Supporting Information

for

Photo-Brook rearrangement of acyl silanes as a strategy for photoaffinity probe design

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Abstract: *Photoaffinity labeling (PAL) is a powerful tool for the identification of non-covalent small molecule-protein interactions that are critical to drug discovery and medicinal chemistry, but this approach is limited to only a small subset of robust photocrosslinkers. The identification of new photoreactive motifs capable of covalent target capture is therefore highly desirable. Herein, we report the design, synthesis, and evaluation of a new class of PAL warheads based on the UV-triggered 1,2-photo Brook rearrangement of acyl silanes, which hitherto have not been explored for PAL workflows. Irradiation of a series of probes in cell lysate revealed an* i*Pr-substituted acyl silane with superior photolabeling and minimal thermal background labeling compared to other substituted acyl silanes. Further, small molecule (+)-JQ1- and rapamycin-derived* i*Pr acyl silanes were shown to selectively label recombinant BRD4-BD1 and FKBP12, respectively, with minimal background. Together, these data highlight the untapped potential of acyl silanes as a novel, tunable scaffold for photoaffinity labeling.*

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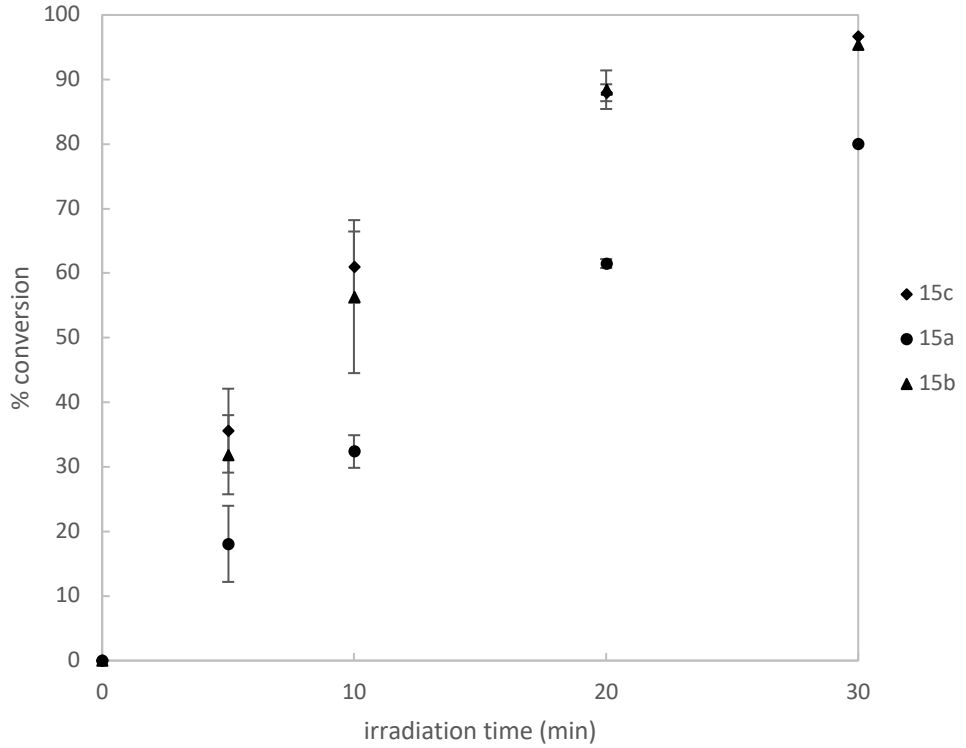


Figure S1: Irradiation time course of acyl silanes **15a-c** in CD_3OD at 365 nm using a 6 W hand-held UV lamp at 25 ˚C. Acyl silane prepared as a stock solution in CD_3OD was added to an NMR tube with dimethylsulfone as an internal standard for a total volume of 50 µL or 0.024 M. Reactions were run in triplicate and analyzed by ^1H NMR (d1 = 10 s).

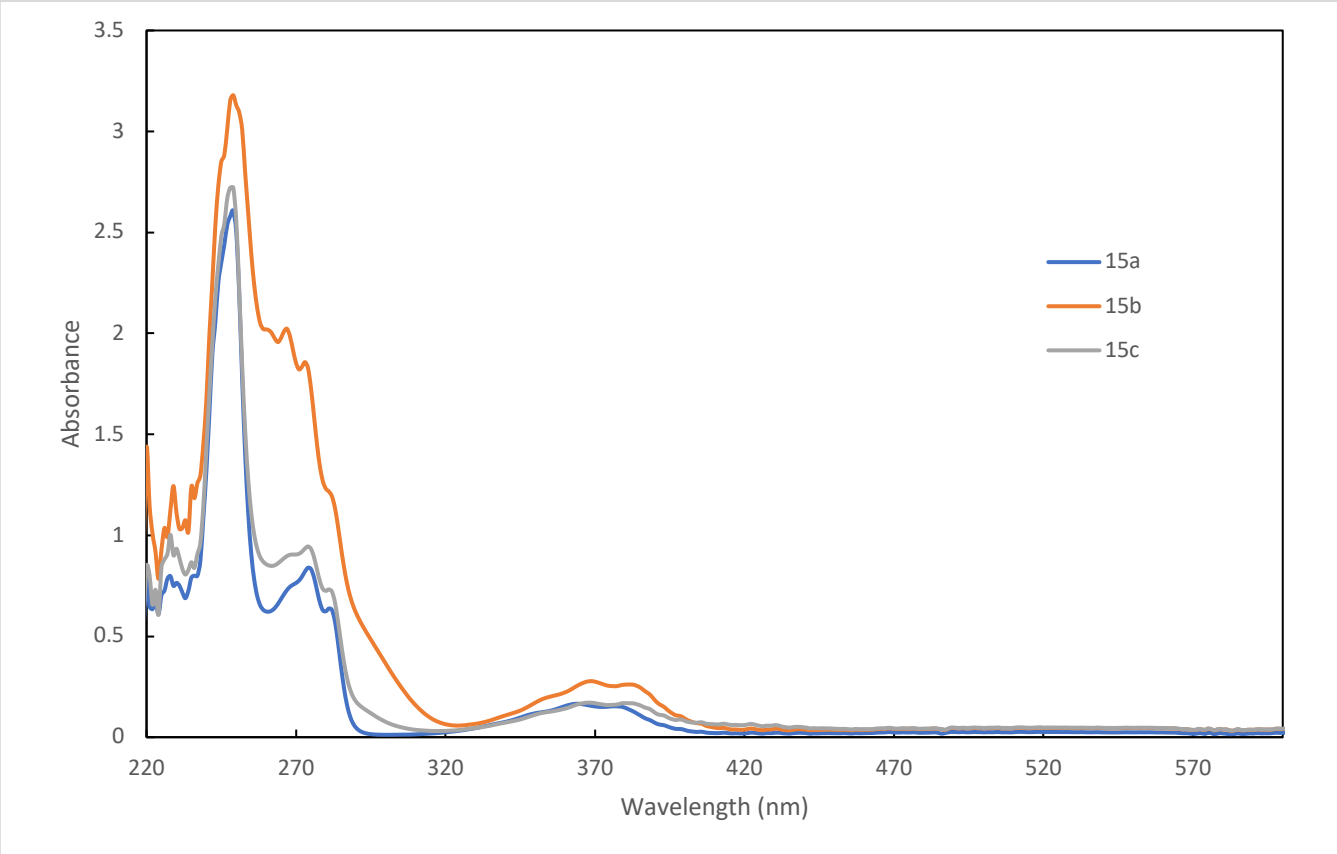
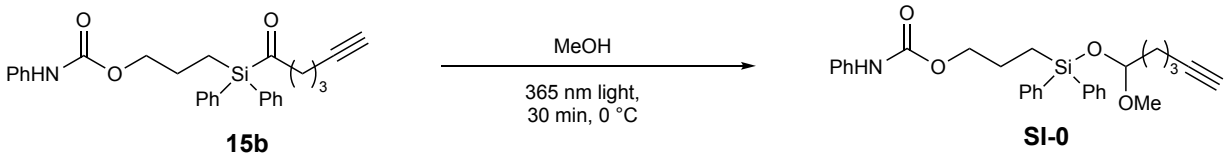


Figure S2: UV-Visible spectra of acyl silanes **15a-c** in MeOH. Acyl silanes **15a**, **15b**, and **15c** show a λ_{max} = 364 nm, 370 nm, and 368 nm, respectively, and an ε = 115.7 $M^{-1}cm^{-1}$, 236.5 $M^{-1}cm^{-1}$, and 111.0 $M^{-1}cm^{-1}$, respectively, at 5mM concentration.



15b **SI-0**

Irradiation of probe 15b in MeOH: Product was characterized from the crude reaction mixture. **^{1}H NMR** (600.1 MHz, DMSO-*d*6): *Aromatic region contains multiple overlapped species*. 9.54 (br. s), 7.60 – 7.54 (m), 7.50 – 7.40 (m), 7.29-7.24 (m), 7.00 – 6.95 (m), 4.77 (dd, J = 4.5, 5.6 Hz, 1H, C*H*OCH$_3$), 4.06 (t, J = 6.9 Hz, 2H), 3.12 (s, 3H, OC*H*$_3$), 2.72 (t, J = 2.6 Hz, 1H, spC–*H*), 2.08 (dt, J = 7.1, 2.7 Hz, 2H), 1.70 – 1.60 (m, 2 or 4 H), overlap with 1.63 (dt, J = 4.5, 7.6 Hz, 2H) 1.45 (dt, J = 14.7, 7.3 Hz, 2H), 1.29 – 1.26 (m, 2H).
HRMS (ESI$^+$): calculated for [C$_{29}$H$_{33}$NO$_4$Si+Na]$^+$ required *m/z* 510.2071, found *m/z* 510.2065.

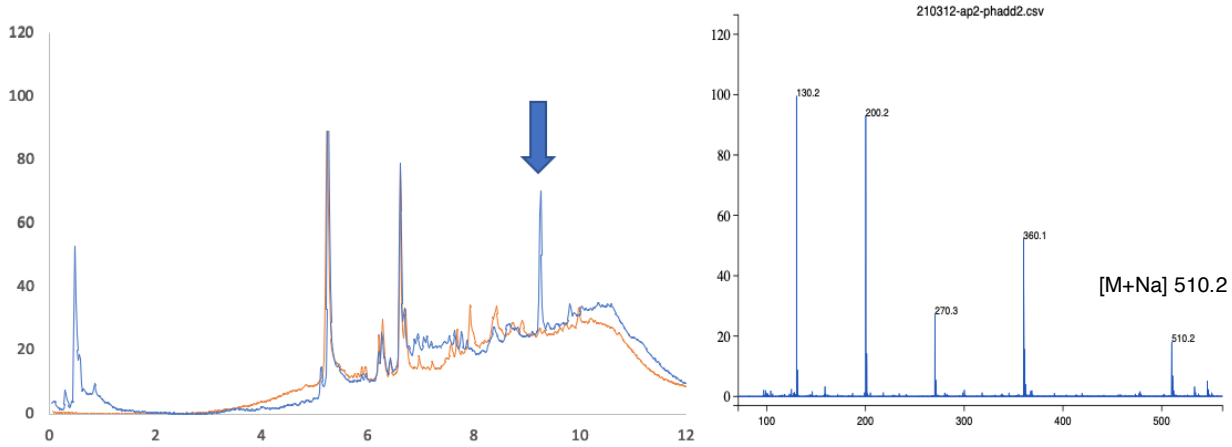


Figure S3. A) LCMS trace (MeCN:H$_2$O 5-95% with 0.1% formic acid over 12 minutes) of MeOH insertion adduct of **15b**. Background profile after injection of blank sample is shown in orange. Trace following irradiation of **15b** in MeOH for 30 min at 0 ºC shown in blue, with acetal adduct indicated by arrow. B) Expansion of mass spectrum of acetal. LCMS (ESI$^+$) calculated for [C$_{29}$H$_{33}$NNaO$_4$Si]$^+$ requires *m/z* 510.2, found *m/z* 510.2.

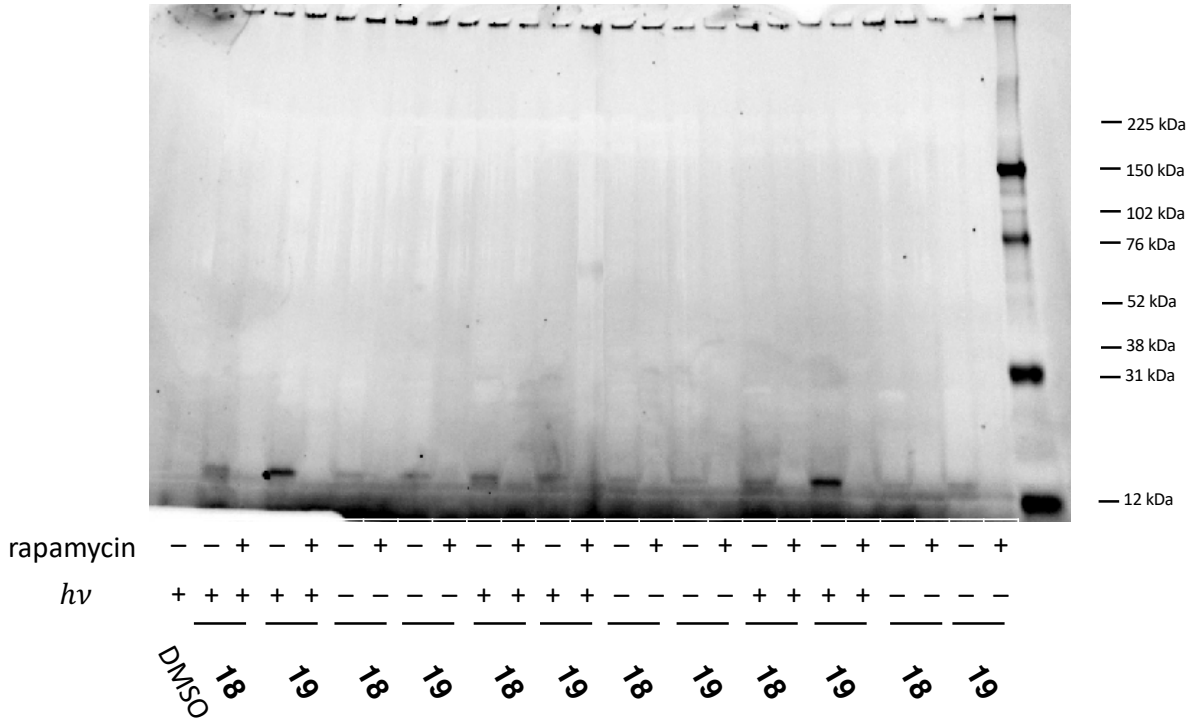


Figure S4: Full gel image of rapamycin PAL probe labeling of FKBP12. FKBP12 (1.0 μg, appx. 1.5 μM) in pH 7.4 PBS (containing 0.1% Triton X-100) was treated with either DMSO or rapamycin (100 μM) and incubated at RT for 30 min. Rapamycin probe **18** or **19** was added (10 μM), and the samples were incubated for 30 min at RT in the dark. Samples were then irradiated for 30 min at 4 ˚C with a 6 W handheld UV lamp. Labeled protein was visualized following Cu click reaction with Rh-N_3.

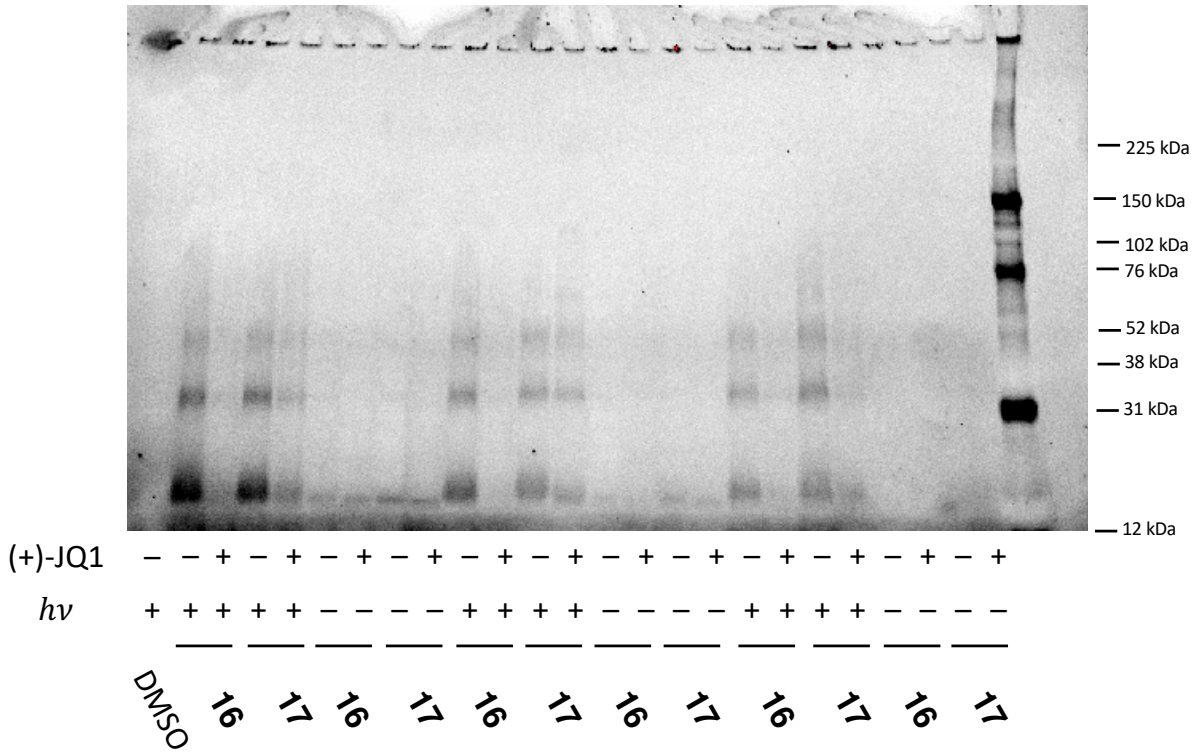


Figure S5: Full gel image of (+)-JQ1 PAL probe labeling of BRD4-BD1. BRD4-BD1 (0.6 μg, appx. 0.7 μM) in pH 7.4 PBS was treated with either DMSO or (+)-JQ1 (100 μM) and incubated at RT for 30 min. (+)-JQ1 probe **16** or **17** was added (10 μM), and the samples were incubated for 30 min at RT in the dark. Samples were then irradiated for 30 min at 4 ˚C with a 6 W handheld UV lamp. Labeled protein was visualized following Cu click reaction with Rh-N_3.

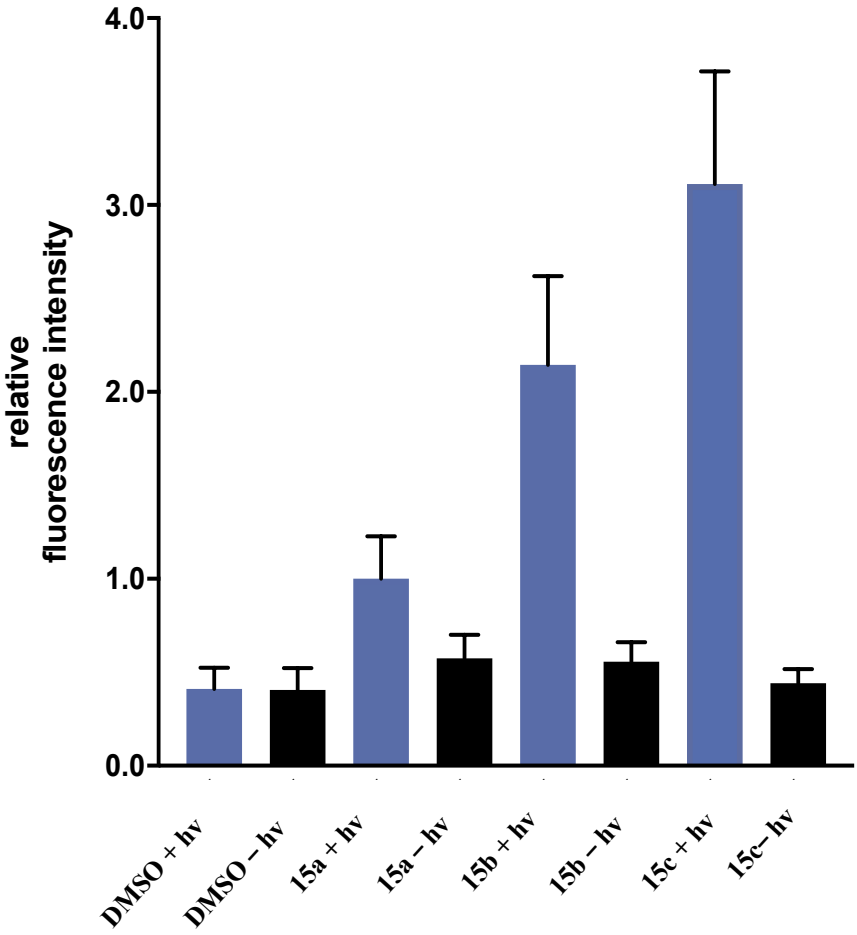


Figure S6. Quantitation of in-gel fluorescence for Figure 3A normalized to protein levels.

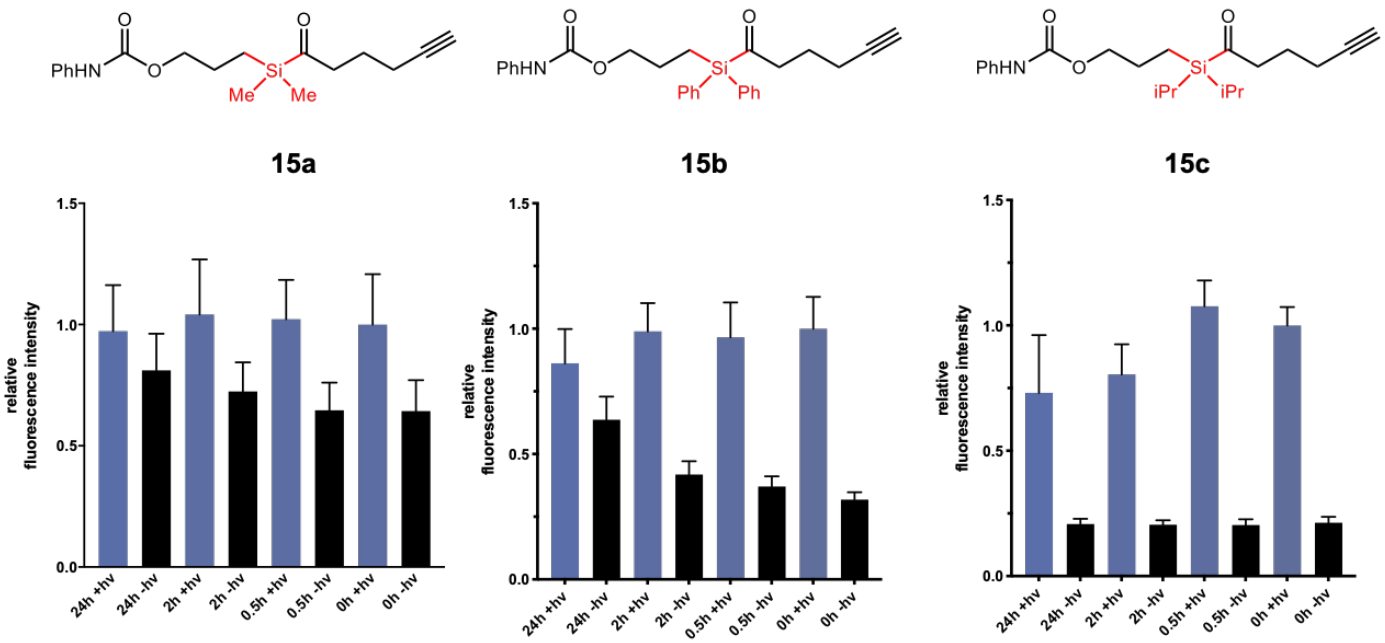


Figure S7. Quantitation of in-gel fluorescence for Figure 3B for probes **15a**–**c** normalized to protein levels.

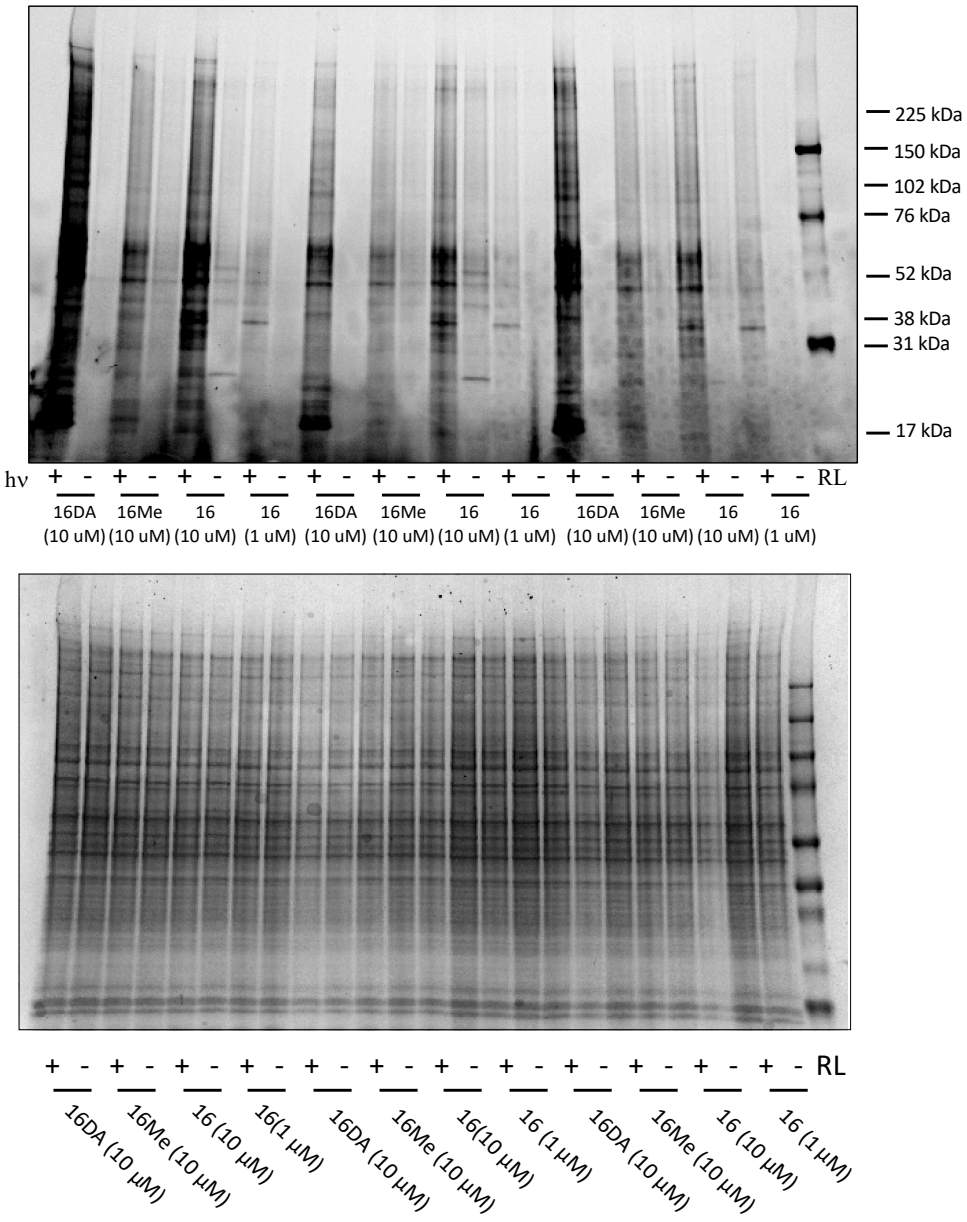


Figure S8. Full gel image of (+)-JQ1 probes **16, 16DA, 16Me** labeling 231MFP cell lysate (top image). SafeStain gel image confirming protein labeling (bottom image)

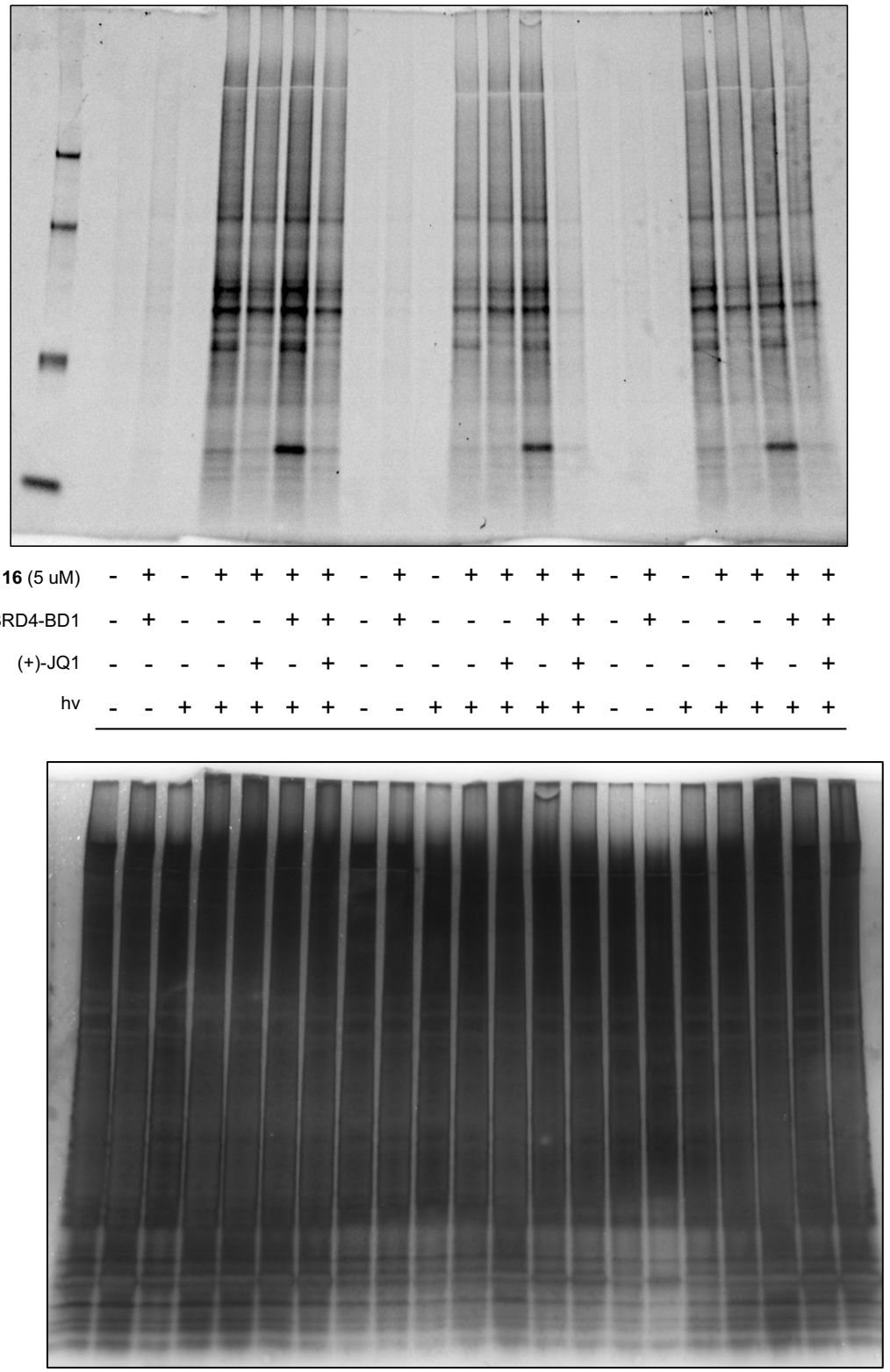
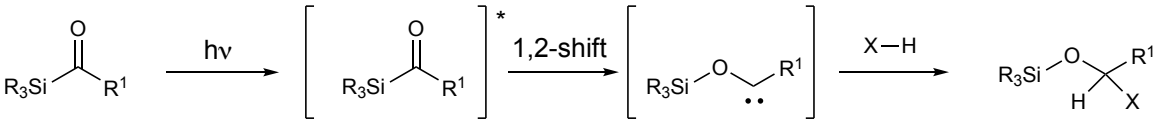
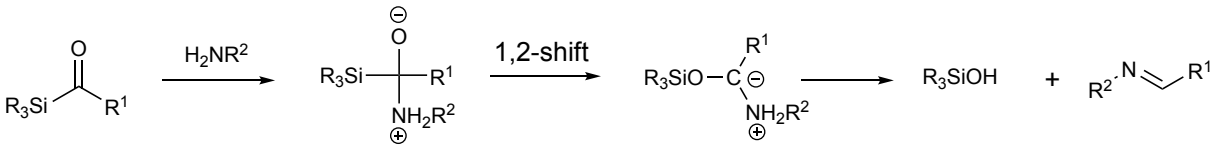


Figure S9. Full gel image of (+)-JQ1 PAL probe **16** labeling of 231MFP lysate spiked with BRD4-BD1 visualized by TAMRA-N_3 (top image). Full gel image of Ag stain (bottom image)

Photochemical 1,2-Brook Rearrangement:



Thermal 1,2-Brook Rearrangement:



Scheme S1. Mechanism of photochemical and thermal 1,2-Brook rearrangements.[1,2]

General Information

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without further purification. Tetrahydrofuran, dichloromethane, diethyl ether, toluene, trimethylamine, and N,N-dimethylformamide were purified by passage through an activated alumina column under argon. Thin-layer chromatography (TLC) analysis of reaction mixtures was performed using Merck silica gel 60 F254 TLC plates and visualized under UV or by staining with $KMnO_4$ or *p*-anisaldehyde. Column chromatography was performed on Merck Silica Gel 60 Å, 230 X 400 mesh. Nuclear magnetic resonance (NMR) spectra were recorded using Bruker AV-600, AV-500, DRX-500, Neo-500, AVB-400, AVQ-400, and AV-300 spectrometers. These CoC-NMR instruments at UC Berkeley are funded in part by the NIH (S10OD024998). ^{1}H and ^{13}C chemical shifts are reported in ppm downfield of tetramethylsilane and referenced to residual solvent peak ($CHCl_3$; $\delta H = 7.268$ ppm and $\delta C = 77.16$ppm). Multiplicities are reported using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, hept = heptet/septet, m = multiplet, br = broad, dt = doublet of triplet resonance. Mass spectral data for EMM were obtained from the QB3 mass spectral facility at the University of California, Berkeley on a Thermo LTQ-FTICR (7T, ESI) and in the Center of Catalysis at the University of California, Berkeley. Solvent abbreviations are reported as follows: EtOAc = ethyl acetate, hex = hexanes, DCM = dichloromethane, Et_2O = diethyl ether, MeOH = methanol, THF = tetrahydrofuran, DMSO = dimethylsulfoxide, Et_3N = trimethylamine, MeCN = acetonitrile.

Chemicals:

Rapamycin (53123-88-9) and (+)-JQ1 (1268524-70-4) were purchased from MedChemExpress (HY-10219 and HY-13030, respectively.). TAMRA-PEG4-Azide was purchased from Click Chemistry Tools (AZ109). (+)-JQ1-OH was prepared from commercial (+)-JQ1 according to literature precedent without modification.[3] N-boc-2-nitrobenzenesulfonamide (**SI-1**) was prepared according to literature precedent without modification.[4] 2-(3-(but-3-yn-1-yl)-3*H*-diazirin-3-yl)ethan-1-amine (**SI-12**) was prepared according to literature precedent.[5]

Biological Materials: 231MFP cells were obtained from Benjamin Cravatt and were derived from MDA-MB-231 cells. Pure recombinant BRD4-BD1 and FKBP12 proteins were purchased from Cayman Chemicals and Origene, respectively.

Analysis of small molecule probes by in-gel fluorescence

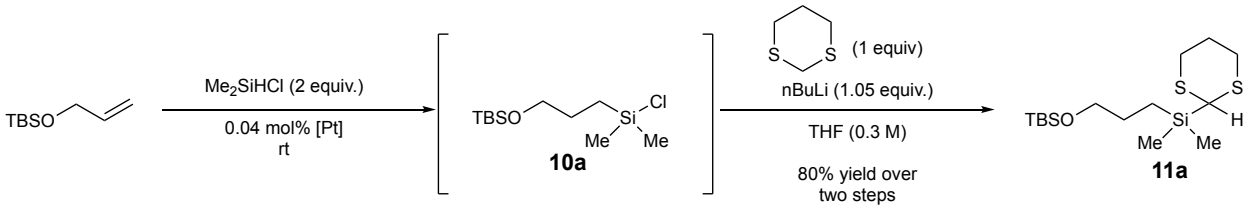
(+)-JQ1 probes: BRD4-BD1 (0.6 μg, appx. 0.7 μM) in pH 7.4 PBS (50 μL) was treated with a prepared stock solution of (+)-JQ1 acyl silane probe in DMSO and incubated in the dark for 30 min at RT. During competition, BRD4-BD1 was treated with a prepared stock solution of (+)-JQ1 (10x final concentration of acyl silane) prior to acyl silane addition and incubated at RT for 30 min. Samples were irradiated for 30 min on ice using a 6 W handheld UV lamp at 365 nm. Labeled protein was visualized following Cu-catalyzed click reaction, performed by sequential addition of $CuSO_4$, (1 mM), tris(2-carboxyethyl)phosphine (1 mM), tris[(1-benzyl-1H-1,2,3-triazol-4-yl)methyl]amine (34 μM) and TAMRA azide (25 μM).[6] Following click reaction, proteins were denatured by the addition of 4X Laemmli SDS loading buffer (30 μL) and run on a 16 cm Protean II xi 10% resolving SDS-PAGE gel system (Bio-Rad) and scanned using a ChemiDoc MP (Bio-Rad).

Rapamycin probes: FKBP12 (1.0 μg, appx. 1.5 μM) in pH 7.4 PBS (0.1% Triton X-100) (50 μL) was treated with a prepared stock solution of rapamycin acyl silane probe in DMSO and incubated in the dark for 30 min at RT. During competition, FKBP12 was treated with a prepared stock solution of rapamycin (10x final concentration of acyl silane) prior to acyl silane addition and incubated at RT for 30 min. Samples were irradiated for 30 min on ice using a 6 W handheld UV lamp at 365 nm. Labeled protein was visualized following Cu-catalyzed click reaction, performed by sequential addition of $CuSO_4$, (1 mM), tris(2-carboxyethyl)phosphine (1 mM), tris[(1-benzyl-1H-1,2,3-triazol-4-yl)methyl]amine (34 μM) and TAMRA azide (25 μM).[6] Following click reaction, proteins were denatured by the addition of 4X Laemmli SDS loading buffer (30 μL) and run on a 16 cm Protean II xi 10% resolving SDS-PAGE gel system (Bio-Rad) and scanned using a ChemiDoc MP (Bio-Rad).

(+)-JQ1 probes in cellular lysate: 231MFP cell lysate (1.0 μg/ μL) in pH 7.4 PBS (50 μL) was treated with a prepared stock solution of (+)-JQ1 probe in DMSO and incubated in the dark for 30 min at RT. Samples were irradiated for 30 min on ice using a 6 W handheld UV lamp at 365 nm. Labeled protein was visualized following Cu-catalyzed click reaction, performed by sequential addition of $CuSO_4$, (1 mM), tris(2-carboxyethyl)phosphine (1 mM), tris[(1-benzyl-1H-1,2,3-triazol-4-yl)methyl]amine (34 μM) and TAMRA azide (25 μM).[6] Following click reaction, proteins were denatured by the addition of 4X Laemmli SDS loading buffer (30 μL) and run on a 16 cm Protean II xi 10% resolving SDS-PAGE gel system (Bio-Rad) and scanned using a ChemiDoc MP (Bio-Rad).

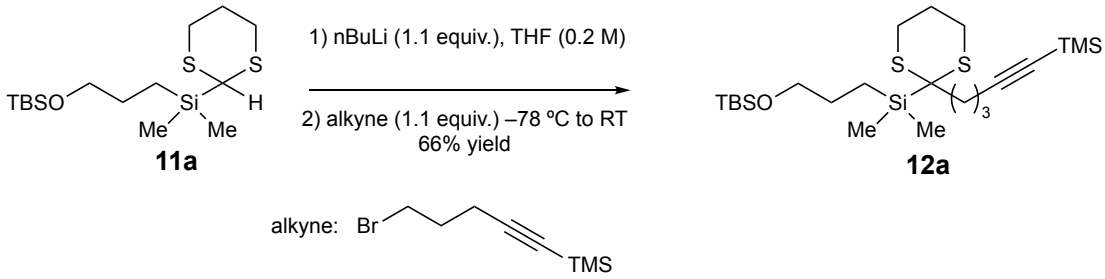
(+)-JQ1 probes in spiked cellular lysate: 231MFP cell lysate (1.0 μg/ μL) in pH 7.4 PBS (50 μL) was treated with 0.2 μg of BRD4-BD1 or DMSO control. A prepared stock solution of (+)-JQ1 probe in DMSO was added and incubated in the dark for 30 min at RT. For competition experiments, 231MFP lysate was treated with a prepared stock solution of (+)-JQ1 (100x final concentration of acyl silane) prior to acyl silane addition and incubated at RT for 30 min. Samples were irradiated for 30 min on ice using a 6 W handheld UV lamp at 365 nm. Labeled protein was visualized following Cu-catalyzed click reaction, performed by sequential addition of $CuSO_4$, (1 mM), tris(2-carboxyethyl)phosphine (1 mM), tris[(1-benzyl-1H-1,2,3-triazol-4-yl)methyl]amine (34 μM) and TAMRA azide (25 μM).[6] Following click reaction, proteins were denatured by the addition of 4X Laemmli SDS loading buffer (30 μL) and run on a 16 cm Protean II xi 10% resolving SDS-PAGE gel system (Bio-Rad) and scanned using a ChemiDoc MP (Bio-Rad).

Synthesis of acyl silane 15a



(3-((1,3-dithian-2-yl)dimethylsilyl)propoxy)(*tert*-butyl)dimethylsilane (11a): To an oven-dried Schlenk flask fitted with a rubber septum and cooled under N_2 was added platinum(0)-1,3-divinyl 1,1,1,3,3-tetramethyldisiloxane complex solution (Karstedt's catalyst) [0.1 M in vinyl terminated poly(dimethylsiloxane), ca 19 µL, 0.04 mol%] and Me_2SiHCl (9.3 mmol, 1.03 mL, 2.0 equiv.) by syringe drop-wise. After stirring at room temperature for 10 min, (allyloxy)(*tert*-butyl)dimethylsilane (4.65 mmol, 800 mg, 1.0 equiv.) was added dropwise over 15 min. After an additional 15 min stirring, the solution was cooled to 0 °C and evacuated under vacuum for 15 min to remove excess $ClSiMe_2H$. After purging with N_2 for an additional 15 min, silyl chloride **10a** was obtained (4.14 mmol, 1.09 g, 89% yield) and used immediately without further purification. **^{1}H NMR** (400.0 MHz, $CDCl_3$): δ 3.60 (t, *J* = 6.6 Hz, 2H), 1.67 – 1.58 (m, 2H), 0.90 (s, 9H), 0.86 – 0.79 (m, 2H), 0.42 (s, 6H), 0.06 (s, 6H). A flame dried 50 mL round bottom flask cooled under vacuum was charged with 1,3-dithiane (0.411 g, 3.42 mmol, 1.0 equiv.) and THF (9 mL, 0.3 M). The reaction vessel was cooled to –30 ˚C and a solution of *n*BuLi (2.2 M in hexanes, 1.64 mL, 3.59 mmol, 1.05 equiv.) was added dropwise. The solution was allowed to warm to room temperature and stir for 1 h before cooling to –78 ˚C and adding **10a** (1.2 equiv.) dropwise. The reaction mixture was allowed to warm to room temperature overnight and the resulting orange solution was quenched by addition of sat. aqueous NH_4Cl solution and extracted with Et_2O three times. The combined organic layers were washed with saturated brine, dried over $MgSO_4$, and concentrated *in vacuo.* The residual 1,3-dithiane was removed by Kugelrohr distillation under full vacuum at 70–100 °C to give **11a** (1.04 g, 3.08 mmol, 90% yield) as a pale oil.

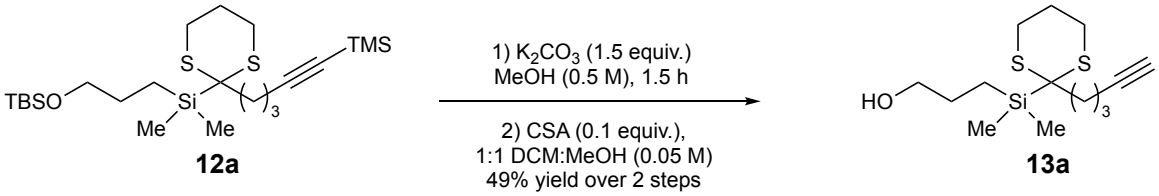
^{1}H NMR (400.0 MHz, $CDCl_3$): δ 3.73 (s, 1H), 3.56 (t, *J* = 6.9 Hz, 2H), 2.91 – 2.83 (m, 2H), 2.74 – 2.68 (m, 2H), 2.15 – 2.08 (m, 1H), 2.05 – 1.95 (m, 1H), 1.61 – 1.52 (m, 2H), 0.89 (s, 9H) (overlap with m, 2H), 0.67 – 0.61 (m, 2H), 0.14 (s, 6H), 0.05 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 68.1, 66.1, 33.7, 31.3, 27.1, 26.4, 26.2, 18.5, 9.3, –4.8, –5.1. **HRMS** (ESI): calculated for $[C_{15}H_{34}OS_2Si_2+H]^+$ required *m/z* 351.1662, found *m/z* 351.1664.



***tert*-butyl(3-(dimethyl(2-(5-(trimethylsilyl)pent-4-yn-1-yl)-1,3-dithian-2-yl)silyl)propoxy)dimethylsilane (12a):** A flame dried 50 mL round bottom flask cooled under vacuum was charged with **11a** (840 mg, 2.5 mmol, 1.0 equiv.) and THF (5 mL, 0.2 M) and cooled to –30 ˚C, followed by the dropwise addition of *n*BuLi (2.2 M, 1.2 mL, 1.1 equiv.). After stirring for 45 min at –30 ˚C, a solution of (5-bromopent-1-yn-1-yl)trimethylsilane (539 mg, 2.63 mmol, 1.1 equiv.) in THF (5 mL) was added dropwise. The reaction was then allowed to warm to room temperature and stir overnight. After 16 h, the reaction was quenched by the addition of sat. aqueous NH_4Cl and extracted with a 1:1 mixture of Et_2O/hexanes. The combined organics were washed with saturated brine, dried over $MgSO_4$, and concentrated to an oil. Purification of the crude material by flash

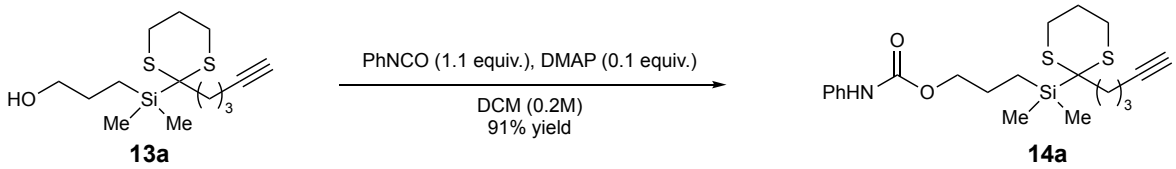
column chromatography on silica gel in 95:5 hex/EtOAc yielded the desired product **12a** as a clear, colorless oil (817 mg, 66% yield).

^{1}H NMR (500.0 MHz, $CDCl_3$): δ 3.57 (t, *J* = 7.0 Hz, 2H), 3.12 – 3.05 (m, 2H), 3.42 (dt, *J* = 14.3, 4.1 Hz, 2H), 2.39 – 2.33 (m, 2H), 2.30 (t, *J* = 6.7 Hz, 2H), 2.09–2.01 (m, 1H), 1.96 – 1.85 (m, 1H), 1.74 – 1.65 (m, 2H), 1.61 – 1.52 (m, 2H), 0.89 (s, 9H), 0.74 – 0.68 (m, 2H), 0.18 (s, 6H), 0.15 (s, 9H), 0.05 (s, 6H). **^{13}C NMR** (125.7 MHz, $CDCl_3$): δ 107.3, 85.2, 66.2, 38.9, 36.1, 27.5, 26.7, 26.1, 25.3, 23.3, 20.2, 18.5, 14.2, 9.3, 0.3, –4.4, –5.1. **HRMS** (ESI^+): calculated for $[C_{12}H_{48}OS_2Si_3+H]^+$ required *m/z* 489.2527, found *m/z* 489.2524.



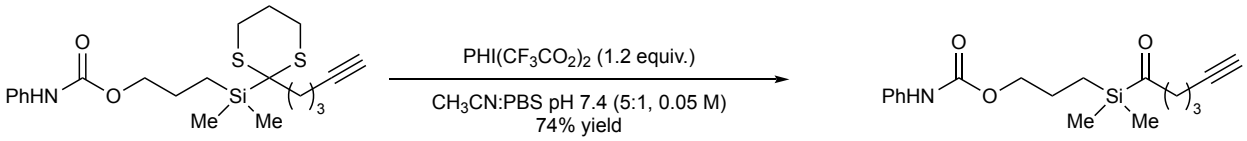
3-(dimethyl(2-(pent-4-yn-1-yl)-1,3-dithian-2-yl)silyl)propyl benzoate (13a): To a solution of **12a** (331 mg, 0.697 mmol, 1.0 equiv.) in MeOH (1.5 mL, 0.5 M) was added potassium carbonate (140 mg, 1.02 mmol, 1.5 equiv.). The reaction was monitored by TLC and after 4 h quenched by addition of sat. aqueous NH_4Cl, diluted with sat. aqueous brine, and extracted with Et_2O three times. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give a residue that was subsequently added to a solution of camphorsulfonic acid (15 mg, 0.068 mmol, 0.1 equiv.) in a 1:1 mixture of DCM:MeOH (0.05 M) and stirred at room temperature. After 3 h, the solution was diluted with 1:1 hex:EtOAc, washed with sat. aqueous $NaHCO_3$ and sat. aqueous brine, dried, filtered, and concentrated to an oil. Purification of the crude material by gradient elution of 10–30% EtOAc in hex by flash column chromatography gave **13a** (130 mg, 49% over two steps) as a clear oil.

^{1}H NMR (600.1 MHz, $CDCl_3$): δ 3.56 (t, *J* = 6.7 Hz, 2H), 3.05 – 2.97 (m, 2H), 2.38 (dt, *J* = 14.4, 3.7 Hz, 2H), 2.32 – 2.28 (m, 2H), 2.21 (td, *J* = 6.8, 2.7 Hz, 2H), 2.04 – 1.93 (m, 3H), 1.84 (ddq, *J* = 3.2, 3.2, 12.6 Hz, 1H), 1.70 – 1.63 (m, 2H), 1.61 – 1.54 (m, 2H), 0.75 – 0.68 (m, 2H), 0.14 (s, 6H). **^{13}C NMR** (150.9 MHz, $CDCl_3$): δ 84.13, 68.80, 65.42, 38.50, 36.20, 27.16, 26.47, 25.00, 23.21, 18.69, 9.25, –4.47. **HRMS** (ESI^+): calculated for $[C_{14}H_{26}OS_2Si+Na]^+$ required *m/z* 325.1087, found *m/z* 325.1089.



3-(dimethyl(2-(pent-4-yn-1-yl)-1,3-dithian-2-yl)silyl)propyl benzoate (14a): A flame-dried screw-capped culture tube cooled under vacuum was charged with **13a** (161 mg, 0.532 mmol, 1.0 equiv.) and DCM (2.66 mL, 0.2 M). Phenylisocyanate (64 mL, 0.585 mmol, 1.1 equiv.) and DMAP (6.5 mg, 0.053 mmol, 0.1 equiv.) were quickly added and the resulting mixture was stirred under N_2 at room temperature overnight. After 16 h, the resulting cloudy mixture was diluted with DCM, washed sequentially with sat. aqueous NH_4Cl, H_2O, and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give **14a** (204 mg, 0.483 mmol, 91% yield) as a pale yellow oil which was used in the next step without further purification.

^{1}H NMR (500.0 MHz, $CDCl_3$): δ 7.41 – 7.36 (m, 2H), 7.3 (t, *J* = 7.5 Hz, 2H), 7.05 (tt, *J* = 1.2, 7.5 Hz, 1H), 4.14 (t, *J* = 6.8 Hz, 2H), 3.07 (ddd, *J* = 2.7, 12.5, 14.7 Hz, 2H), 2.44 (ddd, *J* = 2.7 2.7, 14.3 Hz, 2H), 2.38 – 2.34 (m *J* = 3.7, 5.0, 7.9 Hz, 2H), 2.27 (ddd, *J* = 2.7, 6.7, 6.7 Hz, 2H), 2.09 – 2.02 (m, 1H), 2.00 (t, *J* = 2.5 Hz, 1H), 1.90 (ddq, *J* = 3.3, 3.3, 12.7 Hz, 1H), 1.80 – 1.69 (m, 4H), 0.85 – 0.80 (m, 2H), 0.21 (s, 6H).

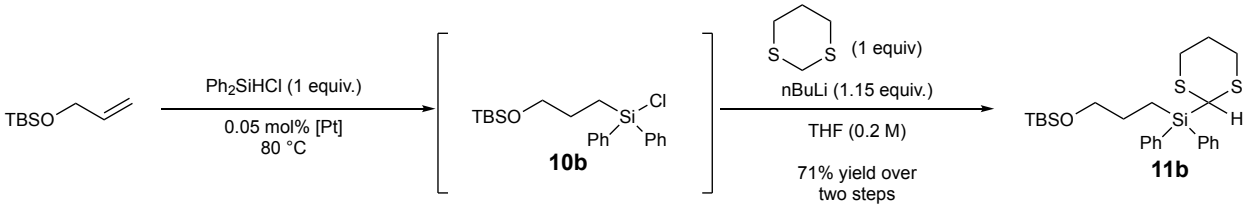


14a **15a**

3-(hex-5-ynoyldimethylsilyl)propyl phenylcarbamate (15a) A flame-dried scintillation vial was charged with **14a** (138 mg, 0.328 mmol 1.0 equiv.) and a 5:1 solution of MeCN:PBS 7.4 buffer (0.05 M, 6 mL). To the rapidly stirred mixture was added PIFA (169 mg, 0.393 mmol, 1.2 equiv.), and the resulting solution was allowed to stir at room temperature. After 2 h, the mixture was diluted with Et_2O, washed sequentially with sat. aqueous NH_4Cl, H_2O, and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude material was purified using flash column chromatography (hex:EtOAc 90:10) to give acyl silane **15a** (80 mg, 74% yield) as a colorless clear oil.

^{1}H NMR (600.1 MHz, $CDCl_3$): δ 7.48 – 7.36 (m, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.06 (t, *J* = 7.2 Hz, 1H), 6.68 (br. s, 1H), 4.12 (t, *J* = 6.6 Hz, 2H), 2.77 (t, *J* = 7.1 Hz, 2H), 2.20 (dt, *J* = 2.6, 6.8 Hz, 2H), 1.93 (t, *J* = 2.6 Hz, 1H), 1.75 (ddd, *J* = 7.0, 7.0, 13.9 Hz, 2H), 1.73 – 1.68 (m, 2H), 0.82 – 0.77 (m, 2H), 0.23 (s, 6H). **^{13}C NMR** (150.9 MHz, $CDCl_3$): δ 247.3, 153.6, 138.1, 129.2, 123.5, 118.8, 83.9, 69.1, 67.3, 47.2, 23.4, 20.8, 17.9, 10.0, –4.6. **HRMS** (ESI^+): calculated for $[C_{18}H_{25}NO_3Si+Na]^+$ required *m/z* 354.1496, found *m/z* 354.1499.

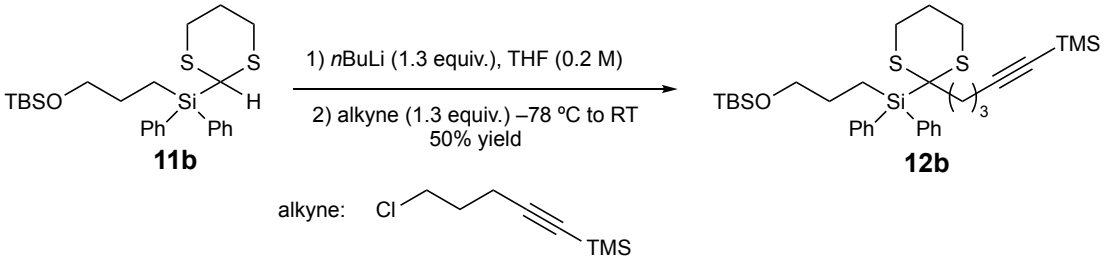
Synthesis of acyl silane 15b



(3-((1,3-dithian-2-yl)diphenylsilyl)propoxy)(*tert*-butyl)dimethylsilane (11b): To an oven-dried Schlenk flask fitted with a rubber septum and cooled under N_2 was added platinum(0)-1,3-divinyl 1,1,1,3,3-tetramethyldisiloxane complex solution (Karstedt's catalyst) [0.1 M in vinyl terminated poly(dimethylsiloxane), ca 15 µL, 0.05 mol%] and Ph_2SiHCl (0.6 mL, 3.09 mmol, 1 equiv.) by syringe drop-wise. The resulting solution was stirred for 10 min at room temperature, then (allyloxy)(*tert*-butyl)dimethylsilane (0.531 g, 3.09 mmol, 1 equiv.) was added as a neat liquid by syringe and the solution was heated in an 80 °C oil bath for 25 min. After cooling to room temperature, the reaction mixture (**10b**) was used immediately in the next step without further purification. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.66 – 7.60 (m, 4H), 7.47 – 7.39 (m, 6H), 3.61 (t, *J* = 6.4 Hz, 2H), 1.76 – 1.66 (m, 2H), 1.42 – 1.35 (m, 2H), 0.89 (s, 9H), 0.03 (s, 6H).

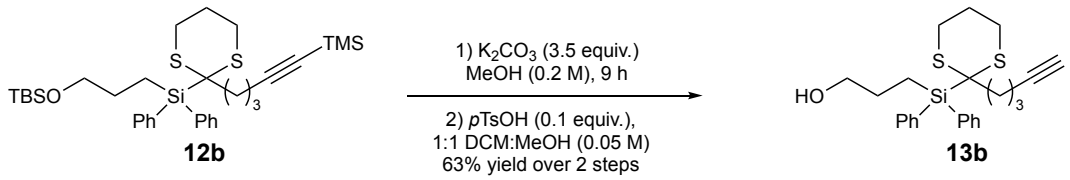
A flame dried 50 mL round bottom flask cooled under vacuum was charged with 1,3-dithiane (0.312 g, 2.6 mmol, 1.0 equiv.) and THF (13 mL, 0.2 M). The reaction vessel was cooled to –30 ˚C and a solution of *n*BuLi (2.99 mmol, 1.15 equiv.) was added dropwise. The solution was allowed to warm to room temperature and stir for 1 h before cooling to –78 ˚C and adding **10b** (1.2 equiv.) dropwise. The reaction mixture was allowed to warm to room temperature overnight and the resulting orange solution was quenched by addition of sat. aqueous NH_4Cl solution and extracted with EtOAc three times. The combined organic layers were washed with saturated brine, dried over $MgSO_4$, and concentrated *in vacuo*. The resulting oil was purified using flash column chromatography (hex:EtOAc 95:5) to give **11b** (0.894 g, 1.84 mmol, 71% over two steps) as an oil.

^{1}H NMR (300.1 MHz, $CDCl_3$): δ 7.70 – 7.63 (m, 4H), 7.46 – 7.34 (m, 6H), 4.25 (s, 1H), 3.60 (t, *J* = 6.6 Hz, 2H), 2.92 (ddd, *J* = 3.3, 11.6, 14.3 Hz, 2H), 2.71 (dt, *J* = 14.1, 3.7 Hz, 2H), 2.16 – 1.99 (m, 2H), 1.74 – 1.61 (m, 2H), 1.32 – 1.23 (m, 2H), 0.89 (s, 9H), 0.03 (s, 6H). **^{13}C NMR** (125.7 MHz, $CDCl_3$): δ 135.8, 132.5, 130.0, 127.9, 65.8, 32.6, 31.8, 27.1, 26.15, 26.10, 22.15, 18.5, 7.5, –5.1 **HRMS** (ESI^+): calculated for $[C_{25}H_{38}OS_2Si_2+Na]^+$ required *m/z* 497.1795, found *m/z* 497.1792.



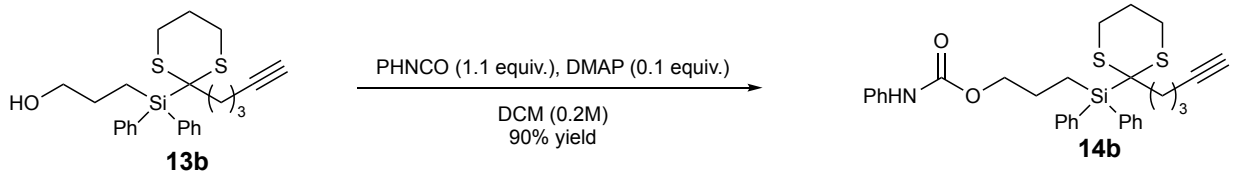
***tert*-butyl(3-(diphenyl(2-(5-(trimethylsilyl)pent-4-yn-1-yl)-1,3-dithian-2-yl)silyl)propoxy)dimethylsilane (12b):** A flame dried 50 mL round bottomed flask cooled under vacuum was charged with **11b** (0.500 g, 1.05 mmol, 1.0 equiv.) and THF (5.27 mL, 0.2 M) and cooled to –78 ˚C, followed by the dropwise addition of *n*BuLi (2.4 M, 0.57 mL, 1.3 equiv.). After stirring for 5 min at –78 ˚C, the reaction was allowed to warm to room temperature over an hour, then returned to –78 ˚C prior to the dropwise addition of (5-chloropent-1-yn-1-yl) trimethylsilane (0.239 g, 1.37 mmol, 1.3 equiv.). The reaction was then allowed to warm to room temperature and stir overnight. After 16 h, the reaction was quenched by the addition of sat. aqueous NH_4Cl and extracted with a 1:1 mixture of Et_2O/hexanes. The combined organics were washed with saturated brine, dried over $MgSO_4$, and concentrated to an oil. Purification of the crude material by flash column chromatography on silica gel in 95:5 hex/EtOAc yielded the desired product **12b** as a clear, colorless oil (0.333 g, 50% yield).

^{1}H NMR (500.0 MHz, CDCl3): δ 7.81 (br.d *J* = 7 Hz, 4H), 7.46 – 7.31 (m, 6H), 3.53 (t, *J* = 6.0 Hz, 2H), 3.14 – 3.05 (m, 2H), 2.47 – 2.40 (m, 2H), 2.30 – 2.25 (m, 2H), 2.09 (t, *J* = 6.6 Hz, 2H), 1.60 – 1.53 (m, 2H), 1.48 – 1.42 (m, 2H), 1.41 – 1.35 (m, 2H), 1.34 – 1.24 (m, 2H), 0.87 (s, 9H), 0.12 (s, 9H), 0.0 (s, 6H). **^{13}C NMR** (125.7 MHz, $CDCl_3$): δ 136.57, 132.52, 129.81, 127.68, 107.27, 84.89, 65.71, 39.69, 36.44, 27.57, 26.42, 26.09, 25.38, 24.98, 23.93, 18.44, 7.66, 0.27, –5.14. **HRMS** (ESI^+): calculated for $[C_{33}H_{52}OS_2Si_3+H]^+$ required *m/z* 613.2840, found *m/z* 613.2838.



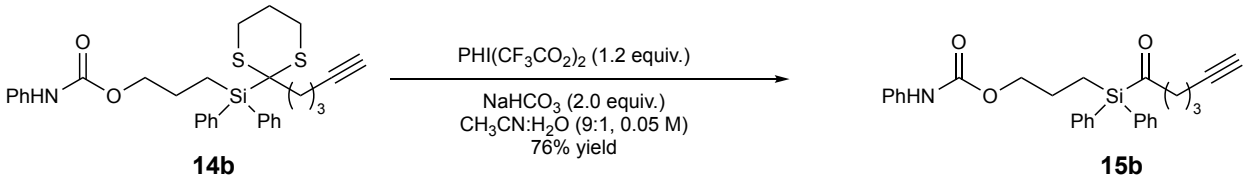
3-((2-(pent-4-yn-1-yl)-1,3-dithian-2-yl)diphenylsilyl)propan-1-ol (13b): A flame dried scintillation vial was charged with **12b** (0.436 g, 0.711 mmol, 1 equiv.), K_2CO_3 (146 mg, 1.06 mmol, 1.5 equiv.) and MeOH (1.5 mL, 0.5 M) and stirred rapidly. Partial conversion was observed by TLC after workup following 6 h of stirring, at which point the material was charged with an additional batch of K_2CO_3 (278 mg, 2.0 equiv) and MeOH (3mL), until full consumption of **12b** was observed by TLC, approximately 3 h. The reaction was transferred to a separatory funnel with Et_2O and hexanes, washed with water, dried over $MgSO_4$, and concentrated. The crude material was then transferred to a scintillation vial charged with *p*-toluenesulfonic acid (13 mg, 0.075 mmol, 0.1 equiv.) and a 1:1 solution of DCM:MeOH (0.05 M, 14 mL). After stirring for 4 h, the solution was diluted with EtOAc, washed sequentially with sat. aqueous NH_4Cl, H_2O, and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give **13b** (191 mg, 0.448 mmol, 63% yield over two steps) as a viscous oil.

^{1}H NMR (500.0 MHz, $CDCl_3$): δ 7.80 (app d, *J* = 7.5 Hz, 4H), 7.45 – 7.35 (m, 6H), 3.57 (t, *J* = 6.4 Hz, 2H), 3.07 (ddd, *J* = 3.1, 12.0, 14.7 Hz, 2H), 2.45 (dt, *J* = 14.4, 3.8 Hz, 2H), 2.30 – 2.26 (m, 2H), 2.08 – 2.01 (m, 2H), 2.07 – 1.93 (m, 2H), 1.88 (t, *J* = 2.5 Hz, 1H), 1.64 – 1.56 (m, 2H), 1.55 – 1.47 (m, 2H), 1.46 – 1.40 (m, 2H). **^{13}C NMR** (125.7 MHz, $CDCl_3$): δ 136.48, 132.22, 129.84, 127.68, 84.12, 68.63, 65.51, 39.49, 36.64, 27.56, 26.42, 24.80, 23.94, 18.56, 7.72. **HRMS** (ESI^+): calculated for $[C_{24}H_{30}OS_2Si+Na]^+$ required *m/z* 449.1400, found *m/z* 449.1396.



3-((2-(pent-4-yn-1-yl)-1,3-dithian-2-yl)diphenylsilyl)propyl benzoate (14b): A flame-dried screw-capped culture tube cooled under vacuum was charged with **13b** (156.4 mg, 0.36 mmol, 1.0 equiv.) and DCM (0.91 mL, 0.2 M). Phenylisocyanate (43 mL, 0.40 mmol, 1.1 equiv.) and DMAP (4.4 mg, 0.036 mmol, 0.1 equiv.) were quickly added and the resulting mixture was stirred under N_2 at room temperature overnight. After 16 h, the resulting cloudy mixture was diluted with DCM, washed sequentially with sat. aqueous NH_4Cl, H_2O, and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give **14b** (178.6 mg, 0.327 mmol, 90% yield) as a crude white solid which was used in the next step without further purification.

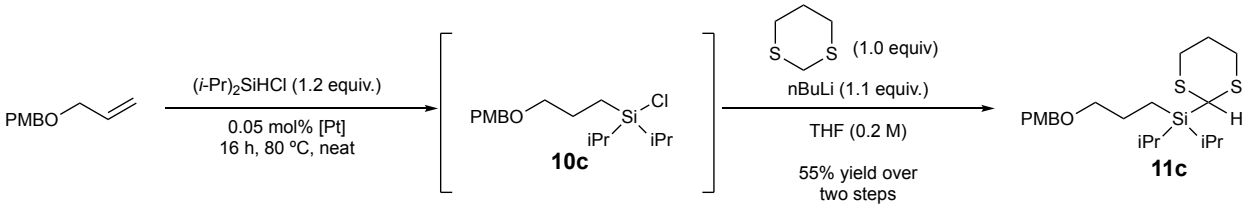
^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.80 (d, J = 7.0 Hz, 4H), 7.48 – 7.28 (m, 10H), 7.09 – 7.02 (m, 1H), 6.55 (br. s, 1H), 4.10 (t, J = 6.5 Hz, 2H), 3.14 – 3.02 (m, 2H), 2.48 (dt, J = 14.1, 2.6 Hz, 2H), 2.34 – 2.26 (m, 2H), 2.08 – 2.03 (m, 2H), 1.88 (t, J = 2.7 Hz, 1H), 1.70 – 1.54 (m, 6H), 1.50 – 1.44 (m, 2H).



3-(hex-5-ynoyldiphenylsilyl)propyl phenylcarbamate (15b): A flame-dried scintillation vial was charged with **14b** (17 mg, 0.037 mmol 1.0 equiv.), $NaHCO_3$ (6.2 mg, 0.075 mmol, 2.0 equiv.), and 9:1 solution of MeCN:H_2O (700:75 uL, 0.05 M). To the rapidly stirred mixture was added PIFA (19 mg, 0.045 mmol, 1.2 equiv.), and the resulting orange solution was allowed to stir at room temperature. After 2 h, the mixture was diluted with Et_2O, washed sequentially with sat. aqueous NH_4Cl, H_2O, and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude material was purified using flash column chromatography (hex:EtOAc 95:5) to give **15b** (13 mg, 76% yield) as a pale yellow oil.

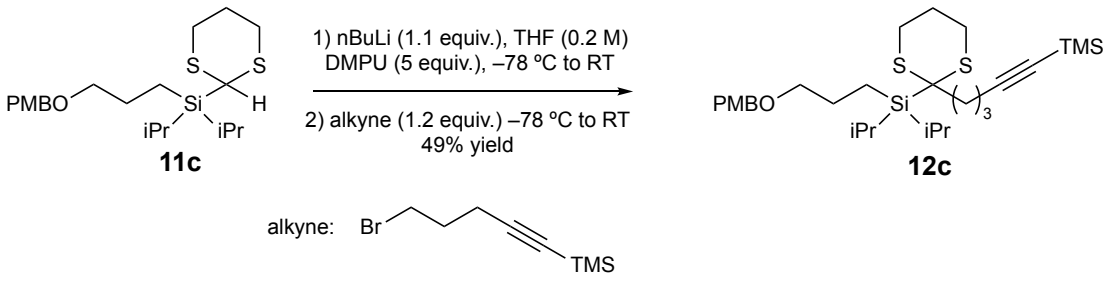
^{1}H NMR (600.1 MHz, $CDCl_3$): δ 7.58 (br. d, J = 7.0 Hz, 4H), 7.46 (tt, J = 6.4, 1.4 Hz, 2H), 7.40 (app. t, J = 7.5 Hz, 4H), 7.35 (br. d, J = 7.5 Hz, 2H), 7.30 (tt, J = 7.3, 2.0 Hz, 2H), 7.05 (t, J = 7.2 Hz, 1H), 6.54 (br. s, 1H), 4.14 (dd, J = 6.5 Hz, 2H), 2.78 (t, J = 7.0 Hz, 2H), 2.12 (td, J = 7.0, 2.6 Hz, 2H), 1.87 (t, J = 2.6 Hz, 1H), 1.82 – 1.76 (m, 2H), 1.71 (ddd, J = 13.9, 7.0, 7.0 Hz, 2H), and 1.38 – 1.33 (m, 2H). **^{13}C NMR** (150.9 MHz, $CDCl_3$): δ 243.76, 187.88, 137.58, 135.38, 131.35, 130.34, 129.04, 128.37, 123.38, 83.67, 68.94, 48.23, 29.72, 23.12, 20.81, 17.70, and 7.83. **HRMS** (ESI^+): calculated for $[C_{28}H_{29}NO_3Si+Na]^+$ required *m/z* 478.1809, found *m/z* 478.1819.

Synthesis of acyl silane 15c



(1,3-dithian-2-yl)diisopropyl(3-((4-methoxybenzyl)oxy)propyl)silane (11c): To an oven-dried Schlenk flask fitted with a rubber septum and cooled under N_2 was added platinum(0)-1,3-divinyl 1,1,1,3,3-tetramethyldisiloxane complex solution (Karstedt's catalyst) [0.1 M in vinyl terminated poly(dimethylsiloxane), ca 150 µL, 0.05 mol%] and *i*Pr$_2$SiHCl (4.5 g, 30 mmol, 1.0 equiv.) by syringe dropwise. The resulting yellow solution was stirred for 10 min at room temperature, then 1-((allyloxy)methyl)-4-methoxybenzene (**9c**, 4.92 g, 30 mmol, 1.0 equiv.) was added as a neat liquid by syringe. The vessel was heated to 80 ˚C in an oil bath for 16 h. After cooling to room temperature, the reaction mixture (**10c**) was used immediately in the next step without further purification. **^{1}H NMR**: (300.1 MHz, $CDCl_3$) δ 7.27 (d, 2H, *J* = 8.7 Hz), 6.90 (d, 2H, *J* = 8.7 Hz), 4.45 (s, 2H), 3.82 (s, 3H), 3.44 (t, 2H, *J* = 6.7 Hz), 1.79–1.69 (m, 2H), 1.11 – 1.06 (m, 14H), 0.89 – 0.83 (m, 2H). A flame dried 250 mL round bottom flask cooled under vacuum was charged with 1,3-dithiane (2.57 g, 21.4 mmol, 1.0 equiv.) and THF (70 mL, 0.3 M). The reaction vessel was cooled to –30 ˚C and a solution of *n*BuLi (2.4 M in hexanes, 9.83 mL, 23.6 mmol, 1.1 equiv.) was added dropwise resulting in a persistent, but faint yellow color. The solution was maintained at –30 ˚C for 1 h before cooling to –78 ˚C and adding **10c** (1.2 equiv.) as a solution in THF (10 mL) dropwise. The reaction mixture was allowed to warm to room temperature overnight and then quenched by addition of 200 mL sat. aqueous NH_4Cl solution and extracted with a 1:1 mixture of Et_2O/hex (3x, 100 mL). The combined organic layers were washed with saturated brine, dried over $MgSO_4$, and concentrated *in vacuo.* The resulting residue was purified by flash column chromatography on silica gel in 95:5 hex/EtOAc to yield a clear, colorless oil (4.84 g, 55% yield).

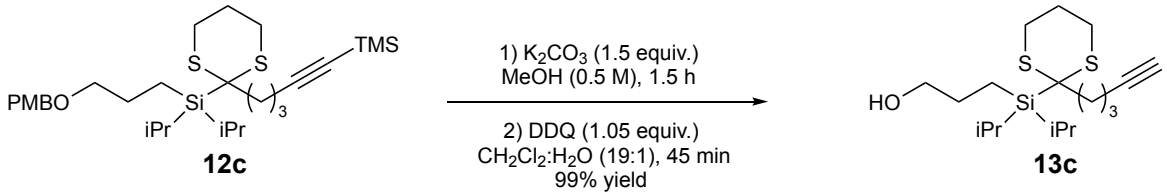
^{1}H NMR: (500.0 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.5 Hz 2H), 6.89 (d, *J* = 8.6 Hz,2H), 4.47 (s, 2H), 3.91 (s, 1H) 3.81 (s, 3H), 3.44 (t, *J* = 7.0 Hz, 2H), 2.90 (ddd, *J* = 14.7, 12.2, 2.8, 2H), 2.71 (dt, *J* = 13.8, 3.9 Hz, 2H), 2.16 – 2.00 (m, 2H), 1.83 – 1.76 (m, 2H), 1.26 – 1.17 (m, 2H), 1.14 (d, *J* = 7.4 Hz, 6H), 1.13 (d, *J* = 7.0 Hz, 6H), 0.77 – 0.72 (m, 2H). **^{13}C NMR** (125.7 MHz) δ 159.1, 130.8, 129.3, 113.8, 73.3, 72.5, 55.3, 32.1, 31.9, 26.6, 24.2, 18.59, 18.56, 11.0, 5.1. **HRMS** (ESI^+): calculated for $[C_{21}H_{36}O_2S_2Si+Na]^+$ required *m/z* 435.1823, found *m/z* 435.1829.



(5-(2-(diisopropyl(3-((4-methoxybenzyl)oxy)propyl)silyl)-1,3-dithian-2-yl)pent-1-yn-1-yl)trimethylsilane (12c): A flame dried 100 mL round bottom flask cooled under vacuum was charged with **11c** (1.95 g, 4.73 mmol, 1.0 equiv.) and THF (24 mL, 0.2 M) and cooled to –78 ˚C, followed by the dropwise addition of *n*BuLi (2.4 M, 2.27 mL, 1.1 equiv.). After stirring for 5 min at –78 ˚C, the reaction was allowed to warm to room temperature over an hour, resulting in an orange solution that was then returned to –78 ˚C prior to the addition of anhydrous DMPU (2.7 mL, 23.7 mmol, 5 equiv.) and (5-bromopent-1-yn-1-yl) trimethylsilane (1.24 g, 5.66 mmol, 1.2 equiv.). The reaction was then allowed to warm to room temperature and stir overnight.

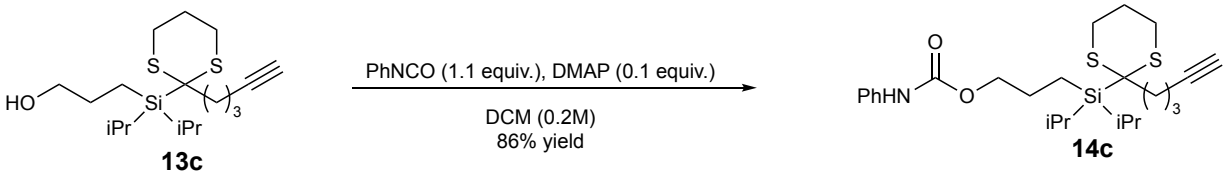
After 16 h, the reaction was quenched by the addition of 100 mL sat. NH_4Cl and extracted with a 1:1 mixture of Et_2O/hexanes (3x50 mL). The combined organics were washed with saturated brine, dried over $MgSO_4$, filtered, and concentrated to an oil. Purification of the crude material by flash column chromatography on silica gel in 95:5 hex/EtOAc yielded the desired product as a clear, colorless oil (1.29 g, 49% yield).

^{1}H NMR (500.0 MHz, $CDCl_3$) δ 7.28 (d, *J* = 9.2 Hz, 1H), 6.88 (d, *J* = 8.8 Hz, 1H), 4.45 (s, 2H), 3.81 (s, 3H), 3.42 (t, *J* = 6.9 Hz, 2H), 3.14 (ddd, *J* = 14.3, 11.8, 2.7 Hz, 2H), 2.49 – 2.44 (m, 2H), 2.38 (dt, *J* = 14.1, 3.5 Hz, 2H), 2.33 (t, *J* = 6.5 Hz, 2H), 2.07 – 2.00 (m, 1H), 1.99 – 1.89 (m, 1H), 1.87 – 1.80 (m, 1H), 1.80 – 1.73 (m, 2H), 1.37 (hept, *J* = 7.5 Hz, 2H), 1.19 (d, *J* = 7.2, 6H), 1.18 (d, *J* = 7.5, 6H), 0.16 (s, 9H). **^{13}C NMR** (125.7 MHz, $CDCl_3$) δ 159.2, 131.0, 129.4, 113.9, 107.3, 85.2, 73.5, 72.5, 55.4, 40.5, 36.9, 26.9, 25.2, 25.0, 23.8, 20.2, 19.8, 19.8, 12.3, 6.4, 0.3. **HRMS** (ESI^+) calculated for $[C_{29}H_{50}O_2S_2Si_2+Na]^+$ required *m/z* 573.2683, found *m/z* 573.2686.



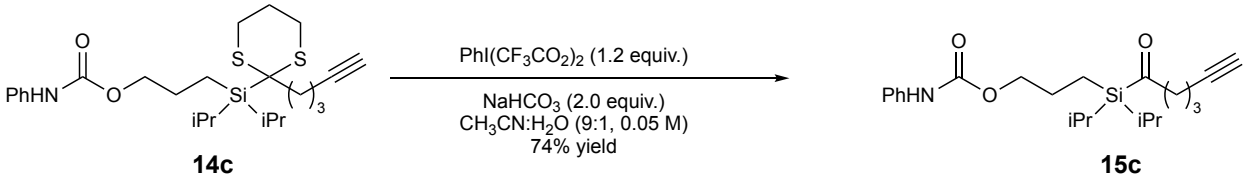
3-(diisopropyl(2-(pent-4-yn-1-yl)-1,3-dithian-2-yl)silyl)propan-1-ol (13c): A flame dried 25 mL round bottom flask was charged with **5** (1.29 g, 2.24 mmol, 1 equiv.), K_2CO_3 (464 mg, 3.36 mmol, 1.5 equiv.) and MeOH (5 mL, 0.5 M) and stirred rapidly until full consumption of **5c** was observed by TLC, approximately 1.5 h. The reaction was transferred to a separatory funnel with Et_2O, washed with water, dried over $MgSO_4$, and concentrated. The crude product was transferred to a 25 mL round bottom flask and dissolved in a mixture of CH_2Cl_2:H_2O (19:1, 12 mL). To the stirred solution was added DDQ (497 mg, 2.19 mmol, 1.05 equiv.) resulting in a dark purple color. After stirring for 45 min, the reaction was quenched by the addition of sat. $NaHCO_3$ sol. and filtered through a short pad of Celite washing with CH_2Cl_2. The filtrate was washed with water, brine, dried over $MgSO_4$, and concentrated to a colored oil. The crude material was purified by a gradient column (9:1 to 8:2 hex:EtOAc) to yield the desired product as a clear, colorless oil (735 mg, 99% yield).

^{1}H NMR (300.1 MHz, $CDCl_3$): δ 3.60 (t, *J* = 6.7 Hz, 2H), 3.09 (ddd, 14.9, 12.7, 3.0 Hz, 2H), 2.45 – 2.42 (m, 2H), 2.38 (dt, *J* = 14.3, 3.9 Hz, 2H), 2.28 (td, *J* = 6.74, 2.70, 2H), 2.05 – 2.02 (m, 1H), 1.99 (t, *J* = 2.63 Hz, 1H), 1.96 – 1.88 (m, 1H), 1.82–1.75 (m, 4H), 1.67 (br. s, 1H) 1.39 – 1.33 (m, 2H), 1.18 – 1.16 (m, 12H), 0.85 – 0.82 (m, 2H). **^{13}C NMR** (125.7 MHz, $CDCl_3$): δ 84.3, 69.0, 66.1, 40.4, 37.2, 28.0, 27.0, 25.1, 23.9, 19.8, 19.7, 18.8, 12.3, 6.1. **HRMS** (ESI^+) calculated for $[C_{18}H_{34}OS_2Si+Na]^+$ required *m/z* 381.1740 , found *m/z* 381.1712.



3-(diisopropyl(2-(pent-4-yn-1-yl)-1,3-dithian-2-yl)silyl)propyl phenylcarbamate (14c): A flame-dried culture tube cooled under vacuum was charged with **13c** (65 mg, 0.18 mmol, 1.0 equiv.) and DCM (0.91 mL, 0.2 M). Phenylisocyanate (22 mL, 0.20 mmol, 1.1 equiv.) and DMAP (2.2 mg, 0.018 mmol, 0.1 equiv.) were quickly added and the resulting mixture was stirred under N_2 at room temperature overnight. After 16 h, the resulting cloudy mixture was diluted with DCM, washed sequentially with sat. aqueous NH_4Cl, H_2O, and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give **14c** (74.2 mg, 0.155 mmol, 86% yield) as a crude white solid which was used in the next step without further purification.

^{1}H NMR (400.0 MHz, $CDCl_3$): 7.41 – 7.36 (m, 2H), 7.33 – 7.28 (m, 2H), 7.09 – 7.03 (m, 1H), 6.61 (br. s, 1H), 4.14 (t, J = 6.7 Hz, 2H), 3.15 – 3.05 (m, 2H), 2.49 – 2.35 (m, 4H), 2.29 (dt, J = 2.7, 6.7 Hz, 2H), 2.08 – 2.00 (m, 2H), 1.97 – 1.88 (m, 2H), 1.84 – 1.75 (m, 2H), 1.43 – 1.33 (m, 2H), 1.21 – 1.16 (m, 12 H), 0.92 – 0.85 (m, 2H).

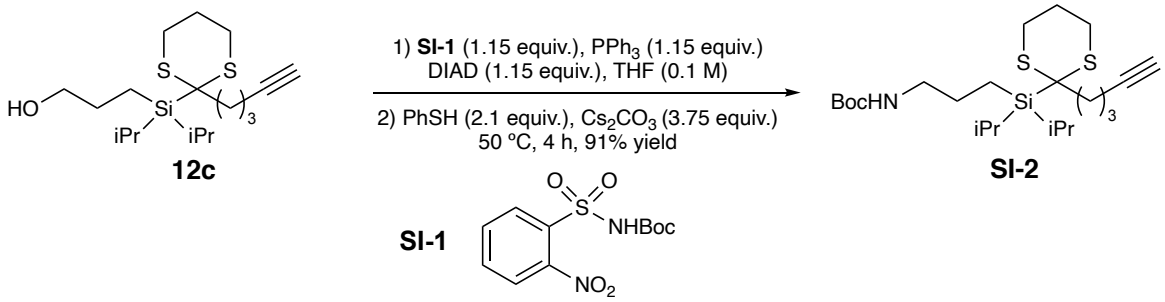


14c **15c**

3-(hex-5-ynoyldiisopropylsilyl)propyl phenylcarbamate (15c): A flame-dried scintillation vial was charged with **14c** (9 mg, 0.023 mmol, 1.0 equiv.), $NaHCO_3$ (3.9 mg, 0.047 mmol, 2.0 equiv.), and a solution of MeCN:H_2O (9:1, 0.05 M, 0.5 mL). To the rapidly stirred mixture was added PIFA (12 mg, 0.028 mmol, 1.2 equiv.), and the resulting yellow solution was allowed to stir at room temperature. After 30 min, the mixture was diluted with Et_2O, washed sequentially with sat. aqueous NH_4Cl, H_2O, and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude material was purified using flash column chromatography (hex:EtOAc 95:5) to give acylsilane **15c** (6.7 mg, 0.017 mmol, 74% yield) as a clear solid.

^{1}H NMR (500.0 MHz, $CDCl_3$): 7.42 – 7.34 (m, 2H), 7.33-7.28 (m, 2H), 7.06 (t, J = 7.3 Hz, 1H), 6.62 (br. s, 1H), 4.14 (t, J = 6.7 Hz, 2H), 2.73 (t, J = 7.0 Hz, 2H), 2.20 (dt, J = 6.9, 2.7 Hz, 2H), 1.95 (t, J = 2.7 Hz, 1H), 1.80 – 1.72 (m, 4H), 1.28 – 1.17 (m, 2H (overlap with EtOAc)), 1.09 – 1.04 (m, 12H), 0.88 – 0.83 (m, 2H). **^{13}C NMR** (125.7 MHz, $CDCl_3$): 137.9, 135.4, 129.1, 128.4, 123.4, 83.7, 69.0, 67.6, 49.3, 23.5, 20.4, 18.2, 18.1, 17.8, 10.6, 4.7. **HRMS** (ESI^+): calculated for $[C_{22}H_{33}NO_3Si+Na]^+$ required *m/z* 410.2122, found *m/z* 410.2126.

Synthesis of acyl silane (+)-JQ1 probes



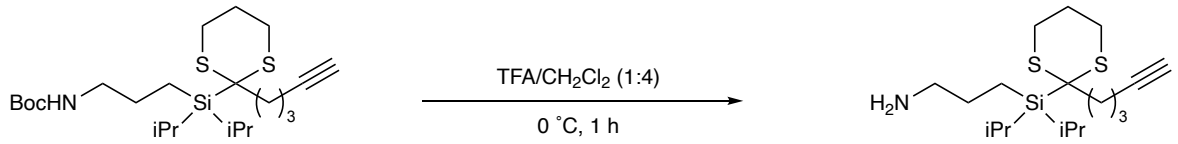
12c **SI-2**

SI-1

***tert*-butyl (3-(diisopropyl(2-(pent-4-yn-1-yl)-1,3-dithian-2-yl)silyl)propyl)carbamate (SI-2):** A 10 mL flame dried round bottom flask cooled under vacuum was charged with **13c** (100 mg, 0.280 mmol, 1 equiv.), N-boc-2-nitrobenzenesulfonamide (**SI-1**, 100 mg, 0.32 mmol, 1.15 equiv., prepared according to Fukumaya, T.; Cheung, M.; Kan, T. *Synlett* **1999**, 1301–1303), triphenyl phosphine (84 mg, 0.32 mmol, 1.15 equiv.), and DIAD (63 µL, 0.32 mmol, 1.15 equiv.) in THF (0.1 M). The mixture was stirred for 16 h before the addition of thiophenol (60 µL, 0.588 mmol, 2.1 equiv.) and Cs_2CO_3 (340 mg, 1.05 mmol, 3.75 equiv.). The reaction was heated to 50 ˚C and vigorously stirred for 4 h before cooling to room temperature. The reaction was quenched by the addition of 5 mL 0.5 M NaOH (5 mL) and extracted with Et_2O (3 x 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ before concentrating to an oil. Purification of the crude product by flash chromatography by gradient elution of 9:1 to 8:2 hex:EtOAc yield the *N*-Boc protected amine (115 mg, 91% yield). The product appears faintly on TLC under UV, but presents as a significant dark band upon heating in *p*-anisaldehyde stain.

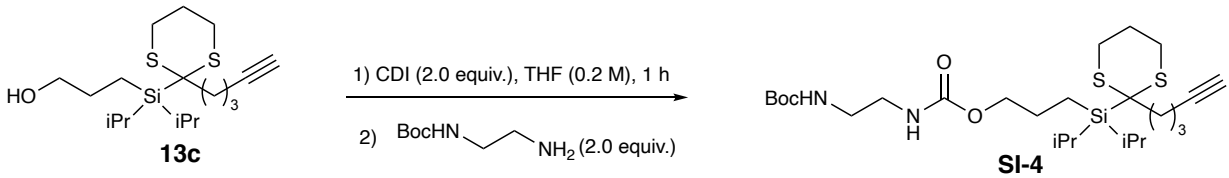
^{1}H NMR: (500.0 MHz, $CDCl_3$) δ 4.64 (bs, 1H), 3.10 (apparent t, J = 13.2 Hz, 2H) 2.45 – 2.41 (m, 2H), 2.38 (dt, J = 14.3, 3.74 Hz, 2H,), 2.28 (td, J = 6.7, 2.6 Hz, 2H), 2.06 – 2.02 (m, 1H), 2.34 (t, J = 2.34 Hz, 1H), 1.96–1.88 (m, 1H), 1.81 – 1.75 (m, 2H), 1.74 – 1.67 (m, 2H), 1.44 (s, 9H), 1.34 (hept, J = 7.4 Hz, 1H) 1.17 (d, J = 7.4 Hz, 6H), 1.16 (d, J = 7.6 Hz, 6H), 0.83

– 0.79 (m, 2H). **^{13}C NMR** (125.7 MHz, $CDCl_3$) δ 156.1, 84.3, 79.0, 69.1, 44.1, 40.3, 37.3, 28.6, 27.0, 25.1, 23.9, 19.8, 19.7, 18.9, 12.3, 7.5. **HRMS** (ESI^+) calculated for $[C_{23}H_{43}NO_2S_2Si+H]^+$ required *m/z* 458.2577, found *m/z* 458.2609.



SI-3 **SI-4**

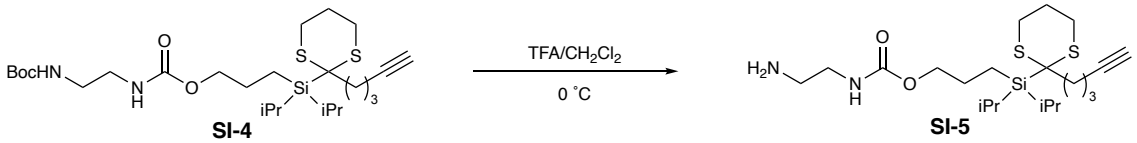
Amine linker SI-4: N-Boc protected amine **SI-3** (91 mg, 0.200 mmol, 1 equiv.) was dissolved in DCM (1 mL, 0.2 M) and cooled to 4 °C before adding TFA (0.25 mL). After 1 h, the reaction was complete by TLC and concentrated, diluted with Et_2O and washed with 1 N NaOH. The organic layer was concentrated to a yellow oil and immediately used in the next reaction without further purification (crude mass 70 mg, crude yield 98%).



13c **SI-4**

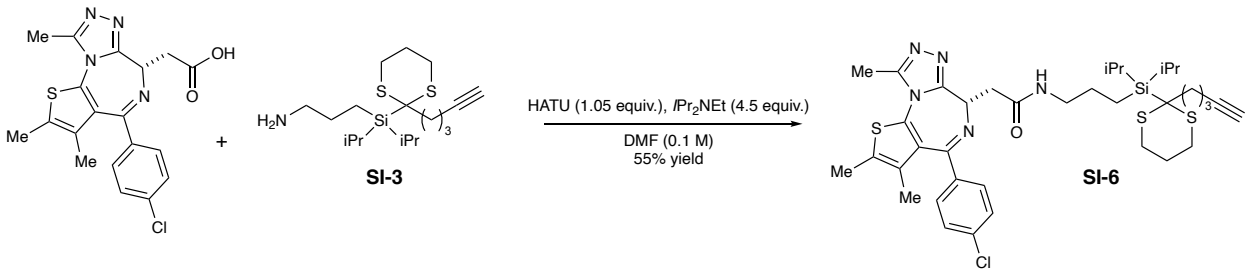
N-Boc protected amine linker SI-4: A 1 dram vial was charged with **13c** (50 mg, 0.140 mmol, 1.0 equiv.), THF (0.7 mL, 0.2 M), and CDI (45 mg, 0.280 mmol, 2.0 equiv) and stirred at ambient temperature for 1 h. Subsequently, N-boc-ethylenediamine (67 mg, 0.420 mmol, 3.0 equiv.) and DMAP (51 mg, 0.420 mmol, 3.0 equiv.) were added. The reaction was stirred overnight before diluting with water and extracting the mixture with EtOAc. The organic extract was washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography of EtOAc in hexanes to yield **SI-4** (67 mg, 88% yield).

^{1}H NMR (500.0 MHz, $CDCl_3$) δ 5.11 (s, 1H), 4.93 (s, 1H), 4.00 (t, *J* = 6.1 Hz, 2H) 3.26 – 3.24 (m, 4H), 3.09 (td, *J* = 14.9, 12.8, 2.7 Hz, 2H), 2.45 – 2.40 (m, 2H) 2.38 (dt, *J* = 14.2, 3.7 Hz, 2H), 2.28 (td, *J* = 6.7, 2.7 Hz, 2H), 2.05 – 2.00 (m, 2H), 1.95–1.76 (m, 5H), 1.42 (s, 9H), 1.35 (hept, *J* = 7.4 Hz, 2H), 1.17 (d, *J* = 7.5 Hz, 6H), 1.16 (d, *J* = 7.6 Hz, 6H), 0.88 – 0.77 (m, 2H). **^{13}C NMR** (125.7 MHz, $CDCl_3$) δ 157.2, 156.5, 84.3, 79.6, 69.1, 67.9, 41.4, 40.8, 40.3, 37.3, 28.5, 27.0, 25.0, 24.4, 23.9, 19.8, 19.7, 18.9, 12.3, 6.3. **HRMS** (ESI^+) calculated for $[C_{26}H_{48}O_4S_2Si+Na]^+$ required *m/z* 567.2717, found *m/z* 567.2718.



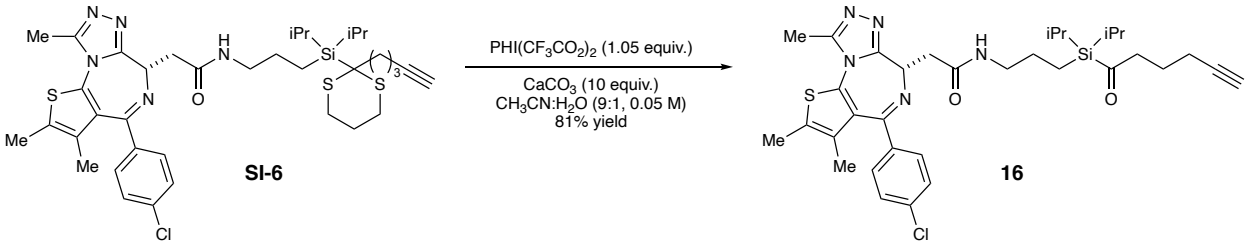
SI-4 **SI-5**

Amine linker SI-5: A 1 dram vial was charged with **SI-4** (67 mg, 0.123 mmol) and DCM (1.4 mL, 0.09 M) and cooled in an ice bath. Subsequently, TFA (0.11 mL, 1.4 mmol, 11.3 equiv.) was added and stirred until complete by TLC. The reaction was concentrated, diluted with Et_2O and washed with 1 N NaOH. The organic layer was concentrated to a 84 mg of a yellow oil and immediately used in the next reaction without further purification.



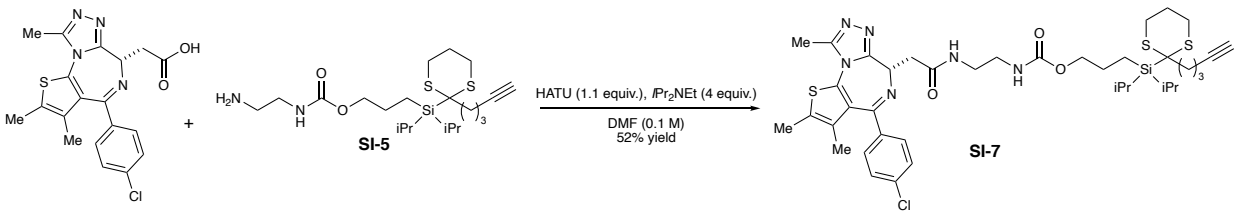
Acyl silane dithiane precursor to 16 (SI-6): To a solution of (+)-JQ1-OH (50 mg, 0.125 mmol, 1.0 equiv.) in a 2 dram vial was added DMF (1.25 mL, 0.1 M), HATU (50 mg, 0.131 mmol, 1.05 equiv.), and *i*-PrNEt$_2$ (65 µL, 0.575 mmol, 4.5 equiv.). After 10 min, freshly prepared **SI-3** was added (46 mg, 0.138 mmol, 1.05 equiv.) and the reaction was allowed to stir for 16 h before removing the DMF *in vacuo* and purifying by silica gel chromatography using a gradient elution of 99.5:0.05-96:4 DCM/MeOH. The product was isolated as a white solid (50 mg, 55% yield).

^{1}H NMR (500.0 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.5 Hz, 2H), 7.31 (d, *J* = 8.7 Hz, 2H), 6.70 (t, *J* = 5.7 Hz, 1H), 4.61 (t, *J* = 6.8 Hz, 1H), 3.71 (hept, *J* = 6.7 Hz, 1H), 3.51 (dd, *J* = 14.4, 6.9 Hz, 1H), 3.37 – 3.29 (m, 2H), 3.25 – 3.14 (m, 2H), 3.08 (ddd, *J* = 15.2, 12.8, 2.7 Hz, 2H), 2.65 (s, 3H), 2.45 – 2.40 (m, 2H), 2.38 (s, 4H), 2.35 (dt, *J* = 14.0, 3.8 Hz, 2H), 2.27 (td, *J* = 6.7, 2.7 Hz, 2H), 2.03 – 1.99 (m, 1H), 2.01 (s, *J* = 2.6 Hz, 1 H), 1.98 – 1.86 (m, 1H), 1.82 – 1.72 (m, 4H), 1.36 – 1.29 (m, 1H), 1.18 – 1.10 (m, 12H), 0.84 – 0.78 (m, 2H). **^{13}C NMR** (125.7 MHz, $CDCl_3$) δ 170.4, 164.0, 155.8, 150.0, 136.8, 136.7, 132.2, 131.0, 130.5, 129.9, 128.8, 84.3, 69.1, 54.5, 43.7, 43.3, 40.3, 39.4, 37.2, 26.9, 25.0, 24.8, 23.9, 19.8, 19.8, 19.7, 18.8, 14.4, 13.2, 12.22, 12.21, 11.9, 7.7. **HRMS** (ESI$^+$) calculated for $[C_{37}H_{51}N_5OClS_3Si+H]^+$ required *m/z* 740.2714, found *m/z* 740.2708.



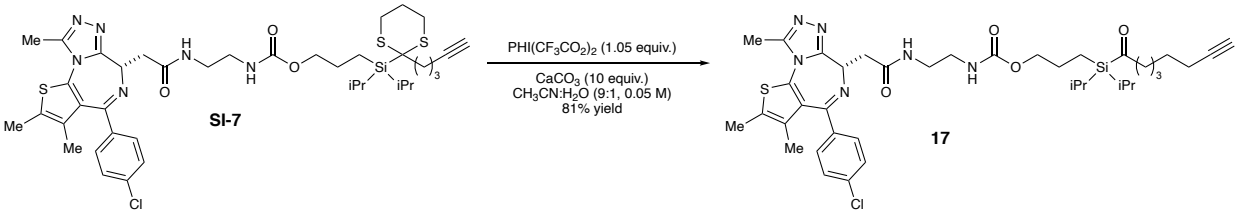
Acyl silane 16: To a solution of **SI-6** (48 mg, 0.0649 mmol, 1 equiv.) and $CaCO_3$ (64.9 mg, 0.649 mmol, 10 equiv.) in CH_3CN:H_2O (9:1, 0.05 M, 1.4 mL) cooled in an ice bath to 4 °C was added PIFA (29.3 mg, 0.0681 mmol, 1.05 equiv.) dropwise in CH_3CN (0.1 mL). The solution was stirred for 30 min in the ice bath before dilution with EtOAc. The resulting mixture was washed with sat. aqueous $NaHCO_3$, brine, and dried over $MgSO_4$ before concentrating *in vacuo.* The crude material was purified by flash column chromatography using a gradient elution of 99.5:0.05–96:4 DCM/MeOH to give **16** as a white solid (34 mg, 81% yield).

^{1}H NMR (500.0 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.3 Hz, 2H), 7.26 (d, *J* = 8.6 Hz, 2H), 6.76 (t, *J* = 6.0 Hz, 1H), 4.57 (t, *J* = 6.9 Hz, 1H), 3.50 (dd, *J* = 14.3, 7.5 Hz, 1H), 3.29 (dd, *J* = 14.4, 6.3 Hz, 1H), 3.24 (p, *J* = 6.6 Hz, 1H), 3.19 (p, *J* = 6.6 Hz, 1H), 2.64 (t, *J* = 7.0 Hz, 2H), 2.60 (s, 3H), 2.33 (s, 3H), 2.12 (td, *J* = 6.9, 2.6 Hz, 2H), 1.90 (t, *J* = 2.6 Hz, 1H), 1.67 (p, *J* = 6.9 Hz, 2H), 1.60 (s, 3H), 1.59–1.49 (m, 2H), 1.11 (hept, *J* = 7.3 Hz, 2H), 1.00 – 0.92 (m, 12H), 0.74 – 0.68 (m, 2H). **^{13}C NMR** (125.7 MHz, $CDCl_3$) δ 246.6, 170.2, 164.7, 155.4, 150.2, 137.5, 135.9, 132.2, 131.7, 131.3, 130.5, 130.2, 128.9, 84.0, 69.1, 54.3, 49.5, 43.0, 38.8, 24.1, 20.6, 18.3, 18.2, 17.9, 14.5, 13.3, 11.8, 10.7, 5.9. **HRMS** (ESI$^+$) calculated for $[C_{34}H_{45}N_5O_2ClSSi+H]^+$ required *m/z* 650.2752, found *m/z* 650.2744.



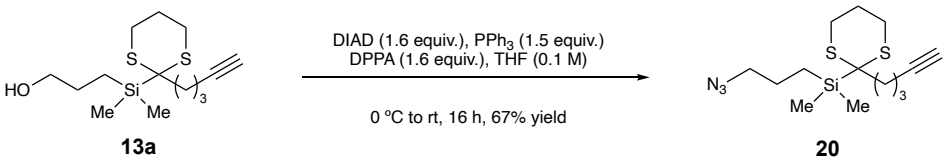
Acyl silane dithiane precursor to 17 SI-7: To a solution of (+)-JQ1-OH (30 mg, 0.075 mmol, 1.0 equiv.) in a 2 dram vial was added DMF (0.75 mL, 0.1 M), HATU (31 mg, 0.0825 mmol, 1.1 equiv.), and *i*-PrNEt$_2$ (52 µL, 0.30 mmol, 4.0 equiv.). After 10 min, freshly prepared **SI-5** was added (36 mg, 0.0825 mmol, 1.1 equiv.) and the reaction was allowed to stir for 16 h before removing the DMF *in vacuo* and purifying by silica gel chromatography using a gradient elution of 99.5:0.05 – 96:4 DCM/MeOH. The product was isolated as a white solid (32 mg, 52% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (br. s, 1H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.6 Hz, 2H), 6.03 (m, 1H), 4.69 (t, *J* = 7.0 Hz, 1H), 4.00 – 3.93 (m, 1H), 3.58 (dd, *J* = 14.7, 7.7 Hz, 1H), 3.54 – 3.46 (m, 1H), 3.43 (dd, *J* = 14.6, 5.9, Hz, 1H), 3.40–3.25 (m, 3H), 3.08 (d, *J* = 13.1 Hz, 2H), 2.69 (s, 3H), 2.44 – 2.36 (m, 2H), 2.40 (s, 3H), 2.30 – 2.22 (m, 2H), 2.06 – 1.99 (m, 2H), 1.97 – 1.89 (m, 1H), 1.88 – 1.73 (m, 4H), 1.67 (s, 3H), 1.35 (hept, *J* = 7.3 Hz, 2H), 1.20 – 1.14 (m, 12H), 0.85 – 0.78 (m, 2H). **^{13}C NMR** (125.7 MHz, $CDCl_3$) δ 171.2, 164.1, 157.2, 155.9, 150.1, 136.9, 136.6, 132.1, 131.1, 131.0, 130.7, 130.0, 128.9, 84.3, 69.1, 67.9, 54.4, 53.6, 41.2, 40.3, 39.9, 39.0, 37.3, 26.9, 25.1, 24.5, 23.9, 19.8, 19.7, 18.9, 14.5, 13.2, 12.3, 11.9, 6.2. **HRMS** (ESI$^+$) calculated for $[C_{40}H_{44}N_6O_3ClS_3Si+H]^+$ required *m/z* 827.3034, found *m/z* 827.3034.



Acyl silane 17: To a solution of **SI-7** (32 mg, 0.0387 mmol, 1 equiv.) and $CaCO_3$ (38.7 mg, 0.387 mmol, 10 equiv.) in CH_3CN:H_2O (9:1, 0.05 M, 0.8 mL) cooled in an ice bath to 4 °C was added PIFA (17.5 mg, 0.0407 mmol, 1.05 equiv.) dropwise in CH_3CN (0.1 mL). The solution was stirred for 30 min in the ice bath before dilution with EtOAc. The resulting mixture was washed with sat. aqueous $NaHCO_3$, brine, and dried over $MgSO_4$ before concentrating *in vacuo*. The crude material was purified by flash column chromatography using a gradient elution of 99.5:0.05–96:4 DCM/MeOH to give **17** as a white solid (23 mg, 81% yield).

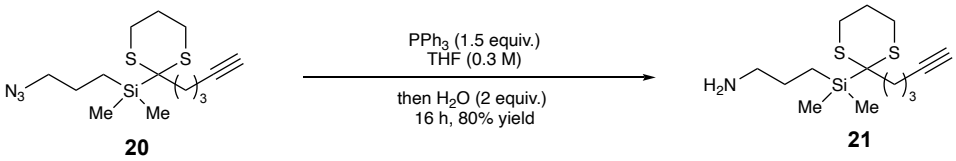
^{1}H NMR (500.0 MHz, $CDCl_3$) δ 7.59 (t, *J* = 5.6 Hz, 1H), 7.39 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 5.91 (t, *J* = 5.5 Hz, 1H), 4.70 (t, *J* = 7.1 Hz, 1H), 4.03 – 3.97 (m, 2H), 3.59 (dd, *J* = 14.7, 7.7 Hz, 1H), 3.52 – 3.46 (m, 1H), 3.43 (dd, *J* = 14.7, 6.5 Hz, 1H), 3.40 – 3.25 (m, 3H), 2.71 (t, *J* = 7.0 Hz, 2H), 2.69 (s, 3H), 2.41 (s, 3H), 2.19 (td, *J* = 6.9, 2.6 Hz, 2H), 1.96 (t, *J* = 2.6 Hz, 1H), 1.73 (p, *J* = 6.9 Hz, 2H), 1.67 (s, 3H), 1.20 (m, 1H), 1.05 (d, *J* = 4.8 Hz, 7H), 1.03 (d, *J* = 4.9 Hz, 6H), 0.82 – 0.75 (m, 2H). **^{13}C NMR** (125.7 MHz, $CDCl_3$) δ 246.6, 170.8, 165.1, 157.1, 155.3, 150.3, 137.7, 135.5, 132.5, 131.8, 130.4, 128.9, 84.0, 69.1, 67.4, 54.1, 49.5, 41.1, 40.0, 38.4, 23.7, 20.6, 18.3, 18.2, 17.9, 14.6, 13.3, 11.9, 10.7, 4.6. **HRMS** (ESI$^+$) calculated for $[C_{37}H_{49}N_6O_4ClSSi+H]^+$ required *m/z* 737.3072, found *m/z* 737.3075.



(3-azidopropyl)dimethyl(2-(pent-4-yn-1-yl)-1,3-dithian-2-yl)silane (20): To a solution of triphenylphosphine (0.393 g, 1.5 mmol, 1.5 equiv.) in THF (6 mL) at 0 °C was added DIAD (0.316 mL, 1.6 mmol, 1.6 equiv.). After stirring for 10 minutes,

alcohol **13a** (0.302 g, 1.00 mmol, 1.0 equiv.) was added to the cloudy white suspension and allowed to stir at 0 °C for 30 minutes, at which point diphenylphosphoylazide (0.346 mL, 1.6 mmol, 1.6 equiv.) was added dropwise and the reaction was allowed to stir overnight. After 16h, the reaction was quenched by addition of H_2O, extracted thrice with EtOAc, and concentrated to an oil. The crude residue was purified by flash column chromatography (hex:EtOAc = 93:7) to give **20** (220 mg, 67% yield) as a clear oil which contained 92% product by mass.

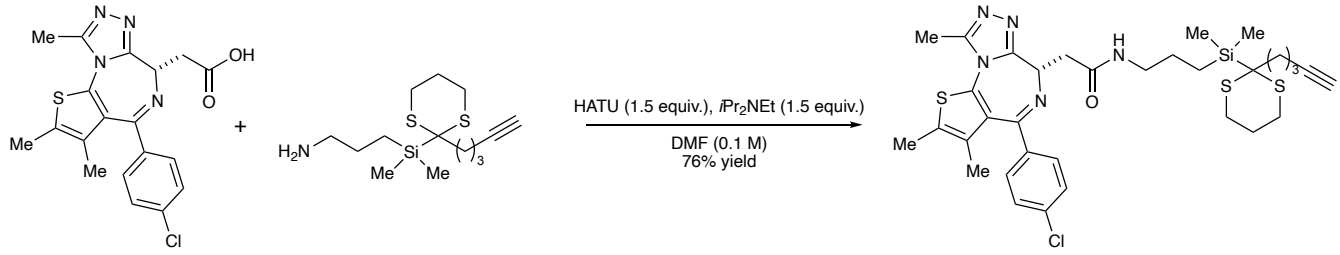
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.26 (td, *J* = 7.0, 1.4 Hz, 2H), 3.11 – 3.01 (m, 2H), 2.48 – 2.39 (m, 2H), 2.38 – 2.29 (m, 2H), 2.05 (dddt, *J* = 12.9, 4.5, 3.0, 1.5 Hz, 1H), 1.99 (td, *J* = 2.6, 1.1 Hz, 1H), 1.96 – 1.83 (m, 1H), 1.76 – 1.64 (m, 4H), 0.85 – 0.76 (m, 2H), 0.19 (d, *J* = 1.4 Hz, 6H). **^{13}C NMR** (125.7 MHz, $CDCl_3$): δ 84.17, 68.85, 54.43, 38.46, 36.38, 26.59, 25.06, 23.89, 23.35, 18.79, 11.07, -4.37. **HRMS** (EI^+) calculated for $[C_{37}H_{49}N_6O_4ClSSi+H]^+$ required *m/z* 327.1259, found *m/z* 327.1259.



20 **21**

3-(dimethyl(2-(pent-4-yn-1-yl)-1,3-dithian-2-yl)silyl)propan-1-amine (21) To a solution of **20** (110 mg, 0.336 mmol, 1.0 equiv.) in THF (1 mL) cooled to 0 °C was added triphenylphosphine (132 mg, 0.505 mmol, 1.5 equiv.) and the mixture was allowed to stir for 1 h at room temperature before adding H_2O (10 uL, 0.672 mmol, 2.0 equiv.) and the reaction was allowed to stir for 16 h. The mixture was concentrated and purified by flash column chromatography using a gradient elution of 98:2 to 8:2 DCM/MeOH to give **21** (88 mg, 80% yield) as a clear oil.

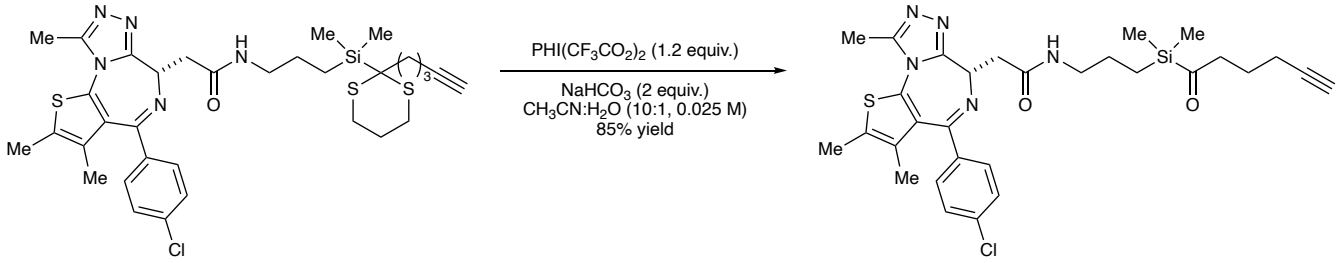
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.06 (ddd, *J* = 14.8, 12.6, 2.7 Hz, 2H), 2.76 – 2.70 (m, 2H), 2.43 (dt, *J* = 14.2, 3.8 Hz, 2H), 2.38 – 2.32 (m, 2H), 2.26 (td, *J* = 6.7, 2.7 Hz, 5H), 2.10 – 2.01 (m, 1H), 1.99 (t, *J* = 2.6 Hz, 1H), 1.90 (qt, *J* = 13.0, 3.4 Hz, 1H), 1.71 (dq, *J* = 11.8, 6.9 Hz, 2H), 1.54 (ddd, *J* = 16.6, 11.1, 5.9 Hz, 2H), 0.80 – 0.73 (m, 2H), 0.18 (s, 6H). **^{13}C NMR** (125.7 MHz, $CDCl_3$) : δ 84.24, 68.83, 45.09, 38.60, 36.34, 27.49, 26.59, 25.10, 23.33, 18.80, 10.68, -4.37. **HRMS** (ESI^+) calculated for $[C_{14}H_{27}NS_2Si+H]^+$ required *m/z* 302.1247, found *m/z* 302.1243.



Dithiane precursor to acylsilane 16Me SI-8. To a solution of (+)-JQ1-OH (26 mg, 0.0625 mmol, 1.0 equiv.) in a 2 dram vial was added DMF (0.625 mL, 0.1 M), HATU (35.6 mg, 0.0938 mmol, 1.5 equiv.), and *i*-$PrNEt_2$ (16 µL, 0.0938 mmol, 1.5 equiv.). After 10 min, **21** was added (19.7 mg, 0.0656 mmol, 1.05 equiv.) and the reaction was allowed to stir for 16 h before removing the DMF *in vacuo* and purifying by silica gel chromatography using a gradient elution of 99:1 – 96:4 DCM/MeOH. The product was isolated as a white solid (33 mg, 76% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 (dd, *J* = 8.7, 3.6 Hz, 2H), 7.32 (d, *J* = 8.6 Hz, 2H), 6.57 (t, *J* = 5.8 Hz, 1H), 4.62 (t, *J* = 6.9 Hz, 1H), 3.71 (pd, *J* = 6.7, 4.1 Hz, 1H), 3.56 – 3.49 (m, 1H), 3.33 (dt, *J* = 13.1, 6.5 Hz, 2H), 3.22 (dt, *J* = 12.7, 6.3 Hz, 1H), 3.17 (qd, *J* = 7.4, 4.2 Hz, 1H), 3.09 – 3.01 (m, 2H), 2.66 (s, 3H), 2.45 – 2.40 (m, 2H), 2.39 (s, 3H), 2.37 – 2.30 (m, 2H), 2.26 (td, *J* = 6.7, 2.7 Hz, 2H), 2.08 – 2.04 (m, 1H), 2.01 (t, *J* = 2.6 Hz, 1H), 1.90 (qt, *J* = 12.7, 3.3 Hz, 1H), 1.74 – 1.67 (m, 2H), 1.66 (s, 3H), 1.65 – 1.57 (m, 2H), 1.44 (d, *J* = 6.6 Hz, 2H), 1.41 (d, *J* = 6.6 Hz, 2H), 0.80 – 0.72 (m, 2H), 0.17 (d, *J* = 1.6 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 170.48, 164.06, 155.80, 150.02, 136.94, 136.73, 132.25, 131.07, 131.01, 130.61, 129.96, 128.87, 84.35, 69.02, 55.63, 54.60, 43.62, 42.91, 39.52, 38.70, 36.47, 28.29, 26.70, 25.20, 24.44, 23.46, 18.90, 18.72, 17.33,

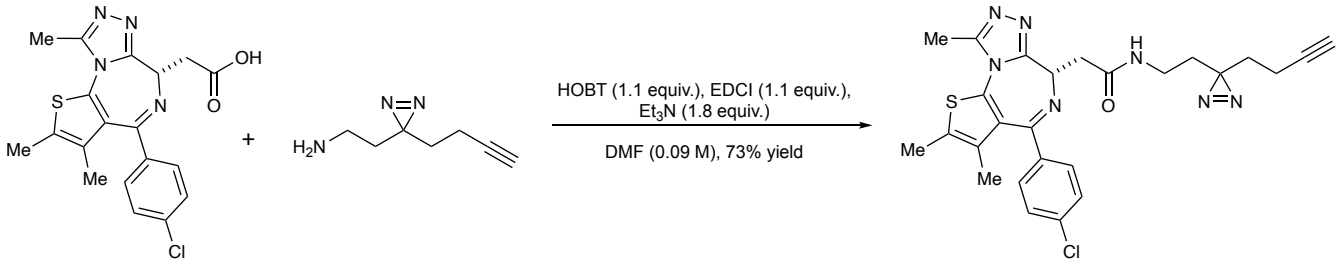
14.50, 13.21, 12.63, 11.94, 11.16, -4.21 (2 extraneous peaks). **HRMS** (ESI$^+$): calculated for $[C_{33}H_{42}ClN_5OS_3Si+H]^+$ required *m/z* 684.2082, found *m/z* 684.2094.



Acyl silane 16Me. To a solution of **SI-8** (5 mg, 0.00714 mmol, 1.0 equiv.) and $NaHCO_3$ (1.2 mg, 0.0413 mmol, 2.0 equiv.) in a solution of MeCN:H_2O (0.025 M, 270 uL:30 uL) was added PIFA (3.7 mg, 0.00857 mmol, 1.2 equiv.) and the resulting yellow solution was allowed to stir for 30 minutes, at which point the solvent was removed in vacuo and the residue was purified by flash column chromatography using a gradient elution of 99:1 to 97:3 DCM:MeOH to give **16Me** (3.7 mg, 85% yield) as a white powder.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.5 Hz, 2H), 7.33 (d, *J* = 8.7 Hz, 2H), 6.62 (t, *J* = 6.0 Hz, 1H), 4.60 (dd, *J* = 7.9, 6.1 Hz, 1H), 3.57 (dd, *J* = 14.1, 8.0 Hz, 1H), 3.36 – 3.19 (m, 3H), 2.74 (t, *J* = 7.1 Hz, 2H), 2.67 (s, 3H), 2.40 (s, 3H), 2.19 (td, *J* = 6.9, 2.7 Hz, 2H), 1.97 (t, *J* = 2.6 Hz, 1H), 1.74 (p, *J* = 7.0 Hz, 2H), 1.57 – 1.48 (m, 2H), 0.72 – 0.65 (m, 2H), 0.19 (d, *J* = 4.6 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 247.08, 170.54, 164.04, 155.75, 150.02, 136.94, 136.71, 132.23, 131.03, 130.97, 130.61, 129.92, 128.86, 83.90, 69.13, 54.68, 47.27, 42.50, 39.66, 29.80, 23.84, 22.79?, 20.75, 17.89, 14.47, 13.19, 11.91, 10.71, -4.74. **HRMS** (ESI$^+$) calculated for $[C_{30}H_{36}ClN_5O_2SSi+H]^+$ required *m/z* 594.2121, found *m/z* 594.2127.

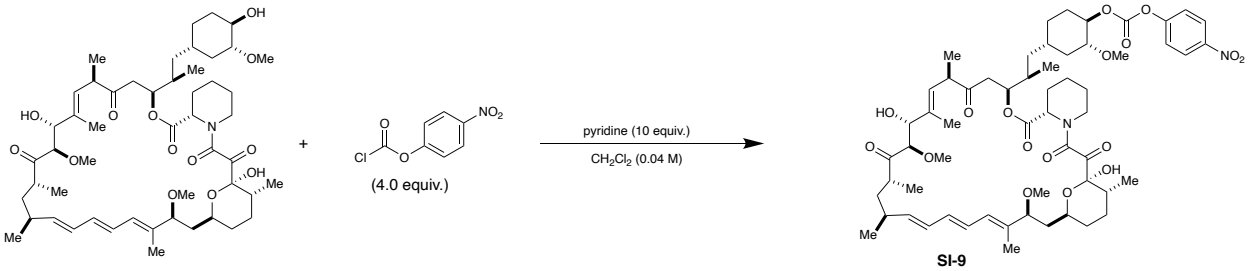
Synthesis of diazirine (+)-JQ1 probe



Diazirine 16-DA. To a solution of (+)-JQ1-OH (14.6 mg, 0.0365 mmol, 1.0 equiv.) in a 2 dram vial was added DMF (0.2 mL), HOBT (5.4 mg, 0.0402 mmol, 1.1 equiv.), EDCI (6.2 mg, 0.0402 mmol, 1.1 equiv.), and NEt_3 (9.1 mg, 0.0657 mmol, 1.8 equiv.). After 10 min, 2-(3-(but-3-yn-1-yl)-3*H*-diazirin-3-yl)ethan-1-amine (**SI-12**) was added (5.0 mg, 0.0365 mmol, 1.0 equiv.) in DMF (0.6 mL) and the reaction was allowed to stir for 12 h at which point the solution was diluted with H_2O extracted 5 times with EtOAc, and the combined organic layers were passed through a short silica plug with EtOAc and concentrated. The material was purified by silica gel chromatography using a gradient elution of 99:1-95:5 DCM:MeOH. The product was isolated as a white solid (13.7 mg, 73% yield).

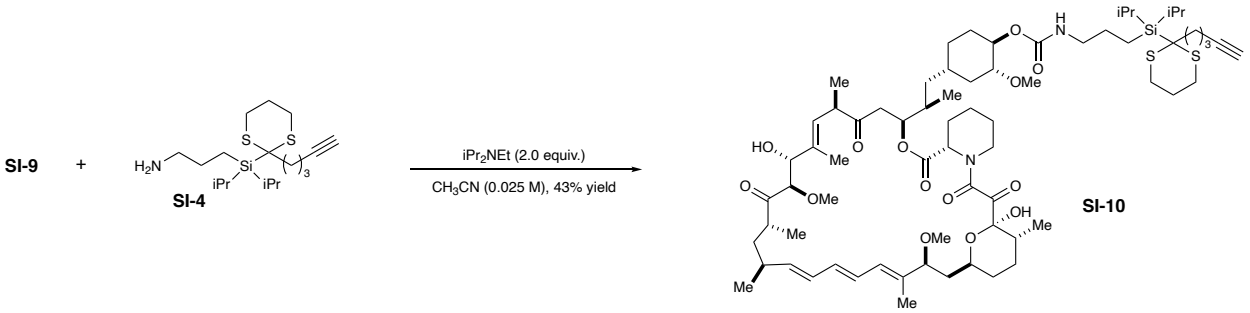
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.2 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 6.89 (t, *J* = 6.0 Hz, 1H), 4.63 (dd, *J* = 7.8, 6.0 Hz, 1H), 3.61 (dd, *J* = 14.3, 7.8 Hz, 1H), 3.37 (dd, *J* = 14.3, 6.1 Hz, 1H), 3.17 (ddt, *J* = 16.8, 13.9, 7.0 Hz, 2H), 2.68 (s, 3H), 2.41 (s, 3H), 2.05 – 1.95 (m, 3H), 1.68 (s, 3H), 1.72 – 1.58 (m, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.62, 164.15, 137.05, 136.55, 131.11, 131.09, 130.62, 130.00, 128.87, 82.86, 69.51, 54.58, 39.43, 34.57, 32.77, 32.14, 31.71, 26.89, 22.78, 14.52, 14.25, 13.36, 13.23, 11.93, 1.14. **HRMS** (ESI$^+$): calculated for $[C_{26}H_{26}ClN_7OS+Na]^+$: required *m/z* 542.1500, found *m/z* 542.1502.

Synthesis of rapamycin acyl silane probes



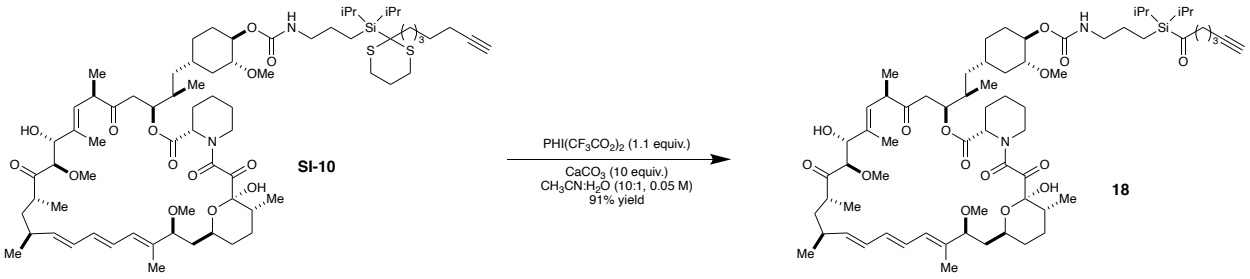
Rapamycin *p*-nitrophenyl carbonate (SI-9): A two-dram vial was charged with rapamycin (35 mg, 0.0385 mmol, 1.0 equiv.) and CH_2Cl_2 (1 mL) followed by pyridine (31 µL, 0.385 mmol, 10 equiv.). A solution of *p*-nitrophenylchloroformate (31 mg, 0.155 mmol, 4.0 equiv.) in CH_2Cl_2 (0.4 mL) was added dropwise. After complete addition, the reaction was stirred for 30 min before diluting with EtOAc and washing with 0.5 M HCl cooled in an ice bath. The organic layer was concentrated and the crude material was purified by flash column chromatography using a gradient of 99:1 to 96:4 DCM/MeOH. The product was isolated as a white crystalline solid (37 mg, 89% yield). For NMR data see Table **S1**.

HRMS (ESI^+) calculated for $[C_{58}H_{82}N_2O_{17}+Na]^+$ required *m/z* 1101.5511, found *m/z* 1101.5491.



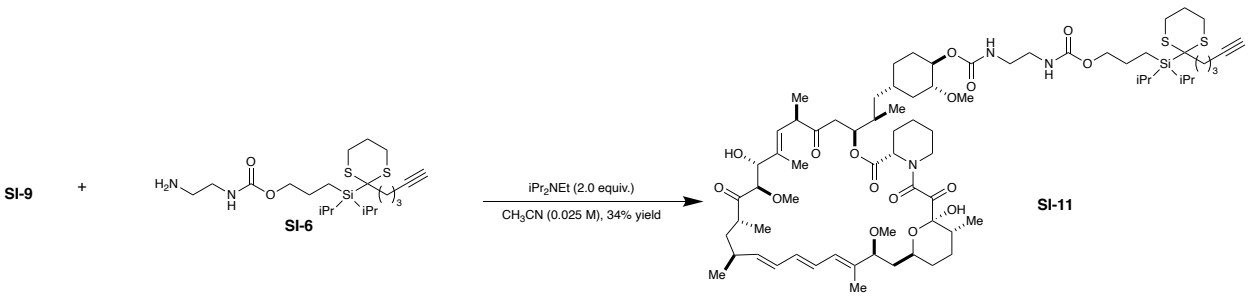
Dithiane rapamycin precursor (SI-10): A two-dram vial was charged with **SI-9** (32 mg, 0.0300 mmol, 1 equiv.), freshly prepared **SI-4** (14 mg, 0.0306 mmol, 1.3 equiv.), *i*-Pr_2NEt (10.4 µL, 0.0600 mmol, 2.0 equiv.) and CH_3CN (0.6 mL, 0.05 M). The reaction was stirred for 16 h before diluted with EtOAc. The solution was washed with 0.5 M HCl cooled in an ice bath and brine, before drying over $NaSO_4$ and concentrating *in vacuo*. The crude material was purified by flash column chromatography using a gradient of 99:1 to 96:4 CH_2Cl_2:MeOH. The product was isolated as a white solid (20 mg, 53% yield). For NMR data see Table **S1.**

HRMS (ESI^+) calculated for $[C_{70}H_{112}N_2O_{14}S_2Si+Na]^+$ required *m/z* 1319.7222, found *m/z* 1319.7217.



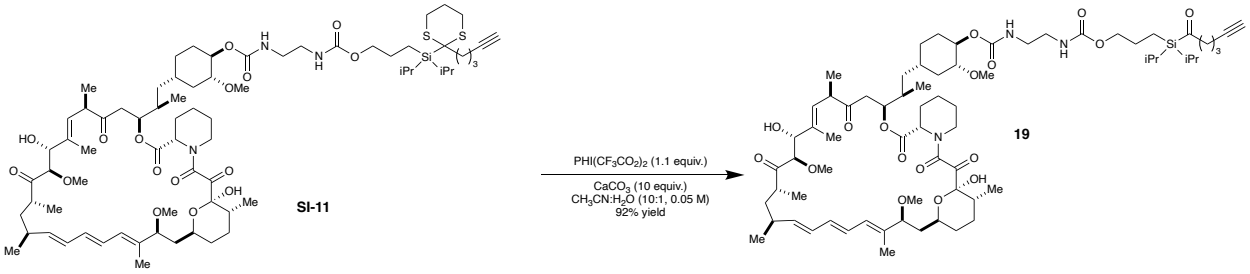
Rapamycin acyl silane (18): To a solution of **SI-10** (20 mg, 0.0154 mmol, 1 equiv.) and $CaCO_3$ (16 mg, 0.154 mmol, 10 equiv.) in CH_3CN:H_2O (9:1, 0.025 M, 0.62 mL) cooled in an ice bath to 4 °C was added PIFA (7.0 mg, 0.0163 mmol, 1.06 equiv.) dropwise in CH_3CN (0.1 mL). The solution was stirred for 30 min in the ice bath before dilution with EtOAc. The resulting mixture was washed with sat. aqueous $NaHCO_3$, brine, and dried over $MgSO_4$ before concentrating *in vacuo*. The crude material was purified by flash column chromatography using a gradient elution of 99:1-96:4 DCM/MeOH to give **18** as a white solid (17 mg, 91% yield). For NMR data see Table **S1.**

HRMS (ESI^+) calculated for $[C_{67}H_{106}N_2O_{15}Si+Na]^+$ required *m/z* 1229.7260, found *m/z* 1229.7241.



Dithiane rapamycin precursor (SI-11): A two-dram vial was charged with **SI-9** (50 mg, 0.0463 mmol, 1 equiv), freshly prepared **SI-6** (22.2 mg, 0.0510 mmol, 1.1 equiv.), *i*-Pr_2NEt (16.2 µL, 0.0930 mmol, 2.0 equiv.) and CH_3CN (1.85 mL, 0.025 M). The reaction was stirred for 16 h before diluted with EtOAc. The solution was washed with 0.5 M HCl cooled in an ice bath and brine, before drying over $NaSO_4$ and concentrating *in vacuo*. The crude material was purified by flash column chromatography using a gradient of 99:1 to 96:4 CH_2Cl_2:MeOH. The product was isolated as a white solid (22 mg, 34% yield). For NMR data see Table **S1.**

HRMS (ESI$^+$) calculated for $[C_{73}H_{117}N_3O_{16}S_2Si+Na]^+$ required *m/z* 1406.7542, found *m/z* 1406.7537.



Rapamycin acyl silane (19): To a solution of **SI-11** (22 mg, 0.0152 mmol, 1 equiv.) and $CaCO_3$ (15.2 mg, 0.152 mmol, 10 equiv.) in CH_3CN:H_2O (9:1, 0.05 M, 0.3 mL) cooled in an ice bath to 4 °C was added PIFA (6.8 mg, 0.0159 mmol, 1.05 equiv.) dropwise in CH_3CN (0.1 mL). The solution was stirred for 30 min in the ice bath before dilution with EtOAc. The resulting mixture was washed with sat. aqueous $NaHCO_3$, brine, and dried over $MgSO_4$ before concentrating *in vacuo*. The crude material was purified by flash column chromatography using a gradient elution of 99:1-96:4 DCM/MeOH to give **19** as a white solid (17 mg, 92% yield). For NMR data see Table **S1.**

HRMS (ESI$^+$) calculated for $[C_{71}H_{114}N_3O_{17}Si+Na]^+$ required *m/z* 1316.7580, found *m/z* 1316.7569.

References:

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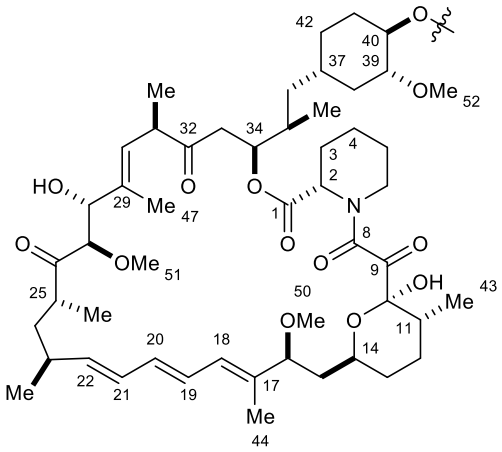
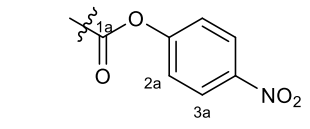
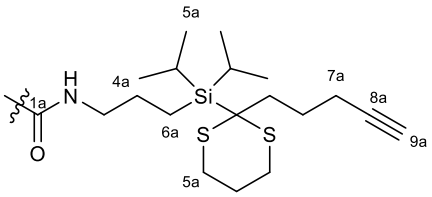
Table S1. Structural assignment for rapamycin probes:

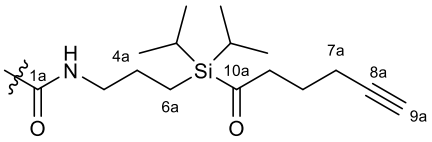




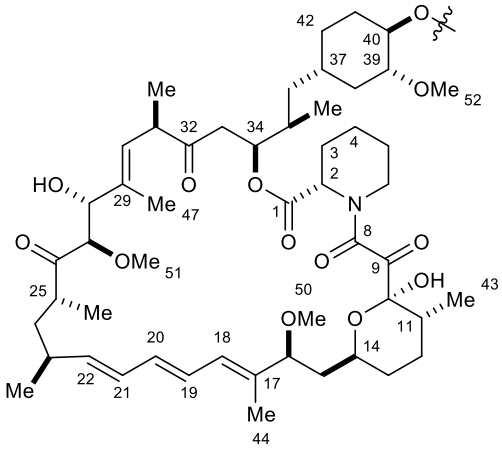
SI-9

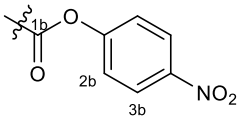


SI-10

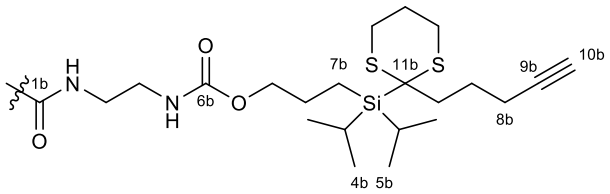


18

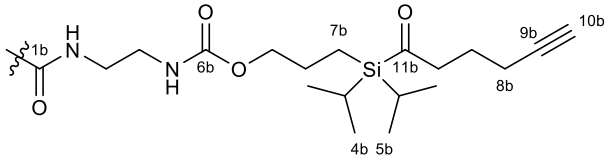




SI-9



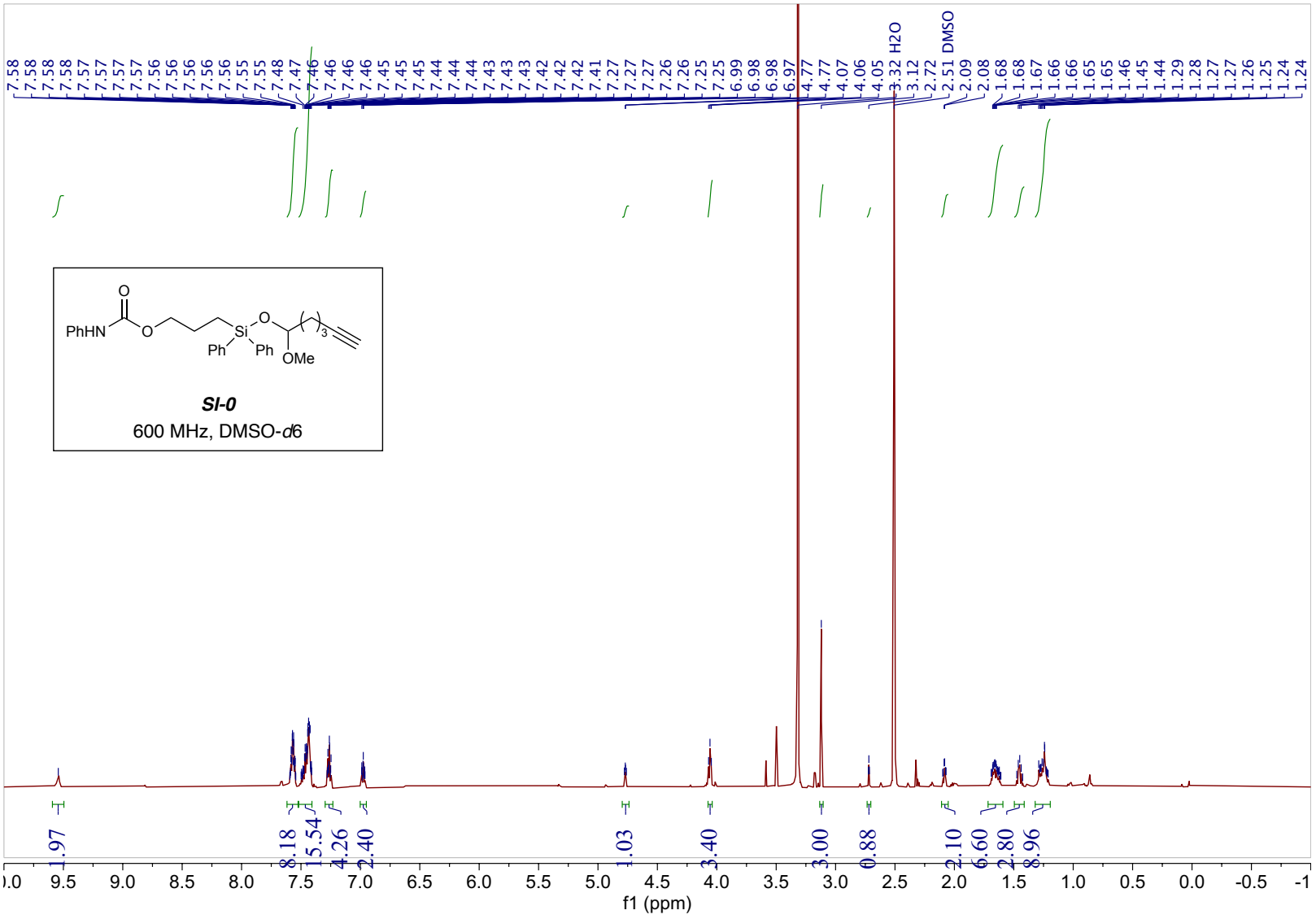
SI-11



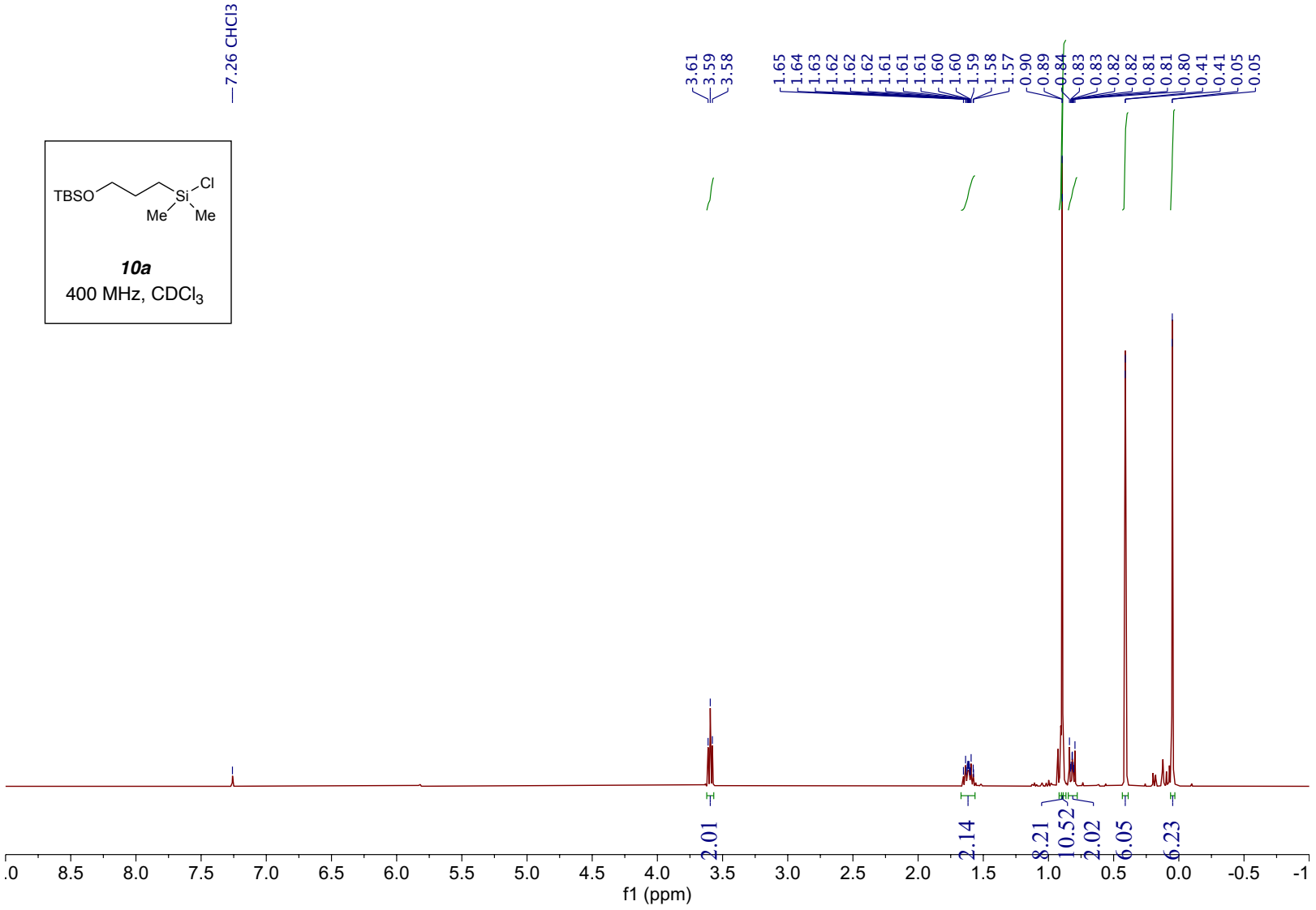
19

	SI-9		Dithiane precursor SI-10		Acyl silane 18	
Carbon #	Major Carbon (δ)	Major Proton (δ)	Major Carbon (δ)	Major Proton (δ)	Major Carbon (δ)	Major Proton (δ)
1	169.3		169.3		169.4	
2	51.3	5.26	51.4	5.27	51.4	5.28
3	27.0	2.32	27.2	2.32	27.2	2.35
4	20.7		20.8		20.8	
6		3.63, 3.54		3.65, 3.56		3.66, 3.57
8	166.8		166.9		166.9	
9	192.8		192.7		192.6	
10	98.5		98.6		98.6	
11	??	1.95				
14	67.2	3.86	67.3	3.86	67.3	3.86
15		1.85		1.85		1.85
16	84.3	3.65	84.3	3.68	84.5	3.68
17	135.9		135.7		135.7	
18	129.4	5.94	129.7	5.96	129.7	5.97
19		6.36		6.38		6.39
20	133.5	6.27	133.7	6.30	133.8	6.31
21	130.3	6.11	130.3	6.13	130.3	6.14
22	140.0	5.50	140.2	5.54	140.3	5.55
26	215.1		215.4		215.6	
27	84.7	3.74	84.9	3.74	84.9	3.74
28		4.17		4.18		4.18
29	136.1		136.1		136.2	
30		5.38		5.41		5.42
31	46.6		46.7		46.8	
32	208.2		208.4		208.4	
33						
34	75.7	5.17	75.6	5.16	75.6	5.17
40		3.27				
44		1.62		1.65		1.65
47		1.74		1.75		1.75
50	55.9	3.10	56.0	3.13	56.0	3.14
51	59.2	3.30	59.4	3.32	59.5	3.33
52		3.41		3.37		3.38
1a	155.7		156.3		156.3	
2a	125.3	7.34				
3a	121.8	8.26				
4a			19.8	1.16	18.3	1.06
5a			19.7	1.15	18.2	1.04
6a			7.5		5.7	0.78
7a				2.28		2.20
8a			69.1		69.1	
9a			84.4	2.02	84.0	1.96
10a					246.6	

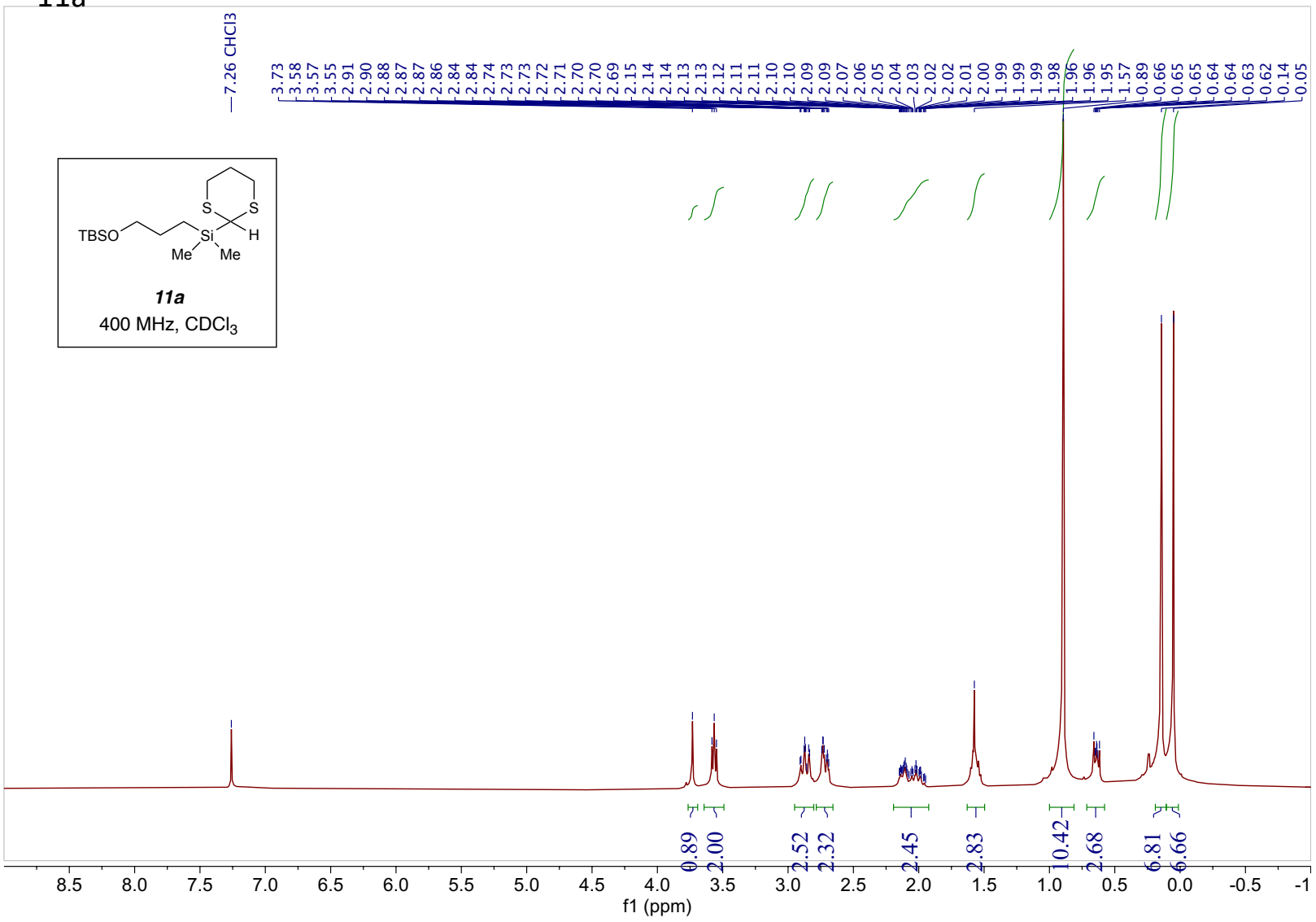
	SI-9		Dithiane precursor SI-11		Acyl silane 19	
Carbon #	Major Carbon (δ)	Major Proton (δ)	Major Carbon (δ)	Major Proton (δ)	Major Carbon (δ)	Major Proton (δ)
1	169.3		169.4		169.4	
2	51.3	5.26	51.4	5.27	51.4	5.28
3	27.0	2.32	27.2	2.32	27.2	2.35
4	20.7		20.8		20.8	
6		3.63, 3.54		3.66, 3.57		3.66, 3.57
8	166.8		166.9		166.9	
9	192.8		192.6		192.7	
10	98.5		98.6		98.6	
11		1.95				
14	67.2	3.86	67.3	3.86	67.3	3.86
15		1.83		1.85		1.85
16	84.3	3.65	84.5	3.68	84.5	3.68
17	135.9		135.7		135.7	
18	129.4	5.94	129.7	5.96	129.7	5.97
19		6.36		6.38		6.38
20	133.5	6.27	133.7	6.31	133.8	6.31
21	130.3	6.11	130.3	6.14	130.3	6.14
22	140.0	5.50	140.3	5.55	140.3	5.55
26	215.1		215.5		215.5	
27	84.7	3.74	84.9	3.73	84.9	3.73
28		4.17		4.18		4.19
29	136.1		136.2		136.2	
30		5.38		5.41		5.41
31	46.6		46.8		46.8	
32	208.2		208.4		208.4	
33						
34	75.4	5.17	75.6	5.16	75.6	5.17
40		3.27				
44		1.62		1.65		1.65
47		1.73		1.75		1.75
50	55.9	3.10	56.0	3.14	56.0	3.14
51	59.2	3.30	59.5	3.33	59.5	3.33
52		3.41		3.37		3.38
1b	155.7		156.7		156.7	
2b	125.3	7.34				
3b	121.8	8.26				
4b			19.8	1.18	18.3	1.05
5b			19.7	1.17	18.2	1.04
6b			157.3		157.2	
7b			6.4		4.7	0.78
8b				2.29		2.20
9b			69.1		69.1	
10b			84.3	2.02	84.0	1.96
11b					246.5	


PhHN
O
O
Si
O
Ph
Ph
OMe
3
SI-0
600 MHz, DMSO-d6
H2O
DMSO
f1 (ppm)

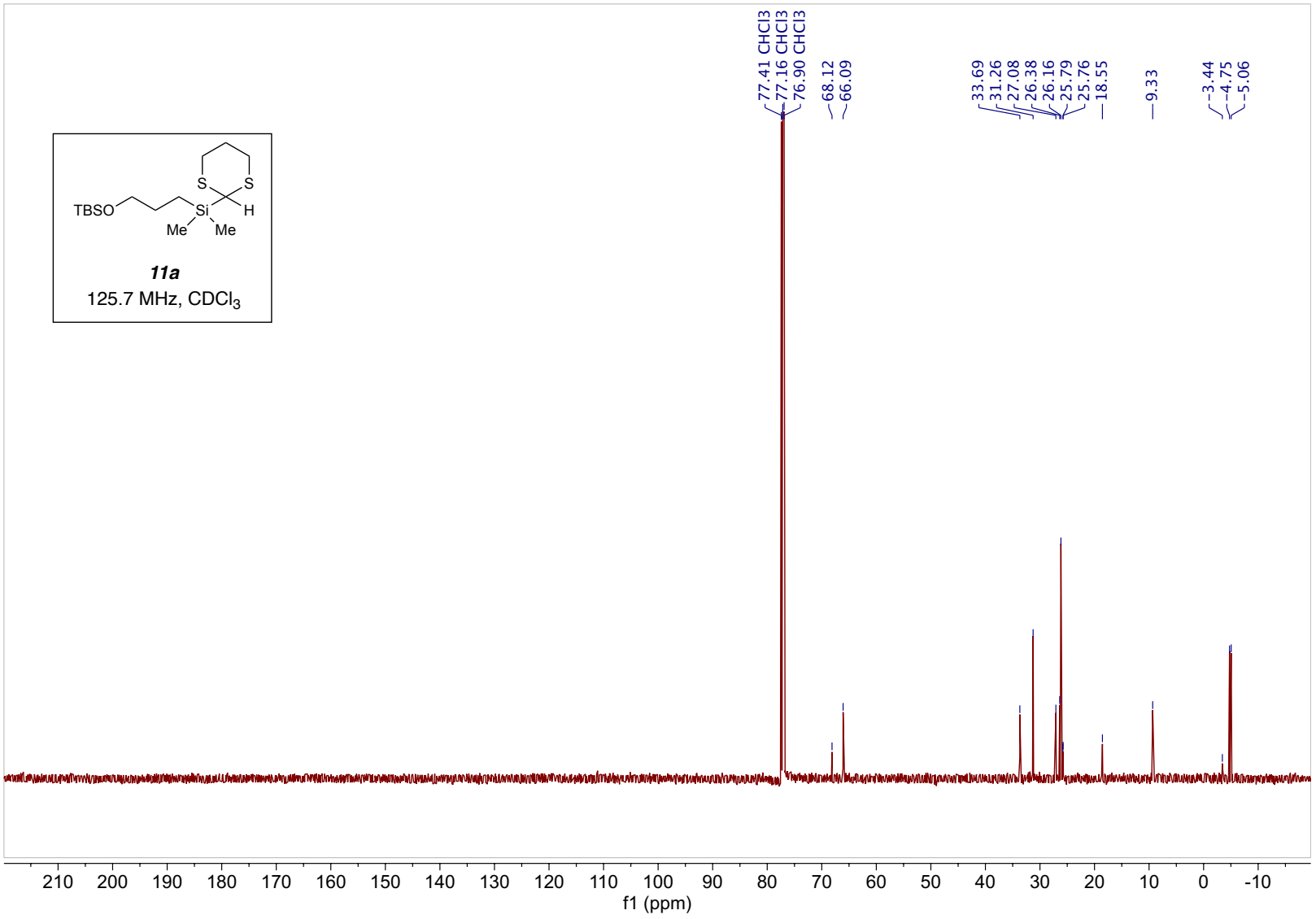
10a


7.26 CHCl3
3.61
3.59
3.58
1.65
1.64
1.63
1.62
1.62
1.62
1.61
1.61
1.61
1.60
1.60
1.59
1.58
1.57
0.90
0.89
0.84
0.83
0.83
0.82
0.82
0.81
0.81
0.80
0.41
0.41
0.05
0.05
TBSO
Si
Cl
Me
Me
10a
400 MHz, CDCl3
2.01
2.14
8.21
10.52
2.02
6.05
6.23
f1 (ppm)

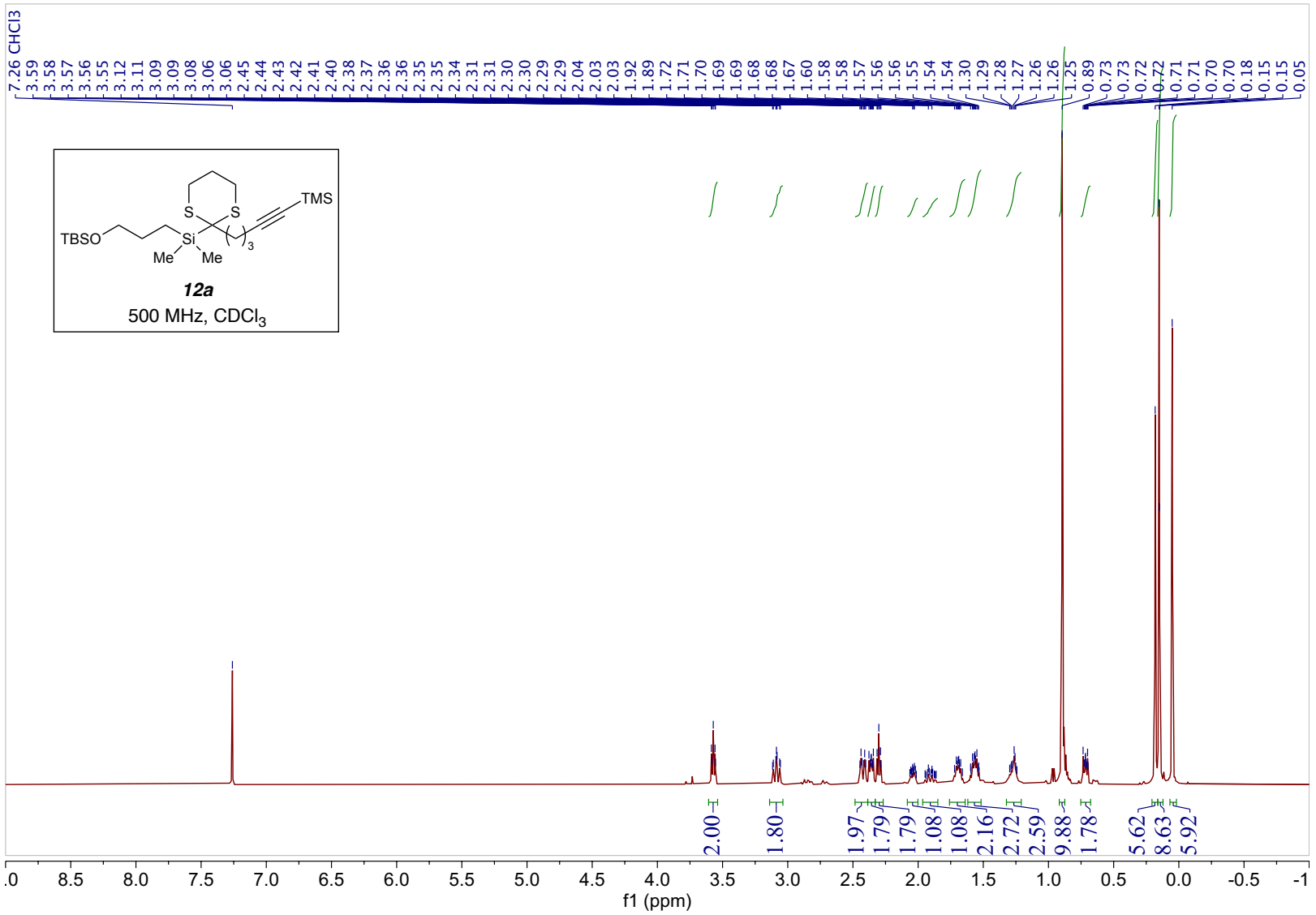
11a


7.26 CHCl3
3.73
3.58
3.57
3.55
2.91
2.90
2.88
2.87
2.87
2.86
2.84
2.84
2.74
2.73
2.73
2.72
2.71
2.70
2.70
2.69
2.15
2.14
2.14
2.13
2.13
2.12
2.11
2.11
2.10
2.10
2.09
2.09
2.07
2.06
2.05
2.04
2.03
2.02
2.02
2.01
2.00
1.99
1.99
1.99
1.98
1.96
1.96
1.95
1.57
0.89
0.66
0.65
0.65
0.64
0.64
0.63
0.62
0.14
0.05
TBSO
Si
S
S
H
Me
Me
11a
400 MHz, CDCl3
0.89
2.00
2.52
2.32
2.45
2.83
10.42
2.68
6.81
6.66
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

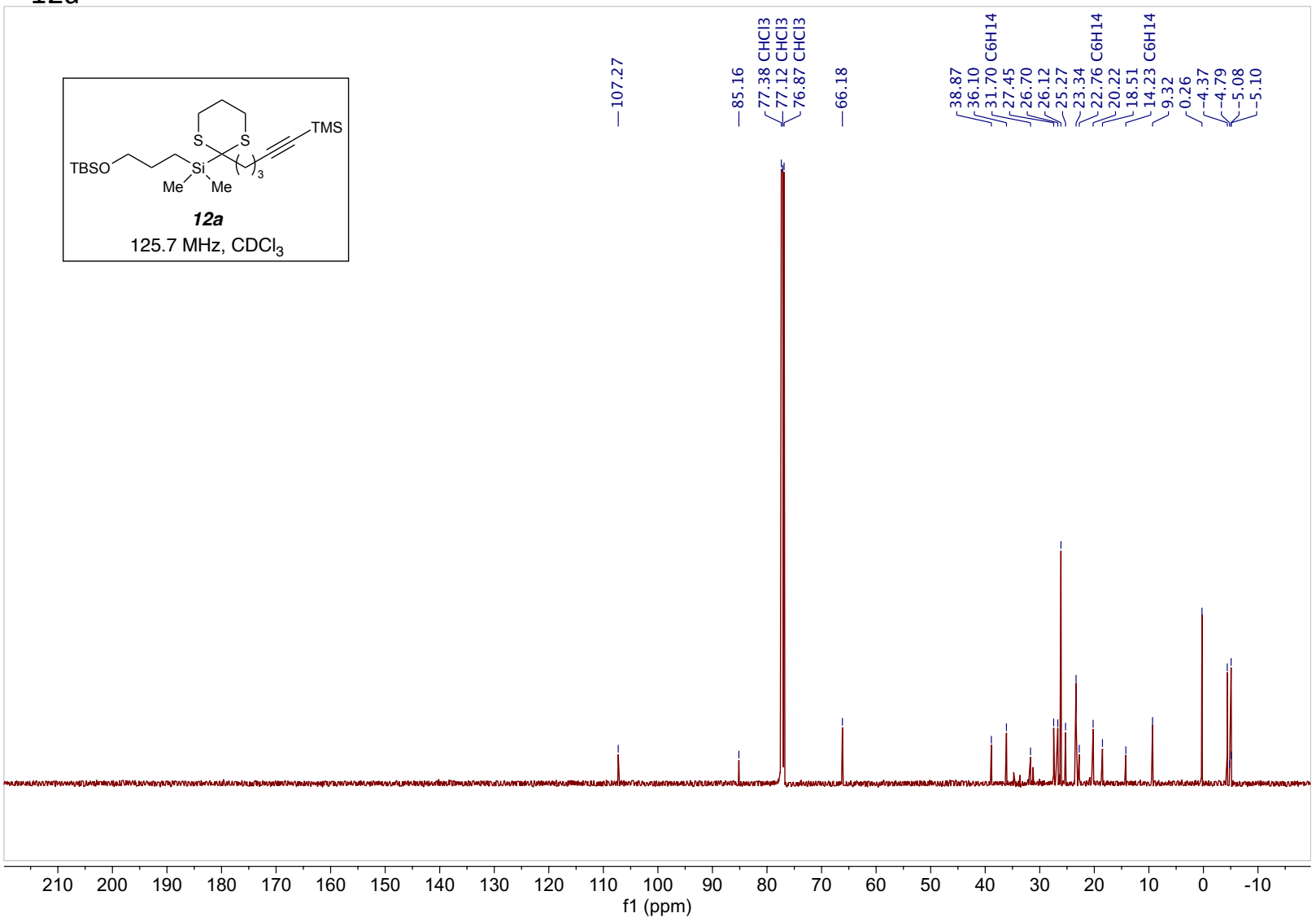
11a


77.41 CHCl3
77.16 CHCl3
76.90 CHCl3
68.12
66.09
33.69
31.26
27.08
26.38
26.16
25.79
25.76
18.55
9.33
-3.44
-4.75
-5.06
TBSO
Si
S
S
H
Me
Me
11a
125.7 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

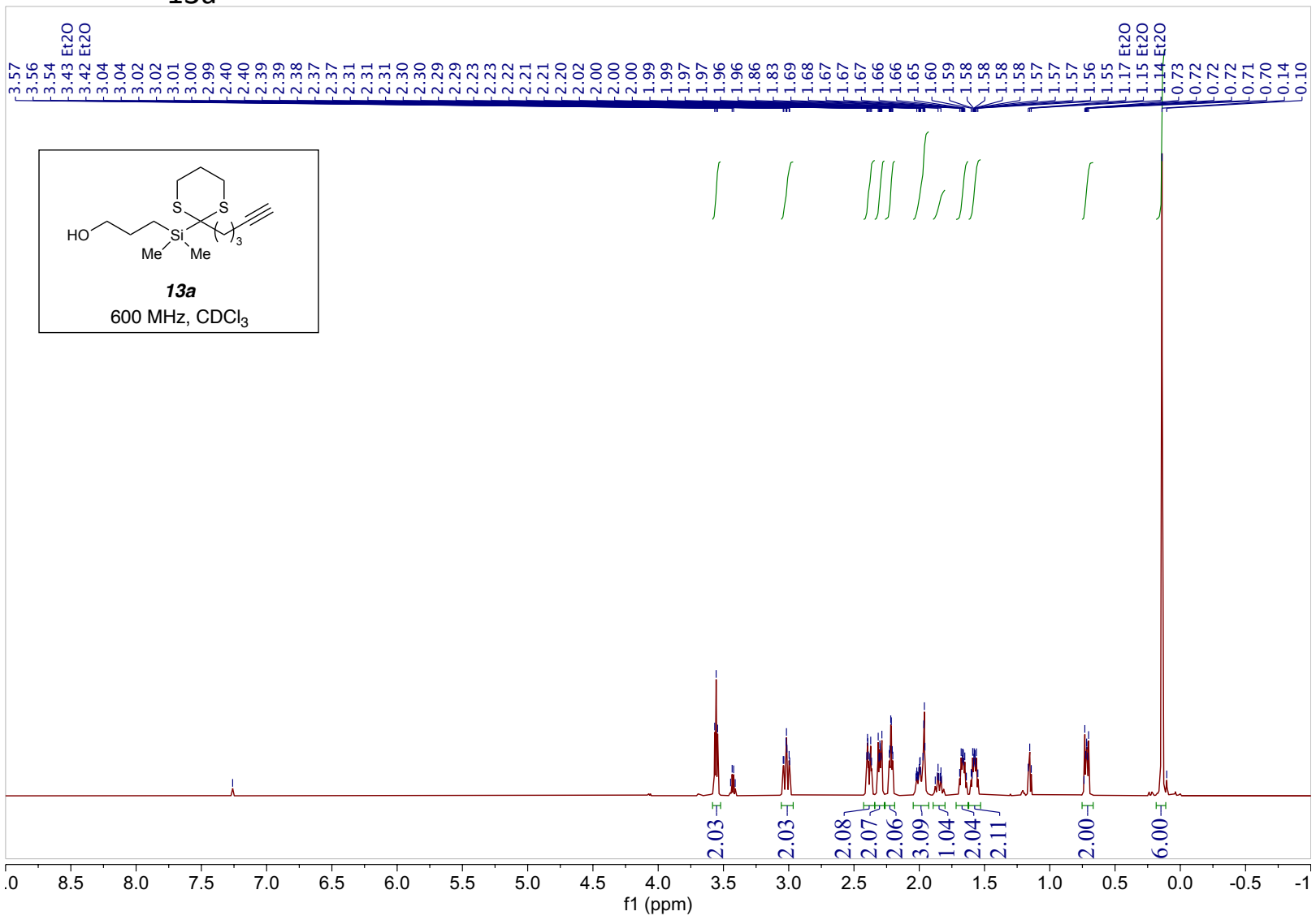
12a


7.26 CHCl3
TMS
TBSO
S
S
Si
Me
Me
3
12a
500 MHz, CDCl3
2.00
1.80
1.97
1.79
1.79
1.08
1.08
2.16
2.72
2.59
9.88
1.78
5.62
8.63
5.92
f1 (ppm)

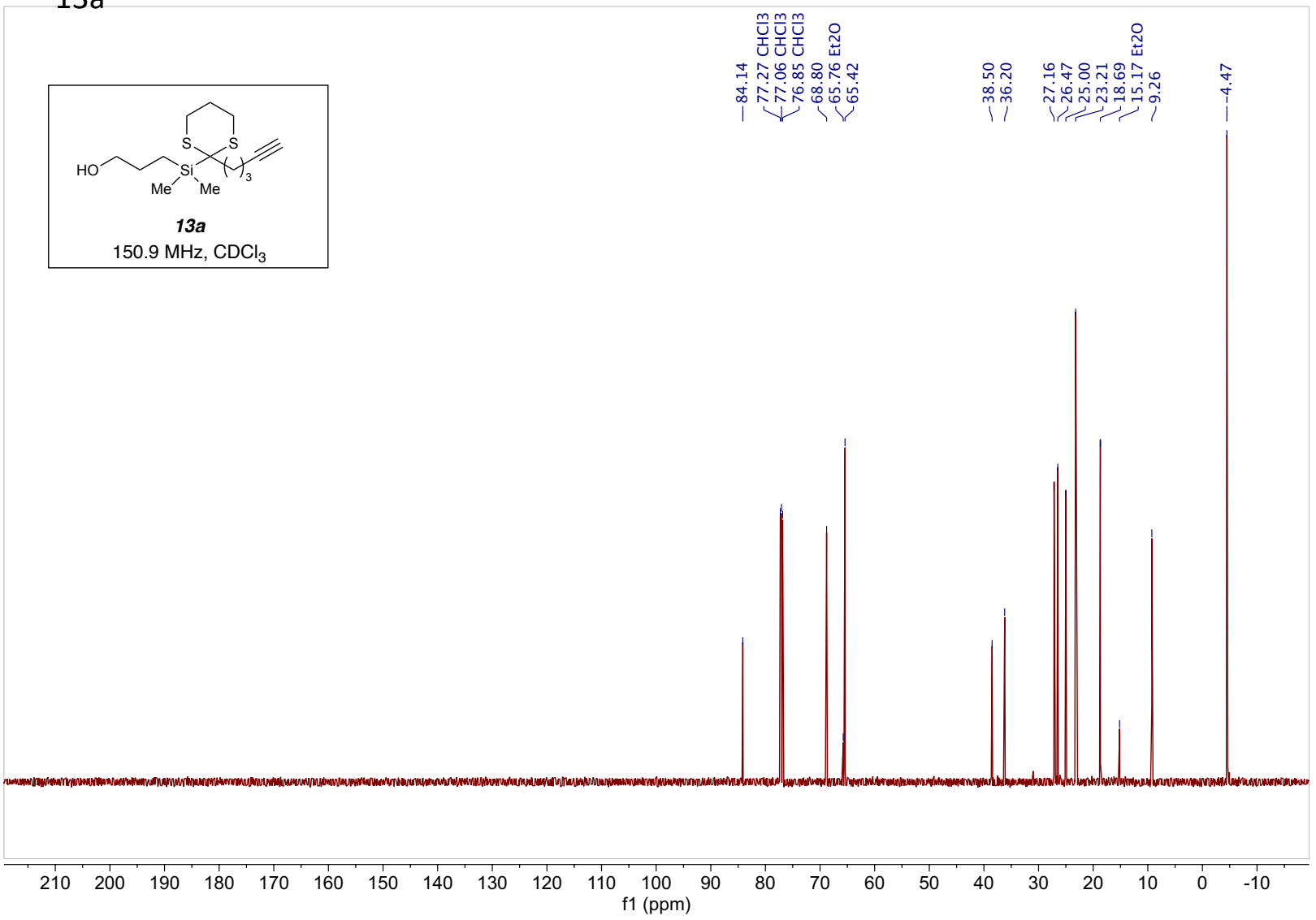
12a


TBSO
Si
Me
Me
S
S
TMS
3
12a
125.7 MHz, CDCl3
107.27
85.16
77.38 CHCl3
77.12 CHCl3
76.87 CHCl3
66.18
38.87
36.10
31.70 C6H14
27.45
26.70
26.12
25.27
23.34
22.76 C6H14
20.22
18.51
14.23 C6H14
9.32
0.26
-4.37
-4.79
-5.08
-5.10
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

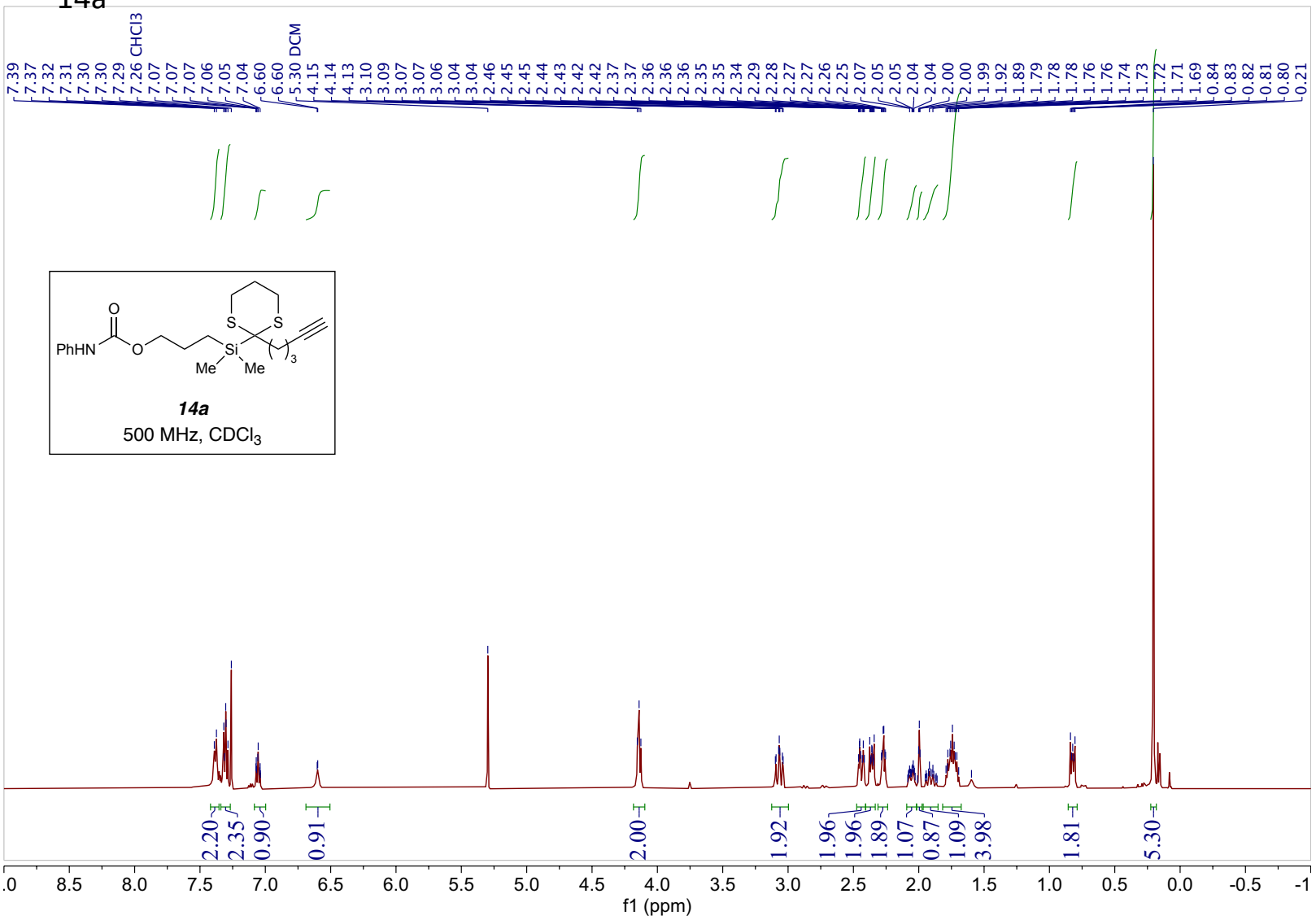
13a



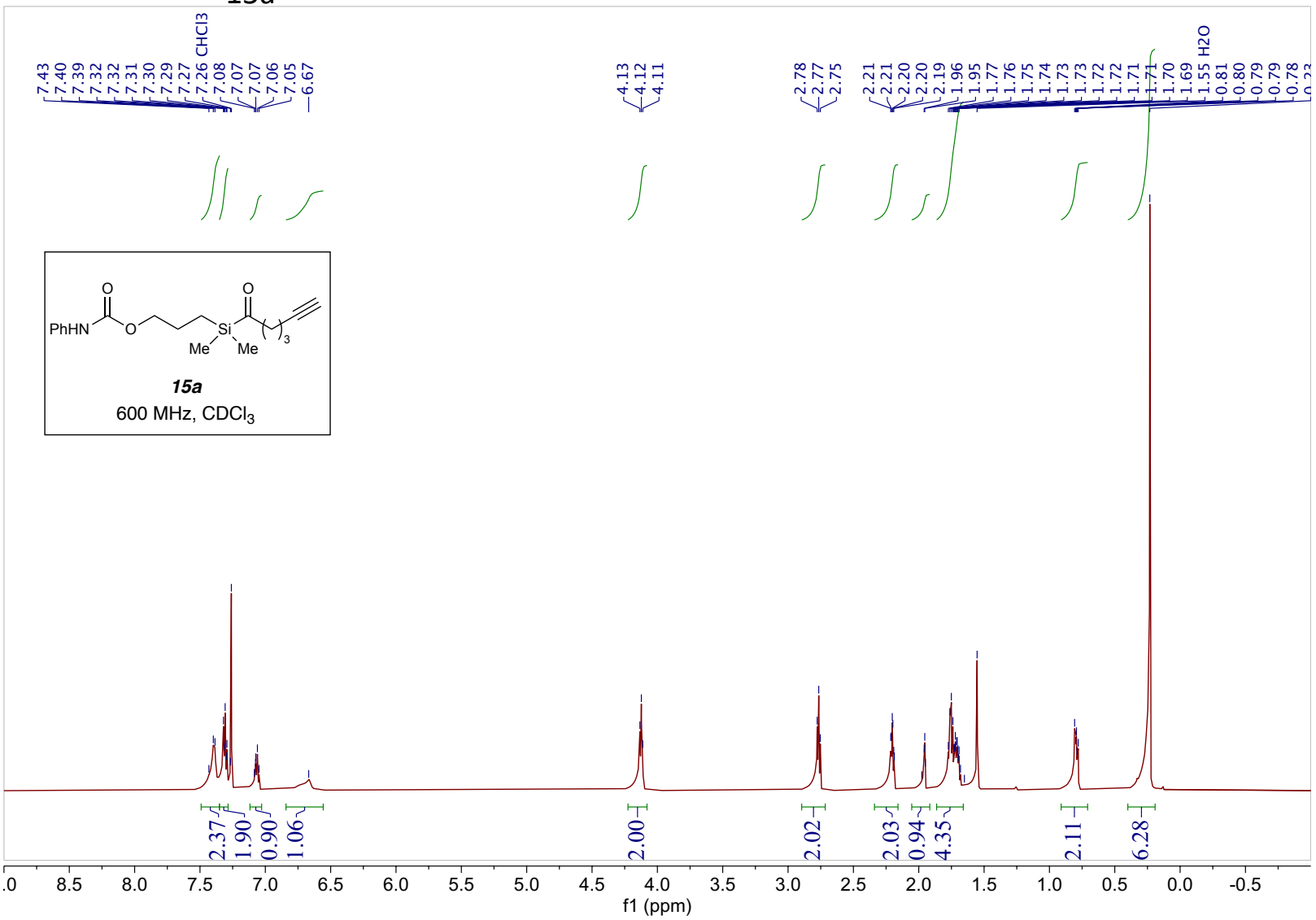
13a


HO
S
S
Si
Me
Me
3
13a
150.9 MHz, CDCl3
84.14
77.27 CHCl3
77.06 CHCl3
76.85 CHCl3
68.80
65.76 Et2O
65.42
38.50
36.20
27.16
26.47
25.00
23.21
18.69
15.17 Et2O
9.26
-4.47
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

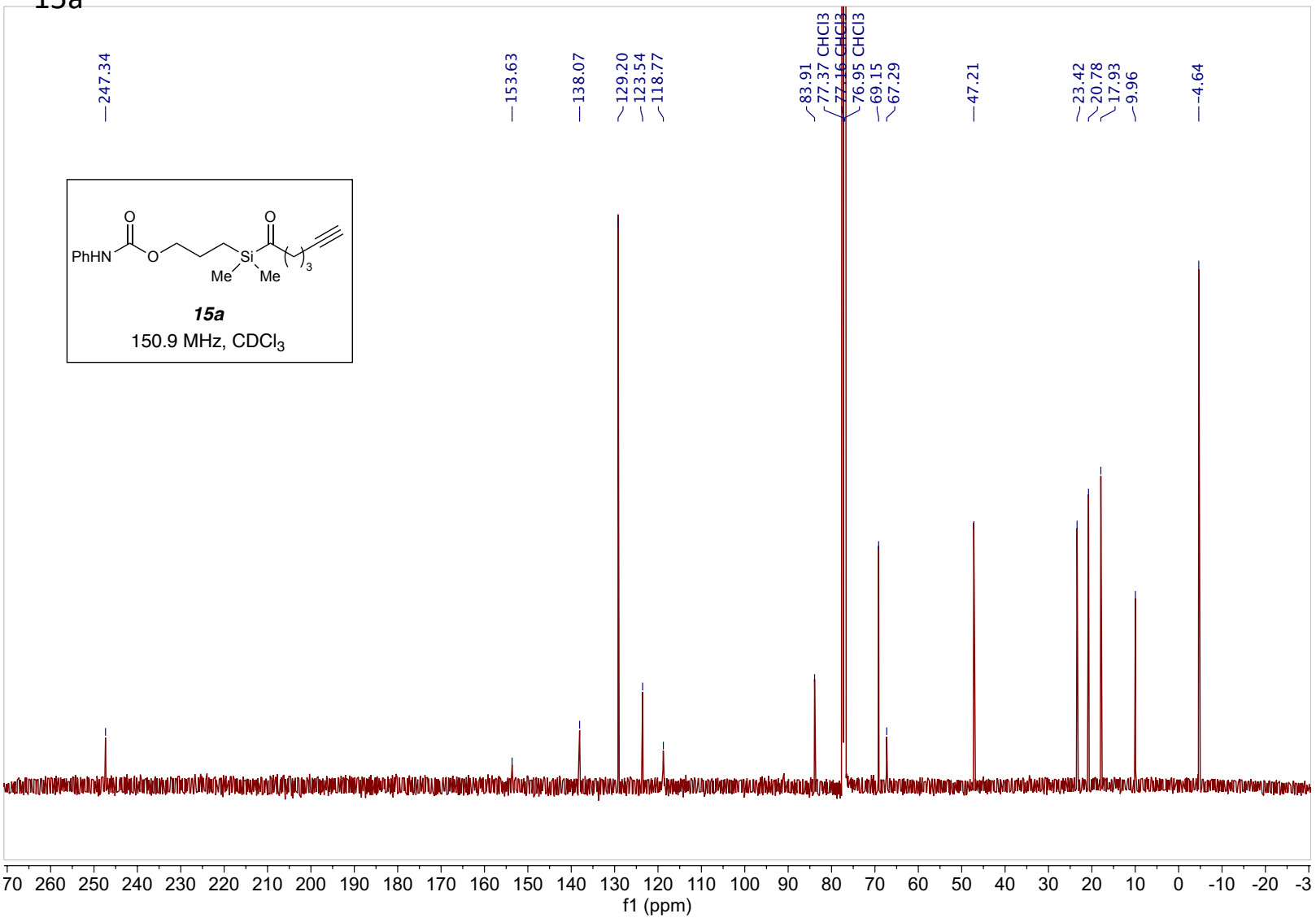
14a


CHCl3
DCM
7.39 7.37 7.32 7.31 7.30 7.30 7.29 7.26 7.07 7.07 7.07 7.06 7.05 7.04 6.60 6.60 5.30 4.15 4.14 4.13 3.10 3.09 3.07 3.07 3.06 3.04 3.04 2.46 2.45 2.45 2.44 2.43 2.42 2.42 2.37 2.37 2.36 2.36 2.35 2.35 2.34 2.29 2.28 2.27 2.27 2.26 2.25 2.07 2.05 2.05 2.04 2.04 2.00 2.00 1.99 1.92 1.89 1.79 1.78 1.78 1.76 1.76 1.74 1.73 1.72 1.71 1.69 0.84 0.83 0.82 0.81 0.80 0.21
PhHN
O
O
S
S
Si
Me
Me
3
14a
500 MHz, CDCl3
2.20 2.35 0.90 0.91 2.00 1.92 1.96 1.96 1.89 1.07 0.87 1.09 3.98 1.81 5.30
f1 (ppm)

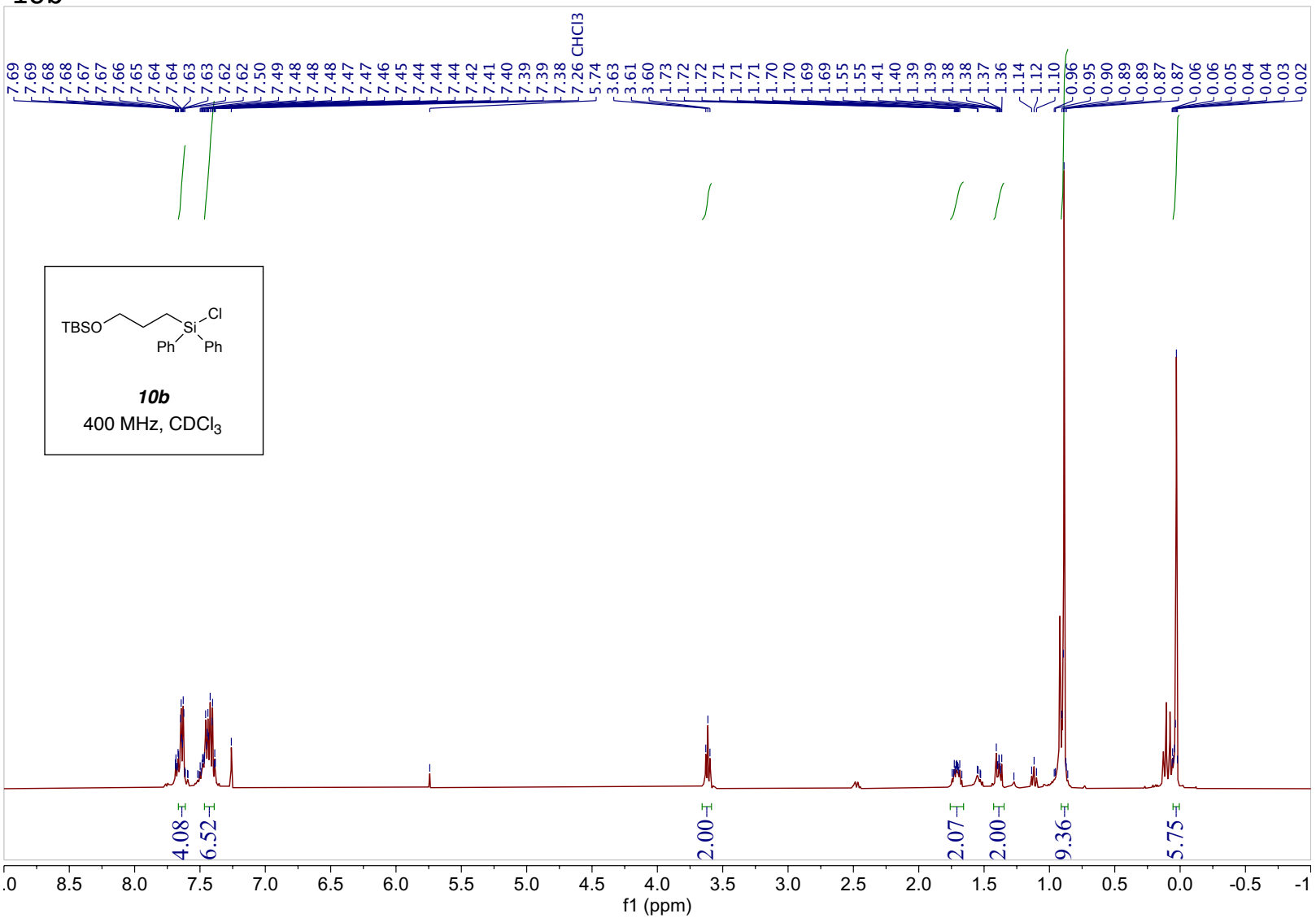
15a


7.43
7.40
7.39
7.32
7.32
7.31
7.30
7.29
7.27
7.26 CHCl3
7.08
7.07
7.07
7.06
7.05
6.67
4.13
4.12
4.11
2.78
2.77
2.75
2.21
2.21
2.20
2.20
2.19
1.96
1.95
1.77
1.76
1.75
1.74
1.73
1.73
1.72
1.72
1.71
1.71
1.70
1.69
1.55 H2O
0.81
0.80
0.79
0.79
0.78
PhHN
O
O
O
Si
Me
Me
3
15a
600 MHz, CDCl3
2.37
1.90
0.90
1.06
2.00
2.02
2.03
0.94
4.35
2.11
6.28
f1 (ppm)

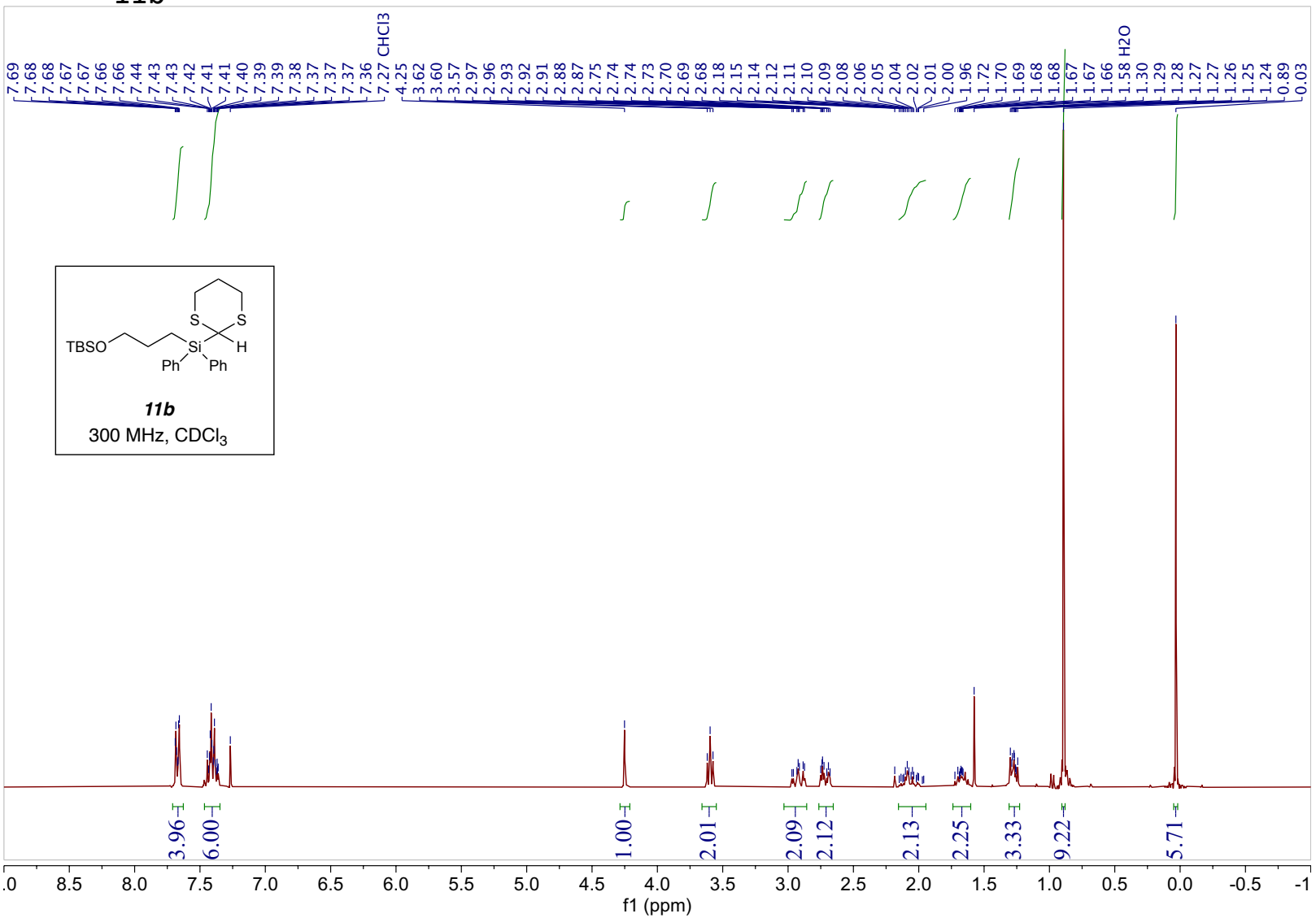
15a


247.34
153.63
138.07
129.20
123.54
118.77
83.91
77.37 CHCl3
77.16 CHCl3
76.95 CHCl3
69.15
67.29
47.21
23.42
20.78
17.93
9.96
-4.64
PhHN
O
O
O
Si
Me
Me
3
15a
150.9 MHz, CDCl3
70 260 250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -3
f1 (ppm)

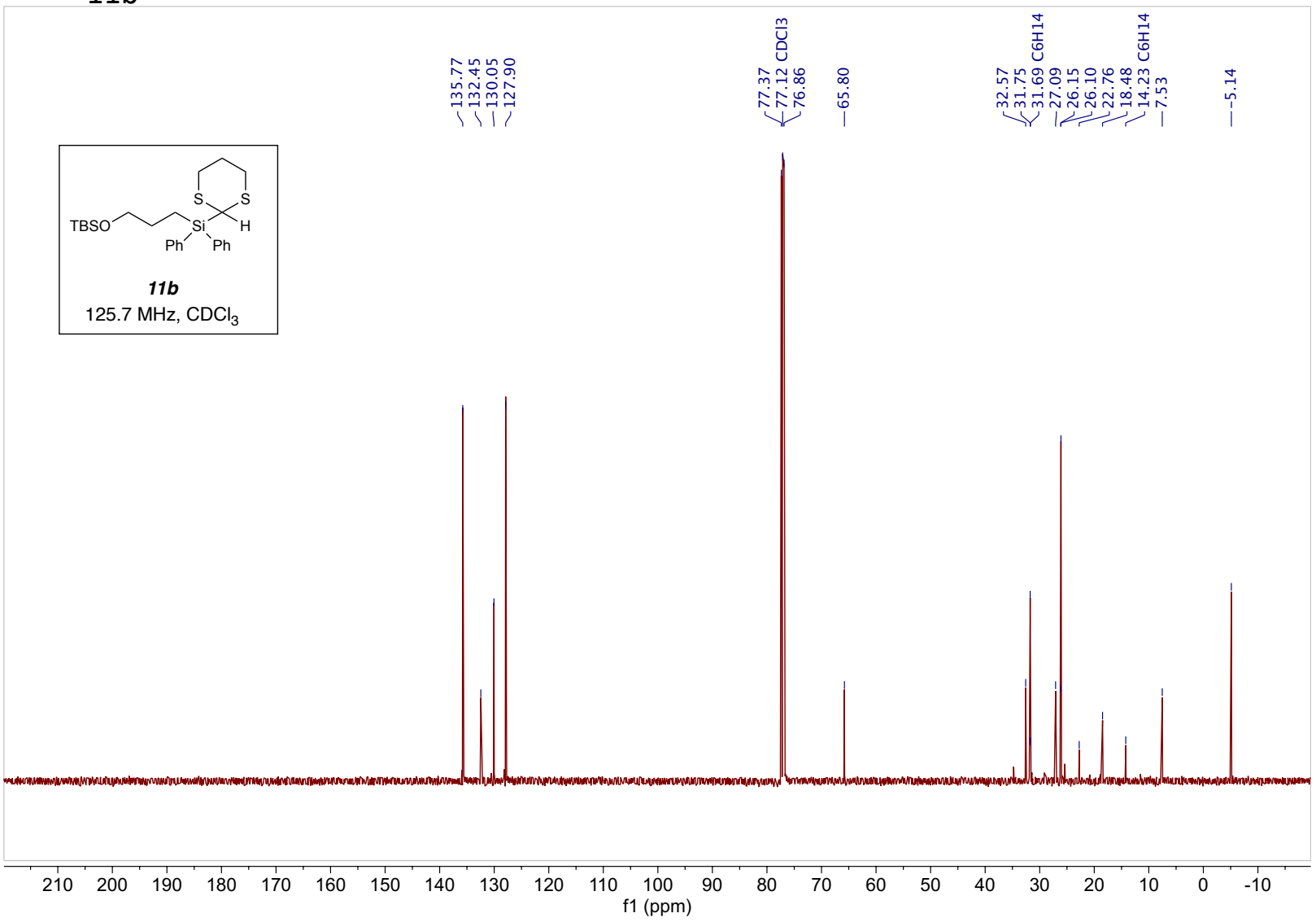
10b


TBSO
Si
Cl
Ph
Ph
10b
400 MHz, CDCl3
CHCl3
4.08
6.52
2.00
2.07
2.00
9.36
5.75
f1 (ppm)

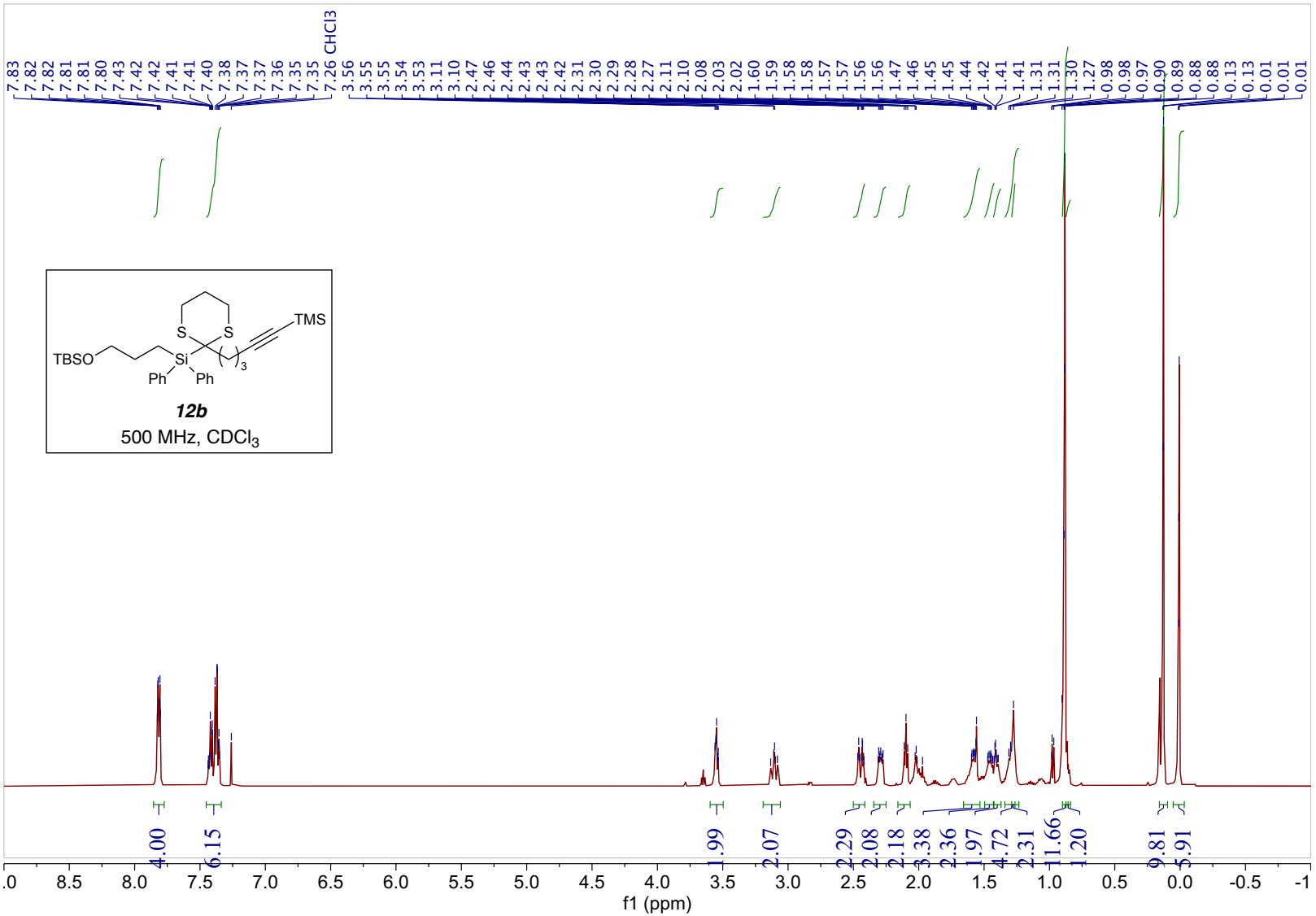
11b


CHCl3
H2O
TBSO
S
S
Si
H
Ph
Ph
11b
300 MHz, CDCl3
3.96
6.00
1.00
2.01
2.09
2.12
2.13
2.25
3.33
9.22
5.71
f1 (ppm)

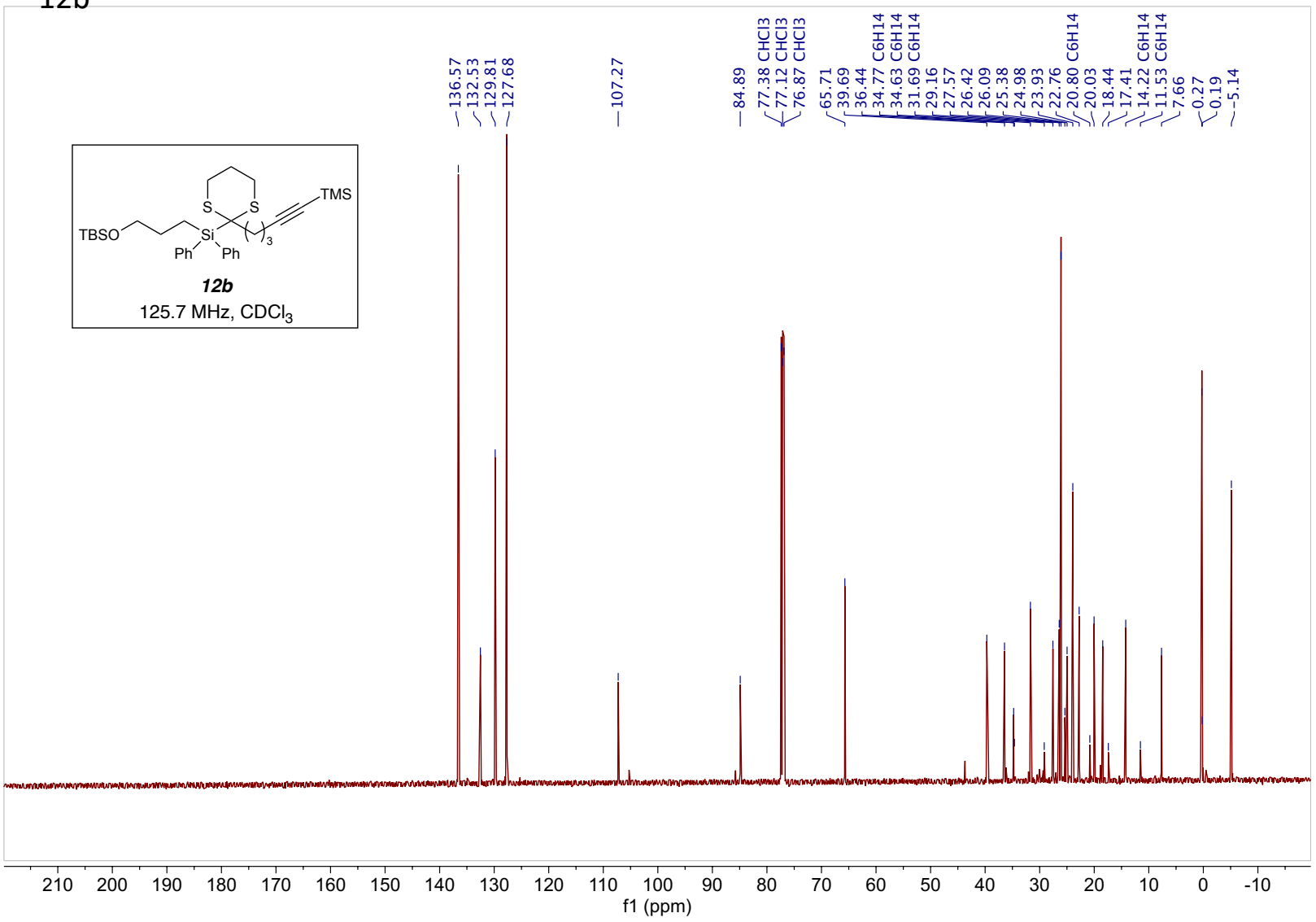
11b


135.77
132.45
130.05
127.90
77.37
77.12 CDCl3
76.86
65.80
32.57
31.75
31.69 C6H14
27.09
26.15
26.10
22.76
18.48
14.23 C6H14
7.53
-5.14
TBSO
Si
S
S
H
Ph
Ph
11b
125.7 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

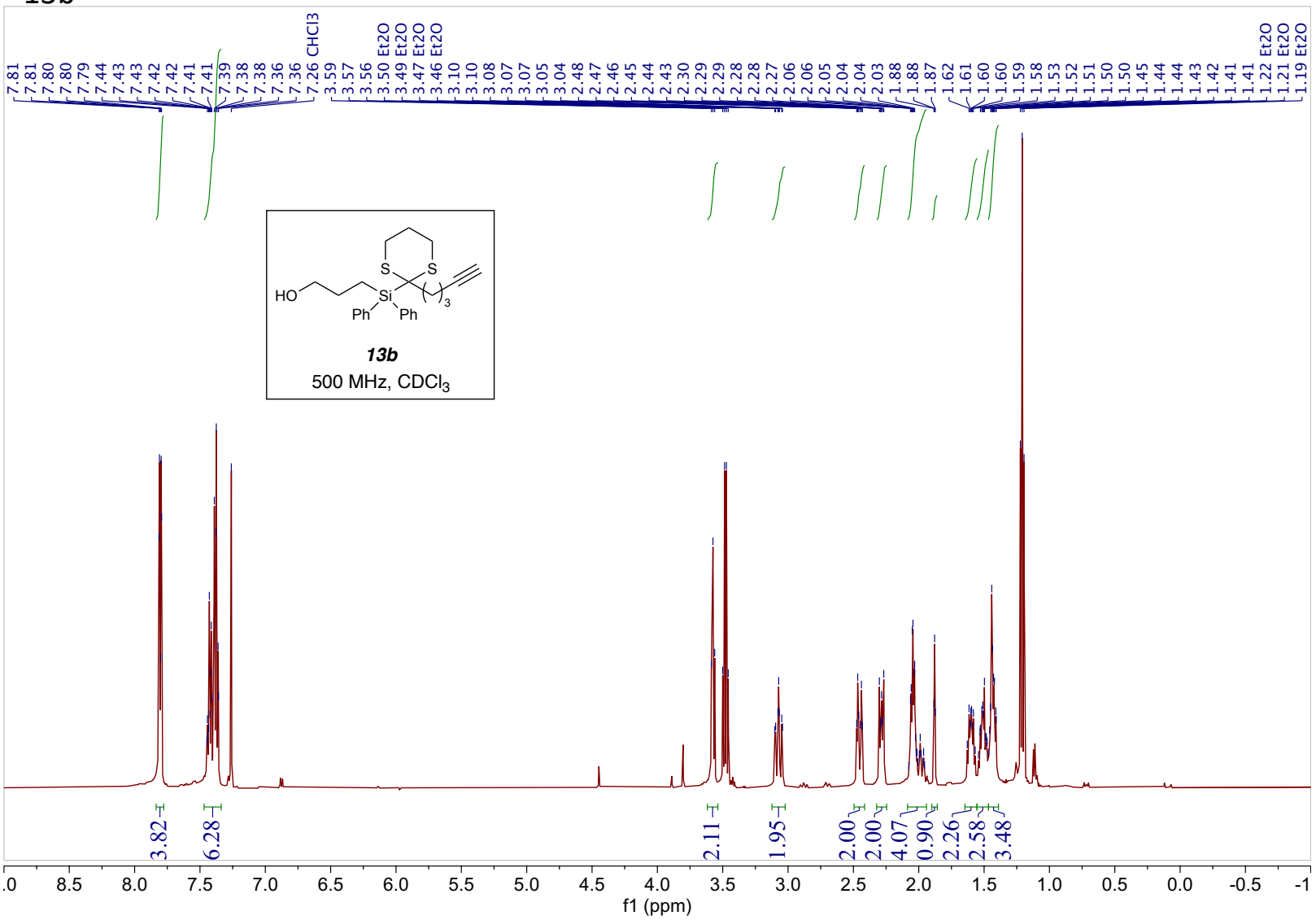
12b


CHCl3
TMS
TBSO
Si
S
S
Ph
Ph
3
12b
500 MHz, CDCl3
4.00
6.15
1.99
2.07
2.29
2.08
2.18
3.38
2.36
1.97
4.72
2.31
11.66
1.20
9.81
5.91
f1 (ppm)

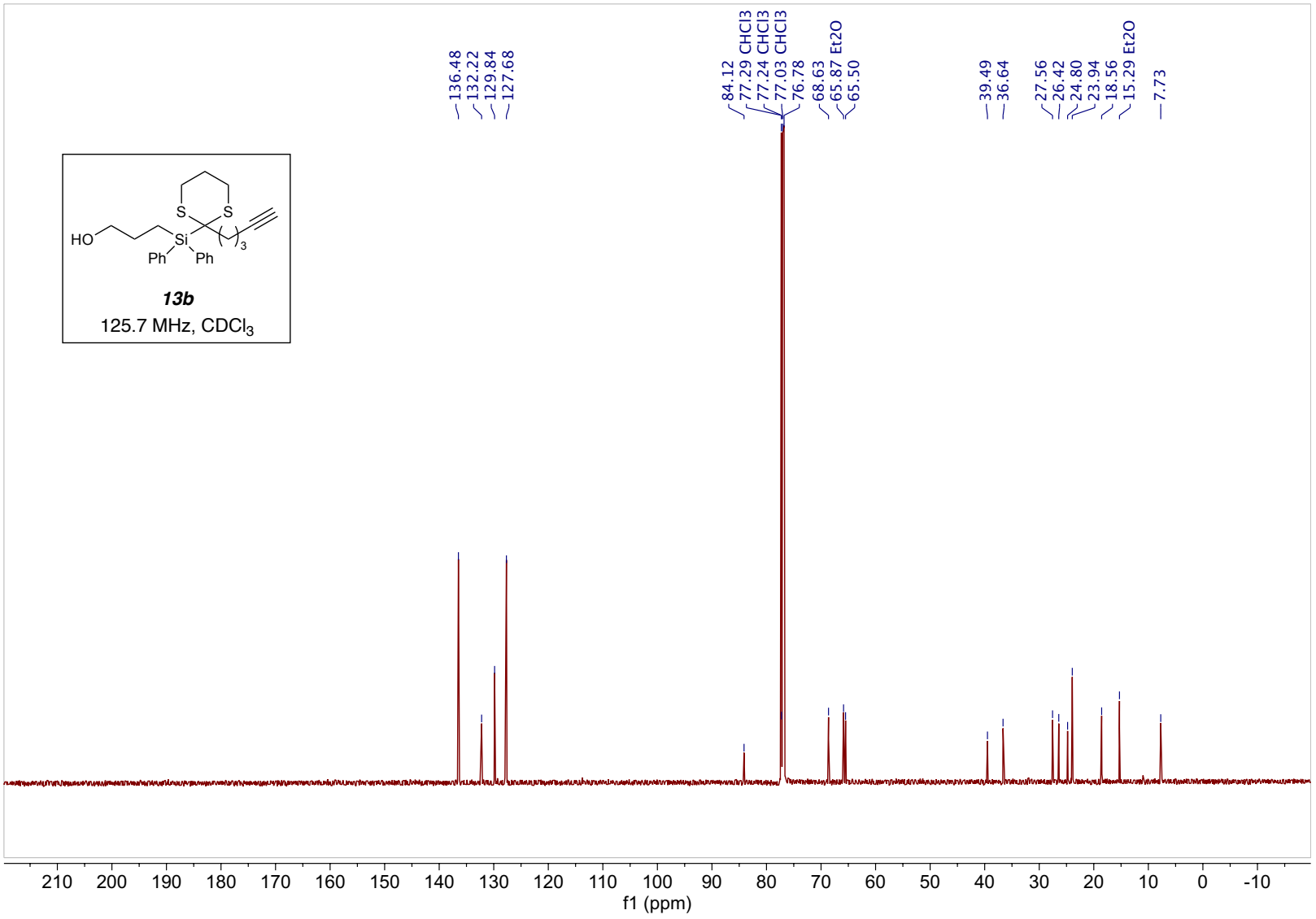
12b


136.57
132.53
129.81
127.68
107.27
84.89
77.38 CHCl3
77.12 CHCl3
76.87 CHCl3
65.71
39.69
36.44
34.77 C6H14
34.63 C6H14
31.69 C6H14
29.16
27.57
26.42
26.09
25.38
24.98
23.93
22.76
20.80 C6H14
20.03
18.44
17.41
14.22 C6H14
11.53 C6H14
7.66
0.27
0.19
-5.14
TMS
TBSO
S
S
Si
Ph
Ph
3
12b
125.7 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

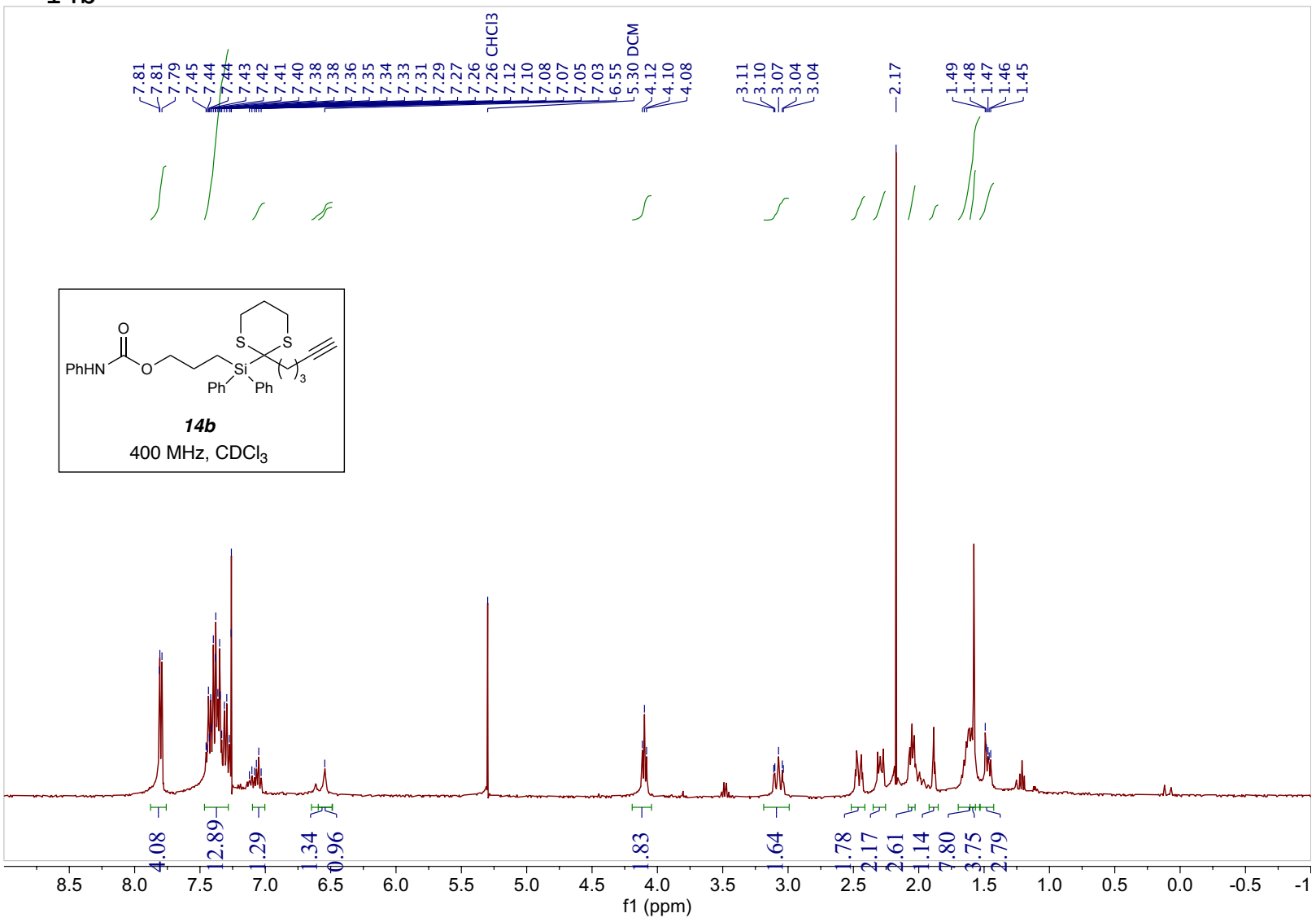
13b


7.81 7.81 7.80 7.80 7.79 7.44 7.43 7.43 7.42 7.42 7.41 7.41 7.39 7.38 7.38 7.36 7.36 CHCl3 7.26
3.59 3.57 3.56 3.50 Et2O 3.49 Et2O 3.47 Et2O 3.46 Et2O 3.10 3.10 3.08 3.07 3.07 3.05 3.04 2.48 2.47 2.46 2.45 2.44 2.43 2.30 2.29 2.29 2.28 2.28 2.27 2.06 2.06 2.05 2.04 2.04 2.03 1.88 1.88 1.87
1.62 1.61 1.60 1.60 1.59 1.58 1.53 1.52 1.51 1.50 1.50 1.45 1.44 1.44 1.43 1.42 1.41 1.41 1.22 Et2O 1.21 Et2O 1.19 Et2O
HO
Si
Ph
Ph
S
S
3
13b
500 MHz, CDCl3
3.82
6.28
2.11
1.95
2.00
2.00
4.07
0.90
2.26
2.58
3.48
f1 (ppm)

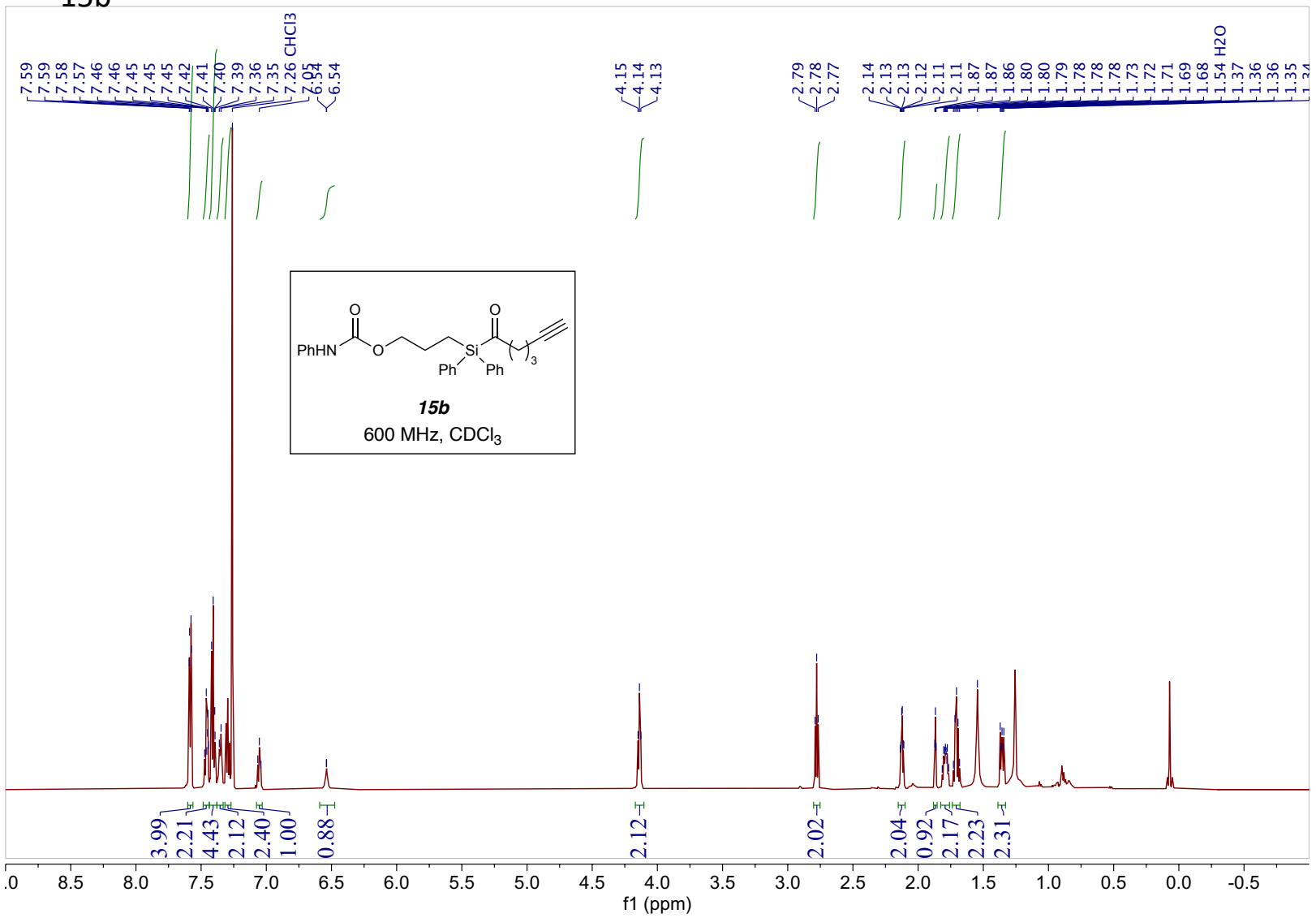
13b


136.48
132.22
129.84
127.68
84.12
77.29 CHCl3
77.24 CHCl3
77.03 CHCl3
76.78
68.63
65.87 Et2O
65.50
39.49
36.64
27.56
26.42
24.80
23.94
18.56
15.29 Et2O
7.73
HO
Si
Ph
Ph
S
S
3
13b
125.7 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

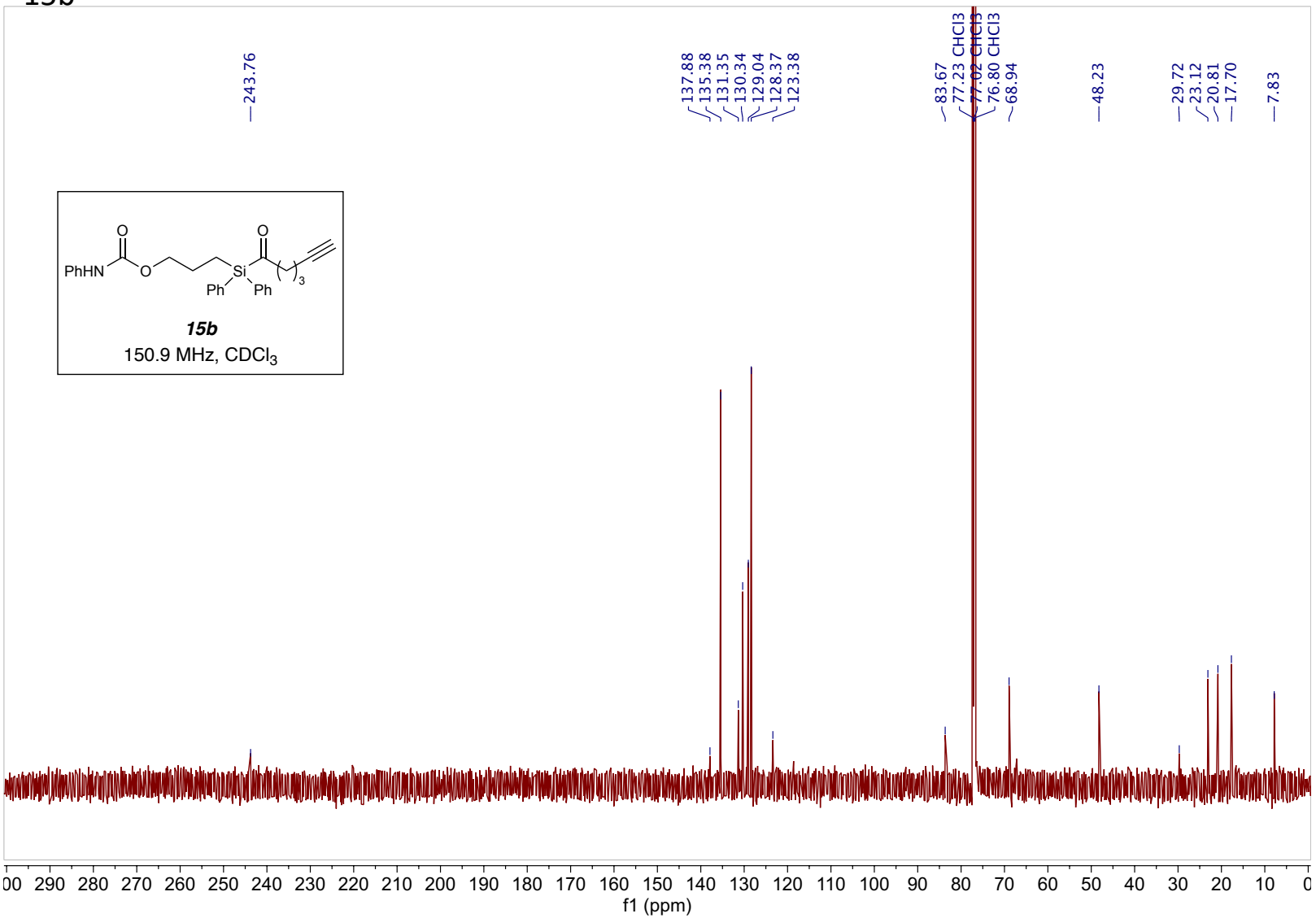
14b


7.81
7.81
7.79
7.45
7.44
7.44
7.43
7.42
7.41
7.40
7.38
7.38
7.36
7.35
7.34
7.33
7.31
7.29
7.27
7.26 CHCl3
7.12
7.10
7.08
7.07
7.05
7.03
6.55
5.30 DCM
4.12
4.10
4.08
3.11
3.10
3.07
3.04
3.04
2.17
1.49
1.48
1.47
1.46
1.45
PhHN
O
O
S
S
Si
Ph
Ph
3
14b
400 MHz, CDCl3
4.08
2.89
1.29
1.34
0.96
1.83
1.64
1.78
2.17
2.61
1.14
7.80
3.75
2.79
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

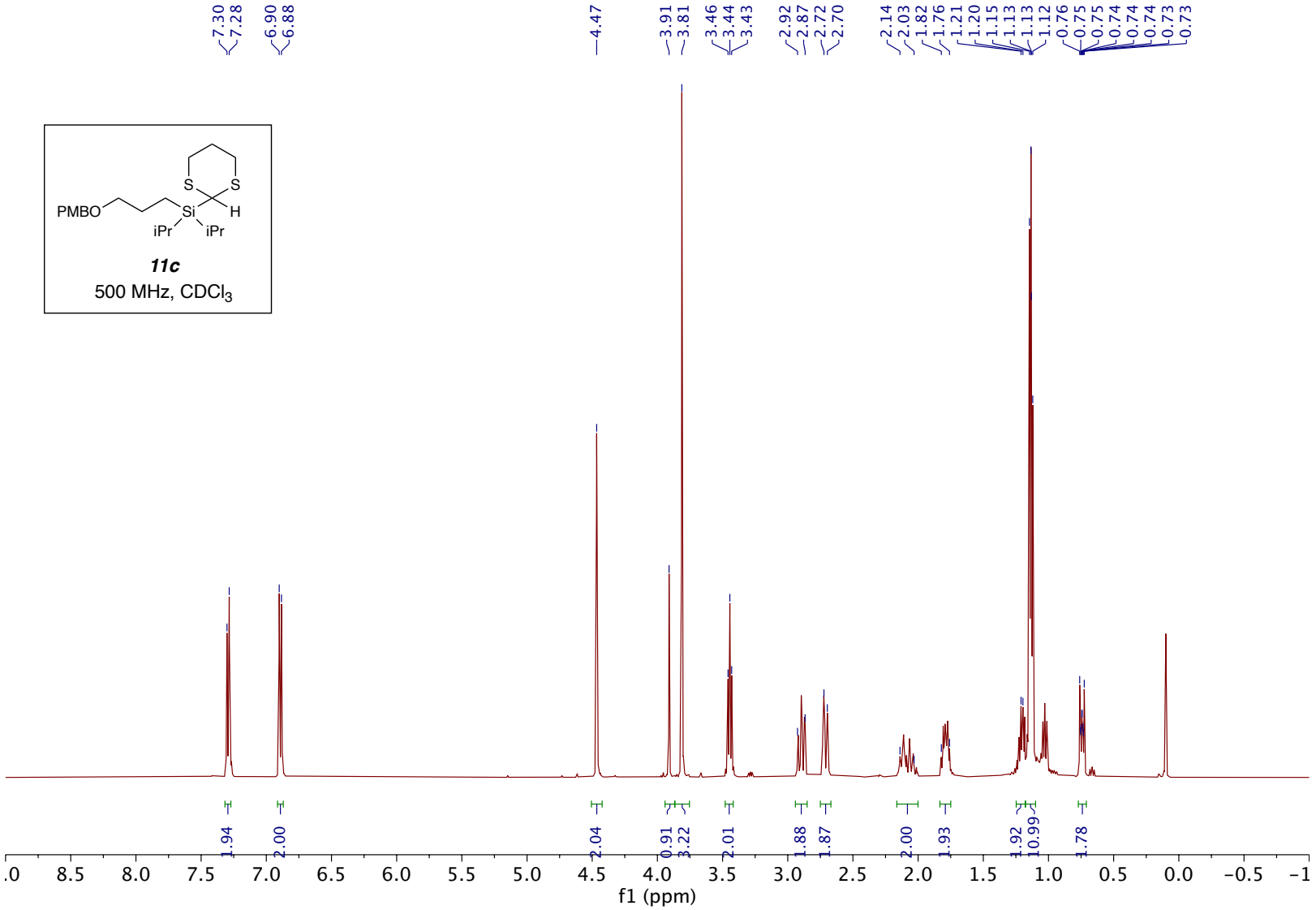
15b


7.59
7.59
7.58
7.57
7.46
7.46
7.45
7.45
7.45
7.42
7.41
7.40
7.39
7.36
7.35
CHCl3
7.26
7.05
6.54
6.54
4.15
4.14
4.13
2.79
2.78
2.77
2.14
2.13
2.13
2.12
2.11
2.11
1.87
1.87
1.86
1.80
1.80
1.79
1.78
1.78
1.78
1.73
1.72
1.71
1.69
1.68
1.54 H2O
1.37
1.36
1.36
1.35
PhHN
O
O
O
Si
Ph
Ph
3
15b
600 MHz, CDCl3
3.99
2.21
4.43
2.12
2.40
1.00
0.88
2.12
2.02
2.04
0.92
2.17
2.23
2.31
f1 (ppm)

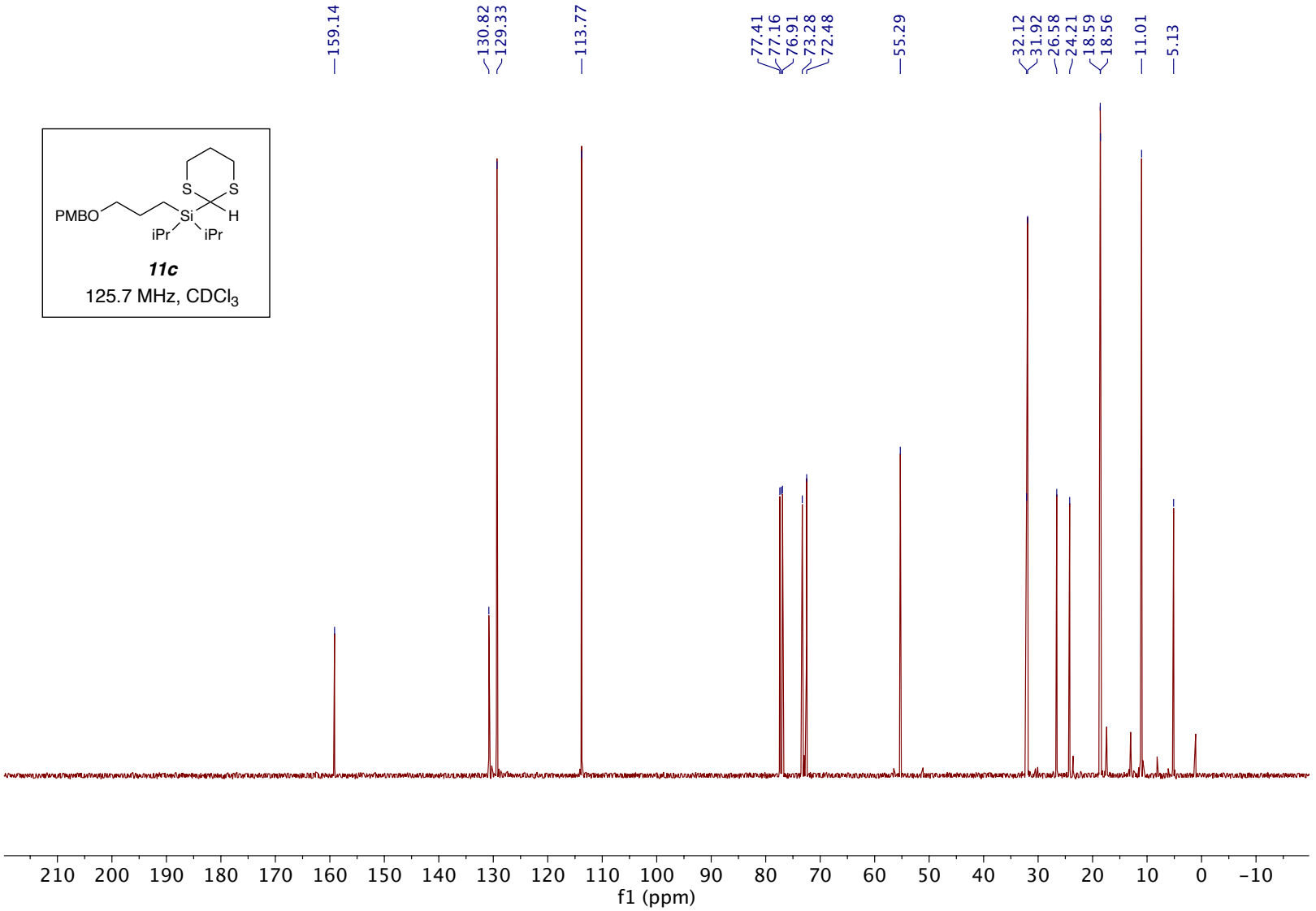
15b


243.76
137.88
135.38
131.35
130.34
129.04
128.37
123.38
83.67
77.23 CHCl3
77.02 CHCl3
76.80 CHCl3
68.94
48.23
29.72
23.12
20.81
17.70
7.83
PhHN
O
O
O
Si
Ph
Ph
3
15b
150.9 MHz, CDCl3
f1 (ppm)

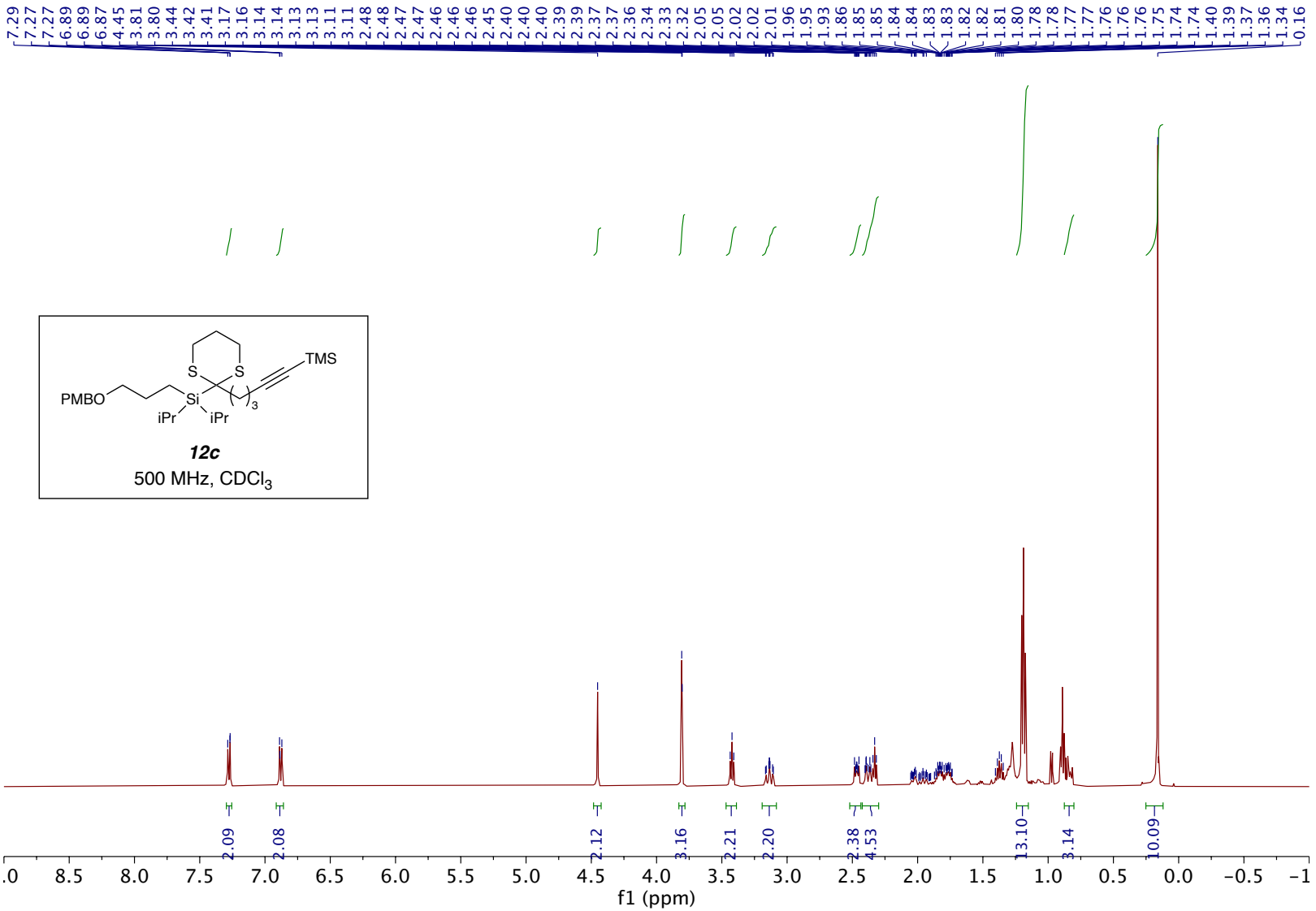
11c


7.30
7.28
6.90
6.88
4.47
3.91
3.81
3.46
3.44
3.43
2.92
2.87
2.72
2.70
2.14
2.03
1.82
1.76
1.21
1.20
1.15
1.13
1.13
1.12
0.76
0.75
0.75
0.74
0.74
0.74
0.73
0.73
PMBO
S
S
Si
H
iPr
iPr
11c
500 MHz, CDCl3
1.94
2.00
2.04
0.91
3.22
2.01
1.88
1.87
2.00
1.93
1.92
10.99
1.78
f1 (ppm)

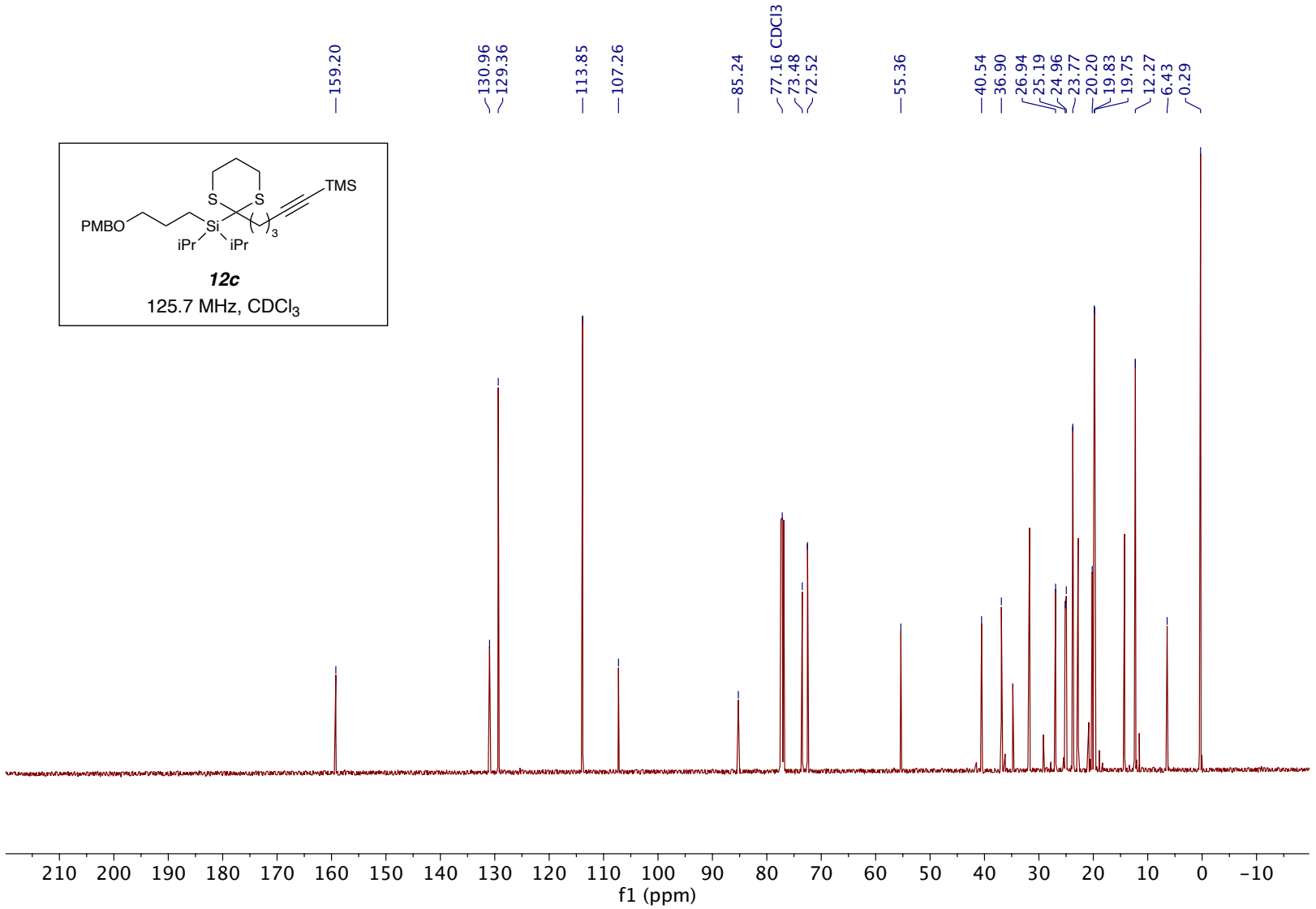
11c


159.14
130.82
129.33
113.77
77.41
77.16
76.91
73.28
72.48
55.29
32.12
31.92
26.58
24.21
18.59
18.56
11.01
5.13
PMBO
Si
S
S
H
iPr
iPr
11c
125.7 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

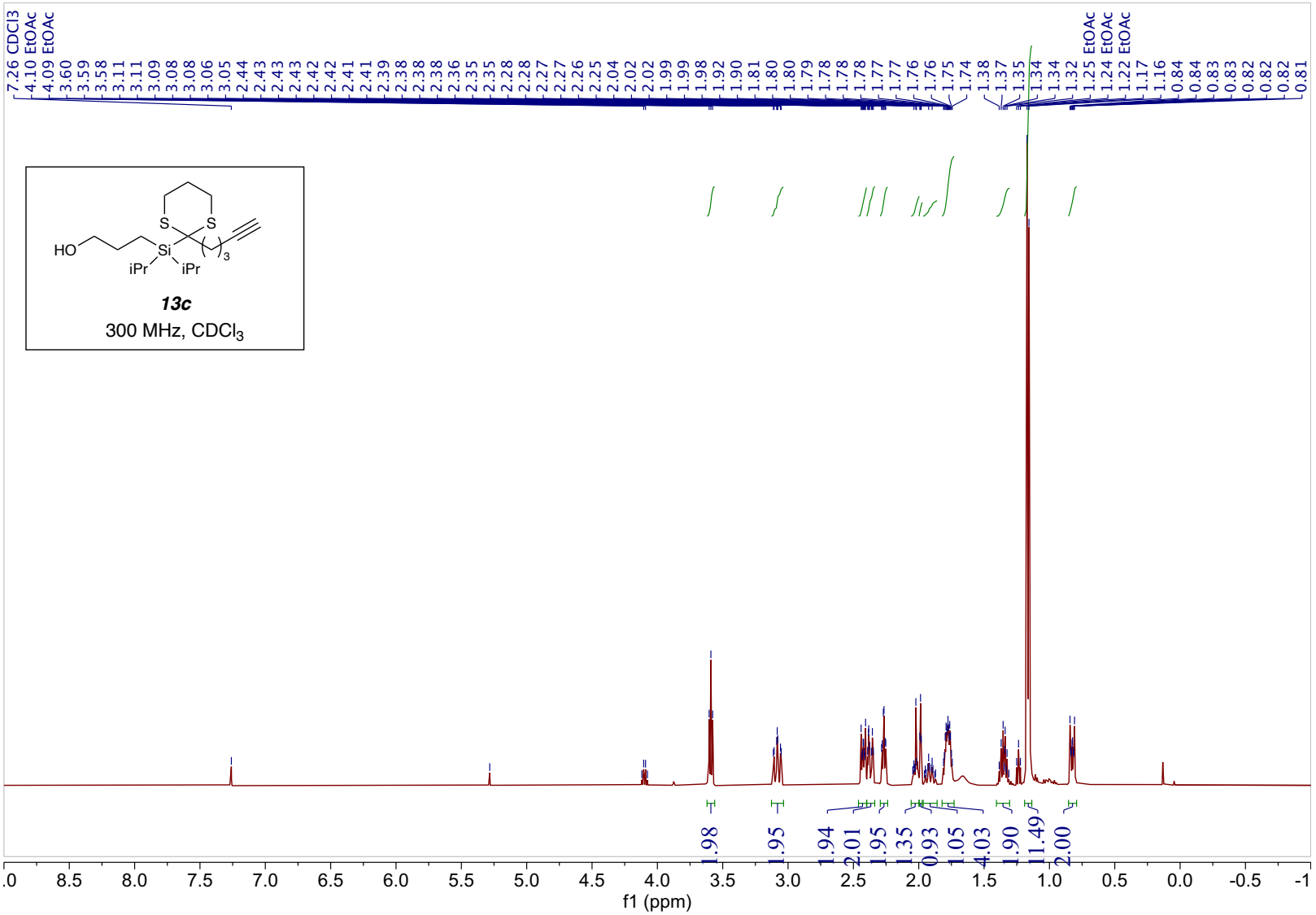
12c


7.29 7.27 7.27 6.89 6.87 4.45 3.81 3.80 3.44 3.42 3.41 3.17 3.16 3.14 3.14 3.13 3.13 3.11 3.11 2.48 2.48 2.47 2.47 2.46 2.46 2.46 2.45 2.40 2.40 2.40 2.39 2.39 2.37 2.37 2.36 2.34 2.33 2.32 2.05 2.02 2.02 2.01 1.96 1.95 1.93 1.86 1.85 1.85 1.84 1.84 1.83 1.82 1.82 1.81 1.80 1.78 1.78 1.77 1.77 1.76 1.76 1.76 1.75 1.74 1.74 1.40 1.39 1.37 1.36 1.34 0.16
PMBO
Si
iPr
iPr
S
S
TMS
3
12c
500 MHz, CDCl3
2.09
2.08
2.12
3.16
2.21
2.20
2.38
4.53
13.10
3.14
10.09
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

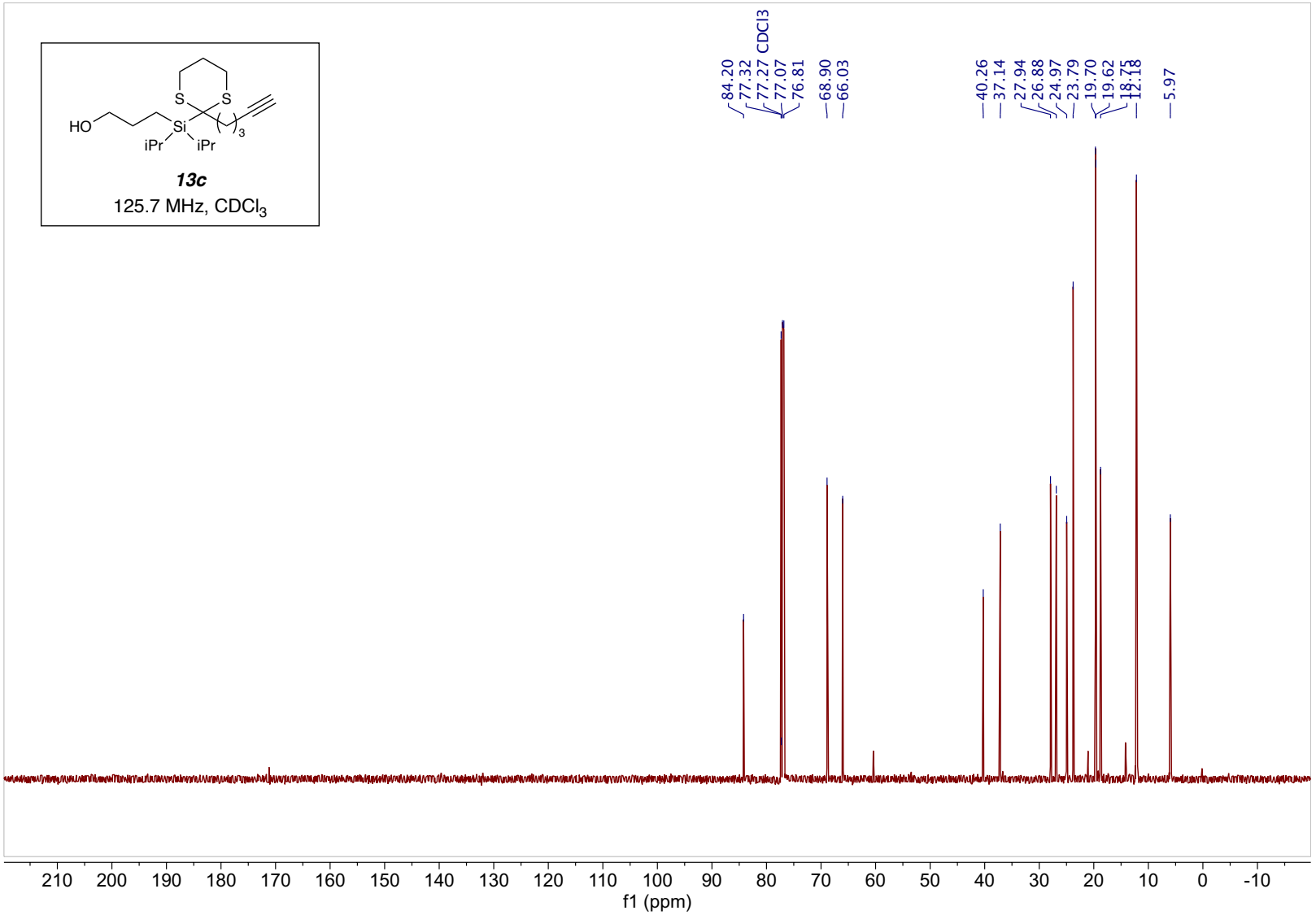
12c


159.20
130.96
129.36
113.85
107.26
85.24
77.16 CDCl3
73.48
72.52
55.36
40.54
36.90
26.94
25.19
24.96
23.77
20.20
19.83
19.75
12.27
6.43
0.29
S
S
TMS
PMBO
Si
iPr
iPr
3
12c
125.7 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

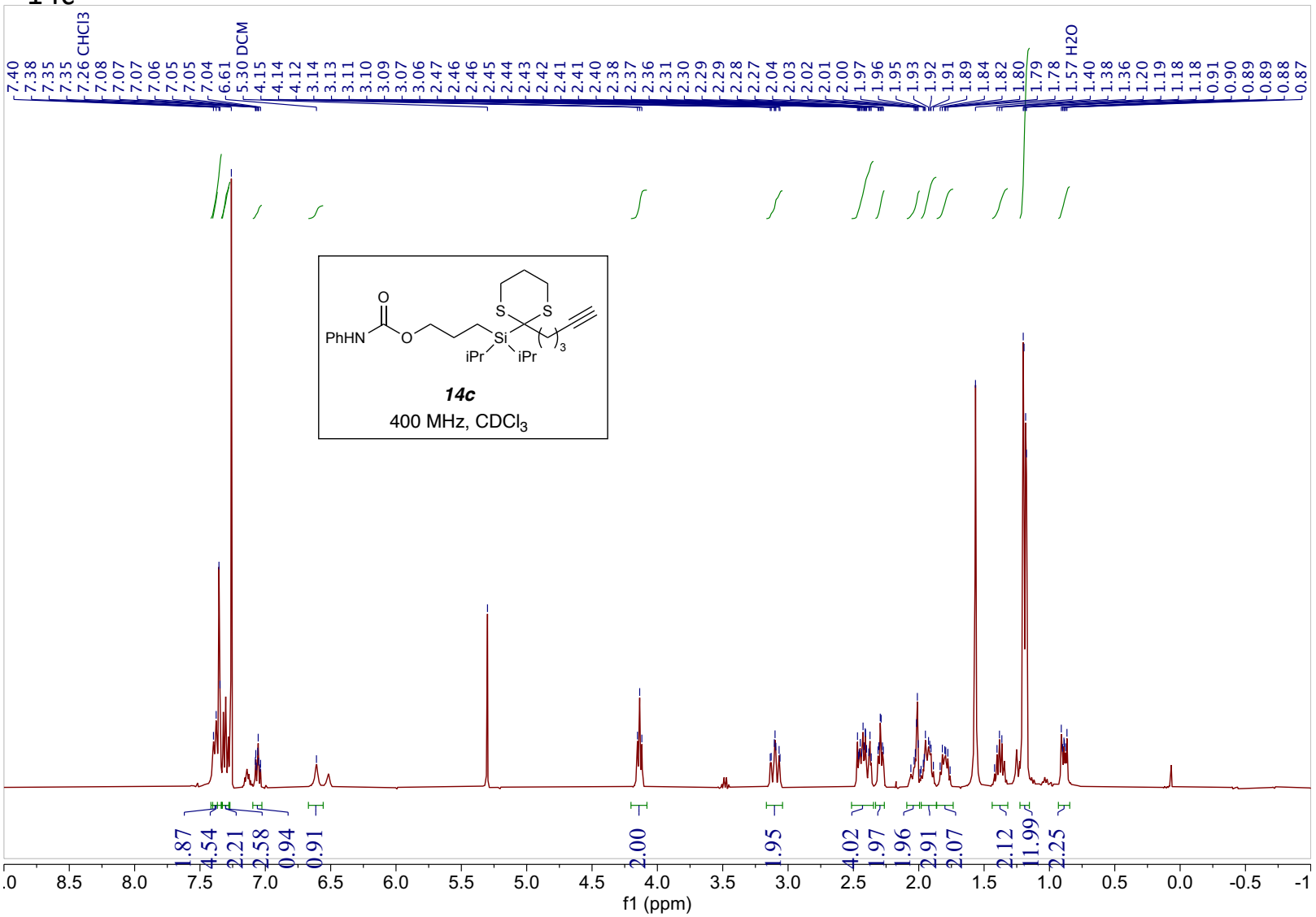
13c


7.26 CDCl3
4.10 EtOAc
4.09 EtOAc
1.25 EtOAc
1.24 EtOAc
1.22 EtOAc
HO
S
S
Si
iPr
iPr
3
13c
300 MHz, CDCl3
1.98
1.95
1.94
2.01
1.95
1.35
0.93
1.05
4.03
1.90
11.49
2.00
f1 (ppm)

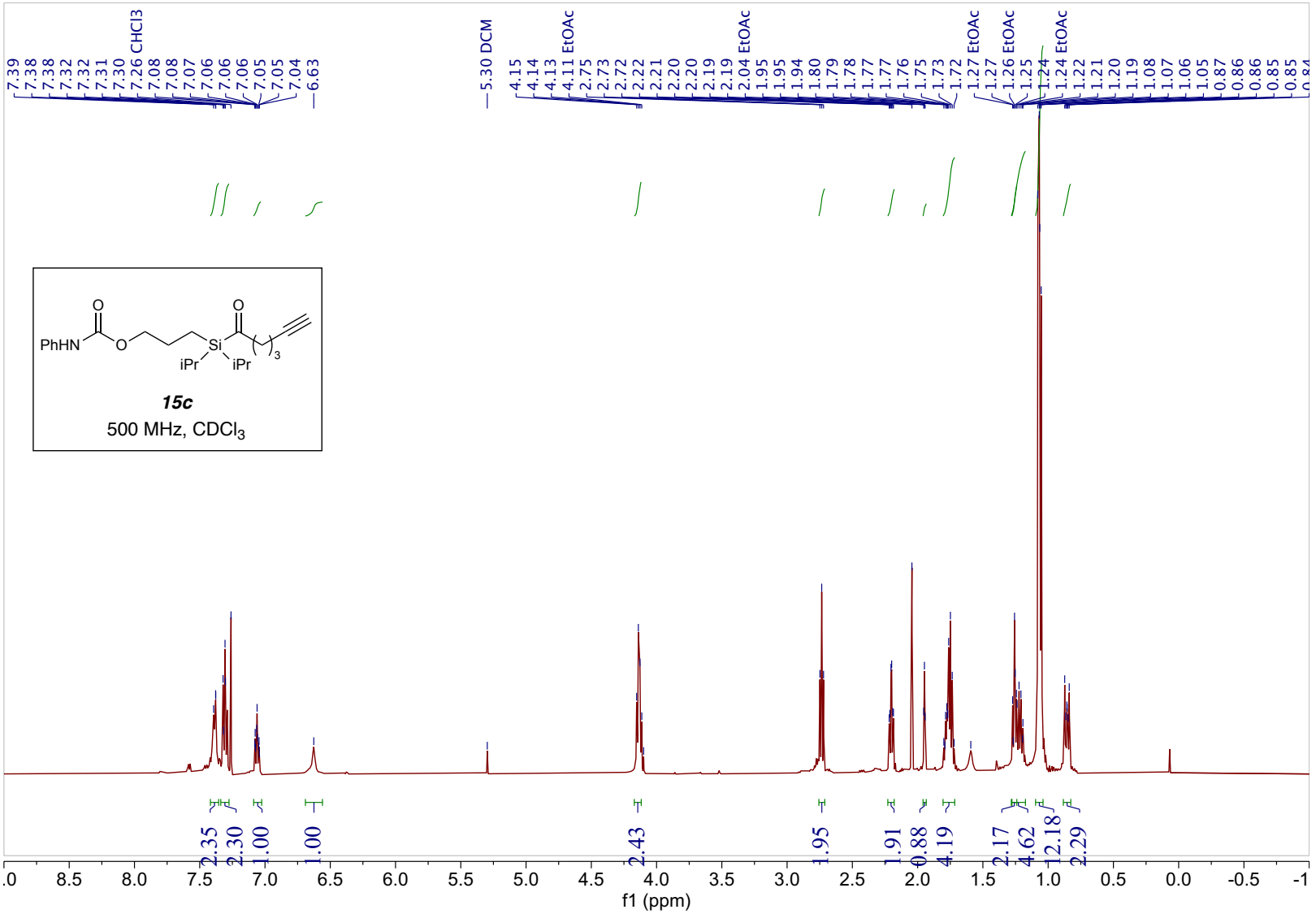
13c


HO
Si
iPr
iPr
S
S
3
13c
125.7 MHz, CDCl3
84.20
77.32
77.27 CDCl3
77.07
76.81
68.90
66.03
40.26
37.14
27.94
26.88
24.97
23.79
19.70
19.62
18.75
18.18
12.15
5.97
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

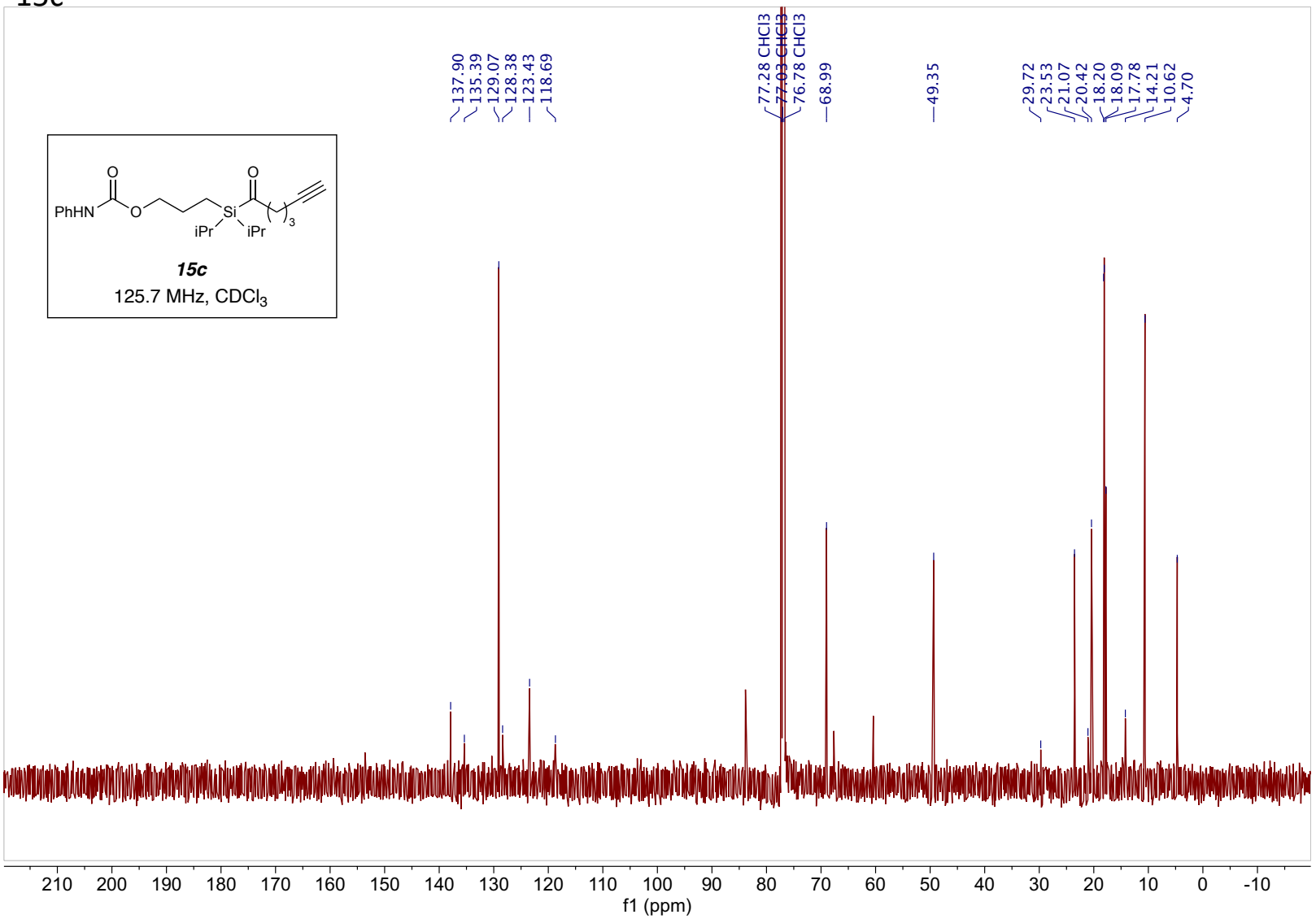
14c


7.40 7.38 7.35 7.35 CHCl3 7.26 7.08 7.07 7.07 7.06 7.05 7.05 7.04 6.61 5.30 DCM 4.15 4.14 4.12 3.14 3.13 3.11 3.10 3.09 3.07 3.06 2.47 2.46 2.46 2.45 2.44 2.43 2.42 2.41 2.41 2.40 2.38 2.37 2.36 2.31 2.30 2.29 2.29 2.28 2.27 2.04 2.03 2.02 2.01 2.00 1.97 1.96 1.95 1.93 1.92 1.91 1.89 1.84 1.82 1.80 1.79 1.78 1.57 H2O 1.40 1.38 1.36 1.20 1.19 1.18 0.91 0.90 0.89 0.89 0.88 0.87
PhHN
O
O
S
S
Si
iPr
iPr
3
14c
400 MHz, CDCl3
1.87 4.54 2.21 2.58 0.94 0.91 2.00 1.95 4.02 1.97 1.96 2.91 2.07 2.12 11.99 2.25
f1 (ppm)

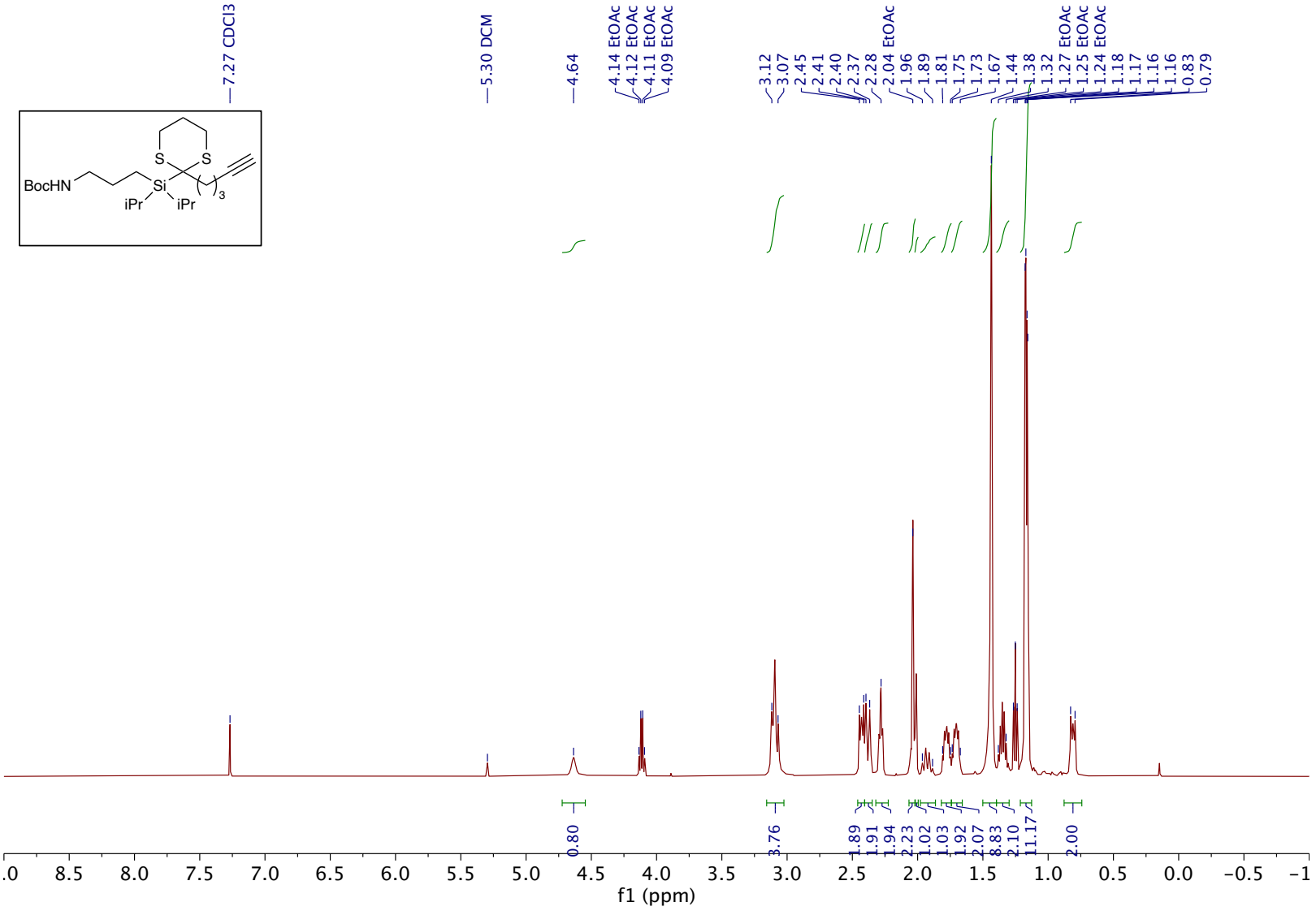
15c


7.39
7.38
7.38
7.32
7.32
7.31
7.30
7.26 CHCl3
7.08
7.08
7.07
7.06
7.06
7.06
7.05
7.05
7.04
6.63
5.30 DCM
4.15
4.14
4.13
4.11 EtOAc
2.75
2.73
2.72
2.22
2.21
2.20
2.20
2.19
2.19
2.04 EtOAc
1.95
1.94
1.80
1.79
1.78
1.77
1.77
1.76
1.75
1.73
1.72
1.27 EtOAc
1.27
1.26 EtOAc
1.25
1.24
1.24 EtOAc
1.22
1.21
1.20
1.19
1.08
1.07
1.06
1.05
0.87
0.86
0.86
0.85
0.85
PhHN
O
O
O
Si
iPr
iPr
3
15c
500 MHz, CDCl3
2.35
2.30
1.00
1.00
2.43
1.95
1.91
0.88
4.19
2.17
4.62
12.18
2.29
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

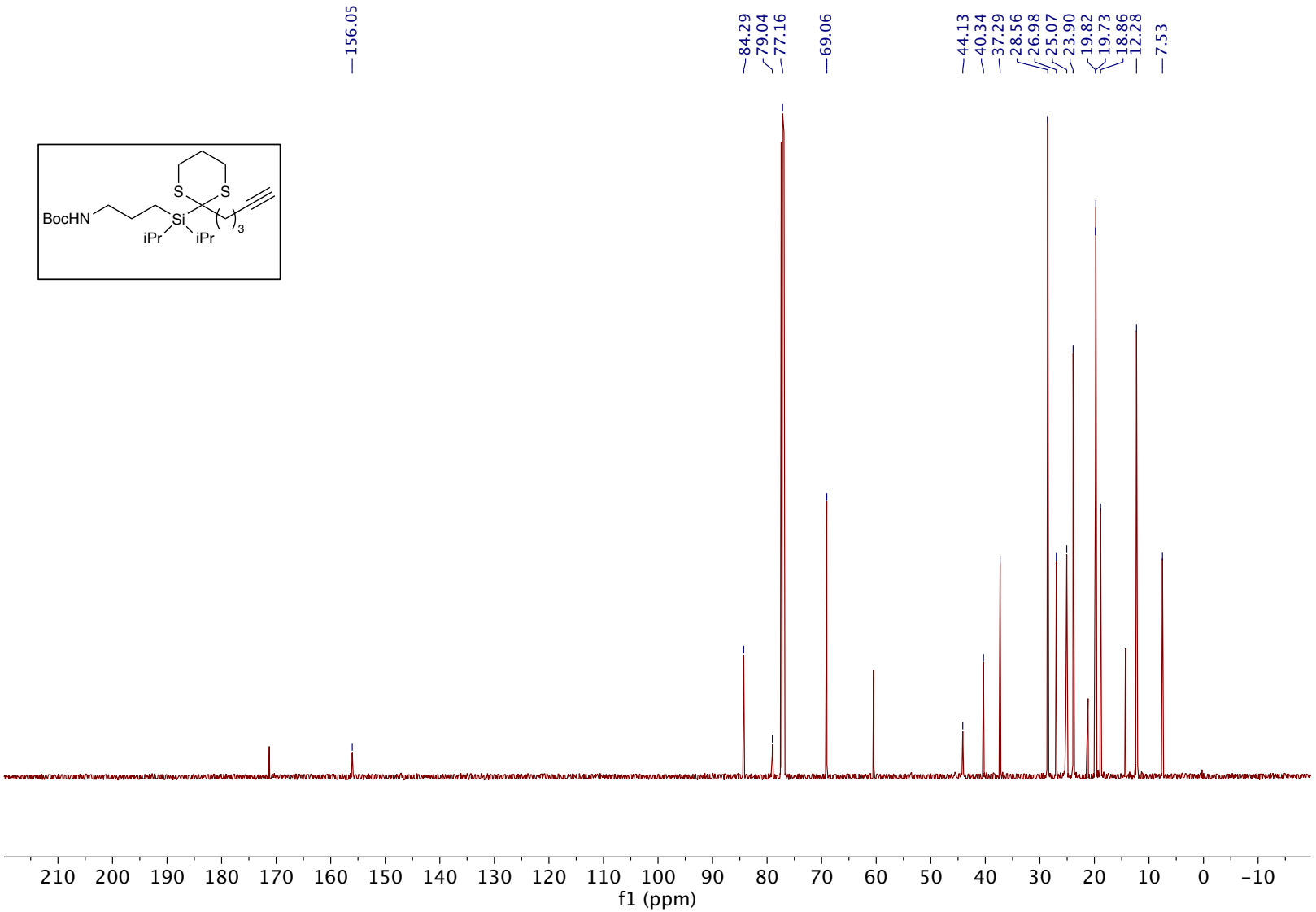
15c


137.90
135.39
129.07
128.38
123.43
118.69
77.28 CHCl3
77.03 CHCl3
76.78 CHCl3
68.99
49.35
29.72
23.53
21.07
20.42
18.20
18.09
17.78
14.21
10.62
4.70
PhHN
O
O
Si
iPr
iPr
3
15c
125.7 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

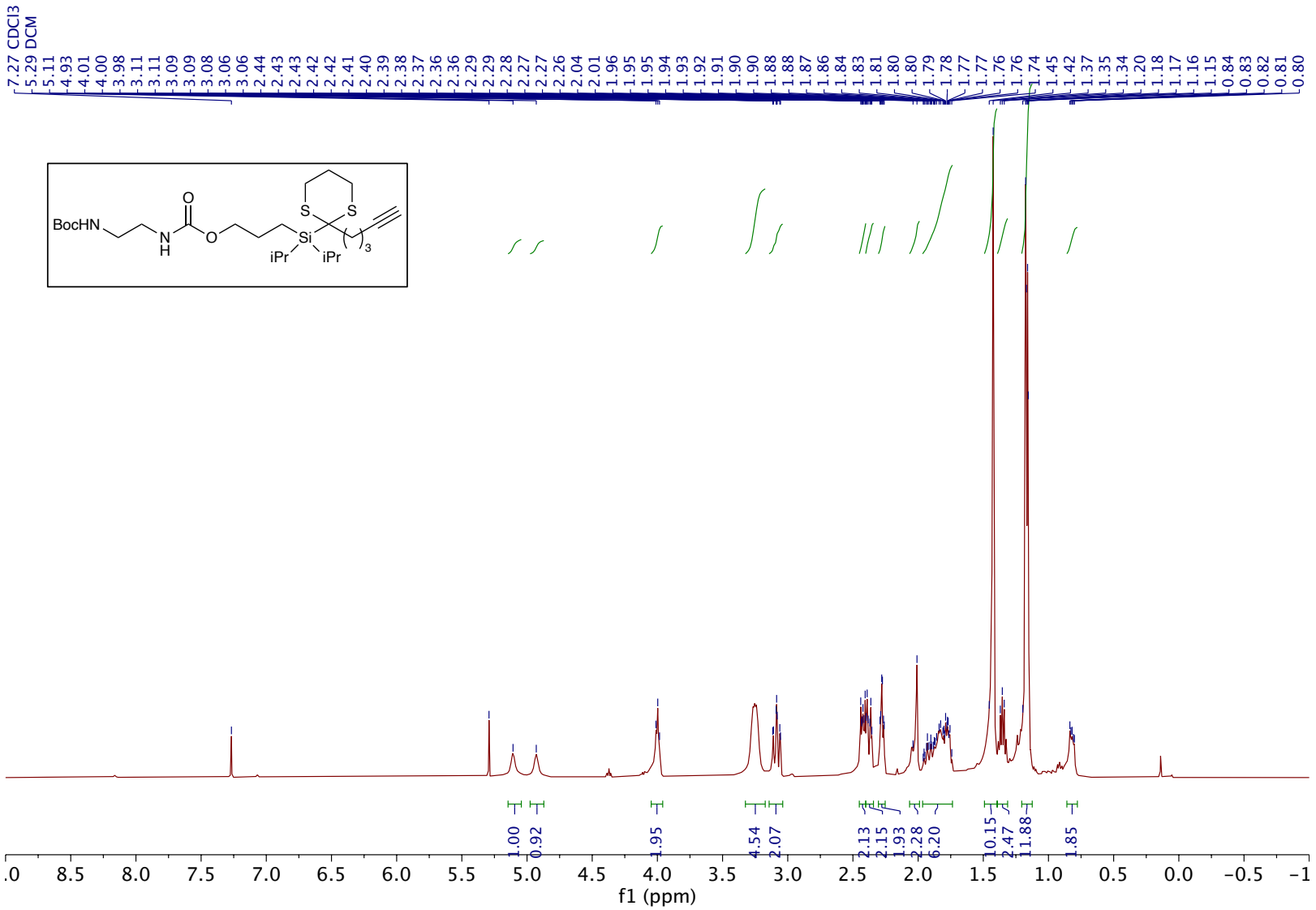
SI-2


7.27 CDCl3
5.30 DCM
4.64
4.14 EtOAc
4.12 EtOAc
4.11 EtOAc
4.09 EtOAc
3.12
3.07
2.45
2.41
2.40
2.37
2.28
2.04 EtOAc
1.96
1.89
1.81
1.75
1.73
1.67
1.44
1.38
1.32
1.27 EtOAc
1.25 EtOAc
1.24 EtOAc
1.18
1.17
1.16
0.83
0.79
BocHN
Si
iPr
iPr
S
S
3
0.80
3.76
1.89
1.91
1.94
2.23
1.02
1.03
1.92
2.07
8.83
2.10
11.17
2.00
f1 (ppm)

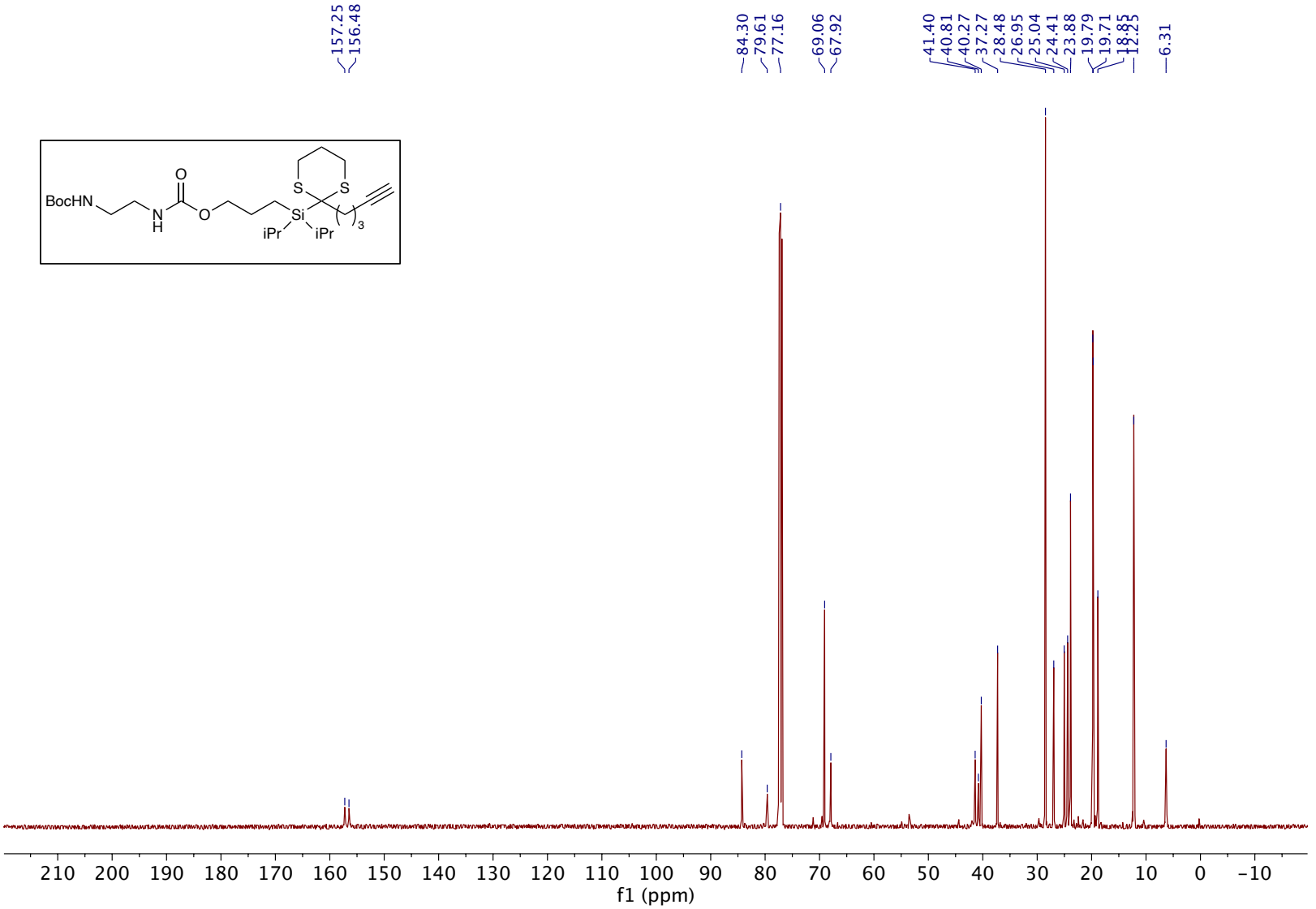
SI-2


156.05
84.29
79.04
77.16
69.06
44.13
40.34
37.29
28.56
26.98
25.07
23.90
19.82
19.73
18.86
12.28
7.53
BocHN
Si
iPr
iPr
S
S
3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

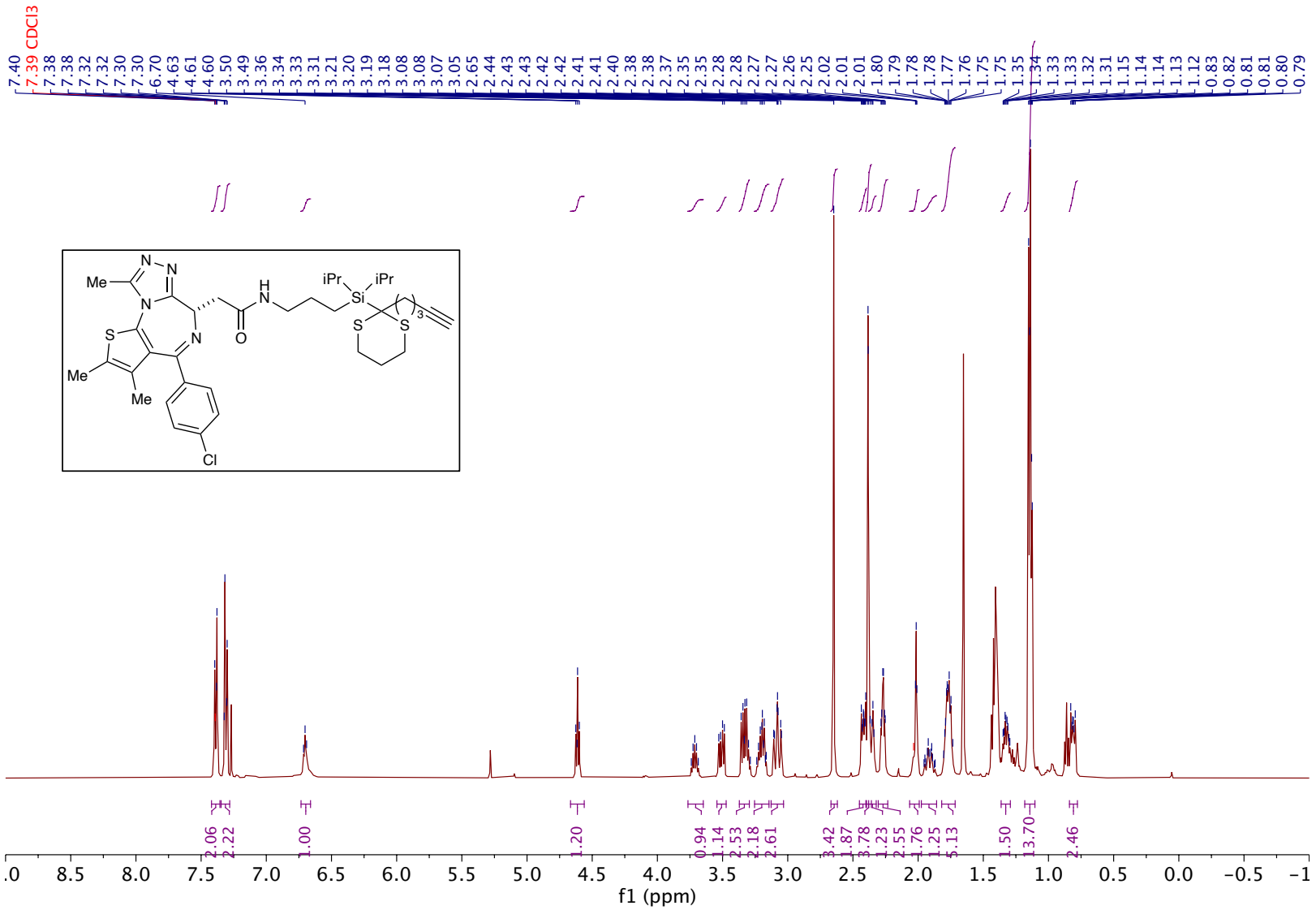
SI-4


7.27 CDCl3
5.29 DCM
BocHN
N
H
O
O
Si
iPr
iPr
S
S
3
1.00
0.92
1.95
4.54
2.07
2.13
2.15
1.93
2.28
6.20
10.15
2.47
11.88
1.85
f1 (ppm)

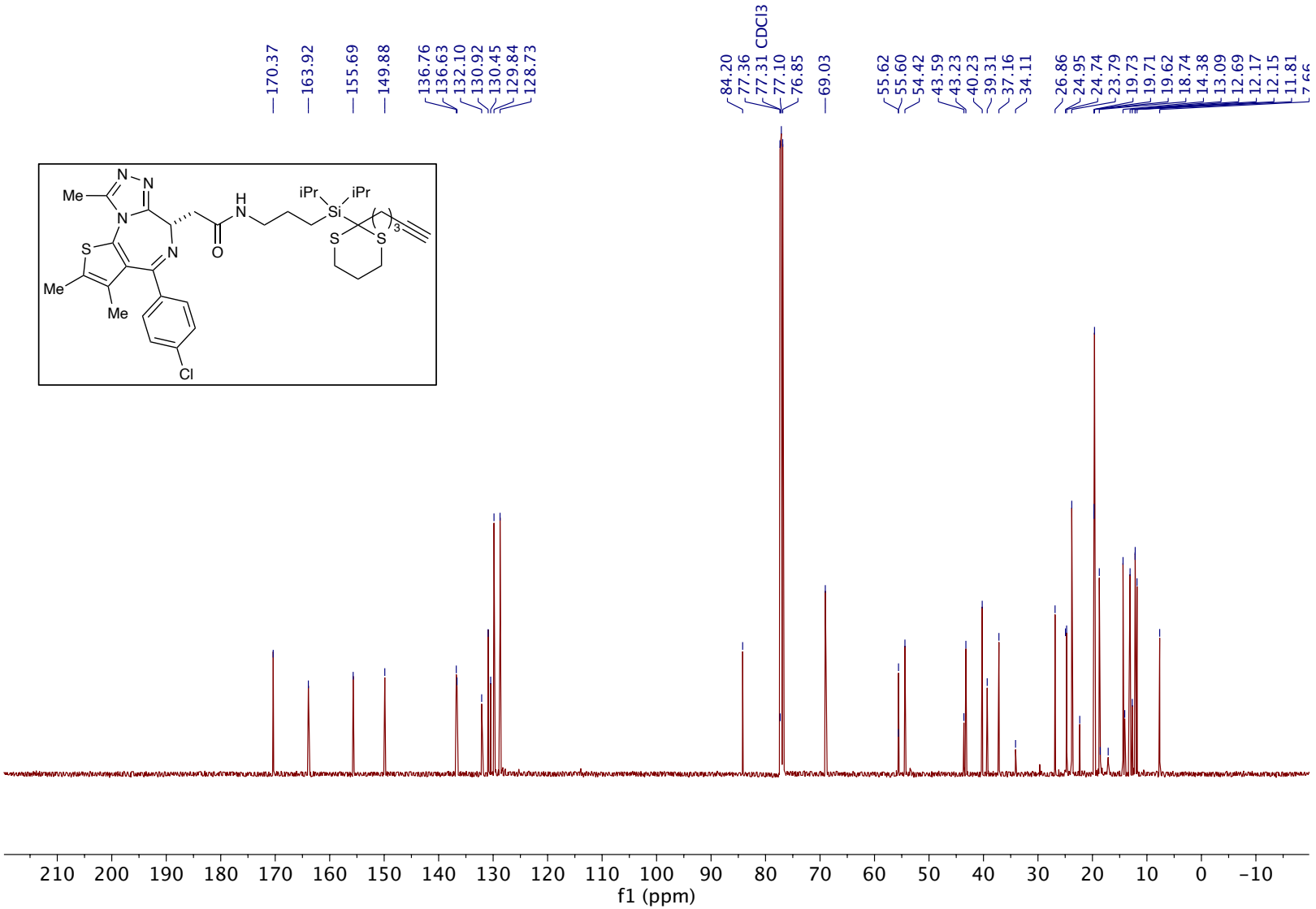
SI-4


157.25
156.48
84.30
79.61
77.16
69.06
67.92
41.40
40.81
40.27
37.27
28.48
26.95
25.04
24.41
23.88
19.79
19.71
18.85
12.25
6.31
BocHN
N
H
O
O
S
S
Si
iPr
iPr
3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

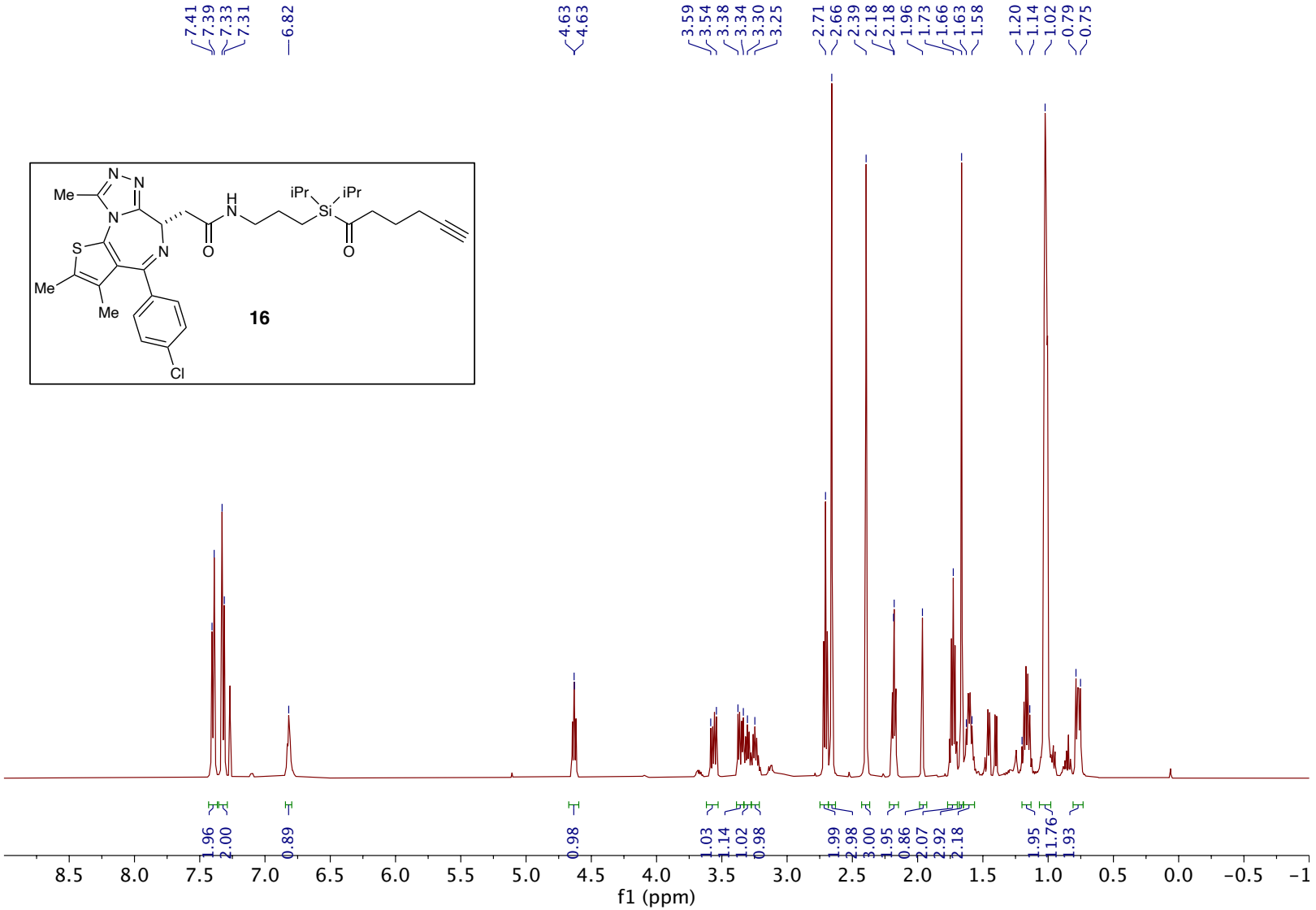
SI-6


7.40
7.39 CDCl3
7.38
7.38
7.32
7.32
7.30
7.30
6.70
4.63
4.61
4.60
3.50
3.49
3.36
3.34
3.33
3.31
3.21
3.20
3.19
3.18
3.08
3.08
3.07
3.05
2.65
2.44
2.43
2.43
2.42
2.42
2.41
2.41
2.40
2.38
2.38
2.37
2.35
2.35
2.28
2.28
2.27
2.27
2.26
2.25
2.02
2.01
2.01
1.80
1.79
1.78
1.78
1.77
1.76
1.75
1.75
1.35
1.34
1.33
1.33
1.32
1.31
1.15
1.14
1.14
1.13
1.12
0.83
0.82
0.81
0.81
0.80
0.79
Me
N
N
N
S
N
H
N
O
iPr
iPr
Si
S
S
3
Me
Me
Cl
2.06
2.22
1.00
1.20
0.94
1.14
2.53
2.18
2.61
3.42
1.87
3.78
1.23
2.55
1.76
1.25
5.13
1.50
13.70
2.46
f1 (ppm)

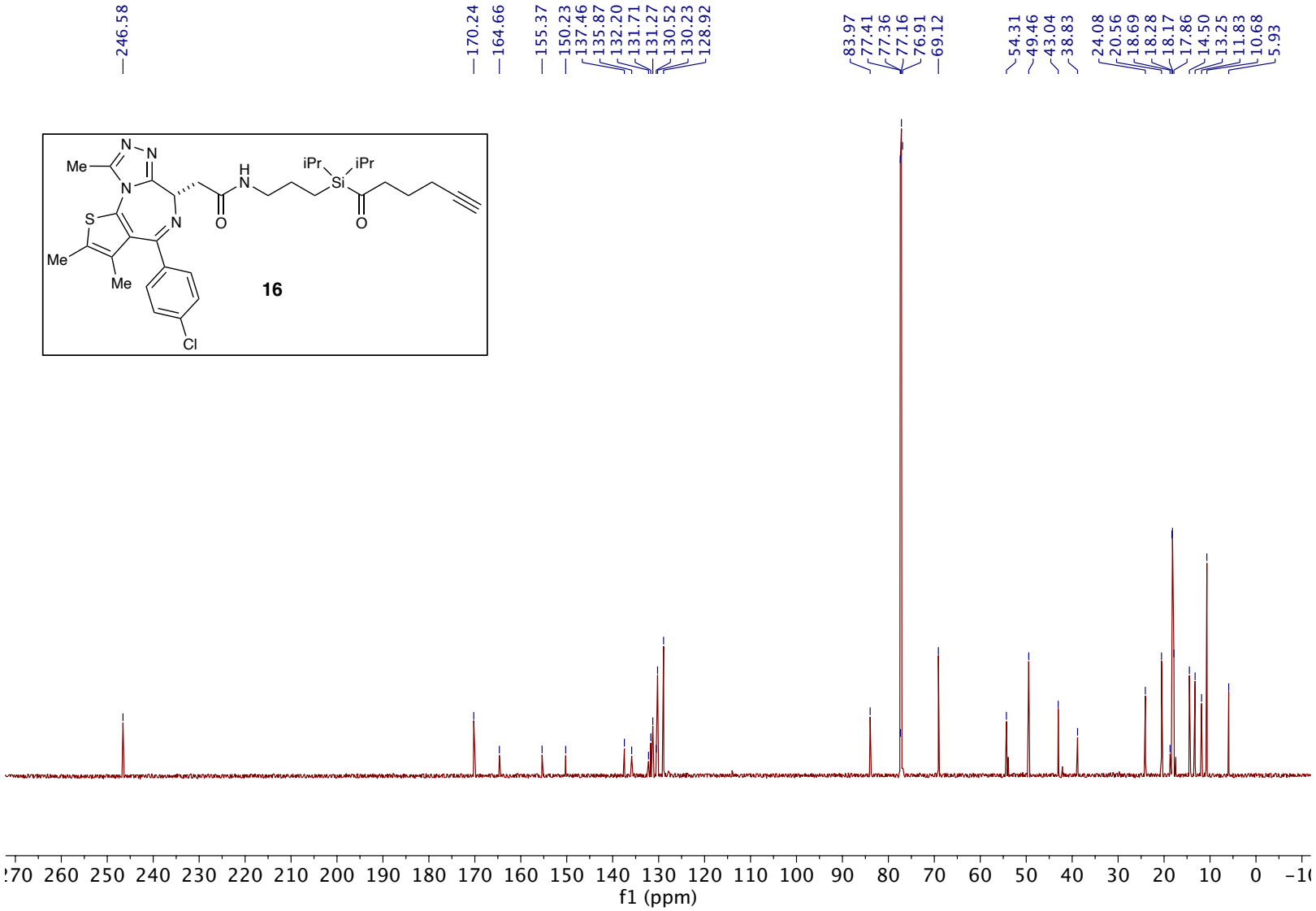
SI-6


170.37
163.92
155.69
149.88
136.76
136.63
132.10
130.92
130.45
129.84
128.73
84.20
77.36
77.31 CDCl3
77.10
76.85
69.03
55.62
55.60
54.42
43.59
43.23
40.23
39.31
37.16
34.11
26.86
24.95
24.74
23.79
19.73
19.71
19.62
18.74
14.38
13.09
12.69
12.17
12.15
11.81
Me
N
N
N
H
N
O
iPr
iPr
Si
S
S
3
S
Me
Me
N
Cl
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

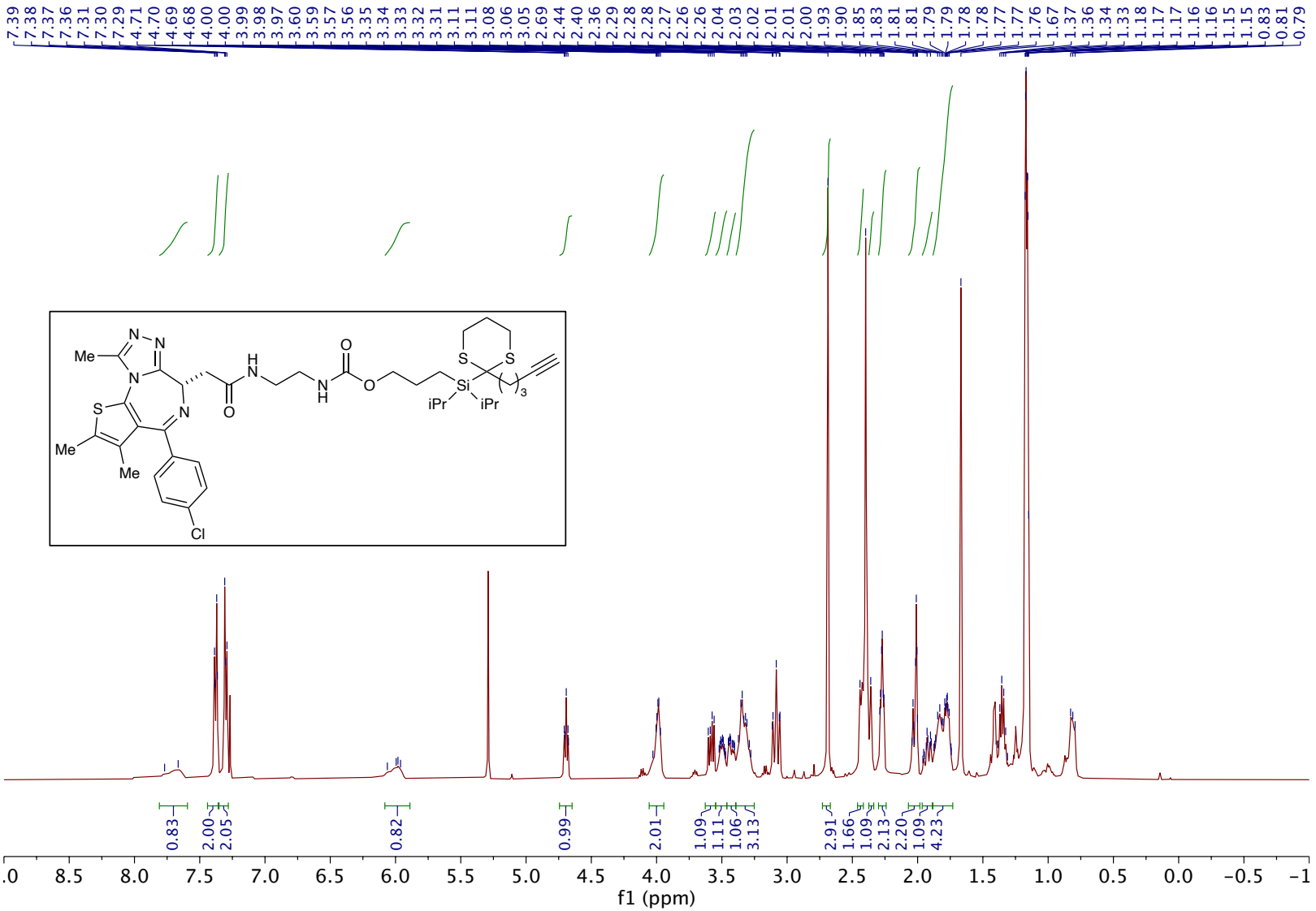
16


7.41
7.39
7.33
7.31
6.82
4.63
4.63
3.59
3.54
3.38
3.34
3.30
3.25
2.71
2.66
2.39
2.18
2.18
1.96
1.73
1.66
1.63
1.58
1.20
1.14
1.02
0.79
0.75
Me
N
N
N
H
N
iPr
Si
iPr
S
N
O
O
Me
Me
16
Cl
1.96
2.00
0.89
0.98
1.03
1.14
1.02
0.98
1.99
2.98
3.00
1.95
0.86
2.07
2.92
2.18
1.95
11.76
1.93
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

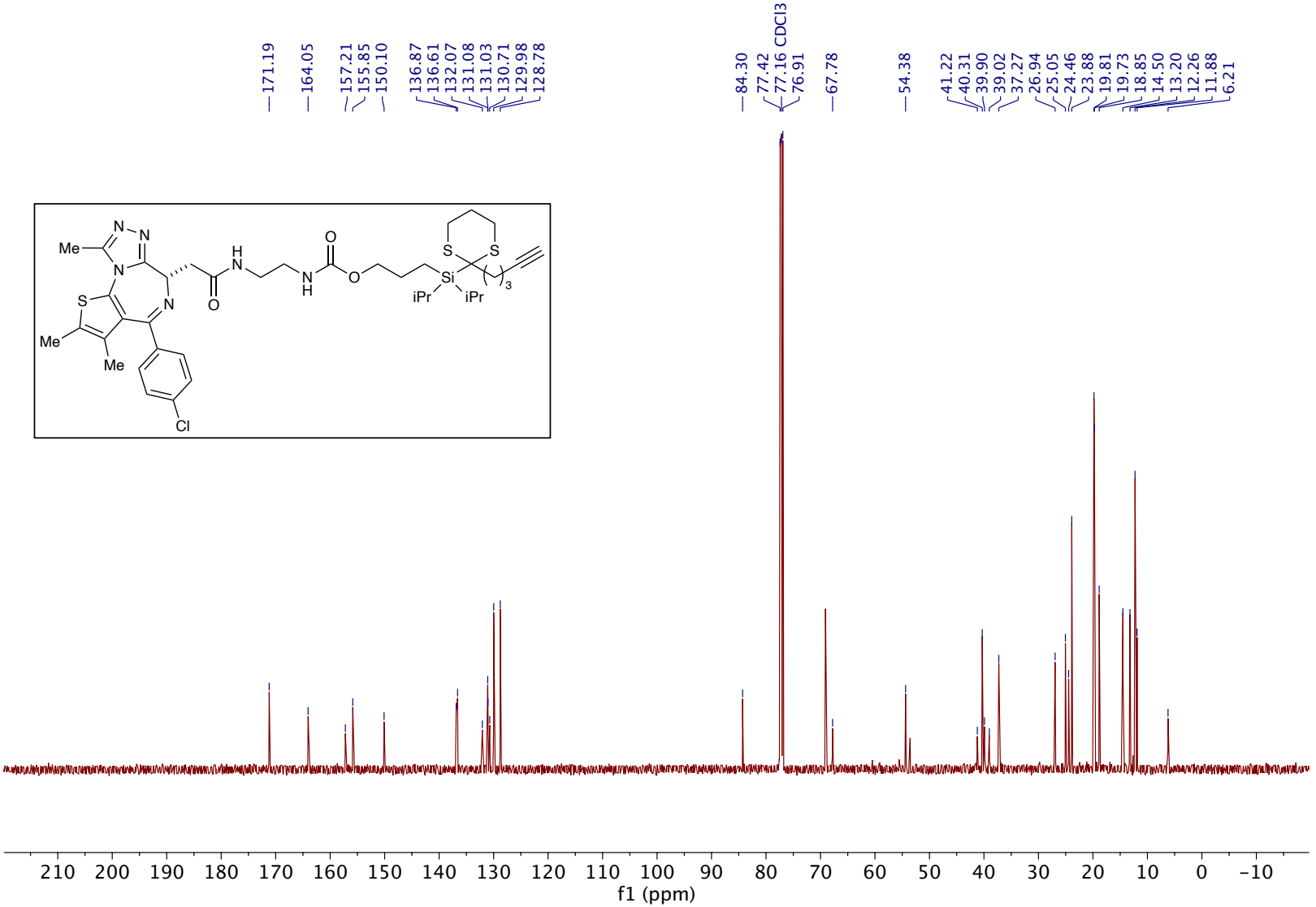
16


246.58
170.24
164.66
155.37
150.23
137.46
135.87
132.20
131.71
131.27
130.52
130.23
128.92
83.97
77.41
77.36
77.16
76.91
69.12
54.31
49.46
43.04
38.83
24.08
20.56
18.69
18.28
18.17
17.86
14.50
13.25
11.83
10.68
5.93
Me
N
N
N
S
N
H
N
O
iPr
Si
iPr
O
Me
Me
Cl
16
f1 (ppm)

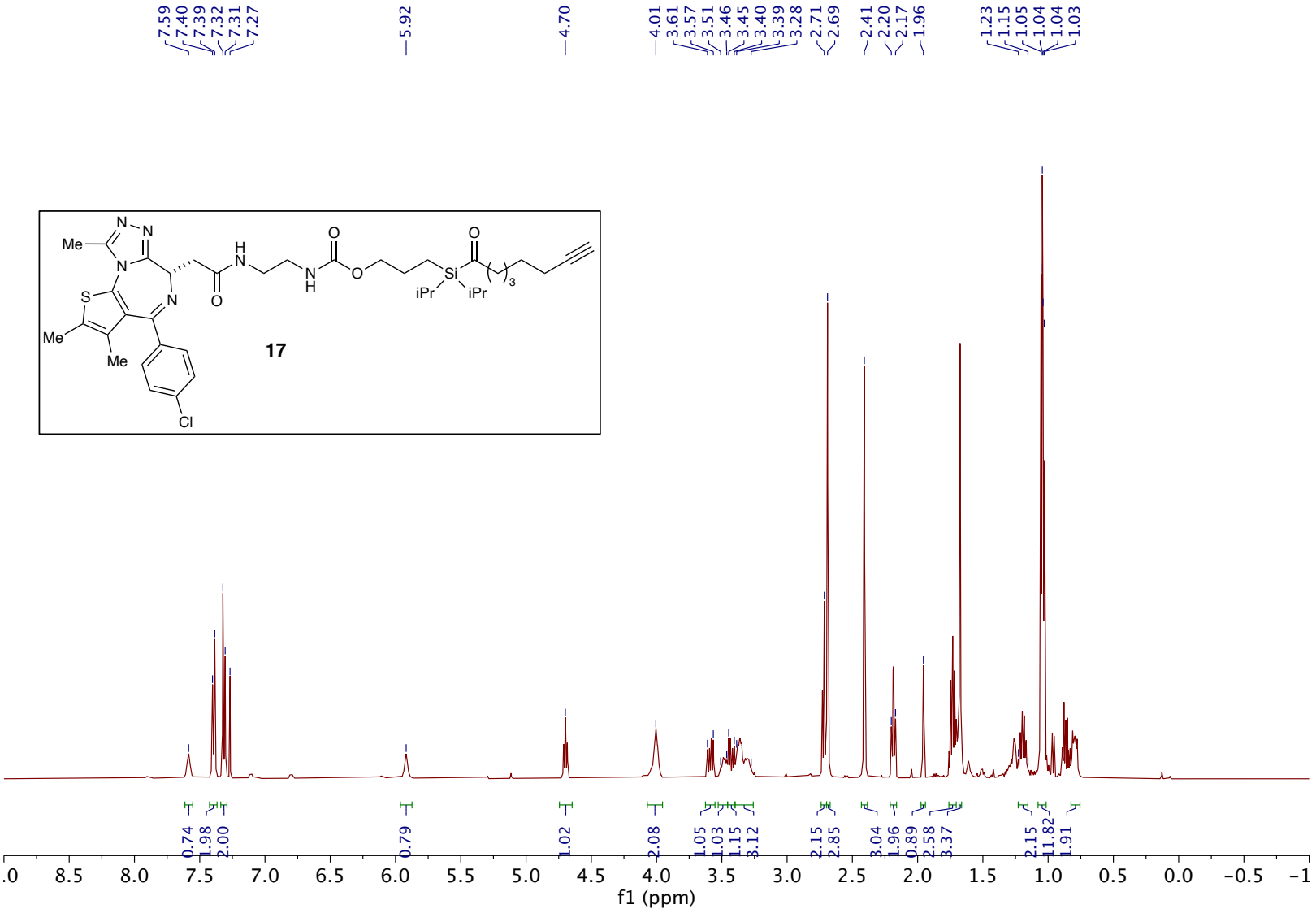
SI-7


7.39 7.38 7.37 7.36 7.31 7.30 7.29 4.71 4.70 4.69 4.68 4.00 4.00 3.99 3.98 3.97 3.60 3.59 3.57 3.56 3.35 3.34 3.33 3.32 3.31 3.11 3.11 3.08 3.06 3.05 2.69 2.44 2.40 2.36 2.29 2.28 2.28 2.27 2.26 2.26 2.04 2.03 2.02 2.01 2.00 1.93 1.90 1.85 1.83 1.81 1.81 1.79 1.79 1.78 1.78 1.77 1.77 1.76 1.67 1.37 1.36 1.34 1.33 1.18 1.17 1.17 1.16 1.16 1.15 1.15 0.83 0.81 0.79
Me
N
N
N
S
N
Me
Me
Cl
O
H
N
O
N
H
O
S
S
Si
iPr
iPr
3
0.83 2.00 2.05 0.82 0.99 2.01 1.09 1.11 1.06 3.13 2.91 1.66 1.09 2.13 2.20 1.09 4.23
.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

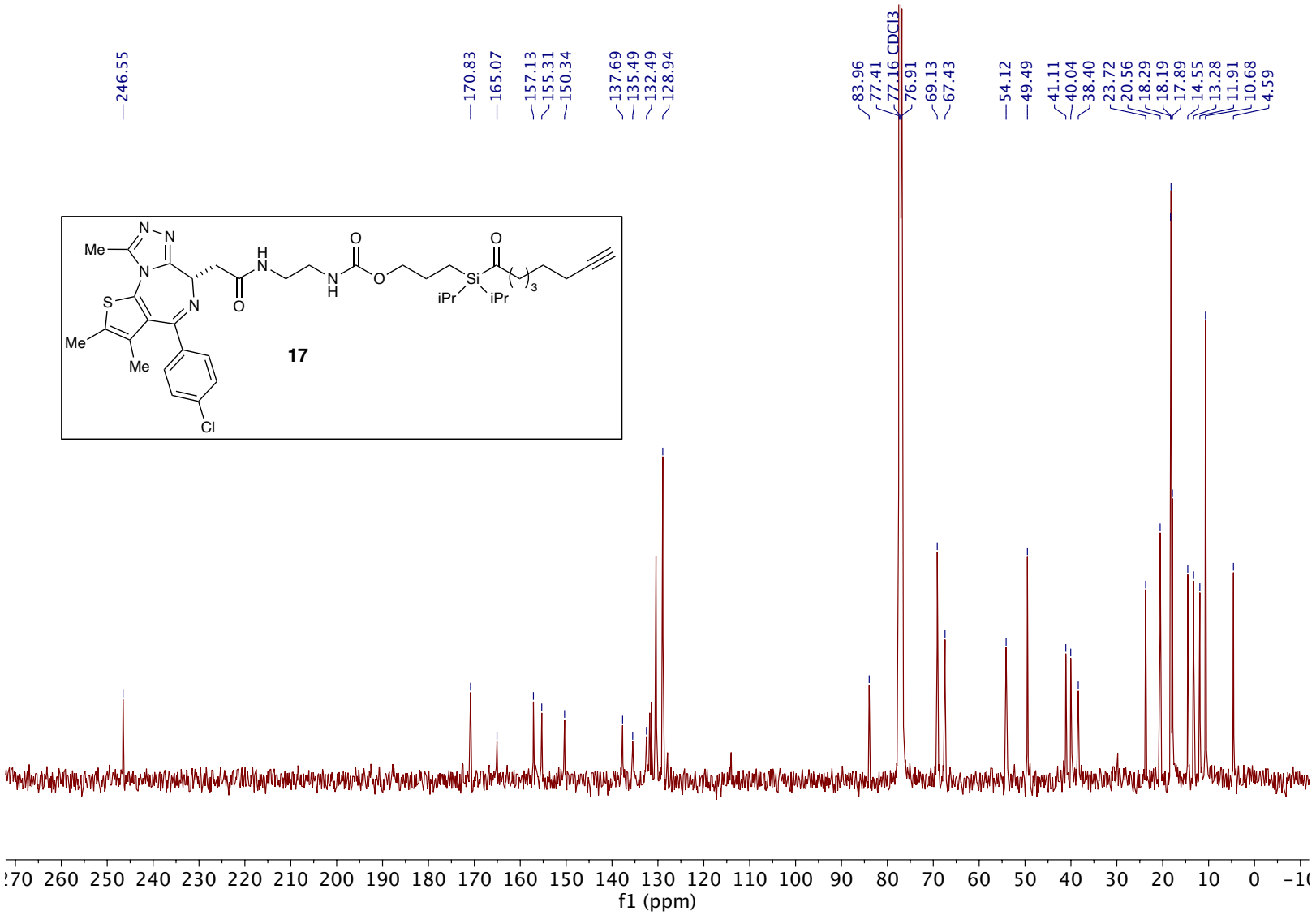
SI-7


171.19
164.05
157.21
155.85
150.10
136.87
136.61
132.07
131.08
131.03
130.71
129.98
128.78
84.30
77.42
77.16 CDCl3
76.91
67.78
54.38
41.22
40.31
39.90
39.02
37.27
26.94
25.05
24.46
23.88
19.81
19.73
18.85
14.50
13.20
12.26
11.88
6.21
Me
N
N
N
H
N
O
O
N
H
O
S
S
S
Si
iPr
iPr
3
Me
Me
Cl
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

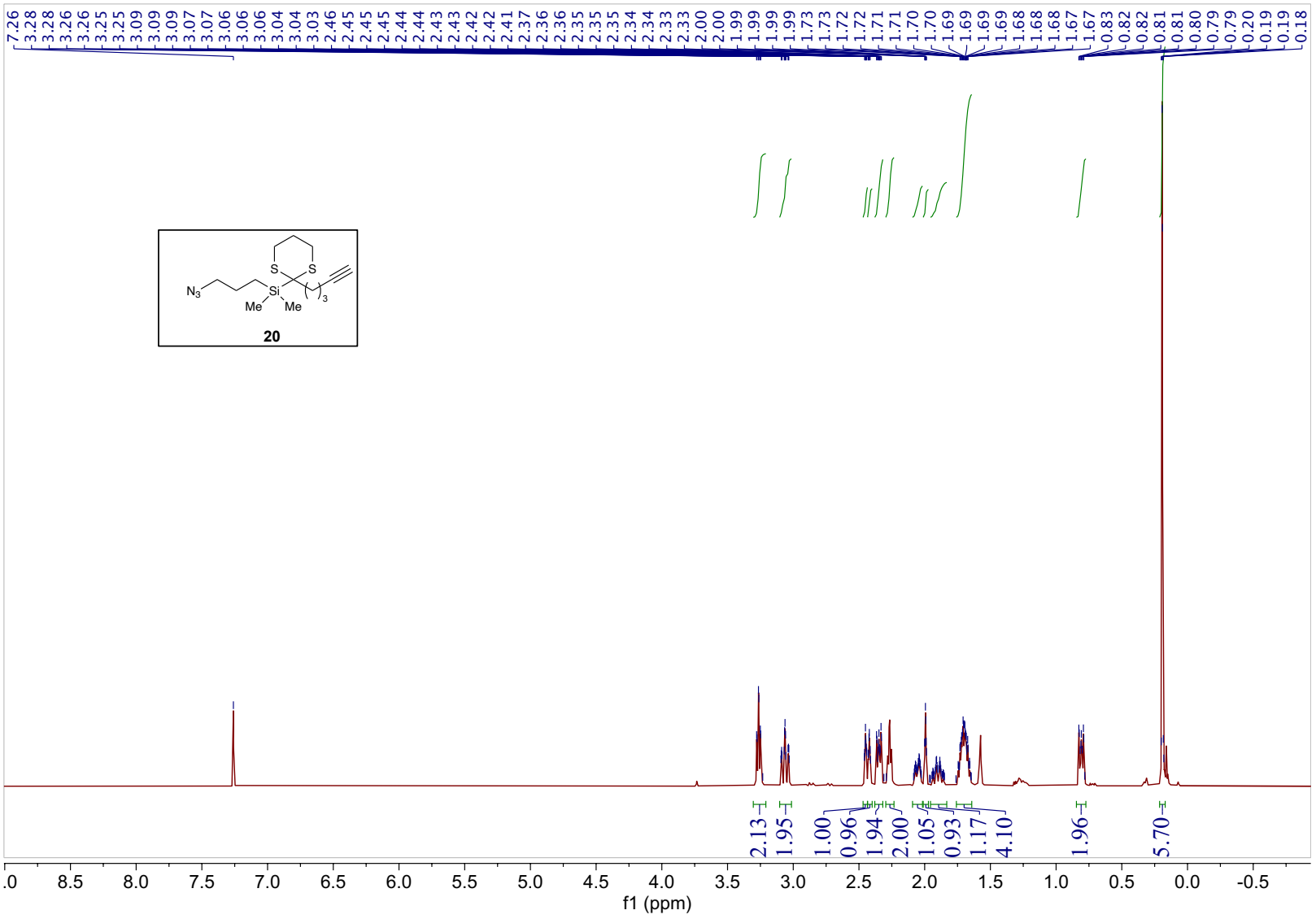
17


7.59
7.40
7.39
7.32
7.31
7.27
5.92
4.70
4.01
3.61
3.57
3.51
3.46
3.45
3.40
3.39
3.28
2.71
2.69
2.41
2.20
2.17
1.96
1.23
1.15
1.05
1.04
1.04
1.03
Me
N
N
N
S
N
H
N
O
O
N
H
O
O
Si
iPr
iPr
3
Me
Me
Cl
17
0.74
1.98
2.00
0.79
1.02
2.08
1.05
1.03
1.15
3.12
2.15
2.85
3.04
1.96
0.89
2.58
3.37
2.15
11.82
1.91
f1 (ppm)

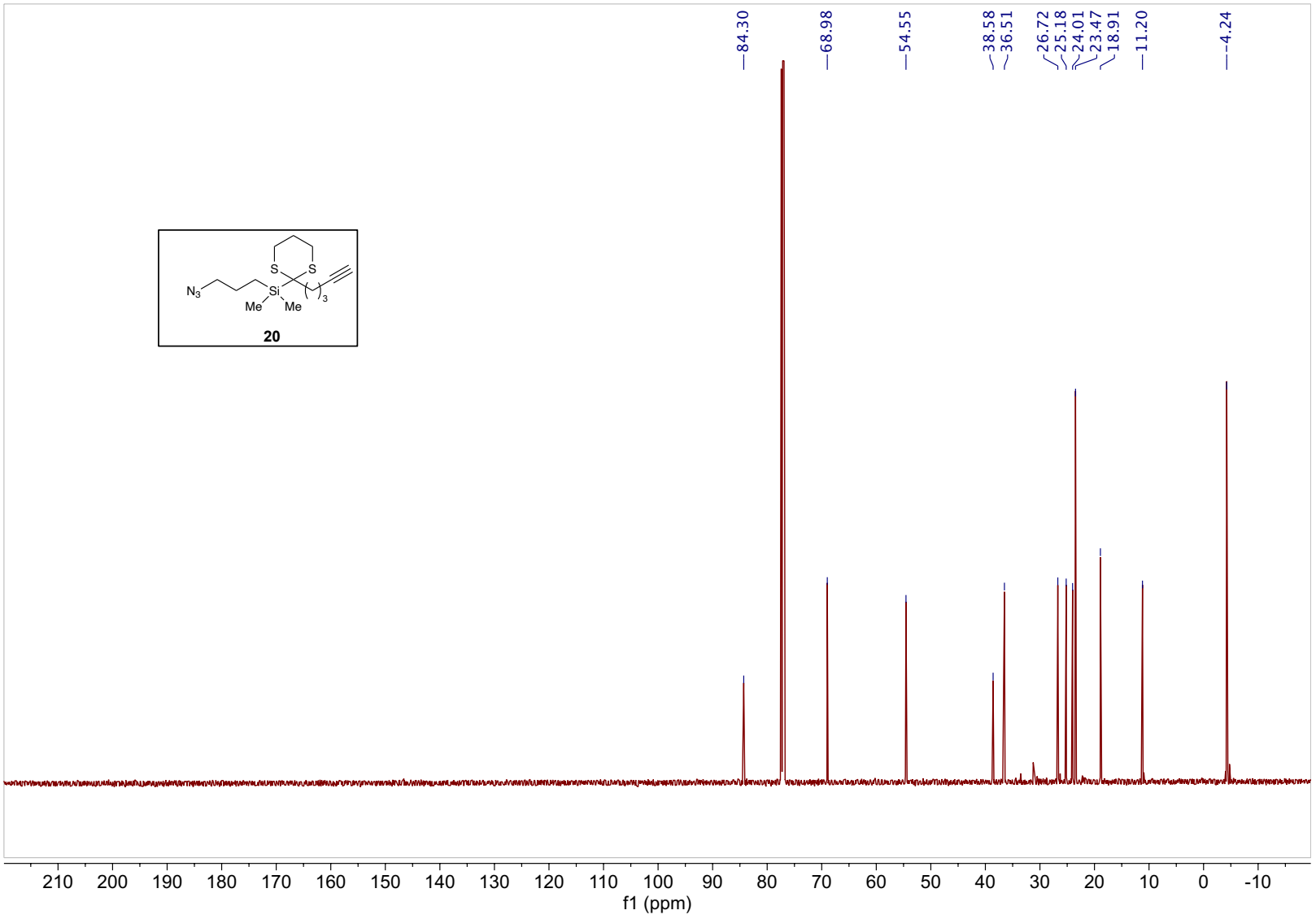
17


246.55
170.83
165.07
157.13
155.31
150.34
137.69
135.49
132.49
128.94
83.96
77.41
77.16 CDCl3
76.91
69.13
67.43
54.12
49.49
41.11
40.04
38.40
23.72
20.56
18.29
18.19
17.89
14.55
13.28
11.91
10.68
4.59
Me
Me
Me
Cl
iPr
iPr
17
f1 (ppm)

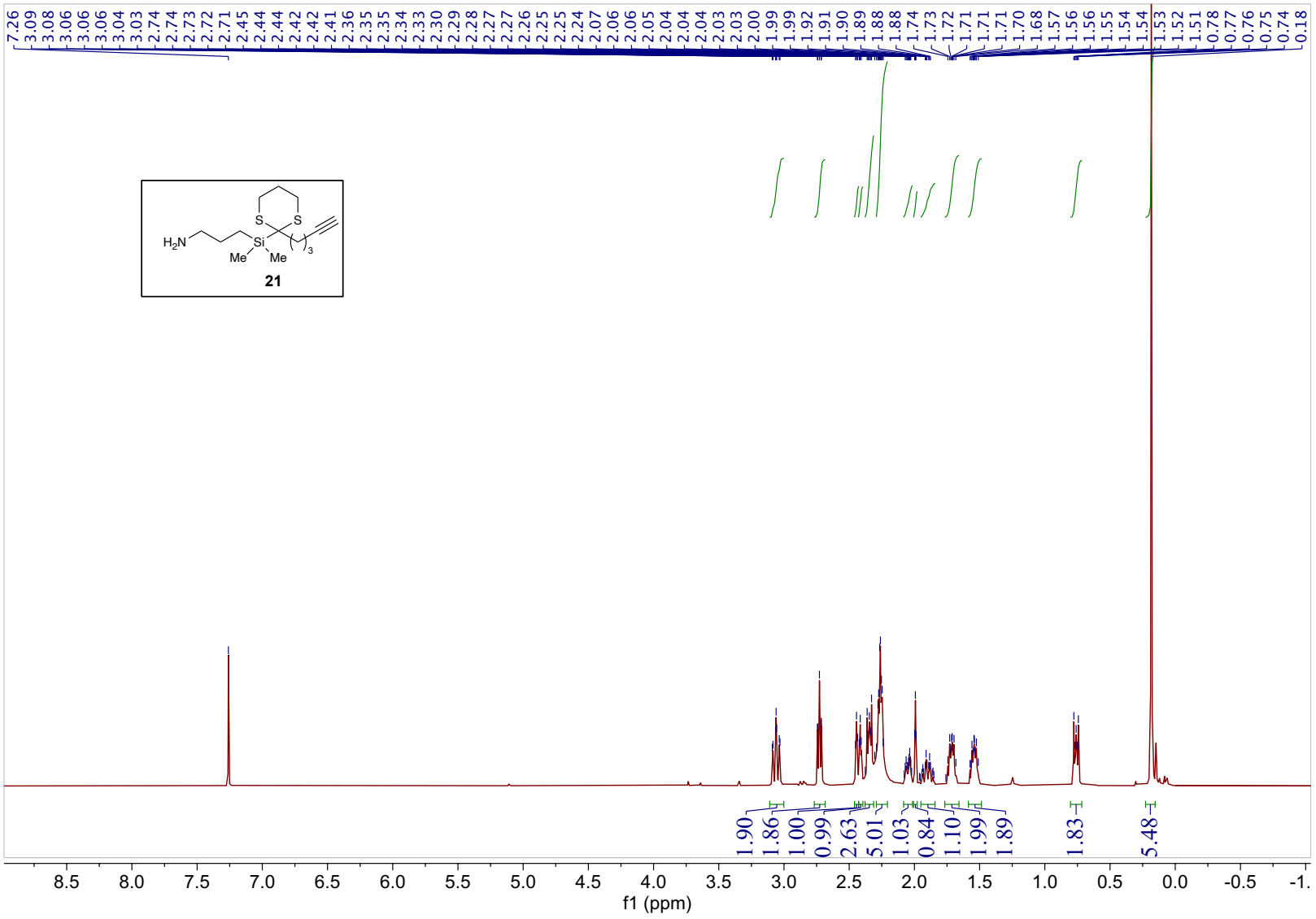
20



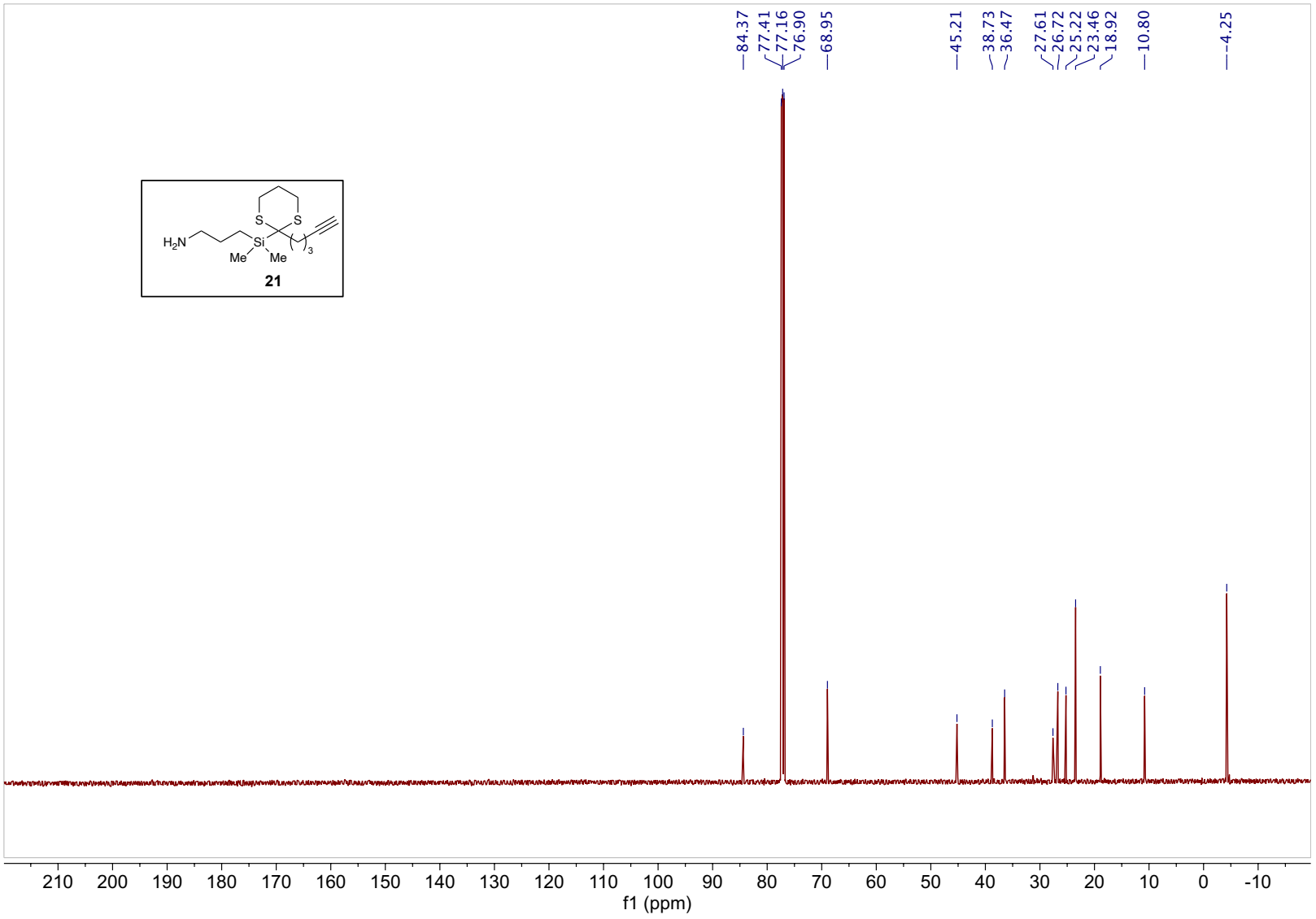
20


84.30
68.98
54.55
38.58
36.51
26.72
25.18
24.01
23.47
18.91
11.20
4.24
S
S
N3
Si
Me
Me
3
20
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

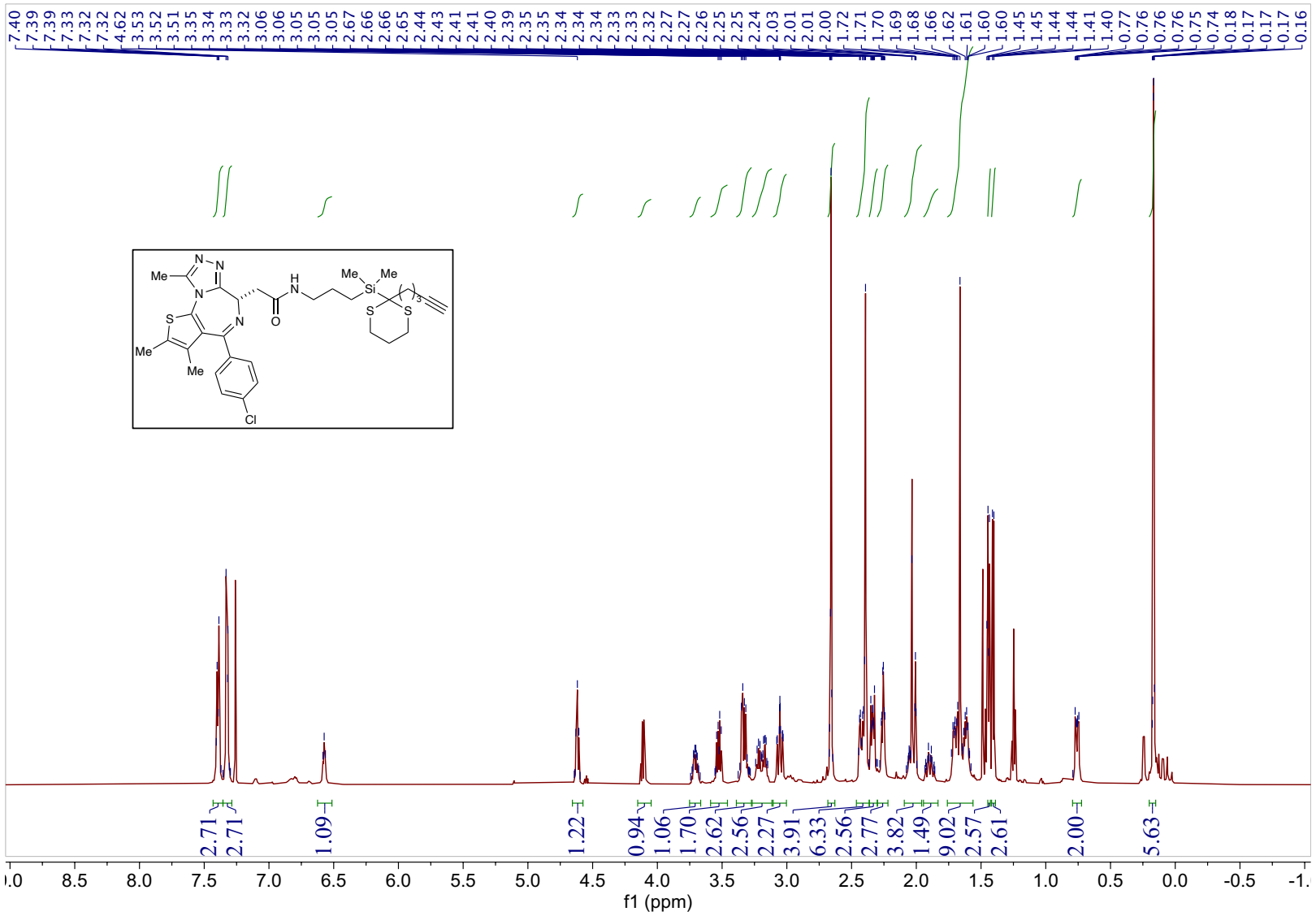
21


7.26 3.09 3.08 3.06 3.06 3.06 3.04 3.03 2.74 2.74 2.73 2.72 2.71 2.45 2.44 2.44 2.42 2.42 2.41 2.36 2.35 2.35 2.34 2.33 2.30 2.29 2.28 2.27 2.27 2.26 2.25 2.25 2.24 2.07 2.06 2.06 2.05 2.04 2.04 2.04 2.03 2.03 2.00 1.99 1.99 1.92 1.91 1.90 1.89 1.88 1.88 1.74 1.73 1.72 1.71 1.71 1.71 1.70 1.68 1.57 1.56 1.56 1.55 1.54 1.54 1.53 1.52 1.51 0.78 0.77 0.76 0.75 0.74 0.18
H2N
Si
S
S
Me
Me
3
21
1.90 1.86 1.00 0.99 2.63 5.01 1.03 0.84 1.10 1.99 1.89 1.83 5.48
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

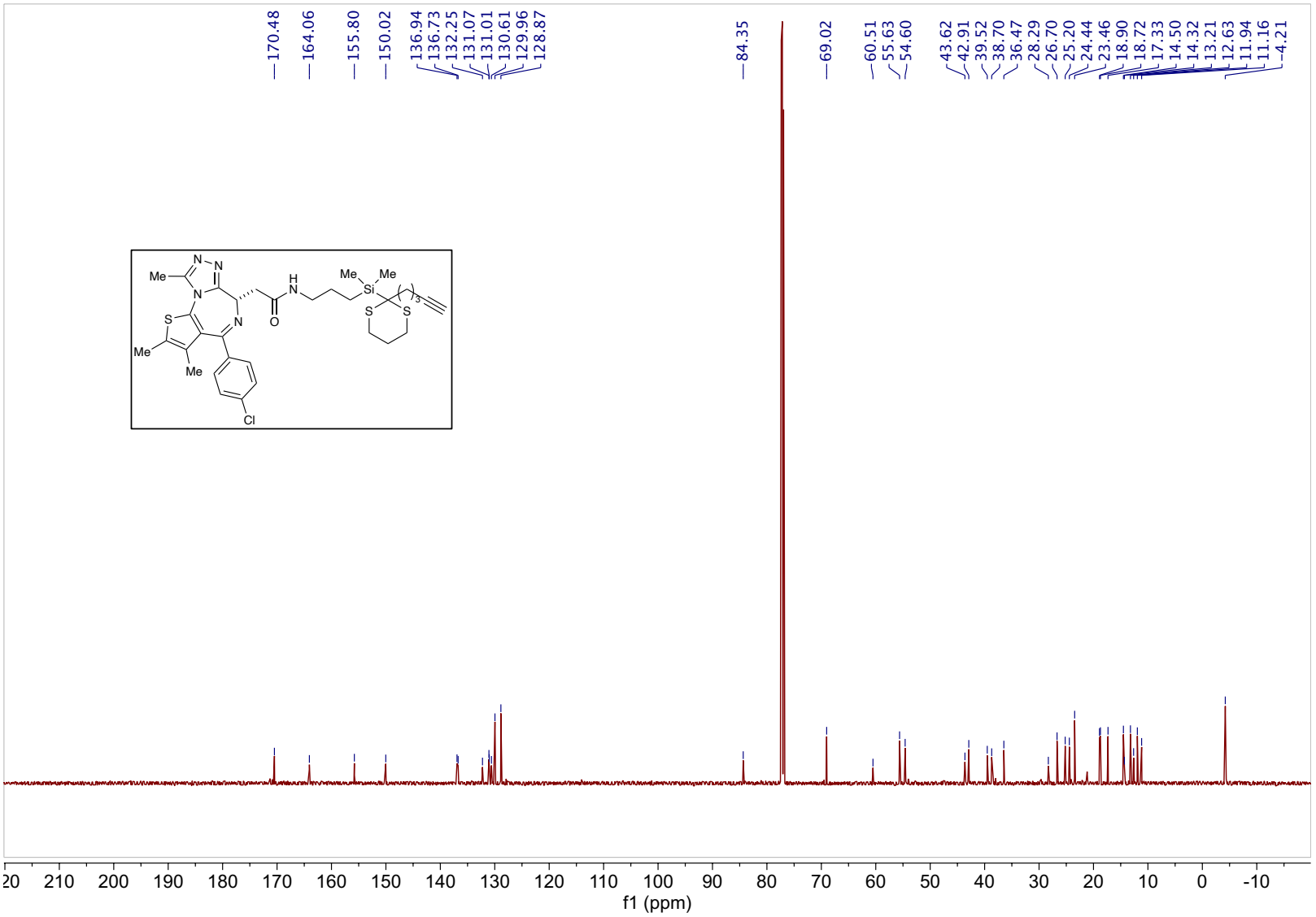
21


84.37
77.41
77.16
76.90
68.95
45.21
38.73
36.47
27.61
26.72
25.22
23.46
18.92
10.80
4.25
S
S
Si
Me
Me
H_2N
3
21
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

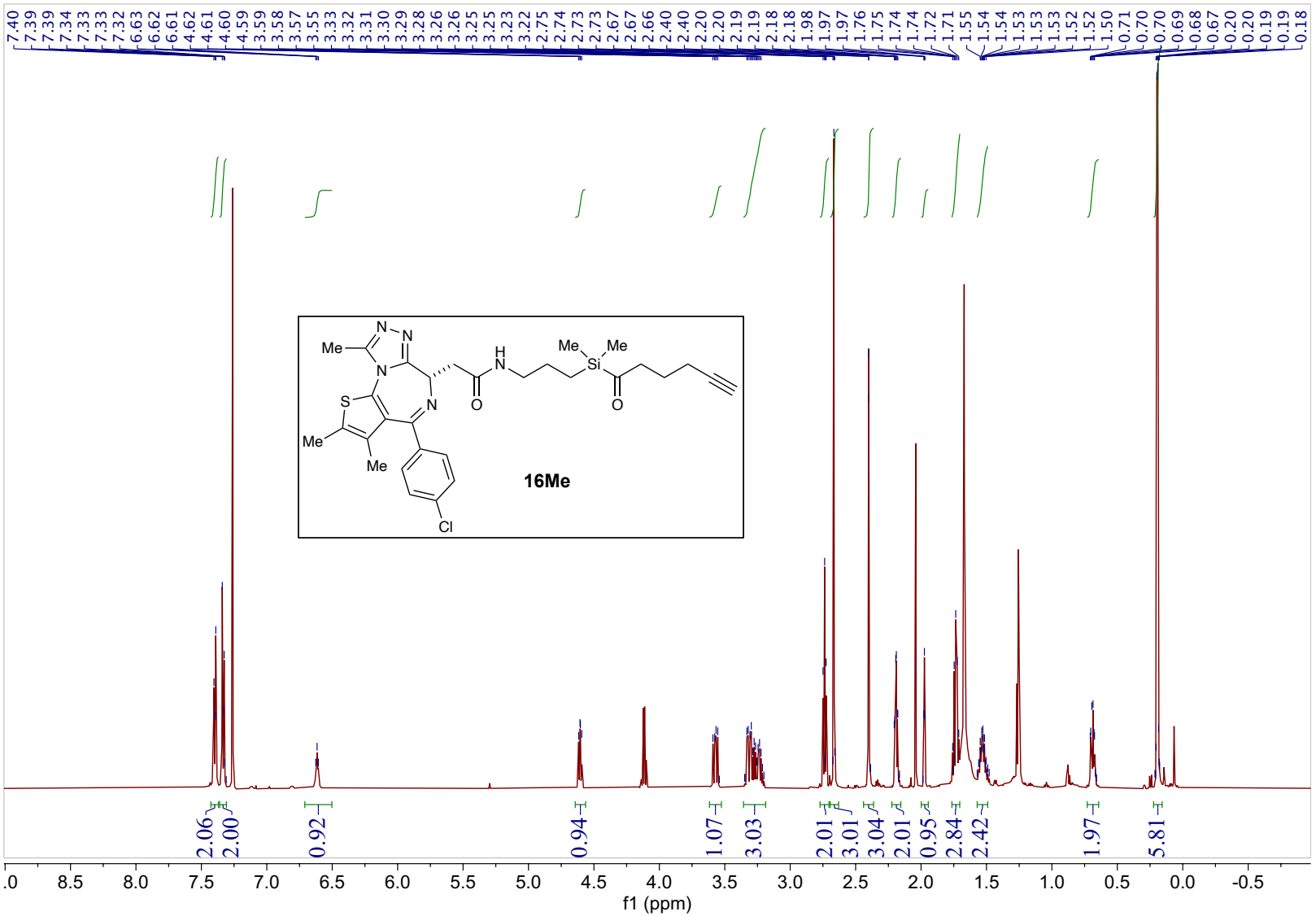
SI-8


7.40 7.39 7.39 7.33 7.32 7.32 4.62 3.53 3.52 3.51 3.35 3.34 3.33 3.32 3.06 3.06 3.05 3.05 3.05 2.67 2.66 2.66 2.65 2.44 2.43 2.41 2.41 2.40 2.39 2.35 2.35 2.34 2.34 2.34 2.33 2.33 2.32 2.27 2.27 2.26 2.25 2.25 2.24 2.03 2.01 2.01 2.00 1.72 1.71 1.70 1.69 1.68 1.66 1.62 1.61 1.60 1.60 1.45 1.45 1.44 1.44 1.41 1.40 0.77 0.76 0.76 0.76 0.75 0.74 0.18 0.17 0.17 0.17 0.16
Me
N
N
N
S
Me
Me
N
O
H
N
Me
Si
Me
S
S
5
Cl
2.71 2.71 1.09 1.22 0.94 1.06 1.70 2.62 2.56 2.27 3.91 6.33 2.56 2.77 3.82 1.49 9.02 2.57 2.61 2.00 5.63
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

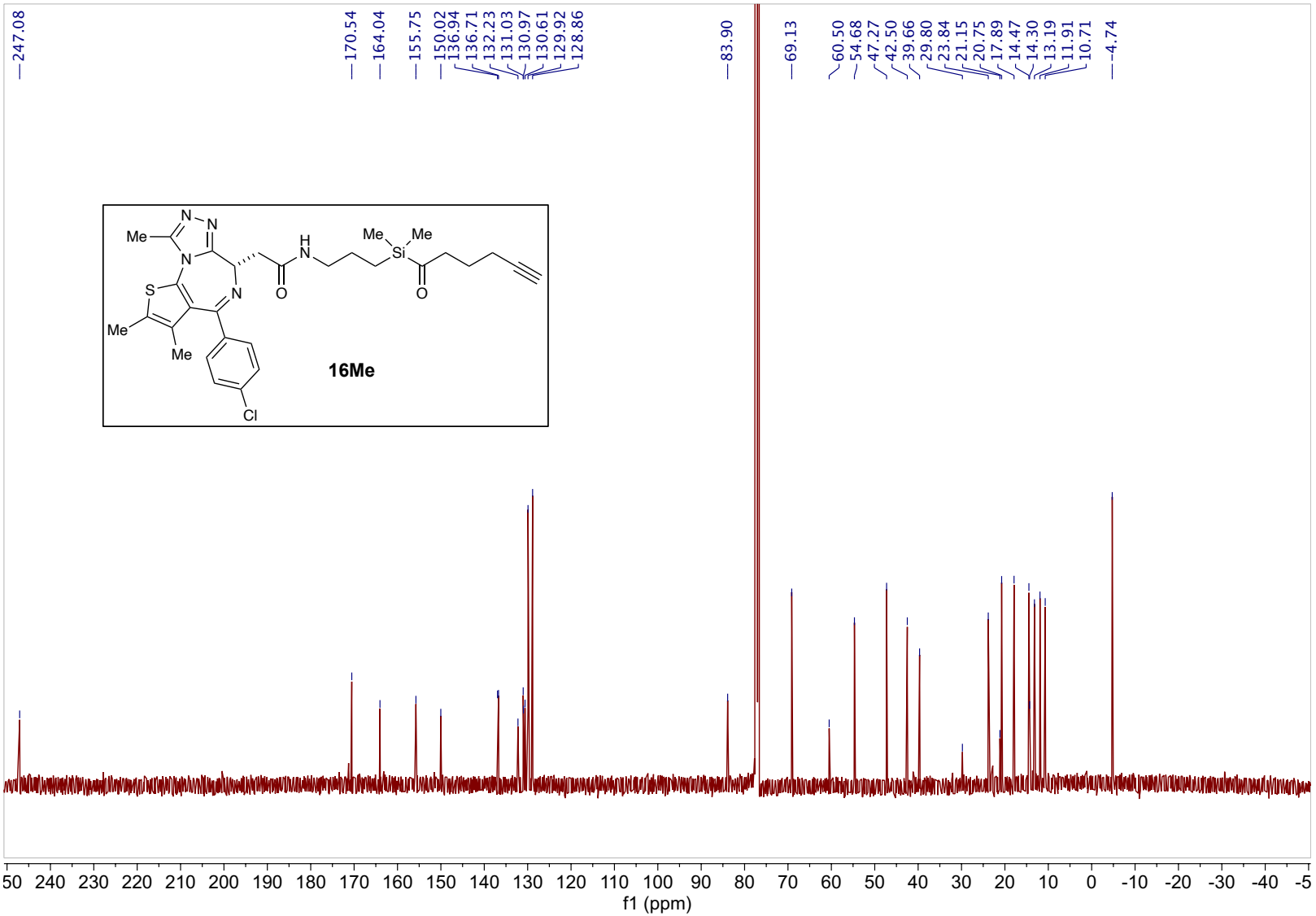
SI-8


170.48
164.06
155.80
150.02
136.94
136.73
132.25
131.07
131.01
130.61
129.96
128.87
84.35
69.02
60.51
55.63
54.60
43.62
42.91
39.52
38.70
36.47
28.29
26.70
25.20
24.44
23.46
18.90
18.72
17.33
14.50
14.32
13.21
12.63
11.94
11.16
4.21
Me
N
N
N
S
Me
Me
Cl
H
N
O
Me
Me
Si
S
S
5
f1 (ppm)

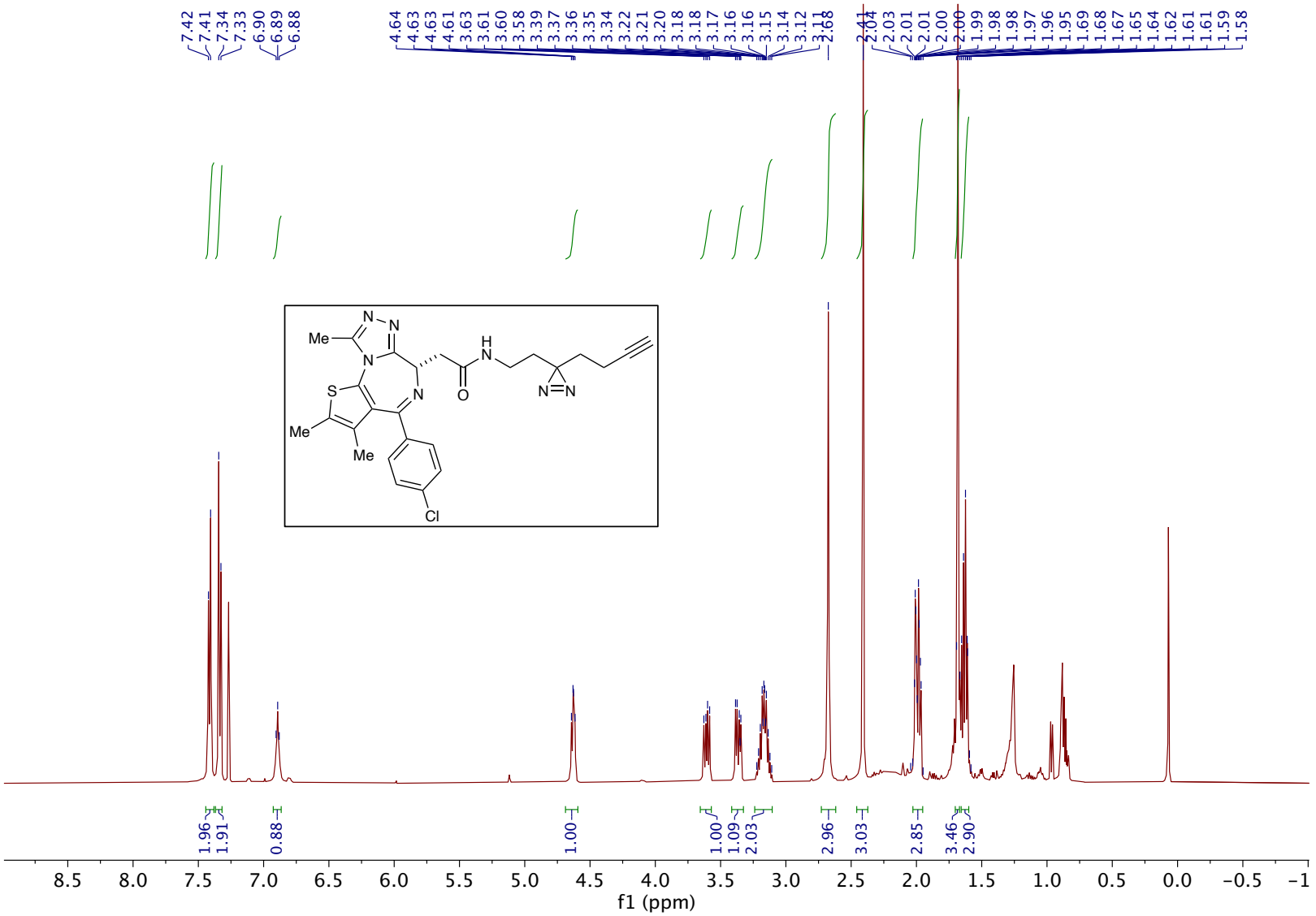
16-Me



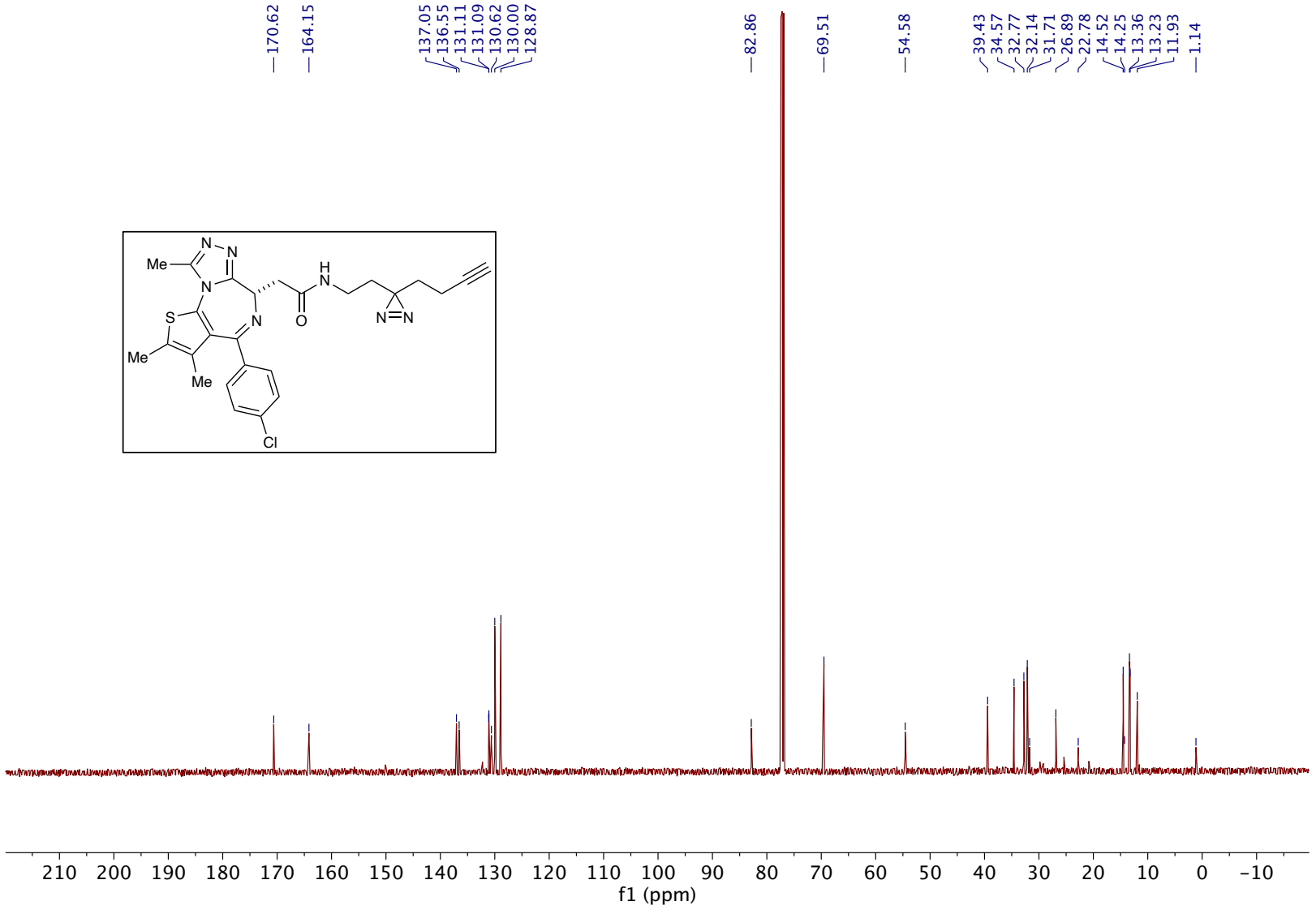
16-Me


247.08
170.54
164.04
155.75
150.02
136.94
136.71
132.23
131.03
130.97
130.61
129.92
128.86
83.90
69.13
60.50
54.68
47.27
42.50
39.66
29.80
23.84
21.15
20.75
17.89
14.47
14.30
13.19
11.91
10.71
4.74
16Me
f1 (ppm)

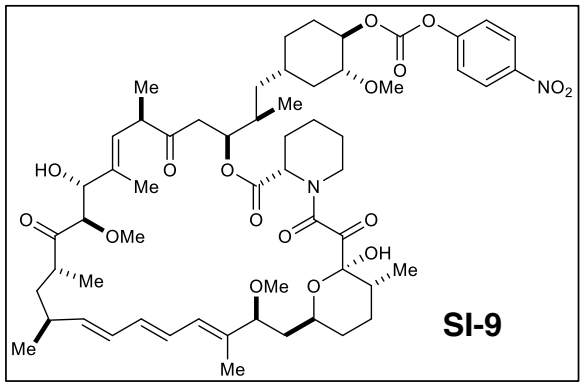
16-DA

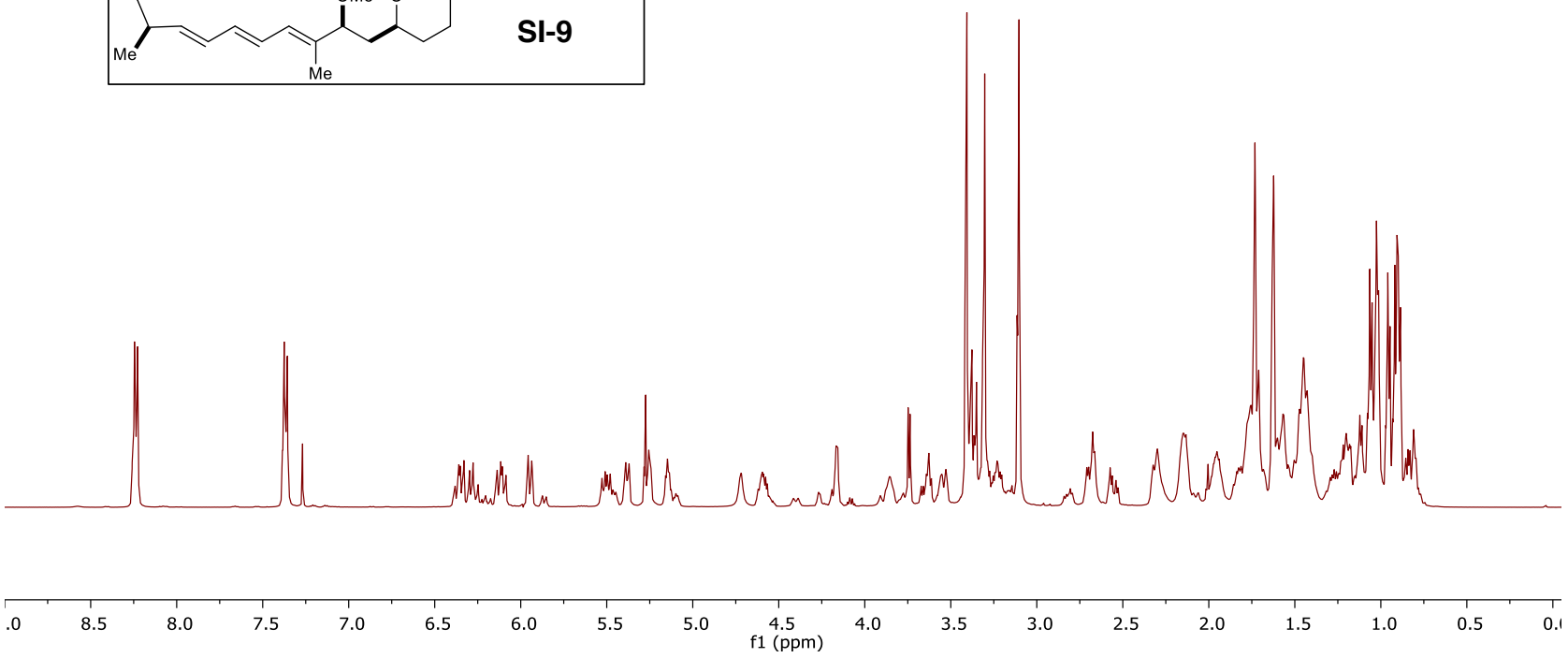

7.42
7.41
7.34
7.33
6.90
6.89
6.88
4.64
4.63
4.63
4.61
4.61
3.63
3.61
3.60
3.58
3.39
3.37
3.36
3.35
3.34
3.22
3.21
3.20
3.18
3.18
3.17
3.16
3.16
3.15
3.14
3.12
3.11
2.68
2.41
2.04
2.03
2.01
2.01
2.00
2.00
1.99
1.98
1.98
1.97
1.96
1.95
1.69
1.68
1.67
1.65
1.64
1.62
1.61
1.61
1.59
1.58
Me
N
N
N
S
N
H
N
O
N=N
Me
Me
Cl
1.96
1.91
0.88
1.00
1.00
1.09
2.03
2.96
3.03
2.85
3.46
2.90
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

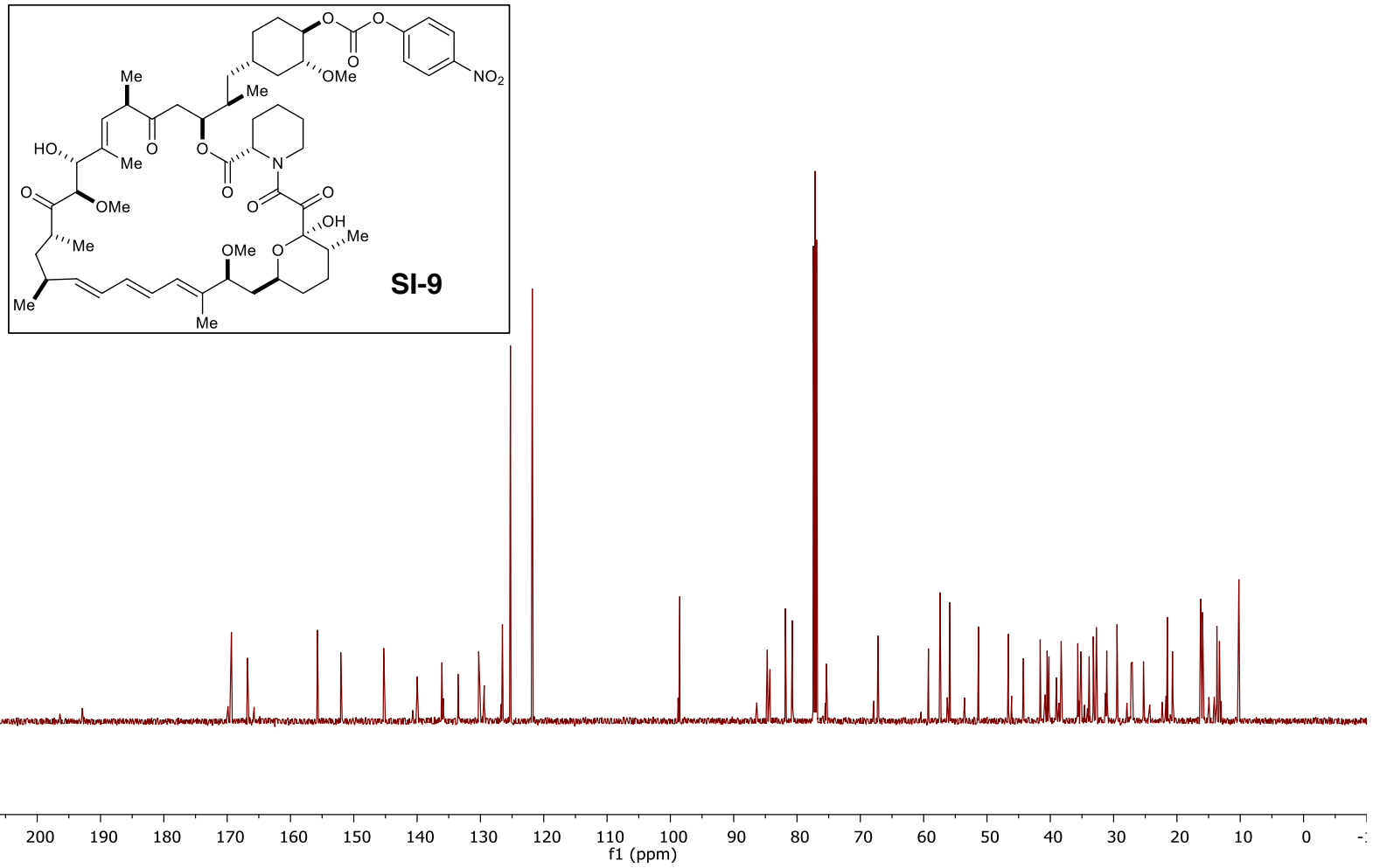
16-DA

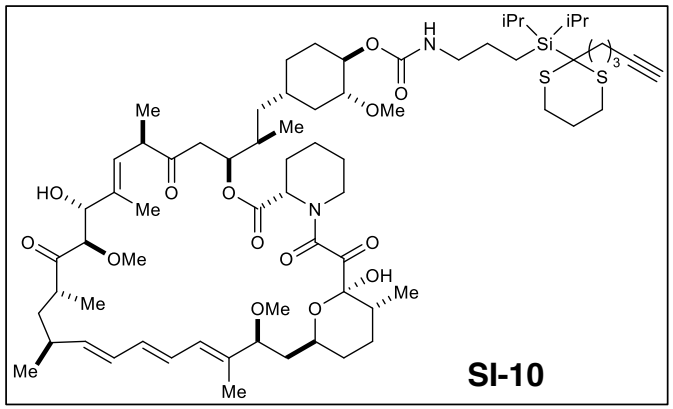

170.62
164.15
137.05
136.55
131.11
131.09
130.62
130.00
128.87
82.86
69.51
54.58
39.43
34.57
32.77
32.14
31.71
26.89
22.78
14.52
14.25
13.36
13.23
11.93
1.14
Me
N
N
N
S
N
H
N
O
N=N
Me
Me
Cl
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

SI-9

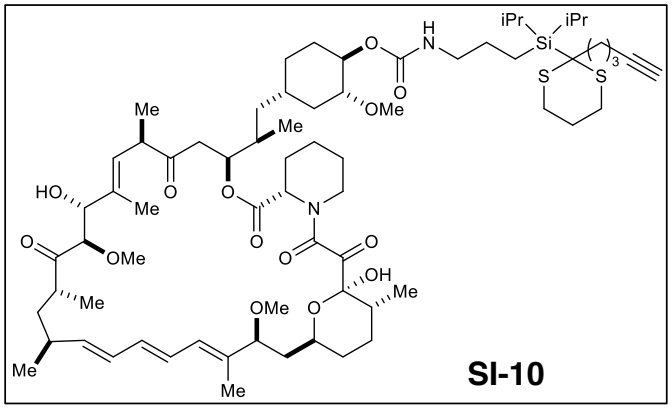





SI-9
f1 (ppm)

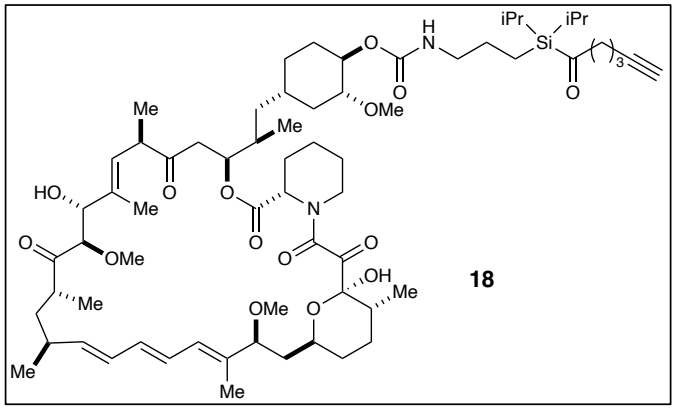

iPr
iPr
Si
H
N
O
O
OMe
Me
Me
HO
Me
O
O
N
O
O
OMe
O
OH
Me
Me
OMe
O
Me
Me
SI-10

7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

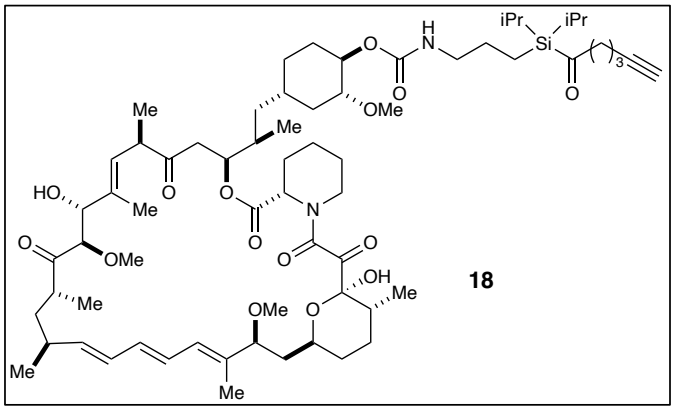

SI-10

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

18

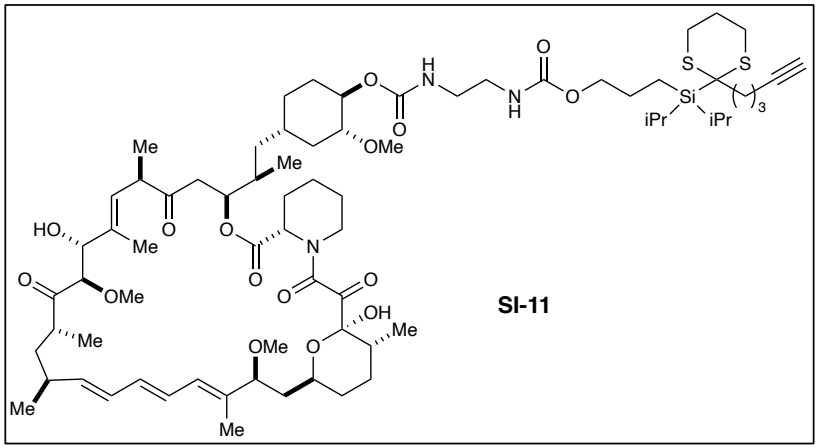


18

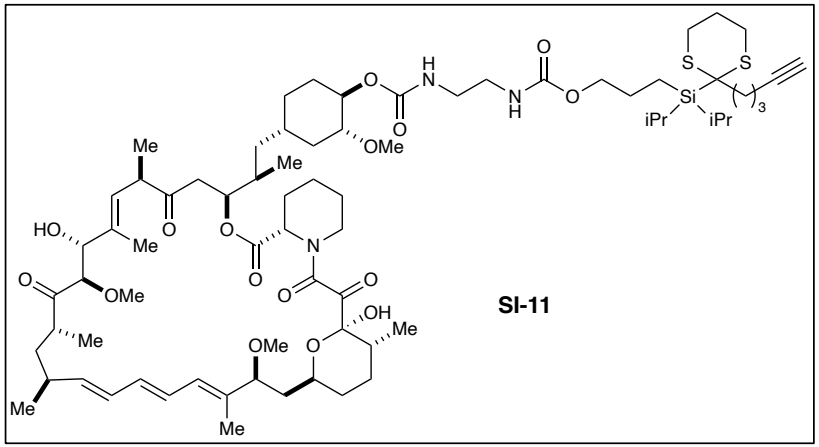

iPr
iPr
Si
H
N
O
OMe
Me
HO
OH
18

60 250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −2
f1 (ppm)

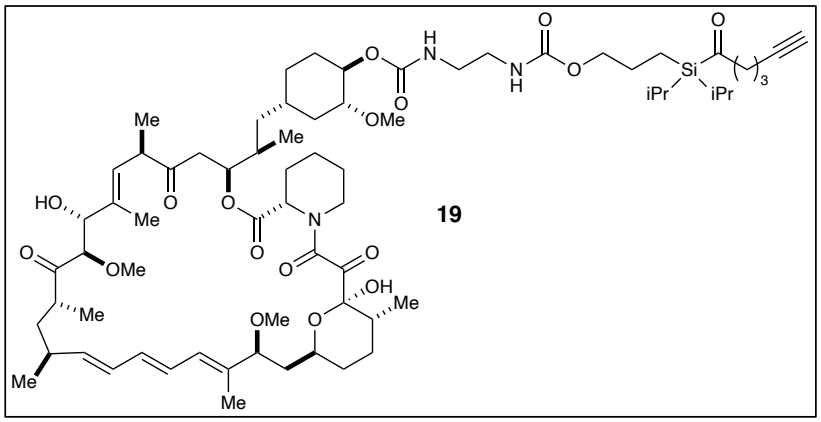
SI-11



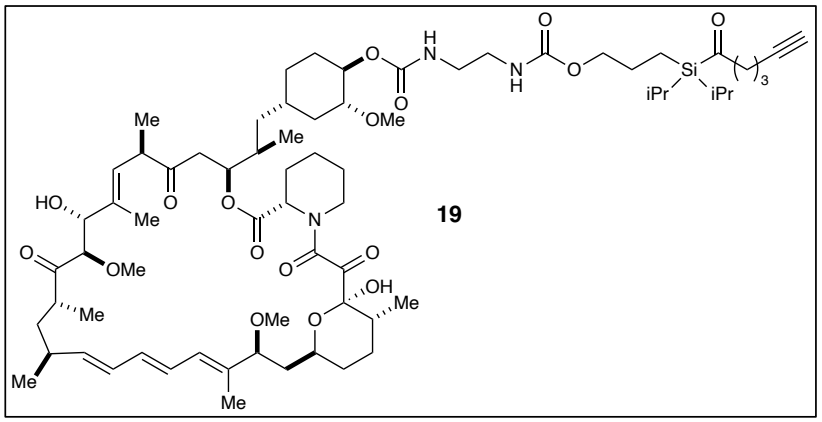
SI-11



19



19


19

60 250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −2
f1 (ppm)