Supporting Information for:

Dearomative Synthetic Entry Into the Altemicidin Alkaloids

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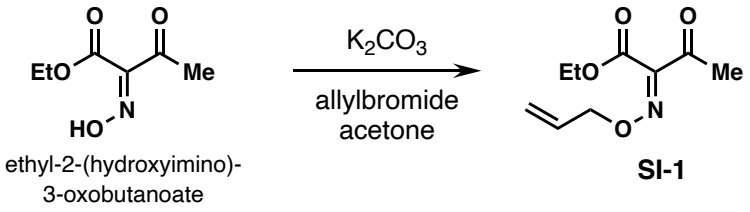
General Procedures

All reactions were performed in flame- or oven-dried glassware under positive pressure of nitrogen or argon, unless otherwise noted. Air- and moisture-sensitive liquids were transferred via syringe. When indicated, solvents or reagents were degassed by sparging with argon for 10 minutes in an ultrasound bath at 25 ˚C. Volatile solvents were removed under reduced pressure rotary evaporation. Analytical and preparative thin-layer chromatography (TLC) were performed using glass plates coated with silica gel (0.25-mm, 60-Å pore size, Merck TLC Silicagel 60 F254) impregnated with a fluorescent indicator (254 nm). TLC plates were visualized by exposure to ultraviolet light (UV) and then were stained by submersion in an ethanolic anisaldehyde solution, potassium permanganate solution, or ninhydrin solution followed by brief heating on a hot plate. Flash column chromatography was performed with silica gel purchased from Silicycle (SiliaFlash®, 60 Å, 230-40 mesh, 40-63 μM). Reverse phase C18 silica was purchased from Acros Organics (C18-RP, 10%C. ca 0.6 mmol/g, part size 40-63 μM). All samples, unless otherwise noted, were dry loaded onto the column either by resuspension of the crude mixture in Et_2O, acetone, or MeOH with an appropriate amount of silica gel and careful concentration to dryness *in vacuo*. 7N NH_3 in MeOH solution for TLC and column chromatography was made according to Appendix A: Ammonia Methanol Solution. Triethylamine, chlorotrimethylsilane, phenyl chloroformate, DBU, and acetyl chloride were distilled over calcium hydride prior to use. All other reagents were used as received from commercial sources, unless otherwise noted. Anhydrous acetonitrile (MeCN), dichloromethane (DCM), tetrahydrofuran (THF), and dimethylformamide (DMF) were obtained by passing these previously degassed solvents through activated alumina columns. Anhydrous methanol (MeOH), trifluorotoluene (CF_3Ph), 1,4-dioxane, ethanol (EtOH), and pyridine were purchased from Sigma Aldrich. Proton nuclear magnetic resonance (^{1}H NMR)

spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on Bruker AV300, AV500, AV600, and AV700 spectrometers at 23 ˚C. Proton chemical shifts are expressed as parts per million (ppm, δ scale) and are referenced to residual solvent ($CHCl_3$, δ 7.26 (s), C_6DH_5, δ 7.16 (s), CD_2HOD δ 3.31 (p), 4.87 (s, DOH), DOH δ 4.80 (s)). Carbon chemical shifts are expressed as parts per million (ppm, δ scale) and are referenced to the solvent ($CDCl_3$, δ 77.16, C_6D_6, δ 128.1, CD_3OD δ 49.00). Data is presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, ddd = doublet of doublet of doublet, dt = triplet of doublet, t = triplet, q = quartet, m = multiplet, br = broad, coupling constant (*J*) in Hertz (Hz), and integration. Infrared (IR) spectra were recorded on a Bruker Alpha FT - IR spectrometer as thin films and are reported in frequency of absorption (cm^{-1}). Only selected resonances are reported. High-resolution mass spectra (HRMS) were obtained by the mass spectrometry facility at the University of California Berkeley using a Finnigan LTQFT mass spectrometer (Thermo Electron Corporation). X-ray diffraction data was collected at the Small Molecule X-ray Crystallography Facility (CheXray) at the University of California, Berkeley using a Rigaku XtaLAB P200 equipped with a MicroMax 007HF rotating anoted an Pilatus3 R 200K-A hybrid pixel array detector. Data were collected using CuKa radiation (l = 1.5418 Å).

Compound Preparation and Characterization Data



Allyl oxime SI-1: To a solution of ethyl-2-(hydroxyimino)-3-oxobutanoate (44.0 g, 276.6 mmol, 1.0 equiv.) in acetone (300 mL) was added potassium carbonate (57.3 g, 414.9 mmol, 1.5 equiv.) followed by allyl bromide (35.9 mL, 414.9 mmol, 1.5 equiv.) at room temperature. Vigorous stirring was maintained for 45 minutes or until TLC showed consumption of starting material. The reaction mixture was then filtered through a pad of Celite®, concentrated, and purified by silica flash column chromatography (5, 10, 15% Et_2O/Hexanes) to yield allyl oxime **SI-1** (45.5 g, 228.5 mmol, 83% yield) after concentrating three times with toluene and drying overnight on a vacuum line to remove residual water.

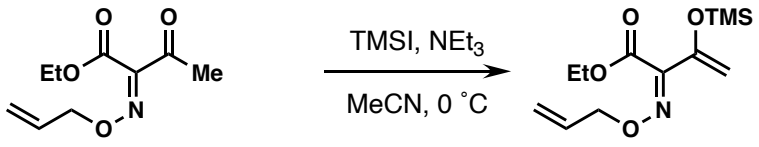
TLC: R_f = 0.57 (25% EtOAc in hexanes).

^{1}H NMR (700 MHz, $CDCl_3$) δ 5.97 (ddt, *J* = 17.3, 10.5, 5.7 Hz, 1H), 5.34 (dd, *J* = 17.3, 1.6 Hz, 1H), 5.28 (dd, *J* = 10.5, 1.6 Hz, 1H), 4.77 (d, *J* = 5.7 Hz, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 2.39 (s, 3H), 1.33 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (176 MHz, $CDCl_3$) δ 193.1, 161.3, 150.5, 132.4, 119.2, 77.6, 77.3, 77.2, 77.0, 62.2, 25.3, 14.2.

HRMS (m/z): (ESI) calcd. for $C_{19}H_{13}NO_4Na$ $[M+Na]^+$: 222.0737, found 222.0738.

IR (thin film) ν_{max} (cm^{-1}): 2984, 1744, 1698, 1369, 1234, 1009.



SI-1 **6**

Silyl enol ether 6: To a 500-mL round bottom flask containing **SI-1** (22.1 g, 110.9 mmol, 1.0 equiv.) and sodium iodide (18.3g, 122.0 mmol, 1.1 equiv.) was added MeCN (139 mL). The mixture was cooled to 0 ˚C and stirred vigorously until dissolution of the sodium iodide. To the cooled solution was added triethylamine (61.8 mL, 443.8 mmol, 4.0 equiv.) followed by chlorotrimethylsilane (21.1 mL, 166.4 mmol, 1.5 equiv.). The resulting suspension was removed from the cooling bath and warmed to room temperature. Upon consumption of starting material as indicated by ^{1}H NMR of an aliquot, the reaction mixture was concentrated *in vacuo* to a brown solid, which was resuspended in 3:1 Et_2O:Hexanes, filtered through Celite® , and concentrated *in vacuo*. The resulting brown oil was resuspended in copious hexanes, filtered through Celite®, and concentrated *in vacuo* to afford silyl enol ether **6** (30.1 g, 110.9 mmol, quant. yield) as a yellow oil.

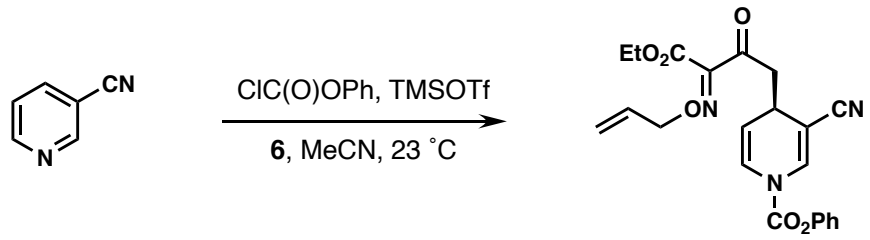
TLC: not stable to silica.

^{1}H NMR (300 MHz, C_6D_6) δ 5.78 (ddt, *J* = 17.2, 10.7, 5.4 Hz, 1H), 5.16 (dq, *J* = 17.2, 1.6 Hz, 1H), 4.98 (dq, *J* = 10.7, 1.4 Hz, 1H), 4.89 (d, *J* = 1.9 Hz, 1H), 4.66 (d, *J* = 1.9 Hz, 1H), 4.49 (dt, *J* = 5.4, 1.6 Hz, 2H), 4.07 (q, *J* = 7.1 Hz, 2H), 0.95 (t, *J* = 7.1 Hz, 3H), 0.19 (s, 9H).

^{13}C NMR (151 MHz, C_6D_6) δ 163.0, 150.8, 149.3, 134.0, 117.6, 100.2, 76.1, 61.5, 14.1, 0.2.

IR (thin film) ν_{max} (cm^{-1}): 2961 (w), 1739 (s), 1613 (m), 1371 (m), 1350 (m), 1323 (s), 1182 (s), 1015 (s), 843 (s).

HRMS (m/z): (ESI) calcd. for $C_{12}H_{22}NO_4Si$ $[M+H]^+$: 272.1313, found 272.1314.



SI-2

Dehydropyridine SI-2: To a 1-L round bottom flask containing 3-cyanopyridine (1.9 g, 18.2 mmol, 1.0 equiv) was added MeCN (80 mL) followed by phenyl chloroformate (3.0 mL, 23.4 mmol, 1.3 equiv.) and TMSOTf (0.350 mL, 1.8 mmol, 0.10 equiv.). After 15 minutes, silyl enol ether **6** (9.8 g, 36.1 mmol, 1.5 equiv.) was added dropwise via cannula as a solution in MeCN (80 mL), and the flask was washed with additional MeCN (20 mL), which was added to the reaction mixture. Upon consumption of 3-cyanopyridine, as indicated by TLC, the reaction mixture was quenched by cannulation into vigorously stirring *aq.* NaOH (1M, 300 mL) at 0 ˚C. The biphasic mixture was warmed to room temperature, poured into a separatory funnel, and extracted with EtOAc (3 x 200 mL). The combined organic layers were washed with *aq.* $NaHCO_3$ (1 x 100 mL), brine (1 x 100 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The orange oil was purified by column chromatography (3, 4, 5, 6 % Et2O in 3:1 hexanes/DCM) to give the desired C-4 dehydropyridine adduct **SI-2** (5.91 g, 14.0 mmol, 77 % yield) as a yellow oil.

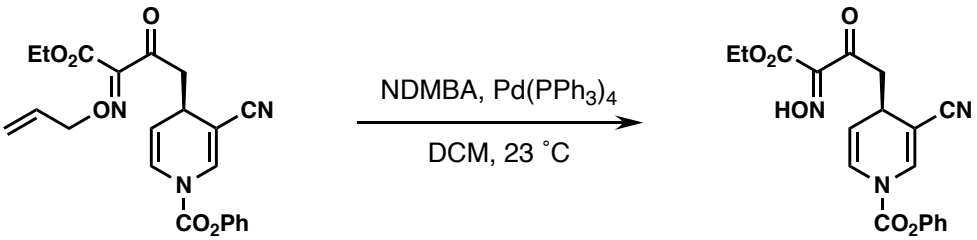
TLC: R_f = 0.43 (25% EtOAc in hexanes).

^{1}H NMR (600 MHz, MeOD) δ 7.76 (s, 1H), 7.43 (dd, *J* = 8.6, 7.3 Hz, 2H), 7.30 (t, *J* = 7.4 Hz, 1H), 7.23 (d, *J* = 7.4 Hz, 2H), 7.02 – 6.89 (m, 1H), 6.03 (ddt, *J* = 17.3, 10.5, 5.8 Hz, 1H), 5.38 (dd, *J* = 17.3, 1.6 Hz, 1H), 5.31 (dd, *J* = 10.5, 1.4 Hz, 1H), 5.19 (dd, *J* = 8.1, 4.5 Hz, 1H), 4.86 – 4.82 (m, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 3.71 (dt, *J* = 7.9, 4.5 Hz, 1H), 3.20 (dd, *J* = 16.5, 4.4 Hz, 1H), 3.11 (dd, *J* = 16.5, 7.9 Hz, 1H), 1.31 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, MeOD) δ 193.6, 162.3, 151.9, 151.5, 150.3 (br), 137.6, 133.8, 130.6, 127.6, 123.3, 122.5, 119.6, 118.9, 110.6 (br), 94.3 (br), 78.8, 63.2, 45.0, 31.5, 14.4.

IR (thin film) ν_{max} (cm^{-1}): 2926, 2213, 1745, 1688, 1322, 1202, 1013.

HRMS (m/z): (ESI) calcd. for $C_{22}H_{21}N_3O_6Na$ $[M+Na]^+$: 446.1323, found 446.1318.



SI-2 **7**

De-allyl dehydropyridine 7: 1,3-Dimethylbarbituric acid (NDMBA, 3.04 g, 19.5 mmol, 0.50 equiv.) and **SI-2** (16.2g, 38.2 mmol, 1.0 equiv.) were loaded into a 500-mL round bottom flask. DCM (382 mL) was added, and the mixture was degassed. To this mixture was added palladium-tetrakis(triphenylphosphine) (441 mg, 0.382 mmol, 0.01 equiv.). Upon consumption of dehydropyridine XX as indicated by TLC, the reaction was quenched by addition of Et_2O (20 mL), followed by *p*-nitrobenzaldehyde (3.00 g, 19.9 mmol, 0.52 equiv.) and H_2O (10 mL) to consume excess NDMBA and ease purification. After stirring for 30 minutes, *sat. aq.* NH_4Cl (300 mL) was added and the resulting biphasic mixture was transferred to a separatory funnel, extracted with EtOAc (3 x 300 mL), washed with brine (1 x 100 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The resulting brown oil was purified by column chromatography (6, 8, 10% Et_2O in 3:1 hexanes/DCM, then 20% Et_2O in 3:1 hexanes/DCM) to give **7** (13.5 g, 35.1 mmol, 92% yield) as a pale yellow foam, which was dried overnight under hi-vac.

TLC: R_f = 0.46 (1:1 EtOAc in hexanes).

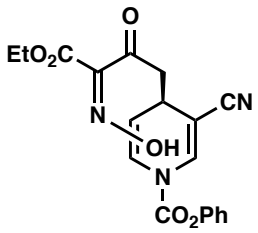
^{1}H NMR (300 MHz, MeOD) δ 7.71 (s, 1H), 7.43 – 7.34 (m, 2H), 7.29 – 7.22 (m, 1H), 7.22 – 7.14 (m, 2H), 6.90 (s, 1H), 5.14 (dd, *J* = 8.7, 4.0 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 3.66 (dt, *J* = 7.4, 3.7 Hz, 1H), 3.27 (p, *J* = 1.6 Hz, 1H), 3.19 (dd, *J* = 16.8, 4.4 Hz, 1H), 3.05 (dd, *J* = 16.8, 8.4 Hz, 1H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, MeOD) δ 194.6, 163.4, 152.2, 151.9, 150.3, 137.5, 130.6, 127.5, 123.2, 122.5, 118.9, 110.7, 94.4, 62.9, 44.9, 31.3, 14.4.

IR (thin film) ν_{max} (cm^{-1}): 3290 (br), 2981 (w), 2925 (w), 2856 (w), 2216 (m), 2216 (m), 1742 (s), 1687 (s), 1321 (s), 1199 (s), 1021 (m).

HRMS (m/z): (ESI) calcd. for $C_{19}H_{17}N_3O_6Na$ $[M+Na]^+$: 406.1010, found 406.1007.

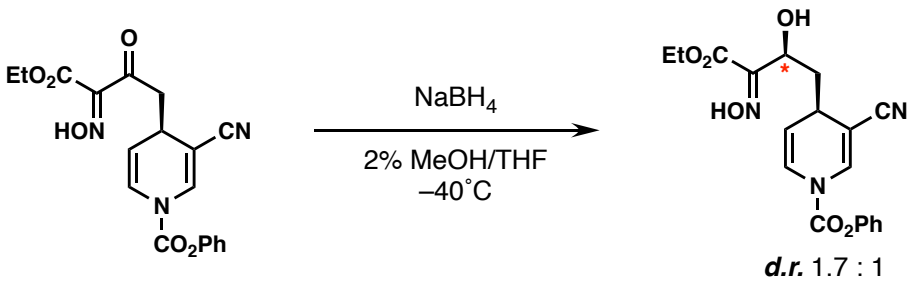
(*E*)-oxime isomer (**SI-3**): (isolated ~5% yield)



SI-3

^{1}H NMR (600 MHz, MeOD) δ 7.74 (s, 1H), 7.48 – 7.41 (m, 2H), 7.33 – 7.25 (m, 1H), 7.25 – 7.17 (m, 2H), 6.95 (s, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 3.73 (dq, *J* = 6.4, 3.8 Hz, 1H), 3.14 (dd, *J* = 18.1, 3.6 Hz, 1H), 3.04 (dd, *J* = 18.1, 8.8 Hz, 1H), 1.32 (t, *J* = 7.1 Hz, 3H).

TLC: R_f = 0.3 (1:1 EtOAc in hexanes).



7 **8**

Alcohol 8: To a 2-L round bottom flask containing **7** (7.88 g, 20.6 mmol, 1.0 equiv.) was added THF (1.0 L) and MeOH (20.6 mL). The solution was cooled to –40 ˚C in a dry ice-acetone bath equipped with a thermometer. Next, the rubber septum and nitrogen inlet were briefly removed to add sodium borohydride (3.11 g, 82.2 mmol, 4.0 equiv) in a single portion. The reaction mixture was kept between –40 ˚C and –30 ˚C until consumption of **7**, as indicated by TLC. The reaction mixture was quenched by careful addition of *aq*. HCl (1M, 103 mL) at –40 ˚C. The biphasic mixture was warmed to room temperature, transferred to a separatory funnel, extracted with EtOAc (3 x 300 mL), washed with *sat. aq.* $NaHCO_3$ (1 x 300 mL) and brine (1 x 300 mL), dried with Na_2SO_4, and concentrated *in vacuo*. The resulting orange oil was purified by column chromatography (20% EtOAc in hexanes —> 40% EtOAc in hexanes) to yield **8** (5.15 g, 13.4 mmol, 65% yield, 1.7 : 1 *dr*) as a yellow foam.

TLC: R_f = 0.25 (1:1 EtOAc in hexanes).

bold=major epimer
normal=minor epimer
underline=superimposed peaks of major and minor epimer

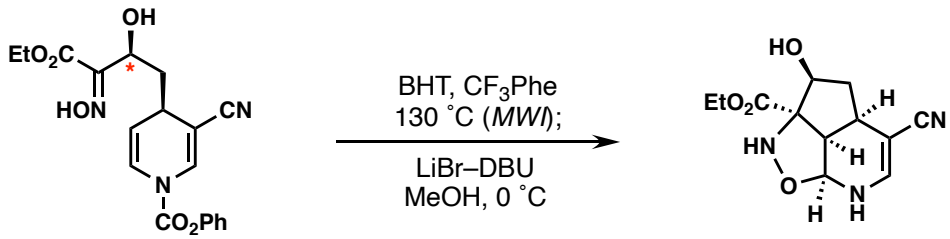
^{1}H NMR (600 MHz, MeOD) δ 7.72 (br s), 7.42 (dd, *J* = 8.6, 7.4 Hz), 7.32 – 7.25 (m), 7.22 (dq, *J* = 7.9, 1.3 Hz), 6.95 (br s), **5.33** (br s), 5.28 (br s), **4.64** (dd, *J* = 7.7, 6.7 Hz), 4.60 (dd, *J* = 9.9, 3.9 Hz), 4.39 – 4.23 (m), **3.40** (dddd, *J* = 9.3, 4.1, 3.2, 1.0 Hz), 3.34 – 3.31 (m), **2.22 – 2.16** (m), 2.16

– 2.11 (m), 1.99 (dt, *J* = 13.8, 7.8 Hz), **1.90** (ddd, *J* = 13.7, 9.5, 4.0 Hz, 2H), 1.34 (td, *J* = 7.1, 3.9 Hz, 9H).

^{13}C NMR (151 MHz, MeOD) δ **164.8**, 164.6, **154.2**, 153.9, 151.9, 150.4 (br), **137.1**, 136.9, 130.6, 127.5, 122.8, 122.5 (br), 119.4, **119.2**, 111.5 (br), **110.8** (br), 95.8 (br), 68.7, **67.3**, 62.5, **62.4**, **42.9**, 42.8, 32.2, **31.4**, **14.5**, 14.5.

IR (thin film) ν_{max} (cm^{-1}): 3370 (br), 2925 (w), 2856 (w), 2213 (m), 1738 (s), 1685 (s), 1619 (m), 1344 (m), 1319 (s), 1285 (m), 1184 (s), 1166 (s), 1154 (m).

HRMS (m/z): (ESI) calcd. for $C_{19}H_{19}N_3O_6Na$ $[M+Na]^+$: 408.1166, found 408.1165.



d.r. 1.7 : 1

8 **9**

Isoxazolidine 9: Six 20-mL Biotage microwave vial were equipped with stir bars and backfilled with nitrogen, to these was added a solution of butylated hydroxytoluene (BHT, 6 x 100 mg, 2.73 mmol, 0.35 equiv.) in trifluorotoluene (6 x 19 mL), which had been previously degassed by sparging with argon. This was followed by a solution of alcohols **8** and *epi*-**8** (6 x 500 mg, 1.29 mmol, 1.0 equiv.) in DCM (6 x 1 mL). The vials were crimped shut and heated each to 130 ˚C for 8 hours in a Biotage microwave reactor over a period of 24 hours. Next a 500-mL flame dried round bottom flask was equipped with a stir bar and oven-dried 3 Å pelleted molecular sieves and put under positive nitrogen pressure. Using a syringe and thick-gauge needle the reaction mixture was transferred to the round bottom flask using methanol (70 mL) and sonication to completely

transfer all solids. To this was added lithium bromide (3.38 g, 38.9 mmol, 5.0 equiv.) in methanol (8 mL), and this mixture was allowed to stir for 15 minutes at room temperature. The mixture was then cooled to 0 ˚C in an ice bath and DBU was added (1.16 mL, 7.78 mmol, 1.0 equiv.) dropwise. Upon reaction completion as indicated by TLC, roughly 2 h, pivalic acid (1.59 g, 15.6 mmol, 2 equiv.) in methanol (5 mL) was transferred to the reaction flask via syringe. The mixture was allowed to warm to room temperature and concentrated *in vacuo* (rotovap bath no higher than 33 ˚C). The crude mixture was purified by column chromatography (1 → 4% MeOH in DCM + 0.07% NH_4OH) and triturated with ether to remove remaining pivalic acid to yield **9** as a fine pale yellow powder (890 mg, 3.50 mmol, 45% yield). The pure material could be crystallized by slow evaporation from hot methanol.

TLC: R_f = 0.35 (10% MeOH in 2:1 DCM/hexanes, run twice).

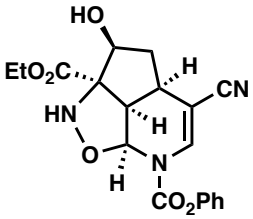
^{1}H NMR (500 MHz, MeOD) δ 7.00 (s, 1H), 5.00 (d, *J* = 4.8 Hz, 1H), 4.46 (dd, *J* = 11.9, 6.3 Hz, 1H), 3.82 (s, 3H), 2.79 (dd, *J* = 9.0, 4.8 Hz, 1H), 2.72 (td, *J* = 10.6, 9.0, 6.3 Hz, 1H), 2.29 (dt, *J* = 11.9, 6.3 Hz, 1H), 1.57 (q, *J* = 11.9 Hz, 1H).

^{13}C NMR (151 MHz, MeOD) δ 173.4, 142.1, 122.5, 85.6, 80.6, 78.9, 74.7, 53.5, 47.5, 40.6, 31.7.

IR (thin film) ν_{max} (cm^{-1}): 3278 (br), 3214 (m), 3033 (m), 2853 (w), 2193 (s), 1730 (s), 1637 (s), 1384 (s), 1275 (s), 1224 (s), 1053 (s).

HRMS (m/z): (ESI) calcd. for $C_{11}H_{14}N_3O_4$ $[M+H]^+$: 252.0979, found 252.0981.

<u>The carbamate-protected isoxazolidine (**SI-4**) can also be isolated:</u>



SI-4

TLC: R_f = 0.57 (10% MeOH in 2:1 DCM/Hexanes).

^{1}H NMR (700 MHz, MeOD) δ 7.80 (br s, 1H), 7.43 (dd, *J* = 8.5, 7.4 Hz, 2H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 7.6 Hz, 2H), 5.90 (br s, 1H), 4.55 (dd, *J* = 11.9, 6.4 Hz, 1H), 4.30 (qd, *J* = 7.1, 1.3 Hz, 2H), 3.31 (s, 1H), 3.17

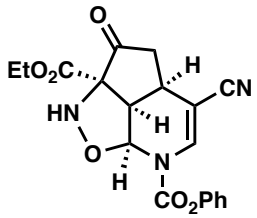
(dd, *J* = 9.3, 5.0 Hz, 1H), 2.87 (ddd, *J* = 12.6, 9.3, 6.4 Hz, 1H), 2.41 (dt, *J* = 11.9, 6.4 Hz, 1H), 1.65 (q, *J* = 12.6, 11.9 Hz, 1H), 1.33 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, MeOD) δ 172.3, 152.2 (br), 152.0, 135.3, 130.7, 127.6, 122.5, 119.4, 94.8, 85.0, 78.9, 75.3, 63.6, 49.4-46.8 (under solvent peak, see provided HSQC), 40.2, 31.7, 14.3.

IR (thin film) ν_{max} (cm^{-1}): 3462 (br), 3238 (br), 2982 (br), 2215 (m), 1735 (s), 1650 (m), 1317 (s), 1197 (s), 1169 (s).

HRMS (m/z): (ESI) calcd. for $C_{19}H_{20}N_3O_6Na$ $[M+H]^+$: 386.1347, found 386.1344.

Ketone isoxazolidine (SI-5): See general procedure for **9**. After microwave reaction the crude mixture was concentrated and purified by preparatory TLC.

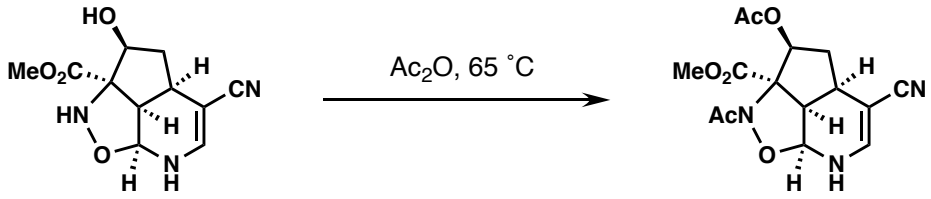


SI-5

TLC: R_f = 0.3 (1:1 EtOAc/Hexanes).

^{1}H NMR (700 MHz, MeOD) δ 7.91 (s, 1H), 7.53 – 7.37 (m, 2H), 7.36 – 7.28 (m, 1H), 7.28 – 7.04 (m, 2H), 5.94 (s, 1H), 4.37 – 4.28 (m, 2H), 3.65 (dd, *J* = 9.5, 5.7 Hz, 1H), 2.93 (dd, *J* = 17.6, 8.5 Hz, 1H), 2.43 (dd, *J* = 17.6, 11.8 Hz, 1H), 1.30 (t, *J* = 7.1 Hz, 3H).

HRMS (m/z): (ESI) calcd. for $C_{19}H_{18}N_3O_6Na$ $[M+H]^+$: 384.1190, found 384.1191.



9 **10**

Bisacyl-isoxalidine 10: A 100-mL round bottom flask was loaded with **9** (600 mg, 2.36 mmol, 1.0 equiv.) and acetic anhydride (12 mL). The resulting mixture was stirred at 65 ˚C. After 12

hours, full conversion to product was achieved, as indicated by TLC and NMR of aliquots. The presence of an overlapping less polar spot indicates the mono *O*-acyl reaction intermediate, and steady heating should be maintained to achieve full conversion. The reaction mixture was then cooled to room temperature and concentrated *in vacuo*. The crude material was purified by column chromatography (1→ 4% MeOH in 3:1 DCM/hexanes) to provide **10** as a fine pale yellow powder (700 mg, 2.09 mmol, 89% yield). On large scales, **10** can be purified by recrystallization from hot methanol.

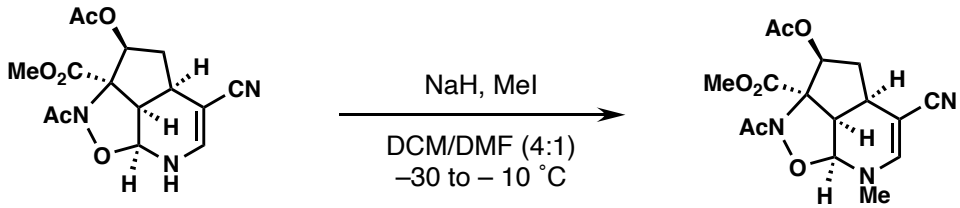
TLC: R^f= 0.5 (10% MeOH in 3:1 DCM/hexanes).

^{1}H NMR (700 MHz, MeOD) δ 7.07 (s, 1H), 5.75 (dd, *J* = 12.0, 6.6 Hz, 1H), 5.47 (d, *J* = 4.7 Hz, 1H), 3.75 (s, 3H), 3.08 (dd, *J* = 9.9, 4.7 Hz, 1H), 2.85 (ddd, *J* = 12.8, 9.8, 6.7 Hz, 1H), 2.49 (dt, *J* = 12.0, 6.6 Hz, 1H), 2.13 (s, 3H), 1.98 (s, 3H), 1.63 (q, *J* = 12.8, 12.0 Hz, 1H).

^{13}C NMR (151 MHz, MeOD) δ 171.8, 169.7, 169.3, 141.8, 121.5, 84.1, 81.6, 76.8, 73.1, 53.5, 49.0, 48.5, 37.1, 30.5, 20.7, 20.7.

IR (thin film) ν_{max} (cm^{-1}): 3376 (br), 3041(w), 2956 (w), 2925 (w), 2853 (w), 2201 (m), 1745 (s), 1647 9s), 1435 (m), 1265 (s), 1237 (s).

HRMS (m/z): (ESI) calcd. for $C_{15}H_{17}N_3O_6Na$ $[M+Na]^+$: 358.1010, found 358.1008.



10 **11**

***N*-methyl isoxazolidine 11:** A suspension of NaH (90%, 615 mg, 25.6 mmol, 20 equiv.) in DCM (30 mL) was cooled to –30 ˚C and to this was added a suspension of **10** (430 mg, 1.28 mmol, 1.0

equiv.) and oven-dried powdered 3 Å molecular sieves (~50 mg) in DCM (20 mL) and DMF (12 mL) under positive nitrogen pressure. This was rapidly followed by addition of iodomethane (3.2 mL, 51.3 mmol, 40 equiv.), which had itself been stirred for several minutes over P_2O_5. The reaction is extremely moisture-sensitive. The reaction mixture was allowed to warm to –10 ˚C and stirred at this temperature until reaction completion as indicated by TLC, approximately 2 hours. The mixture was carefully poured into ice cold 1M HCl (30 mL), after a few minutes, the mixture was neutralized to pH 7 by slow addition of solid $NaHCO_3$ (2.5 g). The biphasic mixture was allowed to warm to room temperature and extracted with DCM (3x10 mL), washed with brine, dried over Na_2SO_4, and concentrated *in vacuo.* The resulting yellow oil was purified by column chromatography (1→ 4 % MeOH in 2:1 DCM/Hexanes) to yield the desired product as a pale yellow solid (440 mg, 1.26 mmol, 98 % yield). **11** can be crystallized by slow evaporation from methanol.

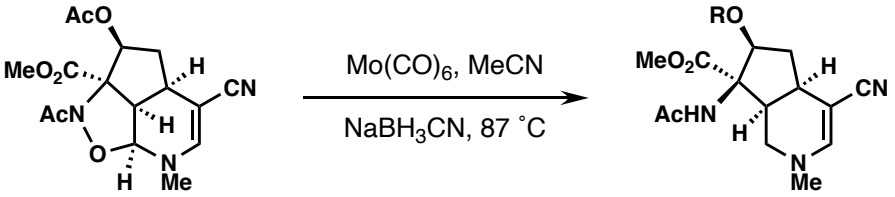
TLC: R_f = 0.7 (10% Methanol in 2:1 DCM/Hexanes).

^{1}H NMR (600 MHz, MeOD) δ 7.05 (s, 1H), 5.75 (dd, *J* = 11.7, 6.4 Hz, 1H), 5.39 (d, *J* = 4.8 Hz, 1H), 3.75 (s, 3H), 3.19 (s, 3H), 3.16 (dd, *J* = 9.5, 4.4 Hz, 1H), 2.80 (ddd, *J* = 12.8, 10.0, 6.8 Hz, 1H), 2.48 (dt, *J* = 11.6, 6.5 Hz, 1H), 2.15 (s, 3H), 1.97 (s, 3H), 1.58 (dt, *J* = 12.9, 11.7 Hz, 1H).

^{13}C NMR (151 MHz, MeOD) δ 171.7, 169.8, 169.2, 145.6, 121.4, 89.6, 81.6, 76.7, 73.3, 53.5, 49.1 (behind solvent peak, see HSQC data), 41.9, 37.3, 29.7, 20.7, 20.7.

HRMS (m/z): (ESI) calcd. for $C_{16}H_{19}N_3O_6Na$ $[M+Na]^+$: 372.1166, found 372.1170.

IR (thin film) ν_{max} (cm^{-1}): 2956 (w), 2925 (w), 2855 (w), 2200 (m), 1749 (s), 1671 (m), 1645 (s), 1436 (m), 1237 (s).



11 **12**

Acylamine 12: [CAUTION: $Mo(CO)_6$, $NaBH_3CN$, AND THEIR BYPRODUCTS SHOULD BE HANDLED WITH CARE IN A WELL-VENTILATED FUME HOOD]. A 25-mL three-necked round bottom flask was sealed with two rubber septa, equipped with a reflux condenser, and loaded with hexacarbonylmolybdenum (160 mg, 0.59 mmol, 1.01 equiv.). To this was added MeCN (3 mL) and the resulting solution was refluxed in a 95 ˚C oil bath for 4–6 hours during which time the mixture turned from pale to dark brown. Separately, a 50-mL round bottom flask was loaded with **11** (203 mg, 0.58 mmol, 1.0 equiv.) and sodium cyanoborohydride (527 mg, 8.40 mmol, 15.0 equiv.), which were dissolved in MeCN (3 mL) and transferred dropwise to the refluxing reaction mixture. The resulting dark brown reaction mixture was allowed to reflux until consumption of starting material **11**, as indicated by TLC. The mixture was cooled to room temperature and carefully poured into a 0 ˚C *aq.* phosphate buffer solution (1M, pH 7) with vigorous stirring. The biphasic mixture was allowed to warm to room temperature with continued stirring and transferred to a separatory funnel. The aqueous layer was extracted with ^{i}PrOH/chloroform (1:3, 3 x 300 mL). The combined organic layers were washed with brine (1 x 300 mL), dried over Na2SO4, and concentrated *in vacuo*. The resulting pale brown oil was purified by column chromatography (3% → 6% MeOH in 2:1 DCM/hexanes) to yield an inconsequential mixture of bis-acyl and mono-acyl product **12** (160 mg, 0.48 mmol, 82 % yield) as a pale brown powder.

<u>R = Ac</u>

TLC: R_f = 0.6 (10% Methanol in 2:1 DCM/Hexanes).

^{1}H NMR (600 MHz, MeOD) δ 6.95 (d, *J* = 1.0 Hz, 1H), 5.41 (t, *J* = 7.7 Hz, 1H), 3.67 (s, 3H), 3.23 (dd, *J* = 13.0, 6.9 Hz, 1H), 3.07 (ddd, *J* = 13.0, 5.4, 1.0 Hz, 1H), 2.94 (td, *J* = 7.2, 5.5 Hz, 1H), 2.80 (q, *J* = 7.8 Hz, 1H), 2.63 (dt, *J* = 13.9, 8.3 Hz, 1H), 2.07 (s, 3H), 1.98 (s, 3H), 1.76 (dt, *J* = 13.8, 7.6 Hz, 1H).

^{13}C NMR (151 MHz, MeOD) δ 173.8, 173.3, 171.2, 149.2, 123.9, 77.6, 75.8, 68.4, 53.1, 45.7, 42.6, 41.9, 38.2, 31.8, 22.0, 20.8.

HRMS (m/z): (ESI) calcd. for $C_{16}H_{22}N_3O_5$ $[M+H]^+$: 336.1565, found 336.1560.

IR (thin film) ν_{max} (cm^{-1}): 3332 (br), 2925 (w), 2184 (m), 1737 (s), 1663 (m), 1629 (s), 1520 (w), 1425 (w), 1372 (w), 1237 (s).

<u>R= H</u>

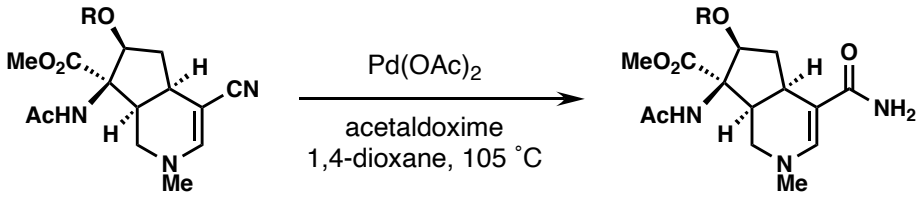
TLC: R_f = 0.5 (10% Methanol in 2:1 DCM/Hexanes).

^{1}H NMR (600 MHz, MeOD) δ 6.97 (s, 1H), 4.17 (t, *J* = 7.9 Hz, 1H), 3.69 (s, 3H), 2.96 – 2.95 (m, 1H), 2.91 (s, 3H), 2.82 – 2.76 (m, 1H), 2.69 (dt, *J* = 11.2, 6.6 Hz, 1H), 2.53 (dt, *J* = 13.1, 7.3 Hz, 1H), 2.03 (s, 3H), 1.45 (ddd, *J* = 13.1, 11.1, 8.4 Hz, 1H).

^{13}C NMR (151 MHz, MeOD) δ 175.0, 173.7, 149.5, 124.3, 76.2, 75.7, 68.1, 53.0, 45.6, 42.8, 42.4, 41.1, 33.4, 22.2.

HRMS (m/z): (ESI) calcd. for $C_{14}H_{19}N_3O_4Na$ $[M+Na]^+$: 316.1268, found 316.1269.

IR (thin film) ν_{max} (cm^{-1}): 3349 (br), 2200 (m), 1734 (m), 1640 (s), 1498 (w), 1434 (w), 1412 (w), 1351 (w), 1295 (m).



R = Ac and H

12

R = Ac and H

13

Amide 13: A 50-mL two-necked round bottom flask bottom flask equipped with a reflux condenser was loaded with nitrile **12** (1.9 :1 molar ratio, 471 mg, 1.78 mmol, 1.0 equiv.), palladium(II) acetate (40 mg, 0.178 mmol, 10 mol %), acetaldoxime (300 mg, 17.8 mmol, 10. equiv.), and 1,4-dioxane (24 mL). The mixture was degassed with argon and refluxed in a 105 ˚C oil bath. Upon reaction completion, roughly 12 hours, as indicated by the consumption of starting material by TLC visualization, the reaction mixture was cooled to room temperature, filtered through Celite®, and concentrated *in vacuo*. The crude product was purified by column chromatography (4% → 8% MeOH with NH_4OH in DCM) to yield **13** *O*-acyl amide (364 mg, 1.03 mmol). and *O*-deacyl amide (132 mg, 0.424 mmol) with an overall yield of 82% yield. NOTE: care must be taken to completely remove the acetamide byproduct which is formed from rearrangement of acetaldoxime and is noticeable in ^{1}H NMRs at 1.8 ppm.

<u>R=Ac</u>

TLC: R_f = 0.3 (10% Methanol in 3:1 DCM/Hexanes).

^{1}H NMR (600 MHz, MeOD) δ 7.31 (s, 1H), 5.46 (t, *J* = 7.2 Hz, 1H), 3.70 (s, 3H), 3.09 – 2.98 (m, 2H), 2.97 (s, 3H), 2.93 (dd, *J* = 10.2, 7.2 Hz, 1H), 2.89 – 2.79 (m, 2H), 2.06 (s, 3H), 2.01 (s, 3H), 1.40 (ddd, *J* = 13.7, 10.3, 6.8 Hz, 1H).

^{13}C NMR (151 MHz, MeOD) δ 174.0, 173.9, 173.7, 171.1, 145.9, 100.8, 75.9, 68.8, 53.2, 45.6, 43.0, 42.4, 40.7, 31.8, 21.9, 20.9.

IR (thin film) ν_{max} (cm^{-1}): 3352 (br), 2951 (w), 1730 (s), 1645 (s), 1650 (s), 1538 (m), 1291 (m), 1245 (s).

HRMS (m/z): (ESI) calcd. for $C_{16}H_{23}N_3O_6Na$ $[M+Na]^+$: 376.1490, found 376.1487.

R=H

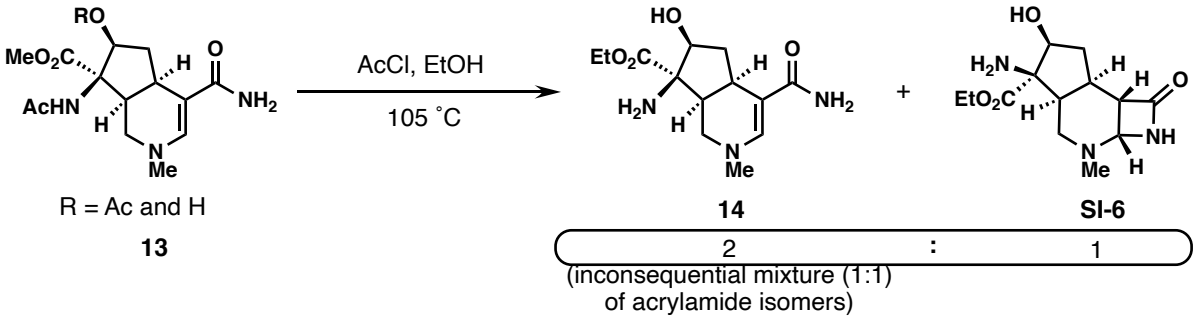
TLC: R_f = 0.2 (10% Methanol in 3:1 DCM/Hexanes).

^{1}H NMR (600 MHz, MeOD) δ 7.33 (s, 1H), 4.19 (dd, *J* = 8.7, 7.2 Hz, 1H), 3.70 (s, 3H), 2.96 (s, 3H), 2.96 – 2.85 (m, 2H), 2.87 (q, *J* = 12.5, 11.8 Hz, 2H), 2.72 (dd, *J* = 12.0, 5.2 Hz, 1H), 2.63 (dt, *J* = 13.0, 6.8 Hz, 1H), 2.05 (s, 3H), 1.24 (td, *J* = 12.6, 8.7 Hz, 1H).

^{13}C NMR (151 MHz, MeOD) δ 175.4, 173.9, 173.6, 146.1, 100.0, 75.8, 67.7, 53.0, 45.8, 43.1, 43.1, 41.4, 32.3, 22.2.

IR (thin film) ν_{max} (cm^{-1}): 3348 (br), 3284 (br), 2955 (w), 2923 (w), 1834 (m), 1650 (s), 1530 (s), 1434 (m), 1381 (m), 1289 (s).

HRMS (m/z): (ESI) calcd. for $C_{14}H_{21}N_3O_5Na$ $[M+Na]^+$: 334.1373, found 334.1377.



Amino alcohol 14: Amide **13** (26 mg, 0.084 mmol, 1.0 equiv.) was concentrated with 3x1mL toluene, dried thoroughly on hi-vac, and transferred as a solution in EtOH (8.4 mL) to a large flame dried microwave vial equipped with a stir bar under positive nitrogen pressure. To this solution was added freshly distilled acetyl chloride (0.90 mL, 1.5 M) dropwise at room temperature. The

nitrogen line was removed and the microwave vial was carefully sealed with a new, unperforated cap. The reaction was submerged in a 105 ˚C oil bath and heated for 1.75h. Upon reaction completion as determined by TLC and removal of an aliquot and NMR analysis, the pale brown solution was cooled and concentrated *in vacuo* to yield a brown oil. The crude product was purified by column chromatography (5, 10, 15, 20 7N NH_3/MeOH in DCM) to yield **14** (15 mg, 0.053 mmol, 63 % yield) as an inconsequential mixture of two isomers converging over time in MeOH or by being subjected to the subsequent reaction conditions. The isomers are chromatographically separable and can be collected either separately or together.

TLC: R_f = 0.46 (isomer A), 0.18 (isomer B) (15% 7N NH_3/MeOH in DCM)

14-Isomer A

^{1}H NMR (500 MHz, MeOD) δ 7.28 (s, 1H), 4.29 (dd, *J* = 8.7, 7.2 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.04 (dd, *J* = 12.7, 5.7 Hz, 1H), 3.00 – 2.92 (m, 1H), 2.96 (s, 3H), 2.86 (dt, *J* = 10.7, 7.4 Hz, 1H), 2.65 (dt, *J* = 13.0, 7.2 Hz, 1H), 2.56 (td, *J* = 8.3, 5.7 Hz, 1H), 1.36 – 1.32 (m, 1H), 1.30 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, MeOD) δ 177.0, 174.0, 146.0, 102.0, 76.6, 68.4, 62.6, 46.0, 43.4, 43.0, 42.2, 31.2, 14.4.

HRMS (m/z): (ESI) calcd. for $C_{13}H_{23}N_3O_4$ $[M+H]^+$:284.1605, found 284.1606.

IR (thin film) ν_{max} (cm^{-1}): 3352 (br), 3237 (br), 2940 (w), 1722 (m), 1643 (s), 1551 (m), 1386 (w), 1340 (w), 1290 (w).

14-Isomer B

(See NMR appendix B for evidence of slow conversion)

^{1}H NMR (600 MHz, MeOD) δ 7.29 (s, 1H), 4.57 (dd, *J* = 10.4, 3.6 Hz, 1H), 4.38 – 4.24 (m, 2H), 3.02 – 2.92 (m, 3H), 2.74 (dt, *J* = 9.3, 3.7 Hz, 1H), 2.70 (s, 3H), 2.52 (ddd, *J* = 13.6, 10.5, 6.2 Hz, 1H), 1.80 (dd, *J* = 13.6, 3.5 Hz, 1H), 1.35 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, MeOD) 173.4, 171.8, 141.1, 104.3, 83.6, 70.2, 63.5, 47.6, 46.1, 38.4, 36.8, 34.4, 14.4.

β-lactam **SI-6**:

TLC: R_f = 0.9 (15% 7N NH_3/MeOH in DCM)

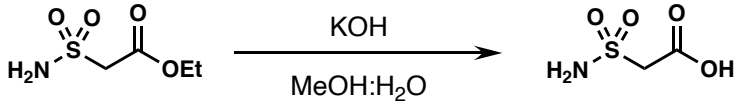
^{1}H NMR (500 MHz, MeOD) δ 4.31 (dd, *J* = 9.5, 3.3 Hz, 1H), 4.26 (qd, *J* = 7.1, 1.2 Hz, 2H), 3.57 (d, *J* = 1.8 Hz, 1H), 2.97 (dd, *J* = 12.4, 1.8 Hz, 1H), 2.55 (dd, *J* = 12.1, 3.1 Hz, 1H), 2.42 (ddd, *J* = 14.0, 9.9, 6.9 Hz, 1H), 2.35 (s, 3H), 2.24 (t, *J* = 5.4 Hz, 1H), 2.21 (dd, *J* = 4.9, 2.5 Hz, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.29-1.26 (m, 1H), 1.26 (dd, *J* = 13.8, 3.5 Hz, 1H).

^{13}C NMR (151 MHz, MeOD) δ 175.7, 175.2, 77.4, 68.2, 65.6, 62.9, 49.*, 44.2, 42.0, 40.9, 35.0, 30.4, 14.5. *behind solvent peak, identified by HSQC

Stereochemical determination correlations are shown in NOE spectrum in Appendix B.

HRMS (m/z): (ESI) calcd. for $C_{13}H_{22}N_3O_4$ $[M+H]^+$:284.1605, found 284.1607, also found $C_{12}H_{21}N_2O_3$ $[M–(N=C=O)]^+$: 241.1547, found 241.1545.

IR (thin film) ν_{max} (cm^{-1}): 3331 (br), 2936 (m), 2857 (m), 1724 (s), 1653 (m), 1445 (m), 1271 (s), 1215(s), 1084 (s).



15

2-sulfamoylacetic acid 15: (Ethoxycarbonyl)methanesulfonamide[1] (60 mg, 0.359 mmol, 1.0 equiv.) was dissolved in MeOH/H_2O (1:1, 3.6 mL) and to this was added crushed potassium

hydroxide (60 mg, 1.08 mmol, 3.0 equiv.). After 120 min the reaction was complete, as indicated by TLC. The reaction was carefully acidified to pH 2 with *aq*. 1 M HCl (1.5 mL) and the mixture was concentrated to dryness. The resulting white powder was resuspended in ^{i}PrOH/$CHCl_3$ (1:3) (10 mL) with the aid of sonication, filtered, concentrated *in vacuo* to yield 2-sulfamoyl acetic acid **15** (50 mg, 0.357 mmol, 99% yield) as a white powder.

TLC: R_f = 0.05 (10% MeOH/DCM).

^{1}H NMR (600 MHz, MeOD) δ 4.05 (s, 2H).

^{13}C NMR (151 MHz, MeOD) δ 167.6, 59.8.

HRMS (m/z): (ESI) calcd. for $C_2H_4NO_4S$ $[M–H]^-$: 137.9867, found 137.9825.

IR (thin film) ν_{max} (cm^{-1}): 3534 (br), 3363 (br), 3269 (br), 2930 (w), 1725 (s), 1333 (s), 1160 (s), 1138 (s).

14 16

Ethyl altemicidin 16: Isomers A and B of amino alcohol **14** (46 mg, 0.162 mmol, 1.0 equiv.) was dissolved in DMF (1.5 mL). To this solution was added sidechain **15** (22 mg, 0.17 mmol, 1.1 equiv.), DMAP (21 mg, 0.017 mmol, 1.1 equiv.), and N,N'-dicyclohexylcarbodiimide (DCC, 33 mg, 0.17 mmol, 1.1 equiv.). The reaction was stirred for at least 12 hours or until TLC indicated consumption of starting material and concentrated to dryness *in vacuo.* The yellow residue was resuspended in distilled water with the aid of sonication and filtered through a pad of Celite® to remove the dicyclohexylurea byproduct. The resulting aqueous solution was concentrated *in vacuo*

and purified column chromatography (5, 10, 15 7N NH_3/MeOH in DCM). The desired **16** was isolated as a pale yellow oil (48 mg, 0.12 mmol, 73% yield).

TLC: R_f = 0.22 (20% Methanol, 2% NH_4OH in DCM) or R_f = 0.18 (15% 7N NH_3/MeOH in DCM)

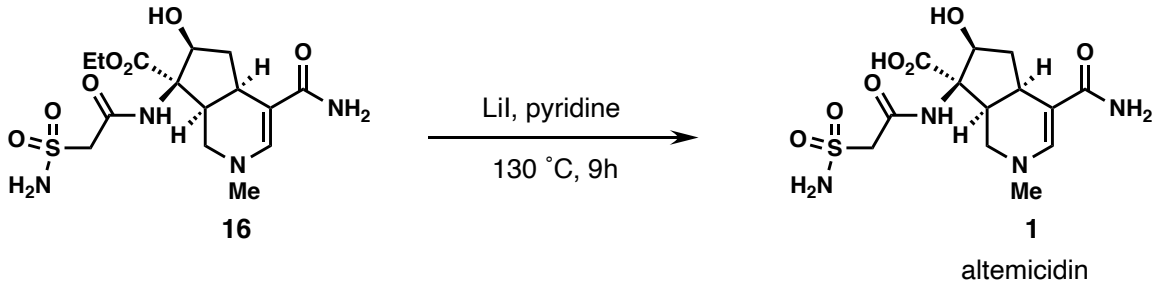
^{1}H NMR (600 MHz, MeOD) δ 7.34 (s, 1H), 4.22 (dd, *J* = 8.4, 7.2 Hz, 1H), 4.21 (d, *J* = 14.2 Hz, 1H, exchangeable), 4.18 (q, *J* = 7.1 Hz, 2H), 4.10 (d, *J* = 14.2 Hz, 1H, exchangeable), 2.96 (s, 3H), 2.95 – 2.81 (m, 4H), 2.66 (dt, *J* = 12.9, 6.9 Hz, 1H), 1.30 – 1.25 (m, 1H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, MeOD) δ 174.5, 174.0, 165.2, 146.1, 99.7, 75.9, 68.0, 62.8, 60.7, 45.8, 43.2, 43.0, 41.4, 32.6, 14.4.

HRMS (m/z): (ESI) calcd. for $C_{15}H_{25}N_4O_7S$ $[M+H]^+$: 405.1438, found 405.1439.

Deuterated compound: $C_{15}H_{23}D_2N_4O_7S$ $[M+H]^+$: 407.1564, found 407.1565.

IR (thin film) ν_{max} (cm^{-1}): 3133 (br), 3041 (br), 2926 (m), 2853 (m), 1646 (s), 1403 (s), 1338 (m), 1203 (m), 1182 (w), 1160 (m), 1134 (m).



Altemicidin 1: Ethyl altemicidin **16** (11 mg, 0.027 mmol, 1.0 equiv.) was transferred to a reaction tube with methanol and concentrated three times with toluene to remove any residual water. The reaction tube was equipped with a stir bar, brought into a glove box, and loaded with LiI (45 mg, 0.34 mmol, 12. equiv.). Pyridine (1 mL) was added to the reaction tube, which was sealed with parafilm and wrapped tightly in foil before being placed in a 130 ˚C oil bath for 9 hours. After 9 hours the reaction mixture was cooled to room temperature and concentrated down at room

temperature by blowing down with nitrogen. The resulting brown solid was resuspended in 1:1 DCM/Ethyl acetate and filtered through Celite®. The filtrate was discarded and the remaining solid was eluted into a fresh flask with 1:1 methanol/water and concentrated by blowing down with nitrogen. The crude mixture was loaded onto a C18 reverse phase column and eluted with 5% MeOH in 10 mM NH_4OAc (aq.). Fractions containing altemicidin-oxazoline were heated for 10-12 h at 60 ˚C to produce altemicidin. Combined fractions were subjected to a second C18 reverse phase column to remove the NH_4OAc (5% MeCN/H_2O) to yield altemicidin **1** (7 mg, 0.018 mmol, 67% yield) as a white powder.

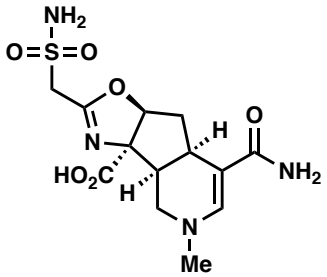
TLC: R_f = 0.2 (25% 7N NH_3/Methanol in DCM)

^{1}H NMR (700 MHz, D_2O) δ 7.39 (s, 1H), 4.38 (d, *J* = 14.1 Hz, 1H), 4.29 (d, *J* = 14.1 Hz, 1H), 4.28 (m, 1H), 2.98 (s, 2H), 2.92 (dd, *J* = 13.3, 7.2 Hz, 1H), 2.89 – 2.81 (m, 3H), 2.67 (m, 1H), 1.26 (dt, *J* = 12.8, 8.8 Hz, 1H).

^{13}C NMR (226 MHz, D_2O) δ 179.7, 174.2, 164.4, 147.3, 97.1, 76.0, 69.1, 60.1, 45.5, 43.2, 41.3, 40.8, 31.7.

HRMS (m/z): (ESI) calcd. for $C_{13}H_{19}N_4O_7S$ $[M–H]^–$: 375.0980, found 375.0981.

IR (thin film) ν_{max} (cm^{-1}): 3214 (br), 1644 (m), 1557 (s), 1406 (s), 1334 (m), 1135 (s).



18

altemicidin oxazoline

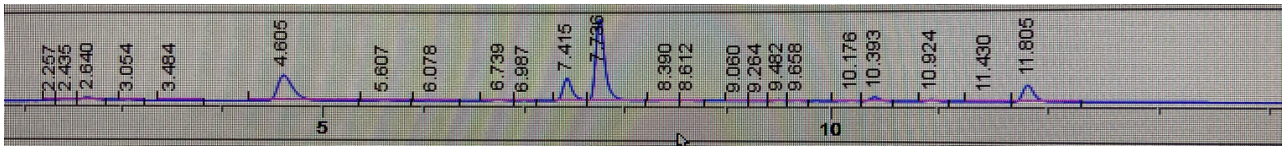
TLC: R_f = 0.3 (25% 7N NH_3/Methanol in DCM)

^{1}H NMR (700 MHz, D_2O) δ 7.38 (s, 1H), 5.44 (dd, *J* = 10.0, 2.2 Hz, 1H), 4.39 (d, *J* = 14.7 Hz, 1H), 4.37 (d, *J* = 14.8 Hz, 1H), 3.10 – 2.02 (m, 2H), 2.97 (dd, *J* = 5.9, 3.4 Hz, 1H), 2.83 (dt, *J* = 9.0, 3.6 Hz, 1H), 2.70 (s, 3H), 2.58 (ddd, *J* = 14.3, 10.1, 5.7 Hz, 1H), 2.18 (dd, *J* = 14.3, 2.2 Hz, 1H).

^{13}C NMR (151 MHz, D_2O) δ 173.13, 172.32, 164.78, 141.49, 101.00, 84.44, 67.23, 58.07, 45.41, 41.86, 38.68, 35.64, 33.46.

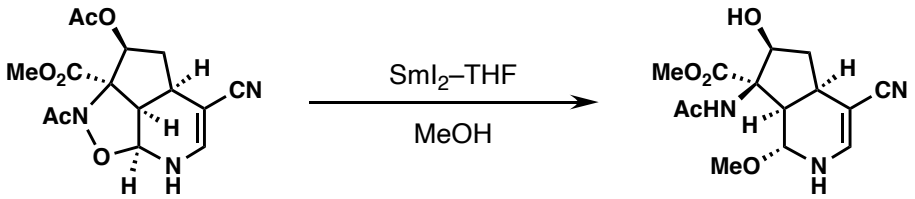
HRMS (m/z): (ESI) calcd. for $C_{13}H_{19}N_4O_6S$ $[M+H]^+$: 359.1020, found 359.1021.

LCMS Trace: 2-90% MeOH/50mM NH_4Oac, Luna C18 100 Å column



Retention time: compound
4.605: ethylpyridinium iodide
7.415: impurity
7.736: altemicidin oxazoline (**18**)
11.805: ethyl altemicidin oxazoline (**17**)

Table 1 Procedures and Characterization Data:



10 **21**

Aminal 18: 21 (4 mg, 0.01 mmol, 1.0 equiv.) was suspended in methanol (200 μL), equipped with a stir bar, and degassed thoroughly with argon. To this was added a freshly made samarium diiodide solution in THF[2] (1.6 of a ~0.05M solution, 0.08 mmol, 8.0 equiv.) and the reaction was allowed to stir at room temperature until consumption of the samarium diiodide as indicated by a change from a deep blue mixture to a pale purple solution. The reaction was diluted with methanol and concentrated. Purification by preparative TLC with 6% MeOH/3:1 DCM/Hexanes to give pure compound **21**.

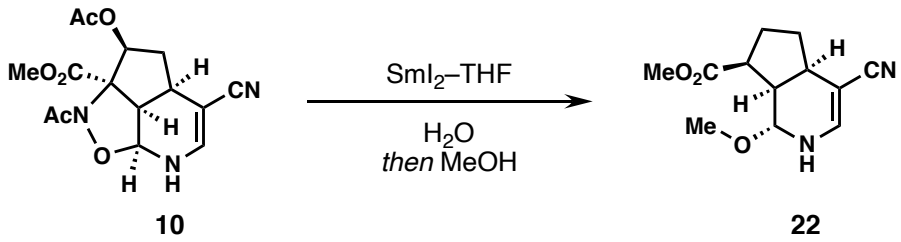
TLC: R_f = 0.4 (10% MeOH, 4:1 DCM/Hex).

^{1}H NMR (700 MHz, MeOD) δ 6.82 (d, *J* = 1.5 Hz, 1H), 4.71 (d, *J* = 1.8 Hz, 1H), 4.25 – 4.14 (m, 1H), 3.69 (s, 3H), 3.27 (s, 3H), 3.05 (dd, *J* = 9.3, 1.9 Hz, 1H), 2.83 (tdd, *J* = 9.1, 4.4, 1.4 Hz, 1H), 2.48 (dt, *J* = 13.9, 8.8 Hz, 1H), 1.94 (s, 3H), 1.88 (ddd, *J* = 13.9, 7.9, 4.4 Hz, 1H).

^{13}C NMR (151 MHz, MeOD) δ 174.1, 174.0, 143.1, 123.2, 82.3, 80.3, 76.6, 67.8, 54.3, 52.9, 45.0, 37.9, 29.1, 22.4.

IR (thin film) ν_{max} (cm^{-1}): 3328 (br), 2925(m), 2190 (m), 1729 (m), 1639 (s), 1513 (m), 1376 (w), 1268 (m), 1083 (m), 1063 (m).

HRMS (m/z): (ESI) calcd. for $C_{14}H_{19}N_3O_5Na$ $[M+Na]^+$: 332.1217, found 332.1216.



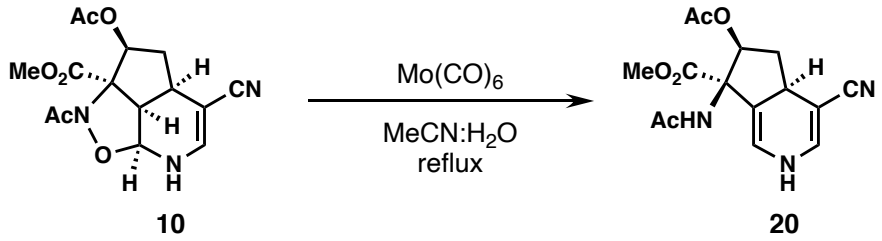
22: 10 (4mg, 0.01 mmol, 1.0 equiv.) was suspended in water (200 μL), equipped with a stir bar, and degassed thoroughly with argon. To this was added a freshly made samarium diiodide solution in THF (1.6 of a ~0.05M solution, 0.08 mmol, 8.0 equiv.) and the reaction was allowed to stir at room temperature until consumption of the samarium diiodide as indicated by a change from a deep purple mixture to a pale purple solution. The reaction was diluted with methanol and concentrated. Purification by preparative TLC with 6% MeOH/3:1 DCM/Hexanes to give pure compound **22**.

TLC: R_f = 0.9 (10% Methanol in 3:1 DCM/Hexanes).

^{1}H NMR (700 MHz, MeOD) δ 6.93 (s, 1H), 4.38 (s, 1H), 3.69 (s, 3H), 3.31 (s, 3H)*, 2.87 (s, 1H), 2.53 (dd, *J* = 15.2, 4.9 Hz, 1H), 2.53 – 2.46 (m, 1H), 2.04 – 1.93 (m, 2H), 1.93 – 1.87 (m, 2H). *underneath solvent peak, see HSQC

^{13}C NMR (151 MHz, MeOD) δ 177.4, 144.1, 122.4, 82.3, 80.7, 54.7, 52.5, 46.6, 45.5, 35.3, 30.1, 27.4.

HRMS (m/z): (ESI) calcd. for $C_{12}H_{16}N_2O_3Na$ $[M+Na]^+$:259.1059, found 249.1056.



Dihydropyridine 17: **10** (3.4 mg, 0.01 mmol, 1.0 equiv.) was combined with molybdenum hexacarbonyl (2.6 mg, 0.01 mmol, 1.0 equiv.) in a reaction tube equipped with a stir bar and backfilled with nitrogen to this was added a 9:1 mixture of MeCN/H_2O (0.55 mL) which had been degassed by sparging with argon and concomitant sonication. The reaction mixture was heated to 85 ˚C for 16 h. Upon cooling to room temperature the reaction mixture was filtered through Celite®, concentrated, and passed through a plug of silica with 10% MeOH/DCM to remove molybdenum byproducts. Further purification by preparative TLC (10% MeOH in 3:1 DCM/Hexanes) provided **20** as the exclusive product of the reaction.

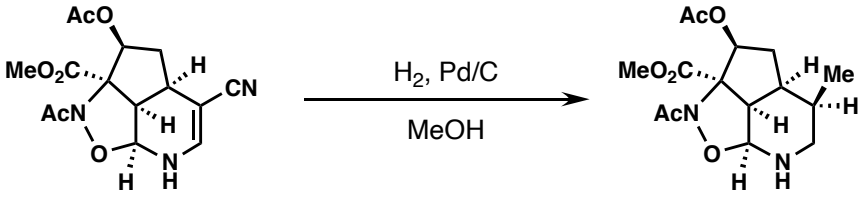
TLC: R_f = 0.4 (10% Methanol in 3:1 DCM/Hexanes).

^{1}H NMR (600 MHz, MeOD) δ 6.86 (s, 1H), 6.34 (d, *J* = 2.2 Hz, 1H), 5.83 (t, *J* = 6.8 Hz, 1H), 3.68 (s, 3H), 3.33 (q, *J* = 2.0 Hz, 1H), 2.64 (dt, *J* = 12.6, 7.1 Hz, 1H), 1.99 (s, 3H), 1.97 (s, 3H), 1.83 (ddd, *J* = 12.6, 9.5, 6.9 Hz, 1H).

^{13}C NMR (151 MHz, MeOD) δ 173.2, 171.7, 171.5, 141.1, 123.4, 121.3, 113.6, 80.1, 73.1, 67.9, 53.2, 39.0, 33.2, 22.0, 20.8.

HRMS (m/z): (ESI) calcd. for $C_{15}H_{17}N_3O_5Na$ $[M+Na]^+$: 342.4060, found 342.1061.

IR (thin film) ν_{max} (cm^{-1}): 3352 (br), 2955 (w), 2928 (w), 2199 (m), 1736 (s), 1662 (m), 1496 (m), 1237 (s).



10 **23**

Piperidine 20: 10 (3.4 mg, 0.01 mmol, 1.0 equiv.) was combined with 10% Pd/C and suspended in methanol (1 mL) in a reaction tube equipped with a stir bar. The tube was sealed with a septum and equipped with a hydrogen balloon which was engaged via an 18-gauge needle. The reaction

mixture was sparged with hydrogen for 10 minutes and the mixture was allowed to stir 12 h under positive hydrogen pressure. Upon reaction completion the mixture was filtered through Celite® with methanol and concentrated *in vacuo.* The crude mixture was further purified by preparatory TLC (8% Methanol in 3:1 DCM/Hexanes) to yield **23** as the main product of the reaction.

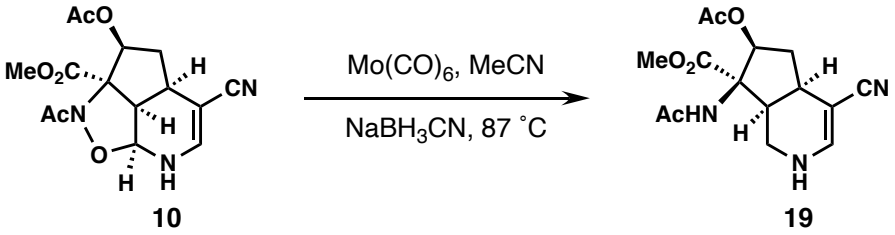
TLC: R_f = 0.7 (10% Methanol in 3:1 DCM/Hexanes).

^{1}H NMR (600 MHz, MeOD) δ 5.76 (dd, *J* = 11.6, 6.5 Hz, 1H), 5.24 (d, *J* = 5.3 Hz, 1H), 3.72 (s, 3H), 2.93 (dd, *J* = 8.8, 5.4 Hz, 1H), 2.80 (t, *J* = 11.7 Hz, 1H), 2.51 (dd, *J* = 11.7, 4.2 Hz, 1H), 2.26 (ddt, *J* = 14.3, 8.8, 5.7 Hz, 1H), 2.09 (s, 3H), 2.01 (dt, *J* = 12.2, 6.3 Hz, 1H), 1.97 (s, 3H), 1.94 (m, 1H), 1.77 (dt, *J* = 13.9, 11.5 Hz, 1H), 0.92 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (151 MHz, MeOD) δ 171.9, 170.1, 168.4, 91.9, 75.9, 75.3, 53.3, 51.9, 49.4, 40.6, 36.3, 30.5, 30.4, 20.8, 20.5, 17.2.

HRMS (m/z): (ESI) calcd. for $C_{15}H_{22}N_2O_6Na$ $[M+Na]^+$: 349.1370, found 349.1370.

IR (thin film) ν_{max} (cm^{-1}): 3371 (br), 2957 (w), 2877 (w), 1745 (s), 1655 (s), 1435 (w), 1236 (s).



19: Prepared in analogous fashion to **12**.

TLC: R_f: 0.55 (15% MeOH in 2:1 DCM/hexanes).

^{1}H NMR (700 MHz, MeOD) δ 7.08 (s, 1H), 5.44 (t, *J* = 7.8, 6.4 Hz, 1H), 3.69 (s, 3H), 3.23 (ddd, *J* = 12.9, 5.2, 1.4 Hz, 1H), 3.13 (dd, *J* = 12.9, 8.8 Hz, 1H), 2.83 – 2.73 (m, 2H), 2.67 (dt, *J* = 14.0, 7.8 Hz, 1H), 2.06 (s, 3H), 2.00 (s, 3H), 1.67 (ddd, *J* = 14.0, 8.7, 6.4 Hz, 1H).

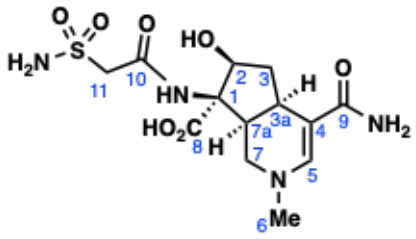
^{13}C NMR (176 MHz, MeOD) δ 173.9, 173.8, 171.1, 146.8, 124.0, 76.8, 75.8, 68.9, 53.2, 41.6, 39.8, 38.3, 33.9, 21.9, 20.8.

HRMS (m/z): (ESI) calcd. for $C_{15}H_{19}N_3O_5Na$ $[M+Na]^+$: 344.1217, found 344.1215.

IR (thin film) ν_{max} (cm^{-1}): 3366 (br), 2954 (w), 2928 (w), 2855 (w), 2186 (s), 1734 (s), 1626 (s), 1506 (s), 1235 (s).

Natural Product Spectral Comparisons

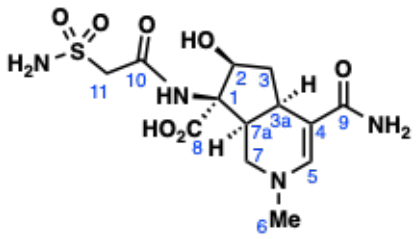
Altemicidin ^{1}H NMR Spectra Comparison:



XX
altemicidin

Position	^{1}H (δ) Natural Sample (400 MHz, D_2O) *[ref. 2]*[3]	^{1}H (δ) Synthetic Sample (600 MHz, D_2O)
2-H	4.28 (dd, *J* = 7.6, 9.0 Hz, 1H)	4.28 (m, 1H)
3-H_a	1.26 (dt, *J* = 9.0,12.6 Hz, 1H)	1.26 (dt, *J* = 8.8, 12.8 Hz, 1H)
3-H_b	2.67 (dt, *J* = 7.6, 12.6 Hz, 1H)	2.67 (m, 1H)
3a-H	~2.93 (m)	2.92 (dd, *J* = 13.3, 7.2 Hz, 1H)
5-H	7.39 (s, 1H)	7.39 (s, 1H)
6-H	2.98 (s, 3H)	2.98 (s, 3H)
7-H_a	~2.86 (m)	2.89-2.81 (m)
7-H_b	~2.86 (m)	2.89-2.81 (m)
7a-H	~2.86 (m)	2.89-2.81 (m)
11-H_a	4.29 (d, *J* = 14.0 Hz, 1H)	4.29 (d, *J* = 14.1 Hz, 1H)
11-H_b	4.38 (d, *J* = 14.0 Hz, 1H)	4.38 (d, *J* = 14.1 Hz, 1H)

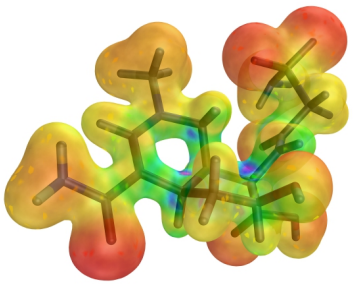
Altemicidin ^{13}C NMR Spectra Comparison:



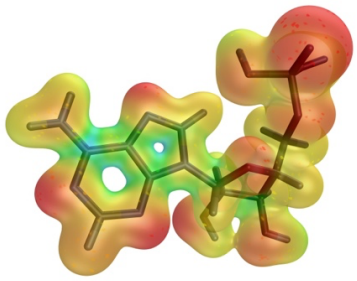
XX
altemicidin

Position	^{13}C (δ) Natural Sample (100 MHz, D_2O) *[ref. 2]*	^{13}C (δ) Synthetic Sample (151 MHz, D_2O)
1	69.1	69.1
2	76.0	76.0
3	41.4	41.3
3a	31.7	31.7
4	97.1	97.1
5	147.3	147.3
6	43.2	43.2
7	45.5	45.5
7a	40.8	40.8
8	179.7	179.7
9	174.2	174.2
10	164.4	164.4
11	60.3	60.1

ESP Surface Data



ESP altemicidin (**1**)



ESP AMP (**4**)

Electrostatic potential (ESP) surfaces for altemicidin (**1**) and AMP (**4**) were generated by Macromodel minimization of the 3D structure in Maestro,[4] followed by optimization and frequency calculations in Gaussian 16[5] (B3LYP/6-31+g(d)). The ESP surfaces were visualized with IQmol[6] (isovalue = 0.05, rainbow color gradient -0.1054 (red) to 0.4041 (purple)).

Gaussian title card:

opt freq=noraman b3lyp/6-31+g(d) scrf=(iefpcm,solvent=water) geom=connectivity empiricaldispersion=gd3bj integral=ultrafinegrid

Altemicidin (**1**) Cartesian coordinates:

$altemicidin-opt-freq

0 1

C	-2.5184	3.157	-4.712
C	-2.2758	1.9694	-5.6676
C	-3.5003	1.933	-6.5927
C	-4.1233	3.4014	-6.5484
C	-3.1883	4.223	-5.6084
C	-2.1277	5.0349	-6.3697
N	-1.1968	5.6398	-5.4211
C	-0.7538	4.882	-4.3765
C	-1.2938	3.6847	-4.0054
O	-3.1814	1.6063	-7.951
N	-4.2334	3.9221	-7.9048
C	-5.5225	3.2728	-5.9106
O	-5.7734	3.4489	-4.7409
O	-6.4437	2.8289	-6.7998
C	-0.409	6.7633	-5.9075
C	-0.8104	2.9109	-2.8501
N	0.4082	3.2668	-2.2828

O	-1.465	1.9798	-2.3686
C	-4.8817	5.0673	-8.1947
C	-4.8783	5.4805	-9.6605
O	-5.4254	5.7734	-7.3383
S	-4.1247	7.1461	-9.834
O	-2.8554	7.091	-9.1034
O	-4.1859	7.5026	-11.2529
N	-5.127	8.2059	-9.0208
H	-3.2326	2.8415	-3.9451
H	-1.3875	2.1506	-6.2831
H	-2.1295	1.03	-5.1278
H	-4.2511	1.2227	-6.2289
H	-3.7817	4.9148	-5.0085
H	-1.5741	4.3989	-7.0799
H	-2.5836	5.8376	-6.9505
H	0.0494	5.3363	-3.8031
H	-3.0125	0.659	-8.0221
H	-3.8694	3.3263	-8.6393
H	-7.2824	2.7466	-6.315
H	-1.0699	7.5254	-6.3292
H	0.1507	7.2069	-5.0803
H	0.3022	6.4585	-6.691
H	1.1286	3.6627	-2.8684
H	0.7343	2.6155	-1.5814
H	-4.2849	4.8292	-10.3067
H	-5.8988	5.5467	-10.0452
H	-5.9415	8.4419	-9.5816
H	-5.3775	7.8345	-8.1017

$end

AMP (**4**) Cartesian coordinates:

$AMP-opt-freq_1
0 1

P	3.70172300	-1.58513900	-0.19284100
O	0.72536200	0.89617100	-0.95742300
O	-1.07002300	3.00024900	1.36234100
O	0.75114600	3.95828100	-0.34193800
O	3.29705900	-0.13094800	-0.70659000
O	2.37614700	-2.01802300	0.61192800
O	4.75191600	-1.39992400	1.02099900
O	4.15939300	-2.45581700	-1.30418900
N	-1.29178400	0.13679700	-0.07812400
N	-1.83881900	-1.93541800	0.61839200
N	-3.51318500	0.92332100	-0.76098600

N	-5.21407000	-0.75424300	-0.40910600
N	-4.78715100	-2.84745500	0.52040300
C	-0.07882100	2.12064600	0.89009600
C	1.19652600	2.81596300	0.38861600
C	-0.49271000	1.31156500	-0.35776200
C	1.81502100	1.74597300	-0.52675700
C	2.86112600	0.91403700	0.19643200
C	-2.65571000	0.01887800	-0.26247600
C	-0.86240900	-1.06773000	0.45190800
C	-2.97466600	-1.27020300	0.18016700
C	-4.33174400	-1.64553000	0.09197000
C	-4.76412000	0.45061400	-0.79955100
H	0.16072400	1.43115800	1.70431500
H	1.86088200	3.11209600	1.20560000
H	-1.08402500	1.93522200	-1.03645800
H	2.25545600	2.20256200	-1.41799000
H	2.45530000	0.47265100	1.10996900
H	3.72900000	1.53046900	0.44648600
H	-1.01605700	3.80532000	0.81313700
H	1.47472700	4.59874100	-0.42356500
H	0.18269300	-1.25452000	0.65436400
H	-5.51806600	1.12486000	-1.19793600
H	-4.12429100	-3.58566100	0.71539600
H	-5.72655600	-3.12395900	0.26637100
H	2.45636100	-2.86079500	1.09371400
H	5.68012700	-1.43726500	0.72828200

$end

References

(1) Wolckenhauer, S. A.; Devlin, A. S.; Du Bois, J. δ-Sultone Formation Through Rh-Catalyzed C−H Insertion. *Org. Lett.* **2007**, 9 (*21*), 4363.

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(4) Schrödinger Release 2021-1: Maestro, Schrödinger, LLC, New York, NY, 2021.

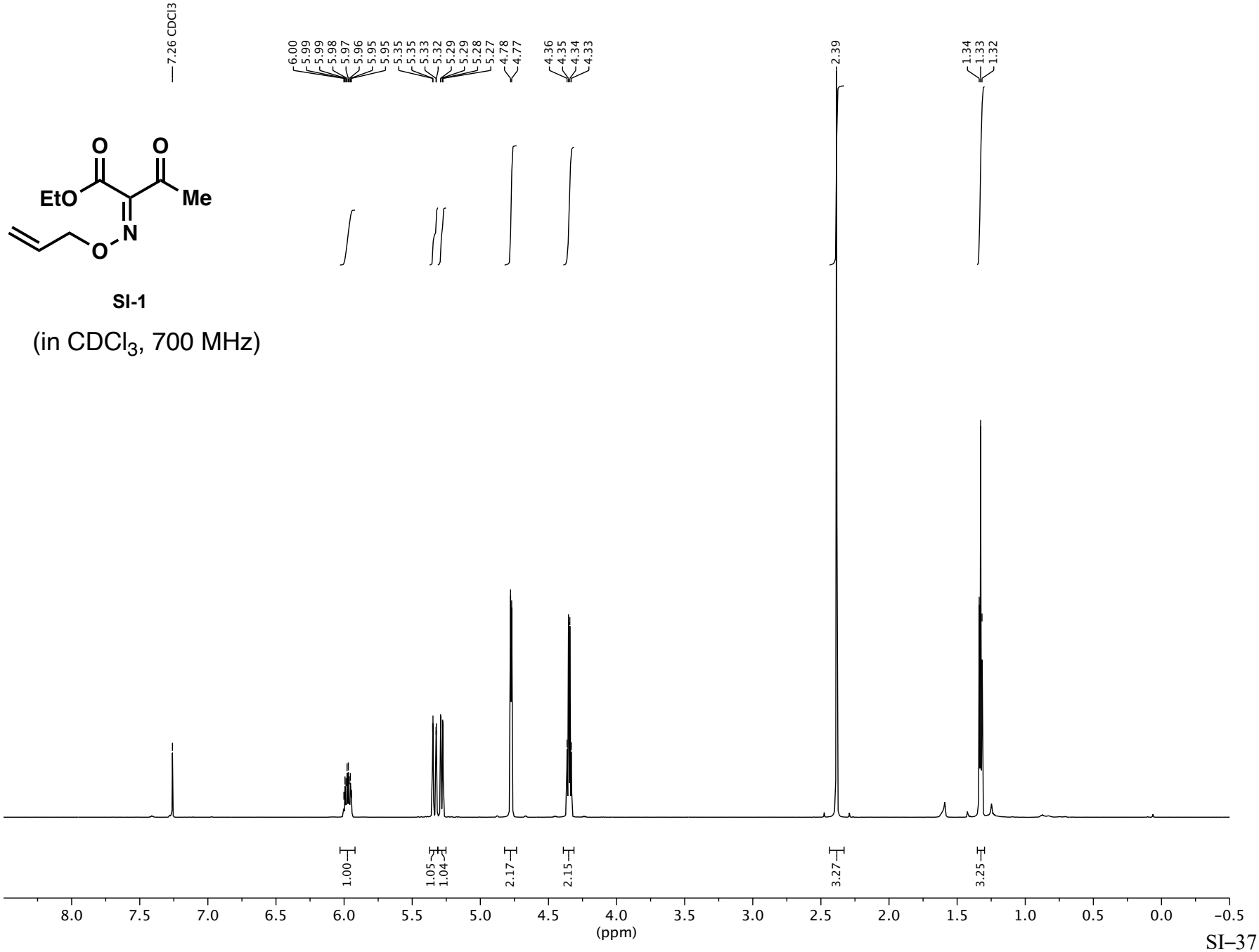
(5) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. Gaussian 16 Rev. C.01; Wallingford, CT, 2016.

(6) Gilbert, A. IQMol; 2020.

Appendix A: Ammonia Methanol Solution

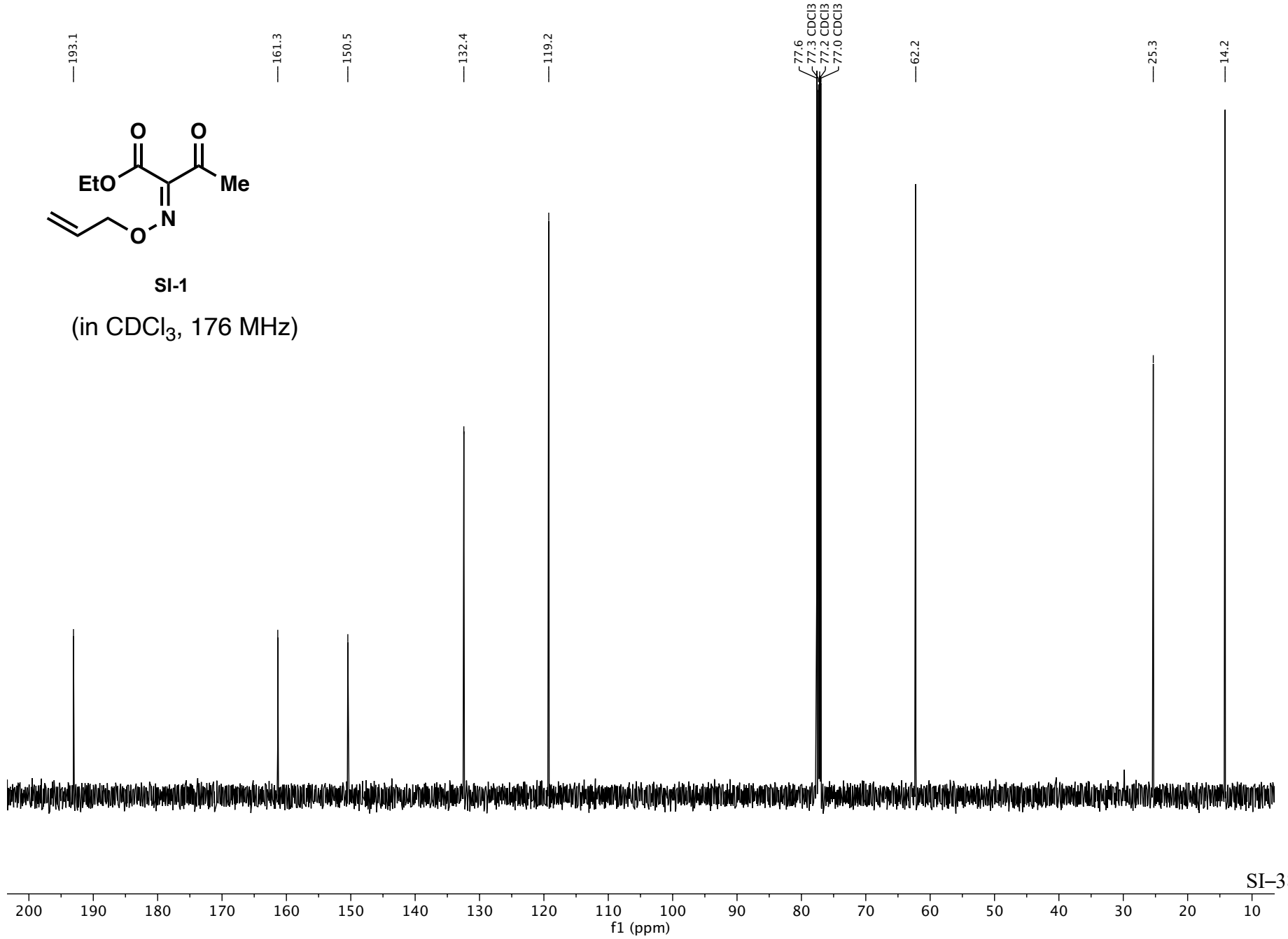
A standard 4L glass bottle of MeOH was clamped securely in a well ventilated hood and cooled to 0 to 10 ˚C in a large ice-water bath, with the bath covering the entire body of the bottle. A tank of ammonia gas was appropriately secured in the hood and equipped with a standard regulator. An outlet hose connected to a 9 inch glass pipet was inserted into the MeOH and attached to the regulator as shown in SI-Figure 1. Ammonia gas was bubbled into the MeOH in a steady stream until saturation was reached as indicated by visible bubbling of the solution. Care was taken to maintain the ice bath replenished as the process is somewhat exothermic. The resulting solution was stored at 4 ˚C when not in use.

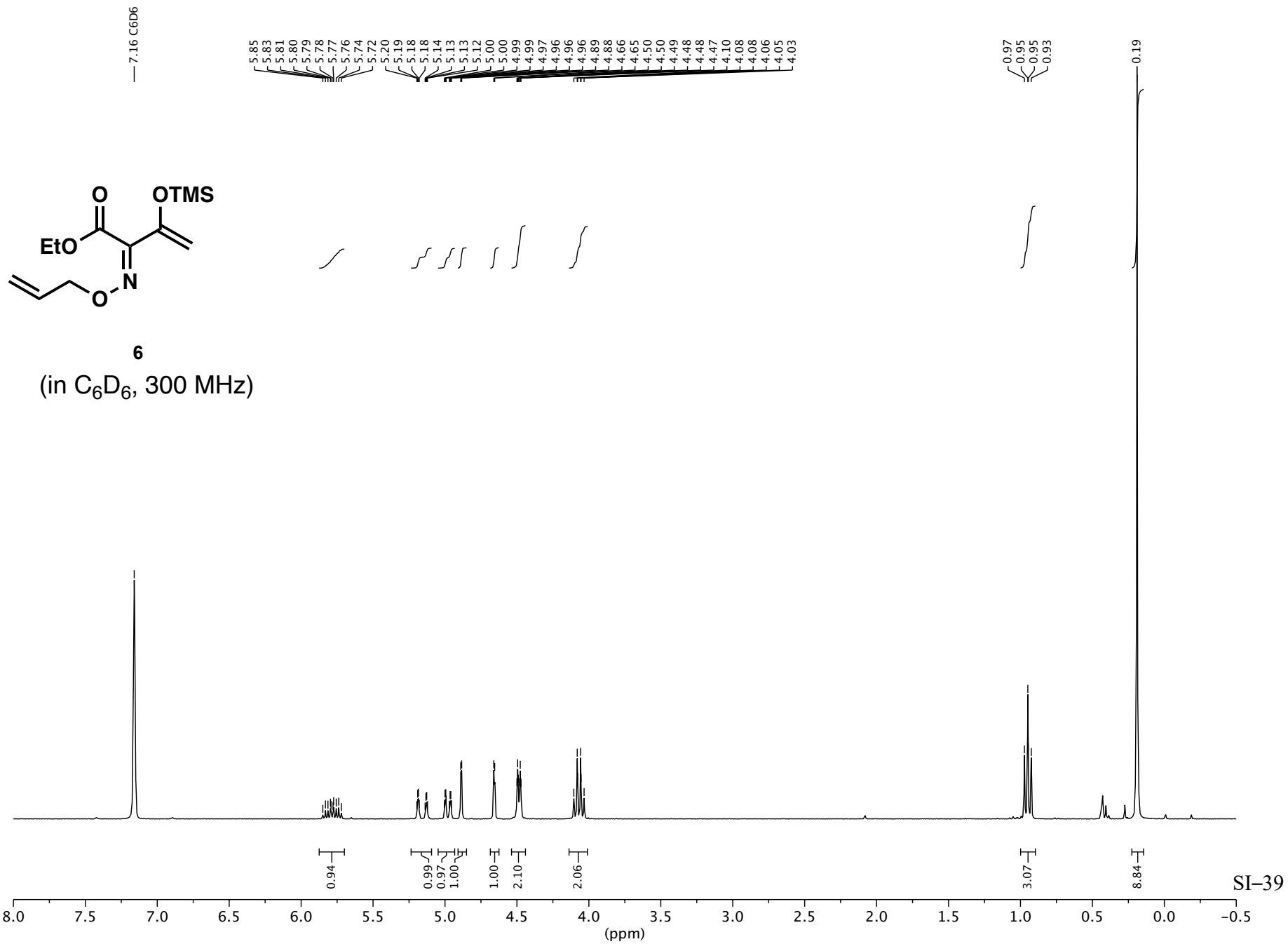
SI-Figure 1: Ammonia gas is bubbled into a cooled 4L of MeOH.



SI-1

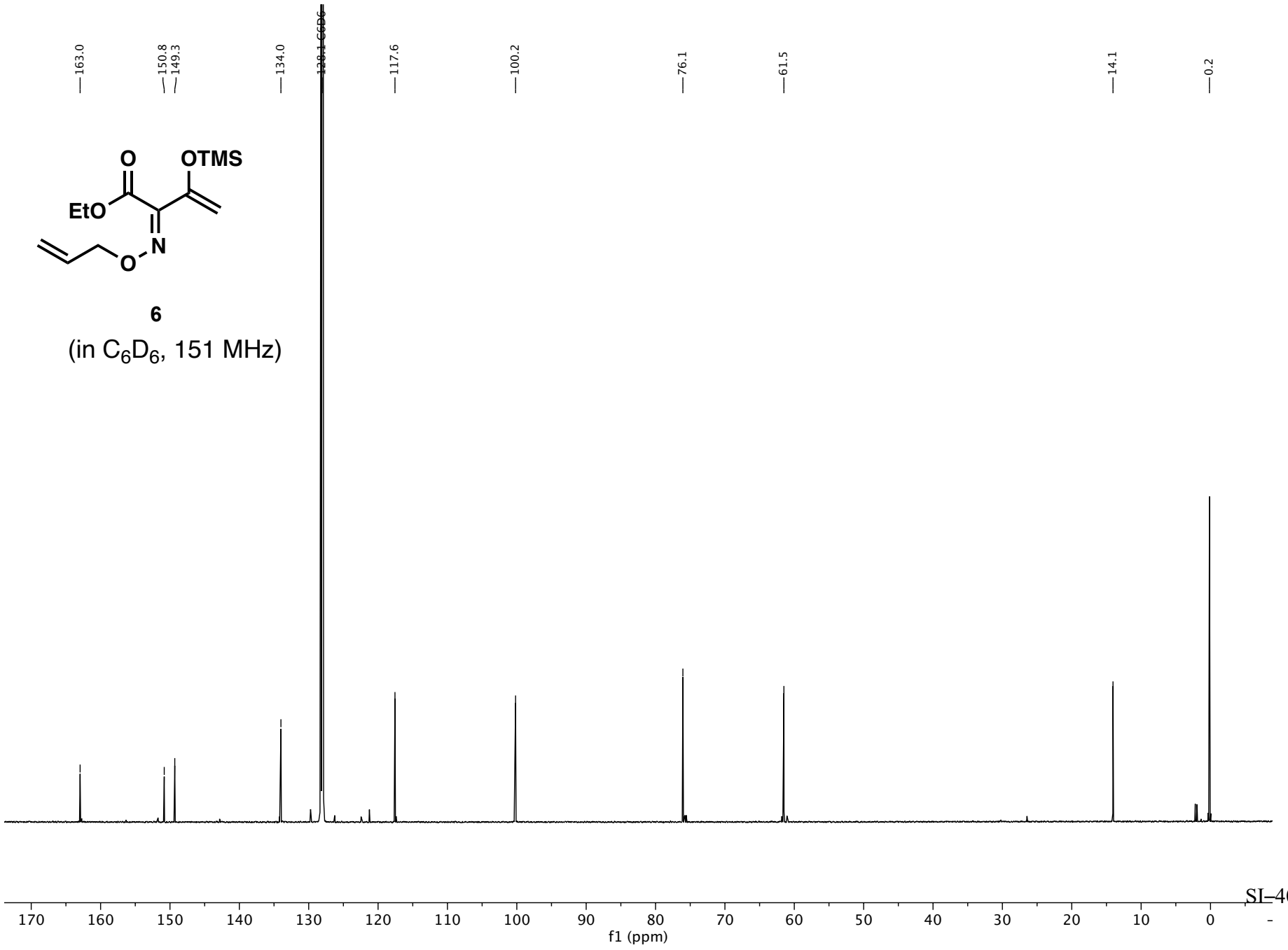
(in $CDCl_3$, 700 MHz)

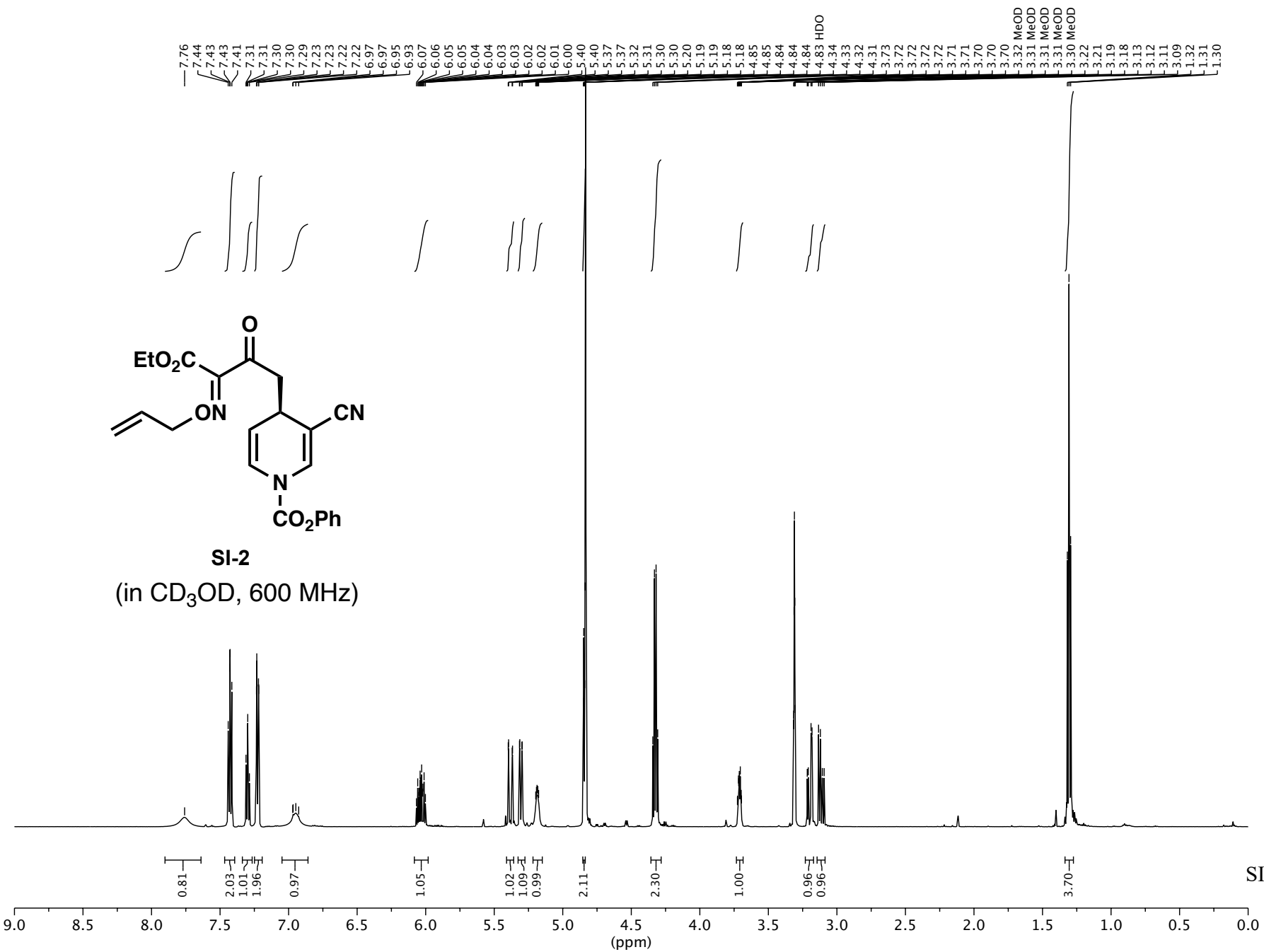

193.1
161.3
150.5
132.4
119.2
77.6
77.3 CDCl3
77.2 CDCl3
77.0 CDCl3
62.2
25.3
14.2
O
O
EtO
Me
N
O
SI-1
(in CDCl3, 176 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



6

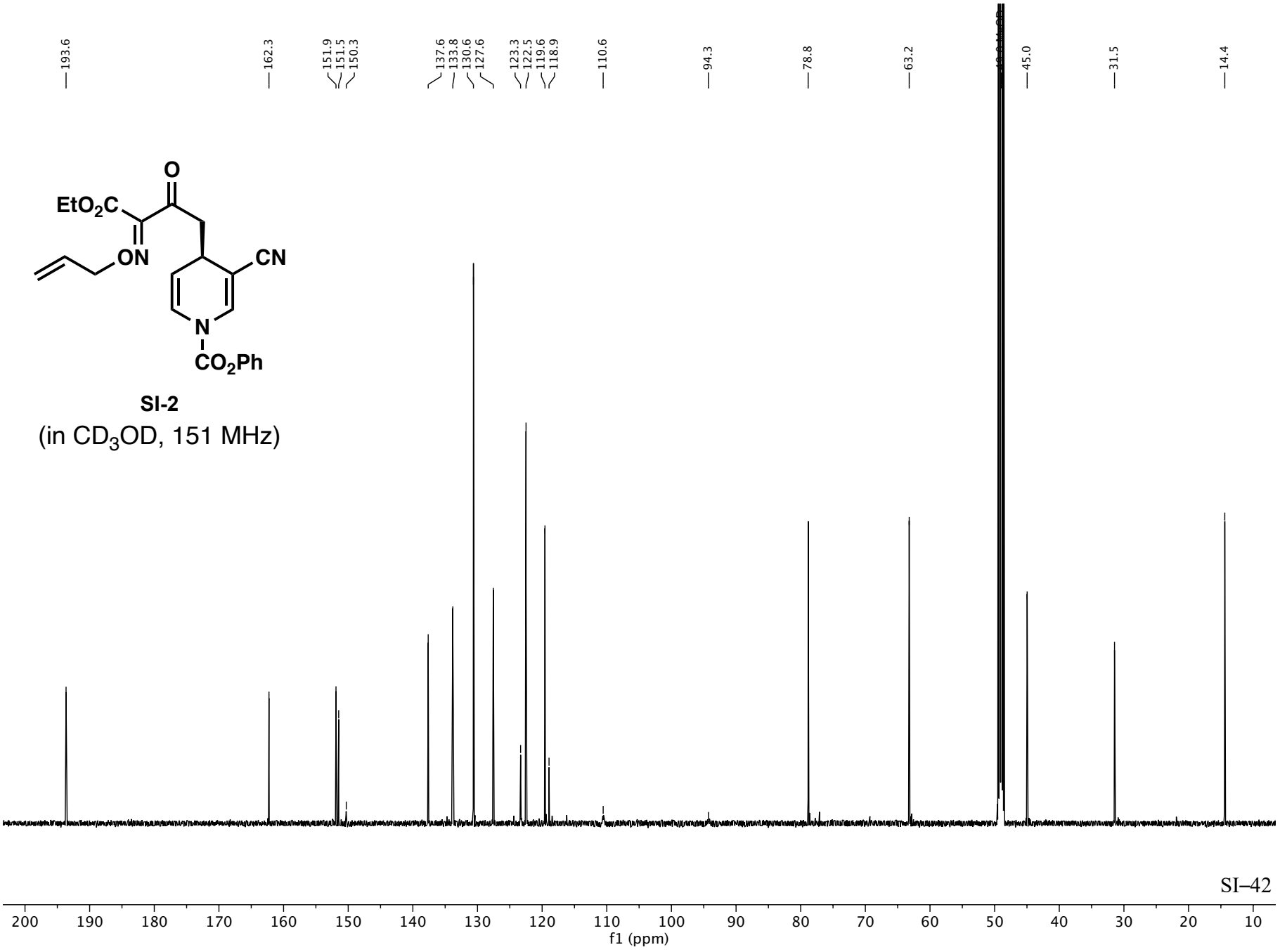
(in C_6D_6, 300 MHz)

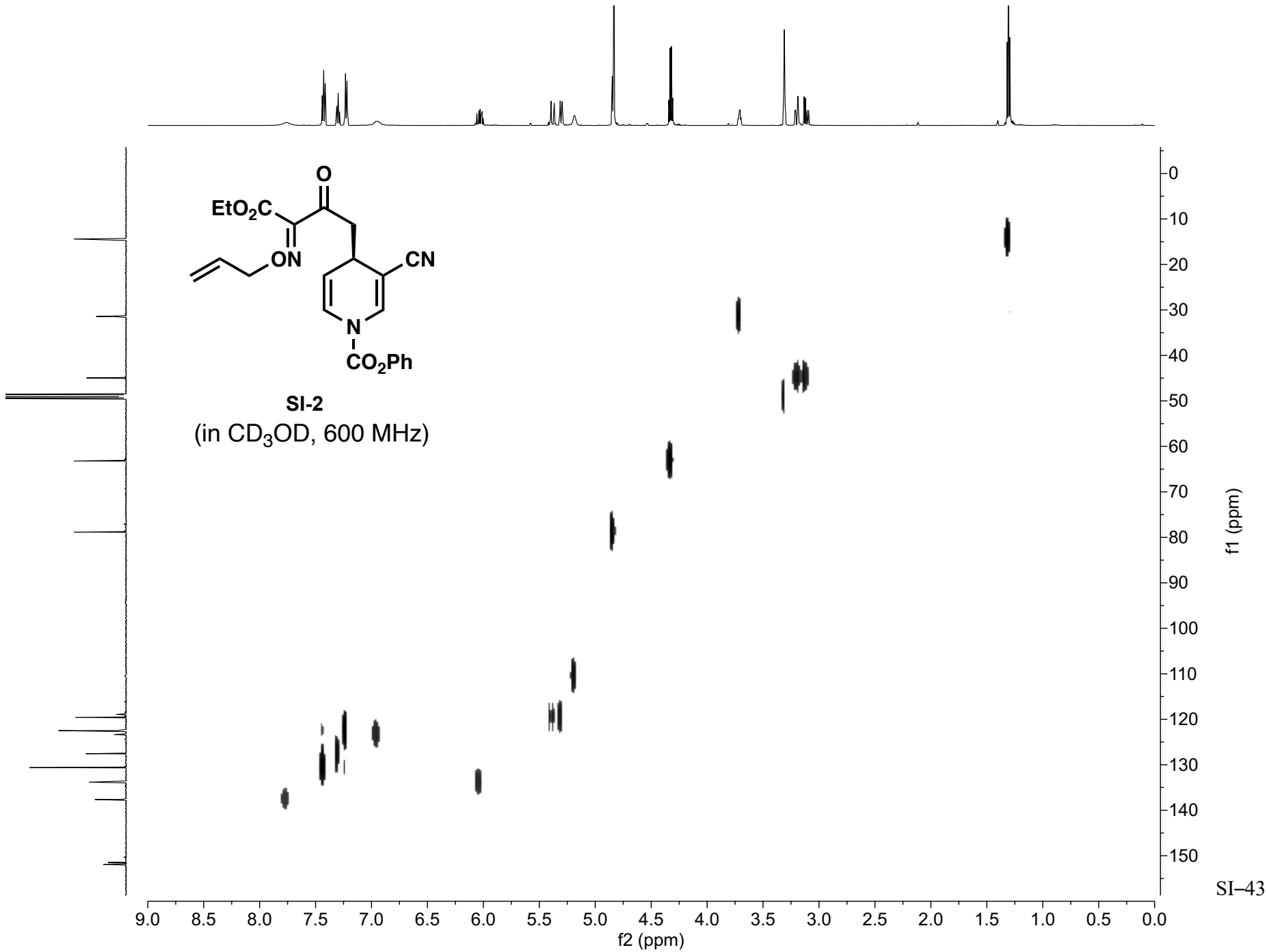

163.0
150.8
149.3
134.0
128.4
117.6
100.2
76.1
61.5
14.1
0.2
O
OTMS
EtO
N
O
6
(in C6D6, 151 MHz)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

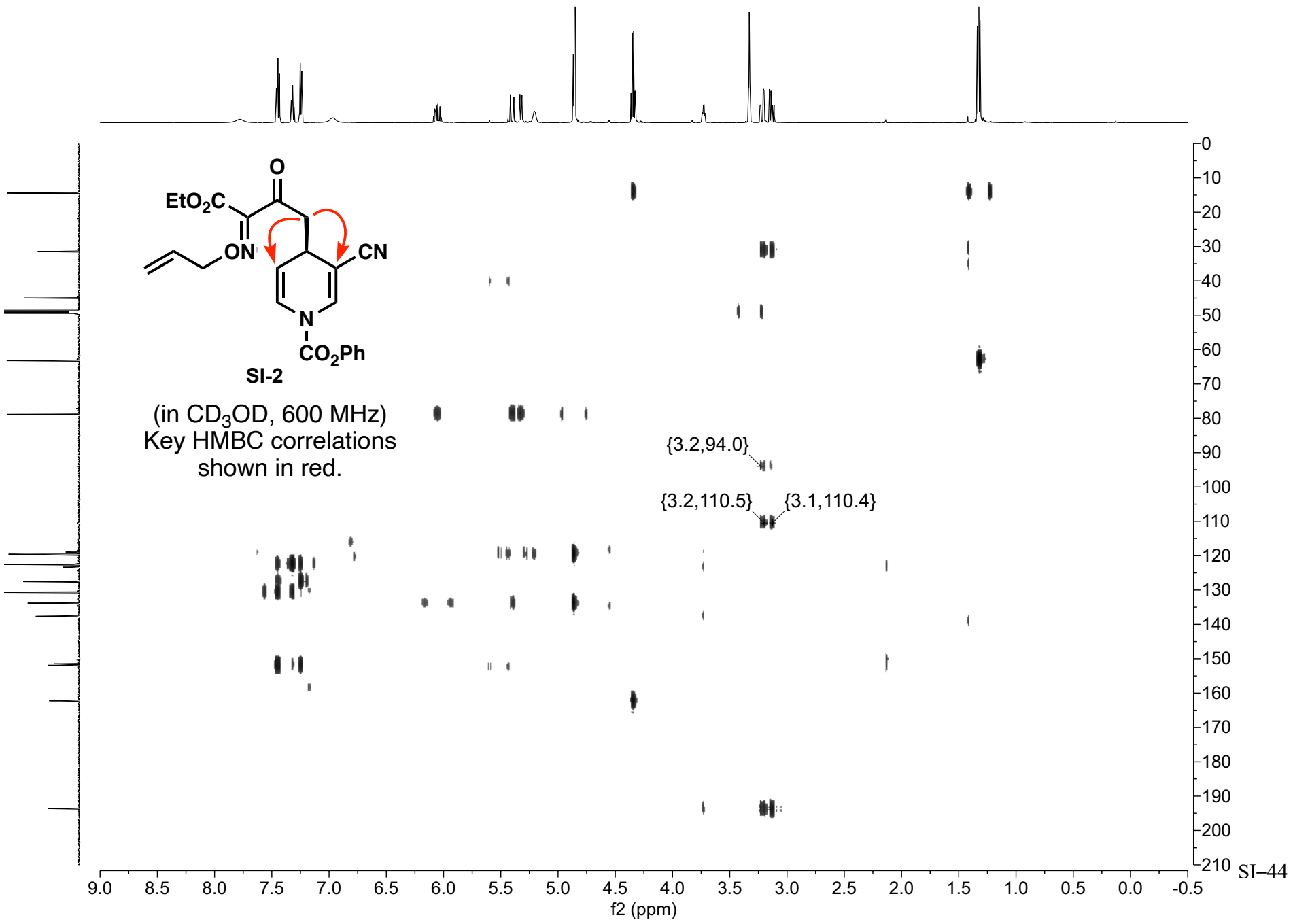


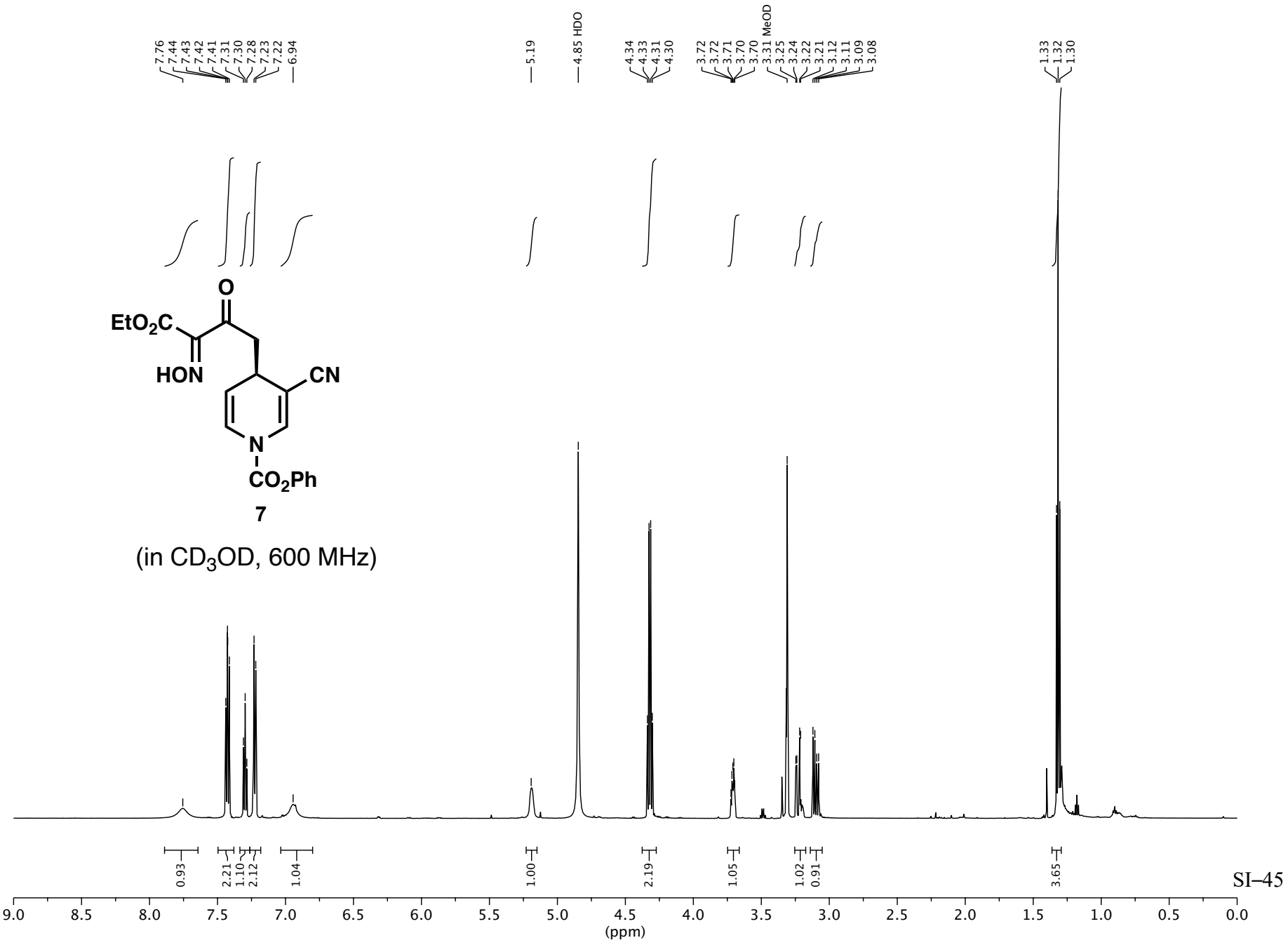
SI-2

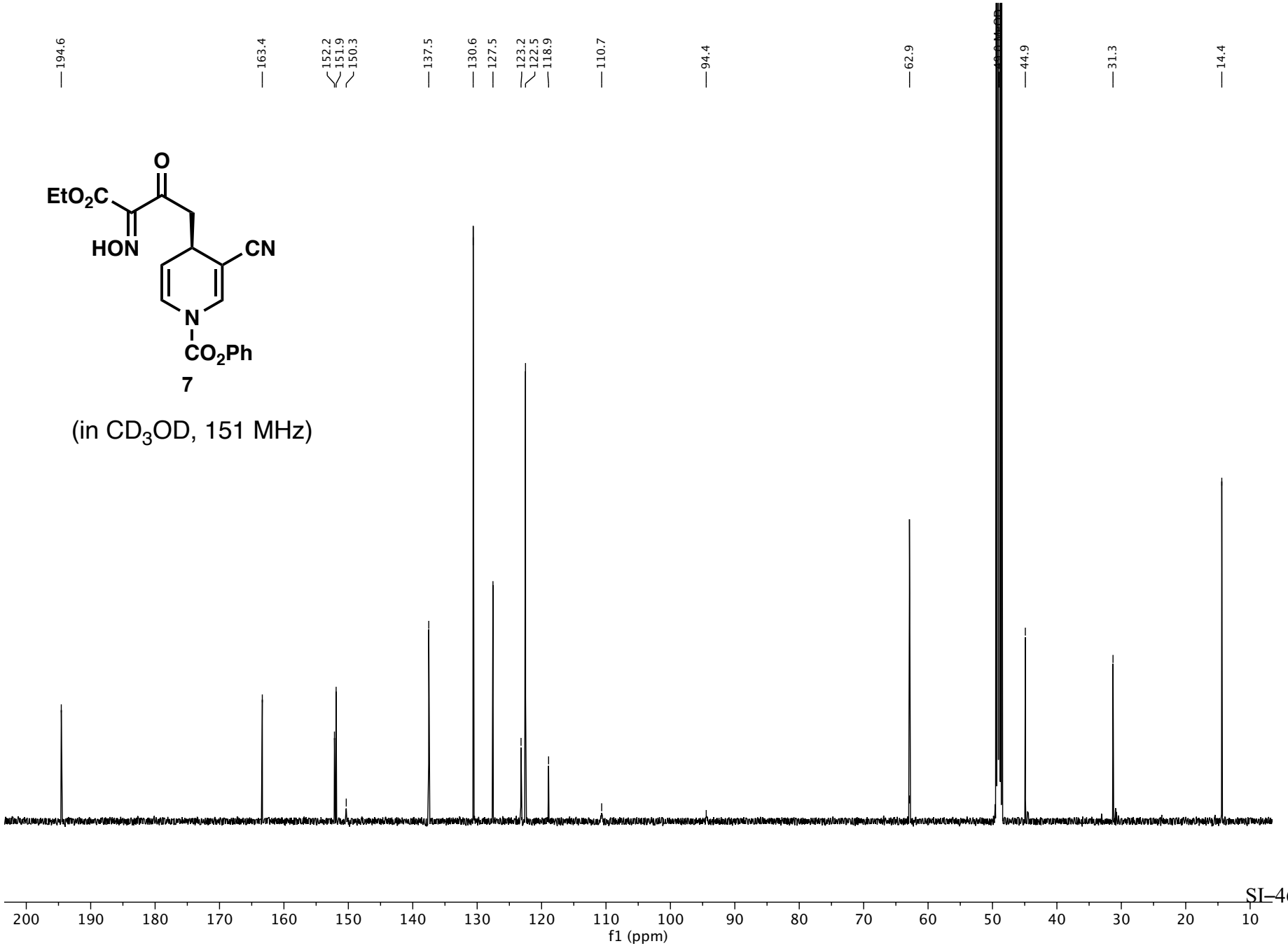
(in CD_3OD, 600 MHz)

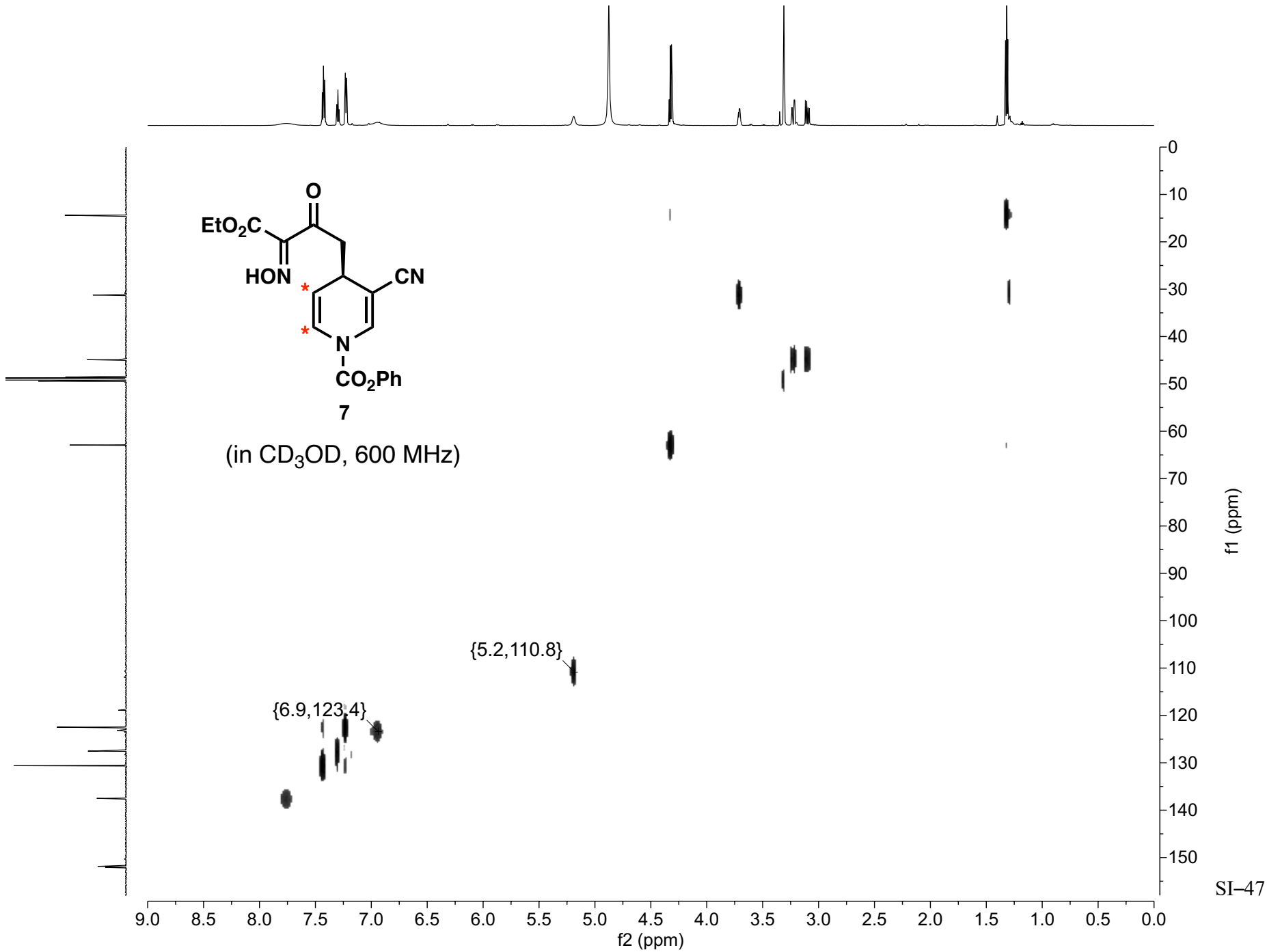

193.6
162.3
151.9
151.5
150.3
137.6
133.8
130.6
127.6
123.3
122.5
119.6
118.9
110.6
94.3
78.8
63.2
45.0
31.5
14.4
O
EtO2C
ON
CN
N
CO2Ph
SI-2
(in CD3OD, 151 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

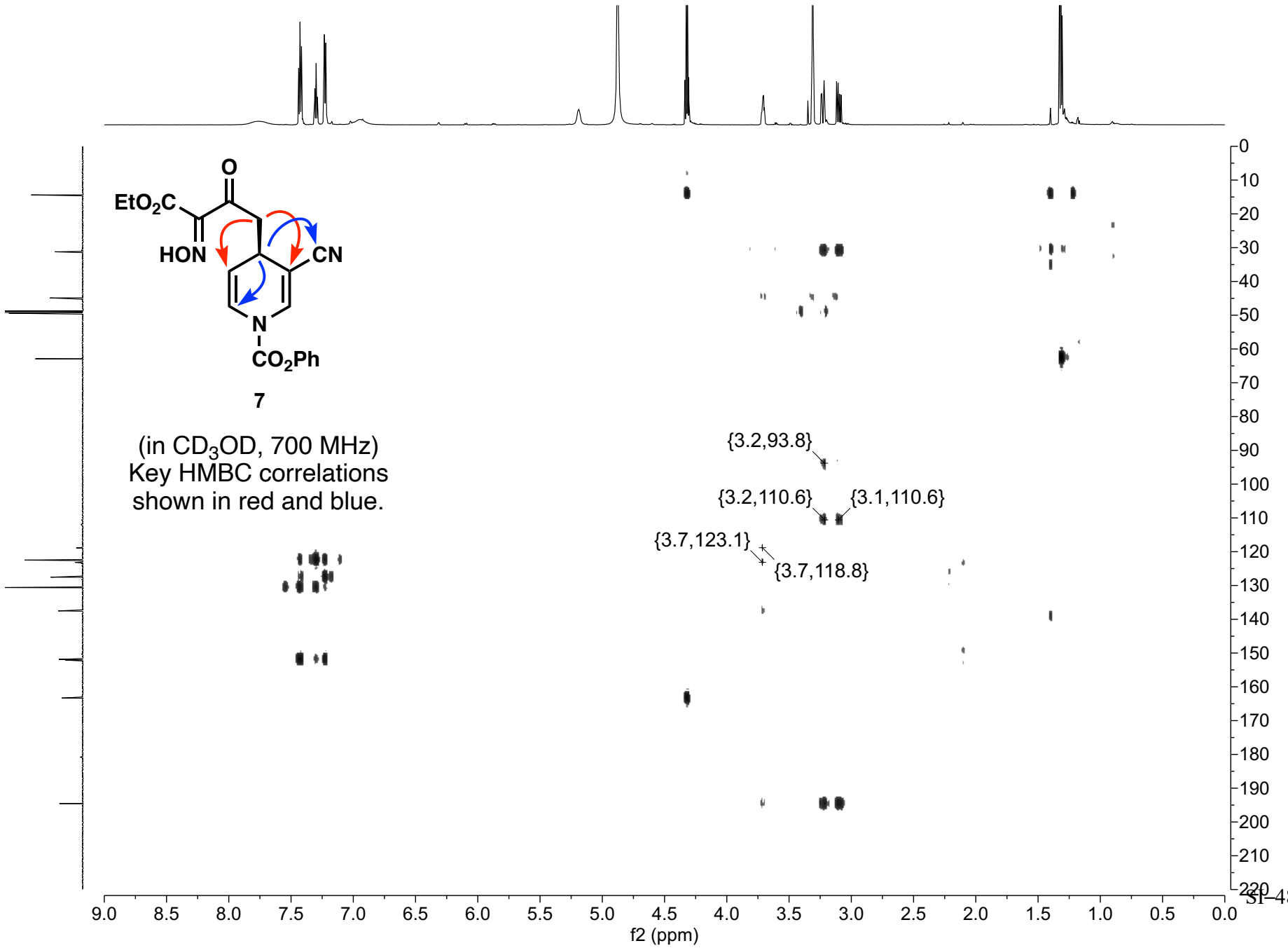

O
EtO2C
ON
CN
N
CO2Ph
SI-2
(in CD3OD, 600 MHz)
f2 (ppm)
f1 (ppm)

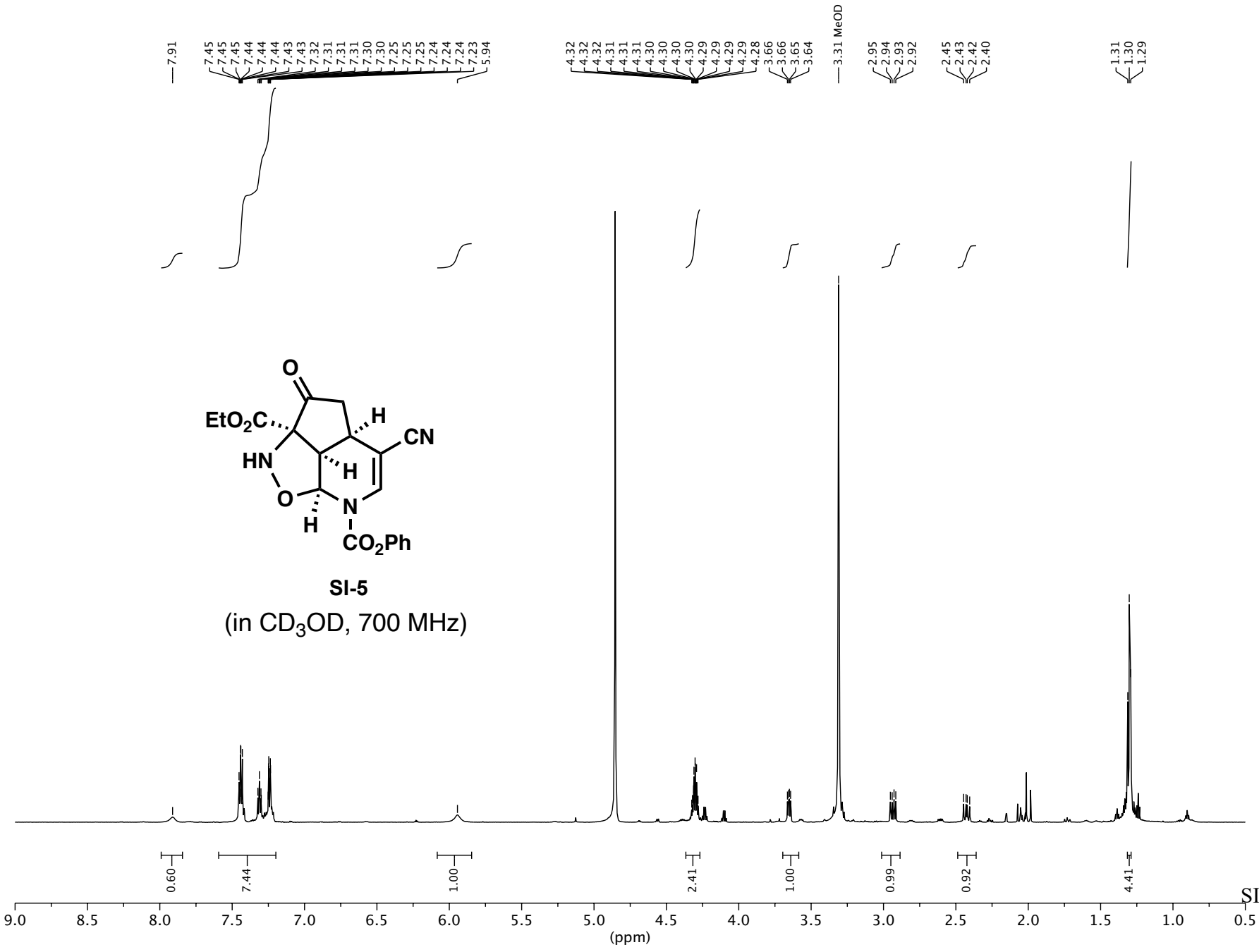

O
EtO2C
ON
CN
N
CO2Ph
SI-2
(in CD3OD, 600 MHz)
Key HMBC correlations
shown in red.
{3.2,94.0}
{3.2,110.5}
{3.1,110.4}
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f2 (ppm)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210


7.76
7.44
7.43
7.42
7.41
7.31
7.30
7.28
7.23
7.22
6.94
5.19
4.85 HDO
4.34
4.33
4.31
4.30
3.72
3.72
3.71
3.70
3.70
3.31 MeOD
3.25
3.24
3.22
3.21
3.12
3.11
3.09
3.08
1.33
1.32
1.30
O
EtO2C
HON
CN
N
CO2Ph
7
(in CD3OD, 600 MHz)
0.93
2.21
1.10
2.12
1.04
1.00
2.19
1.05
1.02
0.91
3.65
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
(ppm)


194.6
163.4
152.2
151.9
150.3
137.5
130.6
127.5
123.2
122.5
118.9
110.7
94.4
62.9
44.9
31.3
14.4
O
EtO2C
HON
CN
N
CO2Ph
7
(in CD3OD, 151 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

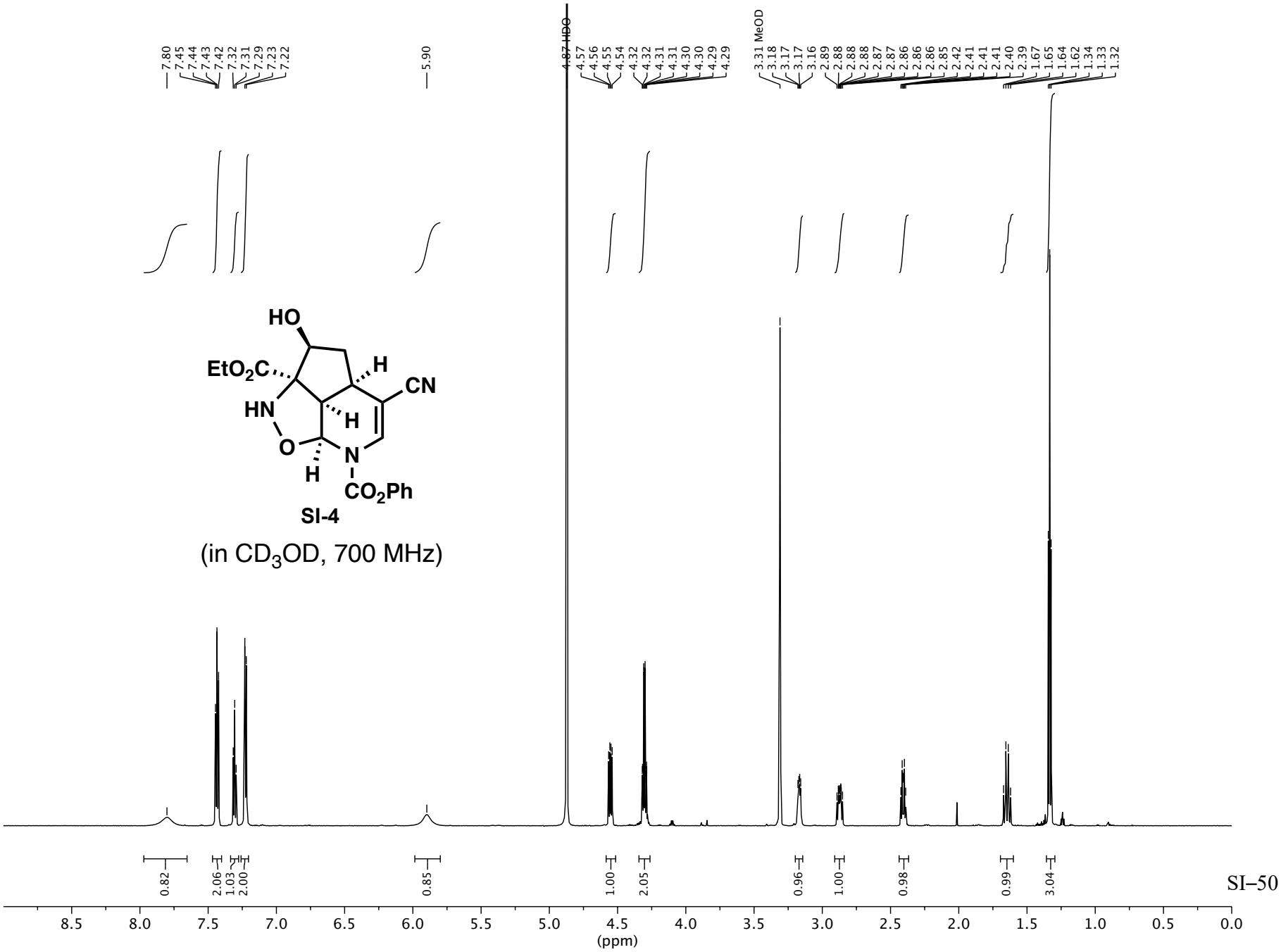

O
EtO2C
HON
CN
N
CO2Ph
7
(in CD3OD, 600 MHz)
{5.2,110.8}
{6.9,123.4}
f2 (ppm)
f1 (ppm)


O
EtO2C
HON
CN
N
CO2Ph
7
(in CD3OD, 700 MHz)
Key HMBC correlations
shown in red and blue.
{3.2,93.8}
{3.2,110.6}
{3.1,110.6}
{3.7,123.1}
{3.7,118.8}
f2 (ppm)



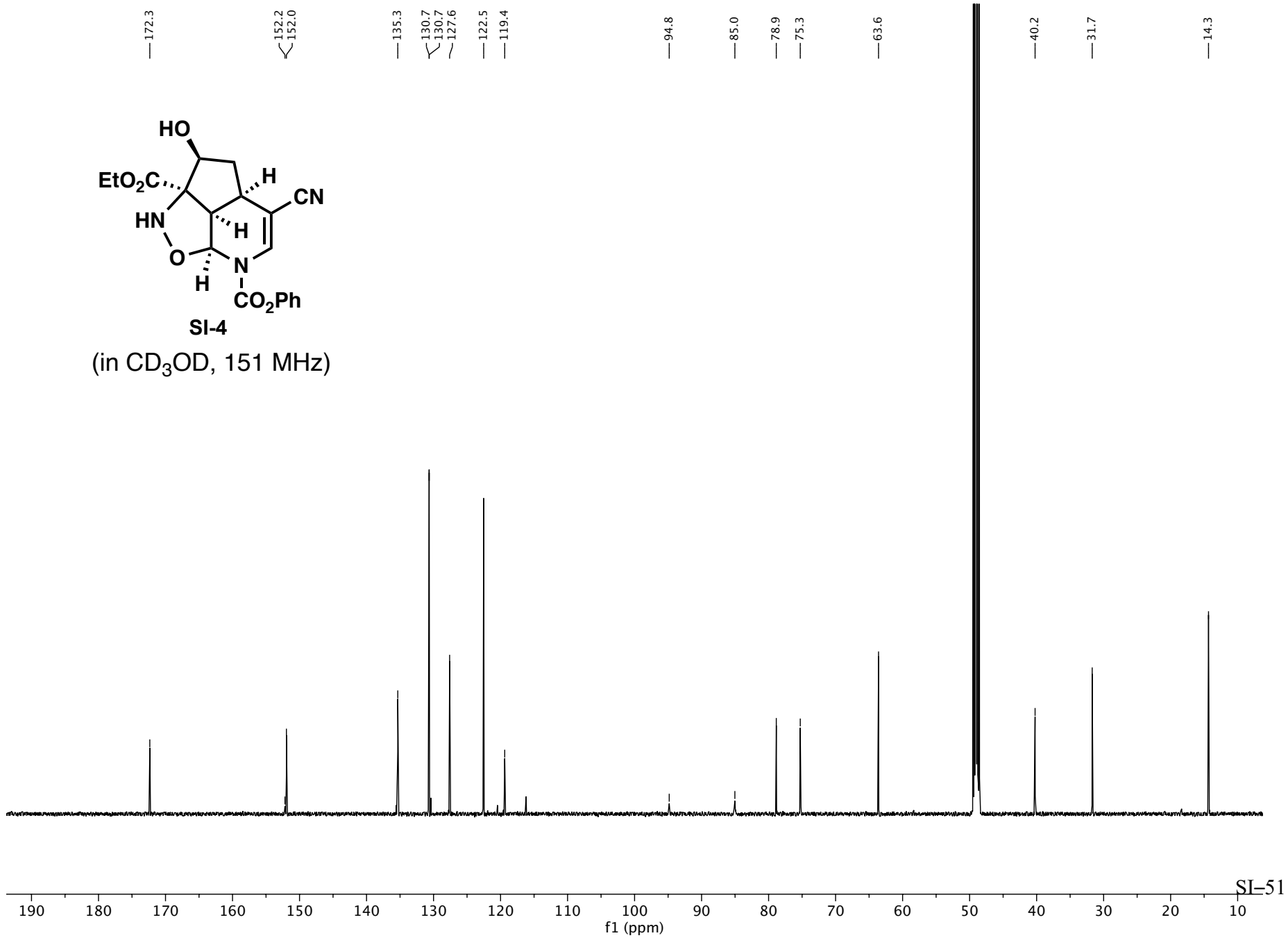
SI-5

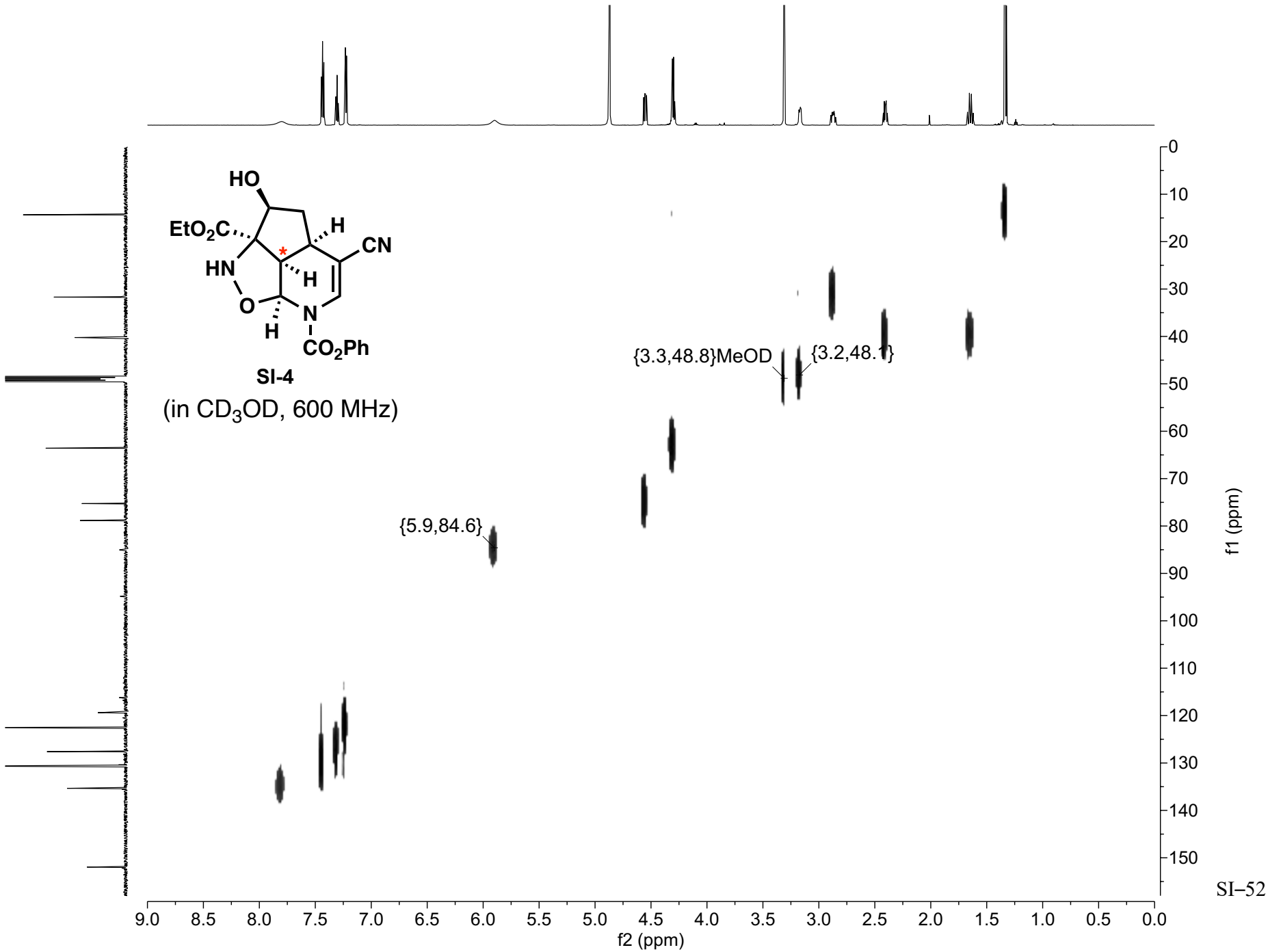
(in CD_3OD, 700 MHz)

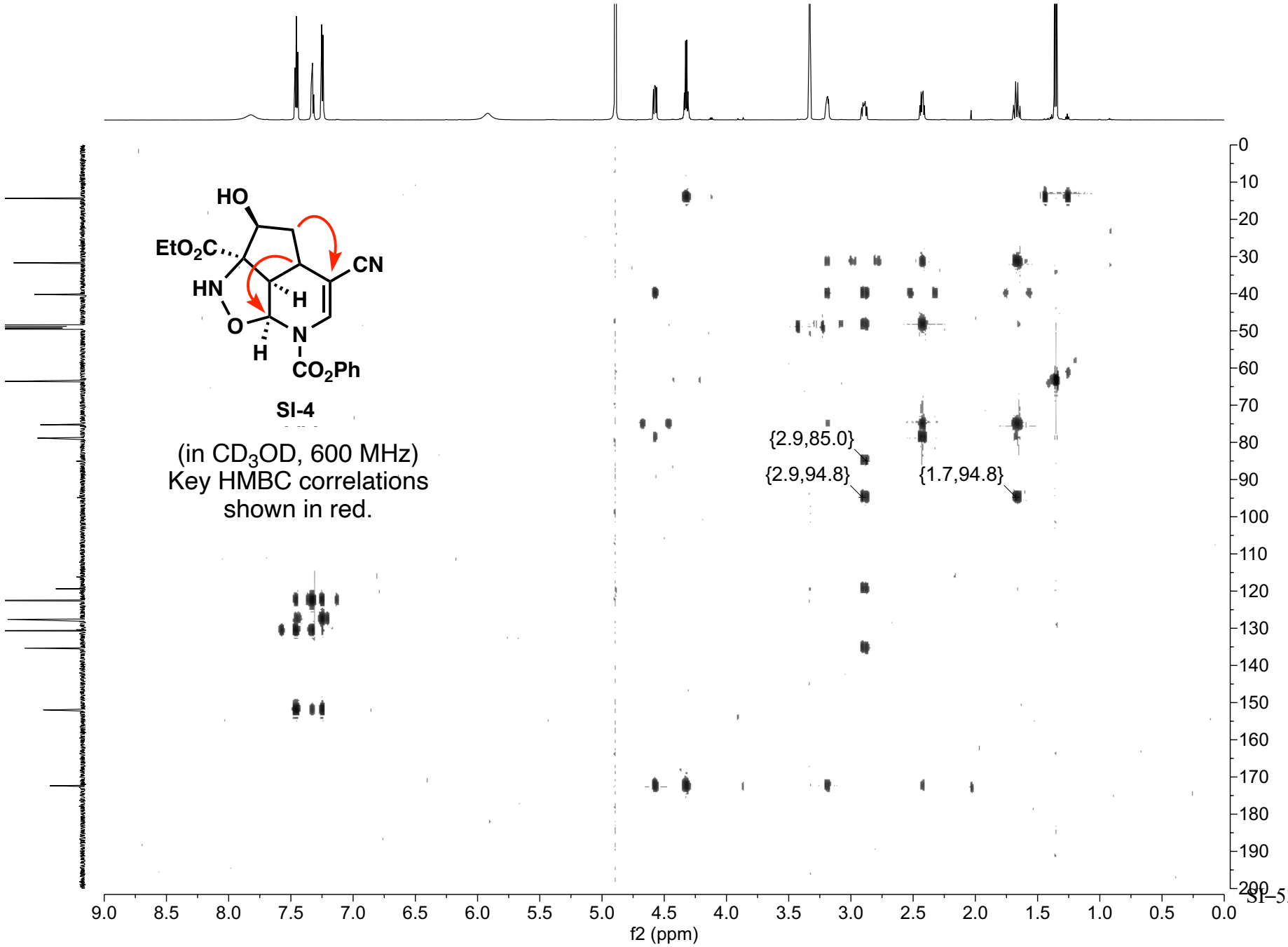


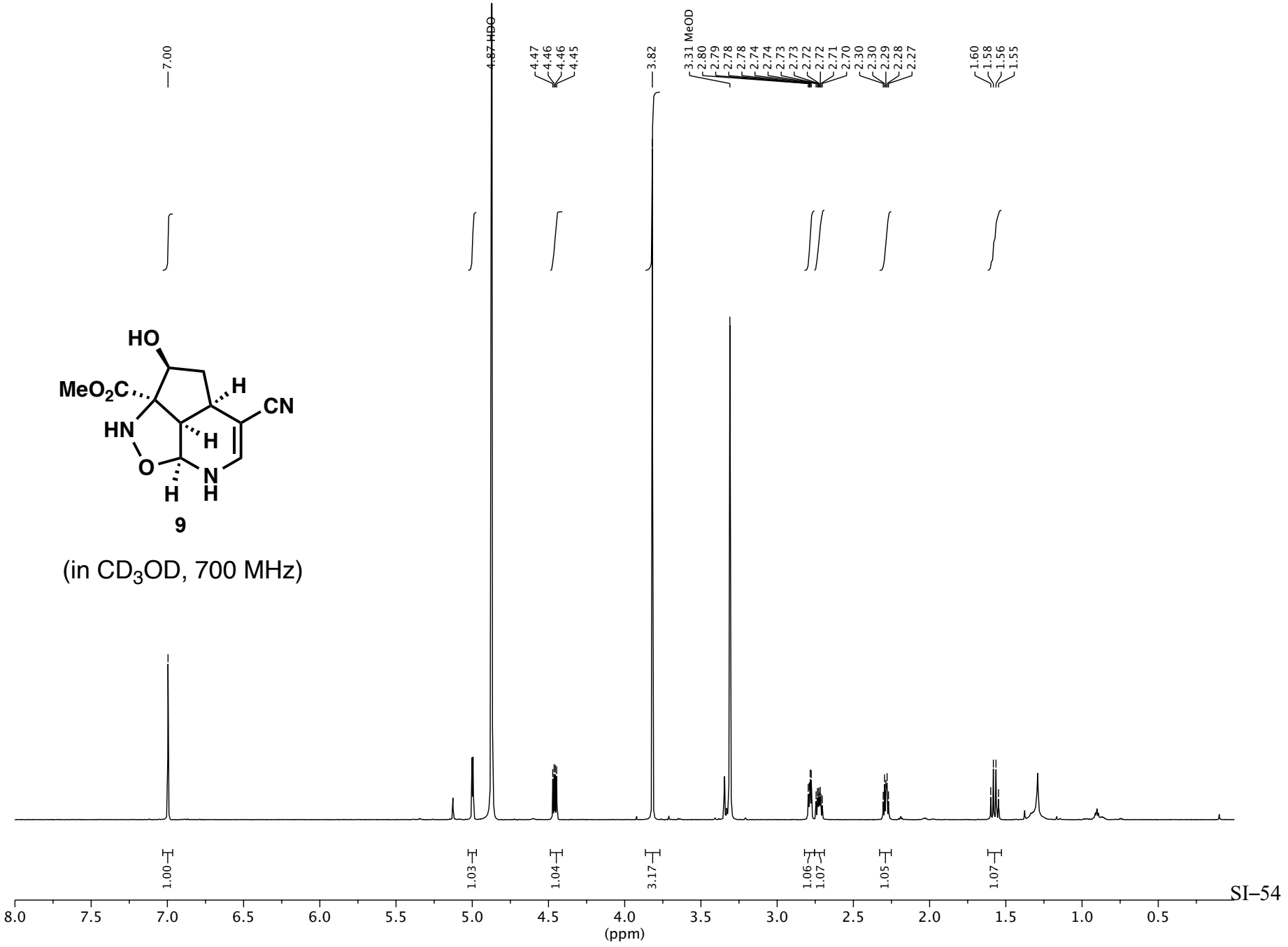
SI-4

(in CD_3OD, 700 MHz)


172.3
152.2
152.0
135.3
130.7
130.7
127.6
122.5
119.4
94.8
85.0
78.9
75.3
63.6
40.2
31.7
14.3
HO
EtO2C
H
CN
HN
H
O
N
H
CO2Ph
SI-4
(in CD3OD, 151 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

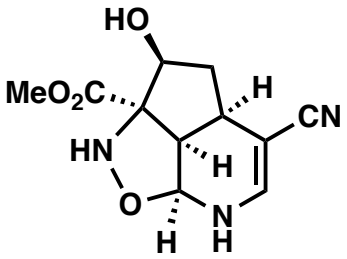

HO
EtO2C
H
CN
HN
O
H
H
N
CO2Ph
SI-4
(in CD3OD, 600 MHz)
{3.3,48.8}MeOD
{3.2,48.1}
{5.9,84.6}
f1 (ppm)
f2 (ppm)


HO
EtO2C
CN
HN
H
O
N
H
CO2Ph
SI-4
(in CD3OD, 600 MHz)
Key HMBC correlations
shown in red.
{2.9,85.0}
{2.9,94.8}
{1.7,94.8}
f2 (ppm)



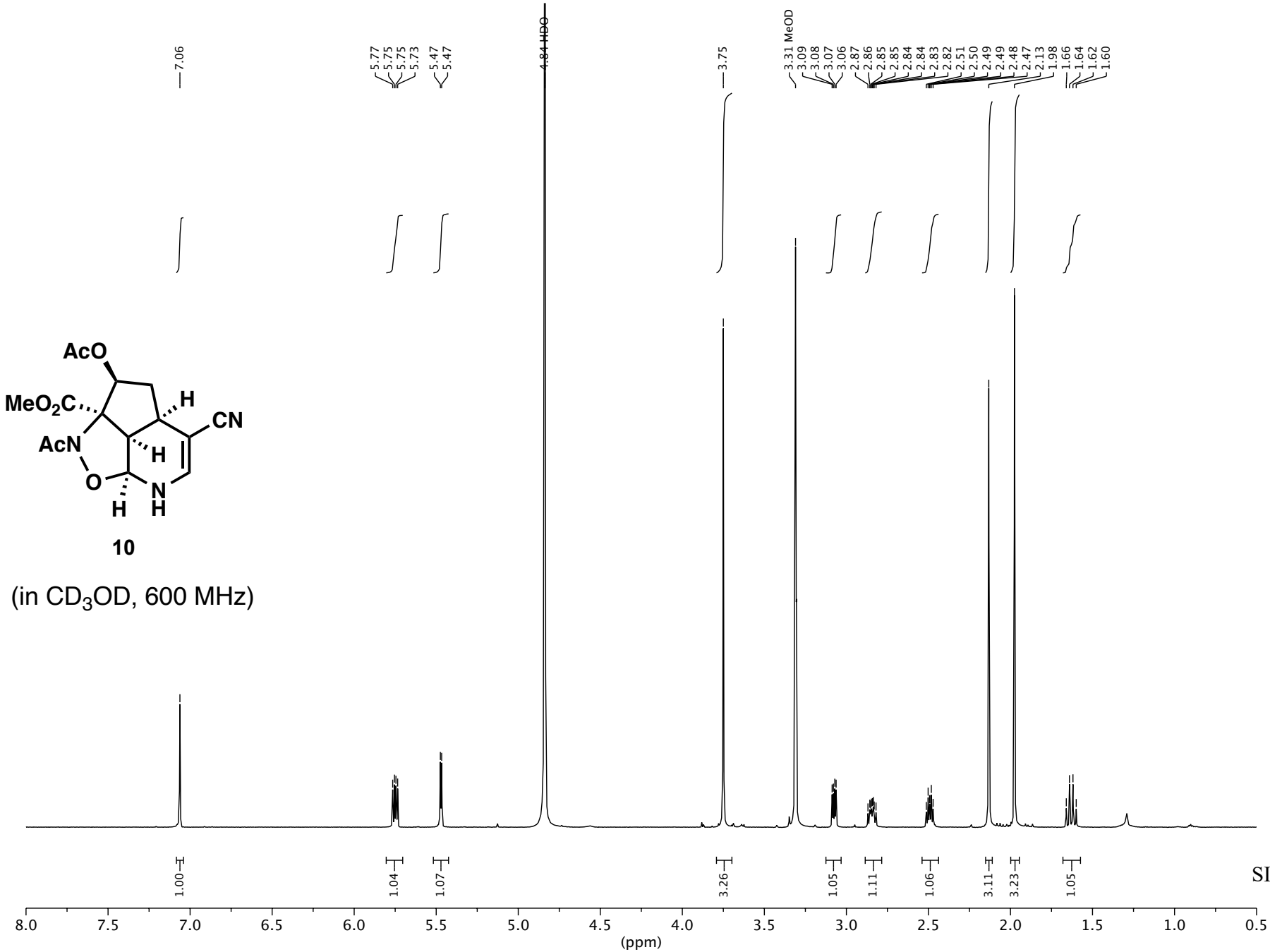
9

(in CD_3OD, 700 MHz)



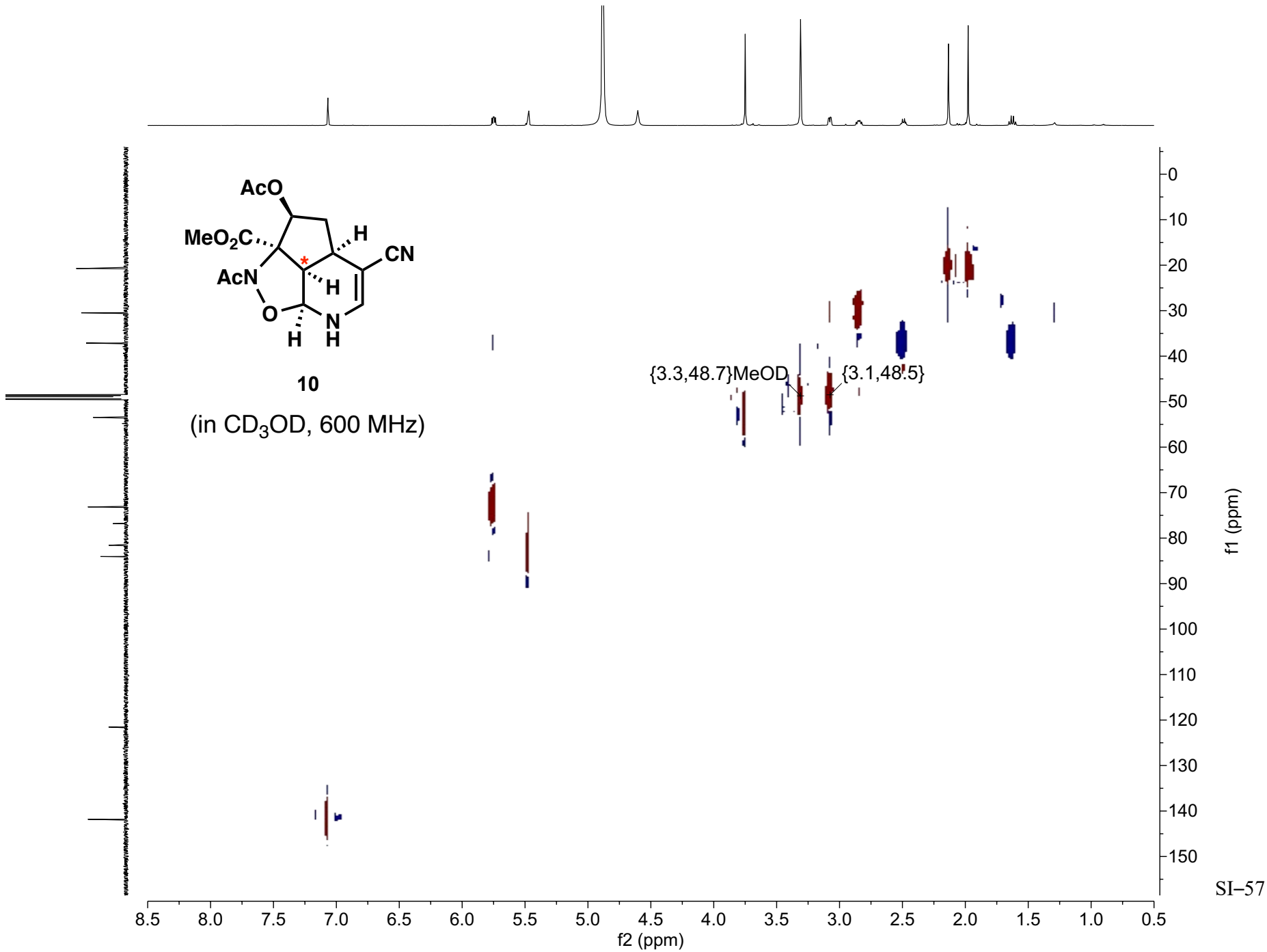
9

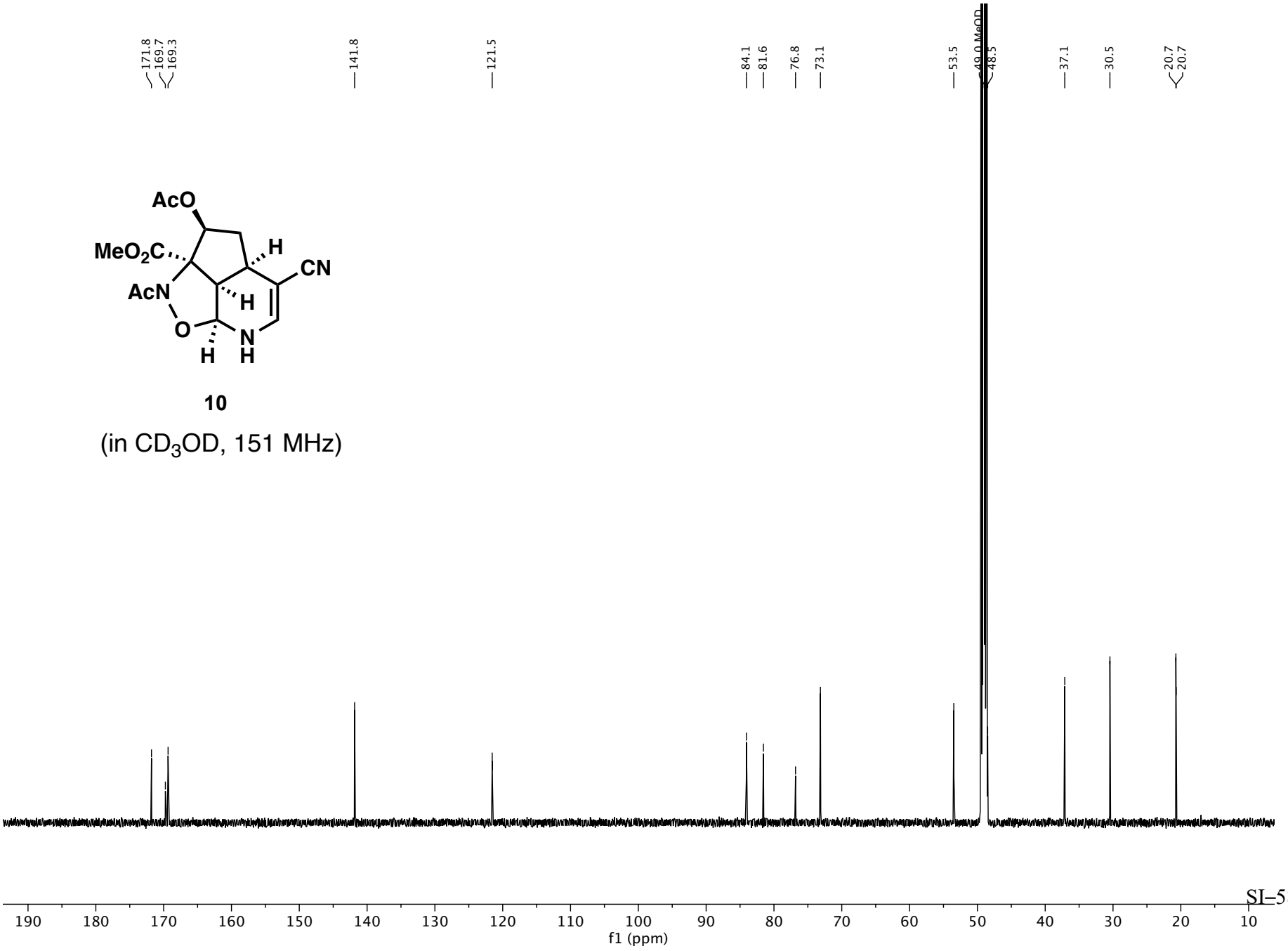
(in CD_3OD, 151 MHz)

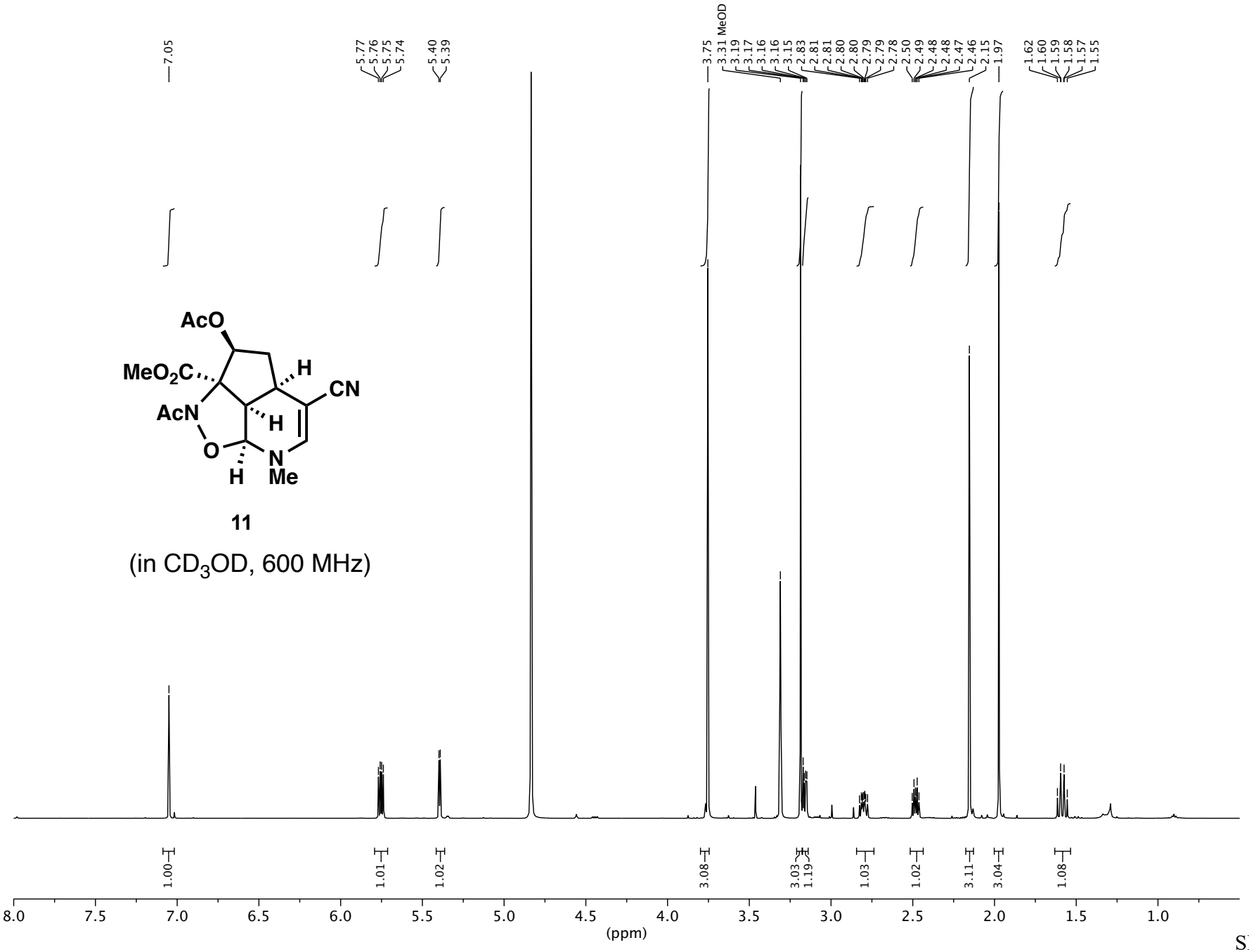


10

(in CD_3OD, 600 MHz)

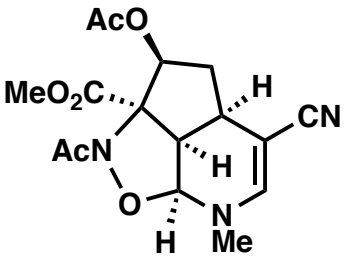

AcO
MeO2C
H
CN
AcN
H
O
N
H
H
10
(in CD3OD, 600 MHz)
{3.3,48.7}MeOD
{3.1,48.5}
f2 (ppm)
f1 (ppm)


171.8
169.7
169.3
141.8
121.5
84.1
81.6
76.8
73.1
53.5
49.0 MeOD
48.5
37.1
30.5
20.7
20.7
AcO
MeO2C
H
CN
AcN
H
O
N
H
H
10
(in CD3OD, 151 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



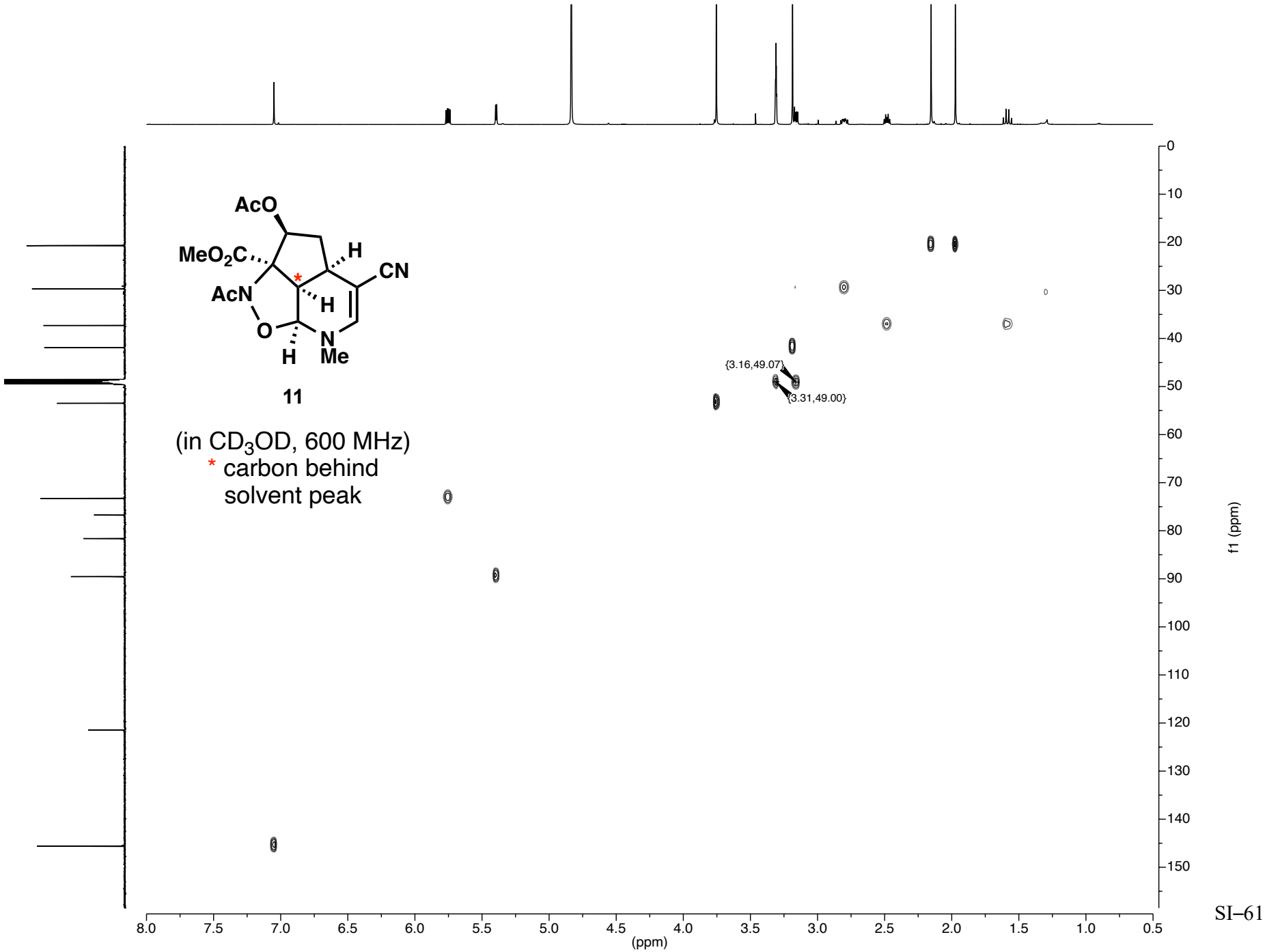
11

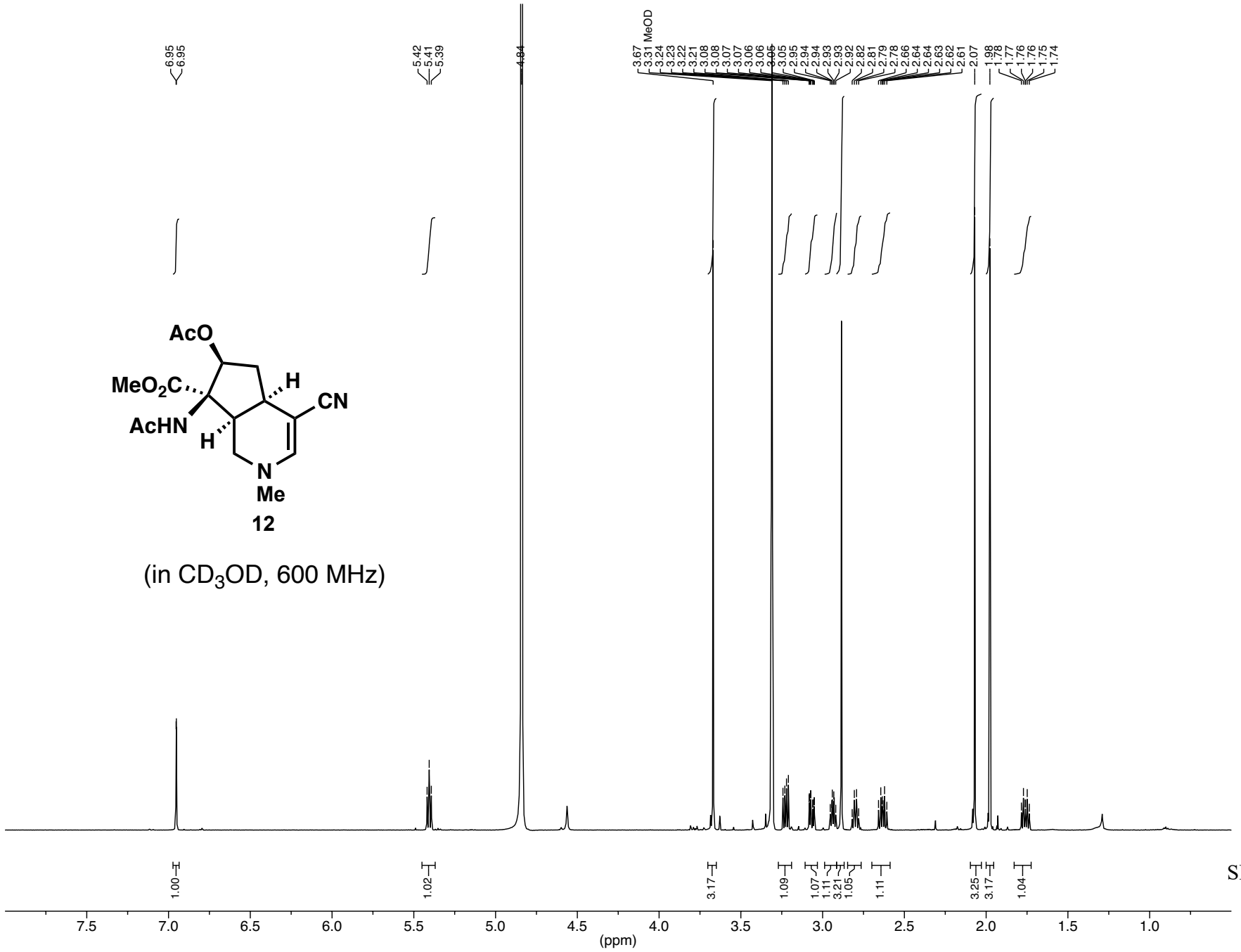
(in CD_3OD, 600 MHz)

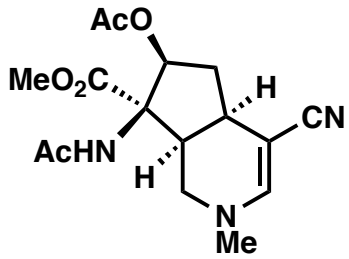


11

(in CD_3OD, 151 MHz)

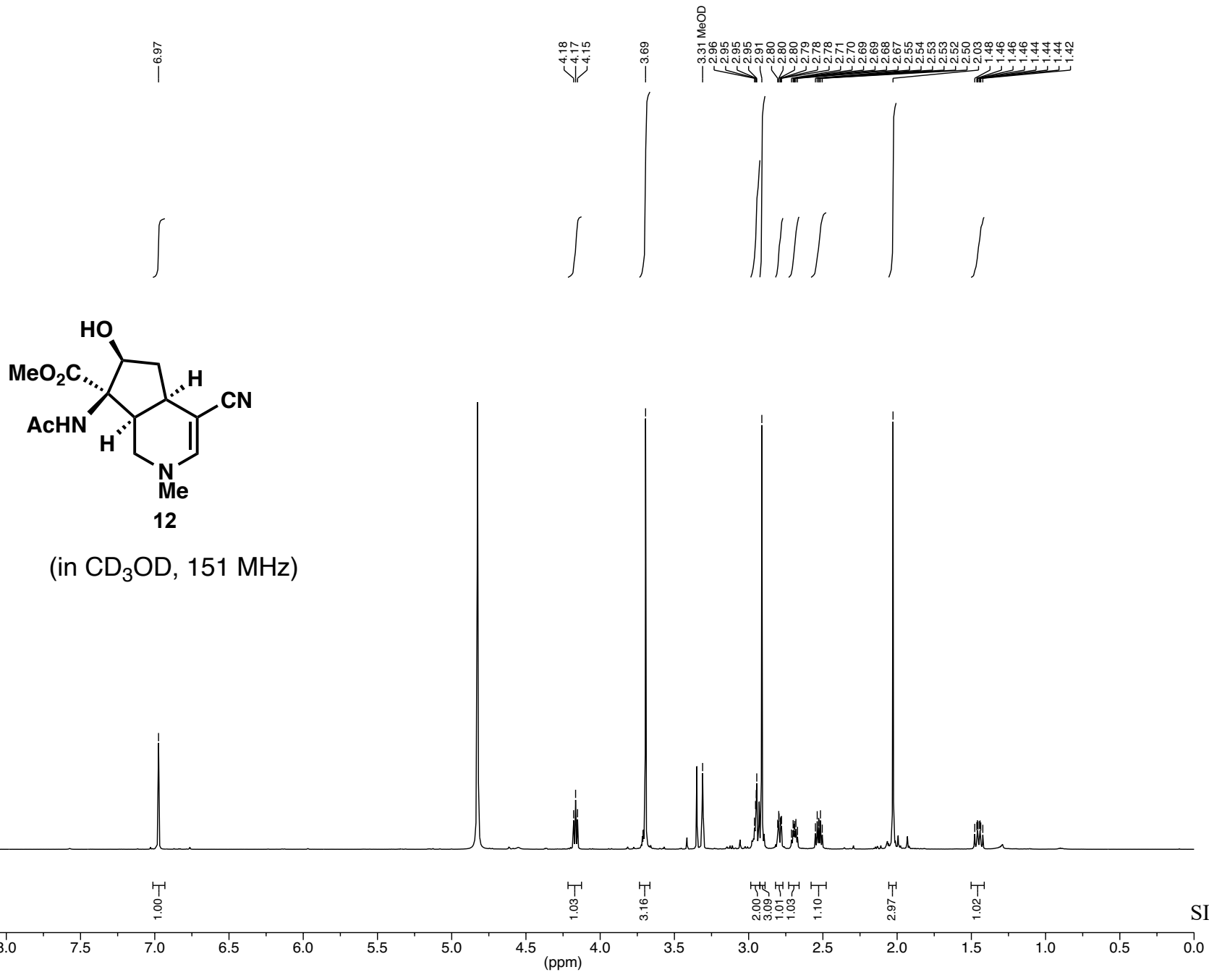

AcO
MeO2C
H
CN
AcN
H
O
N
H
Me
11
(in CD3OD, 600 MHz)
* carbon behind
solvent peak
{3.16,49.07}
{3.31,49.00}
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
(ppm)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
f1 (ppm)

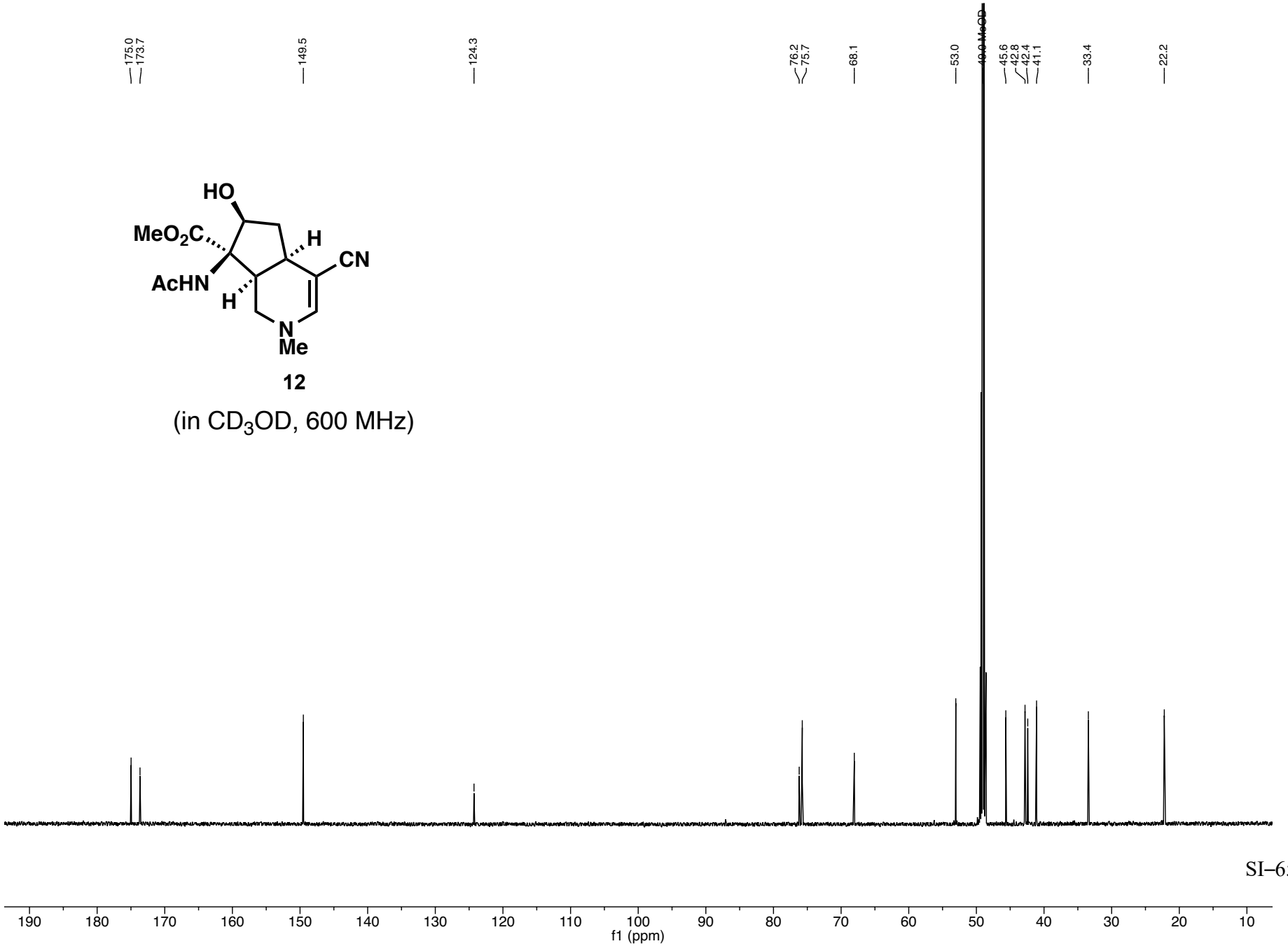

6.95
6.95
5.42
5.41
5.39
4.84
3.67
3.31 MeOD
3.24
3.23
3.22
3.21
3.08
3.08
3.07
3.07
3.06
3.06
3.05
3.05
2.95
2.94
2.94
2.93
2.93
2.92
2.82
2.81
2.79
2.78
2.66
2.64
2.64
2.63
2.62
2.61
2.07
1.98
1.78
1.77
1.76
1.76
1.75
1.74
AcO
MeO2C
H
CN
AcHN
H
N
Me
12
(in CD3OD, 600 MHz)
1.00
1.02
3.17
1.09
1.07
1.11
3.21
1.05
1.11
3.25
3.17
1.04
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
(ppm)



12

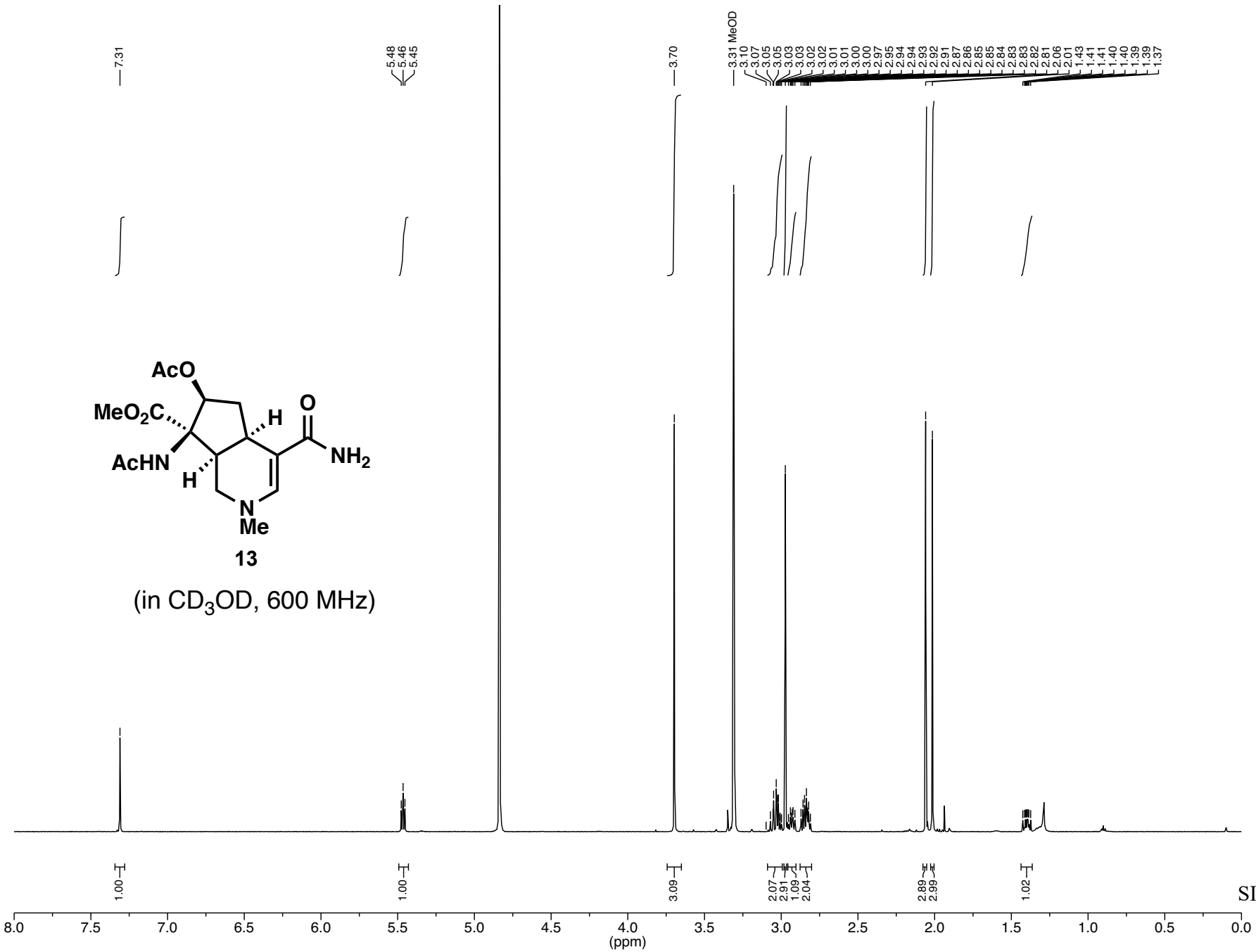
(in CD_3OD, 151 MHz)

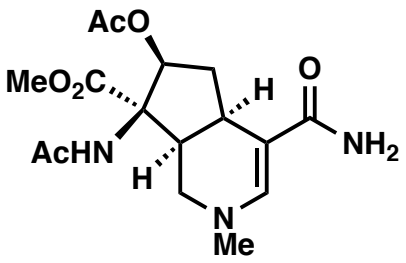

6.97
4.18
4.17
4.15
3.69
3.31 MeOD
2.96
2.95
2.95
2.95
2.91
2.80
2.80
2.80
2.79
2.78
2.78
2.71
2.70
2.69
2.69
2.68
2.67
2.55
2.54
2.53
2.53
2.52
2.50
2.03
1.48
1.46
1.46
1.46
1.44
1.44
1.44
1.42
HO
MeO2C
H
CN
AcHN
H
N
Me
12
(in CD3OD, 151 MHz)
1.00
1.03
3.16
2.00
3.09
1.01
1.03
1.10
2.97
1.02
8.5
8.0
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
(ppm)



12

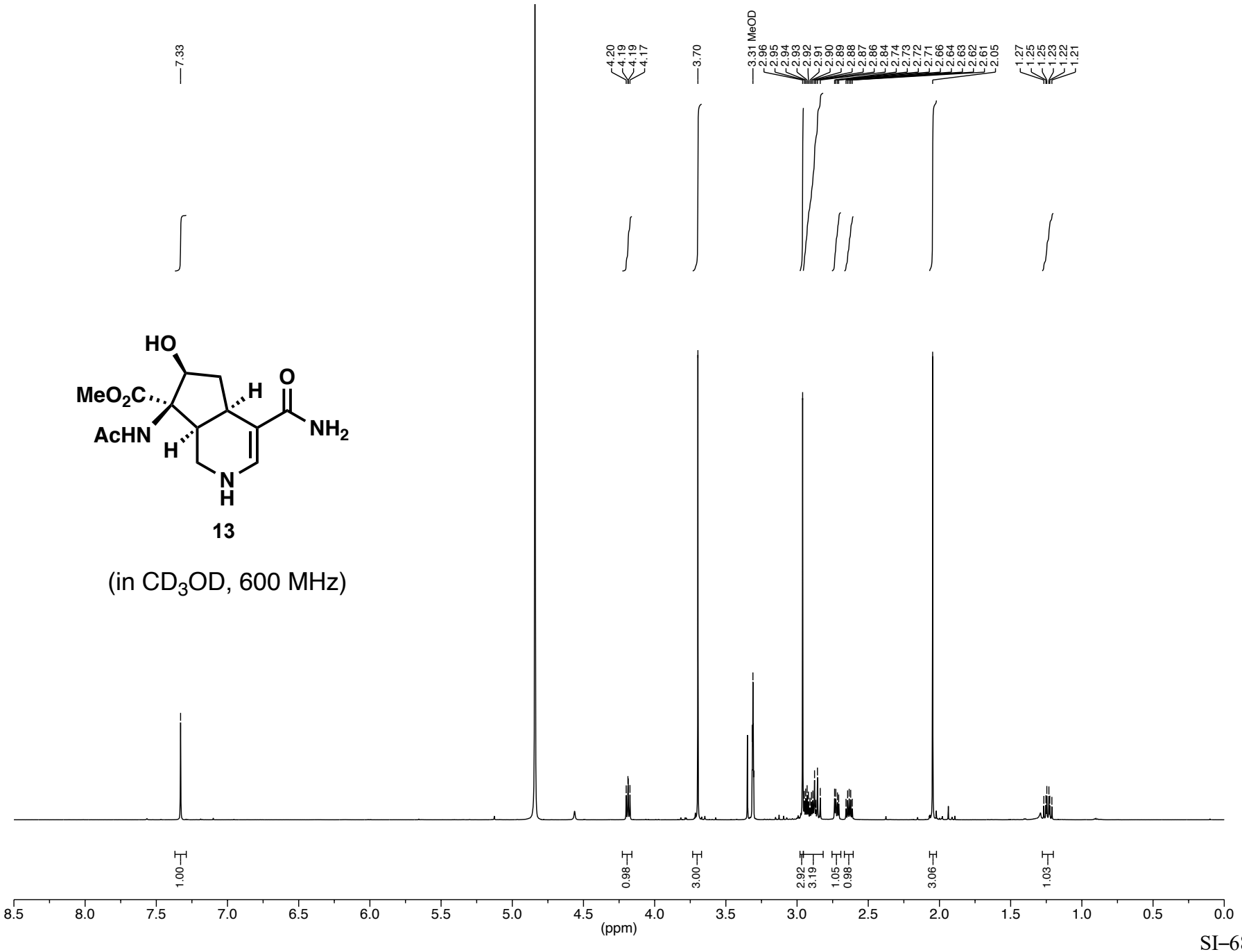
(in CD_3OD, 600 MHz)


7.31
5.48
5.46
5.45
3.70
3.31 MeOD
3.10
3.07
3.05
3.05
3.03
3.03
3.02
3.02
3.01
3.01
3.00
3.00
2.97
2.95
2.94
2.94
2.93
2.92
2.91
2.87
2.86
2.85
2.85
2.84
2.83
2.83
2.82
2.81
2.06
2.01
1.43
1.41
1.41
1.40
1.40
1.39
1.39
1.37
AcO
MeO2C
H
O
AcHN
NH2
H
N
Me
13
(in CD3OD, 600 MHz)
1.00
1.00
3.09
2.07
2.91
1.09
2.04
2.89
2.99
1.02
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
(ppm)



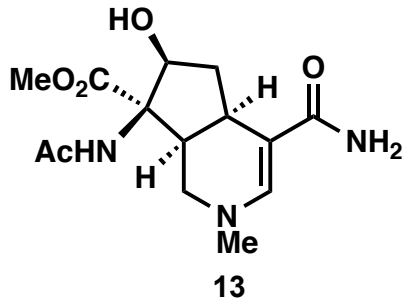
13

(in CD_3OD, 151 MHz)



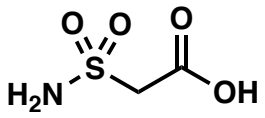
13

(in CD_3OD, 600 MHz)



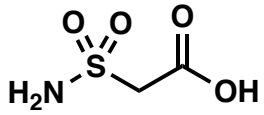
13

(in CD_3OD, 151 MHz)



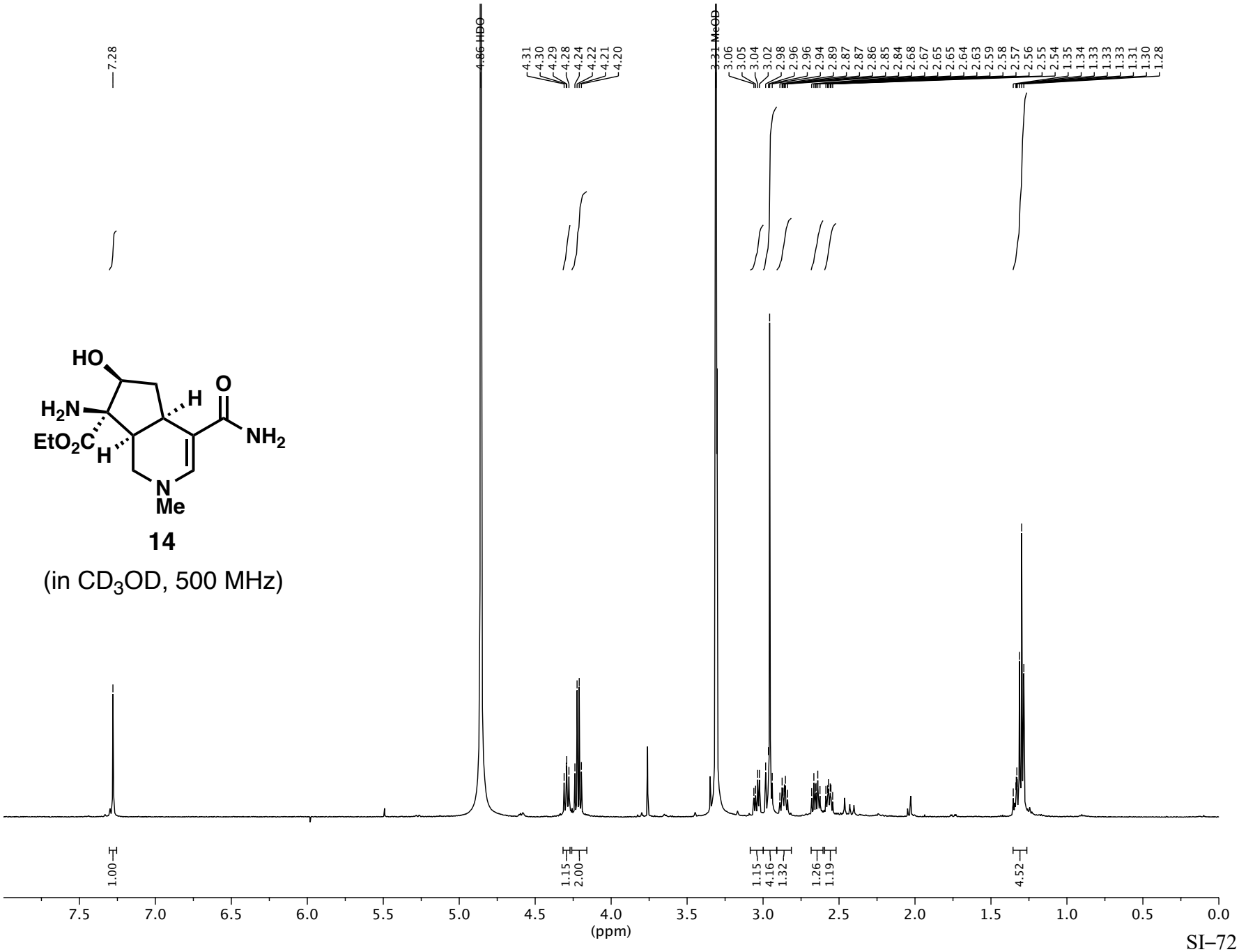
15

(in CD_3OD, 600 MHz)



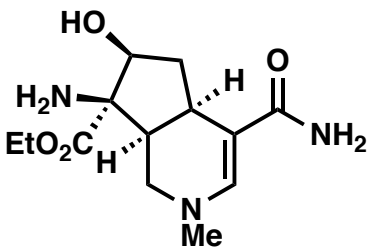
15

(in CD_3OD, 151 MHz)



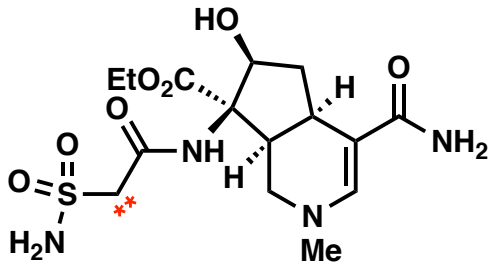
14

(in CD_3OD, 500 MHz)



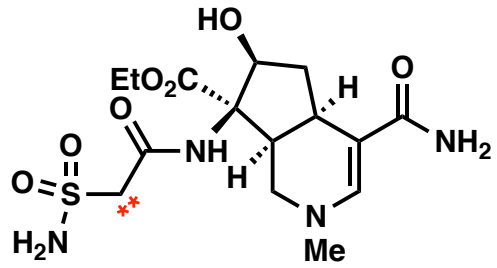
14

(in CD_3OD, 151 MHz)



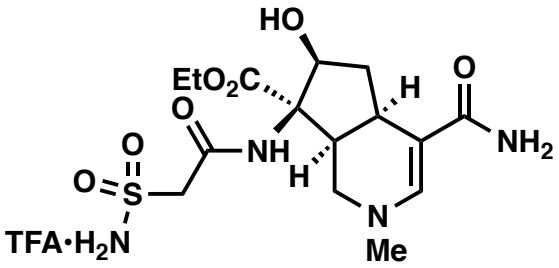
16

(in CD_3OD, 600 MHz)
*exchangeable protons



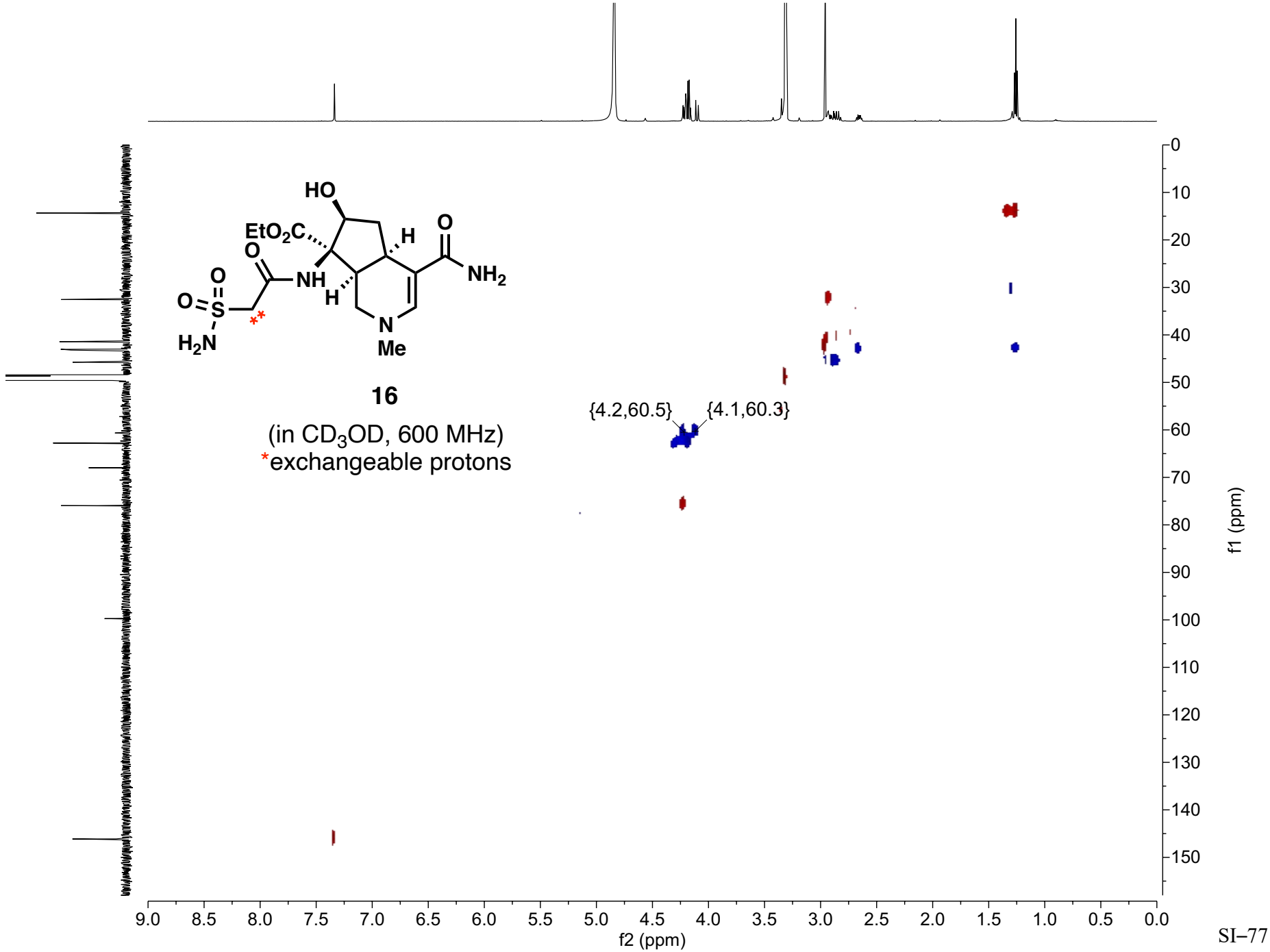
16

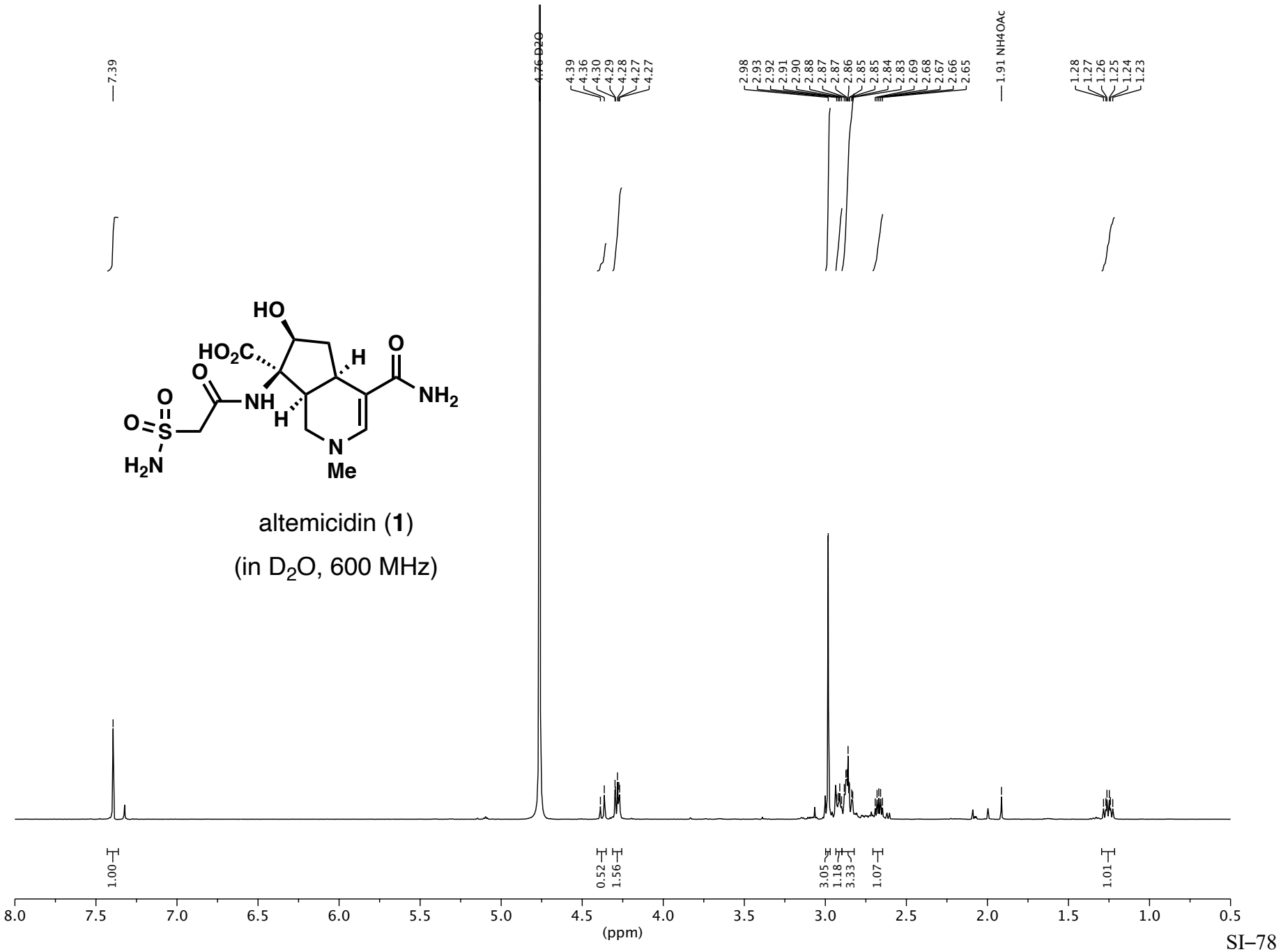
(in CD_3OD, 151 MHz)
*exchangeable protons

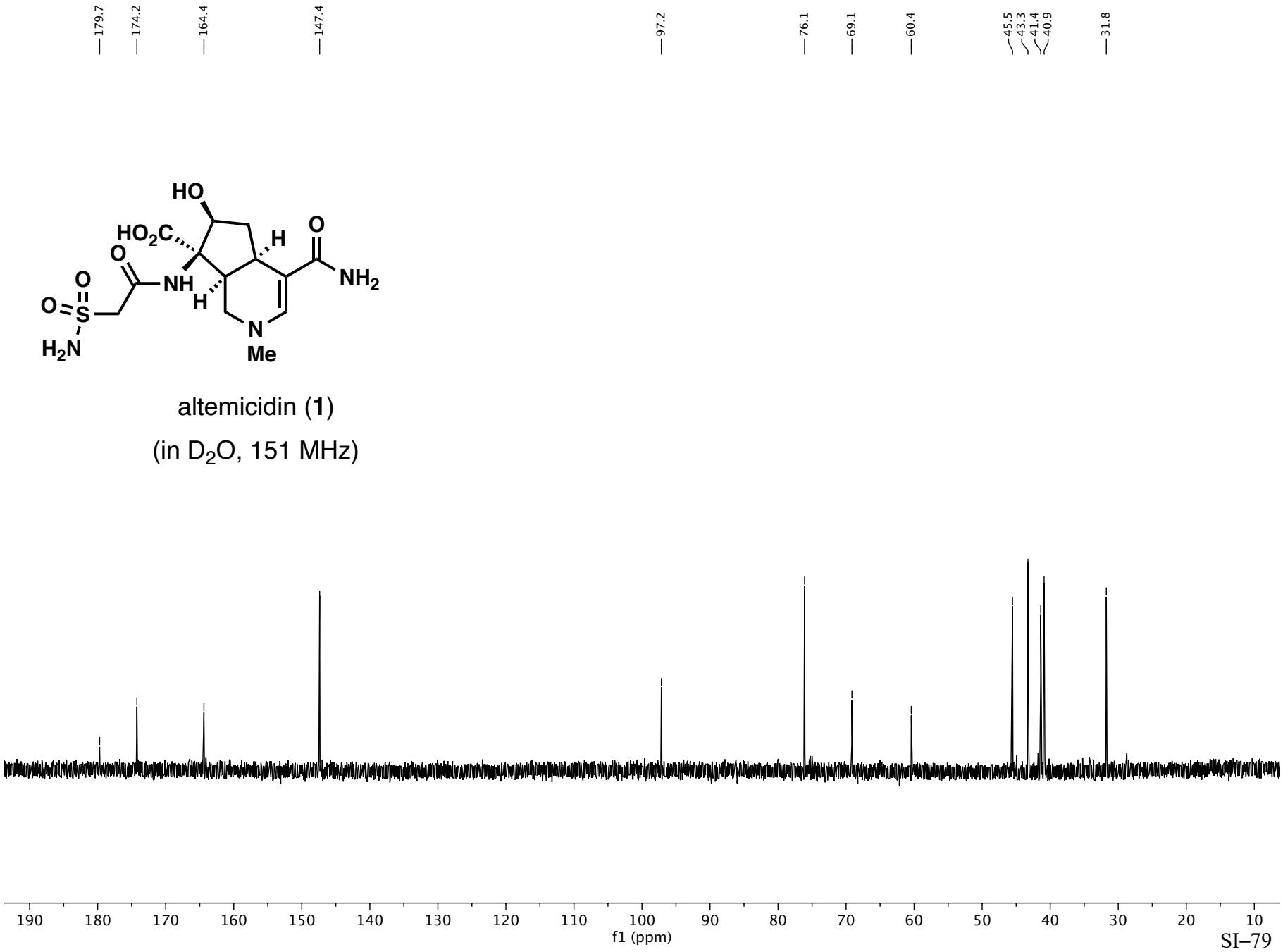


16

(in CD_3OD, 151 MHz)
TFA = trifluoroacetic acid

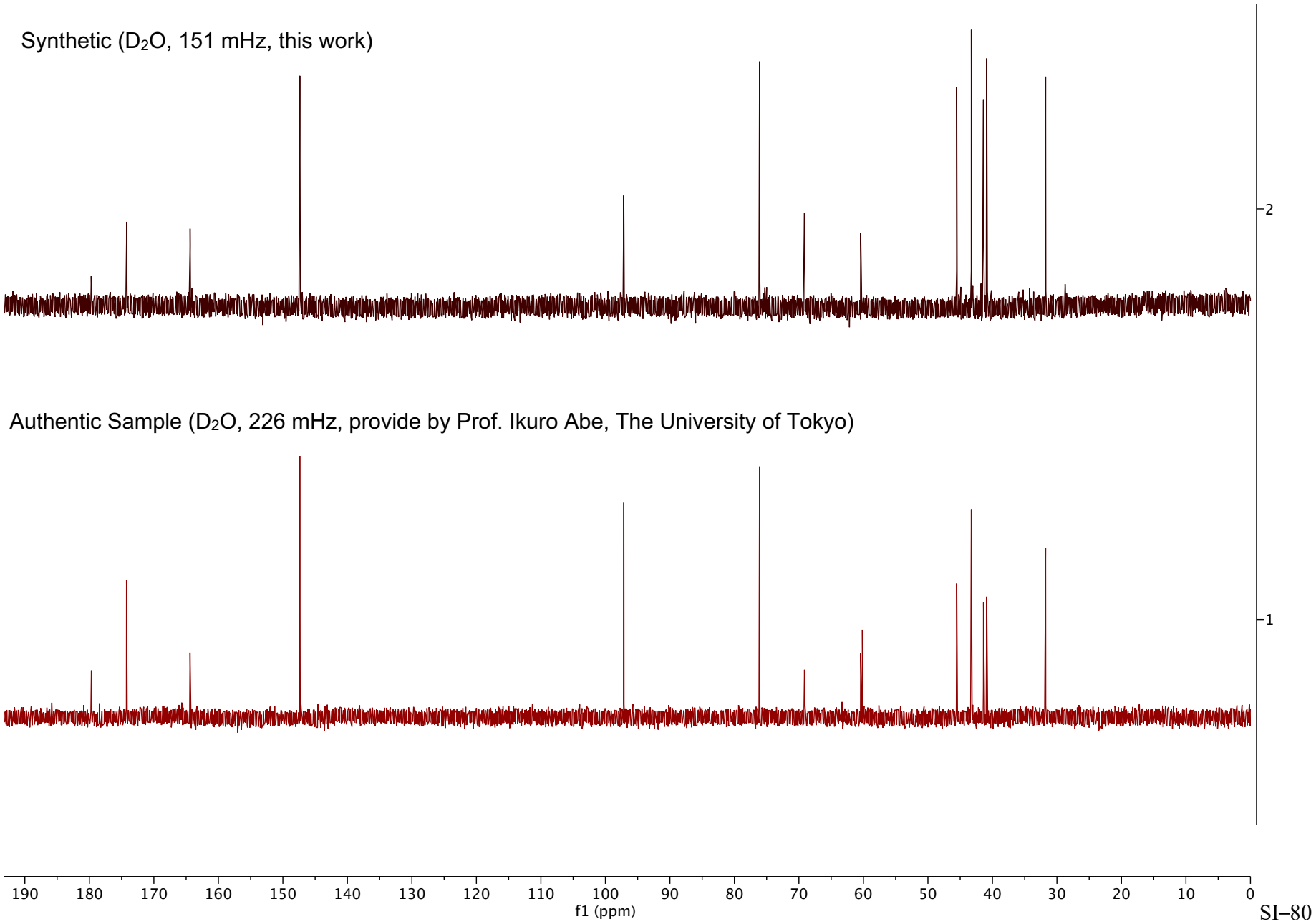

HO
EtO2C
O
H
O
NH2
NH
H
O
S
O
H2N
**
N
Me
16
(in CD3OD, 600 MHz)
*exchangeable protons
{4.2,60.5}
{4.1,60.3}
f2 (ppm)
f1 (ppm)

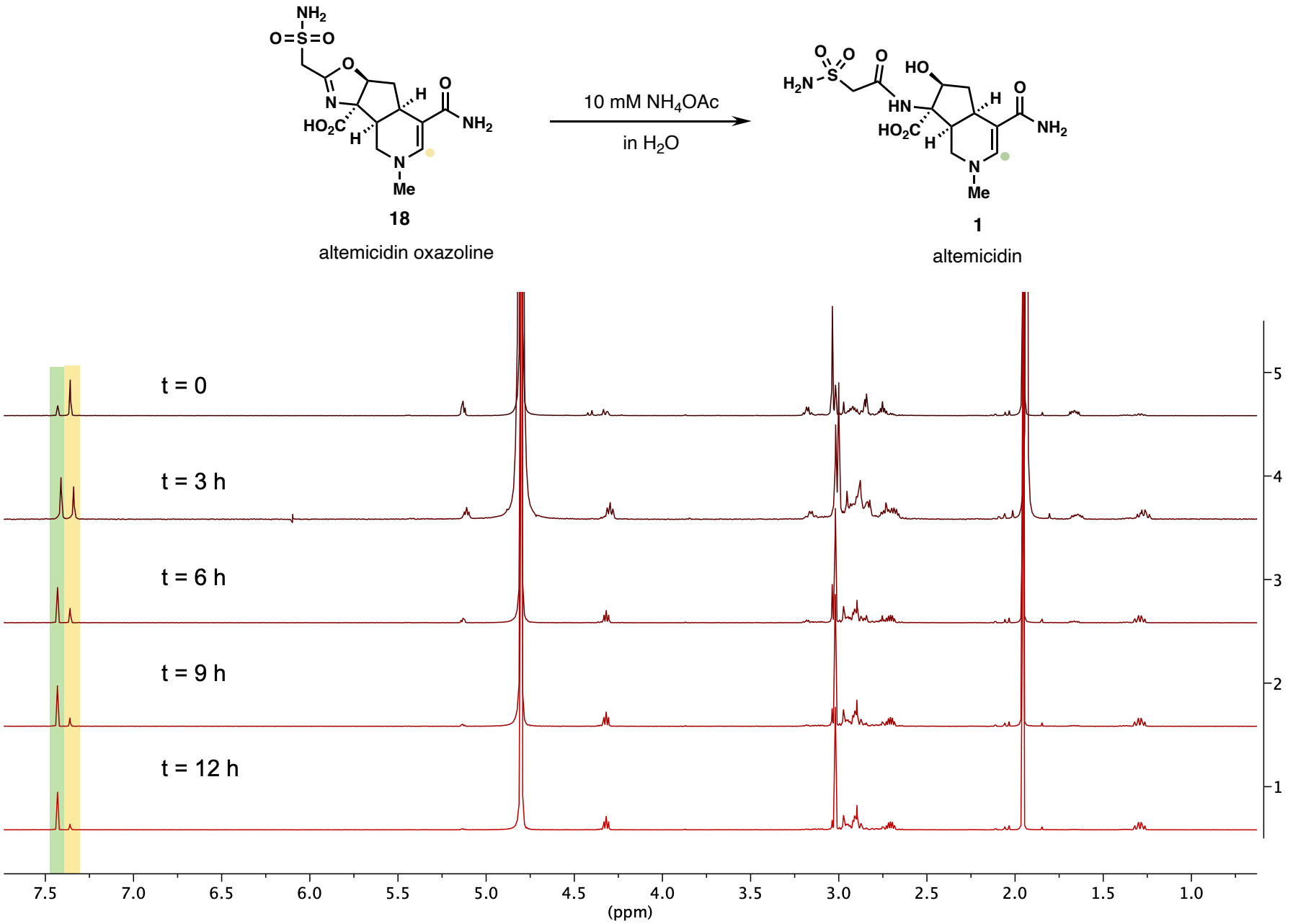

7.39
4.76 D2O
4.39
4.36
4.30
4.29
4.28
4.27
4.27
2.98
2.93
2.92
2.91
2.90
2.88
2.87
2.87
2.86
2.85
2.85
2.84
2.83
2.69
2.68
2.67
2.66
2.65
1.91 NH4OAc
1.28
1.27
1.26
1.25
1.24
1.23
HO
HO2C
O
H
O
NH2
O
NH
H
O
S
N
Me
H2N
altemicidin (1)
(in D2O, 600 MHz)
1.00
0.52
1.56
3.05
1.18
3.33
1.07
1.01
8.0
7.5
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
(ppm)

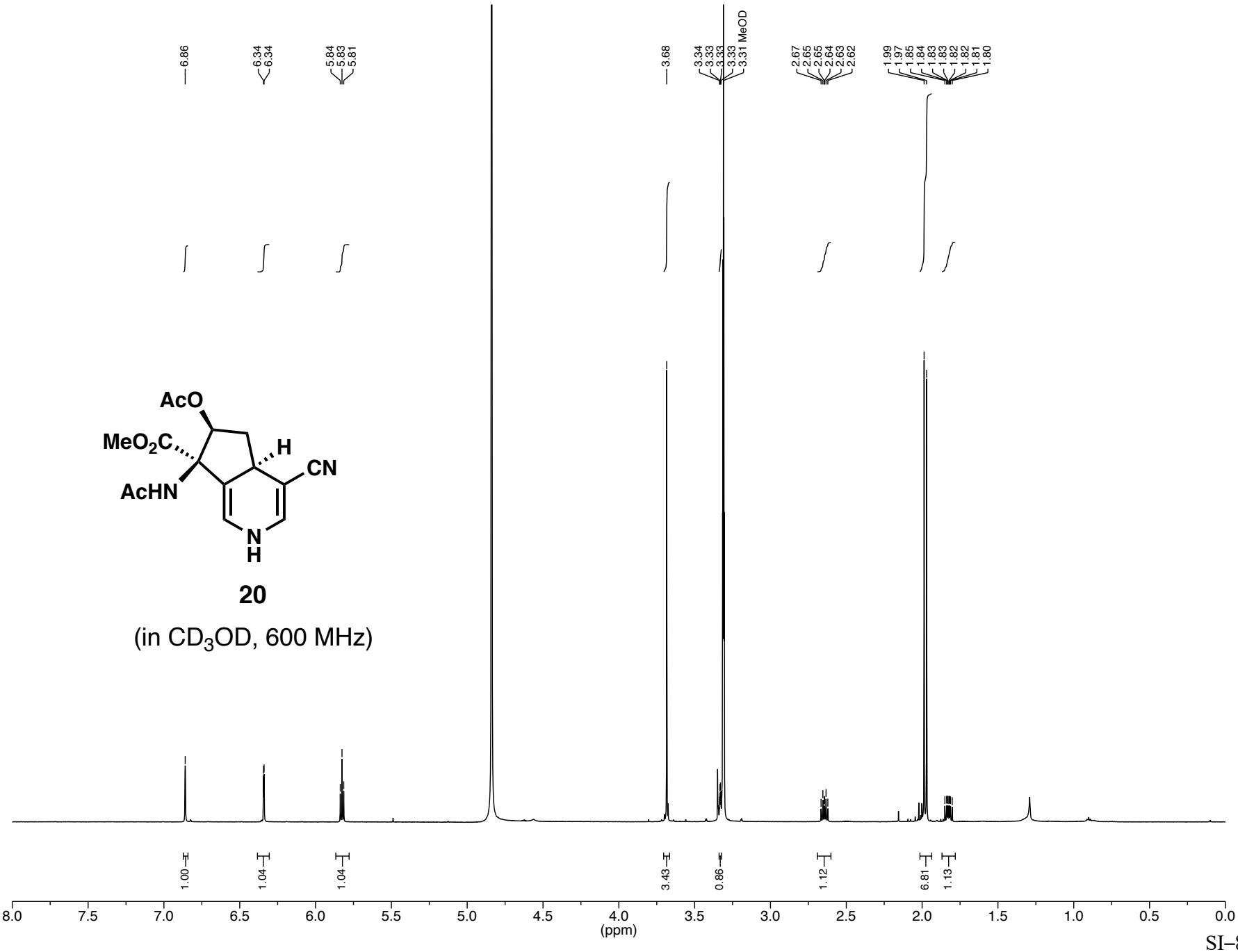


altemicidin (**1**)

(in D_2O, 151 MHz)

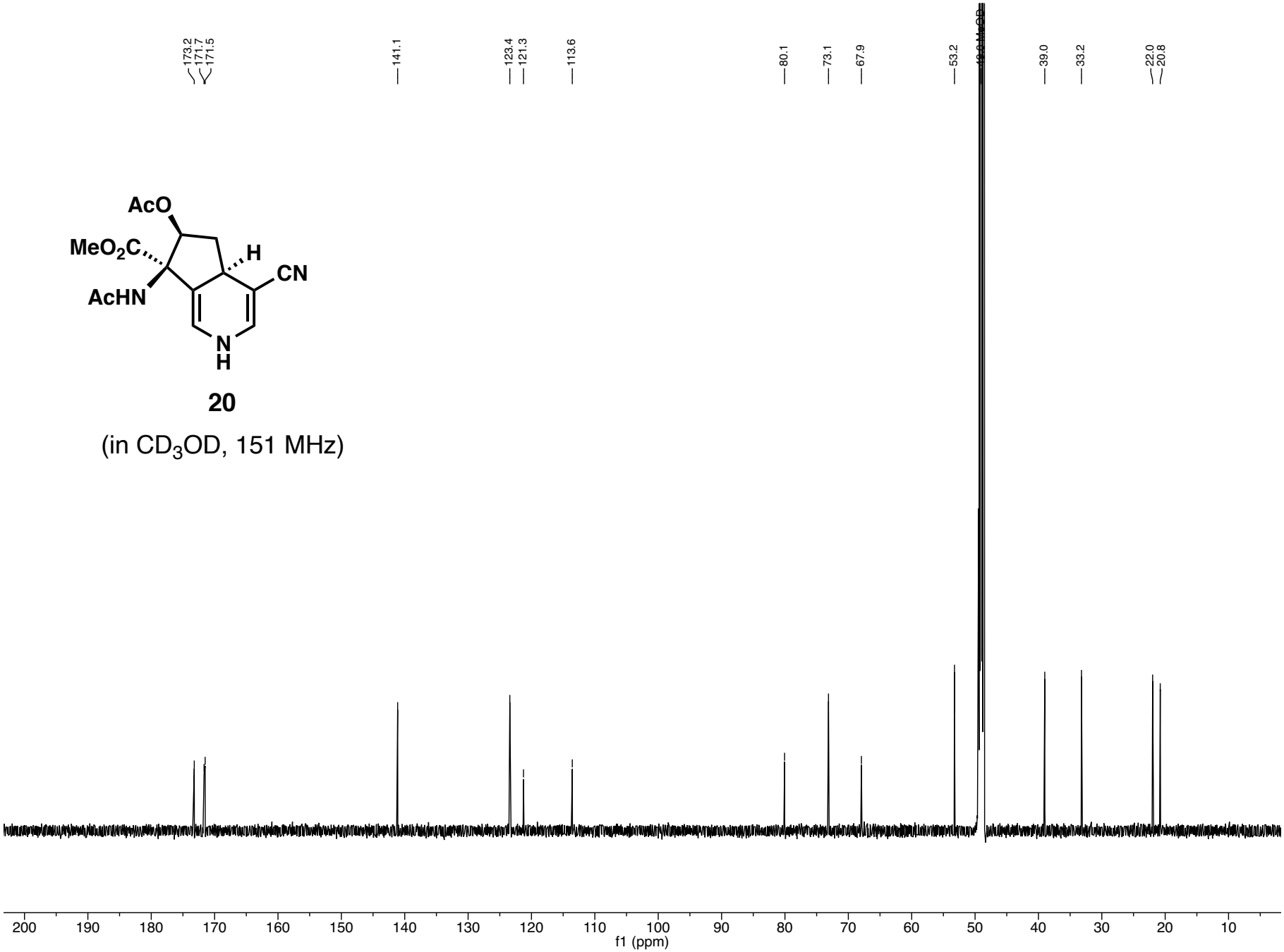

Synthetic (D_2O, 151 mHz, this work)
Authentic Sample (D_2O, 226 mHz, provide by Prof. Ikuro Abe, The University of Tokyo)
2
1
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


10 mM NH4OAc
in H2O
18
altemicidin oxazoline
1
altemicidin
t = 0
t = 3 h
t = 6 h
t = 9 h
t = 12 h
(ppm)



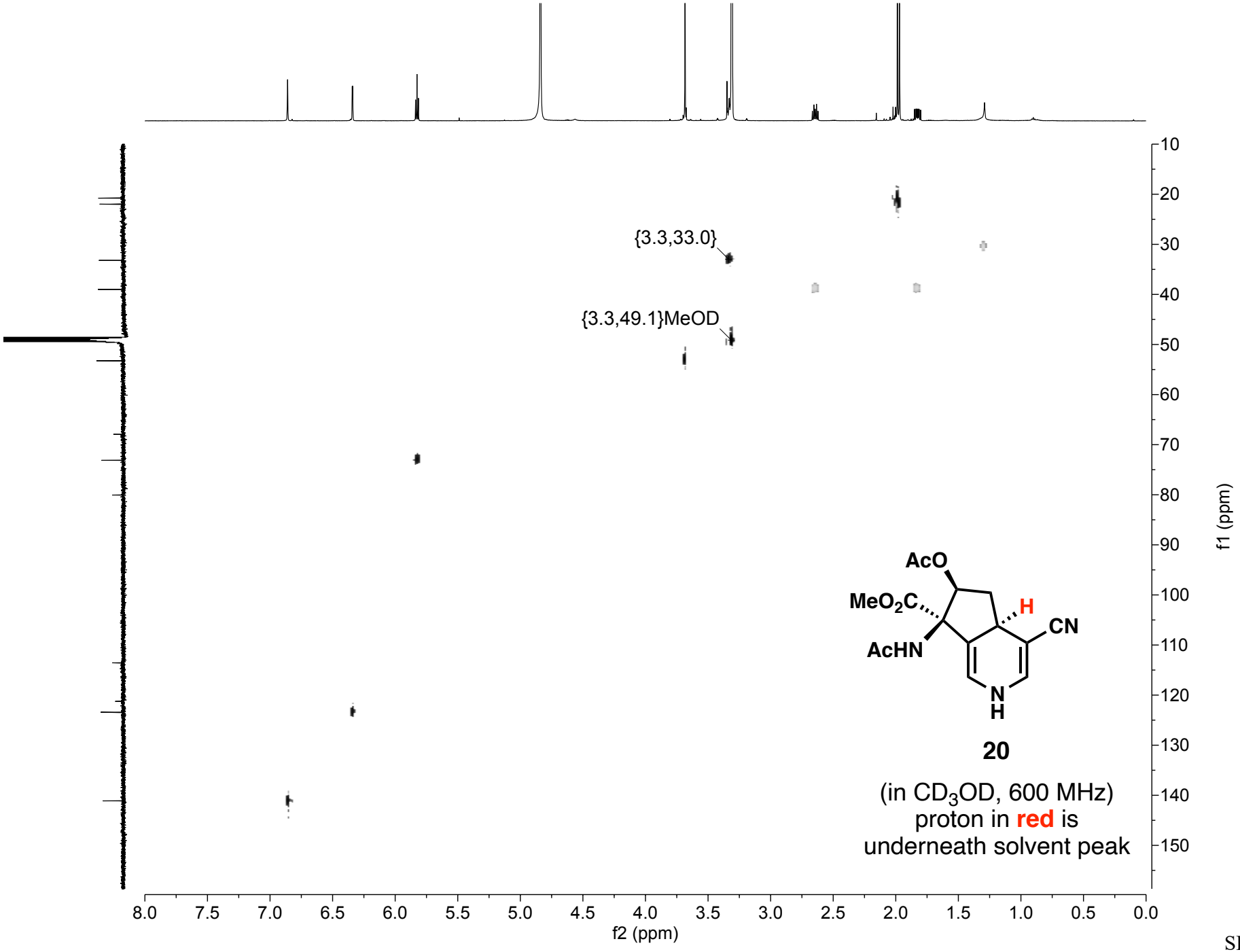
20

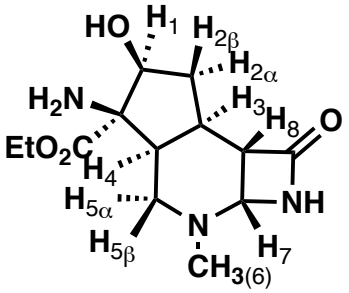
(in CD_3OD, 600 MHz)



20

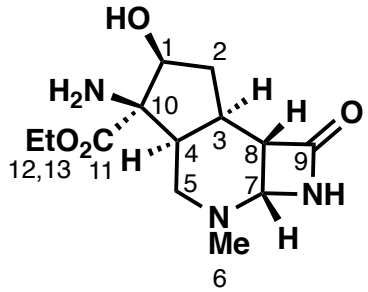
(in CD_3OD, 151 MHz)


{3.3,33.0}
{3.3,49.1}MeOD
AcO
MeO2C
H
CN
AcHN
N
H
20
(in CD3OD, 600 MHz)
proton in red is
underneath solvent peak
f2 (ppm)
f1 (ppm)



SI-6
(in CD_3OD, 600 MHz)

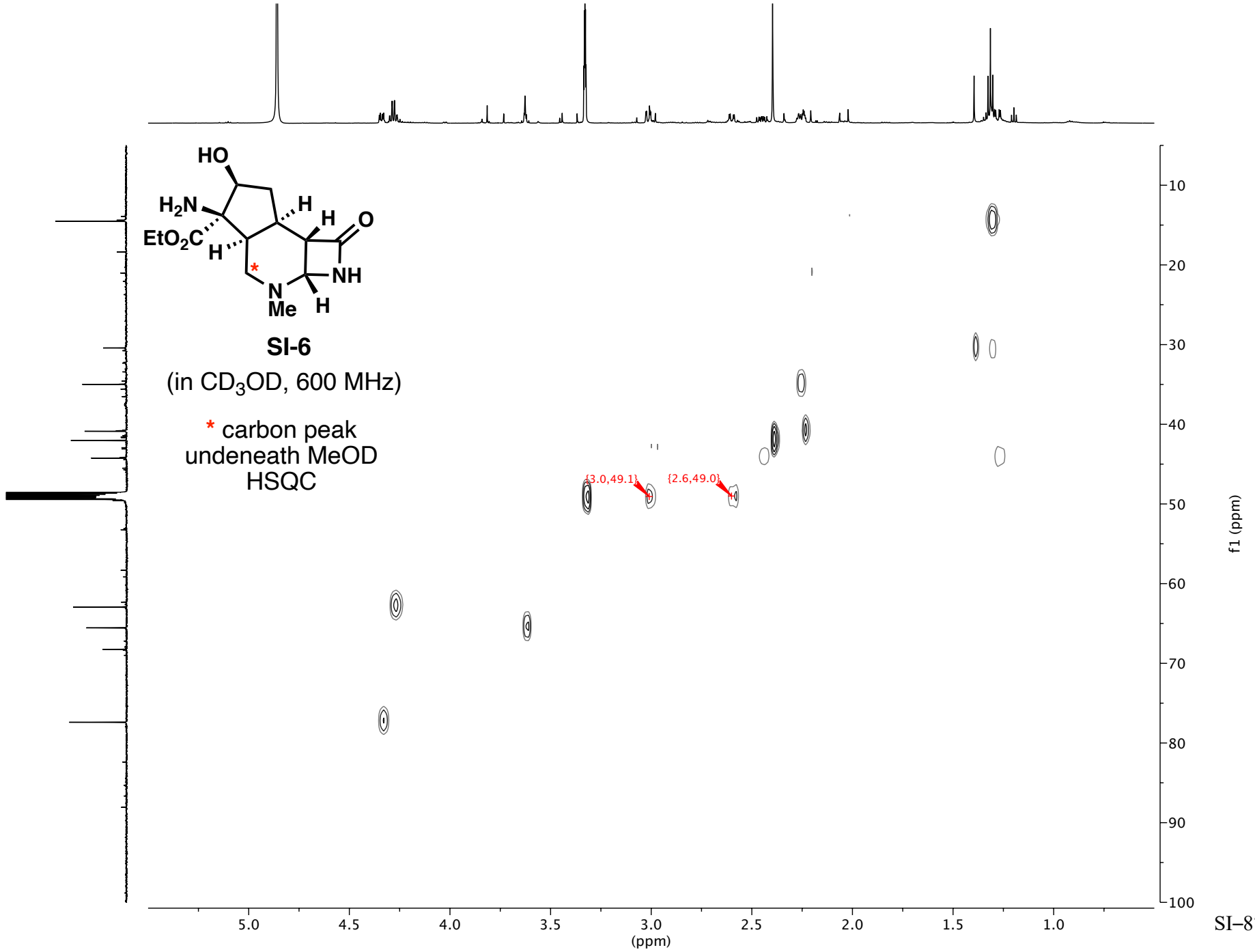
Proton	δ (ppm)
H-1	4.31 (dd)
H-2α	2.42 (ddd)
H-2β	1.26 (dd)
H-3	1.29-1.26 (m)
H-4	2.21 (dd)
H-5α	2.55 (dd)
H-5β	2.97 (dd)
H-6	2.35 (s)
H-7	3.57 (d)
H-8	2.24 (t)

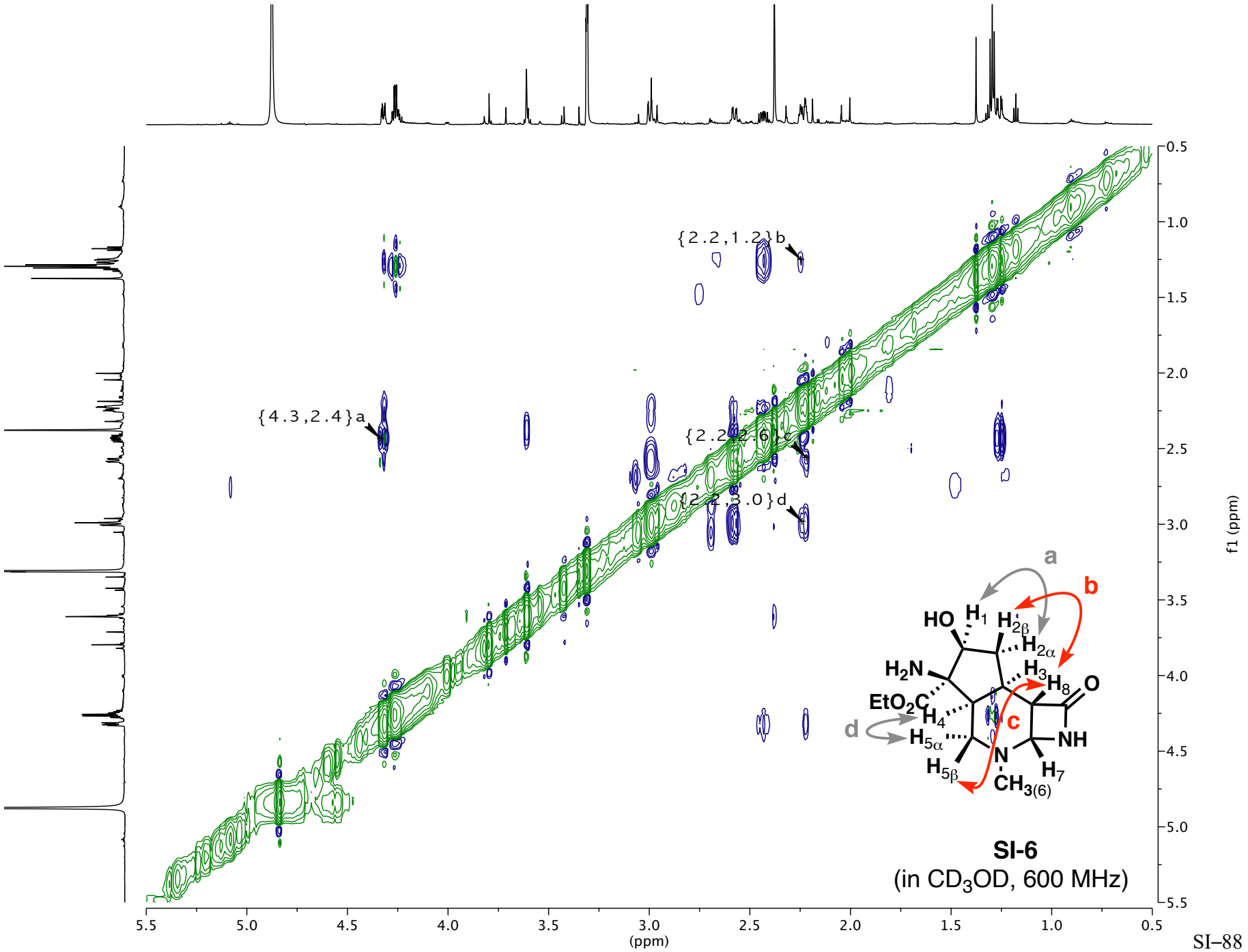


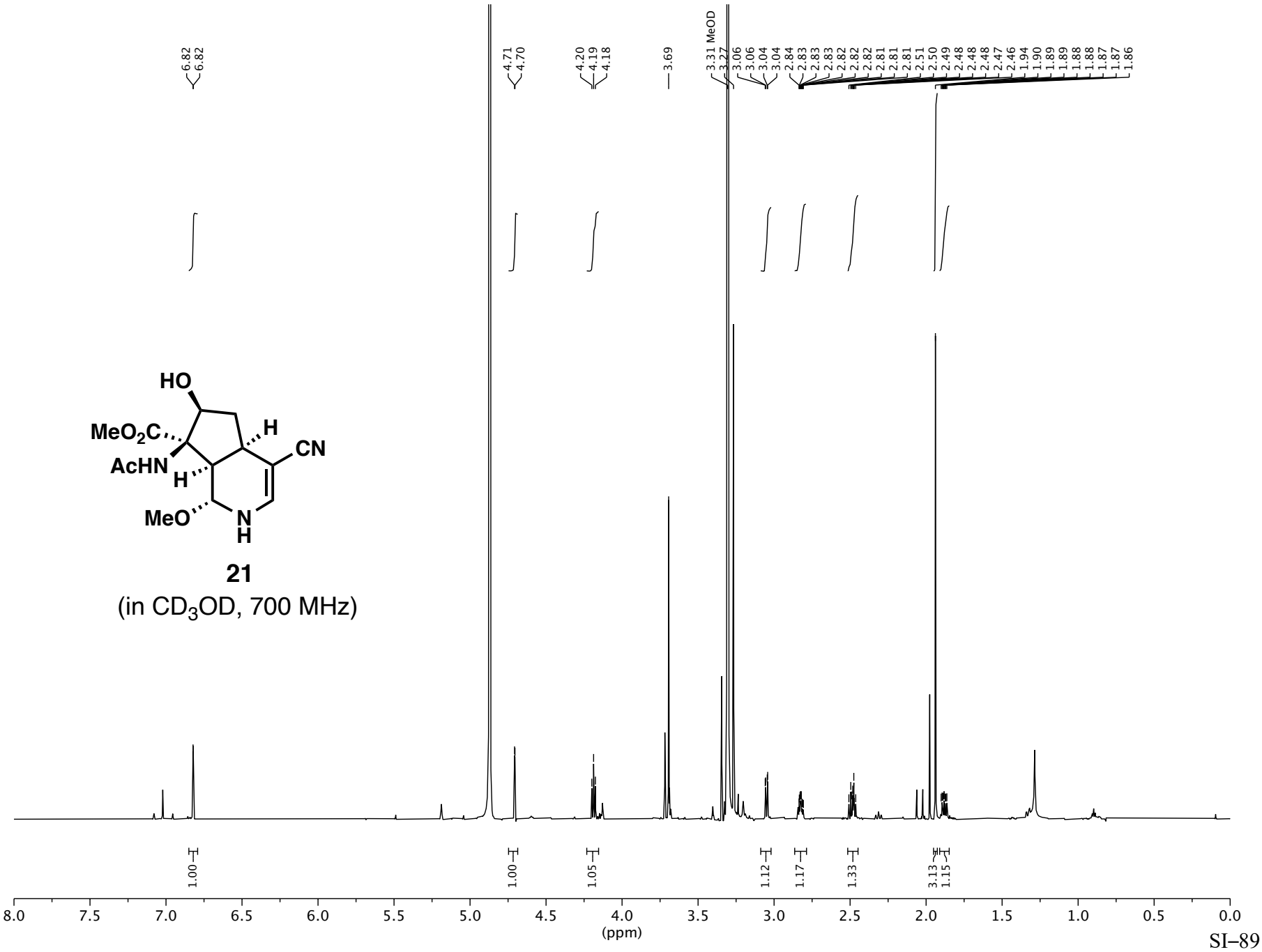
SI-6

(in CD_3OD, 151 MHz)

Carbon	δ (ppm)
C-1	77.4
C-2	44.2
C-3	30.4
C-4	35.0
C-5	49.
C-6	42.0
C-7	65.6
C-8	40.9
C-9	175.7
C-10	68.3
C-11	175.2
C-12,13	62.9, 14.5

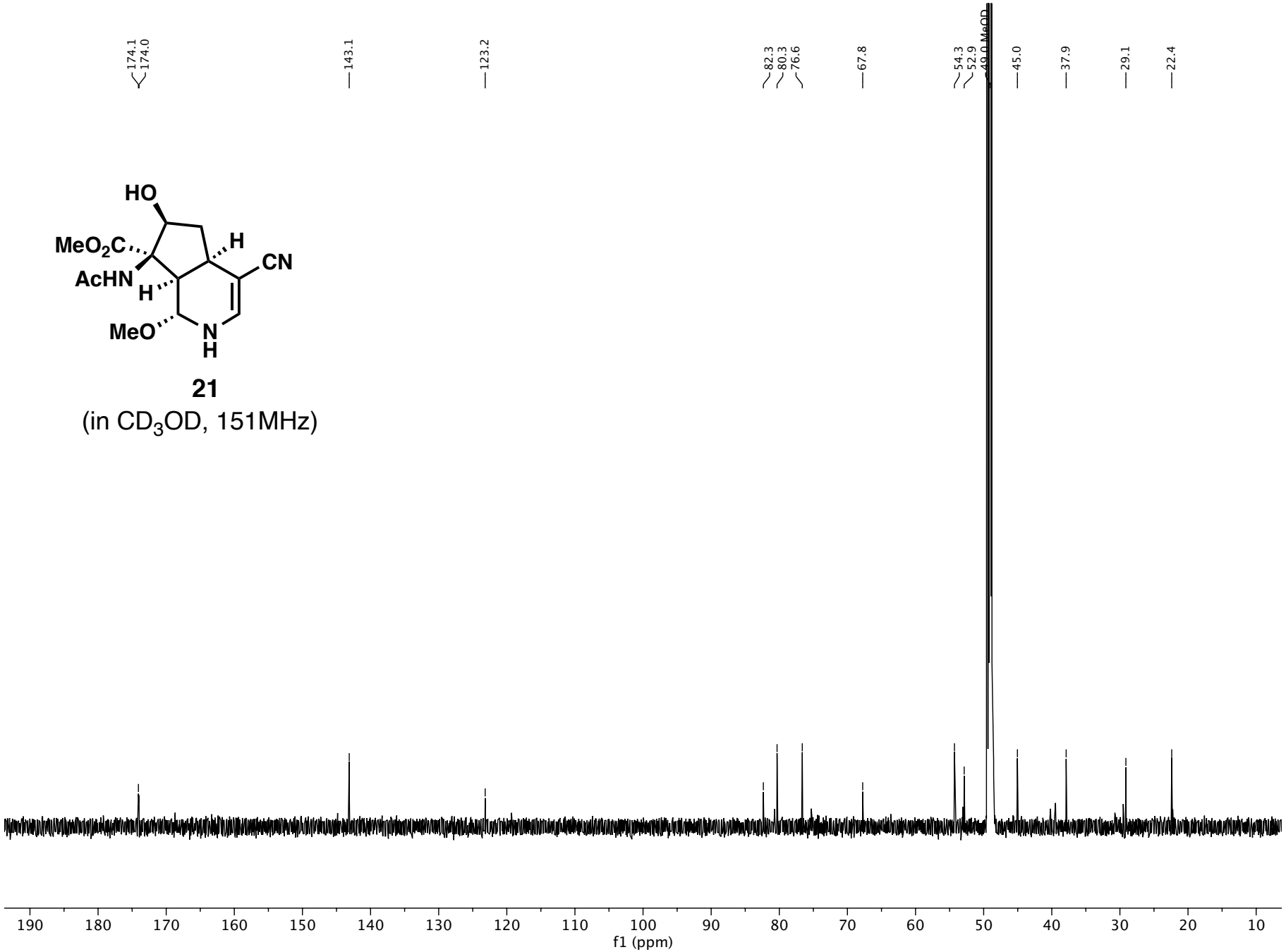

HO
H2N
EtO2C
H
H
H
O
NH
N
Me
H
*
SI-6
(in CD3OD, 600 MHz)
* carbon peak
undeneath MeOD
HSQC
{3.0,49.1}
{2.6,49.0}
f1 (ppm)
10
20
30
40
50
60
70
80
90
100
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
(ppm)


{2.2,1.2}b
{4.3,2.4}a
{2.2,2.6}c
{2.2,3.0}d
a
b
c
d
HO
H1
H2β
H2α
H2N
H3
H8
O
EtO2C
H4
H5α
NH
N
H5β
CH3(6)
H7
SI-6
(in CD3OD, 600 MHz)
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
(ppm)
f1 (ppm)



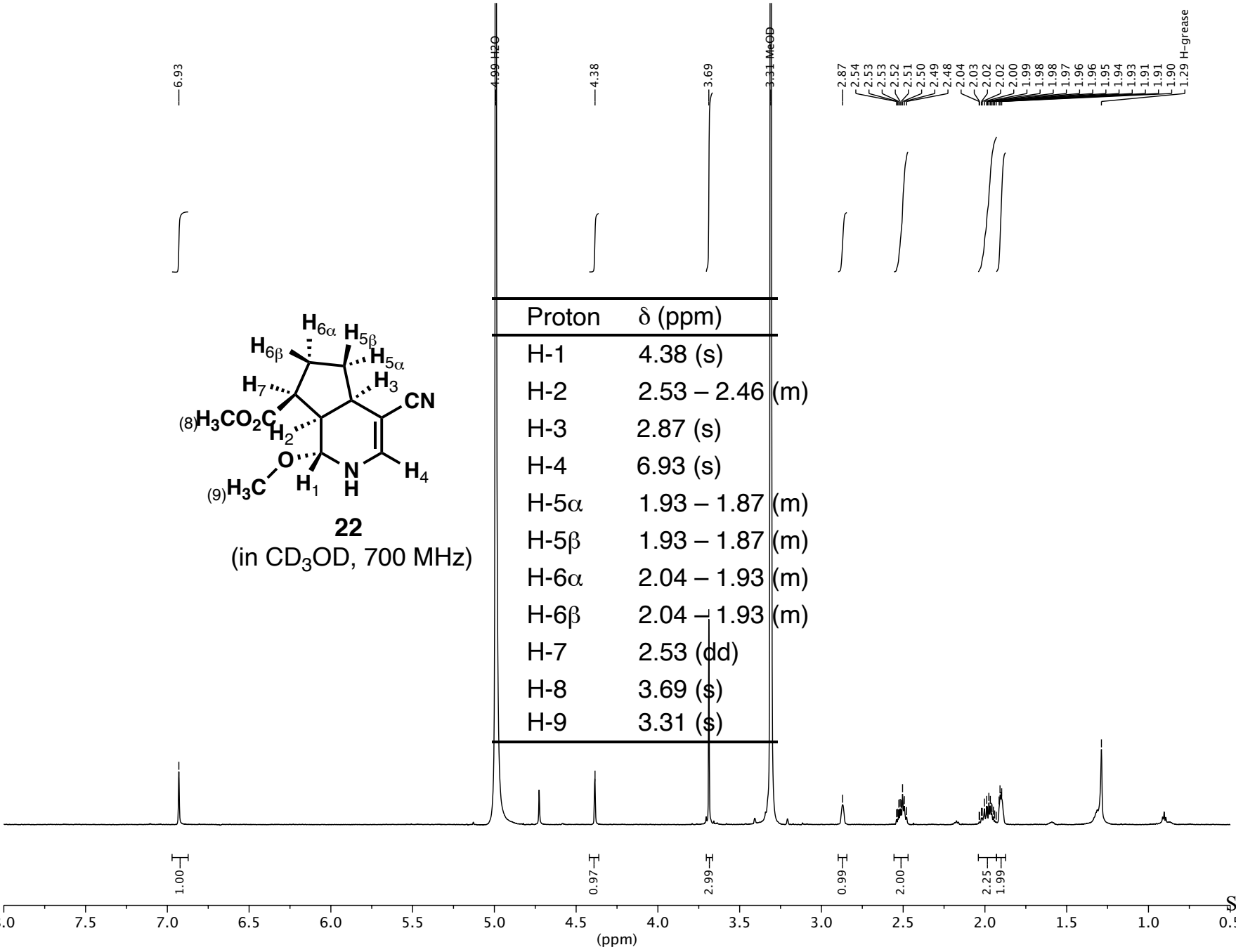
21

(in CD_3OD, 700 MHz)



21

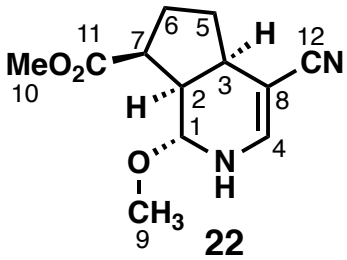
(in CD_3OD, 151MHz)



22

(in CD_3OD, 700 MHz)

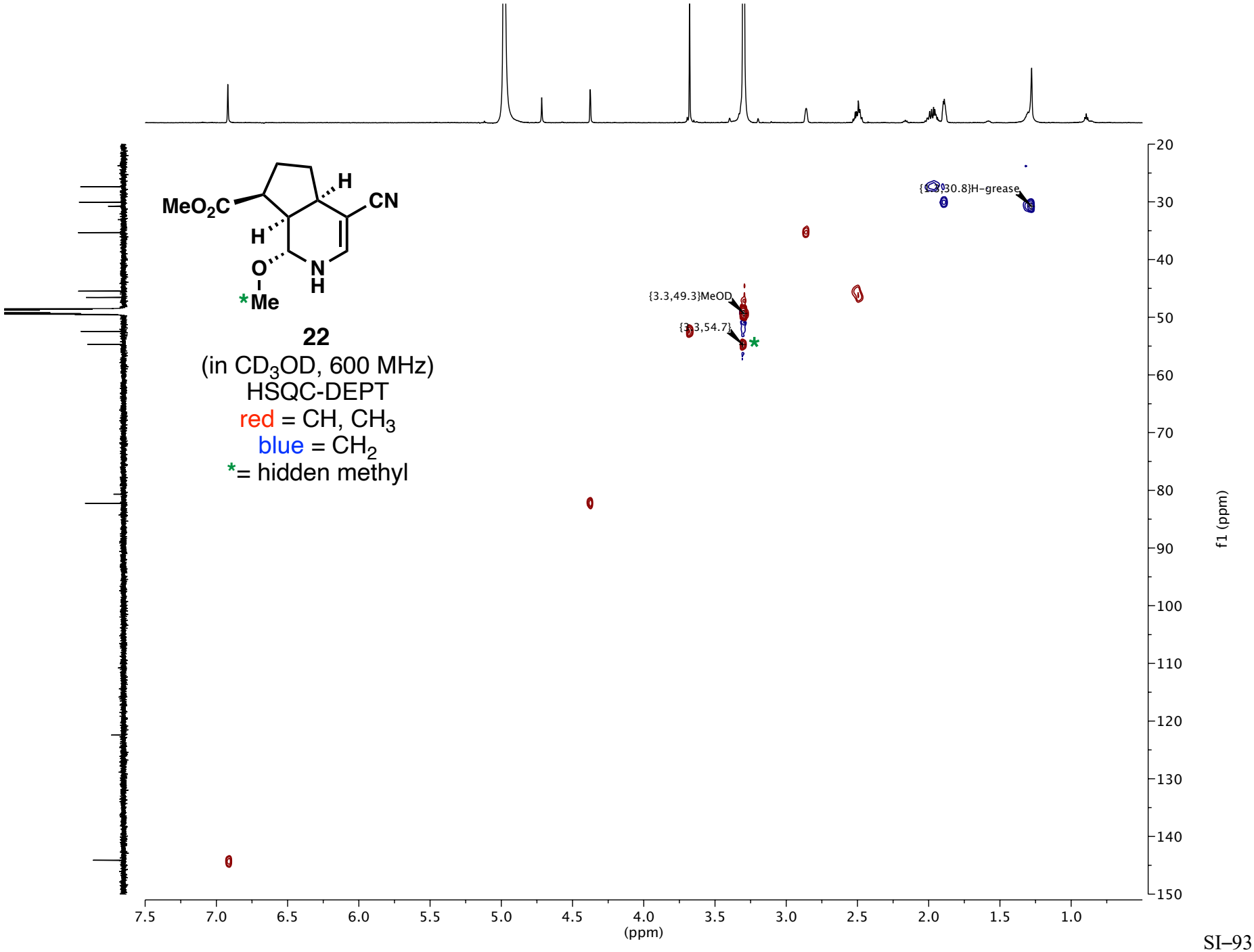
Proton	δ (ppm)
H-1	4.38 (s)
H-2	2.53 – 2.46 (m)
H-3	2.87 (s)
H-4	6.93 (s)
H-5α	1.93 – 1.87 (m)
H-5β	1.93 – 1.87 (m)
H-6α	2.04 – 1.93 (m)
H-6β	2.04 – 1.93 (m)
H-7	2.53 (dd)
H-8	3.69 (s)
H-9	3.31 (s)

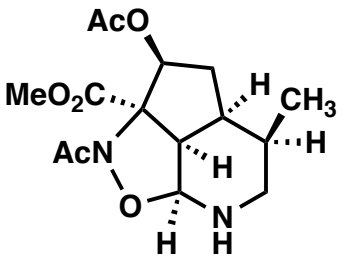


22

(in CD_3OD, 151 MHz)

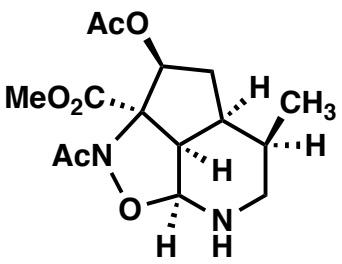
Carbon	δ (ppm)
C-1	82.3
C-2	45.5
C-3	35.3
C-4	144.1
C-5	30.1
C-6	27.4
C-7	46.6
C-8	80.7
C-9	54.7
C-10	52.5
C-11	177.4
C-12	122.4


MeO2C
H
CN
H
O
N
H
*Me
22
(in CD3OD, 600 MHz)
HSQC-DEPT
red = CH, CH3
blue = CH2
*= hidden methyl
{3.3,49.3}MeOD
{3.3,54.7}
{1.3,30.8}H-grease
f1 (ppm)
(ppm)



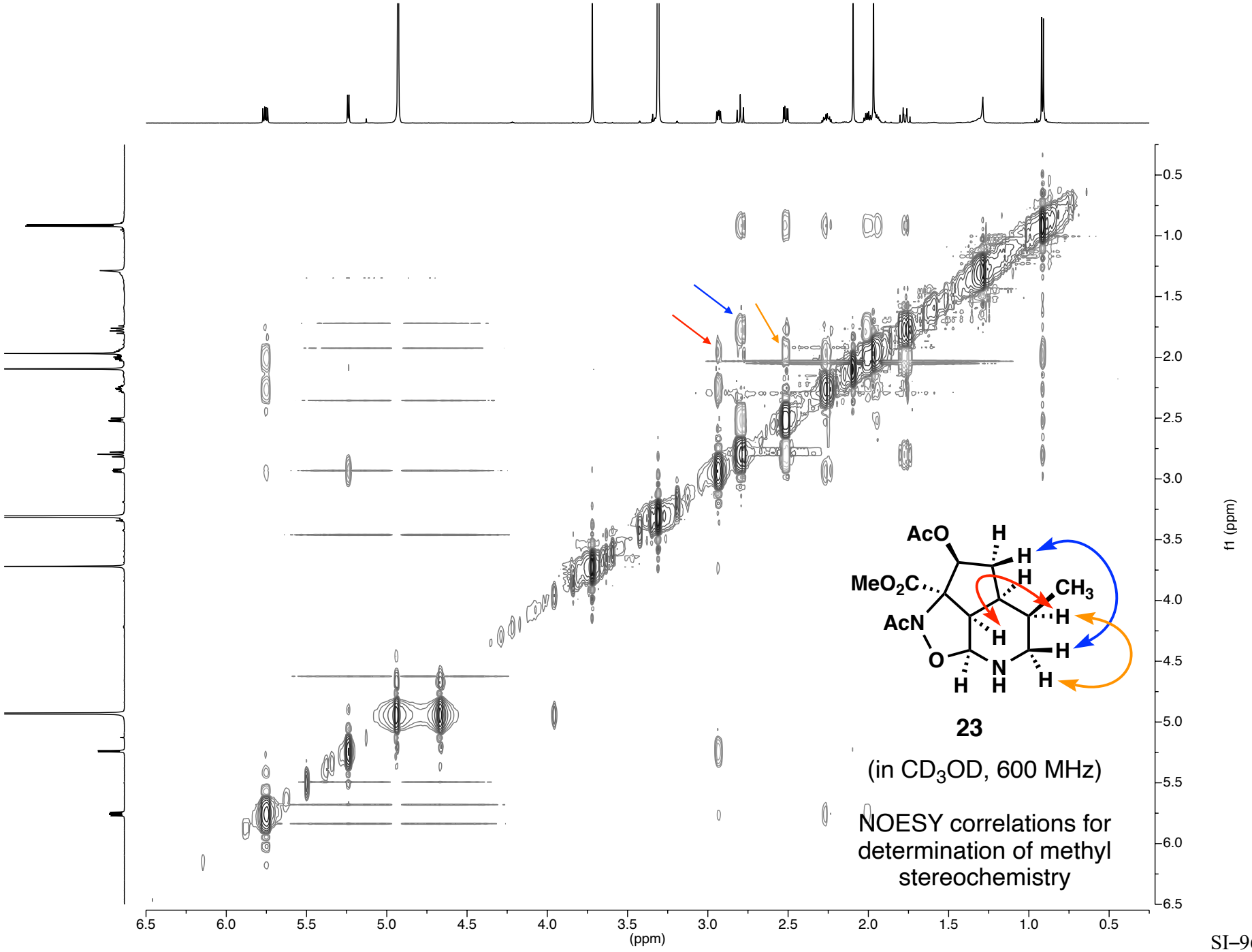
23

(in CD_3OD, 600 MHz)



23

(in CD_3OD, 151 MHz)


AcO
H
H
H
MeO2C
CH3
AcN
H
H
O
N
H
H
H
23
(in CD3OD, 600 MHz)
NOESY correlations for determination of methyl stereochemistry
f1 (ppm)
(ppm)