



## Supporting Information

### **Total Synthesis of Kibdelomycin**

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# Supplementary Materials

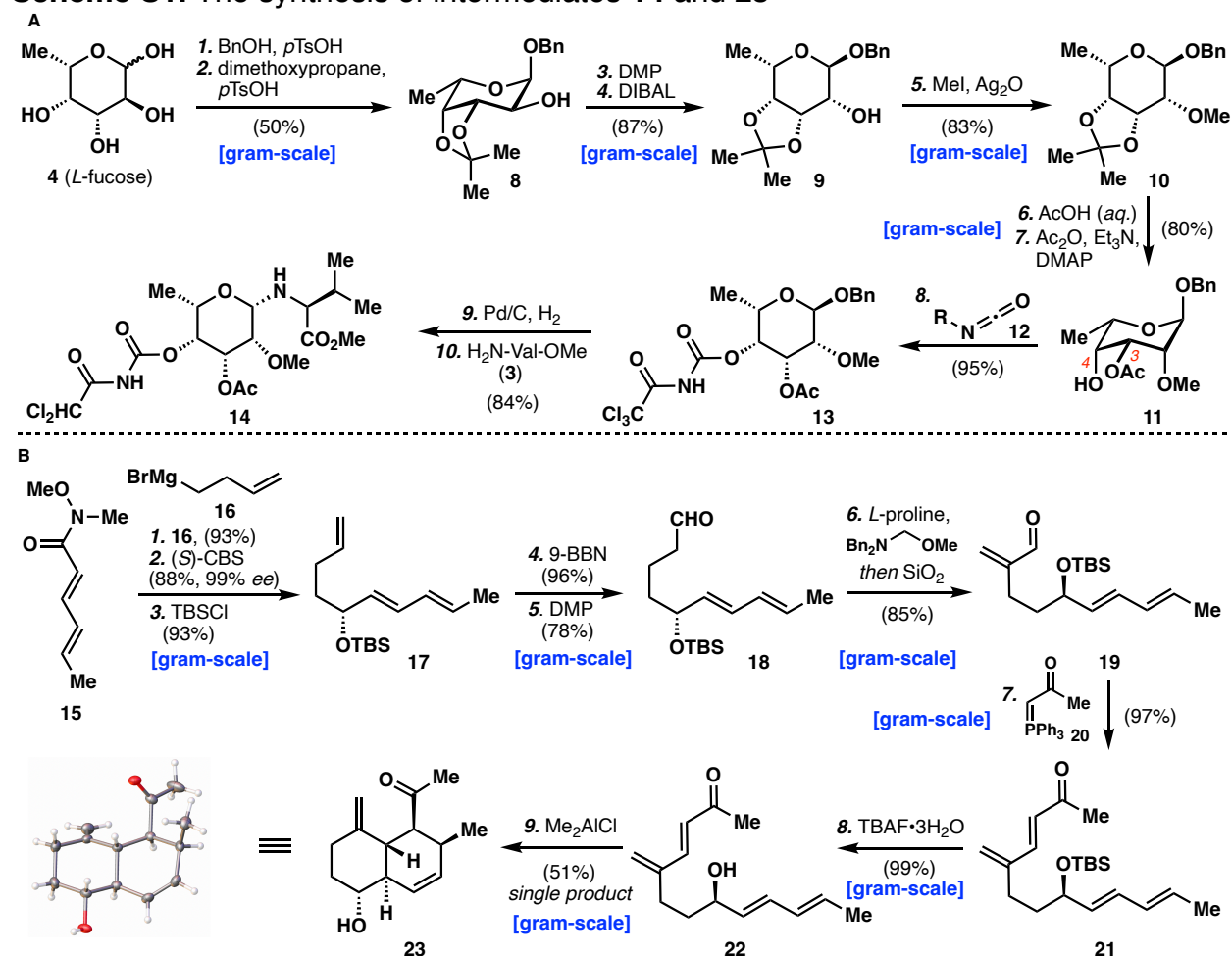
- I) Experimental Section
- II) Chiral SFC Results
- III) X-Ray Crystallography Data
- IV) References
- V) NMR Spectra

## I) General Experimental

All reactions were carried out under an inert argon atmosphere with dry solvents under anhydrous conditions unless otherwise stated. Dry acetonitrile (MeCN), dichloromethane (DCM), diethyl ether (Et<sub>2</sub>O), tetrahydrofuran (THF), toluene (PhMe), dimethylformamide (DMF), benzene, and triethylamine (Et<sub>3</sub>N) were obtained by passing the previously degassed solvents through activated alumina columns. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Yields refer to chromatographically and spectroscopically (<sup>1</sup>H NMR) homogeneous material, unless otherwise stated. Reactions were monitored by thin layer chromatography (TLC) carried out on 0.25 mm E. Merck silica plates (60F-254), using UV light as the visualizing agent and/or phosphomolybdic acid and heat as a developing agent. Flash silica gel chromatography was performed using E. Merck silica gel (60, particle size 0.043 – 0.063 mm). NMR spectra were recorded on Bruker DRX-600 and AMX-400 instruments and were calibrated using residual undeuterated solvent as an internal reference (CDCl<sub>3</sub>: <sup>1</sup>H NMR δ = 7.26 ppm, <sup>13</sup>C NMR δ = 77.16 ppm; acetone-*d*<sub>6</sub>: <sup>1</sup>H NMR δ = 2.05 ppm, <sup>13</sup>C NMR δ = 49.84 ppm; CD<sub>3</sub>OD: <sup>1</sup>H NMR δ = 3.31 ppm, <sup>13</sup>C NMR δ = 49.00 ppm). The following abbreviations were used to explain NMR peak multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, p = quint, m = multiplet, br = broad. High-resolution mass spectra (HRMS) were recorded on an Agilent LC/MSD TOF mass spectrometer by electrospray ionization time-of-flight (ESI-TOF) reflectron experiments.

## The detailed route and conditions:

**Scheme S1.** The synthesis of intermediates **14** and **23**<sup>a</sup>



<sup>a</sup>Reagents and conditions:

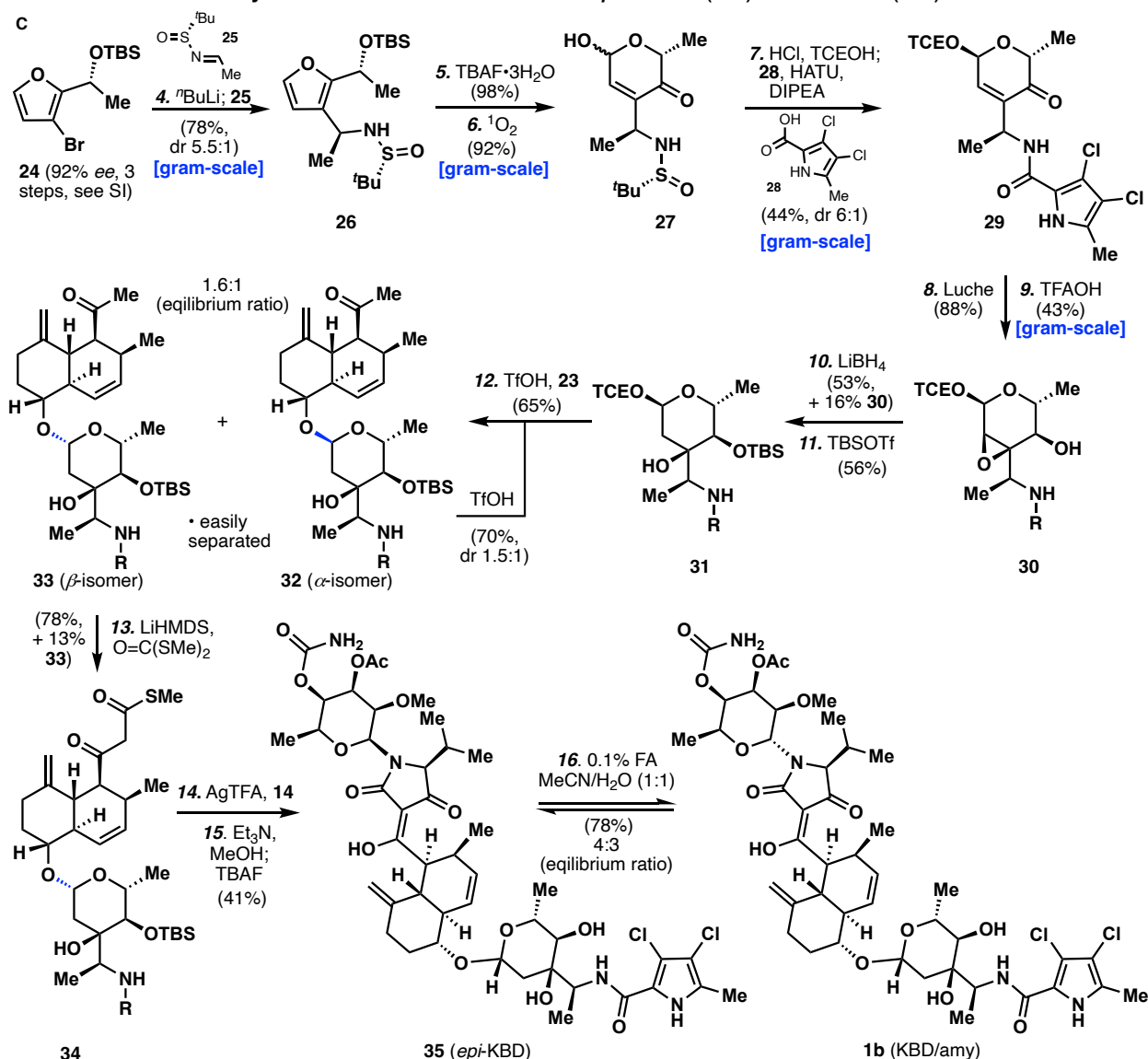
**A** (for **14**): (1) BnOH (10.0 eq.), *p*TsOH (0.1 eq.), 80 °C, overnight; (2) 2,2-dimethoxypropane (3.0 eq.), *p*TsOH (0.2 eq.), DMF, rt, overnight, 50% (2 steps); (3) DMP (1.75 eq.), DCM, rt, 2 h; (4) DIBAL (2.5 eq.), THF, -78 °C to rt, overnight, 87% (2 steps); (5) MeI (6.0 eq.), Ag<sub>2</sub>O (3.0 eq.), CH<sub>3</sub>CN, 75 °C, overnight, 83%; (6) 80% *aq.* AcOH, 80 °C, 1 h; (7) Ac<sub>2</sub>O (1.05 eq.), Et<sub>3</sub>N (1.1 eq.), DMAP (0.05 eq.), DCM, rt, overnight, 80% (2 steps); (8) **12** (2.0 eq.), DCM, 0 °C to rt, 1 h, 95%; (9) Pd/C (10% w/w), EtOAc, rt, 3 h; (10) H<sub>2</sub>N-Val-OMe (1.8 eq.), PPTS (0.2 eq.), DCM, rt, 6 h, 84% (2 steps).

**B** (for **23**): (1) **16** (1.4 eq.), THF, 0 °C, 4 h, 93%; (2) (*S*)-CBS (2.0 eq.), BH<sub>3</sub>·THF (2.2 eq.), THF, -78 °C, 5 h, 88% yield, 99% *ee*; (3) TBSCl (1.5 eq.), imidazole (3.0 eq.), DMF, 50 °C, overnight, 93%; (4) 9-BBN (1.4 eq.), THF, 0 °C to rt, 5 h, then NaBO<sub>3</sub>·4H<sub>2</sub>O (4.0 eq.), H<sub>2</sub>O, 0 °C to rt, overnight, 96%; (5) DMP (1.4 eq.), DCM, rt, 2.5 h, 78%; (6) Bn<sub>2</sub>NCH<sub>2</sub>OMe (1.1 eq.), *L*-proline (0.2 eq.), DMF, 0 °C to rt, 2 h, then SiO<sub>2</sub>, DCM, rt, 5 h, 85%; (7) **20** (1.8 eq.), DCM, 45 °C, 24 h, 97%; (8) TBAF·3H<sub>2</sub>O (1.0 eq.), DCM, rt, 1 h, 99%; (9) Me<sub>2</sub>AlCl (1.0 eq.), DCM, rt, 1 h, 51% (single product).

(8) TBAF·3H<sub>2</sub>O (2.0 eq.), THF, 0 °C to rt, 2 h, 99%; (9) Me<sub>2</sub>AlCl (1.0 eq.), DCM, -20 °C to rt, 18 h, 51%.

Abbreviations: Bn, benzyl; *p*TsOH, *p*-toluenesulfonic acid; DMF, *N,N*-dimethylformamide; DMP, Dess-Martin periodinane; DCM, dichloromethane; DIBAL, diisobutylaluminum hydride; THF, tetrahydrofuran; Ac, acetyl; DMAP, *N,N*-4-dimethylaminopyridine; PPTS, pyridinium *p*-toluenesulfonate; CBS, Corey-Bakshi-Shibata reagent; TBSCl, *tert*-butyldimethylsilyl chloride; 9-BBN, 9-borabicyclo[3.3.1]nonane; TBAF, *tetra-n*-butylammonium fluoride.

**Scheme S2.** The synthesis of intermediates *epi*-KBD (**35**) and KBD (**1b**)<sup>a</sup>



<sup>a</sup>) Reagents and conditions:

**C** (for **35** and **1b**): For the synthesis of compound **24**, see steps 1-3: (1) 2-bromofuran (1.0 eq.), AcCl (3.2 eq.), AlCl<sub>3</sub> (2.9 eq.), DCM, 0 °C to rt, 75 min, 93%; (2) [RuCl<sub>2</sub>(<sup>p</sup>Cymene)]<sub>2</sub> (0.0075 eq.), *N*-((1*R*,2*R*)-2-amino-1,2-diphenylethyl)-4-methylbenzenesulfonamide (0.018 eq.), HCO<sub>2</sub>Na (5.0 eq.), THF/H<sub>2</sub>O (1/2, v:v), 40 °C, 48 h, 92% yield, 92% *ee*; (3) TBSCl (1.5 eq.), imidazole (3.0 eq.), DMF, rt, overnight, 95%; (4) *n*-BuLi (1.1 eq.), Et<sub>2</sub>O, -40 °C, 1 h, then **25** (1.2 eq.), -78 °C to rt, 2 h, 78% (*d.r.* 5.5:1); (5) TBAF·3H<sub>2</sub>O (2.0 eq.), THF, rt, 0.5 h, 98%; (6) MB (0.0014 eq.), O<sub>2</sub>, DCM, -78 °C, 2.5 h, then Me<sub>2</sub>S (5.0 eq.), -78 °C to rt, 2 h, 92%; (7) *p*TsOH (0.2 eq.), TCEOH, rt, 1.5 h, then HCl (2.0 eq.), rt, 1.5 h, then HATU (2.0 eq.), **28** (2.0 eq.), DIPEA (5.5 eq.), DMF, rt, 8 h, 44% (*d.r.* 6:1); (8) NaBH<sub>4</sub> (4.0 eq.), CeCl<sub>3</sub>·7H<sub>2</sub>O (0.4 eq.), MeOH, 0 °C, 20 min, 88%; (9) TFAOH (1.36 eq.), DCM, -40 °C to rt, 2 h, 43%; (10) LiBH<sub>4</sub> (6.0 eq.), toluene, 60 °C, 3 h, 53% **S9** + 16% **30**; (11) TBSOTf (6.0 eq.), Et<sub>3</sub>N (10.0 eq.), DCE, 7 h, 56%; (12) **23** (2.0 eq.), 4 A MS, TfOH (1.0 eq.), DCM, rt, 2.5 h, 65% (1.6:1, β:α); (12') **23** (2.0 eq.), TCEOH (1.0 eq.), 4 A MS, TfOH (2.0 eq.),

DCM, rt, 2.5 h, 70% (1.5:1,  $\beta$ : $\alpha$ ); (13) LiHMDS (20.0 eq.), CO(SMe)<sub>2</sub> (12.0 eq.), THF, -78 to 30 °C, 6.5 h, 78% **34** + 13% **33**; (14) **14** (3.0 eq.), 4 Å MS, AgTFA (5.0 eq.), THF, rt, 2 h; (15) Et<sub>3</sub>N (5.0 eq.), MeOH, rt, 10 min, then TBAF (8.0 eq.), THF, rt, 0.5 h, 41% (2 steps); (16) 0.1% HCO<sub>2</sub>H (4.4 eq.) in MeCN/H<sub>2</sub>O, rt, 24 h, 78% (4:3, **35/1b**). Abbreviations: Bu, butyl; MB, methylene blue; TCE, trichloroethyl; HATU, *O*-(7-azabenzotriazol-1-yl)-*N,N,N,N*-tetramethyluronium hexafluorophosphate; DIPEA, diisopropylethylamine; TFAOH, trifluoroacetic acid; AgTFA, silver trifluoroacetate; Tf, trifluoromethanesulfonyl; DCE, dichloroethane; LiHMDS, lithium *bis*(trimethylsilyl)amide.





**Table S1.** Minimum inhibitory concentration (MIC) of kibelomycin (**1b**) and analogs<sup>a</sup> (μg/mL)

| Organism                           | 1b (KBD)     | 35 ( <i>epi</i> -KBD) | 36   | 37   | 38   | 39   | 40   | 41   | 42   | ciprofloxacin |
|------------------------------------|--------------|-----------------------|------|------|------|------|------|------|------|---------------|
| <i>E. coli</i> MG1655 <sup>b</sup> | 32           | >256                  | >256 | >256 | >256 | >256 | >256 | >256 | >256 | ≤0.015        |
| <i>E. coli</i> W0153 <sup>c</sup>  | 4            | 2                     | 128  | >256 | >256 | 64   | 64   | >256 | >256 | ≤0.015        |
| <i>S. aureus</i> FDA209P           | 0.5          | 1                     | -    | -    | -    | -    | -    | 256  | >128 | 0.25          |
| <i>S. aureus</i> HG003             | <sup>d</sup> | -                     | >64  | >64  | >64  | >64  | >64  | -    | -    | 0.25          |
| <i>S. aureus</i> SH1000            | -            | -                     | >128 | >128 | >128 | >128 | >128 | -    | -    | 0.25          |
| <i>S. aureus</i> UAMS-1            | -            | -                     | >128 | >128 | >128 | >128 | >128 | -    | -    | 0.25          |
| <i>S. aureus</i> USA300            | -            | -                     | >128 | >128 | >128 | >128 | >128 | -    | -    | -             |

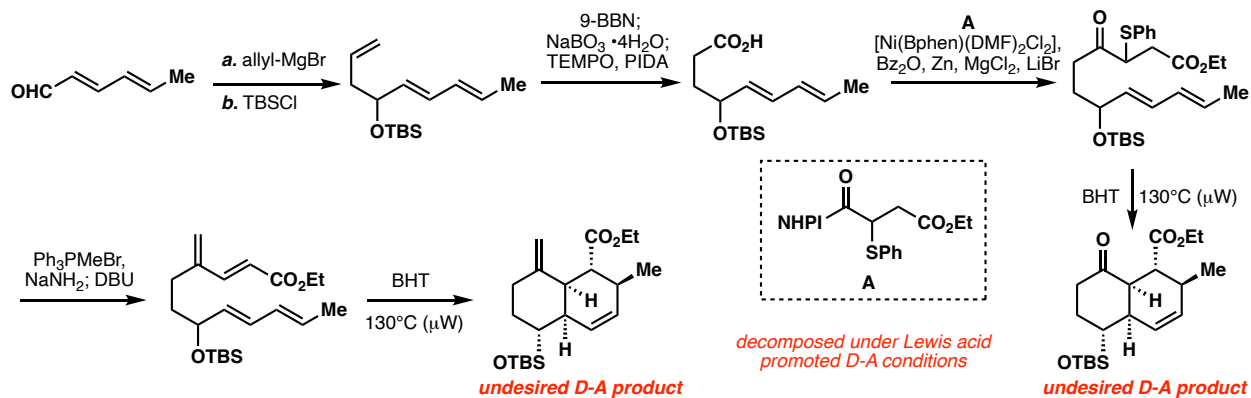
<sup>a</sup> MIC was determined by microdilution assay using Mueller Hinton II Broth.

<sup>b</sup> wild-type strain. <sup>c</sup> permeabilized. <sup>d</sup> - = not available.

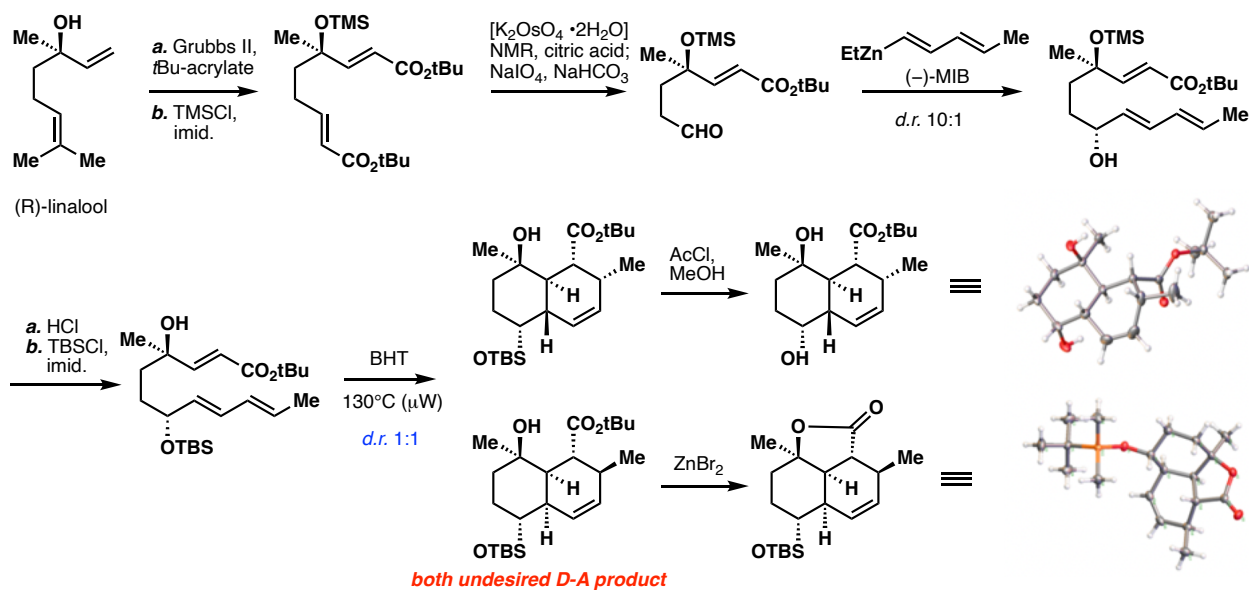
### MIC determination

The microbroth dilution Minimum Inhibitory Concentration (MIC) method was used to determine the *in vitro* antibacterial activity of Kibelomycin and its analogs against bacterial strains. Briefly, assay plates were prepared by two-fold dilution of each compound across the plate, and included a positive and growth control. Overnight liquid cultures of bacterial strains (*E. coli* MG1655, *E. coli* W0153, and *S. aureus* FDA209P) were diluted into the assay plate to achieve 5 x 10<sup>5</sup> CFU/mL and incubated at 37°C for 16-20 hours. The MIC was determined as the lowest concentration of the compound that inhibits growth of the bacteria as determined by the unaided eye. All assays were repeated in triplicate.

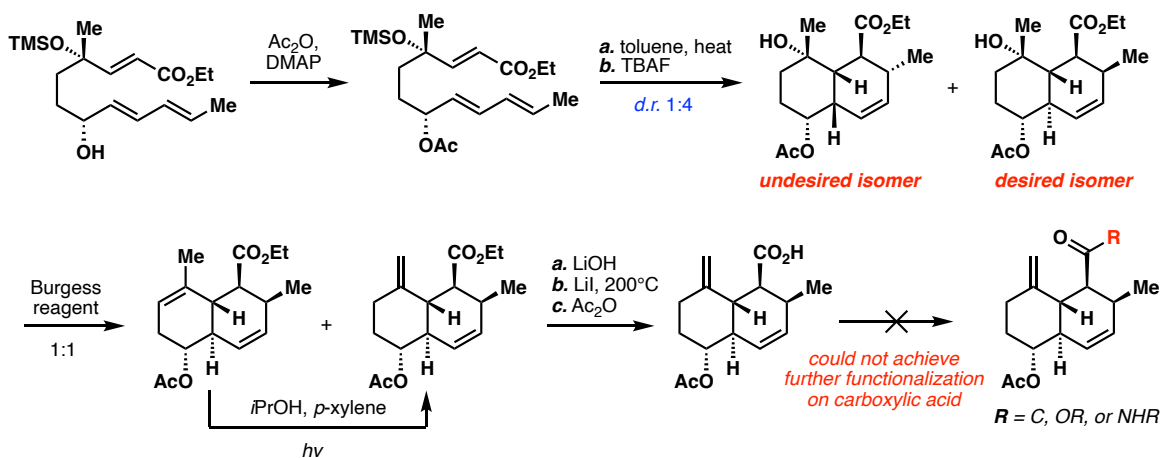
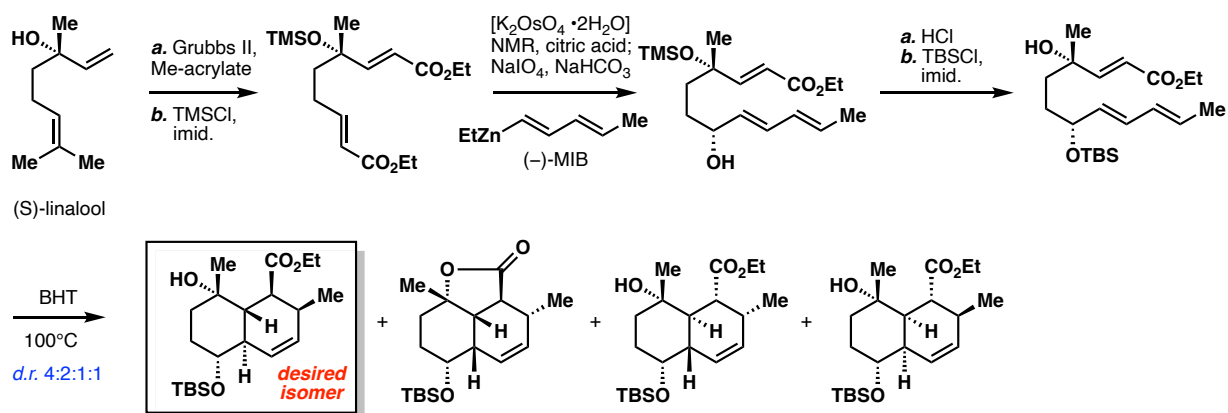
## The development of the routes for decalin synthesis and related Diels-Alder outcomes:



**Scheme S4.** The failed 1<sup>st</sup> generation route

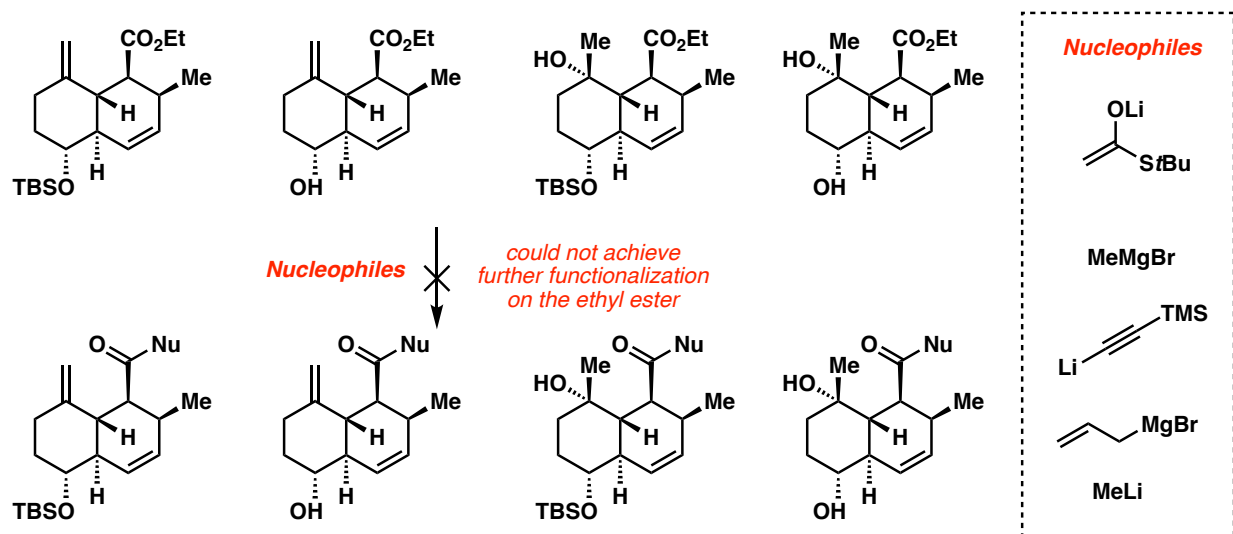


**Scheme S5.** The failed 2<sup>nd</sup> generation route starts from (R)-linalool

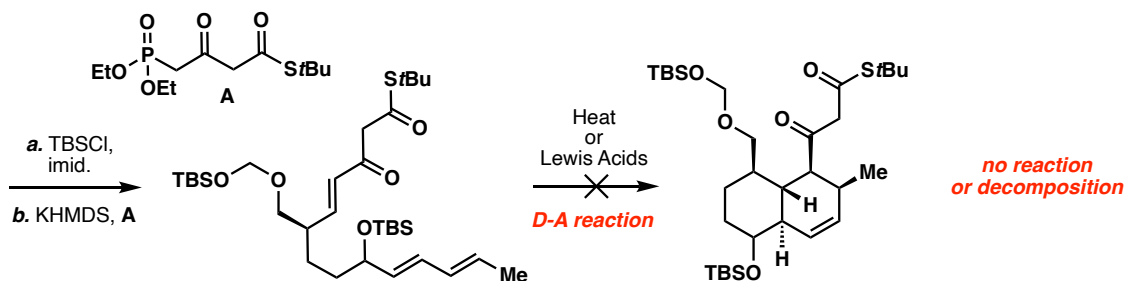
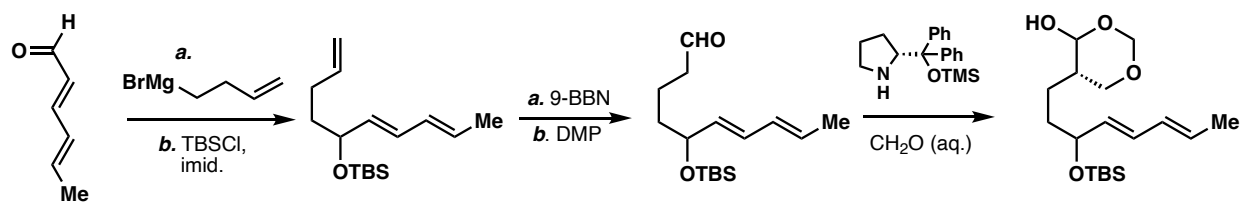


**Scheme S6.** The failed further functionalization on the 2<sup>nd</sup> generation D-A product

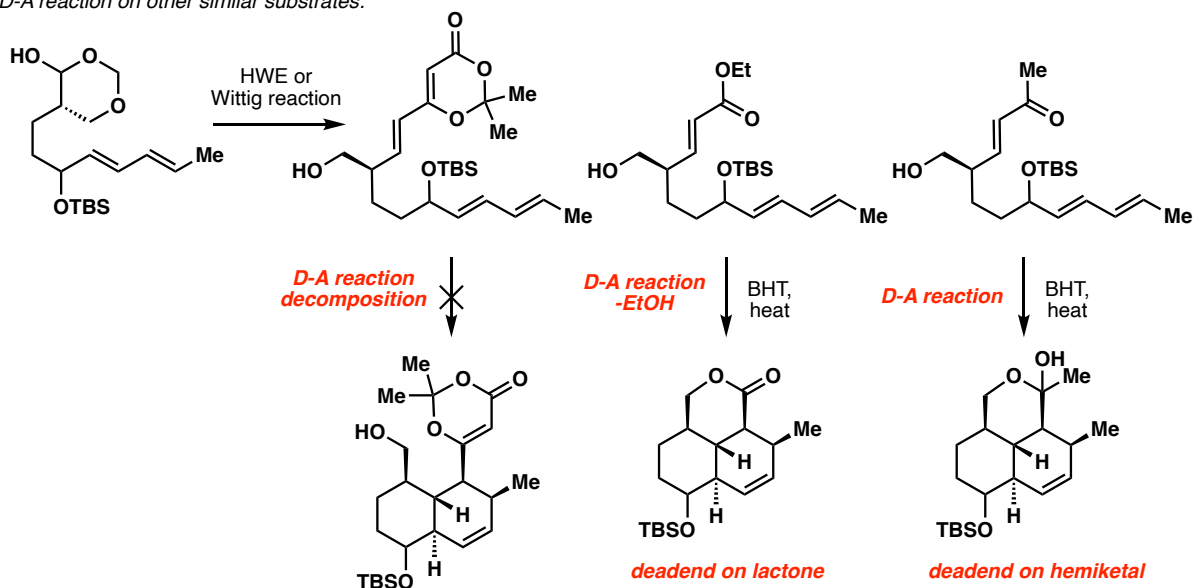
Other dead-end intermediates:



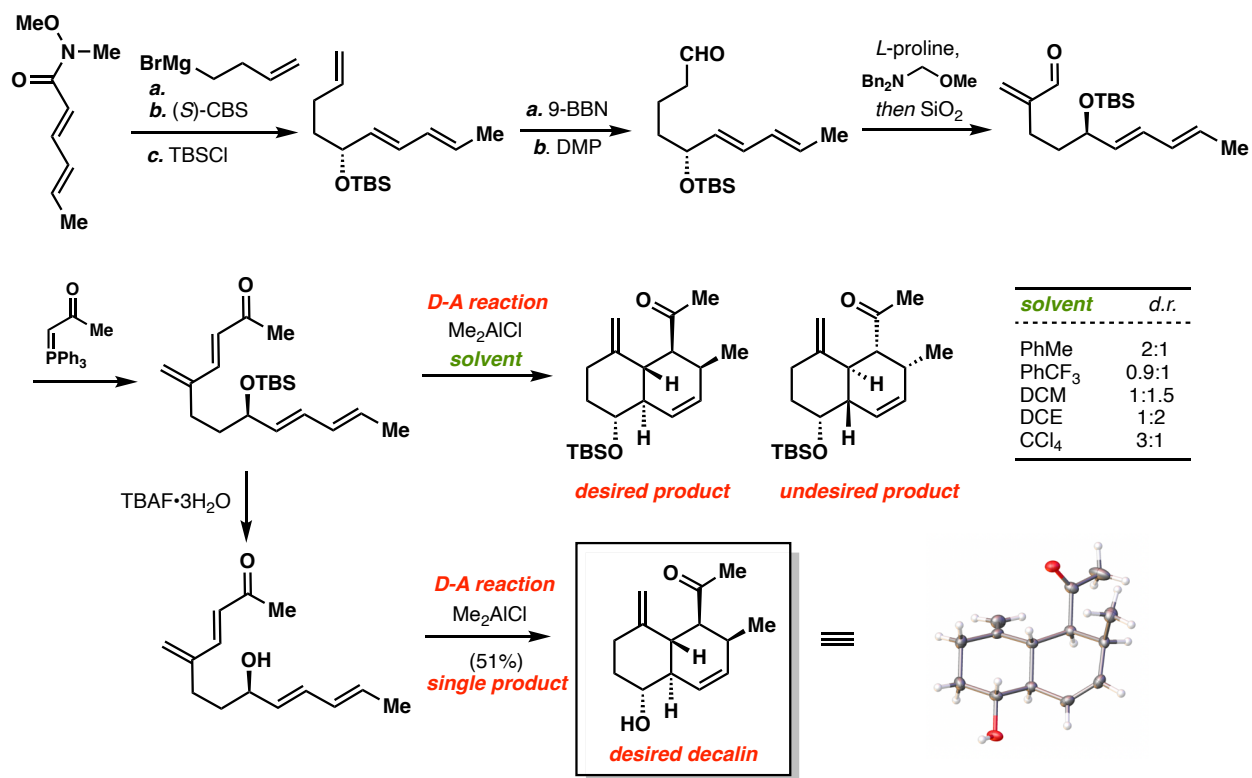
**Scheme S7.** Other dead-end intermediates in the 2<sup>nd</sup> generation route



D-A reaction on other similar substrates:

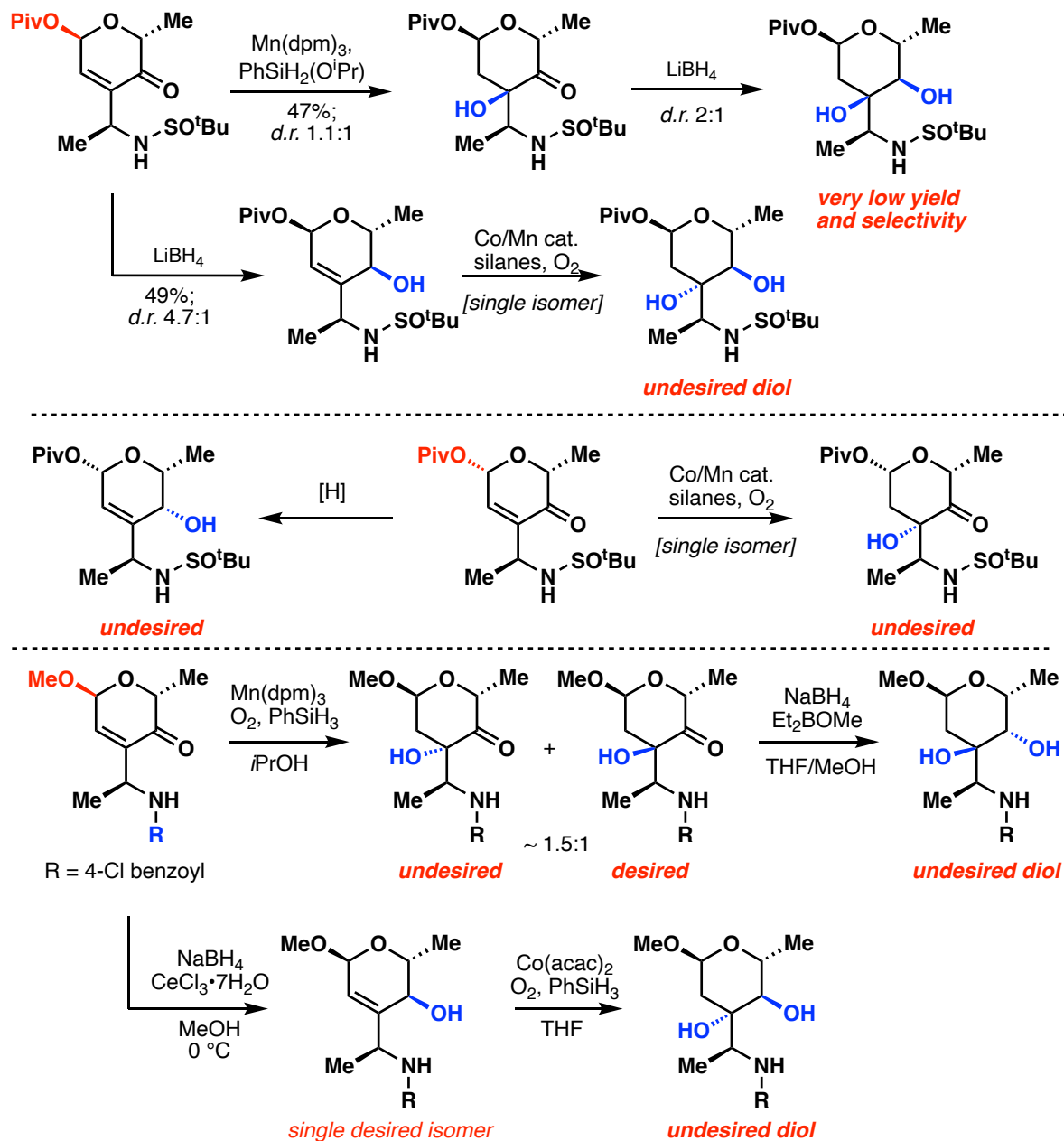


**Scheme S8.** The 3<sup>rd</sup> generation route and the related intermediates for D-A reaction



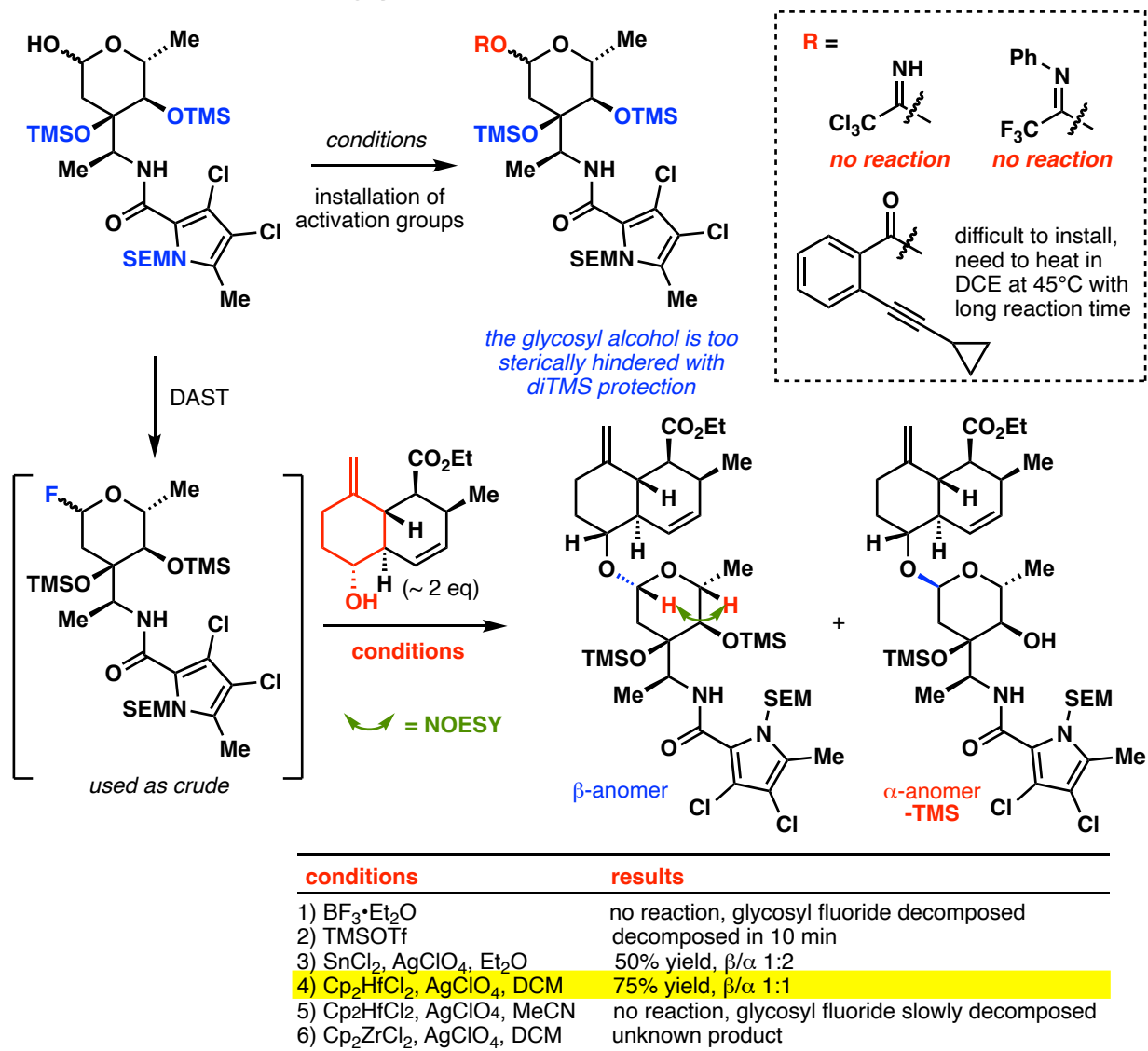
Scheme S9. The final route for decalin

## The *cis*-diol construction through reduction/hydration sequence:

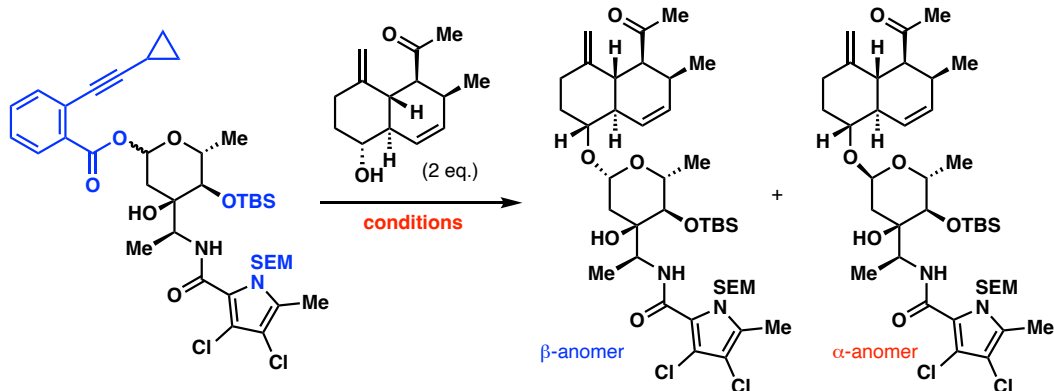


**Scheme S10.** The poor selectivity of the reduction/hydration strategy

## The efforts on the *O*-glycosidation:

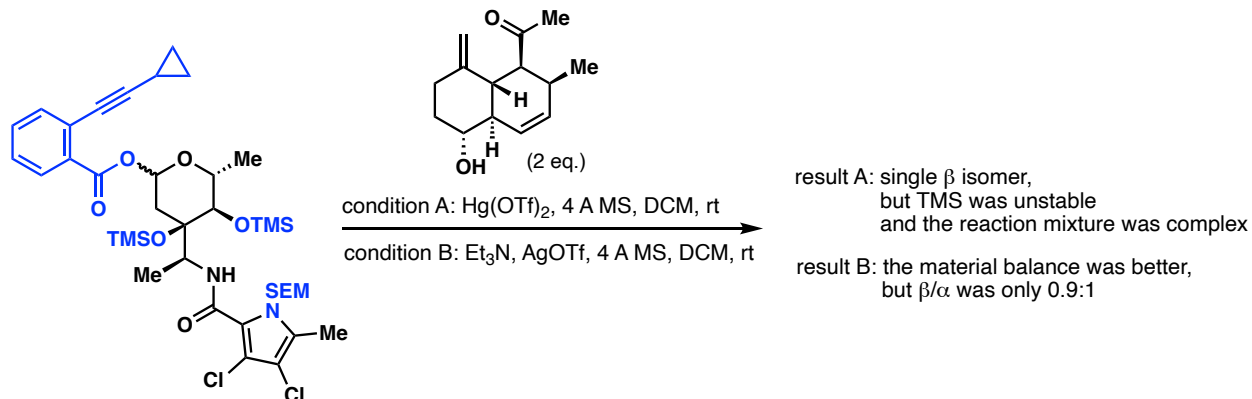


**Scheme S11.** The *O*-glycosidation through glycosyl fluoride



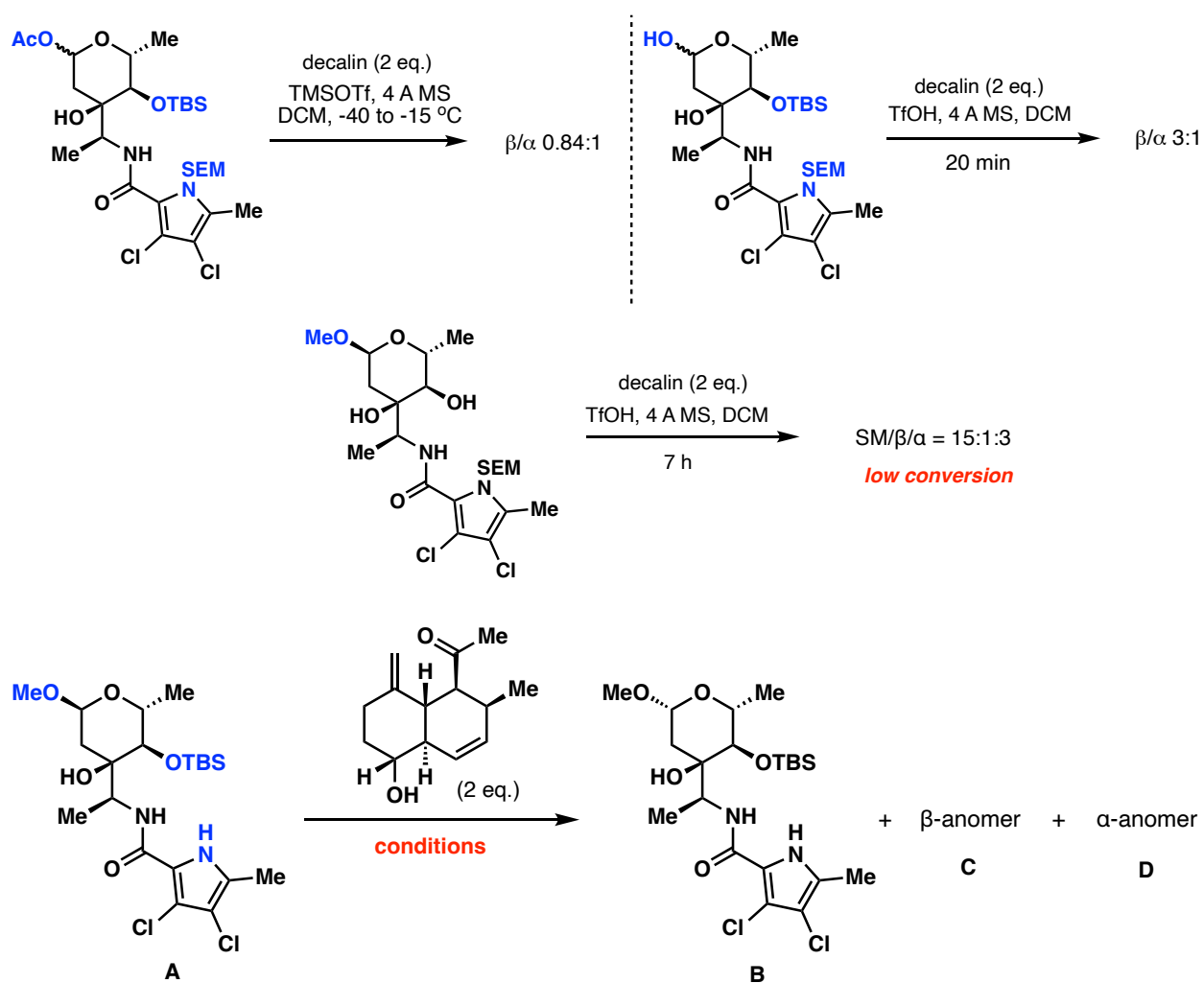
| conditions  | results ( $\beta$ : $\alpha$ ) | conditions  | results ( $\beta$ : $\alpha$ ) |
|---|--------------------------------|---|--------------------------------|
| AgOTf, 4 A MS, DCM, rt  | 2:1                            | AgOTf, 4 A MS, CHCl <sub>3</sub> or EtOAc or Et <sub>2</sub> O, rt                                      | no $\beta$ anomer              |
| AgOTf, 4 A MS, DCM, rt, c = 0.0025M   | 1.6:1                          | AgOTf, 3 A MS, DCM, rt  | 1.2:1                          |
| AgOTf, 4 A MS, DCM/toluene, rt  | 0.6:1                          | I <sub>2</sub> , 3 A MS, DCM, rt  | 0.2:1                          |
| AgOTf, Gd(OTf) <sub>3</sub> , 4 A MS, DCM, rt   | 1.1:1                          | Hg(OAc) <sub>2</sub> , 4 A MS, DCM, rt  | no pdt                         |
| AgOTf, 4 A MS, DCM, 0 °C  | 1.3:1                          | Hg(OAc) <sub>2</sub> , 4 A MS, DCM/CH <sub>3</sub> CN, rt   | 1.5:1                          |
| Ag <sub>2</sub> O or AgNO <sub>3</sub> or Ag <sub>2</sub> SO <sub>4</sub> , 4 A MS, DCM, rt | NR                             | <b>Hg(OTf)<sub>2</sub>, 4 A MS, DCM, rt<sup>a</sup></b>   | <b>2.4:1</b>                   |
| AgClO <sub>4</sub> , 4 A MS, DCM, rt  | 2:1                            | Hg(OTf) <sub>2</sub> , In(OTf) <sub>3</sub> , 4 A MS, DCM, rt   | 2:1                            |
| AgClO <sub>4</sub> , 4 A MS, DCM, rt  | 2:1                            | Hg(OTf) <sub>2</sub> , 4 A MS, DCM, -20 °C to rt  | low conv.                      |
| AgClO <sub>4</sub> , 4 A MS, DMSO, rt   | NR                             | Hg(OTf) <sub>2</sub> , 4 A MS, CH <sub>3</sub> CN, rt   | complex, little $\beta$ anomer |
| AgSbF <sub>6</sub> , 4 A MS, DCM, rt  | no pdt                         | Ph <sub>3</sub> PAuNTf <sub>2</sub> , 4 A MS, DCM, -40 °C to rt   | 0.12:1                         |
| AgOTf, 4 A MS, toluene, rt  | 0.3:1                          | SPhosAuNTf <sub>2</sub> , 4 A MS, DCM, -40 °C   | low conv.                      |
| AgOTf, 4 A MS, DCE, rt  | 1.5:1                          | Pt(NH <sub>3</sub> ) <sub>2</sub> Cl <sub>2</sub> or K <sub>2</sub> PtCl <sub>4</sub> , 4 A MS, DCE, rt | NR                             |

<sup>a</sup> 200 mg scale,  $\beta$ : 53%,  $\alpha$ : 20%.



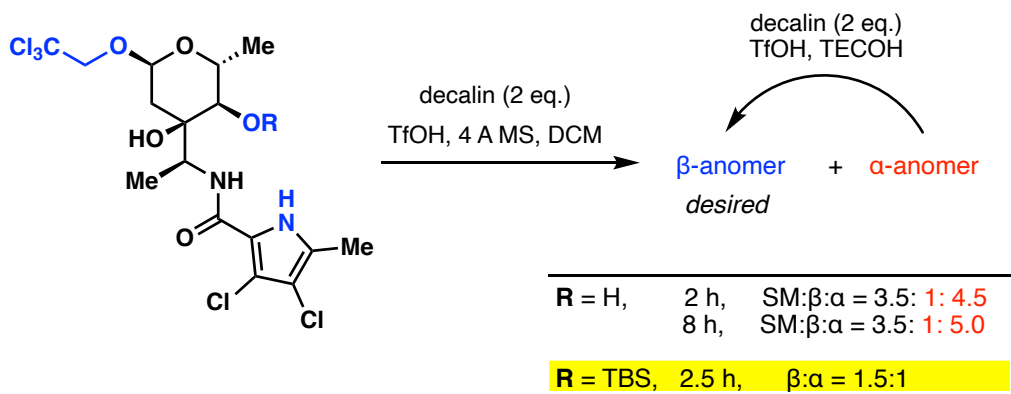
**Scheme S12.** The *O*-glycosidation with alkyne benzoic ester as the activating group



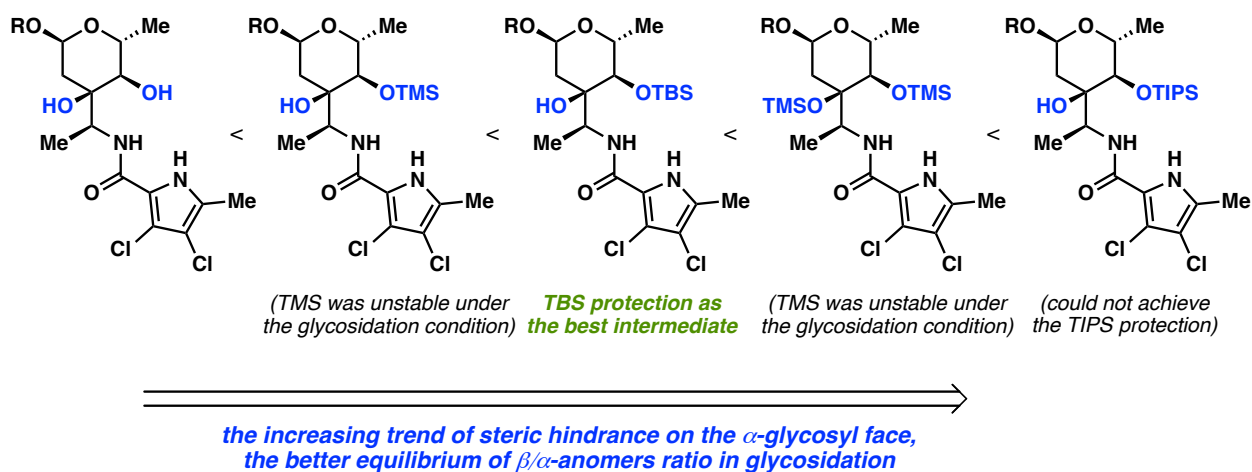


| conditions                              | result                         |
|---|--------------------------------|
| TfOH, DCM                               | low conversion                 |
| TfOH, DCM, TMSCl                        | low conversion                 |
| TfOH, DCM, TBSOTf                       | low conversion                 |
| Tf <sub>2</sub> NH, DCM                 | low conversion                 |
| BF <sub>3</sub> •Et <sub>2</sub> O, DCM | A: 25%, B: 20%, C: 15%, D: 15% |

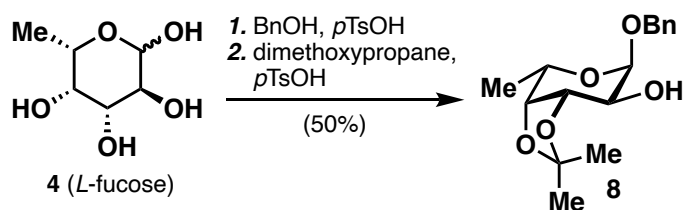
**Scheme S13.** The poor selectivity of *O*-glycosidation with other activating groups



**Scheme S14.** The final *O*-glycosidation substrate with mono TBS protection and TCE as the activating group achieves the good conversion and equilibrium



**Scheme S15.** The control of *O*-glycosidation selectivity based on the steric hindrance of the substrate



**Experimental:** To a flame-dried round bottom flask fixed with a stirbar, was added *L*-fucose (4.105 g, 25.00 mmol). The flask was placed under argon and BnOH (10.0 mL, 10.0 eq.) was added via syringe. The mixture was stirred until all solids were dissolved at which point *p*-TsOH (4.305 g, 2.5 mmol, 0.10 eq.) was added, and the flask was quickly resealed. The solution was then placed on an oil bath preheated to 80 °C and was allowed to stir at this temperature overnight. Upon completion, the flask was removed from the oil bath and allowed to cool. The crude reaction mixture was then loaded directly onto a column and purified by flash column chromatography (SiO<sub>2</sub>; DCM/MeOH 20:1 to 10:1) and used directly in the next reaction.

The benzylated fucopyranose was placed in a round bottom flask fixed with a stirbar and placed under argon. DMF was added (70 mL, 0.36M) and stirred until the solids were dissolved. *p*-TsOH (0.861 g, 5.00 mmol, 0.20 eq.) was added, and once all materials were dissolved, 2,2-dimethoxypropane (9.20 mL, 75.00 mmol, 3.0 eq.) was added dropwise. The resulting solution was stirred overnight at room temperature. When complete, the DMF was removed by rotary evaporation. The resulting residue was re-dissolved in chloroform (70.0 mL). This solution was rinsed sequentially with NaHCO<sub>3</sub> (*sat. aq.*), 5% LiCl (*aq.*), and brine. The organic layer was dried over MgSO<sub>4</sub>, filtered, and concentrated under reduced pressure. The desired product was purified by flash column chromatography (SiO<sub>2</sub>; 30% EtOAc in hexanes) yielding **8** (3.62 g, 50% yield).

**NOTE:** Both  $\alpha$  and  $\beta$  anomers result. In the above eluent, the alpha anomer has a higher  $R_f$  ( $\alpha = 0.30$ ;  $\beta = 0.25$ ). The beta anomer provided unsatisfactory diastereoselectivity in subsequent reactions and thus was discarded.

**Physical State:** colorless oil;

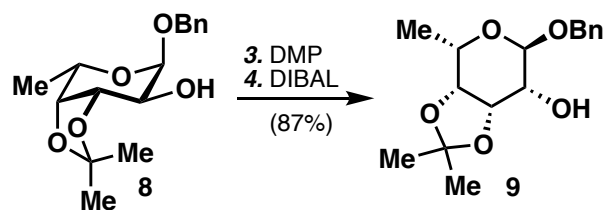
**R<sub>f</sub> Value:** 0.30 (30% EtOAc in hexanes);

**<sup>1</sup>H NMR** (600 MHz, C<sub>6</sub>D<sub>6</sub>) δ 7.21 – 7.18 (m, 2H), 7.16 – 7.13 (m, 2H), 7.11 – 7.07 (m, 1H), 4.88 (d, *J* = 3.9 Hz, 1H), 4.60 (d, *J* = 11.9 Hz, 1H), 4.30 (d, *J* = 12.0 Hz, 1H), 4.25 (t, *J* = 6.2 Hz, 1H), 4.04 (dq, *J* = 2.3, 6.6 Hz, 1H), 3.95 (m, 1H), 3.72 (dd, *J* = 6.3, 2.3 Hz, 1H), 2.24 (d, *J* = 5.5 Hz, 1H), 1.47 (s, 3H), 1.33 (d, *J* = 6.6 Hz, 3H), 1.23 (s, 3H), 0.59 ppm (s, 1H);

**<sup>13</sup>C NMR** (151 MHz, C<sub>6</sub>D<sub>6</sub>) δ 138.2, 128.7 (2C), 238.4, 128.0 (2C), 109.0, 97.2, 76.3, 75.9, 69.6, 69.4, 64.8, 27.8, 25.9, 16.6 ppm;

**Optical Rotation:** [α]<sub>D</sub><sup>20</sup> = -126.0° (c = 0.50 g / 100 mL, CHCl<sub>3</sub>);

**HRMS** (m/z): calc'd for C<sub>16</sub>H<sub>22</sub>O<sub>5</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 317.1359, found 317.1364.



**Experimental:** To a flame-dried round bottom flask fixed with a stir bar, was added **8** (3.62 g, 12.3 mmol) and  $\text{CH}_2\text{Cl}_2$  (120 mL, 0.1M). Dess-Martin-Periodinane (9.13 g, 21.5 mmol, 1.75 eq.) was added in one portion and the reaction mixture was stirred for 2 h at room temperature. The reaction mixture was concentrated under reduced pressure. The crude solids were re-dissolved in  $\text{Et}_2\text{O}$  (0.1M) and run through a plug of silica. The silica plug was rinsed with three more volumes of  $\text{Et}_2\text{O}$ , and the resulting eluent was concentrated under reduced pressure. Finally, the resulting residue was azeotroped with toluene twice on a rotary evaporator (in order to remove any residual acetic acid) yielding a white solid that was used directly in the next reaction.

The above ketone (3.62 g, 12.3 mmol) was dissolved in THF (120 mL, 0.1M) under argon, and the solution was cooled to  $-78^\circ\text{C}$ . DIBAL-H (1.0 M in hexanes; 30.75 mL, 30.75 mmol, 2.5 eq.) was then added dropwise. After stirring the reaction mixture at  $-78^\circ\text{C}$  for 2 h and overnight at room temperature, saturated  $\text{NH}_4\text{Cl}$  (aq.) (35 mL) was added. Next, a saturated aqueous solution of Rochelle's salt (35 mL) and EtOAc (35 mL) were added, and the mixture was stirred vigorously for 30 min. The aqueous phase was extracted with EtOAc (3 x 50 mL). The combined organic layers were rinsed with brine, dried over anhydrous  $\text{Na}_2\text{SO}_4$ , and filtered. The solvent was removed under reduced pressure. The crude product was purified *via* flash column chromatography ( $\text{SiO}_2$ ; 30% EtOAc in hexanes) yielding **9** (3.15 g; 87% yield) as a colorless oil.

**Physical State:** colorless oil;

**R<sub>f</sub> Value:** 0.30 (30% EtOAc in hexanes);

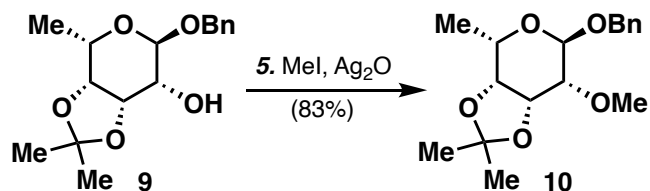
**<sup>1</sup>H NMR** (600 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  7.32 – 7.29 (m, 2H), 7.18 – 7.15 (m, 2H), 7.11 – 7.07 (m, 1H), 4.90 (d,  $J = 5.4$  Hz, 1H), 4.73 (d,  $J = 12.1$  Hz, 1H), 4.44 (d,  $J = 12.1$  Hz, 1H), 4.16 (dd,  $J$

= 7.3, 3.4 Hz, 1H), 3.63 – 3.60 (m, 1H), 3.48 (m, 2H), 2.16 (s, 1H), 1.51 (s, 3H), 1.22 (d,  $J = 6.4$  Hz, 3H), 1.20 ppm (s, 3H);

**$^{13}\text{C}$  NMR** (151 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  138.9, 128.6 (2C), 128.0 (2C), 127.7, 109.8, 101.0, 76.5, 74.5, 69.5, 69.3, 65.4, 26.4, 25.5, 16.1 ppm;

**Optical Rotation:**  $[\alpha]_{\text{D}}^{20} = -94.4^\circ$  ( $c = 0.50$  g / 100 mL,  $\text{CHCl}_3$ );

**HRMS** ( $m/z$ ): calc'd for  $\text{C}_{16}\text{H}_{22}\text{O}_5\text{Na}^+$   $[\text{M}+\text{Na}]^+$  317.1359, found 317.1364.



**Experimental:** To a flame-dried round bottom flask fixed with a stir bar, was added the sugar alcohol **9** (2.22 g, 7.5 mmol) and  $\text{Ag}_2\text{O}$  (3.15 g, 22.5 mmol, 3.0 eq.). The flask was placed under argon and MeCN (75 mL, 0.1M) was added. Next, methyl iodide (2.8 mL, 24.0 mmol, 6.0 eq.) was added via syringe, and the resulting mixture was heated on an oil bath to 75 °C. After stirring overnight at this temperature, the reaction was allowed to cool, then was filtered through celite ( $\text{CHCl}_3$ ). The solvent was removed under reduced pressure and the crude product was purified *via* flash column chromatography ( $\text{SiO}_2$ ; 30%  $\text{Et}_2\text{O}$  in hexanes) yielding **10** (1.92 g, 83% yield).

**Physical State:** colorless oil;

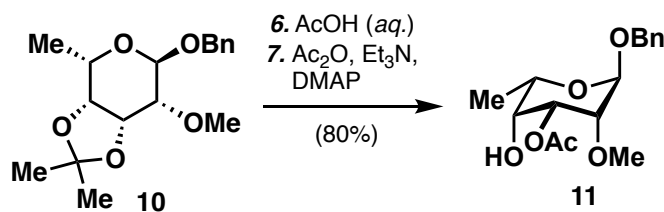
**R<sub>f</sub> Value:** 0.30 (30%  $\text{Et}_2\text{O}$  in hexanes);

**<sup>1</sup>H NMR** (600 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  7.32 – 7.29 (m, 2H), 7.17 – 7.15 (m, 2H), 7.10 – 7.06 (m, 1H), 5.14 (d,  $J = 5.9$  Hz, 1H), 4.78 (d,  $J = 12.0$  Hz, 1H), 4.45 (d,  $J = 12.0$  Hz, 1H), 4.32 (dd,  $J = 7.5, 2.7$  Hz, 1H), 3.57 (dd,  $J = 7.6, 2.0$  Hz, 1H), 3.50 (dq,  $J = 2.0, 6.4$  Hz, 1H), 3.33 (s, 3H), 3.15 (dd,  $J = 5.9, 2.7$  Hz, 1H), 1.56 (s, 3H), 1.27 (s, 3H), 1.24 ppm (d,  $J = 6.4$  Hz, 3H);

**<sup>13</sup>C NMR** (151 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  139.3, 128.5 (2C), 128.0 (2C), 127.6, 110.1, 100.4, 78.9, 77.1, 72.8, 69.4, 66.0, 58.1, 26.6, 25.7, 15.8 ppm;

**Optical Rotation:**  $[\alpha]_{\text{D}}^{20} = -70.6^\circ$  ( $c = 0.50$  g / 100 mL,  $\text{CHCl}_3$ );

**HRMS** ( $m/z$ ): calc'd for  $\text{C}_{17}\text{H}_{24}\text{O}_5\text{Na}^+$   $[\text{M}+\text{Na}]^+$  331.1516, found 331.1520.



**Experimental:** The methylated product **10** (1.90 g, 6.17 mmol) was placed in a round bottom flask fixed with a stir bar. To this was added an aqueous solution of acetic acid (80% AcOH (v/v), 62 mL, 0.1M). The resulting solution was placed on an oil bath preheated to 80 °C. The reaction was monitored by TLC and upon completion (about 1 h), the solvent was removed under reduced pressure. Trace amounts of water and acetic acid were removed by azeotrope with toluene (2 x 30 mL). The resulting diol was directly used in the next step.

The crude diol was placed in a round bottom flask fixed with a stir bar and placed under argon. CH<sub>2</sub>Cl<sub>2</sub> (62.0 mL, 0.1M) and Et<sub>3</sub>N (0.95 mL, 6.80 mmol, 1.1 eq.) were added via syringe. Next, DMAP (0.0378 g, 0.31 mmol, 0.05 eq.) was added to the flask followed by the dropwise addition of Ac<sub>2</sub>O (6.16 mL, 6.51 mmol, 1.05 eq.). The reaction was stirred overnight at room temperature. Upon completion, the reaction was quenched with NH<sub>4</sub>Cl (*sat.*, *aq.*). The aqueous phase was extracted with Et<sub>2</sub>O (3x). The combined organic layers were rinsed with brine, dried over MgSO<sub>4</sub>, and filtered. The solvent was removed under reduced pressure. The crude material was purified by flash column chromatography (SiO<sub>2</sub>; 30% to 40% EtOAc in hexanes) to yield **11** (1.53 g, 80% yield).

**Physical State:** colorless oil;

**R<sub>f</sub> Value:** 0.30 (40% EtOAc in hexanes);

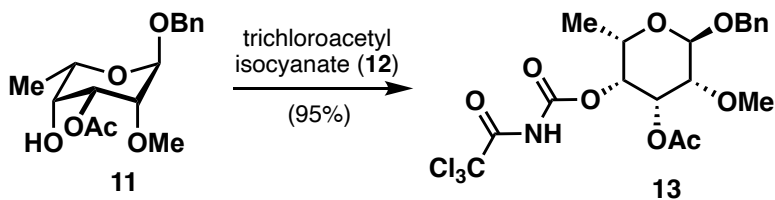
**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>) δ 7.38 – 7.29 (m, 5H), 5.08 (t, *J* = 3.2 Hz, 1H), 5.01 (d, *J* = 1.7 Hz, 1H), 4.73 (d, *J* = 11.9 Hz, 1H), 4.55 (d, *J* = 11.9 Hz, 1H), 3.95 (q, *J* = 6.6 Hz, 1H), 3.70 (s, 1H), 3.57 (m, 1H), 3.49 (s, 3H), 2.16 (s, 3H), 1.28 ppm (d, *J* = 6.5 Hz, 3H);

**<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>) δ 170.5, 137.1, 128.6 (2C), 128.1 (3C), 96.9, 78.7, 71.0, 69.9, 69.5, 67.7, 59.8, 21.3, 16.4 ppm;

**Optical Rotation:** [α]<sub>D</sub><sup>20</sup> = -113.6° (c = 0.50 g / 100 mL, CHCl<sub>3</sub>);

**HRMS** (m/z): calc'd for C<sub>16</sub>H<sub>22</sub>O<sub>6</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 333.1309, found 333.1308.





**Experimental:** To the starting material **11** (205 mg, 0.661 mmol) was added DCM (6.6 mL), and the resulting solution was cooled to 0°C. Trichloroacetyl isocyanate **12** (0.16 mL, 1.33 mmol, 2.0 eq.) was added dropwise *via* syringe and the resulting mixture was stirred at 0°C for 30 min followed by another 30 min at room temperature. Upon completion (as determined by TLC; product  $R_f = 0.30$  in hexanes/EtOAc 2:1), the reaction was quenched by MeOH (0.5 mL) and stirred for 10 minutes. All solvent was removed under reduced pressure, and the resulting material was purified by flash column chromatography (SiO<sub>2</sub>; hexanes/EtOAc 3:1 to 2:1) to yield **13** (312 mg, 95% yield).

**Physical State:** white foam;

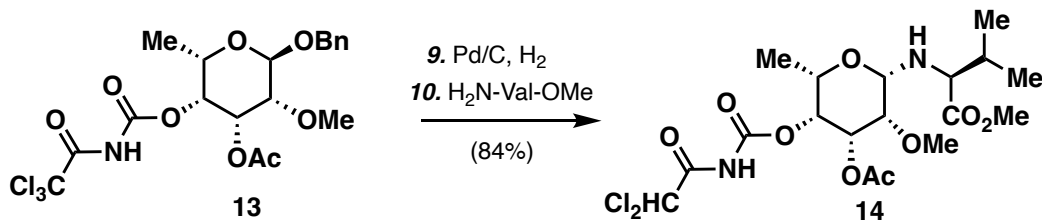
**R<sub>f</sub> Value:** 0.30 (hexanes/EtOAc 2:1);

**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>) δ 8.95 (s, 1H), 7.40 – 7.29 (m, 5H), 5.27 (t,  $J = 3.5$  Hz, 1H), 5.18 (m, 1H), 5.01 (d,  $J = 1.6$  Hz, 1H), 4.71 (d,  $J = 11.9$  Hz, 1H), 4.56 (d,  $J = 11.9$  Hz, 1H), 4.16 (qd,  $J = 6.5, 1.6$  Hz, 1H), 3.49 – 3.47 (m, 1H), 3.47 (s, 3H), 2.10 (s, 3H), 1.25 ppm (d,  $J = 6.6$  Hz, 3H);

**<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>) δ 170.1, 158.2, 149.8, 136.8, 128.7 (2C), 128.3, 128.2 (2C), 97.8, 91.9, 76.8, 72.9, 69.8, 68.3, 64.8, 60.2, 21.0, 16.2 ppm;

**Optical Rotation:**  $[\alpha]_D^{25} = -82.2^\circ$  ( $c = 1.00$  g / 100 mL, CHCl<sub>3</sub>);

**HRMS** ( $m/z$ ): calc'd for C<sub>19</sub>H<sub>23</sub>Cl<sub>3</sub>NO<sub>8</sub><sup>+</sup>  $[M+H]^+$  498.0484, found 498.0489.



**Experimental:** To the starting material **13** (325 mg, 0.654 mmol) in EtOAc (10 mL), was added Pd/C (10% Pd/wt; 33 mg, 10 wt/wt %). The flask was evacuated and backfilled with H<sub>2</sub> (in a balloon) three times. Finally, the flask was fitted with a balloon of H<sub>2</sub> and the reaction mixture was vigorously stirred at room temperature for 3 h until complete as determined by TLC. Upon completion, the reaction mixture was filtered through a pad of celite (EtOAc) and the solvent was removed under reduced pressure yielding the product as a white foam, which was used directly in the next step with no further purification.

The PPTS (32.8 mg, 0.13 mmol, 0.2 eq) and *L*-valine methyl ester (154 mg, 1.17 mmol, 1.8 eq) were added to 5 mL of DCM, and the mixture was stirred for 10 min before adding to another flask of the dried crude material above. The reaction was stirred at room temperature for 6 h and quenched with excess solid NaHCO<sub>3</sub>. The mixture was filtered (washed with EtOAc), and the solvent was removed under reduced pressure. The crude material was purified by flash column chromatography (SiO<sub>2</sub>; hexanes/acetone 8:1) to yield **14** (267 mg, 84% yield over 2 steps).

**Note:** The product is almost a single  $\beta$ -isomer. The very trace amount of  $\alpha$ -isomer was removed by the silica gel chromatography.

**Physical State:** white foam;

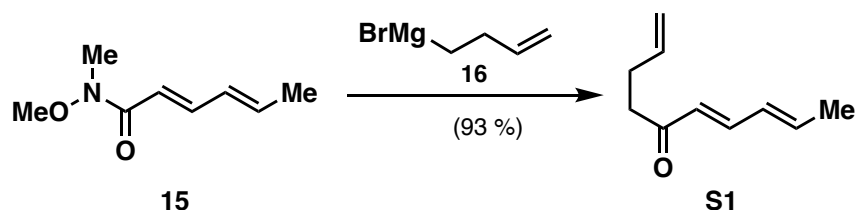
**R<sub>f</sub> Value:** 0.40 (hexanes/acetone 2:1);

**<sup>1</sup>H NMR** (600 MHz, Acetone-*d*<sub>6</sub>)  $\delta$  10.59 (s, 1H), 6.97 (s, 1H), 5.02 (t, *J* = 3.6 Hz, 1H), 4.98 (m, 1H), 4.17 (dd, *J* = 12.7, 1.4 Hz, 1H), 3.76 (dd, *J* = 6.5, 1.5 Hz, 1H), 3.68 (s, 3H), 3.51 (dd, *J* = 3.5, 1.3 Hz, 1H), 3.49 (s, 3H), 3.09 (dd, *J* = 9.8, 6.8 Hz, 1H), 2.92 (dd, *J* = 12.6, 9.7 Hz, 1H), 2.02 (s, 3H), 1.82 – 1.73 (m, 1H), 1.08 (d, *J* = 6.4 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 4H), 0.89 ppm (d, *J* = 6.8 Hz, 3H);

**<sup>13</sup>C NMR** (151 MHz, Acetone-d<sub>6</sub>) δ 176.4, 170.1, 164.0, 152.2, 89.4, 78.2, 73.0, 72.2, 70.3, 67.1, 65.2, 61.6, 51.6, 33.0, 20.9, 19.3, 18.8, 16.4 ppm;

**Optical Rotation:**  $[\alpha]_{\text{D}}^{25} = -23.5^{\circ}$  (c = 0.95 g / 100 mL, CHCl<sub>3</sub>);

**HRMS** (m/z): calc'd for C<sub>18</sub>H<sub>29</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>9</sub> + [M+H]<sup>+</sup> 487.1245, found 487.1241.



**Experimental:** An oven-dried round bottom flask was placed under argon and 210 mL of THF was added to it followed by 4-bromobutene (15.0 mL, 150.0 mmol). A separate oven-dried two-neck round bottom flask was fitted with a stir bar. To this flask was added magnesium turnings (5.40 g, 150 mmol, 1.0 eq.) and I<sub>2</sub> (381 mg, 1.50 mmol, 0.01 eq.) under argon. About 9 mL of the 4-bromobutene solution was added to the iodine and magnesium turnings *via* syringe, and the resulting mixture was heated with a heat gun while being stirred until the brown color disappeared completely. At this point, the entirety of the remaining 4-bromobutene solution was cannulated into the 2-neck flask while occasionally heating the solution to near-reflux with a heat gun. Upon complete addition, the resulting mixture was allowed to stir at room temperature for 1 h. The resulting Grignard reagent **16** was then titrated using the method outlined in the supporting information of the former publication.<sup>[1]</sup>

Afterward, Weinreb amide **15** (9.31 g, 60 mmol) was placed in a round bottom flask fixed with a stir bar. THF (350.0 mL) was added *via* syringe and stirring was started. Cooled the solution down to 0 °C and added the Grignard reagent **16** (1.4 eq.) slowly into the reaction mixture. After the addition of the Grignard reagent, the mixture was stirred for another 4 h. The reaction was quenched with NH<sub>4</sub>Cl (*sat.*, *aq.*, 200 mL), and the aqueous layer was extracted with Et<sub>2</sub>O (3 x 200 mL). The combined organic layers were washed with brine, dried with MgSO<sub>4</sub>, and filtered. The solvent was removed under reduced pressure and the crude material was purified by flash column chromatography (SiO<sub>2</sub>; 0% to 10% Et<sub>2</sub>O in hexanes), yielding the product **S1** (8.38 g, 93% yield).

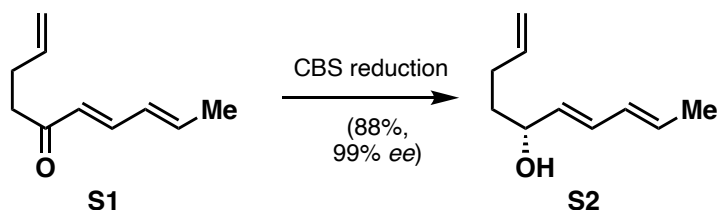
**Physical State:** colorless oil;

**TLC:** R<sub>f</sub> = 0.50 (30% Et<sub>2</sub>O in hexanes);

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.22 – 6.98 (m, 1H), 6.33 – 6.16 (m, 2H), 6.13 – 6.01 (m, 1H), 5.93 – 5.76 (m, 1H), 5.16 – 4.84 (m, 2H), 2.78 – 2.56 (m, 2H), 2.48 – 2.30 (m, 2H), 1.92 – 1.76 ppm (m, 3H);

**<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>) δ 200.1, 143.1, 140.5, 137.5, 130.5, 127.8, 115.3, 39.7, 28.4, 19.0 ppm;

**HRMS** (m/z): calc'd for, C<sub>10</sub>H<sub>15</sub>O<sup>+</sup> [M+H]<sup>+</sup> 151.1117, found 151.1122.



**Experimental:** The (*S*)-CBS catalyst (27.72 g, 2.0 eq) was placed in a round bottom flask fixed with a stir bar and flushed with argon 3 times. THF (250.0 mL) was added *via* syringe and stirring was started. The resulting solution was cooled down to 0 °C and BH<sub>3</sub>/THF complex solution (1.0 M in THF, 80 ml, 1.6 eq.) was added into the mixture slowly. After 20 mins, the solution was cooled down to -78 °C and a THF solution (30 ml) of ketone **S1** (7.51 g, 1.0 eq.) was added *via* a syringe pump over 45 min. 1 h after the addition of ketone **S1**, another 0.6 eq. of BH<sub>3</sub>/THF complex solution (1.0 M in THF, 30 ml) was added to the mixture slowly. 4 h later, the reaction was quenched with NH<sub>4</sub>Cl (*sat.*, *aq.*, 200 mL), and the aqueous layer was extracted Et<sub>2</sub>O (3 x 300 mL). The combined organic layers were washed with brine and dried over MgSO<sub>4</sub>. The solvent was removed under reduced pressure and the crude material was purified by flash column chromatography (SiO<sub>2</sub>; 0% to 50% Et<sub>2</sub>O in hexanes), yielding the product **S2** (6.69 g, 88% yield).

**Physical State:** colorless oil;

**TLC:** R<sub>f</sub> = 0.30 (40% Et<sub>2</sub>O in hexanes);

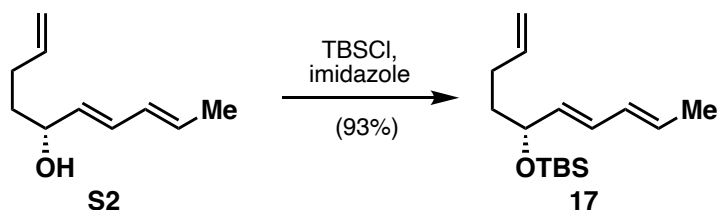
**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>) δ 6.19 (dd, *J* = 15.2, 10.4 Hz, 1H), 6.10 – 5.98 (m, 1H), 5.85 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.79 – 5.65 (m, 1H), 5.61 – 5.50 (m, 1H), 5.06 (dq, *J* = 17.1, 1.7 Hz, 1H), 4.99 (ddt, *J* = 10.2, 2.2, 1.3 Hz, 1H), 4.16 (q, *J* = 6.7 Hz, 1H), 2.15 (dtdd, *J* = 15.3, 8.0, 4.7, 1.4 Hz, 2H), 1.83 – 1.74 (m, 3H), 1.74 – 1.56 ppm (m, 2H);

**<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>) δ 138.4, 133.2, 131.1, 130.9, 130.2, 115.0, 72.4, 36.4, 29.8, 18.2 ppm;

**Optical Rotation:** [α]<sub>D</sub><sup>20</sup> = -5.3° (*c* = 1.00 g / 100 mL, CHCl<sub>3</sub>);

**Enantiomeric excess:** 99% *ee* (measured at Diels-Alder product **23**, see part II)

**HRMS** (*m/z*): calc'd for, C<sub>10</sub>H<sub>17</sub>O<sup>+</sup> [M+H]<sup>+</sup> 153.1274, found 153.1278.



**Experimental:** The reduction product **S2** (9.52 g) was placed in a round bottom flask fixed with a stir bar. DMF (250.0 mL) was added *via* syringe and stirring was started. Imidazole (12.79 g, 187.8 mmol, 3.0 eq.) was added and stirred until dissolved. Finally, TBSCl (14.15 g, 93.9 mmol, 1.5 eq.) was added then the reaction was heated to 50 °C and stirred until complete (as determined by TLC). The reaction was quenched with NaHCO<sub>3</sub> (*sat., aq.*, 500 mL). The aqueous layer was extracted three times with Et<sub>2</sub>O. The combined organic layers were rinsed with LiCl (10% *aq.*, 300 mL x 2) and brine (300 mL), dried over MgSO<sub>4</sub> and filtered. The solvent was removed under reduced pressure and the crude material was purified by flash column chromatography (SiO<sub>2</sub>; 0% to 5% Et<sub>2</sub>O in hexanes), yielding the product **17** (15.5 g, 93% yield).

**Physical State:** colorless oil;

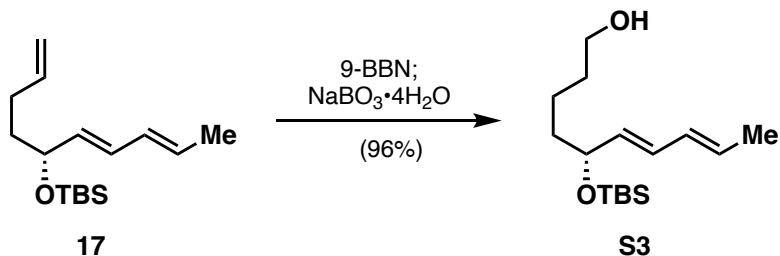
**TLC:** R<sub>f</sub> = 0.50 (1% Et<sub>2</sub>O in hexanes);

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 6.13 – 5.97 (m, 2H), 5.87 – 5.75 (m, 1H), 5.72 – 5.57 (m, 1H), 5.57 – 5.41 (m, 1H), 5.06 – 4.90 (m, 2H), 4.12 (q, *J* = 6.4 Hz, 1H), 2.16 – 2.00 (m, 2H), 1.78 – 1.72 (m, 3H), 1.69 – 1.47 (d, *J* = 6.4, 2H), 0.90 (s, 9H), 0.04 (s, 3H), 0.02 ppm (s, 3H);

**<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>) δ 138.9, 134.3, 131.2, 129.8, 129.0, 114.5, 73.0, 37.8, 29.7, 26.1 (3C), 18.4, 18.2, -4.1, -4.6 ppm;

**Optical Rotation:** [α]<sub>D</sub><sup>20</sup> = -13.9° (c = 1.00 g / 100 mL, CHCl<sub>3</sub>);

**HRMS** (m/z): calc'd for, C<sub>16</sub>H<sub>31</sub>OSi<sup>+</sup> [M+H]<sup>+</sup> 267.2139, found 267.2138.



**Experimental:** The silyl ether **17** (15.5 g, 58.2 mmol) was placed in an oven-dried round bottom flask fixed with a stir bar and placed under nitrogen. THF (500.0 mL) was added to the flask and the contents were cooled to 0 °C. A solution of 9-BBN (0.5 M in THF, 163.0 mL, 81.5 mmol, 1.4 eq.) was then slowly added *via* syringe. The resulting solution was stirred for 30 min at the same temperature before stirring at room temperature for 4.5 h. Upon completion, the reaction was again cooled to 0 °C and sodium perborate tetrahydrate (35.84 g, 232.9 mmol, 4.0 eq.) was added in one portion. Then 200 mL of water was slowly added. Afterward, the reaction was warmed to room temperature and stirred overnight. The mixture was filtered through a pad of celite then transferred to a separatory funnel and extracted with Et<sub>2</sub>O (3 x 300 mL). The combined organic layers were rinsed with brine, dried over MgSO<sub>4</sub>, and filtered. The solvent was removed under reduced pressure and the crude material was purified by flash column chromatography (SiO<sub>2</sub>; 30% Et<sub>2</sub>O in hexanes), yielding the product **S3** (15.90 g, 96% yield).

**Physical State:** colorless oil;

**TLC:** R<sub>f</sub> = 0.22 (30% Et<sub>2</sub>O in hexanes);

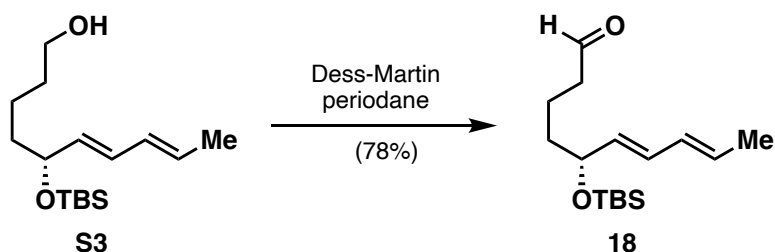
**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>) δ 6.10 – 5.97 (m, 2H), 5.69 – 5.61 (m, 1H), 5.49 (dd, *J* = 14.5, 6.7 Hz, 1H), 4.10 (q, *J* = 6.3 Hz, 1H), 3.63 (t, *J* = 6.6 Hz, 2H), 1.75 (dd, *J* = 6.7, 1.6 Hz, 3H), 1.64 – 1.17 (m, 6H), 0.89 (s, 9H), 0.04 (s, 3H), 0.02 ppm (s, 3H);

**<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>) δ 134.3, 131.2, 129.8, 129.0, 73.4, 63.1, 38.3, 32.9, 26.1 (3C), 21.5, 18.4, 18.2, -4.1, -4.6 ppm;

**Optical Rotation:** [α]<sub>D</sub><sup>20</sup> = +2.0° (c = 1.00 g / 100 mL, CHCl<sub>3</sub>);

**HRMS** (m/z): calc'd for, C<sub>16</sub>H<sub>33</sub>O<sub>2</sub>Si<sup>+</sup> [M+H]<sup>+</sup> 285.2244, found 285.2245.





**Experimental:** The primary alcohol **S3** (15.9 g, 55.94 mmol) was placed in an oven-dried round bottom flask fixed with a stir. CH<sub>2</sub>Cl<sub>2</sub> (350 mL) was added to the flask *via* syringe and the solution was stirred. To the flask was added Dess-Martin periodane (33.22 g, 78.32 mmol, 1.4 eq.) The reaction was stirred for 2.5 h at room temperature. Upon completion, the reaction is directly filtered through a pad of celite using CH<sub>2</sub>Cl<sub>2</sub> to rinse. The excess DMP was quenched with Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (*sat.*, *aq.*, 200 mL), and the mixture was extracted with DCM (3 x 200 mL). The combined organic phase was washed with NaHCO<sub>3</sub> (*sat.*, *aq.*) and brine. The solvent was removed under reduced pressure. This material was then suspended in hexanes and again filtered through a pad of celite, using hexanes to rinse. The solvent was removed under reduced pressure and the material was purified by using a short plug of silica gel (SiO<sub>2</sub>; CH<sub>2</sub>Cl<sub>2</sub>) to remove any residual polar impurities, yielding the product **18** (12.3 g, 78% yield).

**Physical State:** colorless oil;

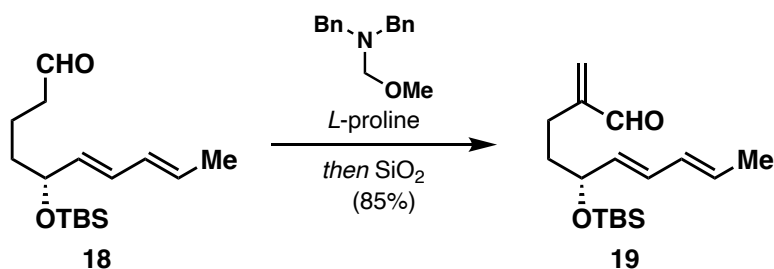
**TLC:** R<sub>f</sub> = 0.71 (30% Et<sub>2</sub>O in hexanes);

**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>) δ 9.74 (t, *J* = 1.8 Hz, 1H), 6.11 – 5.95 (m, 2H), 5.66 (dq, *J* = 13.6, 6.7 Hz, 1H), 5.48 (dd, *J* = 14.9, 6.7 Hz, 1H), 4.12 (q, *J* = 6.3 Hz, 1H), 2.42 (td, *J* = 7.5, 1.8 Hz, 2H), 1.75 (d, *J* = 6.9 Hz, 3H), 1.72 – 1.58 (m, 2H), 1.52 (m, 2H), 0.88 (s, 9H), 0.04 (s, 3H), 0.02 ppm (s, 3H);

**<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>) δ 202.8, 133.8, 131.1, 130.1, 129.3, 73.1, 44.0, 37.9, 26.0 (3C), 18.4, 18.2, 18.0, -4.1, -4.7 ppm;

**Optical Rotation:** [α]<sub>D</sub><sup>20</sup> = +2.5° (c = 1.00 g / 100 mL, CHCl<sub>3</sub>);

**HRMS** (m/z): calc'd for, C<sub>16</sub>H<sub>31</sub>O<sub>2</sub>Si<sup>+</sup> [M+H]<sup>+</sup> 283.2088, found 283.2086.



**Experimental:** The aldehyde (1.36 g, 4.81 mmol) was added to a round bottom flask fixed with a stir bar and placed under argon. DMF (6.4 mL) was added via syringe and the solution was cooled to 0 °C. *L*-proline (110.7 mg, 0.962 mmol, 0.20 eq.) was added to the flask and the resulting solution was stirred for 5 minutes. Next, the aminal (1.22 mL, 1.278 g, 5.29 mmol, 1.1 eq.) was added *via* syringe and the reaction was stirred for 2 hours. Upon completion, the reaction was quenched with NH<sub>4</sub>Cl (*sat.*, *aq.*, 25 mL) and extracted with Et<sub>2</sub>O (3 x 40 mL). The combined organic layers were rinsed with LiCl (10% *aq.*, 50 mL), then brine, dried over MgSO<sub>4</sub>, and filtered. The solvent was removed under reduced pressure. The crude material was redissolved in DCM (50 mL) and SiO<sub>2</sub> (15.0 g) was added to the flask. The resulting slurry was stirred at room temperature for 5 h. Upon completion, the slurry was filtered, and the solids were rinsed with DCM. The solvent was removed under reduced pressure and the crude material was purified by flash column chromatography (SiO<sub>2</sub>; 0% to 5% Et<sub>2</sub>O in hexanes), yielding the product **19** (1.20 g, 85% yield).

**Physical State:** colorless oil;

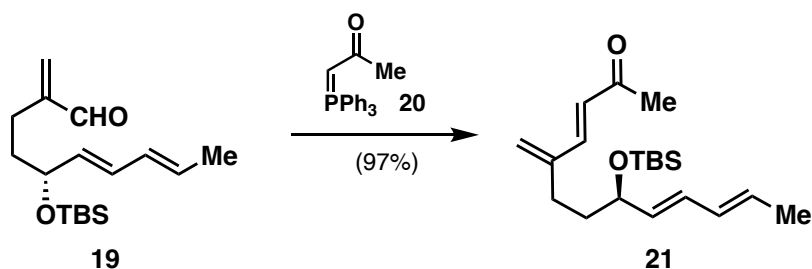
**TLC:** R<sub>f</sub> = 0.56 (10% Et<sub>2</sub>O in hexanes);

**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>) δ 9.53 (s, 1H), 6.23 (s, 1H), 6.10 – 5.96 (m, 2H), 6.02 (ddd, *J* = 13.9, 11.3, 1.7 Hz, 1H), 5.97 (s, 1H), 5.66 (dq, *J* = 13.6, 6.7 Hz, 1H), 5.49 (dd, *J* = 15.0, 6.7 Hz, 1H), 4.13 (q, *J* = 6.3 Hz, 1H), 2.36 – 2.19 (m, 2H), 1.74 (dd, *J* = 7.4 Hz, 3H), 1.69 – 1.57 (m, 2H), 0.89 (s, 9H), 0.04 (s, 3H), 0.02 ppm (s, 3H);

**<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>) δ 194.8, 150.5, 133.9, 133.7, 131.1, 130.2, 129.3, 73.1, 36.5, 26.0 (3C), 23.9, 18.4, 18.2, -4.1, -4.6 ppm;

**Optical Rotation:** [α]<sub>D</sub><sup>20</sup> = +6.9° (c = 1.00 g / 100 mL, CHCl<sub>3</sub>);

**HRMS** (*m/z*): calc'd for C<sub>17</sub>H<sub>31</sub>O<sub>2</sub>Si<sup>+</sup> [M+H]<sup>+</sup> 295.2088, found 295.2100.



**Experimental:** To a flame dried vial was added the enal **19** (8.82 g, 30.0 mmol). The vial was placed under argon and DCM (30.0 mL) was added *via* syringe. After becoming homogeneous, acetylmethylene-triphenylphosphorane **20** (17.17 g, 54.0 mmol, 1.8 eq.) was added, and the vial was tightly sealed. The reaction was heated to 45 °C and stirred at this temperature for 24 h. Upon completion, the reaction was diluted with hexanes and stirred rapidly for 5 min. The resulting slurry was filtered over a pad of celite and rinsed with excess hexanes. The solvent was removed under reduced pressure and the crude material was purified by flash column chromatography (SiO<sub>2</sub>; 5% to 10% Et<sub>2</sub>O in hexanes), yielding the product **21** (9.72 g, 97% yield).

**Physical State:** colorless oil;

**TLC:** R<sub>f</sub> = 0.35 (10% Et<sub>2</sub>O in hexanes);

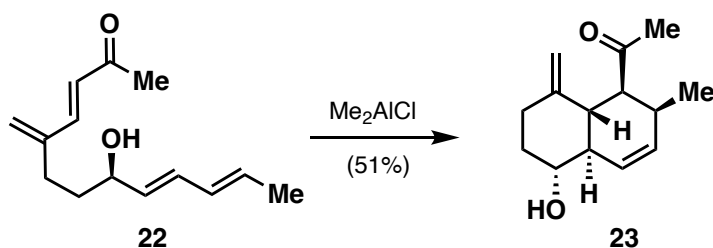
**<sup>1</sup>H NMR** (600 MHz, C<sub>6</sub>D<sub>6</sub>) δ 7.12 (d, *J* = 16.2, 1H), 6.36 (d, *J* = 16.2 Hz, 1H), 6.27 (dd, *J* = 15.3, 10.4 Hz, 1H), 6.14 – 6.06 (m, 1H), 5.68 – 5.58 (m, 2H), 5.22 (d, *J* = 1.4 Hz, 1H), 5.17 (s, 1H), 4.19 (t, *J* = 6.0 Hz, 1H), 2.42 (dq, *J* = 14.9, 5.3, 1H), 2.32 (dq, *J* = 14.8, 5.3, 1H), 1.98 (s, 3H), 1.86 – 1.71 (m, 2H), 1.67 (dd, *J* = 6.8, 1.7 Hz, 3H), 1.12 (s, 9H), 0.20 (s, 3H), 0.20 ppm (s, 3H);

**<sup>13</sup>C NMR** (151 MHz, C<sub>6</sub>D<sub>6</sub>) δ 196.6, 145.5, 144.2, 134.0, 131.5, 130.6, 129.4, 127.7, 123.2, 73.3, 37.4, 27.6, 27.3, 26.2 (3C), 18.5, 18.1, -3.9, -4.6 ppm;

**Optical Rotation:** [α]<sub>D</sub><sup>20</sup> = +3.5° (c = 1.00 g / 100 mL, CHCl<sub>3</sub>);

**HRMS** (m/z): calc'd for C<sub>20</sub>H<sub>35</sub>O<sub>2</sub>Si<sup>+</sup> [M+H]<sup>+</sup> 335.2401, found 335.2409.





**Experimental:** To a flame dried flask fixed with a stir bar and sealed under argon was added the tetraene **22** (1.58 g, 7.2 mmol) *via* syringe. DCM (140.0 mL) was then added and the resulting solution was cooled to  $-20\text{ }^\circ\text{C}$ .  $\text{Me}_2\text{AlCl}$  (0.9 M in heptane; 8.0 mL, 7.2 mmol, 1.0 eq.) was then added dropwise. The reaction was then allowed to stir while slowly warming up to room temperature for 18 hours. Upon completion, the reaction was quenched with  $\text{NH}_4\text{Cl}$  (*sat.*, *aq.*, 30 mL), and a solution of Rochelle's salt (*sat.*, *aq.*, 100 mL) was added to the flask. The biphasic mixture was stirred vigorously for 30 min. The mixture was transferred to a separatory funnel and extracted with  $\text{Et}_2\text{O}$  (2 x 150 mL). The combined organic layers were rinsed with brine, dried over  $\text{MgSO}_4$ , and filtered. The solvent was removed under reduced pressure and the crude material was purified by flash column chromatography ( $\text{SiO}_2$ ; 25% to 35%  $\text{EtOAc}$  in hexanes), yielding the product **23** (802 mg, 51% yield).

**Physical state:** white crystalline solid;

**Melting point:** 151-152  $^\circ\text{C}$

**R<sub>f</sub> Value:** 0.36 (35%  $\text{EtOAc}$  in hexanes);

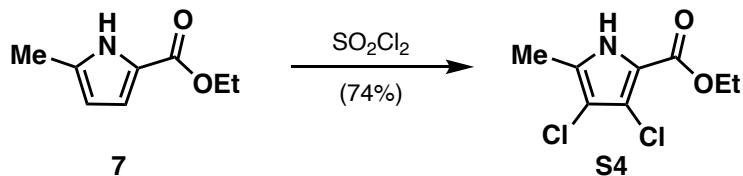
**$^1\text{H NMR}$**  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  5.94 (dt,  $J = 10.0, 1.8$  Hz, 1H), 5.74 (ddd,  $J = 10.0, 4.7, 2.6$  Hz, 1H), 4.76 – 4.72 (s, 1H), 4.19 (s, 1H), 3.47 (td,  $J = 10.4, 4.5$  Hz, 1H), 3.08 (dd,  $J = 11.7, 6.1$  Hz, 1H), 2.68 – 2.61 (m, 1H), 2.38 – 2.33 (m, 1H), 2.26 – 2.16 (m, 6H), 1.78 (tq,  $J = 10.5, 2.2$  Hz, 1H), 1.48 – 1.37 (m, 1H), 0.83 ppm (d,  $J = 7.2$  Hz, 3H);

**$^{13}\text{C NMR}$**  (151 MHz,  $\text{CDCl}_3$ )  $\delta$  210.2, 150.1, 132.0, 125.4, 105.6, 73.8, 52.2, 50.4, 38.3, 38.2, 34.8, 31.3, 30.4, 17.9 ppm;

**Optical Rotation:**  $[\alpha]_{\text{D}}^{20} = +172.2^\circ$  ( $c = 1.00$  g / 100 mL,  $\text{CHCl}_3$ );

**Enantiomeric excess:** 99% *ee* (measured by analytical SFC, see part II)

**HRMS** ( $m/z$ ): calc'd for  $\text{C}_{14}\text{H}_{21}\text{O}_2^+$   $[\text{M}+\text{H}]^+$  221.1536, found 221.1543.



**Experimental:** In a round bottom flask fixed with a stirbar was placed ethyl 5-methyl-1*H*-pyrrole-2-carboxylate (7.65 g, 50.0 mmol). The flask was placed under argon and CCl<sub>4</sub> (35 mL) was added. The resulting mixture was cooled to -20 °C and SO<sub>2</sub>Cl<sub>2</sub> (8.88 ml, 14.85 g, 110 mmol, 2.2 eq.) was added dropwise *via* syringe. The reaction was allowed to stir for 4 h, after which the mixture was filtered to collect a pink solid. The solid was washed by CCl<sub>4</sub> (10 ml) twice to give the crude product. The crude product **S4** (8.18 g, 74 % yield) was dried under reduced pressure and ready for next step without further purification.

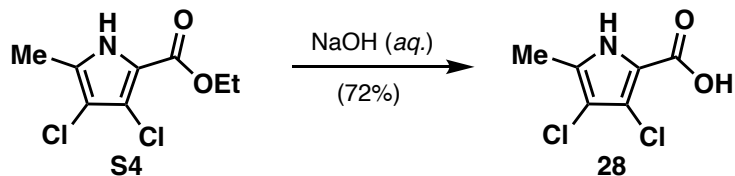
**Physical State:** pink solid;

**R<sub>f</sub> Value:** 0.60 (40% EtOAc in hexanes);

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>): δ (ppm) 9.23 (s, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 2.29 (s, 3H), 1.39 ppm (t, *J* = 7.1 Hz, 3H);

**<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>) δ (ppm) 160.1, 129.2, 117.6, 116.2, 111.9, 61.1, 14.5, 11.6 ppm;

**HRMS** (*m/z*): calc'd for C<sub>8</sub>H<sub>10</sub>Cl<sub>2</sub>NO<sub>2</sub><sup>+</sup> [M+H]<sup>+</sup> 222.0089, found 222.0083.



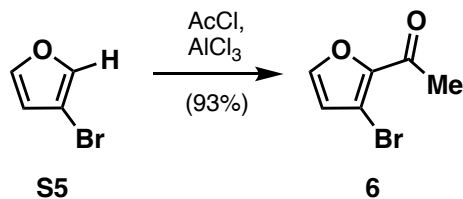
**Experimental:** The starting material **S4** (3.20 g, 14.48 mmol) was dissolved in MeOH (80.0 mL). To this was added 2.0 M NaOH (*aq.*) (80.0 mL, equal volume). The flask was then fitted with a reflux condenser and the solution was heated to 60 °C for 4 h. Upon completion, the reaction was allowed to cool to room temperature. The MeOH in the reaction mixture was removed first under reduced pressure, then the reaction mixture was brought to a pH of ~2 *via* the addition of 2.0 M HCl (*aq.*) and extracted 3 times with DCM. The combined organic layers were rinsed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> then filtered. The solvent was removed under reduced pressure yielding the desired compound **28** (2.0 g, 72% yield), which was used directly without further purification.

**Physical State:** purple solid;

**R<sub>f</sub> Value:** 0.35 (10% MeOH in DCM);

**<sup>1</sup>H NMR** (400 MHz, CD<sub>3</sub>OD): δ 2.23 ppm (s, 3H);

*NOTE: The data was identical to the reported literature.* <sup>[2]</sup>



**Experimental:** According to Lit.:<sup>[3]</sup> To 0 °C cold DCM (550 mL) was added AlCl<sub>3</sub> (66.67 g, 500.0 mmol, 2.94 eq.) portion wise. After stirring for 15 min at 0 °C, a solution of freshly distilled acetyl chloride (38.8 mL, 544.0 mmol, 3.2 eq.) in DCM (550 mL) was added dropwise. After stirring for 30 minutes at 0 °C, a solution of distilled 3-bromofuran **S5** (15.3 mL, 170.0 mmol) in DCM (550 mL) was added dropwise. The reaction mixture was stirred for 20 min at 0 °C, 10 min at room temperature and then cooled to 0 °C. At 0 °C, H<sub>2</sub>O (1.5 L) was added slowly. The reaction mixture was transferred to a separatory funnel and the aqueous phase was extracted with DCM (3x 200 mL). The combined organic phases were washed with H<sub>2</sub>O (3x 200 mL), NaHCO<sub>3</sub> (*sat.*, *aq.*, 3x 300 mL) and brine (500 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and evaporated. The obtained crude product was purified *via* column chromatography on SiO<sub>2</sub> (*n*-pentane/Et<sub>2</sub>O 10/1 to 5/1) to obtain the acylated bromofuran **6** (29.97 g, 93% yield). The spectral data are in good agreement with previous reports.

**Physical State:** red-orange solid;

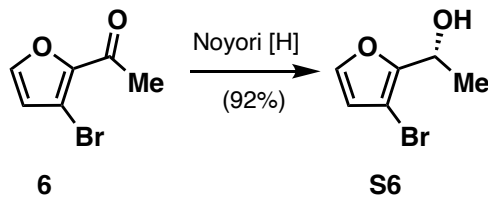
**R<sub>f</sub> Value:** 0.28 (*n*-pentane/Et<sub>2</sub>O 10:1);

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.49 (d, *J* = 1.8 Hz, 1H), 6.62 (d, *J* = 1.9 Hz, 1H), 2.55 ppm (s, 3H);

**<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>) δ 186.7, 148.5, 145.5, 117.6, 107.2, 27.6 ppm;

**HRMS** (*m/z*) calc'd for C<sub>6</sub>H<sub>6</sub>BrO<sub>2</sub><sup>+</sup> [M+H]<sup>+</sup> 188.9546, found 188.9548.





**Experimental:** Similar to Lit.:<sup>[4]</sup> To Ar freeze-pump degassed (4x) H<sub>2</sub>O (300 mL) was added [RuCl<sub>2</sub>(*p*-cymene)]<sub>2</sub> (0.712 g, 1.16 mmol, 0.0075 eq.) and *N*-((1*R*,2*R*)-2-amino-1,2-diphenylethyl)-4-methylbenzenesulfonamide (1.03 g, 2.8 mmol, 0.018 eq.). After stirring the mixture at 70 °C for 1.5 h and cooling to room temperature, a solution of ketone **6** (29.3 g, 155.0 mmol) in THF (150 mL) and sodium formate (52.71 g, 775.0 mmol, 5.0 eq.) was added. The reaction mixture was stirred at 40 °C for 2 days, cooled to room temperature, and extracted with EtOAc (3x 200 mL). The combined org. layers were washed with H<sub>2</sub>O (3x 100 mL) and brine (400 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and evaporated. The obtained crude product was purified *via* column chromatography on SiO<sub>2</sub> (*n*-pentane/Et<sub>2</sub>O 2:1) to obtain the corresponding alcohol **S6** (27.32 g, 92% yield).

**Physical State:** colorless liquid;

**R<sub>f</sub> Value:** 0.56 (*n*-pentane/Et<sub>2</sub>O 2:1);

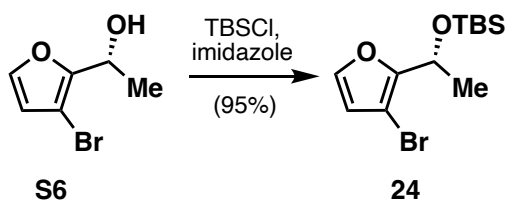
**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>) δ 7.33 – 7.34 (m, 1H), 6.39 – 6.39 (m, 1H), 4.98 – 5.03 (m, 1H), 1.96 (s, broad, 1H), 1.56 ppm (dd, *J* = 1.6, 6.7 Hz, 3H);

**<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>) δ 153.1, 142.2, 114.1, 96.6, 62.0, 21.0 ppm;

**Optical Rotation:** [α]<sub>D</sub><sup>20</sup> = +11.6° (c = 0.50 g / 100 mL, CHCl<sub>3</sub>);

**Enantiomeric excess:** 92% (as determined *via* analytical SFC, see part II);

**HRMS** (m/z): calc'd for C<sub>6</sub>H<sub>6</sub>BrO<sup>+</sup> [M-OH]<sup>+</sup> 172.9597, found 172.9602.



**Experimental:** To a solution of alcohol **S6** (26.74 g, 140.0 mmol) in DMF (450 mL) was added imidazole (28.59 g, 420.0 mmol, 3.0 eq.) and TBDMSCl (31.65 g, 210.0 mmol, 1.5 eq.). After stirring the reaction mixture overnight at room temperature, H<sub>2</sub>O (1.5 L) was added slowly, and the aq. phase was extracted with *n*-pentane (5x 200 mL). The combined org. layers were washed with brine (500 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and evaporated. The obtained crude product was purified via column chromatography on SiO<sub>2</sub> (*n*-pentane/Et<sub>2</sub>O 20:1) to obtain the corresponding silyl ether **24** (40.64 g, 95% yield).

**Physical State:** colorless liquid;

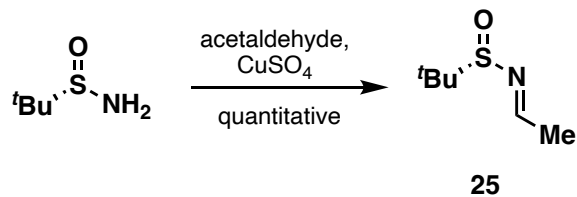
**R<sub>f</sub> Value:** 0.84 (*n*-pentane/Et<sub>2</sub>O 20:1);

**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>) δ 7.33 (d, *J* = 1.9 Hz, 1H), 6.35 (d, *J* = 1.9 Hz, 1H), 4.97 (q, *J* = 6.6 Hz, 1H), 1.47 (d, *J* = 6.6 Hz, 3H), 0.86 (s, 9 H), 0.07 (s, 3H), -0.05 ppm (s, 3H);

**<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>) δ 153.7, 142.0, 113.7, 95.6, 62.5, 25.9 (3C), 22.8, 18.3, -4.9 (2C) ppm;

**Optical Rotation:** [α]<sub>D</sub><sup>20</sup> = +9.4° (c = 0.50 g / 100 mL, CHCl<sub>3</sub>);

**HRMS** (m/z): calc'd for C<sub>12</sub>H<sub>22</sub>BrO<sub>2</sub>Si<sup>+</sup> [M+H]<sup>+</sup> 305.0567, found 305.0574.



**Experimental:** According to Lit.:<sup>[5]</sup> To a suspension of anhydrous CuSO<sub>4</sub> (143.65 g, 900.0 mmol) and (S)-methylpropansulfonamide (36.36 g, 300.0 mmol) in 1,2-dichloroethane (500 mL) was added acetaldehyde (33.75 mL, 600.0 mmol). After stirring the reaction mixture overnight at 60 °C, the mixture was cooled to room temperature, filtered and evaporated. The obtained crude product was purified via column chromatography on SiO<sub>2</sub> (CHCl<sub>3</sub>/MeOH 25:1) to obtain the corresponding sulfinyl imine **25** (44.11g, quantitative yield). The spectral data are in good agreement with previous reports.

**Physical State:** slightly orange liquid;

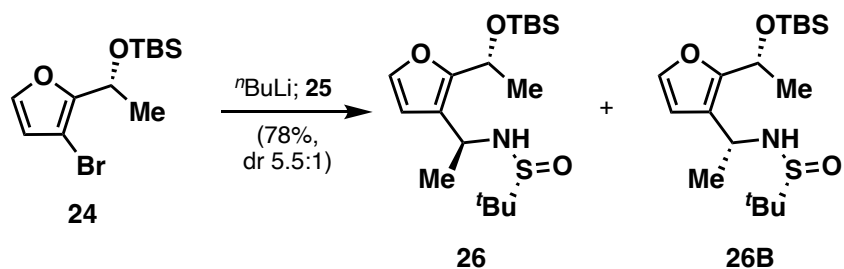
**R<sub>f</sub> Value:** 0.32 (CHCl<sub>3</sub>/MeOH 25:1);

**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>) δ 8.08 (q, *J* = 5.1 Hz, 1H), 2.23 (d, *J* = 5.1 Hz, 3H), 1.19 ppm (s, 3H);

**<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>) δ 166.1, 56.7, 22.6, 22.5 (3C) ppm;

**Optical Rotation:** [α]<sub>D</sub><sup>20</sup> = +310.2° (c = 0.5 g / 100 mL, CHCl<sub>3</sub>);

**HRMS** (method, m/z) calcd. for C<sub>6</sub>H<sub>14</sub>NOS<sup>+</sup> [M+H]<sup>+</sup> 148.0791, found: 148.0794.



**Experimental:** To a  $-78\text{ }^\circ\text{C}$  cold solution of chiral bromide **24** (15.27 g, 50.0 mmol) in  $\text{Et}_2\text{O}$  (250 mL) was added  $n\text{BuLi}$  (2.5 M in hexanes, 22.0 mL, 55.0 mmol, 1.1 eq.). After stirring the reaction mixture at  $-40\text{ }^\circ\text{C}$  for 1 hour, it was re-cooled to  $-78\text{ }^\circ\text{C}$  and a solution of sulfinimine **25** (8.82 g, 60.0 mmol, 1.2 eq.) in  $\text{Et}_2\text{O}$  (20 mL) was added dropwise. The reaction was stirred for 30 min at  $-78\text{ }^\circ\text{C}$  and 1.5 hours at room temperature, before  $\text{NH}_4\text{Cl}$  (*sat.*, *aq.*, 250 mL) was added and the *aq.* phase was extracted with  $\text{Et}_2\text{O}$  (3 x 125 mL). The combined organic layers were dried over anhydrous  $\text{Na}_2\text{SO}_4$ , filtered, and evaporated. The obtained crude product was purified *via* column chromatography on  $\text{SiO}_2$  (hexanes/ $\text{EtOAc}$  3:1 to 1:1) to obtain the corresponding sulfonamide **26** (12.29 g, 66% yield) and related diastereomer **26B** (2.24g, 12%).

Major compound **26**:

**Physical State:** slightly yellow oil;

**R<sub>f</sub> Value:** 0.47 (hexanes/ $\text{EtOAc}$  1:1);

**$^1\text{H NMR}$**  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.25 (d,  $J = 1.9\text{ Hz}$ , 1H), 6.32 (d,  $J = 2.0\text{ Hz}$ , 1H), 4.96 (q,  $J = 6.5\text{ Hz}$ , 1H), 4.72 (dq,  $J = 2.5, 6.5\text{ Hz}$ , 1H), 3.28 (s, 1H), 1.47 (d,  $J = 6.6\text{ Hz}$ , 3H), 1.40 (d,  $J = 6.5\text{ Hz}$ , 3H), 1.19 (s, 9H), 0.85 (s, 9H), 0.04 (s, 3H),  $-0.03\text{ ppm}$  (s, 3H);

**$^{13}\text{C NMR}$**  (151 MHz,  $\text{CDCl}_3$ )  $\delta$  152.8, 141.1, 122.2, 109.2, 64.0, 55.4, 45.0, 25.9 (3C), 24.1, 22.7 (3C), 22.5, 18.3,  $-4.8$  (2C) ppm;

**Optical Rotation:**  $[\alpha]_{\text{D}}^{20} = +108.2^\circ$  ( $c = 0.50\text{ g} / 100\text{ mL}$ ,  $\text{CHCl}_3$ );

**HRMS** ( $m/z$ ) calc'd for  $\text{C}_{18}\text{H}_{36}\text{NO}_3\text{SSi}^+$   $[\text{M}+\text{H}]^+$  374.2180, found 374.2186.

Minor compound **26B**:

**Physical State:** slightly yellow oil;

**R<sub>f</sub> Value:** 0.42 (hexanes/EtOAc 1:1)

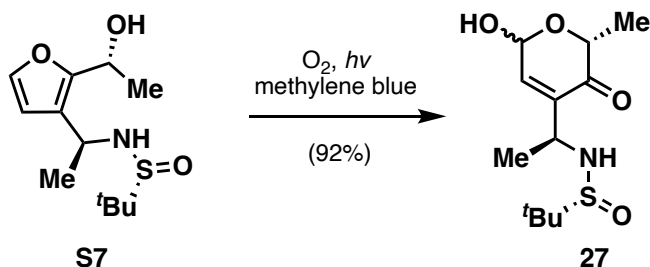
**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>) δ 7.31 (d, *J* = 1.9 Hz, 1H), 6.26 (d, *J* = 1.8 Hz, 1H), 5.01 (q, *J* = 6.5 Hz, 1H), 4.65 – 4.59 (m, 1H), 3.25 (s, 1H), 1.52 (d, *J* = 6.5 Hz, 3H), 1.48 (d, *J* = 6.6 Hz, 3H), 1.16 (s, 9H), 0.86 (s, 9H), 0.04 (s, 3H), -0.03 ppm (s, 3H);

**<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>) δ 153.4, 141.6, 120.9, 108.7, 62.9, 55.4, 45.6, 26.0 (3C), 23.8, 23.6, 22.7 (3C), 18.3, -4.7 (2C) ppm;

**Optical Rotation:** [α]<sub>D</sub><sup>20</sup> = +51.9° (c = 0.42 g / 100 mL, CHCl<sub>3</sub>);

**HRMS** (m/z) calc'd for C<sub>18</sub>H<sub>36</sub>NO<sub>3</sub>SSi<sup>+</sup> [M+H]<sup>+</sup> 374.2180, found 374.2183.





**Experimental:** A  $-78\text{ }^\circ\text{C}$  cold solution of alcohol **17** (3.501 g, 13.5 mmol) and methylene blue (64.0 mg, 0.135 mmol, 0.01 eq.) in  $\text{CH}_2\text{Cl}_2$  (200 mL) was irradiated with a 125 W visible-light lamp, while  $\text{O}_2$  was constantly bubbled through the solution, until all starting material was consumed (checked *via* TLC, usually about 4 h). After addition of  $\text{Me}_2\text{S}$  (5.0 eq), the mixture was stirred for 1 hour at  $-78\text{ }^\circ\text{C}$  and 1 hour at room temperature. The crude reaction mixture was concentrated under reduced pressure and purified *via* column chromatography on  $\text{SiO}_2$  (EtOAc) to obtain the corresponding enone **27** as a mixture of anomers (3.44 g, 92% yield).

**Physical State:** hygroscopic yellow solid;

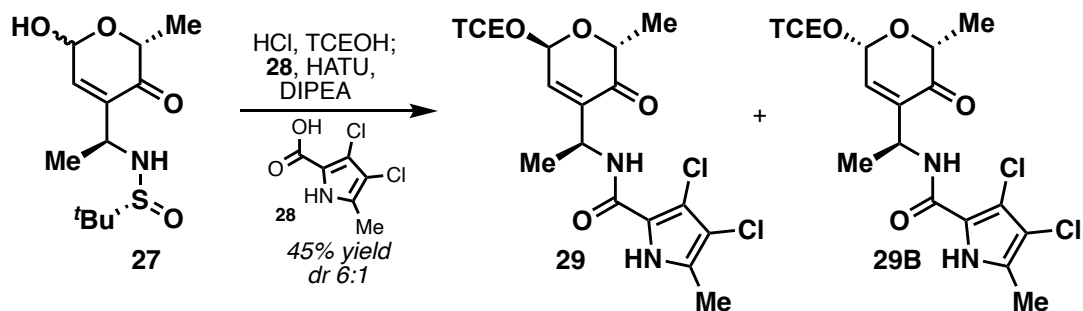
**R<sub>f</sub> Value:** 0.27 (EtOAc);

**$^1\text{H NMR}$**  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  6.79 (d,  $J = 3.4$  Hz, 1H), 5.59 (m, 1H), 4.65 (q,  $J = 6.7$  Hz, 1H), 4.23 – 4.29 (m, 1H), 4.05 (d,  $J = 8.8$  Hz, 1H), 1.38 (d,  $J = 6.9$  Hz, 3H), 1.34 (d,  $J = 6.9$  Hz, 3H), 1.21 ppm (s, 9H);

**$^{13}\text{C NMR}$**  (151 MHz,  $\text{CDCl}_3$ )  $\delta$  197.1, 197.0, 143.8, 140.1, 139.8, 139.2, 91.1, 88.0, 75.1, 70.4, 56.4 (2C), 53.8, 51.3, 22.7 (6 C), 21.8 (2C), 16.3, 15.6 ppm;

*NOTE: 1 carbon ( $t\text{Bu}$ ) was not observed due to incidental equivalence.*

**HRMS** (m/z) calc'd for  $\text{C}_{12}\text{H}_{21}\text{NO}_4\text{SNa}^+$  [ $\text{M}+\text{Na}$ ] $^+$  298.1083, found: 298.1091.



**Experimental:** To a solution of compound **27** (1.1 g, 4.0 mmol) in 7 mL dry trichloroethanol was added anhydrous PTSA (137.6 mg, 0.8 mmol, 0.2 eq.) at room temperature. The reaction was stirred at room temperature for 1.5 h and HCl (4.0 M in dioxane, 2.0 mL, 8.0 mmol, 2.0 equiv) was added. The resulting reaction mixture was stirred at room temperature for another 1.5 h. Most of the volatiles were removed under reduced pressure and the crude material was placed under high vacuum for at least 1 h.

HATU (2.3 g, 6.0 mmol, 1.5 eq.) and **28** (1.2 g, 6.0 mmol, 1.5 eq.) were dissolved in 50 mL DMF in another flask and DIPEA (2.8 mL, 16.0 mmol, 4.0 eq.) was added. After stirred at room temperature for 15 min, the resulting mixture was transferred to the crude amine salt obtained above. After stirring at room temperature for 4 h, another portion of mixture of HATU (0.8 g, 2.0 mmol, 0.5 eq.), **28** (0.4 g, 2.0 mmol, 0.5 eq.) and DIPEA (1.0 mL, 6.0 mmol, 1.5 eq.) in 17 mL DMF was added. Stirring was continued for another 4 h before the reaction mixture was quenched with sat. aq. NaHCO<sub>3</sub>. The mixture was extracted with EtOAc (3x50 mL) and the combined organic layers were washed with 10% aq. LiCl (2 x 20 ml), brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and filtered. The solvent was removed under reduced pressure and the crude product was purified *via* column chromatography on SiO<sub>2</sub> (hexanes/EtOAc 7:1 to 3:1) to obtain the corresponding amide **29** (716 mg, 39% yield) and **29B** (119 mg, 6% yield).

Major anomer **29**:

**Physical State:** yellow foam;

**R<sub>f</sub> Value:** 0.67 (Hexanes/EtOAc 1:1);



**<sup>1</sup>H NMR** (600 MHz, acetone-*d*<sub>6</sub>) δ 7.23 (d, *J* = 8.4 Hz, 1H), 6.97 (dd, *J* = 3.7, 1.0 Hz, 1H), 5.66 (d, *J* = 3.7 Hz, 1H), 5.09 (pd, *J* = 7.0, 1.2 Hz, 1H), 4.72 (q, *J* = 6.7 Hz, 1H), 4.46 (d, *J* = 11.7 Hz, 1H), 4.42 (d, *J* = 11.7 Hz, 1H), 2.28 (s, 3H), 1.40 (d, *J* = 7.0 Hz, 3H), 1.35 ppm (d, *J* = 6.7 Hz, 3H);

**<sup>13</sup>C NMR** (151 MHz, acetone-*d*<sub>6</sub>) δ 197.1, 158.8, 140.1, 137.6, 129.2, 119.9, 111.0, 110.0, 97.7, 95.1, 80.7, 71.4, 45.4, 21.0, 15.6, 11.0 ppm;

**Optical Rotation:**  $[\alpha]_{\text{D}}^{25} = +32.9^{\circ}$  (*c* = 1.00 g / 100 mL, CHCl<sub>3</sub>);

**HRMS** (*m/z*) calc'd for C<sub>16</sub>H<sub>17</sub>Cl<sub>5</sub>N<sub>2</sub>O<sub>4</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 498.9523, found: 498.9518.

Minor anomer **29B**:

**Physical State:** yellow oil;

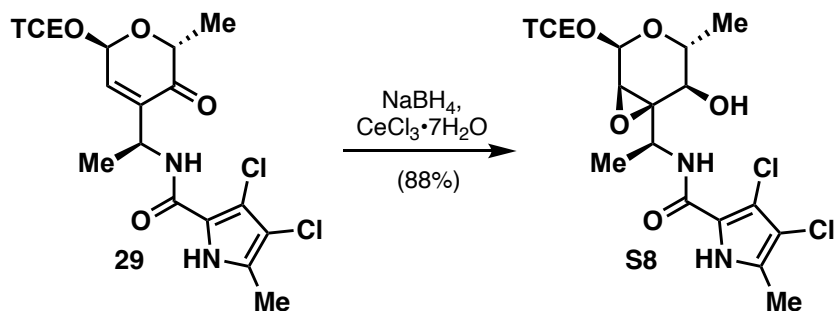
**R<sub>f</sub> Value:** 0.67 (Hexanes/EtOAc 1:1);

**<sup>1</sup>H NMR** (600 MHz, acetone-*d*<sub>6</sub>) δ 7.30 (d, *J* = 8.2 Hz, 1H), 7.01 (dd, *J* = 2.1, 1.0 Hz, 1H), 5.84 (dt, *J* = 2.0, 1.0 Hz, 1H), 5.09 – 5.03 (m, 1H), 4.50 (d, *J* = 11.7 Hz, 1H), 4.44 (d, *J* = 11.7 Hz, 1H), 4.39 (qd, *J* = 6.8, 1.0 Hz, 1H), 2.29 (s, 3H), 1.45 (d, *J* = 6.8 Hz, 3H), 1.42 ppm (d, *J* = 7.0 Hz, 3H);

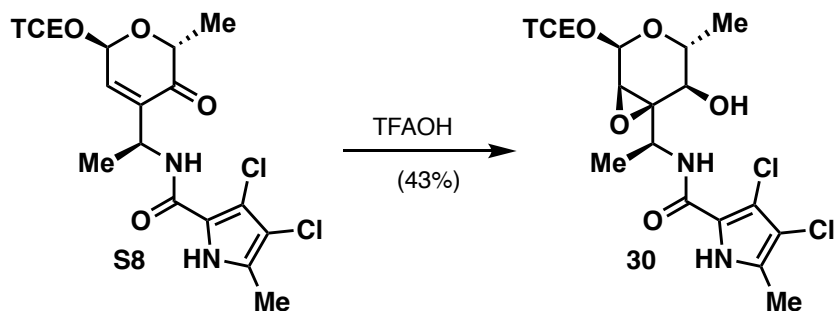
**<sup>13</sup>C NMR** (151 MHz, acetone-*d*<sub>6</sub>) δ 197.1, 158.6, 141.0, 140.2, 129.0, 120.2, 110.9, 109.9, 97.5, 97.5, 80.6, 75.8, 45.3, 20.7, 17.5, 11.0 ppm;

**Optical Rotation:**  $[\alpha]_{\text{D}}^{25} = +18.0^{\circ}$  (*c* = 0.15 g / 100 mL, CHCl<sub>3</sub>);

**HRMS** (*m/z*) calc'd for C<sub>16</sub>H<sub>17</sub>Cl<sub>5</sub>N<sub>2</sub>O<sub>4</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 498.9523, found: 498.9525.



**Experimental:** Compound **29** (1.60 g, 3.36 mmol) was dissolved in MeOH (36.0 mL). The solution was cooled to 0 °C and  $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$  (501 mg, 1.34 mmol, 0.4 eq.) was added to the vial. The resulting solution was stirred for 5 min, after which  $\text{NaBH}_4$  (508 mg, 13.45 mmol, 4.0 eq.) was added. After 20 mins, the reaction was quenched with acetone (10.0 mL), and stirred for 5 min at 0 °C and 5 min at room temperature. The volatiles were removed under reduced pressure and the crude material was placed under high vacuum briefly. The crude material was resuspended in DCM and rinsed with water then brine. The organic layer was dried over  $\text{MgSO}_4$ , and filtered. The solvent was removed under reduced pressure and the crude material was quickly passed through a pad of  $\text{SiO}_2$  (Hexane/EtOAc 1:0 to 1:1) to obtain the corresponding semi pure allylic alcohol **S8** (1.41 g, 88% yield), which could be directly used for the next step.



**Experimental:** To a suspension of urea hydrogen peroxide (320 mg, 3.4 mmol, 1.36 eq.) in dry DCM (20 mL) at 0 °C was added trifluoroacetic anhydride (0.715 g, 0.473 ml, 3.4 mmol, 1.36 eq.) and the reaction mixture was stirred for 1 h at the same temperature before stirring for 1 h at room temperature. This solution was kept at 0 °C and used as trifluoroperacetic acid solution.

Compound **S8** (1.19 g, 2.5 mmol, 1.0 eq) was placed in a flask with a stir bar and dissolved in dry DCM (8 ml). The resulting solution was cooled down to -15 °C then the premade trifluoroperacetic acid solution was added in one portion. Remove the cold bath and let the reaction gradually warm up. After 2 h, the reaction was quenched with aqueous saturated sodium sulfite and stirred at room temperature for 15 min. The aqueous layer was extracted three times with DCM. The combined organic layers were rinsed with sat. aqueous NaHCO<sub>3</sub> then brine. The organic layer was dried over MgSO<sub>4</sub> and filtered. The solvent was removed under reduced pressure. The crude material was purified by flash column chromatography (SiO<sub>2</sub>; 20% to 50% EtOAc in hexanes) to provide epoxide **30** (531 mg, 43% yield).

**Physical State:** yellow foam;

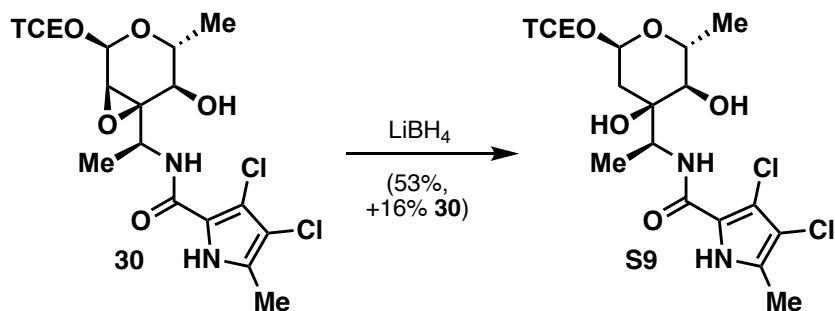
**R<sub>f</sub> Value:** 0.45 (50% EtOAc in hexanes);

**<sup>1</sup>H NMR** (600 MHz, acetone-*d*<sub>6</sub>) δ 6.80 (d, *J* = 7.7 Hz, 1H), 5.28 (dd, *J* = 3.1, 0.6 Hz, 1H), 4.58 (p, *J* = 7.0 Hz, 1H), 4.43 (d, *J* = 8.3 Hz, 1H), 4.34 – 4.27 (m, 2H), 3.90 – 3.84 (m, 1H), 3.72 – 3.67 (m, 2H), 2.29 (s, 3H), 1.43 (d, *J* = 6.9 Hz, 3H), 1.21 ppm (d, *J* = 6.3 Hz, 3H);

**<sup>13</sup>C NMR** (151 MHz, acetone-*d*<sub>6</sub>) δ 159.4, 129.0, 120.1, 110.8, 109.8, 98.0, 94.9, 79.8, 71.7, 67.2, 63.1, 58.7, 45.8, 17.8, 17.7, 11.0 ppm;

**Optical Rotation:** [α]<sub>D</sub><sup>25</sup> = +58.7° (c = 1.66 g / 100 mL, CHCl<sub>3</sub>);

**HRMS** (m/z) calc'd for C<sub>16</sub>H<sub>19</sub>Cl<sub>5</sub>N<sub>2</sub>O<sub>5</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 516.9629, found: 516.9634.



**Experimental:** To a solution of **30** (220.0 mg, 0.45 mmol) in 9 mL dry toluene was added  $\text{LiBH}_4$  (2.0 M in THF, 0.45 mL, 0.89 mmol, 2.0 eq.) at room temperature. After stirred at 60 °C for 1 h,  $\text{LiBH}_4$  (2.0 M in THF, 0.23 mL x 4, 0.45 mmol x 4, 1.0 eq. x 4) was added in four portions every 0.5 h. The reaction was cooled to room temperature and slowly quenched by the addition of  $\text{NH}_4\text{Cl}$  (*sat.*, *aq.*, 15 mL). The reaction mixture was extracted with EtOAc (3 x 20 mL), and the combined organic layers were dried over anhydrous  $\text{Na}_2\text{SO}_4$ , filtered, and evaporated. The obtained crude product was purified *via* column chromatography on  $\text{SiO}_2$  (hexanes/EtOAc 4:1 to 2:3) to obtain the corresponding alcohol **S9** (128.0 mg, 53% yield) and recovered **30** (37 mg, 16%).

**Physical State:** white foam;

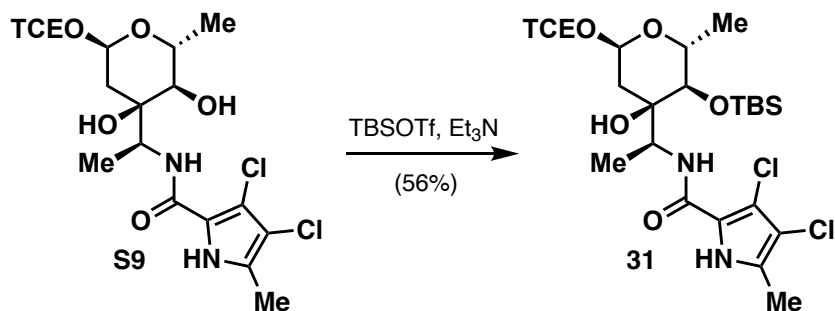
**R<sub>f</sub> Value:** 0.45 (Hexanes/EtOAc 1:2);

**<sup>1</sup>H NMR** (600 MHz, acetone-*d*<sub>6</sub>)  $\delta$  11.02 (s, 1H), 7.06 (d,  $J = 8.1$  Hz, 1H), 5.28 (dd,  $J = 4.2, 2.0$  Hz, 1H), 4.36 (d,  $J = 11.5$  Hz, 1H), 4.33 (dq,  $J = 8.1, 6.8$  Hz, 1H), 4.24 (d,  $J = 11.5$  Hz, 1H), 3.99 (dq,  $J = 9.1, 6.2$  Hz, 1H), 3.93 (s, 1H), 3.72 (d,  $J = 9.4$  Hz, 1H), 3.29 (t,  $J = 8.8$  Hz, 1H), 2.29 (s, 3H), 2.11 (dd,  $J = 14.7, 2.1$  Hz, 1H), 2.05 (dd,  $J = 14.7, 4.2$  Hz, 1H), 1.28 (d,  $J = 6.2$  Hz, 3H), 1.27 ppm (d,  $J = 6.8$  Hz, 3H);

**<sup>13</sup>C NMR** (151 MHz, acetone-*d*<sub>6</sub>)  $\delta$  159.5, 128.7, 120.7, 110.5, 109.9, 99.1, 97.8, 79.9, 75.0, 73.8, 67.2, 52.0, 36.2, 18.6, 16.6, 11.0 ppm;

**Optical Rotation:**  $[\alpha]_{\text{D}}^{25} = +62.6^\circ$  ( $c = 0.27$  g / 100 mL,  $\text{CHCl}_3$ );

**HRMS** ( $m/z$ ) calc'd for  $\text{C}_{16}\text{H}_{21}\text{Cl}_5\text{N}_2\text{O}_5\text{Na}^+$   $[\text{M}+\text{Na}]^+$  518.9785, found: 518.9786.



**Experimental:** To a solution of **S9** (166.0 mg, 0.335 mmol), Et<sub>3</sub>N (0.47 mL, 3.35 mmol, 10.0 eq.) in 7 mL DCE was added TBSOTf (0.23 mL, 1.01 mmol, 3.0 eq.) at room temperature. After stirred at 40 °C for 4 h, another portion of TBSOTf (0.23 mL, 1.01 mmol, 3.0 eq.) was added and stirring was continued for another 3 h.

The reaction was cooled to room temperature and quenched by the addition of NaHCO<sub>3</sub> (sat., aq., 15 mL). The reaction mixture was extracted with DCM (2 x 15 mL) and the combined organic layers were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and evaporated. The obtained crude product was purified *via* column chromatography on SiO<sub>2</sub> (hexanes/EtOAc 10:1 to 6:1) to obtain **31** (115.0 mg, 56% yield).

**Physical State:** white foam;

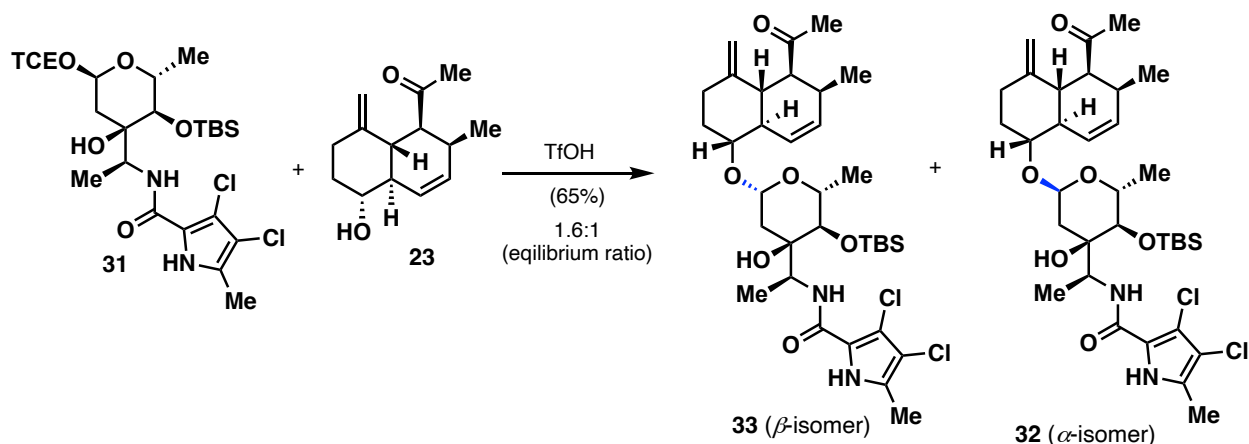
**R<sub>f</sub> Values:** 0.56 (Hexanes/EtOAc 4:1);

**<sup>1</sup>H NMR** (600 MHz, acetone-*d*<sub>6</sub>) δ 11.02 (s, 1H), 7.02 (d, *J* = 9.0 Hz, 1H), 5.22 (t, *J* = 6.1 Hz, 1H), 4.45 (dq, *J* = 9.0, 7.6 Hz, 1H), 4.34 (d, *J* = 11.6 Hz, 1H), 4.25 (d, *J* = 11.6 Hz, 1H), 3.97 (p, *J* = 6.5 Hz, 1H), 3.51 (dd, *J* = 7.1, 1.3 Hz, 1H), 3.44 (d, *J* = 1.0 Hz, 1H), 2.31 (s, 3H), 2.13 (dd, *J* = 5.9, 1.4 Hz, 1H), 2.05 (dd, *J* = 5.9, 1.4 Hz, 1H), 1.28 (d, *J* = 6.0 Hz, 3H), 1.27 (d, *J* = 6.8 Hz, 3H), 0.92 (s, 9H), 0.12 (s, 3H), 0.07 ppm (s, 3H);

**<sup>13</sup>C NMR** (151 MHz, acetone-*d*<sub>6</sub>) δ 159.3, 128.9, 120.4, 110.4, 109.9, 98.5, 98.2, 79.8, 76.3, 74.0, 70.6, 49.2, 34.7, 26.5 (3C), 20.2, 19.0, 16.7, 11.1, -3.4, -3.8 ppm;

**Optical Rotation:** [α]<sub>D</sub><sup>25</sup> = +57.4° (c = 1.72 g / 100 mL, CHCl<sub>3</sub>);

**HRMS** (m/z) calc'd for C<sub>22</sub>H<sub>35</sub>Cl<sub>5</sub>N<sub>2</sub>O<sub>5</sub>SiNa<sup>+</sup> [M+Na]<sup>+</sup> 633.0650, found: 633.0648.



**Experimental:** A solution of **31** (56 mg, 0.092 mmol), **23** (41 mg, 0.184 mmol, 2.0 eq.), 20 mg 4A MS in 6 mL dry DCM was stirred for 15 min at room temperature. TfOH (8.1  $\mu$ L, 0.092 mmol, 1.0 eq.) was added, and stirring was continued for 2.5 h at room temperature. The reaction mixture was quenched with NaHCO<sub>3</sub> (sat., aq., 15 mL), extracted with DCM (3 x 15 mL). The combined organic layers were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and evaporated. The obtained crude product was purified via column chromatography on SiO<sub>2</sub> (hexanes/EtOAc 10:1 to 6:1 to 3:1) to obtain the corresponding  $\beta$ -anomer **33** (25.1 mg, 40% yield) and  $\alpha$ -anomer **32** (14.5 mg, 25%).

For  $\beta$ -anomer **33**:

**Physical State:** white foam;

**R<sub>f</sub> Value:** R<sub>f</sub> = 0.57 (Hexanes/EtOAc 4:1);

**<sup>1</sup>H NMR** (600 MHz, acetone-*d*<sub>6</sub>):  $\delta$  6.73 (d, *J* = 8.0 Hz, 1H), 6.02 (dt, *J* = 10.1, 1.8 Hz, 1H), 5.65 (ddd, *J* = 10.1, 4.6, 2.7 Hz, 1H), 4.93 (dd, *J* = 9.2, 2.1 Hz, 1H), 4.66 (s, 1H), 4.52 (p, *J* = 7.4 Hz, 1H), 4.21 (s, 1H), 3.73 (dq, *J* = 8.8, 6.3 Hz, 1H), 3.59 (td, *J* = 10.6, 4.5 Hz, 1H), 3.49 (d, *J* = 8.7 Hz, 1H), 3.31 (brs, 1H), 3.09 (dd, *J* = 11.7, 6.2 Hz, 1H), 2.69 – 2.62 (s, 1H), 2.29 (s, 3H), 2.29 – 2.24 (m, 2H), 2.19 (t, *J* = 11.3 Hz, 1H), 2.17 (s, 3H), 2.11 (td, *J* = 13.0, 4.4 Hz, 1H), 1.80 (dd, *J* = 13.0, 2.1 Hz, 1H), 1.76 (tq, *J* = 8.6, 2.2 Hz, 1H), 1.53 (dd, *J* = 13.1, 9.2 Hz, 1H), 1.27 (d, *J* = 6.9 Hz, 3H), 1.25 (d, *J* = 6.3 Hz, 3H), 1.24 – 1.20 (m, 1H), 0.97 (s, 9H), 0.78 (d, *J* = 7.2 Hz, 3H), 0.24 (s, 3H), 0.22 ppm (s, 3H);

**<sup>13</sup>C NMR** (151 MHz, acetone-*d*<sub>6</sub>) δ 209.2, 161.0, 151.5, 131.7, 129.0, 127.3, 120.2, 110.9, 110.0, 105.6, 96.2, 78.1, 77.4, 75.7, 71.2, 52.9, 49.8, 49.4, 39.3, 36.5, 35.1, 35.0, 31.7, 30.4, 26.8 (3C), 19.8, 19.2, 18.4, 16.4, 11.1, -2.8, -2.9 ppm;

**Optical Rotation:**  $[\alpha]_{\text{D}}^{25} = +53.7^\circ$  (c = 0.75 g / 100 mL, CHCl<sub>3</sub>);

**HRMS** (m/z) calc'd for C<sub>34</sub>H<sub>53</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>6</sub>Si<sup>+</sup> [M+H]<sup>+</sup> 683.3044, found: 683.3043.

For  $\alpha$ -anomer **32**:

**Physical State:** white foam;

**R<sub>f</sub> Value:** 0.23 (Hexanes/EtOAc 4:1);

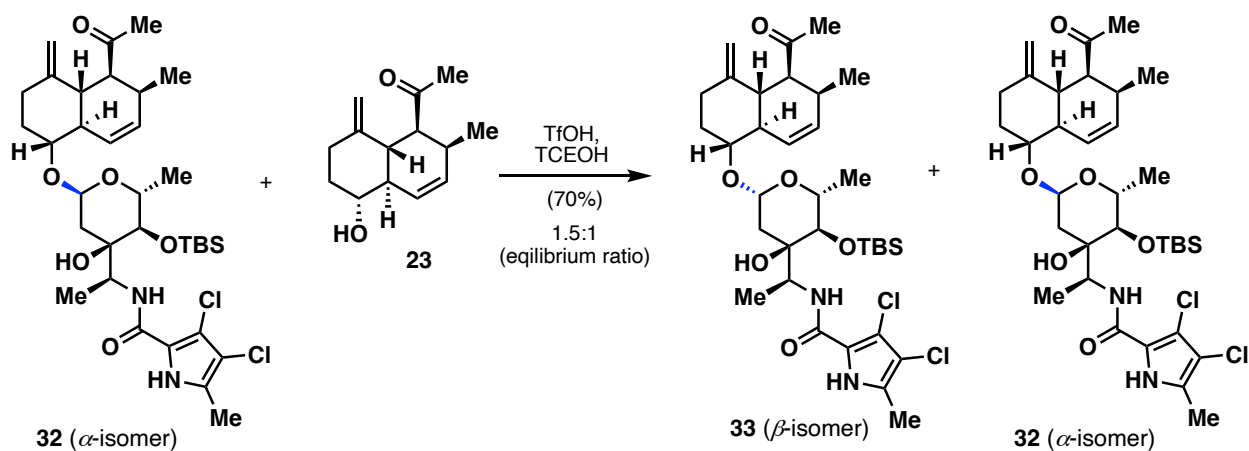
**<sup>1</sup>H NMR** (600 MHz, acetone-*d*<sub>6</sub>) δ 7.02 (d, *J* = 8.6 Hz, 1H), 5.79 (dt, *J* = 10.0, 1.6 Hz, 1H), 5.73 (ddd, *J* = 10.0, 4.7, 2.5 Hz, 1H), 5.02 (t, *J* = 5.7 Hz, 1H), 4.66 (s, 1H), 4.44 (p, *J* = 7.2 Hz, 1H), 4.21 (s, 1H), 3.89 (p, *J* = 6.5 Hz, 1H), 3.47 (d, *J* = 6.3 Hz, 1H), 3.47 (s, 1H), 3.40 (td, *J* = 10.6, 4.7 Hz, 1H), 3.09 (dd, *J* = 11.7, 6.1 Hz, 1H), 2.71 – 2.64 (m, 1H), 2.35 – 2.28 (m, 2H), 2.30 (s, 3H), 2.22 (t, *J* = 11.2 Hz, 1H), 2.19 – 2.16 (m, 1H), 2.18 (s, 3H), 2.10 – 2.06 (m, 1H), 1.95 (dd, *J* = 13.9, 5.8 Hz, 1H), 1.82 – 1.79 (m, 2H), 1.49 – 1.41 (m, 1H), 1.26 (d, *J* = 6.8 Hz, 3H), 1.24 (d, *J* = 6.3 Hz, 3H), 0.91 (s, 9H), 0.79 (d, *J* = 7.1 Hz, 3H), 0.12 (s, 3H), 0.07 (s, 3H).

**<sup>13</sup>C NMR** (151 MHz, acetone-*d*<sub>6</sub>) δ 209.0, 159.3, 151.4, 132.9, 128.7, 126.3, 120.5, 110.3, 109.9, 105.4, 99.8, 82.5, 76.5, 74.2, 69.4, 52.5, 50.0, 49.2, 39.4, 37.4, 35.4, 35.2, 31.8, 30.3, 26.6 (3C), 20.2, 19.1, 18.2, 16.7, 11.1, -3.3, -3.6.

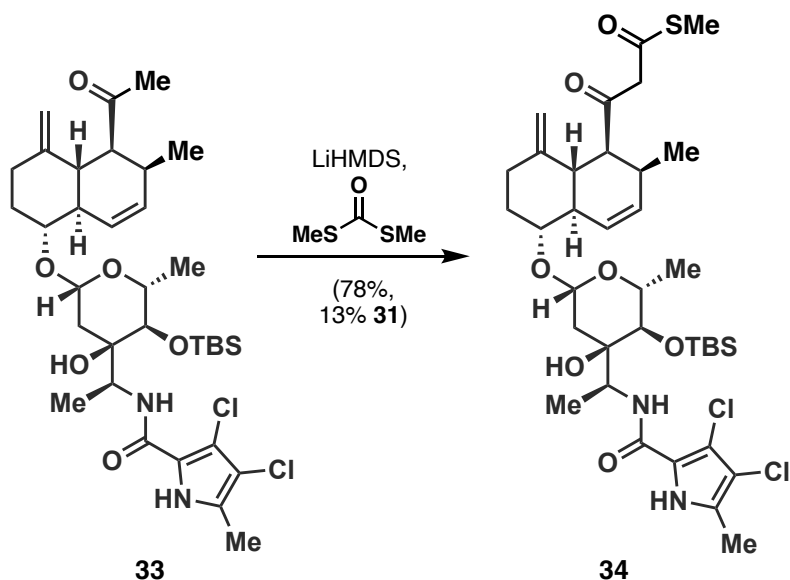
**Optical Rotation:**  $[\alpha]_{\text{D}}^{25} = +45.5^\circ$  (c = 0.29 g / 100 mL, CHCl<sub>3</sub>);

**HRMS** (m/z) calc'd for C<sub>34</sub>H<sub>53</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>6</sub>Si<sup>+</sup> [M+H]<sup>+</sup> 683.3044, found: 683.3051.





**Experimental:** A solution of **32** (3.3 mg, 0.0049 mmol), **23** (2.1 mg, 0.0098 mmol, 2.0 eq.),  $\text{Cl}_3\text{CCH}_2\text{OH}$  (0.5  $\mu\text{L}$ , 0.0049 mmol, 1.0 eq.) and 1.6 mg 4 A MS in 0.3 mL DCM was stirred at room temperature for 10 min before TfOH (0.8  $\mu\text{L}$ , 0.0098 mmol, 2.0 eq.) was added. After stirred at room temperature for 2.5 h, the reaction mixture was quenched with ]  $\text{NaHCO}_3$  (*sat.*, *aq.*, 10 mL) and extracted with DCM (2 x 10 mL). The combined organic layers were dried over anhydrous  $\text{Na}_2\text{SO}_4$ , filtered, and evaporated. The obtained crude product was purified via column chromatography on  $\text{SiO}_2$  (hexanes/EtOAc 10:1 to 6:1 to 3:1) to obtain the corresponding  $\beta$ -anomer **33** (1.4 mg, 42% yield) and recover  $\alpha$ -anomer **32** (0.9 mg, 28%).



**Experimental:** To a flame dried vial was added the ketone **33** (30 mg, 0.044 mmol) and THF (2.0 mL) under argon. The solution was cooled to  $-78\text{ }^{\circ}\text{C}$ , and LiHMDS (1 M solution in THF; 0.88 mL, 0.880 mmol, 20 eq.) was added dropwise. The resulting mixture was stirred at this temperature for 30 min. Thereafter, *S,S'*-dimethyl dithiocarbonate (55  $\mu\text{L}$ , 0.528 mmol, 12.0 eq.) was added dropwise. The reaction was removed from the bath and allowed to warm to room temperature (for about 10 min) before being placed in an oil bath preheated to  $30\text{ }^{\circ}\text{C}$ . The reaction was stirred at this temperature for 6 h, after which it was cooled back to room temperature. The reaction was quenched by the addition of  $\text{NH}_4\text{Cl}$  (*sat., aq.*, 6 mL). The aqueous layer was extracted with EtOAc (3 x 12 mL), and the combined organic layers were rinsed with brine, dried over  $\text{Na}_2\text{SO}_4$ , and filtered. The solvent was removed under reduced pressure and the crude material was purified by preparatory thin-layer chromatography (PTLC) ( $\text{SiO}_2$ ; hexanes/EtOAc 3:1), yielding the product **34** (25.9 mg, 78% yield) and recovering start material **33** (4.0 mg, 13%).

**Physical State:** pale yellow foam;

**R<sub>f</sub> Value:** 0.60 (hexanes/EtOAc 3:1);

**<sup>1</sup>H NMR** (600 MHz, acetone-*d*<sub>6</sub>, major isomer)  $\delta$  10.97 (s, 1H), 6.73 (d,  $J = 8.0$  Hz, 1H), 6.03 (dd,  $J = 10.1, 2.0$  Hz, 1H), 5.68 (m, 1H), 4.95 – 4.90 (m, 1H), 4.68 (s, 1H), 4.52 (p,  $J$

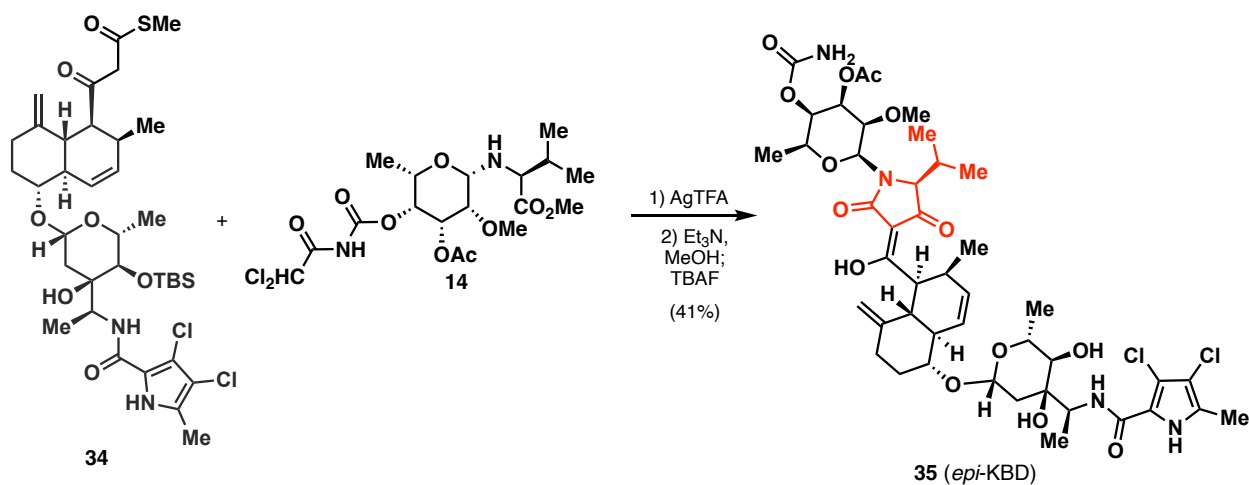
= 7.2 Hz, 1H), 4.28 (s, 1H), 4.01 – 3.90 (m, 1H), 3.77 – 3.68 (m, 1H), 3.59 (td,  $J = 10.8$ , 4.5 Hz, 1H), 3.49 (d,  $J = 8.7$  Hz, 1H), 3.31 (d,  $J = 2.1$  Hz, 1H), 3.27 (dd,  $J = 11.6$ , 6.1 Hz, 1H), 2.78 (m, 1H), 2.32 (s, 3H), 2.30 (s, 3H), 2.28 – 2.25 (m, 1H), 2.20 – 2.17 (m, 1H), 2.11 (td,  $J = 12.2$ , 11.4, 3.3 Hz, 1H), 1.81 – 1.74 (m, 2H), 1.53 (ddd,  $J = 12.9$ , 9.4, 2.3 Hz, 1H), 1.27 (d,  $J = 6.9$  Hz, 3H), 1.24 (d,  $J = 6.3$  Hz, 2H), 0.97 (s, 9H), 0.82 (d,  $J = 7.1$  Hz, 2H), 0.23 ppm (d,  $J = 10.9$  Hz, 6H);

**$^{13}\text{C}$  NMR** (151 MHz, acetone- $d_6$ , major isomer)  $\delta$  202.8, 192.7, 160.8, 150.7, 131.3, 128.9, 127.2, 120.2, 110.7, 109.9, 106.0, 96.1, 77.9, 77.2, 75.6, 71.1, 57.6, 52.4, 49.8, 49.4, 39.1, 36.5, 35.0, 34.9, 31.3, 26.7 (3C), 19.6, 19.1, 18.3, 16.2, 11.9, 10.9, -3.0, -3.1 ppm;

*NOTE: The product has an equilibrium between the keto/enol isomers.*

**Optical Rotation:**  $[\alpha]_{\text{D}}^{25} = +16.3^\circ$  ( $c = 1.00$  g / 100 mL,  $\text{CHCl}_3$ );

**HRMS** ( $m/z$ ) calc'd for  $\text{C}_{36}\text{H}_{55}\text{Cl}_2\text{N}_2\text{O}_7\text{SSi}^+$   $[\text{M}+\text{H}]^+$  757.2871, found: 757.2862.



**Experimental:** To a flame dried vial fixed with a stir bar, and under argon was added the thioester (11.0 mg, 0.014 mmol) and the amino sugar (21.2 mg, 0.044 mmol, 3.0 eq.) as a solution in benzene (1 mL). The benzene was frozen (acetone/dry ice bath) then promptly placed under a high vacuum and left there until all benzene was removed. The fresh-dried 4-A molecular sieves (20 mg) were added to the vial, and it was then evacuated and backfilled with argon. Next, THF (0.2 mL) was added to the vial *via* syringe, and the mixture was stirred for 10 minutes. The vial was wrapped in foil, and AgCO<sub>2</sub>CF<sub>3</sub> (16.0 mg, 0.073 mmol, 5.0 eq.) was quickly added at once. The reaction was stirred for 2 hours at room temperature after which it was diluted with EtOAc and filtered through a pad of celite. The filtrate was then rinsed with 0.5 M HCl (*aq.*, 2 x 10 mL) then brine and NaHCO<sub>3</sub> (*sat, aq.*, 15 mL). The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub> and filtered. The solvent was removed under reduced pressure and the crude material was used in the next step without purification.

The crude material was placed under argon in a flame-dried vial fixed with a stir bar. MeOH (0.8 mL) was added and followed by Et<sub>3</sub>N (10  $\mu$ L, 0.073 mmol, 5 eq.). The reaction was stirred at room temperature for 10 minutes and the solvent was removed quickly under reduced pressure.

The crude mixture above was placed under argon with THF (1 mL). TBAF solution (1.0 M in THF, 0.12 mL, 8 eq.) was added, and the mixture was stirred at room

temperature for 30 minutes. Upon completion, formic acid was added to quench the reaction. The mixture was diluted with acetonitrile (2 mL) and directly purified by prep. HPLC. The eluents containing the product were lyophilized to afford *epi*-KBD **33** (5.6 mg, 41% over 2 steps) as a white solid.

*NOTE: The first step is extremely sensitive to H<sub>2</sub>O in the reaction. It is necessary to use benzene and fresh dried 4A MS to remove H<sub>2</sub>O entirely.*

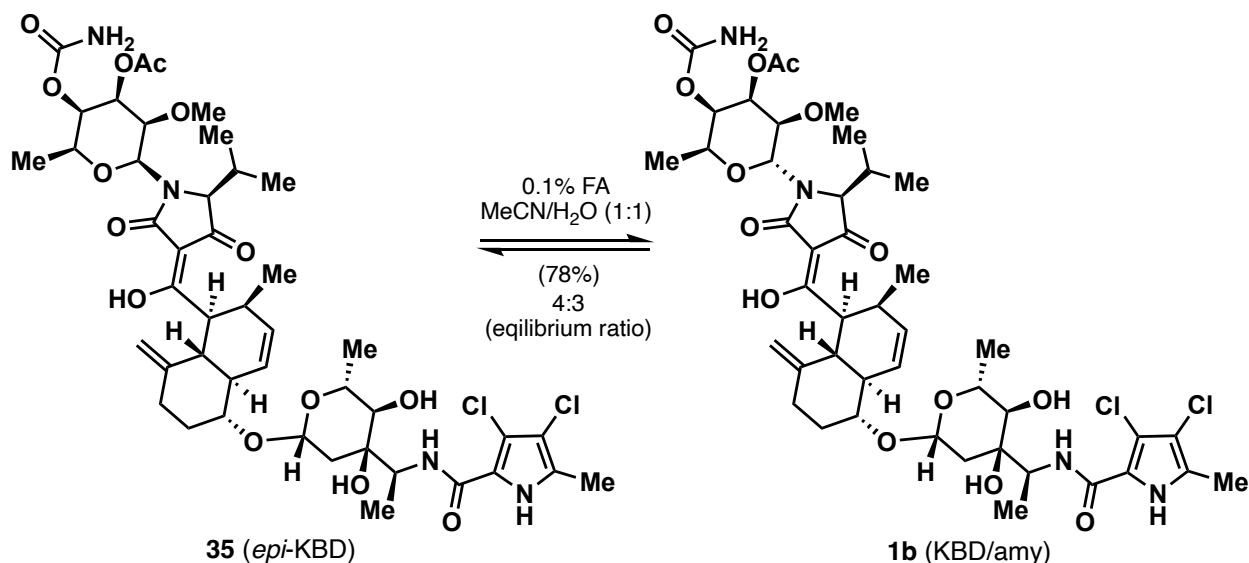
**<sup>1</sup>H NMR** (600 MHz, CD<sub>3</sub>OD) δ 5.95 (d, *J* = 10.1 Hz, 1H), 5.67 – 5.60 (m, 1H), 5.52 (s, 1H), 5.09 (t, *J* = 3.6 Hz, 1H), 4.98 – 4.95 (m, 1H), 4.59 (s, 1H), 4.44 (s, 1H), 4.41 – 4.35 (m, 2H), 3.90 – 3.85 (m, 1H), 3.85 (d, *J* = 3.0 Hz, 1H), 3.71 – 3.65 (m, 2H), 3.57 (dt, *J* = 10.5, 5.3 Hz, 1H), 3.54 (s, 3H), 3.19 (d, *J* = 9.3 Hz, 1H), 2.71 – 2.63 (m, 2H), 2.31 – 2.24 (m, 3H), 2.23 (s, 3H), 2.17 – 2.09 (m, 1H), 2.06 (s, 3H), 1.85 – 1.77 (m, 2H), 1.59 (dd, *J* = 13.4, 9.3 Hz, 1H), 1.27 (d, *J* = 6.1 Hz, 3H), 1.25 (d, *J* = 7.1 Hz, 3H), 1.19 (d, *J* = 6.3 Hz, 3H), 1.15 (d, *J* = 7.1 Hz, 3H), 0.82 (d, *J* = 7.2 Hz, 3H), 0.77 ppm (d, *J* = 6.8 Hz, 3H);

**<sup>13</sup>C NMR** (151 MHz, CD<sub>3</sub>OD) δ 197.9, 176.2, 171.2, 161.8, 159.9, 152.3, 133.6, 129.4, 126.6, 120.0, 112.4, 110.7, 106.1, 103.9, 96.9, 80.8, 79.8, 79.6, 76.4, 74.9, 74.1, 73.9, 71.7, 70.4, 68.5, 60.9, 52.4, 50.0, 47.8, 39.4, 38.5, 35.6, 35.3, 31.7, 30.8, 20.9, 19.5, 19.0, 18.6, 16.6, 16.2, 15.8, 10.8 ppm;

*NOTE: one ketone's carbon did not show up in NMR.*

**Optical Rotation:** [α]<sub>D</sub><sup>25</sup> = -26.0° (c = 0.10 g / 100 mL, MeOH);

**HRMS** (m/z) calc'd for C<sub>44</sub>H<sub>61</sub>Cl<sub>2</sub>N<sub>4</sub>O<sub>14</sub><sup>+</sup> [M+H]<sup>+</sup> 939.3556, found: 939.3560.



**Experimental:** To a vial of purified *epi*-KBD (5.6 mg, 0.006 mmol) was added 1 mL of 0.1% formic acid in acetonitrile/H<sub>2</sub>O (1:1). The mixture was shaken well and kept at room temperature for 24 hours. The reaction was monitored by LC-MS until the equilibrium, and the mixture was directly purified by prep. HPLC. The eluents containing *epi*-KBD and KBD were collected separately and lyophilized to afford *epi*-KBD (2.6 mg, 46% yield) and KBD (1.8 mg, 32% yield), respectively. The NMR spectra and Mass fragments are well-matched to the isolated natural product <sup>[6]</sup> (see **figure S15** to **S17** below).

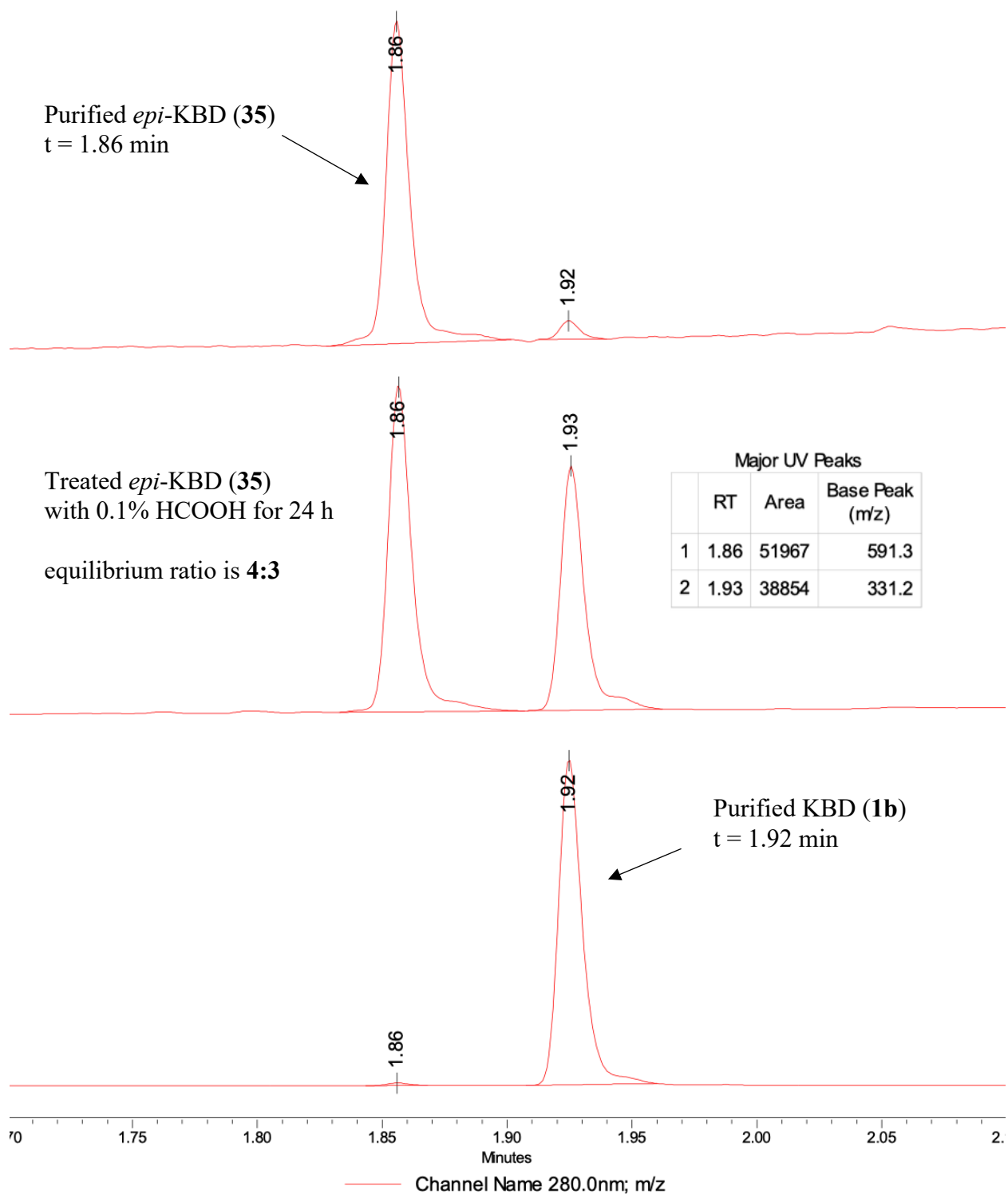
**NOTE:** The mass balance of the reaction was well based on LC-MS results (see **figure S14** below). The major reason of losing material was due to the HPLC purification.

**<sup>1</sup>H NMR** (600 MHz, CD<sub>3</sub>OD)  $\delta$  5.94 (d,  $J$  = 10.2 Hz, 1H), 5.90 (t,  $J$  = 3.4 Hz, 1H), 5.66 – 5.60 (m, 1H), 5.06 (d,  $J$  = 8.0 Hz, 1H), 4.96 (dd,  $J$  = 9.5, 2.2 Hz, 1H), 4.92 (dd,  $z$  = 6.2, 3.5 Hz, 1H), 4.58 (s, 1H), 4.45 (s, 1H), 4.39 (q,  $J$  = 6.8 Hz, 1H), 4.36 – 4.28 (m, 3H), 3.73 – 3.65 (m, 1H), 3.61 – 3.53 (m, 2H), 3.30 (s, 3H), 3.19 (d,  $J$  = 9.1 Hz, 1H), 2.66 (s, 1H), 2.32 – 2.24 (m, 3H), 2.23 (s, 3H), 2.19 – 2.13 (m, 2H), 2.12 (s, 3H), 1.84 – 1.77 (m, 2H), 1.58 (dd,  $J$  = 13.4, 9.4 Hz, 1H), 1.41 (d,  $J$  = 7.0 Hz, 3H), 1.27 (d,  $J$  = 6.3 Hz, 3H), 1.25 (d,  $J$  = 6.9 Hz, 3H), 1.09 (d,  $J$  = 6.9 Hz, 3H), 0.98 (d,  $J$  = 6.9 Hz, 3H), 0.82 (d,  $J$  = 7.2 Hz, 3H).

**<sup>13</sup>C NMR** (151 MHz, CD<sub>3</sub>OD) δ 198.1, 196.7, 178.2, 172.0, 161.7, 158.4, 152.2, 133.7, 129.4, 126.5, 120.0, 112.4, 110.7, 106.2, 105.3, 96.8, 79.6, 77.4, 76.4, 75.6, 74.9, 71.7, 71.4, 69.9, 69.8, 69.6, 57.4, 52.4, 49.9, 48.0, 39.5, 38.5, 35.6, 35.3, 32.1, 32.0, 21.0, 19.0, 18.5, 17.9, 17.7, 16.2, 14.6, 10.8 ppm;

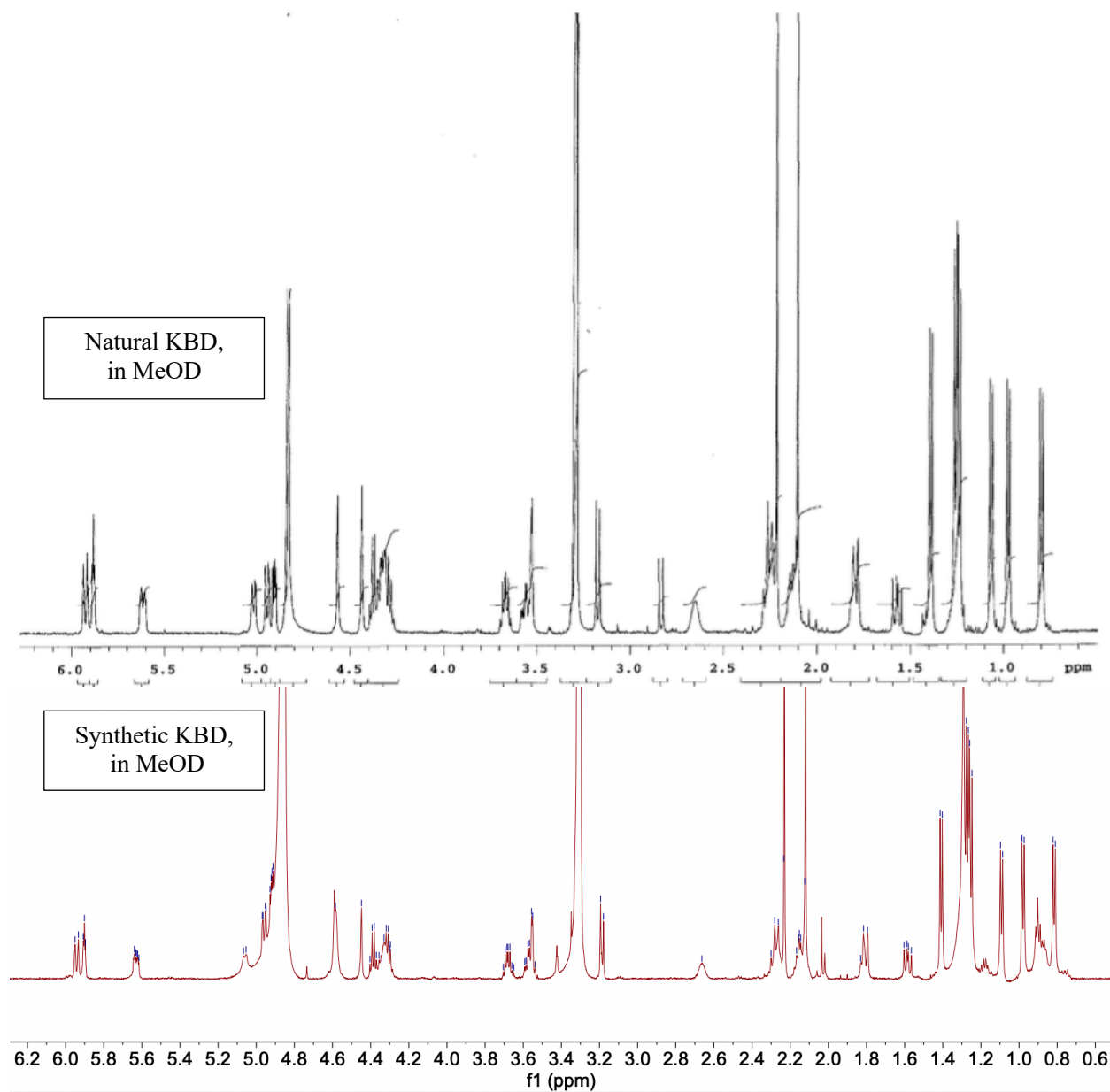
**Optical Rotation:**  $[\alpha]_D^{25} = -20.0^\circ$  (c = 0.23 g / 100 mL, MeOH);

**HRMS** (m/z) calc'd for C<sub>44</sub>H<sub>61</sub>Cl<sub>2</sub>N<sub>4</sub>O<sub>14</sub><sup>+</sup> [M+H]<sup>+</sup> 939.3556, found: 393.3566.

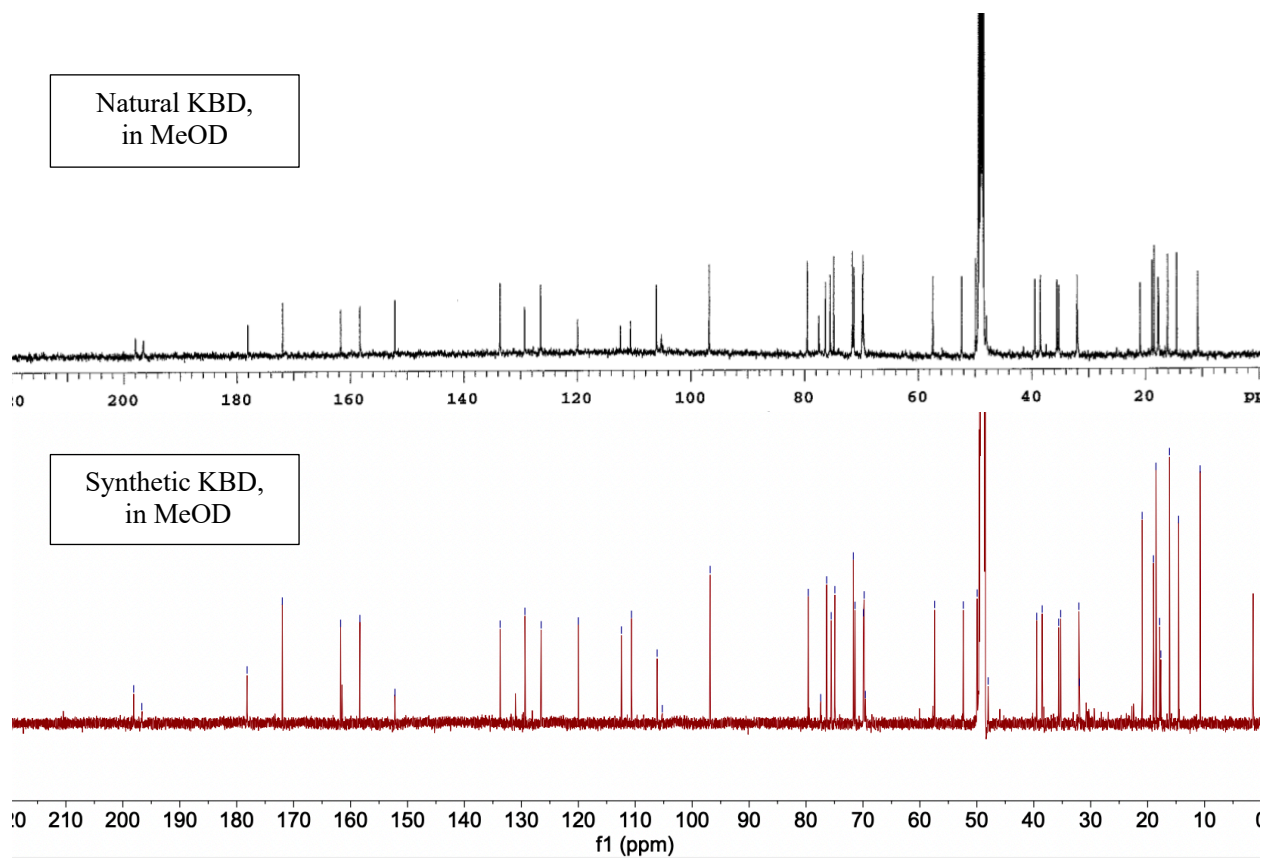


**Figure S16.** The equilibrium of *epi*-KBD and KBD under 0.1% HCOOH condition





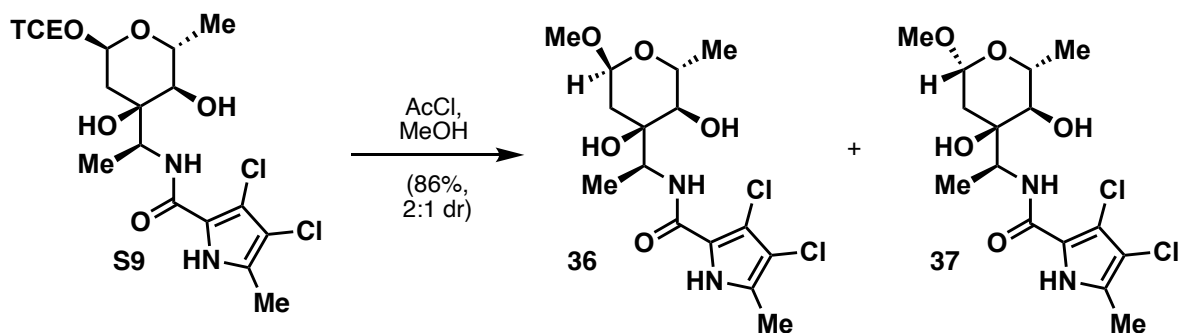
**Figure S17.** Comparison of <sup>1</sup>H NMR of the Natural <sup>[6]</sup> and Synthetic Kibdelomycin (**1b**)



**Figure S18.** Comparison of <sup>13</sup>C NMR of the Natural <sup>[6]</sup> and Synthetic Kibdelomycin (**1b**)



## The procedures for analogs synthesis:



**Experimental:** To a solution of **S9** (40 mg, 0.115 mmol) in 1.5 mL dry MeOH, AcCl (8.1  $\mu$ L, 0.115 mmol, 1.0 eq.) was added at room temperature. The stirring was continued for 30 min at room temperature. The reaction mixture was quenched with NaHCO<sub>3</sub> (*sat.*, *aq.*, 15 mL), extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and evaporated. The obtained crude product was purified preparatory thin-layer chromatography (PTLC) (SiO<sub>2</sub>; Hexanes/EtOAc 1:2) to obtain the corresponding  $\alpha$ -anomer **36** (12.7 mg, 29% yield) and  $\beta$ -anomer **37** (24.9 mg, 57%).

For  $\alpha$ -anomer **36**:

**Physical State:** white foam;

**R<sub>f</sub> Value:** R<sub>f</sub> = 0.5 (Hexanes/EtOAc 1:2);

**<sup>1</sup>H NMR** (600 MHz, acetone-*d*<sub>6</sub>):  $\delta$  7.02 (d, *J* = 7.8 Hz, 1H), 4.82 (dd, *J* = 3.8, 1.8 Hz, 1H), 4.31 – 4.25 (m, 1H), 3.79 – 3.73 (m, 1H), 3.34 (s, 3H), 3.20 (d, *J* = 9.4 Hz, 1H), 2.28 (s, 3H), 1.96 – 1.87 (m, 2H), 1.25 (d, *J* = 6.2 Hz, 3H), 1.23 ppm (d, *J* = 6.8 Hz, 3H);

**<sup>13</sup>C NMR** (151 MHz, acetone-*d*<sub>6</sub>)  $\delta$  159.3, 128.4, 120.7, 110.2, 109.7, 99.0, 75.1, 73.9, 65.9, 55.0, 51.7, 36.2, 18.5, 16.4, 10.9 ppm;

**Optical Rotation:**  $[\alpha]_{\text{D}}^{25} = +61.5^\circ$  (*c* = 0.4 g / 100 mL, MeOH);

**HRMS** (*m/z*) calc'd for C<sub>15</sub>H<sub>22</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>5</sub>Na<sup>+</sup> [*M*+Na]<sup>+</sup> 381.0798, found: 403.0799.

For  $\beta$ -anomer **37**:

**Physical State:** white foam;

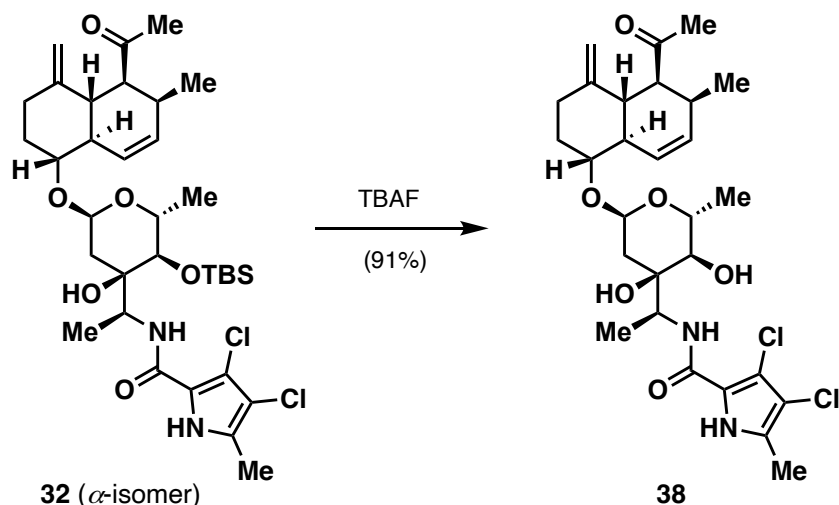
**R<sub>f</sub> Value:** 0.55 (Hexanes/EtOAc 1:2);

**<sup>1</sup>H NMR** (600 MHz, acetone-*d*<sub>6</sub>)  $\delta$  11.08 (s, 1H), 6.87 (d, *J* = 7.7 Hz, 1H), 4.65 (dd, *J* = 9.3, 2.1 Hz, 1H), 4.42 (p, *J* = 7.1 Hz, 1H), 4.25 (s, 1H), 3.88 (d, *J* = 8.8 Hz, 1H), 3.64 (dq, *J* = 9.0, 6.2 Hz, 1H), 3.37 (s, 3H), 3.17 (t, *J* = 8.9 Hz, 1H), 2.29 (s, 3H), 1.82 (dd, *J* = 13.2, 2.1 Hz, 1H), 1.48 (ddd, *J* = 13.2, 9.4, 1.3 Hz, 1H), 1.26 (d, *J* = 6.9 Hz, 3H), 1.24 ppm (d, *J* = 6.2 Hz, 3H);

**<sup>13</sup>C NMR** (151 MHz, acetone-*d*<sub>6</sub>)  $\delta$  160.8, 129.0, 120.0, 111.1, 110.0, 100.5, 76.2, 74.6, 71.1, 56.1, 52.2, 37.3, 18.6, 16.1, 10.9 ppm;

**Optical Rotation:**  $[\alpha]_{\text{D}}^{25} = +11.4^\circ$  (*c* = 0.48 g / 100 mL, MeOH);

**HRMS** (*m/z*) calc'd for C<sub>15</sub>H<sub>23</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>5</sub><sup>+</sup> [M+H]<sup>+</sup> 381.0979, found: 381.0968.



**Experimental:** To a solution of **32** (45 mg, 0.066 mmol) in 2 mL THF, TBAF (1.0 M in THF, 132  $\mu\text{L}$ , 0.132 mmol, 2.0 eq.) was added at room temperature. After 20 min, the reaction mixture was quenched with  $\text{NH}_4\text{Cl}$  (*sat.*, *aq.*, 15 mL), extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over anhydrous  $\text{Na}_2\text{SO}_4$ , filtered, and evaporated. The obtained crude product was purified preparatory thin-layer chromatography (PTLC) ( $\text{SiO}_2$ ; Hexanes/EtOAc: 1:2) to obtain the corresponding analog **38** (34.1 mg, 91% yield).

**Physical State:** white foam;

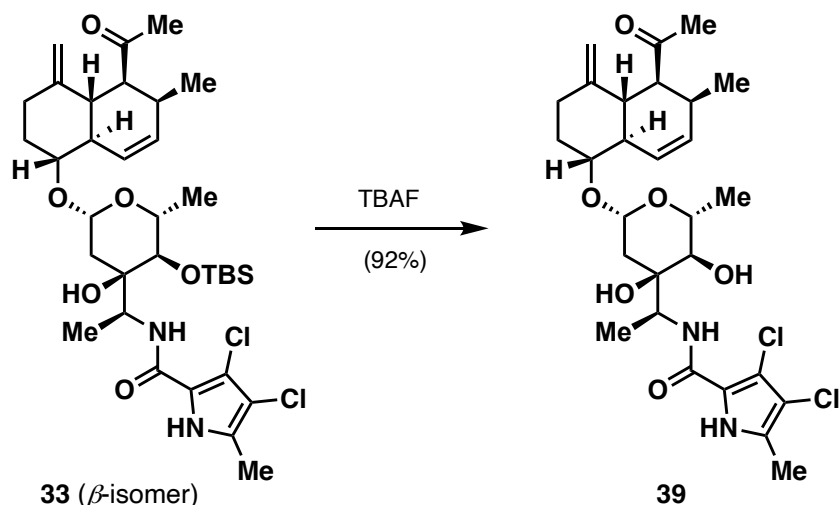
**TLC:**  $R_f = 0.45$  (Hexanes/EtOAc: 1:2);

**$^1\text{H NMR}$**  (600 MHz, acetone- $d_6$ ):  $\delta$  7.04 (d,  $J = 7.7$  Hz, 1H), 5.81 – 5.72 (m, 2H), 5.07 (dd,  $J = 4.3, 1.8$  Hz, 1H), 4.67 (d,  $J = 1.4$  Hz, 1H), 4.32 – 4.26 (m, 1H), 4.24 – 4.21 (m, 1H), 4.02 (s, 1H), 3.92 (dd,  $J = 9.4, 6.2$  Hz, 1H), 3.46 (d,  $J = 10.0$  Hz, 1H), 3.42 (td,  $J = 10.7, 4.7$  Hz, 1H), 3.22 (t,  $J = 9.6$  Hz, 1H), 3.11 (dd,  $J = 11.7, 6.1$  Hz, 1H), 2.73 – 2.65 (m, 1H), 2.38 – 2.34 (m, 1H), 2.33 – 2.30 (m, 1H), 2.28 (s, 3H), 2.24 (t,  $J = 11.2$  Hz, 1H), 2.18 (s, 3H), 2.09 – 2.06 (m, 1H), 1.93 (dd,  $J = 14.3, 4.2$  Hz, 1H), 1.89 – 1.83 (m, 1H), 1.56 – 1.48 (m, 1H), 1.24 (d,  $J = 4.3$  Hz, 3H), 1.23 (d,  $J = 3.8$  Hz, 3H), 0.79 ppm (d,  $J = 7.1$  Hz, 3H);

**<sup>13</sup>C NMR** (151 MHz, acetone- *d*<sub>6</sub>): δ 208.8, 159.3, 151.1, 133.1, 128.4, 125.9, 120.8, 110.2, 109.7, 105.5, 100.4, 83.7, 75.1, 73.8, 66.6, 52.4, 51.6, 49.9, 39.2, 37.0, 36.5, 35.2, 31.6, 30.2, 18.3, 18.0, 16.4, 10.9 ppm;

**Optical Rotation:** [α]<sub>D</sub><sup>25</sup> = +114.3° (c = 0.23 g / 100 mL, CHCl<sub>3</sub>);

**HRMS** (m/z) calc'd for C<sub>28</sub>H<sub>38</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>6</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 591.1999, found: 591.2008.



**Experimental:** To a solution of **33** (33 mg, 0.048 mmol) in 2 mL THF, TBAF (1.0 M in THF, 96  $\mu$ L, 0.096 mmol, 2.0 eq.) was added at room temperature. After 20 min, the reaction mixture was quenched with  $\text{NH}_4\text{Cl}$  (sat., aq., 15 mL), extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over anhydrous  $\text{Na}_2\text{SO}_4$ , filtered, and evaporated. The obtained crude product was purified preparatory thin-layer chromatography (PTLC) ( $\text{SiO}_2$ ; Hexanes/EtOAc: 1:2) to obtain the corresponding analog **39** (25.3 mg, 92% yield).

**Physical State:** white foam;

**TLC:**  $R_f$  = 0.45 (Hexanes/EtOAc: 1:2);

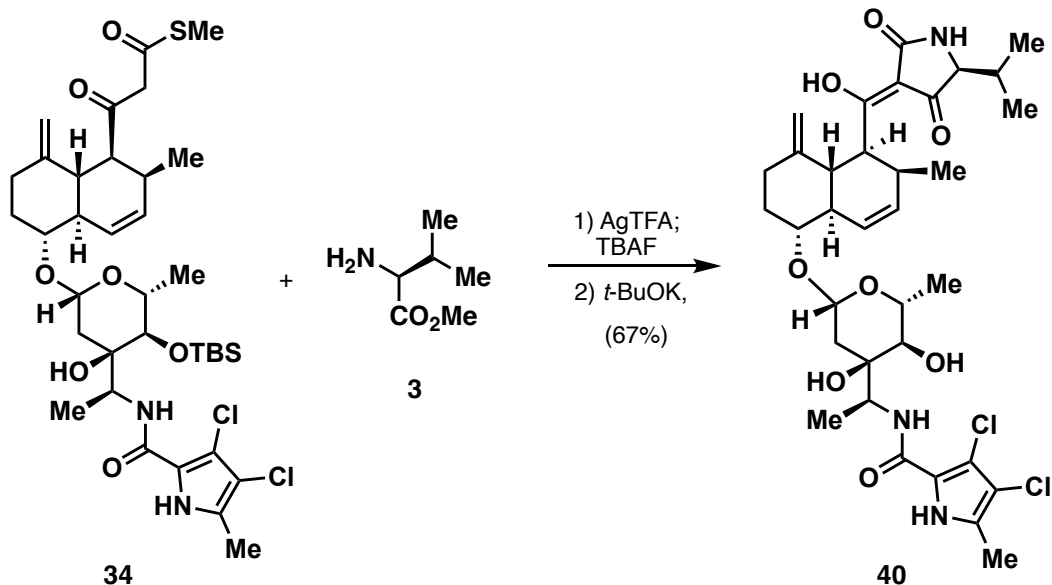
**$^1\text{H}$  NMR** (600 MHz, acetone- $d_6$ ):  $\delta$  6.87 (d,  $J$  = 7.7 Hz, 1H), 6.02 (dt,  $J$  = 10.0, 1.8 Hz, 1H), 5.65 (ddd,  $J$  = 10.1, 4.6, 2.6 Hz, 1H), 4.94 (dd,  $J$  = 9.3, 2.1 Hz, 1H), 4.66 (s, 1H), 4.46 – 4.39 (m, 1H), 4.32 (s, 1H), 4.21 (s, 1H), 3.82 (d,  $J$  = 8.9 Hz, 1H), 3.67 – 3.62 (m, 1H), 3.59 (td,  $J$  = 10.6, 4.4 Hz, 1H), 3.18 (t,  $J$  = 9.0 Hz, 1H), 3.09 (dd,  $J$  = 11.7, 6.2 Hz, 1H), 2.70 – 2.63 (m, 1H), 2.32 – 2.25 (m, 5H), 2.20 (d,  $J$  = 11.2 Hz, 1H), 2.17 (s, 3H), 2.15 – 2.10 (m, 1H), 1.80 – 1.72 (m, 2H), 1.53 (ddd,  $J$  = 13.2, 9.3, 1.2 Hz, 1H), 1.28 (d,  $J$  = 6.9 Hz, 3H), 1.23 (d,  $J$  = 6.2 Hz, 3H), 0.77 ppm (d,  $J$  = 7.1 Hz, 3H);

**$^{13}\text{C}$  NMR** (151 MHz, acetone- $d_6$ ):  $\delta$  207.6, 159.5, 150.1, 130.2, 127.7, 125.9, 118.7, 109.8, 108.6, 104.1, 94.9, 76.5, 75.0, 73.3, 69.8, 51.4, 50.9, 48.0, 37.8, 36.8, 33.7, 33.5, 30.2, 28.8, 17.3, 16.9, 14.8, 9.6 ppm;



**Optical Rotation:**  $[\alpha]_{\text{D}}^{25} = +19.7^{\circ}$  (c = 0.32 g / 100 mL,  $\text{CHCl}_3$ );

**HRMS** (m/z) calc'd for  $\text{C}_{28}\text{H}_{39}\text{Cl}_2\text{N}_2\text{O}_6^+$   $[\text{M}+\text{H}]^+$  569.2180, found: 569.2189.



**Experimental:** A flame-dried vial of the thioester **34** (11.0 mg, 0.014 mmol), the valine methyl ester **3** (5.7 mg, 0.044 mmol, 3.0 eq.), and the fresh-dried 4A MS (10 mg) were evacuated and backfilled with argon. THF (0.4 mL) was added to the vial *via* syringe, and the mixture was stirred for 10 min. The vial was wrapped in foil, and AgCO<sub>2</sub>CF<sub>3</sub> (16.0 mg, 0.073 mmol, 5.0 eq.) was quickly added at once. The reaction was stirred for 2 h at room temperature, after which it was added TBAF (1.0 M in THF, 44  $\mu$ L, 0.044 mmol, 3.0 eq.). After 10 min, the reaction mixture was diluted with EtOAc and filtered through a pad of SiO<sub>2</sub>. The filtrate was then rinsed two times with 0.5 M HCl (*aq.*, 10 mL), then brine and NaHCO<sub>3</sub> (*sat.*, *aq.*, 10 mL). The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub> and filtered. The solvent was removed under reduced pressure and the crude material was quickly passed through a SiO<sub>2</sub> pipet column (Acetone/DCM 1:3), and the semi pure product was directly used in the next step.

The semi pure mixture above was placed under argon with THF (1 mL). *t*BuOK solution (1.0 M in THF, 73  $\mu$ L, 0.073 mmol, 5 eq.) was added at 0 °C, and the mixture was stirred at the same temperature for 30 min. Upon completion, the reaction was quenched with 0.5M HCl (*aq.*, 15 mL), and the mixture was extracted with EtOAc (3 x 15 mL). The combined organic layers were washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub>, and filtered. The solvent was removed under reduced pressure and the crude material was

purified by prep. HPLC. The eluents containing the product were lyophilized to afford **40** (6.8 mg, 67% over 2 steps).

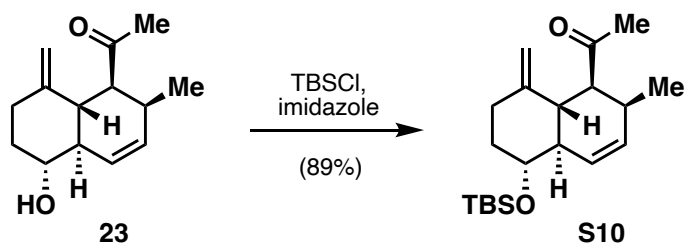
**<sup>1</sup>H NMR** (600 MHz, CD<sub>3</sub>OD) δ 6.01 (d, *J* = 10.1 Hz, 1H), 5.68 (ddd, *J* = 10.0, 4.8, 2.6 Hz, 1H), 4.95 (dd, *J* = 9.5, 2.1 Hz, 1H), 4.70 (d, *J* = 14.2 Hz, 1H), 4.38 (q, *J* = 6.8 Hz, 1H), 4.30 (d, *J* = 10.1 Hz, 1H), 4.26 (t, *J* = 5.2 Hz, 1H), 3.72 – 3.65 (m, 1H), 3.57 (td, *J* = 10.6, 4.6 Hz, 1H), 3.18 (d, *J* = 9.2 Hz, 1H), 2.82 – 2.72 (s, 1H), 2.35 – 2.26 (m, 2H), 2.23 (s, 3H), 2.22 – 2.10 (m, 2H), 1.80 (dd, *J* = 13.3, 2.1 Hz, 1H), 1.58 (dd, *J* = 13.4, 9.4 Hz, 1H), 1.26 (d, *J* = 6.1 Hz, 3H), 1.25 (d, *J* = 6.9 Hz, 3H), 0.97 – 0.90 (m, 6H), 0.82 ppm (dd, *J* = 8.2, 7.1 Hz, 3H);

**<sup>13</sup>C NMR** (151 MHz, CD<sub>3</sub>OD) δ 208.2, 208.0, 170.3, 167.9, 167.8, 161.7, 150.8, 131.8, 129.4, 127.2 (2C), 120.0, 112.4, 110.6, 106.6 (2C), 96.9, 79.2, 76.3, 74.9, 71.7, 61.5, 53.4, 53.2, 52.4, 49.7 (2C), 39.6, 39.5, 38.5, 35.4, 35.2, 32.7 (2C), 32.0, 31.9, 20.3, 20.2, 18.5, 18.4 (2C), 18.2 (2C), 16.2, 10.8 ppm;

*NOTE: The product contains a pair of E/Z isomers on tetramic acid part.*

**Optical Rotation:**  $[\alpha]_{\text{D}}^{25} = +17.2^{\circ}$  (*c* = 0.29 g / 100 mL, MeOH);

**HRMS** (*m/z*): calc'd for C<sub>34</sub>H<sub>46</sub>Cl<sub>2</sub>N<sub>3</sub>O<sub>8</sub><sup>+</sup> [M+H]<sup>+</sup> 694.2656, found 694.2664.



**Experimental:** To a solution of **23** (85 mg, 0.386 mmol, 1.0 equiv) in 3 mL DMF, imidazole (131 mg, 1.93 mmol, 5.0 eq.) and TBSCl (145, 0.966 mmol, 2.5 eq.) were added at 0 °C. The reaction mixture was warmed up to room temperature. After 3 h, the reaction was quenched with NH<sub>4</sub>Cl (*sat.*, *aq.*, 25 mL), extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with brine (2 x 50 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and evaporated. The obtained crude product was purified by column chromatography (SiO<sub>2</sub>; Hexanes/EtOAc 50:1) to obtain the corresponding **S10** (115 mg, 89% yield).

**Physical State:** colorless oil;

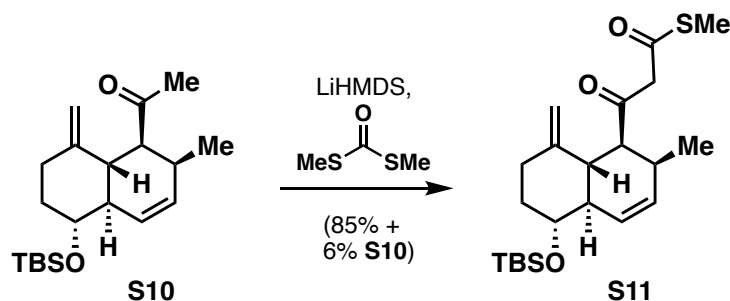
**TLC:** R<sub>f</sub> = 0.2 (Hexanes/EtOAc 50:1);

**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>) δ 5.89 – 5.83 (m, 1H), 5.68 (ddd, *J* = 10.1, 4.8, 2.6 Hz, 1H), 4.70 (s, 1H), 4.16 (s, 1H), 3.44 (td, *J* = 10.3, 4.6 Hz, 1H), 3.05 (dd, *J* = 11.7, 6.1 Hz, 1H), 2.66 – 2.57 (m, 1H), 2.34 – 2.27 (m, 1H), 2.21 – 2.14 (s, 5H), 2.06 (dtd, *J* = 12.2, 4.8, 2.3 Hz, 1H), 1.85 – 1.77 (m, 1H), 1.45 (dddd, *J* = 13.8, 12.5, 10.6, 4.9 Hz, 1H), 0.89 (s, 9H), 0.82 (d, *J* = 7.1 Hz, 3H), 0.07 (s, 3H), 0.06 ppm (s, 3H);

**<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>) δ 210.4, 150.4, 131.2, 126.5, 105.1, 74.5, 52.3, 50.6, 38.3, 34.8, 31.3, 30.3, 26.0 (3C), 18.2, 18.0, -3.9 (2C), -4.5 ppm;

**Optical Rotation:** [α]<sub>D</sub><sup>25</sup> = +62.0° (c = 0.64 g / 100 mL, CHCl<sub>3</sub>);

**HRMS** (*m/z*): calc'd for C<sub>20</sub>H<sub>35</sub>O<sub>2</sub>Si<sup>+</sup> [M+H]<sup>+</sup> 335.2401, found 335.2400.



**Experimental:** To a solution of **S10** (112 mg, 0.335 mmol) in 3 mL THF at -78 °C, LiHMDS (1.0 M in THF, 2.0 mL, 2.0 mmol, 6.0 eq.) was added dropwise. The resulting solution was allowed to stir at this temperature for 30 min. After this period, *S,S'*-dimethyl dithiocarbonate (140  $\mu$ L, 0.134 mmol, 4.0 eq.) was added dropwise. The reaction was removed from the bath and allowed to warm to room temperature (for about 10 min) before being placed in an oil bath preheated to 30 °C. The reaction was stirred at this temperature for 8 h, after which it was cooled back to room temperature. The reaction was quenched by the addition of  $\text{NH}_4\text{Cl}$  (*sat.*, *aq.*, 6 mL). The aqueous layer was extracted three times with EtOAc (3 x 15 mL), and the combined organic layers were rinsed with brine, dried over  $\text{Na}_2\text{SO}_4$ , and filtered. The solvent was removed under reduced pressure and the crude material was purified by column chromatography ( $\text{SiO}_2$ ; Hexanes/EtOAc 60:1) to obtain the corresponding **S11** (116 mg, 85% yield) and recover **S10** (8.2 mg, 6% yield).

**Physical State:** pale yellow oil;

**TLC:**  $R_f = 0.25$  (Hexanes/EtOAc 50:1);

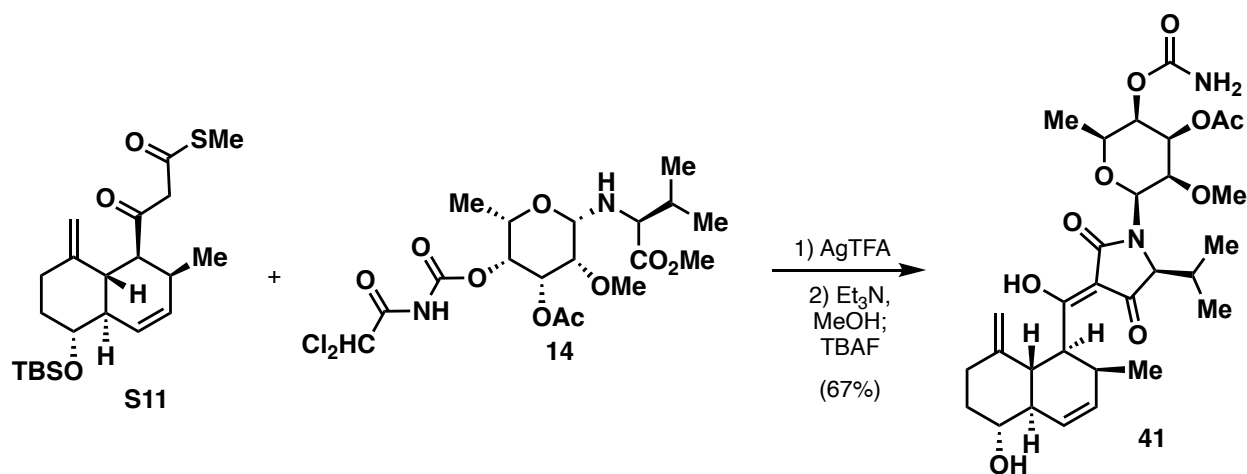
**$^1\text{H NMR}$**  (600 MHz, acetone-*d*6)  $\delta$  5.91 – 5.87 (m, 1H), 5.77 – 5.73 (m, 1H), 4.71 (s, 0.34 H), 4.67 (s, 0.7H), 4.61 (s, 0.34H), 4.28 (s, 0.7H), 4.00 – 3.89 (m, 1H), 3.55 (td,  $J = 10.4$ , 4.6 Hz, 1H), 3.25 (dd,  $J = 11.7$ , 6.0 Hz, 0.7H), 2.83 – 2.75 (m, 2H), 2.33 (s, 1H), 2.31 (s, 2H), 2.30 – 2.09 (m, 4H), 1.82 – 1.73 (m, 1H), 1.45 – 1.36 (m, 1H), 0.93 (d,  $J = 7.1$  Hz, 1H), 0.91 (s, 3H), 0.91 (s, 6H), 0.81 (d,  $J = 7.1$  Hz, 2H), 0.12 – 0.08 ppm (m, 6H);

**<sup>13</sup>C NMR** (151 MHz, acetone-*d*<sub>6</sub>) δ 202.9, 192.7, 151.1, 150.9, 132.4, 132.0, 126.8, 126.7, 105.6, 101.2, 75.2, 75.1, 57.6, 52.2, 52.1, 51.6, 45.3, 39.3 (2C), 38.8, 37.9, 35.4, 35.2, 31.4, 26.2 (6C), 18.6, 18.2, 18.1, 11.9, 10.7, -3.8 (4C), -4.5, -4.6 ppm;

*NOTE: contains 2:1 keto/enol isomers.*

**Optical Rotation:**  $[\alpha]_{\text{D}}^{25} = +51.0^{\circ}$  (c = 0.87 g / 100 mL, CHCl<sub>3</sub>);

**HRMS** (m/z): calc'd for C<sub>22</sub>H<sub>37</sub>O<sub>3</sub>SSi<sup>+</sup> [M+H]<sup>+</sup> 409.2227, found 409.2229.



**Experimental:** To a flame dried vial fixed with a stir bar, and under argon was added the thioester **S11** (22.0 mg, 0.054 mmol) and the amino sugar **14** (78.6 mg, 0.162 mmol, 3.0 eq.) as a solution in benzene (1 mL). The benzene was frozen (acetone/dry ice bath) then promptly placed under a high vacuum and left there until all benzene was removed. The fresh-dried 4A MS (20 mg) were added to the vial, and it was then evacuated and backfilled with argon. Next, THF (0.4 mL) was added to the vial *via* syringe, and the mixture was stirred for 10 min. The vial was wrapped in foil, and AgCO<sub>2</sub>CF<sub>3</sub> (59 mg, 0.270 mmol, 5.0 eq.) was quickly added at once. The reaction was stirred for 2 h at room temperature after which it was diluted with EtOAc and filtered through a pad of celite. The filtrate was then rinsed two times with 0.5 M HCl (*aq.*, 2 x 15 mL), then brine and NaHCO<sub>3</sub> (sat, *aq.*, 10 mL). The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, and filtered. The solvent was removed under reduced pressure and the crude material was used in the next step without purification.

The above crude material was placed under argon in a flame-dried vial fixed with a stir bar. MeOH (0.8 mL) was added and followed by Et<sub>3</sub>N (37  $\mu$ L, 0.270 mmol, 5 eq.). The reaction was stirred at room temperature for 10 min and the solvent was removed quickly under reduced pressure.

The crude mixture above was placed under argon with THF (1 mL). TBAF solution (1.0 M in THF, 0.43 mL, 0.43 mmol, 8 eq.) was added, and the mixture was stirred at room temperature for 30 min. Upon completion, formic acid was added to quench the reaction. The mixture was diluted with acetonitrile (2 mL) and directly purified by prep.

HPLC. The eluents containing the product were lyophilized to afford **41** (21.3 mg, 67% over 2 steps) as a white solid.

*NOTE: The first step is extremely sensitive to H<sub>2</sub>O in the reaction. It is necessary to use benzene and fresh dried 4A MS to remove H<sub>2</sub>O entirely.*

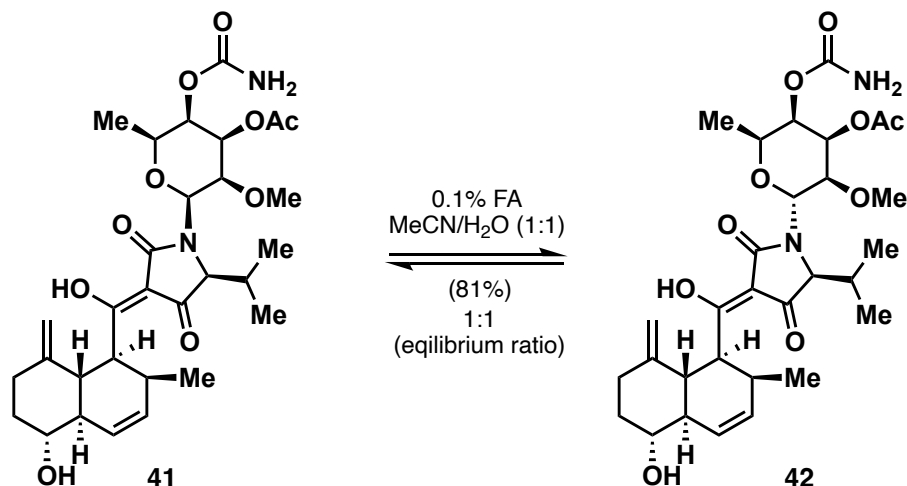
**<sup>1</sup>H NMR** (600 MHz, CD<sub>3</sub>OD) δ 5.92 (dt, *J* = 10.2, 1.7 Hz, 1H), 5.71 (ddd, *J* = 10.1, 4.7, 2.6 Hz, 1H), 5.53 (s, 1H), 5.10 (t, *J* = 3.5 Hz, 1H), 4.97 (dt, *J* = 3.8, 1.4 Hz, 1H), 4.60 (s, 1H), 4.41 (s, 1H), 4.29 (dd, *J* = 11.9, 6.1 Hz, 1H), 3.96 (s, 1H), 3.89 (dd, *J* = 6.4, 1.8 Hz, 1H), 3.72 (d, *J* = 3.1 Hz, 1H), 3.55 (s, 3H), 3.40 – 3.33 (m, 1H), 2.76 – 2.60 (m, 2H), 2.32 – 2.24 (m, 1H), 2.23 – 2.15 (m, 1H), 2.15 – 2.09 (m, 1H), 2.06 (s, 3H), 1.77 (td, *J* = 10.6, 2.3 Hz, 1H), 1.40 (dt, *J* = 12.2, 6.2 Hz, 1H), 1.20 (d, *J* = 6.4 Hz, 3H), 1.16 (d, *J* = 7.2 Hz, 3H), 0.85 (d, *J* = 7.2 Hz, 3H), 0.76 ppm (d, *J* = 6.9 Hz, 3H);

**<sup>13</sup>C NMR** (151 MHz, CD<sub>3</sub>OD) δ 171.5, 159.9, 152.3, 133.8, 126.2, 105.7, 80.8, 79.4, 74.5, 74.0, 70.4, 60.8, 51.8, 49.6, 46.5, 39.0 (2C), 35.9, 32.6, 31.7, 20.8, 19.4, 18.7, 16.6, 15.6 ppm;

**Optical Rotation:** [α]<sub>D</sub><sup>25</sup> = -7.9° (c = 0.19 g / 100 mL, MeOH);

**HRMS** (m/z): calc'd for C<sub>30</sub>H<sub>43</sub>N<sub>2</sub>O<sub>10</sub><sup>+</sup> [M+H]<sup>+</sup> 591.2913, found 591.2916.





**Experimental:** To a vial of **41** (9.8 mg, 0.017 mmol) was added 1 mL of 0.1% formic acid in acetonitrile/H<sub>2</sub>O (1:1). The mixture was shaken well and kept at room temperature for 24 h. The reaction was monitored by LC-MS until the equilibrium, and the mixture was directly purified by prep. HPLC. The eluents containing **41** and **42** were collected separately and lyophilized to afford **41** (4.0 mg, 41% yield) and **42** (3.9 mg, 40% yield), respectively.

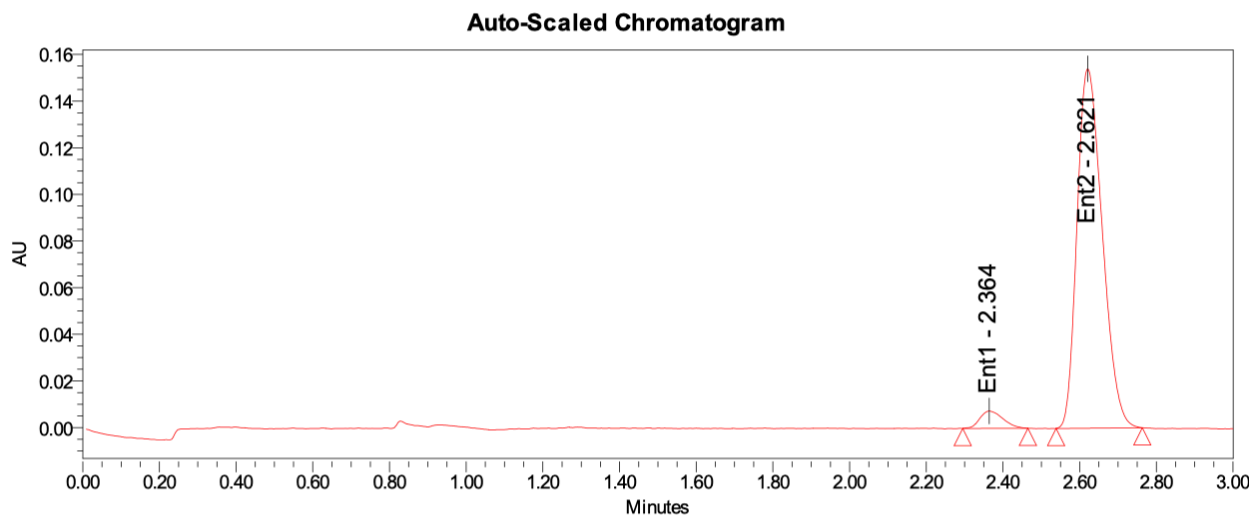
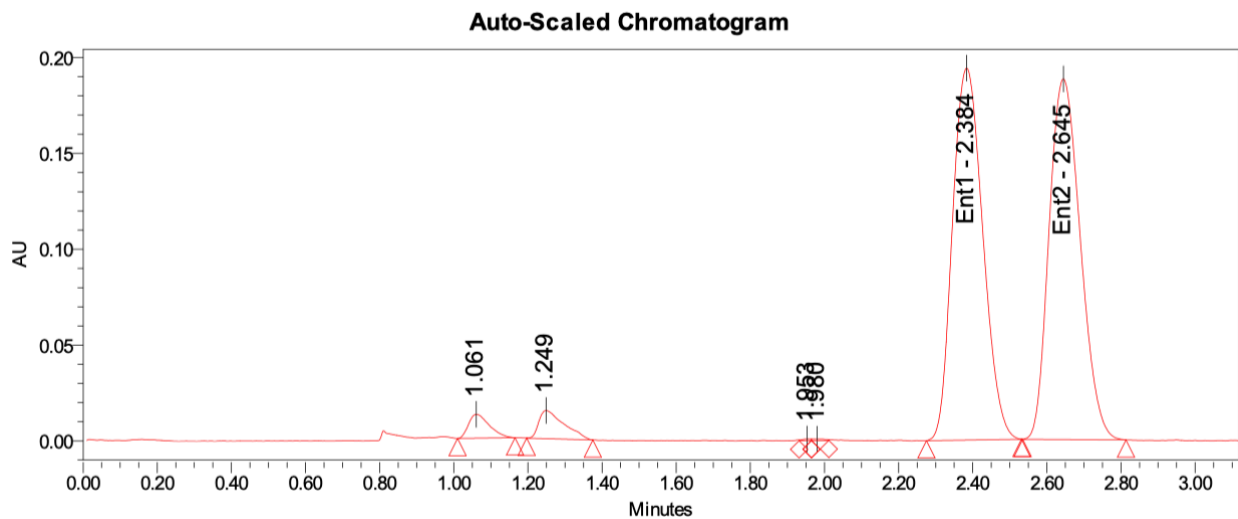
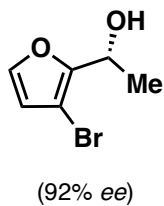
**<sup>1</sup>H NMR** (600 MHz, CD<sub>3</sub>OD)  $\delta$  5.92 – 5.89 (m, 2H), 5.71 (ddd,  $J = 10.0, 4.7, 2.6$  Hz, 1H), 5.07 (d,  $J = 8.9$  Hz, 1H), 4.93 (dd,  $J = 6.2, 3.4$  Hz, 1H), 4.60 (s, 1H), 4.42 (s, 1H), 4.35 – 4.25 (m, 3H), 3.64 (d,  $J = 2.9$  Hz, 1H), 3.36 (dt,  $J = 10.6, 5.3$  Hz, 1H), 3.30 (s, 3H), 2.71 – 2.61 (s, 1H), 2.31 – 2.24 (m, 2H), 2.23 – 2.15 (m, 2H), 2.12 (s, 3H), 2.11 – 2.09 (m, 1H), 1.76 (td,  $J = 10.4, 2.2$  Hz, 1H), 1.41 (d,  $J = 7.0$  Hz, 3H), 1.40 – 1.34 (m, 1H), 1.11 (d,  $J = 7.0$  Hz, 3H), 0.97 (d,  $J = 6.9$  Hz, 3H), 0.84 ppm (d,  $J = 7.2$  Hz, 3H);

**<sup>13</sup>C NMR** (151 MHz, CD<sub>3</sub>OD)  $\delta$  171.9, 158.3, 152.3, 134.0, 126.1, 105.8, 77.3, 75.6, 74.6, 71.5, 69.8, 69.7, 57.4, 51.9, 47.0, 39.2, 39.0, 35.9, 32.4, 32.0, 21.0, 18.7, 18.0, 17.3, 14.5 ppm;

**Optical Rotation:**  $[\alpha]_{\text{D}}^{25} = -8.8^\circ$  ( $c = 0.16$  g / 100 mL, MeOH);

**HRMS** ( $m/z$ ): calc'd for C<sub>30</sub>H<sub>43</sub>N<sub>2</sub>O<sub>10</sub><sup>+</sup> [M+H]<sup>+</sup> 591.2913, found 591.2913.

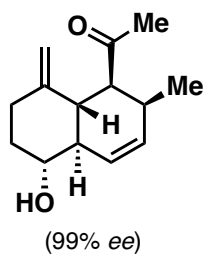
## II) Chiral SFC Results Compound S6



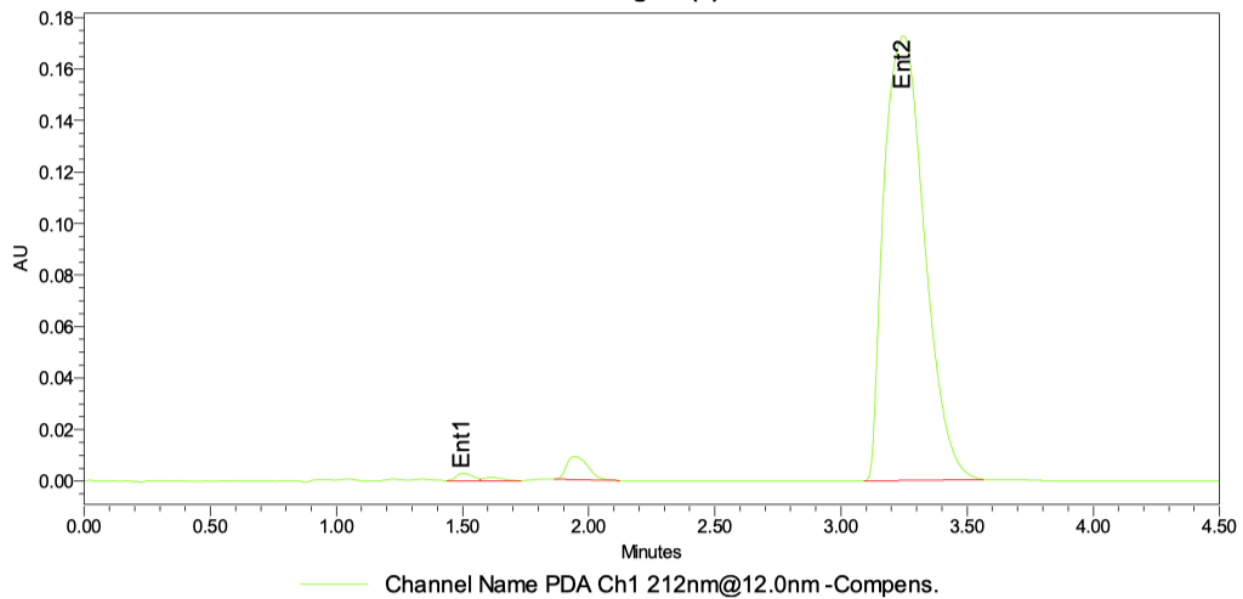
### Area Summarized by Name

|           |       |       |        |         |         |
|-----------|-------|-------|--------|---------|---------|
| JT1-020-P | 50.02 | 49.98 | 0.04   | 1100965 | 1100185 |
| JT1-027-P | 4.22  | 95.78 | -91.57 | 31008   | 704352  |
| JT1-026-P | 4.06  | 95.94 | -91.88 | 21991   | 519563  |

# Compound 23



Chromatogram(s)



Peak Info

|   | Channel Name                   | Name | RT   | Area    | Height (μV) | ent1 | ent2  | ee     |
|---|--------------------------------|------|------|---------|-------------|------|-------|--------|
| 1 | PDA Ch1 212nm@12.0nm -Compens. | Ent1 | 1.50 | 12459   | 2798        | 0.64 | 99.36 | -98.71 |
| 2 | PDA Ch1 212nm@12.0nm -Compens. |      | 1.61 | 5935    | 1223        | 0.64 | 99.36 | -98.71 |
| 3 | PDA Ch1 212nm@12.0nm -Compens. |      | 1.94 | 52939   | 9044        | 0.64 | 99.36 | -98.71 |
| 4 | PDA Ch1 212nm@12.0nm -Compens. | Ent2 | 3.25 | 1920511 | 172689      | 0.64 | 99.36 | -98.71 |

### III) X-ray data of **23** (CCDC# 2086623)

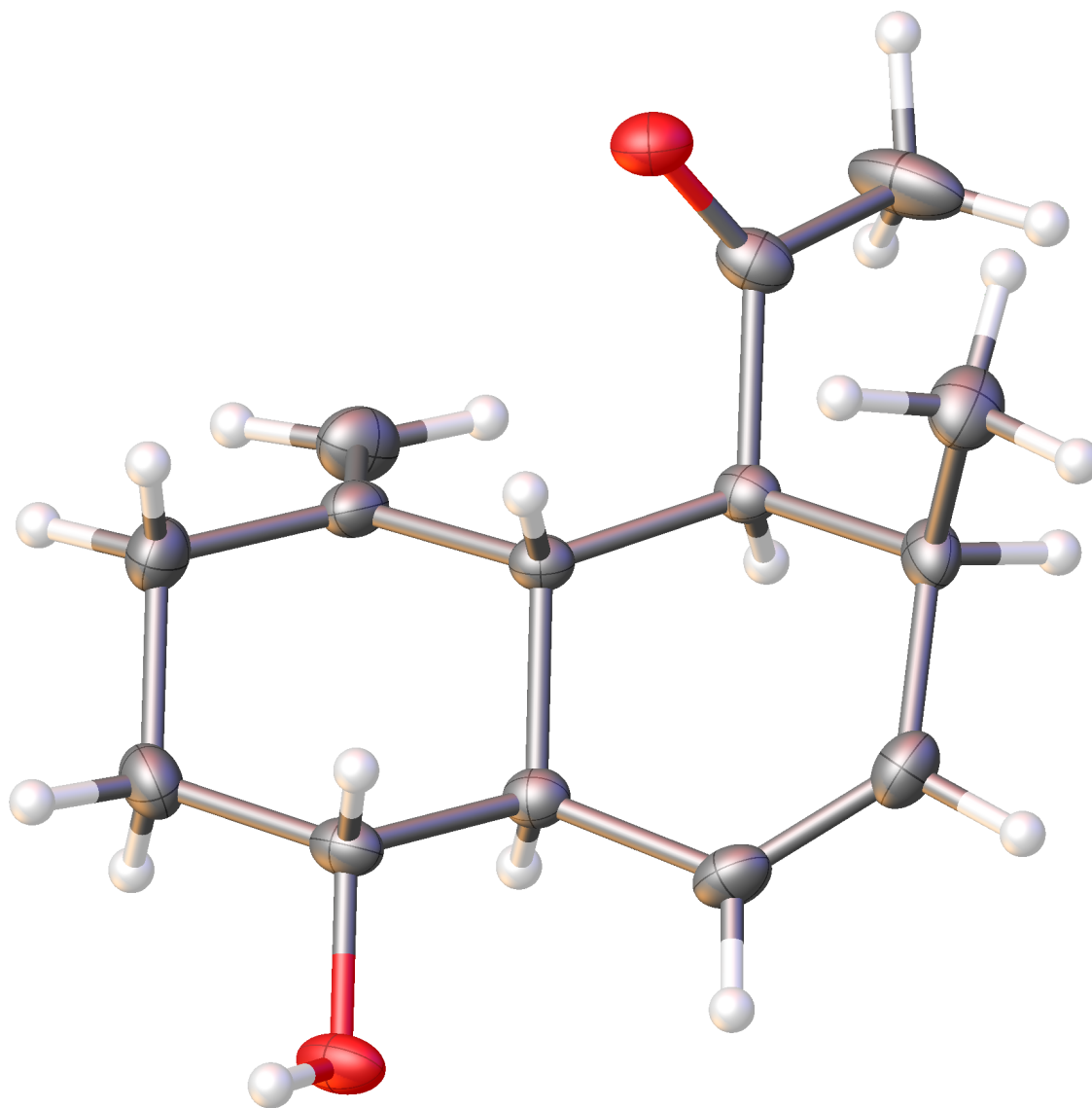
The single crystal X-ray diffraction studies were carried out on a Bruker SMART Apex II CCD diffractometer equipped with Cu K<sub>α</sub> radiation ( $\lambda = 1.54178$ ). Crystals of the subject compound were used as received (grown from Ethylacetate and Pentane). A 0.280 x 0.12 x 0.110 mm colorless block crystal was mounted on a Cryoloop with Paratone oil.

Data were collected in a nitrogen gas stream at 100(2) K using  $\phi$  and  $\omega$  scans. Crystal-to-detector distance was 40 mm using exposure time 2.0, 3.0, and 6.0 second (depending on the  $2\theta$  position) with a scan width of 1.40°. Data collection was 100.0% complete to 67.679° in  $\theta$ . A total of 20851 reflections were collected. 2353 reflections were found to be symmetry independent, with a  $R_{\text{int}}$  of 0.0353. Indexing and unit cell refinement indicated a **Primitive Orthorhombic** lattice. The space group was found to be ***P2<sub>1</sub>2<sub>1</sub>2<sub>1</sub>***. The data were integrated using the Bruker SAINT Software program and scaled using the SADABS software program. Solution by direct methods (SHELXT) produced a complete phasing model consistent with the proposed structure.

All nonhydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All carbon bonded hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014.

Notes: Excellent data and refinement.

Absolute structure parameter 0.07(7) (conclusive)



**Figure S20.** X-ray structure of **23** (CCDC# 2086623)

**Table S2.** Crystal data and structure refinement for **23**.

|                                   |  |          |
|-----------------------------------|--|----------|
| Identification code               | baran786                                       |          |
| Empirical formula                 | C <sub>14</sub> H <sub>20</sub> O <sub>2</sub> |          |
| Formula weight                    | 220.30   |          |
| Temperature                       | 100.0 K  |          |
| Wavelength                        | 1.54178 Å                                      |          |
| Crystal system                    | Orthorhombic                                   |          |
| Space group                       | P2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>  |          |
| Unit cell dimensions              | a = 5.0390(2) Å                                | α = 90°. |
|                                   | b = 14.3672(6) Å                               | β = 90°. |
|                                   | c = 17.1969(8) Å                               | γ = 90°. |
| Volume                            | 1244.99(9) Å <sup>3</sup>                      |          |
| Z                                 | 4  |          |
| Density (calculated)              | 1.175 Mg/m <sup>3</sup>                        |          |
| Absorption coefficient            | 0.604 mm <sup>-1</sup>                         |          |
| F(000)                            | 480  |          |
| Crystal size                      | 0.28 x 0.12 x 0.11 mm <sup>3</sup>             |          |
| Theta range for data collection   | 4.009 to 70.245°.                              |          |
| Index ranges                      | -6 ≤ h ≤ 6, -17 ≤ k ≤ 17, -21 ≤ l ≤ 19         |          |
| Reflections collected             | 20851  |          |
| Independent reflections           | 2353 [R(int) = 0.0353]                         |          |
| Completeness to theta = 67.679°   | 100.0 %  |          |
| Absorption correction             | Semi-empirical from equivalents                |          |
| Max. and min. transmission        | 0.6620 and 0.5685                              |          |
| Refinement method                 | Full-matrix least-squares on F <sup>2</sup>    |          |
| Data / restraints / parameters    | 2353 / 0 / 148                                 |          |
| Goodness-of-fit on F <sup>2</sup> | 1.049  |          |
| Final R indices [I > 2σ(I)]       | R1 = 0.0332, wR2 = 0.0864                      |          |
| R indices (all data)              | R1 = 0.0351, wR2 = 0.0881                      |          |
| Absolute structure parameter      | 0.07(7)  |          |
| Extinction coefficient            | n/a  |          |
| Largest diff. peak and hole       | 0.184 and -0.184 e.Å <sup>-3</sup>             |          |

**Table S3.** Atomic coordinates ( $\times 10^4$ ) and equivalent isotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ) for **23**.  $U(\text{eq})$  is defined as one-third of the trace of the orthogonalized  $U^{ij}$  tensor.

|       | x       | y       | z       | $U(\text{eq})$ |
|-------|---------|---------|---------|----------------|
| O(1)  | 3551(3) | 7155(1) | 5205(1) | 26(1)          |
| O(2)  | 6019(3) | 3026(1) | 6525(1) | 25(1)          |
| C(1)  | 4519(4) | 6221(1) | 5285(1) | 21(1)          |
| C(2)  | 4569(4) | 5742(1) | 4496(1) | 26(1)          |
| C(3)  | 5324(4) | 4707(1) | 4557(1) | 26(1)          |
| C(4)  | 3666(4) | 4224(1) | 5164(1) | 21(1)          |
| C(5)  | 3896(3) | 4699(1) | 5948(1) | 17(1)          |
| C(6)  | 2751(3) | 5690(1) | 5854(1) | 18(1)          |
| C(7)  | 2438(4) | 6178(1) | 6620(1) | 23(1)          |
| C(8)  | 2494(4) | 5744(1) | 7298(1) | 24(1)          |
| C(9)  | 2959(4) | 4719(1) | 7408(1) | 21(1)          |
| C(10) | 2621(3) | 4183(1) | 6626(1) | 18(1)          |
| C(11) | 2069(4) | 3518(1) | 5004(1) | 28(1)          |
| C(12) | 5670(4) | 4581(1) | 7796(1) | 29(1)          |
| C(13) | 3789(4) | 3212(1) | 6732(1) | 22(1)          |
| C(14) | 2069(4) | 2521(1) | 7150(2) | 40(1)          |

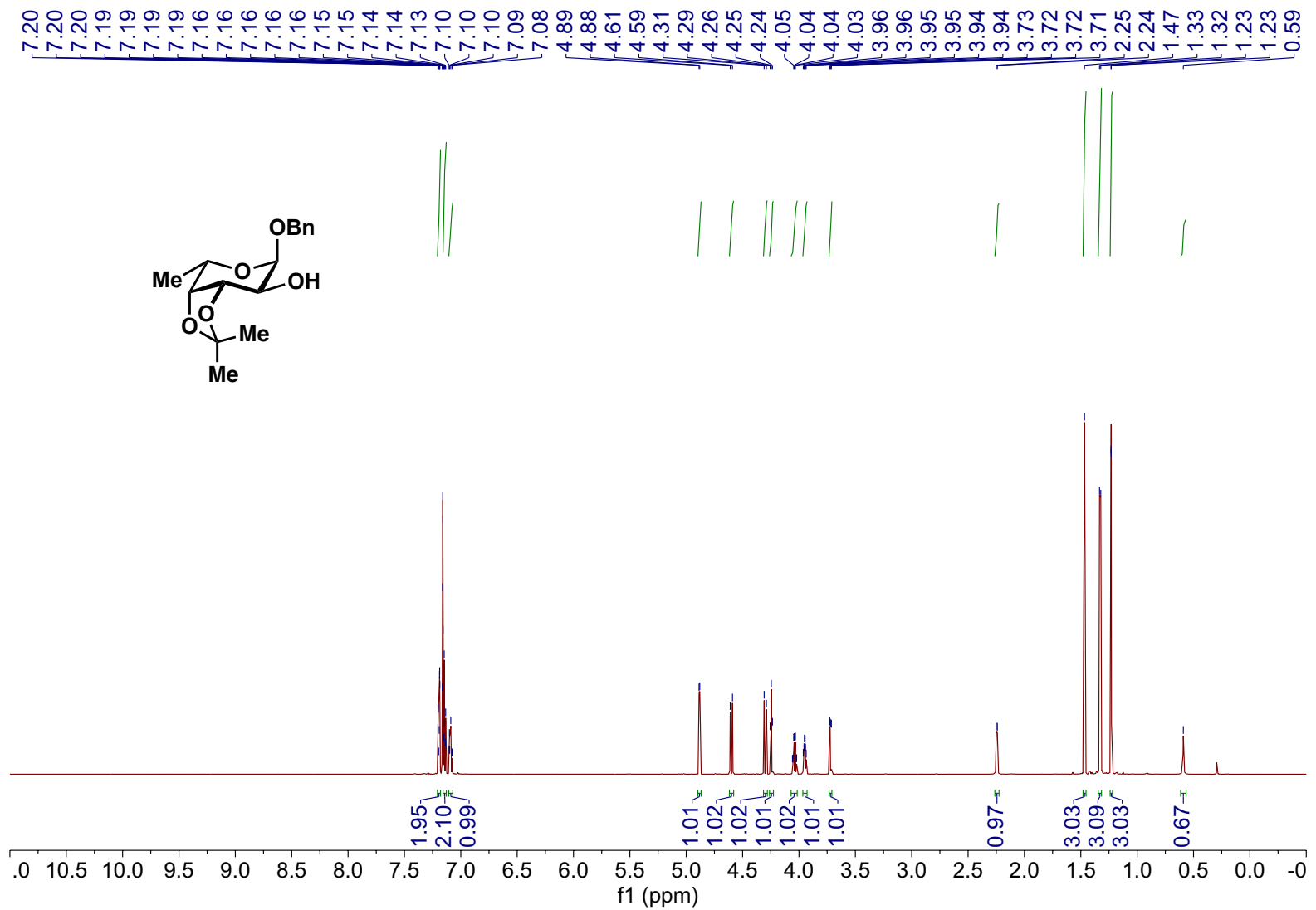
#### IV) References:

- [1] Qin, T.; Cornella, J.; Li, C.; Malins, L.; Edwards, J. T.; Kawamura, S.; Maxwell, B. D.; Eastgate, M. D.; Baran, P. S. *Science* **2016**, *352*, 801.
- [2] Yu, L.-F., Hu, H.-N., Nan, F.-J. *J. Org. Chem.* **2011**, *76*,1448.
- [3] Pelly, S. C.; Parkinson, C. J.; van Otterlo, W. A. L.; de Koning, C. B. *J. Org. Chem.* **2005**, *70*, 10474.
- [4] Mackman, R. L.; Steadman, V. A.; Dean, D. K. *et. al. J. Med. Chem.* **2018**, *61*, 9473.
- [5] Yao, Q.; Yuan, C. *J. Org. Chem.* **2013**, *78*, 6962.
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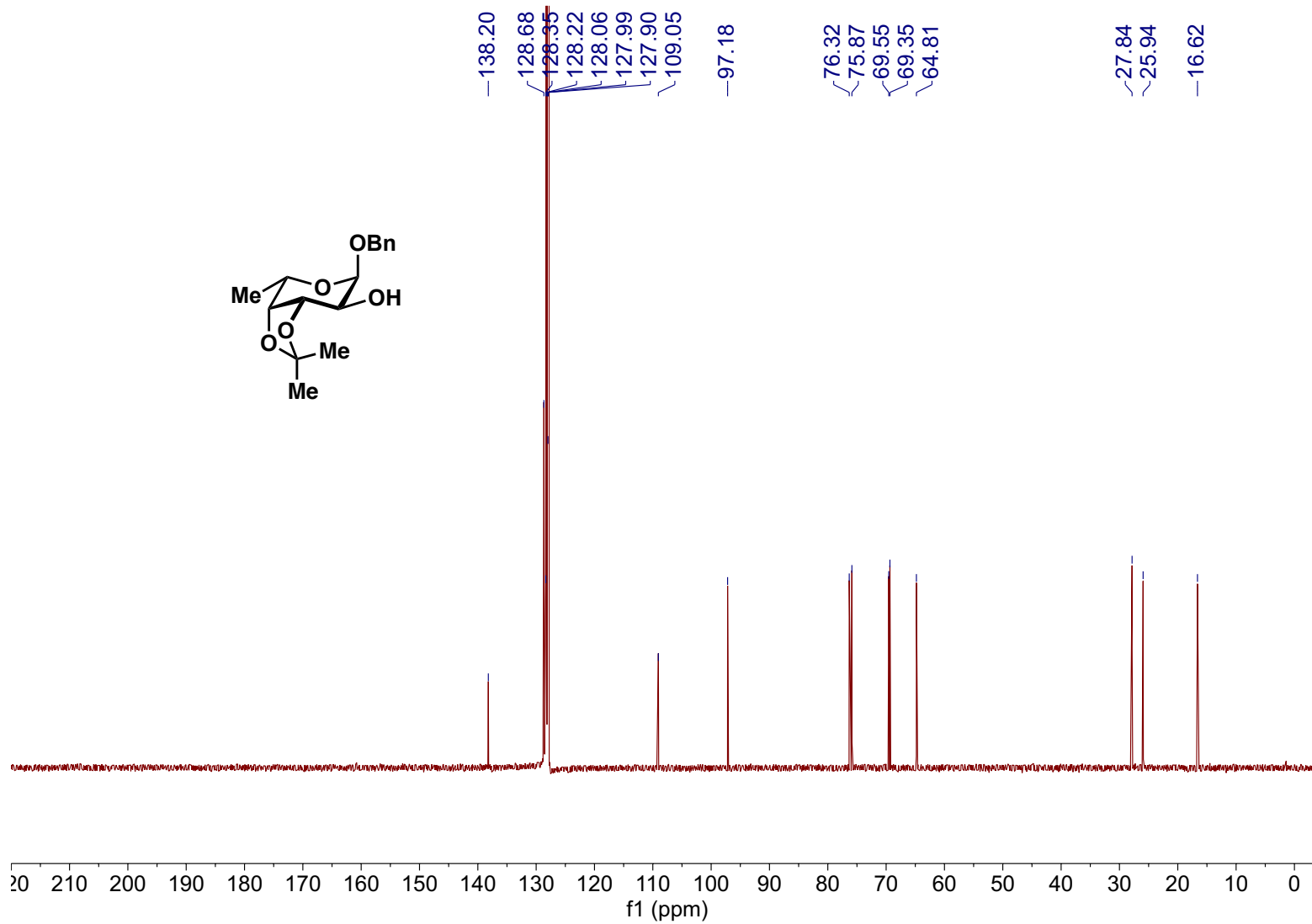
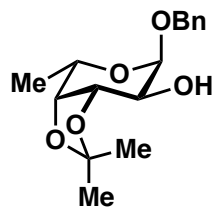


## V) NMR Spectra

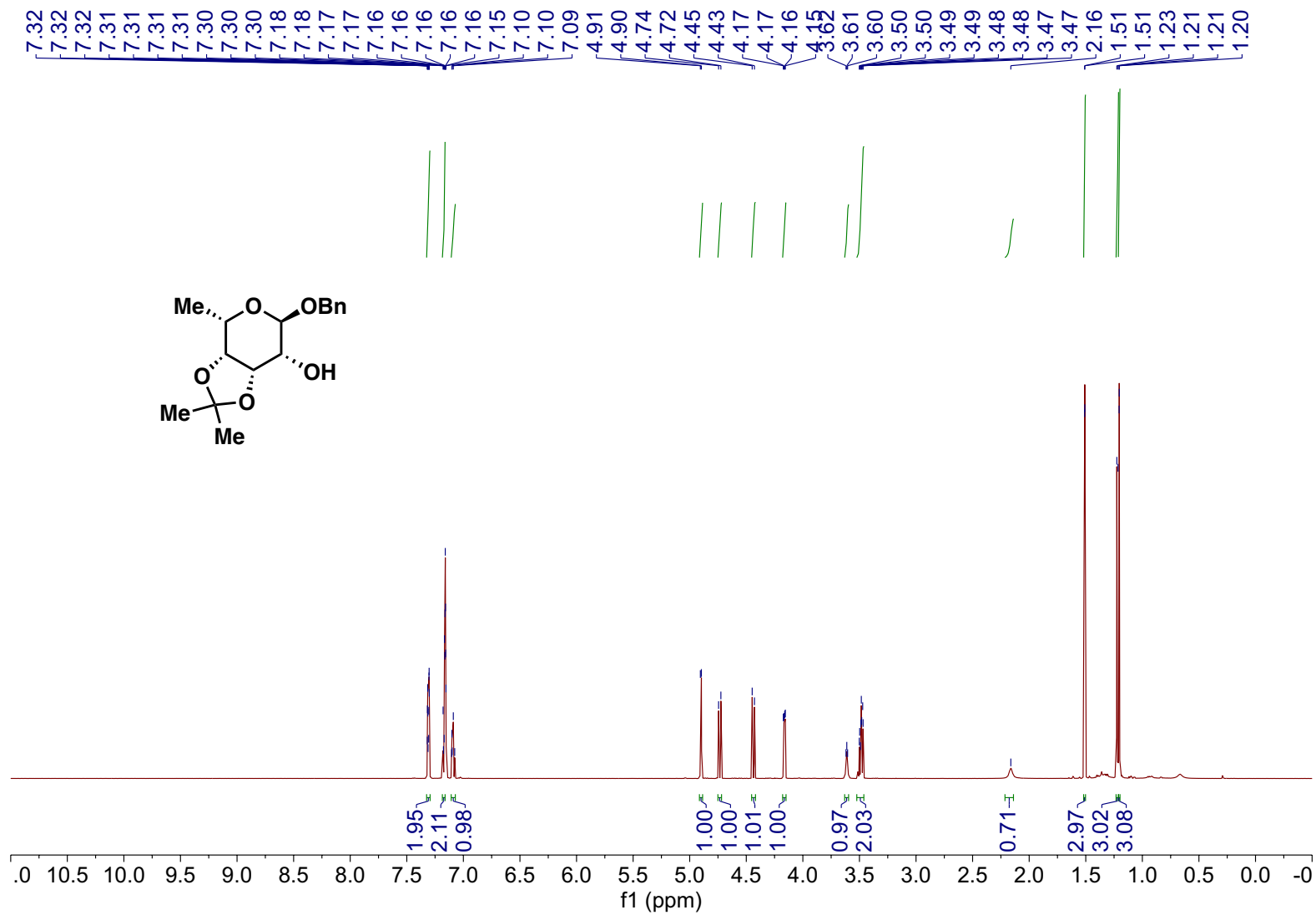
<sup>1</sup>H NMR of **8**



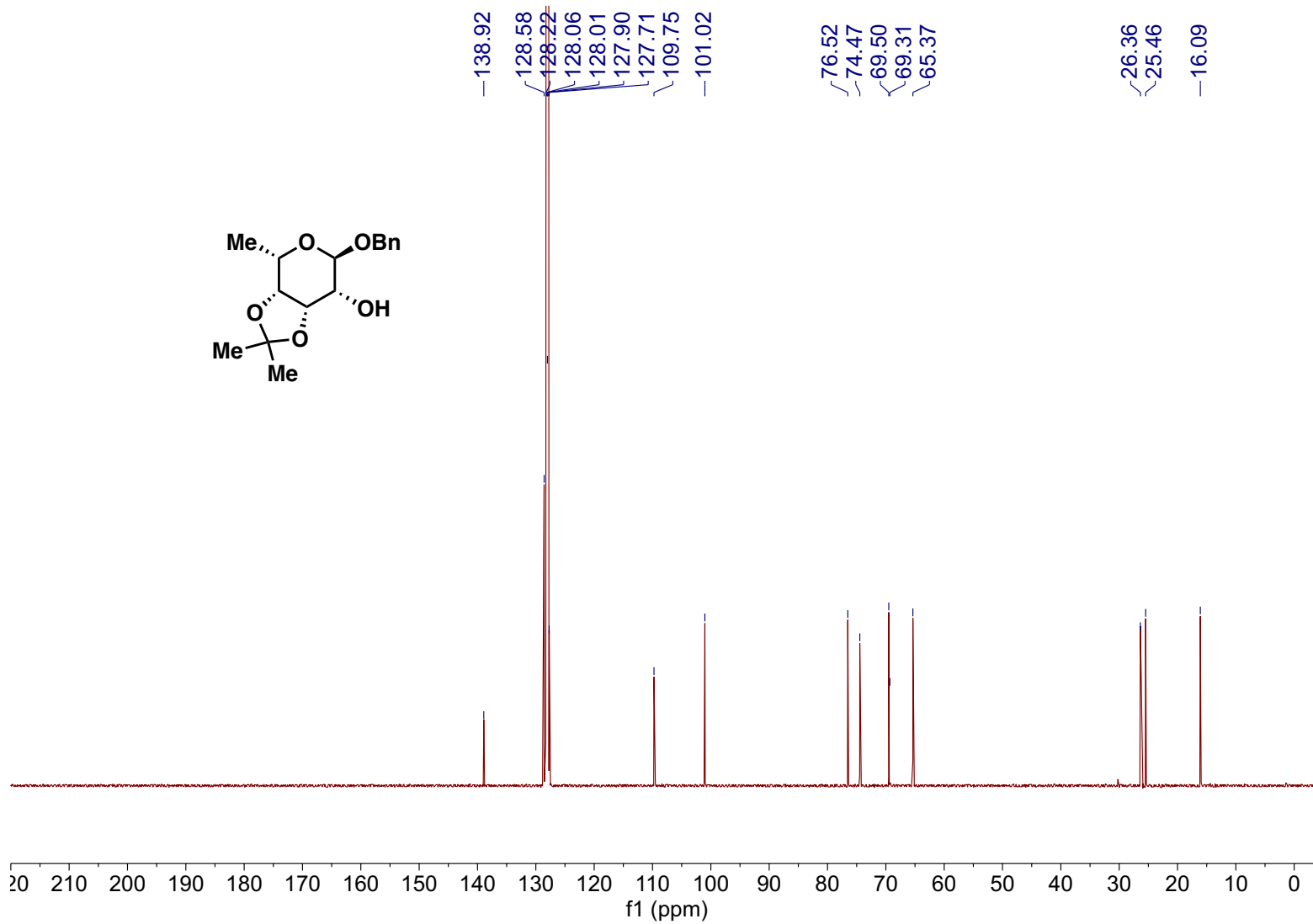
<sup>13</sup>C NMR of **8**



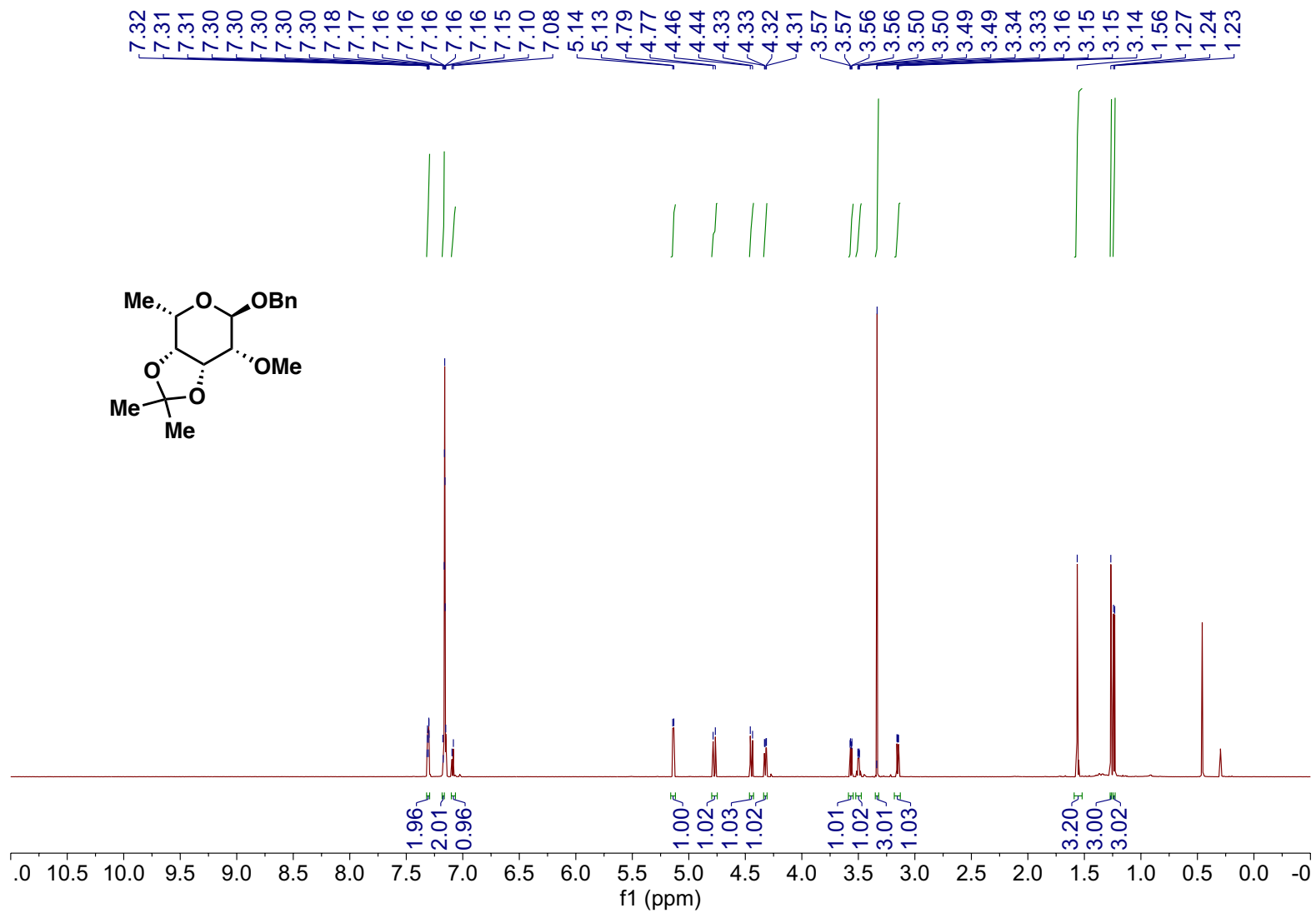
<sup>1</sup>H NMR of 9



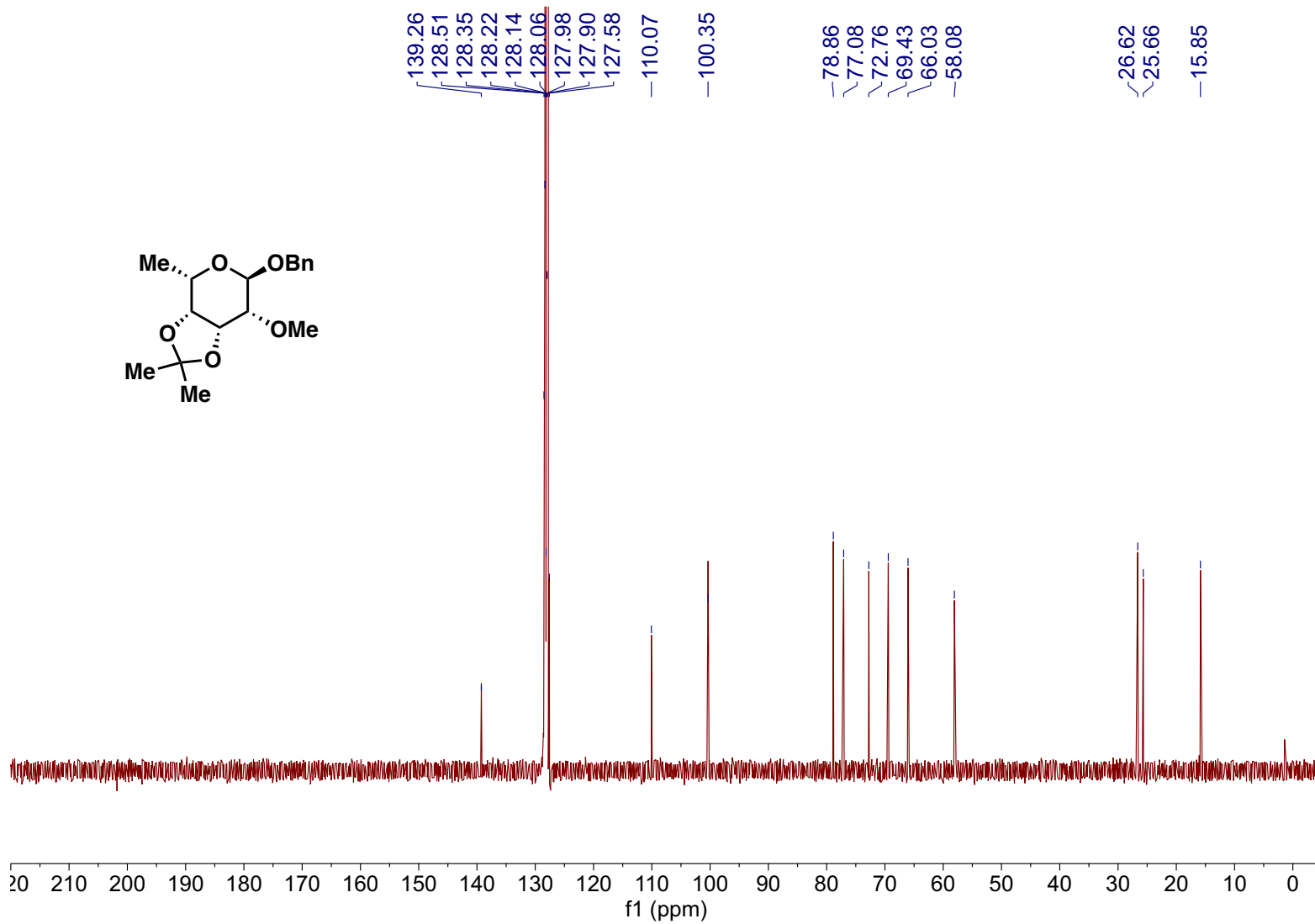
<sup>13</sup>C NMR of **9**



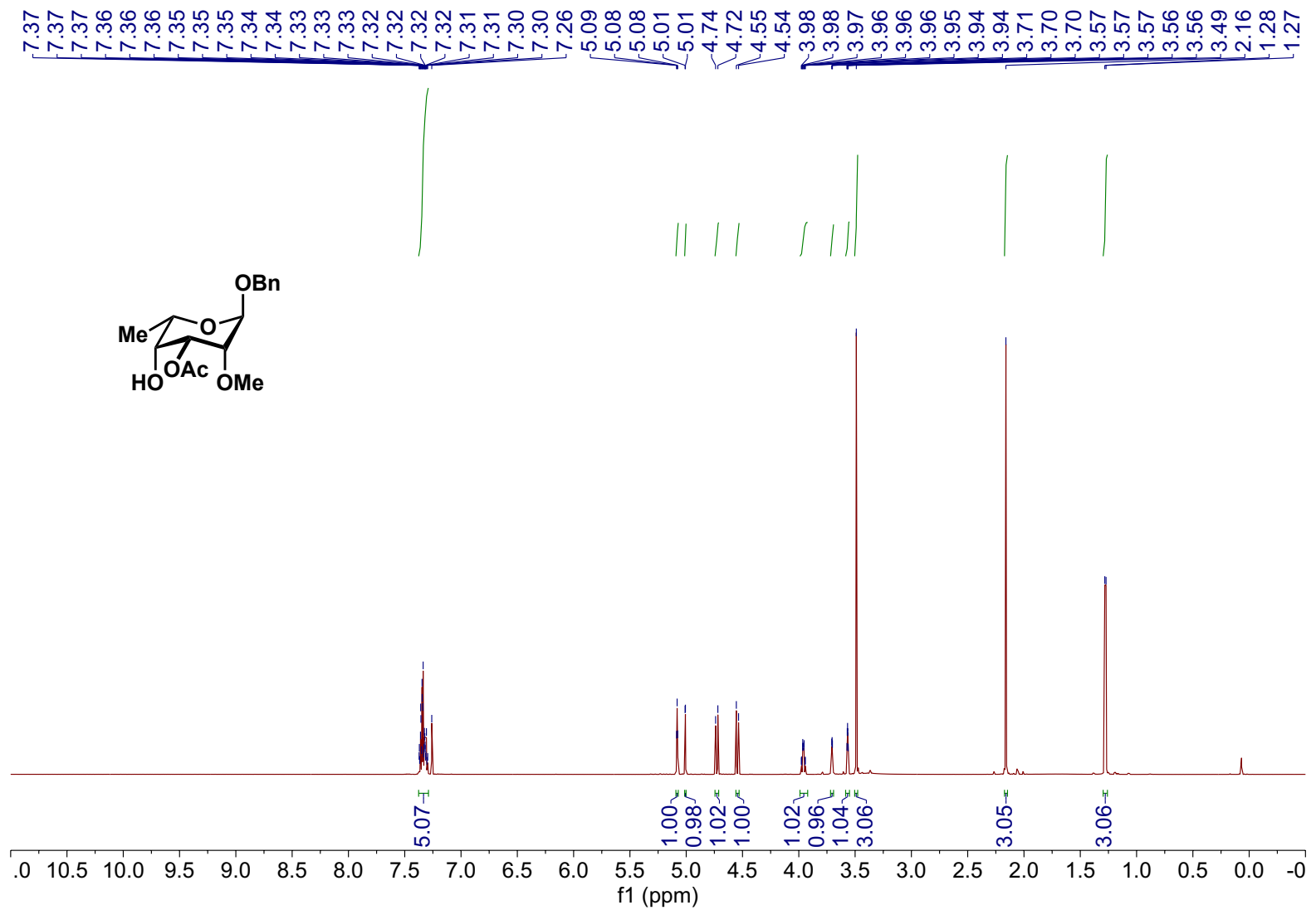
<sup>1</sup>H NMR of 10



<sup>13</sup>C NMR of **10**

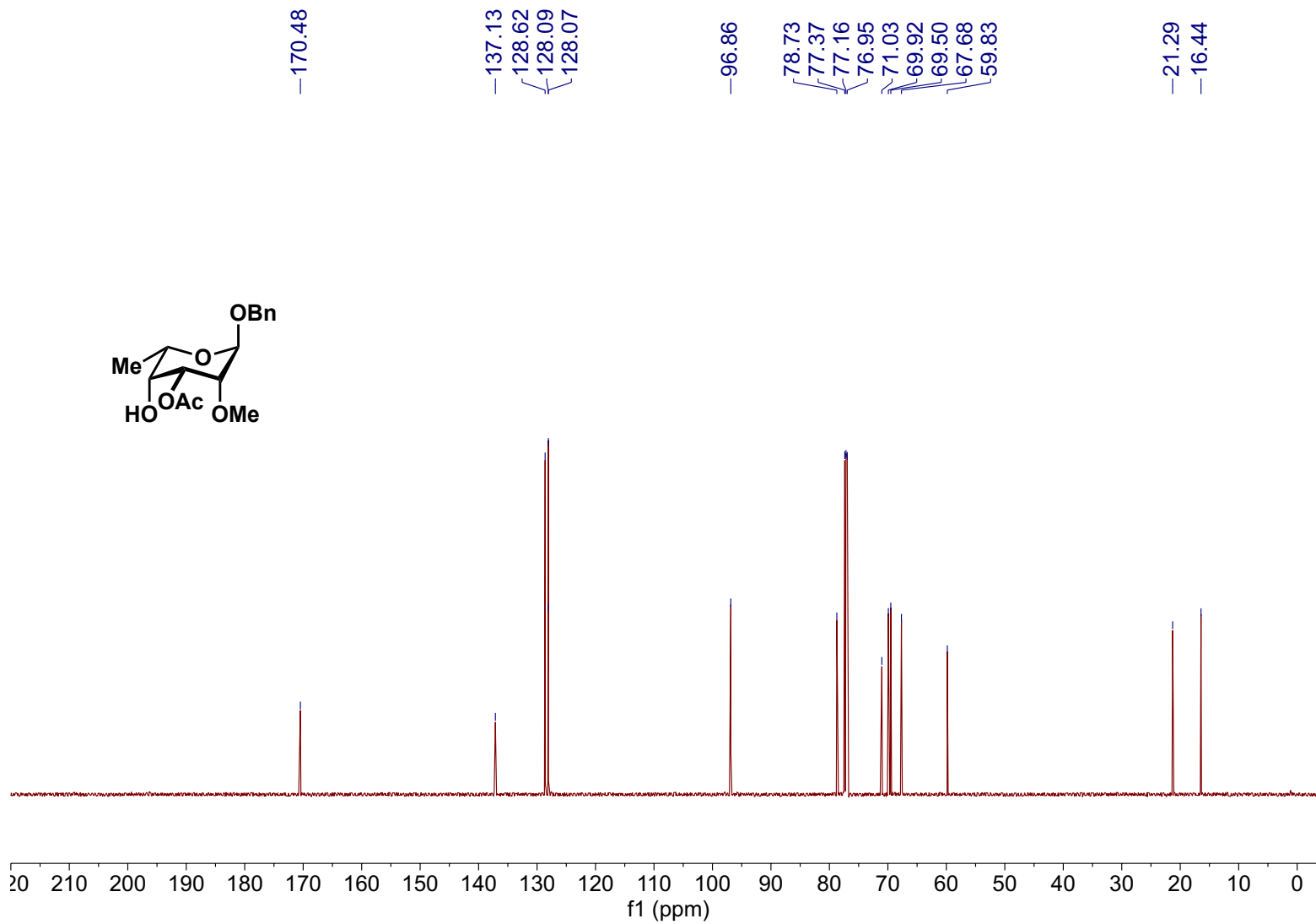


<sup>1</sup>H NMR of 11

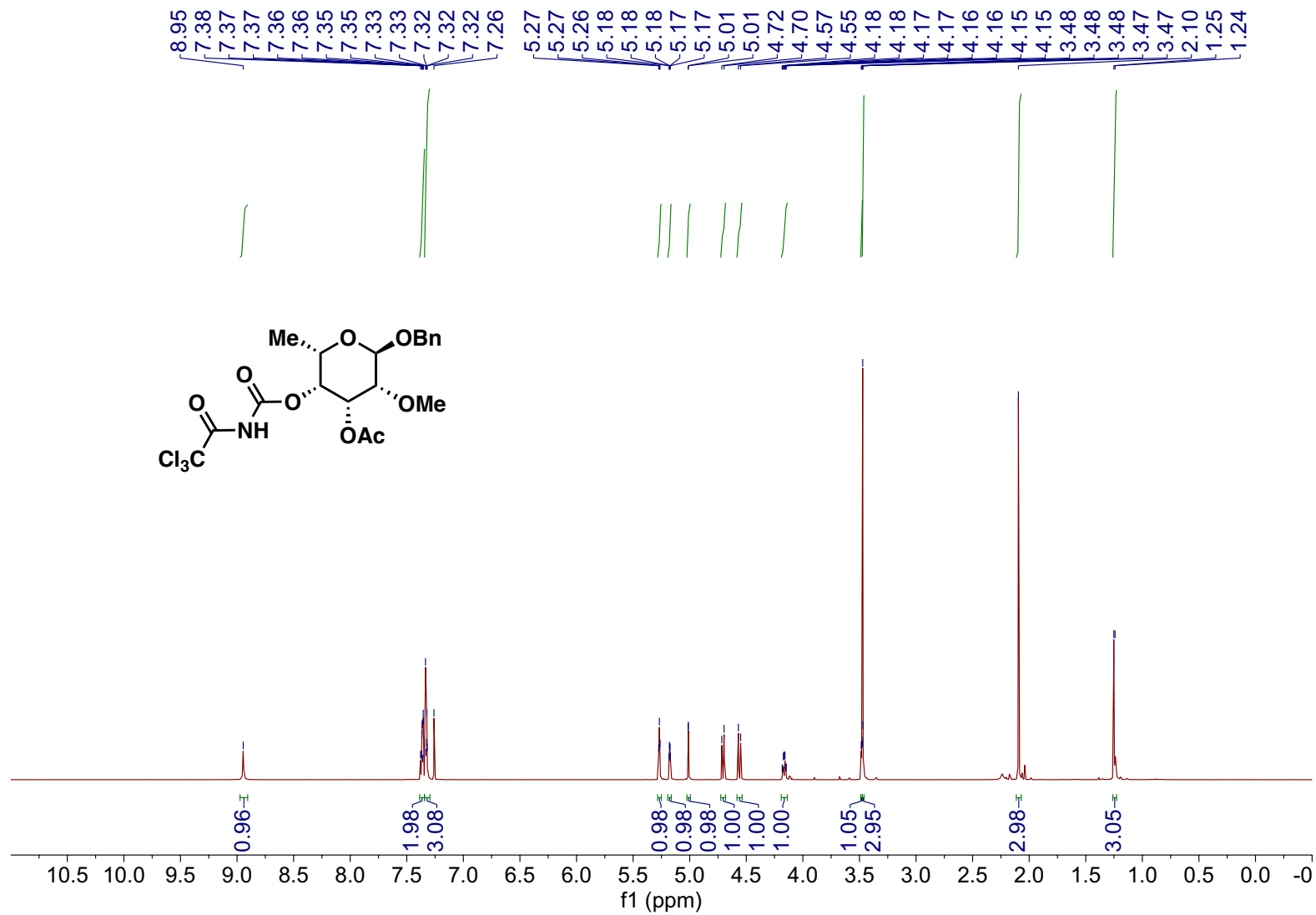




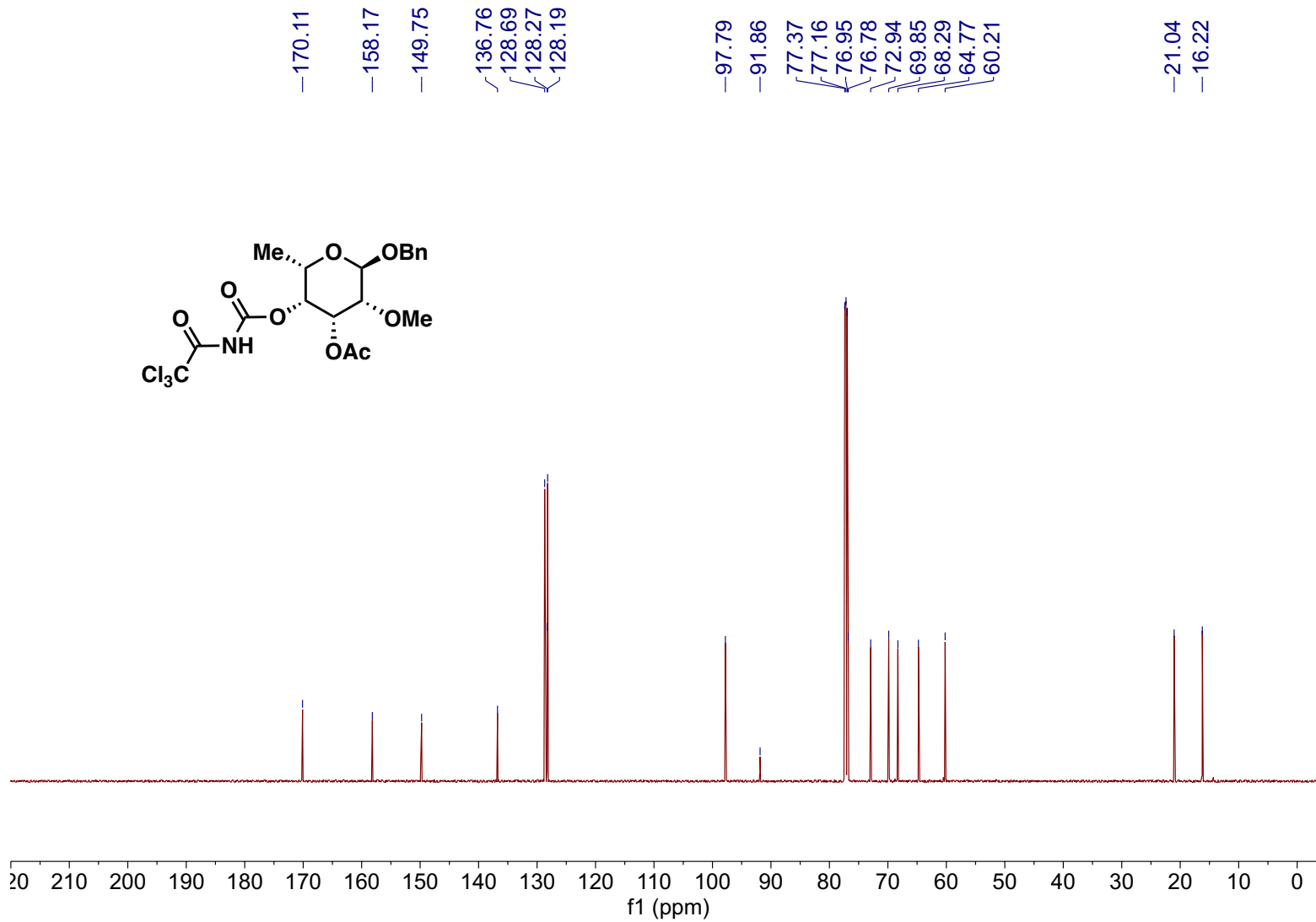
<sup>13</sup>C NMR of **11**



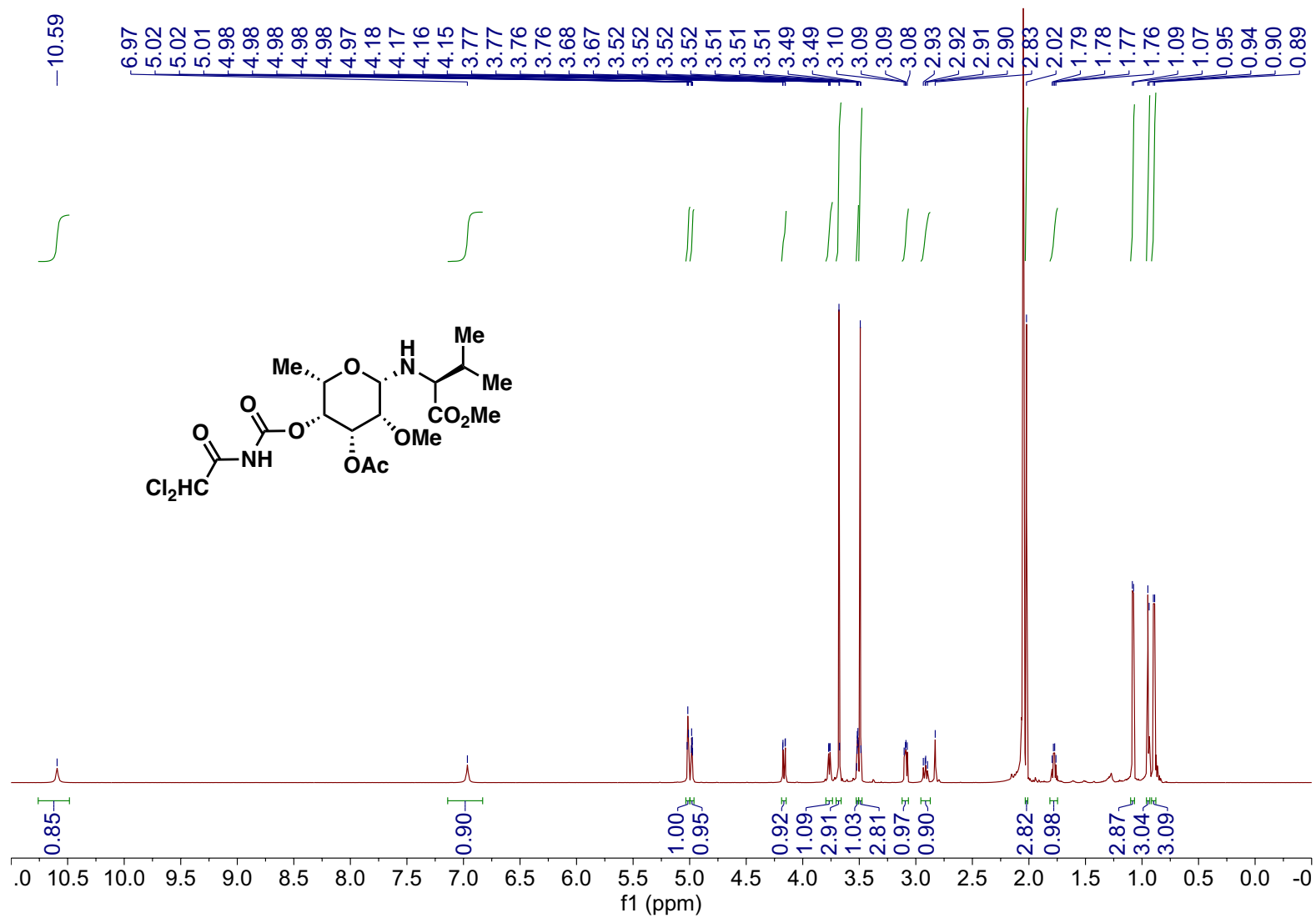
<sup>1</sup>H NMR of 13



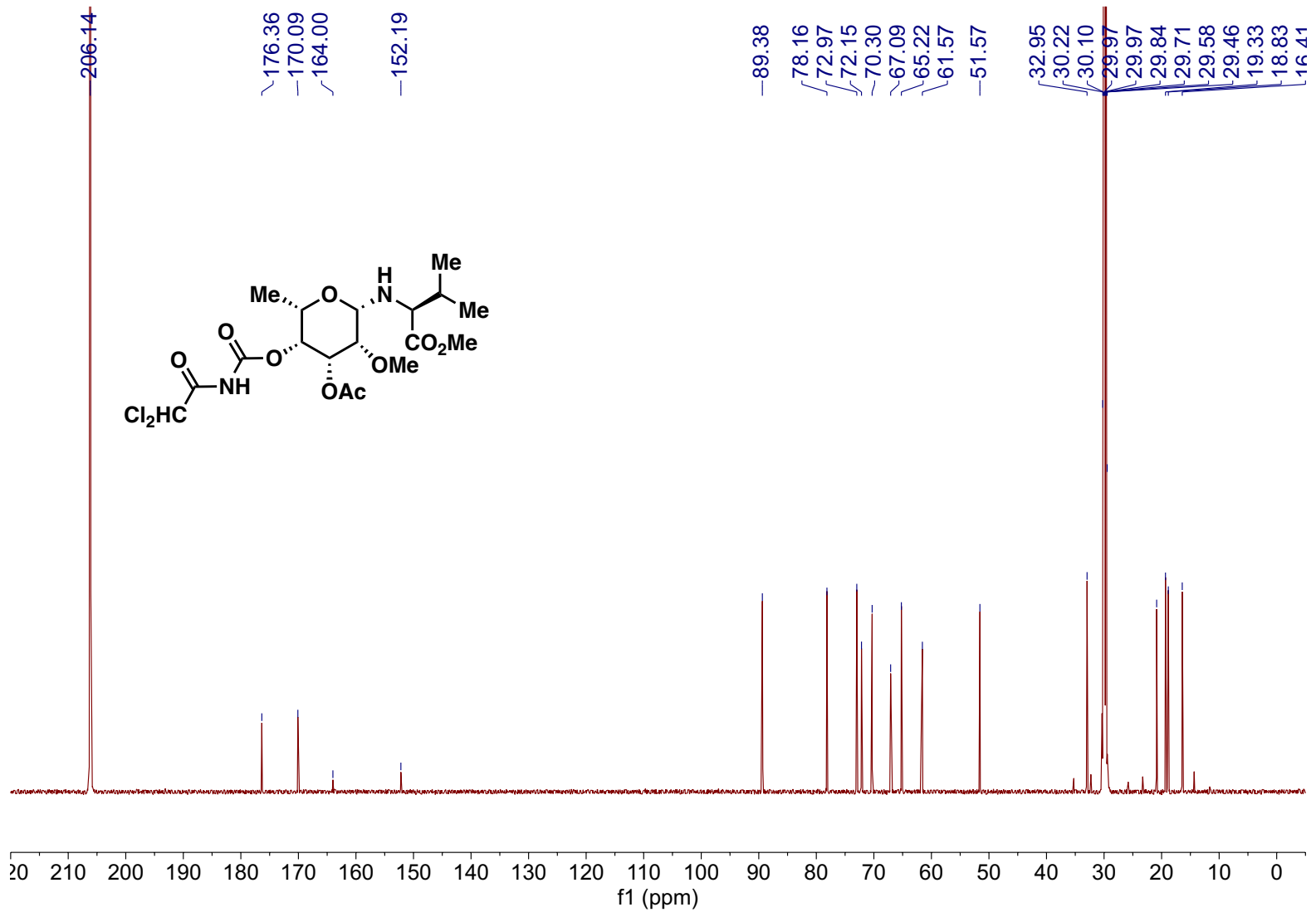
<sup>13</sup>C NMR of **13**



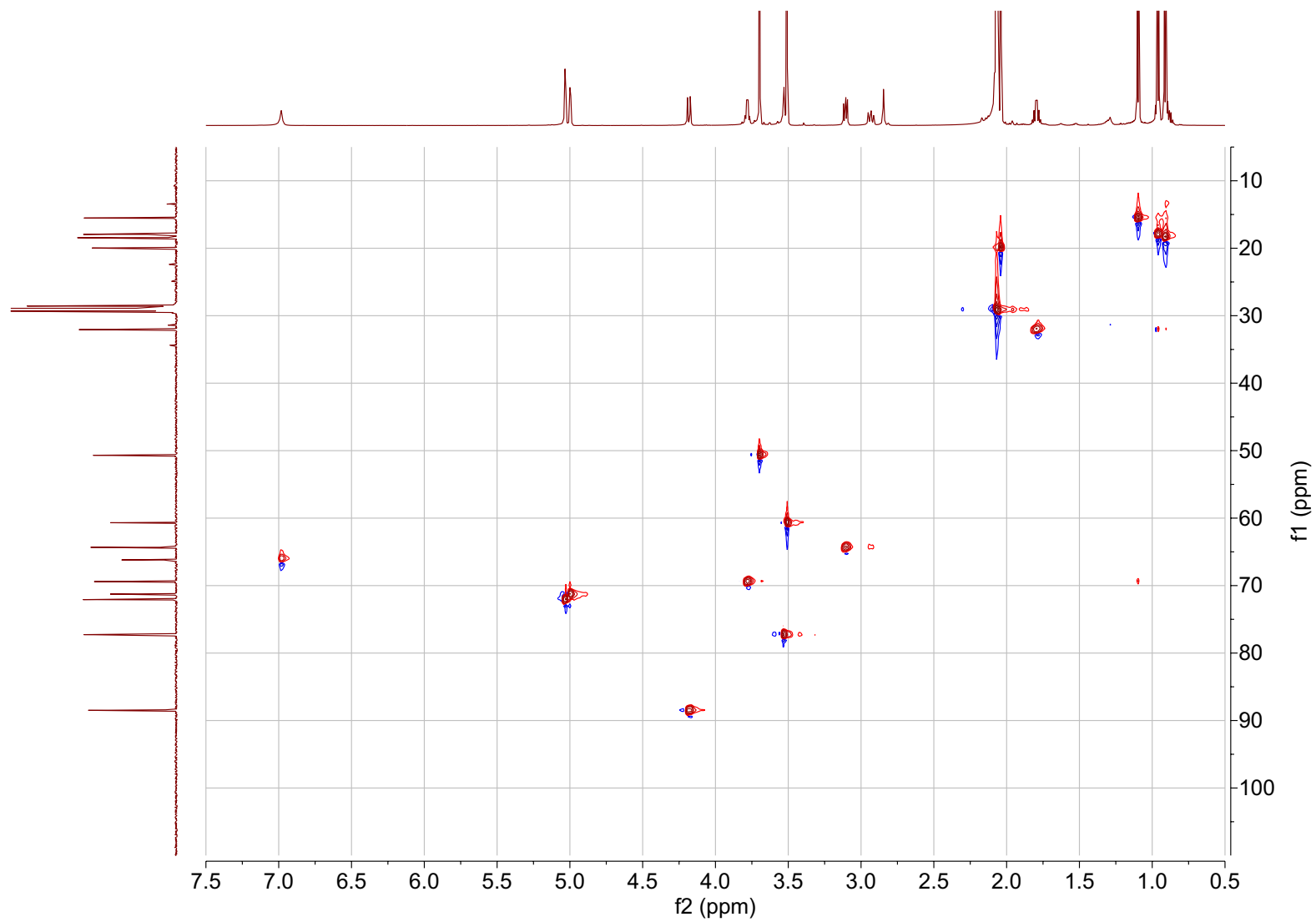
<sup>1</sup>H NMR of 14



<sup>13</sup>C NMR of **14**

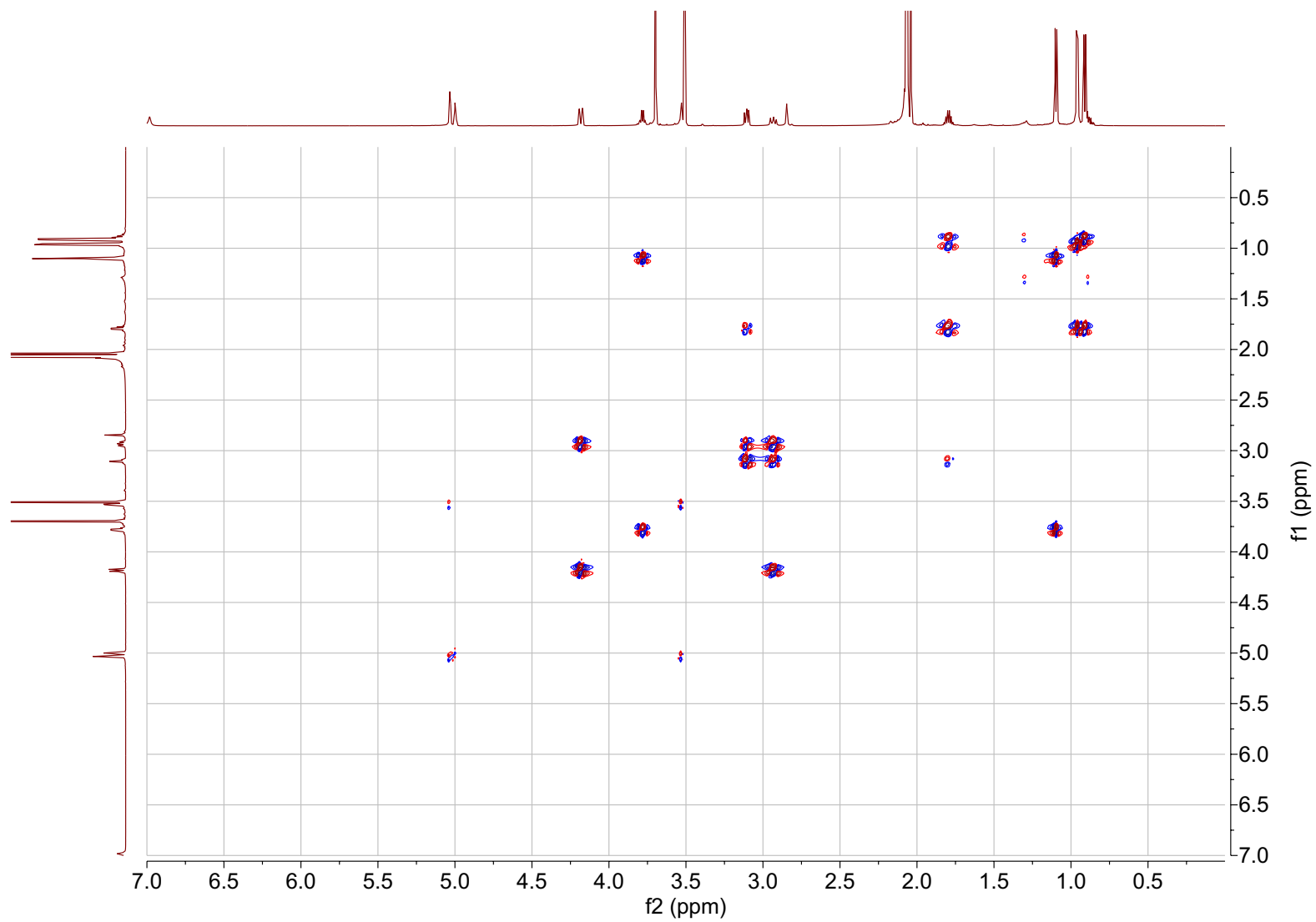


HSQC of 14



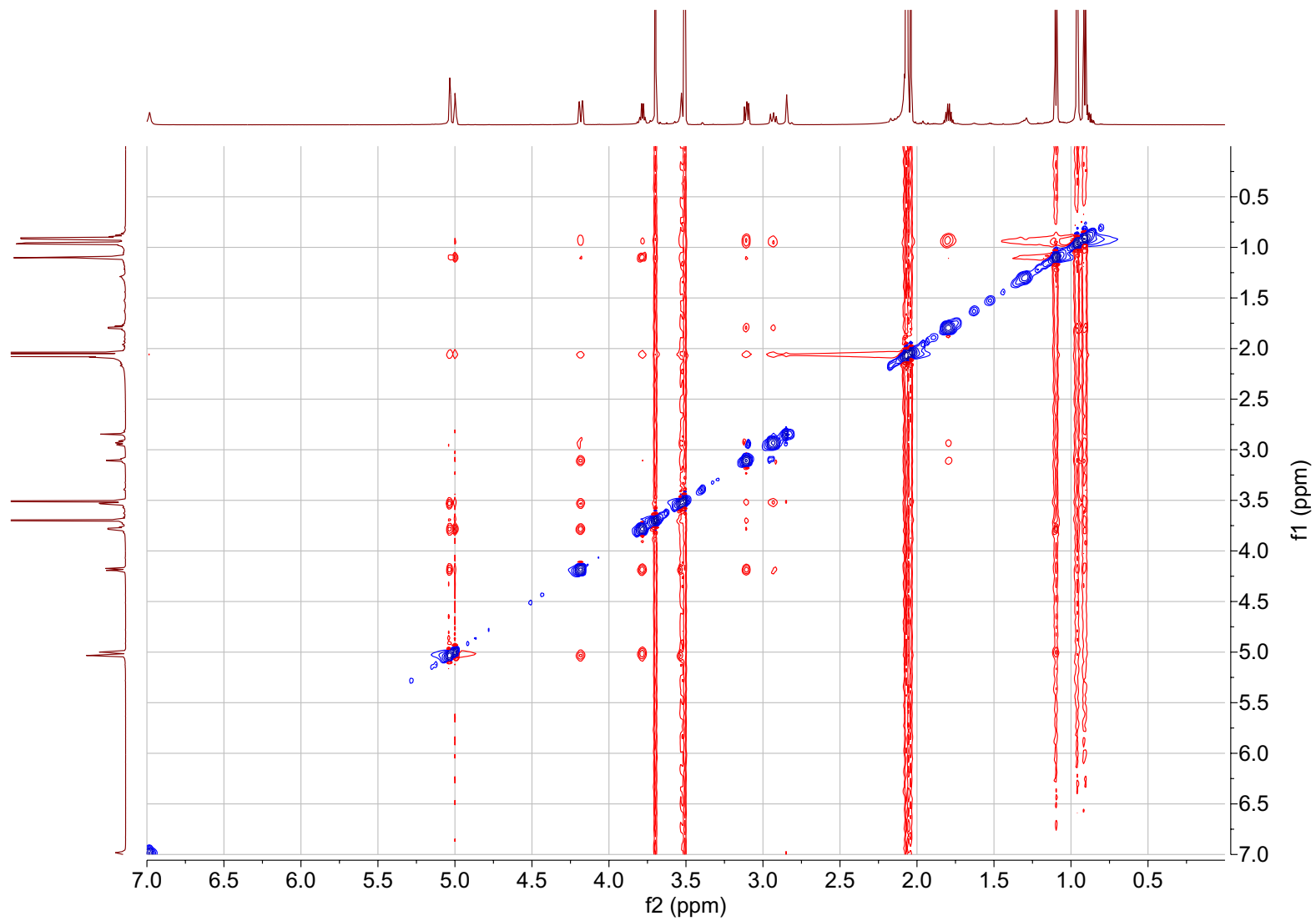
S101

COSY of 14



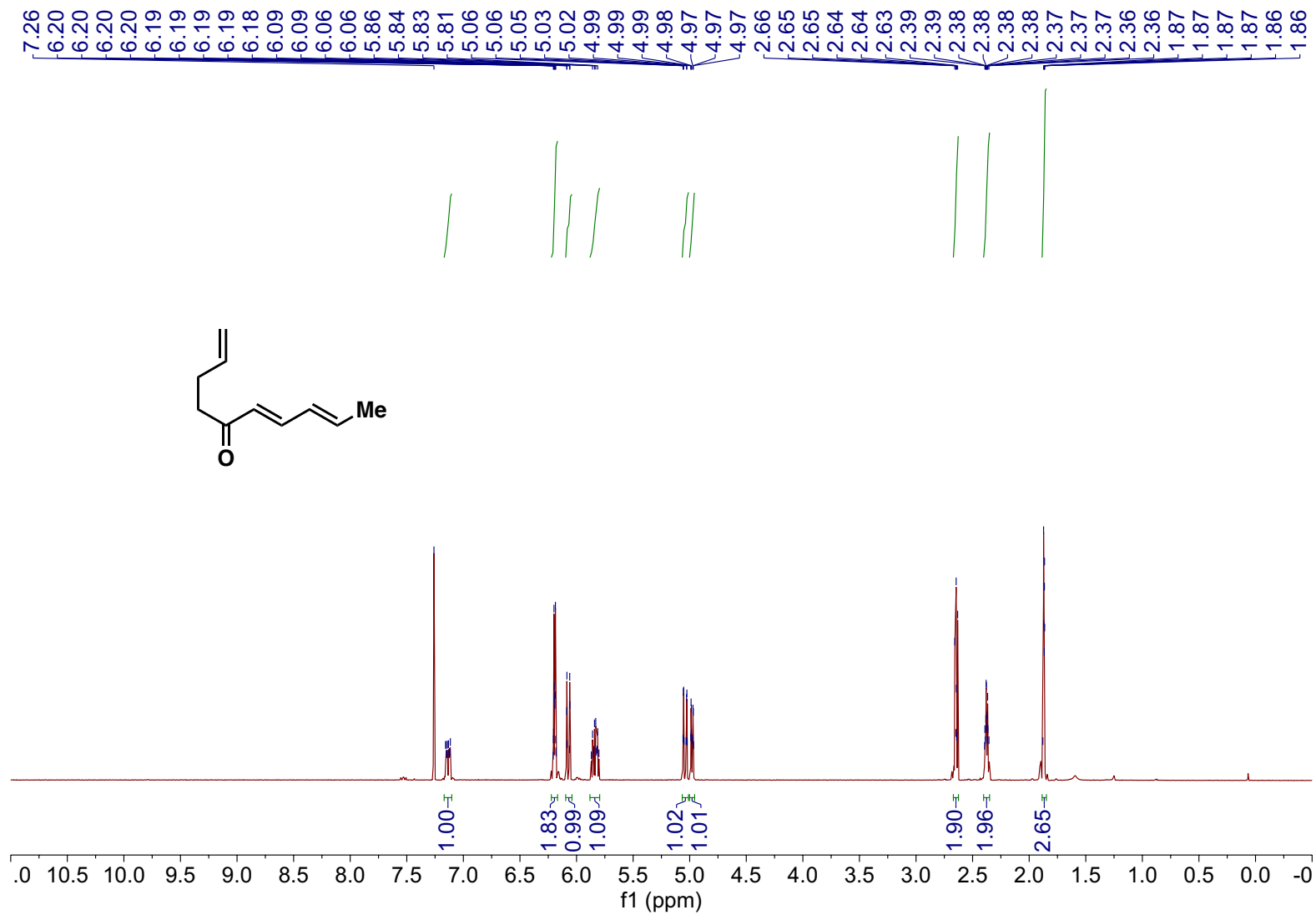
S102

NOESY of 14

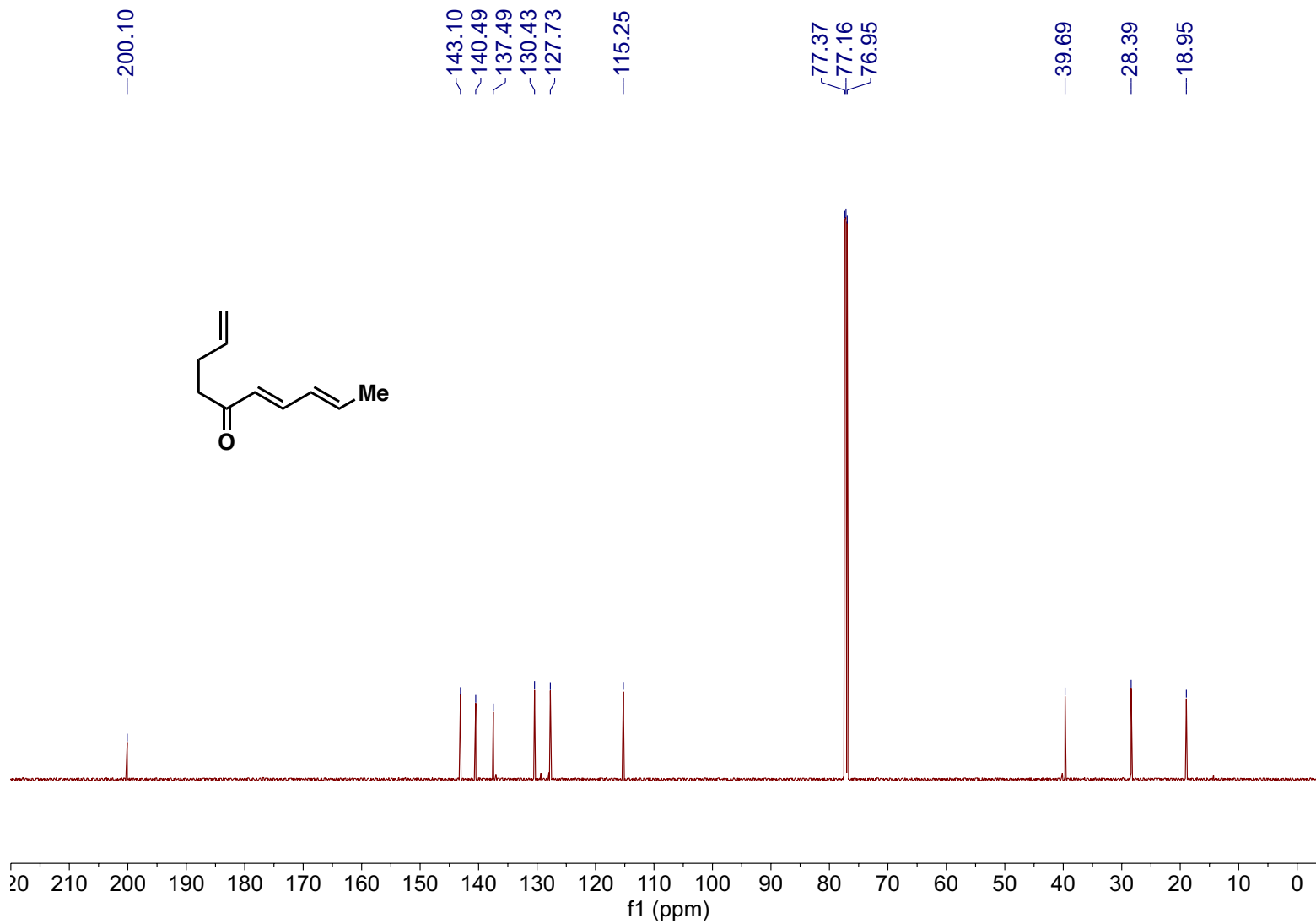




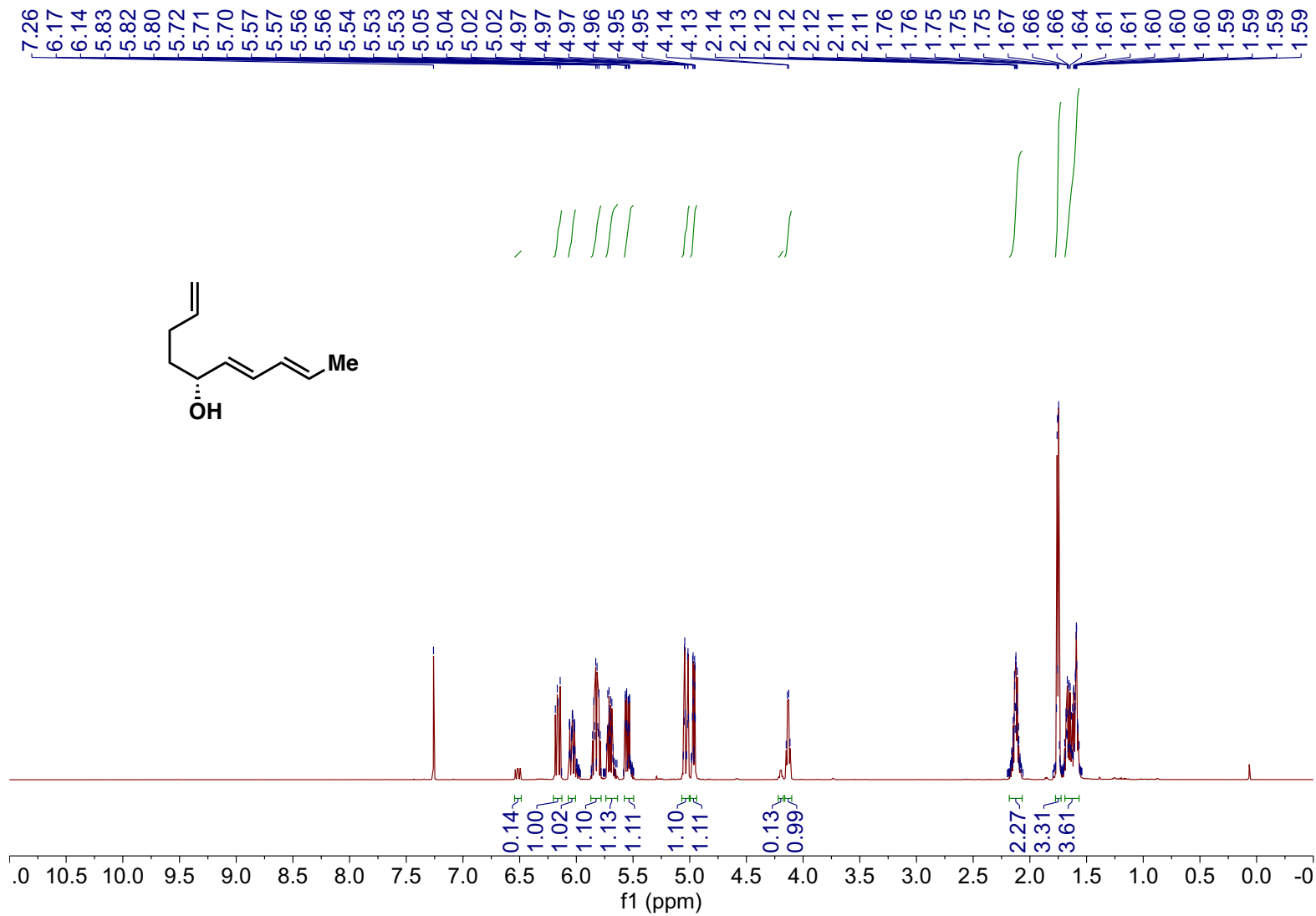
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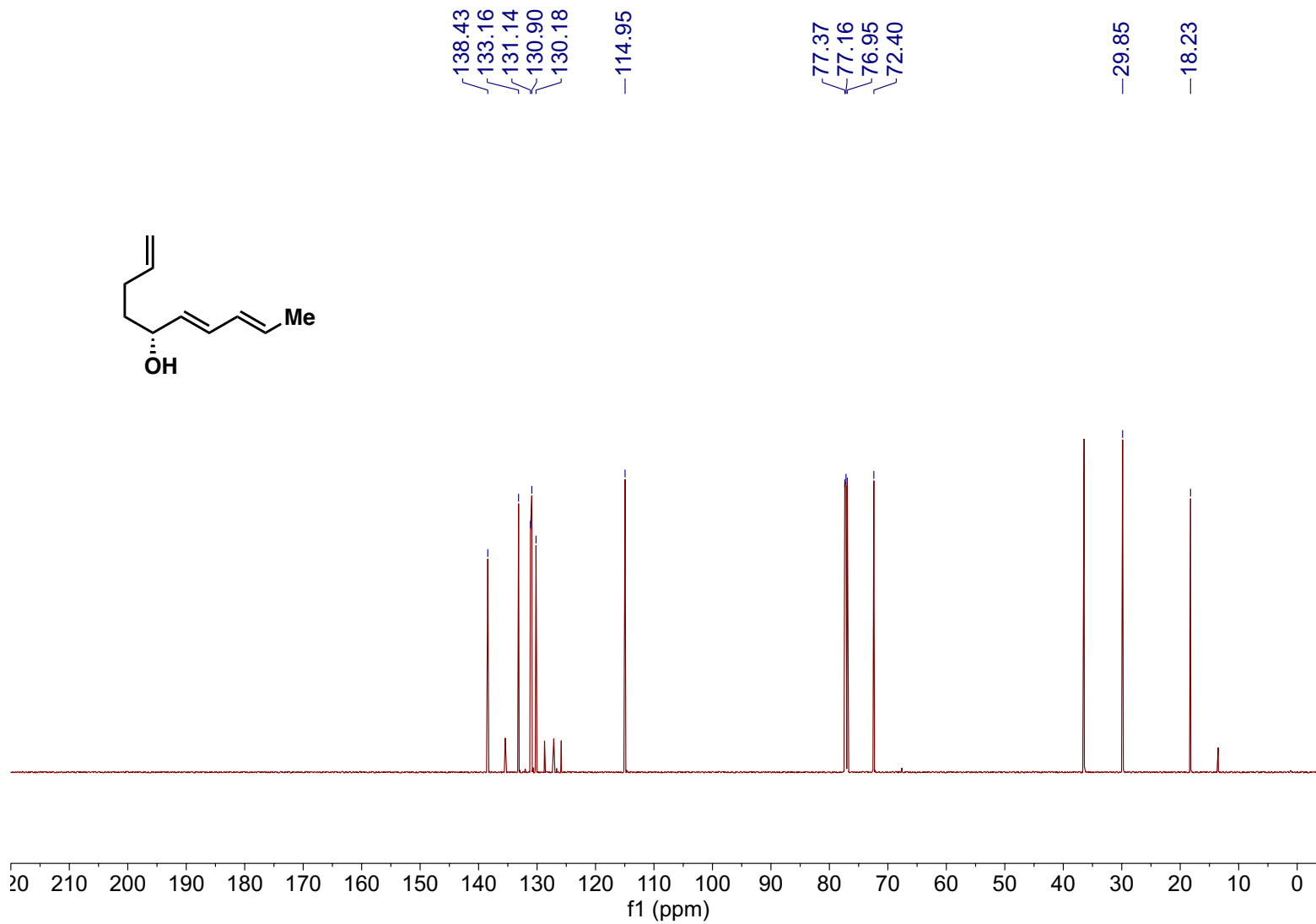
<sup>13</sup>C NMR of S1



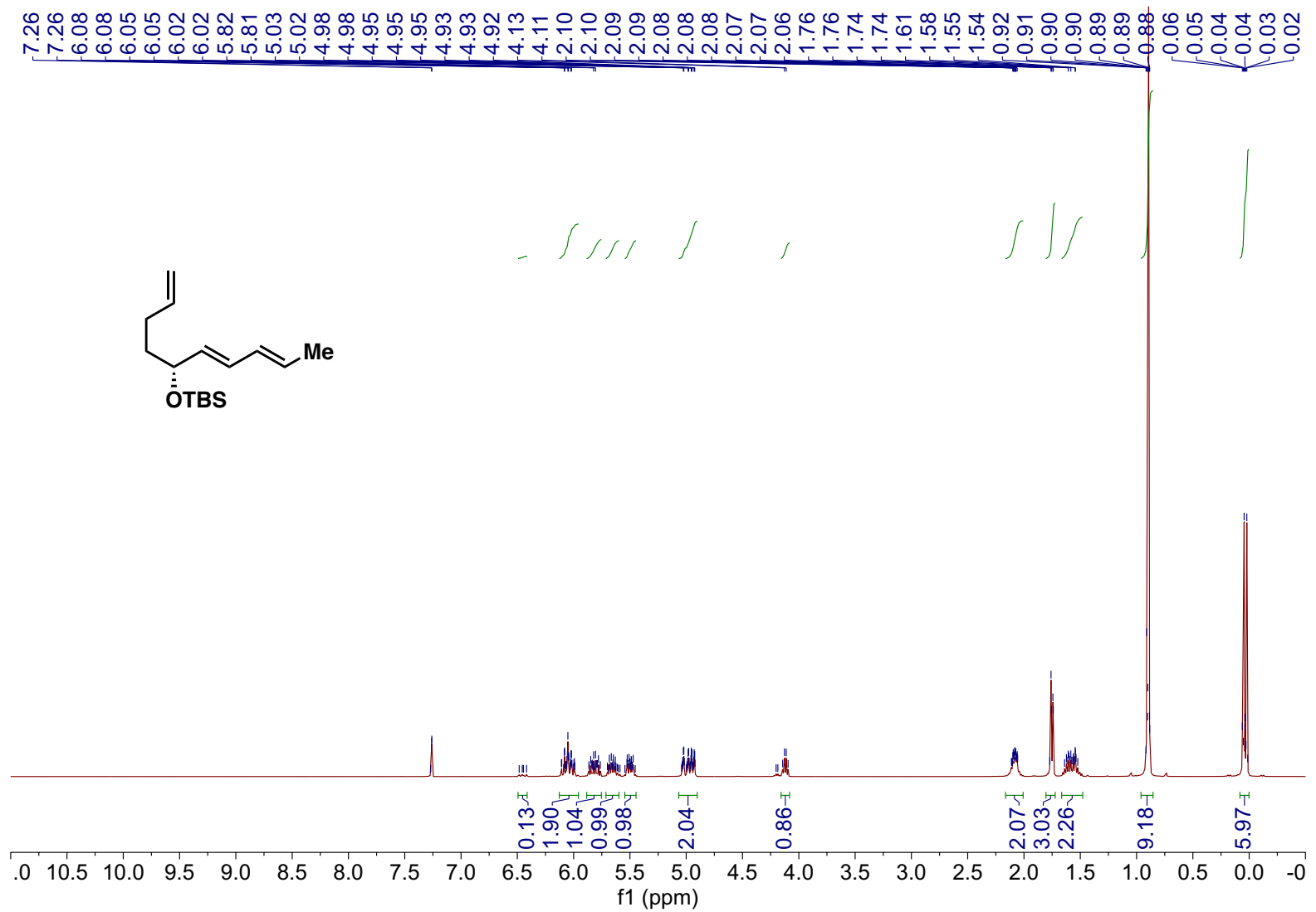
<sup>1</sup>H NMR of S2



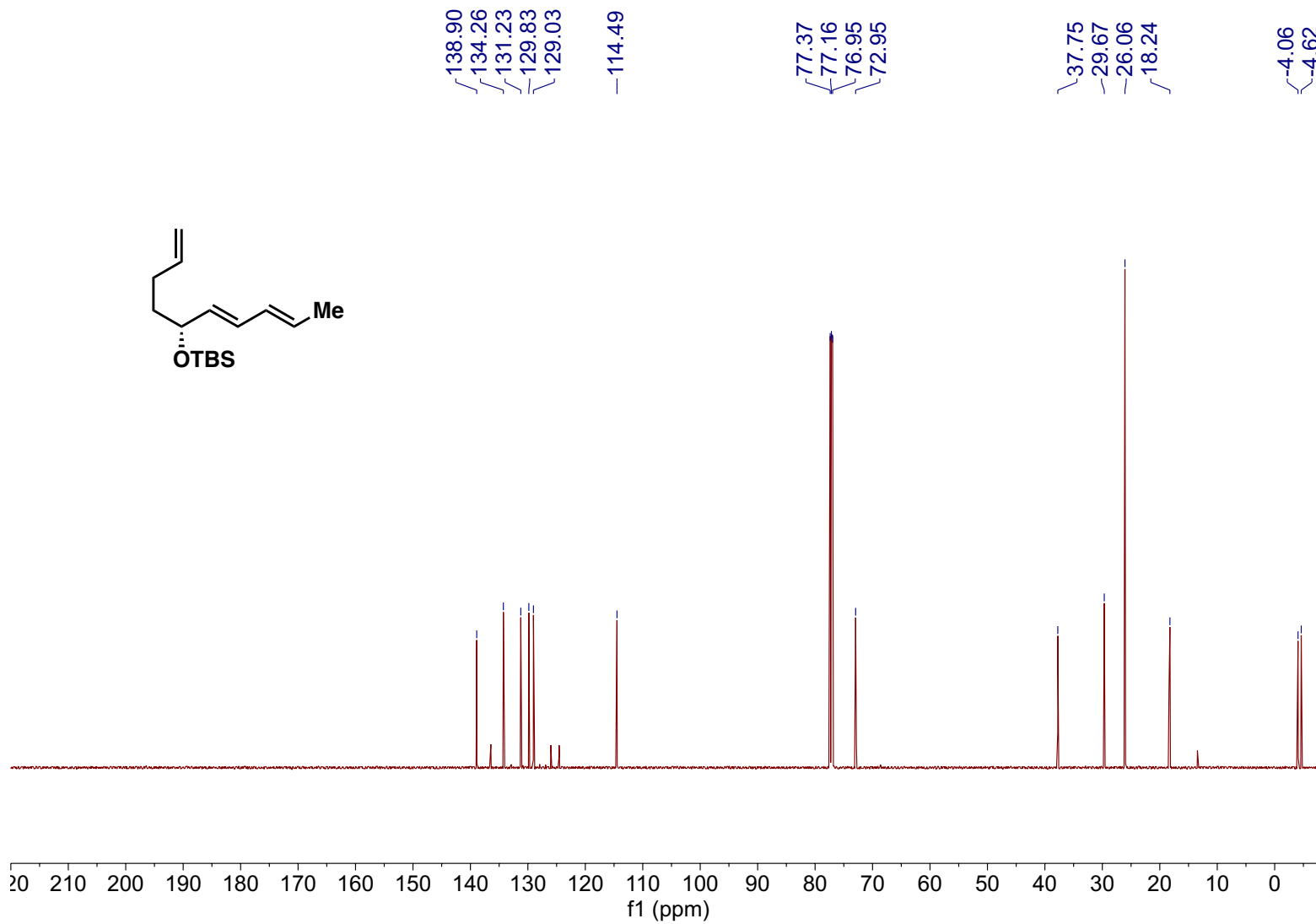
<sup>13</sup>C NMR of S2



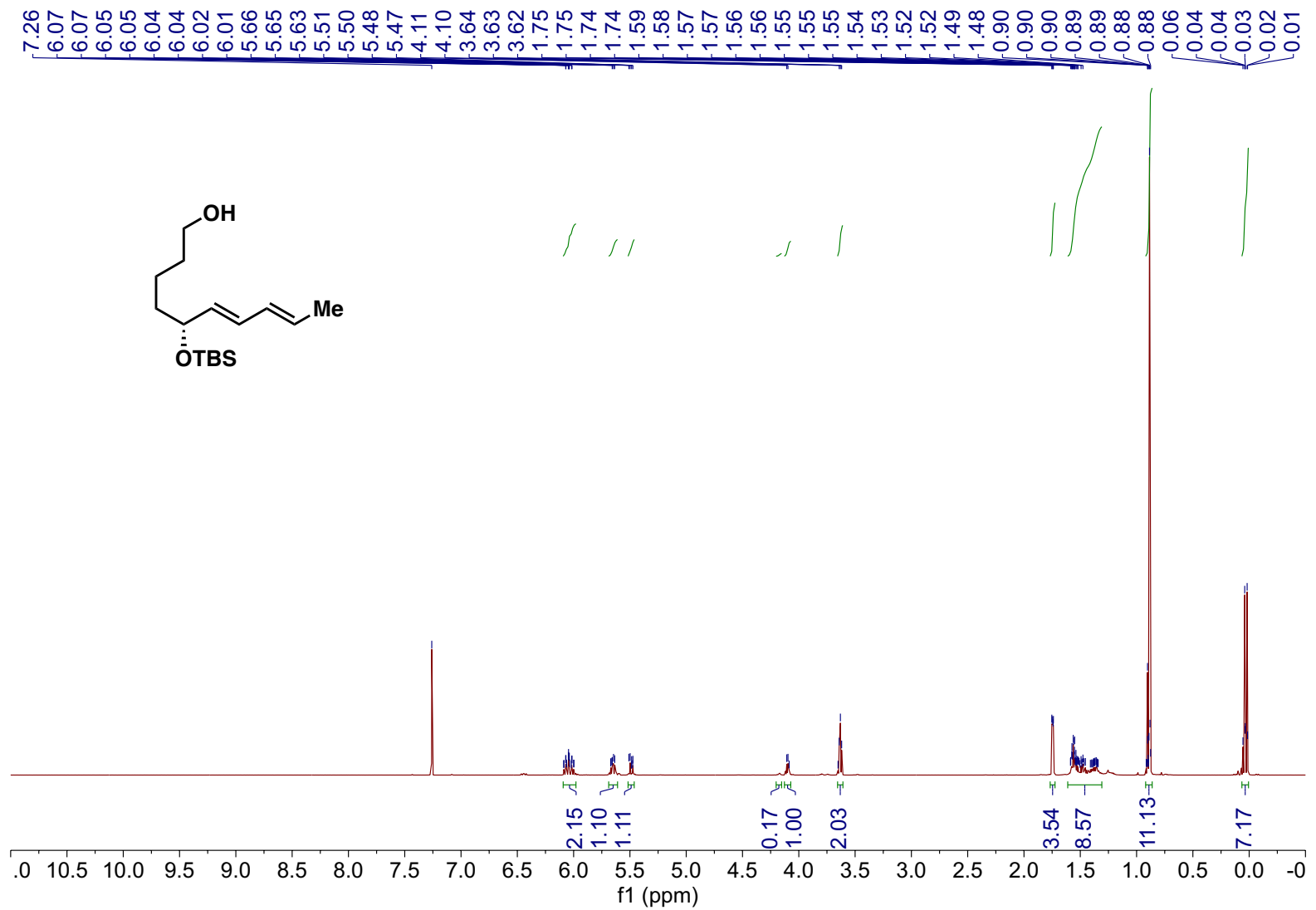
<sup>1</sup>H NMR of 17



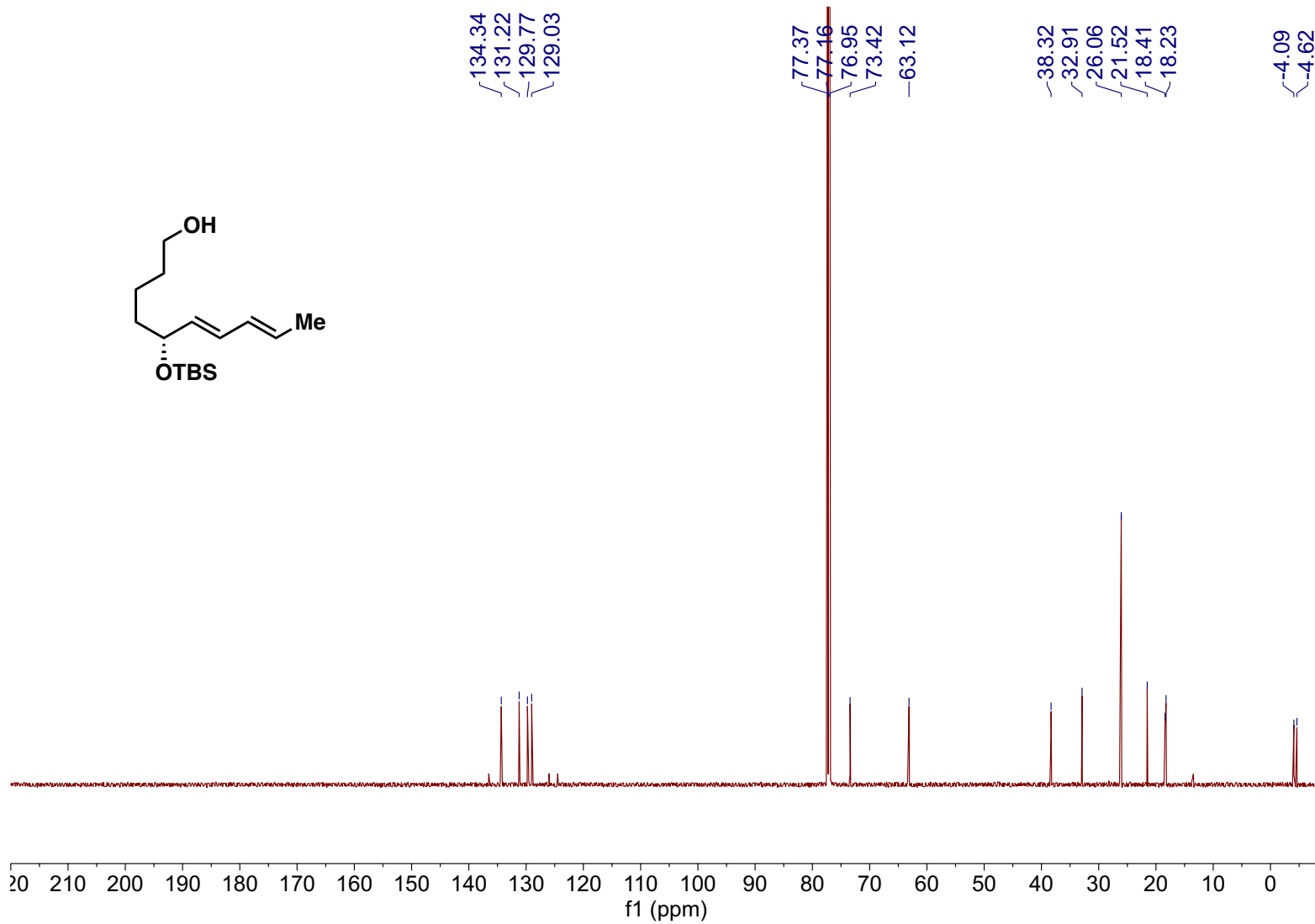
<sup>13</sup>C NMR of 17



<sup>1</sup>H NMR of S3

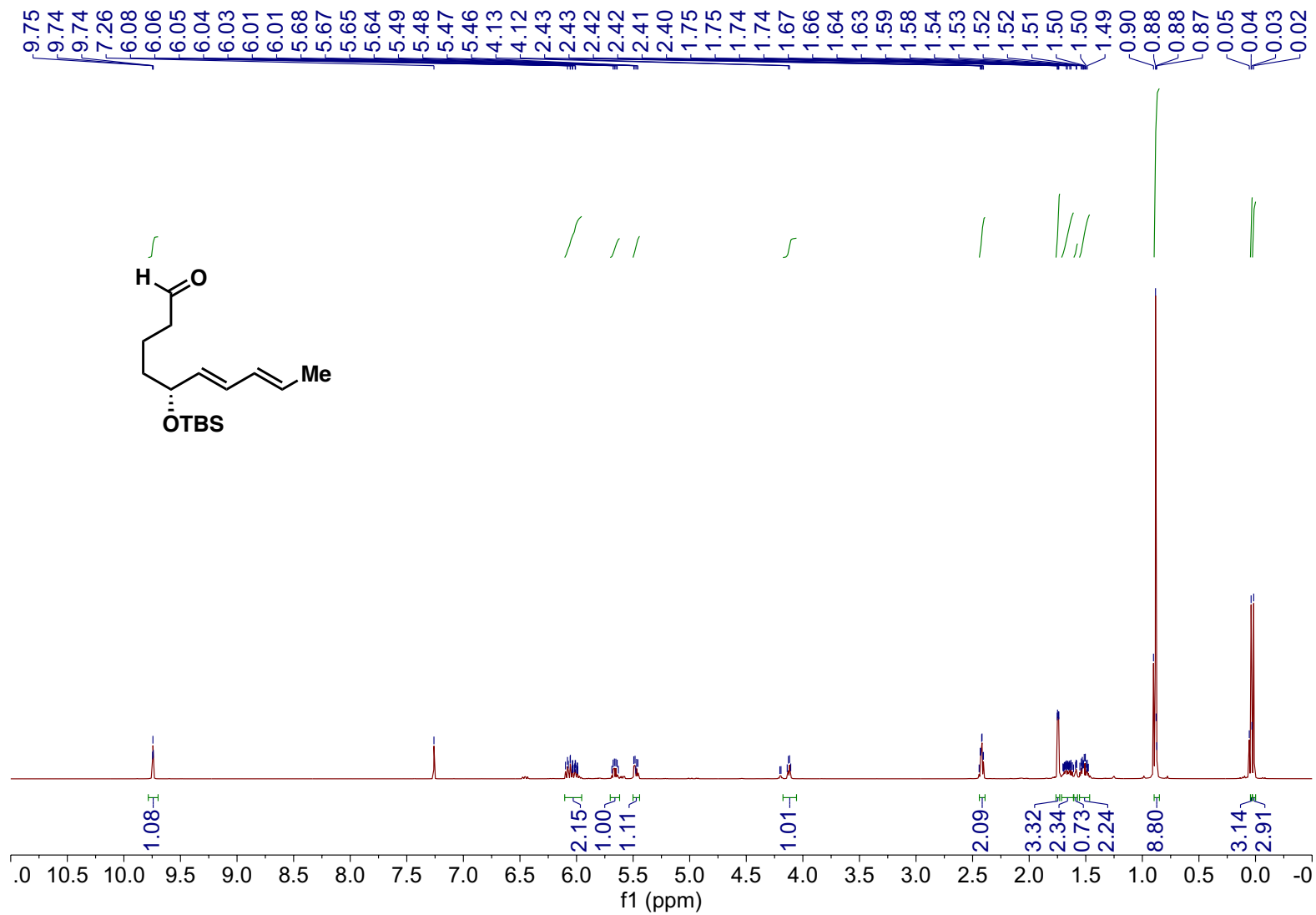


<sup>13</sup>C NMR of **S3**

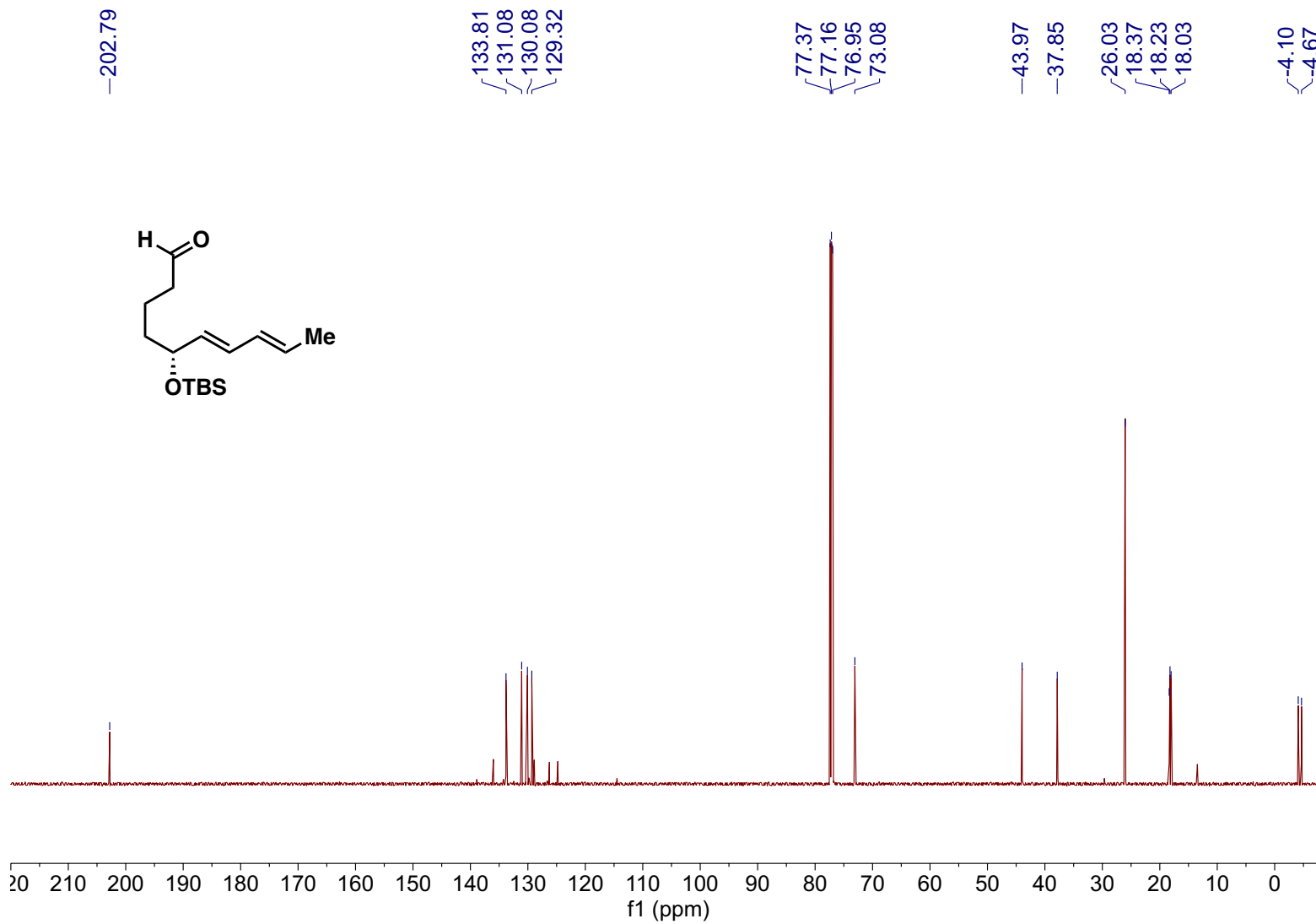




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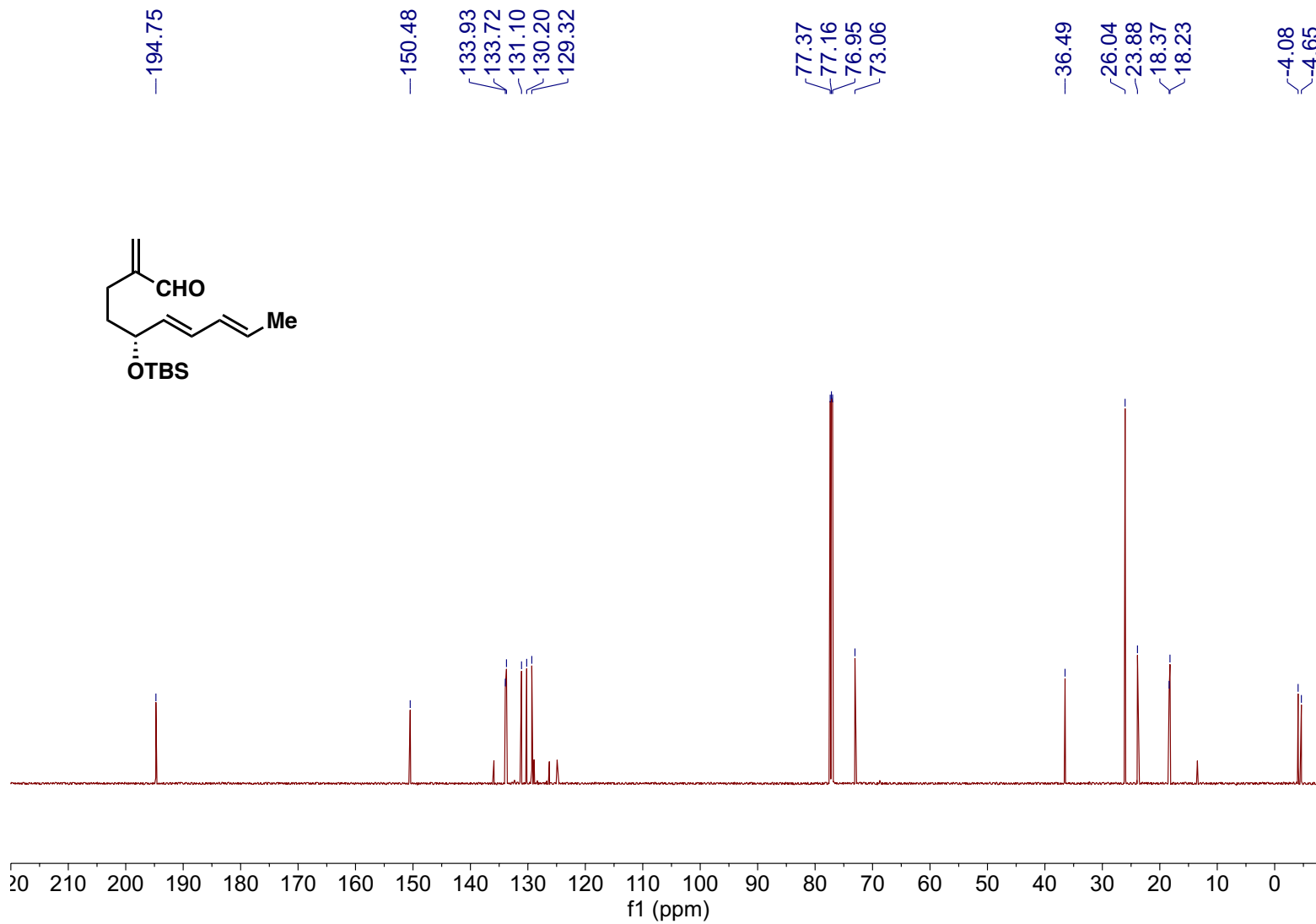


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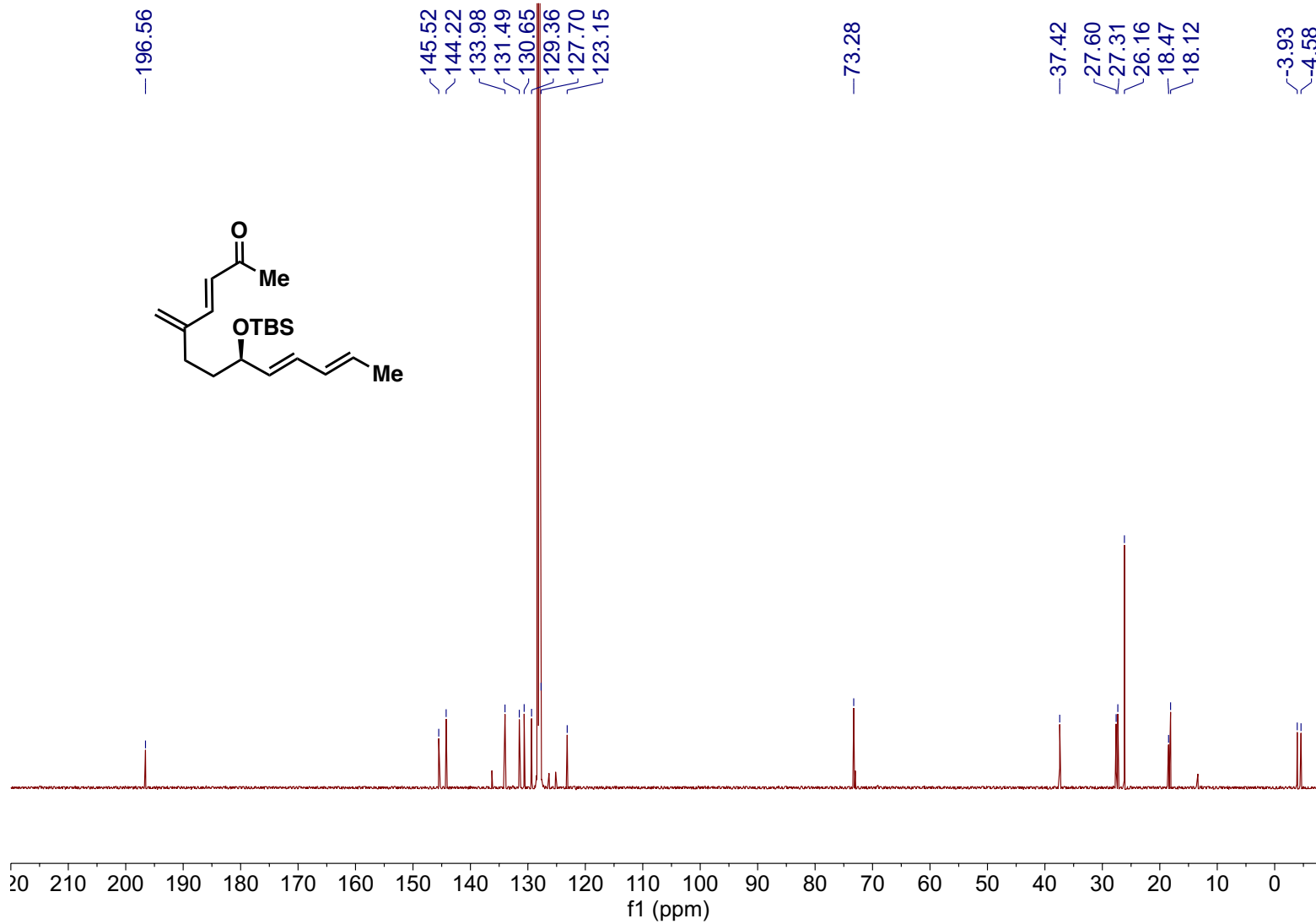


<sup>13</sup>C NMR of **19**

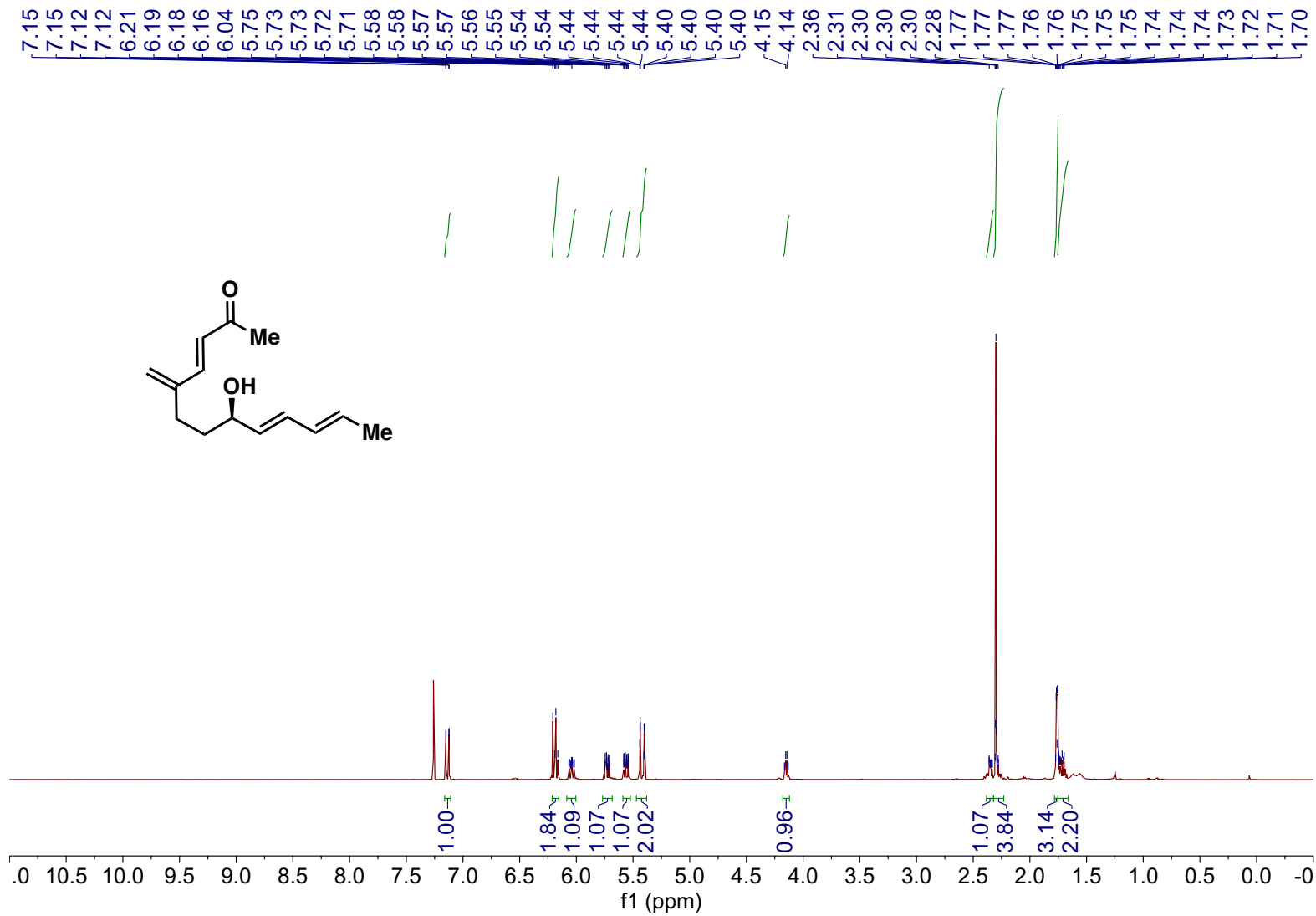




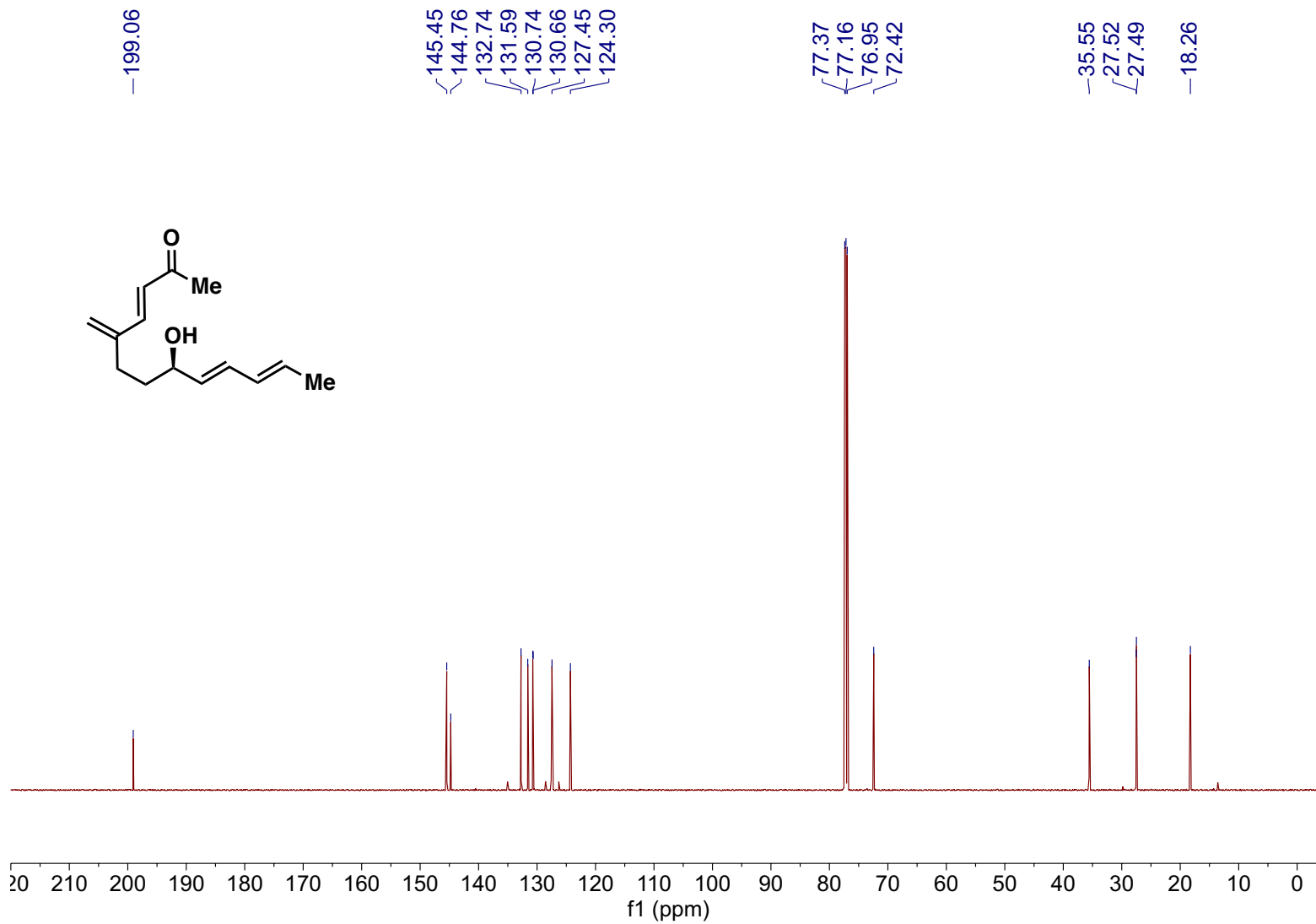
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<sup>1</sup>H NMR of 22

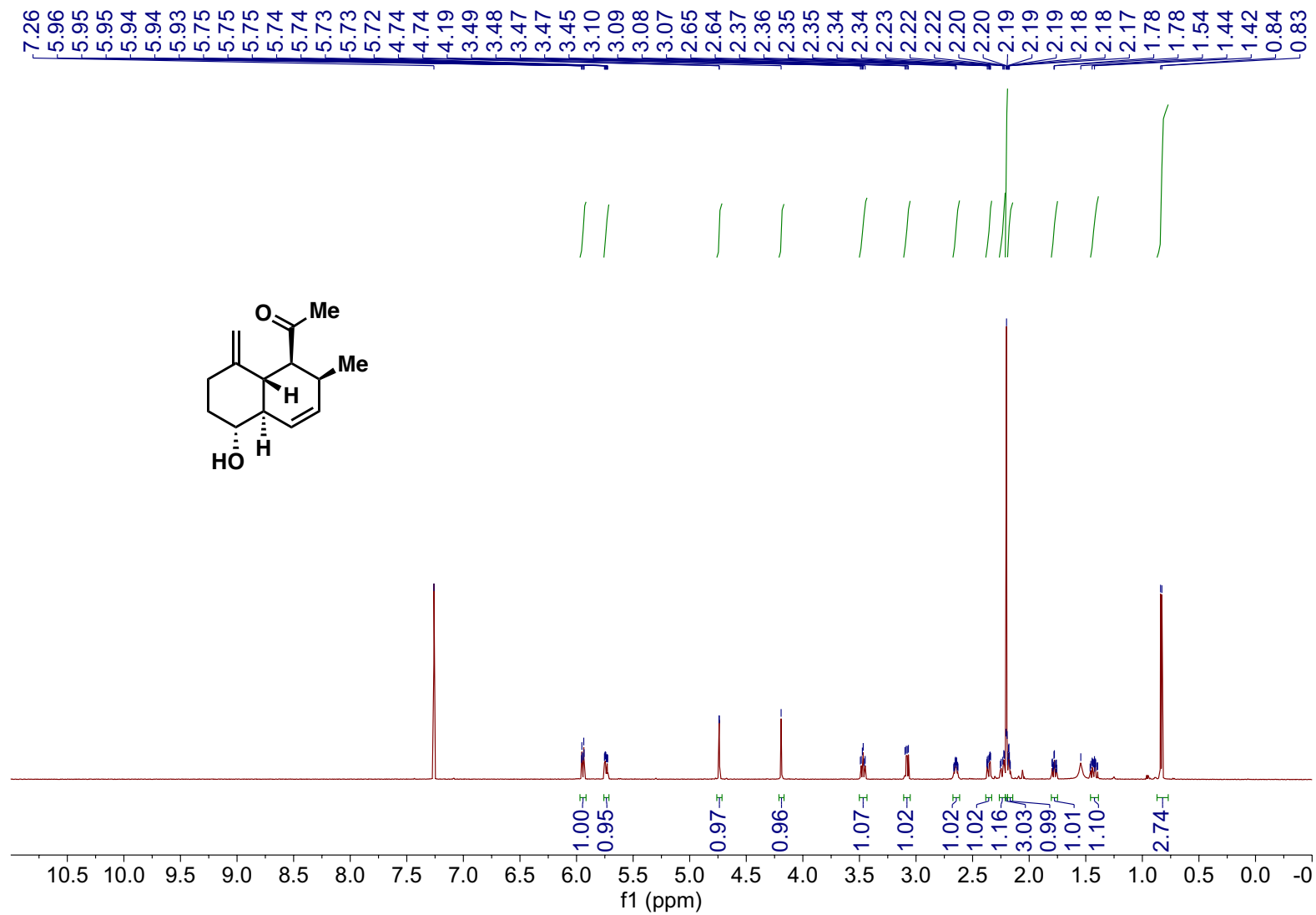


<sup>13</sup>C NMR of **22**

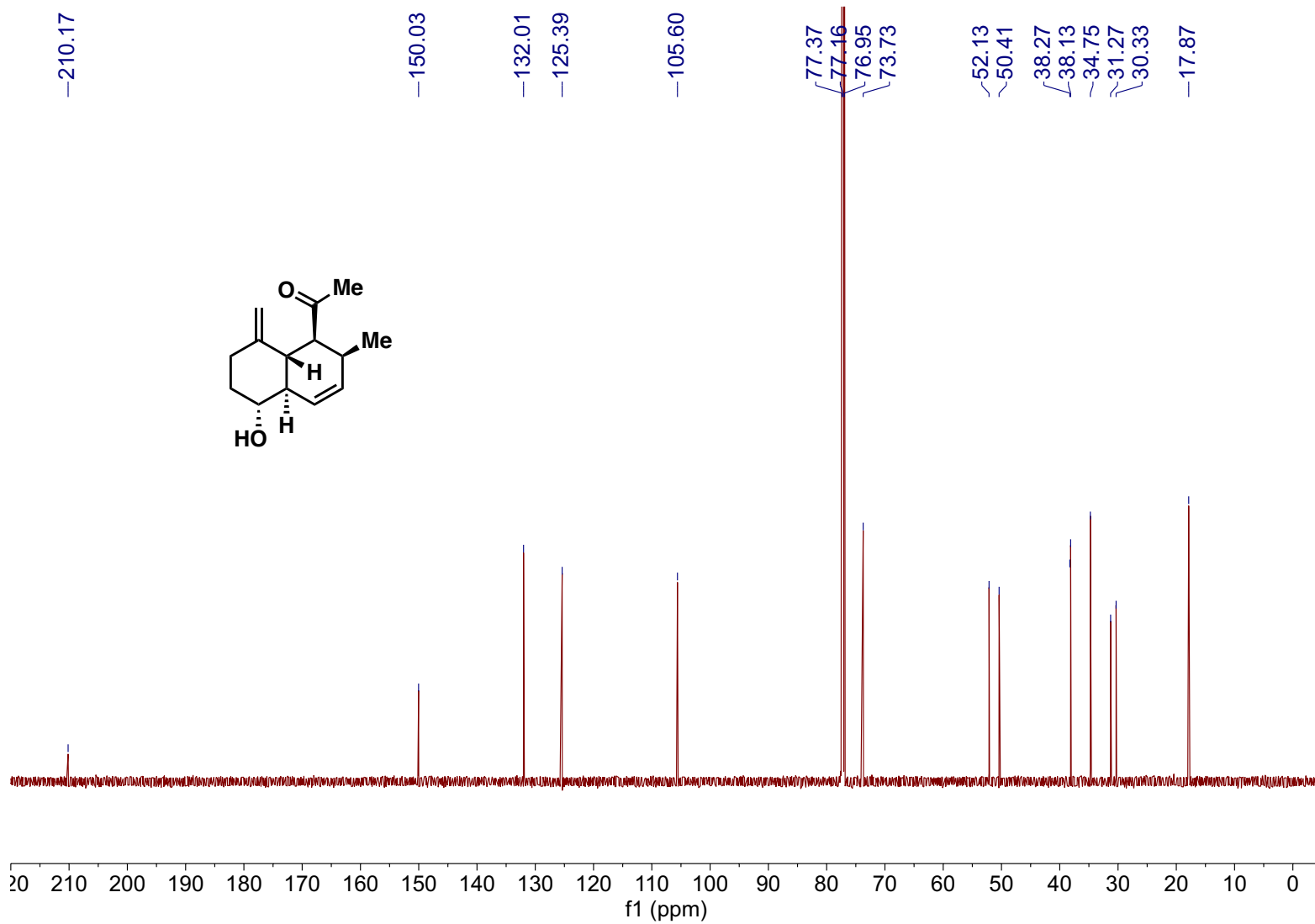




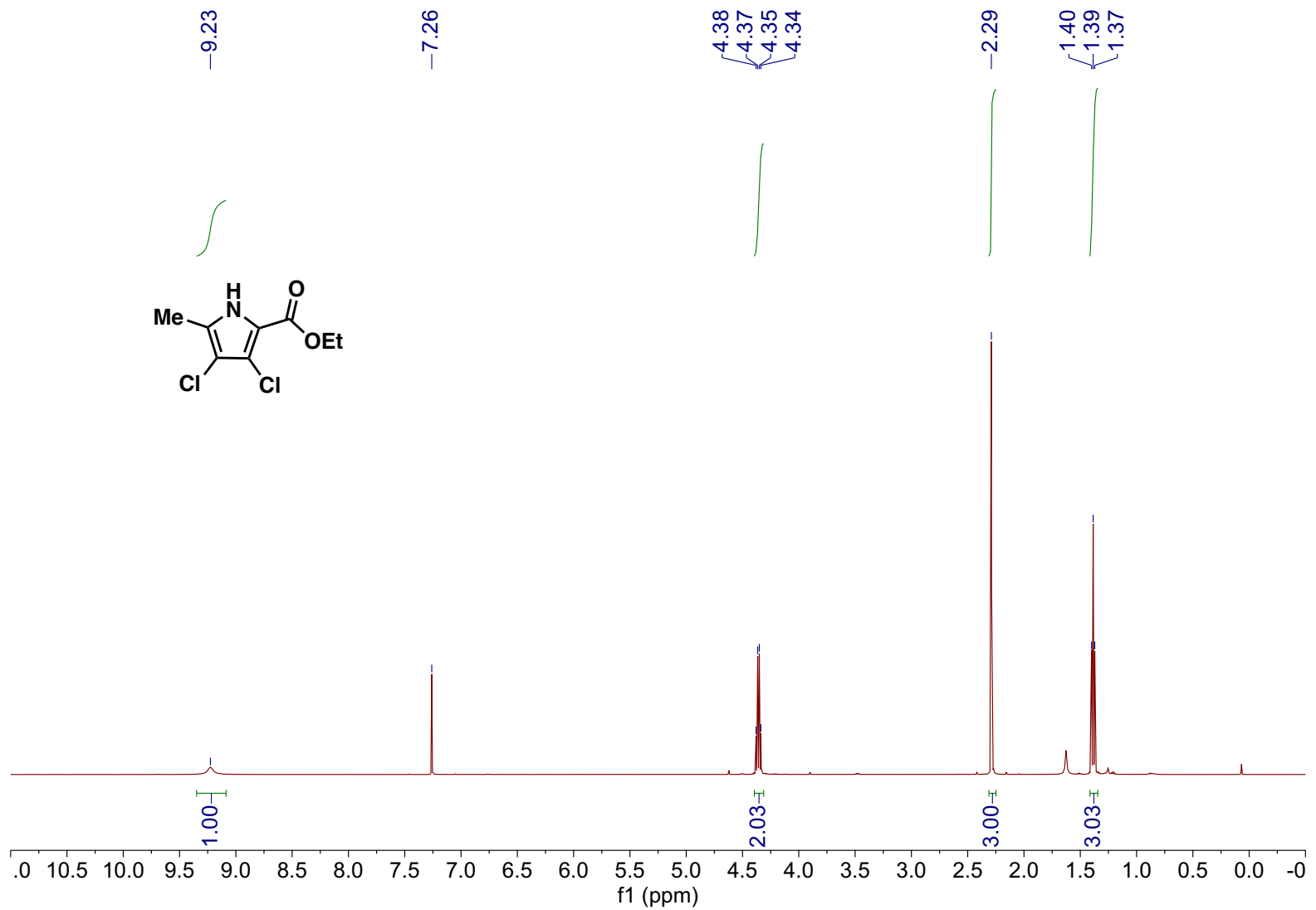
<sup>1</sup>H NMR of 23



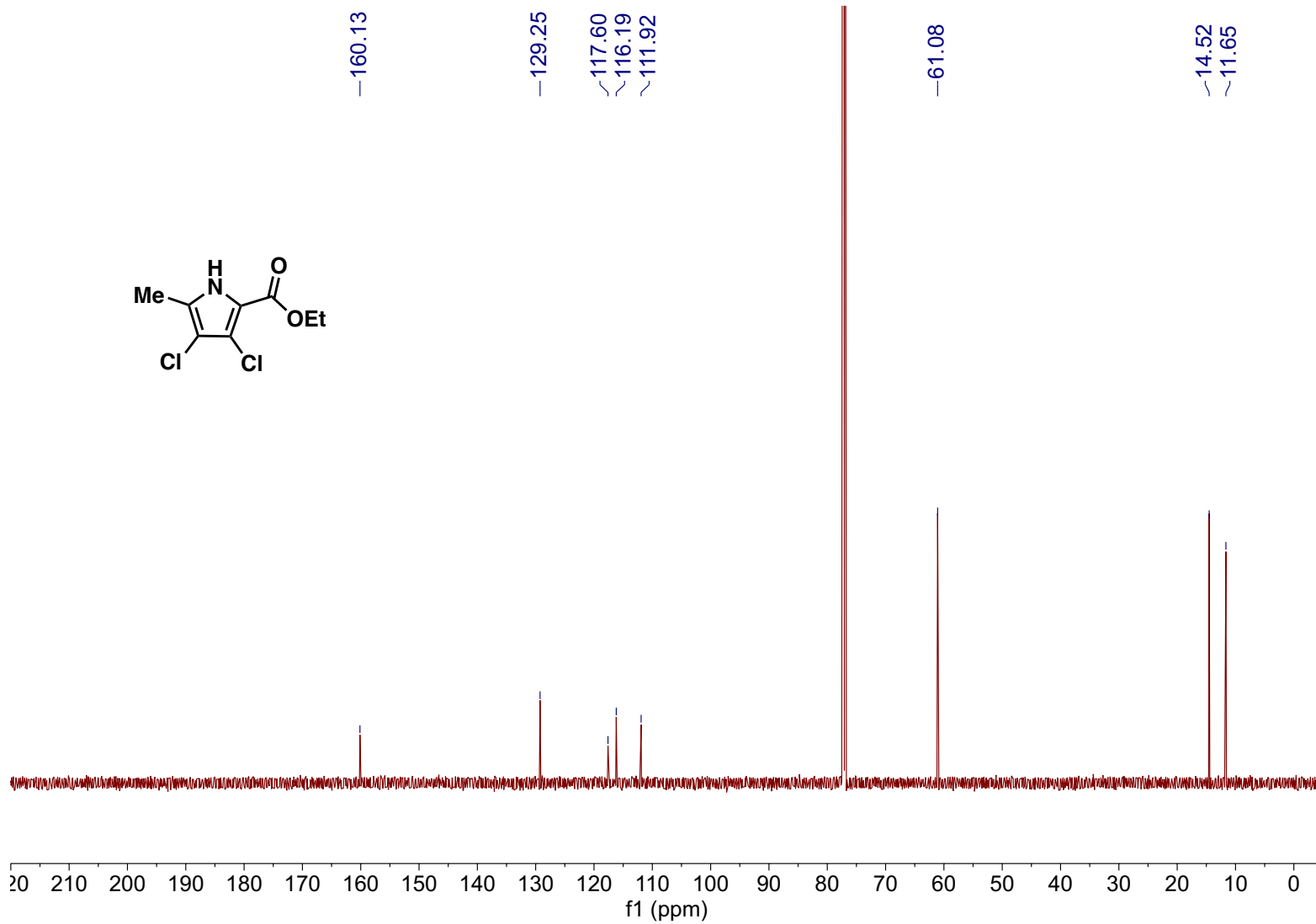
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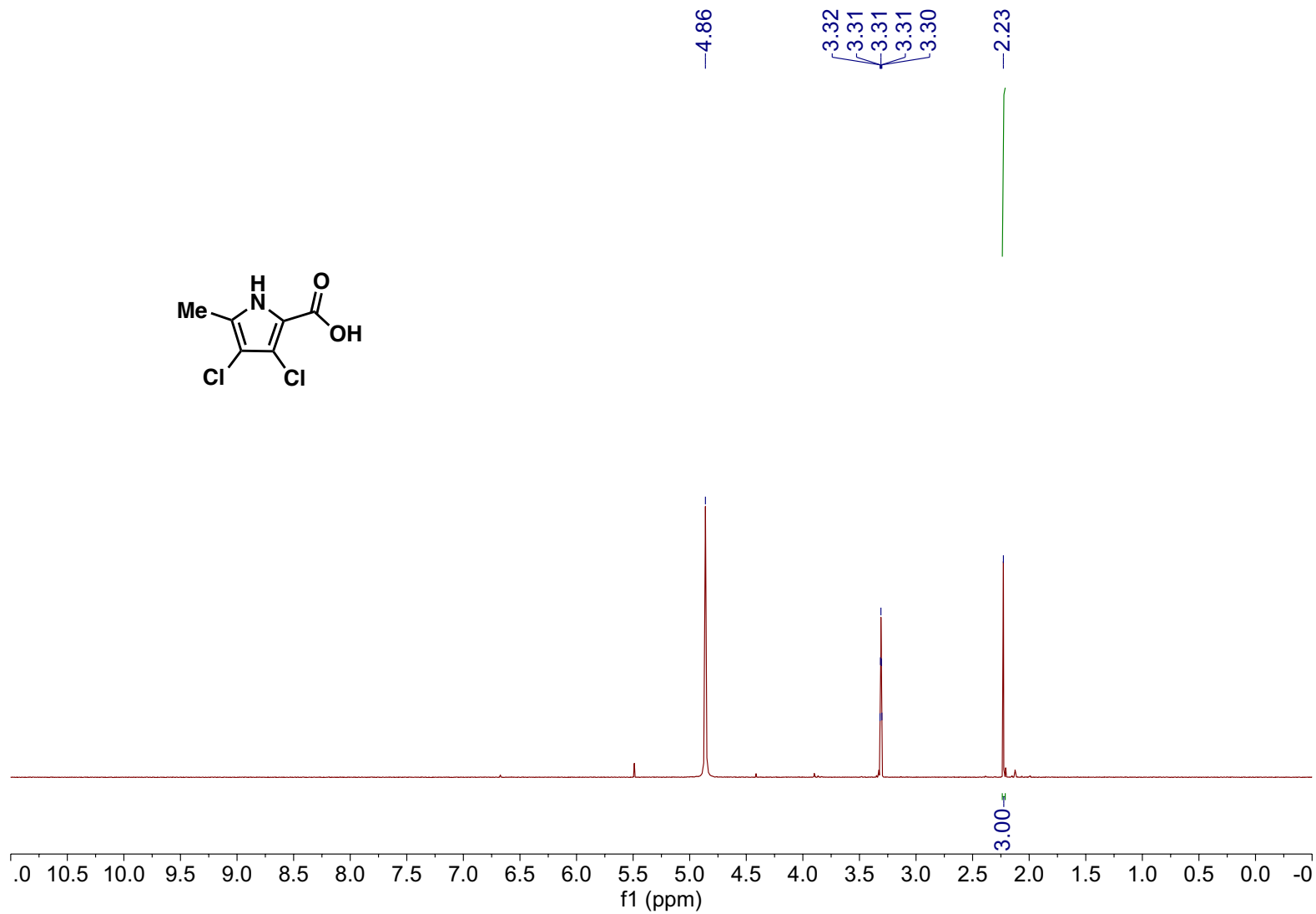
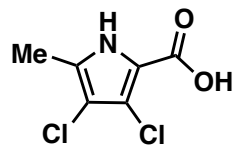
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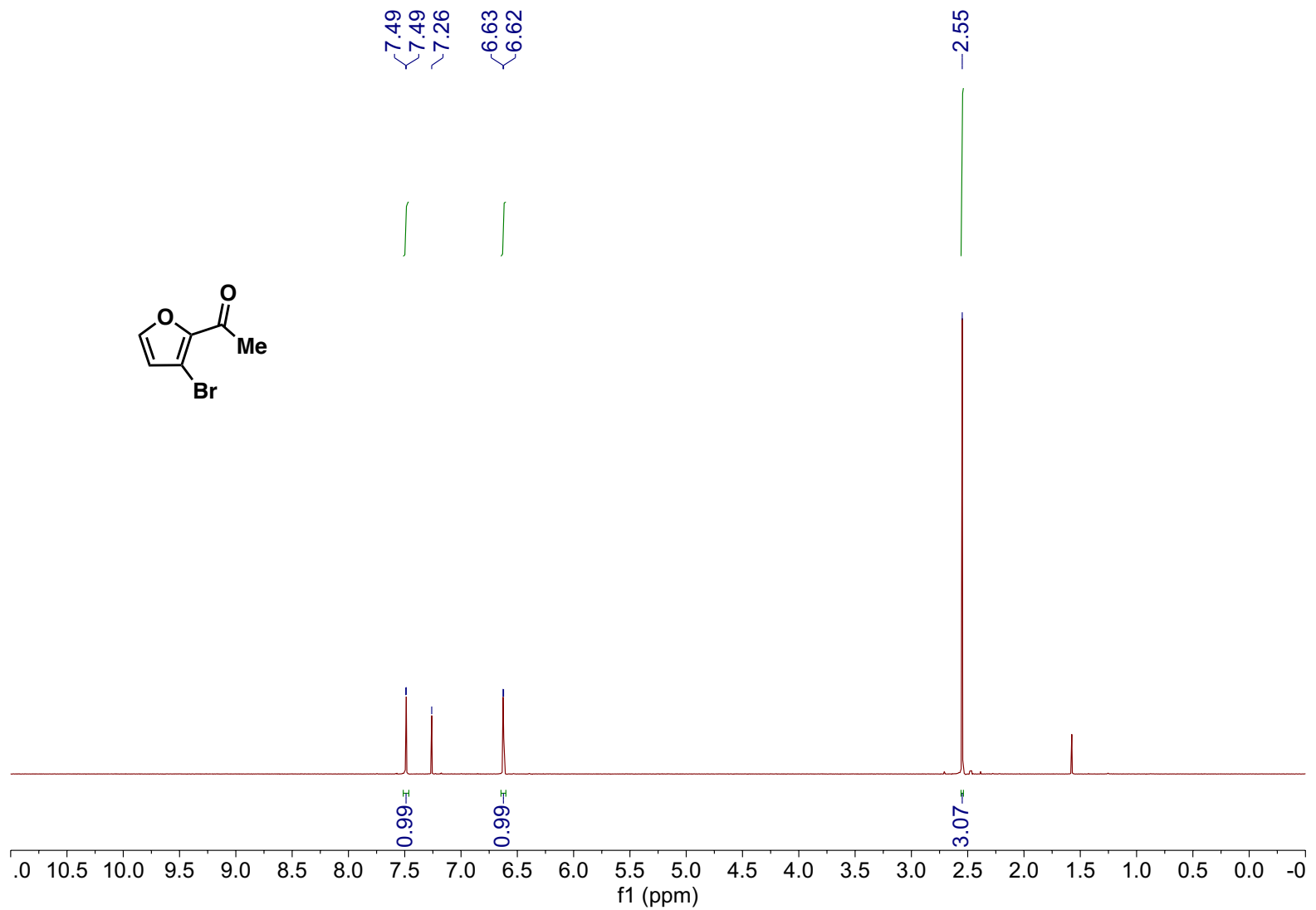
<sup>13</sup>C NMR of **S4**



<sup>1</sup>H NMR of 28



<sup>1</sup>H NMR of **6**



<sup>13</sup>C NMR of **6**

—186.71

—148.53

—145.51

—117.57

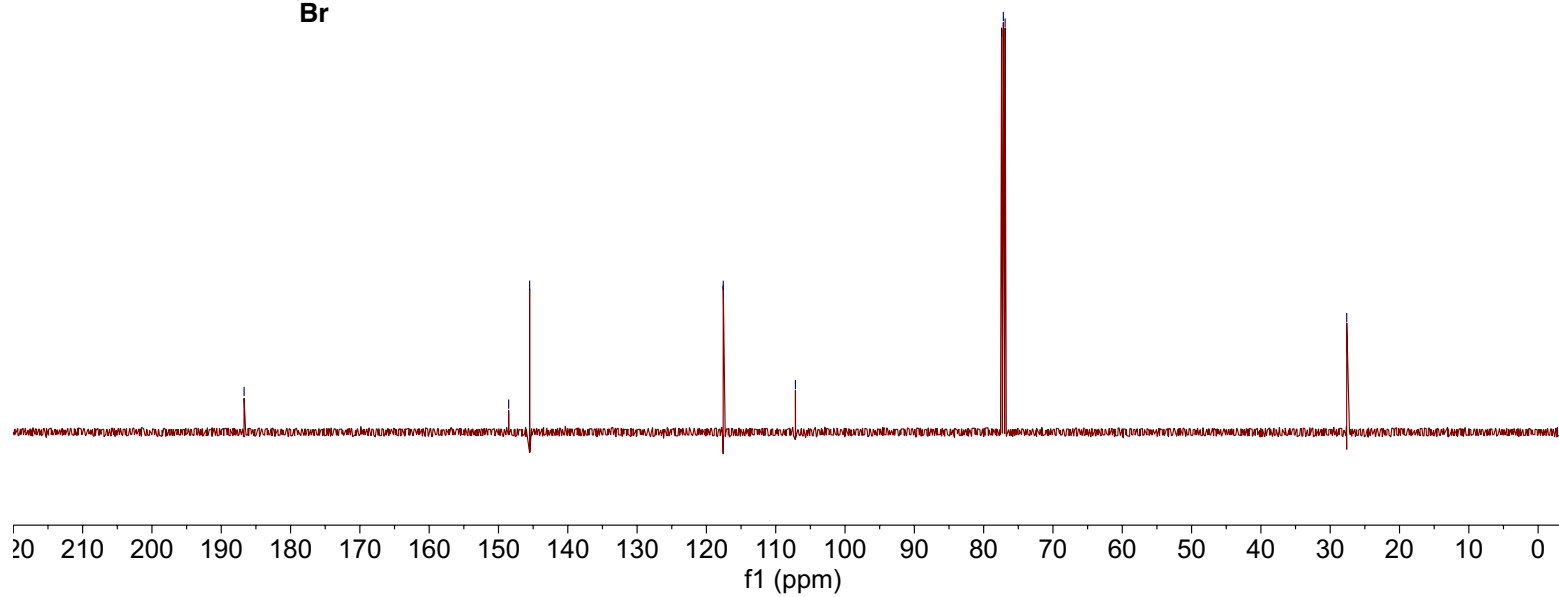
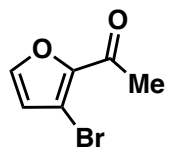
—107.16

77.41

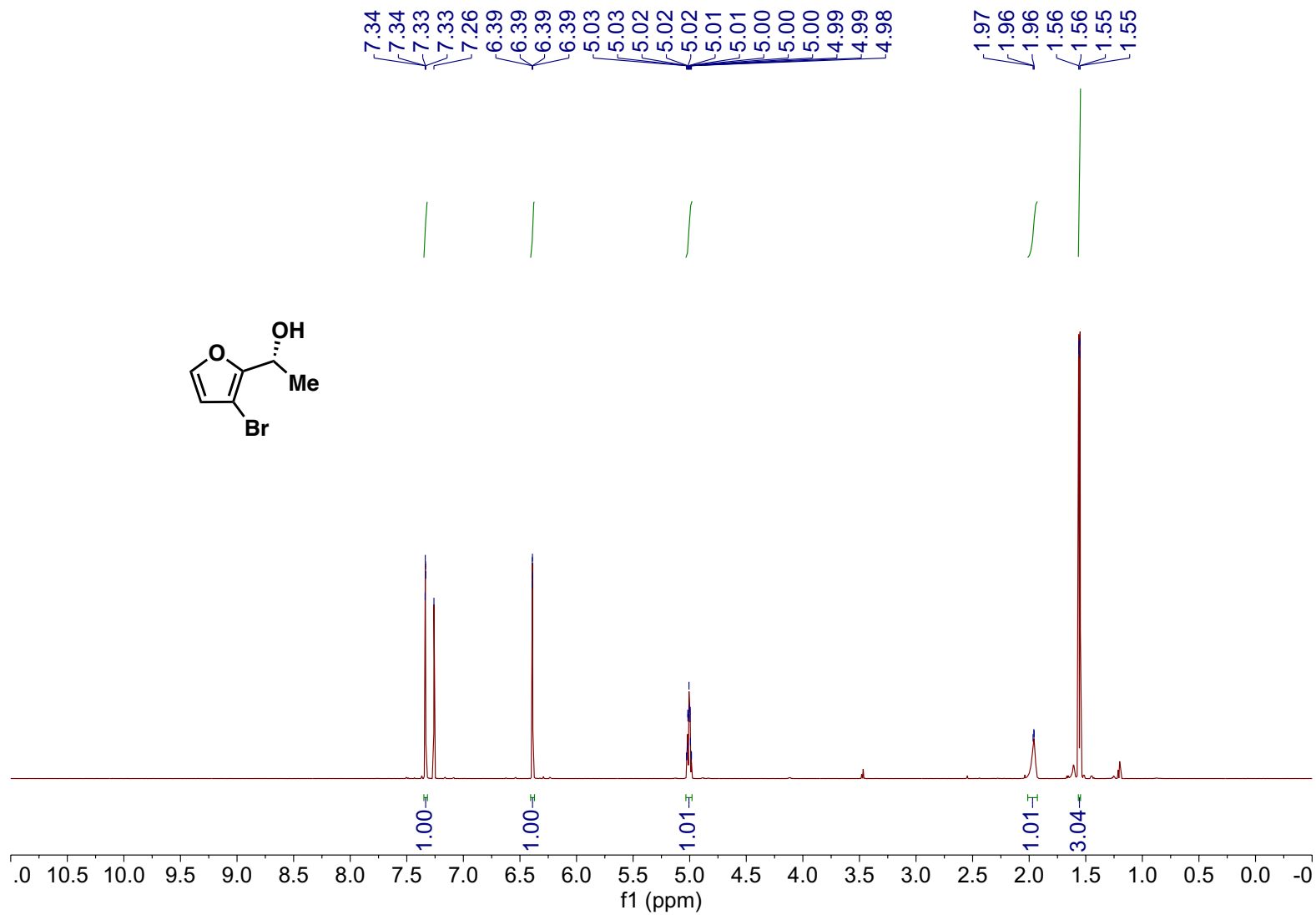
77.16

76.91

—27.61

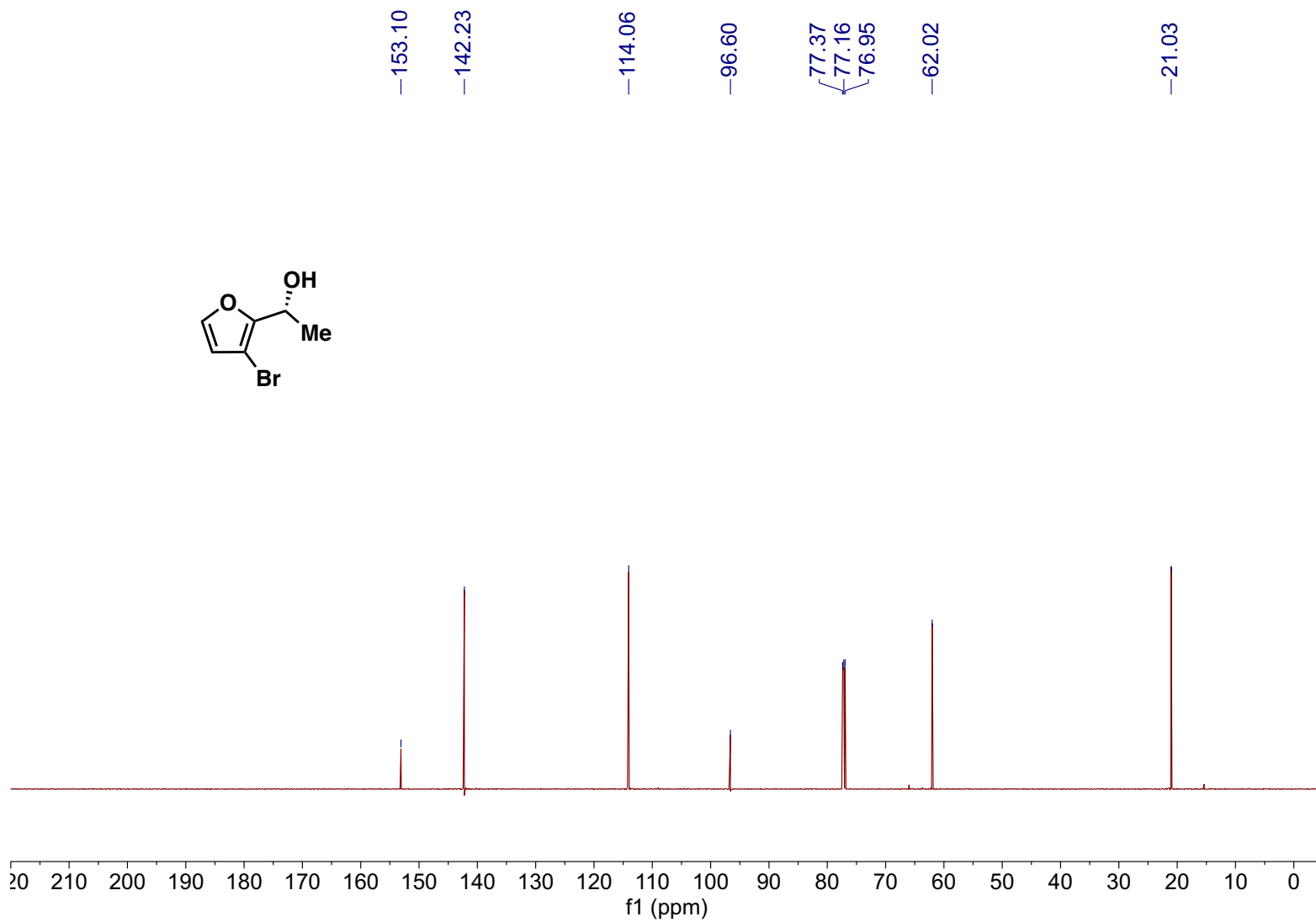


<sup>1</sup>H NMR of S6

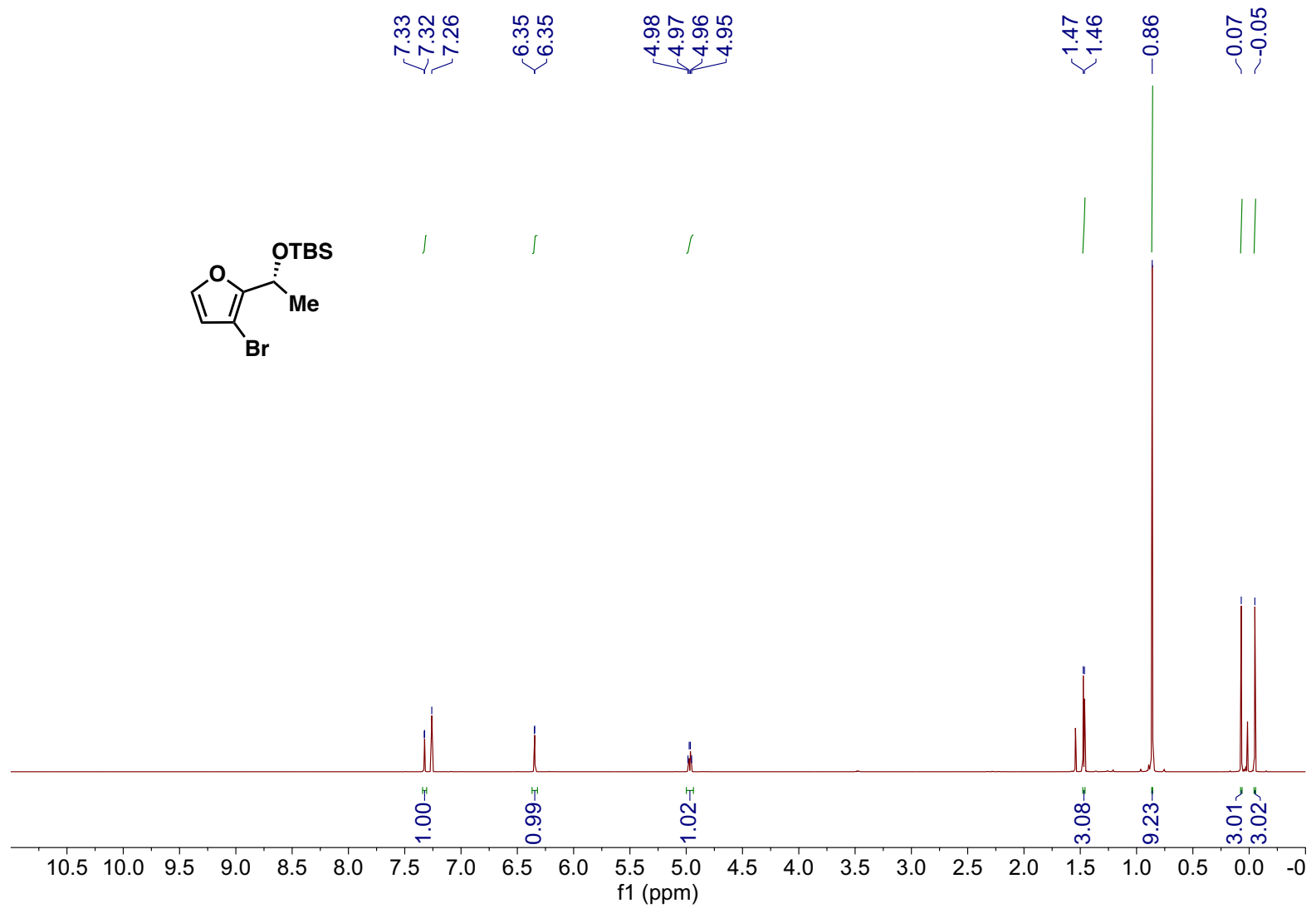




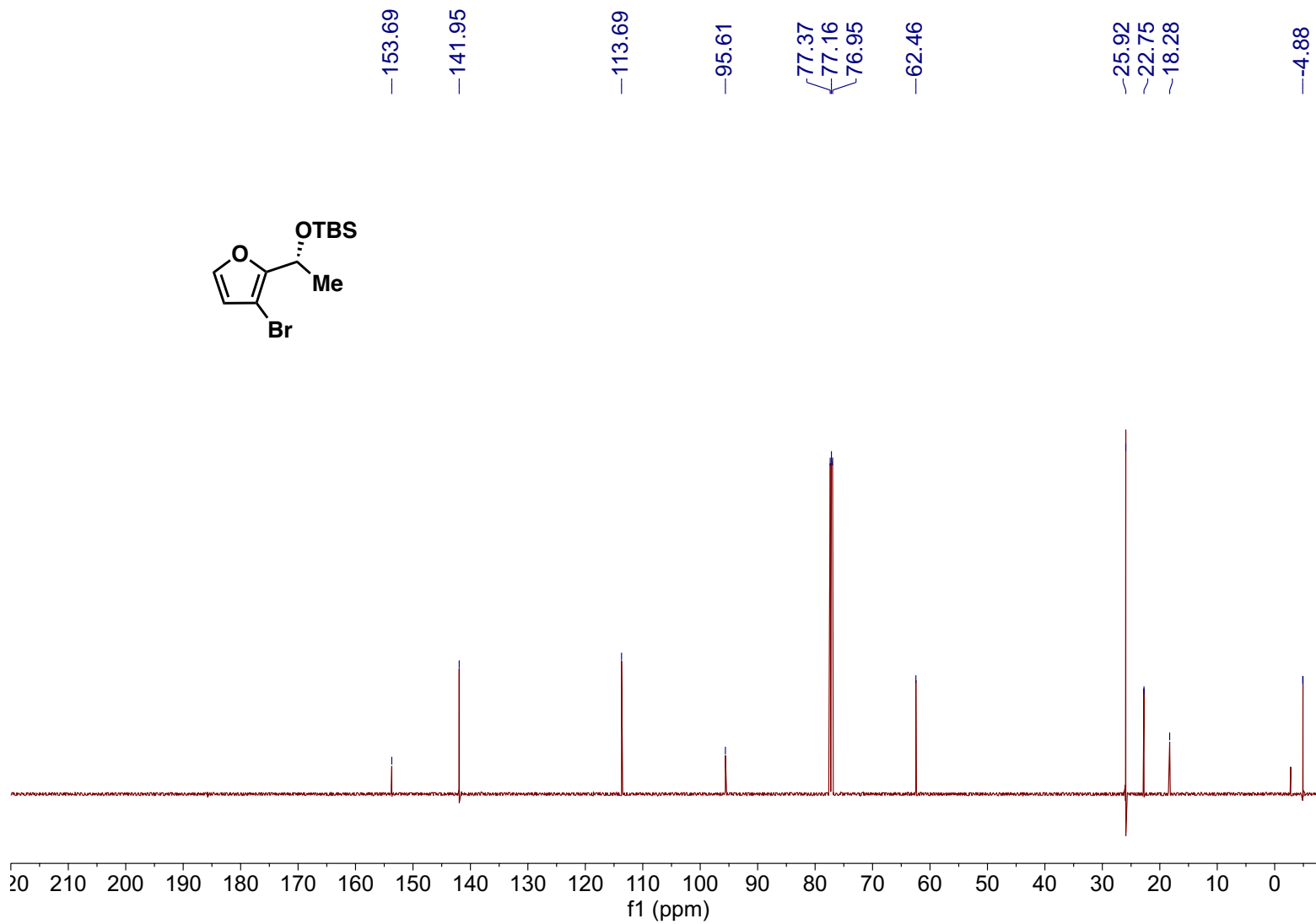
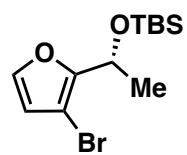
<sup>13</sup>C NMR of **S6**



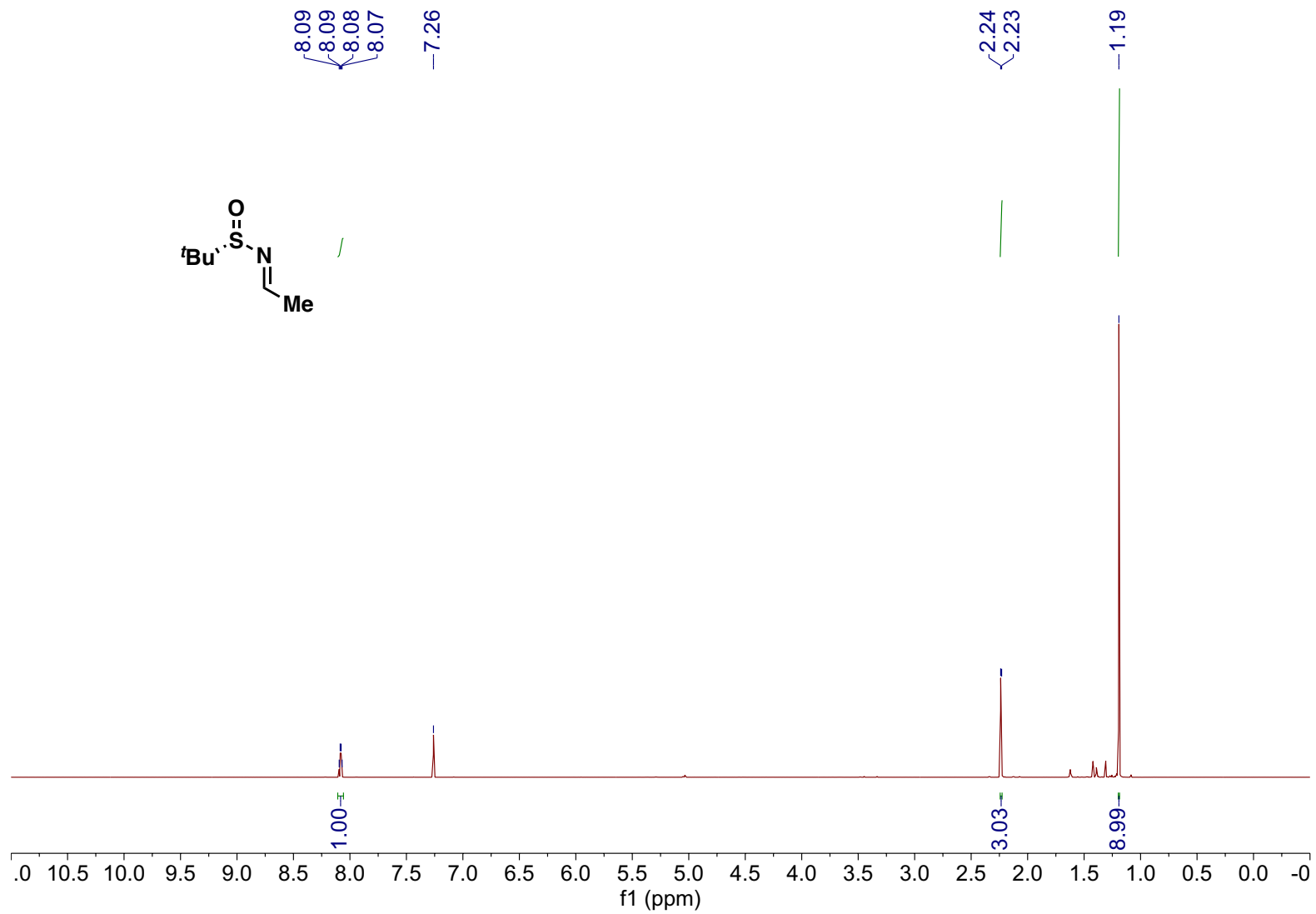
<sup>1</sup>H NMR of 24



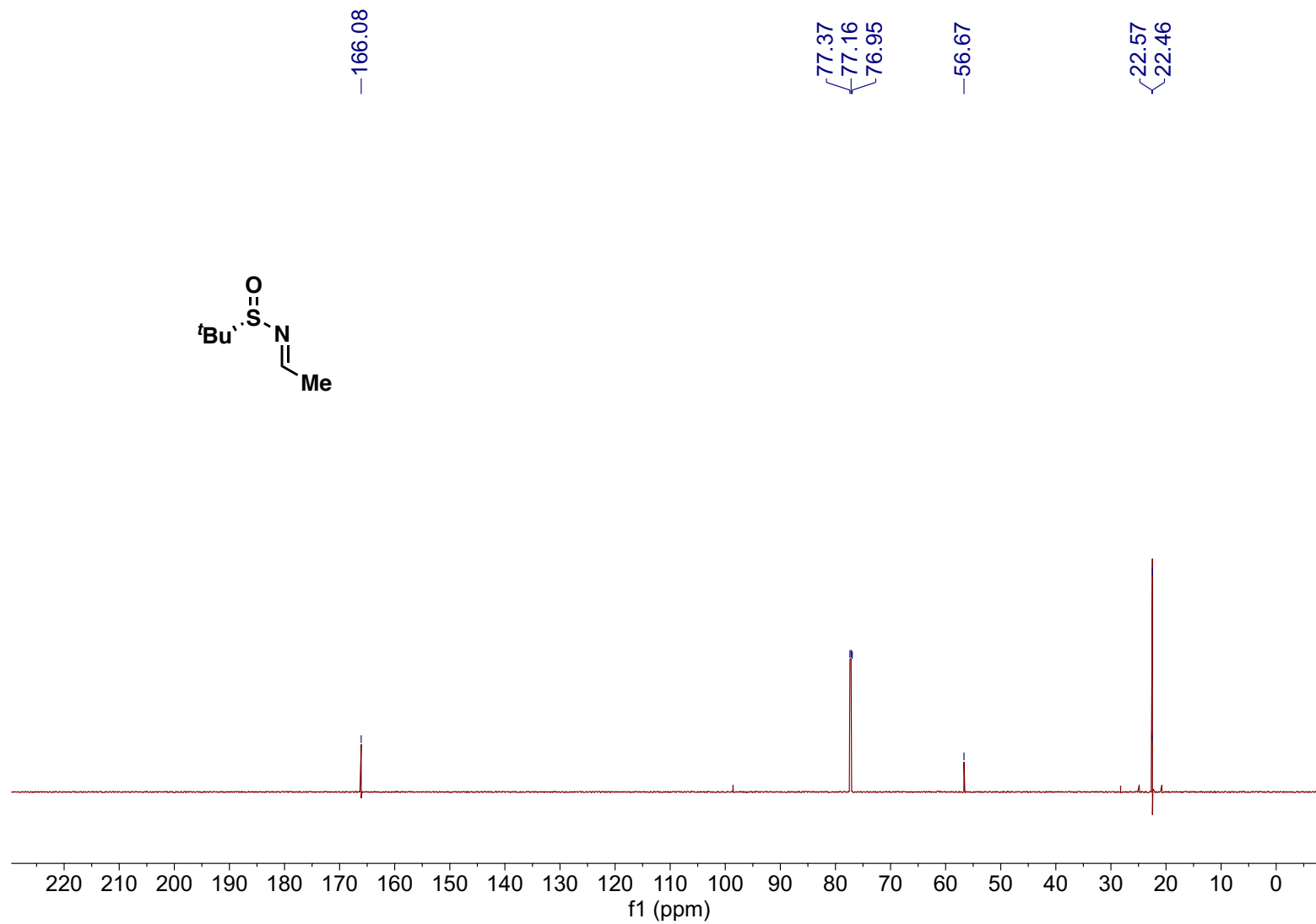
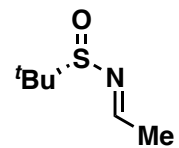
<sup>13</sup>C NMR of **24**



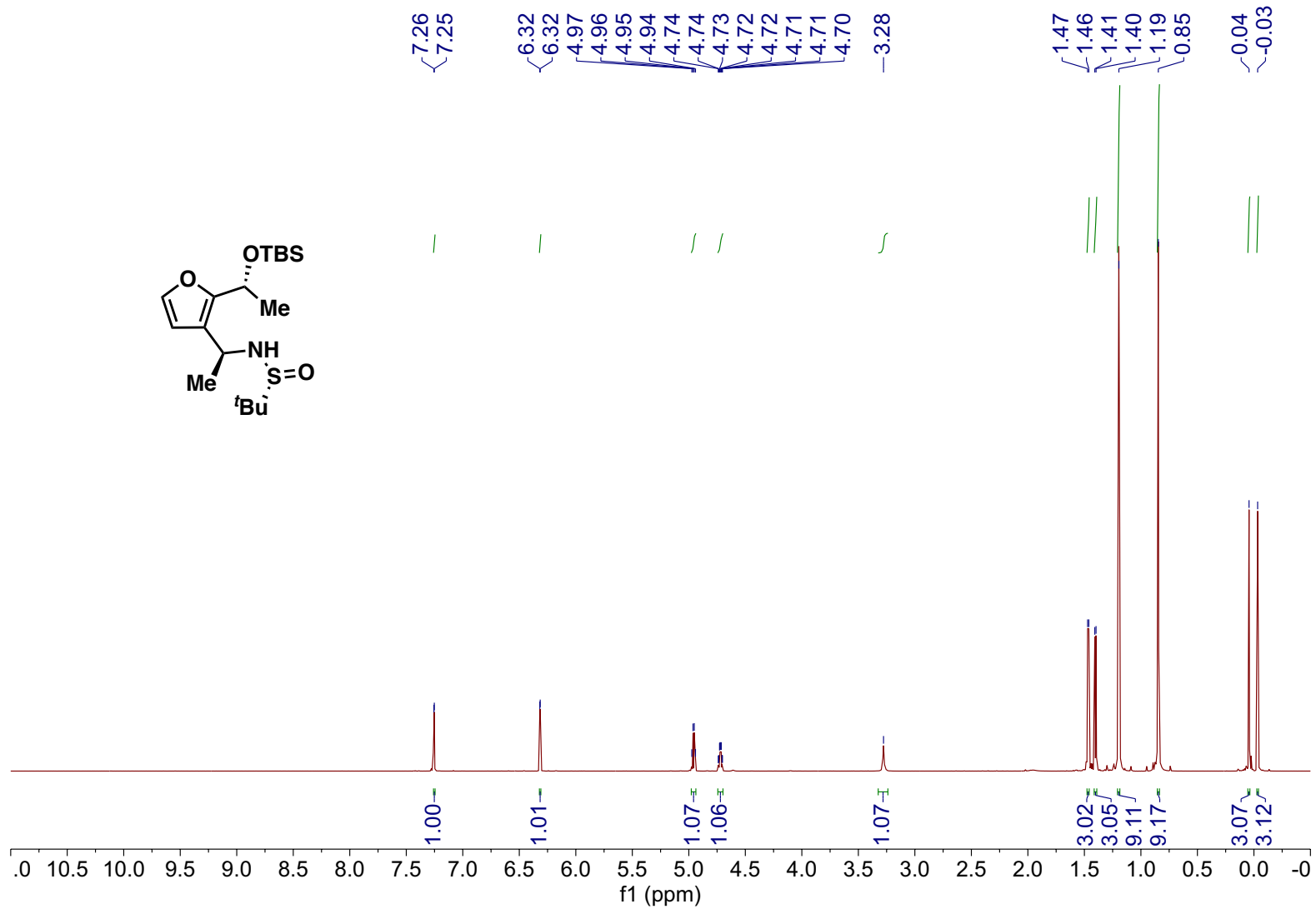
<sup>1</sup>H NMR of 25



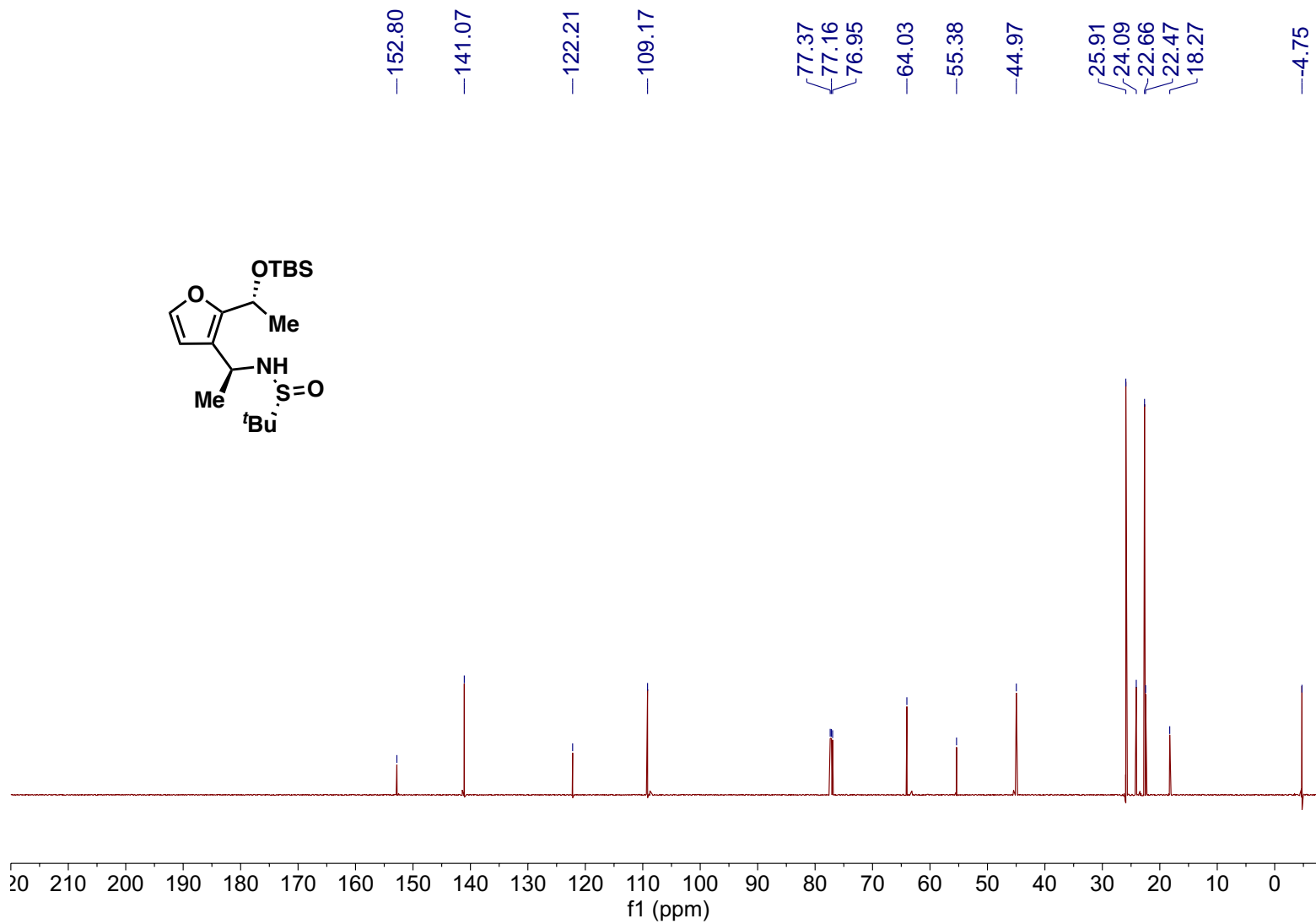
<sup>13</sup>C NMR of **25**



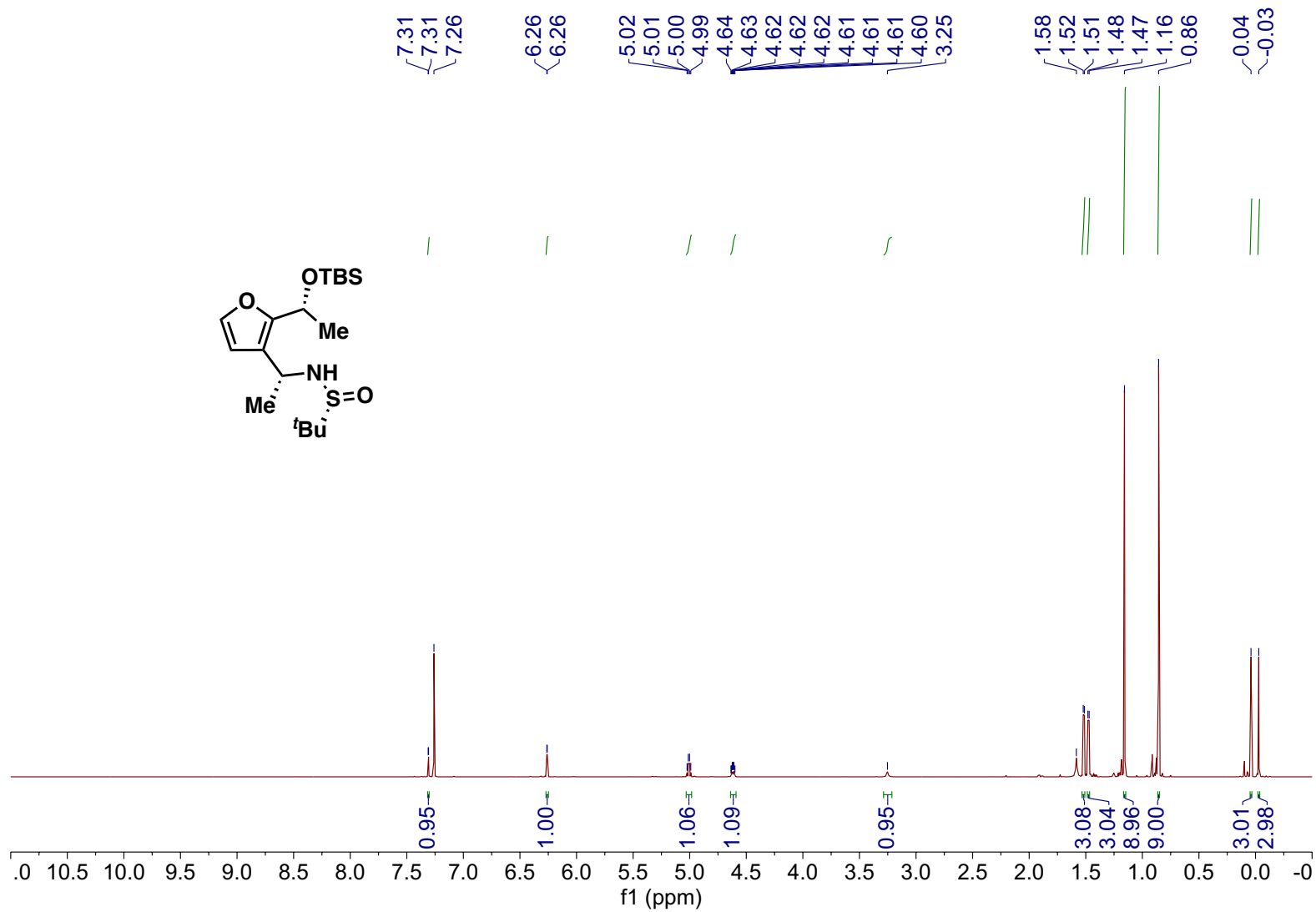
<sup>1</sup>H NMR of 26



<sup>13</sup>C NMR of **26**

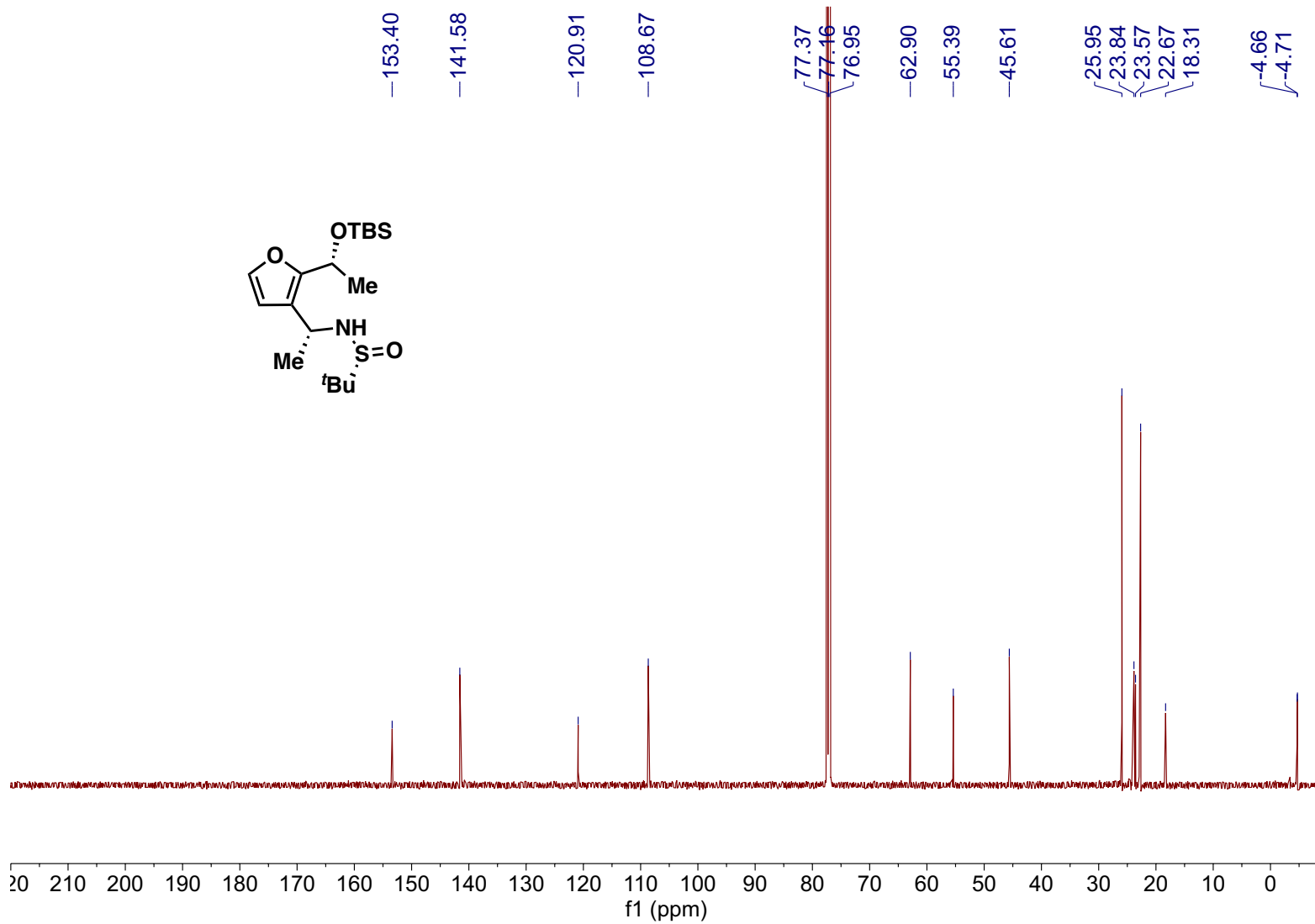


<sup>1</sup>H NMR of **26B**

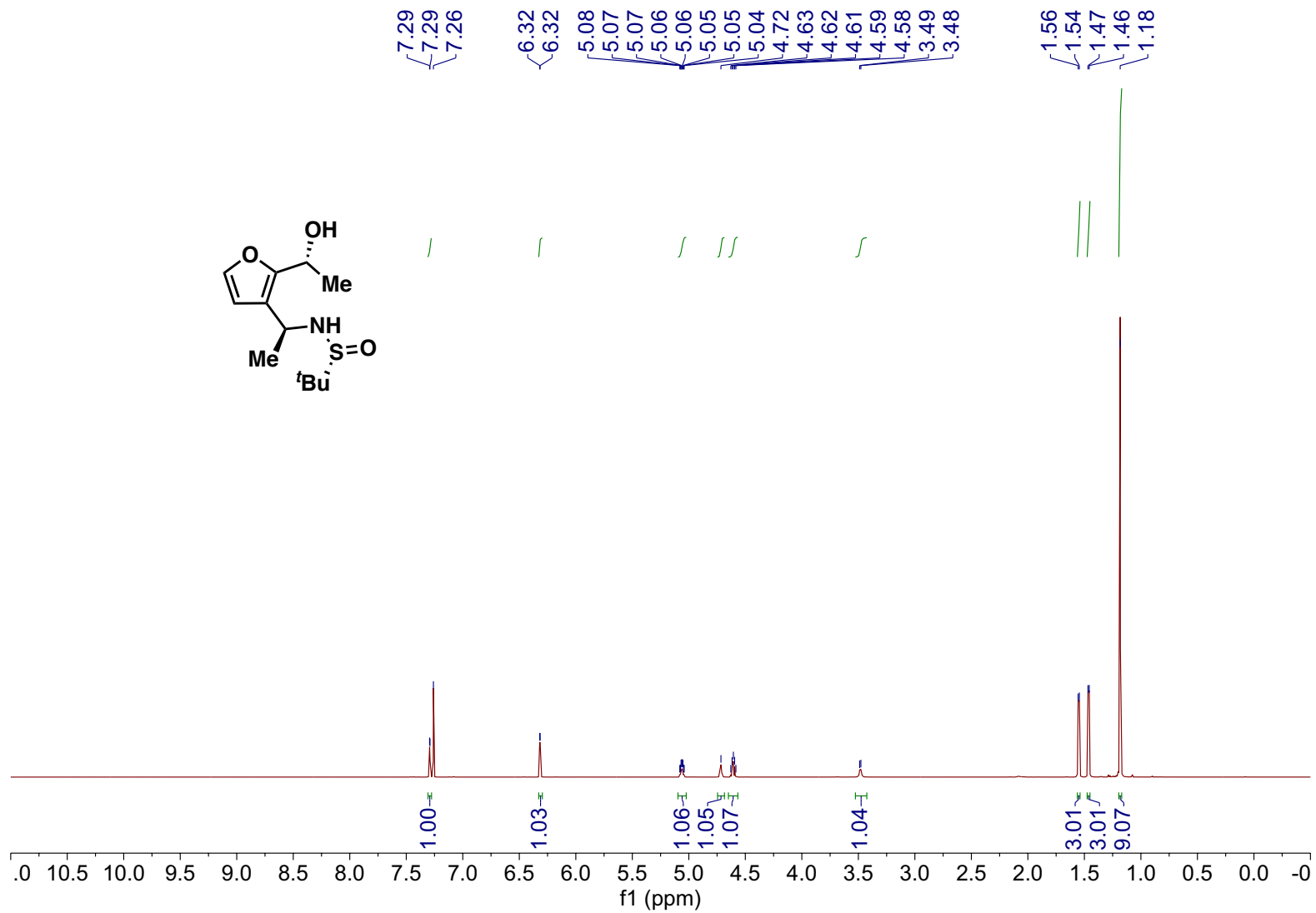




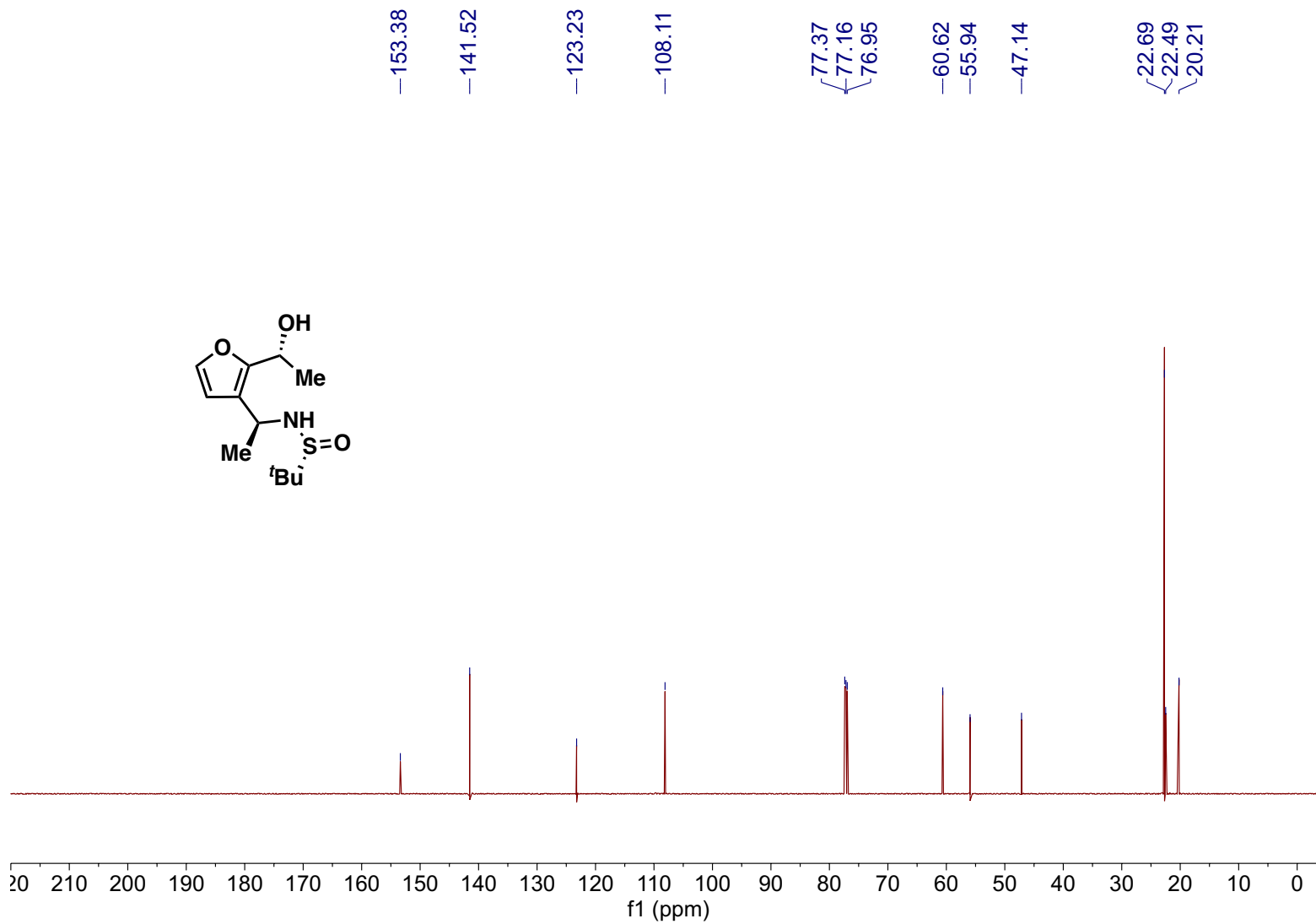
<sup>13</sup>C NMR of **26B**



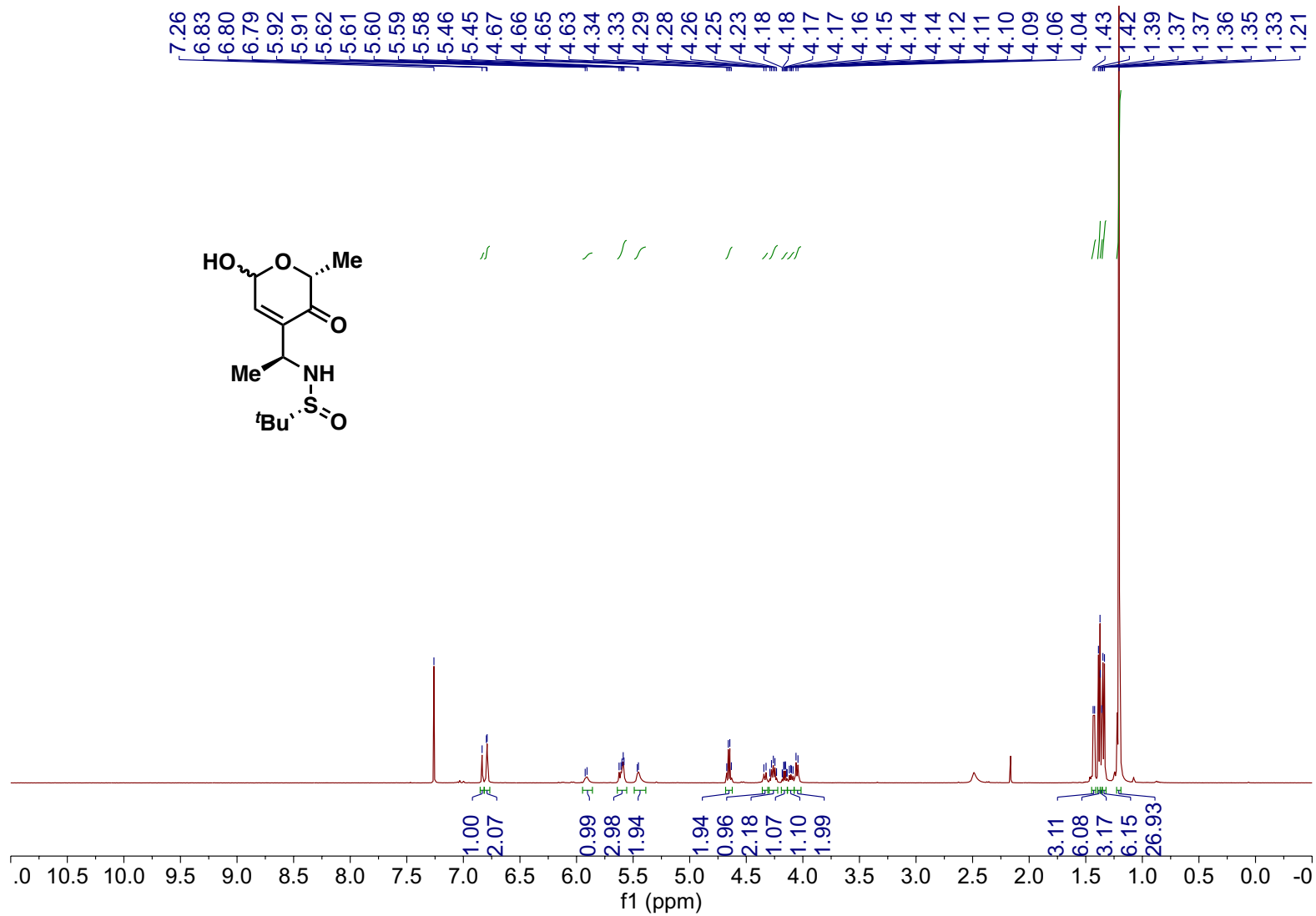
<sup>1</sup>H NMR of **S7**



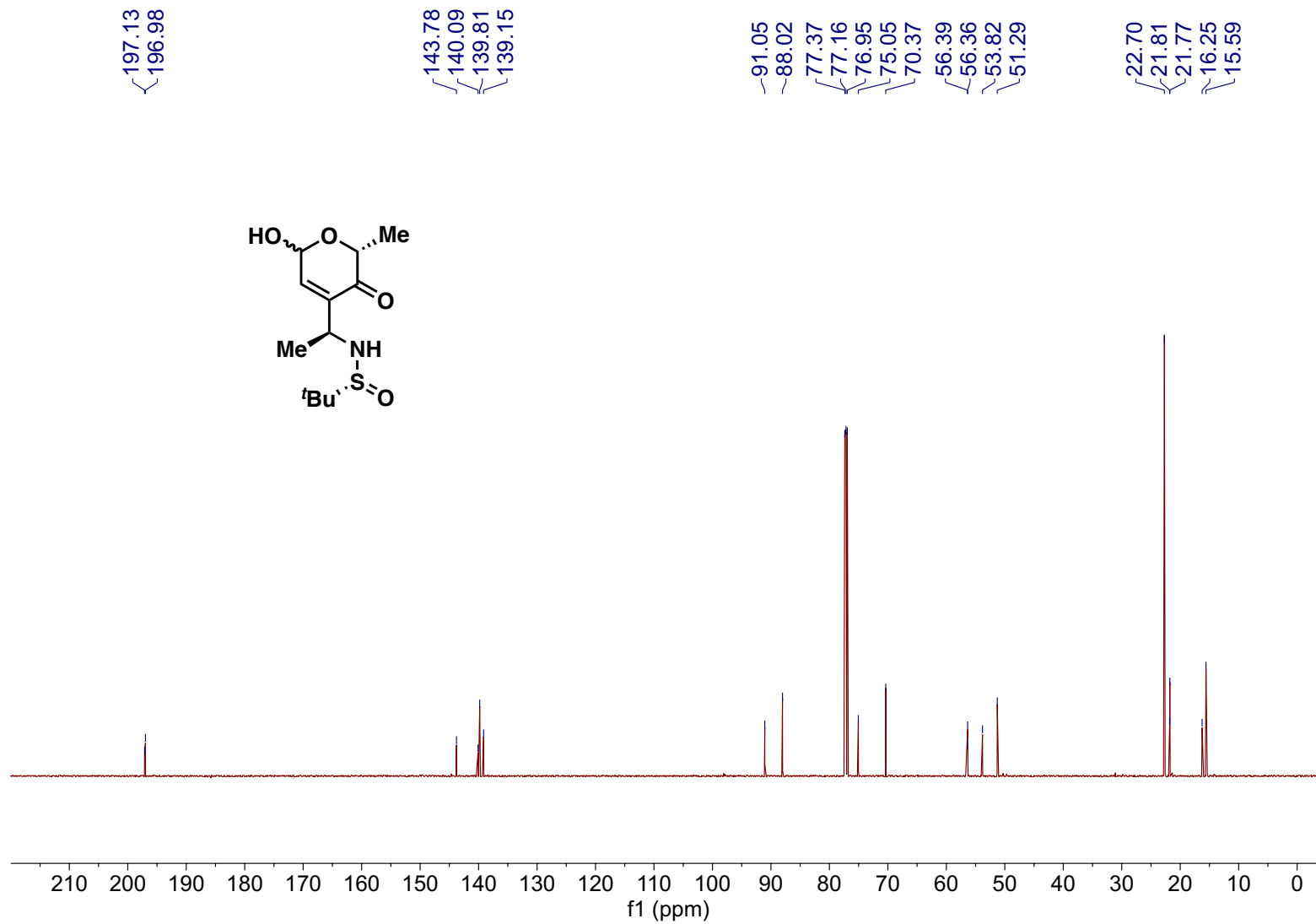
<sup>13</sup>C NMR of **S7**



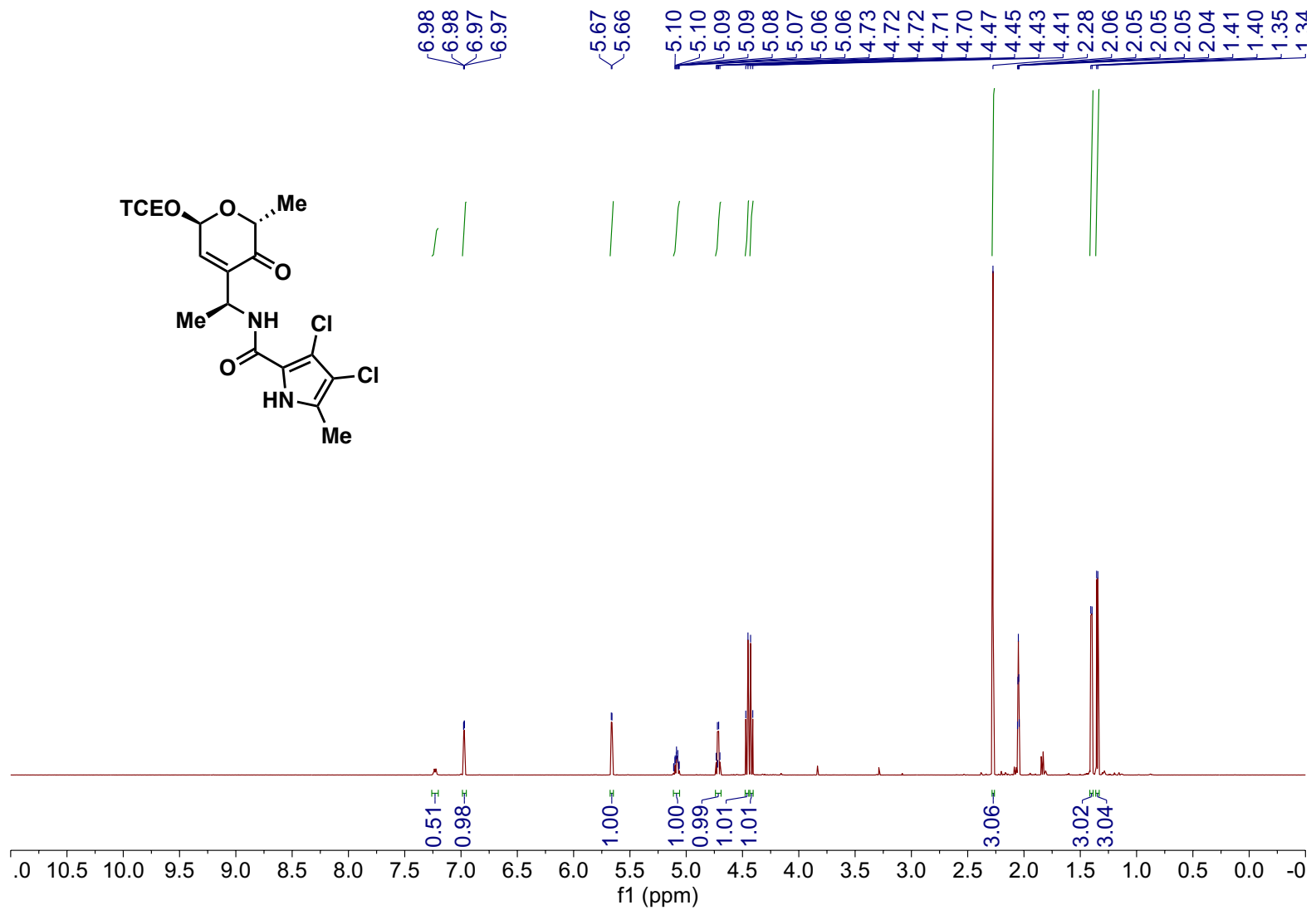
<sup>1</sup>H NMR of 27



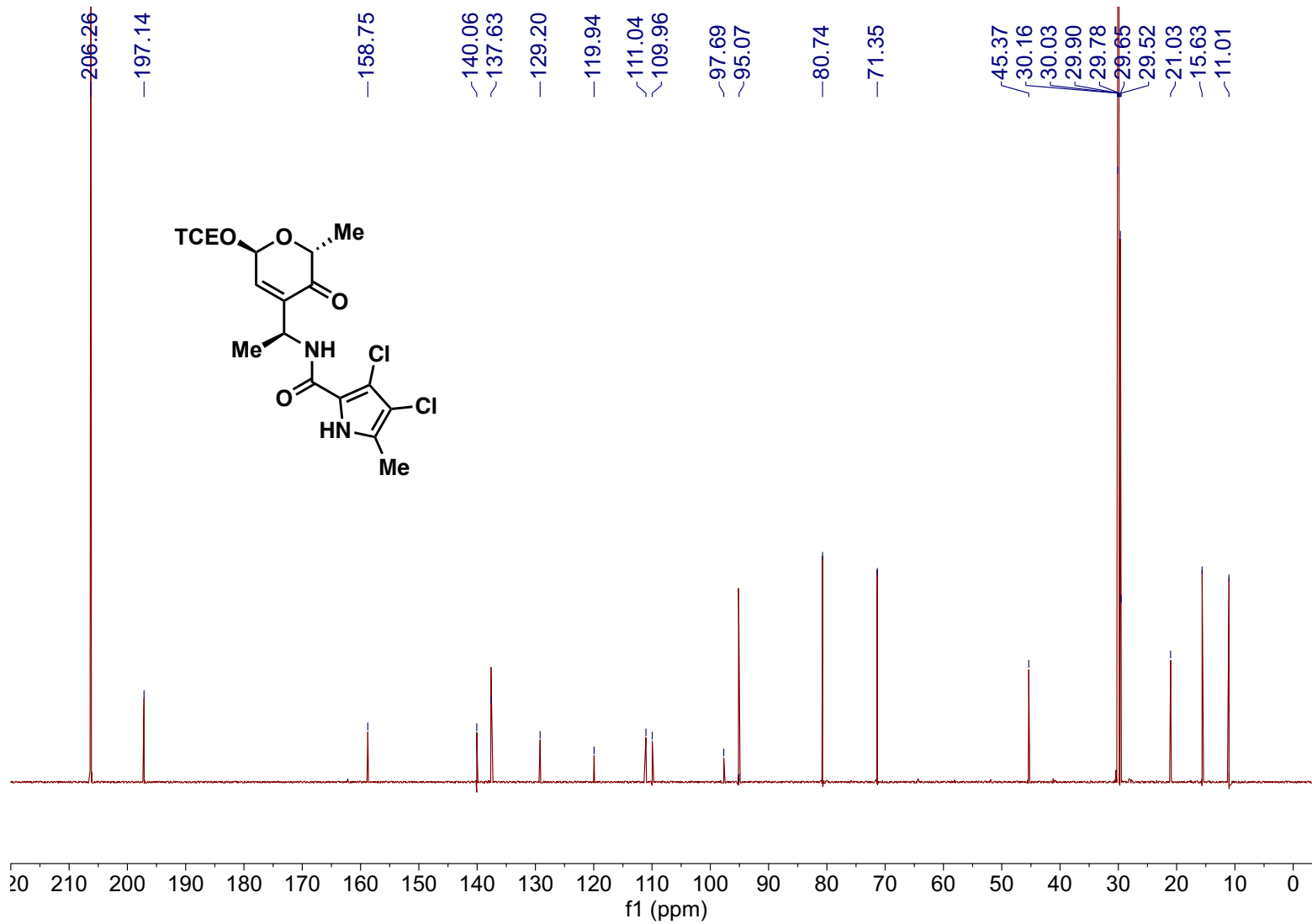
<sup>13</sup>C NMR of **27**



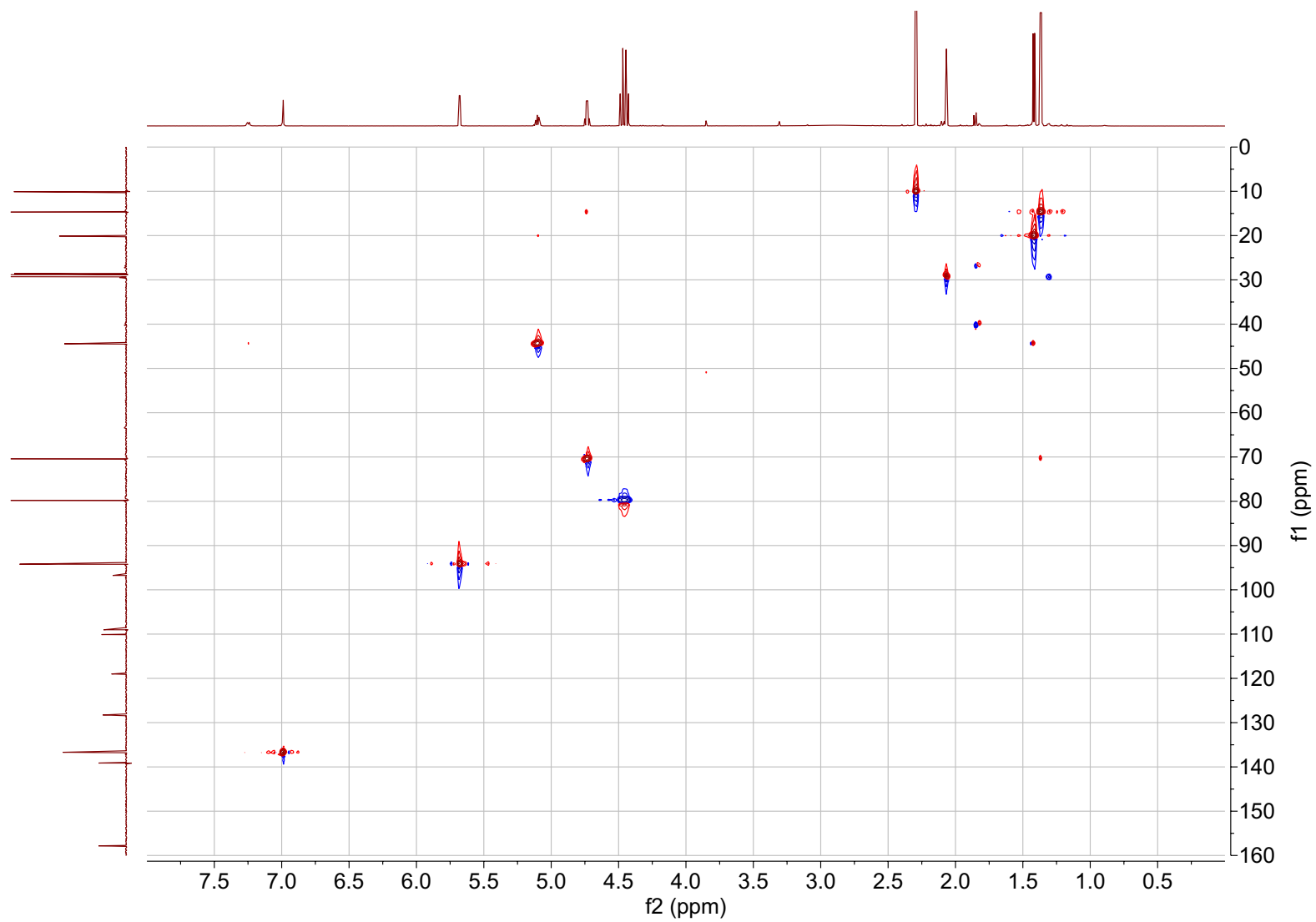
<sup>1</sup>H NMR of 29



<sup>13</sup>C NMR of **29**

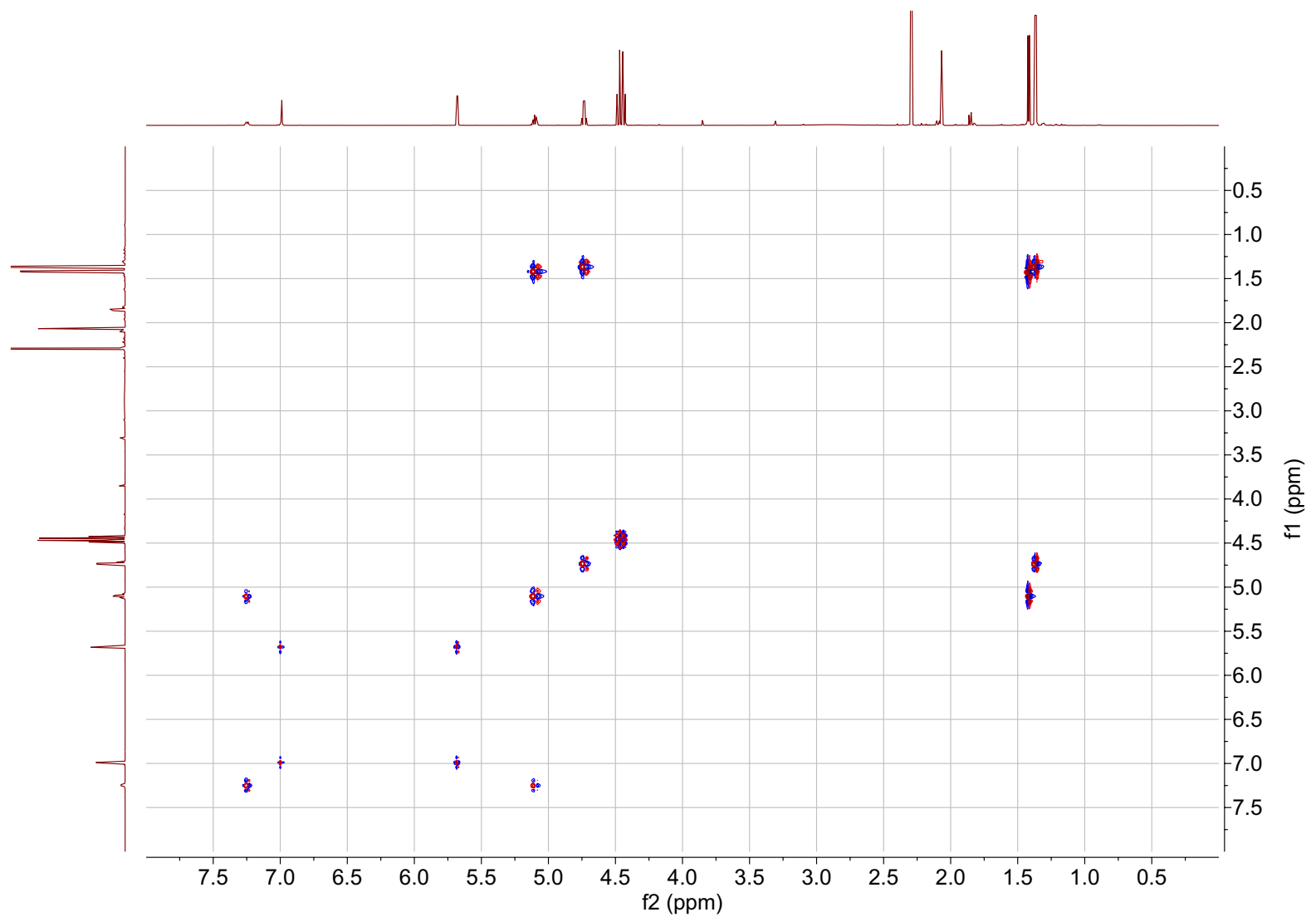


HSQC of 29

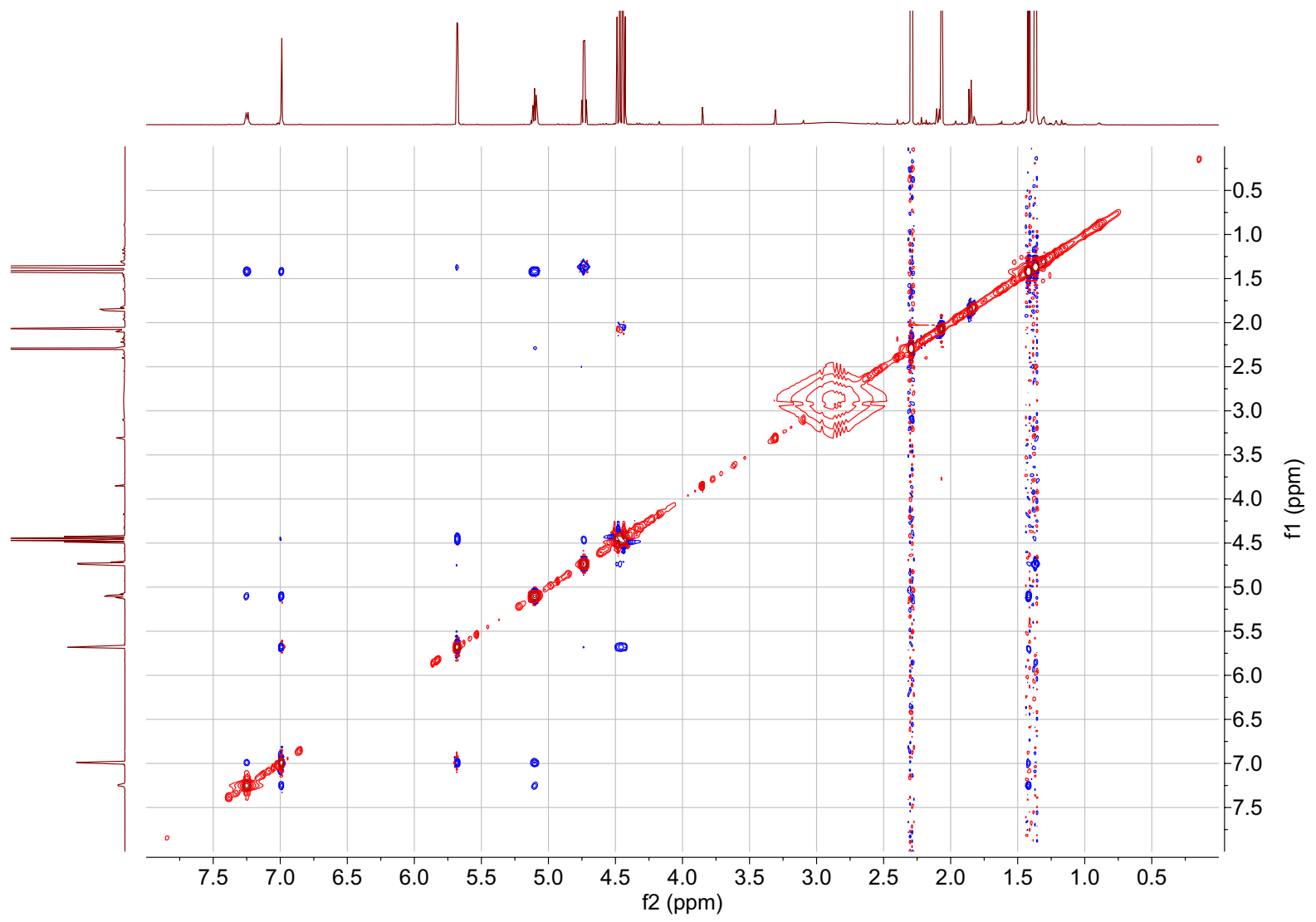




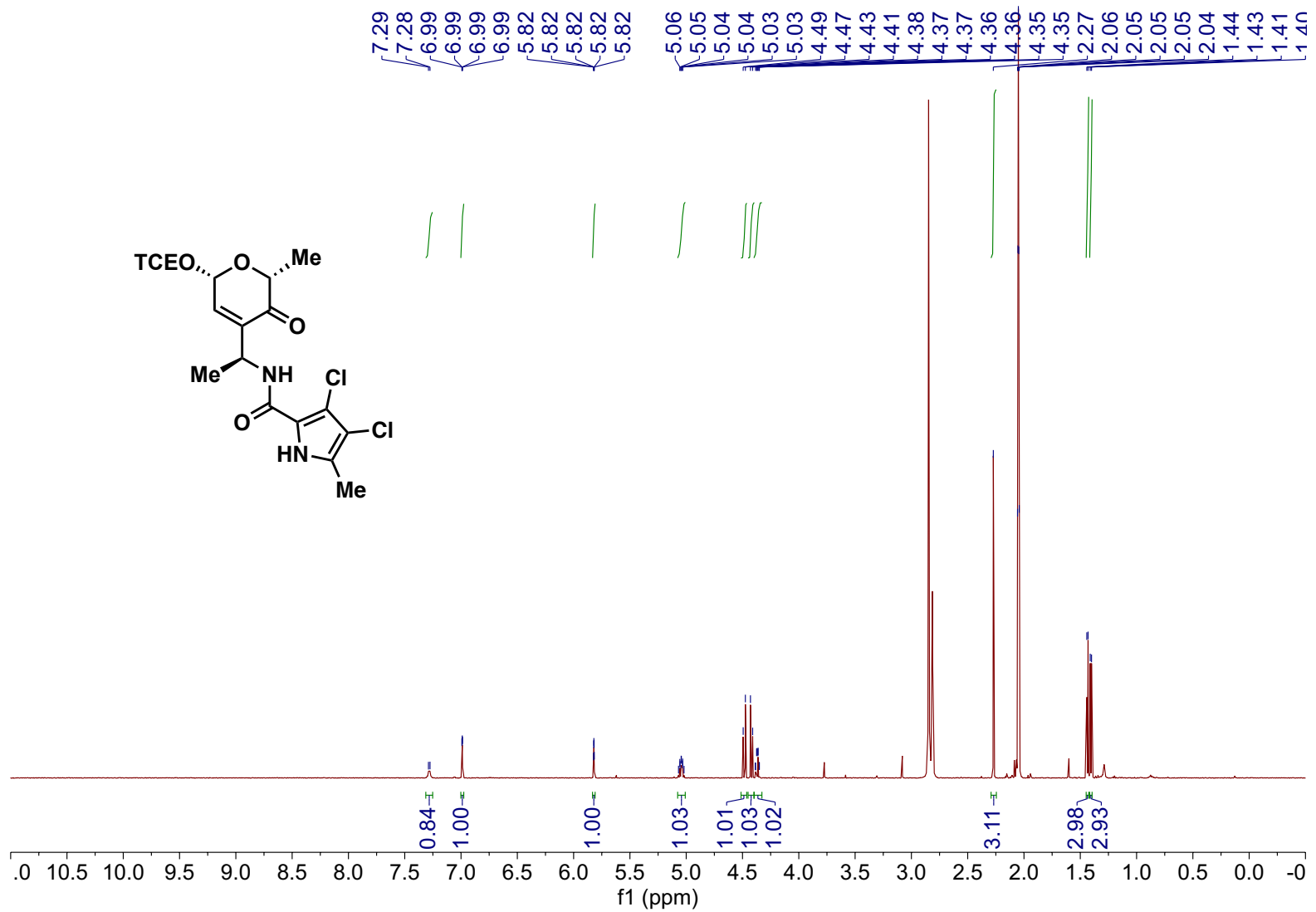
COSY of 29



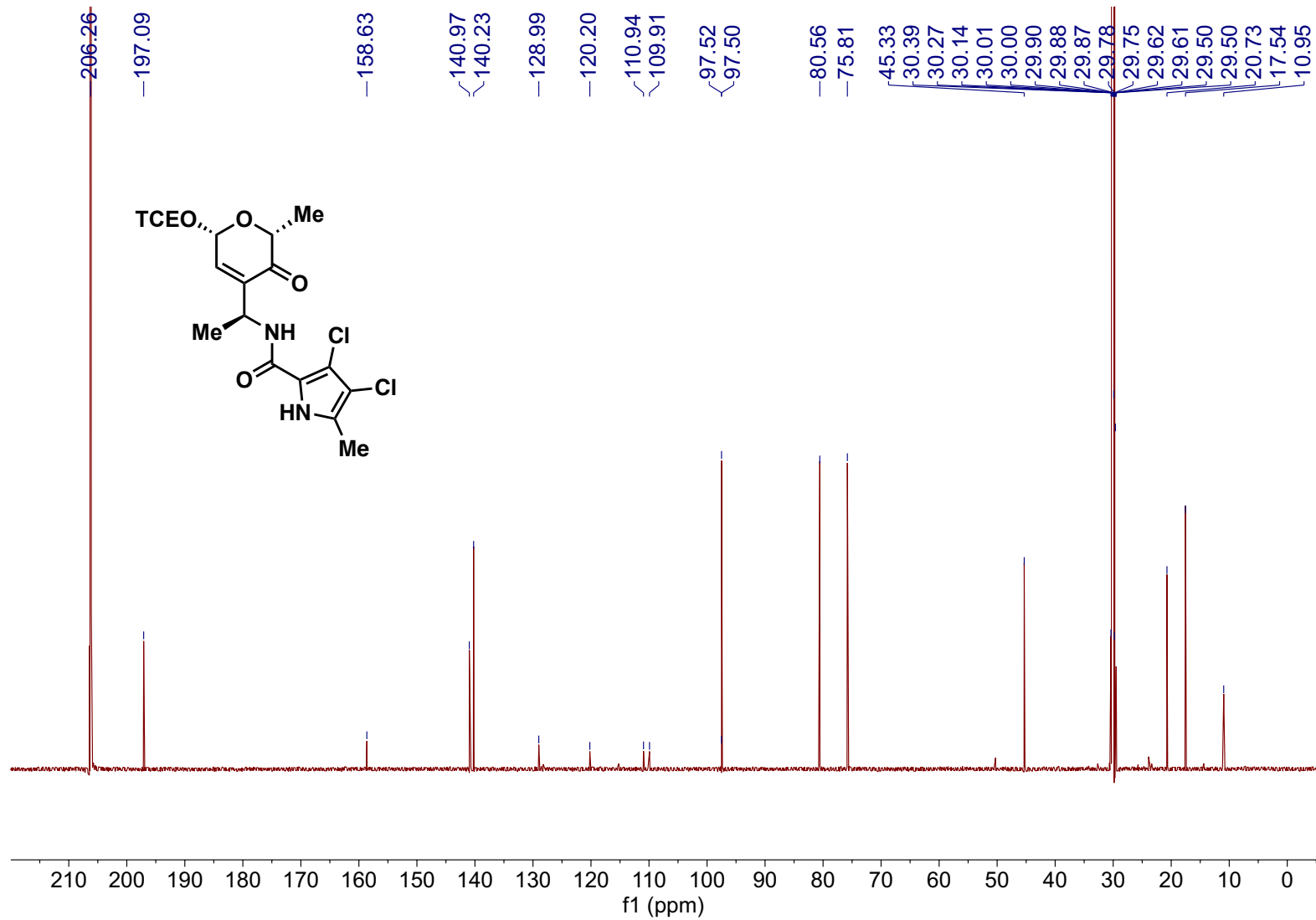
NOESY of 29



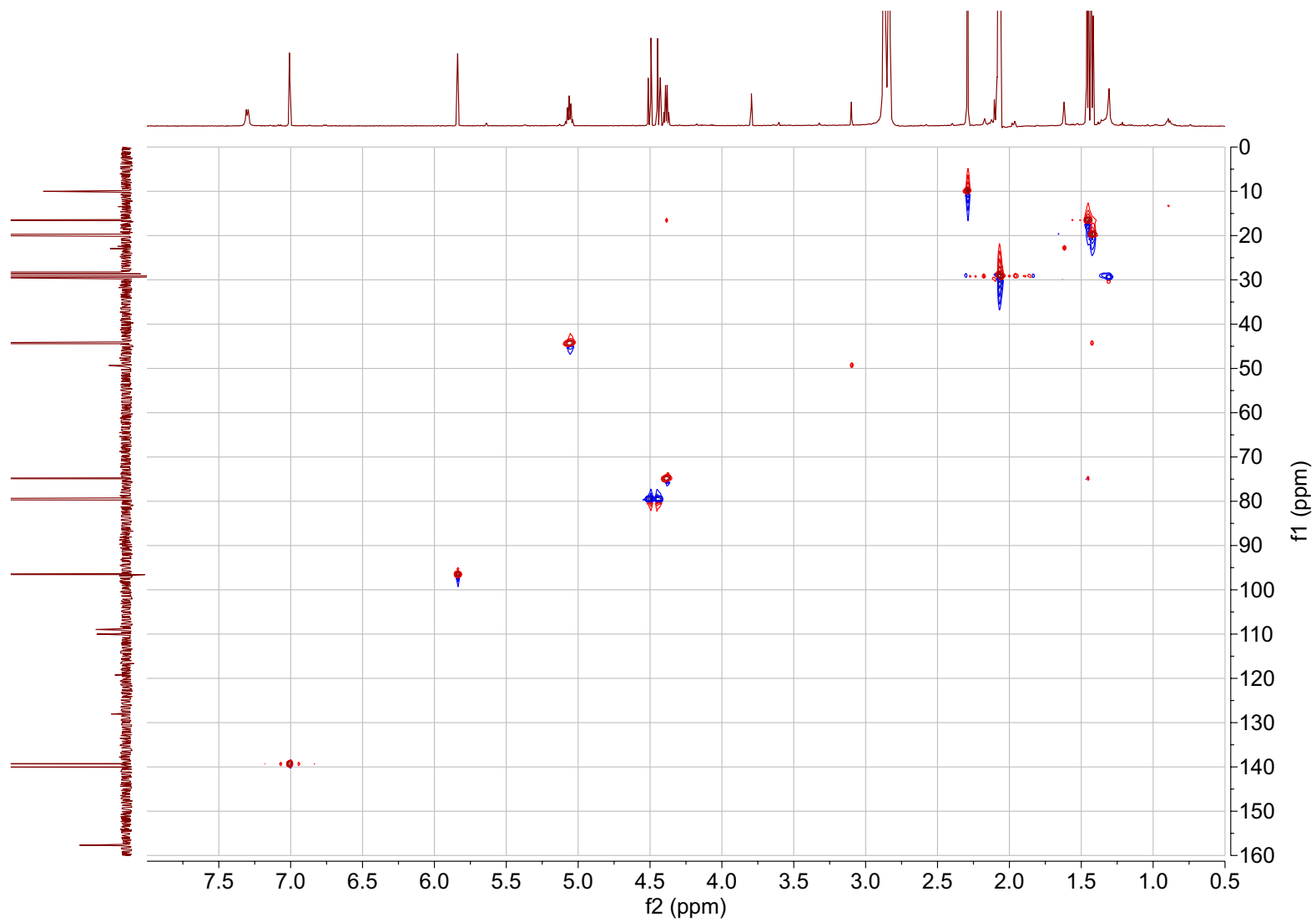
<sup>1</sup>H NMR of 29B



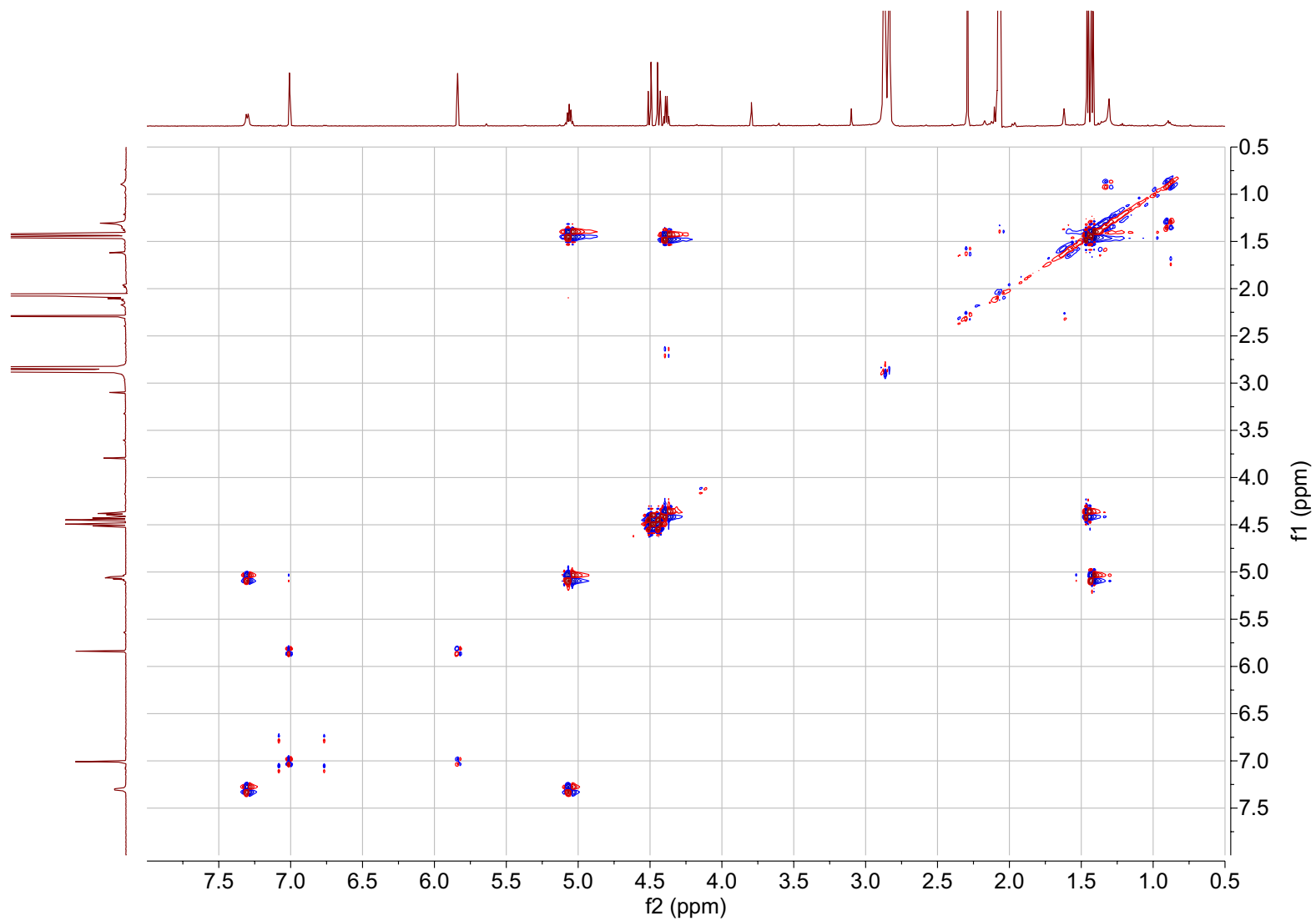
<sup>13</sup>C NMR of **29B**



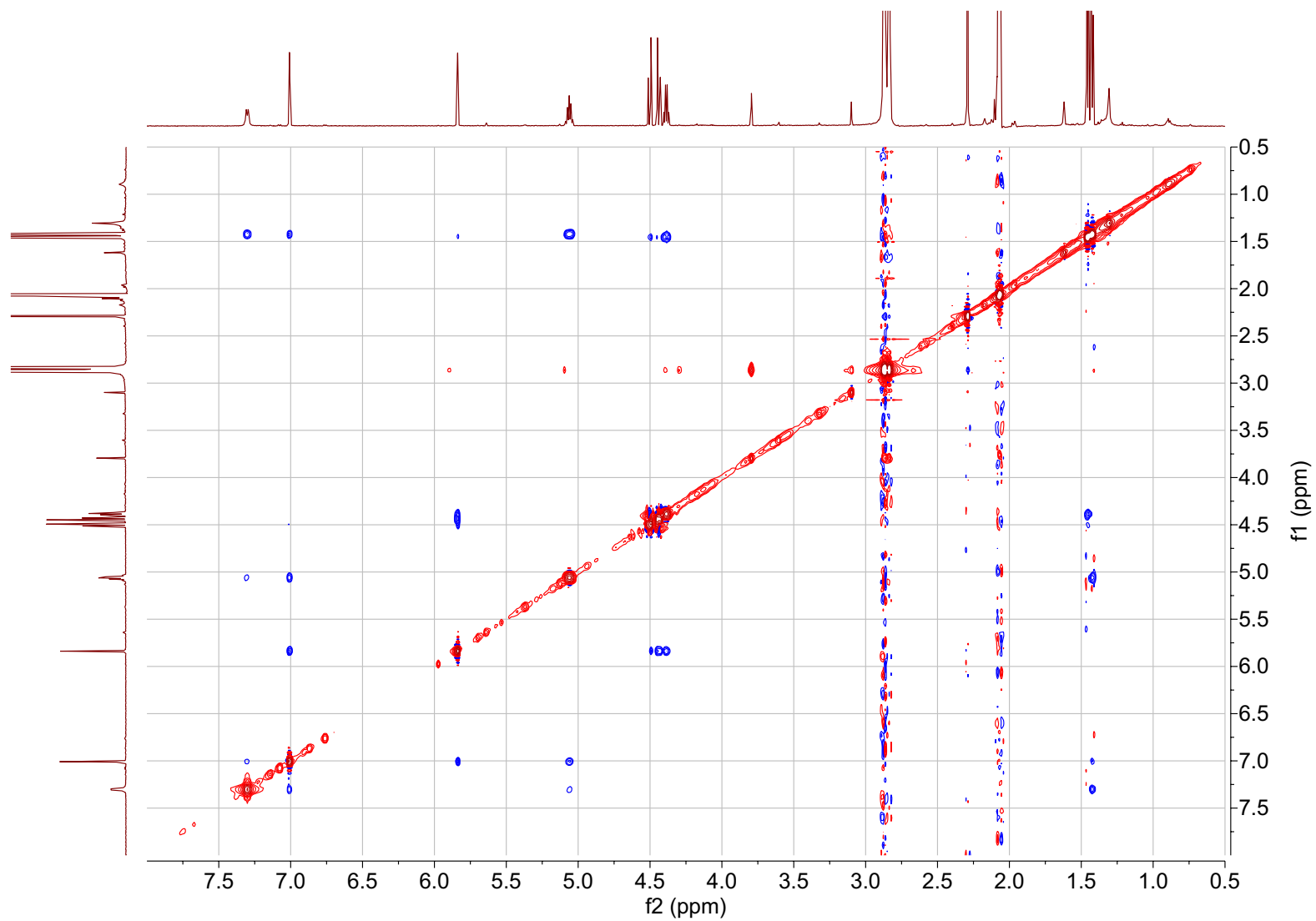
HSQC of 29B



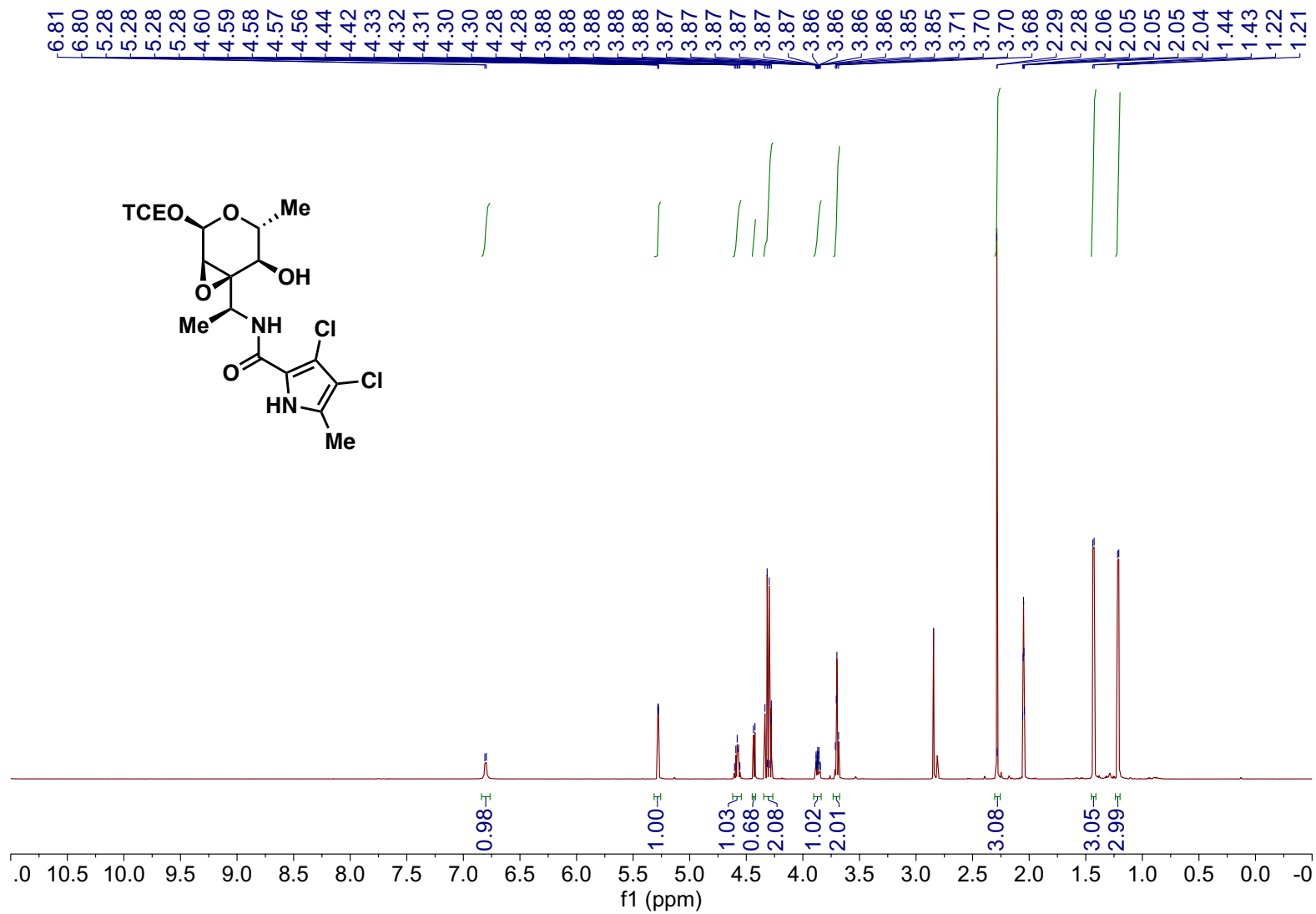
COSY of 29B



NOESY of **29B**

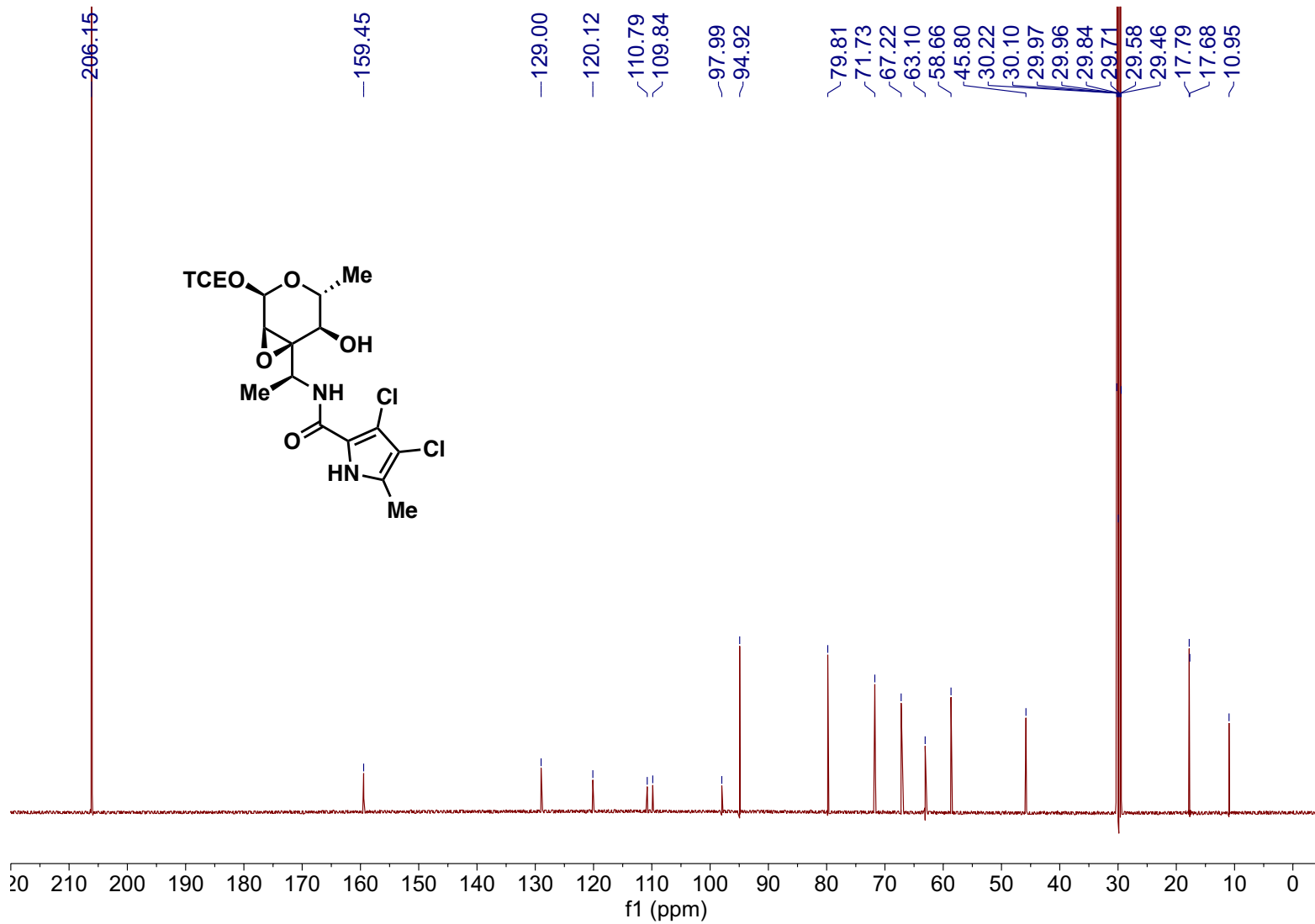


<sup>1</sup>H NMR of 30

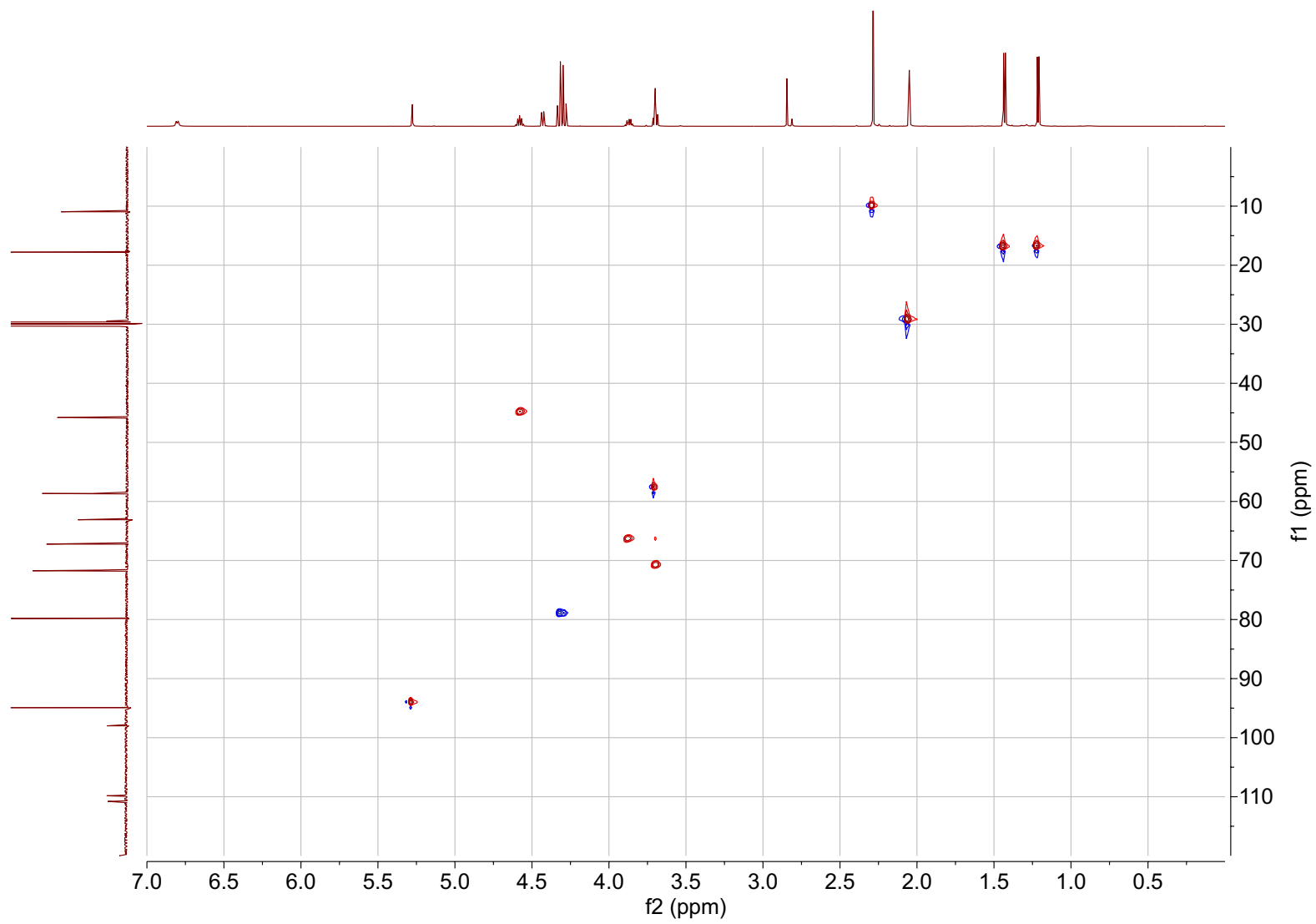




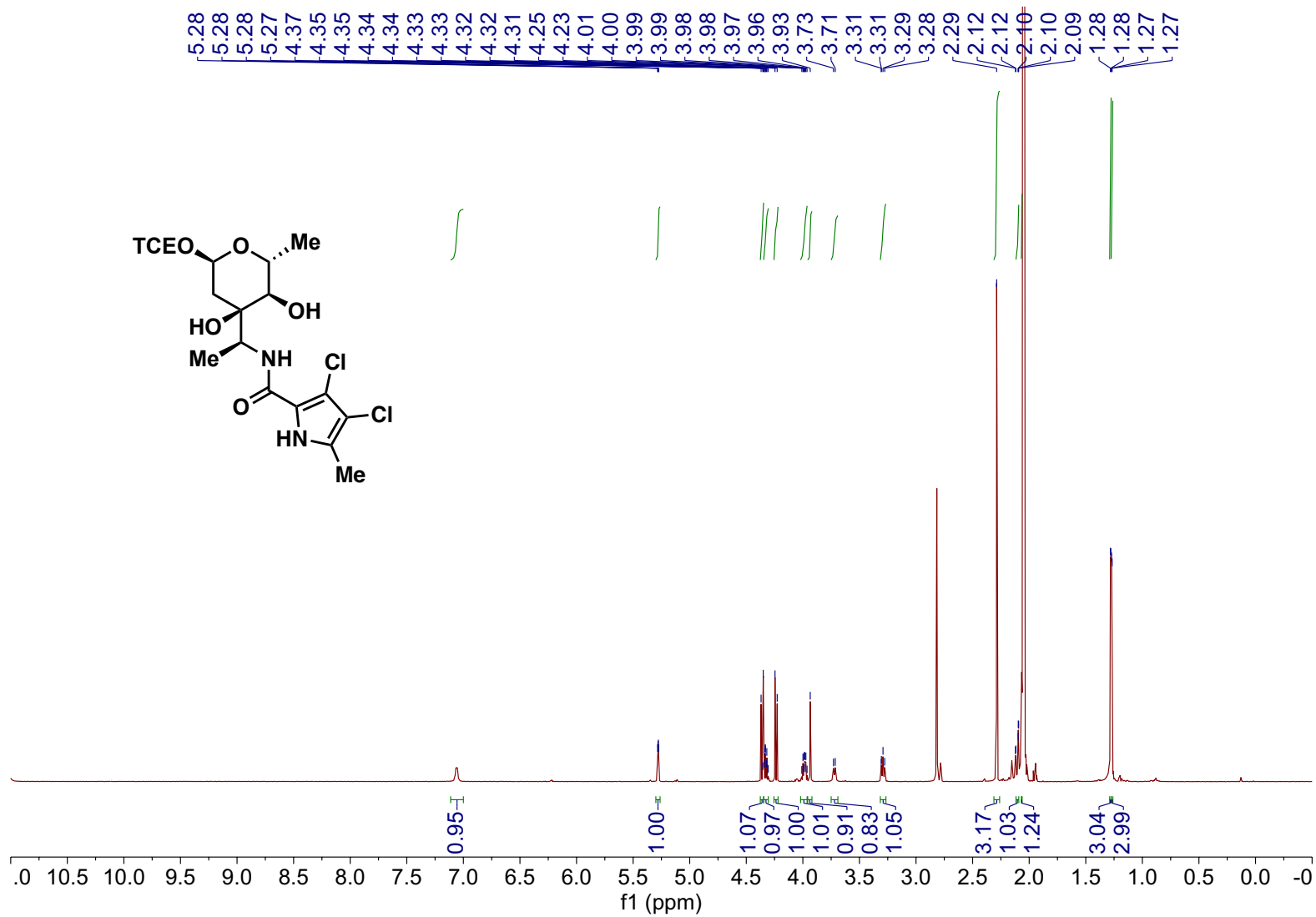
<sup>13</sup>C NMR of **30**



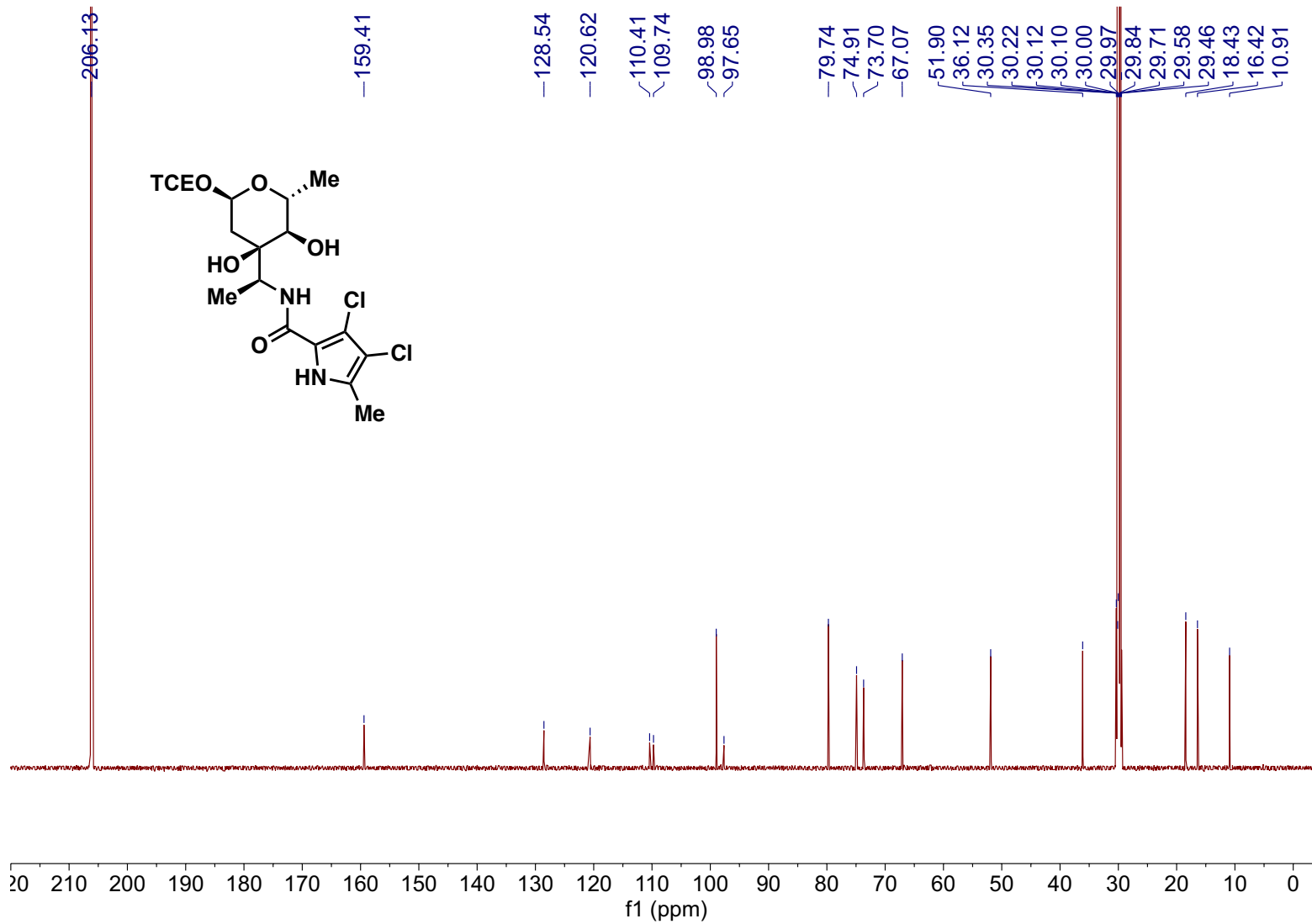
HSQC of 30



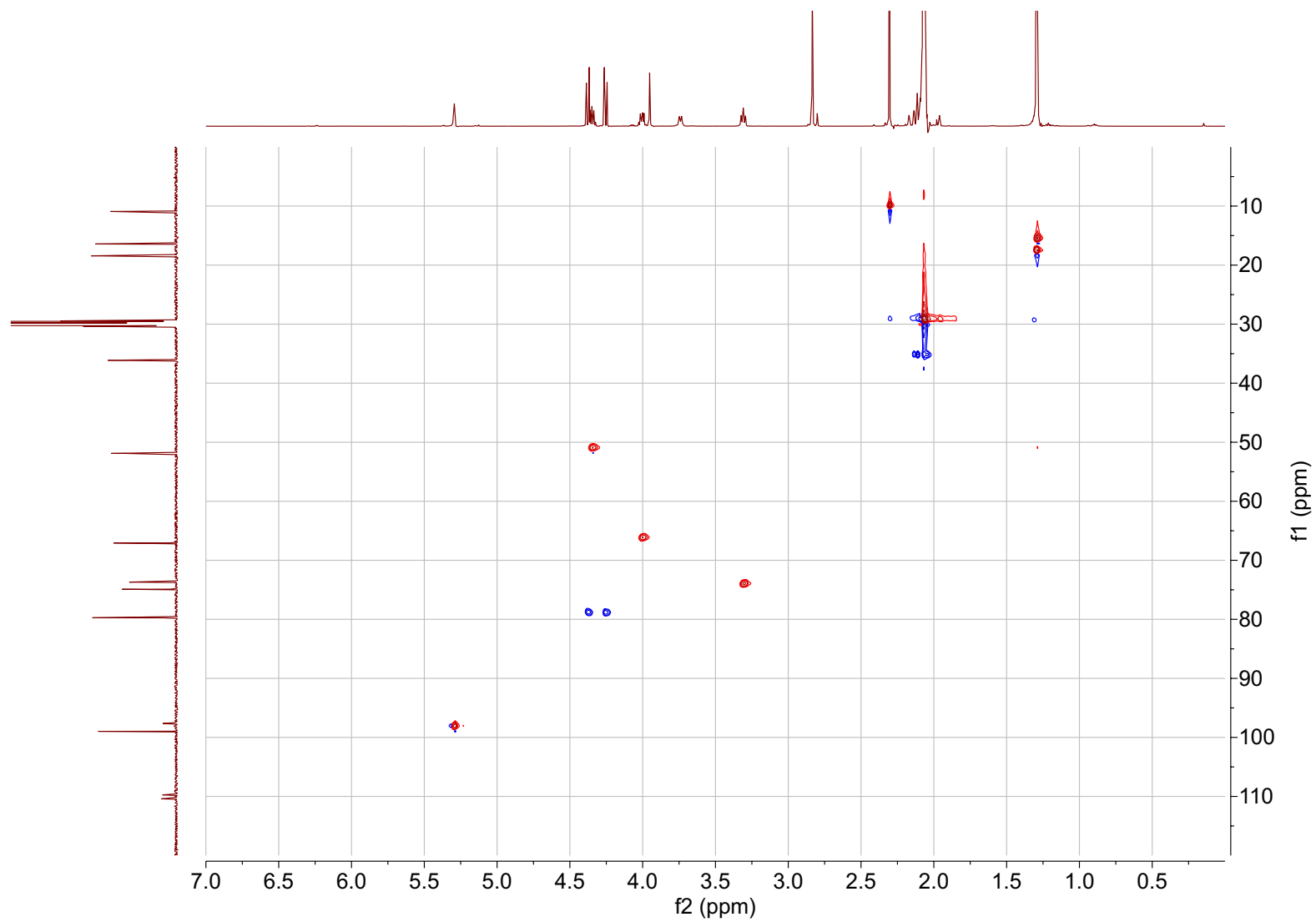
<sup>1</sup>H NMR of S9



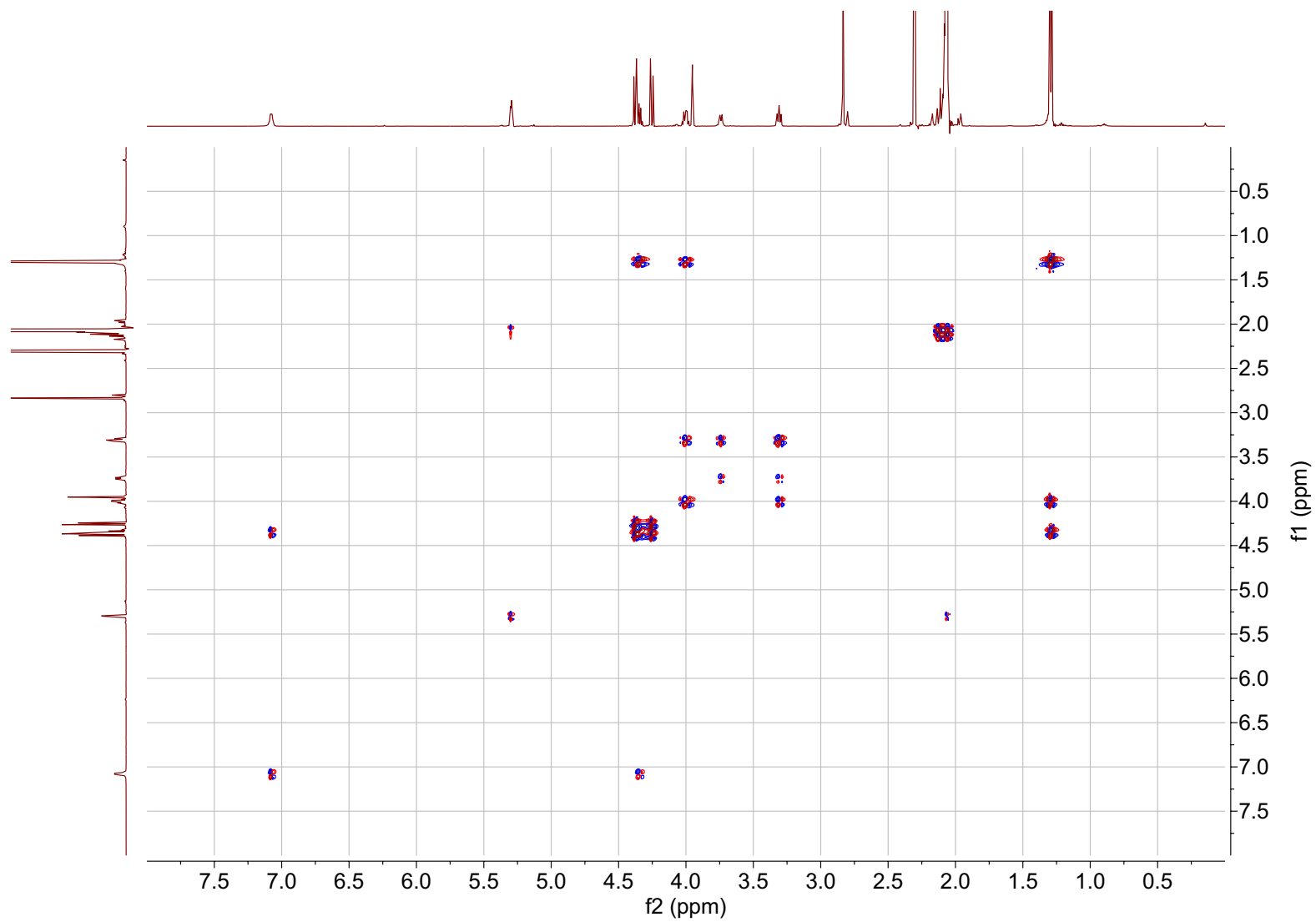
<sup>13</sup>C NMR of **S9**



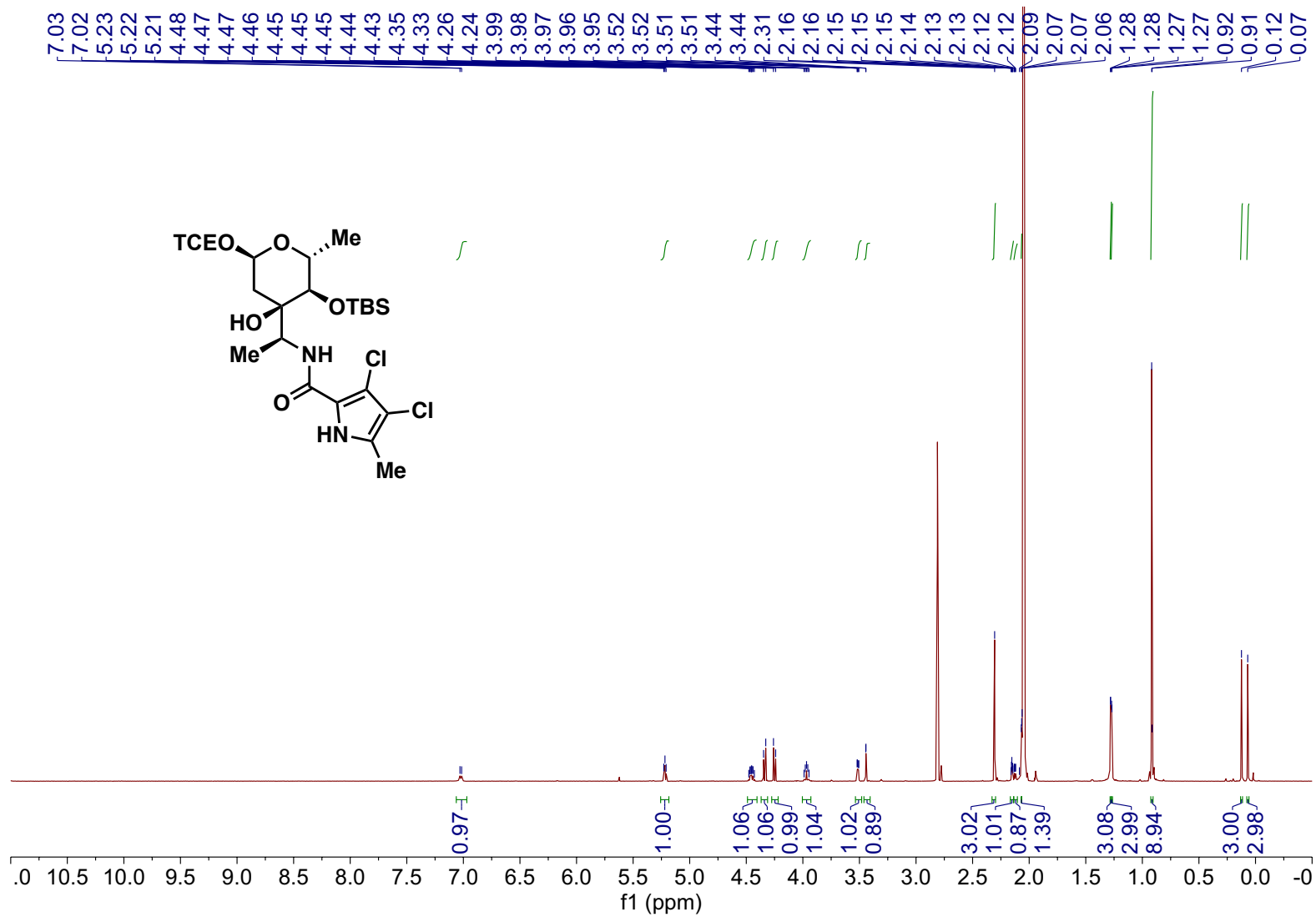
HSQC of S9



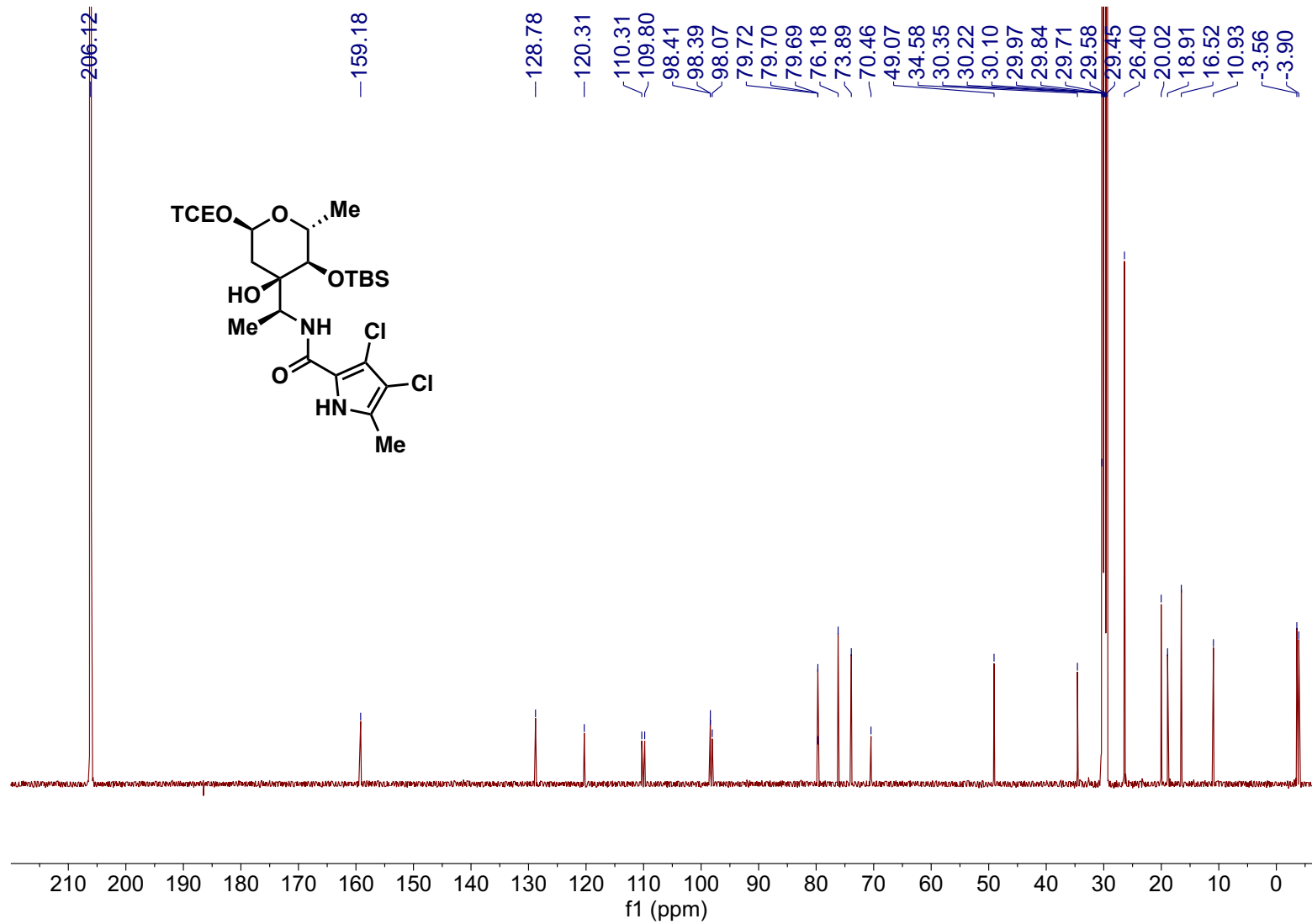
COSY of **S9**



<sup>1</sup>H NMR of 31

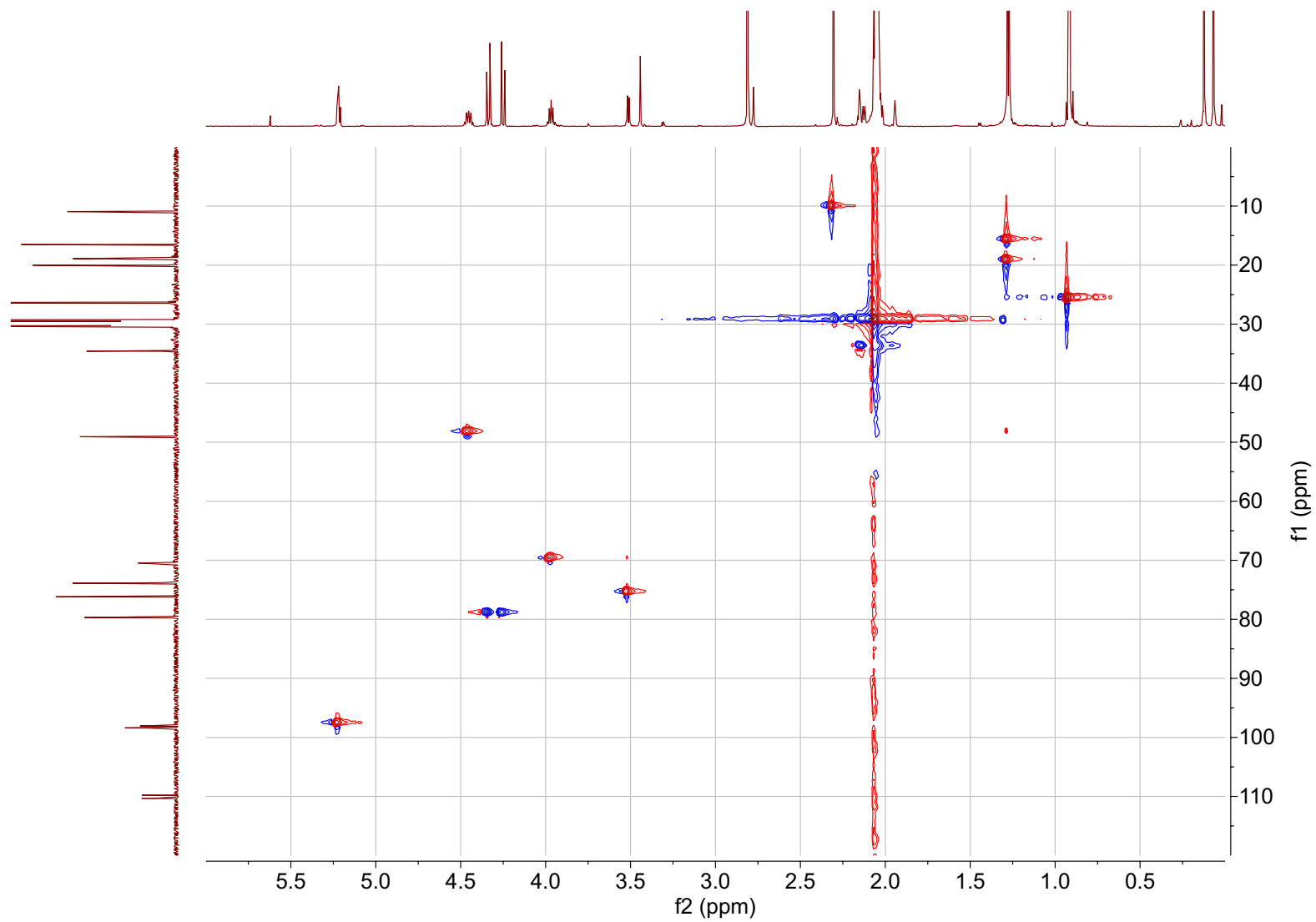


<sup>13</sup>C NMR of **31**

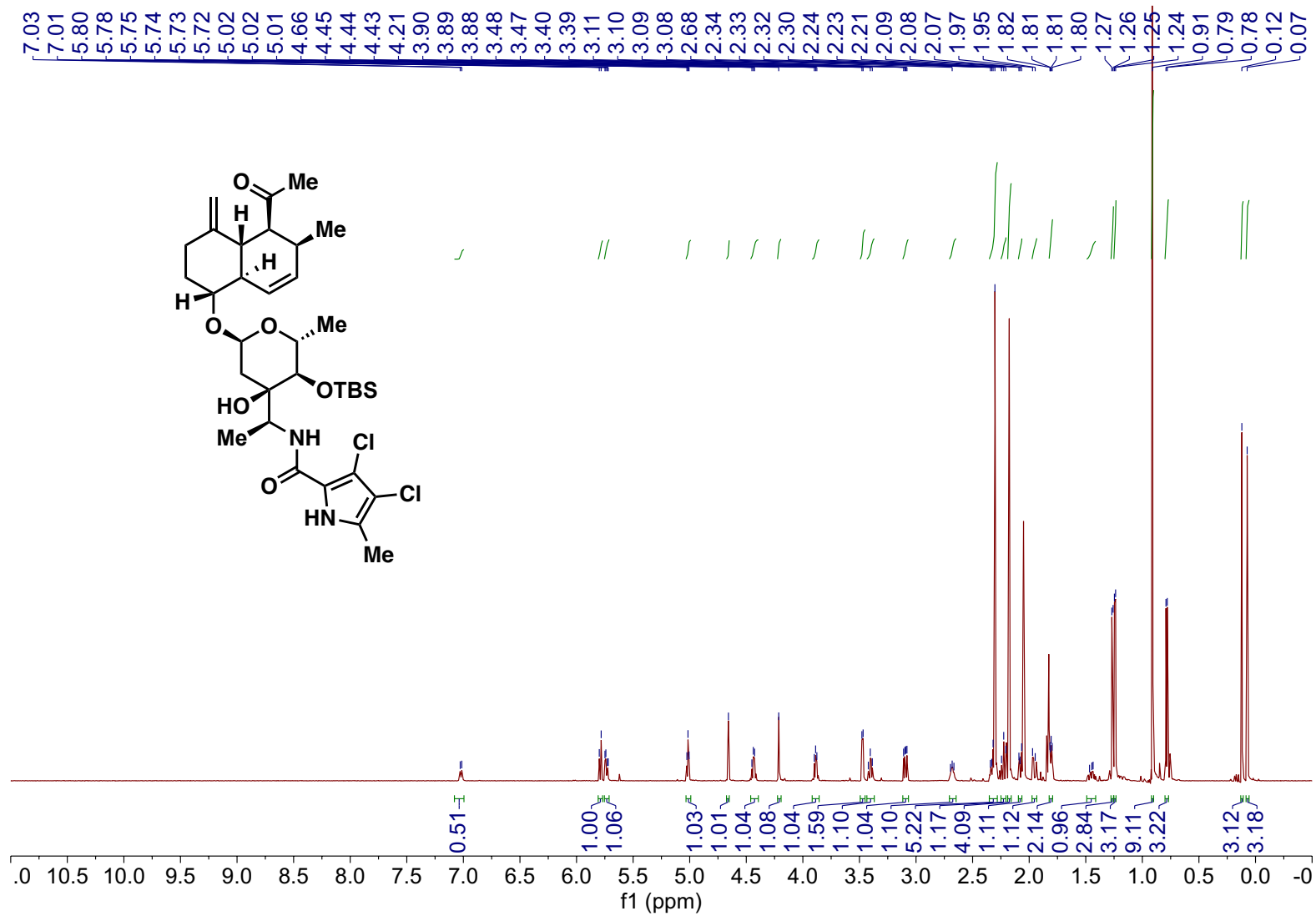




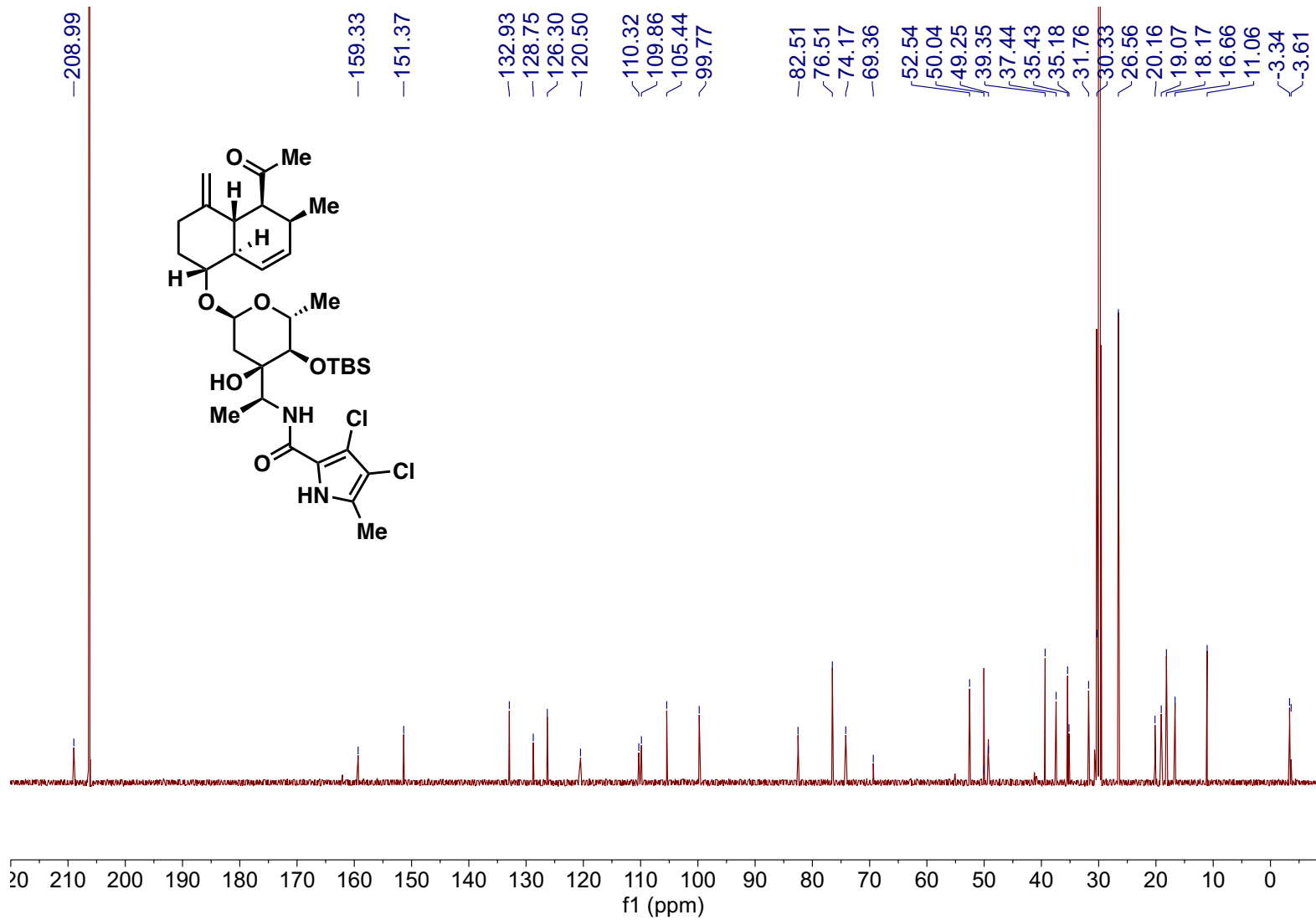
HSQC of 31



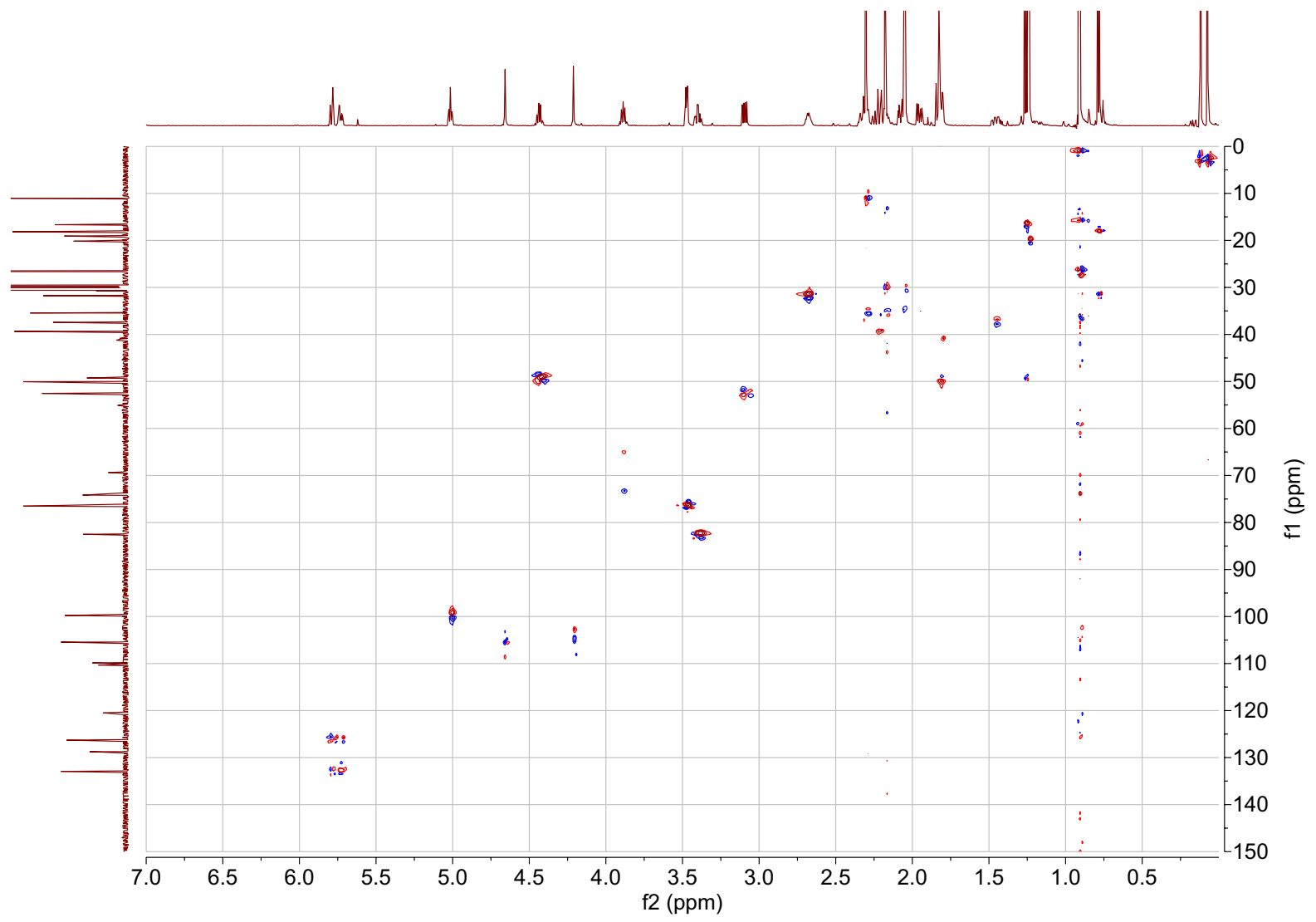
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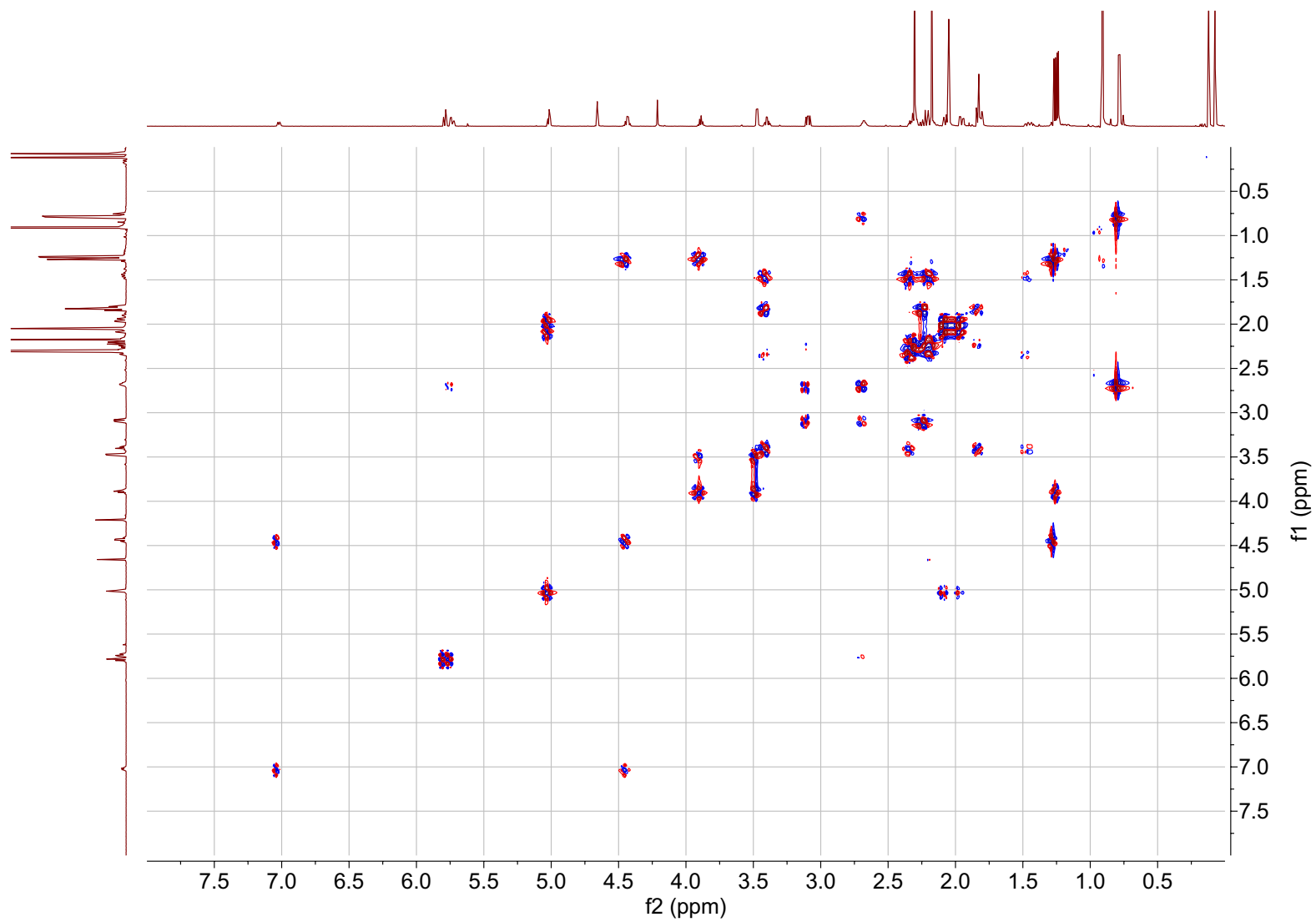
<sup>13</sup>C NMR of **32**



HSQC of 32

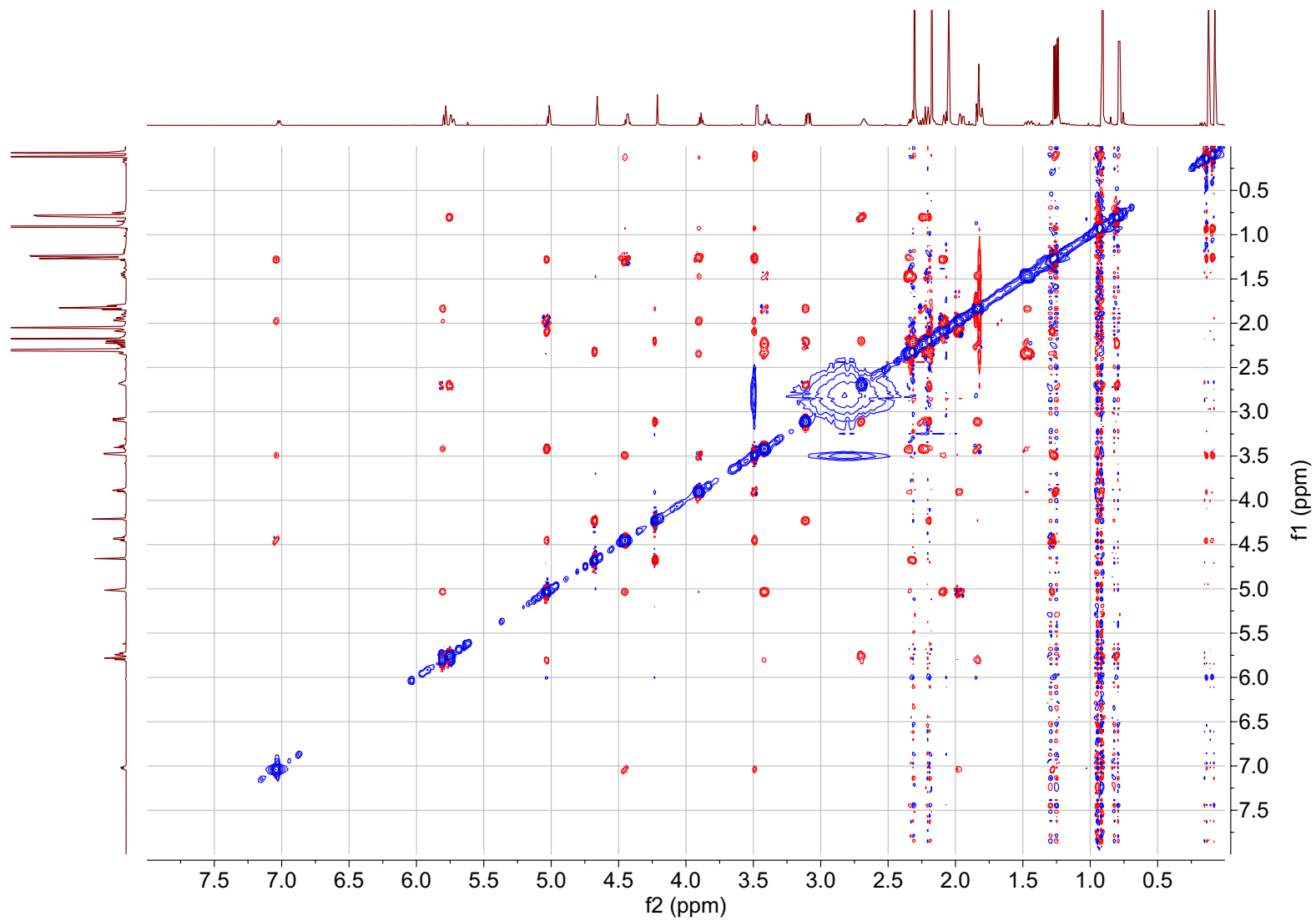


COSY of 32

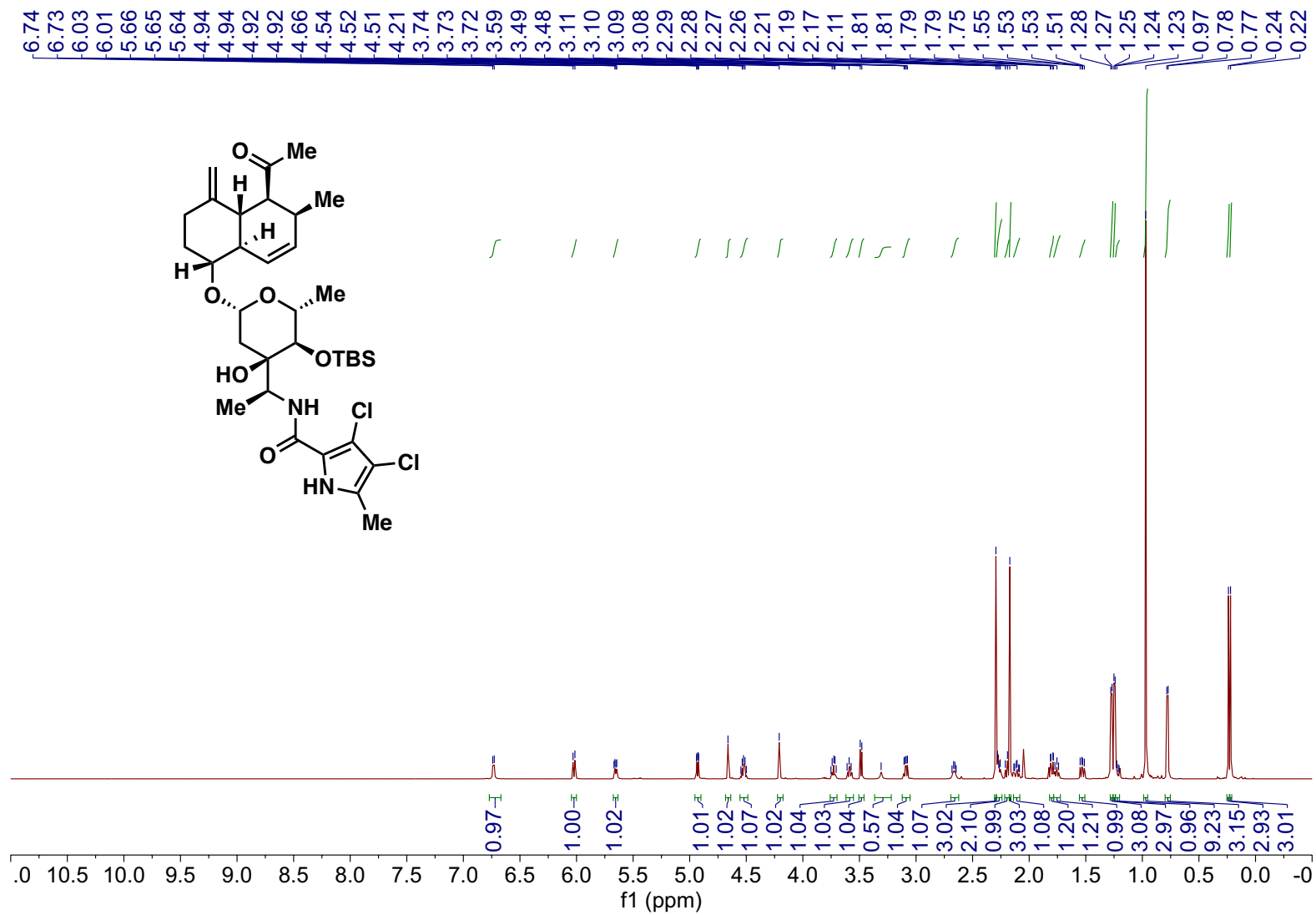


S164

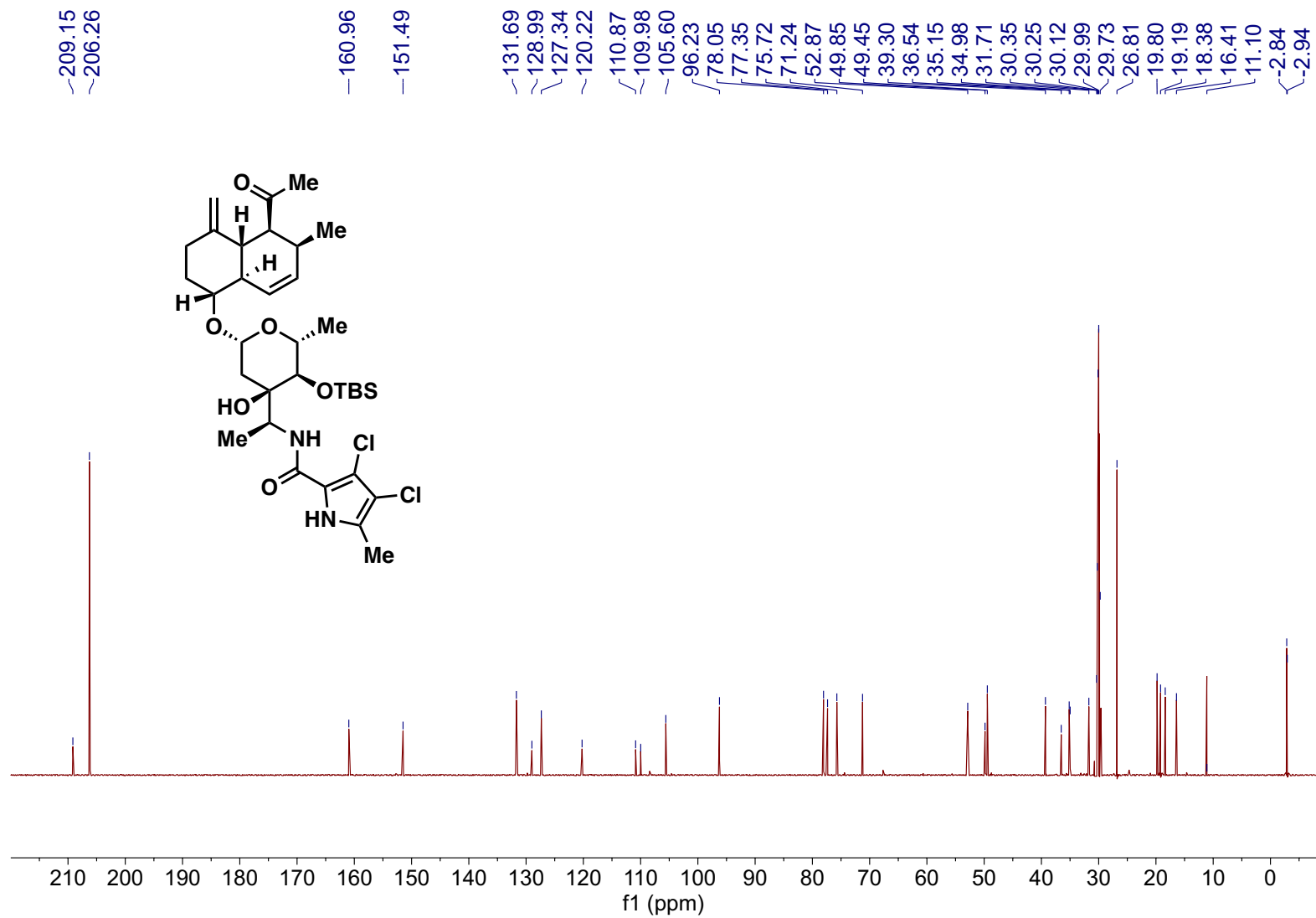
NOESY of 32



<sup>1</sup>H NMR of 33

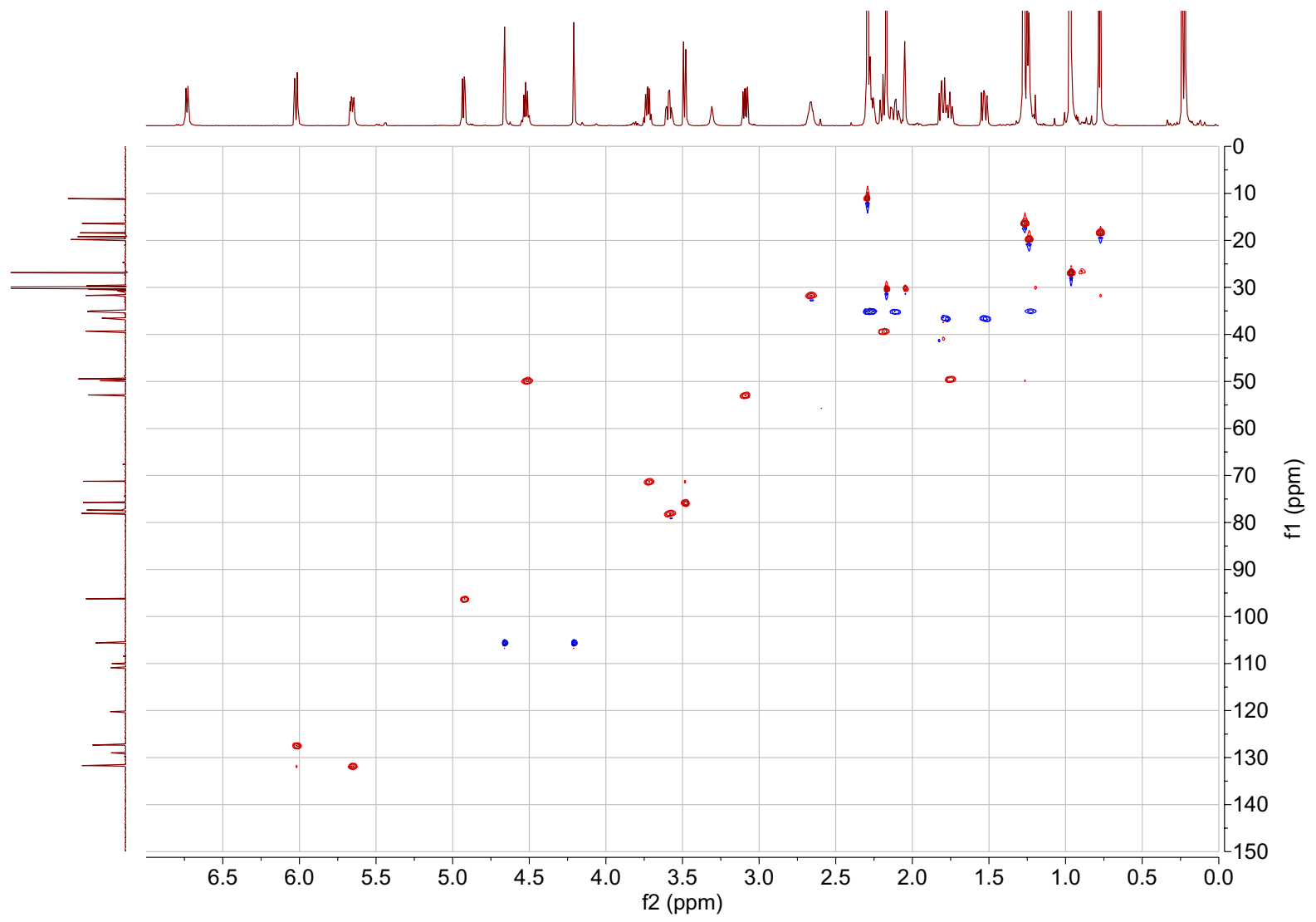


<sup>13</sup>C NMR of **33**

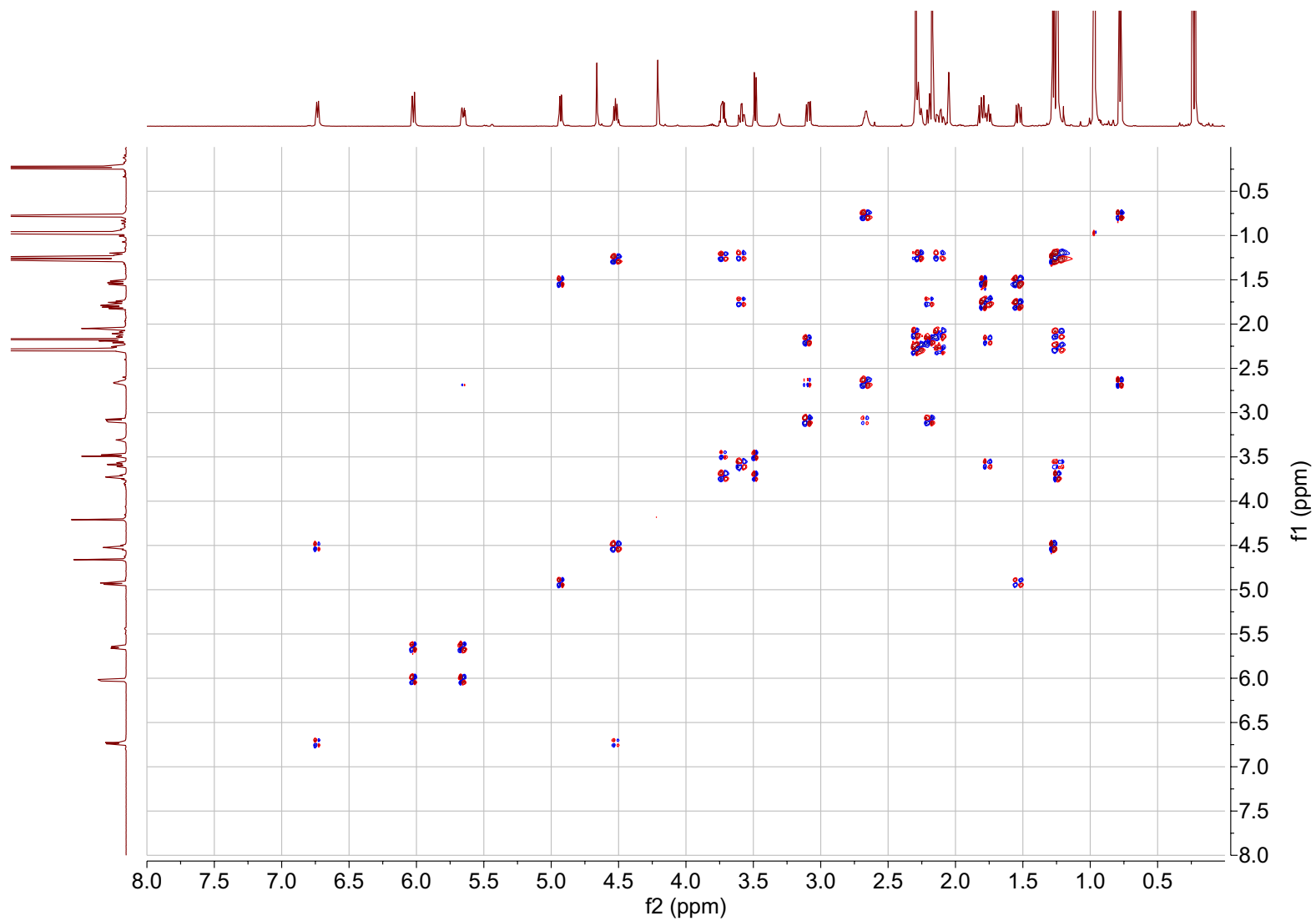




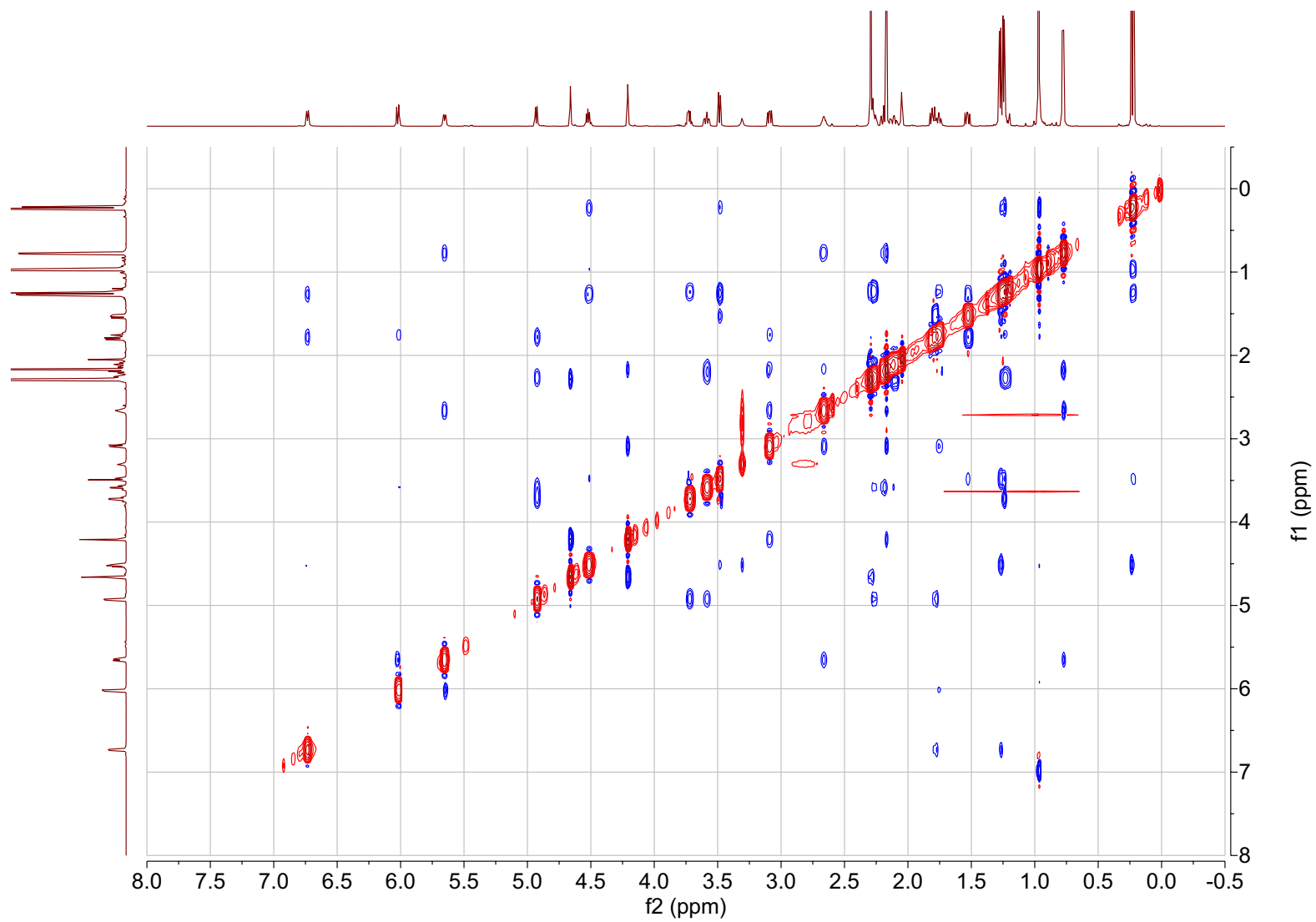
HSQC of 33



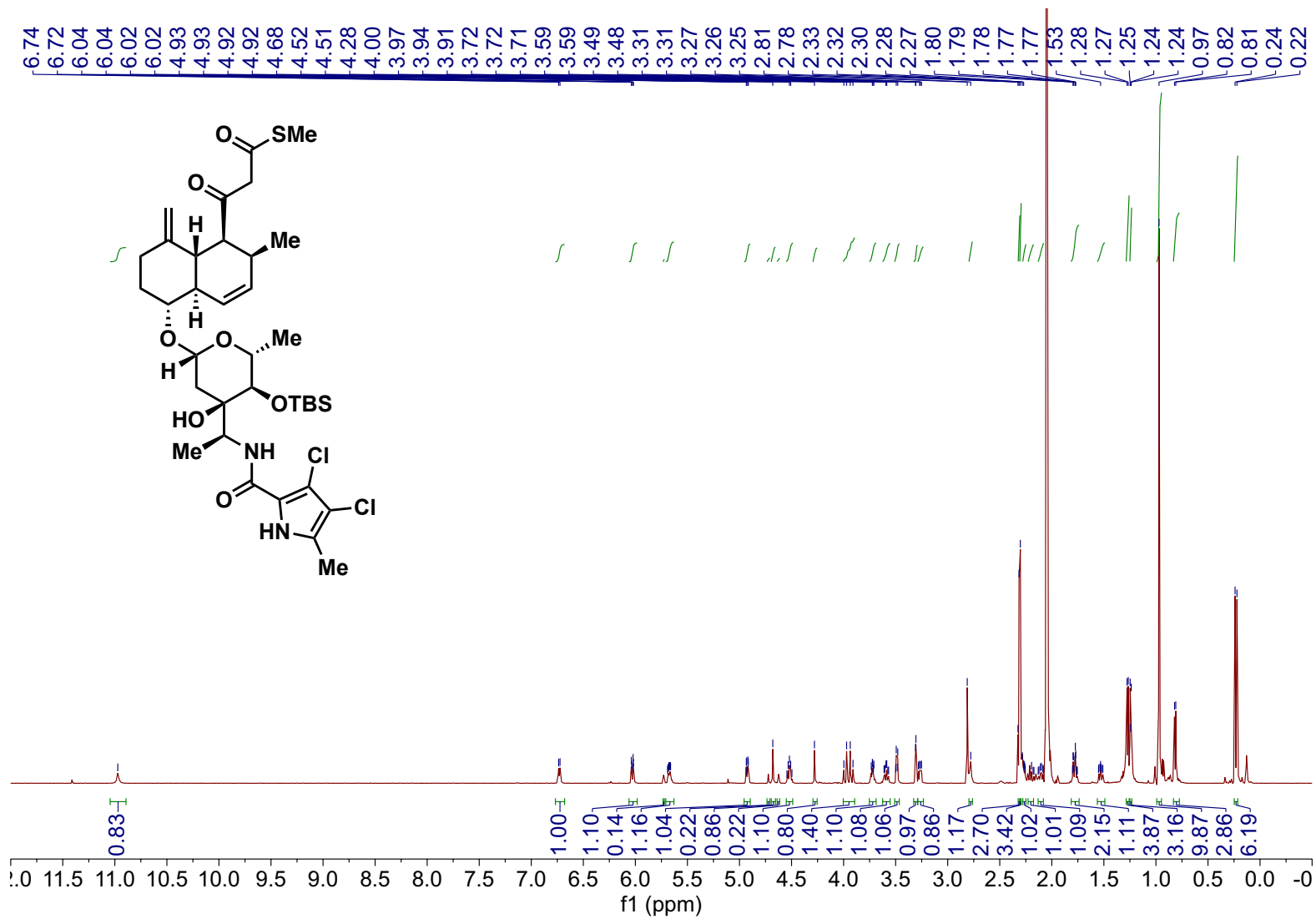
COSY of 33



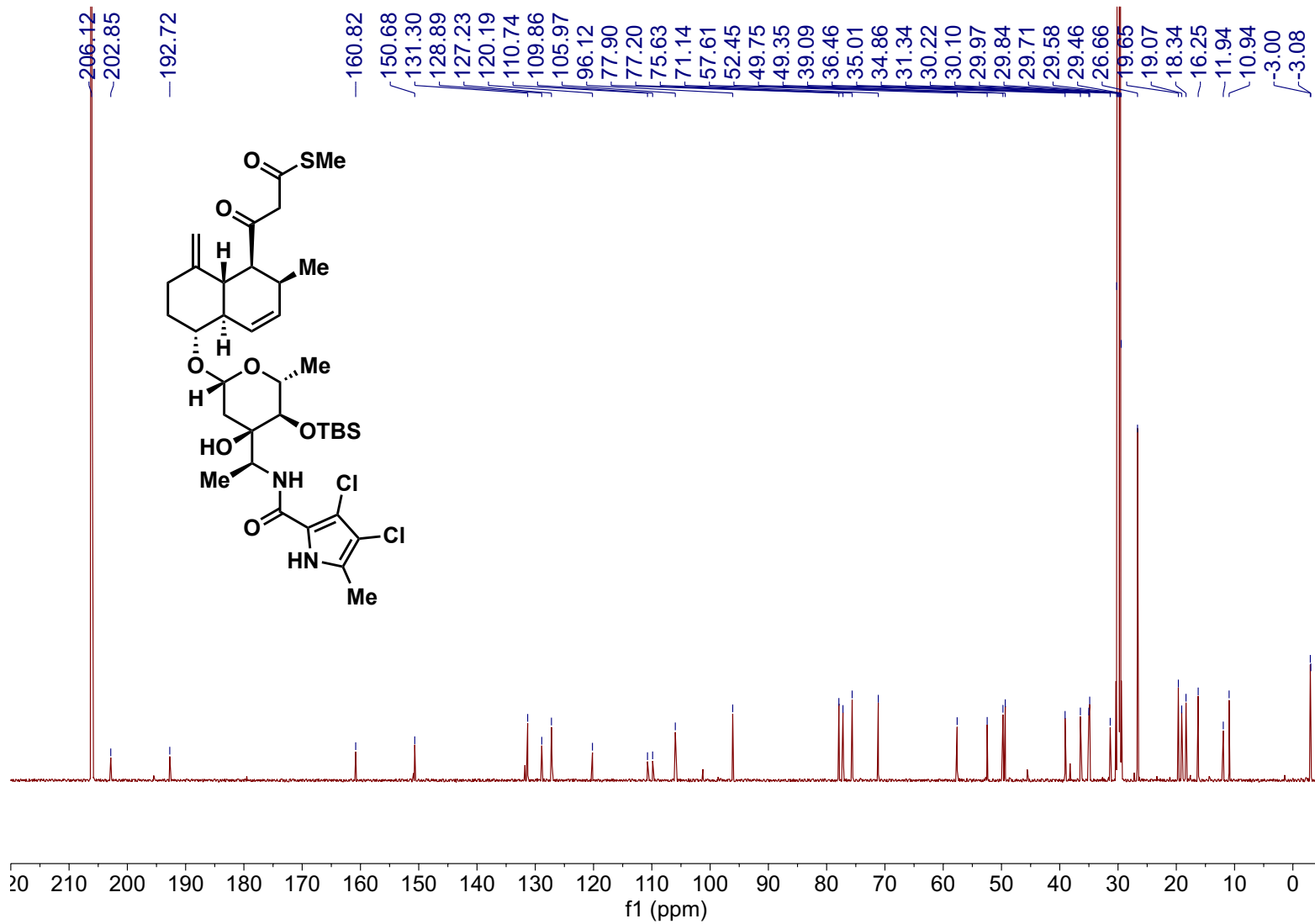
NOESY of 33



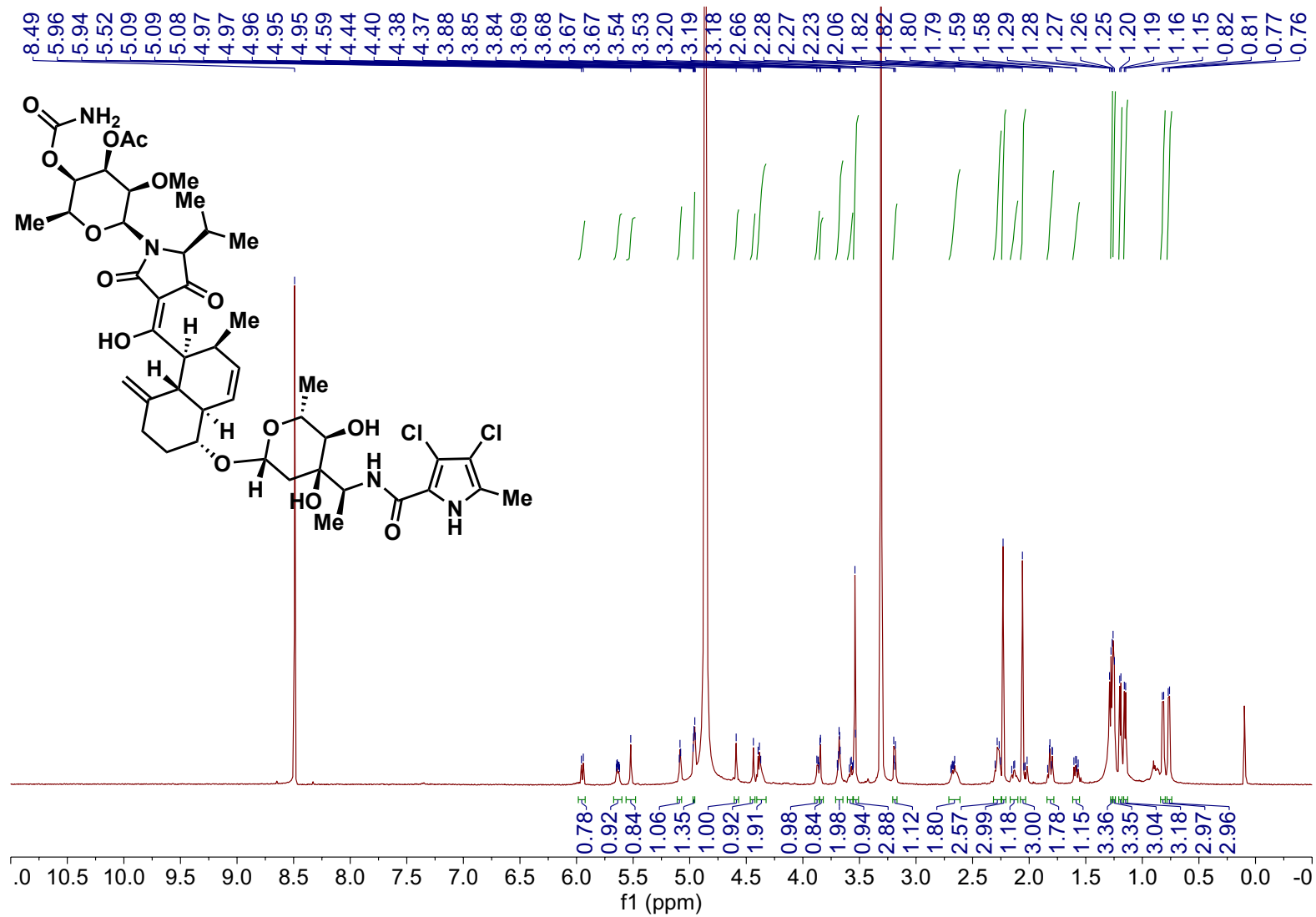
<sup>1</sup>H NMR of 34



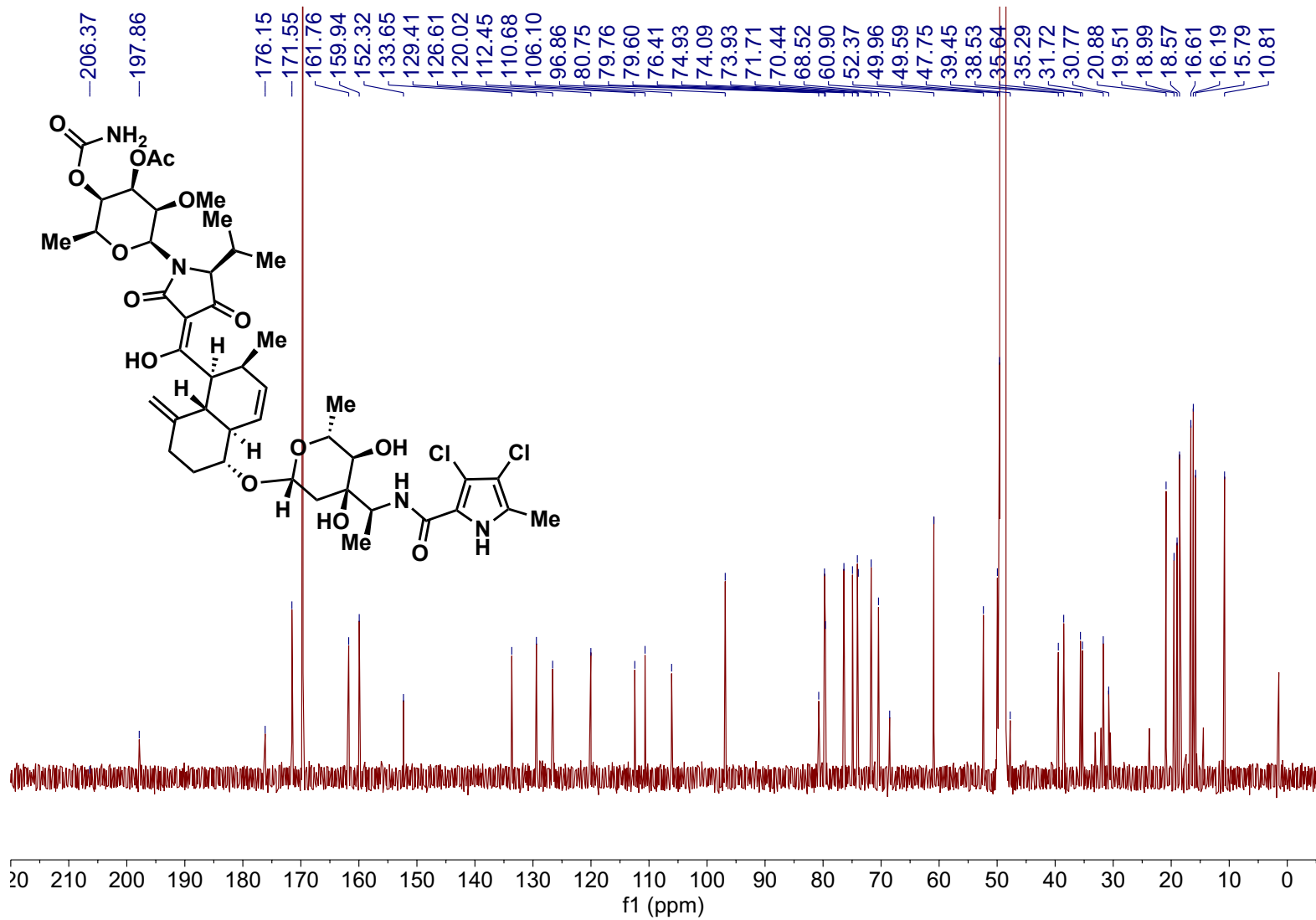
<sup>13</sup>C NMR of **34**



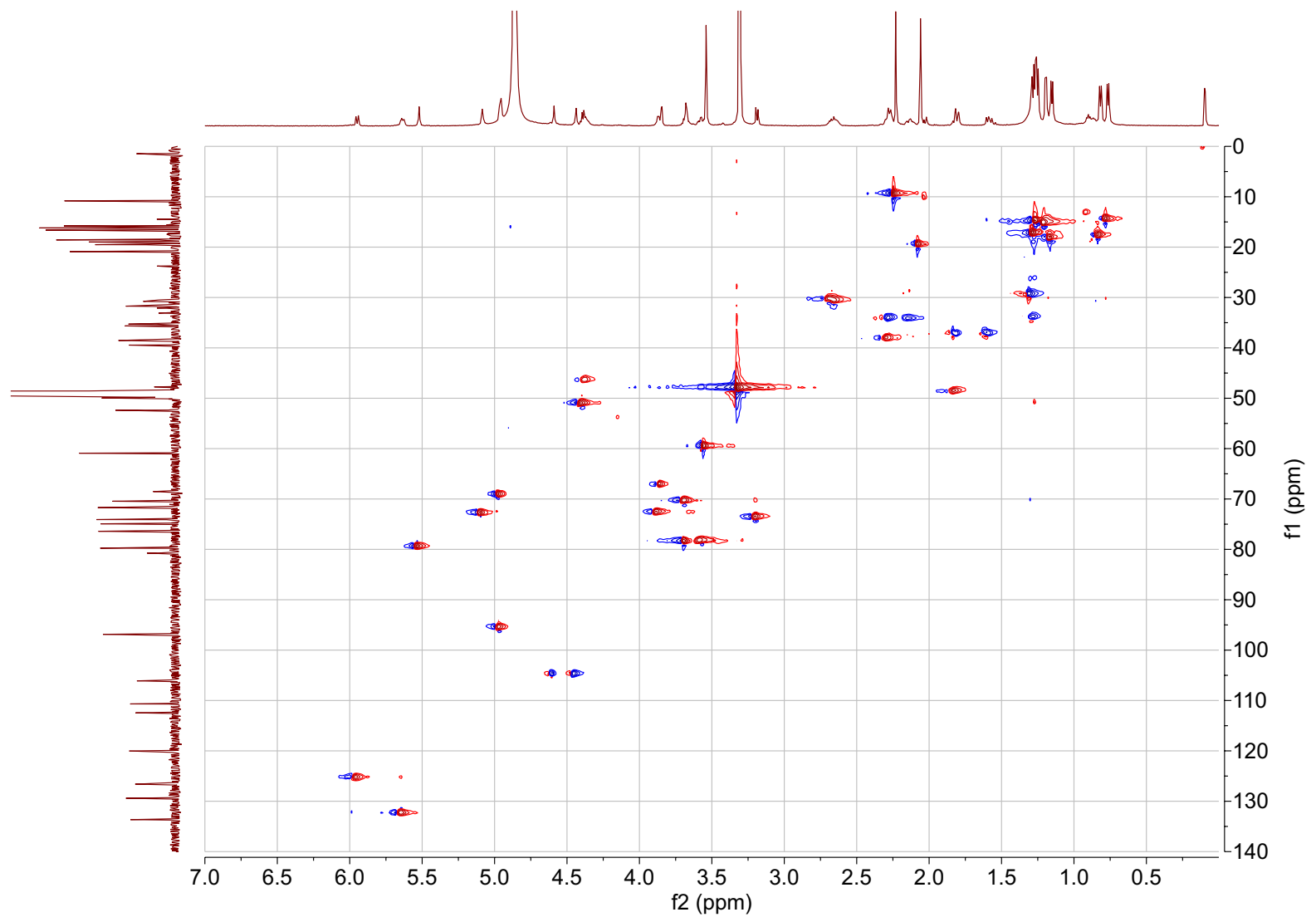
<sup>1</sup>H NMR of **35** (*epi*-KBD)



<sup>13</sup>C NMR of **35** (*epi*-KBD)

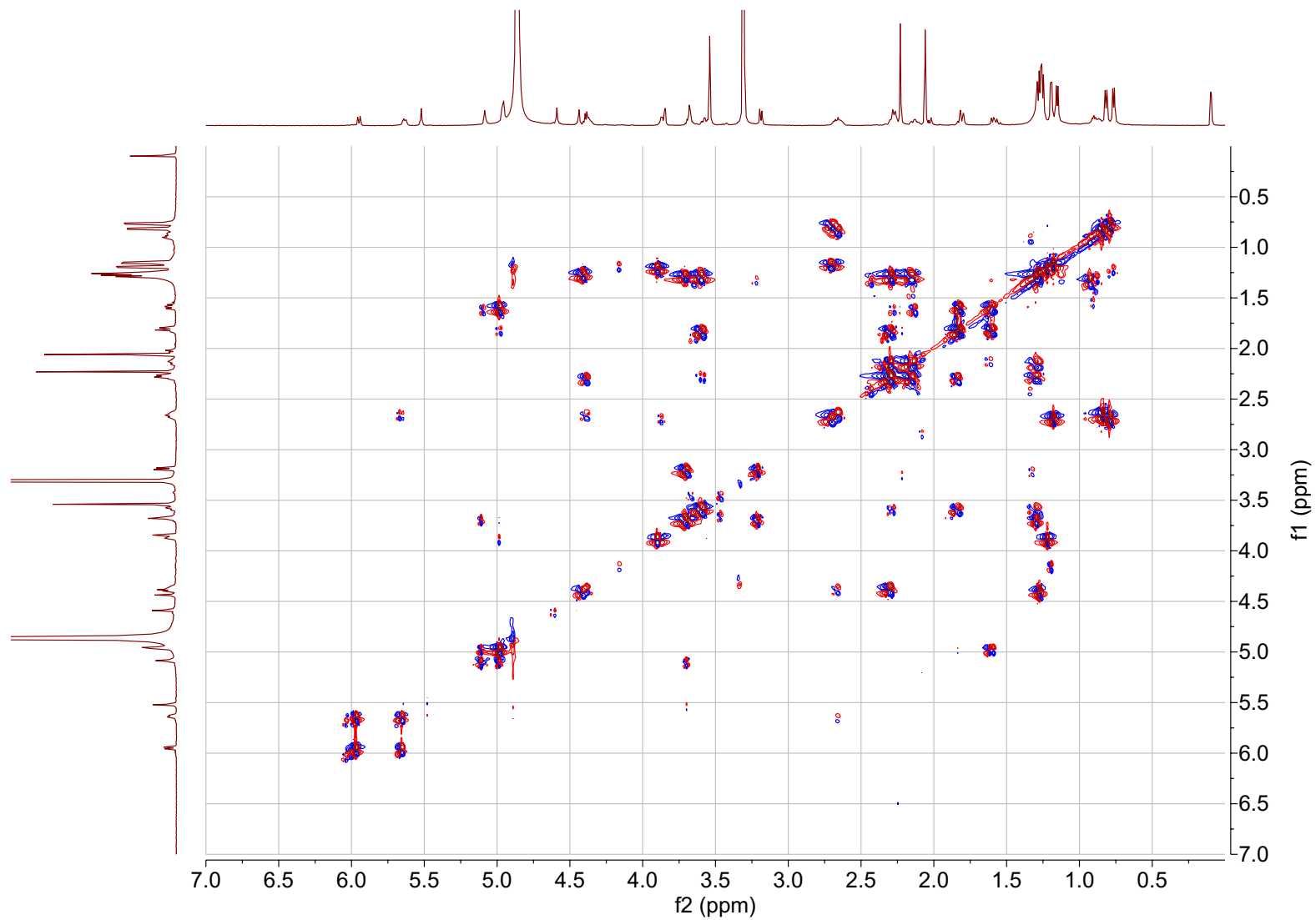


HSQC of **35** (*epi*-KBD)

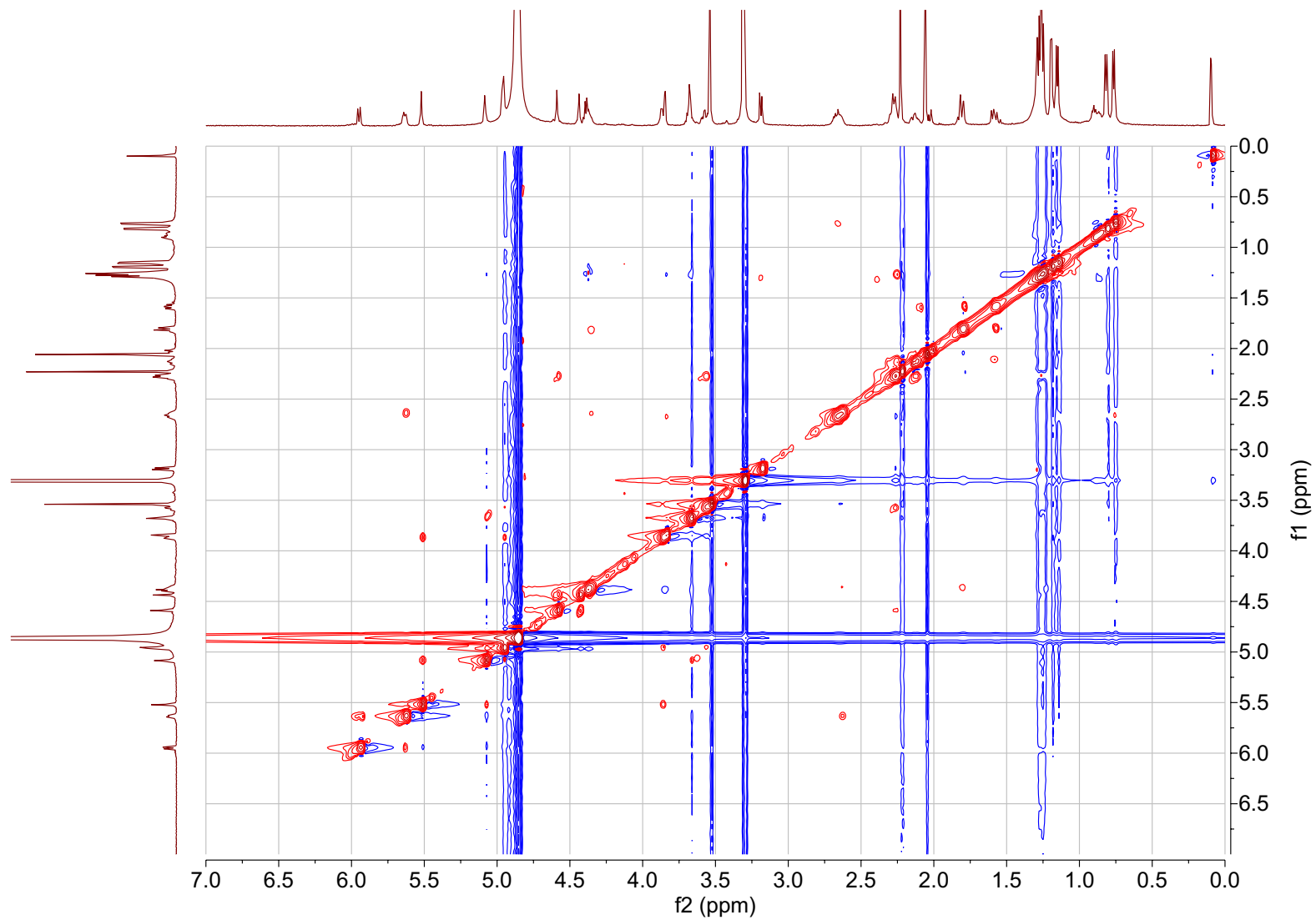




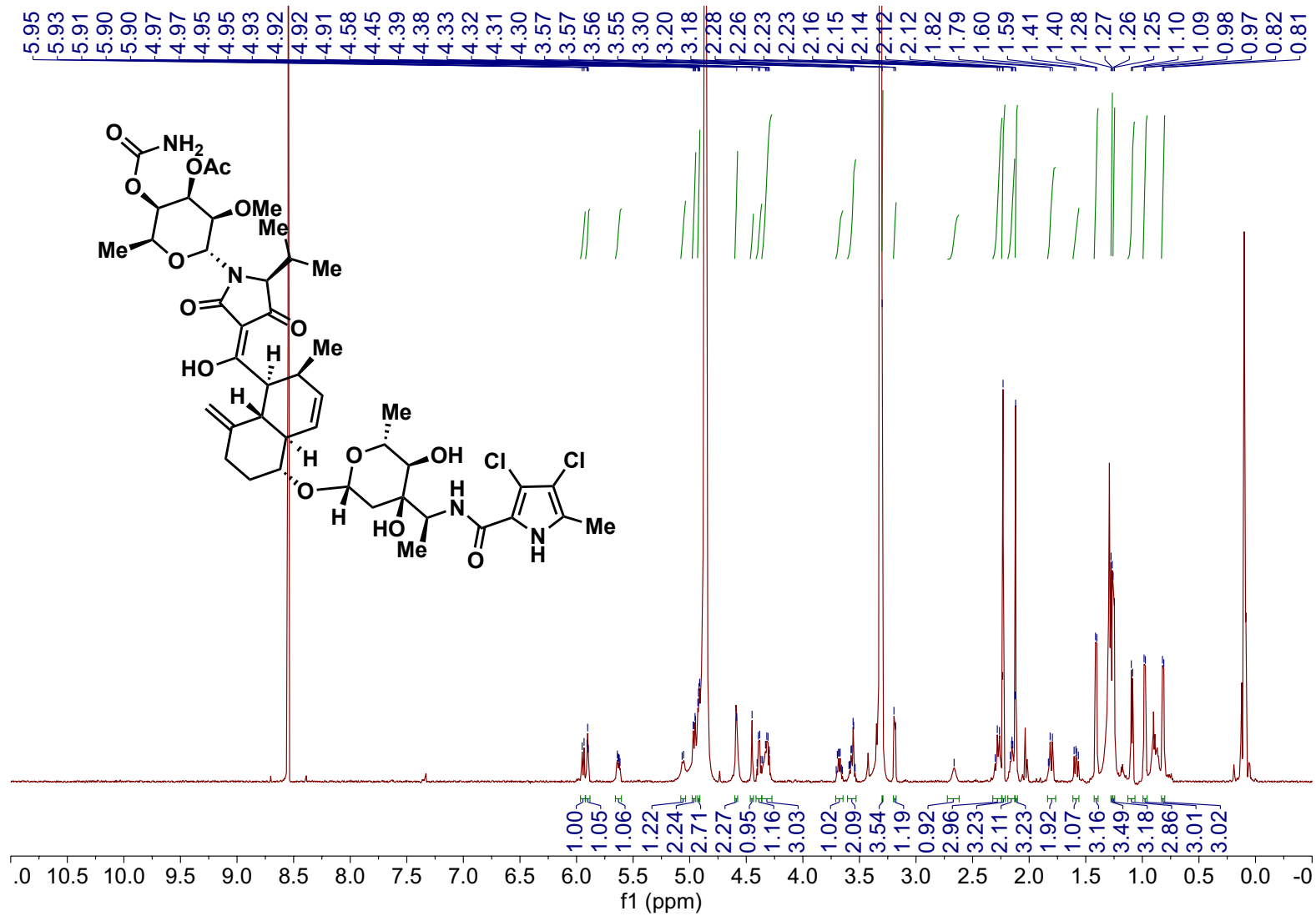
COSY of **35** (*epi*-KBD)



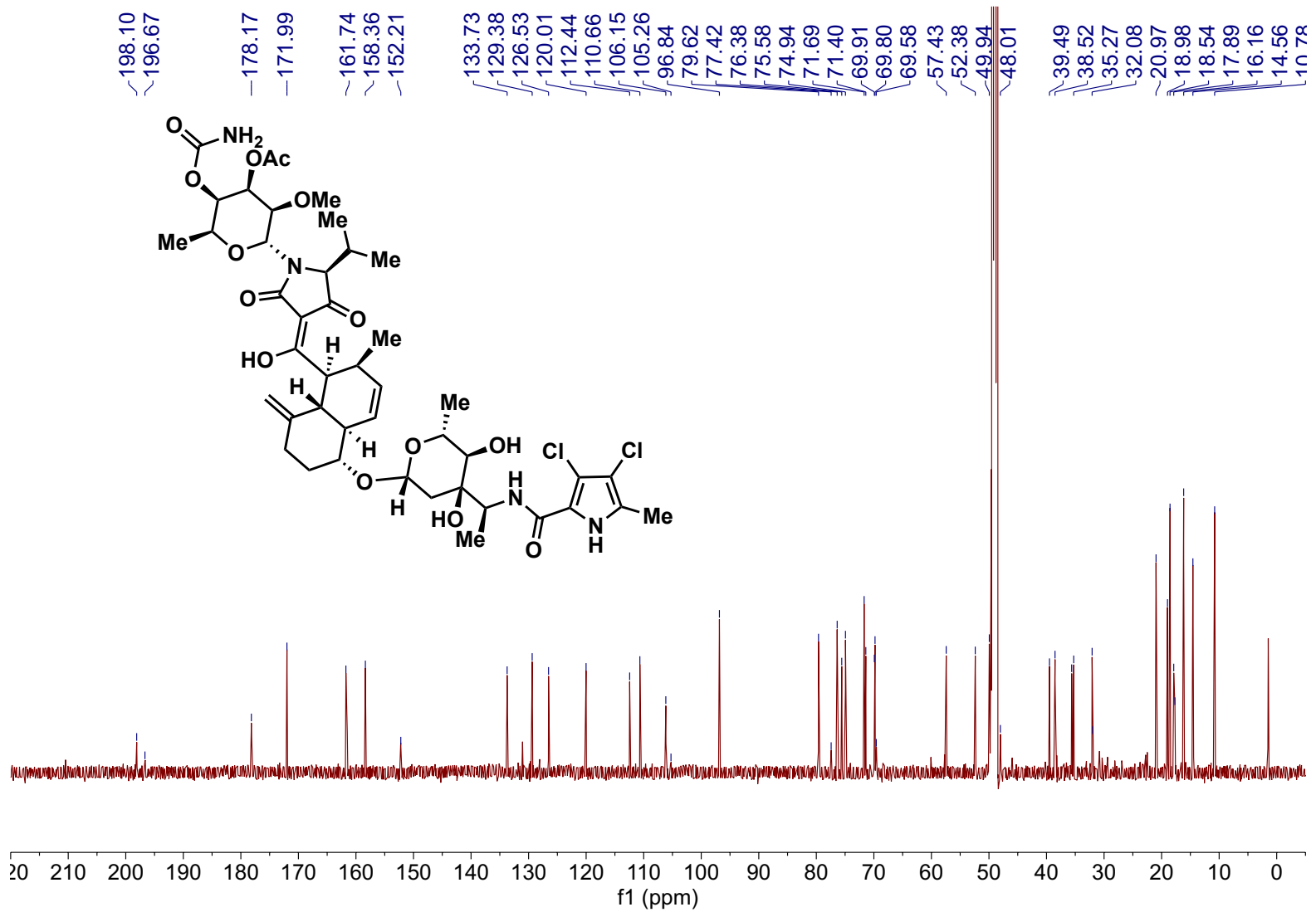
NOESY of **35** (*epi*-KBD)



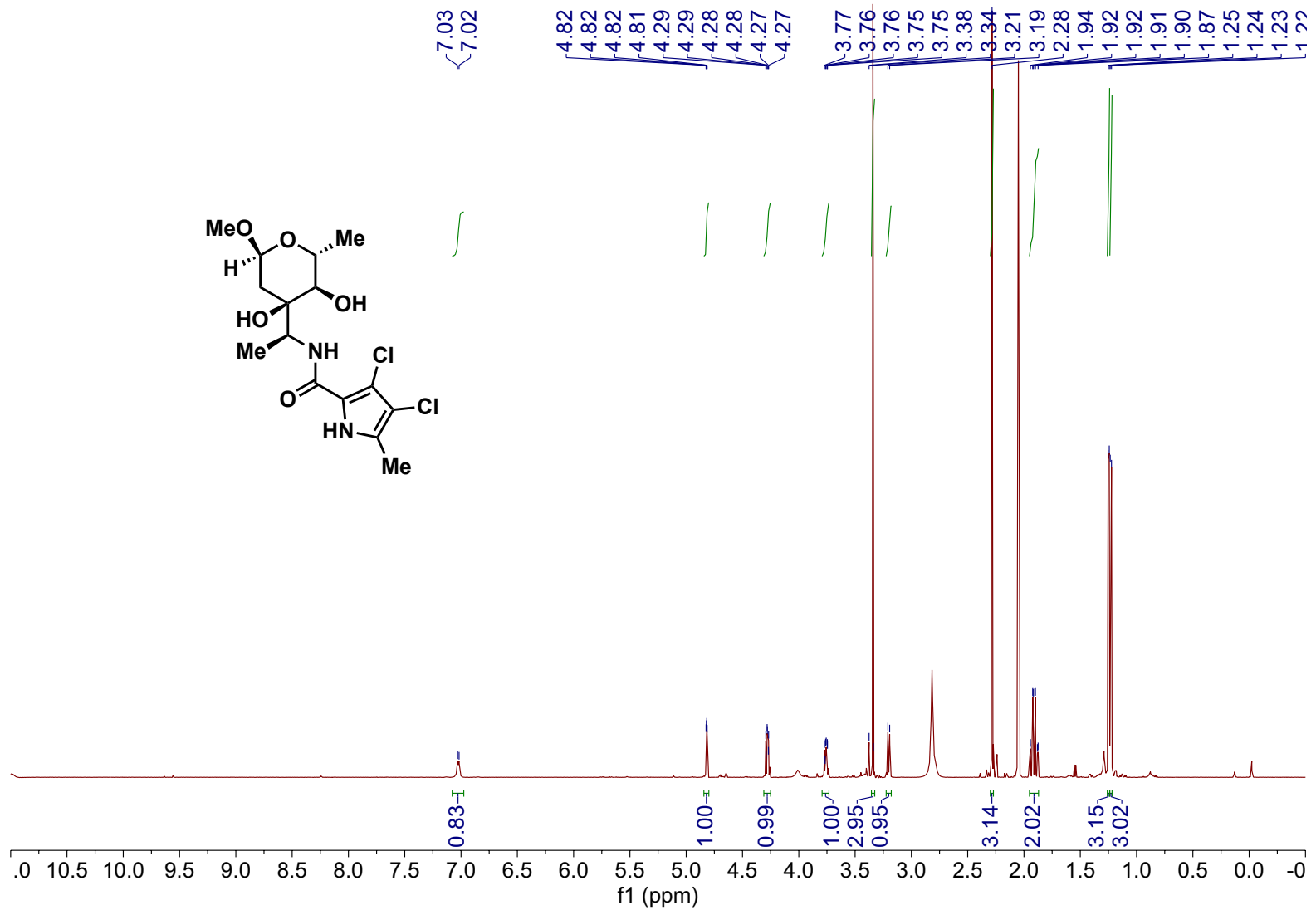
<sup>1</sup>H NMR of **1b** (KBD/amy)



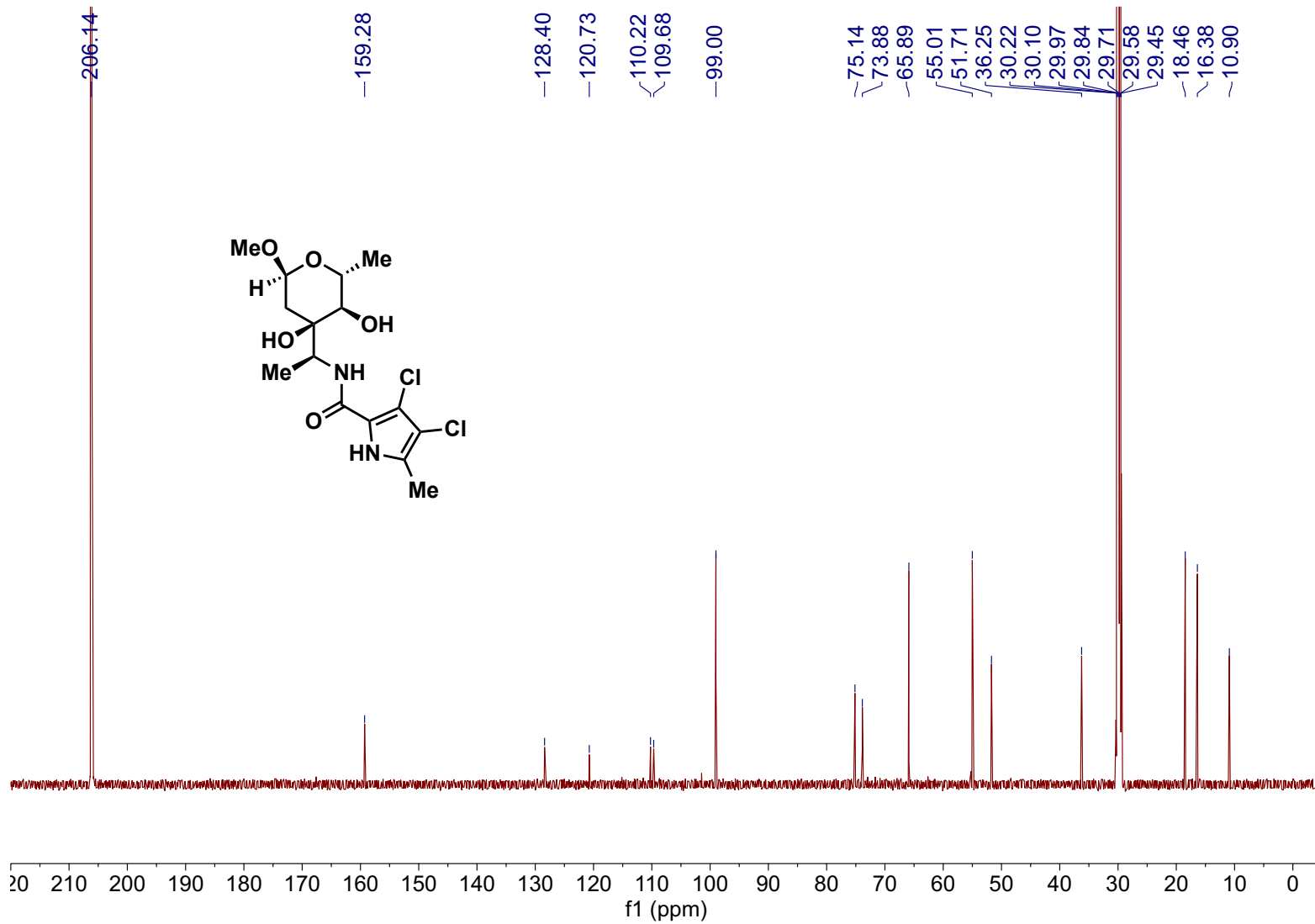
<sup>13</sup>C NMR of **1b** (KBD/amy)



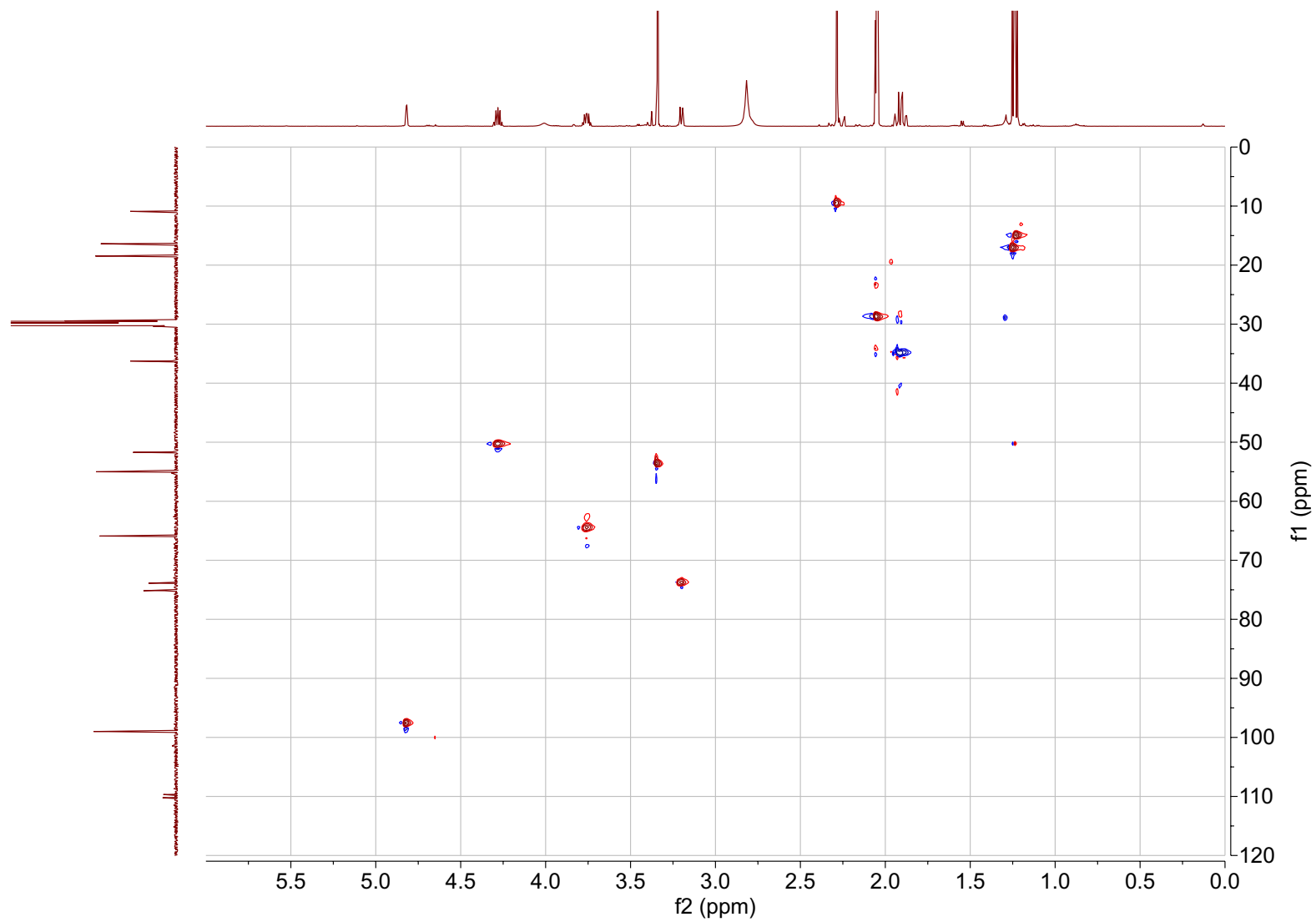
<sup>1</sup>H NMR of 36



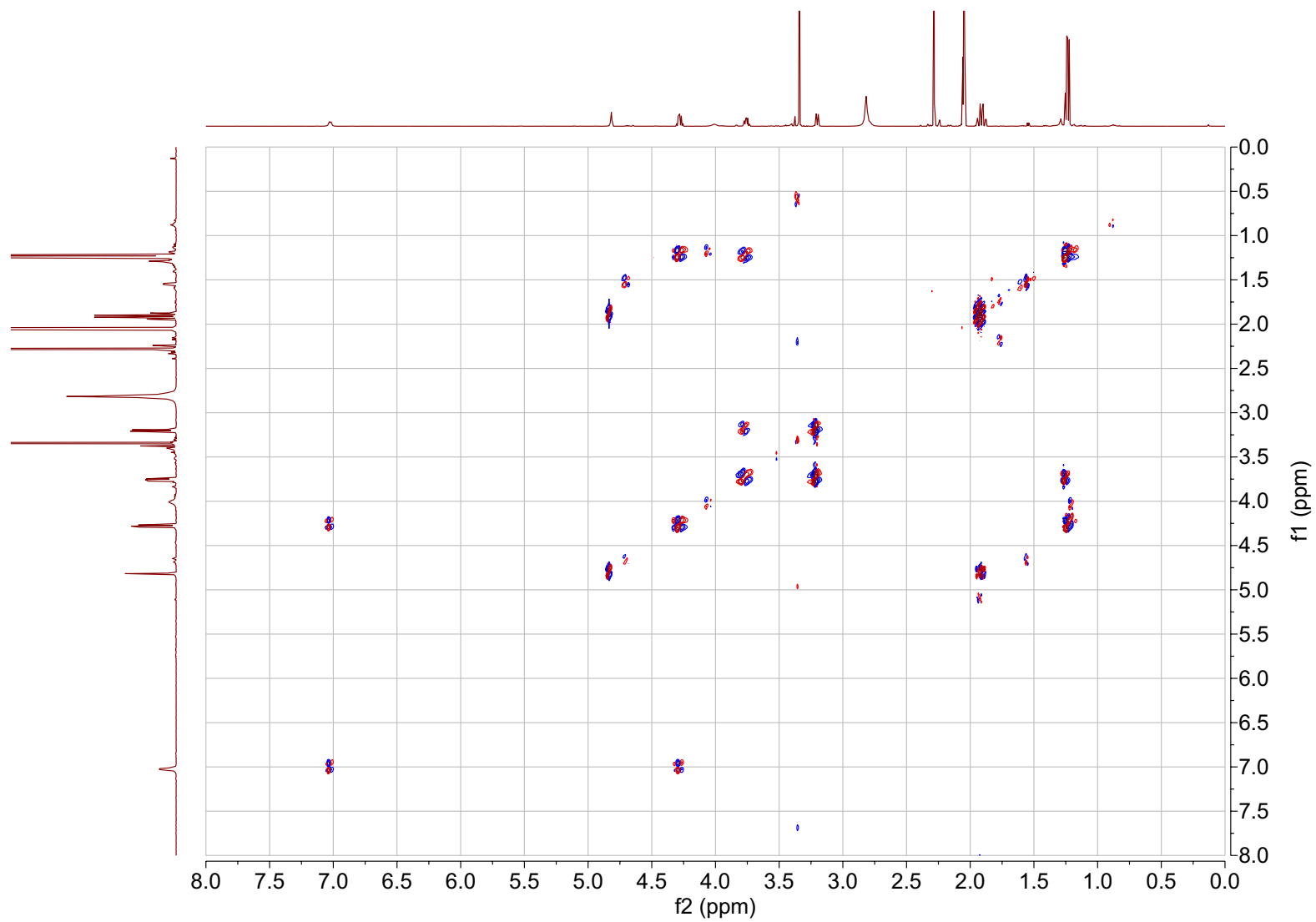
<sup>13</sup>C NMR of **36**



HSQC of 36

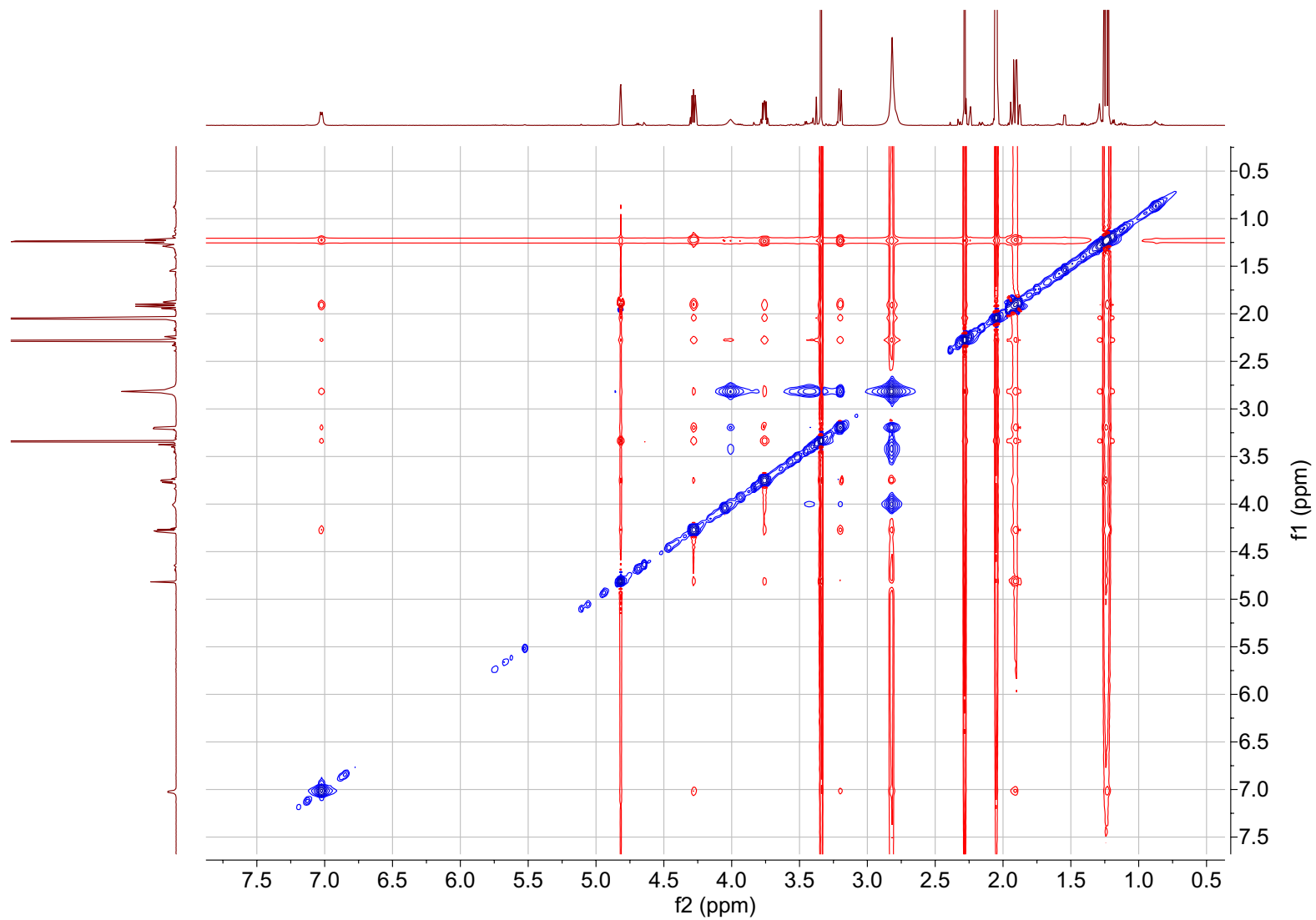


COSY of 36

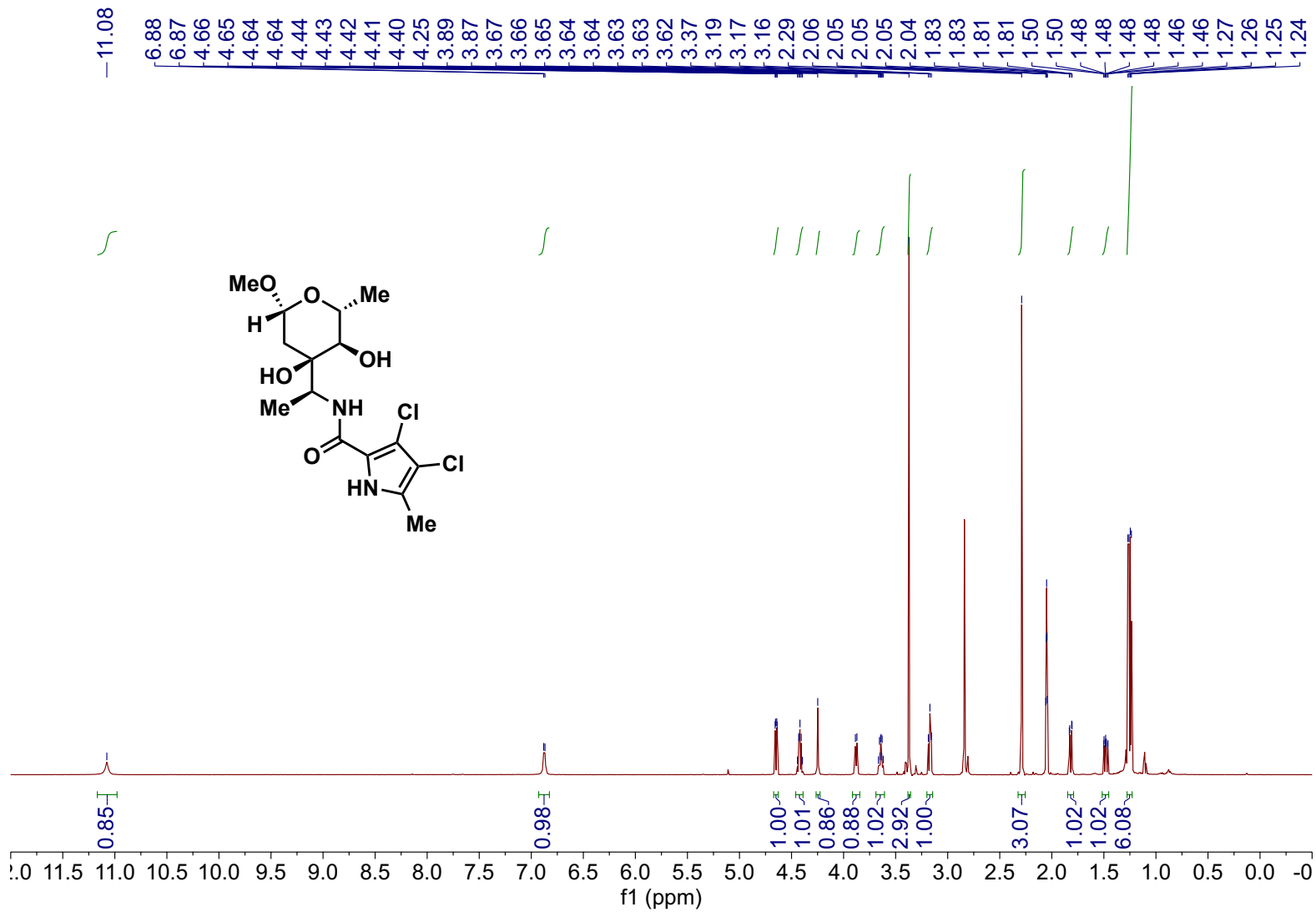




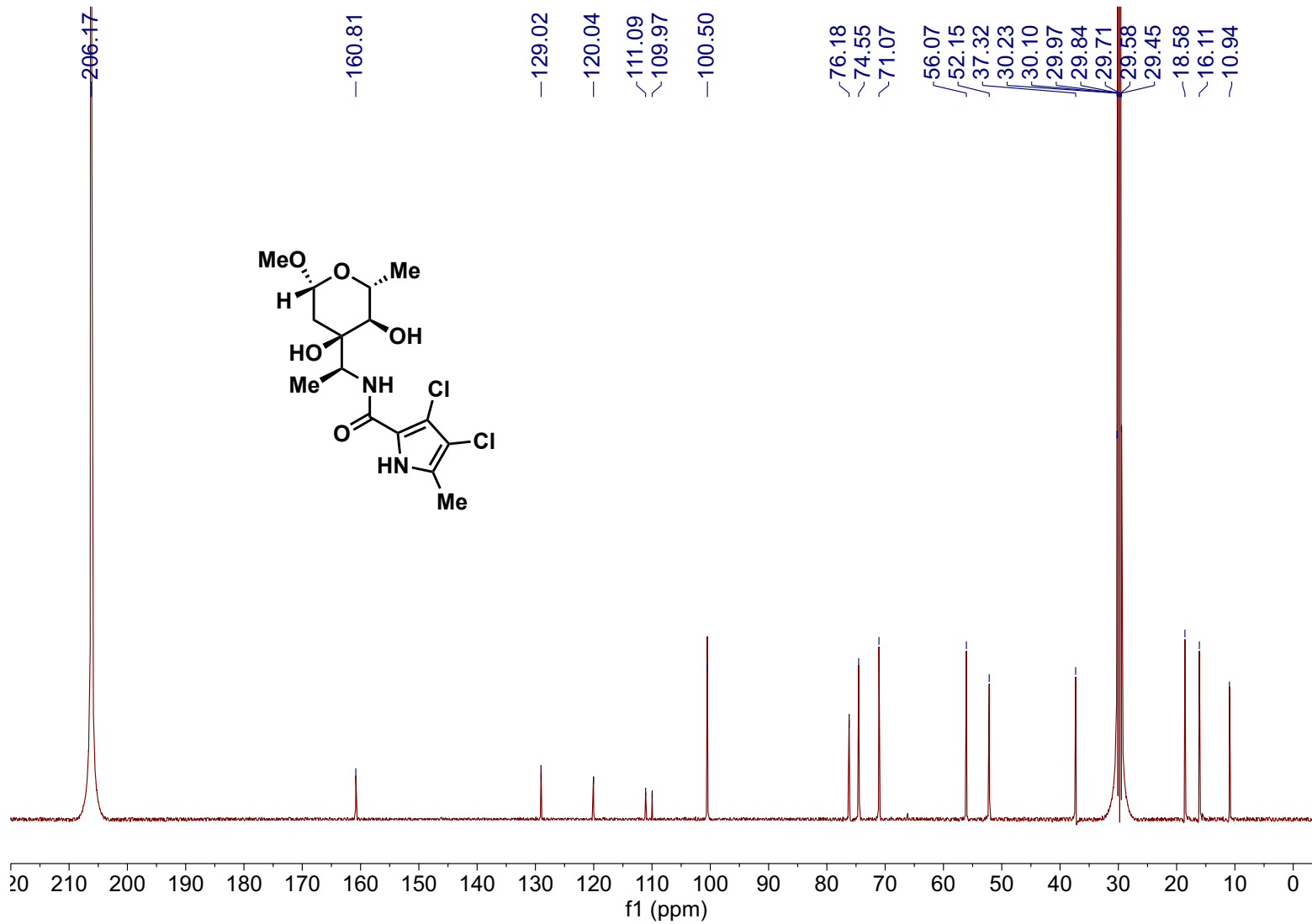
NOESY of 36



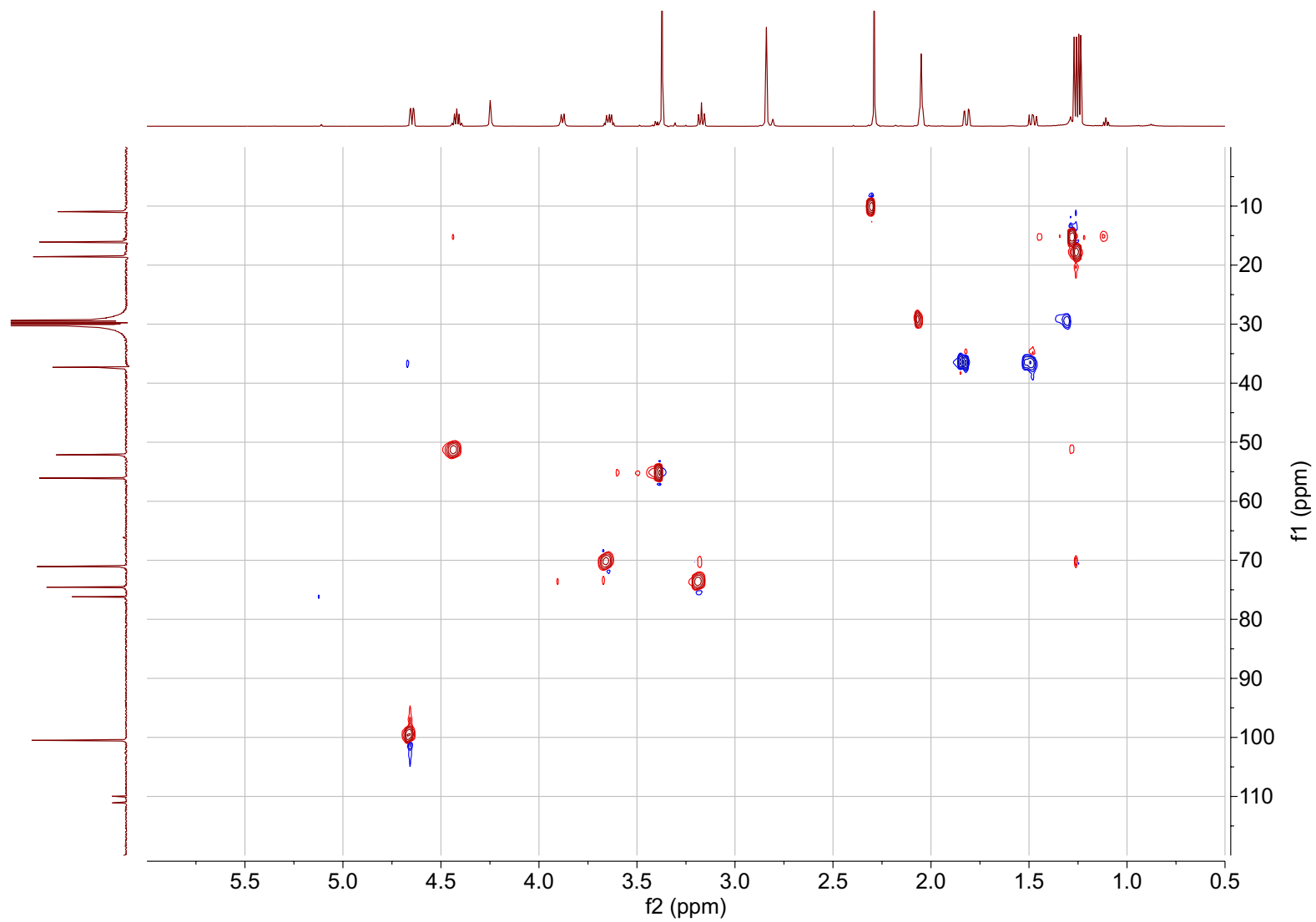
<sup>1</sup>H NMR of 37



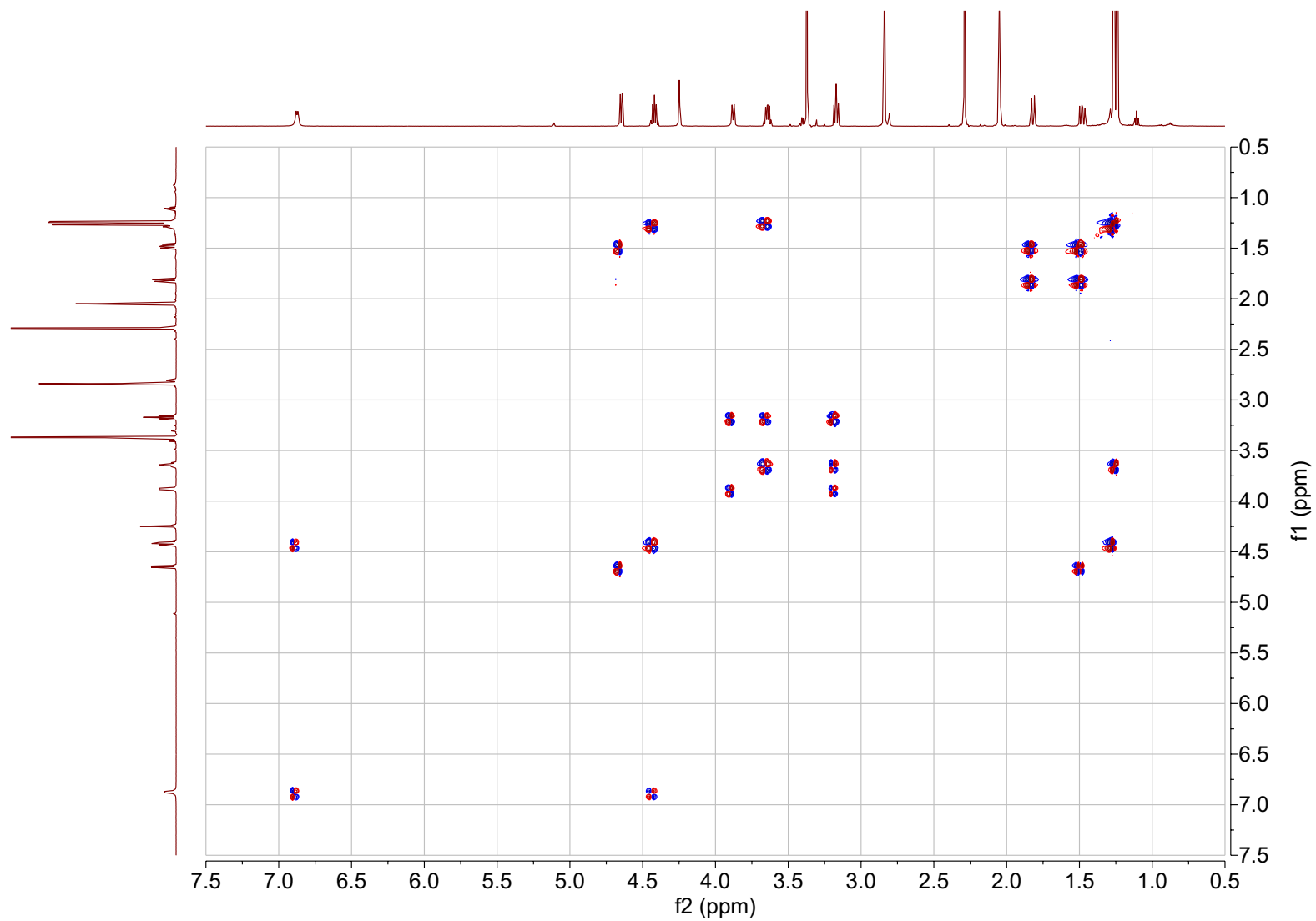
<sup>13</sup>C NMR of **37**



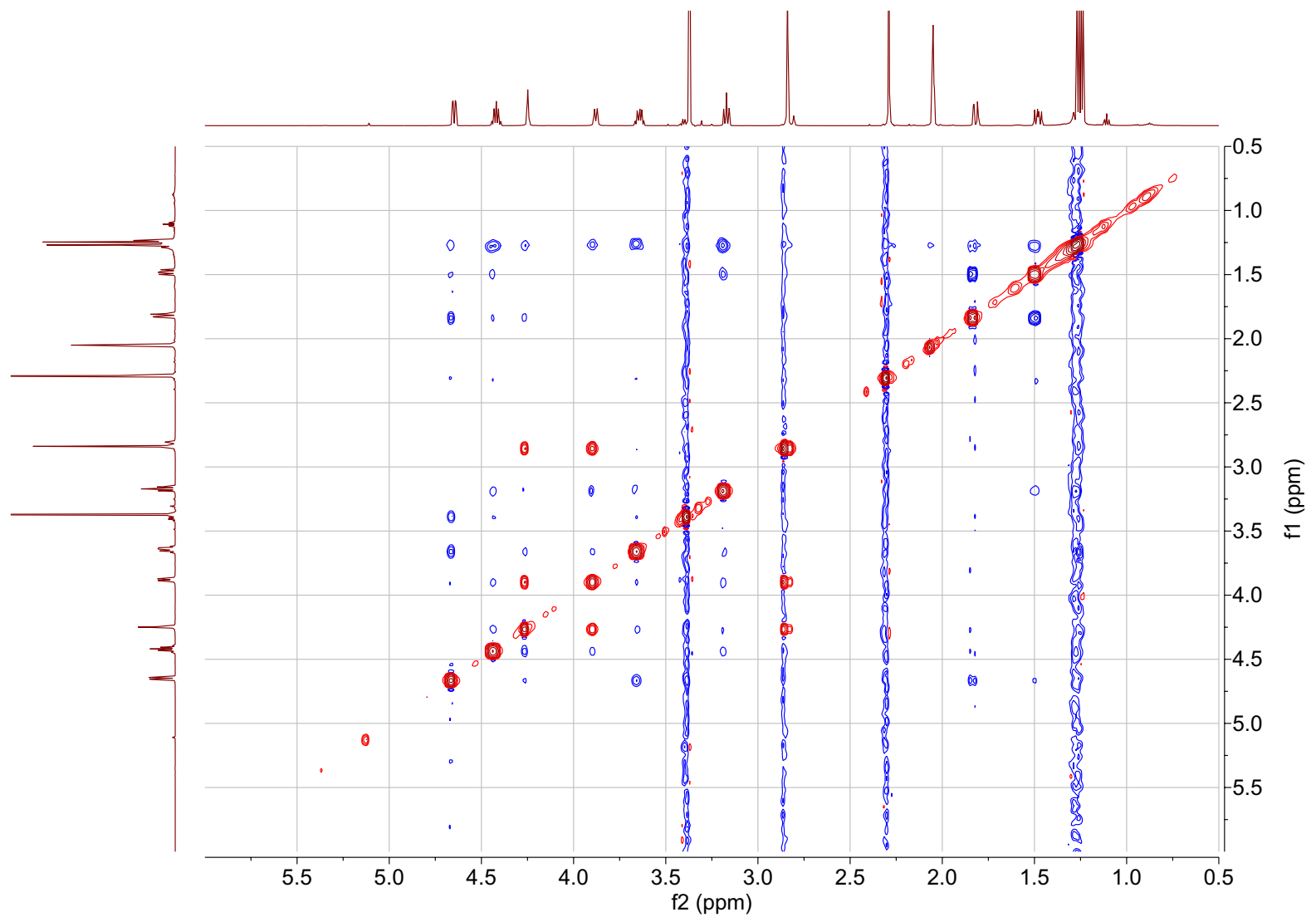
HSQC of 37



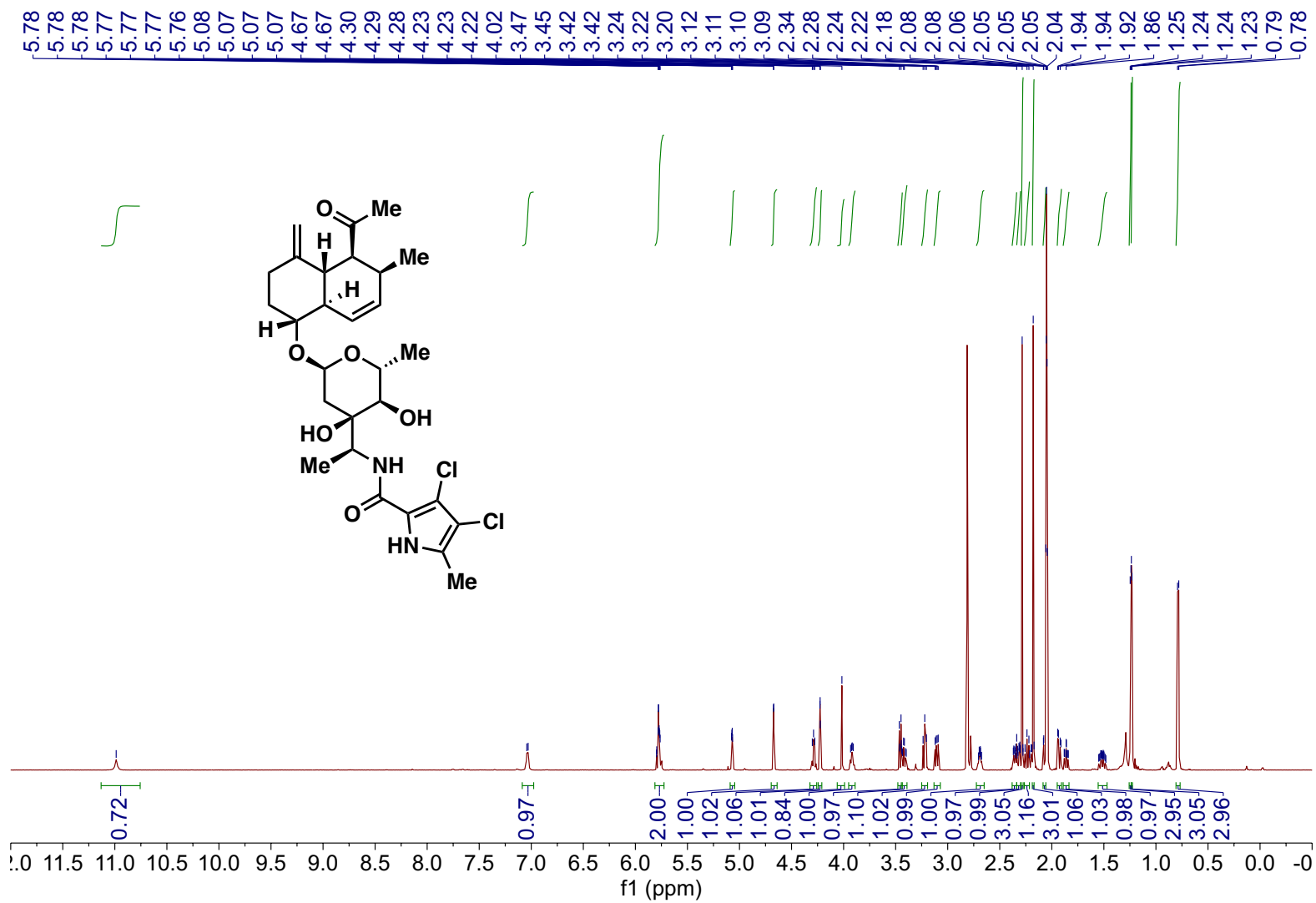
COSY of 37



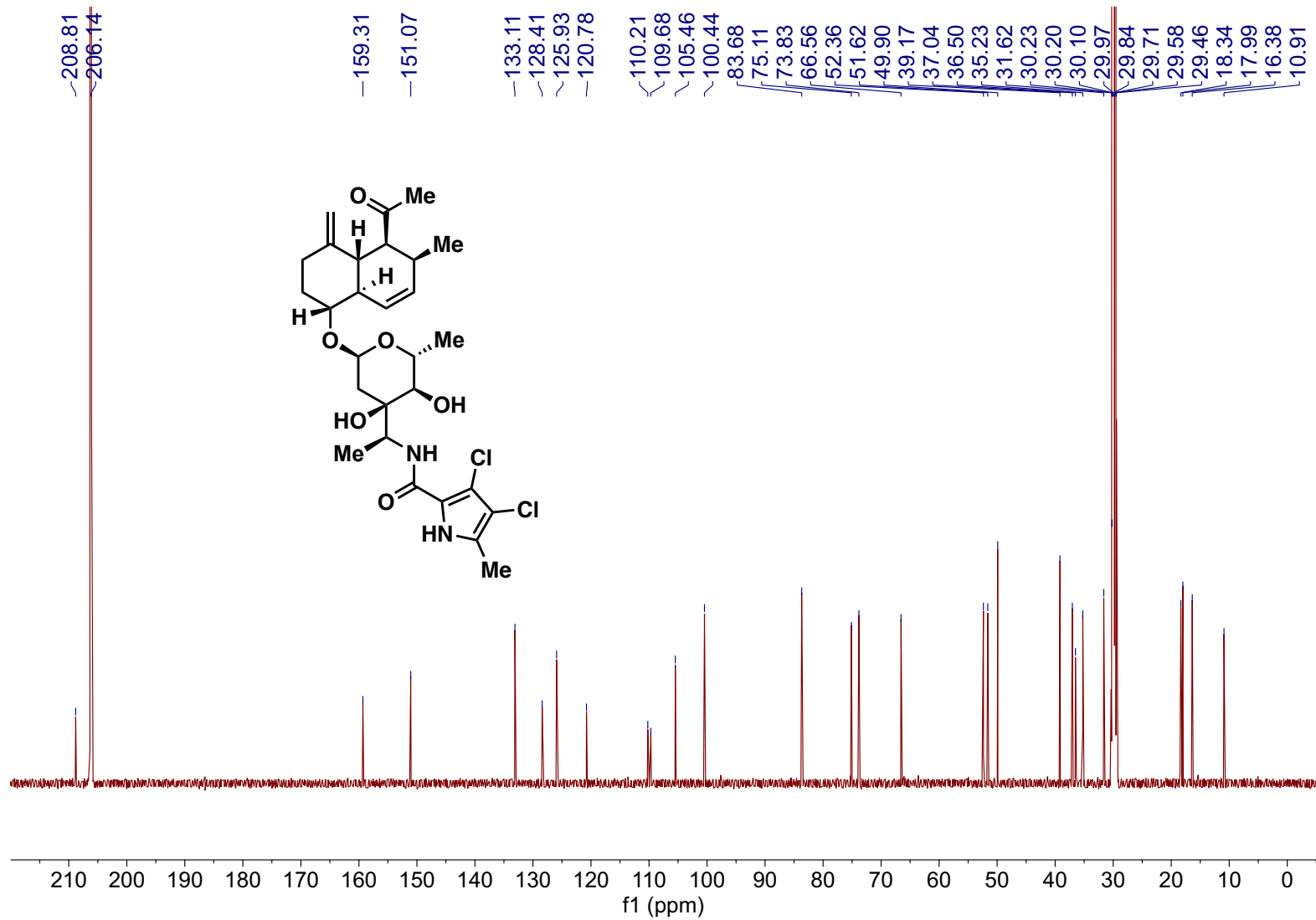
NOESY of 37



<sup>1</sup>H NMR of 38

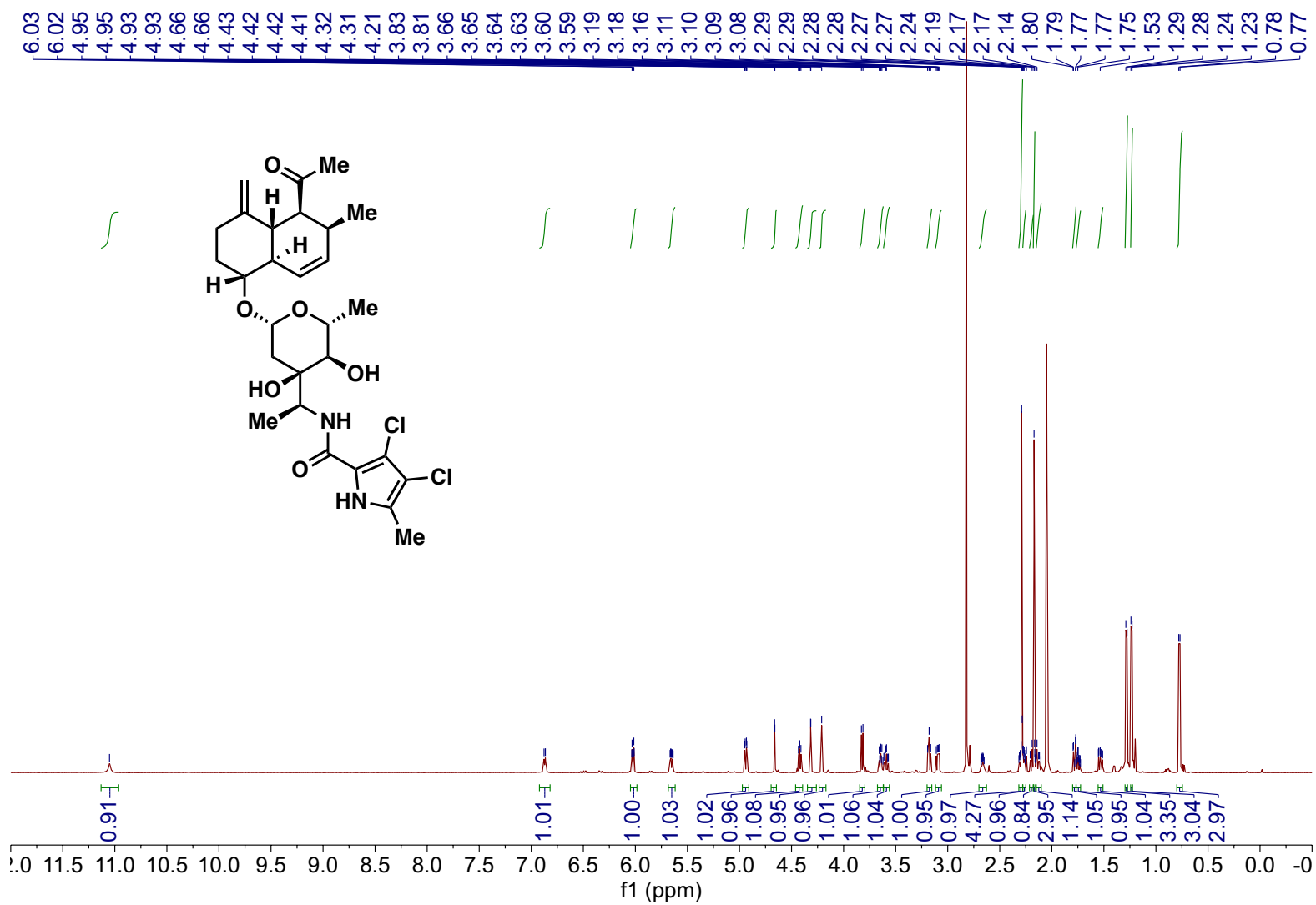


<sup>13</sup>C NMR of **38**

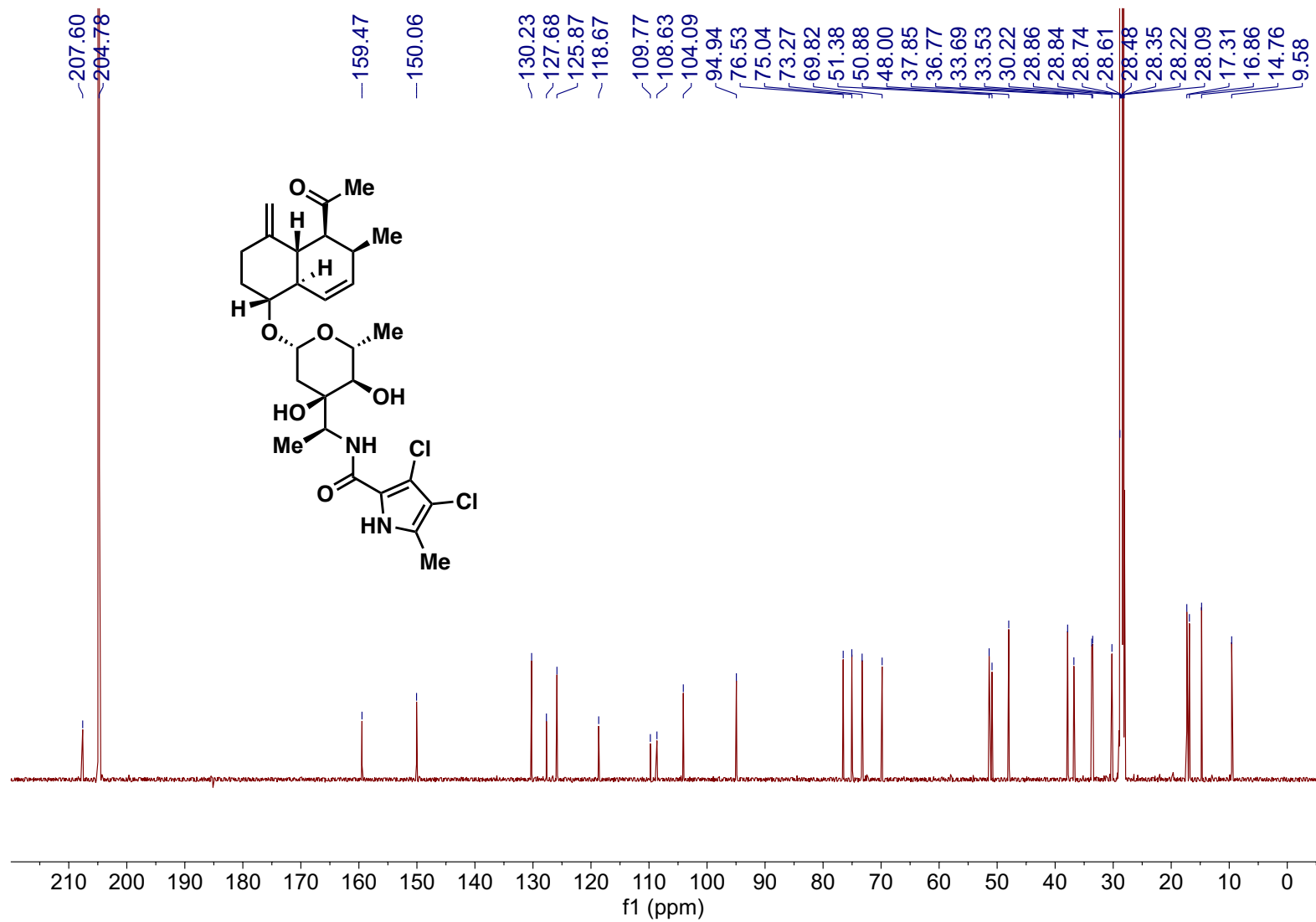




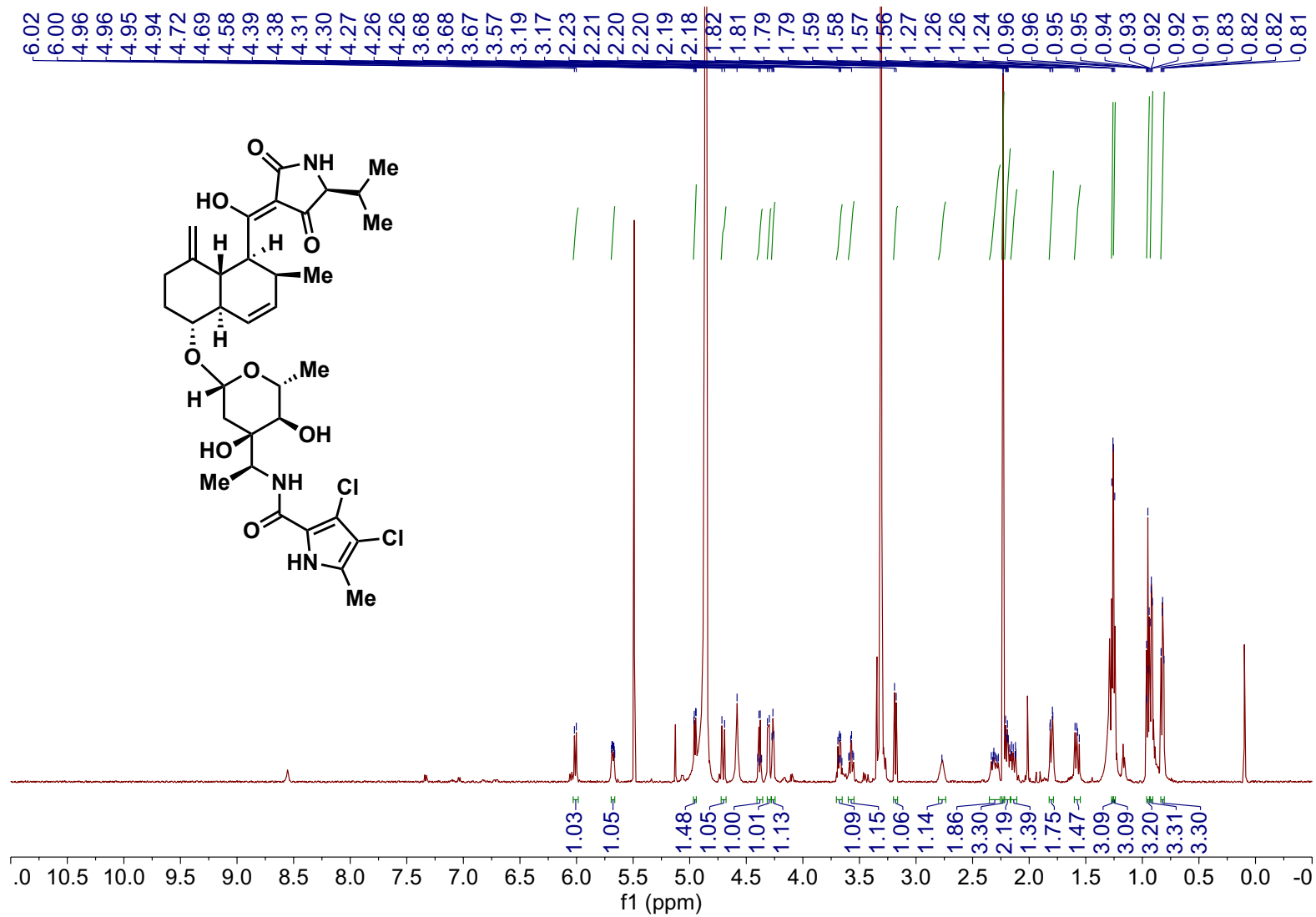
<sup>1</sup>H NMR of 39



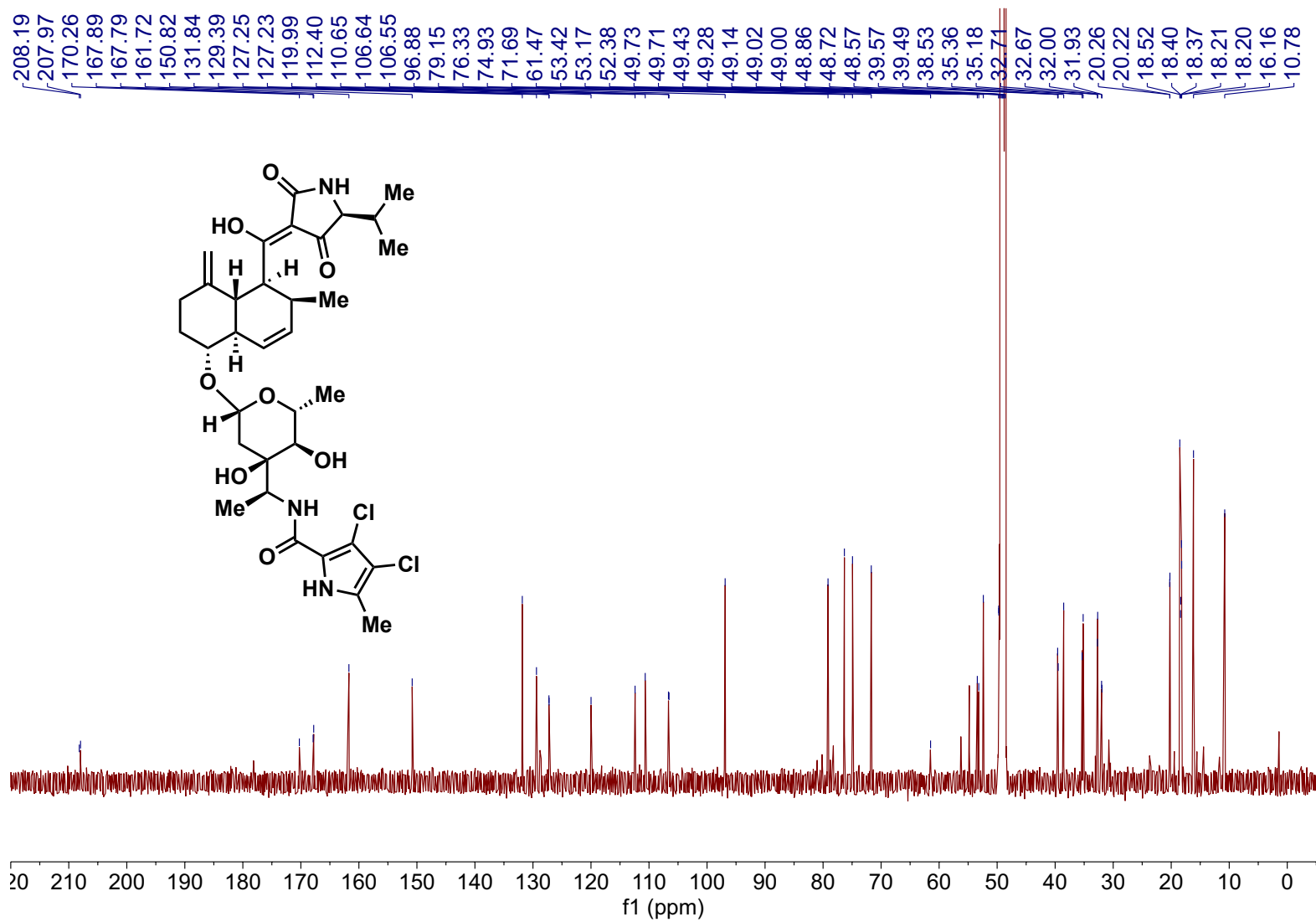
<sup>13</sup>C NMR of **39**



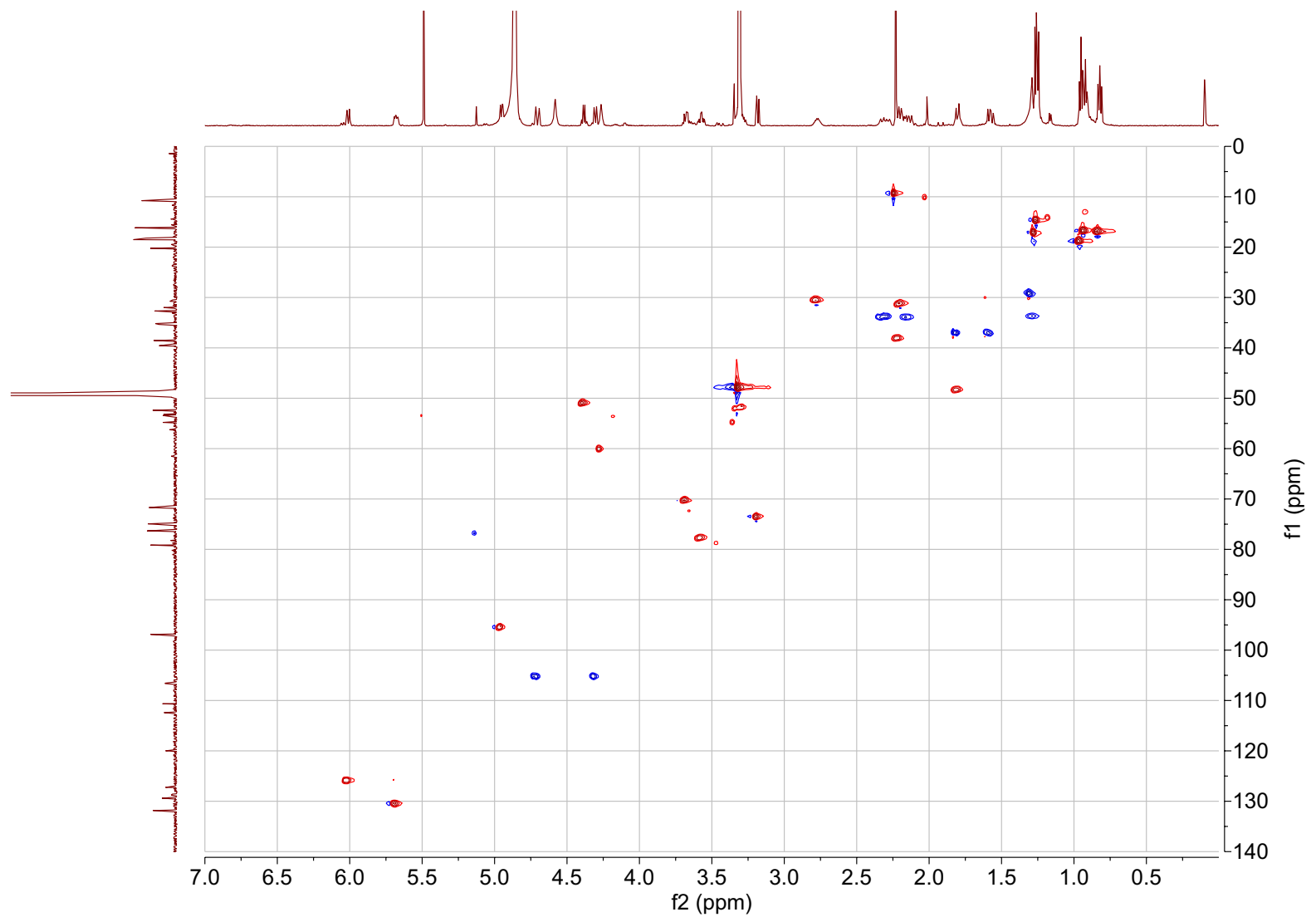
<sup>1</sup>H NMR of 40



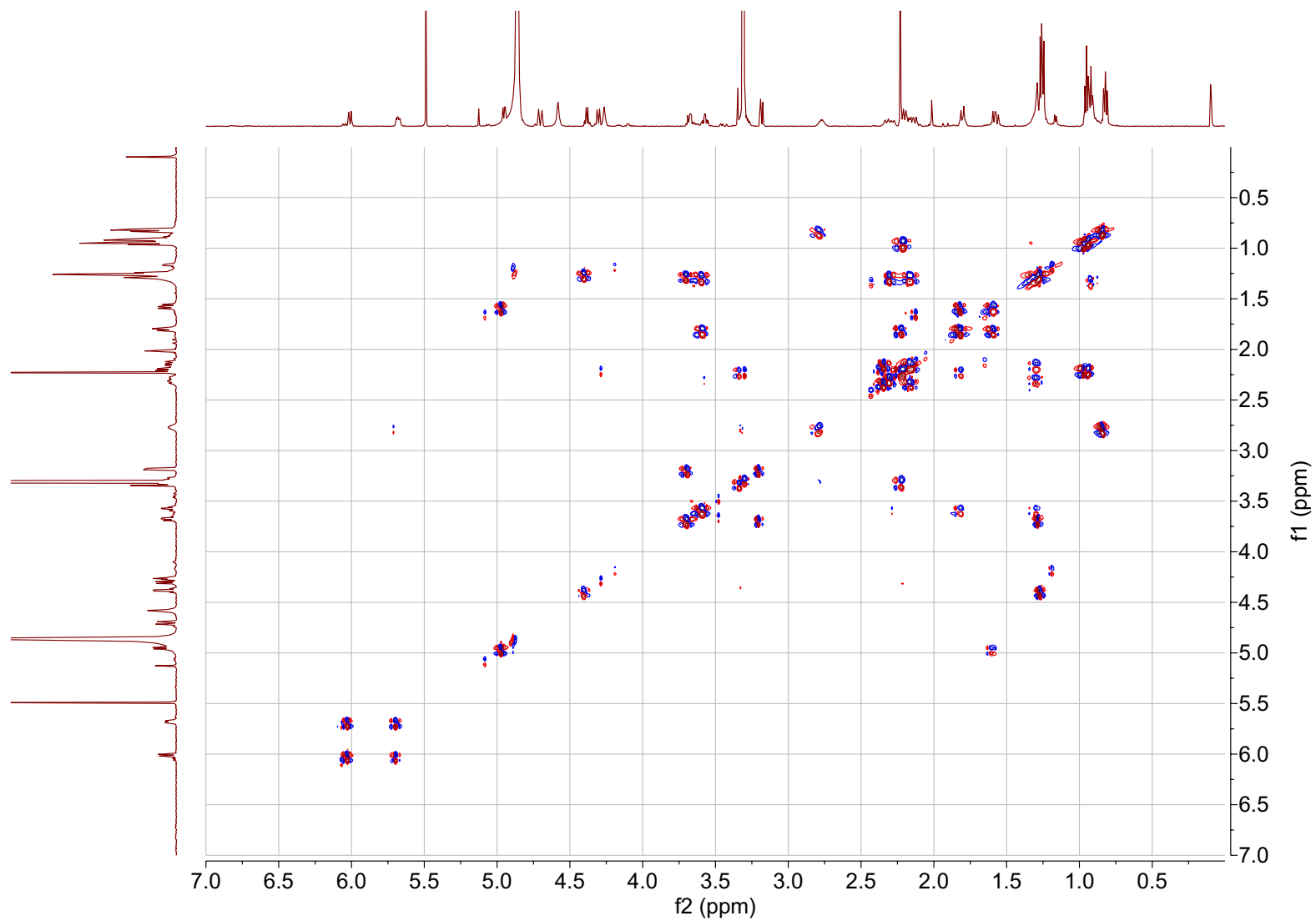
<sup>13</sup>C NMR of **40**



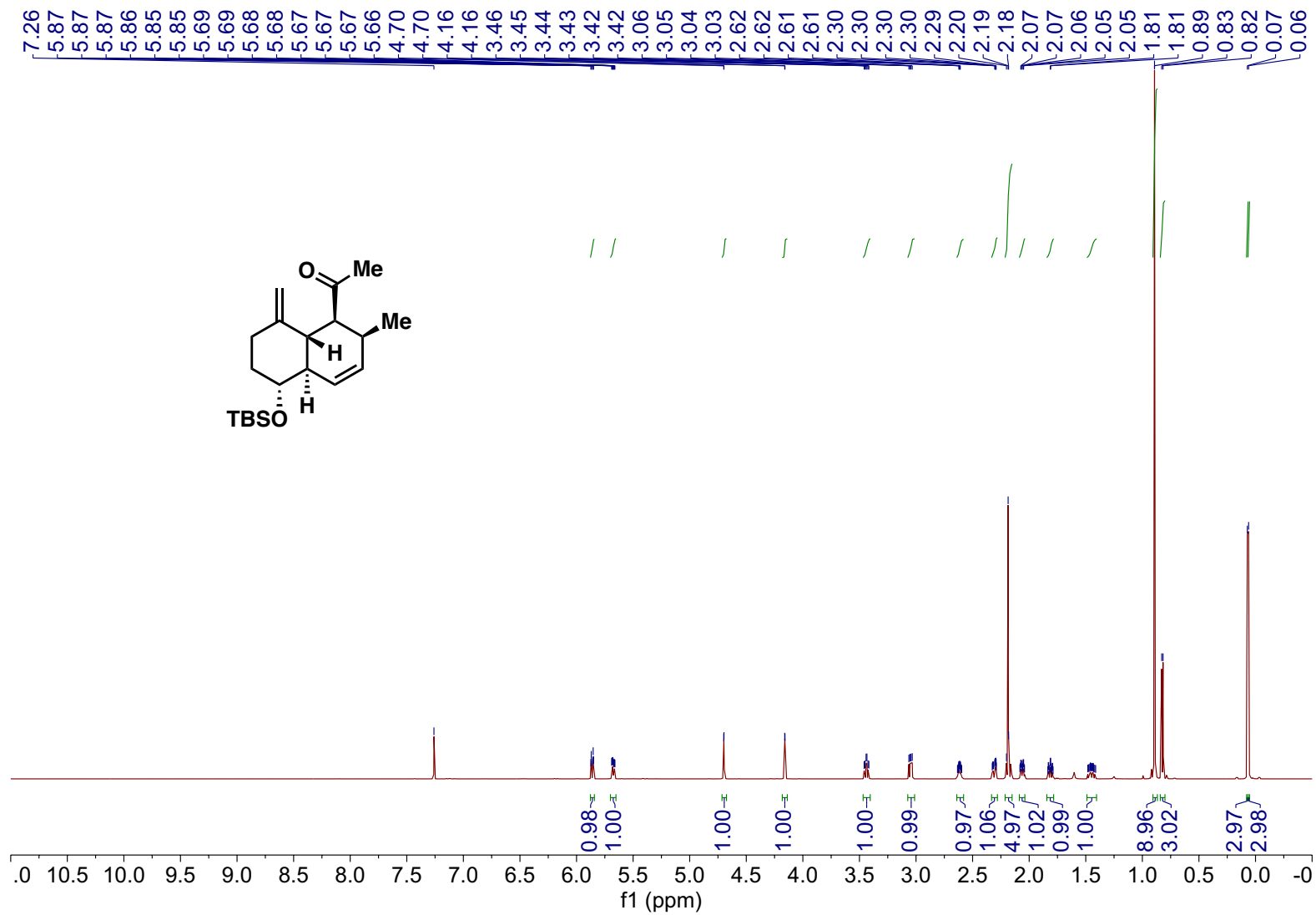
HSQC of 40



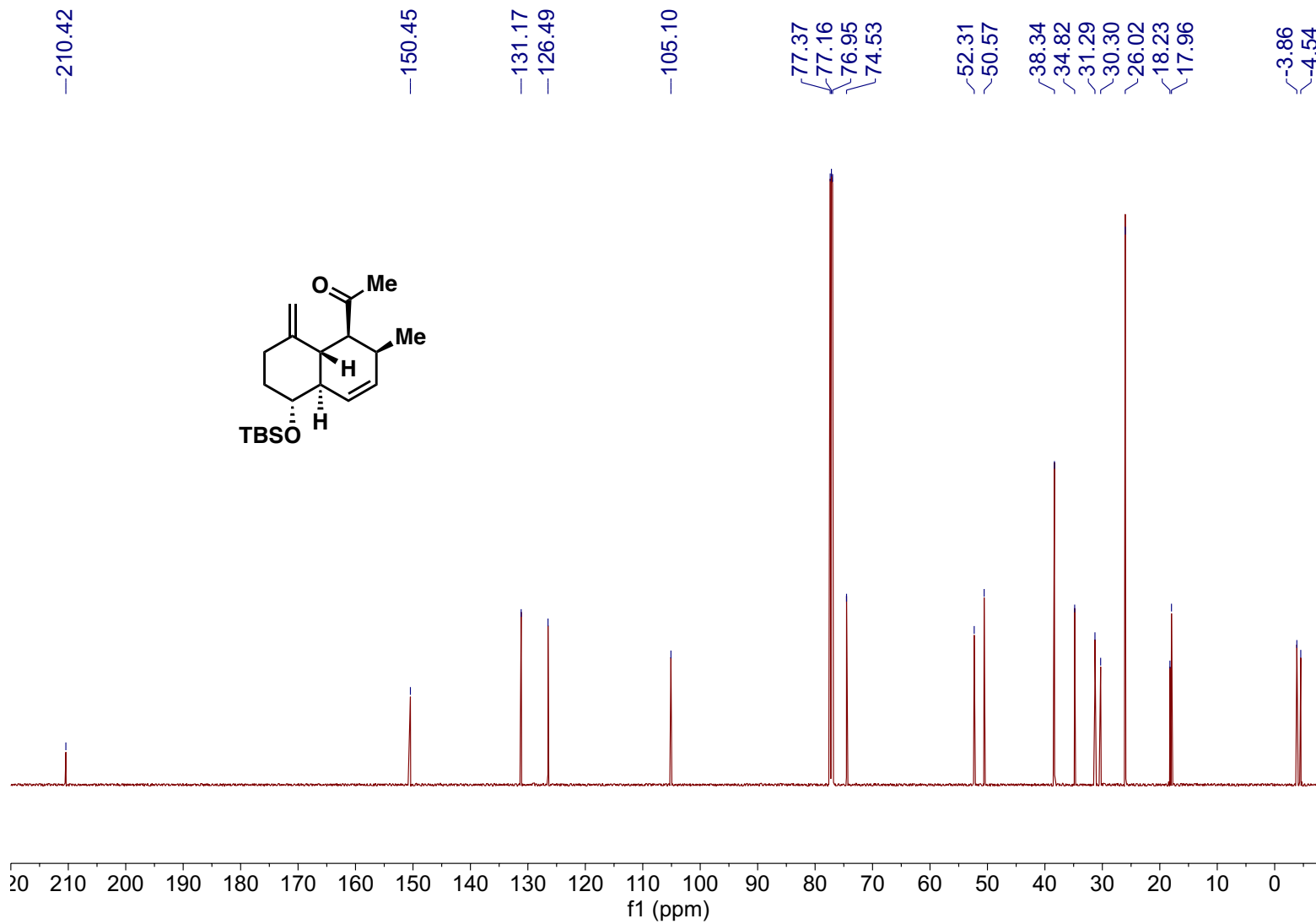
COSY of 40



<sup>1</sup>H NMR of S10

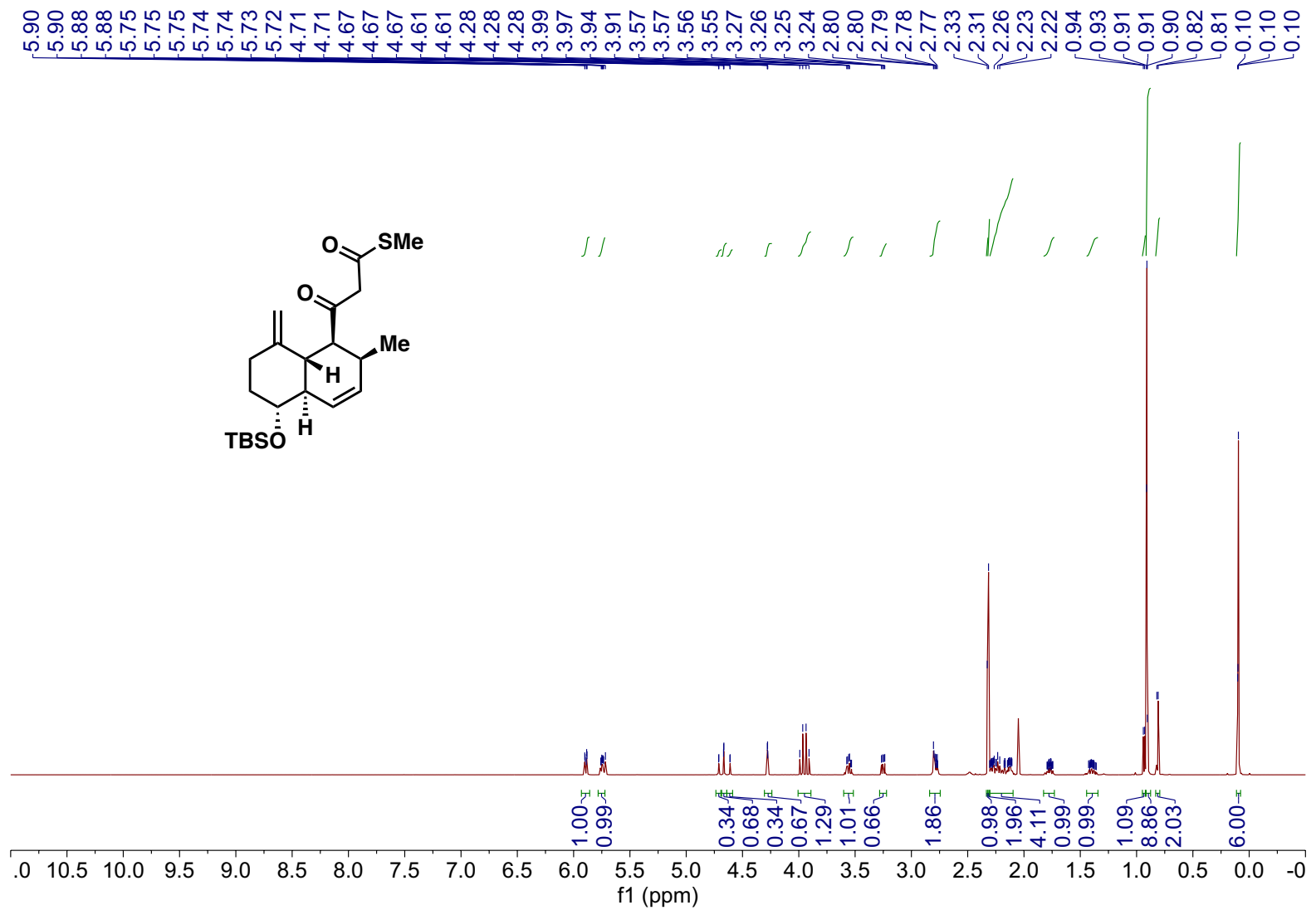


<sup>13</sup>C NMR of **S10**

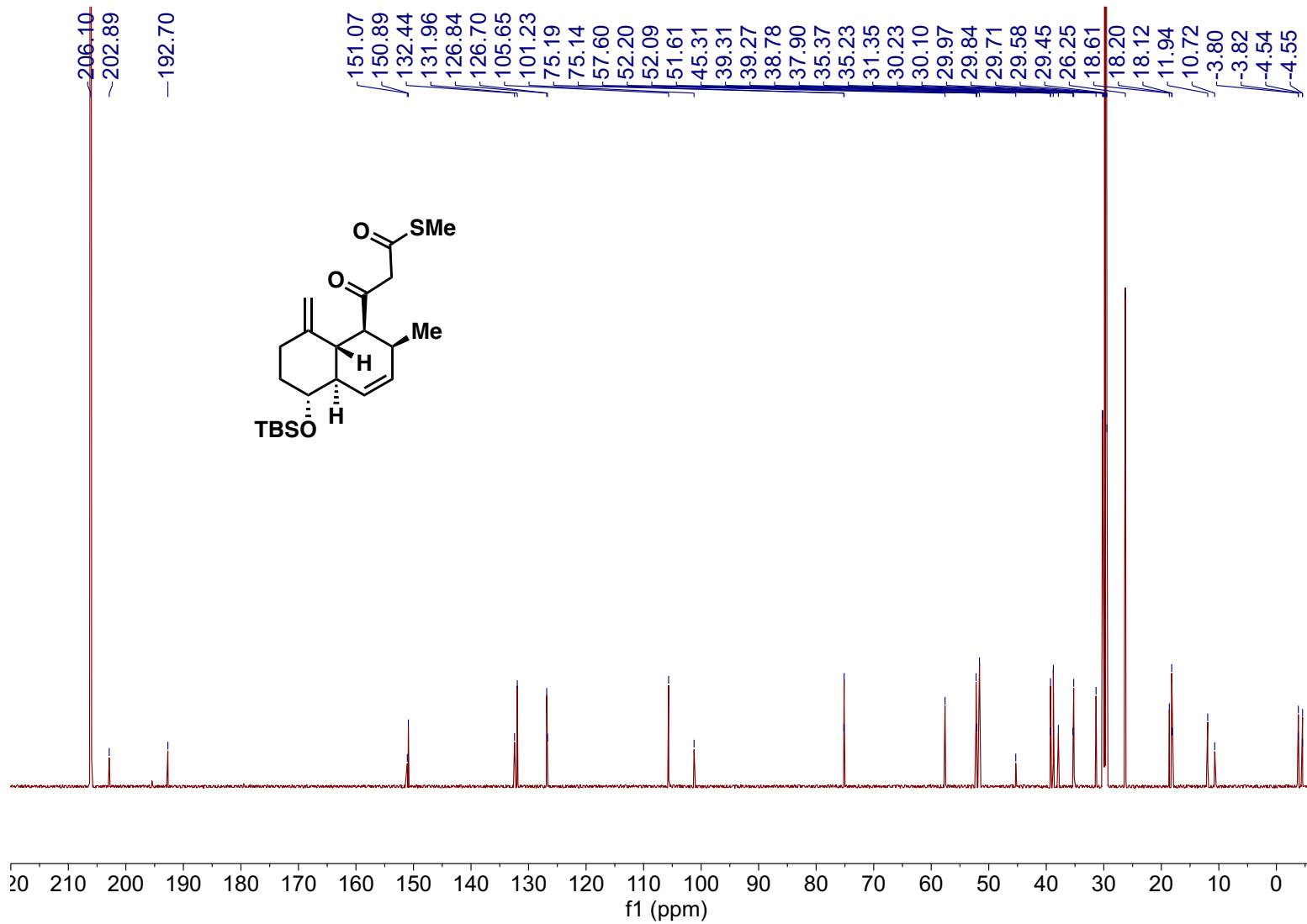




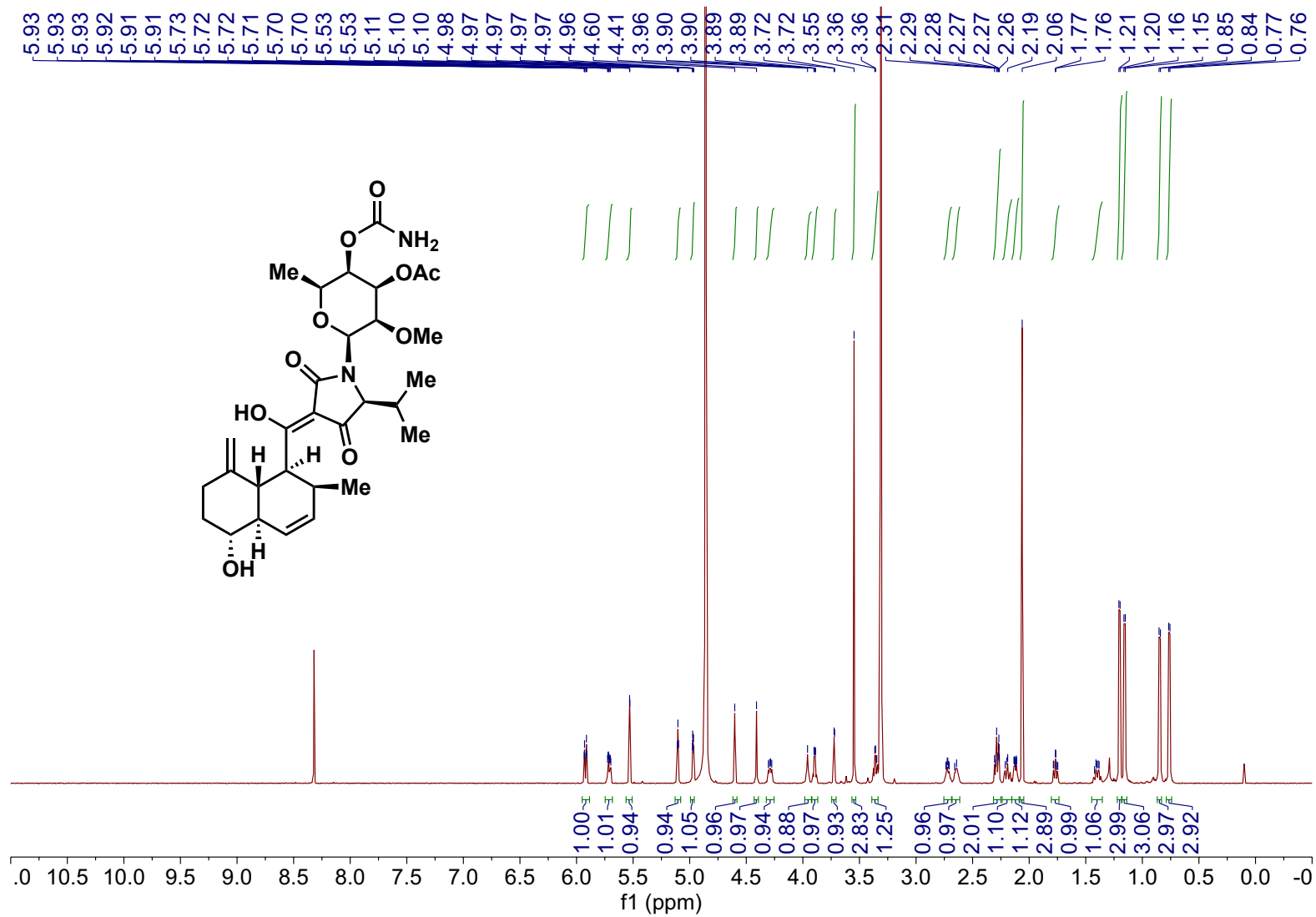
<sup>1</sup>H NMR of S11



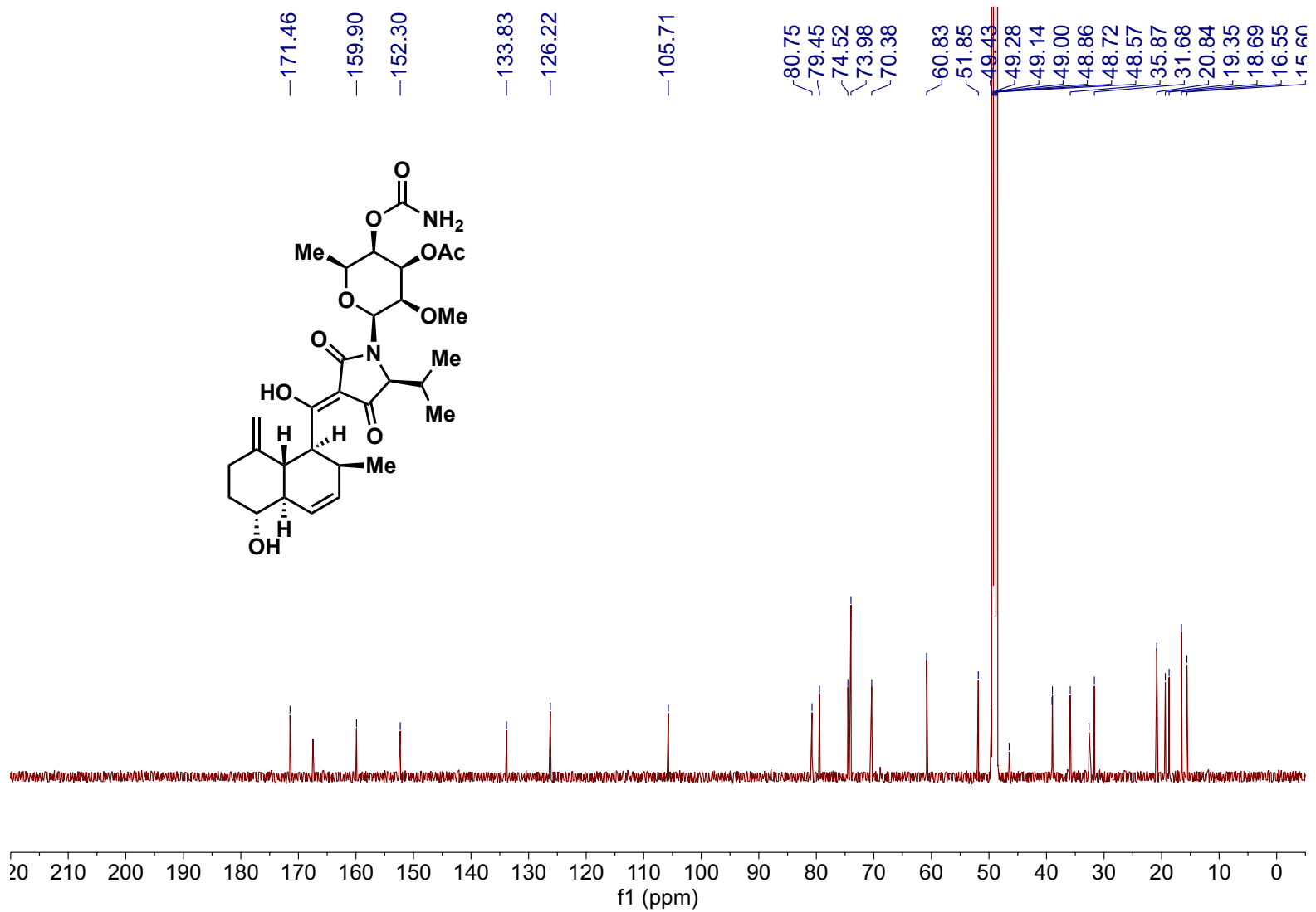
<sup>13</sup>C NMR of **S11**



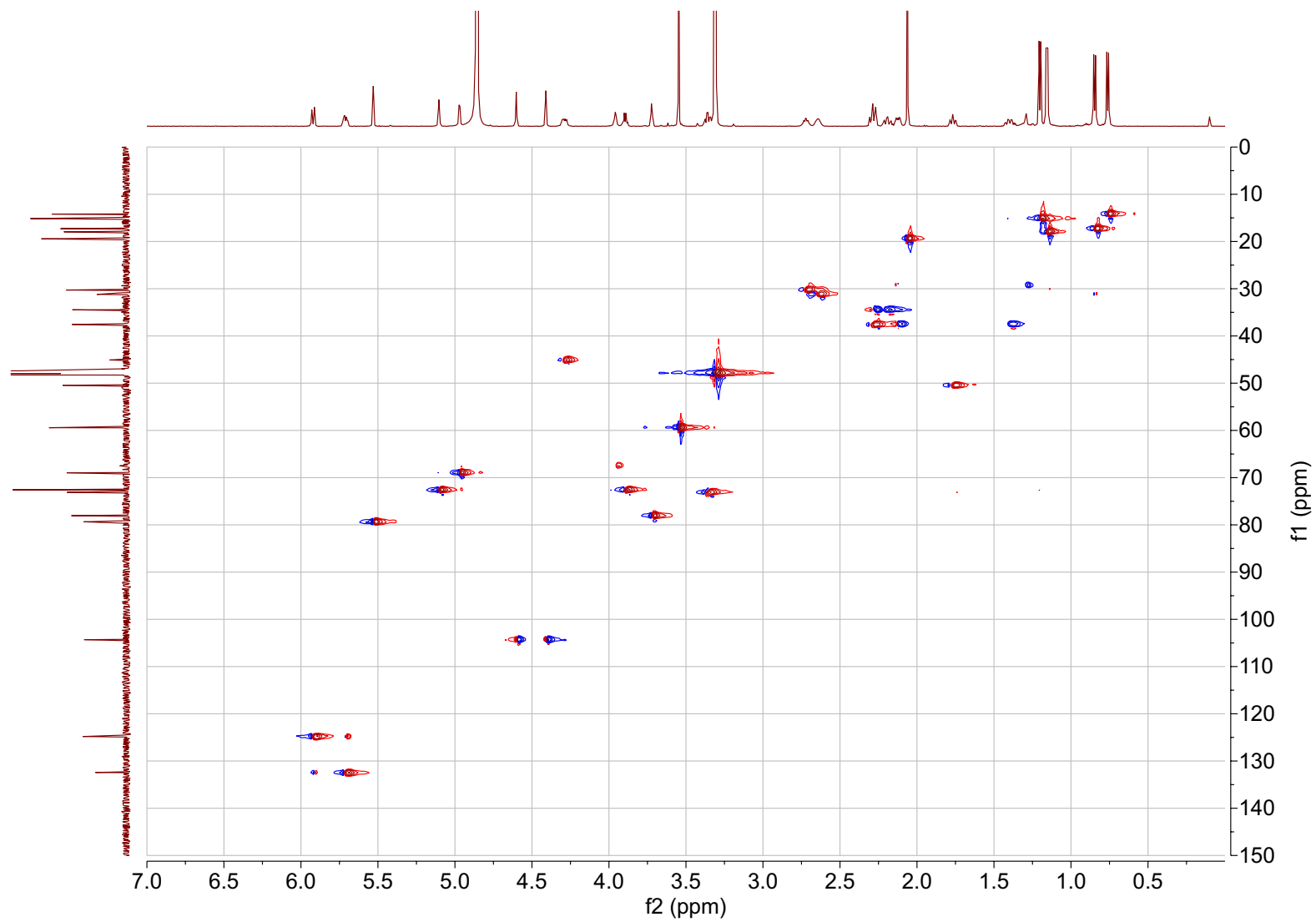
<sup>1</sup>H NMR of 41



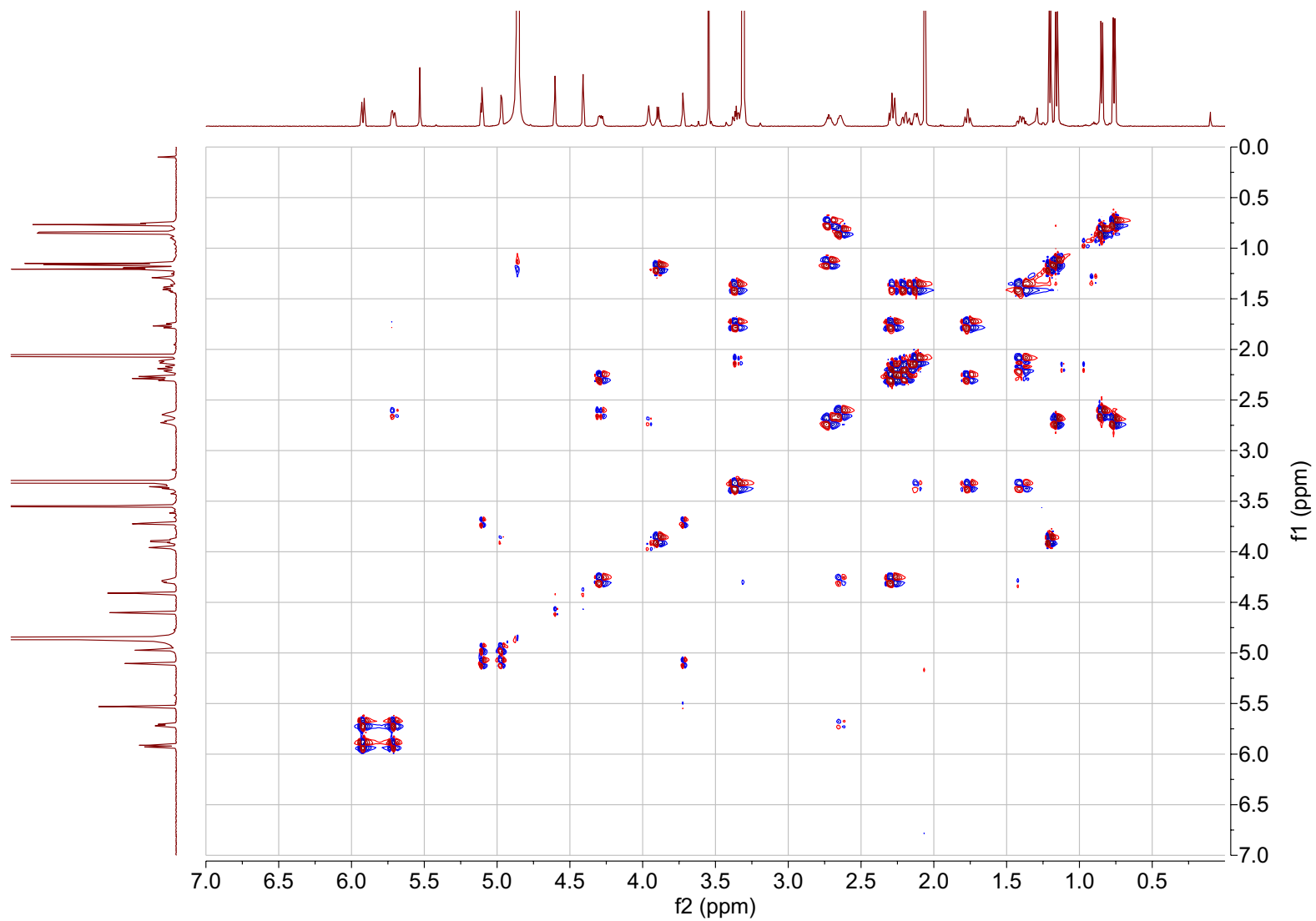
<sup>13</sup>C NMR of **41**



HSQC of 41

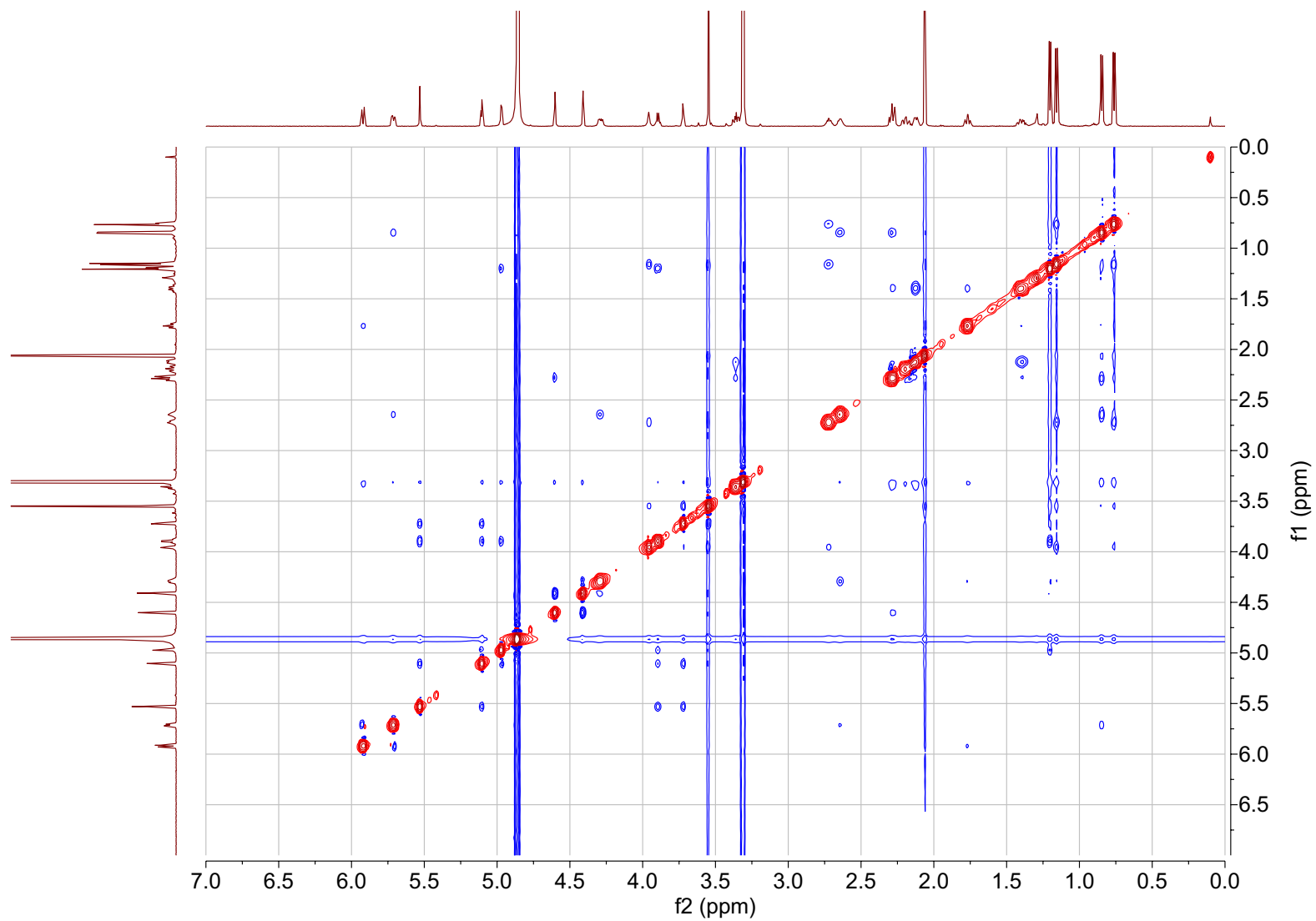


COSY of 41

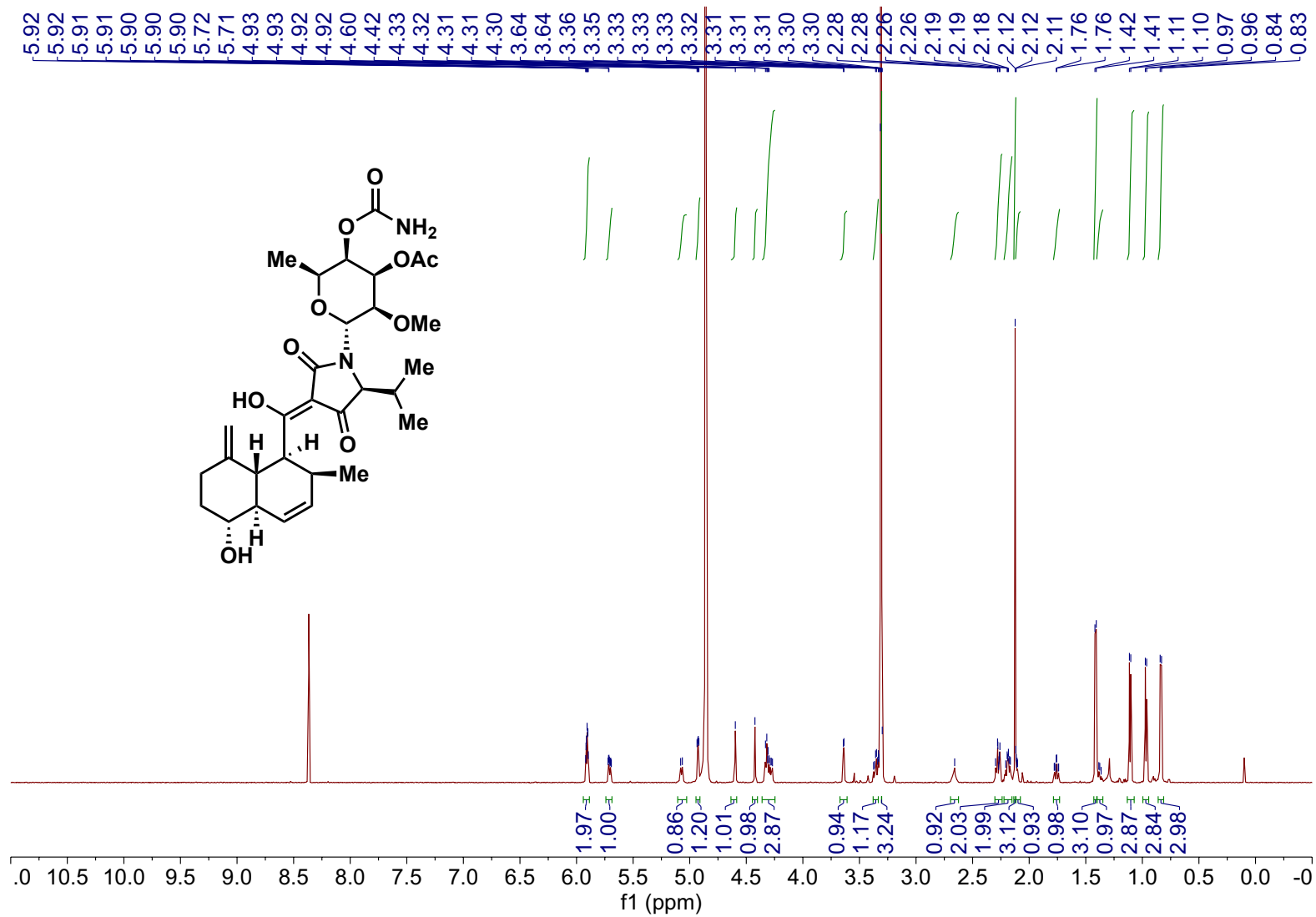


S205

NOESY of 41

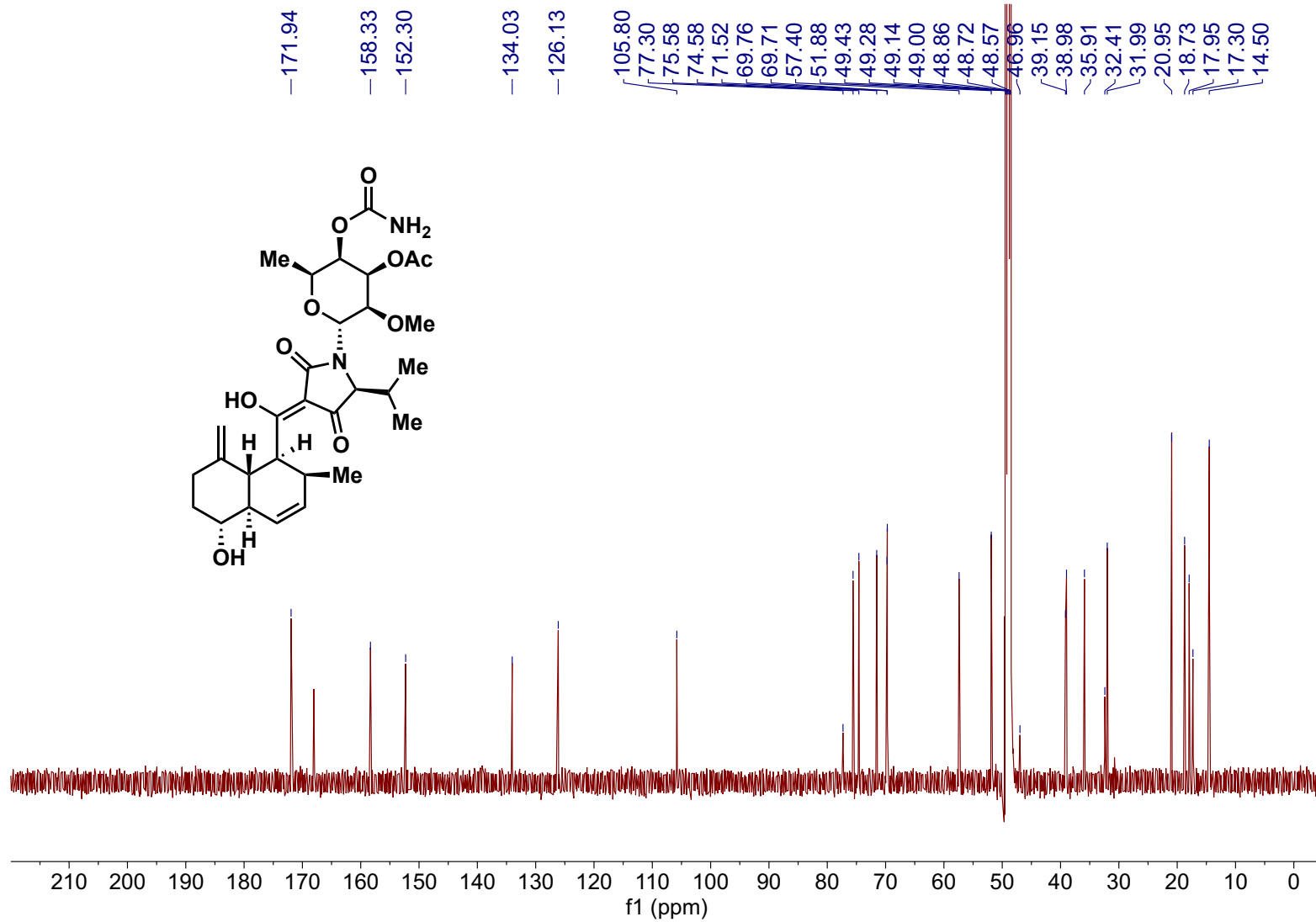


<sup>1</sup>H NMR of 42

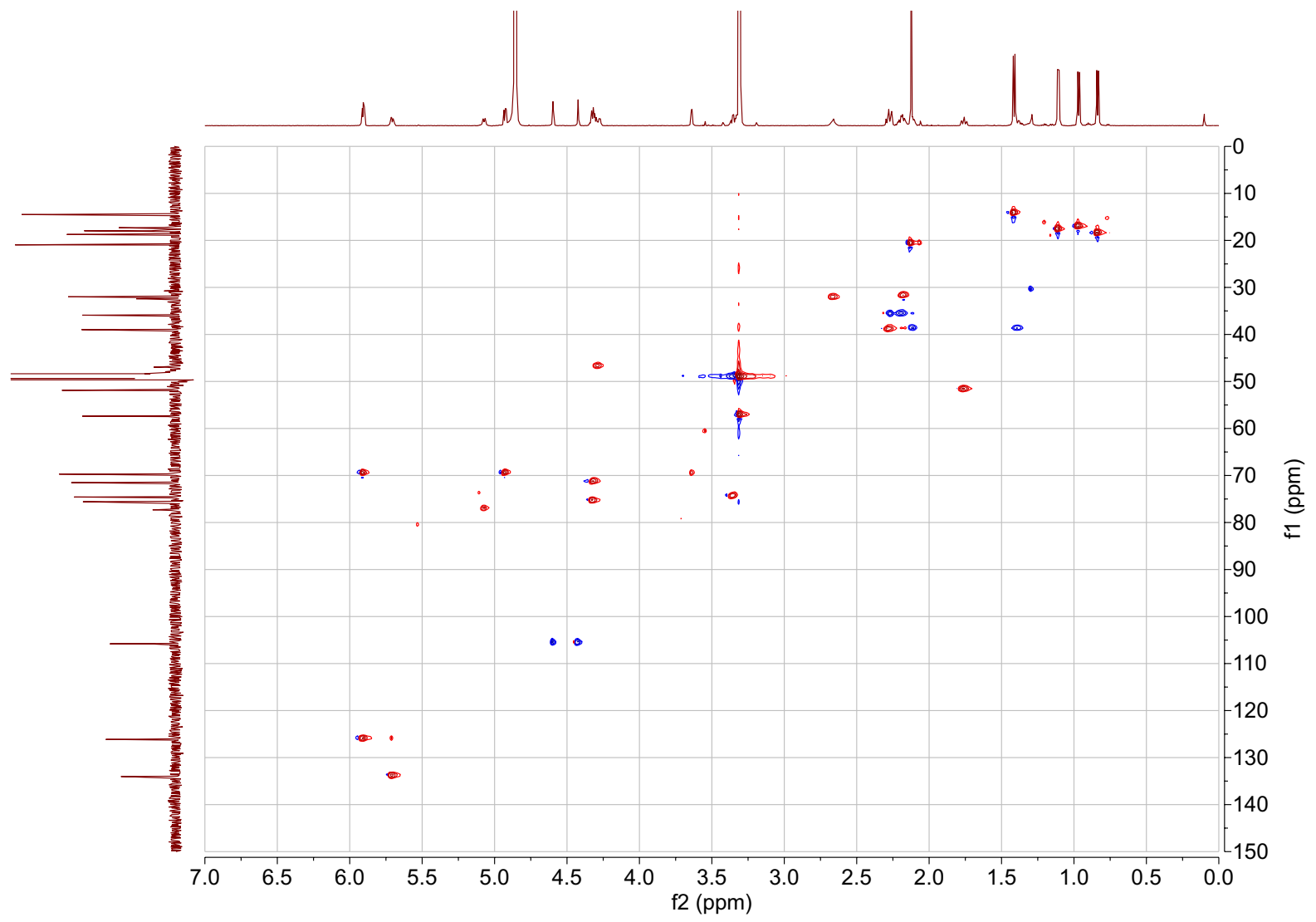




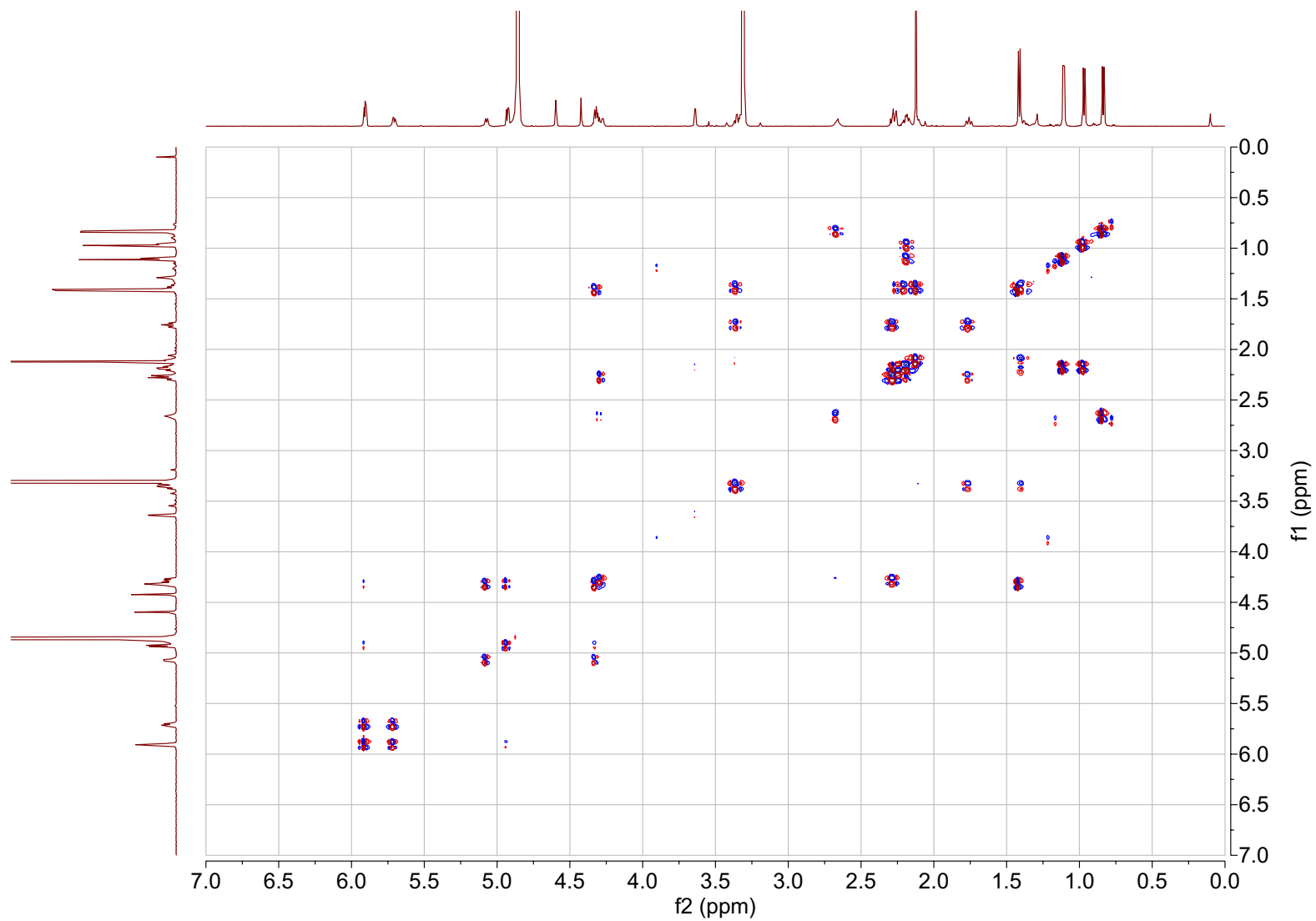
<sup>13</sup>C NMR of **42**



HSQC of 42



COSY of 42



S210

NOESY of 42

