

# Supporting Information

## “Click, Click, Cyclize”: A DOS Approach to Sultams Utilizing Vinyl Sulfonamide Linchpins

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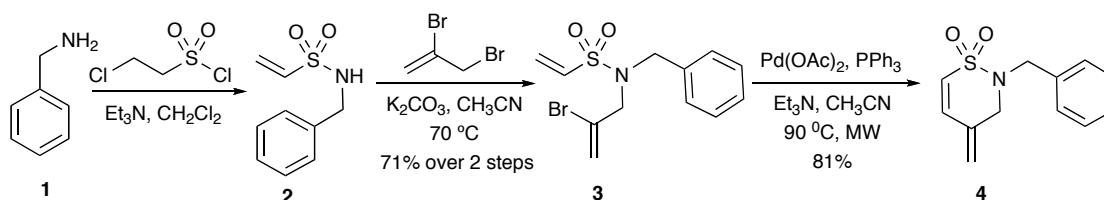
### General Experimental Methods

All reactions were carried out under argon atmosphere. Stirring was achieved with oven-dried magnetic stir bars. Et<sub>2</sub>O, toluene, THF and CH<sub>2</sub>Cl<sub>2</sub> were purified by passage through the Solv-Tek purification system employing activated Al<sub>2</sub>O<sub>3</sub> (Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518-1520). Et<sub>3</sub>N was purified by passage over basic alumina and stored over KOH. Butyl lithium was purchased from Aldrich and titrated prior to use. Glycidol ether was acquired from Daiso Co., Ltd., Fine Chemical Department and used without further purification. Flash column chromatography was performed with Sorbent Technologies (30930M-25, Silica Gel 60A, 40-63 μm). Thin layer chromatography was performed on silica gel 60F254 plates (EM-5717, Merck). Deuterated solvents were purchased from Cambridge Isotope laboratories. <sup>1</sup>H, <sup>13</sup>C NMR spectra were recorded on a Bruker DRX-400 spectrometer

operating at 400 MHz, 100 MHz respectively. Observed rotations at 589 nm were measured using AUTOPOL IV Model automatic polarimeter. High-resolution mass spectrometry (HRMS) was recorded on a LCT Premier Spectrometer (Micromass UK Limited) operating on ESI (MeOH).

## Experimental Data and Characterization Data

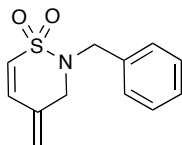
### Procedure of Intramolecular Heck Reaction to Make Sultam



2-Chloroethanesulfonyl chloride (0.21 mL, 2.1 mmol) was added drop wise to a stirred solution of benzyl amine **1** (220 mg, 2.1 mmol) with Et<sub>3</sub>N (1.0 mL, 7.3 mmol.) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) at 0 °C. After addition, stirring was continued at 0 °C for 2 h. Then the mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (10 mL), washed with brine (2x5 mL), dried (MgSO<sub>4</sub>) and concentrated under reduced pressure. The crude mixture **2** was re-dissolved in CH<sub>3</sub>CN (5 mL), 2,3-dibromopropene (0.27 mL, 2.1 mmol, 80% solution) and K<sub>2</sub>CO<sub>3</sub> (580 mg, 4.2 mmol) were added and the mixture was heated at 70 °C for 2-5 h (the reaction was monitored by TLC). After TLC indicated the reaction was complete, it was cooled to rt, filtered and concentrated. Crude product **3** was purified by flash chromatography (8:1 hexane/EtOAc) to give 460 mg (71% over 2 steps) of pure product **3** as a colorless oil.

The Heck reaction was carried out at 90 °C under microwave conditions. Vinyl sulfonamide **3** (100 mg, 0.32 mmol) was added into a 1 mL microwave tube with 0.6 mL CH<sub>3</sub>CN and Et<sub>3</sub>N (0.18 mL, 1.27 mmol). The reaction mixture was degassed with argon for 5 minutes, Pd(OAc)<sub>2</sub> (10 % mol) and PPh<sub>3</sub> (17 mg, 20 % mol) were added and the reaction was heated under microwave conditions at 90 °C for 30 minutes. The reaction mixture was cooled to rt, concentrated under reduced pressure and purified by flash chromatography (8:1 hexane/EtOAc) to afford sultam **4** (60.0 mg, 0.26 mmol) in 81% yield as a clear oil.

#### ***N*-2-Benzyl-4-methylene-1,2-thiazine-1,1-dioxide (4)**



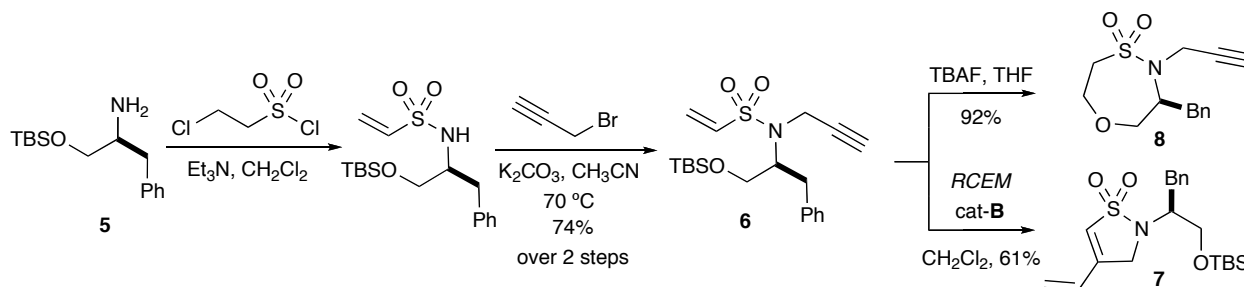
**FTIR** (neat): 2970, 1425, 1320, 1130  $\text{cm}^{-1}$ , colorless oil;

**$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  (ppm) 7.41-7.35 (aromatic H, 5H), 6.73 (d,  $J = 10.4$  Hz, 1H), 6.51 (d,  $J = 10.8$  Hz, 1H), 5.51 (s, 1H), 5.30 (s, 1H), 4.20 (s, 2H), 4.14 (s, 2H);

**$^{13}\text{C-NMR}$**  ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  (ppm) 136.5, 134.9, 132.1, 128.9, 128.2, 128.0(2), 125.3(2), 124.0, 52.0, 49.8;

**HRMS** (ESI)  $m/z$  calculated for  $\text{C}_{12}\text{H}_{13}\text{NO}_2\text{SH}$  236.0745 ( $\text{M}+\text{H}^+$ ), found 236.0740.

#### **Procedure of Intramolecular Enyne Metathesis to Make Sultam Scaffold.**

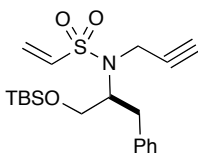


2-Chloroethanesulfonyl chloride (0.1 mL, 1.0 mmol) was added drop wise to a stirred solution of TBS-protected amino alcohol **5** (265 mg, 1.0 mmol) with  $\text{Et}_3\text{N}$  (0.49 mL, 3.5 mmol) in  $\text{CH}_2\text{Cl}_2$  (5 mL) at 0 °C. After addition, stirring was continued at 0 °C for 2 h. The mixture was diluted with  $\text{CH}_2\text{Cl}_2$  (10 mL), washed with brine (2x5 mL), dried ( $\text{MgSO}_4$ ) and concentrated under reduced pressure. Without further purification, the crude mixture was dissolved in  $\text{CH}_3\text{CN}$  (5 mL) and propargyl bromide (0.12 mL, 1.05 mmol, 80 wt.% in toluene) and  $\text{K}_2\text{CO}_3$  (276 mg, 2.0 mmol) were added. The mixture was heated at 70 °C for 2-5 h (reaction was monitored by TLC), and the reaction mixture was cooled down to rt, filtered and concentrated under reduced pressure. The crude product **6** was purified by flash chromatography (10:1 hexane/ $\text{EtOAc}$ ) to afford product **6** (290 mg, 0.74 mmol) in 74% yield over two steps as a colorless oil. Vinyl sulfonamide **6** (202 mg, 0.51 mmol) was redissolved into 50 mL  $\text{CH}_2\text{Cl}_2$ , after it was degassed by argon for 5 minutes, Grubbs cat-**B** [10 mol%,  $(\text{IMesH}_2)(\text{PCy}_3)(\text{Cl})_2\text{Ru}=\text{CHPh}$ ] was added, the mixture solution was refluxed at 55 °C (oil bath) for overnight, and then cooled to rt,

concentrated under reduced pressure and purified by flash chromatography (10:1 hexane/EtOAc) to afford the  $\gamma$ -sultam **7** (123 mg, 0.31 mmol) in 61% yield.

To a solution of vinyl sulfonamide **6** (88 mg, 0.22 mmol) in THF (3 mL) was added TBAF (0.22 mL, 1M in THF). Stirring was continued for 2 h, NH<sub>4</sub>Cl (1 mL, sat'd) was added and the organic layer was extracted by CH<sub>2</sub>Cl<sub>2</sub> (2x2 mL) and dried (MgSO<sub>4</sub>). The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (4:1 hexane/EtOAc) to yield sultam **8** (57 mg, 0.20 mmol) in 92% yield.

**(S)-N-(1-(tert-Butyldimethylsilyloxy)-3-phenylpropan-2-yl)-N-(prop-2-ynyl)ethane-sulfonamide (6)**



$[\alpha]_D^{20}$  -17.3 (c 5.50, CH<sub>2</sub>Cl<sub>2</sub>), colorless oil;

**FTIR** (neat): 3282, 2953, 1456, 1340, 1149, 837, 777 cm<sup>-1</sup>;

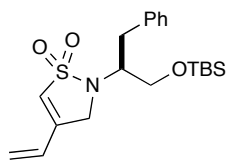
**<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 400 MHz):  $\delta$  (ppm) 7.34-7.23 (aromatic H, 5H), 6.33 (dd,  $J$  = 16.4, 9.6 Hz, 1H), 6.18 (d,  $J$  = 16.8 Hz, 1H), 5.78 (d,  $J$  = 9.6 Hz, 1H), 4.20 (d,  $J$  = 2.4 Hz, 2H), 4.00 (m, 1H), 3.76 (m, 2H), 3.12 (dd,  $J$  = 13.6, 8.4 Hz, 1H), 3.0 (dd,  $J$  = 13.6, 6.4 Hz, 1H), 2.33 (t,  $J$  = 2.4 Hz, 1H), 0.92 (s, 9H), 0.06 (s, 6H);

**<sup>13</sup>C-NMR** (CDCl<sub>3</sub>, 100 MHz):  $\delta$  (ppm) 138.1, 136.3, 129.4(2), 128.5(2), 126.7, 125.5, 80.4, 72.6, 63.8, 61.3, 36.0, 33.8, 25.9(3), 18.2, -5.5(2);

**HRMS** (ESI)  $m/z$  calculated for C<sub>20</sub>H<sub>31</sub>NO<sub>3</sub>SSiNa 416.1692 (M+Na)<sup>+</sup>, found 416.1700.



**(S)-N-2-((tert-Butyldimethylsilyloxy)-3-phenylpropan-2-yl)-4-vinylisosthiazole -1,1-dioxide**  
**(7)**



$[\alpha]_D^{20}$  -8.5 (c 5.50, CH<sub>2</sub>Cl<sub>2</sub>), colorless oil;

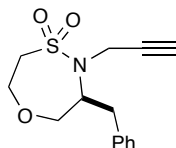
**FTIR** (neat): 2928, 1286, 1109, 837, 777 cm<sup>-1</sup>;

**<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 400 MHz): δ (ppm) 7.34-7.25 (aromatic H, 5H), 6.57 (dd, *J* = 17.4, 10.6 Hz, 1H), 6.52 (s, 1H), 5.78 (d, *J* = 10.4 Hz, 1H), 5.54 (d, *J* = 16.8 Hz, 1H), 4.49 (d, *J* = 15.7 Hz, 1H), 4.26 (d, *J* = 15.8 Hz, 1H), 4.0 (m, 1H), 3.91 (dd, *J* = 10.5, 2.6 Hz, 1H), 3.71 (dd, *J* = 10.5, 3.2 Hz, 1H), 3.22 (dd, *J* = 13.1, 9.7 Hz, 1H), 3.05 (dd, *J* = 13.0, 5.1 Hz, 1H), 0.97 (s, 9H), 0.06 (s, 6H);

**<sup>13</sup>C-NMR** (CDCl<sub>3</sub>, 100 MHz): δ (ppm) 144.6, 137.9, 129.3, 129.0, 128.6, 126.7(2), 122.4(2), 121.9, 63.6, 55.1, 48.1, 34.8, 25.9(3), 18.1, -5.6(2);

**HRMS** *m/z* calculated for C<sub>20</sub>H<sub>31</sub>NO<sub>3</sub>SiSNa 416.1692 (M+Na)<sup>+</sup>, found 416.1692.

**(S)-N-2-Propargyl-3-benzylisosthiazole -5,1,2-dioxide (8)**



$[\alpha]_D^{20}$  -34.1 (c 2.30, CH<sub>2</sub>Cl<sub>2</sub>), colorless oil;

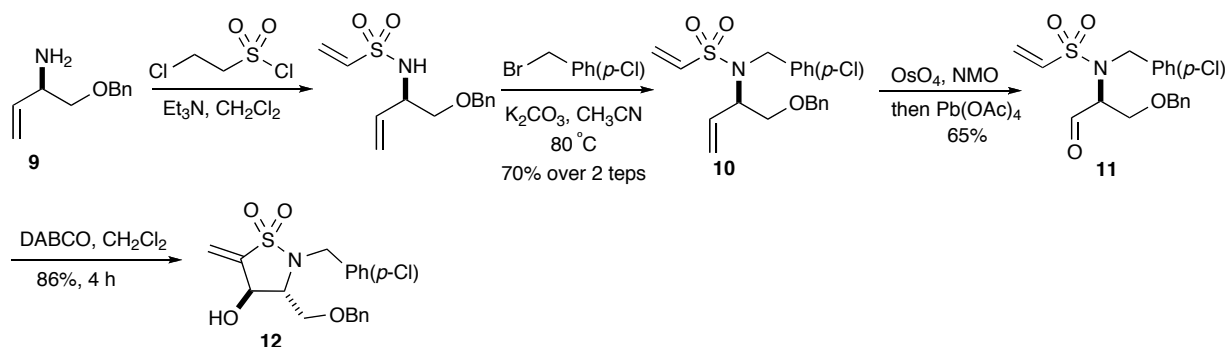
**FTIR** (neat): 2949, 1350, 1144, 1032, 702 cm<sup>-1</sup>;

**<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 400 MHz): δ (ppm) 7.35-7.26 (aromatic H, 5H), 4.25 (m, 1H), 4.18 (m, 2H), 3.98 (dd, *J* = 13.3, 11.2 Hz, 1H), 3.84 (ddd, *J* = 13.1, 11.9, 2.3 Hz, 1H), 3.60 (m, 2H), 3.28 (ddd, *J* = 14.2, 2.0, 2.0 Hz, 1H), 3.08 (dd, *J* = 19.0, 2.4 Hz, 1H), 2.88 (dd, *J* = 13.5, 9.0 Hz, 1H), 2.72 (dd, *J* = 13.4, 5.4 Hz, 1H), 2.34 (dd, *J* = 2.5, 2.4 Hz, 1H);

**<sup>13</sup>C-NMR** (CDCl<sub>3</sub>, 100 MHz): δ (ppm) 137.6, 129.3(2), 128.8(2), 126.8, 78.2, 75.6, 73.8, 67.1, 61.2, 55.9, 40.6, 38.2;

**HRMS** (ESI) *m/z* calculated for C<sub>14</sub>H<sub>17</sub>NO<sub>3</sub>SNa 302.0827 (M+Na)<sup>+</sup>, found 302.0846.

## Selective Oxidation of Chiral Vinyl Sulfonamide to Make Baylis-Hillman Precursor

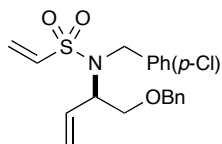


2-Chloroethanesulfonyl chloride (0.1 mL, 1.0 mmol) was added drop wise to a stirred solution of allyl amine alcohol **9** (177 mg, 1.0 mmol) with Et<sub>3</sub>N (0.49 mL, 3.5 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL) at 0 °C. After addition, stirring was continued at 0 °C for 2 h, the reaction mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (5 mL), washed with brine solution (2x3 mL), dried (MgSO<sub>4</sub>) and concentrated under reduced pressure. The crude product was directly used for the next benzylation step. 4-Chlorobenzyl bromide (216 mg, 1.05 mmol) was added to the mixture of resultant vinyl sulfonamide and K<sub>2</sub>CO<sub>3</sub> (276 mg, 2.0 mmol) in CH<sub>3</sub>CN (4 mL). The mixture was refluxed at 80 °C until TLC analysis indicated that the SM was consumed. The reaction mixture was cooled down to rt, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (8:1 hexane/EtOAc) to afford sultam **10** (274 mg, 0.70 mmol) in 70% yield over 2 steps.

A catalytic amount of OsO<sub>4</sub> (2% solution, 0.05 equiv.) was added to the solution of benzylated vinyl sulfonamide **10** (87 mg, 0.22 mmol) and NMO (1.5 equiv.) in THF (3 mL). Stirring was continued until TLC analysis indicated that the SM was consumed. The solution was washed with NaHSO<sub>3</sub> solution twice (2x3 mL), the organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and concentrated. Pb(OAc)<sub>4</sub> (147 mg, 0.33 mmol) was added to the above residue solution in CH<sub>2</sub>Cl<sub>2</sub> (5 mL) at rt, after 4 h, the reaction mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (2x5 mL), the organic layer was washed with brine solution, dried (MgSO<sub>4</sub>), concentrated under reduced pressure and purified by flash chromatography (8:1 hexane/EtOAc) to produce aldehyde vinyl sulfonamide **11** (57 mg, 0.14 mmol) in 65% yield. DABCO (0.10 equiv.) was added to the solution of aldehyde vinyl sulfonamide in CH<sub>2</sub>Cl<sub>2</sub> (4 mL), stirring was continued until TLC analysis indicated that the SM was consumed (normally about 4 h). The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (2:1

hexane/EtOAc) to yield final product **12** (49 mg, 0.12 mmol) in 86% yield with 4:1 diastereoselectivity.

**(R)-N-(1-(Benzyloxy)but-3-en-2-yl)-N-(p-chlorobenzyl)ethenensulfonamide (10)**



$[\alpha]_D^{20}$  23.5 (c 7.65, CH<sub>2</sub>Cl<sub>2</sub>), colorless oil;

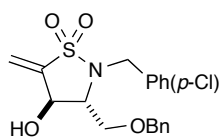
**FTIR:** 3030, 2925, 2862, 1490, 1350, 1189, 1093 cm<sup>-1</sup>;

**<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 400 MHz): δ (ppm) 7.40-7.26 (m, 9H), 6.50 (dd, *J* = 16.4, 10.0 Hz, 1H), 6.18 (d, *J* = 16.4 Hz, 1H), 5.81 (d, *J* = 10.0 Hz, 1H), 5.70 (m, 1H), 5.21 (d, *J* = 11.2 Hz, 1H), 5.20 (d, *J* = 16.4 Hz, 1H), 4.56 (m, 1H), 4.41 (dd, *J* = 19.0, 11.0 Hz, 2H), 4.30 (s, 2H), 3.59 (dd, *J* = 9.2, 8.8 Hz, 1H), 3.48 (dd, *J* = 10.0, 5.2 Hz, 1H);

**<sup>13</sup>C-NMR** (CDCl<sub>3</sub>, 100 MHz): δ (ppm) 137.6, 136.5, 136.0, 133.8, 133.2, 129.8, 129.6, 128.5, 127.9, 127.8, 126.0, 119.4, 73.1, 69.9, 60.1, 47.8;

**HRMS** (ESI) *m/z* calculated for C<sub>20</sub>H<sub>22</sub>NO<sub>3</sub>ClSNa 414.0907 (M+Na)<sup>+</sup>, found 414.0893.

**N-2-(p-Chlorobenzyl)-3(S)-(Benzyloxymethyl)-4(S)-hydroxy-5-methylene-iso-thiazolidine (12)**



dr ratio = 4:1

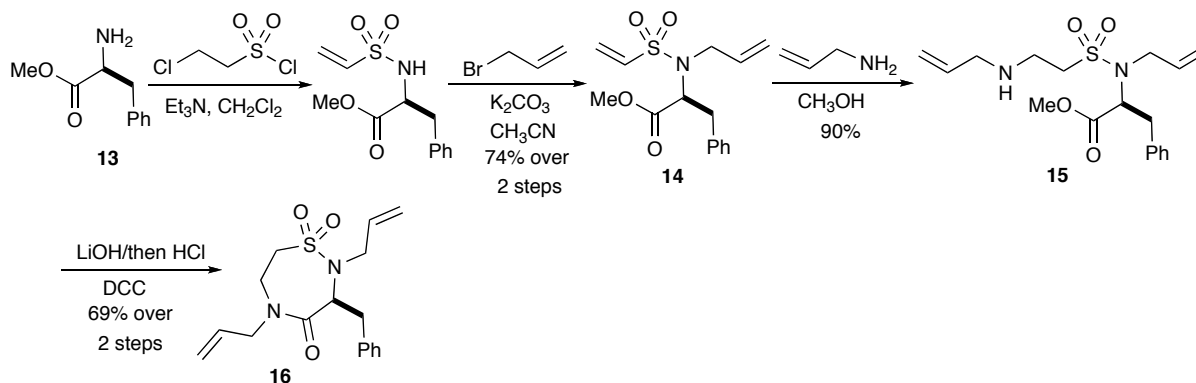
**FTIR:** 3446, 2923, 1490, 1290, 1143, 1092 cm<sup>-1</sup>, colorless oil;

**<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 400 MHz): δ (ppm) 7.40-7.25 (m, 9H), 6.25 (s, 1H), 5.97 (s, 1H), 4.97 (m, 1H), 4.41 (d, *J* = 3.2 Hz, 2H), 4.31 (s, 2H), 3.61 (m, 1H), 3.60 (s, 2H), 3.33 (d, *J* = 8.4 Hz, 1H);

**<sup>13</sup>C-NMR** (CDCl<sub>3</sub>, 100 MHz): δ (ppm) 147.1, 136.6(2), 134.0(2), 129.8, 128.9, 128.8, 128.7, 128.6(2), 128.3(2), 127.9, 117.7, 73.7, 67.6, 66.8, 59.1, 45.5;

**HRMS** (ESI) *m/z* calculated for C<sub>19</sub>H<sub>20</sub>NO<sub>4</sub>ClSNa 416.0699 (M+Na)<sup>+</sup>, found 416.0685.

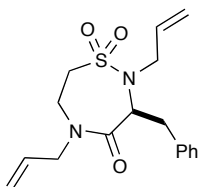
## Procedure for Intermolecular aza-Michael Reaction of Vinyl Sulfonamide.



2-Chloroethanesulfonyl chloride (0.2 mL, 2.0 mmol) was added drop wise to a stirred solution of phenylalanine methyl ester hydrogen chloride **13** (431 mg, 2.0 mmol) with Et<sub>3</sub>N (1.25 mL, 9.0 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) at 0 °C. After addition, stirring was continued at 0 °C for 2 h. The mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (10 mL), and then washed with brine (2x8 mL), dried (MgSO<sub>4</sub>) and concentrated under reduced pressure. The crude mixture was redissolved in CH<sub>3</sub>CN (10 mL), allyl bromide (0.19 mL, 2.1 mmol) and K<sub>2</sub>CO<sub>3</sub> (550 mg, 4.0 mmol) were added and the mixture was heated at 70 °C for 2-5 h (reaction was monitored by TLC). The reaction mixture was cooled to rt, filtered and concentrated under reduced pressure. The crude product **14** was purified by flash chromatography (6:1 hexane/EtOAc) to afford pure product **14** (460 mg, 1.49 mmol) in 74% yield over 2 steps as a colorless oil.

Vinyl sulfonamide **14** (300 mg, 0.97 mmol) and allyl amine (0.09 mL, 1.10 mmol) were dissolved into CH<sub>3</sub>OH (5 mL), the mixture was refluxed overnight and the reaction was cooled to rt, concentrated and purified by flash chromatography (pure EtOAc) to afford **15** (317 mg, 0.86 mmol) in 90% yield as a clear oil. 2*N* LiOH solution (5 mL) was added to **15** (180 mg, 0.49 mmol), stirring was kept until TLC showed the disappearance of SM (3 to 5 h). Acid (1*N* HCl) was added to neutralize the above solution until the pH value was about 6 to 7. The solution was extracted by CH<sub>2</sub>Cl<sub>2</sub> (2x5 mL), dried (MgSO<sub>4</sub>) and filtered. DCC (2.0 equiv.) was added into the above filtrate, the mixture was stirred overnight, filtered, concentrated under reduced pressure and purified by flash chromatography (1:1 hexane/EtOAc) to afford the 7-membered sultam **16** (113 mg, 0.34 mmol) in 69% yield over 2 steps.

**(S)-N-2-Allyl-3-benzyl-N-5-allyl-1,2,5-thiadiazepine-1,1,4-trioxide (16)**



$[\alpha]_D^{20} - 31.3$  (c 0.80, CH<sub>2</sub>Cl<sub>2</sub>), colorless oil;

**FTIR** (neat): 2960, 1655, 1337, 1148, 737 cm<sup>-1</sup>;

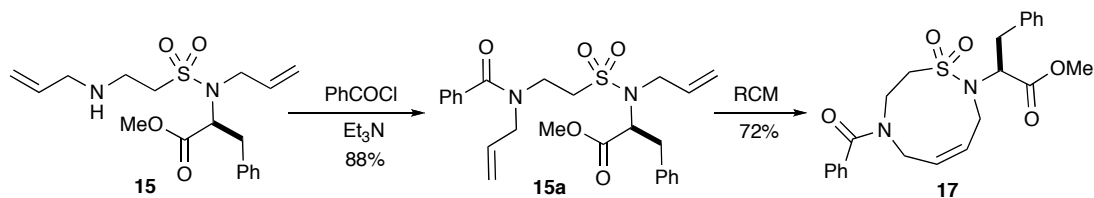
**<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 400 MHz):  $\delta$  (ppm) 7.31-7.23 (aromatic H, 5H), 5.80 (m, 2H), 5.24 (m, 4H), 4.78 (dd,  $J = 6.9, 6.8$  Hz, 1H), 4.11 (dd,  $J = 14.4, 6.2$  Hz, 1H), 3.97 (dd,  $J = 16.6, 5.5$  Hz, 2H), 3.82 (dd,  $J = 16.0, 4.0$  Hz, 1H), 3.68 (dd,  $J = 16.0, 7.2$  Hz, 1H), 3.47 (dd,  $J = 16.9, 4.0$  Hz, 1H), 3.38 (dd,  $J = 14.2, 7.6$  Hz, 1H), 3.18 (dd,  $J = 14.3, 5.1$  Hz, 1H), 3.00 (m, 2H);

**<sup>13</sup>C-NMR** (CDCl<sub>3</sub>, 100 MHz):  $\delta$  (ppm) 170.7, 137.1, 133.6, 132.3, 129.5, 128.4, 126.6(2), 119.4(2), 118.9, 59.3, 51.3, 50.0, 47.5, 43.0, 35.6;

**HRMS** (ESI)  $m/z$  calculated for C<sub>17</sub>H<sub>22</sub>N<sub>2</sub>O<sub>3</sub>SNa 357.1249 (M+Na)<sup>+</sup>, found 357.1221.

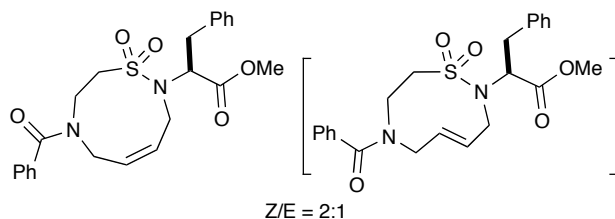
**(S)-N-2-(Phenylmethyl methyl ester)-N-7-Benzoyl-1,2,7-thiadiazepine-1,1-dioxide (17)**

**(mixture of Z/E isomers, Z/E = 2:1)**



Benzoyl chloride (80 mg, 0.58 mmol) was added drop wise to the solution of **15** (209 mg, 0.57 mmol) with Et<sub>3</sub>N (0.12 mL, 0.86 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL) at rt, after stirring the mixture for 2 h, the reaction mixture was washed with water (2x3 mL). The organic layer was dried (MgSO<sub>4</sub>), concentrated under reduced and purified by flash chromatography (4:1 hexane/EtOAc) to afford **15a** (240 mg 0.51 mmol) in 88% yield. The purified compound **15a** was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (50 mL), and degassed with argon gas for 5 minutes, and Grubbs cat-**B** [10 mol%, (IMesH<sub>2</sub>)(PCy<sub>3</sub>)-(Cl)<sub>2</sub>Ru=CHPh] was added into the solution, and refluxed overnight. The mixture was concentrated under reduced pressure and subjected to flash chromatography (4:1

hexane/EtOAc) to afford final product **17** (163 mg 0.37 mmol) in 63% yield over 2 steps as a Z/E mixture (Z/E = 2:1).

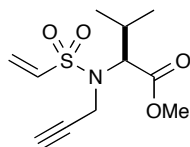


**FTIR** (neat): 3028, 2951, 1742, 1634, 1333, 1144, 735  $\text{cm}^{-1}$ , colorless oil;

**$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  (ppm) 7.42-7.23 (aromatic H, 15H), 6.02 (ddd,  $J = 9.2, 8.1, 8.1$  Hz, 1H), 5.88 (overlap, 1H), 5.80 (ddd,  $J = 9.4, 7.9, 7.9$  Hz, 1H), 4.86 (dd,  $J = 7.3, 7.2$  Hz, 1H), 4.26 (d,  $J = 6.3$  Hz, 1H), 4.10 (overlap, 6H), 3.78 (overlap, 8H), 3.48 (overlap, 3H), 3.15 (m, 3H);  **$^{13}\text{C-NMR}$**  ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  (ppm) 172.0(171.8), 171.0(171.2), 136.4(136.5), 136.0, 132.4, 130.5, 129.8, 129.5, 128.7, 128.6, 127.3(127.2), 126.7(126.4), 61.8(60.4), 52.6(53.8), 47.0, 40.2(43.3), 36.6(38.2), 21.1, 14.2;

**HRMS** (ESI)  $m/z$  calculated for  $\text{C}_{23}\text{H}_{26}\text{N}_2\text{O}_5\text{SNa}$  465.1460 ( $\text{M}+\text{Na}$ ) $^+$ , found 465.1442.

**(S)-Methyl-3-methyl-2-(N-(prop-2-ynyl)vinylsulfonamido)butanoate (19)**



$[\alpha]_D^{20}$   $-59.5$  (c 1.31,  $\text{CH}_2\text{Cl}_2$ ), colorless oil;

**FTIR** (neat): 3279, 2968, 1740, 1344, 1148, 1049  $\text{cm}^{-1}$ ;

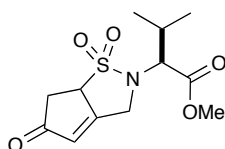
**$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  (ppm) 6.54 (dd,  $J = 16.8, 10.0$  Hz, 1H), 6.20 (d,  $J = 16.5, 10.0$  Hz, 1H), 5.91 (d,  $J = 9.9$  Hz, 1H), 4.27 (dd,  $J = 18.6, 2.3$  Hz, 1H), 3.95 (dd,  $J = 18.4, 2.3$  Hz, 1H), 3.90 (s, 1H), 3.67 (s, 3H), 2.27 (dd,  $J = 2.3, 2.3$  Hz, 1H), 2.17 (m, 1H), 1.00 (d,  $J = 6.7$  Hz, 3H), 0.91 (d,  $J = 6.5$  Hz, 3H);

**$^{13}\text{C-NMR}$**  ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  (ppm) 170.6, 135.5, 126.9, 78.7, 72.6, 64.9, 51.8, 33.4, 28.0, 19.5, 19.3;

**HRMS** (ESI)  $m/z$  Calculated for  $\text{C}_{11}\text{H}_{17}\text{NO}_4\text{SNa}$  282.0776 ( $\text{M}+\text{Na}$ ) $^+$ , found. 282.0781.

**(2S)-Methyl-3-methyl-2-(5-oxo-3,5,6,6a)-tetrahydro-2H-cyclopenta[d]isosthiazole-1,1-dioxide (20)** (mixture of diastereoismer dr = 2:1)

To a solution of **19** (110 mg, 0.42 mmol) in toluene (10 mL) was added  $\text{Co}_2(\text{CO})_8$  (144 mg, 0.42 mmol). The reaction temperature was kept at 80 °C until TLC showed the reaction was over, the mixture was concentrated under reduced pressure and subjected to flash chromatography (4:1 hexane/EtOAc) to yield sultam **20** (66.3 mg, 0.23 mmol) in 55% yield as a 2:1 mixture of diastereomers.



**FTIR** (neat): 2955, 1635, 1219, 1144, 755  $\text{cm}^{-1}$ , colorless oil;

**$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  (ppm) 6.35 (s, 1H), 4.81 (d,  $J = 12.0$  Hz, 0.67H), 4.70 (d,  $J = 12.0$  Hz, 0.33H-Minor), 4.37-4.32 (m, 2H), 4.11 (d,  $J = 6.8$  Hz, 0.67H), 3.91 (d,  $J = 8.4$  Hz, 0.33H-Minor), 3.69 (s, 3H), 2.75 (m, 2H), 2.15 (m, 1H), 1.04 (d,  $J = 6.8$  Hz, 3H), 0.98 (d,  $J = 6.8$  Hz, 3H);

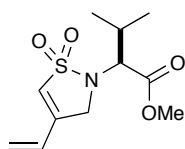
**$^{13}\text{C-NMR}$**  ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  (ppm)

**Major** 204.2, 172.6, 167.5, 130.9, 63.4, 60.9, 52.3, 46.8, 36.0, 29.6, 20.0, 19.7;

**Minor** 203.5, 171.2, 165.7, 130.4, 60.5, 59.5, 52.3, 44.9, 35.6, 27.8, 19.1, 19.0;

**HRMS** (ESI)  $m/z$  Calculated for  $\text{C}_{12}\text{H}_{17}\text{NO}_5\text{SNa}$  310.0725 ( $\text{M}+\text{Na}$ )<sup>+</sup>, found 310.0707.

**(S)-N-2-(3-Methylbutanoate)-4-vinylisothiazole -1,1-dioxide (21)**



**$[\alpha]_D^{20}$**  34.1 (c 1.16,  $\text{CH}_2\text{Cl}_2$ ), colorless oil;

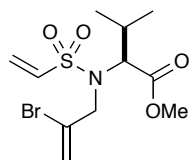
**FTIR** (neat): 2955, 1735, 1290, 1197, 1163  $\text{cm}^{-1}$ ;

**$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  (ppm) 6.55 (m, 2H), 5.60 (dd,  $J = 10.4, 3.6$  Hz, 2H), 4.82 (d,  $J = 15.2$  Hz, 1H), 4.16 (d,  $J = 15.2$  Hz, 1H), 3.89 (d,  $J = 10.0$  Hz, 1H), 3.80 (s, 3H), 2.19 (m, 1H), 1.09 (d,  $J = 6.8$  Hz, 3H), 1.03 (d,  $J = 6.8$  Hz, 3H);

$^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  (ppm) 172.3, 144.6, 128.8, 122.6, 121.7, 59.6, 52.0, 46.5, 29.1, 19.7, 19.2;

**HRMS** (ESI)  $m/z$  Calculated for  $\text{C}_{11}\text{H}_{17}\text{NO}_4\text{SNa}$  282.0776 ( $\text{M}+\text{Na}$ ) $^+$ , found 282.0774.

**(S)-Methyl-2-(N-(2-bromoallyl)vinylsulfonamido)-3-Methylbutanoate (22)**



$[\alpha]_{\text{D}}^{20}$  -23.5 (c 1.65,  $\text{CH}_2\text{Cl}_2$ ), colorless oil;

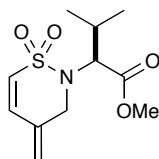
**FTIR** (neat): 2952, 1740, 1346, 1148, 762  $\text{cm}^{-1}$ ;

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  (ppm) 6.52 (dd,  $J = 16.4, 10.0\text{Hz}$ , 1H), 6.24 (d,  $J = 16.4\text{ Hz}$ , 1H), 6.01 (s, 1H), 5.96 (d,  $J = 8.8\text{ Hz}$ , 1H), 5.65 (s, 1H), 4.30 (d,  $J = 17.2\text{ Hz}$ , 1H), 4.09 (m, 2H), 3.72 (s, 3H), 2.19 (m, 1H), 1.03 (d,  $J = 13.2\text{ Hz}$ , 3H), 0.98 (d,  $J = 7.8\text{ Hz}$ , 3H);

$^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  (ppm) 170.8, 134.9, 128.4, 127.4, 120.1, 66.0, 52.6, 51.9, 28.6, 20.1, 19.4;

**HRMS** (ESI)  $m/z$  calculated for  $\text{C}_{11}\text{H}_{18}\text{NO}_4\text{SBrNa}$  362.0038 ( $\text{M}+\text{Na}$ ) $^+$ , found 362. 0032.

**(S)-N-2-(3-Methylbutanoate)-4-methylene-1,2-thiazepine-1,1-dioxide (23)**



$[\alpha]_{\text{D}}^{20}$  -27.4 (c 0.27,  $\text{CH}_2\text{Cl}_2$ ), colorless oil;

**FTIR** (neat): 2959, 1720, 1330, 1150  $\text{cm}^{-1}$ ;

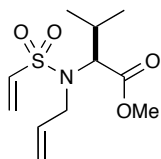
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  (ppm) 6.67 (d,  $J = 10.8\text{ Hz}$ , 1H), 6.49 (d,  $J = 10.4\text{ Hz}$ , 1H), 5.30 (d,  $J = 22.0\text{ Hz}$ , 2H), 4.53 (d,  $J = 16.8\text{ Hz}$ , 1H), 4.26 (d,  $J = 16.8\text{ Hz}$ , 1H), 4.13 (d,  $J = 10.4\text{ Hz}$ , 1H), 3.64 (s, 3H), 2.13 (m, 1H), 0.98 (d,  $J = 6.8\text{ Hz}$ , 3H), 0.85 (d,  $J = 6.8\text{ Hz}$ , 3H);

$^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  (ppm) 170.7, 135.7, 133.9, 127.4, 121.1, 63.4, 51.7, 46.8, 27.8, 19.15, 19.1;

**HRMS** (ESI)  $m/z$  calculated for  $\text{C}_{11}\text{H}_{17}\text{NO}_4\text{SNa}$  282.0776 ( $\text{M}+\text{Na}$ ) $^+$ , found 282.0789.



**(S)-Methyl-2-(N-allylvinylsulfonamido)-3-methylbutanoate (24)**



$[\alpha]_D^{20}$   $-66.3$  (c 6.60,  $\text{CH}_2\text{Cl}_2$ ), colorless oil;

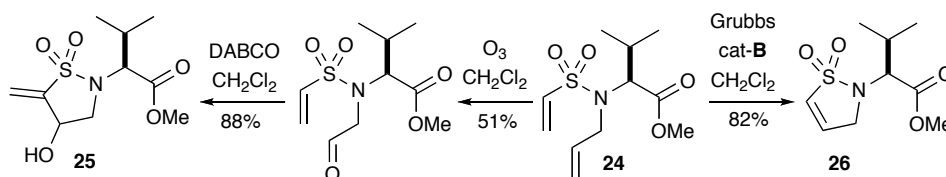
**FTIR** (neat): 2966, 1740, 1342, 1157, 1140  $\text{cm}^{-1}$ ;

**$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  (ppm) 6.42 (dd,  $J = 16.5, 9.9$  Hz, 1H), 6.15 (d,  $J = 16.5$  Hz, 1H), 5.87 (d,  $J = 9.9$  Hz, 1H), 5.80 (m, 1H), 5.17 (d,  $J = 17.1$  Hz, 1H), 5.09 (d,  $J = 10.1$  Hz, 1H), 3.97 (d,  $J = 10.6$  Hz, 1H), 3.91 (dd,  $J = 16.2, 7.7$  Hz, 1H), 3.75 (dd,  $J = 16.2, 5.4$  Hz, 1H), 3.68 (s, 3H), 2.15 (m, 1H), 0.98 (d,  $J = 6.7$  Hz, 3H), 0.90 (d,  $J = 6.7$  Hz, 3H);

**$^{13}\text{C-NMR}$**  ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  (ppm) 171.1, 135.4, 134.5, 126.5, 118.2, 65.5, 51.7, 47.5, 27.9, 19.5(2);

**HRMS** (ESI)  $m/z$  calculated for  $\text{C}_{11}\text{H}_{19}\text{NO}_4\text{SNa}$  284.0932( $\text{M}+\text{Na}$ ) $^+$ , found 320.0802.

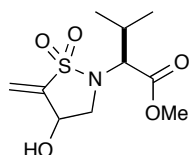
**Selective Oxidation/Baylis-Hillman and RCM Reactions of Vinyl Sulfonamide 24**



Ozone was bubbled through a solution of allyl vinyl sulfonamide **24** (120 mg, 0.46 mmol) and Sudan III indicator (trace amount) in  $\text{CH}_2\text{Cl}_2$  (20 mL) at  $-78$  °C. Once the color was changed from pink to dark brown, the addition of ozone was stopped. Dimethyl sulfide (31 mg, 0.5 mmol) was added drop wise, and the reaction mixture was slowly allowed to warm to rt. The solvent was removed under reduced pressure, and the crude product was purified by flash column chromatography (6:1 hexane/EtOAc) to generate the aldehyde vinyl sulfonamide (63 mg, 0.24 mmol) in 51% yield. DABCO (0.10 equiv.) was added to the solution of aldehyde vinyl sulfonamide (50 mg, 0.19 mmol) in  $\text{CH}_2\text{Cl}_2$  (3 mL), stirring was continued until TLC analysis indicated that the SM was totally consumed (normally 2 to 4 h), the solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (2:1 hexane/EtOAc) to produce sultam **25** (44 mg, 0.17 mmol) in 88% with dr = 1.2:1.

Vinyl sulfonamide **24** (150 mg, 0.57 mmol) was added into CH<sub>2</sub>Cl<sub>2</sub> (50 mL), the solution was degassed by argon gas for 5 minutes. Grubbs cat-**B** [10 mol%, (IMesH<sub>2</sub>)(PCy<sub>3</sub>)-(Cl)<sub>2</sub>Ru=CHPh] was added, the reaction temperature was increased to 55 °C and kept overnight. The reaction was cooled to rt, concentrated under reduced pressure and purified by flash column chromatography (6:1 hexane/EtOAc) to produce sultam **26** (109 mg, 0.47 mmol) in 82% yield.

**(S)-N-2-(3-Methylbutanoate)-4-hydroxy-5-methyleneisothiazolidine (25) (mixture of diastereoisomers, dr = 1.2:1)**



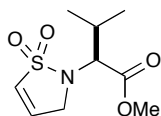
**FTIR:** 3468, 2966, 1740, 1298, 1203, 1145 cm<sup>-1</sup>, colorless oil;

**<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 400MHz): δ (ppm) 5.97(5.96) (s, 1H), 4.92(4.80) (m, 1H), 3.92(3.85) (dd, *J* = 25.6, 9.6 Hz, 3H), 3.74(3.72) (overlap, 4H), 3.53(3.28) (dd, *J* = 10.8, 5.2 Hz, 1H), 2.14 (m, 1H), 0.99(0.97) (d, *J* = 6.7 Hz, 6H);

**<sup>13</sup>C-NMR** (CDCl<sub>3</sub>, 100MHz): δ (ppm) 172.2(171.5), 148.0(147.8), 118.4(118.3), 66.4(66.5), 60.6(60.0), 52.3(52.1), 49.3, 28.8(28.7), 19.4(19.3), 19.2(19.1);

**HRMS** (ESI) *m/z* calculated for C<sub>10</sub>H<sub>17</sub>NO<sub>5</sub>SNa 286.0725 (M+Na)<sup>+</sup>, found 286.0662.

**N-2-(3-Methylbutanoate)-iso-thiazole-1,1-dioxide (26)**



[α]<sub>D</sub><sup>20</sup> -19.0 (c 1.93, CH<sub>2</sub>Cl<sub>2</sub>), colorless oil;

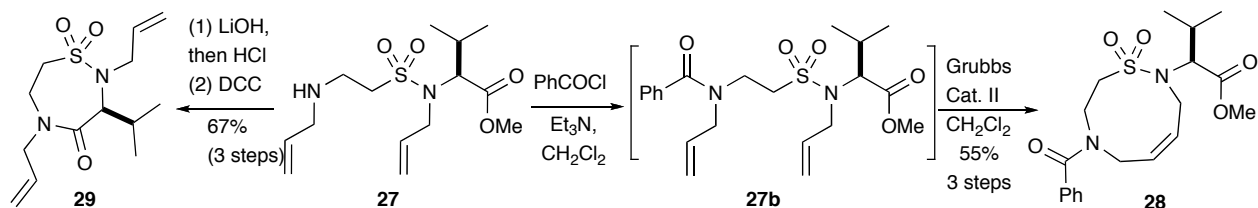
**FTIR** (neat): 2968, 1735, 1286, 1147, 707 cm<sup>-1</sup>;

**<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 400 MHz): δ (ppm) 6.89 (d, *J* = 6.8 Hz, 1H), 6.62 (ddd, *J* = 7.0, 2.3, 2.0 Hz, 1H), 4.67 (ddd, *J* = 16.9, 1.9, 1.9 Hz, 1H), 4.01 (ddd, *J* = 17.0, 2.1, 2.1 Hz, 1H), 3.75 (d, *J* = 10.0 Hz, 1H), 3.65 (s, 3H), 2.07 (m, 1H), 0.98 (d, *J* = 6.6 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H);

**<sup>13</sup>C-NMR** (CDCl<sub>3</sub>, 100 MHz): δ (ppm) 172.0, 136.0, 126.1, 59.5, 51.9, 47.9, 29.1, 19.6, 19.1;

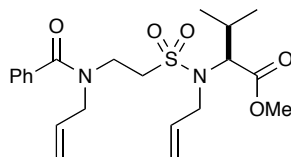
**HRMS** (ESI) *m/z* calculated for C<sub>9</sub>H<sub>15</sub>NO<sub>4</sub>SNa 256.0619 (M+Na)<sup>+</sup>, found 256.0467.

## An Amidation and RCM Sequence to Sultams **28** and **29**.



Vinyl sulfonamide **24** (100 mg, 0.38 mmol) and allyl amine (23 mg, 0.40 mmol) were dissolved into CH<sub>3</sub>OH (4 mL) and the mixture was refluxed overnight. The reaction mixture was cooled down to rt and concentrated under reduced pressure. CH<sub>2</sub>Cl<sub>2</sub> (5 mL) and Et<sub>3</sub>N (106 mL, 0.76 mmol) were added into the crude product, followed by the addition of benzoyl chloride (56.3 mg, 0.40 mmol). After stirring for 3 h, brine solution (1 mL) was added, the organic layer was separated, dried (MgSO<sub>4</sub>) and concentrated under reduced pressure. The crude product was purified by flash column chromatography (4:1 hexane/EtOAc) to produce an intermediate sulfonamide **27b** (131 mg, 0.31 mmol).

### (*S*)-Methyl-2-(*N*-allyl-2-(*N*-allylbenzamido)ethylsulfonamido)-3-methylbutanoate (**27b**).



$[\alpha]_D^{20}$  -45.2 (c 4.92, CH<sub>2</sub>Cl<sub>2</sub>), colorless oil;

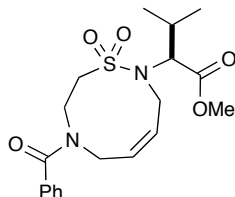
**FTIR** (neat): 2966, 1740, 1336, 1155, 1137, 702 cm<sup>-1</sup>;

**<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 400 MHz):  $\delta$  (ppm) 7.53-7.39 (m, 5H), 5.86 (m, 1H), 5.70 (m, 1H), 5.26 (d,  $J$  = 17.0 Hz, 1H), 5.24 (d,  $J$  = 9.7 Hz, 1H), 5.20 (d,  $J$  = 17.0 Hz, 1H), 5.18 (d,  $J$  = 9.7 Hz, 1H), 4.00 (m, 4H), 3.86 (m, 3H), 3.76 (s, 3H), 3.44 (s, 2H), 2.20 (m, 1H), 1.02 (d,  $J$  = 5.8 Hz, 3H), 0.95 (d,  $J$  = 6.4 Hz, 3H);

**<sup>13</sup>C-NMR** (CDCl<sub>3</sub>, 100 MHz):  $\delta$  (ppm) 172.2, 171.2, 135.8, 133.9, 133.1, 129.8, 128.4, 126.6(2), 119.2(2), 118.0, 65.4, 53.1, 52.1, 50.9, 47.4, 40.8, 27.7, 19.5, 19.3;

**HRMS** (ESI)  $m/z$  calculated for C<sub>21</sub>H<sub>30</sub>N<sub>2</sub>O<sub>5</sub>SNa 445.1773 (M+Na)<sup>+</sup>, found 445.1756.

**(S)-N-2-(iso-Propylmethyl methyl ester)-N-7-Benzoyl-1,2,7-thiaidazepine-1,1-dioxide (28) (a mixture of Z/E diastereoisomers)**



The amide sulfonamide **27b** (103.0 mg, 0.24 mmol) was added into 50 mL CH<sub>2</sub>Cl<sub>2</sub>, the solution was degassed for 5 minutes, and Grubbs cat-**B** [10 mol%, (IMesH<sub>2</sub>)(PCy<sub>3</sub>)-(Cl)<sub>2</sub>Ru=CHPh] was added. The reaction mixture was refluxed at 55 °C overnight, cooled to rt, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (4:1 hexane/EtOAc) to produce amide sultam **28** (64 mg, 0.16 mmol) in 55% yield over 3 steps as a 2:1 mixture of Z/E diastereomers.

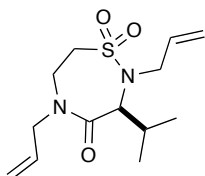
**FTIR** (neat): 2968, 1742, 1637, 1335, 1132, 709 cm<sup>-1</sup>, colorless oil;

**<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 400 MHz): δ (ppm) 7.38-7.35 (aromatic H, 5H), 6.0 (ddd, *J* = 9.2, 8.2, 8.2 Hz, 1H), 5.60(5.84) (ddd, *J* = 9.2, 7.9, 7.9 Hz, 1H), 4.36 (m, 2H), 4.09 (overlap, 2H), 3.90 (m, 1H), 3.70 (s, 3H), 3.69 (m, 3H), 3.39 (m, 1H), 2.32 (m, 1H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.94 (d, *J* = 6.4 Hz, 3H);

**<sup>13</sup>C-NMR** (CDCl<sub>3</sub>, 100 MHz): δ (ppm) 172.0, 171.3, 136.0, 133.0, 130.3, 129.8(2), 128.6(2), 126.6, 64.8, 53.3, 52.2, 47.0, 38.4, 37.9, 26.3, 19.6, 18.6;

**HRMS** (ESI) *m/z* calculated for C<sub>19</sub>H<sub>26</sub>N<sub>2</sub>O<sub>5</sub>SNa 417.1460 (M+Na)<sup>+</sup>, found 417.1419.

**(S)-N-2,5-Allyl-3-iso-propyl-5,1,2-thiadiazepine-1,1-dioxide (29)**



2*N* LiOH solution (5 mL) was added to the product **27** (105 mg, 0.33 mmol), stirring was kept until TLC showed the disappearance of starting material **27** (3 to 5 h), then acid (1*N* HCl) was added to neutralize the above solution until pH value was about 6 to 7. The solution was extracted by CH<sub>2</sub>Cl<sub>2</sub> (2x3 mL), dried (MgSO<sub>4</sub>) and filtered. DCC (2.0 equiv.) was added into the above filtrate, the mixture was stirred overnight, filtered and concentrated under reduced

pressure. The crude product was purified by flash chromatography (2:1 hexane/EtOAc) to afford 7-membered sultam **29** (70 mg, 0.25 mmol) in 67% yield over three steps.

$[\alpha]_D^{20}$  -22.8 (c 9.00, CH<sub>2</sub>Cl<sub>2</sub>), colorless oil;

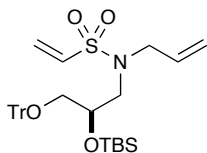
**FTIR** (neat): 2964, 1658.7, 1337, 1144, 933, 742 cm<sup>-1</sup>;

**<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 400 MHz): δ (ppm) 5.75 (m, 2H), 5.24 (overlap, 4H), 4.04 (m, 3H), 3.38 (d, *J* = 10.5 Hz, 1H), 3.63 (d, *J* = 16.6 Hz, 2H), 3.48 (dd, *J* = 16.7, 4.0 Hz, 1H), 3.15 (dd, *J* = 14.3, 5.2 Hz, 1H), 2.93 (dd, *J* = 12.5, 12.6 Hz, 1H), 2.30 (m, 1H), 1.00 (d, *J* = 6.7 Hz, 3H), 0.95 (d, *J* = 6.7 Hz, 3H);

**<sup>13</sup>C-NMR** (CDCl<sub>3</sub>, 100 MHz): δ (ppm) 170.3, 133.1, 132.4, 119.5, 119.1, 63.9, 50.8, 50.1, 47.5, 43.0, 26.3, 20.4, 19.1;

**HRMS** (ESI) *m/z* calculated for C<sub>13</sub>H<sub>22</sub>N<sub>2</sub>O<sub>3</sub>SNa 287.1429 (M+H)<sup>+</sup>, found 287.1435.

**(*R*)-*N*-(2-(*tert*-Butyldimethylsilyloxy)-3-(trityloxy)propyl)-*N*-allylethanesulfonamide (**30**)**



$[\alpha]_D^{20}$  -75.6 (c 0.78, CH<sub>2</sub>Cl<sub>2</sub>), colorless oil;

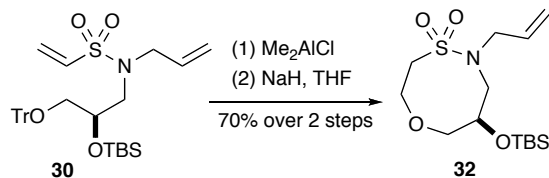
**FTIR** (neat): 2928, 1448, 1348, 1148, 776 cm<sup>-1</sup>;

**<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 400 MHz): δ (ppm) 7.50-7.25 (aromatic H, 15H), 6.33 (dd, *J* = 16.0, 6.0 Hz, 1H), 6.20 (d, *J* = 16.0 Hz, 1H), 5.88 (d, *J* = 16.0 Hz, 1H), 5.74 (m, 1H), 5.23 (d, *J* = 9.1 Hz, 1H), 5.20 (d, *J* = 10.5 Hz, 1H), 4.14 (m, 1H), 3.79 (d, *J* = 6.4 Hz, 2H), 3.42 (dd, *J* = 14.7, 5.7 Hz, 1H), 3.13 (m, 3H), 0.93 (s, 9H), 0.14 (s, 3H), 0.07 (s, 3H);

**<sup>13</sup>C-NMR** (CDCl<sub>3</sub>, 100 MHz): δ (ppm) 143.9, 135.4, 132.8, 128.7, 127.8(3), 127.1(6), 126.4(6), 119.5(3), 86.6, 71.5, 65.5, 51.8, 49.6, 25.9(3), 18.0, -4.7(2);

**HRMS** (ESI) *m/z* Calculated for C<sub>33</sub>H<sub>43</sub>NO<sub>4</sub>SiSNa 600.2580 (M+Na)<sup>+</sup>, found 600.2571.

### 6,1,2-Oxathiazepine-*N*-(allyl)-4-(*S*)-(tert-butyldimethylsilyloxy)-1,1-dioxide (**32**)



To a solution of vinyl sulfonamide **30** (98 mg, 0.17 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (4 mL) was added a small amount of Me<sub>2</sub>AlCl solution (1 M in CH<sub>2</sub>Cl<sub>2</sub>) at -10 °C. After the reaction was completed, water (1 mL) was added; the solution was extracted by CH<sub>2</sub>Cl<sub>2</sub> (2x2 mL), dried (MgSO<sub>4</sub>) and concentrated under reduced pressure. NaH (6.8 mg, 60% dispersion in mineral oil, 0.26 mmol) was added to a solution of crude vinyl sulfonamide alcohol in THF (3 mL), stirring was continued until TLC showed the SM disappeared, a small amount of water was added to remove residual NaH. The organic layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 x3 mL), the organic layers were combined, dried (MgSO<sub>4</sub>), concentrated under reduced pressure and purified by flash chromatography (10:1 hexane/EtOAc) to afford the 8-membered sultam **32** (40 mg, 0.12 mmol) in 70% yield.

[ $\alpha$ ]<sub>D</sub><sup>20</sup> -10.6 (c 0.50, CH<sub>2</sub>Cl<sub>2</sub>), colorless oil;

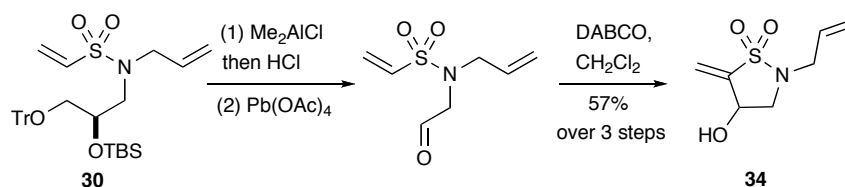
**FTIR** (neat): 2930, 1337, 1142, 1109, 837 cm<sup>-1</sup>;

**<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 400 MHz):  $\delta$  (ppm) 5.84 (m, 1H), 5.28 (dd, *J* = 13.2, 1.2 Hz, 1H), 5.26 (dd, *J* = 10.2, 1.0 Hz, 1H), 4.29 (ddd, *J* = 13.7, 5.4, 3.6 Hz, 1H), 4.08 (ddd, *J* = 15.0, 9.8, 4.8 Hz, 1H), 3.99 (dd, *J* = 15.1, 5.9 Hz, 1H), 3.85 (m, 2H), 3.65 (d, *J* = 4.9 Hz, 2H), 3.43 (dd, *J* = 15.0, 10.2 Hz, 1H), 3.32 (m, 3H), 0.91 (s, 9H), 0.08 (s, 6H);

**<sup>13</sup>C-NMR** (CDCl<sub>3</sub>, 100 MHz):  $\delta$  (ppm) 133.1, 118.9, 79.9, 64.3, 63.2, 55.5, 51.7, 45.5, 25.8(3), 18.3, -5.4(2);

**HRMS** (ESI) *m/z* calculated for C<sub>14</sub>H<sub>29</sub>NO<sub>4</sub>SSiNa 358.1484 (M+Na)<sup>+</sup>, found 358.1475.

***N*-Allyl-4-hydroxy-5-methylene-1,2-thiazine, tetrahydro-1,1-dioxide (34)**



To a solution of vinyl sulfonamide **30** (280 mg, 0.49 mmol) in  $\text{CH}_2\text{Cl}_2$  (5 mL) was added small amount of  $\text{Me}_2\text{AlCl}$ . After trityl deprotection was complete (as monitored by TLC), 20 mol% HCl solution was added to remove the TBS group. The solution was extracted with  $\text{CH}_2\text{Cl}_2$  (2x5 mL), dried ( $\text{Na}_2\text{SO}_4$ ), and partially concentrated to half volume.  $\text{Pb}(\text{OAc})_4$  (323 mg, 0.73 mmol) was added and once the reaction was complete (as monitored by TLC), the reaction mixture was concentrated under reduced pressure and purified by flash chromatography (4:1 hexane/EtOAc) to afford aldehyde vinyl sulfonamide (59 mg, 0.31 mmol) in 63% yield over 2 steps.

To the solution of aldehyde vinyl sulfonamide (50 mg, 0.26 mmol) in  $\text{CH}_2\text{Cl}_2$  (3 mL) was added DABCO (0.1 equiv.), after the reaction was over (as monitored by TLC), the reaction mixture was concentrated under reduced pressure and purified by flash chromatography (2:1 hexane/EtOAc) to afford sultam **34** (45 mg, 0.24 mmol) in 91% yield.

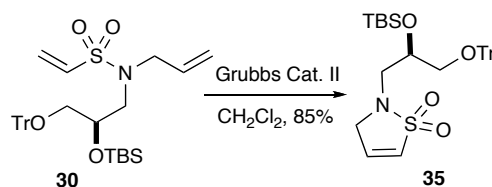
**FTIR** (neat): 3470, 2921, 1421, 1297, 1198, 1185, 935  $\text{cm}^{-1}$ , colorless oil;

**$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  (ppm) 6.24 (s, 1H), 6.00 (s, 1H), 5.87 (ddt,  $J = 17.0, 13.0, 7.0$  Hz, 1H), 5.33 (m, 2H), 4.86 (m, 1H), 3.71 (d,  $J = 6.8$  Hz, 2H), 3.48 (dd,  $J = 10.0, 6.0$  Hz, 1H), 3.10 (dd,  $J = 10.4, 4.8$  Hz, 1H);

**$^{13}\text{C-NMR}$**  ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  (ppm) 148.3, 131.6, 120.3, 119.1, 65.1, 52.7, 46.6;

**HRMS** (ESI)  $m/z$  calculated for  $\text{C}_7\text{H}_{11}\text{NO}_3\text{SNa}$  190.0538 ( $\text{M}+\text{H}$ )<sup>+</sup>, found 190.0538.

***(S)*-*N*-2-(2-(*tert*-Butyldimethylsilyloxy)-3-(trityloxy)propyl)-1,2-oxathiazepine-1,1-dioxide (35)**



Amide sulfonamide **30** (206 mg, 0.36 mmol) was added into CH<sub>2</sub>Cl<sub>2</sub> (50 mL) and the solution was degassed for 5 minutes. Grubbs cat-**B** [10 mol%, (IMesH<sub>2</sub>)(PCy<sub>3</sub>)-(Cl)<sub>2</sub>Ru=CHPh] (10 mol %) was added, the reaction mixture was refluxed at 55 °C overnight, cooled to rt, and concentrated under reduced pressure. The crude product was purified by flash chromatography (12:1 hexanes/EtOAc) to afford amide sultam **35** (168 mg, 0.31 mmol) in 85% yield.

[ $\alpha$ ]<sub>D</sub><sup>20</sup> 6.5 (c 8.28, CH<sub>2</sub>Cl<sub>2</sub>), colorless oil;

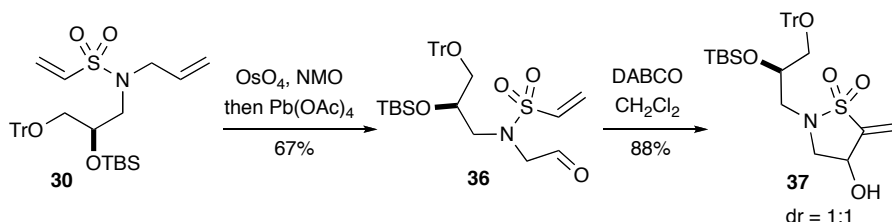
FTIR (neat): 2932, 1448, 1337, 1144, 700 cm<sup>-1</sup>;

<sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz):  $\delta$  (ppm) 7.53-7.25 (aromatic H, 15H), 6.74 (d, *J* = 6.8 Hz, 1H), 6.64 (d, *J* = 7.2 Hz, 1H), 4.01 (dd, *J* = 5.1, 4.7 Hz, 1H), 3.97 (s, 2H), 3.48 (m, 2H), 3.30 (dd, *J* = 9.0, 6.7 Hz, 1H), 3.16 (dd, *J* = 9.6, 4.2 Hz, 1H), 0.91 (s, 9H), 0.07 (s, 3H), 0.01 (s, 3H);

<sup>13</sup>C-NMR (CDCl<sub>3</sub>, 100 MHz):  $\delta$  (ppm) 143.9, 135.3, 128.8(3), 127.9(6), 127.1(6), 127.0(3), 86.8, 71.2, 65.0, 54.8, 47.7, 25.8(3), 18.0, -4.74, -4.88;

HRMS (ESI) *m/z* calculated for C<sub>31</sub>H<sub>39</sub>NO<sub>4</sub>SSiNa 572.2267 (M+Na)<sup>+</sup>, found 572.2254.

**(S)-N-(2-(tert-Butyldimethylsilyloxy)-3-(trityloxy)propyl)-4-hydroxy-5-methyleneethenesulfonamide (37) (a mixture of diastereoisomers dr = 1:1)**



A catalytic amount of OsO<sub>4</sub> (2% solution, 0.05 equiv.) was added to the solution of vinyl sulfonamide **30** (135 mg, 0.23 mmol) and NMO (0.35 mmol) in THF (5 mL). Stirring was continued until TLC indicated that the SM was totally consumed. The solution was washed with NaHSO<sub>3</sub> (2x3 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), and filtered. Pb(OAc)<sub>4</sub> (156 mg, 0.35 mmol) was added to the above filtrate solution at rt and stirring was continued for 4 h. After 4 hours, the reaction mixture was passed thru a SiO<sub>2</sub> SPE and the resulting filtrate was extracted with CH<sub>2</sub>Cl<sub>2</sub> (2x5 mL), washed with brine solution, dried (MgSO<sub>4</sub>) and concentrated under reduced pressure. The crude product was purified by flash chromatography (10:1 hexanes/EtOAc) to produce aldehyde sulfonamide **36** (89 mg, 0.15 mmol) in 67% yield over 2 steps.



DABCO (0.10 equiv.) was added to the solution of aldehyde vinyl sulfonamide **36** (50 mg, 0.09 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (3 mL), stirring was continued until TLC analysis indicated that the SM was totally consumed (normally about 4 h). The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (8:1 hexane/EtOAc) to afford sultam **37** (44 mg, 0.08 mmol) in 88% yield.

**FTIR** (neat): 3474, 2928, 1448, 1304, 1085, 835, 775 cm<sup>-1</sup>, colorless oil;

**<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 400 MHz): δ (ppm) 7.50-7.24 (aromatic H, 15H), 6.18 (d, *J* = 9.8 Hz, 1H), 5.94 (d, *J* = 12.6 Hz, 1H), 4.75(4.65)<sub>Minor</sub> (m, 1H), 3.99(3.94)<sub>Minor</sub> (m, 1H), 3.58(3.47)<sub>Minor</sub> (dd, *J* = 10.2, 7.0 Hz, 1H), 3.40-3.10 (m, 5H), 2.58(2.34)<sub>Minor</sub> (d, *J* = 8.1 Hz, 1H), 0.90(0.89)<sub>Minor</sub> (s, 9H), 0.06 (s, 3H), -0.01 (s, 3H);

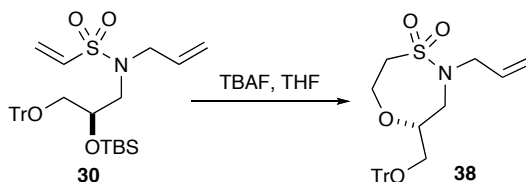
**<sup>13</sup>C-NMR** (CDCl<sub>3</sub>, 100 MHz): δ (ppm)

**Major** 147.9, 143.8, 128.7[3], 127.9[6], 127.1[6], 118.3[3], 86.7, 70.6, 65.4, 64.7, 55.5, 47.1, 25.8[3], 18.0, -4.75[2];

**Minor** 147.8, 143.8, 128.7[3], 127.9[6], 127.1[6], 118.9[3], 86.7, 70.7, 65.4, 64.7, 55.0, 47.1, 25.8[3], 18.0, -4.75[2];

**HRMS** (ESI) *m/z* calculated for C<sub>32</sub>H<sub>41</sub>NO<sub>5</sub>SiSNa 602.2372 (M+Na)<sup>+</sup>, found 602.2411.

### *N*-Allyl-4-trityloxymethyl-5,1,2-oxathiazepine-1,1-dioxide (**38**)



TBAF (0.5 mL) in THF (1.0 M in THF) was added to the stirred solution of vinyl sulfonamide **30** (70 mg, 0.12 mmol) in THF (2 mL). Stirring was continued for 2 h at rt, NH<sub>4</sub>Cl (1 mL, sat'd) was added and the organic layer was extracted by CH<sub>2</sub>Cl<sub>2</sub> (2x2 mL) and dried (MgSO<sub>4</sub>). The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (16:1 Hexane/EtOAc) to yield sultam **38** (50 mg, 0.11 mmol) in 90% yield.

[α]<sub>D</sub><sup>20</sup> 3.6 (c 5.60, CH<sub>2</sub>Cl<sub>2</sub>), colorless oil;

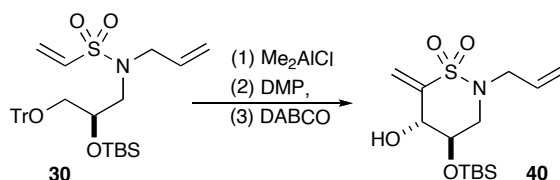
**FTIR** (neat): 2927, 1294, 1151, 706 cm<sup>-1</sup>;

**<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 400 MHz): δ (ppm) 7.40-7.26 (m, 15H), 5.82 (dddd, *J* = 16.1, 10.8, 6 and 6 Hz, 1H), 5.29 (d, *J* = 16.0 Hz, 1H), 5.26 (d, *J* = 9.6 Hz, 1H), 4.26 (m, 2H), 4.00 (dd, *J* = 15.1, 5.6 Hz, 1H), 3.91-3.82 (m, 2H), 3.43-3.24 (overlap, 5H), 3.10 (dd, *J* = 10.0, 3.4 Hz, 1H);

**<sup>13</sup>C-NMR** (CDCl<sub>3</sub>, 100 MHz): δ (ppm) 143.6, 133.0, 128.7(3), 128.0(6), 127.2(6), 119.1(3), 86.8, 78.7, 64.5, 62.9, 55.4, 51.6, 45.9;

**HRMS** (ESI) *m/z* calculated for C<sub>27</sub>H<sub>29</sub>NO<sub>4</sub>SNa 486.1715 (M+Na)<sup>+</sup>, found 486.1698.

***N*-(*iso*-Allyl)-4-(*S*)-(tert-butyldimethylsilyloxy)-5-(*R*)-hydroxy-6-methylene-1,2-thiazine, tetrahydro-1,1-dioxide (**40**)**



To a solution of **30** (82 mg, 0.14 mmol) in 3 mL CH<sub>2</sub>Cl<sub>2</sub> at -10 °C was added small amount of Me<sub>2</sub>AlCl (1 M in CH<sub>2</sub>Cl<sub>2</sub>), stirring was continued until TLC analysis indicated that trityl-deprotection was complete. A brine solution (2 mL) was added to the reaction mixture, which was next extracted with CH<sub>2</sub>Cl<sub>2</sub> (2x2 mL). The combined organic layers were dried (MgSO<sub>4</sub>) and concentrated under reduced pressure. To the crude mixture was added CH<sub>2</sub>Cl<sub>2</sub> (3 mL) and the Dess-Martin agent (115 mg, 0.27 mmol). After 4 hours, the reaction mixture was washed with NaHCO<sub>3</sub> (sat'd, aq.), and the organic layer was dried (MgSO<sub>4</sub>) and partially concentrated under reduced pressure to yield aldehyde vinyl sulfonamide. To the solution of aldehyde vinyl sulfonamide was added DABCO (0.10 equiv.). The reaction was monitored by TLC (normally 2 to 4 h). Upon completion, the solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (4:1 hexanes/EtOAc) to afford the 6-membered ring sultam **40** in 67% yield (32 mg, 0.09 mmol) over 3 steps (dr > 95:5).

[α]<sub>D</sub><sup>20</sup> -32.8 (c 0.35, CH<sub>2</sub>Cl<sub>2</sub>), colorless oil;

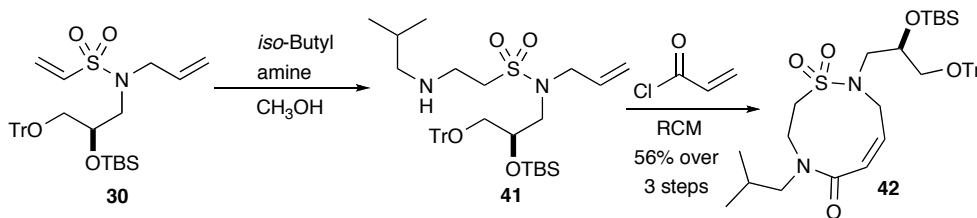
**FTIR** (neat): 3504, 2955, 1339, 1130, 1105, 838, 781 cm<sup>-1</sup>;

**<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 400 MHz): δ (ppm) 6.06 (d, *J* = 1.6 Hz, 1H), 5.91 (d, *J* = 1.8 Hz, 1H), 5.81 (m, 1H), 5.31 (overlap, 1H), 5.28 (overlap, 1H), 4.53 (m, 1H), 3.89 (dd, *J* = 14.6 5.8 Hz, 1H), 3.67 (m, 2H), 3.35 (m, 2H), 2.85 (d, *J* = 4.3 Hz, 1H), 0.91 (s, 9H), 0.13 (s, 3H), 0.00 (s, 3H);

**<sup>13</sup>C-NMR** (CDCl<sub>3</sub>, 100 MHz): δ (ppm) 143.7, 132.9, 119.5, 118.1, 74.7, 72.8, 51.4, 48.6, 25.7(3), 17.9, -4.6(2);

**HRMS** (ESI)  $m/z$  calculated for  $C_{14}H_{27}NO_4SSiNa$  356.1328 ( $M+Na$ )<sup>+</sup>, found 356.1324.

***N*-(2-*tert*-Butyldimethylsilyloxy)-3-(trityloxy)propan)sultam)ethyl)-*N*-isobutylacrylamide  
(42) (Mixture of diastereoisomers)**



To the solution of vinyl sulfonamide **30** (87 mg, 0.15 mmol) in methanol (2 mL) was added *iso*-butyl amine (11 mg, 0.15 mmol), the mixture was heated at 60 °C until starting material was consumed, then reaction mixture was cooled down and concentrated. 5 mL CH<sub>2</sub>Cl<sub>2</sub> was added into the pure product, followed by the addition of triethyl amine (42 mL, 0.30 mmol) and acryloyl chloride (15 mg, 0.16 mmol), after stirring for 3 h, 2 mL brine solution was added, and then the solution was extracted by CH<sub>2</sub>Cl<sub>2</sub> (2x3 mL), dried over MgSO<sub>4</sub>, concentrated and purified to give RCM reaction precursor (87 mg, 0.12 mmol). The purified precursor was dissolved in 50 mL CH<sub>2</sub>Cl<sub>2</sub>, and then the solution was degassed for 5 minutes, Grubbs catalyst II was added (10 mol%). The reaction mixture was refluxed at 55 °C overnight, then reaction was cooled down to rt, concentrated and purified by chromatography (6:1 hexanes:EtOAc) to give amide sultam **42** (57 mg, 0.08 mmol) in 56% yield over the whole process.

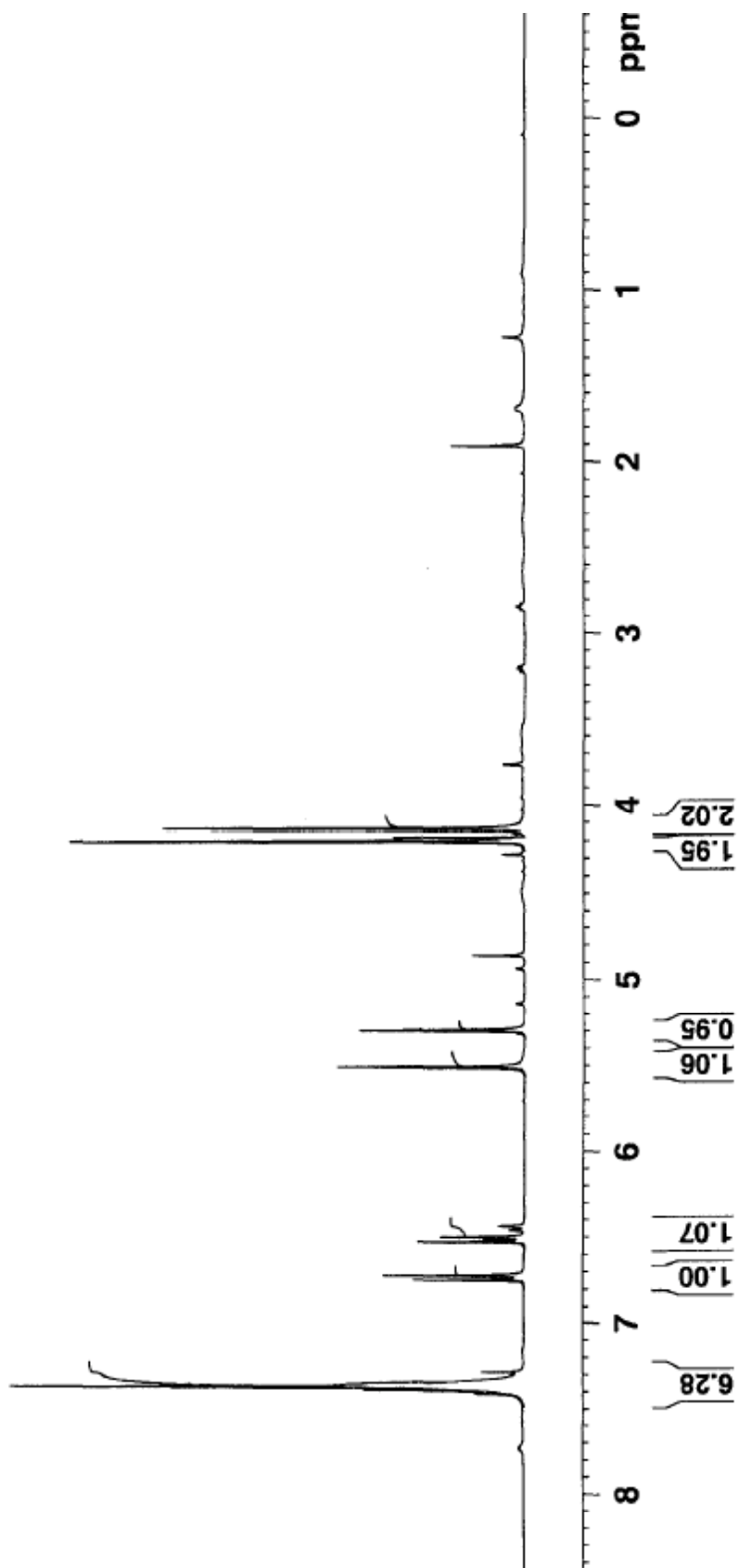
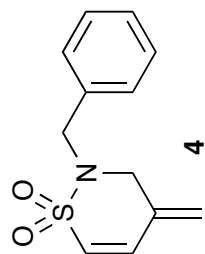
**FTIR** (neat): 2957, 1626, 1448, 1337, 1140, 733 cm<sup>-1</sup>, colorless oil;

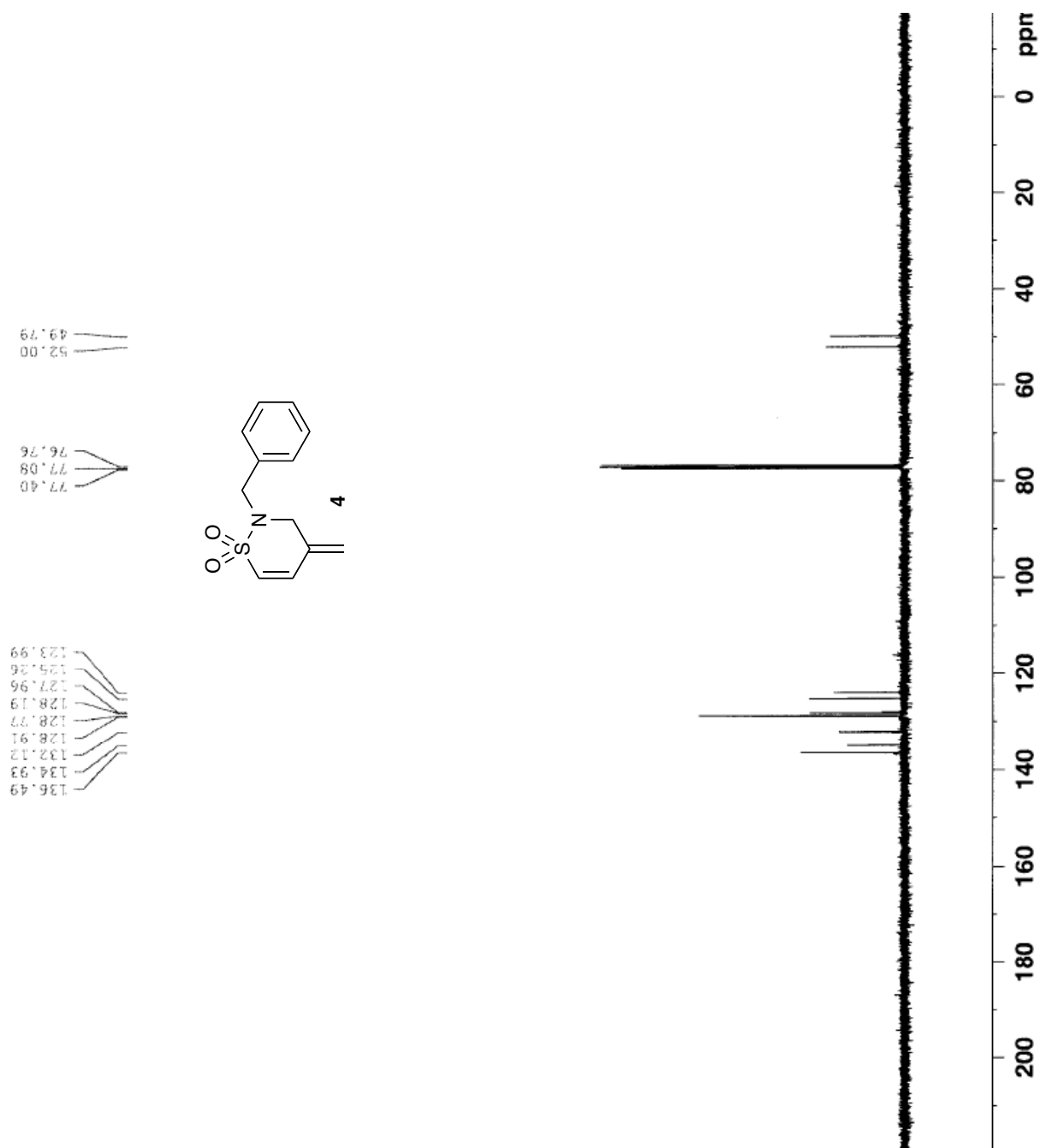
**<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 400 MHz): δ (ppm) 7.44-7.22 (aromatic H, 15H), 6.08 (d,  $J$  = 11.4 Hz, 1H), 5.88 (m, 1H), 4.28 (dd,  $J$  = 13.9, 13.6 Hz, 1H), 4.18 (m, 1H), 4.03-3.89 (overlap, 3H), 3.48 (dd,  $J$  = 14.0, 13.1 Hz, 2H), 3.36 (overlap, 1H), 3.05 (overlap, 4H), 2.52 (m, 1H), 2.00 (m, 1H), 0.89 (overlap, 15H), 0.07 (s, 3H), -0.14 (s, 3H);

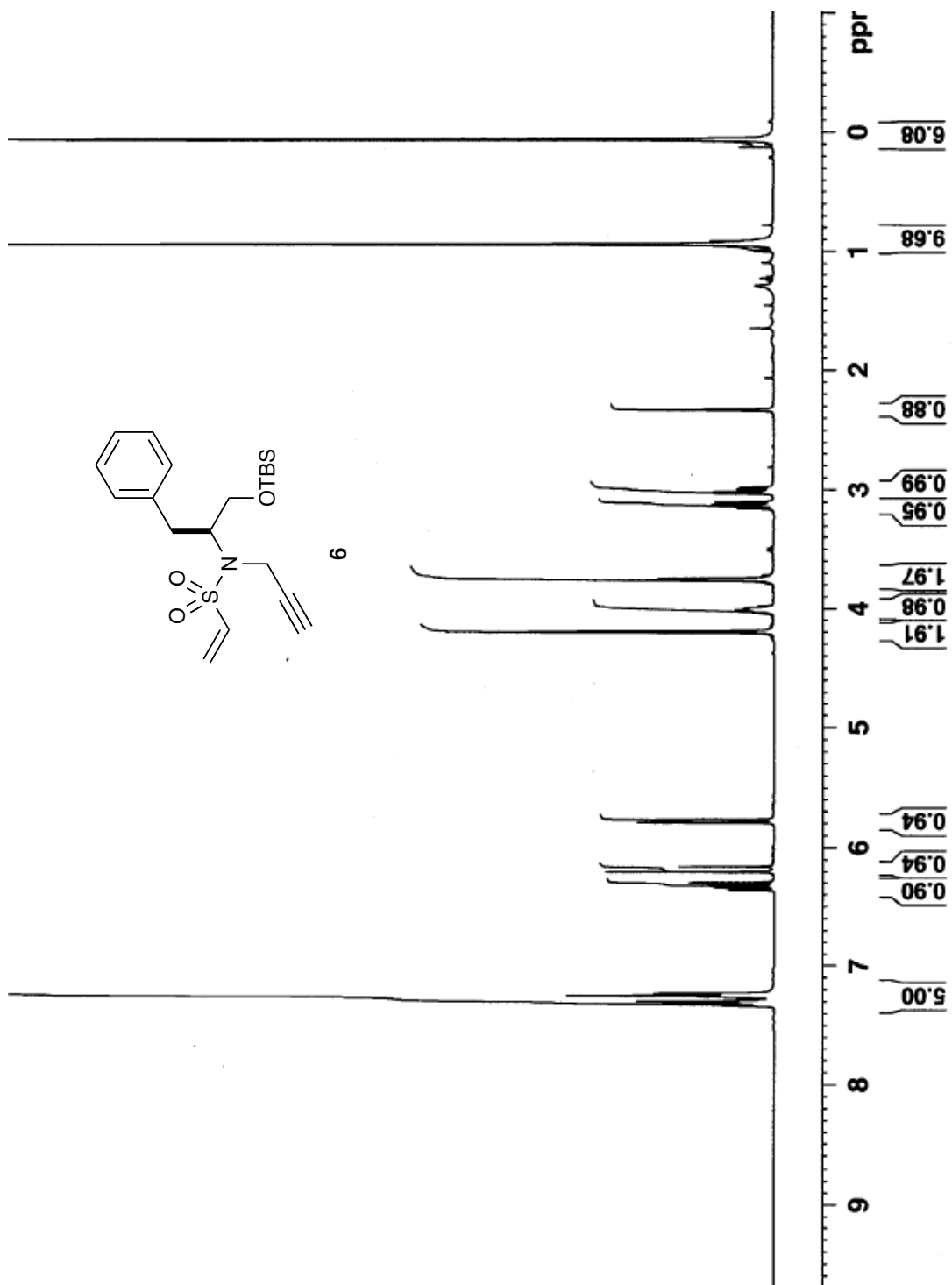
**<sup>13</sup>C-NMR** (CDCl<sub>3</sub>, 100 MHz): δ (ppm) 169.3, 143.8, 131.6, 128.6(3), 127.9(6), 127.1(6), 126.4(3), 86.6, 71.5, 65.5, 51.9, 49.2, 47.4, 45.5, 42.1, 25.9(3), 20.3, 19.8, 17.8, -4.74(2);

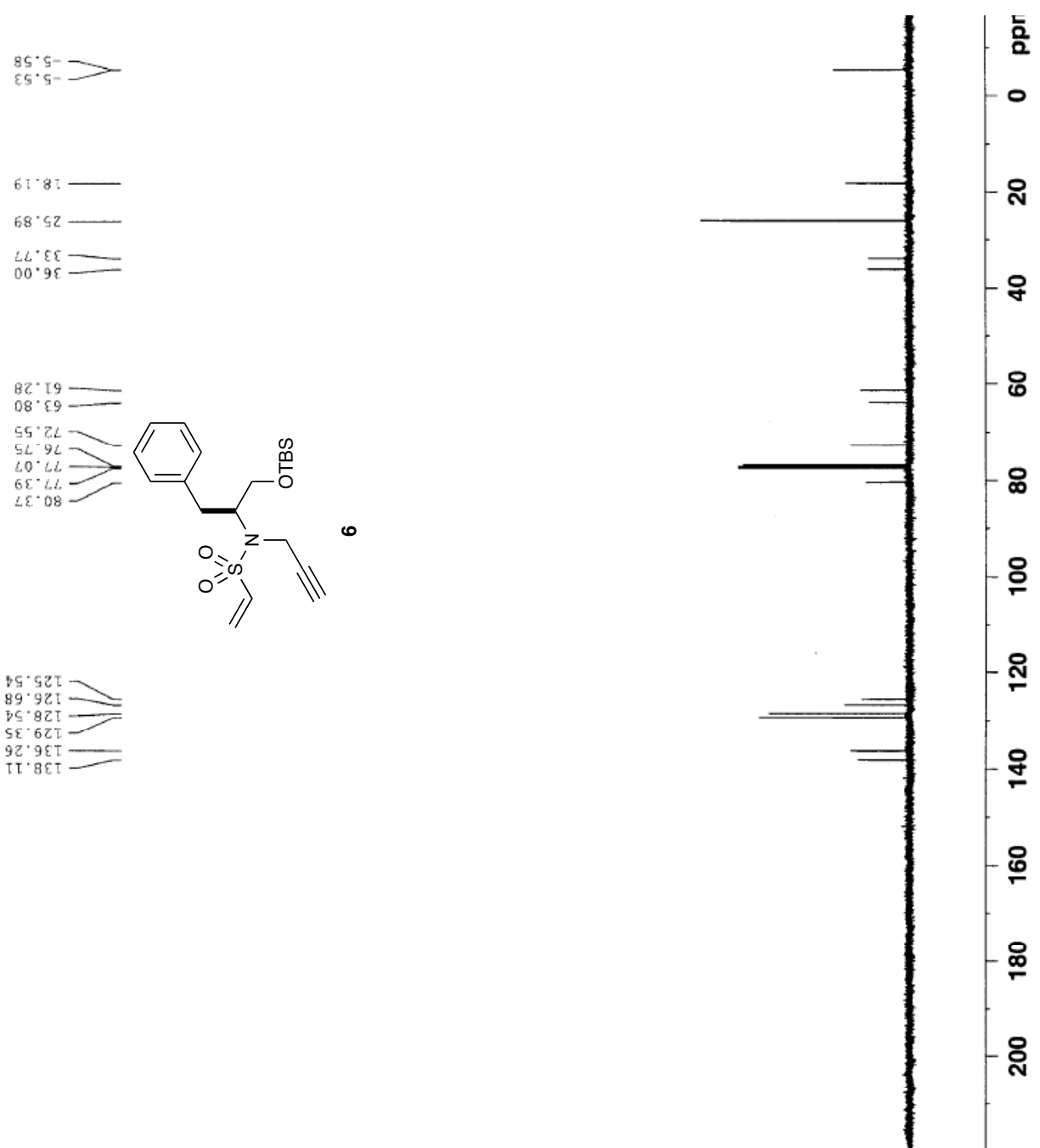
**HRMS** (ESI)  $m/z$  calculated for  $C_{38}H_{52}N_2O_5SiSNa$  699.3264 ( $M+Na$ )<sup>+</sup>, found 699.3252.

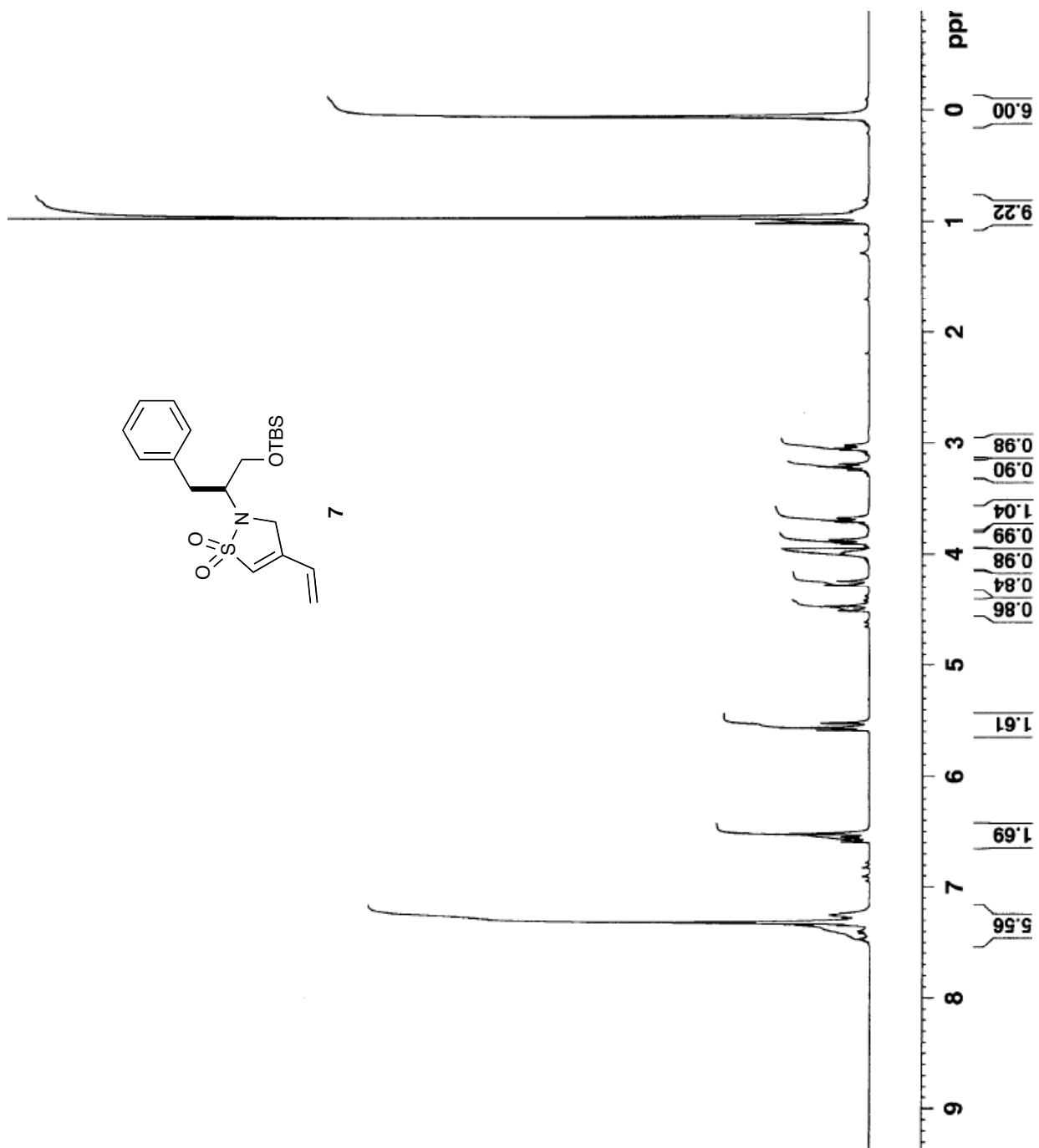
# $^1\text{H}$ , $^{13}\text{C}$ -NMR Spectra for New Compounds



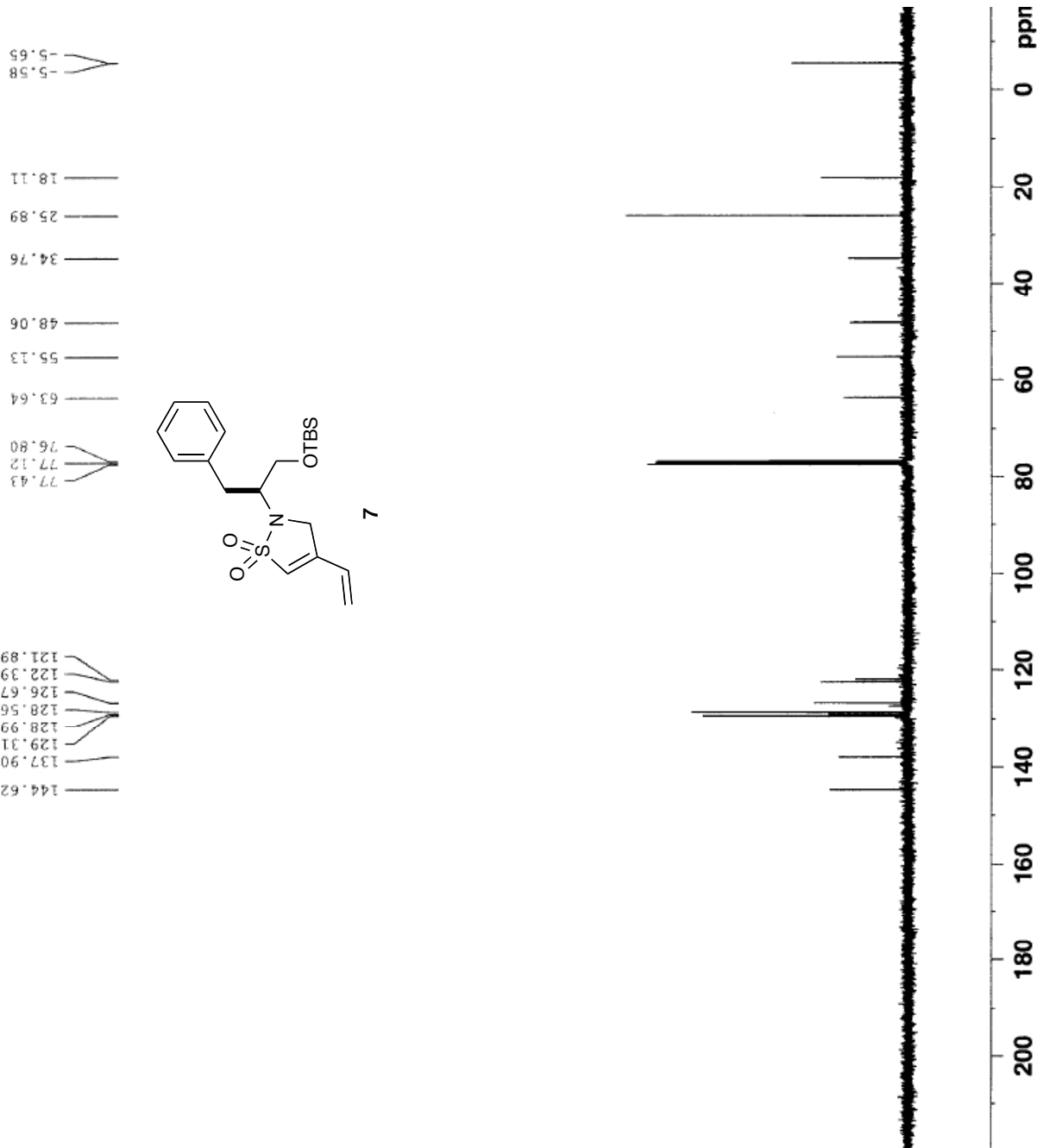


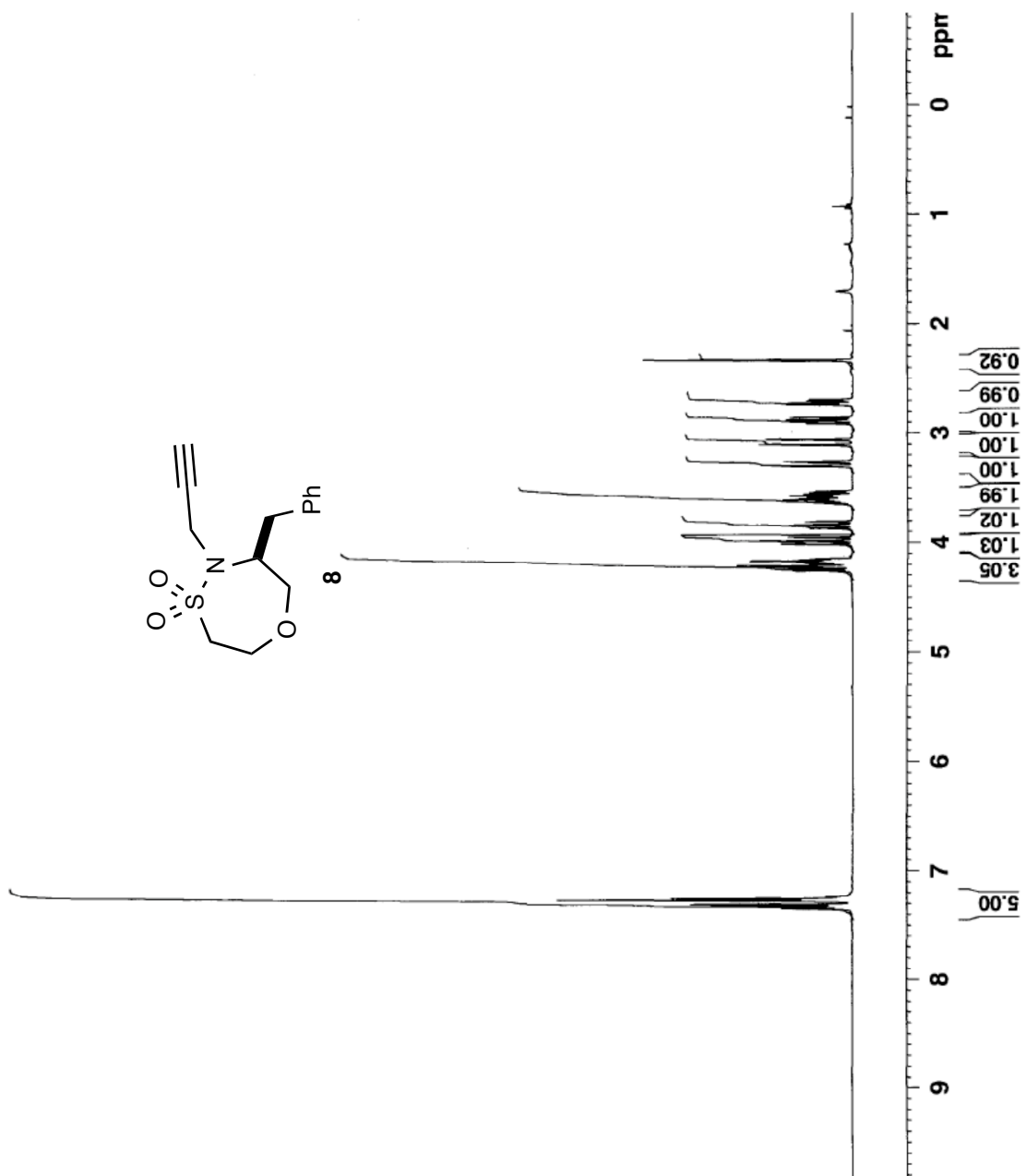


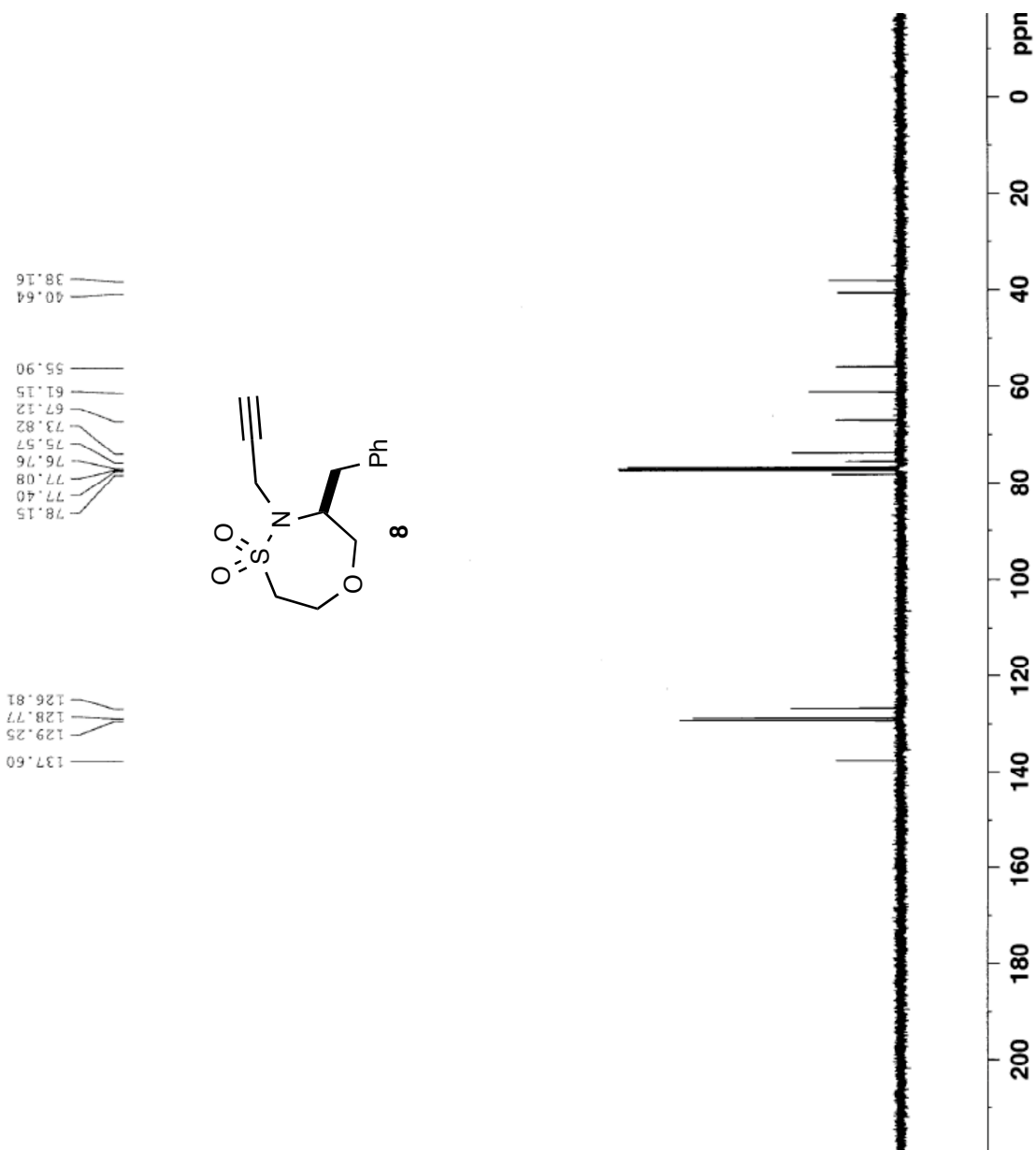


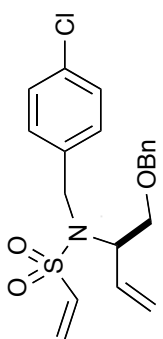




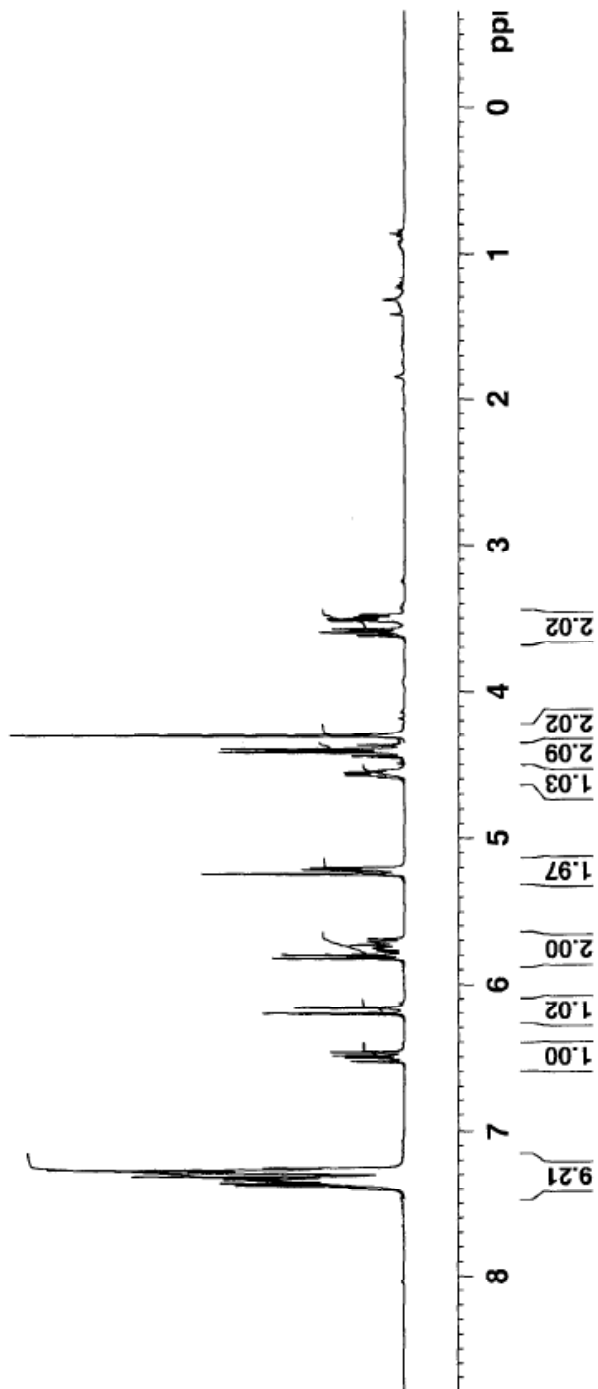


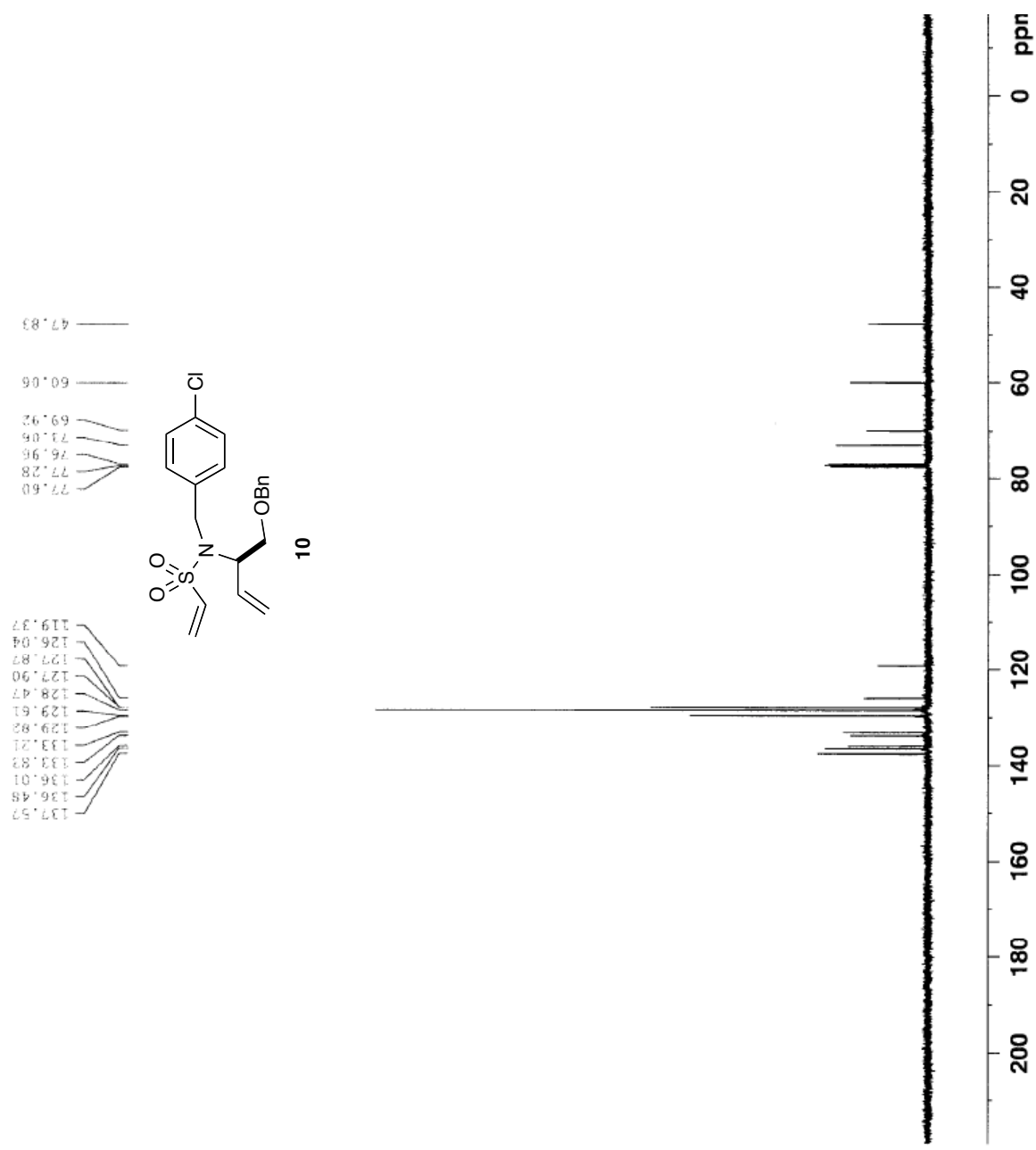


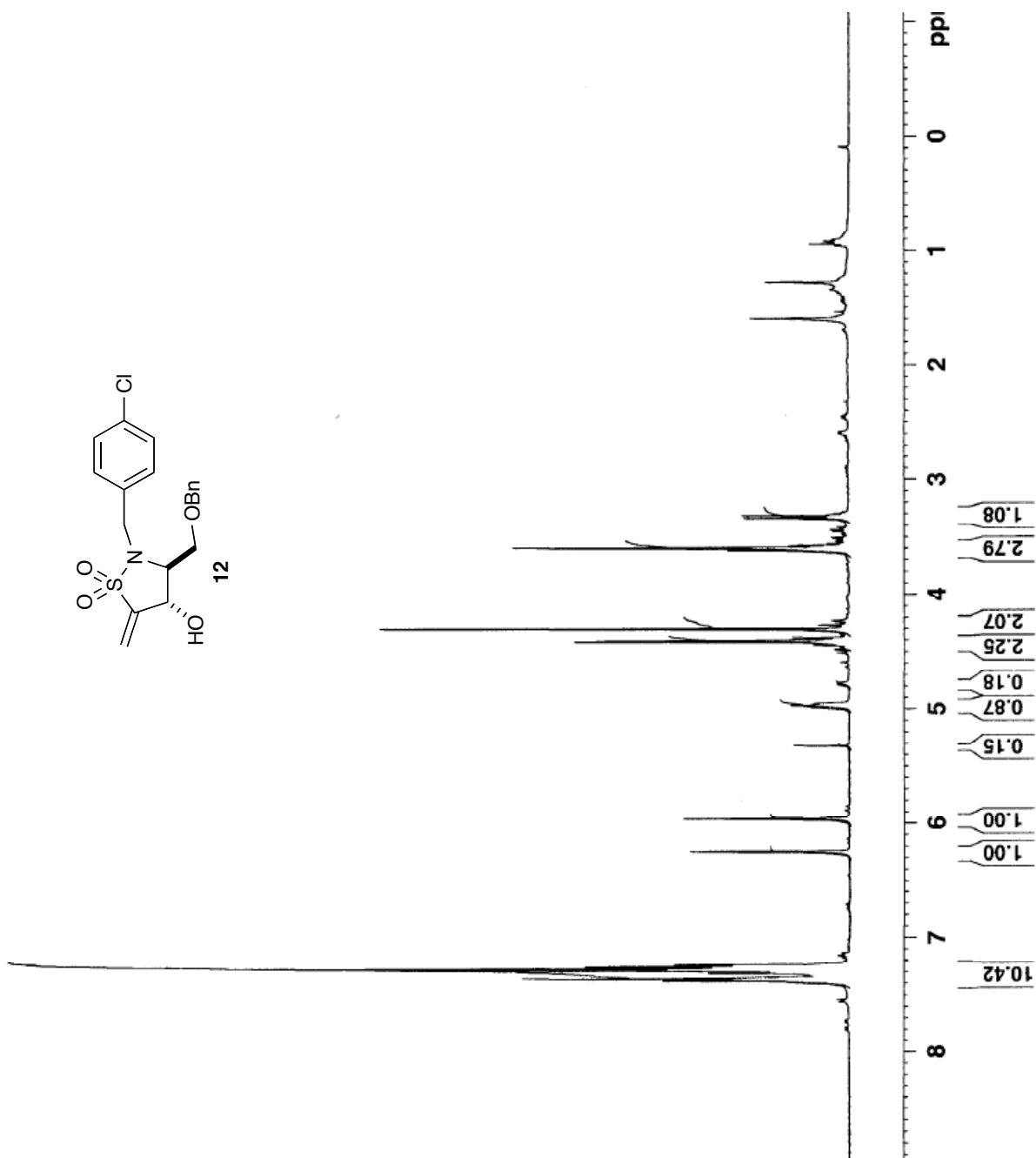


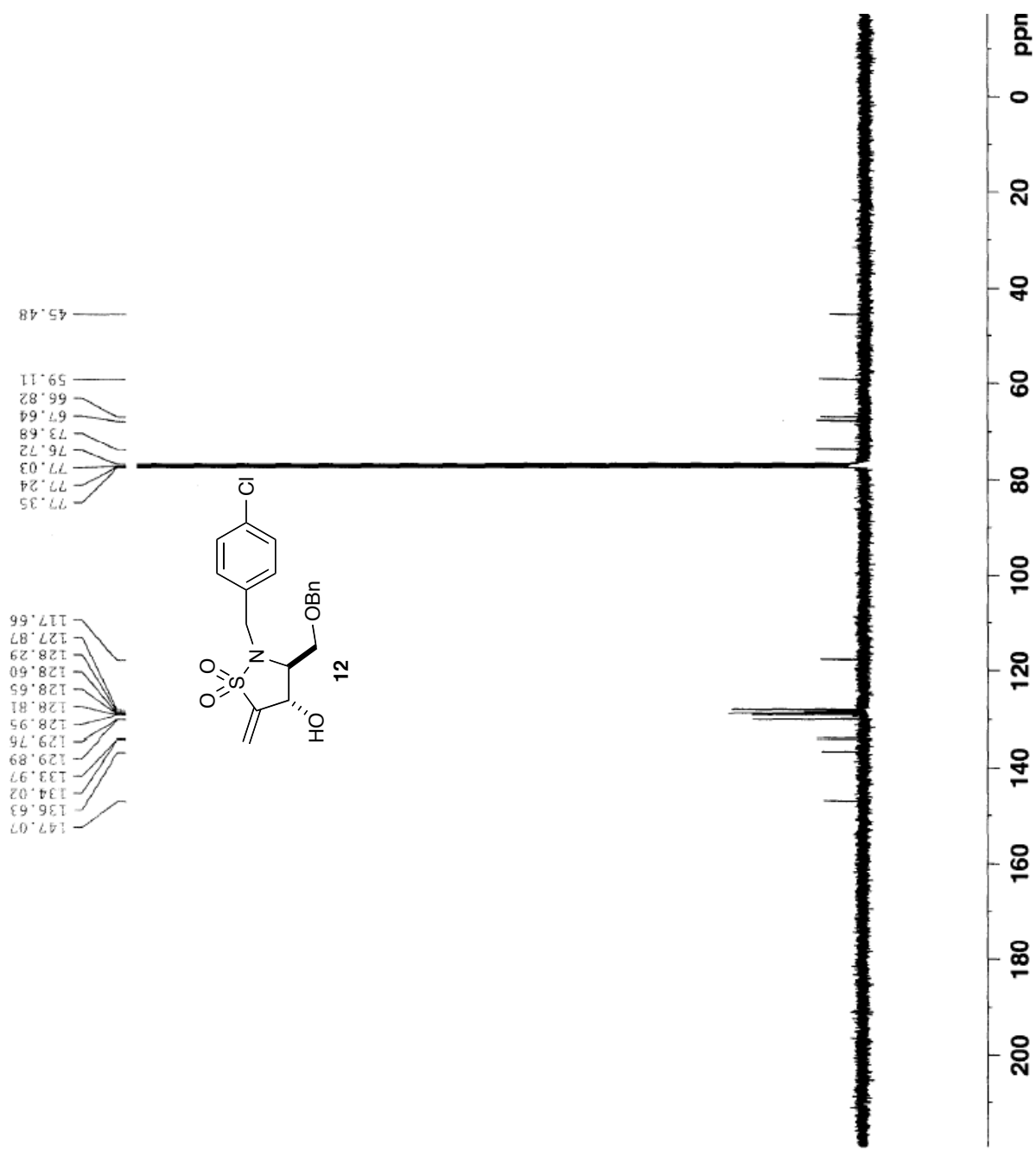


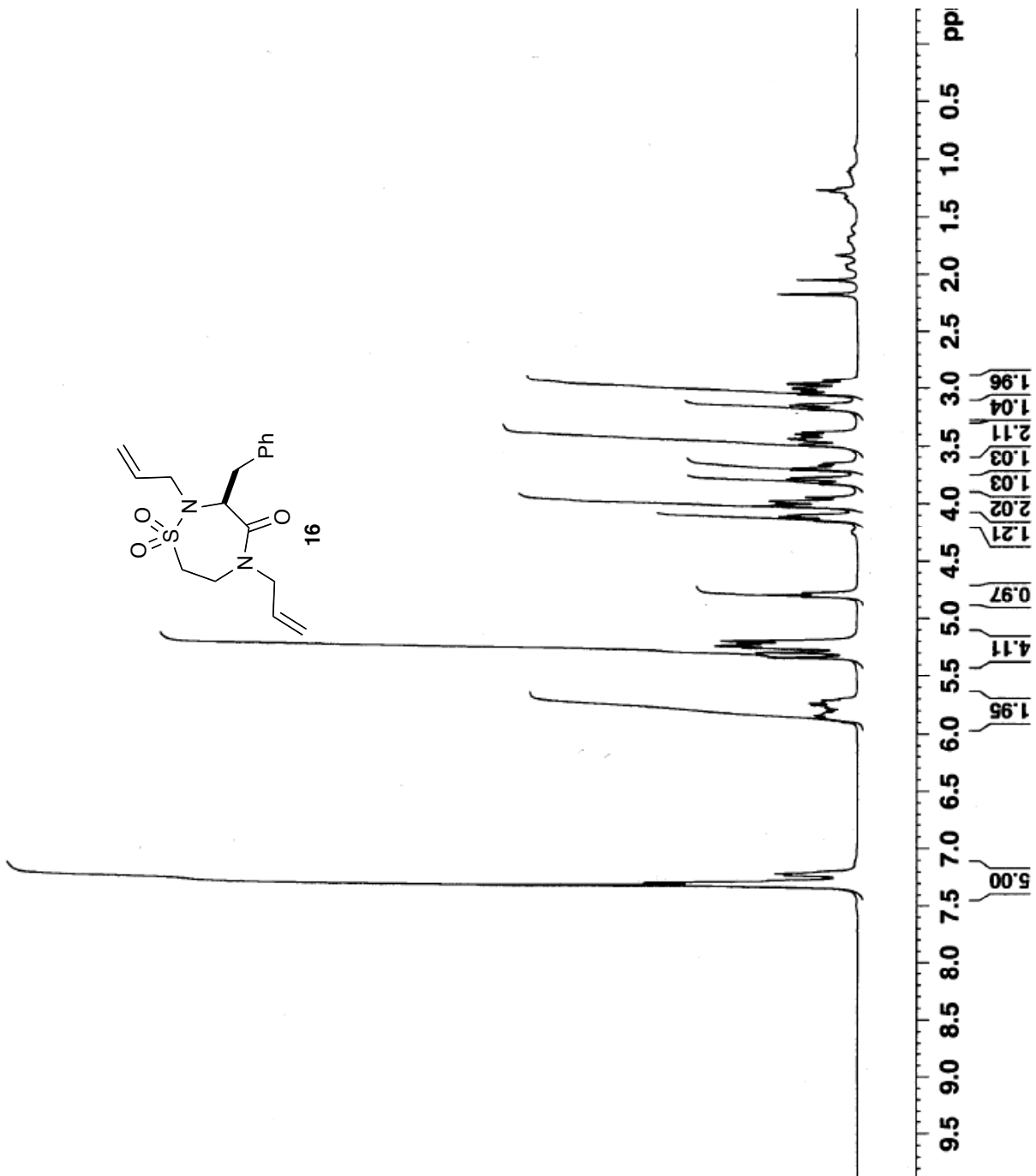
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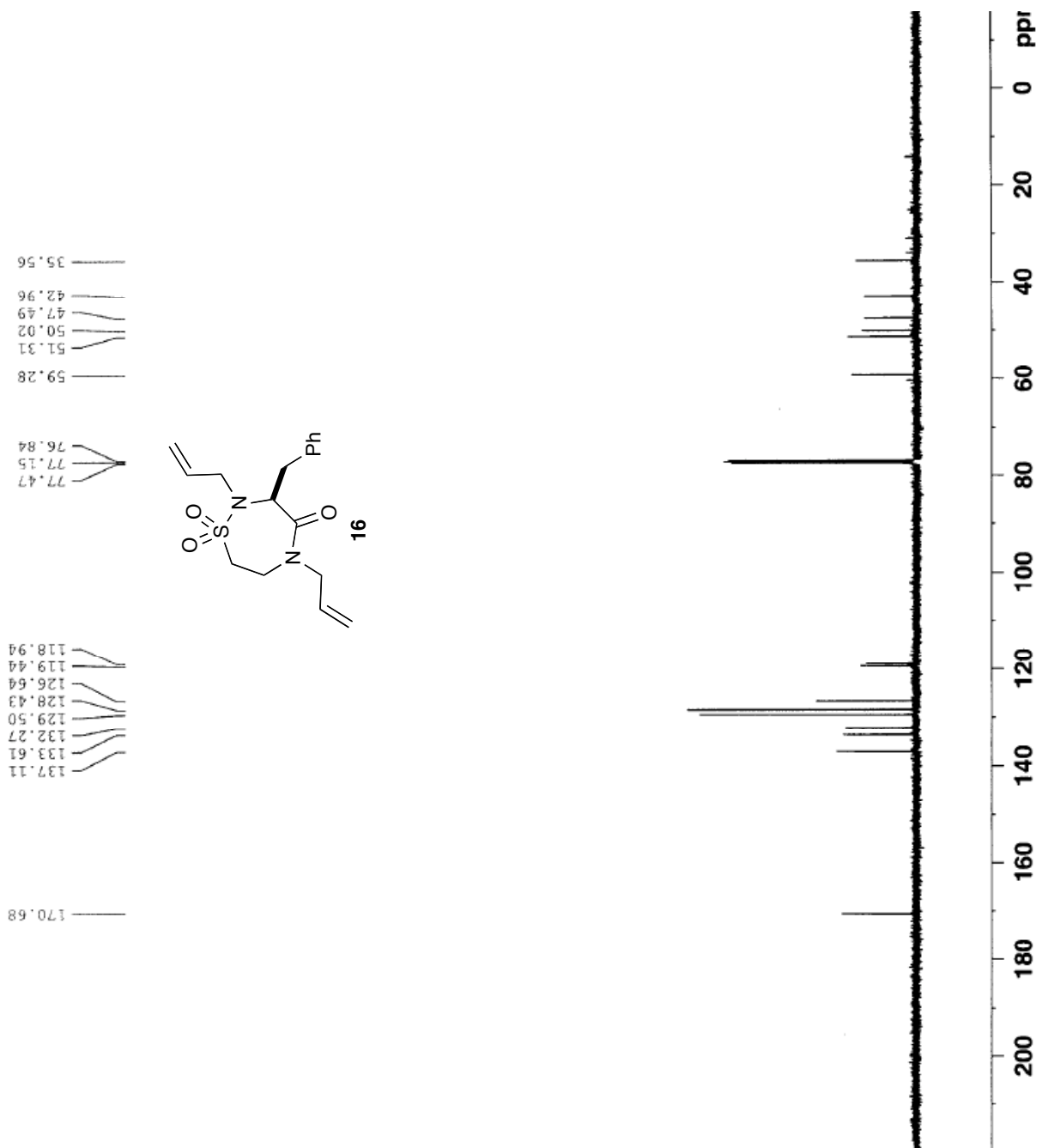


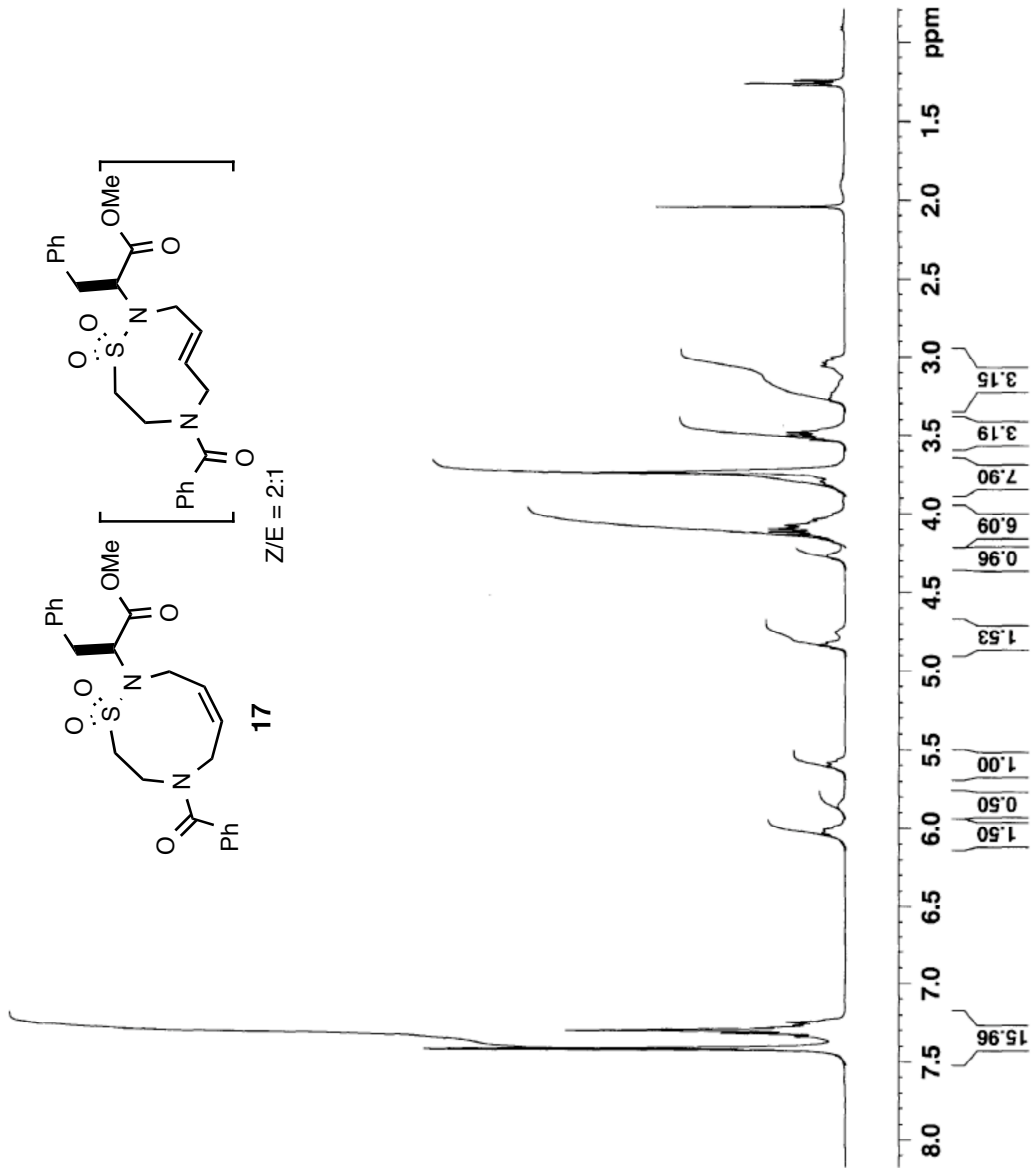


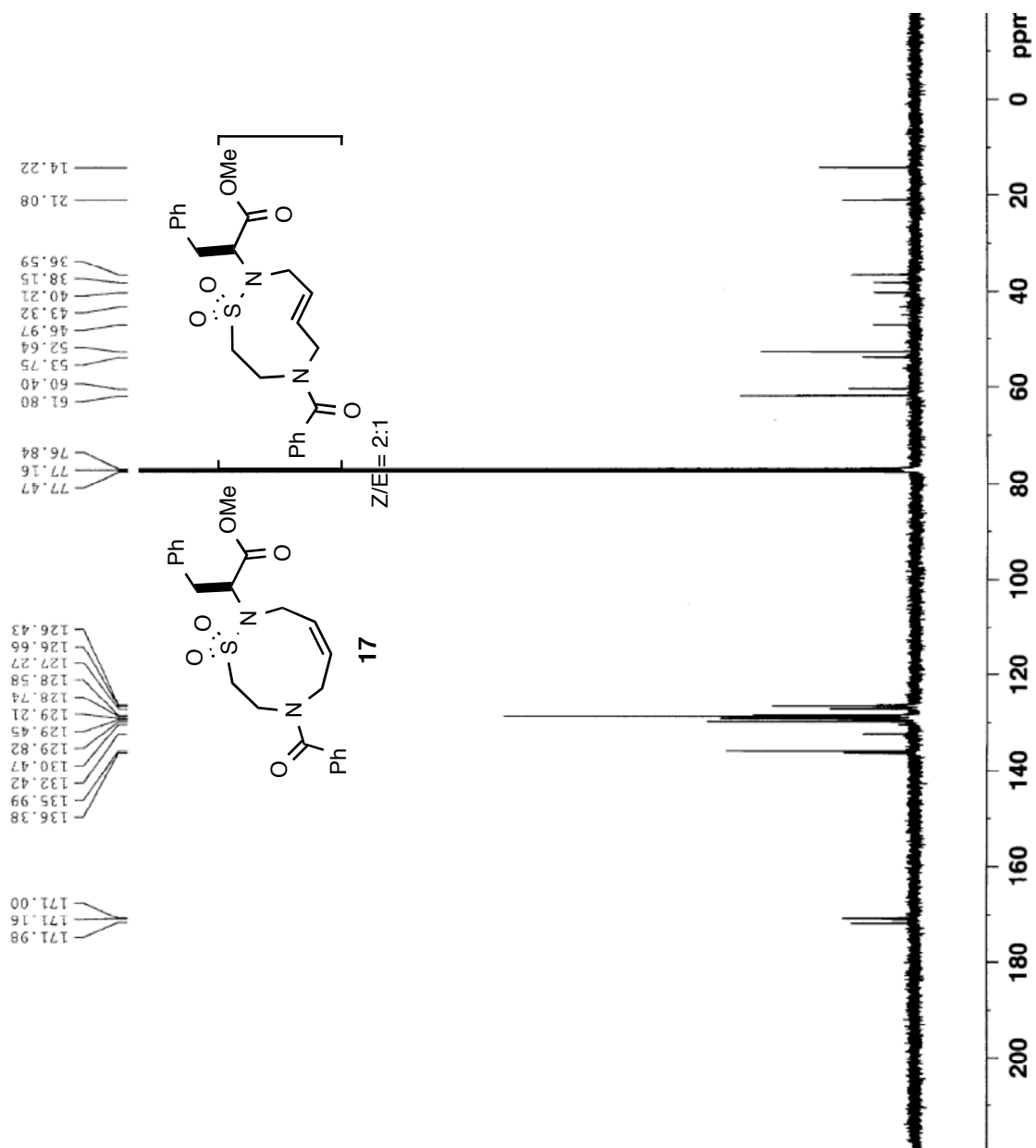


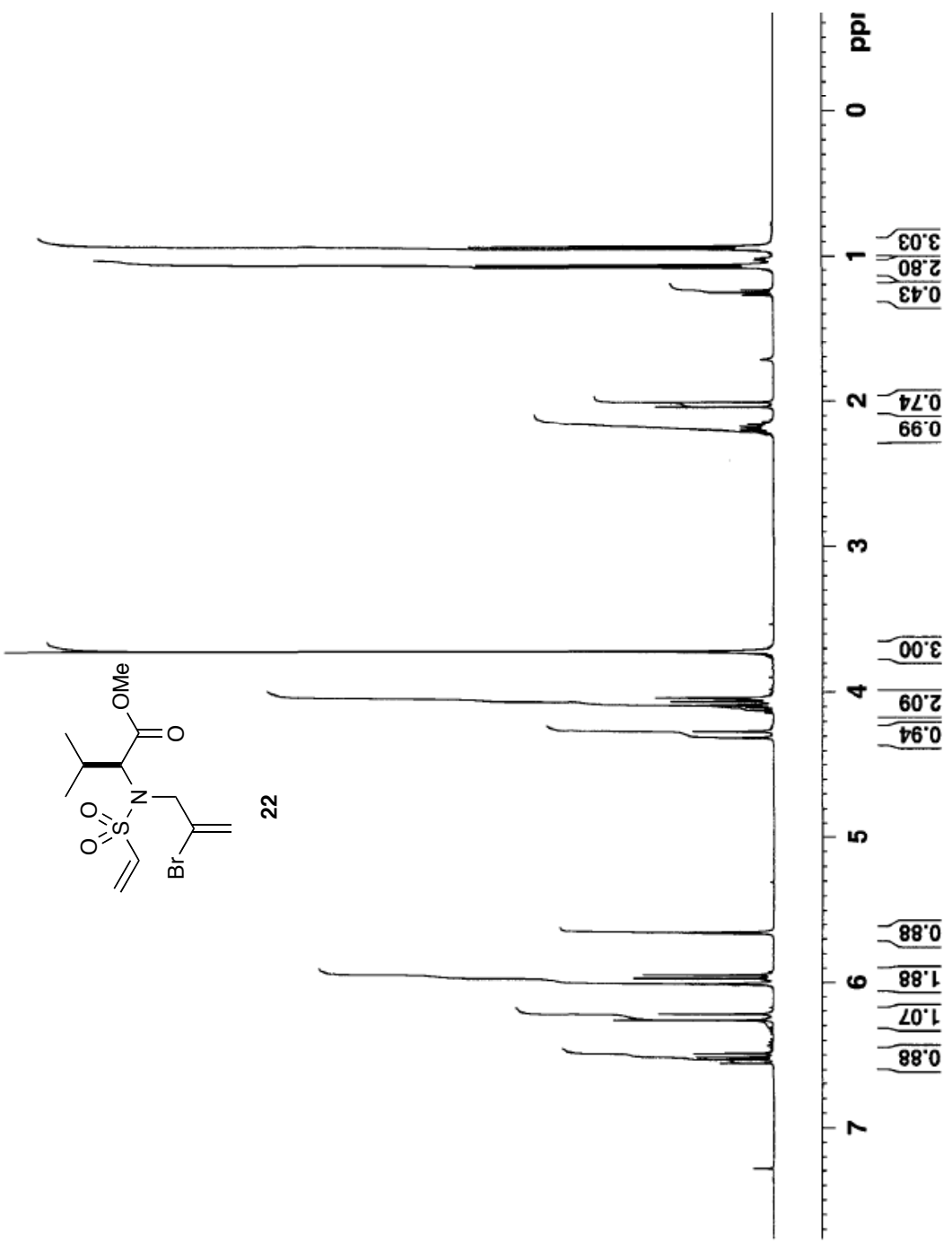


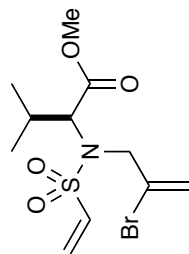
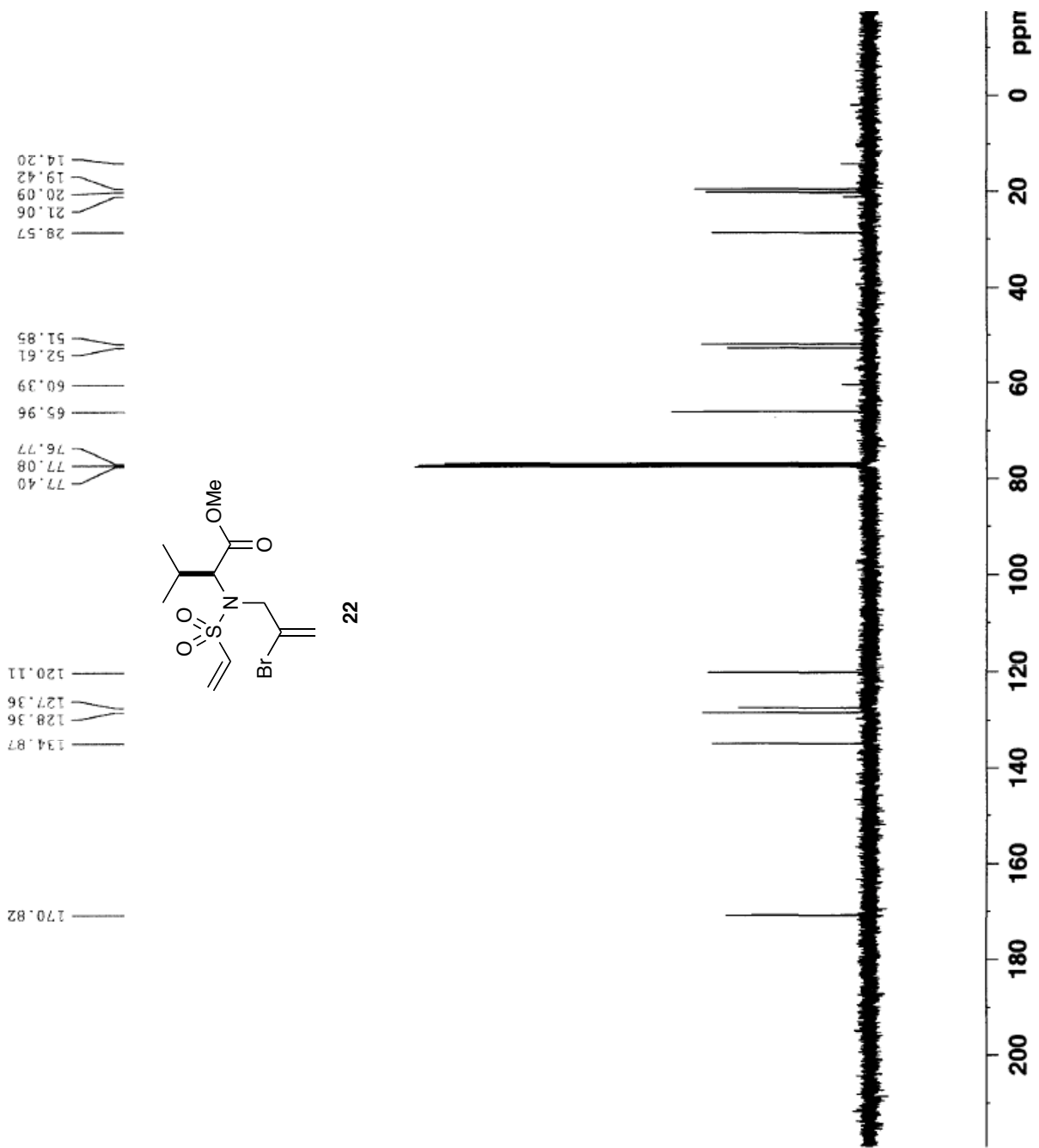




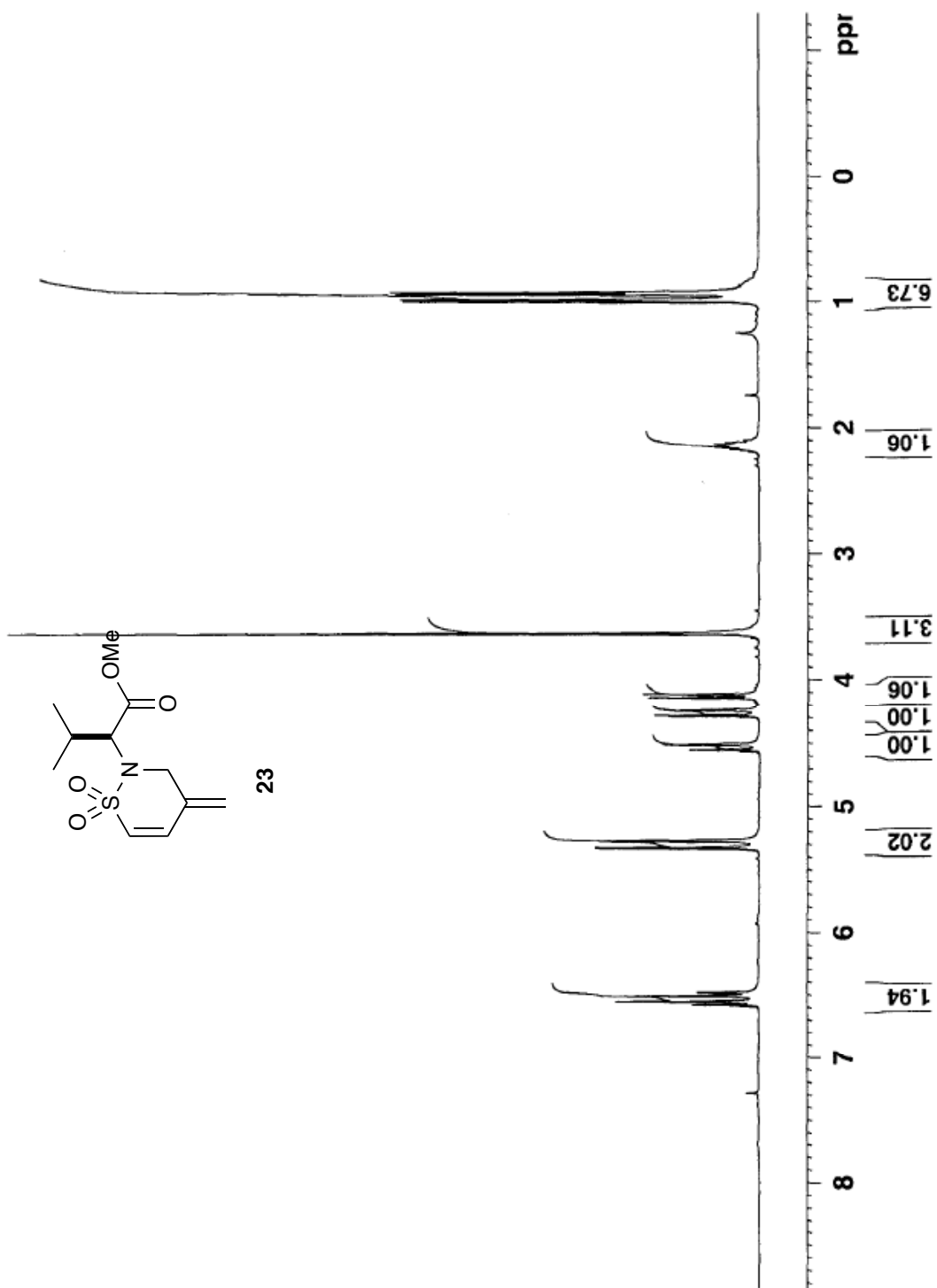


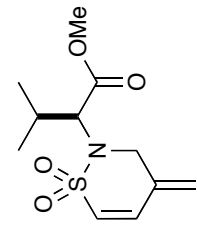
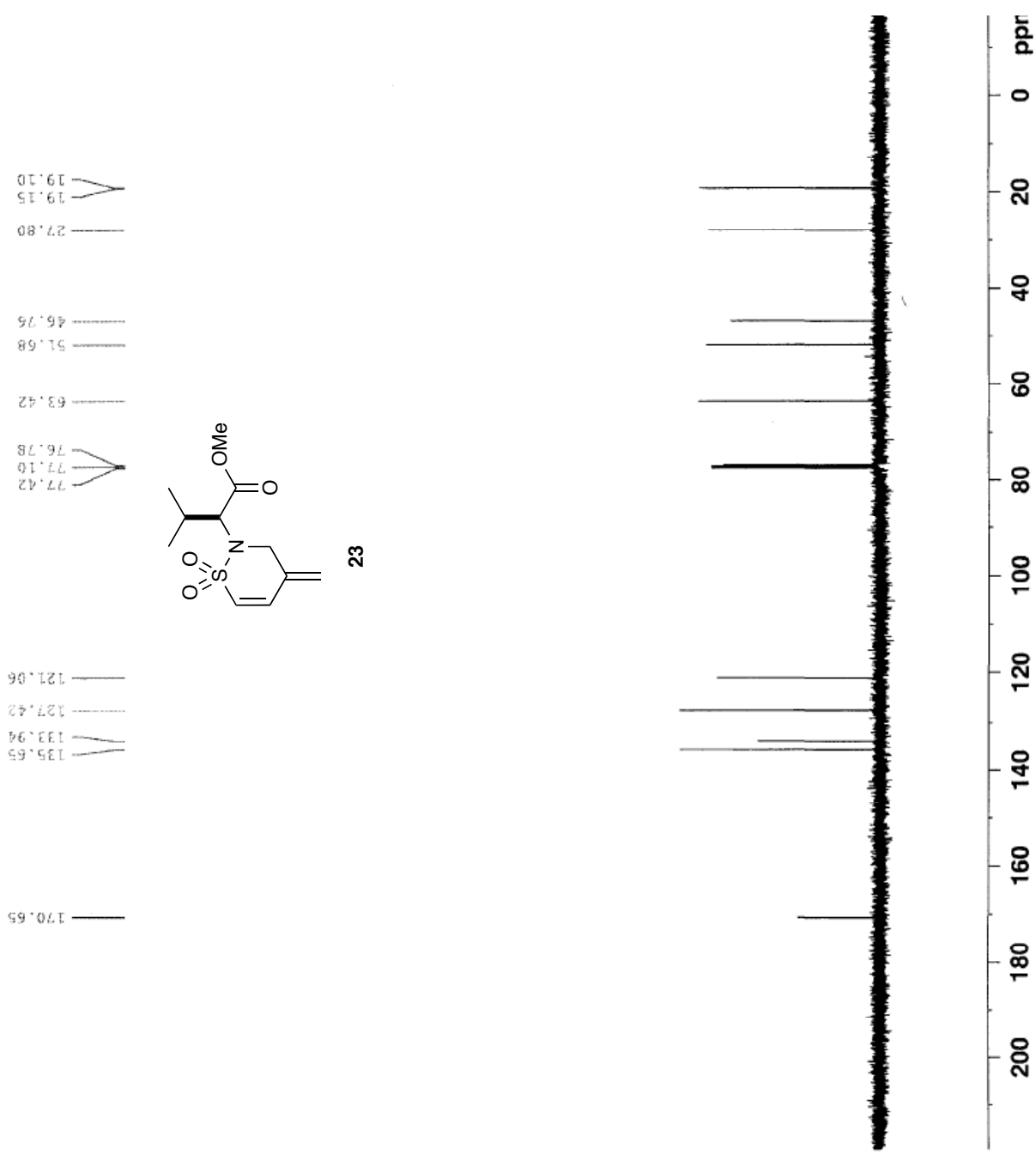




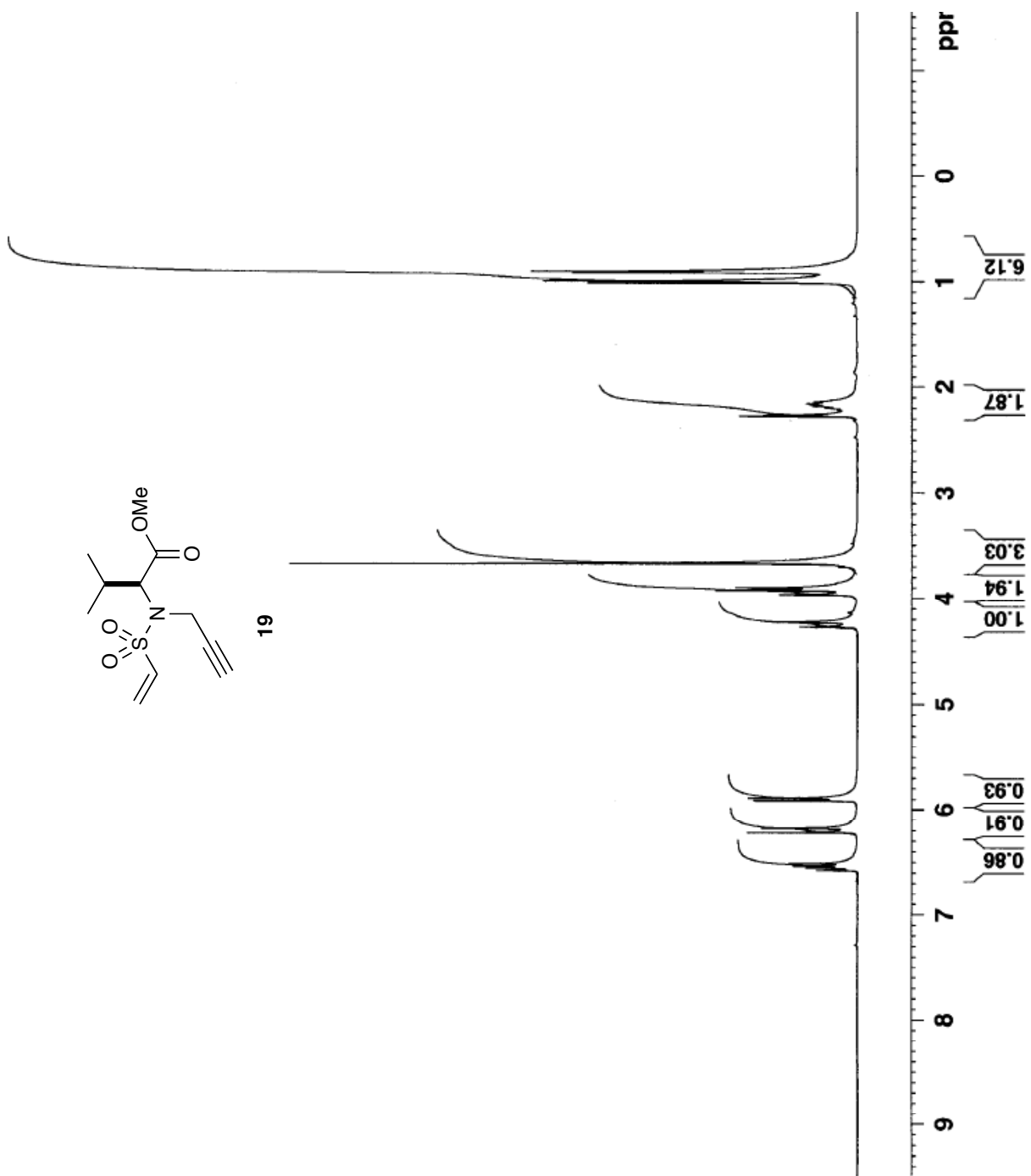


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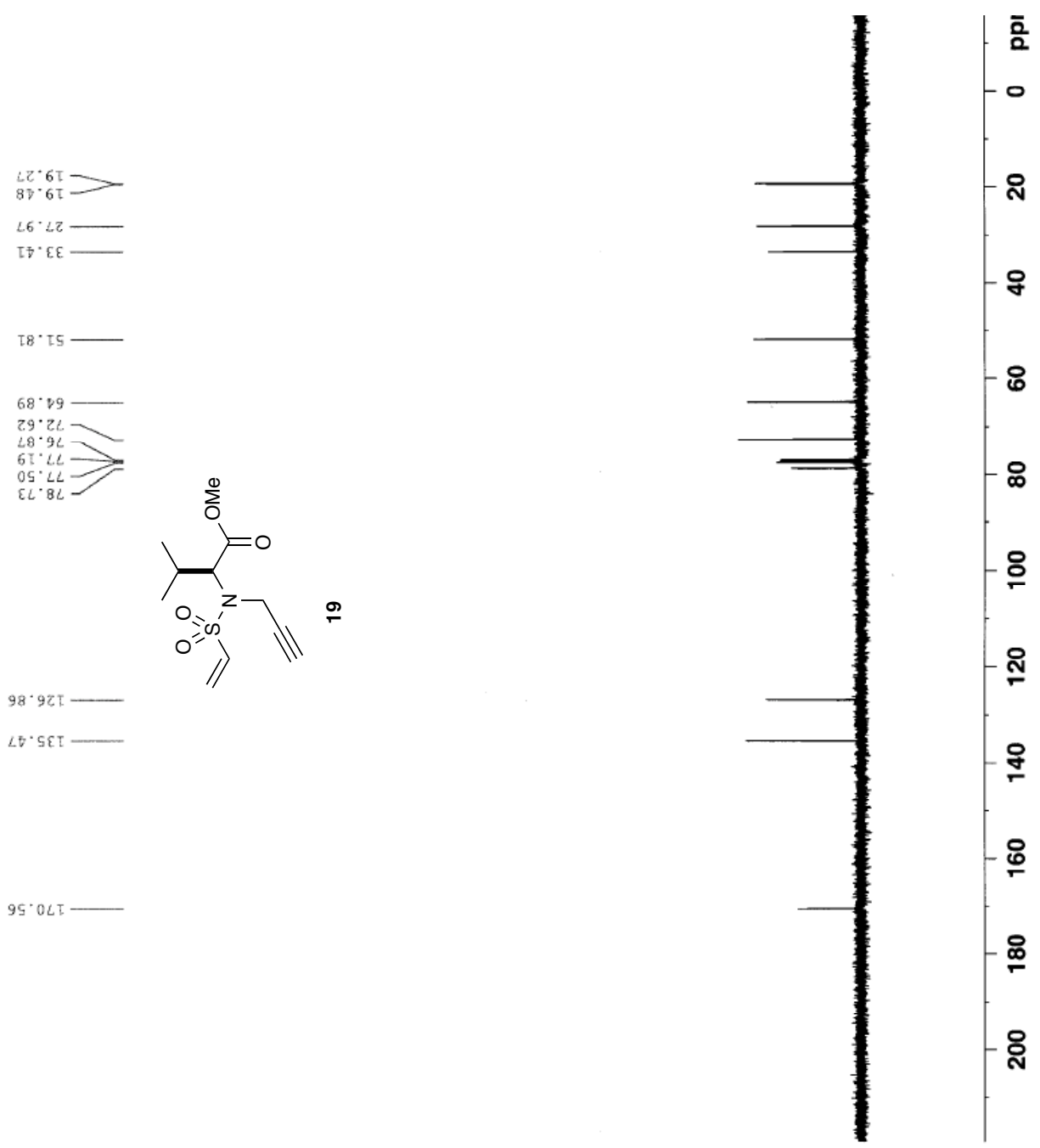


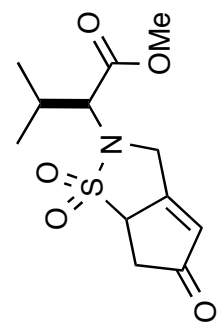


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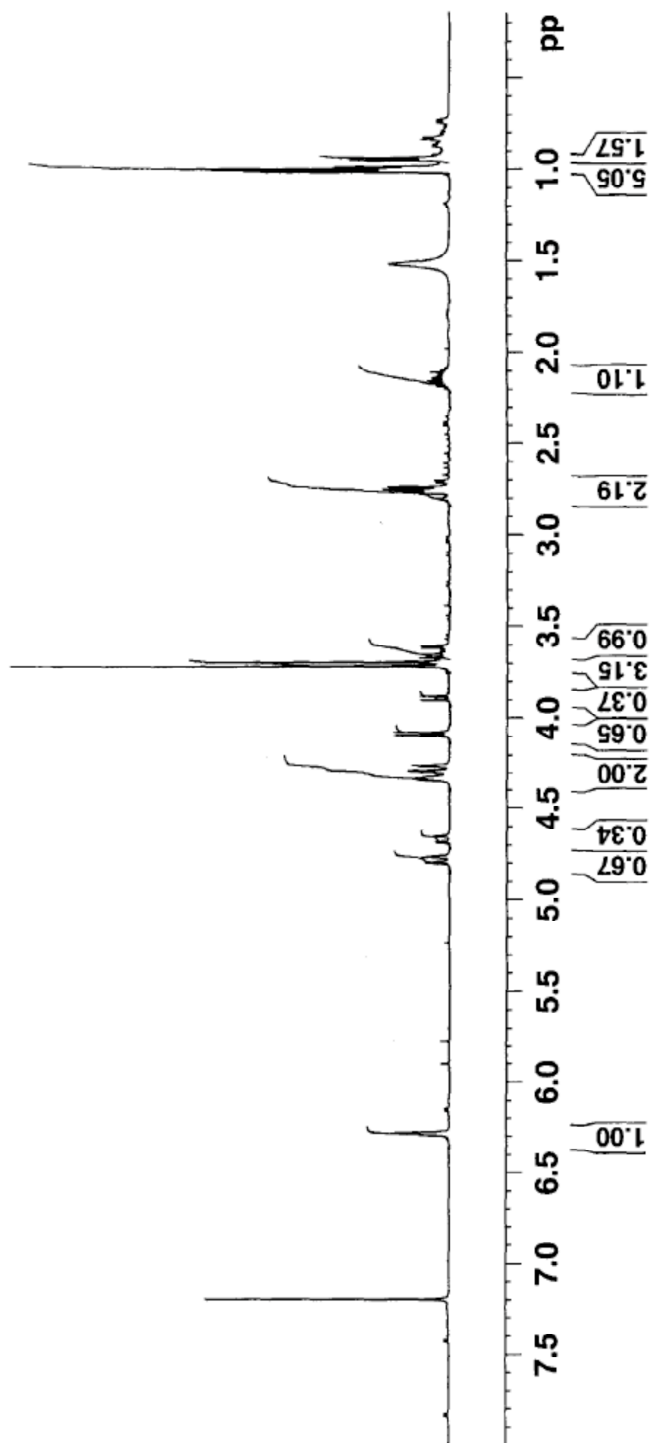








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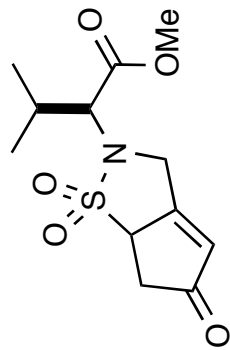


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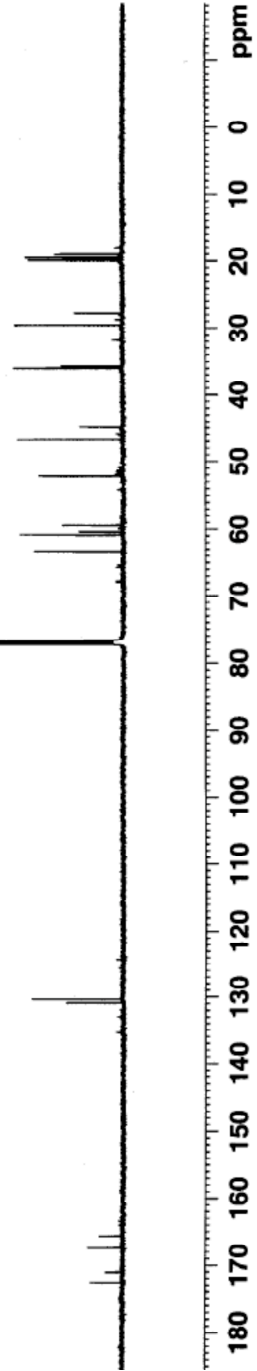
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171.15  
167.49  
165.72

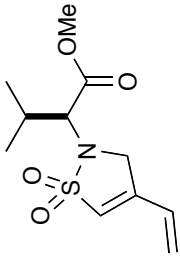
130.92  
130.39

63.35  
60.91  
60.45  
59.50  
52.25  
52.24  
46.79  
44.90  
36.00  
35.64  
29.58  
27.83  
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19.66  
19.61  
19.13  
19.04

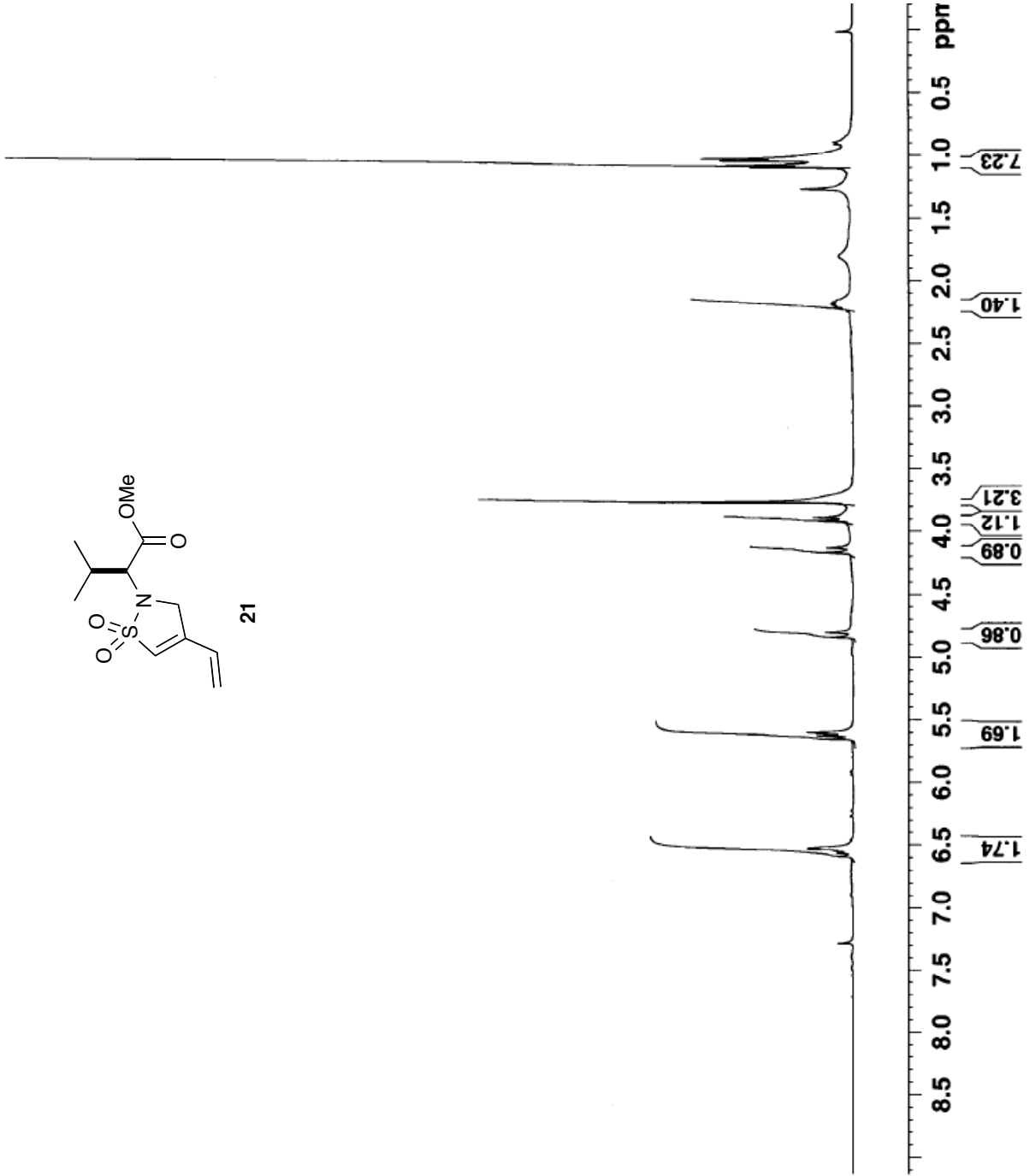


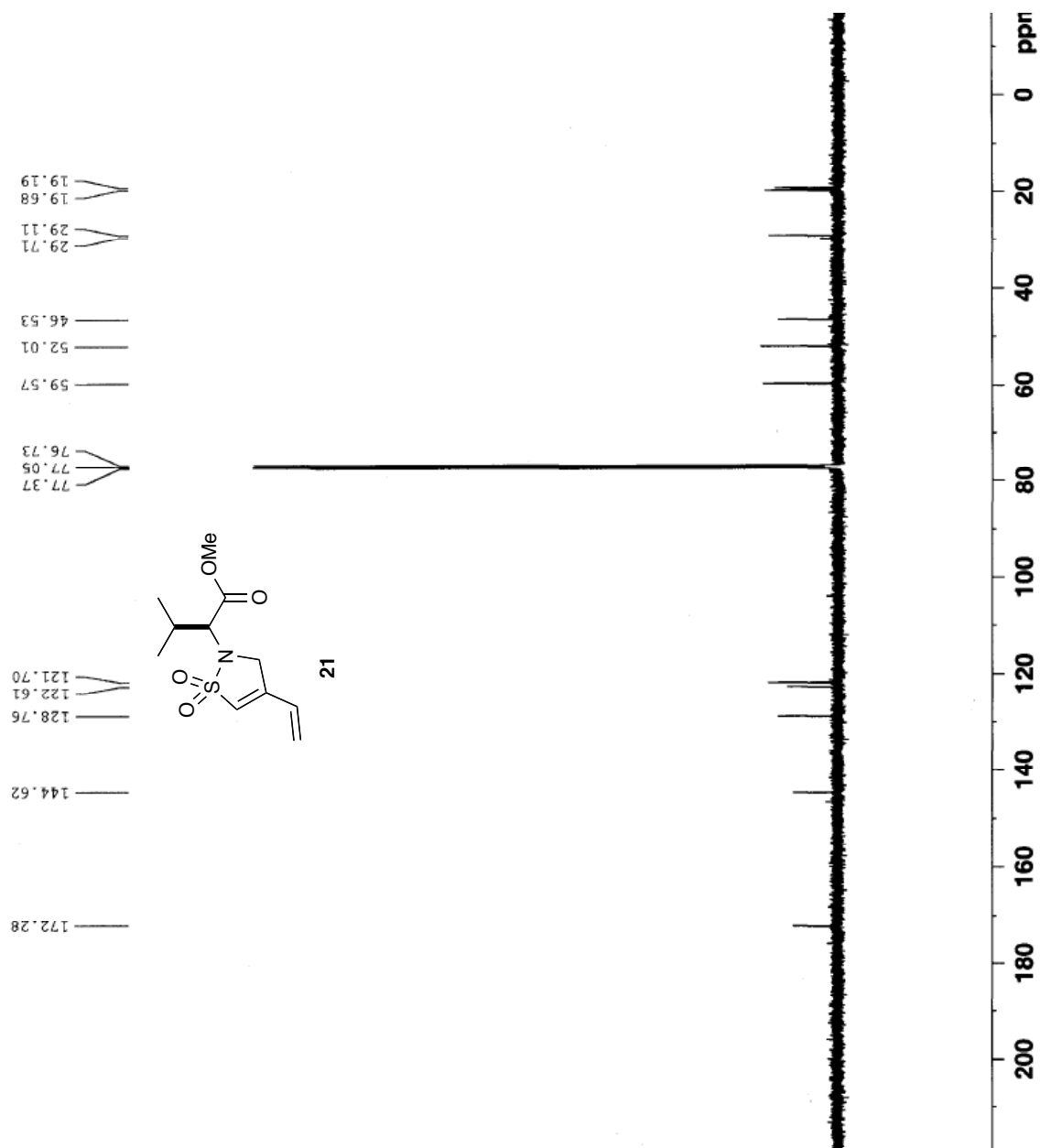
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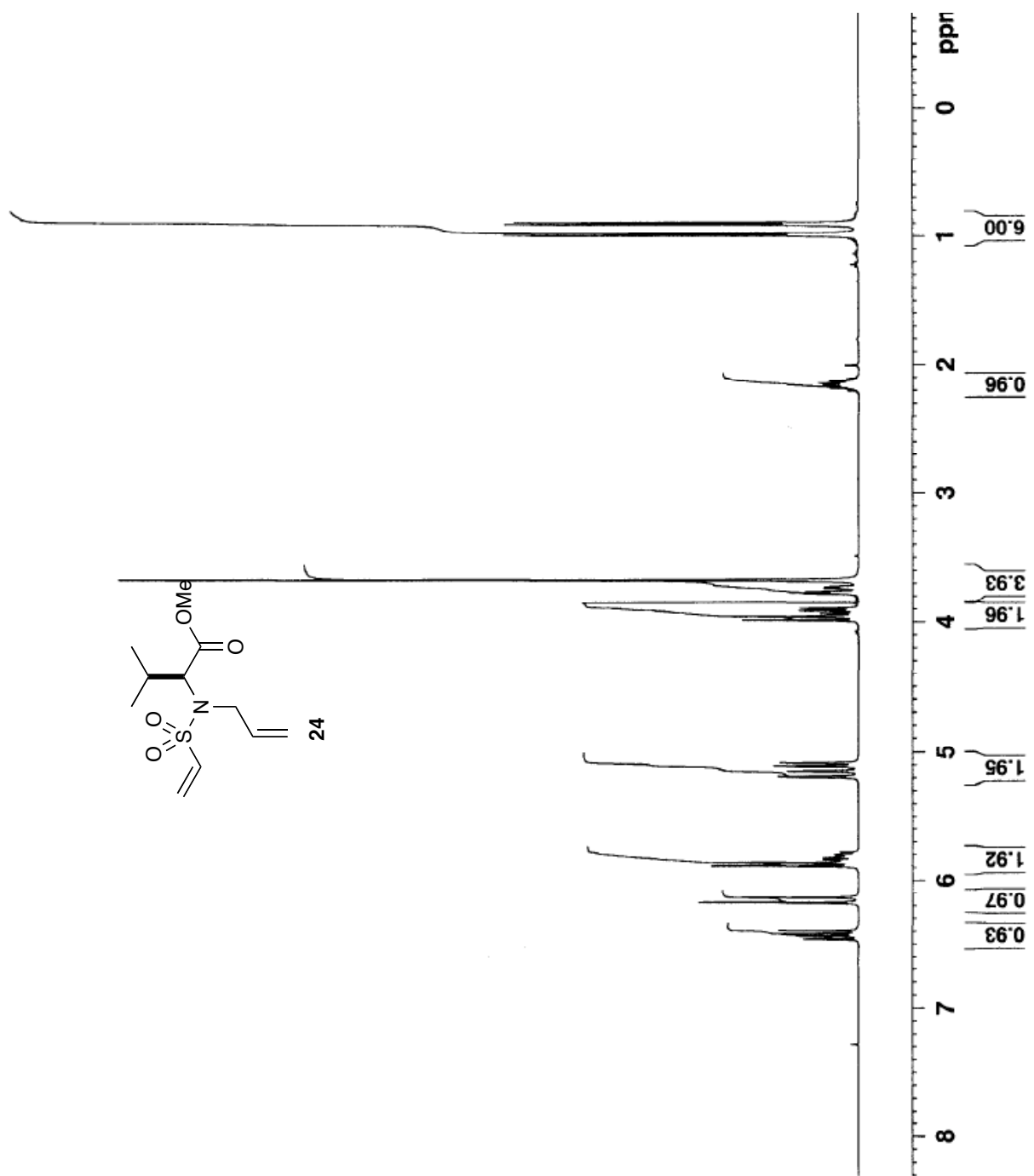


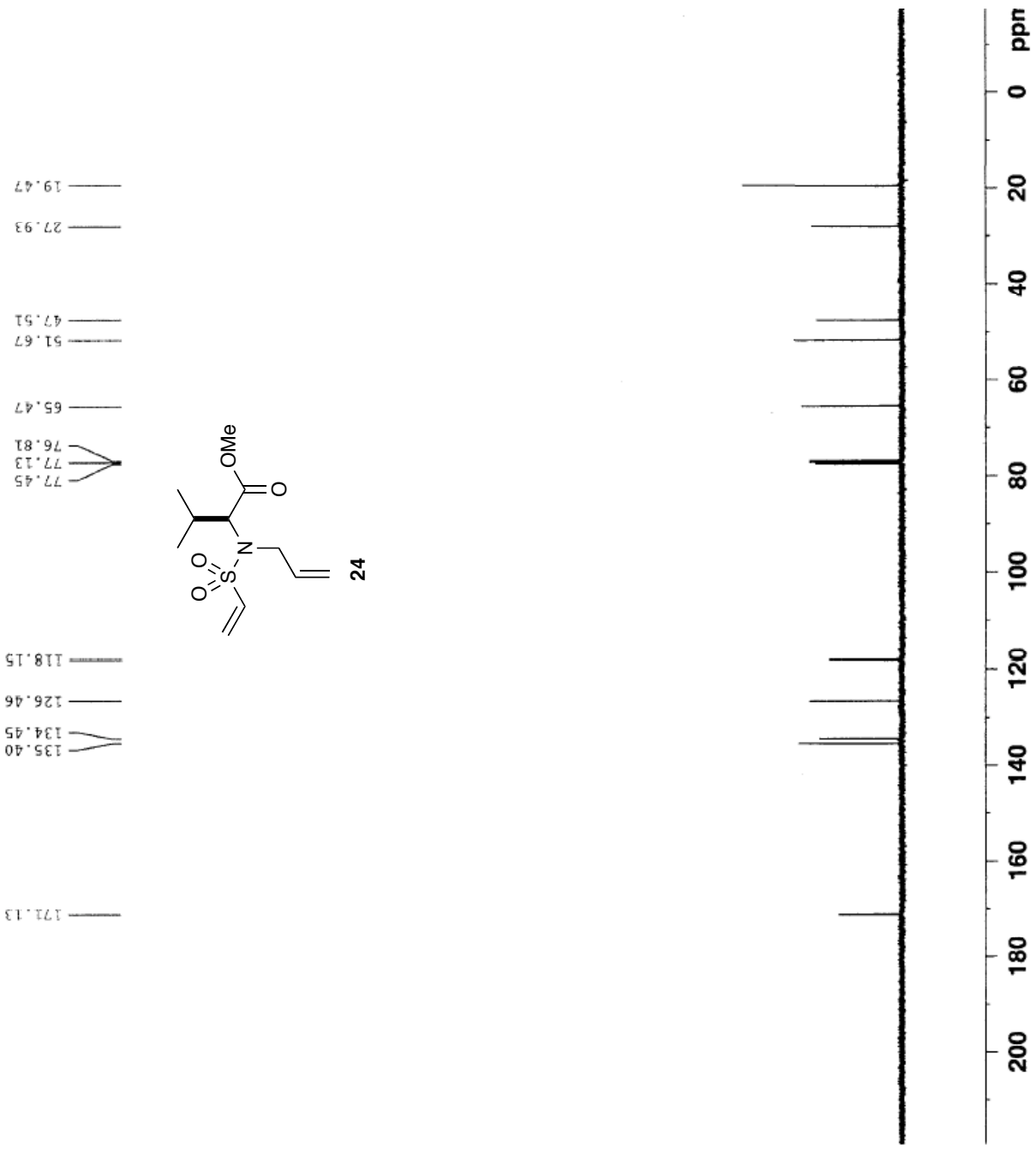


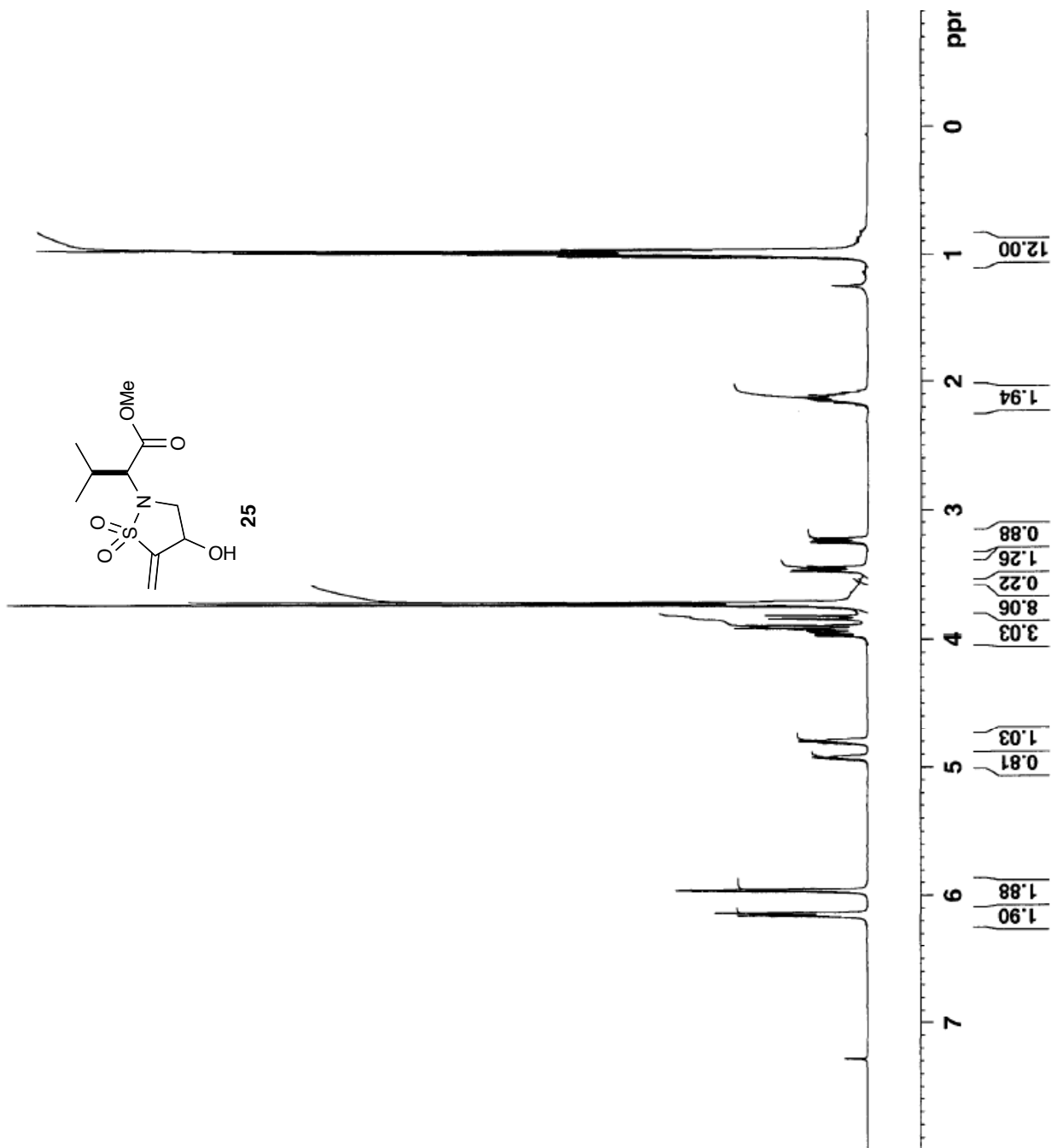
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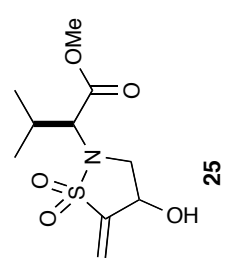
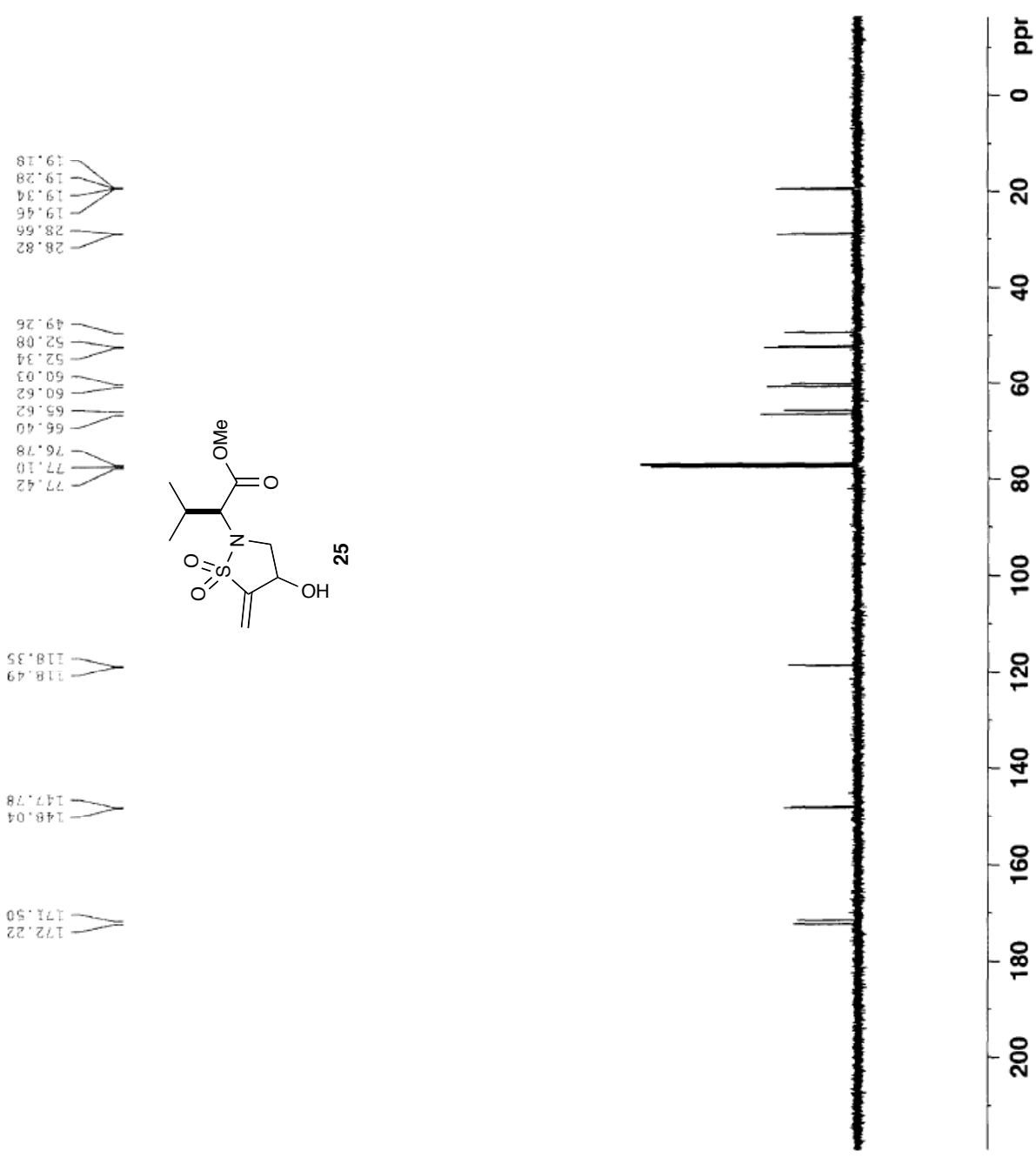


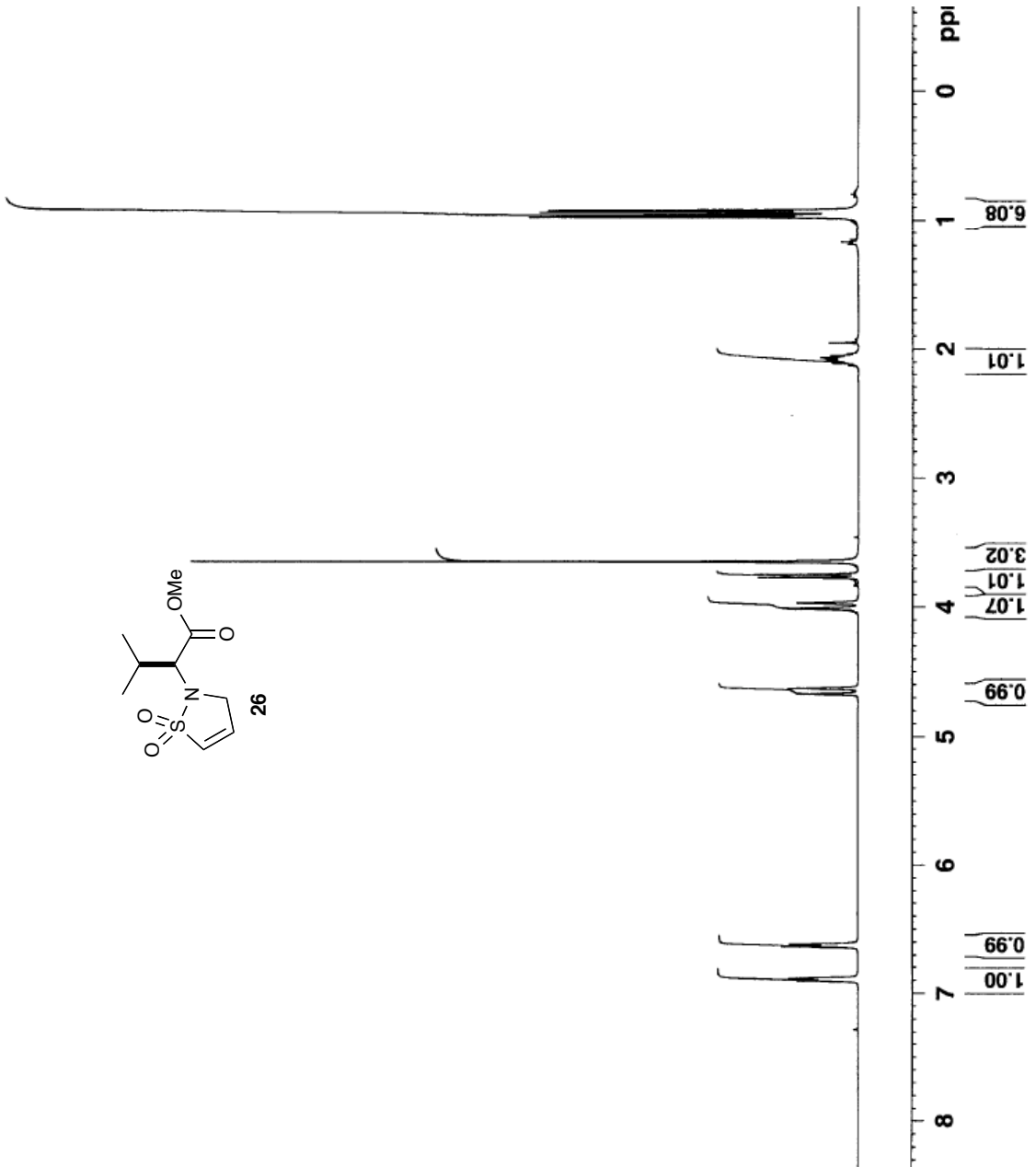


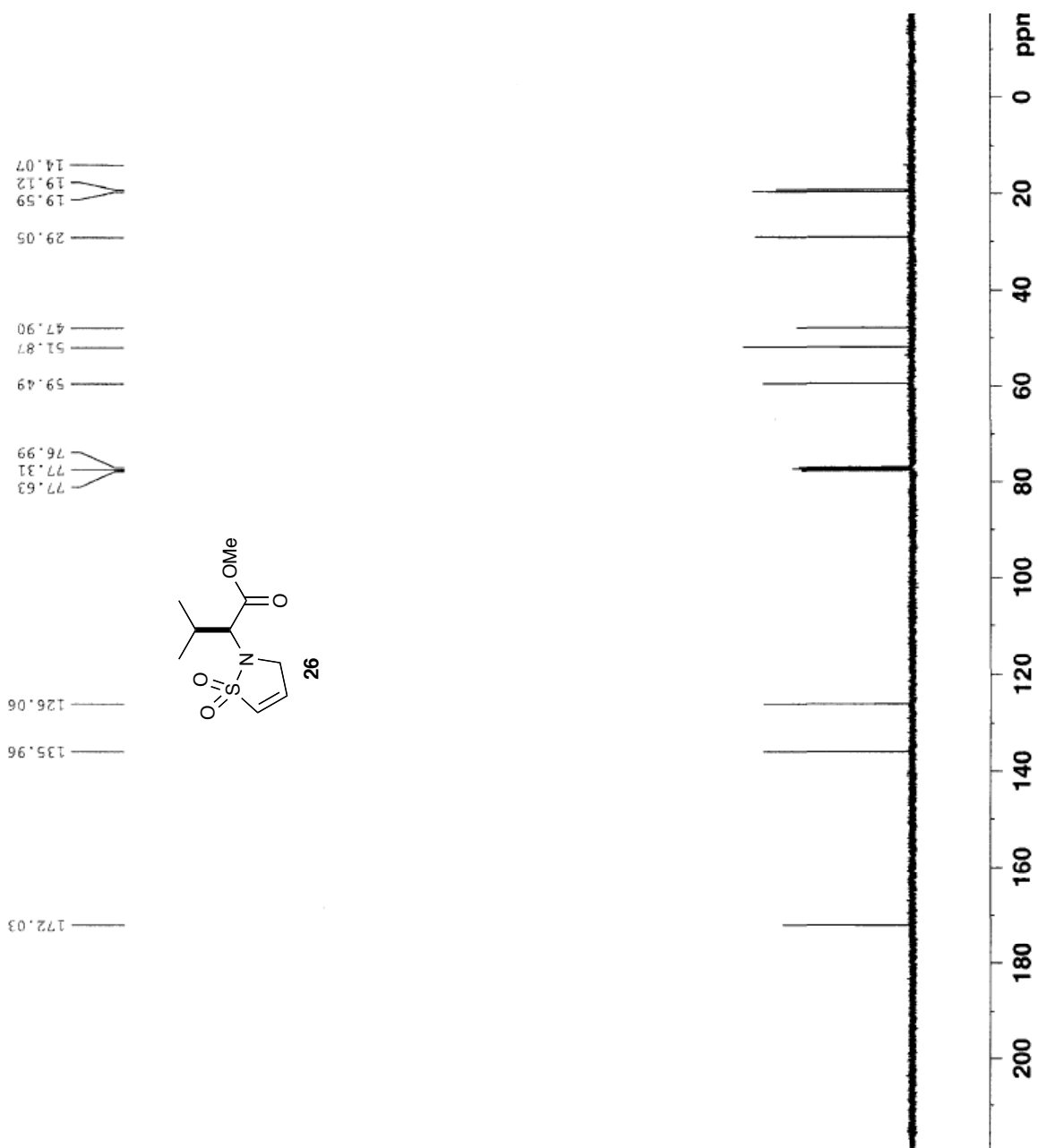


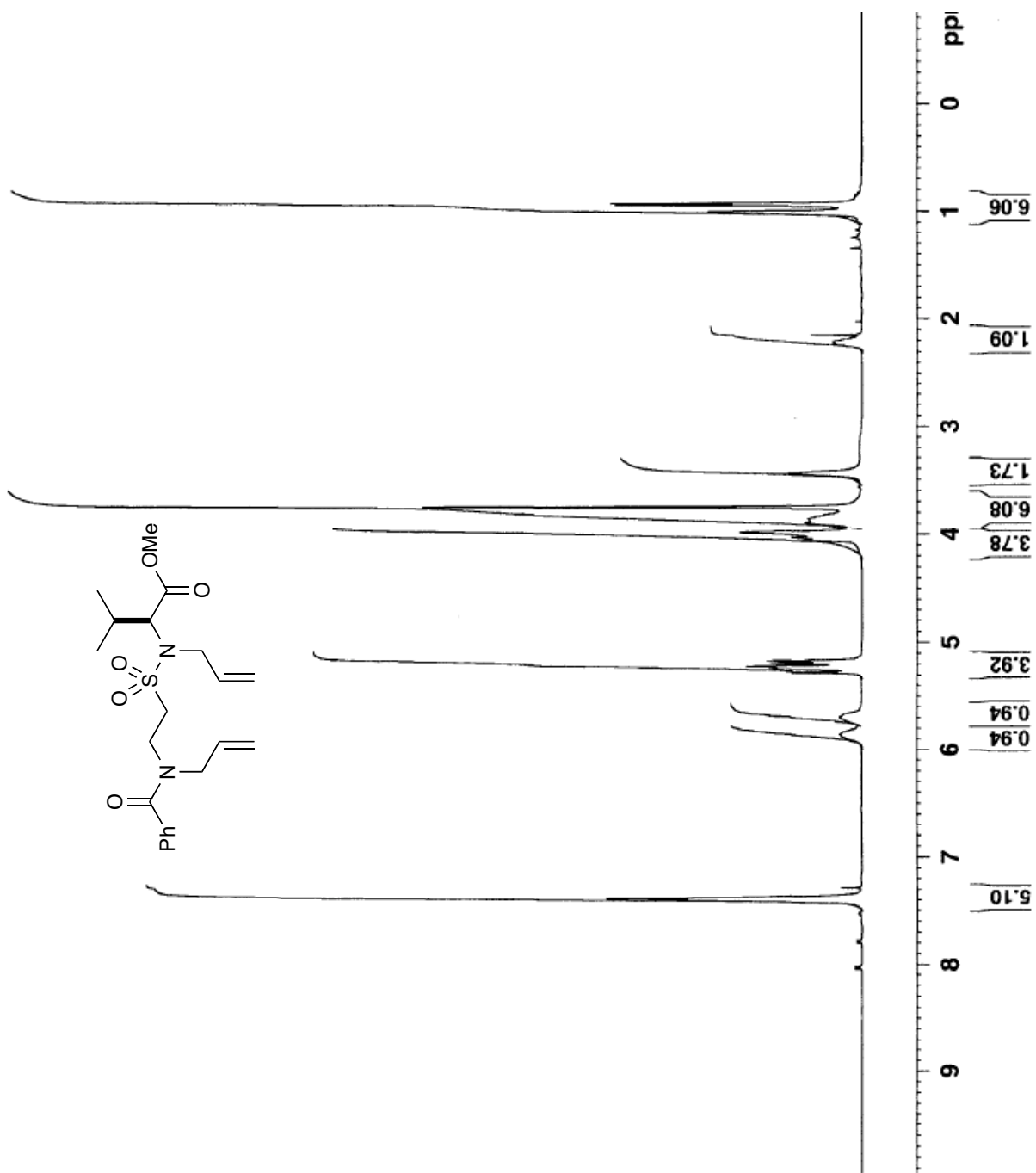


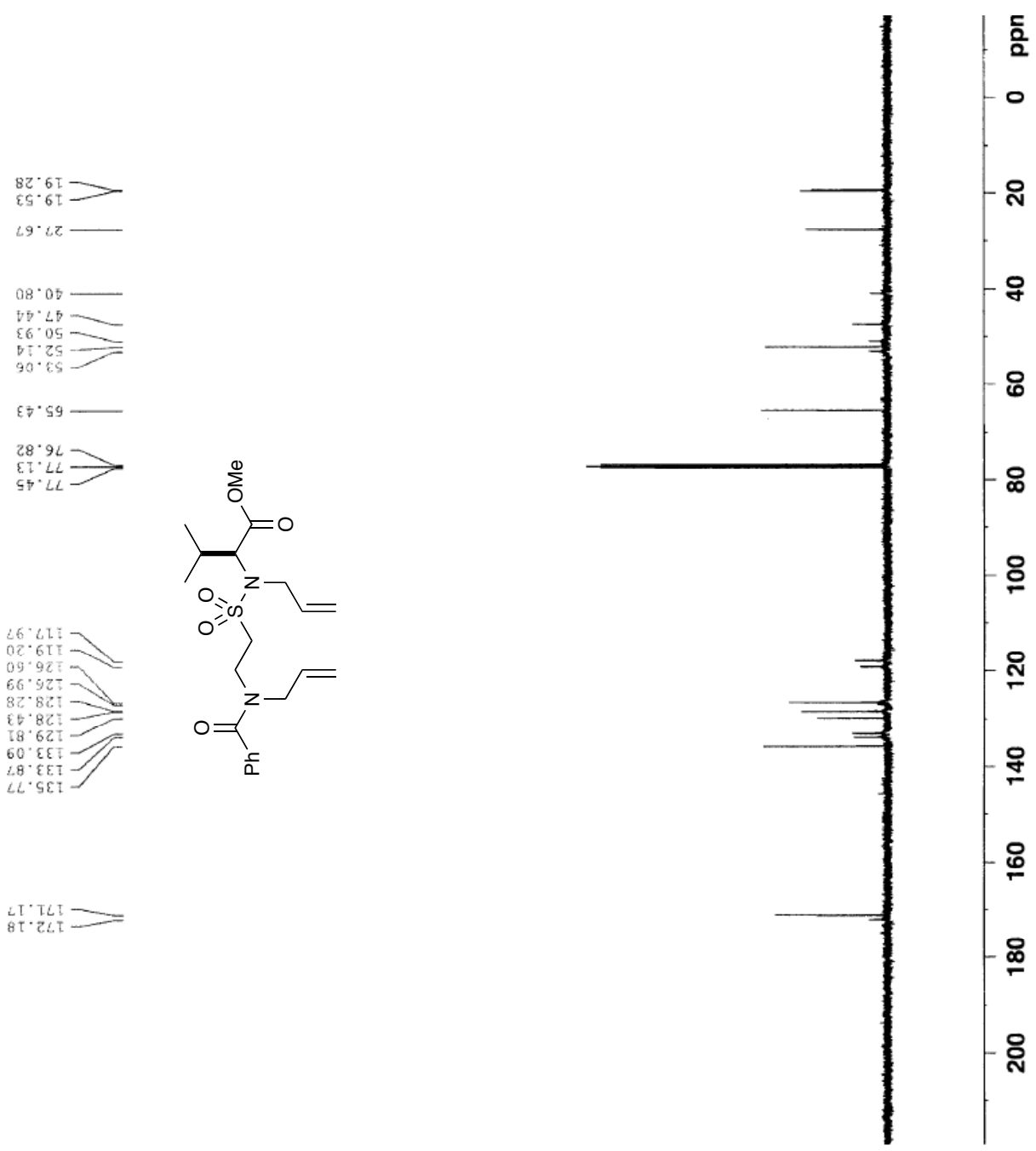


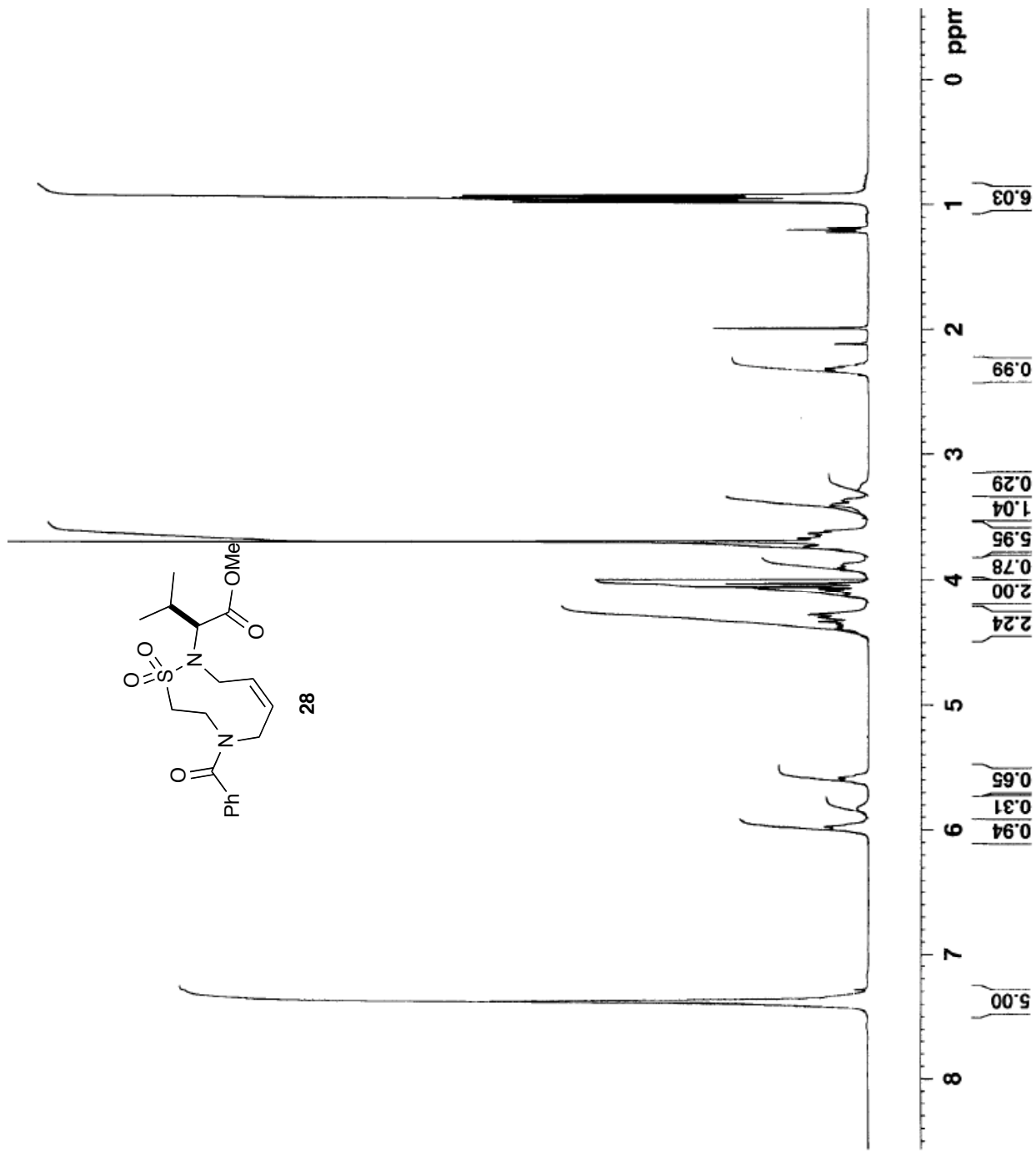


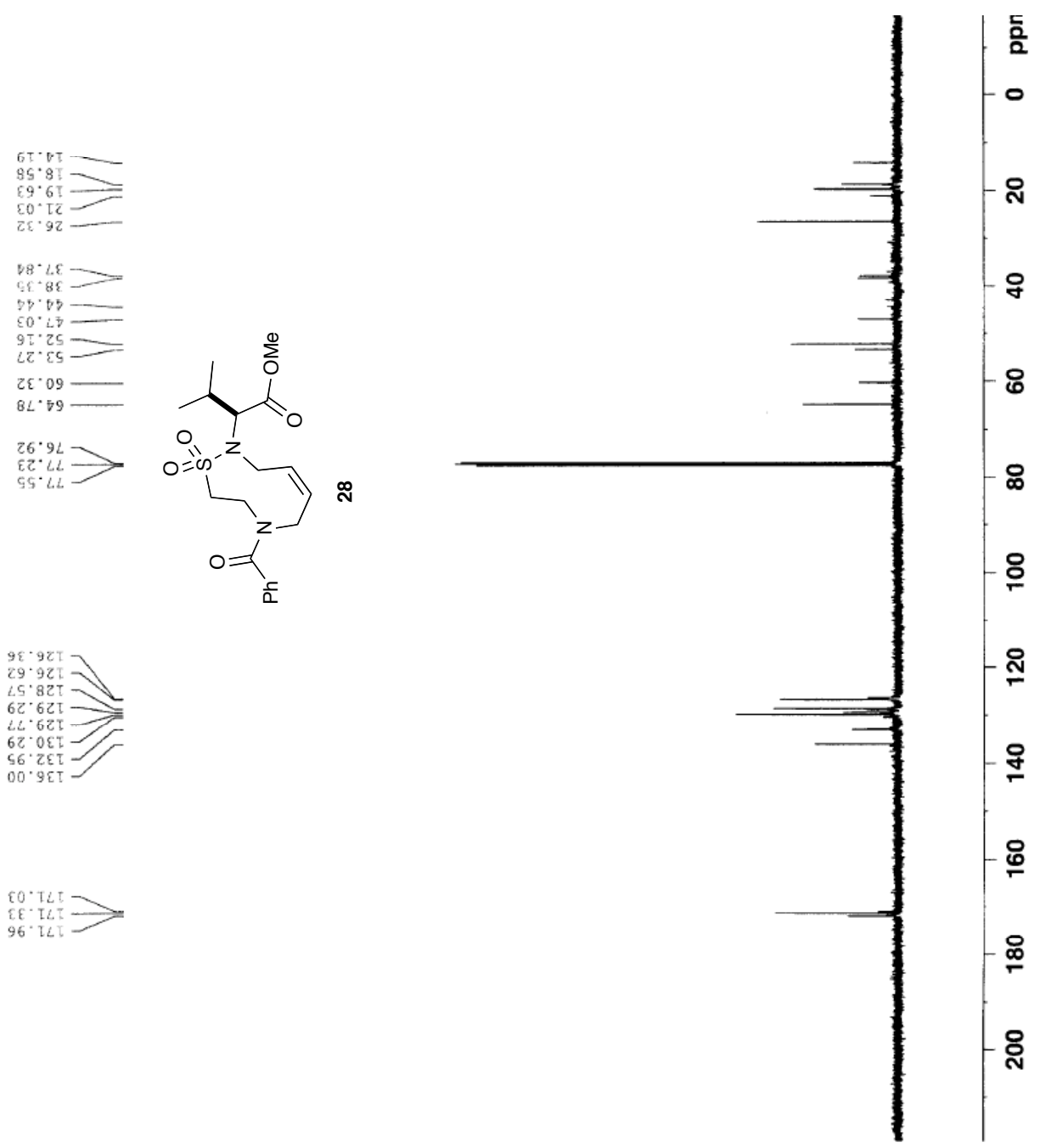


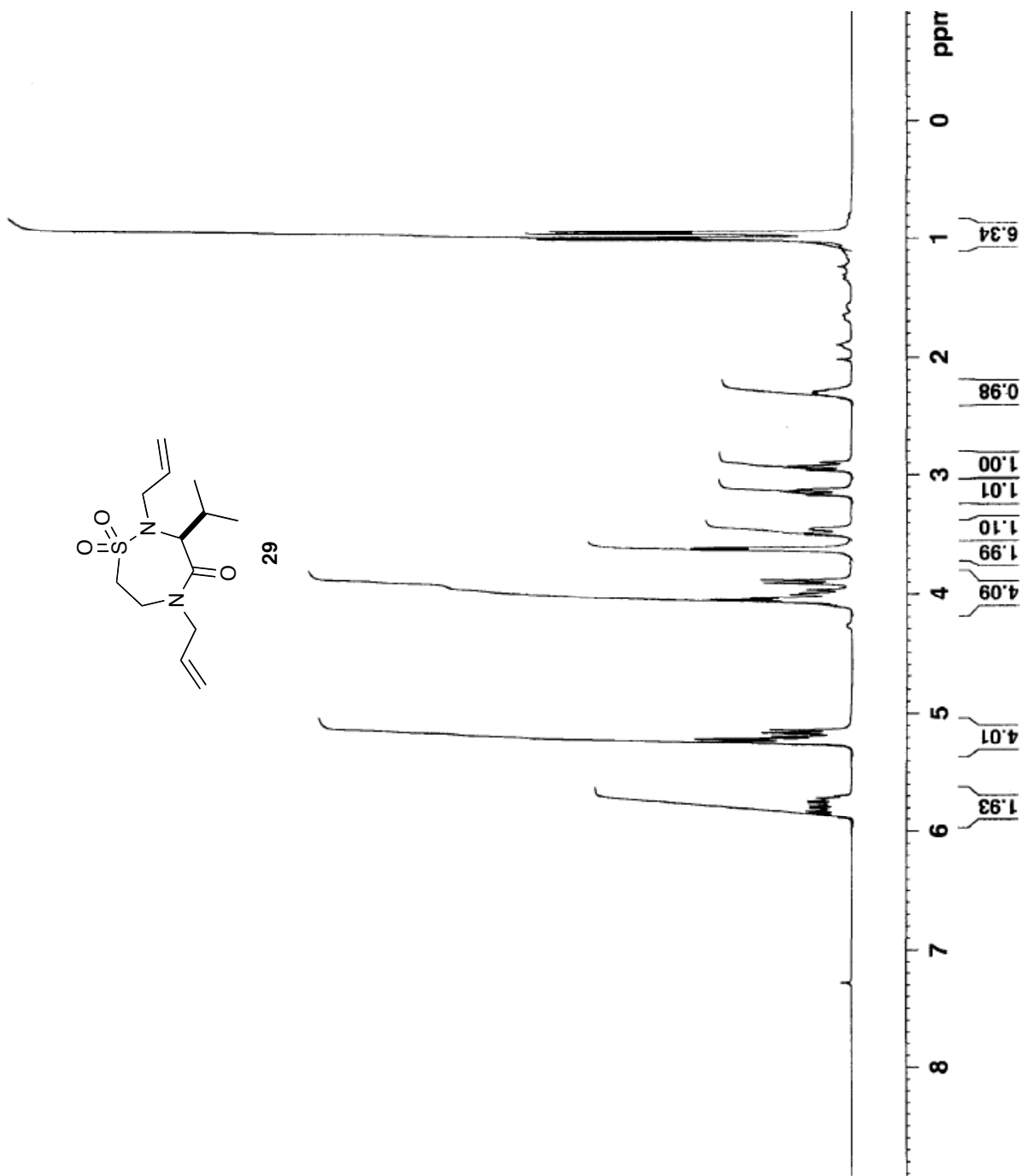




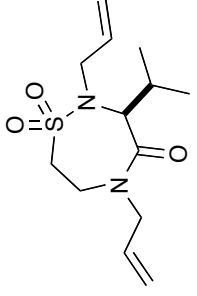
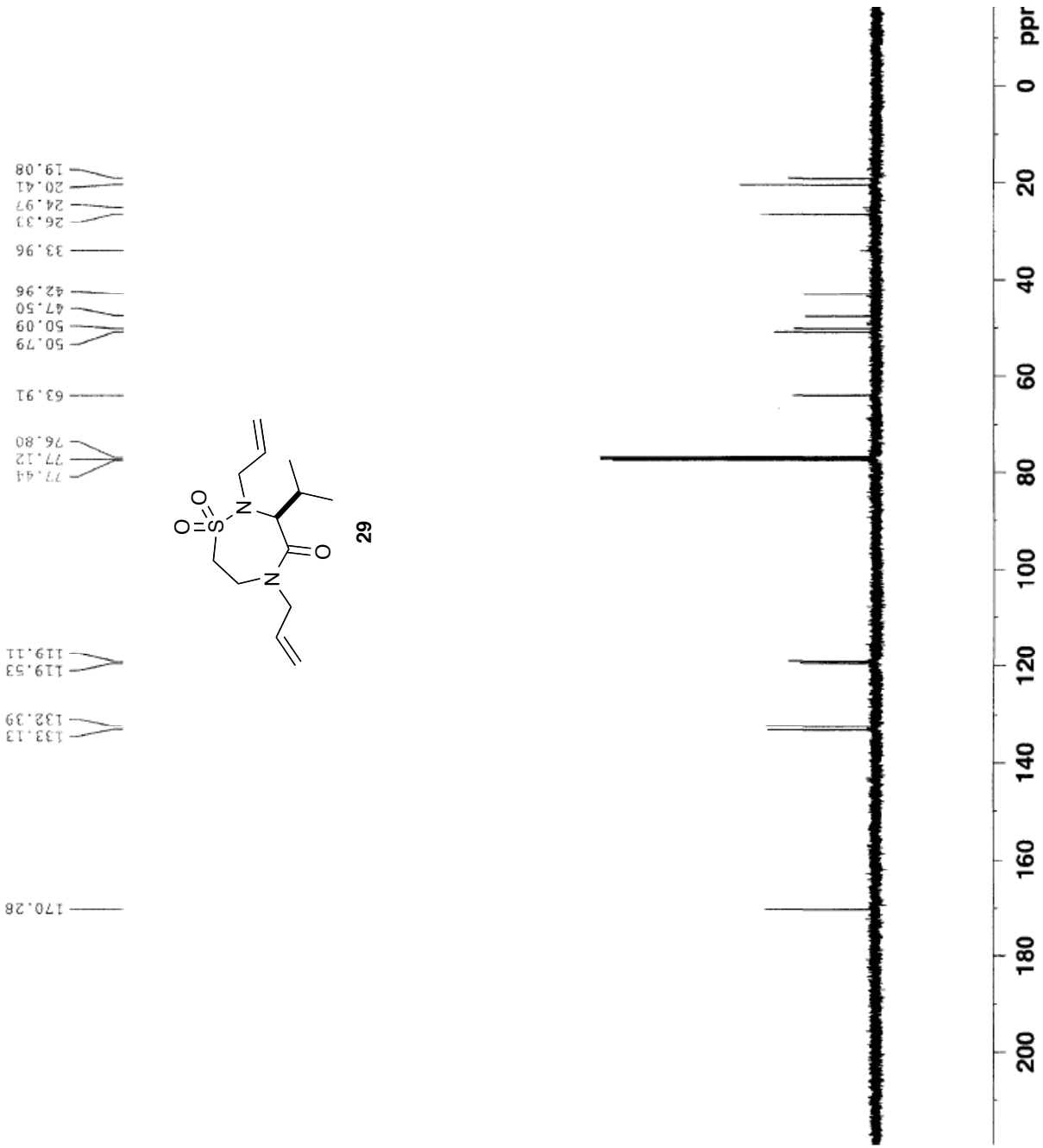


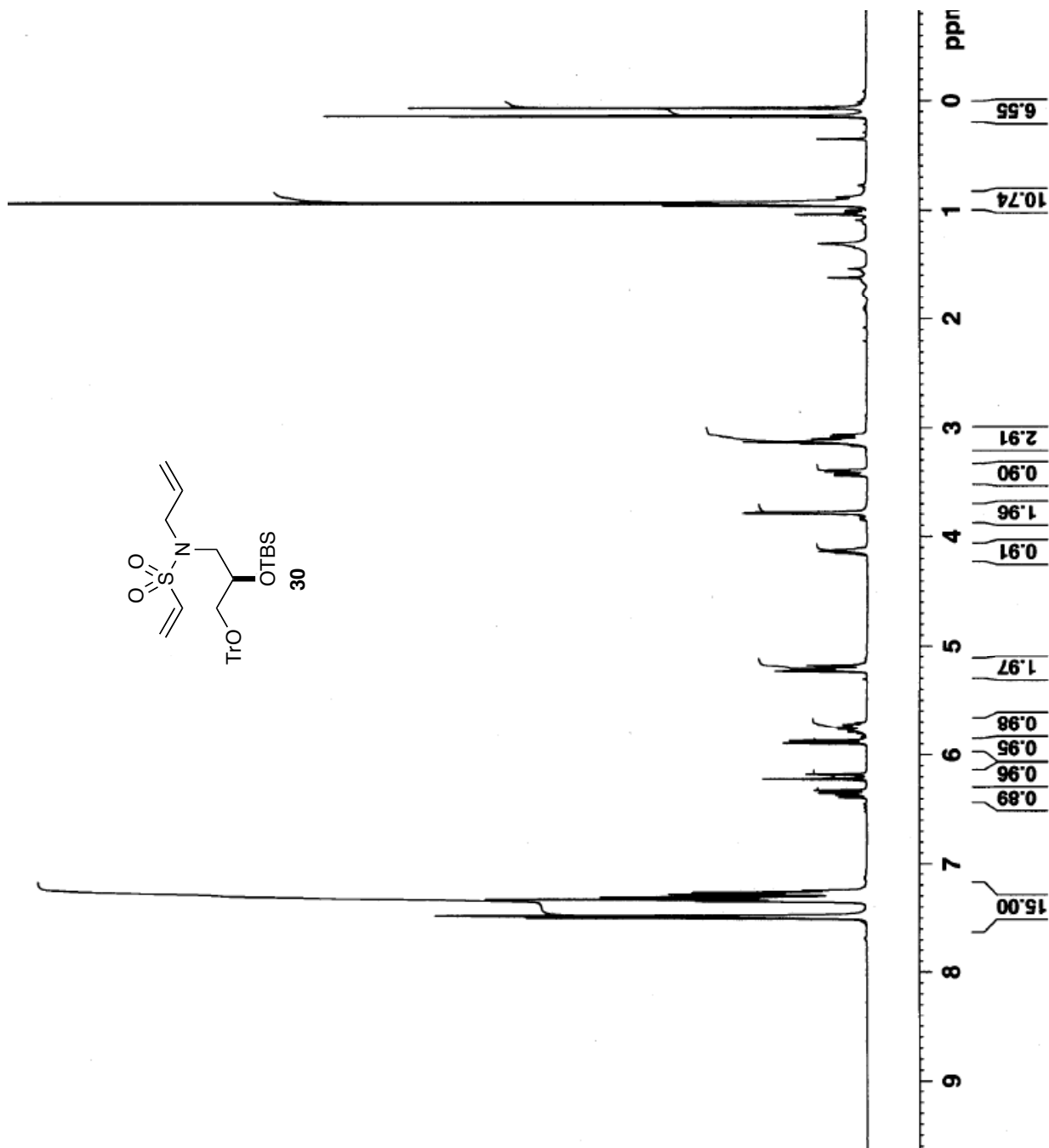




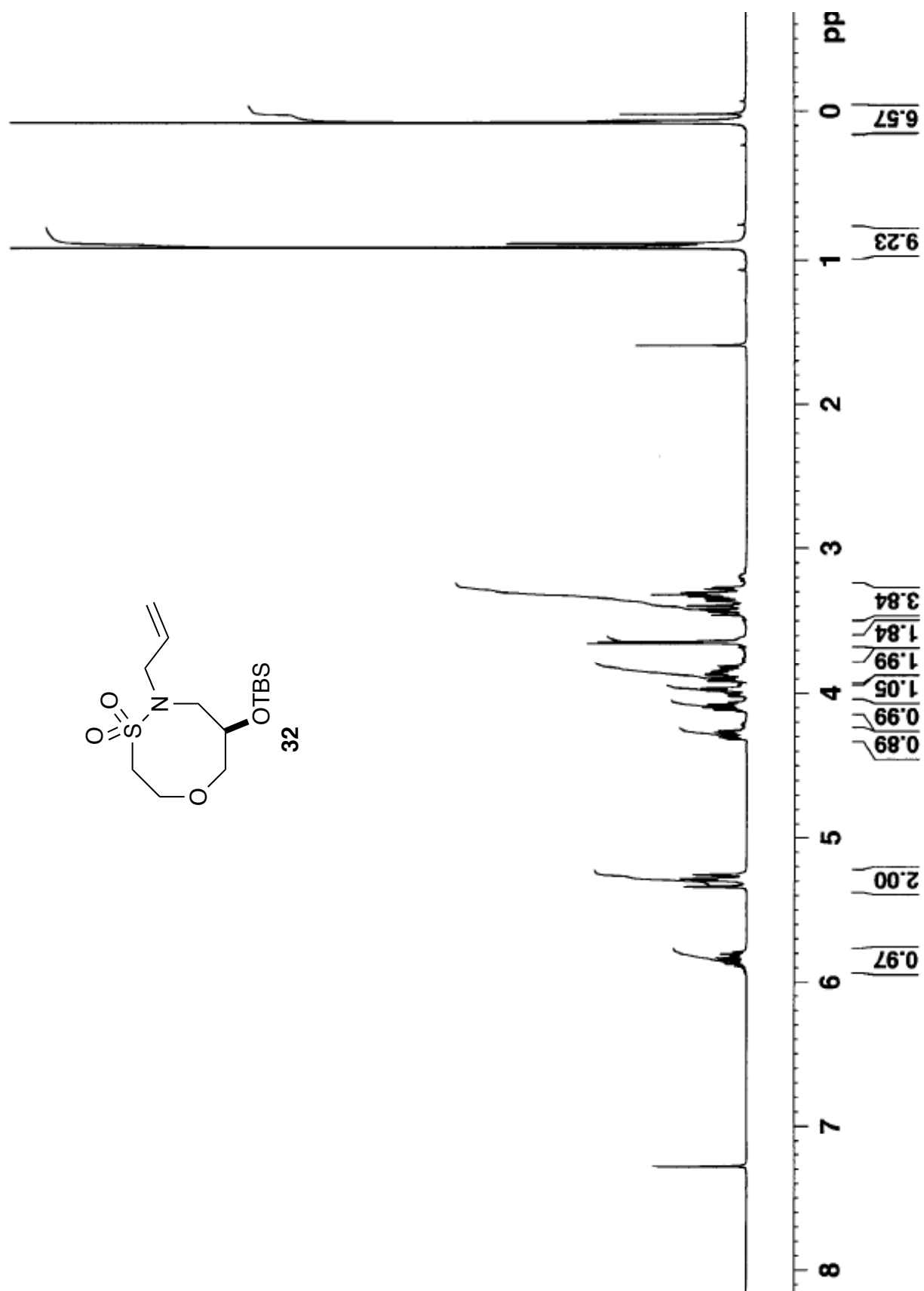


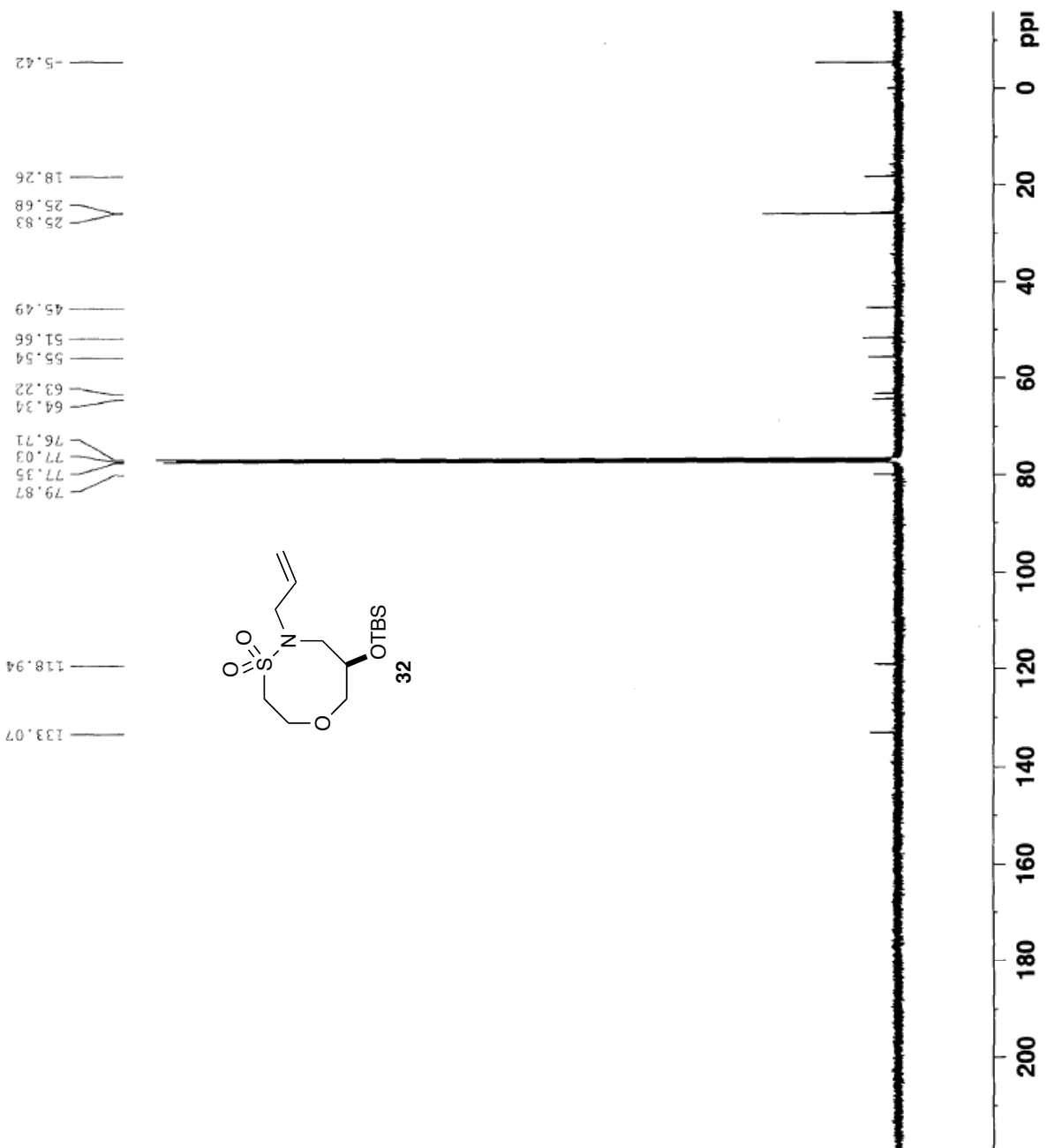


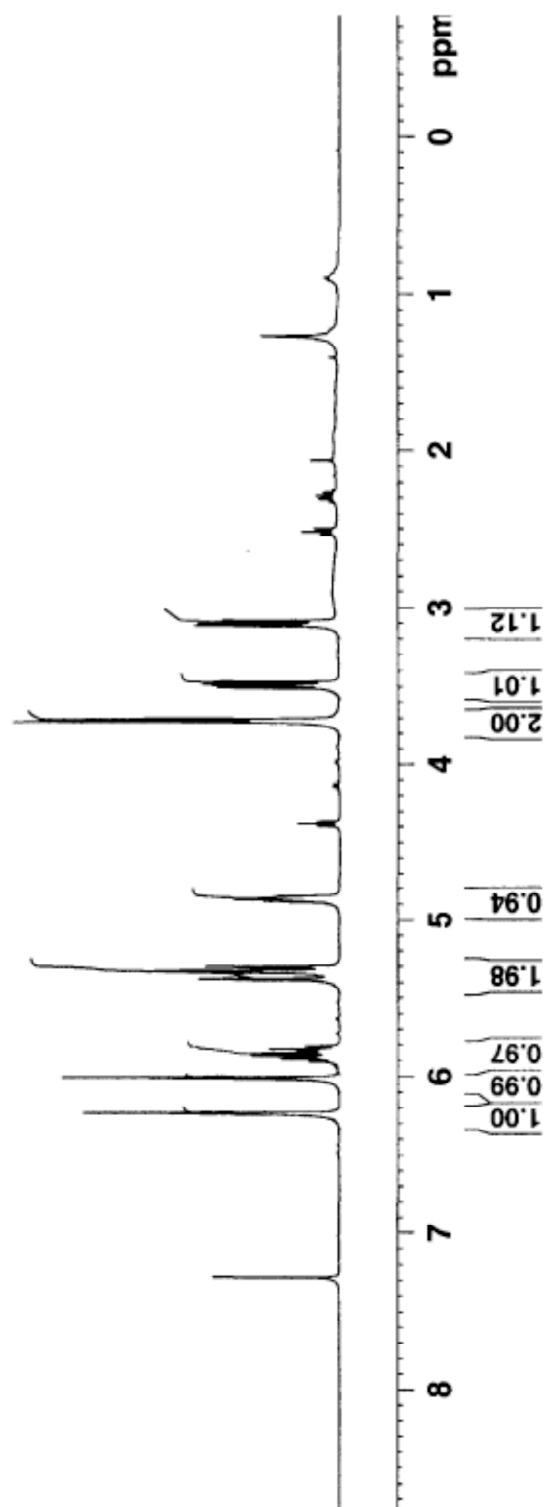
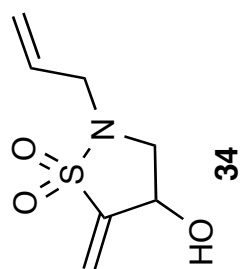


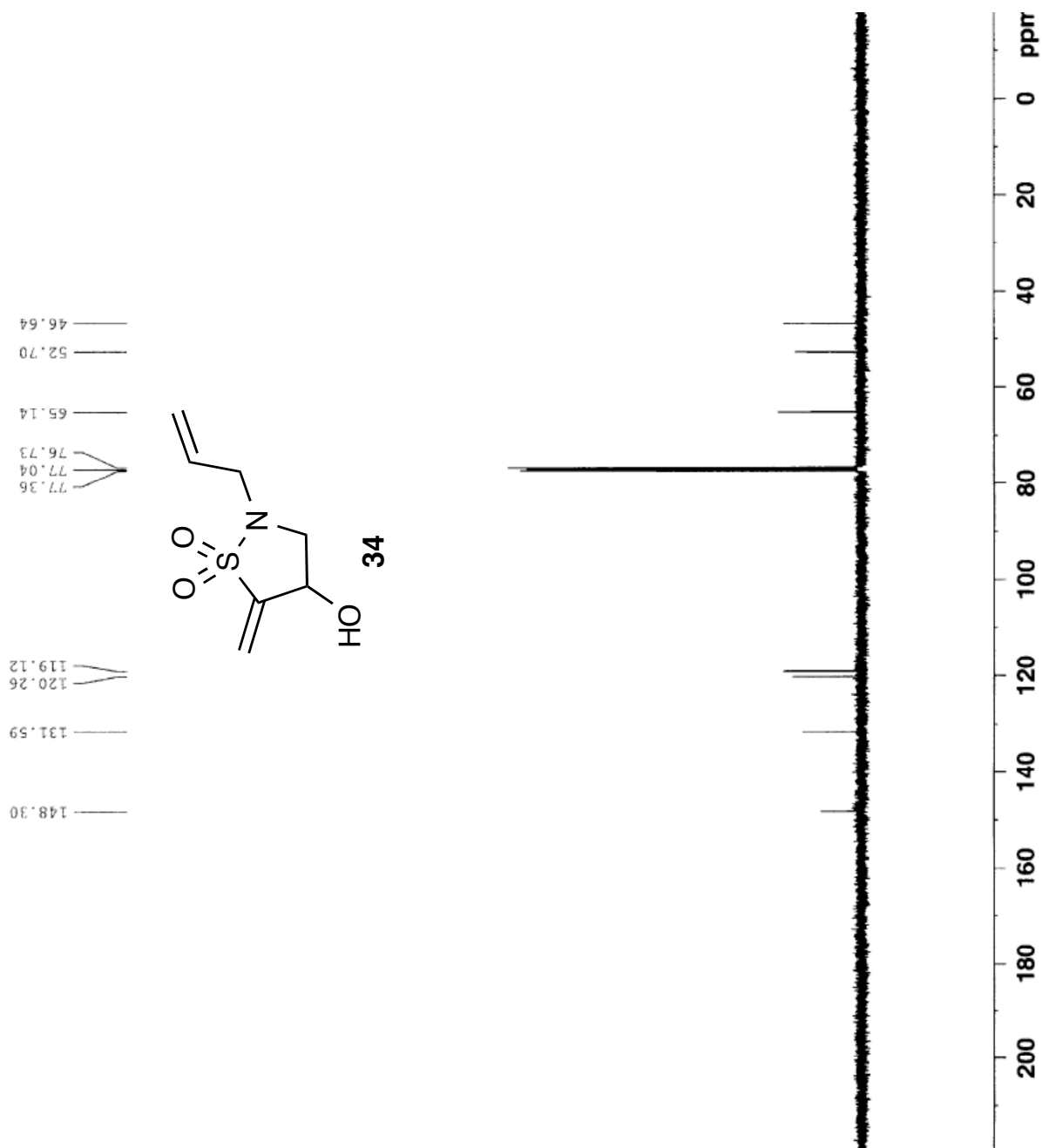


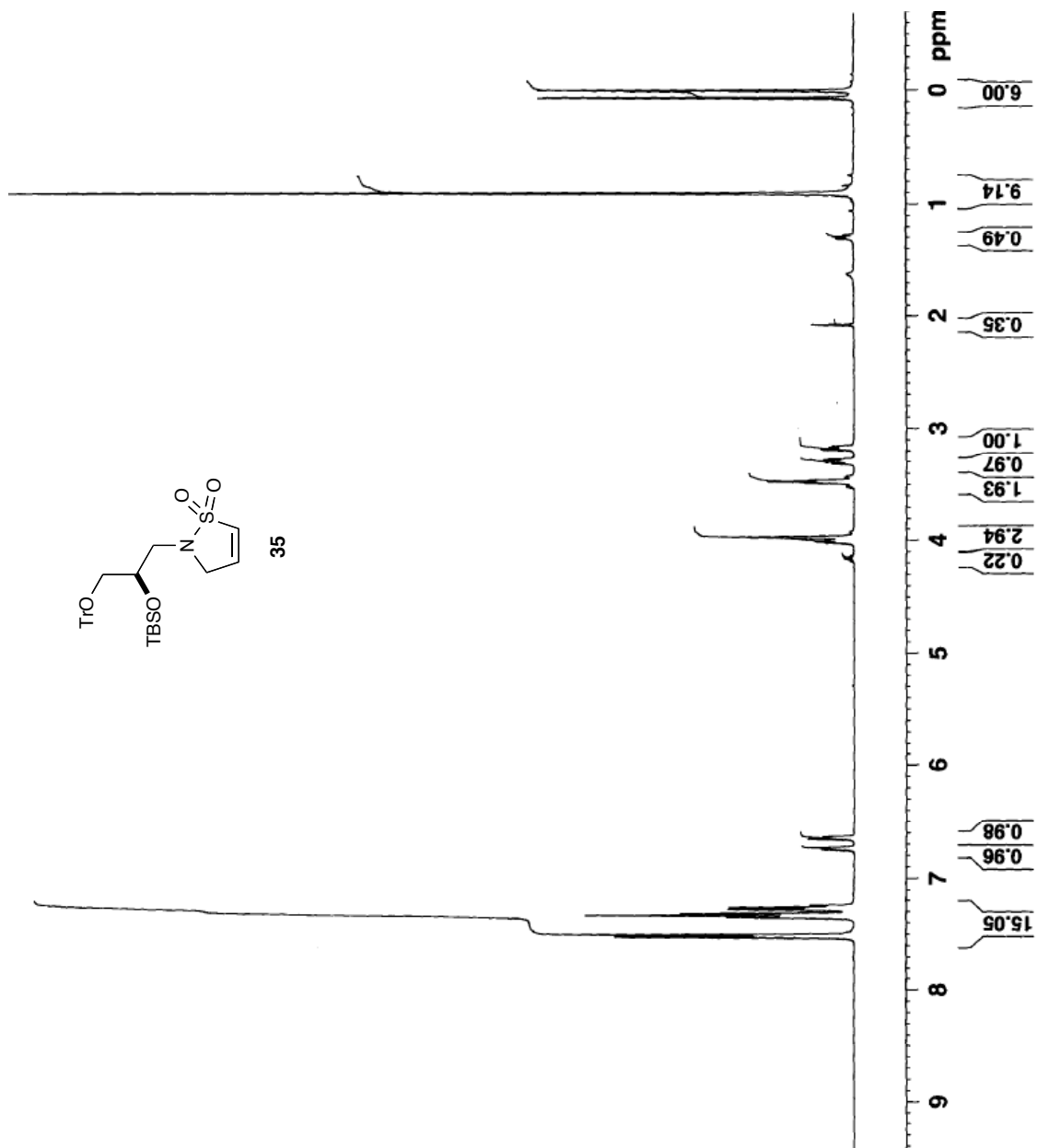




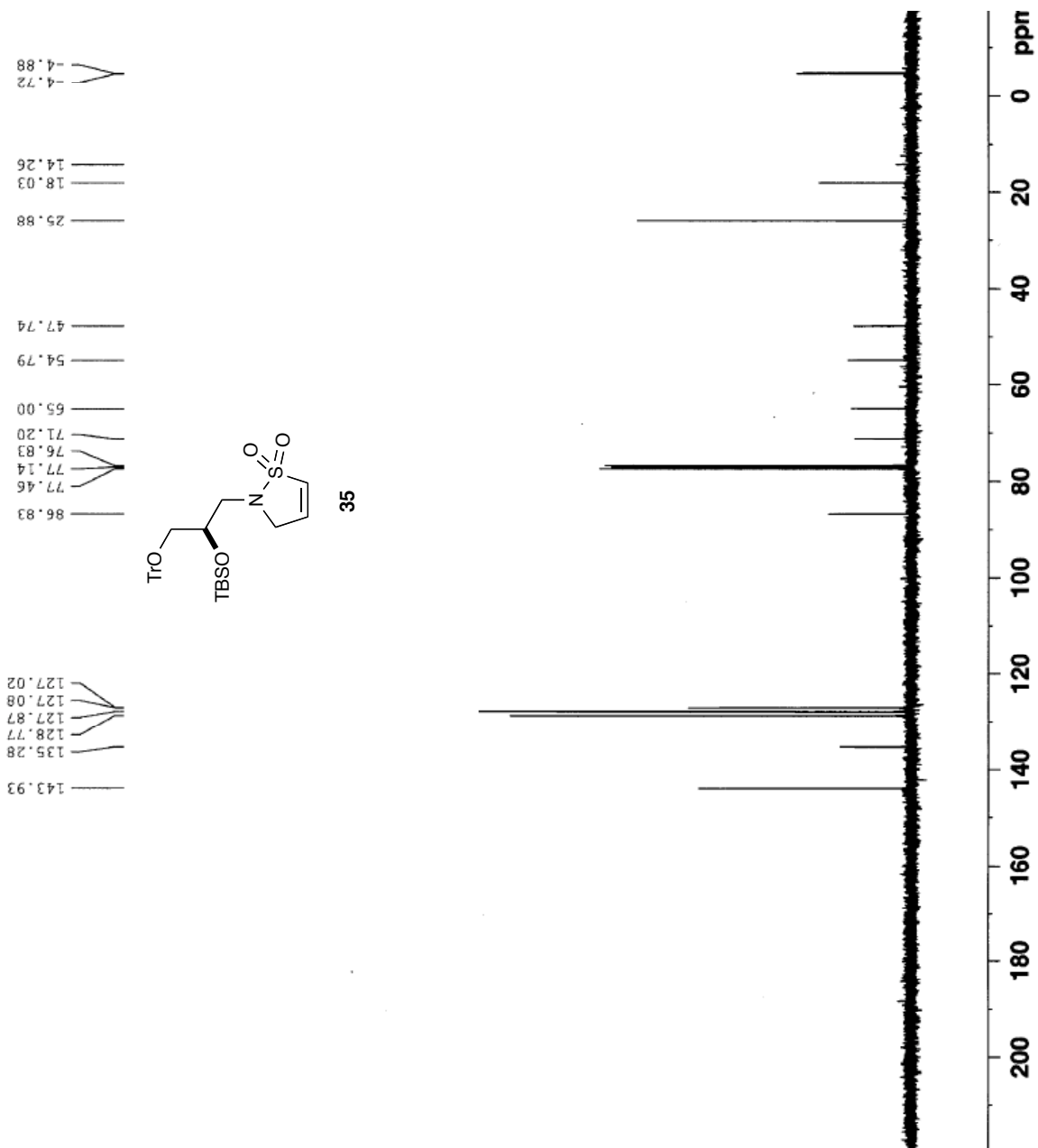


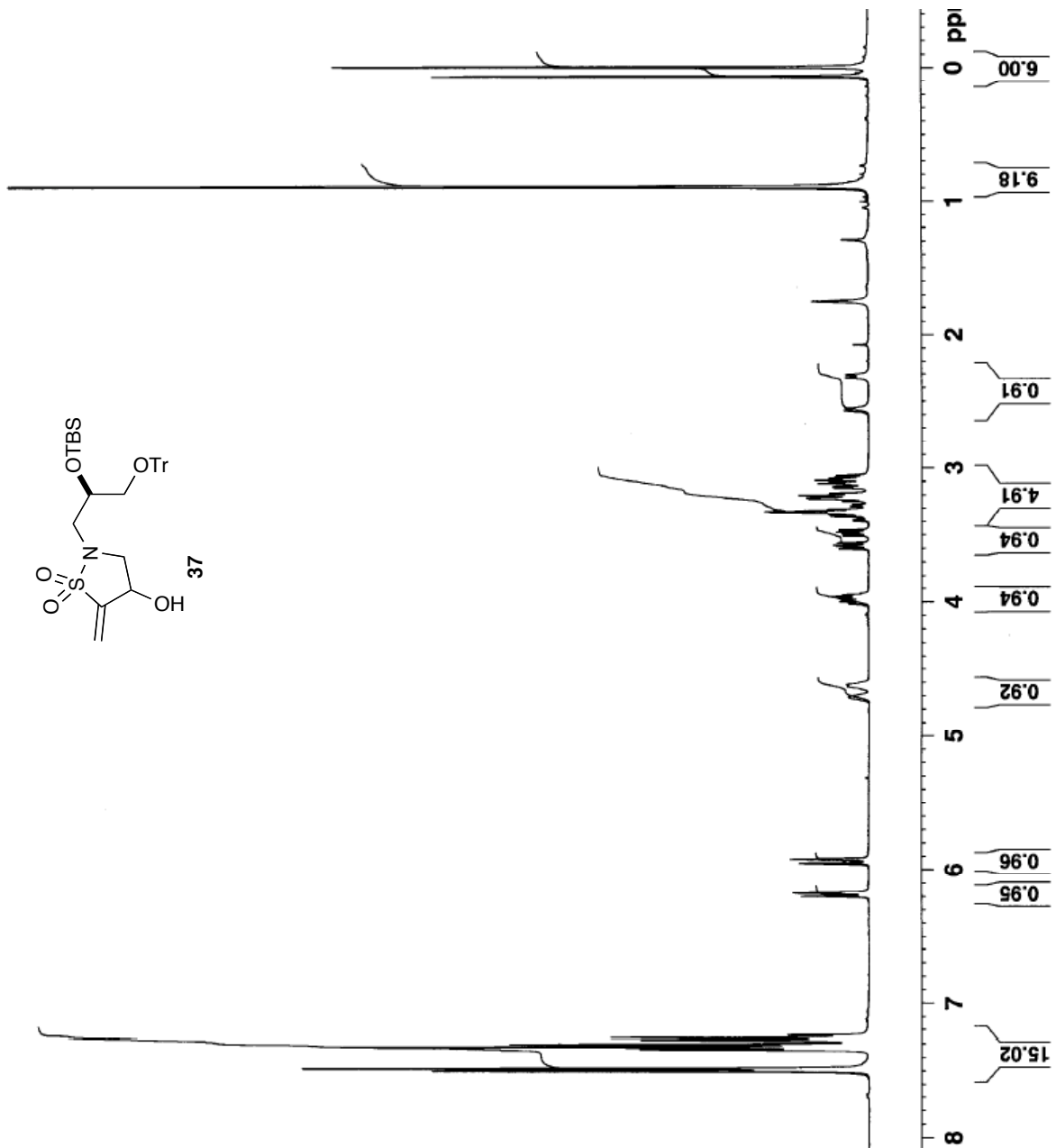


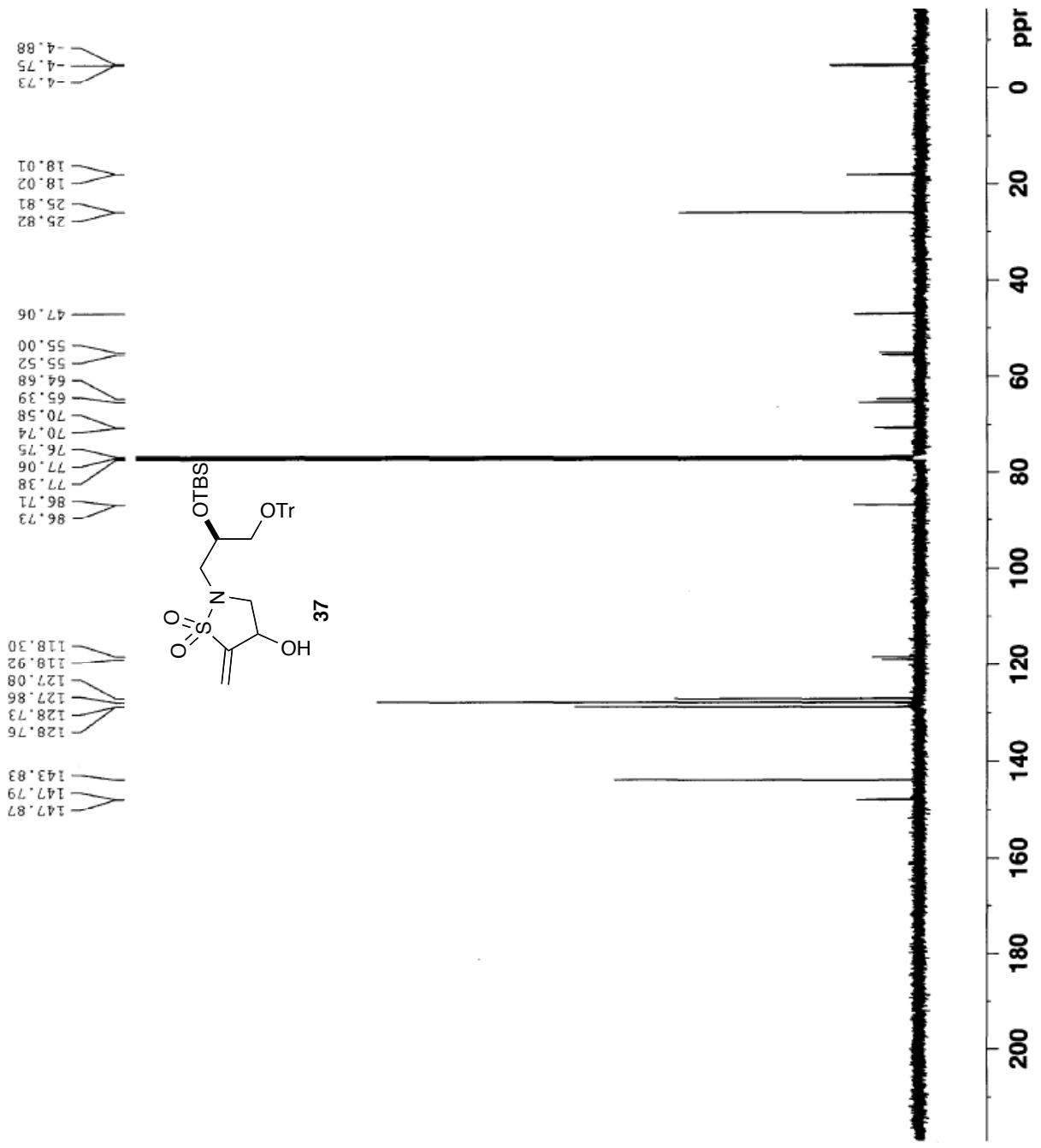


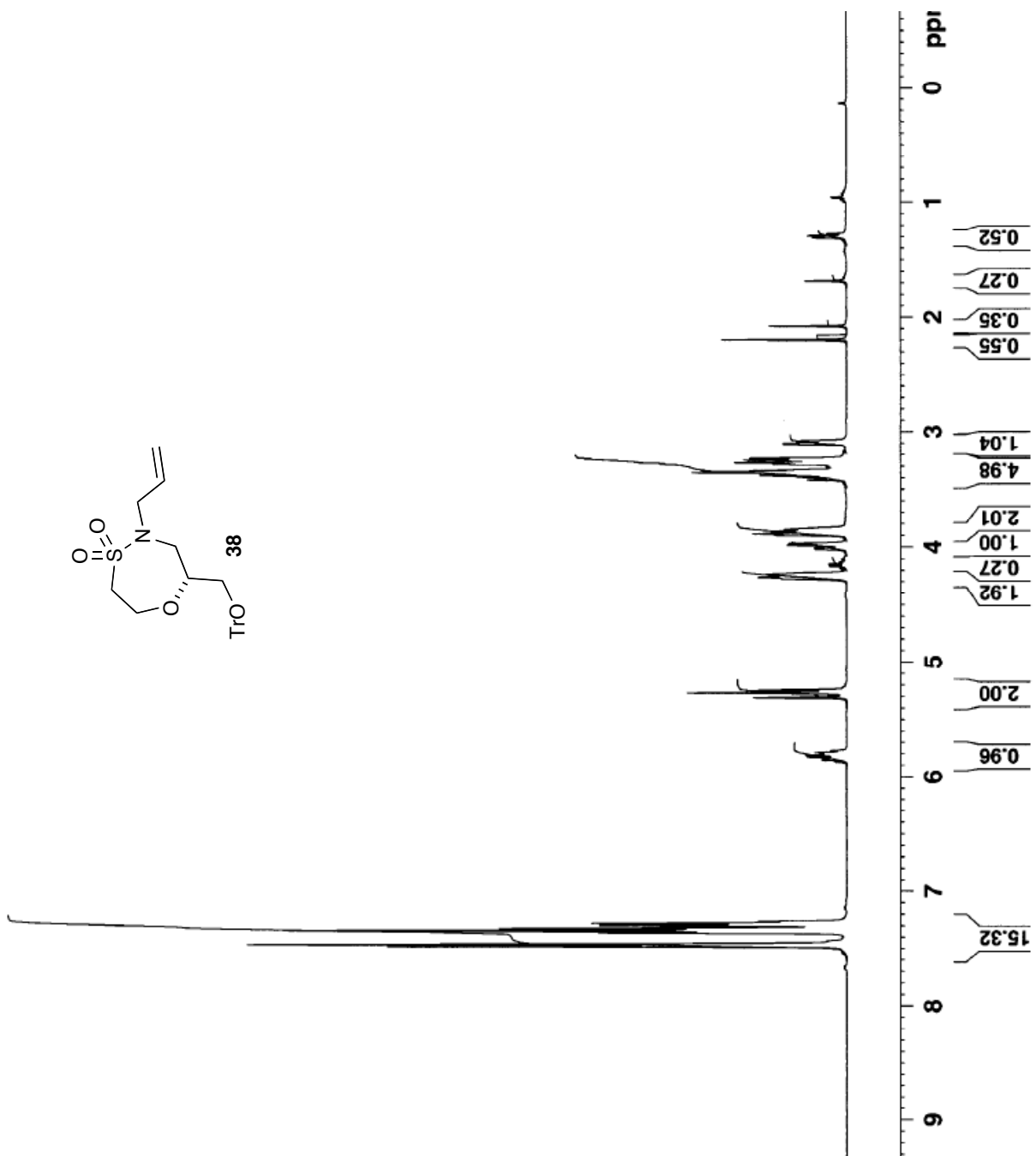


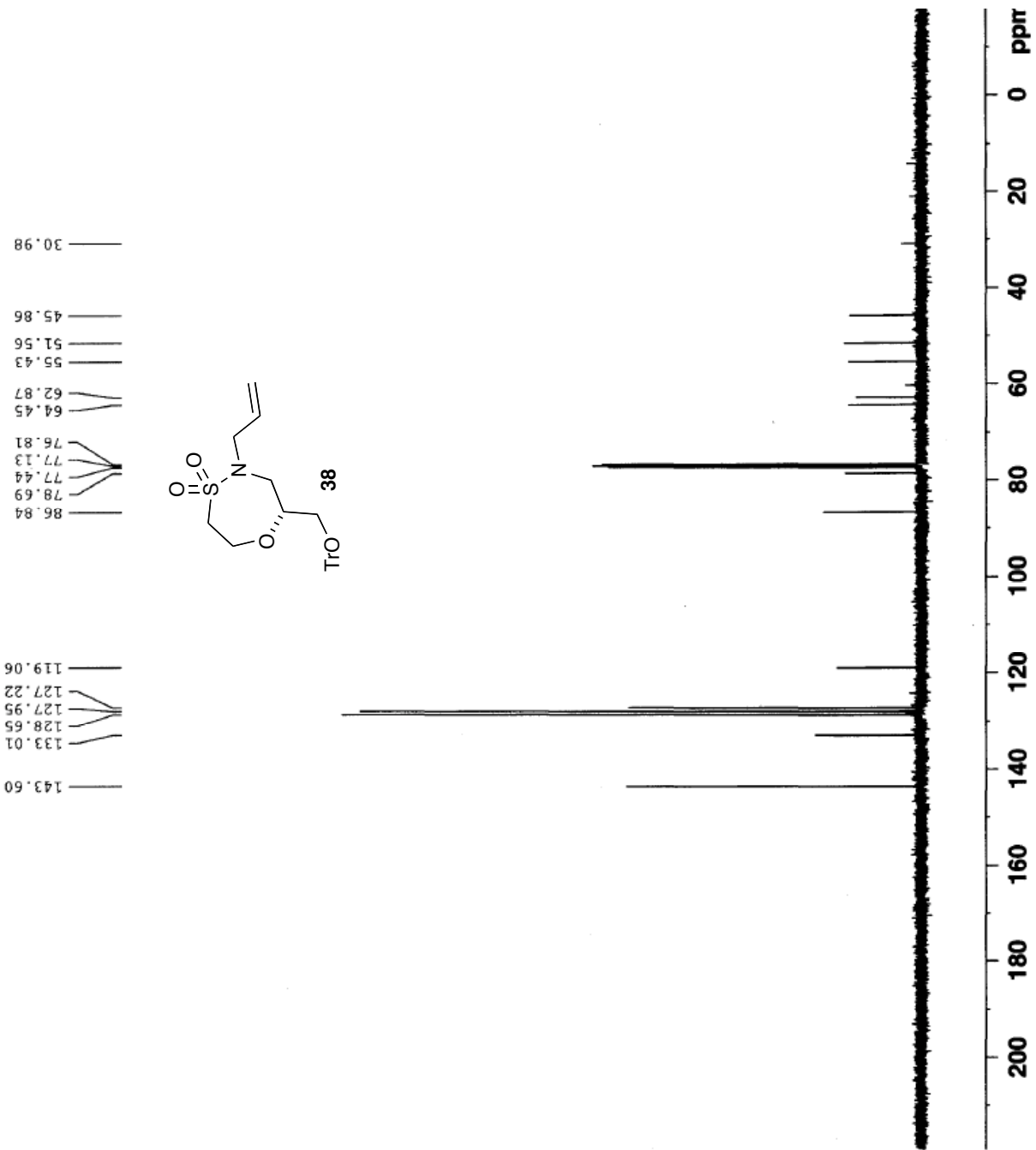


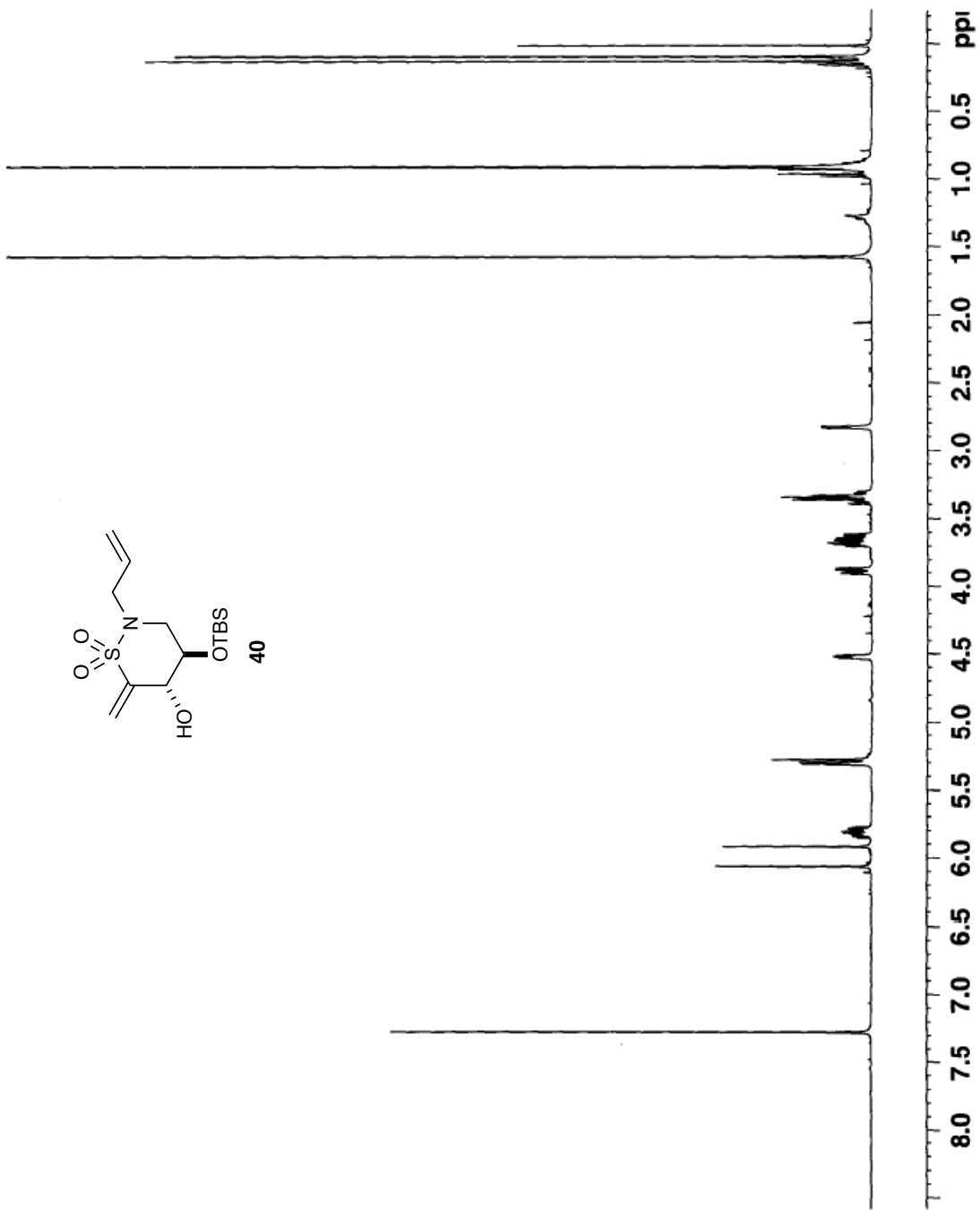


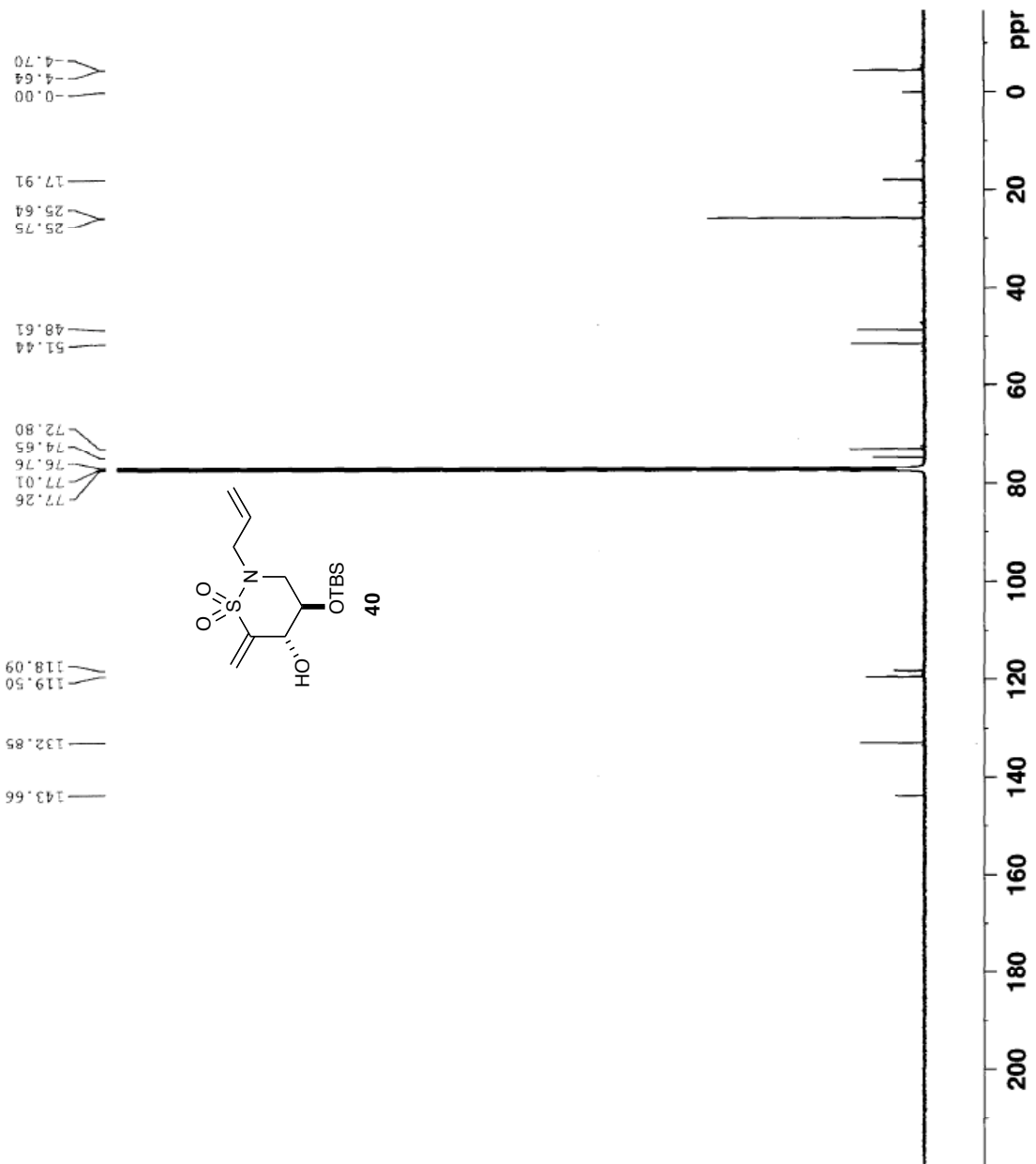


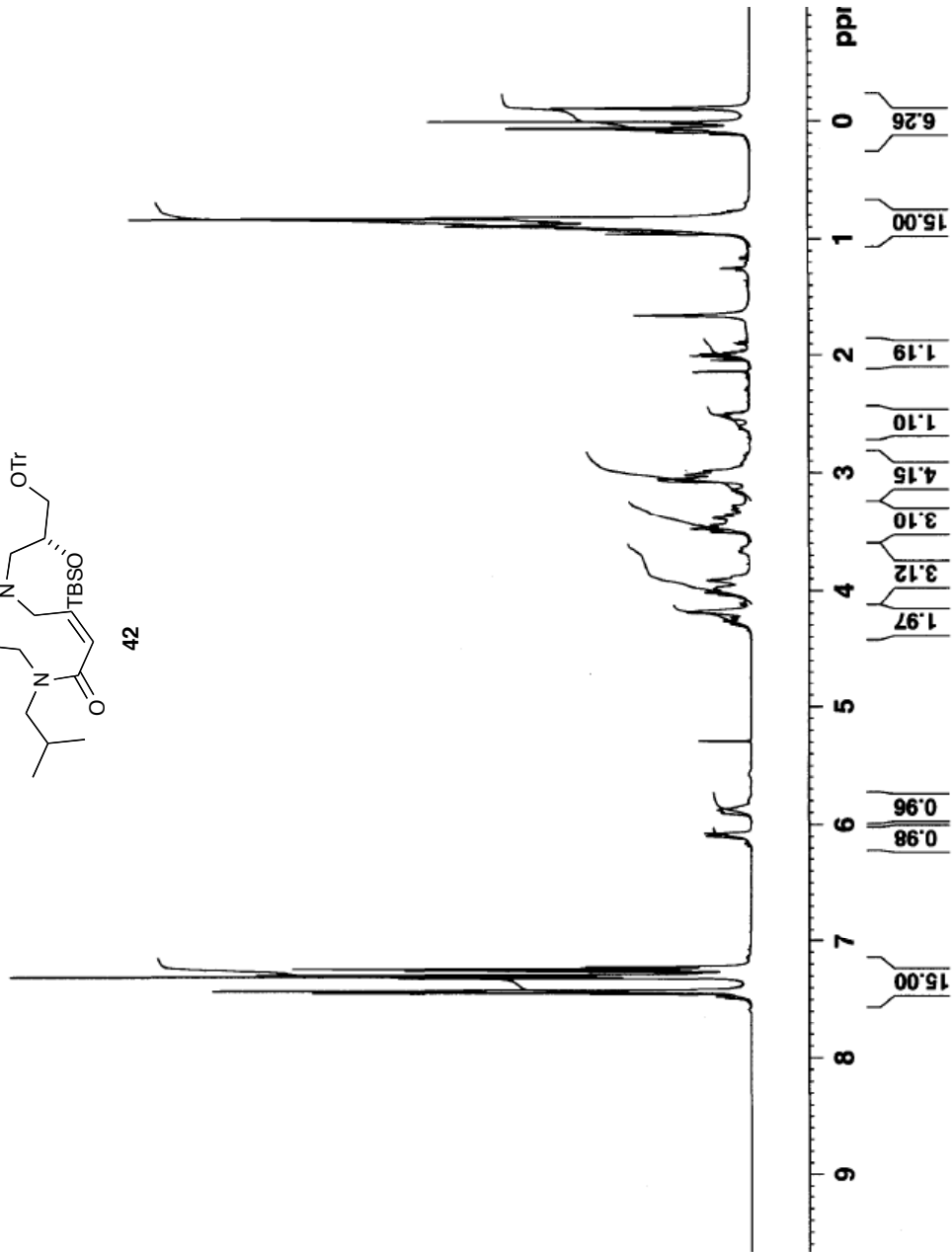
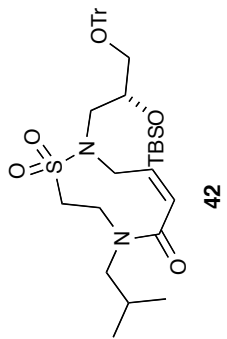




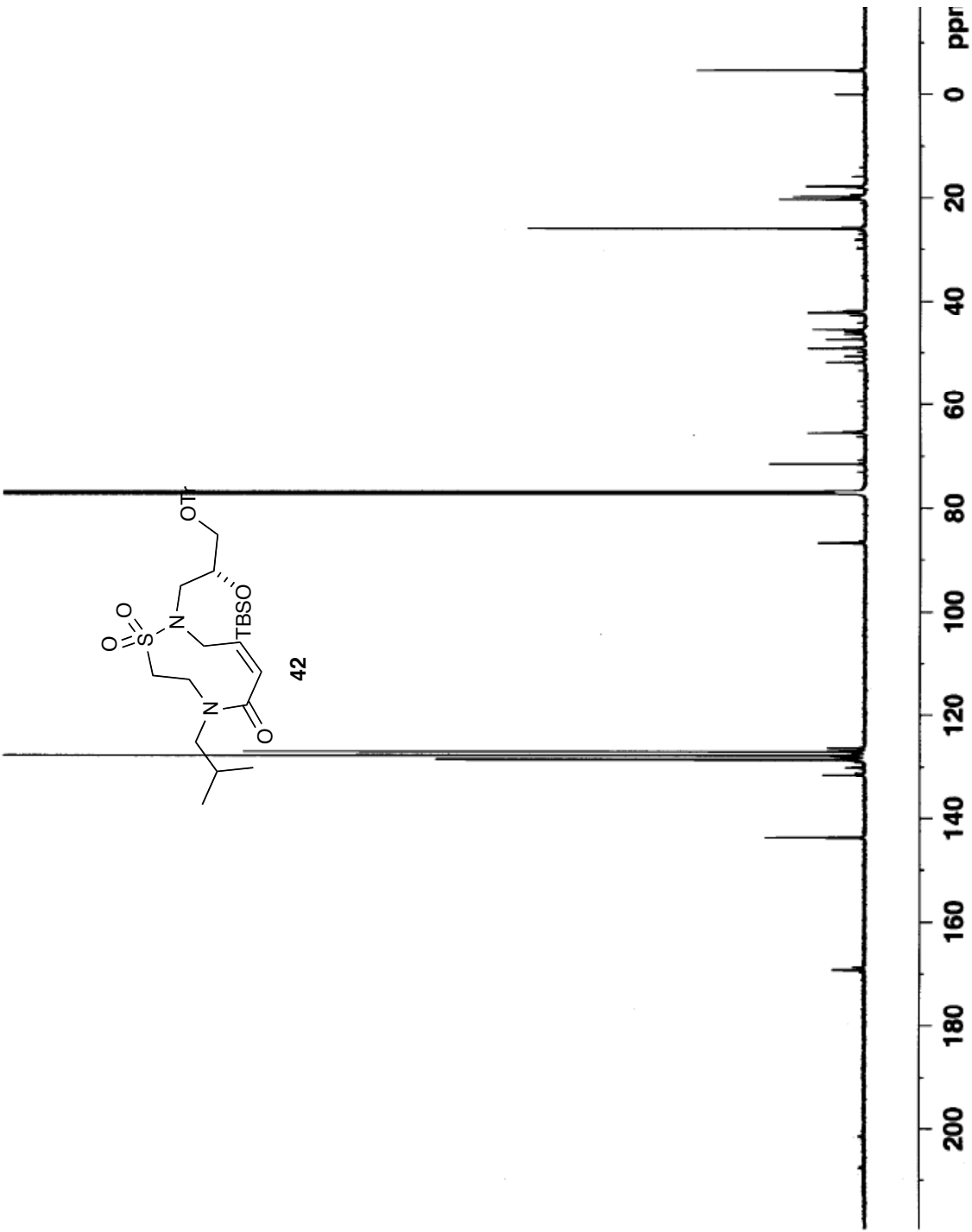


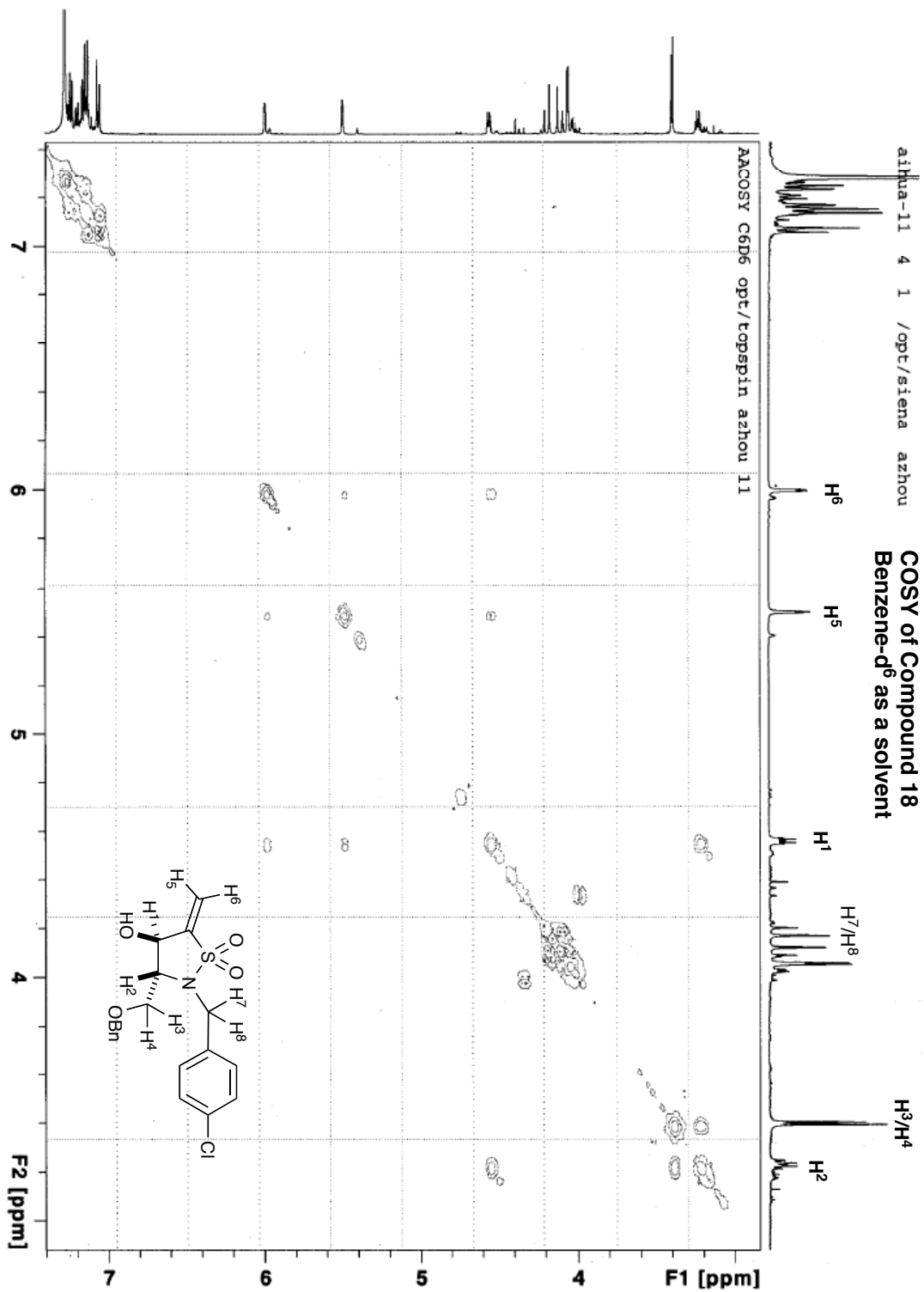


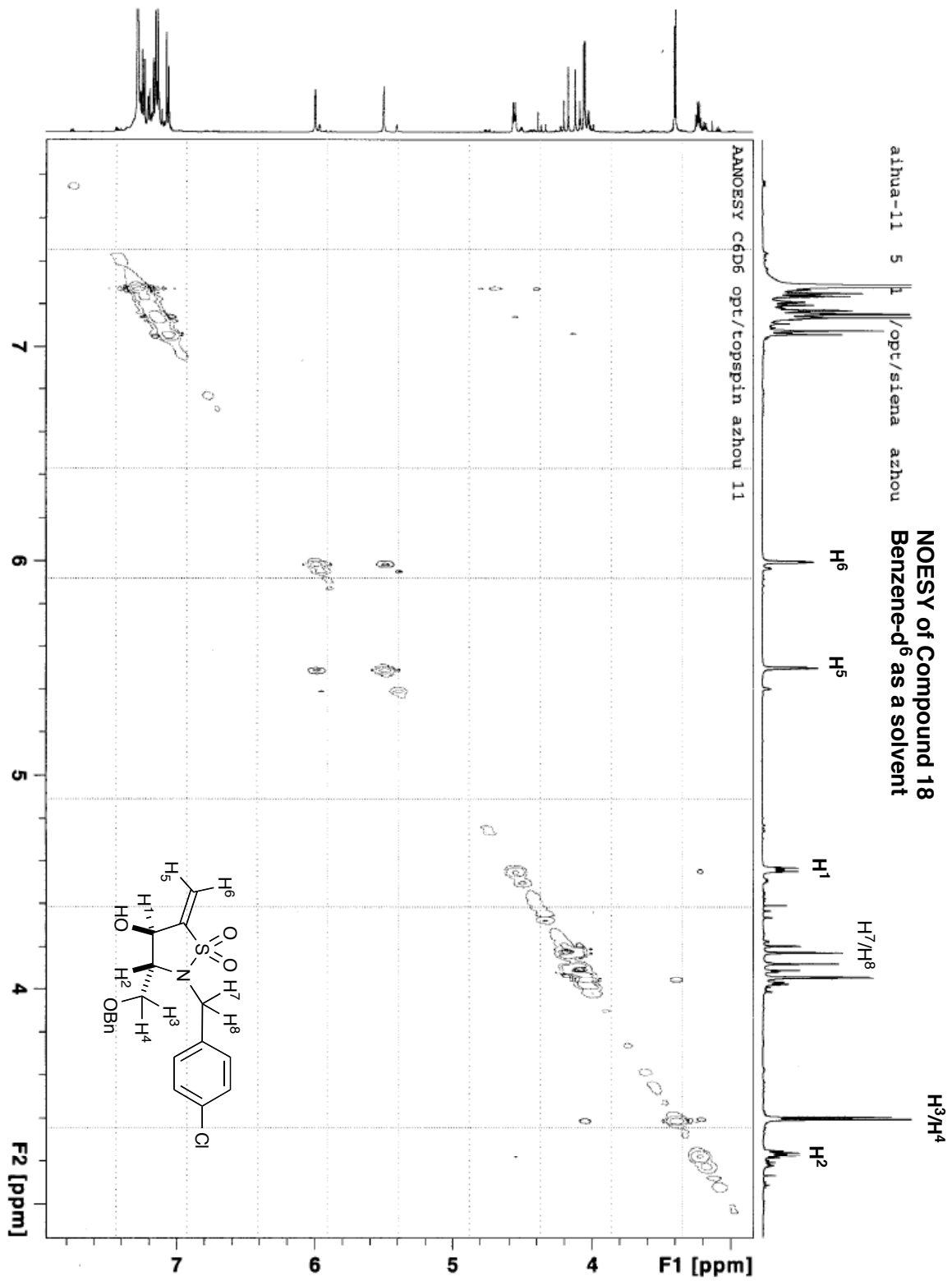












# COSY of Compound 40

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