

*Supporting Information*

**Oxazoline-Oxazinone Oxidative Rearrangement. Divergent Syntheses of (2*S*,3*S*)-  
4,4,4-Trifluorovaline and (2*S*,4*S*)-5,5,5-Trifluoroisoleucine**

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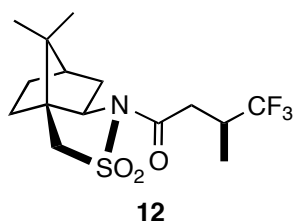
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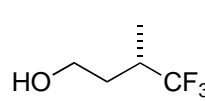
mmol) in toluene (60 mL) was added dropwise to a suspension of NaH (60% wt in mineral oil, washed twice with dry hexanes, 800 mg, 20.0 mmol) in toluene (40 mL) at 0 °C and the mixture stirred at r.t. for 30 minutes. The acid chloride (1.50 g) in toluene (40 mL) was added and the mixture stirred at r.t. for one hour. The reaction was quenched with water and the aqueous phase extracted with EtOAc. The combined organic extracts were washed with water and brine, dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated under reduced pressure to give the crude product. Purification by flash chromatography (1:4 EtOAc:hexanes, dry-load) gave butenamide **11** (1.73 g, 49% from **9**) as a viscous colorless oil as well as amide **11b** (174 mg, 5% from **9**); Data for **11**: FTIR (ATR, neat):  $\nu$  2960, 2886, 1681, 1456, 1413, 1394, 1376, 1335, 1299, 1273, 1240, 1221, 1168, 1135, 1100, 1068, 1048, 1001, 912, 892, 859, 776, 764, 733 cm<sup>-1</sup>;  $[\alpha]_D^{19}$  -71.1 (*c* 1.16, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  6.89 (br s, 1H), 3.91 (dd, *J* = 7.2, 5.6 Hz, 1H), 3.47 (ABq, *J* = 14.0 Hz, 2H), 2.17 (d, *J* = 1.6 Hz, 3H), 2.12-2.09 (m, 2H), 1.94-1.88 (m, 3H), 1.45-1.35 (m, 2H), 1.14 (s, 3H), 0.96 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  162.7 (C), 141.9 (q, *J* = 30.6 Hz, C), 122.9 (q, *J* = 273 Hz, CF<sub>3</sub>), 121.0 (q, *J* = 5.8 Hz, CH), 64.9 (CH), 52.9 (CH<sub>2</sub>), 48.6 (C), 47.8 (C), 44.6 (CH), 38.3 (CH<sub>2</sub>), 32.7 (CH<sub>2</sub>), 26.4 (CH<sub>2</sub>), 20.7 (CH<sub>3</sub>), 19.7 (CH<sub>3</sub>), 13.0 (CH<sub>3</sub>); HRESIMS *m/z* 352.1192 [M+H]<sup>+</sup>, calcd. 352.1189 for C<sub>15</sub>H<sub>21</sub>F<sub>3</sub>NO<sub>3</sub>S. Data for **11b**: FTIR (ATR, neat):  $\nu$  1701 cm<sup>-1</sup>;  $[\alpha]_D^{21}$  -96.8 (*c* 1.0, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  5.95-5.93 (m, 1H), 5.60-5.58 (m, 1H), 3.89 (dd, *J* = 7.3, 4.9 Hz, 1H), 3.65 (AXq, *J* = 17.6 Hz, 2H), 3.49 (ABq, *J* = 13.6 Hz, 2H), 2.15-2.08 (m, 1H), 2.08 (ddd, *J* = 13.7, 13.7, 7.3 Hz, 1H), 1.97-1.84 (m, 3H), 1.45-1.31 (m, 2H), 1.14 (s, 3H), 0.97 (s, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  167.3 (C), 130.9 (q, *J* = 31.6 Hz, C), 123.9 (q, *J* = 5.4 Hz, CH<sub>2</sub>), 123.1 (q, *J* = 273.3 Hz, CF<sub>3</sub>), 65.5 (CH), 53.0 (CH<sub>2</sub>), 48.7 (C), 47.9 (C), 44.7 (CH), 38.4 (CH<sub>2</sub>), 36.4 (q, *J* = 1.2 Hz, CH<sub>2</sub>), 32.9 (CH<sub>2</sub>), 26.5 (CH<sub>2</sub>), 20.8 (CH<sub>3</sub>), 20.0 (CH<sub>3</sub>). HRESI-TOFMS *m/z* 352.1190 [M+H]<sup>+</sup>, calcd. 352.1189 for C<sub>15</sub>H<sub>21</sub>F<sub>3</sub>NO<sub>3</sub>S.



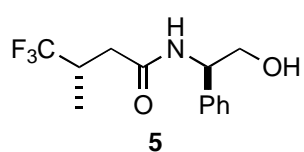
**Camphor sultam, 4,4,4-trifluoro-3-methylbutanamide (12).** A mixture of alkene **11** (506 mg, 1.44 mmol) and Pd/C (10% wt, 76.3 mg) in absolute EtOH (50 mL) was shaken in a thick-walled Parr hydrogenation reaction vessel under 90 psi of H<sub>2</sub> for 1.5 hours. The reaction mixture was filtered through a pad of Celite and concentrated under reduced pressure to give the crude product. Purification by flash chromatography (1:4 EtOAc:hexanes) gave butanamide **12** (482 mg, 95%, *dr* 4:1 by integration of the <sup>1</sup>H NMR

spectrum) as a white solid. Data for the 4:1 mixture of 3*S*:3*R*-**12**: FTIR (ATR, neat):  $\nu$  2960, 2887, 1694, 1466, 1415, 1392, 1374, 1330, 1312, 1267, 1235, 1217, 1167, 1119, 1086, 1063, 1039, 1017, 988, 911, 875, 823, 810, 775, 732, 659  $\text{cm}^{-1}$ ;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  168.6 (C), 127.7 (q,  $J = 277$  Hz,  $\text{CF}_3$ ), 65.1 (CH), 52.8 ( $\text{CH}_2$ ), 48.4 (C), 47.7 (C), 44.5 (CH), 38.2 ( $\text{CH}_2$ ), 35.7 (d,  $J = 2.3$  Hz,  $\text{CH}_2$ ), 34.3 (q,  $J = 27.6$  Hz, CH), 32.7 ( $\text{CH}_2$ ), 26.3 ( $\text{CH}_2$ ), 20.6 ( $\text{CH}_3$ ), 19.7 ( $\text{CH}_3$ ), 13.1 (d,  $J = 2.2$  Hz,  $\text{CH}_3$ ); HRESIMS  $m/z$  354.1348  $[\text{M}+\text{H}]^+$ , calcd. 354.1345 for  $\text{C}_{15}\text{H}_{23}\text{F}_3\text{NO}_3\text{S}$ . The two diastereomers could be separated by chiral HPLC (Cellulose-2 column, see paragraph below for details). Data for 3*S*-**12**:  $[\alpha]_D^{21} -63.8$  ( $c$  0.17,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  3.86 (dd,  $J = 6.8, 5.6$  Hz, 1H), 3.46 (ABq,  $J = 13.6$  Hz, 2H), 3.02 (dd,  $J = 16.8, 4.8$  Hz, 1H), 2.92 (m, 1H), 2.70 (dd,  $J = 16.8, 8.0$  Hz, 1H), 2.12-2.01 (m, 2H), 1.95-1.86 (m, 3H), 1.42-1.33 (m, 2H), 1.15 (d,  $J = 6.4$  Hz, 3H), 1.11 (s, 3H), 0.95 (s, 3H). Data for 3*R*-**12**:  $[\alpha]_D^{21} -59.0$  ( $c$  0.17,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  3.88 (dd,  $J = 6.8$  Hz, 1H), 3.49 (ABq,  $J = 14.0$  Hz, 2H), 3.01 (dd,  $J = 16.0, 3.6$  Hz, 1H), 2.98-2.86 (m, 1H), 2.80 (dd,  $J = 16.4, 8.8$  Hz, 1H), 2.12-2.08 (m, 2H), 1.97-1.85 (m, 3H), 1.45-1.32 (m, 2H), 1.16 (d,  $J = 6.8$  Hz, 3H), 1.15 (s, 3H), 0.98 (s, 3H).

Reductions of **11** to 3*S*-**12** and 3*R*-**12** from Table 1: HPLC analysis to determine the diastereomeric ratio of **12** was performed using an Agilent 1100 Series HPLC with a Lux Cellulose-2 chiral column (5  $\mu$ , 250 mm x 4.6 mm) eluting with 10% *i*-PrOH/hexanes at a flow rate of 1 mL/min. The retention time of 3*S*-**12** was 7.43 min and the retention time of 3*R*-**12** was 8.96 min. The areas under the peaks were measured at two wavelengths,  $\lambda = 210$  nm and  $\lambda = 230$  nm, and the diastereomeric ratio represented in Table 1 is an average of the two values. For those entries that contain remaining starting material (entries 7 and 8), the diastereomeric ratio of the product could not be obtained using the HPLC conditions described above due to incomplete separation of the starting material (**11**) from the 3*R*-diastereomer. In these cases, analysis was performed using  $^{19}\text{F}$  NMR (470 MHz,  $\text{CDCl}_3$ ): (**11**)  $\delta -71.0$  (d,  $J = 1.4$  Hz,  $\text{CF}_3$ ); 3*R*-**12**  $\delta -73.27$  (d,  $J = 9.0$  Hz,  $\text{CF}_3$ ); 3*S*-**12**  $\delta -73.37$  (d,  $J = 8.6$  Hz,  $\text{CF}_3$ ).

 (*S*)-4,4,4-Trifluoro-3-methylbutan-1-ol (**13**). To  $\text{LiAlH}_4$  (248 mg, 6.53 mmol) in THF (30 mL) was added the sultam amide (2.31 g, 6.53 mmol) in THF (35 mL) via cannula at rt. After 1.5 h, the reaction was quenched slowly with  $\text{H}_2\text{O}$ ,

dropwise, until the bubbling ceased, at which time Na<sub>2</sub>SO<sub>4</sub> was added until a free-flowing solid was noticed. The reaction was filtered through a pad of Celite and washed with Et<sub>2</sub>O. The ether was concentrated on low vacuum. Cold pentane was added and the solid sultam was triturated with ether. The Et<sub>2</sub>O layer was concentrated again under low vacuum. The oil was then distilled to remove the excess Et<sub>2</sub>O (which distilled from 50-150 °C) and the temperature was lowered and house vacuum was applied to distill the desired alcohol (55-60 °C, house vacuum, 598 mg, 66%, 60% *ee*). [ $\alpha$ ]<sub>D</sub><sup>23</sup> -8.9 (*c* 2.0, CHCl<sub>3</sub>); literature<sup>2</sup> (42% *ee*): [ $\alpha$ ]<sub>D</sub><sup>20</sup> -7.3 (*c* 1.3, CHCl<sub>3</sub>). *R*<sub>f</sub> = 0.12 (20% EtOAc/hexanes); IR (neat)  $\nu$  1264 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  3.80-3.72 (m, 1H), 3.71-3.63 (m, 1H), 2.44-2.32 (m, 1H), 1.98-1.90 (m, 1H), 1.79 (br s, 1H, *OH*), 1.55-1.47 (m, 1H), 1.12 (d, *J* = 6.9 Hz, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) ppm 128.5 (q, *J* = 280 Hz, CF<sub>3</sub>), 59.6 (CH<sub>2</sub>), 34.5 (q, *J* = 26.4 Hz, CH), 32.3 (CH<sub>2</sub>), 12.6 (CH<sub>3</sub>); HR GCMS-Cl *m/z* [M+H]<sup>+</sup> 143.0683, calcd for C<sub>5</sub>H<sub>10</sub>F<sub>3</sub>O<sub>3</sub> 143.0684.

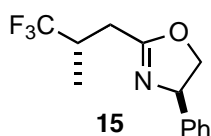


**(S)-4,4,4-Trifluoro-N-((R)-2-hydroxy-1-phenylethyl)-3-**

**methylbutanamide (5).** LiOH (1.25 M in water, 15.6 mL, 19.5 mmol) was added to amide **12** (*dr* 4:1, 858 mg, 2.43 mmol) in THF (16.3 mL) and water (6.9 mL) and the mixture stirred at r.t. for 12 hours. The

reaction was further basified with 20% aq. NaOH (2 mL) and the aqueous phase extracted with CH<sub>2</sub>Cl<sub>2</sub>. The aqueous layer was then acidified to pH 2 using 2 M HCl and re-extracted with CH<sub>2</sub>Cl<sub>2</sub>. The organic extracts from the second extraction were washed with water and brine, dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated under reduced pressure to give the crude acid (*S*)-**7** (379 mg) as a yellow oil that was used in the next step without purification; FTIR (ATR, neat):  $\nu$  3053 (br), 2991, 2952, 2678 (br), 1714, 1469, 11421, 1380, 1344, 1305, 1267, 1171, 1127, 1089, 1018, 938, 893 cm<sup>-1</sup>; [ $\alpha$ ]<sub>D</sub><sup>22</sup> -15.6 (*c* 2.0, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  2.82-2.70 (m, 2H), 2.36 (dd, *J* = 16.8, 10.2 Hz, 1H), 1.21 (d, *J* = 6.8 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  177.2 (C), 127.5 (q, *J* = 278 Hz, CF<sub>3</sub>), 34.9 (q, *J* = 27.8 Hz, CH), 34.5 (q, *J* = 3.0 Hz, CH<sub>2</sub>), 13.0 (q, *J* = 2.3 Hz, CH<sub>3</sub>); HRESIMS *m/z* 155.0324 [M-H]<sup>-</sup>, calcd. 155.0325 for C<sub>5</sub>H<sub>6</sub>F<sub>3</sub>O<sub>2</sub>. HATU (1.11 g, 2.91 mmol) and *i*-Pr<sub>2</sub>NEt (677  $\mu$ L, 3.88 mmol) were added to a solution of acid (*S*)-**7** (379 mg, 2.43 mmol) and (*R*)-phenylglycinol (**14**) (400 mg, 2.91 mmol) in DMF (55 mL) and the mixture stirred at r.t. for 15 hours. Evaporation of the solvent under reduced pressure gave the crude product, which was purified by flash chromatography (2:3 EtOAc:hexanes, dry-load) to give

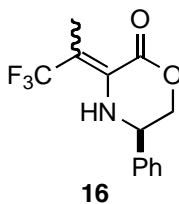
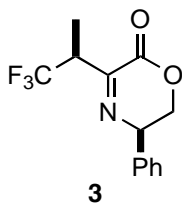
amide **5** (506 mg, 75% from **12**) as a glassy yellow solid. A portion of this sample (376 mg, 56%) was obtained as a single diastereomer and carried through the remainder of the sequence; FTIR (ATR, neat):  $\nu$  3294, 3067, 3033, 2924, 2851, 1646, 1548, 1496, 1467, 1456, 1389, 1358, 1307, 1268, 1171, 1129, 1085, 1020, 758, 700  $\text{cm}^{-1}$ ;  $[\alpha]_D^{19}$   $-60.2$  ( $c$  0.915,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.37-7.24 (m, 5H), 6.65 (br s, 1H), 5.02 (app q,  $J = 5.6$  Hz, 1H), 3.86-3.78 (m, 2H), 2.80 (m, 1H), 2.56 (dd,  $J = 14.8, 4.4$  Hz, 1H), 2.15 (dd,  $J = 14.8, 9.6$  Hz, 1H), 1.15 (d,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  170.1 (C), 138.5 (CH), 127.8 (q,  $J = 279$  Hz,  $\text{CF}_3$ ), 128.9 (CH), 127.9 (CH), 126.6 (CH), 66.2 ( $\text{CH}_2$ ), 55.8 (CH), 36.5 (d,  $J = 3.0$  Hz,  $\text{CH}_2$ ), 35.1 (q,  $J = 27.3$  Hz, CH), 12.9 (d,  $J = 3.0$  Hz,  $\text{CH}_3$ ); HRESIMS  $m/z$  276.1210  $[\text{M}+\text{H}]^+$ , calcd. 276.1206 for  $\text{C}_{13}\text{H}_{17}\text{F}_3\text{NO}_2$ .



**(R)-4-Phenyl-2-((S)-3,3,3-trifluoro-2-methylpropyl)-4,5-dihydrooxazole**

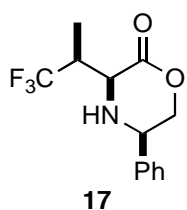
**(15)**. DAST (70.4  $\mu\text{L}$ , 0.533 mmol) was added to a solution of amide **5** (122 mg, 0.444 mmol) in  $\text{CH}_2\text{Cl}_2$  (4.5 mL) at  $-78$   $^\circ\text{C}$  and the mixture stirred at  $-78$   $^\circ\text{C}$  for one hour.  $\text{K}_2\text{CO}_3$  (92.1 mg, 0.666 mmol) was added in a single portion

and the mixture warmed to r.t. over 1.5 hours. The reaction was quenched with sat. aq.  $\text{NaHCO}_3$  and the aqueous phase extracted with  $\text{CH}_2\text{Cl}_2$ . The combined organic extracts were washed with water and brine, dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated to give the crude product. Purification by flash chromatography (3:17 EtOAc:hexanes) gave oxazoline **15** (106 mg, 93%,  $dr >15:1$  by integration of the  $^1\text{H}$  NMR spectrum) as a colorless oil; FTIR (ATR, neat):  $\nu$  3064, 3032, 2986, 2901, 2849, 1669, 1494, 1467, 1455, 1434, 1386, 1357, 1268, 1242, 1169, 1127, 1086, 1020, 984, 928, 761, 699  $\text{cm}^{-1}$ ;  $[\alpha]_D^{20}$   $+36.9$  ( $c$  0.915,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.37-7.22 (m, 5H), 5.20 (t,  $J = 9.2$  Hz, 1H), 4.63 (td,  $J = 9.4, 1.5$  Hz, 1H), 4.10 (td,  $J = 8.4, 1.4$  Hz, 1H), 2.88-2.74 (m, 2H), 2.39 (dd,  $J = 15.3, 9.9$  Hz, 1H), 1.25 (d,  $J = 6.7$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  165.6 (C), 141.9 (C), 128.7 (CH), 127.6 (q,  $J = 279$  Hz,  $\text{CF}_3$ ), 127.6 (CH), 126.4 (CH), 74.7 ( $\text{CH}_2$ ), 69.6 (CH), 35.7 (q,  $J = 27.6$  Hz, CH), 28.5 (q,  $J = 2.7$  Hz,  $\text{CH}_2$ ), 12.8 (q,  $J = 2.7$  Hz,  $\text{CH}_3$ ); HRESIMS  $m/z$  258.1101  $[\text{M}+\text{H}]^+$ , calcd. 258.1100 for  $\text{C}_{13}\text{H}_{15}\text{F}_3\text{NO}$ .



**(R)-5-Phenyl-3-((S)-1,1,1-trifluoropropan-2-yl)-5,6-dihydro-2H-1,4-oxazin-2-one (3) and (R)-5-Phenyl-3-(1,1,1-**

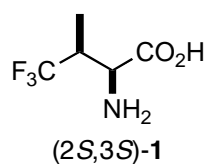
**trifluoropropan-2-ylidene)morpholin-2-one (16).** Oxazoline **15** (110 mg, 0.428 mmol) in freshly-distilled 1,4-dioxane (1.4 mL) was added to a suspension of SeO<sub>2</sub> (94.9 mg, 0.855 mmol) in 1,4-dioxane (1.4 mL) and the mixture heated at reflux for 50 minutes. The reaction mixture was cooled to r.t. and then filtered through a pad of Florisil. Evaporation of the solvent under reduced pressure gave the crude product, which was purified by flash chromatography (3:37 EtOAc:hexanes) to give oxazinone **3** (75.6 mg, 65%, *dr* 7:1, <sup>1</sup>H NMR) as a yellow oil and enamine **16** (9.1 mg, 8%, 1.2:1 *E:Z*, arbitrary assignment) as a yellow oil. Data for **3**: FTIR (ATR, neat): ν 3065, 3033, 3000, 2952, 2894, 1742, 1645, 1497, 1456, 1384, 1342, 1308, 1260, 1224, 1172, 1115, 1078, 1049, 1037, 1030, 1001, 984, 920, 870, 819, 795, 758, 697, 670, 662 cm<sup>-1</sup>; [α]<sub>D</sub><sup>20</sup> -110 (*c* 1.20, CHCl<sub>3</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.46-7.29 (m, 5H), 5.06 (dd, *J* = 9.2, 4.4 Hz, 1H), 4.64 (dd, *J* = 11.6, 4.4 Hz, 1H), 4.31 (dd, *J* = 11.6, 9.2 Hz, 1H), 4.16 (m, 1H), 1.49 (d, *J* = 7.2 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 159.0 (C), 154.6 (C), 136.2 (C), 129.4 (CH), 128.8 (CH), 127.2 (CH), 126.1 (q, *J* = 281 Hz, CF<sub>3</sub>), 71.4 (CH<sub>2</sub>), 59.9 (CH), 41.1 (q, *J* = 28.2 Hz, CH), 12.7 (CH<sub>3</sub>); HREIMS *m/z* 271.0812 [M]<sup>+</sup>, calcd. 271.0815 for C<sub>13</sub>H<sub>12</sub>F<sub>3</sub>NO<sub>2</sub>. Data for **16**: FTIR (ATR, neat): ν 3420 (br), 1747, 1725, 1637, 1454, 1396, 1286, 1169, 1140, 1099, 1053, 999, 759, 699 cm<sup>-1</sup>; (for the following NMR data, \* indicates a signal for the major geometrical isomer, \*\* indicates the a signal for the minor isomer and no asterisk indicates only a single signal was observed) <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.47-7.38 (m, 3H), 7.32-7.29 (m, 2H), 5.59\*\* (s, 1H), 5.25\* (s, 1H), 5.06\*\* (dd, *J* = 11.7, 11.7 Hz, 1H), 5.05\* (dd, *J* = 11.7, 11.7 Hz, 1H), 4.63\*\* (dd, *J* = 11.7, 9.2 Hz, 1H), 4.62\*\* (dd, *J* = 11.7, 9.2 Hz, 1H), 4.25\*\* (dd, *J* = 11.7, 10.9 Hz, 1H), 4.23\*\* (dd, *J* = 11.7, 11.7 Hz, 1H), 1.91\* (s, 3H), 1.77 (s, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): 159.3\* (C), 158.3\*\* (C), 154.7\* (C), 153.4\*\* (C), 135.5\*\* (C), 135.4\* (C), 129.6\* (CH), 129.5\*\* (CH), 129.3\* (CH), 129.2\*\* (CH), 127.3 (CH), 71.6 (CH<sub>2</sub>), 60.7\* (CH), 60.6\*\* (CH), 20.7\* (CH<sub>3</sub>), 20.0\*\* (CH<sub>3</sub>) {note: CF<sub>3</sub> signal was not observed}; <sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>): -78.8\* (s), -78.9\*\* (s). HRESIMS *m/z* 271.0820 [M+H]<sup>+</sup>, calcd. 271.0815 for C<sub>12</sub>H<sub>13</sub>F<sub>3</sub>NO<sub>2</sub>.



**(3S,5R)-5-Phenyl-3-((S)-1,1,1-trifluoropropan-2-yl)morpholin-2-one (17).**

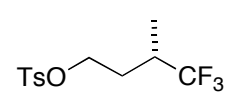
A mixture of oxazinone **3** (*dr* 7:1, 16.6 mg, 61.2 μmol) and PtO<sub>2</sub> (9.7 mg, 39.6 μmol) in PhCF<sub>3</sub> (1.5 mL) was evacuated twice and then stirred under 1 atm of

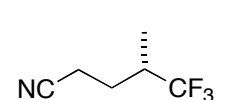
H<sub>2</sub> for 1.5 hours. The reaction mixture was filtered through a plug of cotton wool and concentrated under reduced pressure to give the crude product. Purification by flash chromatography (1:19 → 1:9 EtOAc:hexanes) gave **17** (9.1 mg, 54%) as a colorless oil; FTIR (ATR, neat):  $\nu$  3338, 3065, 3033, 2989, 2952, 2917, 2848, 1737, 1497, 1458, 1407, 1389, 1371, 1323, 1288, 1260, 1208, 1178, 1154, 1118, 1092, 1069, 1040, 977, 920, 875, 802, 782, 760, 701, 665 cm<sup>-1</sup>;  $[\alpha]_D^{20}$  -57.6 (*c* 2.76, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>)  $\delta$  7.04-7.02 (m, 3H), 6.96-6.94 (m, 2H), 3.86 (m, 1H), 3.68 (td, *J* = 10.6, 1.8 Hz, 1H), 3.61 (dq, *J* = 10.6, 3.0 Hz, 1H), 3.34 (m, 1H), 3.27 (m, 1H), 1.44 (br s, 1H), 1.11 (d, *J* = 6.9 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  167.3 (C), 137.1 (C), 129.0 (CH), 128.9 (CH), 127.7 (q, *J* = 278 Hz, CF<sub>3</sub>), 127.1 (CH), 74.9 (CH<sub>2</sub>), 58.5 (d, *J* = 2.3 Hz, CH), 56.7 (CH), 40.5 (q, *J* = 25.8 Hz, CH), 8.37 (d, *J* = 2.3 Hz, CH<sub>3</sub>); HREIMS *m/z* 273.0970 [M]<sup>+</sup>, calcd. 273.0971 for C<sub>13</sub>H<sub>14</sub>F<sub>3</sub>NO<sub>2</sub>. HPLC analysis (Econosil 5  $\mu$  silica column, 3:7 Et<sub>2</sub>O:hexanes, flow rate 1 mL/min, UV detection at  $\lambda$  210/220 nm) showed a retention time of 5.7 min for **17**. Repeating the reaction using **3** as a single diastereomer gave a mixture of products that was analysed under the HPLC conditions described above. Integration of the peaks for **17** (*t*<sub>R</sub> 5.7 min) and the minor diastereomer (*t*<sub>R</sub> 13.7 min) indicated a *dr* of 3:1.



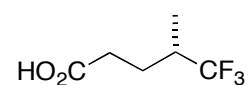
**(2S,3S)-4,4,4-Trifluorovaline (1)**. Pd(OH)<sub>2</sub> (20 % wt, 25.1 mg, 0.0471 mmol) and 2.4 M HCl (314  $\mu$ L, 0.753 mmol) were added to morpholinone **17** (51.5 mg, 0.188 mmol) in MeOH (6 mL) and H<sub>2</sub>O (0.4 mL) and the mixture shaken under 90 psi of H<sub>2</sub> in a thick-walled Parr hydrogenation vessel for two hours.

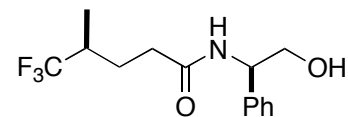
The reaction mixture filtered through a pad of Celite and concentrated under reduced pressure, then re-dissolved in 6 M HCl (6 mL) and heated at 110 °C for 20 hours. The reaction mixture was again concentrated under reduced to give **1**•HCl (40.0 mg) as an orange solid;  $[\alpha]_D^{24}$  +7.0 (*c* 1.0, 1.0 N HCl); lit.<sup>4</sup>  $[\alpha]_D^{24}$  +7.2 (*c* 0.75, 1.0 N HCl); <sup>1</sup>H NMR (500 MHz, D<sub>2</sub>O):  $\delta$  4.33 (d, *J* = 2.6 Hz, 1H), 3.25 (m, 1H), 1.21 (d, *J* = 7.4 Hz, 3H); <sup>19</sup>F NMR (471 MHz, D<sub>2</sub>O/1% CF<sub>3</sub>CO<sub>2</sub>H):  $\delta$  71.62 (s); lit.<sup>5a</sup> <sup>19</sup>F NMR (283 MHz, D<sub>2</sub>O/CF<sub>3</sub>CO<sub>2</sub>H):  $\delta$  71.69 (d, *J* = 9.3 Hz). Ion-exchange chromatography (Dowex 50X2-400, strongly acidic cation resin, 200-400 dry-mesh, eluting with 2.0 M NH<sub>4</sub>OH) gave free amino acid **5** (28.7 mg, 89%) as a white solid;  $[\alpha]_D^{22}$  +0.22 (*c* 1.0, D<sub>2</sub>O); <sup>1</sup>H NMR (500 MHz, D<sub>2</sub>O):  $\delta$  4.08 (d, *J* = 2.3 Hz, 1H), 3.16 (m, 1H), 1.18 (d, *J* = 7.5 Hz, 3H); HRESIMS *m/z* 172.0579 [M+H]<sup>+</sup>, calcd. 172.0580 for C<sub>5</sub>H<sub>9</sub>F<sub>3</sub>NO<sub>2</sub>.

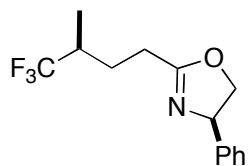

**(S)-4,4,4-Trifluoro-3-methylbutyl-4-methylbenzenesulfonate (18).** The sultam amide (2.74 g, 7.75 mmol, dr 4:1) in THF (48 mL) was cannulated into a mixture of LiAlH<sub>4</sub> (294 mg, 7.75 mmol) in THF (30 mL) at rt and was stirred for 1.25 h. It was then quenched slowly with H<sub>2</sub>O until the bubbling ceased and then solid Na<sub>2</sub>SO<sub>4</sub> was added. The reaction was filtered through a pad of Celite and concentrated *in vacuo* on low heat and low vacuum since the primary alcohol is volatile. To the crude was added pentane (50 mL) and it was cooled to 0 °C which cause the sultam byproduct to precipitate. The solid was filtered and the filtrate was concentrated *in vacuo* again on low heat/low vacuum. The crude oil was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (15 mL) and DABCO (1.74 g, 15.5 mmol) was added and the reaction was cooled to 0 °C. TsCl (2.2 g, 11.6 mmol) was added in small portions and the reaction was stirred for 21 h and then filtered through a pad of Celite. The filtrate was extracted with 2 M HCl and then 10% NaHCO<sub>3</sub> and dried over MgSO<sub>4</sub>. The crude pale yellow oil was chromatographed (SiO<sub>2</sub>, 5:95 → 10:90 → 15:85 EtOAc:hexanes) to provide the tosylate as a colorless oil (1.27 g, 55%, 60% *ee*).  $[\alpha]_D^{23} -7.2$  (*c* 1.0, CHCl<sub>3</sub>);  $R_f = 0.24$  (30% EtOAc/hexanes); IR (neat)  $\nu$  1360 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.79 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 4.14-4.06 (m, 2H), 2.45 (s, 3H), 2.38-2.27 (m, 1H), 2.05 (dddd, *J* = 14.6, 8.0, 6.3, 5.2 Hz, 1H), 1.61 (dddd, *J* = 14.3, 8.6, 5.2, 5.2 Hz, 1H), 1.07 (d, *J* = 6.8 Hz, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  145.2 (C), 132.8 (C), 130.1 (CH), 129.5 (q, *J* = 279.5 Hz, CF<sub>3</sub>), 128.0 (CH), 67.1 (CH<sub>2</sub>), 34.5 (q, *J* = 27.6 Hz, CH), 29.0 (CH<sub>2</sub>), 21.8 (CH), 12.4 (q, *J* = 2.4 Hz, CH<sub>3</sub>); HR ESIMS *m/z* [M+NH<sub>4</sub>]<sup>+</sup> 314.1039, calcd for C<sub>12</sub>H<sub>19</sub>F<sub>3</sub>NO<sub>3</sub>S 314.1038.


**(S)-5,5,5-Trifluoro-4-methylpentanenitrile (19).** NaI (42.1 mg, 286 μmol) was added to the tosylate (849 mg, 2.86 mmol) and NaCN (700 mg, 14.3 mmol) in DMSO (5.7 mL) and the reaction was heated to 60 °C for 1.5 h. After cooling to rt, added Et<sub>2</sub>O and then extracted the Et<sub>2</sub>O layer with H<sub>2</sub>O then brine and dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed *in vacuo* under low heat and the excess Et<sub>2</sub>O was removed by distillation at 100 °C. The remaining oil left behind contained the pure nitrile (345 mg, 80%, 60% *ee*).  $[\alpha]_D^{22} -7.8$  (*c* 2.0, CHCl<sub>3</sub>);  $R_f = 0.47$  (30% EtOAc/hexanes); IR (neat)  $\nu$  2250 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  2.54-2.31 (m, 3H), 2.05 (dq, *J* = 14.3, 9.4 Hz, 1H), 1.70 (dq, *J* = 14.3, 7.2 Hz, 1H), 1.66 (d, *J* = 7.2 Hz, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  127.7 (q, *J* = 279.5 Hz, CF<sub>3</sub>), 118.7 (C),

37.1 (q,  $J = 26.4$  Hz, CH), 25.6 (q,  $J = 2.4$  Hz, CH<sub>2</sub>), 14.9 (CH<sub>2</sub>), 12.5 (q,  $J = 2.4$  Hz, CH<sub>3</sub>); HR TOFMS-CI  $m/z$  [M+H]<sup>+</sup> 152.0676, calcd for C<sub>6</sub>H<sub>9</sub>F<sub>3</sub>N 152.0682.

 **(S)-5,5,5-Trifluoro-4-methylpentanoic acid (8).** Concentrated HCl (3.5 mL) was added to the nitrile (172 mg, 1.14 mmol) and the reaction was heated to 100 °C for 2.5 h and then cooled. Water was added and the reaction was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined CH<sub>2</sub>Cl<sub>2</sub> layers were dried over MgSO<sub>4</sub>, filtered, and concentrated to a pale yellow oil that was clean by <sup>1</sup>H NMR (140 mg, 73%, 60% *ee*). [ $\alpha$ ]<sub>D</sub><sup>22</sup> -9.4 (*c* 1.0, CHCl<sub>3</sub>); IR (neat)  $\nu$  1713 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  10.75 (br s, 1H), 2.50 (ddd,  $J = 16.6, 8.6, 6.3$  Hz, 1H), 2.43 (ddd,  $J = 16.6, 8.3, 6.9$  Hz, 1H), 2.31-2.20 (m, 1H), 2.02 (dddd,  $J = 14.3, 8.6, 7.2, 5.5$  Hz, 1H), 1.66 (dddd,  $J = 14.6, 8.6, 8.6, 6.3$  Hz, 1H), 1.12 (d,  $J = 6.9$  Hz, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  179.4 (C), 128.2 (q,  $J = 280$  Hz, CF<sub>3</sub>), 37.2 (q,  $J = 26.4$  Hz, CH), 31.1 (CH<sub>2</sub>), 24.6 (CH<sub>2</sub>), 12.7 (CH<sub>3</sub>); HR ESIMS  $m/z$  [M-H]<sup>+</sup> 169.0481, calcd for C<sub>6</sub>H<sub>8</sub>F<sub>3</sub>O<sub>2</sub> 169.0476.

 **(S)-5,5,5-Trifluoro-N-((R)-2-hydroxy-1-phenylethyl)-4-methylpentanamide (6).** To the carboxylic acid (117 mg, 688  $\mu$ mol) and *R*-phenylglycinol (189 mg, 1.38 mmol) in DMF (6.8 mL) at rt was added Et<sub>3</sub>N (240  $\mu$ L, 1.72 mmol) and then HATU (523 mg, 1.38 mmol). The reaction was stirred for 15 h and then brine was added and the reaction was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined CH<sub>2</sub>Cl<sub>2</sub> layers were dried over MgSO<sub>4</sub> and concentrated to a tan oil. Ether was added and then washed with H<sub>2</sub>O, to remove excess DMF, and was then dried again over MgSO<sub>4</sub> and concentrated to a crude oil. Column chromatography (SiO<sub>2</sub>, 50:50  $\rightarrow$  70:30  $\rightarrow$  90:10 EtOAc:hexanes) provided the oxazoline as a colorless oil (168 mg, 84% yield, 4:1 *dr*). The two diastereomers could not be separated and only one set of peaks was observed in the <sup>1</sup>H NMR. [ $\alpha$ ]<sub>D</sub><sup>22</sup> -47.6 (*c* 1.0, CHCl<sub>3</sub>); IR (neat)  $\nu$  3300 (br), 1644 cm<sup>-1</sup>;  $R_f = 0.10$  (60% EtOAc/hexanes); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.38-7.23 (m, 5H), 6.59 (br d,  $J = 6.8$  Hz, 1H, *NH*), 5.00 (dd,  $J = 12.4, 5.6$  Hz, 1H), 3.82-3.77 (m, 2H), 3.17 (br t,  $J = 5.2$  Hz, 1H, *OH*), 2.37-2.12 (m, 3H), 1.98 (dddd,  $J = 14.4, 8.8, 6.8, 6.0$  Hz, 1H), 1.73-1.62 (m, 1H), 1.09 (d,  $J = 7.2$  Hz, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  172.5 (C), 139.0 (C), 128.9 (CH), 128.7 (q,  $J = 279.5$  Hz, CF<sub>3</sub>), 127.9 (CH), 126.7 (CH), 66.3 (CH<sub>2</sub>), 55.9 (CH), 37.2 (q,  $J = 26.4$  Hz, CH), 33.3 (CH<sub>2</sub>), 25.5 (CH<sub>2</sub>), 12.9 (CH<sub>3</sub>); HR ESIMS  $m/z$  [M+H]<sup>+</sup> 290.1366, calcd for C<sub>14</sub>H<sub>19</sub>F<sub>3</sub>NO<sub>2</sub> 290.1362.



**(R)-4-Phenyl-2-((S)-4,4,4-trifluoro-3-methylbutyl)-4,5-dihydrooxazole (20).** DAST (89.0  $\mu\text{L}$ , 678  $\mu\text{mol}$ ) was added dropwise to the amide (178 mg, 617  $\mu\text{mol}$ ) in  $\text{CH}_2\text{Cl}_2$  (6.2 mL) at  $-78^\circ\text{C}$ . After 1.2 h, the reaction was complete by TLC and quenched with  $\text{K}_2\text{CO}_3$  (128 mg, 925  $\mu\text{mol}$ ) and

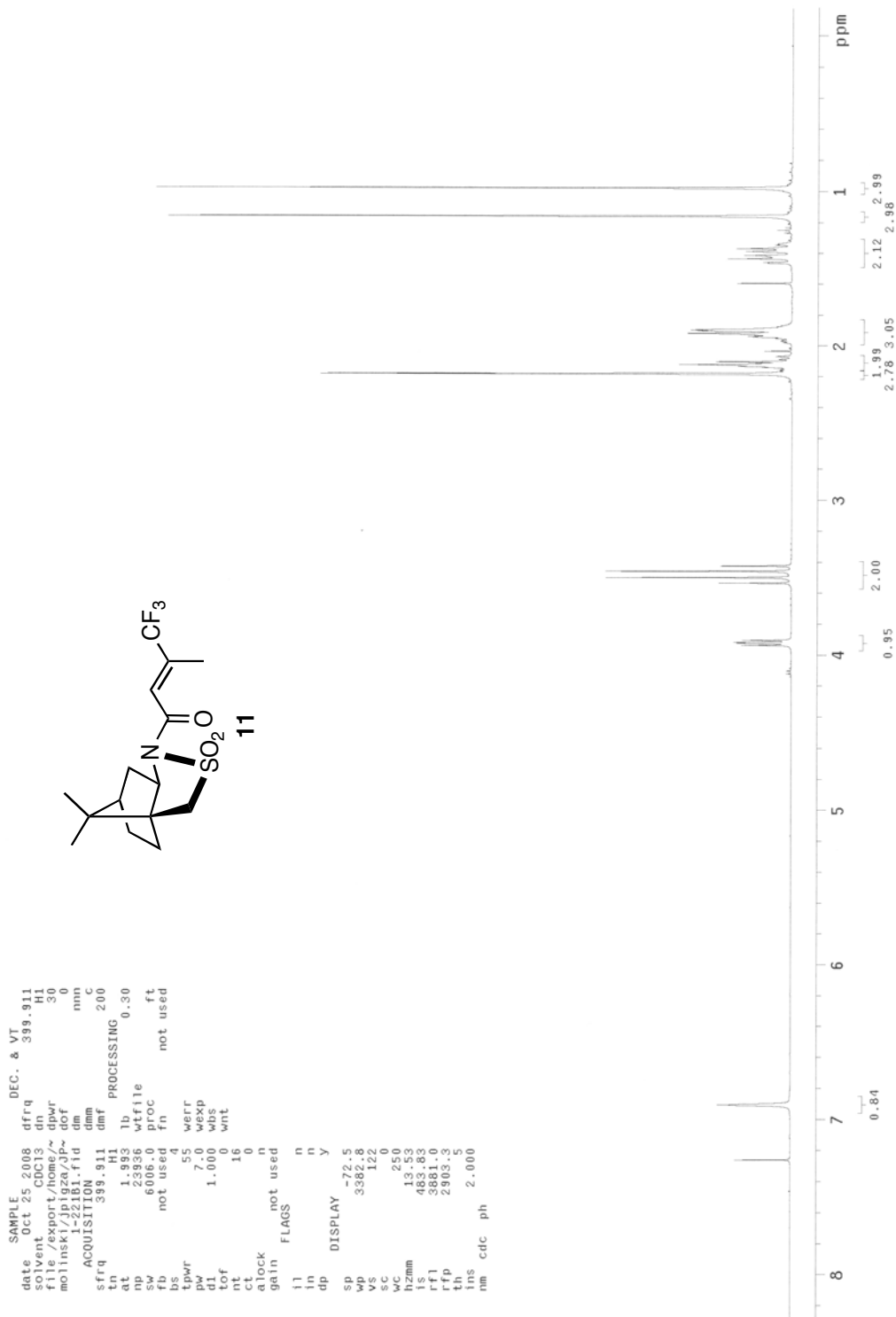
allowed to stir at  $-78^\circ\text{C}$  for 15 min before warming to rt for 1 h. Then satd. aq.  $\text{NaHCO}_3$  was added and the reaction was stirred for 10 min before extraction with  $\text{CH}_2\text{Cl}_2$ . The combined organic layers were dried over  $\text{MgSO}_4$ , filtered, and concentrated to a pale yellow oil. Column chromatography ( $\text{SiO}_2$ , 10-20-30% EtOAc/hexanes) provided the desired oxazole product as a colorless oil (144 mg, 86%, 4:1 *dr*). The two diastereomers could not be separated and only one set of peaks was observed in the  $^1\text{H}$  NMR.  $[\alpha]_D^{22} +22.6$  (*c* 2.0,  $\text{CHCl}_3$ );  $R_f = 0.12$  (20:80 EtOAc:hexanes); IR (neat)  $\nu$  1666  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.37-7.32 (m, 2H), 7.30-7.26 (m, 1H), 7.24-7.22 (m, 2H), 5.17 (dd,  $J = 9.2, 9.2$  Hz, 1H), 4.60 (dd,  $J = 8.5, 8.5$  Hz, 1H), 4.08 (dd,  $J = 8.6, 8.6$  Hz, 1H), 2.52 (ddd,  $J = 15.5, 9.2, 5.7$  Hz, 1H), 2.44 (ddd,  $J = 15.8, 9.1, 7.2$  Hz, 1H), 2.36-2.26 (m, 1H), 2.12 (dddd,  $J = 14.4, 9.4, 6.6, 5.2$  Hz, 1H), 1.75 (dddd,  $J = 14.3, 8.6, 8.6, 5.7$  Hz, 1H), 1.15 (d,  $J = 6.9$  Hz, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  167.9 (C), 142.3 (C), 128.8 (CH), 128.3 (q,  $J = 279.5$  Hz,  $\text{CF}_3$ ), 127.7 (CH), 126.6 (CH), 74.7 ( $\text{CH}_2$ ), 69.7 (CH), 37.3 (q,  $J = 26.4$  Hz, CH), 26.0 ( $\text{CH}_2$ ), 25.3 ( $\text{CH}_2$ ), 12.6 ( $\text{CH}_3$ ); HR ESIMS  $m/z$   $[\text{M}+\text{H}]^+$  272.1258, calcd for  $\text{C}_{14}\text{H}_{17}\text{F}_3\text{NO}$  272.1262.

## References

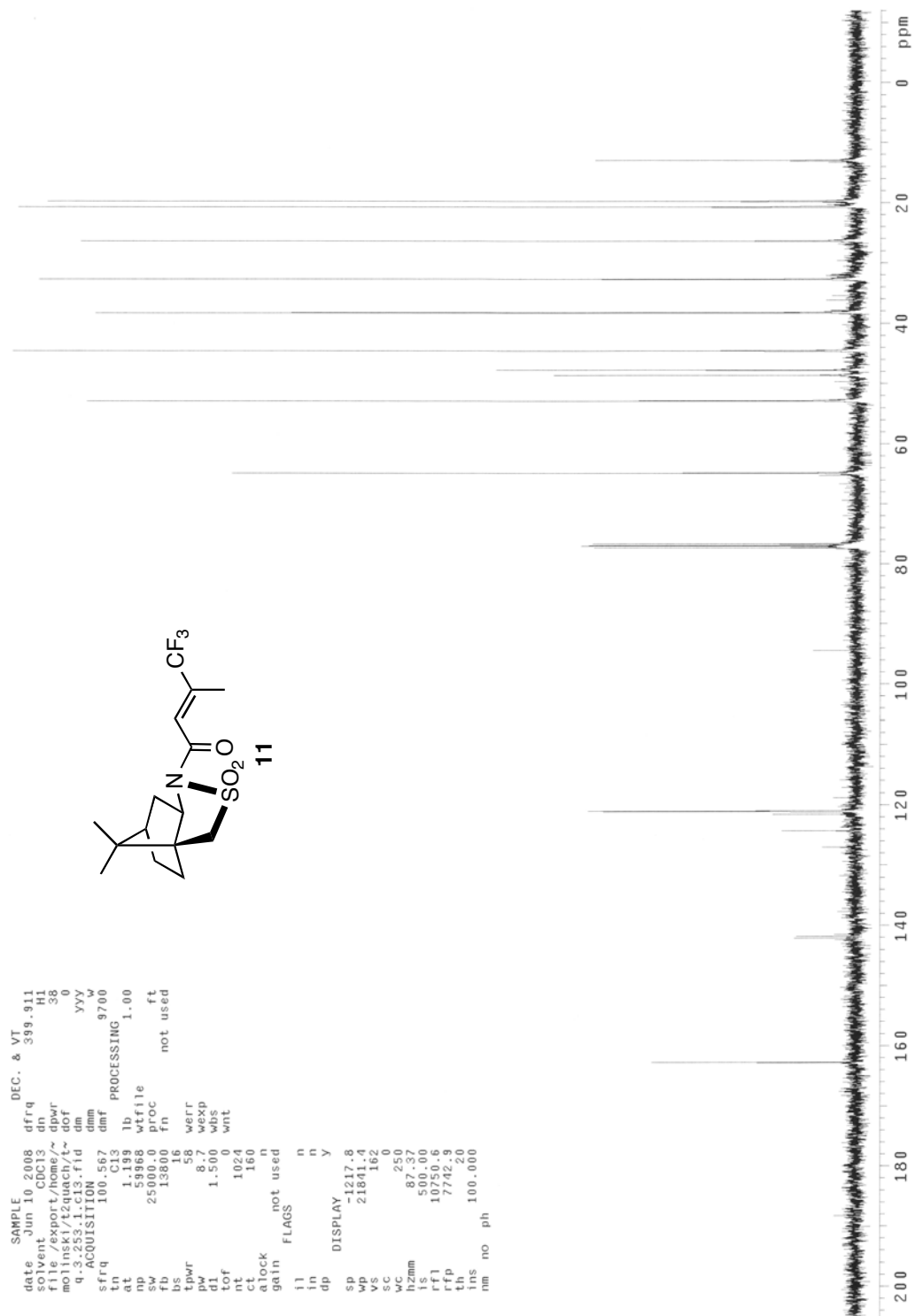
1. Oppolzer, W.; Mills, R. J.; Reglier, M. *Tetrahedron Lett.* **1986**, 27, 183.
2. Weinges, K.; Kromm, E. *Liebigs Ann. Chem.* **1985**, 90.
3. Acid **7**
4. (a) Xing, X.; Fichera, A.; Kumar, K. *J. Org. Chem.* **2002**, 67, 1722. (b) Xing, X.; Fichera, A.; Kumar, K. *J. Org. Chem.* **2002**, 67, 8290 (correction to ref 5a).

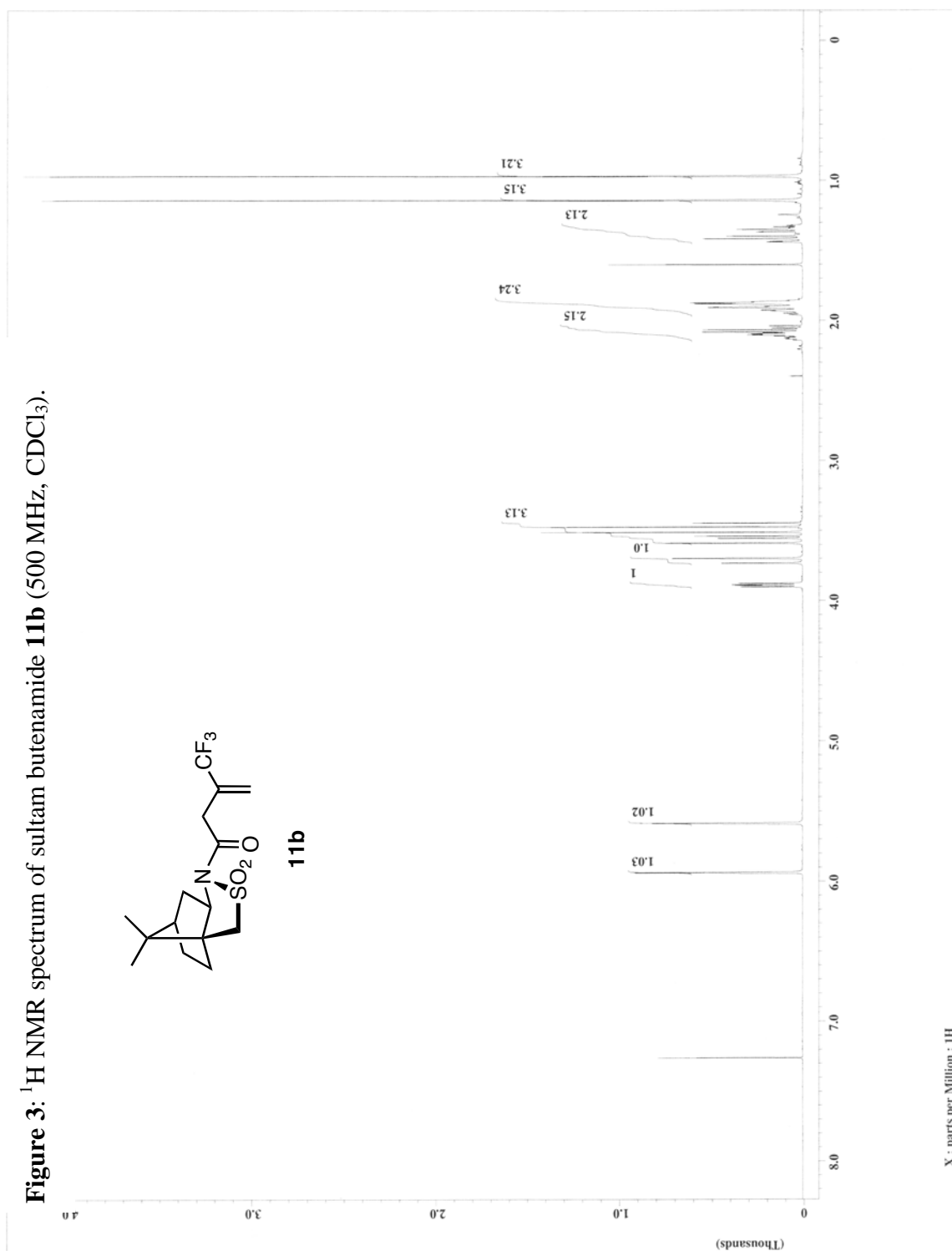
# NMR spectra of compounds

**Figure 1:** <sup>1</sup>H NMR spectrum of sultam butenamide **11** (400 MHz, CDCl<sub>3</sub>).

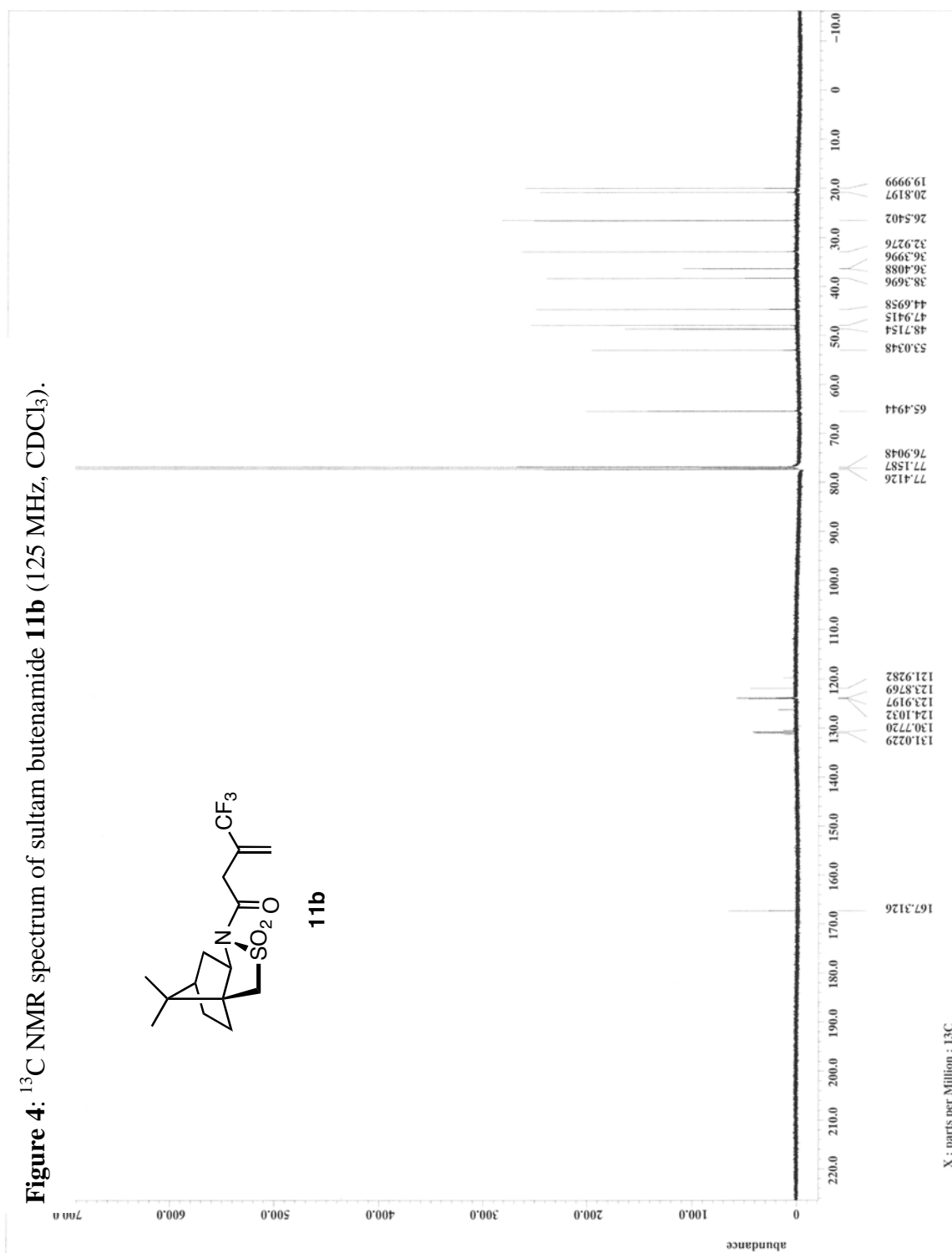


**Figure 2:**  $^{13}\text{C}$  NMR spectrum of sultam butenamide **11** (100 MHz,  $\text{CDCl}_3$ ).

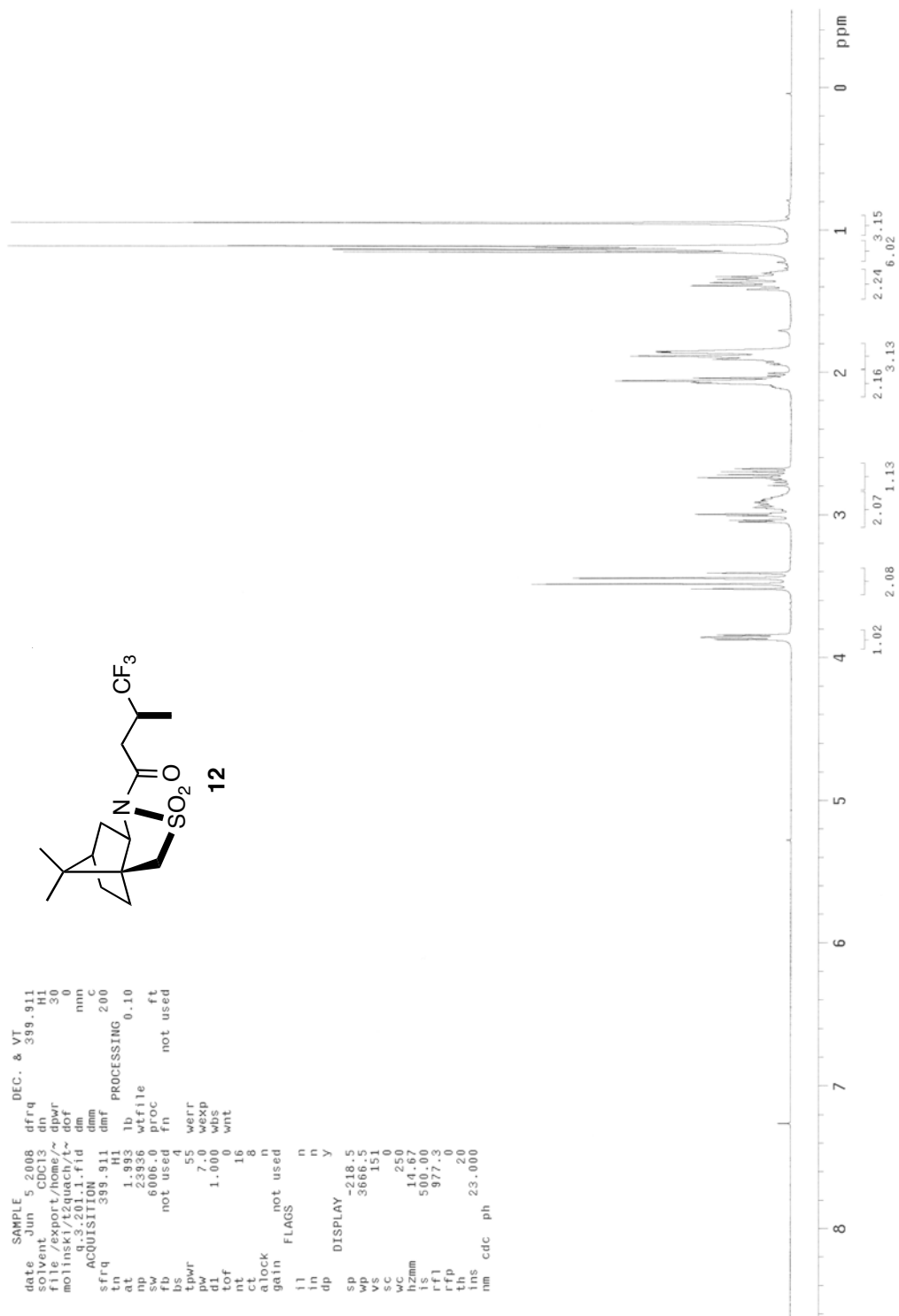




**Figure 4:**  $^{13}\text{C}$  NMR spectrum of sultam butenamide **11b** (125 MHz,  $\text{CDCl}_3$ ).



**Figure 5:**  $^1\text{H}$  NMR spectrum of sultam butanamide **12** (400 MHz,  $\text{CDCl}_3$ ).



**Figure 6:**  $^{13}\text{C}$  NMR spectrum of sultam butanamide **12** (100 MHz,  $\text{CDCl}_3$ ).

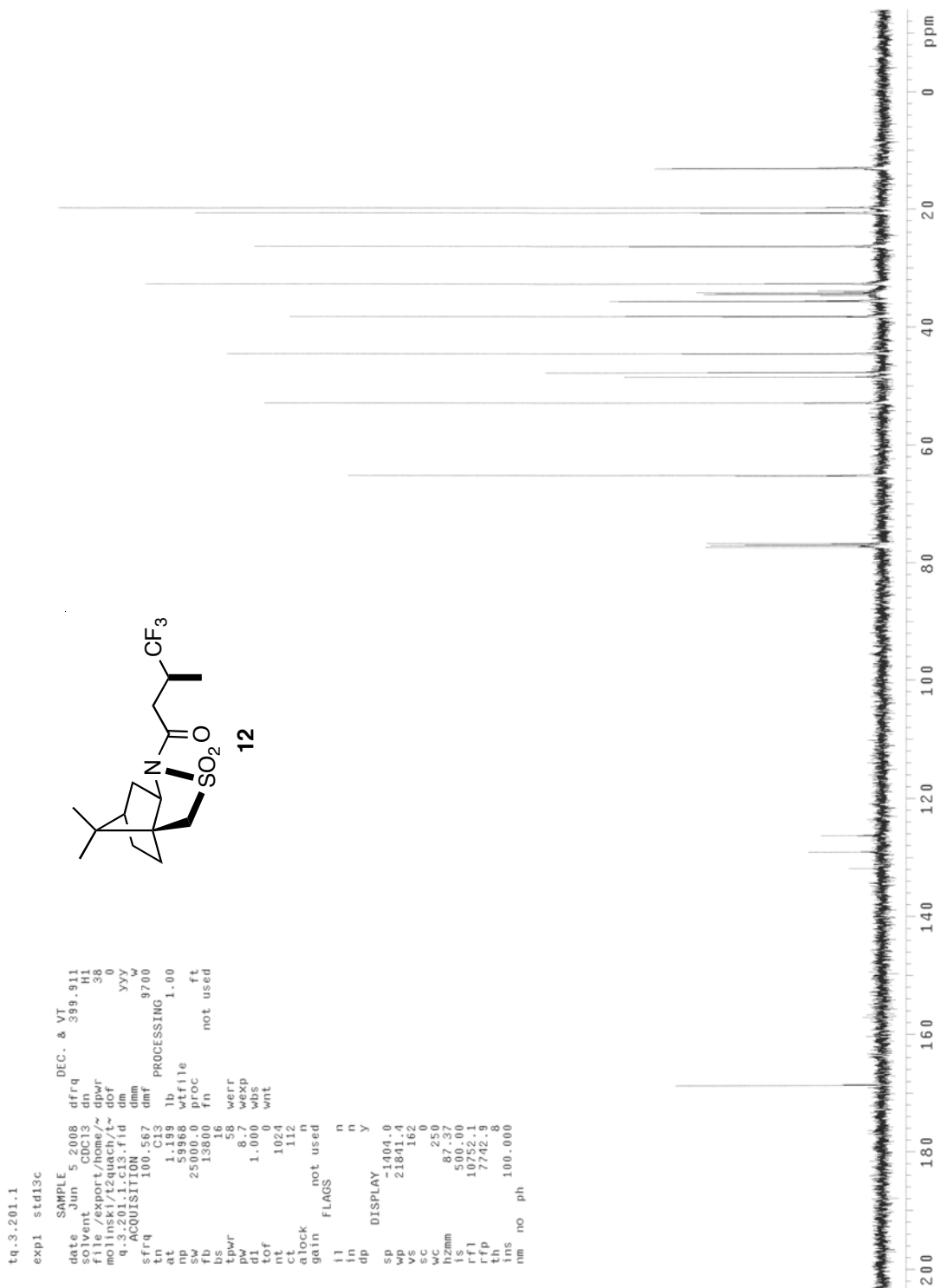
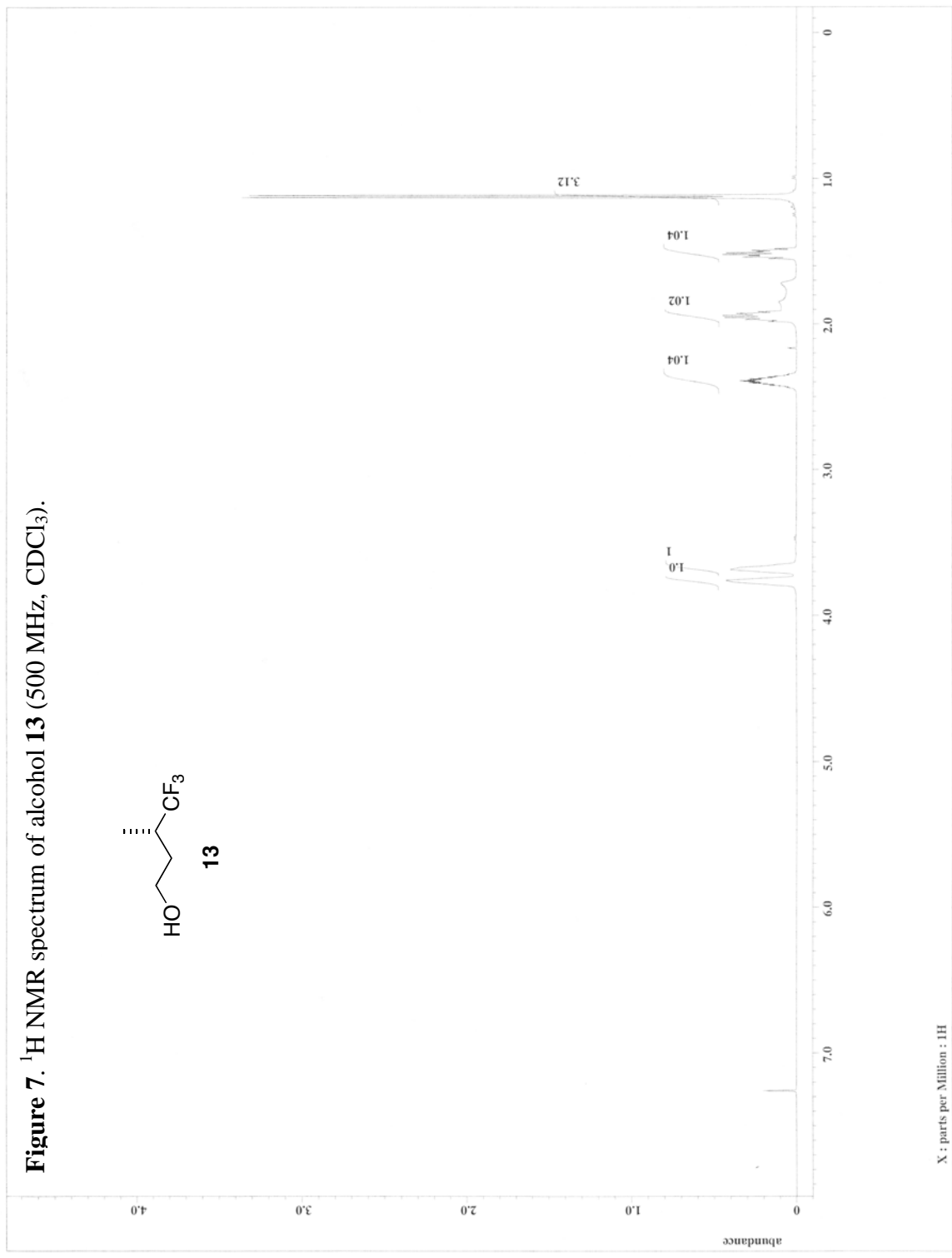
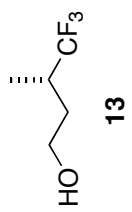
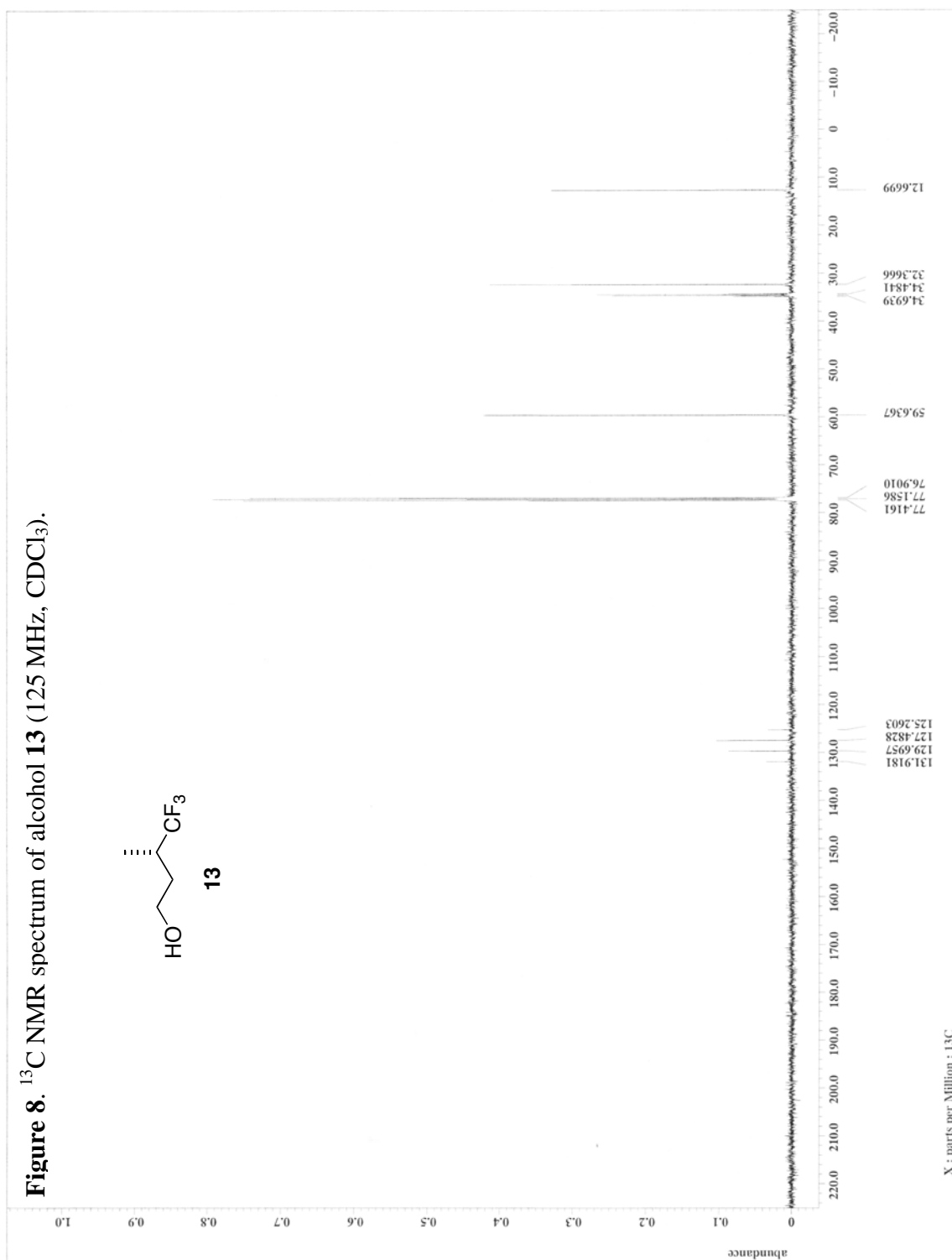


Figure 7. <sup>1</sup>H NMR spectrum of alcohol **13** (500 MHz, CDCl<sub>3</sub>).



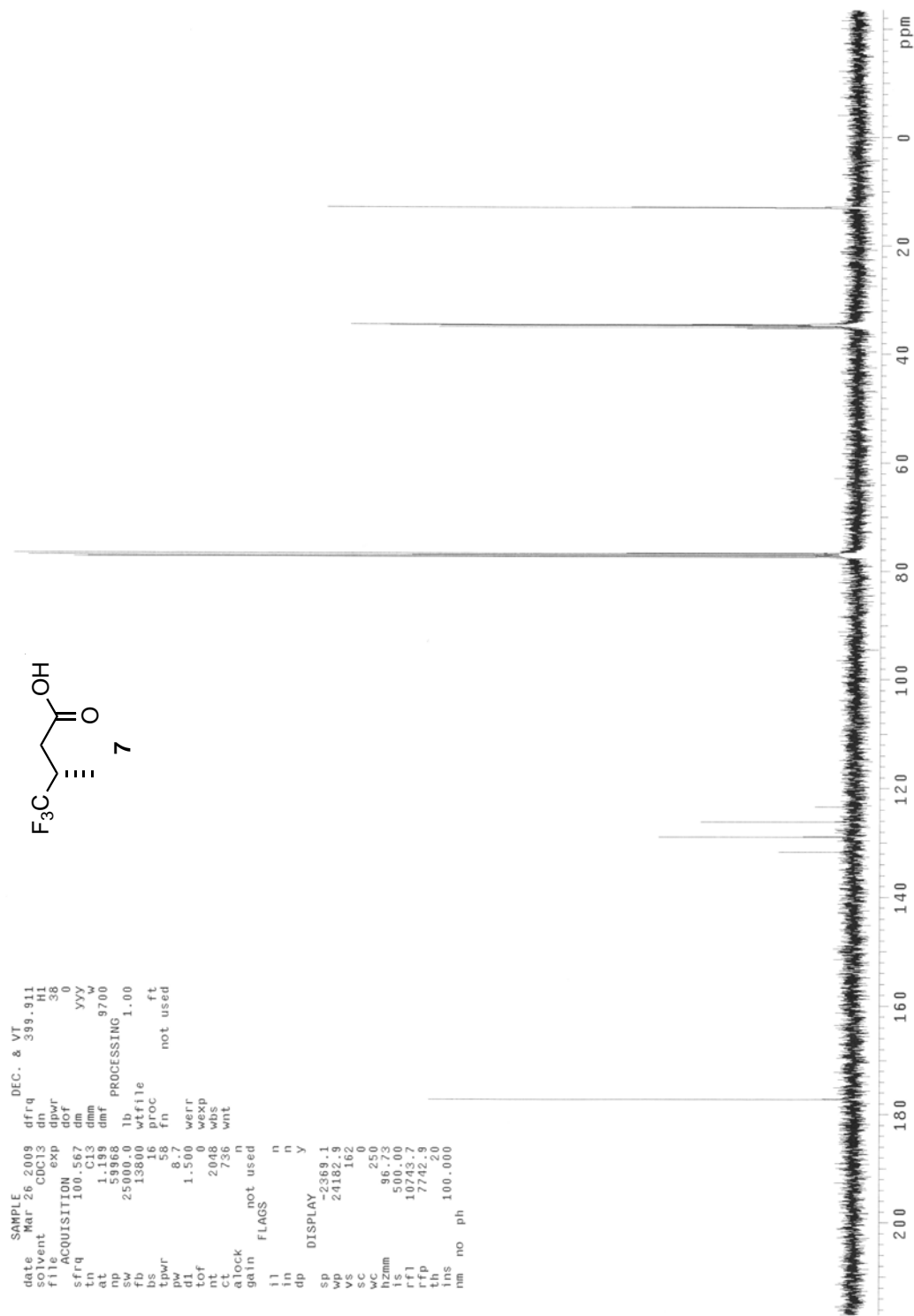
X : parts per Million : 1H



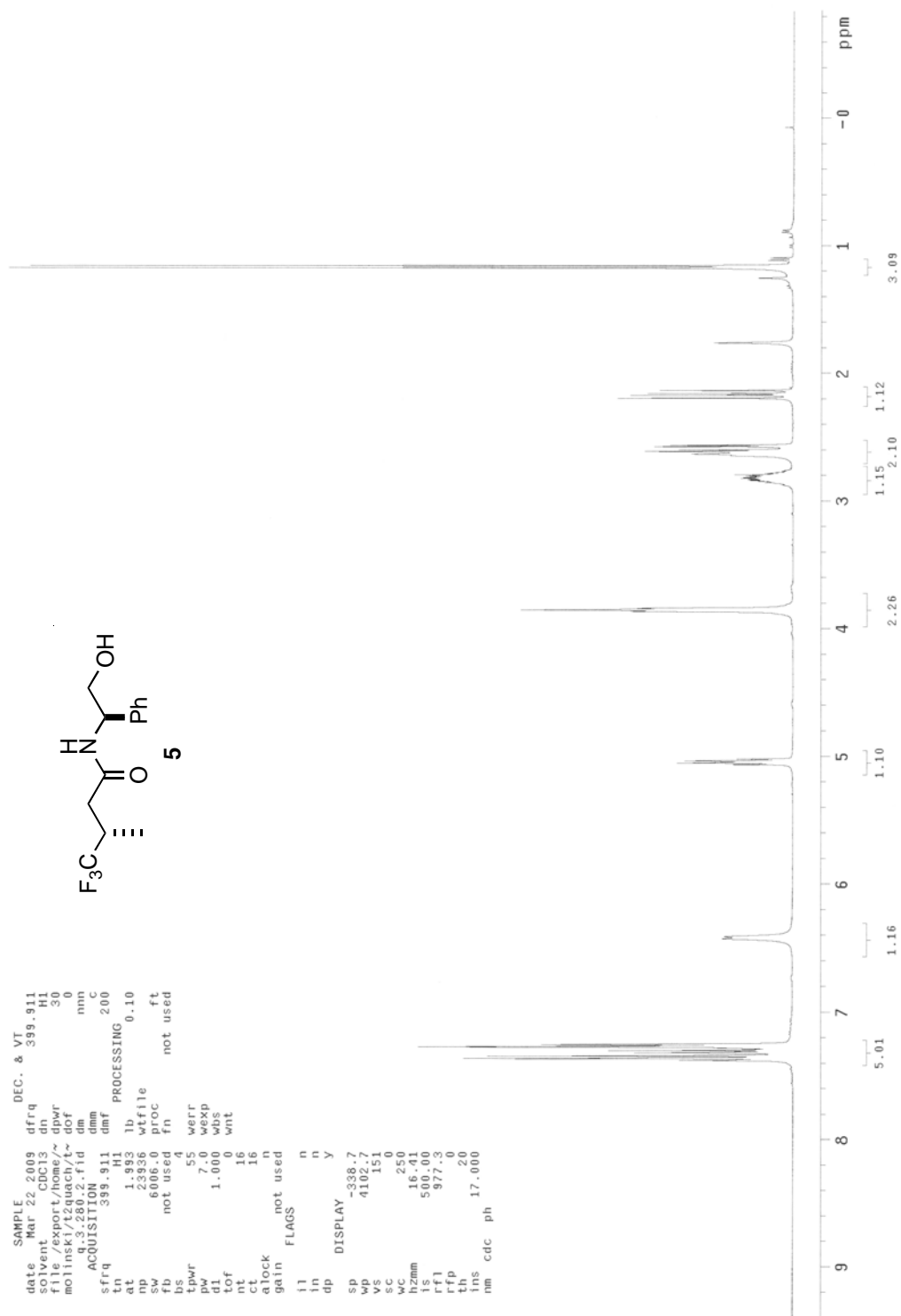
**Figure 9:**  $^1\text{H}$  NMR spectrum of acid **7** (400 MHz,  $\text{CDCl}_3$ ).



**Figure 10:**  $^{13}\text{C}$  NMR spectrum of acid **7** (100 MHz,  $\text{CDCl}_3$ ).



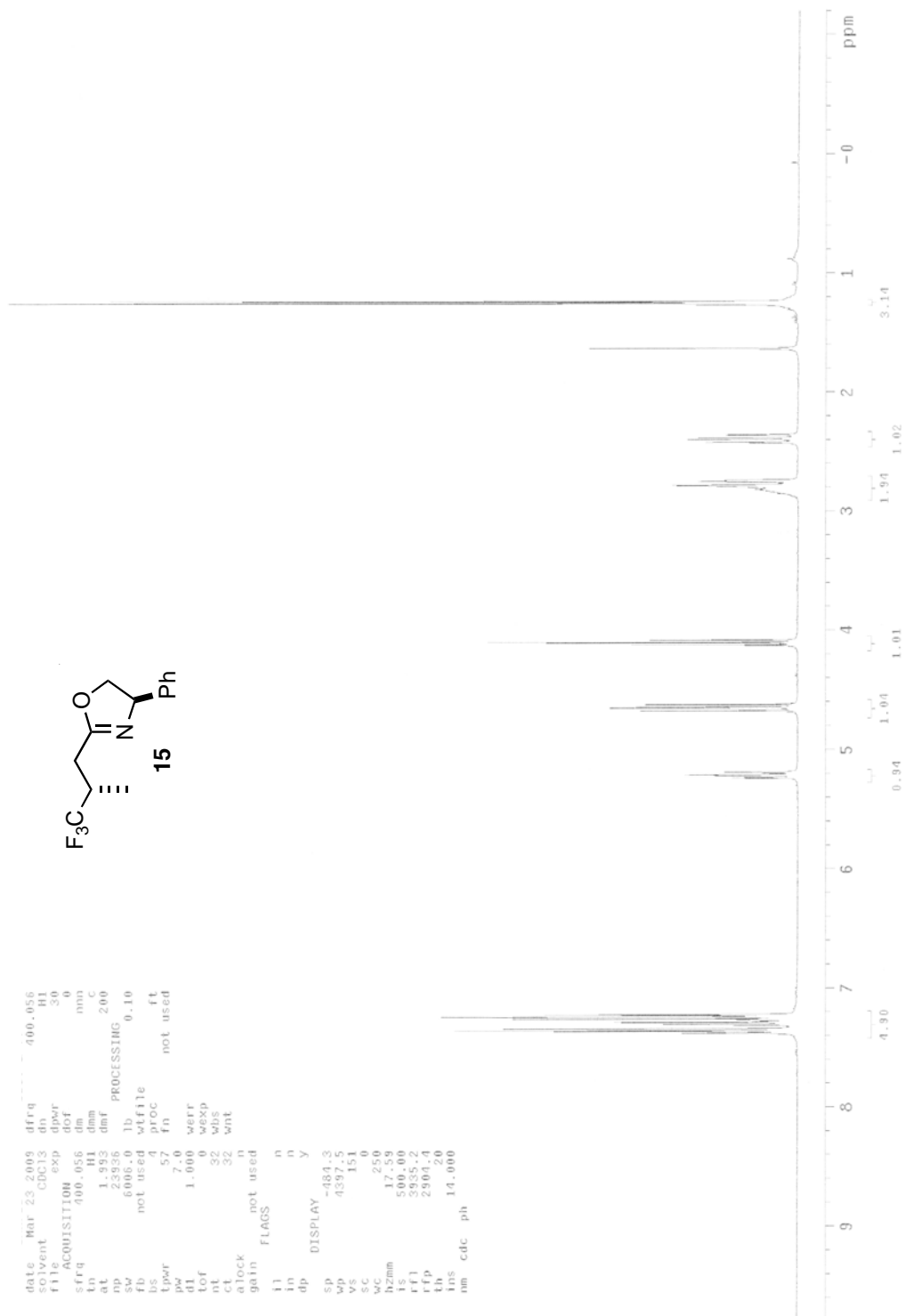
**Figure 11:**  $^1\text{H}$  NMR spectrum of amide **5** (400 MHz,  $\text{CDCl}_3$ ).



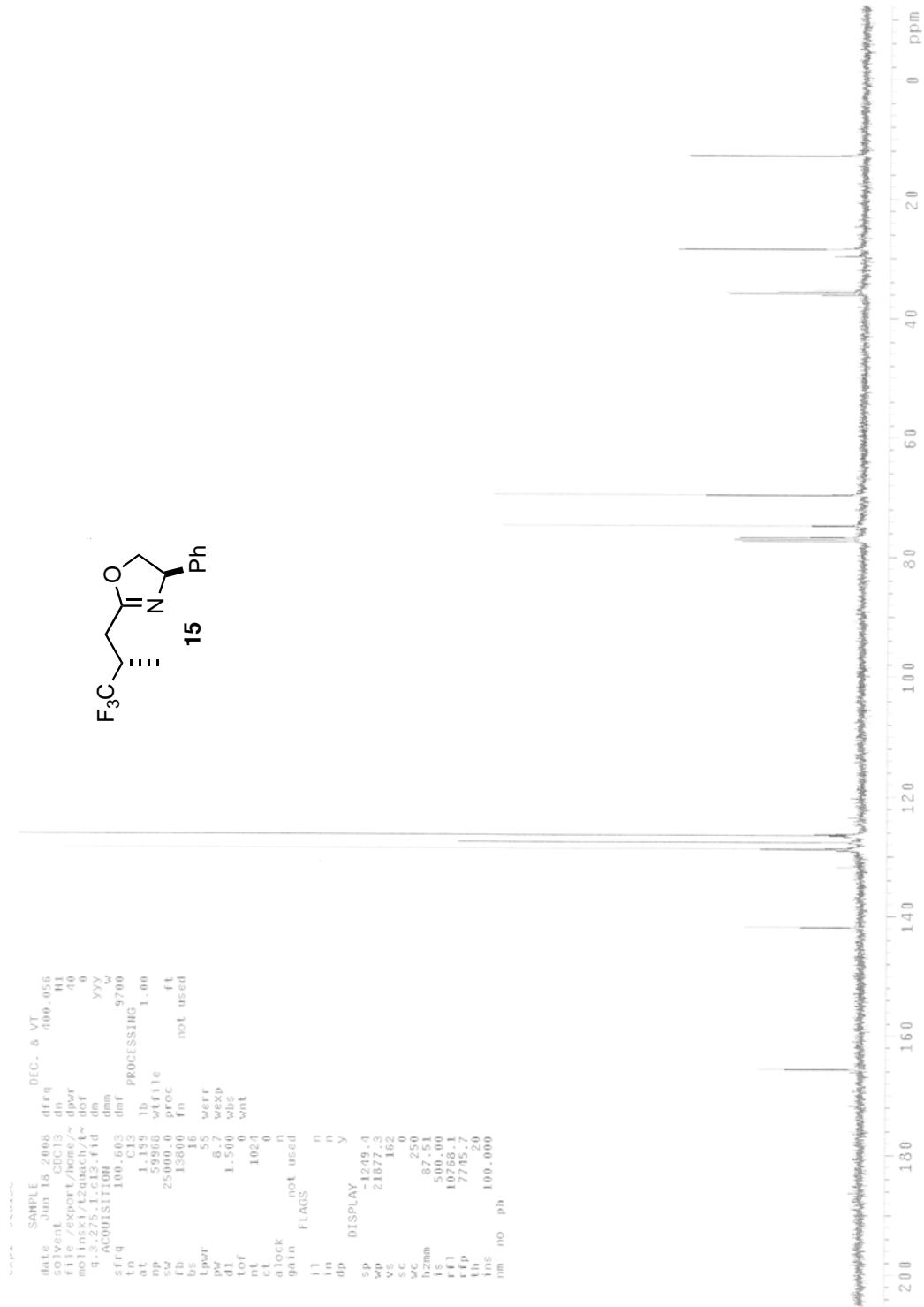
**Figure 12:**  $^{13}\text{C}$  NMR spectrum of amide **5** (100 MHz,  $\text{CDCl}_3$ ).



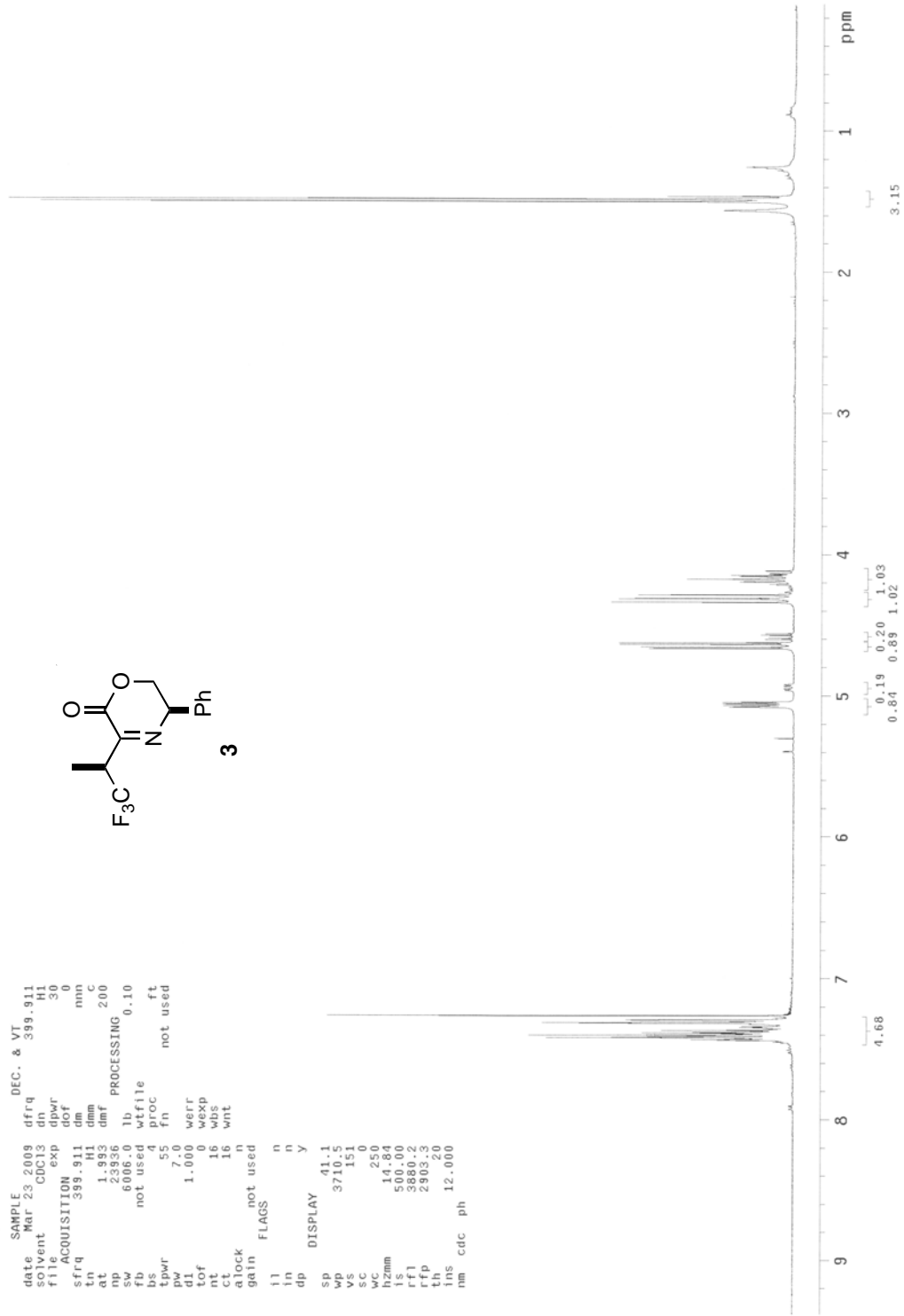
**Figure 13:**  $^1\text{H}$  NMR spectrum of oxazoline **15** (400 MHz,  $\text{CDCl}_3$ ).



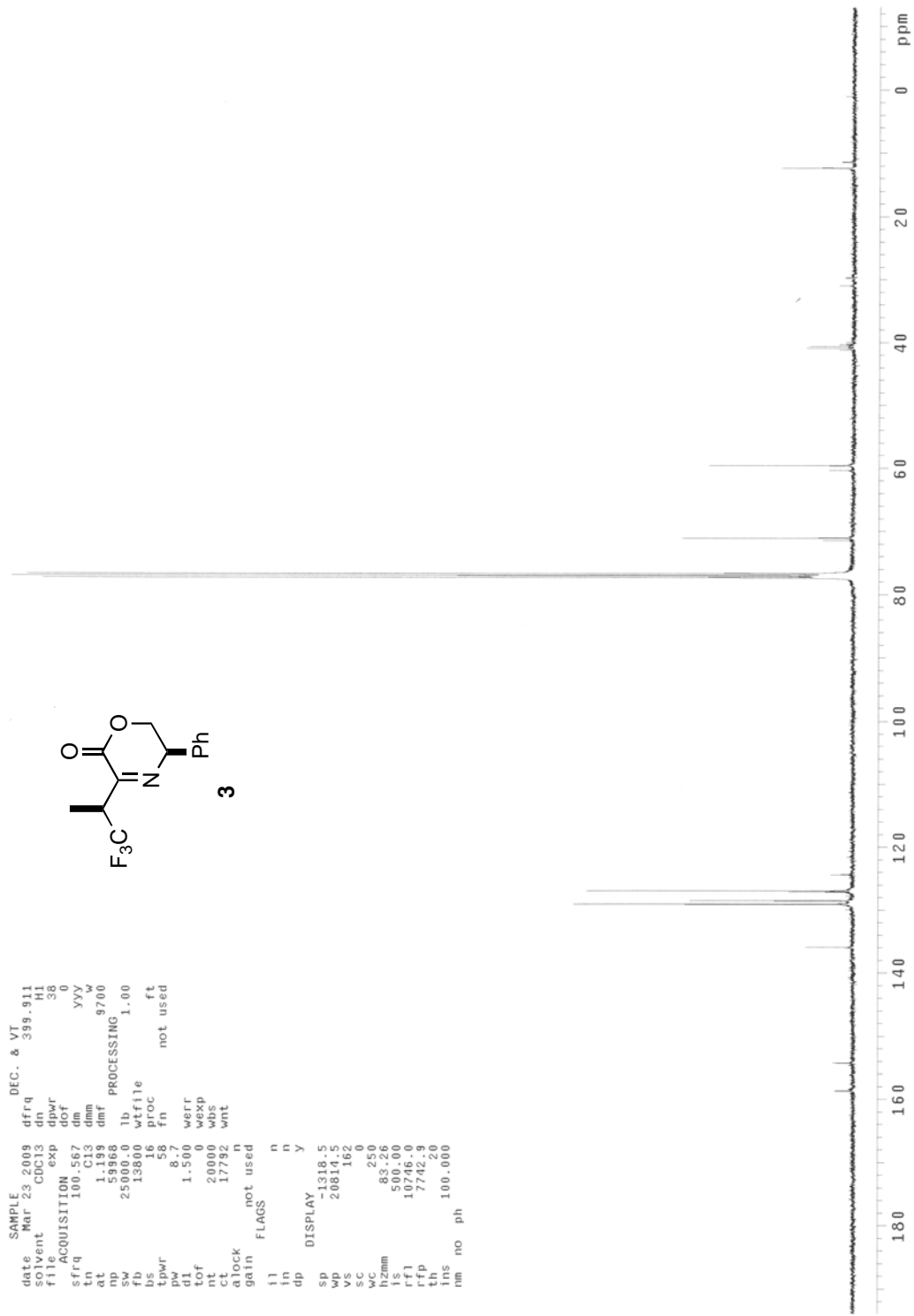
**Figure 14:**  $^{13}\text{C}$  NMR spectrum of oxazoline **15** (100 MHz,  $\text{CDCl}_3$ ).



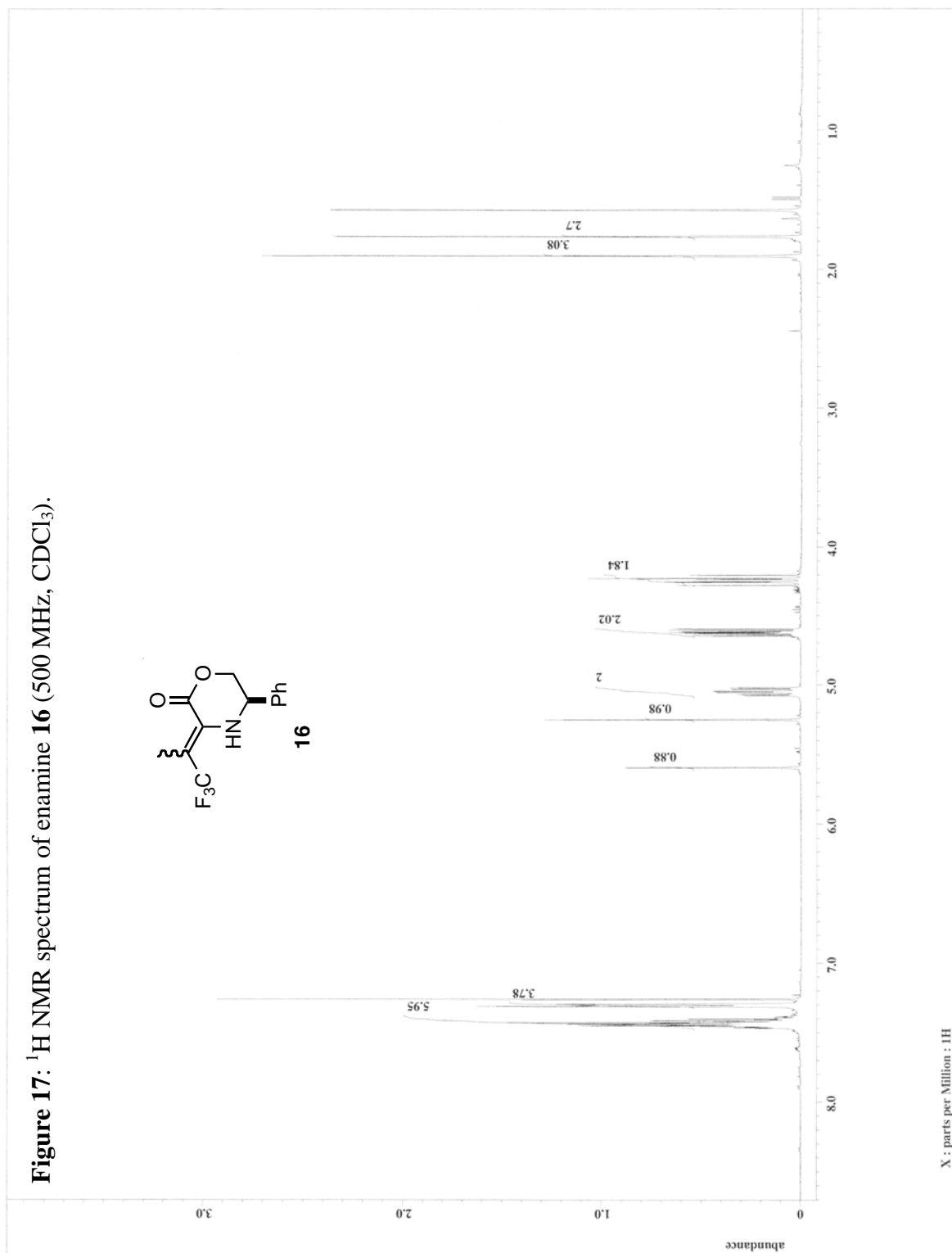
**Figure 15:**  $^1\text{H}$  NMR spectrum of oxazinone **3** (400 MHz,  $\text{CDCl}_3$ ).



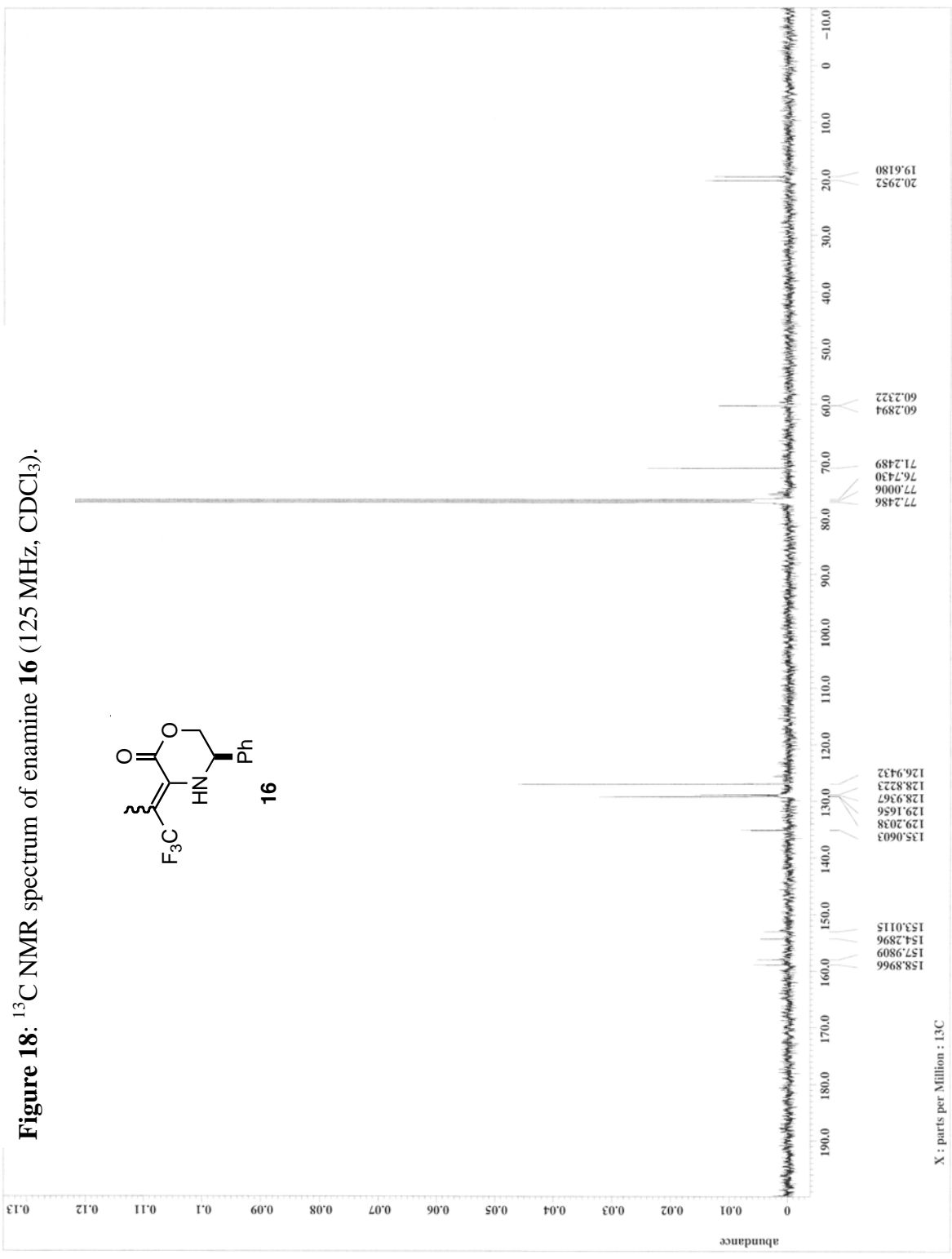
**Figure 16:**  $^{13}\text{C}$  NMR spectrum of oxazinone **3** (100 MHz,  $\text{CDCl}_3$ ).



**Figure 17:**  $^1\text{H}$  NMR spectrum of enamine **16** (500 MHz,  $\text{CDCl}_3$ ).



X : parts per Million : 1H



**Figure 19:**  $^{19}\text{F}$  NMR spectrum of enamine **16** (471 MHz,  $\text{CDCl}_3$ ).

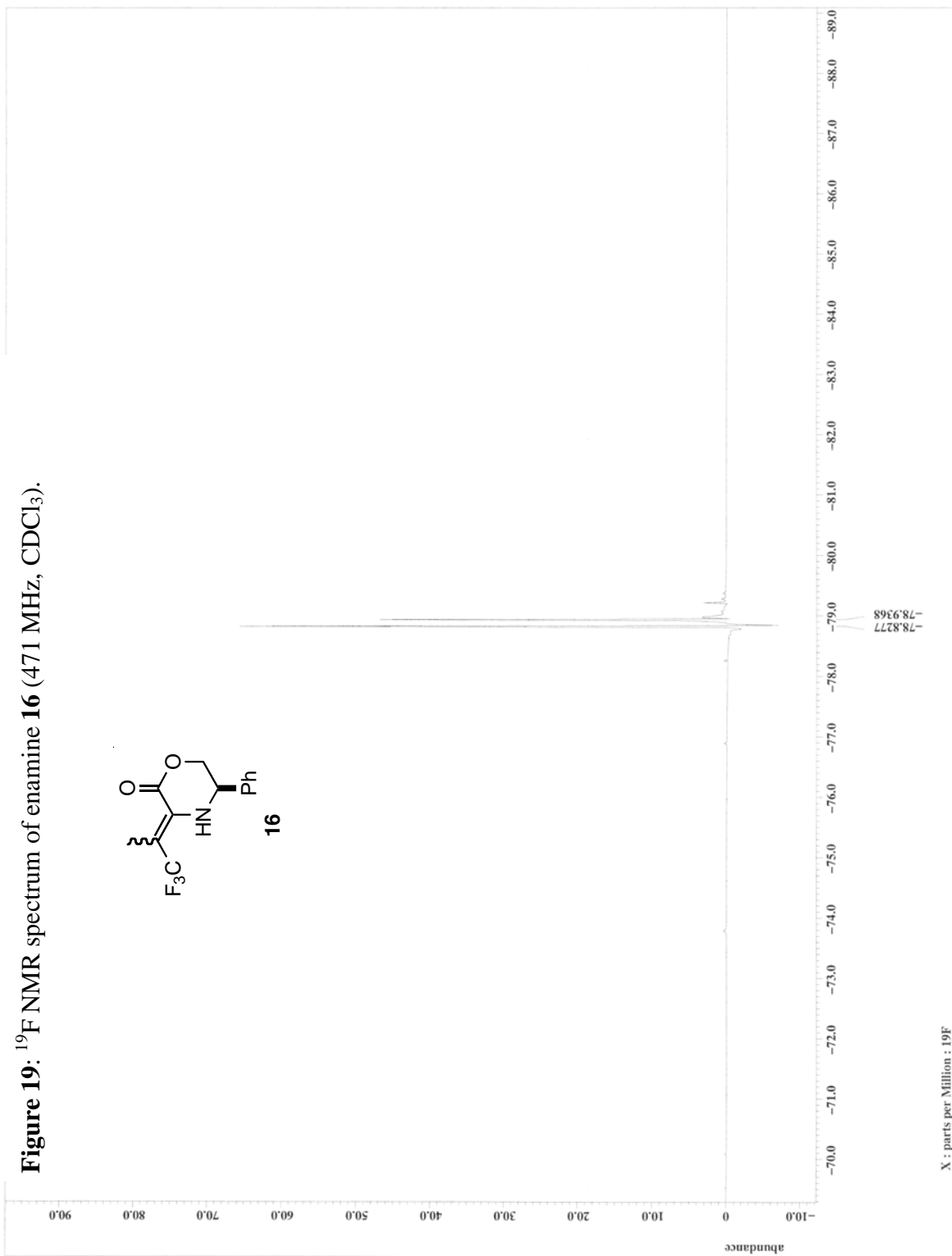
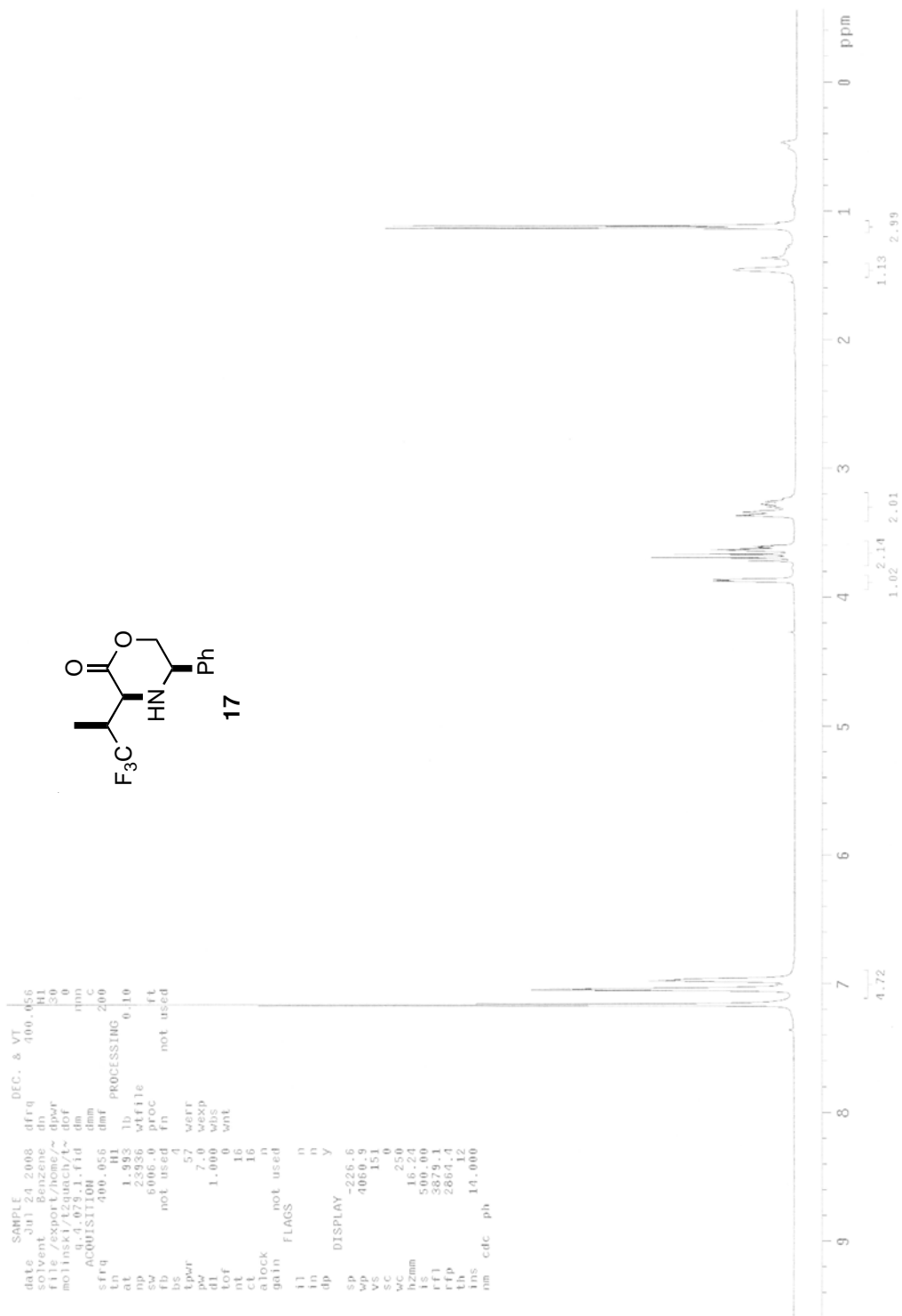


Figure 20: <sup>1</sup>H NMR spectrum of morpholinone **17** (400 MHz, C<sub>6</sub>D<sub>6</sub>).



**Figure 21:**  $^{13}\text{C}$  NMR spectrum of morpholinone **17** (100 MHz,  $\text{CDCl}_3$ ).

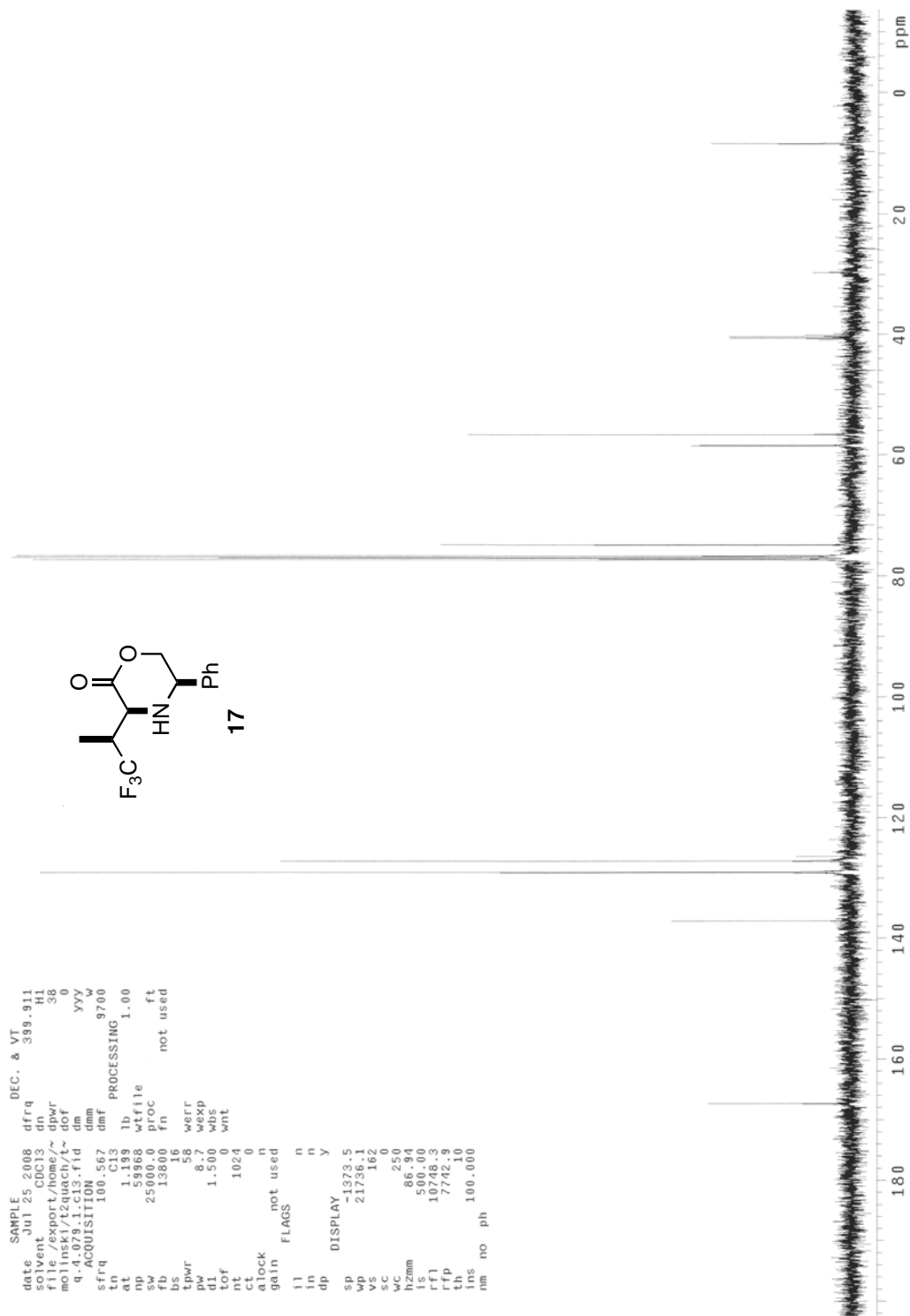
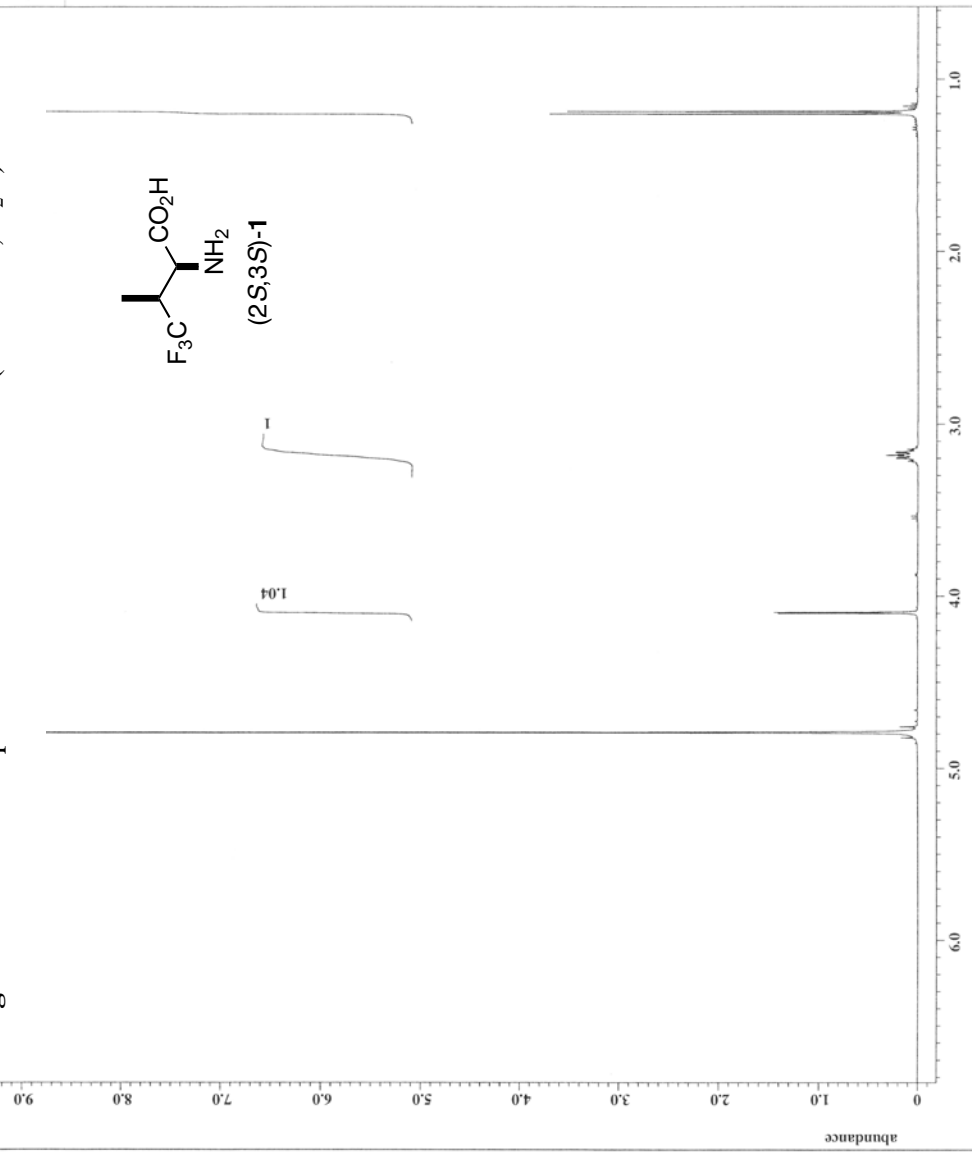
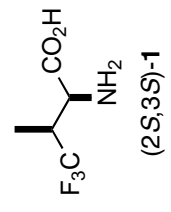




Figure 22: <sup>1</sup>H NMR spectrum of trifluorovaline **1** (500 MHz, D<sub>2</sub>O).

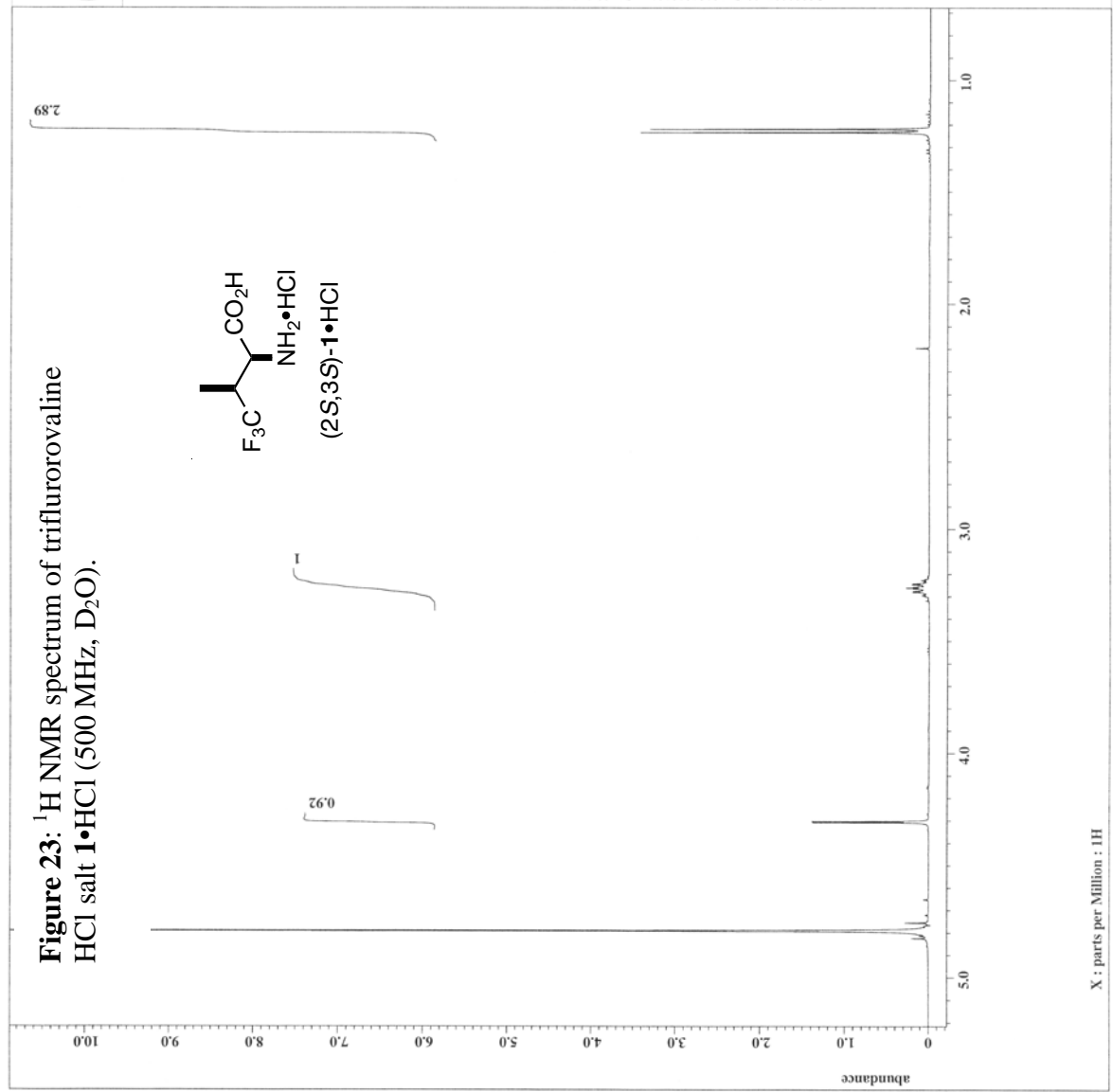
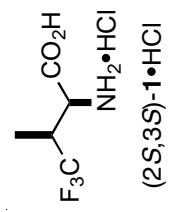


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Revision_time = 27-MAR-2009 13:38:15
Current_time = 27-MAR-2009 13:38:24
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Dim1_units = [ppm]
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Spectrometer = JNM-ECA500
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X_domain = 1H
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X_points = 32768
X_prescans = 1
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X_sweep = 9.38438438[MHz]
Irr_domain = 1H
Irr_freq = 500.15991521[MHz]
Irr_offset = 5.0[ppm]
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Tri_domain = 1H
Tri_offset = 5.0[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 33
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X_acq_time = 3.49175808[s]
X_angle = 8[deg]
X_pulse = 3.87[us]
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Recvr_gain = 52
Relaxation_delay = 2[s]
Repetition_time = 5.49175808[s]
Temp_set = 21.2[degC]
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X : parts per Million : 1H



**Figure 23:** <sup>1</sup>H NMR spectrum of trifluorovaline HCl salt **1**•HCl (500 MHz, D<sub>2</sub>O).



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Author = t2mcb
Experiment = 1D single pulse
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Revision_time = 27-MAR-2009 14:58:51
Current_time = 27-MAR-2009 14:58:58

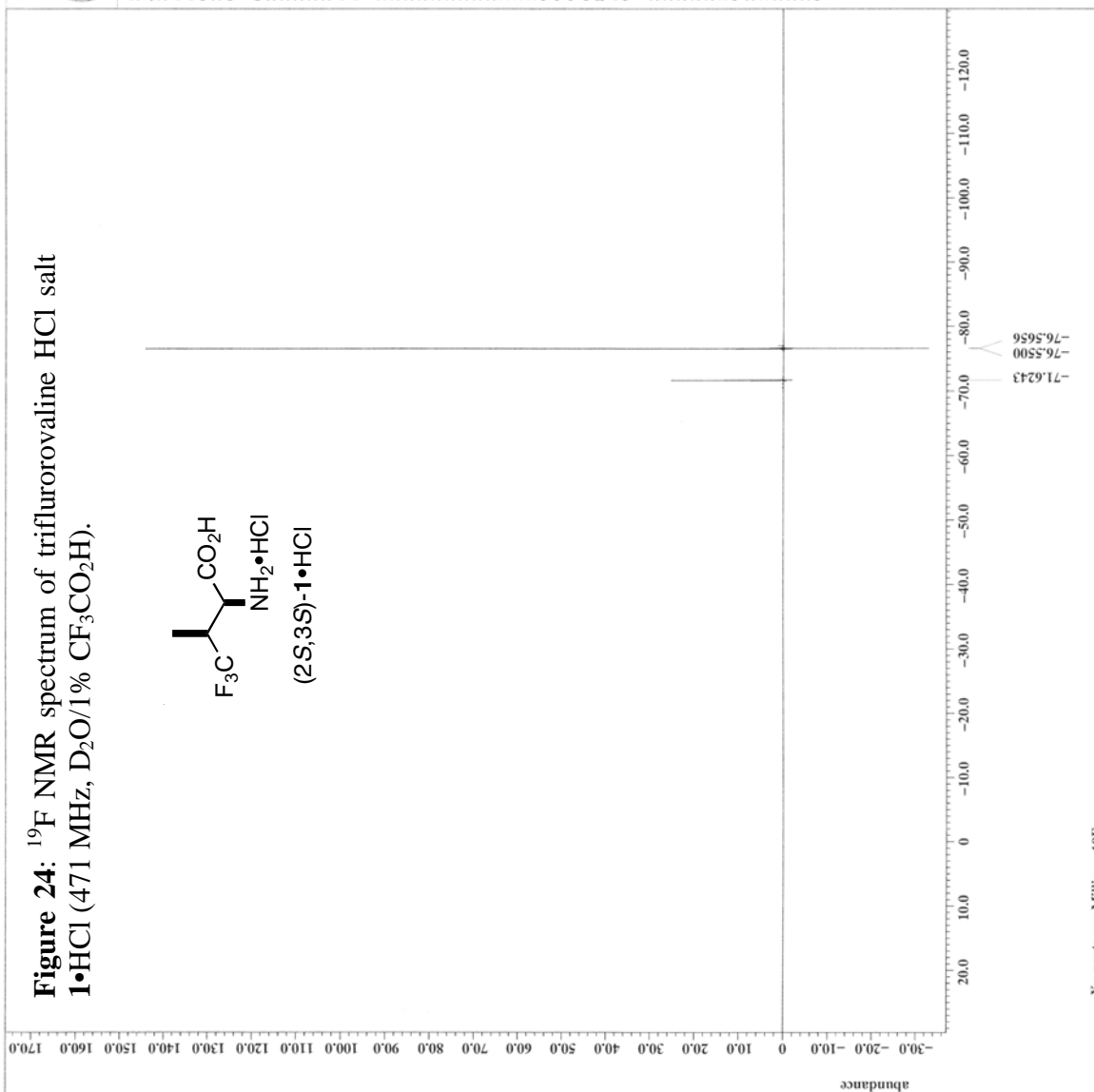
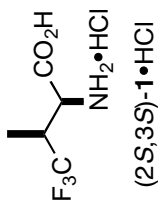
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Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
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Spectrometer = JNM-ECA500

Field_strength = 11.7473579 [T] (500 [MH
X_acq_duration = 1.49175808 [s]
X_domain = 500.15991521 [MHz]
X_offset = 5.0 [ppm]
X_points = 32768
X_prescans = 1
X_resolution = 0.28638868 [Hz]
X_sweep = 9.38438438 [kHz]
Irr_domain = 1H
Irr_freq = 500.15991521 [MHz]
Irr_offset = 1.0 [ppm]
Irr_domain = 1H
T1_freq = 500.15991521 [MHz]
T1_offset = 5.0 [ppm]
Clipped = FALSE
Mod_return = 1
Scans = 32
Total_scans = 32

X_90_width = 7.74 [us]
X_acq_time = 1.49175808 [s]
X_gate = 45.6475808 [s]
X_atn = 8 [dB]
X_pulse = 3.87 [us]
Irr_mode = Off
Tri_mode = Off
Dante_presat = FALSE
Initial_wait = 1 [s]
Revr_gain = 54
Relaxation_delay = 2 [s]
Repetition_time = 1.49175808 [s]
Temp_get = 21.3 [C]
  
```

X : parts per Million : 1H

**Figure 24:**  $^{19}\text{F}$  NMR spectrum of trifluorovaline HCl salt  
**1•HCl** (471 MHz,  $\text{D}_2\text{O}/1\% \text{CF}_3\text{CO}_2\text{H}$ ).



```

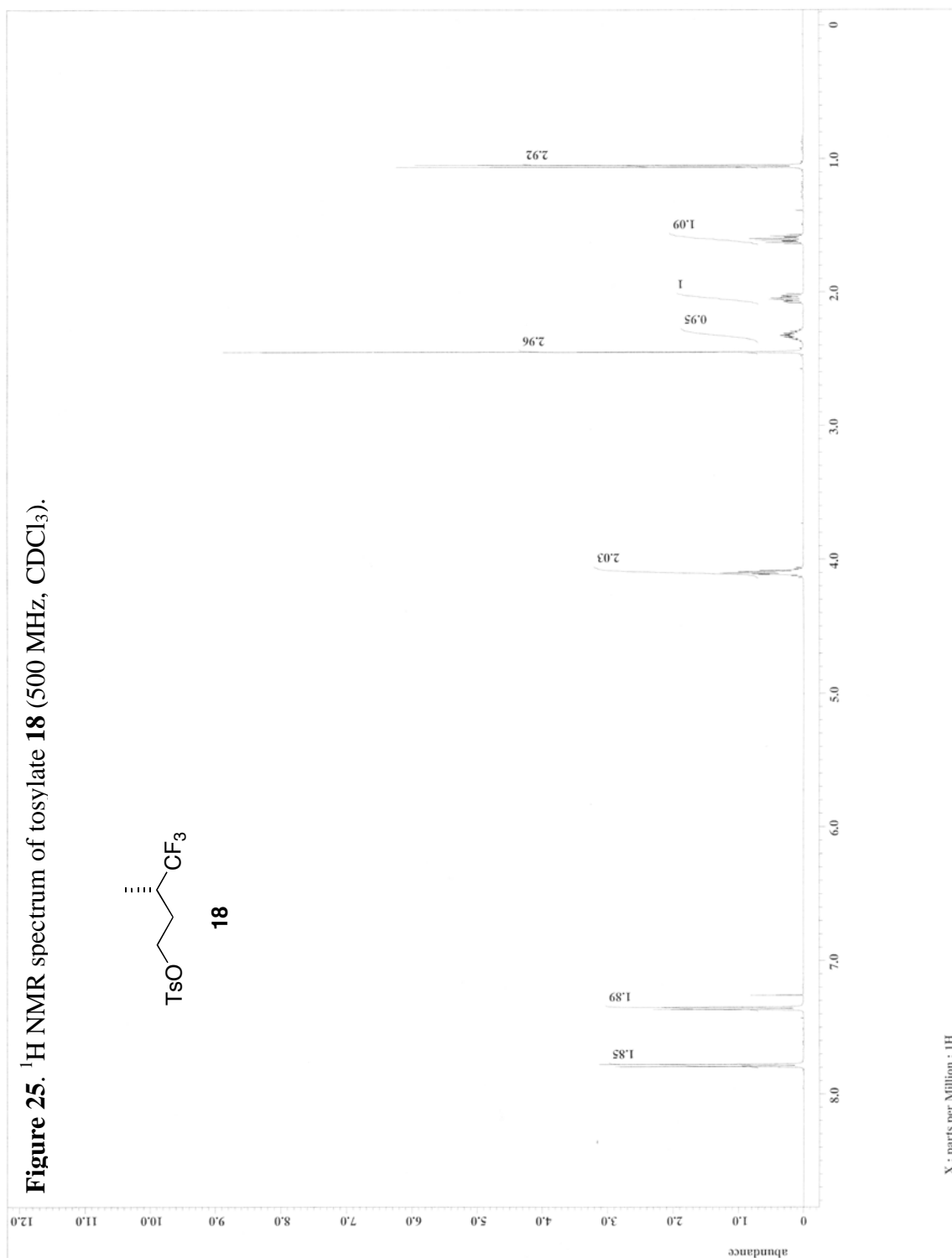
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Revision_time = 27-MAR-2009 14:56:55
Current_time = 27-MAR-2009 14:57:04

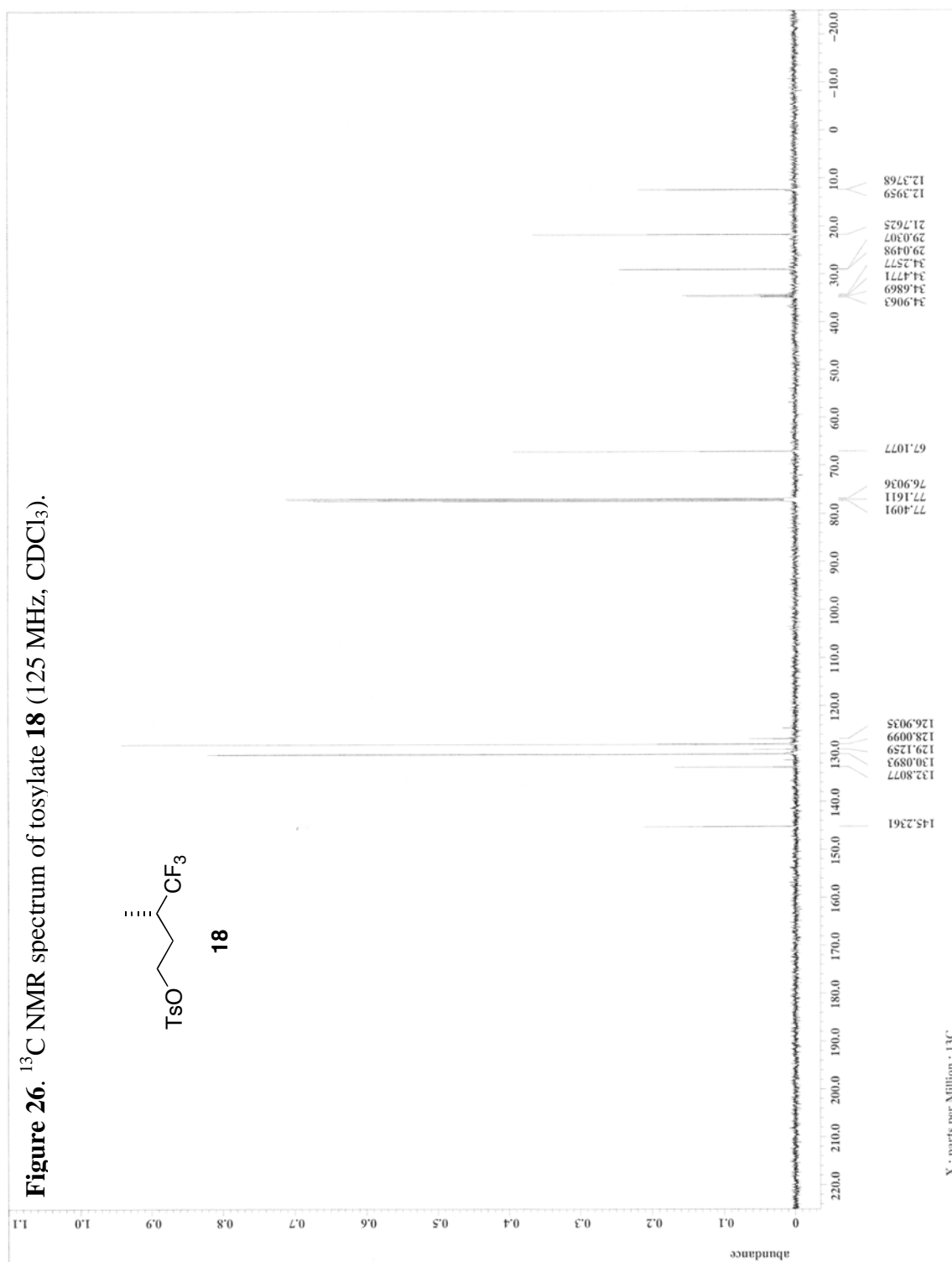
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X_offset = 0 [ppm]
X_points = 32768
X_prescans = 1
X_resolution = 7.33595628 [Hz]
X_sweep = 240.38461538 [kHz]
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Irr_freq = 470.62046084 [MHz]
Irr_offset = 1 [ppm]
Irr_phase = 180
Mod_return = 5 [ppm]
Tri_freq = 470.62046084 [MHz]
Tri_offset = FALSE
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Mod_return = 161
Total_scans = 161

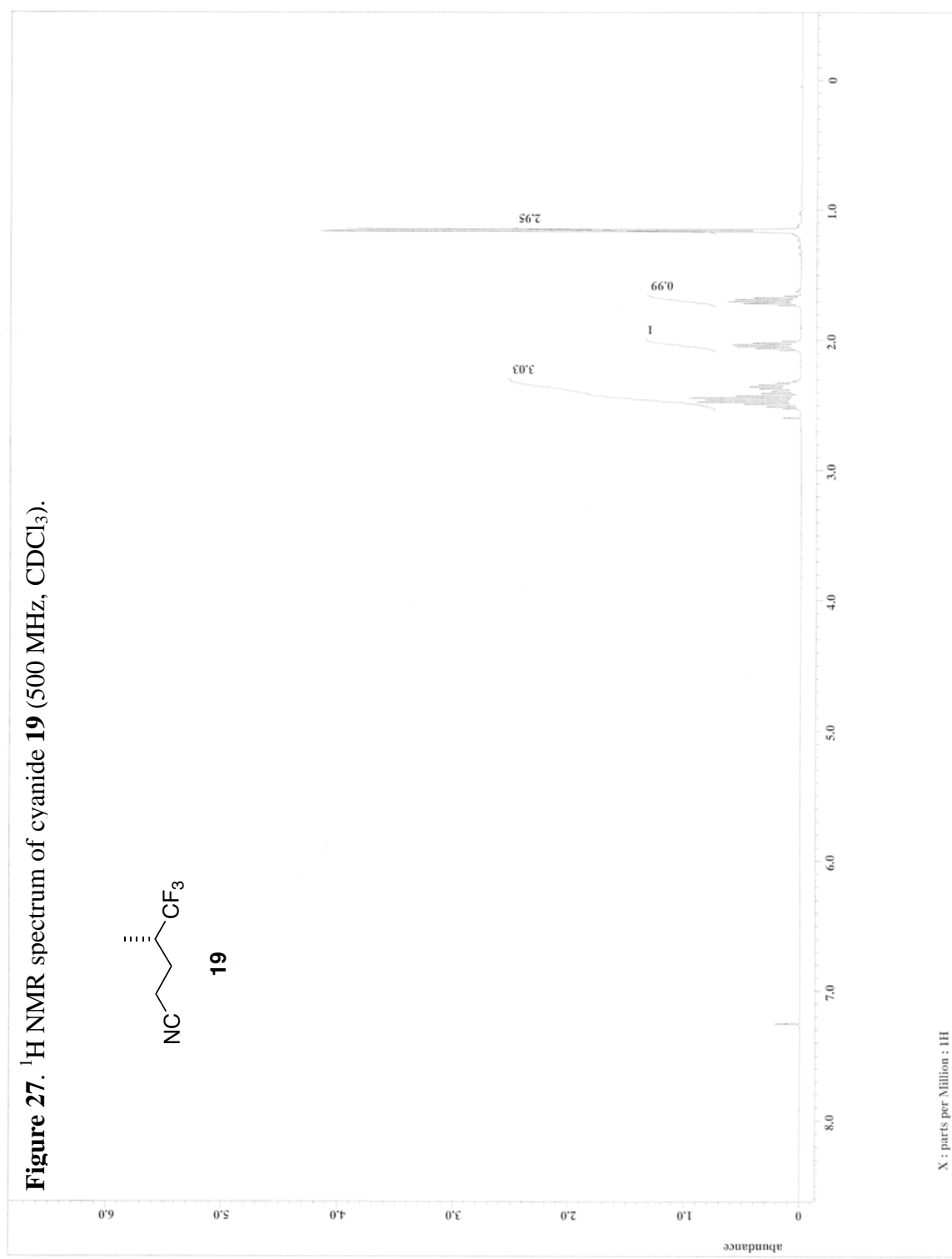
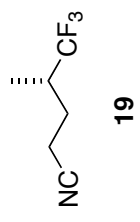
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X_acq_time = 45.13631488 [s]
X_delay = 6 [dB]
X_atn = 3.8125 [us]
X_pulse = Off
Irr_mode = Off
Dante_presat = FALSE
Initial_wait = 1 [s]
Recvr_gain = 50
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Temp_set = 21 [dC]
  
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X : parts per Million : 19F

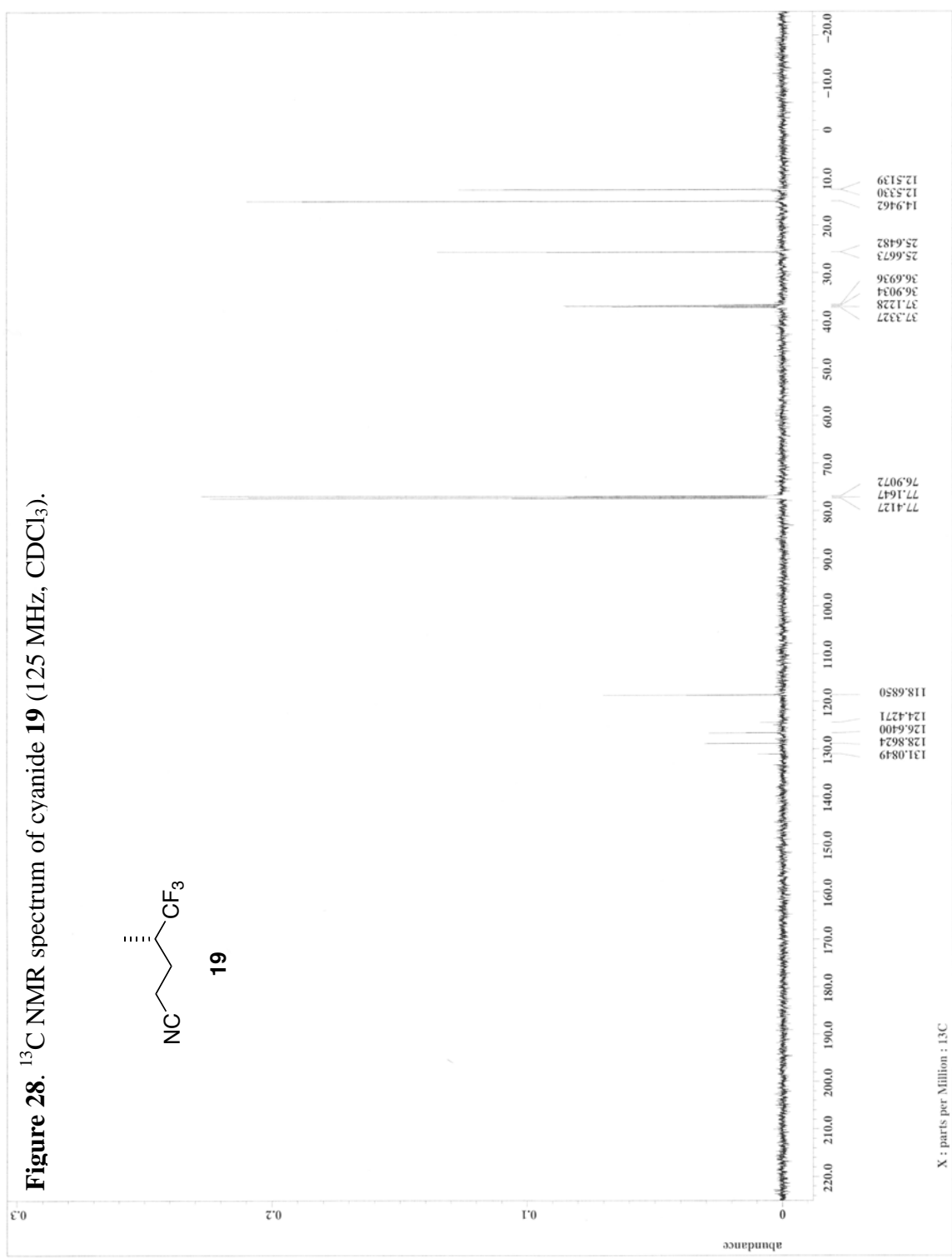




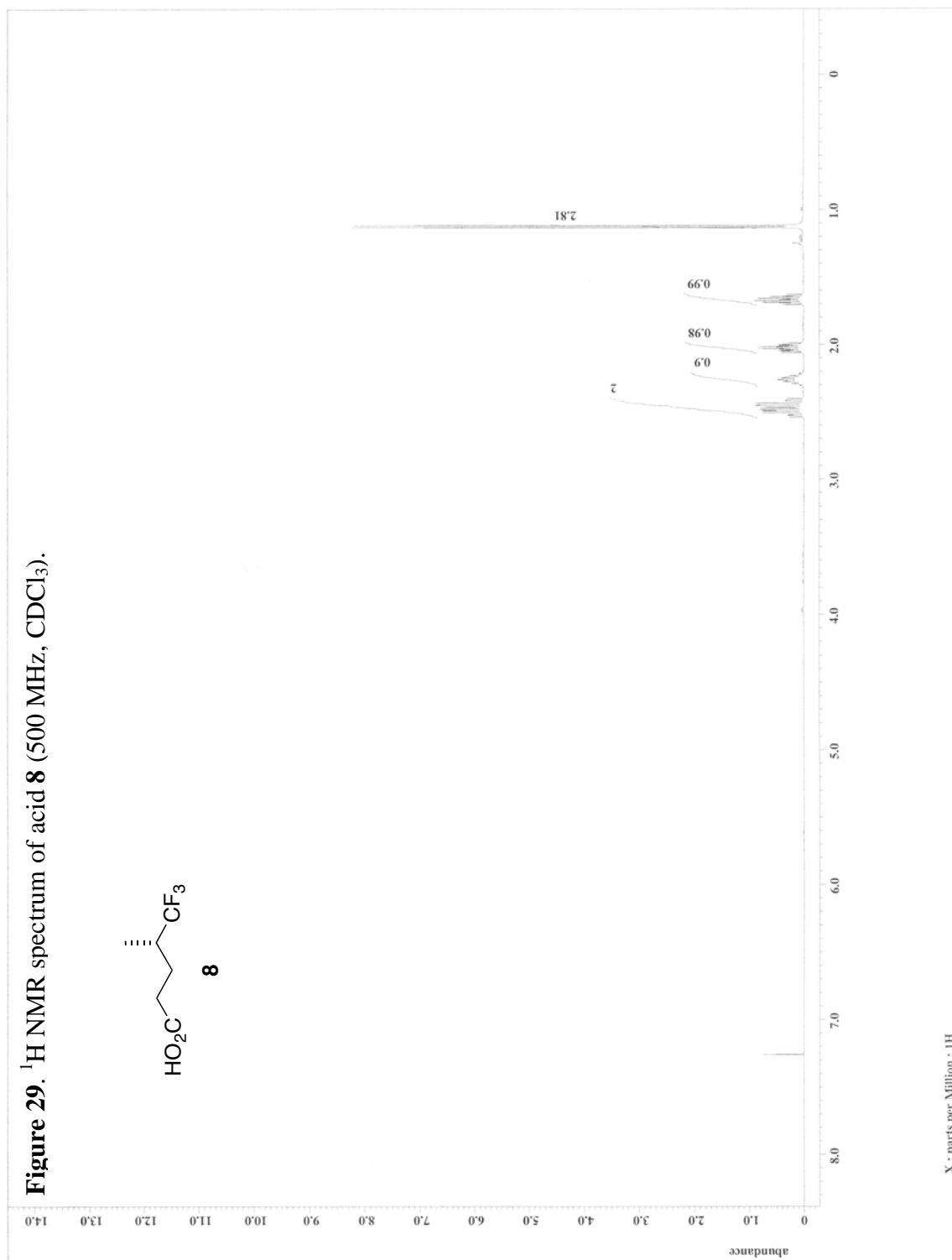
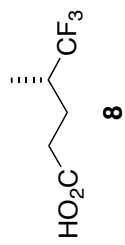
**Figure 27.**  $^1\text{H}$  NMR spectrum of cyanide **19** (500 MHz,  $\text{CDCl}_3$ ).



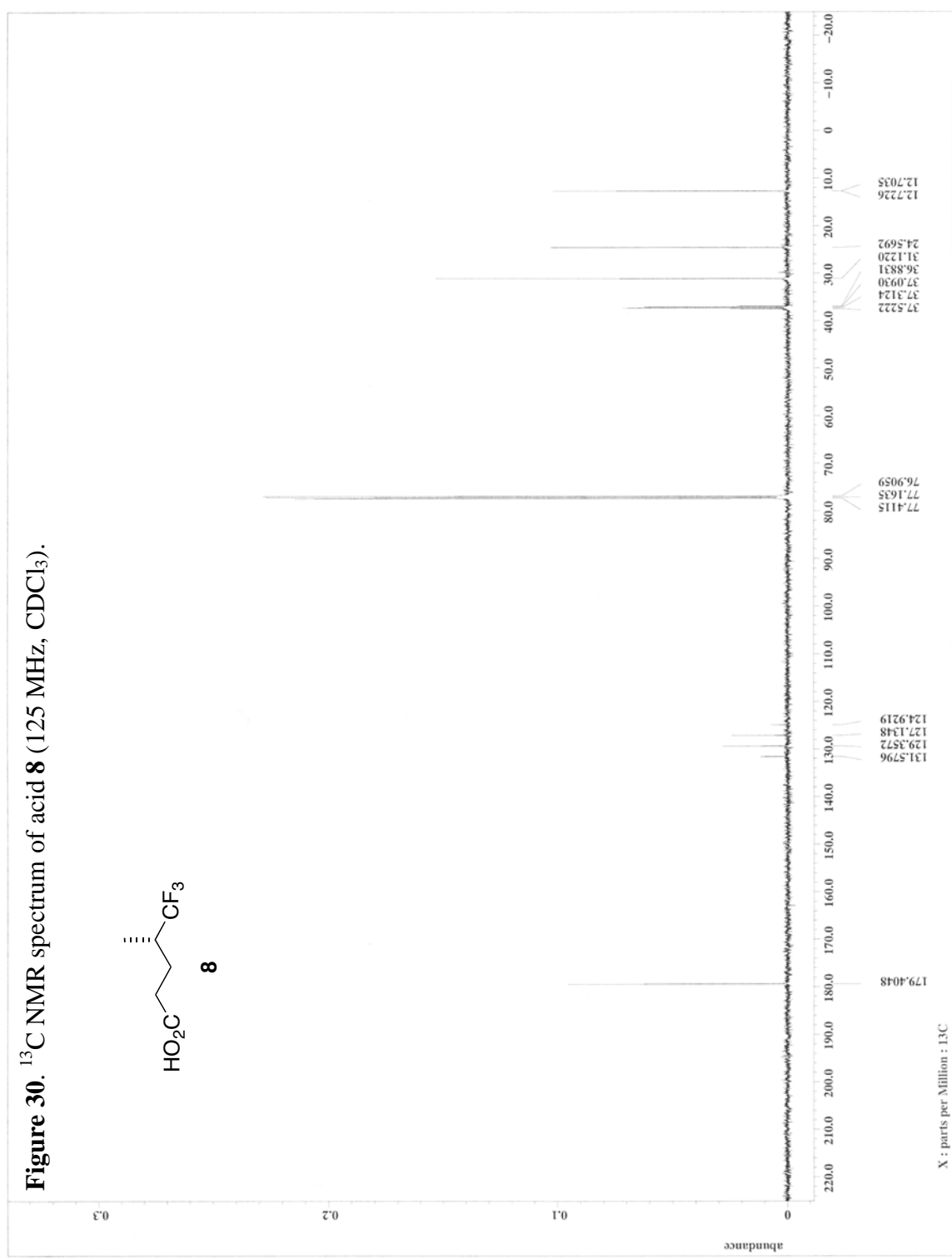
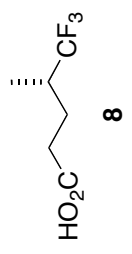
X : parts per Million : 1H



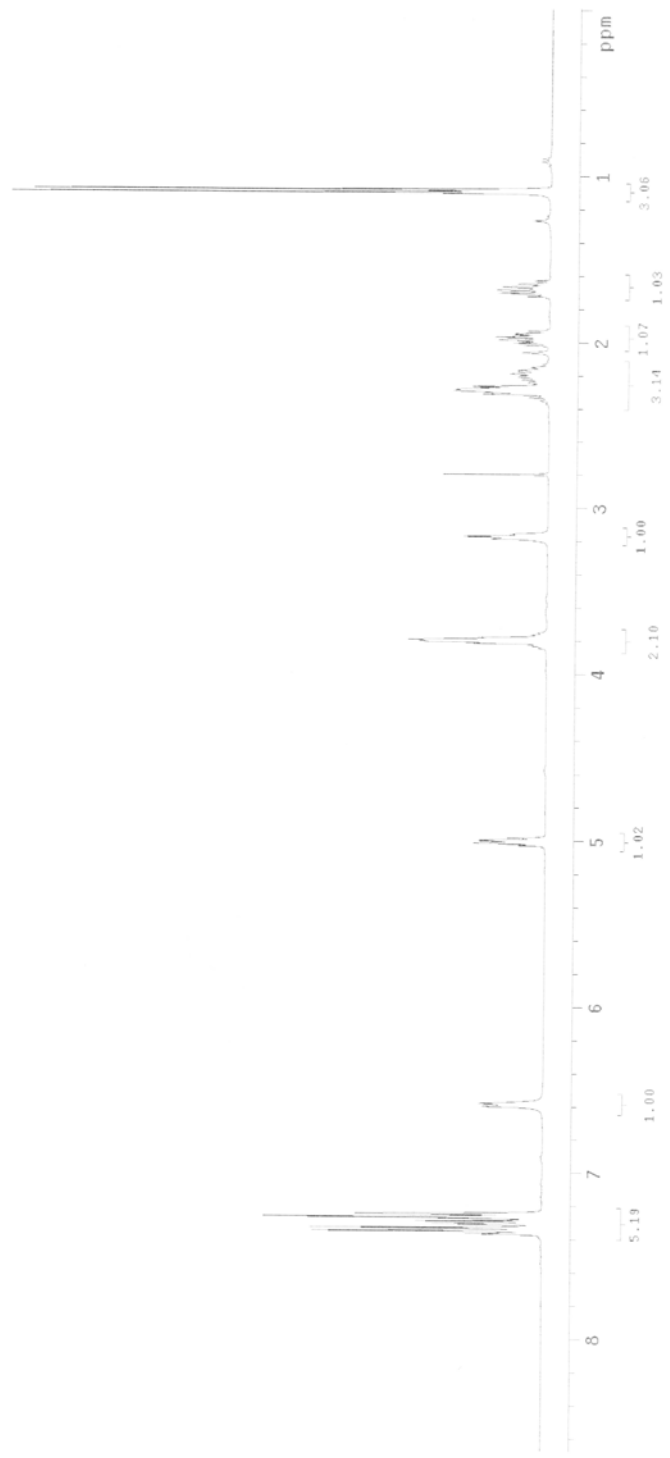
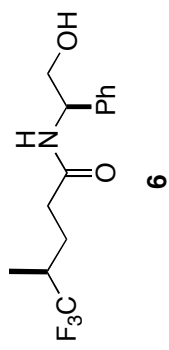
**Figure 29.**  $^1\text{H}$  NMR spectrum of acid **8** (500 MHz,  $\text{CDCl}_3$ ).

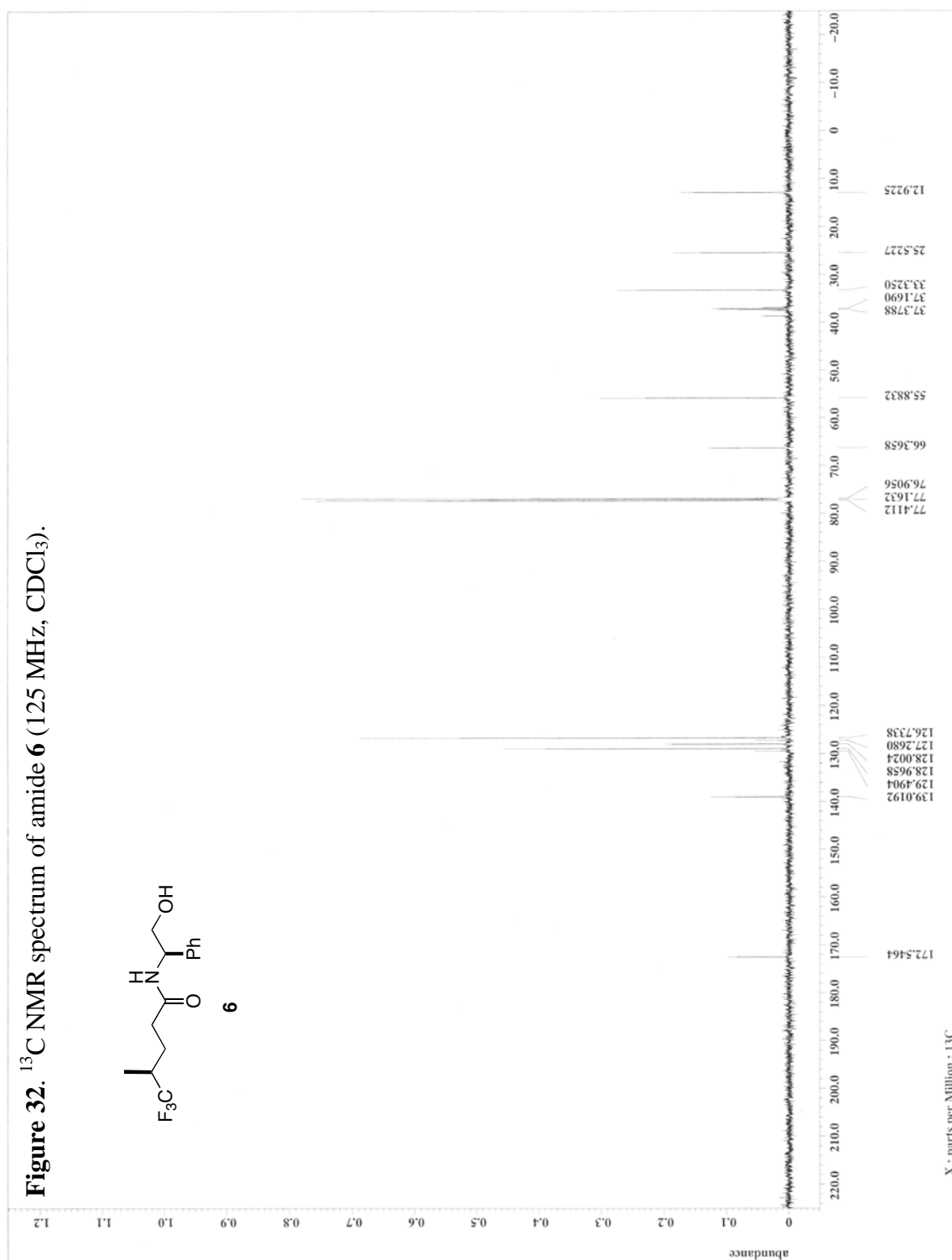


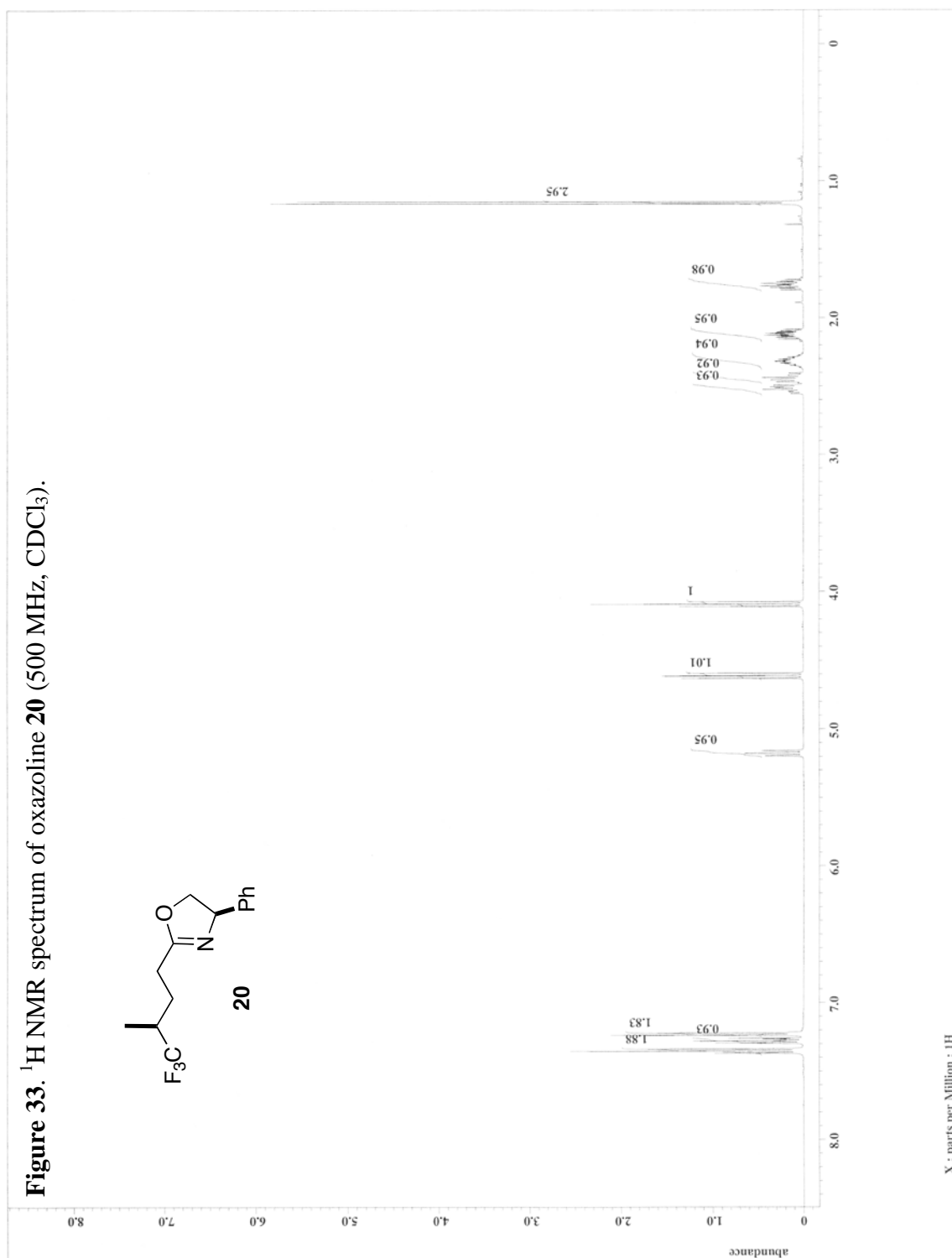
**Figure 30.**  $^{13}\text{C}$  NMR spectrum of acid **8** (125 MHz,  $\text{CDCl}_3$ ).

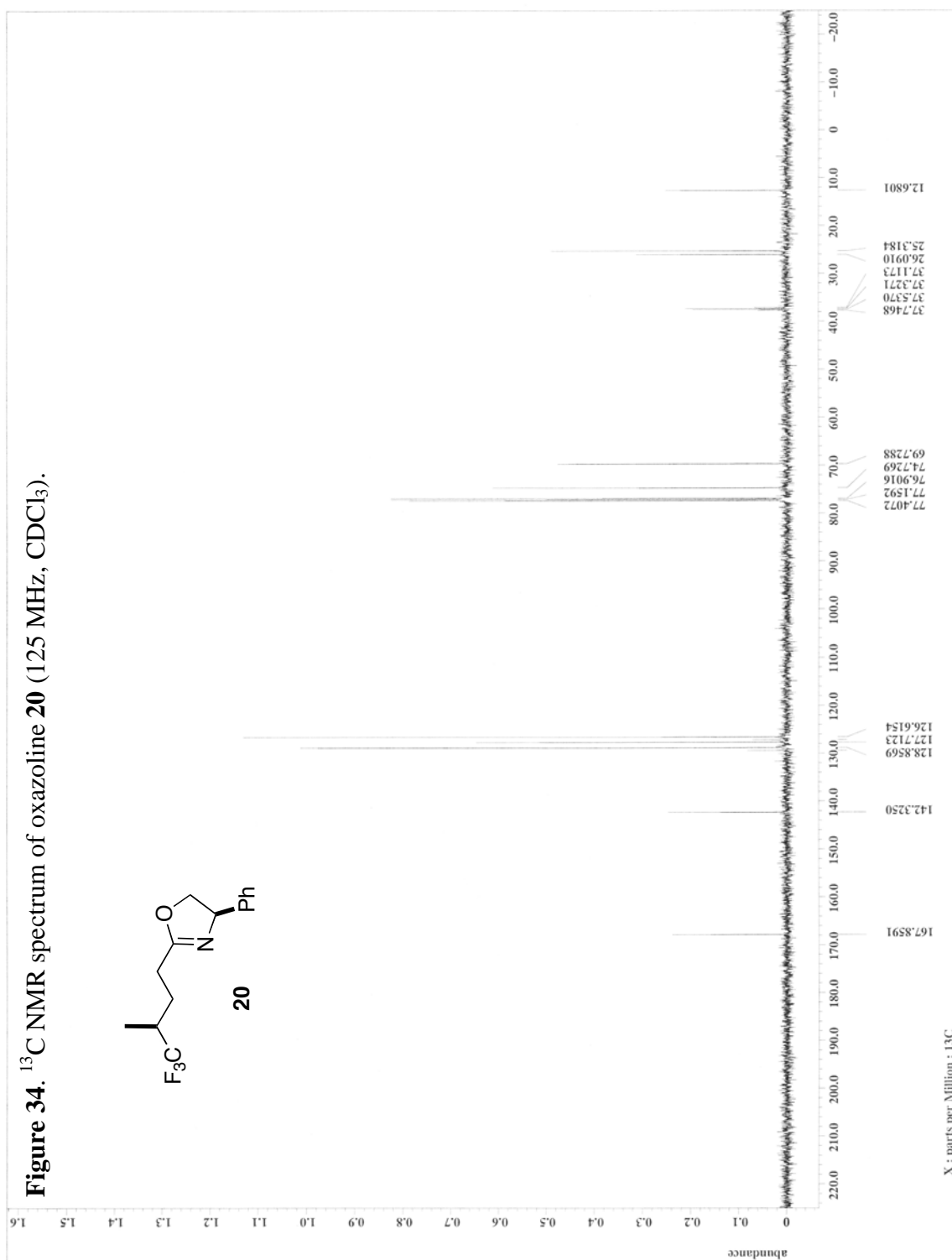


**Figure 31.**  $^1\text{H}$  NMR spectrum of amide **6** (400 MHz,  $\text{CDCl}_3$ ).



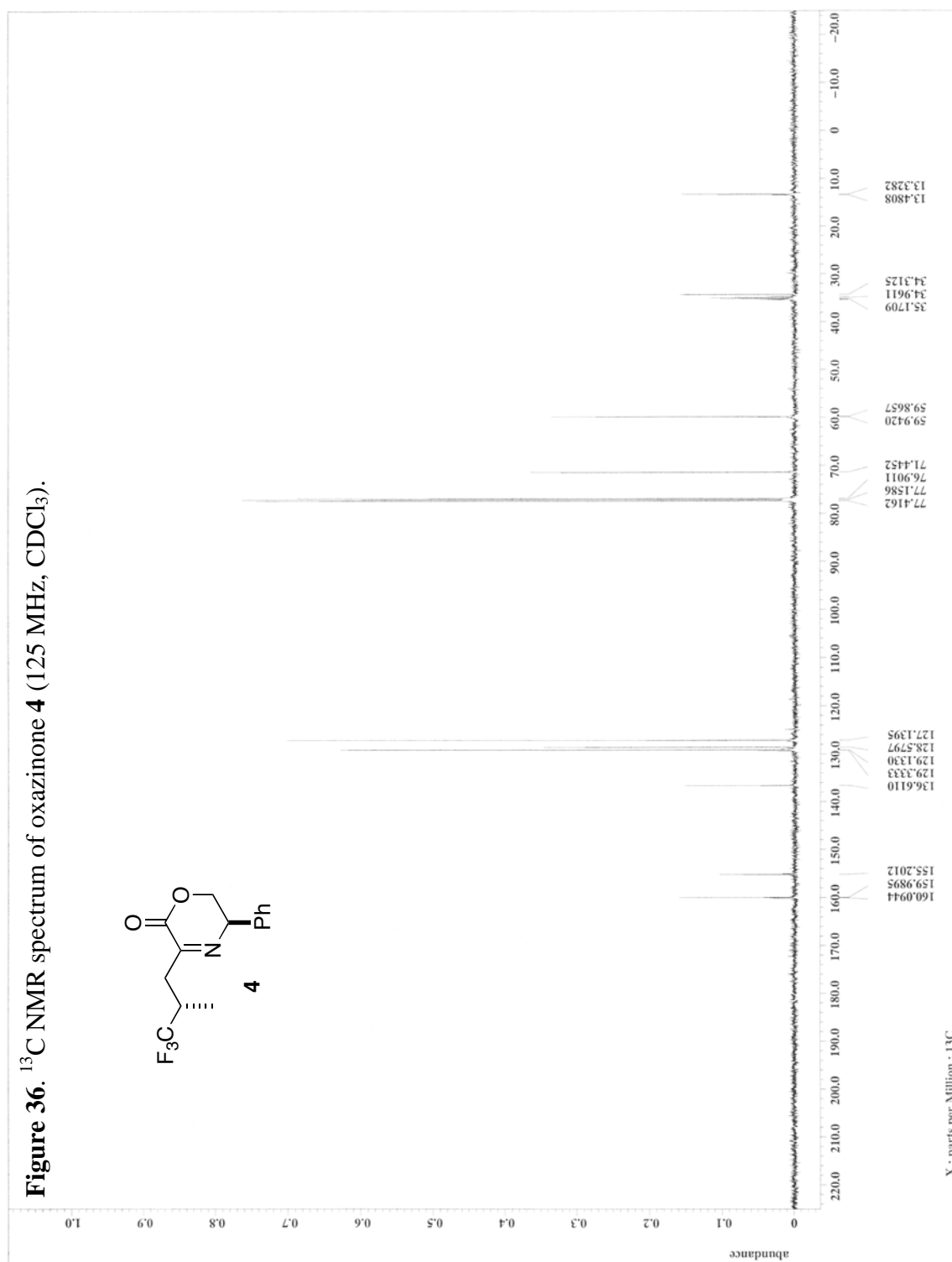








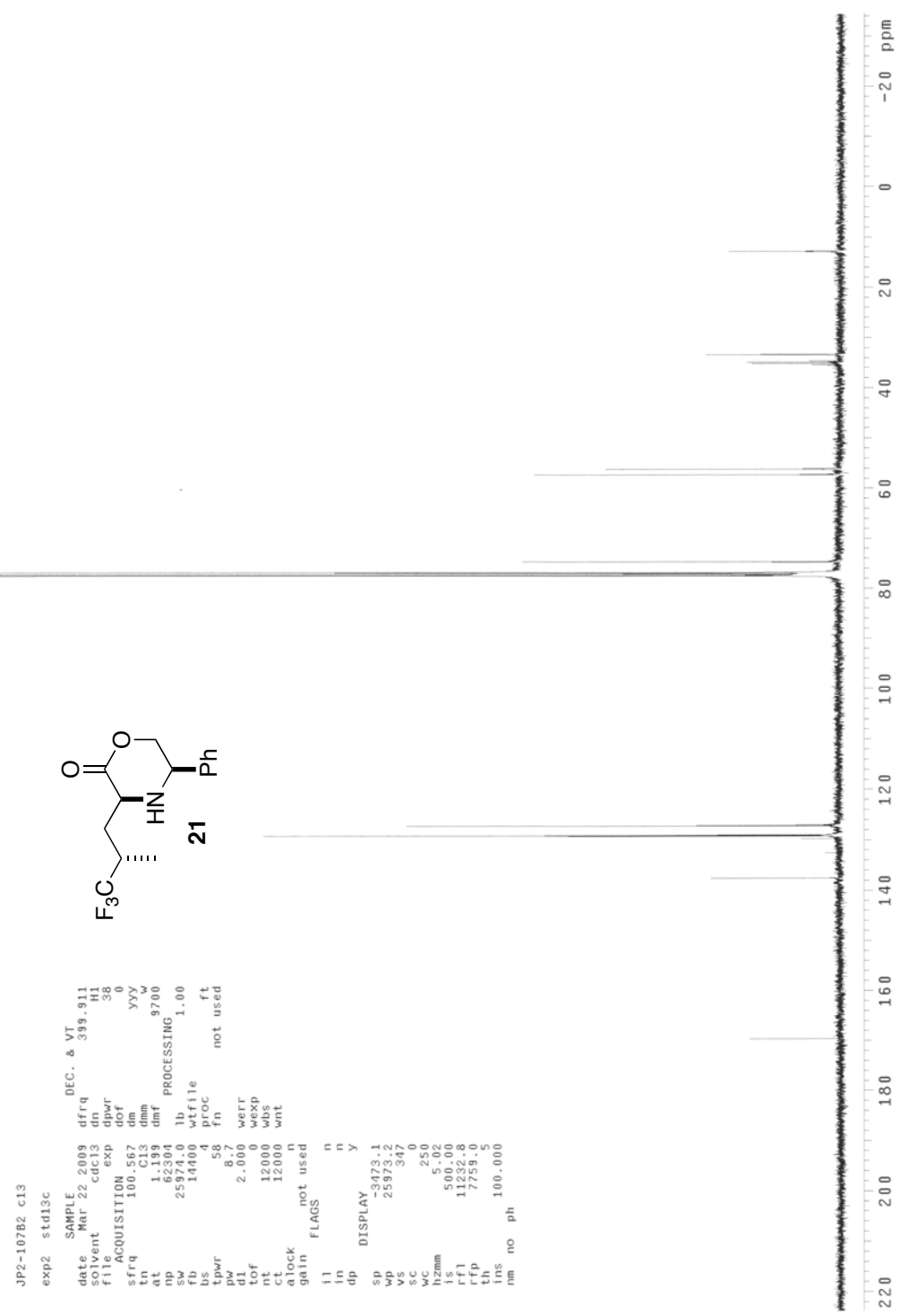
**Figure 36.**  $^{13}\text{C}$  NMR spectrum of oxazinone **4** (125 MHz,  $\text{CDCl}_3$ ).

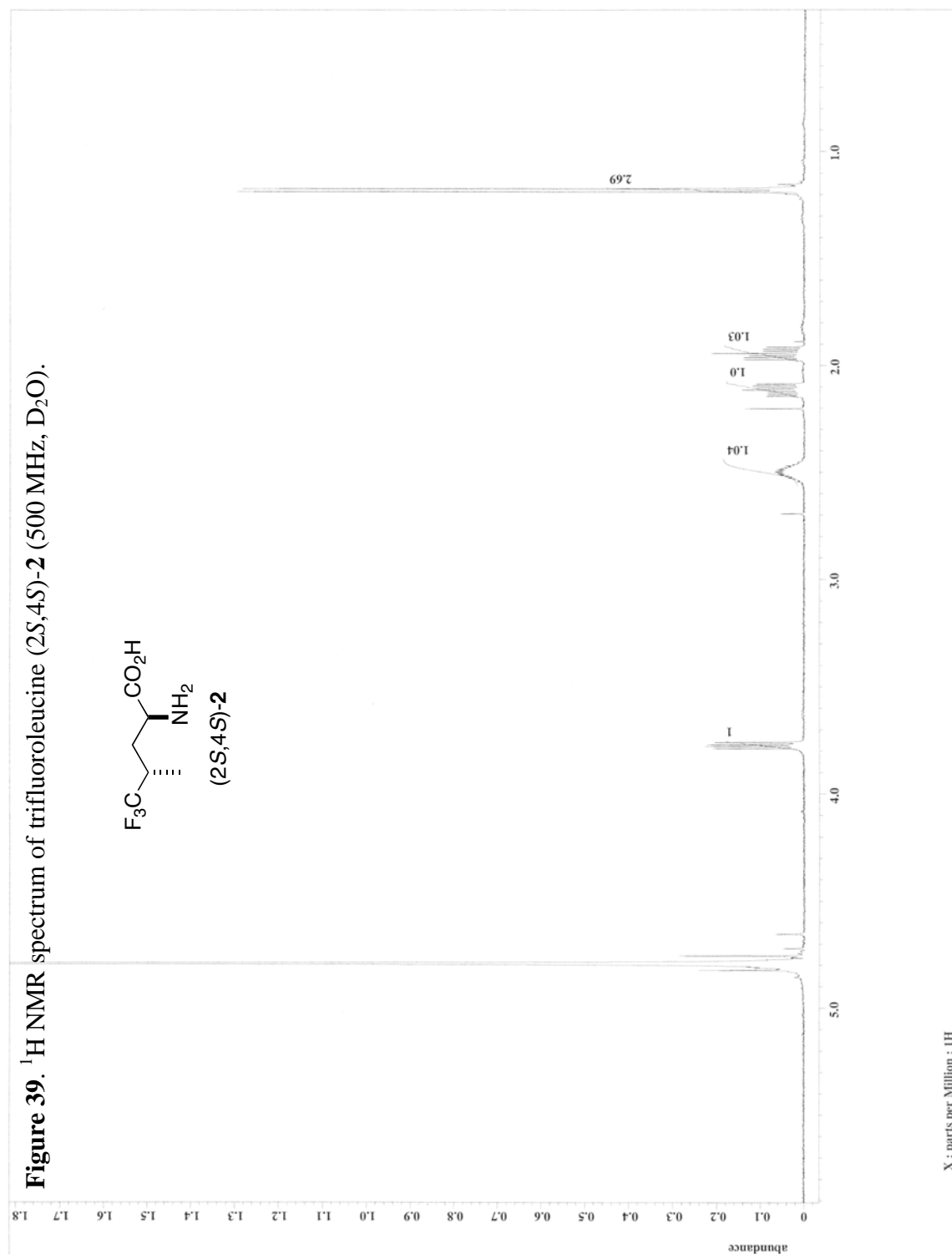


**Figure 37.**  $^1\text{H}$  NMR spectrum of morpholinone **21** (400 MHz,  $\text{CDCl}_3$ ).

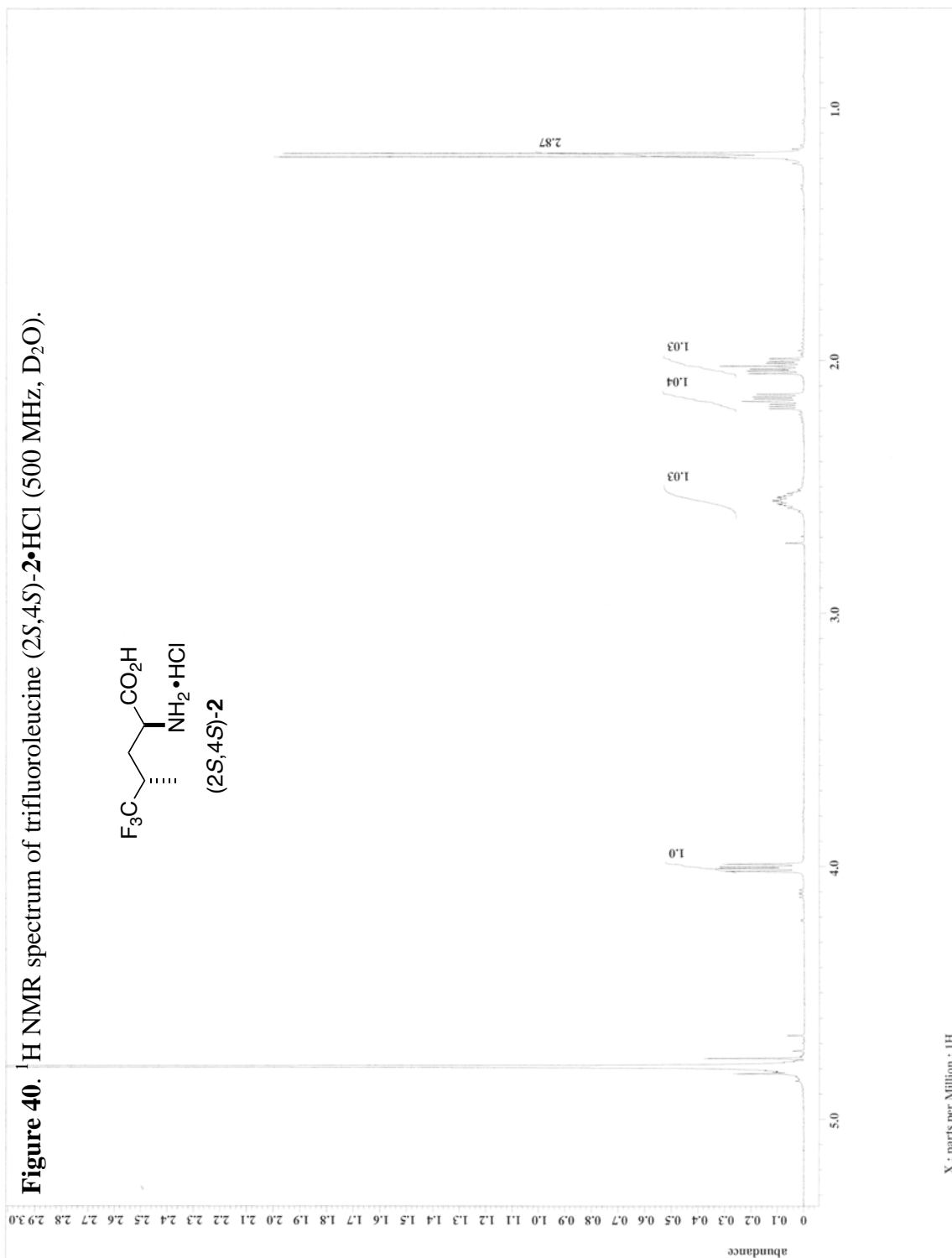


**Figure 38.** <sup>13</sup>C NMR spectrum of morpholinone **21** (100 MHz, CDCl<sub>3</sub>).





**Figure 40.**  $^1\text{H}$  NMR spectrum of trifluoroisoleucine (2*S*,4*S*)-**2**•HCl (500 MHz,  $\text{D}_2\text{O}$ ).



**Figure 41.**  $^{19}\text{F}$  NMR spectrum of trifluoroleucine (2*S*,4*S*)-2•HCl (471 MHz,  $\text{D}_2\text{O}$  w/1%  $\text{CF}_3\text{CO}_2\text{H}$ ).

