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Supporting Information

Nitrogen-interrupted *halo*-Prins/*halo*-Nazarov fragment coupling cascade for the synthesis of indolines

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General Remarks

All vacuum/argon flushes and flame drying techniques were performed using a Schlenk line, along with septa and needles (no Schlenk flasks or multi-neck flasks were used, unless specifically stated). Reagents were used as obtained from commercial suppliers without further purification, unless otherwise noted. Tetrahydrofuran (THF, BHT stabilized), methylene chloride (DCM), methanol and dimethylformamide (DMF) were purchased from Fisher and dried by the addition of vacuum/flame dried 4 Å molecular sieves (typically with a ~ 2 cm layer of ball-shaped sieves per solvent bottle, over at least three days). The solvents were used under air atmosphere. 4 Å and 5 Å molecular sieves were purchased from Aldrich and stored in an oven (120 °C) prior to use. The sieves were further dried using a Tirrill burner under vacuum before use (followed by cooling to room temperature under vacuum, and then being exposed to argon). Screw-top tubes and flasks were made of heavy glass walls, for the purpose of withstanding higher pressures than the common round bottom flasks (see CG-1880 on Chemglass). Celite 545 was purchased from EMD. ACS-grade hexanes, toluene, ethyl acetate and DCM were used for column chromatography. Thin-layer chromatography (TLC) was performed on pre-coated silica gel 60 F254 glass-supported plates from EMD, and visualization was performed with a UV lamp followed by staining with *p*-anisaldehyde or CAM solution followed by heating (using a hot plate for *p*-anisaldehyde stain and using a heat gun-lower heating setting carefully with breaks until the background becomes pale blue). *p*-Anisaldehyde staining solution was prepared by dissolving 0.7 mL of *p*-anisaldehyde in 250 mL of ethanol solution containing 9.5 mL of conc. sulfuric acid (98% aq) and 2.7 mL of glacial acetic acid (ethanol solution needs to be carefully prepared using an ice/water bath). CAM staining solution was prepared by dissolving 2.5 g of $(NH_4)_6Mo_7O_{24}$ and 1.0 g of $Ce(SO_4)_2$ in 90 mL of water and 10 mL of conc. H_2SO_4 (98% aq, add carefully with cooling). Column chromatography was carried out on EM Science silica gel (60 Å pore size, 230-400 mesh). Preparatory thin-layer chromatography (prep-TLC) was performed on pre-coated silica gel 60 F254 glass-supported plates from EMD (same plates that were cut into smaller plates for the regular TLC analysis). Deuterated solvents were purchased from Cambridge Isotope Laboratories. Potassium carbonate was flame-dried in a flask under vacuum, let to cool to room temperature, filled with argon, and as such added to bottles of deuterated chloroform to remove any acids formed due to the spontaneous decomposition of chloroform in the presence of light and oxygen. For the preparation of NMR samples, about 0.70-0.75 mL of $CDCl_3/K_2CO_3$, measured with a syringe and

needle, was filtered through a small pad of cotton (placed in a Pasteur pipette), and a pipette bulb was used to push out the residual chloroform from the cotton pad. Other deuterated solvents were used as received. Trifluoromethanesulfonic acid was purchased from Oakwood Chemicals (100 mL bottle) and was distilled under reduced pressure using a Buchi Kugelrohr. A few drops of trifluoromethanesulfonic anhydride were added to the distillation flask prior to distillation, and the distilled acid was quickly transferred to a glass bottle, under argon, followed by a few drops of trifluoromethanesulfonic anhydride. Trifluoromethanesulfonic acid can only be handled using glass (micro)syringes and steel needles. Disposable plastic syringes and needles cannot be used, as they dissolve/melt in the presence of TfOH. TfOH fumes in air and over time forms crystalline TfOH•H_2O (which cannot be used). Therefore, 2 dram vials were flame dried under vacuum, refilled with argon when cooled to room temperature, and a PTFE tape (2 layers) was wrapped on the closing threads of the vial (in the clockwise direction). The septum was briefly removed and a partially filled 9'' Pasteur pipet was used to fill the vial with a small amount of the distilled TfOH. Both the vial and the bottle with the distilled TfOH were quickly closed with their corresponding caps, and then wrapped with two layers of electric tape (3M), followed by parafilm (a piece of parafilm used for wrapping was folded in half to increase the thickness and tightness of the wrapped layer). Triflic acid was stored in freezer (-20 °C) when not in use.

^{1}H NMR spectra were recorded at room temperature (unless otherwise stated) on a 500 MHz Bruker Avance spectrometer or a 400 MHz Bruker Avance spectrometer, using TopSpin v1.3, and processed in MNova v12.0.2. Chemical shifts are given in parts per million (ppm) referenced to solvent residual proton resonance (δ = 7.26 for $CHCl_3$, or using the built-in reference values for other solvents in MNova 12). NMR data are reported as: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet/quintet, m = multiplet, and any combination of d, t, q, and p e.g., dt = doublet of triplets), coupling constants (*J*) given in Hz, and integration. In cases where two or more diastereoisomers are present, chemical shifts from both diastereoisomers are listed, and the most resolved peaks that do not overlap with other peaks were used for the determination of the diastereometic ratio (dr).

^{13}C NMR spectra were recorded at room temperature (unless otherwise stated) on a 126 MHz or 101 MHz Bruker Avance spectrometer with proton decoupling. Chemical shifts are given in parts per million (ppm), referenced to solvent carbon resonance (δ = 77.0 for $CHCl_3$, or using the built-in reference values for other solvents in MNova 12). In cases where two or more diastereoisomers are present, chemical shifts from both diastereoisomers are listed. In some cases, the observed number of peaks is less than the expected number for the proposed structure, and this happens in the case of nosyl (2-nitrophenylsulfonyl) and the boron-containing compound **SI-10**. These peaks belong to the carbon atoms bonded directly to either a nitro group or a boron atom. The quadrupolar relaxation of the most abundant isotopes of boron and nitrogen occurs at a fast rate that leads to a broadening of the multiplets expected for the appropriate carbon atoms, and yet it is not fast enough for the peaks to be effectively decoupled and to appear as singlets, resulting in broadened peak shapes that are lost in the baseline (noise).[1]

^{19}F NMR spectra were recorded at room temperature on a 376 MHz Bruker Avance spectrometer. Chemical shifts are given in parts per million (ppm), referenced according to TopSpin v1.3 based on the deuterium frequency of $CDCl_3$ used as solvent for shim/lock purposes.

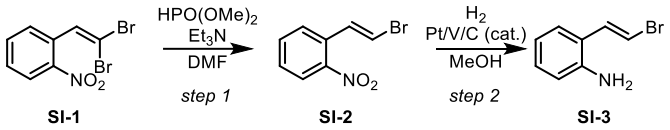
X-ray crystallography data was collected by Dr. Bill Brennessel at the X-ray Crystallographic Facility of the University of Rochester, Rochester, NY 14627 (USA). High-resolution mass spectra (HRMS) were measured at the University of Rochester Mass Spectrometry Resource Lab by Kevin Welle.

Normal phase (NP) high-pressure liquid chromatography (HPLC) was performed using Shimadzu SCL-10AVP/LC-20AD/LC-20AD/DGU-20A(3R)/CTO-20A/SPD-20A/Rheodyne 20 μL sample loop. Column: Luna Silica(2) 5 μm, 100 Å, 250 x 4.6 mm 00G-4274-E0. Solvents: Fisher Scientific Hexanes HPLC grade; Sigma-Aldrich 2-Propanol HPLC grade. Detection: D2 254 nm. Chromatography was performed in isocratic mode. Injection size (manual): 10 μL of 1 mg/mL solutions in 10% isopropanol/hexanes (HPLC grade, filtered using 0.45 μm syringe filters before injection).

Note: Thioglycolic acid and the thioglycolic acid byproducts have a pungent, "skunky" odor.

Experimental Details

Enyne substrates 1



Compound **SI-1** was prepared according to the literature procedure.[2]

Step 1 (Hirao reduction):[3] To a 250 mL round-bottom flask, equipped with a stir-bar, **SI-1** (7 g, 22.8 mmol, 1.0 equiv.) was added, followed by the addition of triethylamine (16 mL, 114 mmol, 5.0 equiv.) and DMF (18 mL). The flask was closed using a yellow cap (Caplugs) and the mixture was stirred and cooled to 0 °C using an ice/water bath. Once cooled, the flask was opened and dimethyl phosphite (8.4 mL, 91.2 mmol, 4.0 equiv.) was added using a graduated pipette (the flask was capped again following the addition). *Note: the addition of dimethyl phosphite is exothermic and the reaction mixture immediately darkens*. After 5-10 min, the flask is taken out of the water/ice bath (the water/ice bath is only necessary for controlling the described exotherm) and the reaction was left to stir overnight at room temperature. *Quench:* The reaction mixture was diluted with water and the mixture was transferred to a separatory funnel using diethyl ether. The aqueous layer was extracted with ether and the layers were separated. The organic layer was washed with 2 M aq. HCl (the pH level was checked using a universal pH strip to confirm that there was an excess of HCl), then sat. aq. sodium bicarbonate, then brine. The organic layer was collected, dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium-grade fritted funnel under vacuum), and the solvents were removed by vacuum distillation using a rotary evaporator (at 30 °C). The crude was purified by flash column chromatography (SiO_2, 10% ethyl acetate/hexanes, Rf ~ 0.3) to obtain 4.044 g (78%) of **SI-2** as a light yellow fluffy solid. *The product is not bench stable and its color changes to dark green if left to stay at room temperature overnight (under air, argon, or high vacuum). The compound remains unchanged if left in freezer (-20 °C) for at least six months.*
M.P. 42-43 °C
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.65 (d, *J* = 13.8 Hz, 1H), 7.60 (td, *J* = 7.6, 1.4 Hz, 1H), 7.52 – 7.45 (m, 2H), 6.79 (d, *J* = 13.8 Hz, 1H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 133.5, 133.0, 131.5, 129.0, 128.8, 125.0, 111.1.
HRMS (ESI) *m/z* calc'd for $C_8H_6{}^{79}BrNO_2$ $[M+H]^+$: 227.9655, found: 227.9650.

Step 2:[2] To a 250 mL Paar shaker (hydrogenator) pressure bottle was added **SI-2** (4.034 g, 17.7 mmol, 1.0 equiv.), followed by methanol (90 mL, in portions with stirring, by hand, to dissolve **SI-2**). To this solution, the hydrogenation catalyst (1% Pt/2% V on activated carbon, 50-70% wetted powder, Evonik Noblyst P8078, purchased from Strem) was added (957 mg, 0.018 mmol Pt, 0.1 mol% Pt; the batch used had a 63.3% water content, as determined by the supplier). The bottle was attached to the Paar hydrogenator and evacuated using a vacuum pump (to ~20-30 Torr, dry ice/acetone-cooled trap was used to protect the pump from the solvent vapor). The bottle was then refilled with hydrogen gas (to 40 Psi) and this procedure was repeated two more times. The shaker was then turned on and the gas pressure was monitored in 10-30 min intervals. Whenever the pressure became low, the shaking was stopped and the bottle was refilled with additional hydrogen gas (to 40 Psi) and then the shaking was resumed. Two refills were necessary on this scale. *Quench:* When the TLC showed full consumption of the starting material (10% ethyl acetate/hexanes, the product has a slightly smaller Rf value than **SI-2**, the product spot appearing just below the spot of the substrate) the reaction mixture was vacuum filtered through celite (medium fritted funnel, celite was packed by physically being pressed down using the bottom of a 20 mL vial or a glass stopper *under vacuum*) and the celite was washed using copious amounts of ethyl acetate. The solvents were removed by vacuum distillation using a rotary evaporator and the crude was purified by flash column chromatography (SiO_2, 10% ethyl acetate/hexanes, Rf ~ 0.3) to obtain 2.714 g (83%) of **SI-3** as a pale orange solid.
Note: Unlike different dry Pd/C catalysts which are highly pyrophoric (an attempt to use 5% Pd/C for this transformation resulted in the spontaneous ignition of the reaction mixture on a small scale using a similar procedure), this catalyst never exhibited any pyrophoric behavior. Additionally, filtration of the catalyst was allowed to proceed to dryness of the filter cake (on celite) without exhibiting any pyrophoric behavior. Nevertheless, we still

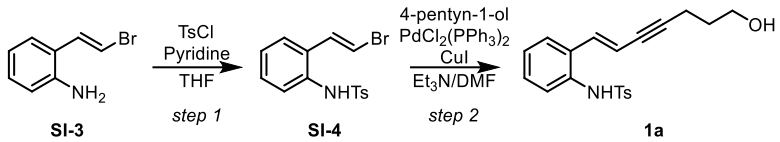
suggest that the standard safety precautions should be followed, as with any reactions that involve potentially pyrophoric materials.

M.P. 74-75 °C

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 – 7.09 (m, 3H), 6.75 (t, *J* = 7.5 Hz, 1H), 6.71 – 6.62 (m, 2H), 3.72 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 143.4, 133.4, 129.4, 127.6, 122.4, 119.1, 116.3, 107.5.

HRMS (ESI) *m/z* calc'd for $C_8H_8{}^{79}BrN$ $[M+H]^+$: 197.9913, found: 197.9914.



SI-3 **SI-4** **1a**

Step 1: To a flame-dried 25 mL round-bottom flask, equipped with a stir bar, under argon, **SI-3** (725 mg, 3.66 mmol, 1.0 equiv.) was added. The flask was closed with a septum and evacuated/refilled with argon once using a Schlenk line. To the flask, anhydrous THF (4.6 mL) and pyridine (0.63 mL) were added. The mixture was cooled to 0 °C using an ice/water bath and then *p*-toluenesulfonyl chloride (803 mg, 4.21 mmol, 1.15 equiv.) was added in portions (by briefly removing the septum, adding the solid with a spatula, placing back the septum and then repeating the procedure until all solid has been added). The reaction mixture was let to warm up to room temperature (by keeping the flask in the ice/water bath and allowing the ice to melt) and stirred overnight. *Quench*: When the TLC showed full consumption of the starting material (30% ethyl acetate/hexanes, product is slightly more polar than **SI-3**), the reaction mixture was diluted with dichloromethane and transferred to a separatory funnel. The mixture was washed with water and the layers were separated. Aqueous layer was washed three times with dichloromethane, and then the combined organic layer was washed with brine. Organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography (SiO_2, 15% ethyl acetate/hexanes, Rf ~ 0.2; *note:* crude was loaded on silica using hot toluene and the product solidified on the column during chromatography, obstructing the flow of the eluent) to obtain 1.194 g (93%) of **SI-4** as a white/colorless solid.

M.P. 153-154 °C

^{1}H NMR (500 MHz, CD_3CN) δ 7.48 – 7.43 (m, 2H), 7.36 – 7.30 (m, 1H), 7.27 – 7.22 (m, 2H), 7.20 – 7.14 (m, 2H), 7.05 – 6.99 (m, 1H), 6.98 (d, *J* = 13.8 Hz, 1H), 6.65 (d, *J* = 13.9 Hz, 1H), 2.33 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.2, 137.5, 134.0, 133.7, 133.5, 130.7, 129.9, 128.8, 128.4, 128.0, 127.4, 109.8, 21.5.

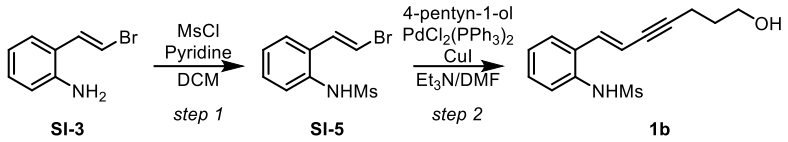
HRMS (ESI) *m/z* calc'd for $C_{15}H_{14}{}^{79}BrNO_2S$ $[M+H]^+$: 352.0002, found: 351.9990.

Step 2 (general conditions for the Sonogashira coupling): To a 100 mL round-bottom flask, equipped with a stir bar, **SI-4** (1.039 g, 2.95 mmol, 1.0 equiv.) was added, followed by triethylamine (15 mL) and DMF (3 mL). The flask was closed with a septum, and the mixture was sparged with argon (using a long needle connected to a Schlenk line with an argon line, and another bleed needle) with stirring for around 30 min. After this time, while still sparging, the septum was removed and $PdCl_2(PPh_3)_2$ (41 mg, 0.059 mmol, 2 mol%), CuI (22 mg, 0.118 mmol, 4 mol%) and 4-pentyn-1-ol (0.30 mL, 3.25 mmol, 1.1 equiv.) were quickly added in succession. The flask was capped with a septum, connected to the argon line, and the mixture was stirred at room temperature overnight. *Note: The reaction quickly darkens after the addition of 4-pentyn-1-ol. Quench*: When the TLC showed full consumption of the starting material (40% ethyl acetate/hexanes, product Rf ~ 0.08) the reaction was diluted with ethyl acetate and vacuum filtered through celite into a separatory funnel. Celite was washed with copious amounts of ethyl acetate. The mixture was washed with 2 M aq. HCl (the pH level was checked using a universal pH strip to confirm that there was excess of HCl), water, sat. aq. sodium bicarbonate, and brine. Organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography (SiO_2, toluene was used first to remove a yellow band of palladium impurities, then 30% ethyl acetate/hexanes to remove toluene, then 80% ethyl acetate/hexanes to elute product) to obtain 849 mg (81%) of **1a** as an orange solid.

M.P. 108-110 °C

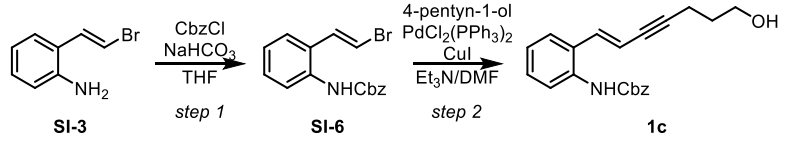
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 7.7 Hz, 1H), 7.28 – 7.24 (m, 1H), 7.24 – 7.11 (m, 4H), 6.80 (s, 1H), 6.73 (d, *J* = 16.0 Hz, 1H), 5.87 (dt, *J* = 16.0, 2.3 Hz, 1H), 3.80 (t, *J* = 6.2 Hz, 2H), 2.49 (td, *J* = 6.9, 2.2 Hz, 2H), 2.38 (s, 3H), 1.87 (s, 1H), 1.83 (p, *J* = 6.6 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 143.9, 136.2, 134.3, 132.9, 131.8, 129.6, 129.0, 127.2, 126.7, 126.0, 125.7, 112.0, 92.7, 79.9, 61.6, 31.2, 21.5, 16.1.
HRMS (ESI) *m/z* calc'd for $C_{20}H_{21}NO_3S$ $[M+H]^+$: 356.1315, found: 356.1300.



Step 1: To a flame-dried 25 mL round-bottom flask, equipped with a stir bar, under argon, **SI-3** (905 mg, 4.56 mmol, 1.0 equiv.) was added. The flask was closed with a septum and evacuated/refilled with argon once using a Schlenk line. To the flask, pyridine (0.74 mL, 9.12 mmol, 2.0 equiv.) and dichloromethane (5 mL) were added. The mixture was cooled to 0 °C using an ice/water bath and then methanesulfonyl chloride (0.53 mL, 6.84 mmol, 1.5 equiv.) was added to it dropwise. The reaction mixture was let to warm up to room temperature (by keeping the flask in the ice/water bath and allowing the ice to melt) and stirred overnight. *Quench*: When the TLC showed full consumption of the starting material (30% ethyl acetate/hexanes, product Rf ~ 0.22) the reaction mixture was diluted with dichloromethane and transferred to a separatory funnel. The organic layer was washed with 2 M aq. HCl (the pH level was checked using a universal pH strip to confirm that there was excess of HCl), and then the aqueous layer was back-extracted once with dichloromethane. The organic layers were combined and washed with sat. aq. sodium bicarbonate, then brine. Organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was used in the next step without purification. Crude **SI-5** (1.184 g, 82%) was obtained as a white/colorless solid in a ~2:1 (mol) ratio with respect to dichloromethane (yield was corrected to account for dichloromethane).
^{1}H NMR (*crude*) (500 MHz, Acetone-d_6) δ 8.29 (s, 1H), 7.67 – 7.59 (m, 2H), 7.52 – 7.46 (m, 1H), 7.42 – 7.34 (m, 1H), 7.33 – 7.26 (m, 1H), 7.11 – 7.03 (m, 1H), 3.02 (s, 3H).

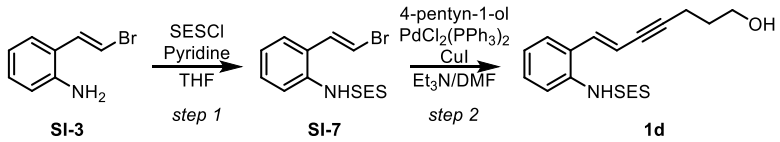
Step 2: Sonogashira coupling was performed according to the general conditions (see **1a**), using **SI-5** (330 mg, 1.04 mmol, 1.0 equiv.; presence of dichloromethane was taken into consideration). The crude was purified by flash column chromatography (SiO_2, 60% ethyl acetate/hexanes, *note*: the crude was dry-loaded on silica by adding dry silica to the acetone solution of the crude material) to obtain 238 mg (82%) of **1b** as a tan solid.
M.P. 126-127 °C
^{1}H NMR (500 MHz, Acetone-d_6) δ 8.22 (s, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.44 (d, *J* = 7.9 Hz, 1H), 7.35 – 7.28 (m, 2H), 7.25 (t, *J* = 7.6 Hz, 1H), 6.27 – 6.19 (m, 1H), 3.62 (t, *J* = 6.2 Hz, 2H), 2.98 (s, 3H), 2.84 (s, 1H), 2.47 – 2.40 (m, 2H), 1.71 (p, *J* = 6.6 Hz, 2H).
^{13}C NMR (126 MHz, Acetone-d_6) δ 136.1, 135.0, 133.8, 129.7, 127.6, 127.6, 126.4, 111.6, 93.6, 80.6, 60.9, 40.1, 32.6, 16.4.
HRMS (ESI) *m/z* calc'd for $C_{14}H_{17}NO_3S$ $[M+H]^+$: 280.1002, found: 280.0995.



Step 1: To a flame-dried 10 mL round-bottom flask, equipped with a stir bar, under argon, **SI-3** (198 mg, 1.0 mmol, 1.0 equiv.) was added, followed by sodium bicarbonate (92 mg, 1.1 mmol, 1.1 equiv.). The flask was closed with a septum and evacuated/refilled with argon once using a Schlenk line. To the flask, anhydrous THF (2.5 mL) was added and the mixture was cooled to 0 °C using an ice/water bath. To the cooled mixture, benzyl chloroformate (CbzCl, 0.16 mL, 1.1 mmol, 1.1 equiv.) was added dropwise. The reaction mixture was let to warm up to room temperature (by keeping the flask in the ice/water bath and allowing the ice to melt) and stirred overnight. *Quench*: The mixture was diluted with dichloromethane/water and transferred to a separatory funnel. Organic layer was separated, and the aqueous layer was extracted two more times with dichloromethane. Combined organic layers were washed with brine, collected, and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was

used in the next step without purification (the product had sufficient purity based on the acquired ^{1}H NMR of the crude material). The yield was quantitative based on the mass of the obtained crude material (white/colorless solid). *Note*: The authors were not able to find a solvent system in which **SI-3** and **SI-6** had different Rf values. Instead, staining the TLC plate using the CAM stain proved effective, where **SI-3** (and any other unprotected aniline in general, prepared for this manuscript), immediately upon exposure to the stain, stains orange, while **SI-6** (and any other protected aniline, prepared for this manuscript) only stains grey/black upon heating.
^{1}H NMR (*crude*) (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.46 – 7.26 (m, 8H), 7.17 (d, *J* = 13.8 Hz, 1H), 7.11 (t, *J* = 7.6 Hz, 1H), 6.49 (s, 1H), 5.22 (s, 2H).

Step 2: Sonogashira coupling was performed according to the general conditions (see **1a**), using **SI-6** (332 mg, 1.0 mmol, 1.0 equiv.; the crude material was assumed to be pure for the stoichiometric calculations). The crude was purified by flash column chromatography (SiO_2, 50% ethyl acetate/hexanes, Rf ~ 0.3) to obtain 295 mg (88%) of **1c** as an amber oil.
^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) δ 7.78 (d, *J* = 8.2 Hz, 1H), 7.44 – 7.31 (m, 6H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 16.0 Hz, 1H), 6.56 (s, 1H), 6.05 (dt, *J* = 16.0, 2.3 Hz, 1H), 5.22 (s, 2H), 3.78 (t, *J* = 6.1 Hz, 2H), 2.50 (td, *J* = 7.0, 2.2 Hz, 2H), 1.83 (p, *J* = 6.6 Hz, 2H), 1.45 (s, 1H).
^{13}C NMR (126 MHz, $CDCl_3$, 50 °C) δ 153.8, 136.2, 134.8, 134.5, 129.1, 128.6, 128.3, 126.3, 124.8, 122.7, 122.7, 112.4, 92.6, 80.1, 67.3, 61.8, 31.5, 16.2.
HRMS (ESI) *m/z* calc'd for $C_{21}H_{21}NO_3$ $[M+H]^+$: 336.1594, found: 336.1581.



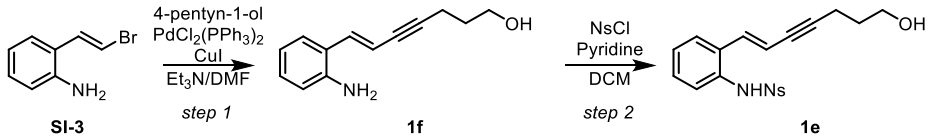
SI-3 SI-7 1d

Step 1: To a flame-dried 10 mL round-bottom flask, equipped with a stir bar, under argon, **SI-3** (198 mg, 1.0 mmol, 1.0 equiv.) was added. The flask was closed with a septum and evacuated/refilled with argon once using a Schlenk line. To the flask, anhydrous THF (1.3 mL) and pyridine (0.16 mL) were added. The mixture was cooled to 0 °C using an ice/water bath and then 2-(trimethylsilyl)ethanesulfonyl chloride (241 mg, 1.2 mmol, 1.2 equiv.) was added dropwise. The reaction mixture was let to warm up to room temperature (by keeping the flask in the ice/water bath and allowing the ice to melt) and stirred overnight. *Quench*: When the TLC showed full consumption of the starting material (30% ethyl acetate/hexanes, product Rf ~ 0.52 similar to **SI-3**, distinguished by staining with CAM), the reaction mixture was diluted with dichloromethane and transferred to a separatory funnel. The mixture was washed with water and the layers were separated. Aqueous layer was extracted three times with dichloromethane, and then the combined organic layer was washed with brine. Organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography (SiO_2, 20% ethyl acetate/hexanes, Rf ~ 0.36) to obtain 274 mg (76%) of **SI-7** as an off-white solid.
M.P. 123-125 °C
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 – 7.43 (m, 1H), 7.40 – 7.30 (m, 3H), 7.23 – 7.18 (m, 1H), 6.75 (d, *J* = 13.9 Hz, 1H), 6.54 (s, 1H), 3.07 – 2.99 (m, 2H), 1.10 – 1.03 (m, 2H), 0.02 (s, 9H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 133.2, 132.5, 130.6, 129.5, 127.3, 126.6, 124.5, 110.1, 48.8, 10.4, -2.1.
HRMS (ESI) *m/z* calc'd for $C_{13}H_{20}BrNO_2SSi$ $[M+H]^+$: 362.0240, found: 362.0239.

Note: 2-(trimethylsilyl)ethanesulfonyl chloride was prepared in two steps according to the literature procedures, starting from trimethylvinylsilane. The first step was done according to the procedure described by Weinreb et al.[4] The second step was done according to the work described by Robins et al.[5], which is a modified version of the second step described in the first paper, but does not produce the corresponding sulfonic anhydride byproduct. It should be noted that the procedure described by Robins et al. has stoichiometric inconsistencies with the main text in their publication, and the procedure that is consistent with the authors' observations (described in the experimental section, with corrected stoichiometry according to the main text) , and that was used in this work, is described below. Sodium 2-(trimethylsilyl)ethanesulfonate (5.59 g, 27.4 mmol, 1.0 equiv.) was crushed to a fine powder using a mortar and pestle and was transferred to a flame-dried 100 mL round-bottom flask, equipped with a stir bar (and previously filled with argon). A pressure-equalizing addition funnel was attached to the flask. The funnel was closed with a septum and evacuated/refilled with argon once using a Schlenk line. To the funnel, thionyl chloride (31 mL, 425

mmol, 15.5 equiv.) was added, and only a bleed needle was left on the septum on top of the addition funnel. The flask was cooled to 0 °C using an ice/water bath. With rapid stirring, thionyl chloride was slowly added dropwise, while maintaining the ice/water bath temperature at 0 °C. Upon completion of the addition, the addition funnel was removed, and the flask was closed with a septum (with a bleed needle). To this mixture, DMF (0.78 mL, 10.14 mmol, 0.37 equiv.) was added dropwise. The reaction mixture was let to warm up to room temperature (by keeping the flask in the ice/water bath and allowing the ice to melt) and stirred overnight. *Quench*: The reaction was quenched according to the procedure by Robins et al.[5] The product was obtained as an orange liquid (3.85 g, 70%). The spectral data were consistent with the literature and no contamination of the desired sulfonyl chloride with the sulfonic anhydride was observed.

Step 2: Sonogashira coupling was performed using the procedure described for the preparation of **1a**, using **SI-7** (274 mg, 1.0 mmol, 1.0 equiv). The crude was purified by flash column chromatography (SiO_2, 50% ethyl acetate/hexanes, Rf ~ 0.32) to obtain 256 mg (93%) of **1d** as an orange foamy oil.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 – 7.41 (m, 2H), 7.29 (t, *J* = 7.8 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.09 (d, *J* = 16.0 Hz, 1H), 6.40 (s, 1H), 6.13 – 6.05 (m, 1H), 3.80 (t, *J* = 6.2 Hz, 2H), 3.05 – 2.97 (m, 2H), 2.54 – 2.47 (m, 2H), 1.84 (p, *J* = 6.4 Hz, 2H), 1.61 (s, 1H), 1.10 – 1.00 (m, 2H), 0.00 (s, 9H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 134.3, 133.4, 130.6, 129.4, 126.5, 126.3, 124.0, 112.9, 93.3, 79.8, 61.6, 48.7, 31.2, 16.1, 10.5, -2.1.
HRMS (ESI) *m/z* calc'd for $C_{18}H_{27}NO_3SSi$ $[M+H]^+$: 366.1554, found: 366.1543.



Step 1 (Sonogashira coupling): To a 250 mL round-bottom flask, equipped with a stir bar, **SI-3** (1.367 g, 6.9 mmol, 1.0 equiv.) was added, followed by triethylamine (35 mL) and DMF (7 mL). The flask was closed with a septum, and the mixture was sparged with argon (using a long steel needle connected to a Schlenk line with an argon line, and another bleed needle) with stirring for around 30 min. After this time, while still sparging, the septum was removed and $PdCl_2(PPh_3)_2$ (98 mg, 0.14 mmol, 2 mol%), CuI (53 mg, 0.28 mmol, 4 mol%) and 4-pentyn-1-ol (0.71 mL, 7.6 mmol, 1.1 equiv.) were quickly added in succession. The flask was capped with a septum, pierced with one (short) needle connected to the argon line, and the mixture was stirred at room temperature overnight. *Note: The reaction quickly darkens after the addition of 4-pentyn-1-ol. Quench*: When the TLC showed full consumption of the starting material (50% ethyl acetate/hexanes, product Rf ~ 0.22, UV fluorescent, pale blue) the reaction was diluted with ethyl acetate and vacuum filtered through celite. Celite was washed with copious amounts of ethyl acetate. Solvents were removed by vacuum distillation using a rotary evaporator (ethyl acetate and triethylamine were removed at 30 °C using a two-stage diaphragm pump; most of the DMF was removed at 50 °C using a high-vac rotary vane pump, which condensed in a bump trap). The crude was purified by flash column chromatography (SiO_2, toluene was used first to remove yellow palladium impurities, then hexanes to remove toluene, then 50% ethyl acetate/hexanes to elute product) to obtain 1.13 g (81%) of **1f** as a yellow solid.
M.P. 66-68 °C
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 – 7.22 (m, 1H), 7.11 – 7.06 (m, 1H), 6.95 (d, *J* = 16.0 Hz, 1H), 6.74 (t, *J* = 7.5 Hz, 1H), 6.68 – 6.63 (m, 1H), 6.03 (dt, *J* = 16.0, 2.3 Hz, 1H), 3.80 (s, 2H), 3.77 (t, *J* = 6.2 Hz, 2H), 2.49 (td, *J* = 7.0, 2.3 Hz, 2H), 2.23 (s, 1H), 1.81 (p, *J* = 6.6 Hz, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 143.6, 135.7, 129.2, 126.5, 122.5, 118.9, 116.3, 109.4, 91.3, 80.5, 61.5, 31.3, 16.1.
HRMS (ESI) *m/z* calc'd for $C_{13}H_{15}NO$ $[M+H]^+$: 202.1226, found: 202.1230.

Step 2: To a 100 mL round-bottom flask, equipped with a stir bar, **1f** (1.13 g, 6.45 mmol, 1.0 equiv.) was added, followed by dichloromethane (13 mL) and pyridine (0.55 mL, 6.77 mmol, 1.05 equiv.). While stirring, 2-nitrobenzenesulfonyl chloride (NsCl, 1.5 g, 6.77 mmol, 1.05 equiv.) was added, slowly, in portions. Once the addition was complete, the flask was closed using a yellow cap, and the mixture was stirred overnight. *Quench:* The reaction mixture was diluted with ethyl acetate and transferred to a separatory funnel. 2 M aqueous HCl was added to the funnel, and the contents were mixed. The aqueous layer was removed (the pH level was checked using a universal pH strip to confirm that there was excess of HCl). The organic layer was washed with saturated aqueous sodium bicarbonate, then with brine. Organic layer was collected, dried by the addition of excess anhydrous magnesium sulfate

(filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography (SiO_2, 50% ethyl acetate/hexanes, Rf ~ 0.2) to obtain 1.676 g (67%) of **1e** as an orange solid.

*Note: Performing this sequence in the opposite order (N-nosylation first, followed by the Sonogashira coupling) leads to significantly lower yields of the final product **1e** (formation of the N-nosyl indole is observed as the major side product).*

M.P. 106-108 °C

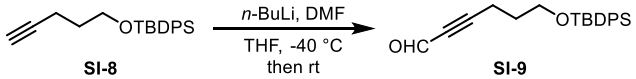
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.9 Hz, 1H), 7.76 – 7.67 (m, 2H), 7.58 (t, *J* = 7.7 Hz, 1H), 7.43 – 7.35 (m, 1H), 7.27 (d, *J* = 5.2 Hz, 1H), 7.25 – 7.20 (m, 3H), 7.04 (d, *J* = 16.0 Hz, 1H), 5.91 – 5.80 (m, 1H), 3.78 (t, *J* = 6.1 Hz, 2H), 2.50 – 2.42 (m, 2H), 1.80 (p, *J* = 6.4 Hz, 2H), 1.67 (s, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 148.0, 134.6, 133.9, 133.7, 132.9, 132.6, 132.0, 131.3, 129.0, 128.0, 127.8, 125.9, 125.5, 111.9, 93.0, 79.9, 61.6, 31.2, 16.1.

HRMS (ESI) *m/z* calc'd for $C_{19}H_{18}N_2O_5S$ $[M+H]^+$: 387.1009, found: 387.1006.

SI-8

To a vacuum/flame dried 250 mL round bottom flask, equipped with a stir bar, cooled to room temperature and filled with argon, 2.8 mL (30 mmol, 1 equiv) of 4-pentyn-1-ol and 120 mL of anhydrous DMF were added. The mixture was stirred and 4.5 g (2.2 equiv) of imidazole was added in one portion. When imidazole dissolved, *t*-butyldiphenylsilyl chloride (TBDPSCl, 8.6 mL, 1.1 equiv) was added dropwise. The mixture was stirred for 5 h at room temperature (until TLC showed full consumption of the starting material). *Quench*: The stir bar was removed and the reaction mixture was transferred to a 500 mL separatory funnel using 240 mL of diethyl ether (addition of ether causes the mixture to become white/cloudy). Saturated aq NH_4Cl was added, and the layers were separated after shaking. The aqueous layer was back extracted once with ether. Organic layers were combined and washed with water three times. The organic layer was collected and dried with excess anhydrous magnesium sulfate. The mixture was filtered over a medium grade fritted funnel under vacuum and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by filtration through a large silica plug (~150 g, 5% diethyl ether/hexanes) to obtain 9.422 g (97%) of **SI-8** as a colorless liquid. The spectral data was consistent with the literature.[6]



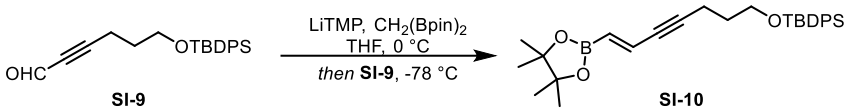
SI-8 **SI-9**

A 250 mL round bottom flask, containing **SI-8** (9.422 g, 29.2 mmol, 1.0 equiv) and a stir bar, was vacuum/argon flushed three times. The flask was briefly opened and 70 mL of anhydrous THF was added via an open graduated cylinder. The flaks was closed, and the mixture was stirred and cooled to -40 °C using a dry ice/acetone bath (pieces of dry ice were carefully added until the temperature reached -40 °C, checked with a thermometer). Once the mixture was cooled, *n*-BuLi (2.5 M in hexanes, 11.7 mL, 1 equiv) was added (the addition was not slow and dropwise, but not necessarily as fast as possible – it was as fast as the syringe and needle could safely handle the flow rate). This addition was followed by the addition of anhydrous DMF (4.5 mL, 2 equiv) in a similar manner as *n*-BuLi, without any unnecessary delay (or rush). The cooling bath was removed and the mixture was let to stir for 1.5 h.

During this time, about 1 h after the cooling bath removal, a 10% aqueous solution of KH_2PO_4 was prepared (4 equiv, 16 g in 160 mL water). To this solution, 160 mL of diethyl ether was added and the mixture was rapidly stirred in a large Erlenmeyer flask. This mixture was cooled with an ice/water bath.

Quench: After 1.5 h of stirring, the flask containing the reaction mixture was opened and the stirring was stopped. Using an external magnet, the stir bar was held in place in the flask, and the reaction mixture was poured into the previously prepared and chilled phosphate/ether biphasic solution that was rapidly stirred. The flask was washed with ether. The stirring in the Erlenmeyer flask was stopped and the stir bar was removed. The mixture was transferred into a large separatory funnel and the layers were separated. The aqueous layer was back extracted once with ether. The organic layers were combined and washed twice with water and once with brine. The organic layer was collected and dried with excess anhydrous magnesium sulfate. The mixture was filtered over a medium grade fritted funnel under vacuum and the solvents were removed by vacuum distillation using a rotary evaporator. The crude mass of the product **SI-9** was 10.532 g (pale yellow liquid). TLC analysis (10% ethyl acetate/hexanes) showed that the product was pure and it was used in the next step without purification or characterization. The yield was assumed to be quantitative.

Note: Compound **SI-9** is known in the literature,[6] although the reported methods for its preparation are often significantly lower yielding, due to the issues described in the paper by Journet and Cai et al.[7] Lower yields arise from side reactions during the workup, and the workup described above (adapted from the ref. 7) solves this problem. Changes in the way workup is done are not recommended.



SI-9 **SI-10**

Boron-Wittig reaction:[8] To a vacuum/flame dried 250 mL round bottom flask, equipped with a stir bar, 2,2,6,6-tetramethylpiperidine (5.9 mL, 1.2 equiv) and anhydrous THF (35 mL) were added. The mixture was stirred and cooled to 0 °C using an ice/water bath. To the chilled mixture *n*-BuLi (2.5 M in hexanes, 14 mL, 1.2 equiv) was added dropwise and the mixture was stirred for 10 min. In the meanwhile, $CH_2(Bpin)_2$ (9.38 g, 1.2 equiv) and 70 mL of anhydrous THF (measured by an open graduated cylinder, added in portions to dissolve the solid reagent) were added to an Erlenmeyer flask. The flask containing the prepared solution of LiTMP was briefly opened and the solution of $CH_2(Bpin)_2$ in THF was poured into it. The flask was closed and the mixture was stirred for 5 min at 0 °C. In the meanwhile, aldehyde **SI-9** (29.2 mmol, 1 equiv, total amount of previously prepared aldehyde) was dissolved in 35 mL of anhydrous THF in a pear-shaped flask (pointy bottom, flask closed with a septum). The flask containing the prepared $LiCH(Bpin)_2$ in THF was removed from the ice/water bath and placed in an acetone bath. The bath was cooled to -78 °C using excess amount of dry ice. Once the mixture was cooled, solution of **SI-9** in THF was cannula transferred (dropwise addition) into it, and the mixture was let to stir at -78 °C for 4 h.

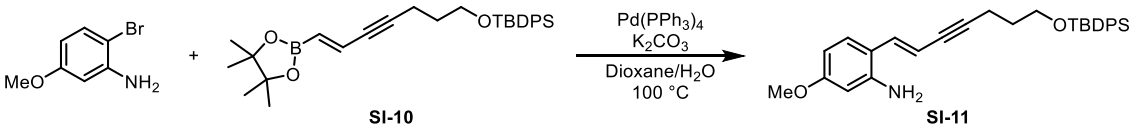
Quench: After 4 h, the flask was removed from the dry ice/acetone bath and was let to stir and warm up to room temperature. The stirring was then stopped and the stir bar removed. The solvents were removed by vacuum distillation using a rotary evaporator. The residual thick liquid was redissolved with copious amount diethylether and transferred to a separatory funnel. The organic layer was washed with 2 M aq HCl, then with water. The collected aqueous layers were back extracted once with diethylether. The organic layers were combined and washed with saturated aq $NaHCO_3$, then with brine. The organic layer was collected and dried with excess anhydrous magnesium sulfate. The mixture was filtered over a medium grade fritted funnel under vacuum and the solvents were removed by vacuum distillation using a rotary evaporator. The product was purified by flash column chromatography (SiO_2, 2.5% ethyl acetate/hexanes) and 8.64 g (62% over two steps) of **SI-10** was isolated as a pale yellow viscous liquid.

*Note: **SI-10** streaks on the TLC plate*[9]*, and streaks during column chromatography, requiring a large volume of the eluent to fully elute.*

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 – 7.64 (m, 4H), 7.44 – 7.35 (m, 6H), 6.41 (dt, *J* = 18.4, 2.1 Hz, 1H), 5.91 (d, *J* = 18.4 Hz, 1H), 3.74 (t, *J* = 6.0 Hz, 2H), 2.50 (td, *J* = 7.2, 2.2 Hz, 2H), 1.78 (tt, *J* = 7.1, 5.9 Hz, 2H), 1.27 (s, 12H), 1.05 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 135.53, 133.81, 130.19, 129.55, 127.62, 94.60, 83.39, 80.98, 62.33, 31.45, 26.83, 24.71, 19.23, 16.12.

HRMS (ESI) *m/z* calc'd for $C_{29}H_{39}BO_3Si$ $[M+H]^+$: 475.2834, found: 475.2843.



SI-10 **SI-11**

Suzuki-Miyaura coupling (general conditions for enyne synthesis): To a 40 mL screw-top pressure vessel, equipped with a stir bar, 2-bromo-5-methoxyaniline (202 mg, 1 mmol, 1 equiv), **SI-10** (498 mg, 1.05 equiv, added with a 9'' Pasteur pipet into the open vessel placed on a balance), anhydrous K_2CO_3 (276 mg, 2 equiv), 1,4-dioxane (8 mL) and DI water (2 mL) were added. The vessel was closed with a septum and the stirring mixture was sparged with argon for 15-30 min. In the meanwhile, lemon-yellow $Pd(PPh_3)_4$, stored at -40 °C in the N_2-filled glovebox, was measured into a small vial (about 60 mg, 5 mol%). The vial was closed and removed from the glovebox. After the sparging was stopped, the vessel was quickly opened and the catalyst was quickly added. The vessel was closed with a screw top and then placed into a preheated oil bath at 100 °C, behind a blast shield. The reaction mixture was rapidly stirred overnight.

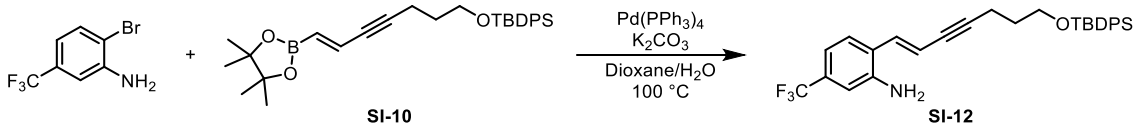
Quench: The vessel was removed from the oil bath and let to cool down to room temperature while stirring. Once cooled, the stirring was stopped and the flask was carefully opened to air (caution: CO_2 evolution builds up pressure and the flask needs to be opened slowly and carefully). The mixture was diluted with diethylether and transferred to

a separatory funnel. The organic layer was washed with water, then sat. aq. sodium bicarbonate, then brine. The organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography (12% ethyl acetate/hexanes), to obtain 346 mg (74%) of **SI-11**, as a yellow-orange viscous liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 – 7.66 (m, 4H), 7.46 – 7.33 (m, 7H), 7.19 (d, *J* = 8.6 Hz, 1H), 6.84 (d, *J* = 16.0 Hz, 1H), 6.34 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.21 (d, *J* = 2.5 Hz, 1H), 5.91 (dt, *J* = 16.0, 2.2 Hz, 1H), 3.81 – 3.75 (m, 7H), 2.53 (td, *J* = 7.1, 2.3 Hz, 2H), 1.82 (p, *J* = 6.9 Hz, 2H), 1.07 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 160.77, 144.98, 135.58, 135.19, 133.85, 129.55, 127.86, 127.62, 115.96, 107.53, 105.18, 101.23, 91.15, 80.40, 62.43, 55.16, 31.70, 26.83, 19.23, 16.16.

HRMS (ESI) *m/z* calc'd for $C_{30}H_{35}NO_2Si$ $[M+H]^+$: 470.2510, found: 470.2521.



SI-10 **SI-12**

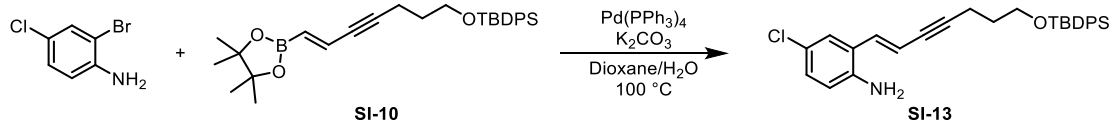
SI-12 was prepared according to the general conditions for the Suzuki-Miyaura coupling for enyne synthesis, using 2-bromo-5-(trifluoromethyl)aniline (202 mg, 1 mmol, 1 equiv) and **SI-10** (498 mg, 1.05 equiv). The crude was purified by flash column chromatography (8% ethyl acetate/hexanes), to obtain 505 mg (99%) of **SI-12**, as a yellow-orange viscous liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 – 7.67 (m, 4H), 7.47 – 7.35 (m, 6H), 7.32 (d, *J* = 8.1 Hz, 1H), 6.98 (d, *J* = 8.1 Hz, 0H), 6.91 – 6.88 (m, 1H), 6.85 (d, *J* = 16.0 Hz, 1H), 6.08 (dt, *J* = 16.0, 2.2 Hz, 1H), 3.90 (s, 2H), 3.79 (t, *J* = 5.9 Hz, 2H), 2.55 (td, *J* = 7.1, 2.3 Hz, 2H), 1.87 – 1.79 (m, 2H), 1.07 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 143.71, 135.59, 134.15, 133.84, 130.94 (q, $^2J_{CF}$ = 32.1 Hz), 129.59, 127.65, 127.06, 125.67 (q, $^4J_{CF}$ = 1.4 Hz), 124.04 (q, $^1J_{CF}$ = 272.1 Hz), 115.30 (q, $^3J_{CF}$ = 3.8 Hz), 112.60 (q, $^3J_{CF}$ = 3.9 Hz), 112.28, 93.38, 79.73, 62.38, 31.55, 26.85, 19.25, 16.18.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.08 (s, 3F).

HRMS (ESI) *m/z* calc'd for $C_{30}H_{32}F_3NOSi$ $[M+H]^+$: 508.2278, found: 508.2292.



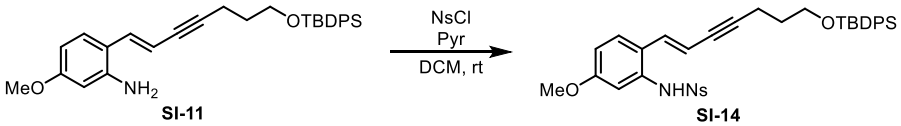
SI-10 **SI-13**

SI-13 was prepared according to the general conditions for the Suzuki-Miyaura coupling for enyne synthesis, using 2-bromo-4-chloroaniline (454 mg, 2.2 mmol, 1 equiv) and **SI-10** (1.14 g, 1.1 equiv). The crude was purified by flash column chromatography (10% ethyl acetate/hexanes), to obtain 996 mg (95%) of **SI-13**, as a yellow-orange viscous liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 – 7.67 (m, 4H), 7.47 – 7.32 (m, 6H), 7.22 (d, *J* = 2.4 Hz, 1H), 7.04 (dd, *J* = 8.5, 2.4 Hz, 1H), 6.80 (d, *J* = 15.9 Hz, 1H), 6.60 (d, *J* = 8.5 Hz, 1H), 6.01 (dt, *J* = 16.0, 2.2 Hz, 1H), 3.79 (t, *J* = 5.9 Hz, 2H), 3.74 – 3.71 (m, 2H), 2.54 (td, *J* = 7.1, 2.2 Hz, 2H), 1.87 – 1.78 (m, 2H), 1.07 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.14, 135.57, 134.13, 133.81, 129.58, 128.83, 127.63, 126.07, 124.04, 123.65, 117.35, 111.17, 92.90, 79.79, 62.36, 31.55, 26.83, 19.24, 16.16.

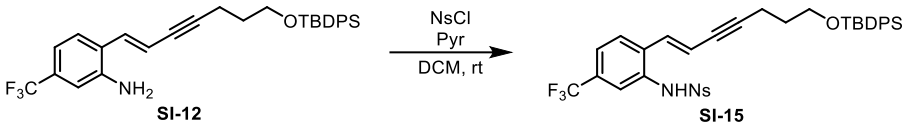
HRMS (ESI) *m/z* calc'd for $C_{29}H_{32}{}^{35}ClNOSi$ $[M+H]^+$: 474.2014, found: 474.2028.



SI-11 **SI-14**

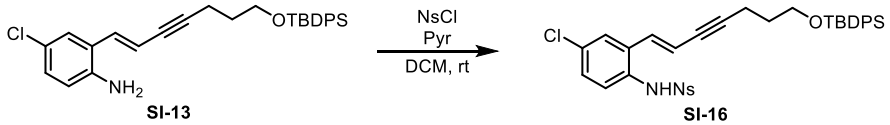
To a 20 mL scintillation vial, equipped with a stir bar, **SI-11** (347 mg, 0.74 mmol, 1.0 equiv.) was added, followed by dichloromethane (1.5 mL) and pyridine (90 μL, 1.5 equiv.). While stirring, 2-nitrobenzenesulfonyl chloride (NsCl, 246 mg, 1.5 equiv.) was added, slowly, in portions. Once the addition was complete, the vial was closed, and the mixture was stirred overnight at room temperature. *Quench:* The solvent was removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography (SiO_2, 20% ethyl acetate/hexanes) to obtain 470 mg (97%) of **SI-14** as an orange viscous liquid (partially contaminated with NsCl).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.75 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.73 – 7.66 (m, 4H), 7.63 (td, *J* = 7.7, 1.5 Hz, 1H), 7.56 (td, *J* = 7.7, 1.3 Hz, 1H), 7.46 – 7.33 (m, 6H), 7.30 (d, *J* = 8.7 Hz, 1H), 7.21 (s, 1H), 6.90 – 6.83 (m, 2H), 6.79 (dd, *J* = 8.6, 2.6 Hz, 1H), 5.72 (dt, *J* = 15.9, 2.2 Hz, 1H), 3.79 – 3.73 (m, 5H), 2.47 (td, *J* = 7.1, 2.2 Hz, 2H), 1.83 – 1.74 (m, 2H), 1.07 (s, 9H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 160.00, 147.97, 136.44, 135.57, 133.91, 133.82, 133.64, 132.83, 132.58, 131.18, 129.59, 127.65, 126.80, 125.85, 125.40, 114.32, 112.37, 110.16, 92.75, 79.60, 62.40, 55.48, 31.66, 26.84, 19.23, 16.12.
HRMS (ESI) *m/z* calc'd for $C_{36}H_{38}N_2O_6SSi$ $[M+H]^+$: 655.2293, found: 655.2301.



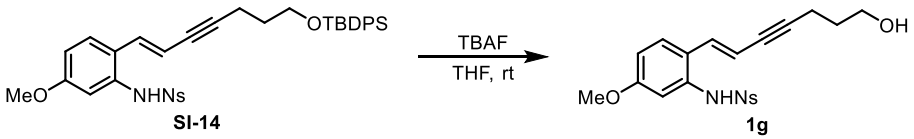
SI-12 **SI-15**

To a 20 mL scintillation vial, equipped with a stir bar, **SI-12** (505 mg, 0.99 mmol, 1.0 equiv.) was added, followed by dichloromethane (2 mL) and pyridine (89 µL, 1.1 equiv.). While stirring, 2-nitrobenzenesulfonyl chloride (NsCl, 244 mg, 1.1 equiv.) was added, slowly, in portions. Once the addition was complete, the vial was closed, and the mixture was stirred overnight at room temperature. *Quench:* The solvent was removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography (SiO_2, 10% ethyl acetate/hexanes) to obtain 600 mg (87%) of **SI-15** as an orange viscous liquid.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.76 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.74 – 7.65 (m, 5H), 7.60 (td, *J* = 7.7, 1.3 Hz, 1H), 7.54 – 7.48 (m, 3H), 7.48 – 7.39 (m, 4H), 7.42 – 7.32 (m, 2H), 7.31 (s, 1H), 7.00 (d, *J* = 16.0 Hz, 1H), 5.97 (dt, *J* = 16.0, 2.2 Hz, 1H), 3.77 (t, *J* = 5.9 Hz, 2H), 2.52 (td, *J* = 7.2, 2.2 Hz, 2H), 1.85 – 1.75 (m, 2H), 1.08 (s, 9H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 147.99, 136.88 (q, $^4J_{CF}$ = 1.2 Hz), 135.58, 134.24, 133.80, 132.74, 132.60, 132.54, 131.25, 130.76 (q, $^2J_{CF}$ = 33.2 Hz), 129.62, 127.67, 126.56, 125.59, 124.41 (q, $^3J_{CF}$ = 3.9 Hz), 124.17 (q, $^3J_{CF}$ = 3.8 Hz), 123.30 (q, $^1J_{CF}$ = 272.2 Hz), 114.99, 95.53, 79.12, 62.36, 31.50, 26.85, 19.25, 16.21.
^{19}F NMR (376 MHz, $CDCl_3$) δ -63.66 (s, 3F).
HRMS (ESI) *m/z* calc'd for $C_{36}H_{35}F_3N_2O_5SSi$ $[M+H]^+$: 693.2061, found: 693.2066.



SI-13 **SI-16**

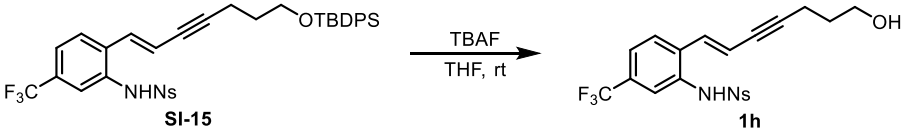
To a 20 mL scintillation vial, equipped with a stir bar, **SI-13** (943 mg, 1.99 mmol, 1.0 equiv.) was added, followed by dichloromethane (4 mL) and pyridine (0.18 mL, 1.1 equiv.). While stirring, 2-nitrobenzenesulfonyl chloride (NsCl, 485 mg, 1.1 equiv.) was added, slowly, in portions. Once the addition was complete, the vial was closed, and the mixture was stirred overnight at room temperature. *Quench:* The solvent was removed by vacuum distillation using a rotary evaporator. The crude product **SI-16** (1.334 g, orange liquid) was used without further purification (assumed quantitative yield).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.70 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.70 – 7.64 (m, 4H), 7.63 (td, *J* = 7.7, 1.5 Hz, 1H), 7.56 (td, *J* = 7.7, 1.3 Hz, 1H), 7.46 – 7.31 (m, 6H), 7.35 – 7.33 (m, 1H), 7.22 – 7.14 (m, 3H), 6.87 (d, *J* = 16.0 Hz, 1H), 5.81 (dt, *J* = 16.0, 2.2 Hz, 1H), 3.74 (t, *J* = 5.9 Hz, 2H), 2.47 (td, *J* = 7.1, 2.2 Hz, 2H), 1.81 – 1.72 (m, 2H), 1.05 (s, 9H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 148.73, 137.17, 136.34, 136.17, 134.81, 134.69, 134.55, 133.63, 133.47, 131.98, 131.29, 130.38, 129.97, 129.56, 128.43, 126.56, 126.27, 114.44, 95.58, 79.88, 63.11, 32.29, 27.61, 20.00, 16.93.
HRMS (ESI) *m/z* calc'd for $C_{35}H_{35}{}^{35}ClN_2O_5SSi$ $[M+H]^+$: 659.1797, found: 659.1803.



SI-14 **1g**

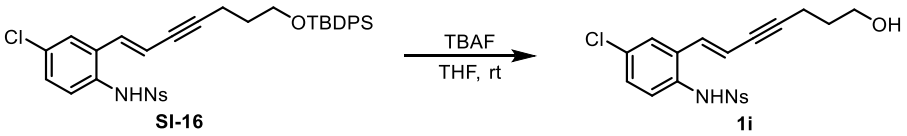
TBDPS deprotection (general procedure): To a 20 mL scintillation vial, equipped with a stir bar, **SI-14** (430 mg, 0.66 mmol, 1.0 equiv.) was added, followed by anhydrous THF (6.6 mL) and tetrabutylammonium fluoride (1 M in THF, 1.3 mL, 2 equiv.). The vial was closed, and the mixture was stirred overnight at room temperature. *Quench:* The reaction mixture was diluted with diethylether and transferred to a separatory funnel. The organic layer was washed

with saturated aq NH_4Cl once, and then twice with brine. The organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography (45% ethyl acetate/hexanes), to obtain 149 mg (55%) of **1g**, as a yellow-orange viscous foamy liquid.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.77 – 7.69 (m, 2H), 7.59 (td, *J* = 7.7, 1.2 Hz, 1H), 7.29 (d, *J* = 8.7 Hz, 1H), 6.90 (d, *J* = 15.9 Hz, 1H), 6.84 (d, *J* = 2.6 Hz, 1H), 6.78 (dd, *J* = 8.7, 2.6 Hz, 1H), 5.72 (dt, *J* = 16.0, 2.3 Hz, 1H), 3.81 – 3.74 (m, 5H), 2.45 (td, *J* = 6.9, 2.3 Hz, 2H), 1.83 – 1.74 (m, 2H), 1.64 (s, 1H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 160.06, 147.96, 134.02, 133.98, 133.09, 132.85, 132.63, 131.21, 126.75, 125.71, 125.49, 114.34, 112.44, 109.78, 92.05, 80.05, 61.61, 55.48, 31.23, 16.09.
HRMS (ESI) *m/z* calc'd for $C_{20}H_{20}N_2O_6S$ $[M+H]^+$: 417.1115, found: 417.1120.



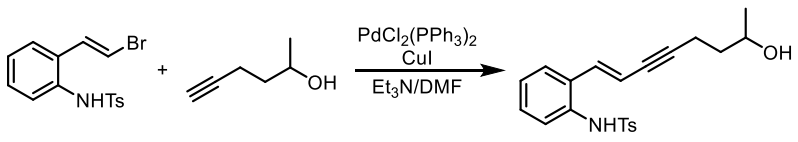
SI-15 **1h**

1h was prepared according to the general procedure for TBDPS deprotection, using **SI-15** (544 mg, 0.79 mmol). The crude was purified by flash column chromatography (45% ethyl acetate/hexanes), to obtain 201 mg (56%) of **1h**, as a yellow solid.
M.P. 147-148 °C
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 – 7.88 (m, 1H), 7.77 – 7.69 (m, 2H), 7.64 – 7.57 (m, 1H), 7.52 – 7.46 (m, 2H), 7.46 – 7.41 (m, 1H), 7.03 (d, *J* = 16.0 Hz, 1H), 5.96 (dt, *J* = 16.0, 2.3 Hz, 1H), 3.77 (t, *J* = 6.1 Hz, 2H), 2.47 (tdd, *J* = 6.9, 2.2, 0.7 Hz, 2H), 1.84 – 1.74 (m, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 148.00 (q, $^4J_{CF}$ = 1.3 Hz), 136.70 (q, $^4J_{CF}$ = 1.2 Hz), 134.26, 133.21, 132.77, 132.75, 132.64, 131.27, 130.85 (q, $^2J_{CF}$ = 33.2 Hz), 126.54, 125.66, 124.32 (q, $^3J_{CF}$ = 3.5 Hz), 124.16 (q, $^3J_{CF}$ = 3.8 Hz), 123.30 (q, $^1J_{CF}$ = 272.4 Hz), 114.62, 94.74, 79.53, 61.56, 31.13, 16.16.
^{19}F NMR (376 MHz, $CDCl_3$) δ -63.01 (s, 3F).
HRMS (ESI) *m/z* calc'd for $C_{20}H_{17}F_3N_2O_5S$ $[M+H]^+$: 455.0883, found: 455.0889.



SI-16 **1i**

1i was prepared according to the general procedure for TBDPS deprotection, using **SI-16** (1.99 mmol, total amount of previously prepared material). The crude was purified by flash column chromatography (45% ethyl acetate/hexanes), to obtain 419 mg (50%) of **1i**, as a yellow solid.
M.P. 151-152 °C
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 – 7.88 (m, 1H), 7.77 – 7.69 (m, 2H), 7.64 – 7.57 (m, 1H), 7.36 (d, *J* = 2.2 Hz, 1H), 7.24 – 7.15 (m, 2H), 6.95 (d, *J* = 16.0 Hz, 1H), 5.85 (dt, *J* = 16.0, 2.2 Hz, 1H), 3.77 (t, *J* = 6.1 Hz, 2H), 2.47 (td, *J* = 6.9, 2.3 Hz, 2H), 1.84 – 1.76 (m, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 135.2, 134.0, 133.7, 133.4, 132.9, 132.7, 131.2, 130.9, 129.1, 128.9, 125.8, 125.6, 113.2, 94.0, 79.6, 61.6, 31.2, 16.1.
HRMS (ESI) *m/z* calc'd for $C_{19}H_{17}{}^{35}ClN_2O_5S$ $[M+H]^+$: 421.0619, found: 421.0627.



SI-4 **1j**

Sonogashira coupling was performed according to the general conditions (see **1a**), using **SI-4** (1.194 g, 3.4 mmol, 1.0 equiv) and 5-hexyn-2-ol (0.56 mL, 5.6 mmol, 2.0 equiv). The crude was purified by flash column chromatography (SiO_2, 50% ethyl acetate/hexanes, Rf ~ 0.3) to obtain 1.007 g (80%) of **1j** as an orange viscous oil.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 – 7.58 (m, 2H), 7.33 – 7.30 (m, 1H), 7.29 – 7.26 (m, 1H), 7.24 – 7.18 (m, 3H), 7.16 – 7.11 (m, 1H), 6.69 (d, *J* = 16.0 Hz, 1H), 6.51 (s, 1H), 5.88 (dt, *J* = 16.0, 2.3 Hz, 1H), 4.03 – 3.94 (m, 1H), 2.54 – 2.45 (m, 2H), 2.39 (s, 3H), 1.74 – 1.68 (m, 2H), 1.68 – 1.64 (m, 1H), 1.26 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.0, 136.2, 134.2, 132.9, 131.7, 129.7, 129.0, 127.2, 126.7, 126.2, 125.5, 112.3, 93.0, 79.8, 67.1, 37.6, 23.5, 21.5, 16.2.
HRMS (ESI) *m/z* calc'd for $C_{21}H_{23}NO_3S$ $[M+H]^+$: 370.1471, found: 370.1461.

Carbonyl Compounds 2 and 5

Carbonyl compounds **2b**-**2e**, **2g**, **2h'/''**, **2i**-**2j**, **2l**, and **5d** were obtained from commercial suppliers (Sigma Aldrich, Oakwood Chemicals, Combi Blocks, Ambeed, Alfa Aesar or Fisher Scientific) and were used as received. Benzaldehyde **2a** was obtained from a commercial source and was vacuum distilled. The distilled benzaldehyde was kept in a glass bottle, under argon, closed with a septum and kept in a jar with drierite under argon in the fridge (to avoid the formation of benzoic acid). Isobutyraldehyde **2j** was distilled using a Hickman still head under argon and used immediately. Aldehydes **2f, 2k, 2m** were prepared according to reported literature procedures.[10–12] Compound **2n** was prepared from 4-(hydroxymethyl)piperidine (commercially available) in two steps, according to the procedure outlined in the work by Skrydstrup et al.[13] (SI, page 11, using 2-nitrobenzenesulfonyl chloride instead of *p*-toluenesulfonyl chloride) and was used as crude.
Enol ethers **5a-5c, 5e** were prepared from the corresponding ketals[14,15] using a general procedure described by Napolitano et. al.[16] and were used as crude (after removing the solvents by vacuum distillation using a rotary evaporator). Cyclohexanone (**5a** ketone) was obtained from Sigma-Aldrich and used as received. 1,1-Dimethoxycyclohexane (**5a** ketal) was obtained from TCI and used as received.
Note: enol ethers are acid-sensitive and readily hydrolyze on the silica gel. They should be used as crude or purified by vacuum distillation. If silica gel chromatography purification is attempted, then the following should be considered: 1% triethylamine should be present in all eluents; silica should be packed using the slurry method with 1% triethylamine in the solvent used for preparing the slurry; some triethylamine should be added to the solvent used for dissolving the crude that is to be loaded onto the column (for wet loading). TLC monitoring is done with TLCs that are first labelled (marked with a pencil), then fully dipped into a 1% triethylamine/hexanes solution, briefly (air) dried until they appear dry and then spotted (some triethylamine should always be present in the solution that is being spotted onto the plate). If $CDCl_3$ is used for preparing NMR samples of enol ethers, it should be stored above vacuum flame-dried potassium carbonate prior to use.

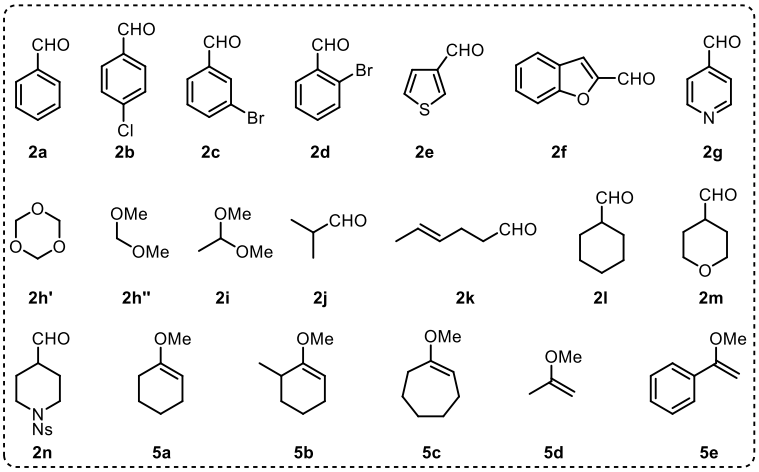
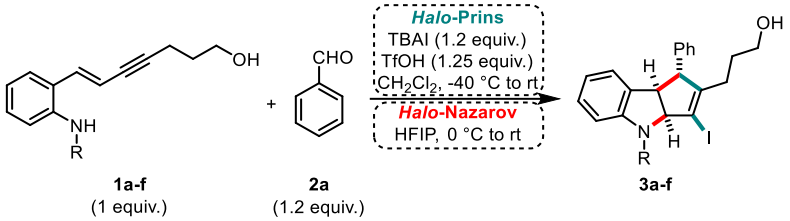
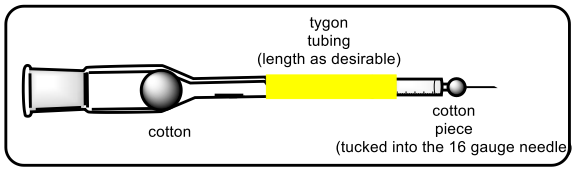


Table S1. Starting materials: carbonyl compounds.

General Procedure for the One-Pot *Halo*-Prins/*Halo*-Nazarov Reaction: Nitrogen Substituent Scope

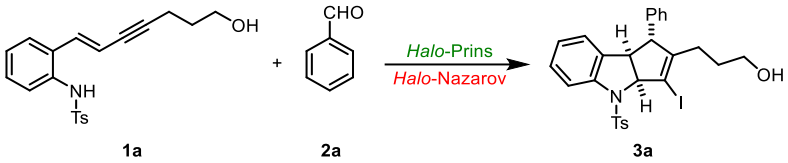


To a 10 mL round bottom flask, equipped with a stir bar, 5 Å powdered molecular sieves (72 mg, 300 mg/mmol benzaldehyde) were added (kept in the oven at 120 °C before use). The flask was closed with a septum, and then flame-dried under vacuum (~ 10 Torr). The flask was let to cool to room temperature and then carefully refilled with argon (*note:* sieves are easily blown and readily end up in the Schlenk line – to protect the Schlenk line from sieves, the authors used a large piece of cotton in between the line and the tubing (inside 24/40 glass adapter) and then a small piece of cotton in between the needle and the piece of a 1 mL syringe attached to the tubing; see the schematic below). The septum was briefly removed (while keeping the needle connected to the argon line, with the flow of argon reduced to prevent the blowing of the sieves, above the ground glass joint of the flask to maintain inert atmosphere) and enyne **1a-f** (0.2 mmol, 1.0 equiv.) and tetrabutylammonium iodide (89 mg, 0.24 mmol, 1.2 equiv.) were added. The flask was closed again and benzaldehyde (24.4 μL, 0.24 mmol, 1.2 equiv.) and anhydrous dichloromethane (2 mL) were added. The mixture was cooled to ~ -40 °C using the dry ice/acetonitrile bath (*note*: dry ice pieces should be added one by one until the bath has a temperature of -40 °C; no excess of dry ice should be used). Using a glass microsyringe, trifluoromethanesulfonic acid (22 μL, 0.25 mmol, 1.25 equiv) was slowly added dropwise to the reaction mixture (*note: trifluoromethanesulfonic acid fumes when exposed to air and this exposure should be minimized due to its hygroscopic nature; see general remarks of the SI for further remarks about the trifluoromethanesulfonic acid*). The reaction mixture was stirred in the acetonitrile bath (which was let to warm up) and the reaction progress was monitored using TLC (40% ethyl acetate/hexanes, consumption of the enyne **1a-f** was monitored, Rf ~ 0.1). Upon full (or near full) consumption of the starting material (typically within 1 h for **1a-1e**, and overnight for **1f**), dry ice/acetonitrile bath was replaced with an ice/water bath and 1,1,1,3,3,3-hexafluoropropan-2-ol (0.2 mL, HFIP) was added in one portion. The reaction was stirred in a slowly melting ice/water bath and monitored using TLC (40% ethyl acetate/hexanes, consumption of the *halo*-Prins intermediate was monitored, Rf ~ 0.5). During this time (typically within one hour), enyne **1a-e** was typically fully converted into the *halo*-Prins intermediate as well (if the full conversion was not observed before the addition of HFIP). *Quench*: When the TLC showed full consumption of the *halo*-Prins intermediate (*vide supra*), sodium bicarbonate (solid/powder) was added to the reaction mixture in excess. The mixture was diluted with ethyl acetate and the mixture was vacuum filtered through celite into a separatory funnel. The celite was washed with copious amounts of ethyl acetate. Following the filtration, the organic layer was washed with sat. aq. sodium bicarbonate, then with brine. The organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography to obtain the desired *halo*-Nazarov product **3a-e.**



Adapter for flame-drying molecular sieves.

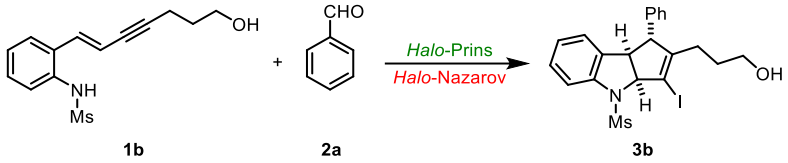
Compound **3a**



1a **2a** **3a**

Using the general procedure for the one-pot *halo*-Prins/*halo*-Nazarov reaction with the enyne **1a**, product **3a** was obtained in 88% (93 mg) as a white/colorless foam. The crude was purified by flash column chromatography (SiO_2, 40% ethyl acetate/hexanes).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.0 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.28 (d, *J* = 9.6 Hz, 2H), 7.16 – 7.09 (m, 4H), 7.06 (d, *J* = 8.0 Hz, 2H), 5.56 – 5.49 (m, 1H), 3.91 – 3.83 (m, 1H), 3.34 – 3.22 (m, 3H), 2.32 – 2.23 (m, 4H), 1.94 – 1.86 (m, 1H), 1.51 – 1.41 (m, 1H), 1.37 – 1.26 (m, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 152.3, 143.9, 141.6, 139.9, 137.0, 134.6, 129.4, 129.1, 128.5, 127.3, 127.1, 127.1, 126.0, 124.2, 119.5, 97.4, 77.7, 61.7, 59.6, 52.4, 29.3, 28.1, 21.4.
HRMS (ESI) *m/z* calc'd for $C_{27}H_{26}INO_3S$ $[M+H]^+$: 572.0756, found: 572.0751.

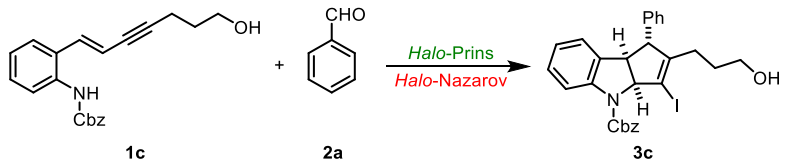
Compound **3b**



1b **2a** **3b**

Using the general procedure for the one-pot *halo*-Prins/*halo*-Nazarov reaction with the enyne **1b**, product **3b** was obtained in 86% (85 mg) as an off-white foam. The crude was purified by flash column chromatography (SiO_2, 40% ethyl acetate/hexanes). Crystals suitable for X-Ray diffraction analysis were obtained by mixing a small amount of material with heptane, heating the heterogeneous mixture to boiling, followed by the drop-by-drop addition of DCM until the hot mixture became homogeneous. The solution was left at room temperature to slowly cool down and evaporate (with the cap placed loosely on top), leading to a few crystals suitable for X-Ray analysis.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.0 Hz, 1H), 7.38 (q, *J* = 7.4 Hz, 3H), 7.33 – 7.27 (m, 2H), 7.23 – 7.17 (m, 3H), 5.66 – 5.59 (m, 1H), 4.04 (s, 1H), 3.95 (d, *J* = 7.3 Hz, 1H), 3.34 (td, *J* = 6.4, 2.3 Hz, 2H), 2.81 (s, 3H), 2.37 – 2.26 (m, 1H), 2.03 – 1.90 (m, 1H), 1.57 – 1.44 (m, 1H), 1.41 – 1.28 (m, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 152.5, 141.5, 139.8, 136.0, 129.2, 129.0, 127.5, 127.1, 125.9, 124.6, 118.2, 97.5, 77.7, 61.8, 59.6, 53.1, 37.3, 29.3, 28.2.
HRMS (ESI) *m/z* calc'd for $C_{14}H_{17}NO_3S$ $[M+H]^+$: 280.1002, found: 280.0995.

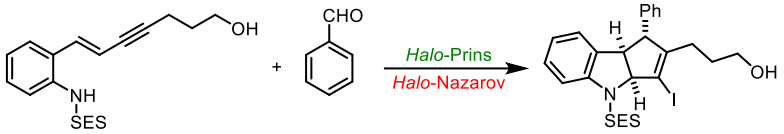
Compound **3c**



1c **2a** **3c**

Using the general procedure for the one-pot *halo*-Prins/*halo*-Nazarov reaction with the enyne **1c**, product **3c** was obtained in 84% (82 mg) as an off-white foam. The crude was purified by flash column chromatography (SiO_2, 40% ethyl acetate/hexanes).
^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) δ 7.81 (s, 1H), 7.53 (d, *J* = 7.4 Hz, 2H), 7.44 – 7.32 (m, 5H), 7.31 – 7.27 (m, 2H), 7.25 – 7.19 (m, 3H), 7.07 (t, *J* = 7.4 Hz, 1H), 5.92 – 5.80 (m, 1H), 5.46 (d, *J* = 12.2 Hz, 1H), 5.31 (d, *J* = 12.2 Hz, 1H), 4.05 (s, 1H), 3.92 (d, *J* = 7.4 Hz, 1H), 3.40 – 3.29 (m, 2H), 2.36 – 2.26 (m, 1H), 2.03 – 1.95 (m, 1H), 1.59 – 1.45 (m, 1H), 1.43 – 1.33 (m, 1H), 1.16 (s, 1H).
^{13}C NMR (126 MHz, $CDCl_3$, 30 °C) δ 152.9, 142.1, 140.5, 136.2, 134.4, 129.1, 128.6, 128.5, 128.5, 128.2, 127.3, 127.3, 123.9, 123.7, 117.0, 96.2, 74.2, 67.6, 61.9, 59.8, 52.7, 29.6, 28.4.
HRMS (ESI) *m/z* calc'd for $C_{28}H_{26}INO_3$ $[M+H]^+$: 552.1036, found: 552.1029.

Compound **3d**



1d **2a** **3d**

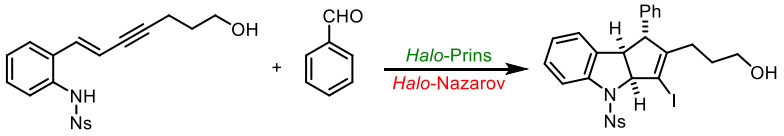
Using the general procedure for the one-pot *halo*-Prins/*halo*-Nazarov reaction with the enyne **1d**, product **3d** was obtained in 71% (81 mg) as a white/colorless foam. The crude was purified by flash column chromatography (SiO_2, 40% ethyl acetate/hexanes).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.0 Hz, 1H), 7.43 – 7.28 (m, 6H), 7.25 – 7.19 (m, 2H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.52 (d, *J* = 14.6 Hz, 1H), 6.47 (s, 1H), 6.16 (s, 1H), 3.78 – 3.62 (m, 2H), 3.11 – 2.98 (m, 3H), 2.52 – 2.39 (m, 1H), 1.99 – 1.86 (m, 1H), 1.76 – 1.67 (m, 1H), 1.16 – 1.05 (m, 2H), 0.02 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.3, 137.8, 133.9, 133.7, 130.7, 129.3, 128.9, 128.8, 127.8, 127.1, 126.9, 126.6, 125.1, 102.8, 76.2, 61.6, 48.9, 36.7, 27.1, 10.4, -2.0.

HRMS (ESI) *m/z* calc'd for $C_{25}H_{32}INO_3SSi$ $[M+H]^+$: 582.0995, found: 582.0987.

Compound **3e**



1e **2a** **3e**

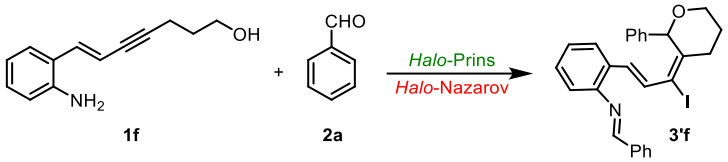
Using the general procedure for the one-pot *halo*-Prins/*halo*-Nazarov reaction with the enyne **1e**, product **3e** was obtained in 74% (62 mg) as a white/colorless foam. The crude was purified by flash column chromatography (SiO_2, 50% ethyl acetate/hexanes).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.82 (m, 1H), 7.65 – 7.56 (m, 2H), 7.56 – 7.47 (m, 2H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.31 (t, *J* = 6.9 Hz, 1H), 7.28 (d, *J* = 1.4 Hz, 2H), 7.25 – 7.22 (m, 1H), 7.16 (t, *J* = 7.4 Hz, 1H), 5.99 – 5.89 (m, 1H), 3.97 (s, 1H), 3.89 (d, *J* = 7.0 Hz, 1H), 3.33 (td, *J* = 6.4, 2.5 Hz, 2H), 2.36 – 2.23 (m, 1H), 2.02 – 1.90 (m, 1H), 1.58 – 1.46 (m, 1H), 1.41 – 1.30 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 152.9, 148.2, 141.5, 138.4, 136.8, 134.1, 132.1, 131.1, 130.9, 129.2, 128.6, 127.4, 127.2, 125.9, 124.8, 124.1, 117.7, 97.0, 78.9, 61.8, 59.3, 52.6, 29.3, 28.2.

HRMS (ESI) *m/z* calc'd for $C_{26}H_{23}IN_2O_5S$ $[M+H]^+$: 603.0445, found: 603.0442.

Compound **3'f**



1f **2a** **3'f**

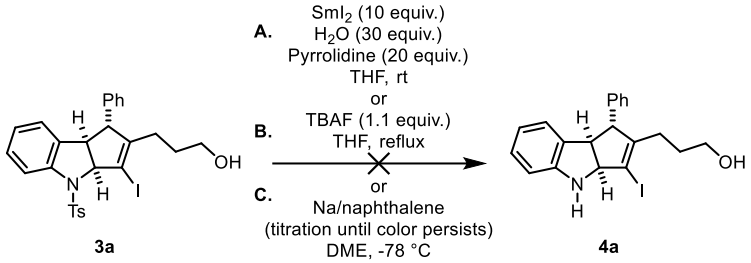
Using the general procedure for the one-pot *halo*-Prins/*halo*-Nazarov reaction with the enyne **1a**, product **3'a** was obtained in 21% (21 mg) as a pale-yellow oil. The crude was purified using preparatory TLC (40% ethyl acetate/hexanes, **3'a** Rf ~ 0.6).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.87 (d, *J* = 7.4 Hz, 2H), 7.51 – 7.29 (m, 11H), 7.14 (t, *J* = 7.6 Hz, 1H), 6.93 (d, *J* = 7.8 Hz, 1H), 6.66 (d, *J* = 14.9 Hz, 1H), 6.15 (s, 1H), 3.73 – 3.60 (m, 2H), 3.05 (d, *J* = 14.8 Hz, 1H), 2.39 (td, *J* = 13.7, 5.1 Hz, 1H), 1.96 – 1.84 (m, 1H), 1.71 – 1.58 (m, 1H).

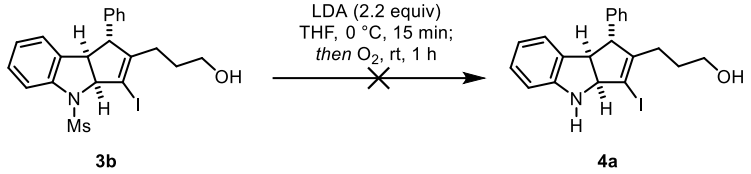
^{13}C NMR (126 MHz, $CDCl_3$) δ 160.1, 150.2, 143.0, 138.1, 136.6, 136.2, 131.4, 130.1, 129.0, 128.9, 128.8, 128.7, 127.5, 127.1, 127.0, 127.0, 126.0, 118.6, 104.7, 76.2, 61.6, 36.6, 27.3.

HRMS (ESI) *m/z* calc'd for $C_{27}H_{24}INO$ $[M+H]^+$: 506.0981, found: 506.0977.

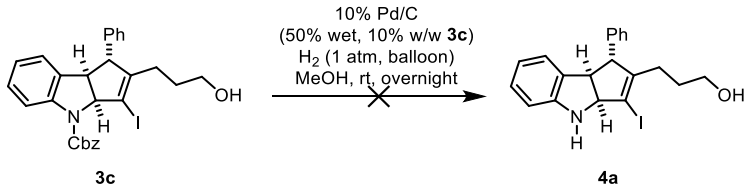
Removal of the Nitrogen Substituent



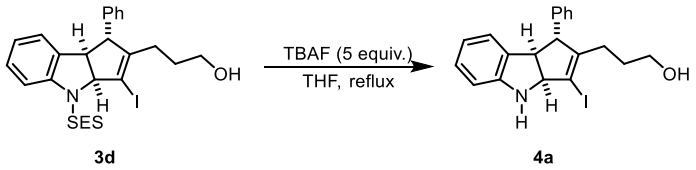
Different methods for the removal of the *p*-toluenesulfonyl (Ts) group in **3a** were attempted, adapted from different literature procedures. Using **A**[17] and **B**[18], **3a** was mostly left unconverted. Method **C**[19] led to full decomposition of **3a**.



Removal of the methanesulfonyl (Ms) group was attempted using the base/oxygen mediated transformation described in the literature[20], resulting in the full decomposition of **3b**.



Removal of the carbobenzyloxy (Cbz) group was attempted using the standard hydrogenolysis conditions, resulting in no reaction.

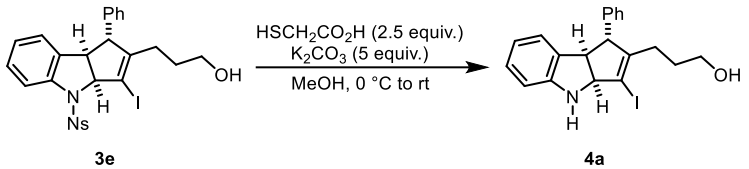


Deprotection of the *N*-2-(trimethylsilyl)ethylsulfonyl group (SES) in **3e** (80 mg, 0.138 mmol, 1.0 equiv.) was accomplished using 5 equiv. of TBAF (1 M solution in THF), according to a procedure from literature.[21] The reaction mixture was refluxed for 27 h in this case. The crude was purified using flash column chromatography (SiO_2, 30% ethyl acetate/hexanes) to obtain **3a** (41 mg, 71%) as pale orange foamy oil. *Note:* Compounds **3e** and **3a** are of similar polarity on TLC (Rf ~ 0.33 vs 0.39 for **3e** and **3a**, respectively, using 40% ethyl acetate/hexanes) but stain differently using the *p*-anisaldehyde stain (**3e** stains yellow, **3a** stains light green) or the CAM stain (**3a** stains orange immediately upon exposure to stain, while **3e** requires heating to stain grey/black).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (t, *J* = 7.5 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.21 (d, *J* = 7.5 Hz, 2H), 7.17 (d, *J* = 7.4 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.79 (t, *J* = 7.4 Hz, 1H), 6.72 (d, *J* = 7.8 Hz, 1H), 4.99 (d, *J* = 7.9 Hz, 1H), 3.97 (s, 1H), 3.87 (d, *J* = 7.9 Hz, 1H), 3.44 – 3.30 (m, 2H), 2.30 – 2.21 (m, 1H), 2.01 – 1.90 (m, 1H), 1.58 – 1.46 (m, 1H), 1.45 – 1.33 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.2, 148.3, 142.7, 131.8, 129.0, 128.3, 127.3, 127.1, 124.4, 119.4, 110.6, 101.0, 73.9, 62.0, 60.6, 54.3, 29.6, 28.0.

HRMS (ESI) *m/z* calc'd for $C_{20}H_{20}INO$ $[M+H]^+$: 418.0662, found: 418.0656.



3e **4a**

Deprotection of the *N*-2-nitrophenylsulfonyl group (Ns) was done according to the procedure adapted from the literature.[22]

To a 10 mL round-bottom flask, equipped with a stir bar, **3f** (120 mg, 0.2 mmol, 1 equiv.) was added, followed by anhydrous potassium carbonate (138 mg, 1.0 mmol, 5.0 equiv.) and anhydrous methanol (3.6 mL). The flask was closed and the mixture was cooled to 0 °C using an ice/water bath. When cooled, the flask was briefly opened and thioglycolic acid (35 μL, 0.5 mmol, 2.5 equiv.) was added dropwise using a glass microsyringe. The flask was closed again and the reaction mixture immediately became clear yellow. The mixture was stirred overnight, while letting the ice/water bath slowly reach room temperature. *Quench:* When the TLC showed full consumption of **3f** (50% ethyl acetate/hexanes, Rf ~ 0.26 **3f**, 0.47 **3a**), the reaction mixture was diluted with copious amounts of ethyl acetate and transferred to a separatory funnel. The organic layer was washed three times using sat. aq. sodium bicarbonate (to remove the yellow thioglycolic acid side products), then with brine. The organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography (SiO_2, 35% ethyl acetate/hexanes) to obtain **3a** (73 mg, 88%) as yellow oil.

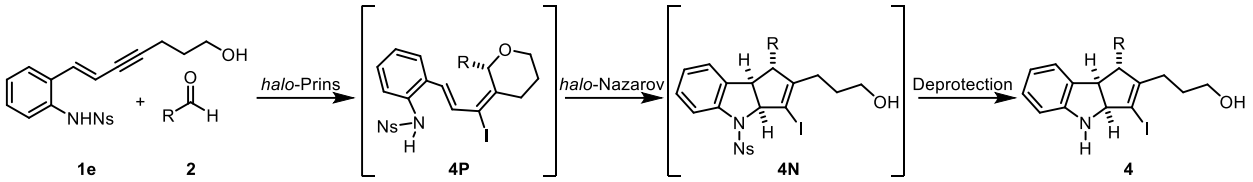
Note: Thioglycolic acid and the thioglycolic acid byproducts have a pungent, "skunky" odor.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (t, *J* = 7.5 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.21 (d, *J* = 7.5 Hz, 2H), 7.17 (d, *J* = 7.4 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.79 (t, *J* = 7.4 Hz, 1H), 6.72 (d, *J* = 7.8 Hz, 1H), 4.99 (d, *J* = 7.9 Hz, 1H), 3.97 (s, 1H), 3.87 (d, *J* = 7.9 Hz, 1H), 3.44 – 3.30 (m, 2H), 2.30 – 2.21 (m, 1H), 2.01 – 1.90 (m, 1H), 1.58 – 1.46 (m, 1H), 1.45 – 1.33 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.2, 148.3, 142.7, 131.8, 129.0, 128.3, 127.3, 127.1, 124.4, 119.4, 110.6, 101.0, 73.9, 62.0, 60.6, 54.3, 29.6, 28.0.

HRMS (ESI) *m/z* calc'd for $C_{20}H_{20}INO$ $[M+H]^+$: 418.0662, found: 418.0656.

General Procedure for the (One-Pot) *Halo*-Prins/*Halo*-Nazarov/Deprotection Sequence: Carbonyl Scope (Aldehydes)



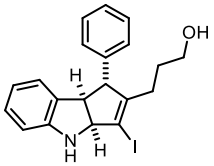
Halo-Prins: To a flask, equipped with a stir bar, 5 Å molecular sieves (300 mg/mmol aldehyde **2**) were added. The flask was closed with a septum and flame-dried under vacuum (~ 10 Torr). The flask was let to cool to room temperature and then carefully refilled with argon (*note:* sieves are easily blown and readily end up in the Schlenk line – to protect the Schlenk line from sieves, the authors have used a large piece of cotton in between the line and the tubing (inside 24/40 glass adapter) and then a small piece of cotton in between the needle and the piece of a 1 mL syringe attached to the tubing). The septum was briefly removed (while keeping the needle connected to the argon line, with the flow of argon reduced to prevent the blowing of the sieves, above the ground glass joint of the flask to maintain inert atmosphere) and enyne **1e** (1.0 equiv.), tetrabutylammonium iodide (1.2 equiv.) and aldehyde **2** (1.2 equiv. added at this point in case it was a solid) were added. The flask was closed again and aldehyde **2** (1.2 equiv. added using a (micro)syringe in case it was a liquid) and anhydrous dichloromethane (to obtain 0.1 mol/L solution with respect to the enyne **1e**) were added. The mixture was cooled to ~ -40 °C using the dry ice/acetonitrile bath (*note*: dry ice pieces should be added one by one until the bath has a temperature of -40 °C; no excess of dry ice should be used). Using a glass (micro)syringe, trifluoromethanesulfonic acid (1.25 equiv) was slowly added dropwise to the reaction mixture (*note: trifluoromethanesulfonic acid fumes when exposed to air and this exposure should be minimized due to its hygroscopic nature; see general remarks of the SI for further remarks about the trifluoromethanesulfonic acid*). The reaction mixture was stirred in the acetonitrile bath (which was let to warm up) and the reaction progress was monitored using TLC (50% ethyl acetate/hexanes, consumption of the enyne **1e** was monitored, Rf ~ 0.15). Typical reaction time was ~ 1 h, after which the consumption of the enyne **1e** was deemed to be full. In case of cyclic aldehydes, full consumption of the enyne **1e** was not observed (even after leaving the reaction to stir at room temperature overnight).

Halo-Nazarov: The *halo*-Prins reaction mixture flask was removed from the dry ice/acetonitrile bath and placed in an ice/water bath. To the flask, 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP, volume added to reach the volume ratio of 10:1 DCM/HFIP) was added dropwise. The reaction mixture was left to stir in a slowly melting ice/water bath and the consumption of the *halo*-Prins product was followed by TLC (50% ethyl acetate/hexanes, typical Rf ~ 0.5, except when using aldehydes **2m-n**, when Rf ~ 0.1-0.3). The *halo*-Nazarov products **4N** were significantly more polar on the TLC (50% ethyl acetate/hexanes, Rf ~ 0.25, except when using aldehydes **2m-n**, when Rf ~ 0.1-0.3 in 70% ethyl acetate/hexanes) compared to the *halo*-Prins products. The reaction typically took 1-2 h to reach completion (judged by the consumption of the *halo*-Prins intermediate on the TLC plate). In case the consumption of the *halo*-Prins intermediate stalled (based on the comparison between TLC plates taken in 30 min – 1 h intervals), the reaction mixture was cooled to 0 °C (ice/water bath) and additional trifluoromethanesulfonic acid (0.2 equiv.) was added dropwise. The reaction was monitored and if the reaction stalled again, the procedure was repeated. In general, the trifluoromethanesulfonic acid was never additionally added more than two times.

Deprotection: To the *halo*-Nazarov reaction mixture, anhydrous potassium carbonate (10 equiv.; increased amounts of potassium carbonate and thioglycolic acid were required for full consumption of the protected *halo*-Nazarov products **4N** in the one-pot procedure) was added, and then the solvents were removed by vacuum distillation using a rotary evaporator. To the mixture, anhydrous methanol (to obtain 0.05 mol/L solution with respect to the amount of enyne **1e** used in the *halo*-Prins reaction) was added. The flask was closed and the mixture was cooled to 0 °C using an ice/water bath. Once cooled, the flask was opened and thioglycolic acid (5 equiv.) was added dropwise using a (micro)syringe. The flask was closed and the mixture was stirred in a slowly melting ice/water bath (left to reach room temperature) overnight. *Quench*: When the TLC showed full consumption of the *halo*-Nazarov intermediate **4N** (50% ethyl acetate/hexanes, deprotected products **4** are less polar on the TLC than the protected products 4**N**, Rf ~ 0.56 for **4**), the mixture was vacuum-filtered through celite into a separatory funnel, using copious amounts of ethyl acetate. The organic layer was washed three times using sat. aq. sodium bicarbonate (to remove the yellow thioglycolic acid side products), then with brine. The organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography.

Scope (Aldehydes)

Compound 4a



4a

Compound **4a** was isolated as yellow oil after column chromatography (DCM, then 30% ethyl acetate/hexanes) in 81% yield (68 mg).

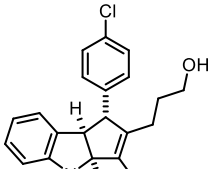
Note: As the *N*-nosyl derivative **3e** is significantly more polar than **4a**, we believe that the higher yield for the one-pot three-step sequence (*halo*-Prins/*halo*-Nazarov/deprotection) that prepares **4a** over the one-pot two-step sequence (*halo*-Prins/*halo*-Nazarov) that prepares **3e** is attributed to the loss of **3e** during the workup, which is diminished in the case of **4a**.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (t, *J* = 7.5 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.21 (d, *J* = 7.5 Hz, 2H), 7.17 (d, *J* = 7.4 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.79 (t, *J* = 7.4 Hz, 1H), 6.72 (d, *J* = 7.8 Hz, 1H), 4.99 (d, *J* = 7.9 Hz, 1H), 3.97 (s, 1H), 3.87 (d, *J* = 7.9 Hz, 1H), 3.44 – 3.30 (m, 2H), 2.30 – 2.21 (m, 1H), 2.01 – 1.90 (m, 1H), 1.58 – 1.46 (m, 1H), 1.45 – 1.33 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.2, 148.3, 142.7, 131.8, 129.0, 128.3, 127.3, 127.1, 124.4, 119.4, 110.6, 101.0, 73.9, 62.0, 60.6, 54.3, 29.6, 28.0.

HRMS (ESI) *m/z* calc'd for $C_{20}H_{20}INO$ $[M+H]^+$: 418.0662, found: 418.0656.

Compound 4b



4b

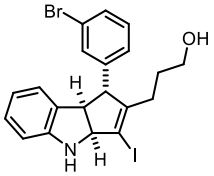
Compound **4b** was isolated as yellow foam after column chromatography (DCM, then 30% ethyl acetate/hexanes) in 69% yield (62 mg).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, *J* = 7.9 Hz, 2H), 7.16 – 7.11 (m, 3H), 7.08 (t, *J* = 7.6 Hz, 1H), 6.78 (t, *J* = 7.4 Hz, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 4.98 – 4.90 (m, 1H), 4.33 (s, 1H), 3.94 (s, 1H), 3.81 (d, *J* = 7.9 Hz, 1H), 3.42 – 3.33 (m, 2H), 2.31 – 2.20 (m, 1H), 1.98 – 1.88 (m, 1H), 1.56 – 1.47 (m, 1H), 1.42 – 1.32 (m, 1H), 1.16 (s, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.7, 148.4, 141.3, 132.9, 131.4, 129.2, 128.6, 128.5, 124.3, 119.4, 110.6, 101.6, 73.8, 61.9, 59.9, 54.4, 29.6, 28.0.

HRMS (ESI) *m/z* calc'd for $C_{20}H_{19}{}^{35}ClINO$ $[M+H]^+$: 452.0273, found: 452.0269.

Compound 4c



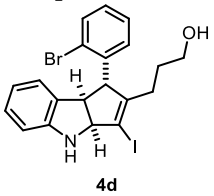
4c

Compound **4c** was isolated as orange oil after column chromatography (DCM, then 30% ethyl acetate/hexanes) in 76% yield (75 mg).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 7.9 Hz, 1H), 7.33 – 7.30 (m, 1H), 7.21 (d, *J* = 7.9 Hz, 1H), 7.15 – 7.09 (m, 2H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.76 (t, *J* = 7.4 Hz, 1H), 6.67 (d, *J* = 7.8 Hz, 1H), 4.97 – 4.89 (m, 1H), 4.31 (s, 1H), 3.90 (s, 1H), 3.80 (d, *J* = 7.9 Hz, 1H), 3.40 – 3.29 (m, 2H), 2.30 – 2.19 (m, 1H), 1.96 – 1.86 (m, 1H), 1.55 – 1.44 (m, 1H), 1.41 – 1.30 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.2, 149.1, 145.9, 132.0, 131.4, 131.1, 131.1, 129.3, 126.7, 125.1, 123.9, 120.2, 111.4, 102.7, 74.5, 62.7, 60.9, 55.0, 30.4, 28.8.
HRMS (ESI) *m/z* calc'd for $C_{20}H_{19}{}^{79}BrINO$ $[M+H]^+$: 495.9767, found: 495.9765.

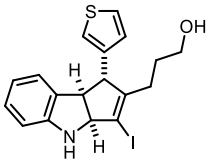
Compound 4d



4d

Compound **4d** was isolated as orange oil after column chromatography (DCM, then 30% ethyl acetate/hexanes) in 66% yield (65 mg).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.47 (d, *J* = 7.4 Hz, 1H), 7.31 (td, *J* = 7.5, 1.3 Hz, 1H), 7.15 (td, *J* = 7.6, 1.7 Hz, 1H), 7.13 – 7.07 (m, 1H), 7.04 – 7.00 (m, 1H), 6.81 (t, *J* = 7.4 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 4.85 – 4.79 (m, 1H), 4.59 (s, 1H), 4.32 (s, 1H), 3.75 (d, *J* = 7.5 Hz, 1H), 3.42 – 3.30 (m, 2H), 2.38 – 2.27 (m, 1H), 1.99 – 1.89 (m, 1H), 1.60 – 1.48 (m, 1H), 1.48 – 1.37 (m, 1H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 150.4, 148.2, 141.2, 133.2, 131.2, 128.7, 128.4, 128.1, 128.0, 125.0, 124.4, 119.5, 110.4, 102.5, 73.1, 61.9, 58.1, 54.0, 29.7, 28.2.
HRMS (ESI) *m/z* calc'd for $C_{20}H_{19}{}^{79}BrINO$ $[M+H]^+$: 495.9767, found: 495.9764.

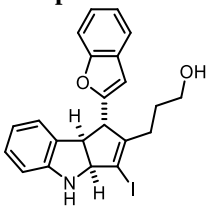
Compound 4e



4e

Compound **4e** was isolated as yellow oil after column chromatography (DCM, then 30% ethyl acetate/hexanes) in 73% yield (62 mg).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (dt, *J* = 5.7, 2.8 Hz, 1H), 7.16 (d, *J* = 7.4 Hz, 1H), 7.10 – 7.07 (m, 2H), 6.93 – 6.92 (m, 1H), 6.79 (td, *J* = 7.5, 2.3 Hz, 1H), 6.72 (d, *J* = 7.7 Hz, 1H), 4.97 – 4.95 (m, 1H), 4.10 (s, 1H), 3.87 (d, *J* = 7.8 Hz, 1H), 3.40 – 3.35 (m, 2H), 2.29 – 2.23 (m, 1H), 2.05 – 1.99 (m, 1H), 1.58 – 1.50 (m, 1H), 1.41 – 1.35 (m, 1H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 151.0, 148.3, 143.5, 131.5, 128.4, 126.7, 126.5, 124.3, 120.8, 119.4, 110.6, 100.8, 73.6, 61.9, 55.1, 53.5, 29.6, 28.0.
HRMS (ESI) *m/z* calc'd for $C_{18}H_{18}INOS$ $[M+H]^+$: 424.0227, found: 424.0220.

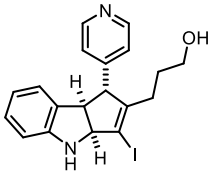
Compound 4f



4f

Compound **4f** was isolated as light brown oil after column chromatography (DCM, then 30% ethyl acetate/hexanes) in 56% yield (51 mg).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.5 Hz, 1H), 7.48 (d, *J* = 8.1 Hz, 1H), 7.29 – 7.19 (m, 3H), 7.11 (t, *J* = 7.6 Hz, 1H), 6.80 (t, *J* = 7.4 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 6.55 (s, 1H), 5.02 (d, *J* = 5.7 Hz, 1H), 4.19 (s, 1H), 4.11 (d, *J* = 7.8 Hz, 1H), 3.45 – 3.37 (m, 2H), 2.34 (dt, *J* = 15.1, 8.0 Hz, 1H), 2.17 (dt, *J* = 14.5, 7.4 Hz, 1H), 1.64 – 1.55 (m, 1H), 1.48 – 1.40 (m, 1H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 157.9, 154.9, 148.4, 147.7, 130.9, 128.6, 128.4, 124.3, 124.0, 122.8, 120.7, 119.5, 111.1, 110.7, 102.9, 102.6, 73.7, 61.9, 53.2, 51.3, 29.6, 28.1.
HRMS (ESI) *m/z* calc'd for $C_{22}H_{20}INO_2$ $[M+H]^+$: 458.0611, found: 458.0599.

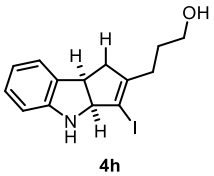
Compound 4g



4g

The synthesis of the compound **4g** was attempted using the one-pot *halo*-Prins/*halo*-Nazarov protocol. The TLC of this reaction sequence and a ^{1}H NMR of the crude mixture indicated a complex mixture, without any signs that the product had been formed. The deprotection was not attempted.

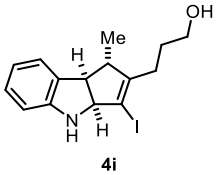
Compound 4h



4h

Attempt to prepare **4h**, beginning with the standard procedure for the *halo*-Prins reaction, with the following modifications: enyne **1e** (1.0 equiv.), 1,3,5-trioxane (0.5 equiv., which corresponds to 1.5 equiv. of formaldehyde) or dimethoxymethane (1.5 equiv.), TBAI (2.0 equiv.), 5 Å molecular sieves (400 mg/mmol enyne **1e**), dichloromethane (5 mL/mmol enyne **1e**) and trifluoromethanesulfonic acid (1.2 equiv.), temperature from -40 °C to +40 °C (reflux), was unsuccessful in the case of 1,3,5-trioxane (no conversion of the enyne **1e** was observed), and in the case of dimethoxymethane led to the formation of MOM-protected enyne (**1e-MOM**) which did not undergo *halo*-Prins cyclization.

Compound 4i



4i

To a flask, equipped with a stir bar, 5 Å molecular sieves (600 mg/mmol 1,1-dimethoxymethane) were added. The flask was closed with a septum and flame-dried under vacuum (~ 10 Torr). The flask was let to cool to room temperature and then carefully refilled with argon (*note:* sieves are easily blown and readily end up in the Schlenk line – to protect the Schlenk line from sieves, the authors have used a large piece of cotton in between the line and the tubing (inside 24/40 glass adapter) and then a small piece of cotton in between the needle and the piece of a 1 mL syringe attached to the tubing). The septum was briefly removed (while keeping the needle connected to the argon line, with the flow of argon reduced to prevent the blowing of the sieves, above the ground glass joint of the flask to maintain inert atmosphere) and enyne **1e** (1.0 equiv.), and tetrabutylammonium iodide (1.2 equiv) were added. The flask was closed again and 1,1-dimethoxymethane (1.2 equiv. added using a (micro)syringe) and anhydrous dichloromethane (to obtain 0.1 mol/L solution with respect to the enyne **1e**) were added. The mixture was cooled to ~ -40 °C using the dry ice/acetonitrile bath (*note*: dry ice pieces should be added one by one until the bath has a temperature of -40 °C; no excess of dry ice should be used). Using a glass (micro)syringe, trifluoromethanesulfonic acid (1.25 equiv) was slowly added dropwise to the reaction mixture (*note: trifluoromethanesulfonic acid fumes when exposed to air and this exposure should be minimized due to its hygroscopic nature; see general remarks of the SI for further remarks about the trifluoromethanesulfonic acid*). The reaction mixture was stirred in the acetonitrile bath (which was let to warm up) and the reaction progress was monitored using TLC (50% ethyl acetate/hexanes, consumption of the enyne **1e** was monitored, Rf ~ 0.15). After 1 h, the dry ice/acetonitrile bath was replaced with ice/water bath, and 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP, volume added to reach the volume ratio of 10:1 DCM/HFIP) was added dropwise, and the reaction was allowed to warm to room temperature. After 16 h, an additional 0.2 equiv. of trifluoromethanesulfonic acid was added dropwise (at room temperature). After another 2 h, an additional 0.2 equiv. of trifluoromethanesulfonic acid was added dropwise. After 1 h, the reaction was quenched with the excess of solid sodium bicarbonate, filtered through a silica plug eluting with 60% ethyl acetate/hexanes, concentrated using

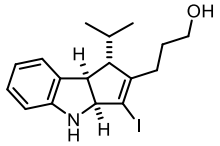
a rotary evaporator, and purified by column chromatography (SiO_2, 25%–50% ethyl acetate/hexanes) to give the protected *halo*-Nazarov product **4Ni** as an orange oil (72 mg, 68%). This oil was then added to a flask followed by MeOH (2.7 mL) and K_2CO_3 (10 equiv.). Afterward, mercaptoacetic acid (5 equiv.) was added to the flask at room temperature overnight. The reaction was worked up by diluting with EtOAc, washing x2 with saturated $NaHCO_3$, x1 with brine, then dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. The crude material was purified by column chromatography from DCM to 25% EtOAc/hexanes to yield **4i** as a colorless oil (21 mg, 45%; 31% over three steps).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 – 7.00 (m, 2H), 6.74 (t, *J* = 7.4 Hz, 1H), 6.68 (d, *J* = 7.7 Hz, 1H), 4.77 (d, *J* = 7.7 Hz, 1H), 3.54 (d, *J* = 7.8 Hz, 1H), 3.51 – 3.35 (m, 2H), 2.90 (q, *J* = 7.2 Hz, 1H), 2.36 – 2.24 (m, 1H), 2.22 – 2.11 (m, 1H), 1.76 – 1.60 (m, 1H), 1.57 – 1.43 (m, 1H), 1.28 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.5, 148.4, 132.1, 128.1, 124.2, 119.3, 110.5, 99.0, 72.9, 62.0, 52.7, 48.2, 29.7, 27.5, 20.8.

HRMS (ESI) *m/z* calc'd for $C_{15}H_{18}INO$ $[M+H]^+$: 356.0506, found: 356.0495.

Compound 4j



4j

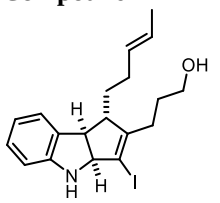
Compound **4j** was isolated as yellow oil after column chromatography (DCM, then 30% ethyl acetate/hexanes) in 69% yield (53 mg).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.07 – 6.97 (m, 2H), 6.73 (t, *J* = 7.4 Hz, 1H), 6.66 (d, *J* = 7.8 Hz, 1H), 4.64 (d, *J* = 7.8 Hz, 1H), 4.26 (s, 1H), 3.62 (d, *J* = 8.0 Hz, 1H), 3.50 – 3.38 (m, 2H), 2.81 (s, 1H), 2.35 – 2.25 (m, 1H), 2.16 – 2.00 (m, 2H), 1.73 – 1.60 (m, 1H), 1.56 – 1.43 (m, 1H), 1.32 (s, 1H), 1.18 (d, *J* = 6.8 Hz, 3H), 0.76 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.7, 148.6, 132.7, 127.9, 124.2, 119.1, 110.3, 100.1, 73.9, 62.1, 60.6, 45.1, 29.6, 28.8, 27.7, 21.5, 16.4.

HRMS (ESI) *m/z* calc'd for $C_{17}H_{22}INO$ $[M+H]^+$: 384.0819, found: 384.0814.

Compound 4k



4k

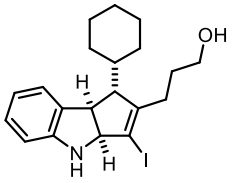
One-pot halo-Prins/halo-Nazarov/deprotection: Compound **4k** was isolated as yellow oil after column chromatography (DCM, then 30% ethyl acetate/hexanes) in 62% yield (51 mg).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.07 – 6.99 (m, 2H), 6.73 (t, *J* = 7.4 Hz, 1H), 6.66 (d, *J* = 7.7 Hz, 1H), 5.60 – 5.43 (m, 2H), 4.73 – 4.68 (m, 1H), 4.24 (s, 1H), 3.65 (d, *J* = 7.8 Hz, 1H), 3.45 – 3.38 (m, 2H), 2.84 – 2.79 (m, 1H), 2.34 – 2.25 (m, 1H), 2.25 – 2.07 (m, 3H), 1.82 – 1.73 (m, 1H), 1.72 – 1.68 (m, 3H), 1.67 – 1.61 (m, 1H), 1.53 – 1.37 (m, 2H), 1.34 – 1.23 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.8, 148.6, 132.2, 130.4, 128.1, 125.8, 124.2, 119.1, 110.3, 99.8, 73.1, 62.0, 53.4, 49.8, 33.4, 30.3, 29.7, 27.6, 17.9.

HRMS (ESI) *m/z* calc'd for $C_{19}H_{24}INO$ $[M+H]^+$: 410.0975, found: 410.0979.

Compound 4l



4l

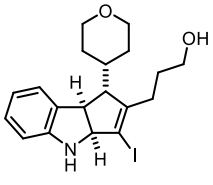
Compound **4l** was isolated as pale-yellow foam after flash column chromatography (DCM, then 30% ethyl acetate/hexanes) in 78% yield (66 mg).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.05 – 7.00 (m, 1H), 7.00 – 6.97 (m, 1H), 6.72 (td, *J* = 7.4, 1.1 Hz, 1H), 6.65 (d, *J* = 7.5 Hz, 1H), 4.61 (dt, *J* = 8.0, 2.1 Hz, 1H), 3.66 (d, *J* = 8.0 Hz, 1H), 3.50 – 3.38 (m, 2H), 2.78 (d, *J* = 3.0 Hz, 1H), 2.33 – 2.23 (m, 1H), 2.17 – 2.07 (m, 1H), 1.90 – 1.82 (m, 1H), 1.82 – 1.61 (m, 6H), 1.54 – 1.32 (m, 5H), 1.23 – 1.12 (m, 2H), 0.95 – 0.83 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.2, 148.6, 132.8, 127.9, 124.2, 119.1, 110.3, 99.8, 73.9, 62.1, 60.2, 46.4, 39.3, 32.2, 29.7, 27.7, 27.1, 26.7, 26.5, 26.3.

HRMS (ESI) *m/z* calc'd for $C_{20}H_{26}INO$ $[M+H]^+$: 424.1132, found: 424.1128.

Compound 4m



4m

The *halo*-Prins product **4Pm** was prepared according to the general procedure (first paragraph) but the reaction profile was deemed too complex (by TLC) for carrying into the subsequent steps in one-pot. The reaction was quenched by the addition of excess solid sodium bicarbonate. The mixture was stirred for 5 min and then vacuum-filtered over a short silica plug, using diethyl ether to elute the crude product The solvents were removed by vacuum distillation using a rotary evaporator (the flask was protected from light using a piece of aluminum foil; the *halo*-Prins products were light-sensitive), and the product was purified by preparative TLC (70% ethyl acetate/hexanes, Rf ~ 0.1) and was used in the next two steps (in one-pot) without characterization.

To a flask, equipped with a stir bar, *halo*-Prins product **4Pm** (1.0 equiv.) was added, followed by anhydrous dichloromethane (DCM, to obtain 0.1 mol/L solution with respect to **4Pm**) and 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP, volume added to reach the volume ratio of 10:1 DCM/HFIP). The flask was closed and the mixture was cooled to 0 °C using an ice/water bath. Once cooled, the flask was briefly opened and trifluoromethanesulfonic acid (0.2 equiv.) was added dropwise. The rest of the procedure was carried out in the same way as described in the second and third paragraph of the general procedure for the one-pot *halo*-Prins/*halo*-Nazarov/deprotection sequence for aldehydes.

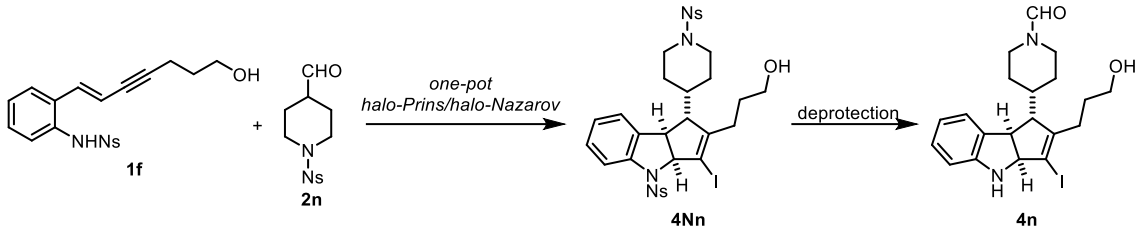
Compound **4Pm** was isolated in 48% yield (59 mg) after preparative TLC. Compound **4m** was isolated as yellow oil after preparative TLC (ethyl acetate, Rf ~ 0.4) in 29% yield (25 mg, 61% yield for the one-pot *halo*-Nazarov/deprotection sequence).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.07 – 7.01 (m, 1H), 6.99 – 6.95 (m, 1H), 6.73 (td, *J* = 7.4, 1.0 Hz, 1H), 6.66 (d, *J* = 7.8 Hz, 1H), 4.64 (dt, *J* = 8.0, 2.0 Hz, 1H), 4.25 (s, 1H), 4.13 – 3.97 (m, 2H), 3.70 (d, *J* = 8.0 Hz, 1H), 3.52 – 3.32 (m, 4H), 2.84 (p, *J* = 1.5 Hz, 1H), 2.36 – 2.27 (m, 1H), 2.18 – 2.08 (m, 1H), 1.96 – 1.88 (m, 1H), 1.81 (qd, *J* = 12.2, 4.6 Hz, 1H), 1.71 – 1.61 (m, 2H), 1.53 – 1.43 (m, 1H), 1.34 – 1.28 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 149.3, 148.5, 132.3, 128.1, 124.1, 119.2, 110.3, 100.6, 73.8, 68.1, 68.1, 62.0, 59.2, 46.3, 36.8, 31.5, 29.6, 27.7, 27.4.

HRMS (ESI) *m/z* calc'd for $C_{19}H_{24}INO_2$ $[M+H]^+$: 426.0924, found: 426.0917.

Compound 4n



Compound **4Nn** was prepared according to the first two paragraphs of the general procedure for the the one-pot *halo*-Prins/*halo*-Nazarov/deprotection sequence for aldehydes. Instead of proceeding with the deprotection step (third paragraph), the reaction was quenched by the addition of excess solid sodium bicarbonate. The mixture was stirred for 5 min and then vacuum-filtered through celite into a separatory funnel, using copious amounts of ethyl acetate. The organic layer was washed using sat. aq. sodium bicarbonate and the layers were separated. The aqueous layer was washed two times with ethyl acetate and the organic layers were combined and washed with brine. The organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography.

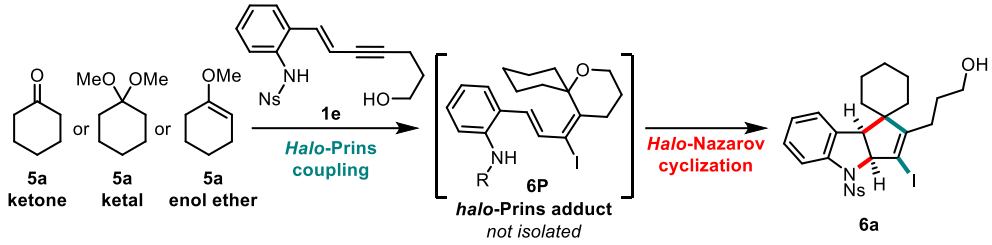
Compound **4Nn** was isolated in 56% yield (89 mg) after flash column chromatography (80% ethyl acetate/hexanes, Rf ~ 0.19) and was used in the next step without characterization. Compound **4n** was prepared using a modified procedure for the deprotection: potassium carbonate (20 equiv.), a mixture of anhydrous DMF and anhydrous methanol (1:1 v/v, to obtain 0.05 mol/L solution with respect to **4Nn**) and thioglycolic acid (10 equiv.) were used. This change was necessary due to low solubility of **4Nn** in methanol, and due to the presence of two nosyl groups in **4Nn**. Compound **4n** was isolated as yellow foam after preparative TLC (94% DCM, 5% methanol, 1% aqueous ammonia (30%), Rf ~ 0.4) in 15% yield (14 mg, 27% yield for the deprotection step).

^{1}H NMR (500 MHz, $CDCl_3$, mixture of conformers) δ 8.07 – 8.00 (m, 1H), 7.07 – 7.01 (m, 1H), 6.97 – 6.91 (m, 1H), 6.76 – 6.70 (m, 1H), 6.68 – 6.62 (m, 1H), 4.64 – 4.49 (m, 2H), 4.28 – 4.22 (m, 1H), 3.84 – 3.72 (m, 1H), 3.72 – 3.65 (m, 1H), 3.64 – 3.56 (m, 1H), 3.50 – 3.40 (m, 2H), 3.22 – 2.99 (m, 1H), 2.91 – 2.85 (m, 1H), 2.71 – 2.49 (m, 1H), 2.38 – 2.29 (m, 1H), 2.18 – 2.09 (m, 1H), 1.99 – 1.90 (m, 1H), 1.89 – 1.78 (m, 1H), 1.69 – 1.58 (m, 2H), 1.57 – 1.43 (m, 2H), 1.19 – 1.04 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$, mixture of conformers) δ 160.8, 149.2, 149.0, 148.5, 148.4, 131.9, 131.9, 128.2, 128.2, 124.0, 123.9, 119.3, 119.1, 110.4, 110.4, 101.1, 101.0, 73.7, 73.7, 64.2, 61.9, 61.9, 58.9, 46.3, 46.3, 46.2, 46.1, 40.0, 39.9, 38.1, 31.6, 30.2, 29.6, 27.7, 27.7, 27.3, 25.8.

HRMS (ESI) *m/z* calc'd for $C_{20}H_{25}IN_2O_2$ $[M+H]^+$: 453.1033, found: 453.1027.

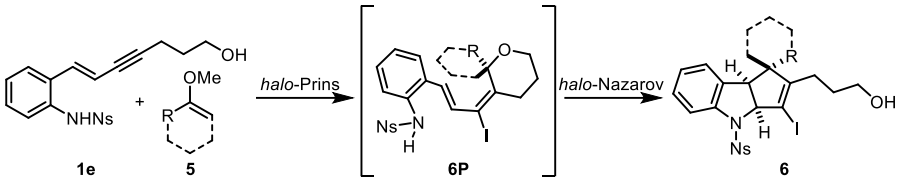
Optimization of the Reaction Conditions for the Ketone *Halo*-Prins/*Halo*-Nazarov Sequence



Halo-Prins: To a flask, equipped with a stir bar, 5 Å molecular sieves (400 mg/mmol **5a**) were added. The flask was closed with a septum and flame-dried under vacuum (~ 10 Torr). The flask was let to cool to room temperature and then carefully refilled with argon (*note:* sieves are easily blown and readily end up in the Schlenk line – to protect the Schlenk line from sieves, the authors have used a large piece of cotton in between the line and the tubing (inside 24/40 glass adapter) and then a small piece of cotton in between the needle and the piece of a 1 mL syringe attached to the tubing). The septum was briefly removed (while keeping the needle connected to the argon line, with the flow of argon reduced to prevent the blowing of the sieves, above the ground glass joint of the flask to maintain inert atmosphere) and enyne **1e** (0.1 mmol, 1.0 equiv.), and tetrabutylammonium iodide (2.0 equiv.) were added. The flask was closed again and **5a** (1.2 or 2.0 equiv. added using a (micro)syringe) and anhydrous dichloromethane (to obtain 0.2 mol/L solution with respect to the enyne **1e**) were added. The mixture was cooled to ~ -40 °C using a Neslab CC-100 immersion cooler. Using a glass (micro)syringe, trifluoromethanesulfonic acid (2.0 equiv) was slowly added dropwise to the reaction mixture (*note: trifluoromethanesulfonic acid fumes when exposed to air and this exposure should be minimized due to its hygroscopic nature; see general remarks of the SI for further remarks about the trifluoromethanesulfonic acid*). The reaction mixture was stirred at -40 °C and the reaction progress was monitored using TLC (50% ethyl acetate/hexanes, consumption of the enyne **1e** was monitored, Rf ~ 0.15). Typical reaction time was ~ 16 h, after which the consumption of the enyne **1e** was deemed to be full or the reaction had stalled, as no change in the consumption of the enyne **1e** could be observed on consecutive TLCs. *Quench:* The reaction was quenched by the addition of excess solid sodium bicarbonate. The mixture was stirred for 5 min and then vacuum-filtered over a short silica plug, using diethyl ether to elute the crude product (TLC, 50% ethyl acetate/hexanes, typical Rf ~ 0.5. The solvents were removed by vacuum distillation using a rotary evaporator (the flask was protected from light using a piece of aluminum foil; the *halo*-Prins products were light-sensitive), and the product was used without further purification.

Halo-Nazarov: To a flask, equipped with a stir bar, *halo*-Prins adduct (1.0 equiv., calculated based on the crude mass of the *halo*-Prins product, assuming that the product was pure for stoichiometric calculations) was added, followed by anhydrous dichloromethane (DCM, to obtain 0.1 mol/L solution with respect to **1e**) and 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP, volume added to reach the volume ratio of 10:1 DCM/HFIP). The flask was closed and the mixture was cooled to 0 °C (stir plate was positioned in a small fridge). Once cooled, the flask was briefly opened and trifluoromethanesulfonic acid (0.2 equiv.) was added dropwise. The flask was closed and the mixture was left to stir for ~ 16 h (product Rf ~ 0.1-0.3 in 50% ethyl acetate/hexanes). *Quench:* The reaction mixture was quenched with the addition of excess aqueous sodium bicarbonate (at room temperature) and was left to stir vigorously for 10 min (during which the typical dark red color of the mixture dissipated to colorless or pale yellow). The mixture was transferred to a separatory funnel using excess dichloromethane. The organic layer was washed with saturated aqueous sodium bicarbonate once and the layers were separated. Aqueous layer was washed once with dichloromethane and the combined organic layers were washed once with brine. Organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by preparatory TLC (50% ethyl acetate/hexanes; the product was extracted from silica using ethyl acetate and then the solvent was removed in the usual way).

General Procedure for the (One-Pot) *Halo*-Prins/*Halo*-Nazarov/Deprotection Sequence: Carbonyl Scope (ketones masked as enol ethers)

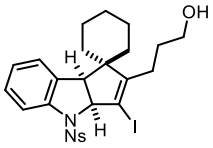


Halo-Prins: To a flask, equipped with a stir bar, 5 Å molecular sieves (400 mg/mmol enol ether **5**) were added. The flask was closed with a septum and flame-dried under vacuum (~ 10 Torr). The flask was let to cool to room temperature and then carefully refilled with argon (*note:* sieves are easily blown and readily end up in the Schlenk line – to protect the Schlenk line from sieves, the authors have used a large piece of cotton in between the line and the tubing (inside 24/40 glass adapter) and then a small piece of cotton in between the needle and the piece of a 1 mL syringe attached to the tubing). The septum was briefly removed (while keeping the needle connected to the argon line, with the flow of argon reduced to prevent the blowing of the sieves, above the ground glass joint of the flask to maintain inert atmosphere) and enyne **1e** (1.0 equiv.), and tetrabutylammonium iodide (2.0 equiv.) were added. The flask was closed again and methyl enol ether **5** (2.0 equiv. added using a (micro)syringe) and anhydrous dichloromethane (to obtain 0.2 mol/L solution with respect to the enyne **1e**) were added. The mixture was cooled to ~ -40 °C using the dry ice/acetonitrile bath (*note*: dry ice pieces should be added one by one until the bath has a temperature of -40 °C; no excess of dry ice should be used). Using a glass (micro)syringe, trifluoromethanesulfonic acid (2.0 equiv) was slowly added dropwise to the reaction mixture (*note: trifluoromethanesulfonic acid fumes when exposed to air and this exposure should be minimized due to its hygroscopic nature; see general remarks of the SI for further remarks about the trifluoromethanesulfonic acid*). The reaction mixture was stirred in the acetonitrile bath (which was let to warm up) and the reaction progress was monitored using TLC (50% ethyl acetate/hexanes, consumption of the enyne **1e** was monitored, Rf ~ 0.15). Typical reaction time was ~ 16 h, after which the consumption of the enyne **1e** was deemed to be full (or the reaction had stalled, as no change in the consumption of the enyne **1e** could be observed on consecutive TLCs). *Quench:* The reaction was quenched by the addition of excess solid sodium bicarbonate. The mixture was stirred for 5 min and then vacuum-filtered over a short silica plug, using diethyl ether to elute the crude product (TLC, 50% ethyl acetate/hexanes, typical Rf ~ 0.5. The solvents were removed by vacuum distillation using a rotary evaporator (the flask was protected from light using a piece of aluminum foil; the *halo*-Prins products were light-sensitive), and the product was used without further purification.

Halo-Nazarov: To a flask, equipped with a stir bar, *halo*-Prins product **6P** (1.0 equiv., calculated based on the crude mass of the *halo*-Prins product, assuming that the product was pure for stoichiometric calculations) was added, followed by anhydrous dichloromethane (DCM, to obtain 0.1 mol/L solution with respect to **6P**) and 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP, volume added to reach the volume ratio of 10:1 DCM/HFIP). The flask was closed and the mixture was cooled to 0 °C using an ice/water bath. Once cooled, the flask was briefly opened and trifluoromethanesulfonic acid (0.2 equiv.) was added dropwise. The flask was closed and the mixture was left to stir in a slowly melting ice/water bath for ~ 16 h (product Rf ~ 0.1-0.3 in 50% ethyl acetate/hexanes). *Quench:* The reaction mixture was quenched with the addition of excess aqueous sodium bicarbonate (at room temperature) and was left to stir vigorously for 10 min (during which the typical dark red color of the mixture dissipated to colorless or pale yellow). The mixture was transferred to a separatory funnel using excess dichloromethane. The organic layer was washed with saturated aqueous sodium bicarbonate once and the layers were separated. Aqueous layer was washed once with dichloromethane and the combined organic layers were washed once with brine. Organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography.

Scope (Ketones)

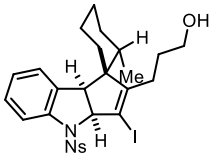
Compound 6a



6a

Compound **6a** was isolated as an off-white foam in 81% yield (96 mg) after flash column chromatography (45% ethyl acetate/hexanes).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, J = 7.9 Hz, 1H), 7.62 (t, J = 7.7 Hz, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.54 (d, J = 7.8 Hz, 1H), 7.48 (t, J = 7.7 Hz, 1H), 7.22 (t, J = 7.8 Hz, 1H), 7.18 (d, J = 7.7 Hz, 1H), 7.04 (t, J = 7.5 Hz, 1H), 5.51 (d, J = 6.2 Hz, 1H), 3.99 (d, J = 6.2 Hz, 1H), 3.59 – 3.47 (m, 2H), 2.30 – 2.19 (m, 1H), 2.15 – 2.06 (m, 1H), 2.00 – 1.93 (m, 1H), 1.87 – 1.80 (m, 1H), 1.80 – 1.72 (m, 2H), 1.64 – 1.23 (m, 8H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 157.8, 148.2, 139.6, 134.0, 133.6, 132.1, 131.1, 131.0, 128.1, 127.1, 125.2, 124.0, 117.4, 96.3, 75.8, 62.4, 53.8, 50.9, 36.8, 31.3, 30.8, 26.8, 25.6, 23.9, 23.8.
HRMS (ESI) *m/z* calc'd for $C_{25}H_{27}IN_2O_5S$ $[M+H]^+$: 595.0758, found: 595.0750.

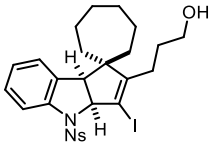
Compound 6b



6b

Compound **6b** was isolated as an off-white foam in 77% yield (94 mg) after flash column chromatography (45% ethyl acetate/hexanes). The diastereomeric ratio was estimated from the ^{1}H NMR to be 6.5:2.8:1.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 – 7.43 (m, 6H), 7.25 – 6.99 (m, 3H), 5.59 – 5.42 (m, 1H), 3.93 (dd, *J* = 108.0, 6.8 Hz, 1H), 3.66 – 3.40 (m, 2H), 2.43 – 1.93 (m, 4H), 1.93 – 1.28 (m, 9H), 1.00 – 0.81 (m, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 157.5, 154.5, 148.2, 140.0, 139.4, 134.0, 133.9, 133.4, 132.2, 132.1, 132.0, 131.1, 131.0, 128.0, 127.4, 127.4, 127.1, 125.1, 125.0, 124.9, 124.0, 117.3, 117.1, 99.2, 97.3, 62.7, 62.6, 62.4, 58.5, 56.6, 56.4, 54.3, 48.5, 39.5, 35.3, 32.5, 32.4, 32.2, 32.2, 31.3, 30.9, 29.1, 26.6, 26.5, 25.1, 23.0, 21.0, 17.0, 16.7.
HRMS (ESI) *m/z* calc'd for $C_{25}H_{27}IN_2O_5S$ $[M+H]^+$: 609.0915, found: 609.0901.

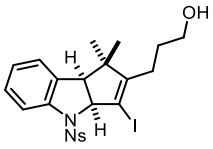
Compound 6c



6c

Compound **6c** was isolated as an off-white foam in 64% yield (78 mg) after flash column chromatography (42% ethyl acetate/hexanes).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.0 Hz, 1H), 7.61 (t, *J* = 7.7 Hz, 1H), 7.57 (d, *J* = 8.3 Hz, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 1H), 7.24 – 7.19 (m, 2H), 7.02 (t, *J* = 7.5 Hz, 1H), 5.51 (d, *J* = 6.2 Hz, 1H), 3.77 (d, *J* = 6.2 Hz, 1H), 3.57 (t, *J* = 6.3 Hz, 2H), 2.32 – 2.23 (m, 1H), 2.22 – 2.12 (m, 1H), 2.04 – 1.95 (m, 1H), 1.82 – 1.45 (m, 14H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 158.1, 148.2, 139.7, 134.0, 133.6, 132.0, 131.0, 131.0, 128.0, 127.5, 125.0, 124.0, 117.4, 96.8, 75.5, 62.6, 56.4, 55.2, 41.6, 34.0, 31.4, 30.1, 29.7, 27.3, 24.0, 23.5.
HRMS (ESI) *m/z* calc'd for $C_{26}H_{29}IN_2O_5S$ $[M+H]^+$: 609.0915, found: 609.0906.

Compound 6d



6d

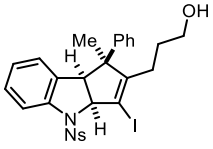
Compound **6d** was isolated as an off-white foam in 36% yield (40 mg) after flash column chromatography (40% ethyl acetate/hexanes).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 – 7.74 (m, 1H), 7.64 – 7.58 (m, 1H), 7.56 – 7.52 (m, 2H), 7.50 – 7.44 (m, 1H), 7.23 – 7.15 (m, 2H), 7.03 (t, *J* = 7.5 Hz, 1H), 5.63 (d, *J* = 6.9 Hz, 1H), 3.64 (d, *J* = 6.9 Hz, 1H), 3.60 (t, *J* = 6.3 Hz, 2H), 2.27 – 2.18 (m, 1H), 2.16 – 2.08 (m, 1H), 1.59 (m, 3H), 1.46 (s, 1H), 1.30 (s, 3H), 1.27 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 156.9, 148.3, 139.5, 134.0, 133.7, 132.1, 131.0, 131.0, 128.0, 127.6, 124.8, 124.1, 117.3, 96.0, 76.0, 62.6, 56.3, 49.6, 31.3, 30.7, 26.5, 24.2.

HRMS (ESI) *m/z* calc'd for $C_{22}H_{23}IN_2O_5S$ $[M+H]^+$: 555.0445, found: 555.0437.

Compound 6e



6e

Compound **6e** was isolated as an off-white foam in 46% yield (57 mg) after flash column chromatography (42% ethyl acetate/hexanes). The diastereomeric ratio was estimated from the ^{1}H NMR to be 3.9:1.

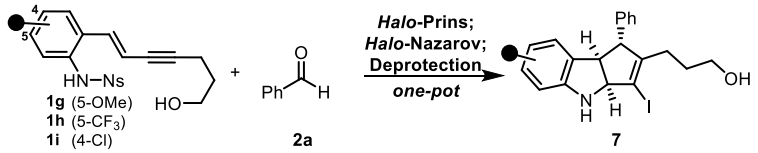
Crystals suitable for X-Ray diffraction analysis were obtained by mixing a small amount of material with heptane, heating the heterogeneous mixture to boiling, followed by the drop-by-drop addition of DCM until the hot mixture became homogeneous. The solution was left at room temperature to slowly cool down and evaporate (with the cap placed loosely on top), leading to a few crystals suitable for X-Ray analysis.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 – 7.28 (m, 8H), 7.24 – 6.90 (m, 3H), 6.54 – 5.26 (m, 3H), 3.91 (dd, *J* = 59.4, 7.5 Hz, 1H), 3.60 – 3.43 (m, 2H), 2.26 – 1.63 (m, 6H), 1.46 – 1.28 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 156.1, 155.5, 148.3, 146.3, 141.7, 139.1, 134.0, 133.2, 132.4, 131.9, 131.3, 131.0, 130.9, 128.9, 128.1, 128.0, 128.0, 127.6, 127.2, 127.0, 126.2, 125.5, 124.8, 124.1, 124.0, 117.4, 116.4, 98.1, 97.9, 76.6, 62.9, 62.6, 58.7, 58.4, 57.9, 57.0, 31.5, 30.9, 27.8, 27.6, 27.0, 22.7.

HRMS (ESI) *m/z* calc'd for $C_{27}H_{25}IN_2O_5S$ $[M+H]^+$: 617.0602, found: 617.0593.

General Procedure for the (One-Pot) *Halo*-Prins/*Halo*-Nazarov/Deprotection Sequence: Aniline Substitution

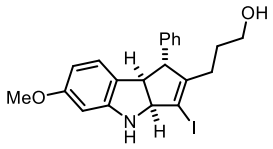


Halo-Prins: To a flask, equipped with a stir bar, 5 Å molecular sieves (36 mg, 300 mg/mmol benzaldehyde **2a**) were added. The flask was closed with a septum and flame-dried under vacuum (~ 10 Torr). The flask was let to cool to room temperature and then carefully refilled with argon (*note:* sieves are easily blown and readily end up in the Schlenk line – to protect the Schlenk line from sieves, the authors have used a large piece of cotton in between the line and the tubing (inside 24/40 glass adapter) and then a small piece of cotton in between the needle and the piece of a 1 mL syringe attached to the tubing). The septum was briefly removed (while keeping the needle connected to the argon line, with the flow of argon reduced to prevent the blowing of the sieves, above the ground glass joint of the flask to maintain inert atmosphere) and enyne **1g-1i** (0.1 mmol, 1.0 equiv.) and tetrabutylammonium iodide (44 mg, 1.2 equiv.) were added. The flask was closed again and benzaldehyde **2a** (12.5 μL, 1.2 equiv.) and anhydrous dichloromethane (1 mL, to obtain 0.1 mol/L solution with respect to the enyne **1**) were added. The mixture was cooled to ~ -40 °C using the dry ice/acetonitrile bath (*note*: dry ice pieces should be added one by one until the bath has a temperature of -40 °C; no excess of dry ice should be used). Using a glass microsyringe, trifluoromethanesulfonic acid (11 μL, 1.25 equiv) was slowly added dropwise to the reaction mixture (*note: trifluoromethanesulfonic acid fumes when exposed to air and this exposure should be minimized due to its hygroscopic nature; see general remarks of the SI for further remarks about the trifluoromethanesulfonic acid*). The reaction mixture was stirred in the acetonitrile bath (which was let to warm up) and the reaction progress was monitored using TLC (50% ethyl acetate/hexanes, consumption of the enyne **1** was monitored, Rf ~ 0.15). Typical reaction time was ~ 1 h, after which the consumption of the enyne **1** was deemed to be full.

Halo-Nazarov: The *halo*-Prins reaction mixture flask was removed from the dry ice/acetonitrile bath and placed in an ice/water bath. To the flask, 1,1,1,3,3,3-hexafluoropropan-2-ol (0.1 mL HFIP, volume added to reach the volume ratio of 10:1 DCM/HFIP) was added dropwise. The reaction mixture was left to stir in a slowly melting ice/water bath and the consumption of the *halo*-Prins product was followed by TLC (50% ethyl acetate/hexanes). The *N*-protected *halo*-Nazarov products were significantly more polar than *halo*-Prins products on the TLC. The reaction typically took 1-2 h to reach completion (judged by the consumption of the *halo*-Prins intermediate on the TLC plate).

Deprotection: To the *halo*-Nazarov reaction mixture, anhydrous potassium carbonate (138 mg, 10 equiv.) was added, and then the solvents were removed by vacuum distillation using a rotary evaporator. To the mixture, anhydrous methanol (2 mL, to obtain 0.05 mol/L solution with respect to the amount of enyne **1** used in the *halo*-Prins reaction) was added. The flask was closed and the mixture was cooled to 0 °C using an ice/water bath. Once cooled, the flask was opened and thioglycolic acid (35 μL, 5 equiv.) was added dropwise. The flask was closed and the mixture was stirred in a slowly melting ice/water bath (left to reach room temperature) overnight. *Quench*: When the TLC showed full consumption of the *N*-protected *halo*-Nazarov intermediate (50% ethyl acetate/hexanes, deprotected products **7** are less polar than the *N*-protected products), the mixture was vacuum-filtered through celite into a separatory funnel, using copious amounts of ethyl acetate. The organic layer was washed three times using sat. aq. sodium bicarbonate (to remove the yellow thioglycolic acid side products), then with brine. The organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography.

Compound 7a



7a

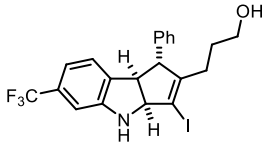
Compound **7a** was isolated as a pale yellow oil in 40% yield (18 mg) after flash column chromatography (DCM, then 25% ethyl acetate/hexanes).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (t, *J* = 7.6 Hz, 2H), 7.33 – 7.25 (m, 1H), 7.21 – 7.15 (m, 2H), 7.04 (dd, *J* = 8.1, 1.2 Hz, 1H), 6.32 (dd, *J* = 8.1, 2.3 Hz, 1H), 6.28 (d, *J* = 2.3 Hz, 1H), 4.98 (dt, *J* = 7.9, 2.0 Hz, 1H), 4.34 (s, 1H), 3.93 – 3.89 (m, 1H), 3.82 – 3.77 (m, 1H), 3.76 (s, 3H), 3.45 – 3.32 (m, 2H), 2.30 – 2.21 (m, 1H), 2.00 – 1.90 (m, 1H), 1.59 – 1.47 (m, 1H), 1.45 – 1.32 (m, 1H), 1.14 (s, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 160.6, 151.1, 149.8, 142.8, 129.0, 127.3, 127.1, 124.6, 124.1, 104.5, 101.1, 96.8, 74.6, 62.0, 60.7, 55.3, 53.7, 29.6, 28.0.

HRMS (ESI) *m/z* calc'd for $C_{21}H_{22}INO_2$ $[M+H]^+$: 448.0768, found: 448.0772.

Compound 7b



7b

Compound **7b** was isolated as a pale yellow foam in 82% yield (40 mg) after preparatory TLC (DCM, first large band above the baseline).

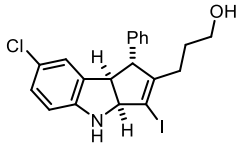
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.35 (m, 2H), 7.33 – 7.26 (m, 1H), 7.25 – 7.17 (m, 3H), 7.04 – 6.98 (m, 1H), 6.90 – 6.86 (m, 1H), 5.04 (dt, *J* = 8.1, 2.0 Hz, 1H), 4.52 (s, 1H), 3.98 – 3.93 (m, 1H), 3.91 – 3.85 (m, 1H), 3.44 – 3.35 (m, 2H), 2.31 – 2.21 (m, 1H), 2.01 – 1.91 (m, 1H), 1.59 – 1.47 (m, 1H), 1.43 – 1.31 (m, 1H), 1.20 (s, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 152.24, 149.55, 143.06, 136.22 (q, $^4J_{CF}$ = 1.2 Hz), 131.57 (q, $^2J_{CF}$ = 31.7 Hz), 129.88, 128.09, 127.98, 125.23, 125.08 (q, $^1J_{CF}$ = 272.2 Hz), 116.86 (q, $^3J_{CF}$ = 4.1 Hz), 107.40 (q, $^3J_{CF}$ = 3.8 Hz), 100.97, 74.95, 62.73, 61.37, 54.74, 30.37, 28.73.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.46 (s, 3F).

HRMS (ESI) *m/z* calc'd for $C_{21}H_{19}F_3INO$ $[M+H]^+$: 486.0536, found: 486.0541.

Compound 7c



7c

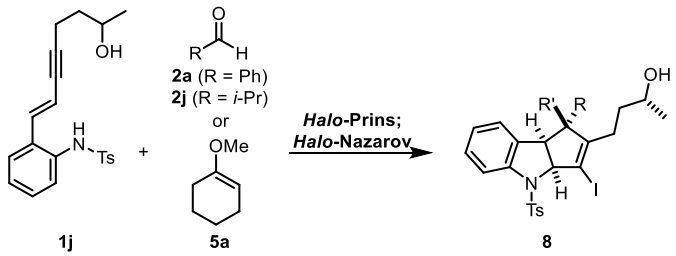
Compound **7c** was isolated as a pale yellow foam in 82% yield (37 mg) after preparatory TLC (DCM, first large band above the baseline).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.34 (m, 2H), 7.32 – 7.25 (m, 1H), 7.21 – 7.15 (m, 2H), 7.13 – 7.09 (m, 1H), 7.05 – 7.00 (m, 1H), 6.60 (d, *J* = 8.3 Hz, 1H), 4.99 (dt, *J* = 8.0, 2.0 Hz, 1H), 4.33 (s, 1H), 3.94 – 3.90 (m, 1H), 3.83 (d, *J* = 7.9 Hz, 1H), 3.46 – 3.34 (m, 2H), 2.31 – 2.21 (m, 1H), 2.00 – 1.90 (m, 1H), 1.59 – 1.47 (m, 1H), 1.46 – 1.32 (m, 1H), 1.19 (s, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.3, 147.1, 142.3, 133.6, 129.1, 128.2, 127.3, 127.2, 124.5, 123.7, 111.2, 100.6, 74.3, 62.0, 60.6, 54.2, 29.6, 28.0.

HRMS (ESI) *m/z* calc'd for $C_{20}H_{19}{}^{35}ClINO$ $[M+H]^+$: 452.0273, found: 452.0282.

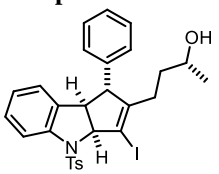
Secondary Alcohols: Chirality Transfer



Halo-Prins: To a flask, equipped with a stir bar, 5 Å molecular sieves (300 mg/mmol **2** or 400 mg/mmol **5**) were added. The flask was closed with a septum and flame-dried under vacuum (~ 10 Torr). The flask was let to cool to room temperature and then carefully refilled with argon (*note:* sieves are easily blown and readily end up in the Schlenk line – to protect the Schlenk line from sieves, the authors have used a large piece of cotton in between the line and the tubing (inside 24/40 glass adapter) and then a small piece of cotton in between the needle and the piece of a 1 mL syringe attached to the tubing). The septum was briefly removed (while keeping the needle connected to the argon line, with the flow of argon reduced to prevent the blowing of the sieves, above the ground glass joint of the flask to maintain inert atmosphere) and enyne **1j** (0.2 mmol, 1.0 equiv.), and tetrabutylammonium iodide (2.0 equiv.) were added. The flask was closed again and aldehyde **2** (1.2 equiv) or methyl enol ether **5** (2.0 equiv) and anhydrous dichloromethane (to obtain 0.2 mol/L solution with respect to the enyne **1g**) were added. The mixture was cooled to ~ -40 °C using the dry ice/acetonitrile bath (*note*: dry ice pieces should be added one by one until the bath has a temperature of -40 °C; no excess of dry ice should be used). Using a glass (micro)syringe, trifluoromethanesulfonic acid (2.0 equiv) was slowly added dropwise to the reaction mixture (*note: trifluoromethanesulfonic acid fumes when exposed to air and this exposure should be minimized due to its hygroscopic nature; see general remarks of the SI for further remarks about the trifluoromethanesulfonic acid*). The reaction mixture was stirred in the acetonitrile bath (which was let to warm up) and the reaction progress was monitored using TLC (50% ethyl acetate/hexanes, consumption of the enyne **1j** was monitored, Rf ~ 0.15). Typical reaction time was 30 min, after which the consumption of the enyne **1j** was deemed to be full (or the reaction had stalled, as no change in the consumption of the enyne **1j** could be observed on consecutive TLCs). *Quench:* The reaction was quenched by the addition of excess solid sodium bicarbonate. The mixture was stirred for 5 min and then vacuum-filtered over a short silica plug, using diethyl ether to elute the crude product (TLC, 20% ethyl acetate/hexanes, typical Rf ~ 0.3). The solvents were removed by vacuum distillation using a rotary evaporator (the flask was protected from light using a piece of aluminum foil; the *halo*-Prins products were light-sensitive), and the product was used without further purification.

Halo-Nazarov: To a flask, equipped with a stir bar, *halo*-Prins adduct (1.0 equiv., calculated based on the crude mass of the *halo*-Prins product, assuming that the product was pure for stoichiometric calculations) was added, followed by anhydrous dichloromethane (DCM, to obtain 0.1 mol/L solution with respect to enyne **1j**) and 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP, volume added to reach the volume ratio of 10:1 DCM/HFIP). The flask was closed and the mixture was cooled to 0 °C (stir plate was positioned in a small fridge). Once cooled, the flask was briefly opened and trifluoromethanesulfonic acid (0.2 equiv.) was added dropwise. The flask was closed and the mixture was left to stir for 30 min (product Rf ~ 0.3 in 40% ethyl acetate/hexanes). *Quench:* The reaction mixture was quenched with the addition of excess aqueous sodium bicarbonate (at room temperature) and was left to stir vigorously for 10 min (during which the typical dark red color of the mixture dissipated to colorless or pale yellow). The mixture was transferred to a separatory funnel using excess dichloromethane. The organic layer was washed with saturated aqueous sodium bicarbonate once and the layers were separated. Aqueous layer was washed once with dichloromethane and the combined organic layers were washed once with brine. Organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography to obtain pure *halo*-Nazarov product **8.**

Compound 8a



8a

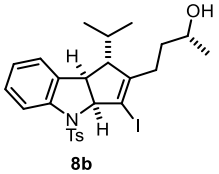
Compound **8a** was isolated as an off-white foam in 81% yield (95 mg) after flash column chromatography (40% ethyl acetate/hexanes). Diastereomeric ratio was determined to be 4.0:1 using normal phase HPLC (unbound silica, 1 mL/min, 1.5% 2-propanol/hexanes).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 7.9 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.30 – 7.27 (m, 2H), 7.17 – 7.08 (m, 4H), 7.06 (d, *J* = 8.0 Hz, 2H), 5.52 (d, *J* = 7.1 Hz, 1H), 3.92 – 3.81 (m, 1H), 3.51 – 3.36 (m, 1H), 3.27 (d, *J* = 7.2 Hz, 1H), 2.34 – 2.23 (m, 4H), 1.96 – 1.83 (m, 1H), 1.64 (s, 1H), 1.36 – 1.27 (m, 1H), 1.22 – 1.12 (m, 1H), 0.98 (d, *J* = 6.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 152.5, 143.9, 141.8, 141.6, 140.0, 137.0, 134.7, 129.5, 129.1, 128.6, 127.3, 127.1, 127.1, 126.0, 124.3, 124.2, 119.6, 119.5, 97.3, 97.2, 77.8, 77.7, 67.3, 67.1, 59.9, 59.4, 52.5, 52.4, 35.6, 35.5, 28.2, 28.1, 23.1, 21.4.

HRMS (ESI) *m/z* calc'd for $C_{28}H_{28}INO_3S$ $[M+H]^+$: 586.0913, found: 586.0906.

Compound 8b



8b

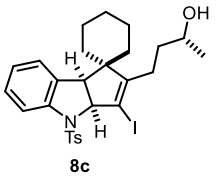
Compound **8b** was isolated as an off-white foam in 53% yield (58 mg) after flash column chromatography (40% ethyl acetate/hexanes). Diastereomeric ratio was determined to be 4.1:1 using normal phase HPLC (unbound silica, 1 mL/min, 1% 2-propanol/hexanes).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.1 Hz, 1H), 7.45 (d, *J* = 7.9 Hz, 2H), 7.22 (t, *J* = 7.8 Hz, 1H), 7.13 (d, *J* = 7.9 Hz, 2H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.96 – 6.89 (m, 1H), 5.21 – 5.16 (m, 1H), 3.62 – 3.43 (m, 1H), 2.95 (d, *J* = 7.2 Hz, 1H), 2.73 – 2.62 (m, 1H), 2.40 – 2.29 (m, 4H), 2.04 – 1.95 (m, 2H), 1.52 – 1.41 (m, 1H), 1.36 – 1.28 (m, 1H), 1.10 (d, *J* = 6.2 Hz, 3H), 1.06 – 0.98 (m, 4H), 0.65 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 152.1, 143.8, 140.3, 138.0, 134.9, 129.4, 128.2, 127.2, 125.8, 124.0, 124.0, 119.4, 96.0, 78.0, 67.6, 67.2, 60.0, 59.4, 43.9, 35.7, 35.5, 28.8, 28.7, 27.9, 27.8, 23.3, 23.2, 21.5, 21.5, 16.4.

HRMS (ESI) *m/z* calc'd for $C_{25}H_{30}INO_3S$ $[M+H]^+$: 552.1069, found: 552.1062.

Compound 8c



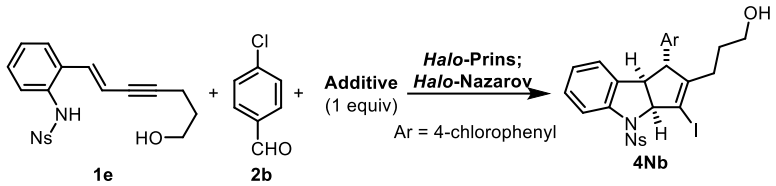
8c

Compound **8c** was isolated as an off-white foam in 64% yield (74 mg) after flash column chromatography (40% ethyl acetate/hexanes). Diastereomeric ratio was determined to be 2.7:1 using normal phase HPLC (unbound silica, 1 mL/min, 1% 2-propanol/hexanes). Crystals suitable for X-Ray diffraction analysis were obtained by mixing a small amount of material with heptane, heating the heterogeneous mixture to boiling, followed by the drop-by-drop addition of DCM until the hot mixture became homogeneous. The solution was left at room temperature to slowly cool down and evaporate (with the cap placed loosely on top), leading to a few crystals suitable for X-Ray analysis.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 – 7.66 (m, 1H), 7.44 – 7.40 (m, 2H), 7.25 – 7.21 (m, 1H), 7.12 (d, *J* = 8.1 Hz, 2H), 7.08 (d, *J* = 7.7 Hz, 1H), 7.06 – 7.00 (m, 1H), 5.22 – 5.17 (m, 1H), 3.79 – 3.66 (m, 1H), 3.39 – 3.28 (m, 1H), 2.41 – 2.25 (m, 4H), 2.22 – 1.92 (m, 2H), 1.91 – 1.83 (m, 1H), 1.82 – 1.74 (m, 1H), 1.73 – 1.64 (m, 2H), 1.56 – 1.40 (m, 4H), 1.40 – 1.17 (m, 4H), 1.17 – 1.08 (m, 3H).

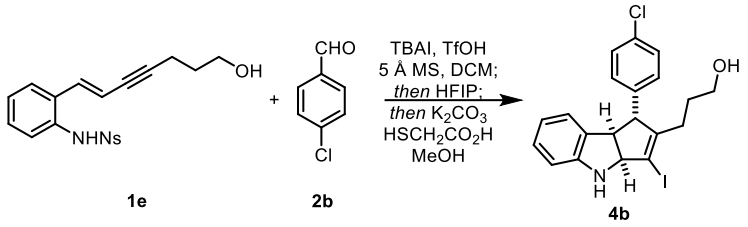
^{13}C NMR (126 MHz, $CDCl_3$) δ 157.4, 143.8, 141.3, 135.1, 133.9, 133.8, 129.4, 128.1, 128.0, 127.2, 126.5, 125.2, 125.2, 119.3, 96.4, 96.3, 74.8, 74.7, 68.0, 67.9, 53.9, 53.8, 50.5, 50.4, 37.4, 36.8, 36.7, 30.7, 29.6, 26.8, 26.5, 25.5, 25.5, 23.9, 23.9, 23.8, 23.4, 23.1, 21.5.
HRMS (ESI) *m/z* calc'd for $C_{27}H_{32}INO_3S$ $[M+H]^+$: 578.1220, found: 578.1224.

Functional Group Compatibility Tests

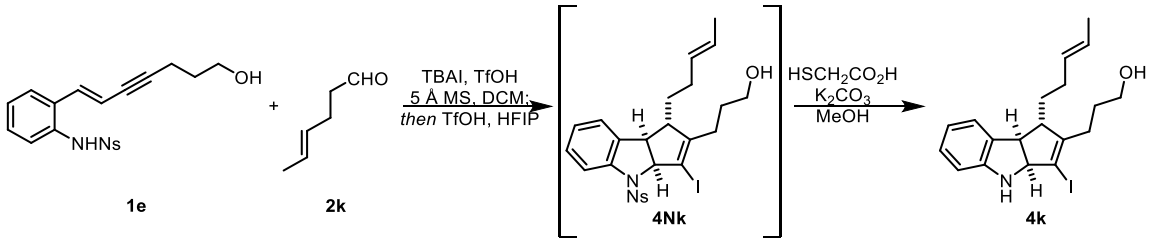


To a 2 dram vial, equipped with a stir bar, powdered 5 Å molecular sieves (36 mg) were added. The vial was closed with a septum and flame-dried under vacuum (~ 10 Torr). The flask was let to cool to room temperature and then carefully refilled with argon (*note:* sieves are easily blown and readily end up in the Schlenk line – to protect the Schlenk line from sieves, the authors have used a large piece of cotton in between the line and the tubing (inside 24/40 glass adapter) and then a small piece of cotton in between the needle and the piece of a 1 mL syringe attached to the tubing). The septum was briefly removed (while keeping the needle connected to the argon line, with the flow of argon reduced to prevent the blowing of the sieves, above the ground glass joint of the flask to maintain inert atmosphere) and enyne **1e** (39 mg, 0.1 mmol, 1.0 equiv.), tetrabutylammonium iodide (44 mg, 1.2 equiv.) and *p*-chlorobenzaldehyde **2b** (17 mg, 1.2 equiv.) were added. The flask was closed again and anhydrous dichloromethane (DCM, 1 mL) was added. To this mixture, **additive** was added (0.1 mmol, 1 equiv). The mixture was cooled to ~ -40 °C using the dry ice/acetonitrile bath (*note*: dry ice pieces should be added one by one until the bath has a temperature of -40 °C; no excess of dry ice should be used). Using a glass microsyringe, trifluoromethanesulfonic acid (11 μL, 1.25 equiv.) was slowly added dropwise to the reaction mixture (*note: trifluoromethanesulfonic acid fumes when exposed to air and this exposure should be minimized due to its hygroscopic nature; see general remarks of the SI for further remarks about the trifluoromethanesulfonic acid*). The reaction mixture was stirred in the acetonitrile bath (which was let to warm up) and the reaction progress was monitored using TLC (50% ethyl acetate/hexanes, consumption of the enyne **1e** was monitored, Rf ~ 0.15). After 1 h, the flask was removed from the dry ice/acetonitrile bath and placed in an ice/water bath. To the flask, 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP, 1.8 mL) was added dropwise. The reaction mixture was left to stir in a slowly melting ice/water bath and the consumption of the *halo*-Prins product was followed by TLC (50% ethyl acetate/hexanes, Rf ~ 0.5). After 3 h, the reaction was quenched by the addition of excess sodium bicarbonate. The mixture was stirred for 5 min and then vacuum-filtered through celite into a separatory funnel, using copious amounts of ethyl acetate. The organic layer was washed using sat. aq. sodium bicarbonate and the layers were separated. The aqueous layer was washed two times with ethyl acetate and the organic layers were combined and washed with brine. The organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude material was transferred to a 20 mL scintillation vial, and the solvent was thoroughly removed (after rotary evaporation) by keeping the vial attached to a high vacuum line (~50 mTorr). This step resulted in a partial or total removal of the volatile additives, and their amounts were not quantified. To this vial, placed on a balance, trichloroethylene (about 0.1 mmol, 9 μL, ~13 mg) was added dropwise and the accurate mass of the added standard was recorded. This sample was immediately dissolved using 0.7-0.75 mL of $CDCl_3$ and transferred to an NMR tube. Quantitative ^{1}H NMR was recorded using a standard proton pulse sequence (90° pulse width, acquisition time aq = 7 s, relaxation delay d1 = 63 s, number of scans ns = 4; exponential multiplication line broadening lb = 0.2 Hz). Trichloroethylene peak is at 6.45 ppm; peak of the product **4Nb** used for integration is at 3.94-3.95 ppm.
Isolated yields were obtained by purification using preparatory TLC (50% ethyl acetate/hexanes).

Large Scale Experiments



To a 100 mL round-bottom flask, equipped with a stir bar, powdered 5 Å molecular sieves (720 mg) were added. The flask was closed with a septum and flame-dried under vacuum (~ 10 Torr). The flask was let to cool to room temperature and then carefully refilled with argon (*note:* sieves are easily blown and readily end up in the Schlenk line – to protect the Schlenk line from sieves, the authors have used a large piece of cotton in between the line and the tubing (inside 24/40 glass adapter) and then a small piece of cotton in between the needle and the piece of a 1 mL syringe attached to the tubing). The septum was briefly removed (while keeping the needle connected to the argon line, with the flow of argon reduced to prevent the blowing of the sieves, above the ground glass joint of the flask to maintain inert atmosphere) and enyne **1e** (773 mg, 2.0 mmol, 1.0 equiv.), tetrabutylammonium iodide (886 mg, 2.4 mmol, 1.2 equiv.) and *p*-chlorobenzaldehyde **2b** (337 mg, 2.4 mmol, 1.2 equiv.) were added. The flask was closed again and anhydrous dichloromethane (DCM, 20 mL) was added. The mixture was cooled to ~ -40 °C using the dry ice/acetonitrile bath (*note*: dry ice pieces should be added one by one until the bath has a temperature of -40 °C; no excess of dry ice should be used). Using a glass syringe (Hamilton 1 mL Gastight Syringe Model 1001 TLL, PTFE Luer Lock), trifluoromethanesulfonic acid (0.22 mL, 2.5 mmol, 1.25 equiv.) was slowly added dropwise to the reaction mixture (*note: trifluoromethanesulfonic acid fumes when exposed to air and this exposure should be minimized due to its hygroscopic nature; see general remarks of the SI for further remarks about the trifluoromethanesulfonic acid*). The reaction mixture was stirred in the acetonitrile bath (which was let to warm up) and the reaction progress was monitored using TLC (50% ethyl acetate/hexanes, consumption of the enyne **1e** was monitored, Rf ~ 0.15). After 1.5 h, the flask was removed from the dry ice/acetonitrile bath and placed in an ice/water bath. To the flask, 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP, 2 mL) was added dropwise. The reaction mixture was left to stir in a slowly melting ice/water bath and the consumption of the *halo*-Prins product was followed by TLC (50% ethyl acetate/hexanes, Rf ~ 0.5). After 3 h, anhydrous potassium carbonate (2.76 g, 20 mmol, 10 equiv.) was added to the flask, and then the solvents were removed by vacuum distillation using a rotary evaporator. To the mixture, anhydrous methanol (40 mL) was added. The flask was closed and the mixture was cooled to 0 °C using an ice/water bath. Once cooled, the flask was opened and thioglycolic acid (0.69 mL, 10 mmol, 5 equiv.) was added dropwise using a plastic syringe. The flask was closed and the mixture was stirred in a slowly melting ice/water bath (left to reach room temperature) overnight. After 16 h, the mixture was vacuum-filtered through celite into a separatory funnel, using copious amounts of ethyl acetate. The organic layer was washed three times using sat. aq. sodium bicarbonate (to remove the yellow thioglycolic acid side products), then with brine. The organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography (DCM, then 30% ethyl acetate/hexanes) to obtain 635 mg (70% over three steps) of **4b**, as a yellow foam.
Spectral data matched the data previously obtained for the compound **4b.**



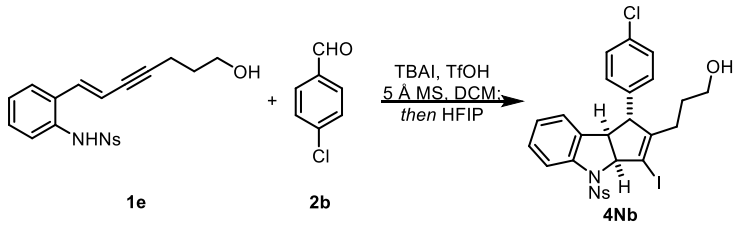
To a 100 mL round-bottom flask, equipped with a stir bar, powdered 5 Å molecular sieves (1.44 g) were added. The flask was closed with a septum and flame-dried under vacuum (~ 10 Torr). The flask was let to cool to room temperature and then carefully refilled with argon (*note:* sieves are easily blown and readily end up in the Schlenk line – to protect the Schlenk line from sieves, the authors have used a large piece of cotton in between the line and the tubing (inside 24/40 glass adapter) and then a small piece of cotton in between the needle and the piece of a 1 mL

syringe attached to the tubing). The septum was briefly removed (while keeping the needle connected to the argon line, with the flow of argon reduced to prevent the blowing of the sieves, above the ground glass joint of the flask to maintain inert atmosphere) and enyne **1e** (1.546 g, 4.0 mmol, 1.0 equiv.) and tetrabutylammonium iodide (1.772 g, 4.8 mmol, 1.2 equiv.) were added. The flask was closed again and (*E*)-4-hexenal **2k** (0.53 mL, 4.8 mmol, 1.2 equiv.) and anhydrous dichloromethane (DCM, 40 mL) was added. The mixture was cooled to ~ -40 °C using the dry ice/acetonitrile bath (*note*: dry ice pieces should be added one by one until the bath has a temperature of -40 °C; no excess of dry ice should be used). Using a glass syringe (Hamilton 1 mL Gastight Syringe Model 1001 TLL, PTFE Luer Lock), trifluoromethanesulfonic acid (0.45 mL, 5.0 mmol, 1.25 equiv.) was slowly added dropwise to the reaction mixture (*note: trifluoromethanesulfonic acid fumes when exposed to air and this exposure should be minimized due to its hygroscopic nature; see general remarks of the SI for further remarks about the trifluoromethanesulfonic acid*). The reaction mixture was stirred in the acetonitrile bath (which was let to warm up) and the reaction progress was monitored using TLC (50% ethyl acetate/hexanes, consumption of the enyne **1e** was monitored, Rf ~ 0.15). After 3.5 h, the flask was removed from the dry ice/acetonitrile bath and placed in an ice/water bath. To the flask, 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP, 4 mL) was added dropwise. The reaction mixture was left to stir in a slowly melting ice/water bath and the consumption of the *halo*-Prins product was followed by TLC (50% ethyl acetate/hexanes, Rf ~ 0.5). After 15 h, additional (second portion) trifluoromethanesulfonic acid (71 μL, 0.8 mmol, 0.2 equiv.) was added. After 6 h, additional (third portion) trifluoromethanesulfonic acid (71 μL, 0.8 mmol, 0.2 equiv.) was added. After 17 h, the reaction was quenched by the addition of excess sodium bicarbonate. The mixture was stirred for 5 min and then vacuum-filtered through celite into a separatory funnel, using copious amounts of ethyl acetate. The organic layer was washed using sat. aq. sodium bicarbonate and the layers were separated. The aqueous layer was washed two times with ethyl acetate and the organic layers were combined and washed with brine. The organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography (50% ethyl acetate/hexanes), to obtain 1.604 g (67% over two steps) of **4Nk**, as a pale-yellow foam. The product was used in the deprotection step without characterization.

To a flask, equipped with a stir bar, protected *halo*-Nazarov product **4Nk** (1.604 g, 2.7 mmol, 1.0 equiv.) was added, followed by anhydrous potassium carbonate (3.731g, 27 mmol, 10 equiv.) and anhydrous methanol (50 mL). The flask was closed and the mixture was cooled to 0 °C using an ice/water bath. Once cooled, the flask was opened and thioglycolic acid (0.94 mL, 13.5 mmol, 5 equiv.) was added dropwise using a syringe. The flask was closed and the mixture was stirred in a slowly melting ice/water bath (left to reach room temperature) overnight. After 17 h, the mixture was vacuum-filtered through celite into a separatory funnel, using copious amounts of ethyl acetate. The organic layer was washed three times using sat. aq. sodium bicarbonate (to remove the yellow thioglycolic acid side products), then with brine. The organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography (DCM, then 30% ethyl acetate/hexanes) to obtain 803 mg (49% over three steps, 73% for the deprotection step) of **4k**, as a yellow oil.

Note: The synthesis of **4k** on a larger scale was not done in one-pot over three steps (unlike the synthesis of **4k** on a smaller scale, described previously). This resulted in easier purification of the final product **4k** on this scale.

Spectral data matched the data previously obtained for the compound **4k.**



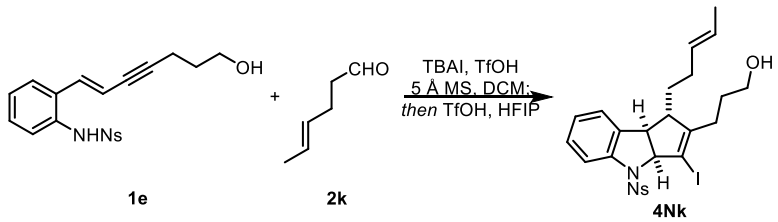
To a 100 mL round-bottom flask, equipped with a stir bar, powdered 5 Å molecular sieves (650 mg) were added. The flask was closed with a septum and flame-dried under vacuum (~ 10 Torr). The flask was let to cool to room temperature and then carefully refilled with argon (*note:* sieves are easily blown and readily end up in the Schlenk line – to protect the Schlenk line from sieves, the authors have used a large piece of cotton in between the line and the tubing (inside 24/40 glass adapter) and then a small piece of cotton in between the needle and the piece of a 1 mL syringe attached to the tubing). The septum was briefly removed (while keeping the needle connected to the argon line, with the flow of argon reduced to prevent the blowing of the sieves, above the ground glass joint of the flask to maintain inert atmosphere) and enyne **1e** (700 mg, 1.81 mmol, 1.0 equiv.), tetrabutylammonium iodide (802 mg, 2.17

mmol, 1.2 equiv.) and *p*-chlorobenzaldehyde **2b** (305 mg, 2.17 mmol, 1.2 equiv.) were added. The flask was closed again and anhydrous dichloromethane (DCM, 18 mL) was added. The mixture was cooled to ~ -40 °C using the dry ice/acetonitrile bath (*note*: dry ice pieces should be added one by one until the bath has a temperature of -40 °C; no excess of dry ice should be used). Using a glass syringe (Hamilton 1 mL Gastight Syringe Model 1001 TLL, PTFE Luer Lock), trifluoromethanesulfonic acid (0.20 mL, 2.26 mmol, 1.25 equiv.) was slowly added dropwise to the reaction mixture (*note: trifluoromethanesulfonic acid fumes when exposed to air and this exposure should be minimized due to its hygroscopic nature; see general remarks of the SI for further remarks about the trifluoromethanesulfonic acid*). The reaction mixture was stirred in the acetonitrile bath (which was let to warm up) and the reaction progress was monitored using TLC (50% ethyl acetate/hexanes, consumption of the enyne **1e** was monitored, Rf ~ 0.15). After 30 min, the flask was removed from the dry ice/acetonitrile bath and placed in an ice/water bath. To the flask, 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP, 1.8 mL) was added dropwise. The reaction mixture was left to stir in a slowly melting ice/water bath and the consumption of the *halo*-Prins product was followed by TLC (50% ethyl acetate/hexanes, Rf ~ 0.5). After 3 h, the reaction was quenched by the addition of excess sodium bicarbonate. The mixture was stirred for 5 min and then vacuum-filtered through celite into a separatory funnel, using copious amounts of ethyl acetate. The organic layer was washed using sat. aq. sodium bicarbonate and the layers were separated. The aqueous layer was washed two times with ethyl acetate and the organic layers were combined and washed with brine. The organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography (40% ethyl acetate/hexanes) to obtain 1.052 g (91% over two steps) of **4Nb** as orange solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.60 (td, *J* = 7.7, 1.3 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.52 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.48 (td, *J* = 7.7, 1.3 Hz, 1H), 7.37 – 7.34 (m, 2H), 7.25 – 7.20 (m, 1H), 7.18 – 7.15 (m, 2H), 7.13 (t, *J* = 7.5 Hz, 1H), 5.89 (dt, *J* = 7.0, 2.1 Hz, 1H), 3.93 (s, 1H), 3.82 (d, *J* = 6.9 Hz, 1H), 3.33 (t, *J* = 6.3 Hz, 2H), 2.34 – 2.24 (m, 1H), 1.97 – 1.88 (m, 1H), 1.56 – 1.45 (m, 1H), 1.38 – 1.29 (m, 1H), 1.15 (s, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 152.5, 148.2, 140.0, 138.4, 136.5, 134.1, 133.3, 132.3, 131.1, 131.0, 129.4, 128.7, 128.5, 125.9, 124.7, 124.2, 117.7, 97.6, 78.8, 61.8, 58.6, 52.6, 29.4, 28.2.

HRMS (ESI) *m/z* calc'd for $C_{26}H_{22}{}^{35}ClIN_2O_5S$ $[M+H]^+$: 637.0055, found: 637.0044.



1e **2k** **4Nk**

To a 50 mL round-bottom flask, equipped with a stir bar, powdered 5 Å molecular sieves (360 mg) were added. The flask was closed with a septum and flame-dried under vacuum (~ 10 Torr). The flask was let to cool to room temperature and then carefully refilled with argon (*note:* sieves are easily blown and readily end up in the Schlenk line – to protect the Schlenk line from sieves, the authors have used a large piece of cotton in between the line and the tubing (inside 24/40 glass adapter) and then a small piece of cotton in between the needle and the piece of a 1 mL syringe attached to the tubing). The septum was briefly removed (while keeping the needle connected to the argon line, with the flow of argon reduced to prevent the blowing of the sieves, above the ground glass joint of the flask to maintain inert atmosphere) and enyne **1e** (386 g, 1.0 mmol, 1.0 equiv.) and tetrabutylammonium iodide (443 mg, 1.2 mmol, 1.2 equiv.) were added. The flask was closed again and (*E*)-4-hexenal **2k** (0.14 mL, 1.2 mmol, 1.2 equiv.) and anhydrous dichloromethane (DCM, 10 mL) was added. The mixture was cooled to ~ -40 °C using the dry ice/acetonitrile bath (*note*: dry ice pieces should be added one by one until the bath has a temperature of -40 °C; no excess of dry ice should be used). Using a glass syringe (Hamilton 1 mL Gastight Syringe Model 1001 TLL, PTFE Luer Lock), trifluoromethanesulfonic acid (0.11 mL, 1.25 mmol, 1.25 equiv.) was slowly added dropwise to the reaction mixture (*note: trifluoromethanesulfonic acid fumes when exposed to air and this exposure should be minimized due to its hygroscopic nature; see general remarks of the SI for further remarks about the trifluoromethanesulfonic acid*). The reaction mixture was stirred in the acetonitrile bath (which was let to warm up) and the reaction progress was monitored using TLC (50% ethyl acetate/hexanes, consumption of the enyne **1e** was monitored, Rf ~ 0.15). After 3 h, the flask was removed from the dry ice/acetonitrile bath and placed in an ice/water bath. To the flask, 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP, 1 mL) and trifluoromethanesulfonic acid (44 μL, 0.5 mmol, 0.5 equiv., added via a glass microsyringe) were added dropwise. The reaction mixture was left to stir in a slowly melting ice/water bath and the consumption of the *halo*-Prins product was followed by TLC (50% ethyl

acetate/hexanes, Rf ~ 0.5). After 1 h, the reaction was quenched by the addition of excess sodium bicarbonate. The mixture was stirred for 5 min and then vacuum-filtered through celite into a separatory funnel, using copious amounts of ethyl acetate. The organic layer was washed using sat. aq. sodium bicarbonate and the layers were separated. The aqueous layer was washed two times with ethyl acetate and the organic layers were combined and washed with brine. The organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography (40% ethyl acetate/hexanes), to obtain 403 mg (68% over two steps) of **4Nk**, as a pale-yellow foam.

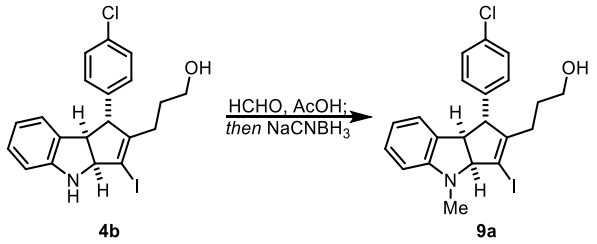
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.61 (td, *J* = 7.7, 1.4 Hz, 1H), 7.55 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.52 – 7.46 (m, 2H), 7.21 – 7.15 (m, 1H), 7.06 – 7.02 (m, 2H), 5.60 (dt, *J* = 6.9, 2.1 Hz, 1H), 5.54 – 5.37 (m, 2H), 3.65 (d, *J* = 6.9 Hz, 1H), 3.39 – 3.27 (m, 2H), 2.84 – 2.78 (m, 1H), 2.38 – 2.27 (m, 1H), 2.17 – 2.02 (m, 3H), 1.80 – 1.68 (m, 1H), 1.66 (dd, *J* = 6.1, 1.4 Hz, 3H), 1.63 – 1.55 (m, 1H), 1.50 – 1.36 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.4, 148.2, 138.5, 137.2, 134.0, 132.4, 131.3, 131.1, 130.1, 128.3, 126.1, 125.6, 124.6, 124.2, 117.3, 95.8, 78.6, 61.8, 52.0, 48.7, 32.8, 30.0, 29.4, 27.8, 17.9.

HRMS (ESI) *m/z* calc'd for $C_{25}H_{27}IN_2O_5S$ $[M+H]^+$: 595.0758, found: 595.0750.

Product Diversification

N-Alkylation



4b **9a**

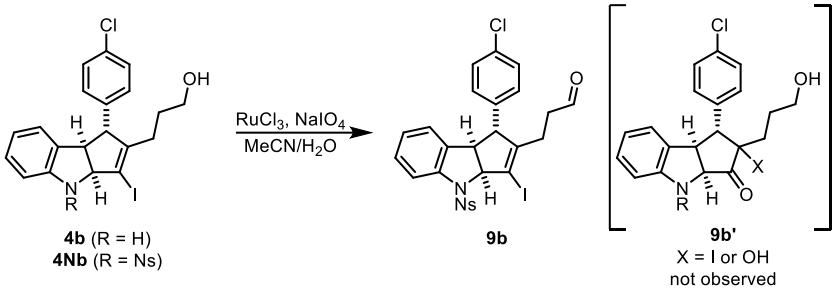
To a 2-dram glass vial, equipped with a stir bar, **4b** (90 mg, 0.2 mmol, 1.0 equiv.), glacial acetic acid (0.6 mL) and 38% aqueous formaldehyde (formalin, 0.16 mL, 2.2 mmol, 11 equiv.) were added. The vial was closed with a plastic cap and the mixture was stirred at room temperature. After 30 min, the vial was opened and sodium cyanoborohydride (42 mg, 0.66 mmol, 3.3 equiv.) was added in one portion (effervescence was observed). The vial was closed again and the mixture was stirred for 1 h. *Quench*: The reaction mixture was diluted with ethyl acetate and transferred to a separatory funnel. Saturated aqueous sodium bicarbonate was added, the layers were mixed and then separated. Organic layer was washed with brine. The organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by preparative TLC (25% ethyl acetate/5% triethylamine/hexanes, middle UV active band), to obtain 39 mg (42%) of **9a**, as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.31 (m, 2H), 7.15 – 7.08 (m, 3H), 6.99 (d, *J* = 7.2 Hz, 1H), 6.67 (t, *J* = 7.4 Hz, 1H), 6.50 (d, *J* = 7.9 Hz, 1H), 4.66 (dt, *J* = 9.1, 1.3 Hz, 1H), 3.93 (dd, *J* = 8.9, 3.4 Hz, 1H), 3.90 – 3.82 (m, 1H), 3.50 – 3.38 (m, 2H), 3.13 (s, 3H), 2.35 – 2.25 (m, 1H), 1.94 – 1.82 (m, 1H), 1.58 – 1.34 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.7, 151.5, 141.6, 132.8, 131.2, 129.1, 128.8, 128.5, 123.7, 117.9, 108.0, 97.4, 81.5, 62.1, 59.6, 55.3, 37.5, 29.5, 27.9.

HRMS (ESI) *m/z* calc'd for $C_{21}H_{21}{}^{35}ClINO$ $[M+H]^+$: 466.0429, found: 466.0429.

Oxidation



4b (R = H)
4Nb (R = Ns)

9b

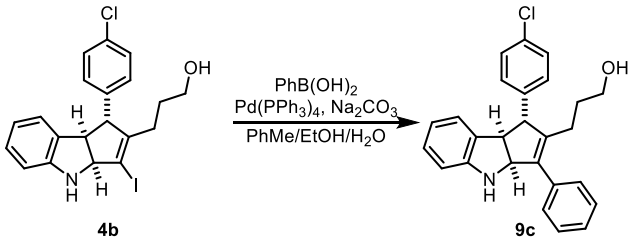
9b'
X = I or OH
not observed

To a 10 mL round-bottom flask, equipped with a stir-bar, **4Nb** (78 mg, 0.122 mmol, 1.0 equiv.), acetonitrile (2 mL), and water (0.4 mL) were added. The flask was closed and the mixture was stirred and cooled to 0 °C using an ice/water bath. To the mixture, ruthenium(III) chloride hydrate (6 mg, 0.0122 mmol, 0.1 equiv., based on 40% Ru content stated by the supplier) and sodium periodate (16 mg, 0.073 mmol, 0.6 equiv.) were added. The reaction was stirred overnight at 0 °C (in a fridge). After 16 h, additional sodium periodate (13 mg, 0.061 mmol, 0.5 equiv.) were added. After stirring for additional 3 h, final portion of sodium periodate (13 mg, 0.061 mmol, 0.5 equiv.) was added. After 30 min, full consumption of **4Nb** was observed based on the TLC (50% ethyl acetate/hexanes, product Rf ~ 0.5). *Quench*: The reaction mixture was diluted with ethyl acetate and transferred to a separatory funnel. The organic layer was washed with 10% aqueous sodium thiosulfate. The layers were separated, and the aqueous layer was back-extracted with ethyl acetate two times. The organic layers were combined and washed with brine. The organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by preparative TLC (50% ethyl acetate/hexanes), to obtain 22 mg (29%) of **9b**, as a pale-yellow oil.
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.51 – 9.47 (m, 1H), 7.83 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.58 (td, *J* = 7.7, 1.4 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.50 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.47 (td, *J* = 7.7, 1.4 Hz, 1H), 7.37 – 7.32 (m, 2H), 7.26 – 7.21 (m, 1H), 7.20 (d, *J* = 7.5 Hz, 1H), 7.17 – 7.14 (m, 2H), 7.11 (td, *J* = 7.6, 1.0 Hz, 1H), 5.88 (dt, *J* = 7.1, 1.9 Hz, 1H), 3.92 – 3.85 (m, 1H), 3.81 (d, *J* = 6.9 Hz, 1H), 2.46 – 2.31 (m, 2H), 2.28 – 2.09 (m, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 200.1, 151.2, 148.3, 139.8, 138.4, 136.3, 134.1, 133.5, 132.3, 131.1, 130.9, 129.5, 128.8, 128.6, 126.0, 124.8, 124.2, 117.7, 98.5, 78.8, 59.3, 52.7, 40.8, 24.5.
HRMS (ESI) *m/z* calc'd for $C_{26}H_{20}{}^{35}ClIN_2O_5S$ $[M+H]^+$: 634.9899, found: 634.9882.

The same reaction was attempted with **4b**. The TLC of the reaction mixture was complex, in the form of a long UV-active streak across the 3/4th of the plate's height (50% ethyl acetate/hexanes). The addition of triethylamine to the eluent or using different eluents with different concentrations of the crude mixture did not have a significant effect on the TLC. The reaction mixture was discarded.

Initially targeted **9b'** was not observed.

Cross Coupling



4b

9c

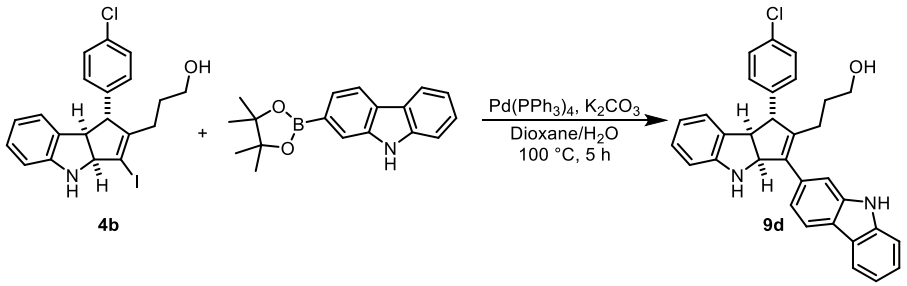
To a 15 mL screw-top tube (sealable tube), equipped with a stir bar, **4b** (90 mg, 0.2 mmol, 1.0 equiv.), phenylboronic acid (37 mg, 0.3 mmol, 1.5 equiv.), toluene (0.6 mL), ethanol (0.2 mL), and 2 M aq. sodium carbonate (0.2 mL) were added. The tube was closed with a septum and the mixture was stirred and degassed with argon (using a long needle connected to a Schlenk line with an argon line, and another bleed needle). After 20 min of continuous degassing, the septum was removed and tetrakis(triphenylphosphine)palladium(0) (6 mg, 0.005 mmol, 2.5 mol%) was quickly added (this air-sensitive palladium(0) complex was weighed in a nitrogen-filled glovebox into a small vial before use). The

mixture was further degassed for 5 min. The septum was removed, and the tube was quickly closed with a screw top. The tube was placed in a preheated oil bath at 80 °C, and the reaction mixture was stirred overnight. *Quench*: After 21 h, the tube was removed from the oil bath and the mixture was let to cool down to room temperature. The tube was carefully opened, and the mixture was diluted with ethyl acetate and transferred to a separatory funnel. The organic layer was washed with water, then sat. aq. sodium bicarbonate, then brine. The organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography (40% ethyl acetate/hexanes, same Rf as **4b**), to obtain 80 mg (100%) of **9c**, as a pale-yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (t, *J* = 7.5 Hz, 2H), 7.39 – 7.31 (m, 5H), 7.25 – 7.18 (m, 3H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.79 (t, *J* = 7.4 Hz, 1H), 6.58 (d, *J* = 7.8 Hz, 1H), 5.35 (d, *J* = 8.1 Hz, 1H), 4.12 (s, 1H), 3.87 (d, *J* = 7.9 Hz, 1H), 3.42 – 3.34 (m, 2H), 2.27 – 2.18 (m, 1H), 1.84 – 1.74 (m, 1H), 1.60 – 1.50 (m, 1H), 1.50 – 1.39 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 149.3, 142.6, 142.4, 139.1, 135.9, 132.4, 132.1, 129.0, 128.9, 128.7, 128.4, 128.1, 127.4, 124.3, 119.0, 110.3, 70.9, 62.3, 61.6, 53.4, 30.5, 23.7.

HRMS (ESI) *m/z* calc'd for $C_{26}H_{24}{}^{35}ClNO$ $[M+H]^+$: 402.1619, found: 402.1615.



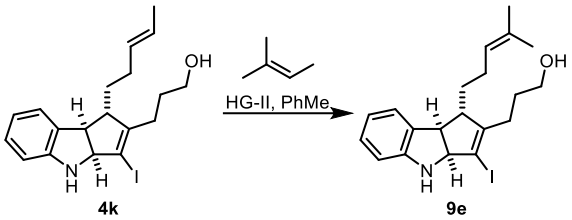
To a 15 mL screw-top tube (sealable tube), equipped with a stir bar, **4b** (32 mg, 0.071 mmol, 1.0 equiv.), (9*H*-carbazolyl)boronic acid pinacol ester (21 mg, 0.071 mmol, 1.0 equiv.), potassium carbonate (20 mg, 0.142 mmol, 2.0 equiv.), dioxane (0.8 mL), and water (0.2 mL) were added. The tube was closed with a septum and the mixture was stirred and degassed with argon (using a long needle connected to a Schlenk line with an argon line, and another bleed needle). After 20 min of continuous degassing, the septum was removed and tetrakis(triphenylphosphine)palladium(0) (4 mg, 0.0036 mmol, 5 mol%) was quickly added (this air-sensitive lemon yellow palladium(0) complex was weighed in a nitrogen-filled glovebox into a small vial before use). The mixture was further degassed for 5 min. The septum was removed, and the tube was quickly closed with a screw top. The tube was placed in a preheated oil bath at 100 °C, and the reaction mixture was stirred for 5 h. *Quench*: The tube was removed from the oil bath and the mixture was let to cool down to room temperature. The tube was carefully opened, and the mixture was diluted with ethyl acetate and transferred to a separatory funnel. The organic layer was washed with water, then sat. aq. sodium bicarbonate, then brine. The organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by preparative TLC (40% ethyl acetate/hexanes, large mid-plate UV active and slightly fluorescent band), to obtain 32 mg (91%) of **9d**, as a pale-yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (s, 1H), 8.08 (t, *J* = 7.9 Hz, 2H), 7.44 – 7.39 (m, 1H), 7.37 – 7.34 (m, 3H), 7.30 (s, 1H), 7.25 – 7.18 (m, 4H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.80 (t, *J* = 7.4 Hz, 1H), 6.55 (d, *J* = 7.7 Hz, 1H), 5.46 – 5.37 (m, 1H), 4.11 (s, 1H), 3.87 (d, *J* = 8.0 Hz, 1H), 3.40 – 3.32 (m, 2H), 2.34 – 2.22 (m, 1H), 1.82 – 1.71 (m, 1H), 1.58 – 1.39 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 149.3, 142.7, 142.0, 139.8, 139.8, 139.7, 133.3, 132.4, 132.3, 129.0, 128.9, 128.1, 126.0, 124.4, 122.9, 122.6, 120.5, 120.3, 119.6, 119.6, 119.1, 110.7, 110.7, 110.4, 71.1, 62.3, 61.8, 53.3, 30.4, 23.8.

HRMS (ESI) *m/z* calc'd for $C_{32}H_{27}ClN_2O$ $[M+H]^+$: 491.1885, found: 491.1875.

Cross Metathesis



4k **9e**

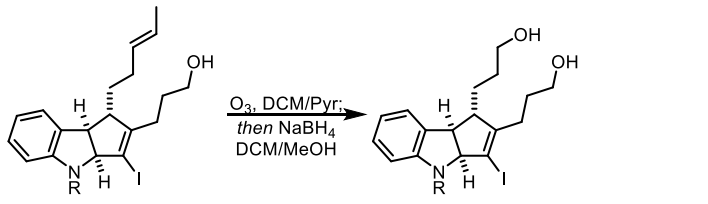
To a 2-dram glass vial, equipped with a stir-bar, flame-dried under vacuum (~ 10 Torr) and refilled with argon (once it cooled to room temperature), **4k** (72 mg, 0.176 mmol, 1.0 equiv.), freshly distilled 2-methyl-2-butene (0.22 mL, 2 mmol, 11.4 equiv., distilled using a Minum-Ware Hickman Still Head in argon atmosphere immediately before use), Hoveyda-Grubbs second generation catalyst (2 mg, 0.002 mmol, 1 mol%, Umicore M720, this air-sensitive ruthenium(II) complex was weighed in a nitrogen-filled glovebox into a small vial before use), and anhydrous toluene (1 mL) were added. The vial was closed with a plastic cap and placed in a preheated oil bath at 60 °C. The reaction mixture was stirred overnight at this temperature. *Quench*: The vial was removed from the oil bath and the mixture was let to cool down to room temperature. Once cooled, the mixture was diluted with ethyl acetate and the mixture was filtered through celite, using copious amounts of ethyl acetate. The filtrate was collected, and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography (30% ethyl acetate/hexanes), to obtain 57 mg of **9e**, contaminated with a small amount of inseparable **4k** (70% yield of **9e** or 77% yield of **9e**, based on the recovery of starting material).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.07 – 6.98 (m, 2H), 6.73 (td, *J* = 7.4, 1.1 Hz, 1H), 6.66 (d, *J* = 7.7 Hz, 1H), 5.21 – 5.12 (m, 1H), 4.72 (dt, *J* = 7.9, 2.1 Hz, 1H), 4.25 (s, 1H), 3.67 (d, *J* = 7.9 Hz, 1H), 3.47 – 3.37 (m, 2H), 2.85 – 2.78 (m, 1H), 2.37 – 2.24 (m, 1H), 2.24 – 2.09 (m, 3H), 1.83 – 1.75 (m, 1H), 1.74 (s, 3H), 1.67 (s, 3H), 1.65 – 1.60 (m, 1H), 1.55 – 1.33 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.8, 148.6, 132.3, 132.2, 128.0, 124.2, 123.6, 119.1, 110.3, 99.7, 73.2, 62.0, 53.5, 49.8, 33.7, 29.7, 27.6, 25.7, 25.7, 17.9.

HRMS (ESI) *m/z* calc'd for $C_{20}H_{26}INO$ $[M+H]^+$: 424.1132, found: 424.1130.

Ozonolysis



4Nk (R = Ns)
4k (R = H)

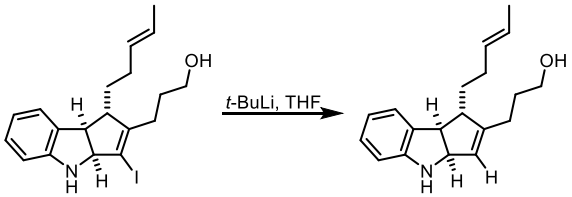
9f (R = Ns)
9g (R = H)

To a 10 mL pear-shaped flask, **4Nk** (108 mg, 0.182 mmol, 1.0 equiv.), dichloromethane (4 mL) and pyridine (48 μL, 0.6 mmol, 3.3 equiv.) were added. The mixture was cooled to -78 °C using a dry ice/acetone bath and purged with bubbling oxygen for 5 min (oxygen was passed through the ozone generator that was off, and was delivered into the flask through a long, stainless-steel needle; note: the flask was not closed with a septum – it was left open and a stir-bar was not used). After degassing, the ozone generator was turned on for 1 min (bubbling of ozone/oxygen gas mixture was enough to stir it) after which it was stopped, and the gas-delivery needle was removed from the flask (oxygen was left to pass through it). The consumption of **4Nk** was monitored by TLC (50 % ethyl acetate/hexanes). This procedure was repeated for 3 more times (making total reaction time 4 min on this scale) when the consumption of **4Nk** was deemed to be completed. The mixture was purged with argon to remove any residual dissolved ozone. The flask was placed in an ice/water bath and a stir-bar was added into it. The mixture was stirred and methanol (2 mL), and sodium borohydride (38 mg, 1.0 mmol, 5 equiv.) were added (effervescence was observed). The mixture was let to stir overnight in a slowly melting ice/water bath. *Quench*: The mixture was diluted with ethyl acetate and transferred to a separatory funnel. Organic layer was washed with 2 M aq. HCl, then sat. aq. sodium bicarbonate, then brine. The organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary

evaporator. The crude was purified by flash column chromatography (10% methanol/DCM), to obtain 60 mg (57%) of **9f**, as a pale-yellow foam.
Note: An attempt to perform ozonolysis using **4k** resulted in the formation of precipitate that could not be dissolved in either $CDCl_3$ or DMSO-d_6.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.62 (td, *J* = 7.7, 1.4 Hz, 1H), 7.55 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.53 – 7.46 (m, 2H), 7.19 (td, *J* = 7.7, 1.6 Hz, 1H), 7.11 – 7.03 (m, 2H), 5.60 (dt, *J* = 7.0, 2.1 Hz, 1H), 3.69 (t, *J* = 6.1 Hz, 2H), 3.64 (d, *J* = 6.9 Hz, 1H), 3.37 (t, *J* = 6.3 Hz, 2H), 2.92 – 2.86 (m, 1H), 2.36 – 2.27 (m, 1H), 2.18 – 2.09 (m, 1H), 1.88 – 1.78 (m, 1H), 1.69 – 1.57 (m, 3H), 1.57 – 1.48 (m, 1H), 1.47 – 1.38 (m, 1H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 153.3, 148.2, 138.5, 137.1, 134.1, 132.2, 131.2, 131.1, 128.3, 125.7, 124.7, 124.2, 117.4, 95.8, 78.6, 62.4, 61.7, 52.4, 48.9, 29.6, 29.5, 29.4, 27.8.
HRMS (ESI) *m/z* calc'd for $C_{23}H_{25}IN_2O_6S$ $[M+H]^+$: 585.0551, found: 585.0550.

To a 10 mL round-bottom flask, equipped with a stir-bar, **9f** (60 mg, 0.103 mmol, 1.0 equiv.), anhydrous potassium carbonate (138 mg, 1 mmol, 10 equiv.) and anhydrous methanol (2 mL) were added. The flask was closed with a plastic cap and the mixture was stirred and cooled to 0 °C using a ice/water bath. Once cooled, the flask was opened and thioglycolic acid (35 μL, 0.5 mmol, 5 equiv.) was added dropwise. The flask was closed again, and the mixture was let to stir overnight in a slowly-melting ice/water bath. *Quench:* The reaction was quenched by the addition of excess sodium bicarbonate. The mixture was stirred for 5 min and then vacuum-filtered through celite using copious amounts of ethyl acetate. The solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by flash column chromatography (ethyl acetate) to obtain 24 mg (60%; 34% over two steps) of **9g**, as colorless oil.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.07 – 6.99 (m, 2H), 6.73 (t, *J* = 7.4 Hz, 1H), 6.66 (d, *J* = 7.7 Hz, 1H), 4.75 – 4.69 (m, 1H), 3.73 (t, *J* = 6.3 Hz, 2H), 3.63 (d, *J* = 7.9 Hz, 1H), 3.47 – 3.36 (m, 2H), 2.85 (d, *J* = 8.8 Hz, 1H), 2.33 – 2.25 (m, 1H), 2.21 – 2.12 (m, 1H), 1.90 – 1.59 (m, 6H), 1.55 – 1.41 (m, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 151.5, 148.6, 132.1, 128.1, 124.2, 119.2, 110.4, 99.9, 73.3, 62.6, 62.0, 53.7, 50.0, 30.1, 29.9, 29.7, 27.6.
HRMS (ESI) *m/z* calc'd for $C_{17}H_{22}INO_2$ $[M+H]^+$: 400.0768, found: 400.0771.

Deiodination



4k **9h**

To a 10 mL round-bottom flask, equipped with a stir-bar, flame-dried under vacuum (~ 10 Torr) and refilled with argon (once it cooled to room temperature), **4k** (82 mg, 0.2 mmol, 1.0 equiv.), and anhydrous THF (2 mL) were added. The flask was cooled to -78 °C using a dry ice/acetone bath and the mixture was stirred. To the mixture, 1.6 M solution of *t*-BuLi in pentane (0.5 mL, 0.8 mmol, 4.0 equiv.) was added slowly dropwise (color change was observed). The dry ice pieces were removed (using long metal tweezers) and the reaction mixture was stirred for 1 h, while letting the bath temperature increase to -40 °C. *Quench*: The reaction was quenched cold by the slow and careful addition of sat. aq. ammonium chloride. The mixture was warmed up to room temperature and transferred to a separatory funnel using excess of ethyl acetate. More sat. aq. ammonium chloride was added, and the layers were separated. Organic layer was washed with brine. The organic layer was collected and dried by the addition of excess anhydrous magnesium sulfate (filtered over a medium grade fritted funnel under vacuum) and the solvents were removed by vacuum distillation using a rotary evaporator. The crude was purified by preparative TLC (70% ethyl acetate/hexanes), to obtain 49 mg (86%) of **9h**, as a yellow oil.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.05 (d, *J* = 7.3 Hz, 1H), 7.01 (t, *J* = 7.6 Hz, 1H), 6.73 (t, *J* = 7.4 Hz, 1H), 6.61 (t, *J* = 7.8 Hz, 1H), 5.58 – 5.45 (m, 2H), 5.27 – 5.24 (m, 1H), 4.82 – 4.77 (m, 1H), 3.68 (d, *J* = 8.1 Hz, 1H), 3.53 (t, *J* = 6.4 Hz, 2H), 2.74 – 2.68 (m, 2H), 2.66 (s, 1H), 2.27 – 2.07 (m, 3H), 2.03 – 1.94 (m, 1H), 1.81 – 1.72 (m, 1H), 1.70 (d, *J* = 5.0 Hz, 3H), 1.68 – 1.58 (m, 2H), 1.39 – 1.29 (m, 1H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 149.6, 149.5, 133.5, 130.9, 127.7, 125.3, 124.8, 124.5, 119.0, 110.6, 67.3, 62.5, 55.4, 51.0, 33.8, 30.6, 30.3, 25.3, 17.9.
HRMS (ESI) *m/z* calc'd for $C_{19}H_{25}NO$ $[M+H]^+$: 284.2009, found: 284.2007.

References

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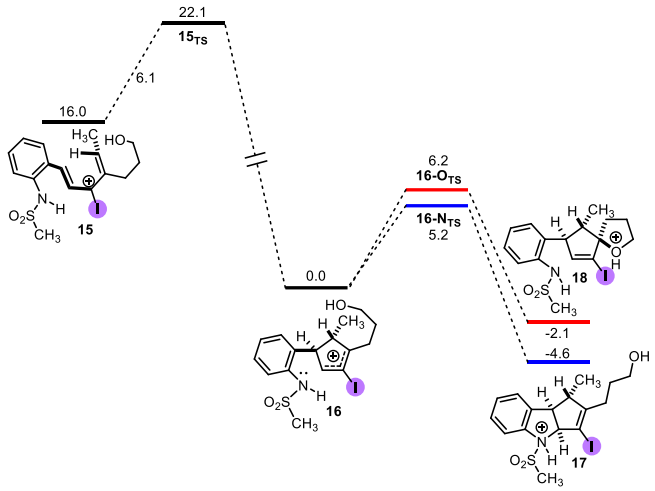
Computational Methods

Input files for ground state or transition state intermediates of a given reaction were prepared locally using GaussView 6.0 and transferred to the University of Rochester Blue Hive Linux cluster where DFT calculations were carried out in the Gaussian 16 suite of programs. Optimization calculations (either to a ground state or a transition state) were carried out at the M06-2x functional and Def2-TZVP basis set level of theory, with implicit solvation using the Solvation Model Based on Density (SMD = dichloromethane). Intrinsic reaction coordinate (IRC) calculations were carried out on the transition state structures to verify that they connected to the associated reactant and product structures. Frequency calculations, ran at the M06- 2x/Def2-TZVP level of theory (SMD = dichloromethane) for the obtained optimized structures, were carried out to confirm that ground state structures had zero imaginary frequencies and that transition states had a single imaginary frequency. All shown free energies are ZPE and thermally corrected (reported in Hartree units, at 298.15 K and 1 atm) and were obtained from the frequency calculations.

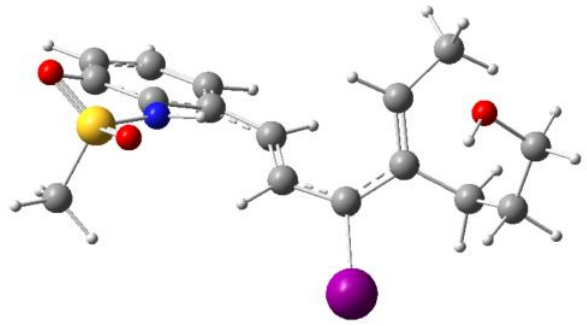


Gaussian 16, Revision C.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2019.

DFT Optimized Structures (M06-2x/Def2-TZVP, SMD = dichloromethane)

All energies (EE + Thermal Free Energy Correction) have the unit Hartree. Coordinates are provided in format ATOM-X-Y-Z.

15



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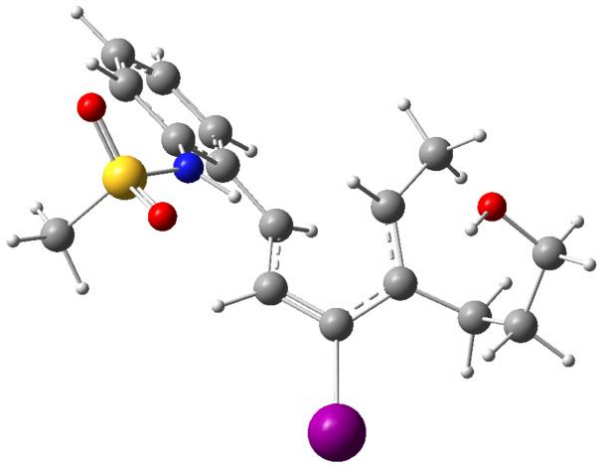
15TS



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C	-3.27614300	0.26243800	-1.71379500
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C	-0.89283500	-0.26742900	-0.95610800
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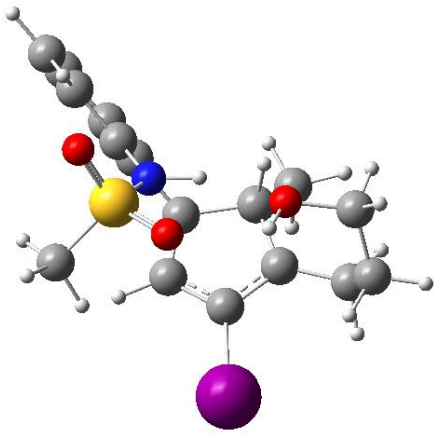
16



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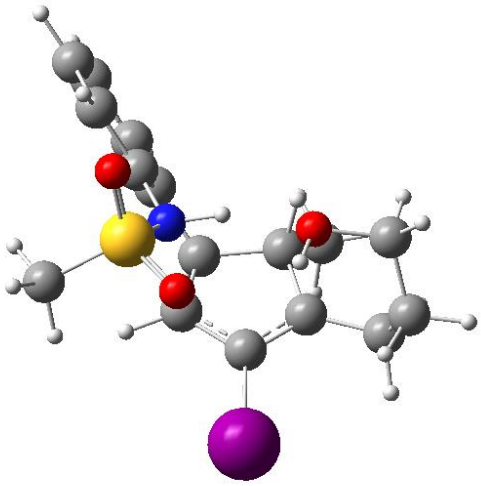
16-N_{TS}



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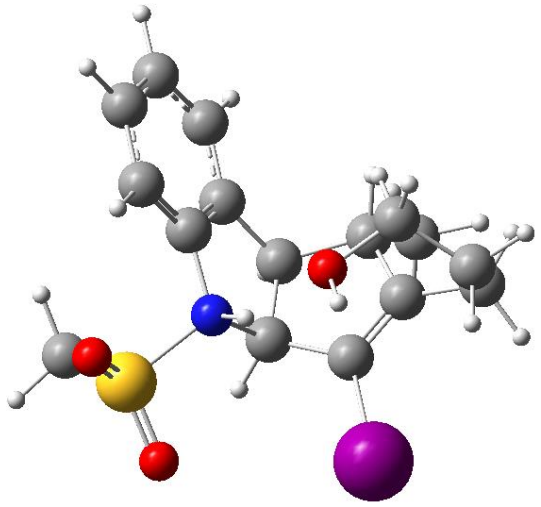
H	-6.24705600	1.39906000	-3.07511800
H	-6.76227100	-0.91582700	-2.38693400
H	-5.10075300	-2.25288100	-1.14748400
H	-4.03300200	2.38696300	-2.55033800
H	-0.80545900	-0.65102200	-2.04073800
H	-1.58476900	1.81199100	-1.93330400
H	-2.58902700	1.34091000	0.87452800
H	-1.84887400	-4.42379700	-2.17155100
H	-2.63266800	-2.93188100	-2.76345400
H	-0.88356600	-2.92264300	-2.30505500
H	-2.20584400	0.80374300	3.29046900
H	-1.59819500	-0.53402000	4.27044700
H	0.26383200	0.92561000	4.06345500
H	0.57544900	-0.39668600	2.94952100
H	1.18556400	1.65219100	1.85069600
H	-0.31051500	2.46058500	2.34135500
H	-0.98712100	3.64353700	-0.34575600
H	-2.75319700	3.56945200	-0.24809400
H	-1.79799600	3.63971300	1.23106300
I	1.66163700	-0.99783000	0.07739600
H	-1.31720400	-1.69051800	2.26933400
H	-2.49248600	-1.01287000	0.53319900

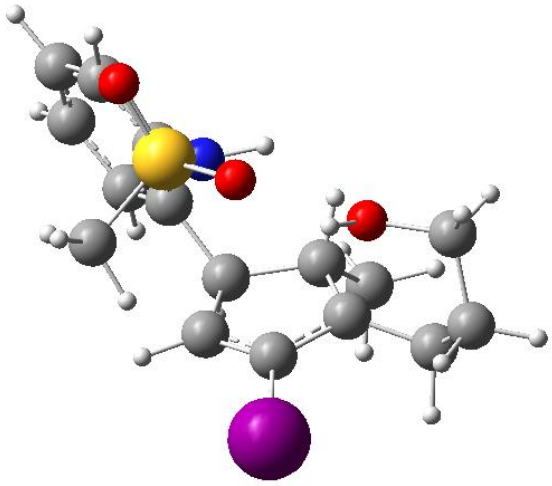
17



Imaginary Frequencies = 0
EE + Thermal Free Energy Correction = -1598.066616

C	-5.54619900	0.48728400	-1.39779900
C	-5.63564300	-0.80269700	-0.87801800
C	-4.49166500	-1.51932200	-0.55531100
C	-3.28128600	-0.89184600	-0.78827600
C	-3.16128900	0.39403700	-1.26994800
C	-4.31451400	1.09950400	-1.58498900
N	-1.95684200	-1.48197200	-0.54837300
C	-0.90985800	-0.38070100	-0.89888800
C	-1.74106800	0.87129000	-1.25832800
C	-0.17533800	-0.00809400	0.34511200
C	-0.59787400	1.14352400	0.85937000
C	-1.48004200	1.88998600	-0.11316200
S	-1.69532400	-3.04776300	-1.41508500
C	-2.20418000	-2.63854200	-3.03836300
O	-0.29042700	-3.26038900	-1.35215600
O	-2.60218000	-3.94587500	-0.78492400
O	-2.22888300	-1.11203000	2.26678800
C	-2.36683100	0.15655900	2.92318000
C	-1.03233400	0.78877000	3.31685600
C	-0.35171600	1.66400500	2.23854600
C	-0.79838700	3.16373000	-0.60792500
H	-6.45260300	1.02491000	-1.64458000
H	-6.60585100	-1.25399000	-0.71903400
H	-4.54705100	-2.51801900	-0.14548100
H	-4.25013400	2.11348100	-1.95964600
H	-0.29379700	-0.77731100	-1.70214400
H	-1.43620600	1.27921900	-2.22112000
H	-2.41918200	2.16252600	0.37625400
H	-1.93661700	-3.51521500	-3.63236000
H	-3.27922100	-2.47706400	-3.05379800
H	-1.64659600	-1.76858200	-3.38520200
H	-2.92357900	0.79016300	2.23044300
H	-2.98517800	0.01865100	3.81256900
H	-1.19248900	1.41135700	4.19850100
H	-0.36021500	-0.01535900	3.62442900
H	0.72041900	1.71419400	2.44261300
H	-0.74119800	2.68071700	2.30132400
H	0.13159400	2.92068800	-1.12572700
H	-1.45243500	3.69653800	-1.30004300
H	-0.56629500	3.83171900	0.22259800
I	1.20745900	-1.29100200	1.21621800
H	-1.84710100	-1.73643200	2.89784000
H	-1.87890300	-1.69287100	0.47277900

16-O$_{TS}$



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EE + Thermal Free Energy Correction = -1598.049452

C	-5.35938300	0.71863700	-3.04402800
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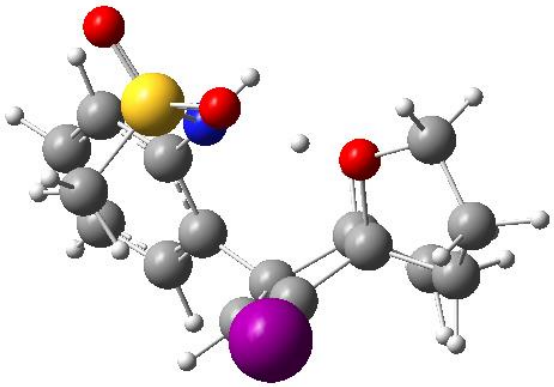
C	-5.10194200	-1.19755600	-1.61784400
C	-3.90649800	-0.67718000	-1.13995000
C	-3.41368600	0.54533400	-1.61442700
C	-4.16557100	1.23588800	-2.55918100
N	-3.14800200	-1.35078000	-0.13554000
C	-0.92761500	0.19890800	-1.32262700
C	-2.08860000	1.11459500	-1.14967100
C	-0.14984300	0.11977700	-0.22705700
C	-0.69589100	0.92701600	0.83033900
C	-1.95952100	1.58424900	0.32163900
S	-2.74215000	-2.93017500	-0.14707300
C	-1.73632500	-3.10030400	-1.57469800
O	-1.92987200	-3.08884600	1.04088300
O	-3.87850300	-3.79198300	-0.29845000
O	-1.53184900	-0.54190100	2.08740600
C	-0.94987100	-0.22516000	3.35618600
C	0.37334000	0.45094900	3.07050100
C	0.09401600	1.47861900	1.96586700
C	-1.93331900	3.11069000	0.42988200
H	-5.92313500	1.27027200	-3.78518100
H	-6.75166200	-0.91373200	-2.95320500
H	-5.46447300	-2.13817200	-1.22613200
H	-3.79945500	2.18630600	-2.92860100
H	-0.72131700	-0.30042900	-2.26236200
H	-1.88479500	1.98036200	-1.79093500
H	-2.79438000	1.21912700	0.92344800
H	-1.55257200	-4.16789000	-1.69315000
H	-2.28116000	-2.71920700	-2.43823500
H	-0.80207500	-2.56590100	-1.41124800
H	-1.64397000	0.45010800	3.85620300
H	-0.83834500	-1.13341800	3.94805800
H	0.76202200	0.95694700	3.95313700
H	1.10585500	-0.28552700	2.74448000
H	1.03912000	1.83306900	1.54050100
H	-0.43278900	2.32812400	2.39487100
H	-1.04640700	3.52131400	-0.05601500
H	-2.81560000	3.50646500	-0.07382800
H	-1.95936400	3.44537600	1.46486700
I	1.60836200	-0.97381200	-0.14285700
H	-1.28947800	-1.44602400	1.80528500
H	-3.15806100	-0.96303200	0.80390100

18



Imaginary Frequencies = 0
EE + Thermal Free Energy Correction = -1598.062603

C	-5.13186500	0.61432000	-3.33209900
C	-5.66549000	-0.56830400	-2.84109600
C	-5.07768300	-1.17873900	-1.74281700
C	-3.95162000	-0.61449100	-1.16015700
C	-3.39025200	0.57219500	-1.64356000
C	-4.01085300	1.17543200	-2.73501400
N	-3.34435800	-1.21756700	-0.00416600
C	-0.91960000	0.33003700	-1.31066200
C	-2.12651000	1.18825800	-1.06859500
C	-0.24976400	0.05745200	-0.20091400
C	-0.84815700	0.70551200	1.01914800
C	-2.08231100	1.48338400	0.46011500
S	-2.77060500	-2.74064200	0.04782500
C	-1.95404800	-2.97612000	-1.47947000
O	-1.77689000	-2.67999000	1.13144900
O	-3.77609200	-3.74716200	0.20741900
O	-1.34291200	-0.37302500	1.95080100
C	-0.67146200	-0.34189300	3.25844700
C	0.57362000	0.47612000	3.00845800
C	0.13018800	1.46112200	1.92465800
C	-2.05648700	2.98693100	0.70765400
H	-5.58930100	1.10520300	-4.18153100
H	-6.54031500	-1.00940800	-3.30032000
H	-5.48899100	-2.09120100	-1.32791200
H	-3.60109400	2.09924500	-3.12502200
H	-0.64729400	-0.00958700	-2.30227500
H	-1.98033100	2.13074400	-1.60311800
H	-2.96559700	1.07818100	0.94972200
H	-1.55445800	-3.98952400	-1.42290500
H	-2.68207800	-2.90670300	-2.28620900
H	-1.15006400	-2.25285500	-1.58465600
H	-1.36822500	0.13819400	3.94184100
H	-0.50038600	-1.37566000	3.54866900
H	0.88795100	0.99179300	3.91341800
H	1.38647100	-0.15944200	2.66603700
H	0.96476000	1.84035300	1.33668600
H	-0.37428400	2.30509300	2.38826000
H	-1.13997300	3.43733800	0.32026200
H	-2.90198700	3.44187900	0.18951600
H	-2.14795900	3.23100700	1.76542900
I	1.45288600	-1.13542600	-0.15563200
H	-1.44995100	-1.33711900	1.55270900
H	-3.78368600	-0.97715600	0.88435100

HPLC Traces

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: AM400		
Sample ID	: 0.75f-IPA-1%;		
Data Filename	: AM400-5.lcd		
Method Filename	: 0.75f_IPA_1%60min.lcm		
Batch Filename	:		
Vial #	: 1-1	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 1/31/2023 3:10:29 PM	Acquired by	: System Administrator
Date Processed	: 1/31/2023 4:39:37 PM	Processed by	: System Administrator

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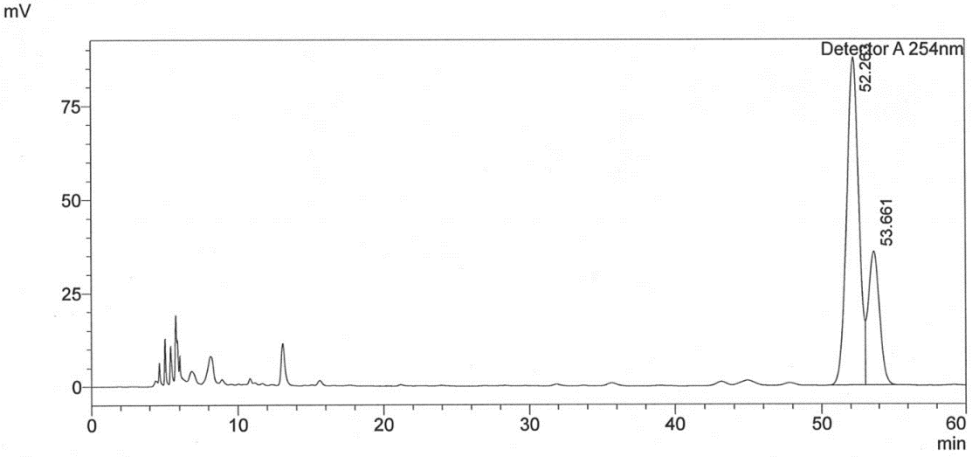
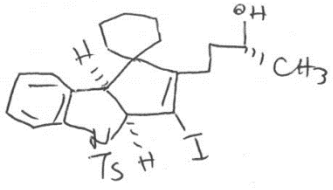


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	52.263	5194743	87651	72.535	2.90		
2	53.661	1966945	35905	27.465	1.00	V	
Total		7161688	123556				



SHIMADZU LabSolutions

Analysis Report

<Sample Information>

Sample Name	: AM423		
Sample ID	: 1.0f-IPA-1.5%;		
Data Filename	: AM423-005.lcd		
Method Filename	: 1.0_IPA_1.5%60min.lcm		
Batch Filename	:		
Vial #	: 1-1	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 1/17/2023 9:43:56 AM	Acquired by	: System Administrator
Date Processed	: 1/23/2023 11:40:14 AM	Processed by	: System Administrator

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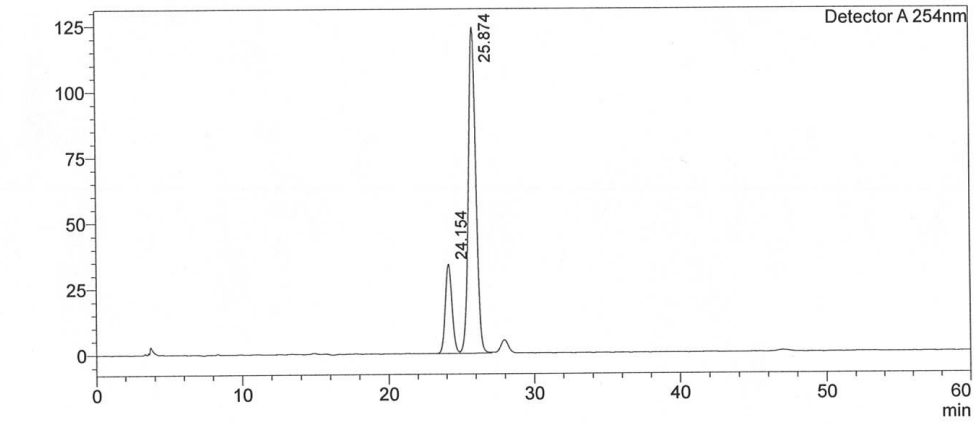
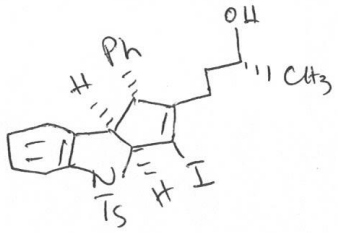


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	24.154	1103397	33938	20.007	1.0	V	
2	25.874	4411753	124019	79.993	4.0	V	
Total		5515150	157957				



SHIMADZU LabSolutions

Analysis Report

<Sample Information>

Sample Name	: AM432		
Sample ID	: 1f-IPA-1%;		
Data Filename	: AM432-1.lcd		
Method Filename	: 1.0_IPA_1%60min.lcm		
Batch Filename	:		
Vial #	: 1-1	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 1/30/2023 1:35:32 PM	Acquired by	: System Administrator
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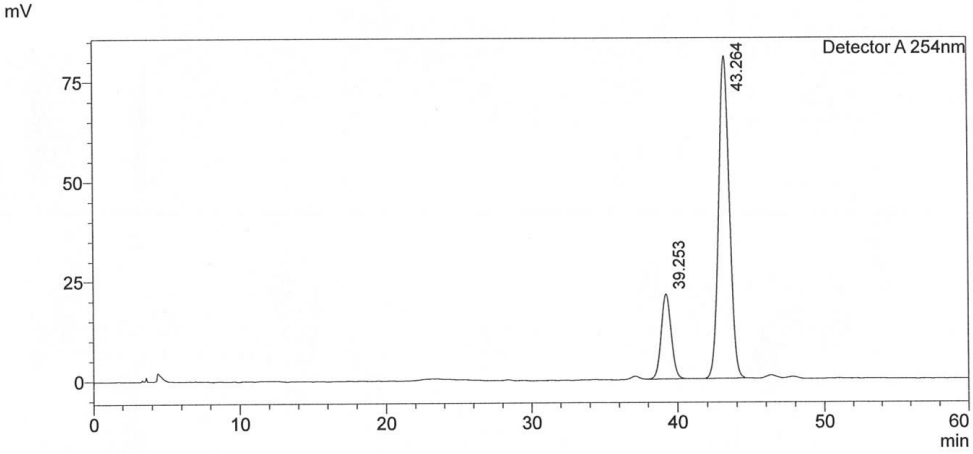
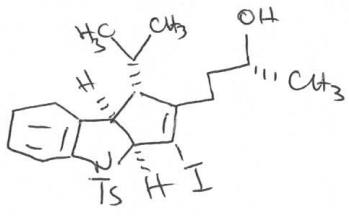


<Peak Table>

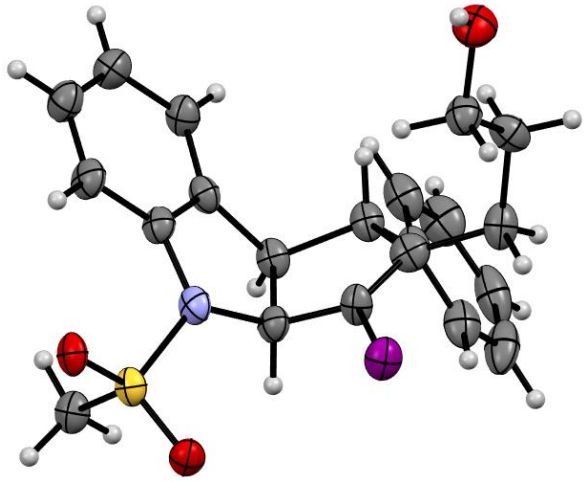
Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	39.253	1011913	21372	19.617	1.0	V	
2	43.264	4146534	80789	80.383	4.1		
Total		5158447	102161				



X-Ray Data

Compound 3b (CCDC Deposition Number 2240473)

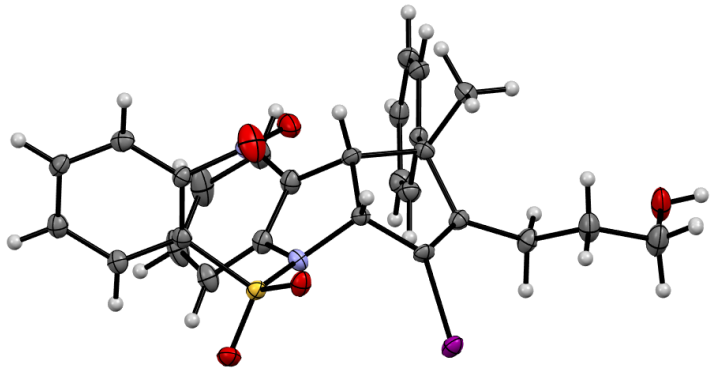


Crystal data and structure refinement for **3b**.

Identification code	**3b**	
Empirical formula	C21 H22 I N O3 S	
Formula weight	495.35	
Temperature	100.00(10) K	
Wavelength	1.54184 Å	
Crystal system	triclinic	
Space group	*P*-1	
Unit cell dimensions	*a* = 10.9449(2) Å	α = 77.386(3)°
	b = 13.1560(5) Å	β = 82.198(3)°
	c = 14.6317(6) Å	γ = 89.881(2)°
Volume	2036.12(12) Å^3	
Z	4	
Density (calculated)	1.616 Mg/m^3	
Absorption coefficient	13.488 mm^{-1}	
F(000)	992	
Crystal color, morphology	colourless, needle	
Crystal size	0.106 x 0.026 x 0.019 mm^3	
Theta range for data collection	3.444 to 80.720°	
Index ranges	$-13 \le h \le 13$, $-16 \le k \le 15$, $-18 \le l \le 18$	
Reflections collected	60921	
Independent reflections	13917 [*R*(int) = 0.075]	

Observed reflections	10953
Completeness to theta = 67.684°	99.9%
Absorption correction	Multi-scan
Max. and min. transmission	1.00000 and 0.59652
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	13917 / 0 / 492
Goodness-of-fit on F^2	1.059
Final *R* indices [*I*>2sigma(*I*)]	*R*1 = 0.0655, *wR*2 = 0.1814
R indices (all data)	*R*1 = 0.0819, *wR*2 = 0.1963
Largest diff. peak and hole	2.278 and -1.940 e.Å^{-3}

Compound 6e (CCDC Deposition Number 2240474)

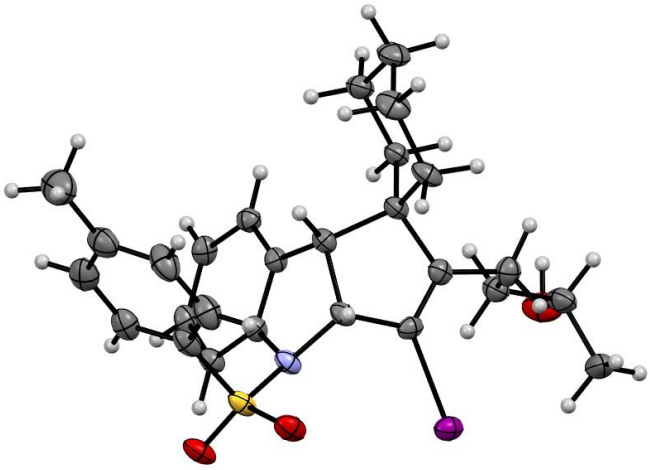


Crystal data and structure refinement for **6e** (major diastereomer).

Identification code	**6e**	
Empirical formula	C27 H25 I N2 O5 S	
Formula weight	616.45	
Temperature	100.00(10) K	
Wavelength	1.54184 Å	
Crystal system	triclinic	
Space group	*P*-1	
Unit cell dimensions	*a* = 10.3499(2) Å	α = 83.790(2)°
	b = 11.4812(2) Å	β = 76.551(2)°
	c = 11.8168(2) Å	γ = 65.058(2)°
Volume	1238.23(4) Å^3	
Z	2	
Density (calculated)	1.653 Mg/m^3	
Absorption coefficient	11.303 mm^{-1}	

F(000)	620
Crystal color, morphology	colourless, block
Crystal size	0.06 x 0.053 x 0.036 mm^3
Theta range for data collection	3.846 to 80.507°
Index ranges	$-13 \le h \le 13$, $-14 \le k \le 14$, $-14 \le l \le 15$
Reflections collected	41813
Independent reflections	5316 [*R*(int) = 0.0455]
Observed reflections	5092
Completeness to theta = 74.504°	99.7%
Absorption correction	Multi-scan
Max. and min. transmission	1.00000 and 0.83490
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5316 / 0 / 336
Goodness-of-fit on F^2	1.140
Final *R* indices [*I*>2sigma(*I*)]	*R*1 = 0.0281, *wR*2 = 0.0800
R indices (all data)	*R*1 = 0.0292, *wR*2 = 0.0807
Largest diff. peak and hole	1.014 and -1.014 e.$Å^{-3}$

Compound 8c (CCDC Deposition Number 2240475)

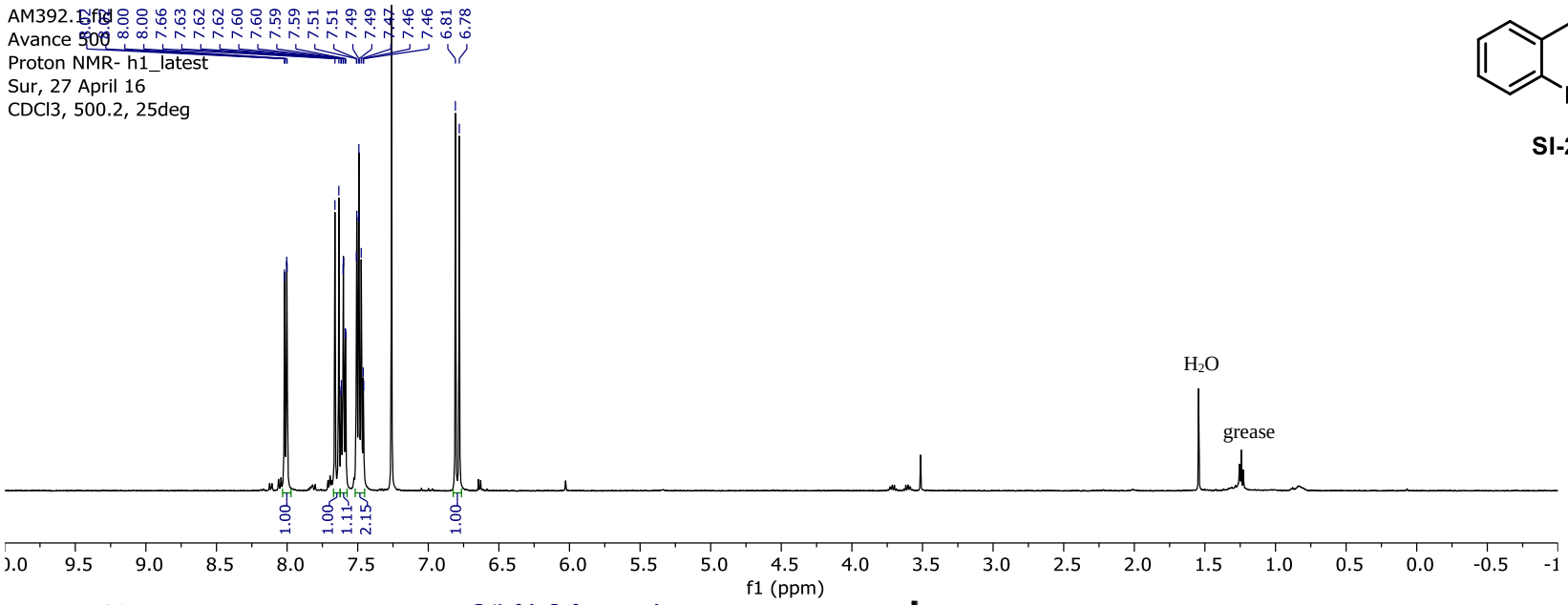


Crystal data and structure refinement for **8c**.

Identification code	**8c**
Empirical formula	C27 H32 I N O3 S
Formula weight	577.49
Temperature	100.00(10) K
Wavelength	1.54184 Å

Crystal system	triclinic	
Space group	*P*-1	
Unit cell dimensions	a = 10.0403(3) Å	α = 82.958(2)°
	b = 10.7542(3) Å	β = 72.346(2)°
	c = 13.6818(2) Å	γ = 62.821(3)°
Volume	1252.07(6) Å^3	
Z	2	
Density (calculated)	1.532 Mg/m^3	
Absorption coefficient	11.054 mm^{-1}	
F(000)	588	
Crystal color, morphology	colourless, plate	
Crystal size	0.2 x 0.143 x 0.052 mm^3	
Theta range for data collection	3.391 to 80.461°	
Index ranges	$-10 \le h \le 12$, $-13 \le k \le 13$, $-17 \le l \le 17$	
Reflections collected	42710	
Independent reflections	5389 [R(int) = 0.0479]	
Observed reflections	5251	
Completeness to theta = 74.504°	99.7%	
Absorption correction	Multi-scan	
Max. and min. transmission	1.00000 and 0.36742	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5389 / 51 / 351	
Goodness-of-fit on F^2	1.092	
Final R indices [I>2sigma(I)]	R1 = 0.0288, wR2 = 0.0727	
R indices (all data)	R1 = 0.0294, wR2 = 0.0732	
Largest diff. peak and hole	0.451 and -0.920 e.Å^{-3}	

NMR Data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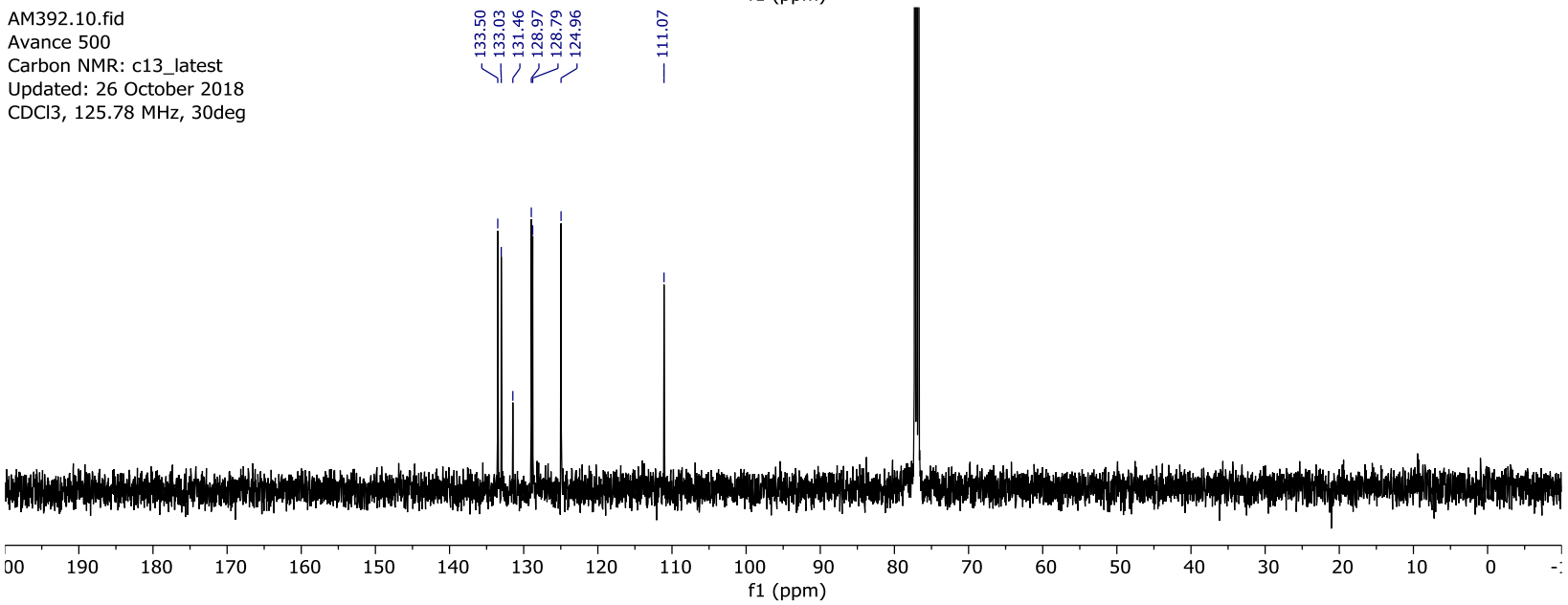
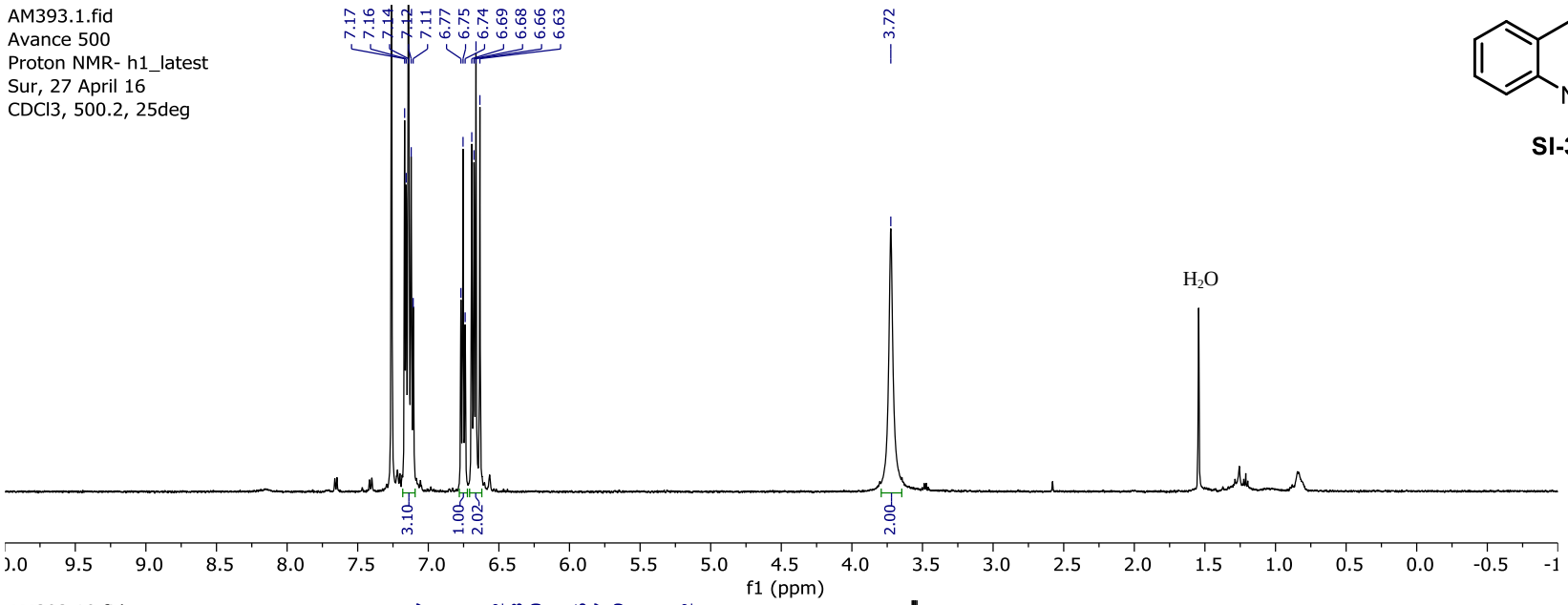
grease
f1 (ppm)

Br
NO2

SI-2

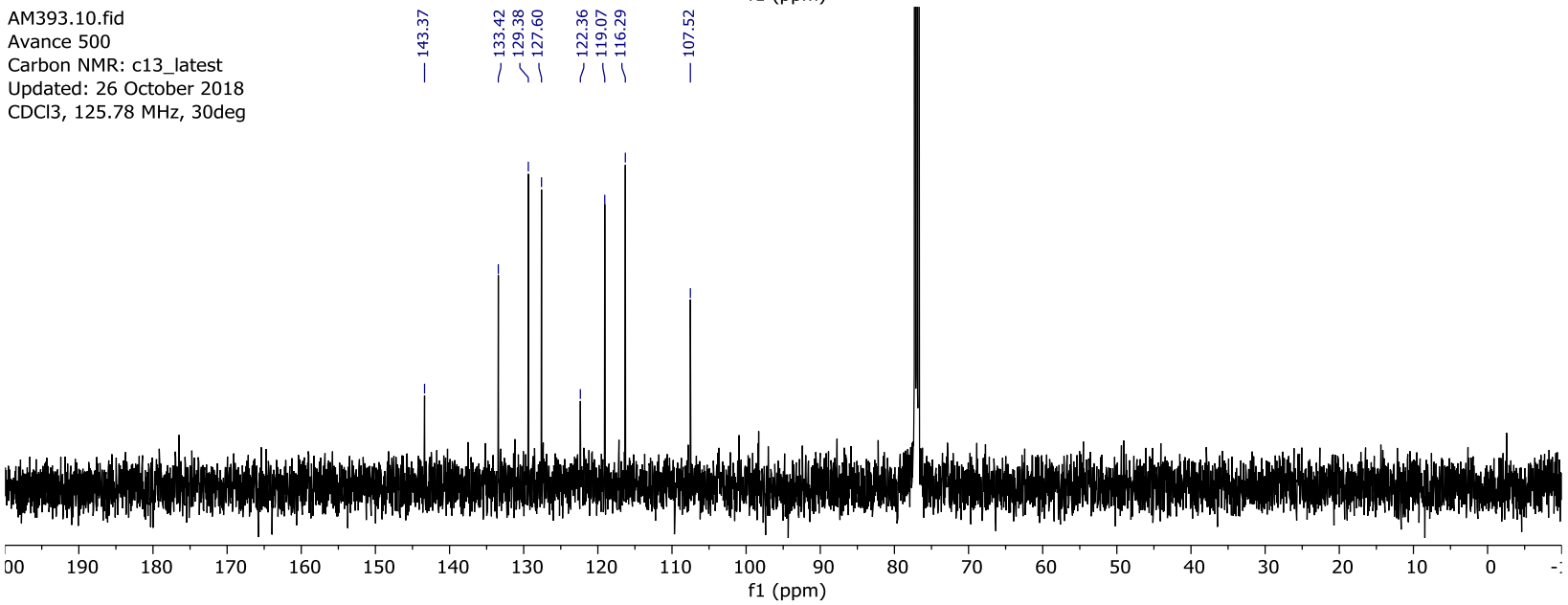

AM392.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
133.50
133.03
131.46
128.97
128.79
124.96
111.07
f1 (ppm)

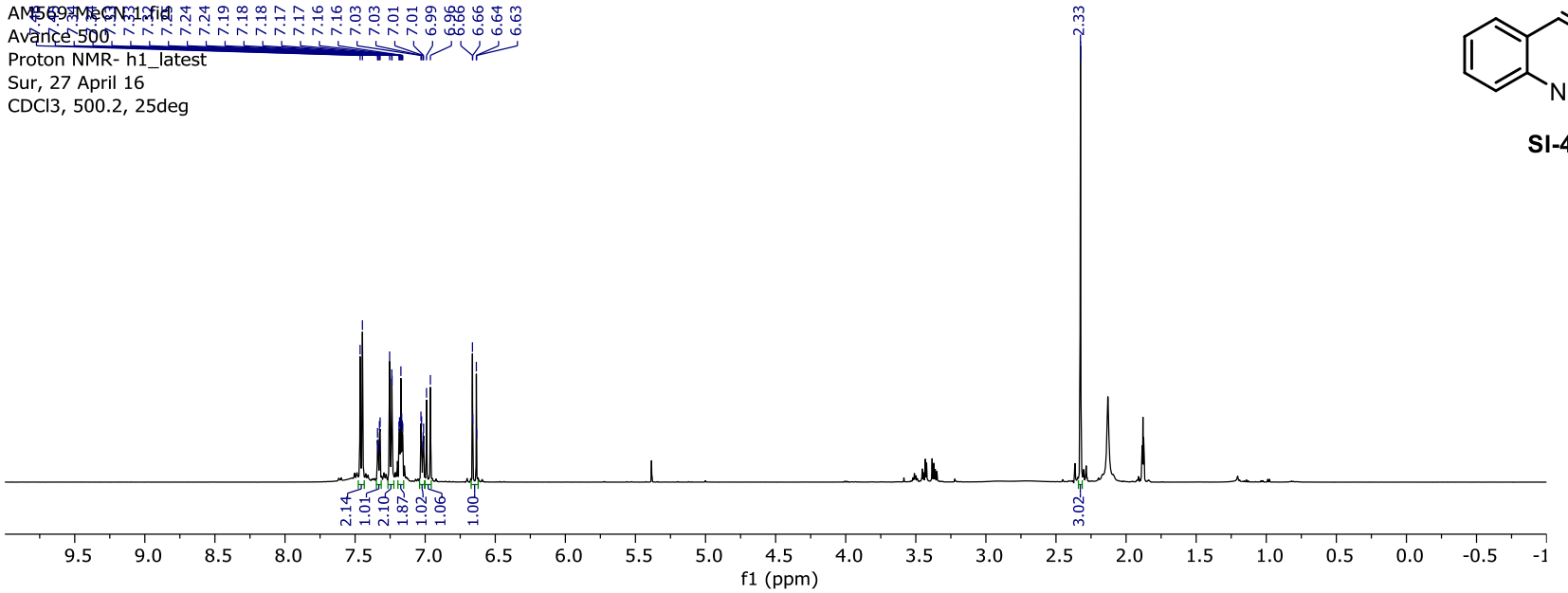
NMR Data


AM393.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
7.17
7.16
7.14
7.12
7.11
6.77
6.75
6.74
6.69
6.68
6.66
6.63
3.72
H2O
3.10
1.00
2.02
2.00
f1 (ppm)

Br
NH2

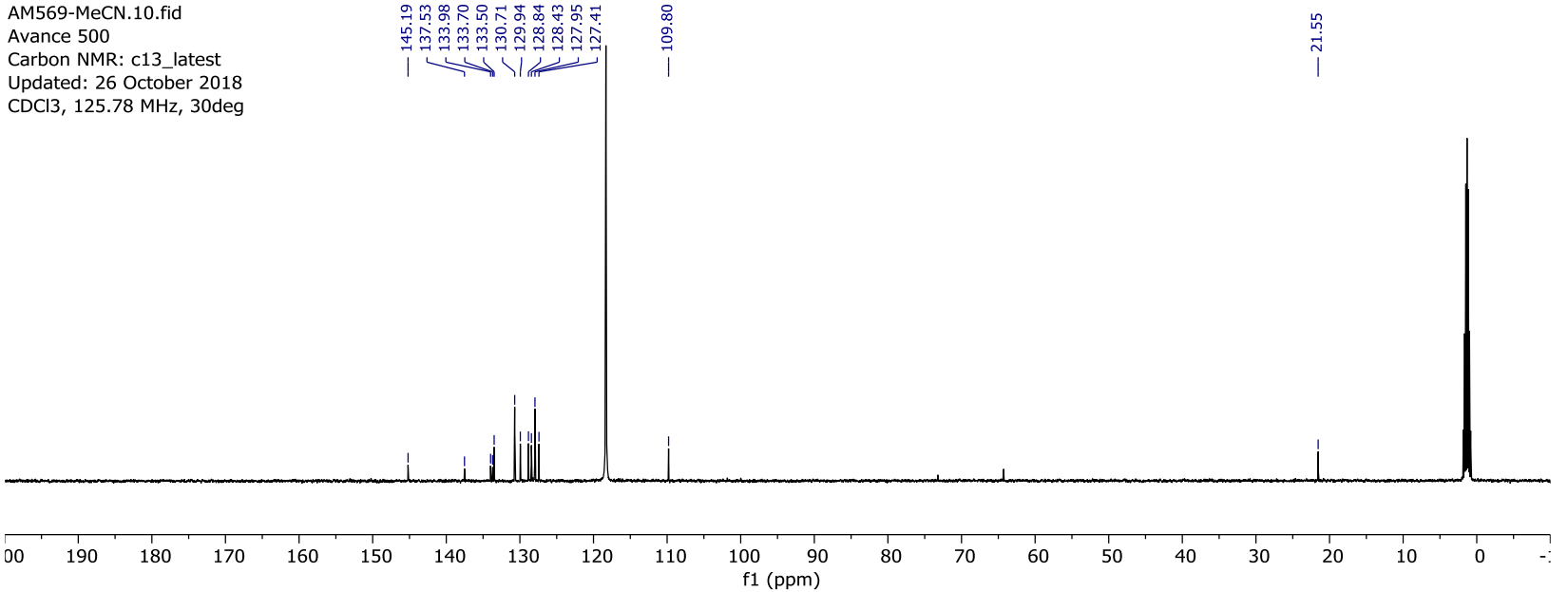
SI-3


AM393.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
143.37
133.42
129.38
127.60
122.36
119.07
116.29
107.52
f1 (ppm)

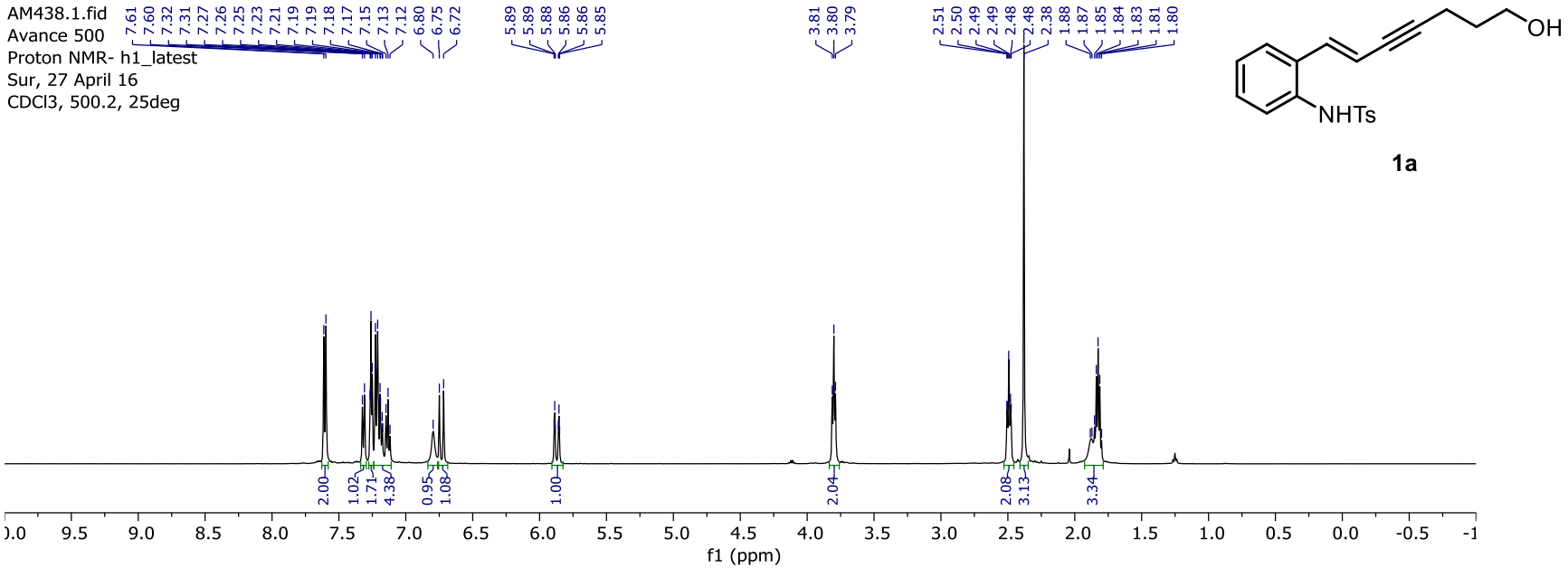

AM569-MeCN.11.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
2.33
2.14
1.01
2.10
1.87
1.02
1.06
1.00
3.02
f1 (ppm)

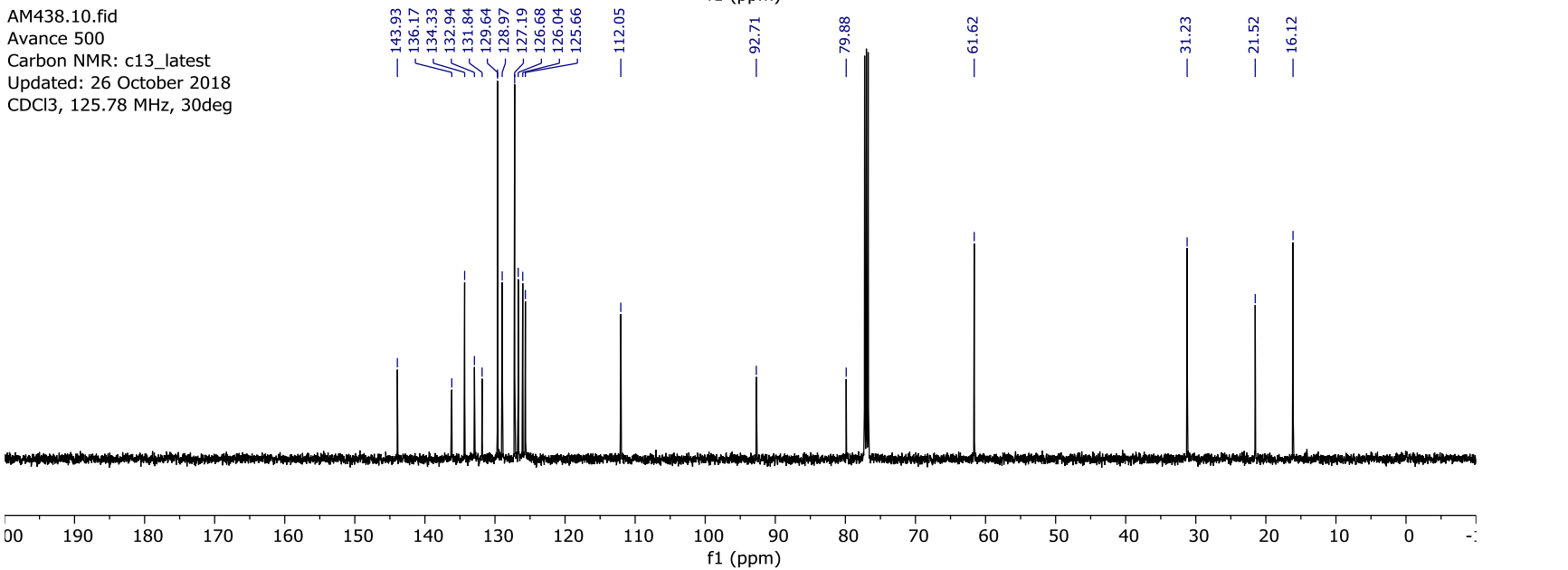
Br
NHTs

SI-4

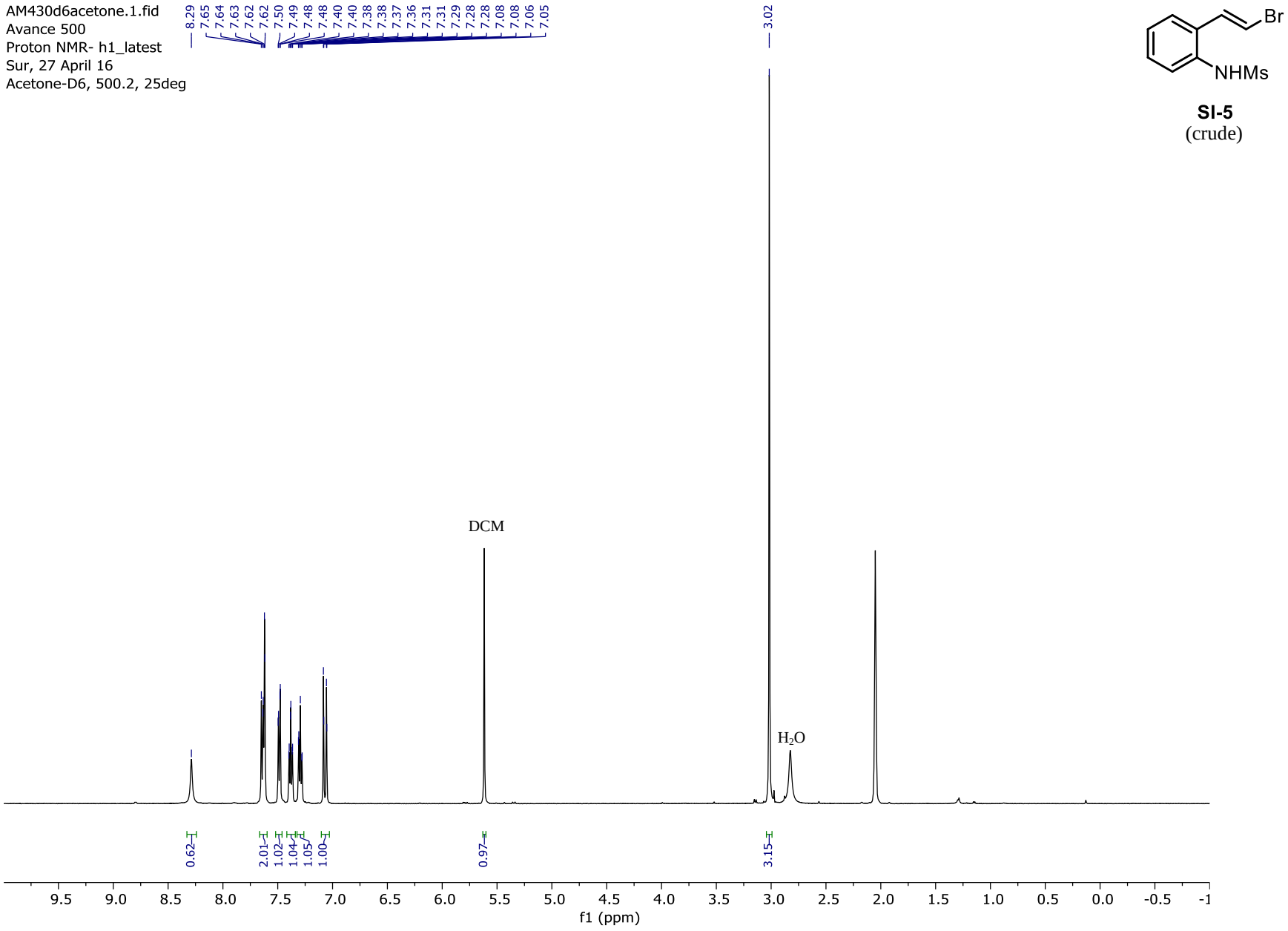

AM569-MeCN.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
145.19
137.53
133.98
133.70
133.50
130.71
129.94
128.84
128.43
127.95
127.41
109.80
21.55
f1 (ppm)

NMR Data


AM438.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
7.61 7.60 7.32 7.31 7.27 7.26 7.25 7.23 7.21 7.19 7.19 7.18 7.17 7.15 7.13 7.12 6.80 6.75 6.72
5.89 5.89 5.88 5.86 5.86 5.85
3.81 3.80 3.79
2.51 2.50 2.49 2.49 2.48 2.48 2.38
1.88 1.87 1.85 1.84 1.83 1.81 1.80
2.00 1.02 1.71 4.38 0.95 1.08 1.00 2.04 2.08 3.13 3.34
f1 (ppm)
OH
NHTs
1a

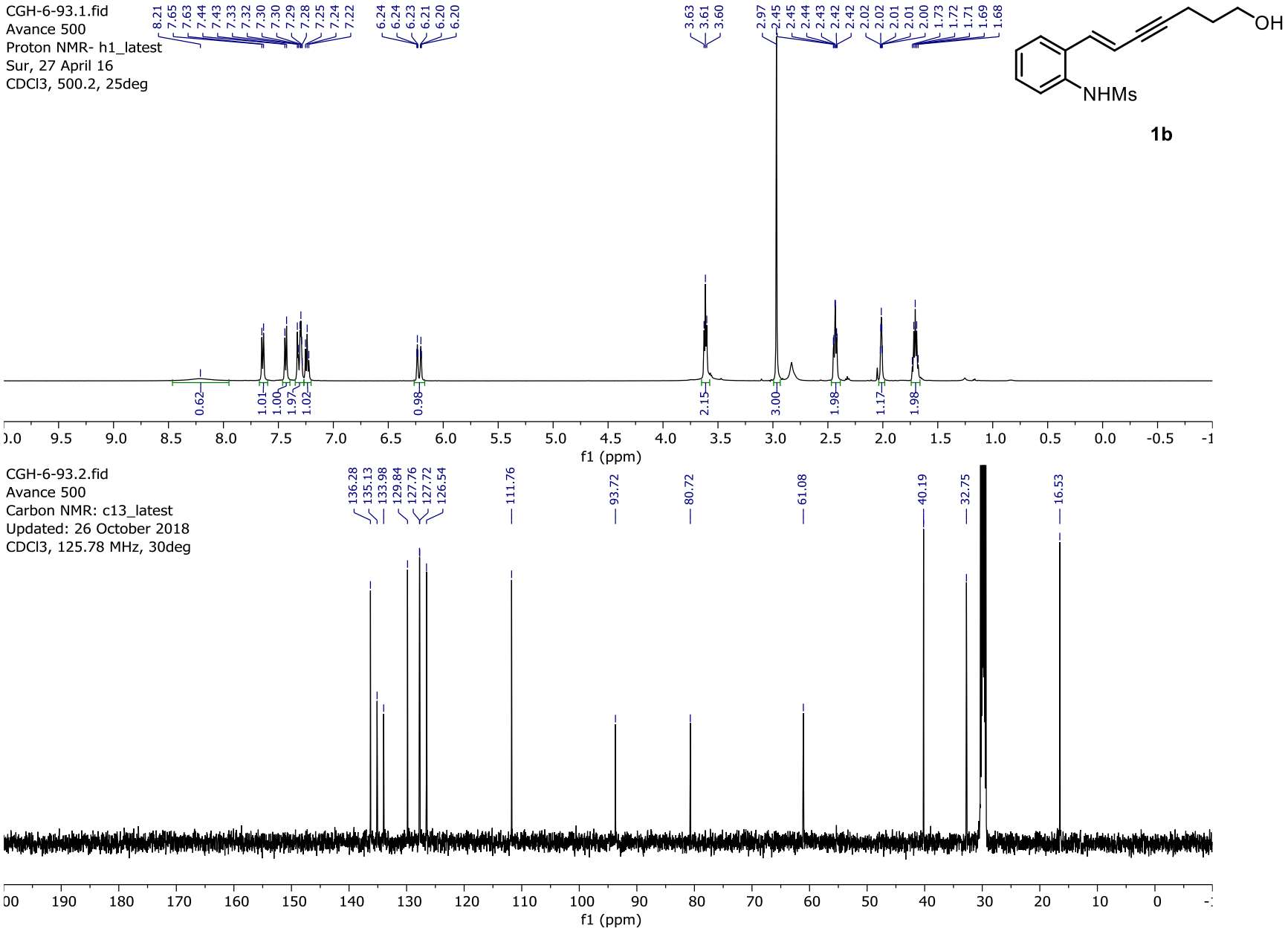

AM438.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
143.93 136.17 134.33 132.94 131.84 129.64 128.97 127.19 126.68 126.04 125.66
112.05
92.71
79.88
61.62
31.23
21.52
16.12
f1 (ppm)

NMR Data

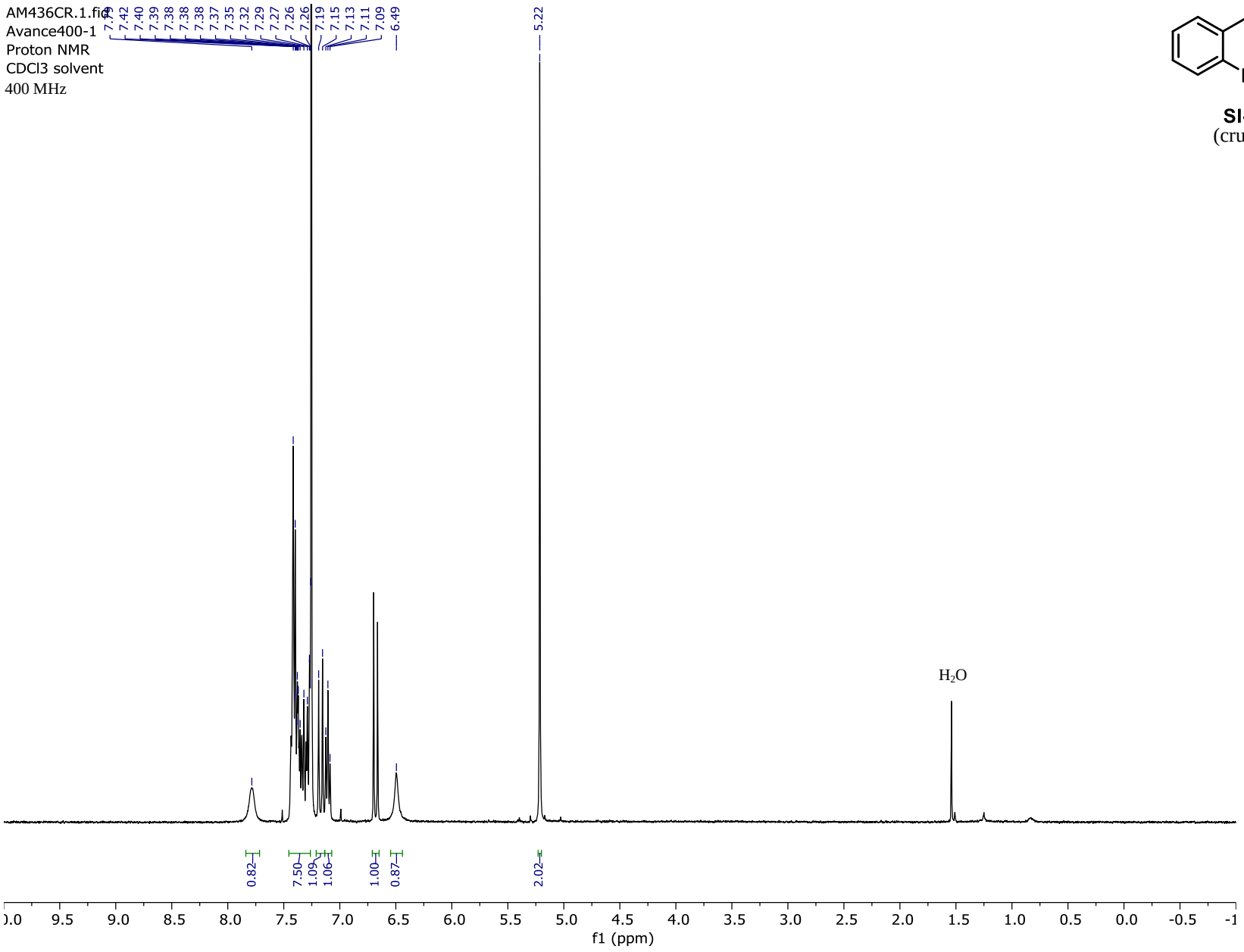


SI-5
(crude)

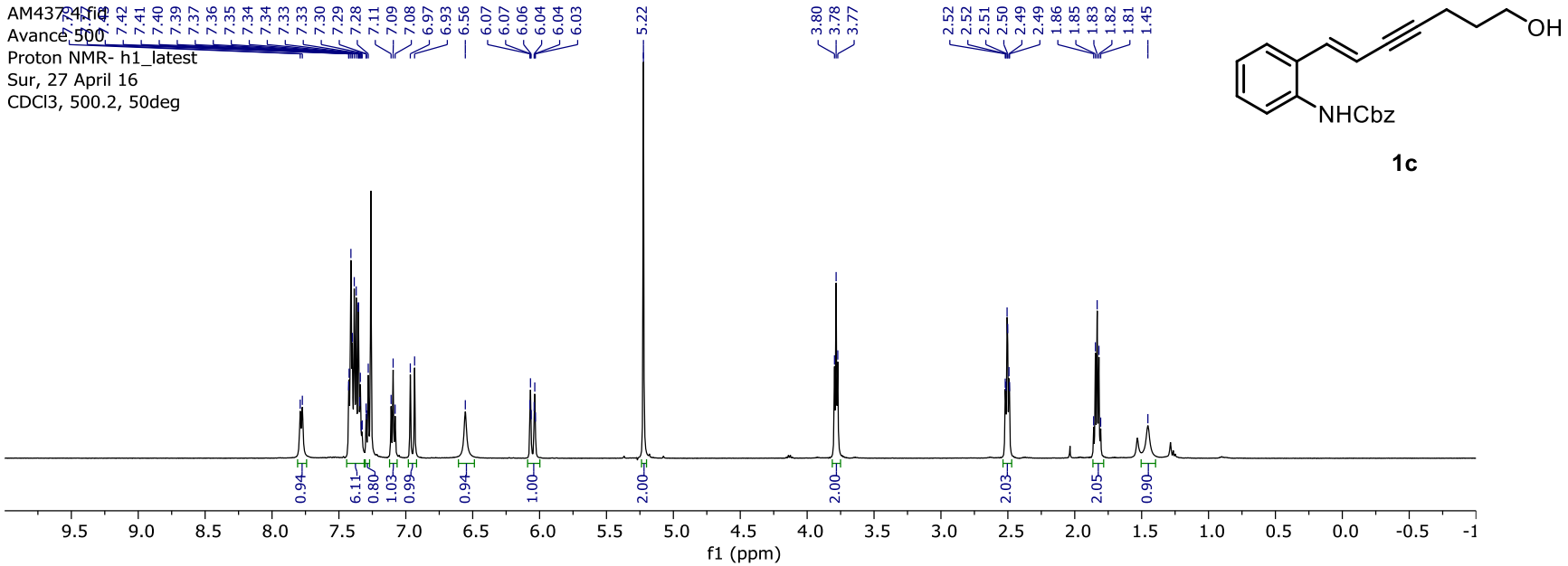
NMR Data

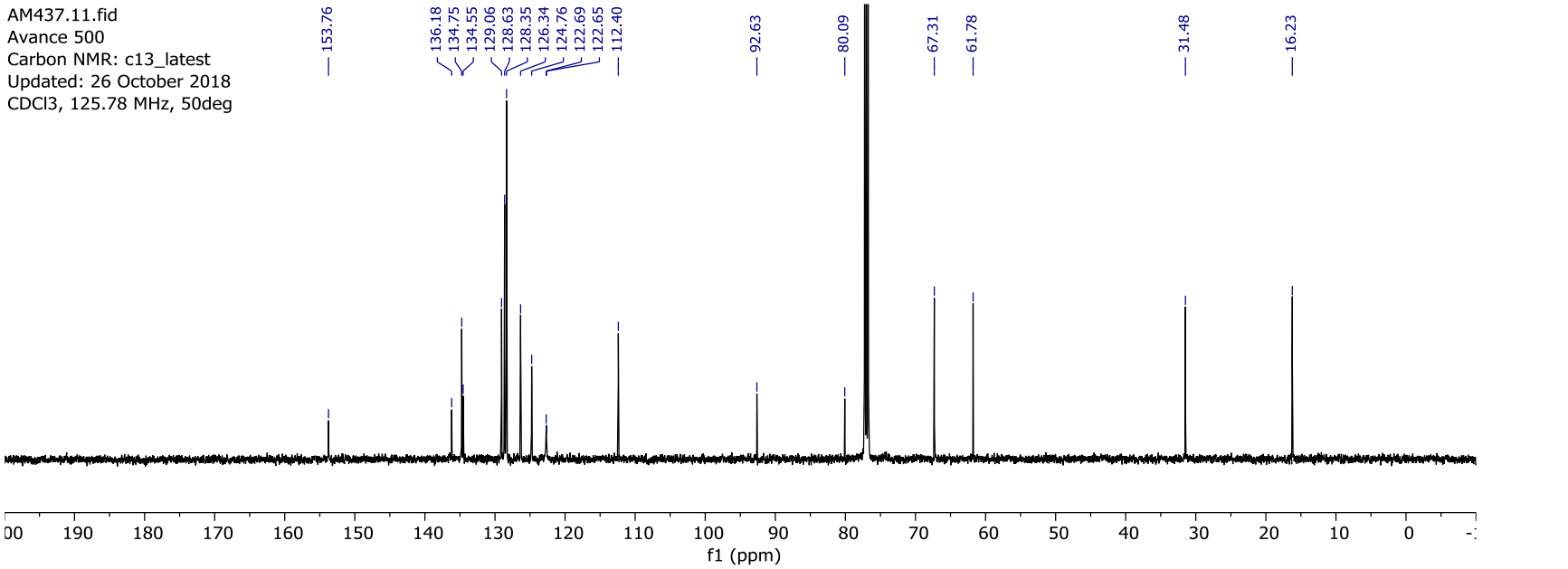

CGH-6-93.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
8.21 7.65 7.63 7.44 7.43 7.33 7.32 7.30 7.30 7.29 7.28 7.25 7.24 7.22
6.24 6.24 6.23 6.21 6.20 6.20
3.63 3.61 3.60
2.97 2.45 2.45 2.44 2.43 2.42 2.42
2.02 2.02 2.01 2.01 2.00 1.73 1.72 1.71 1.69 1.68
0.62 1.01 1.00 1.97 1.02 0.98 2.15 3.00 1.98 1.17 1.98
f1 (ppm)
OH
NHMs
1b
CGH-6-93.2.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
136.28 135.13 133.98 129.84 127.76 127.72 126.54 111.76 93.72 80.72 61.08 40.19 32.75 16.53
f1 (ppm)

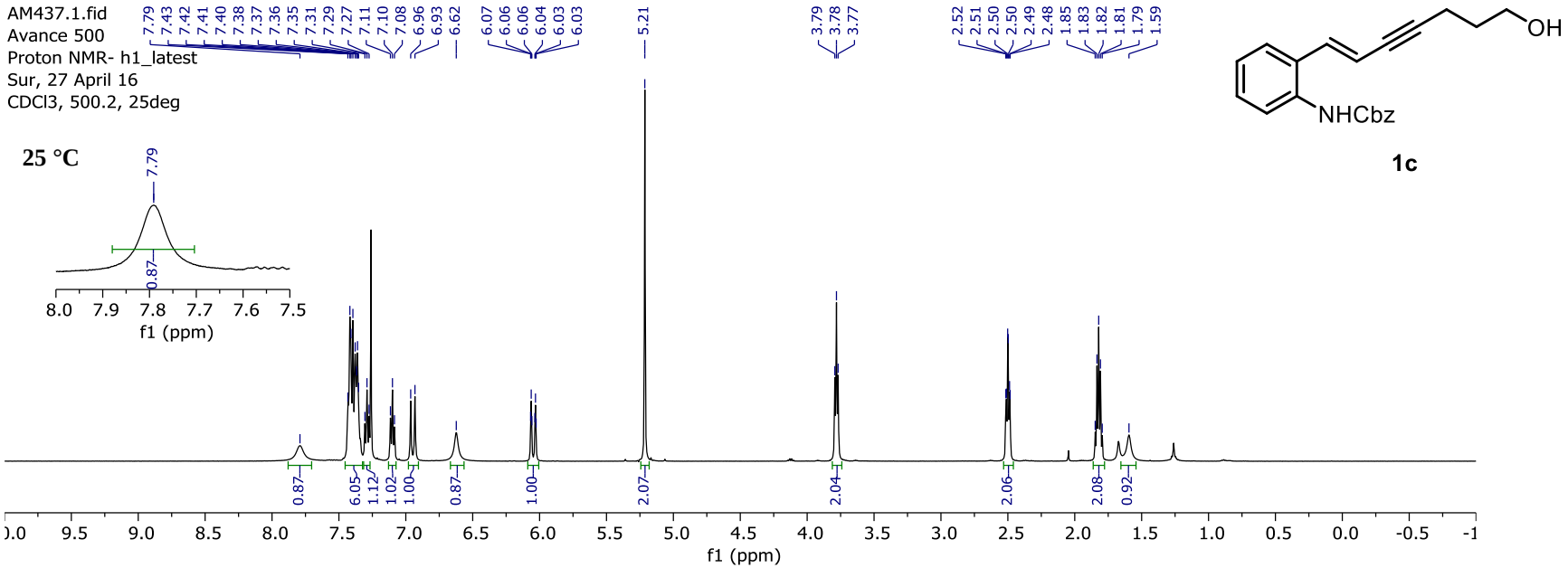
NMR Data



SI-6
(crude)

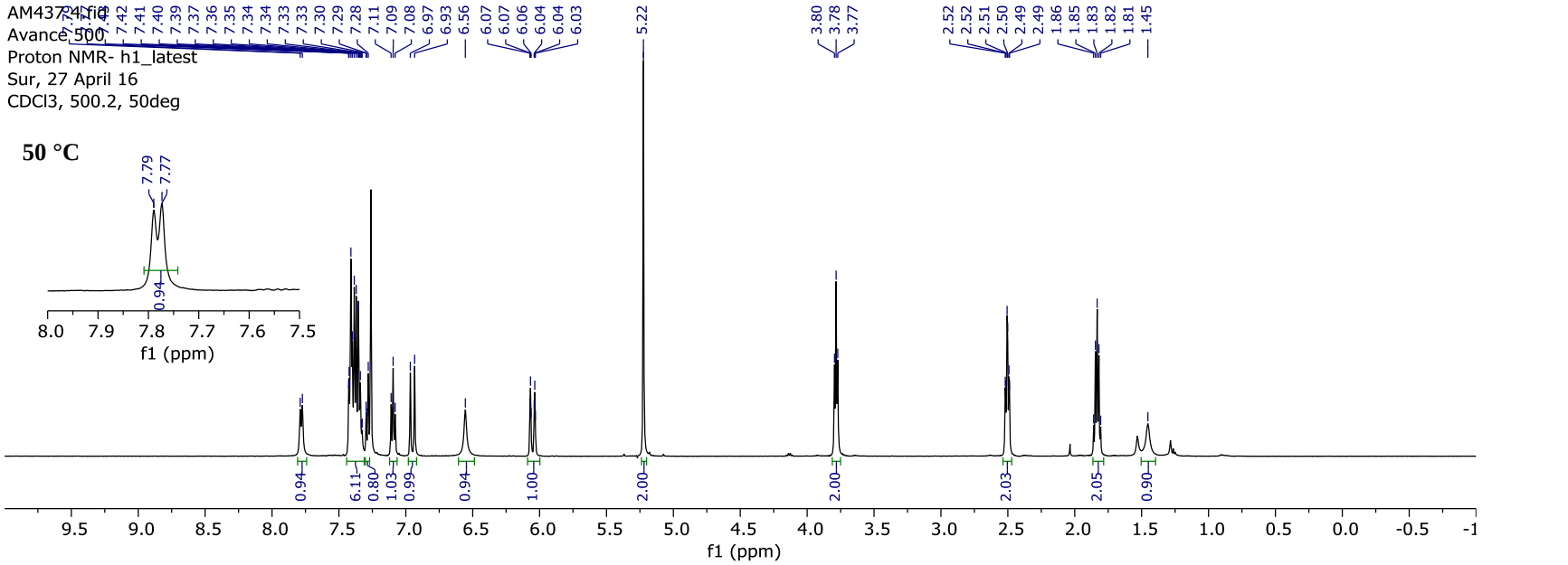

AM437.14.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 50deg
OH
NHCbz
1c
f1 (ppm)


AM437.11.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 50deg
f1 (ppm)

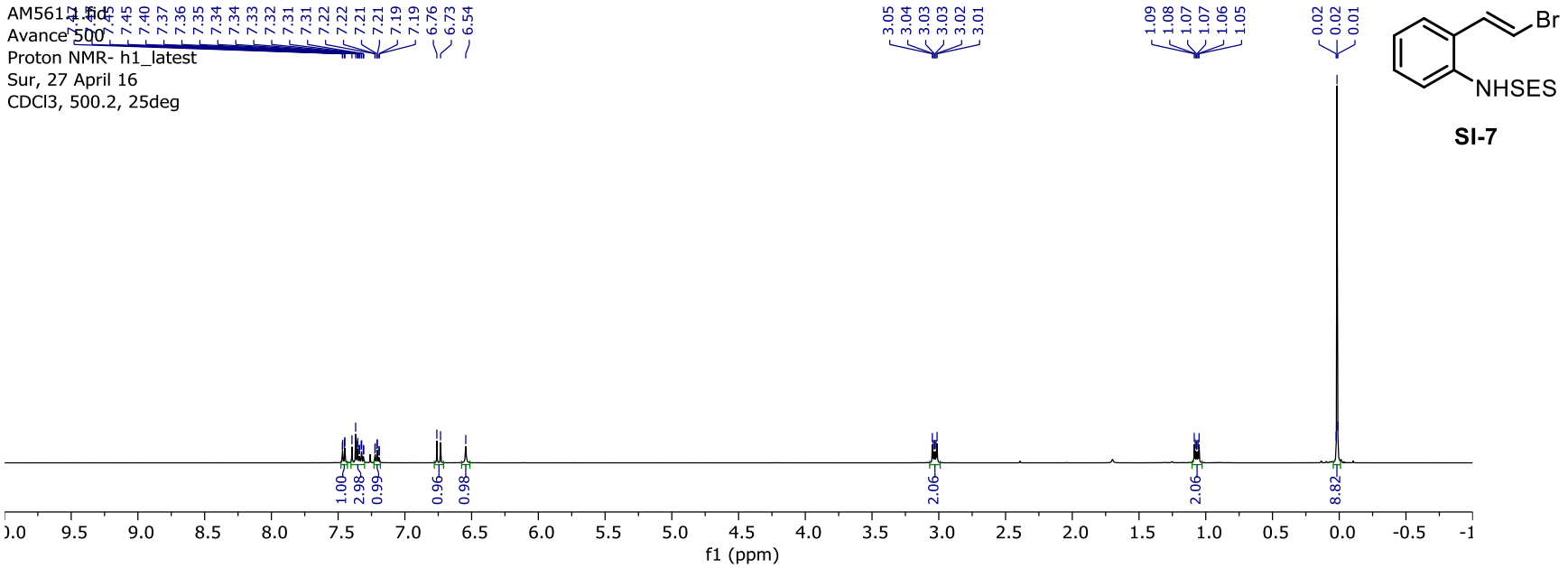

AM437.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
25 °C
f1 (ppm)

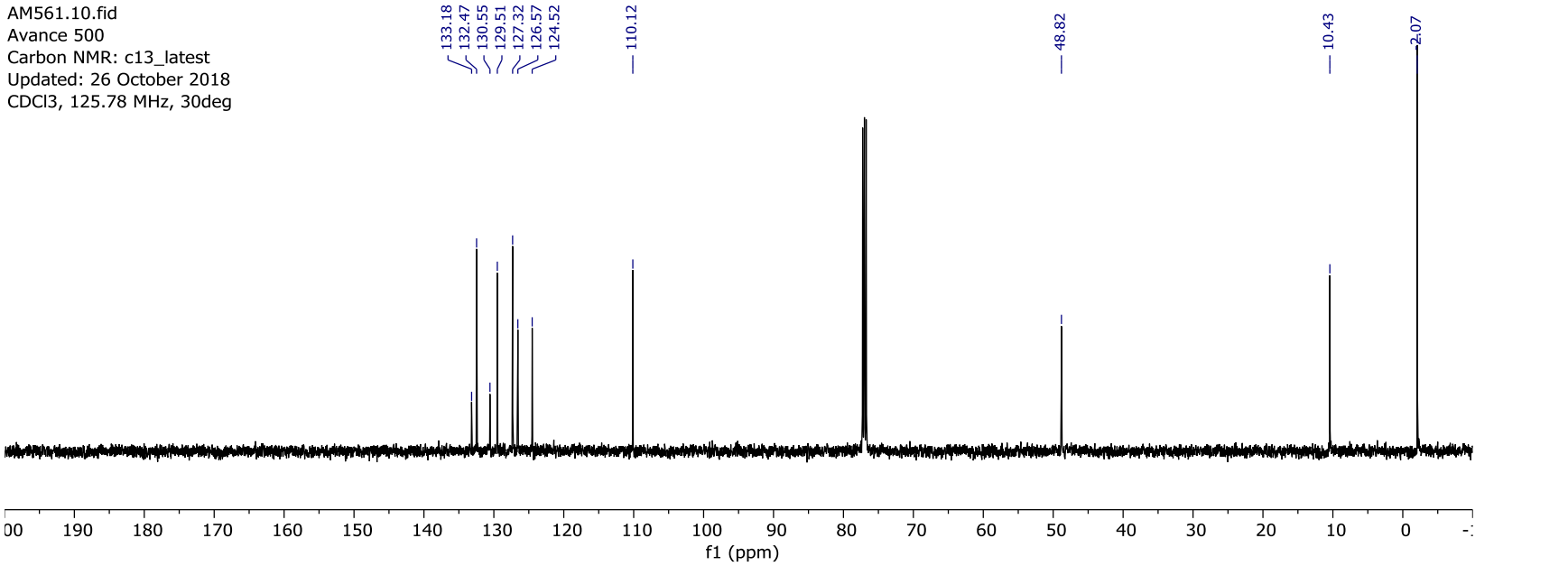
OH
NHCbz

1c

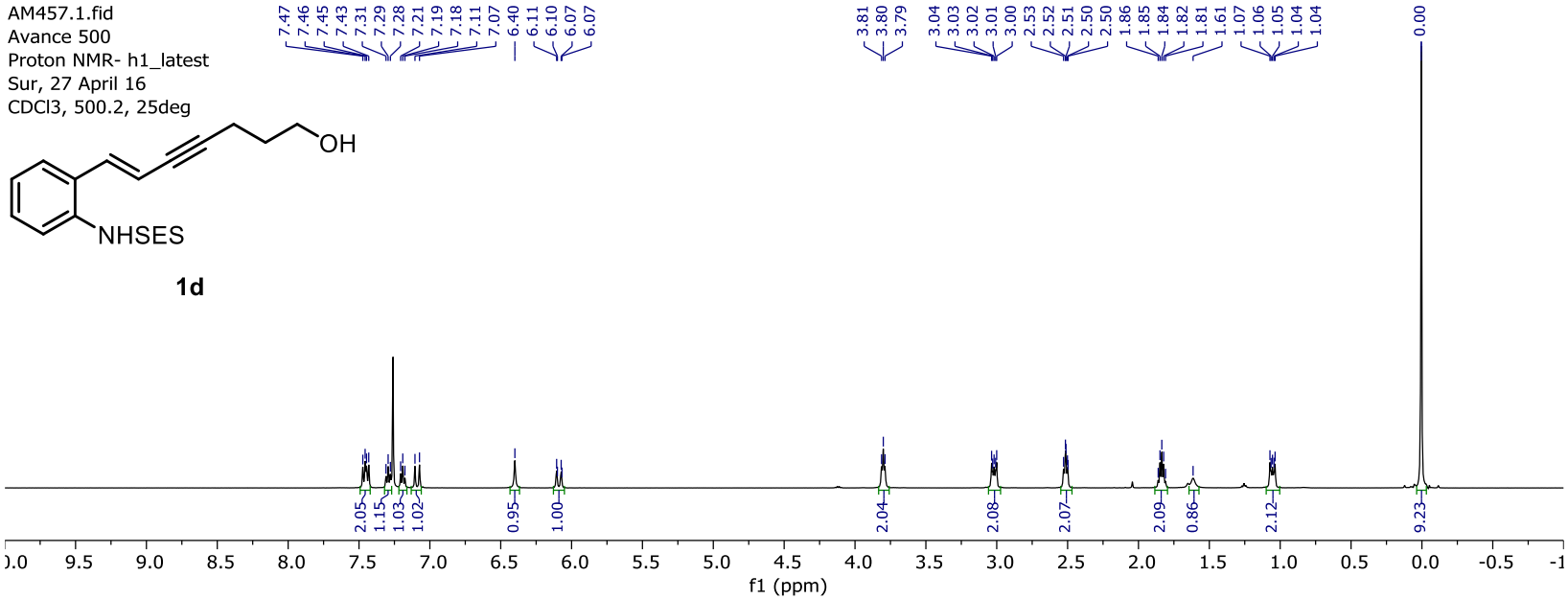

AM437.4.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 50deg
50 °C
f1 (ppm)

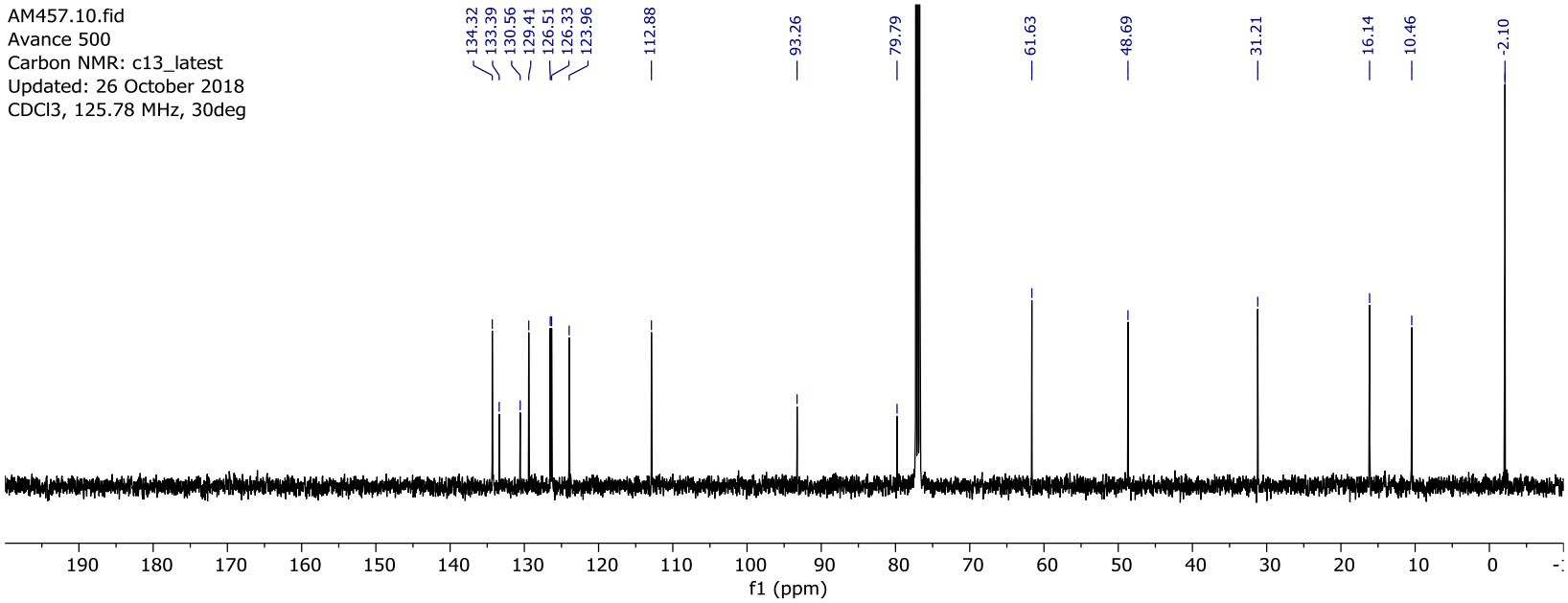
NMR Data


AM561.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
Br
NHSES
SI-7
f1 (ppm)

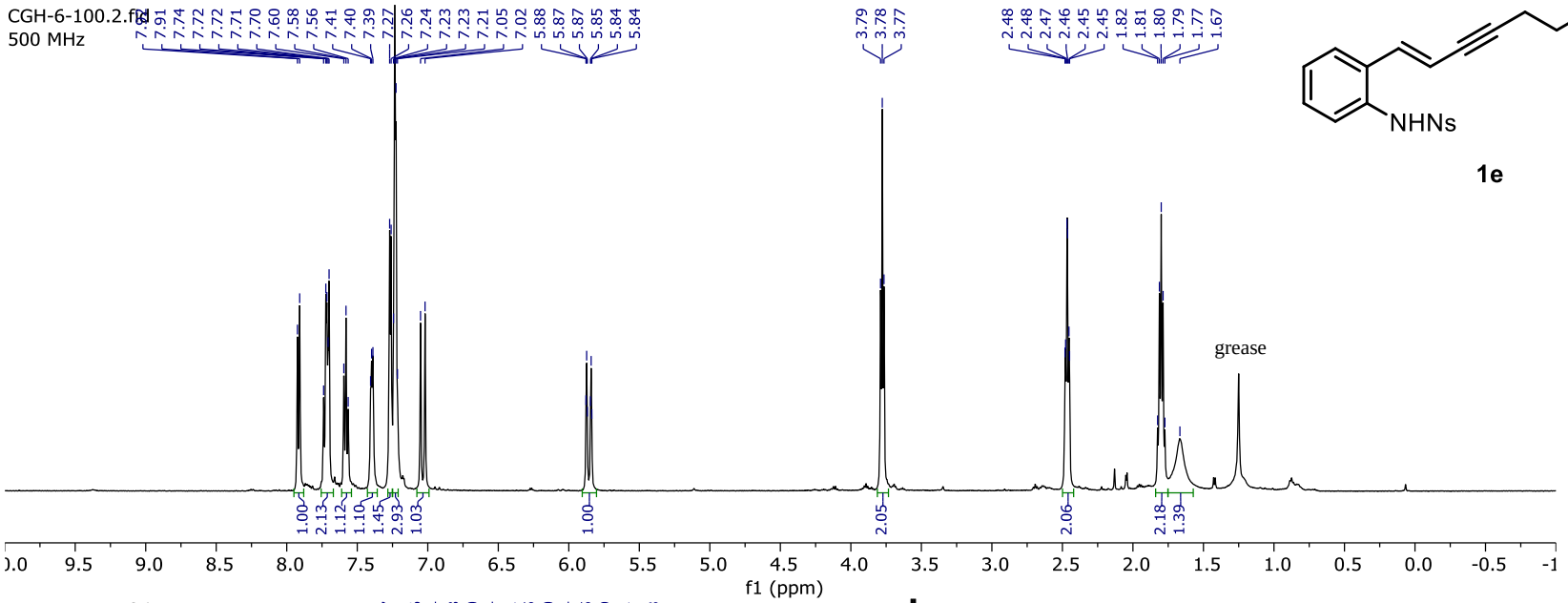

AM561.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

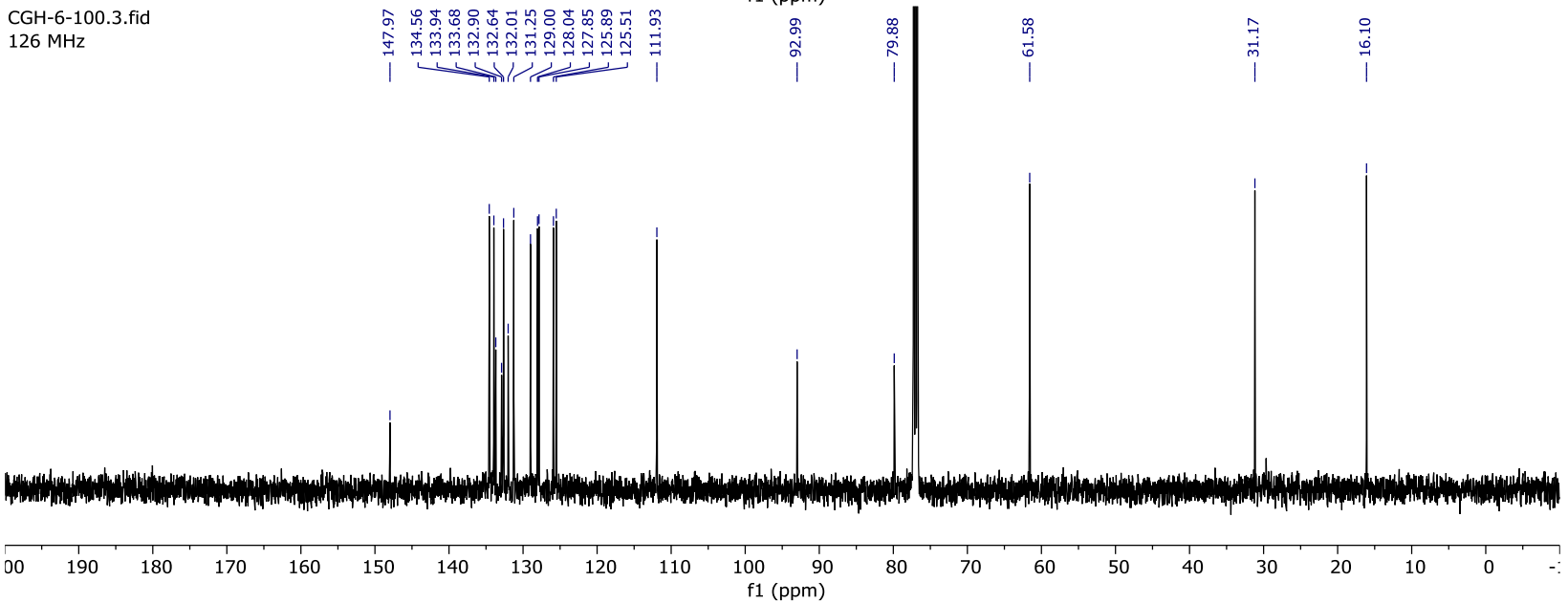
NMR Data


AM457.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
OH
NHSES
1d
f1 (ppm)

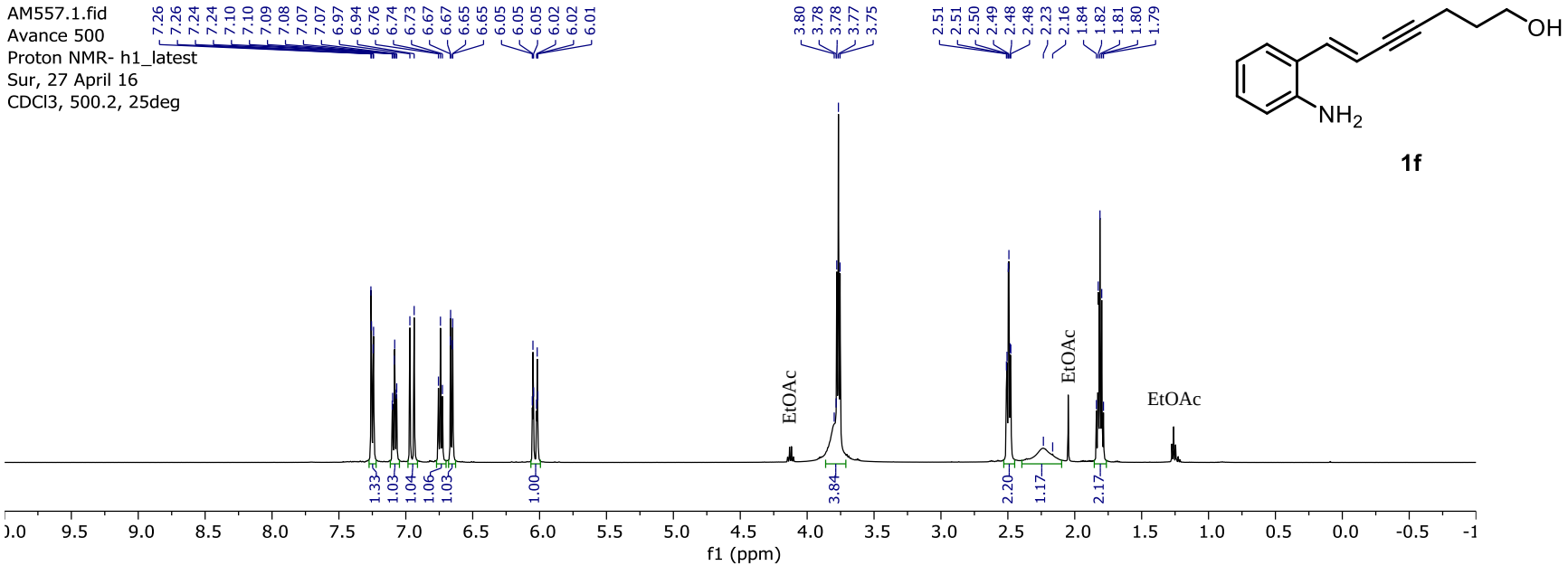

AM457.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

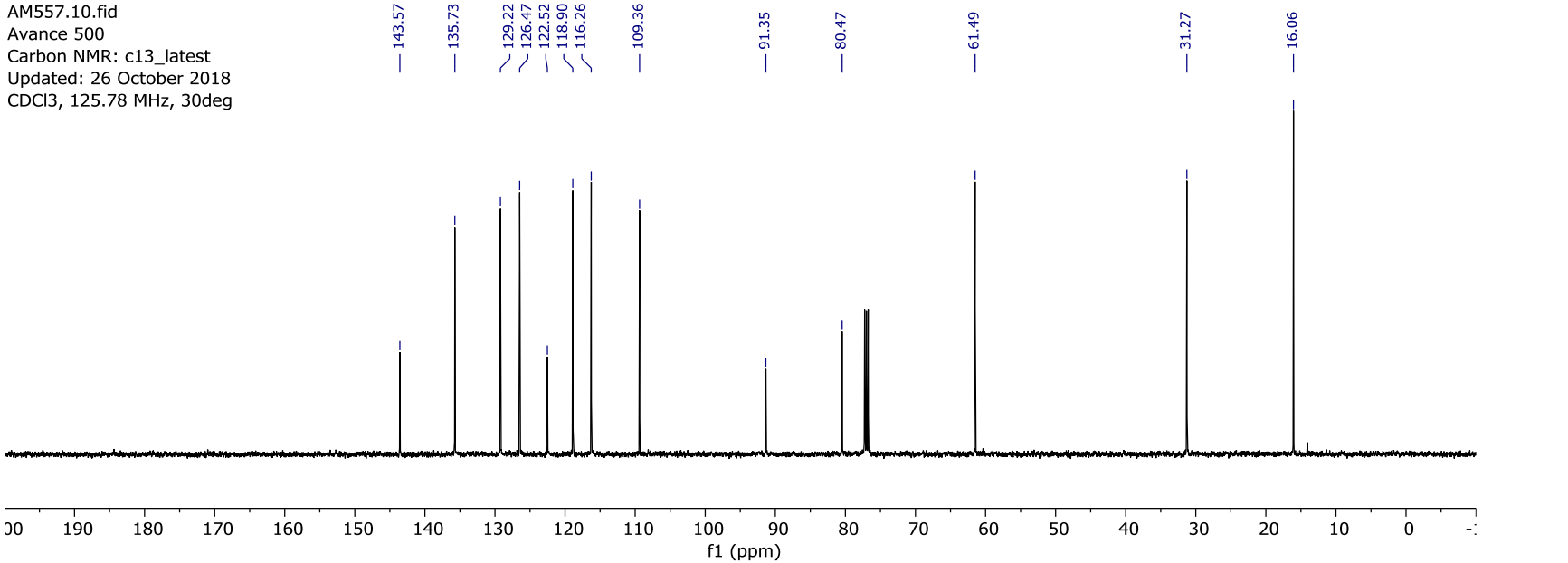
NMR Data


CGH-6-100.2.fid
500 MHz
7.92 7.91 7.74 7.72 7.72 7.71 7.70 7.60 7.58 7.56 7.41 7.40 7.39 7.27 7.26 7.24 7.23 7.21 7.05 7.02 5.88 5.87 5.87 5.85 5.84 5.84
3.79 3.78 3.77
2.48 2.48 2.47 2.46 2.45 2.45 1.82 1.81 1.80 1.79 1.77 1.67
OH
NHNs
1e
grease
1.00 2.13 1.12 1.10 1.45 2.93 1.03 1.00 2.05 2.06 2.18 1.39
f1 (ppm)

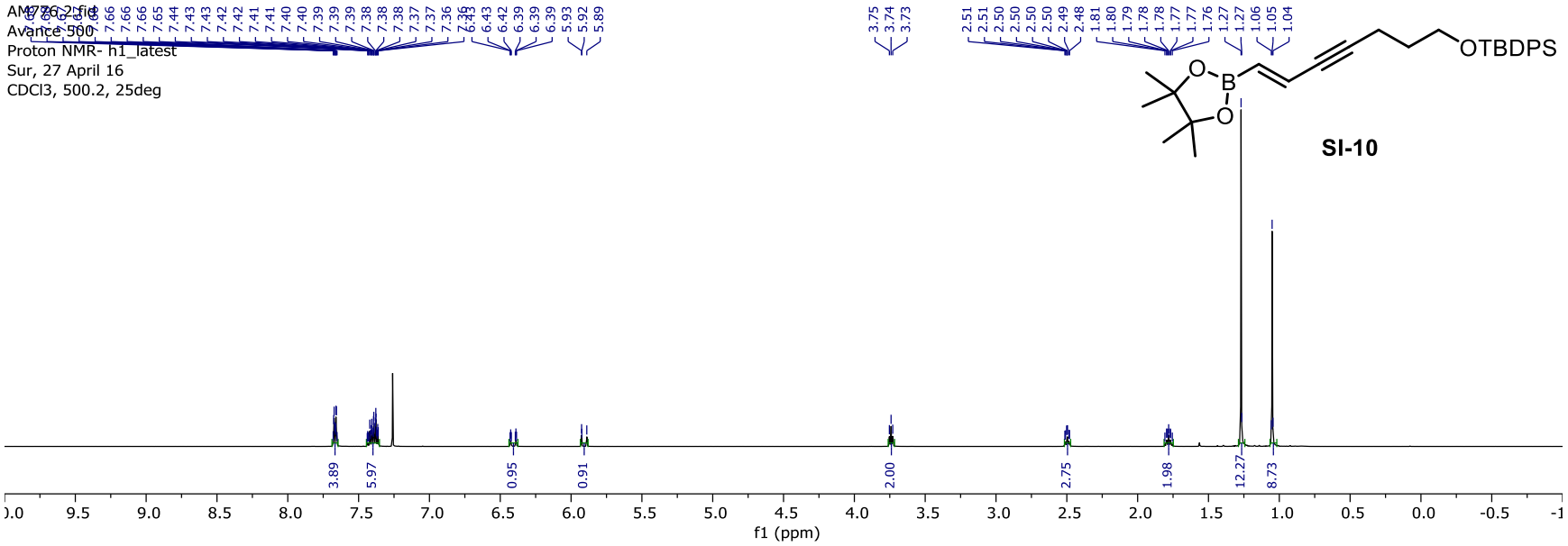

CGH-6-100.3.fid
126 MHz
147.97 134.56 133.94 133.68 132.90 132.64 132.01 131.25 129.00 128.04 127.85 125.89 125.51 111.93 92.99 79.88 61.58 31.17 16.10
f1 (ppm)

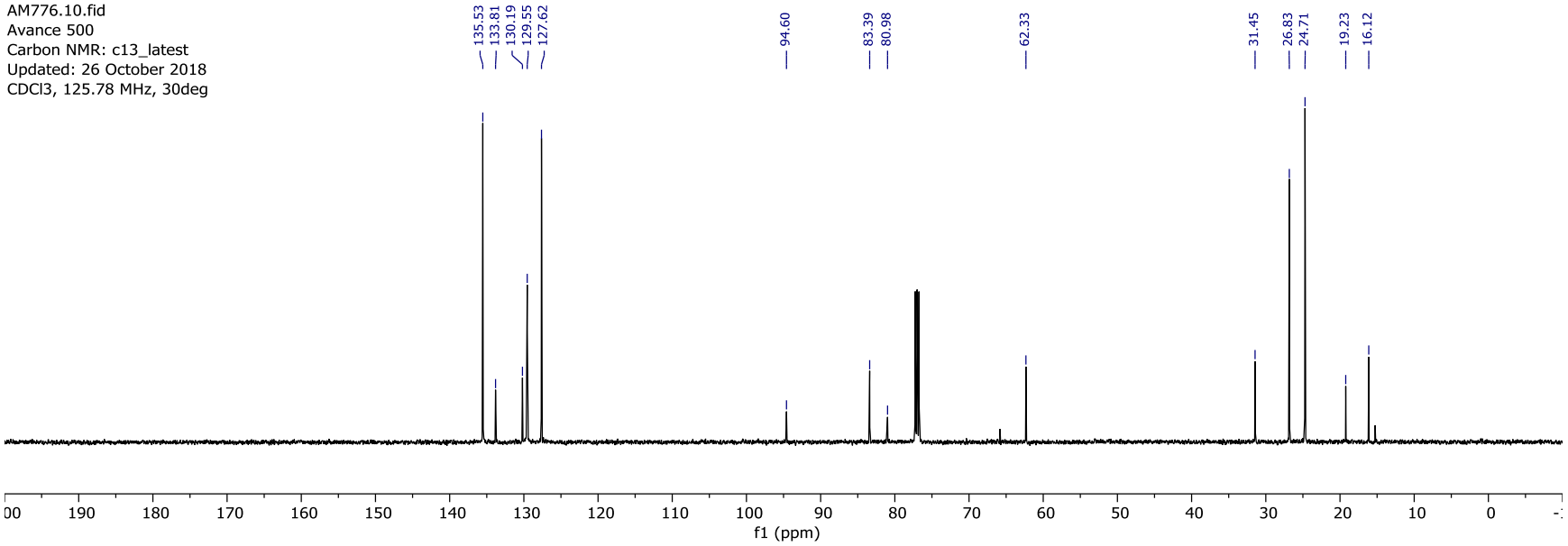
NMR Data


AM557.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
7.26 7.26 7.24 7.24 7.10 7.10 7.09 7.08 7.07 7.07 6.97 6.94 6.76 6.74 6.73 6.67 6.67 6.65 6.65 6.05 6.05 6.05 6.02 6.02 6.01
3.80 3.78 3.78 3.77 3.75
2.51 2.51 2.50 2.49 2.48 2.48 2.23 2.16 1.84 1.82 1.81 1.80 1.79
OH
NH2
1f
EtOAc
EtOAc
EtOAc
1.33 1.03 1.04 1.06 1.03 1.00 3.84 2.20 1.17 2.17
f1 (ppm)

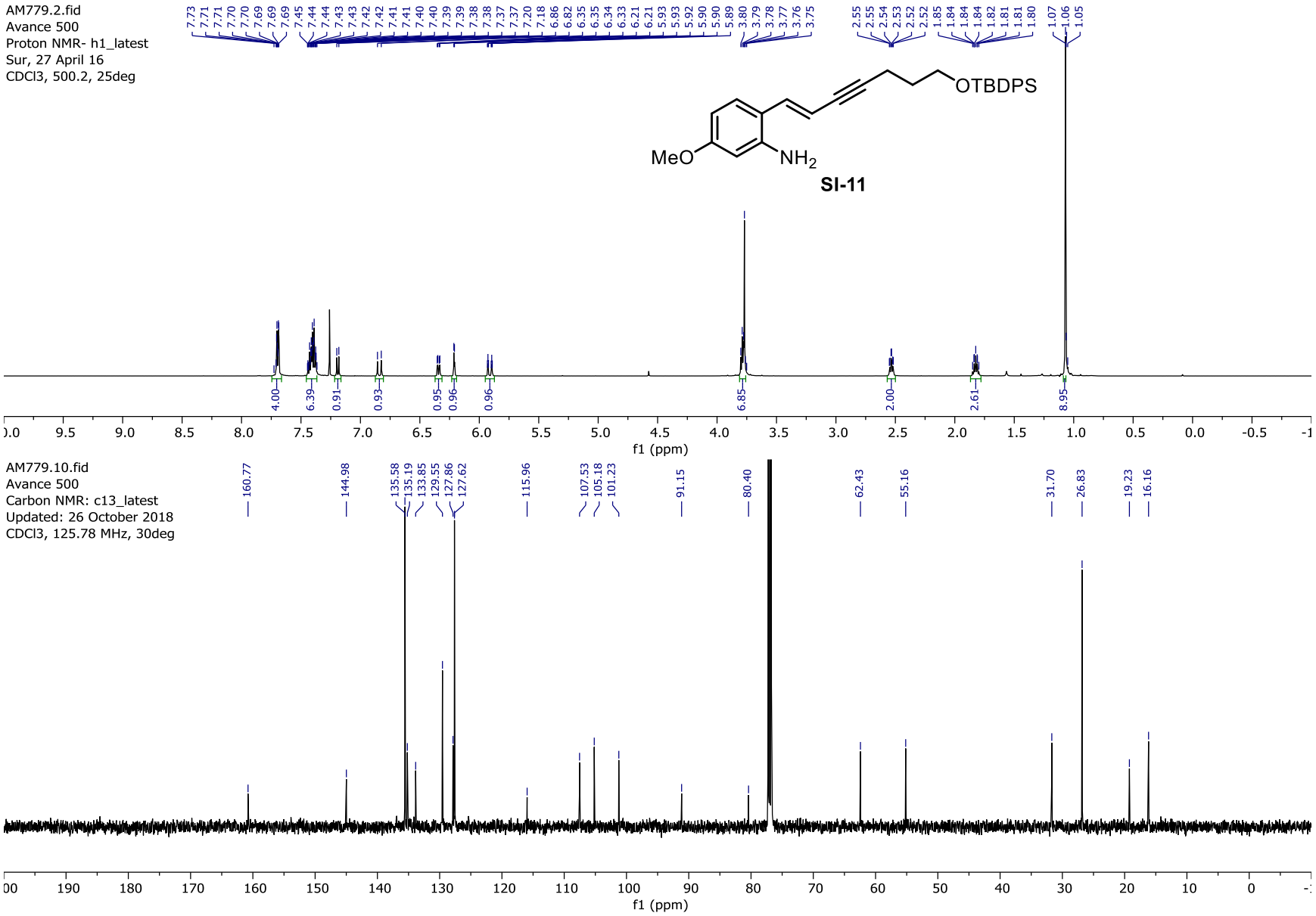

AM557.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
143.57 135.73 129.22 126.47 122.52 118.90 116.26 109.36 91.35 80.47 61.49 31.27 16.06
f1 (ppm)

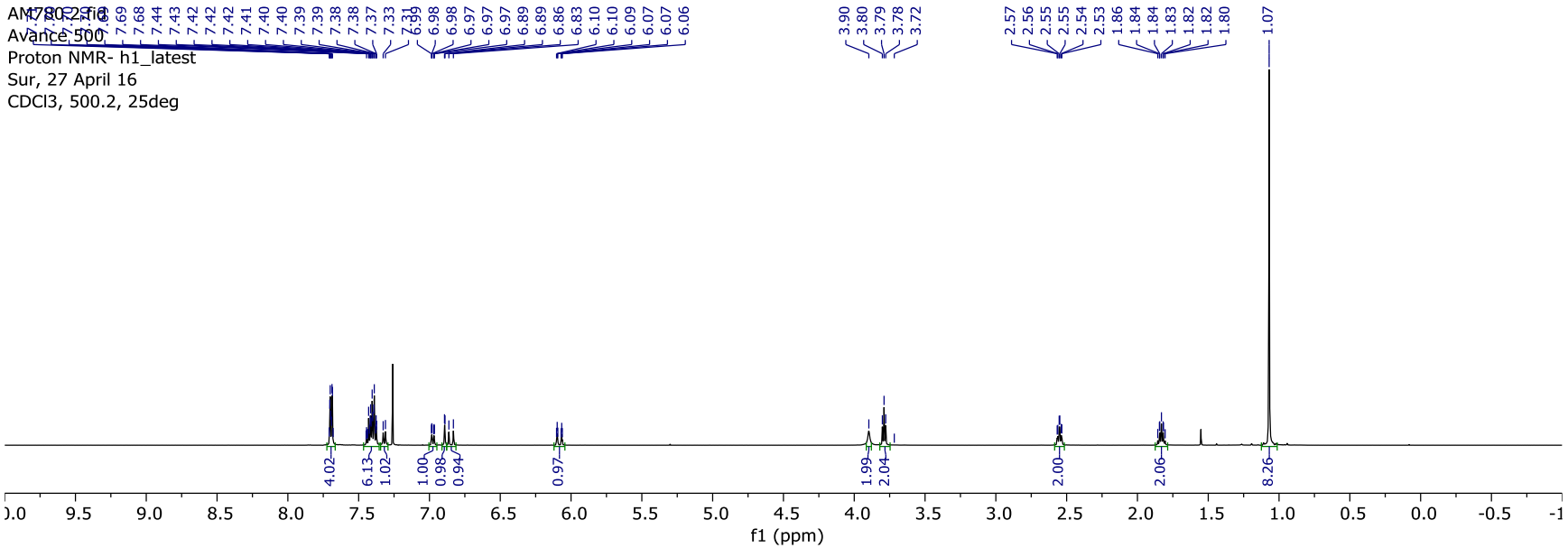
NMR Data

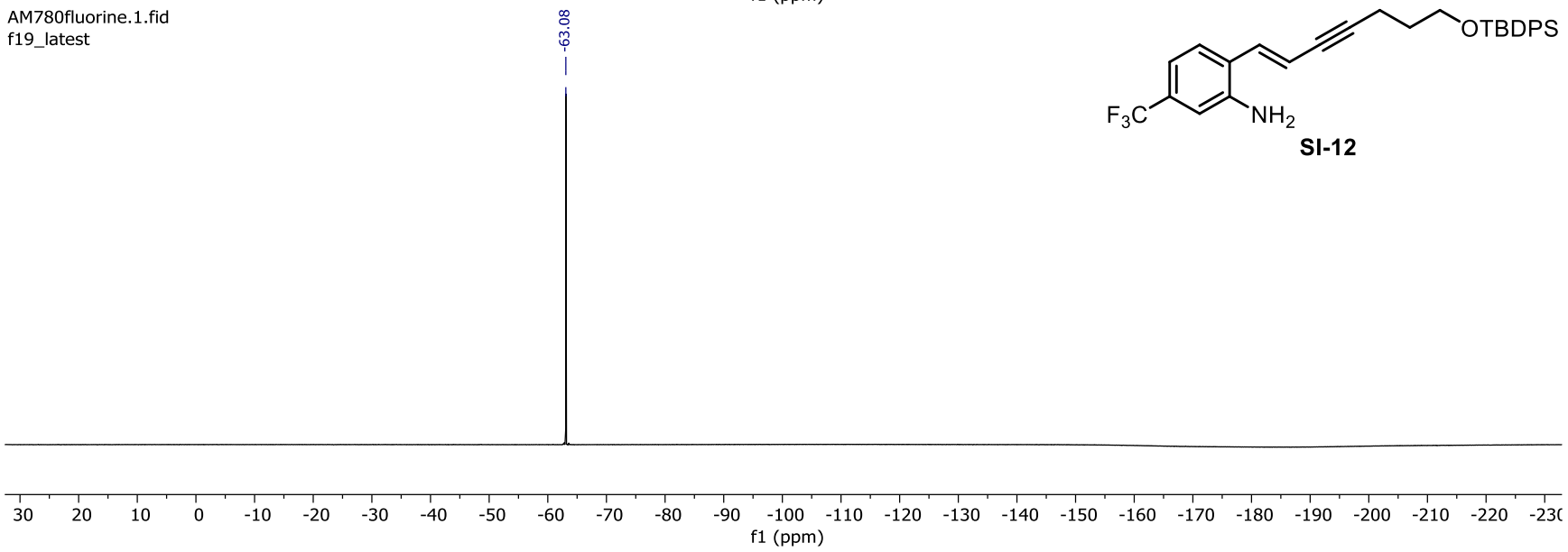

AM776.2.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
OTBDPS
SI-10
3.89
5.97
0.95
0.91
2.00
2.75
1.98
12.27
8.73
f1 (ppm)


AM776.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
135.53
133.81
130.19
129.55
127.62
94.60
83.39
80.98
62.33
31.45
26.83
24.71
19.23
16.12
f1 (ppm)

NMR Data


AM779.2.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
OTBDPS
MeO
NH2
SI-11
f1 (ppm)
AM779.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

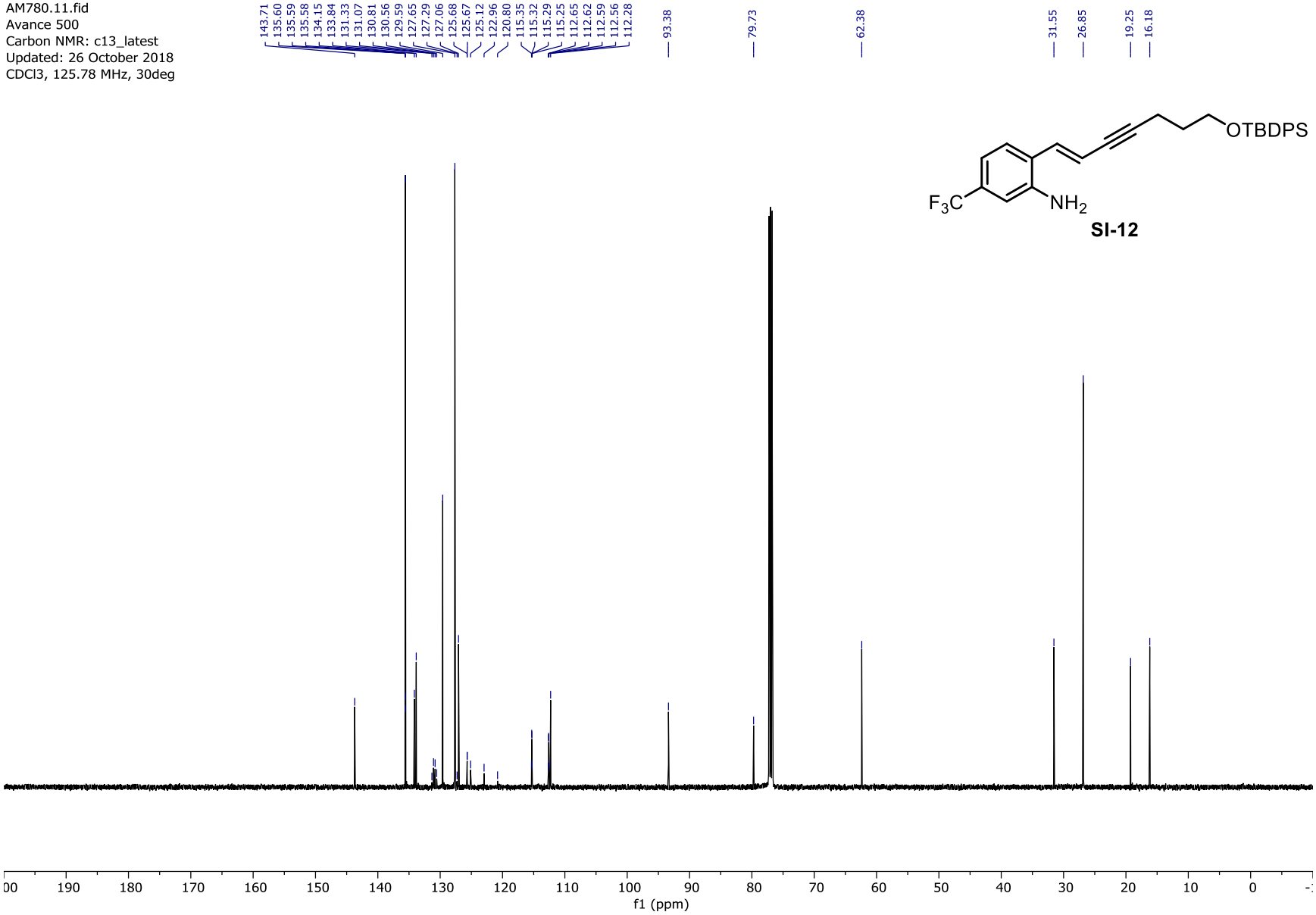

AM780.2.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
f1 (ppm)


AM780fluorine.1.fid
f19_latest
-63.08
f1 (ppm)

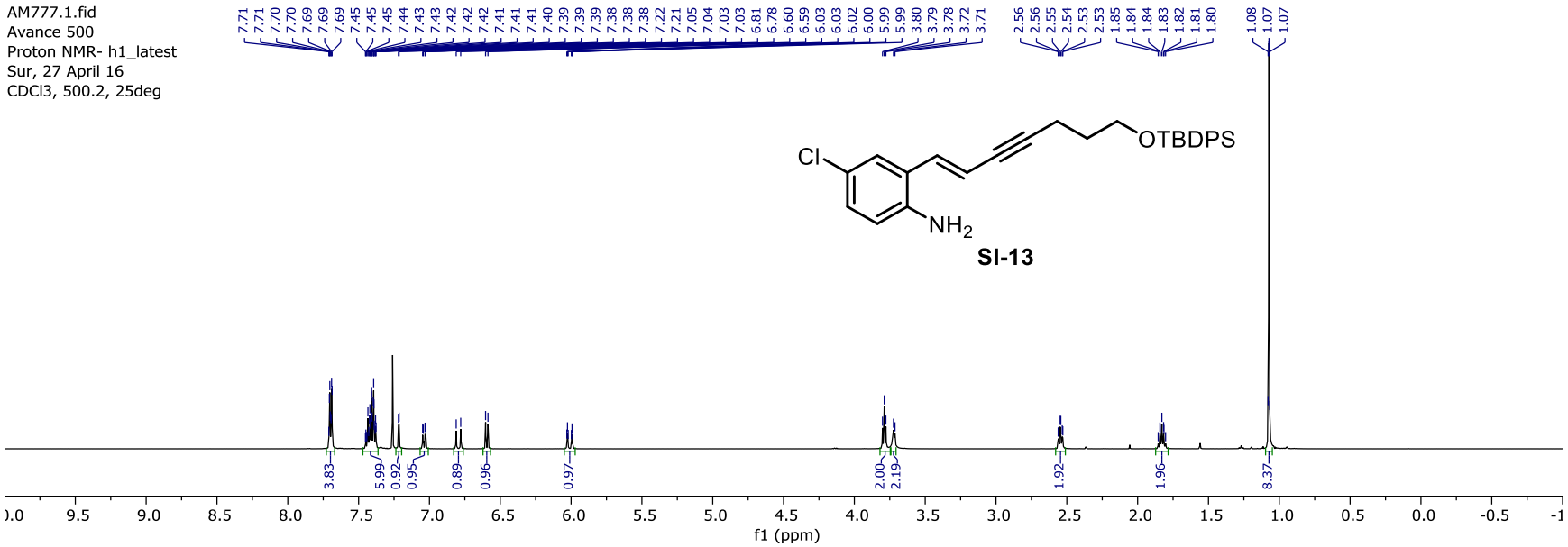
OTBDPS
F3C
NH2

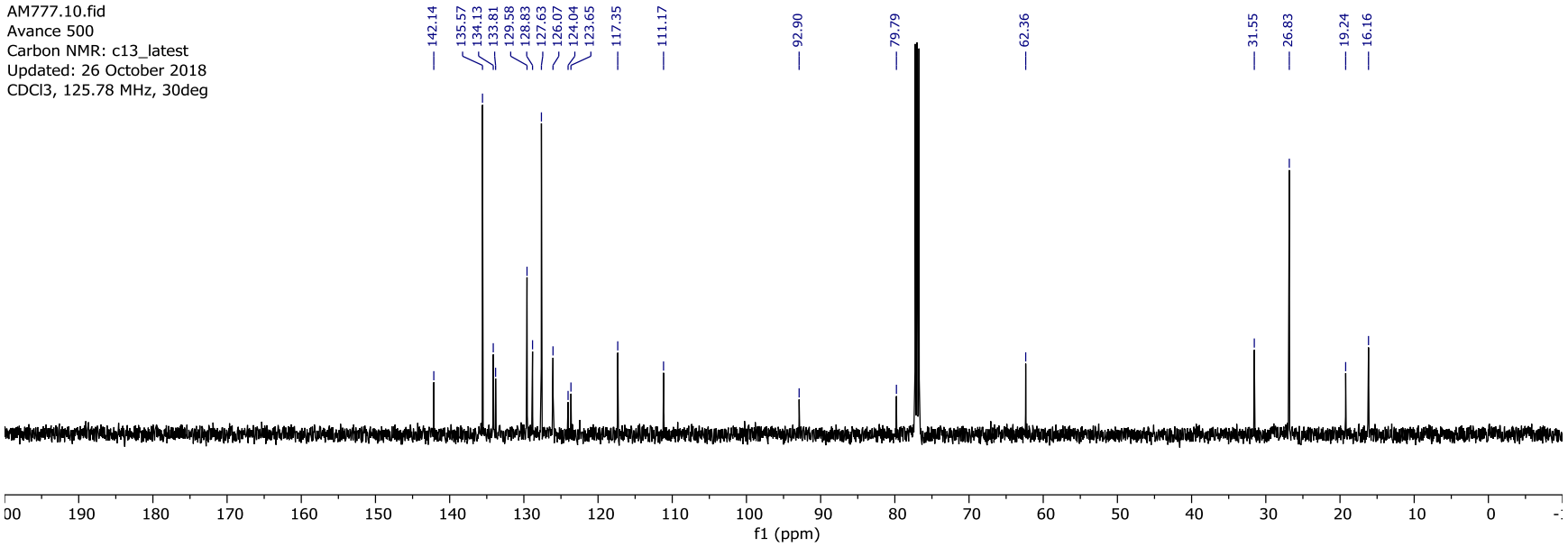
SI-12

AM780.11.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg

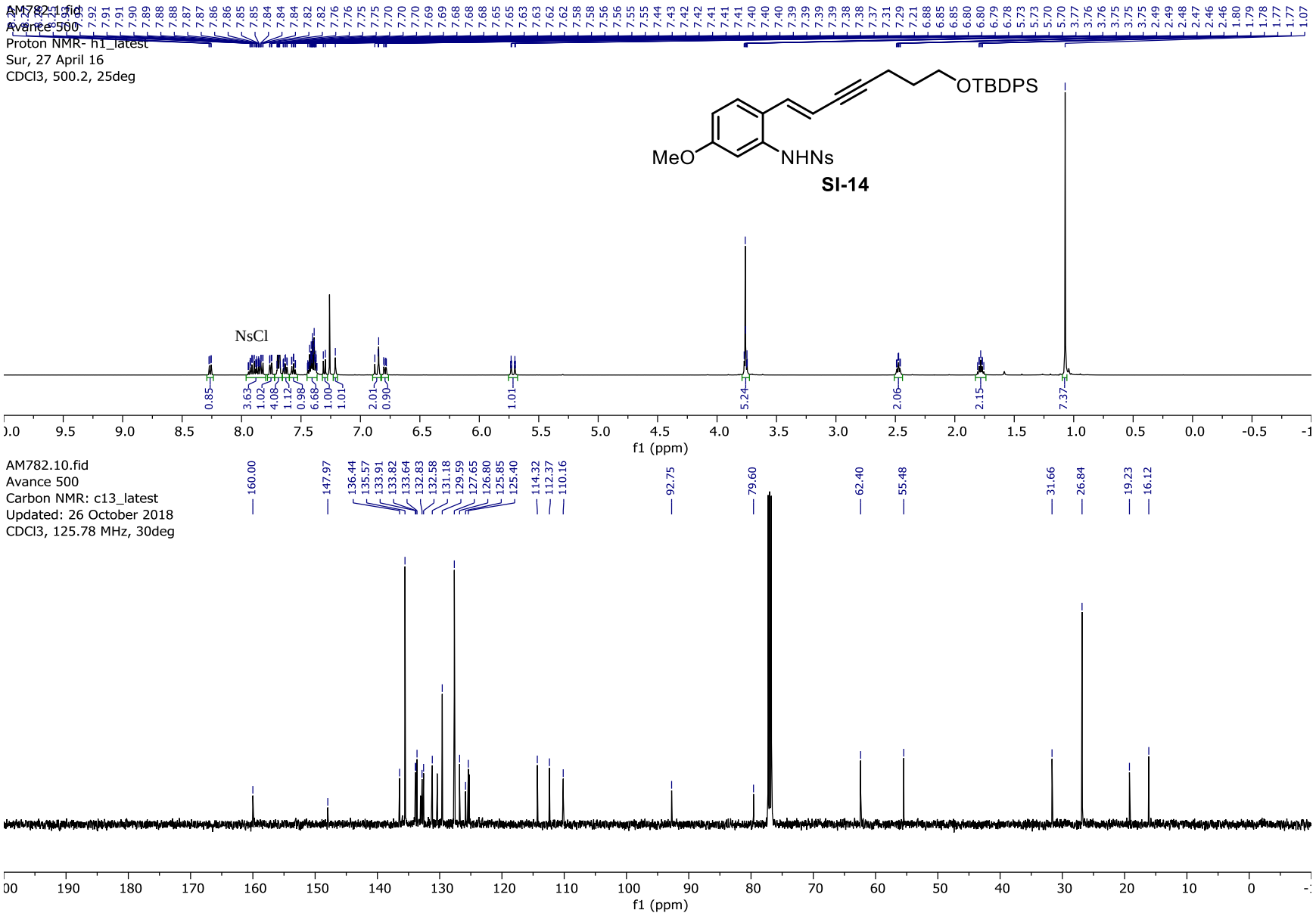


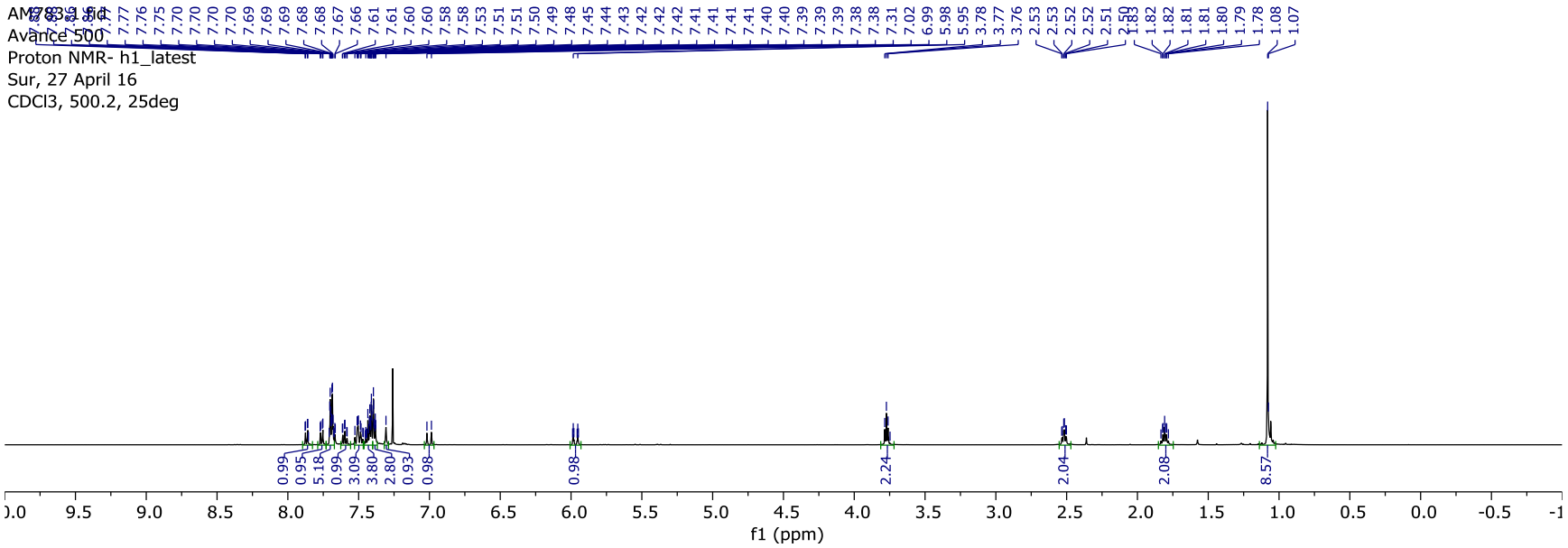
NMR Data

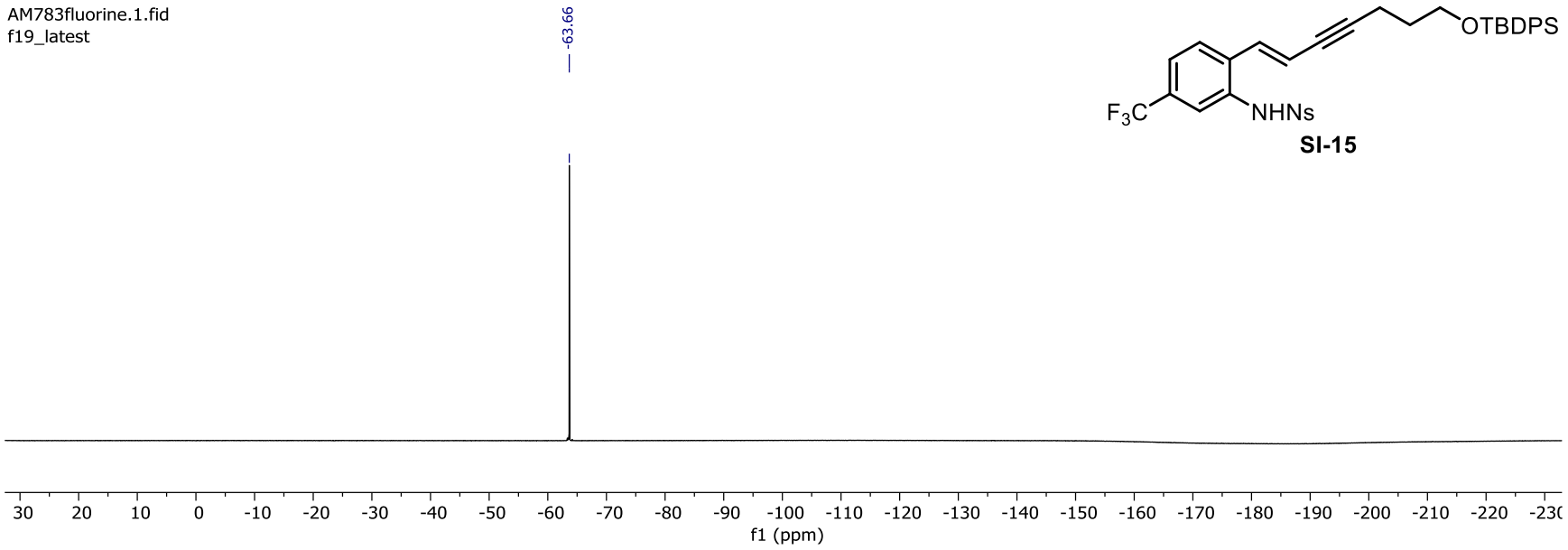

AM777.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
Cl
OTBDPS
NH2
SI-13
f1 (ppm)


AM777.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

NMR Data


AM782.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
OTBDPS
MeO
NHNs
SI-14
NsCl
0.85
3.63
1.02
4.08
1.12
0.98
6.68
1.00
1.01
2.01
0.90
1.01
5.24
2.06
2.15
7.37
f1 (ppm)
AM782.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
160.00
147.97
136.44
135.57
133.91
133.82
133.64
132.83
132.58
131.18
129.59
127.65
126.80
125.85
125.40
114.32
112.37
110.16
92.75
79.60
62.40
55.48
31.66
26.84
19.23
16.12
f1 (ppm)

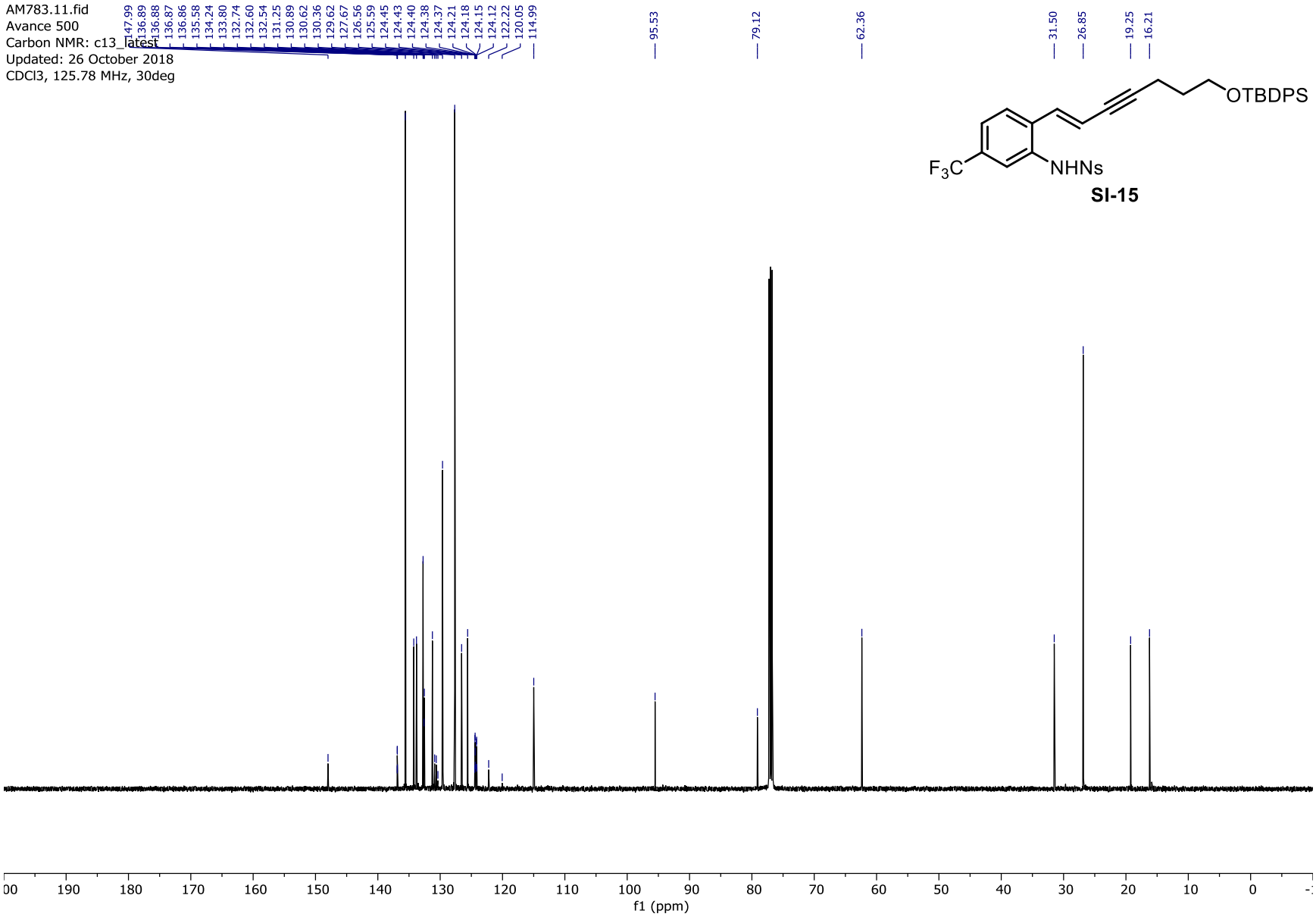

AM783-1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
0.99
0.95
5.18
0.99
3.09
3.80
2.80
0.93
0.98
0.98
2.24
2.04
2.08
8.57
f1 (ppm)


AM783fluorine.1.fid
f19_latest
-63.66
f1 (ppm)

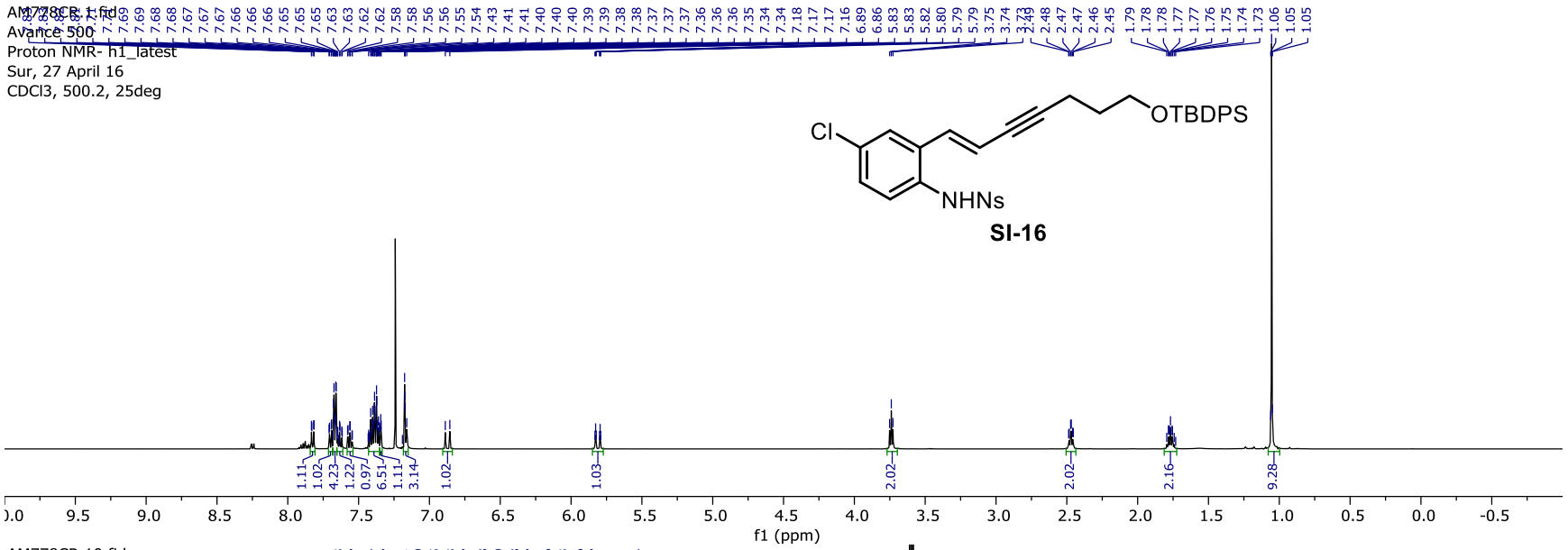
OTBDPS
F3C
NHNs

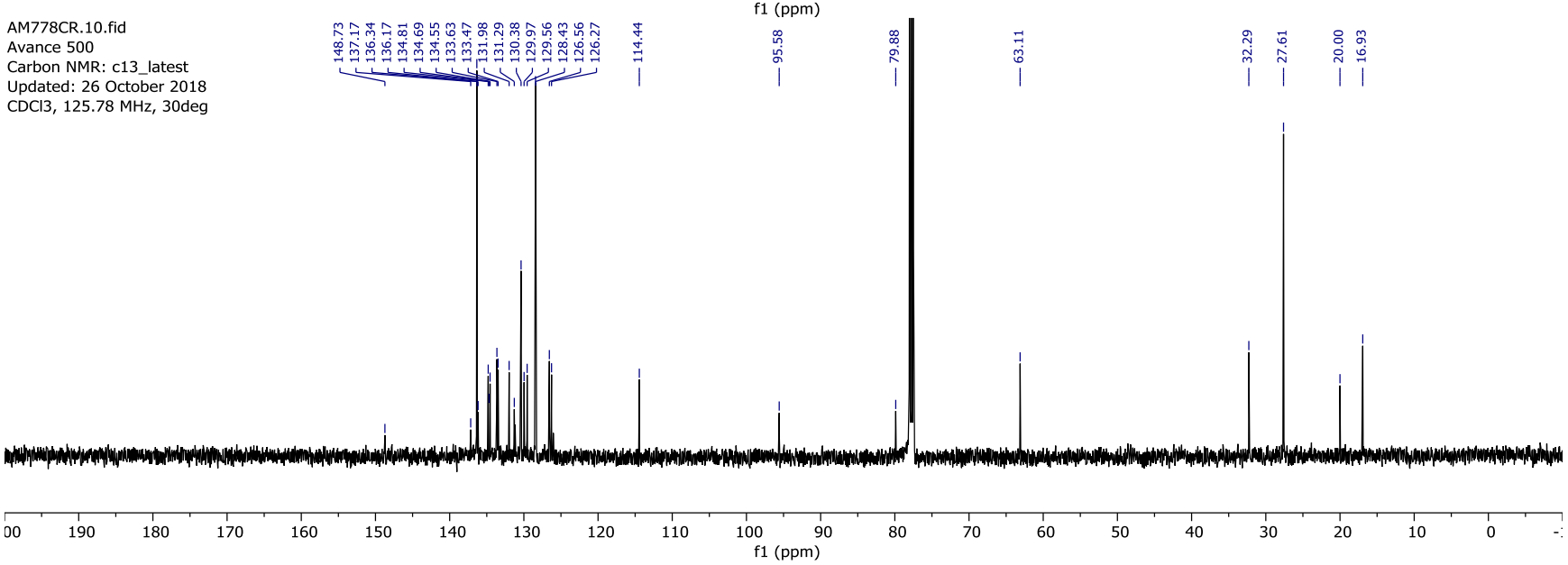
SI-15

NMR Data

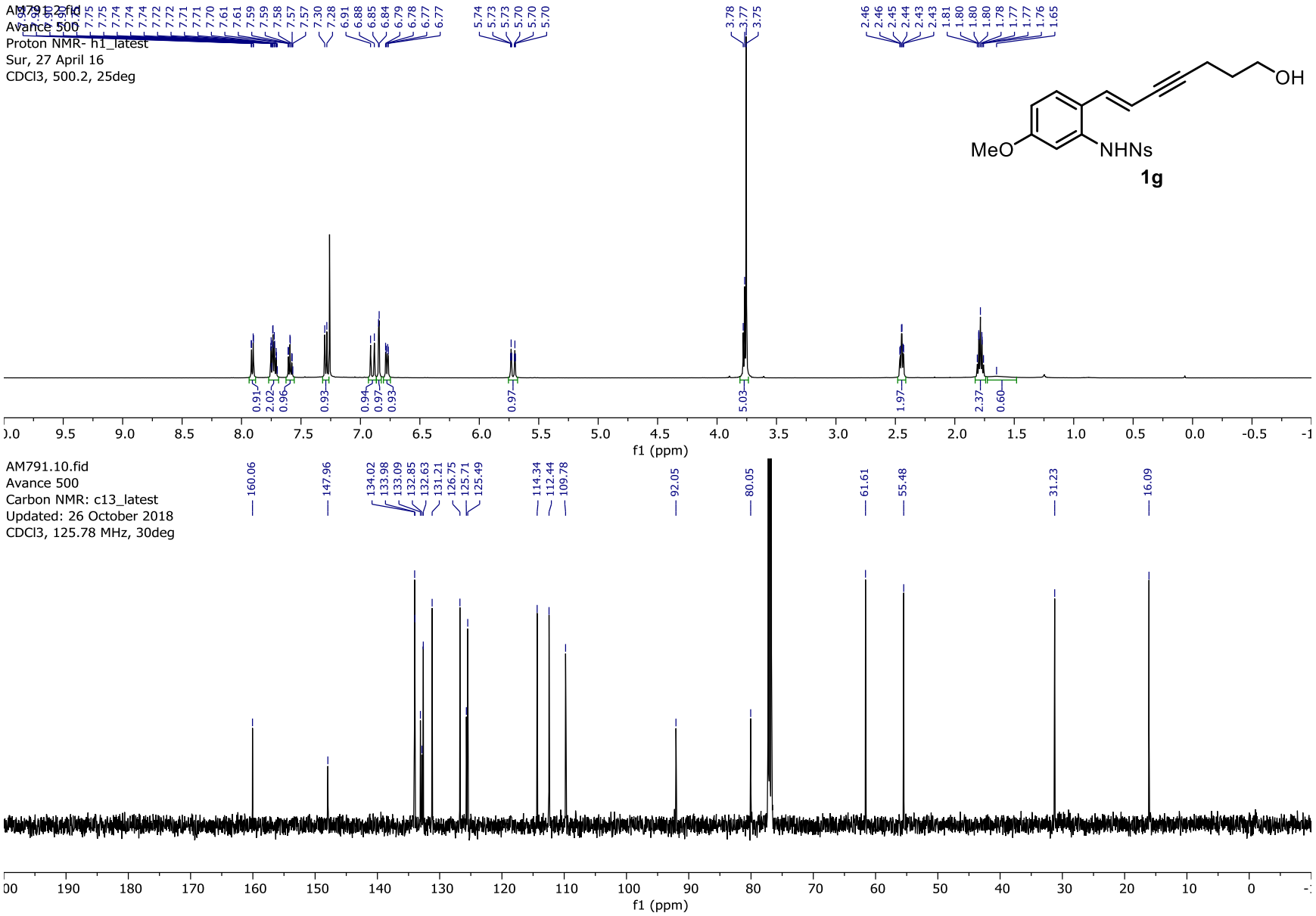

AM783.11.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
147.99
136.89
136.88
136.87
136.86
135.58
134.24
133.80
132.74
132.60
132.54
131.25
130.89
130.62
130.36
129.62
127.67
126.56
125.59
124.45
124.43
124.40
124.38
124.37
124.21
124.18
124.15
124.12
122.22
120.05
114.99
95.53
79.12
62.36
31.50
26.85
19.25
16.21
OTBDPS
F3C
NHNs
SI-15
f1 (ppm)

NMR Data

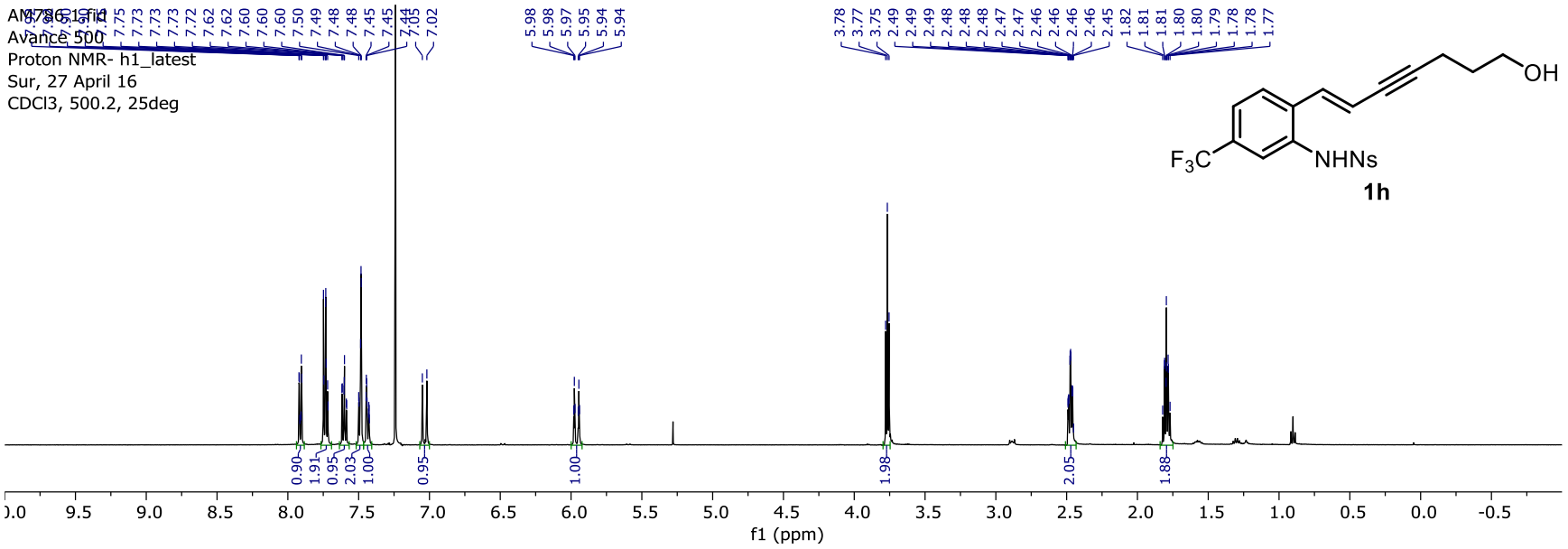

AM778CR.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
Cl
OTBDPS
NHNs
SI-16
f1 (ppm)

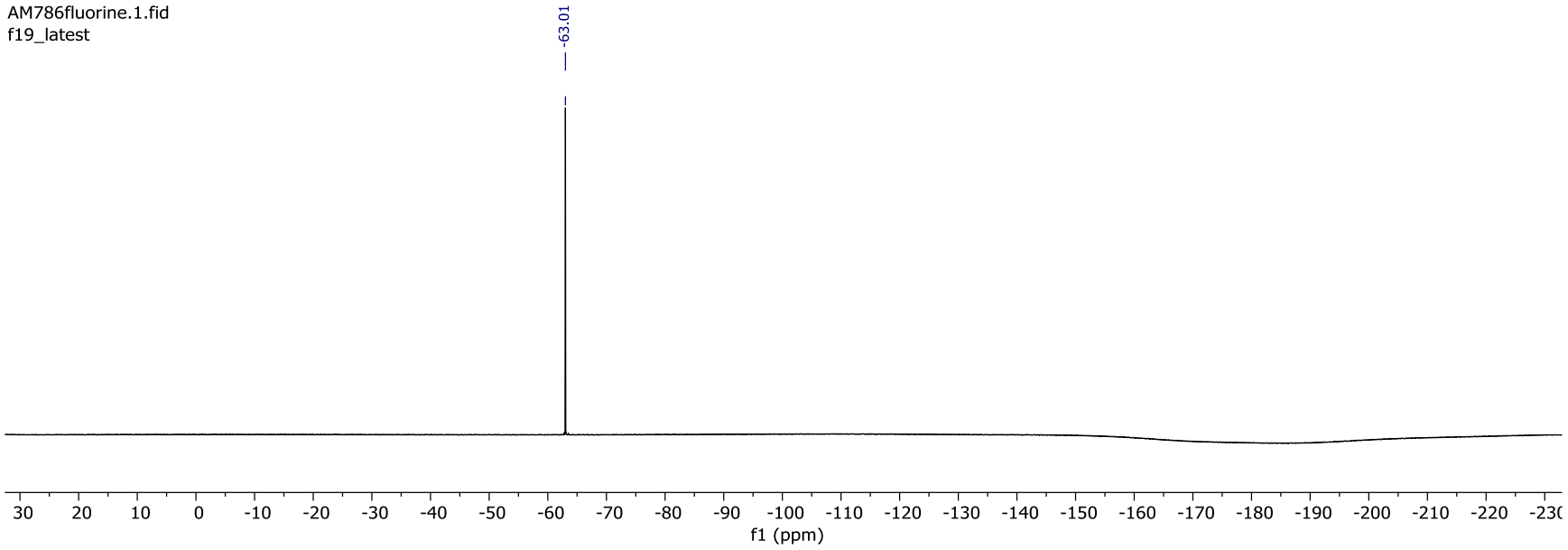

AM778CR.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

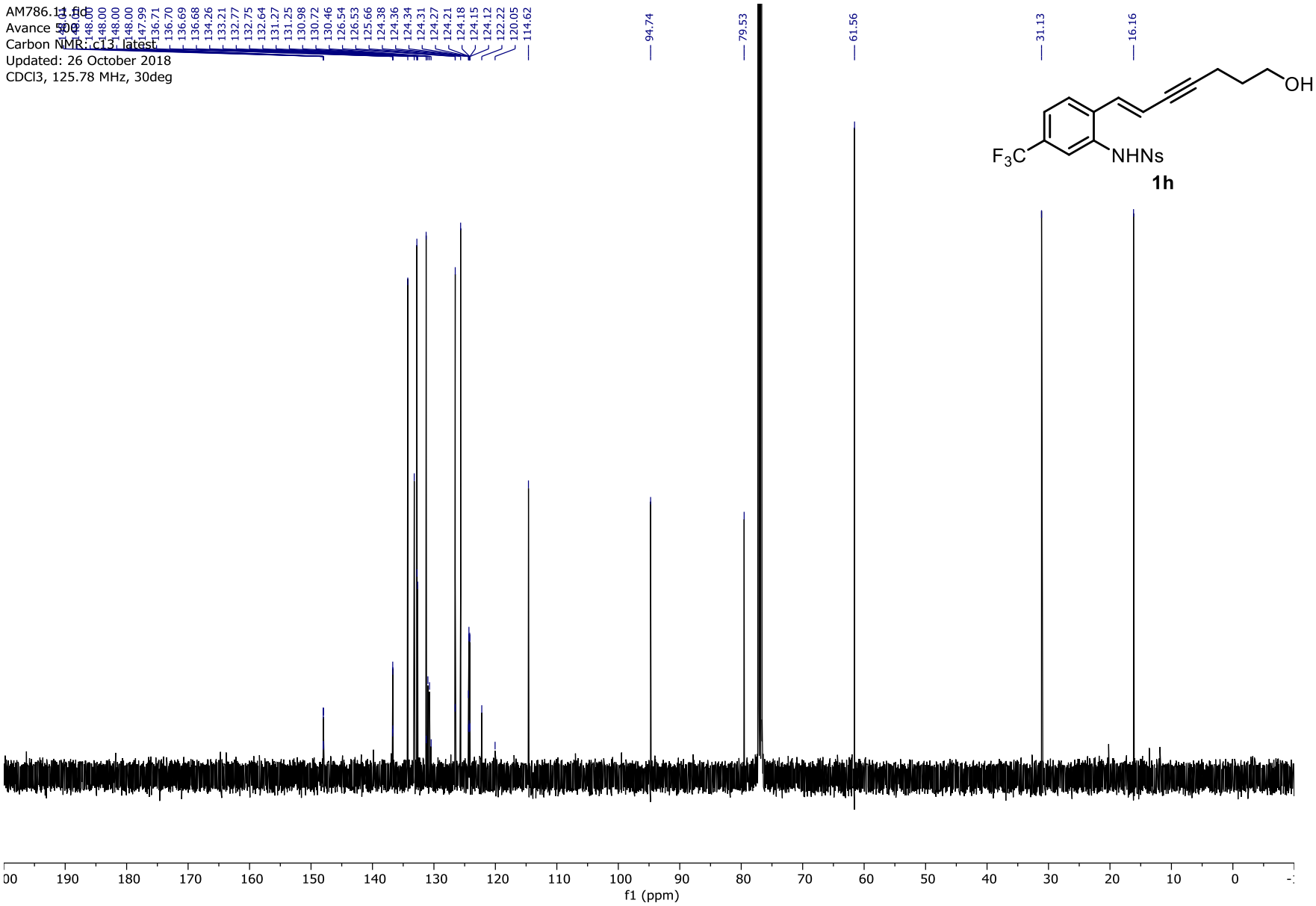
NMR Data

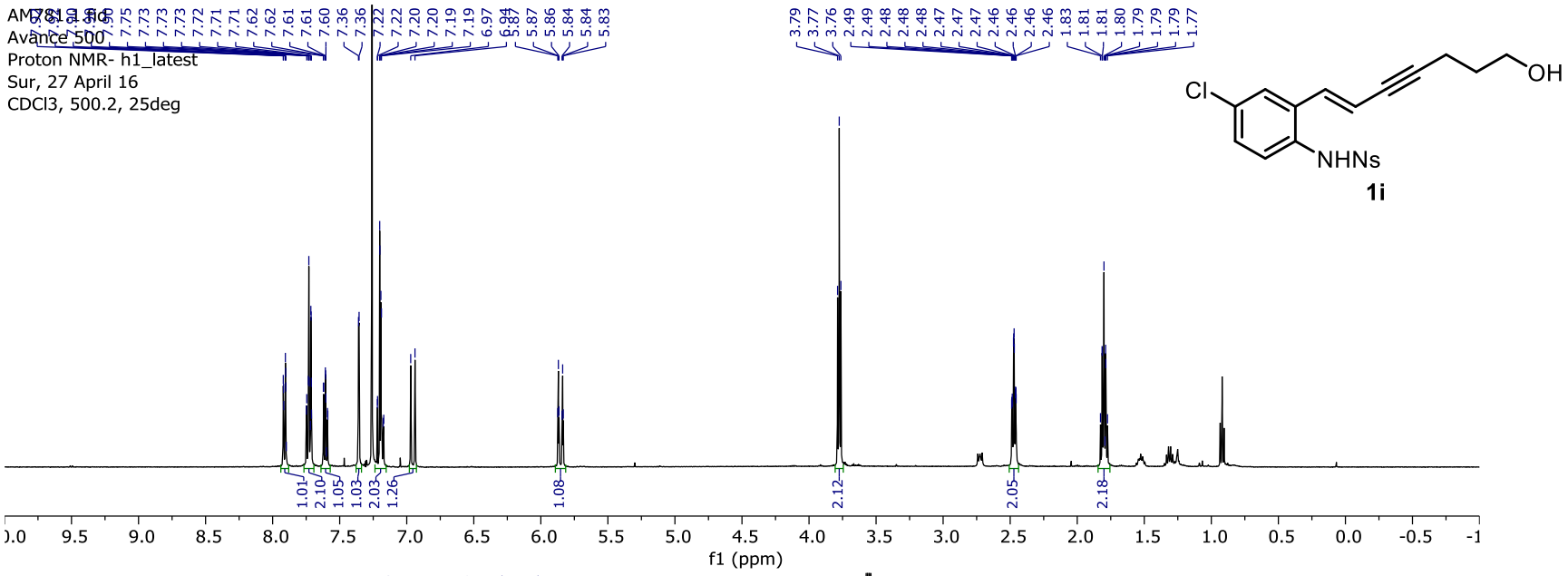

AM791.2.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
OH
MeO
NHNs
1g
f1 (ppm)
AM791.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

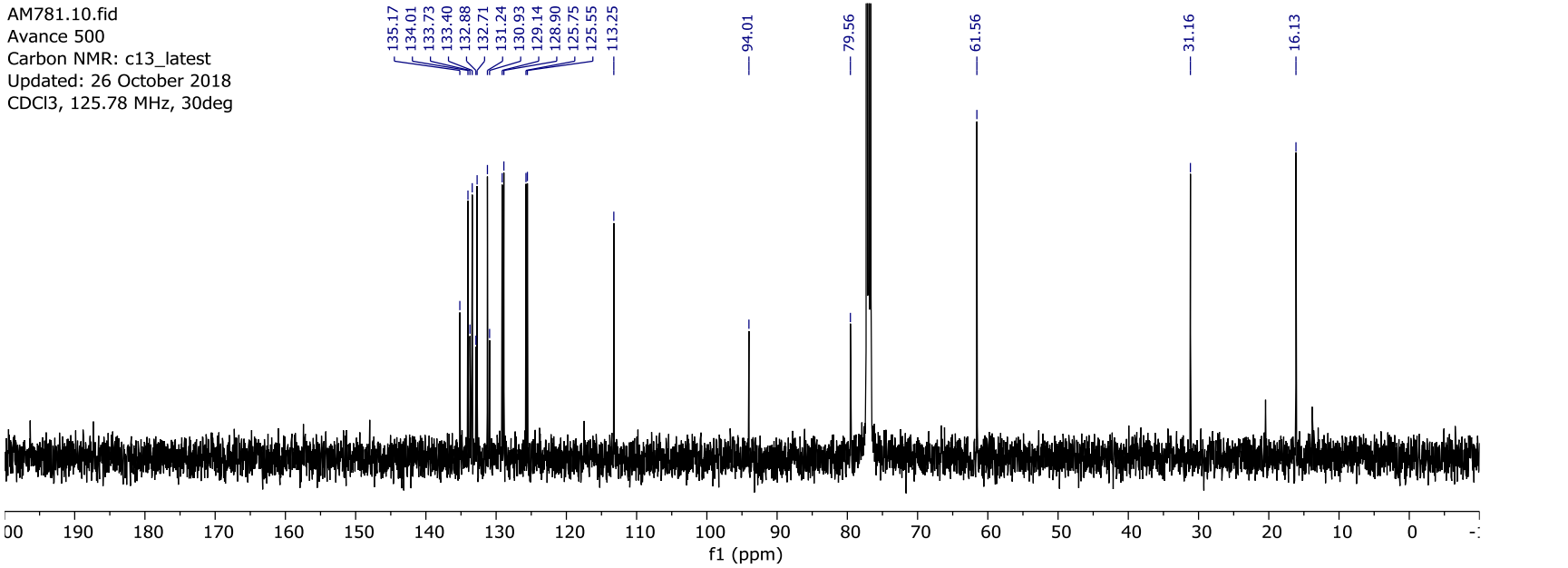
NMR Data


AM786_1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
OH
F3C
NHNs
1h
f1 (ppm)

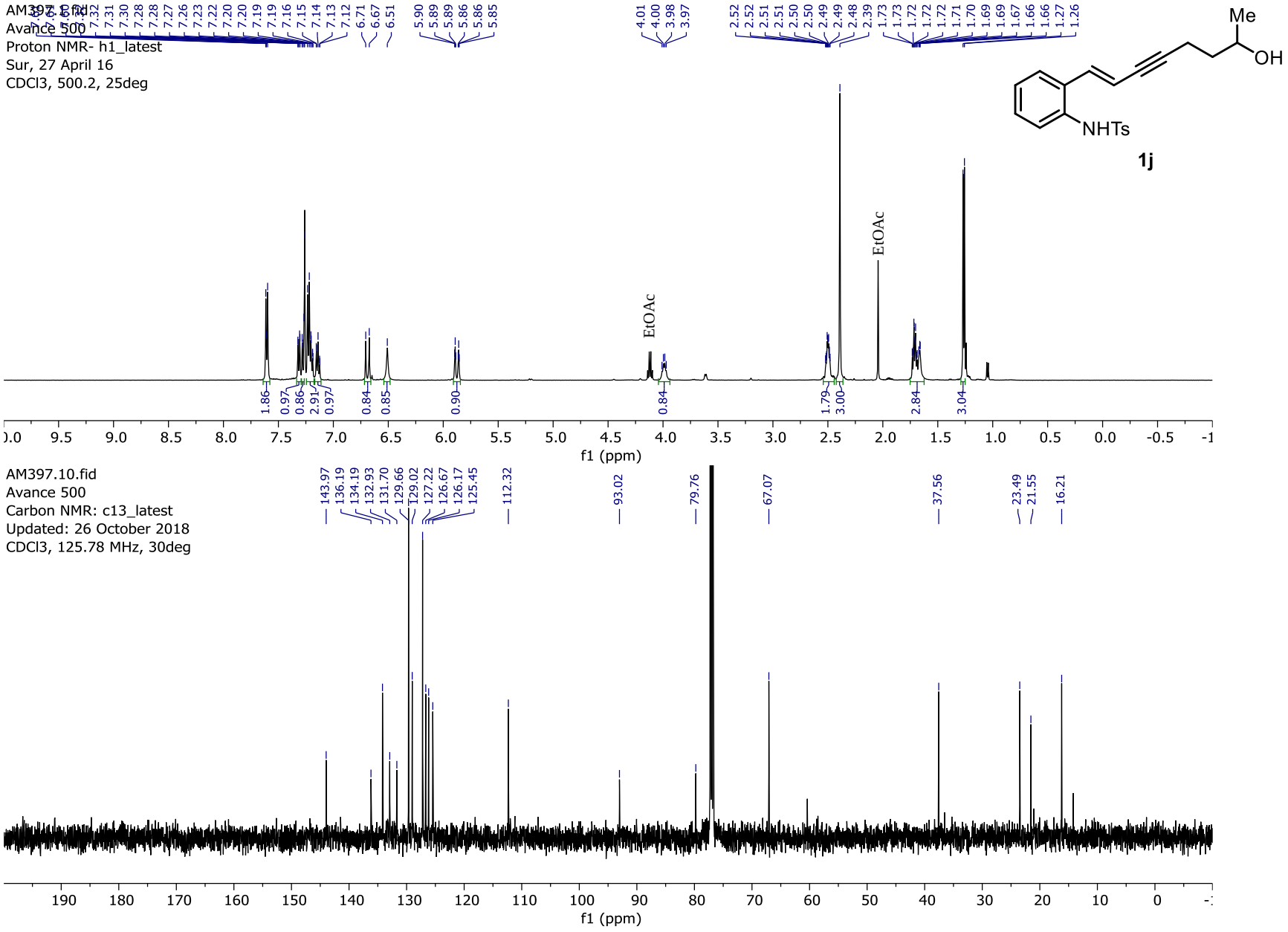

AM786fluorine.1.fid
f19_latest
-63.01
f1 (ppm)


AM786.11.fid
Avance 500
Carbon NMR: c13 latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
94.74
79.53
61.56
31.13
16.16
OH
F3C
NHNs
1h
f1 (ppm)

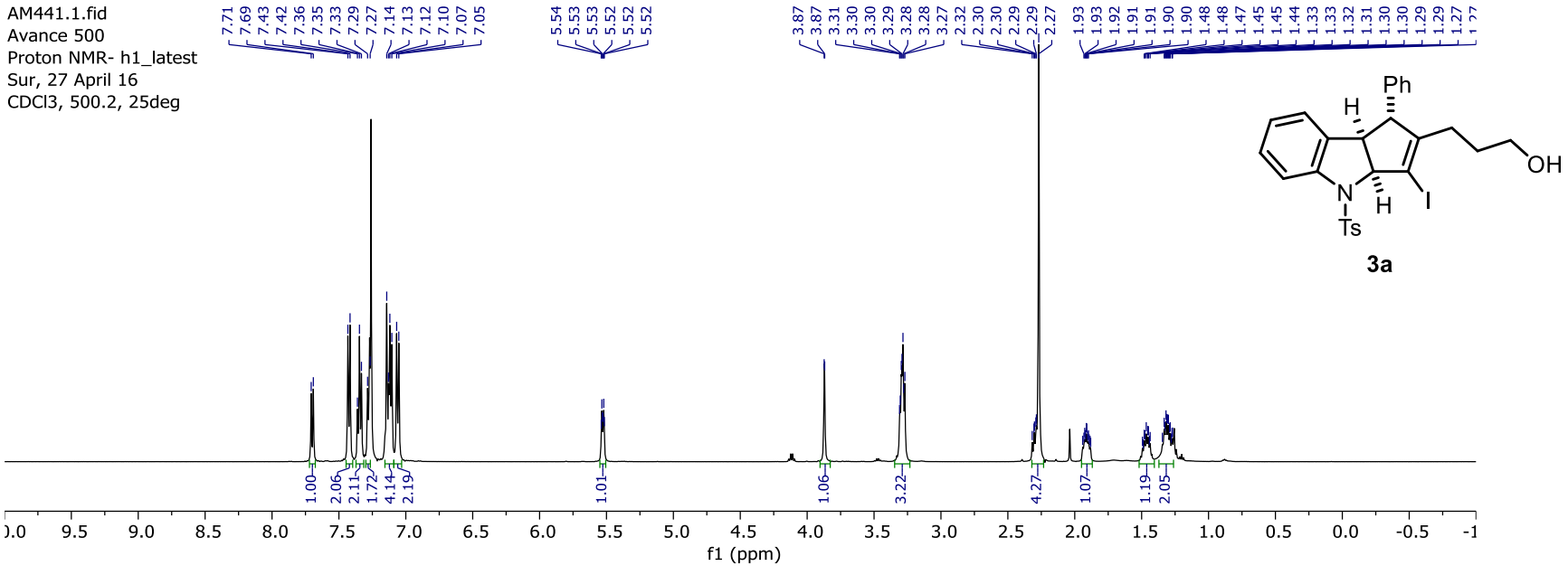

AM781.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
Cl
OH
NHNs
1i
1.01
2.10
1.05
1.03
2.03
1.26
1.08
2.12
2.05
2.18
f1 (ppm)

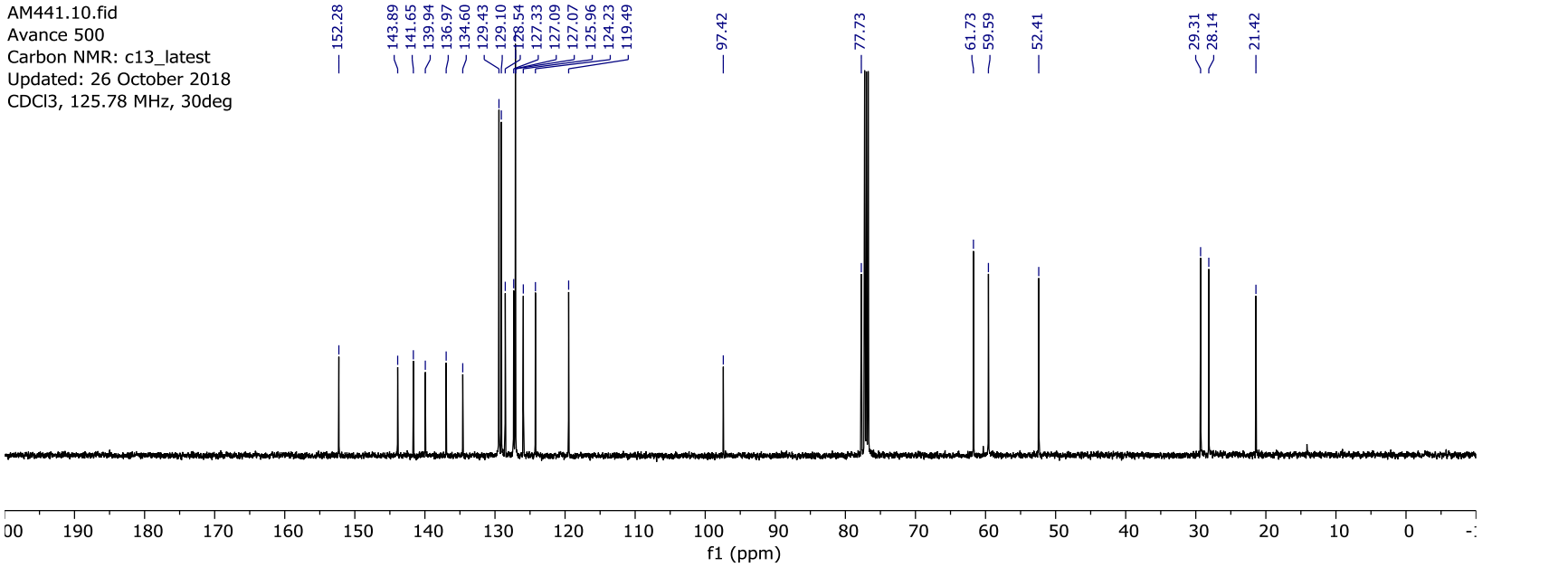

AM781.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
135.17
134.01
133.73
133.40
132.88
132.71
131.24
130.93
129.14
128.90
125.75
125.55
113.25
94.01
79.56
61.56
31.16
16.13
f1 (ppm)

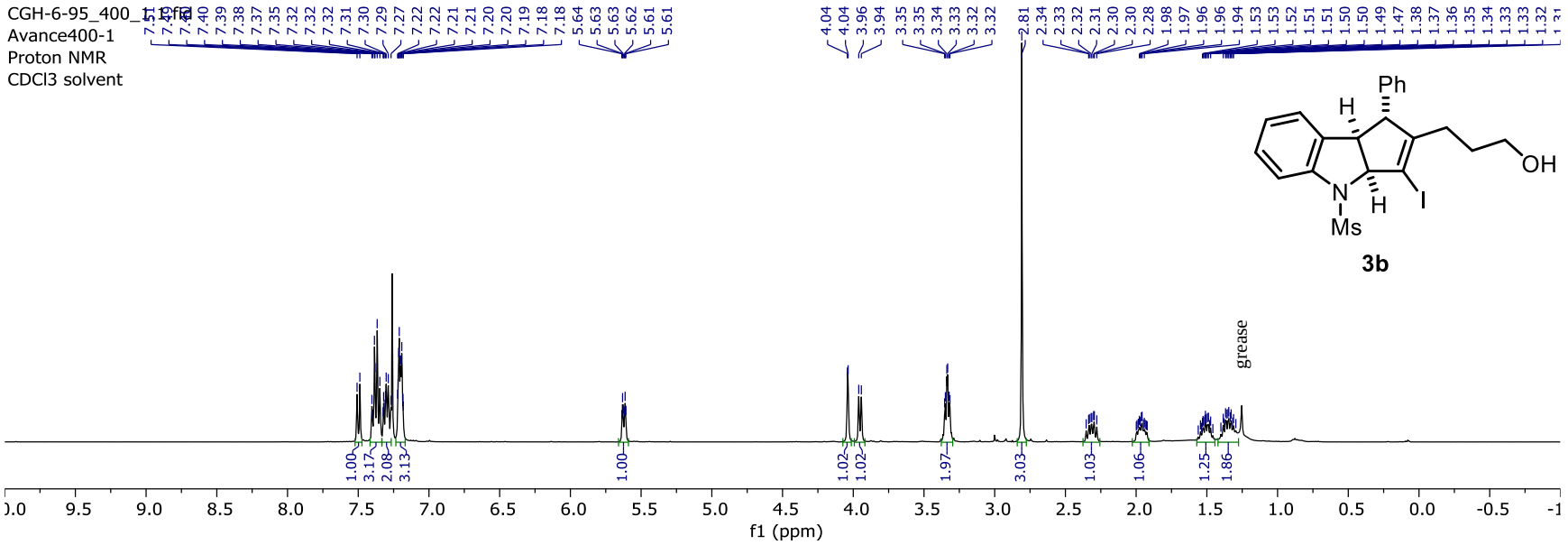
NMR Data

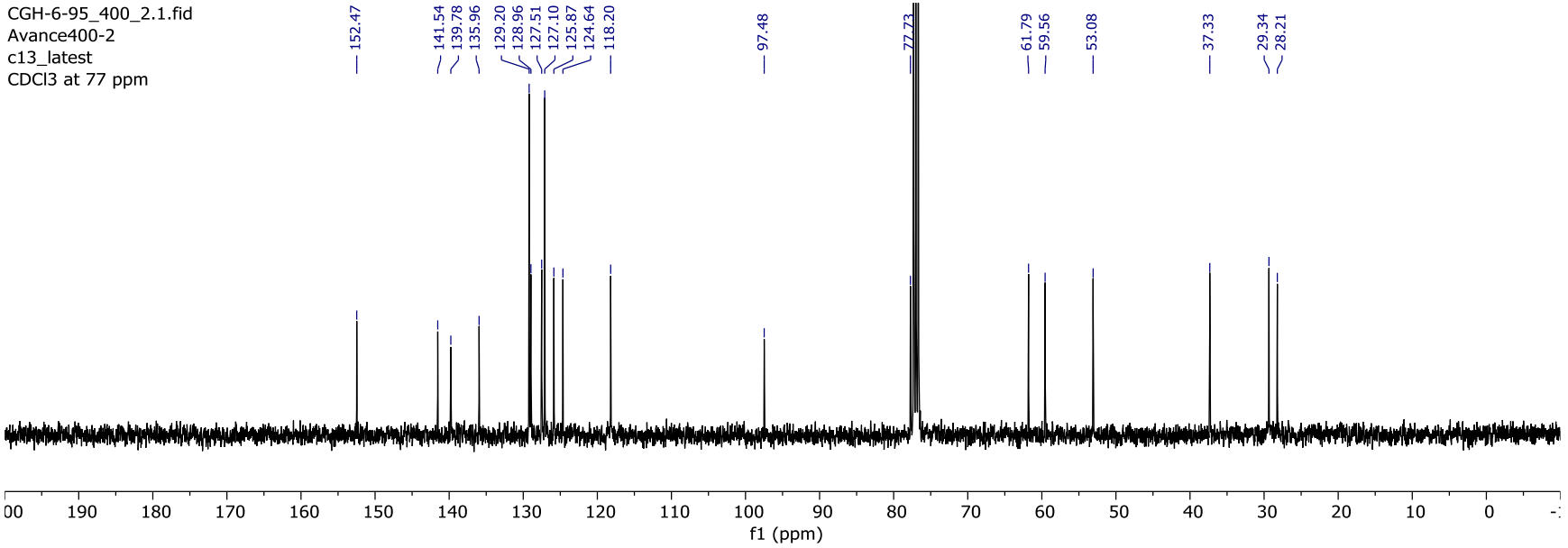

AM397.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
Me
OH
NHTs
1j
EtOAc
EtOAc
f1 (ppm)
AM397.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

NMR Data


AM441.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
Ph
H
OH
N
H
I
Ts
3a
f1 (ppm)

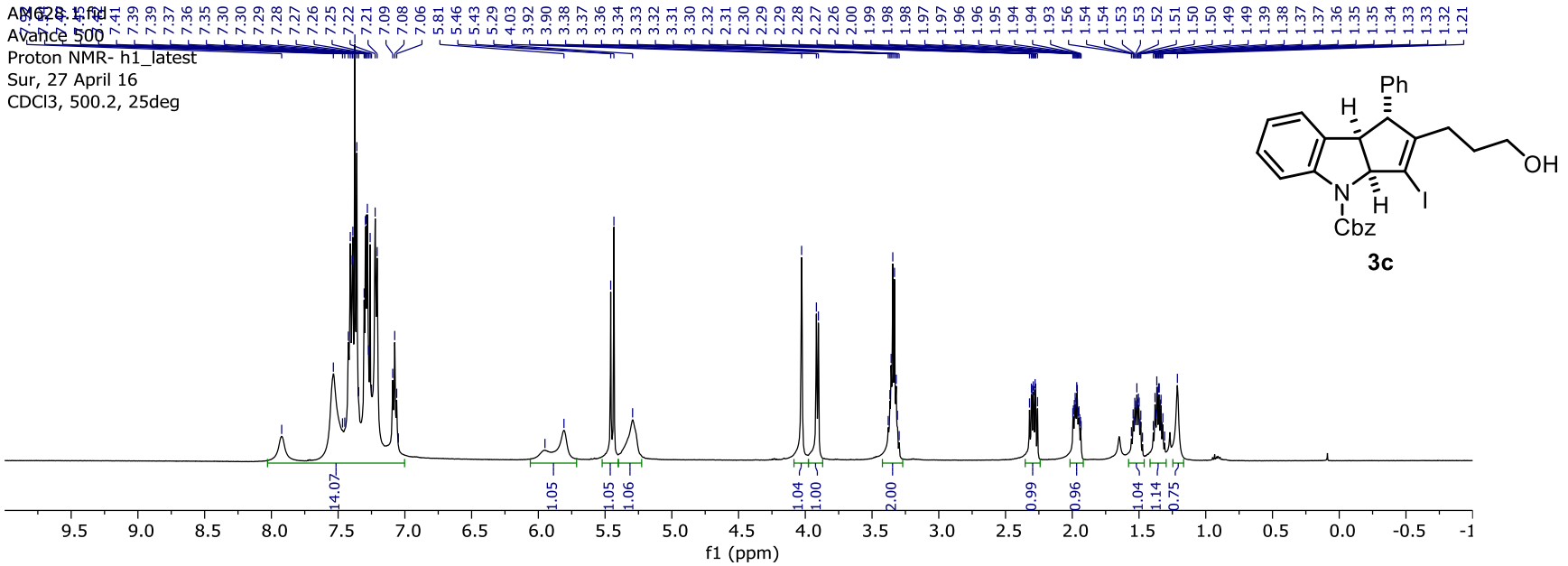

AM441.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

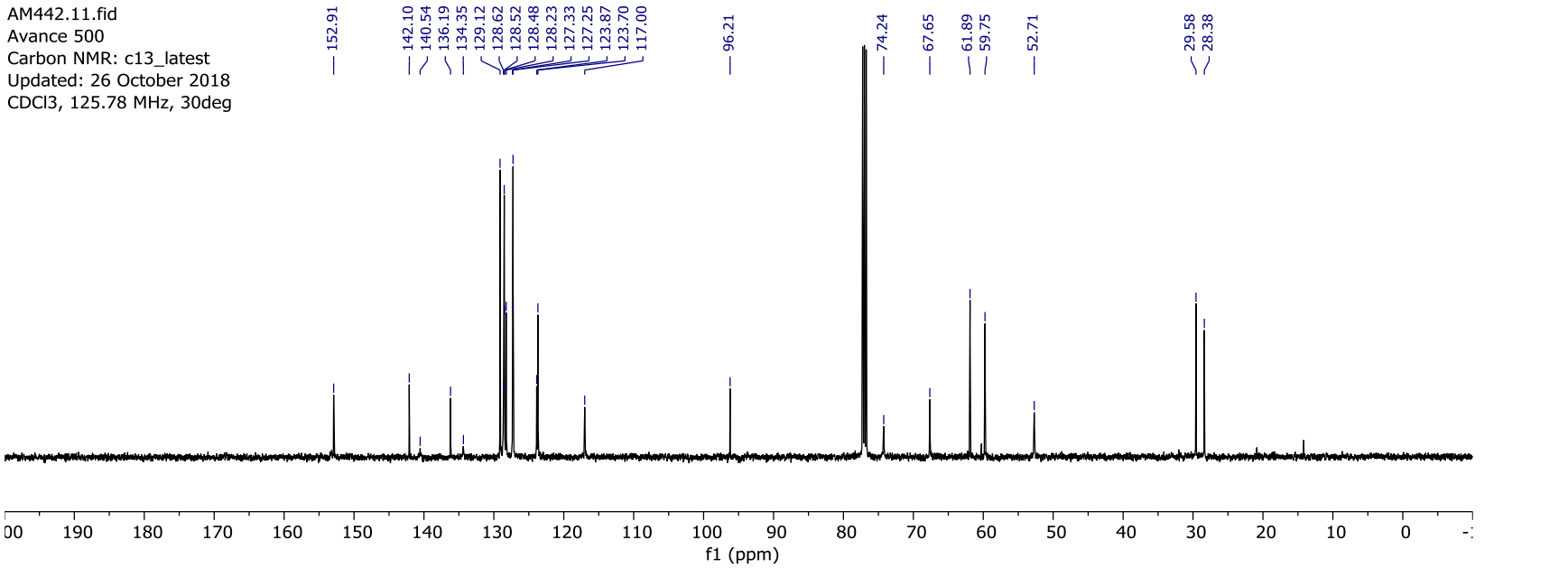

CGH-6-95_400_1.1.fid
Avance400-1
Proton NMR
CDCl3 solvent
Ph
H
OH
N
H
I
Ms
3b
grease
f1 (ppm)


CGH-6-95_400_2.1.fid
Avance400-2
c13_latest
CDCl3 at 77 ppm
f1 (ppm)

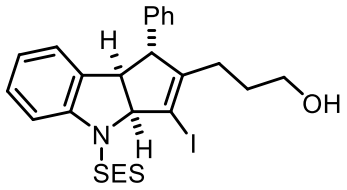
f

NMR Data


AM628.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
Ph
H
OH
N
H
I
Cbz
3c
14.07
1.05
1.05
1.06
1.04
1.00
2.00
0.99
0.96
1.04
1.14
0.75
f1 (ppm)

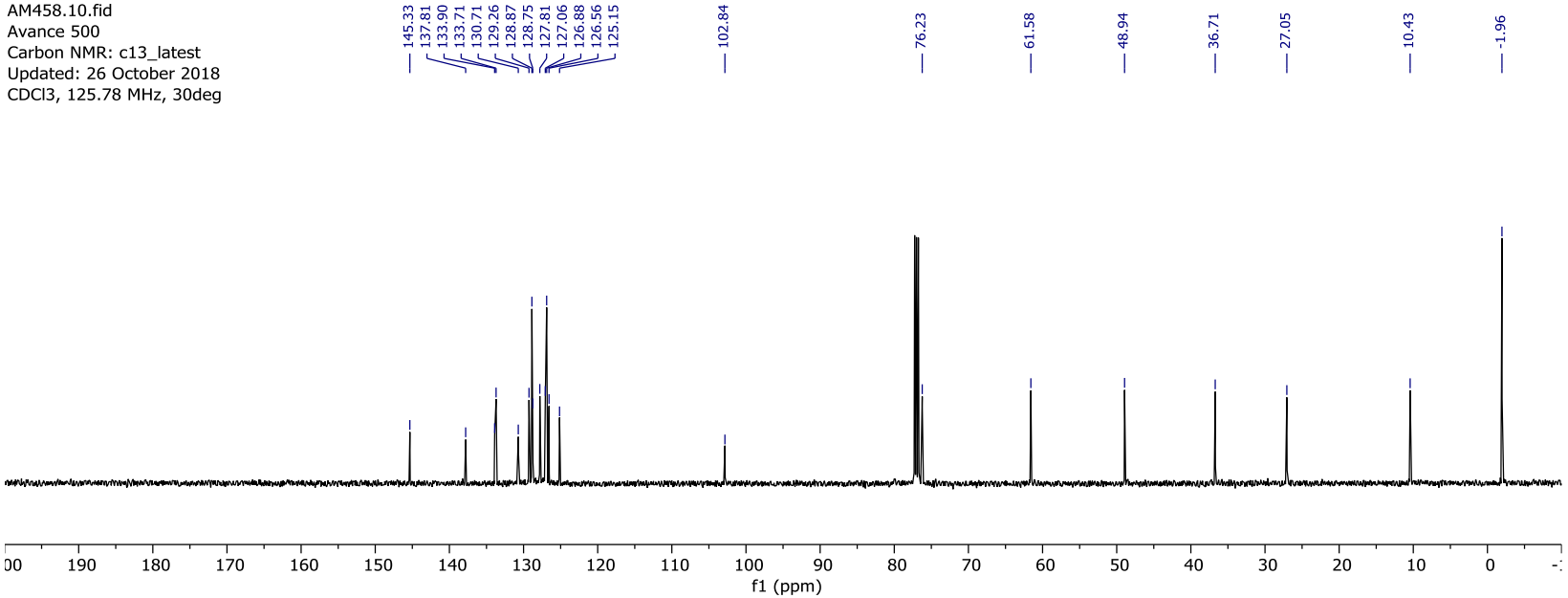

AM442.11.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
152.91
142.10
140.54
136.19
134.35
129.12
128.62
128.52
128.48
128.23
127.33
127.25
123.87
123.70
117.00
96.21
74.24
67.65
61.89
59.75
52.71
29.58
28.38
f1 (ppm)

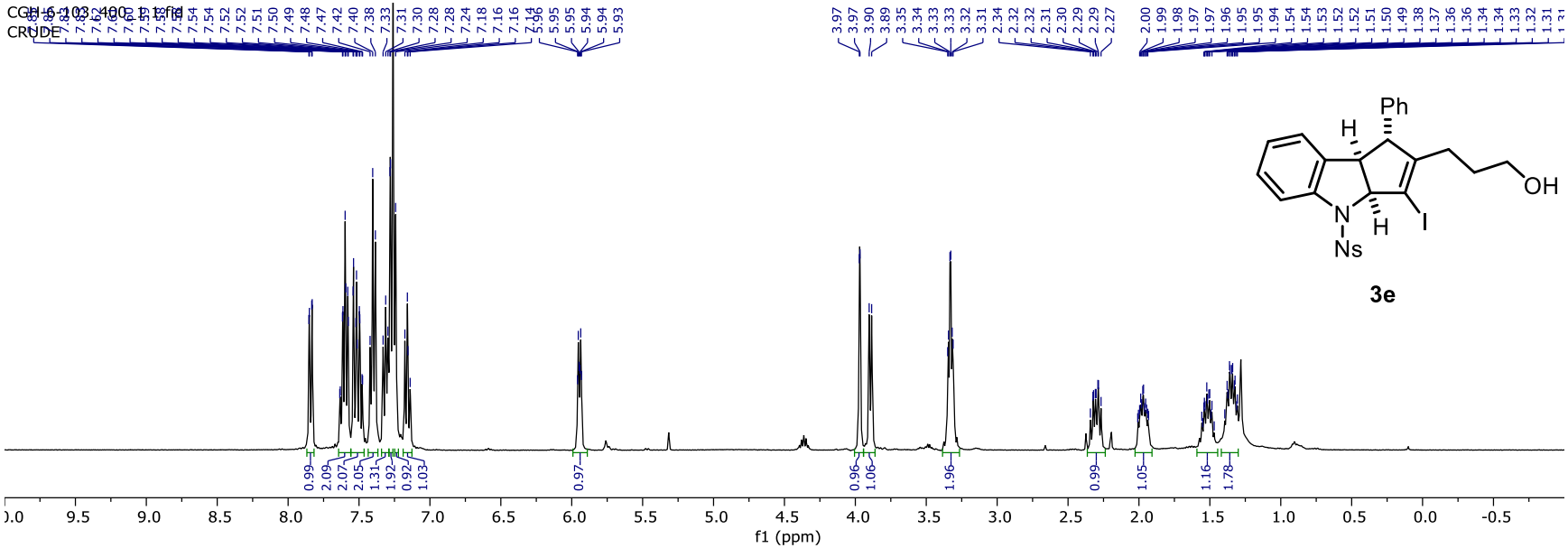
AM458.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg

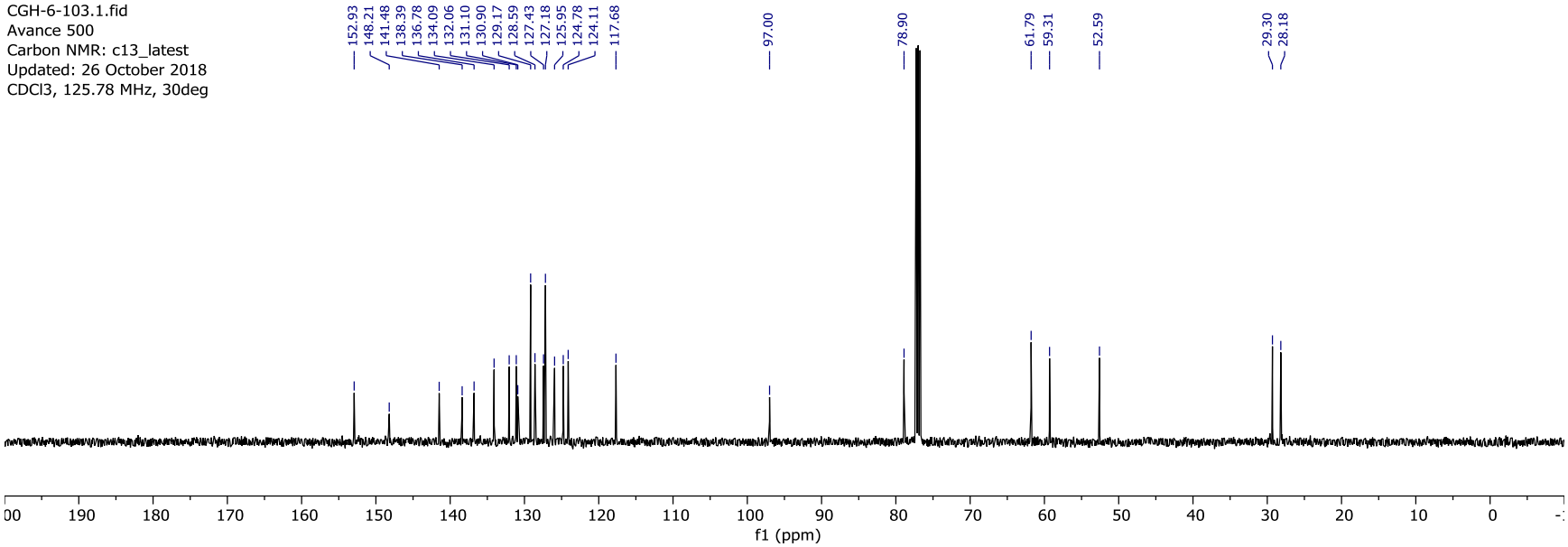


3d

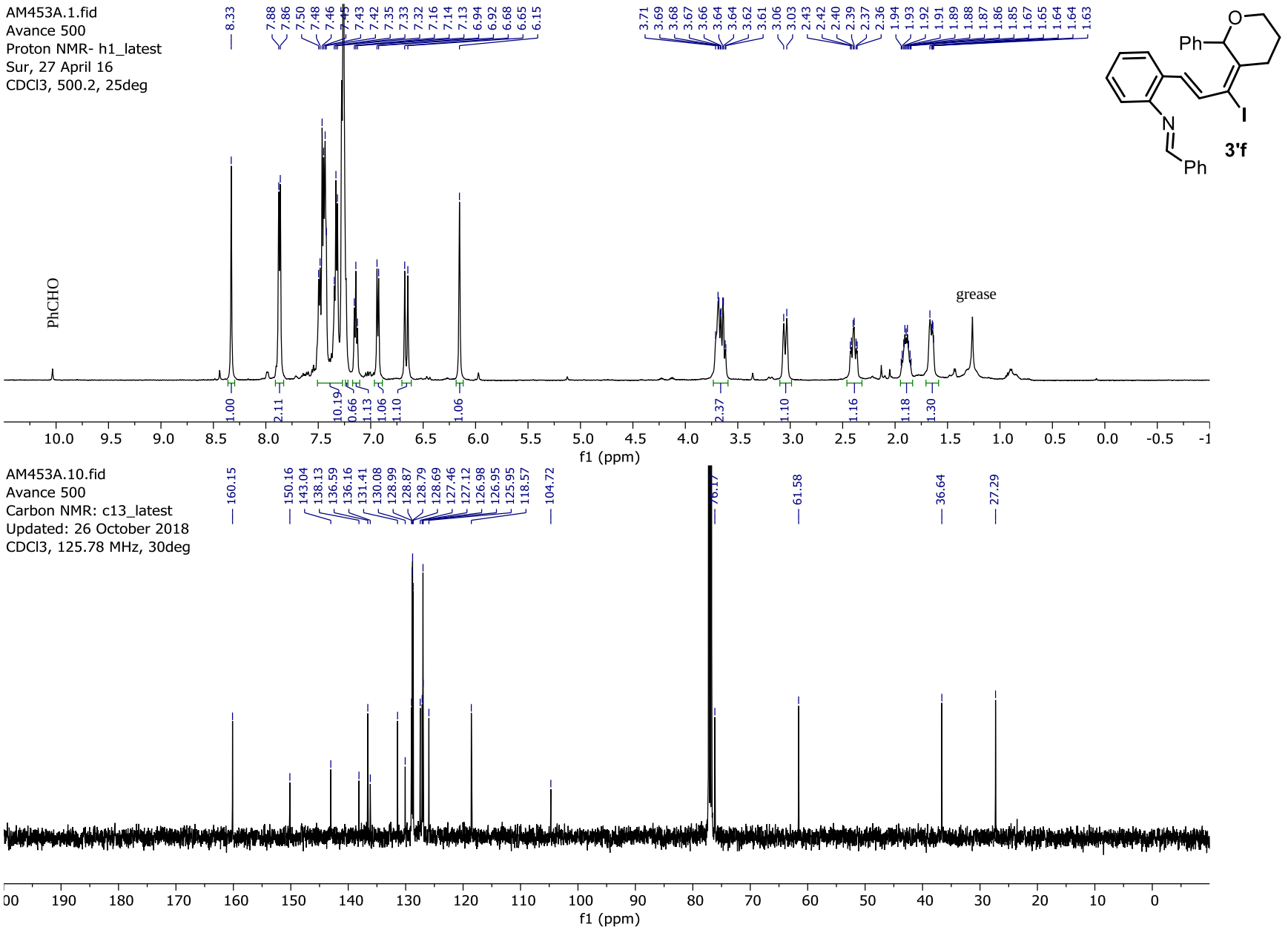
AM458.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg



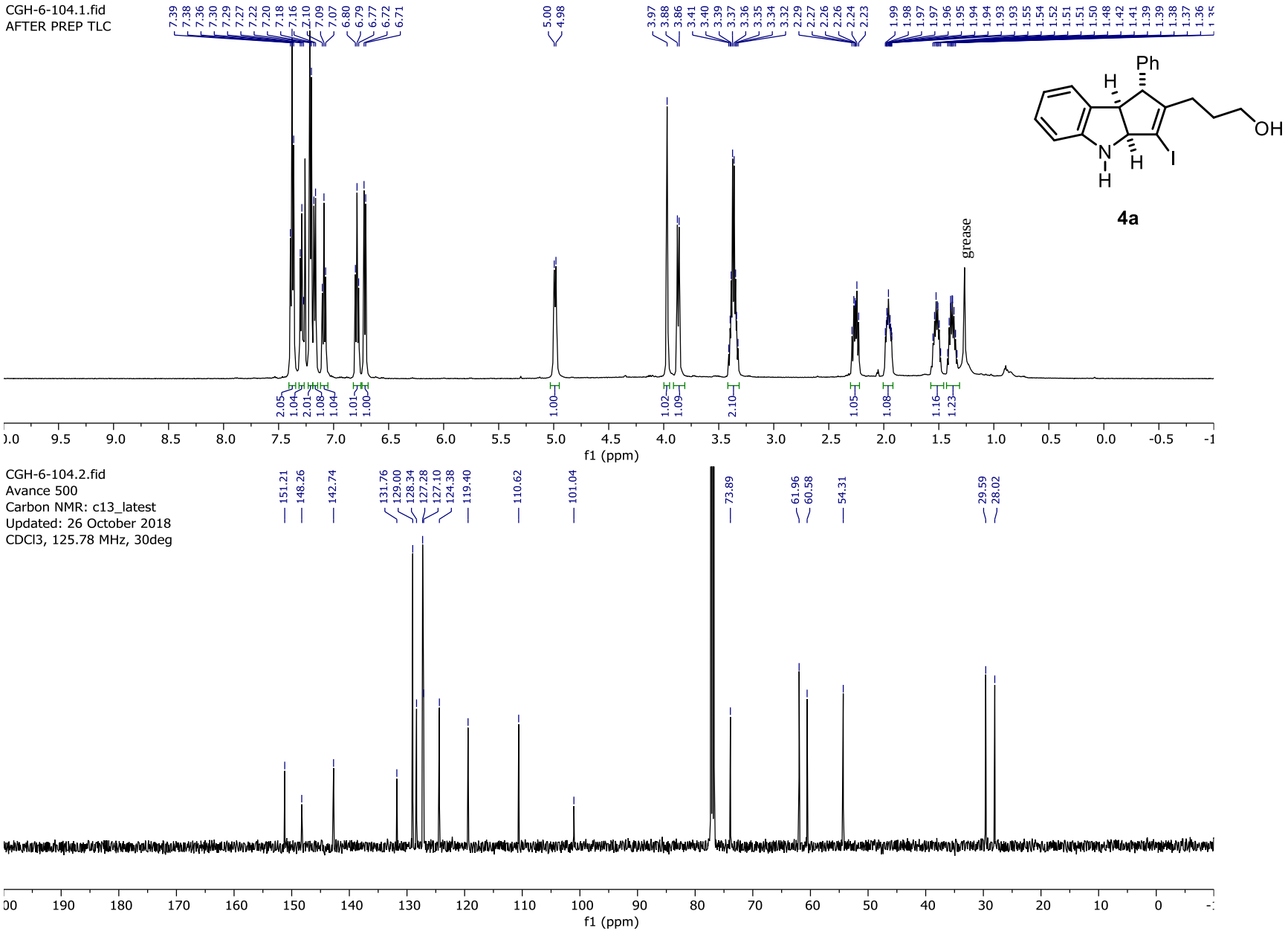

CGH-6-103_400_1_1.fid
CRUDE
Ph
H
OH
N
H
I
Ns
3e
f1 (ppm)


CGH-6-103.1.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

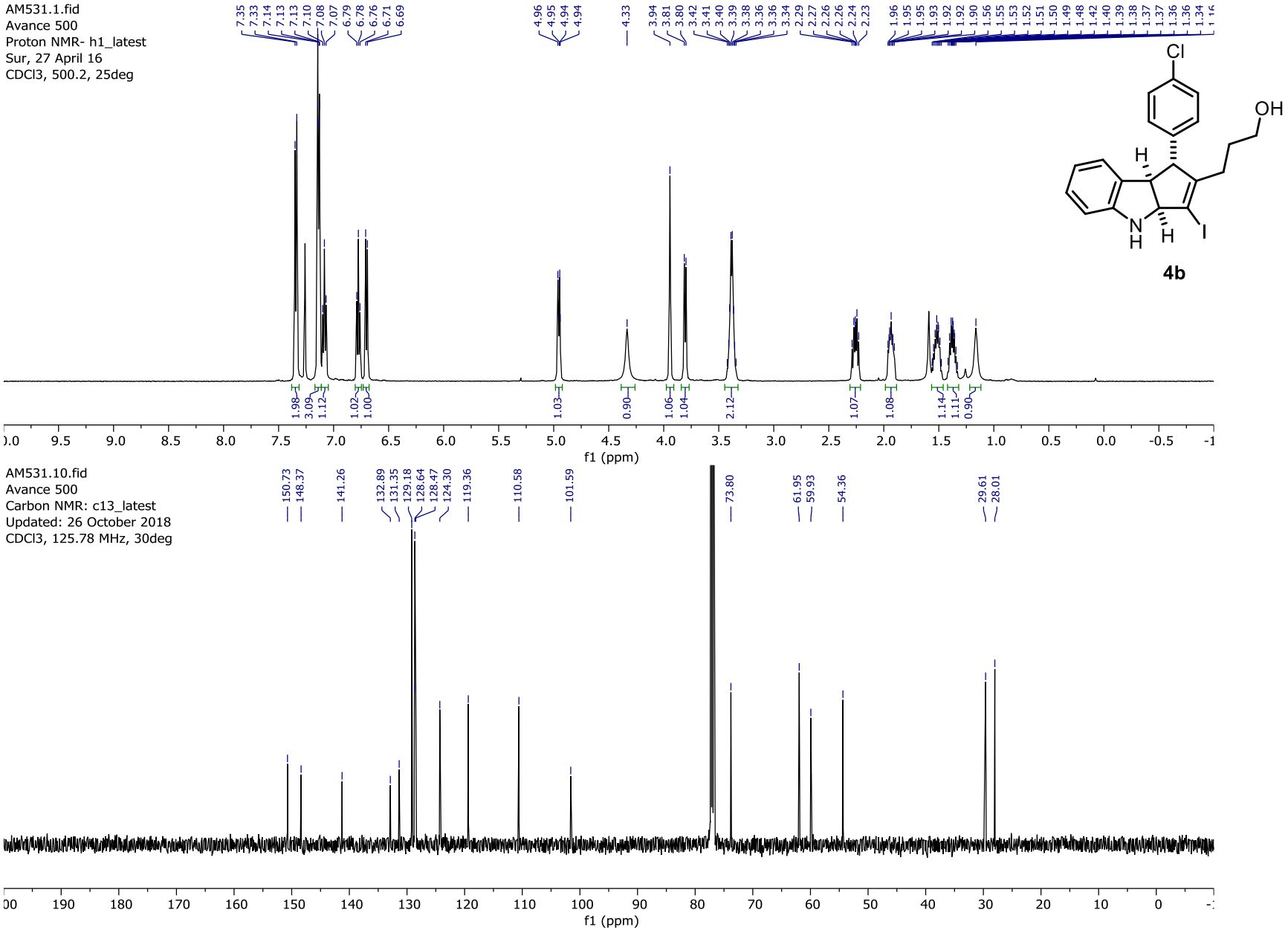
NMR Data


AM453A.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
PhCHO
grease
f1 (ppm)
AM453A.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)
Ph
O
I
N
Ph
3'f

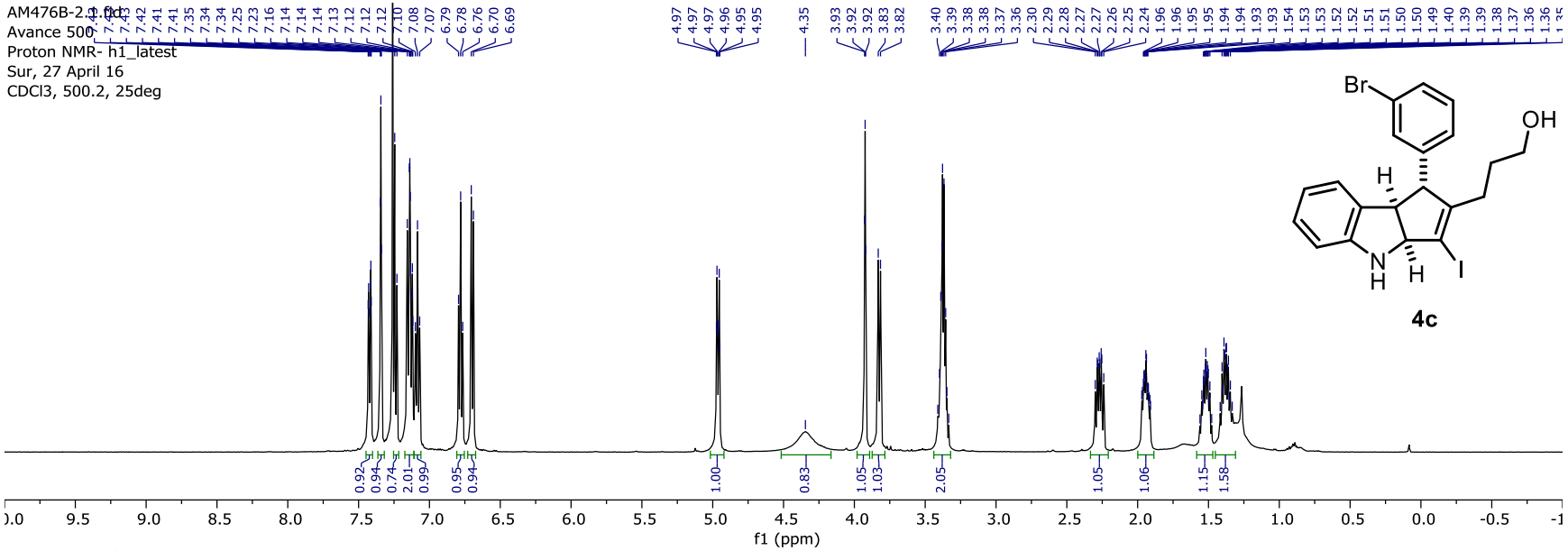
NMR Data

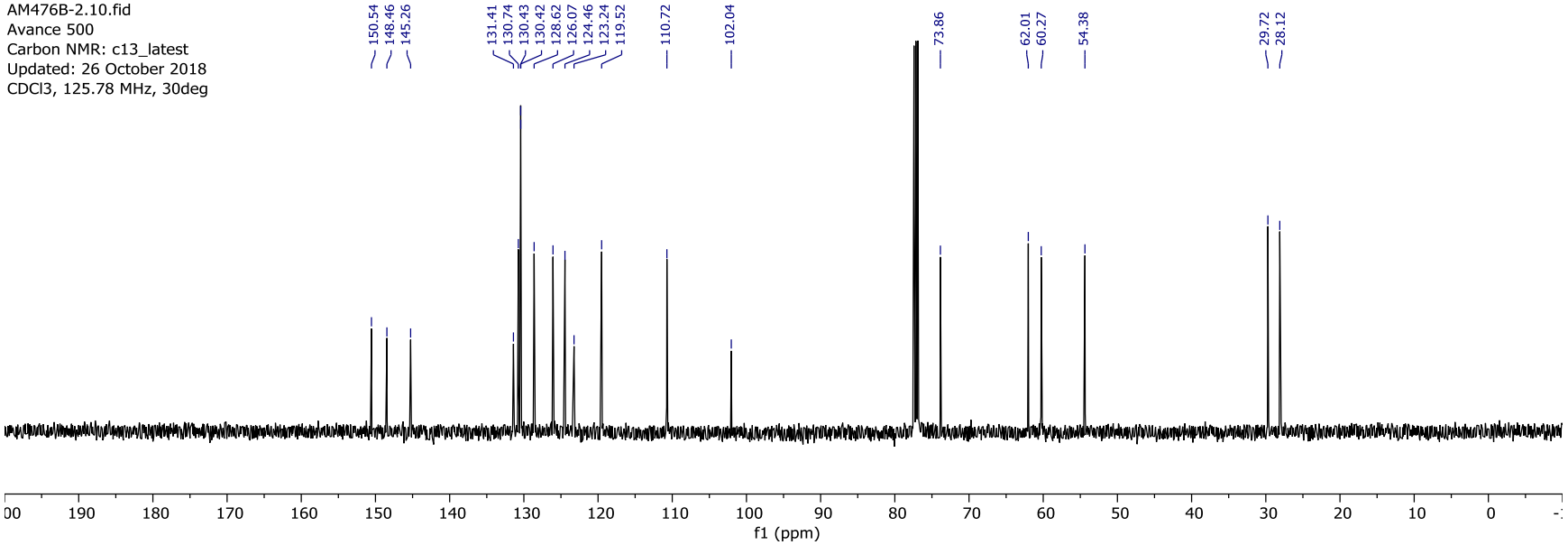

CGH-6-104.1.fid
AFTER PREP TLC
Ph
H
OH
N
H
H
I
4a
grease
f1 (ppm)
CGH-6-104.2.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

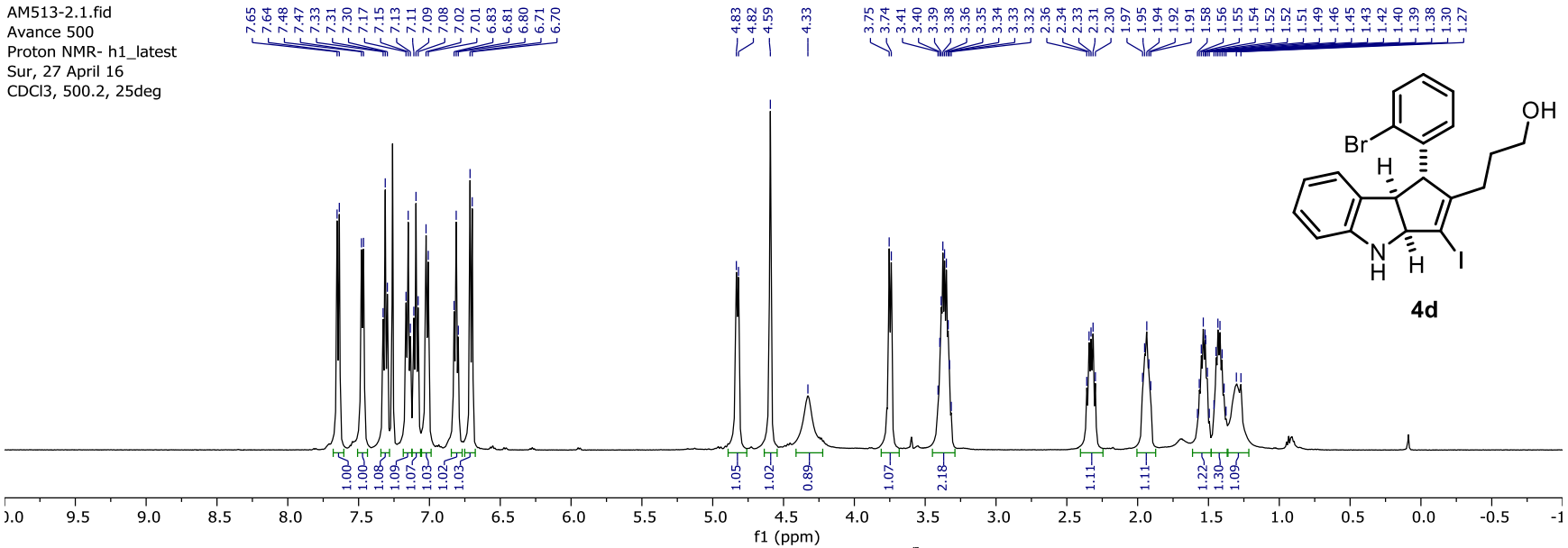
NMR Data

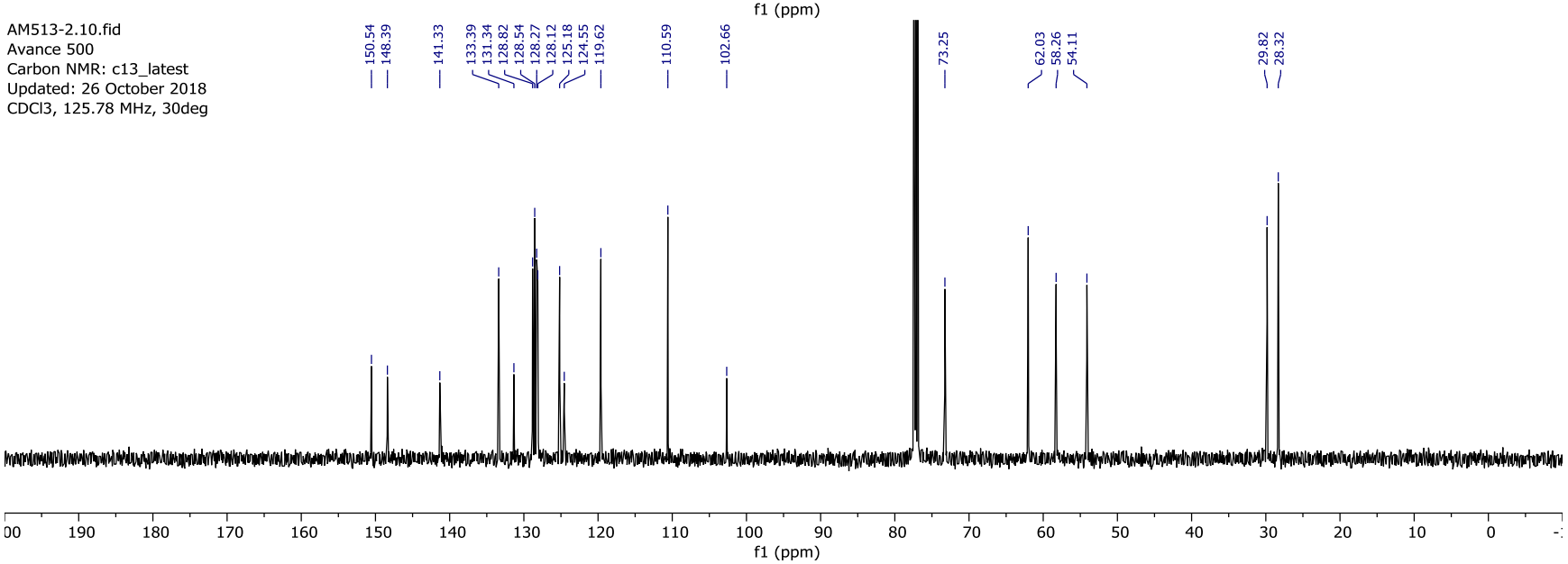

AM531.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
Cl
OH
H
N
H
H
I
4b
f1 (ppm)
AM531.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

NMR Data

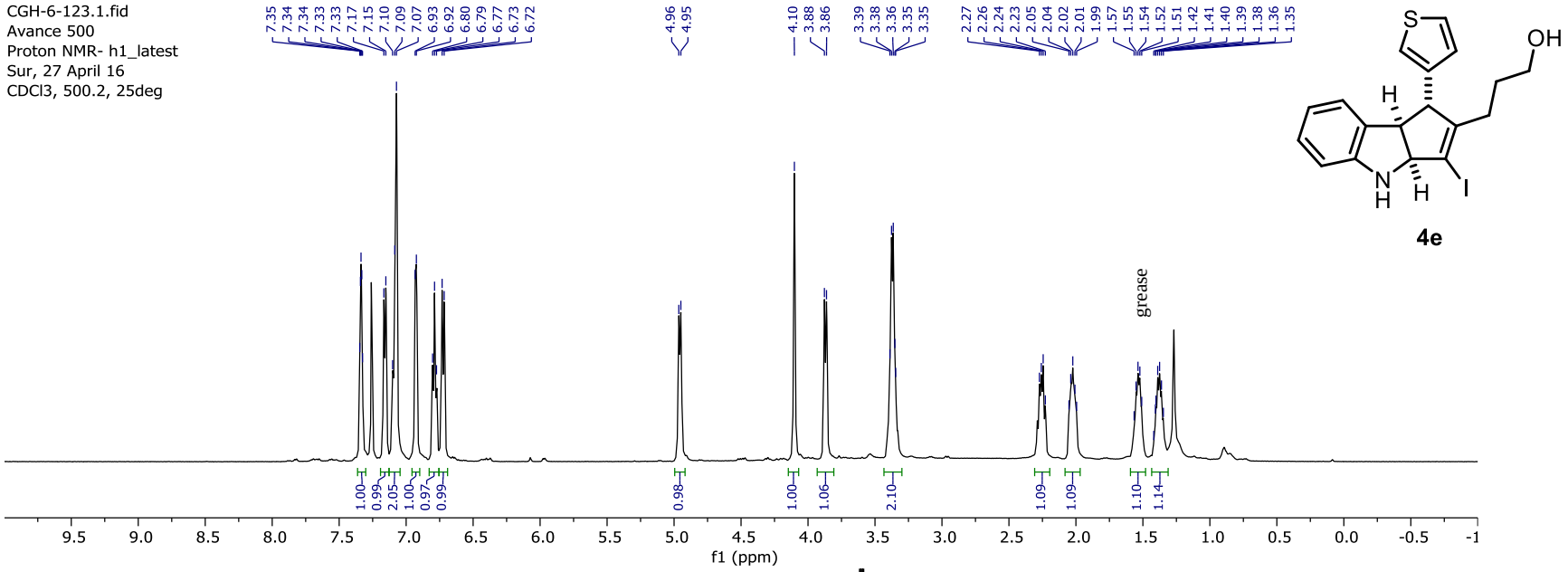

AM476B-2.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
Br
OH
H
N
H
H
I
4c
f1 (ppm)

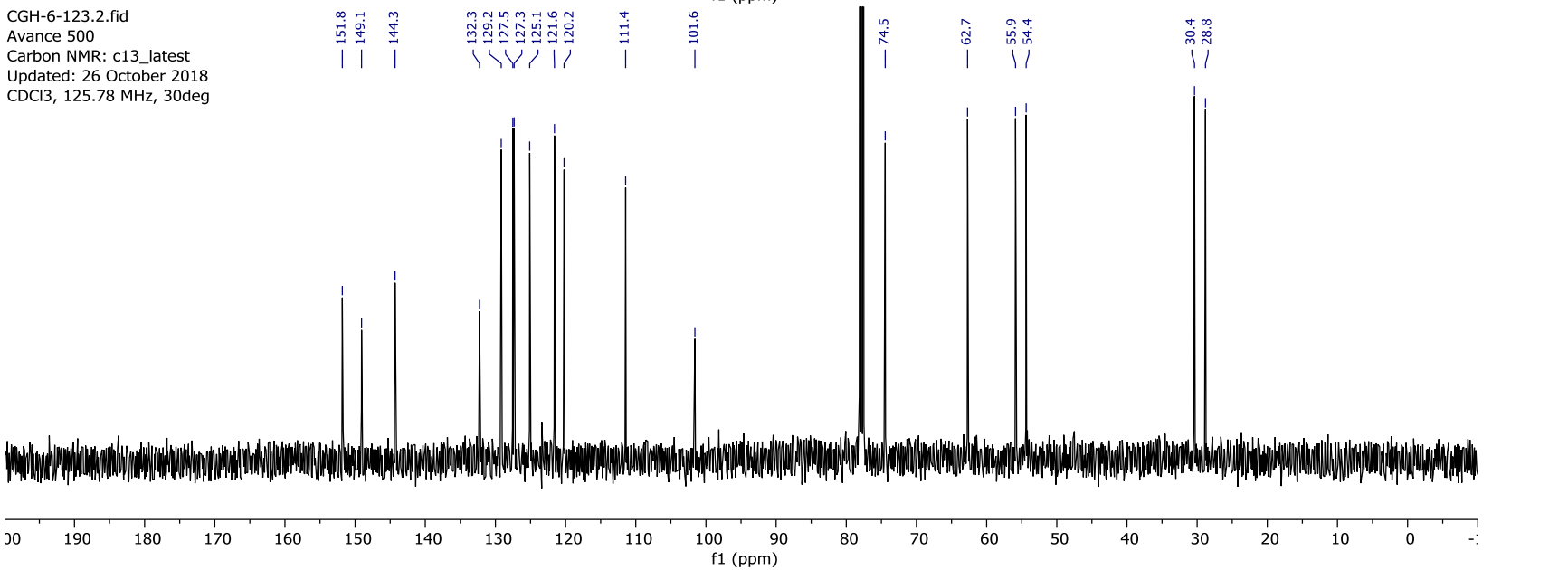

AM476B-2.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)


AM513-2.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
7.65 7.64 7.48 7.47 7.33 7.31 7.30 7.17 7.15 7.13 7.11 7.09 7.08 7.02 7.01 6.83 6.81 6.80 6.71 6.70
4.83 4.82 4.59 4.33
3.75 3.74 3.41 3.40 3.39 3.38 3.36 3.35 3.34 3.33 3.32 2.36 2.34 2.33 2.31 2.30 1.97 1.95 1.94 1.92 1.91 1.58 1.56 1.55 1.54 1.52 1.52 1.51 1.49 1.46 1.45 1.43 1.42 1.40 1.39 1.38 1.30 1.27
1.00 1.00 1.08 1.09 1.07 1.03 1.02 1.03 1.05 1.02 0.89 1.07 2.18 1.11 1.11 1.22 1.30 1.09
f1 (ppm)
Br
OH
H
N
H
H
I
4d

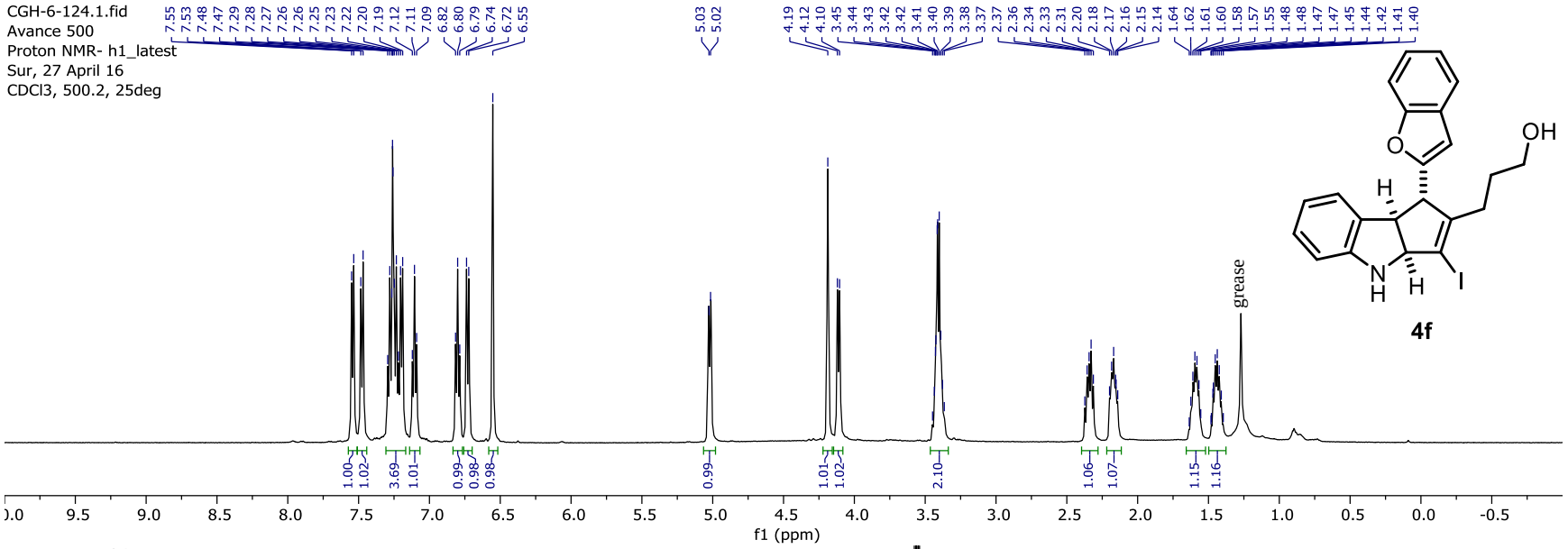

AM513-2.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
150.54 148.39 141.33 133.39 131.34 128.82 128.54 128.27 128.12 125.18 124.55 119.62 110.59 102.66 73.25 62.03 58.26 54.11 29.82 28.32
f1 (ppm)

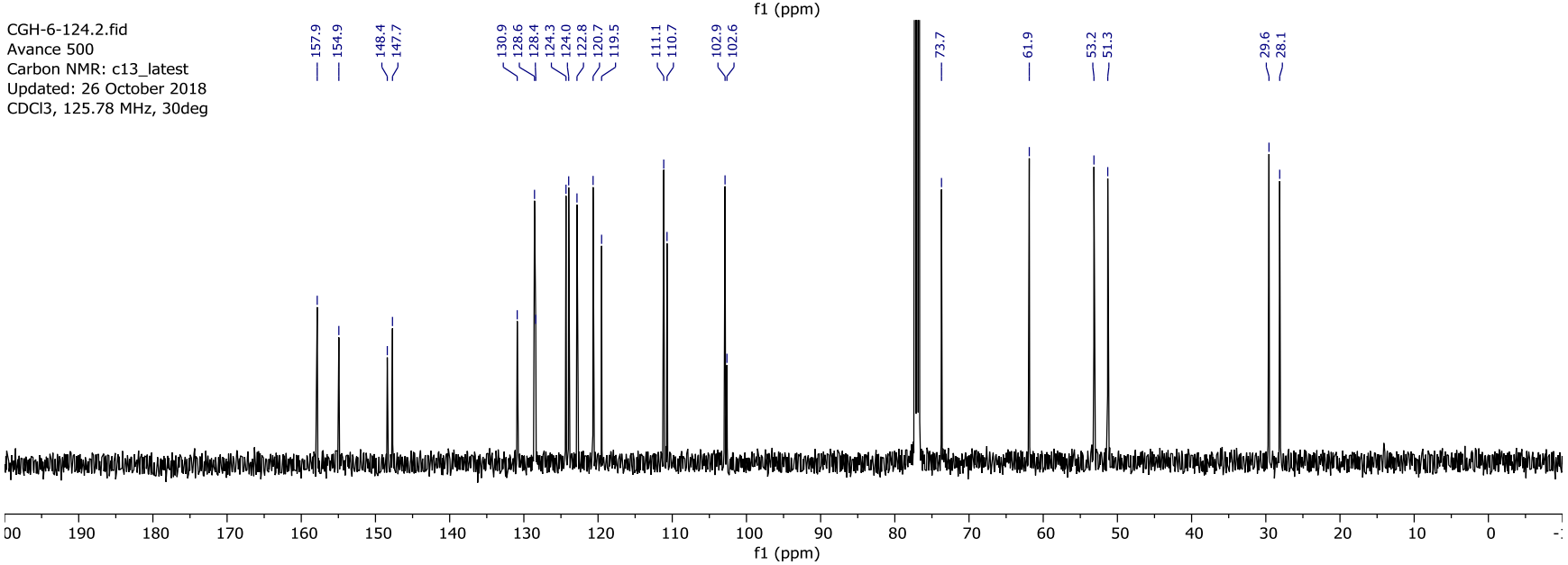
NMR Data


CGH-6-123.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
7.35 7.34 7.34 7.33 7.33 7.17 7.15 7.10 7.09 7.07 6.93 6.92 6.80 6.79 6.77 6.73 6.72
4.96 4.95
4.10 3.88 3.86
3.39 3.38 3.36 3.35 3.35
2.27 2.26 2.24 2.23 2.05 2.04 2.02 2.01 1.99
1.57 1.55 1.54 1.52 1.51 1.42 1.41 1.40 1.39 1.38 1.36 1.35
grease
1.00 0.99 2.05 1.00 0.97 0.99 0.98 1.00 1.06 2.10 1.09 1.09 1.10 1.14
f1 (ppm)
S
OH
H
N
H
H
I
4e

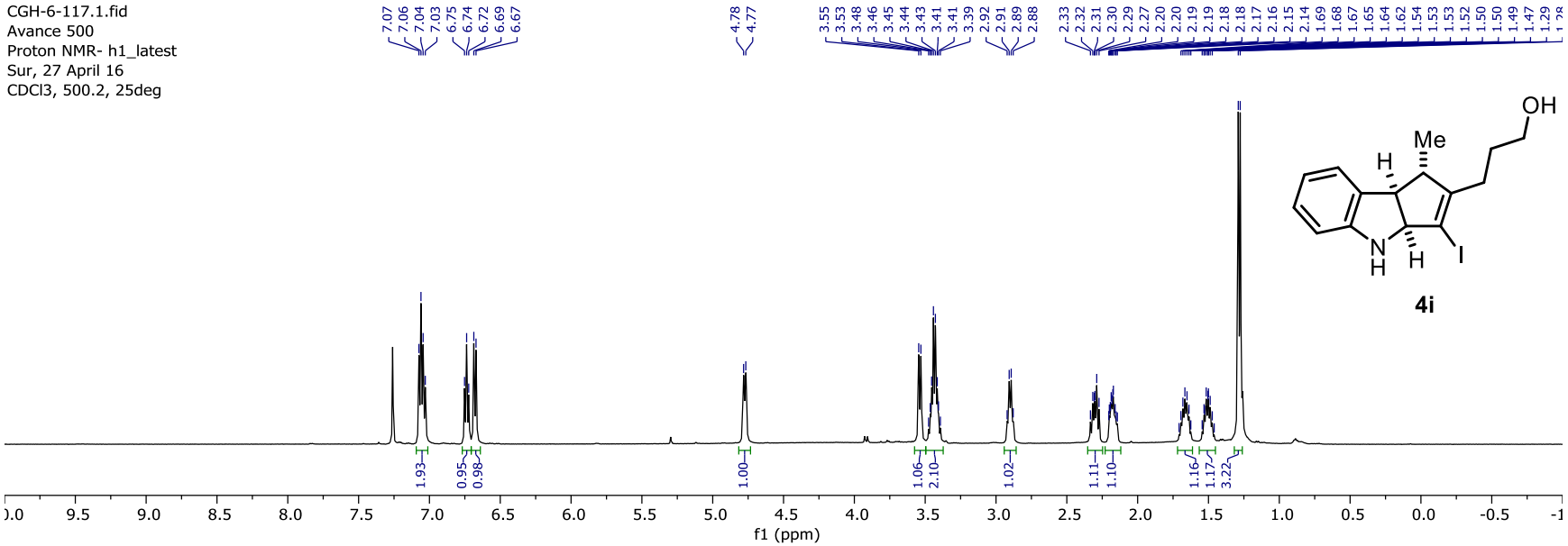

CGH-6-123.2.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
151.8 149.1 144.3 132.3 129.2 127.5 127.3 125.1 121.6 120.2 111.4 101.6 74.5 62.7 55.9 54.4 30.4 28.8
f1 (ppm)

NMR Data


CGH-6-124.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
grease
OH
O
H
N
H
H
I
4f
f1 (ppm)

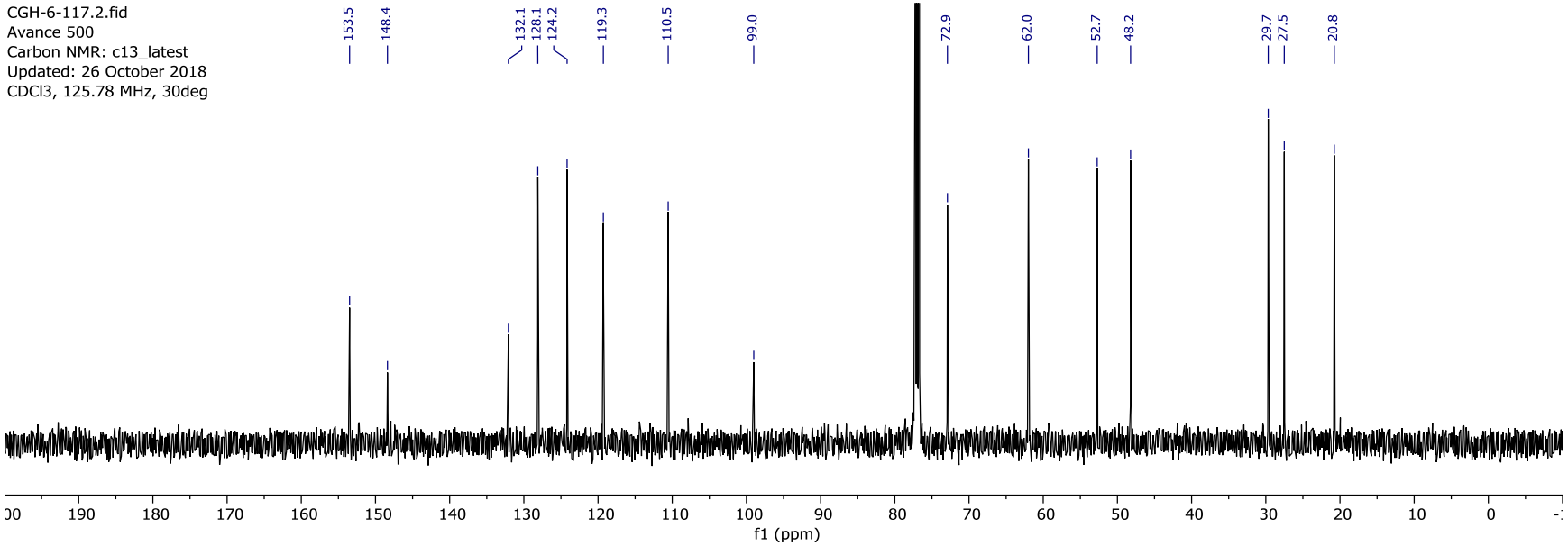

CGH-6-124.2.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

CGH-6-117.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg

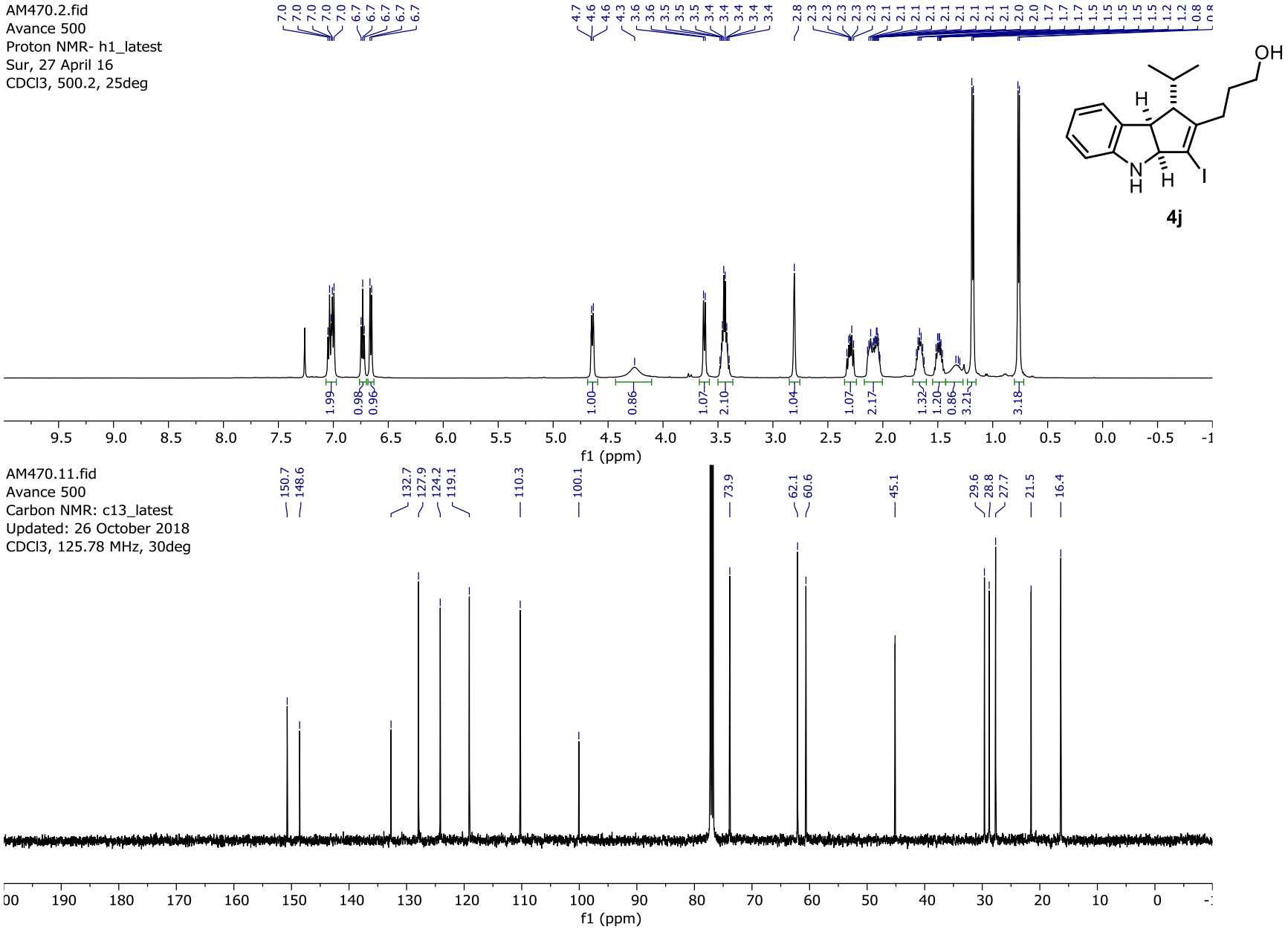


4i

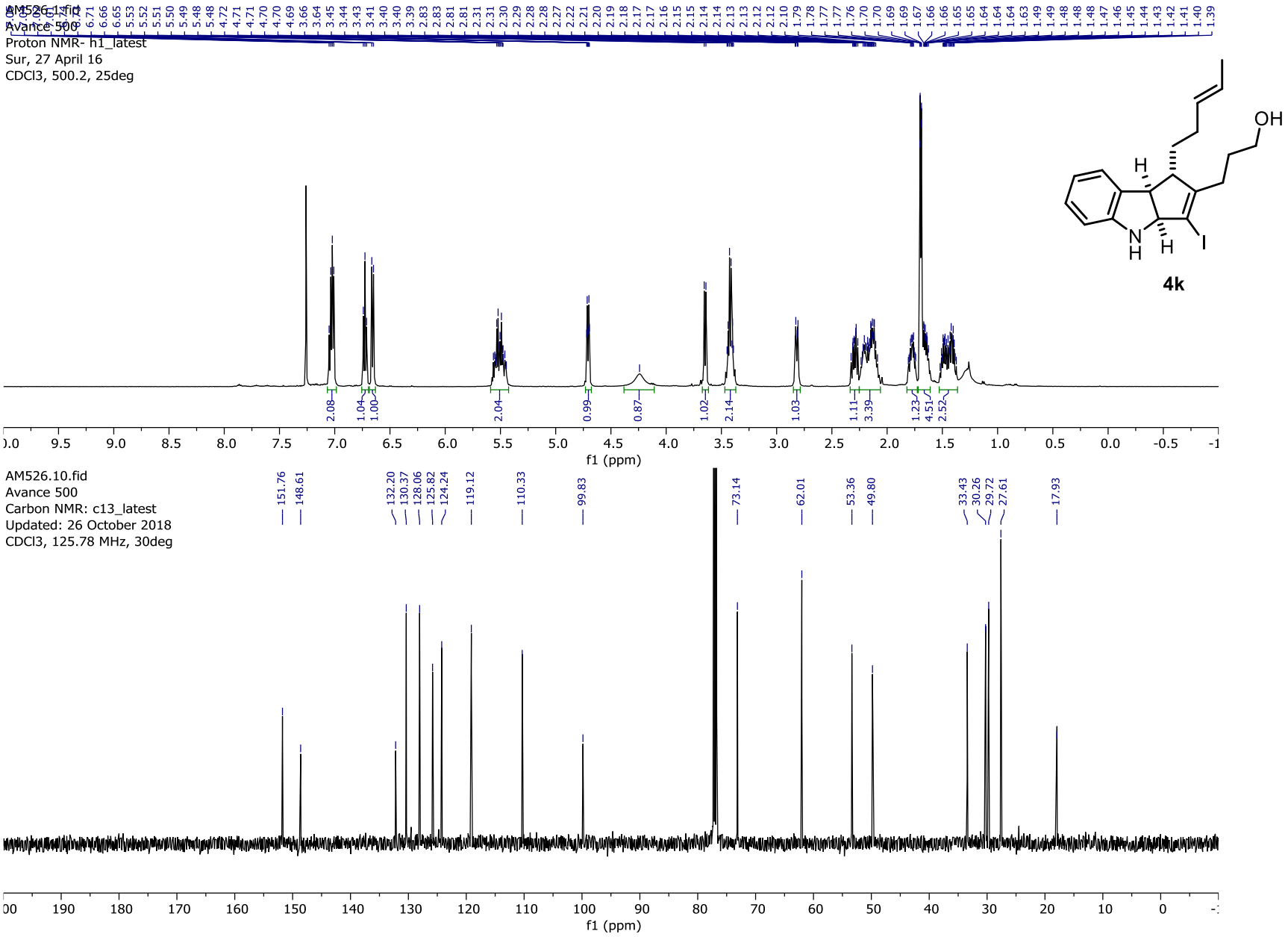
CGH-6-117.2.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg



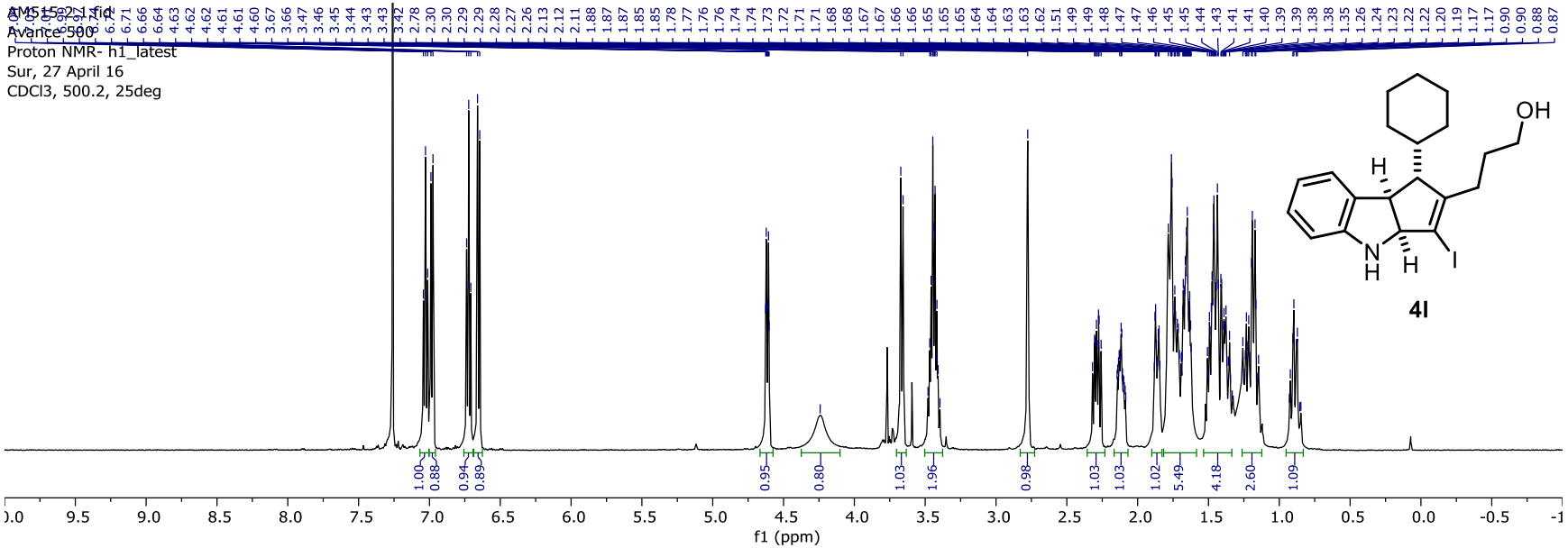
NMR Data

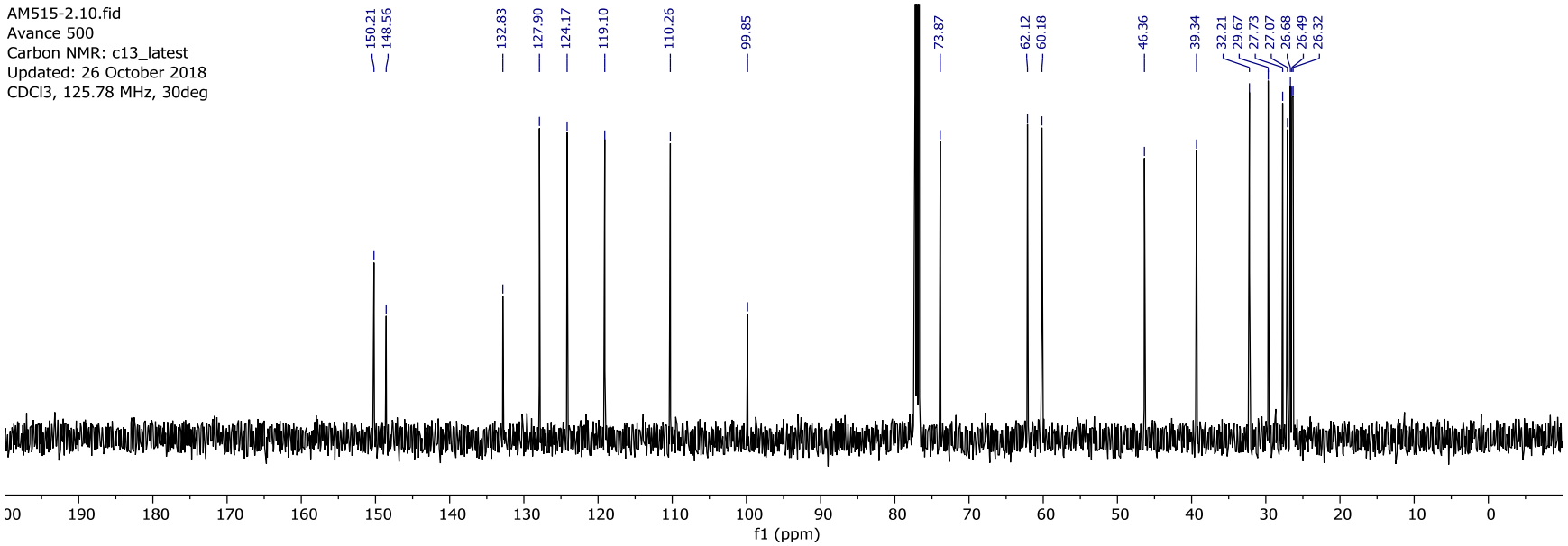

AM470.2.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
OH
H
N
H
H
I
4j
f1 (ppm)
AM470.11.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
150.7
148.6
132.7
127.9
124.2
119.1
110.3
100.1
73.9
62.1
60.6
45.1
29.6
28.8
27.7
21.5
16.4
f1 (ppm)

NMR Data

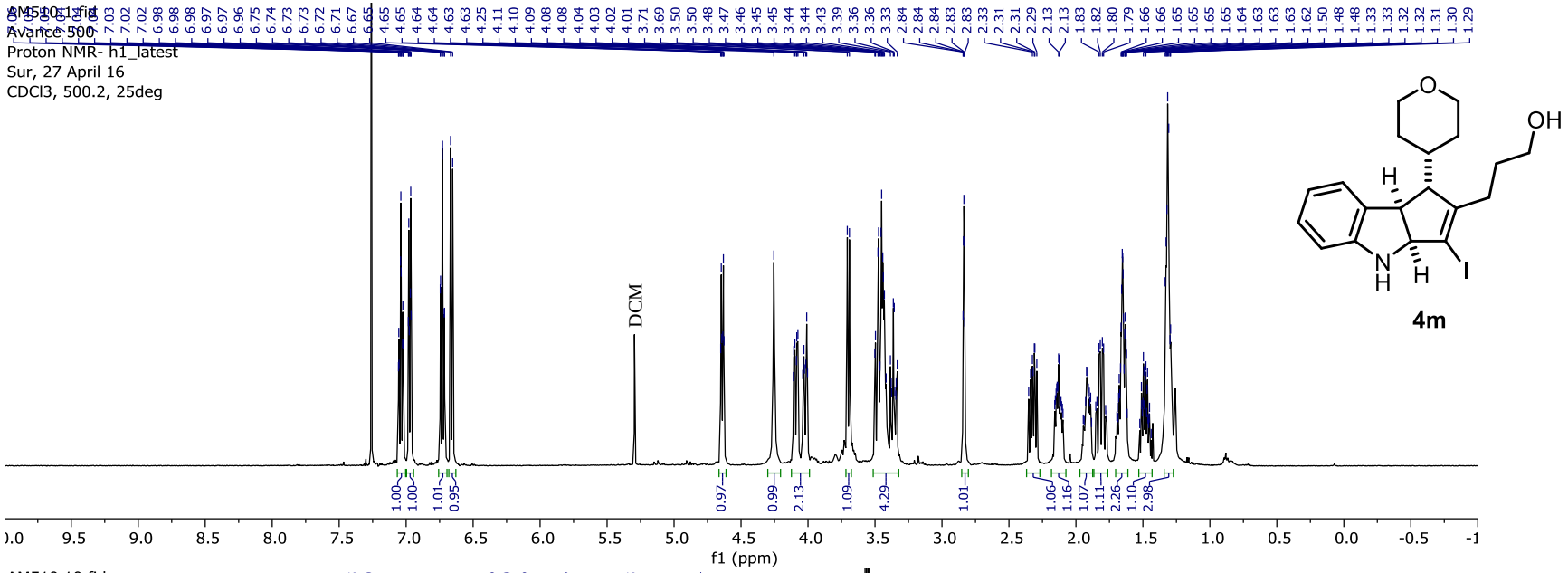

AM526.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
OH
H
N
H
H
I
4k
f1 (ppm)
AM526.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
151.76
148.61
132.20
130.37
128.06
125.82
124.24
119.12
110.33
99.83
73.14
62.01
53.36
49.80
33.43
30.26
29.72
27.61
17.93
f1 (ppm)

NMR Data


AM515-2.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
OH
H
N
H
H
I
4l
f1 (ppm)

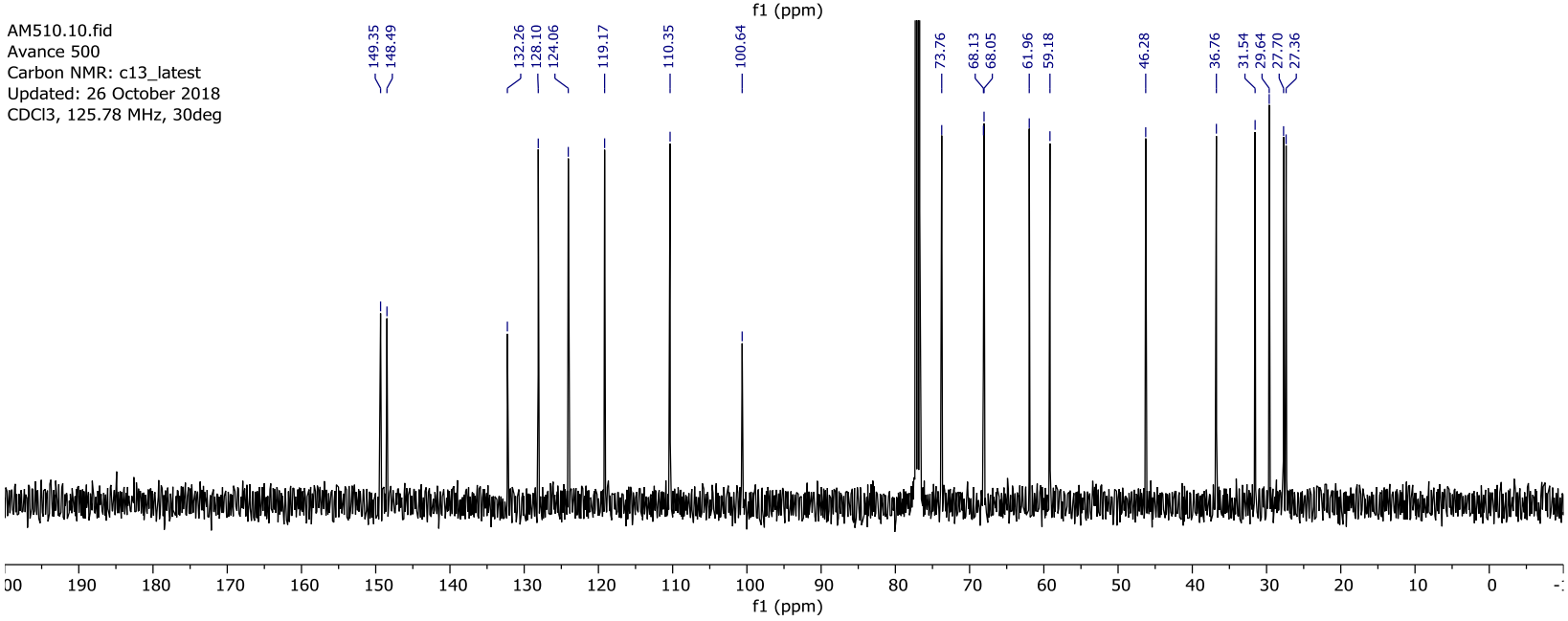

AM515-2.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
150.21
148.56
132.83
127.90
124.17
119.10
110.26
99.85
73.87
62.12
60.18
46.36
39.34
32.21
29.67
27.73
27.07
26.68
26.49
26.32
f1 (ppm)

NMR Data

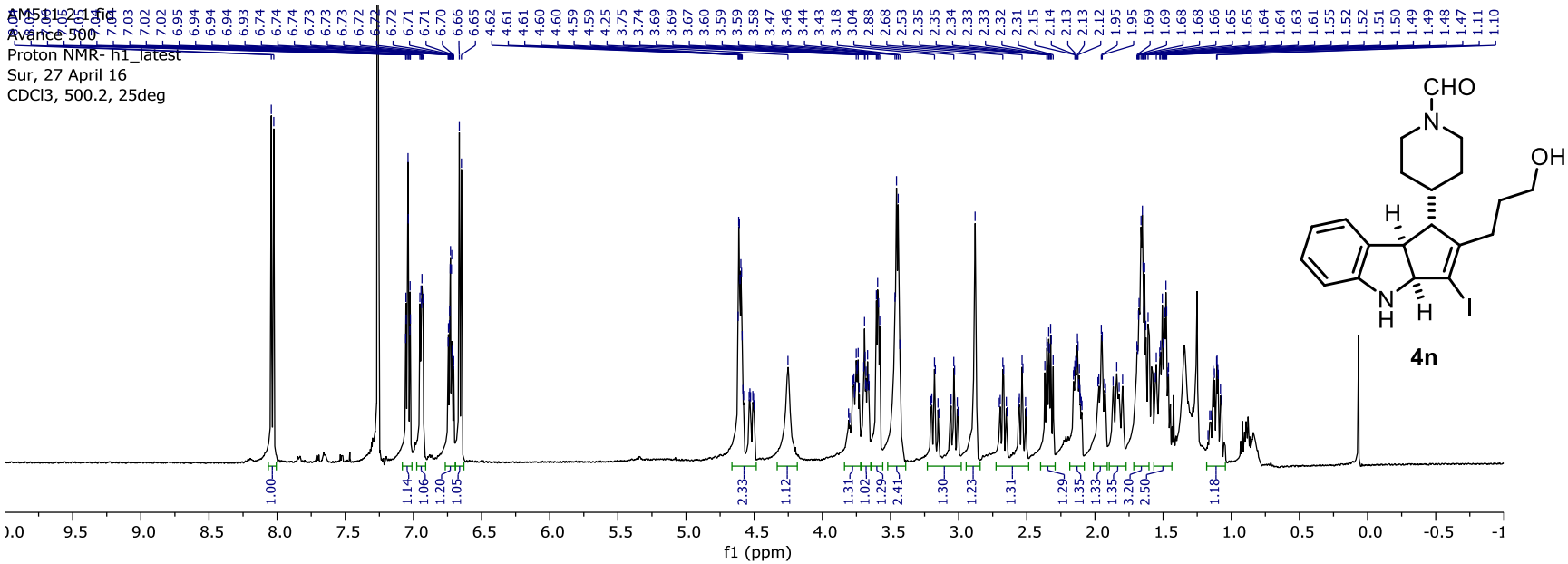

AM510.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
DCM
f1 (ppm)

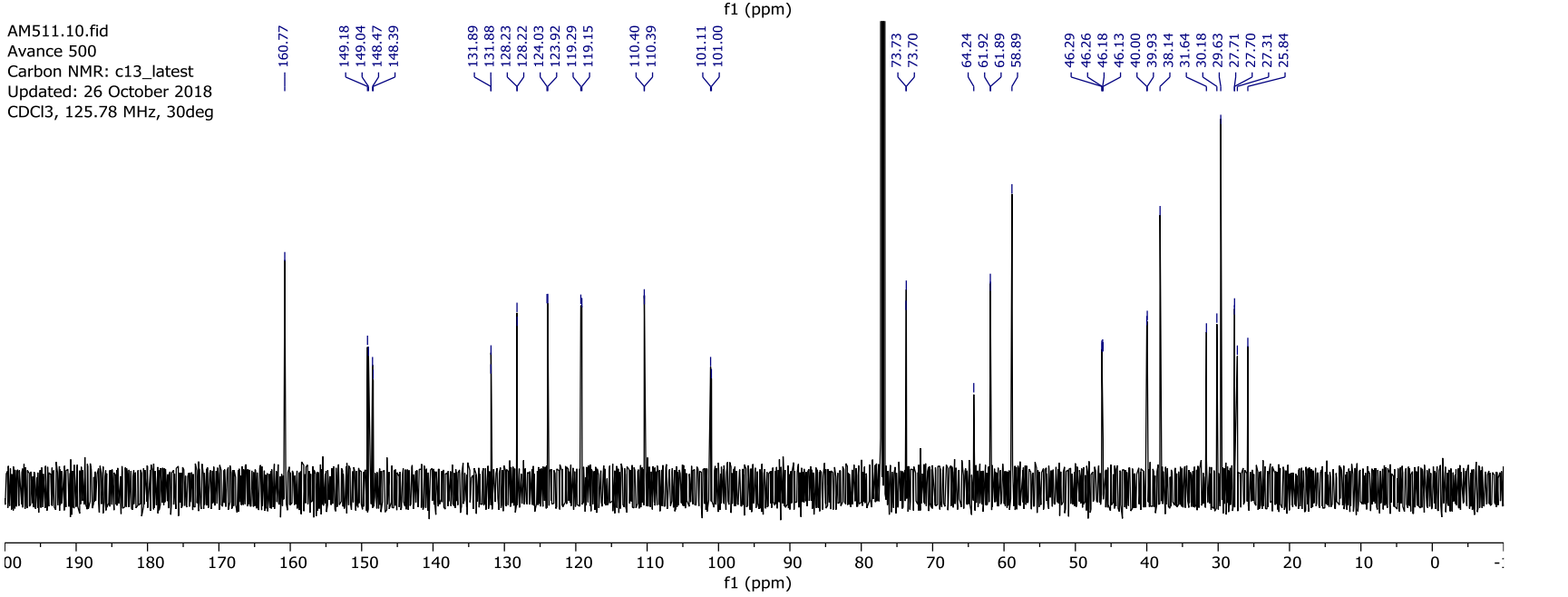
O
OH
H
N
H
H
I

4m

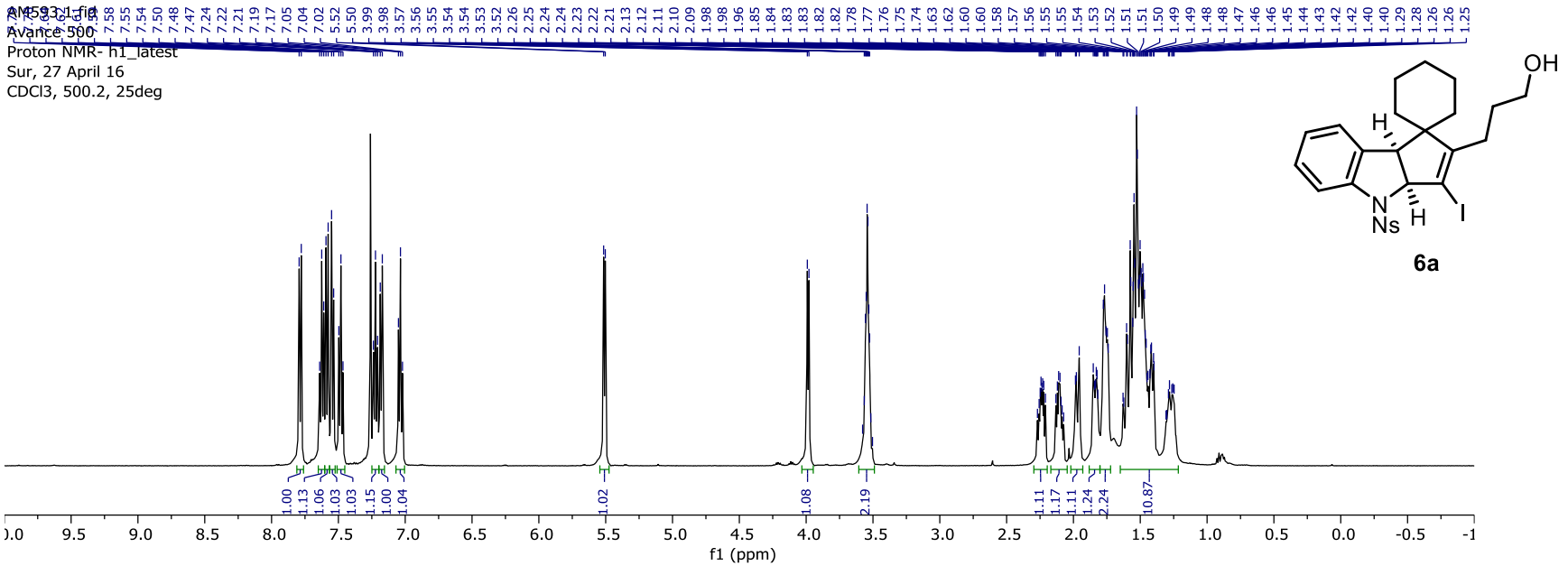

AM510.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
149.35
148.49
132.26
128.10
124.06
119.17
110.35
100.64
73.76
68.13
68.05
61.96
59.18
46.28
36.76
31.54
29.64
27.70
27.36
f1 (ppm)

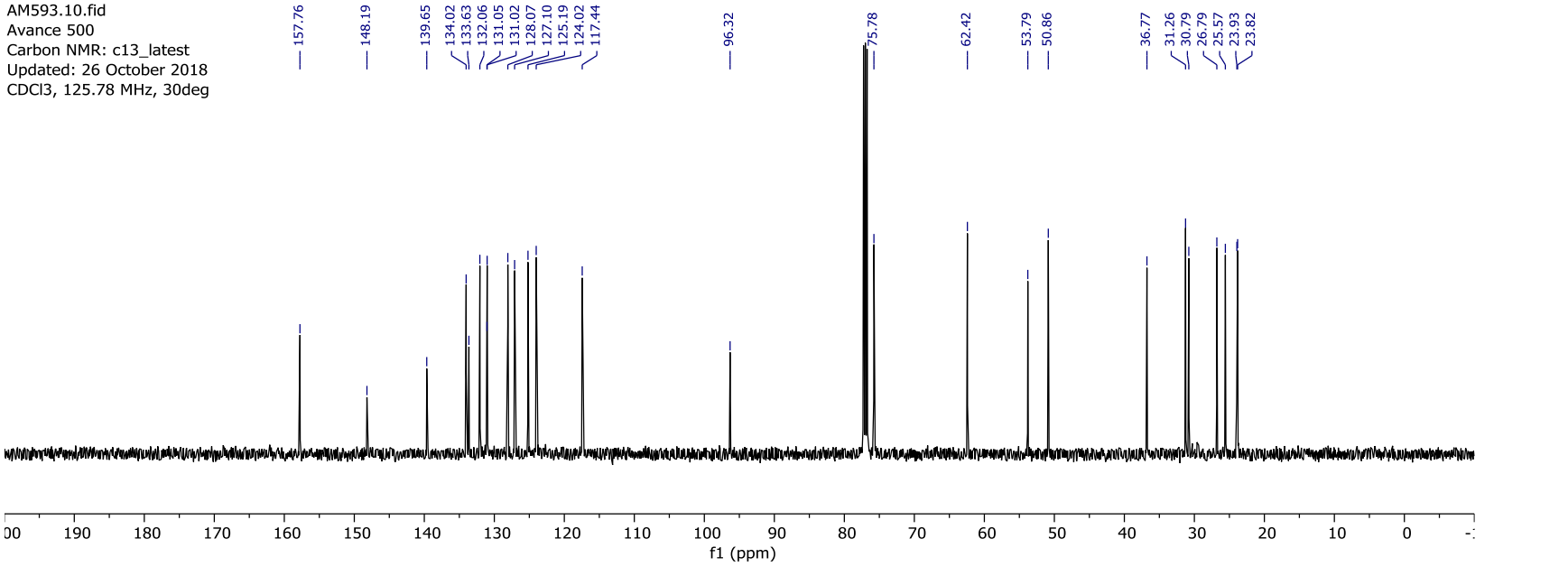
NMR Data


AM511.2.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
CHO
N
OH
H
N
H
H
I
4n
f1 (ppm)

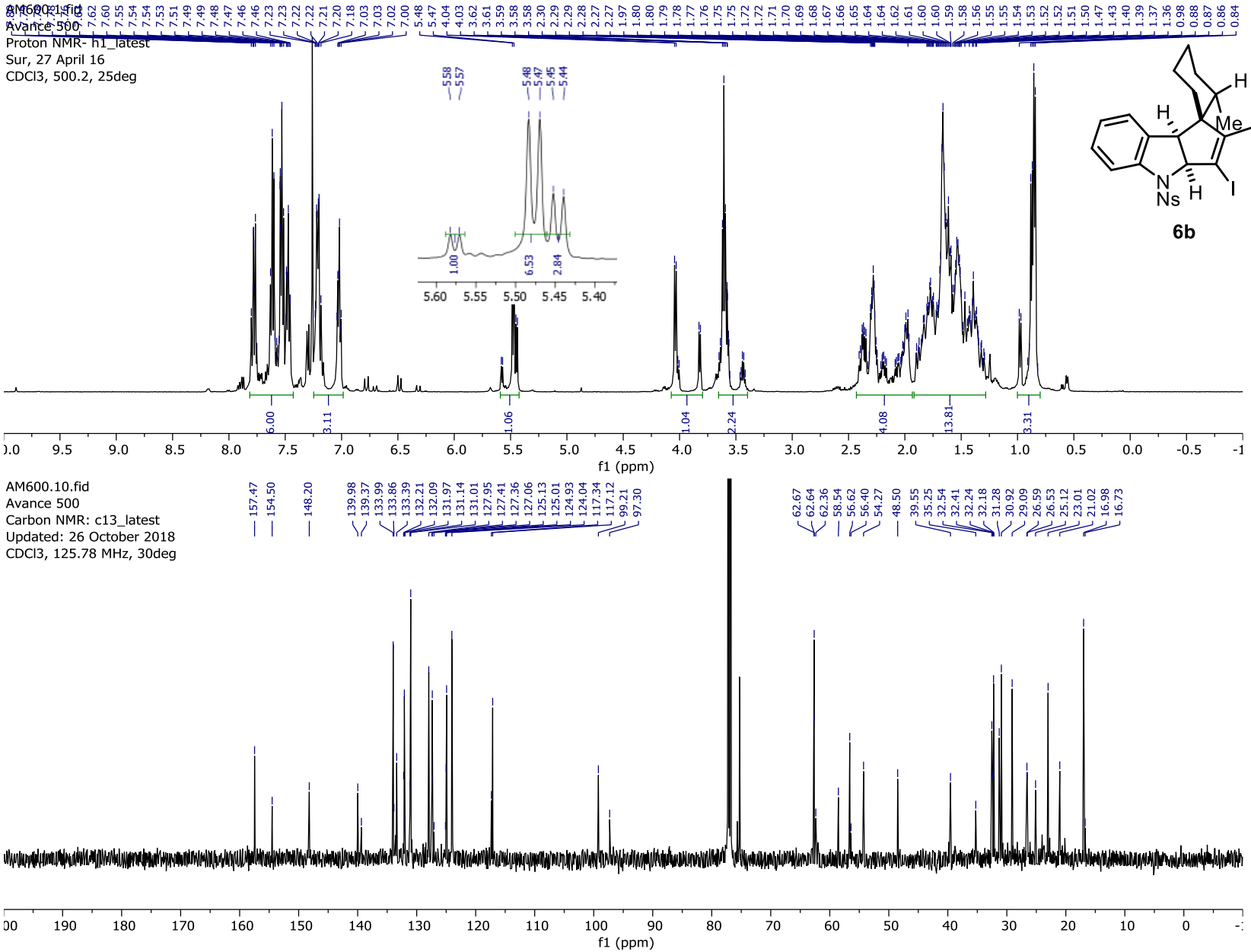

AM511.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

NMR Data

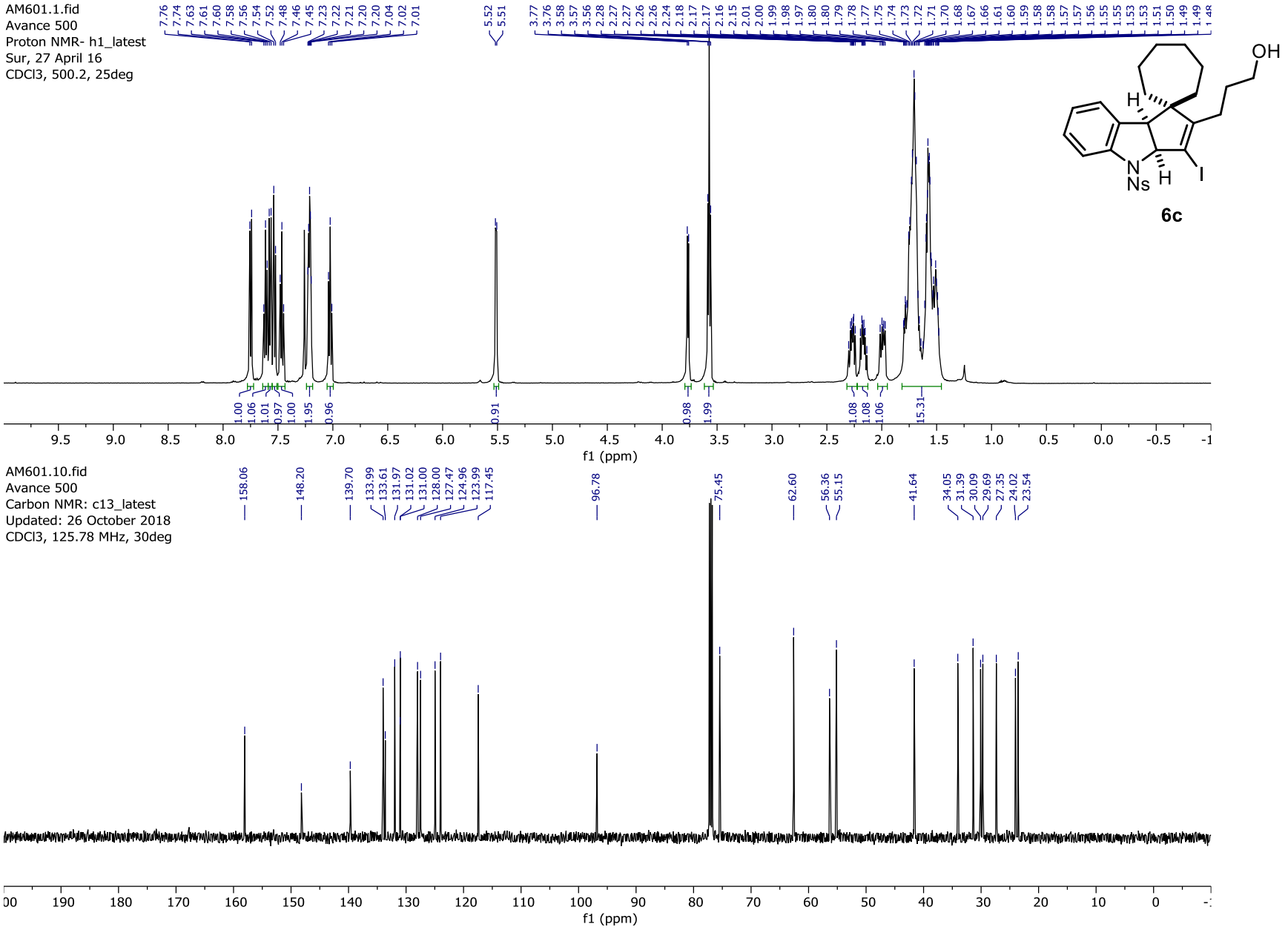

AM593.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
OH
H
N
Ns
H
I
6a
f1 (ppm)

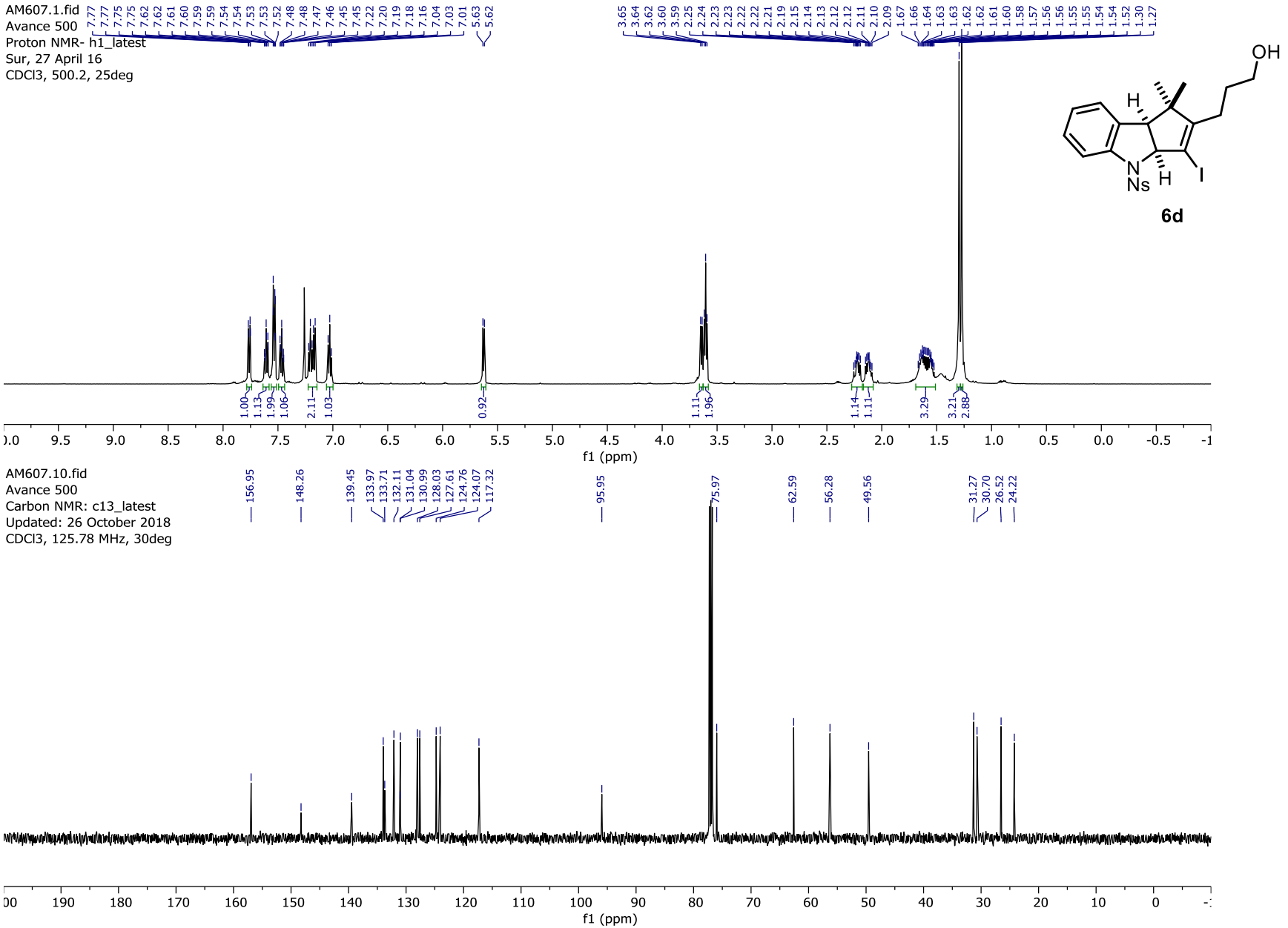

AM593.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

NMR Data

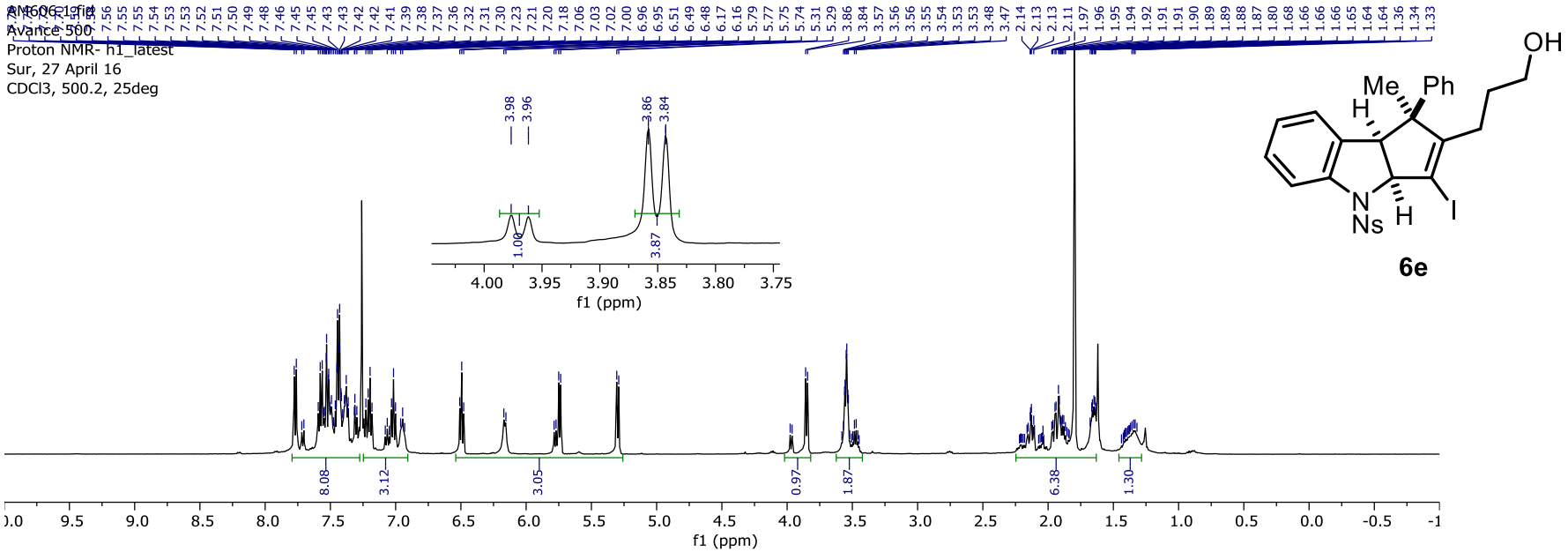

AM600.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
OH
H
H
Me
N
Ns
H
I
6b
f1 (ppm)
AM600.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

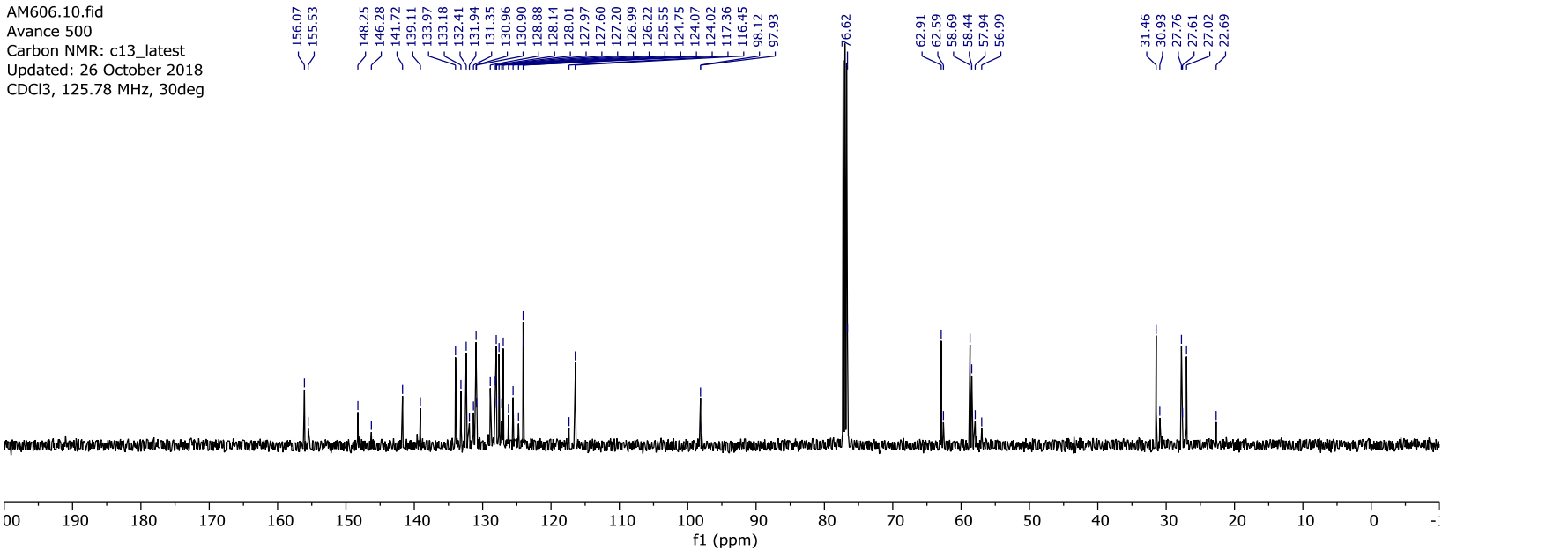
NMR Data


AM601.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
OH
H
N
Ns
H
I
6c
f1 (ppm)
AM601.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

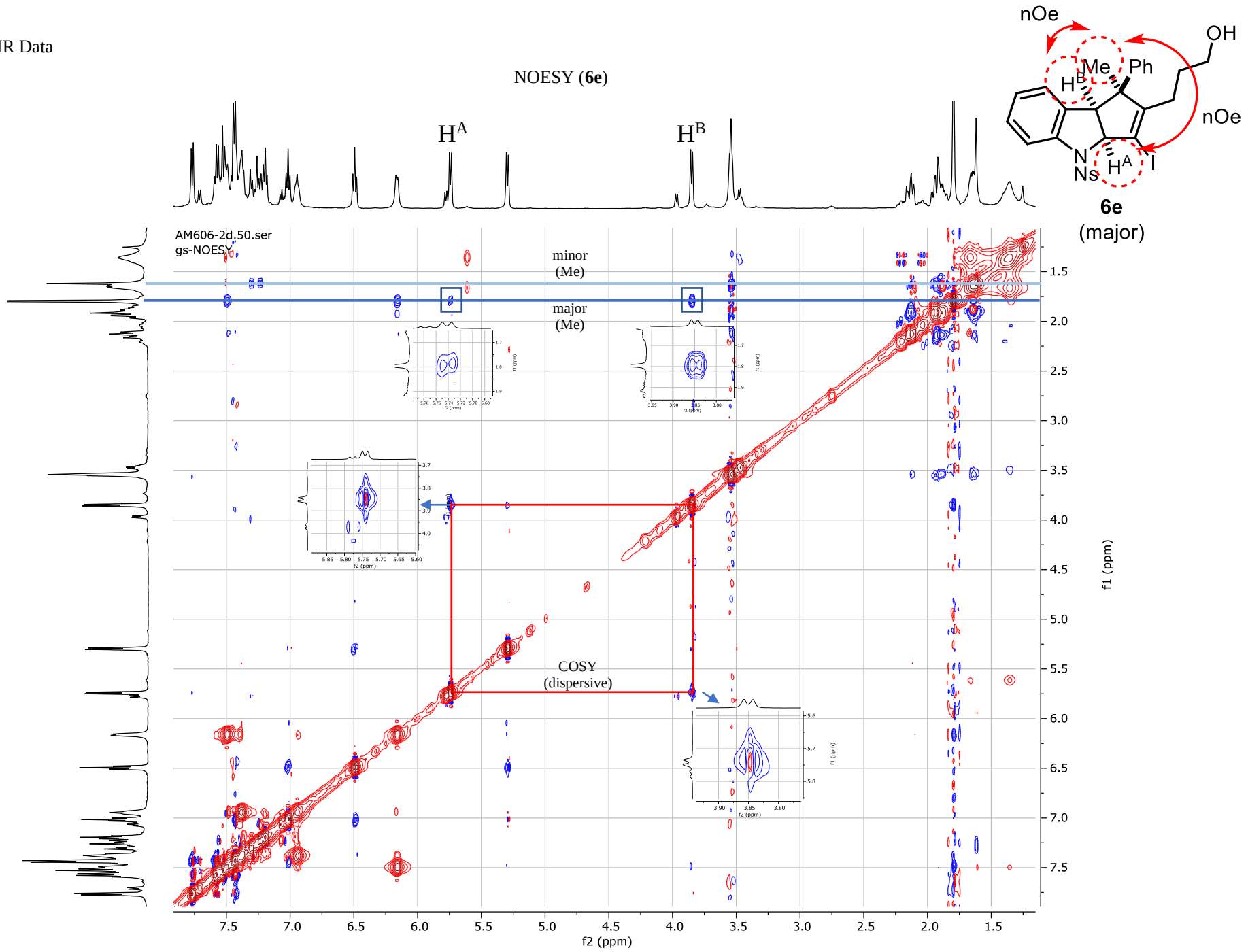

AM607.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
OH
H
N
Ns
H
I
6d
f1 (ppm)
AM607.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

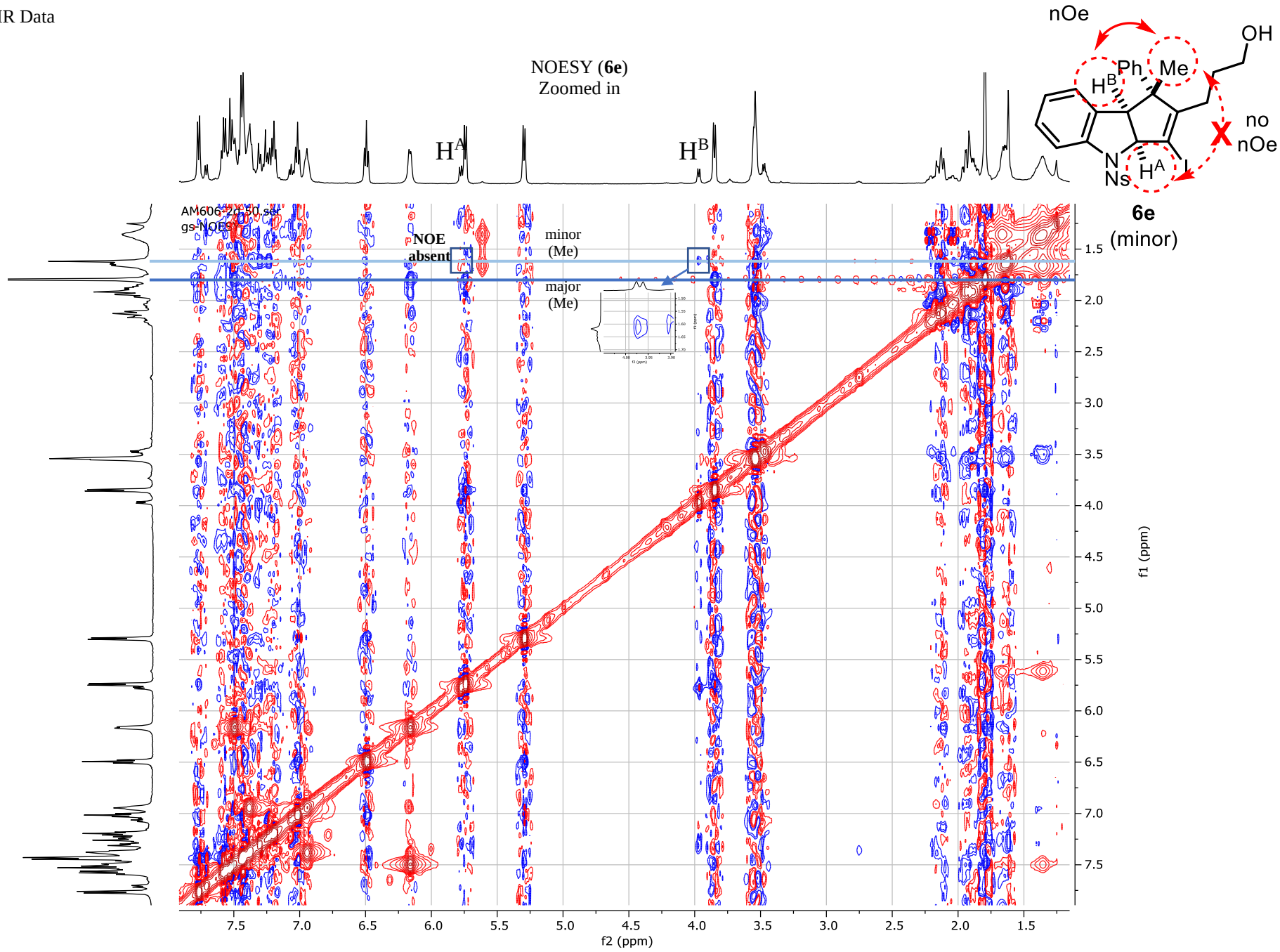
NMR Data

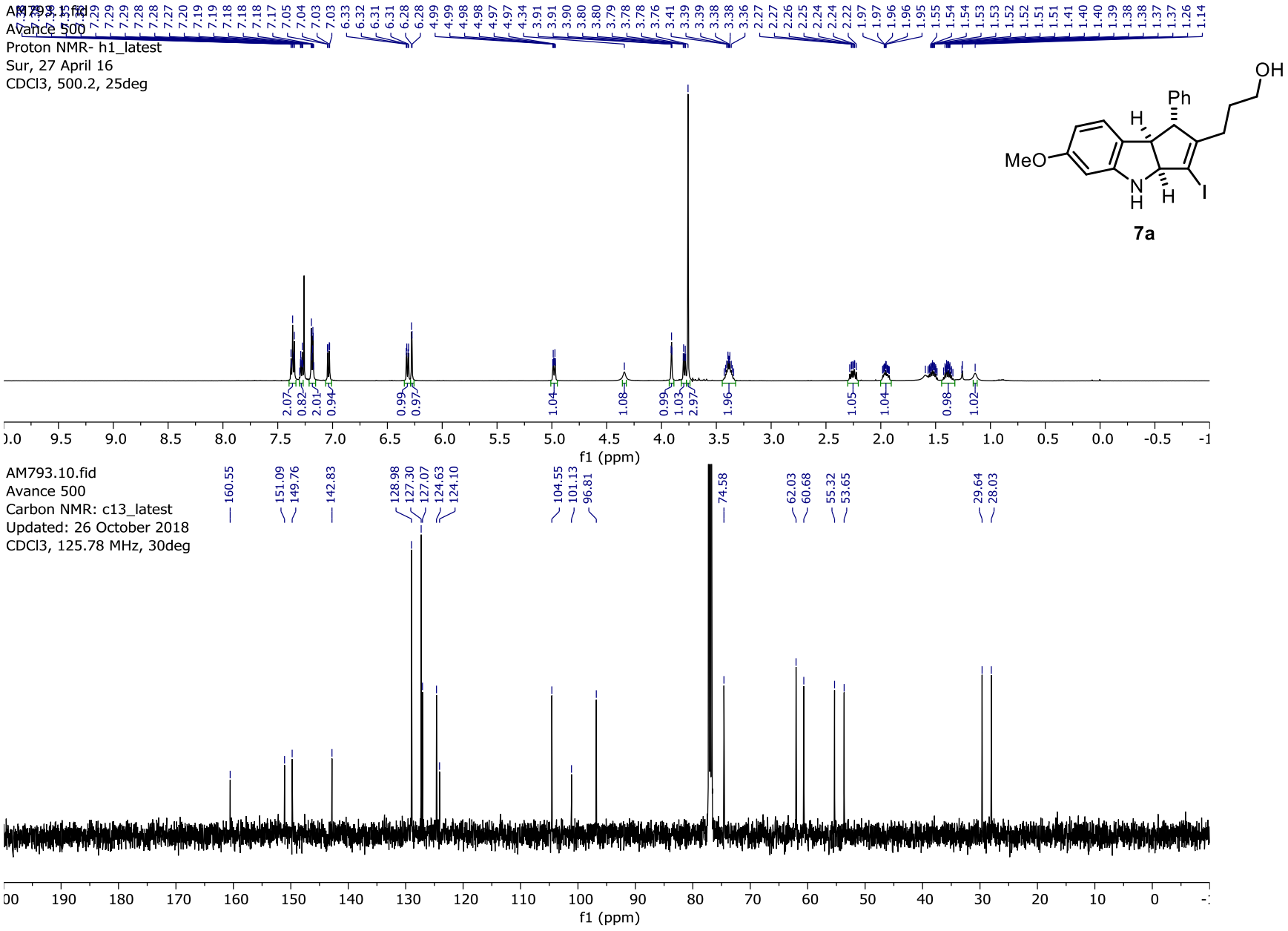

AM606.1H.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
f1 (ppm)
OH
Me
Ph
H
N
Ns
H
I
6e


AM606.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

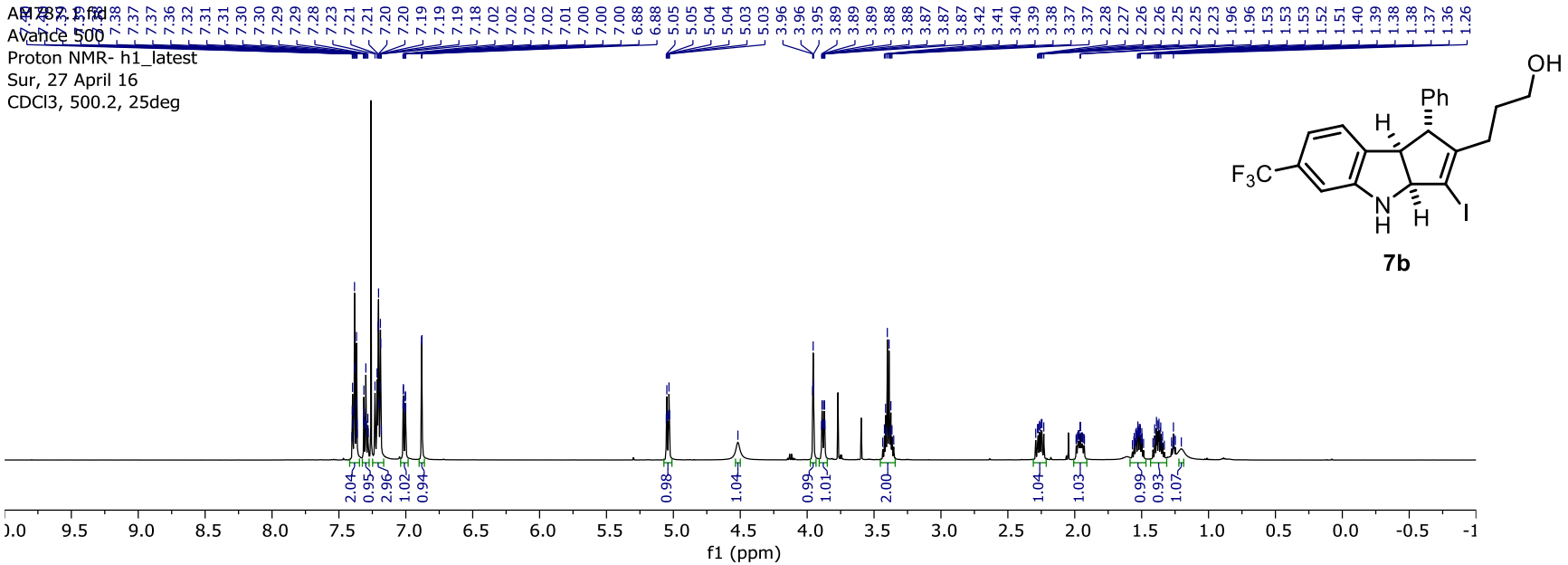
NMR Data

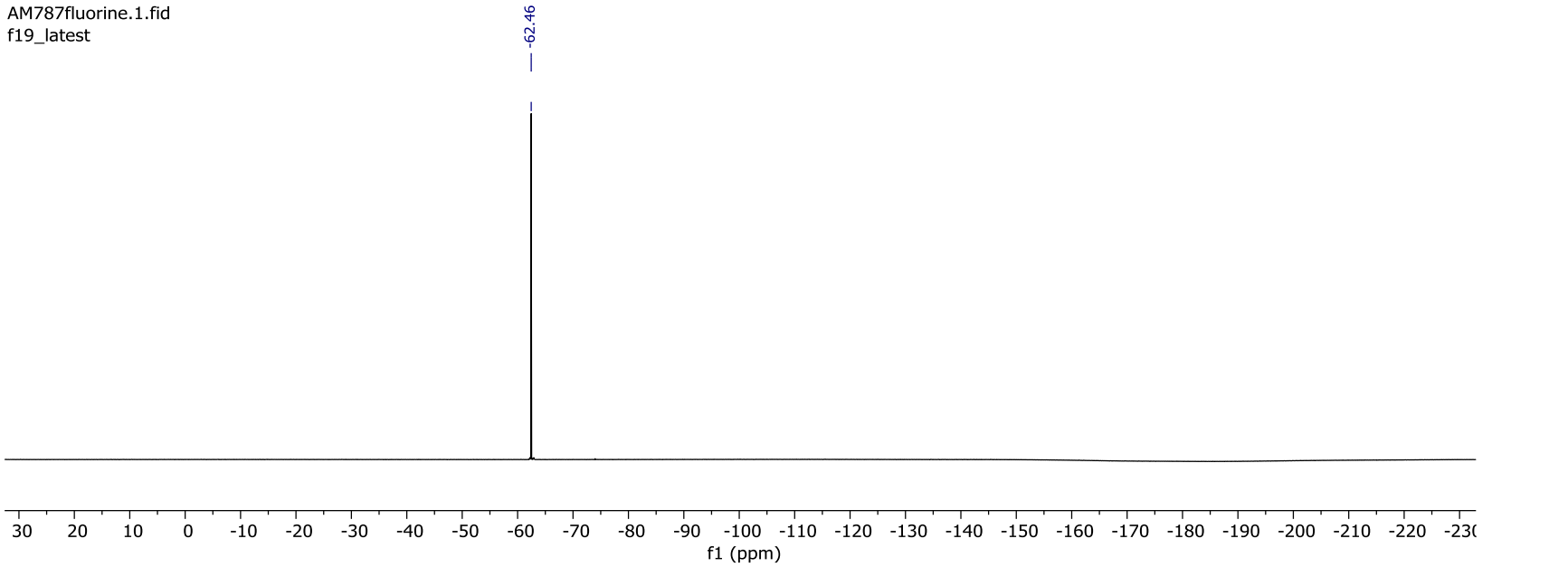

NOESY (6e)
H^A
H^B
nOe
OH
Me
Ph
H^B
nOe
N
Ns
H^A
I
6e
(major)
AM606-2d.50.ser
gs-NOESY
minor
(Me)
major
(Me)
COSY
(dispersive)
f2 (ppm)
f1 (ppm)


NOESY (6e)
Zoomed in
H^A
H^B
nOe
OH
Ph
Me
H^B
no
nOe
N
Ns
H^A
6e
(minor)
AM606-2-050.ser
gs-NOESY
NOE
absent
minor
(Me)
major
(Me)
f1 (ppm)
f2 (ppm)

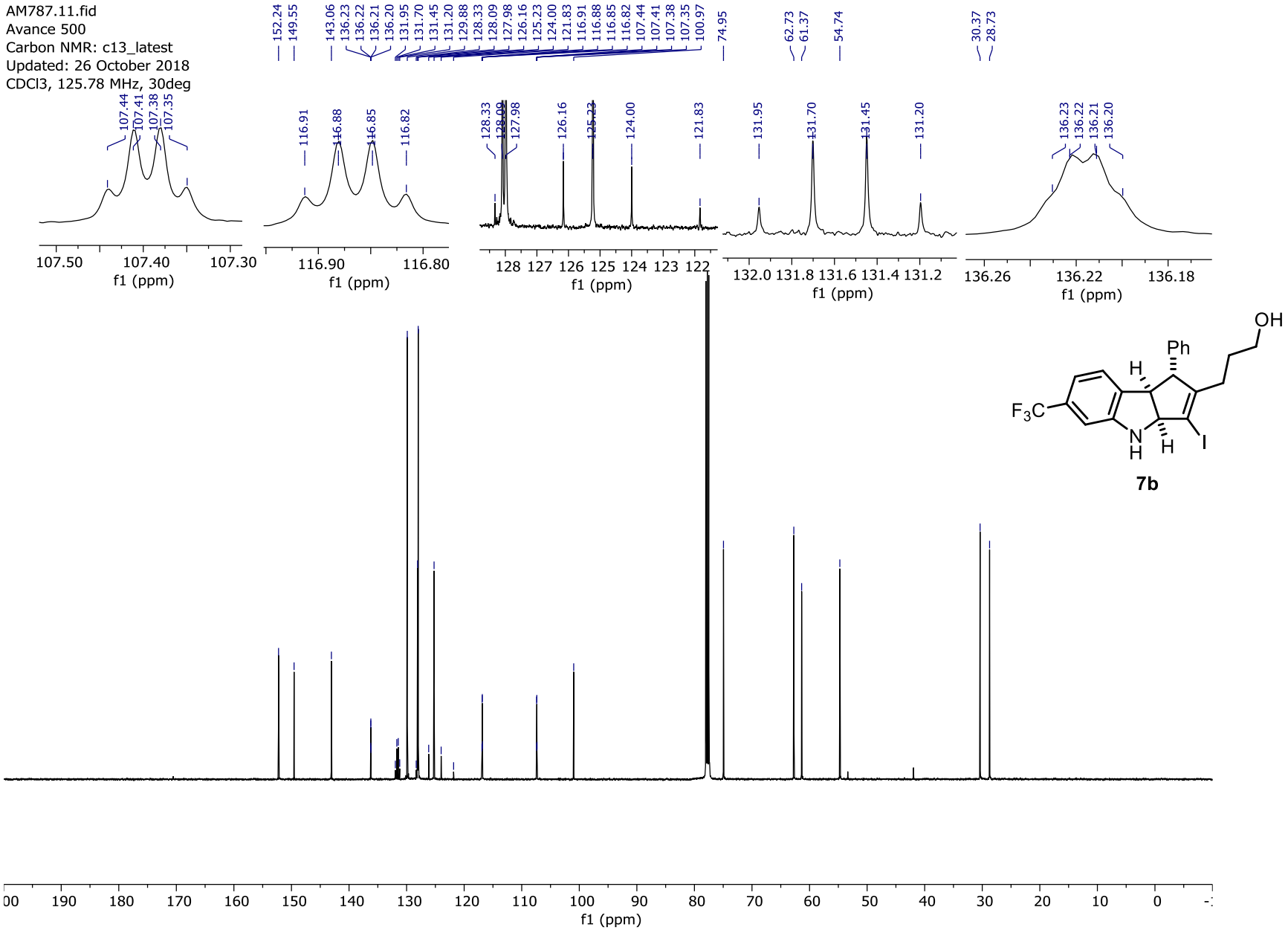

AM793.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
OH
Ph
H
MeO
N
H
H
I
7a
f1 (ppm)
AM793.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
160.55
151.09
149.76
142.83
128.98
127.30
127.07
124.63
124.10
104.55
101.13
96.81
74.58
62.03
60.68
55.32
53.65
29.64
28.03
f1 (ppm)

NMR Data

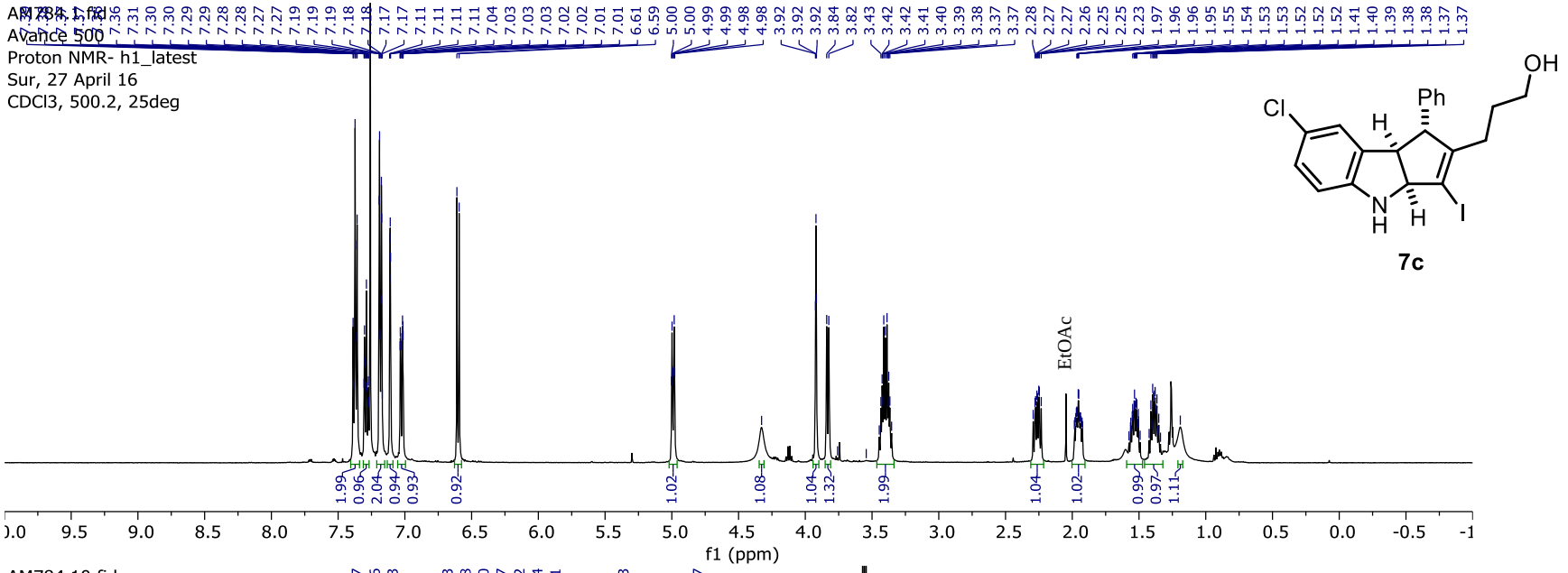

AM787_1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
OH
Ph
H
F3C
N
H
H
I
7b
2.04
0.95
2.96
1.02
0.94
0.98
1.04
0.99
1.01
2.00
1.04
1.03
0.99
0.93
1.07
f1 (ppm)

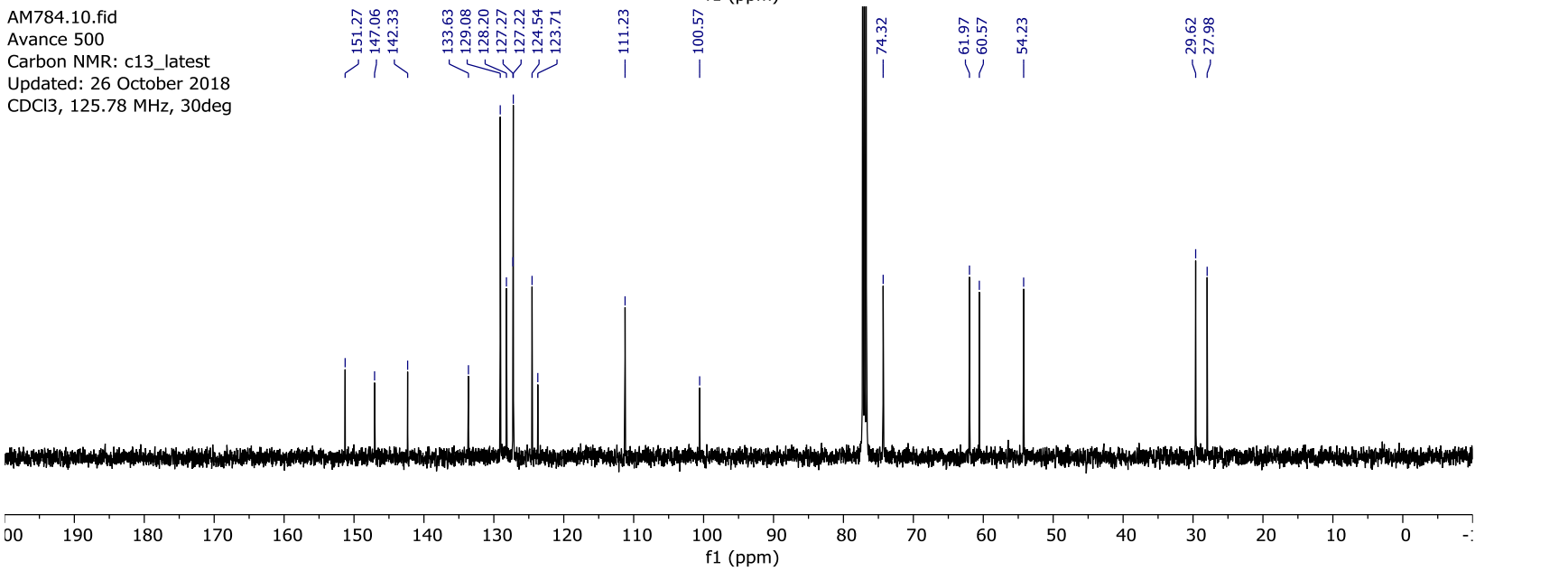

AM787fluorine.1.fid
f19_latest
-62.46
f1 (ppm)

NMR Data

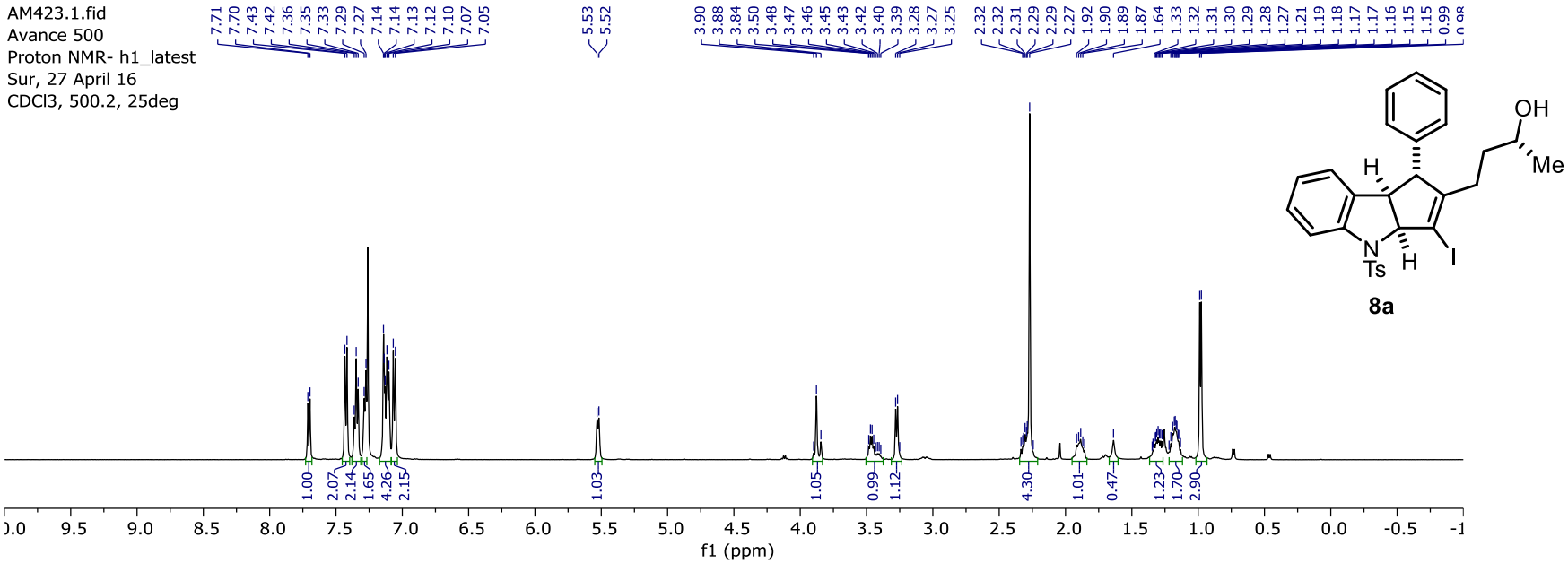

AM787.11.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
152.24
149.55
143.06
136.23
136.22
136.21
136.20
131.95
131.70
131.45
131.20
129.88
128.33
128.09
127.98
126.16
125.23
124.00
121.83
116.91
116.88
116.85
116.82
107.44
107.41
107.38
107.35
100.97
74.95
62.73
61.37
54.74
30.37
28.73
f1 (ppm)
OH
Ph
H
F3C
N
H
H
I
7b

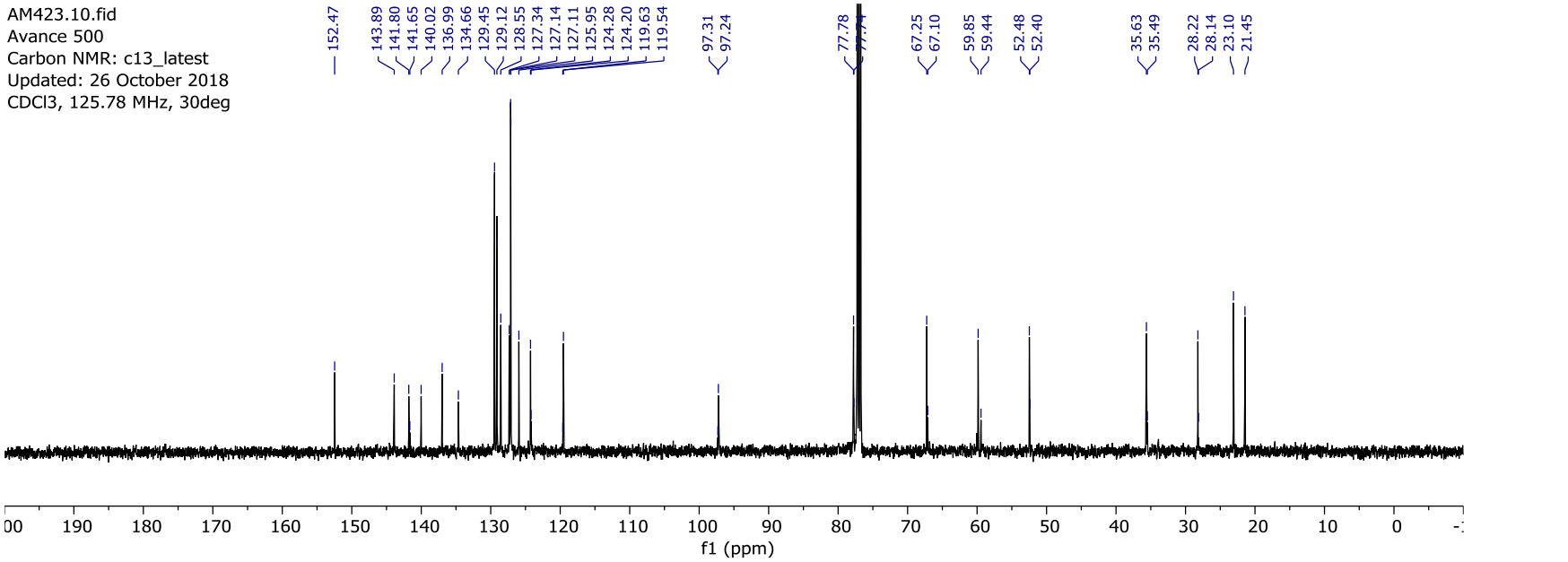
NMR Data


AM784.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
OH
Ph
Cl
H
N
H
H
I
7c
EtOAc
f1 (ppm)

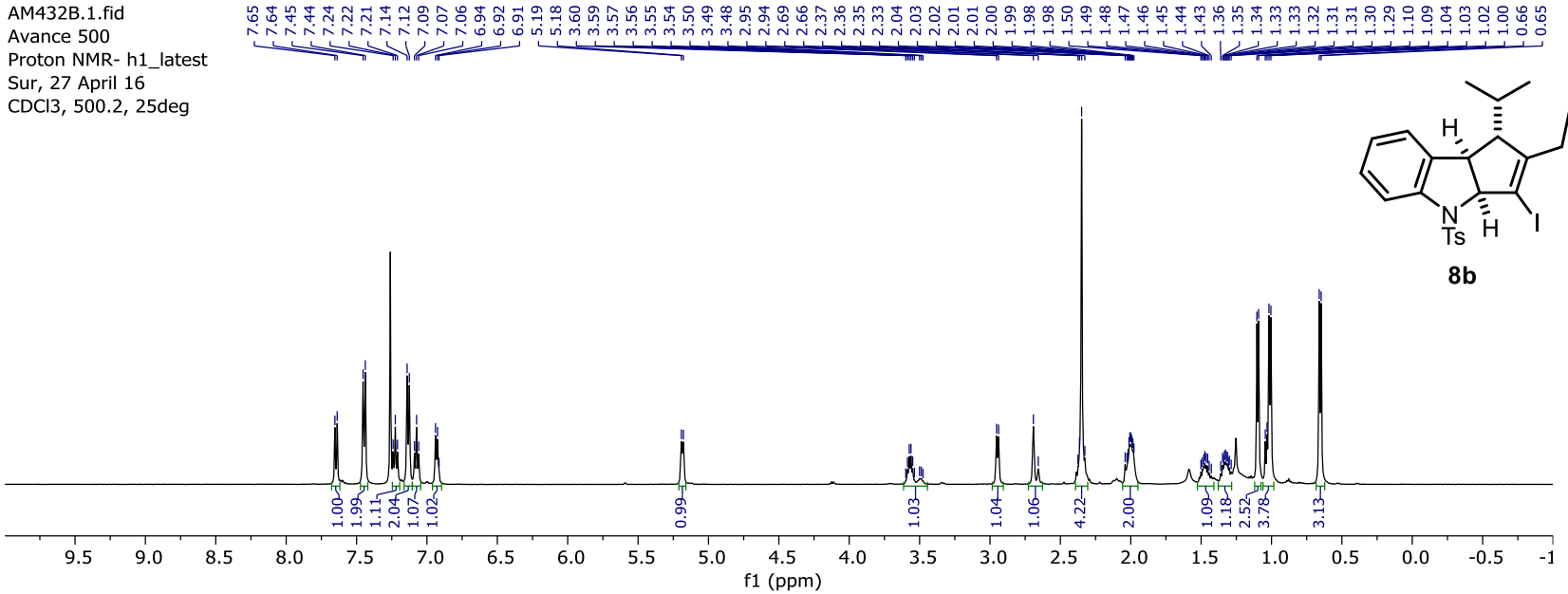

AM784.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
151.27
147.06
142.33
133.63
129.08
128.20
127.27
127.22
124.54
123.71
111.23
100.57
74.32
61.97
60.57
54.23
29.62
27.98
f1 (ppm)

NMR Data


AM423.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
OH
Me
H
N
Ts
H
I
8a
f1 (ppm)

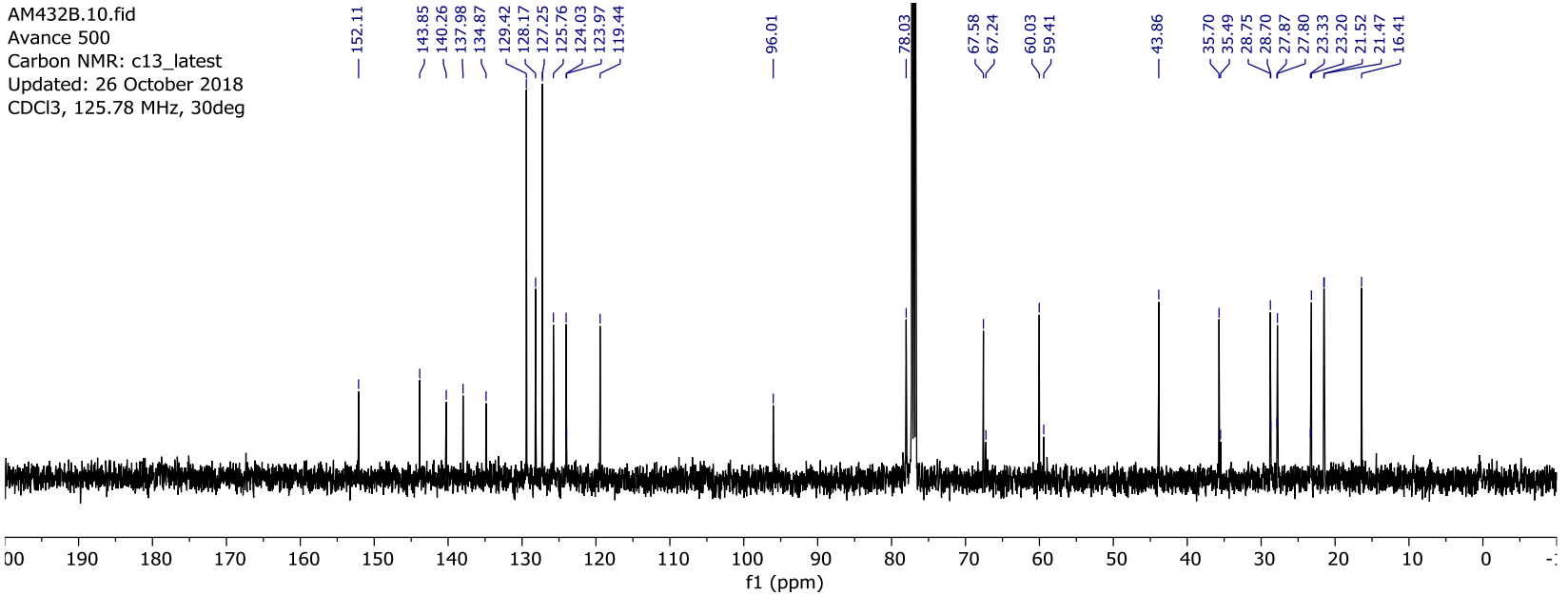

AM423.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

AM432B.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg

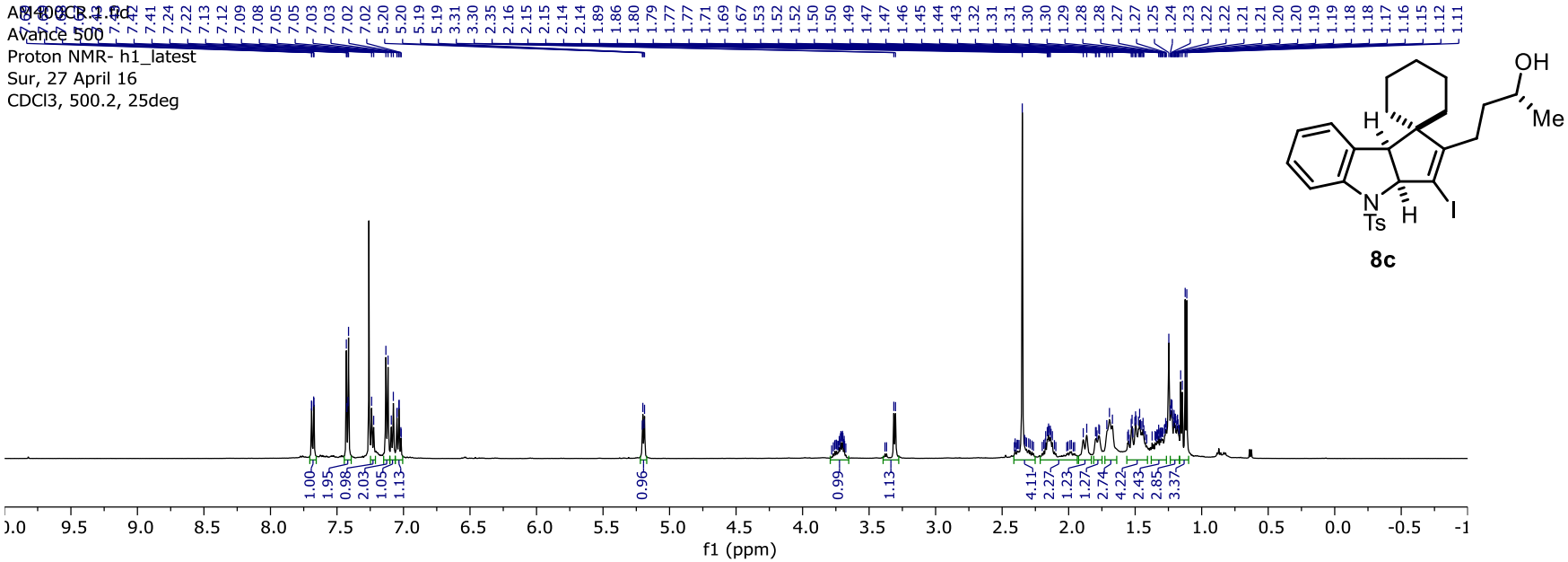


8b

AM432B.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg

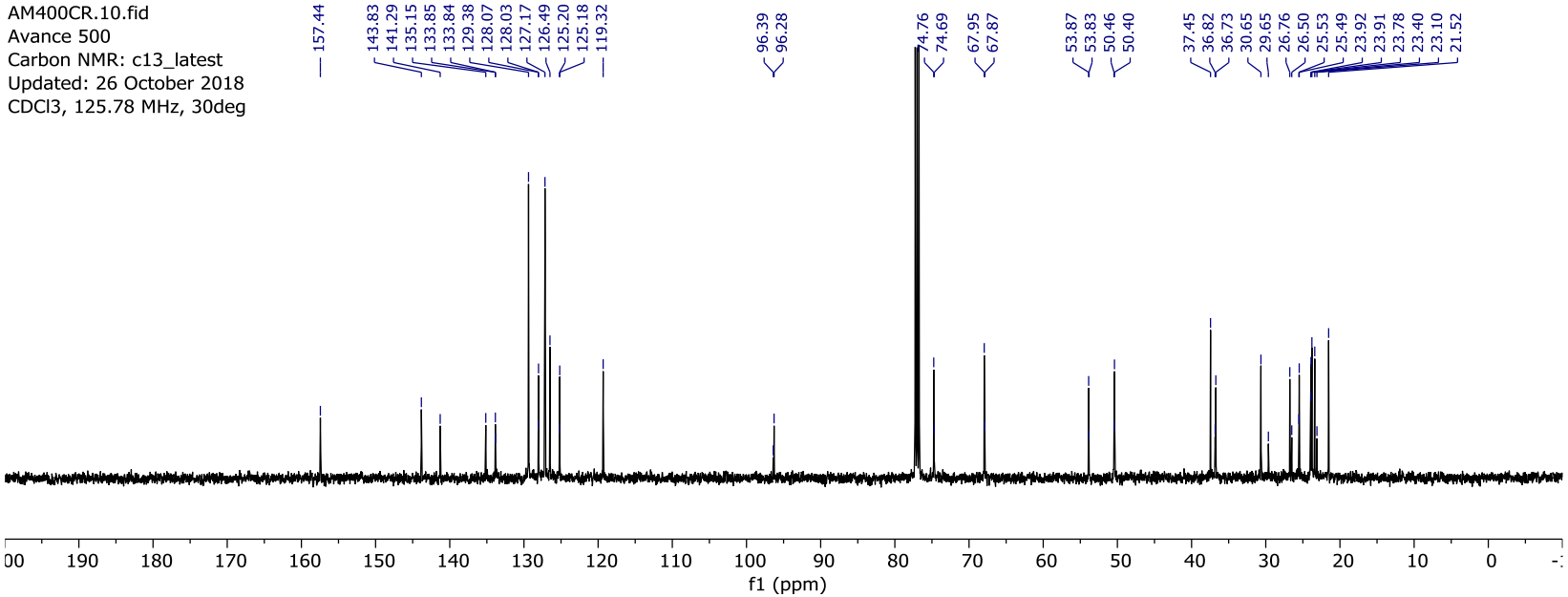


NMR Data

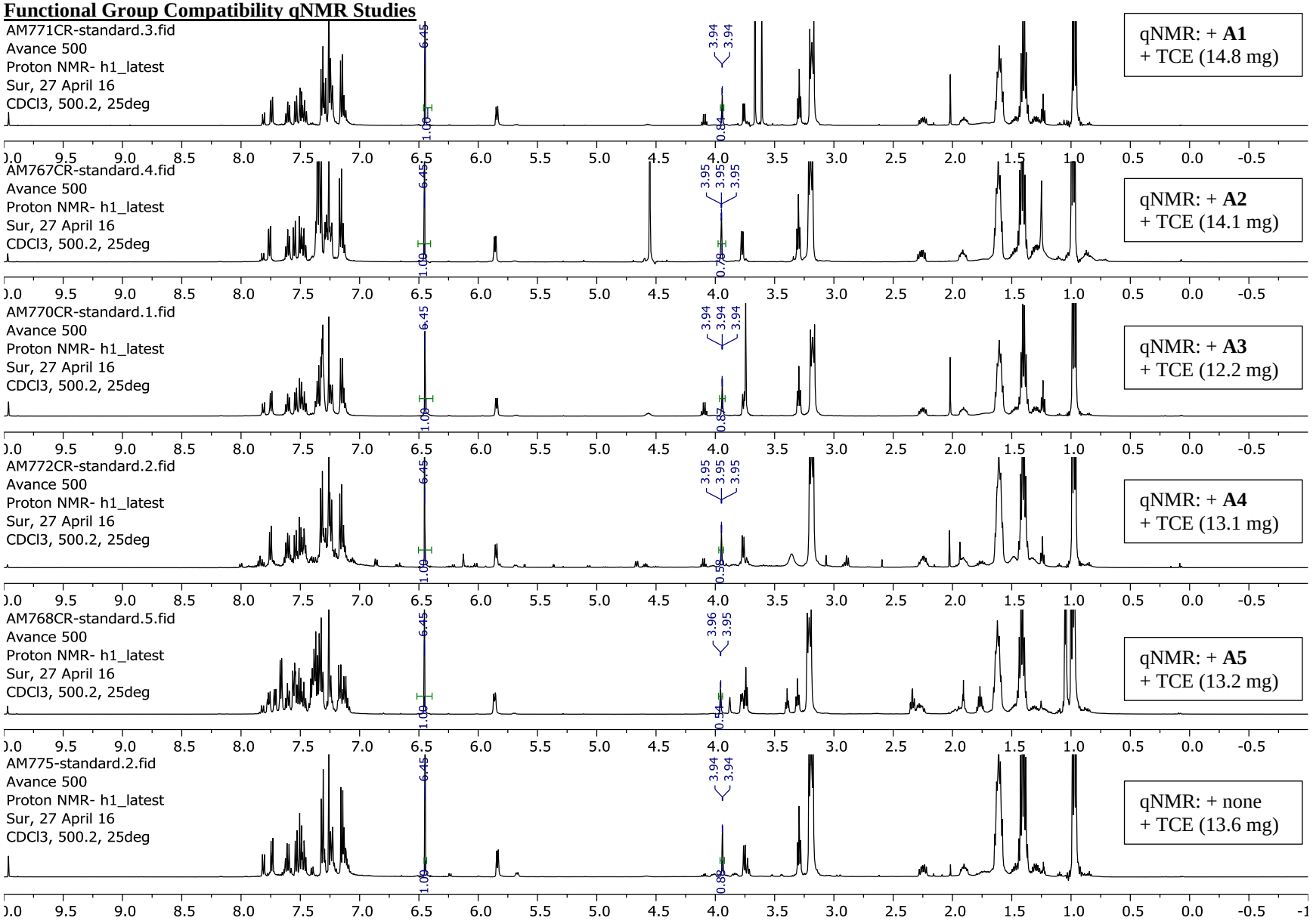

AM400CR.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
f1 (ppm)

OH
Me
H
N
Ts
H
I

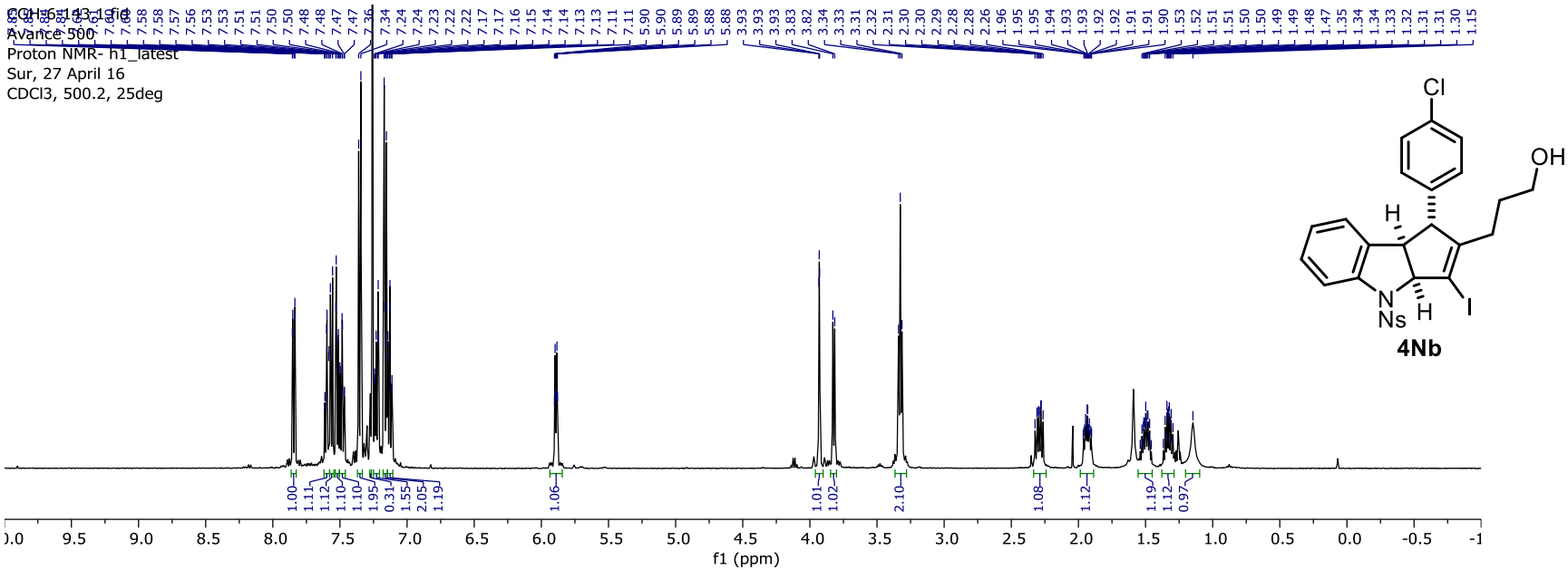
8c

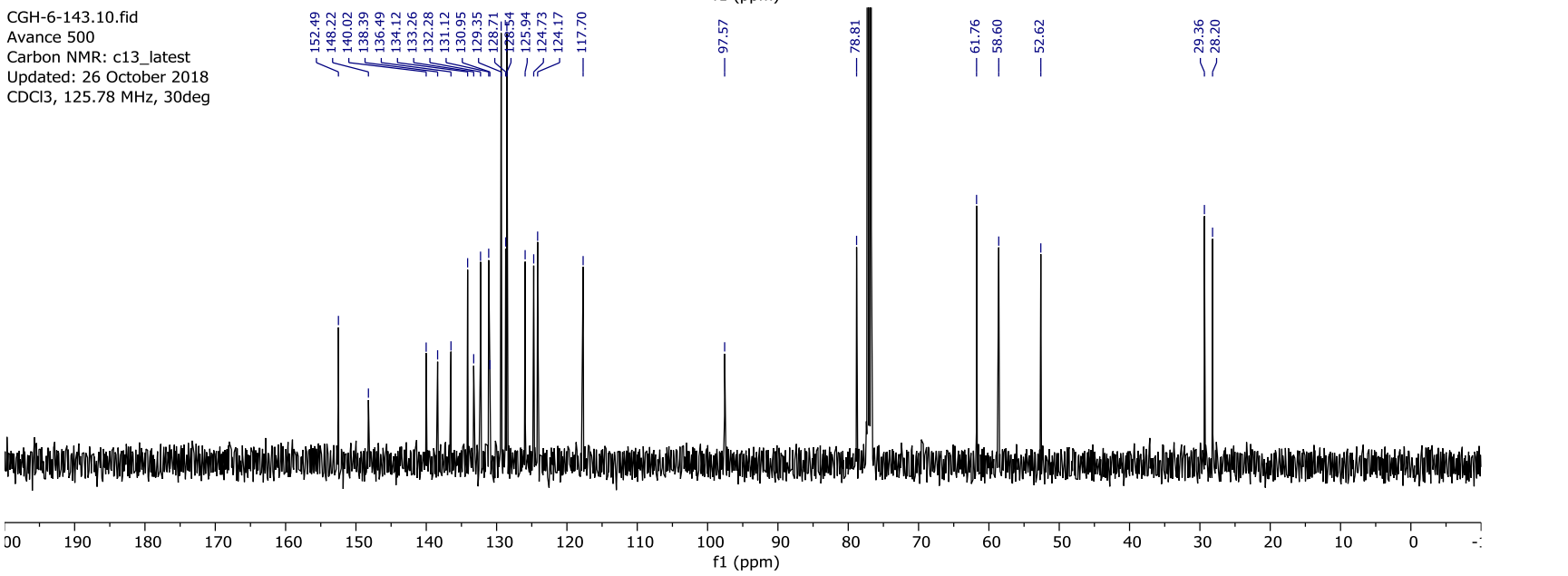

AM400CR.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

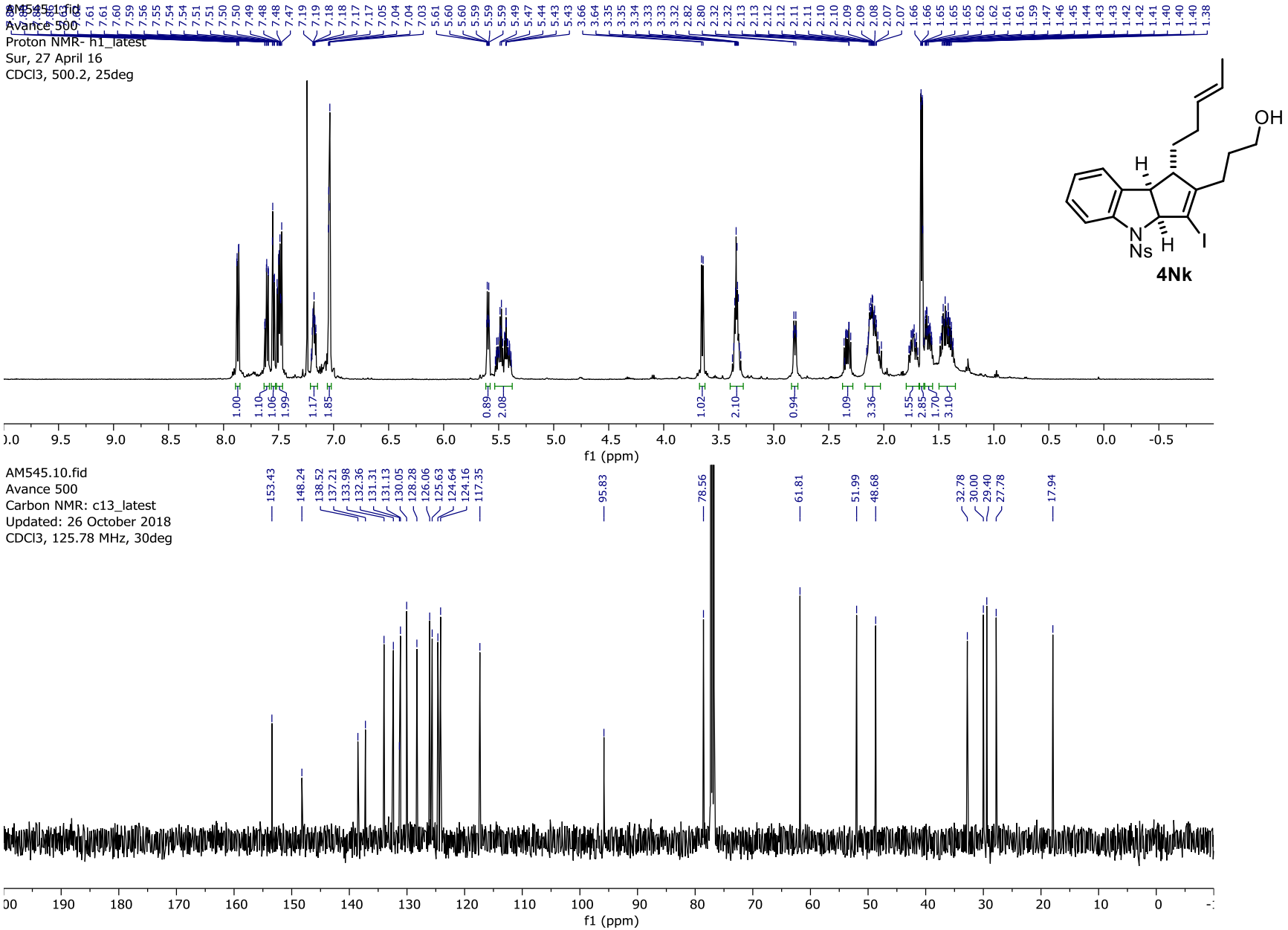
Functional Group Compatibility qNMR Studies



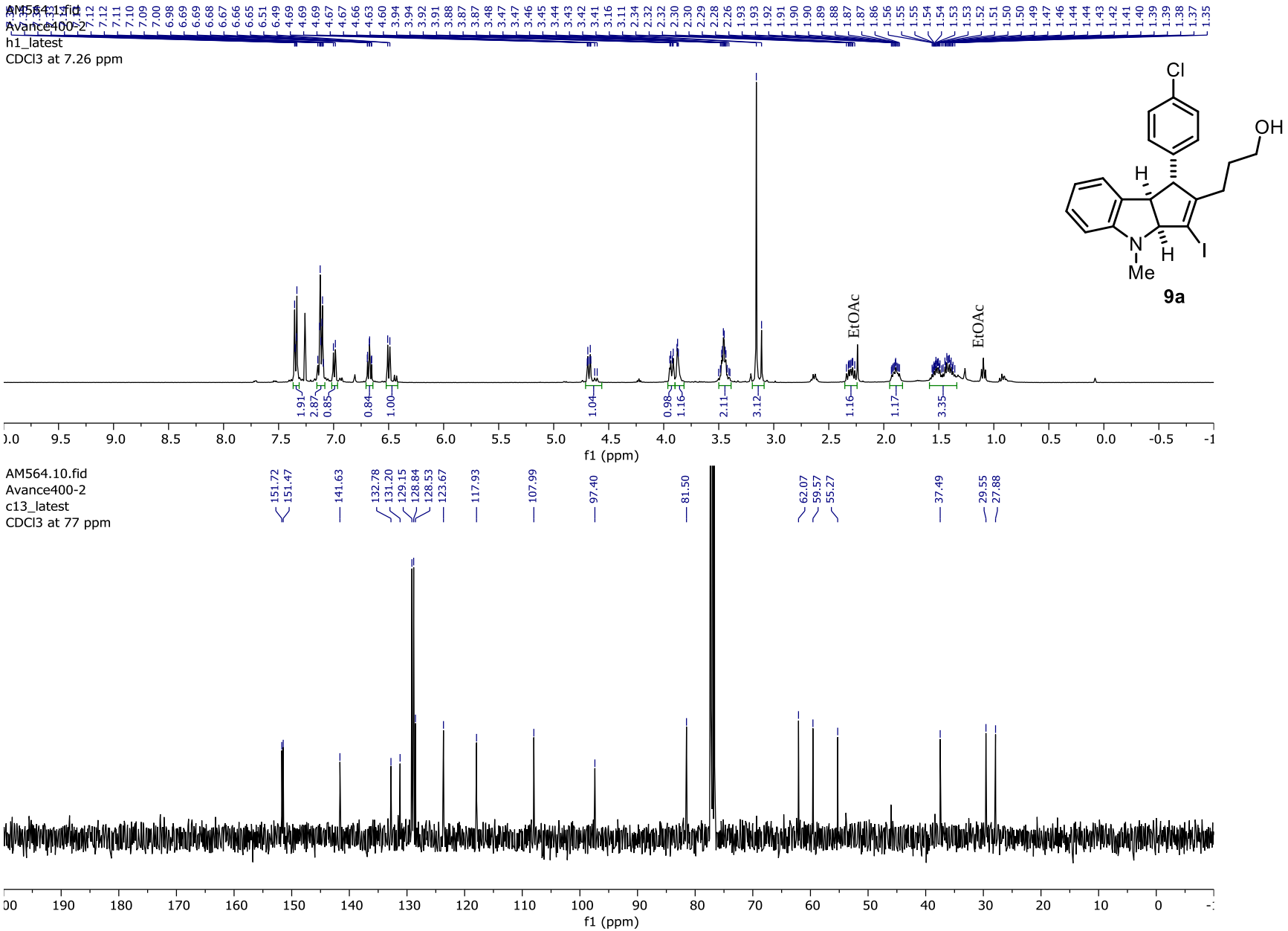
NMR Data

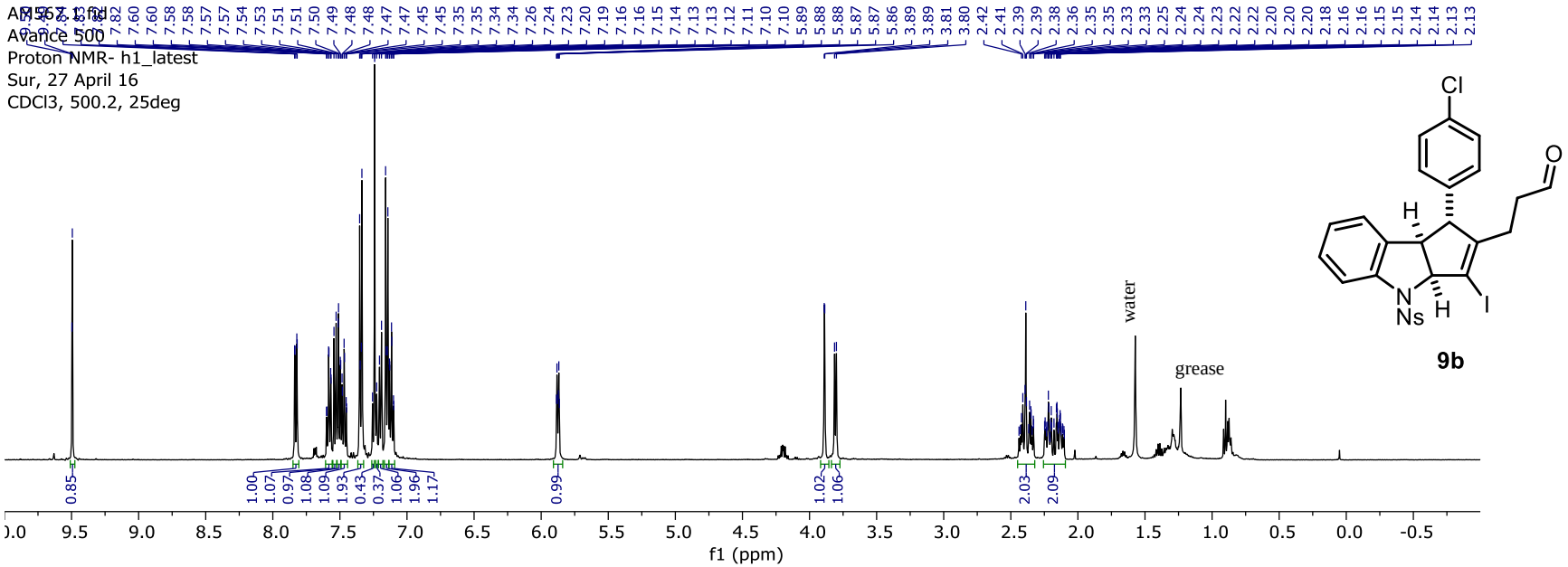

CGH-6-143.1H.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
Cl
OH
H
N
Ns
H
I
4Nb
f1 (ppm)

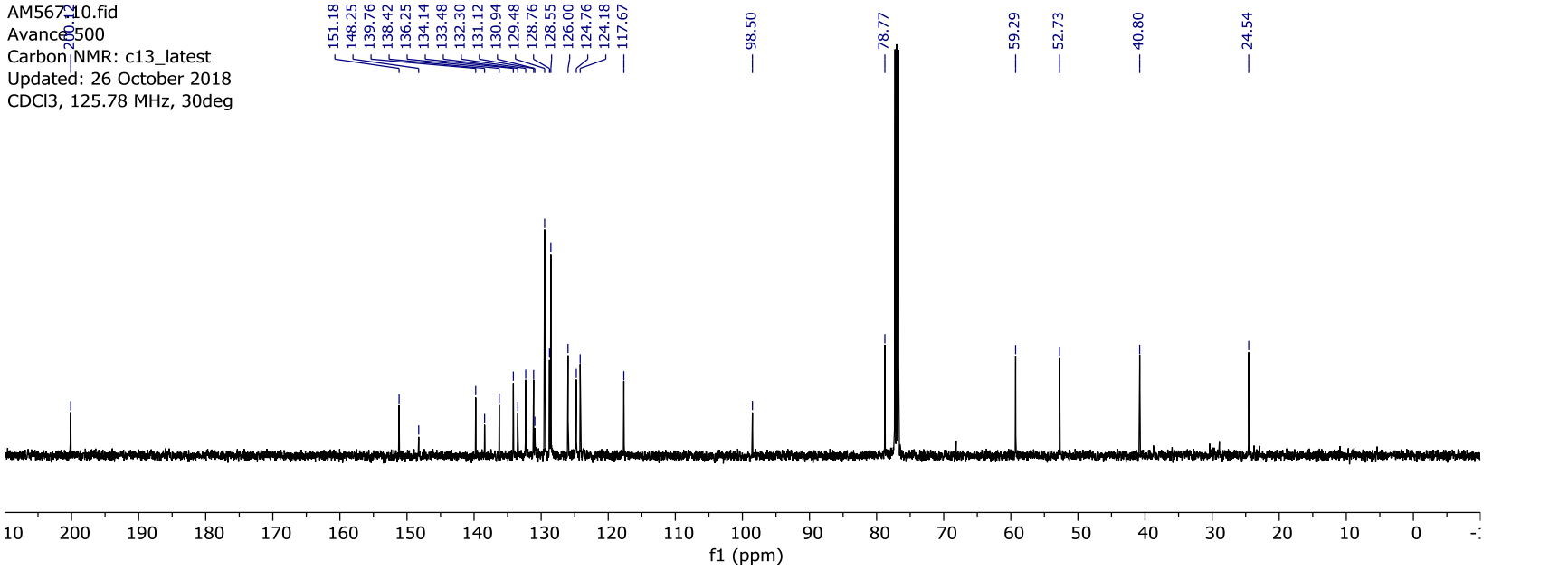

CGH-6-143.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
152.49
148.22
140.02
138.39
136.49
134.12
133.26
132.28
131.12
130.95
129.35
128.71
128.54
125.94
124.73
124.17
117.70
97.57
78.81
61.76
58.60
52.62
29.36
28.20
f1 (ppm)


AM545.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
f1 (ppm)
OH
H
N
Ns
H
I
4Nk
AM545.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
153.43
148.24
138.52
137.21
133.98
132.36
131.31
131.13
130.05
128.28
126.06
125.63
124.64
124.16
117.35
95.83
78.56
61.81
51.99
48.68
32.78
30.00
29.40
27.78
17.94
f1 (ppm)

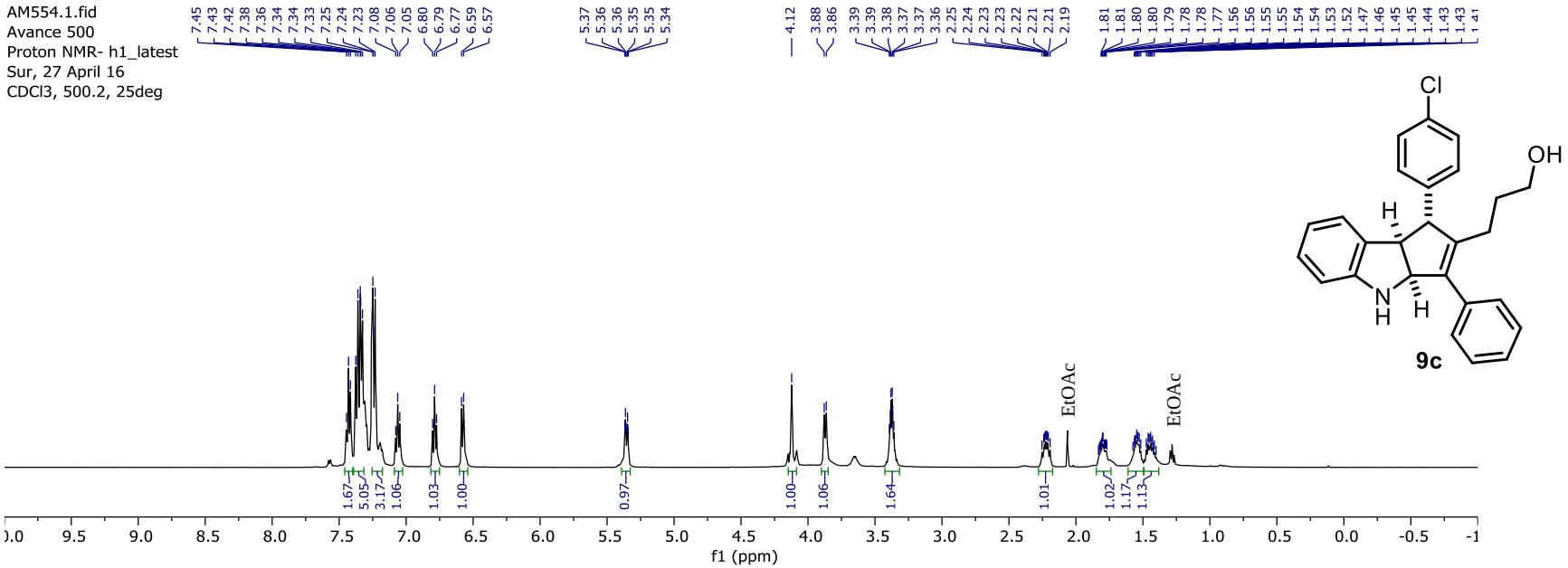
NMR Data

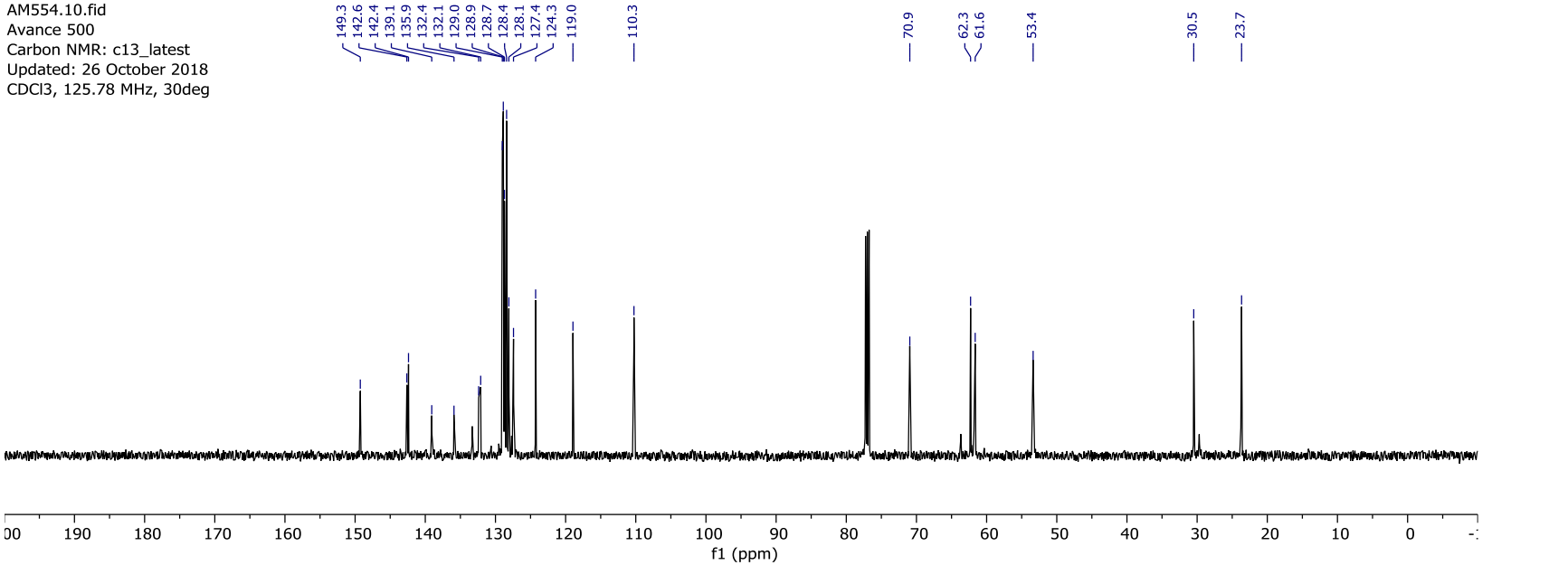

AM564.1.fid
Avance400-2
h1_latest
CDCl3 at 7.26 ppm
Cl
OH
H
N
Me
H
I
9a
EtOAc
EtOAc
1.91
2.87
0.85
0.84
1.00
1.04
0.98
1.16
2.11
3.12
1.16
1.17
3.35
f1 (ppm)
AM564.10.fid
Avance400-2
c13_latest
CDCl3 at 77 ppm
151.72
151.47
141.63
132.78
131.20
129.15
128.84
128.53
123.67
117.93
107.99
97.40
81.50
62.07
59.57
55.27
37.49
29.55
27.88
f1 (ppm)


AM567_1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
water
grease
f1 (ppm)

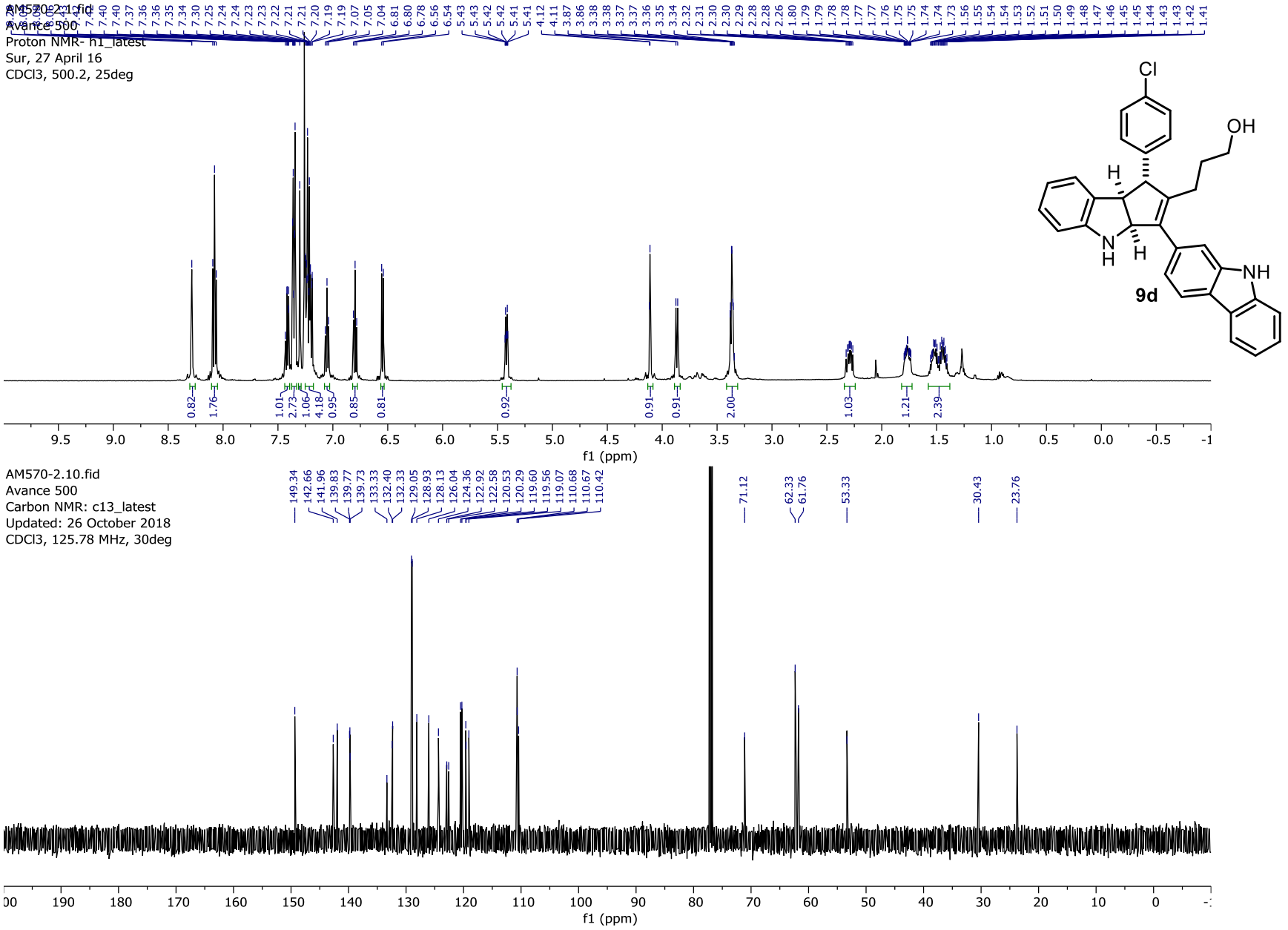

AM567_10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

NMR Data

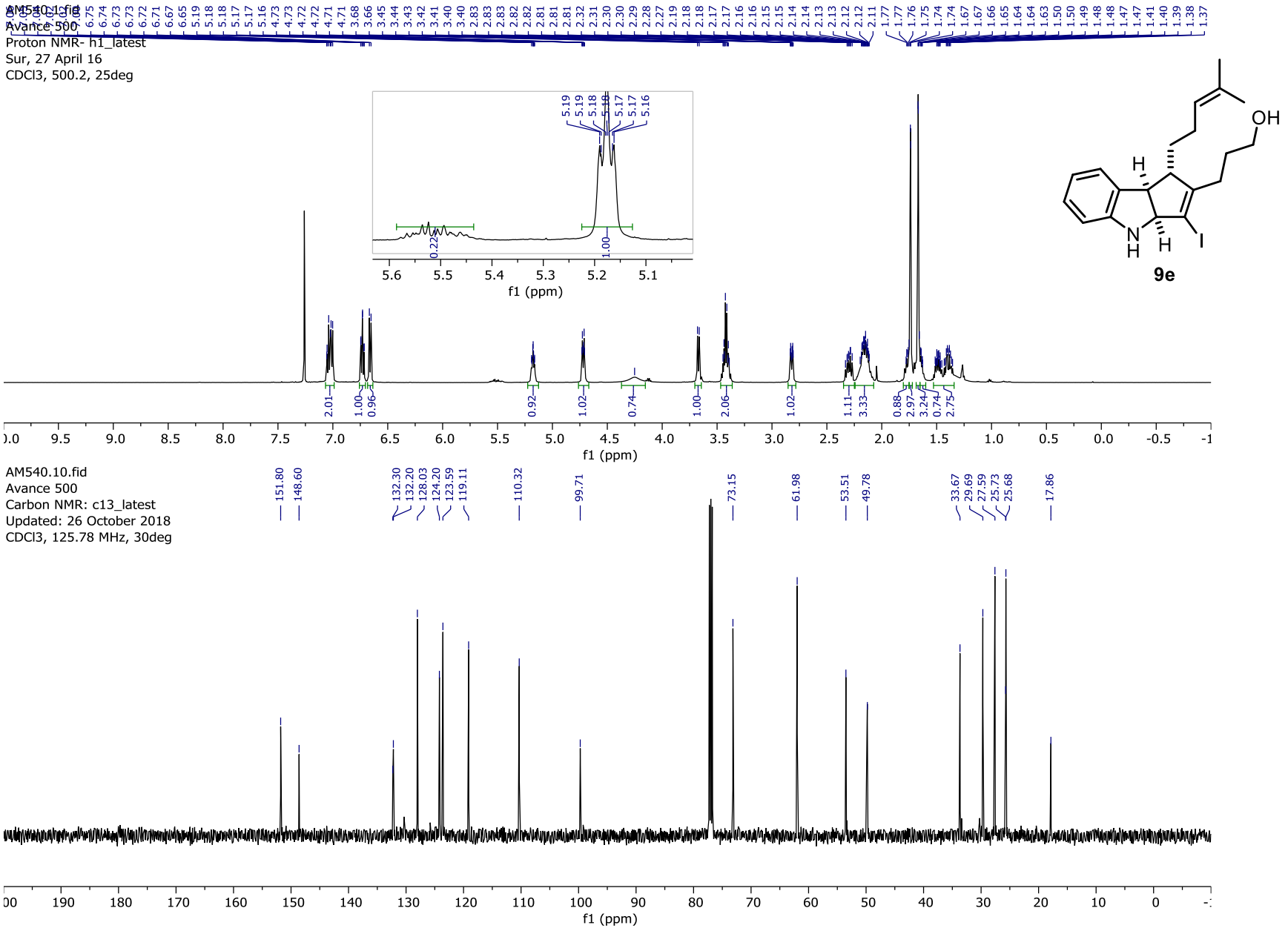

AM554.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
Cl
OH
H
N
H
H
9c
EtOAc
EtOAc
f1 (ppm)

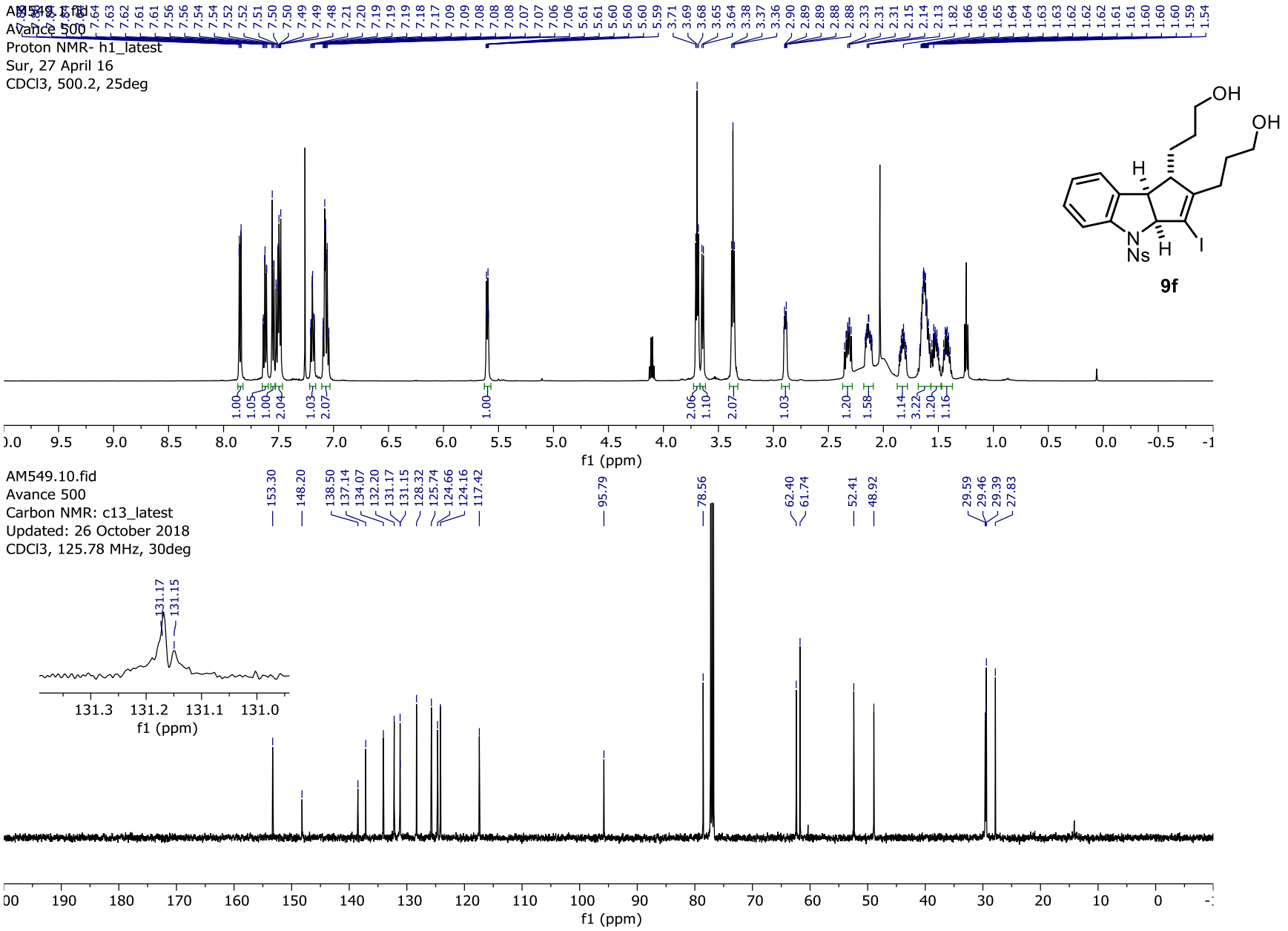

AM554.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

NMR Data

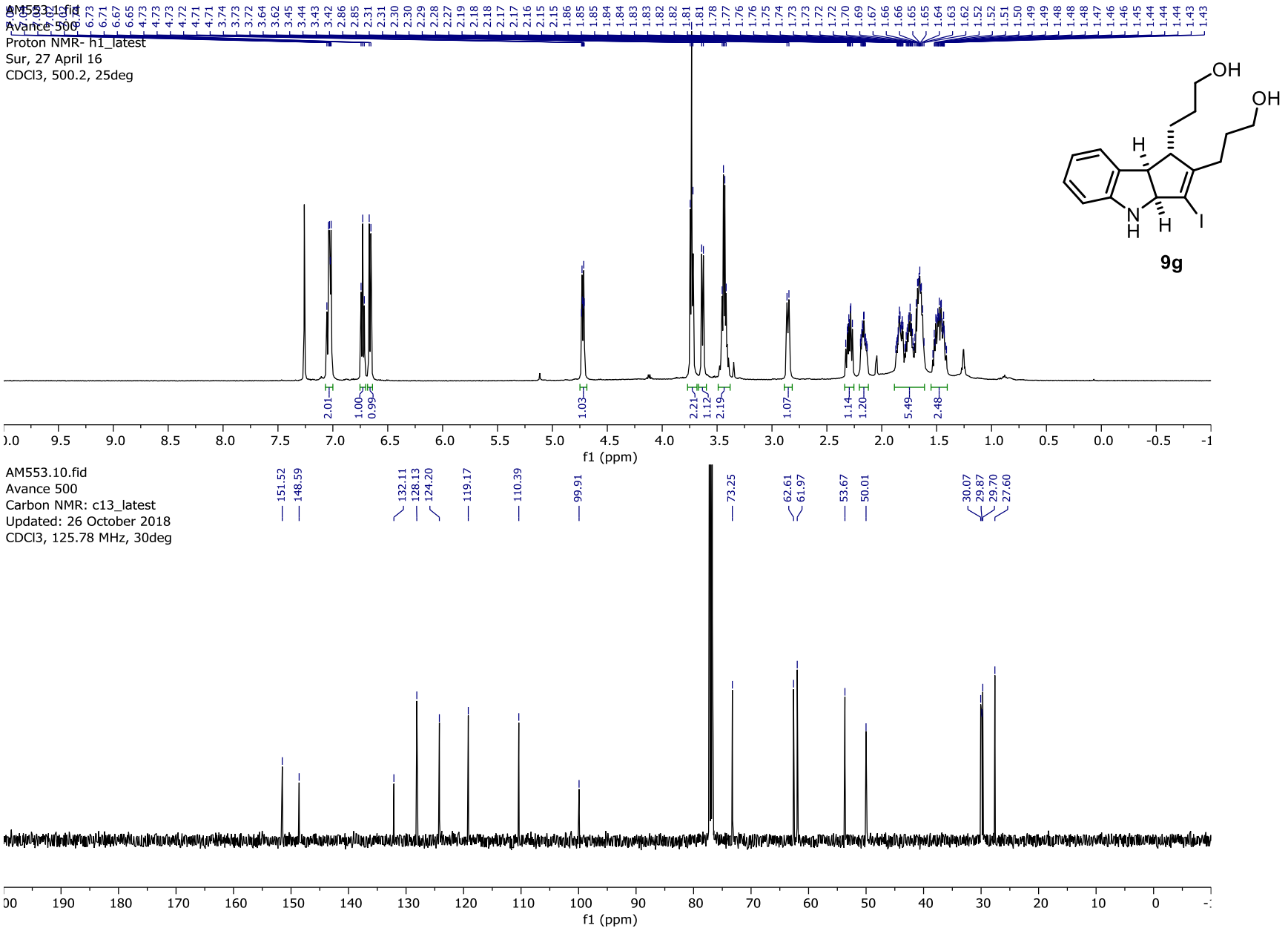

AM570-2.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
Cl
OH
H
N
H
H
NH
9d
f1 (ppm)
AM570-2.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
149.34
142.66
141.96
139.83
139.77
139.73
133.33
132.40
132.33
129.05
128.93
128.13
126.04
124.36
122.92
122.58
120.53
120.29
119.60
119.56
119.07
110.68
110.67
110.42
71.12
62.33
61.76
53.33
30.43
23.76
f1 (ppm)

NMR Data


AM540.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
f1 (ppm)
OH
H
N
H
H
I
9e
AM540.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
151.80
148.60
132.30
132.20
128.03
124.20
123.59
119.11
110.32
99.71
73.15
61.98
53.51
49.78
33.67
29.69
27.59
25.73
25.68
17.86
f1 (ppm)

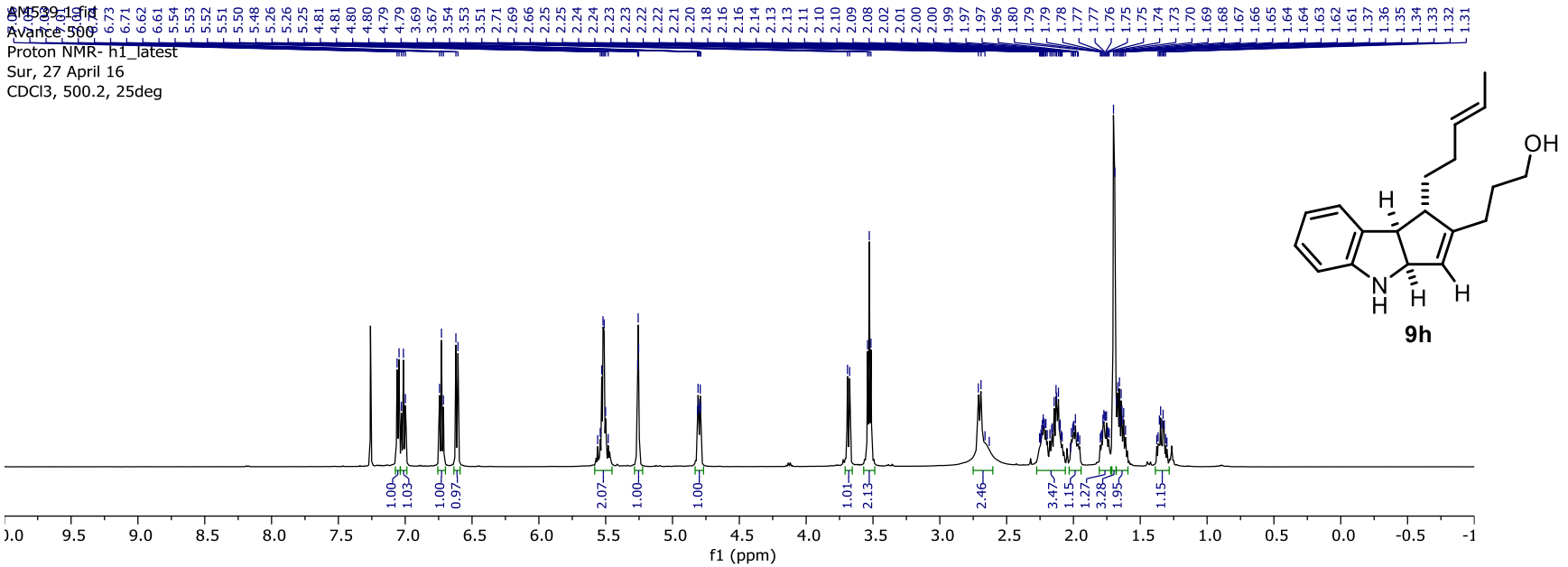

AM549.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
OH
OH
H
N
Ns
H
I
9f
f1 (ppm)
AM549.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
153.30
148.20
138.50
137.14
134.07
132.20
131.17
131.15
128.32
125.74
124.66
124.16
117.42
95.79
78.56
62.40
61.74
52.41
48.92
29.59
29.46
29.39
27.83
131.17
131.15
131.3
131.2
131.1
131.0
f1 (ppm)
f1 (ppm)

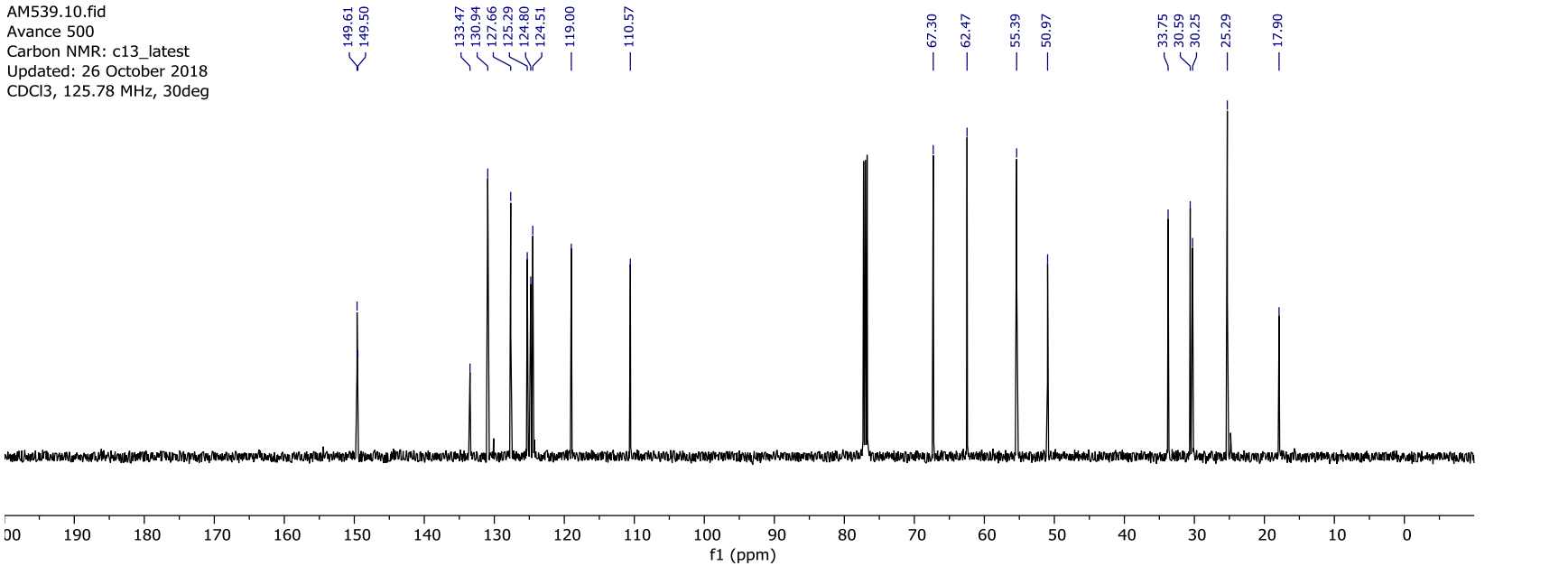
NMR Data


AM553.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
f1 (ppm)
AM553.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)

OH
OH
H
N
H
H
I

9g


AM539.1.fid
Avance 500
Proton NMR- h1_latest
Sur, 27 April 16
CDCl3, 500.2, 25deg
OH
H
N
H
H
H
9h
f1 (ppm)


AM539.10.fid
Avance 500
Carbon NMR: c13_latest
Updated: 26 October 2018
CDCl3, 125.78 MHz, 30deg
f1 (ppm)