Formal and total synthesis of (±)-cycloclavine

Nitinkumar D. Jabre, Teruki Watanabe, and Matthias Brewer

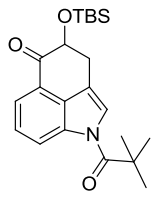
The University of Vermont, Department of Chemistry,
82 University Place, Burlington, VT 05405
Matthias.Brewer@uvm.edu

I) General Experimental Details

All reactions were carried out under an atmosphere of nitrogen using flame-dried glassware unless otherwise noted. A rotary evaporator equipped with a water condenser and attached to a vacuum system was used to concentrate *in vacuo*. Samples were further dried under reduced pressure on a high-vacuum line. Tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), and diethyl ether (Et_2O) were dried via a solvent dispensing system. Commercially available $SnCl_4$ was distilled twice from P_2O_5 under a nitrogen atmosphere and was stored in a sealed tube as a 1M solution in dichloromethane (CH_2Cl_2) or commercially available 1M solutions of $SnCl_4$ in dichloromethane were used as received. Triethylamine (Et_3N) and diisopropylamine (i-Pr_2NH) were distilled from CaH_2 under a nitrogen atmosphere and stored in septum-sealed bottles over solid KOH. All other commercial reagents were used as received. Reactions were cooled to –40 °C or –78 °C via dry ice–acetone baths, to –15 °C via ice–salt baths and to 0 °C via ice–water baths. Silica gel flash column chromatography was performed using Merck grade 60 silica gel (230–400 mesh) and TLC analysis was carried out using Merck 60F–254 silica on glass plates. Visualization of TLC plates was achieved using ultraviolet light, polyphosphomolybdic acid and cerium sulfate in EtOH with H_2SO_4, ceric ammonium molybdate, or iodine vapor. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 25 °C unless otherwise noted. ^1H chemical shifts are reported in ppm (δ units) downfield from tetramethylsilane. Solvent peaks were used as internal references for all ^{13}C NMR. Accurate mass data was acquired in ESI mode using an orbitrap mass analyzer.

II) Experimental procedures and compound characterization data

4-(*tert*-butyldimethylsilyloxy)-1-pivaloyl-3,4-dihydrobenzo[*cd*]indol-5(1*H*)-one (7):

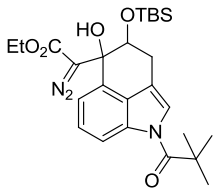


A solution of **3** (4.75 g, 18.6 mmol) and distilled Et_3N (6.50 mL, 46.5 mmol) in dry CH_2Cl_2 (238 mL) was cooled to 0 ºC and TBSOTf (5.10 mL, 22.3 mmol) was added dropwise over the period of 5 min. The reaction mixture was stirred at 0 ºC for 10 min and then at room temperature for 30 min. The reaction mixture was combined with water and the aqueous layer was extracted with CH_2Cl_2 (30 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4 and the solvents were removed in vacuo to give the TBS enol ether as a brown solid which was used in the next step without further purification.

The TBS enol ether was dissolved in CH_2Cl_2 (238 mL) and cooled to 0 ºC. A solution of K_2CO_3 (2.60 g, 18.6 mmol) in H_2O (142 mL) was added and the mixture was maintained at 0 ºC for 10 min at which point the biphasic mixture was stirred vigorously and solid *m*-CPBA (4.60 g, 18.6 mmol) was added in small portions over the period of 30 min. After the addition, the reaction mixture was stirred for an additional 1 h. After consumption of starting material as judged by TLC analysis (R_f = 0.5, 80:20 Hexanes/EtOAc), aq. $NaHCO_3$ (100 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (30 mL × 3). The organic layers were combined, washed with brine, dried over anhydrous Na_2SO_4 and evaporated in vacuo to give a brown viscous oil which was used in the next step without further purification.

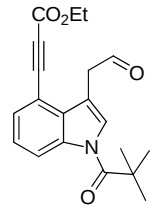
TBSCl (2.80 g, 18.6 mmol) was added to a solution of the crude product from above, imidazole (1.90 g, 27.9 mmol), and N,N-dimethylaminopyridine (228 mg, 1.86 mmol) in CH_2Cl_2 (190 mL) and the resulting mixture was stirred at room temperature for 6 h. The reaction mixture was combined with aq. NH_4Cl and the mixture was extracted with CH_2Cl_2 (30 mL × 3). The organic layers were combined, washed with brine, dried over anhydrous Na_2SO_4 and evaporated to give the crude product as a brown viscous oil which was purified by silica gel flash column chromatography (97:3 Hexanes/EtOAc) to provide 5.00 g (70% yield) of **7** as a viscous oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (dd, *J* = 8.2, 0.5 Hz, 1H), 7.73 (dd, *J* = 7.5, 0.5 Hz, 1H), 7.60 (d, *J* = 1.5 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 1H), 4.68 (dd, *J* = 10.8, 6.8 Hz, 1H), 3.42 (dd, *J* = 15.9, 6.6 Hz, 1H), 3.23 (ddd, *J* = 15.7, 10.8, 2.0 Hz, 1H), 1.54 (s, 9H), 0.95 (s, 9H), 0.24 (s, 3H), 0.12 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.3, 177.0, 135.5, 132.5, 126.5, 125.0, 122.6, 121.6, 120.1, 114.9, 74.9, 41.0, 30.7, 28.6, 25.8, 18.5, -4.5, -5.5. IR (thin film) 1696 cm^{-1}. HRMS (ESI) calcd for [$C_{22}H_{32}NO_3Si$] 386.21460, found 386.21443.

Ethyl 2-(4-(tert-butyldimethylsilyloxy)-5-hydroxy-1-pivaloyl-1,3,4,5-tetrahydrobenzo [*cd*]indol-5-yl)-2-diazoacetate (6) :



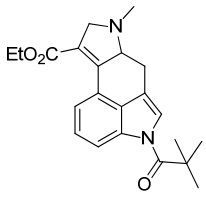
A solution **7** (5.0 g, 13.0 mmol) and ethyl diazoacetate (1.92 g, 16.9 mmol) in THF (215 mL) was cooled to −78 °C and a freshly prepared solution of LDA (15.6 mmol) in THF (45 mL) was added dropwise via cannula over a period of 15 min. The resulting brown solution was maintained at −78 °C for 2 h at which point the reaction was quenched by the addition of MeOH (2 mL) followed by the addition of a saturated aqueous solution of NH_4Cl (100 mL). The mixture was warmed to room temperature, additional saturated NH_4Cl solution (300 mL) was added, and the mixture was extracted with EtOAc (100 mL × 3). The organic layers were combined, dried over anhydrous Na_2SO_4, and evaporated to provide a yellow viscous oil that was purified by silica gel column chromatography (96:4 to 92:8 hexanes/ EtOAc) to give 5.10 g (79% yield) of the title compound. ^{1}H NMR (500 MHz, $CDCl_3$) Major diastereomer: δ ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (dd, *J* = 5.9, 3.1 Hz, 1H), 7.47 (s, 1H), 7.42 – 7.36 (m, 2H), 4.77 – 4.55 (app t, 1H), 4.16 (dddt, *J* = 17.8, 14.2, 10.9, 7.1 Hz, 2H), 3.68 (brs, 1H), 3.16 – 2.96 (m, 2H), 1.54 (s, *J* = 13.0 Hz, 9H), 1.22 (t, *J* = 6.3 Hz, 3H), 0.95 (s, 9H), 0.18 (s, 3H), 0.12 (s, 3H). Minor diastereomer: δ 8.31 (dd, *J* = 8.2, 0.6 Hz, 1H), 7.56 – 7.37 (m, 3H), 5.91 (brs, 1H), 4.43 – 4.20 (m, 3H), 3.16 (dd, *J* = 16.0, 3.0 Hz, 1H), 2.86 (ddd, *J* = 16.1, 7.3, 1.1 Hz, 1H), 1.51 (s, 9H), 1.31 (t, *J* = 7.1 Hz, 3H), 0.80 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.9, 176.8, 168.2, 165.3, 135.2, 135.0, 129.8, 127.6, 127.4, 126.5, 126.3, 120.7, 120.5, 120.2, 119.7, 117.8, 117.6, 115.3, 115.2, 74.5, 72.3, 72.0, 61.0, 60.4, 58.9, 40.8, 28.53, 28.51, 27.2, 25.62, 25.57, 17.82, 17.76, 14.41, 14.38, -4.6, -4.8, -5.0, -5.2. IR (thin film) 3485, 2097, 1690 cm^{-1}. HRMS (ESI) calcd for [$C_{26}H_{37}N_3O_5SiNa$]$^+$ 522.23947, found 522.23935.

Ethyl 3-(3-(2-oxoethyl)-1-pivaloyl-1*H*-indol-4-yl)propiolate (5):



A solution of $SnCl_4$ (1M in CH_2Cl_2, 3.60 mL, 3.60 mmol) was added as a single stream to a 0 °C solution of diazoester **6** (1.80 g, 3.60 mmol) in CH_2Cl_2 (74.0 mL). During the addition gas evolution was noted and the yellow solution became purple. The reaction mixture was maintained at 0 °C until gas evolution ceased (~15 min) at which point saturated aqueous $NaHCO_3$ (8 mL) was added. The mixture was stirred for 5 min at 0 °C, transferred into a separatory funnel containing additional saturated aqueous $NaHCO_3$ (50 mL), and extracted with CH_2Cl_2 (30 mL × 5). The organic layers were combined, washed with brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure to give the crude product as brown solid, which was used in the subsequent cycloaddition step without further purification. Alternatively, the crude product could be purified by silica gel column chromatography (80:20 to 70:30 hexanes/EtOAc) to provide **5** as a colorless oil in 80% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.91 (s, 1H), 8.56 (d, *J* = 8.4 Hz, 1H), 7.75 (s, 1H), 7.41 (d, *J* = 7.4 Hz, 1H), 7.23 (t, *J* = 8.0 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 4.11 (s, 2H), 1.43 (s, 9H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.2, 176.6, 153.6, 137.0, 129.9, 129.8, 126.8, 124.9, 120.3, 112.4, 110.0, 84.9, 84.2, 61.9, 41.2, 40.3, 28.4, 13.9. IR (thin film) 2213, 1725, 1697 cm^{-1}. HRMS (ESI) calcd for [$C_{20}H_{22}NO_4$] 340.15433, found 340.15418.

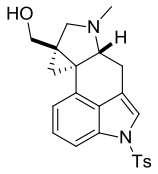
Ethyl 7-methyl-4-pivaloyl-6,6a,7,8-tetrahydro-4*H*-indolo[6,5,4-*cd*]indole-9-carboxylate (9):



A solution of crude **5** (~ 3.60 mmol) in dry toluene (35.0 mL) was cooled to 0 ºC and a solution of freshly prepared and distilled TMS sarcosine ester (581 mg, 3.60 mmol) in dry toluene (1 mL) was added dropwise over a period of 10 min. and the mixture was stirred at 0 ºC for 30 min. In a separate two neck RBF fitted with a water condenser, dry toluene (5.00 mL) was warmed to reflux. The cold reaction mixture was added dropwise to the boiling toluene over a period of 1 h. After the addition, the resulting solution was maintained at 120 ºC for another 1 h and then cooled to room temperature and the solvent was removed in vacuo. The resulting residue was purified by silica gel column chromatography (74:25:1 to 59:40:1 hexanes/EtOAc/Et_3N) to provide 820 mg (62% yield over two steps) of **9** as a brown solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.36 (dd, *J* = 10.8, 8.0 Hz, 2H), 7.47 (d, *J* = 1.8 Hz, 1H), 7.35 (t, *J* = 8.0 Hz, 1H), 4.36 – 4.18 (m, 3H), 3.78 – 3.69 (m, 1H), 3.64 (dd, *J* = 13.8, 5.9 Hz, 1H), 3.30 (dd, *J* = 15.0, 6.3 Hz, 1H), 2.72 (ddd, *J* = 14.7, 11.4, 2.1 Hz, 1H), 2.53 (s, 3H), 1.49 (s, 9H), 1.32 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.8, 164.3, 145.6, 135.0, 129.5, 125.9, 124.1, 123.7, 122.6, 120.0, 119.0, 116.7, 77.2, 72.7, 63.5, 60.3, 40.8, 40.0, 28.5, 14.1. IR (thin film) 1689 cm^{-1}. HRMS (ESI) calcd for [$C_{22}H_{27}N_2O_3$] 367.20162, found 367.20151.

Ethyl 7-methyl-6,6a,7,8-tetrahydro-4*H*-indolo[6,5,4-*cd*]indole-9-carboxylate (4): A mixture of N-pivalyl indole derivative **9** (112 mg, 306 µmol), DBU (183 µL, 1.22 mmol), H_2O (11.0 µL, 611 µmol) and THF (2.00 mL) was warmed to reflux for 19 h. (*Note:* DBU, H_2O and THF were each degassed separately by sparging with N_2 for 30 min prior to their use in the reaction). The reaction mixture was combined with H_2O (15 mL) and the aqueous layer was extracted with EtOAc (10 mL, × 5). The organic layers were combined, dried over anhydrous Na_2SO_4 and evaporated under reduced pressure to give the unprotected indole derivative as a brown viscous oil. The crude product was purified by silica gel column chromatography (49.5:50:0.5 to 29.5:70:0.5 hexanes/EtOAc/Et_3N) to give 64.0 mg (74% yield) of **4**. Spectral data for this material matched published values.[1]

Ethyl 7-methyl-4-tosyl-6,6a,7,8-tetrahydro-4*H*-indolo[6,5,4-*cd*]indole-9-carboxylate (10): A solution of **9** (1.50 g, 4.09 mmol), H_2O (147 µL, 8.20 mmol), DBU (2.50 mL, 16.9 mmol) and THF (26.0 mL) was warmed to reflux for 19 h under an N_2 atmosphere. (*Note:* DBU, H_2O and THF were each degassed separately by sparging with N_2 for 30 min prior to their use in the reaction). After 19 h, the reaction mixture was mixed with H_2O (50 mL) and the aqueous layer was extracted with EtOAc (20 mL × 5). The organic layers were combined, dried over Na_2SO_4 and evaporated to give the unprotected indole derivative as a brown viscous oil (1.47 g). This crude material was dissolved in toluene (44.0 mL) and Bu_4NHSO_4 (139 mg, 0.41 mmol) and 50% aq KOH (2.64 g, 4.71 mmol) were added. The biphasic mixture was stirred vigorously at room temperature for 20 min. at which point tosyl chloride (936 mg, 4.91 mmol) was added in a single portion. The reaction mixture stirred at room temperature for 1 h. If the TLC analysis (R_f = 0.5, 89:10:1 Hexanes/EtOAc/Et_3N) indicated the presence of starting material, an additional 0.2 equiv of tosyl chloride was added and stirring was continued for another 30 min. After consumption of starting material as judged by TLC analysis, the reaction mixture was mixed with water, two layers were separated and the aqueous layer was extracted with EtOAc (20 mL × 3). All of the organic layers were combined, dried over Na_2SO_4 and evaporated to give N-tosyl indole derivative **10** as a foamy solid. This material was purified by silica gel column chromatography (59:40:1 to 49:50:1 hexanes/EtOAc/Et_3N) to provide 1.40 g (78% yield) of **10** as brown solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, *J* = 7.8 Hz, 1H), 7.90 (d, *J* = 8.2 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 2H), 7.35 (t, *J* = 8.0 Hz, 1H), 7.27 (d, *J* = 2.0 Hz, 1H), 7.21 (d, *J* = 8.3 Hz, 2H), 4.37 – 4.17 (m, 3H), 3.77 – 3.67 (m, 1H), 3.64 (dd, *J* = 13.8, 5.9 Hz, 1H), 3.29 (dd, *J* = 15.1, 6.2 Hz, 1H), 2.66 (ddd, *J* = 15.0, 11.2, 2.1 Hz, 1H), 2.52 (s, 3H), 2.33 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.3, 145.2, 144.8, 135.3, 133.4, 131.1, 129.8, 126.7, 125.5, 124.7, 123.6, 123.4, 120.6, 117.8, 115.0, 72.6, 63.5, 60.5, 40.1, 28.5, 21.5, 14.2. IR (thin film) 1708 cm^{-1}. HRMS (ESI) calcd for [$C_{24}H_{25}N_2O_4S$] 437.15295, found 437.15272.

Rel-((1a*R*,3a*R*,9b*S*)-3-methyl-6-tosyl-1a,2,3,3a,4,6-hexahydro-1*H*-cyclopropa[c]indolo[4,3-*ef*]indol-1a-yl)methanol (11): 

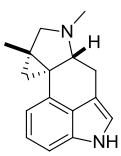
DIBALH (0.70 mL, 687 µmol; 1M in THF) was added dropwise to a 0 ºC solution of N-tosyl indole **10** (100 mg, 229 µmol) in toluene (5.80 mL). The reaction mixture was stirred at 0 ºC for 15 min and then at room temperature for 45 min at which point aq. sodium potassium trartrate (3 mL) and then aq. $NaHCO_3$ (15 mL) were carefully added. The mixture was extracted with EtOAc (7 mL × 5), dried over Na_2SO_4 and evaporated to give the allylic alcohol as a pale yellow solid which was used in the subsequent cyclopropanation reaction. A small portion of the allylic alcohol was purified by silica gel column chromatography (94.5:5:0.5 to 84.5:15:0.5 hexanes/EtOAc/Et_3N): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 – 7.60 (m, 3H), 7.26 – 7.13 (m, 5H), 4.75 (d, *J* = 13.7 Hz, 1H), 4.51 (d, *J* = 13.7 Hz, 1H), 4.16 (dd, *J* = 14.0, 3.4 Hz, 1H), 3.66 – 3.57 (m, 1H), 3.53 (dd, *J* = 14.0, 5.2 Hz, 1H), 3.25 (dd, *J* = 15.0, 6.2 Hz, 1H), 2.59 (ddd, *J* = 14.8, 11.1, 2.0 Hz, 1H), 2.52 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.7, 136.1, 135.5, 133.4, 129.9, 129.8, 129.7, 126.7, 125.5, 125.0, 120.1, 119.6, 118.0, 112.8, 71.2, 63.6, 58.3, 40.1, 28.2, 21.5. IR (thin film) 3376 cm^{-1}. HRMS (ESI) calcd for [$C_{22}H_{23}N_2O_3S$] 395.14239, found 395.14219.

A solution of iodine (233 mg, 0.92 mmol) and Et_2O (167 µL, 1.60 mmol) in dry CH_2Cl_2 (0.9 mL) was maintained at 0 ºC under an N_2 atmosphere and a solution of Et_2Zn (800 µL, 0.80 mmol; 1M in hexane) was added dropwise during which time the purple solution turned colorless. This solution was removed from the ice bath and stirred at room temperature for 10 min and was then again cooled at 0 ºC at which point a solution of CHI_3 (135 mg, 0.34 mmol) in dry CH_2Cl_2 (2.30 mL) was added via cannula followed by the addition of Solution B (*see below*). The reaction mixture was stirred at 0 ºC for approx. 2-3 h and then at room temperature for 15 h at which point the reaction was quenched by the addition of aq. NH_4Cl (1 mL) and then mixed with aq. $NaHCO_3$ (10 mL). The mixture was extracted with $CHCl_3$ (5 mL × 7) and the organic layers were combined, dried over Na_2SO_4 and evaporated to give the crude product as brown solid. Purification of this residue by silica gel column chromatography (20:79:1 to 0:99:1 hexanes/EtOAc/Et_3N then 89:10:1 hexanes/EtOAc/Et_3N) provided 22.5 mg (24% yield) of cyclopropane **11**; δ ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.72 (d, *J* = 8.3 Hz, 1H), 7.24 – 7.13 (m, 4H), 6.86 (d, *J* = 7.4 Hz, 1H), 4.31 (dd, *J* = 11.9, 6.8 Hz, 1H), 4.12 (dd, *J* = 12.1, 3.5 Hz, 1H), 3.20 (d, *J* = 8.6 Hz, 1H), 3.07 (dd, *J* = 14.5, 3.8 Hz, 1H), 2.76 – 2.61 (m, 2H), 2.46 (ddd, *J* = 14.2, 12.0, 1.9 Hz, 1H), 2.35 (s, 3H), 2.34 (s, 3H), 1.70 (d, *J* = 3.9 Hz, 1H), 1.40 (app. t, 1H), 0.58 (d, *J* = 3.8 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.6, 135.4, 134.9, 133.2, 131.1, 129.8, 126.7, 125.6, 119.9, 119.4, 114.6, 111.1, 68.6, 63.6, 61.0, 39.5, 35.0, 34.3, 24.8, 22.8, 21.4. IR (thin film) 3384 cm^{-1}. HRMS (ESI) calcd for [$C_{23}H_{25}N_2O_3S$] 409.15804, found 409.15779.

<u>*Solution B:*</u> A solution of iodine (70.0 mg, 0.28 mmol), Et_2O (60.0 µL, 0.57 mmol) and dry CH_2Cl_2 (0.50 mL) was maintained at 0 ºC under a N_2 atmosphere and a solution of Et_2Zn (275 µL, 0.28 mmol, 1M in hexane) was added dropwise during which the purple solution turned

colorless. The ice bath was removed and the resulting mixture was stirred at room temperature for 15 min and then added to a room temperature CH_2Cl_2 (0.5 mL) solution of the crude allylic alcohol (229 µmol) obtained from the DIBALH reduction of ester **10** (see above). The resulting mixture of zinc alkoxide was stirred at room temperature for 10 min before being used in the above procedure.

(±)-Cycloclavine:



Freshly distilled $MeSO_2Cl$ (6.80 µL, 88.0 µmol) was added dropwise to a 0 ºC solution of **11** (20.0 mg, 49.0 µmol) and Et_3N (13.8 µL, 98.0 µmol) in dry CH_2Cl_2 (2.00 mL). The reaction mixture was stirred at 0 ºC for 1 h and then diluted with CH_2Cl_2 (10 mL). The organic layer was washed with saturated $NaHCO_3$ (5 mL × 2), water (5 mL × 1) and brine (5 mL × 1), dried over Na_2SO_4 and evaporated to give the mesylated product which was used in the next step without further purification. *Note:* The mesylated product was unstable to silica gel chromatography conditions.

A 1M solution of $LiBHEt_3$ (98.0 µL, 98.0 µmol) was added dropwise to a cold solution of the mesyl derivative in THF (0.50 mL). The reaction mixture was maintained at 0 ºC for 45 min, at which point H_2O (5.00 mL) was added. The mixture was added to 10% NaOH (5.00 mL) and the mixture was extracted with EtOAc (10.0 mL × 5). The organic layers were combined, dried over Na_2SO_4 and evaporated to give the reduced product (25.0 mg) which was used in the next step without further purification.

The crude reduced material (10.0 mg) formed above was dissolved in an equal part mixture of aq 20% NaOH and MeOH (4.00 mL) and was then warmed to reflux for 12 h. After cooling to room temperature the MeOH was removed in vacuo and the remainder of the reaction mixture was diluted with water and extracted with EtOAc (5.00 mL × 7). The organic layers were combined, dried over Na_2SO_4 and evaporated to give a residue that was purified by silica gel column chromatography (79:20:1 to 59:40:1 $CHCl_3$/acetone/Et_3N) to provide 2.5 mg of cycloclavine. Spectral data for this material matched published values.[2]

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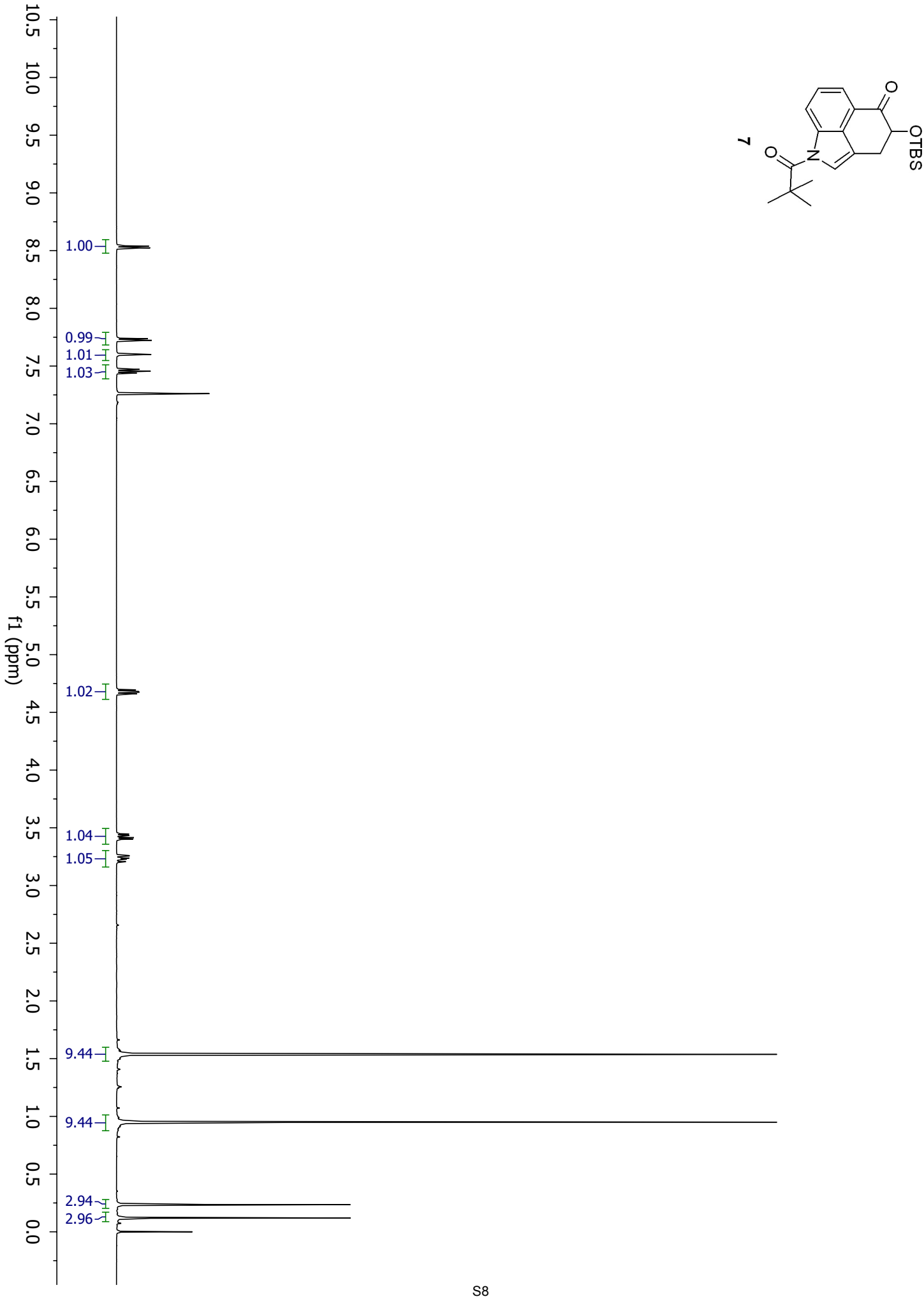
1) Incze, M.; Doernyei, G.; Moldvai, I.; Temesvari-Major, E.; Egyed, O.; Szántay, C., *Tetrahedron* **2008,** *64*(13), 2924-2929.

2) Petronijevic, F. R.; Wipf, P., *J. Am. Chem. Soc.* **2011,** *133*(20), 7704-7707.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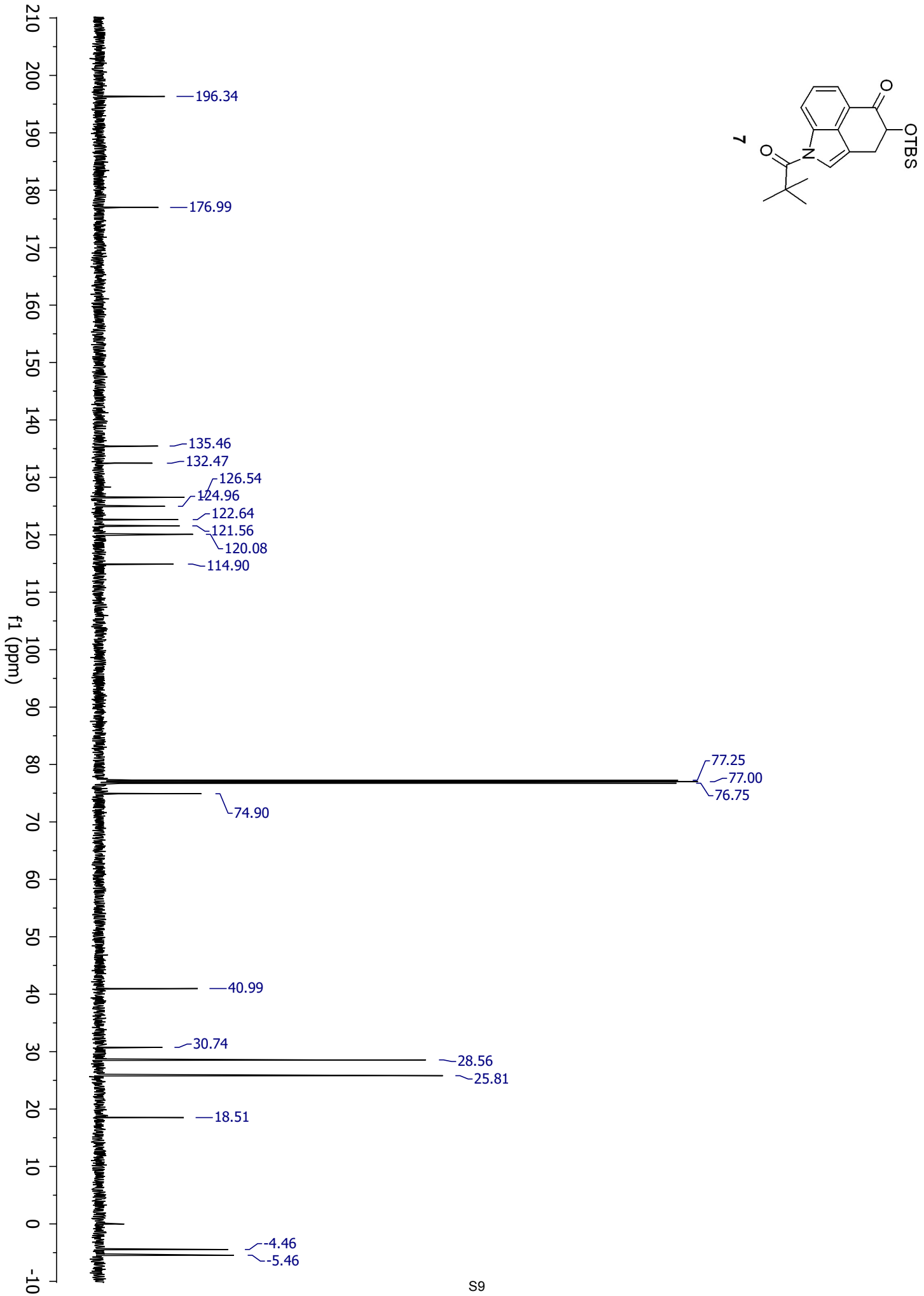
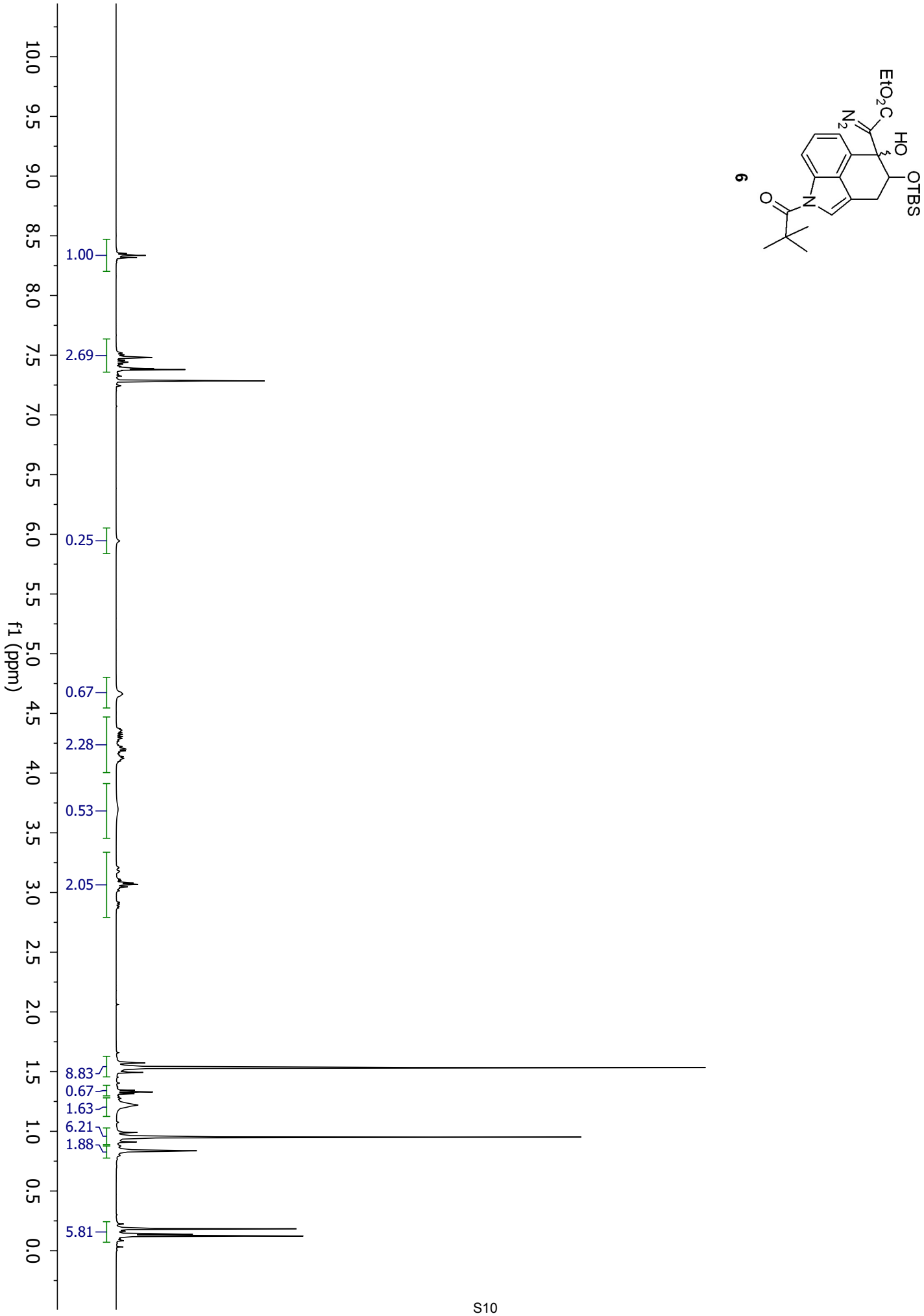
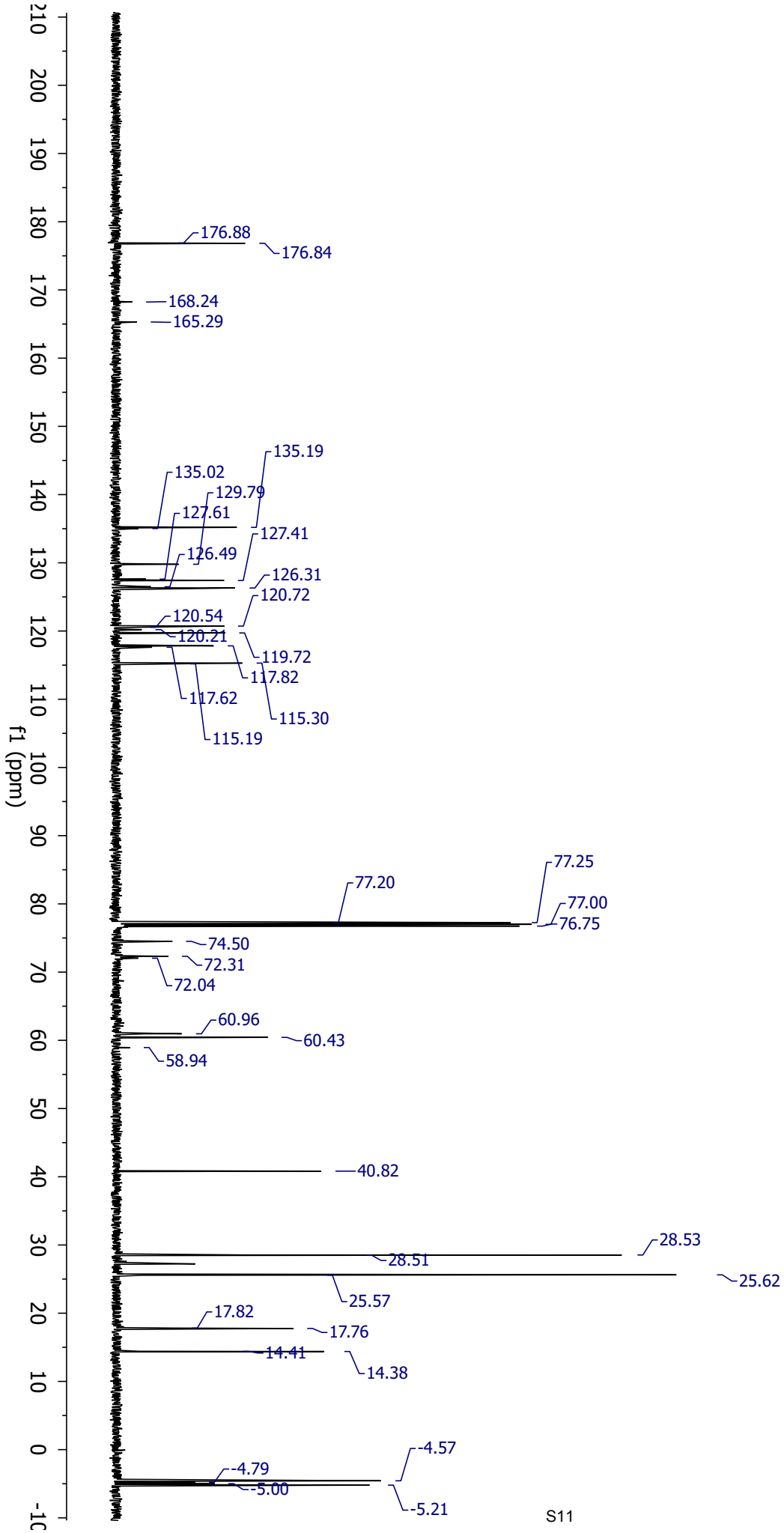
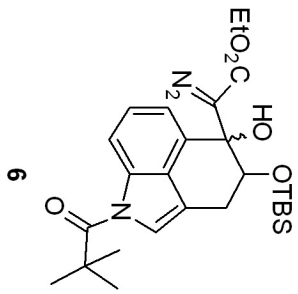
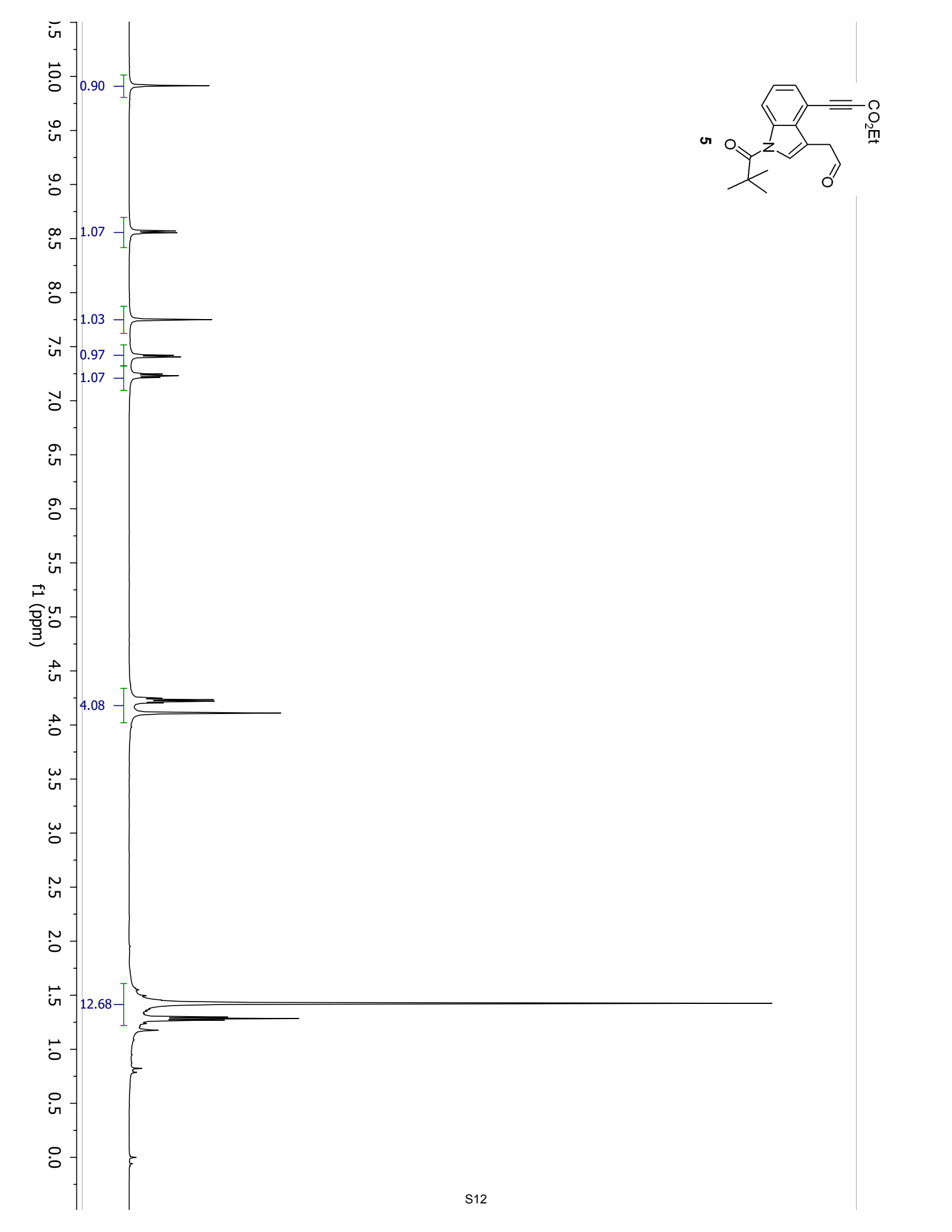
9.44
9.44
2.94
2.96
O
OTBS
N
O
7

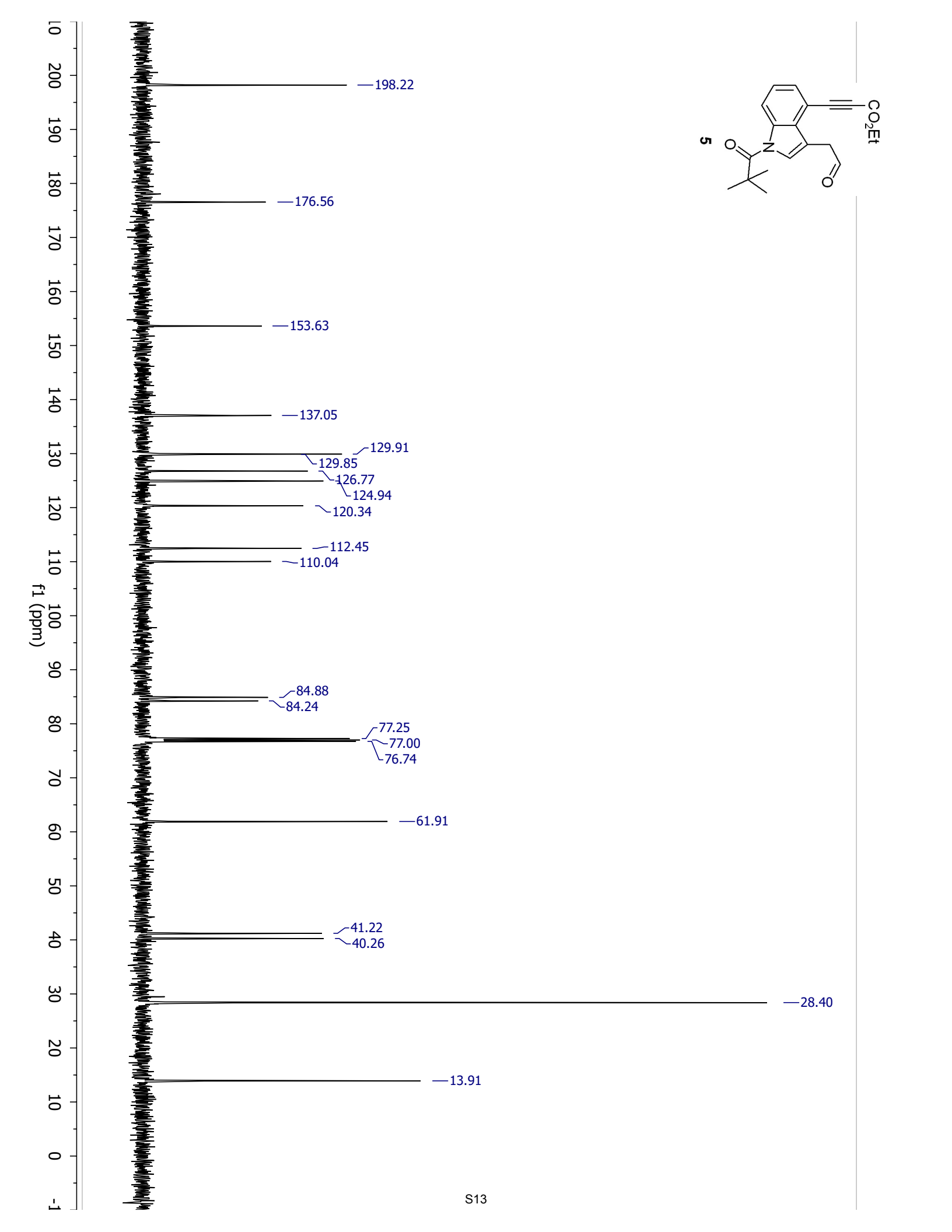

196.34
176.99
135.46
132.47
126.54
124.96
122.64
121.56
120.08
114.90
77.25
77.00
76.75
74.90
40.99
30.74
28.56
25.81
18.51
-4.46
-5.46
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
O
N
O
OTBS
7

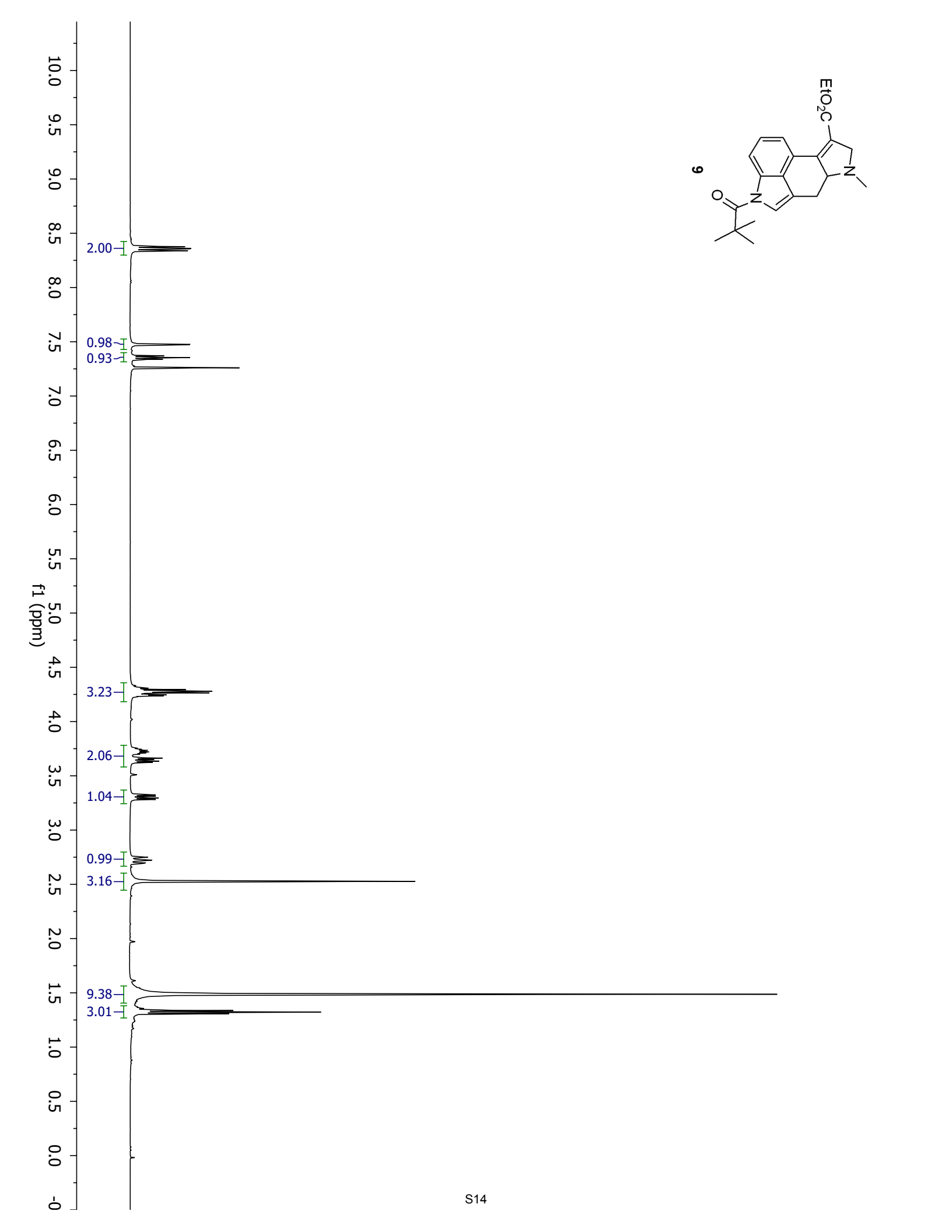

10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
1.00
2.69
0.25
0.67
2.28
0.53
2.05
8.83
0.67
1.63
6.21
1.88
5.81
EtO2C
N2
HO
OTBS
O
N
6

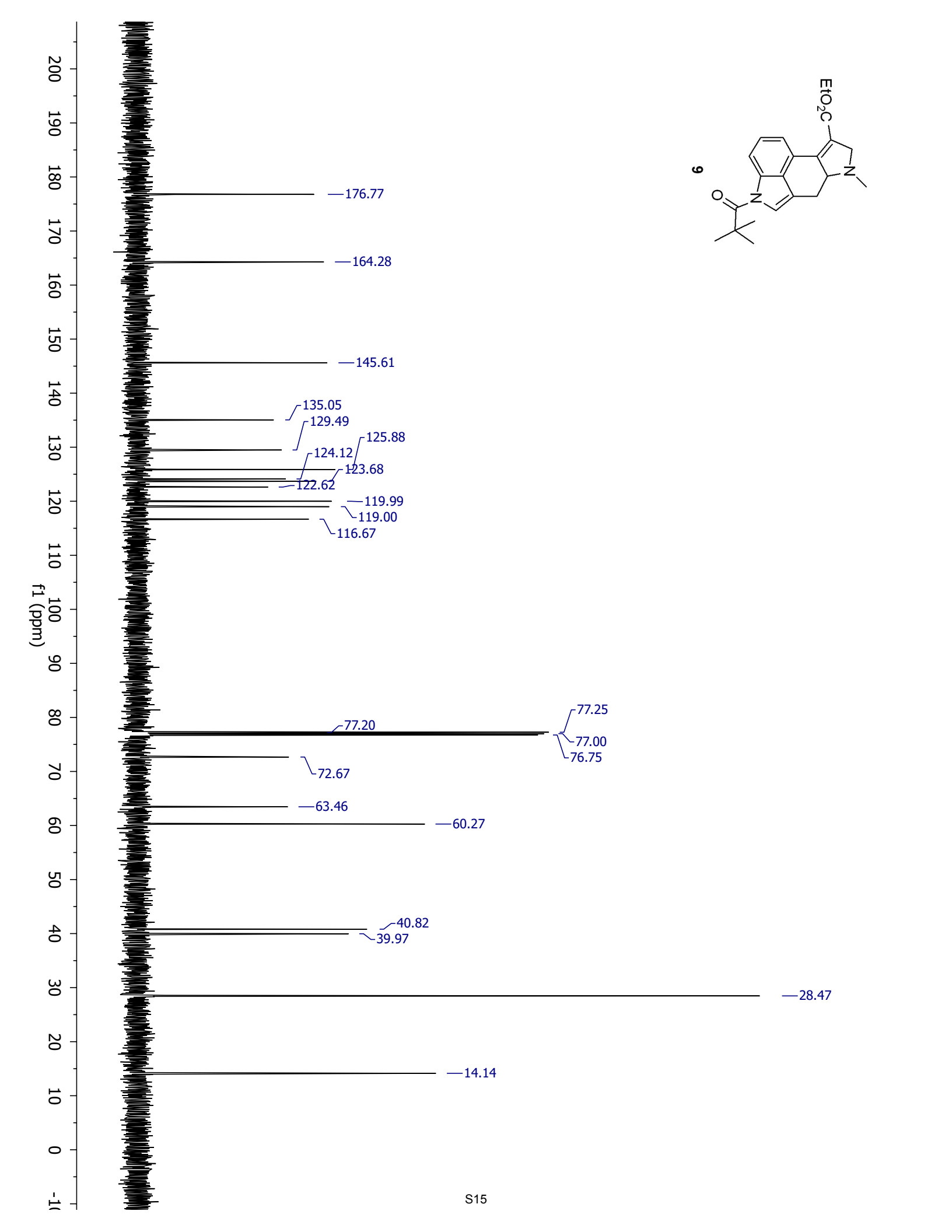

f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
176.88
176.84
168.24
165.29
135.19
135.02
129.79
127.61
127.41
126.49
126.31
120.72
120.54
120.21
119.72
117.82
117.62
115.30
115.19
77.25
77.20
77.00
76.75
74.50
72.31
72.04
60.96
60.43
58.94
40.82
28.53
28.51
25.62
25.57
17.82
17.76
14.41
14.38
-4.57
-4.79
-5.00
-5.21

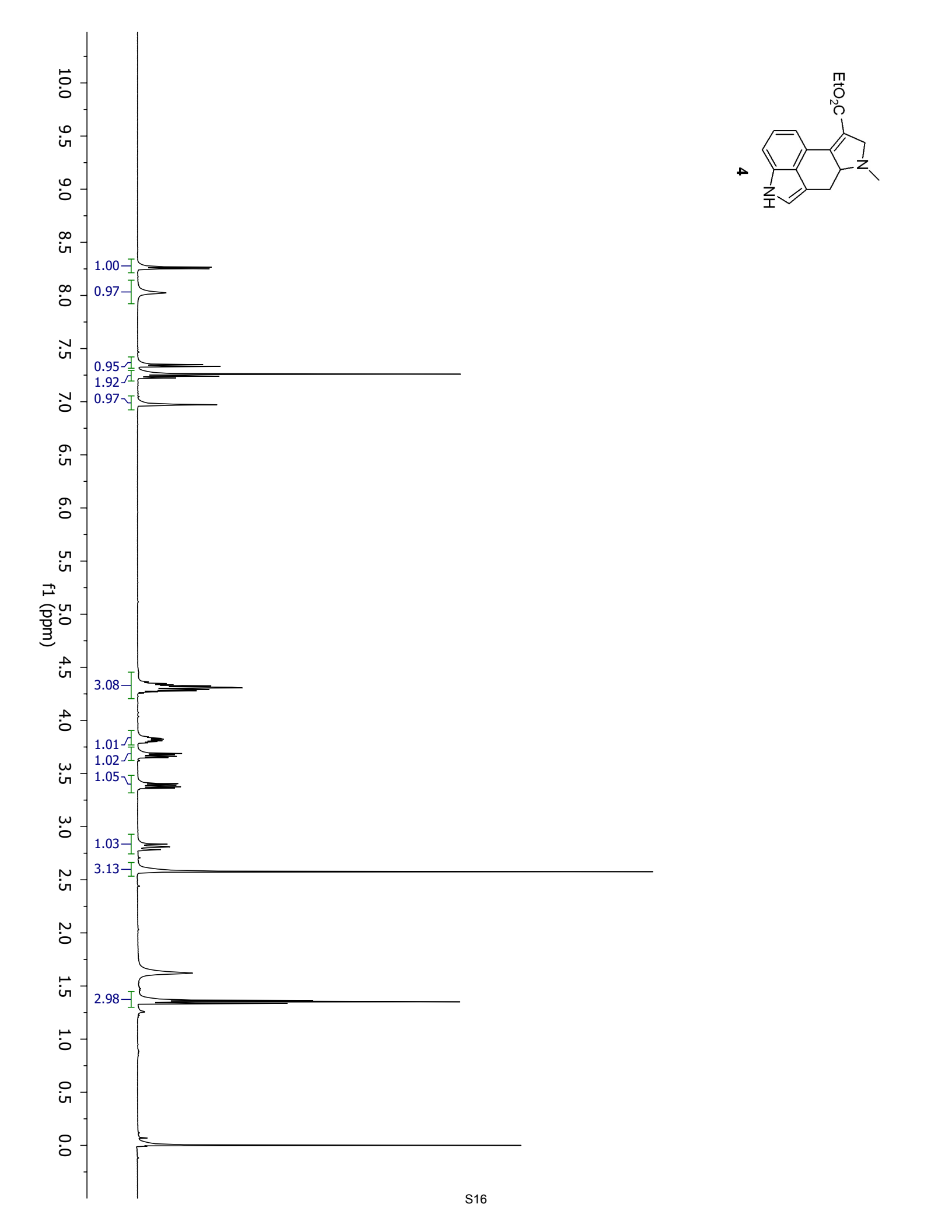

6
EtO2C
N2
HO
OTBS
O
N


0.90
1.07
1.03
0.97
1.07
4.08
12.68
f1 (ppm)
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
CO2Et
O
N
O
O
5

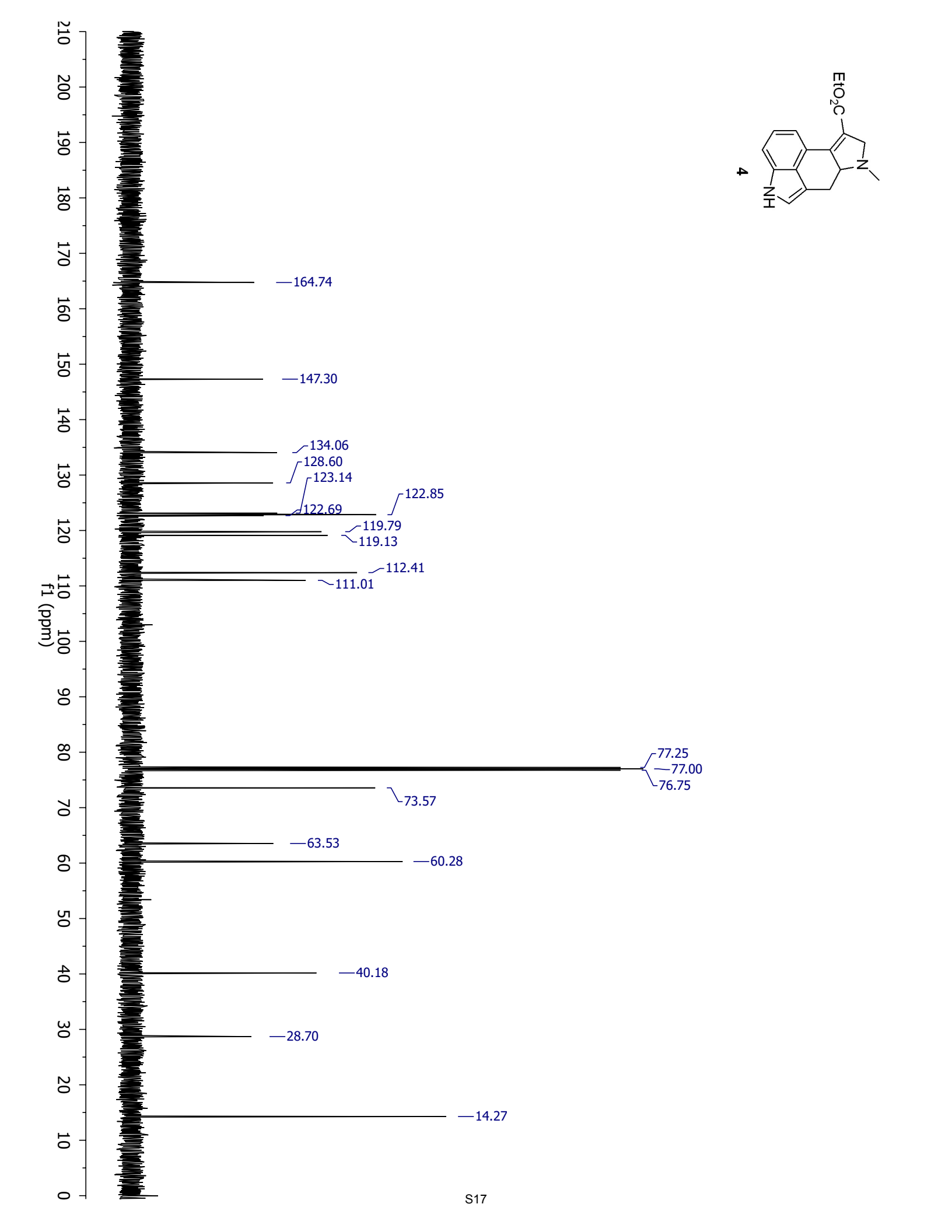

198.22
176.56
153.63
137.05
129.91
129.85
126.77
124.94
120.34
112.45
110.04
84.88
84.24
77.25
77.00
76.74
61.91
41.22
40.26
28.40
13.91
f1 (ppm)
CO2Et
5

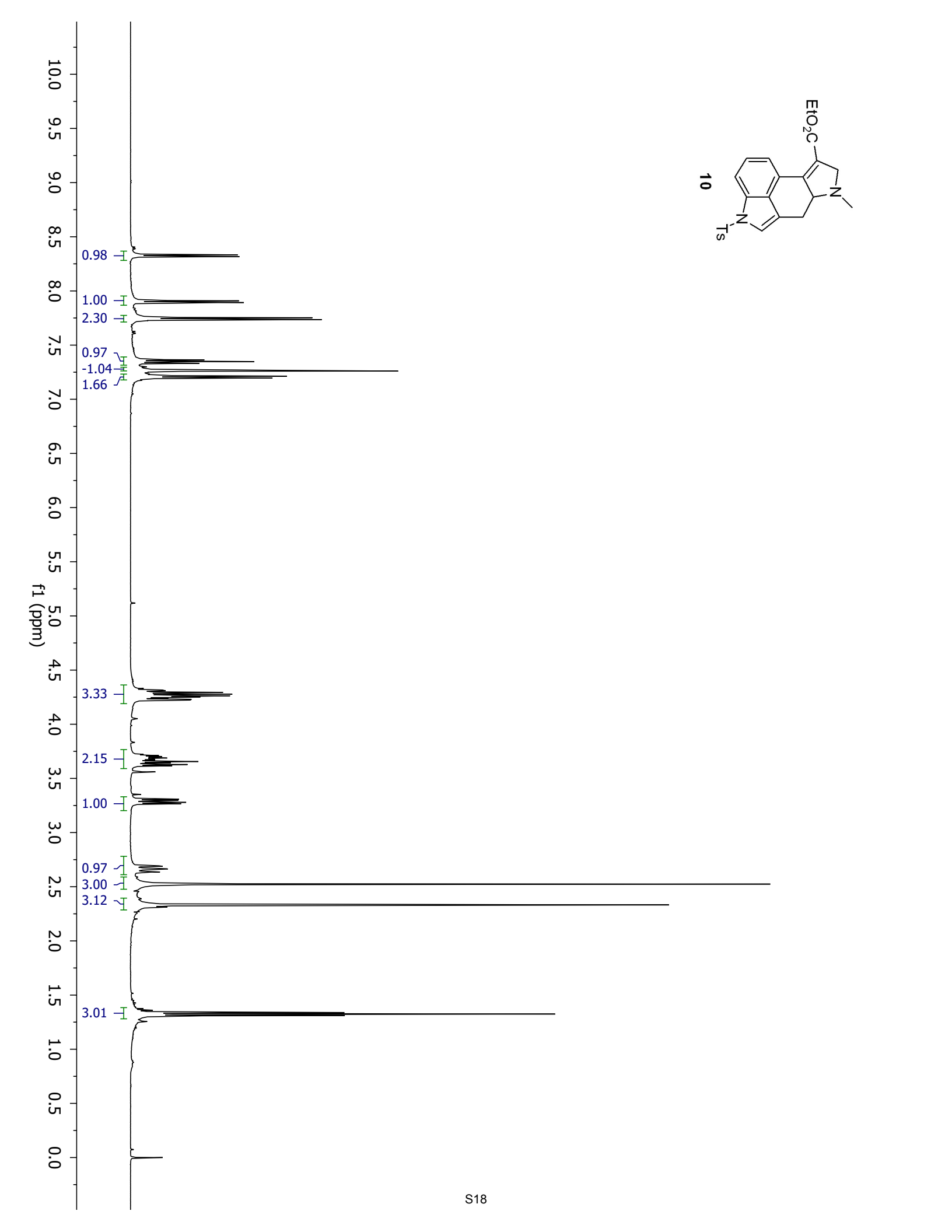

f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
2.00
0.98
0.93
3.23
2.06
1.04
0.99
3.16
9.38
3.01
EtO2C
N
O
N
9


f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1(
176.77
164.28
145.61
135.05
129.49
125.88
124.12
123.68
122.62
119.99
119.00
116.67
77.25
77.20
77.00
76.75
72.67
63.46
60.27
40.82
39.97
28.47
14.14
EtO2C
N
O
N
9

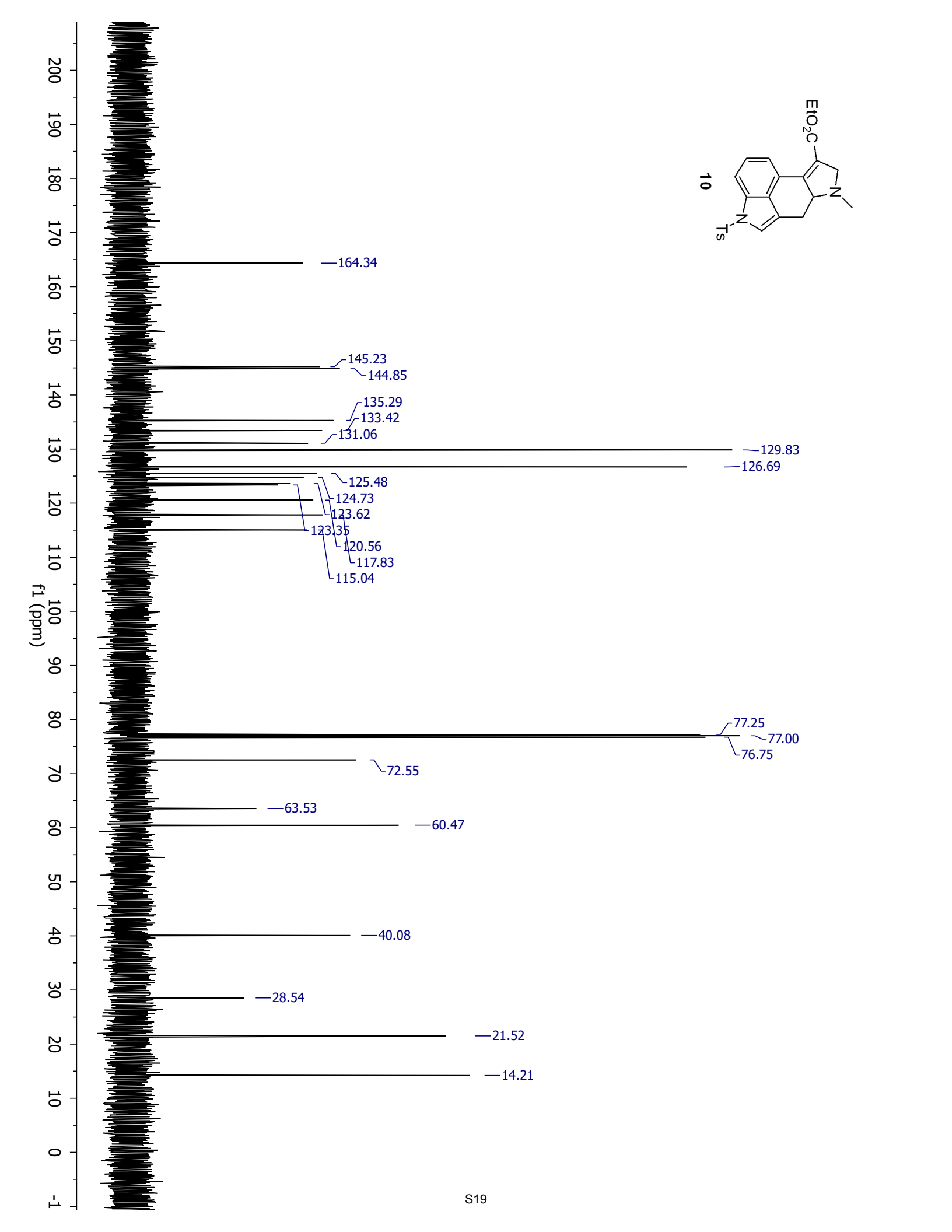

10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
1.00
0.97
0.95
1.92
0.97
3.08
1.01
1.02
1.05
1.03
3.13
2.98
EtO2C
N
NH

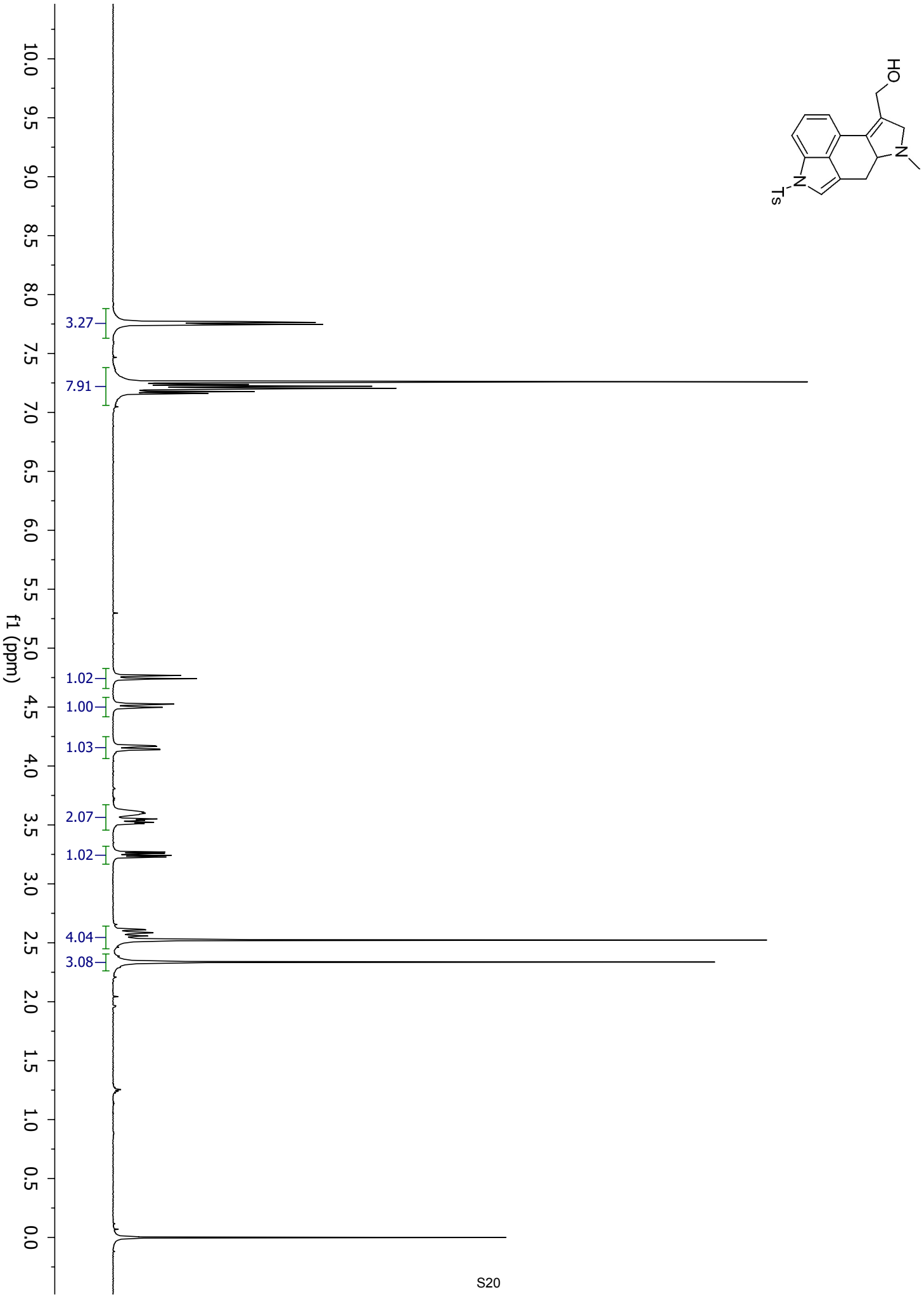
4

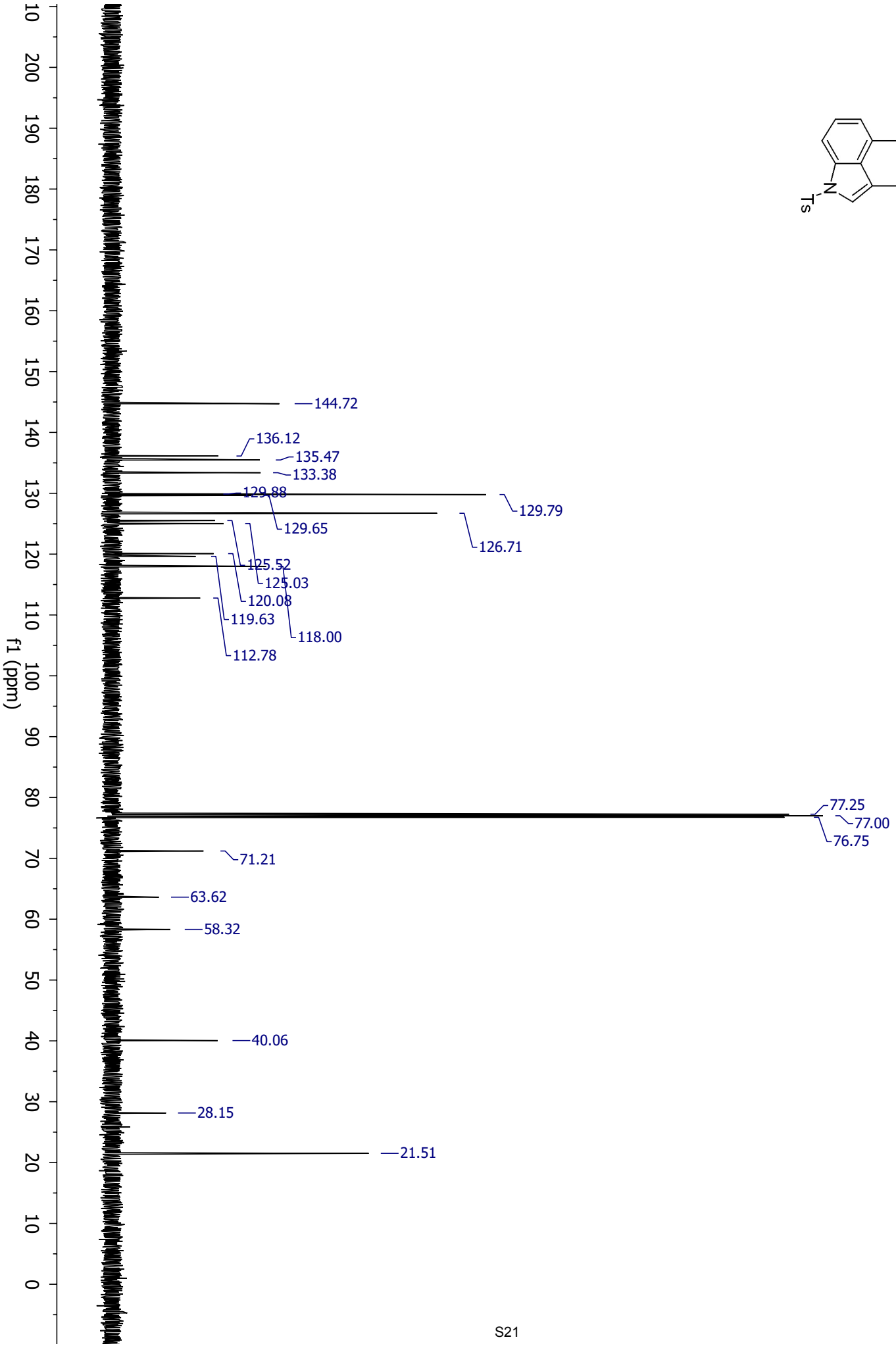

164.74
147.30
134.06
128.60
123.14
122.69
122.85
119.79
119.13
112.41
111.01
77.25
77.00
76.75
73.57
63.53
60.28
40.18
28.70
14.27
f1 (ppm)
EtO2C
NH
N
4

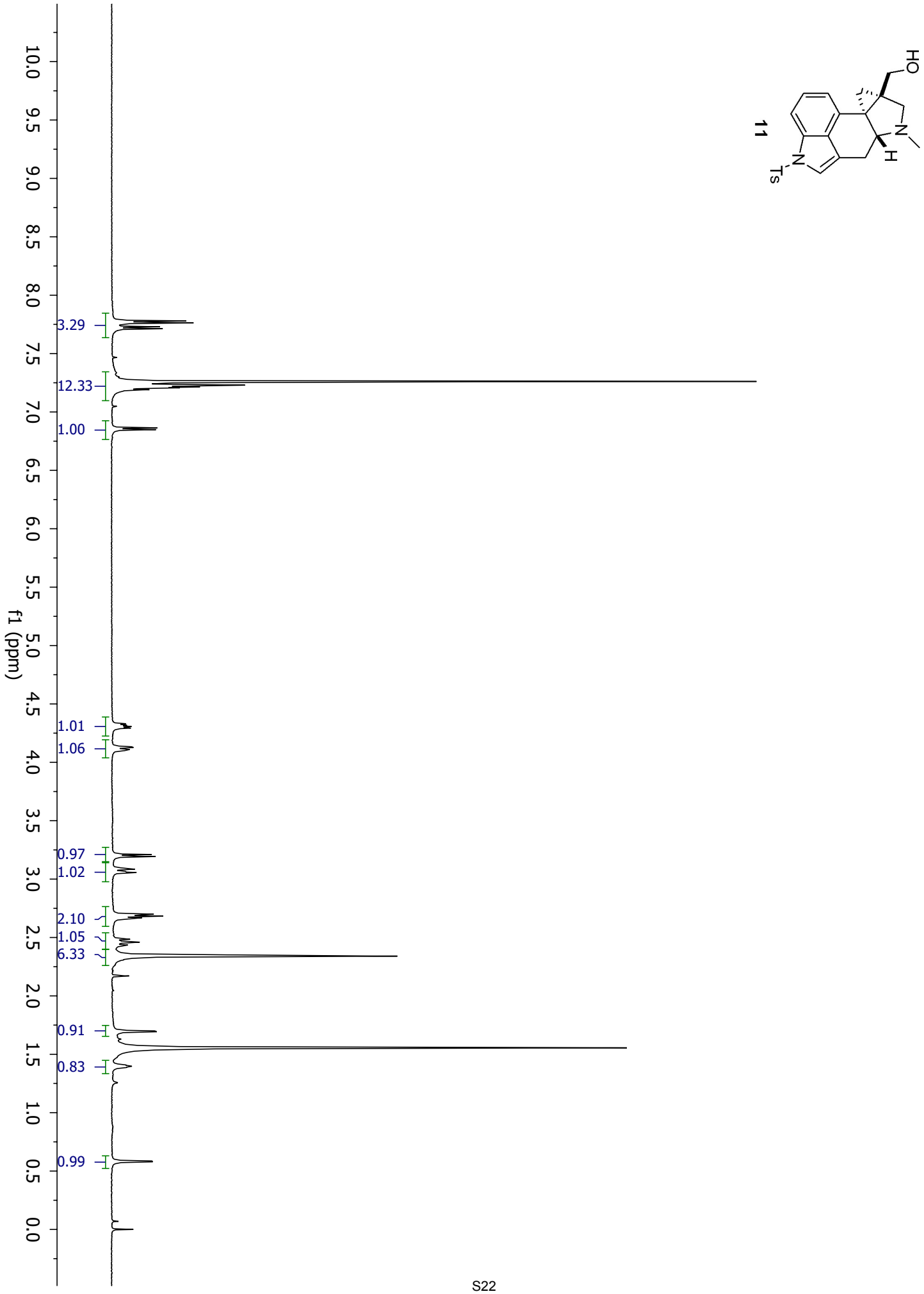

10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
0.98
1.00
2.30
0.97
-1.04
1.66
3.33
2.15
1.00
0.97
3.00
3.12
3.01
EtO2C
N
N
Ts

10


EtO2C
10
N
N
Ts
164.34
145.23
144.85
135.29
133.42
131.06
129.83
126.69
125.48
124.73
123.62
123.35
120.56
117.83
115.04
77.25
77.00
76.75
72.55
63.53
60.47
40.08
28.54
21.52
14.21
f1 (ppm)

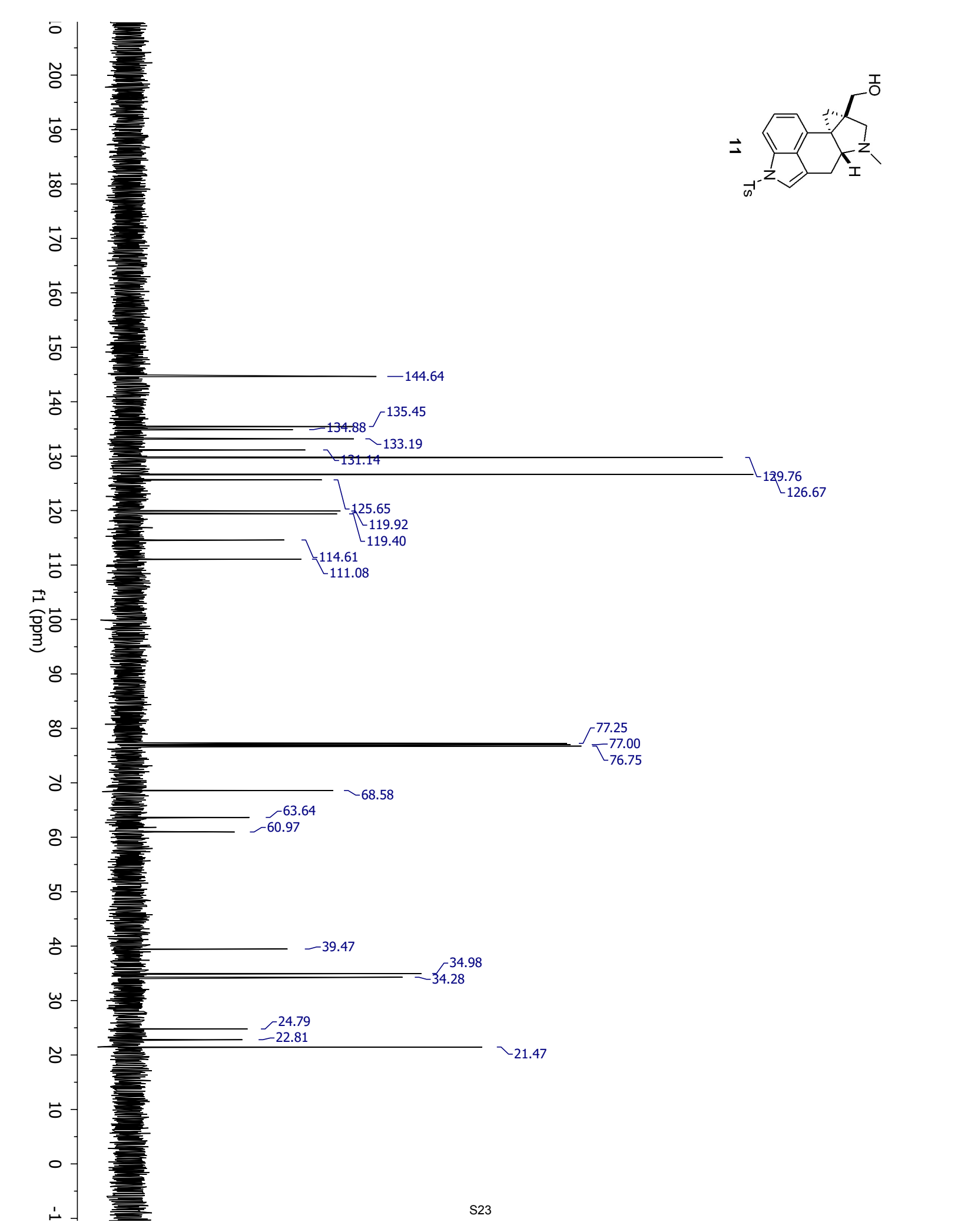

HO
N
N
Ts
3.27
7.91
1.02
1.00
1.03
2.07
1.02
4.04
3.08
f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


144.72
136.12
135.47
133.38
129.88
129.79
129.65
126.71
125.52
125.03
120.08
119.63
118.00
112.78
77.25
77.00
76.75
71.21
63.62
58.32
40.06
28.15
21.51
f1 (ppm)
HO
N
N
Ts


3.29
12.33
1.00
1.01
1.06
0.97
1.02
2.10
1.05
6.33
0.91
0.83
0.99
f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

HO
N
H
N
Ts

11


144.64
135.45
134.88
133.19
131.14
129.76
126.67
125.65
119.92
119.40
114.61
111.08
77.25
77.00
76.75
68.58
63.64
60.97
39.47
34.98
34.28
24.79
22.81
21.47
f1 (ppm)
HO
N
H
N
Ts
11