

*Supporting Information for*

**An RCM Strategy to Stereodiverse  $\delta$ -Sultam Scaffolds**

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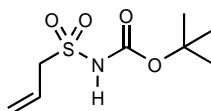
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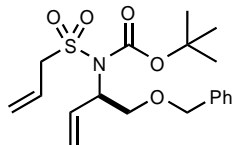
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## General Experimental:

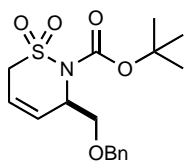
All reactions were carried out in flame-dried glassware under argon. Toluene, THF, Et<sub>2</sub>O, and CH<sub>2</sub>Cl<sub>2</sub> were purified by passage through a purification system (Solv-Tek) employing activated Al<sub>2</sub>O<sub>3</sub>. Et<sub>3</sub>N was distilled from CaH<sub>2</sub>. Flash column chromatography was performed with Merck silica gel (EM-9385-9, 230–400 mesh). Thin layer chromatography (TLC) was performed on silica gel 60F254 plates (EM-5715-7, Merck). <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded in CDCl<sub>3</sub>, MeOD or Acetone-*d*<sub>6</sub> on either a Bruker DRX-400 or a Bruker AM-500 spectrometer operating at 400/100 MHz and 500/125 MHz, respectively. High-resolution mass spectrometry (HRMS) and FAB spectra were obtained on a VG Instrument ZAB double-focusing mass spectrometer. Infrared data was obtained on a Nicolet 320 Fourier Transform Infrared Spectrophotometer. Melting points were obtained on a Thomas Hoover capillary melting point apparatus. Optical rotations were carried out on a Rudolph Automatic Polarimeter (AUTOPOL IV).



**tert-butyl allylsulfonylcarbamate (9):** To a solution of allyl sulfonamide **8** (500 mg, 4.13 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5.2 mL) was added DMAP (50 mg, 0.41 mmol) and Et<sub>3</sub>N (459 mg, 4.53 mmol, 0.63 mL), followed by the dropwise addition of a solution of Boc<sub>2</sub>O (1.04 g, 4.75 mmol, 1.09 mL) in CH<sub>2</sub>Cl<sub>2</sub> (8.3 mL) over 15 min with stirring. The reaction was stirred at rt for 2.5 h after which the solvent was removed. To the crude mixture was added 1N HCl (25 mL) and the solution extracted with EtOAc (4 × 50 mL). The organic layer was washed with water (25 mL) and brine (25 mL), dried over MgSO<sub>4</sub>, filtered and the solvent removed under reduced pressure. Flash chromatography (SiO<sub>2</sub>, 3:1 Heptane/EtOAc) afforded 851 mg (93%) of carbamate **9** as a yellow oil, which solidified to a crystalline yellow solid upon standing in the fridge overnight. A small amount of the bisprotected product (46 mg, 4%) was also isolated. TLC R<sub>f</sub> = 0.32 (1:1 Heptane/EtOAc); Mp = 43–45 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.97 (s, 1H, N-H), 5.90 (dddd, *J* = 17.4, 10.1, 7.4, 7.4 Hz, 1H), 5.49 (dd, *J* = 10.1, 1.0 Hz, 1H), 5.44 (dd, *J* = 17.0, 1.2 Hz, 1H), 4.11 (d, *J* = 7.4 Hz, 2H), 1.51 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 149.8, 124.8, 124.5, 84.1, 56.6, 27.7; FTIR (neat) 3242, 3094, 2982, 1742, 1641 cm<sup>-1</sup>; HRMS (M+Na<sup>+</sup>) calcd for C<sub>8</sub>H<sub>15</sub>NO<sub>4</sub>SNa 244.0619, found 244.0610.

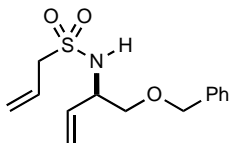


**(R)-tert-butyl allylsulfonyl(1-(benzyloxy)but-3-en-2-yl)carbamate (12):** To a solution of allylic alcohol **11** (120 mg, 0.67 mmol), sulfamoyl carbamate **9** (149 mg, 0.67 mmol) and PPh<sub>3</sub> (228 mg, 0.87 mmol) in THF (13.4 mL) at rt was added DEAD (152 mg, 0.87 mmol, 0.14 mL) dropwise via syringe and the reaction stirred at rt until complete by TLC (usually < 1 h). Flash chromatography (SiO<sub>2</sub>, 6:1 Hexane/EtOAc) afforded 219 mg (79%) of sulfonamide **12** as a yellow oil. TLC R<sub>f</sub> = 0.63 (2:1 Heptane/EtOAc);  $[\alpha]_D^{25} = -9.7$  (c 1.12, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.27-7.19 (m, 5H), 5.92 (ddd, *J* = 17.2, 10.4, 6.5 Hz, 1H), 5.78 (dddd, *J* = 17.4, 10.1, 7.4, 7.4 Hz, 1H), 5.29 (dd, *J* = 9.9, 1.0 Hz, 1H), 5.26 (dd, *J* = 17.1, 1.0 Hz, 1H), 5.23 (dd, *J* = 17.3, 1.0 Hz, 1H), 5.16 (dd, *J* = 10.4, 1.0 Hz, 1H), 4.96-4.90 (m, 1H), 4.52 (d, *J* = 11.8 Hz, 1H), 4.44 (d, *J* = 11.8 Hz, 1H), 4.16 (dd, *J* = 13.8, 7.6 Hz, 1H), 4.05 (dd, *J* = 13.7, 7.2 Hz, 1H), 3.84 (dd, *J* = 9.6, 8.8 Hz, 1H), 3.59 (dd, *J* = 9.7, 6.2 Hz, 1H), 1.43 (s, 9H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 151.0, 137.8, 134.0, 128.4, 127.7, 127.7, 124.7, 124.6, 118.5, 84.6, 73.0, 69.9, 59.3, 58.4, 28.0; FTIR (neat) 3088, 3030, 2978, 2930, 2868, 1726, 1639, 1497 cm<sup>-1</sup>; HRMS (M+Na<sup>+</sup>) calcd for C<sub>19</sub>H<sub>27</sub>NO<sub>5</sub>SNa 404.1508, found 404.1527.

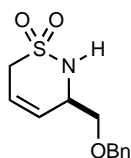


**1,2-thiazine-N-carboxylic acid-3,6-dihydro-3R-[(phenylmethoxy)methyl]-1,1-dimethyl-ethyl ester-1,1-dioxide (13):** To a solution of diene **12** (2.5 g, 6.55 mmol) in degassed toluene (655 mL) was added Grubbs second generation catalyst (278 mg, 0.328 mmol) in one portion and the reaction heated at reflux for 3 h. The solvent was removed under reduced pressure, CH<sub>2</sub>Cl<sub>2</sub> (50 mL) added and the residual ruthenium removed by addition of DMSO (1.28 g, 16.4 mmol, 1.16 mL), followed by stirring at rt for 12 h. Flash chromatography (SiO<sub>2</sub>, 3:1 Hexane/EtOAc) afforded 2.0 g (87 %) of sultam **13** as an ivory solid. TLC R<sub>f</sub> = 0.33 (2:1 Heptane/EtOAc); Mp = 68-73 °C;  $[\alpha]_D^{25} = +120.4$  (c 0.95, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.34-7.27 (m, 5H), 6.01 (dddd, *J* = 10.8, 4.0, 1.6, 1.6 Hz, 1H), 5.78 (dddd, *J* = 10.4, 5.6, 2.8, 1.6 Hz, 1H), 5.27-5.24

(m, 1H), 4.55 (s, 2H), 3.92 (dddd,  $J = 16.4, 2.4, 2.4, 2.4$  Hz, 1H), 3.78 (d,  $J = 6.4$  Hz, 2H), 3.77-3.72 (m, 1H), 1.49 (s, 9H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  150.5, 137.8, 128.3, 127.6, 127.6, 126.8, 118.3, 84.6, 73.2, 70.7, 60.0, 50.3, 27.8; FTIR (neat) 2980, 2928, 2866, 1722, 1454  $\text{cm}^{-1}$ ; HRMS ( $\text{M}+\text{Na}^+$ ) calcd for  $\text{C}_{17}\text{H}_{23}\text{NO}_5\text{SNa}$  376.1195, found 376.1212.

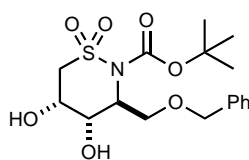


**(R)-N-(1-(benzyloxy)but-3-en-2-yl)prop-2-ene-1-sulfonamide (14):** To a solution of diene **12** (330 mg, 0.87 mmol) in  $\text{CH}_2\text{Cl}_2$  (3 mL) was added an excess of TFA (1 mL) dropwise via syringe and the reaction stirred at rt until all starting material was consumed (~30 min) by TLC analysis. The reaction mixture was quenched with 15 mL of saturated  $\text{NaHCO}_3$  and extracted with  $\text{CH}_2\text{Cl}_2$  ( $4 \times 25$  mL). The organic layers were combined, dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated under reduced pressure. Flash chromatography ( $\text{SiO}_2$ , 3:1 Heptane/EtOAc) afforded 227 mg (93%) of sulfonamide **14** as a light yellow oil. TLC  $R_f = 0.70$  (1:1 Heptane/EtOAc);  $[\alpha]_D^{25} = +4.6$  ( $c$  0.81,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.38-7.28 (m, 5H), 5.90 (dddd,  $J = 17.2, 10.0, 7.2, 7.2$  Hz, 1H), 5.83 (ddd,  $J = 17.2, 10.4, 6.8$  Hz, 1H), 5.38 (dd,  $J = 10.8, 1.0$  Hz, 1H), 5.37 (dd,  $J = 17.2, 1.0$  Hz, 1H), 5.35 (dd,  $J = 17.2, 1.0$  Hz, 1H), 5.26 (dd,  $J = 10.4, 1.0$  Hz, 1H), 4.81 (d,  $J = 7.5$  Hz, 1H), 4.56 (d,  $J = 11.9$  Hz, 1H), 4.51 (d,  $J = 11.8$  Hz, 1H), 4.17-4.11 (m, 1H), 3.73 (dd,  $J = 6.7, 6.0$  Hz, 2H), 3.60 (dd,  $J = 9.5, 4.1$  Hz, 1H), 3.50 (dd,  $J = 9.5, 5.4$  Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  137.3, 135.4, 128.4, 127.8, 127.7, 125.7, 123.7, 117.7, 73.2, 72.3, 57.9, 56.1; FTIR (neat) 3283, 3086, 3030, 2921, 2862, 1641  $\text{cm}^{-1}$ ; HRMS ( $\text{M}+\text{Na}^+$ ) calcd for  $\text{C}_{14}\text{H}_{19}\text{NO}_3\text{SNa}$  304.0983, found 304.1003.

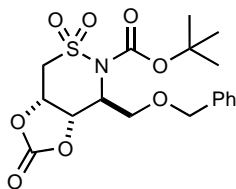


**(R)-2H-1,2-thiazine-3,6-dihydro-3-[(phenylmethoxy)methyl]-1,1-dioxide (15):** In a procedure similar to the preparation of sultam **13**, a solution of sulfonamide **14** (217 mg, 0.77 mmol) in degassed  $\text{CH}_2\text{Cl}_2$  (154 mL) was treated with Grubbs second generation catalyst (33 mg, 0.039 mmol) and the mixture subjected to the RCM reaction. Removal of the residual ruthenium with

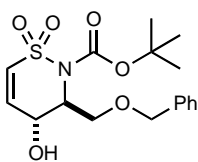
DMSO, followed by purification via flash chromatography (SiO<sub>2</sub>, 3:1 Heptane/EtOAc) afforded 180 mg (92%) of sultam **15** as an ivory solid. TLC R<sub>f</sub> = 0.12 (2:1 Heptane/EtOAc); Mp = 79-83 °C; [α]<sub>D</sub><sup>25</sup> = + 41.7 (*c* = 1.19, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.39-7.29 (m, 5H), 5.86-5.76 (m, 2H), 4.81, (d, *J* = 7.1 Hz, 1H), 4.57 (d, *J* = 12.0 Hz, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.31-4.26 (m, 1H) 3.74-3.68 (m, 1H), 3.64 (d, *J* = 4.4 Hz, 2H), 3.63-3.58 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 137.1, 128.5, 128.0, 127.8, 127.2, 120.9, 73.3, 70.2, 56.8, 47.5; FTIR (neat) 3252, 3032, 2922, 2866, 1653, 1498 cm<sup>-1</sup>; HRMS (M+NH<sub>4</sub><sup>+</sup>) calcd for C<sub>12</sub>H<sub>19</sub>N<sub>2</sub>O<sub>3</sub>S 271.1116, found 271.1108.



**1,2-thiazine-*N*-carboxylic acid-3,4,5,6-tetrahydro-(3*S*)-[(phenylmethoxy)methyl]-(4*R*,5*S*)-dihydroxy-1,1-dimethylethyl ester-1,1-dioxide (16):** To a solution of sultam **13** (566 mg, 1.60 mmol), NMO (255 mg, 1.92 mmol) and citric acid (504 mg, 2.40 mmol) in acetone (3 mL) and water (1 mL) was added a 4 % aqueous solution of OsO<sub>4</sub> (0.016 mmol, 40 μL) and the reaction stirred at rt for 12 h. The reaction was quenched with a 10% aqueous solution of Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (15 mL), extracted with CH<sub>2</sub>Cl<sub>2</sub> (4 × 15 mL), the organic layers combined, dried over MgSO<sub>4</sub>, filtered and concentrated under reduced pressure. Flash chromatography (SiO<sub>2</sub>, 1:1 Hexanes/EtOAc) afforded 598 mg (96%) of diol **16** as a white crystalline solid. TLC R<sub>f</sub> = 0.11 (1:1 Hexane/EtOAc); Mp = 105-110°C; [α]<sub>D</sub><sup>25</sup> = + 14.0 (*c* 1.65, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.37-7.28 (m, 5H), 4.83 (ddd, *J* = 9.2, 6.0, 3.2 Hz, 1H), 4.56 (d, *J* = 11.6 Hz, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.33-4.28 (m, 1H), 4.18 (bs, 1H), 3.76 (dd, *J* = 9.6, 9.2 Hz, 1H), 3.66 (dd, *J* = 10.0, 6.0 Hz, 1H), 3.52 (dd, *J* = 12.8, 10.4 Hz, 1H), 3.33 (dd, *J* = 12.8, 4.4 Hz, 1H), 2.65 (s, 2H, O-H), 1.49 (s, 9H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 151.8, 137.4, 128.5, 128.1, 128.0, 85.3, 73.4, 68.5, 66.4, 65.8, 60.5, 52.3, 27.9; FTIR (neat) 3477 (O-H), 3030, 2982, 2932, 2872, 1724 cm<sup>-1</sup>; HRMS (M+Na<sup>+</sup>) calcd for C<sub>17</sub>H<sub>25</sub>NO<sub>7</sub>SNa 410.1250, found 410.1254.

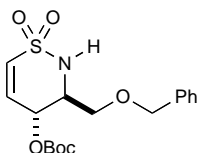


**1,2-thiazine-1,1-dioxide-*N*-carboxylic acid-3,4,5,6-tetrahydro-(3*S*)-[(phenylmethoxy)methyl]-cyclic-(4*R*,5*S*)-cyclocarbonate-1,1-dimethylethyl ester (16a):** To a solution of *cis*-diol **16** (525 mg, 1.36 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (38 mL) at -78 °C was added pyridine (3.22 g, 40.8 mmol) and triphosgene (604 mg, 2.03 mmol) in one portion. After stirring for 10 min at -78 °C the temperature was raised to 0 °C and the reaction stirred at that temperature for 1 h. The crude mixture was quenched with 10 % HCl (15 mL) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (4 × 25 mL), dried over MgSO<sub>4</sub>, filtered and concentrated under reduced pressure. Flash chromatography (SiO<sub>2</sub>, 1.5:1 Hexanes/EtOAc) afforded 544 mg (97%) of the carbonate as a white fluffy solid. TLC R<sub>f</sub> = 0.35 (1:1 Hexane/EtOAc); Mp = 55-65 °C; [α]<sub>D</sub><sup>25</sup> = + 6.2 (*c* 1.40, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.40-7.28 (m, 5H), 5.17 (ddd, *J* = 8.8, 4.4, 2.0 Hz, 1H), 5.07 (dd, *J* = 8.8, 2.0 Hz, 1H), 4.99 (app q, *J* = 2.8 Hz, 1H), 4.56 (d, *J* = 11.6 Hz, 1H), 4.47 (d, *J* = 11.6 Hz, 1H), 4.14 (dd, *J* = 15.6, 4.4 Hz, 1H), 3.86 (dd, *J* = 10.8, 2.8 Hz, 1H), 3.77 (dd, *J* = 10.8, 3.6 Hz, 1H), 3.47 (dd, *J* = 15.2, 2.0 Hz, 1H), 1.55 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 152.2, 151.1, 136.1, 128.9, 128.6, 128.0, 86.2, 74.0, 73.8, 72.4, 70.5, 59.0, 51.6, 27.9; FTIR (neat) 2982, 2939, 1819, 1730, 1454 cm<sup>-1</sup>; HRMS (M+Na<sup>+</sup>) calcd for C<sub>18</sub>H<sub>23</sub>NO<sub>8</sub>SNa 436.1042, found 436.1043.

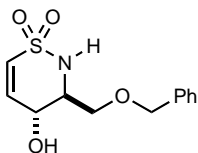


**1, 2thiazine-*N*-carboxylic acid-3, 4-dihydro-(3*S*)-[(phenylmethoxy)methyl]--(4*S*)-hydroxy-1, 1-dimethylethyl ester-1, 1-dioxide (18):** To a solution of the carbonate obtained in the previous reaction (70 mg, 0.174 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (1.7 mL) was added Et<sub>3</sub>N (19.3 mg, 0.19 mmol) and the reaction heated at reflux for 1 h. Flash chromatography (SiO<sub>2</sub>, 2:1 Hexanes/EtOAc) afforded 56.6 mg (91%) of  $\gamma$ -hydroxy sultam **18** as a white solid. TLC R<sub>f</sub> = 0.32 (1:1 Hexanes/EtOAc); Mp = 85-87 °C; [α]<sub>D</sub><sup>25</sup> = -64.4 (*c* 1.03, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.36-7.29 (m, 5H), 6.47 (ddd, *J* = 10.4, 4.8, 1.2 Hz, 1H), 6.43 (d, *J* = 10.8 Hz, 1H), 4.92-4.87 (m, 1H), 4.58 (d, *J* =

11.6 Hz, 1H), 4.49 (d,  $J = 11.6$  Hz, 1H), 4.39-4.35 (m, 1H), 3.70 (dd,  $J = 8.8, 4.8$  Hz, 2H), 2.47 (d,  $J = 8.5$  Hz, 1H), 1.53 (s, 9H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  151.1, 137.3, 133.9, 129.4, 128.4, 127.9, 127.8, 85.7, 73.3, 68.3, 61.4, 61.4, 27.9; FTIR (neat) 3493, 3059, 3035, 2982, 2927, 2872, 1732, 1641  $\text{cm}^{-1}$ ; HRMS ( $\text{M}+\text{Na}^+$ ) calcd for  $\text{C}_{17}\text{H}_{23}\text{NO}_6\text{SNa}$  392.1144, found 392.1150.

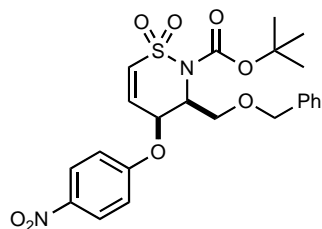


**1,2-thiazine-1,1-dioxide-3,4-dihydro-(3S)-[(phenylmethoxy)methyl]-(4S)-tert-butyl-carbonate (19):** To a solution of sultam **18** (25 mg, 0.067 mmol) in THF (0.67 mL) was added  $\text{Cs}_2\text{CO}_3$  (24 mg, 0.074 mmol) and the reaction stirred at 60 °C for 1 h. The crude product was filtered and purified by flash chromatography ( $\text{SiO}_2$ , 4:1 Hexanes/ EtOAc) to afford 17.9 mg (71%) of sultam **19** as a clear oil. TLC  $R_f = 0.64$  (2:1 Hexanes/EtOAc);  $[\alpha]_D^{25} = -75.9$  ( $c$  0.20,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.38-7.29 (m, 5H), 6.63 (dd,  $J = 11.2, 2.0$  Hz, 1H), 6.36 (dd,  $J = 11.2, 2.0$  Hz, 1H), 5.48 (ddd,  $J = 12.0, 4.0, 2.0$  Hz, 1H), 4.98 (d,  $J = 12.4$  Hz, 1H), 4.58 (d,  $J = 11.6$  Hz, 1H), 4.50 (d,  $J = 11.6$  Hz, 1H), 4.00 (dddd,  $J = 12.5, 5.0, 2.5, 2.5$  Hz, 1H), 3.68 (dd,  $J = 10.0, 1.6$  Hz, 1H), 3.59 (dd,  $J = 10.0, 2.8$  Hz, 1H), 1.50 (s, 9H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  153.3, 137.0, 136.3, 130.3, 128.6, 128.2, 128.0, 83.9, 73.7, 66.7, 66.0, 56.0, 27.7; FTIR (neat) 3285, 3063, 2982, 1743, 1618, 1456, 1369, 1151  $\text{cm}^{-1}$ ; HRMS ( $\text{M}+\text{Na}^+$ ) calcd for  $\text{C}_{17}\text{H}_{23}\text{NO}_6\text{SNa}$  392.1144, found 392.1138.



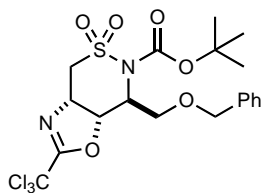
**(3S,4R)-2H-1,2-thiazine-3,4-dihydro-3[(phenylmethoxy)methyl]-4-hydroxy-1,1-dioxide (20):** In a procedure similar to the preparation of sulfonamide **14**,  $\gamma$ -hydroxy sultam **18** (75.0 mg, 0.20 mmol) in  $\text{CH}_2\text{Cl}_2$  (1.0 mL) was treated with TFA (0.1 mL) and the solution stirred at rt for 30 min. Flash chromatography ( $\text{SiO}_2$ , 1:1.5 Hexanes/EtOAc) afforded 49.3 mg (91%) of sultam **20** as a white crystalline solid. TLC  $R_f = 0.30$  (1:1.5 Hexanes/EtOAc); Mp = 115-125 °C;  $[\alpha]_D^{25} =$

-15.7 (*c* 0.25, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.38-7.30 (m, 5H), 6.55 (dd, *J* = 10.8, 2.4 Hz, 1H), 6.37 (dd, *J* = 10.8, 2.0 Hz, 1H), 4.78 (d, *J* = 12.4 Hz, 1H), 4.58 (d, *J* = 11.6 Hz, 1H), 4.53 (d, *J* = 11.6 Hz, 1H), 4.55-4.50 (m, 1H), 3.91 (dd, *J* = 9.6, 2.0 Hz, 1H), 3.84-3.77 (m, 1H), 3.61 (dd, *J* = 9.6, 3.6 Hz, 1H), 2.17 (d, *J* = 7.2 Hz, 1H); <sup>13</sup>C NMR (125 MHz, Acetone-*d*<sub>6</sub>) δ 141.6, 138.5, 128.8, 128.2, 127.5, 127.4, 72.9, 68.4, 62.8, 59.2; FTIR (neat) 3518, 3240, 3060, 2920, 1623, 1406 cm<sup>-1</sup>; HRMS (M+NH<sub>4</sub><sup>+</sup>) calcd for C<sub>12</sub>H<sub>19</sub>N<sub>2</sub>O<sub>4</sub> 287.1066, found 287.1078.

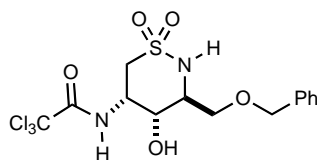


**1,2-thiazine-*N*-carboxylic acid-3,4-dihydro-(3*S*)-[(phenylmethoxy)methyl]-(4*R*)-(p-nitrophenoxy)-1,1-dimethylethyl ester-1, 1-dioxide (21):** To a solution of sultam **18** (50 mg, 0.14 mmol) in THF (0.70 mL) was added *p*-nitrophenol (19.0 mg, 0.14 mmol) and PPh<sub>3</sub> (40 mg, 0.15 mmol), followed by the dropwise addition of DEAD (26.0 mg, 0.15 mmol, 24 μL) at rt. The reaction was stirred at rt until complete consumption of sultam **18** (less than 1 h) by TLC analysis. Flash chromatography (SiO<sub>2</sub>, 2:1 Heptane/EtOAc) afforded 30 mg (45 %) of **21** as an ivory solid. TLC R<sub>f</sub> = 0.69 (1:1 Hexanes/EtOAc); Mp = 148-155 °C; [α]<sub>D</sub><sup>25</sup> = +2.4 (*c* 0.20, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.24 (d, *J* = 9.2 Hz, 2H), 7.33-7.27 (m, 5H), 7.00 (d, *J* = 9.2 Hz, 2H), 6.47 (dd, *J* = 11.2, 2.4 Hz, 1H), 6.40 (ddd, *J* = 11.2, 1.6, 1.6 Hz, 1H), 5.50-5.48 (m, 1H), 5.27-5.21 (m, 1H), 4.55 (d, *J* = 11.2 Hz, 1H), 4.49 (d, *J* = 11.2 Hz, 1H), 4.05 (dd, *J* = 10.0, 10.0 Hz, 1H), 3.89 (dd, *J* = 10.4, 4.4 Hz, 1H), 1.52 (s, 9H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 160.5, 150.8, 142.7, 137.6, 133.6, 129.5, 128.2, 127.8, 127.7, 126.3, 115.2, 85.9, 73.5, 70.0, 65.5, 57.1, 27.8; FTIR (neat) 2980, 2932, 2874, 1732, 1610, 1518, 1342 cm<sup>-1</sup>; HRMS (M+NH<sub>4</sub><sup>+</sup>) calcd for C<sub>23</sub>H<sub>30</sub>N<sub>3</sub>O<sub>8</sub>S 508.1754, found 508.1729.



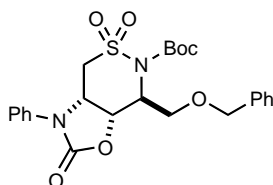


**Trichlorooxazole-containing sultam (22):** To a cold solution (-50 °C) of sultam **18** (50 mg, 0.135 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (1.35 mL) was added Cl<sub>3</sub>CCN (20 μL) and DBU (4.1 mg, 0.027 mmol, 4.0 μL). The reaction was stirred until it slowly reached rt. The reaction was quenched with saturated NH<sub>4</sub>Cl (15 mL) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (4 × 15 mL). The organic layers were combined, dried over MgSO<sub>4</sub>, filtered and concentrated under reduced pressure. Flash chromatography (SiO<sub>2</sub>, 2:1 Hexanes/EtOAc) afforded 66 mg (96 %) of **22** a white solid. TLC R<sub>f</sub> = 0.58 (1:1 Hexanes/EtOAc); Mp = 49-54 °C; [α]<sub>D</sub><sup>25</sup> = +28.4 (*c* = 0.67, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.40-7.30 (m, 5H), 5.27 (dd, *J* = 10.4, 2.0 Hz, 1H), 5.18 (ddd, *J* = 4.4, 4.4, 2.0 Hz, 1H), 4.91 (ddd, *J* = 10.0, 5.6, 2.4 Hz, 1H), 4.59 (d, *J* = 11.6 Hz, 1H), 4.51 (d, *J* = 11.6 Hz, 1H), 4.04 (dd, *J* = 14.8, 5.6 Hz, 1H), 3.79 (d, *J* = 4.4 Hz, 2H), 3.53 (dd, *J* = 14.8, 2.4 Hz, 1H), 1.52 (s, 9H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) 163.1, 151.2, 136.5, 128.7, 128.4, 128.0, 85.6, 80.5, 80.5, 73.9, 70.1, 63.6, 58.9, 51.2, 27.9; FTIR (neat) 2982, 2935, 2972, 1728, 1666, 1454, 1369, 1346 cm<sup>-1</sup>; HRMS (M+H<sup>+</sup>) calcd for C<sub>19</sub>H<sub>24</sub>Cl<sub>3</sub>N<sub>2</sub>O<sub>6</sub>S 513.0421, found 513.0417.

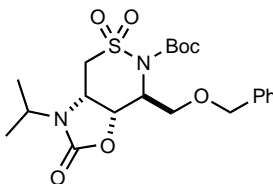


**1,2-thiazine-1,1-dioxide-3,4,5,6-tetrahydrohydro-(3*S*)-[(phenylmethoxy)methyl]-(4*S*)-hydroxy-(5*S*)-(2,2,2-trichloro)acetamide (23):** To a solution of sultam **22** (24.0 mg, 0.047 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.5 mL) was added TFA (0.47 mmol, 35 μL) and the reaction stirred at rt for 1 h. Flash chromatography (SiO<sub>2</sub>, 1:1 Hexanes/EtOAc) afforded 19.4 mg (97%) of trichloroacetimidate **23** as a white solid. TLC R<sub>f</sub> = 0.45 (1:1.5 Hexanes/EtOAc); Mp = 56-64 °C; [α]<sub>D</sub><sup>25</sup> = -41.5 (*c* 0.54, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.51 (d, *J* = 8.8 Hz, 1H), 7.40-7.30 (m, 5H), 4.99 (d, *J* = 9.6 Hz, 1H), 4.90 (dddd, *J* = 8.0, 4.0, 4.0, 4.0 Hz, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.13 (dd, *J* = 10.4, 4.0 Hz, 1H), 3.92 (dd, *J* = 9.6, 2.4 Hz, 1H), 3.63-3.60 (m, 2H), 3.45 (dd, *J* = 14.0, 4.0 Hz, 1H), 3.37 (dd, *J* = 14.0, 4.0 Hz, 1H), 2.70 (s, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 163.9, 137.1, 128.6, 128.2, 128.0, 92.0, 73.7, 67.2, 67.1, 55.1,

51.1, 50.3; FTIR (neat) 3470-3447, 3362, 3064, 3032, 2935, 1713, 1630, 1454  $\text{cm}^{-1}$ ; HRMS ( $\text{M}+\text{H}^+$ ) calcd for  $\text{C}_{14}\text{H}_{18}\text{Cl}_3\text{N}_2\text{O}_5\text{S}$  431.0002, found 431.0026.

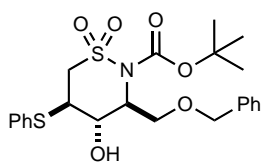


**1,2-thiazine-*N*-carboxylic acid-3,4,5,6-tetrahydro-(3*S*)-[(phenylmethoxy)methyl]-*N'*-phenyl-(4*S*,5*S*)-oxazolidinone-1,1-dimethylethyl ester-1,1-dioxide (24):** To a solution of  $\gamma$ -hydroxy sultam **18** (6.0 mg, 0.016 mmol) in DCE (0.16 mL) was added phenyl isocyanate (2.9 mg, 0.024 mmol) and  $\text{Et}_3\text{N}$  (0.16 mg, 0.016 mmol). The reaction was stirred in a pressure tube at reflux (83  $^\circ\text{C}$ ) until complete by TLC. Flash chromatography ( $\text{SiO}_2$ , 4:1 Hexanes/EtOAc) afforded 5 mg (64%) of bicyclic sultam **24** as a white solid. TLC  $R_f$  = 0.55 (1:1 Hexane/EtOAc); Mp= 160-164  $^\circ\text{C}$ ;  $[\alpha]_D^{25}$  = -52.9 ( $c$  0.17,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.45-7.30 (m, 10H), 5.09 (dd,  $J$  = 9.2, 2.0 Hz, 1H), 5.03-5.01 (m, 1H), 4.93 (ddd,  $J$  = 9.2, 4.8, 2.0 Hz, 1H), 4.59 (d,  $J$  = 11.6 Hz, 1H), 4.53 (d,  $J$  = 11.6 Hz, 1H), 3.93 (dd,  $J$  = 14.8, 4.0 Hz, 1H), 3.89 (dd,  $J$  = 10.4, 3.6 Hz, 1H), 3.83 (dd,  $J$  = 10.8, 3.6 Hz, 1H), 3.22 (dd,  $J$  = 15.2, 2.0 Hz, 1H), 1.55 (s, 9H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  153.5, 151.2, 136.5, 134.7, 129.7, 128.9, 128.5, 128.0, 126.7, 123.7, 85.9, 74.1, 71.0, 70.5, 59.6, 55.4, 48.0, 28.0; FTIR (neat) 3063, 2928, 1765, 1724, 1630, 1599, 1456  $\text{cm}^{-1}$ ; HRMS ( $\text{M}+\text{NH}_4^+$ ) calcd for  $\text{C}_{24}\text{H}_{32}\text{N}_3\text{O}_7\text{S}$  506.1961, found 506.1973.

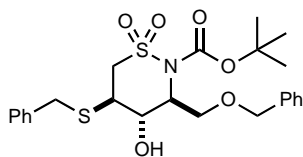


**1,2-thiazine-*N*-carboxylic acid-3, 4, 5, 6-tetrahydro-(3*S*)-[(phenylmethoxy)methyl]-*N'*-isopropyl-(4*S*,5*S*)-oxazolidinone-1,1-dimethylethyl ester-1,1-dioxide (25):** To a solution of  $\gamma$ -hydroxy sultam **18** (41.0 mg, 0.11 mmol) in DCM (0.78 mL) was added isopropyl isocyanate (14.0 mg, 0.166 mmol, 16  $\mu\text{L}$ ) and  $\text{Et}_3\text{N}$  (3.9 mg, 0.039 mmol, 8  $\mu\text{L}$ ). The reaction was heated at 50  $^\circ\text{C}$  in a pressure tube until complete by TLC (~24 h). Flash chromatography ( $\text{SiO}_2$ , 2:1 Hexanes/EtOAc) afforded 39.1 mg (78%) of bicyclic sultam **25** as an ivory solid. TLC  $R_f$  = 0.14

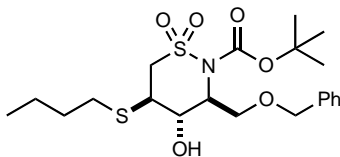
(1:1 Hexanes/EtOAc); Mp = 132-135 °C;  $[\alpha]_D^{25} = -34.5$  ( $c$  0.52,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.40-7.29 (m, 5H), 4.96 (ddd,  $J = 4.0, 4.0, 2.4$  Hz, 1H), 4.79 (dd,  $J = 8.4, 2.0$  Hz, 1H), 4.56 (d,  $J = 11.6$  Hz, 1H), 4.52 (d,  $J = 11.6$  Hz, 1H), 4.33 (ddd,  $J = 8.4, 4.8, 3.2$  Hz, 1H), 3.94 (dd,  $J = 15.2, 5.2$  Hz, 1H), 3.88-3.85 (m, 1H), 3.85 (dd,  $J = 10.8, 4.4$  Hz, 1H), 3.76 (dd,  $J = 10.4, 3.6$  Hz, 1H), 3.26 (dd,  $J = 14.8, 3.2$  Hz, 1H), 1.54 (s, 9H), 1.34 (d,  $J = 7.2$  Hz, 3H), 1.32 (d,  $J = 6.8$  Hz, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  155.1, 151.0, 136.7, 128.8, 128.4, 128.0, 85.7, 73.9, 71.5, 70.3, 59.1, 52.9, 50.6, 46.5, 28.0, 21.5, 20.0; FTIR (neat) 3109, 2980, 1755, 1634, 1520, 1454  $\text{cm}^{-1}$ ; HRMS ( $\text{M}+\text{NH}_4^+$ ) calcd for  $\text{C}_{21}\text{H}_{34}\text{N}_3\text{O}_7\text{S}$  472.2117, found 472.2112.



**1,2-thiazine-*N*-carboxylic acid-3,4,5,6-tetrahydro-(3*S*)-[(phenylmethoxy)methyl]-(4*R*)-hydroxy-(5*R*)-phenylthio-1,1-dimethylethyl ester-1,1-dioxide (26):** To a solution of  $\gamma$ -hydroxy sultam **18** (32 mg, 0.087 mmol) in  $\text{CH}_2\text{Cl}_2$  (0.87 mL) was added PhSH (10.5 mg, 0.095 mmol, 10  $\mu\text{L}$ ) and DMAP (2.0 mg, 0.0174 mmol). The reaction was stirred at rt for 12 h and the solvent removed under reduced pressure. Flash chromatography ( $\text{SiO}_2$ , 4:1 Hexanes/EtOAc) afforded 35 mg (84%, 6:1 mixture of inseparable diastereomers) **26** as a clear oil. (**Major diastereomer**) TLC  $R_f = 0.59$  (1:1 Hexanes/EtOAc);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.44 (dd,  $J = 6.0, 3.0$  Hz, 2H), 7.35-7.28 (m, 6H), 7.22 (dd,  $J = 8.0, 1.5$  Hz, 2H), 4.95 (ddd,  $J = 9.0, 6.0, 2.5$  Hz, 1H), 4.52 (d,  $J = 12.0$  Hz, 1H), 4.42 (d,  $J = 11.5$  Hz, 1H), 4.19 (d,  $J = 2.0$  Hz, 1H), 3.87 (ddd,  $J = 13.0, 3.5, 2.0$  Hz, 1H), 3.74 (dd,  $J = 10.0, 9.0$  Hz, 1H), 3.67 (dd,  $J = 13.5, 12.5$  Hz, 1H), 3.64 (dd,  $J = 10.5, 5.5$  Hz, 1H), 3.22 (dd,  $J = 13.0, 3.5$  Hz, 1H), 2.61 (d,  $J = 3.0$  Hz, 1H), 1.50 (s, 9H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  151.5, 137.5, 132.9, 129.7, 129.7, 128.8, 128.5, 127.9, 127.7, 85.1, 73.3, 68.2, 64.6, 61.7, 50.5, 46.0, 27.9; FTIR (neat) 3504, 3061, 2982, 2932, 1728, 1583, 1454  $\text{cm}^{-1}$ ; HRMS ( $\text{M}+\text{NH}_4^+$ ) calcd for  $\text{C}_{23}\text{H}_{33}\text{N}_2\text{O}_6\text{S}_2$  497.1780, found 497.1778.

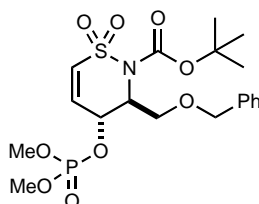


**1,2-thiazine, *N*-carboxylic acid-3,4,5,6-tetrahydro-(3*R*)-[(phenylmethoxy)methyl]-(4*R*)-hydroxy-(5*R*)-benzylthio-1,1-dimethylethyl ester-1,1-dioxide (27):** In a procedure similar to the preparation of sultam **26**, a solution of  $\gamma$ -hydroxy sultam **18** (29 mg, 0.078 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.78 mL) was treated with PhCH<sub>2</sub>SH (10.7 mg, 0.086 mmol, 10  $\mu$ L) and Et<sub>3</sub>N (1.6 mg, 0.0156 mmol, 2.2  $\mu$ L). The reaction was stirred at rt for 12 h and the solvent removed under reduced pressure. Flash chromatography (SiO<sub>2</sub>, 3:1 Hexanes/EtOAc) afforded 38.5 mg (100%) of **27** as a separable mixture of diastereomers (dr ~10:1) as clear oils. (**Major diastereomer**) TLC R<sub>f</sub> = 0.50 (1:1 Hexanes/EtOAc);  $[\alpha]_D^{25} = + 57.7$  (*c* 0.73, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.36-7.25 (m, 10H), 4.88 (ddd, *J* = 8.0, 6.8, 2.4 Hz, 1H), 4.52 (d, *J* = 12.0 Hz, 1H), 4.44 (d, *J* = 12.0 Hz, 1H), 4.00-3.98 (m, 1H), 3.80 (d, *J* = 13.6 Hz, 1H), 3.76 (d, *J* = 13.6 Hz, 1H), 3.58 (dd, *J* = 8.0, 1.2 Hz, 1H), 3.57 (d, *J* = 13.2 Hz, 1H), 3.54 (d, *J* = 13.2 Hz, 1H), 3.39 (ddd, *J* = 13.2, 3.2, 2.0 Hz, 1H), 3.01 (dd, *J* = 13.2, 3.2 Hz, 1H), 2.57 (s, 1H), 1.48 (s, 9H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  150.4, 136.6, 135.7, 127.9, 127.8, 127.4, 126.9, 126.8, 126.7, 83.9, 72.1, 67.3, 63.7, 60.4, 49.5, 40.7, 34.8, 26.9; FTIR (neat) 3504, 2980, 2930, 1726, 1602, 1454, 1138 cm<sup>-1</sup>; HRMS (M+NH<sub>4</sub><sup>+</sup>) calcd for C<sub>24</sub>H<sub>35</sub>N<sub>2</sub>O<sub>6</sub>S<sub>2</sub> 511.1937, found 511.1939.

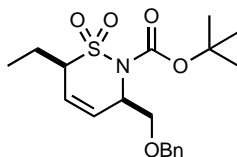


**1,2-thiazine-*N*-carboxylic acid-3,4,5,6-tetrahydro-(3*S*)-[(phenylmethoxy)methyl]-(4*R*)-hydroxy-(5*R*)-butylthio-1,1-dimethylethyl ester-1,1-dioxide (28):** In a procedure similar to the preparation of sultam **27**, a solution of  $\gamma$ -hydroxy sultam **18** (27 mg, 0.073 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.73 mL) was treated with BuSH (7.2mg, 0.080 mmol, 10  $\mu$ L) and Et<sub>3</sub>N (2.2 mg, 0.0219 mmol, 3.0  $\mu$ L). The reaction was stirred at rt for 12 h and the solvent removed under reduced pressure. Flash chromatography (SiO<sub>2</sub>, 3:1 Hexanes/EtOAc) afforded 29.6 mg (88%) of **28** as an inseparable mixture of diastereomers (dr ~4.5:1) as a clear oil. (**Major diastereomer**) TLC R<sub>f</sub> = 0.50 (1:1 Hexanes/EtOAc); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.35-7.29 (m, 5H), 4.97 (ddd, *J* = 9.0, 5.5, 2.5 Hz, 1H), 4.60 (d, *J* = 12.0 Hz, 1H), 4.47 (d, *J* = 12.0 Hz, 1H), 4.12 (app q, *J* = 2.0 Hz, 1H), 3.80 (dd, *J* = 9.5, 9.5 Hz, 1H), 3.67 (dd, *J* = 10.0, 6.0 Hz, 1H), 3.56 (dd, *J* = 13.0, 13.0 Hz, 1H), 3.46 (ddd, *J* = 13.0, 3.0, 2.0 Hz, 1H), 3.17 (dd, *J* = 13.0, 3.0 Hz, 1H), 2.61 (d, *J* = 2.5 Hz,

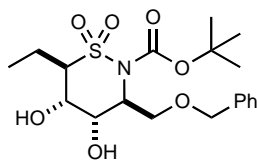
1H), 2.57 (ddd,  $J = 7.5, 7.5, 2.0$  Hz, 2H), 1.57-1.54 (m, 2H), 1.50 (s, 9H), 1.42-1.37 (m, 2H), 0.92 (t,  $J = 7.0$  Hz, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  151.4, 137.6, 128.5, 127.9, 127.8, 85.0, 73.2, 68.2, 64.6, 61.3, 50.7, 42.6, 31.6, 31.3, 27.9, 21.9, 13.6; FTIR (neat) 2959, 2932, 1728, 1624, 1607, 1497, 1454  $\text{cm}^{-1}$ ; HRMS ( $\text{M}+\text{Na}^+$ ) calcd for  $\text{C}_{21}\text{H}_{33}\text{NO}_6\text{S}_2\text{Na}$  482.1647, found 482.1638.



**1,2-thiazine-1,1-dioxide-*N*-carboxylic acid-3, 4-dihydro-(3*S*)-[(phenylmethoxy)-methyl]-1,1-dimethylethyl ester-(4*S*)-dimethylphosphate (29):** To a solution of  $\gamma$ -hydroxy sultam **18** (144 mg, 0.39 mmol) in  $\text{CH}_2\text{Cl}_2$  (4 mL) at 0 °C was added *N*-methylimidazole (96 mg, 1.17 mmol, 84  $\mu\text{L}$ ) and  $(\text{MeO})_2\text{P}(\text{O})\text{Cl}$  (112.6 mg, 0.78 mmol, 84  $\mu\text{L}$ ). The ice bath was removed and the reaction stirred at rt for 1 h. The reaction was quenched with a saturated solution of  $\text{NH}_4\text{Cl}$  (15 mL) and extracted with  $\text{CH}_2\text{Cl}_2$  ( $4 \times 15$  mL). The organic layers were combined, dried over  $\text{MgSO}_4$ , filtered and concentrated under reduced pressure. Flash chromatography ( $\text{SiO}_2$ , 1:2 hexanes/ $\text{EtOAc}$ ) afforded 159 mg (85%) of sultam **29** as a clear oil. TLC  $R_f = 0.37$  (1:2.5 Heptane/ $\text{EtOAc}$ );  $[\alpha]_D^{25} = -83.9$  ( $c$  1.35,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.31-7.23 (m, 5H), 6.46 (d,  $J = 10.6$  Hz, 1H), 6.43 (ddd,  $J = 10.6, 5.3, 1.5$  Hz, 1H), 5.06-5.02 (m, 1H), 4.93 (ddd,  $J = 7.7, 5.4, 2.0$  Hz, 1H), 4.51 (d,  $J = 11.8$  Hz, 1H), 4.43 (d,  $J = 11.7$  Hz, 1H), 3.72 (d,  $J_{\text{HP}} = 11.3$  Hz, 3H), 3.69 (d,  $J_{\text{HP}} = 11.3$  Hz, 3H), 3.62 (dd,  $J = 8.4, 1.3$  Hz, 2H), 1.46 (s, 9H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  150.6, 137.2, 131.6, 129.7 (d,  $J_{\text{CP}} = 15.0$  Hz), 128.5, 128.0, 127.8, 85.8, 73.4, 67.5, 65.2 (d,  $J_{\text{CP}} = 20.0$  Hz), 59.4 (d,  $J_{\text{CP}} = 20.0$  Hz), 54.8 (d,  $J_{\text{CP}} = 25.0$  Hz), 54.8 (d,  $J_{\text{CP}} = 20.0$  Hz), 27.9;  $^{31}\text{P}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.77; FTIR (neat) 3833, 2981, 2959, 1736, 1647, 1456  $\text{cm}^{-1}$ ; HRMS ( $\text{M}+\text{NH}_4^+$ ) calcd for  $\text{C}_{19}\text{H}_{32}\text{N}_2\text{O}_9\text{PS}$  495.1566, found 495.1560.

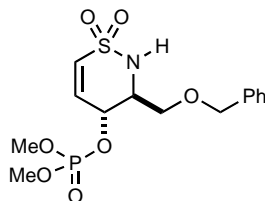


**1,2-thiazine-*N*-carboxylic acid-3,6-dihydro-(3*R*)-[(phenylmethoxy)methyl]-(6*R*)-ethyl- 1,1-dimethylethyl ester-1,1-dioxide (30):** To a solution of CuCN·2 LiCl (1 M, 0.56 mmol) at -78 °C was added Et<sub>2</sub>Zn (1 M, 0.56 mmol) and the mixture stirred at that temperature for 1.5 h. A solution of phosphate **29** (26.5 mg, 0.056 mmol) in THF (0.56 mL) was added to the diethyl cuprate mixture and the solution stirred until it warmed up to -20 °C. The reaction was quenched with a saturated solution of NH<sub>4</sub>Cl (10 mL) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (4 × 10 mL), the organic layers combined, dried over MgSO<sub>4</sub>, filtered and concentrated. Flash chromatography (SiO<sub>2</sub>, 7:1 Hexanes/EtOAc) afforded 15.5 mg (74%) of sultam **30** as a white solid. TLC R<sub>f</sub> = 0.69 (2:1 Hexanes/EtOAc); Mp = 60-65 °C; [α]<sub>D</sub><sup>25</sup> = + 85.7 (*c* 0.68, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.34-7.27 (m, 5H), 5.93 (ddd, *J* = 10.8, 3.2, 3.2 Hz, 1H), 5.60 (ddd, *J* = 10.8, 2.0, 1.6 Hz, 1H), 5.28-5.22 (m, 1H), 4.48 (s, 2H), 3.74-3.67 (m, 3H), 2.11-2.05 (m, 1H), 1.69-1.60 (m, 1H), 1.42 (s, 9H), 1.07 (t, 7.4 Hz, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 150.7, 137.9, 128.1, 127.6, 127.6, 125.8, 122.7, 84.4, 73.1, 70.9, 60.5, 59.9, 27.9, 21.7, 10.9; FTIR (neat) 2978, 2935, 1716, 1616, 1456, 1169 cm<sup>-1</sup>; HRMS (M+NH<sub>4</sub><sup>+</sup>) calcd for C<sub>19</sub>H<sub>31</sub>N<sub>2</sub>O<sub>5</sub>S 399.1954, found 399.1953.

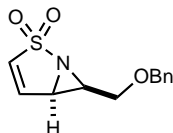


**1,2-thiazine-*N*-carboxylic acid-3,4,5,6-tetrahydro-(3*R*)-[(phenylmethoxy)methyl]-(4*R*,5*S*)-dihydroxy-(6*R*)-ethyl- 1,1-dimethylethyl ester-1,1-dioxide (31):** To a stirring solution of sultam **30** (10.8 mg, 0.028 mmol) in acetone (1.5 mL) and water (0.5 mL) was added citric acid (9.0 mg, 0.042 mmol), NMO (6.0 mg, 0.033 mmol) and 1 drop of OsO<sub>4</sub> (4 % solution in water) via pipet. The reaction was stirred at rt for 12 h, then quenched with a 10% aqueous solution of Na<sub>2</sub>SO<sub>3</sub> and extracted with CH<sub>2</sub>Cl<sub>2</sub> (4 × 15 mL). The organic layers were combined, dried over MgSO<sub>4</sub>, filtered and concentrated under reduced pressure. Flash chromatography (SiO<sub>2</sub>, 1:1 Hexanes/EtOAc) afforded 9.1 mg (78%) of diol **31** as an ivory solid. TLC R<sub>f</sub> = 0.16 (1:1 Hexanes/EtOAc); Mp = 100-105 °C; [α]<sub>D</sub><sup>25</sup> = + 50.8 (*c* 0.13, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.37-7.30 (m, 5H), 4.72 (ddd, *J* = 9.6, 5.6, 4.0 Hz, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.51 (d, *J* = 11.6 Hz, 1H), 4.27 (bs, 1H), 3.98 (dd, *J* = 6.8, 6.0 Hz, 1H), 3.82 (dd, *J* = 9.6, 9.2 Hz, 1H), 3.72 (dd, *J* = 9.6, 5.6 Hz, 1H), 3.38 (ddd, *J* = 8.0, 6.0, 6.0 Hz, 1H), 2.74 (bs, 1H), 2.51 (d, *J* = 7.6 Hz, 1H), 2.04 (ddd, *J* = 13.6, 7.6, 7.6 Hz, 2H), 1.50 (s, 9H), 1.20 (t, *J* = 7.6 Hz, 3H); <sup>13</sup>C NMR

(125 MHz, CDCl<sub>3</sub>)  $\delta$  151.9, 137.4, 128.5, 128.0, 127.9, 84.9, 73.5, 70.3, 69.7, 68.0, 63.9, 59.8, 27.9, 18.8, 11.9; FTIR (neat) 3479, 2979, 2933, 2879, 1722, 1367, 1055 cm<sup>-1</sup>; HRMS (M+Na<sup>+</sup>) calcd for C<sub>19</sub>H<sub>29</sub>NO<sub>7</sub>SNa 438.1563, found 438.1551.

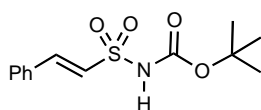


**1,2-thiazine-1,1-dioxide-3,4-dihydro-(3S)-[(phenylmethoxy)methyl]-(4R)-dimethylphosphate (32):** To a stirring solution of sultam **29** (12.0 mg, 0.25 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.25 mL) was added FeCl<sub>3</sub> (4.0 mg, 0.025 mL) in one portion and the reaction stirred at rt for 30 min. The crude mixture was quenched with water (10 mL) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (4 × 15 mL), dried over MgSO<sub>4</sub>, filtered and concentrated under reduced pressure. Flash chromatography (SiO<sub>2</sub>, 1:2 Hexane/EtOAc) afforded 5.6 mg (60%) of sultam **32** as a white solid. TLC R<sub>f</sub> = 0.14 (1:2 Hexanes/EtOAc); Mp = 80-84° C;  $[\alpha]_D^{25} = -49.6$  (c 1.11, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.37-7.32 (m, 5H), 6.64 (dd, *J* = 10.8, 2.0 Hz, 1H), 6.52 (dd, *J* = 10.8, 2.0 Hz, 1H), 5.18 (dddd, *J* = 9.2, 9.2, 2.0, 2.0 Hz, 1H), 5.00 (d, *J* = 12.0 Hz, 1H), 4.59 (d, *J* = 11.6 Hz, 1H), 4.55 (d, *J* = 11.6 Hz, 1H), 4.00-3.95 (m, 1H), 3.87 (dd, *J* = 9.6, 2.0 Hz, 1H), 3.79 (d, *J*<sub>HP</sub> = 11.2 Hz, 3H), 3.75 (d, *J*<sub>HP</sub> = 11.2 Hz, 3H), 3.65 (dd, *J* = 9.6, 2.4 Hz, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  137.1, 136.7, 130.4, 128.6, 128.2, 128.0, 73.7, 67.2 (d, *J*<sub>CP</sub> = 20.0 Hz), 66.9, 57.1 (d, *J*<sub>CP</sub> = 35.0 Hz), 54.9 (d, *J*<sub>CP</sub> = 30.0 Hz), 54.8 (d, *J*<sub>CP</sub> = 30.0 Hz); <sup>31</sup>P NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  1.60; FTIR (neat) 3232, 3119, 2957, 1610, 1454, 1155, 1092 cm<sup>-1</sup>; HRMS (M+Na<sup>+</sup>) calcd for C<sub>14</sub>H<sub>20</sub>NO<sub>7</sub>PSNa 400.0596, found 400.0578.

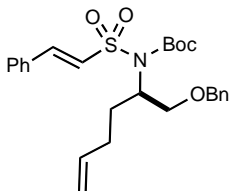


**Aziridine-Containing Sultam (34):** To a solution of sultam **32** (21.7 mg, 0.0575 mmol) in THF (0.58 mL) was added Cs<sub>2</sub>CO<sub>3</sub> (56 mg, 0.173 mmol) and the reaction stirred at 60 °C for 1 h. The

product was filtered and purified by flash chromatography (SiO<sub>2</sub>, 1:1 Hexanes/EtOAc) to afford 15 mg (100%) of aziridine **34** as a light-yellow oil. TLC R<sub>f</sub> = 0.43 (1:2 Hexanes/EtOAc); [α]<sub>D</sub><sup>25</sup> = -38.6 (c 0.35, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.38-7.31 (m, 5H), 6.96 (ddd, *J* = 6.0, 1.0, 1.0 Hz, 1H), 6.40 (d, *J* = 6.0 Hz, 1H), 4.60 (d, *J* = 12.4 Hz, 1H), 4.56 (d, *J* = 12.8 Hz, 1H), 3.80 (dd, *J* = 11.6, 4.4 Hz, 1H), 3.68 (m, 1H), 3.58 (dd, *J* = 11.2, 4.8 Hz, 1H), 2.78 (q, *J* = 4.0 Hz, 1H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 136.8, 136.2, 127.6, 127.0, 126.9, 125.0, 72.6, 66.8, 55.5, 46.2; FTIR (neat) 3080, 2920, 1609 cm<sup>-1</sup>; HRMS (M+Na<sup>+</sup>) calcd for C<sub>12</sub>H<sub>13</sub>NO<sub>3</sub>SNa 274.0514, found 274.0515.



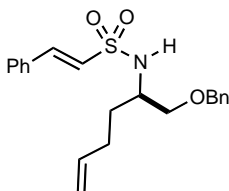
**(E)-tert-butyl styrylsulfonylcarbamate (36):** To a solution of (*E*)-2-phenylethanesulfonamide (1.0 g, 5.46 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (6.8 mL) containing DMAP (66 mg, 0.55 mmol) and Et<sub>3</sub>N (607 mg, 6.0 mmol, 0.84 mL) at rt was added a solution of Boc<sub>2</sub>O (1.37 g, 6.27 mmol, 1.44 mL) in CH<sub>2</sub>Cl<sub>2</sub> (10.9 mL) dropwise with stirring over 20 min. The reaction was stirred for 2 h at rt, followed by removal of the solvent under reduced pressure. The crude product was treated with EtOAc (80 mL) and 1N HCl (53 mL) and the organic layer washed successively with water (50 mL) and brine (50 mL). The water layer was washed with CH<sub>2</sub>Cl<sub>2</sub> (4 × 50 mL), the organic layers combined, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated under reduced pressure. The product was heated in heptane (20 mL), cooled down to rt and filtered to give 1.46 g (94%) of styrylsulfonylcarbamate **36** as an ivory solid. TLC R<sub>f</sub> = 0.51(1:1 Hexanes/EtOAc); Mp = 160-166 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.68 (d, *J* = 15.4 Hz, 1H), 7.54-7.52 (m, 2H), 7.46-7.41 (m, 3H), 7.20 (s, 1H, N-H), 7.00 (d, *J* = 15.4 Hz, 1H), 1.48 (s, 9H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 149.3, 144.6, 132.1, 131.5, 129.2, 128.7, 123.9, 84.3, 28.0; FTIR (neat) 3246, 1736, 1614, 1576 cm<sup>-1</sup>; HRMS (M+Na<sup>+</sup>) calcd for C<sub>13</sub>H<sub>17</sub>NO<sub>4</sub>SNa 306.0776, found 306.0769.



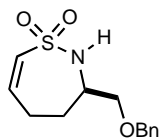
**(R,E)-tert-butyl 1-(benzyloxy)hex-5-en-2-yl(styrylsulfonyl)carbamate (38):** In a procedure similar to the preparation of sulfonamide **12**, a solution of sulfamoyl carbamate **36** (1.42 g, 5.01



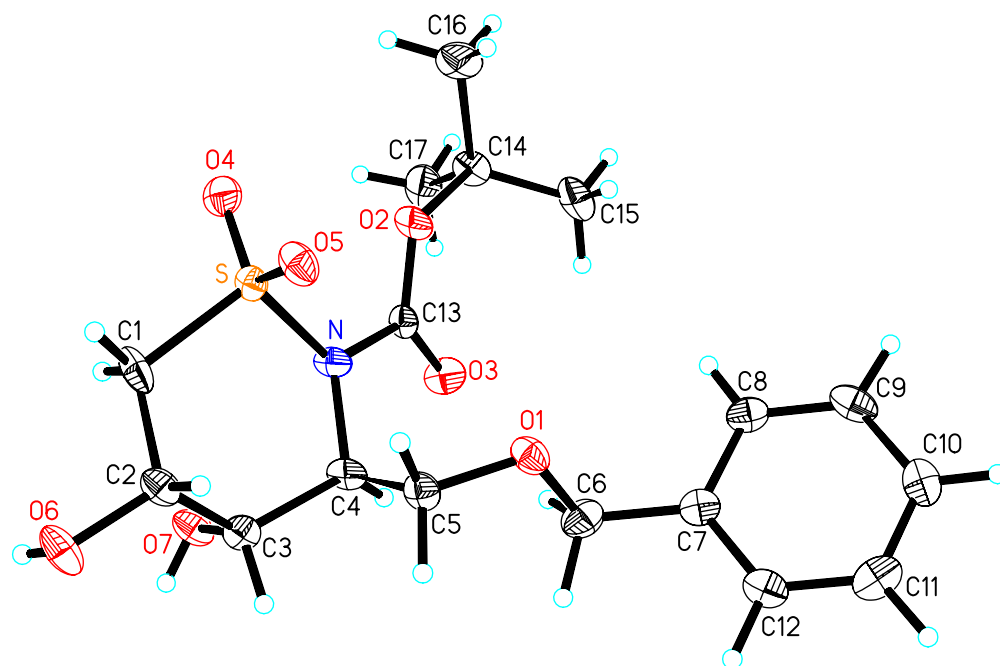
mmol) in THF (3.2 mL) was subjected to the Mitsunobu reaction in the presence of secondary alcohol **37** (1.03 g, 5.01 mmol), PPh<sub>3</sub> (1.71g, 5.51 mmol) and DIAD (1.11 g, 5.51 mmol, 1.07 mL) to yield after flash chromatography (SiO<sub>2</sub>, 10:1 Hexane/EtOAc) 1.93 g (82%) of sulfamoyl carbamate **38** as a yellow oil. TLC R<sub>f</sub> = 0.49 (3:1 Hexanes/EtOAc); [α]<sub>D</sub><sup>25</sup> = -9.1 (c 1.06, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.50 (d, *J* = 15.5 Hz, 1H), 7.41-7.37 (m, 1H), 7.33-7.27 (m, 7H), 7.20 (d, *J* = 7.4 Hz, 2H), 6.98 (d, *J* = 15.5 Hz, 1H), 5.86 (dddd, *J* = 16.8, 10.2, 6.5, 6.3 Hz, 1H), 5.08 (dd, *J* = 17.2, 1.6 Hz, 1H), 5.01 (dd, *J* = 10.2, 1.0 Hz, 1H), 4.74-4.66 (m, 1H), 4.58 (d, *J* = 11.6 Hz, 1H), 4.46 (d, *J* = 11.6 Hz, 1H), 3.96 (dd, *J* = 9.8, 9.8 Hz, 1H), 3.56 (dd, *J* = 9.8, 5.1 Hz, 1H), 2.28-2.16 (m, 2H), 2.14-2.03 (m, 1H), 1.73-1.63 (m, 1H), 1.47 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 150.7, 142.2, 137.7, 137.2, 132.1, 130.5, 128.7, 128.1, 127.9, 127.3, 127.2, 125.2, 114.9, 83.7, 72.7, 69.9, 58.0, 30.2, 29.1, 27.7; FTIR (neat) 3070, 2980, 1726, 1639, 1616, 1578, 1450, 1353, 1145 cm<sup>-1</sup>; HRMS (M+H<sup>+</sup>) calcd for C<sub>26</sub>H<sub>34</sub>NO<sub>5</sub>S 472.2158, found 472.2159.



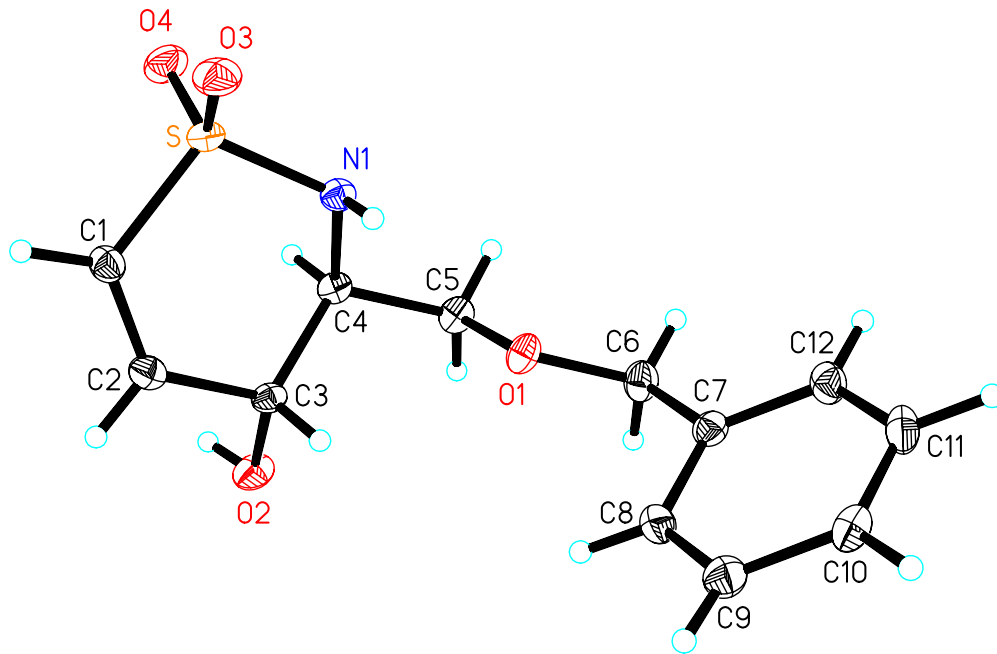
**(*R,E*)-N-(1-(benzyloxy)hex-5-en-2-yl)-2-phenylethanesulfonamide (39):** In a procedure similar to the preparation of sulfonamide **14**, a solution of sulfamoyl carbamate **38** (115 mg, 0.24 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (2.0 mL) was treated with TFA (0.5 mL) to yield after aqueous workup and flash chromatography (SiO<sub>2</sub>, 2:1 Heptane/EtOAc) 91 mg (100%) of sulfonamide **39** as an ivory solid. TLC R<sub>f</sub> = 0.45 (2:1 Hexanes/EtOAc); Mp = 40-43 °C; [α]<sub>D</sub><sup>25</sup> = +18.0 (c 1.13, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.43 (d, *J* = 15.4 Hz, 1H), 7.39-7.27 (m, 10H), 6.67 (d, *J* = 15.4 Hz, 1H), 5.77 (dddd, *J* = 16.8, 10.2, 6.6, 6.6 Hz, 1H), 5.00 (dd, *J* = 17.1, 1.6 Hz, 1H), 4.96 (dd, *J* = 10.2, 1.3 Hz, 1H), 4.62 (d, *J* = 8.3 Hz, 1H), 4.50 (s, 2H), 3.53 (dd, *J* = 8.8, 3.4 Hz, 1H), 3.49-3.42 (m, 2H), 2.22-2.06 (m, 2H), 1.69 (q, *J* = 7.4 Hz, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 140.5, 137.6, 137.5, 132.6, 130.5, 129.0, 128.4, 128.1, 127.8, 127.7, 126.2, 115.3, 73.2, 71.7, 53.3, 31.9, 29.8; FTIR (neat) 3279, 3063, 2928, 1622, 1448, 1363, 1150 cm<sup>-1</sup>; HRMS (M+H<sup>+</sup>) calcd for C<sub>21</sub>H<sub>26</sub>NO<sub>3</sub>S 372.1633, found 372.1643.



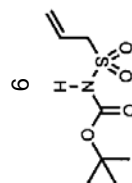
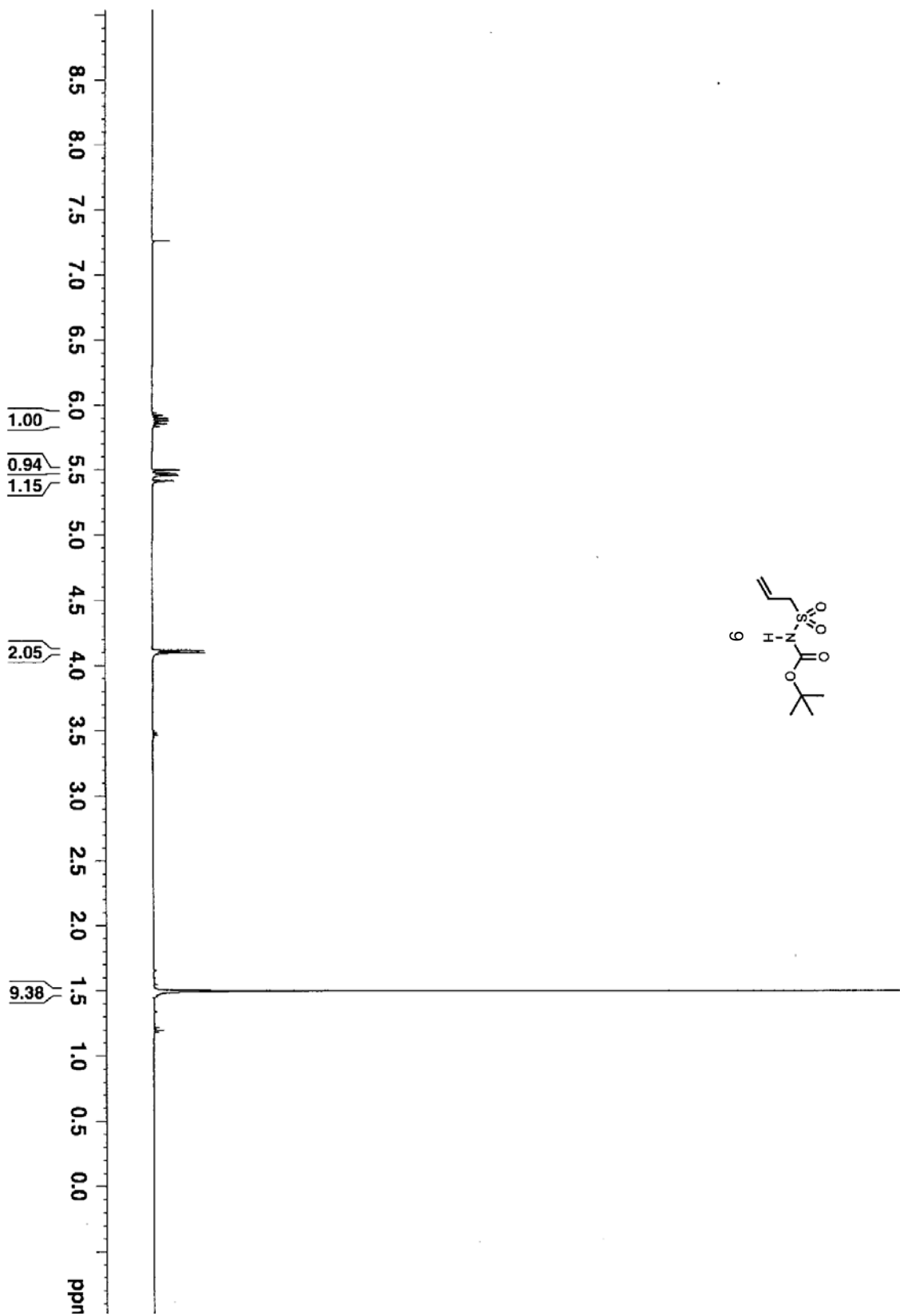
**1,2-thiazepin-3,4,5-trihydro-(3R)-[(phenylmethoxy)methyl]-1,1-dioxide (40):** A solution of sulfonamide **39** (361 mg, 0.97 mmol) in refluxing DCE (194 mL) was subjected to RCM with Grubbs second generation catalyst (5 mol %, 41 mg, 0.049 mmol) and the reaction stirred for 3-6 hrs to afford after flash chromatography (SiO<sub>2</sub>, 3:1 Heptane/EtOAc) 224 mg (86%) of vinylic sultam **40** as a yellow oil. TLC R<sub>f</sub> = 0.28 (1:1 Hexanes/EtOAc); [α]<sub>D</sub><sup>25</sup> = -1.7 (c 0.92, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.38-7.29 (m, 5H), 6.61 (dd, *J* = 11.1, 1.9 Hz, 1H), 6.36 (ddd, *J* = 11.1, 7.2, 5.5 Hz, 1H), 4.89 (d, *J* = 7.9 Hz, 1H), 4.55 (d, *J* = 11.8 Hz, 1H), 4.50 (d, *J* = 11.8 Hz, 1H), 3.80-3.73 (m, 1H), 3.64-3.55 (m, 2H), 2.65-2.57 (m, 2H), 2.04-1.99 (m, 1H), 1.94-1.87 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 139.2, 137.4, 135.0, 128.2, 127.6, 127.5, 73.0, 72.5, 53.8, 28.5, 25.9; FTIR (neat) 3265, 3059, 3030, 2926, 1624, 1496, 1452, 1363 cm<sup>-1</sup>; HRMS (M+Na<sup>+</sup>) calcd for C<sub>13</sub>H<sub>17</sub>NO<sub>3</sub>SNa 290.0827, found 290.0829.

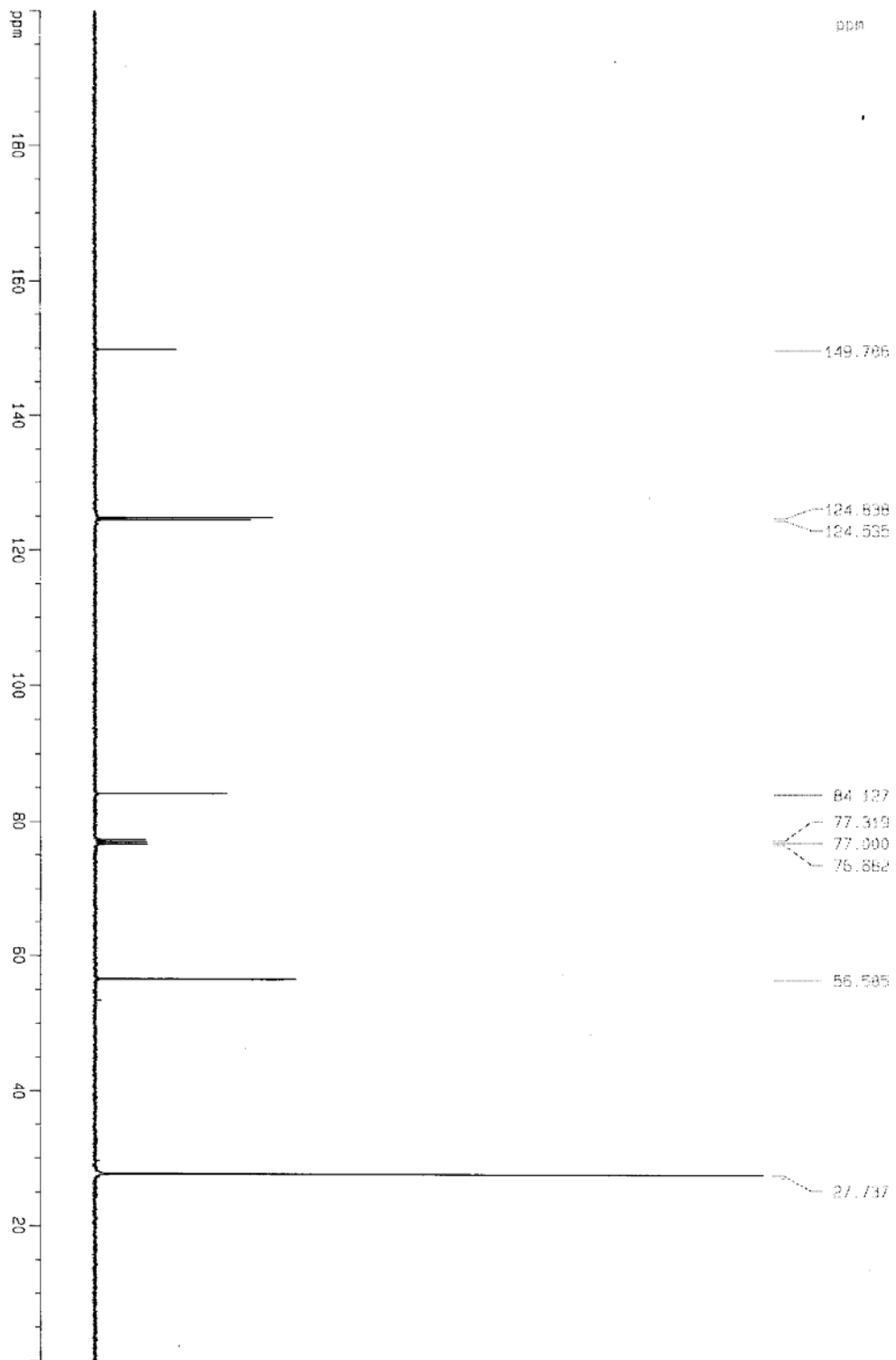


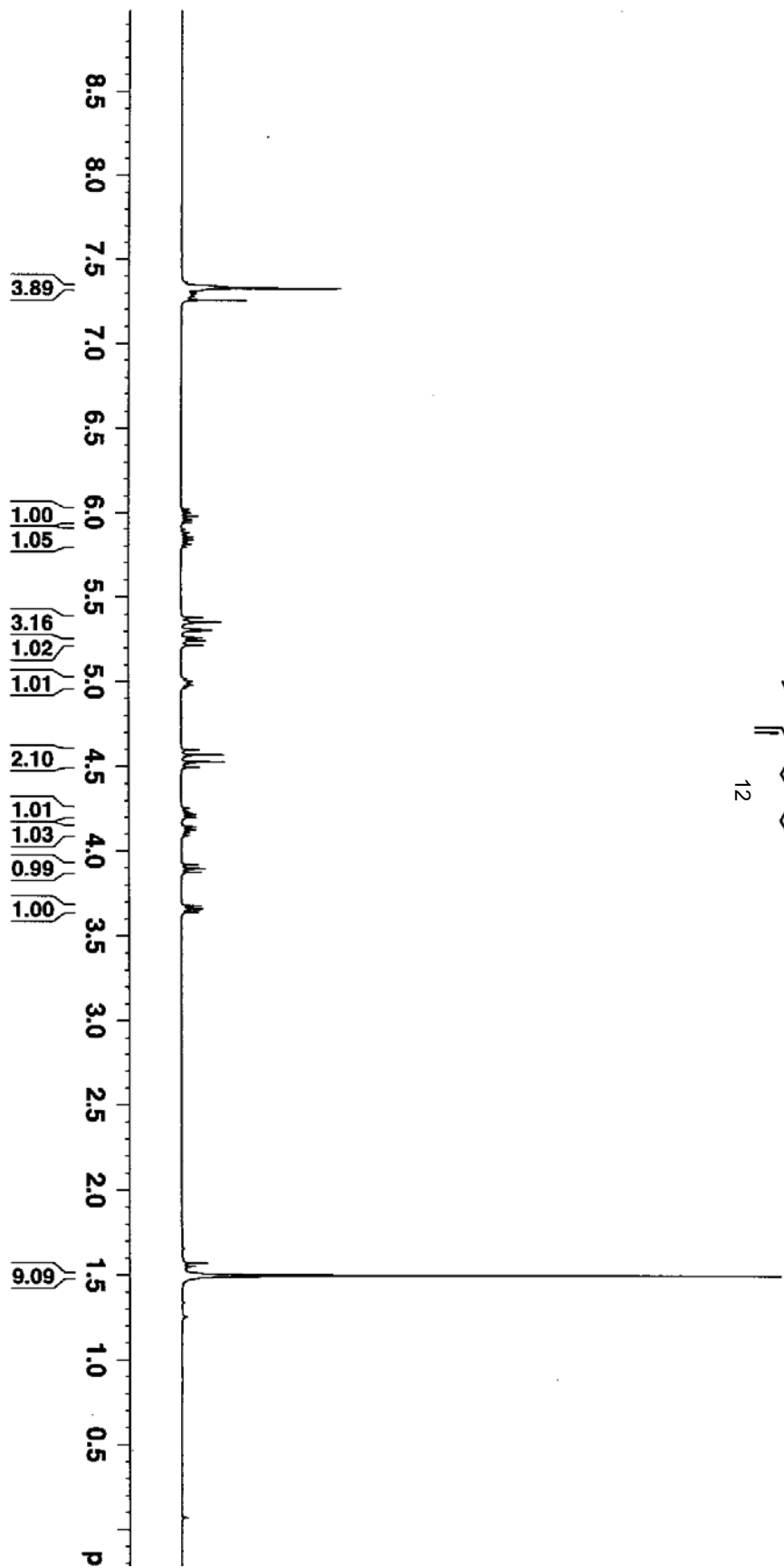
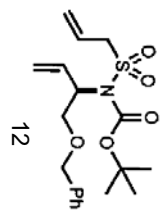
**Figure S1.** Thermal ellipsoid diagram for compound **16**. Ellipsoids are drawn at the 50% probability level.

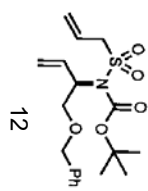
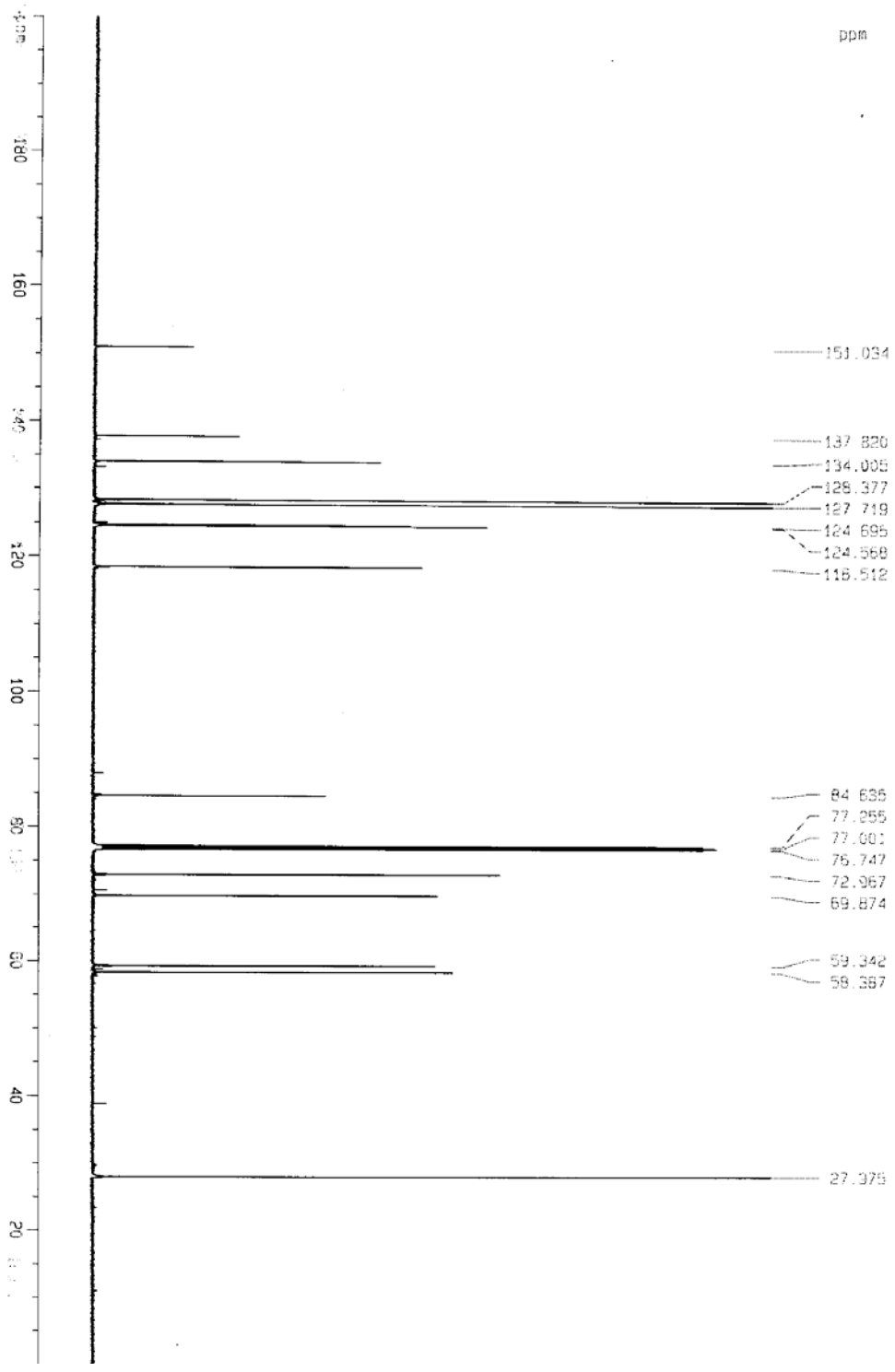


**Figure S2.** Thermal ellipsoid diagram for compound **20**. Ellipsoids are drawn at the 50% probability level.

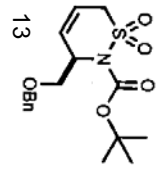
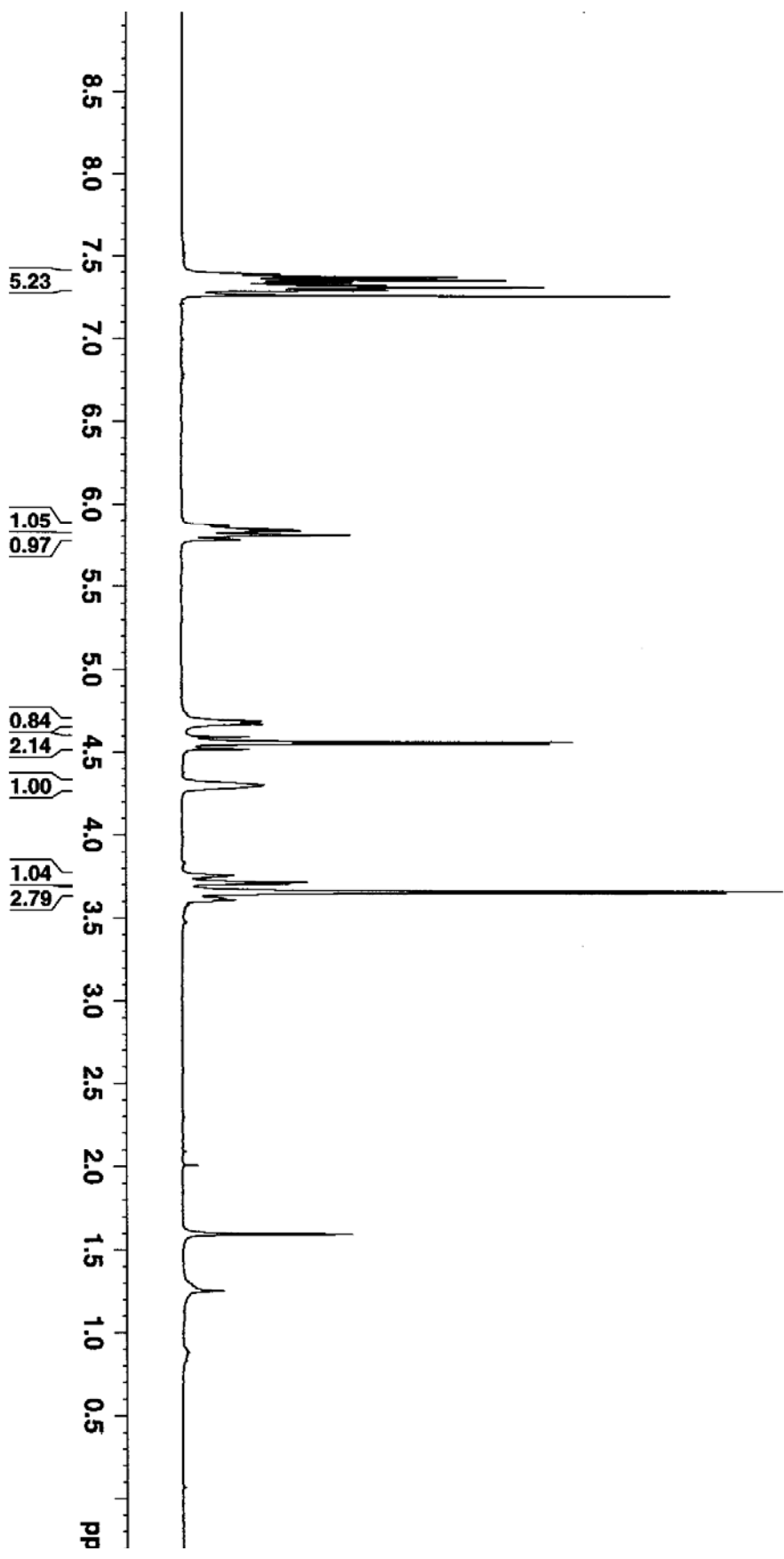


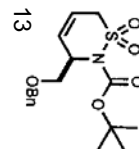
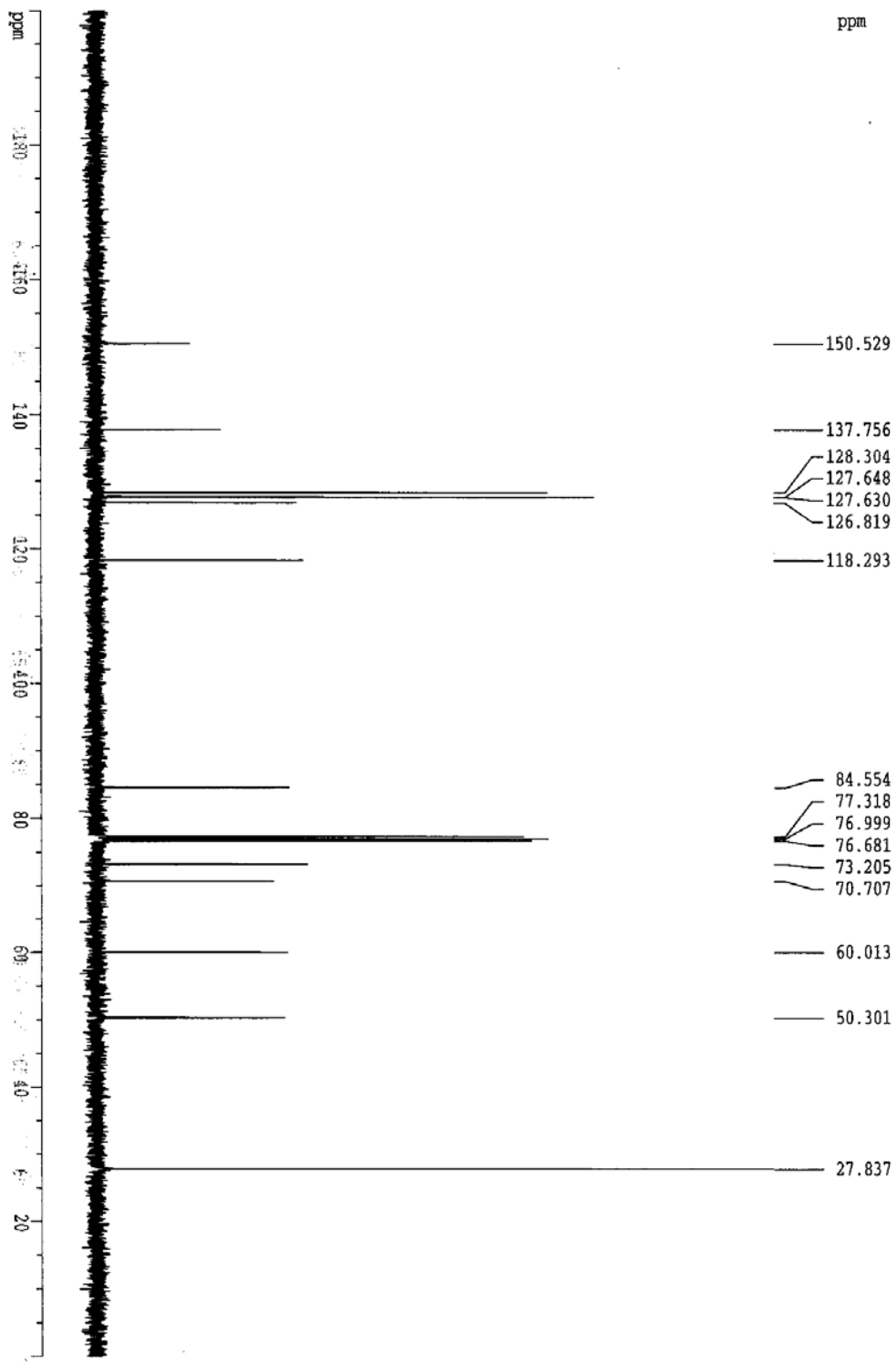


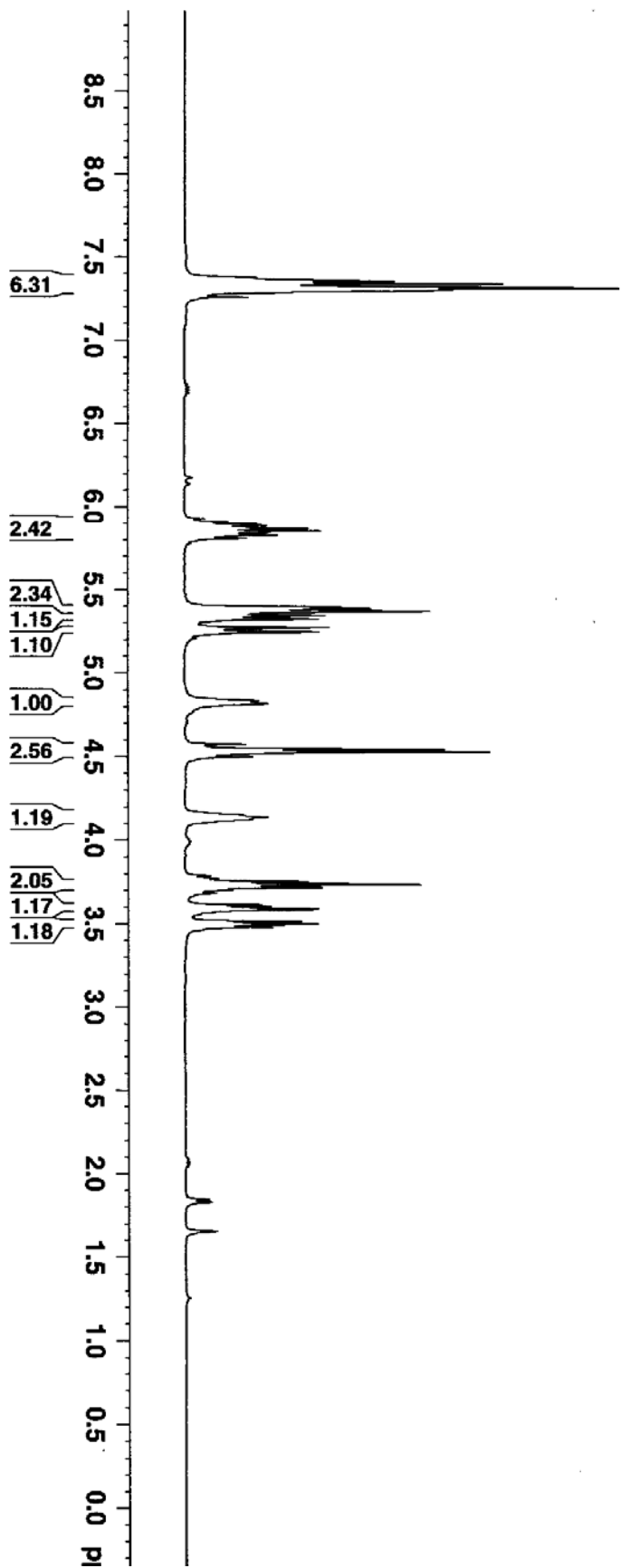
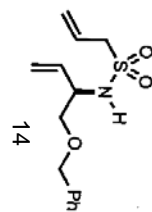


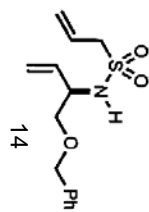
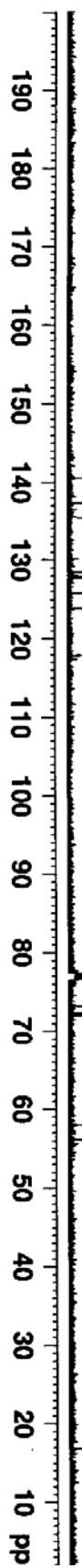












- 137.340
- 135.443
- 128.470
- 127.925
- 127.756
- 125.771
- 123.870
- 117.847

- 77.317
- 77.202
- 76.682
- 73.300
- 72.359

- 58.045
- 56.165

