Supporting Information

Total Synthesis of (−)-Nodulisporic Acids B, C and D:

Evolution of a Unified Synthetic Strategy

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1. Materials and Methods

(1) Preparation of reagents and solvents

All chemicals were purchased from commercial vendors unless otherwise noted. Anhydrous tetrahydrofuran (THF), diethyl ether (Et_2O), and cyclopentyl methyl ether (CPME) were distilled from sodium/benzophenone. Dichloromethane (CH_2Cl_2), and toluene were acquired from a Pure Solve PS-400 solvent purification system. Hexamethylphosphoramide (HMPA) and triethylamine (Et_3N) were distilled from calcium hydride. Commercial tert-butyllithium (*t*-BuLi) solutions were titrated by using diphenylacetic acid.[1]

(2) Reaction equipment and conditions

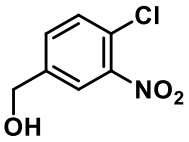
All reactions that require anhydrous conditions were performed in oven- or flame-dried glassware under N_2 or argon atmosphere with the reactant azeotroped with toluene to remove moisture. High pressure glass vials and septa caps required for sealed tube reactions were purchased from Biotage. High vacuum (0.05 torr) was created by using an oil pump (Nandor Model 1400N). All reactions were stirred magnetically unless otherwise mentioned. Ice/water bath was used to create 0~5 °C reaction temperature; dry ice/acetonitrile bath was used create −40 °C reaction temperature; dry ice/acetone bath was used to create −78 °C reaction temperature; and ethanol/liquid nitrogen bath was used to create −105 °C reaction temperature. All yields refer to spectroscopically pure compounds.

(3) Purifications and Analyses

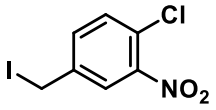
Reactions were monitored by using thin layer chromatography (TLC) with 250 mm pre-coated silica gel plates purchased from Silicycle Technology. Silica gel flash chromatography was conducted by using ACS grade solvents and silica gel which was purchased from Silicycle Technology. Silica gel flash chromatography was conducted under positive pressure by applying pressurized air. Silica gel vacuum liquid chromatography was conducted under negative pressure by applying vacuum created from a water aspirator. Medium pressure liquid chromatography was conducted by using a Varian ProStar 210 Pump equipped with a high-pressure glass column (350 mm × 35 mm or 350 mm × 10 mm) packed with silica gel (Sorbent Technologies, Standard Grade, porosity 60 Å, particle size 32-63 μm). High-performance liquid chromatography (HPLC) was conducted by using Gilson 333/334 Pumps equipped with an UV-Vis dual wavelength detector and a C18 column (VYDAC C18 monomeric, 250 mm × 10 mm, 5 μm particle size). All Infrared spectra were recorded on a Jasco Model FT/IR-480 Plus spectrometer. All melting points were acquired on a Thomas-Hoover apparatus and are uncorrected. All optical rotations were measured on a Jasco P-2000 polarimeter. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Avance III 500 MHz spectrometer equipped with either an Oxford

cryomagnet or a Spectrospin/Bruker cryomagnet (500MHz/52mm) with a 5-mm dual cryo probe by using either 5 mm or 3 mm NMR tubes. High-resolution mass spectra (HRMS) were acquired either on a Waters LC-TOF mass spectrometer (model LCT-XE Premier) or on a waters GCT Premier spectrometer at the University of Pennsylvania. Single crystal X-ray structures were determined at the University of Pennsylvania

2. Experimental Procedures

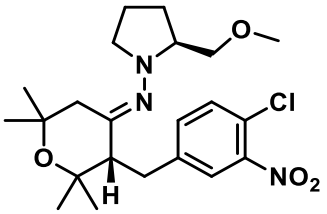


Alcohol S10: In a three-neck round bottom, commercially available 4-chloro-3-nitrobenzoic acid (4 g, 20 mmol, 1 eq.) was dissolved in THF (40 mL). The resulting colorless solution was cooled to 0 °C by using an ice/water bath. BH_3·THF (1M in THF, 40 mL, 40 mmol, 2 eq.) was added dropwise via an addition funnel over 15 minutes. A lot of bubbles were generated upon the addition of BH_3·THF solution, and the solution turned to a cloudy mixture. The ice/water bath was then removed, and the reaction mixture was warmed to room temperature and stirred overnight to form a clean, pale yellow solution which was then cooled to 0 °C again and quenched by careful addition of NaOH (1M aqueous solution), until bubbling ceased, to provide a red mixture. This mixture was stirred at room temperature for 30 minutes and then diluted with EtOAc (40 mL). The organic layer was separated and washed with $NaHCO_3$ (saturated aqueous solution), brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to afford the title compound as a pale yellow, amorphous solid (3.7 g, >95%) without further purification. **IR** 3238, 2917, 2849, 1535, 1354, 1028, 899, 828, 806, 753 (neat) cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 1.6 Hz, 1H), 7.55 – 7.46 (m, 2H), 4.75 (s, 2H), 2.22 (s, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 148.01, 141.46, 131.99, 131.20, 125.81, 123.56, 63.35. **HRMS (CI)** *m/z* 188.0110 [$(M+H)^+$; calcd for $C_7H_7ClNO_3$: 188.0014].

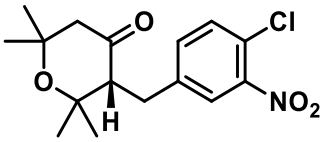


Iodide 12: In a three-neck round bottom flask equipped with an addition funnel, alcohol **S10** (3.7 g, 19.8 mmol, 1 eq.) was dissolved in CH_2Cl_2 (60 mL) and cooled to −20 °C. N-methylimidazole (3.4 g, 41.4 mmol, 2.07 eq.) was added, followed by the addition of iodine (5.3 g, 20.7 mmol, 1.05 eq.) to provide a dark purple solution. PPh_3 (5.4 g, 20.7 mmol, 1.05 eq.) was dissolved in CH_2Cl_2 (30 mL) and was then added dropwise to the reaction mixture via the additional funnel over 10 minutes. The

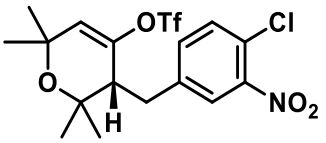
resulting orange solution was warmed to 0 °C, stirred at 0 °C for 1 hour, and filtered through a pad of silica gel (eluted with 5:1 hexanes/EtOAc). The filtrate was concentrated *in vacuo* at 0 °C to provide a pale yellow solid. This solid was then purified by using silica gel flash chromatography (eluted with 7:1 hexanes/EtOAc then 5:1 hexanes/EtOAc). The combined fractions were concentrated *in vacuo* at 0 °C to afford the title compound (5.0 g, 85%) as a white, amorphous solid. **IR** (neat) 3027, 1603, 1563, 1532, 1475, 1430, 1366, 1342, 1295, 1217, 1160, 1131, 1051, 930, 895, 832, 808, 752, 701, 673 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.88 (d, *J* = 2.3 Hz, 1H), 7.55 – 7.45 (m, 2H), 4.42 (s, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 140.0, 133.5, 132.5, 126.4, 125.6, 1.1. **HRMS (CI)** *m/z* 170.0011 [$(M-I)^+$; calcd for $C_7H_5NO_2Cl$: 170.0009].



Hydrazone (+)-13: Hydrazone (+)-**9** (362 mg, 1.35 mmol, 2.1 eq.) was azeotroped with benzene in a round bottom flask under high vacuum and was then backfilled with argon. THF (6 mL) was added. The resulting pale-yellow solution was cooled to −78 °C and treated dropwise with *t*-BuLi (1.1 M in pentane, 1.2 mL, 1.29 mmol, 2.0 eq.). This solution was stirred at −78 °C for 20 minutes and was then cooled to −105 °C. In a separate flask, iodide **12** (191 mg, 0.64 mmol, 1 eq.) was dissolved in THF (6 mL) was cooled to −78 °C and was cannulated into the anion solution of (+)-**9** to provide a dark brown mixture. This mixture was stirred at −105 °C for 30 minutes, then warmed to −78 °C, and stirred at −78 °C for 50 minutes. The reaction was then quenched with $NaHCO_3$ (saturated aqueous solution), warmed to room temperature, and diluted with EtOAc. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to yield the crude product as an orange oil. This oil was then purified by using silica gel flash chromatography (eluted with 20:1 CH_2Cl_2/acetone) to provide the title compound (180 mg, 64%) as a viscous, yellow oil. $[\alpha]_D^{25}$ +20.0 (*c* 3.5, $CHCl_3$). **IR** (neat) 2974, 2930, 2873, 1640, 1536, 1478, 1366, 1307, 1234, 1194, 1134, 1049, 1014, 984, 921, 811, 783, 752 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.38 (q, *J* = 8.2 Hz, 2H), 3.22 (s, 3H), 3.18 – 3.13 (m, 1H), 3.07 – 3.03 (m, 2H), 2.87 (dd, *J* = 14.1, 3.7 Hz, 1H), 2.73 – 2.65 (m, 1H), 2.59 – 2.51 (m, 2H), 2.43 – 2.34 (m, 1H), 2.00 – 1.88 (m, 2H), 1.74 – 1.65 (m, 2H), 1.60 – 1.48 (m, 2H), 1.39 (s, 3H), 1.29 (s, 3H), 1.24 (s, 3H), 1.23 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 147.7, 141.4, 134.4, 131.3, 126.2, 124.2, 75.5, 74.2, 66.1, 59.2, 55.1, 53.2, 39.0, 32.8, 32.1, 31.1, 30.2, 27.0, 26.4, 21.9. **HRMS (ESI)** *m/z* 438.2146 [$(M+H)^+$; calcd for $C_{22}H_{33}N_3O_4Cl$: 438.2160].

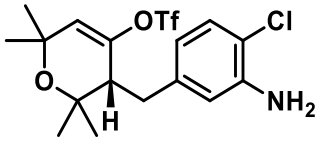


Ketone (+)-14: In a round bottom flask, the solution of (+)-**13** (14 mg, 0.032 mmol, 1 eq.) in CH_2Cl_2 (5 mL) was cooled to −78 °C and purged with O_3/O_2 stream (1 mL/minute) for 3 minutes to provide a faint blue solution. Argon was then purged into the solution for 15 minutes at −78 °C until the faint blue color dissipated to provide a pale-yellow solution. PPh_3 (25 mg, 0.096 mmol, 3 eq.) was then added into the solution at −78 °C. This solution was then warmed to room temperature, stirred for 1 hour, and concentrated *in vacuo* to provide an amber-colored oil. This oil was then purified by using silica gel flash chromatography (eluted with 7:1 hexanes/EtOAc) to provide the title compound (8 mg, 77%) as a viscous, colorless oil. $[\alpha]_D^{25}$ +1.9 (*c* 0.7, $CHCl_3$). **IR** (neat) 2977, 1713, 1536, 1479, 1369, 1300, 1227, 1180, 1137, 1049, 1013, 811 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.41 (s, 2H), 3.13 (dd, *J* = 13.7, 10.6 Hz, 1H), 2.77 (d, *J* = 10.3 Hz, 1H), 2.52 – 2.44 (m, 2H), 2.32 (d, *J* = 12.8 Hz, 1H), 1.48 (s, 3H), 1.35 (s, 3H), 1.26 (s, 3H), 1.20 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 208.2, 147.9, 141.5, 134.3, 131.7, 126.1, 124.7, 80.6, 61.9, 53.8, 33.5, 31.6, 30.4, 29.1, 24.8. **HRMS (ESI)** *m/z* 348.0978 [$(M+Na)^+$; calcd for $C_{16}H_{20}NO_4ClNa$: 348.0982].

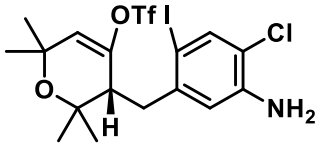


Triflate (+)-S14: In a round bottom flask, ketone (+)-**14** (632 mg, 1.94 mmol, 1 eq.) was dissolved in THF (30 mL) and cooled to −78 °C. To the resulting solution was then added dropwise with LHMDS (1.0 M in THF, 5.82 mL, 5.82 mmol, 3 eq.) and stirred at −78 °C for 30 minutes to provide a dark red solution. In a separate round bottom flask, Comins' reagent (1.90 g, 4.85 mmol, 2.5 eq.) was azeotroped with benzene, added THF (15 mL), and cooled to −78 °C. The resulting solution was then cannulated to the anion solution of (+)-**14**, stirred at −78 °C for 2 hours, quenched with NH_4Cl (saturated aqueous solution), and warmed to room temperature. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and filtered through a pad of silica gel (eluted with 5:1 hexanes/EtOAc). The filtrate was concentrated *in vacuo* to yield the crude product as a colorless oil. This oil was then purified by using silica gel flash chromatography (eluted with 10:1 hexanes/EtOAc) to provide the title compound (890 mg, >95%) as a colorless oil. $[\alpha]_D^{25}$ +134.4 (*c* 4.3, $CHCl_3$). **IR** (neat) 2979, 1537, 1418, 1353, 1247, 1212, 1140, 1051, 995, 922, 832, 807, 754, 611 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.32 (d, *J* = 7.6 Hz, 1H), 5.75 (s, 1H), 3.12 (dd, *J* = 13.4, 5.1 Hz, 1H), 2.81 – 2.64 (m, 1H), 2.51 – 2.37 (m, 1H), 1.48 – 1.13 (m, 12H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 147.8,

147.0, 139.8, 134.0, 131.9, 126.1, 125.1, 125.0, 118.2 (dd, J = 643, 320 Hz), 75.8, 72.7, 48.3, 35.5, 31.6, 28.5, 28.2, 27.7. **HRMS (ESI)** *m/z* 480.0481 [(M+Na)$^+$; calcd for $C_{17}H_{19}NO_6F_3SClNa$: 480.0471].

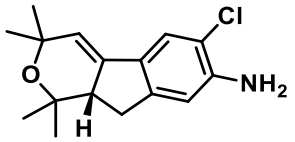


Amine (+)-**15**: In a round bottom flask, a solution of (+)-**S14** (1.10 g, 2.40 mmol, 1 eq.) in THF (24 mL) was added EtOH (24 mL) and H_2O (6 mL). The resulting pale-yellow solution was then added iron powder (1.34 g, 24.0 mmol, 10 eq.) and NH_4Cl (641mg, 12.0 mmol, 5 eq.). The resulting mixture was stirred vigorously to dismiss the fine powder of iron that attached to the magnetic stirring bar. The flask was then equipped with a reflux condenser, and the reaction mixture was heated to 90 °C under argon atmosphere. This mixture was stirred at 90 °C for 100 minutes, and a mirror-like appearance was formed on the wall of the reaction flask. The reaction mixture was then cooled to room temperature, added Celite, and filtered through a pad of silica gel (eluted with Et_2O, then EtOAc). The filtrate was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the title compound (1.04 g, >95%) as a pale-yellow oil without further purification. $[\alpha]_D^{25}$ +138.3 (*c* 3.8, $CHCl_3$). **IR** (neat) 3480, 3384, 2979, 2934, 1688, 1620, 1495, 1417, 1369, 1313, 1247, 1212, 1167, 1141, 1062, 1042, 1012, 995, 925, 895, 870, 834, 784, 760, 660, 613 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.13 (d, J = 8.1 Hz, 1H), 6.57 (s, 1H), 6.49 (d, J = 8.0 Hz, 1H), 5.70 (s, 1H), 4.01 (brs, 2H), 2.92 (dd, J = 13.8, 6.3 Hz, 1H), 2.60 (dd, J = 13.7, 8.0 Hz, 1H), 2.44 (t, J = 7.1 Hz, 1H), 1.44 – 1.29 (m, 9H), 1.25 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 148.1, 142.9, 139.1, 129.4, 123.9, 119.7, 118.4 (dd, J = 643, 328 Hz) 117.4, 116.4, 76.0, 72.5, 48.3, 35.7, 31.7, 28.8, 28.4, 27.7. **HRMS (ESI)** *m/z* 428.0902 [(M+H)$^+$; calcd for $C_{17}H_{22}NO_4F_3SCl$: 428.0910]. **HRMS (ESI)** *m/z* 426.0753 [(M−H)$^-$; calcd for $C_{17}H_{20}NO_4F_3SCl$: 428.0754].

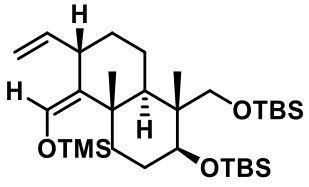


Iodide (+)-**16**: In a 20 mL reaction vial, triflate (+)-**15** (250 mg, 0.576 mmol, 1 eq.) was dissolved in CH_2Cl_2 (3 mL) and MeOH (1.5 mL). To the resulting solution was then added finely ground $CaCO_3$ powder (864 mg, 8.64 mmol, 15 eq.), followed by the addition of BTMA·ICl_2[2] (300 mg, 0.864 mmol, 1.5 eq.) to provide an olive-green mixture. This mixture was stirred at room temperature for 50 minutes and then quenched by dropwise addition of $Na_2S_2O_3$ (saturated aqueous solution) to provide a brown color mixture. This mixture was then diluted with EtOAc, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* at 0 °C to yield the crude product as a brown color oil. This oil was then purified by using silica gel flash chromatography (eluted with 8:1 hexanes/EtOAc) to provide the

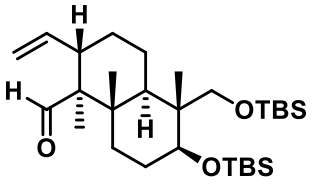
title compound (255 mg, 80%) as an amber color oil. $[\alpha]_D^{25}$ +124.5 (c 3.8, $CHCl_3$). **IR** (neat) 3483, 3395, 2978, 2933, 1687, 1616, 1558, 1473, 1417, 1370, 1271, 1247, 1212, 1140, 1055, 1014, 995, 925, 873, 833, 785, 761, 737, 675, 611 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.64 (s, 1H), 6.55 (s, 1H), 5.74 (s, 1H), 4.01 (brs, 2H), 3.15 (d, *J* = 9.8 Hz, 1H), 2.70 – 2.57 (m, 2H), 1.45 (s, 3H), 1.43 – 1.35 (m, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 147.8, 143.3, 140.7, 138.8, 124.3, 118.7, 118.4 (dd, *J* = 643, 328 Hz), 117.1, 84.5, 75.9, 72.7, 46.3, 40.8, 31.9, 28.6, 28.5, 27.7. **HRMS (ESI)** *m/z* 553.9877 [$(M+H)^+$; calcd for $C_{17}H_{21}NO_4SClF_3I$: 553.9877].



Aniline (–)-7: In a 20 mL high pressure glass vial, LiCl (460 mg, 10.8 mmol, 20.0 eq.) was added and flame dried *in vacuo* to form a free-flowing solid. Iodide (+)-**16** (300 mg, 0.542 mmol, 1 eq.) was then added into the vial, and the mixture was azeotroped with toluene *in vacuo* at 40 °C. $Pd(PPh_3)_4$ (125 mg, 0.108 mmol, 0.2 eq.) was then added to the vial, and the vial was sealed with a septum cap. 1,4-Dioxane (10 mL) was then added into the mixture and stirred at room temperature for 10 minutes. $(Me_3Sn)_2$ (195 mg, 0.596 mmol, 1.1 eq.) was then added via a syringe, and the reaction vial was put into a preheated oil bath (100 °C). The reaction mixture was stirred vigorously at 100 °C for 15 hours and cooled to room temperature. KF/Celite[3] (3 g) was then added, and the reaction mixture was stirred at room temperature for 1 hour and filtered through a pad of Celite. The filtrate was concentrated *in vacuo* to provide the crude product as a pale-yellow oil. This oil was then purified by using silica gel flash chromatography (eluted with 10:1 hexanes/EtOAc) to provide the title compound (114 mg, 76%, >95% ee by chiral SFC analysis) as a viscous, lime green color oil. Lime green crystals (m.p. 94–96 °C) could be acquired by slow evaporation from a solution (5:1 hexanes/EtOAc) for X-ray crystallographic analysis. $[\alpha]_D^{25}$ –47.4 (c 0.6, $CHCl_3$). **IR** (neat) 3351, 2970, 2926, 1619, 1482, 1346, 1244, 1148, 988, 833, 756, 680 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.32 (s, 1H), 6.63 (s, 1H), 5.77 (d, *J* = 2.5 Hz, 1H), 4.08 (brs, 2H), 2.92 (dd, *J* = 15.9, 9.3 Hz, 1H), 2.87 – 2.79 (m, 1H), 2.49 (dd, *J* = 15.9, 7.3 Hz, 1H), 1.35 – 1.28 (m, 9H), 1.06 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 144.73, 142.92, 137.94, 131.75, 121.50, 119.96, 118.45, 111.78, 74.32, 72.64, 48.49, 33.27, 31.90, 30.08, 30.02, 22.12. **HRMS (ESI)** *m/z* 278.1308 [$(M+H)^+$; calcd for $C_{16}H_{21}NOCl$: 278.1312].



Silyl enol ether (−)-17: In a three-neck round bottom flask equipped with an additional funnel, $CuBr{\cdot}Me_2S$[4] (5.7 g, 21.6 mmol, 1.2 eq.) and THF (30 mL) were added, and a white slurry[5] was formed. Upon addition of Me_2S (30 mL), this slurry turned to a clean, colorless solution. This solution was cooled to −78 °C, and a solution of vinyl magnesium bromide[6] (0.37 M in THF, 175 mL, 64.8 mmol, 3.0 eq.) was added via cannula over 10 minutes to provide a dark emerald-green solution.[7] This solution was stirred at −78 °C for 50 minutes, and HMPA (6.3 mL, 36.0 mmol, 2 eq.) was added. In a separate flask, aldehyde (+)-**11**[8] (8.4 g, 18.0 mmol, 1 eq.) was dissolved in THF (15 mL), and was added TMSCl (5.1 mL, 36.0 mmol, 2 eq.). The resulting solution was added to the flask containing the vinyl cuprate species via an addition funnel over 15 minutes. The resulting mixture was stirred at −78 °C for 3 hours, then added TMEDA (5 mL), aqueous ammonia (10 mL), water (100 mL), warmed to room temperature, and stirred at room temperature for 2 hours. The resulting mixture was filtered through a pad of Celite. The organic layer was separated, and the aqueous layer was extracted with hexanes. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to yield the crude product as a brown oil. This oil was then purified by using silica gel vacuum liquid chromatography (eluted with hexanes) to provide the title compound (9.0 g, 88%) as a light lime green oil.[9] $[\alpha]_D^{25}$ −3.4 (c 2.1, $CHCl_3$). **IR** (neat) 2933, 2856, 1702, 1471, 1443, 1386, 1361, 1330, 1254, 1088, 1046, 1030, 1005, 960, 932, 897, 878, 854, 835, 816, 772, 664, 635 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.78 – 5.64 (m, 2H), 4.97 (d, *J* = 5.4 Hz, 1H), 4.94 (s, 1H), 3.74 (dd, *J* = 11.3, 5.1 Hz, 1H), 3.38 (d, *J* = 9.6 Hz, 1H), 3.13 (d, *J* = 9.7 Hz, 1H), 2.82 – 2.71 (m, 1H), 2.23 (dt, *J* = 14.0, 3.6 Hz, 1H), 1.89 (td, *J* = 13.8, 4.3 Hz, 1H), 1.77 (dq, *J* = 12.5, 4.1 Hz, 1H), 1.70 – 1.48 (m, 4H), 1.40 (dtd, *J* = 20.4, 12.1, 10.2, 6.0 Hz, 2H), 1.17 (s, 3H), 0.90 (s, 6H), 0.88 (s, 12H), 0.61 (s, 3H), 0.15 (s, 9H), 0.07 (s, 3H), 0.04 (d, *J* = 3.7 Hz, 3H), 0.02 (s, 3H), 0.01 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 142.9, 131.9, 131.0, 113.9, 72.0, 64.7, 44.6, 43.9, 42.7, 40.4, 36.8, 34.1, 28.5, 26.4, 26.3, 21.6, 21.3, 18.5, 18.5, 12.9, −0.3, −3.2, −4.5, −4.9, −5.4. **HRMS (CI)** *m/z* 566.4034 [$(M)^+$; calcd for $C_{31}H_{62}O_3Si_3$: 566.4007]; *m/z* 551.3791 [$(M-CH_3)^+$; calcd for $C_{30}H_{59}O_3Si_3$: 551.3772]; *m/z* 509.3293 [$(M-C_4H_9)^+$; calcd for $C_{30}H_{59}O_3Si_3$: 509.3303].



Aldehyde (−)-20:

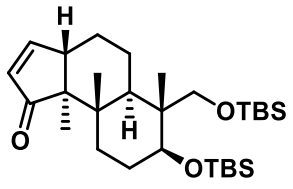
Condition 1:

Silyl enol ether **(−)-17** (4.9 g, 8.64 mmol, 1 eq.) was dissolved in THF (77 mL) and HMPA (8.6 mL). The resulting solution was cooled to 0 °C. MeLi (27 mL, 1.6M in Et_2O, 43.2 mmol, 5 eq.) was added dropwise over a 15 min period. The solution was then cooled to −78 °C and methyl iodide (5.4 mL,

86.4 mmol, 10 eq.) was added dropwise. The reaction was allowed to warm to room temperature and was then quenched with brine. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo* to yield the crude product as a colorless oil. This oil was then purified by using silica gel medium pressure liquid chromatography (eluted with 100:1 hexanes/EtOAc) to provide the title compound (1.8 g, 41%). $[\alpha]_D^{25}$ −31.6 (*c* 1.3, $CHCl_3$). **IR** (neat) 2927, 1712, 1471, 1254, 1085, 919, 857, 836, 772 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.68 (s, 1H), 5.57 (ddd, *J* = 17.3, 10.5, 7.0 Hz, 1H), 5.08 – 4.92 (m, 2H), 3.72 – 3.62 (m, 1H), 3.36 (d, *J* = 9.9 Hz, 1H), 3.12 (d, *J* = 9.8 Hz, 1H), 3.04 (dd, *J* = 12.2, 6.1 Hz, 1H), 1.89 (dd, *J* = 11.7, 3.2 Hz, 1H), 1.78 – 1.71 (m, 1H), 1.62 – 1.33 (m, 7H), 1.20 (s, 3H), 1.01 (s, 3H), 0.92 (s, 9H), 0.86 (s, 9H), 0.63 (s, 3H), 0.06 – 0.00 (m, 12H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 209.3, 140.2, 115.9, 71.6, 64.3, 55.9, 43.9, 40.9, 40.7, 36.6, 32.1, 27.2, 27.1, 26.1, 26.1, 21.2, 18.3, 18.2, 17.3, 13.2, 10.3, −3.4, −4.7, −5.1, −5.5. **HRMS (ESI)** *m/z* 509.3842 [$(M+H)^+$; calcd for $C_{29}H_{57}O_3Si_2$: 509.3846].

Condition 2:

In a round bottom flask, THF (7.7 mL) was added to enol ether (−)-**17** (3.5 g, 6.2 mmol, 1 eq.), and the resulting solution was cooled to −78 °C. MeLi (1.6 M in Et_2O, 7.7 mL, 12.3 mmol, 2 eq.) was then added dropwise to the reaction solution, and the resulting orange solution was stirred at 0 °C for 30 minutes. 12-crown-4 (3.5 mL, 21.6 mmol, 3.5 eq.) was then added to the reaction solution, and the resulting solution was stirred at 0 °C for 20 minutes and was then cooled to −78 °C. MeI (2.3 mL, 37 mmol, 6 eq.) was then added dropwise to the reaction solution, and the resulting solution was stirred at −40 °C for 100 hours. The reaction was then quenched with $Na_2S_2O_3$ (saturated aqueous solution). The organic layer was separated, and the aqueous layer was extracted with hexanes. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to yield the crude product as an oil (3.6 g). This oil was then added MeOH (20 mL) and EtOH (50 mL) and put in a −20 °C refrigerator overnight and then filtered. The titled compound (2.5 g, 80%) was obtained in pure.



Enone (+)-**21**:

Protocol 1:

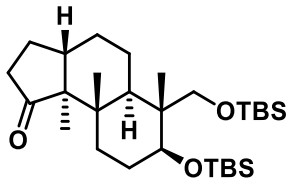
In a round bottom flask, aldehyde (−)-**20** (1.8 g, 3.5 mmol, 1 eq.) was dissolved in THF (35 mL). The resulting solution was cooled to −78 °C and was treated dropwise with vinyl magnesium bromide (1.0 M in THF, 12.6 mL, 12.6 mmol, 3.6 eq.). The reaction solution was allowed to warm to 0 °C over a period of 9 hours and was then quenched with NH_4Cl (saturated aqueous solution). The organic layer

was separated, and the aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered through a pad of silica gel (eluted with Et_2O). The filtrate was concentrated *in vacuo* to yield the crude product as a colorless oil. This oil was then dissolved in CH_2Cl_2 (350 mL), added 2nd generation Grubbs catalyst (297 mg, 0.35 mmol, 0.1 eq.), and stirred at room temperature for 11 hours. To the resulting amber-color solution was then added PCC (1.1 g, 5.3 mmol, 1.5 eq.) and NaOAc (861 mg, 10.5 mmol, 3.0 eq.), and the resulting mixture was stirred at room temperature for 6.5 hours to provide a dark brown solution. Celite and $NaHCO_3$ were then added, and the mixture was filtered through a pad of Celite (eluted with Et_2O). The filtrate was concentrated *in vacuo*, dissolved in Et_2O, and then filtered through a pad of Celite (eluted with Et_2O) again. The filtrate was concentrated *in vacuo* to yield the crude product as a dark brown oil. This oil was then purified by using silica gel flash chromatography (eluted with 20:1 hexanes/EtOAc) to provide the title compound (1.45 g, 82%) as a white, waxy solid. $[\alpha]_D^{25}$ +43.2 (*c* 0.1, $CHCl_3$). **IR** (neat) 2933, 2856, 1702, 1471, 1443, 1386, 1361, 1330, 1254, 1088, 1046, 1030, 1005, 960, 932, 897, 878, 854, 835, 816, 772, 664, 635,772, 664, 635 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.40 (dd, *J* = 6.0, 1.7 Hz, 1H), 5.89 (dd, *J* = 5.9, 3.1 Hz, 1H), 3.81 – 3.71 (m, 1H), 3.67 (dd, *J* = 11.3, 5.2 Hz, 1H), 3.42 (d, *J* = 9.7 Hz, 1H), 3.13 – 3.05 (m, 2H), 2.13 – 2.01 (m, 2H), 1.88 – 1.80 (m, 1H), 1.72 – 1.59 (m, 3H), 1.47 (td, *J* = 13.5, 4.0 Hz, 1H), 1.35 – 1.27 (m, 1H), 1.16 (s, 3H), 1.05 (s, 3H), 0.91 (s, 9H), 0.87 (s, 9H), 0.60 (s, 3H), 0.05 (s, 3H), 0.03 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 213.6, 162.9, 132.1, 72.1, 64.5, 59.6, 47.2, 44.0, 38.8, 37.9, 30.4, 27.7, 26.1, 26.1, 23.4, 23.1, 20.1, 18.9, 18.3, 18.2, 12.5, −3.3, −4.7, −5.0, −5.6. **HRMS (ESI)** *m/z* 507.3687 [$(M+H)^+$; calcd for $C_{29}H_{55}O_3Si_2$: 507.3689].

Protocol 2:

In a round bottom flask, aldehyde (−)-**20** (17 g, 33.5 mmol, 1 eq.) was dissolved in THF (330 mL). The resulting solution was cooled to −78 °C and was treated dropwise with vinyl magnesium bromide (1.0 M in THF, 121 mL, 121 mmol, 3.6 eq.). The reaction solution was allowed to warm to 0 °C over a period of 9 hours and was then quenched with NH_4Cl (saturated aqueous solution). The organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered through a pad of silica gel (eluted with Et_2O). The filtrate was concentrated *in vacuo* to yield the crude product as a colorless oil. Next, the crude product was dissolved in CPME (335 mL), and Hoveyda-Grubbs Catalyst 2nd Generation (210 mg, 0.335 mmol, 0.01 eq.) was dissolved in minimal amount of CPME, and the resulting solution was then added to the reaction solution. The reaction mixture was then stirred at 110 °C under nitrogen for 23 hours then filtered through a silica pad then concentrated *in vacuo* to provide the crude product as off-white solid which was used directly for the next step without further purification. Next, in a 250-mL round bottom flask, powder 4Å molecular sieve (15 g) was heated to approximately 120 °C for 10 minutes under high vacuum to remove moisture. The flask was then cooled to room temperature and was then back filled three times with nitrogen. In another 250 mL round bottom flask, the crude product from the last stage was treated with NMO (5.4 g, 46 mmol, 1.4 eq.), CH_2Cl_2 (60 mL). The resulting solution was cannulated to the flask containing powder 4Å molecular sieve. The resulting mixture was cooled

to 0 °C and added TPAP (275 mg, 0.78 mmol, 0.023 eq.) that was dissolved in CH_2Cl_2 (20 mL). The resulting green mixture was stirred at 0 °C for 7 hours then diluted with hexanes (120 mL) then added Celite. The mixture was then filtered through a silica pad (washed with Et_2O). The filtrate was then concentrated *in vacuo* to provide the crude product as off-white solid which was purified by trituration from acetone to yield the title compound (12 g, 71%).



Ketone (−)-22:

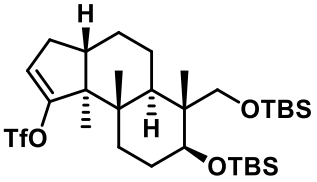
Method 1: from enone (+)-**21**

In a round bottom flask, EtOAc (4 mL) was added, followed by the addition of palladium on carbon (14 mg, 10 wt. %). The resulting mixture was purged with hydrogen for 15 minutes, and (+)-**21** (73 mg, 0.144 mmol, 1 eq.) in EtOAc (2 mL) was added. A hydrogen balloon was then attached, and the reaction mixture was stirred vigorously for 4 hours and was then backfilled with N_2. The mixture was then filtered through a pad of Celite, and the filtrate was concentrated *in vacuo* to provide the title compound (66 mg, 90%) as a white, waxy solid without further purification. An aliquot was recrystallized from Et_2O to yield colorless needles (m.p.=136~140 ˚C). $[\alpha]_D^{25}$ −61 (*c* 1.3, $CHCl_3$). **IR** (neat) 2954, 2856, 1729, 1471, 1444, 1385, 1360, 1254, 1088, 1068, 1005, 974, 927, 892, 856, 835, 772, 736, 664 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.65 (dd, *J* = 11.4, 4.9 Hz, 1H), 3.39 (d, *J* = 9.6 Hz, 1H), 3.08 (d, *J* = 9.7 Hz, 1H), 2.30 (dd, *J* = 19.2, 8.4 Hz, 1H), 2.23 – 2.14 (m, 1H), 2.09 – 2.03 (m, 1H), 1.99 (dt, *J* = 19.0, 9.4 Hz, 1H), 1.87 (dd, *J* = 12.3, 3.1 Hz, 1H), 1.82 – 1.74 (m, 1H), 1.71 – 1.43 (m, 6H), 1.35 – 1.23 (m, 2H), 0.99 (s, 3H), 0.91 (s, 12H), 0.86 (s, 9H), 0.58 (s, 3H), 0.06 – 0.00 (m, 12H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 221.5, 72.0, 64.5, 56.2, 43.8, 40.5, 39.1, 37.7, 30.4, 27.5, 26.1, 26.0, 25.9, 23.9, 22.2, 18.2, 18.1, 17.6, 12.5, 10.5, −3.4, −4.8, −5.1, −5.6. **HRMS (ESI)** *m/z* 509.3827 [$(M+H)^+$; calcd for $C_{29}H_{57}O_3Si_2$: 509.3846].

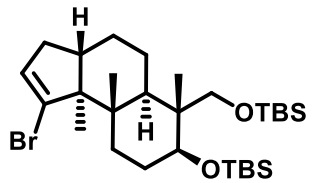
Method 2: from aldehyde (−)-**20**

In a microwave reaction tube, aldehyde (−)-**20** (30 mg, 0.06 mmol, 1 eq.) was added $Rh(NBD)_2BF_4$ (22 mg, 0.06 mmol, 1 eq.), (±)-BINAP (37 mg, 0.06 mmol, 1 eq.), and N,N-dimethylacetamide (1 mL). The reaction was sealed under nitrogen and reacted in a microwave reactor at 220 ˚C for 2 hours. Hexanes was then added followed by the addition of water. The organic phase was separated, and the aqueous phase was extracted with hexanes. The combined organic layers were washed with brine, dried over Na_2SO_4, followed by $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to yield the

crude product which was then purified by using silica gel vacuum liquid chromatography (40:1, hexanes/EtOAc) to provide the title compound (23 mg, 77%).

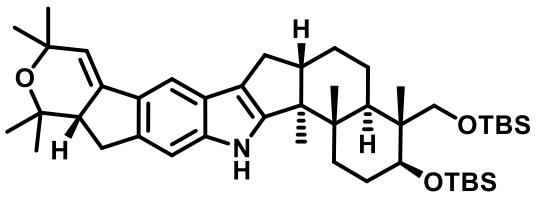


Triflate (−)-**23**: In a 50-mL round-bottom flask, ketone (−)-**22** (2.5 g, 4.92 mmol, 1 eq.) was azeotroped with toluene, and THF (8.2 mL) was then added, and the solution was cooled to −78 °C. The resulting solution was treated with LHMDS (1.0 M in THF, 5.4 mL, 5.40 mmol, 1.1 eq.) and then stirred at −78 °C for 1 hour. A solution of $PhNTf_2$ (1.93 g, 5.40 mmol, 1.1 eq.) in THF (7.4 mL) was added to the reaction solution at −78 °C. The resulting solution was warmed to 0 °C over a period of 1.5 hours and was then diluted with hexanes. The resulting mixture was filtered through a silica pad, and the filtrate was concentrated *in vacuo*. The crude product was dissolved in hexanes and was subsequently washed with HCl (2N, aqueous solution), $NaHCO_3$ (saturated aqueous solution), dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product as a golden-colored oil. This oil was purified using silica gel vacuum chromatography (eluted with a gradient of hexanes, 100:1 hexanes/EtOAc) to provide the title compound (2.55 g, 81%) as a white amorphous solid. $[\alpha]_D^{25}$ −2.5 (*c* 2.3, $CDCl_3$). **IR** (neat) 2953, 2858, 1626, 1472, 1423, 1251, 1213, 1143, 1093, 1046, 1006, 939, 882, 836, 774 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.54 (dd, *J* = 3.3, 1.7 Hz, 1H), 3.66 (dd, *J* = 11.3, 5.1 Hz, 1H), 3.41 (d, *J* = 9.8 Hz, 1H), 3.08 (d, *J* = 9.7 Hz, 1H), 2.32 – 2.20 (m, 1H), 2.15 (ddd, *J* = 14.8, 6.5, 3.3 Hz, 1H), 1.98 (ddd, *J* = 14.8, 11.0, 1.8 Hz, 1H), 1.89 (dd, *J* = 12.5, 3.3 Hz, 1H), 1.75 – 1.42 (m, 6H), 1.34 (dd, *J* = 12.6, 3.7 Hz, 1H), 1.29 – 1.20 (m, 1H), 1.08 (s, 3H), 1.04 (s, 3H), 0.92 (s, 9H), 0.88 (s, 9H), 0.59 (s, 3H), 0.06 (s, 3H), 0.04 (d, *J* = 1.2 Hz, 6H), 0.03 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 158.6, 114.1, 71.8, 64.3, 54.7, 43.9, 42.9, 38.8, 37.6, 31.0, 30.3, 27.8, 26.1, 26.0, 24.5, 22.7, 18.3, 18.2, 18.1, 12.3, 12.1, -3.4, -4.8, -5.1, -5.6. **HRMS (ESI)** *m/z* 641.3270 [$(M+H)^+$; calcd for $C_{30}H_{56}F_3O_5SSi_2$: 641.3339].



Bromide (−)-**8**: In a 50 mL Schlenk flask, triflate (−)-**23** (2.1 g, 3.3 mmol, 1 eq.) was added in turn with N-methyl-2-aminobiphenylpalladium methanesulfonate dimer (85 mg, 0.098 mmol, 0.03 eq.), *t*-BuBrettPhos (143 mg, 0.295 mmol, 0.09 eq.), KF (95 mg, 1.64 mmol, 0.5 eq.), KBr (781 mg, 6.56

mmol, 2 eq.), and Cs_2CO_3 (64 mg, 0.196 mmol, 0.06 eq.). The resulting solid mixture was back filled with argon multiple times. CPME (13 mL) was cannulated to the reaction flask. The resulting mixture was heated to reflux and maintained at reflux under argon for 43 hours while stirring vigorously. This mixture was cooled to room temperature, diluted with hexanes, and was then filtered through a silica pad washed with hexanes. The filtrate was concentrated *in vacuo* to provide the crude product as an off-white amorphous solid (1.58 g, 84%). This solid was used for the next step without further purification. $[\alpha]_D^{25}$ −2.3 (*c* 2.1, $CDCl_3$). **IR** (neat) 2928, 1472, 1255, 1091, 835, 773 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.81 (dd, *J* = 3.1, 1.8 Hz, 1H), 3.67 (dd, *J* = 11.3, 5.1 Hz, 1H), 3.41 (d, *J* = 9.7 Hz, 1H), 3.10 (d, *J* = 9.7 Hz, 1H), 2.36 – 2.19 (m, 2H), 2.05 (ddd, *J* = 14.8, 6.7, 3.1 Hz, 1H), 1.93 – 1.83 (m, 2H), 1.72 – 1.47 (m, 6H), 1.46 – 1.19 (m, 4H), 1.10 (s, 3H), 0.93 (s, 9H), 0.88 (s, 9H), 0.60 (s, 3H), 0.08 (s, 3H), 0.06 (s, 3H), 0.05 – 0.00 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 133.7, 132.4, 71.9, 64.5, 57.5, 44.3, 44.1, 39.8, 38.2, 33.8, 30.2, 27.7, 26.1, 26.1, 25.3, 23.0, 18.3, 18.1, 17.7, 12.6, 12.3, 1.2, -3.4, -4.7, -5.1, -5.6. **HRMS (ESI)** *m/z* 571.2927 [$(M+H)^+$; calcd for $C_{29}H_{56}BrO_2Si_2$: 571.3002].

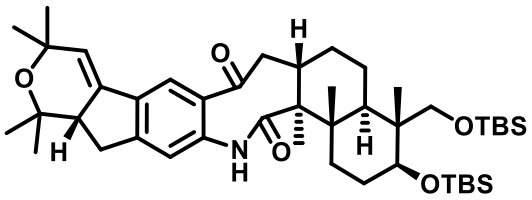


Indole (−)-26: In a reaction vial, aniline (−)-**7** (26 mg, 0.094 mmol, 1 eq.) and triflate (−)-**23** (72 mg, 0.113 mmol, 1.2 eq.) or bromide (−)-**8** (65 mg, 0.113 mmol, 1.2 eq.) were added, followed by the addition of RuPhos Pd GIII (23.5 mg, 0.028 mmol, 0.3 eq.), Cs_2CO_3 (184 mg, 0.546 mmol, 6 eq.), and RuPhos (13 mg, 0.034 mmol, 0.3 eq.) as solids. This mixture was then azeotroped with benzene *in vacuo*, added toluene (2 mL), and sealed with a septum cap. The vial was then backfilled with N_2 and sealed with paraffin wax. The reaction vial was then put into a preheated oil bath (100 °C). The reaction mixture was stirred vigorously at 100 °C for 18 hours, and filtered through a pad of silica gel (eluted with 5:1 hexanes/EtOAc). The filtrate was concentrated *in vacuo* to yield the crude product as a brown oil. This oil was then purified by using silica gel vacuum liquid chromatography (eluted with a gradient elution of 30:1, 20:1, 10:1, 5:1 hexanes/EtOAc) to provide the title compound [38 mg, 56% for triflate (−)-**23**, and 41 mg, 60% for bromide (−)-**8**] as a white foam. $[\alpha]_D^{25}$ −10.0 (*c* 0.3, $CHCl_3$). **IR** 2928, 2856, 1461, 1385, 1251, 1094, 835, 773 (neat) cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.62 (s, 1H), 7.51 (s, 1H), 7.16 (s, 1H), 5.97 (d, *J* = 2.9 Hz, 1H), 3.76 (dd, *J* = 11.0, 4.7 Hz, 1H), 3.44 (d, *J* = 9.8 Hz, 1H), 3.14 (dd, *J* = 12.9, 7.7 Hz, 2H), 2.95 (td, *J* = 9.3, 8.5, 2.9 Hz, 1H), 2.71 (ddt, *J* = 42.4, 19.5, 7.6 Hz, 3H), 2.31 (dd, *J* = 13.2, 10.7 Hz, 1H), 2.12 – 2.04 (m, 1H), 1.93 – 1.79 (m, 2H), 1.73 (tq, *J* = 11.8, 7.2 Hz, 2H), 1.67 – 1.50 (m, 3H), 1.51 – 1.43 (m, 1H), 1.36 (d, *J* = 6.6 Hz, 9H), 1.11 (s, 6H), 0.99 (s, 3H), 0.95 (s, 9H), 0.91 (s, 9H), 0.63 (d, *J* = 2.6 Hz, 3H), 0.08 (dd, *J* = 7.2, 5.6 Hz, 12H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 151.8, 141.3, 139.3, 137.9, 132.7, 125.0, 119.6, 118.3, 109.7, 107.6, 74.6, 72.8, 71.9, 64.3, 53.2, 48.8, 48.8, 43.9, 39.1, 37.1, 34.8, 33.5, 33.4, 32.1, 31.7, 30.2,

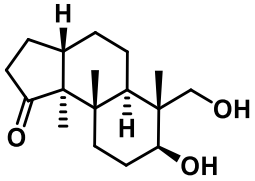
30.1, 27.9, 27.6, 27.1, 26.1, 25.4, 25.2, 22.8, 22.3, 18.9, 18.3, 18.1, 14.4, 12.3, -3.4, -4.7, -5.1, -5.6. **HRMS (ESI)** *m/z* 732.5198 [(M+H)$^+$; calcd for $C_{45}H_{74}NO_3Si_2$: 732.5207].

Purification protocol: Nitrogen-Purged Vacuum Silica Gel Column Chromatography

1) Hexanes was degassed by bubbling through nitrogen gas for 30 minutes and was mixed with silica gel and then loaded on a column. The silica gel loaded on the column was then dried completely through pressurized nitrogen.
2) All solvents for column chromatography were purged with nitrogen for at least 15 minutes before use.
3) During the column chromatography purification, a nitrogen balloon was attached to the top of the column while vacuum was applied at the outlet of the column.
4) Fractions of interest were combined and evaporated using a rotary evaporator at room temperature and backfilled with nitrogen upon finishing evaporating.

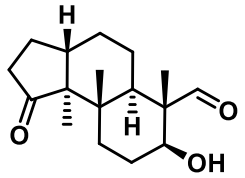


Amide (−)-27: was obtained as a by-product (>50%)[10] in the cases which regular silica gel column purification was applied for indole (−)-**26** under air, or exposure of indole (−)-**26** under air for days. $[\alpha]_D^{25}$ −37.2 (*c* 0.3, $CHCl_3$). **IR** 2954, 1648, 1472, 1250, 1091, 836, 774 (neat) cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.03 (s, 1H), 6.95 (s, 1H), 6.14 (d, *J* = 3.1 Hz, 1H), 3.68 (dd, *J* = 10.0, 5.3 Hz, 1H), 3.35 (d, *J* = 9.8 Hz, 1H), 3.13 (dd, *J* = 16.8, 9.4 Hz, 1H), 3.04 (d, *J* = 9.9 Hz, 1H), 3.00 – 2.85 (m, 3H), 2.61 (dd, *J* = 17.0, 7.7 Hz, 1H), 2.36 (dd, *J* = 18.1, 3.1 Hz, 1H), 1.99 – 1.92 (m, 1H), 1.74 – 1.60 (m, 4H), 1.48 (d, *J* = 11.4 Hz, 1H), 1.40 – 1.30 (m, 15H), 1.07 (s, 3H), 1.02 (s, 3H), 0.92 (s, 9H), 0.86 (s, 9H), 0.51 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H), 0.01 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.8, 176.7, 149.5, 139.6, 137.2, 136.9, 134.2, 130.8, 125.0, 124.1, 121.2, 74.4, 72.8, 71.5, 64.2, 59.7, 48.6, 48.3, 43.7, 41.1, 36.0, 35.3, 33.6, 32.2, 31.6, 30.2, 30.0, 29.8, 27.5, 26.0, 22.1, 21.7, 18.5, 18.2, 18.1, 14.9, 12.7, -3.5, -4.8, -5.2, -5.6. **HRMS (ESI)** *m/z* 764.5123 [(M+H)$^+$; calcd for $C_{45}H_{74}NO_5Si_2$: 764.5106].

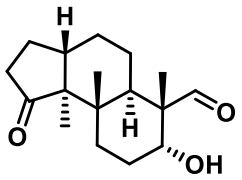


Diol (−)-28: In a polyethylene reaction vial, a solution of (−)-**22** (200 mg, 0.393 mmol, 1 eq.) in CH_2Cl_2 (4 mL) and MeCN (4 mL) was added, cooled to 0 °C, and then treated dropwise with HF (6

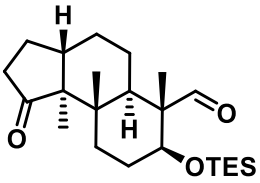
mL, 48 wt. % in H_2O) to provide a white slurry. This slurry was then warmed to room temperature and stirred for 2 hours to provide a light pink solution. This solution was then added slowly into a vigorously stirred $NaHCO_3$ (saturated aqueous solution) by using a plastic dropper, and powered $NaHCO_3$ was then added to neutralize the remaining HF. This mixture was stirred at room temperature for 10 minutes until the solution turned basic (by using red litmus paper test) and then diluted with EtOAc. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, followed by $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to yield the crude product as a pale-yellow oil. This oil was then purified by using silica gel vacuum liquid chromatography (eluted with a gradient elution of 20:1, 10:1, then 5:1 CH_2Cl_2/MeOH) to provide the title compound (115 mg, >95%) as a white foam. $[\alpha]_D^{25}$ −43.3 (*c* 2.2, $CHCl_3$). **IR** (neat) 3398, 2943, 1729, 1448, 1385, 1109, 1033, 969, 916, 732 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.81 – 3.50 (m, 2H), 3.40 (d, *J* = 10.3 Hz, 1H), 2.40 – 2.08 (m, 4H), 2.08 – 1.94 (m, 2H), 1.86 – 1.74 (m, 1H), 1.74 – 1.64 (m, 3H), 1.62 – 1.43 (m, 4H), 1.42 – 1.24 (m, 2H), 1.01 (s, 3H), 0.94 (s, 3H), 0.87 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 221.7, 76.2, 71.1, 56.2, 42.5, 40.9, 40.4, 39.5, 37.8, 30.7, 27.0, 25.9, 24.0, 22.5, 18.0, 11.5, 10.7. **HRMS (CI)** *m/z* 280.2037 [$(M)^+$; calcd for $C_{17}H_{28}O_3$: 280.2038].



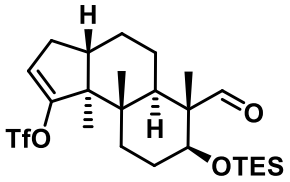
Aldehyde (−)-29: In a reaction vial, a solution of (−)-**28** (22 mg, 0.079 mmol, 1 eq.) in CH_2Cl_2 (0.5 mL) and H_2O (0.5 mL) was added TEMPO (13.5 mg, 0.086 mmol, 1.1 eq.) and BAIB (28 mg, 0.086 mmol, 1.1 eq.). The resulting biphasic system was stirred vigorously at room temperature for 55 minutes, and then quenched with $Na_2S_2O_3$ (saturated aqueous solution), followed by $NaHCO_3$ (saturated aqueous solution). After stirring at room temperature for 10 minutes, the organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over $MgSO_4$ and filtered. The filtrate was concentrated *in vacuo* to yield the crude product as an orange oil. This oil was then purified by using silica gel flash chromatography (eluted with 3:1 hexanes/EtOAc) to provide the title compound (22 mg, >95%) as a colorless, amorphous solid. $[\alpha]_D^{25}$ −40.7 (*c* 1.3, $CHCl_3$). **IR** (neat) 3438, 2944, 2359, 1729, 1447, 1380, 1245, 1112, 1058, 1039, 974, 950, 918, 752, 974, 950, 918, 752 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.41 – 9.29 (m, 1H), 3.71 (d, *J* = 9.6 Hz, 1H), 2.31 (dd, *J* = 19.5, 8.5 Hz, 1H), 2.23 – 2.11 (m, 2H), 2.07 – 1.94 (m, 1H), 1.89 – 1.48 (m, 9H), 1.49 – 1.31 (m, 2H), 1.04 (s, 3H), 1.00 (s, 3H), 0.95 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 220.8, 207.0, 72.4, 55.9, 55.4, 40.5, 40.1, 38.7, 37.5, 30.6, 26.6, 25.7, 24.8, 24.0, 17.7, 10.7, 8.8. **HRMS (CI)** *m/z* 278.1882 [$(M)^+$; calcd for $C_{17}H_{26}O_3$: 278.1882]; *m/z* 261.1844 [$(M–OH)^+$; calcd for $C_{17}H_{25}O_2$: 278.1855].



Aldehyde (−)-31: Isolated as a by-product (7.7 mg, 35%) from the above-mentioned protocol using only CH_2Cl_2 as the solvent without adding H_2O. $[\alpha]_D^{25}$ −75.7 (*c* 0.6, $CHCl_3$). **IR** (neat) 3454, 2949, 1716, 1453, 1404, 1377, 1286, 1227, 1111, 1077, 1022, 970, 929, 906, 755, 647 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.79 (s, 1H), 4.10 (s, 1H), 2.32 (dd, *J* = 19.3, 8.5 Hz, 1H), 2.22 (tdd, *J* = 12.6, 10.0, 6.8 Hz, 1H), 2.11 (dd, *J* = 13.5, 3.3 Hz, 1H), 2.06 – 1.96 (m, 1H), 1.96 – 1.88 (m, 2H), 1.88 – 1.74 (m, 3H), 1.74 – 1.51 (m, 4H), 1.45 (qd, *J* = 12.6, 4.0 Hz, 2H), 1.10 (s, 3H), 1.00 (s, 3H), 0.88 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 220.8, 204.8, 69.9, 55.1, 52.3, 42.0, 40.6, 40.0, 37.5, 26.5, 26.4, 25.4, 23.9, 22.2, 20.8, 15.4, 11.0. **HRMS (CI)** *m/z* 278.1880 [$(M)^+$; calcd for $C_{17}H_{26}O_3$: 278.1882]

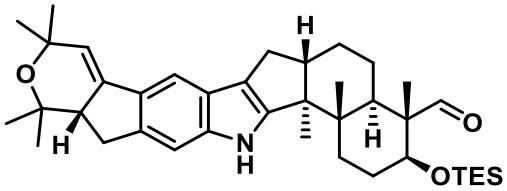


Silyl ether (−)-32: In a reaction vial, a solution of (−)-**29** (85 mg, 0.305 mmol, 1 eq.) in CH_2Cl_2 (1.5 mL) was cooled to −78 °C. This solution was treated dropwise with 2,6-lutidine (140 uL, 1.22 mmol, 4 eq.), followed by dropwise addition of TESOTf (138 uL, 0.61 mmol, 2 eq.) via a micro syringe. The resulting mixture was stirred at −78 °C for 3 minutes, quenched with NH_4Cl (saturated aqueous solution), and then diluted with Et_2O. The organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic layers were dried over $MgSO_4$ and filtered through a pad of silica gel (eluted with Et_2O). The filtrate was concentrated *in vacuo* to yield the crude product as an oil. This oil was then purified by using silica gel vacuum liquid chromatography (eluted with a gradient elution of hexanes, then 10:1 hexanes/EtOAc) to provide the title compound (122 mg, >95%) as a colorless oil. $[\alpha]_D^{25}$ −11.1 (*c* 0.7, $CHCl_3$). **IR** (neat) 2955, 2682, 1733, 1687, 1633, 1615, 1457, 1413, 1379, 1239, 1115, 1017, 975, 949, 924, 863, 822, 776, 745, 638 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.29 (s, 1H), 3.73 (d, *J* = 9.4 Hz, 1H), 2.31 (dd, *J* = 19.3, 8.5 Hz, 1H), 2.22 – 2.09 (m, 2H), 1.99 (dt, *J* = 19.2, 9.4 Hz, 1H), 1.87 – 1.60 (m, 6H), 1.61 – 1.45 (m, 2H), 1.45 – 1.27 (m, 2H), 1.05 (s, 3H), 1.00 (s, 3H), 0.96 (s, 3H), 0.91 – 0.86 (m, 9H), 0.51 (qt, *J* = 8.0, 4.1 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 220.8, 207.4, 73.9, 56.1, 56.0, 40.5, 39.8, 38.6, 37.6, 30.7, 27.2, 25.8, 24.8, 24.0, 17.8, 10.7, 9.5, 7.1, 5.4. **HRMS (CI)** *m/z* 393.2838 [$(M+H)^+$; calcd for $C_{23}H_{41}O_3Si$: 393.2825]; *m/z* 363.2358 [$(M-C_2H_5)^+$; calcd for $C_{21}H_{36}O_3Si$: 363.2355].



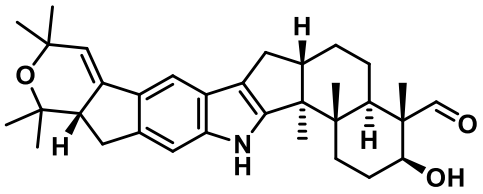
Triflate (−)-33: In a reaction vial, a solution of (−)-**32** (58 mg, 0.148 mmol, 1 eq.) in THF (4.5 mL) was cooled to −78 °C and treated dropwise with LHMDS (1.0 M in THF, 326 uL, 0.326 mmol, 2.2 eq.). The resulting pale-yellow solution was stirred at −78 °C for 15 minutes. In a separate reaction vial, $PhNTf_2$ (211 mg, 0.591 mmol, 4 eq.) was azeotroped with benzene, dissolved in THF (4.5 mL), and then added dropwise to the anion solution of (−)-**32**. The resulting mixture was stirred at −78 °C for 15 minutes, then warmed to room temperature over a period of 15 minutes and was stirred at room temperature for 1 hour to provide an orange solution. This solution was then added MeOH (1 mL), Et_3N (200 uL), DMAP (30 mg), acetone (15 mL), and stirred at room temperature for 1 hour to decompose the remaining $PhNTf_2$. This mixture was then diluted with Et_2O, washed with NH_4Cl (saturated aqueous solution), brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to yield the crude product as a pale-yellow oil. This oil was then purified by using silica gel vacuum liquid chromatography (eluted with 40:1 hexanes/EtOAc) to provide the title compound (59 mg, 76%) as a colorless oil. $[\alpha]_D^{25}$ −1.1 (*c* 3.0, $CHCl_3$). **IR** (neat) 2952, 2876, 1734, 1626, 1457, 1421, 1250, 1213, 1142, 1102, 1069, 1052, 995, 940, 921, 896, 857, 823, 807, 745 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.30 (s, 1H), 5.55 (s, 1H), 3.80 – 3.68 (m, 1H), 2.30 – 2.20 (m, 1H), 2.20 – 2.10 (m, 1H), 2.05 – 1.93 (m, 1H), 1.88 – 1.62 (m, 5H), 1.60 – 1.49 (m, 2H), 1.45 – 1.30 (m, 2H), 1.13 – 1.02 (m, 9H), 0.95 – 0.85 (m, 9H), 0.59 – 0.45 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 207.3, 158.1, 118.8 (dd, *J* = 643, 315 Hz) 114.7, 73.7, 56.2, 54.6, 43.0, 39.8, 38.5, 31.2, 30.5, 27.5, 25.5, 24.5, 18.5, 12.4, 9.3, 7.1, 5.4. **HRMS (ESI)** *m/z* 547.2116 [$(M+Na)^+$; calcd for $C_{24}H_{39}F_3O_5SSiNa$: 547.2137].

Note: Purifications of all indole-containing compounds below were carried out according to the *nitrogen-purged vacuum silica gel column chromatography proto*col (see above) unless otherwise mentioned.



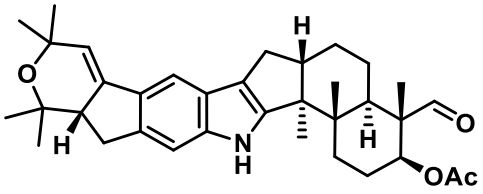
Indole (−)-34: In a 5 mL high pressure glass vial, aniline (−)-**7** (41 mg, 0.148 mmol, 1.5 eq.) and triflate (−)-**33** (52 mg, 0.099 mmol, 1 eq.) were added, followed by the addition of RuPhos Pd GIII (25 mg, 0.030 mmol, 0.3 eq.), Cs_2CO_3 (97 mg, 0.297 mmol, 3.0 eq.), and RuPhos (41 mg, 0.089 mmol, 0.9 eq.)

as solids. This mixture was then azeotroped with benzene *in vacuo*, added toluene (1 mL), and sealed with a septum cap. The vial was then backfilled with N_2 and sealed with paraffin wax. The reaction vial was then put into a preheated oil bath (70 °C). The reaction mixture was stirred vigorously at 70 °C for 24 hours, and filtered through a pad of silica gel (eluted with 5:1 hexanes/EtOAc). The filtrate was concentrated *in vacuo* to yield the crude product as a brown oil. This oil was then purified by using silica gel vacuum liquid chromatography (eluted with a gradient elution of 30:1, 20:1, 10:1, 5:1 hexanes/EtOAc) to provide the title compound (42 mg, 69%) as a white foam. $[\alpha]_D^{25}$ −10.0 (*c* 1.0, $CHCl_3$). **IR** 3407, 2934, 2875, 1726, 1457, 1377, 1362, 1248, 1110, 1038, 1001, 921, 862, 824, 750 (neat) cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.36 (s, 1H), 7.61 (s, 1H), 7.50 (s, 1H), 7.15 (s, 1H), 5.96 (d, *J* = 2.5 Hz, 2H), 3.84 (dd, *J* = 10.7, 4.0 Hz, 1H), 3.19 – 3.06 (m, 1H), 3.01 – 2.89 (m, 1H), 2.81 – 2.59 (m, 3H), 2.37 – 2.24 (m, 1H), 2.08 – 1.99 (m, 1H), 1.99 – 1.82 (m, 2H), 1.83 – 1.74 (m, 1H), 1.74 – 1.67 (m, 1H), 1.67 – 1.40 (m, 3H), 1.40 – 1.29 (m, 9H), 1.19 – 1.00 (m, 12H), 0.99 – 0.81 (m, 9H), 0.66 – 0.45 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 207.4, 193.7, 150.9, 141.6, 139.4, 138.5, 133.0, 125.1, 120.0, 118.7, 110.1, 107.8, 74.8, 73.8, 73.0, 56.3, 53.2, 48.9, 48.9, 39.6, 38.8, 33.7, 33.5, 32.3, 30.4, 30.3, 27.8, 27.6, 25.6, 25.2, 22.4, 19.1, 14.7, 9.2, 7.2, 5.4. **HRMS (ESI)** *m/z* 616.4161 [$(M+H)^+$; calcd for $C_{39}H_{58}NO_3Si$: 616.4186].

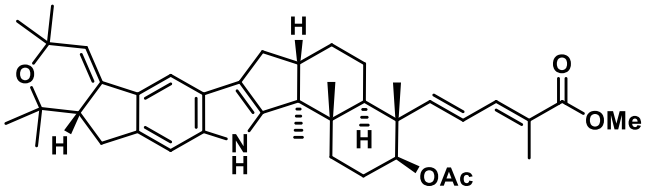


Alcohol (−)-37: In a 5 mL glass vial, (−)-**34** (42 mg, 0.068 mmol, 1 eq.) was added, and the vial was sealed with a septum cap, backfilled with N_2, and then charged with THF (680 uL), followed by the addition of TBAF (1M in THF, 102 uL, 0.102 mmol, 1.5 eq.) and H_2O (50 uL). The resulting mixture was stirred at room temperature for 10 hours and then diluted with EtOAc. The EtOAc solution was washed with H_2O, brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to yield the crude product as a pale-yellow oil. This oil was then purified by using silica gel vacuum liquid chromatography (eluted with a gradient elution of 10:1, 5:1, 2.5:1, 1:1 hexanes/EtOAc) to provide the title compound (26 mg, 76%) as a white foam. $[\alpha]_D^{25}$ −34.7 (*c* 1.1, $CHCl_3$). **IR** (neat) 3398, 2971, 2930, 2862, 1724, 1623, 1457, 1377, 1350, 1272, 1249, 1229, 1215, 1147, 1130, 1109, 1094, 1077, 1030, 986, 969, 919, 832, 755, 696, 969, 919, 832, 755, 696 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.43 (s, 1H), 7.67 (s, 1H), 7.50 (s, 1H), 7.15 (s, 1H), 5.96 (d, *J* = 2.6 Hz, 1H), 3.83 (d, *J* = 10.9 Hz, 1H), 3.18 – 3.06 (m, 1H), 2.98 – 2.88 (m, 1H), 2.80 – 2.58 (m, 3H), 2.39 – 2.27 (m, 1H), 2.15 – 1.80 (m, 4H), 1.80 – 1.70 (m, 1H), 1.70 – 1.49 (m, 2H), 1.40 – 1.29 (m, 9H), 1.28 – 1.17 (m, 3H), 1.16 – 0.99 (m, 12H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 207.0, 150.7, 141.7, 139.4, 138.5, 133.1, 125.1, 120.0, 118.7, 110.1, 107.9, 74.8, 73.0, 72.3, 55.5, 53.1, 49.0, 48.8, 40.0, 38.9, 33.7, 33.4, 32.3, 30.4, 30.3, 27.7, 26.9,

25.6, 25.2, 22.5, 19.1, 14.7, 8.7. **HRMS (ESI)** *m/z* 502.3319 [$(M+H)^+$; calcd for $C_{33}H_{44}NO_3$: 502.3321].

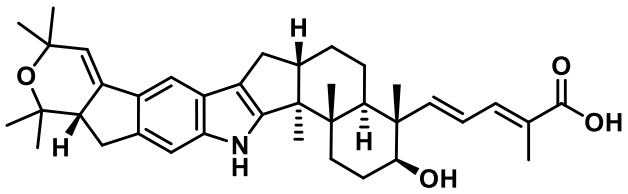


Acetate (−)-40: In a 5 mL glass vial, a solution of (−)-**37** (21 mg, 0.042 mmol, 1 eq.) in $CHCl_3$ (200 uL) was cooled to 0 °C, and DMAP (0.24 mg, 0.002 mmol, 0.05 eq.), Et_3N (23 uL, 0.168 mmol, 4 eq.), and Ac_2O (8.4 uL, 0.084 mmol, 2 eq.) were added in sequence. The resulting mixture was then warmed to room temperature and stirred for 1 hour. Another portion of Ac_2O (8.4 uL, 0.084 mmol, 2 eq.) was then added, and the resulting mixture was stirred at room temperature for 30 minutes. The solvent was removed *in vacuo*, and the resulting mixture was then purified by using silica gel vacuum liquid chromatography (eluted with a gradient elution of 5:1, 3:1, 1:1 hexanes/EtOAc) to provide the title compound (26 mg, >95%) as a pale-yellow foam. $[\alpha]_D^{25}$ −16.2 (*c* 1.3, $CHCl_3$). **IR** (neat) 3398, 2970, 2930, 2862, 1732, 1456, 1377, 1363, 1239, 1147, 1131, 1093, 1073, 1028, 990, 923, 894, 832, 756, 666 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.31 (s, 1H), 7.74 (brs, *J* = 23.2 Hz, 1H), 7.50 (s, 1H), 7.16 (s, 1H), 5.96 (d, *J* = 2.5 Hz, 1H), 5.03 (dd, *J* = 10.8, 4.2 Hz, 1H), 3.21 – 3.05 (m, 1H), 2.99 – 2.86 (m, 1H), 2.79 – 2.61 (m, 3H), 2.40 – 2.26 (m, 1H), 2.18 – 1.84 (m, 8H), 1.77 – 1.43 (m, 4H), 1.41 – 1.28 (m, 9H), 1.20 – 0.98 (m, 12H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 204.5, 170.7, 150.5, 141.7, 139.4, 138.5, 133.1, 125.0, 120.0, 118.7, 110.1, 107.9, 74.8, 73.6, 73.0, 54.5, 53.2, 49.0, 48.8, 39.7, 38.8, 33.7, 33.1, 32.3, 30.4, 30.3, 27.7, 25.4, 25.1, 23.3, 22.5, 21.4, 19.1, 14.7, 9.2. **HRMS (ESI)** *m/z* 544.3401 [$(M+H)^+$; calcd for $C_{35}H_{46}NO_4$: 544.3427].



Dienolate (−)-41: In a 5 mL high pressure glass vial, phosphonate **35**[11] (317 mg, 1.43 mmol, 30 eq.) was azeotroped with benzene, and the vial was sealed with a septum cap. THF (1.4 mL) was added and the resulting solution was cooled to −78 °C and treated dropwise with LHMDS (1.0 M in THF, 1.43 mL, 1.43 mmol, 30 eq.) to provide an orange solution. This solution was stirred at −78 °C for 5 minutes, warmed to 0 °C, and stirred at 0 °C for 15 minutes. To the resulting red solution was added (−)-**40** (26 mg, 0.048 mmol, 1 eq.) in THF (1.4 mL). The resulting solution was warmed to room temperature, stirred for 14 hours, and quenched with $NaHCO_3$ (saturated aqueous solution). This

mixture was then diluted with hexanes and filtered through a pad of silica gel (eluted with 5:1 hexanes/EtOAc). The filtrate was concentrated *in vacuo* and then purified by using silica gel vacuum liquid chromatography (eluted with a gradient elution of 10:1, 5:1, 3:1 hexanes/EtOAc) to provide the title compound (15 mg, 60%) as a pale-yellow foam. $[\alpha]_D^{25}$ −31.4 (*c* 0.2, $CHCl_3$). **IR** (neat) 3388, 2970, 2930, 2860, 1713, 1634, 1457, 1435, 1362, 1288, 1247, 1148, 1131, 1108, 1067, 1028, 992, 869, 831, 751, 736 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.49 (s, 1H), 7.19 (d, *J* = 11.2 Hz, 1H), 7.15 (s, 1H), 6.27 (dd, *J* = 15.8, 11.7 Hz, 1H), 5.96 (s, 1H), 5.82 (d, *J* = 15.4 Hz, 1H), 4.81 – 4.66 (m, 1H), 3.76 (s, 3H), 3.13 (dd, *J* = 15.8, 9.5 Hz, 1H), 3.00 – 2.88 (m, 1H), 2.82 – 2.57 (m, 3H), 2.36 – 2.23 (m, 1H), 2.13 – 1.79 (m, 9H), 1.73 (t, *J* = 14.0 Hz, 1H), 1.67 – 1.24 (m, 14H), 1.22 – 0.94 (m, 12H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.8, 169.3, 152.0, 150.9, 141.6, 139.4, 138.9, 138.4, 133.0, 125.8, 125.2, 125.1, 120.0, 118.7, 110.0, 107.8, 78.3, 74.8, 73.0, 53.5, 52.1, 49.0, 48.9, 45.8, 45.1, 39.3, 33.7, 33.4, 32.3, 30.4, 30.3, 27.7, 25.4, 24.6, 24.0, 22.5, 21.5, 19.5, 14.7, 13.1, 12.4. **HRMS (ESI)** *m/z* 662.3821 [$(M+Na)^+$; calcd for $C_{41}H_{53}NO_5Na$: 662.3821].



(−)-Nodulisporic Acid D (4): A solution of THF (2 mL), MeOH (4 mL), and LiOH (2mL, 1M aqueous solution) was purged through N_2 for 15 minutes and added to (−)-**41** (15 mg, 0.023 mmol, 1 eq.) in a 20 mL reaction vial. The resulting mixture was stirred at room temperature for 15 hours, and the organic solvent was removed *in vacuo*. The resulting aqueous mixture was then adjusted to pH=2.5 by using citric acid and extracted multiple times with CH_2Cl_2 until no product could be detected by TLC. The combined organic layers were dried over $MgSO_4$ and filtered. The filtrate was concentrated *in vacuo* and purified by high-performance liquid chromatography (detected at λ=270 nm) with a reversed-phase C18 column (VYDAC C18 monomeric, 25 mm × 10 mm, 5 μm particle size) that eluted with a linear gradient elution of 10% MeCN in H_2O (the H_2O gradient contained 0.05 M NH_4HCO_3) to 100% MeCN over 15 minutes, with the flow rate of 5 mL/minute.[12] The product containing fractions were lyophilized to provide the title compound (10 mg, 72%) as a white foam. $[\alpha]_D^{25}$ −93.2 (*c* 0.1, $CHCl_3$). **IR** (neat) 3344, 2968, 2929, 2858, 1683, 1634, 1555, 1457, 1376, 1362, 1249, 1226, 1147, 1130, 1095, 1072, 1029, 980, 831, 757, 737 cm^{-1}. **^{1}H NMR** (500 MHz, CD_3OD) δ 7.38 (s, 1H), 7.26 (d, *J* = 11.1 Hz, 1H), 7.15 (s, 1H), 6.36 (dd, *J* = 15.4, 11.3 Hz, 1H), 5.94 – 5.87 (m, 2H), 3.41 (d, *J* = 9.7 Hz, 1H), 3.08 (dd, *J* = 15.7, 9.2 Hz, 1H), 2.85 (q, *J* = 7.9 Hz, 1H), 2.67 (dd, *J* = 15.7, 7.7 Hz, 1H), 2.58 (q, *J* = 6.1 Hz, 2H), 2.24 (t, *J* = 14.1 Hz, 1H), 1.93 (s, 3H), 1.90 – 1.37 (m, 10H), 1.37 – 1.22 (m, 9H), 1.13 – 0.95 (m, 12H). **^{13}C NMR** (126 MHz, CD_3OD) δ 172.1, 155.2, 152.6, 143.6, 141.3, 140.7, 138.4, 132.6, 126.2, 126.1, 118.9, 118.1, 110.1, 108.5, 77.8, 76.2, 74.3, 54.3, 50.2,

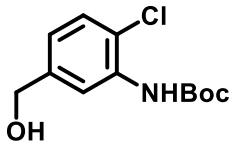
50.1, 48.1, 45.6, 40.0, 34.2, 33.6, 32.1, 30.7, 30.5, 30.1, 28.2, 27.8, 26.3, 25.7, 22.5, 19.3, 14.7, 12.8, 11.8. **HRMS (ESI)** *m/z* 584.3737 [$(M+H)^+$; calcd for $C_{38}H_{50}NO_4$: 584.3740].

^{13}C NMR shifts of (−)-nodulisporic acid D [natural (100 MHz) vs. synthetic (126 MHz)]

Atom No.	Natural[a]	Synthetic[b]	Δ δ (ppm)
1			
2	152.6	152.6	0.0
3	54.2	54.3	+0.1
4	39.9	40.0	+0.1
5	33.6	33.6	0.0
6	27.8	27.8	0.0
7	77.8	77.8	0.0
8	48.1	48.1	0.0
9	45.6	45.6	0.0
10	25.6	25.7	+0.1
11	26.4	26.3	-0.1
12	50.1	50.2	+0.1
13	28.3	28.2	-0.1
14	118.1	118.1	0.0
15	126.1	126.1	0.0
16	110.2	110.1	-0.1
17	138.3	138.4	+0.1
18	141.3	141.3	0.0
19	118.8	118.9	+0.1
20	74.3	74.3	0.0
21			
22	76.2	76.2	0.0
23	50.1	50.1	0.0
24	34.2	34.2	0.0
25	132.6	132.6	0.0
26	108.5	108.5	0.0
27	143.6	143.6	0.0
28	14.6	14.7	+0.1
29	19.3	19.3	0.0
30	11.9	11.8	-0.1
31	30.2	30.1	-0.1
32	32.2	32.1	-0.1
33	22.6	22.5	-0.1
34	30.5	30.5	0.0
1''	155.2	155.2	0.0
2''	126.1	126.1	0.0
3''	140.6	140.7	+0.1
4''	126.1	126.2	+0.1
5''	172.2	172.1	-0.1
6''	12.9	12.8	-0.1

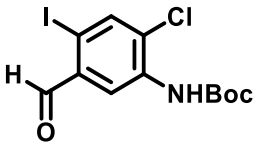
Note 1: spectra comparison was based on the publication "Singh, S. B.; Ondeyka, J. G.; Jayasuriya, H.; Zink, D. L.; Ha, S. N.; Dahl-Roshak, A.; Greene, J.; Kim, J. A.; Smith, M. M.; Shoop, W.; Tkacz, J. S. *J Nat Prod* **2004**, 67, 1496."

Note 2: ^{1}H NMR comparison of the synthetic nodulisporic acid D (**4**) with the natural nodulisporic acid D was made by spectra overlap (see spectroscopic data section).

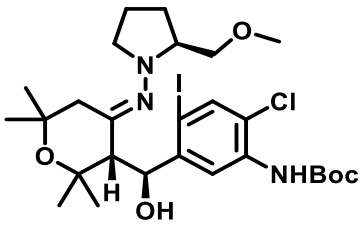


Alcohol 50: In a three-neck round-bottom flask, commercially available 3-[(*tert*-butoxycarbonyl-)amino]-4-chlorobenzoic acid (560 mg, 2.1 mmol, 1 eq.) was dissolved in THF (3 mL). The resulting solution was cooled to 0 °C. BH_3-THF (4.4 mL, 1M solution in THF, 4.4 mmol, 2.1 eq.) was then added dropwise to the solution via a plastic syringe. The reaction mixture was warmed to room temperature and stirred for 15 hours. The reaction solution was then cooled to 0 °C and quenched with MeOH (2 mL). The resulting mixture was diluted with ethyl acetate, washed with sodium hydroxide (1N, aqueous solution), dried over Na_2SO_4, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product (520 mg, >95%) as a white amorphous solid. This solid was used for the next step without further purification. **IR** (neat) 3426, 2979, 1733, 1589, 1523, 1453, 1431, 1392, 1368, 1251, 1227, 1157, 1070, 1040, 869, 812, 768, 735 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.29 (dd, *J* = 8.2, 2.5 Hz, 1H), 7.10 – 6.90 (m, 2H), 4.63 (s, 2H), 2.52 (s, 1H), 1.53 (d, *J* = 1.8 Hz, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 152.6, 141.1, 135.1, 129.1, 121.9, 120.9, 118.3, 81.4, 64.8, 28.4. **HRMS (ESI)** *m/z* 280.0729 [$(M+Na)^+$; calcd for $C_{12}H_{16}ClNNaO_3$: 280.0716].

Iodide 51: In a round-bottom flask, alcohol **50** (900 mg, 3.5 mmol, 1 eq.) was dissolved in CH_2Cl_2 (6 mL) and CH_3CN (6 mL). The resulting solution was treated with $AgNO_3$ (887 mg, 5.2 mmol, 1.5 eq.) followed by I_2 (1.1 g, 4.3 mmol, 1.2 eq.). The resulting off-white suspension was stirred at room temperature for 2 hours. This mixture was then diluted with CH_2Cl_2 and filtered. The filtrate was washed in turn with $Na_2S_2O_3$ (saturated aqueous solution) and brine, dried over Na_2SO_4, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product as a pale-yellow solid which was purified using silica gel flash chromatography (eluted with 5:1 hexanes/EtOAc) to provide the title compound (1.3 g, > 95%) as a white foam. **IR** (neat) 3422, 2977, 2929, 1736, 1573, 1501, 1444, 1390, 1368, 1254, 1226, 1155, 1044, 871, 766, 734, 689 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.66 (s, 1H), 6.93 (s, 1H), 4.64 – 4.38 (m, 2H), 3.31 (s, 1H), 1.51 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 152.3, 142.8, 138.1, 135.5, 121.3, 119.3, 87.6, 81.7, 68.7, 28.4. **HRMS (EI)** *m/z* 382.9797 [$(M)^+$; calcd for $C_{12}H_{15}ClINO_3$: 382.9785].

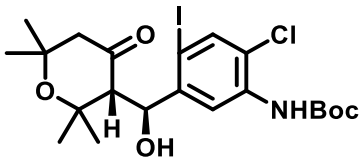


Aldehyde 52: In a round-bottom flask, activated MnO_2 powder (44 g, 506 mmol, 4.8 eq.) was heated to 150 °C under vacuum to remove moisture until formed a free-flowing powder. This flask was then cooled to room temperature and was added a solution of **51** (40 g, 104 mmol, 1 eq.) in CPME (70 mL) and cyclohexane (300 mL). The resulting black mixture was stirred at 60 °C for 15 hours and was then cooled to room temperature, filtered through Celite. The filtrate was concentrated *in vacuo* to provide the crude product as an off-white amorphous solid which was purified using silica gel flash chromatography (eluted with 20:1 hexanes/EtOAc) to provide the title compound (38 g, >95%) as an orange colored amorphous solid. **IR** (neat) 3427, 2927, 1738, 1696, 1581, 1564, 1499, 1384, 1368, 1253, 1224, 1154, 1071, 1047, 872, 768 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.90 (d, J = 1.5 Hz, 1H), 8.62 (s, 1H), 7.85 (s, 1H), 7.00 (s, 1H), 1.51 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 193.9, 151.7, 139.9, 136.4, 134.3, 128.3, 121.0, 89.9, 82.1, 28.3. **HRMS (EI)** *m/z* 280.9117 [$(M-Boc)^+$; calcd for C_7H_4ClINO: 280.9104].

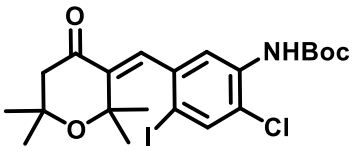


Hydrazone (+)-53: In a three-neck flask equipped with a thermometer, SAMP hydrazone (+)-**9** (2.4 g, 8.9 mmol, 2 eq.) was placed and was then added HMPA (3.1 mL) and THF (26.7 mL). The resulting solution was cooled to −78 °C and was then treated dropwise with *t*-BuLi (6.0 mL, 1.49 M in pentane, 8.9 mmol, 2 eq.) while keeping the solution temperature <−40 °C. The resulting orange colored solution was stirred at −78 °C for 2.5 hours then cooled by using a liquid N_2 bath until the solution completely frozen. A solution of aldehyde **52** (1.7 g, 4.5 mmol, 1 eq.) in THF (8 mL) was added slowly to the frozen reaction mixture at a rate such that the reaction mixture remained frozen.[13] After finishing addition, the flask was put into a liquid nitrogen/EtOH bath until the reaction mixture melted. The resulting orange solution was stirred for 3 hours at −105 °C, 2 hours at −78 °C, and was then quenched with aqueous pH 7 buffer solution, warmed to room temperature, and diluted with EtOAc. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product as a pale-yellow oil. This oil was purified using silica gel flash

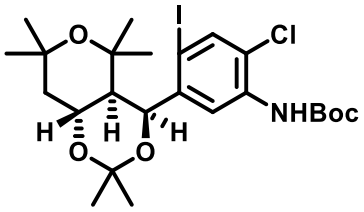
chromatography (eluted with a gradient of 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc, 6:1 hexanes/EtOAc, 3:1 hexanes/EtOAc, 1:1 hexanes/EtOAc) to provide the title compound (1.72 g, 59%) as a pale yellow-green foam. $[\alpha]_D^{25}$ +33.4 (*c* 0.2, $CHCl_3$). **IR** (neat) 3427, 2975, 2931, 1738, 1569, 1498, 1445, 1384, 1367, 1249, 1224, 1155, 1072, 1044, 1012, 872, 757 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.46 (s, 1H), 7.75 (s, 1H), 6.93 (s, 1H), 6.38 (s, 1H), 5.46 (d, *J* = 4.5 Hz, 1H), 3.62 (d, *J* = 4.6 Hz, 1H), 3.54 – 3.43 (m, 1H), 3.43 – 3.35 (m, 1H), 3.32 (s, 1H), 3.24 (s, 3H), 3.12 – 3.03 (m, 1H), 2.81 (dd, *J* = 36.3, 14.2 Hz, 1H), 2.60 (q, *J* = 8.8 Hz, 1H), 2.50 – 2.26 (m, 2H), 2.11 – 1.95 (m, 1H), 1.94 – 1.77 (m, 2H), 1.52 (s, 9H), 1.30 (d, *J* = 2.4 Hz, 3H), 1.25 (s, 3H), 1.22 (s, 3H), 1.16 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.8, 165.4, 151.7, 145.1, 138.5, 135.7, 121.5, 119.4, 90.7, 81.4, 76.2, 75.7, 75.6, 75.6, 74.3, 74.2, 73.7, 66.3, 66.1, 59.3, 58.9, 54.8, 54.3, 54.1, 45.1, 44.2, 40.4, 33.2, 32.1, 31.6, 31.3, 30.6, 30.2, 28.4, 27.8, 26.7, 26.6, 22.2, 22.1. **HRMS (ESI)** *m/z* 650.1852 [$(M+H)^+$; calcd for $C_{27}H_{42}ClIN_3O_5$: 650.1858].



Ketone (−)-54: In a round-bottom flask, hydrazone (+)-**53** (2.8 g, 4.3 mmol, 1 eq.) was dissolved in MeOH (43 mL) and was added pH 7 buffer solution (4.3 mL) followed by the addition of SeO_2 (717 mg, 6.5 mmol, 1.5 eq.). H_2O_2 (4.3 mL, 30 wt. % in H_2O) was then added slowly to the reaction mixture. The resulting mixture was stirred vigorously at room temperature for 15 hours and was then cooled to 0 °C. $NaHCO_3$ (saturated aqueous solution) was then added. The resulting mixture was diluted with Et_2O, and brine was then added. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with $Na_2S_2O_3$ (saturated aqueous solution), until a peroxide paper test indicating no peroxide was detectable (failure to remove all peroxide may result in a severe explosion upon concentration). The organic layer was washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product. The crude product was purified using silica gel vacuum chromatography (eluted with a gradient of hexanes, 50:1 hexanes/EtOAc, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc, 6:1 hexanes/EtOAc, 3:1 hexanes/EtOAc) to provide the title compound (1.32 g, 57%) as a white foam. $[\alpha]_D^{25}$ −19.0 (*c* 0.05, $CHCl_3$). **IR** (neat) 3428, 2975, 1721, 1570, 1498, 1368, 1260, 1154 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.73 (s, 1H), 6.92 (s, 1H), 5.27 (s, 1H), 3.35 (t, J = 6.2 Hz, 1H), 3.12 – 2.92 (m, 1H), 2.52 (dd, J = 13.2, 4.7 Hz, 1H), 2.42 (d, J = 13.0 Hz, 1H), 1.52 (s, 9H), 1.46 (s, 3H), 1.32 (s, 3H), 1.29 (s, 3H), 1.17 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 210.5, 152.0, 144.2, 138.7, 135.9, 121.6, 119.0, 88.6, 81.6, 80.4, 76.1, 74.5, 62.5, 53.4, 53.4, 32.8, 32.7, 30.0, 28.4, 27.1, 14.6. **HRMS (ESI)** *m/z* 536.0689 [$(M-H)^-$; calcd for $C_{21}H_{28}ClINO_5$: 536.0701].



Enone 55: was obtained as a byproduct from the above-mentioned procedure as a pale-yellow amorphous solid (670 mg, 30%). A colorless crystal (m.p.=109~110 °C) was obtained from crystallization of the pure product from hexanes. **IR** (neat) 3427, 2978, 2932, 1735, 1699, 1614, 1566, 1493, 1444, 1382, 1368, 1314, 1254, 1223, 1155, 1071, 1050, 1017, 952, 872, 795, 767, 711, 635 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.06 (d, *J* = 2.4 Hz, 1H), 7.75 (d, *J* = 2.8 Hz, 1H), 7.34 (d, *J* = 2.6 Hz, 1H), 6.95 (s, 1H), 2.60 (d, *J* = 2.6 Hz, 2H), 1.49 (s, 9H), 1.32 (s, 6H), 1.30 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 197.9, 151.8, 142.3, 141.8, 137.9, 137.7, 135.3, 121.3, 119.0, 88.3, 81.7, 75.6, 72.2, 50.6, 32.0, 29.8, 28.4, 28.4. **HRMS (ESI)** *m/z* 520.0733 [$(M+H)^+$; calcd for $C_{21}H_{28}ClINO_4$: 520.0752].

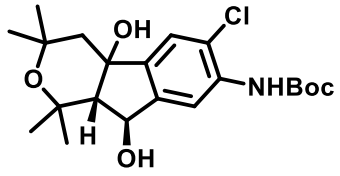


Acetal (−)-56:

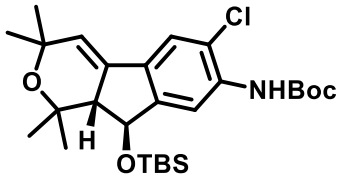
In a reaction vial, ketone (−)-**54** (40 mg, 0.074 mmol, 1 eq.) was dissolved in THF (1 mL), and the resulting solution was cooled to 0 °C. Pinacolborane (55 μL, 0.38 mmol, 5 eq.) was added to the solution, and the resulting solution was stirred at 0 °C for 2.5 hours and at room temperature overnight. $NaHCO_3$ (saturated aqueous solution) was then added, followed by diluting the mixture with Et_2O. The organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered through a silica pad. The filtrate was concentrated *in vacuo* to provide the crude product which was used for the next stage without further purification.

The crude product from the last stage was dissolved in CH_2Cl_2 (2 mL), and 2,2-dimethoxypropane (830 μL, 6.73 mmol, 91 eq.) and PPTS (13.3 mg, 0.053 mmol, 0.7 eq.) were added. The resulting solution was stirred at room temperature for 4 hours and was then diluted with Et_2O and added $NaHCO_3$ (saturated aqueous solution). The organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered through a silica pad. The filtrate was concentrated *in vacuo* to provide the crude product which was purified by silica gel vacuum chromatography (eluted with a gradient of hexanes, 50:1 hexanes/EtOAc, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc, 6:1 hexanes/EtOAc, 3:1 hexanes/EtOAc) to provide the title compound (28 mg, 65% over the 2 steps) as a colorless oil. $[\alpha]_D^{25}$ −25.2 (*c* 0.1, $CHCl_3$). **IR** (neat) 3427, 2979, 2934, 1739, 1570, 1499, 1445, 1390, 1368, 1313, 1224, 1175, 1155,

1123, 1073, 1046, 1010, 979, 897, 873, 825, 757 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.72 (s, 1H), 6.90 (s, 1H), 5.24 (d, *J* = 8.1 Hz, 1H), 4.36 (ddd, *J* = 14.5, 11.0, 3.8 Hz, 1H), 2.46 (dd, *J* = 10.6, 8.1 Hz, 1H), 1.91 (dd, *J* = 11.8, 3.8 Hz, 1H), 1.72 (t, *J* = 12.0 Hz, 1H), 1.54 (s, 9H), 1.43 (d, *J* = 4.0 Hz, 3H), 1.34 (s, 3H), 1.29 (s, 3H), 1.25 (s, 6H), 0.70 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 151.9, 142.3, 137.6, 135.3, 121.5, 120.4, 102.6, 90.3, 82.8, 81.5, 74.4, 73.4, 64.6, 55.4, 44.5, 34.1, 30.8, 29.9, 29.3, 28.4, 24.9, 24.9, 24.7, 23.6. **HRMS (EI)** *m/z* 579.1277 [$(M)^+$; calcd for $C_{24}H_{35}ClINO_5$: 579.1248].

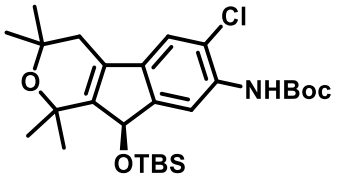


Diol (+)-57: In a reaction vial, $NiCl_2$ (7.5 mg, 0.058 mmol, 0.2 eq.) and $CrCl_2$ (177 mg, 1.44 mmol, 5 eq.) were heated under high vacuum until a grey-colored free-flowing powder was formed. The reaction vial was back filled with argon, and ketone (−)-**54** (155 mg, 0.29 mmol, 1 eq.) was added as a solution in anhydrous DMF (1.44 mL, degassed by using freeze-pump-thaw technique). The resulting dark-green mixture was stirred vigorously at room temperature for 19 hours and was then quenched with aqueous pH 7 buffer. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product. The crude product was used directly for the next step without further purification. The crude product can be purified using silica gel vacuum chromatography[14] (eluted with a gradient of 3:1 hexanes/EtOAc, 1:1 hexanes/EtOAc, 1:2 hexanes/EtOAc; each elution solvent systems contained 0.5% Et_3N) to provide the title compound (94 mg, 79%) as an oil. $[\alpha]_D^{25}$ +5.1 (*c* 0.1, $CHCl_3$). **IR** (neat) 3427, 2974, 1733, 1666, 1590, 1516, 1367, 1237, 1156, 1062, 1023, 880, 801 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.33 (s, 1H), 7.07 (s, 1H), 4.88 (d, *J* = 4.6 Hz, 1H), 2.88 (brs, 1H), 2.20 (d, *J* = 14.7 Hz, 1H), 2.16 (d, *J* = 4.8 Hz, 1H), 1.71 (d, *J* = 14.7 Hz, 1H), 1.56 (s, 9H), 1.49 (s, 3H), 1.41 (s, 3H), 1.21 (d, *J* = 6.8 Hz, 1H), 1.17 (s, 3H), 1.01 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.9, 152.6, 144.4, 142.3, 135.1, 123.2, 123.0, 116.1, 81.3, 74.5, 72.7, 70.9, 64.6, 44.8, 36.7, 32.8, 31.6, 31.2, 30.9, 29.0, 28.4. **HRMS (ESI)** *m/z* 410.1715 [$(M-H)^-$; calcd for $C_{21}H_{29}ClNO_5$: 410.1734].

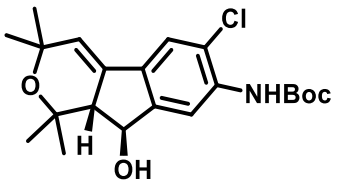


Olefin (−)-58: In a round-bottom flask, diol (+)-**57** (600 mg, 1.46 mmol, 1 eq.) was added CH_2Cl_2 (15 mL), 2,6-lutidine (678 μL, 5.82 mmol, 4 eq.), and the resulting solution was cooled to −78 °C. TBSOTf (669 μL, 2.9 mmol, 2 eq.) was added dropwise to the solution at −78 °C, and the resulting solution was stirred at −78 °C for 2 hours and was then poured into $NaHCO_3$ (saturated aqueous solution) and diluted with Et_2O. The organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered through Celite. The filtrate was concentrated *in vacuo* to provide the crude product which was used for the next step without further purification.

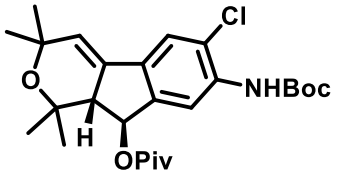
To the crude product in a round-bottom flask was added DMAP (180 mg, 1.47 mmol, 1 eq.) and pyridine (14.6 mL). The resulting solution was cooled to 0 °C, and MsCl (1.1 mL, 14.6 mmol, 10 eq.) was then added dropwise. The resulting mixture was warmed to room temperature and stirred at room temperature for 19 hours and was then poured into $NaHCO_3$ (saturated aqueous solution) and diluted with EtOAc. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product. The crude product was purified using silica gel vacuum chromatography (eluted with a gradient of hexanes, 100:1 hexanes/EtOAc, 50:1 hexanes/EtOAc, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc) to provide the title compound (304 mg, 41% over the two steps) as an oil. $[\alpha]_D^{25}$ −25.7 (*c* 0.1, $CHCl_3$). **IR** (neat) 3356, 2967, 2929, 2857, 1620, 1473, 1433, 1343, 1243, 1135, 1087, 1008, 837, 774, 674 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.41 (s, 1H), 7.03 (s, 1H), 5.93 (d, *J* = 3.0 Hz, 1H), 4.97 (d, *J* = 5.5 Hz, 1H), 2.78 (dd, *J* = 5.6, 2.9 Hz, 1H), 1.54 (s, 9H), 1.45 (s, 3H), 1.33 (s, 3H), 1.32 (s, 3H), 1.08 (s, 3H), 0.95 (s, 9H), 0.31 (s, 3H), 0.19 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 152.1, 146.0, 135.2, 134.1, 133.5, 122.7, 122.5, 120.8, 116.3, 81.0, 74.0, 72.3, 58.9, 31.9, 30.5, 29.8, 28.4, 26.1, 23.3, 18.2, -2.6, -3.6. **HRMS (ESI)** *m/z* 530.2480 [$(M+Na)^+$; calcd for $C_{27}H_{42}ClNNaO_4Si$: 530.2469].



Olefin (−)-59: was obtained as a byproduct from the procedure mentioned above as an oil (70 mg, 10% over the two steps). $[\alpha]_D^{25}$ +54.6 (*c* 0.1, $CHCl_3$). **IR** (neat) 3430, 2930, 1736, 1588, 1505, 1415, 1367, 1335, 1237, 1158, 1061, 1005, 838, 774 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.35 (s, 1H), 7.03 (s, 1H), 6.93 (s, 1H), 5.26 (t, *J* = 2.3 Hz, 1H), 2.30 (qd, *J* = 16.0, 2.2 Hz, 2H), 1.54 (s, 9H), 1.52 (s, 3H), 1.45 (s, 3H), 1.36 (s, 3H), 1.24 (s, 3H), 0.95 (s, 9H), 0.39 (s, 3H), 0.29 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 152.2, 146.4, 145.2, 138.1, 132.8, 131.8, 121.3, 118.6, 116.1, 80.8, 73.7, 71.1, 34.3, 30.1, 30.1, 29.7, 29.3, 28.4, 26.1, 18.3, -3.0, -3.5. **HRMS (ESI)** *m/z* 530.2461 [$(M+Na)^+$; calcd for $C_{27}H_{42}ClNNaO_4Si$: 530.2469].

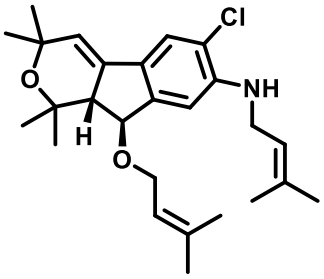


Alcohol (−)-48: In a plastic reaction vial, carbamate olefin (−)-**58** (600 mg, 1.18 mmol, 1 eq.) was dissolved in CH_2Cl_2 (12 mL) and MeCN (12 mL). The resulting solution was cooled to 0 °C, and HF (8.8 mL, 48 wt. % in H_2O) was then added dropwise. The resulting mixture was stirred at 0 °C for 2.5 hours and then poured into $NaHCO_3$ (saturated aqueous solution). The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product. The crude product was purified using silica gel vacuum chromatography (eluted with a gradient of hexanes, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc, 6:1 hexanes/EtOAc, 3:1 hexanes/EtOAc) to provide the title compound (353 mg, 76%) as a pale-green foam. $[\alpha]_D^{25}$ −51.9 (*c* 0.1, $CHCl_3$). **IR** (neat) 3422, 2975, 1738, 1584, 1508, 1367, 1241, 1156, 1064, 756 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.40 (s, 1H), 7.06 (s, 1H), 5.92 (d, *J* = 2.9 Hz, 1H), 4.82 (d, *J* = 5.9 Hz, 1H), 2.72 (s, 1H), 2.64 (dd, *J* = 5.9, 2.9 Hz, 1H), 1.52 (s, 9H), 1.43 (s, 3H), 1.32 (s, 3H), 1.30 (s, 3H), 1.05 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 152.5, 145.7, 135.2, 133.7, 133.7, 123.2, 123.1, 121.1, 116.0, 81.5, 76.3, 73.8, 72.5, 59.1, 31.8, 30.0, 29.7, 28.4, 23.1. **HRMS (ESI)** *m/z* 392.1618 [$(M-H)^-$; calcd for $C_{21}H_{27}ClNO_4$: 392.1629].



Pivalate (−)-60: In reaction vial containing alcohol (−)-**48** (67 mg, 0.17 mmol, 1 eq.) was added DMAP (55 mg, 0.45 mmol, 2.6 eq.) and CH_2Cl_2 (1.5 mL). The resulting solution was cooled to −78 °C. PivCl (22 μL, 0.19 mmol, 1.1 eq.) was added to the solution, and the resulting solution was warned from −78 °C to room temperature over a period of 2 hours and was then stirred at room temperature for 0.5 hour. $NaHCO_3$ (saturated aqueous solution) was added. The organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product. The crude product was purified using silica gel vacuum chromatography (eluted with a gradient of hexanes, 50:1 hexanes/EtOAc, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc, 6:1 hexanes/EtOAc, 3:1 hexanes/EtOAc) to provide the title compound (60 mg, 84%) as a white amorphous solid. This solid was crystalized from hexanes to provide colorless needles (m.p.=158~160 °C). $[\alpha]_D^{25}$ −54.2 (*c* 0.2, $CHCl_3$). **IR** (neat) 3429, 2975, 2932, 1734, 1611, 1582, 1508, 1480, 1460, 1422, 1394, 1367, 1339, 1281, 1241,

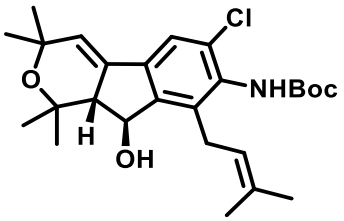
1225, 1154, 1061, 1034, 1000, 939, 876, 843, 768, 739 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.44 (s, 1H), 7.01 (s, 1H), 6.18 (d, *J* = 6.1 Hz, 1H), 5.98 (d, *J* = 2.9 Hz, 1H), 2.88 (dd, *J* = 6.1, 2.9 Hz, 1H), 1.52 (s, 9H), 1.34 (s, 3H), 1.32 (s, 3H), 1.28 (s, 9H), 1.26 (s, 3H), 1.16 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 178.4, 152.0, 142.4, 135.6, 134.0, 133.3, 123.5, 123.4, 121.1, 116.0, 81.3, 76.0, 73.6, 72.6, 55.8, 38.8, 31.8, 29.8, 29.6, 28.4, 27.2, 26.6, 22.9. **HRMS (ESI)** *m/z* 500.2199 [$(M+Na)^+$; calcd for $C_{26}H_{36}ClNO_5Na$: 500.2180].



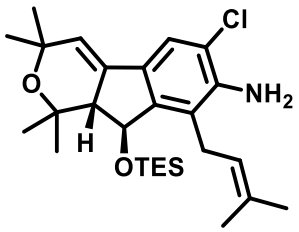
Amine (−)-**63**: In a 5-mL reaction vial, alcohol (−)-**48** (33 mg, 0.084 mmol, 1 eq.) was azeotroped with toluene, and CPME (840 μL) was then added followed by HMPA (42 μL). The resulting solution was cooled to −78 °C and was then treated dropwise with *t*-BuLi solution (1.55 M in pentane, 325 μL, 0.504 mmol, 6 eq.) to provide a dark red solution. This solution was warmed to −15 °C and stirred at −15 °C for 3 hours. The resulting red solution was cooled to −78 °C, and THF (840 μL) was then added followed by the addition of prenyl bromide (145 μL, 1.26 mmol, 15 eq.). The resulting solution was warmed from −78 °C to room temperature over a period of 1.5 hours and was then quenched with $NaHCO_3$ (saturated aqueous solution). The organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product. The crude product was purified using silica gel vacuum chromatography (eluted with a gradient of hexanes, 50:1 hexanes/EtOAc, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc, 6:1 hexanes/EtOAc, 3:1 hexanes/EtOAc) to provide the crude product.

The crude product from the last stage was dissolved in CH_2Cl_2 (1 mL) and cooled to 0 °C. 2,6-lutidine (144 μL, 1.24 mmol, 15 eq.) was added to the solution followed by the addition of TMSOTf (90 μL, 0.5 mmol, 6 eq.). The resulting solution was stirred at 0 °C for 1 hour and was then diluted with hexanes and filtered through a silica pad. The filtrate was concentrated *in vacuo* to provide the crude product as an oil. This oil was purified using silica gel vacuum chromatography (eluted with a gradient of hexanes, 50:1 hexanes/EtOAc, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc, 6:1 hexanes/EtOAc, 3:1 hexanes/EtOAc) to provide the title compound (18 mg, 49% over the 2 steps) as an oil. $[\alpha]_D^{25}$ −140.0 (*c* 0.3, $CHCl_3$). **IR** (neat) 3424, 2972, 2928, 1706, 1676, 1606, 1573, 1501, 1425, 1376, 1363, 1337, 1298, 1245, 1185, 1136, 1074, 1010, 986, 881, 835, 782, 700 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.37 (s, 1H), 6.71 (s, 1H), 5.78 (d, *J* = 2.7 Hz, 1H), 5.49 – 5.39 (m, 1H), 5.40 – 5.32 (m, 1H), 4.80 (d, *J* = 5.9 Hz, 1H), 4.40 (s, 1H), 4.14 (dd, *J* = 11.1, 7.1 Hz, 1H), 4.04 (dd, *J* = 10.9, 7.2 Hz, 1H), 3.77 (t, *J* =

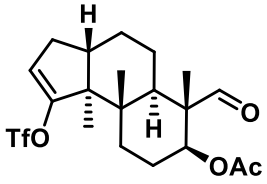
5.8 Hz, 2H), 2.88 (dd, *J* = 6.0, 2.8 Hz, 1H), 1.78 (s, 6H), 1.75 (s, 3H), 1.70 (s, 3H), 1.46 (s, 3H), 1.32 (s, 6H), 1.09 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 144.5, 144.1, 137.3, 136.5, 134.3, 128.5, 121.4, 121.4, 121.0, 120.5, 120.1, 106.7, 83.0, 74.0, 72.6, 63.5, 53.8, 42.0, 32.0, 30.1, 30.0, 26.0, 25.8, 23.1, 18.2, 18.2. **HRMS (ESI)** *m/z* 452.2356 [$(M+Na)^+$; calcd for $C_{26}H_{36}ClNNaO_2$: 452.2332].



Alcohol (−)-64: In a 5-mL reaction vial, alcohol (−)-**48** (130 mg, 0.33 mmol, 1 eq.) was azeotroped with toluene, and CPME (3.3 mL) was then added followed by HMPA (165 μL). The resulting solution was cooled to −78 °C and was then treated dropwise with *t*-BuLi solution (1.47 M in pentane, 1.35 mL, 1.98 mmol, 6 eq.) to provide a dark red solution.[15] This solution was warmed to −40 °C and stirred for 3 hours. During this period, CuCN (177 mg, 1.98 mmol, 6 eq.) was added to a 20-mL reaction vial and was heated to 120 °C under high vacuum for 2.5 hours. This vial was backed filled with nitrogen multiple times, and THF (3.3 mL) was added. The CuCN/THF mixture was cooled to −78 °C. The red anion solution was cannulated to the slurry of CuCN/THF, and the resulting brown slurry was stirred at −13 °C for 1 hour. The reaction vial was then cooled to −78 °C, and prenyl bromide (572 μL, 4.95 mmol, 15 eq.) was added dropwise. The resulting dark brown mixture was stirred at −78 °C for 1 hour, −40 °C for 1 hour, −15 °C for 1h, and was then quenched with $NaHCO_3$ (saturated aqueous solution) followed by the addition of ammonium hydroxide solution (30-32%). The resulting mixture was warmed to room temperature and stirred for 0.5 hour until all copper salts dissolved. This mixture was then diluted with EtOAc. The organic layer was separated, and the aqueous layer was extracted with EtOAc. After the extraction, the aqueous layer was added $KMnO_4$ before discard. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product as a brown-colored oil. This oil was purified using silica gel vacuum chromatography (eluted with a gradient of 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc, 6:1 hexanes/EtOAc, 3:1 hexanes/EtOAc) to provide the title compound (110 mg, 72%) as a white foam.[16] $[\alpha]_D^{25}$ −55.4 (*c* 0.3, $CHCl_3$). **IR** (neat) 3426, 2975, 2930, 1738, 1609, 1582, 1506, 1418, 1392, 1367, 1241, 1157, 1063, 1008, 986, 923, 884, 842, 768, 739, 703 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.40 (s, 1H), 6.09 (s, 1H), 6.00 (d, *J* = 2.9 Hz, 1H), 5.16 – 5.01 (m, 1H), 4.93 (s, 1H), 3.66 (dd, *J* = 15.1, 7.3 Hz, 1H), 3.46 (dd, *J* = 15.1, 6.0 Hz, 1H), 2.65 (t, *J* = 3.9 Hz, 1H), 2.26 (s, 1H), 1.80 (s, 3H), 1.71 (s, 3H), 1.50 (s, 9H), 1.46 (s, 3H), 1.33 (s, 6H), 1.04 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 134.0, 124.5, 119.4, 76.3, 73.8, 72.6, 59.4, 31.7, 29.9, 29.8, 29.7, 28.4, 28.2, 25.8, 22.9, 18.1. **HRMS (ESI)** *m/z* 484.2212 [$(M+Na)^+$; calcd for $C_{26}H_{36}ClNNaO_4$: 484.2231].



Aniline (–)-46: In a 5-mL reaction vial, alcohol (–)-**64** (50 mg, 0.11 mmol, 1 eq.) was treated with CH_2Cl_2 (1.4 mL) and 2,6-lutidine (314 μL, 2.7 mmol, 25 eq.). The resulting solution was cooled to −78 °C, and TESOTf (120 μL, 0.53 mmol, 4.8 eq.) was added. This solution was warmed to 0 °C and stirred at 0 °C for 1 hour. TMSOTf (98 μL, 0.54 mmol, 4.9 eq.) was added to the reaction solution at 0 °C, and the solution was stirred at 0 °C for an additional 30 minutes. Hexanes were then added to the reaction solution, and the resulting mixture was filtered through a silica pad, washed with Et_2O. The filtrate was concentrated *in vacuo* to provide the crude product as a pale-yellow oil. This oil was purified by silica gel vacuum chromatography (eluted with a gradient of hexanes, 50:1 hexanes/EtOAc, 25:1 hexanes/EtOAc, 6:1 hexanes/EtOAc) to provide the title compound (52 mg, > 95%) as a colorless oil. $[\alpha]_D^{25}$ −23.3 (*c* 0.1, $CHCl_3$). **IR** (neat) 3467, 3376, 2968, 2913, 2876, 1674, 1615, 1457, 1377, 1363, 1342, 1243, 1153, 1141, 1089, 1009, 986, 828, 778, 740, 683 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29 (s, 1H), 5.81 (d, *J* = 2.7 Hz, 1H), 5.10 (d, *J* = 3.9 Hz, 1H), 5.05 (t, *J* = 6.5 Hz, 1H), 4.20 (s, 2H), 3.71 (dd, *J* = 16.3, 5.8 Hz, 1H), 3.32 (dd, *J* = 16.1, 6.9 Hz, 1H), 2.73 (t, *J* = 3.3 Hz, 1H), 1.82 (s, 3H), 1.74 (d, *J* = 1.7 Hz, 3H), 1.47 (s, 3H), 1.34 (s, 3H), 1.30 (s, 3H), 0.94 (s, 3H), 0.87 (t, *J* = 7.9 Hz, 9H), 0.52 (q, *J* = 7.9 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 143.5, 142.3, 135.6, 134.4, 130.3, 124.6, 121.6, 121.4, 120.6, 119.0, 77.6, 74.4, 72.8, 58.0, 31.8, 30.1, 29.9, 27.3, 25.7, 22.2, 18.1, 7.1, 6.4. **HRMS (EI)** *m/z* 475.2675 [$(M)^+$; calcd for $C_{27}H_{42}ClNO_2Si$: 475.2673].

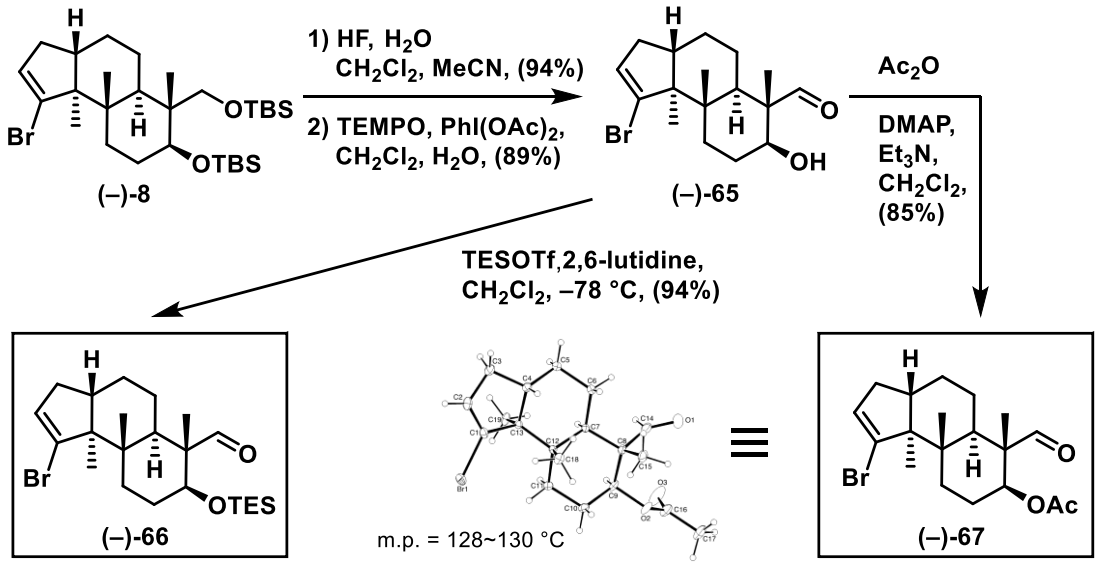


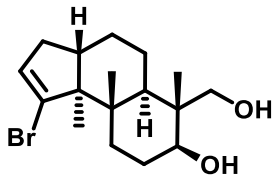
Triflate (–)-47: In a round bottom flask, THF (1 mL) was added to triflate (–)-**33** (52 mg, 0.1 mmol, 1 eq.), and TBAF (1M in THF, 200 uL, 0.2 mmol, 2 eq.) was then added. The resulting solution was stirred at room temperature for 2 hours. The solvent was then removed under vacuum, and the residual was added CH_2Cl_2 (1 mL), Et_3N (138 uL, 1 mmol, 10 eq.), DMAP (1.2 mg, 0.01 mmol, 0.1 eq.), and Ac_2O (47 uL, 0.5 mmol, 5 eq.). The resulting mixture was stirred at room temperature for 2 hours and was quenched with $NaHCO_3$ (saturated aqueous solution). The organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product as a pale-yellow oil. This oil was purified using silica gel vacuum chromatography (eluted with a gradient 25:1

hexanes/EtOAc, 13:1 hexanes/EtOAc, 6:1 hexanes/EtOAc, 3:1 hexanes/EtOAc) to provide the title compound (36 mg, 80%) as a white amorphous solid. $[\alpha]_D^{25}$ −41.9 (*c* 0.1, $CHCl_3$). **IR** (neat) 2947, 1736, 1627, 1420, 1382, 1215, 1142, 1051, 1031, 997, 941, 893, 863, 831, 807, 766 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.26 (s, 1H), 5.59 (s, 1H), 4.95 (dd, *J* = 11.1, 5.1 Hz, 1H), 2.26 (d, *J* = 10.1 Hz, 1H), 2.20 (ddd, *J* = 14.7, 6.4, 3.2 Hz, 1H), 2.08 – 2.02 (m, 1H), 1.98 (s, 3H), 1.83 (ddd, *J* = 23.9, 10.1, 4.3 Hz, 3H), 1.77 – 1.69 (m, 3H), 1.61 (d, *J* = 8.4 Hz, 1H), 1.43 (p, *J* = 12.1 Hz, 2H), 1.14 (s, 3H), 1.13 (s, 3H), 1.11 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 141.2, 129.2, 77.4, 72.2, 64.4, 55.2, 44.1, 43.8, 38.2, 36.9, 34.3, 31.6, 28.0, 26.1, 26.1, 24.9, 22.9, 18.3, 18.1, 13.8, 12.3, -3.4, -4.8, -5.1, -5.6. **HRMS (EI)** *m/z* 452.1460 [$(M)^+$; calcd for $C_{20}H_{27}F_3O_6S$: 452.1480].

Note: Bromide variants of the eastern hemisphere were also prepared for investigation of the union reaction.

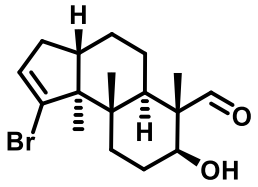
Scheme S1. Synthesis of the Bromide Eastern Hemisphere



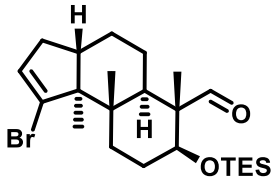


Diol (−)-S8: In a 500-mL plastic reaction flask, bromide (−)-**8** (1.58 g, 2.76 mmol, 1 eq.) was dissolved in CH_2Cl_2 (23 mL) and MeCN (23 mL). The resulting solution was cooled to 0 °C, and HF (16.6 mL, 48 wt. % in H_2O) was then added dropwise. The resulting mixture was warmed to room temperature and stirred vigorously for 2 hours and was then diluted with EtOAc (200 mL). Sodium hydroxide (180 mL, 3N, aqueous solution) was added slowly to neutralize HF until the red litmus test paper showed a

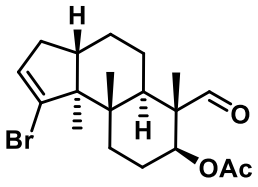
blue color. The organic layer was separated, and the aqueous layer was extracted five times with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product as an off-white colored amorphous solid (890 mg, 94%). This solid was used for the next step without further purification. $[\alpha]_D^{25}$ −13.0 (*c* 1.3, $CDCl_3$). **IR** (neat) 3356, 2936, 1586, 1450, 1378, 1079, 1040, 999, 975, 911, 804, 734 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.82 (dd, *J* = 3.2, 1.8 Hz, 1H), 3.69 (d, *J* = 10.4 Hz, 1H), 3.66 – 3.54 (m, 1H), 3.40 (d, *J* = 10.4 Hz, 1H), 2.69 (t, *J* = 8.1 Hz, 1H), 2.55 (s, 1H), 2.36 (dt, *J* = 13.5, 3.6 Hz, 1H), 2.31 – 2.21 (m, 1H), 2.06 (ddd, *J* = 15.0, 6.6, 3.1 Hz, 1H), 1.87 (ddd, *J* = 15.0, 11.2, 1.8 Hz, 1H), 1.75 – 1.63 (m, 2H), 1.61 – 1.46 (m, 3H), 1.43 – 1.29 (m, 3H), 1.12 (s, 3H), 0.95 (s, 3H), 0.88 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 133.1, 132.7, 76.0, 71.3, 57.4, 44.0, 42.7, 41.4, 40.1, 33.8, 30.4, 27.3, 25.2, 23.2, 17.9, 12.7, 11.2. **HRMS (ESI)** *m/z* 365.1198 [$(M+Na)^+$; calcd for $C_{17}H_{27}BrNaO_2$: 365.1092].



Aldehyde (−)-65: In a 100-mL round-bottom flask, diol (−)-**S8** (890 mg, 2.59 mmol, 1 eq.) was dissolved in CH_2Cl_2 (16.6 mL) and was then added H_2O (16.6 mL). To the resulting biphasic mixture was added a solid mixture of TEMPO (445 mg, 2.85 mmol, 1.1 eq.) and $PhI(OAc)_2$ (1.25 g, 3.88 mmol, 1.5 eq.) in one portion. The resulting mixture was stirred vigorously at room temperature for 2.5 hours and was then diluted with EtOAc. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product as an orange-colored oil. This oil was purified using silica gel vacuum chromatography (eluted with a gradient of hexanes, 6:1 hexanes/EtOAc, 3:1 hexanes/EtOAc, 1:1 hexanes/EtOAc) to provide the title compound (783 mg, 89%) as a colorless oil. $[\alpha]_D^{25}$ −28.0 (*c* 2.2, $CDCl_3$). **IR** (neat) 3437, 2938, 2864, 1725, 1587, 1449, 1379, 1266, 1082, 1036, 1001, 976, 914, 864, 805, 733 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.37 (s, 1H), 5.84 (dd, *J* = 3.1, 1.8 Hz, 1H), 3.74 (dd, *J* = 11.5, 4.8 Hz, 1H), 2.41 (dt, *J* = 13.7, 3.5 Hz, 1H), 2.26 (dddd, *J* = 12.6, 10.9, 6.6, 2.9 Hz, 1H), 2.08 (ddd, *J* = 15.0, 6.6, 3.1 Hz, 1H), 1.94 – 1.86 (m, 2H), 1.85 – 1.78 (m, 1H), 1.73 (ddd, *J* = 13.1, 3.6, 1.6 Hz, 1H), 1.68 – 1.61 (m, 1H), 1.56 (td, *J* = 13.4, 3.8 Hz, 1H), 1.51 – 1.39 (m, 2H), 1.29 – 1.23 (m, 1H), 1.19 (s, 1H), 1.13 (d, *J* = 0.9 Hz, 3H), 1.09 (s, 3H), 1.00 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ206.7, 132.7, 71.9, 57.2, 55.6, 44.2, 40.5, 39.3, 33.8, 30.3, 26.6, 25.8, 25.0, 17.7, 12.7, 8.4. **HRMS (ESI)** *m/z* 363.0947 [$(M+Na)^+$; calcd for $C_{17}H_{25}BrNaO_2$: 363.0936].

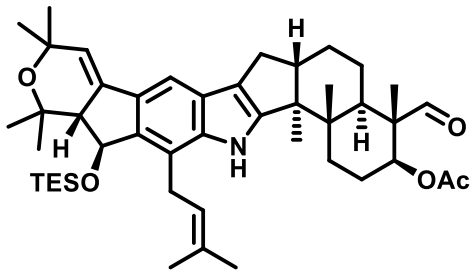


Bromide (−)-**66**: In a round bottom flask, aldehyde (−)-**65** (874 mg, 2.56 mmol, 1 eq.) was added CH_2Cl_2 (13 mL) and 2,6-lutidine (1.2 mL, 10.3 mmol, 4 eq.). The resulting solution was cooled to −78 °C and was added dropwise with TESOTf (1.16 mL, 5.1 mmol, 2 eq.). The reaction was stirred at −78 °C for 20 minutes and was then quenched with $NaHCO_3$ (saturated aqueous solution). The organic layer was separated, and the aqueous layer was extracted with hexanes. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product as a colorless oil. This oil was purified using silica gel vacuum chromatography (eluted with a gradient of hexanes, 50:1 hexanes/EtOAc, 13:1 hexanes/EtOAc) to provide the title compound (1.12 g, 96%) as a colorless solid after placed under high vacuum overnight. $[\alpha]_D^{25}$ −46.2 (*c* 0.3, $CHCl_3$). **IR** (neat) 2951, 2875, 2674, 1732, 1596, 1456, 1414, 1379, 1238, 1100, 1067, 1047, 1015, 986, 970, 931, 861, 822, 777, 747, 726, 698, 607 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.30 (s, 1H), 5.83 (dd, *J* = 3.1, 1.9 Hz, 1H), 3.75 (dd, *J* = 11.1, 5.0 Hz, 1H), 2.36 (dt, *J* = 13.7, 3.6 Hz, 1H), 2.30 – 2.20 (m, 1H), 2.06 (ddd, *J* = 15.0, 6.6, 3.1 Hz, 1H), 1.95 – 1.81 (m, 2H), 1.79 – 1.65 (m, 2H), 1.60 (dq, *J* = 8.9, 3.5, 3.0 Hz, 1H), 1.51 (td, *J* = 13.4, 4.0 Hz, 1H), 1.40 (tdd, *J* = 14.2, 7.2, 3.8 Hz, 3H), 1.11 (s, 3H), 1.08 (s, 3H), 1.00 (s, 3H), 0.91 (t, *J* = 7.9 Hz, 9H), 0.53 (qd, *J* = 7.9, 3.7 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 207.1, 132.6, 73.5, 57.3, 56.3, 44.2, 40.2, 39.2, 33.8, 30.4, 27.3, 25.7, 25.1, 17.7, 12.7, 9.0, 6.9, 5.2. **HRMS (CI)** *m/z* 425.1541 [$(M-C_2H_5)^+$; calcd for $C_{21}H_{34}BrO_2Si$: 425.1506].



Bromide (−)-67: In a 10-mL reaction flask containing aldehyde (−)-**65** (341 mg, 1 mmol, 1 eq.) and DMAP (12.2 mg, 0.1 mmol, 0.1 eq.), CH_2Cl_2 (2.5 mL) was added. Et_3N (553 μL, 4 mmol, 4 eq.) was added to the solution followed by the addition of Ac_2O (189 μL, 2 mmol, 2 eq.). The resulting solution was stirred at room temperature for 0.5 hour, and the solvent was remove by flushing with nitrogen gas. The resulting solid was purified using silica gel vacuum chromatography (eluted with a gradient of hexanes, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc, 6:1 hexanes/EtOAc, 3:1 hexanes/EtOAc) to provide the title compound (325 mg, 85%) as a white amorphous solid. An aliquot was recrystallized from hexane/ethyl acetate (1:1) to yield colorless needles (m.p.=128~130 °C). $[\alpha]_D^{25}$ −14.2 (*c* 0.2, $CHCl_3$). **IR** (neat) 2933, 1736, 1587, 1451, 1420, 1379, 1240, 1142, 1076, 1030, 974, 930, 896, 867,

804 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.25 (s, 1H), 5.84 (dd, *J* = 3.1, 1.7 Hz, 1H), 4.94 (dd, *J* = 11.4, 5.1 Hz, 1H), 2.44 (dd, *J* = 13.6, 3.4 Hz, 1H), 2.25 (s, 1H), 2.13 – 2.04 (m, 1H), 2.02 – 1.94 (m, 5H), 1.94 – 1.72 (m, 3H), 1.65 (td, *J* = 11.4, 9.2, 3.8 Hz, 2H), 1.51 – 1.36 (m, 2H), 1.14 (s, 3H), 1.10 (s, 3H), 1.01 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 204.1, 170.3, 132.8, 132.3, 73.2, 57.2, 54.6, 44.2, 40.3, 39.2, 33.7, 30.2, 25.5, 24.9, 23.0, 21.1, 17.7, 12.7, 9.0. **HRMS (ESI)** *m/z* 405.1039 [$(M+Na)^+$; calcd for $C_{19}H_{27}BrNaO_3$: 405.1041].



Indole (+)-72:

Method 1: using triflate (−)-47

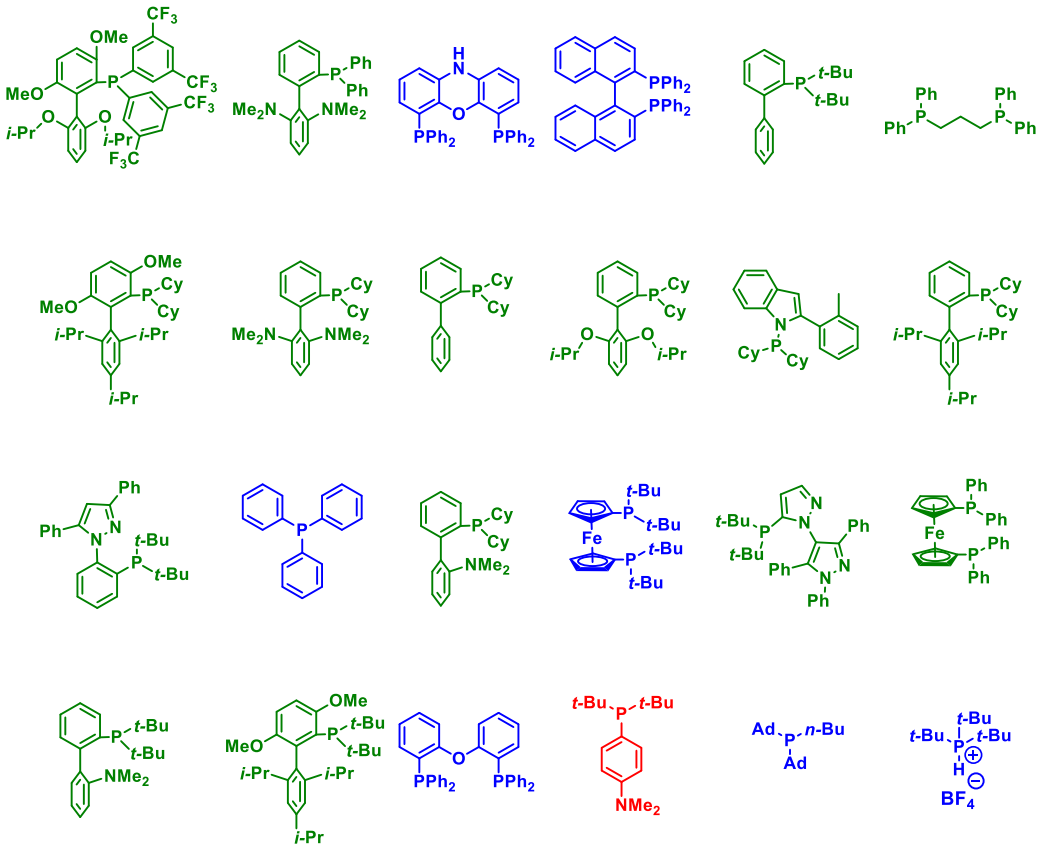
In a 1 mL reaction vial, $Pd(OAc)_2$ (1.7 mg, 0.0076 mmol, 0.3 eq.) and APhos (6 mg, 0.0225 mmol, 0.9 eq.) were dissolved in THF (100 μL) under nitrogen atmosphere. The resulting solution was stirred at room temperature under nitrogen for 3 minutes, and the solvent was then removed under vacuum. To the resulting orange-colored residue was added CPME (167 μL) to produce a yellow solution. This solution was then added to a reaction vial containing a mixture of aniline (−)-**46** (12 mg, 0.025 mmol, 1 eq.) and triflate (−)-**47** (23 mg, 0.05 mmol, 2 eq.), K_3PO_4 (32 mg, 0.15 mmol, 6 eq.), and sand (ca. 5~10 mg). The reaction vial was sealed under nitrogen, heated to 110 °C, and then stirred vigorously at 110 °C for 16 hours, then 115 °C for 24 hours. The resulting dark-brown colored mixture was cooled to room temperature, diluted with Et_2O, and filtered through a plug of silica. The filtrate was concentrated and purified using medium pressure liquid chromatographic (MPLC) (eluted with a gradient of hexanes, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc, 6:1 hexanes/EtOAc, 3:1 hexanes/EtOAc)[17] to provide the title compound (9.4 mg, 51%) as an off-white amorphous solid. $[\alpha]_D^{25}$ +30.7 (*c* 0.1, $CHCl_3$). **IR** (neat) 3443, 2967, 1733, 1644, 1555, 1418, 1378, 1240, 1139, 1074, 1027, 787, 738, 737 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.33 (s, 1H), 7.86 (s, 1H), 7.38 (s, 1H), 5.96 (d, *J* = 2.8 Hz, 1H), 5.40 (d, *J* = 7.3 Hz, 1H), 5.28 (d, *J* = 4.0 Hz, 1H), 5.03 (dd, *J* = 11.5, 4.9 Hz, 1H), 3.83 (dd, *J* = 16.2, 7.3 Hz, 1H), 3.71 (dd, *J* = 16.2, 7.1 Hz, 1H), 2.83 (t, *J* = 3.4 Hz, 1H), 2.76 (d, *J* = 17.4 Hz, 1H), 2.68 (dd, *J* = 13.3, 6.4 Hz, 1H), 2.32 (dd, *J* = 13.3, 10.6 Hz, 1H), 2.23 – 2.06 (m, 2H), 2.01 (s, 6H), 1.89 (s, 3H), 1.85 – 1.72 (m, 4H), 1.73 – 1.52 (m, 3H), 1.52 (d, *J* = 7.7 Hz, 3H), 1.37 (s, 3H), 1.31 (s, 3H), 1.20 (s, 3H), 1.17 (s, 3H), 1.04 (s, 3H), 0.96 (s, 3H), 0.87 (t, *J* = 7.8 Hz, 9H), 0.52 (q, *J* = 7.9 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 204.2, 170.4, 151.2, 141.5, 137.2, 136.7, 132.8, 132.2, 126.7, 123.5, 121.6, 120.4, 118.4, 107.3, 77.7, 74.5, 73.5, 72.8, 58.5, 54.3, 52.8, 48.6, 39.5, 38.6, 32.9,

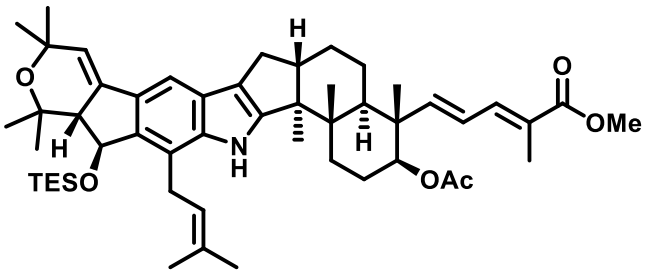
32.0, 30.2, 30.0, 27.6, 27.4, 25.7, 25.2, 24.9, 23.1, 22.3, 21.1, 19.0, 18.2, 14.6, 9.1, 7.2, 6.5. **HRMS (ESI)** *m/z* 742.4884 [(M+H)$^+$; calcd for $C_{46}H_{68}NO_5Si$: 742.4867].

Method 2: using bromide (−)-67

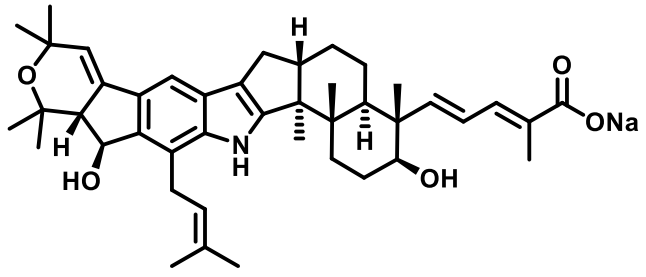
In a 1 mL reaction vial, $Pd(OAc)_2$ (1.7 mg, 0.0075 mmol, 0.3 eq.) and APhos (6 mg, 0.0225 mmol, 0.9 eq.) were dissolved in THF (100 μL) under nitrogen atmosphere. The resulting solution was stirred at room temperature under nitrogen for 3 minutes, and the solvent was then removed under vacuum. To the resulting orange-colored residue was added CPME (167 μL) to produce a yellow solution. This solution was then added to a reaction vial containing a mixture of aniline (−)-**46** (11 mg, 0.025 mmol, 1.0 eq.), bromide (−)-**67** (19.1 mg, 0.05 mmol, 2.0 eq.), K_3PO_4 (32 mg, 0.15 mmol, 6.0 eq.), and sand (ca. 5~10 mg). The reaction vial was sealed under nitrogen, heated to 110 °C, and then stirred vigorously at 110 °C for 16 hours, then 115 °C for 24 hours. The resulting dark-brown colored mixture was cooled to room temperature, diluted with Et_2O, and filtered through a plug of silica. The filtrate was concentrated and purified using medium pressure liquid chromatographic (MPLC) (eluted with a gradient of hexanes, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc, 6:1 hexanes/EtOAc, 3:1 hexanes/EtOAc)[18] to provide the title compound (8 mg, 43%) as an off-white amorphous solid.

Ligands that were investigated for the above-mentioned reaction using aniline (−)-**46** and bromide (−)-**67**.





Indole (+)-73: In a 5-mL reaction vial, phosphonate **35** (24 mg, 0.11 mmol, 10 eq.) was dissolved in THF (187 μL). The resulting solution was cooled to −78 °C, and LHMDS (1M in THF, 100 μL, 0.1 mmol, 9 eq.) was then added. This solution was warmed to 0 °C and stirred for 15 minutes at 0 °C. Indole (+)-**72** (8 mg, 0.011 mmol, 1 eq.) dissolved in 187 μL THF was added to the anion solution, and the resulting pale-yellow solution was warmed to room temperature and stirred for 15 hours, and then was diluted with hexanes. The resulting mixture was filtered through a silica pad, and the filtrate was concentrated and purified using nitrogen purged silica gel vacuum chromatography (eluted with a gradient of hexanes, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc, 6:1 hexanes/EtOAc, 3:1 hexanes/EtOAc) to provide the title compound (9.2 mg, > 95%) as an off-white amorphous solid. $[\alpha]_D^{25}$ +7.4 (*c* 0.1, $CHCl_3$). **IR** (neat) 3394, 2956, 2926, 2873, 1712, 1629, 1579, 1437, 1378, 1289, 1247, 1226, 1119, 1072, 1009, 976, 937, 832, 787, 748 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.38 (s, 1H), 7.20 (d, *J* = 11.2 Hz, 1H), 6.29 (dd, *J* = 15.4, 11.2 Hz, 1H), 5.96 (d, *J* = 2.8 Hz, 1H), 5.84 (d, *J* = 15.4 Hz, 1H), 5.39 (t, *J* = 7.1 Hz, 1H), 5.28 (d, *J* = 3.9 Hz, 1H), 4.73 (t, *J* = 8.1 Hz, 1H), 3.83 (dd, *J* = 16.6, 7.0 Hz, 1H), 3.77 (s, 3H), 3.71 (dd, *J* = 16.2, 7.0 Hz, 1H), 2.82 (t, *J* = 3.3 Hz, 1H), 2.80 – 2.70 (m, 1H), 2.65 (dd, *J* = 13.3, 6.4 Hz, 1H), 2.30 (dd, *J* = 13.3, 10.6 Hz, 1H), 2.07 (q, *J* = 11.2, 9.9 Hz, 1H), 1.98 (s, 3H), 1.96 (d, *J* = 1.3 Hz, 3H), 1.95 – 1.90 (m, 1H), 1.89 (s, 3H), 1.77 (s, 3H), 1.75 (d, *J* = 3.5 Hz, 1H), 1.66 – 1.58 (m, 1H), 1.56 (s, 3H), 1.51 (s, 3H), 1.46 – 1.40 (m, 1H), 1.37 (s, 3H), 1.31 (s, 3H), 1.20 (s, 3H), 1.17 (s, 3H), 1.13 – 1.05 (m, 1H), 0.99 (s, 3H), 0.96 (s, 3H), 0.87 (t, *J* = 7.9 Hz, 9H), 0.58 – 0.48 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.6, 169.1, 151.7, 151.6, 141.5, 138.7, 137.1, 136.8, 132.8, 132.1, 126.8, 125.7, 125.0, 123.5, 121.5, 120.3, 118.4, 107.2, 78.1, 77.7, 74.5, 72.8, 58.5, 53.1, 51.9, 48.8, 45.6, 44.9, 39.2, 33.1, 32.0, 30.2, 30.0, 27.6, 27.4, 25.7, 25.2, 24.5, 23.8, 22.3, 21.2, 19.5, 18.2, 14.5, 12.9, 12.3, 7.2, 6.5. **HRMS (ESI)** *m/z* 860.5261 [(M+Na)$^+$; calcd for $C_{52}H_{75}NNaO_6Si$: 860.5261].



(−)-Nodulisporic Acid C (3) Sodium Salt: In a 5-mL reaction vial containing indole (+)-**73** (5.0 mg, 6 μmol, 1 eq.), a mixture containing LiOH (250 μL, 1N, aqueous solution), MeOH (500 μL), and THF (250 μL) was added. The resulting mixture was heated to 50 °C and stirred for 3 hours at 50 °C and was then cooled to room temperature. The solvent was then removed under high vacuum, and the residue was added HOAc (550 μL, 1M, in EtOAc). An excessive amount of Na_2CO_3 powder was added to neutralize HOAc, and the solvent was then removed under high vacuum. To the residue was added $(CD_3)_2CO$, and the solution was then filtered through a Celite plug into a NMR tube. Na_2CO_3 powder (ca. 10 mg) was added to the NMR tube, and the NMR data of (−)-nodulisporic acid C sodium salt was acquired. After completing the spectra acquisition, the sample was filtered through Celite, concentrated in vacuum to yield white film (5 mg, >95%). $[\alpha]_D^{25}$ −65.1 (*c* 0.3, $CHCl_3$). **IR** (neat) 3385, 2924, 2853, 1682, 1633, 1454, 1377, 1258, 1097, 1030, 979, 805, 739 cm^{-1}. **^{1}H NMR** [500 MHz, $(CD_3)_2CO$] δ 9.03 (brs, 1H), 7.29 (s, 1H), 7.20 (d, *J* = 10.9 Hz, 1H), 6.36 (dd, *J* = 15.3, 11.3 Hz, 1H), 5.98 (d, *J* = 16.2 Hz, 1H), 5.95 (d, *J* = 2.9 Hz, 1H), 5.28 (t, *J* = 6.8 Hz, 1H), 5.00 (d, *J* = 5.0 Hz, 1H), 4.01 (dd, *J* = 14.2, 7.3 Hz, 1H), 3.68 (dd, *J* = 14.5, 5.2 Hz, 1H), 3.47 (dd, *J* = 10.8, 4.7 Hz, 1H), 2.74 (m, 1H), 2.66 (dd, *J* = 4.7, 2.9 Hz, 1H), 2.61 (dd, *J* = 13.1, 6.3 Hz, 1H), 2.27 (dd, *J* = 12.9, 11.0 Hz, 1H), 1.90 (brs, 3H), 1.85 (m, 2H), 1.81 (s, 3H), 1.79 (m, 1H), 1.77 (m, 1H), 1.74 (m, 1H), 1.65 (s, 3H), 1.59 (m, 2H), 1.46 (m, 2H), 1.38 (s, 3H), 1.25 (s, 3H), 1.24 (s, 3H), 1.14 (s, 3H), 1.07 (s, 3H), 1.05 (s, 3H), 0.99 (s, 3H). **^{13}C NMR** [126 MHz, $(CD_3)_2CO$] δ 169.6, 154.9, 152.9, 142.1, 139.7, 137.5, 137.1, 132.1, 131.5, 127.2, 125.5, 124.2, 123.2, 119.6, 118.7, 107.4, 76.8, 76.3, 74.1, 72.6, 60.6, 54.2, 49.7, 47.8, 44.9, 39.6, 33.3, 32.2, 30.3, 30.2, 27.8, 27.5, 26.5, 25.9, 25.6, 25.3, 23.0, 19.2, 18.0, 14.6, 12.7, 11.6. **HRMS (ESI)** *m/z* 668.4318 [$(M+H)^+$; calcd for $C_{43}H_{58}NO_5$: 668.4315 for the free acid].

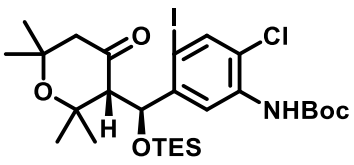
	Natural	Synthetic	Difference
Carbon	δHn	δHs	Δ=δHs-δHn
2			
3			
4			
5	1.85 (m, 2H)	1.85 (m, 2H)	0.00
6	1.78 (m), 1.81 (m)	1.77 (m), 1.79 (m)	-0.01, -0.02
7	3.45 (dd, *J*=4.5, 10.5)	3.47 (dd, *J*=4.7, 10.8)	0.02
8			
9	1.75 (m)	1.74 (m)	-0.01
10	1.46 (m, 2H)	1.46 (m, 2H)	0.00
11	1.60 (m, 2H)	1.59 (m, 2H)	-0.01
12	2.75 (m)	2.74 (m)	-0.01
13	2.25 (dd, *J*=10.5, 13.0)	2.27 (dd, *J*=10.8, 12.9)	0.02
	2.60 (dd, *J*=6.5, 13.0)	2.61 (dd, *J*=6.3, 13.1)	0.01
14			
15			
16	7.31 (s)	7.29 (s)	-0.02
17			
18			

19	5.96 (d, *J*=3.0)	5.95 (d, *J*=2.9)	-0.01
20			
22			
23	2.70 (dd, *J*=3.0, 6.0)	2.66 (dd, *J*=2.9, 4.9)	-0.04
24	5.00 (d, *J*=3.0)	5.00 (d, *J*=5.0)	0.00
25			
26			
27			
28	1.05 (s)	1.05 (s)	0.00
29	1.13 (s)	1.14 (s)	0.01
30	1.07 (s)	1.07 (s)	0.00
31	1.26 (s)	1.24 (s)	-0.02
32	1.27 (s)	1.25 (s)	-0.02
33	1.00 (s)	0.99 (s)	-0.01
34	1.40 (s)	1.38 (s)	-0.02
1'	3.70 (dd, *J*=6.0, 15.0)	3.68 (dd, *J*=5.2, 14.5)	-0.02
	4.00 (dd, *J*=8.0, 15.0)	4.01 (dd, *J*=7.3, 14.2)	0.01
2'	5.30 (t, *J*=6.0, 8.0)	5.28 (t, *J*=6.8)	-0.02
3'			
4'	1.80 (s)	1.81 (s)	0.01
5'	1.67 (s)	1.65 (s)	-0.02
1''	5.96 (d, *J*=15.0)	5.98 (d, *J*=16.2)	0.02
2''	6.38 (dd, *J*=11.5, 15.0)	6.37 (dd, *J*=11.3, 15.3)	-0.01
3''	7.22 (d, *J*=11.5)	7.21 (d, *J*=10.9)	-0.01
4''			
5''			
6''	1.90 (d, *J*=1.2)	1.90 (brs)	0.00
NH	9.00 (brs)	9.03 (brs)	0.03

	Natural	Synthetic	Difference
Carbon	δCn	δCs	Δ=δCs-δCn
2	153.0	152.9	-0.1
3	54.3	54.2	-0.1
4	39.7	39.6	-0.1
5	33.4	33.3	-0.1
6	27.6	27.5	-0.1
7	76.9	76.8	-0.1
8	47.9	47.8	-0.1
9	45.0	44.9	-0.1
10	25.4	25.3	-0.1
11	26.0	25.9	-0.1
12	49.7	49.7	0.0
13	27.9	27.8	-0.1
14	118.8	118.7	-0.1

15	127.4	127.2	-0.2
16	107.6	107.4	-0.2
17	132.2	132.1	-0.1
18	137.2	137.5	0.3
19	119.8	119.6	-0.2
20	72.7	72.6	-0.1
22	74.2	74.1	-0.1
23	60.7	60.6	-0.1
24	76.5	76.3	-0.2
25	137.1	137.1	0.0
26	123.3	123.2	-0.1
27	142.1	142.1	0.0
28	14.7	14.6	-0.1
29	19.4	19.2	-0.2
30	11.7	11.6	-0.1
31	30.3	30.3	0.0
32	32.3	32.2	-0.1
33	23.1	23.0	-0.1
34	30.3	30.2	-0.1
1'	26.6	26.5	-0.1
2'	124.4	124.2	-0.2
3'	131.7	131.5	-0.2
4'	25.4	25.6	0.2
5'	18.1	18.0	-0.1
1''	155.2	154.9	-0.3
2''	125.6	125.5	-0.1
3''	140.1	139.7	-0.4
4''	125.4	125.5	0.1
5''	170.0	169.6	-0.4
6''	12.7	12.7	0.0

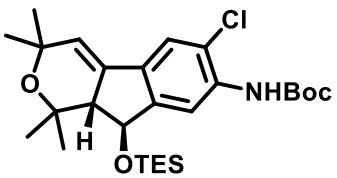
Note 1: spectra comparison was based on the publication: Ondeyka, J. G.; Byrne, K.; Vesey, D.; Zink, D. L.; Shoop, W. L.; Goetz, M. A.; Singh, S. B. J. Nat. Prod. **2003**, 66, 121.



Ketone (–)-77: In a round-bottom flask, (+)-**53** (31 g, 47.7 mmol, 1 eq.) was added imidazole (9.7 g, 143 mmol., 3.0 eq.). The mixture was dissolved in CH_2Cl_2 (475 mL) and was then added CaH_2 (1g). TESCl (16 mL, 95 mmol, 2 eq.) was added dropwise via a syringe, and the resulting mixture was stirred at room temperature for 25 hours. The mixture was then quenched with $NaHCO_3$ (saturated aqueous

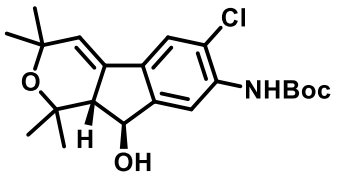
solution), warmed to room temperature, and was then diluted with Et_2O. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with water and then brine, and then dried over $MgSO_4$ and filtered through a silica pad. The filtrate was concentrated *in vacuo* to provide the crude product as a pale-yellow oil. This oil was used directly for the next step without further purification.

In a three-neck round-bottom flask equipped with a mechanical stirrer and an addition funnel, the crude product from last step was dissolved in cyclohexane (500 mL) and was added pH 6 buffer solution (73.4 mL). SeO_2 (12 g, 110 mmol, 2.3 eq.) was added in one portion followed by dropwise addition of H_2O_2 (73.4 mL, 35 wt. % in H_2O) over a period of 10 minutes. The internal temperature raised from 25 ˚C to 50 ˚C after finishing adding H_2O_2. The mixture was stirred vigorously using the mechanical stirring blade for 25 hours. Another portion of SeO_2 (12 g, 110 mmol, 2.3 eq.) was then added to the reaction mixture which was then stirred vigorously using the mechanical stirring blade for another 12 hours. The reaction flask was then cooled to 0 ˚C and quenched dropwise with $Na_2S_2O_3$ (saturated aqueous solution) (caution exothermic!) while maintaining the internal temperature less than 15 ˚C. until peroxide paper indicating no peroxide was detectable [failure to remove all peroxide may result severe explosion (!) upon concentration], the mixture was then filtered through Celite. The organic layer was separated, and the aqueous layer was extracted with hexanes. The combined organic layer was washed with brine, dried over $MgSO_4$ and then filtered. The filtrate was concentrated *in vacuo* to provide the crude product as a pale-yellow oil. This oil was then purified by using silica gel flash chromatography (eluted with a gradient of hexanes, 50:1 hexanes/EtOAc, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc) to provide the title compound (18.6 g, 60%, 2 steps) as an oil. $[\alpha]_D^{25}$ −31.4 (*c* 0.5, $CHCl_3$). **IR** (neat) 3428, 2973, 2876, 1739, 1716, 1569, 1495, 1444, 1386, 1367, 1299, 1222, 1154, 1072, 1044, 1008, 943, 870, 845, 802, 742 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.41 (s, 1H), 7.73 (s, 1H), 6.89 (s, 1H), 5.42 (d, *J* = 5.4 Hz, 1H), 3.08 (d, *J* = 5.4 Hz, 1H), 2.64 (d, *J* = 13.9 Hz, 1H), 2.44 (d, *J* = 13.9 Hz, 1H), 1.56 (s, 3H), 1.54 (s, 9H), 1.34 (s, 3H), 1.25 (s, 3H), 0.87 (t, *J* = 7.9 Hz, 9H), 0.51 (qd, *J* = 7.8, 3.4 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 208.7, 151.6, 145.5, 138.4, 135.6, 121.2, 119.8, 100.1, 88.4, 81.3, 78.8, 76.3, 74.8, 64.3, 52.2, 34.8, 32.8, 32.7, 31.7, 30.8, 28.4, 27.2, 22.8, 14.2, 6.9, 4.9. **HRMS (ESI)** *m/z* 674.1516 [$(M+Na)^+$; calcd for $C_{27}H_{43}ClINNaO_5Si$: 674.1541].



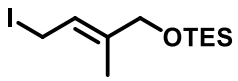
Olefin (−)-79: In a reaction vial, $NiCl_2$ (127 mg, 0.98 mmol, 0.2 eq.) and $CrCl_2$ (3 g, 24.4 mmol, 5 eq.) were heated under high vacuum until forming a grey-colored free-flowing powder. Then the reaction vial was back filled with argon and was added ketone (−)-**77** (3.2 g, 4.9 mmol, 1 eq.) as a solution in anhydrous DMF (25 mL, degassed by using freeze-pump-thaw technique). The resulting dark green

mixture was stirred vigorously at room temperature for 15 hours. This mixture was then poured into a stirring mixture of Et_2O/hexanes 1:1 and was then added $NaHCO_3$ (saturated aqueous solution). The organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, and then filtered through a pad of silica gel. The filtrate was concentrated *in vacuo* to provide the crude product. The crude product was used directly for the next step without further purification. The crude product (2.5 g) in a round-bottom flask was added DMAP (116 mg, 0.95 mmol, 0.2 eq.), CH_2Cl_2 (47 mL), and 2,6-lutidine (8.3 mL, 71.3 mmol, 15 eq.). The resulting solution was then cooled to 0 °C, and MsCl (1.1 mL, 14 mmol, 2.9 eq.) was added dropwise. The resulting mixture was then warmed to room temperature and stirred at room temperature for 68 hours and was then poured into $NaHCO_3$ (saturated aqueous solution). The mixture was then diluted with Et2O and stirred vigorously at room temperature for 20 minutes. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and then filtered. The filtrate was concentrated *in vacuo* to provide the crude product. The crude product was purified by using silica gel vacuum chromatography (eluted with a gradient of hexanes, 100:1 hexanes/EtOAc, 50:1 hexanes/EtOAc, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc) to provide the title compound (1.5 g, 60% over the two steps) as an oil. $[\alpha]_D^{25}$ −50.0 (*c* 0.45, $CHCl_3$). **IR** (neat) 3429, 2970, 2934, 2877, 1738, 1610, 1583, 1508, 1460, 1418, 1392, 1366, 1337, 1291, 1239, 1223, 1156, 1093, 1062, 1008, 987, 937, 897, 829, 814, 741, 696, 627 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.40 (s, 1H), 7.02 (s, 1H), 5.92 (d, *J* = 2.9 Hz, 1H), 4.99 (d, *J* = 5.5 Hz, 1H), 2.77 (dd, *J* = 5.6, 2.9 Hz, 1H), 1.58 (s, 3H), 1.54 (s, 9H), 1.45 (s, 3H), 1.33 (s, 3H), 1.31 (s, 3H), 1.08 (s, 3H), 1.02 (t, *J* = 7.9 Hz, 9H), 0.77 (ddt, *J* = 17.4, 15.1, 7.3 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 152.1, 146.1, 135.3, 134.1, 133.5, 122.7, 122.5, 120.9, 116.0, 72.3, 59.0, 31.8, 30.3, 29.8, 28.3, 23.2, 7.2, 5.9. **HRMS (ESI)** *m/z* 530.2468 [$(M+Na)^+$; calcd for $C_{27}H_{42}ClNNaO_4Si$: 530.2469].

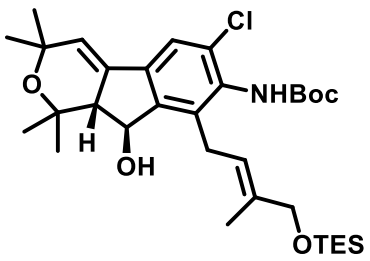


Alcohol (−)-48: In a plastic reaction vial, olefin (−)-**79** (850 mg, 1.67 mmol, 1 eq.) was added THF (16.7 mL) and *t*-BuOH (1.67 mL). Then, H_2SiF_6 (25 wt% in water, 193 uL, 0.33 mmol, 0.2 eq.) was added to the solution, and the resulting solution was stirred at room temperature for 22 hours and was then added another portion of H_2SiF_6 (25 wt% in water, 193 uL, 0.33 mmol, 0.2 eq.). The reaction mixture was then stirred at room temperature for 5 hours and was then added Na_2CO_3 and $MgSO_4$. The reaction vial was then shake, and the mixture was filtered through a silica pad. The filtrate was concentrated *in vacuo* to provide the crude product. The crude product was purified by using silica gel vacuum chromatography (eluted with a gradient of 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc, 6:1

hexanes/EtOAc, 3:1 hexanes/EtOAc) to provide the title compound (620 mg, 94%) as an oil. $[\alpha]_D^{25}$ −51.9 (*c* 0.1, $CHCl_3$). **IR** (neat) 3422, 2975, 1738, 1584, 1508, 1367, 1241, 1156, 1064, 756 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.40 (s, 1H), 7.06 (s, 1H), 5.92 (d, *J* = 2.9 Hz, 1H), 4.82 (d, *J* = 5.9 Hz, 1H), 2.72 (s, 1H), 2.64 (dd, *J* = 5.9, 2.9 Hz, 1H), 1.52 (s, 9H), 1.43 (s, 3H), 1.32 (s, 3H), 1.30 (s, 3H), 1.05 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 152.5, 145.7, 135.2, 133.7, 133.7, 123.2, 123.1, 121.1, 116.0, 81.5, 76.3, 73.8, 72.5, 59.1, 31.8, 30.0, 29.7, 28.4, 23.1. **HRMS (ESI)** *m/z* 392.1618 $[(M-H)^-$; calcd for $C_{21}H_{27}ClNO_4$: 392.1629].

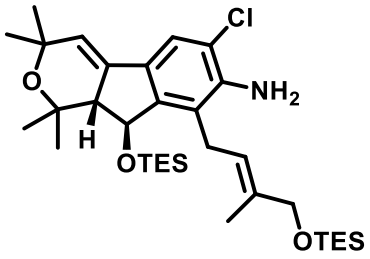


Iodide 80: In a reaction flask, PPh_3 (1.76 g, 6.7 mmol, 1 eq.) and imidazole (1.37 g, 20.1 mmol, 3 eq.) were placed, and CH_2Cl_2 (22 mL) was then added. The resulting solution was cooled to −10 °C, and iodine (1.70 g, 6.7 mmol, 1 eq.) was then added to provide a pale-yellow solution. Next, (*E*)-3-methyl-4-[(triethylsilyl)oxy]but-2-en-1-ol[19] (1.45 g, 6.7 mmol, 1 eq.) was dissolved in CH_2Cl_2 (11 mL) and was added dropwise to the reaction flask. The resulting reaction mixture was stirred at −10 °C for 40 minutes and was quenched by adding $Na_2S_2O_3$ (saturated aqueous solution). The organic layer was separated, and the aqueous layer was extracted with hexanes. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered through a silica pad. To the filtrate was added several pieces of copper wire (ca. 100 mg) and concentrated *in vacuo* at 0 °C to provide the crude product as a pale-yellow oil (1.5 g, 69%), stored over several pieces of copper wire.[20] This oil was used for the next step without further purification. **IR** (neat) 2953, 2875, 1457, 1238, 1146, 1119, 1069, 1007, 723 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.83 (t, *J* = 9.0 Hz, 1H), 4.04 (s, 2H), 3.97 (d, *J* = 8.8 Hz, 2H), 1.63 (s, 3H), 0.98 (t, *J* = 8.0 Hz, 9H), 0.63 (q, *J* = 8.0 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 140.6, 121.0, 67.3, 13.1, 6.9, 4.6, 2.5. **HRMS (EI)** *m/z* 198.1440 $[(M-HI)^+$; calcd for $C_{11}H_{22}OSi$: 198.1440].



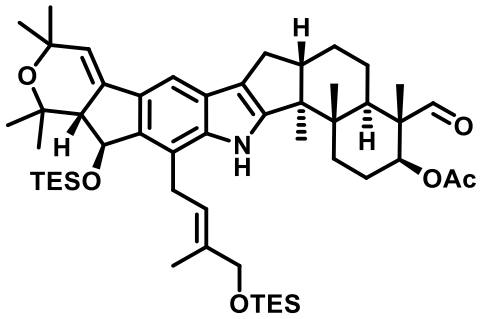
Alcohol (−)-81: In a reaction vial, alcohol (−)-**48** (273 mg, 0.69 mmol, 1 eq.) was azeotroped with toluene and to this residue was then added CPME (6.9 mL) and HMPA (345 μL). The resulting solution was cooled to −78 °C and was then treated dropwise with *t*-BuLi solution (1.43 M in pentane, 2.9 mL, 4.16 mmol, 6 eq.) to provide a dark orange/red solution which was then warmed to −40 °C and stirred for 3 hours at −40 °C. During this period, CuCN (372 mg, 4.16 mmol, 6 eq.) was added to

a 20 mL reaction vial and heated to 120 °C for 2.5 hours under high vacuum. The vial containing CuCN was cooled to room temperature and backed filled with nitrogen. THF (6.9 mL) was then added to CuCN, and the resulting mixture was cooled to −78 °C. The dark orange/red anion solution (−40 °C) was cannulated to the slurry of CuCN/THF, and the resulting brown slurry was stirred at −40 °C for 1 hour then cooled to −78 °C, and iodide **80** (1.56 g, 4.8 mmol, 6.9 eq.) was then added dropwise. The resulting dark brown mixture was stirred at −78 °C for 3.5 hours and was then quenched with ammonium hydroxide solution (30-32%) and stirred vigorously for 20 minutes. The mixture was diluted with EtOAc. The organic layer was separated, and the aqueous layer was extracted with EtOAc. After the extraction, the aqueous layer was added $KMnO_4$ before discard. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product as a pale-yellow oil. This oil was purified using silica gel vacuum chromatography (eluted with a gradient of hexanes, 50:1 hexanes/EtOAc, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc, 6:1 hexanes/EtOAc, 3:1 hexanes/EtOAc) to provide crude fractions. The fraction, containing starting material alcohol (−)-**48** and product alcohol (−)-**81**, was subjected to reverse phase C-18 high-performance liquid chromatography (eluted with a gradient of 30% MeCN/H_2O to 100% MeCN) to provide the starting material alcohol (−)-**48** (102 mg, 37%) and the product alcohol (−)-**81** (184 mg, 45%) both as a white foam. Alcohol (−)-**81**: $[\alpha]_D^{25}$ −48.0 (*c* 0.2, $CHCl_3$). **IR** (neat) 3466, 3377, 2956, 2911, 2876, 2734, 1730, 1671, 1615, 1457, 1415, 1378, 1364, 1342, 1292, 1242, 1153, 1140, 1089, 1008, 909, 868, 829, 780, 741, 681 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.41 (s, 1H), 6.05 (s, 1H), 6.01 (d, *J* = 3.1 Hz, 1H), 5.38 (s, 1H), 4.95 (t, *J* = 7.0 Hz, 1H), 4.02 (s, 2H), 3.74 (s, 1H), 3.54 (dd, *J* = 15.2, 6.0 Hz, 1H), 2.65 (s, 1H), 1.89 (d, *J* = 8.8 Hz, 1H), 1.80 (s, 3H), 1.51 (s, 9H), 1.47 (s, 3H), 1.33 (s, 6H), 1.04 (s, 3H), 0.94 (t, *J* = 7.9 Hz, 9H), 0.59 (q, *J* = 7.9 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 153.9, 142.7, 141.5, 139.5, 138.9, 136.0, 134.4, 134.0, 124.4, 122.3, 119.4, 114.1, 80.7, 76.2, 73.8, 72.6, 68.2, 59.4, 31.7, 29.9, 29.8, 29.7, 28.4, 27.6, 22.8, 13.9, 6.9, 4.5, 4.4.. **HRMS (ESI)** *m/z* 590.3076 [(M−H)$^-$; calcd for $C_{32}H_{49}ClNO_5Si$: 590.3069].



Amine (−)-76: In a round bottom flask, alcohol (−)-**81** (272 mg, 0.46 mmol, 1 eq.) was azeotroped with toluene and was then dissolved in CH_2Cl_2 (9.2 mL). 2,6-lutidine (1.6 mL, 13.8 mmol, 30 eq.) was added to the solution. The resulting solution was cooled to −78 °C, and TESOTf (416 μL, 1.84 mmol, 4 eq.) was then added dropwise. The resulting solution was stirred at −78 °C for 40 minutes and 0 °C for 20 minutes. TMSOTf (332 μL, 1.84 mmol, 4 eq.) was added at 0 °C, and the resulting solution was stirred at 0 °C for 40 minutes and was then quenched with $NaHCO_3$ (saturated aqueous solution).

The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product as a pale-yellow oil. This oil was purified using silica gel vacuum chromatography (eluted with a gradient of hexanes, 50:1 hexanes/EtOAc, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc) to provide the title compound (215 mg, 77%) as a pale-yellow oil. $[\alpha]_D^{25}$ −43.0 (*c* 0.3, $CHCl_3$). **IR** (neat) 3428, 2957, 2877, 1736, 1646, 1582, 1508, 1457, 1419, 1367, 1241, 1216, 1158, 1064, 1008, 884, 804, 744, 604 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29 (s, 1H), 5.80 (d, *J* = 2.8 Hz, 1H), 5.39 – 5.31 (m, 1H), 5.09 (d, *J* = 3.9 Hz, 1H), 4.17 (s, 2H), 4.03 (s, 2H), 3.82 (dd, *J* = 16.3, 6.0 Hz, 1H), 3.33 (dd, *J* = 16.2, 7.1 Hz, 1H), 2.73 (t, *J* = 3.4 Hz, 1H), 1.81 (s, 3H), 1.47 (s, 3H), 1.33 (s, 3H), 1.29 (s, 3H), 0.99 – 0.90 (m, 12H), 0.87 (t, *J* = 7.9 Hz, 9H), 0.59 (q, *J* = 8.0 Hz, 6H), 0.51 (q, *J* = 8.0 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 143.5, 142.3, 137.4, 135.5, 130.3, 124.2, 121.6, 121.3, 120.6, 119.1, 77.6, 74.4, 72.7, 68.0, 57.9, 31.8, 30.1, 29.9, 26.7, 22.1, 13.9, 7.1, 6.9, 6.4, 4.6. **HRMS (ESI)** *m/z* 606.3552 [$(M+H)^+$; calcd for $C_{33}H_{57}ClNO_3Si_2$: 606.3566].



Indole (+)-82:

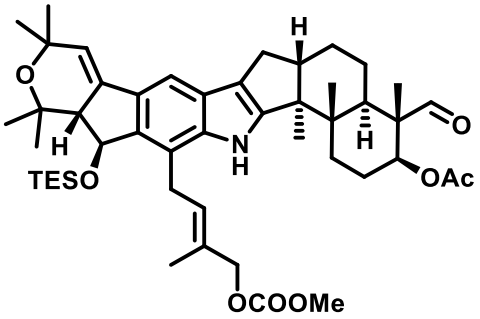
Method 1: using triflate (−)-47

In a reaction vial, aniline (−)-**76** (27 mg, 0.045 mmol, 1 eq.), triflate (−)-**47** (40.2 mg, 0.09 mmol, 2 eq.), K_3PO_4 (57 mg, 0.27 mmol, 6 eq.), and sand (ca. 15 mg) were added. A stock solution containing $Pd(OAc)_2$ (1.26 mg, 5.6 μmol, 0.125 eq.) and APhos (3 mg, 11.2 μmol, 0.25 eq.) in CPME (450 μL) was then added to the reaction vial. The reaction vial was sealed under nitrogen, stirred at 520 RPM, 120 °C for 18 hours. The resulting dark brown colored mixture was cooled to room temperature, diluted with Et_2O, and filtered through a plug of silica. The filtrate was concentrated and purified using silica gel vacuum chromatography (eluted with a gradient of hexanes, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc, 6:1 hexanes/EtOAc) to provide the title compound (13.7 mg, 35%) as an off-white amorphous solid. $[\alpha]_D^{25}$ +18.7 (*c* 0.5, $CHCl_3$). **IR** (neat) 3445, 2954, 2876, 1733, 1616, 1456, 1415, 1377, 1240, 1075, 1007, 781, 741 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.33 (s, 1H), 7.74 (s, 1H), 7.39 (s, 1H), 7.27 (s, 1H), 5.96 (d, *J* = 2.8 Hz, 1H), 5.66 (t, *J* = 7.2 Hz, 1H), 5.27 (d, *J* = 4.0 Hz, 1H), 5.03 (dd, *J* = 11.3, 4.9 Hz, 1H), 4.04 (s, 2H), 3.94 (dd, *J* = 16.5, 7.3 Hz, 1H), 3.70 (dd, *J* = 16.3, 6.9 Hz, 1H), 2.83 (d, *J* = 3.5 Hz, 1H), 2.76 (dd, *J* = 15.5, 6.0 Hz, 1H), 2.71 – 2.63 (m, 1H), 2.32 (dd, *J* = 13.4, 10.5 Hz, 1H), 2.22 – 2.11 (m, 1H), 2.11 – 2.03 (m, 1H), 2.01 (s, 3H), 1.87 (s, 3H), 1.81 – 1.70 (m, 2H), 1.65 (dd, *J* = 26.3, 7.5 Hz, 2H), 1.56 (d, *J* = 13.0 Hz, 2H), 1.50 (s, 4H), 1.37 (s, 3H), 1.31 (s, 3H), 1.28

– 1.23 (m, 1H), 1.20 (s, 3H), 1.15 (s, 3H), 1.12 – 1.06 (m, 1H), 1.03 (s, 3H), 0.97 – 0.90 (m, 9H), 0.85 (t, J = 7.9 Hz, 9H), 0.59 (q, J = 8.0 Hz, 6H), 0.50 (q, J = 7.9 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 204.2, 170.4, 151.2, 141.5, 137.3, 136.6, 135.9, 132.2, 126.7, 122.5, 121.4, 120.5, 118.6, 107.3, 77.7, 74.5, 73.4, 72.8, 67.8, 58.5, 54.3, 52.9, 48.5, 45.6, 39.5, 38.6, 32.9, 32.0, 30.2, 30.0, 27.6, 26.7, 25.9, 25.2, 24.9, 23.1, 22.8, 22.3, 21.2, 19.1, 14.5, 14.0, 9.1, 7.2, 6.9, 6.4, 4.5. **HRMS (ESI)** *m/z* 872.5698[(M+H)$^+$; calcd for $C_{52}H_{82}NO_6Si_2$: 872.5681].

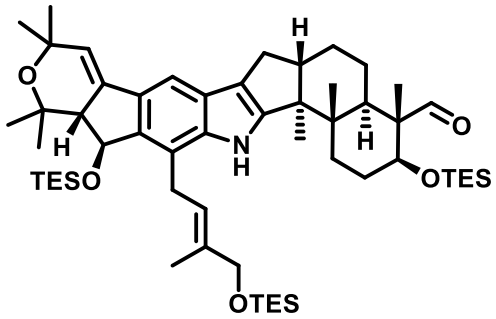
Method 2: using bromide (–)-67

In a 1 mL reaction vial, $Pd(OAc)_2$ (1.3 mg, 5.6 μmol, 0.125 eq.) and APhos (3 mg, 0.011 mmol, 0.25 eq.) were dissolved in THF (100 μL), heated to reflux under nitrogen for 3 minutes, and the solvent was then removed under vacuum. To the resulting orange-colored residue was added CPME (450 μL) to produce a yellow solution. This solution was added to a reaction vial which contained a mixture of aniline (–)-**76** (27 mg, 0.045 mmol, 1 eq.), bromide (–)-**67** (33 mg, 0.09 mmol, 2 eq.), K_3PO_4 (57 mg, 0.27 mmol, 6 eq.), and sand (15 mg). The reaction vial was sealed under nitrogen, stirred at 600 RPM, 120 °C for 18 hours. The resulting dark brown colored mixture was cooled to room temperature, diluted with Et_2O, and filtered through a plug of silica. The filtrate was concentrated and purified using silica gel vacuum chromatography (eluted with a gradient of hexanes, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc, 6:1 hexanes/EtOAc) to provide the title compound (17 mg, 43%) as an off-white amorphous solid.



Carbonate (–)-75: In a reaction vial, indole (+)-**82** (8 mg, 0.0092 mmol, 1 eq.) was dissolved in CH_2Cl_2 (100 uL), MeOH (400 uL). NH_4F (3.4 mg, 0.092 mmol, 10 eq.) was then added to the solution. The resulting mixture was then stirred at room temperature for 1.5 hour then diluted with Et_2O and filtered through a silica pad. The filtrate was concentrated *in vacuo* to provide the crude product as a pale-yellow oil. This oil was used directly for the next step without further purification. The crude product was then dissolved in CH_2Cl_2 (500 uL) and added pyridine (10 uL, 0.123 mmol, 13 eq.). The resulting solution was cooled to 0 °C and added methyl chloroformate (5uL, 0.065 mmol, 7 eq.) then stirred at 0 °C for 1 hour. $NaHCO_3$ (saturated aqueous solution) was then added, and the mixture was stirred at room temperature for 20 minutes. The organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product as a pale-yellow oil. This oil was then purified by using silica gel vacuum chromatography (eluted with a gradient of hexanes, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc, 6:1 hexanes/EtOAc, 3:1 hexanes/EtOAc, 3:1

hexanes/acetone) to provide the title compound (7 mg, 93%, 2 steps) as a pale-yellow foam. $[\alpha]_D^{25}$ −2.6 (*c* 0.1, $CHCl_3$). **IR** (neat) 3447, 2962, 1734, 1541, 1457, 1260, 1027, 799 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.33 (s, 1H), 7.65 (s, 1H), 7.40 (s, 1H), 5.97 (d, *J* = 2.8 Hz, 1H), 5.71 (t, *J* = 7.0 Hz, 1H), 5.27 (d, *J* = 4.0 Hz, 1H), 5.03 (dd, *J* = 11.4, 4.8 Hz, 1H), 4.62 – 4.49 (m, 2H), 3.94 (dd, *J* = 16.3, 6.3 Hz, 1H), 3.79 (d, *J* = 5.7 Hz, 3H), 3.72 (dd, *J* = 16.6, 7.7 Hz, 1H), 2.83 (t, *J* = 3.4 Hz, 1H), 2.80 – 2.73 (m, 1H), 2.72 – 2.61 (m, 1H), 2.32 (dd, *J* = 13.4, 10.6 Hz, 1H), 2.18 – 2.06 (m, 2H), 2.01 (s, 3H), 1.95 (s, 3H), 1.76 (d, *J* = 12.7 Hz, 1H), 1.71 – 1.52 (m, 3H), 1.50 (s, 3H), 1.37 (s, 3H), 1.31 (s, 3H), 1.26 (d, *J* = 1.9 Hz, 3H), 1.20 (s, 3H), 1.16 (s, 3H), 1.04 (s, 3H), 0.96 (s, 3H), 0.86 (t, *J* = 8.0 Hz, 9H), 0.60 – 0.44 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 204.3, 170.4, 155.9, 151.6, 141.3, 137.4, 136.5, 132.3, 131.1, 128.7, 126.8, 120.7, 120.4, 118.7, 107.6, 77.7, 74.5, 73.5, 73.3, 72.8, 58.4, 54.9, 54.3, 53.0, 48.5, 39.5, 38.6, 32.9, 32.0, 30.2, 30.0, 29.8, 29.4, 27.6, 27.0, 25.2, 24.9, 23.1, 22.3, 21.2, 19.1, 14.5, 14.3, 9.1, 7.2, 6.5. **HRMS (ESI)** *m/z* 816.4880 [$(M+H)^+$; calcd for $C_{48}H_{70}NO_8Si$: 816.4871].



Indole (+)-83:

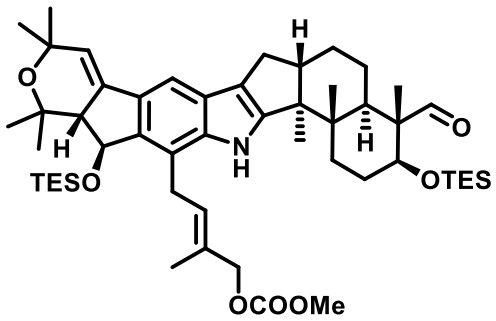
Method 1: using triflate (−)-33

In a 5 mL reaction vial, $Pd(OAc)_2$ (1.4 mg, 6 μmol, 0.125 eq.) and APhos (3.3 mg, 0.0125 mmol, 0.25 eq.) were dissolved in THF (100 μL), heated to reflux under nitrogen for 3 minutes, and the solvent was then removed under vacuum. To the resulting orange-colored residue was added CPME (500 μL) to produce a yellow solution. This solution was added to a reaction vial which contained a mixture of aniline (−)-**76** (30 mg, 0.05 mmol, 1 eq.), triflate (−)-**33** (52 mg, 0.1 mmol, 2 eq.), K_3PO_4 (64 mg, 0.3 mmol, 6 eq.), and sand (10 mg). The reaction vial was sealed under nitrogen, stirred at 600 RPM, 120 °C for 17 hours. The resulting dark brown colored mixture was cooled to room temperature, diluted with Et_2O, and filtered through a plug of silica. The filtrate was concentrated and purified using silica gel vacuum chromatography (eluted with a gradient of hexanes, 50:1 hexanes/EtOAc, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc) to provide the title compound (23 mg, 49%) as an off-white amorphous solid. $[\alpha]_D^{25}$ +18.7 (*c* 0.3, $CHCl_3$). **IR** (neat) 3841, 3446, 2954, 2876, 1732, 1670, 1508, 1457, 1415, 1377, 1362, 1341, 1242, 1100, 1007, 925, 862, 822, 786, 741 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.38 (s, 1H), 7.77 (s, 1H), 7.39 (s, 1H), 5.96 (d, *J* = 2.9 Hz, 1H), 5.69 (t, *J* = 7.0 Hz, 1H), 5.28 (d, *J* = 3.9 Hz, 1H), 4.07 (d, *J* = 3.2 Hz, 1H), 3.93 (dd, *J* = 16.2, 7.4 Hz, 1H), 3.85 (q, *J* = 4.7 Hz, 1H), 3.73 (dd, *J* = 16.3, 7.0 Hz, 1H), 2.83 (t, *J* = 3.3 Hz, 1H), 2.81 – 2.72 (m, 1H), 2.66 (dd, *J* = 13.3,

6.4 Hz, 1H), 2.31 (dd, *J* = 13.3, 10.6 Hz, 1H), 2.02 (dd, *J* = 12.7, 3.3 Hz, 1H), 1.98 – 1.89 (m, 2H), 1.89 (s, 3H), 1.84 – 1.77 (m, 1H), 1.76 – 1.68 (m, 1H), 1.66 – 1.54 (m, 2H), 1.51 (s, 3H), 1.49 – 1.44 (m, 1H), 1.37 (s, 3H), 1.36 – 1.33 (m, 1H), 1.31 (s, 3H), 1.29 – 1.20 (m, 1H), 1.17 (s, 3H), 1.14 (s, 3H), 1.02 (s, 3H), 0.95 (t, *J* = 8.0 Hz, 21H), 0.86 (t, *J* = 7.9 Hz, 9H), 0.65 – 0.46 (m, 18H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 207.2, 151.7, 141.4, 137.2, 136.7, 136.0, 132.1, 126.8, 122.7, 121.3, 120.4, 107.3, 77.7, 74.5, 73.6, 72.8, 67.9, 58.5, 56.0, 52.9, 48.6, 39.4, 38.7, 33.2, 32.0, 30.2, 30.0, 27.6, 27.5, 26.8, 25.4, 25.1, 22.3, 19.1, 14.6, 14.0, 9.1, 7.2, 6.9, 6.9, 6.5, 5.2, 4.6. **HRMS (ESI)** *m/z* 944.6442[(M+H)$^+$; calcd for $C_{56}H_{94}NO_5Si_3$: 944.6440].

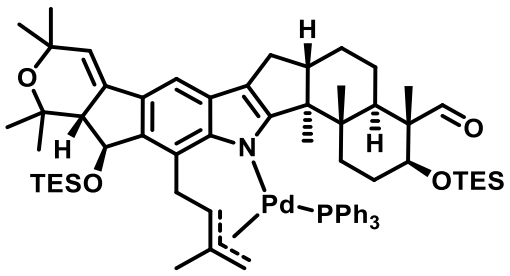
Method 2: using bromide (−)-**66**

In a 1 mL reaction vial, $Pd(OAc)_2$ (2.2 mg, 9.8 μmol, 0.125 eq.) and APhos (5.2 mg, 0.0195 mmol, 0.25 eq.) were dissolved in THF (100 μL), heated to reflux under nitrogen for 3 minutes, and the solvent was then removed under vacuum. To the resulting orange-colored residue was added CPME (780 μL) to produce a yellow solution. This solution was added to a reaction vial which contained a mixture of aniline (−)-**76** (47 mg, 0.078 mmol, 1 eq.), bromide (−)-**66** (71 mg, 0.156 mmol, 2 eq.), K_3PO_4 (100 mg, 0.47 mmol, 6 eq.), and sand (20 mg). The reaction vial was sealed under nitrogen, stirred at 600 RPM, 120 °C for 18 hours. The resulting dark brown colored mixture was cooled to room temperature, diluted with Et_2O, and filtered through a plug of silica. The filtrate was concentrated and purified using silica gel vacuum chromatography (eluted with a gradient of hexanes, 50:1 hexanes/EtOAc, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc) to provide the title compound (50 mg, 68%) as an off-white amorphous solid.



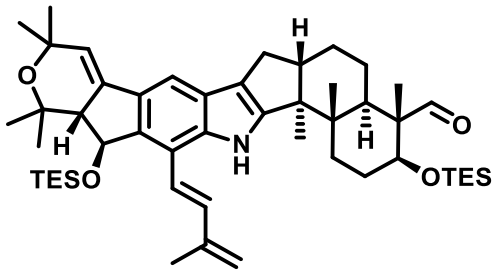
Carbonate (+)-84: In a reaction vial, indole (+)-**83** (74 mg, 0.078 mmol, 1 eq.) was dissolved in CH_2Cl_2 (500 μL), MeOH (2 mL). NH_4F (29 mg, 0.78 mmol, 10 eq.) was added to the solution. The resulting mixture was stirred at room temperature for 1.5 hours, then diluted with Et_2O, and filtered through a silica gel pad. The filtrate was concentrated *in vacuo* to provide the crude product as a pale-yellow oil. This oil was used directly for the next step without further purification. The crude product was dissolved in CH_2Cl_2 (2 mL), and pyridine (63 μL, 0.78 mmol, 10 eq.) was added. The resulting solution was cooled to 0 °C, and methyl chloroformate (24 μL, 0.31 mmol, 4 eq.) was added then

stirred at 0 °C for 1 hour. $NaHCO_3$ (saturated aqueous solution) was added, and the mixture was stirred at room temperature for 20 minutes to hydrolyze remaining methyl chloroformate. The organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product as a pale-yellow oil. This oil was purified using silica gel vacuum chromatography (eluted with a gradient of 50:1 hexanes/EtOAc, 25:1 hexanes/EtOAc, 13:1 hexanes/EtOAc, 6:1 hexanes/EtOAc) to provide the title compound (42 mg, 61%, 2 steps) as a pale-yellow foam. $[\alpha]_D^{25}$ +15.9 (*c* 0.05, $CHCl_3$). **IR** (neat) 3455, 2954, 2876, 1750, 1670, 1457, 1377, 1362, 1340, 1266, 1135, 1098, 1005, 862, 822, 789, 741 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.38 (s, 1H), 7.60 (s, 1H), 7.40 (s, 1H), 5.97 (d, *J* = 2.9 Hz, 1H), 5.74 – 5.65 (m, 1H), 5.27 (d, *J* = 3.9 Hz, 1H), 4.56 (s, 2H), 3.96 (dd, *J* = 16.4, 7.0 Hz, 1H), 3.85 (dd, *J* = 10.8, 4.4 Hz, 1H), 3.79 (s, 3H), 3.70 (dd, *J* = 16.2, 6.8 Hz, 1H), 2.83 (t, *J* = 3.4 Hz, 1H), 2.75 (td, *J* = 10.3, 3.6 Hz, 1H), 2.66 (dd, *J* = 13.3, 6.4 Hz, 1H), 2.31 (dd, *J* = 13.4, 10.6 Hz, 1H), 2.03 (dd, *J* = 12.6, 3.2 Hz, 1H), 1.97 (s, 3H), 1.94 – 1.86 (m, 1H), 1.81 (dd, *J* = 10.3, 6.0 Hz, 1H), 1.76 – 1.69 (m, 1H), 1.62 (ddd, *J* = 16.4, 12.2, 5.6 Hz, 1H), 1.50 (s, 3H), 1.48 – 1.45 (m, 1H), 1.37 (s, 3H), 1.31 (s, 3H), 1.17 (s, 3H), 1.13 (s, 3H), 1.03 (s, 3H), 0.95 (t, *J* = 7.9 Hz, 15H), 0.86 (t, *J* = 7.9 Hz, 9H), 0.57 (qd, *J* = 7.9, 2.8 Hz, 6H), 0.50 (qd, *J* = 7.9, 2.0 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 207.2, 155.9, 152.0, 141.2, 137.3, 136.5, 132.2, 131.0, 128.6, 126.8, 120.6, 120.4, 118.7, 107.6, 77.7, 77.4, 74.5, 73.6, 73.4, 72.8, 58.4, 56.1, 54.9, 53.1, 48.6, 39.4, 38.6, 34.8, 34.7, 33.2, 32.0, 31.7, 30.2, 30.0, 27.6, 27.4, 27.1, 26.8, 25.4, 25.4, 25.1, 22.3, 19.1, 14.6, 14.4, 9.1, 7.2, 7.0, 6.9, 6.5, 5.2, 5.2. **HRMS (ESI)** *m/z* 910.5475 [$(M+Na)^+$; calcd for $C_{52}H_{81}NO_7Si_2Na$: 910.5449].



Palladacycle (+)-85: In a reaction vial containing $[Pd(allyl)Cl]_2$ (4 mg, 0.011 mmol, 0.6 eq.), PPh_3 (12.5 mg, 0.048 mmol, 2.6 eq.) and $C_2H_4Cl_2$ (920 μL) were added. The resulting solution was stirred under nitrogen atmosphere at room temperature for 10 minutes, and the solution was then added to another vial containing carbonate (+)-**84** (16 mg, 0.018 mmol, 1 eq.). The reaction vial was sealed under nitrogen, and was stirred at 50 °C overnight, and the solvent was then removed *in vacuo*. The resulting pale-yellow foam residue was purified using silica gel MPLC (eluted with a gradient of hexanes, 50:1 hexanes/EtOAc, 25:1) to provide the title compound (15 mg, 70%) as a pale-yellow amorphous solid. $[\alpha]_D^{25}$ +39.4 (*c* 0.05, $CHCl_3$). **IR** (neat) 3281, 3055, 2952, 2875, 1731, 1670, 1457, 1436, 1377, 1362, 1339, 1243, 1136, 1096, 1004, 924, 862, 822, 784, 741, 694 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.74 (s, 1H), 9.37 (s, 1H), 7.62 – 7.57 (m, 7H), 7.44 – 7.39 (m, 9H), 5.95 (d, *J* = 3.0

Hz, 1H), 5.18 (d, *J* = 4.1 Hz, 1H), 4.32 – 4.18 (m, 1H), 4.10 (q, *J* = 10.4, 9.7 Hz, 2H), 3.87 – 3.74 (m, 1H), 2.92 (s, 1H), 2.87 – 2.77 (m, 1H), 2.67 (dd, *J* = 13.2, 6.4 Hz, 1H), 2.61 (s, 1H), 2.32 (dd, *J* = 13.3, 10.7 Hz, 2H), 2.10 (s, 3H), 2.01 (dd, *J* = 12.7, 3.3 Hz, 1H), 1.89 – 1.81 (m, 2H), 1.80 – 1.69 (m, 2H), 1.57 (s, 3H), 1.47 (s, 3H), 1.37 (s, 3H), 1.29 (s, 3H), 1.19 (s, 3H), 1.12 (s, 3H), 1.09 (s, 3H), 0.96 – 0.86 (m, 12H), 0.83 (t, *J* = 7.9 Hz, 9H), 0.52 (td, *J* = 8.9, 8.3, 4.0 Hz, 6H), 0.47 (q, *J* = 7.8 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 207.7, 153.1, 141.1, 136.7, 136.4, 134.3, 134.2, 134.2, 134.1, 133.2, 132.9, 131.8, 130.5, 128.7, 128.7, 128.6, 126.9, 121.1, 120.1, 118.0, 107.4, 97.6, 97.4, 78.1, 74.4, 73.9, 72.8, 62.7, 58.4, 56.3, 53.5, 48.8, 39.6, 38.6, 33.3, 32.0, 30.2, 29.8, 27.6, 27.4, 26.3, 25.6, 25.3, 22.2, 19.9, 19.0, 14.7, 9.1, 7.1, 7.0, 6.5, 5.3. **HRMS (ESI)** *m/z* 1180.5910 [$(M+H)^+$; calcd for $C_{68}H_{93}NO_4PPdSi_2$: 1180.5416].



Triene (+)-86: In a reaction vial containing palladacycle (+)-**85** (16 mg, 13 μmol, 1 eq.), toluene (2.7 mL) was added followed by the addition of NaO*t*-Bu (80 μL, 24 mg/mL in toluene, 20 μmol, 1.5 eq.). The reaction vial was sealed under nitrogen and heated to 55 °C for 11 hours. The reaction solution was diluted with hexanes then filtered through a pad of silica gel. The filtrate was then concentrated *in vacuo*. The resulting residue was purified using silica gel vacuum chromatography (eluted with a gradient of 50:1 hexanes/EtOAc, 25:1 hexanes/EtOAc) to provide the title compound (8 mg, 74%) as an amorphous solid. $[\alpha]_D^{25}$ +26.1 (*c* 0.15, $CHCl_3$). **IR** (neat) 2952, 2875, 1732, 1456, 1414, 1377, 1341, 1242, 1099, 1006, 863, 822, 786, 739 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.40 (s, 1H), 7.91 (s, 1H), 7.43 (s, 1H), 7.17 (d, *J* = 16.8 Hz, 1H), 6.88 (d, *J* = 16.7 Hz, 1H), 5.99 (d, *J* = 2.8 Hz, 1H), 5.31 (d, *J* = 4.0 Hz, 1H), 5.18 (s, 2H), 3.87 (d, *J* = 7.3 Hz, 1H), 2.85 (s, 1H), 2.82 (s, 1H), 2.70 (dd, *J* = 13.4, 6.4 Hz, 1H), 2.34 (dd, *J* = 13.2, 10.8 Hz, 1H), 2.12 (s, 3H), 2.09 – 1.87 (m, 3H), 1.85 (s, 1H), 1.75 (s, 1H), 1.64 (d, *J* = 11.6 Hz, 1H), 1.55 (s, 3H), 1.53 (s, 3H), 1.39 (s, 3H), 1.33 (s, 3H), 1.21 (s, 3H), 1.16 (s, 3H), 1.08 (s, 3H), 0.99 (s, 3H), 0.96 (t, *J* = 7.9 Hz, 9H), 0.83 (t, *J* = 7.9 Hz, 9H), 0.58 (qd, *J* = 7.8, 3.2 Hz, 6H), 0.46 (q, *J* = 7.9 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 207.2, 152.0, 142.9, 139.2, 138.0, 136.4, 134.0, 132.2, 127.3, 125.6, 120.8, 119.5, 119.1, 117.3, 108.8, 77.9, 77.4, 74.5, 73.7, 72.8, 58.4, 56.0, 53.3, 48.6, 39.5, 38.8, 33.4, 32.0, 30.2, 29.9, 27.6, 27.5, 25.4, 25.1, 22.3, 19.2, 18.8, 14.7, 9.1, 7.1, 6.9, 6.4, 5.3. **HRMS (ESI)** *m/z* 812.5456 [$(M+H)^+$; calcd for $C_{50}H_{78}NO_4Si_2$: 812.5469].

Note: after the tricyclic indole core was constructed, the late-stage intermediates displayed high instability towards air and acidic conditions. Special handling protocols for these intermediates were applied. Specific operation protocol was as following:

Purification protocol 1: Nitrogen-Purged Vacuum Silica Gel Column Chromatography

1) Hexanes was degassed by bubbling through nitrogen gas for 30 minutes and was mixed with silica gel and then loaded on a column. The silica gel loaded on the column was then dried completely through pressurized nitrogen.

2) All solvents for column chromatography were purged with nitrogen for at least 15 minutes before use.

3) During the column chromatography purification, a nitrogen balloon was attached to the top of the column while vacuum was applied at the outlet of the column.

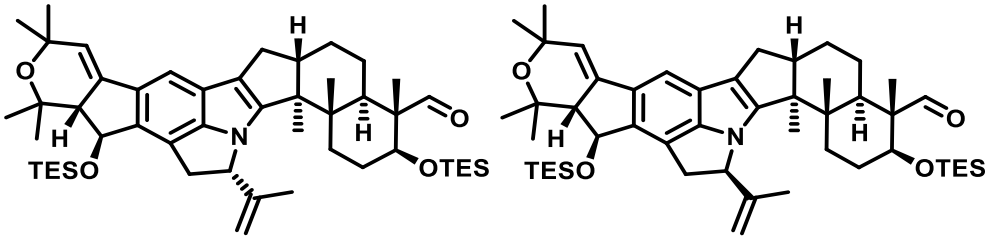
Fractions of interest were combined and evaporated using a rotary evaporator at room temperature and backfilled with nitrogen upon finishing evaporating.

Purification protocol 2: Nitrogen-Purged MPLC Silica Gel Column Chromatography

1) The MPLC silica gel column was completely dried with pressurized nitrogen gas.

2) All solvents for column chromatography were purged with nitrogen for at least 15 minutes before use.

Fractions of interest were combined and evaporated using a rotary evaporator at room temperature and backfilled with nitrogen upon finishing evaporating.



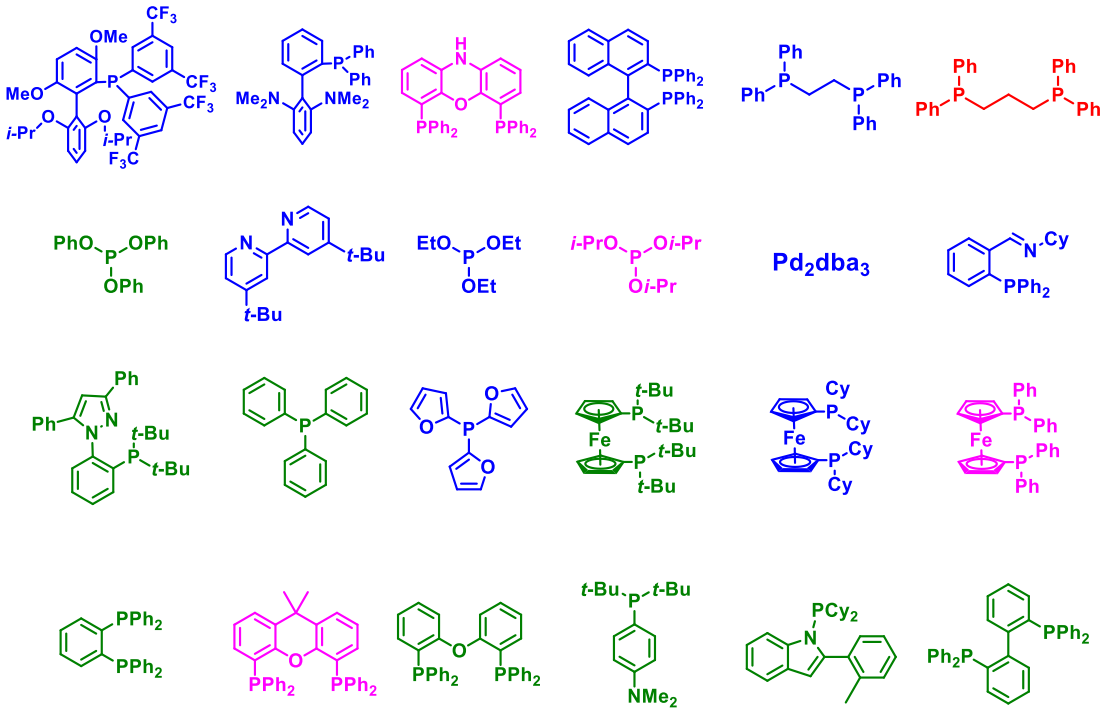
Indole (+)-88 and **Indole (+)-89**:

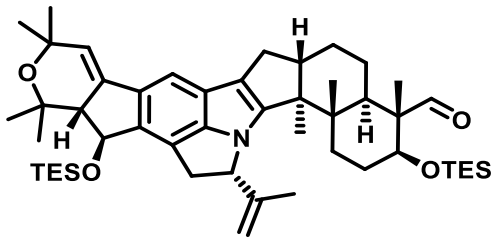
Method 1 (applying achiral ligand): In a reaction flask containing $[Pd(allyl)Cl]_2$ (5 mg, 0.014 mmol) and dppb (24 mg, 0.056 mmol), CH_2Cl_2 (100 μL) was added under nitrogen, and the solvent was then removed *in vacuo*, and the resulting residue was added another CH_2Cl_2 (4 mL) to provide the catalyst stock solution. This $[Pd(allyl)Cl]_2$/dppb catalyst stock solution {107 μL, containing 0.0125 eq. of $[Pd(allyl)Cl]_2$ and 0.05 eq. of dppb} was added to the reaction flask containing carbonate (+)-**84** (25 mg, 0.03 mmol, 1 eq.). The solvent was removed *in vacuo*, and to the resulting residue was added toluene (6 mL) followed by NaO*t*-Bu (179 μL, 24 mg/mL in toluene, 0.045 mmol, 1.5 eq.). The

reaction flask was sealed under nitrogen and stirred at room temperature for 17 hours. The reaction solution was diluted with hexanes and filtered through a pad of silica gel. The filtrate was then concentrated *in vacuo*. The resulting residue was purified using silica gel MPLC (eluted with a gradient of 100:1 hexanes/EtOAc/0.5% Et_3N, 50:1 hexanes/EtOAc/0.5% Et_3N)[21] to provide (+)-**88** (11 mg, 45%) as a white foam. $[\alpha]_D^{25}$ +47.7 (*c* 0.2, $CHCl_3$). **IR** (neat) 2954, 2876, 1733, 1457, 1411, 1377, 1363, 1337, 1300, 1240, 1096, 1043, 1008, 943, 924, 862, 823, 739, 683 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.36 (d, *J* = 2.5 Hz, 1H), 7.31 (s, 1H), 5.95 (d, *J* = 2.9 Hz, 1H), 5.27 (d, *J* = 8.5 Hz, 1H), 5.19 (d, *J* = 4.6 Hz, 1H), 4.88 (s, 1H), 4.76 (s, 1H), 4.19 (dd, *J* = 16.2, 8.7 Hz, 1H), 3.82 (d, *J* = 11.2 Hz, 1H), 3.36 (d, *J* = 16.0 Hz, 1H), 2.90 – 2.79 (m, 1H), 2.80 – 2.70 (m, 1H), 2.61 (dd, *J* = 13.4, 6.3 Hz, 1H), 2.38 (t, *J* = 12.1 Hz, 1H), 2.03 – 1.93 (m, 1H), 1.84 (t, *J* = 12.5 Hz, 1H), 1.71 (q, *J* = 14.5, 12.9 Hz, 4H), 1.64 – 1.55 (m, 1H), 1.51 (s, 3H), 1.46 (d, *J* = 2.4 Hz, 2H), 1.40 (s, 3H), 1.36 (s, 3H), 1.34 (s, 3H), 1.28 (s, 3H), 1.12 (s, 3H), 1.11 (s, 3H), 1.09 (s, 3H), 1.02 – 0.93 (m, 18H), 0.73 – 0.63 (m, 6H), 0.58 (qd, *J* = 7.9, 3.0 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 207.2, 153.3, 151.3, 145.8, 136.9, 133.9, 133.7, 121.5, 119.6, 119.5, 118.0, 112.4, 107.0, 77.3, 76.8, 74.2, 73.4, 72.5, 68.6, 59.3, 56.3, 53.4, 49.7, 41.6, 39.6, 38.8, 33.6, 32.1, 30.5, 30.1, 29.8, 27.8, 27.6, 25.5, 25.4, 22.9, 18.9, 17.7, 14.2, 9.1, 7.3, 6.9, 6.3, 5.3. **HRMS (ESI)** *m/z* 812.5464 [$(M+H)^+$; calcd for $C_{50}H_{78}NO_4Si_2$: 812.5469].

(+)-**89** (9 mg, 37%) was isolated as a white foam $[\alpha]_D^{25}$ +4.9 (*c* 0.1, $CHCl_3$). **IR** (neat) 2954, 2876, 1733, 1457, 1411, 1377, 1363, 1337, 1300, 1240, 1096, 1043, 1008, 943, 924, 862, 823, 739, 683 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.37 (s, 1H), 7.33 (s, 1H), 5.97 (d, *J* = 2.7 Hz, 1H), 5.20 (d, *J* = 8.5 Hz, 1H), 5.17 (d, *J* = 4.6 Hz, 1H), 4.84 (s, 1H), 4.66 (brs, 1H), 4.05 (dd, *J* = 16.1, 8.4 Hz, 1H), 3.92 – 3.79 (m, 1H), 3.52 (d, *J* = 16.1 Hz, 1H), 2.85 (d, *J* = 4.1 Hz, 1H), 2.76 (s, 1H), 2.68 (dd, *J* = 13.8, 6.4 Hz, 1H), 2.31 – 2.19 (m, 1H), 1.93 (dd, *J* = 31.2, 10.8 Hz, 2H), 1.76 (dq, *J* = 30.1, 14.8, 13.5 Hz, 4H), 1.56 (s, 1H), 1.50 (s, 3H), 1.46 – 1.39 (m, 2H), 1.36 (s, 3H), 1.33 (s, 3H), 1.28 (s, 3H), 1.11 (s, 3H), 1.10 (s, 3H), 1.05 (s, 3H), 0.96 (t, *J* = 7.9 Hz, 21H), 0.65 (q, *J* = 7.9 Hz, 6H), 0.57 (qd, *J* = 7.8, 2.6 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 207.3, 154.9, 151.0, 146.0, 136.8, 134.4, 133.9, 123.6, 119.7, 118.0, 112.7, 107.3, 77.4, 74.3, 73.7, 72.6, 68.9, 59.2, 56.3, 55.1, 47.0, 41.3, 39.9, 38.3, 32.1, 32.0, 30.3, 30.2, 29.8, 28.1, 27.2, 25.4, 25.1, 22.8, 18.8, 15.2, 9.1, 7.2, 7.0, 6.5, 5.2. **HRMS (ESI)** *m/z* 812.5481 [$(M+H)^+$; calcd for $C_{50}H_{78}NO_4Si_2$: 812.5469].

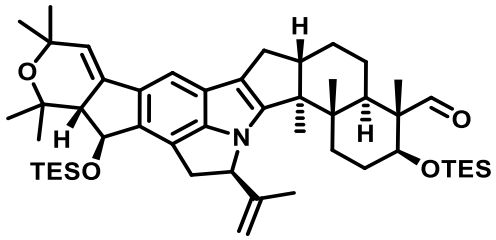
Ligands which were investigated for the above-mentioned reaction.





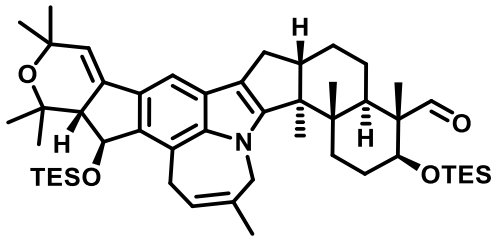
Indole (+)-88:

Method 2 (applying chiral ligand): A stock solution of $[Pd(allyl)Cl]_2$ (0.042 mg, 0.12 μmol, 0.01 eq.)/(*S,S,S*)-MonoPhos-BPA[22] (0.26 mg, 0.48 μmol, 0.04 eq.) in CH_2Cl_2 (20 μL) was added to a reaction flask containing carbonate (+)-**84** (10 mg, 11 μmol, 1 eq.). The solvent was removed *in vacuo*, and to the resulting residue was added toluene (2.4 mL). To the solution was then added NaO*t*-Bu (96 μL, 24 mg/mL in toluene, 0.024 mmol, 2.2 eq.). The reaction flask was sealed under nitrogen and stirred at room temperature for 17 hours. The reaction solution was diluted with hexanes then filtered through a pad of silica gel. The filtrate was concentrated *in vacuo*. The resulting residue was purified using silica gel MPLC (eluted with a gradient of 100:1 hexanes/EtOAc/0.5% Et_3N, 50:1 hexanes/EtOAc/0.5% Et_3N) to provide the title compound (4.2 mg, 47%) as a white foam.



Indole (+)-89:

Method 2: A stock solution of $[Pd(allyl)Cl]_2$ (0.054 mg, 0.15 μmol, 0.0125 eq.)/(*S*)-PipPhos (0.24 mg, 0.6 μmol, 0.05 eq.) in CH_2Cl_2 (20 μL) was added to the reaction flask containing carbonate (+)-**84** (10 mg, 11 μmol, 1 eq.). The solvent was removed *in vacuo*. To the resulting residue was added toluene (2.4 mL) followed by NaO*t*-Bu (96 μL, 24 mg/mL in toluene, 0.024 mmol, 2.2 eq.). The reaction flask was sealed under nitrogen and stirred at room temperature for 17 hours. The reaction solution was diluted with hexanes then filtered through a pad of silica gel. The filtrate was concentrated *in vacuo*. The resulting residue was purified using silica gel MPLC (eluted with a gradient of 100:1 hexanes/EtOAc/0.5% Et_3N, 50:1 hexanes/EtOAc/0.5% Et_3N) to provide the title compound (4 mg, 45%) as a white foam.

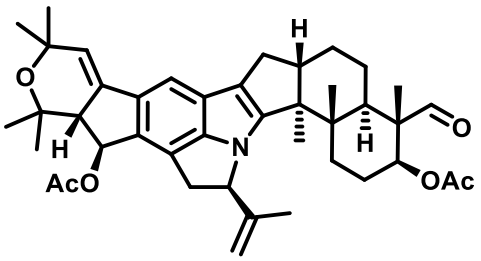


Indole (+)-90:

Method 1: $[PdCl(allyl)]_2$ (0.055 mg, 0.15 μmol, 0.0125 eq.)/dppb (0.26 mg, 0.6 μmol, 0.05 eq.) was added as a stock solution in CH_2Cl_2 (20 μL) to the reaction flask containing carbonate (+)-**84** (10 mg, 0.011 mmol, 1 eq.). The solvent was removed *in vacuo*, and to the resulting residue was added toluene (2.4 mL) followed by NaO*t*-Bu (72 μL, 24 mg/mL in toluene, 0.018 mmol, 1.5 eq.). The reaction flask was sealed under nitrogen and stirred at 55 °C for 17 hours. The reaction solution was diluted with hexanes then filtered through a pad of silica gel. The filtrate was concentrated *in vacuo*. The resulting residue was purified using silica gel MPLC (eluted with a gradient of 100:1 hexanes/EtOAc/0.5% Et_3N, 50:1 hexanes/EtOAc/0.5% Et_3N) to provide the title compound (8 mg, 87%) as a white foam. $[\alpha]_D^{25}$ +14.3 (*c* 0.5, $CHCl_3$). **IR** (neat) 3341, 2953, 2876, 1724, 1457, 1415, 1378, 1243, 1099, 1006, 827, 739 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.36 (s, 1H), 7.30 (s, 1H), 6.04 (t, *J* = 6.8 Hz, 1H), 5.93 (d, *J* = 2.8 Hz, 1H), 5.26 (d, *J* = 4.0 Hz, 1H), 5.09 (d, *J* = 14.1 Hz, 1H), 4.72 (d, *J* = 14.0 Hz, 1H), 3.99 (dd, *J* = 15.9, 6.3 Hz, 1H), 3.85 (q, *J* = 5.0 Hz, 1H), 3.66 (dd, *J* = 15.9, 7.3 Hz, 1H), 2.80 (t, *J* = 3.5 Hz, 2H), 2.62 (dd, *J* = 13.3, 6.6 Hz, 1H), 2.27 – 2.13 (m, 1H), 2.15 – 2.05 (m, 1H), 2.05 – 1.98 (m, 1H),

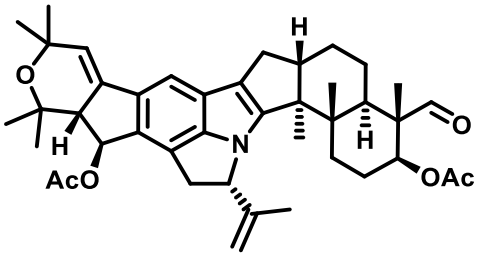
1.94 (d, J = 8.9 Hz, 2H), 1.92 (s, 3H), 1.87 – 1.79 (m, 1H), 1.77 – 1.68 (m, 1H), 1.58 (s, 3H), 1.51 (s, 3H), 1.36 (s, 3H), 1.30 (s, 3H), 1.26 (s, 3H), 1.15 (s, 3H), 1.07 (s, 3H), 0.98 (s, 3H), 0.95 (t, J = 7.9 Hz, 9H), 0.88 (t, J = 8.0 Hz, 9H), 0.58 (tt, J = 8.0, 3.7 Hz, 6H), 0.55 – 0.48 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 207.0, 153.6, 141.6, 136.3, 136.2, 134.8, 131.5, 128.6, 126.6, 122.5, 120.3, 117.9, 107.4, 77.9, 77.4, 74.5, 72.8, 72.8, 58.4, 56.9, 56.6, 49.4, 49.2, 40.8, 40.3, 35.2, 32.0, 30.1, 30.0, 27.8, 27.0, 26.2, 26.1, 25.6, 23.5, 22.4, 19.6, 14.6, 9.1, 7.2, 7.0, 6.5, 5.2. **HRMS (ESI)** *m/z* 812.5461 [$(M+H)^+$; calcd for $C_{50}H_{78}NO_4Si_2$: 812.5469].

Method 2 (the re-subjection experiment): A stock solution of $[Pd(allyl)Cl]_2$ (0.023 mg, 0.06 μmol, 0.0125 eq.)/dppb (0.1 mg, 0.25 μmol, 0.05 eq.) in CH_2Cl_2 (19 μL) was added to the reaction flask containing a 1.3:1 mixture of (+)-**88** and (+)-**89** (4 mg, 5 μmol, 1 eq.). The solvent was removed *in vacuo*, and to the resulting residue was added toluene (1 mL) followed by NaO*t*-Bu (30 μL, 24 mg/mL in toluene, 7.5 μmol, 1.5 eq.). The reaction flask was sealed under nitrogen and stirred at 55 °C for 17 hours. The reaction solution was diluted with hexanes then filtered through a pad of silica gel. The filtrate was concentrated *in vacuo*. The resulting residue was purified using silica gel MPLC (eluted with a gradient of 100:1 hexanes/EtOAc/0.5% Et_3N, 50:1 hexanes/EtOAc/0.5% Et_3N) to provide the title compound (3.6 mg, 90%) as a white foam.

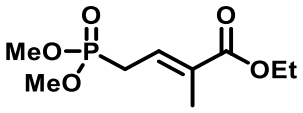


Acetate (−)-95: In a reaction flask, THF (0.5 mL) was added to indole (+)-**89** (19.4 mg, 0.024 mmol, 1 eq.) followed by the addition of TBAF (120 μL, 1M in THF, 0.12 mmol, 5 eq.). The resulting solution was stirred at room temperature for 3 hours. The solvent was removed, and to the residue was added CH_2Cl_2 (0.5 mL) followed by the addition of DMAP (ca. 1 mg), Et_3N (66 μL, 0.47 mmol, 20 eq.), and Ac_2O (25 μL, 0.24 mmol, 10 eq.). The resulting solution was stirred at room temperature for 2 hours and quenched with $NaHCO_3$ (saturated aqueous solution). The organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product as a pale-yellow oil. This oil was purified using silica gel vacuum chromatography (eluted with a gradient of 13:1 hexanes/EtOAc/0.5% Et_3N, 6:1 hexanes/EtOAc/0.5% Et_3N, 3:1 hexanes/EtOAc/0.5% Et_3N) to provide the title compound (10 mg, 62%) as a white amorphous solid. $[\alpha]_D^{25}$ −35.8 (*c* 0.1, $CHCl_3$). **IR** (neat) 2973, 1735, 1442, 1373, 1300, 1237, 1156, 1027, 912, 733, 647 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.30 (s, 1H), 7.33 (s, 1H), 6.29 (d, J = 5.8 Hz, 1H), 5.99 (d, J = 2.9 Hz, 1H), 5.18 (d, J = 8.3 Hz, 1H), 5.00 (dd, J = 11.2, 4.3 Hz, 1H), 4.79 (s, 1H), 4.75 (s, 1H), 3.99 (dd, J = 16.5, 8.3 Hz, 1H), 3.05 (d, J = 16.9 Hz, 1H), 2.97 (dd, J = 5.9, 2.9 Hz, 1H), 2.83 – 2.70 (m, 1H), 2.66 (dd, J = 13.7, 6.7

Hz, 1H), 2.25 (dd, *J* = 13.9, 10.7 Hz, 1H), 2.16 (s, 3H), 2.07 (s, 1H), 2.04 (s, 1H), 2.02 – 2.00 (m, 1H), 1.98 (s, 3H), 1.91 – 1.77 (m, 2H), 1.77 – 1.67 (m, 1H), 1.62 – 1.49 (m, 2H), 1.49 – 1.38 (m, 1H), 1.37 – 1.29 (m, 9H), 1.19 (s, 3H), 1.15 (s, 3H), 1.12 – 1.10 (m, 3H), 1.09 (s, 3H), 0.94 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 204.4, 171.1, 170.5, 154.6, 151.0, 146.3, 135.2, 134.1, 129.7, 123.9, 120.4, 120.0, 118.2, 113.1, 107.8, 76.1, 73.7, 73.6, 72.8, 69.0, 56.0, 55.2, 54.6, 47.1, 41.5, 40.0, 38.2, 32.2, 31.8, 29.9, 29.8, 28.1, 25.3, 25.0, 23.0, 22.9, 21.4, 21.2, 18.9, 15.2, 9.2. **HRMS (ESI)** *m/z* 668.3960 [(M+H)$^+$; calcd for $C_{42}H_{54}NO_6$: 668.3951].

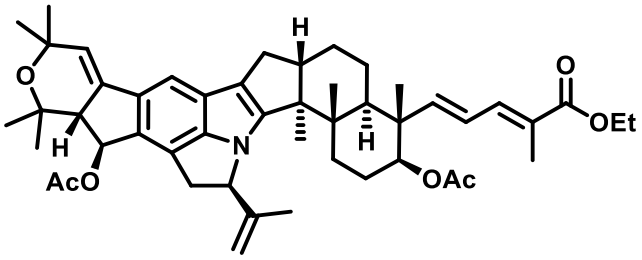


Acetate (−)-91: indole (+)-**88** (11 mg, 0.014 mmol, 1 eq.) was used for the reaction following the above-mentioned procedure to provide the title compound (5.9 mg, 63%) as a white amorphous solid. $[\alpha]_D^{25}$ −43.2 (*c* 0.2, $CHCl_3$). **IR** (neat) 2973, 1735, 1446, 1373, 1236, 1156, 1026, 913, 733 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.31 (s, 1H), 7.34 (s, 1H), 6.35 (d, *J* = 5.8 Hz, 1H), 6.00 (d, *J* = 3.0 Hz, 1H), 5.20 (dd, *J* = 8.7, 2.6 Hz, 1H), 5.01 (d, *J* = 9.8 Hz, 1H), 4.87 (s, 1H), 4.69 (s, 1H), 3.88 (dd, *J* = 16.4, 8.6 Hz, 1H), 3.32 (dd, *J* = 16.3, 2.5 Hz, 1H), 2.96 (dd, *J* = 5.8, 2.9 Hz, 1H), 2.75 (s, 1H), 2.63 (dd, *J* = 13.3, 6.4 Hz, 1H), 2.41 (dd, *J* = 13.4, 10.9 Hz, 1H), 2.16 (s, 3H), 2.15 – 2.06 (m, 1H), 2.01 (s, 3H), 1.97 – 1.83 (m, 3H), 1.80 – 1.69 (m, 3H), 1.69 – 1.60 (m, 1H), 1.60 – 1.49 (m, 1H), 1.43 (s, 3H), 1.41 – 1.31 (m, 9H), 1.20 (s, 3H), 1.18 – 1.09 (m, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 204.2, 170.9, 170.4, 152.9, 151.2, 145.4, 135.3, 134.4, 129.2, 121.7, 120.4, 119.8, 118.1, 112.6, 107.5, 76.1, 73.6, 73.4, 72.7, 68.7, 56.0, 54.5, 53.5, 49.7, 41.4, 39.7, 38.7, 33.4, 32.1, 29.9, 29.8, 27.8, 25.3, 25.2, 23.1, 23.0, 21.2, 21.1, 18.9, 17.8, 14.2, 9.1. **HRMS (ESI)** *m/z* 668.3960 [(M+H)$^+$; calcd for $C_{42}H_{54}NO_6$: 668.3951].

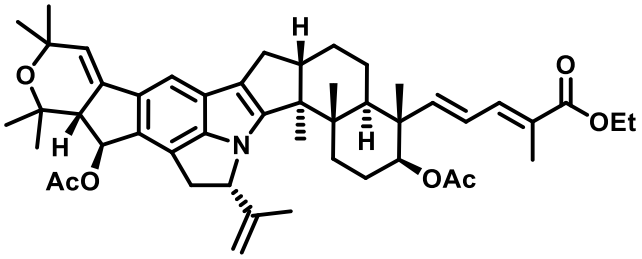


Phosphonate 92: To ethyl (*E*)-4-bromo-2-methylbut-2-enoate[23] (252 mg, 1.2 mmol, 1 eq.) was added trimethyl phosphate (433 μL, 3.7 mmol, 3 eq.). The neat mixture was heated to 100 °C for 2 hours. Excessive trimethyl phosphate was removed by distillation at 100 °C under high vacuum, and the residue was purified using silica gel MPLC (eluted with hexanes/acetone, 3:1) to provide the title compound (250 mg, 88%) as a colorless oil. **IR** (neat) 3480, 2956, 2852, 1709, 1650, 1464, 1367, 1256, 1178, 1106, 1027, 839, 751, 711, 650 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.76 (q, *J* = 6.8 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.79 (d, *J* = 10.9 Hz, 6H), 2.78 (dd, *J* = 23.4, 8.2 Hz, 2H), 1.91 (d, *J* = 3.9 Hz,

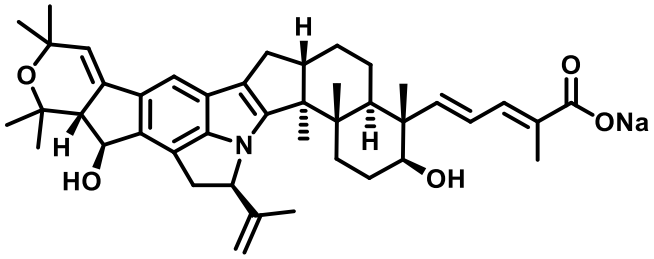
4H), 1.32 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.2 (d, J = 3.6 Hz), 132.0 (d, J = 13.7 Hz), 129.6 (d, J = 11.5 Hz), 60.8, 52.8 (d, J = 6.4 Hz), 27.1, 26.0, 14.2 , 12.5 (d, J = 2.5 Hz). **HRMS (ESI)** *m/z* 237.0886 [$(M+H)^+$; calcd for $C_9H_{18}O_5P$: 237.0892].



Enoate (−)-96: In a reaction flask, THF (1.6 mL) was added to phosphonate **92** (33 mg, 0.14 mmol, 20 eq.) and was cooled to −78 °C. LHMDS (117 μL, 1 M in THF, 0.117 mmol, 17 eq.) was then added at −78 °C, and the resulting yellow solution was stirred at 0 °C for 15 minutes and was then cooled to −78 °C again. Next, acetate (−)-**95** (4.6 mg, 6.9 μmol, 1 eq.) was dissolved in THF (250 μL), and the resulting solution was added via a plastic syringe to the −78 °C anion solution. The resulting solution was warmed slowly to room temperature and stirred for 17 hours and was then quenched with $NaHCO_3$ (saturated aqueous solution). The organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to provide the crude product as a pale-yellow oil. This oil was purified using silica gel vacuum chromatography (eluted with a gradient of 13:1 hexanes/EtOAc/0.5% Et_3N, 6:1 hexanes/EtOAc/0.5% Et_3N, 3:1 hexanes/EtOAc/0.5% Et_3N) to provide the title compound (4.1 mg, 77%) as a white foam after lyophilizing. $[\alpha]_D^{25}$ −45.7 (*c* 0.05, $CHCl_3$). **IR** (neat) 3404, 2928, 2855, 1735, 1698, 1456, 1366, 1242, 1201, 1133, 1067, 1027, 836, 799, 751, 720 cm^{-1}. **^{1}H NMR** [500 MHz, $(CD_3)_2CO$] δ 7.35 (s, 1H), 7.17 (d, J = 11.2 Hz, 1H), 6.40 (dd, J = 15.4, 11.2 Hz, 1H), 6.28 (d, J = 6.1 Hz, 1H), 6.11 (d, J = 2.9 Hz, 1H), 5.99 (d, J = 15.5 Hz, 1H), 5.43 (dd, J = 8.5, 1.9 Hz, 1H), 4.87 (dt, J = 4.6, 2.5 Hz, 2H), 4.75 (dd, J = 10.4, 5.7 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 3.98 (dd, J = 16.5, 8.4 Hz, 1H), 3.15 (dd, J = 16.4, 1.8 Hz, 1H), 2.81 – 2.73 (m, 0H), 2.67 (dd, J = 13.8, 6.5 Hz, 1H), 2.26 (dd, J = 13.8, 10.8 Hz, 1H), 2.16 (s, 3H), 2.11 – 2.08 (m, 1H), 1.93 (d, J = 1.3 Hz, 4H), 1.92 (s, 3H), 1.91 – 1.88 (m, 2H), 1.86 – 1.69 (m, 4H), 1.68 – 1.55 (m, 1H), 1.52 (ddt, J = 9.7, 6.1, 3.7 Hz, 3H), 1.39 – 1.34 (m, 2H), 1.32 (s, 3H), 1.29 (s, 3H), 1.27 (s, 3H), 1.22 (d, J = 5.4 Hz, 3H), 1.18 (s, 3H), 1.16 (s, 3H), 1.14 (s, 3H), 1.03 (s, 3H). **^{13}C NMR** [126 MHz, $(CD_3)_2CO$] δ 170.3, 169.4, 167.5, 154.5, 152.3, 151.5, 146.2, 138.2, 135.3, 133.7, 129.5, 125.4, 124.5, 123.3, 119.9, 118.2, 112.6, 107.6, 77.6, 75.2, 72.9, 72.1, 68.7, 60.0, 56.0, 55.4, 47.1, 45.6, 45.0, 40.8, 38.5, 31.7, 31.4, 29.4, 29.2, 27.6, 25.2, 24.0, 23.3, 22.3, 20.1, 20.1, 18.7, 14.4, 13.7, 11.9, 11.7. **HRMS (ESI)** *m/z* 600.4490 [$(M+Na)^+$; calcd for $C_{49}H_{63}NNaO_7$: 600.4502].



Enoate (–)-93: Acetate (–)-**91** (5.9 mg, 0.088 mmol, 1 eq.) was used for the reaction following the above-mentioned procedure to provide the title compound (5.5 mg, 80%) as a white foam after lyophilizing. $[\alpha]_D^{25}$ –21.4 (*c* 0.03, $CHCl_3$). **IR** (neat) 3429, 2929, 1736, 1703, 1636, 1448, 1372, 1243, 1133, 1028, 837, 799, 751, 720 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33 (s, 1H), 7.18 (d, *J* = 11.0 Hz, 1H), 6.34 (d, *J* = 5.7 Hz, 1H), 6.27 (dd, *J* = 15.4, 11.2 Hz, 1H), 5.98 (d, *J* = 3.0 Hz, 1H), 5.81 (d, *J* = 15.4 Hz, 1H), 5.28 – 5.10 (m, 1H), 4.84 (s, 1H), 4.69 (t, *J* = 7.9 Hz, 1H), 4.66 (s, 1H), 4.22 (q, *J* = 7.2 Hz, 2H), 3.87 (dd, *J* = 16.4, 8.6 Hz, 1H), 3.34 – 3.25 (m, 1H), 2.94 (dd, *J* = 6.0, 2.9 Hz, 1H), 2.71 (s, 1H), 2.60 (dd, *J* = 13.3, 6.3 Hz, 1H), 2.37 (dd, *J* = 13.2, 11.0 Hz, 1H), 2.14 (s, 3H), 1.97 (s, 3H), 1.95 (s, 3H), 1.90 – 1.76 (m, 3H), 1.75 – 1.63 (m, 3H), 1.63 – 1.52 (m, 2H), 1.52 – 1.44 (m, 3H), 1.41 (s, 3H), 1.38 – 1.29 (m, 10H), 1.18 (s, 3H), 1.13 (s, 3H), 1.10 (s, 3H), 1.07 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.9, 170.7, 168.6, 152.8, 151.7, 145.3, 138.4, 135.4, 134.3, 129.0, 126.0, 125.0, 121.7, 120.3, 119.8, 118.1, 112.6, 107.4, 78.1, 77.3, 76.1, 73.6, 72.7, 68.7, 60.7, 56.0, 53.9, 49.8, 45.7, 45.1, 41.3, 39.2, 33.6, 32.1, 29.9, 29.8, 27.8, 25.5, 24.4, 23.8, 23.0, 21.3, 21.2, 19.3, 17.8, 14.5, 14.2, 12.9, 12.3. **HRMS (ESI)** *m/z* 600.4524 [(M+Na)$^+$; calcd for $C_{49}H_{63}NNaO_7$: 600.4502].



(–)-Nodulisporic Acid B (2)-Sodium Salt: In a reaction vial containing enoate (–)-**96** (5 mg, 0.0064 mmol, 1 eq.), LiOH (100 μL, 1M aqueous solution) and 1,4-dioxane (300 μL) were added. The resulting opaque mixture was stirred at room temperature for 24 hours. The solvent was removed *in vacuo*. The resulting residue was added HOAc (100 μL, 1M in EtOAc), and the solvent was again removed *in vacuo*. The residue was next dissolved in minimal amount of CH_2Cl_2 and was loaded on a mini-scale[24] silica gel column (eluted in absence of air, with a gradient of 1:1 hexanes/EtOAc/0.1% HOAc, then 1:2 hexanes/EtOAc/0.1% HOAc) to provide nodulisporic acid B-free acid (2.6 mg, 61%) [note: the free acid is highly unstable. Spontaneous C(24)-OH elimination happened immediately upon storage as the free acid)]. After all volatiles were removed under high vacuum, $(CD_3)_2CO$ (300 μL) was immediately added to the residue followed by the addition of Na_2CO_3 (ca. 2~4 mg).

$[\alpha]_D^{25}$ (lit.) : –40 (c 0.4, MeOH)

$[\alpha]_D^{25}$ (syn.) : –27 (c 0.02, MeOH)

IR (lit.) : 3275, 2920, 2852, 1634, 1454, 1410, 1377, 1224 cm^{-1}

IR (syn.) : 3395, 2927, 2860, 1635, 1442, 1408, 1377, 1227 cm^{-1}

UV (MeOH) λ_{max} (lit.) : 273, 266, 322, 335 nm

UV (MeOH) λ_{max} (syn.): 272, 266, 322, 336 nm

HRMS (lit.) : *m/z* 666.4141 [$(M+H)^+$; calcd for $C_{45}H_{56}NO_5$: 666.4158]

HRMS (syn.): *m/z* 666.4180 [$(M+H)^+$; calcd for $C_{43}H_{56}NO_5$: 666.4158]

No.	Lit. [500 MHz, $(CD_3)_2CO$]	Syn. [500 MHz, $(CD_3)_2CO$]	Difference (ppm)
2			
3			
4			
5	1.8 (m), 2.0 (m)	1.8 (m), 2.0 (m)	0.0, 0.0
6	1.78 (m, 2H)	1.74 (m, 2H)	-0.04
7	3.48 (m)	3.48 (m)	0.00
8			
9	1.75 (m)	1.74 (m)	-0.01
10	1.62 (m, 2H)	1.62 (m, 2H)	0.00
11	1.45 (m, 2H)	1.47 (m, 2H)	+0.02
12	2.70 (m)	2.74 (m)	+0.04
13	2.25 (m), 2.60 (m)	2.21 (m), 2.62 (m)	-0.04, +0.02
14			
15			
16	7.25 (s)	7.24 (s)	-0.01
17			
18			
19	5.93 (d, J=3.0)	5.98 (d, J=2.9)	+0.05
20			
22			
23	2.67 (dd, J=3.0, 6.0)	2.65 (dd, J=2.7, 6.0)	-0.02
24	4.92 (d, J=6.0)	4.91 (d, J=6.1)	-0.01
25			
26			
27			
28	0.96 (s)	0.96 (s)	0.00
29	1.13 (s)	1.11 (s)	-0.02
30	1.07 (s)	1.07 (s)	0.00
31	1.29 (s)	1.28 (s)	-0.01
32	1.25 (s)	1.24 (s)	-0.01
33	1.10 (s)	1.09 (s)	-0.01
34	1.40 (s)	1.38 (s)	-0.02

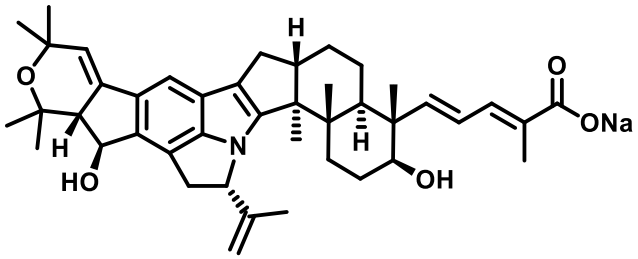
1'	3.5 (d, J=16.0)	3.49 (d, J=15.5)	-0.01
	4.0 (dd, J=8.0, 16.0)	4.05 (dd, J=8.4, 16.4)	+0.05
2'	5.35 (d, J=8.0)	5.37 (d, J=8.5)	+0.02
3'			
4'	4.79 (s), 4.82 (s)	4.79 (s), 4.82 (s)	0.00
5'	1.24 (s)	1.20 (s)	-0.04
1''	5.96 (d, J=15.0)	5.99 (d, J=15.6)	+0.03
2''	6.38 (dd, J=15.0, 13.5)	6.37 (dd, J=15.4, 11.2)	
3''	7.22 (d, J=13.5)	7.21 (d, J=11.2)	-0.01
4''			
5''			
6''	1.9 (brs)	1.9 (d, J=1.1)	0.00

No.	Lit. [500 MHz, $(CD_3)_2CO$]	Syn. [500 MHz, $(CD_3)_2CO$]	Difference (ppm)
2	151.9	152	+0.1
3	56.1	56.3	+0.2
4	39.6	39.5	-0.1
5	32.8	32.9	+0.1
6	27.3	27.5	+0.2
7	76.9	77.1	+0.2
8	47.9	48.1	+0.2
9	45.4	45.5	+0.1
10	25	25.2	+0.2
11	26.2	26.4	+0.2
12	47.9	48	+0.1
13	28.5	28.6	+0.1
14	120.9	120.9	0.0
15	124.1	124.2	+0.1
16	107.9	108.1	+0.2
17	133.9	134	+0.1
18	135.6	135.8	+0.2
19	119.6	119.8	+0.2
20	72.6	72.7	+0.1
22	74.1	74.2	+0.1
23	60.5	60.6	+0.1
24	75.6	75.7	+0.1
25	137.4	137.5	+0.1
26	118.5	118.6	+0.1
27	155.7	155.8	+0.1
28	15.3	15.4	+0.1
29	19.5	19.7	+0.2
30	11.7	11.9	+0.2
31	30.3	30.6	+0.3
32	32.4	32.5	+0.1
33	23.6	23.7	+0.1
34	30.5	30.6	+0.1

1'	41.1	41.2	+0.1
2'	69.8	69.9	+0.1
3'	147.5	147.6	+0.1
4'	112.7	112.9	+0.2
5'	17	17.1	+0.1
1''	154.8	155.2	+0.4
2''	125.7	125.7	0.0
3''	139.6	139.9	+0.3
4''	125.7	125.7	0.0
5''	170.4	169.9	-0.5
6''	12.9	12.9	0.0

Note 1: Spectra comparison of nodulisporic acid B was based on the publication: "Ondeyka, J. G.; Dahl-Roshak, A. M.; Tkacz, J. S.; Zink, D. L.; Zakson-Aiken, M.; Shoop, W. L.; Goetz, M. A.; Singh, S. B. *Bioorg Med Chem Lett* **2002**, *12*, 2941."

Note 2: The value difference of the optical rotation may resulted from various factors such as instrumental stability, solvent purity (degree of oxygen), sample purity, etc.

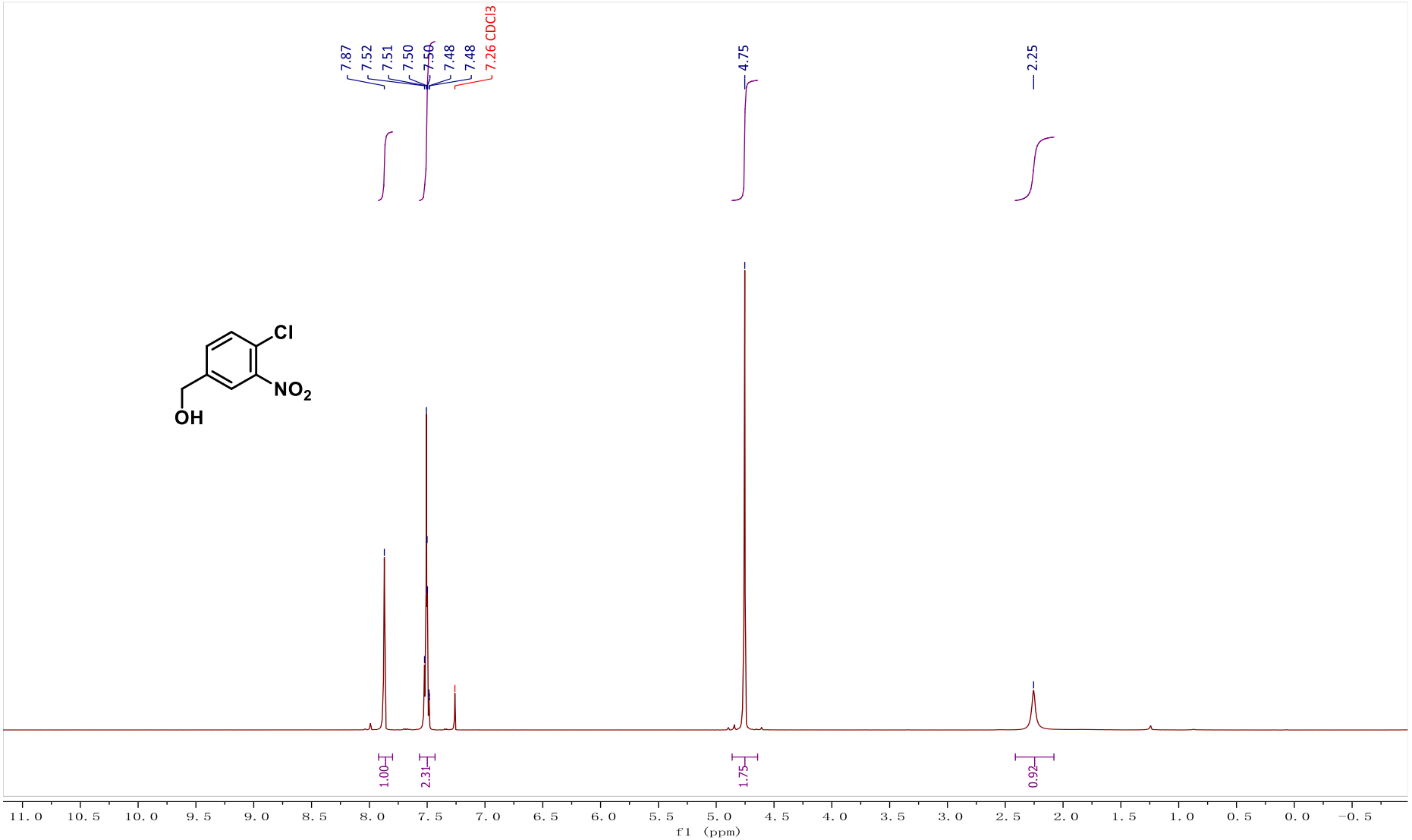


(–)-2-epi-Nodulisporic Acid B (94)-Sodium Salt: Enoate (–)-**93** (7 mg, 0.009 mmol, 1 eq.) was used for the reaction following the above-mentioned procedure to provide 2-epi-Nodulisporic Acid B-free acid (4.7 mg, 78%) which was also immediately added $CDCl_3$ (300 μL) followed by Na_2CO_3 (ca. 2 mg). $[\alpha]_D^{25}$ –4.8 (*c* 0.05, $CHCl_3$). **IR** (neat) 2925, 1706, 1377, 1260, 1031, 800 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.32 – 7.29 (m, 2H), 6.39 (dd, *J* = 15.3, 11.2 Hz, 1H), 5.94 (d, *J* = 2.8 Hz, 1H), 5.85 (d, *J* = 15.4 Hz, 1H), 5.27 (d, *J* = 8.5 Hz, 1H), 5.02 (d, *J* = 5.6 Hz, 1H), 4.86 (s, 1H), 4.71 (s, 1H), 4.20 (dd, *J* = 16.5, 8.6 Hz, 1H), 3.43 (d, *J* = 16.8 Hz, 1H), 3.40 – 3.35 (m, 1H), 2.72 (s, 1H), 2.65 (s, 1H), 2.60 (dd, *J* = 13.2, 6.3 Hz, 1H), 2.42 – 2.32 (m, 1H), 2.15 – 2.02 (m, 1H), 1.98 (s, 3H), 1.80 (dd, *J* = 20.9, 11.2 Hz, 3H), 1.72 – 1.52 (m, 3H), 1.49 (s, 3H), 1.46 (s, 3H), 1.39 (s, 2H), 1.35 (s, 3H), 1.34 (s, 3H), 1.16 (s, 3H), 1.10 (s, 3H), 1.08 (s, 3H), 1.06 (s, 3H). **^{13}C NMR** [126 MHz, $(CD_3)_2CO$] δ 154.0, 152.3, 147.3, 137.6, 135.1, 134.2, 121.8, 120.7, 119.8, 118.5, 112.3, 107.8, 76.8, 75.6, 74.2, 72.7, 69.4, 68.1, 60.8, 54.5, 50.8, 48.1, 47.0, 45.2, 41.7, 40.1, 34.6, 32.6, 30.7, 29.3, 28.4, 27.7, 26.4, 26.2, 25.5, 23.8, 19.5, 18.0, 14.6, 11.8. **HRMS (ESI)** *m/z* 666.4166 [$(M+H)^+$; calcd for $C_{43}H_{56}NO_5$: 666.4158].

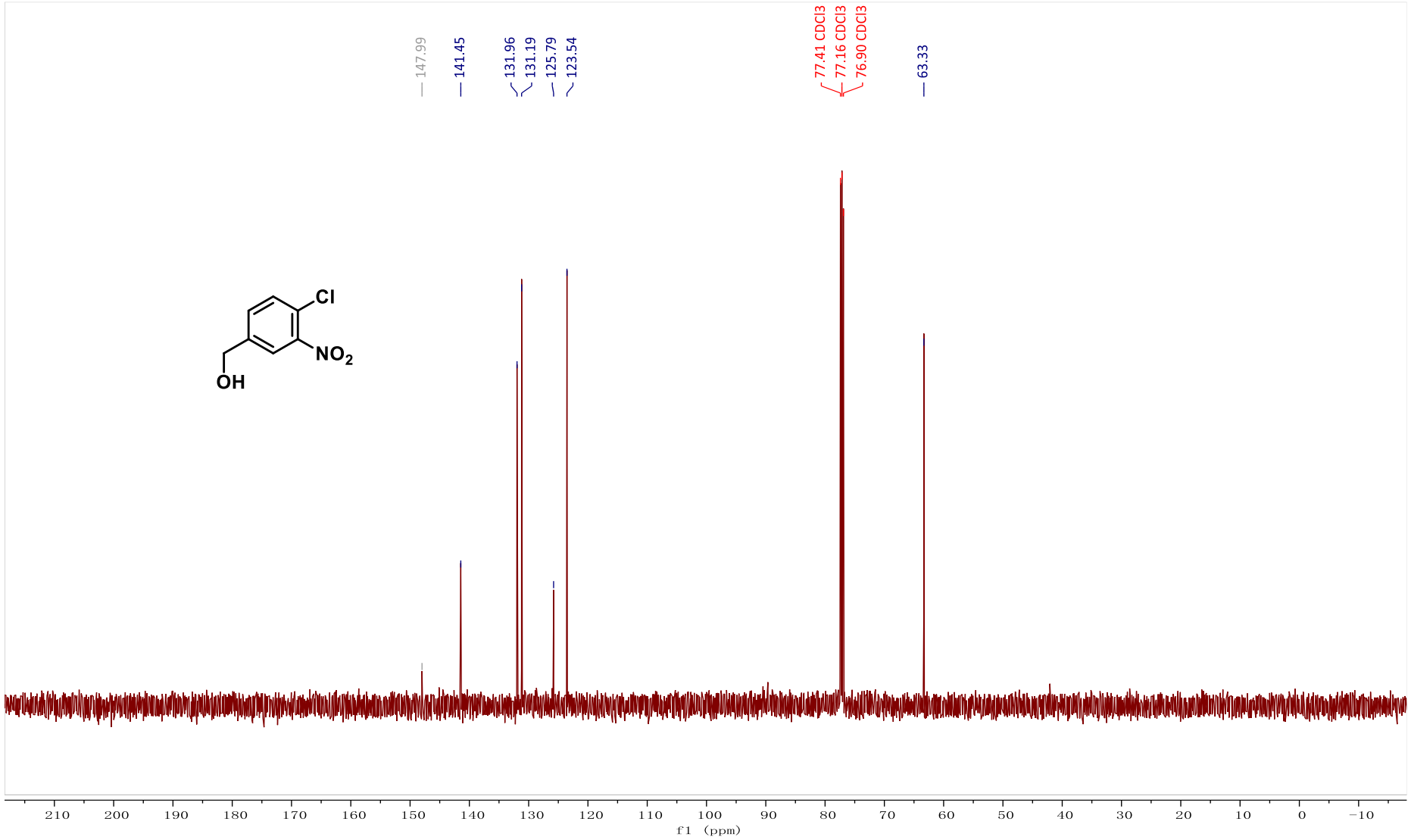
Notes and References

(1) Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879.
(2) Benzyltrimethylammonium dichloroiodide was prepared in a 100-gram scale batch as a yellow, crystalline solid. Kajigaeshi, S.; Kakinami, T.; Yamasaki, H.; Fujisaki, S.; Kondo, M.; Okamoto, T. *Chem. Lett.* **1987**, *16*, 2109.
(3) KF/Celite was prepared according to the following reference: Ando, T.; Yamawaki, J. *Chem. Lett.* **1979**, *8*, 45.
(4) The quality of CuBr·Me_2S is crucial for the success of this reaction. Copper(I) bromide dimethyl sulfide complex was prepared by the method, outlined in the publication (Theis, A. B.; Townsend, C. A. *Synth. Commun.* **1981**, *11*, 157.), as a white, free flowing, crystalline solid. This solid is stable under N_2 for months.
(5) THF should be free of oxygen. If a brown color developed upon addition of THF, this may indicate the presence of oxygen, and this reaction should not be conducted.
(6) Vinyl magnesium bromide solution in THF was prepared by the method (Fuson, R. C.; Mon, M. T. *J. Org. Chem.* **1961**, *26*, 756.) as a clean, light yellow solution with the concentration varied from 0.3 M to 0.7 M, which was titrated by using Love's method (Love, B. E.; Jones, E. G. *J. Org. Chem.* **1999**, *64*, 3755.).
(7) If the solution color was dark orange instead of dark emerald green after finishing addition of vinyl magnesium bromide solution, this may indicate that the cuprate reagent was not generated properly (often because oxygen was not removed from the solvent) and the reaction should not be conducted.
(8) Prepared via the published method: Smith, A. B., III; Kurti, L.; Davulcu, A. H.; Cho, Y. S. *Org. Process Res. Dev.* **2007**, *11*, 19.
(9) This product is stable, in absence of moisture, under N_2 in a −20 °C refrigerator for months.
(10) The yield may vary from factors such as the oxygen content, time of purification, etc.
(11) Prepared via the following published method: Eberbach, W.; Trostmann, U. *Chem. Ber.* **1985**, *118*, 4035.
(12) All solvents were purged through nitrogen for 15 minutes prior to use.
(13) Failure to keep the anion solution frozen upon adding electrophiles may result in mixture of diastereomers.
(14) Only for characterization purpose. The crude product was unstable to silica chromatography and was carried directly to the next step without further purification.
(15) This reaction must be conducted in the absence of air.
(16) Using of CuI, CuBr-Me_2S, or CuTC yielded no product.
(17) All solvents were purged through nitrogen for 15 minutes prior to use.
(18) All solvents were purged through nitrogen for 15 minutes prior to use.
(19) Prepared according to the literature procedure: Martínez, M. M.; Hoppe, D. *Eur. J. Org. Chem.* **2005**, *2005*, 1427.
(20) This product should be freshly prepared prior to use and is highly unstable at −20 °C (ca. several hours). The stability increased upon storage with copper wire at −20 °C (several days).
(21) All solvents were purged through nitrogen for 15 minutes prior to use.
(22) (*S,S,S*)-(+)-(3,5-Dioxa-4-phosphacyclohepta[2,1-a:3,4-a']dinaphthalen-4-yl)bis(1-phenylethyl)amine
(23) Prepared from ethyl tiglate via the procedure from the following publication: Chakor, N. S.; Musso, L.; Dallavalle, S. *J. Org. Chem.* **2009**, *74*, 844.
(24) Glass pipet (0.7 cm wide and 5 cm long) loaded with silica gel.

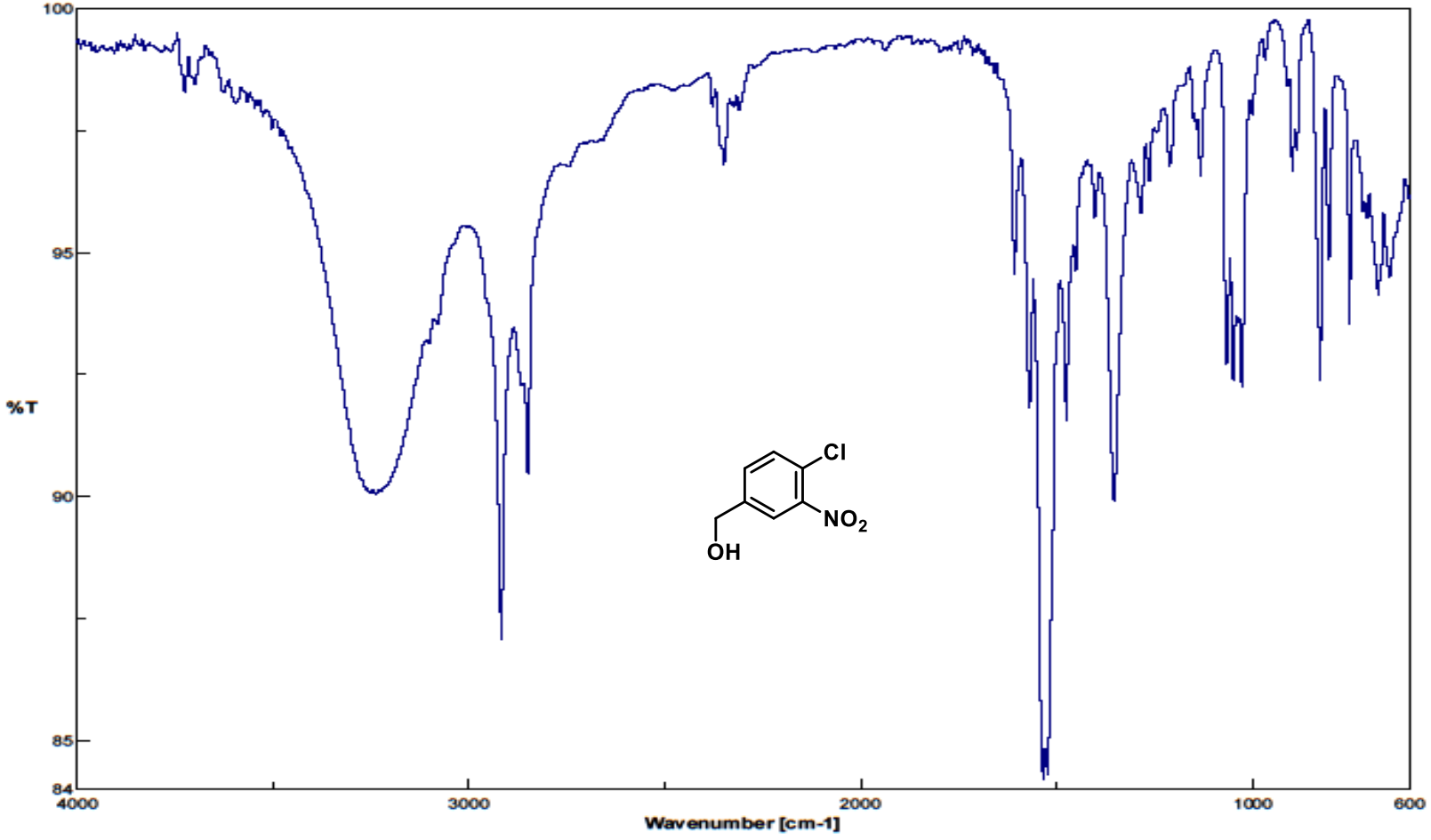
3. Spectroscopic Data



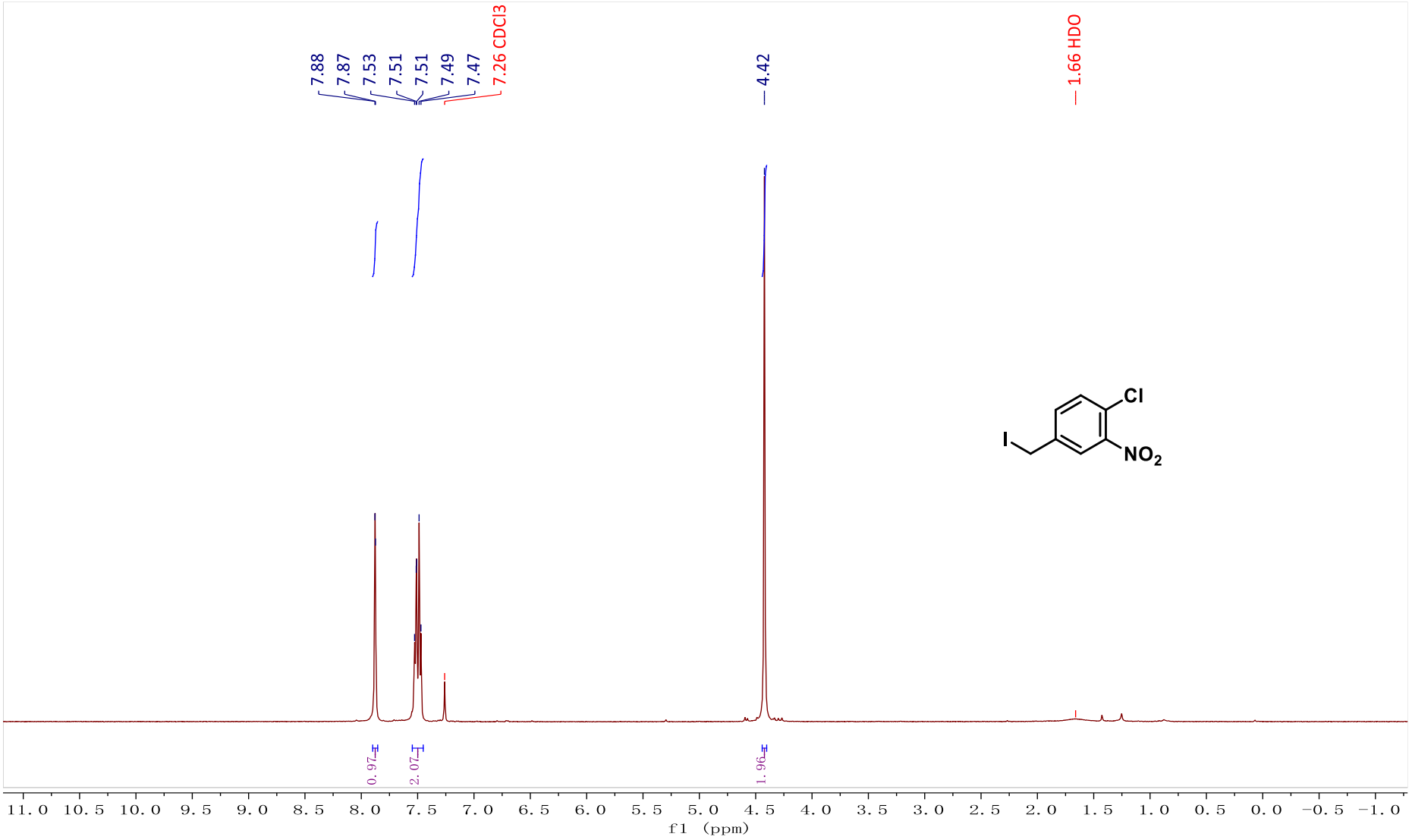
^{1}H NMR (500 MHz) Spectrum of Compound **S10** in $CDCl_3$



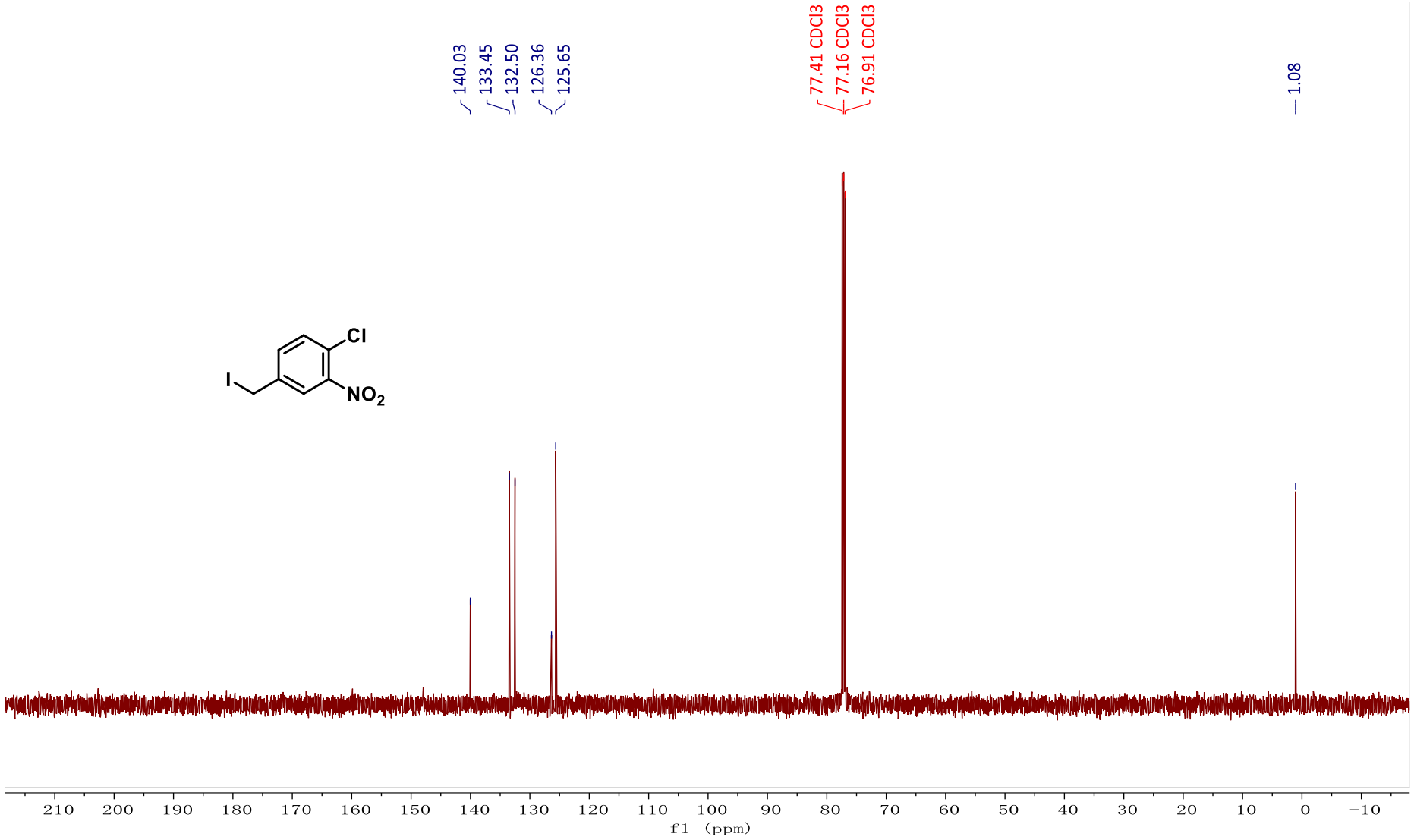
^{13}C NMR (126 MHz) Spectrum of Compound **S10** in $CDCl_3$



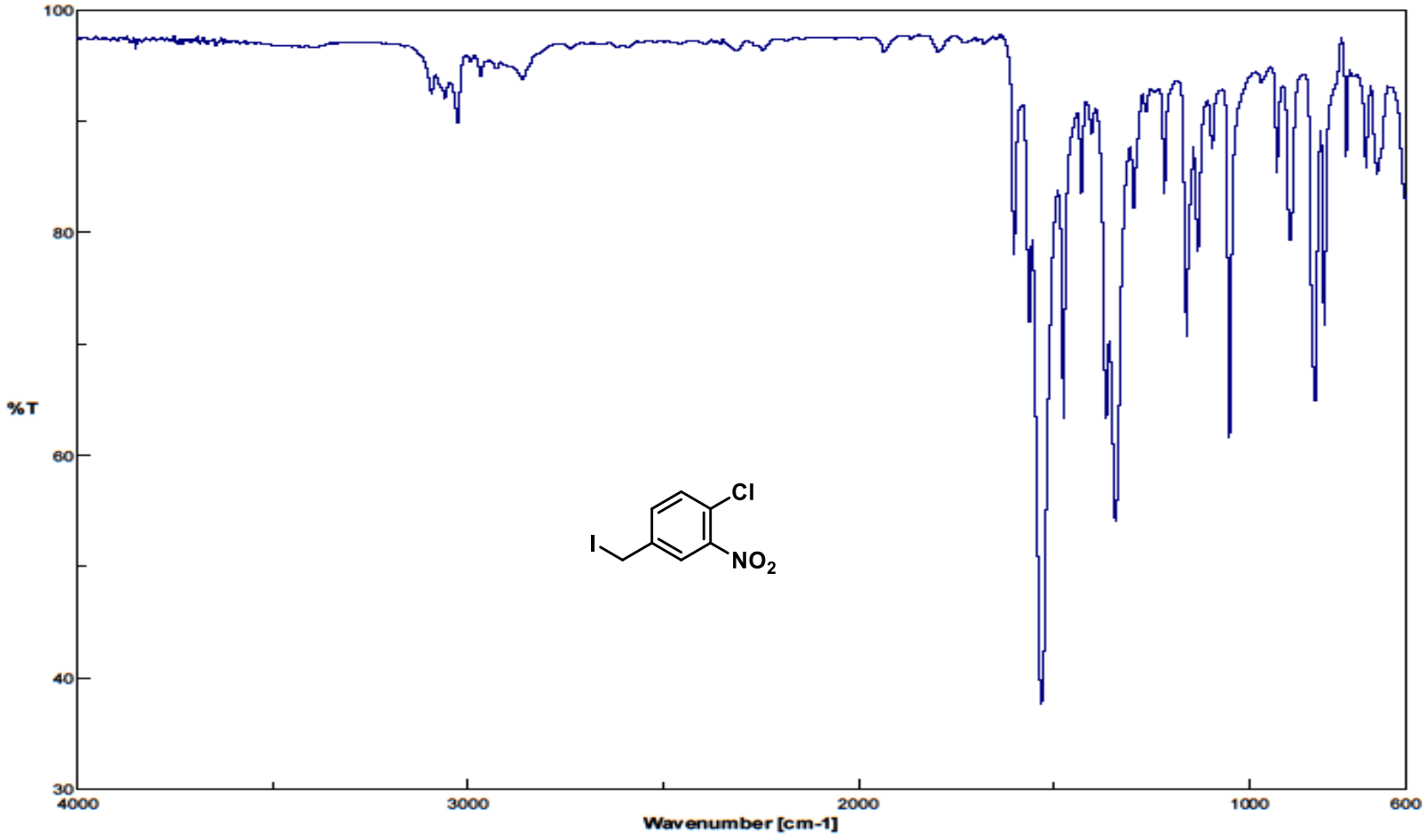
IR Spectrum of Compound **S10**



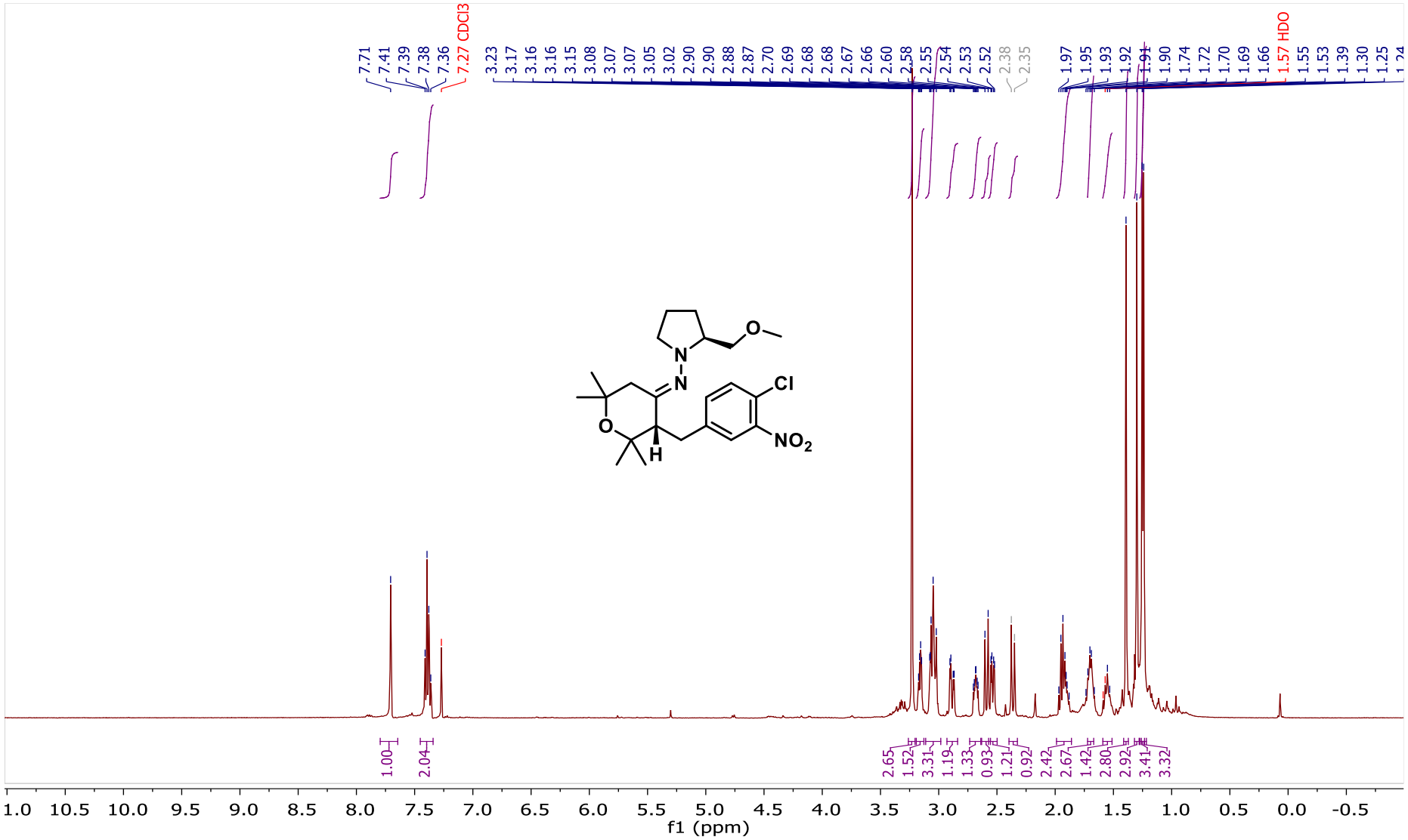
^{1}H NMR (500 MHz) Spectrum of Compound **12** in $CDCl_3$



^{13}C NMR (126 MHz) Spectrum of Compound **12** in $CDCl_3$

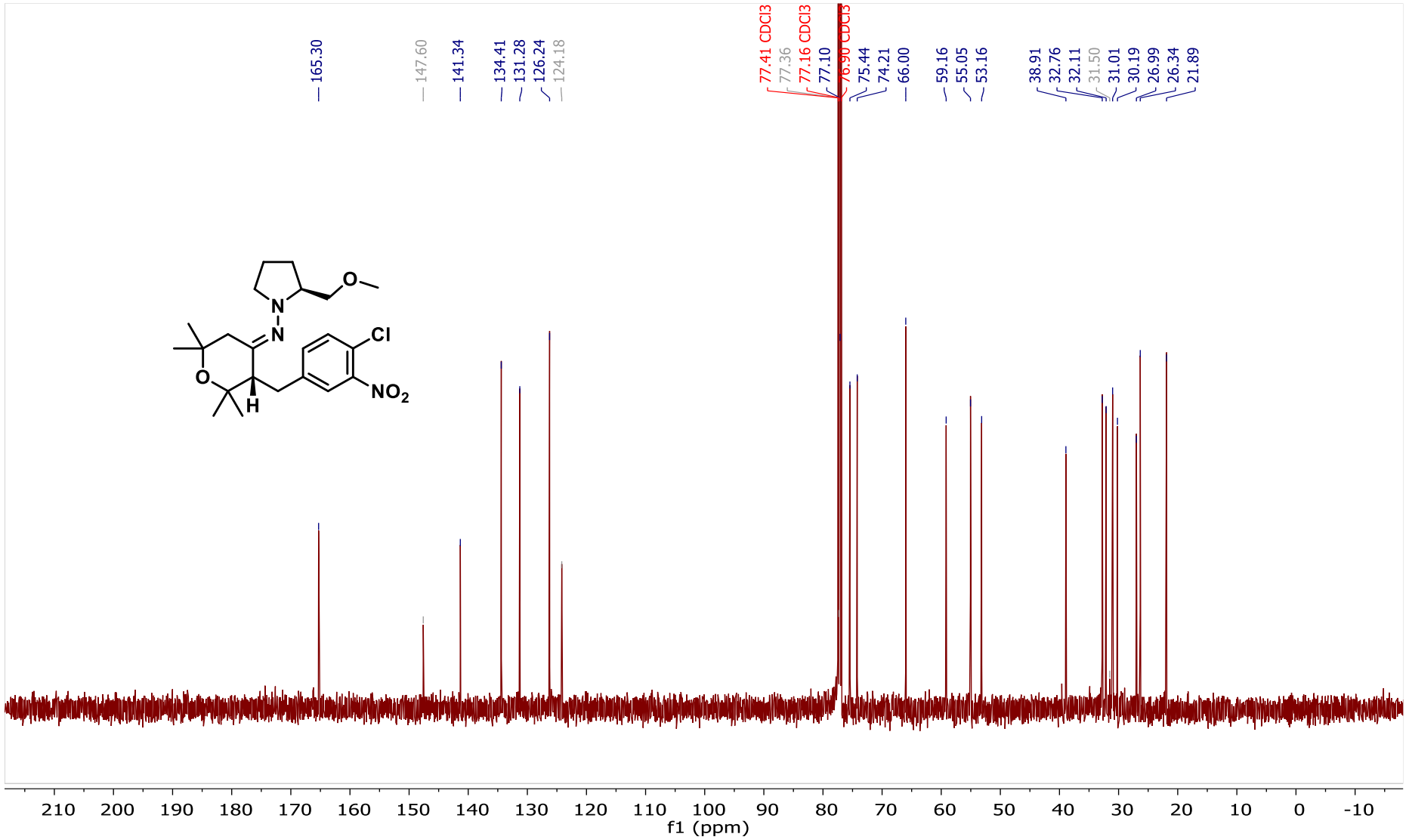


IR Spectrum of Compound **12**



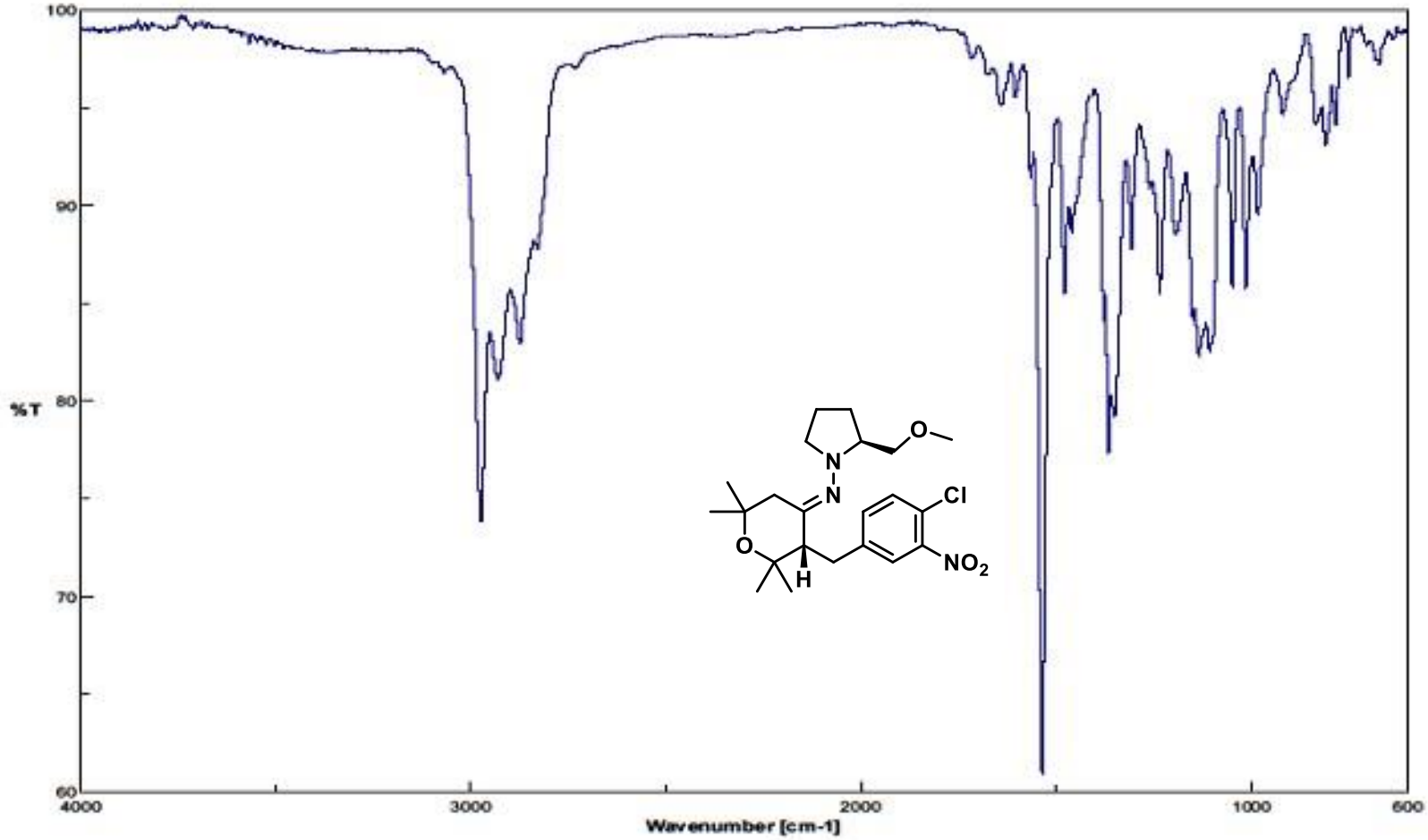
^{1}H NMR (500 MHz) Spectrum of Compound (+)-**13** in $CDCl_3$

(containing Z/E isomers)



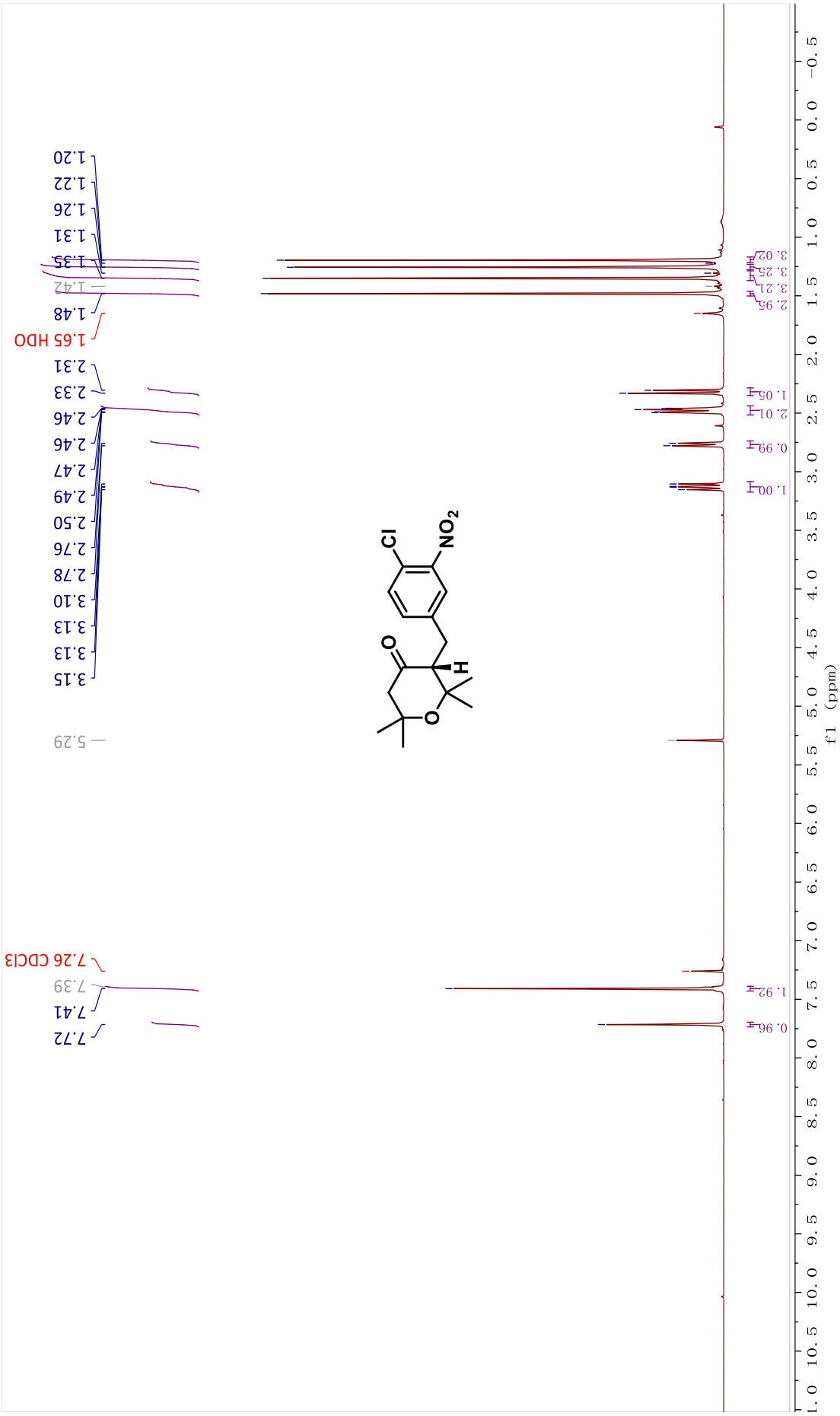
^{13}C NMR (126 MHz) Spectrum of Compound (+)-**13** in $CDCl_3$

(containing Z/E isomers)

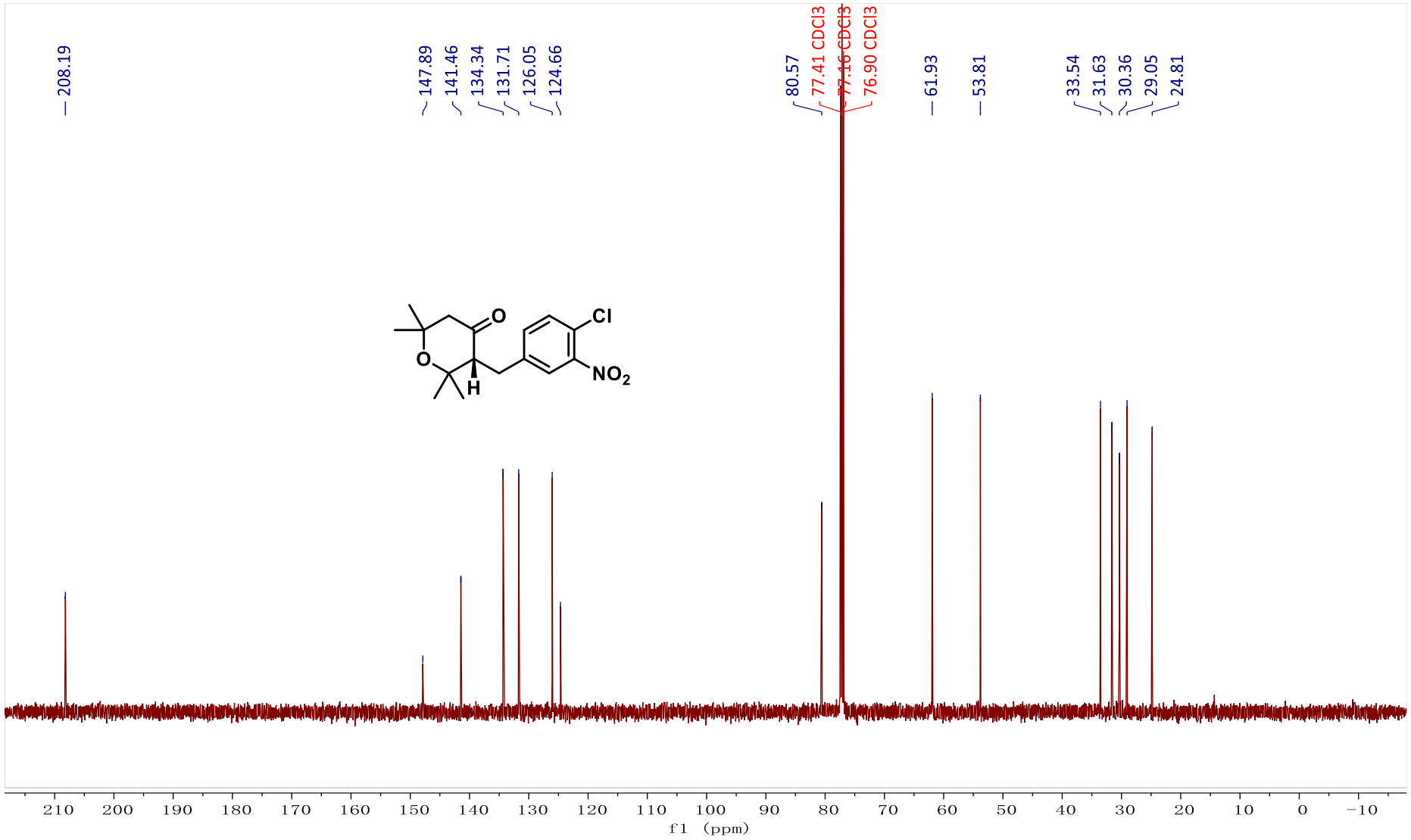


IR Spectrum of Compound (+)-**13**

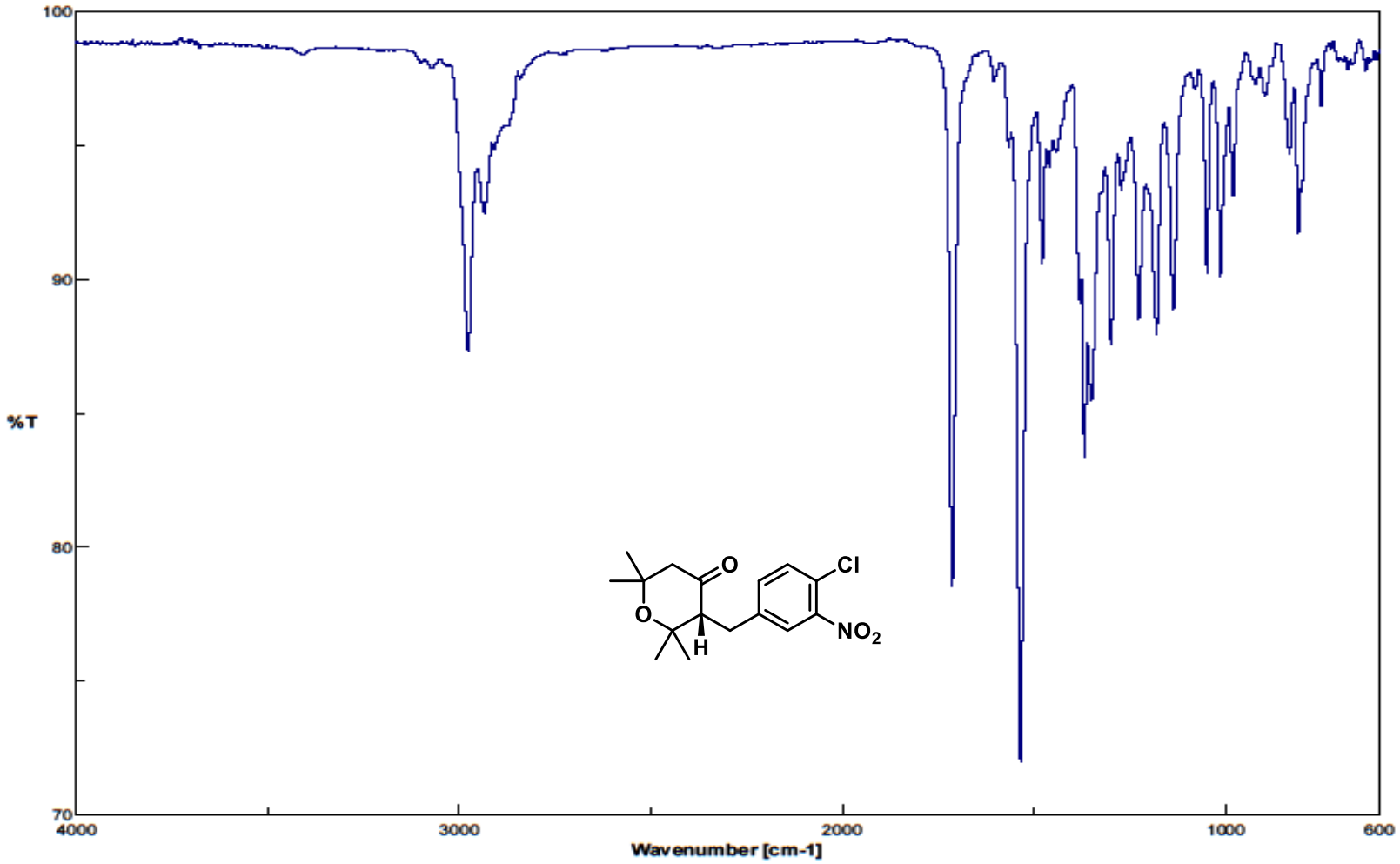
(containing Z/E isomers)



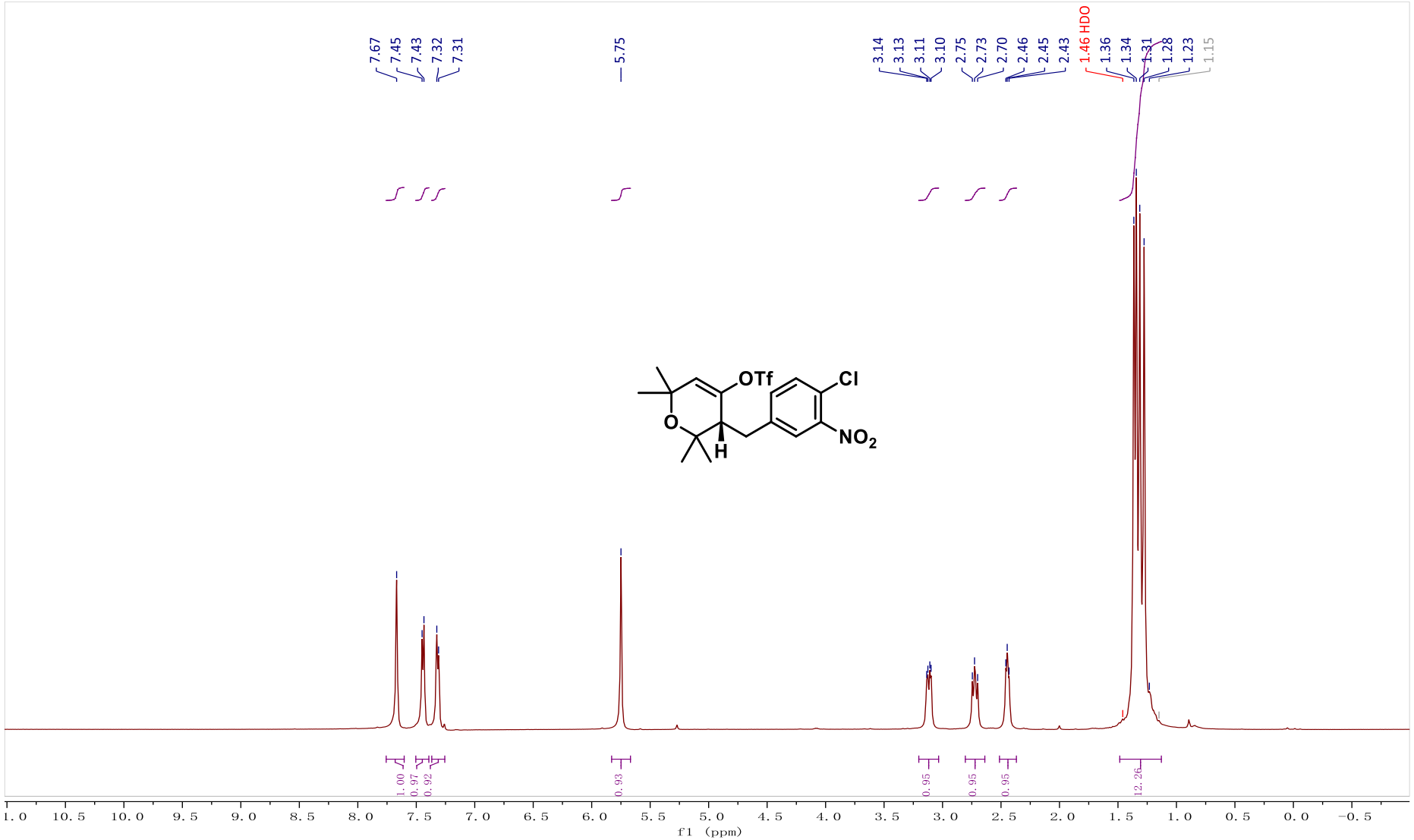
^{1}H NMR (500 MHz) Spectrum of Compound (+)-**14** in $CDCl_3$



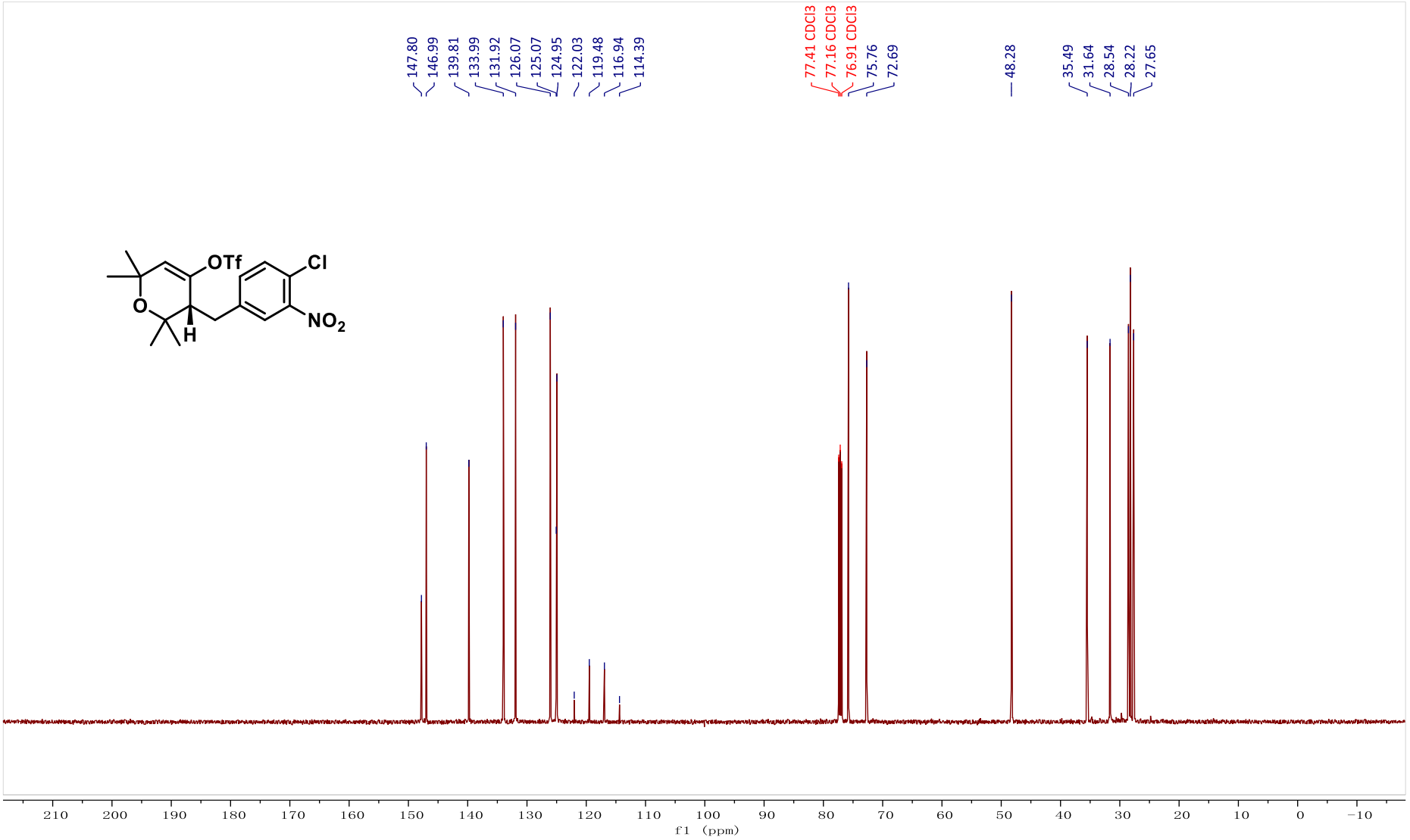
^{13}C NMR (126 MHz) Spectrum of Compound (+)-**14** in $CDCl_3$



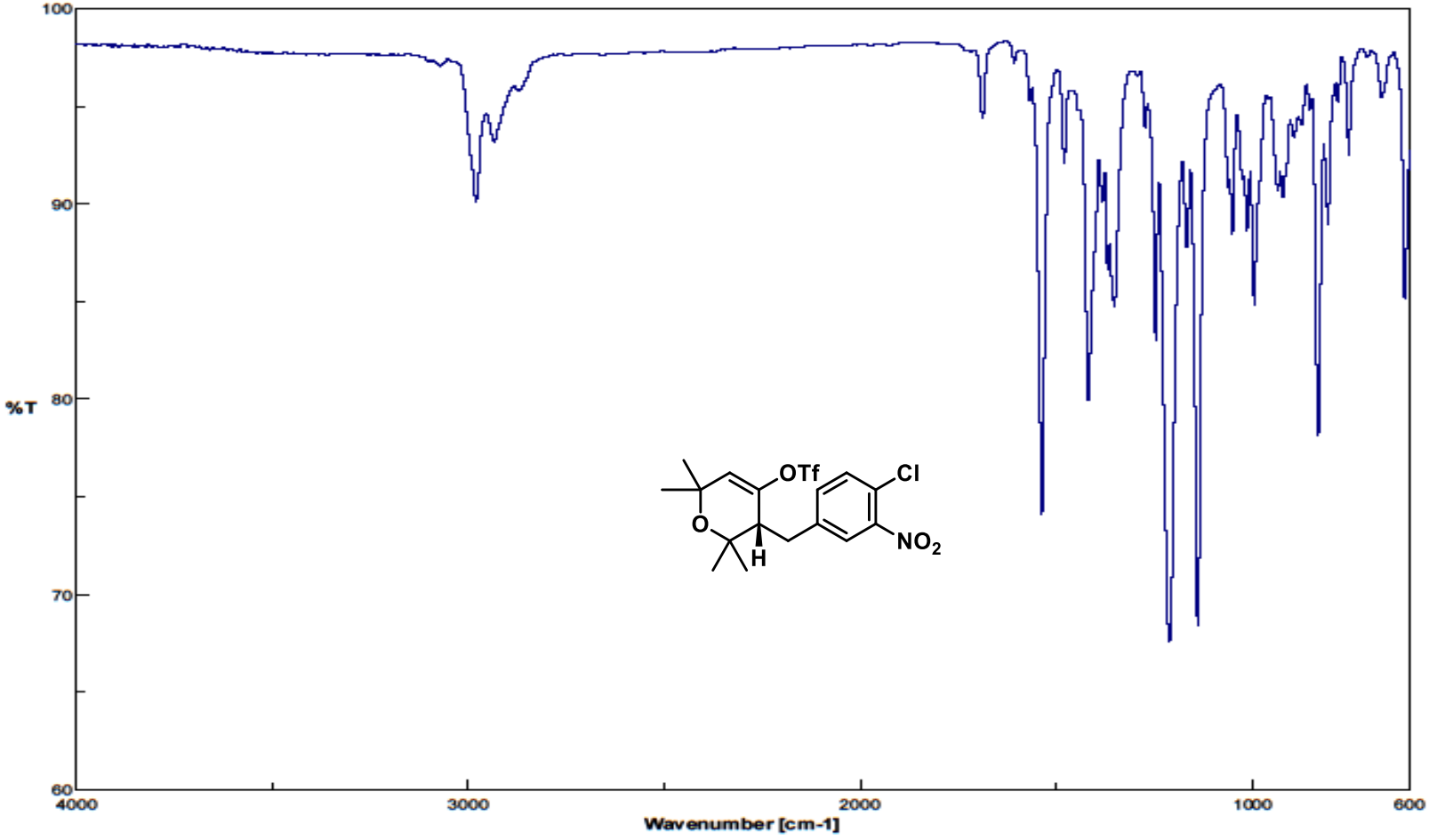
IR Spectrum of Compound (+)-**14**



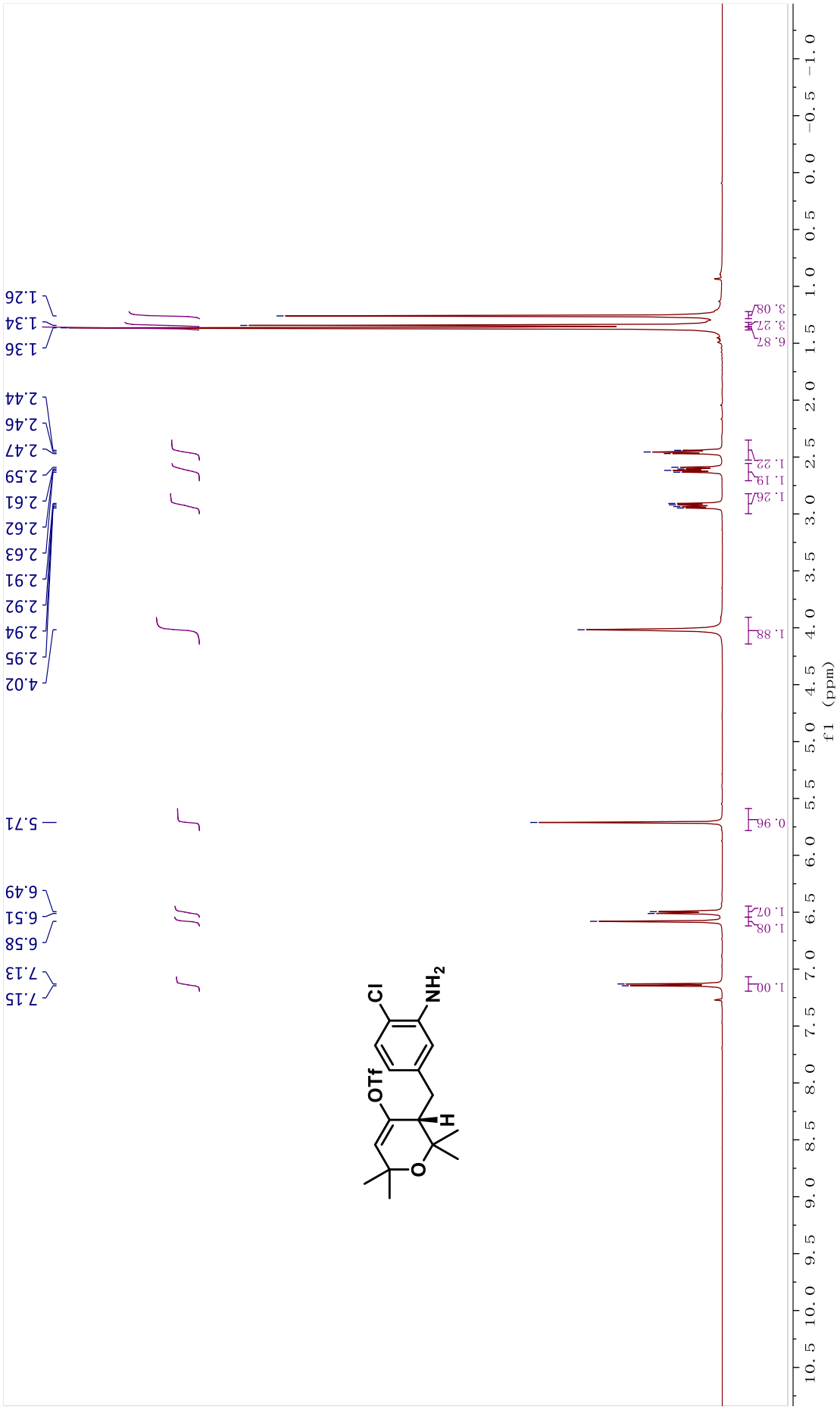
^{1}H NMR (500 MHz) Spectrum of Compound (+)-**S14** in $CDCl_3$



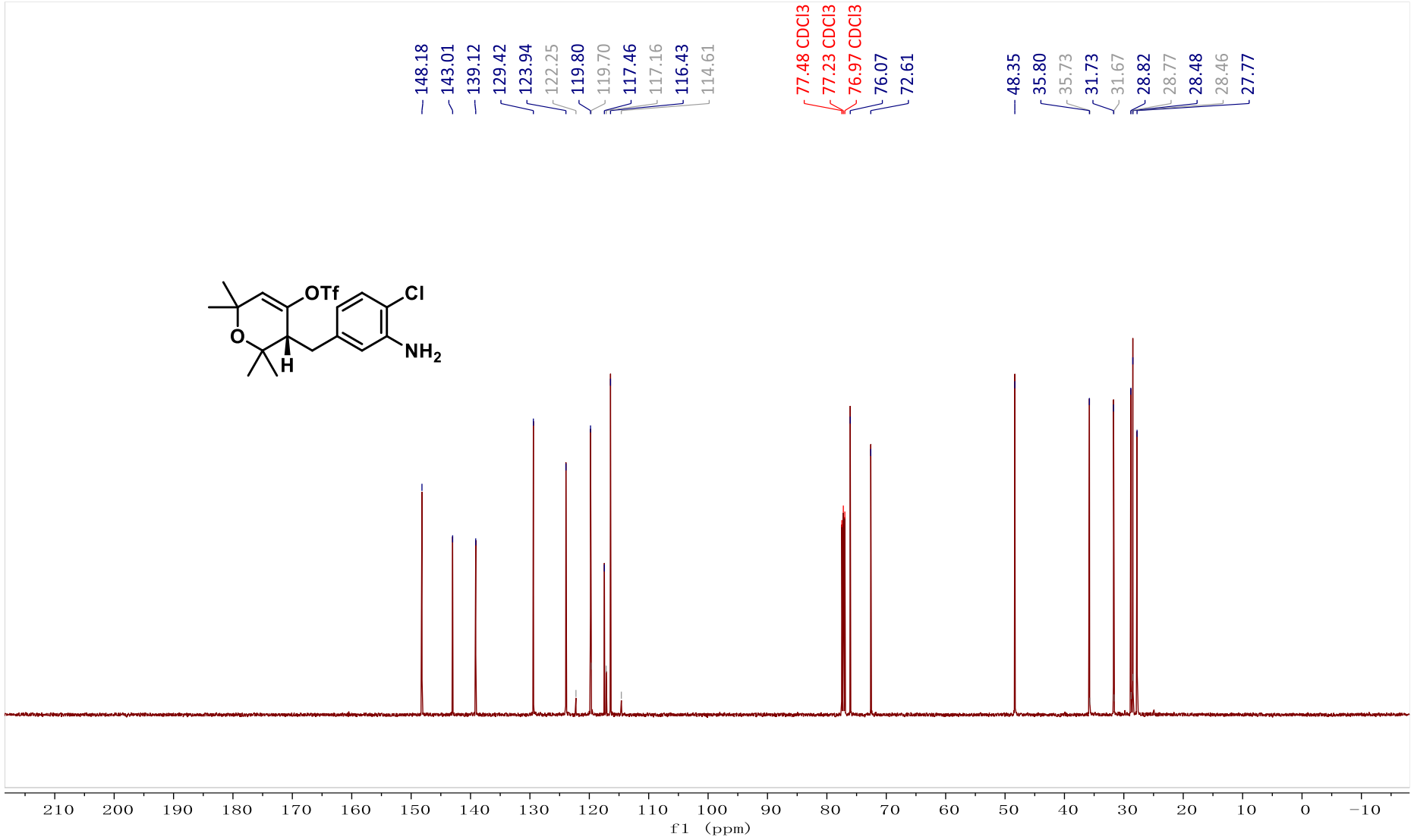
^{13}C NMR (126 MHz) Spectrum of Compound (+)-**S14** in $CDCl_3$



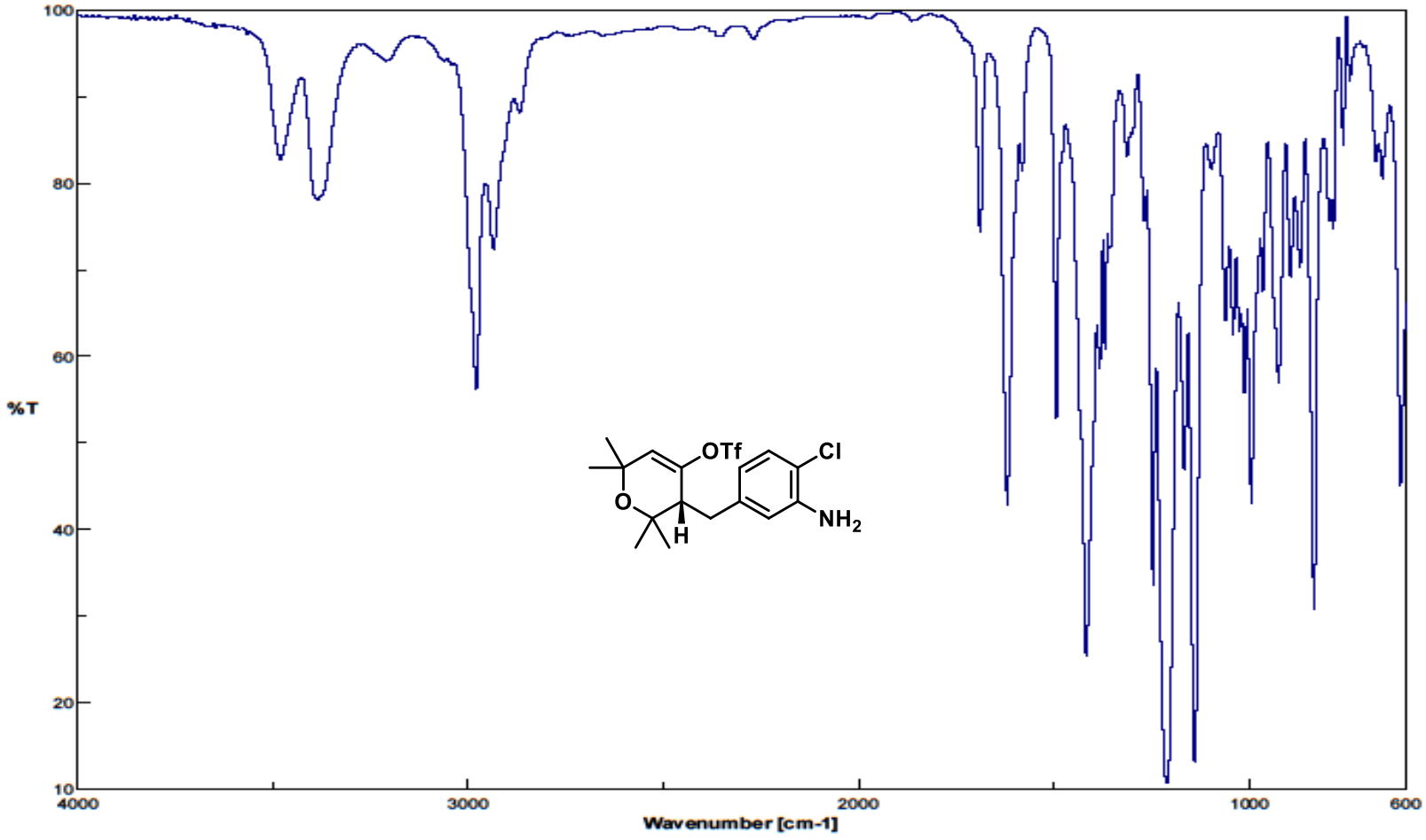
IR Spectrum of Compound (+)-**S14**



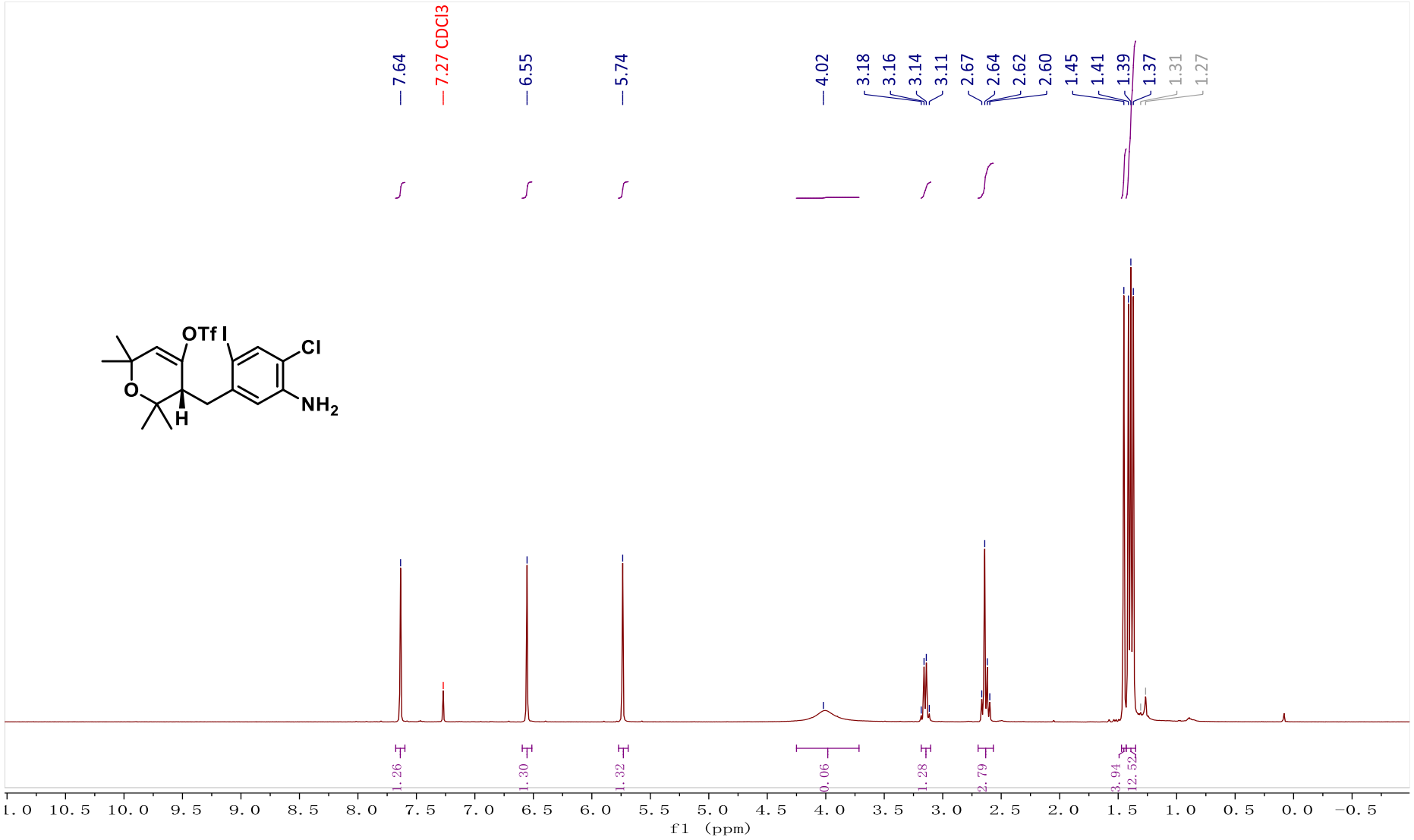
^{1}H NMR (500 MHz) Spectrum of Compound (+)-**15** in $CDCl_3$



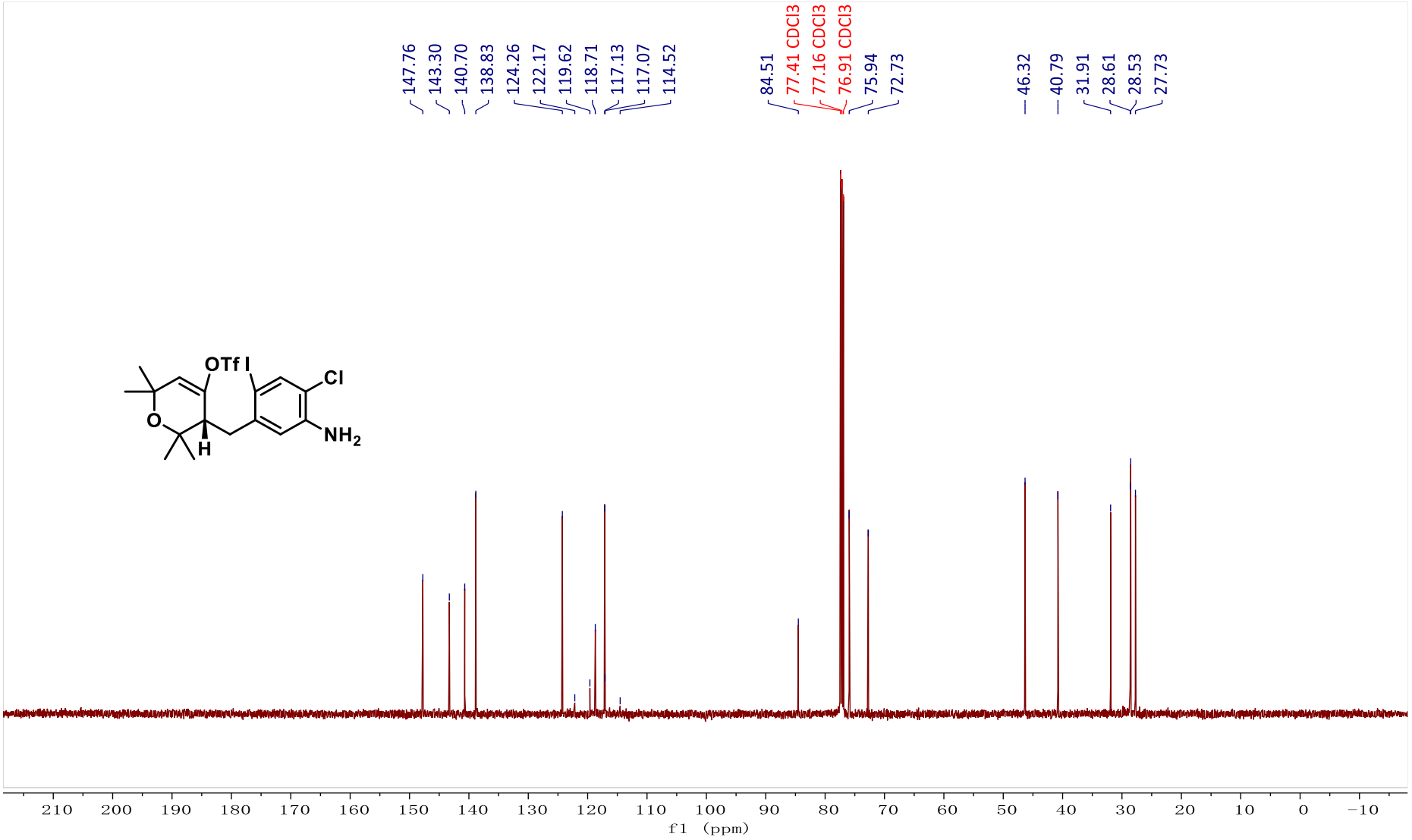
^{13}C NMR (126 MHz) Spectrum of Compound (+)-**15** in $CDCl_3$



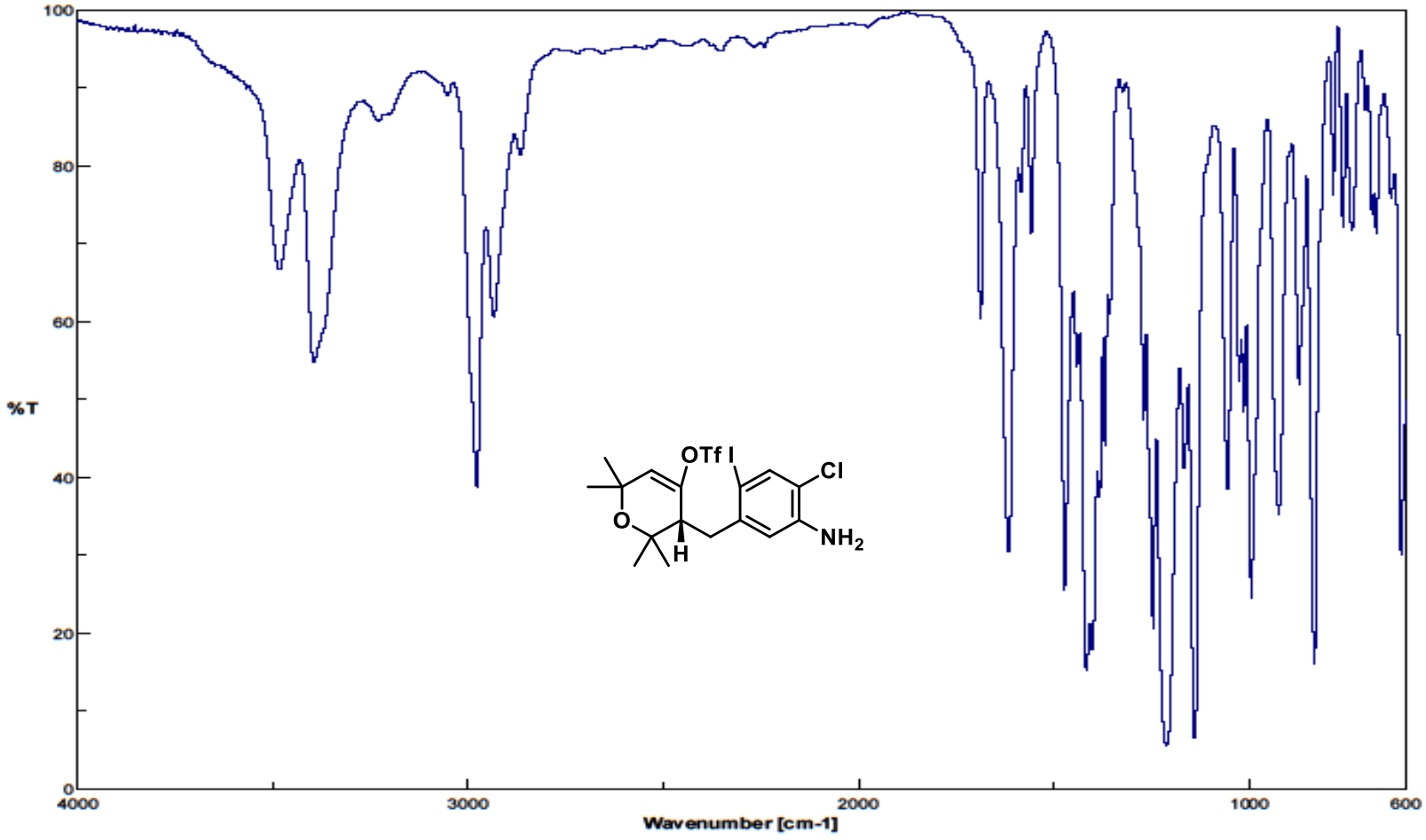
IR Spectrum of Compound (+)-**15**



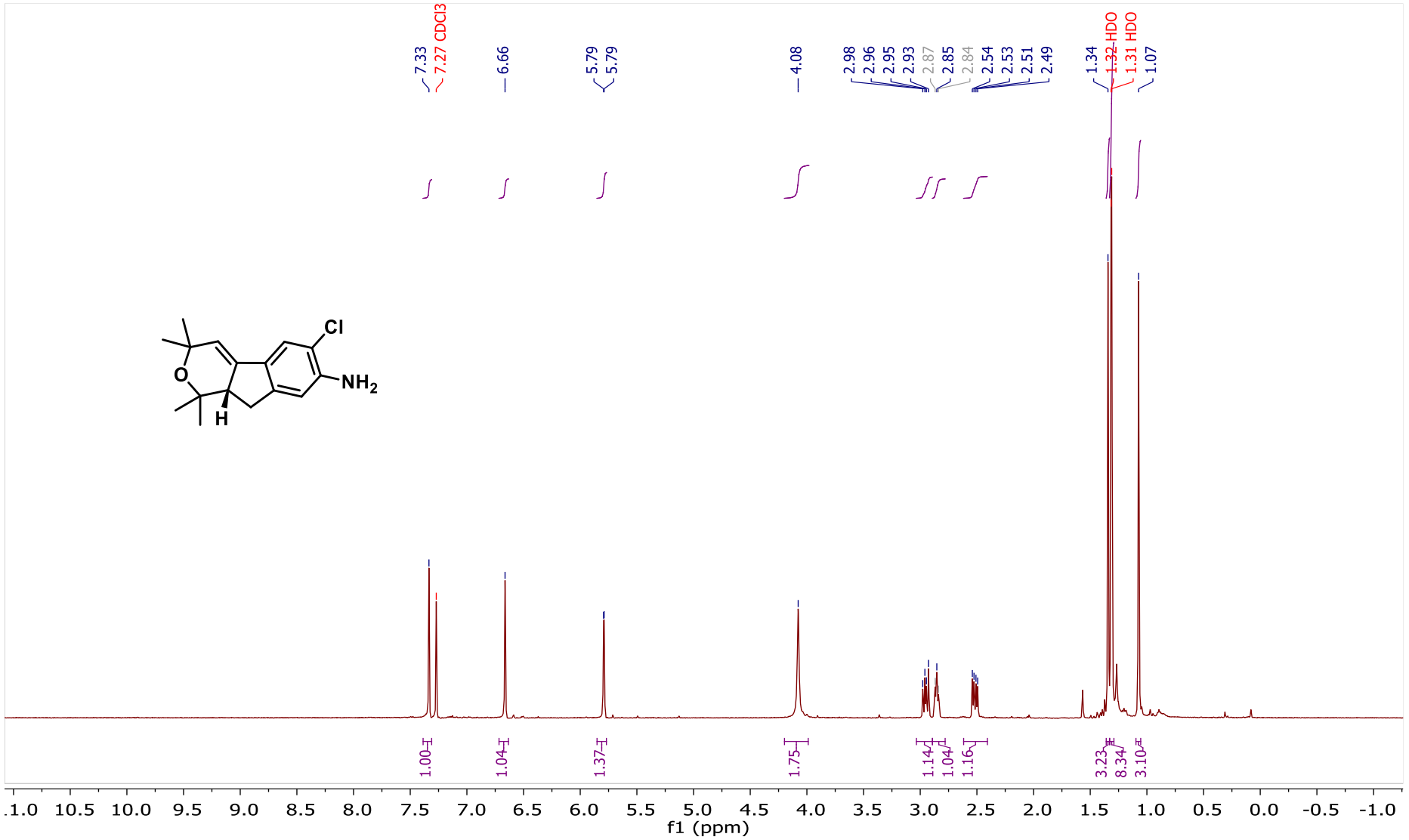
^{1}H NMR (500 MHz) Spectrum of Compound (+)-**16** in $CDCl_3$



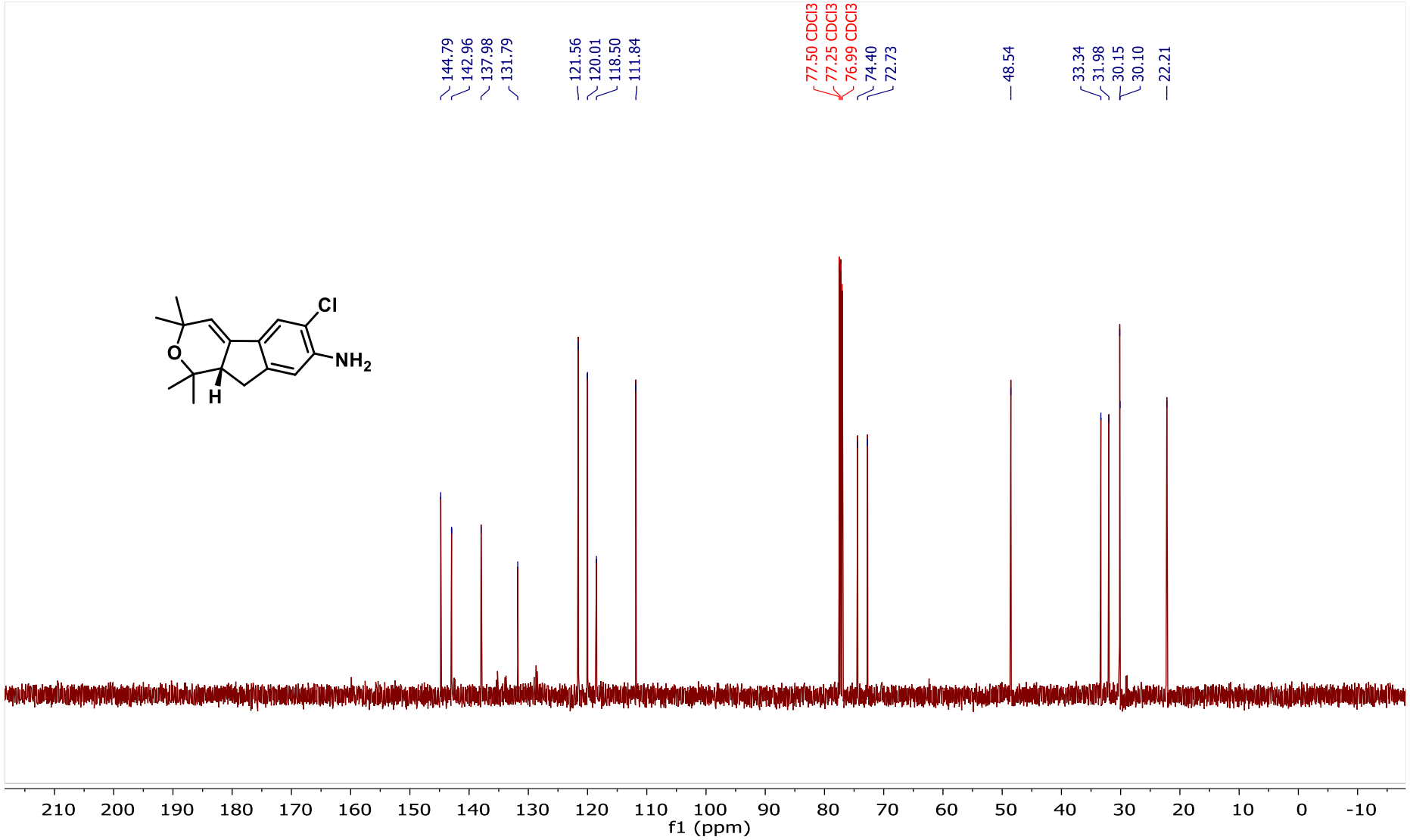
^{13}C NMR (126 MHz) Spectrum of Compound (+)-**16** in $CDCl_3$



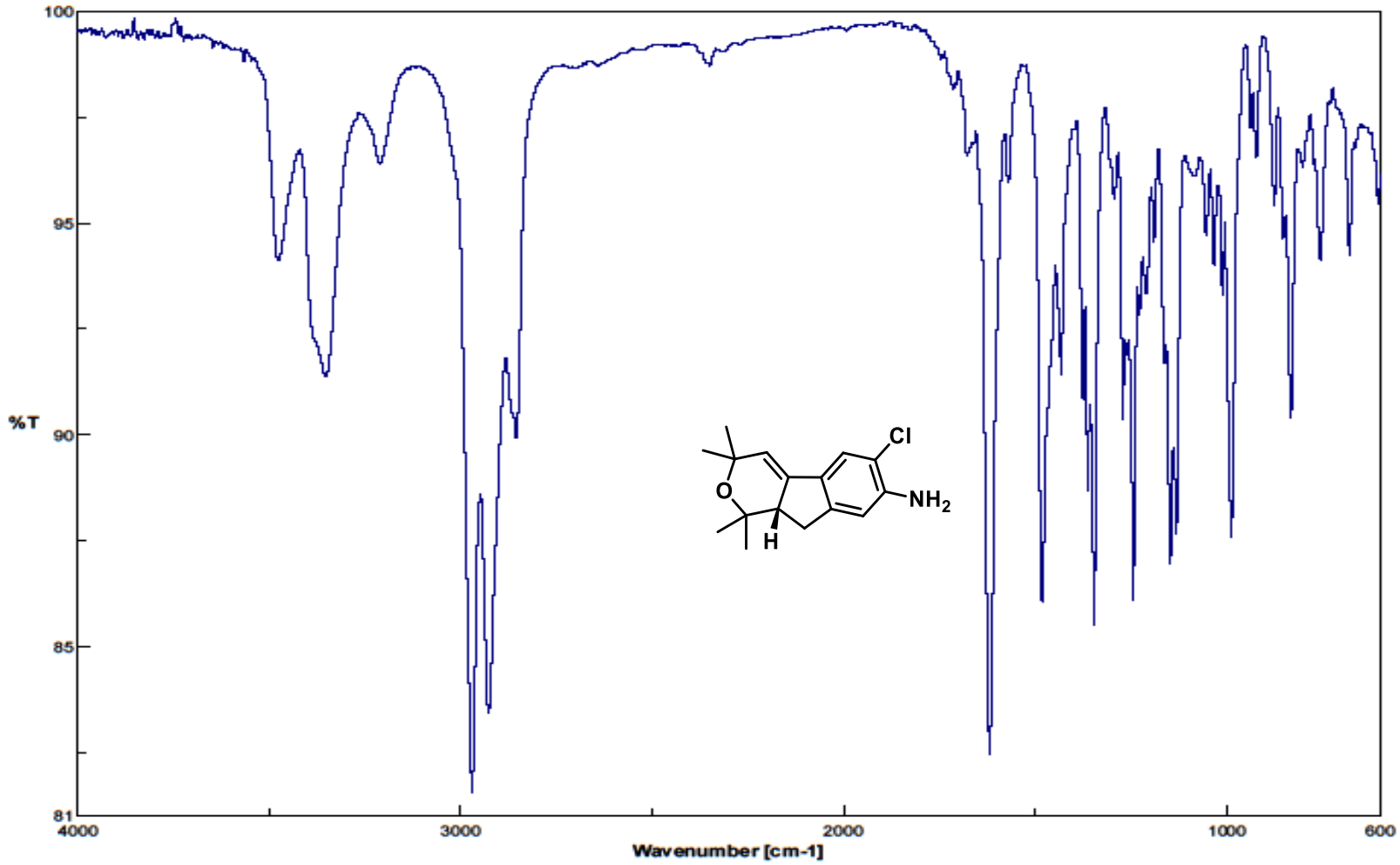
IR Spectrum of Compound (+)-**16**



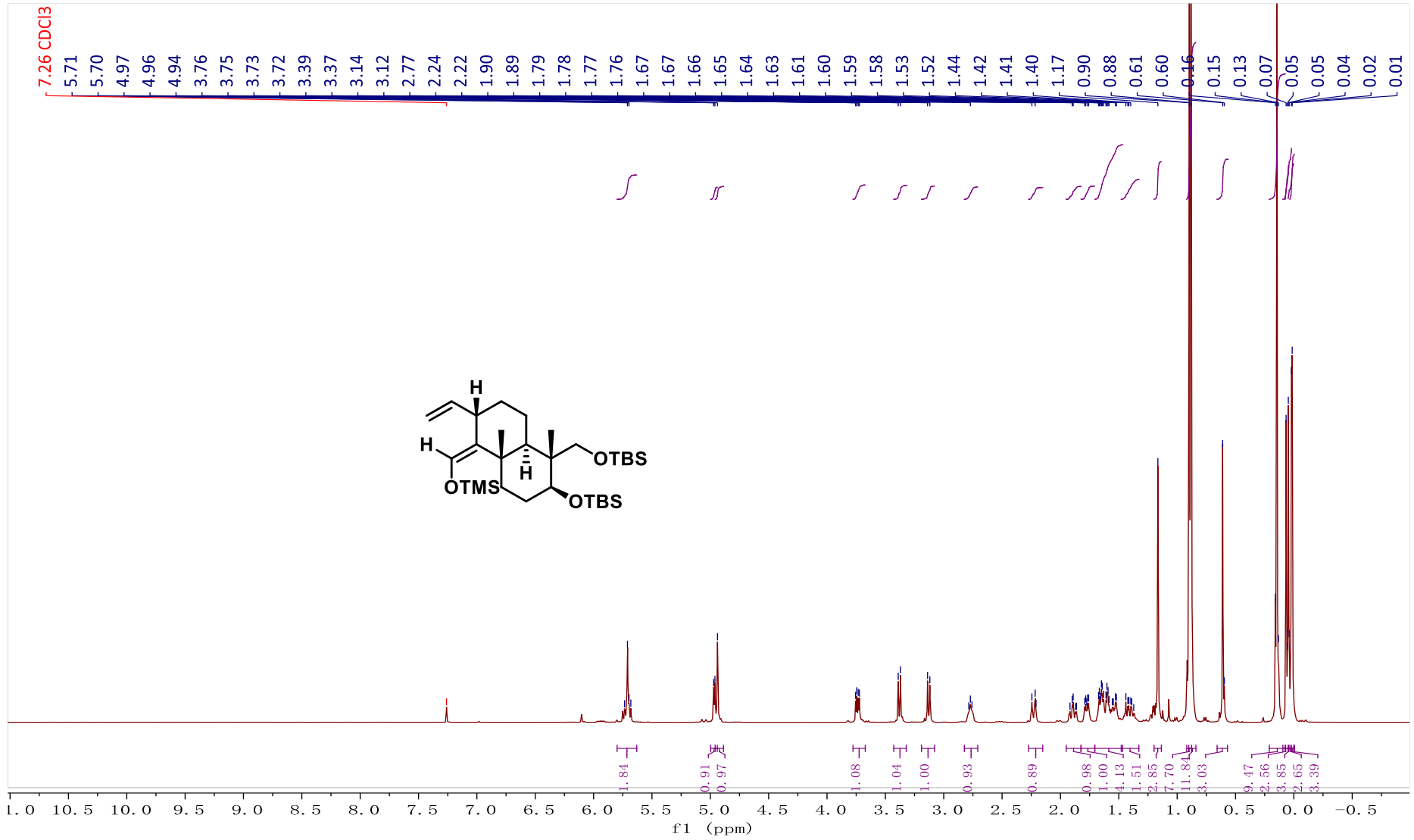
^{1}H NMR (500 MHz) Spectrum of Compound **(–)-7** in $CDCl_3$



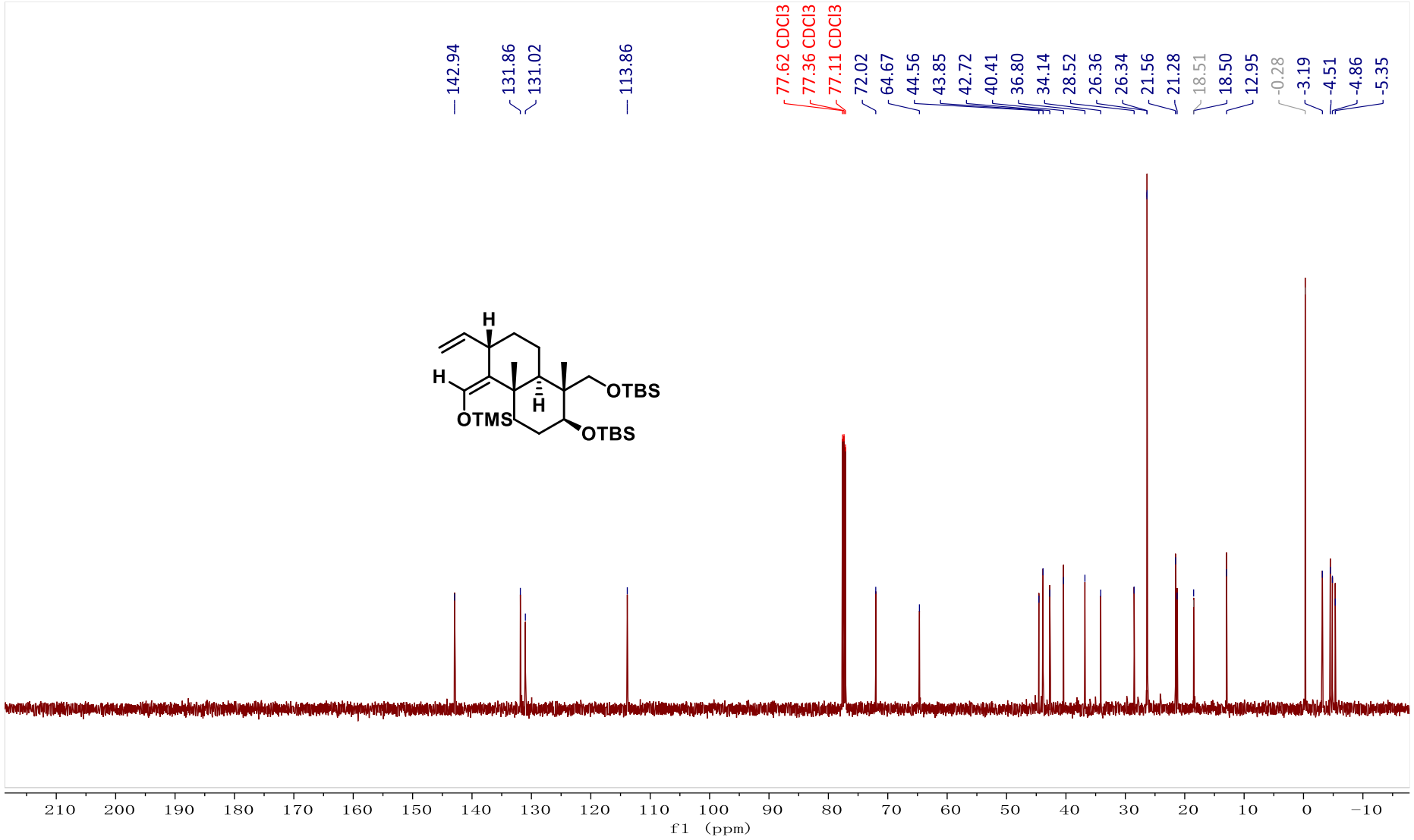
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-7** in $CDCl_3$



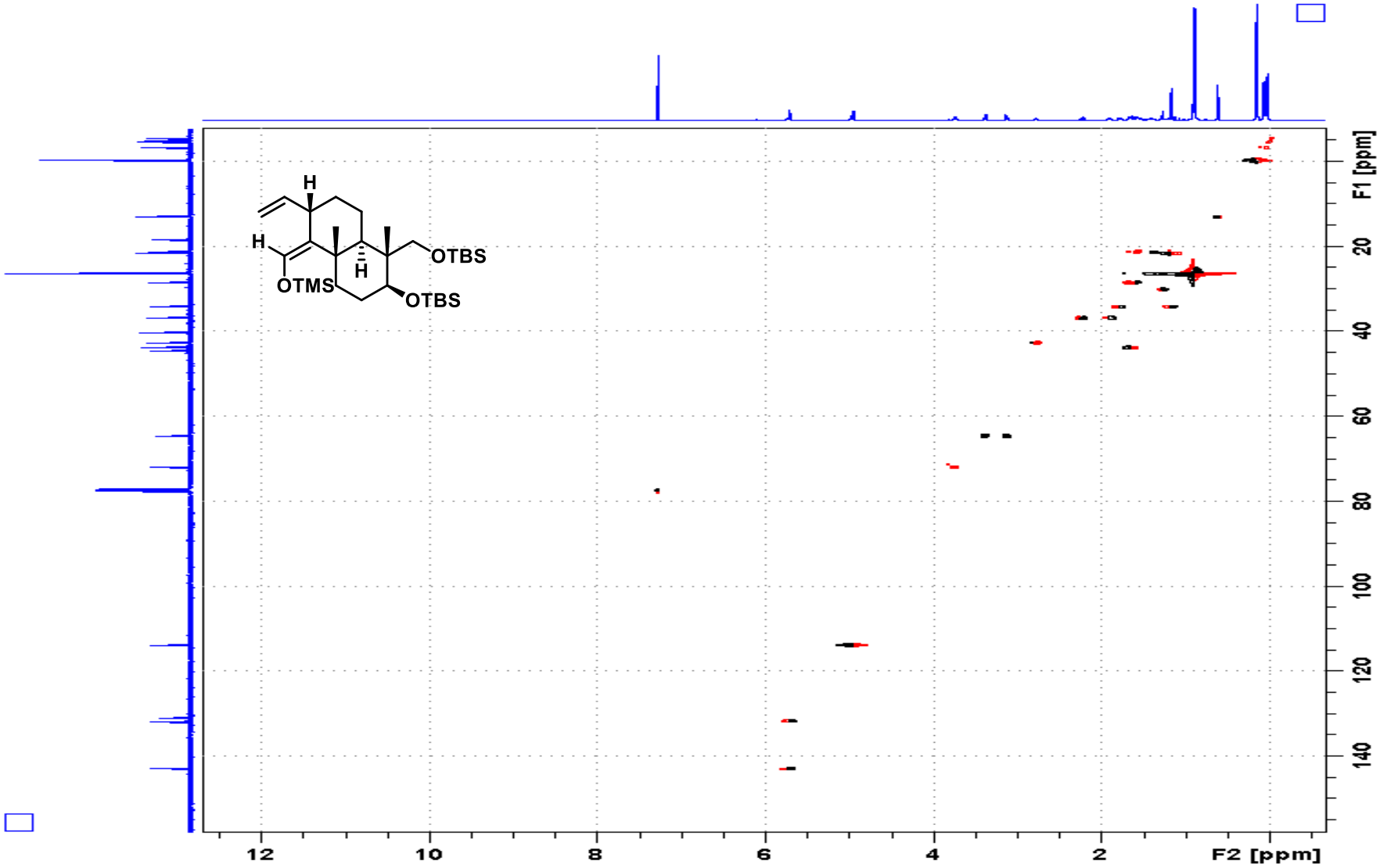
IR Spectrum of Compound (–)-**7**



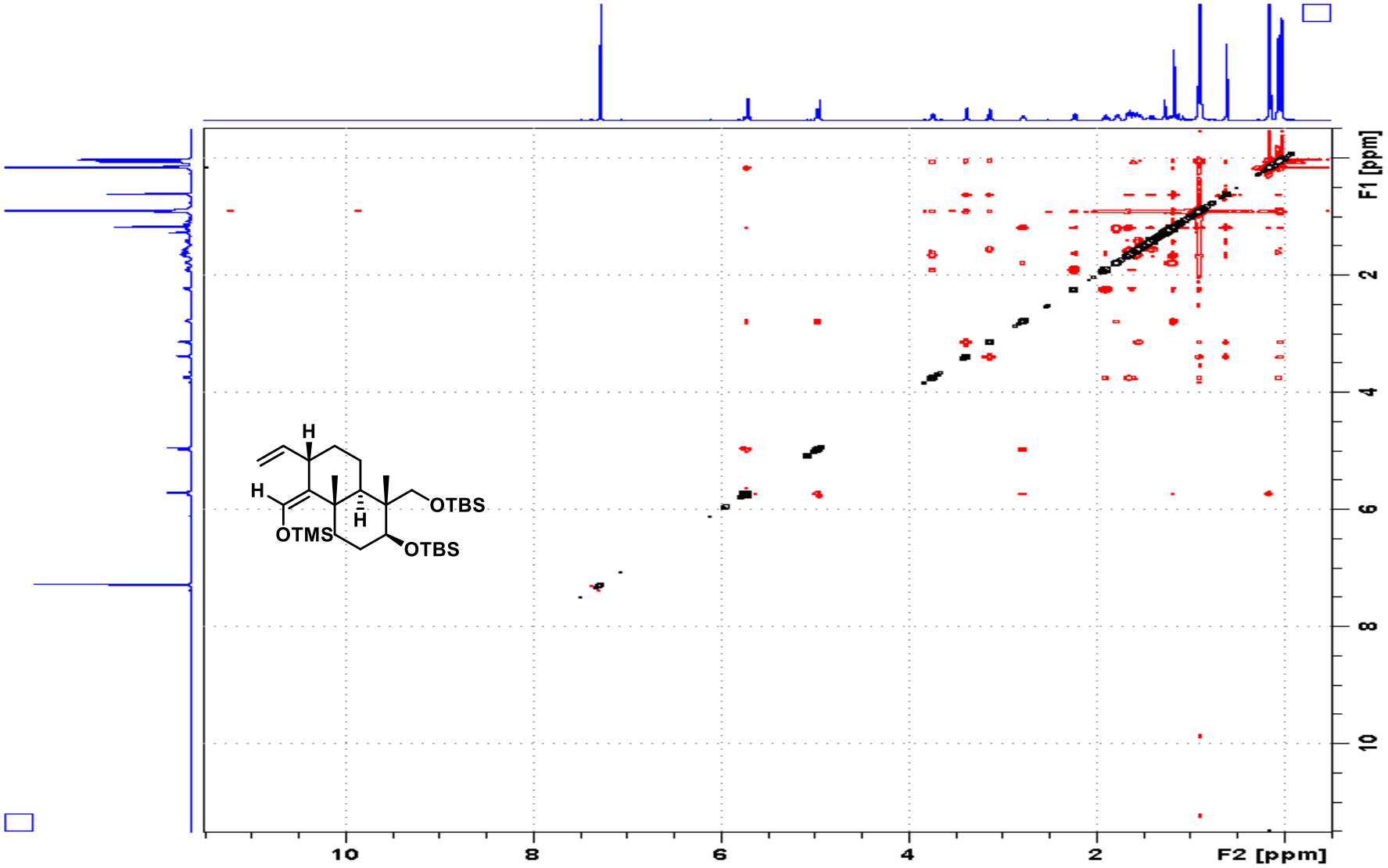
^{1}H NMR (500 MHz) Spectrum of Compound **(−)-17** in $CDCl_3$



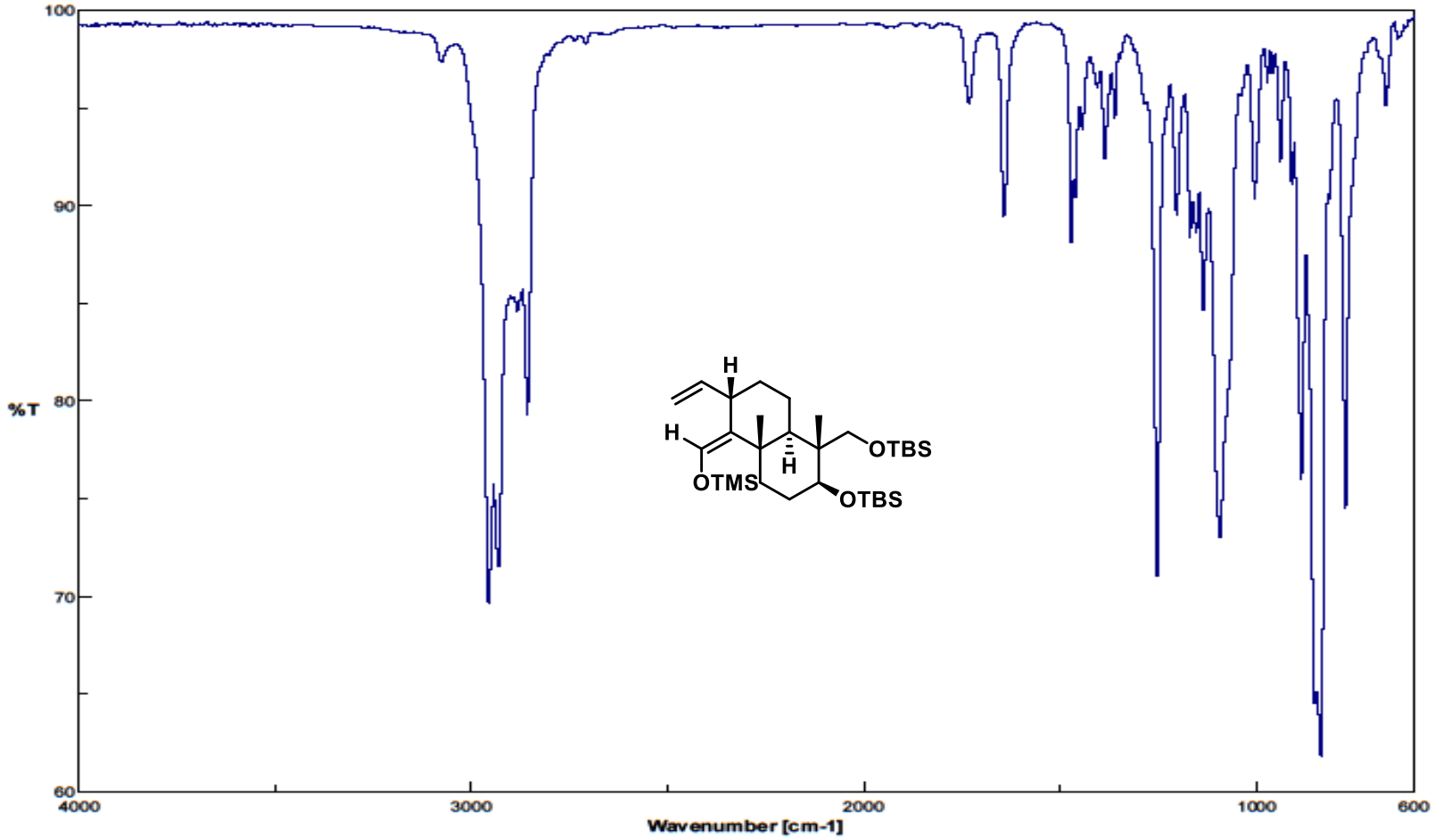
^{13}C NMR (126 MHz) Spectrum of Compound **(−)-17** in $CDCl_3$



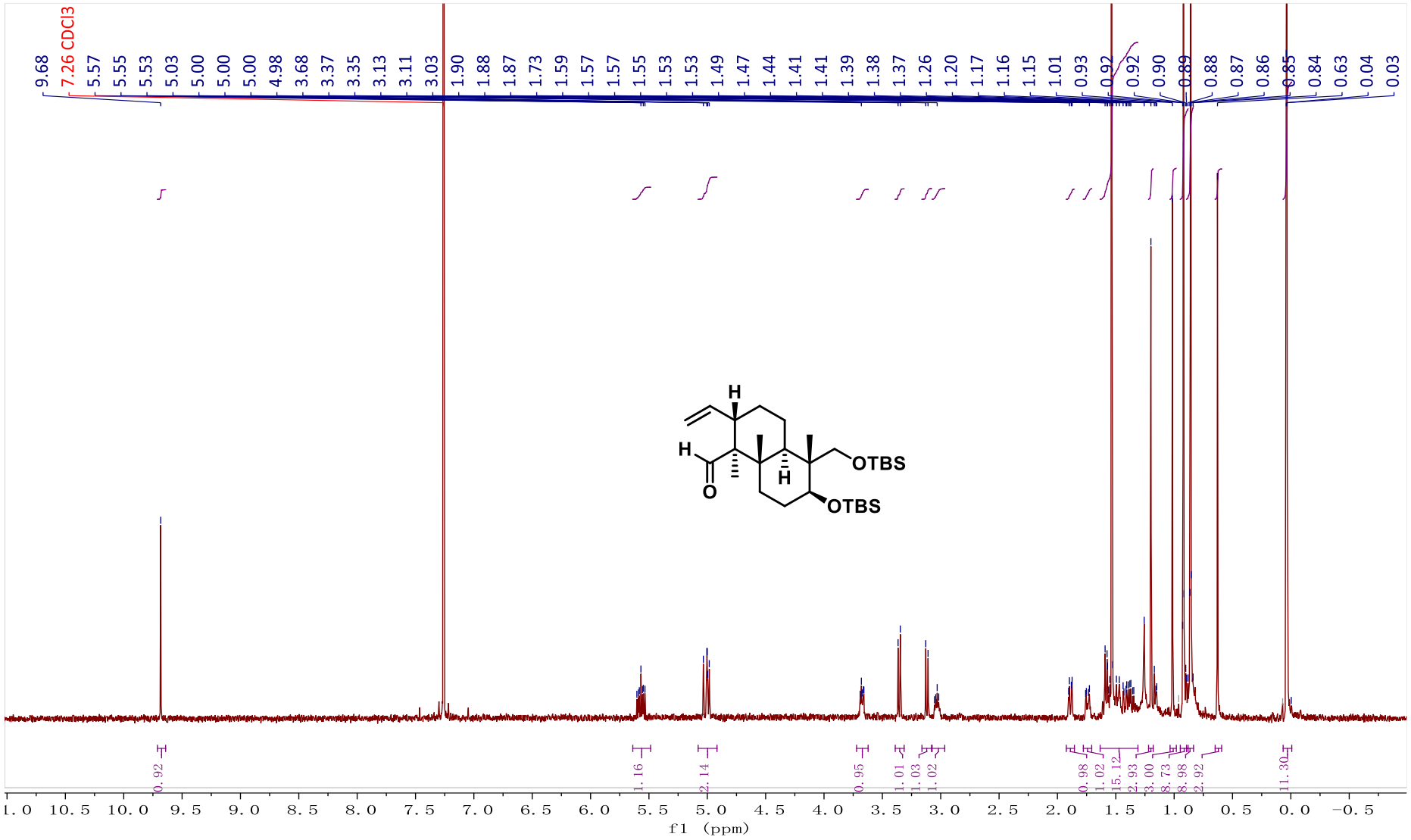
HSQC Spectrum of Compound **(–)-17** in $CDCl_3$



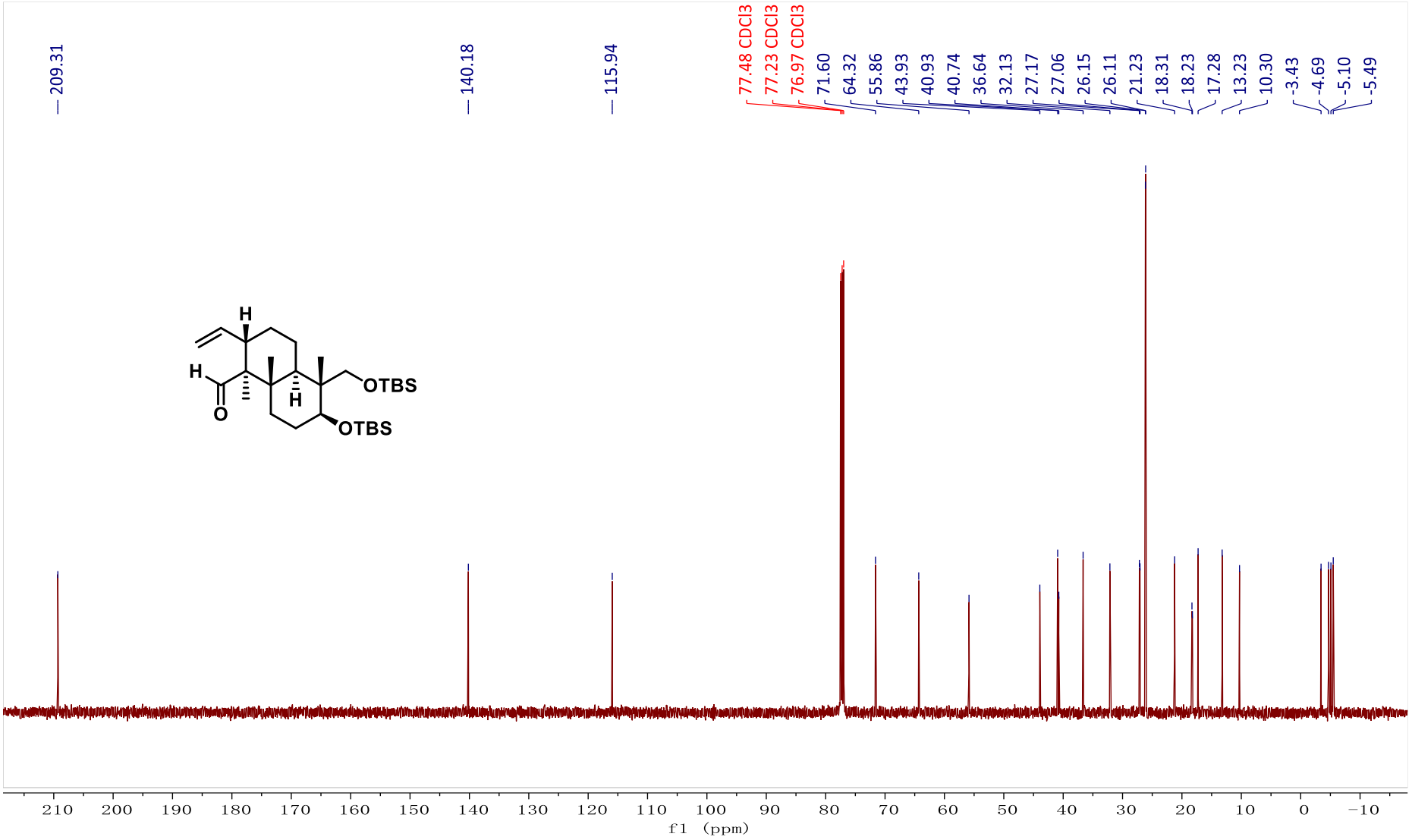
NOESY Spectrum of Compound (–)-**17** in $CDCl_3$



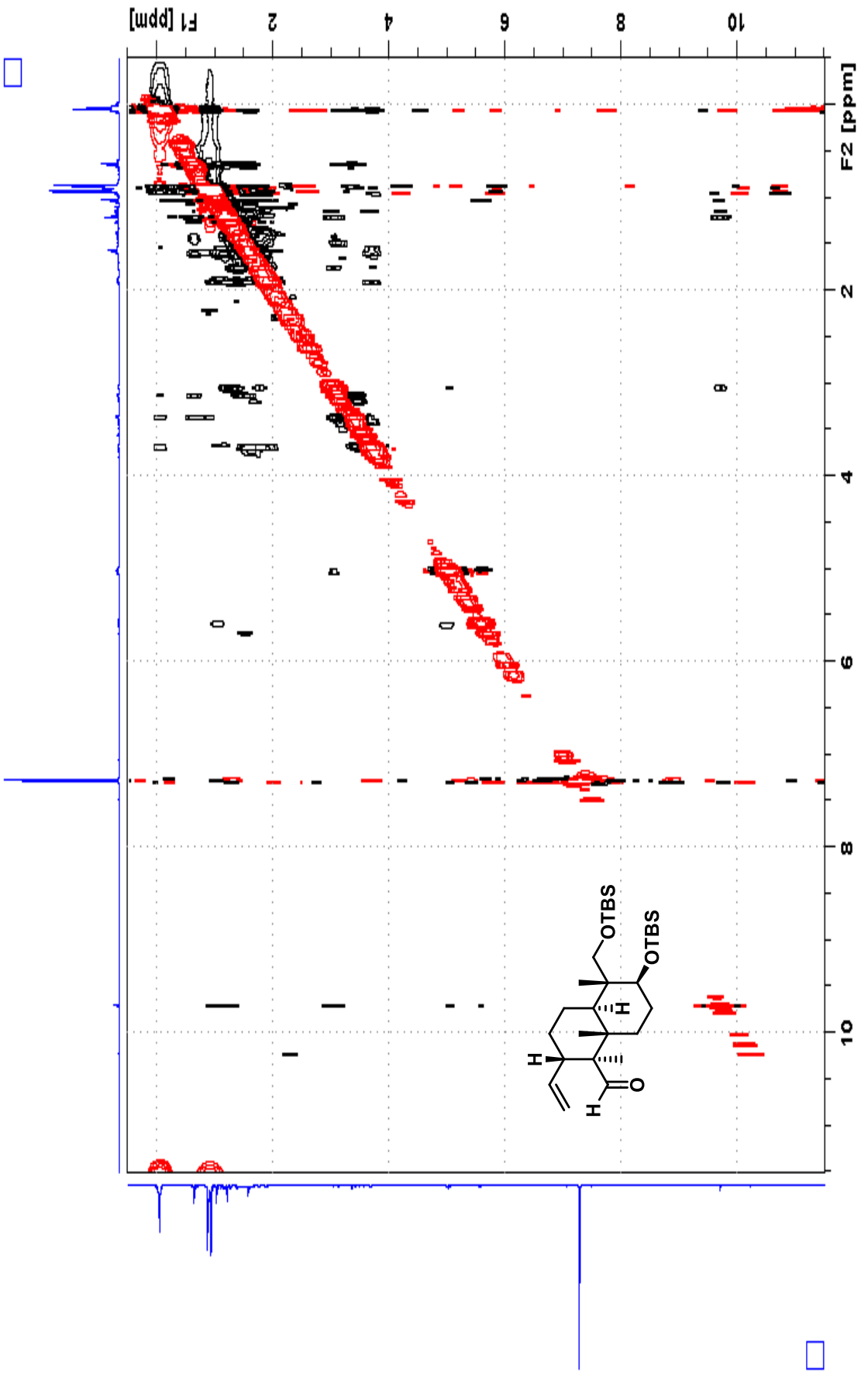
IR Spectrum of Compound (–)-**17**



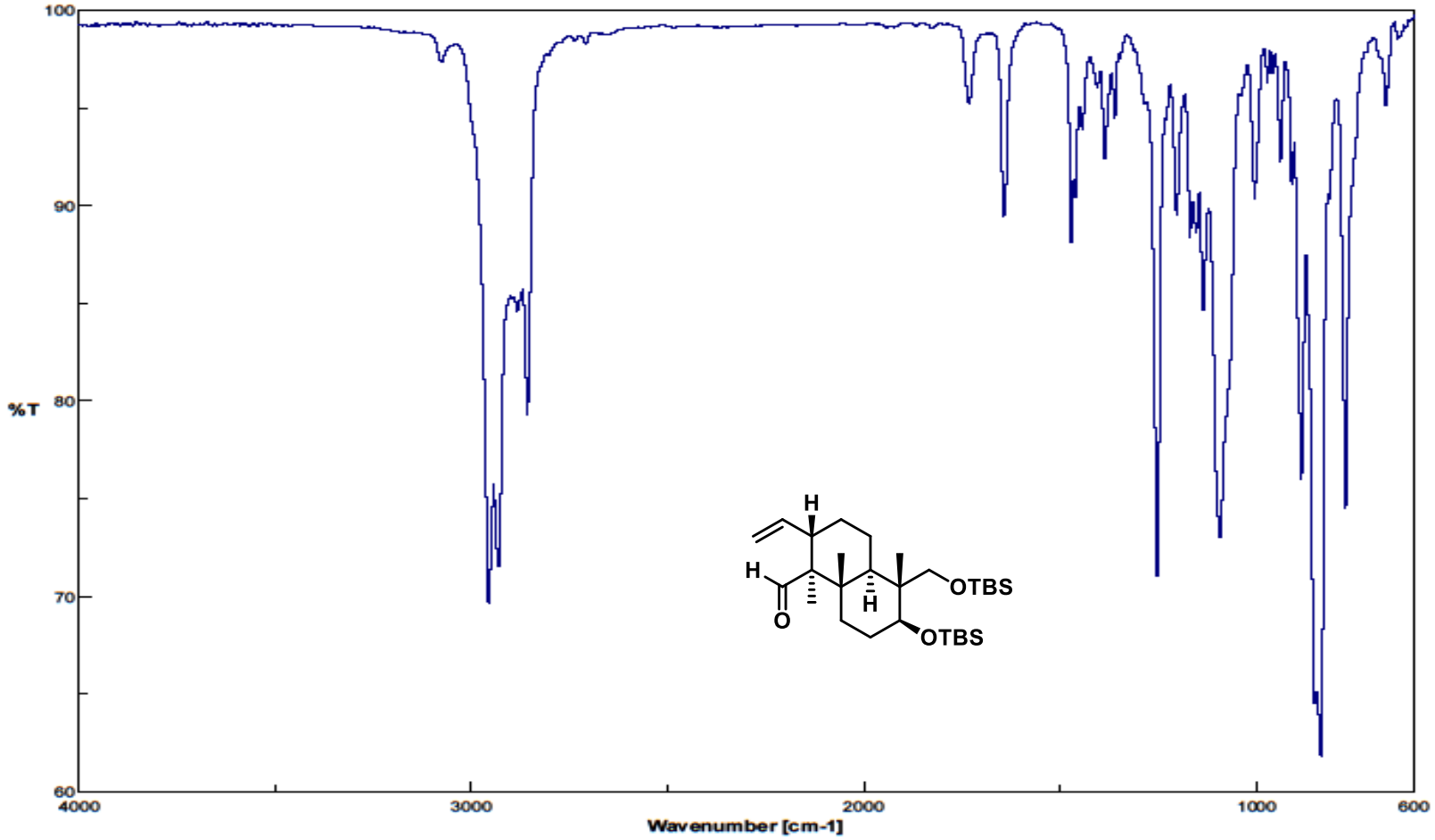
^{1}H NMR (500 MHz) Spectrum of Compound **(−)-20** in $CDCl_3$



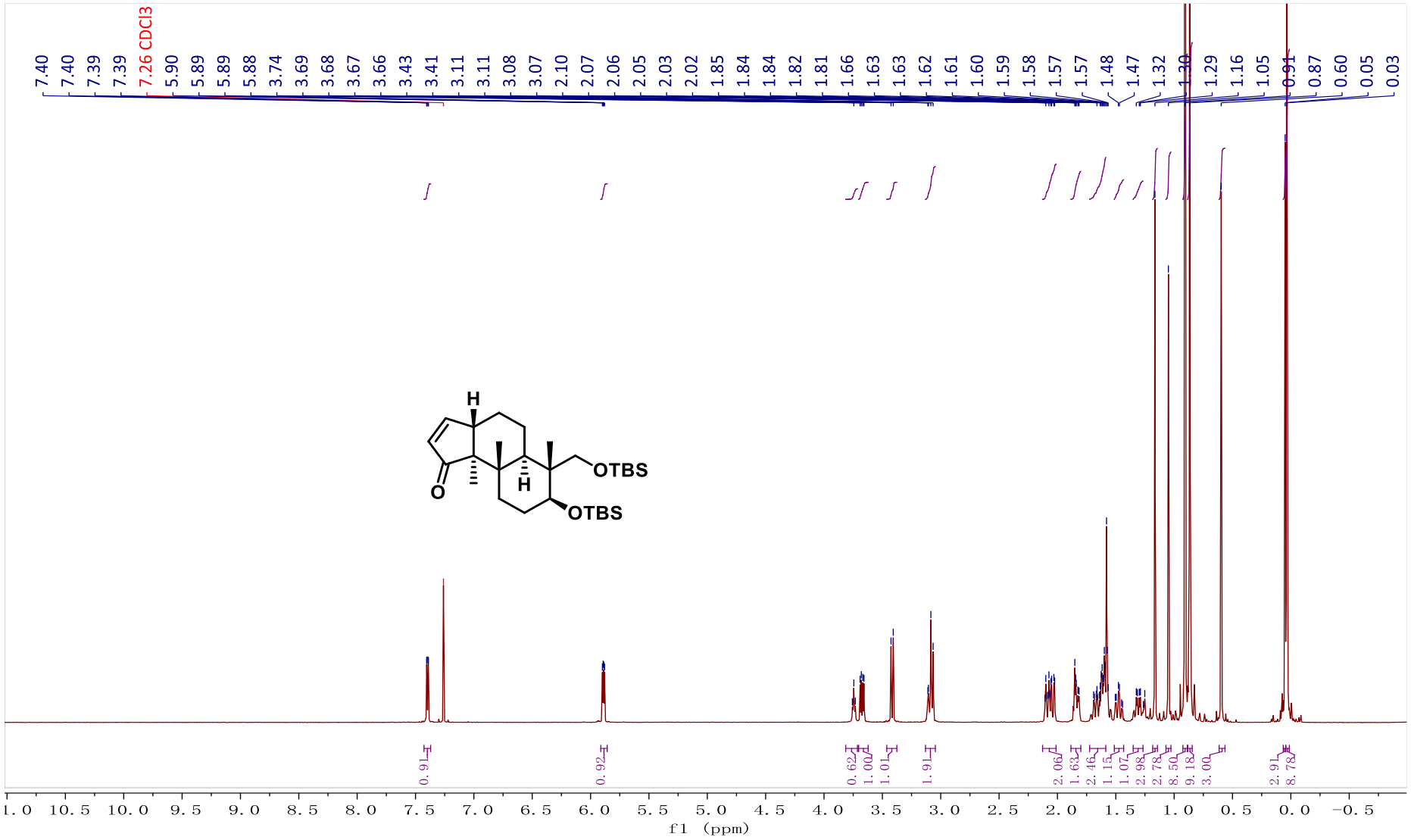
^{13}C NMR (126 MHz) Spectrum of Compound **(−)-20** in $CDCl_3$



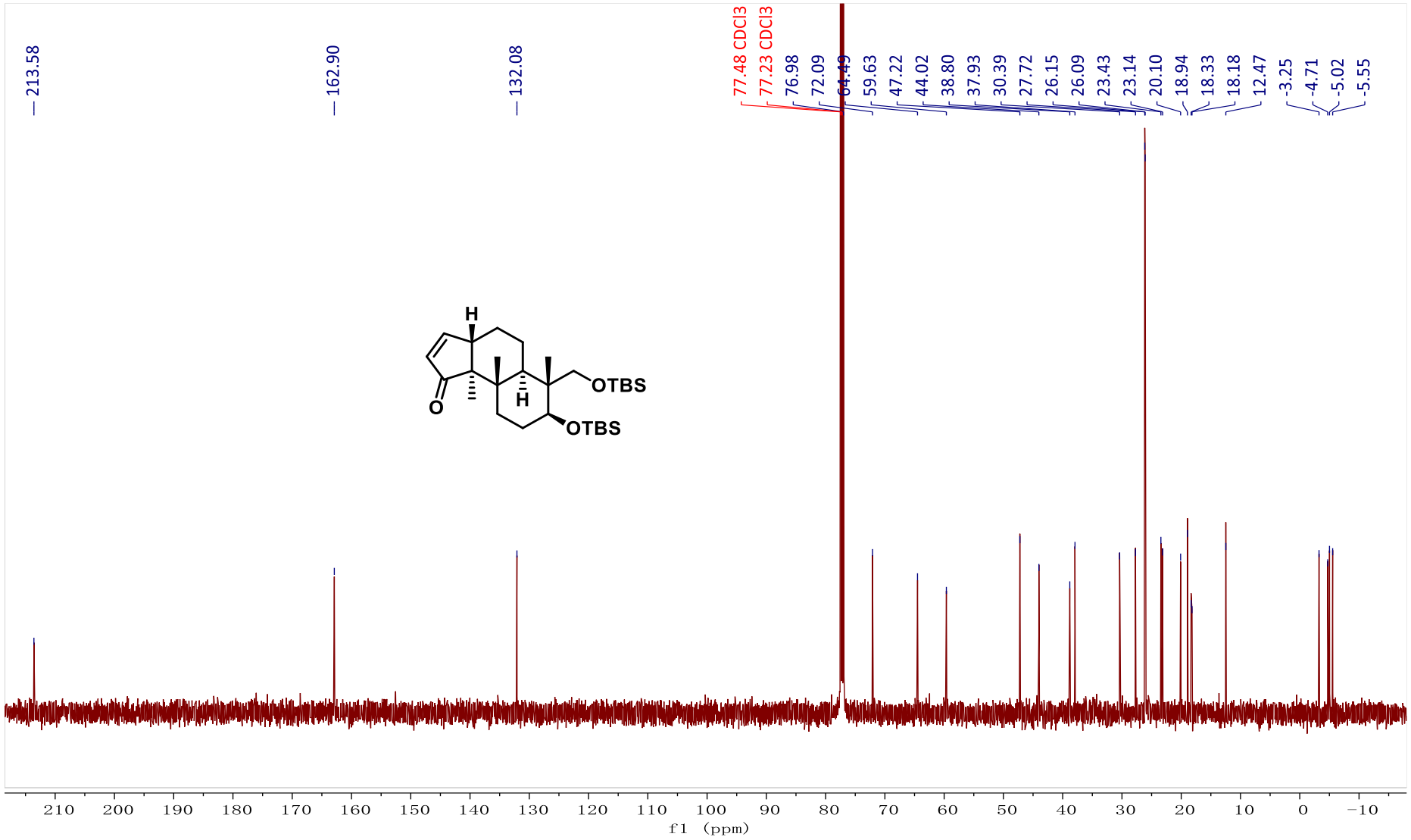
NOESY Spectrum of Compound (–)-**20** in $CDCl_3$



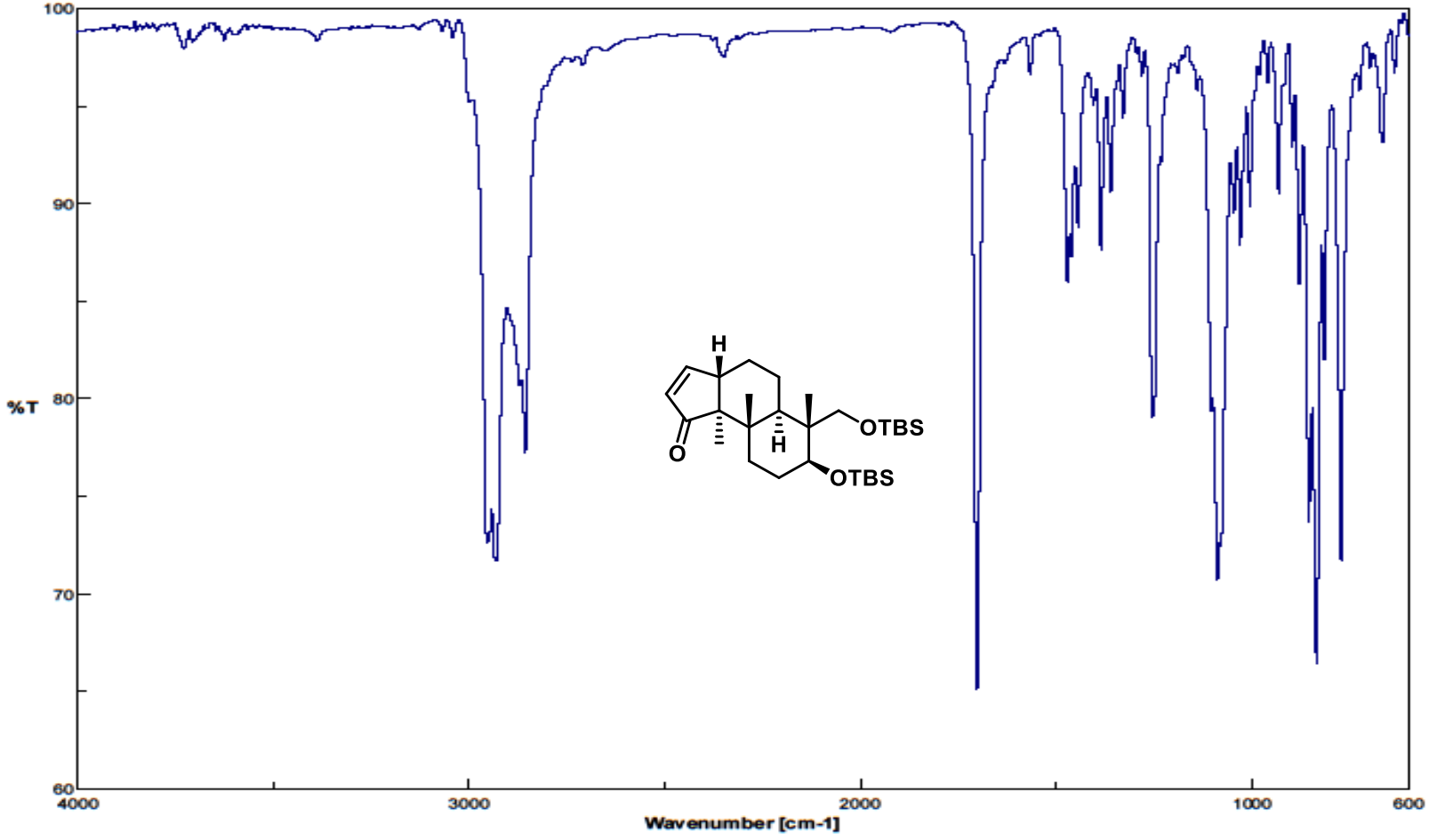
IR Spectrum of Compound (−)-**20**



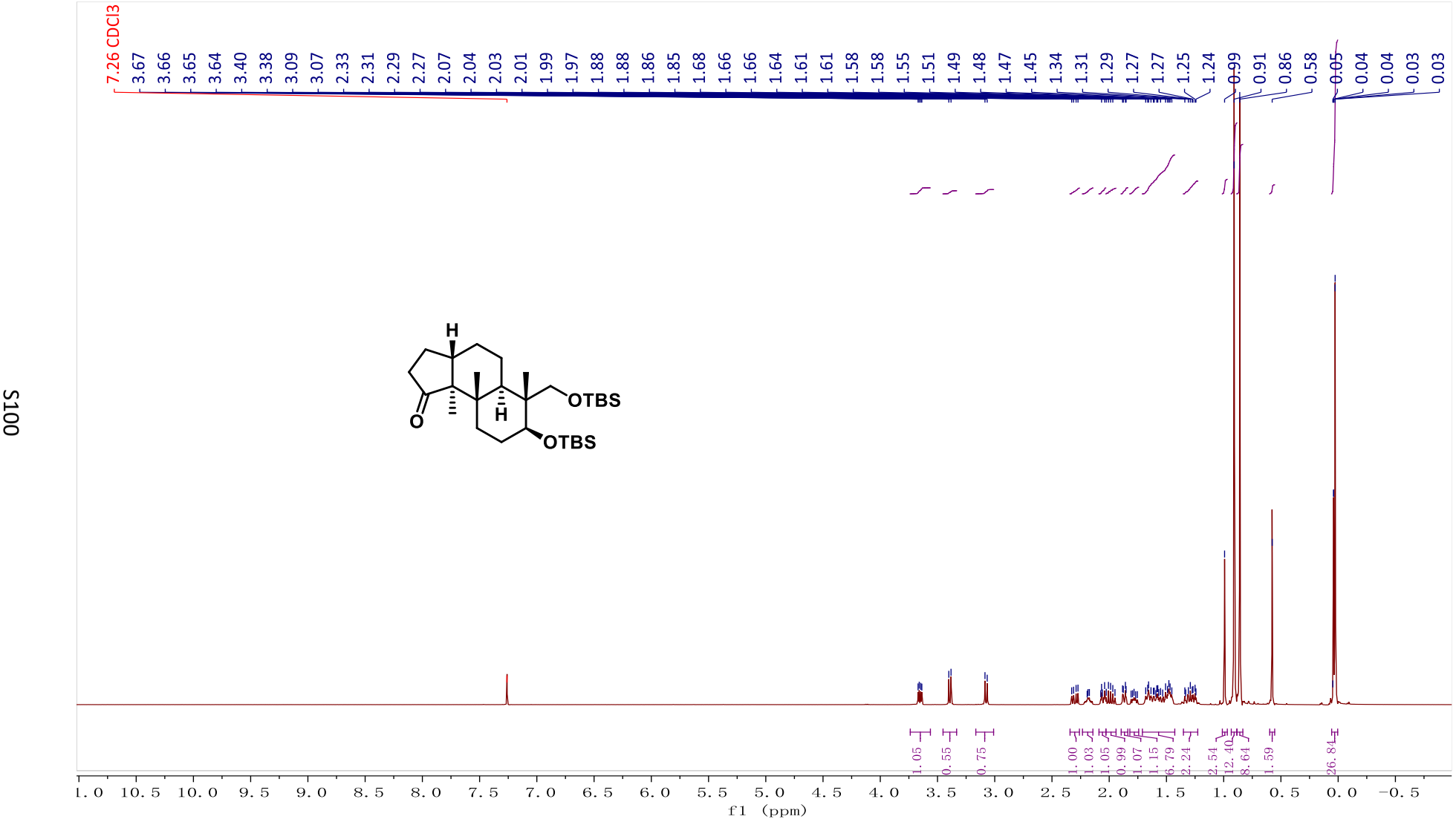
^{1}H NMR (500 MHz) Spectrum of Compound **(+)-21** in $CDCl_3$



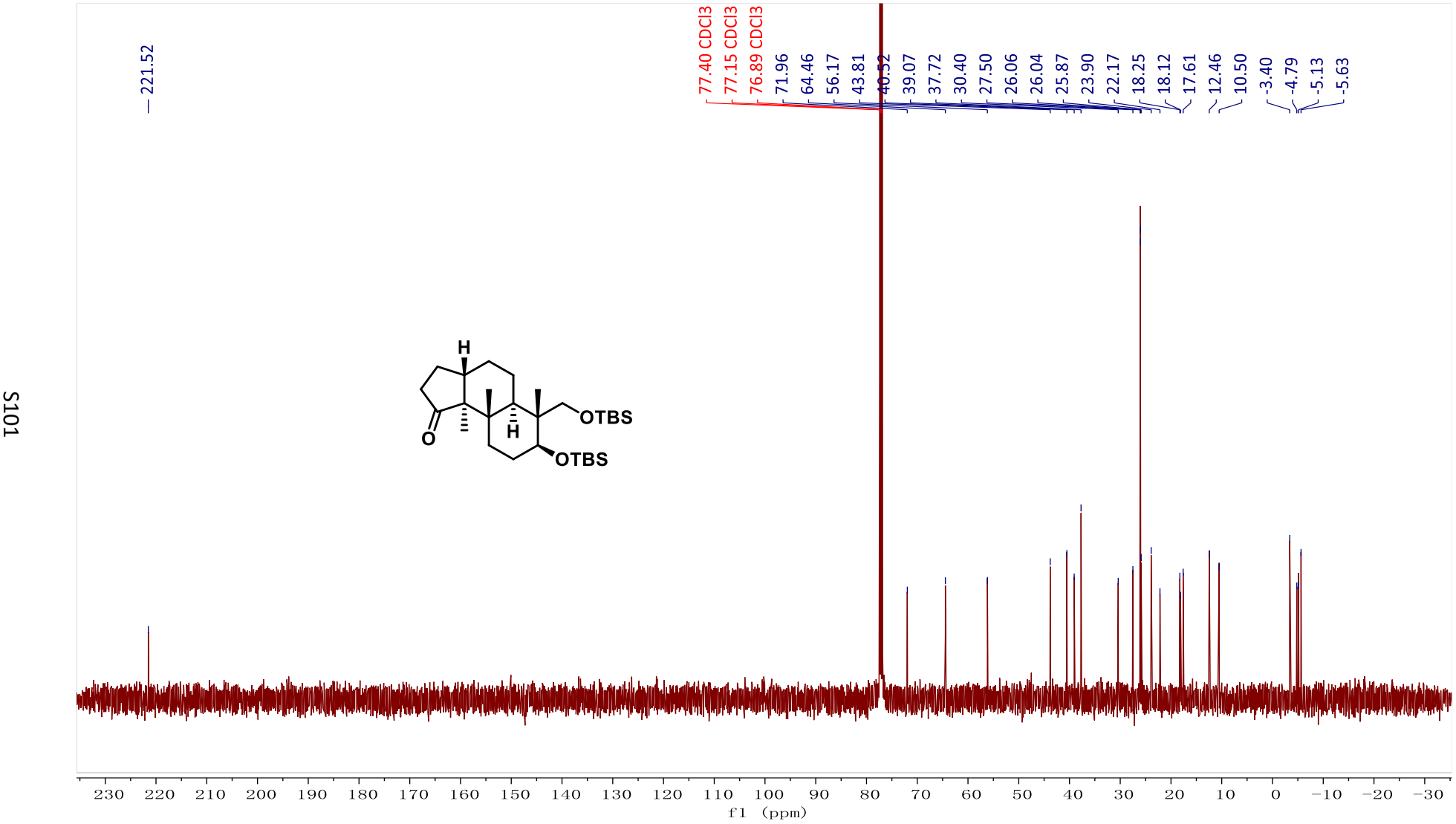
^{13}C NMR (126 MHz) Spectrum of Compound **(+)-21** in $CDCl_3$



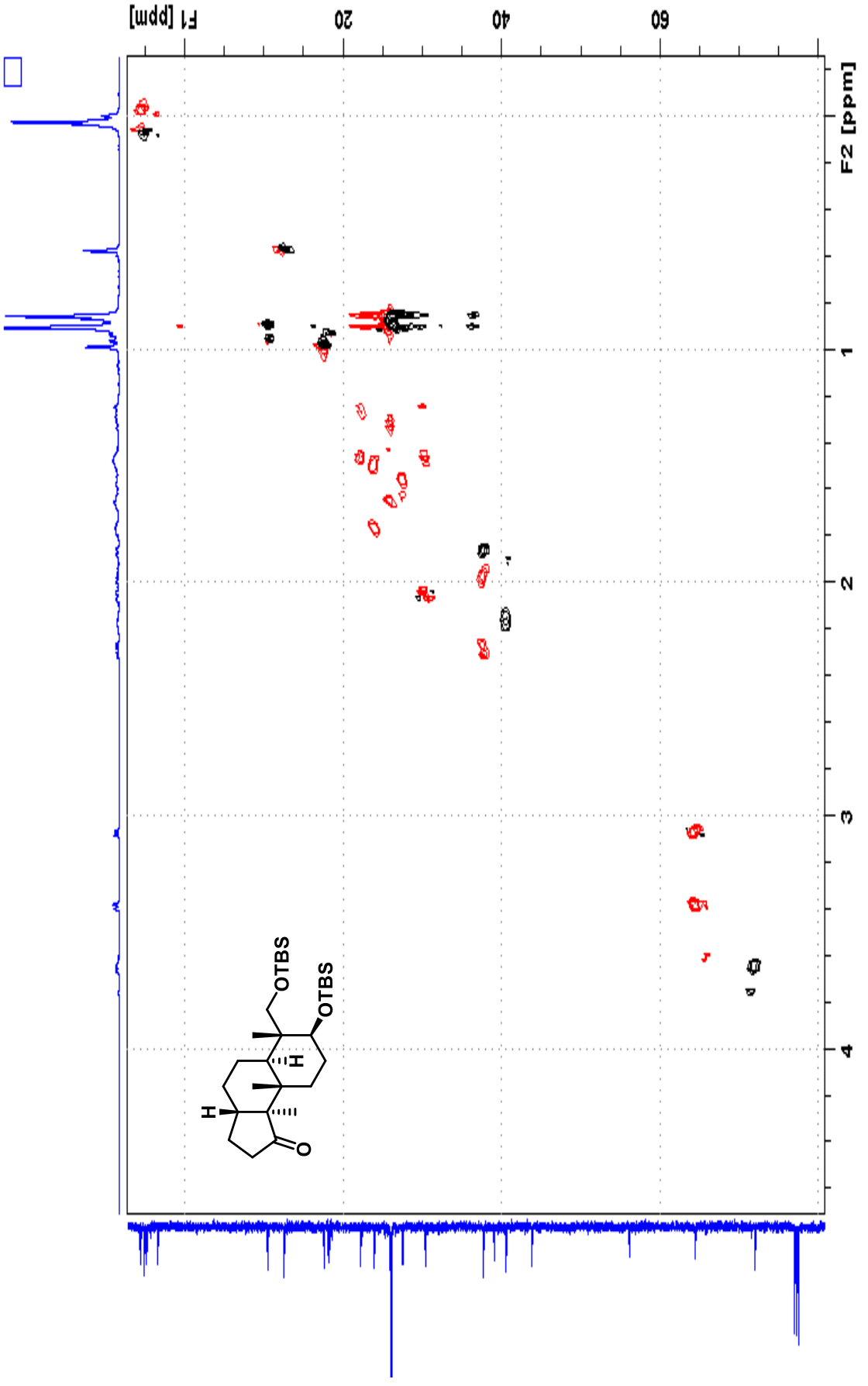
IR Spectrum of Compound **(+)-21**



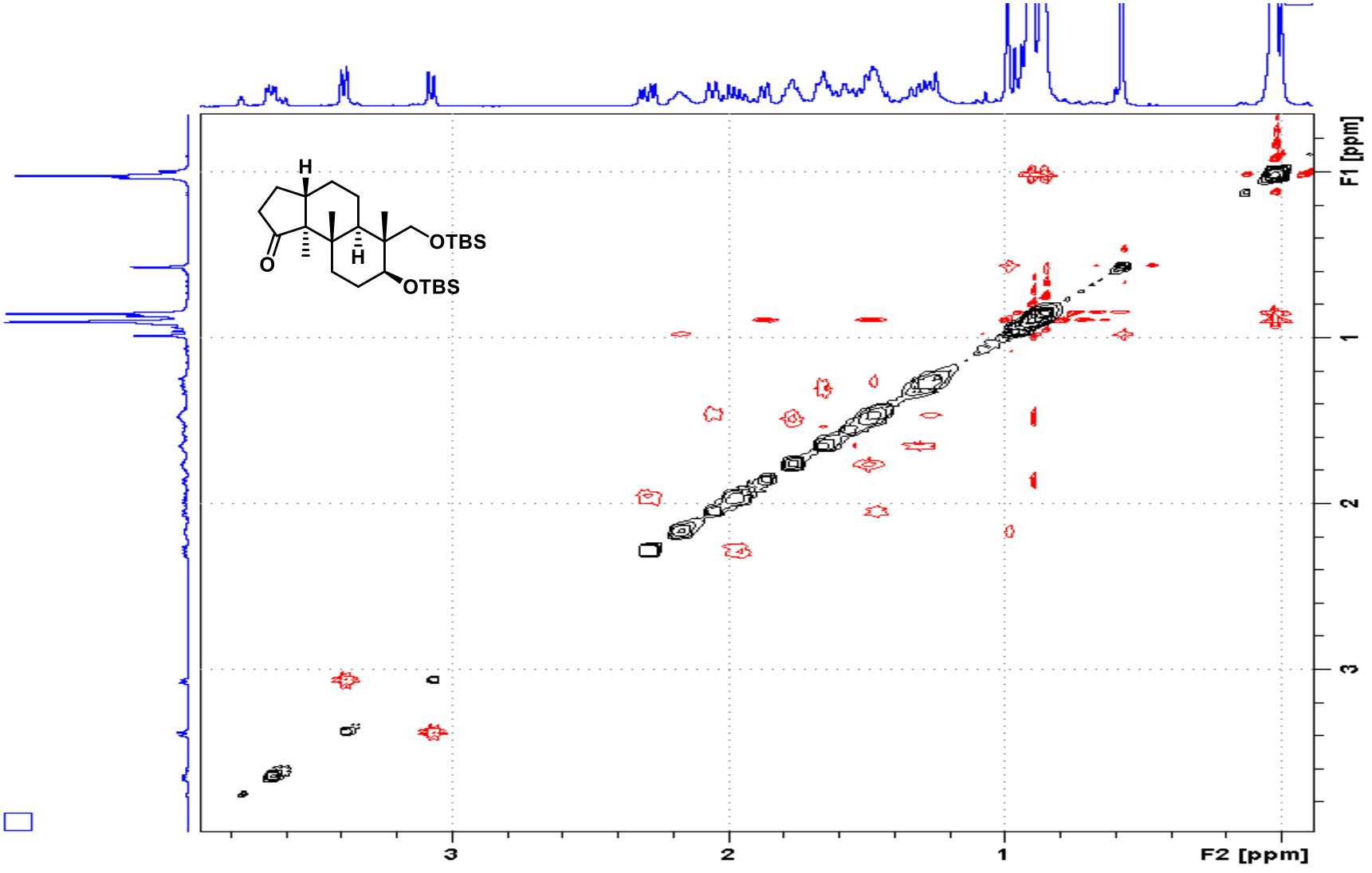
^{1}H NMR (500 MHz) Spectrum of Compound **(−)-22** in $CDCl_3$



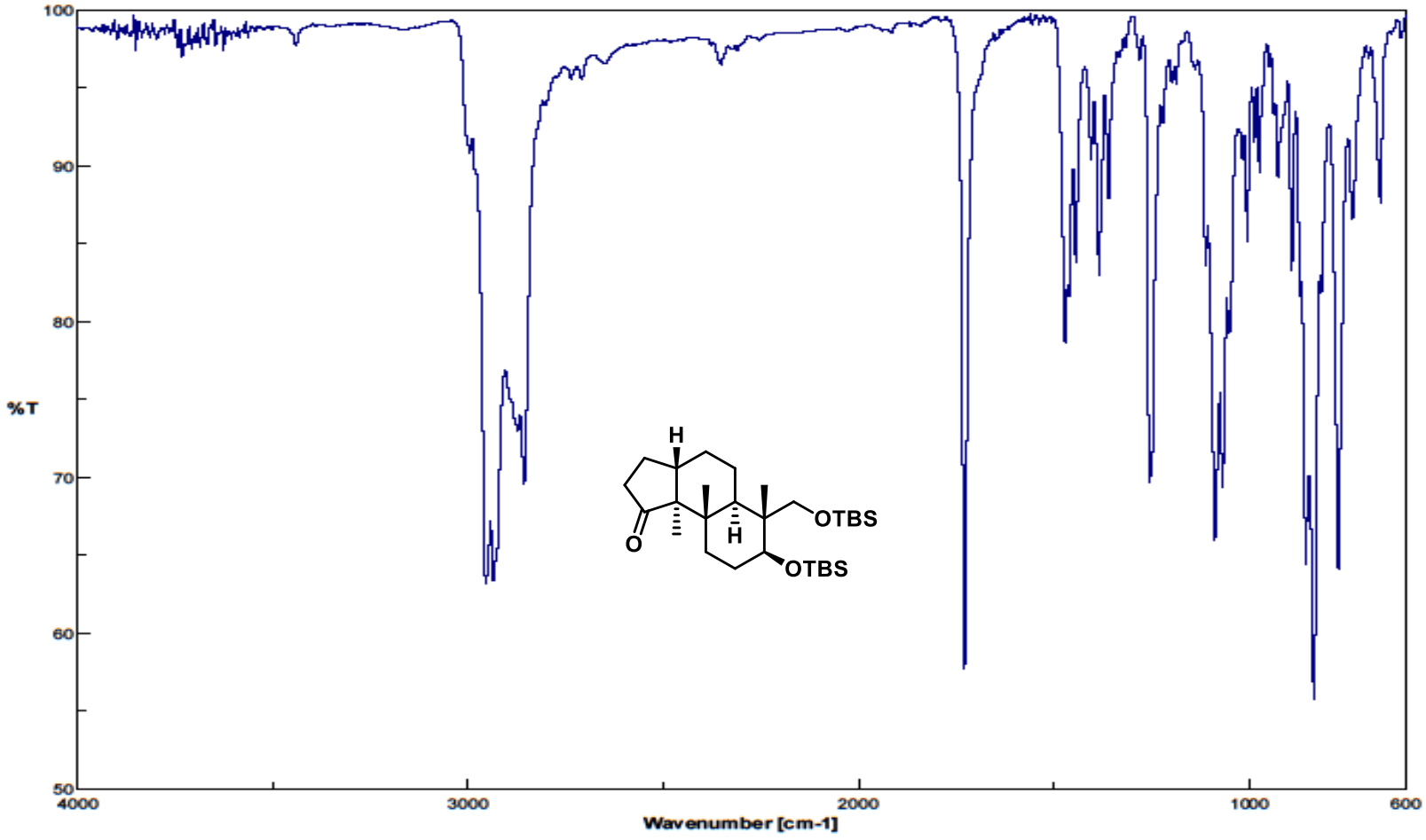
^{13}C NMR (126 MHz) Spectrum of Compound **(−)-22** in $CDCl_3$



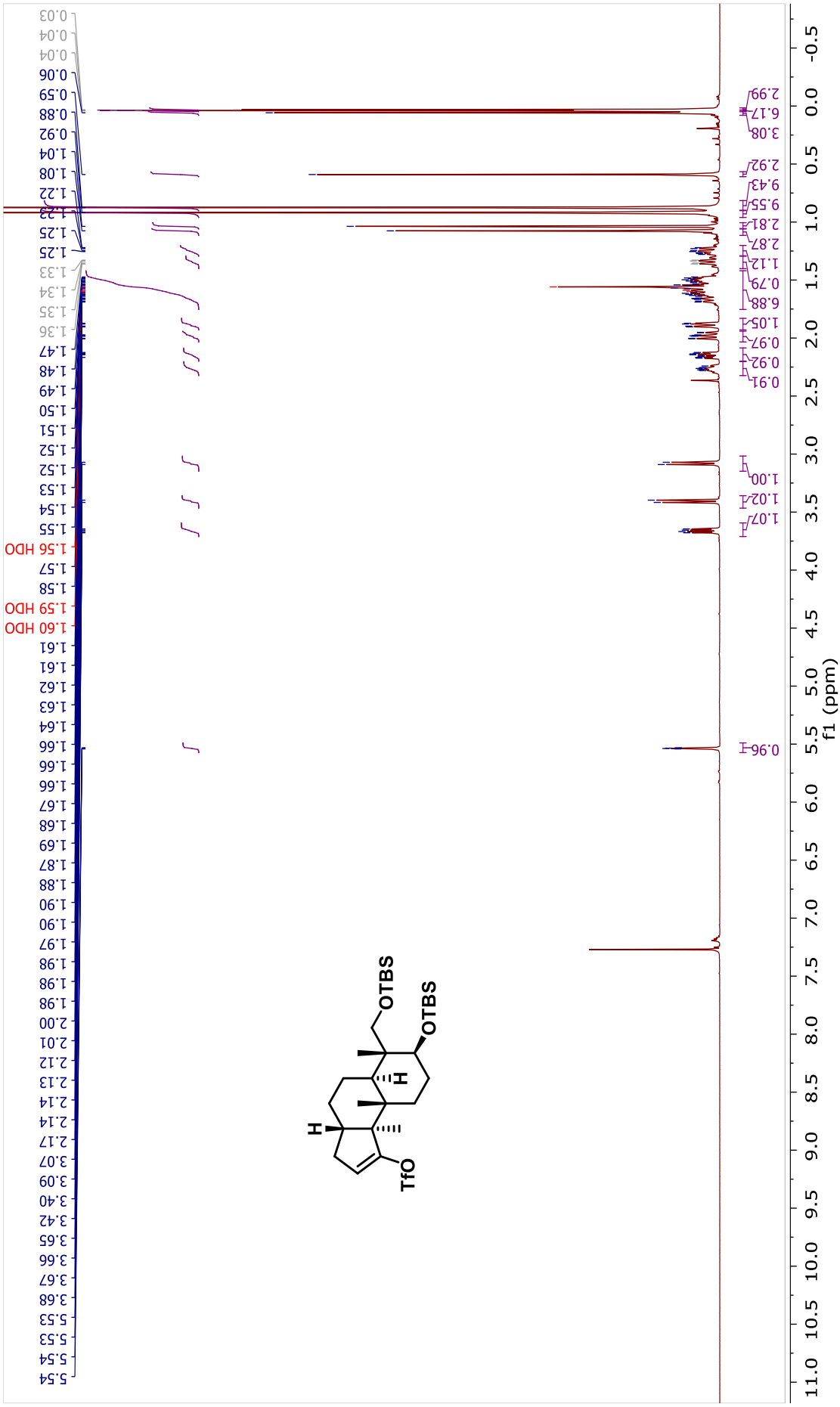
HSQC Spectrum of Compound (−)-**22** in $CDCl_3$



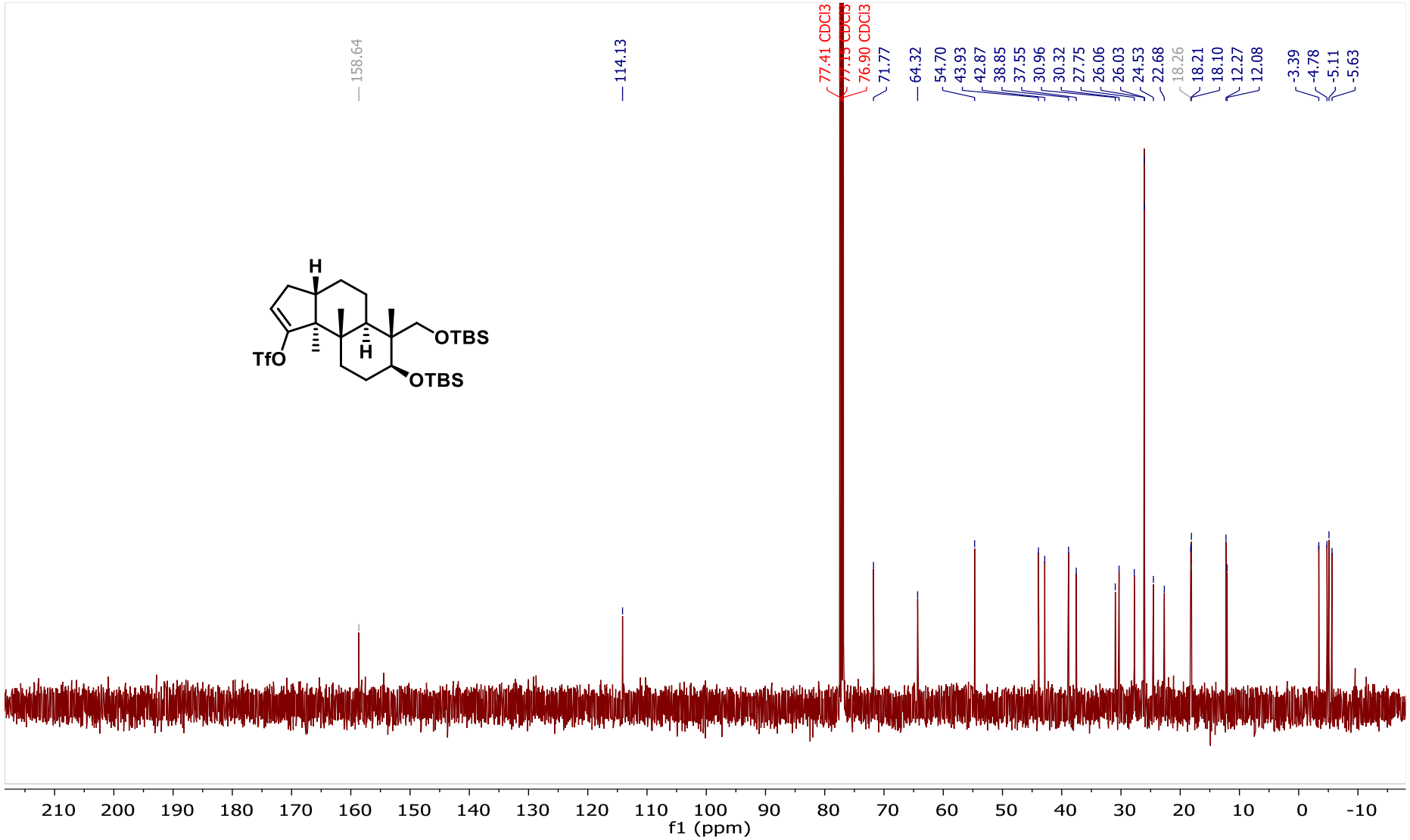
NOESY Spectrum of Compound (−)-**22** in $CDCl_3$



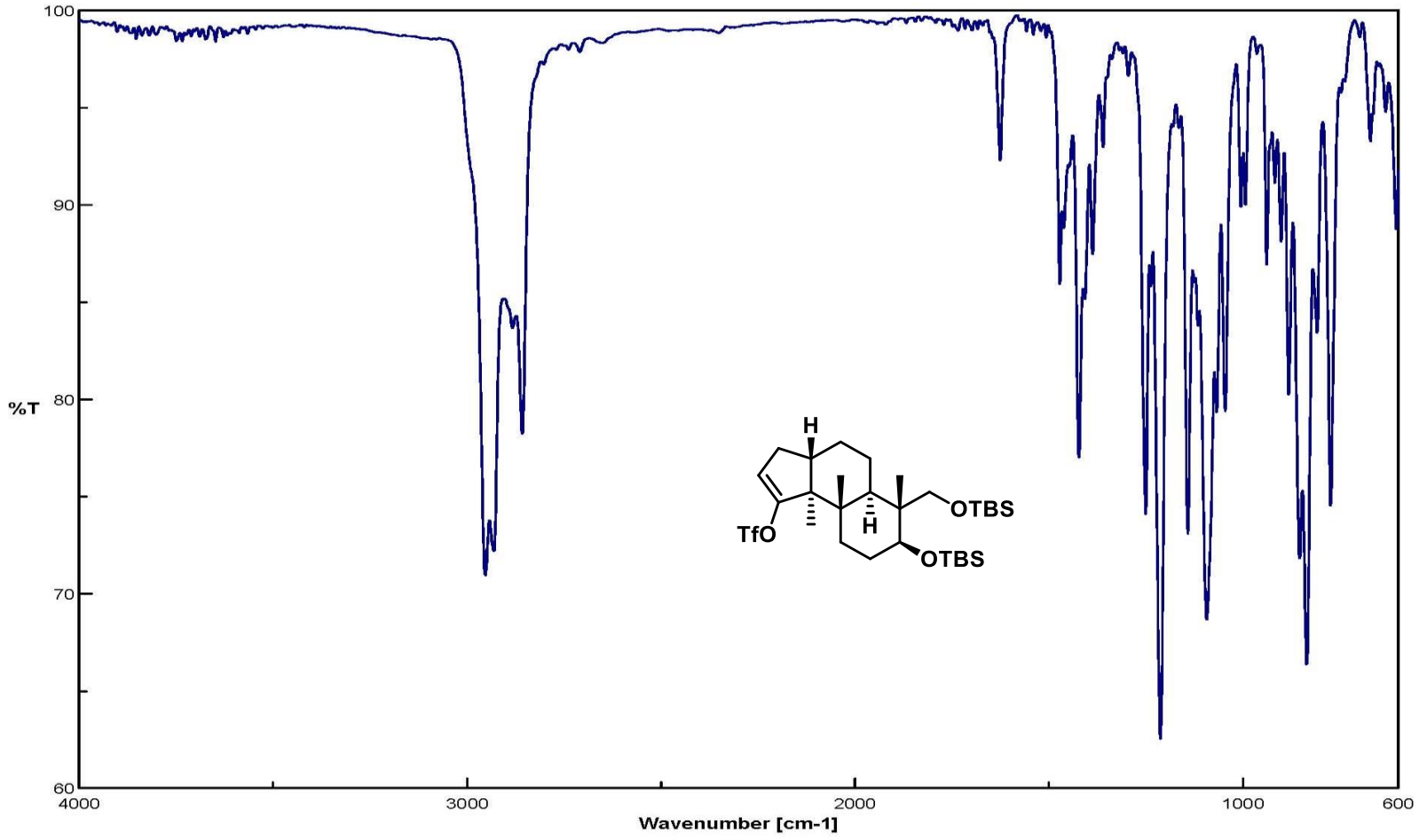
IR Spectrum of Compound (−)-**22**



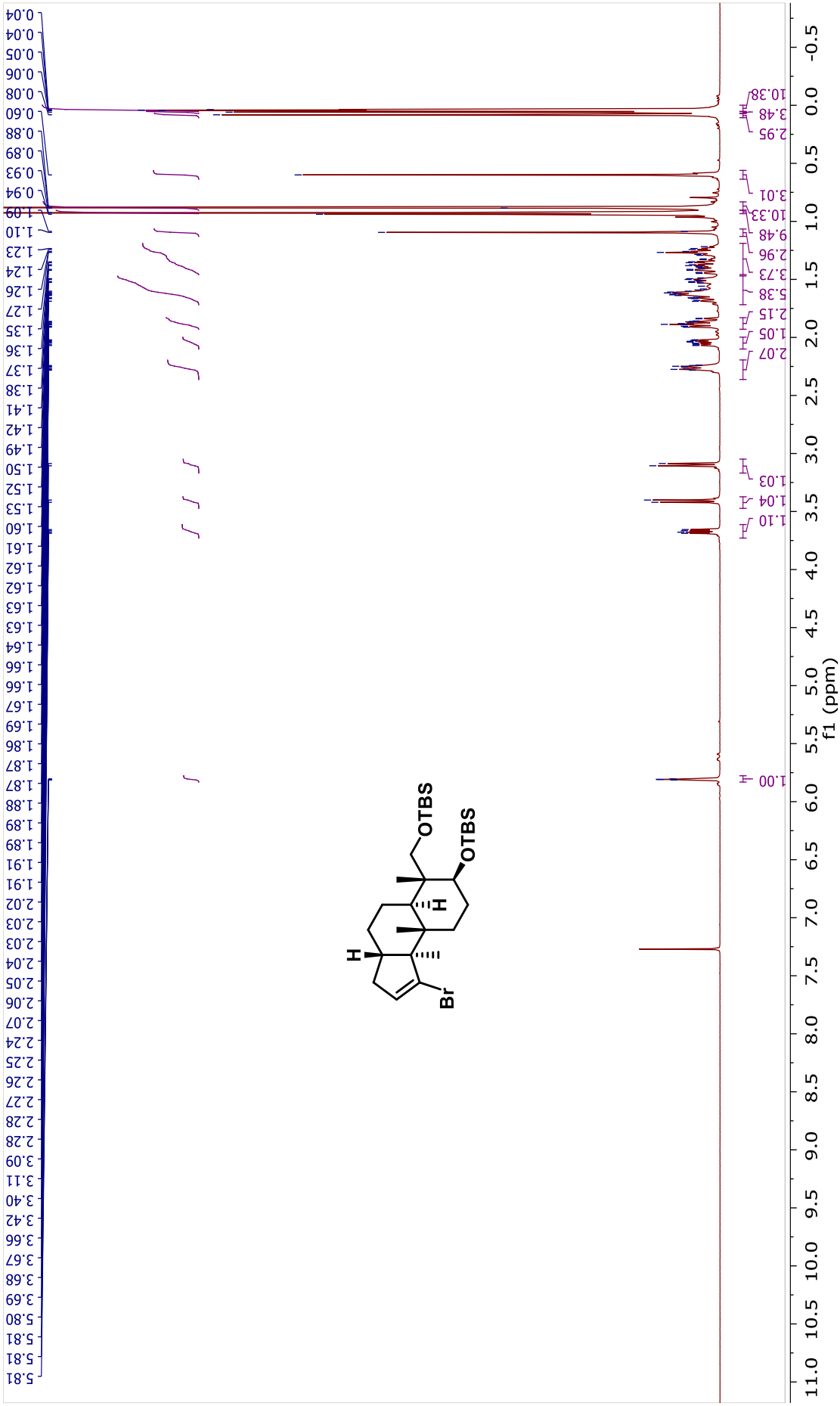
^{1}H NMR (500 MHz) Spectrum of Compound (−)-**23** in $CDCl_3$



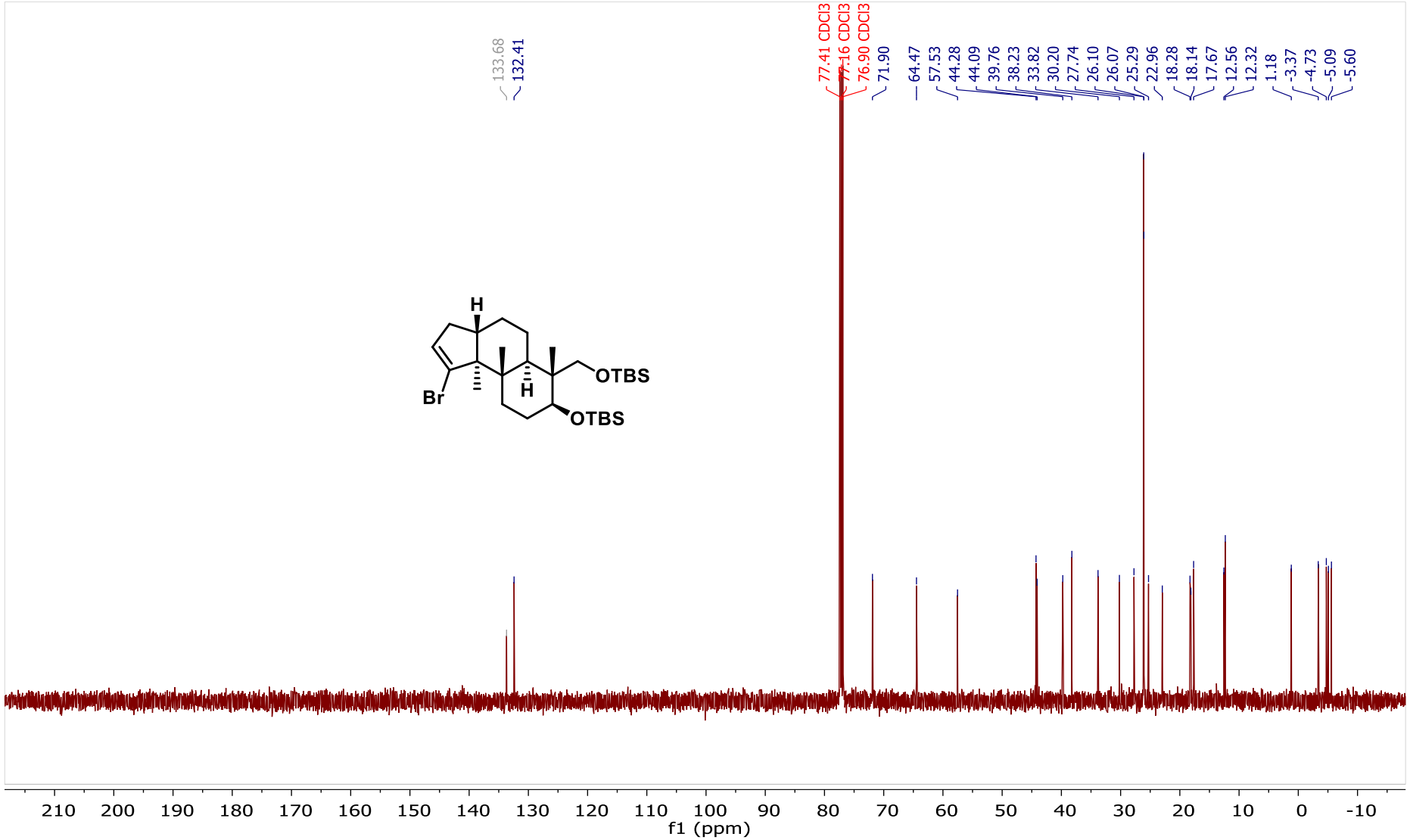
^{13}C NMR (126 MHz) Spectrum of Compound (−)-**23** in $CDCl_3$



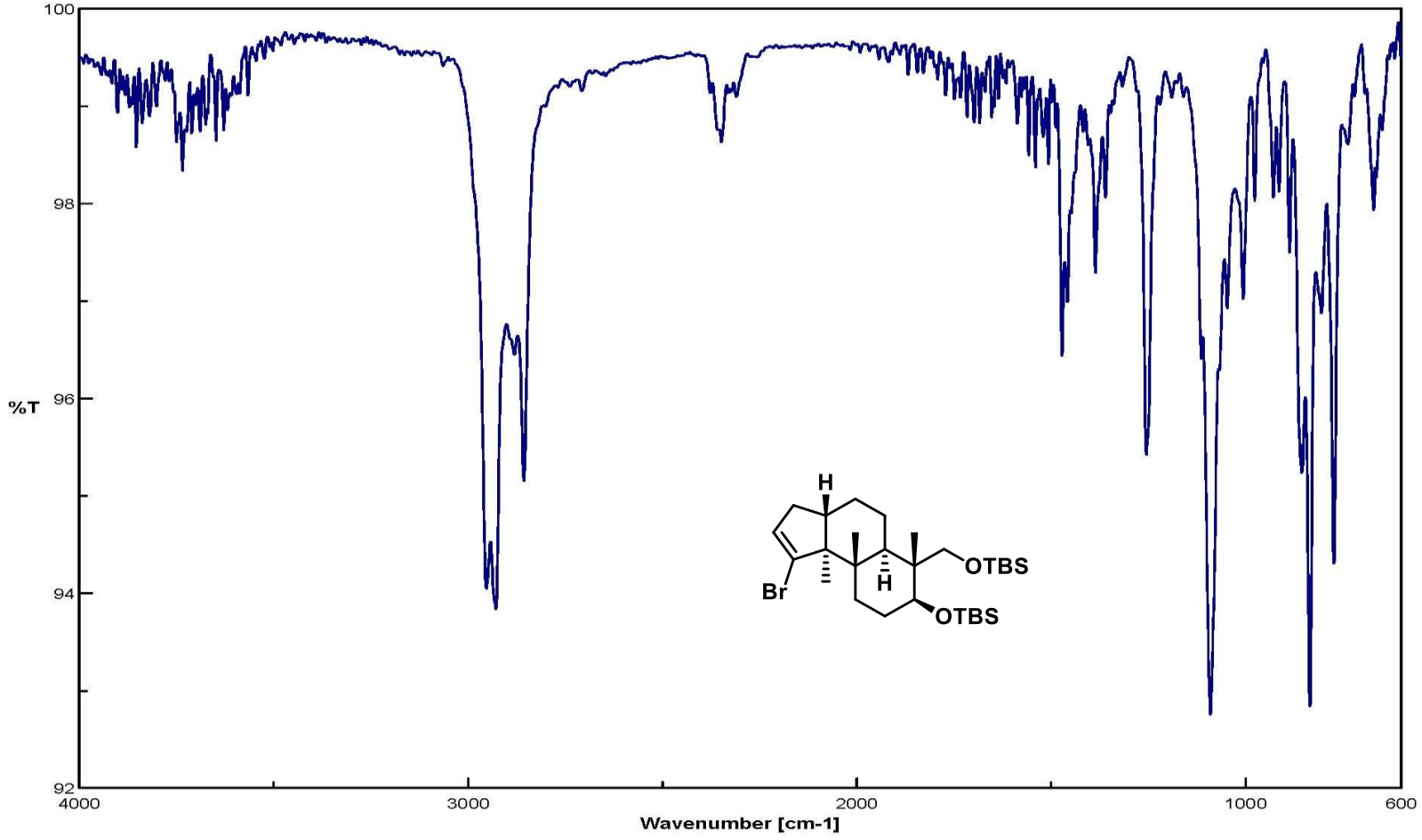
IR Spectrum of Compound (–)-**23**



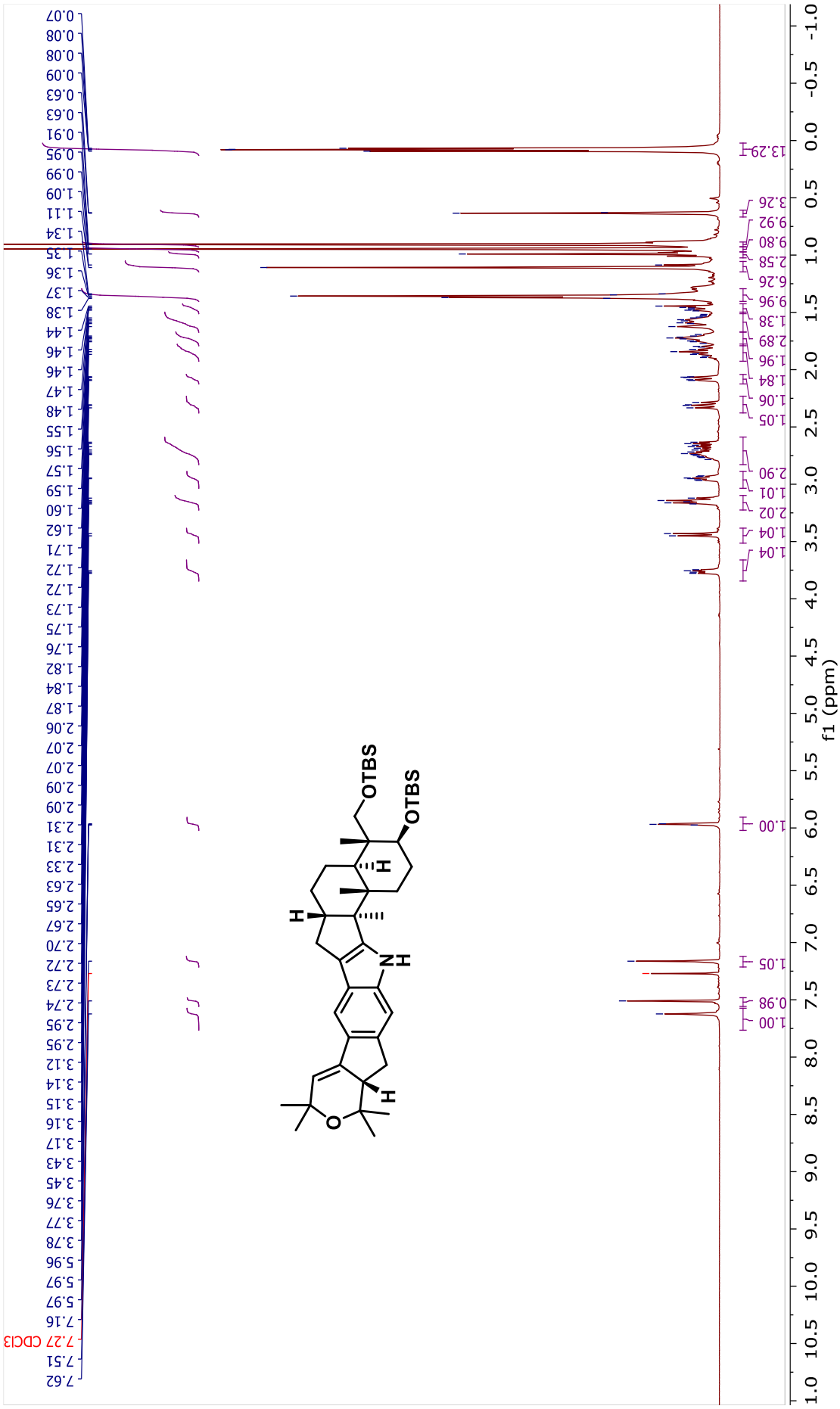
^{1}H NMR (500 MHz) Spectrum of Compound (−)-**8** in $CDCl_3$



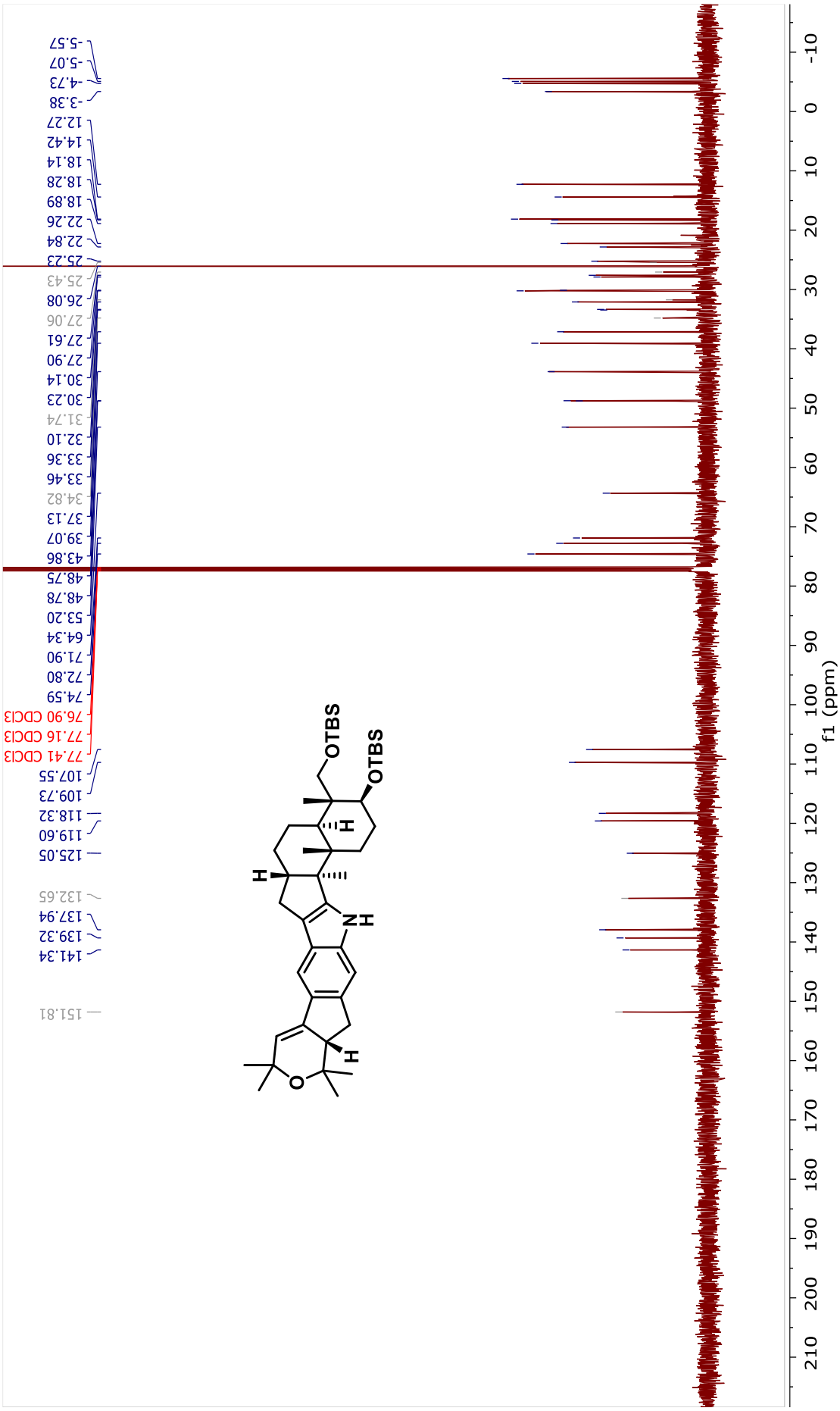
^{13}C NMR (126 MHz) Spectrum of Compound (–)-**8** in $CDCl_3$



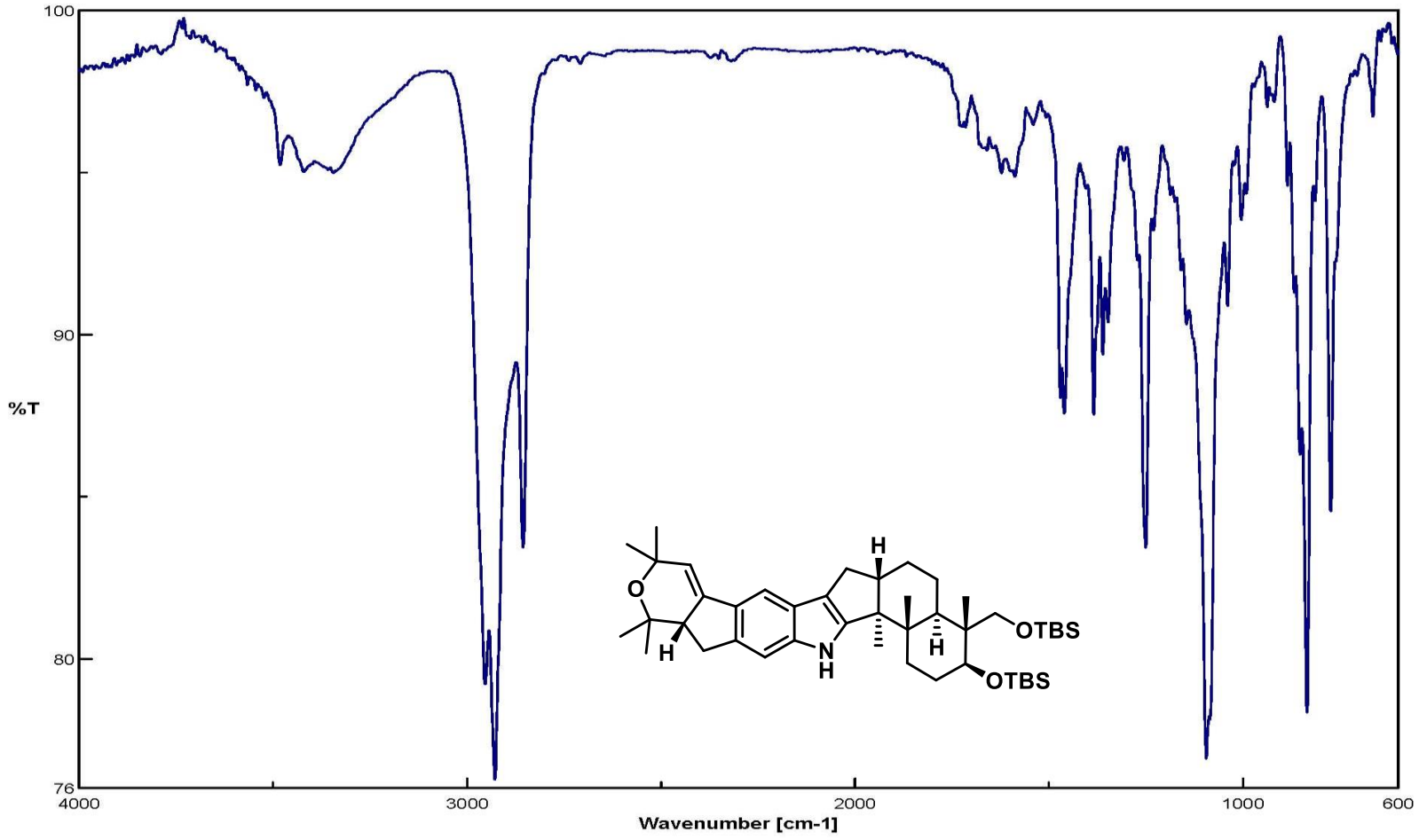
IR Spectrum of Compound (–)-**8**



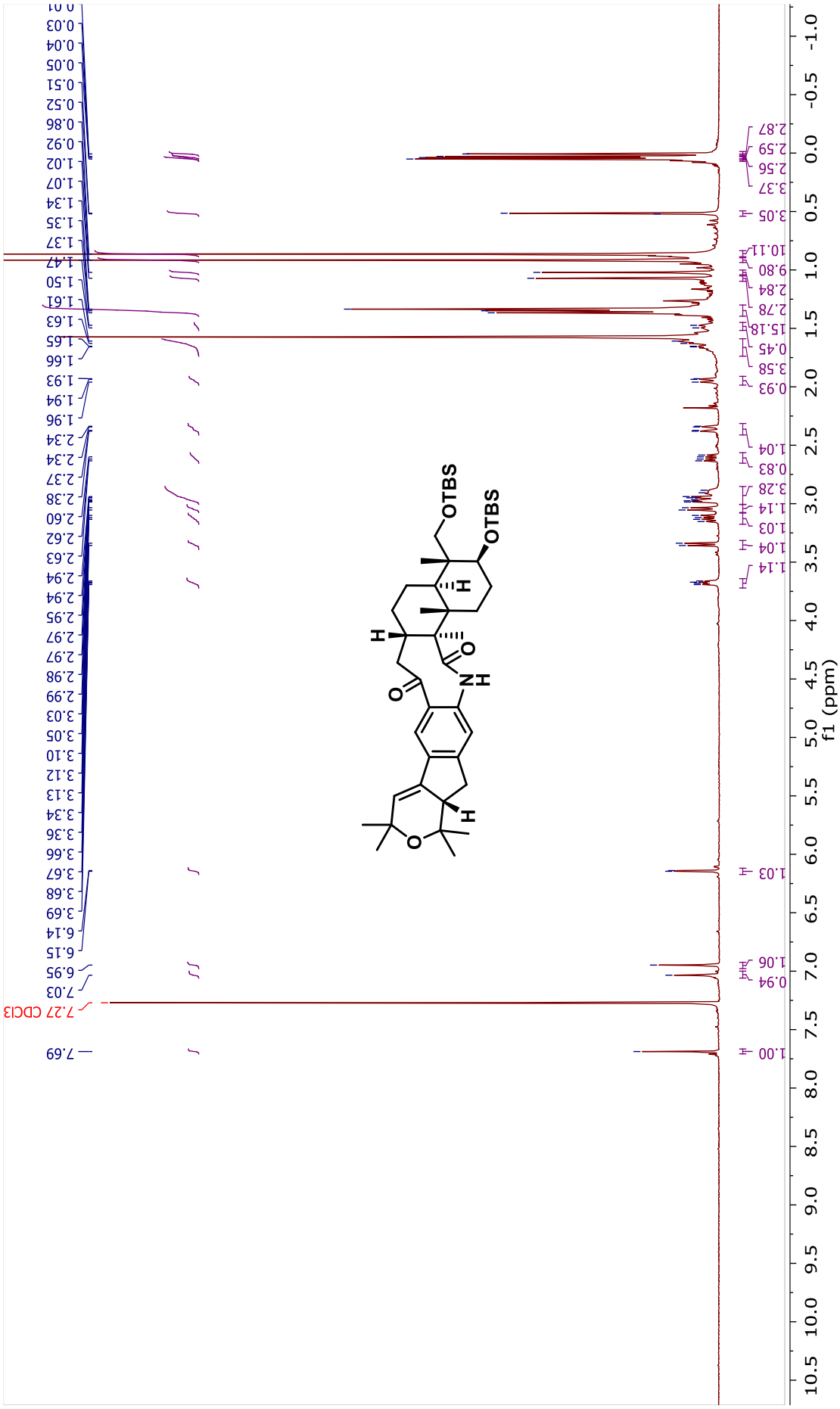
^{1}H NMR (500 MHz) Spectrum of Compound (−)-**26** in $CDCl_3$



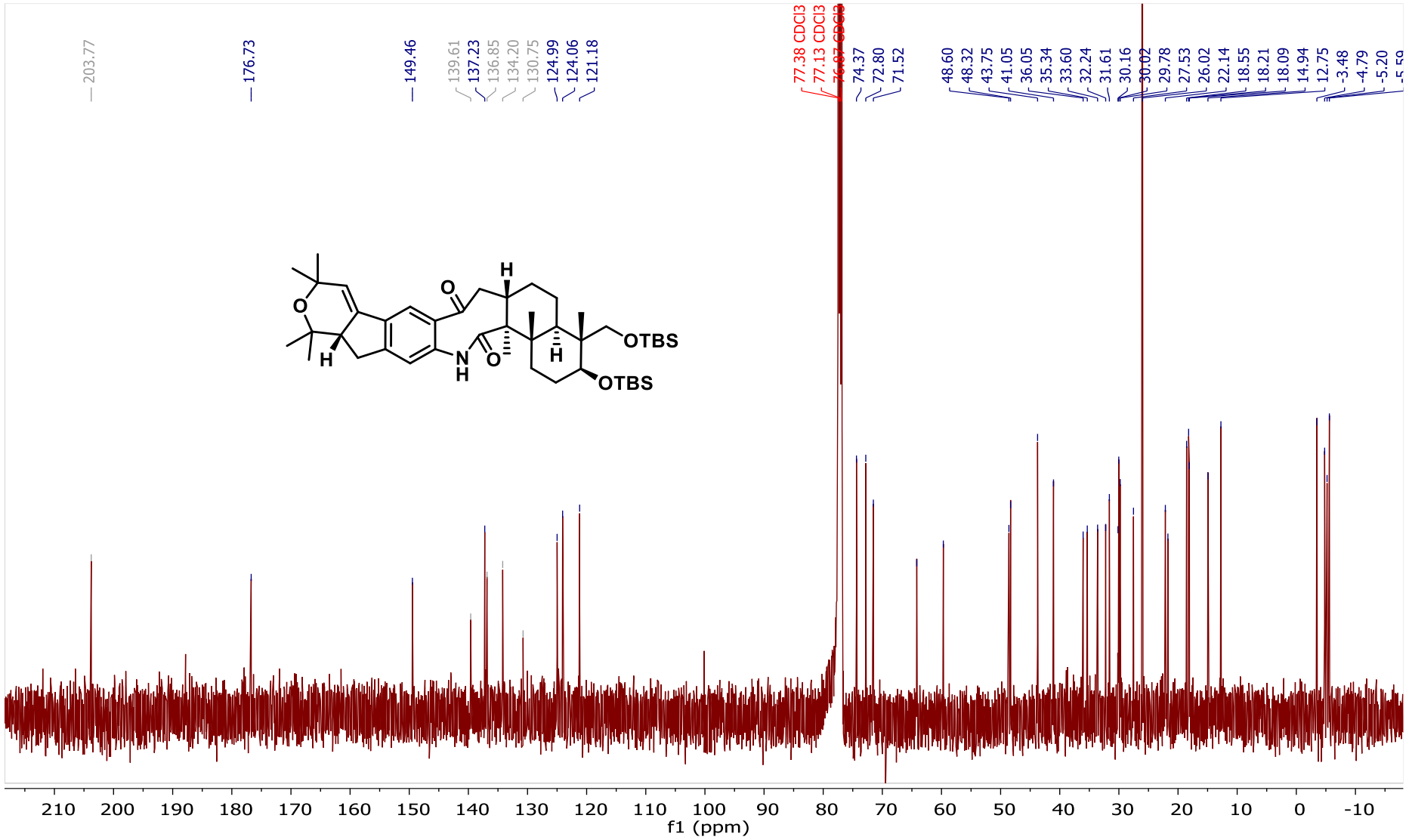
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-26** in $CDCl_3$



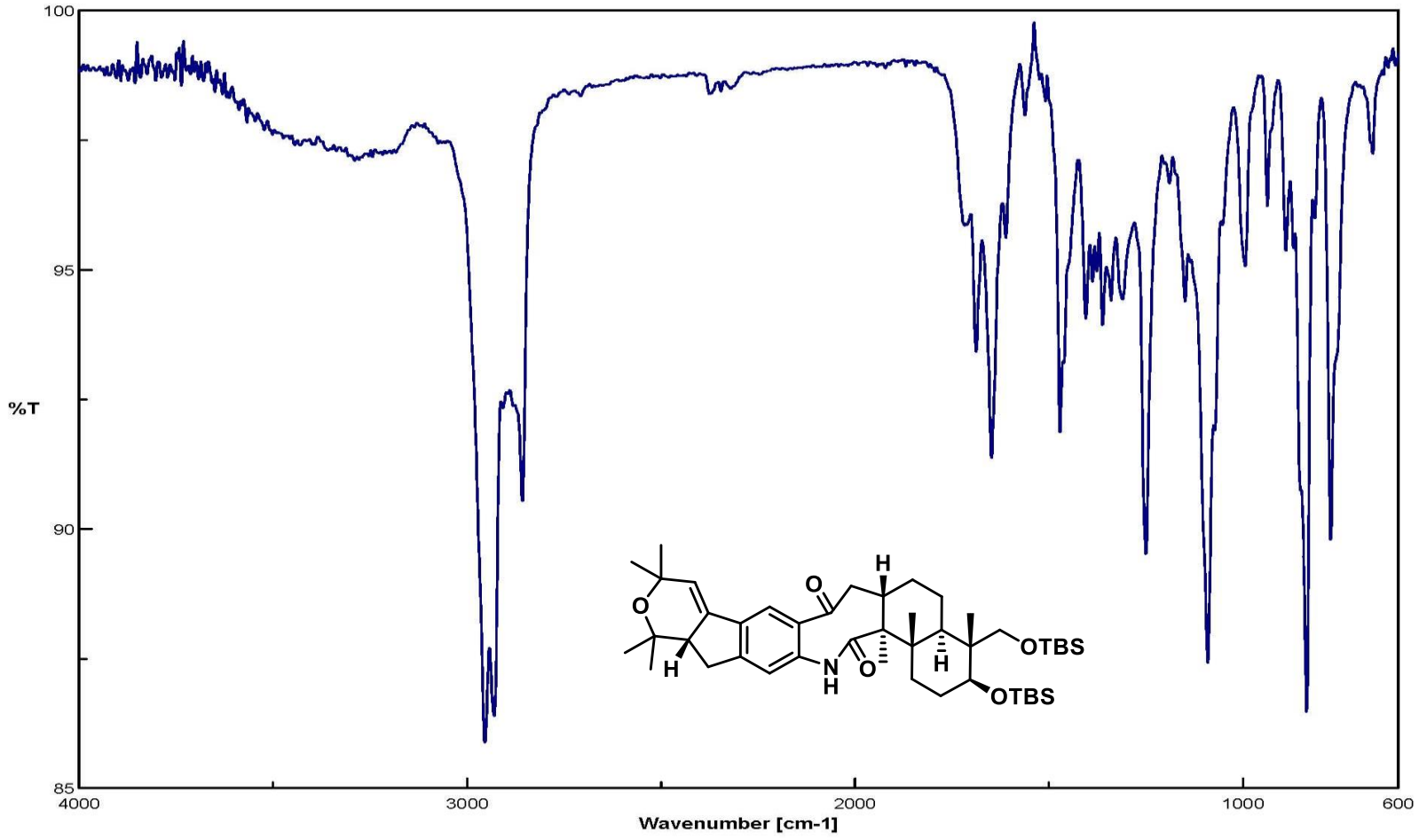
IR Spectrum of Compound (−)-**26**



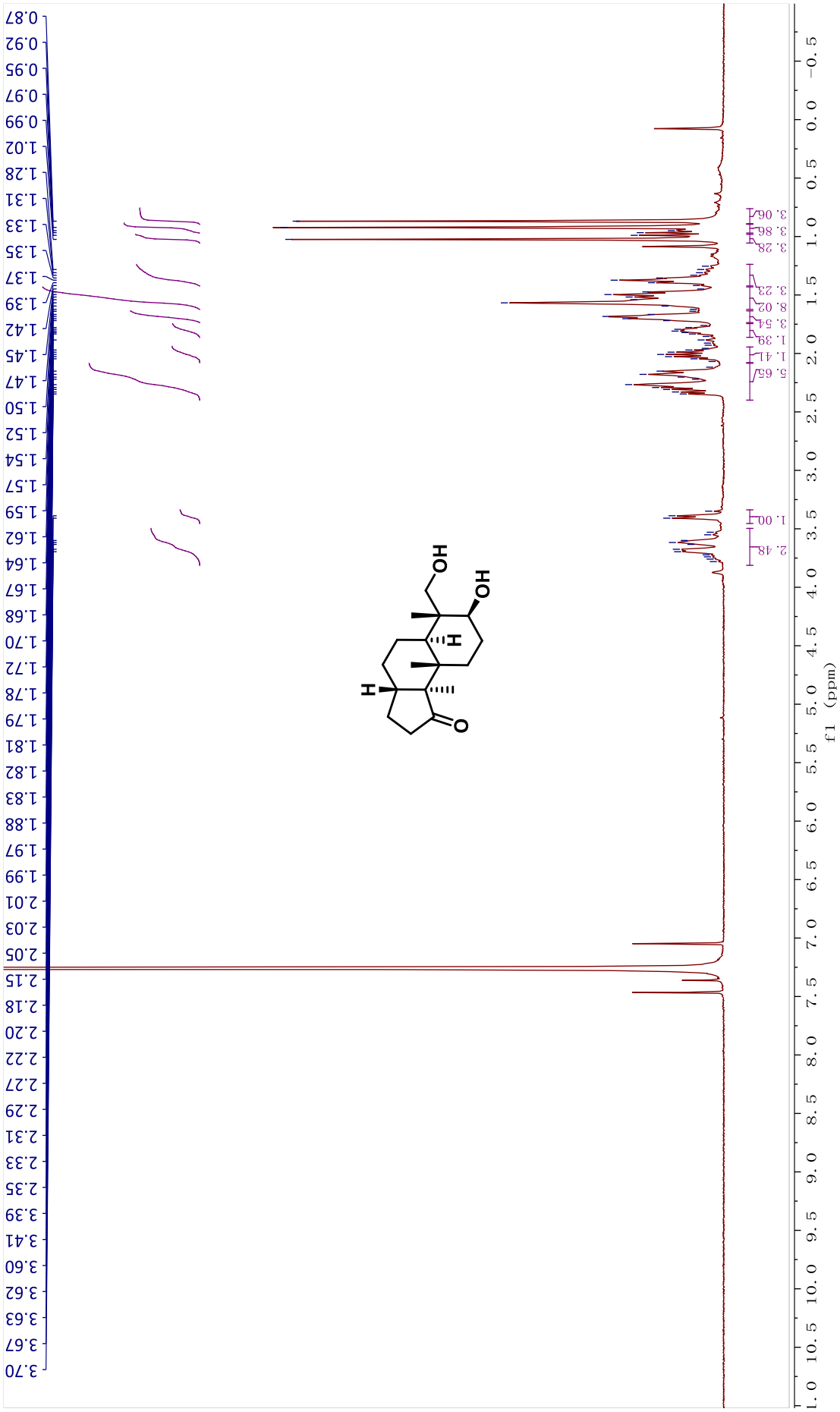
^{1}H NMR (500 MHz) Spectrum of Compound **(–)-27** in $CDCl_3$



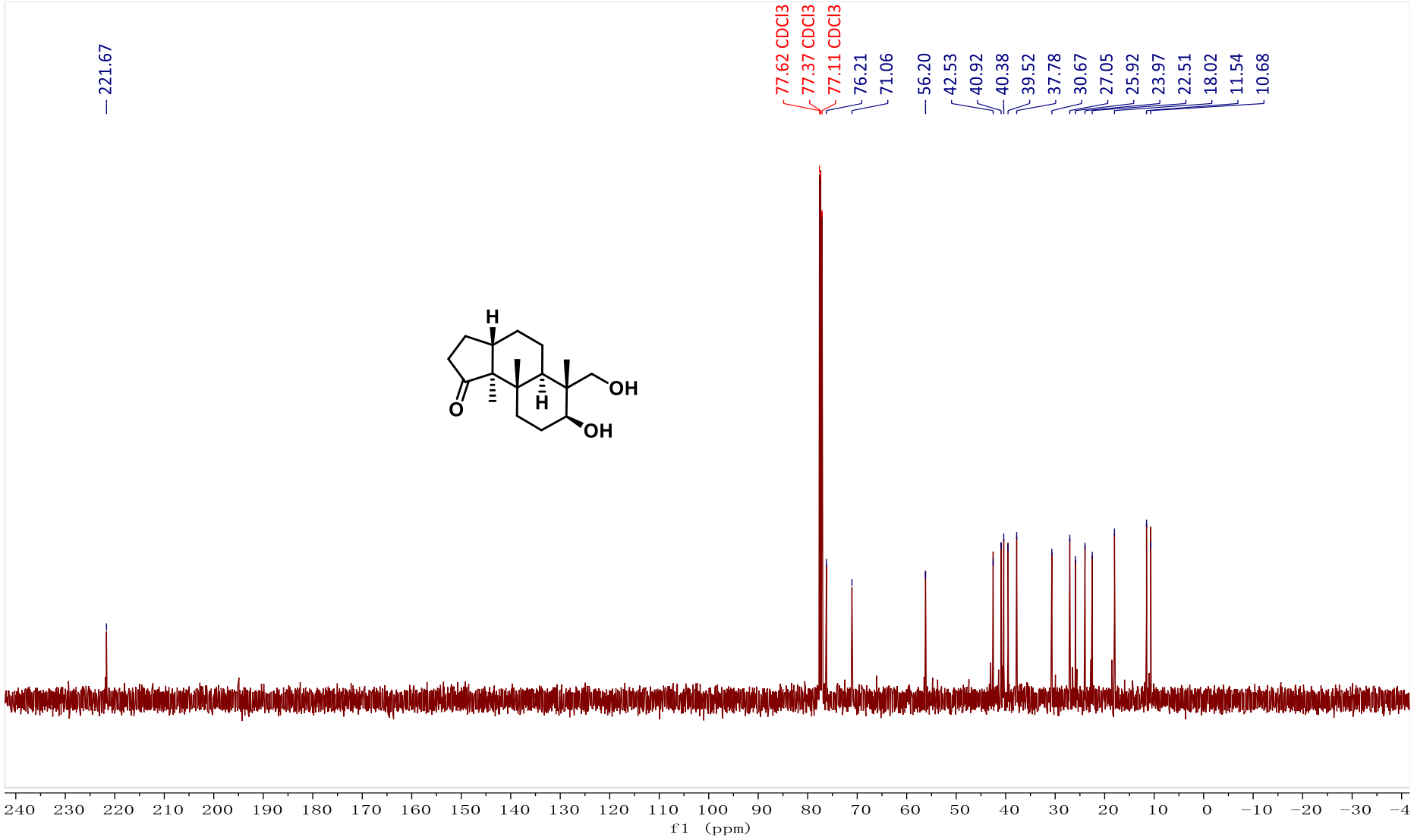
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-27** in $CDCl_3$



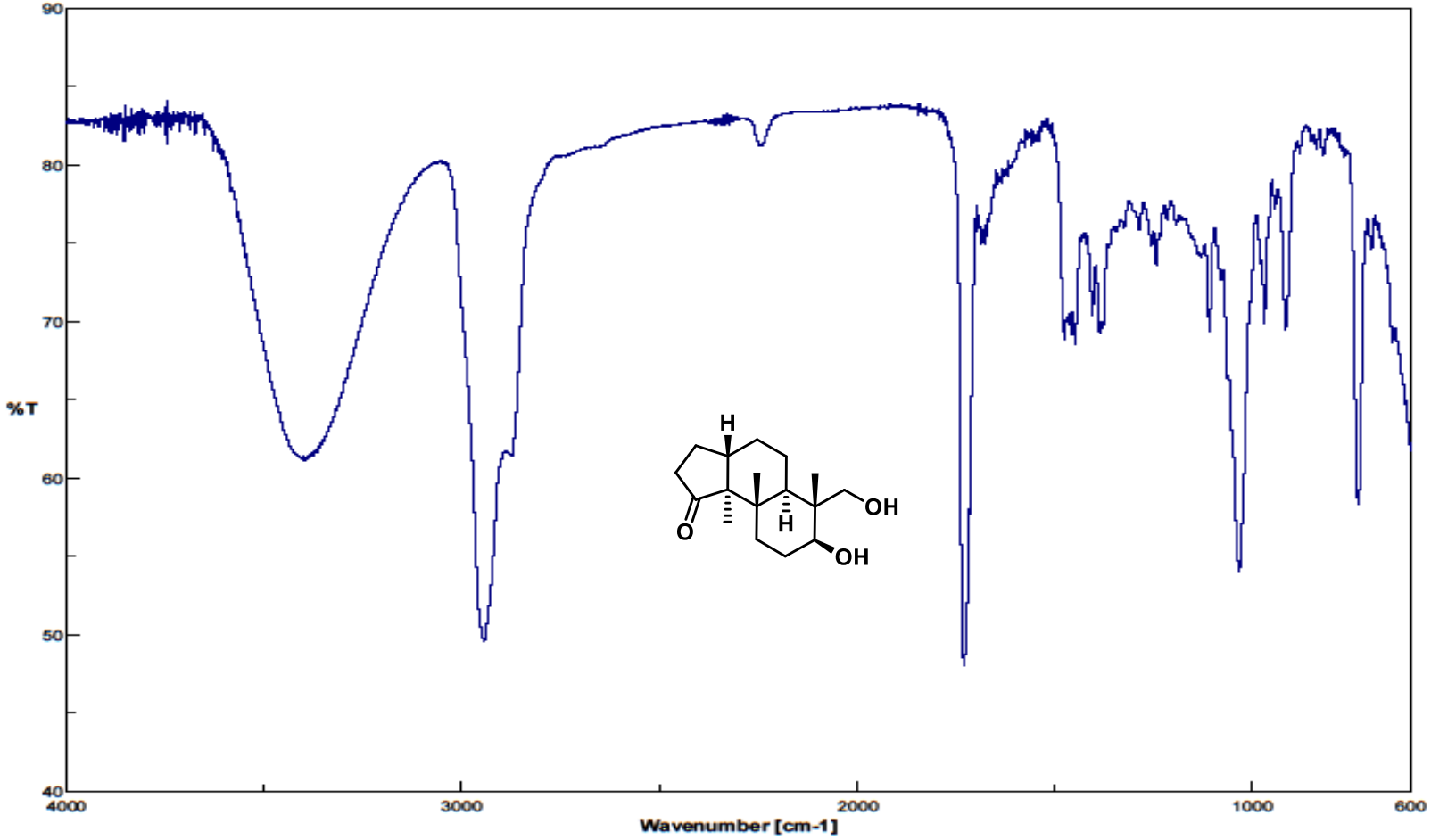
IR Spectrum of Compound **(–)-27**



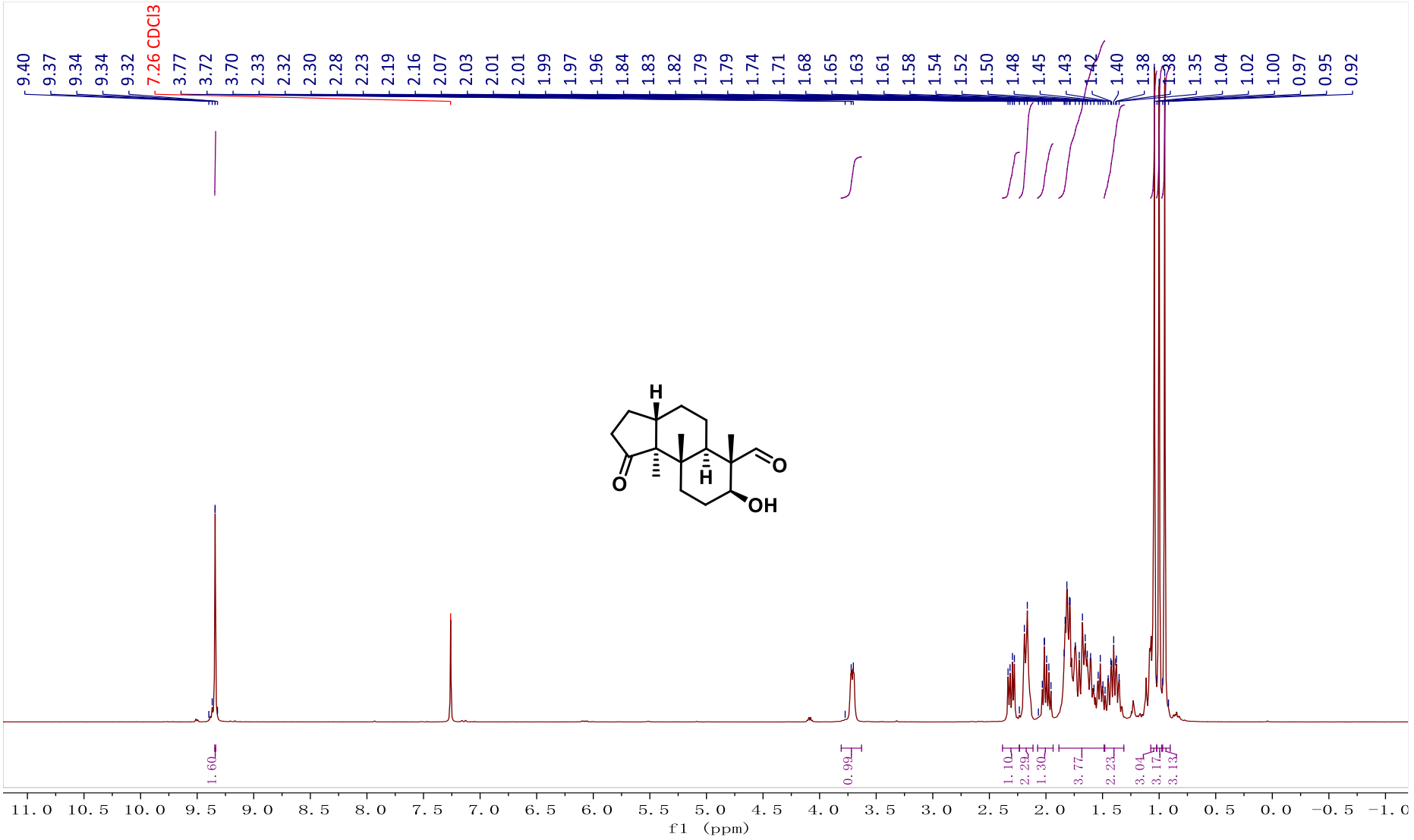
^{1}H NMR (500 MHz) Spectrum of Compound **(−)-28** in $CDCl_3$



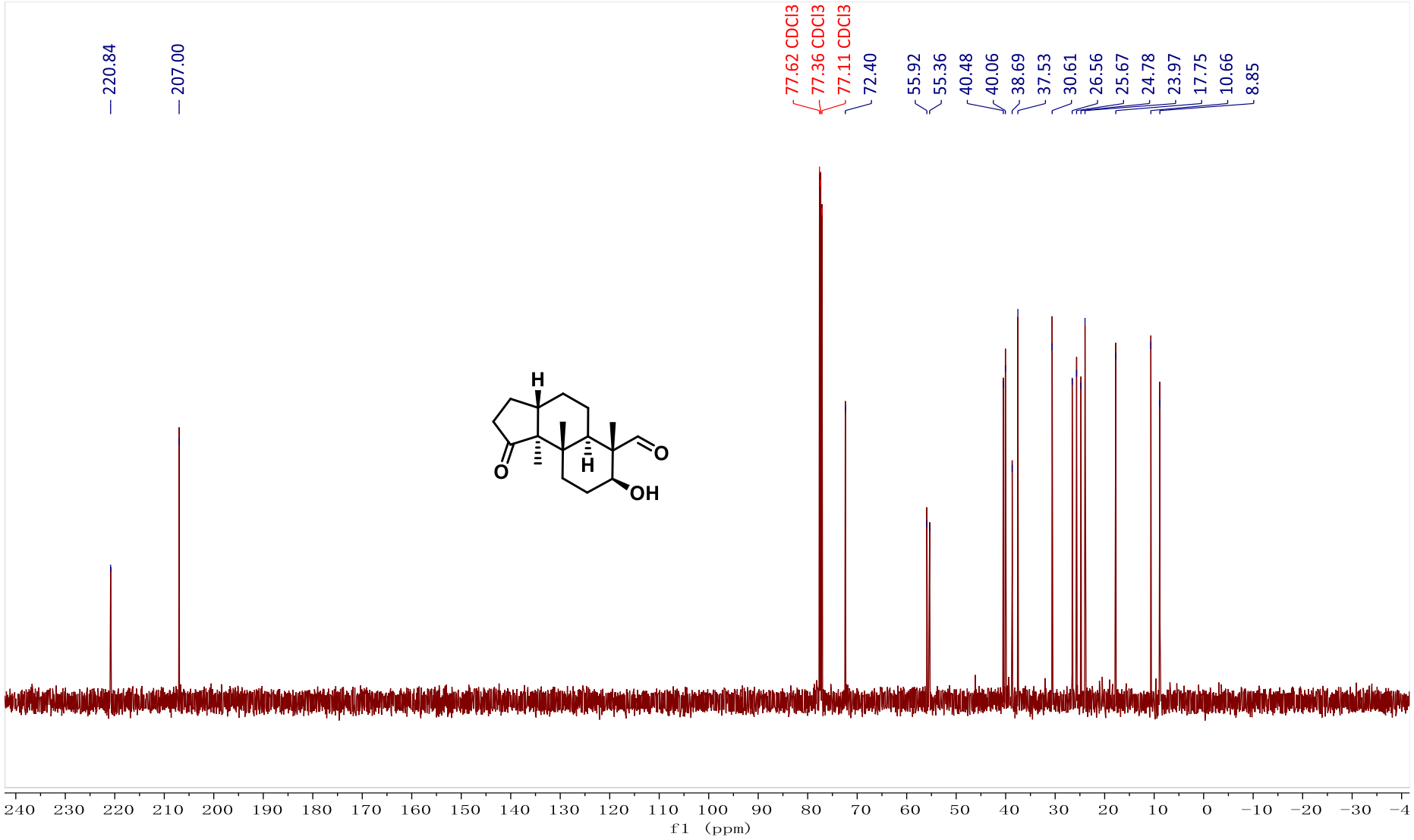
^{13}C NMR (126 MHz) Spectrum of Compound **(−)-28** in $CDCl_3$



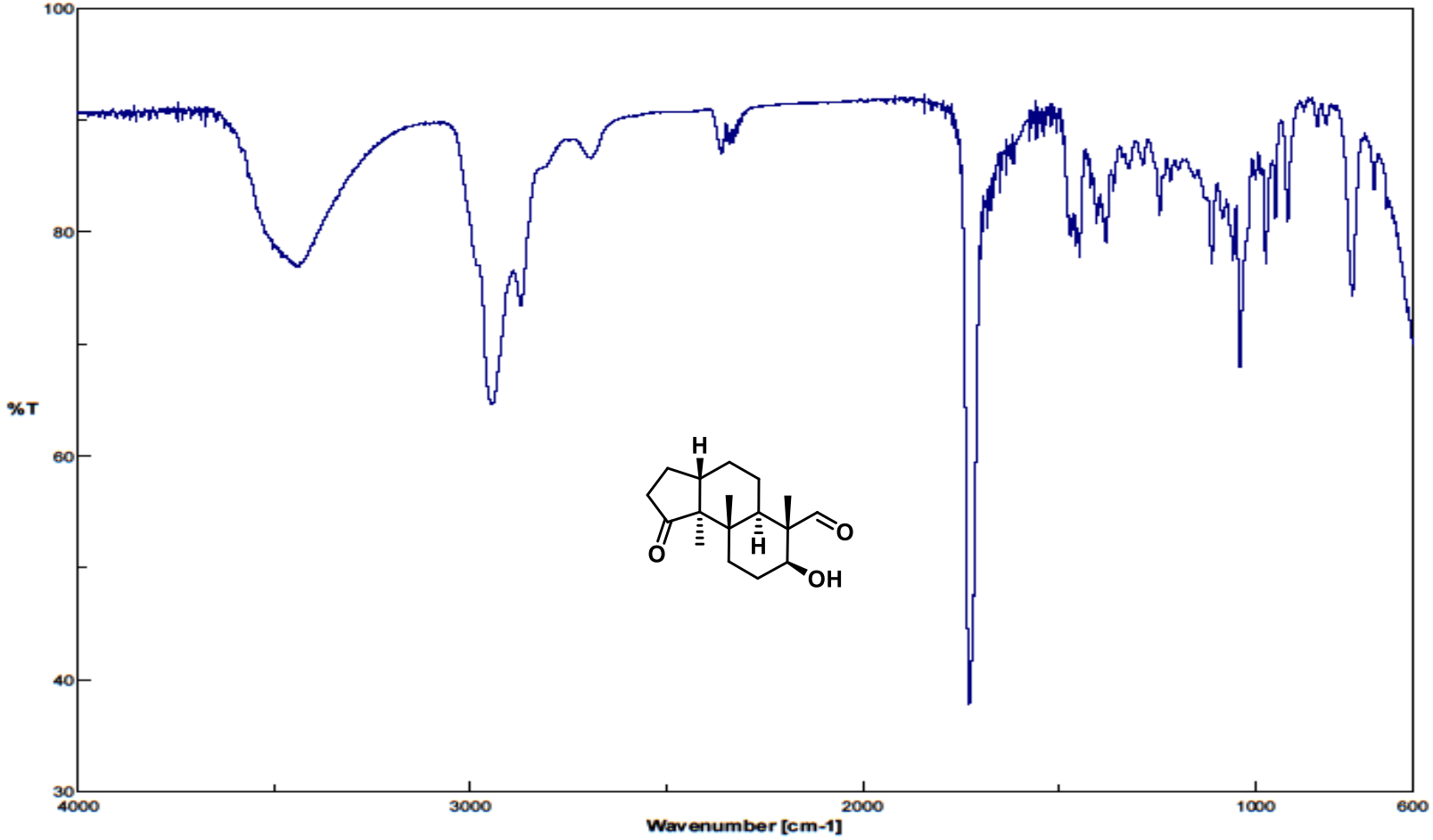
IR Spectrum of Compound (−)-**28**



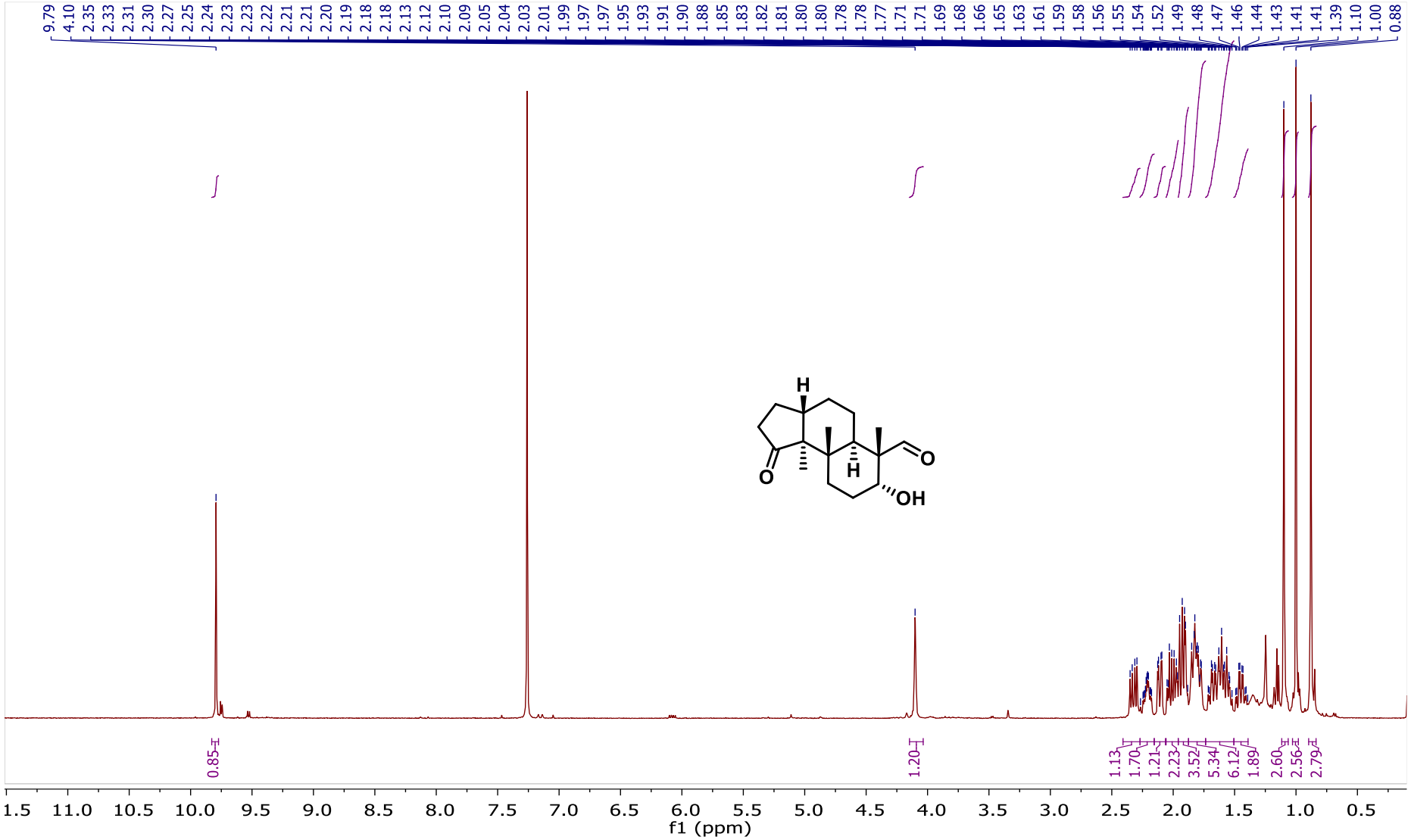
^{1}H NMR (500 MHz) Spectrum of Compound **(−)-29** in $CDCl_3$



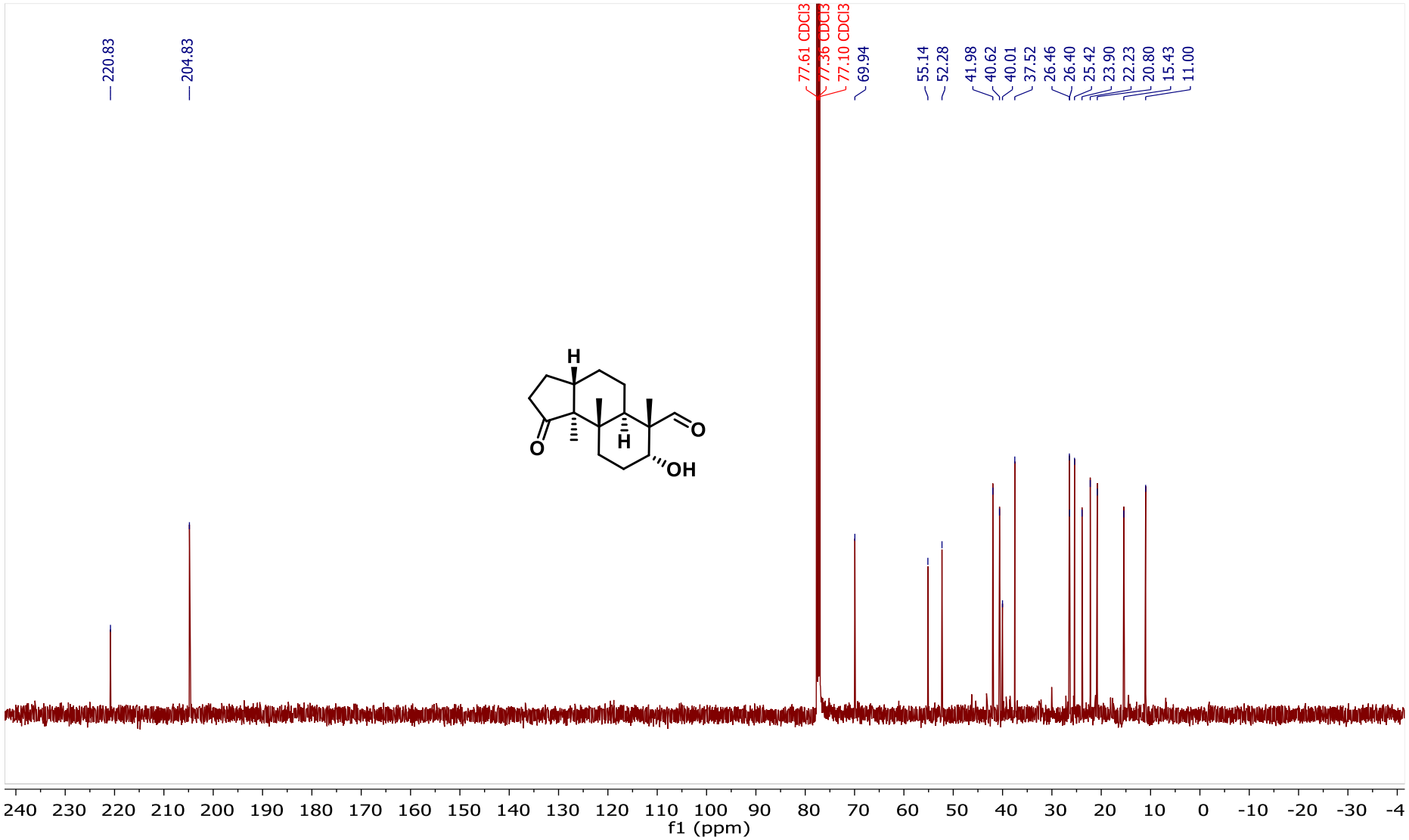
^{13}C NMR (126 MHz) Spectrum of Compound **(−)-29** in $CDCl_3$



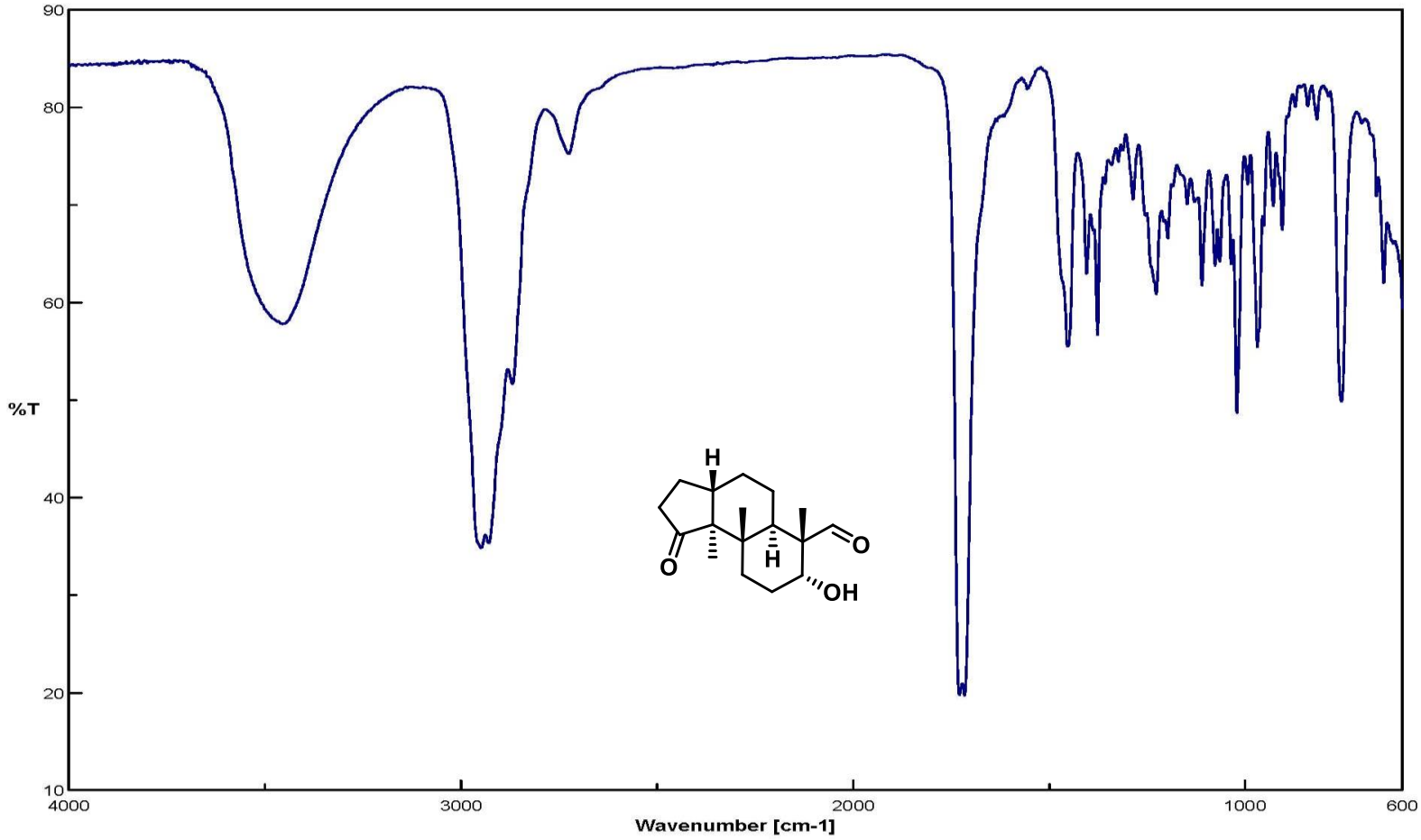
IR Spectrum of Compound (−)-**29**



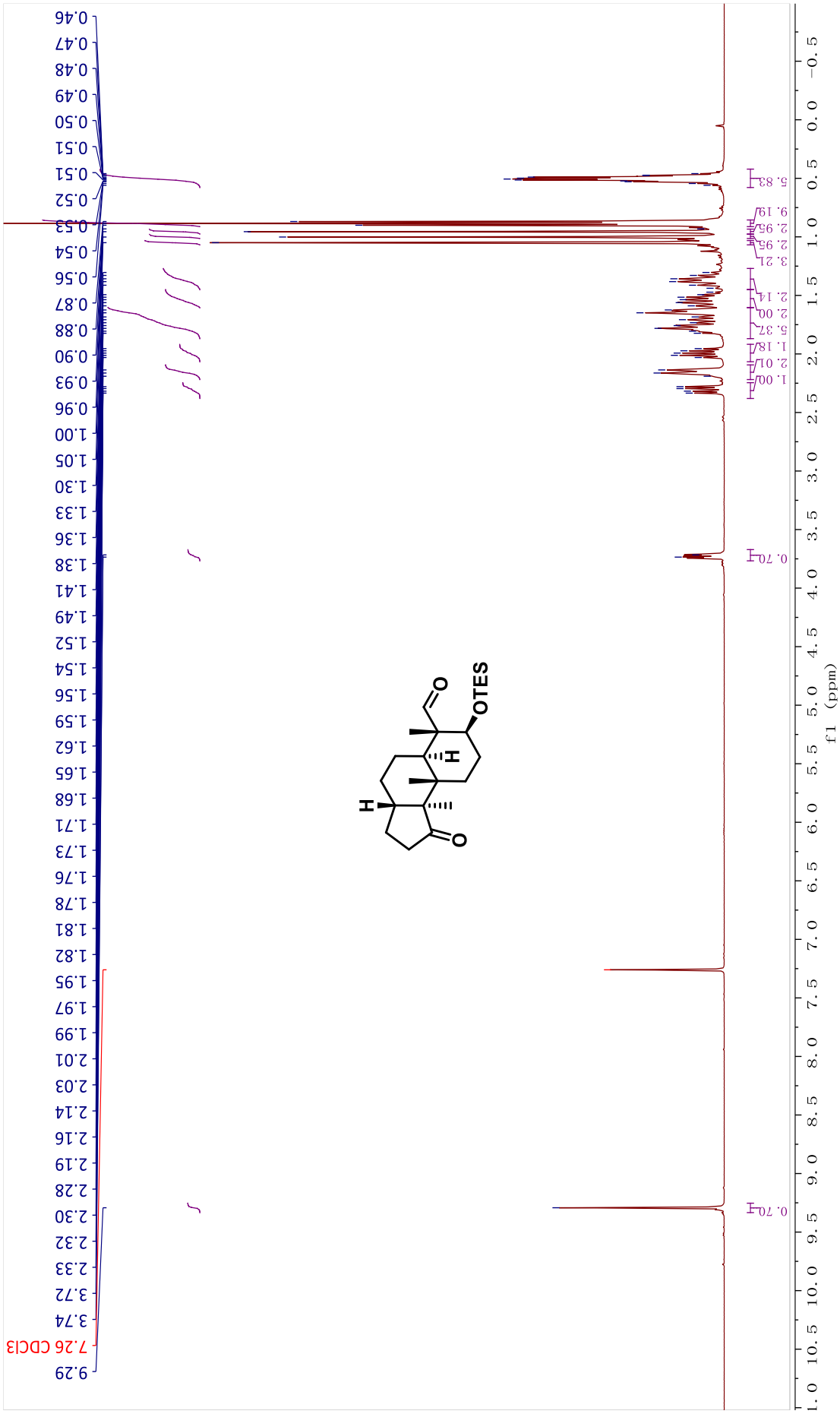
^{1}H NMR (500 MHz) Spectrum of Compound **(−)-31** in $CDCl_3$



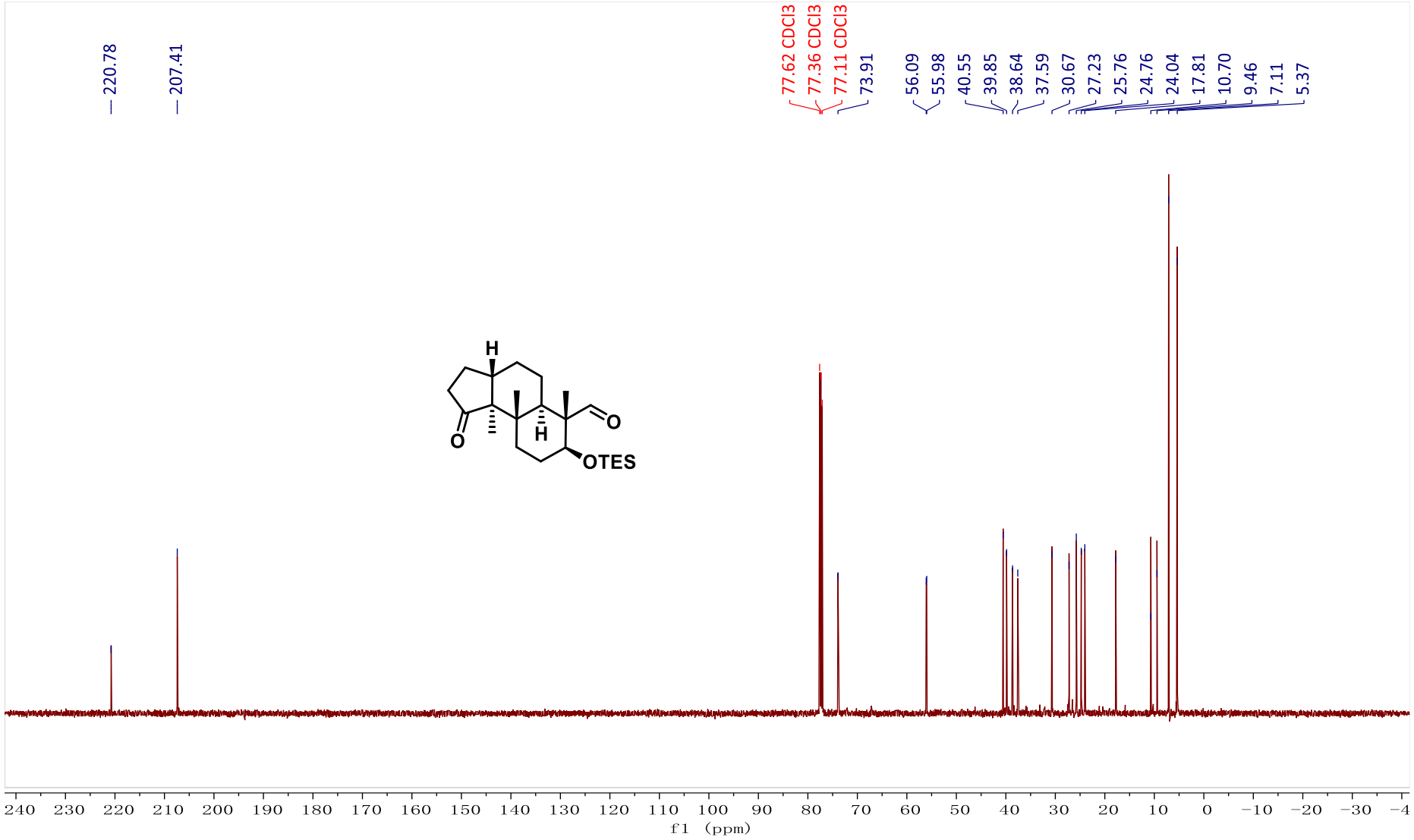
^{13}C NMR (126 MHz) Spectrum of Compound **(−)-31** in $CDCl_3$



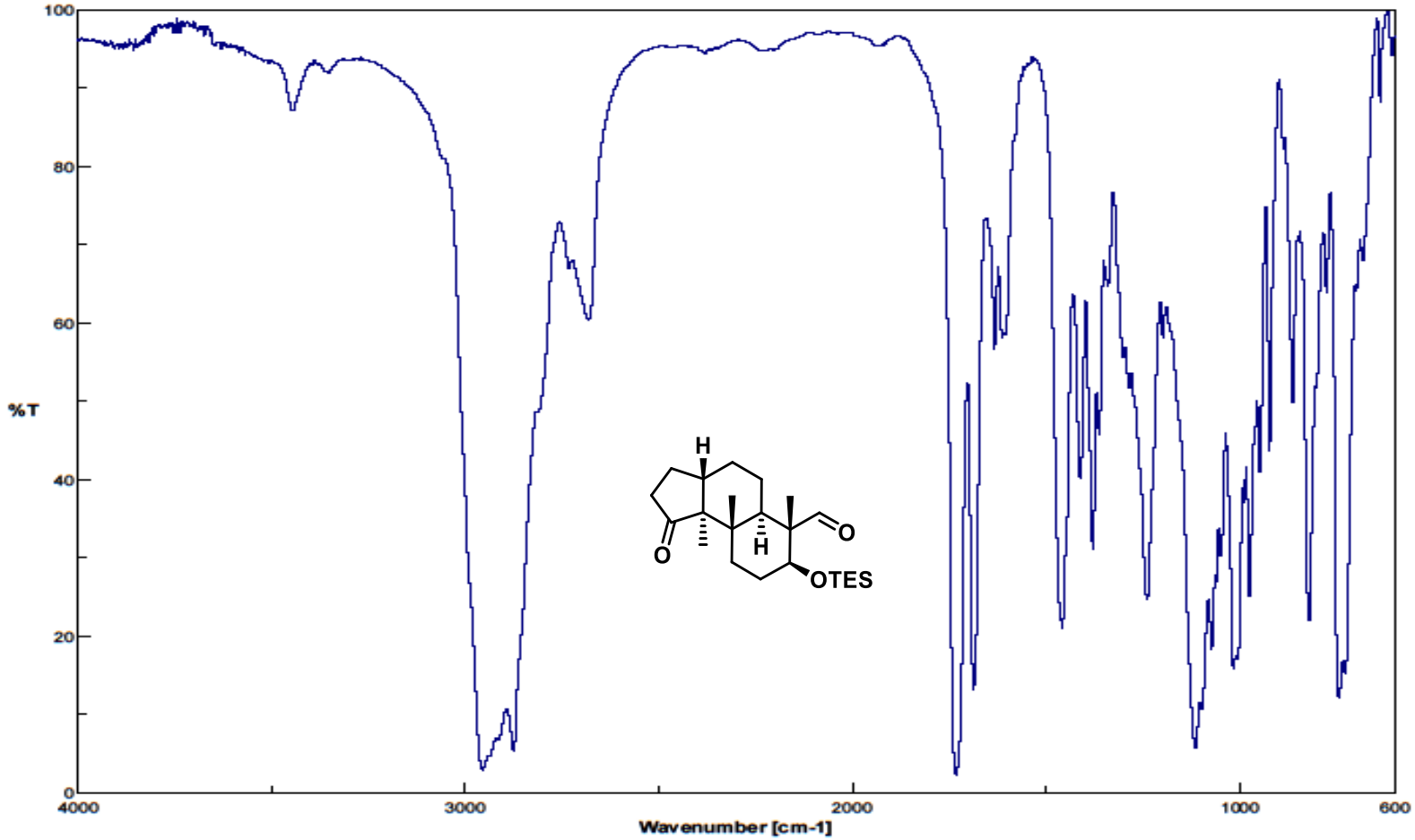
IR Spectrum of Compound (−)-**31**



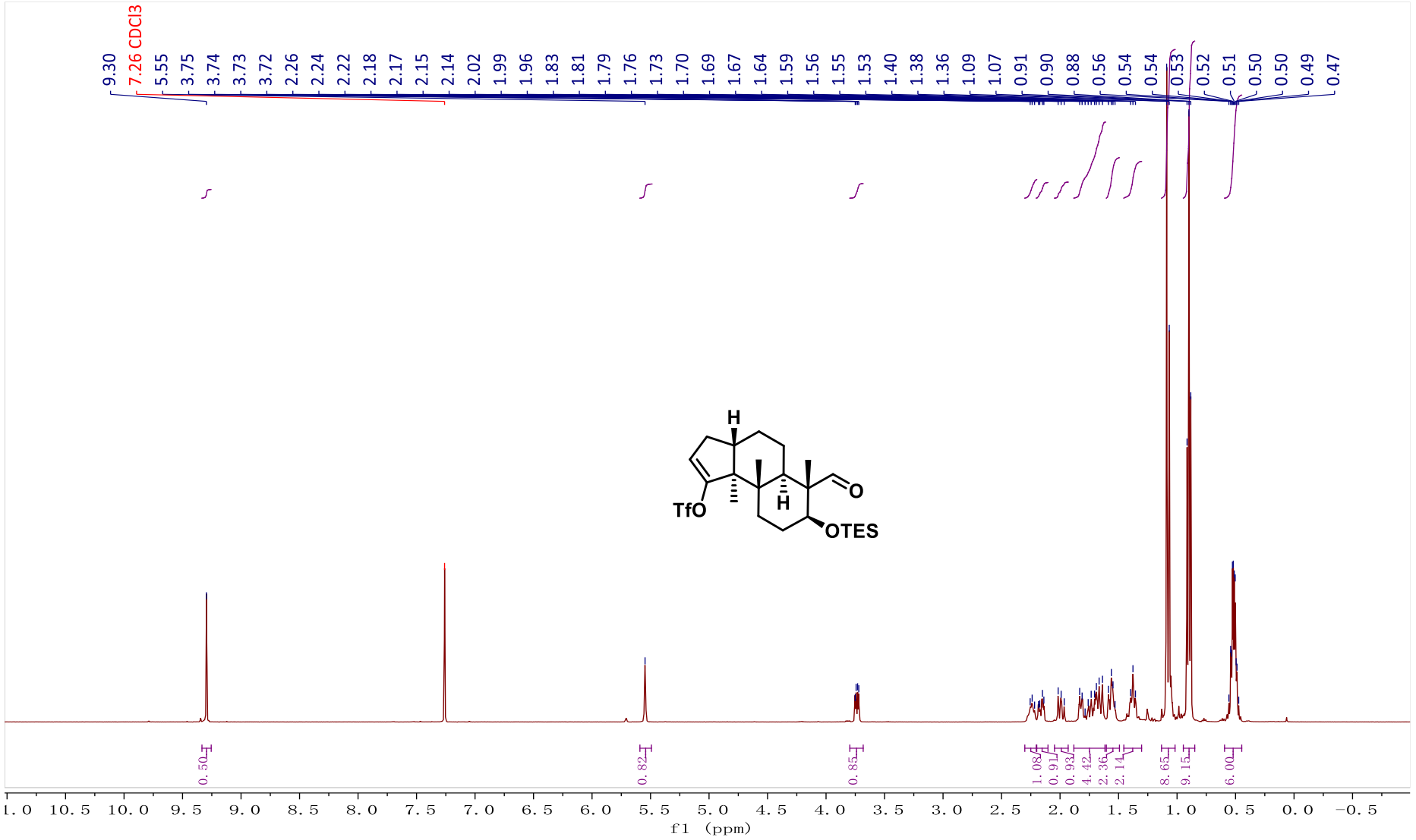
^{1}H NMR (500 MHz) Spectrum of Compound (–)-**32** in $CDCl_3$



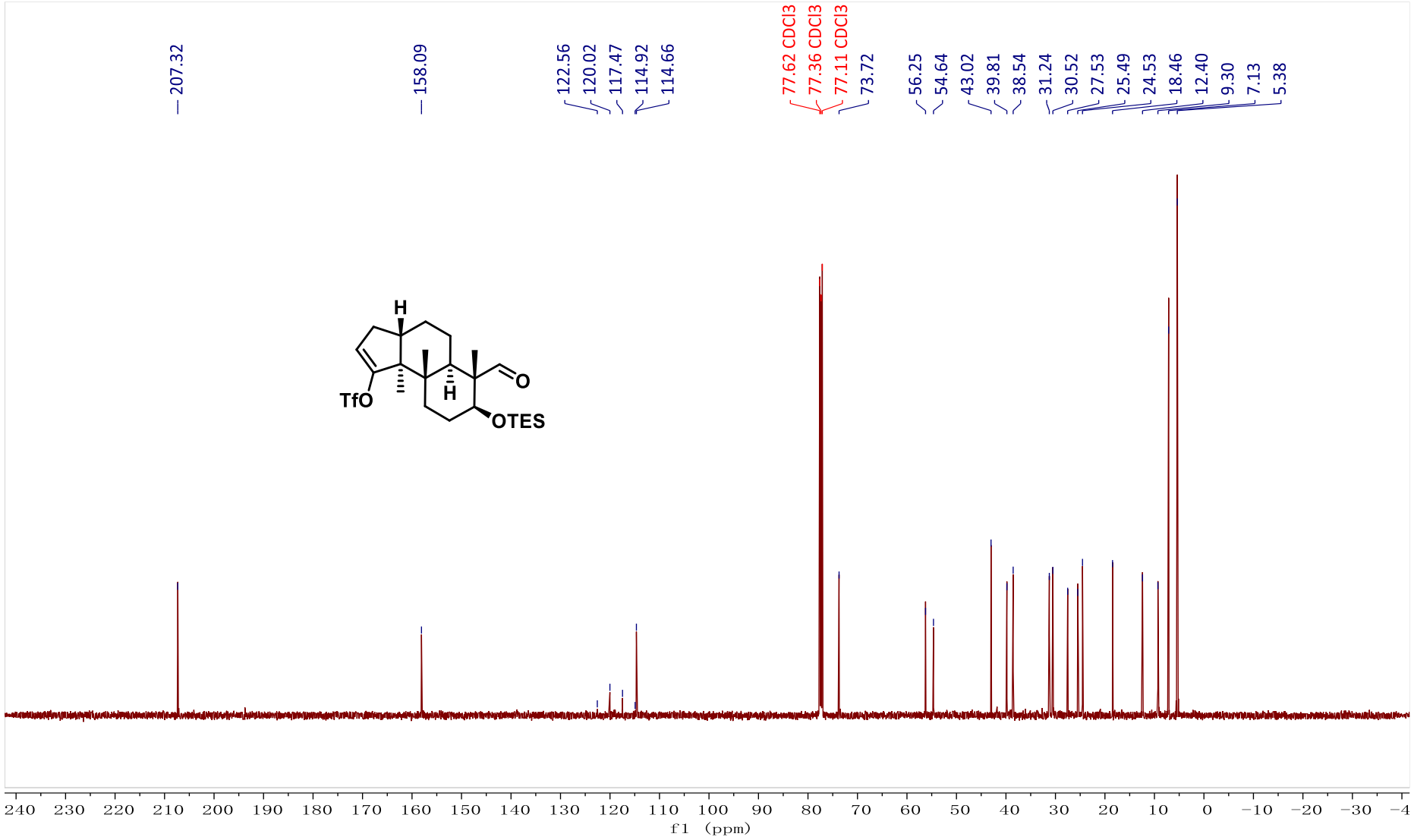
^{13}C NMR (126 MHz) Spectrum of Compound **(−)-32** in $CDCl_3$



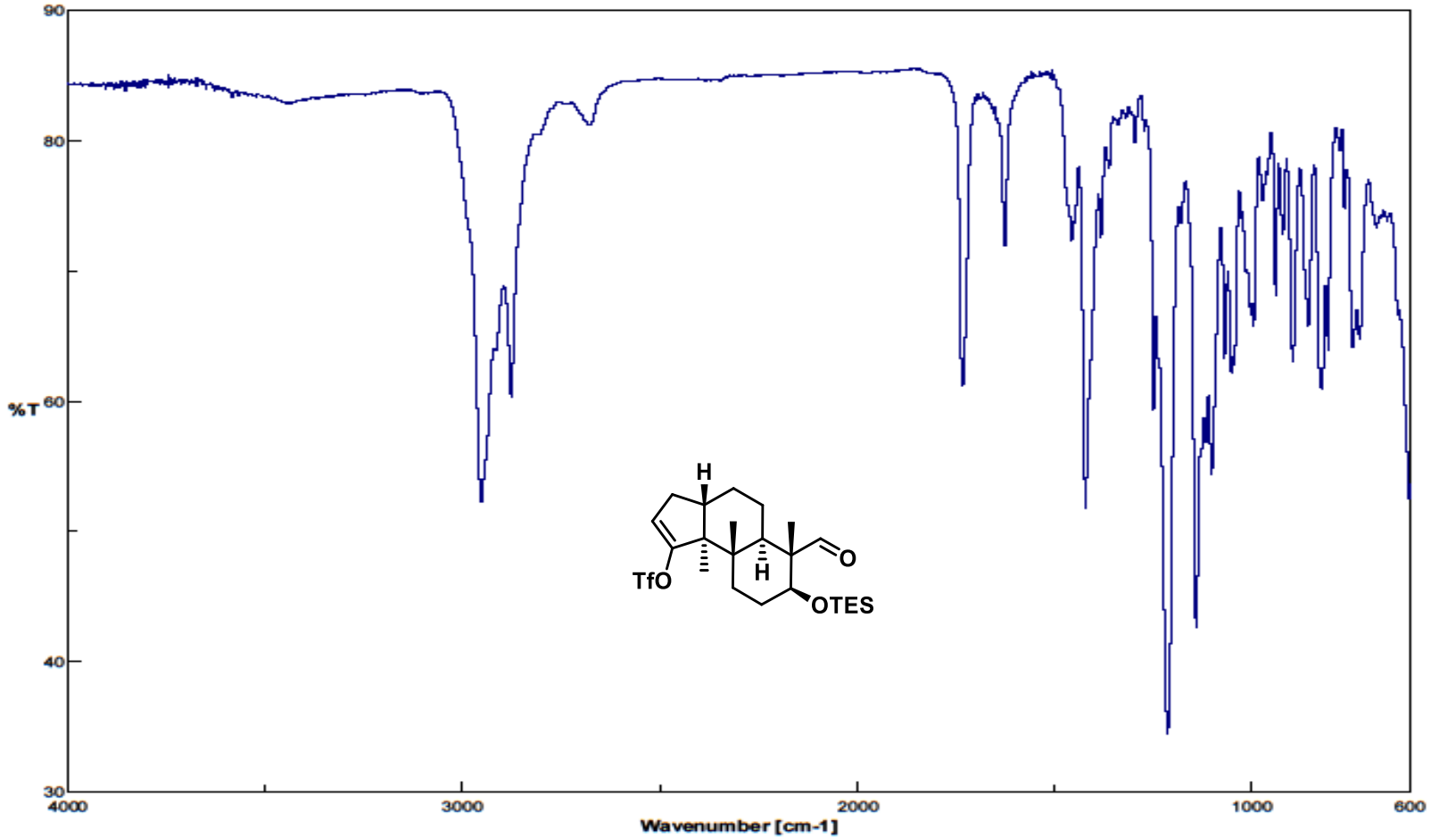
IR Spectrum of Compound (–)-**32**



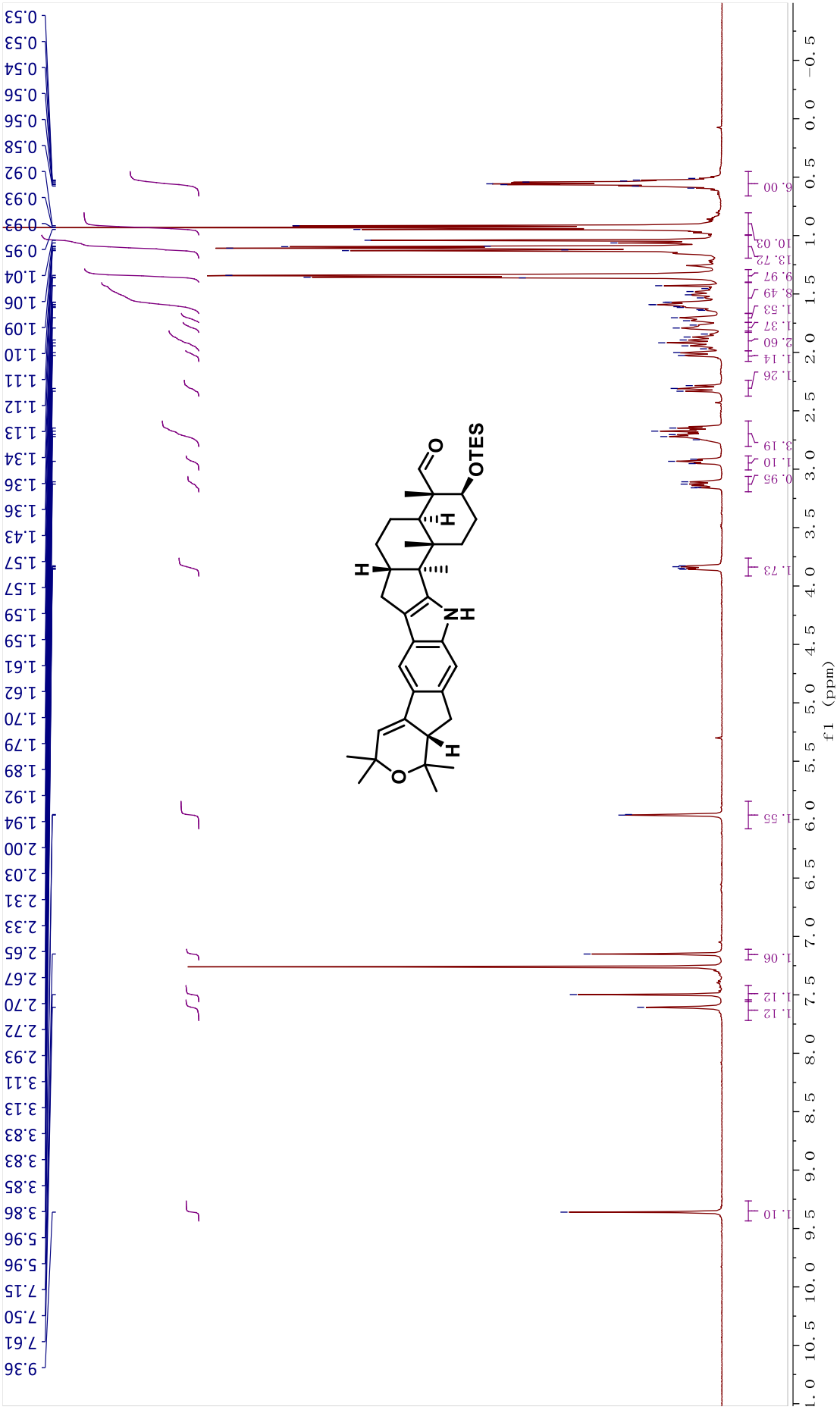
^{1}H NMR (500 MHz) Spectrum of Compound **(−)-33** in $CDCl_3$



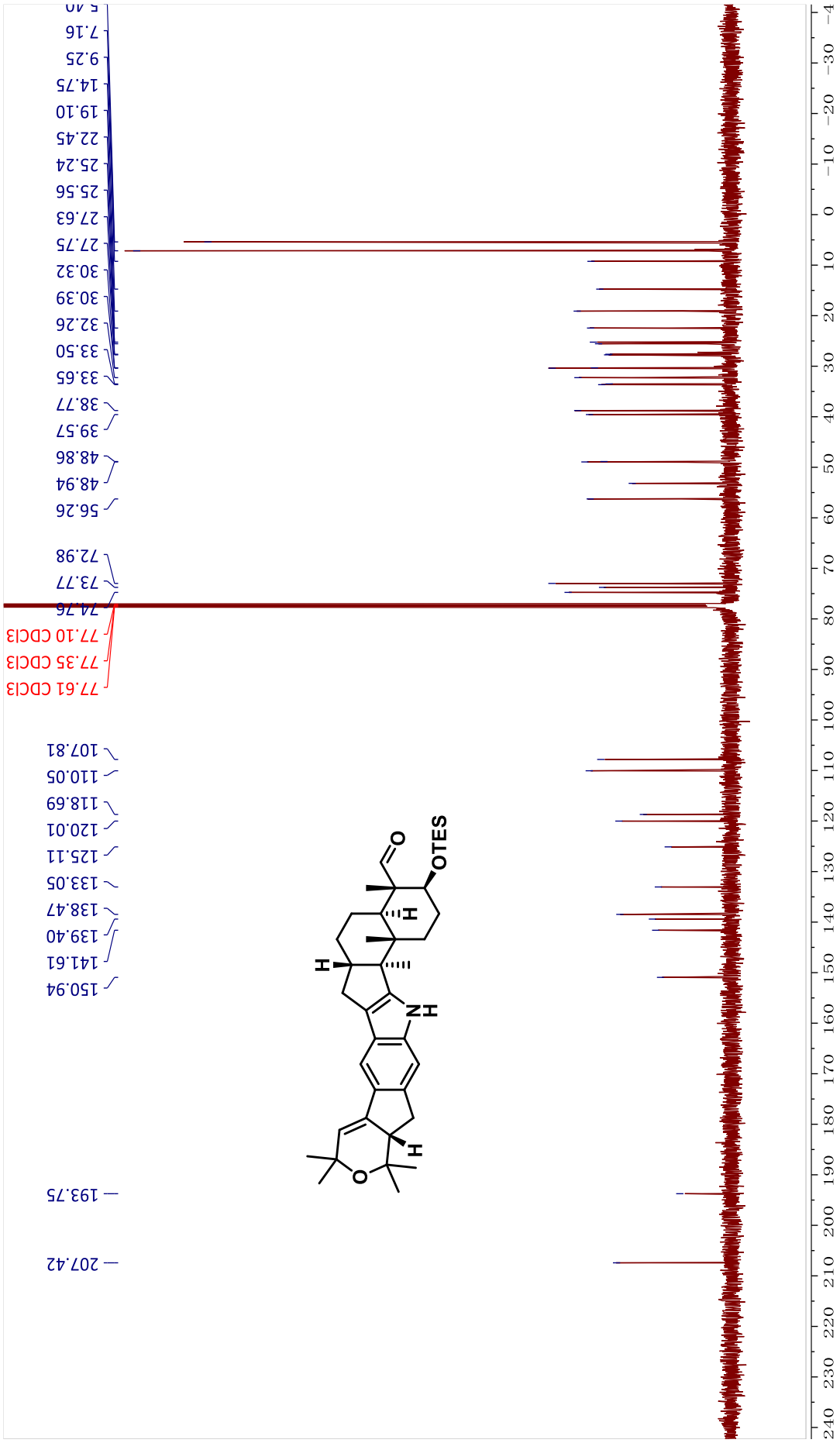
^{13}C NMR (126 MHz) Spectrum of Compound **(−)-33** in $CDCl_3$



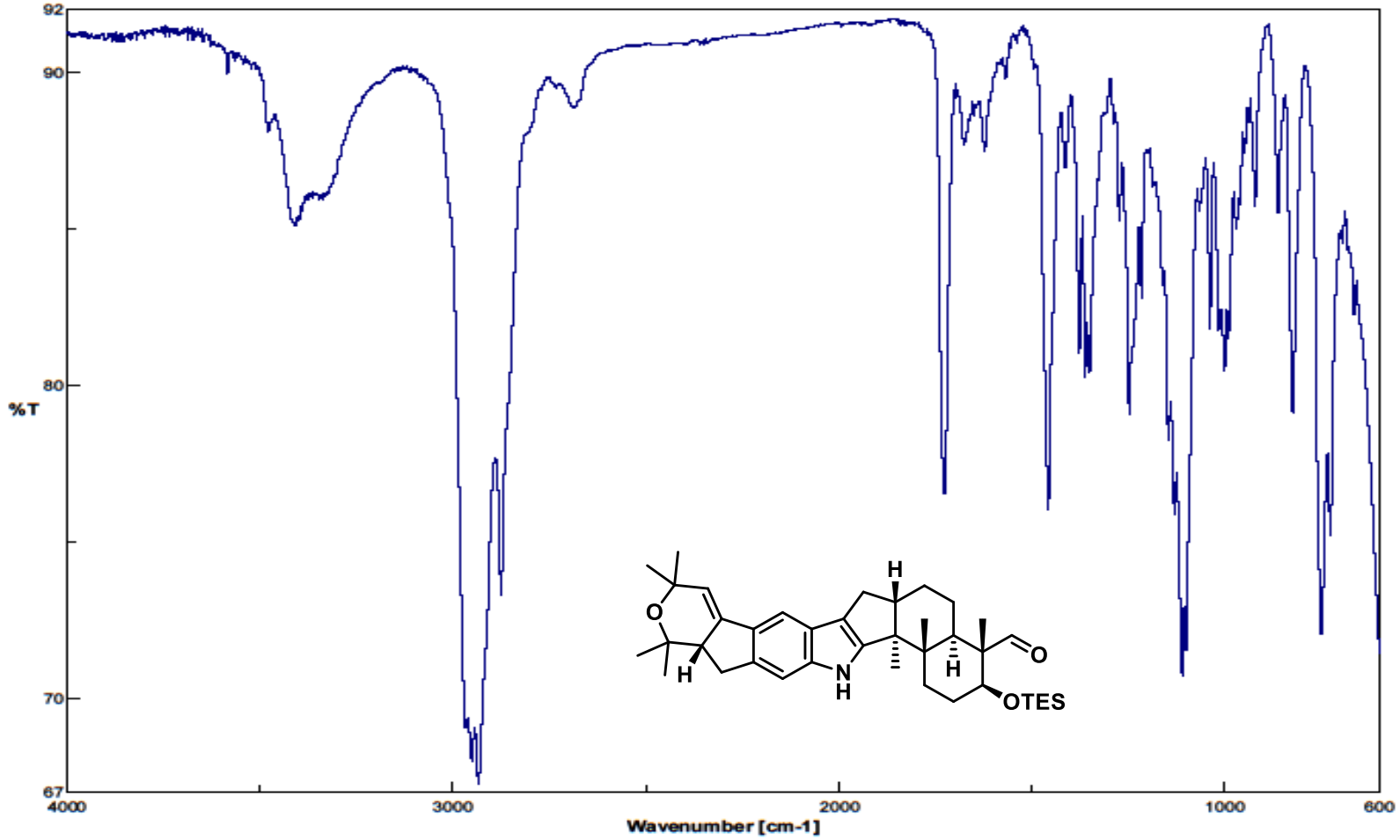
IR Spectrum of Compound (−)-**33**



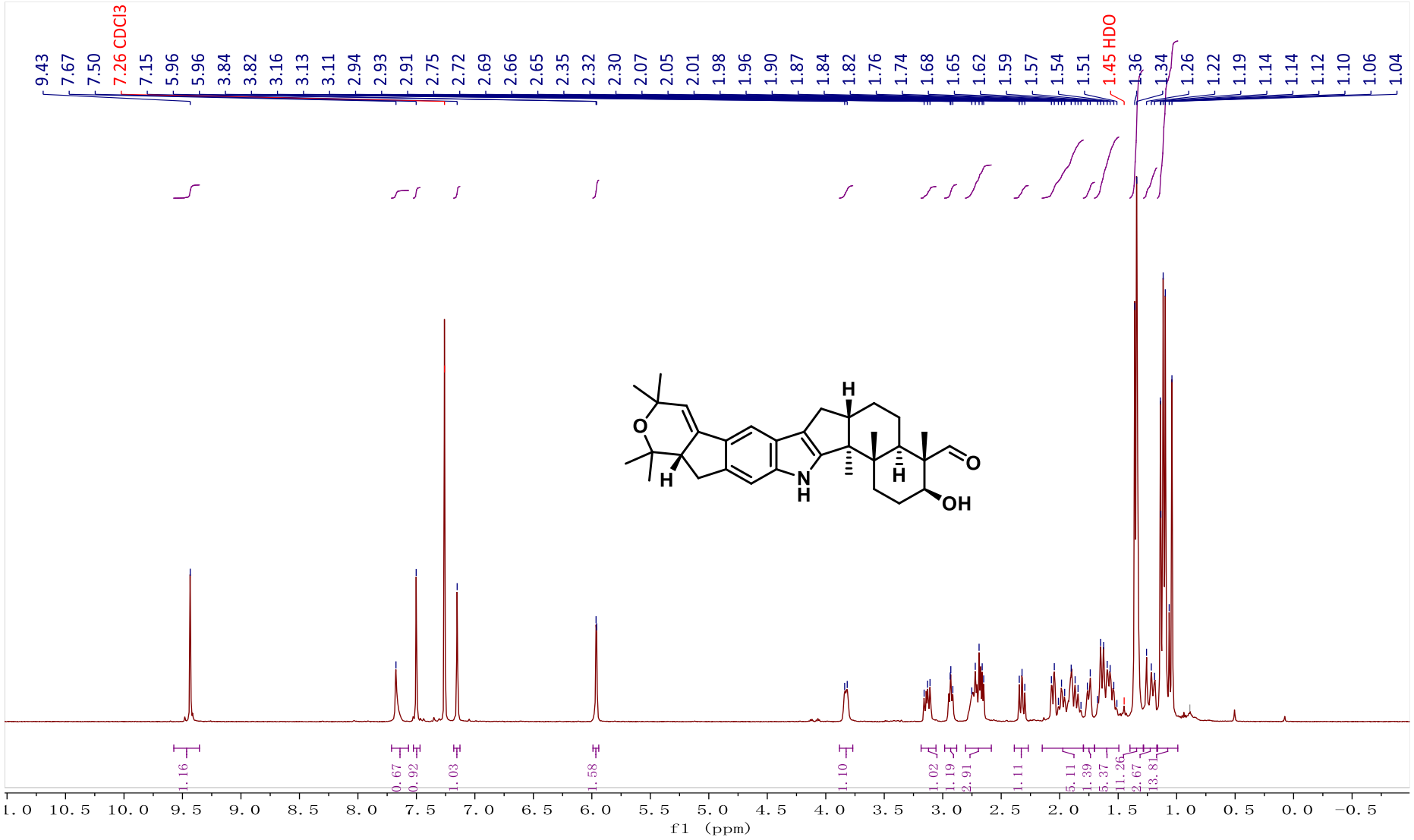
^{1}H NMR (500 MHz) Spectrum of Compound (−)-**34** in $CDCl_3$



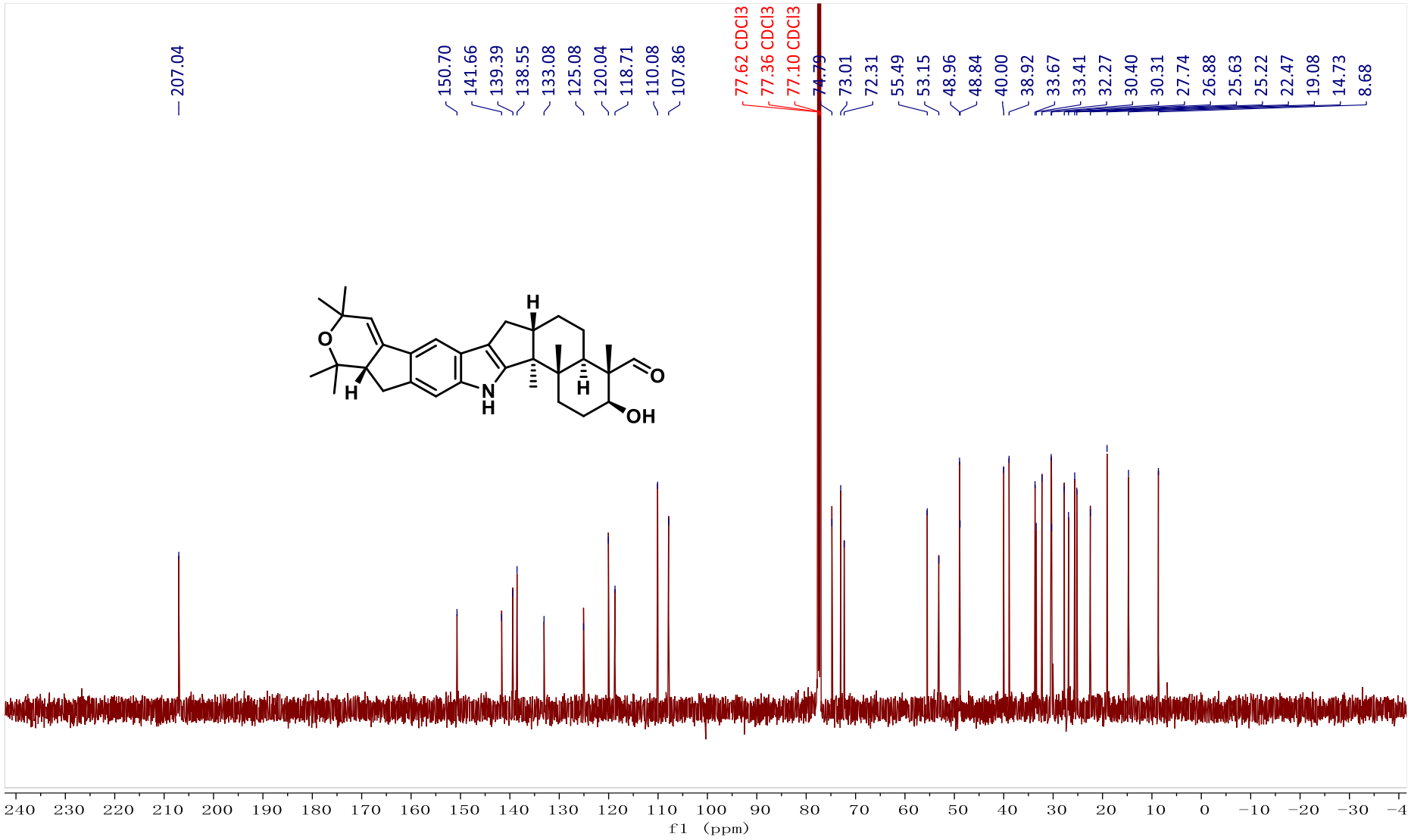
^{13}C NMR (126 MHz) Spectrum of Compound (–)-**34** in $CDCl_3$



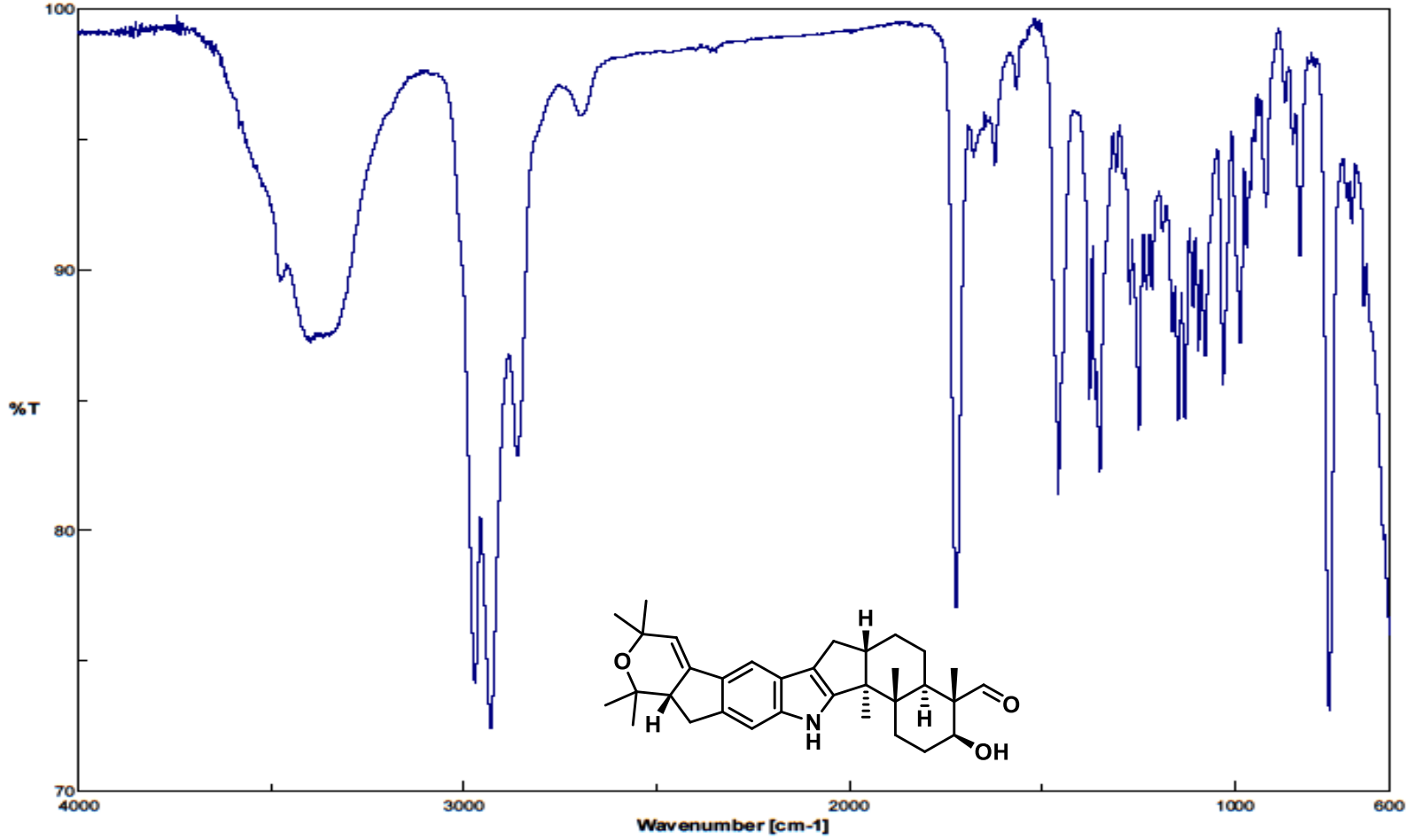
IR Spectrum of Compound (−)-**34**



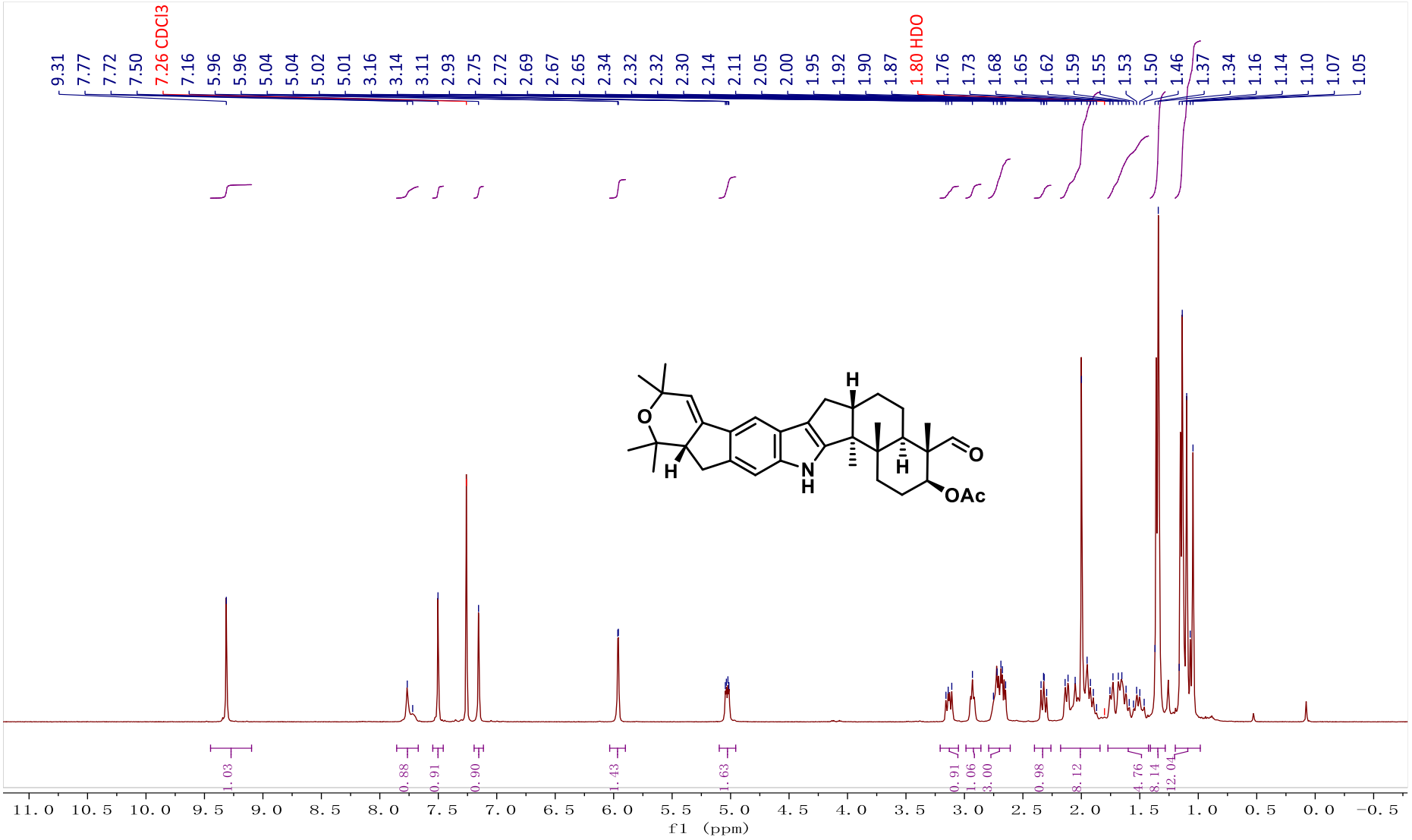
^{1}H NMR (500 MHz) Spectrum of Compound **(−)-37** in $CDCl_3$



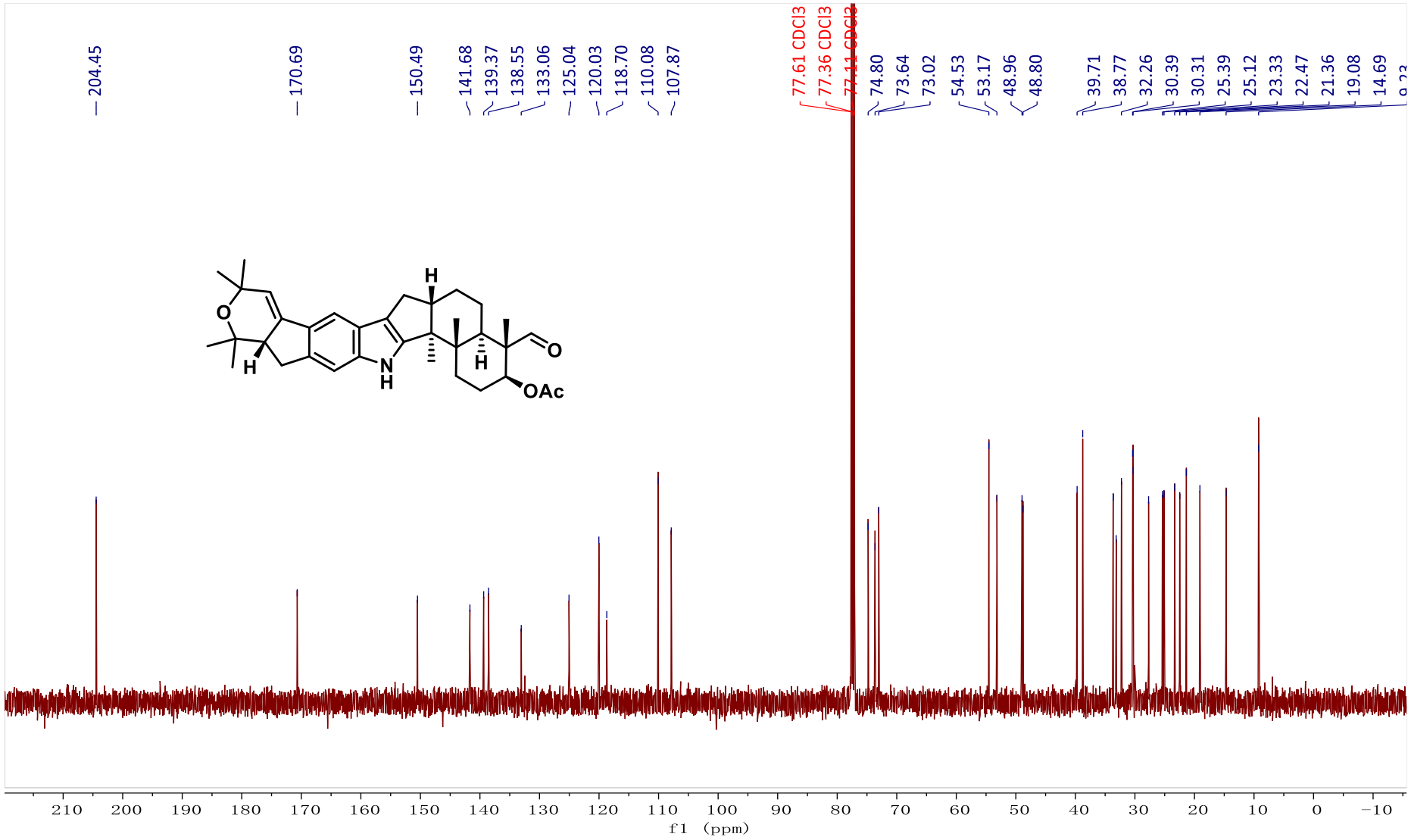
^{13}C NMR (126 MHz) Spectrum of Compound **(−)-37** in $CDCl_3$



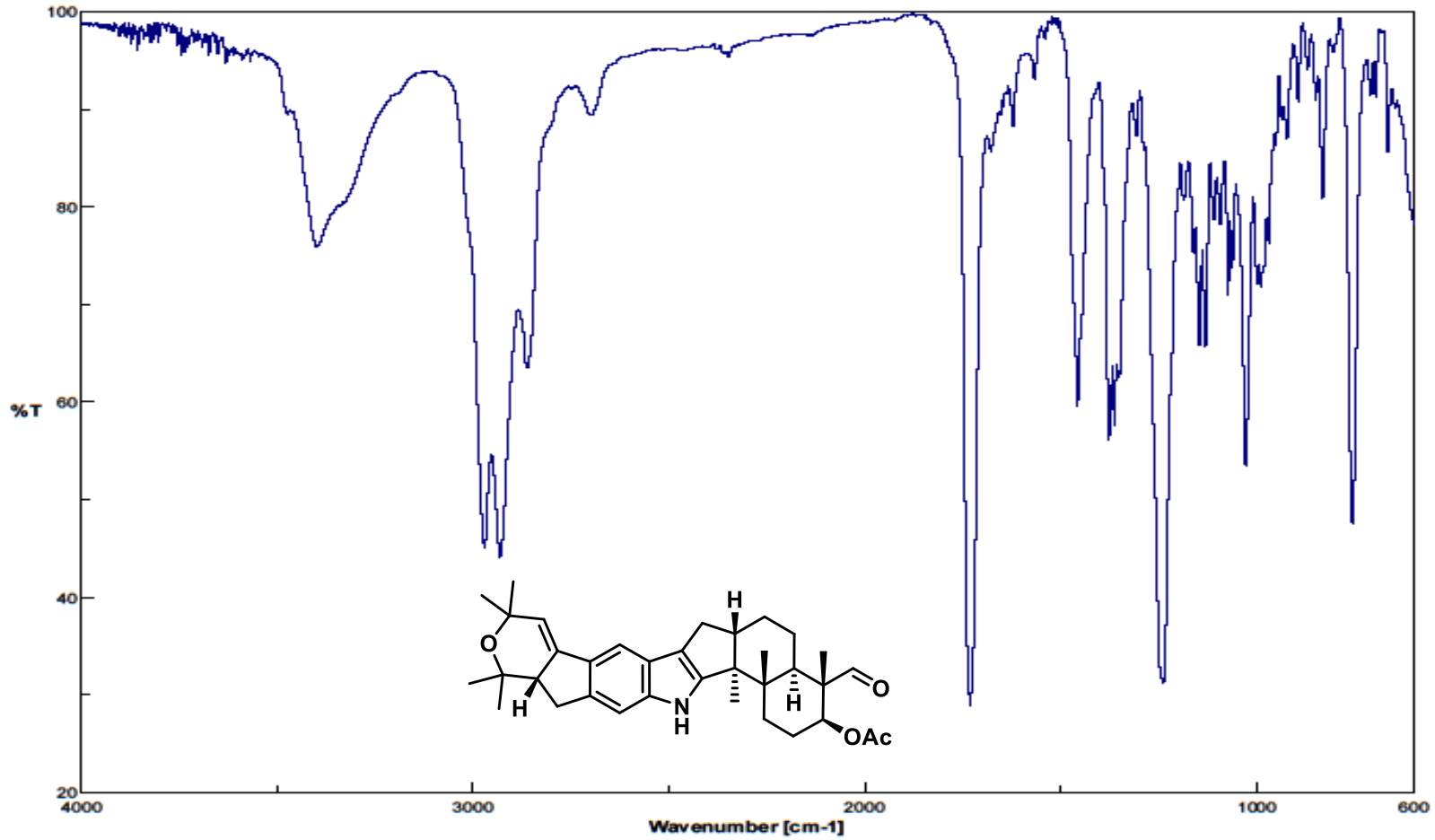
IR Spectrum of Compound (−)-**37**



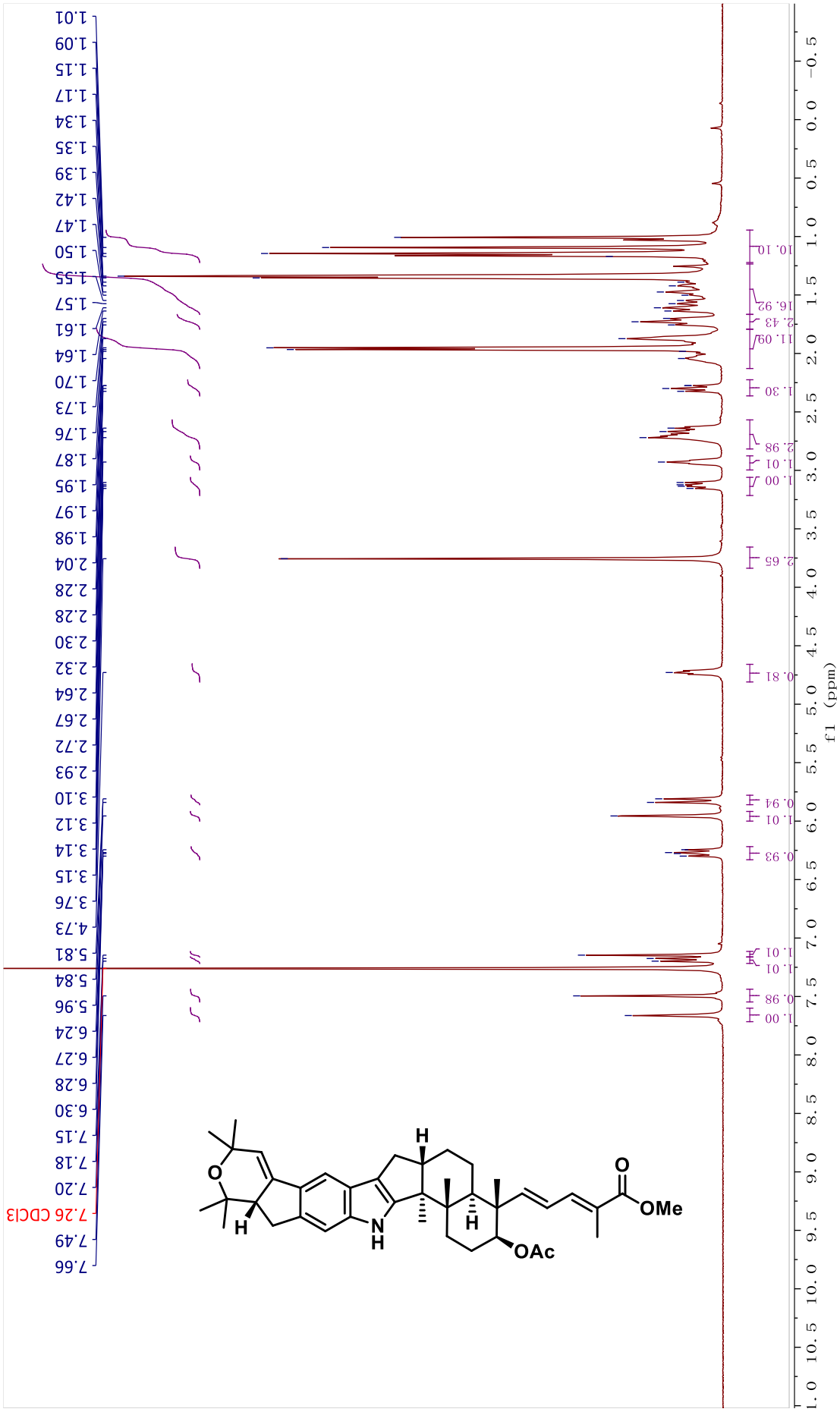
^{1}H NMR (500 MHz) Spectrum of Compound **(−)-40** in $CDCl_3$



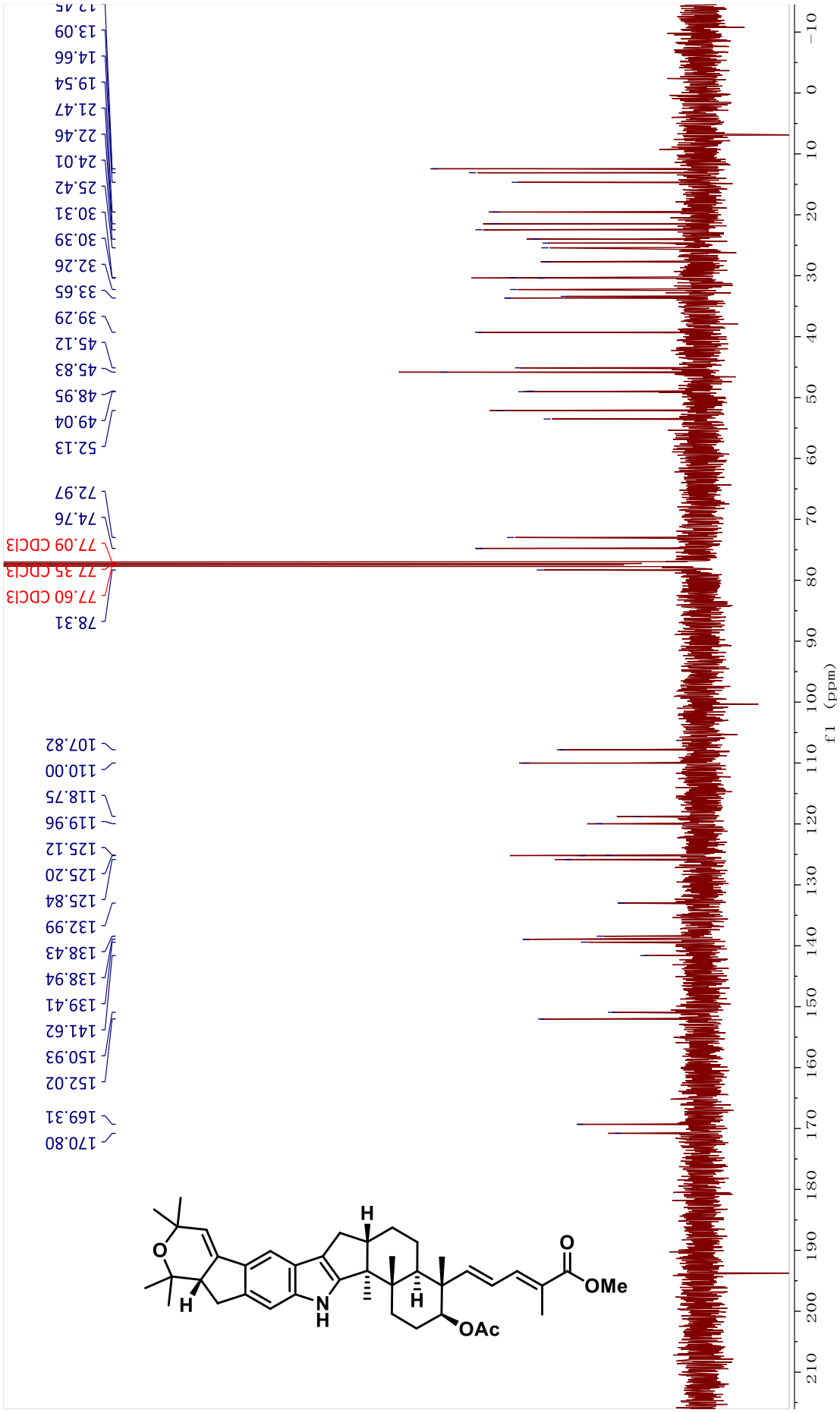
^{13}C NMR (126 MHz) Spectrum of Compound **(−)-40** in $CDCl_3$



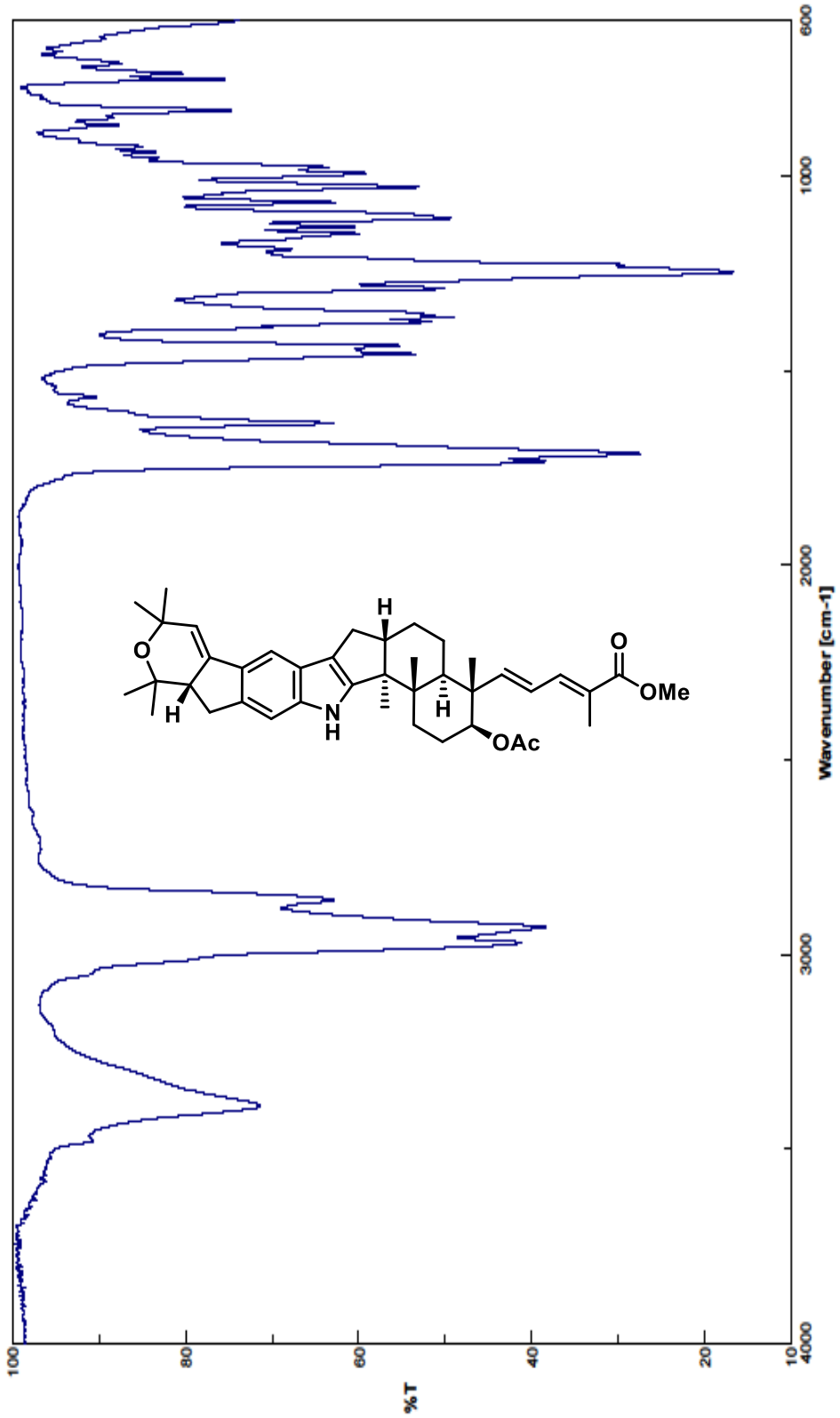
IR Spectrum of Compound (−)-**40**



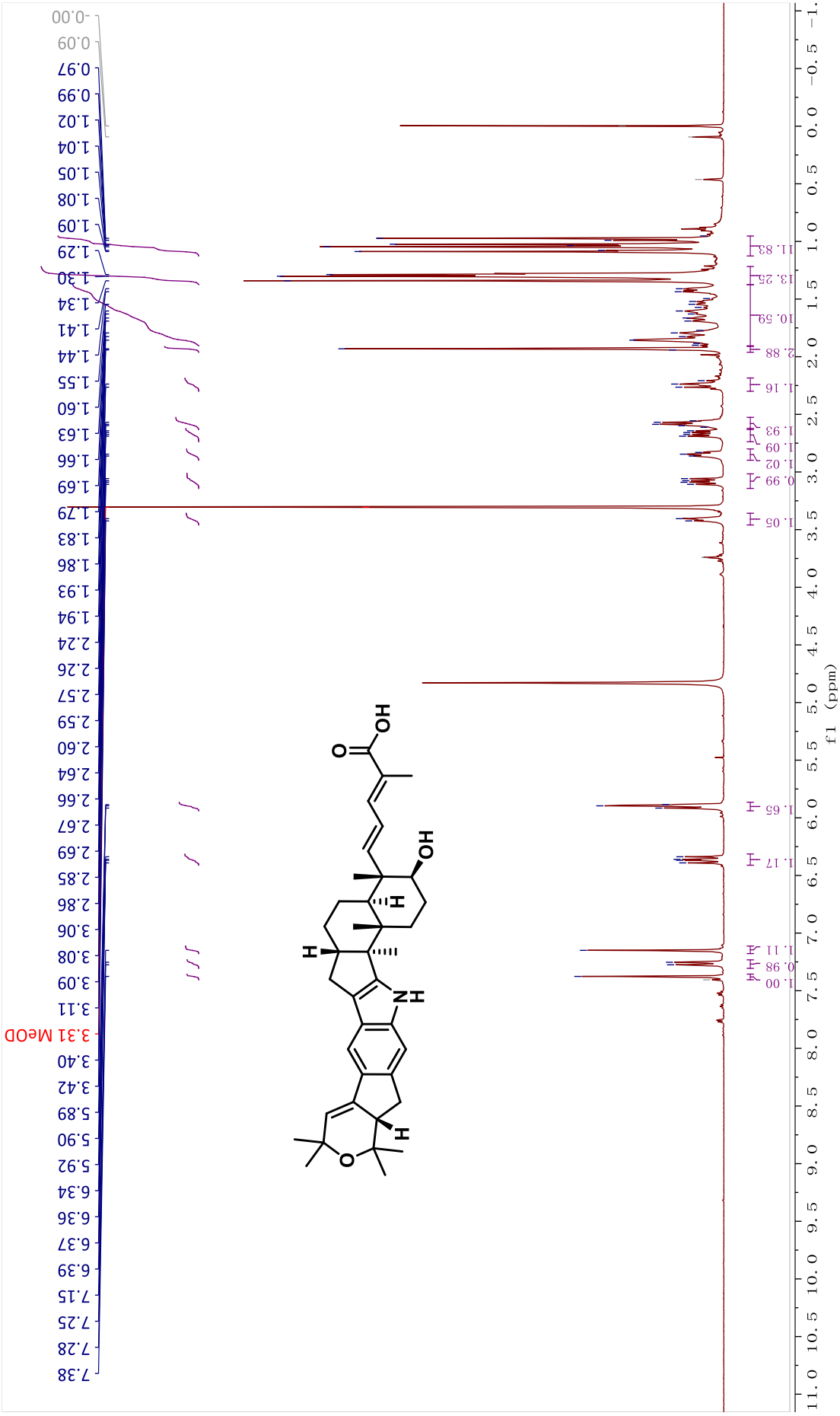
^{1}H NMR (500 MHz) Spectrum of Compound (–)-**41** in $CDCl_3$



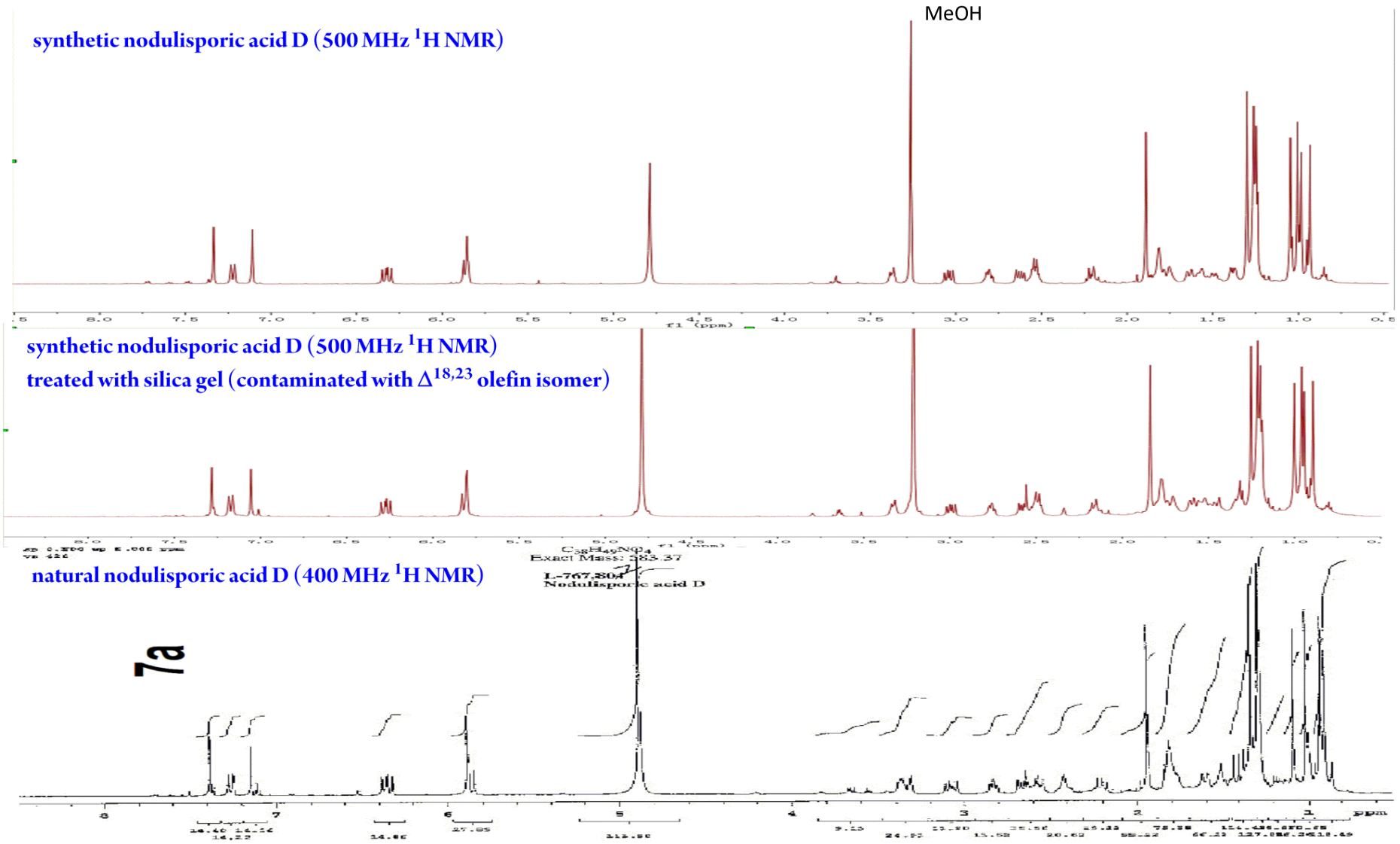
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-41** in $CDCl_3$



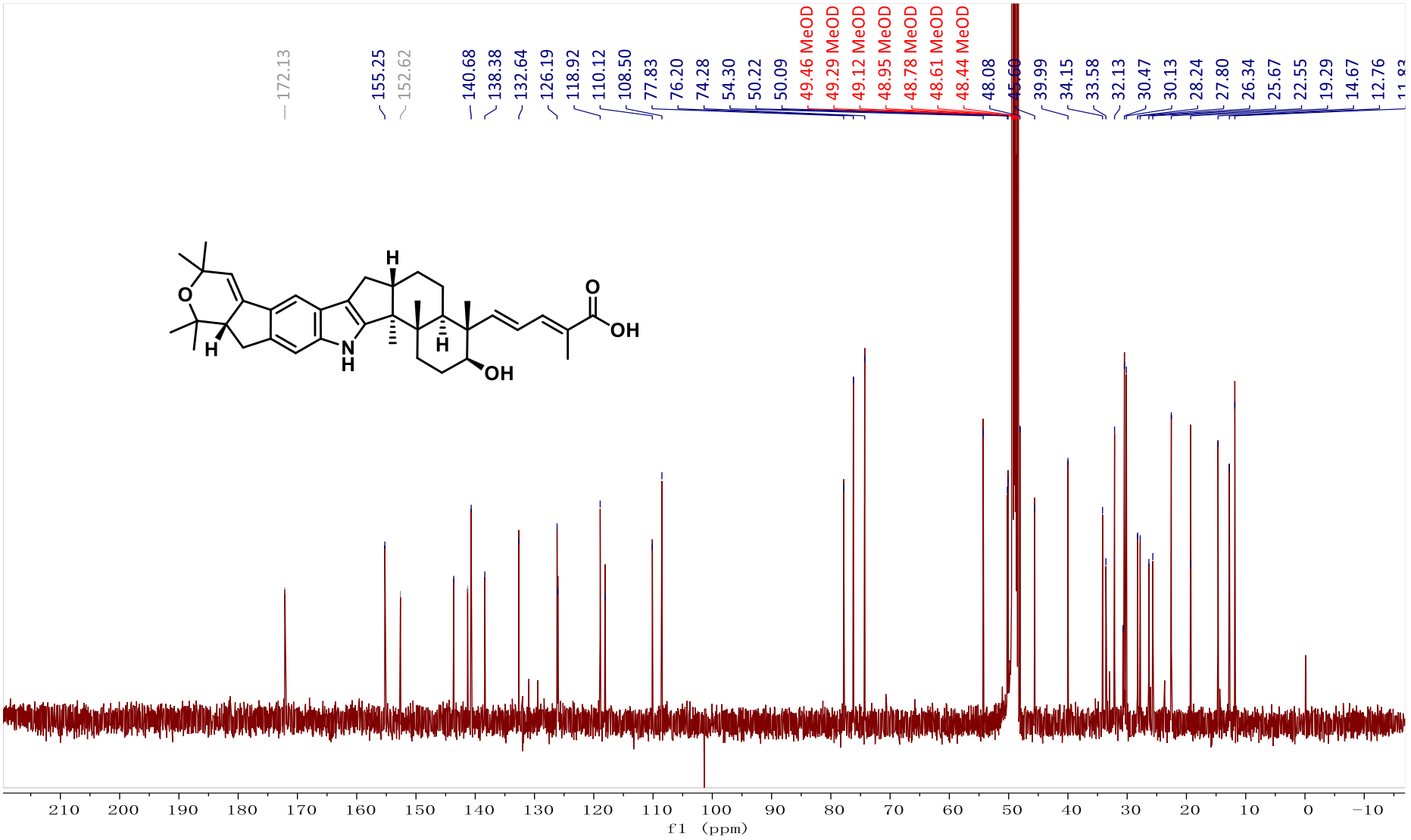
IR Spectrum of Compound (–)-41



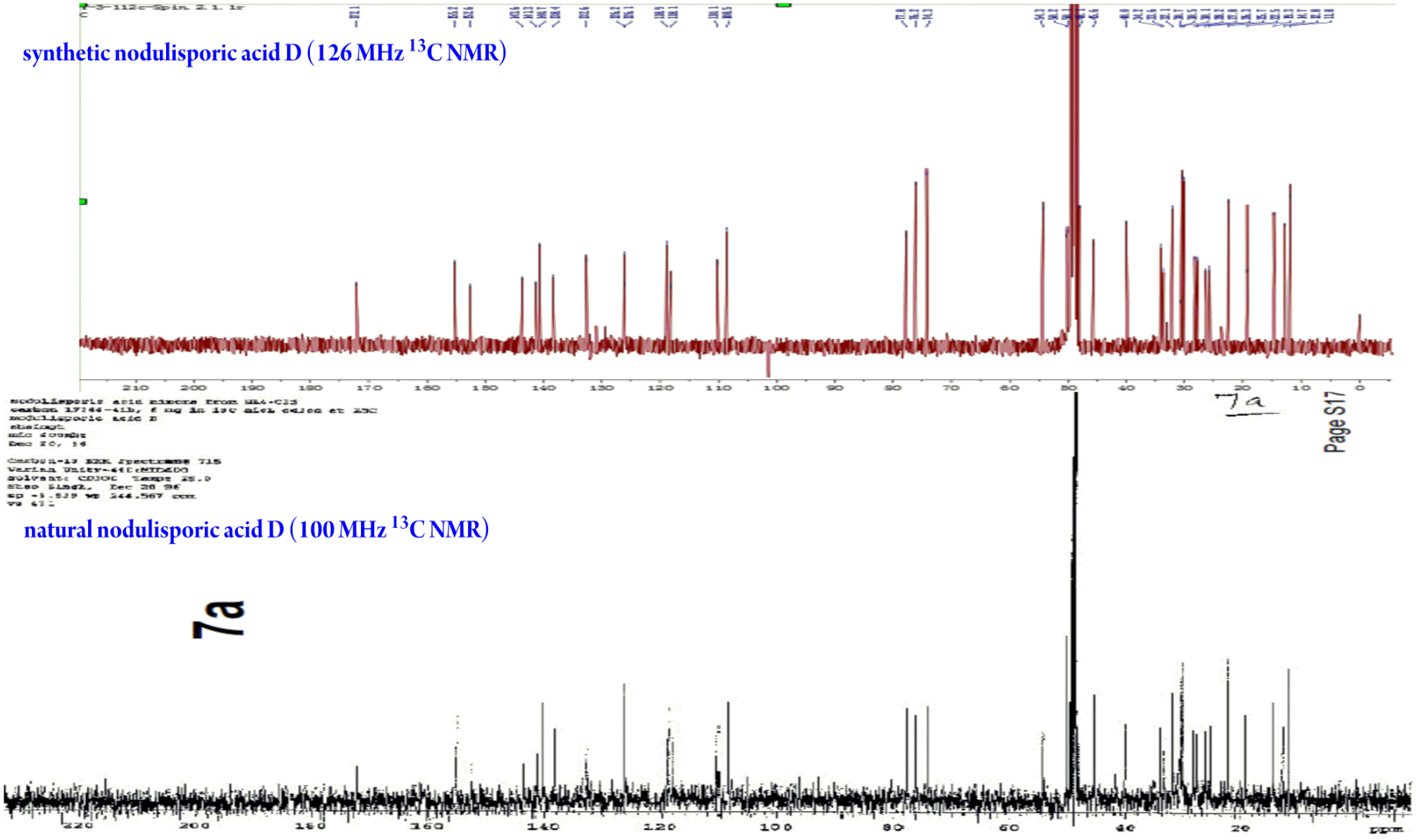
^{1}H NMR (500 MHz) Spectrum of Compound (−) **-4** in CD_3OD



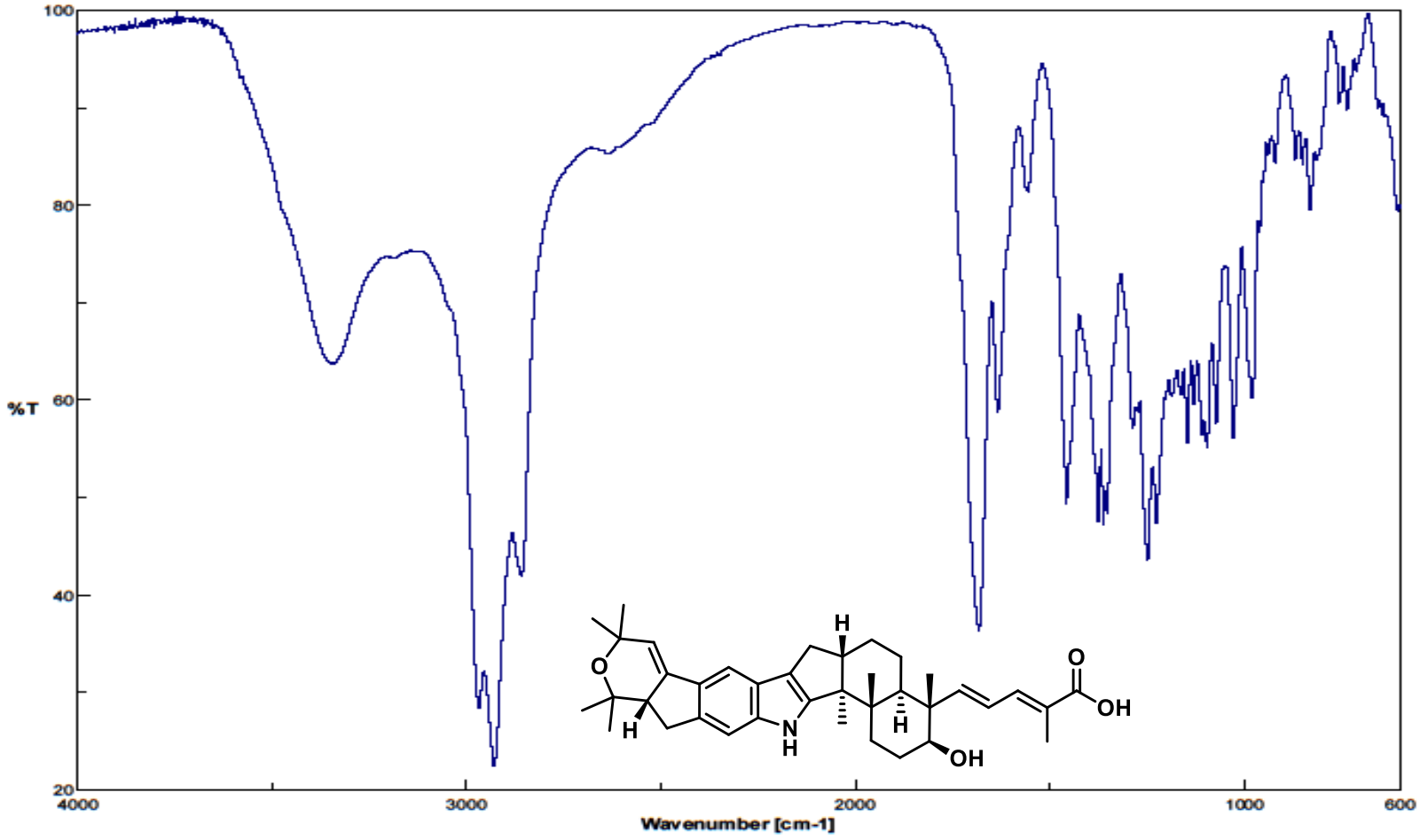
^{1}H NMR Comparison of Natural (400 MHz) and Synthetic (500 MHz) of **(–) -4** in CD_3OD



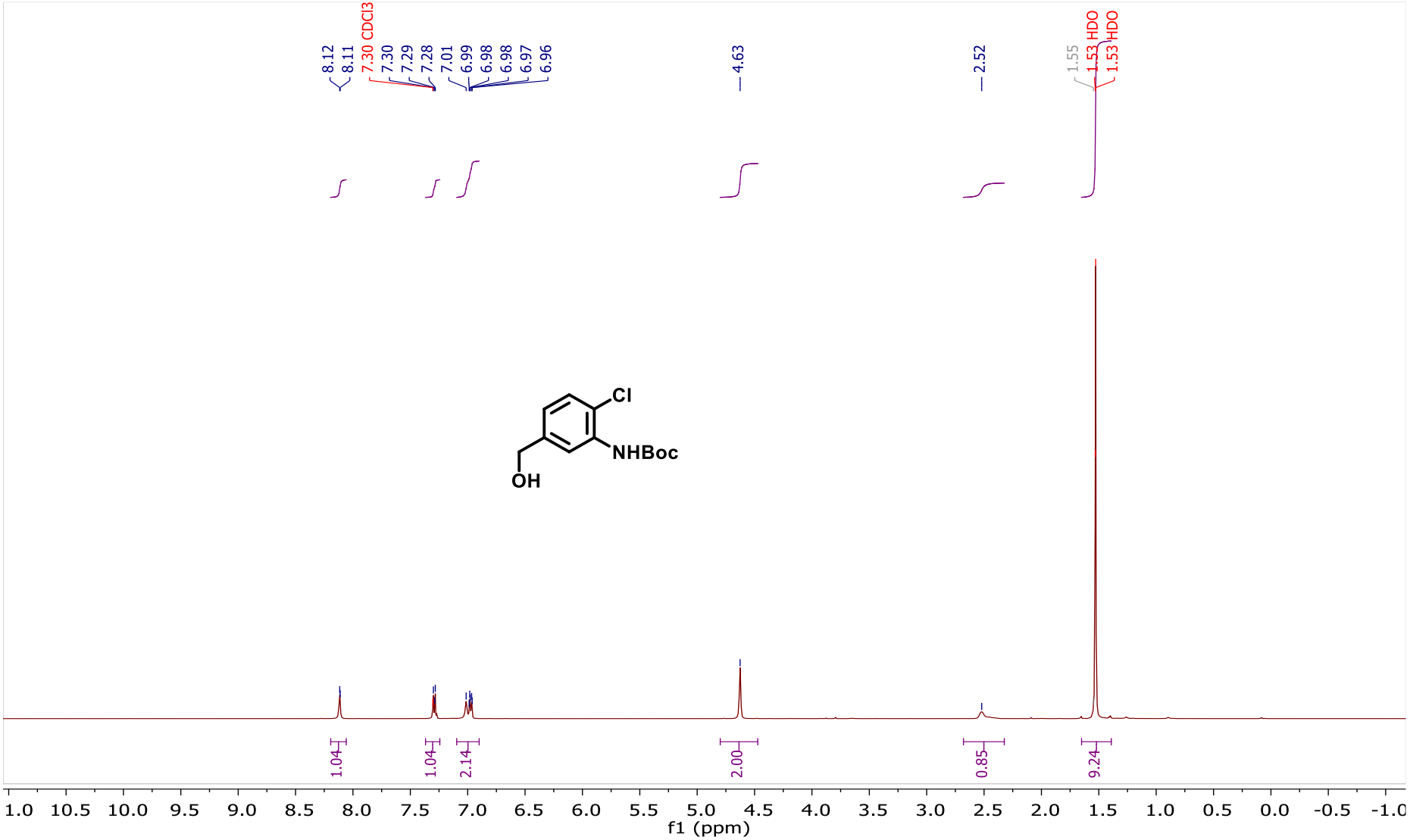
^{13}C NMR (126 MHz) Spectrum of Compound **(–) -4** in CD_3OD



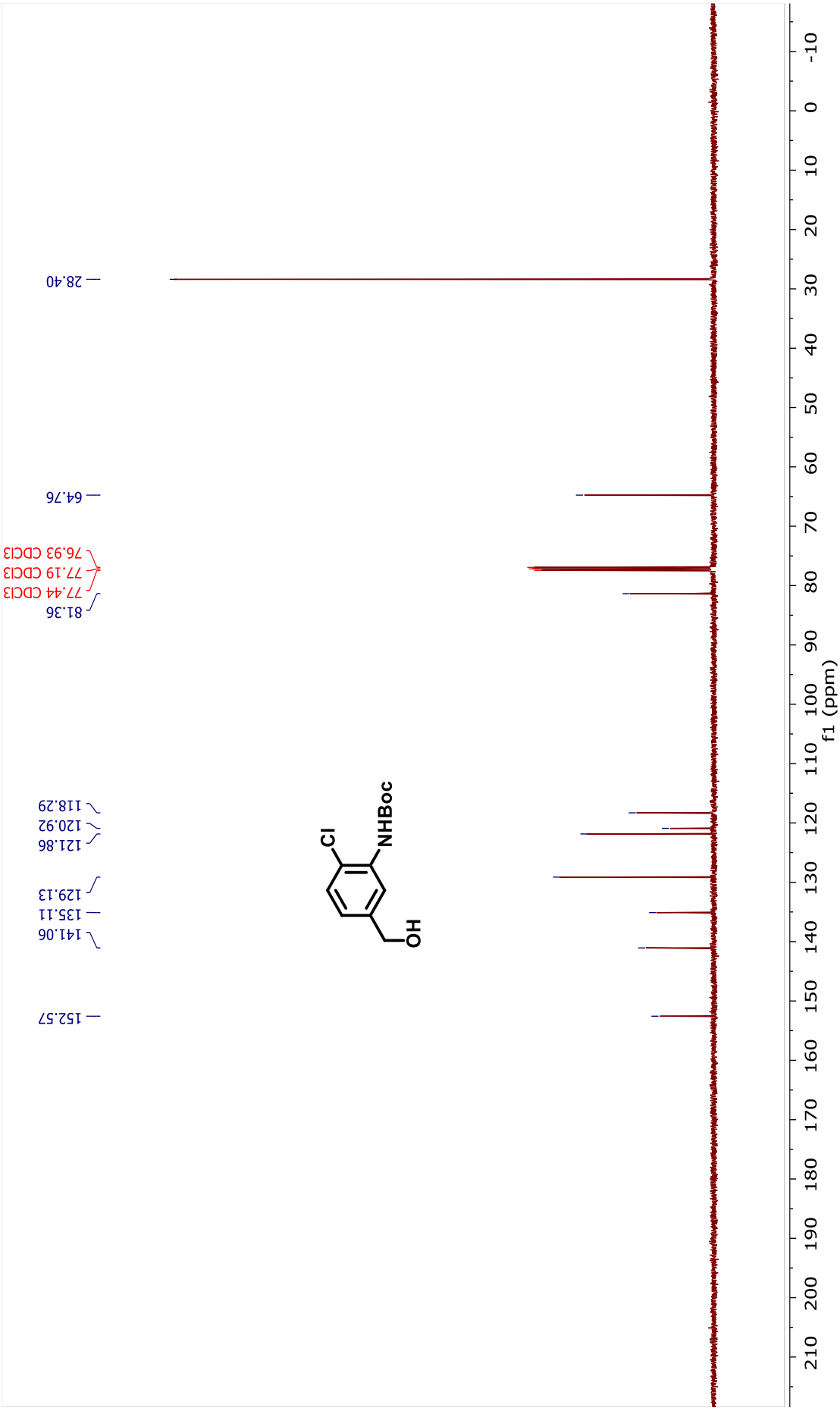
^{13}C NMR Comparison of Natural (100 MHz) and Synthetic (126 MHz) of **(–) -4** in CD_3OD



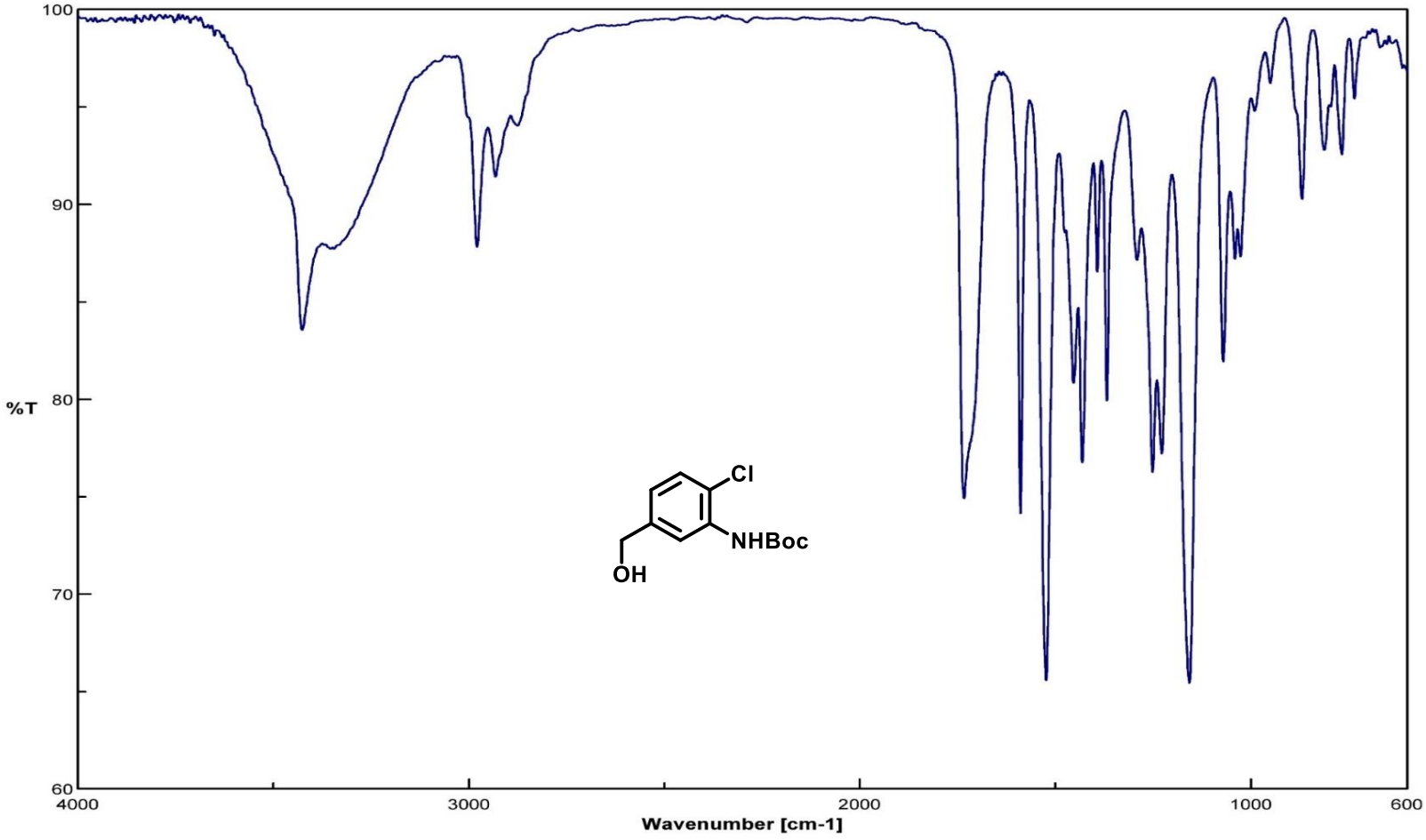
IR Spectrum of Compound **(–) -4**



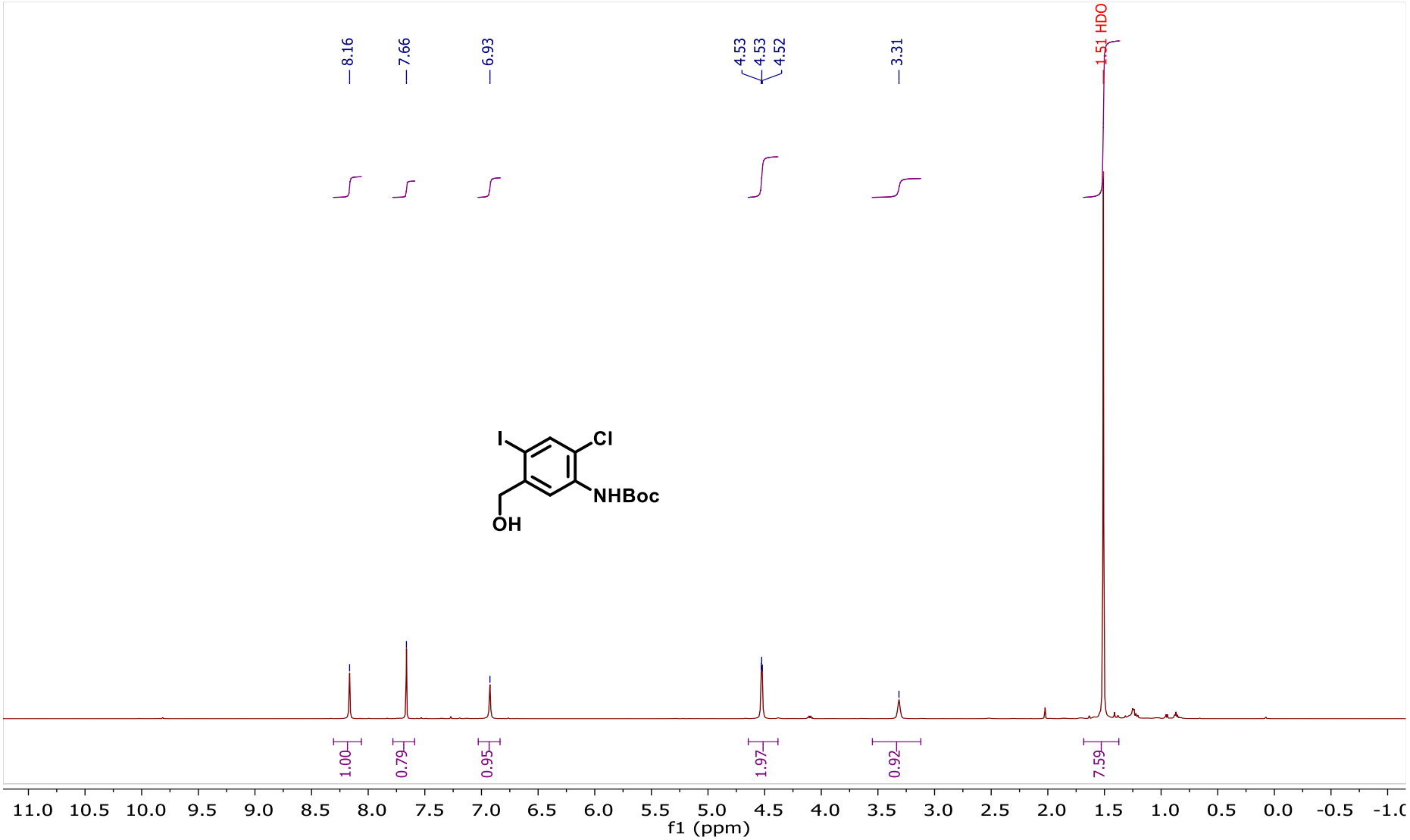
^{1}H NMR (500 MHz) Spectrum of Compound **50** in $CDCl_3$



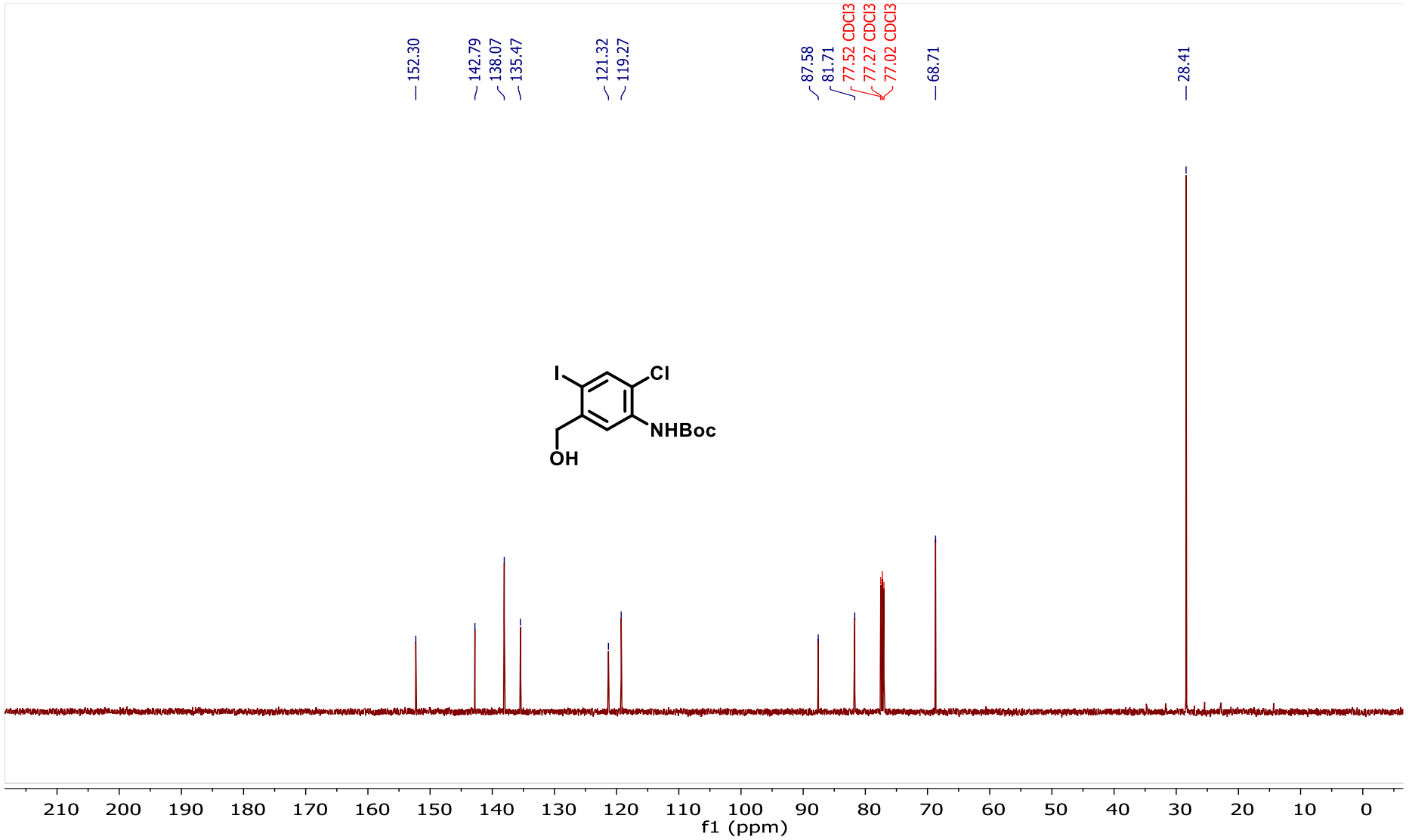
^{13}C NMR (126 MHz) Spectrum of Compound **50** in $CDCl_3$



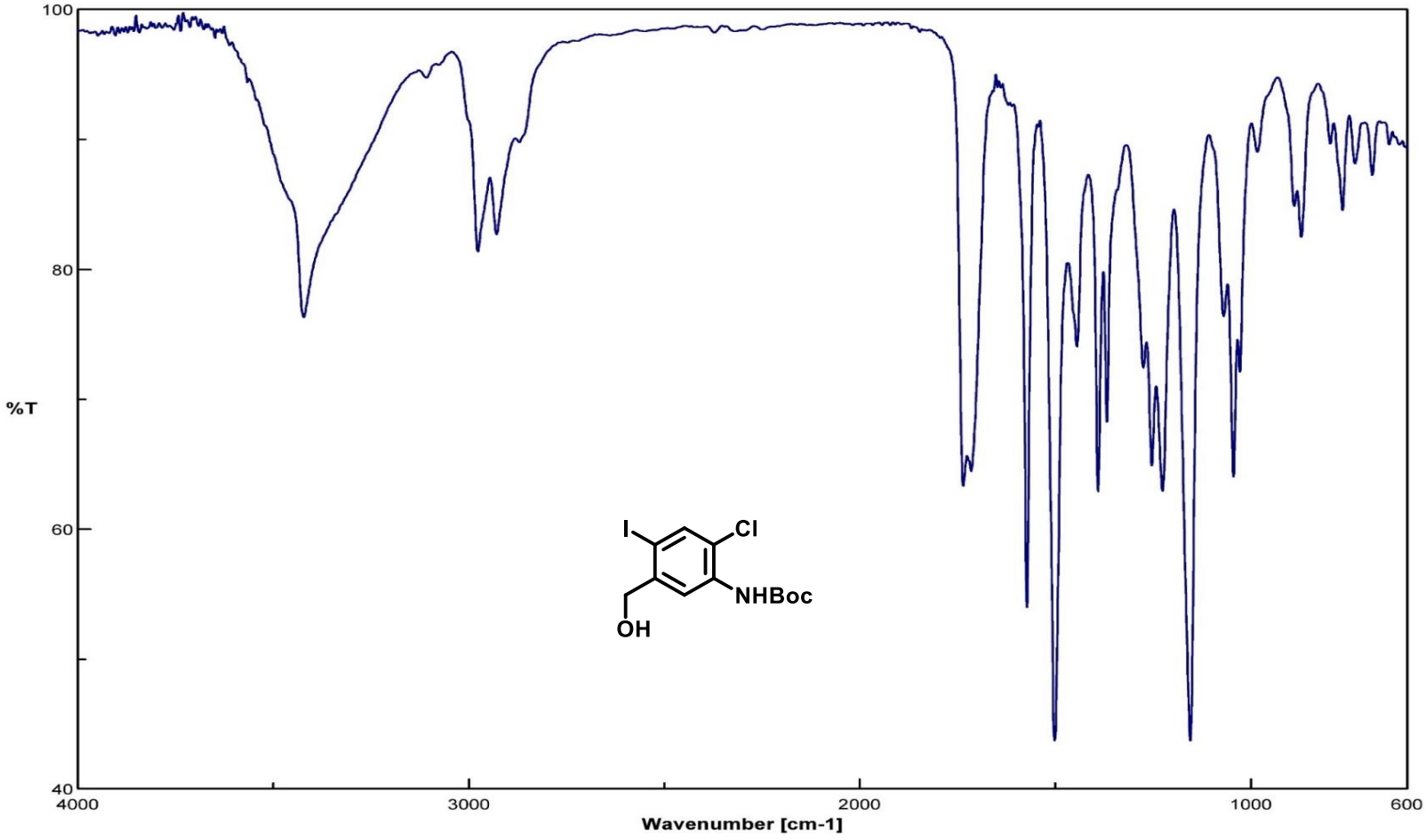
IR Spectrum of Compound **50**



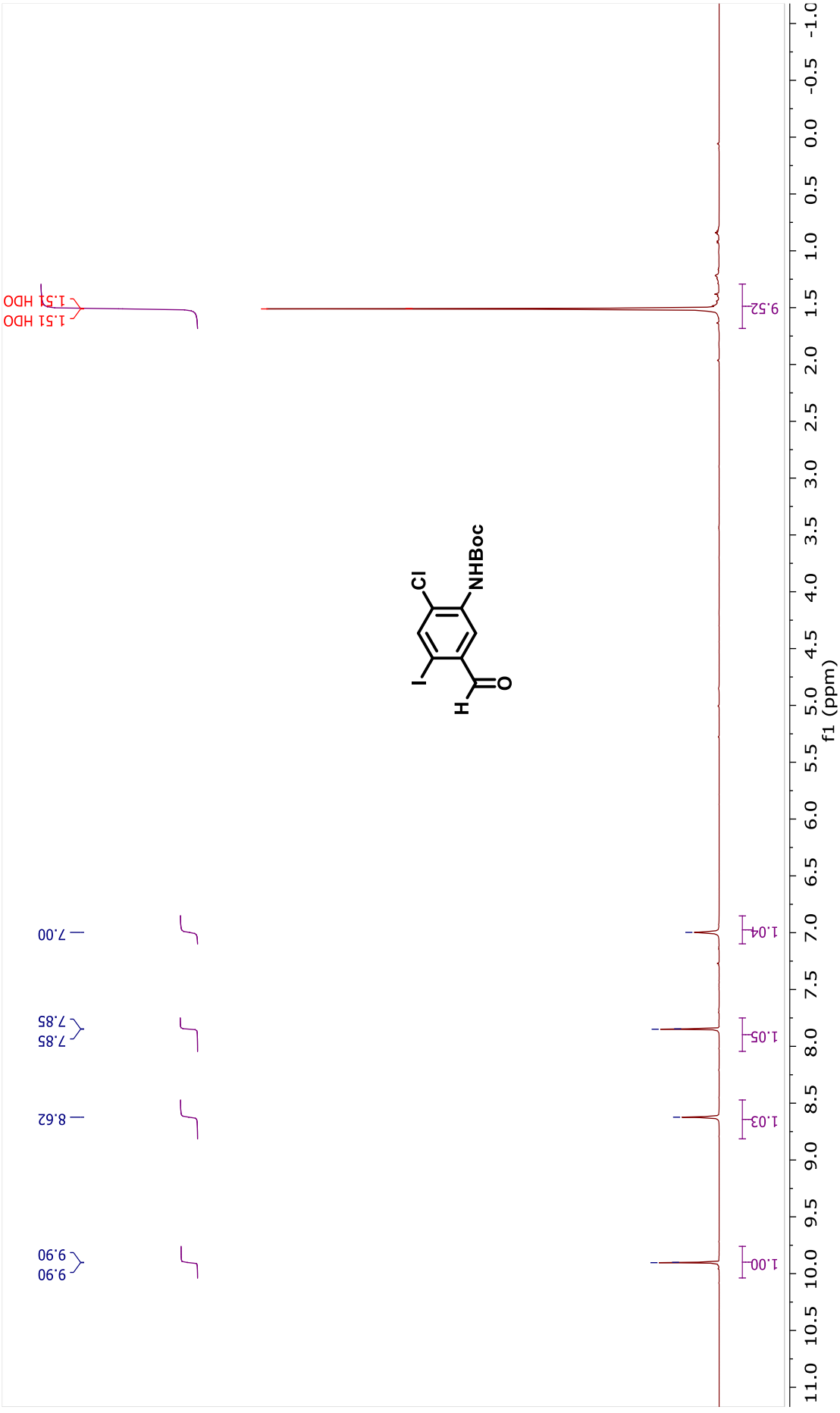
^{1}H NMR (500 MHz) Spectrum of Compound **51** in $CDCl_3$



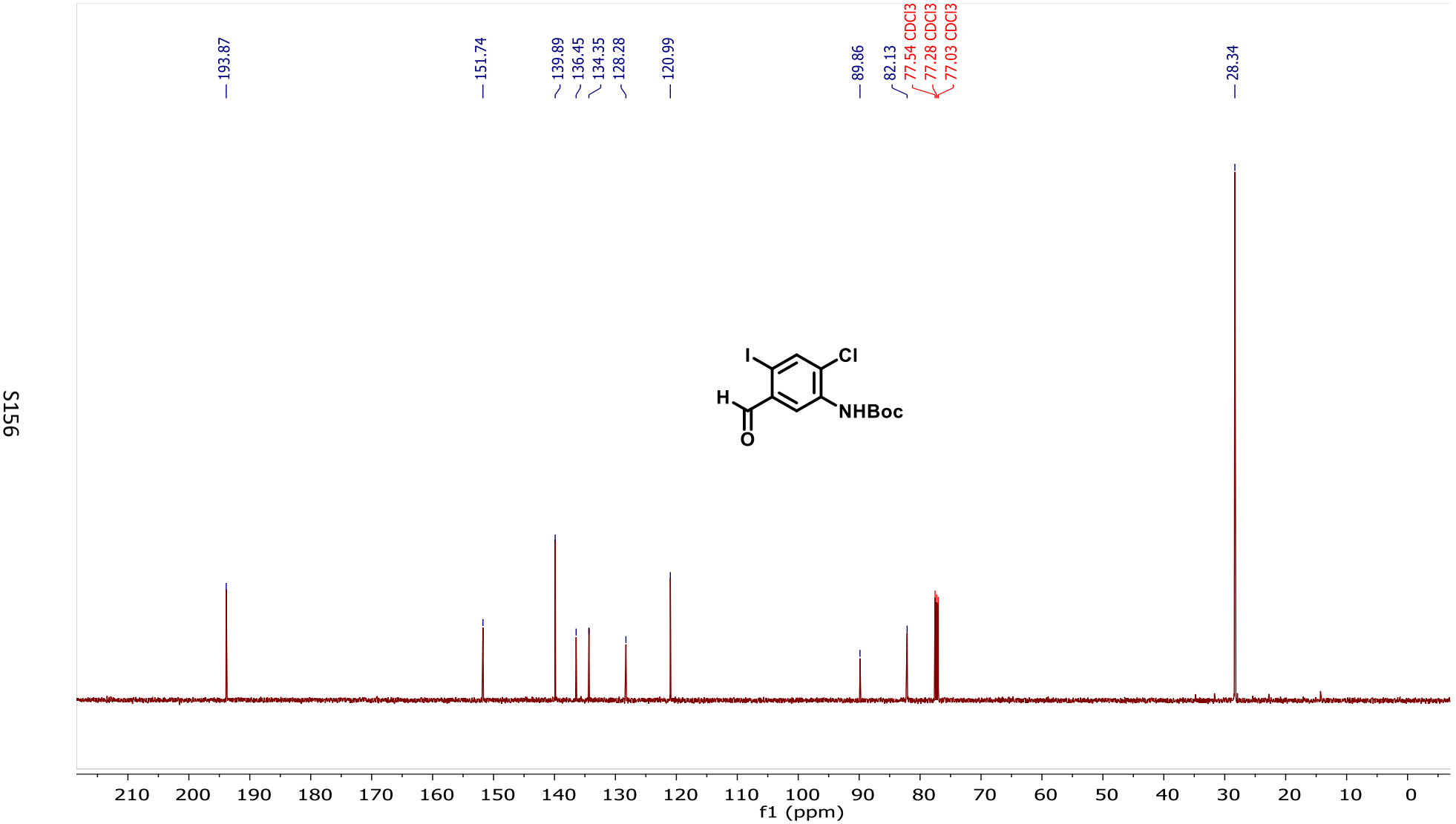
^{13}C NMR (126 MHz) Spectrum of Compound **51** in $CDCl_3$



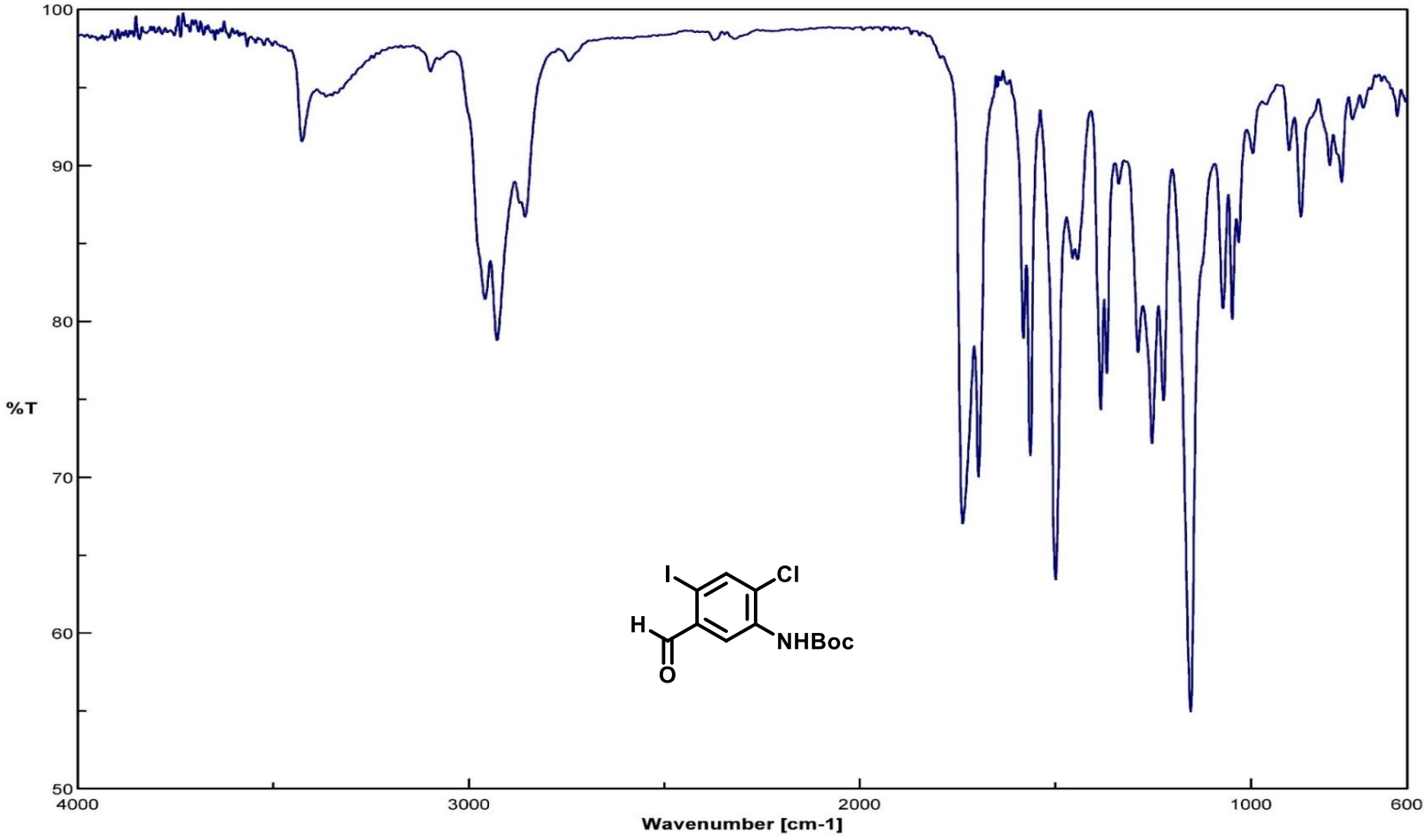
IR Spectrum of Compound **51**



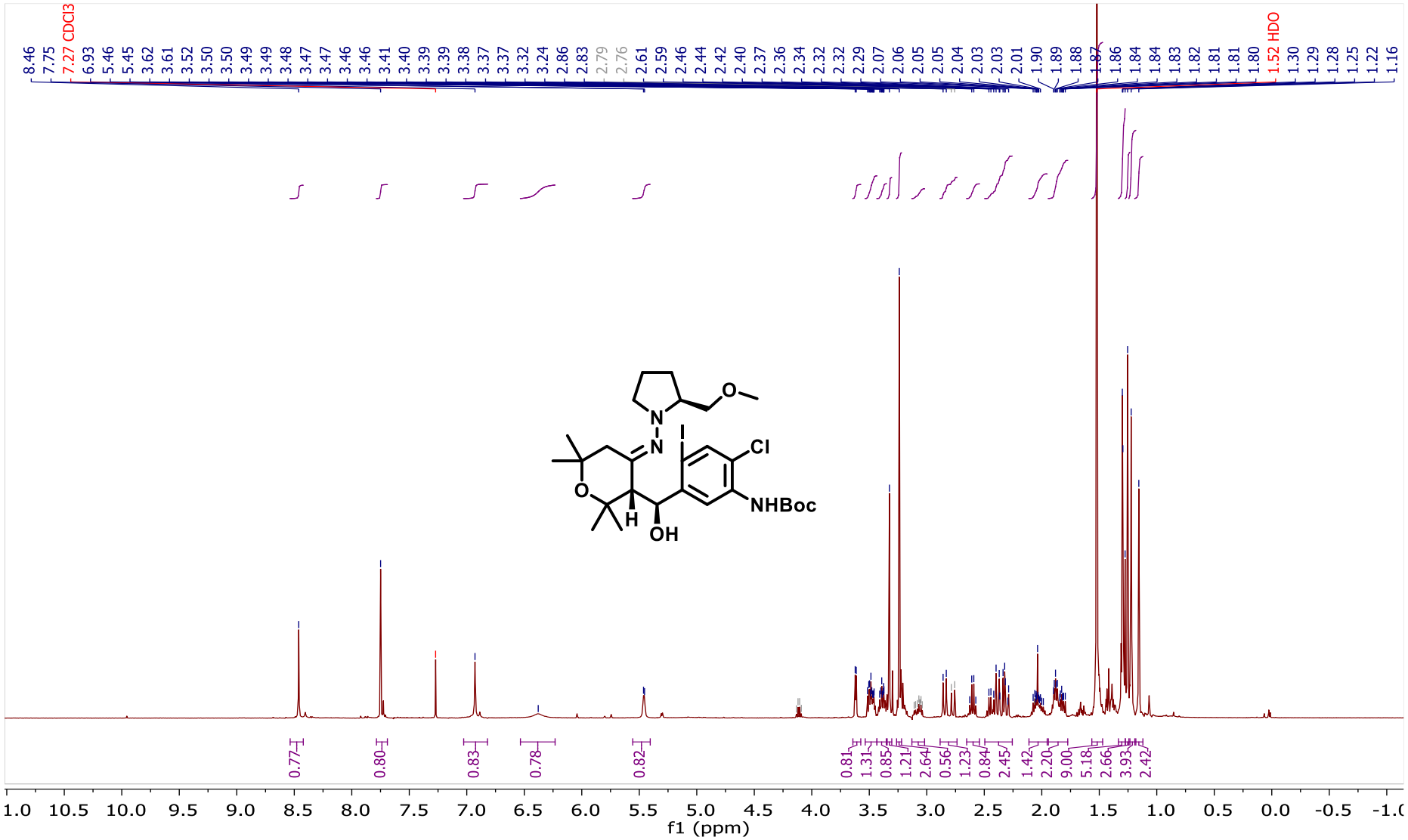
^{1}H NMR (500 MHz) Spectrum of Compound **52** in $CDCl_3$



^{13}C NMR (126 MHz) Spectrum of Compound **52** in $CDCl_3$

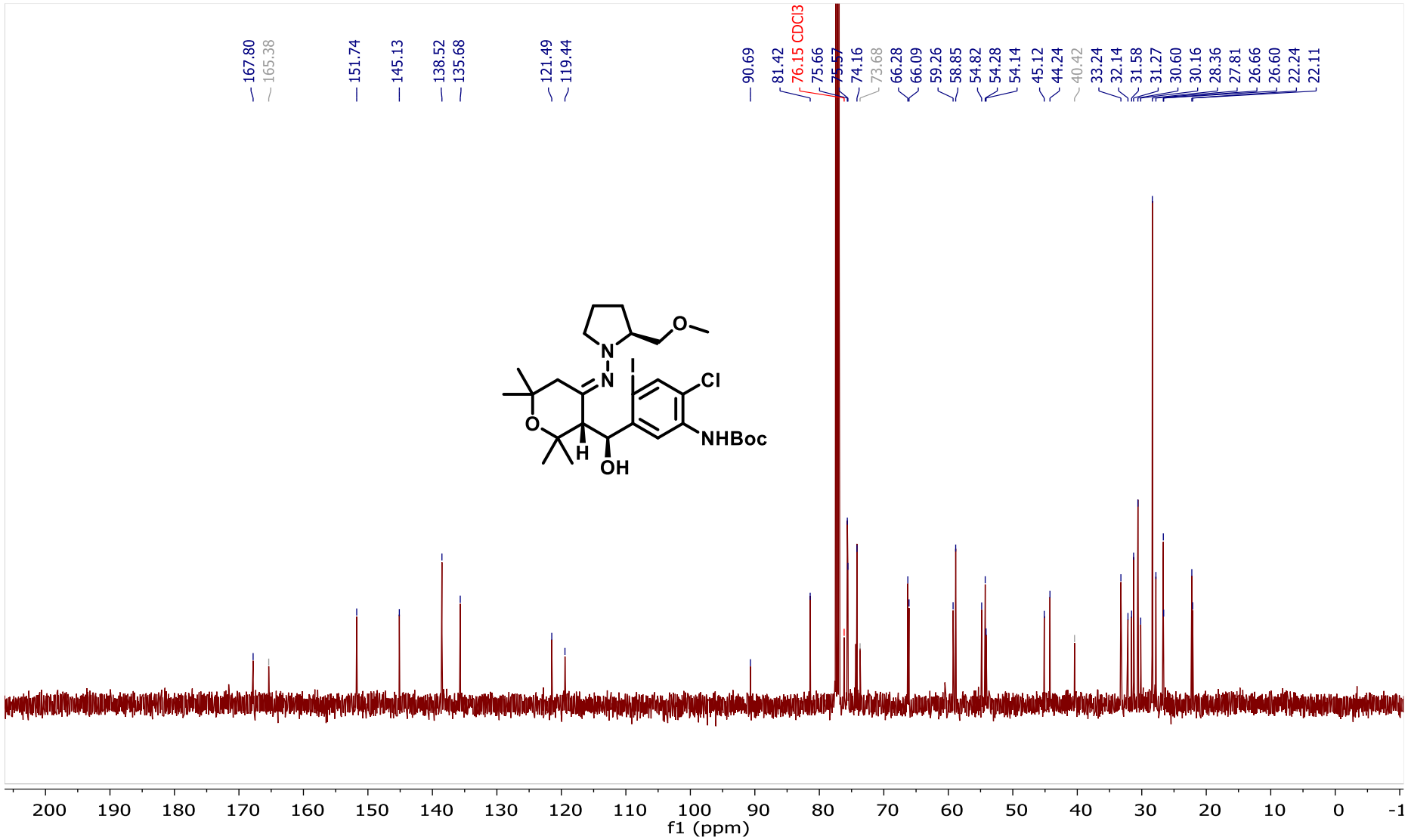


IR Spectrum of Compound **52**



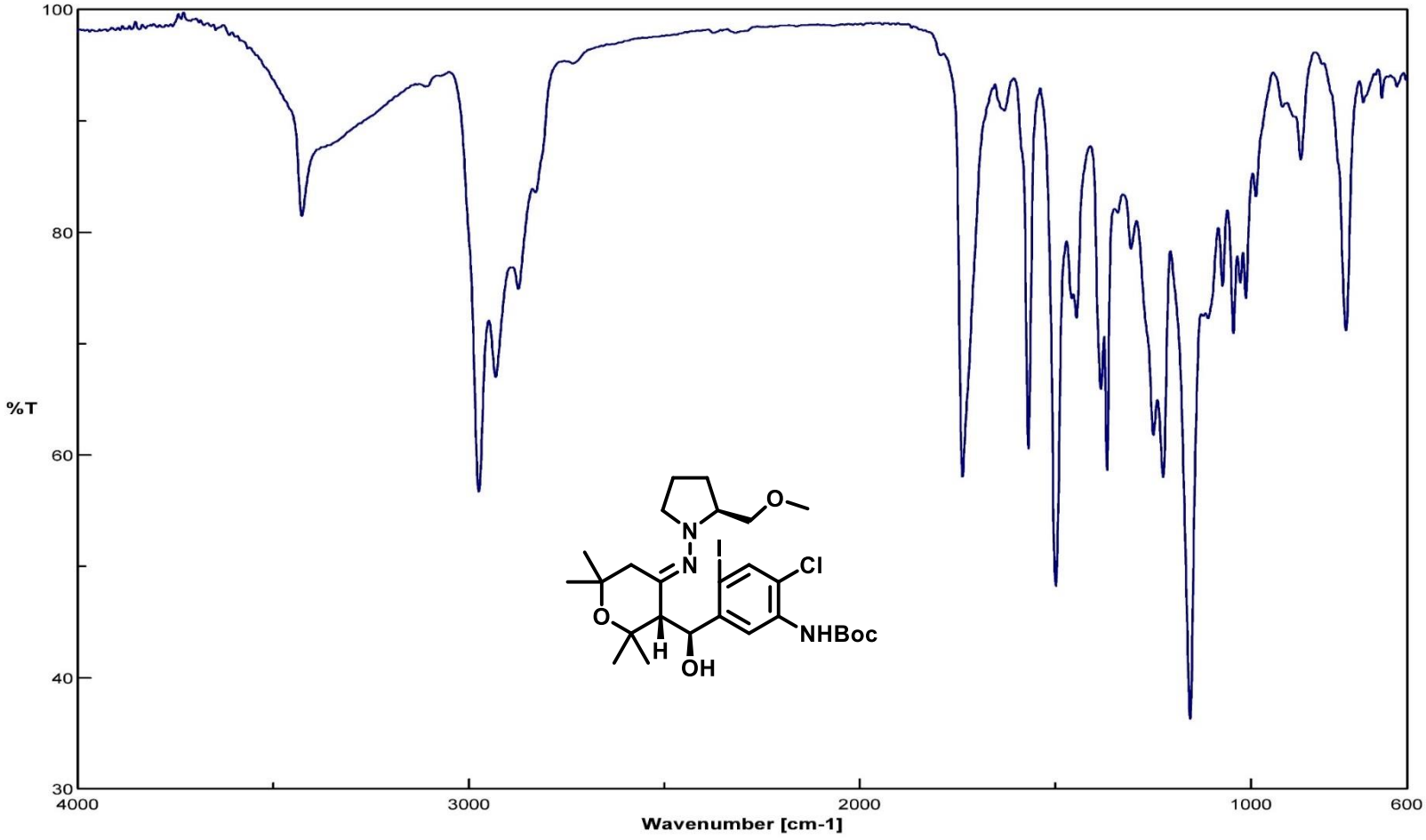
^{1}H NMR (500 MHz) Spectrum of Compound **(+)-53** in $CDCl_3$

(containing Z/E isomers)



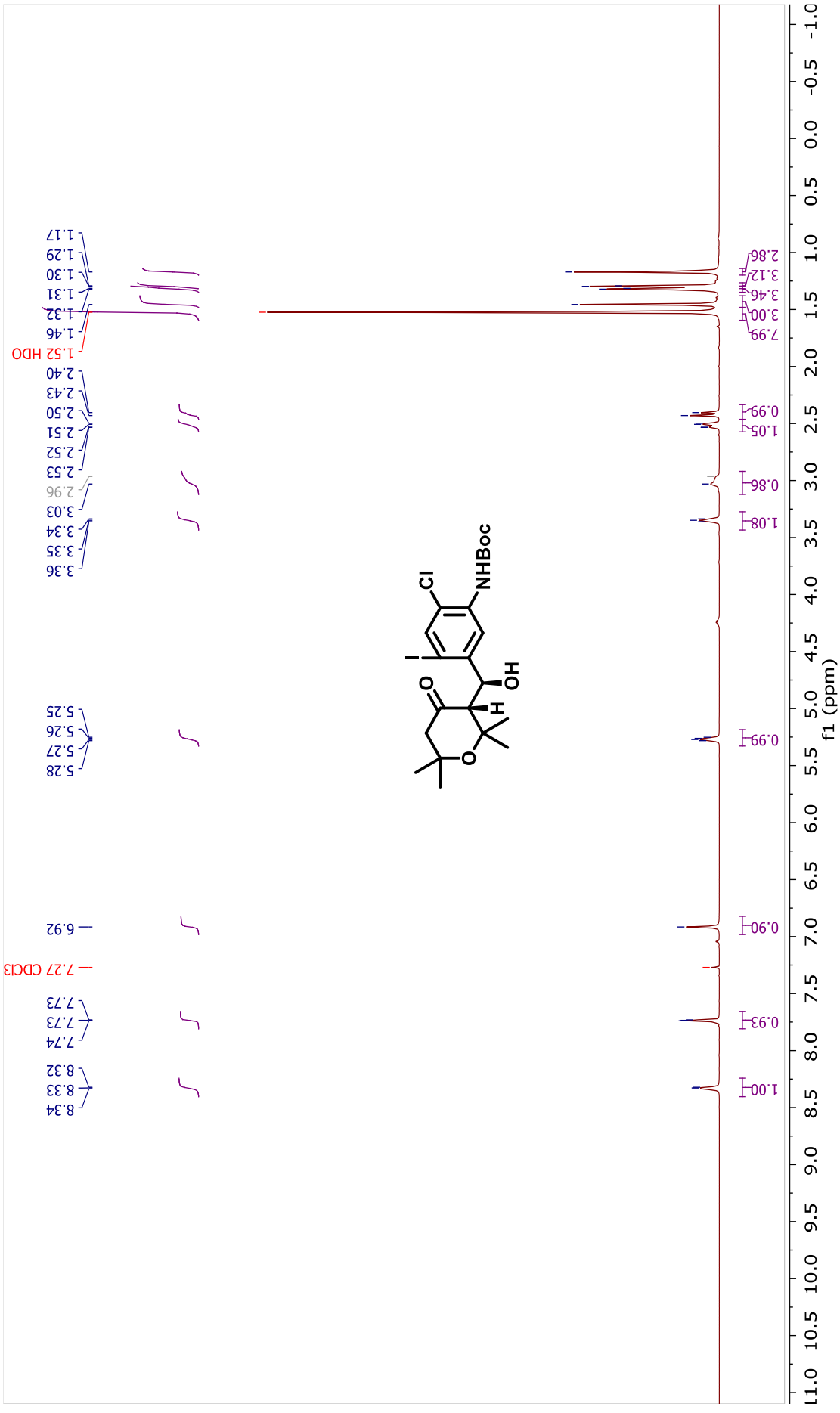
^{13}C NMR (126 MHz) Spectrum of Compound **(+)-53** in $CDCl_3$

(containing Z/E isomers)

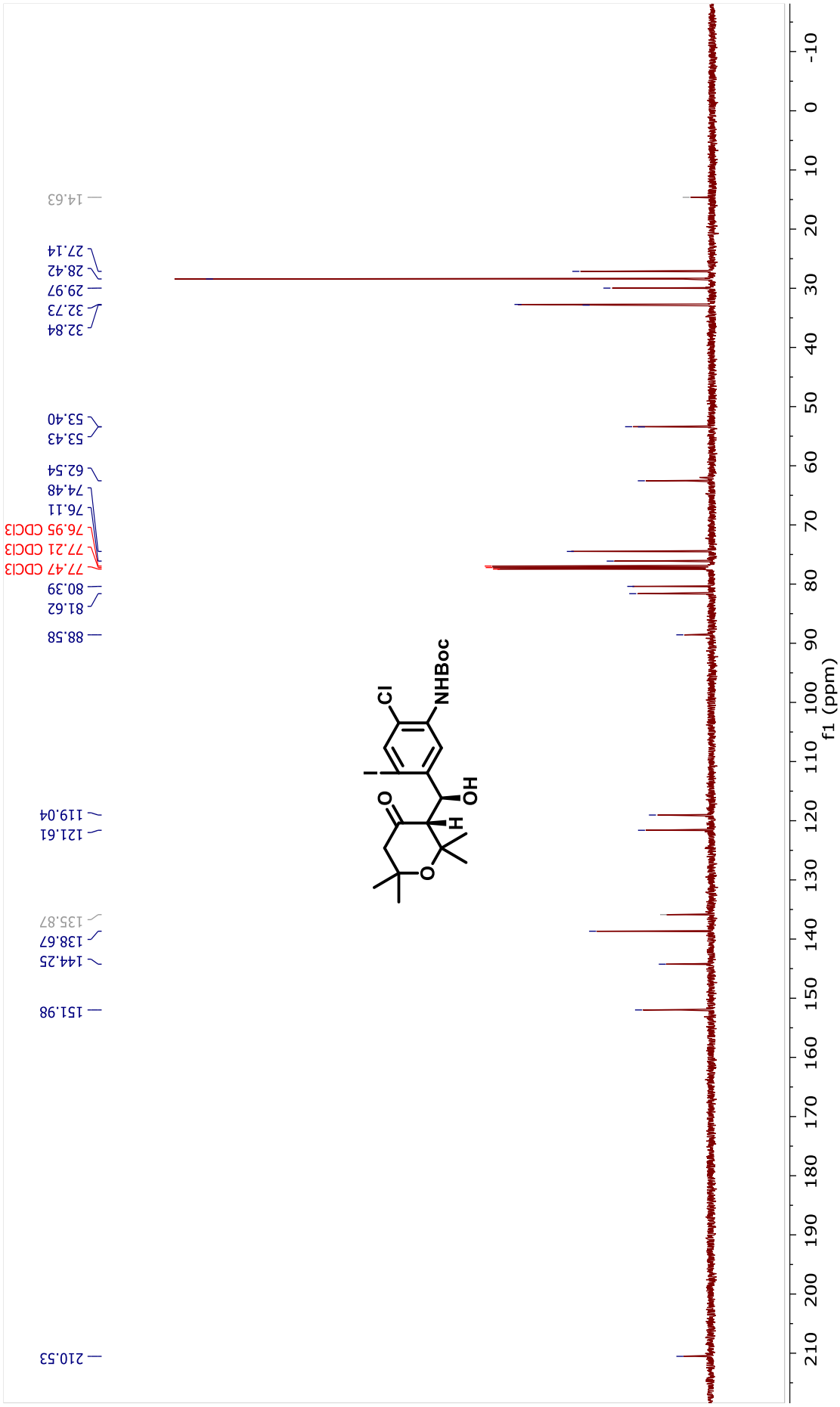


IR Spectrum of Compound **(+)-53**

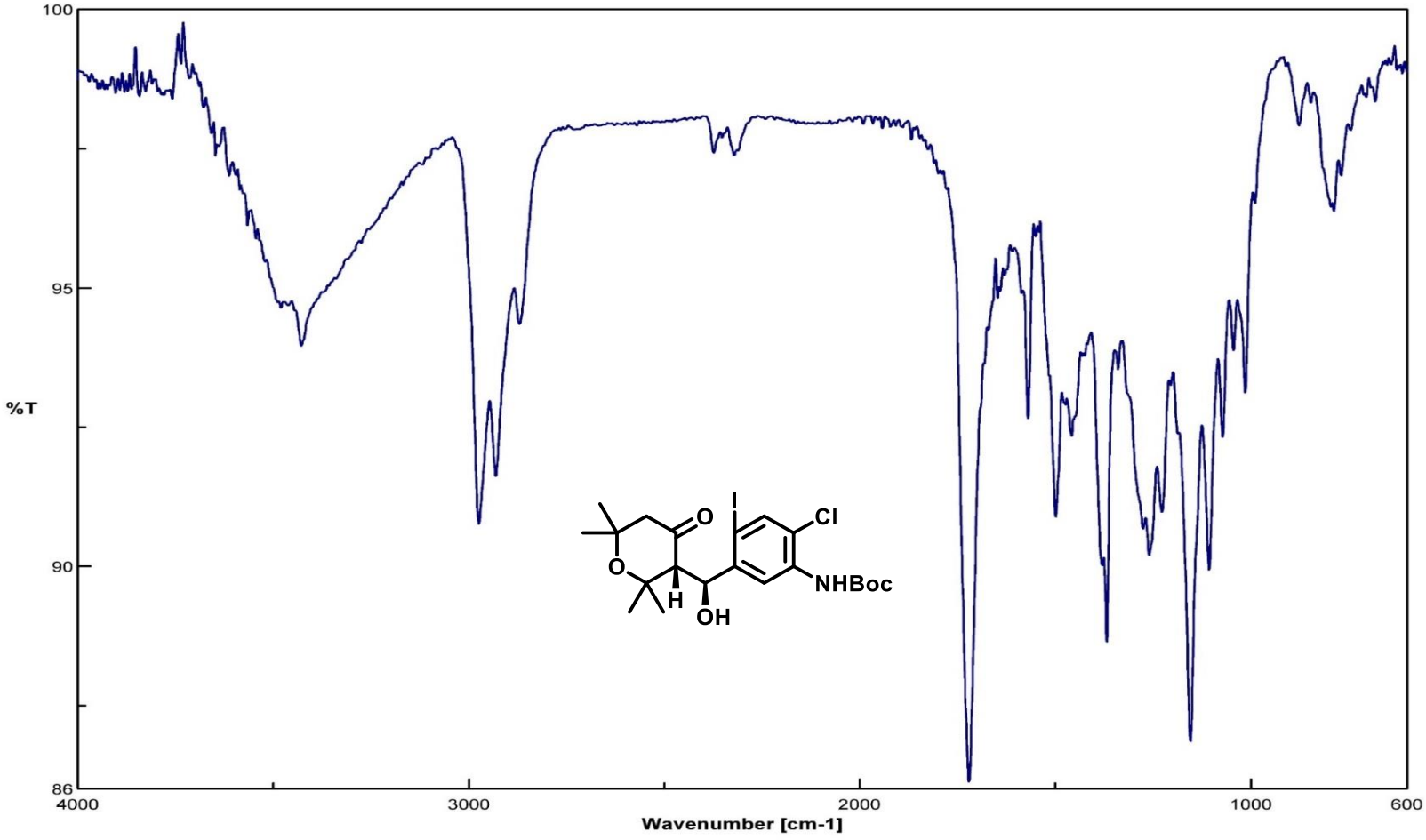
(containing Z/E isomers)



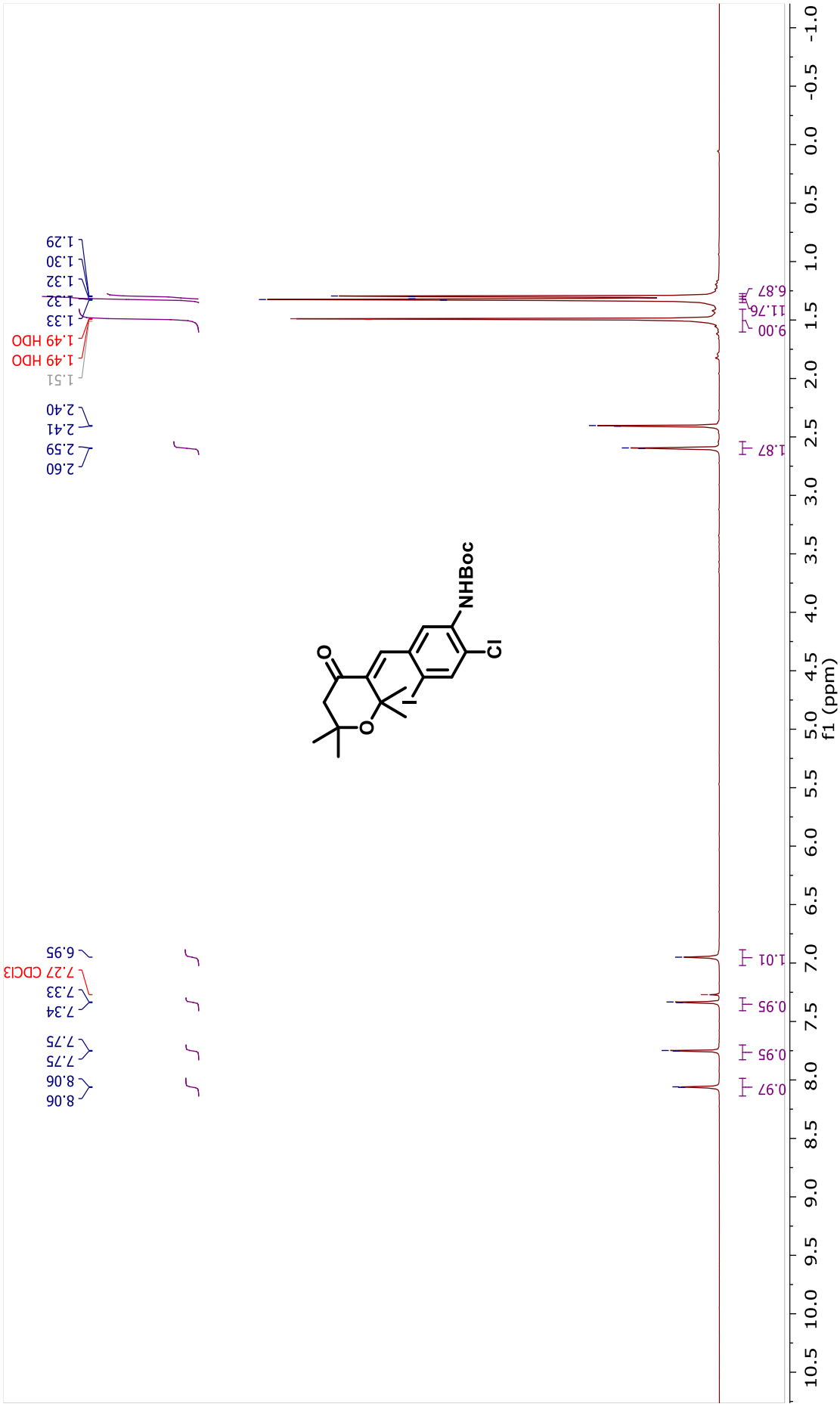
^{1}H NMR (500 MHz) Spectrum of Compound **(–)-54** in $CDCl_3$



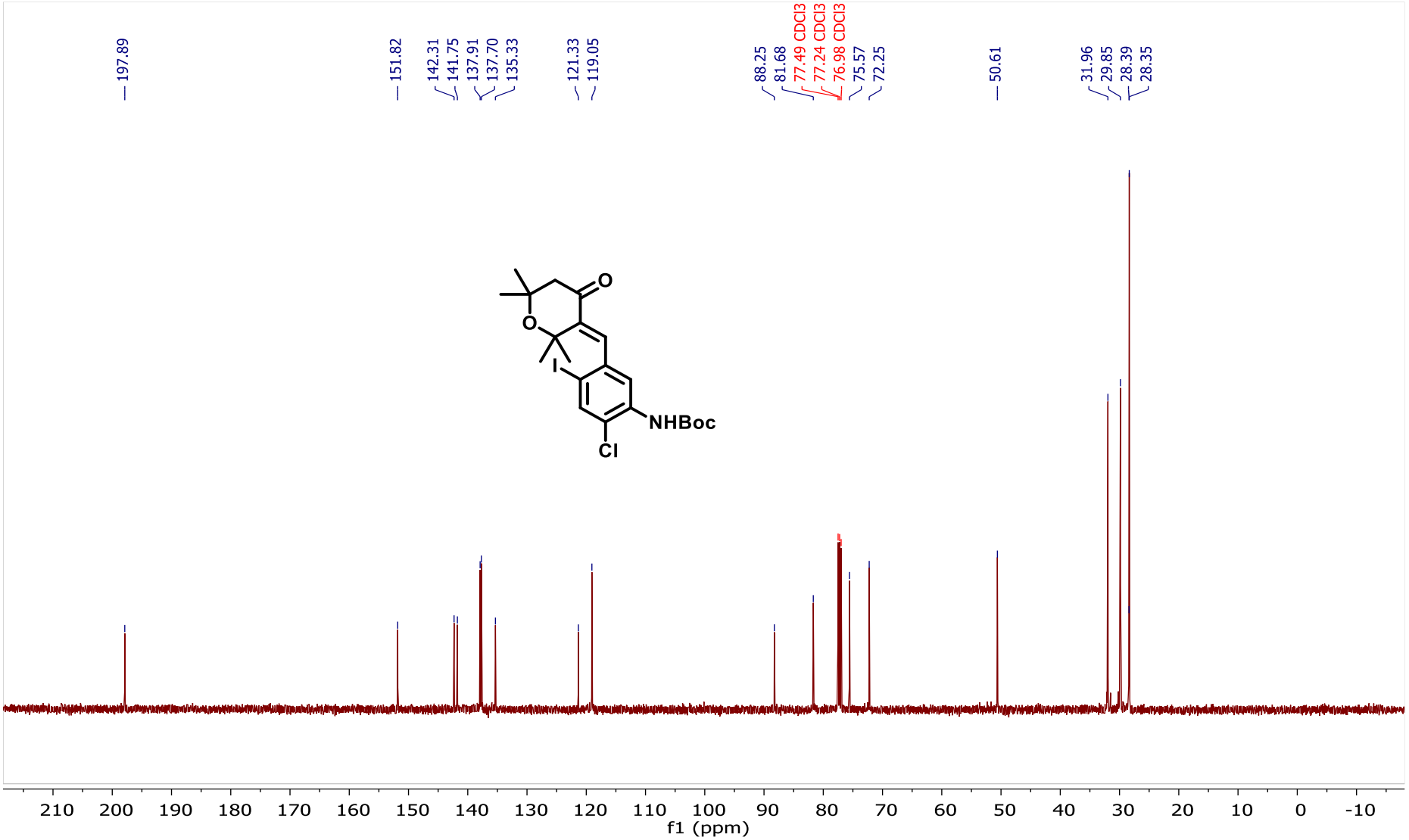
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-54** in $CDCl_3$



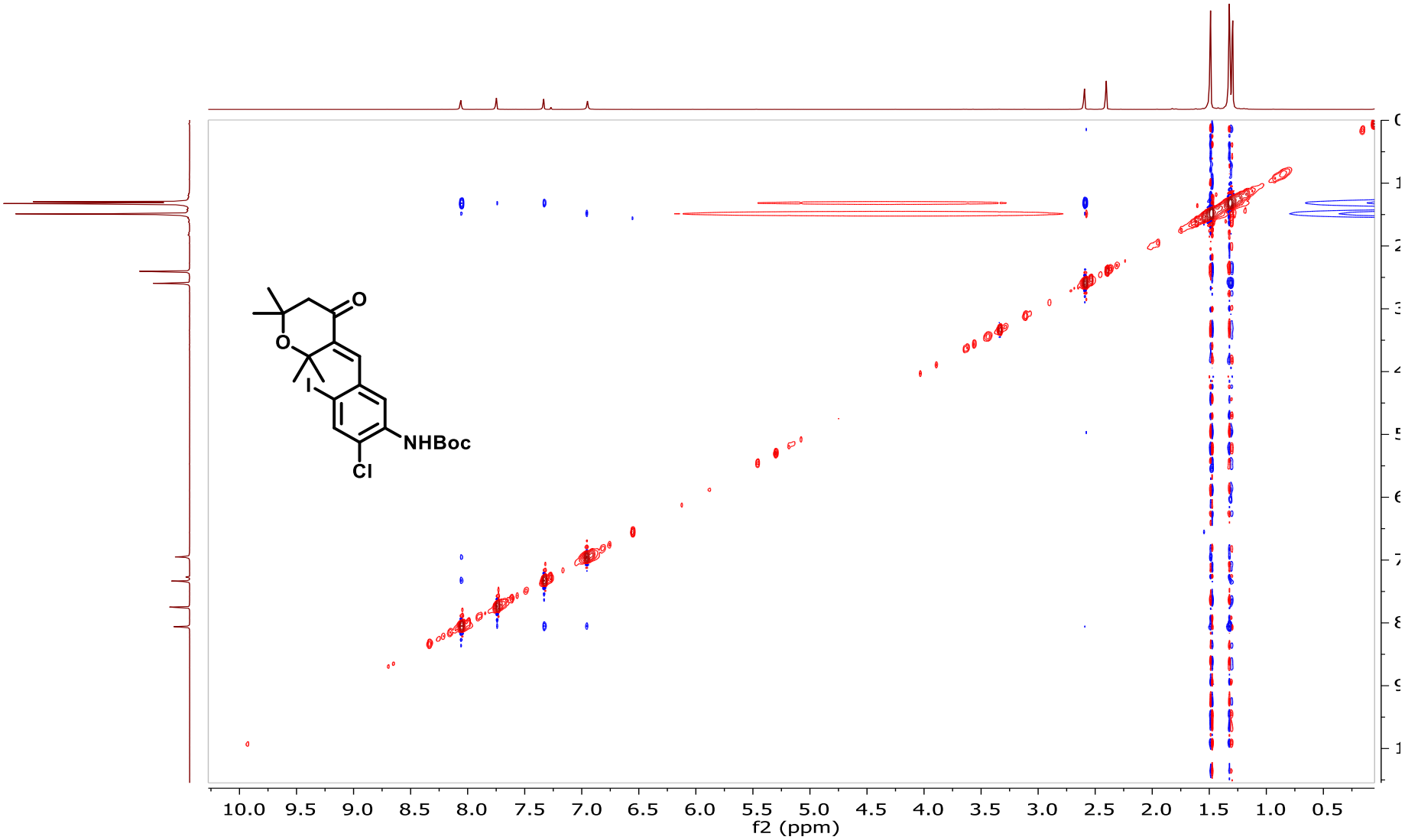
IR Spectrum of Compound (–)-54



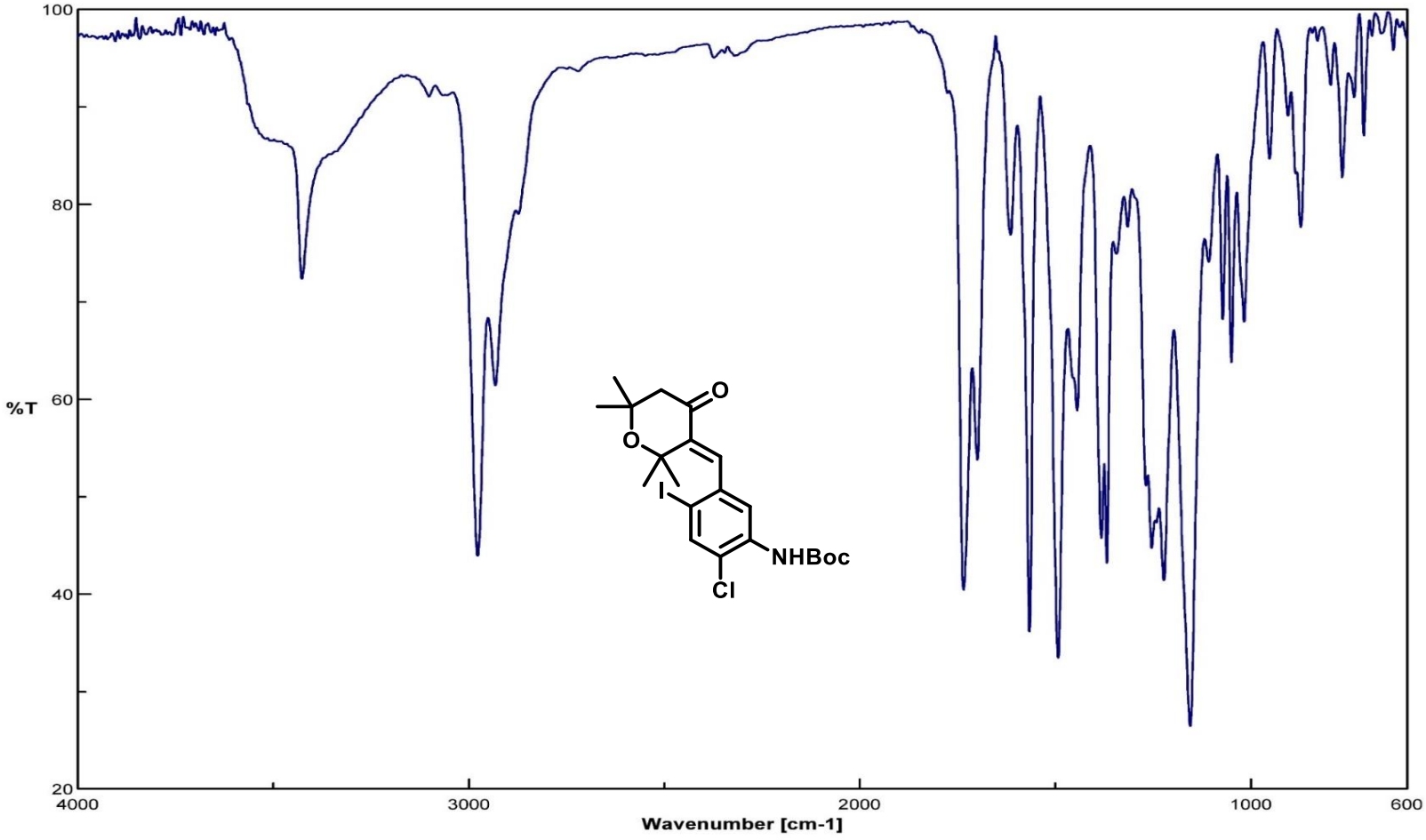
^{1}H NMR (500 MHz) Spectrum of Compound **55** in $CDCl_3$



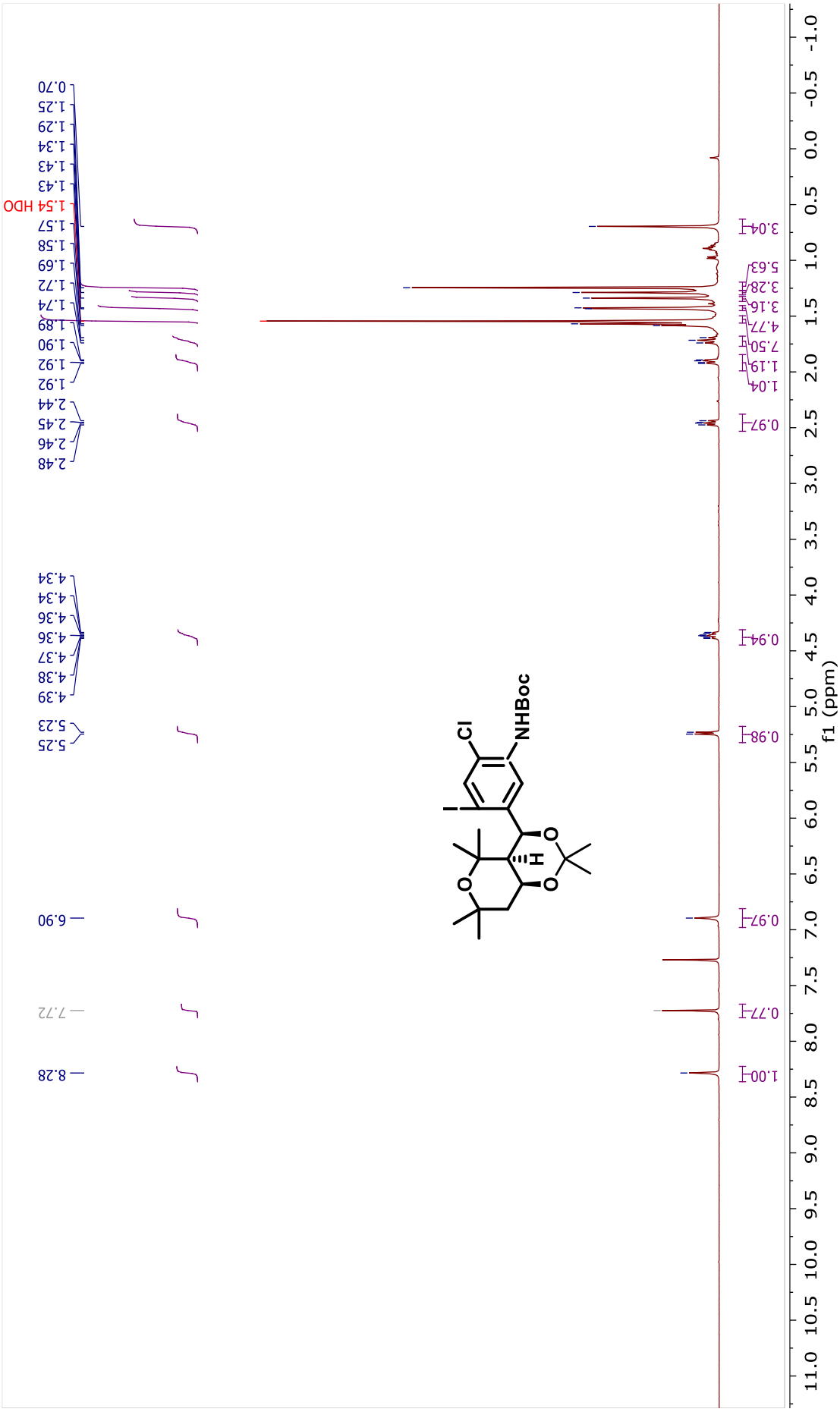
^{13}C NMR (126 MHz) Spectrum of Compound **55** in $CDCl_3$



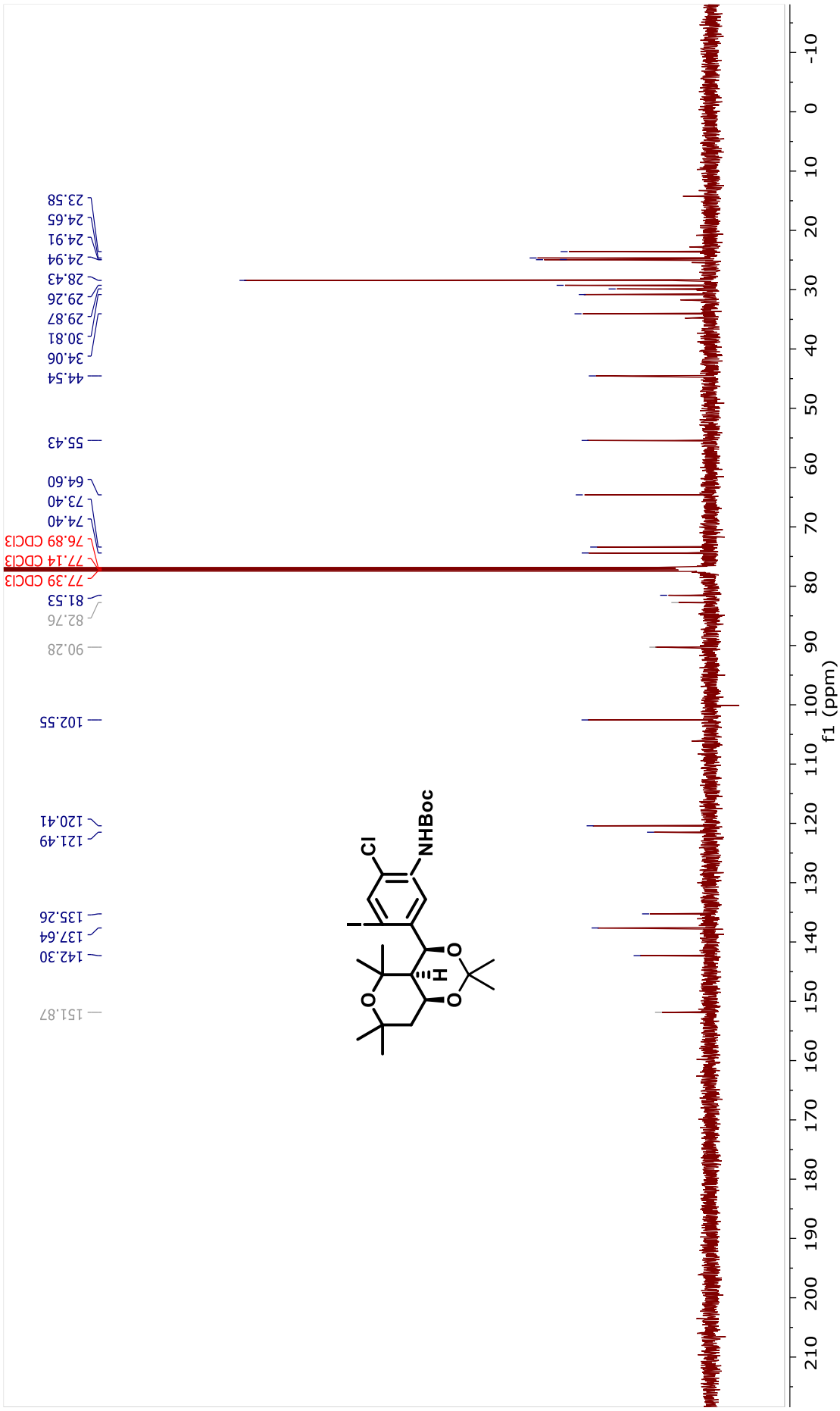
NOESY Spectrum of Compound **55** in $CDCl_3$



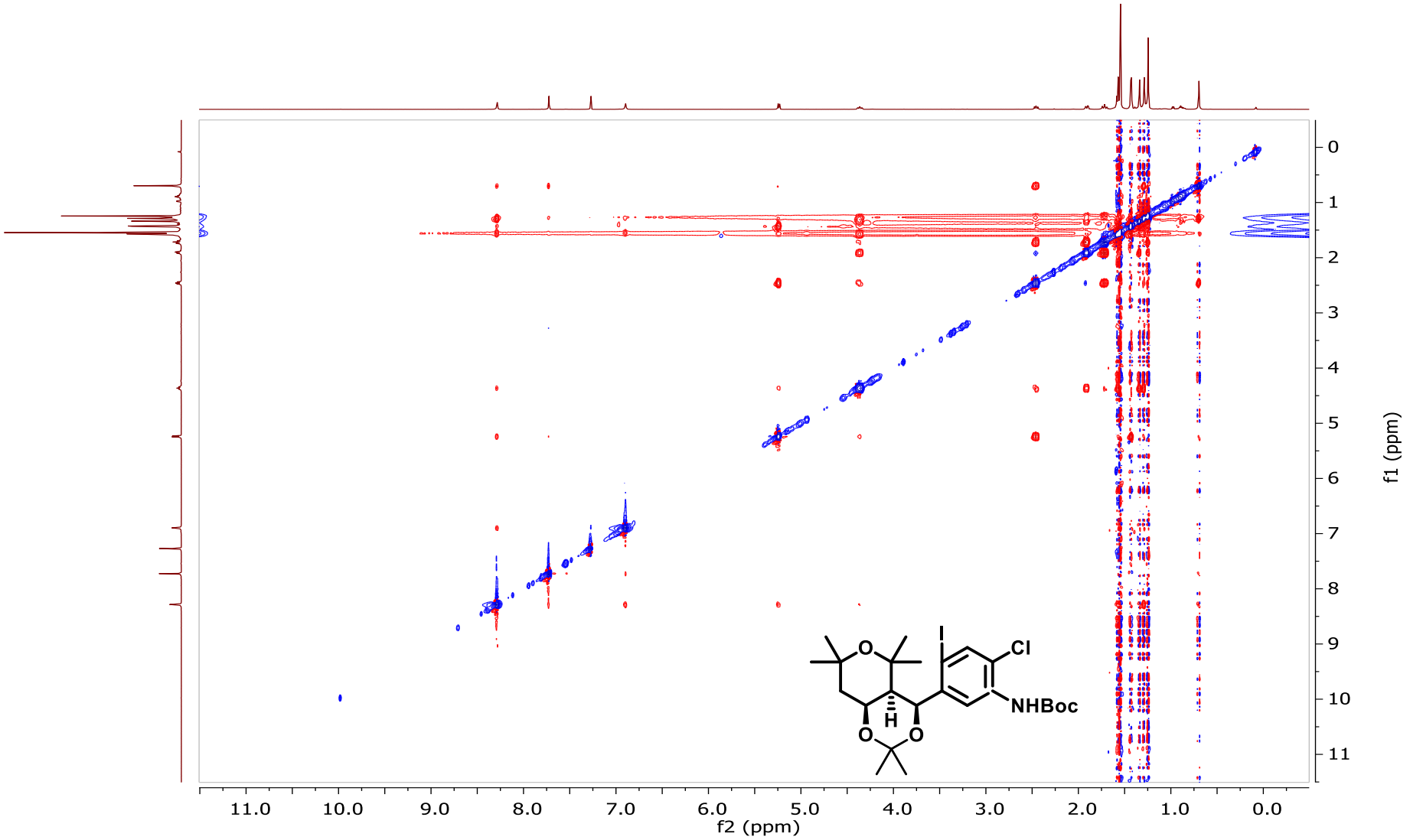
IR Spectrum of Compound **55**



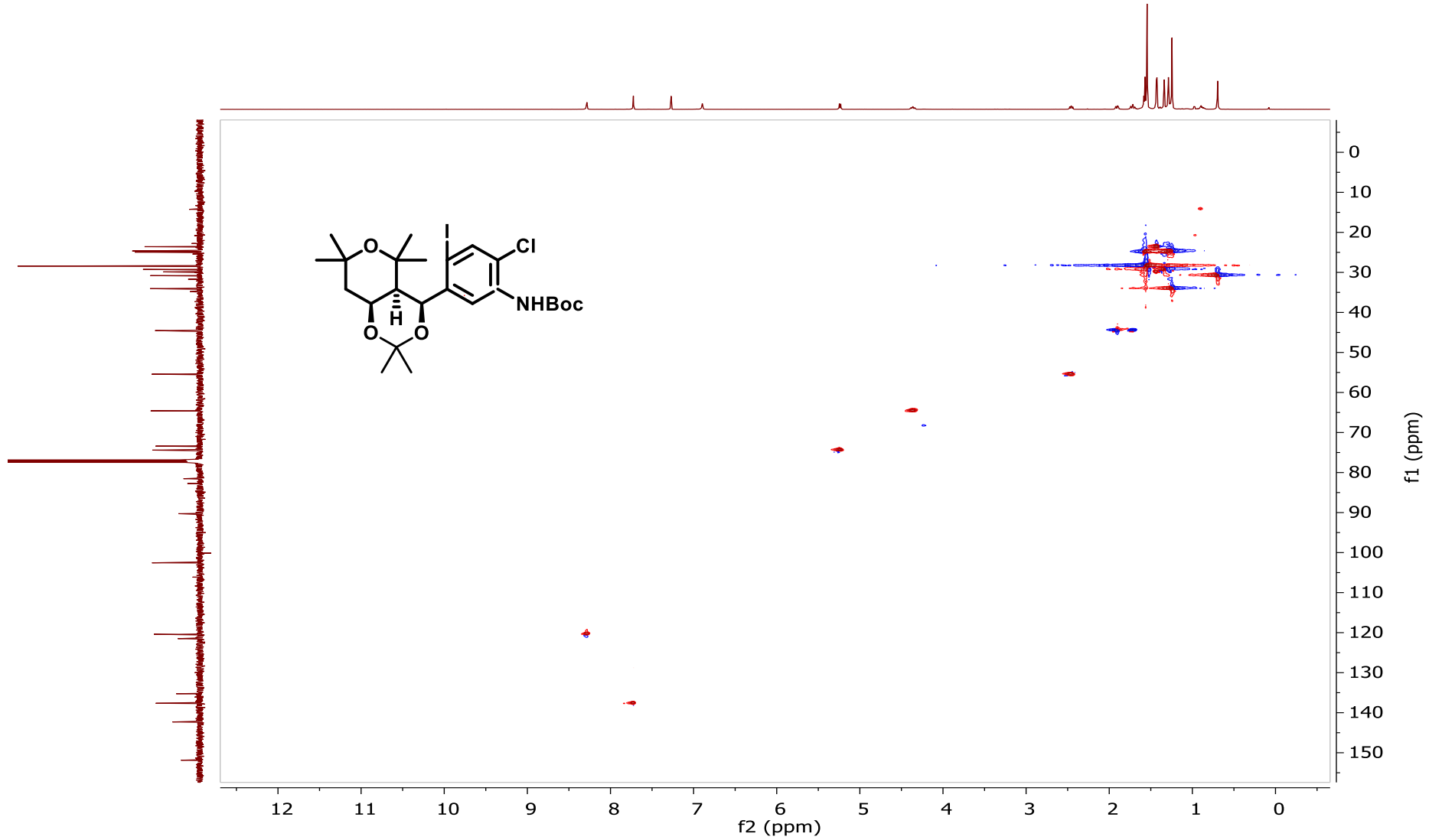
^{1}H NMR (500 MHz) Spectrum of Compound **(–)-56** in $CDCl_3$



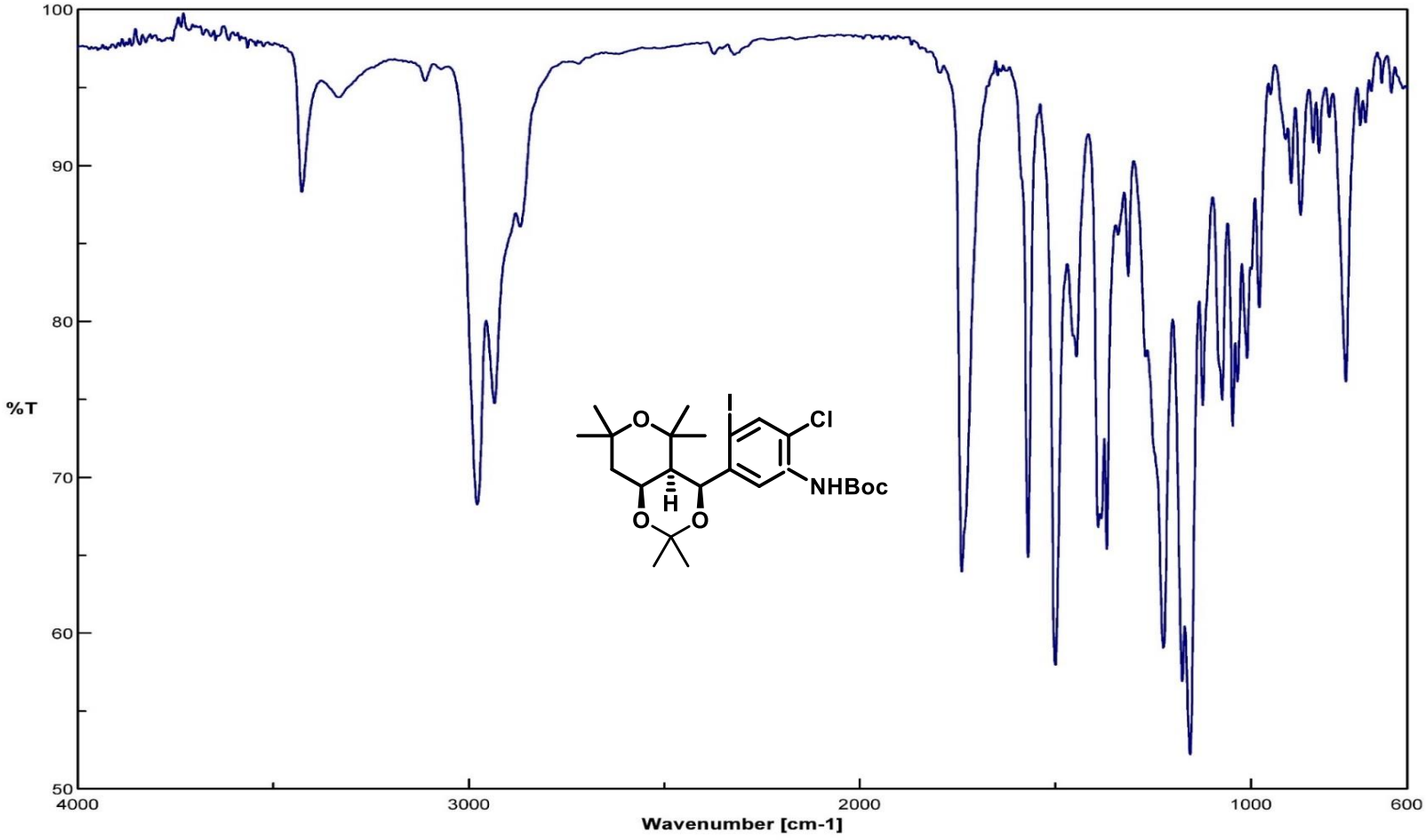
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-56** in $CDCl_3$



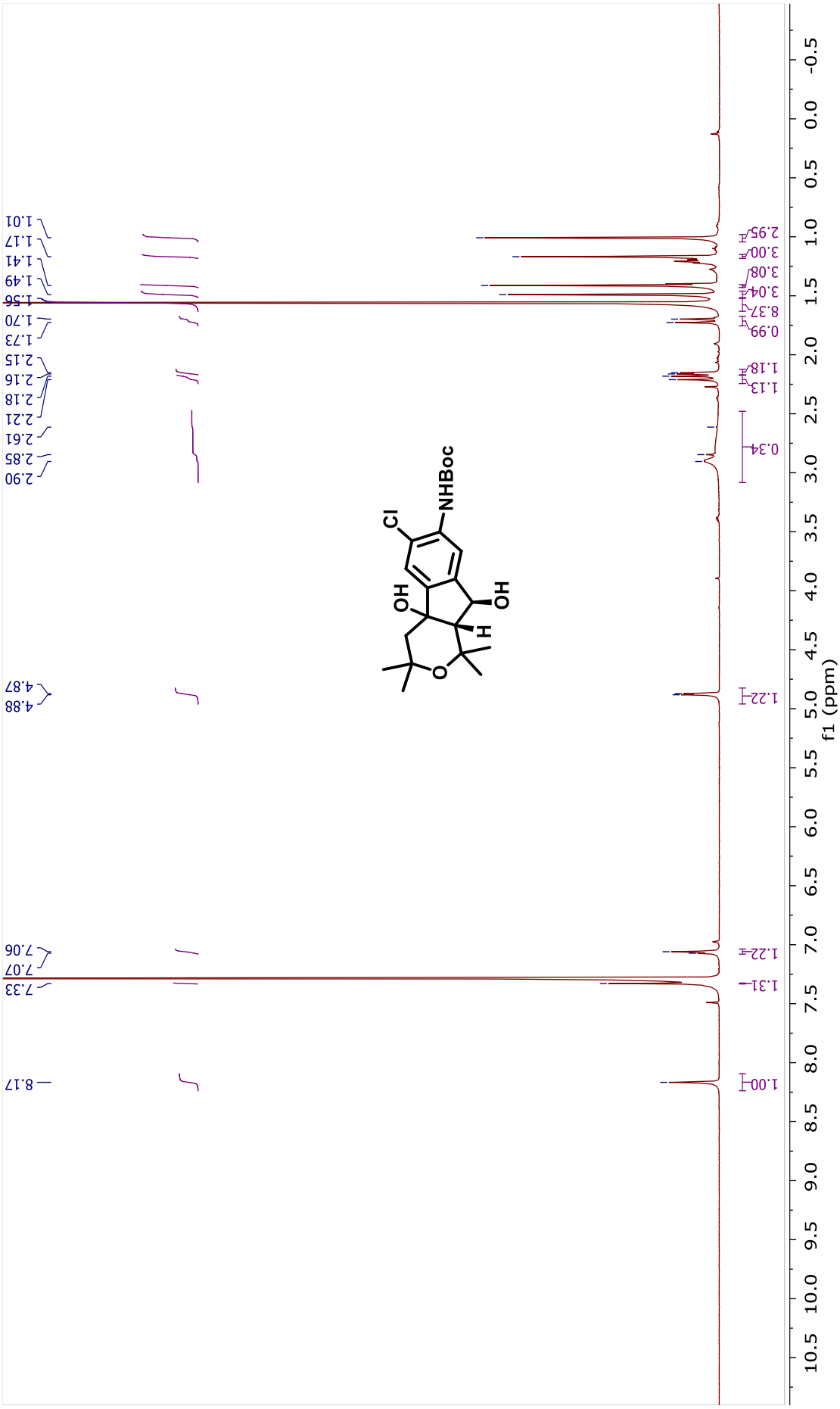
NOESY Spectrum of Compound **(–)-56** in $CDCl_3$



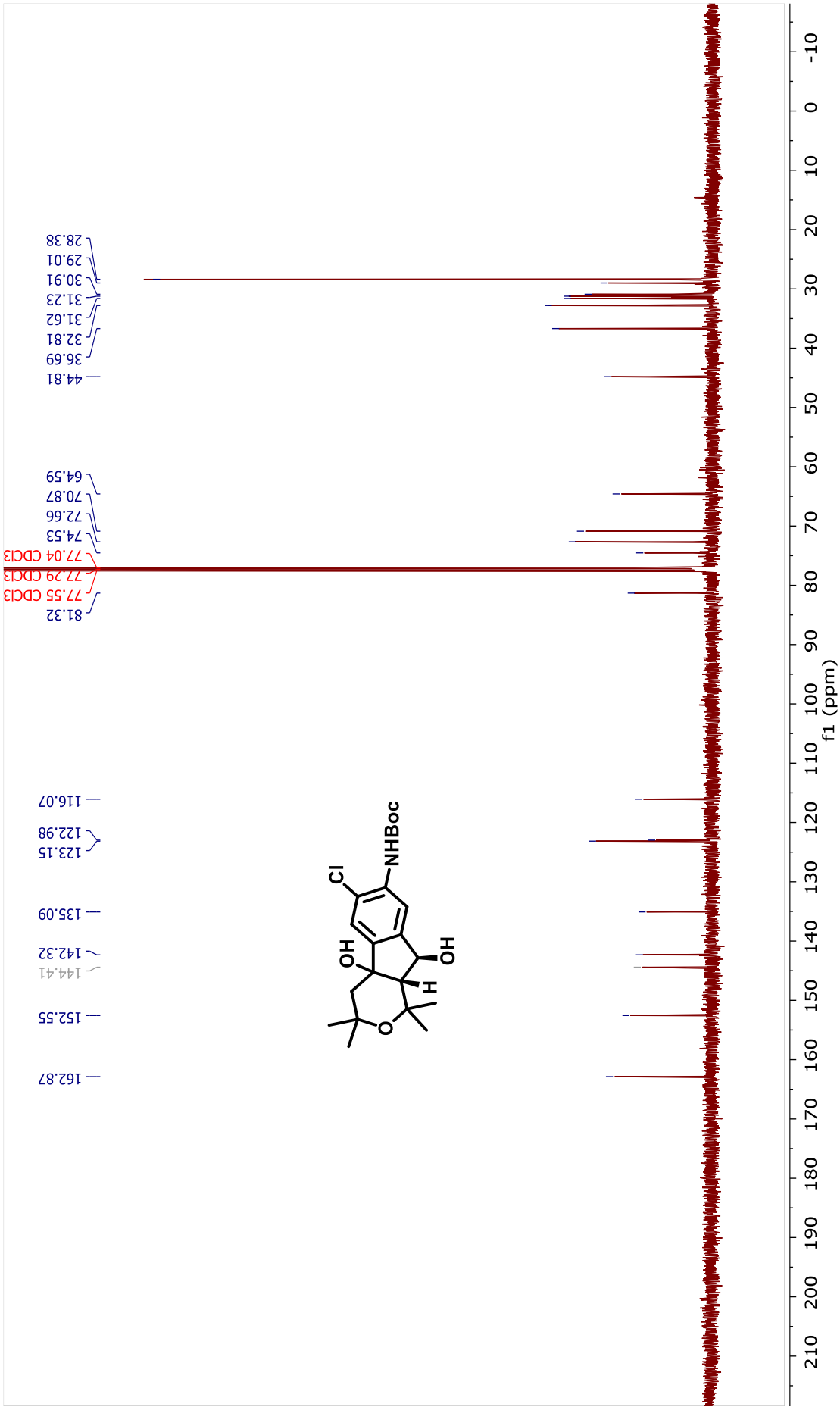
HSQC Spectrum of Compound **(–)-56** in $CDCl_3$



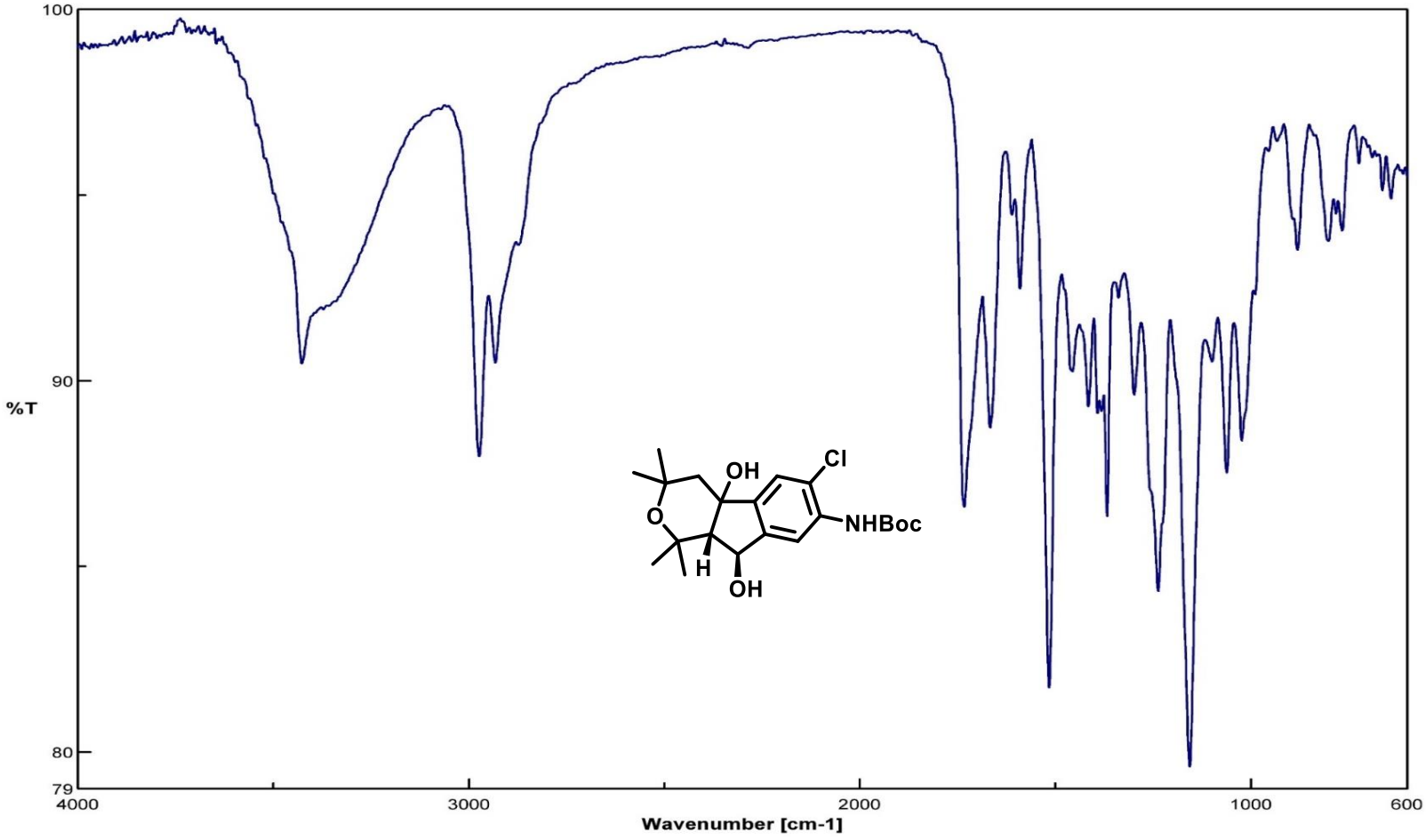
IR Spectrum of Compound **(–)-56**



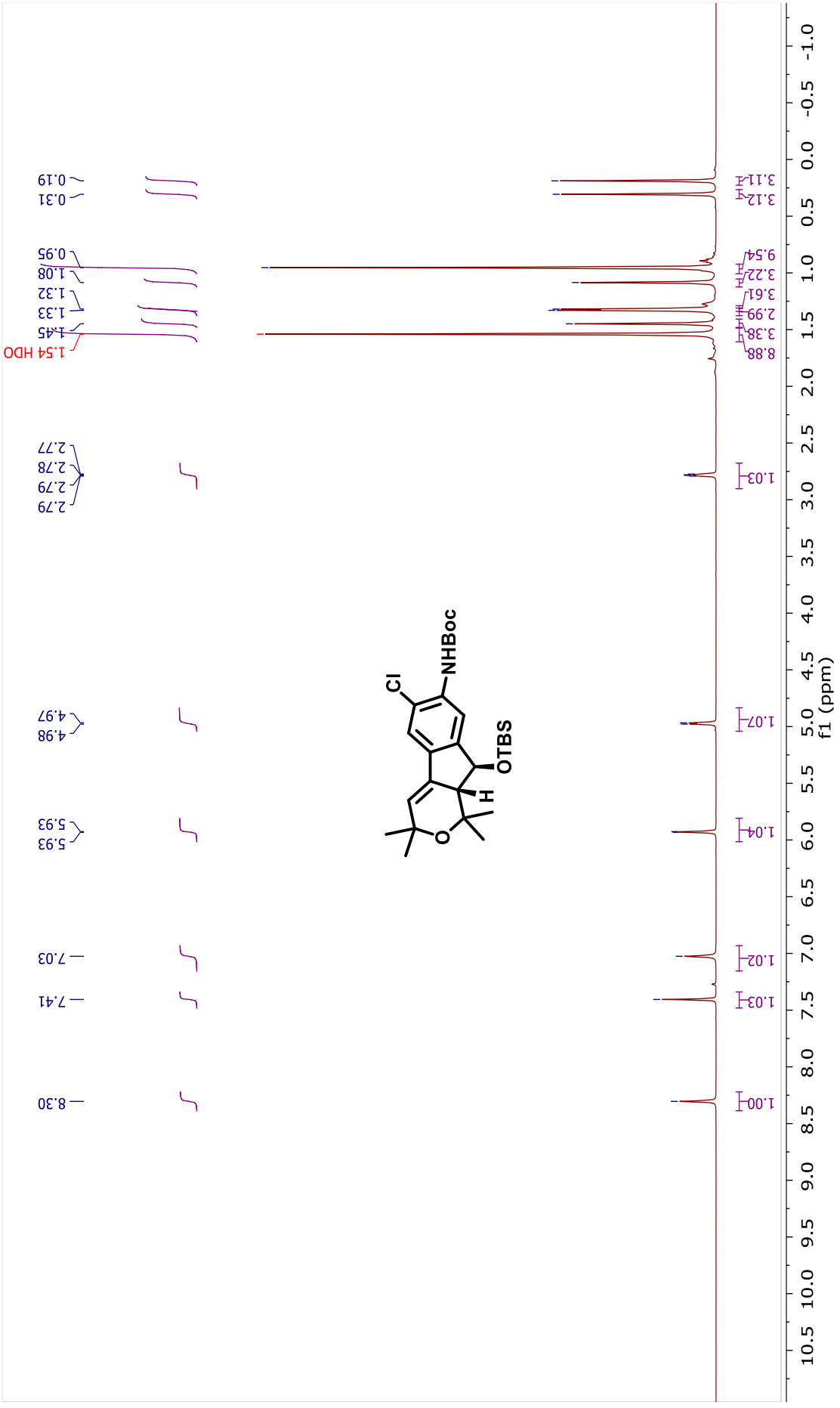
^{1}H NMR (500 MHz) Spectrum of Compound **(+)-57** in $CDCl_3$



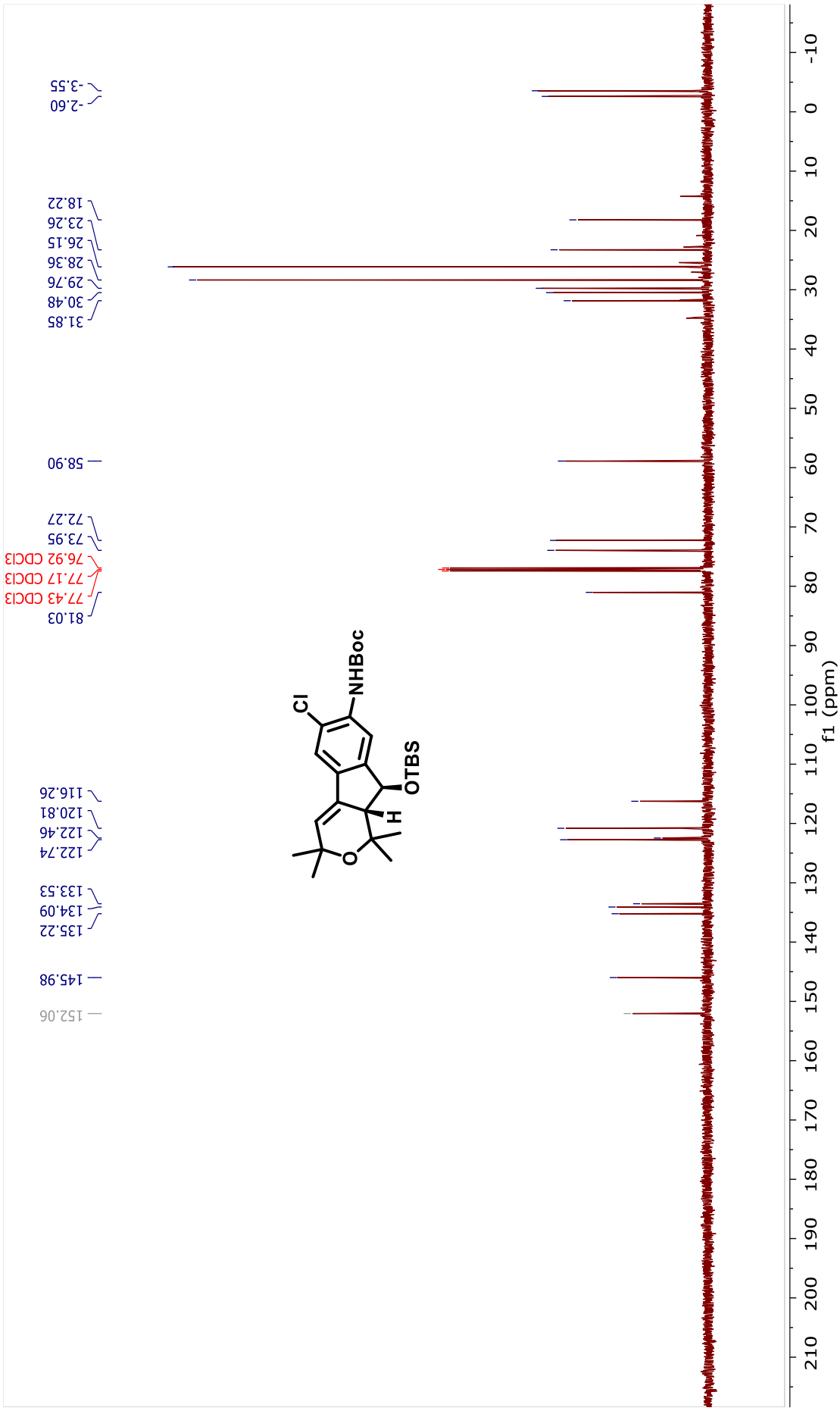
^{13}C NMR (126 MHz) Spectrum of Compound **(+)-57** in $CDCl_3$



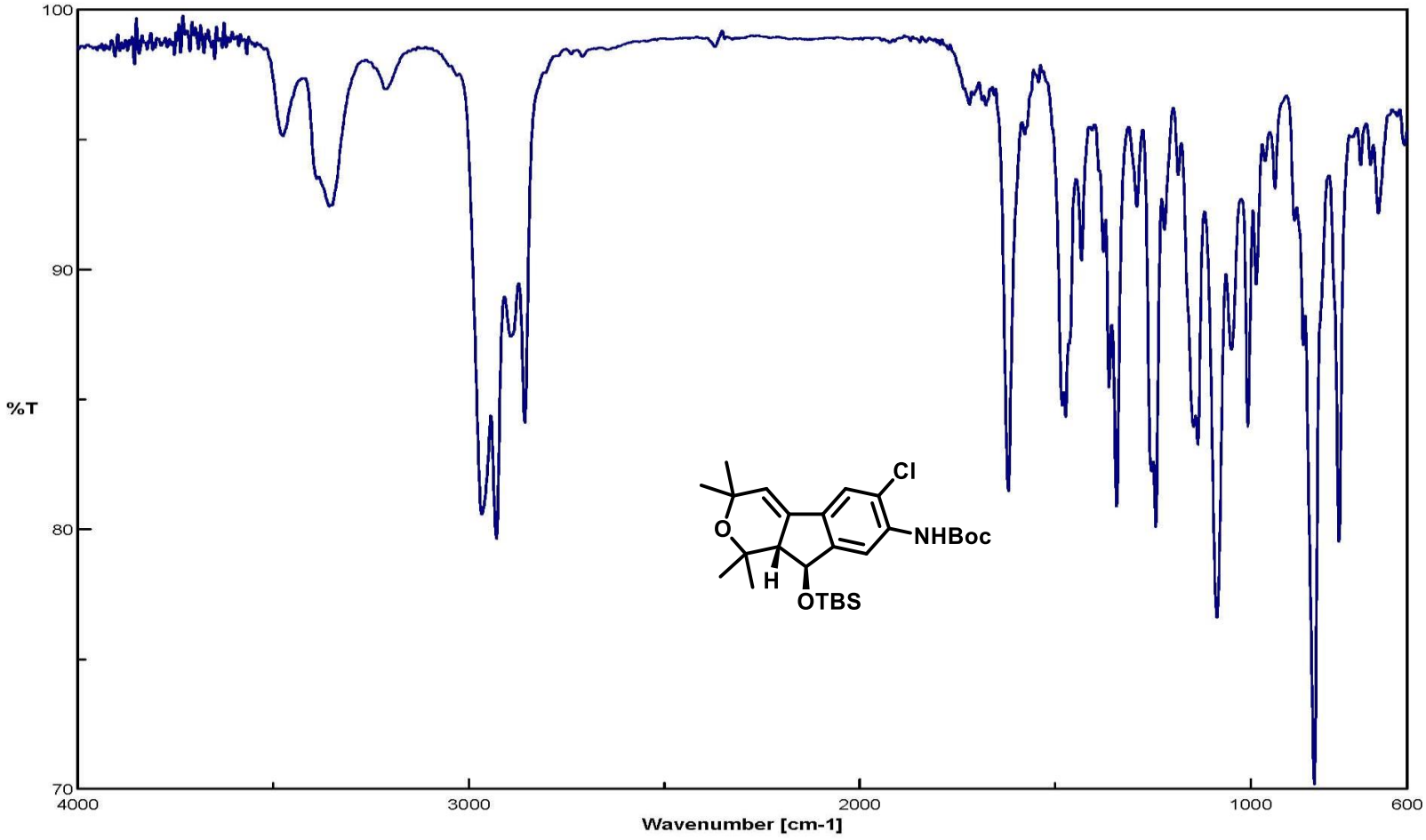
IR Spectrum of Compound **(+)-57**



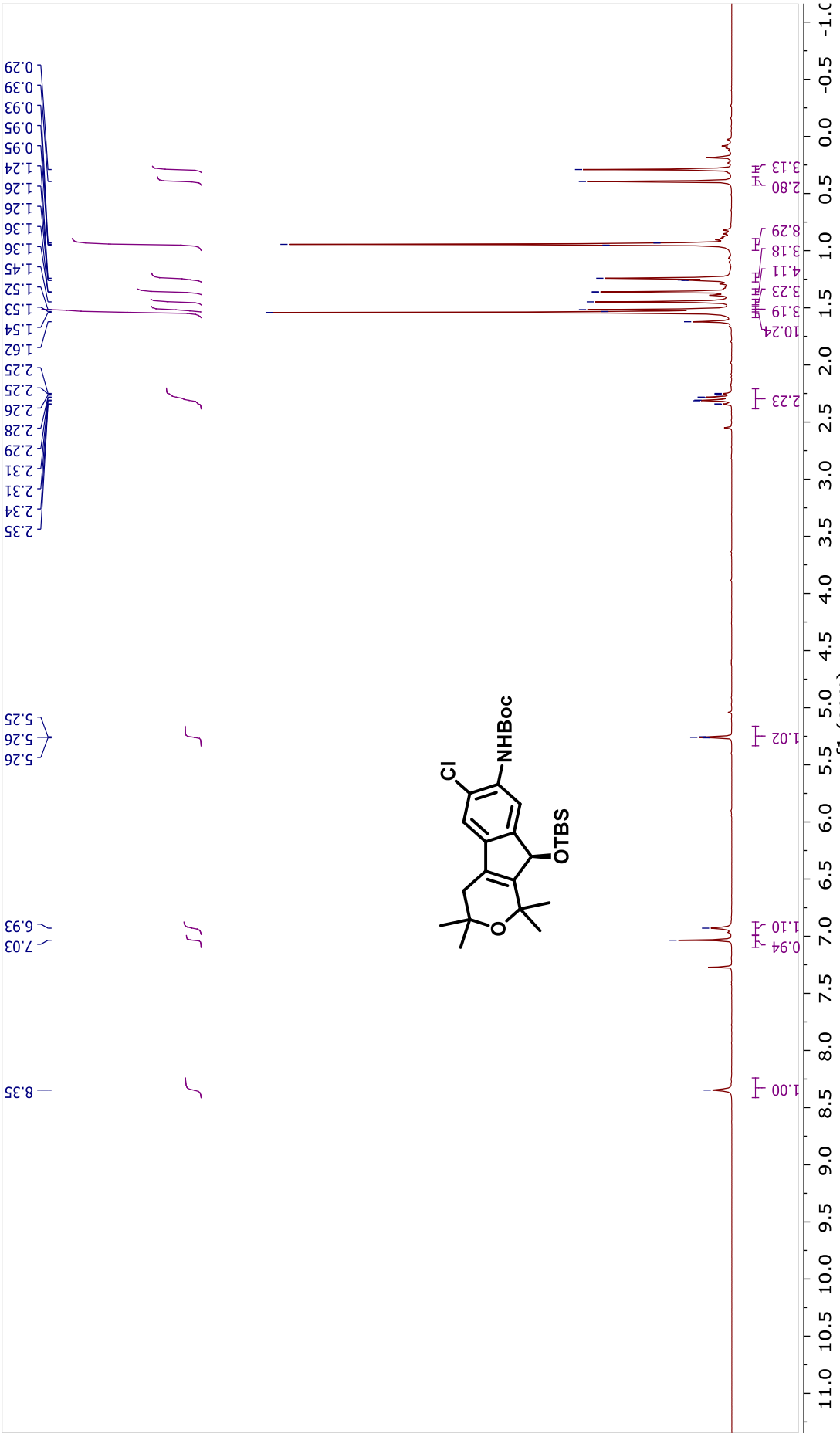
^{1}H NMR (500 MHz) Spectrum of Compound **(–)-58** in $CDCl_3$



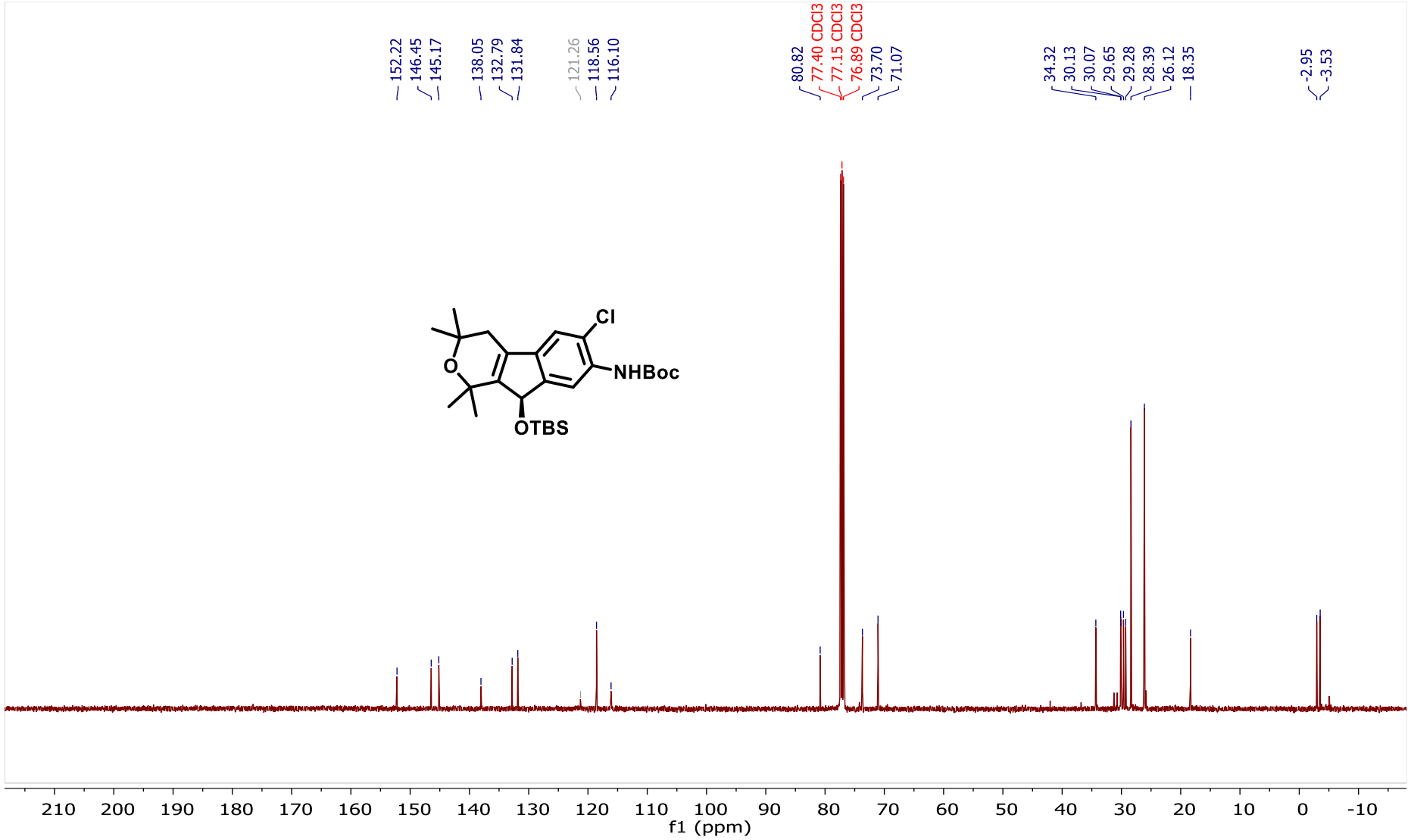
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-58** in $CDCl_3$



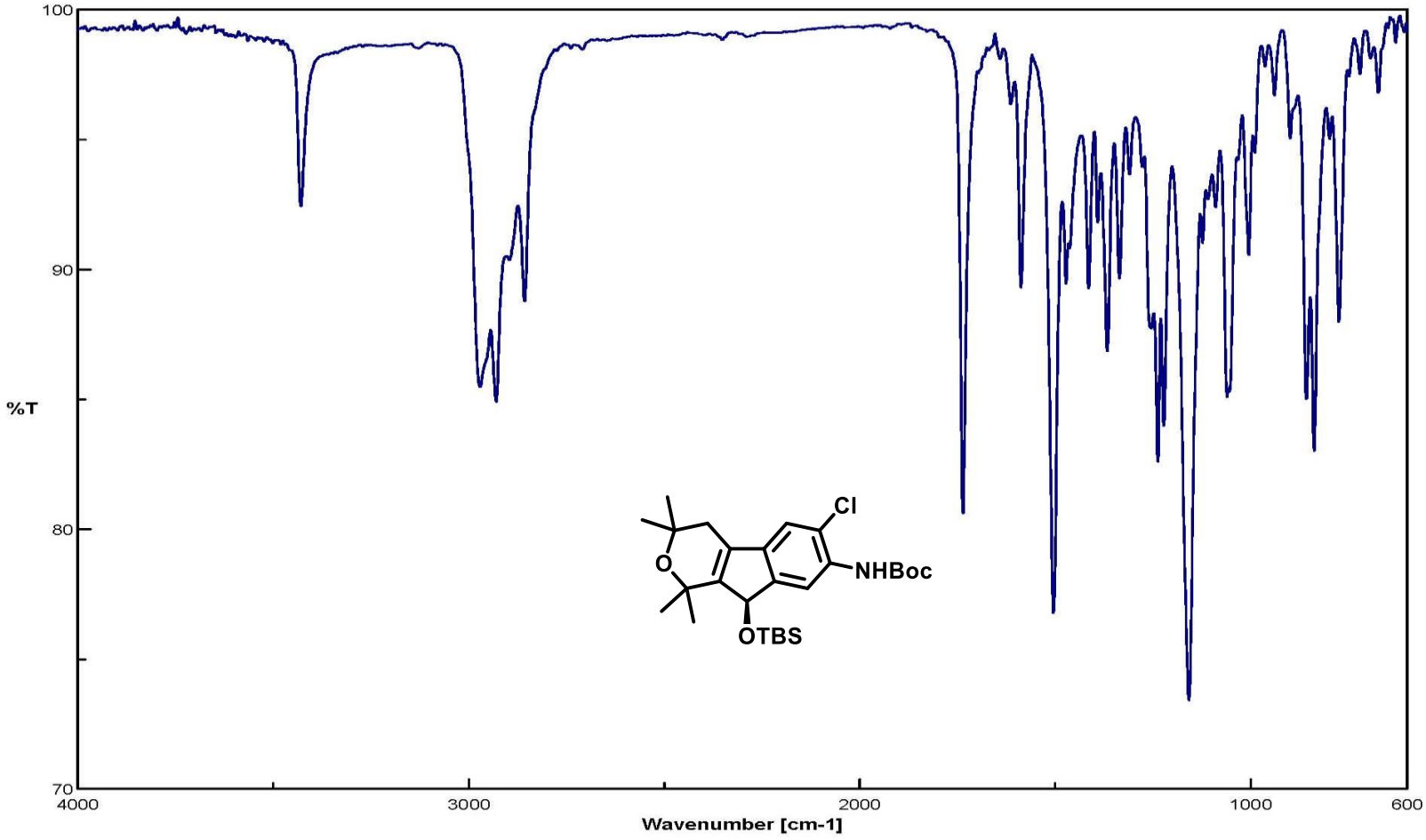
IR Spectrum of Compound (–)-**58**



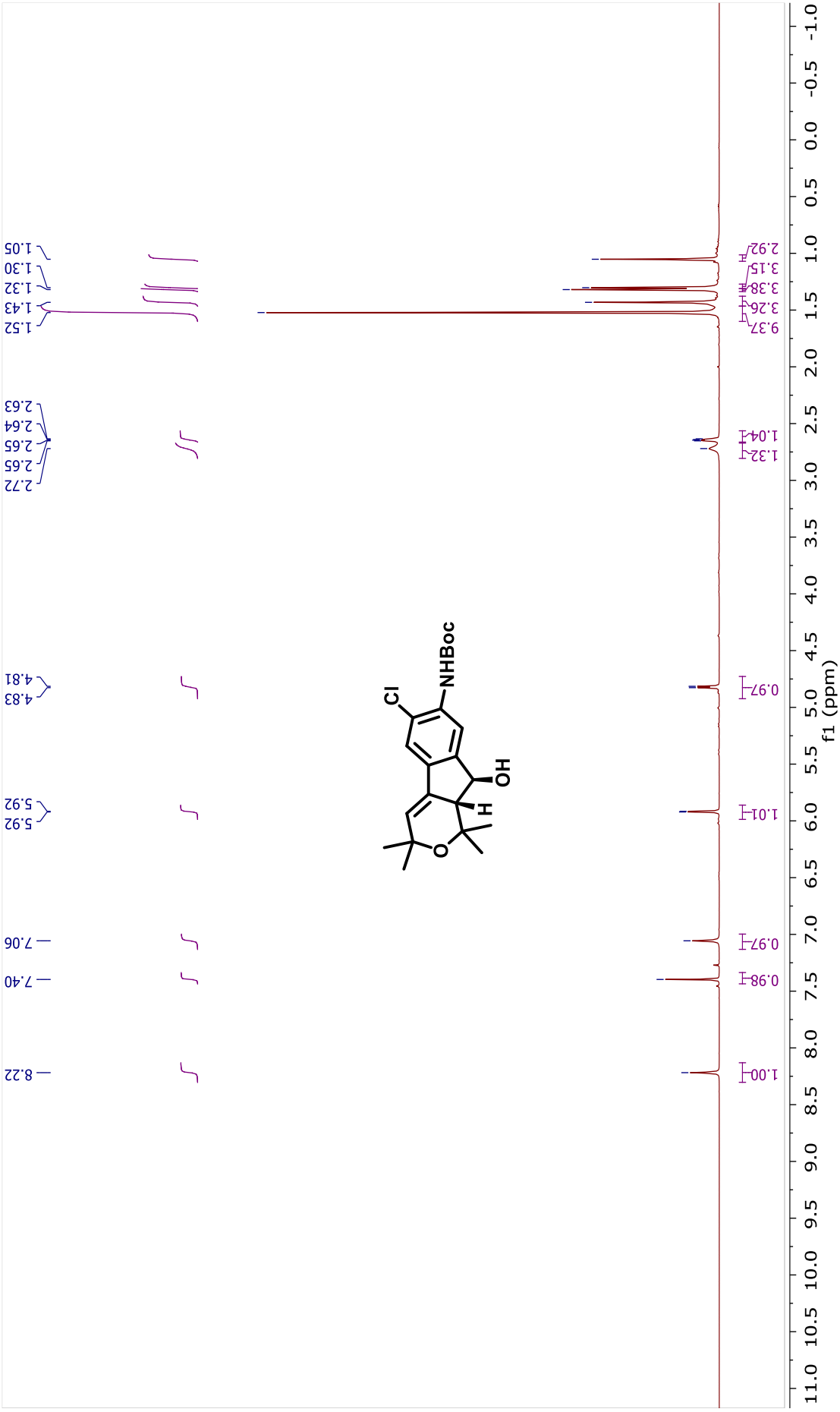
^{1}H NMR (500 MHz) Spectrum of Compound **(–)-59** in $CDCl_3$



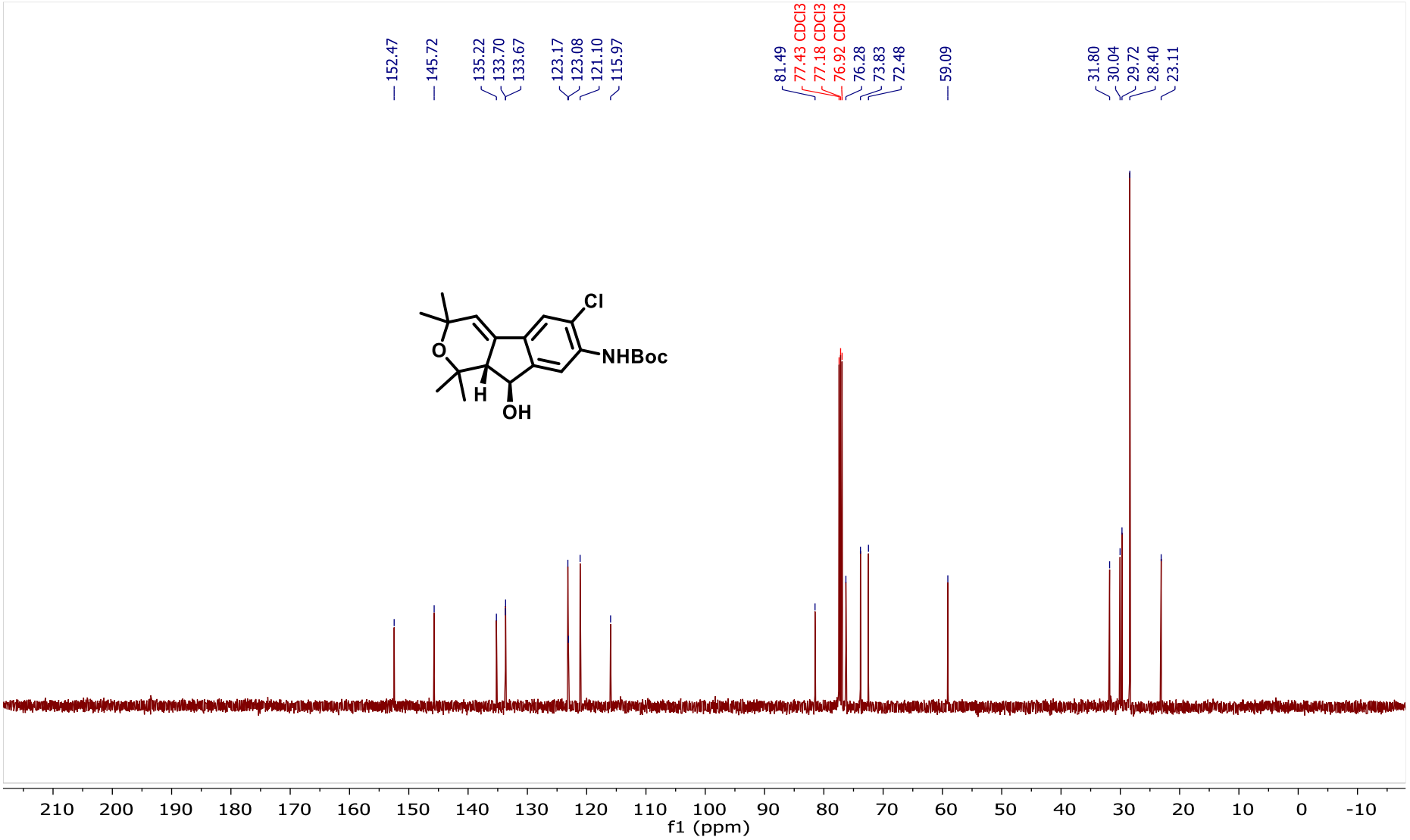
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-59** in $CDCl_3$



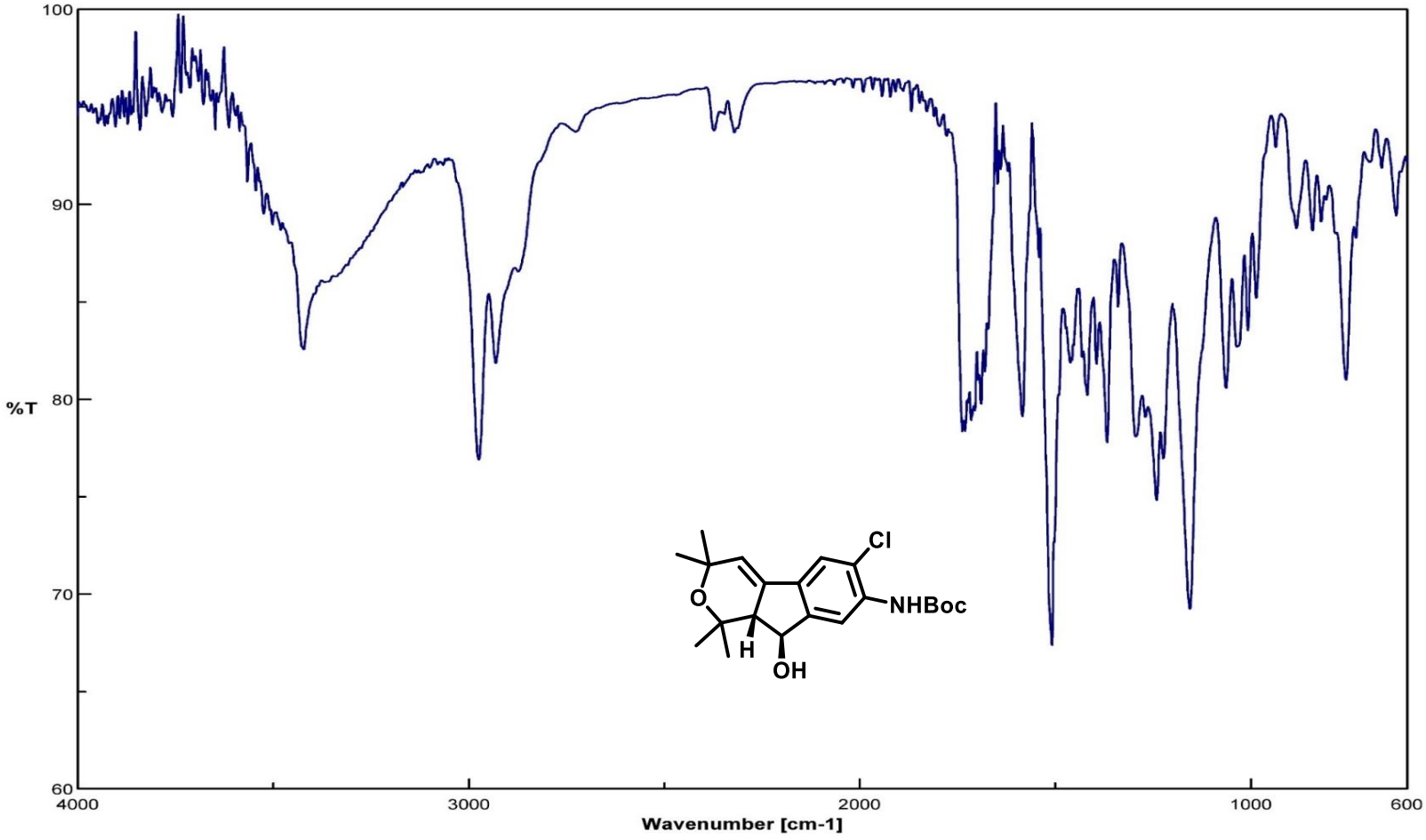
IR Spectrum of Compound (–)-59



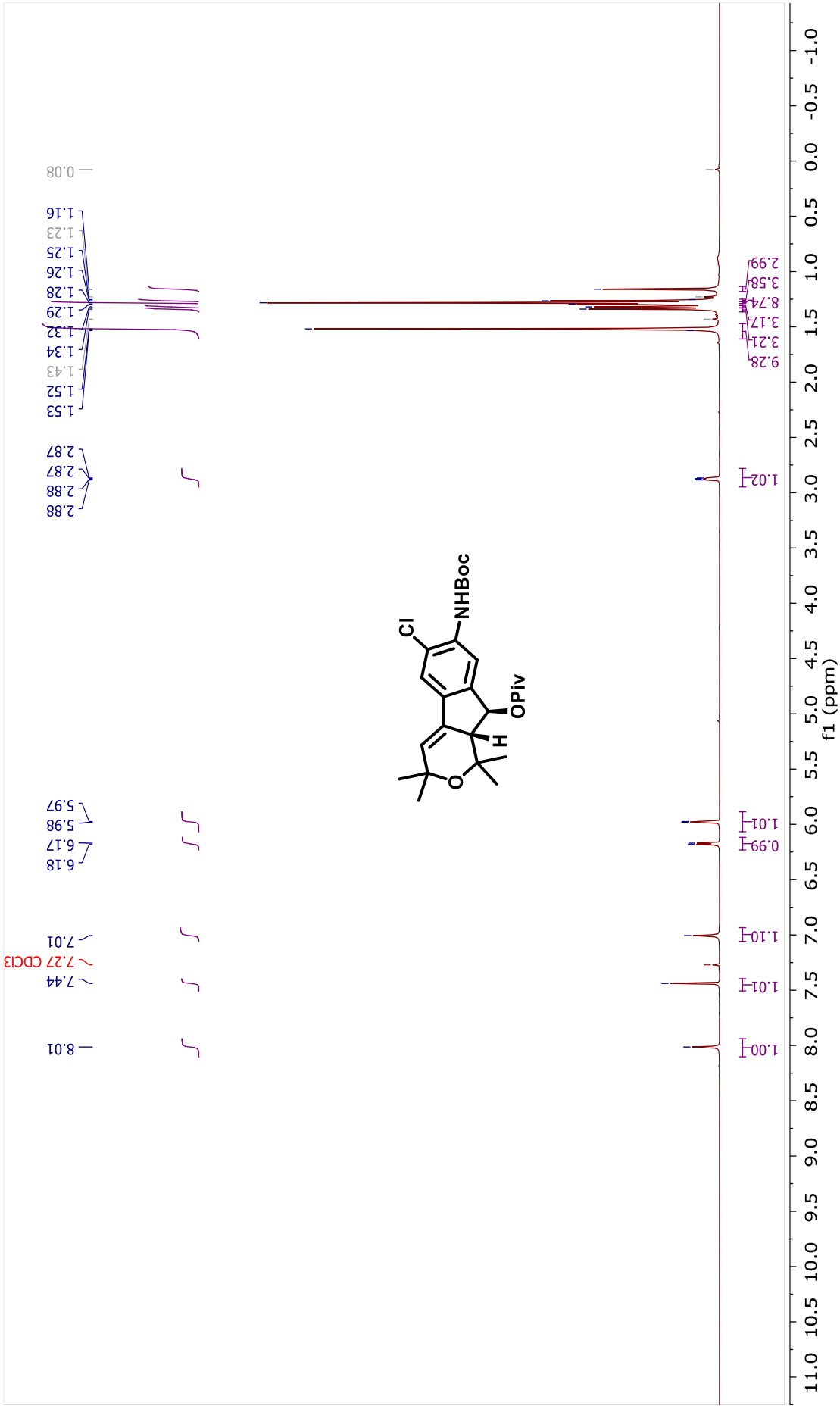
^{1}H NMR (500 MHz) Spectrum of Compound **(–)-48** in $CDCl_3$



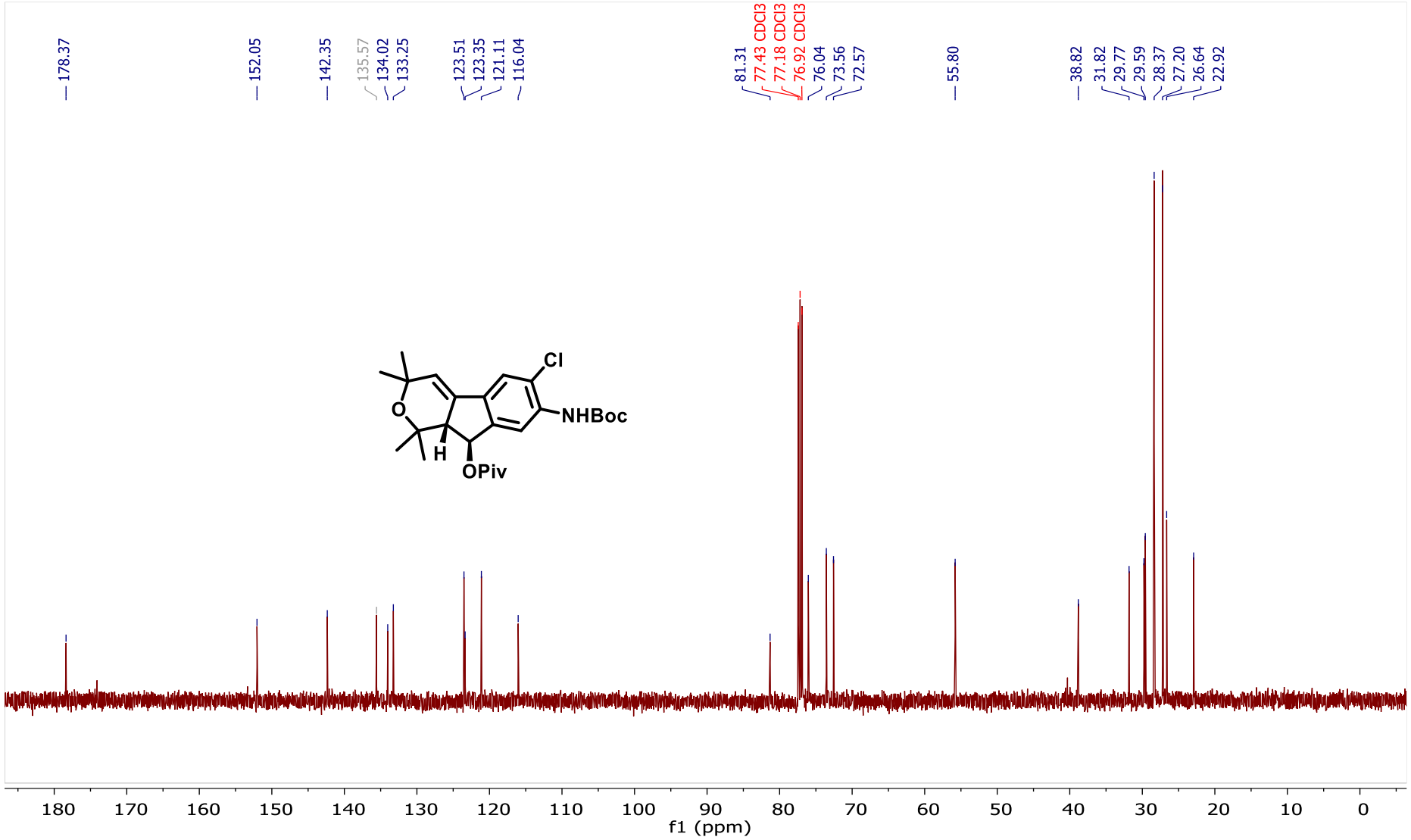
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-48** in $CDCl_3$



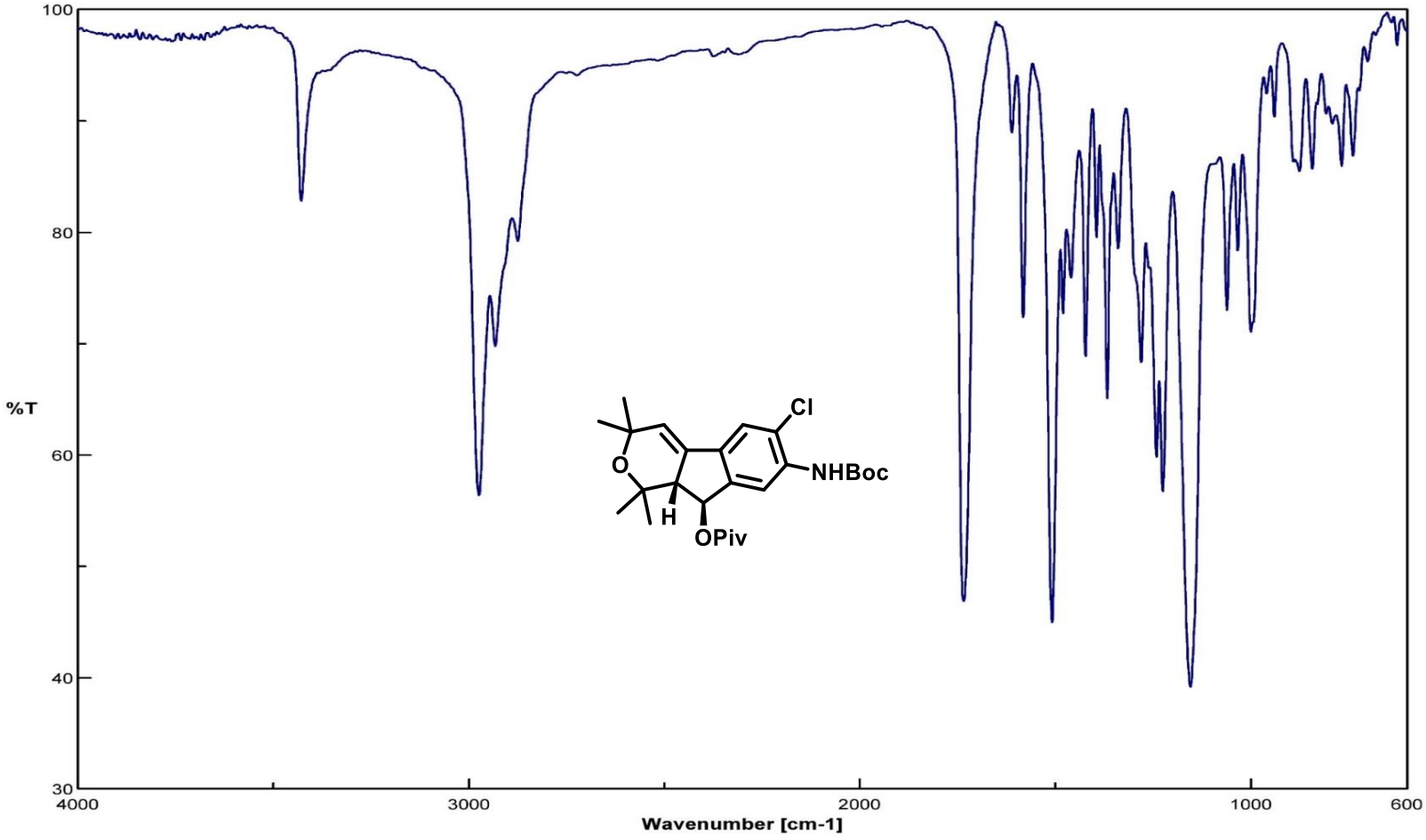
IR Spectrum of Compound **(–)-48**



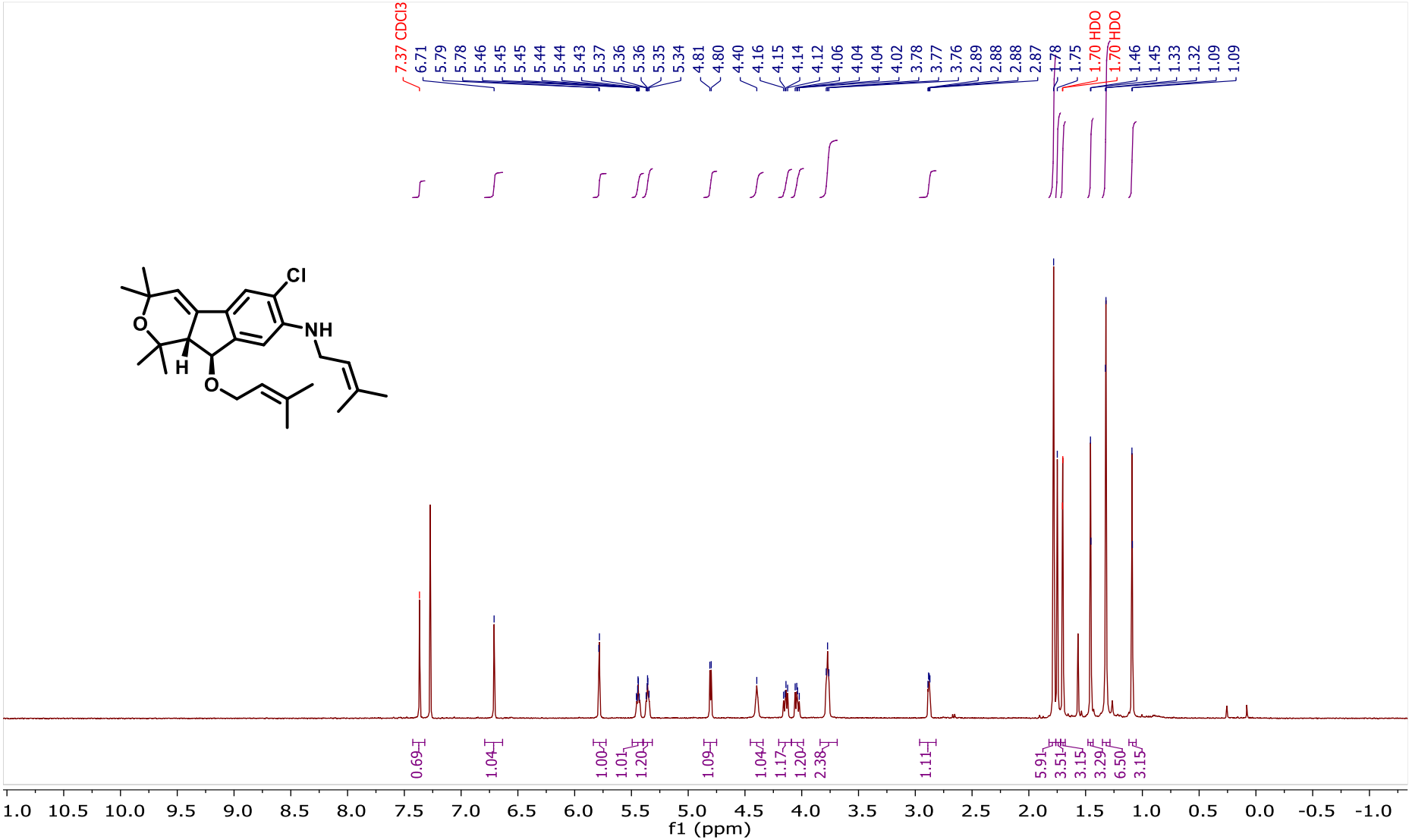
^{1}H NMR (500 MHz) Spectrum of Compound **(–)-60** in $CDCl_3$



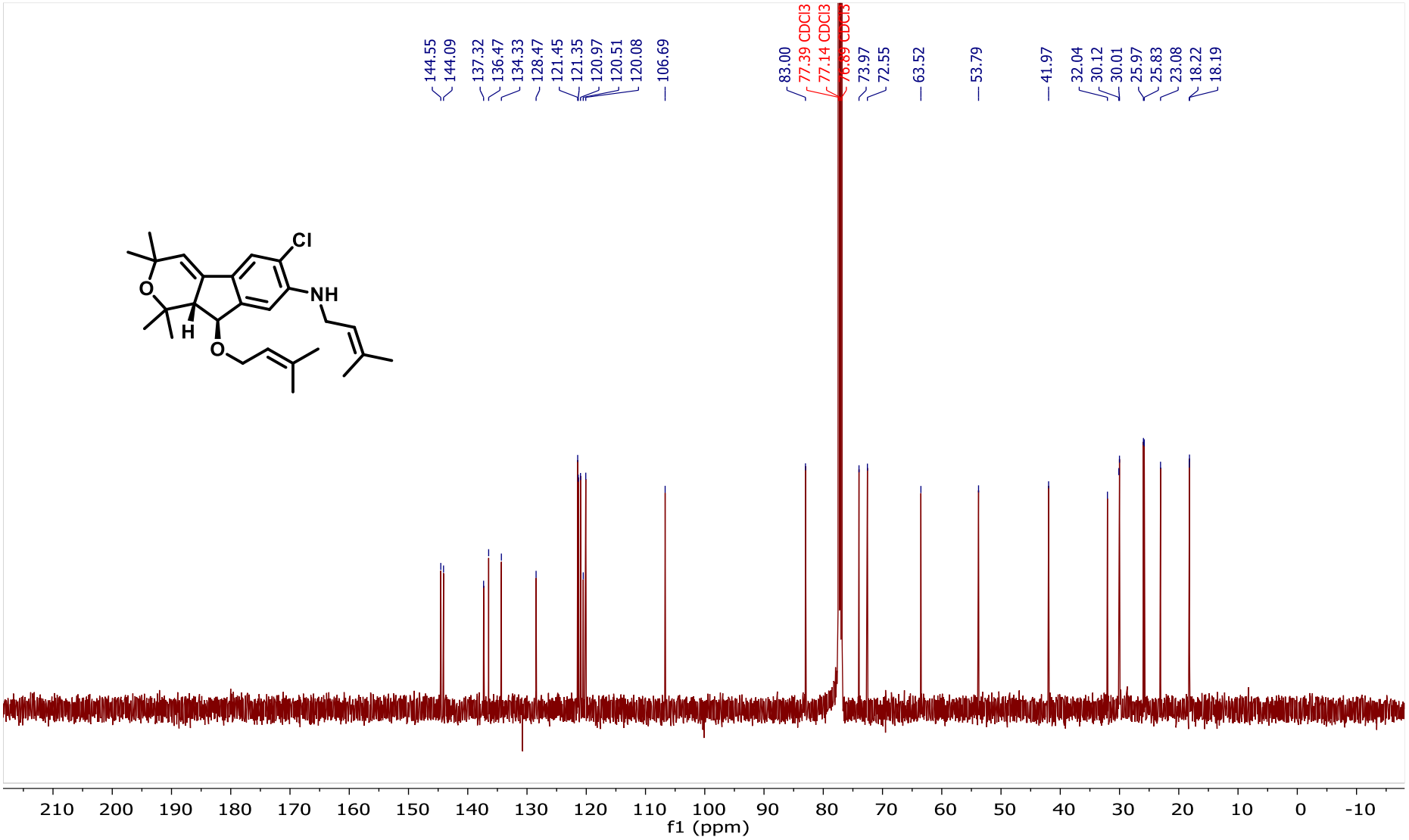
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-60** in $CDCl_3$



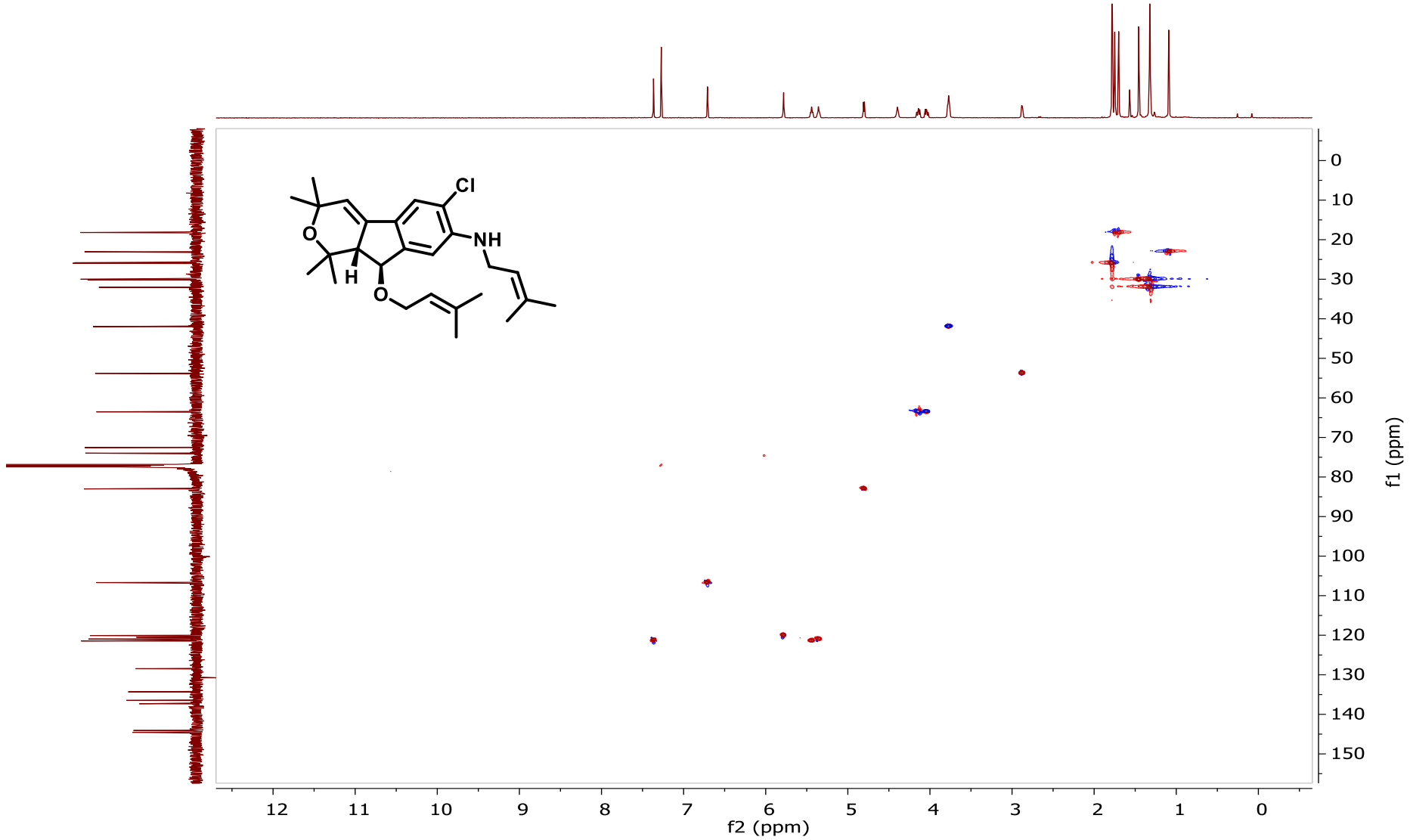
IR Spectrum of Compound **(–)-60**



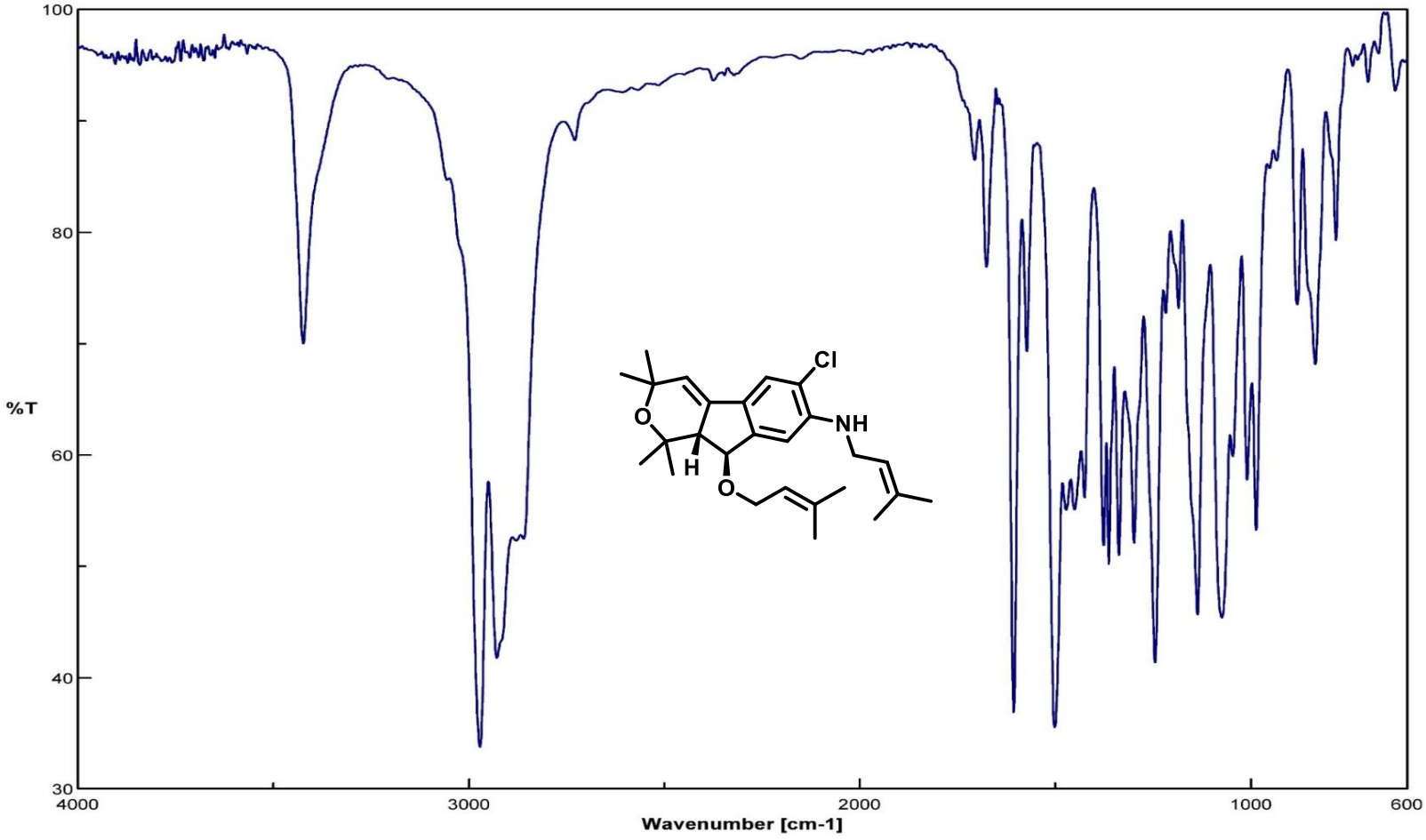
^{1}H NMR (500 MHz) Spectrum of Compound (−)-**63** in $CDCl_3$



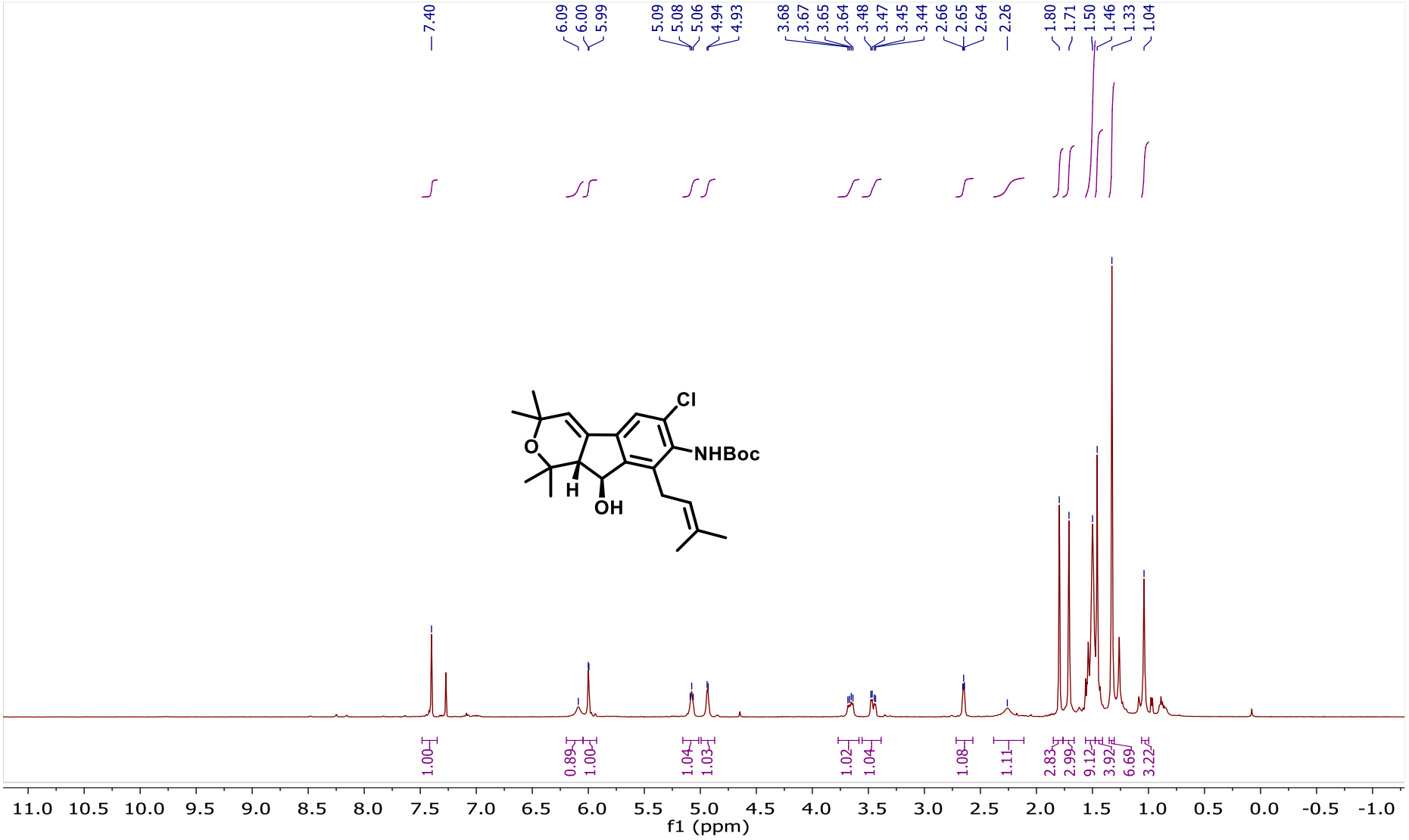
^{13}C NMR (126 MHz) Spectrum of Compound (−)-**63** in $CDCl_3$



HSQC Spectrum of Compound (−)-**63** in $CDCl_3$

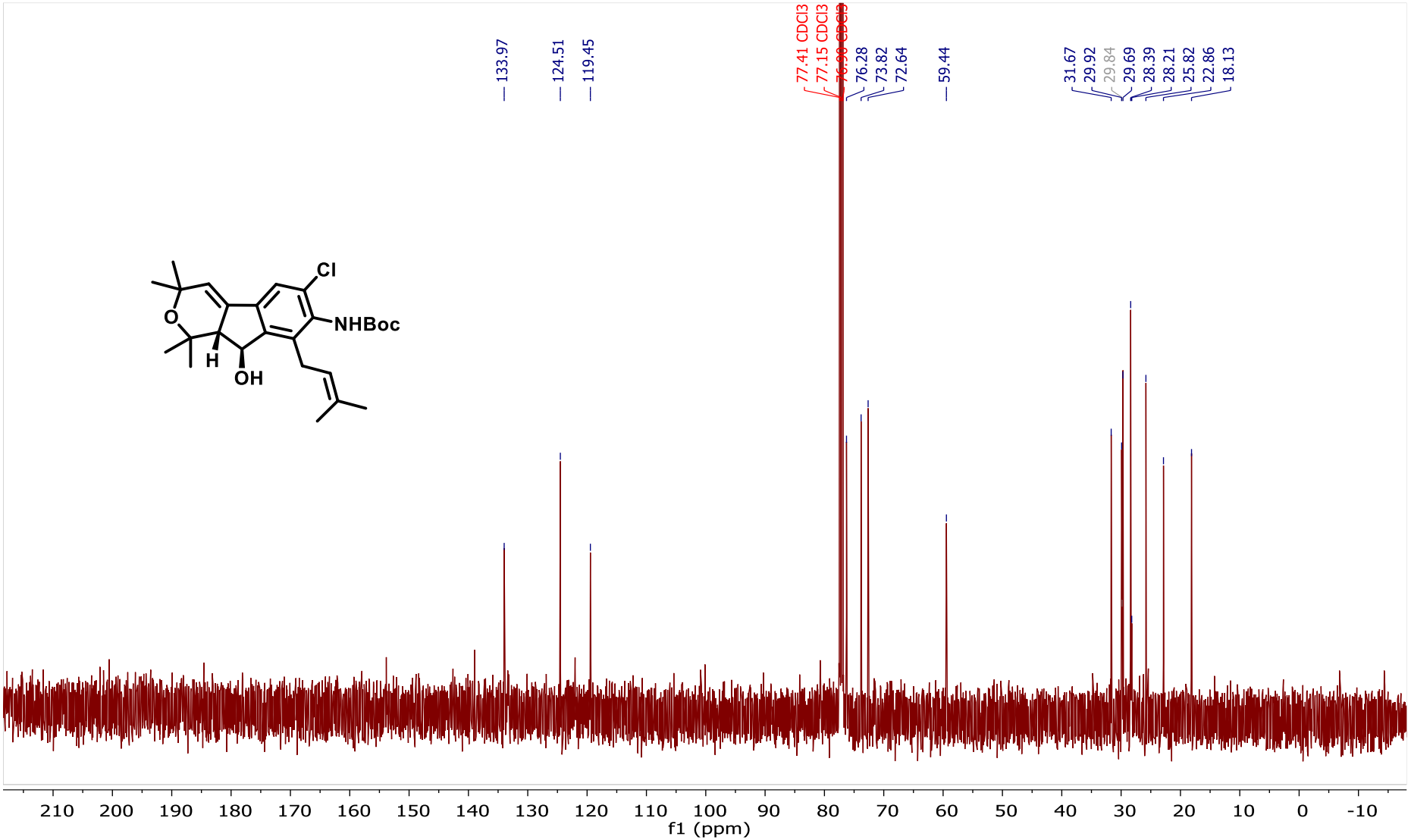


IR Spectrum of Compound (–)-**63**



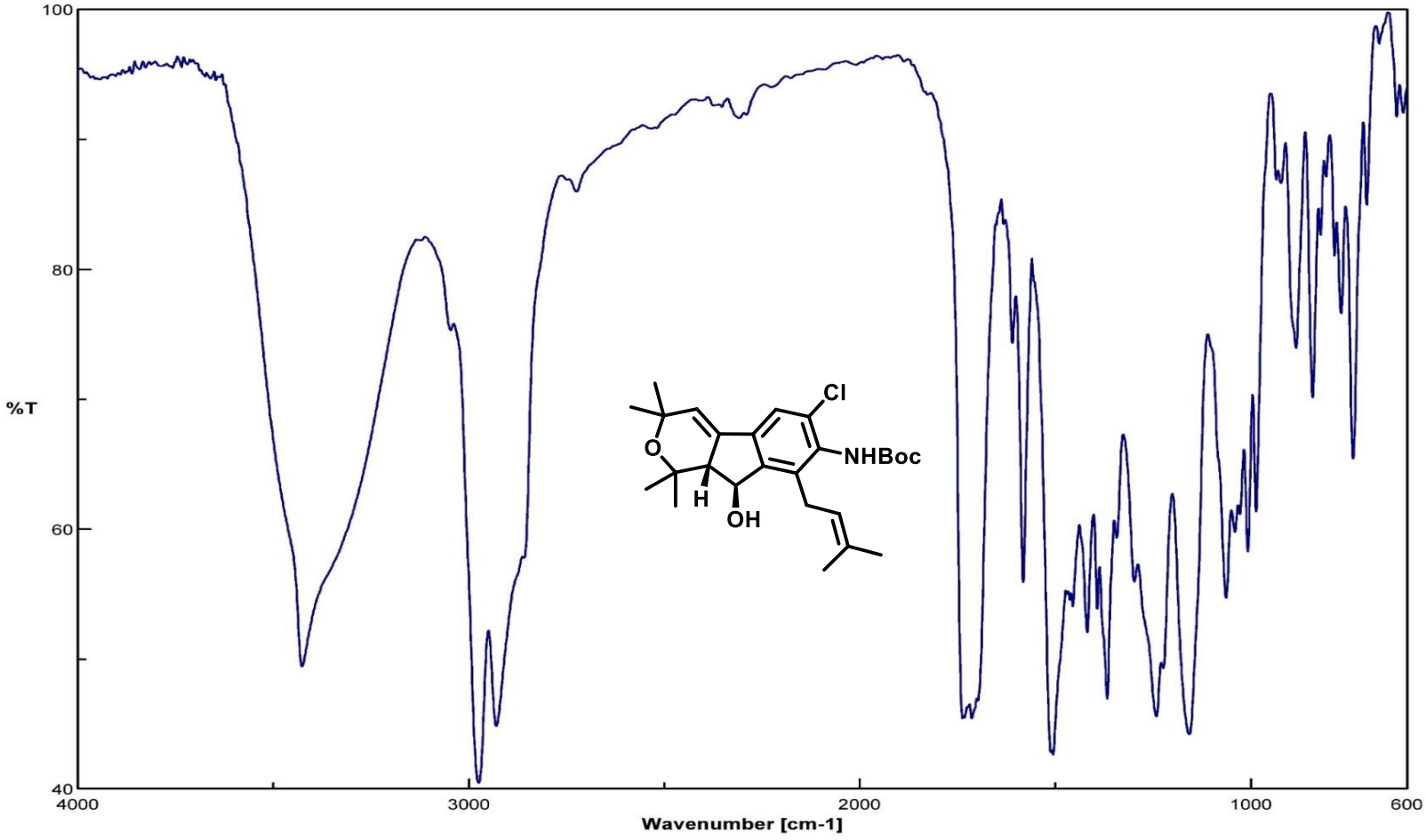
^{1}H NMR (500 MHz) Spectrum of Compound **(–)-64** in $CDCl_3$

(containing rotamers)



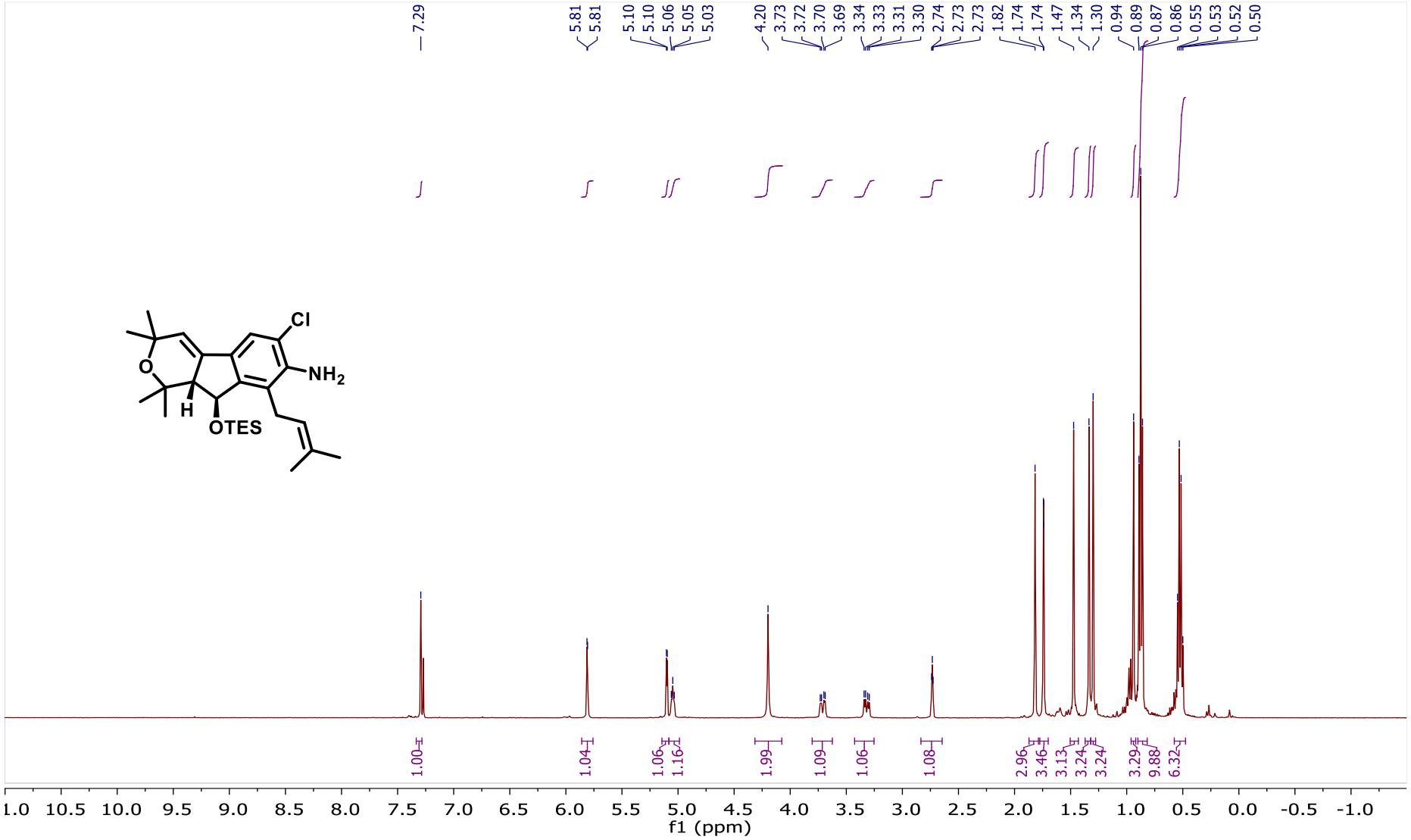
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-64** in $CDCl_3$

(containing rotamers)

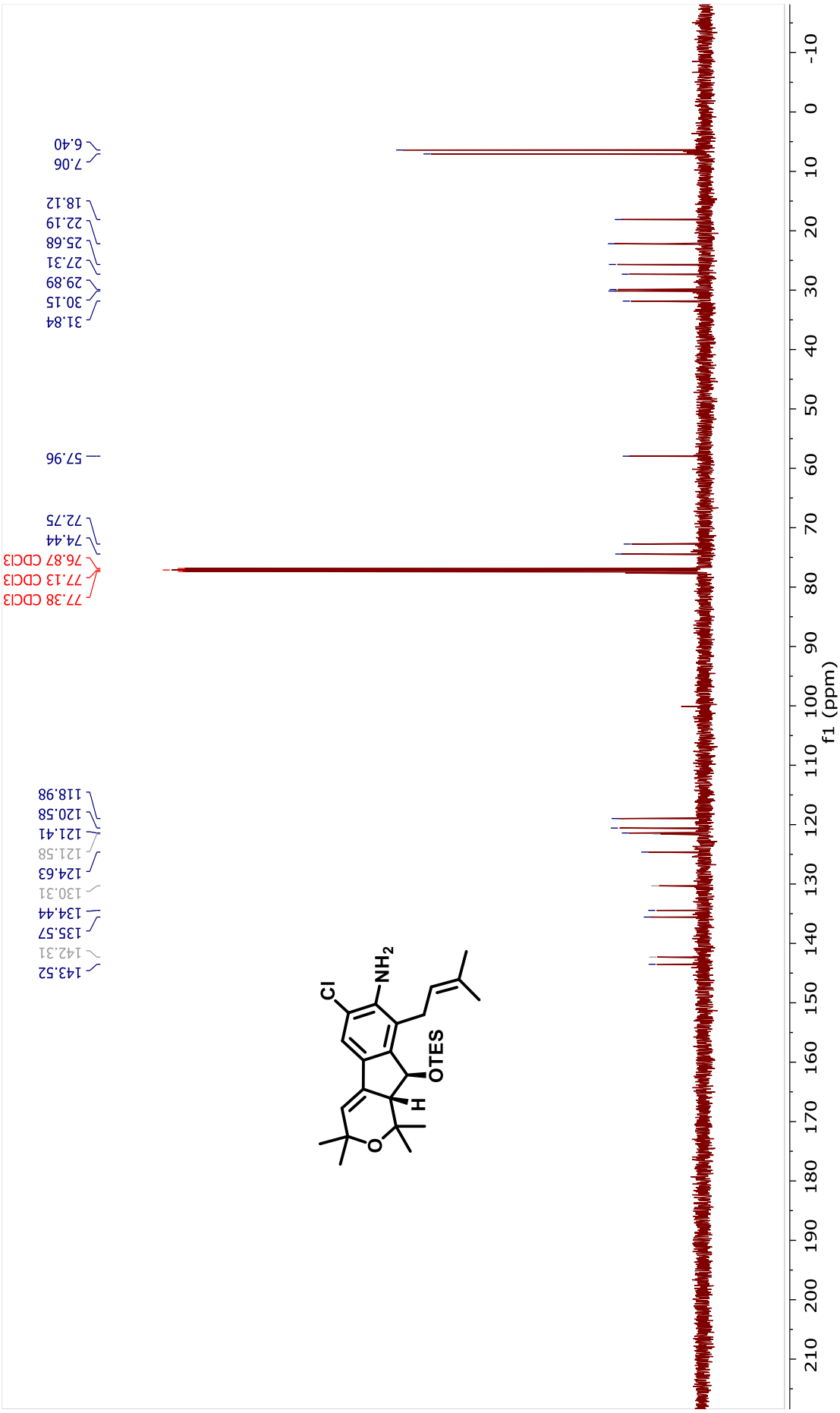


IR Spectrum of Compound **(–)-64**

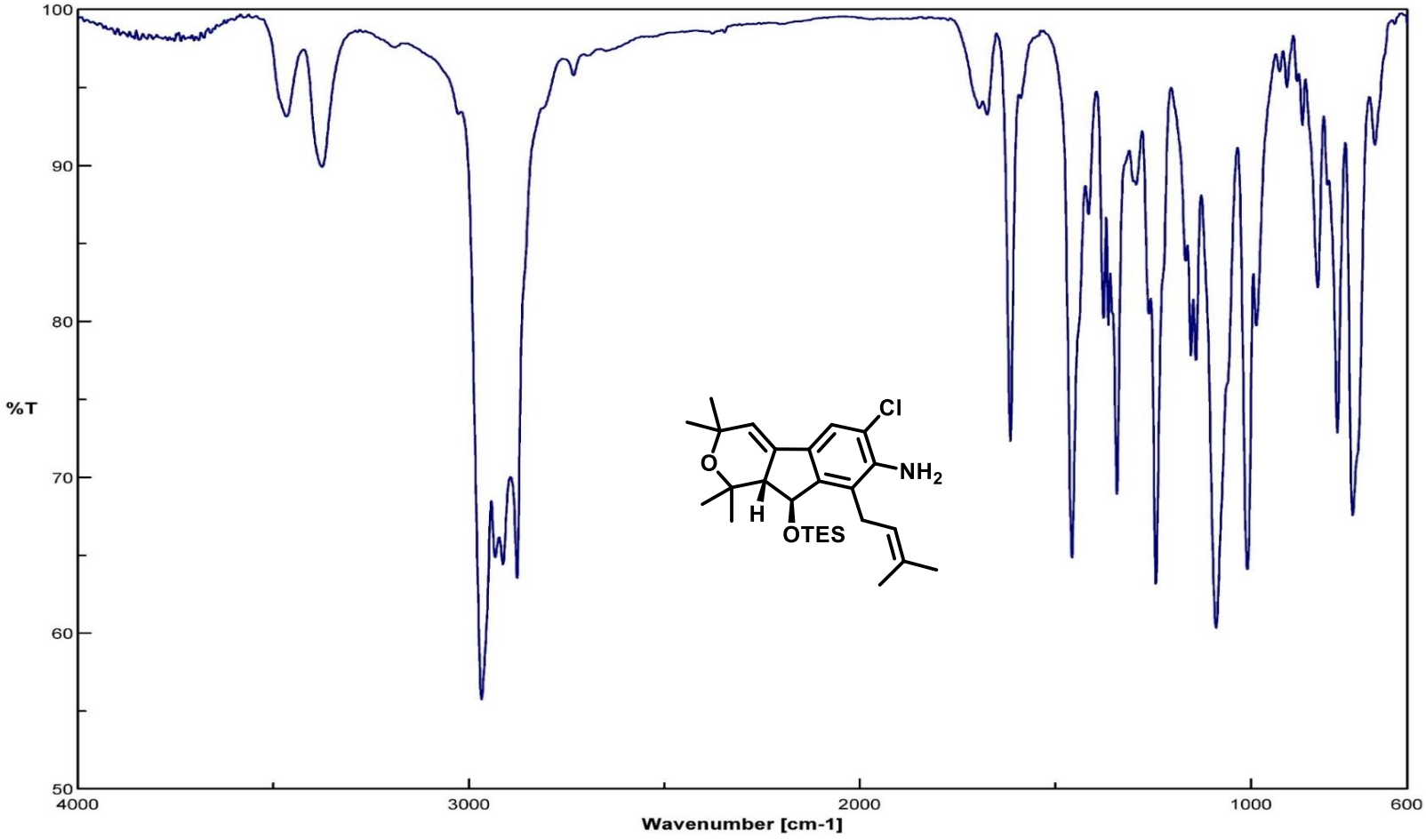
(containing rotamers)



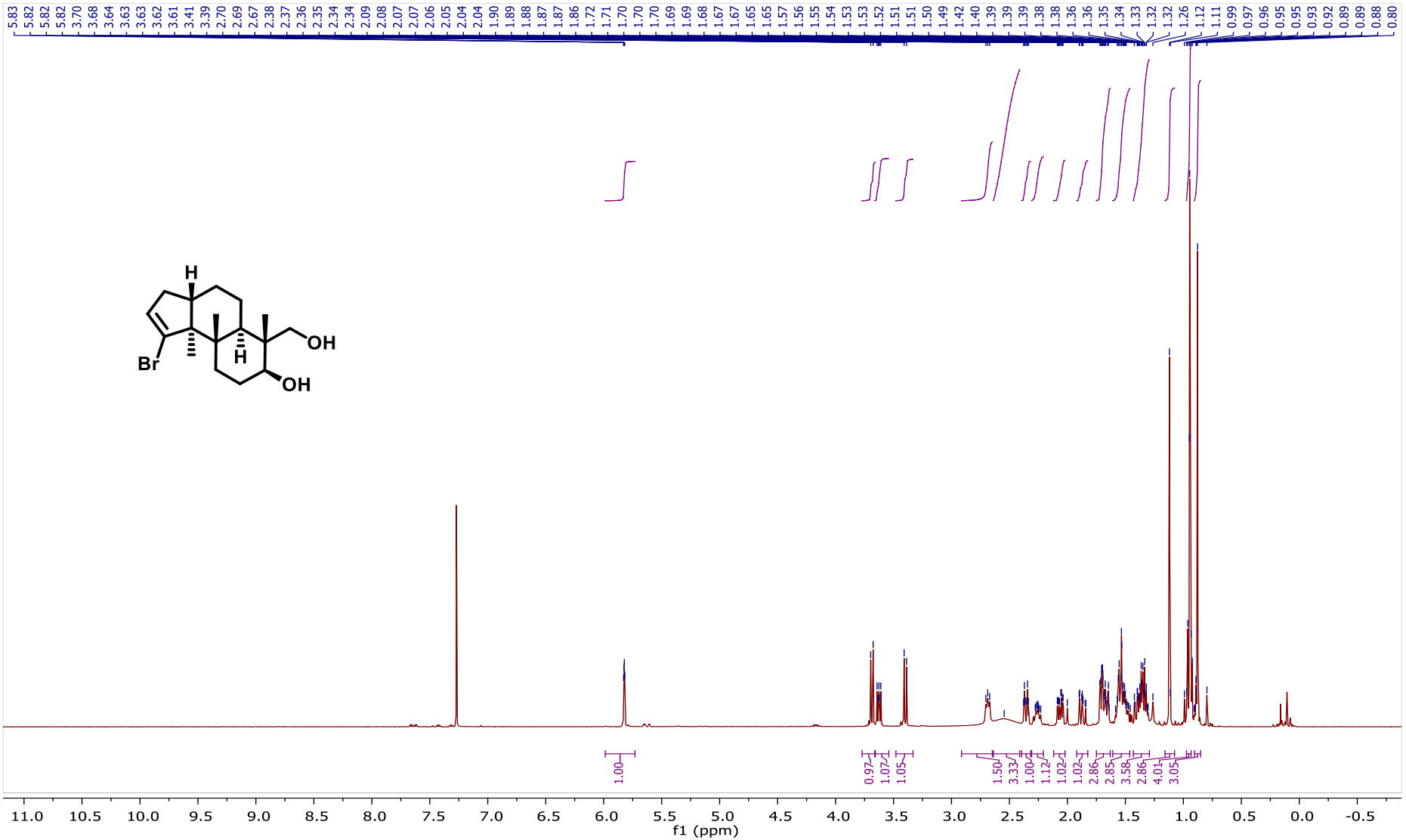
^{1}H NMR (500 MHz) Spectrum of Compound **(–)-46** in $CDCl_3$



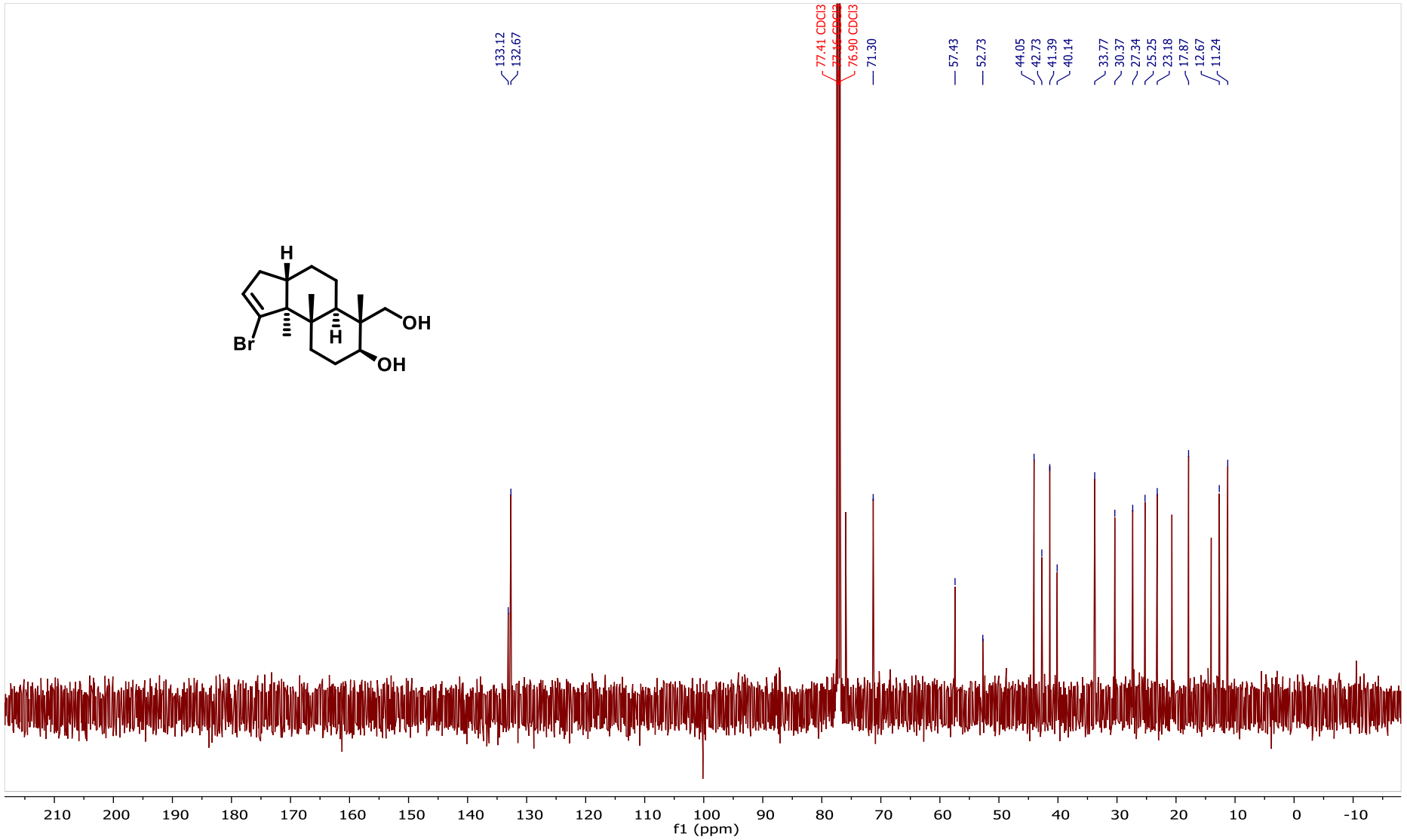
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-46** in $CDCl_3$



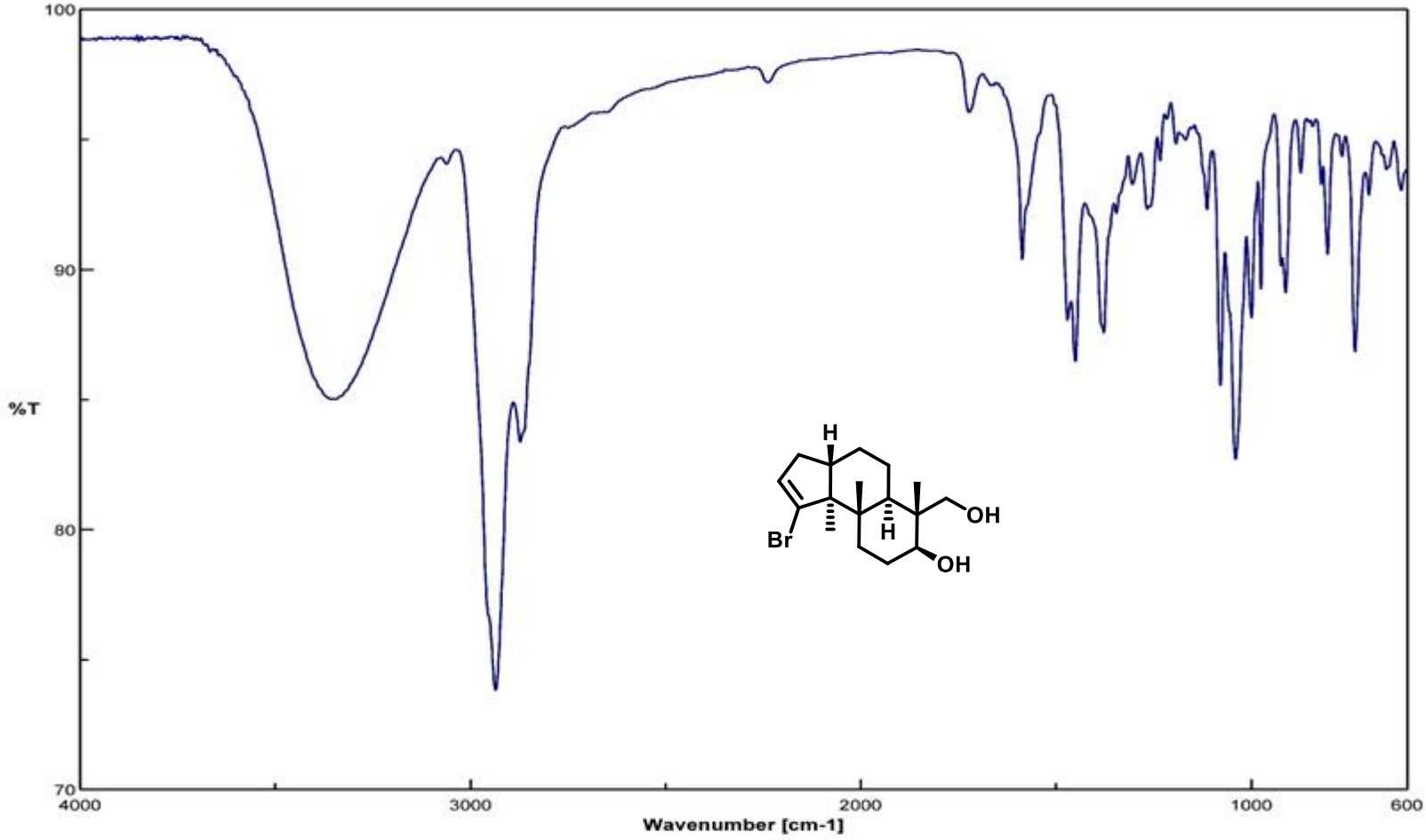
IR Spectrum of Compound **(–)-46**



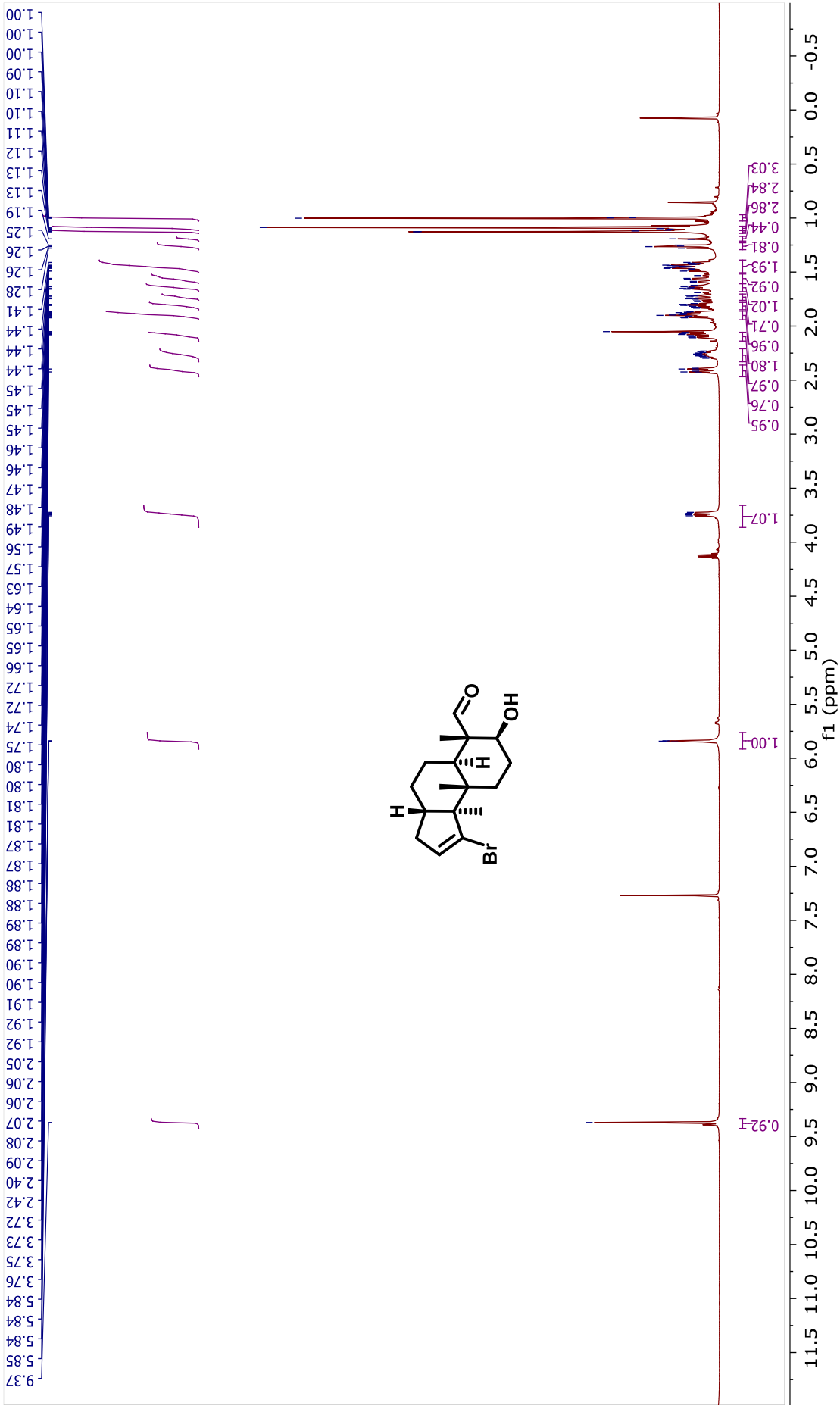
^{1}H NMR (500 MHz) Spectrum of Compound (−)-**S8** in $CDCl_3$



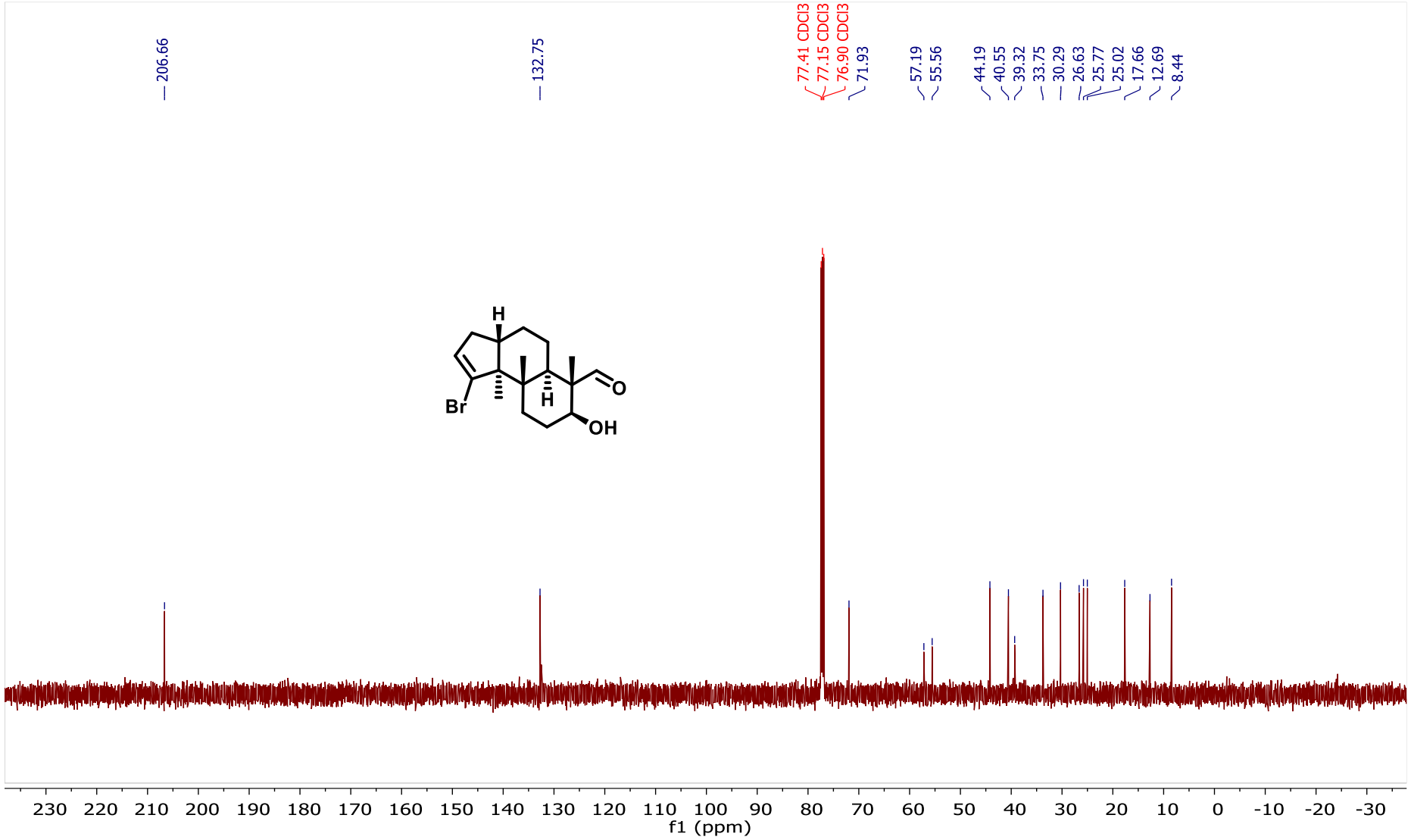
^{13}C NMR (126 MHz) Spectrum of Compound (−)-**S8** in $CDCl_3$



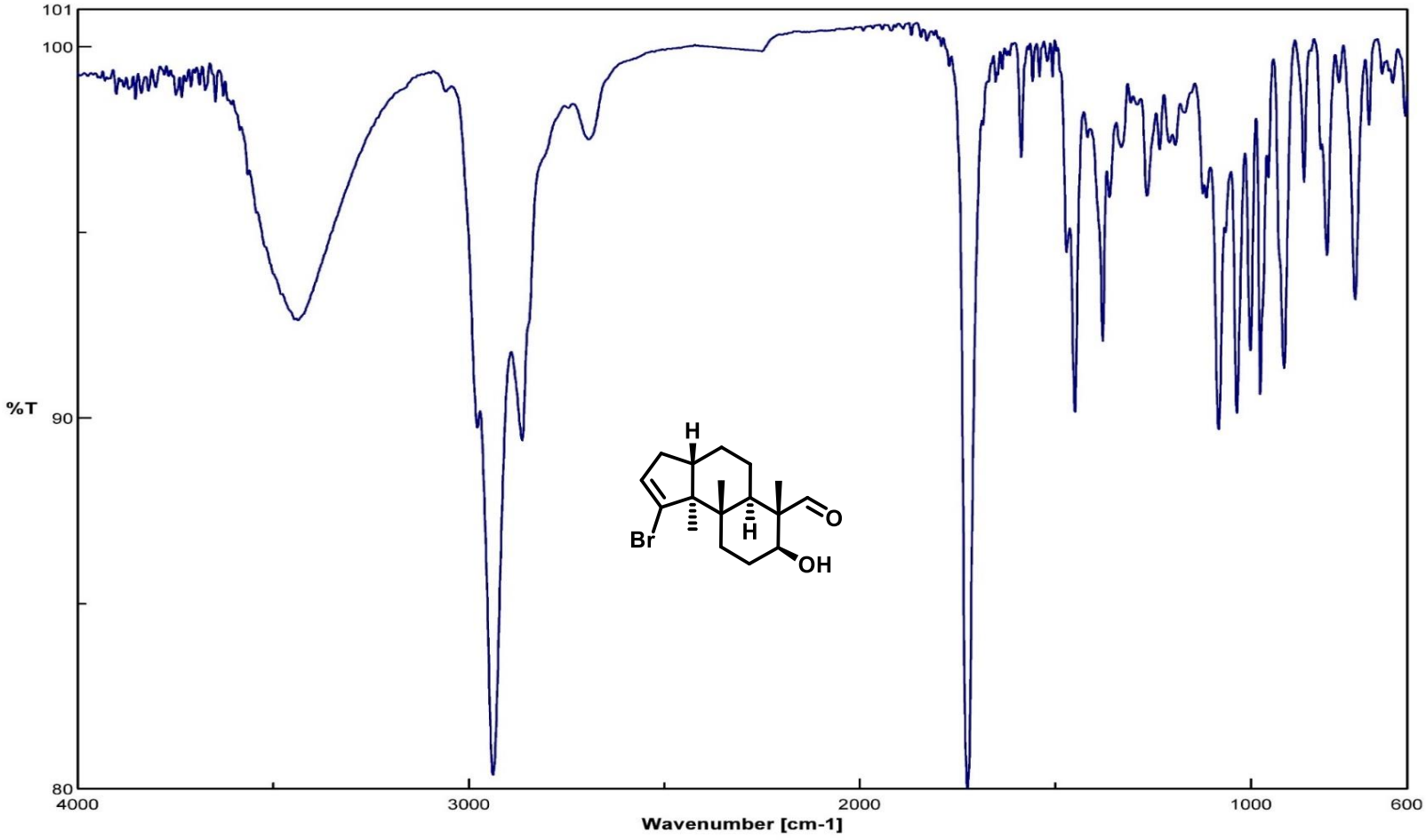
IR Spectrum of Compound (−)-**S8**



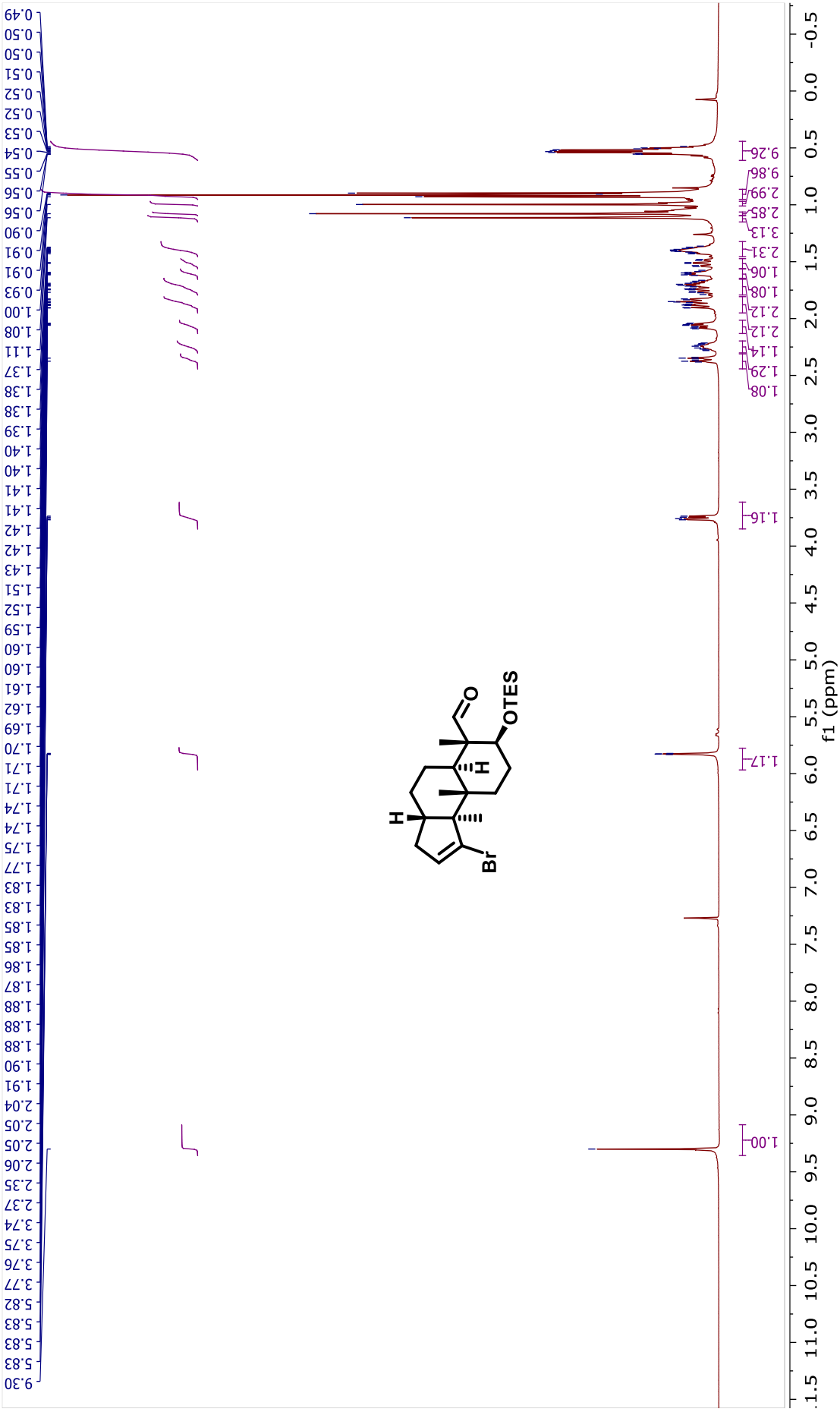
^{1}H NMR (500 MHz) Spectrum of Compound **(–)-65** in $CDCl_3$



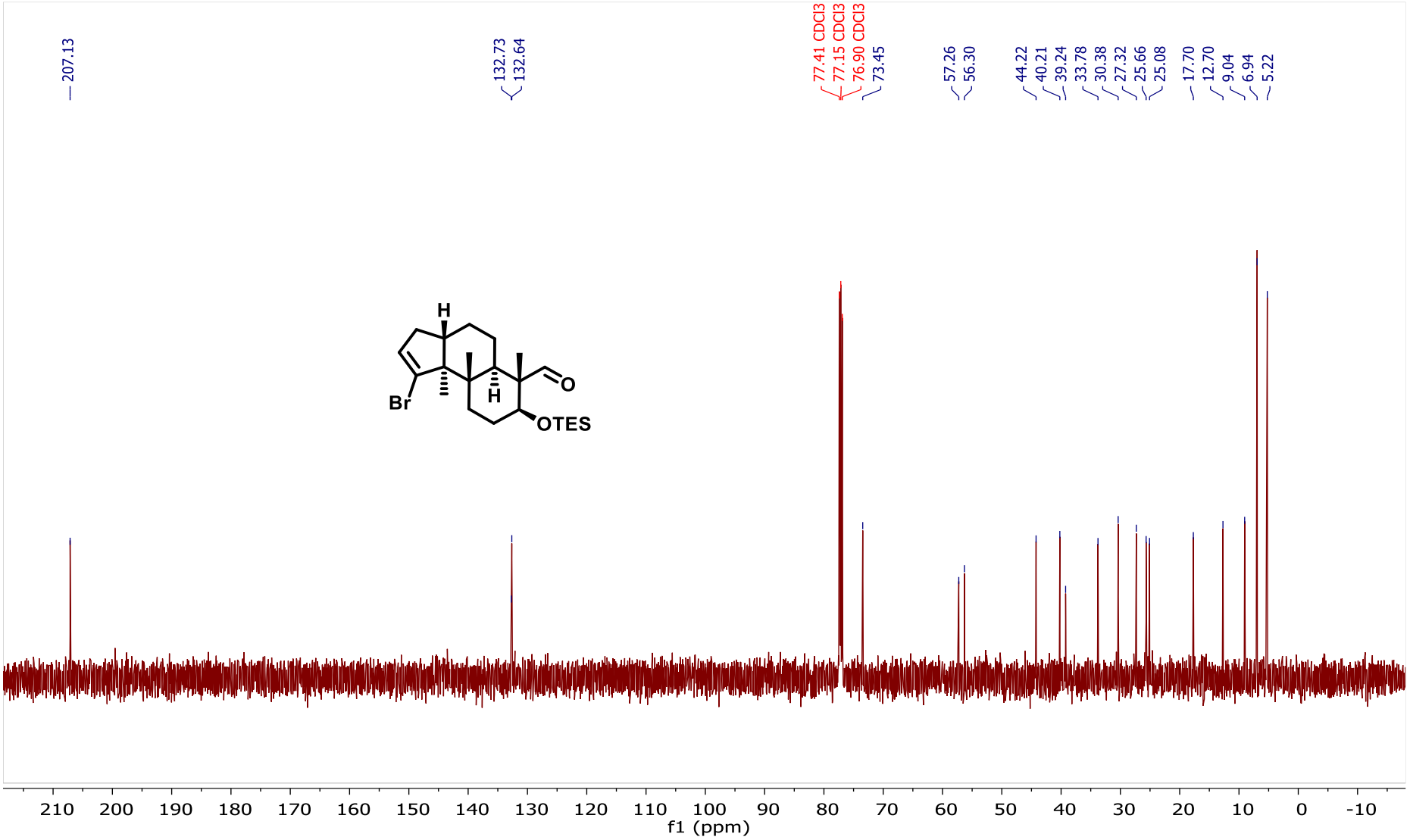
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-65** in $CDCl_3$



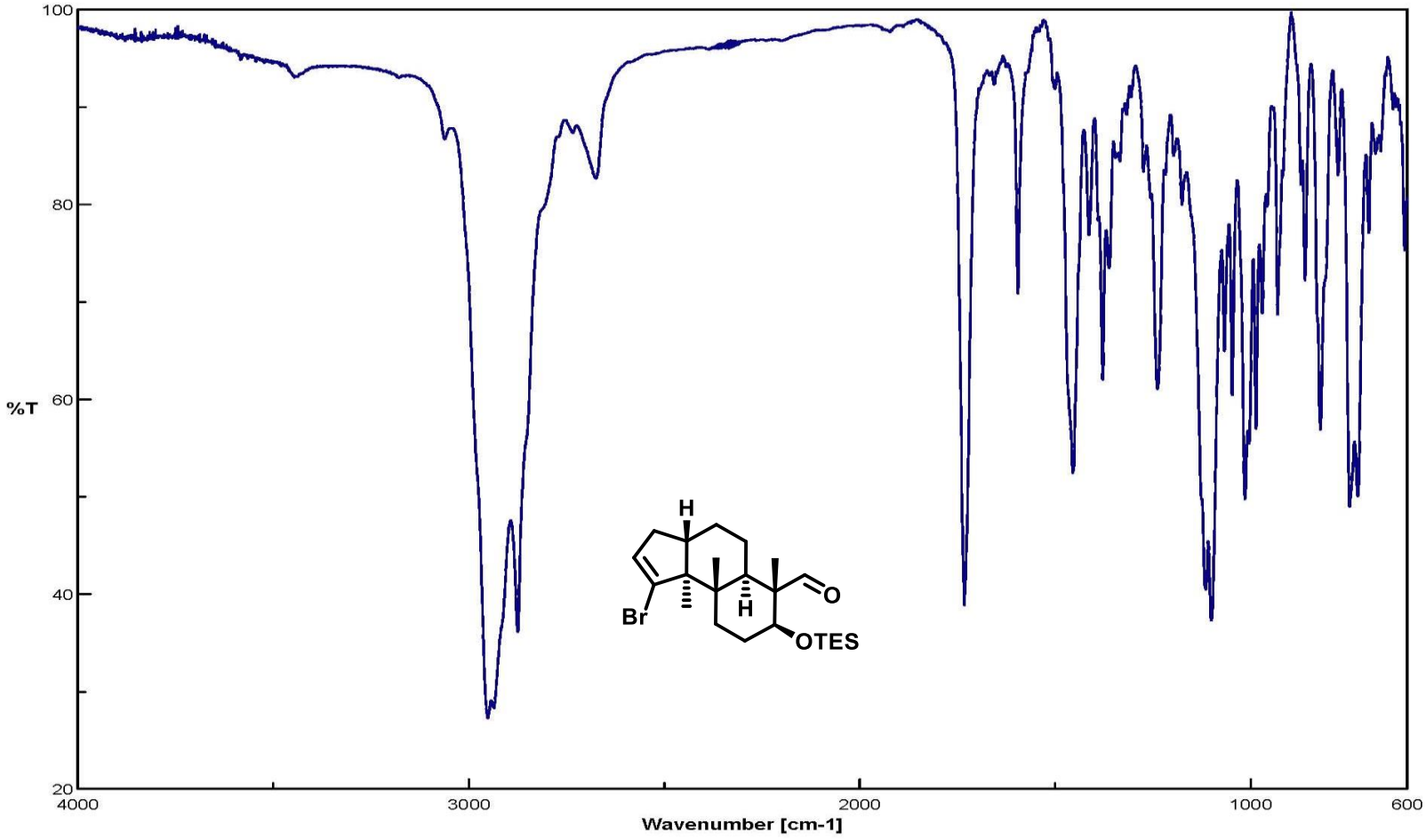
IR Spectrum of Compound **(–)-65**



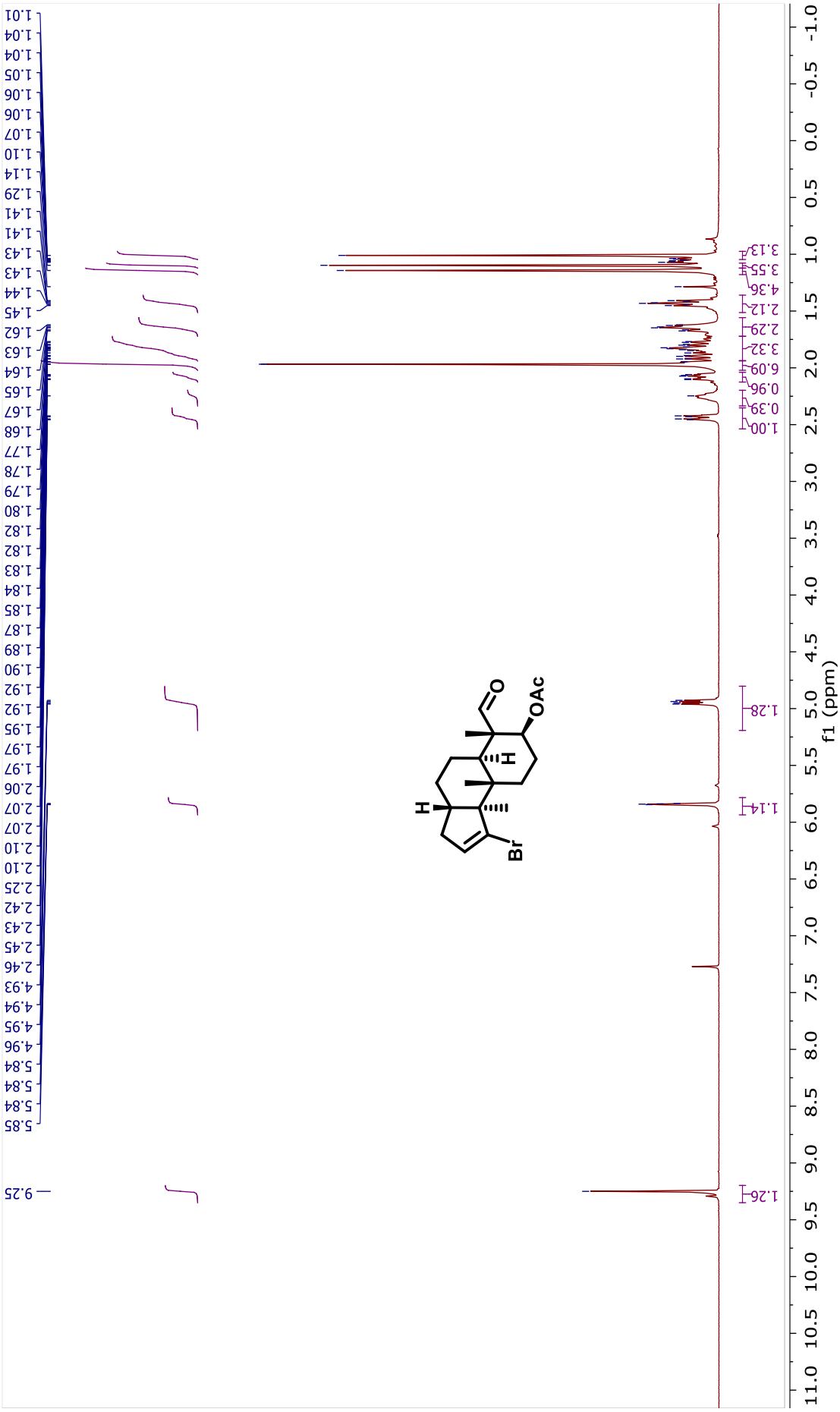
^{1}H NMR (500 MHz) Spectrum of Compound (−)-**66** in $CDCl_3$



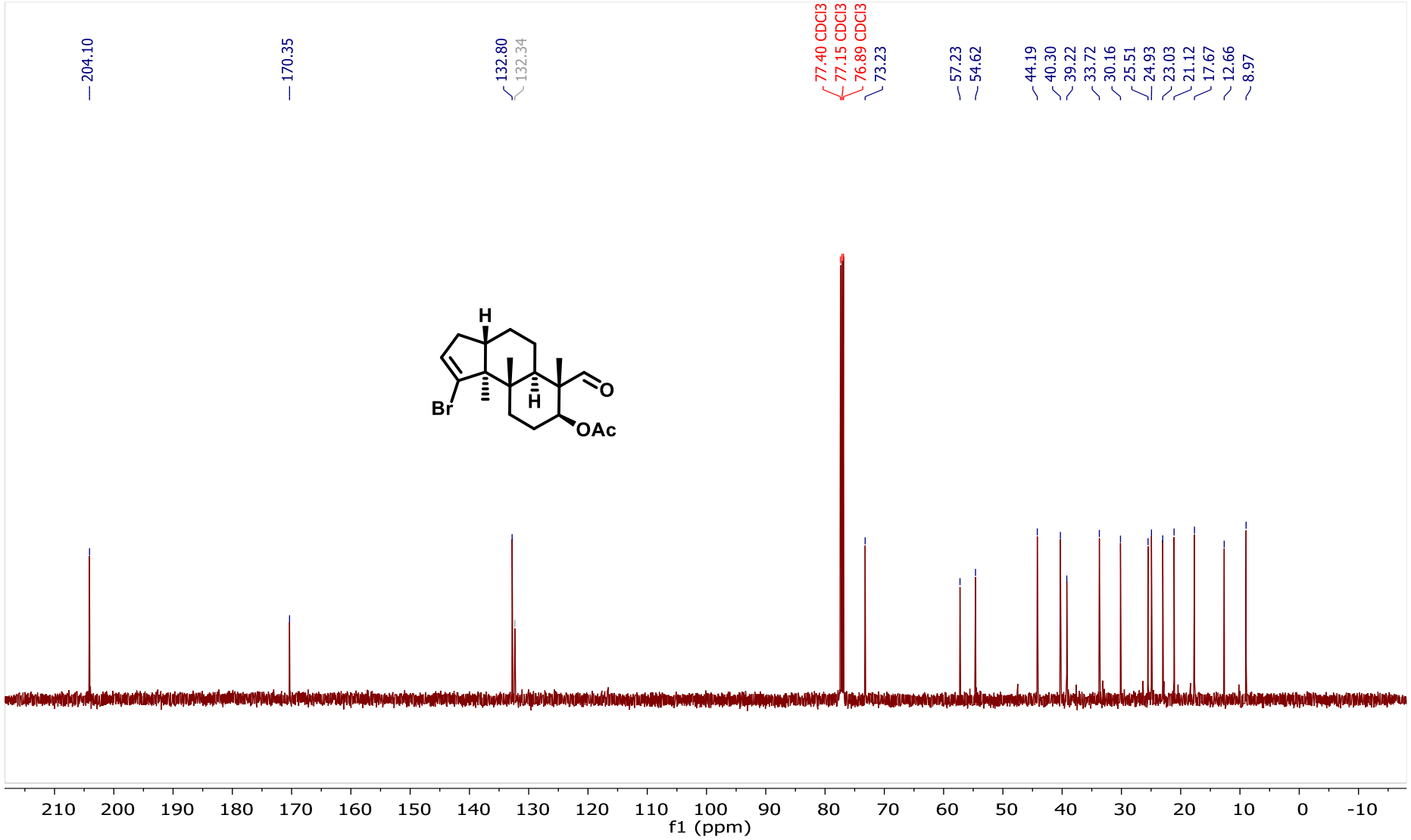
^{13}C NMR (126 MHz) Spectrum of Compound (−)-**66** in $CDCl_3$



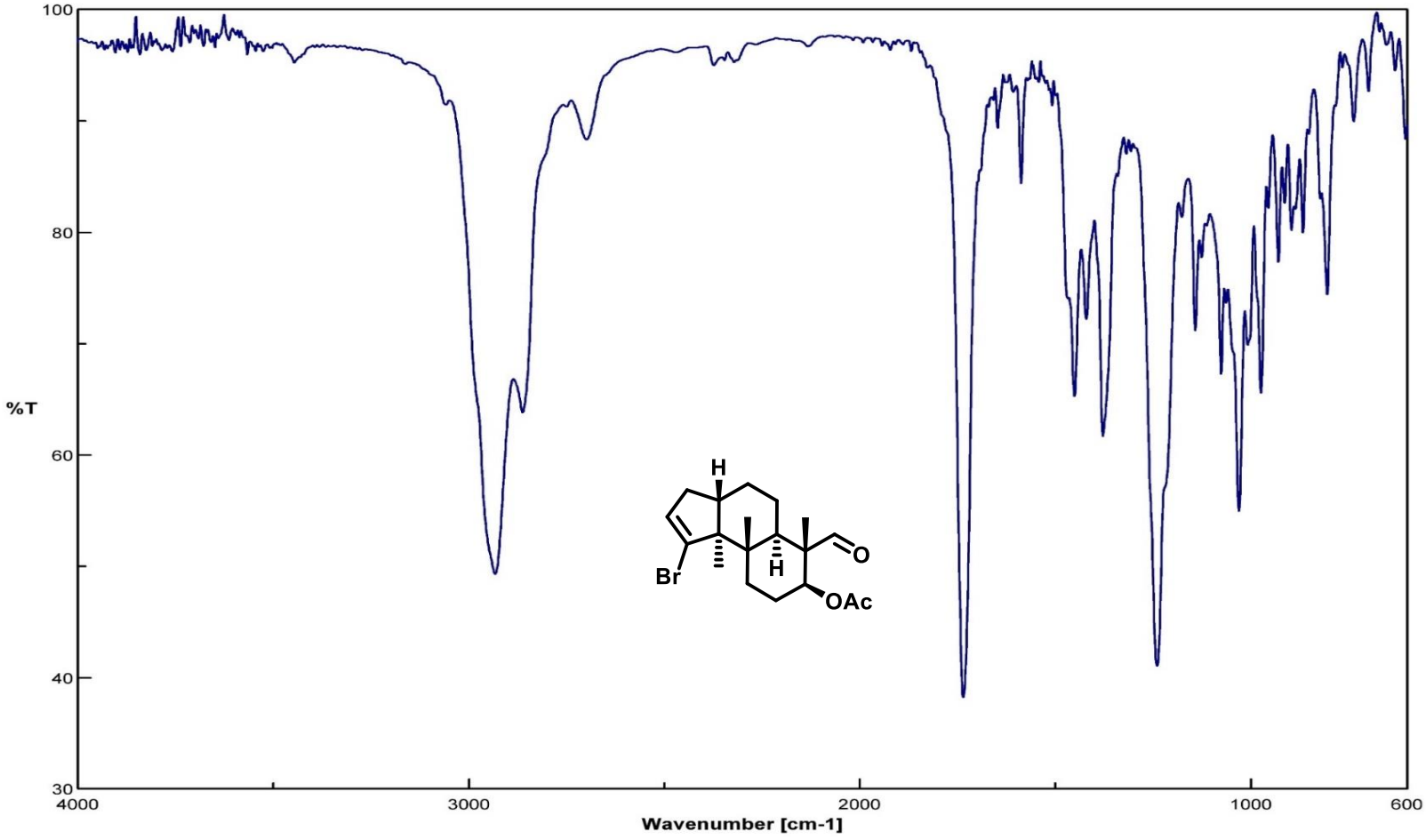
IR Spectrum of Compound (–)-**66**



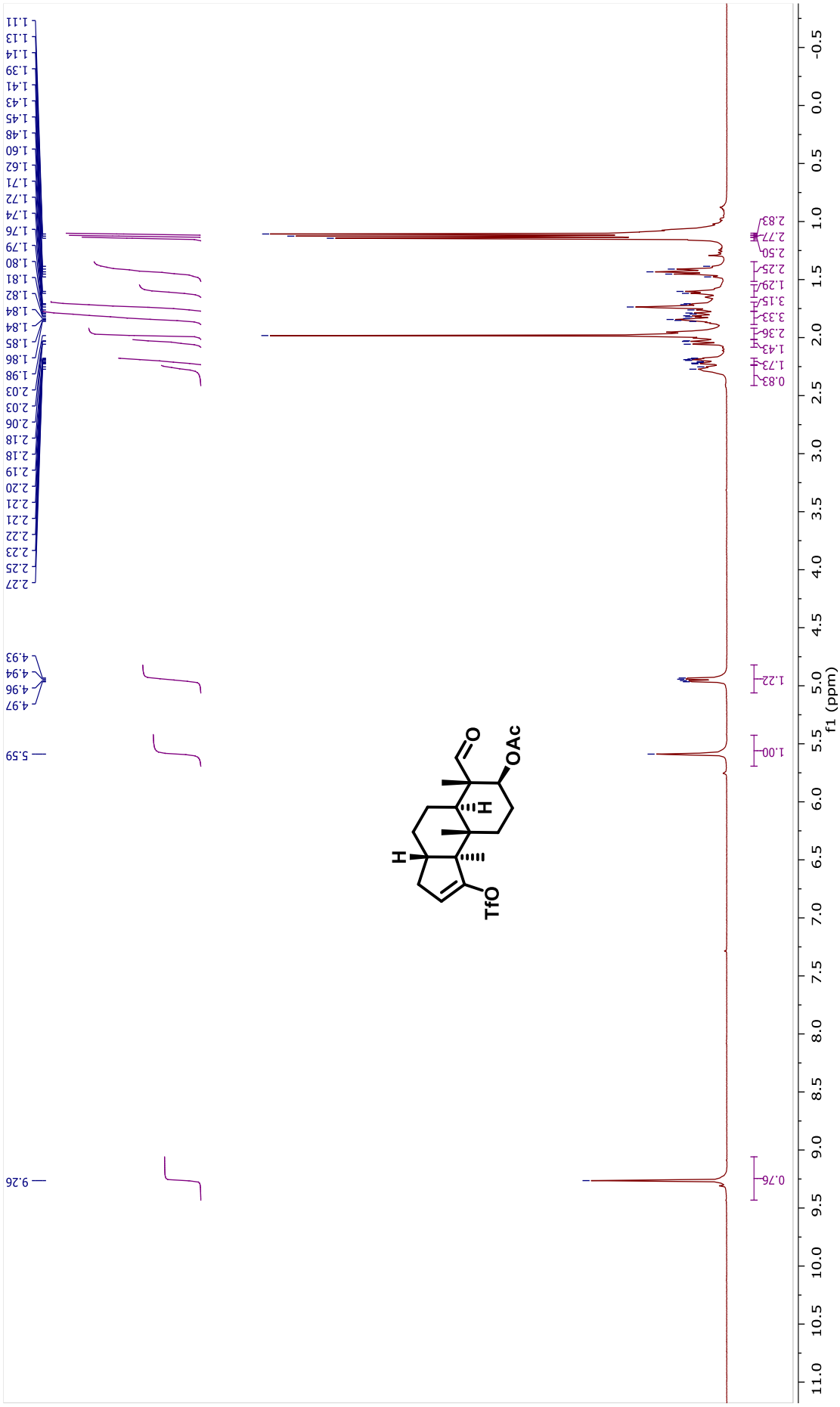
^{1}H NMR (500 MHz) Spectrum of Compound **(–)-67** in $CDCl_3$



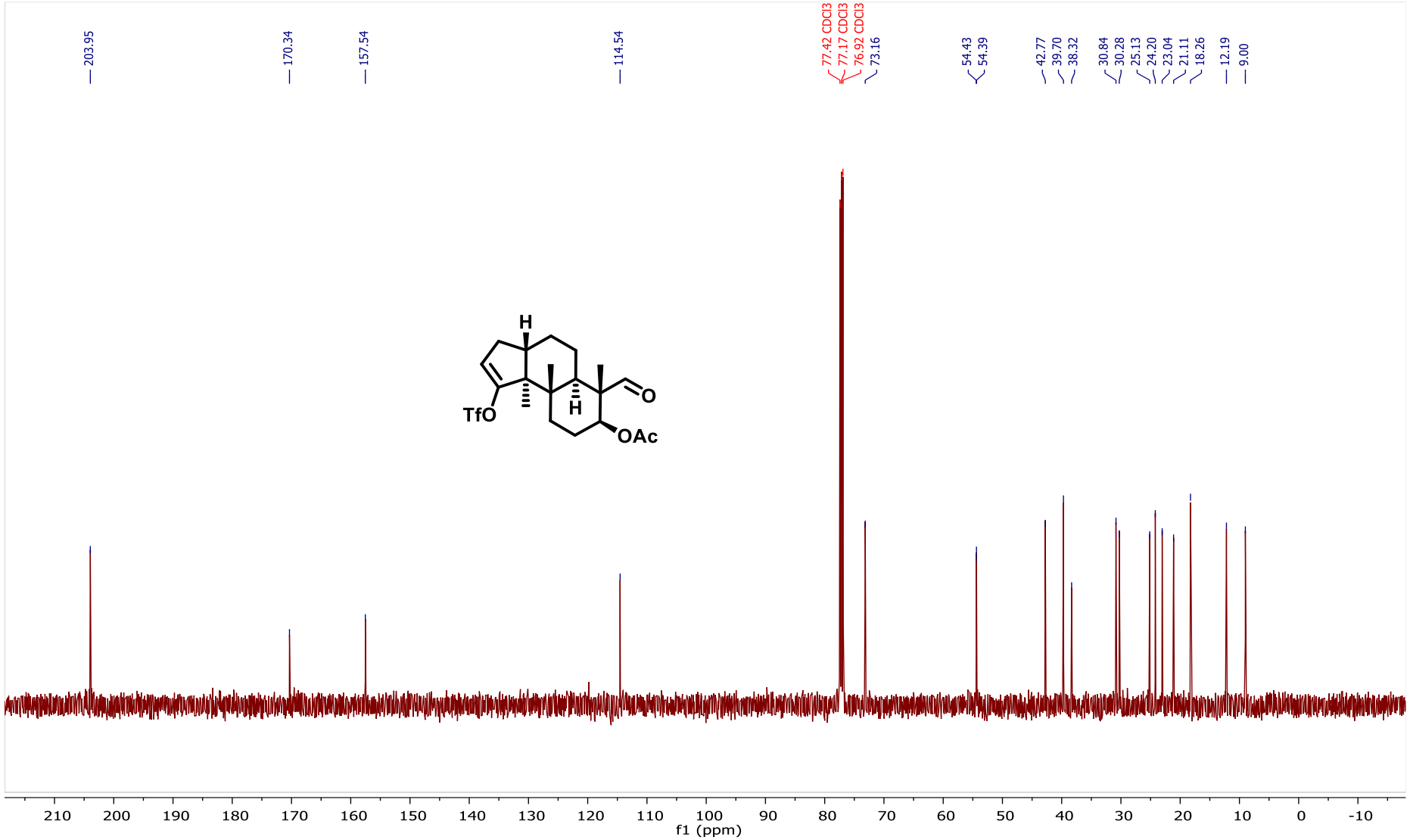
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-67** in $CDCl_3$



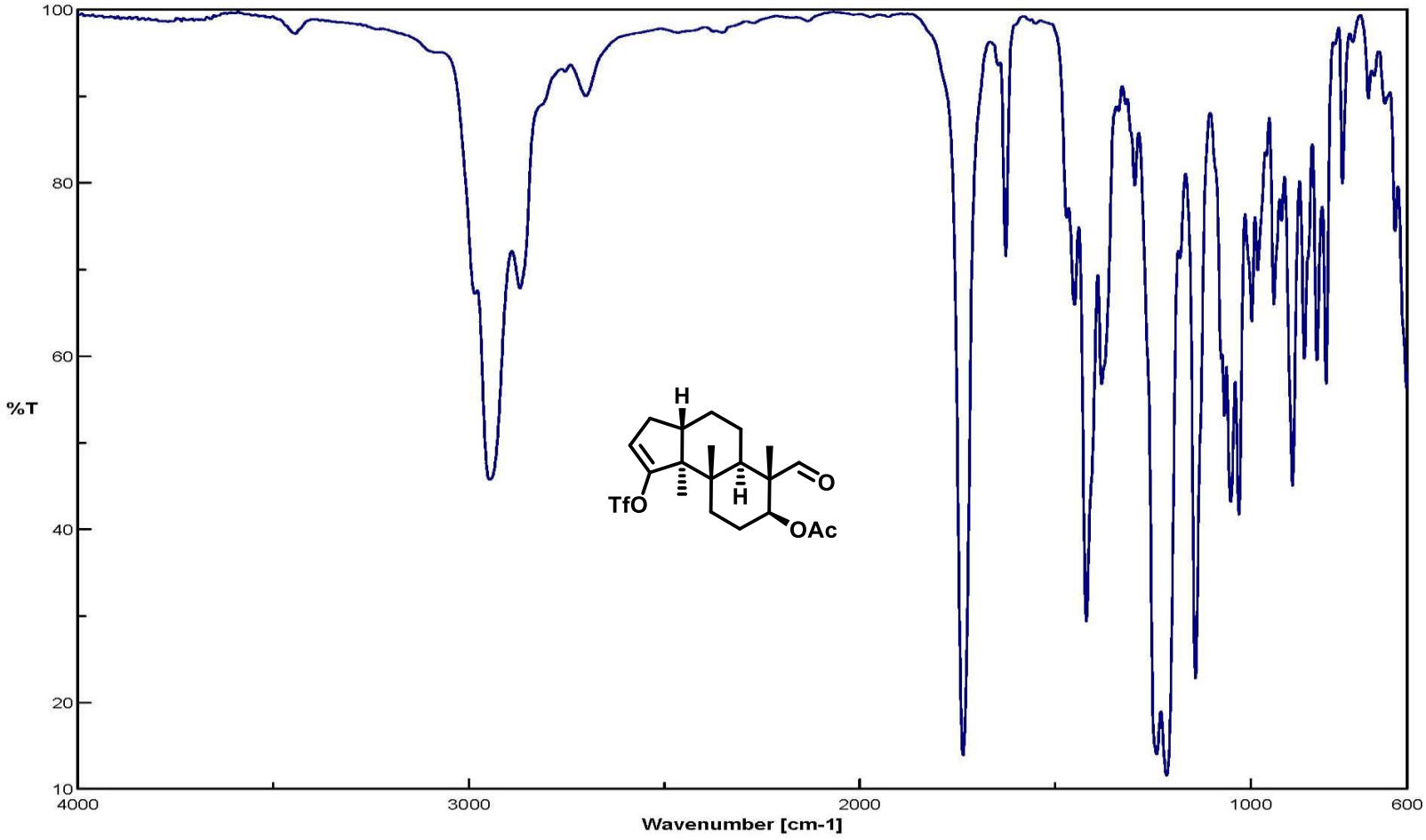
IR Spectrum of Compound **(–)-67**



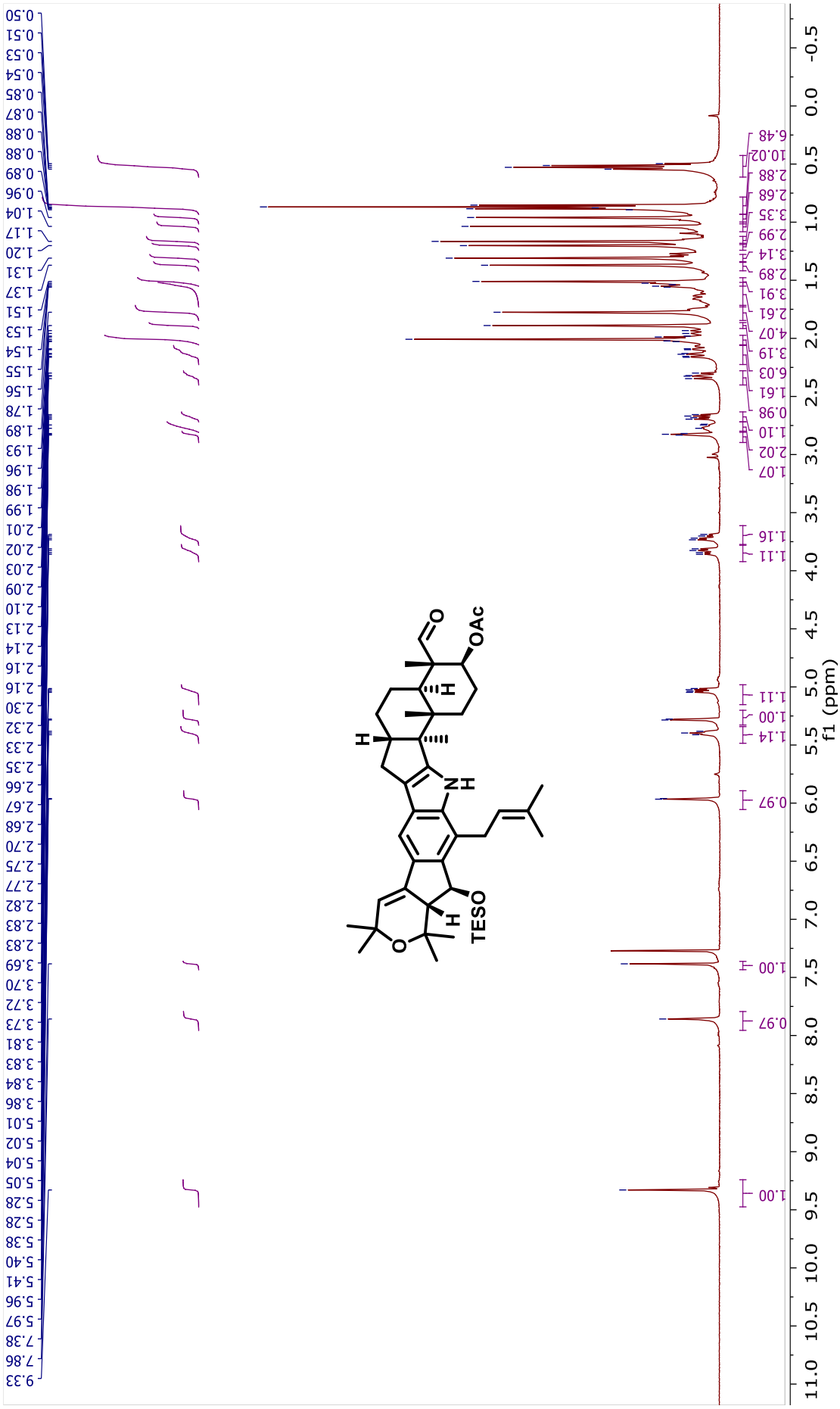
^{1}H NMR (500 MHz) Spectrum of Compound **(–)-47** in $CDCl_3$



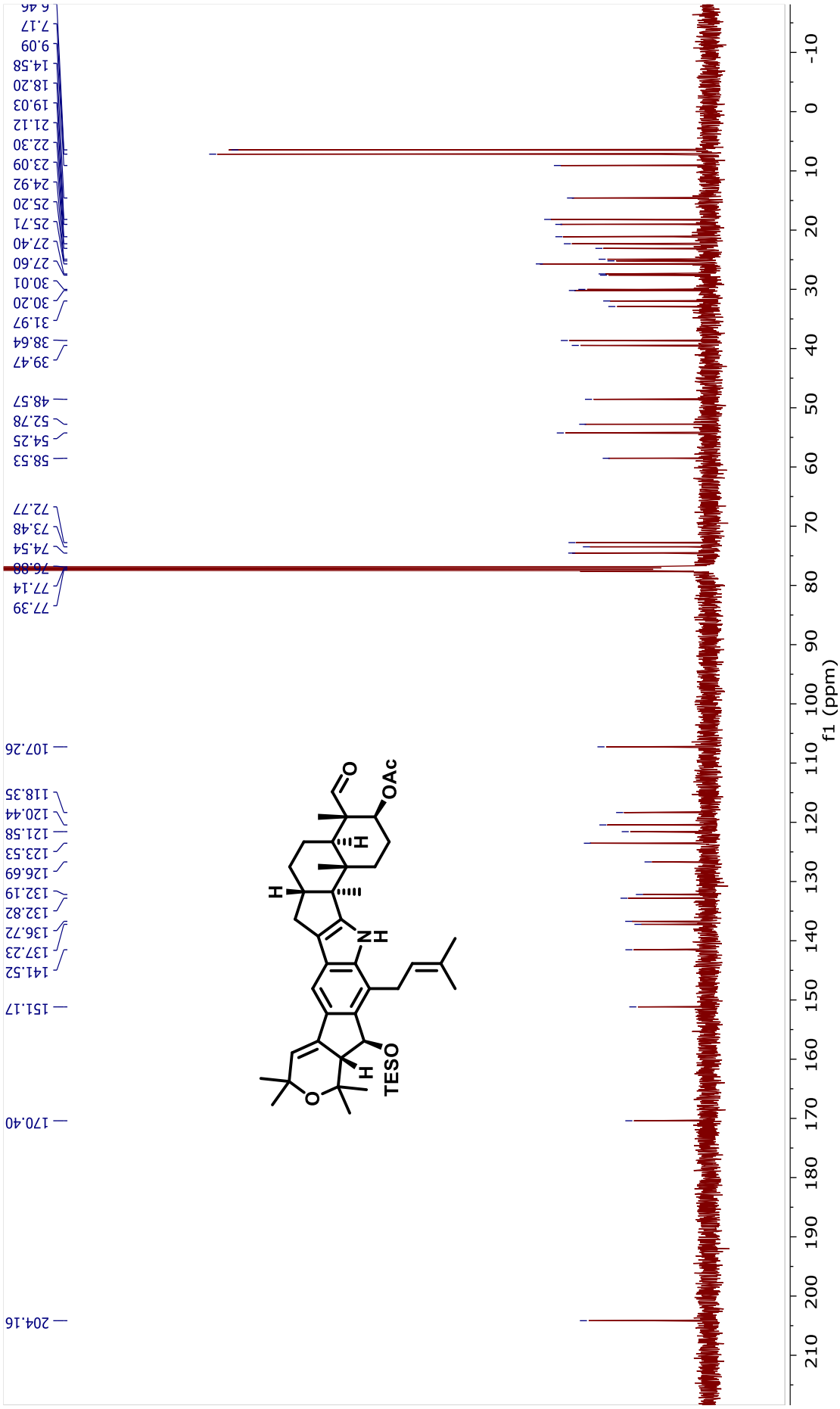
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-47** in $CDCl_3$



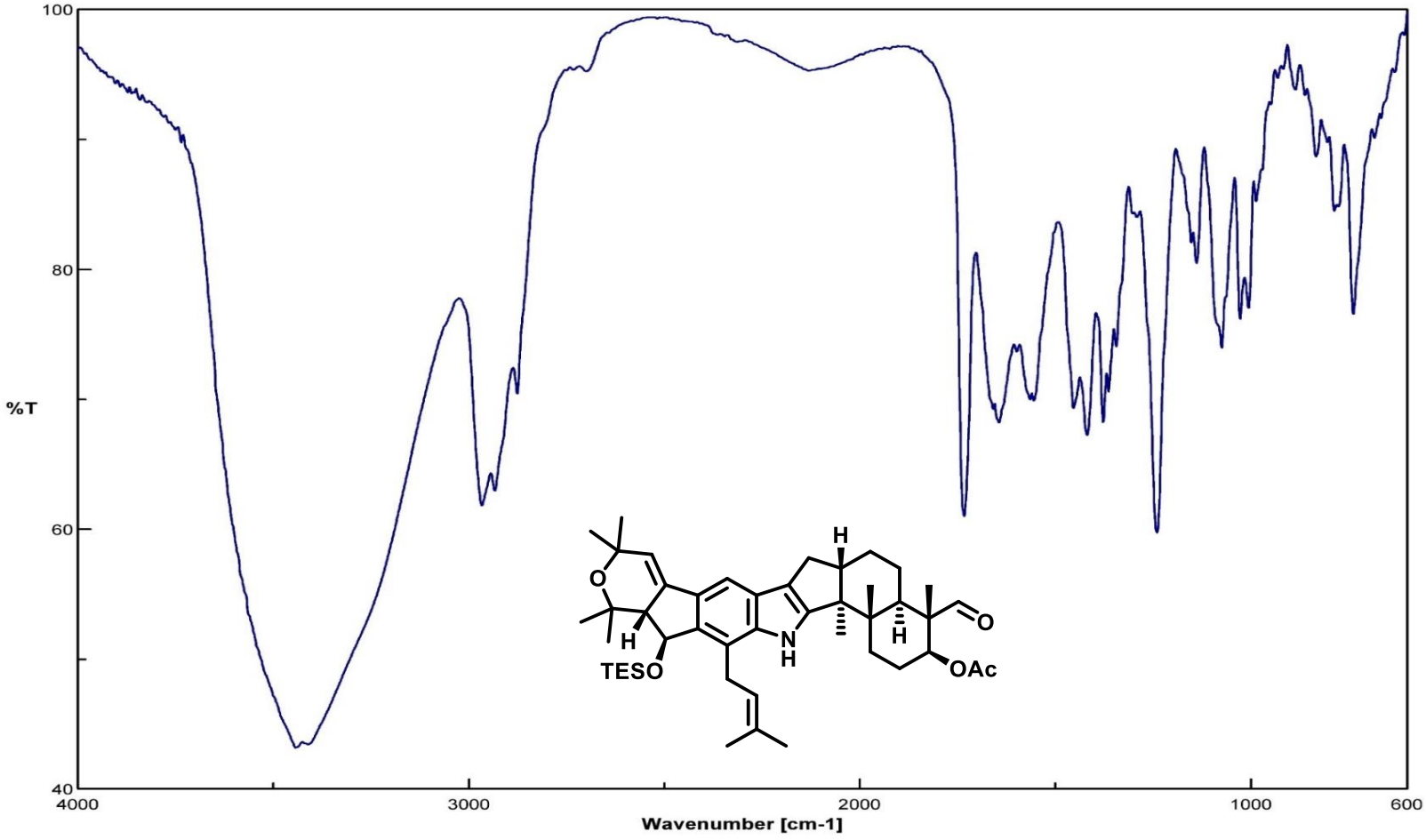
IR Spectrum of Compound **(–)-47**



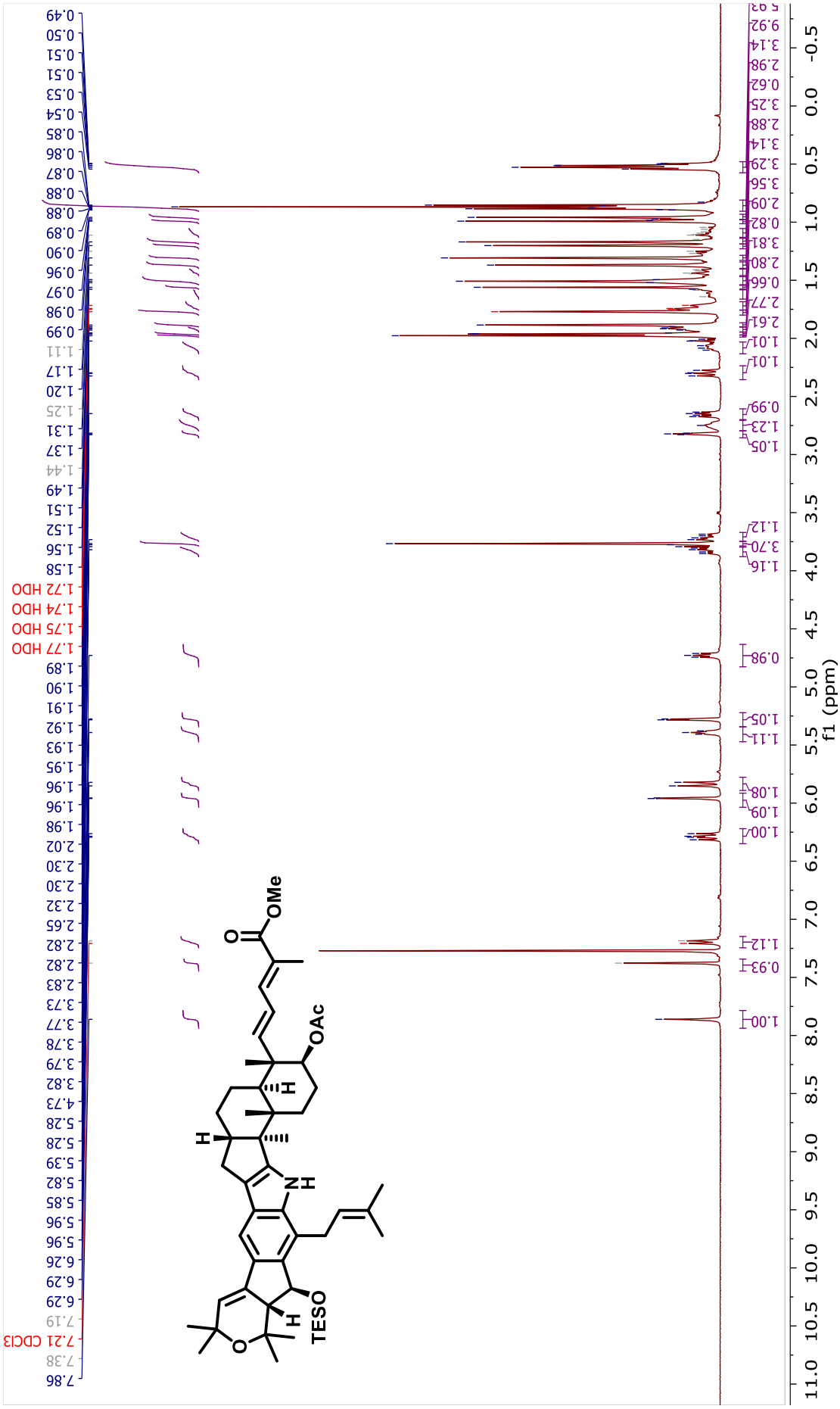
^{1}H NMR (500 MHz) Spectrum of Compound **(+)-72** in $CDCl_3$



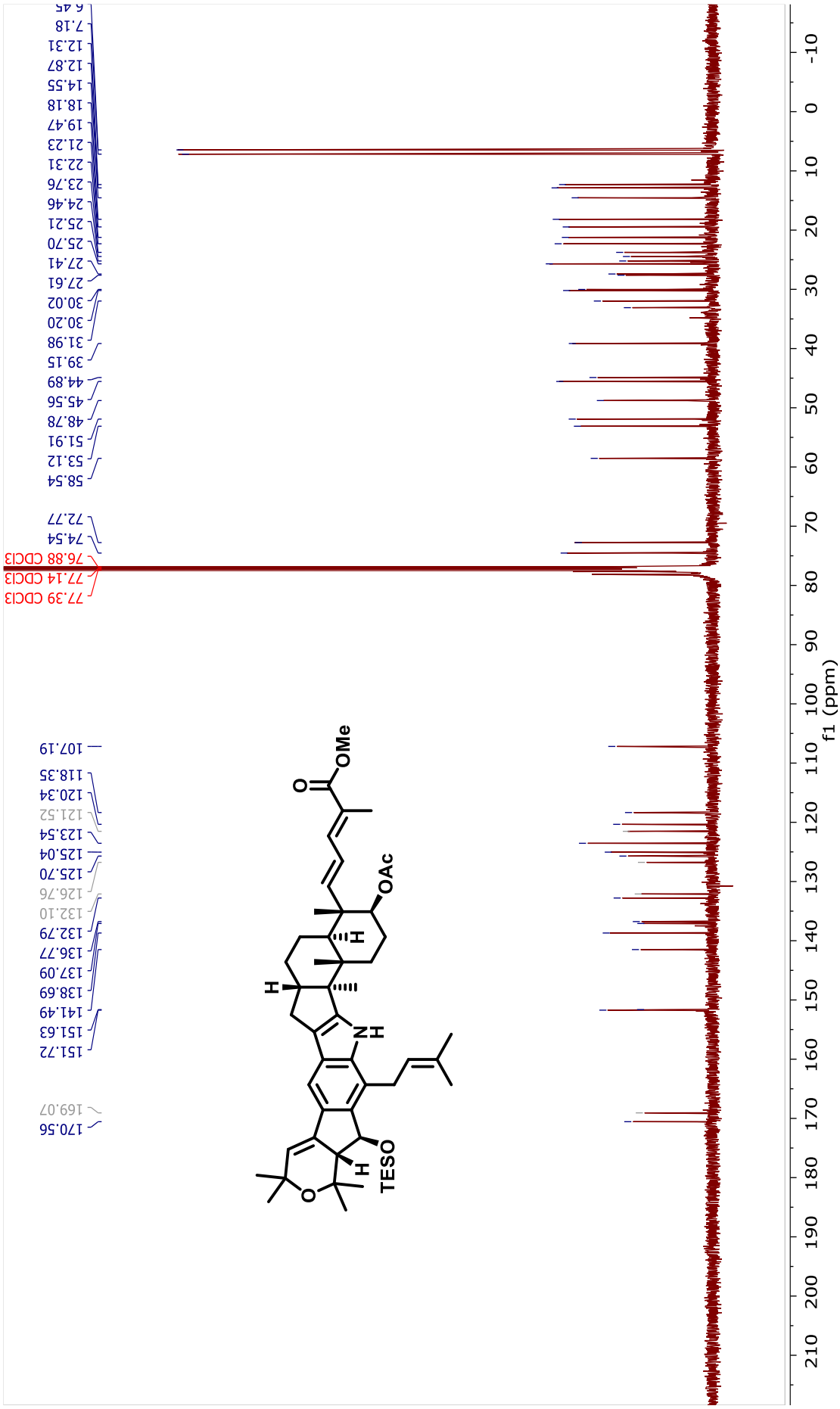
^{13}C NMR (126 MHz) Spectrum of Compound **(+)-72** in $CDCl_3$



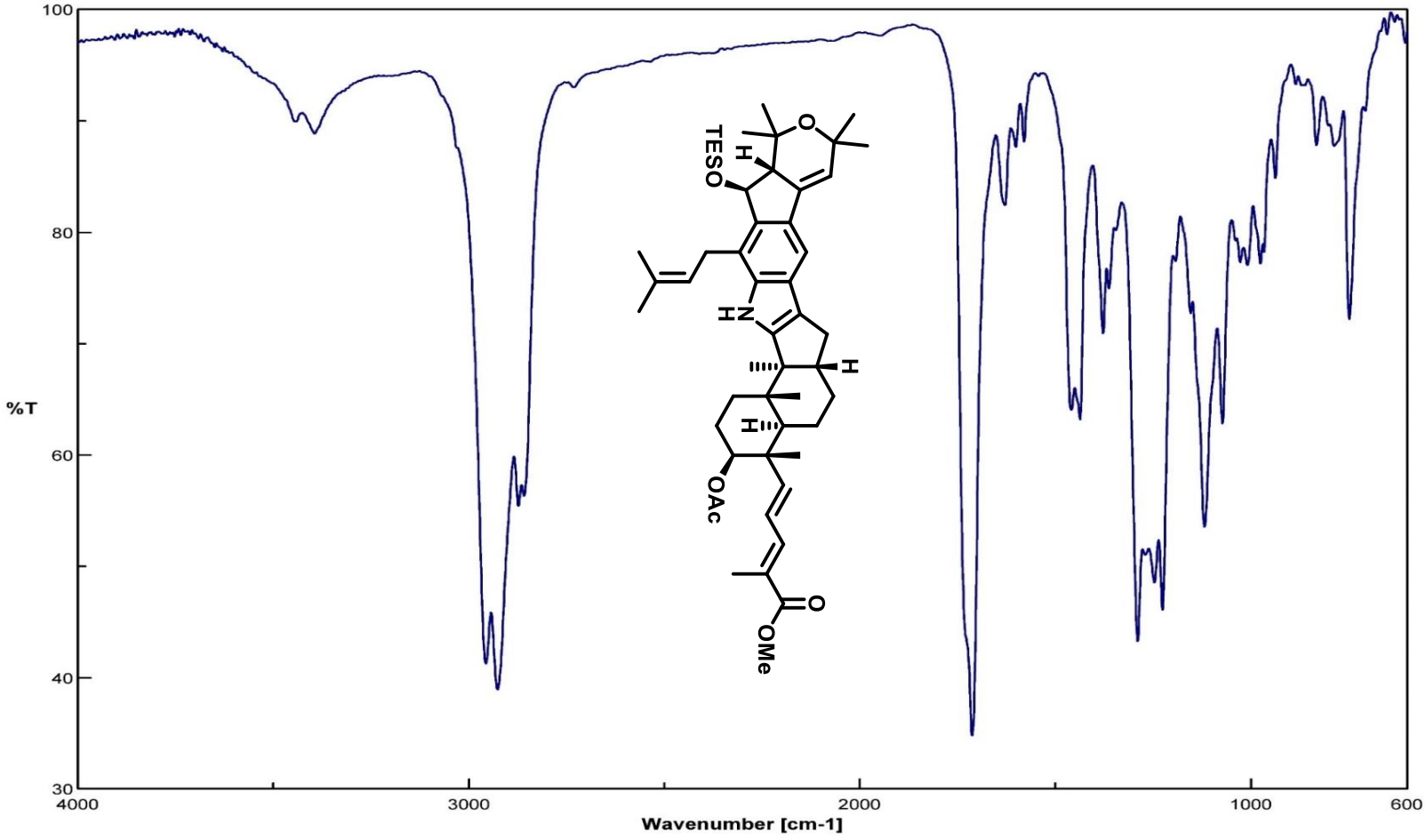
IR Spectrum of Compound **(+)-72**



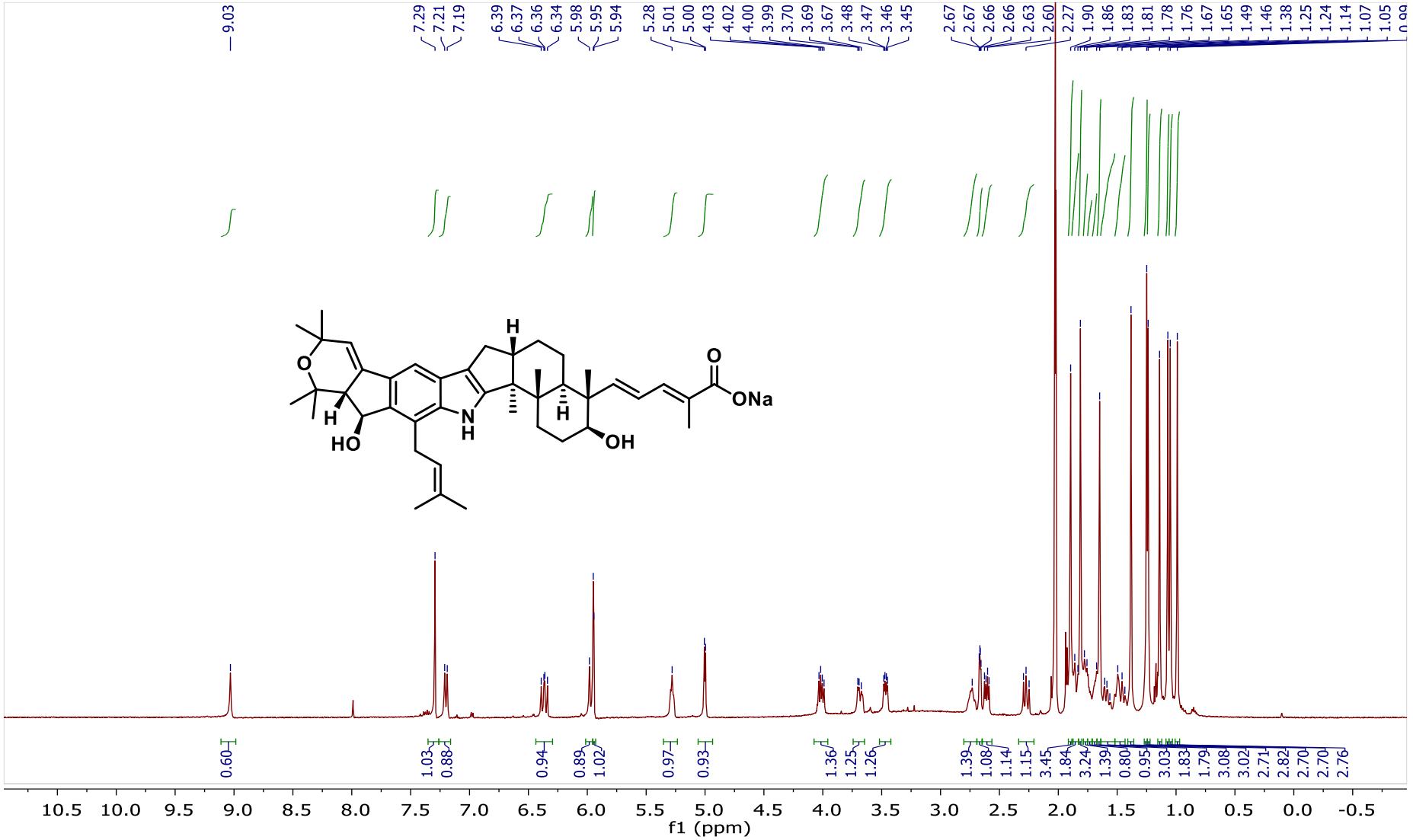
^{1}H NMR (500 MHz) Spectrum of Compound **(+)-73** in $CDCl_3$



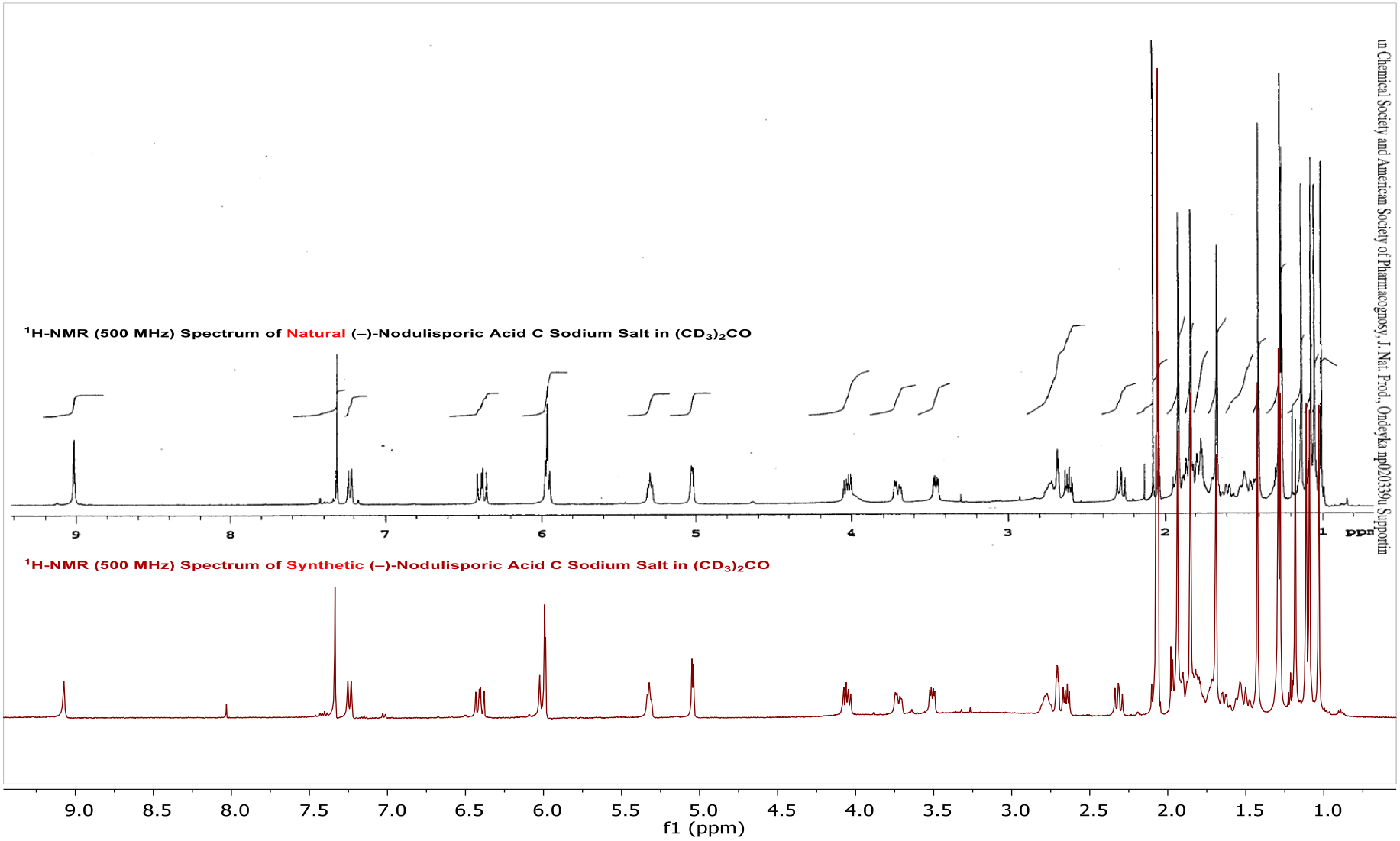
^{13}C NMR (126 MHz) Spectrum of Compound **(+)-73** in $CDCl_3$



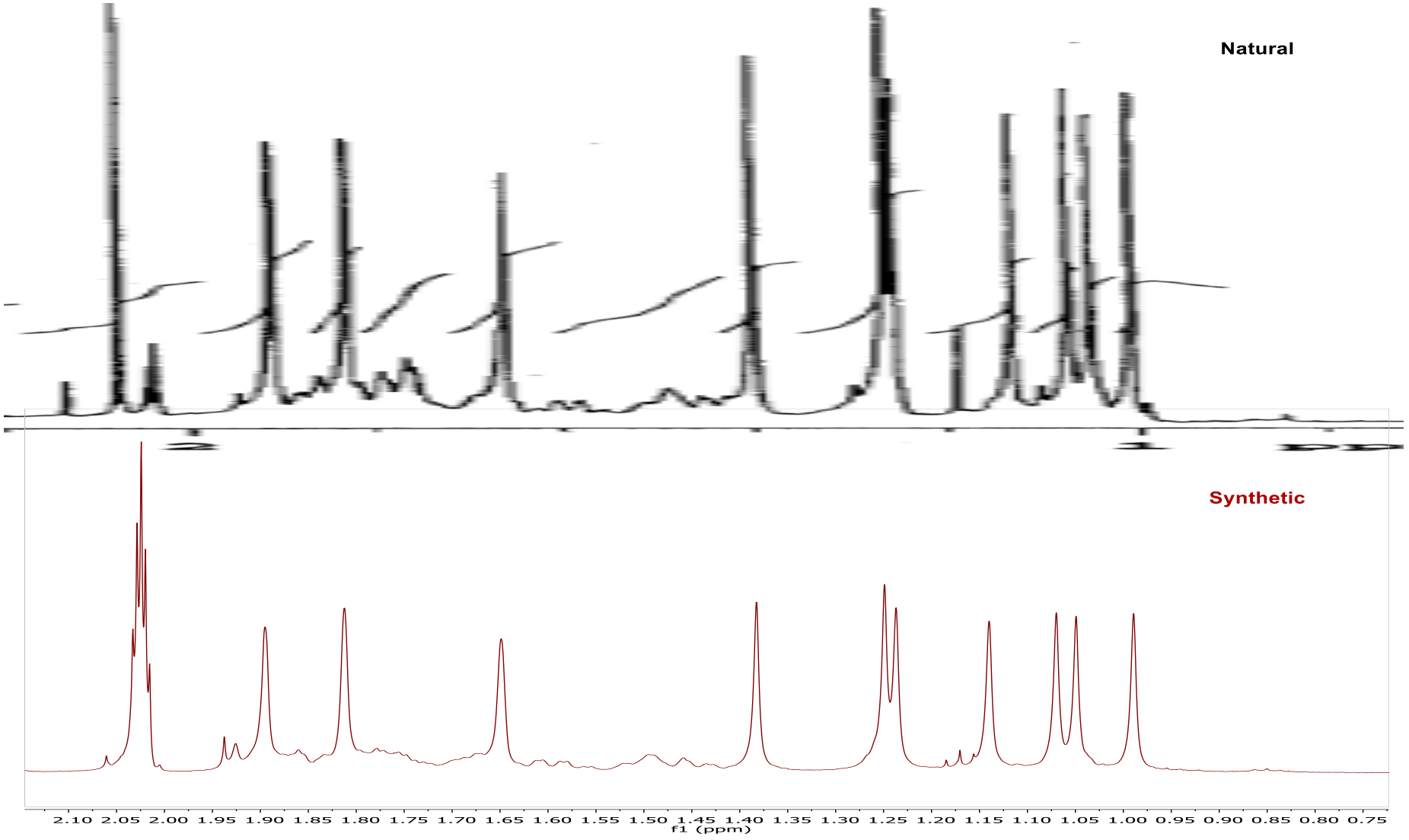
IR Spectrum of Compound **(+)-73**



^{1}H NMR (500 MHz) Spectrum of Compound **(–)-3-Sodium Salt** in $(CD_3)_2CO$

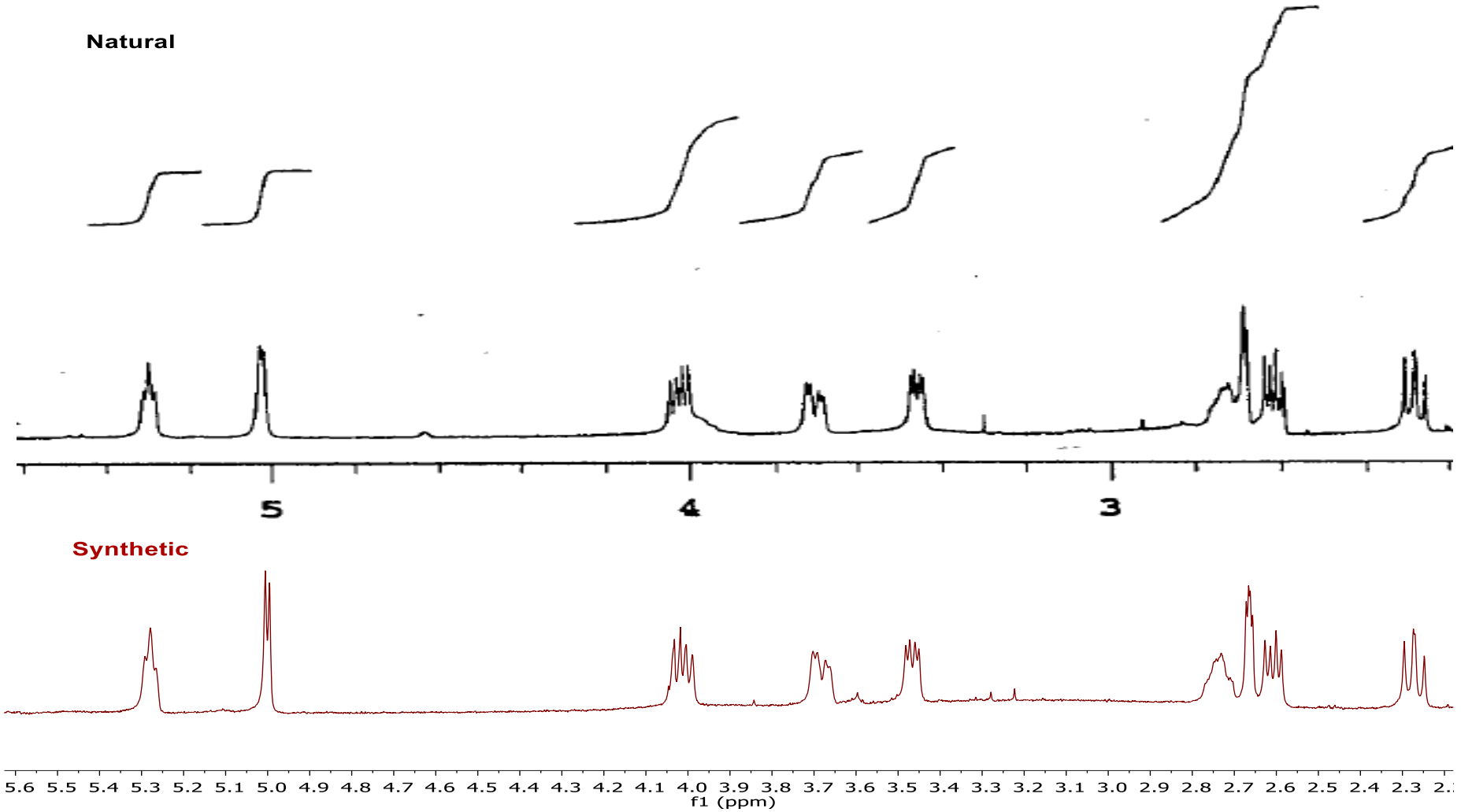


^{1}H NMR Comparison of Natural (500 MHz) and Synthetic (500 MHz) **(–) -3-Sodium Salt** in $(CD_3)_2CO$



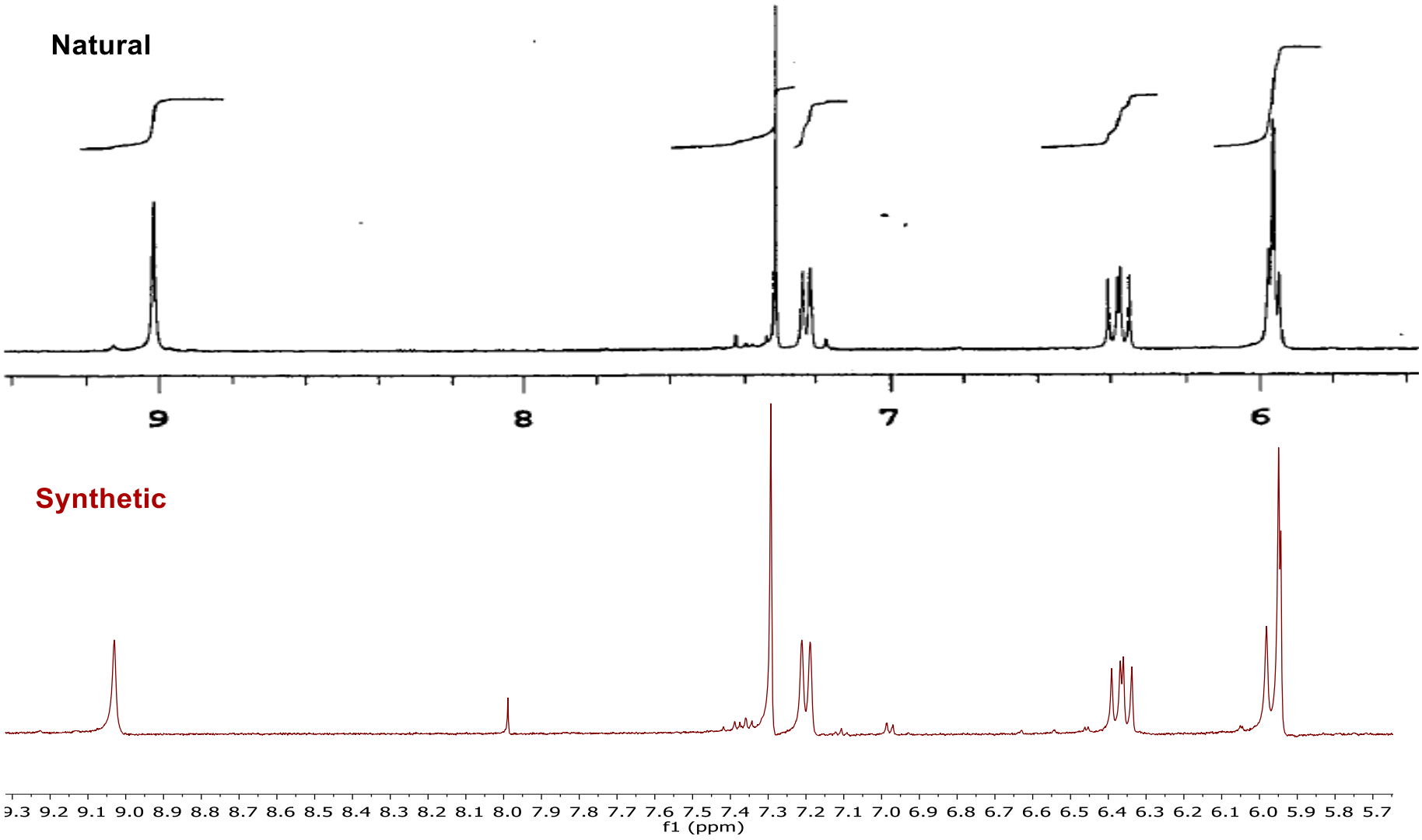
^{1}H NMR Comparison of Natural (500 MHz) and Synthetic (500 MHz) **(–) -3-Sodium Salt** in $(CD_3)_2CO$

(0.7 ppm to 2.2 ppm Expanded View)



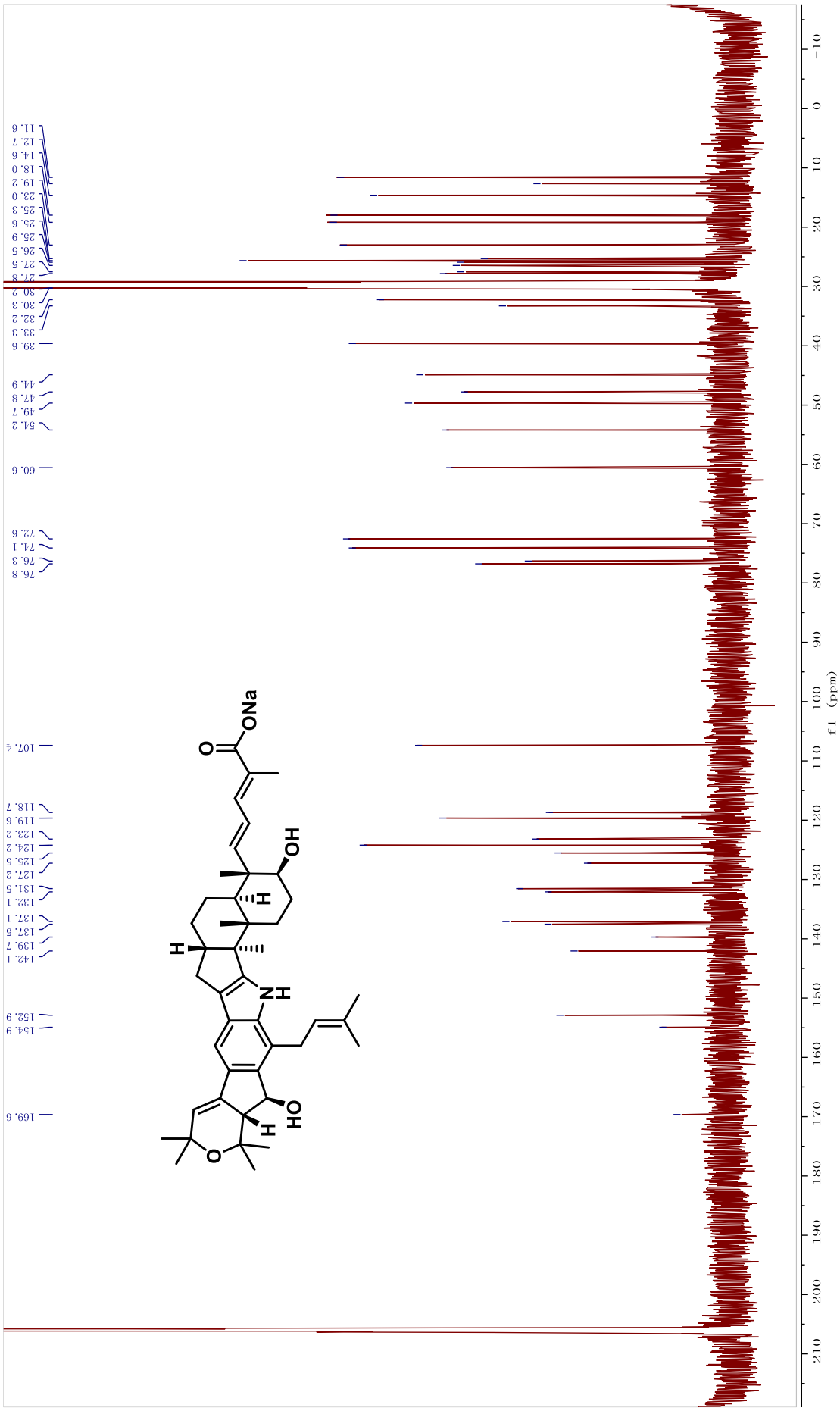
^{1}H NMR Comparison of Natural (500 MHz) and Synthetic (500 MHz) **(–) -3-Sodium Salt** in $(CD_3)_2CO$

(2.2 ppm to 5.6 ppm Expanded View)

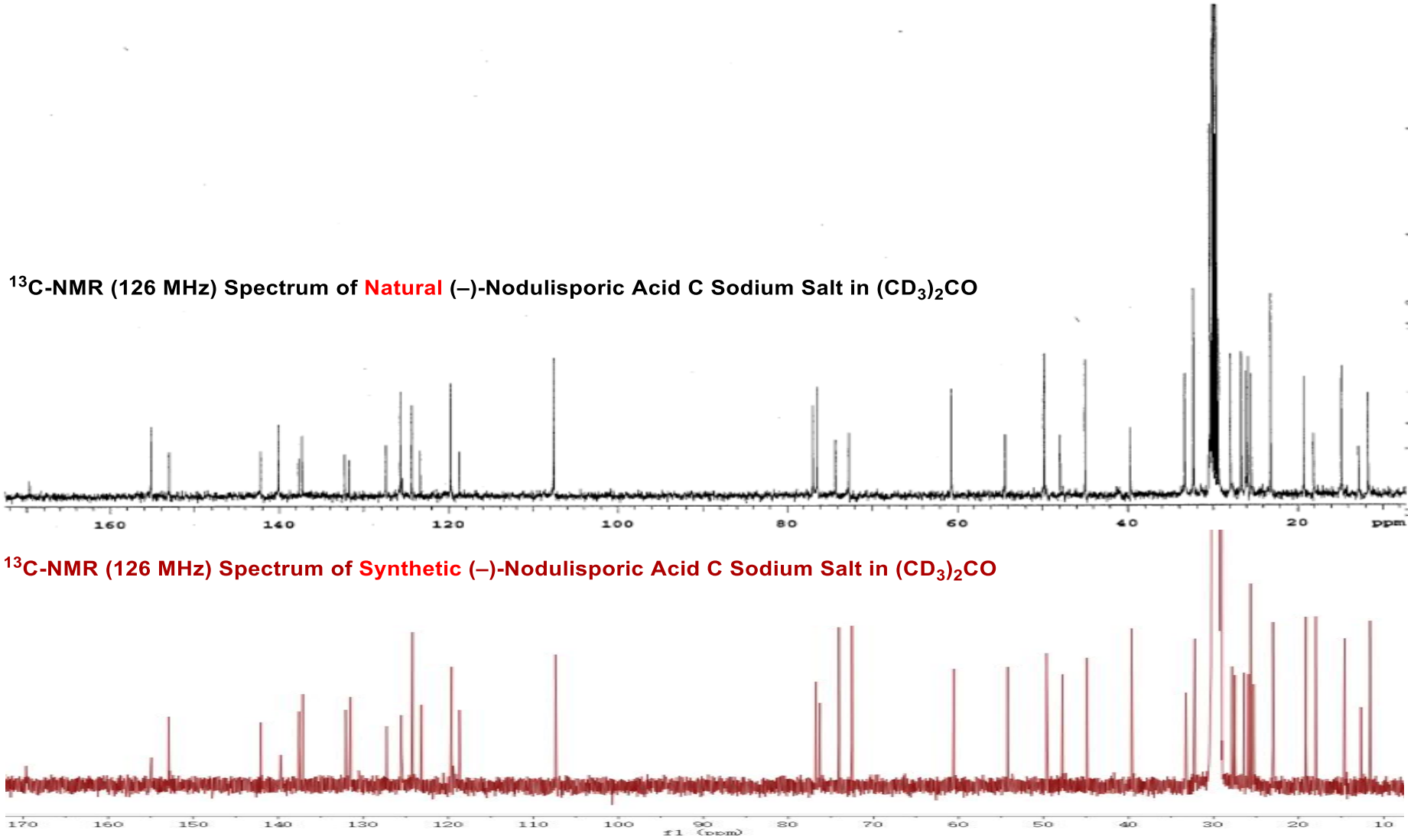


^{1}H NMR Comparison of Natural (500 MHz) and Synthetic (500 MHz) **(–) -3-Sodium Salt** in $(CD_3)_2CO$

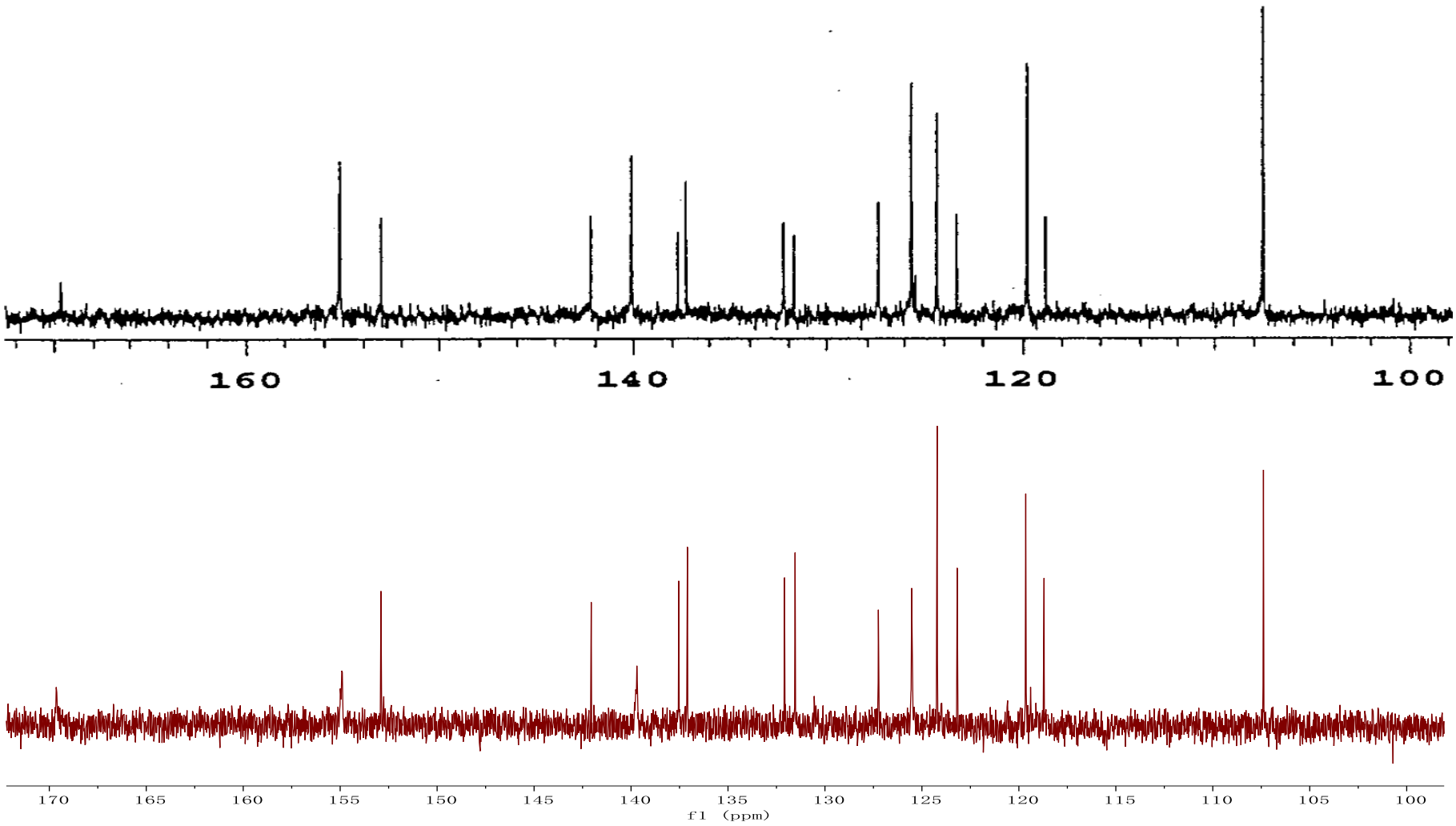
(9.3 ppm to 5.7 ppm Expanded View)



^{13}C NMR (126 MHz) Spectrum of Compound **(–)-3-Sodium Salt** in $(CD_3)_2CO$

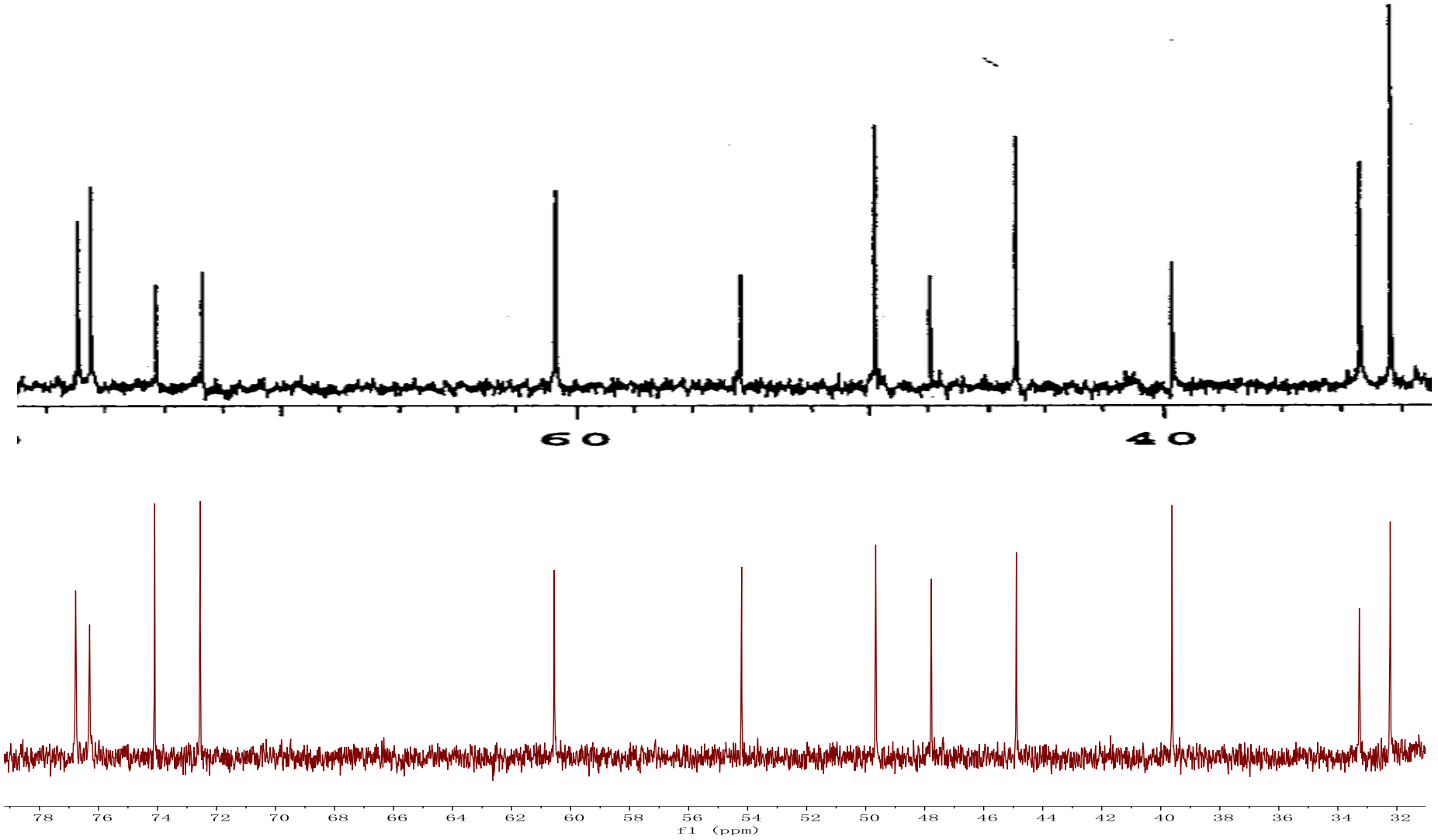


^{13}C NMR Comparison of Natural (126 MHz) and Synthetic (126 MHz) **(–) -3-Sodium Salt** in CD_3OD



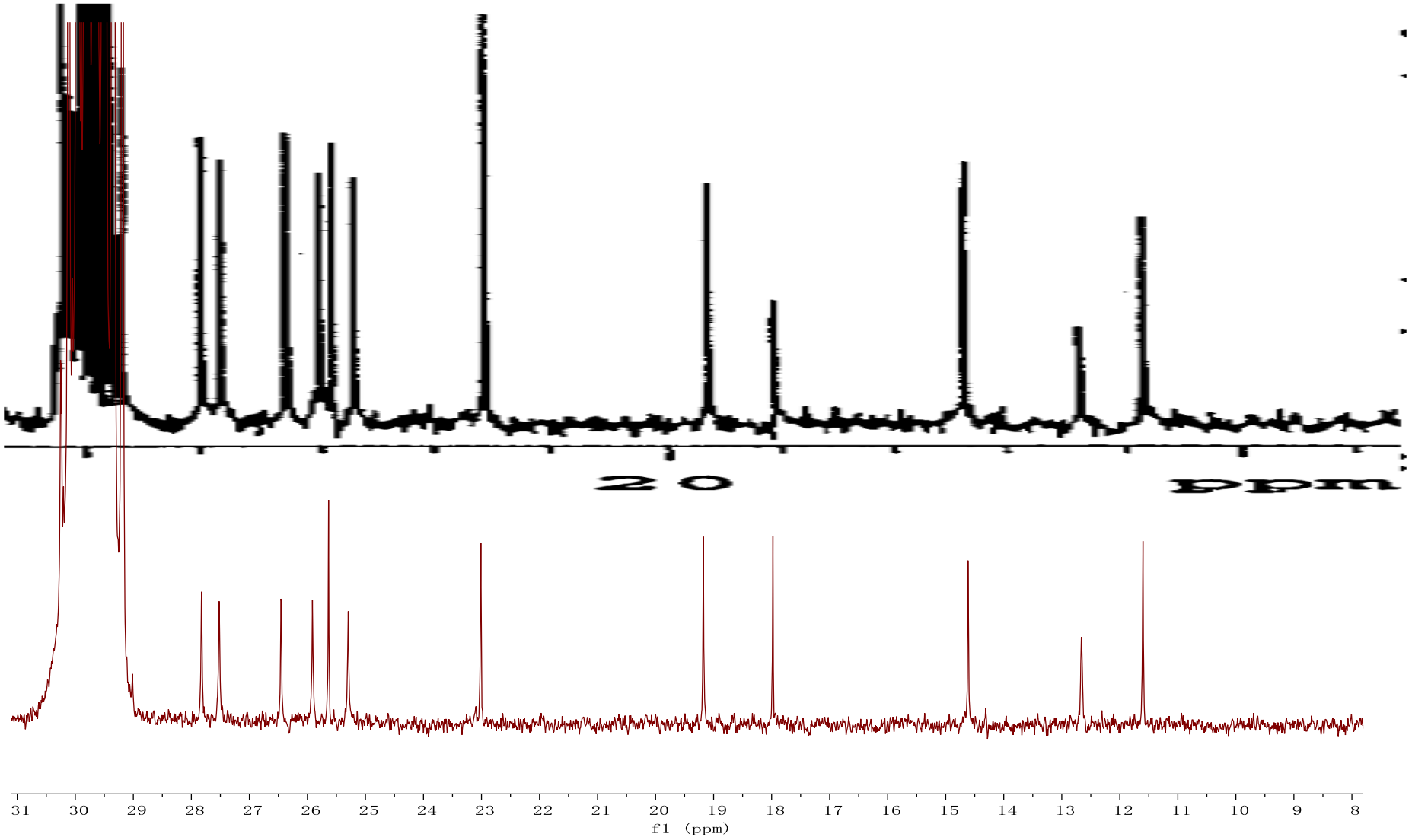
^{13}C NMR Comparison of Natural (126 MHz) and Synthetic (126 MHz) **(–) -3-Sodium Salt** in CD_3OD

(172 ppm to 98 ppm Expanded View)



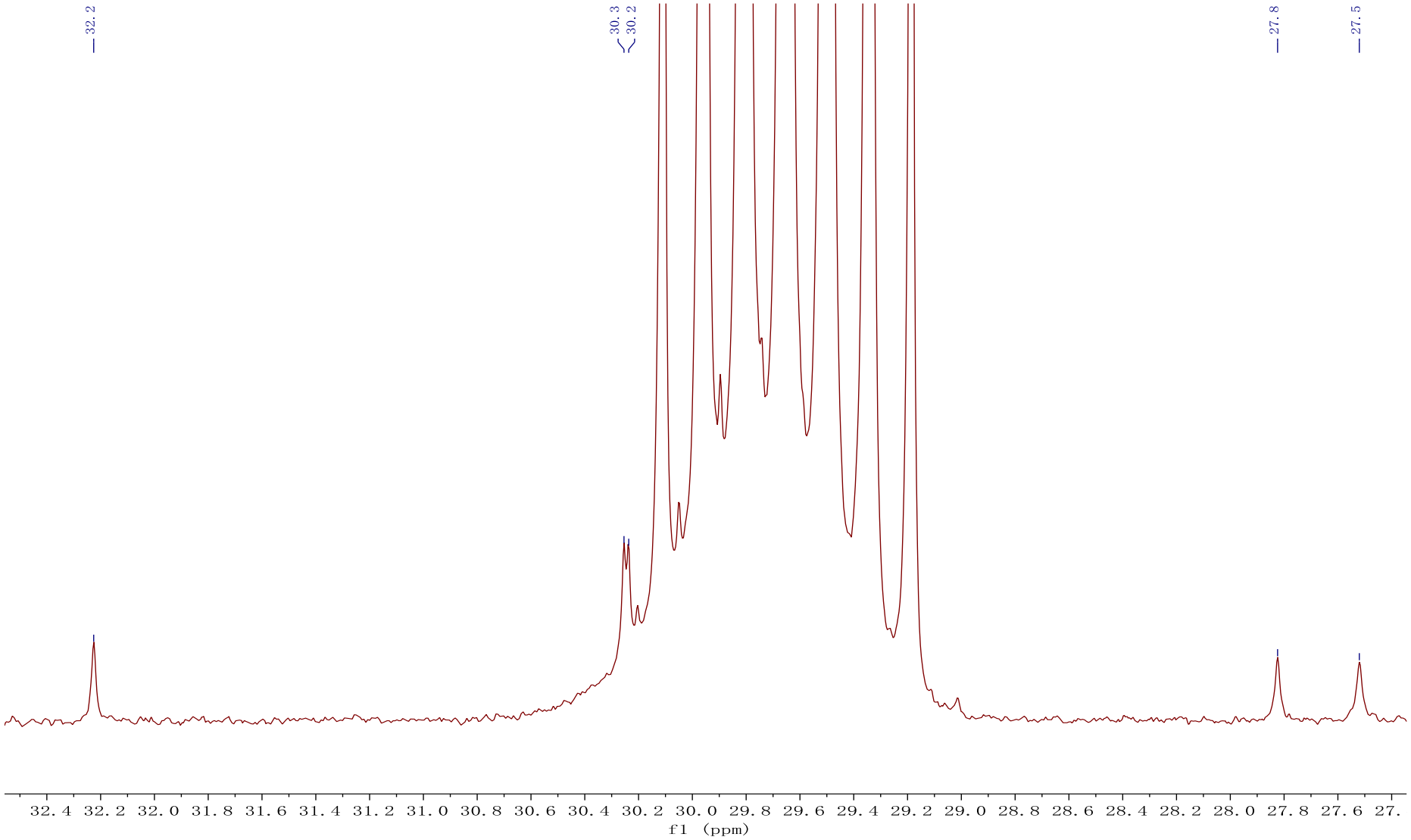
^{13}C NMR Comparison of Natural (126 MHz) and Synthetic (126 MHz) **(–) -3-Sodium Salt** in CD_3OD

(79 ppm to 32 ppm Expanded View)



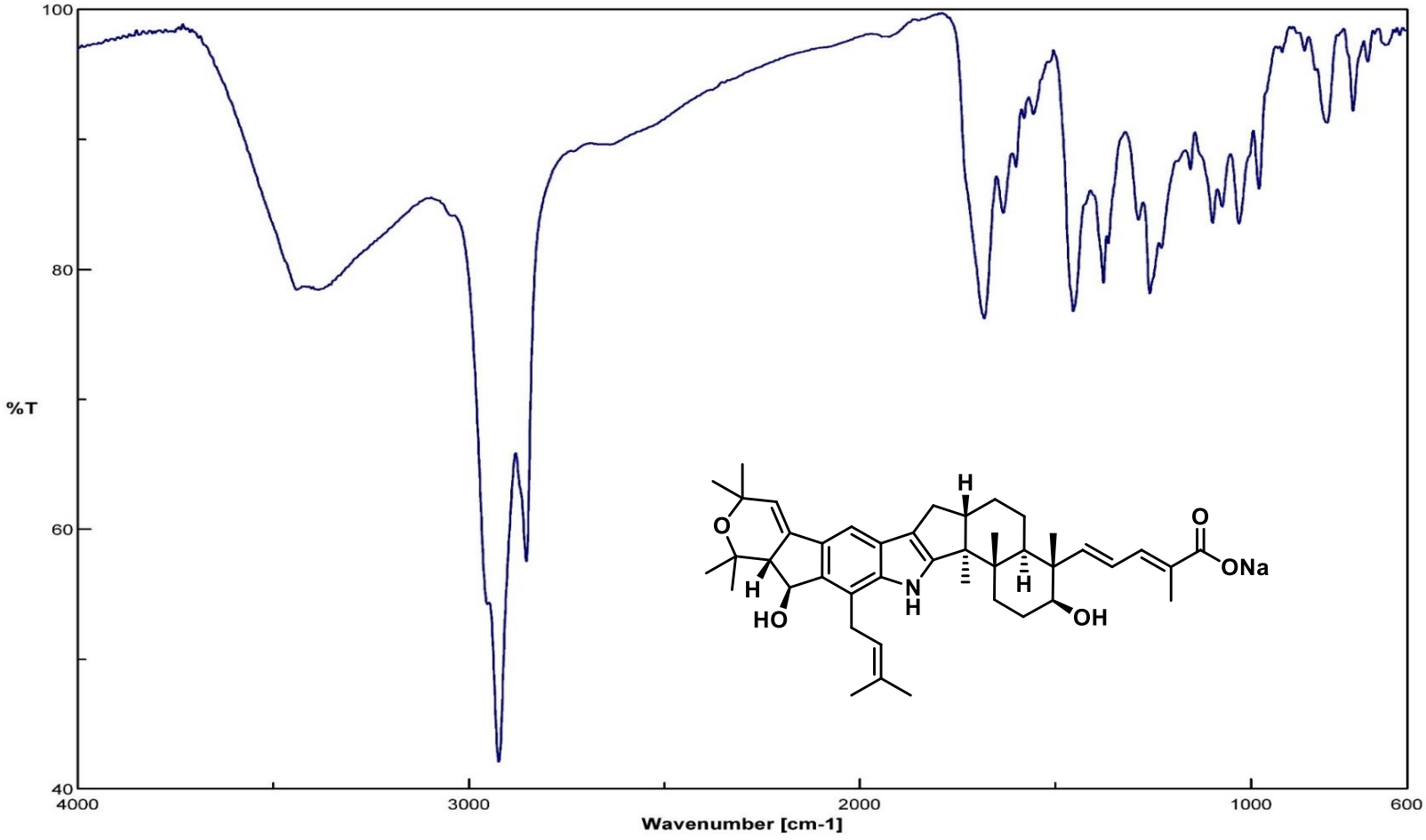
^{13}C NMR Comparison of Natural (126 MHz) and Synthetic (126 MHz) **(–) -3-Sodium Salt** in CD_3OD

(31 ppm to 8 ppm Expanded View)

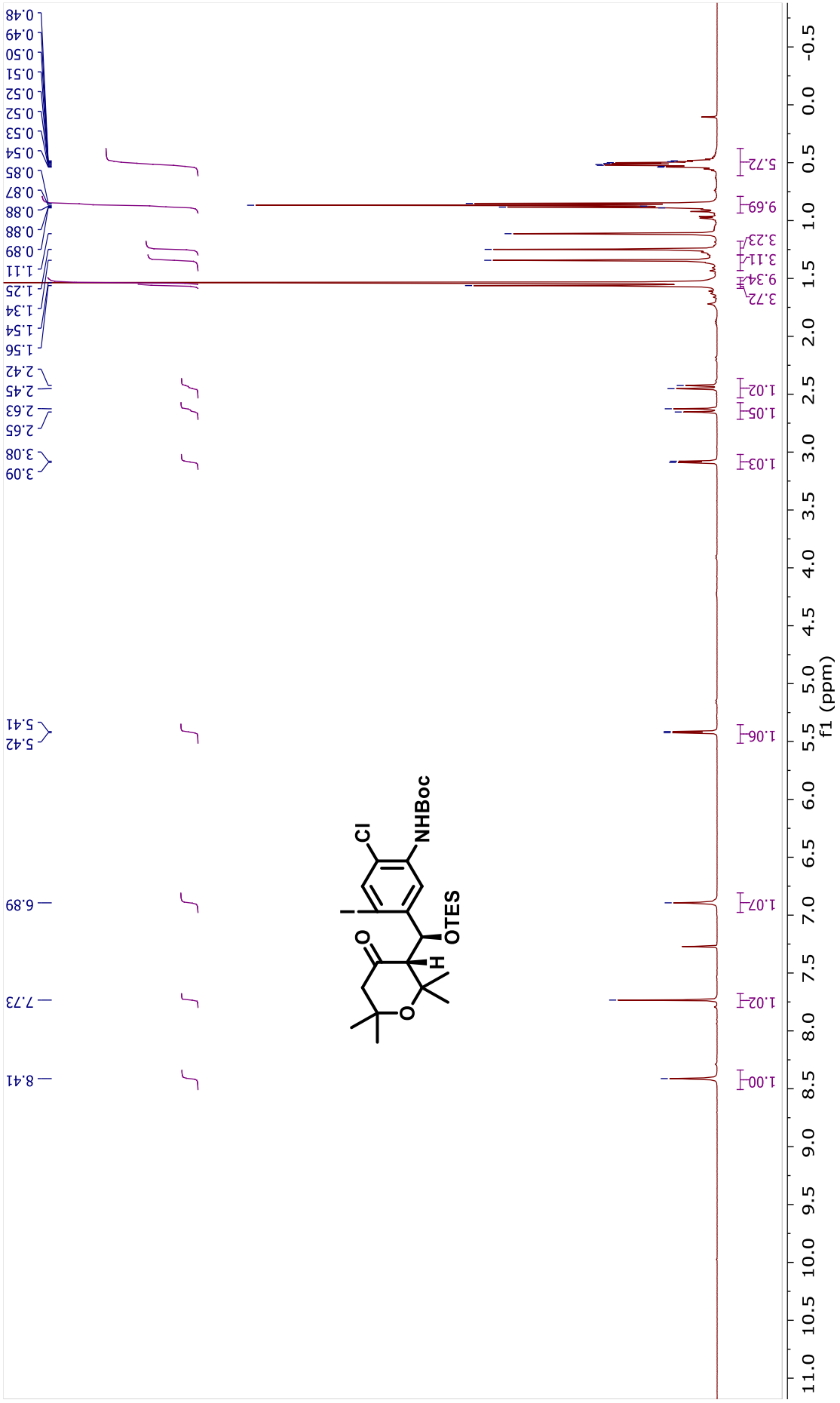


^{13}C NMR of Synthetic (126 MHz) **(–) -3-Sodium Salt** in CD_3OD

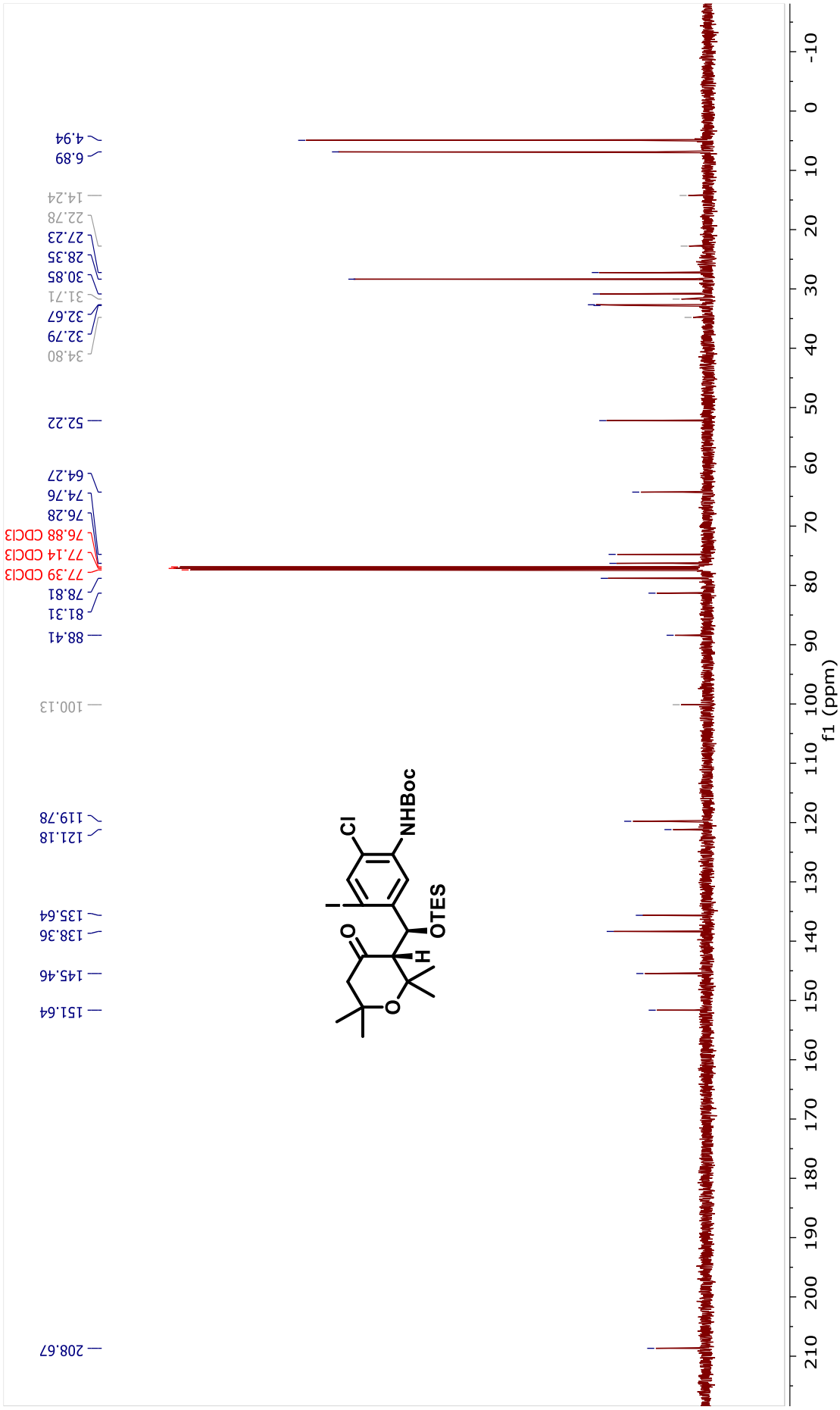
(30.3 ppm and 30.2 ppm Peak Picking Expanded View)



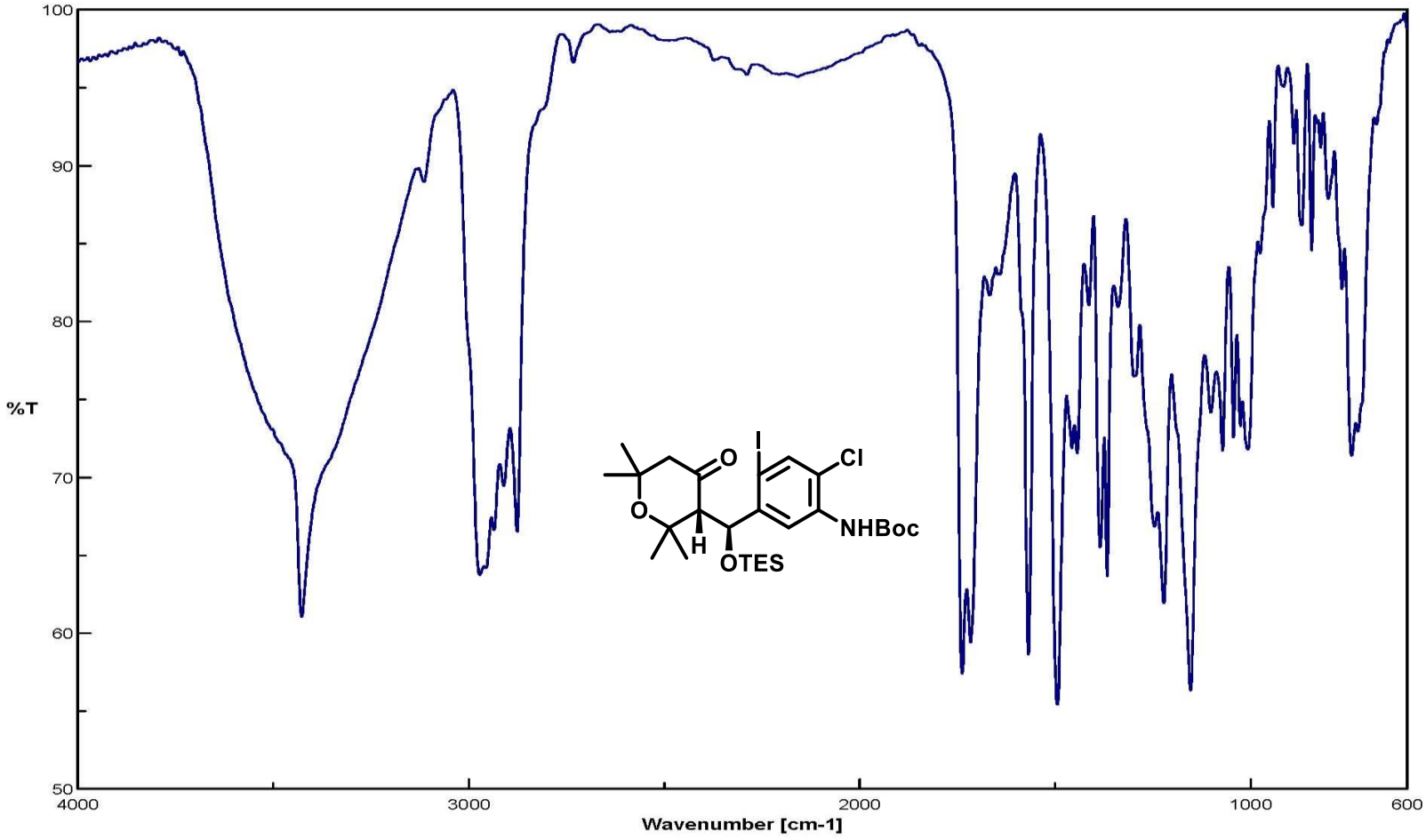
IR Spectrum of Compound **(–)-3-Sodium Salt**



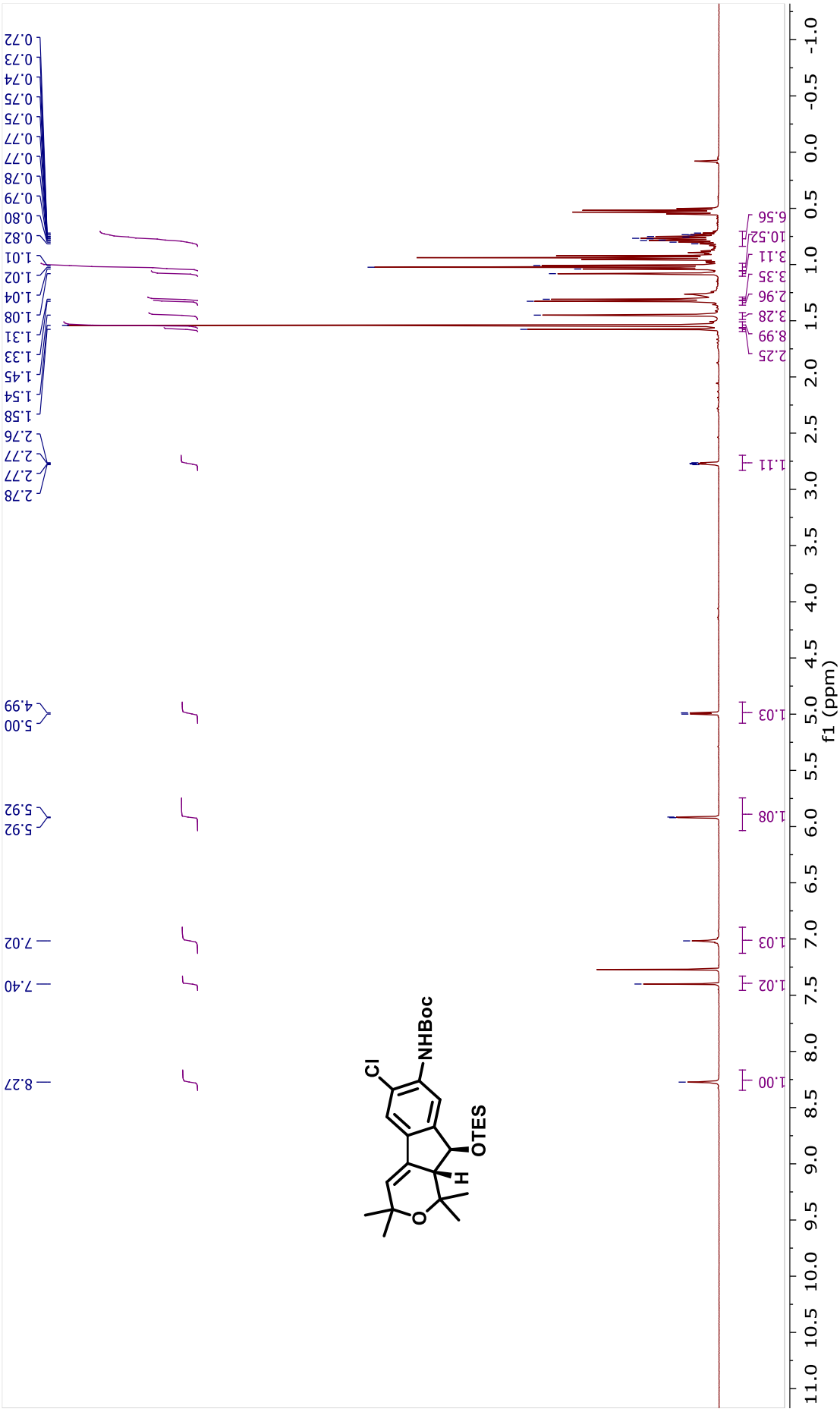
^{1}H NMR (500 MHz) Spectrum of Compound (–)-**77** in $CDCl_3$



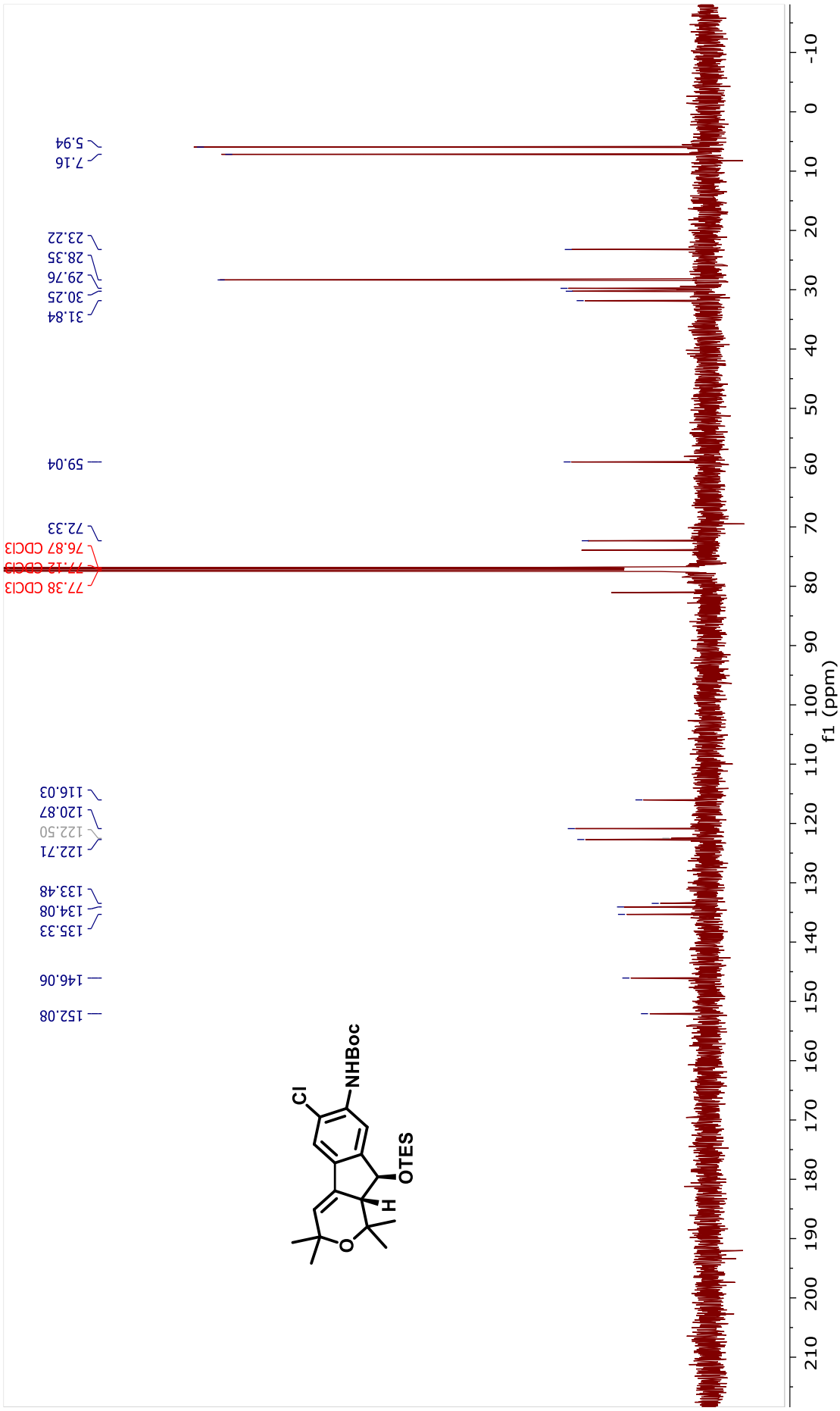
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-77** in $CDCl_3$



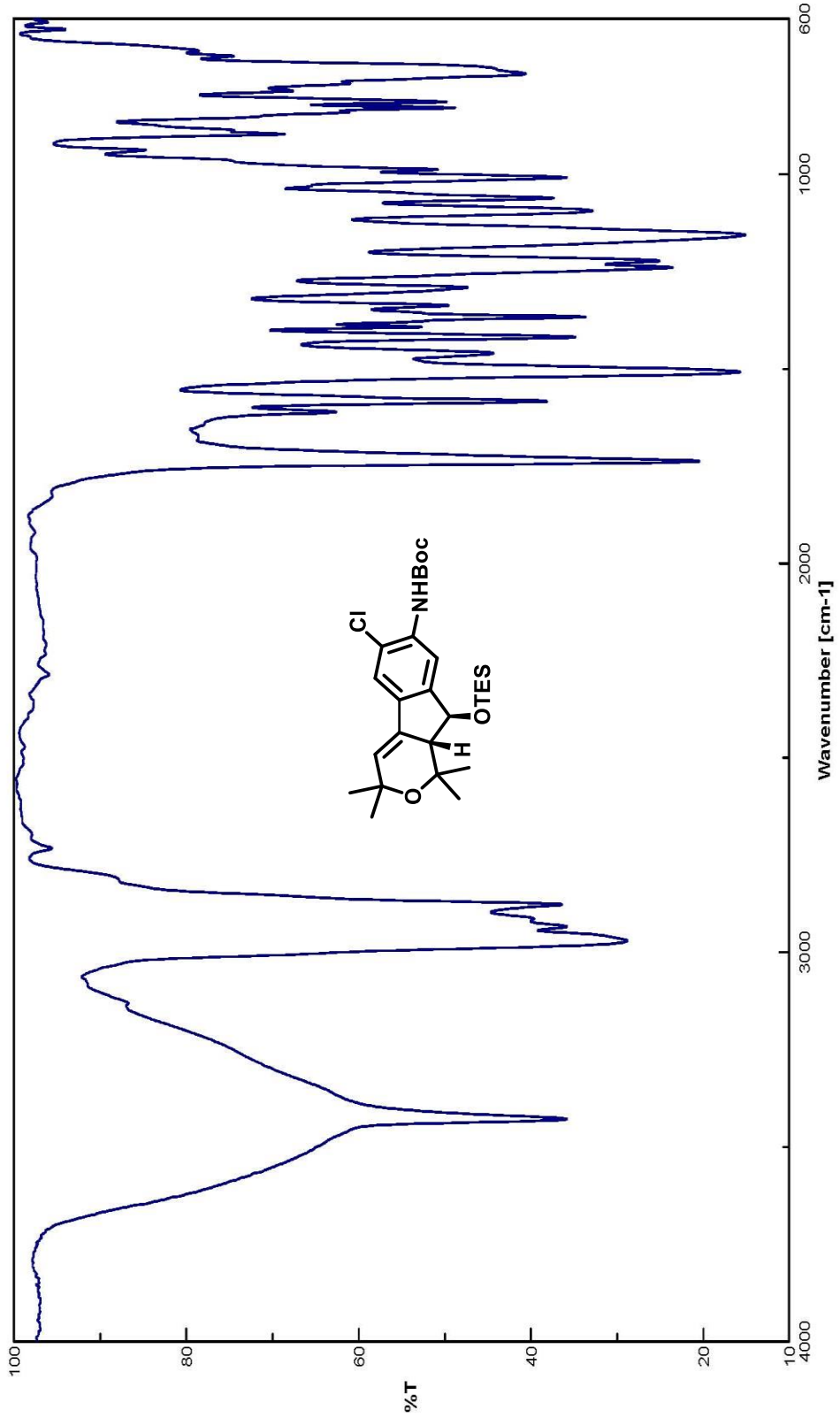
IR Spectrum of Compound(–)-77



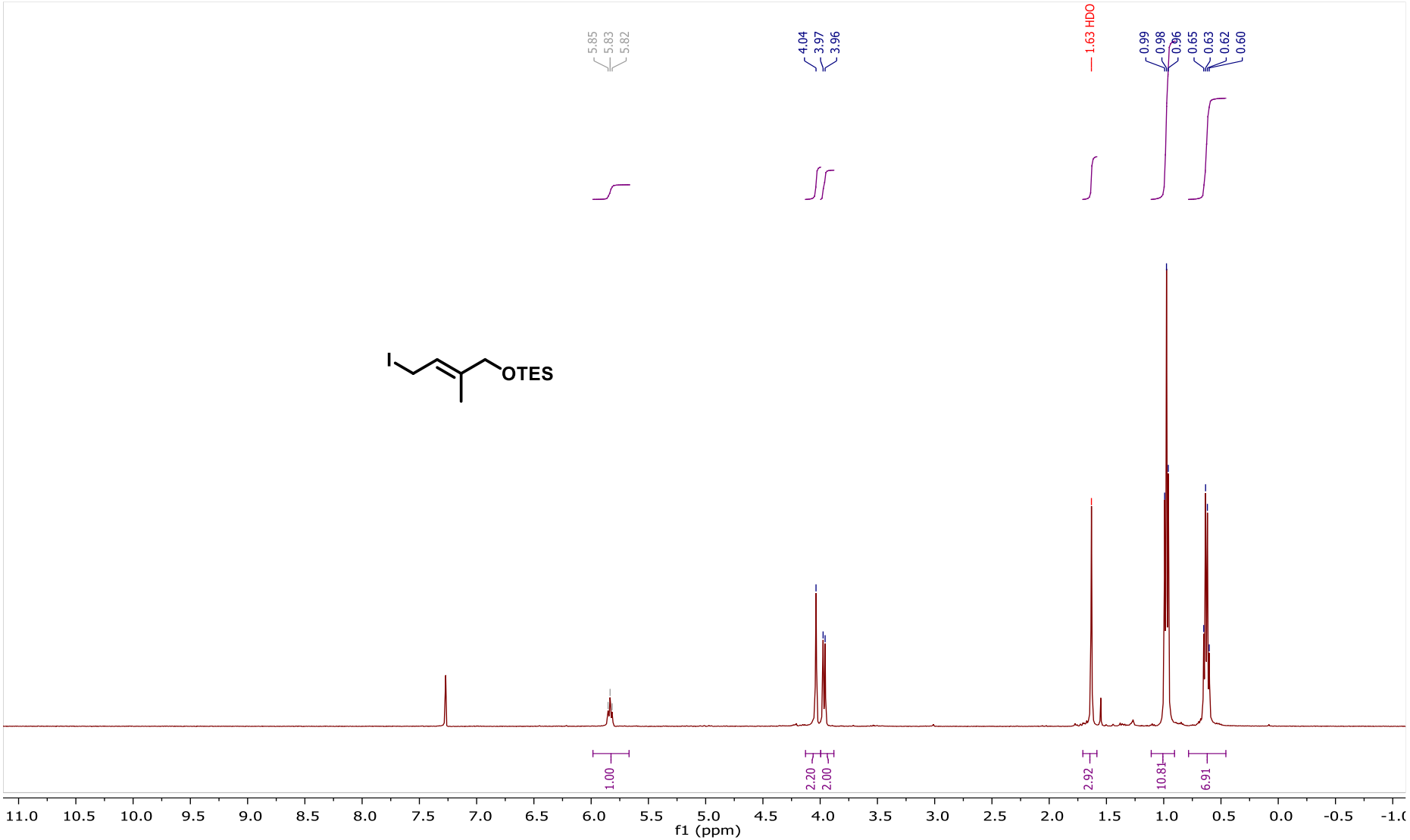
^{1}H NMR (500 MHz) Spectrum of Compound (–)-**79** in $CDCl_3$



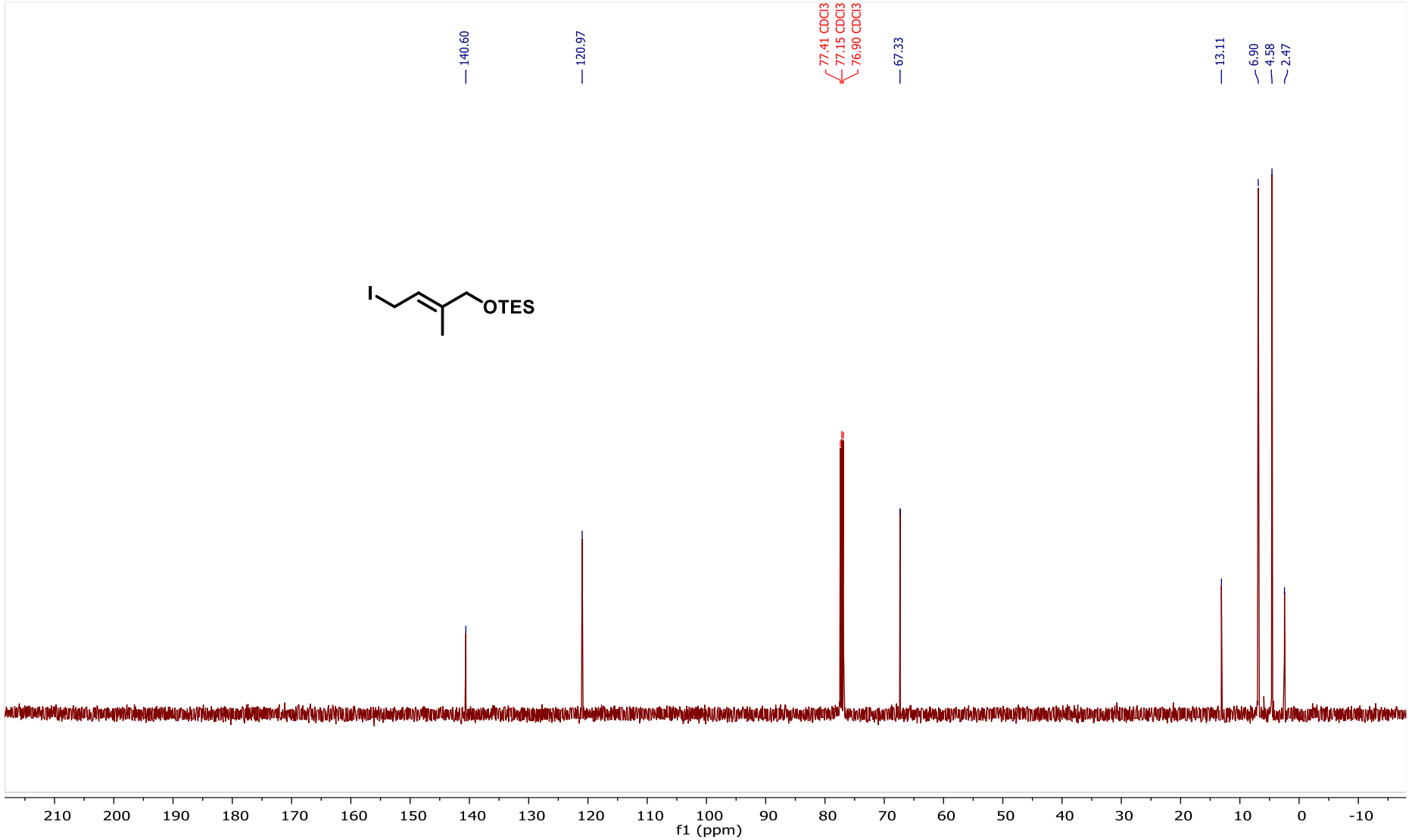
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-79** in $CDCl_3$



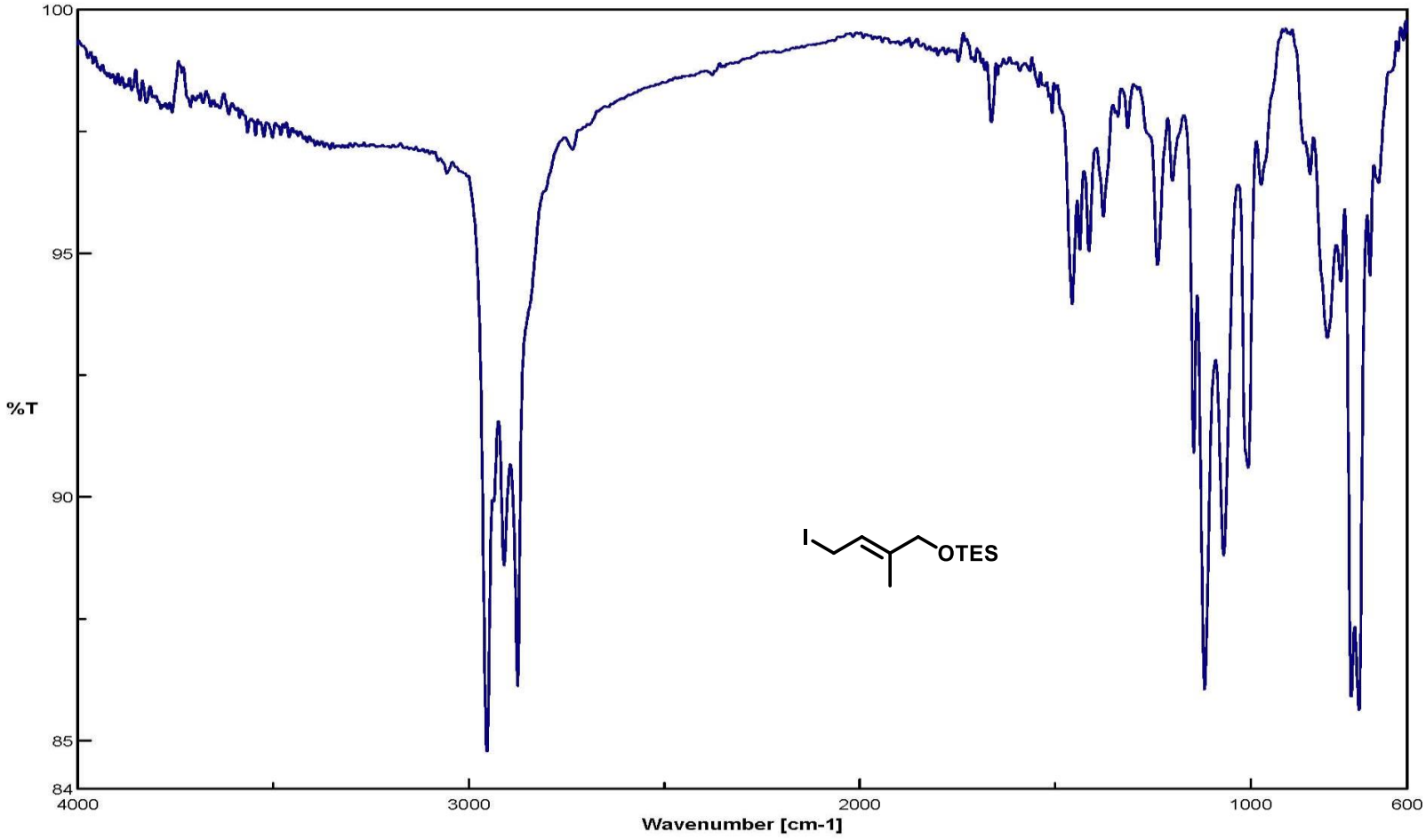
IR Spectrum of Compound (–)-**79**



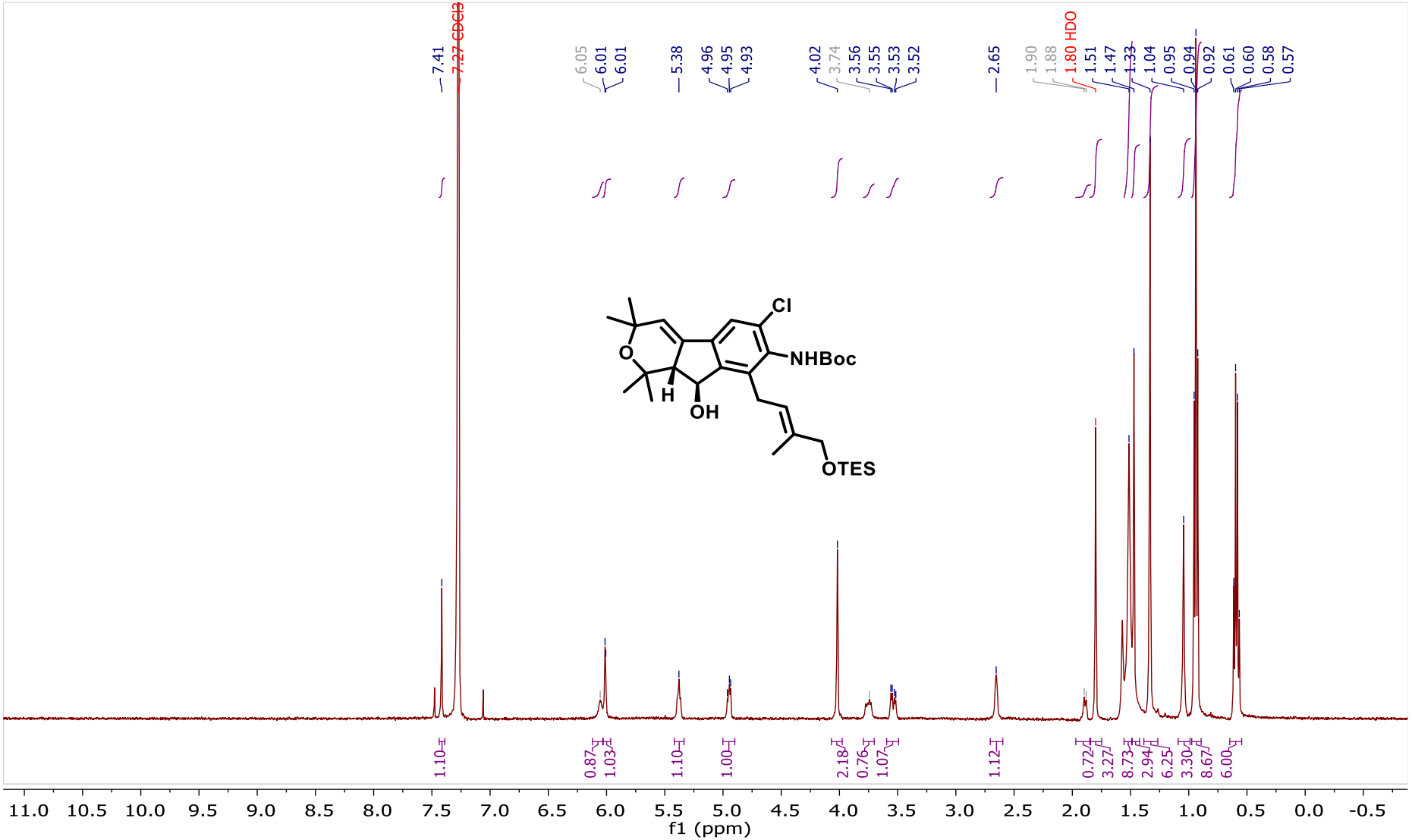
^{1}H NMR (500 MHz) Spectrum of Compound **80** in $CDCl_3$



^{13}C NMR (126 MHz) Spectrum of Compound **80** in $CDCl_3$

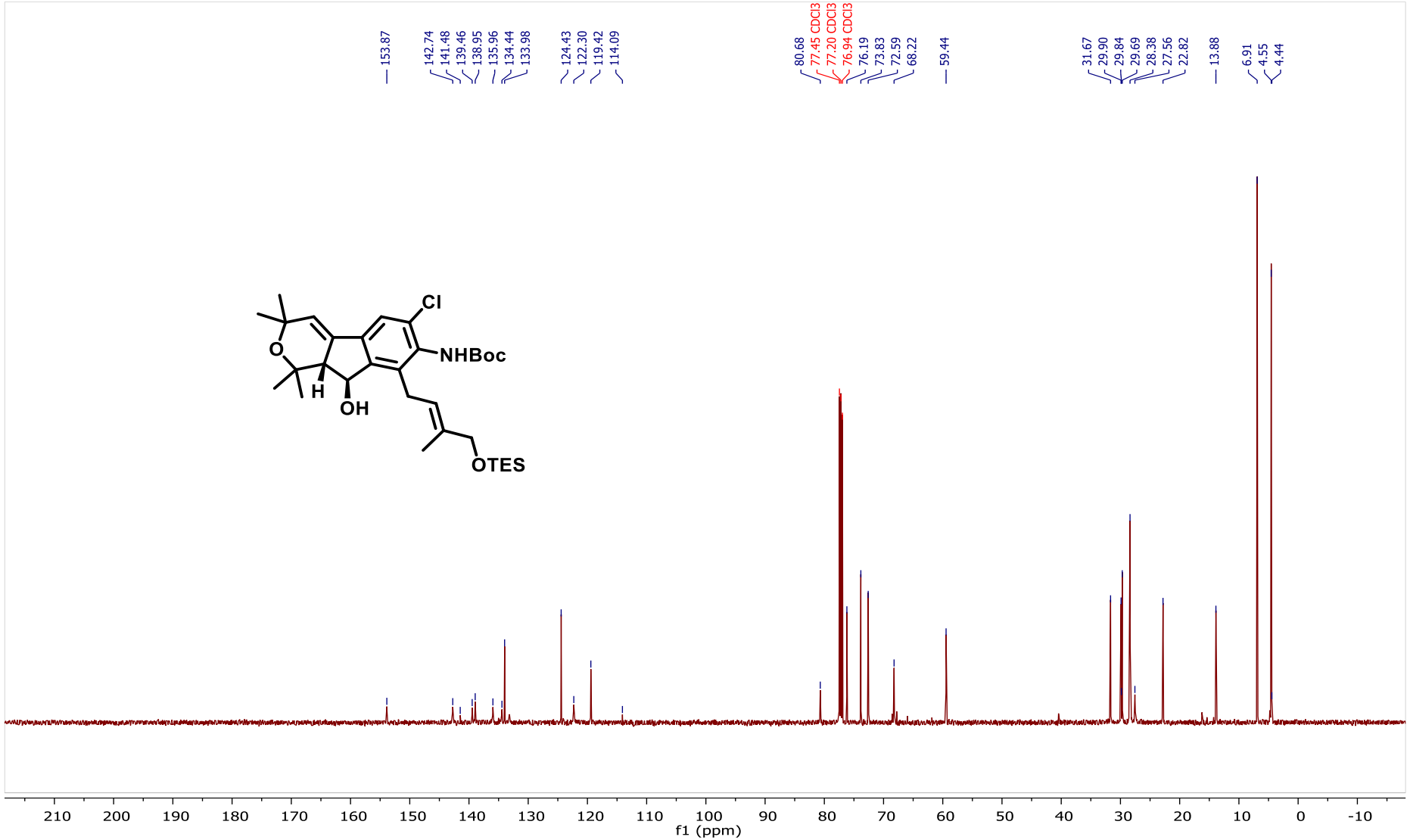


IR Spectrum of Compound **80**



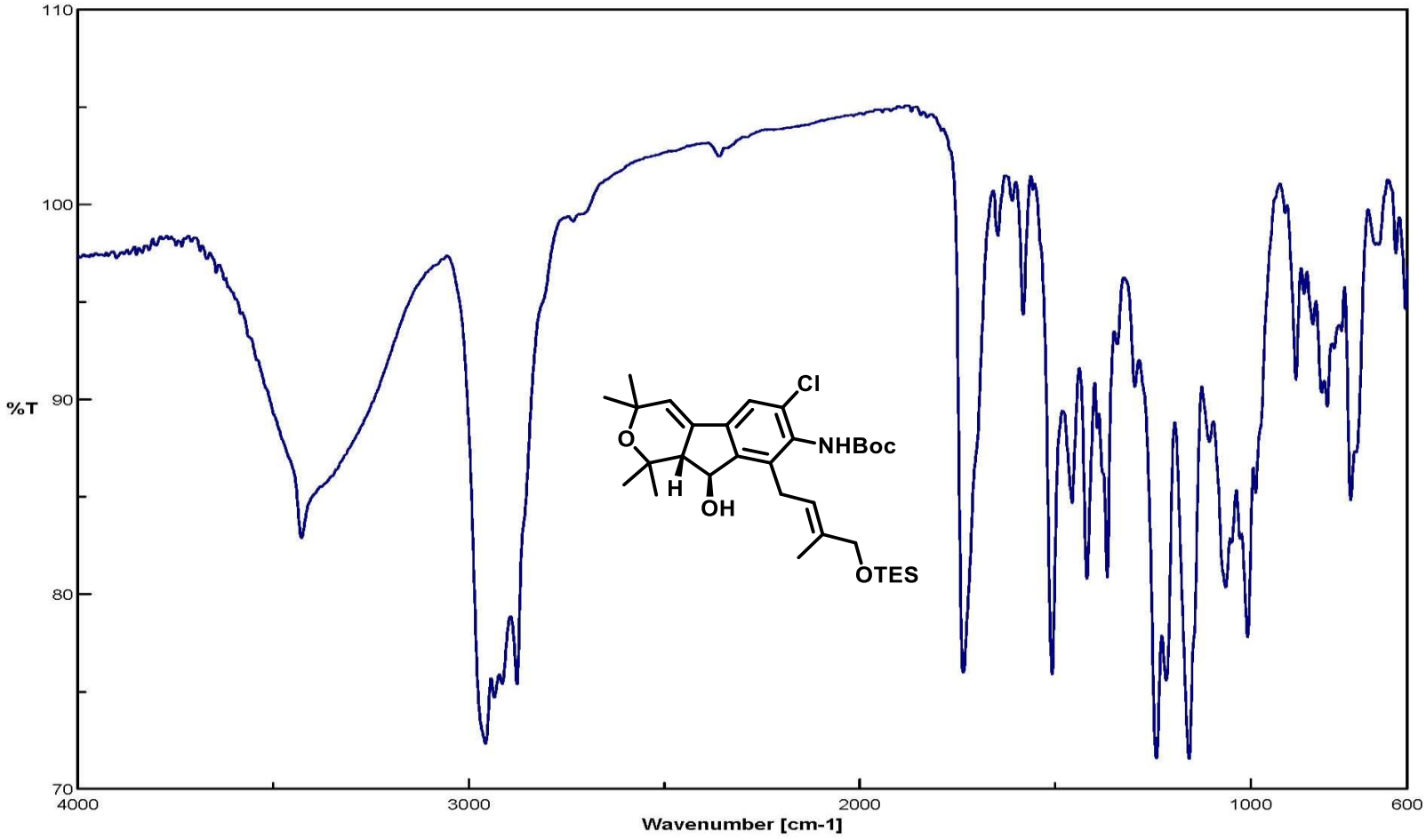
^{1}H NMR (500 MHz) Spectrum of Compound **(–)-81** in $CDCl_3$

(containing rotamers)



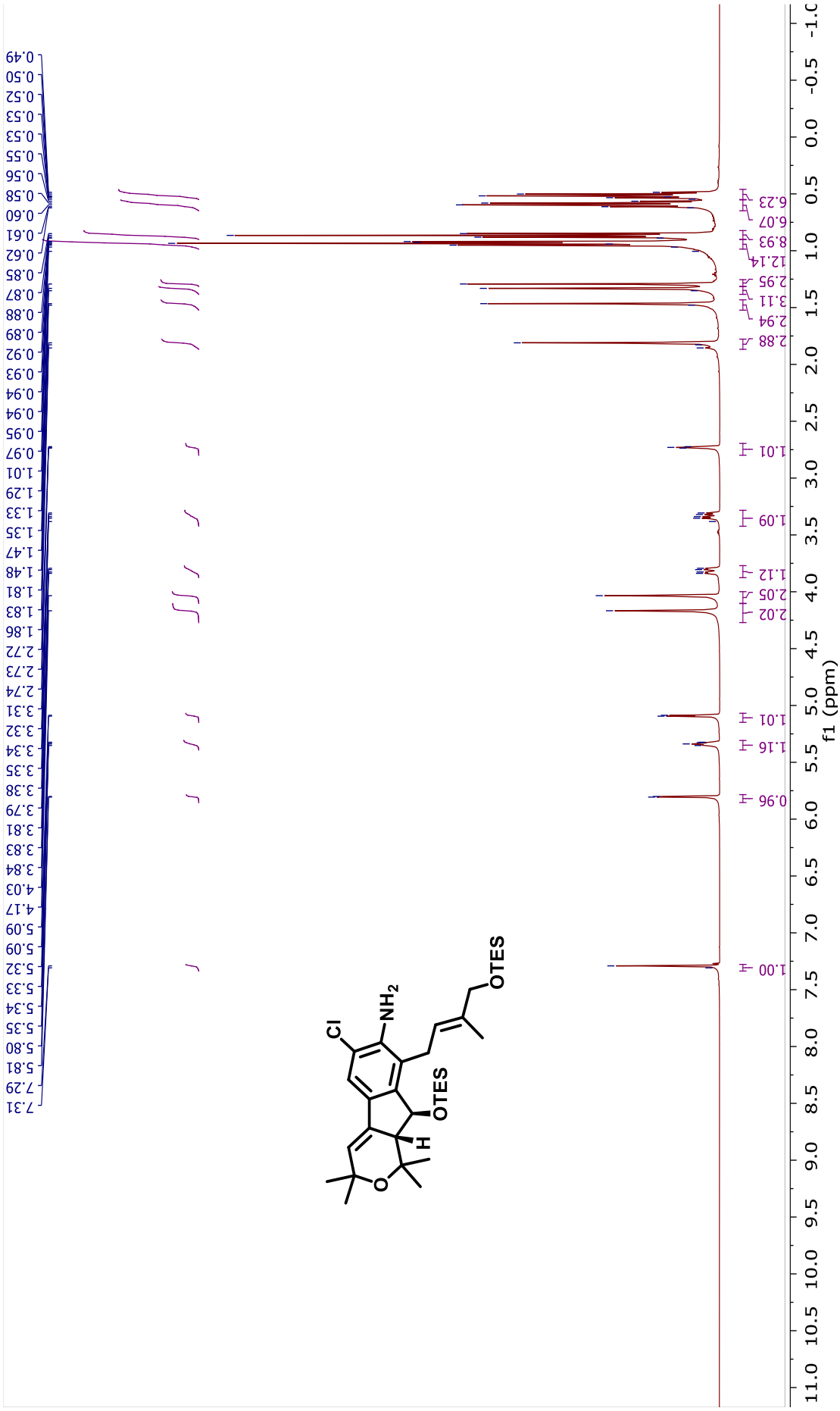
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-81** in $CDCl_3$

(containing rotamers)

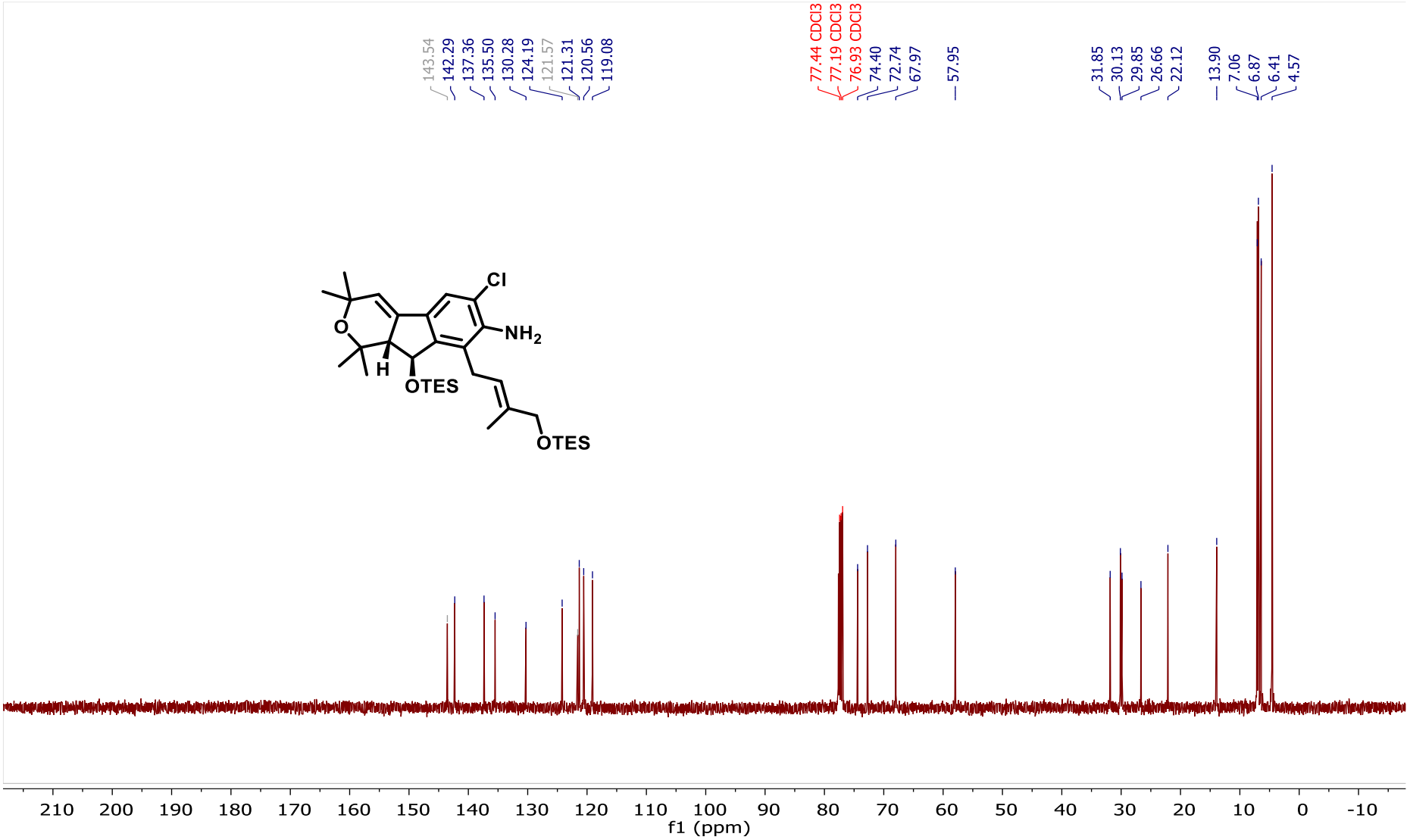


IR Spectrum of Compound **(–)-81**

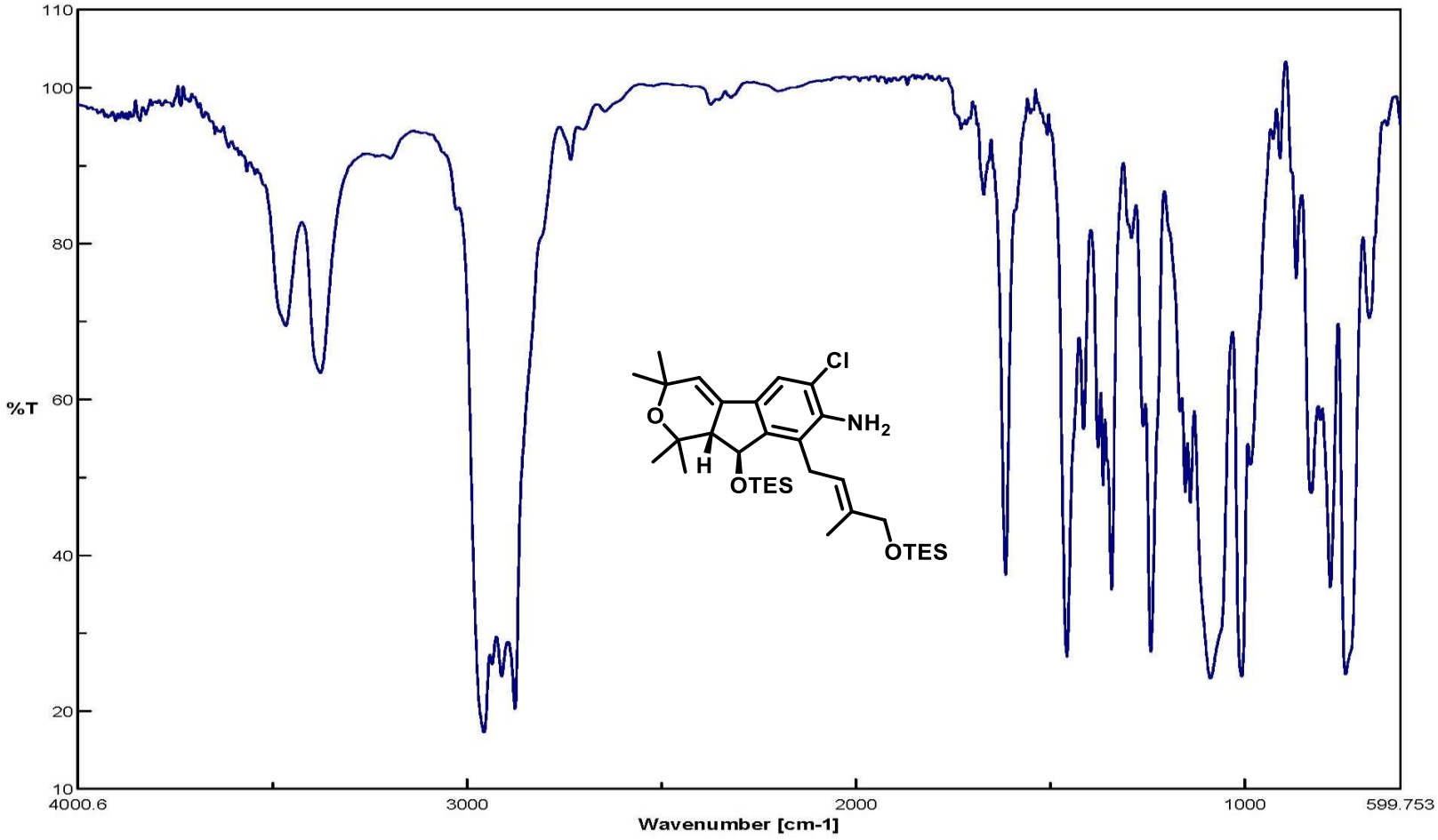
(containing rotamers)



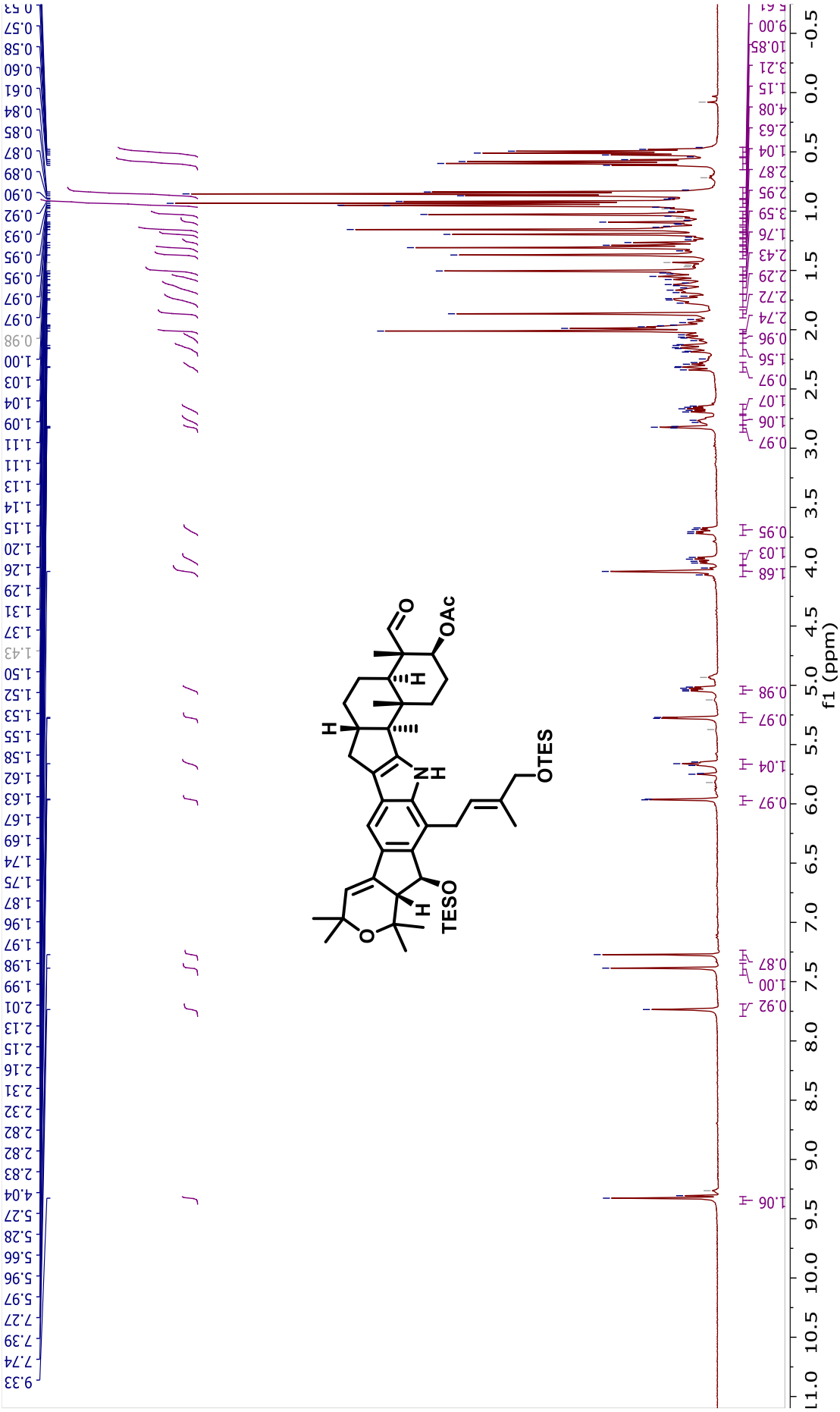
^{1}H NMR (500 MHz) Spectrum of Compound **(–)-76** in $CDCl_3$



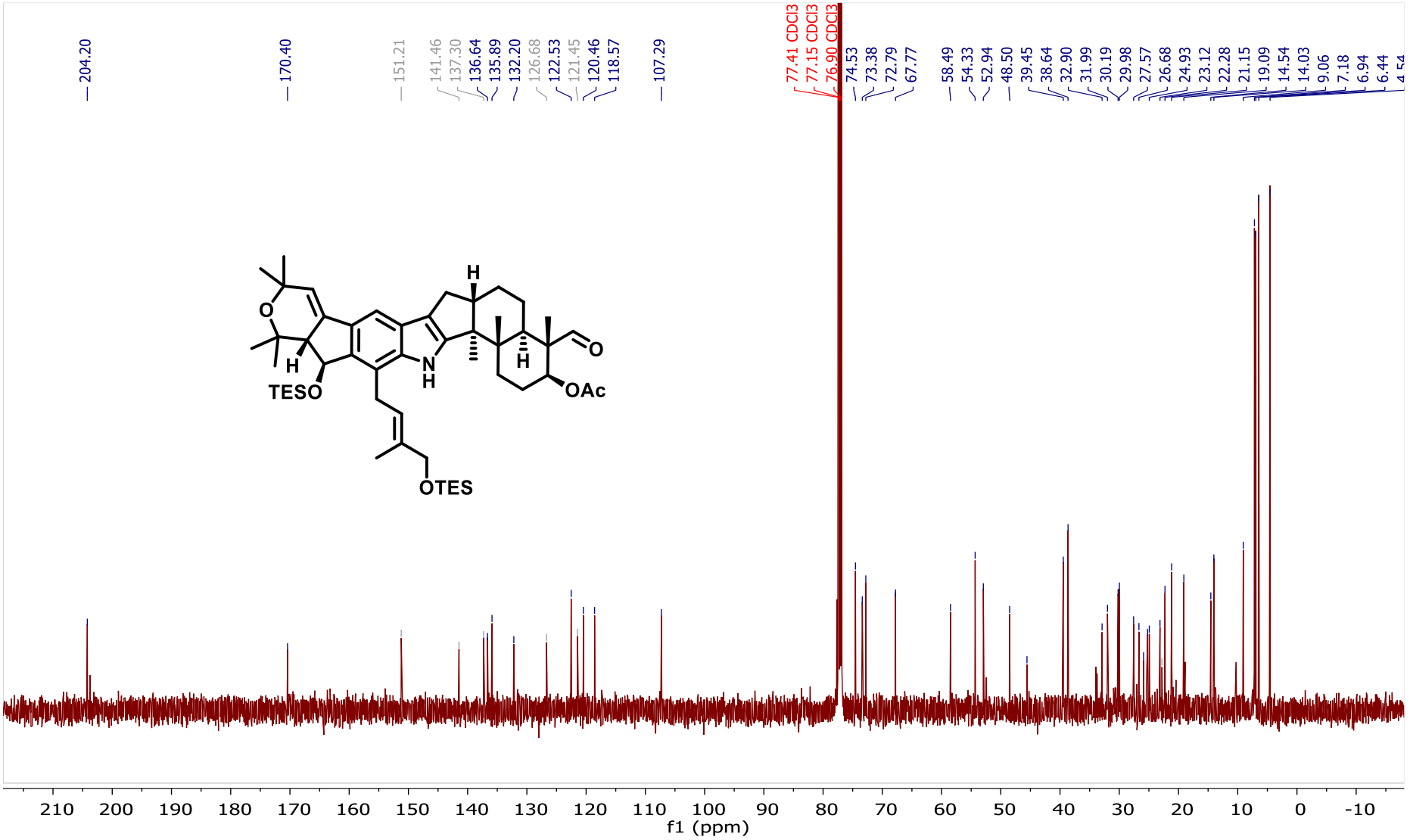
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-76** in $CDCl_3$



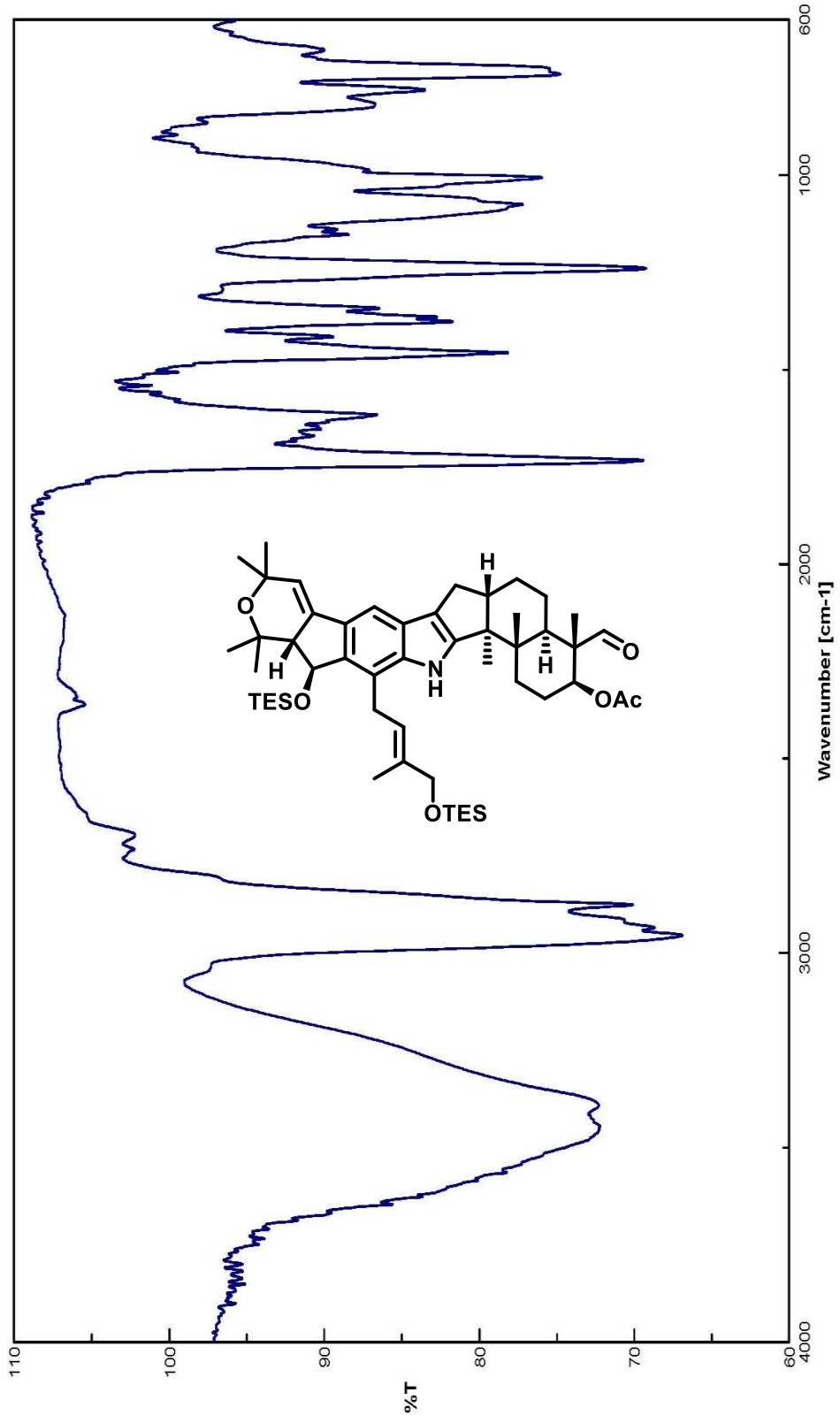
IR Spectrum of Compound **(–)-76**



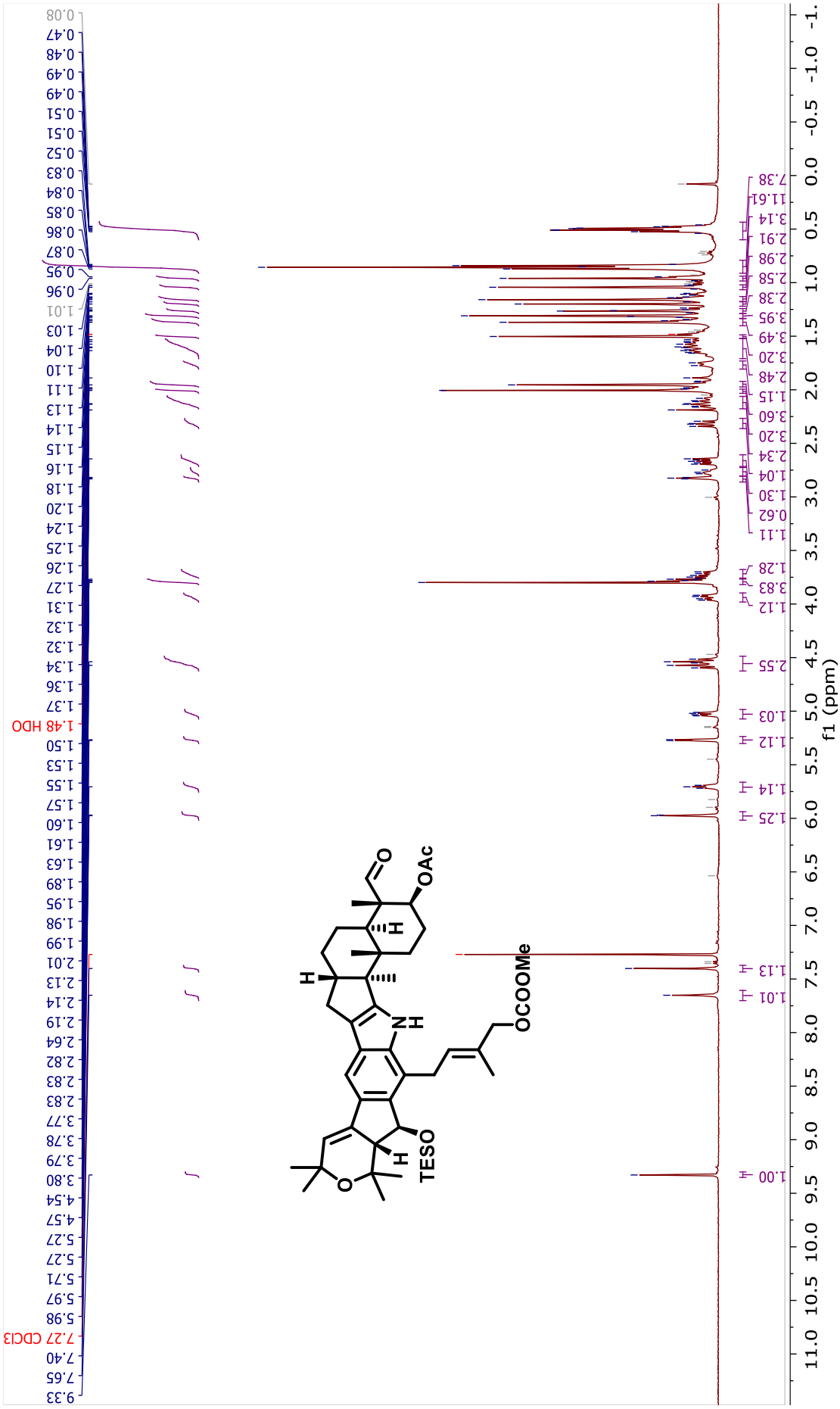
^{1}H NMR (500 MHz) Spectrum of Compound **(+)-82** in $CDCl_3$



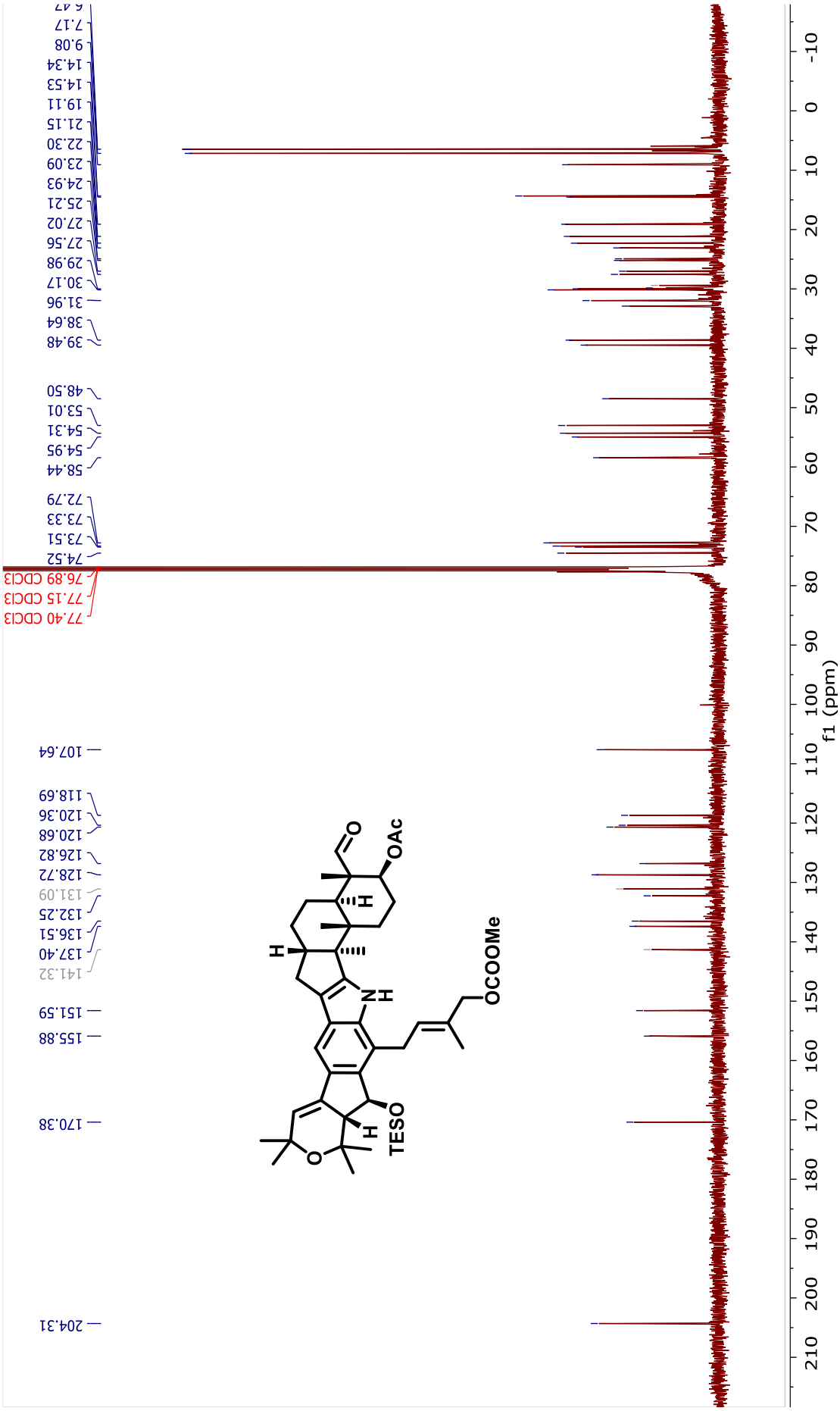
^{13}C NMR (126 MHz) Spectrum of Compound **(+)-82** in $CDCl_3$



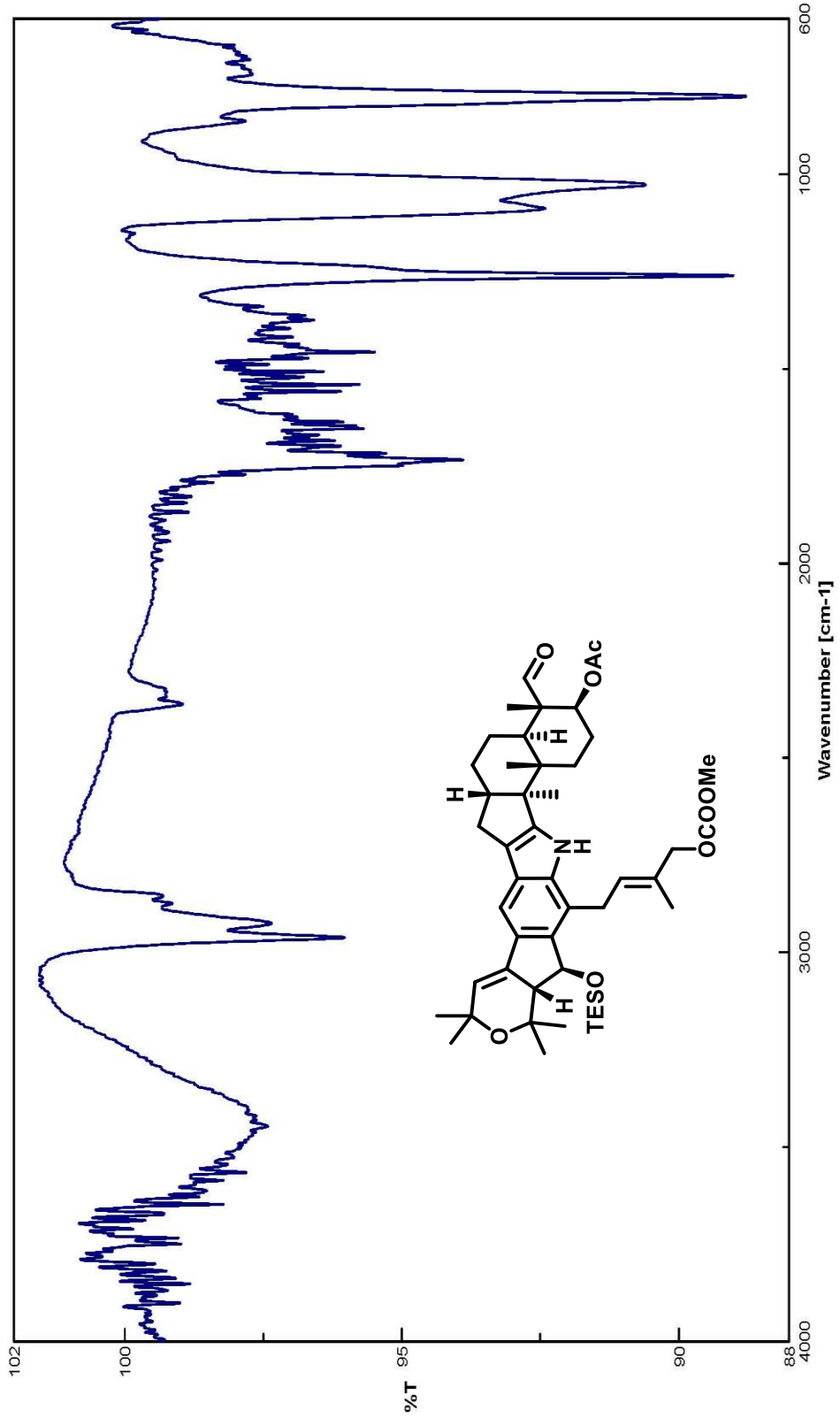
IR Spectrum of Compound (+)-82



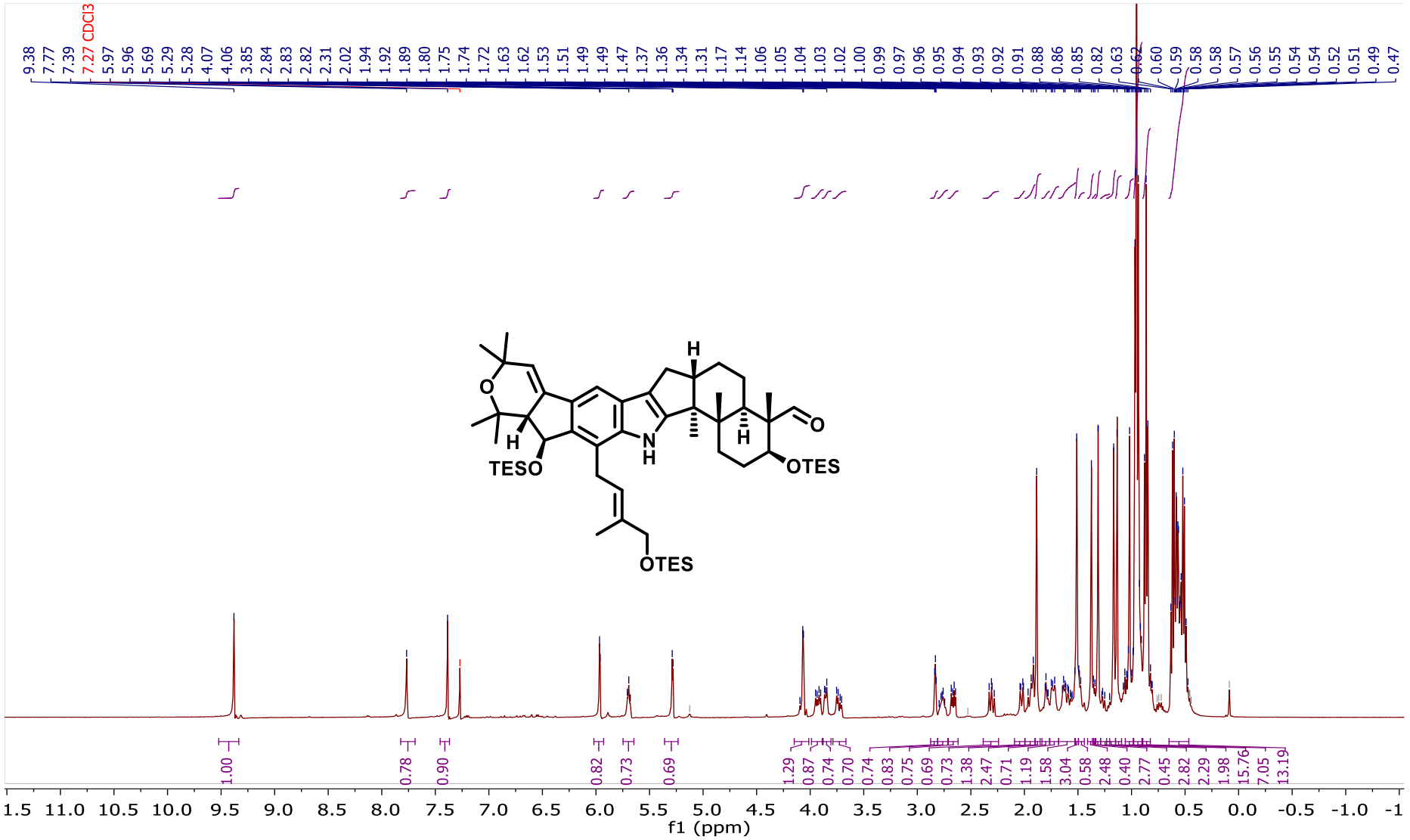
^{1}H NMR (500 MHz) Spectrum of Compound **(–)-75** in $CDCl_3$



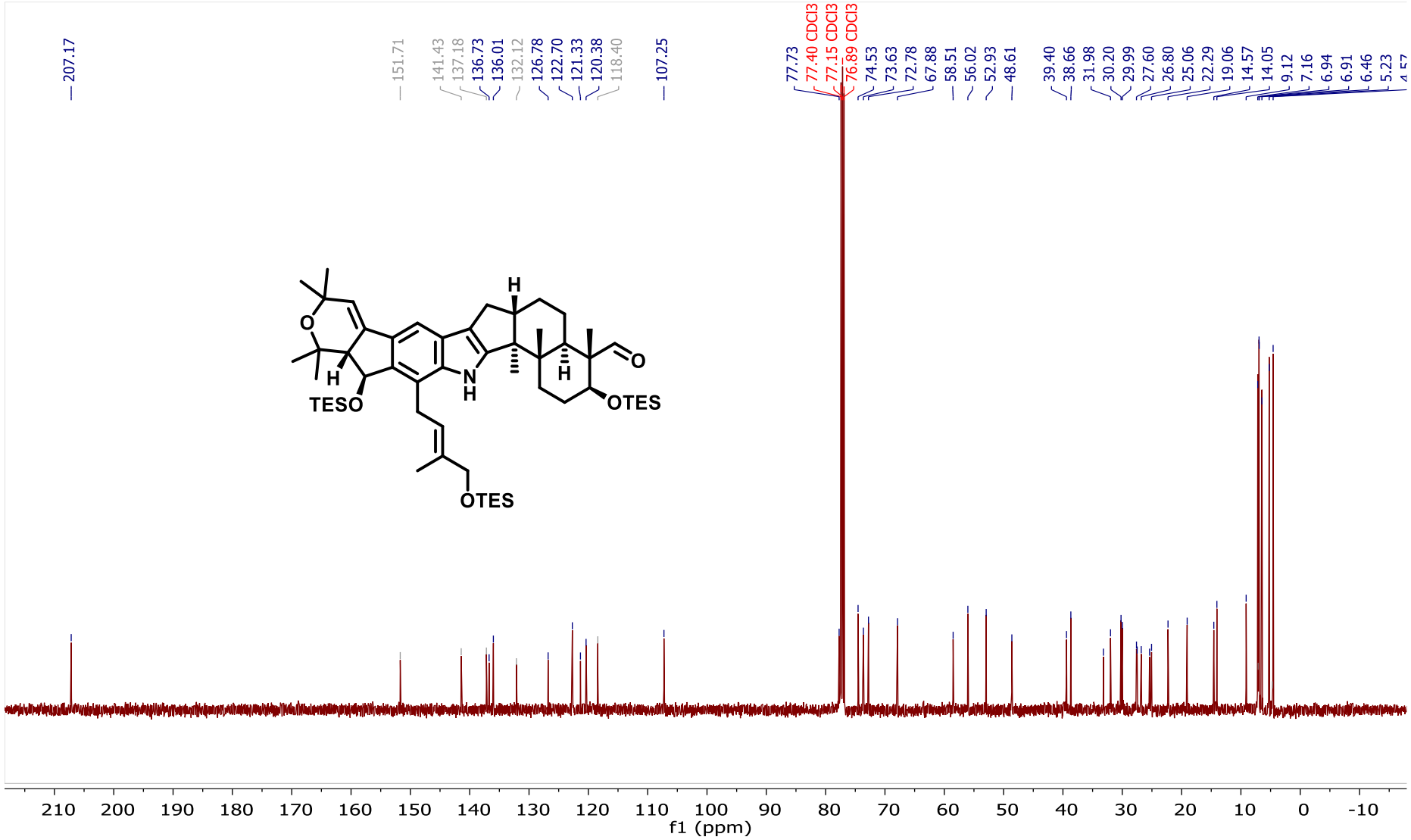
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-75** in $CDCl_3$



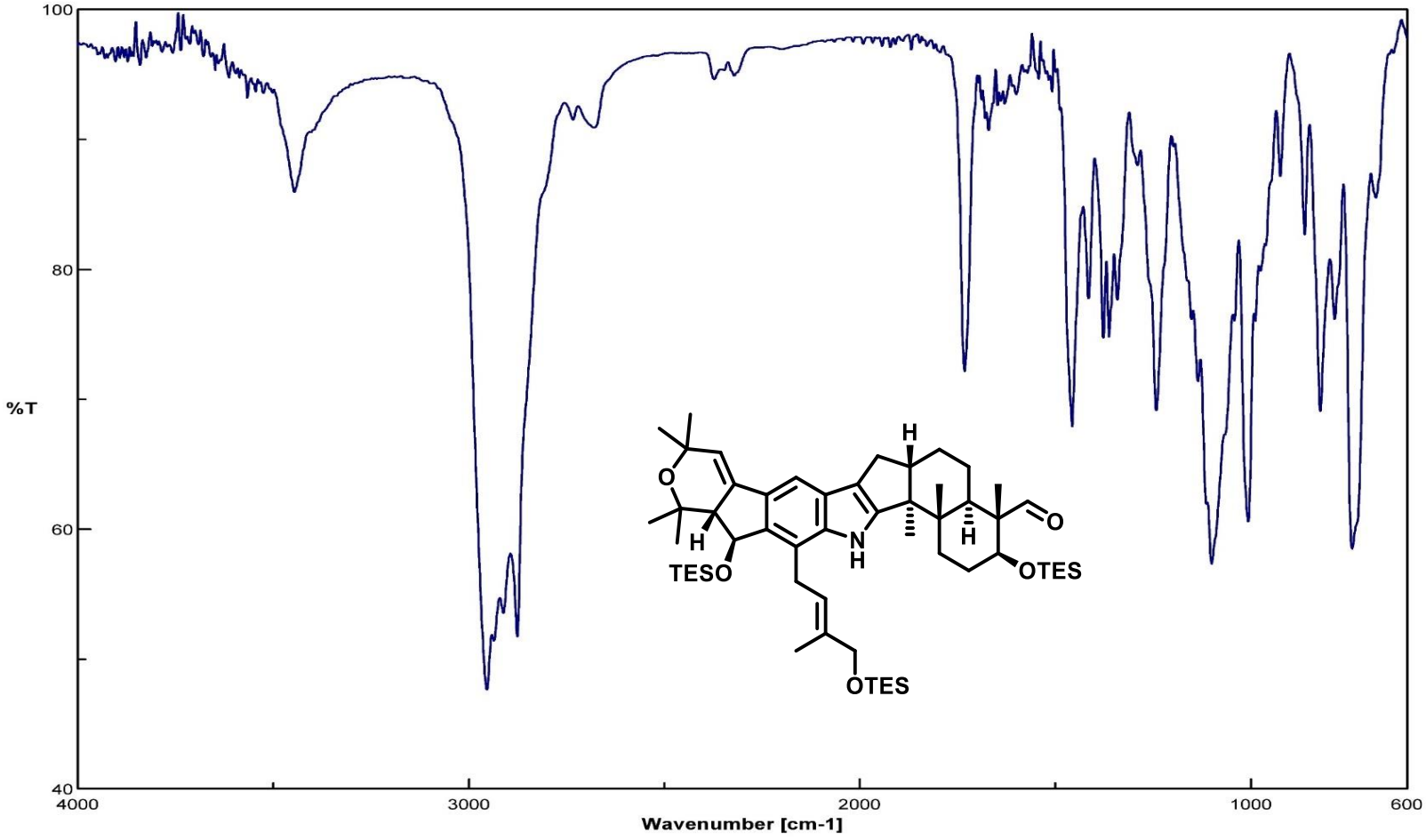
IR Spectrum of Compound (–)-75



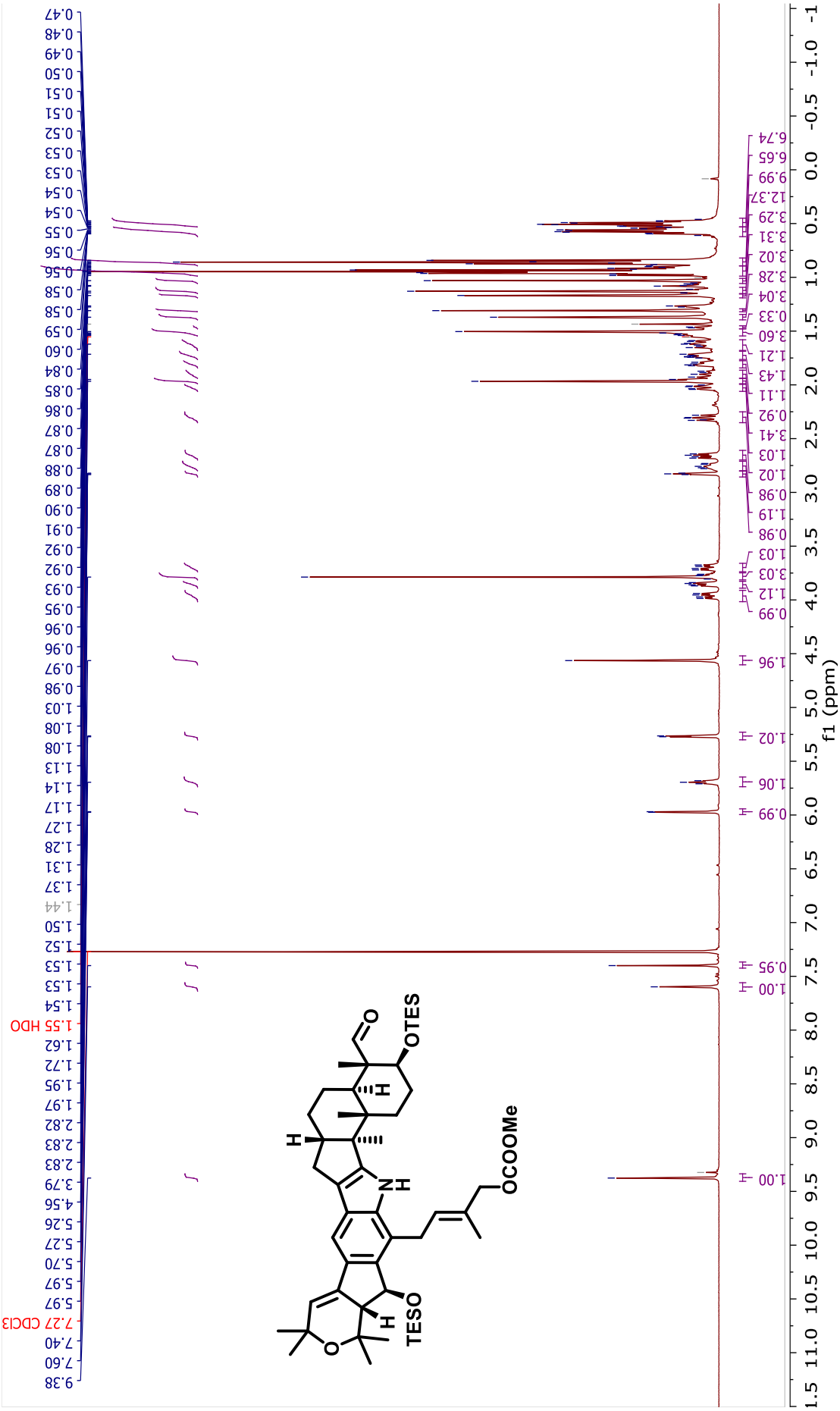
^{1}H NMR (500 MHz) Spectrum of Compound **(+)-83** in $CDCl_3$



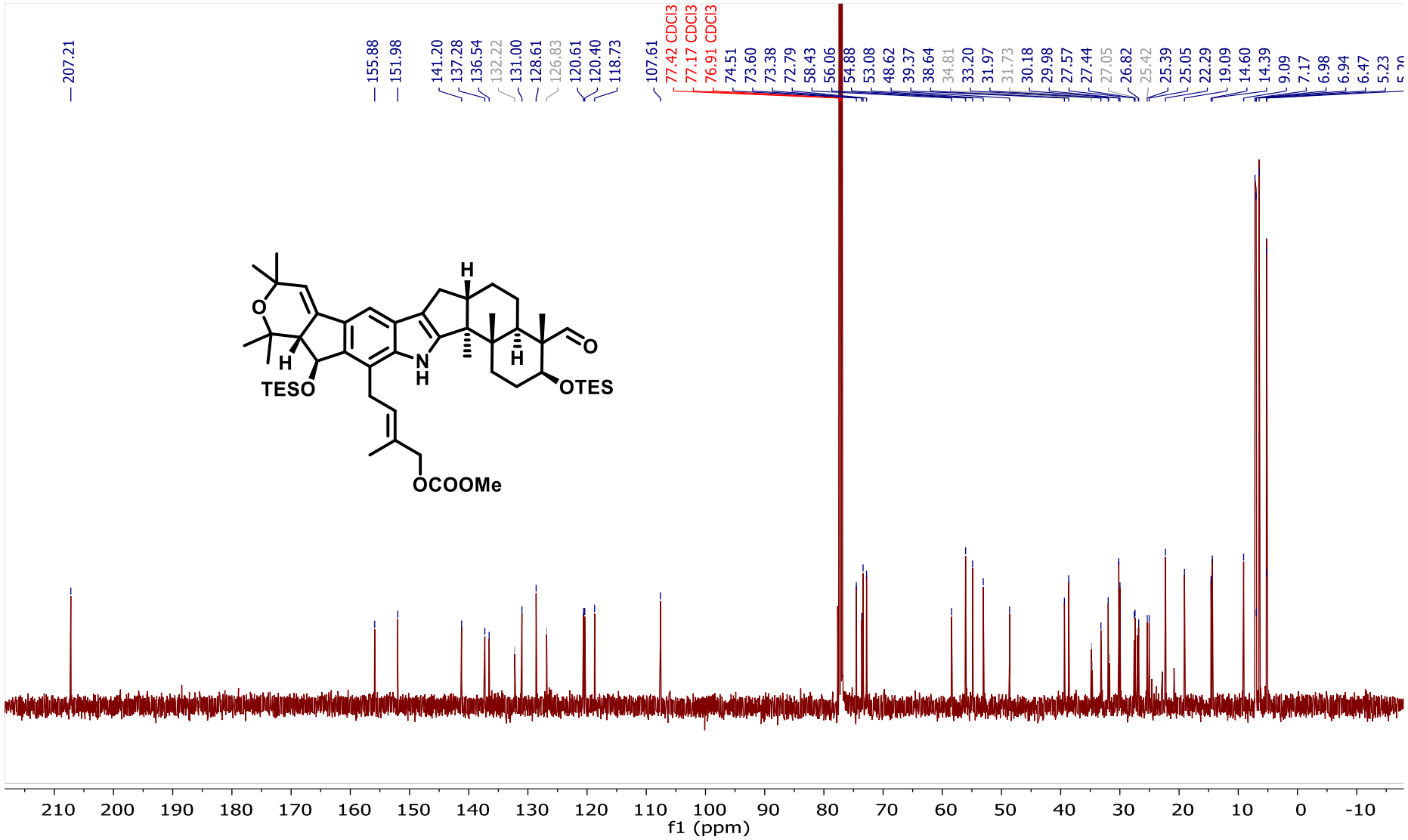
^{13}C NMR (126 MHz) Spectrum of Compound **(+)-83** in $CDCl_3$



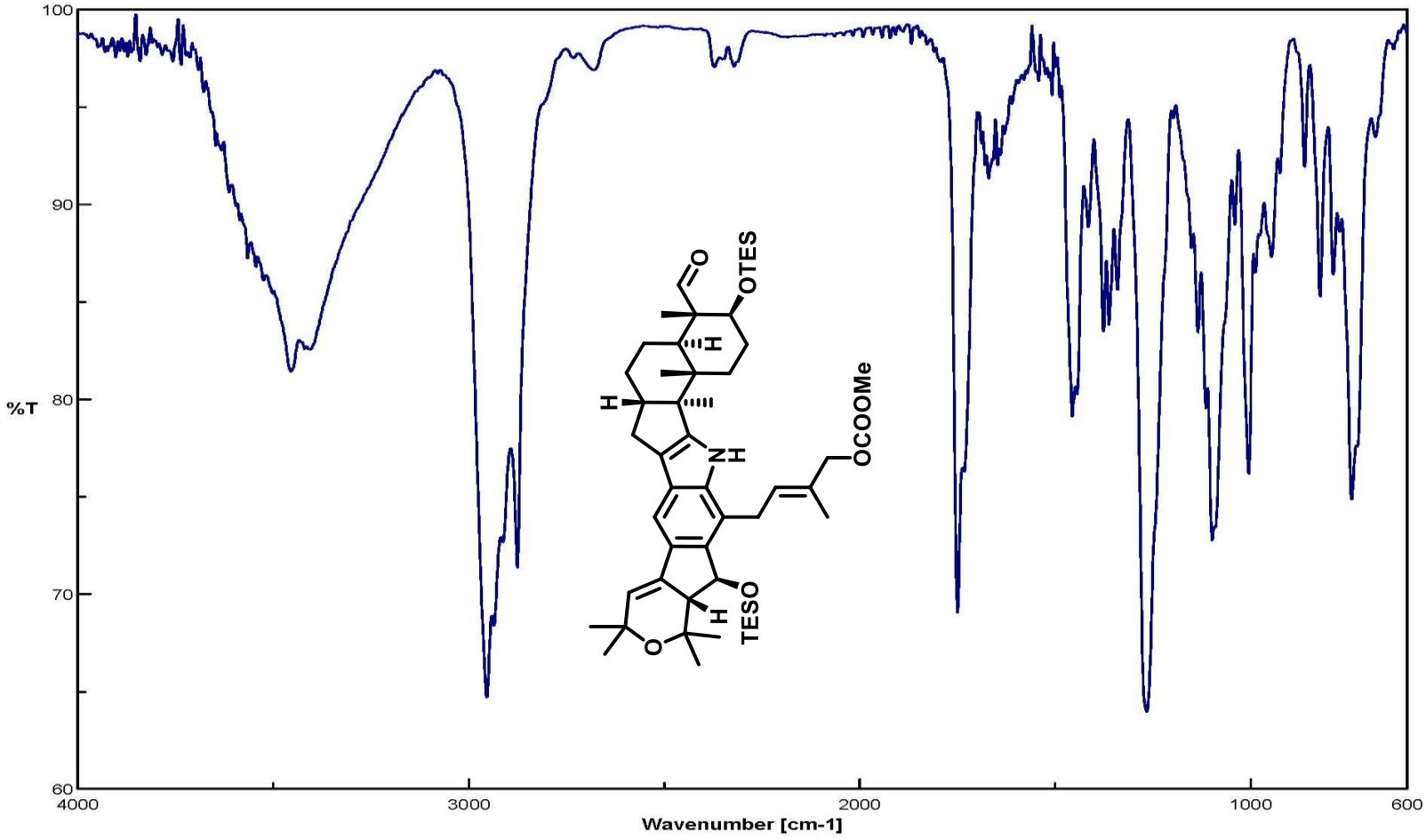
IR Spectrum of Compound **(+)-83**



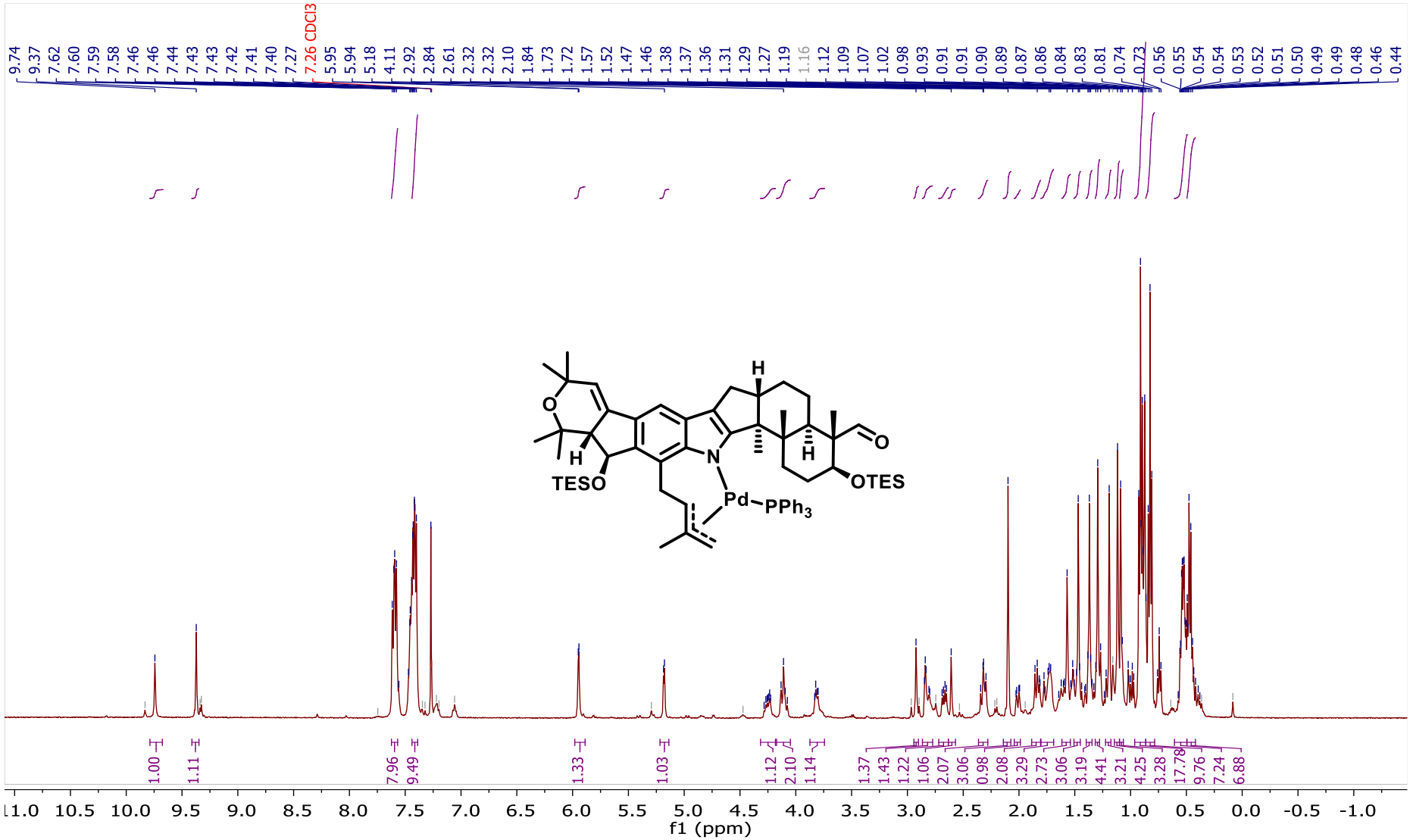
^{1}H NMR (500 MHz) Spectrum of Compound **(+)-84** in $CDCl_3$



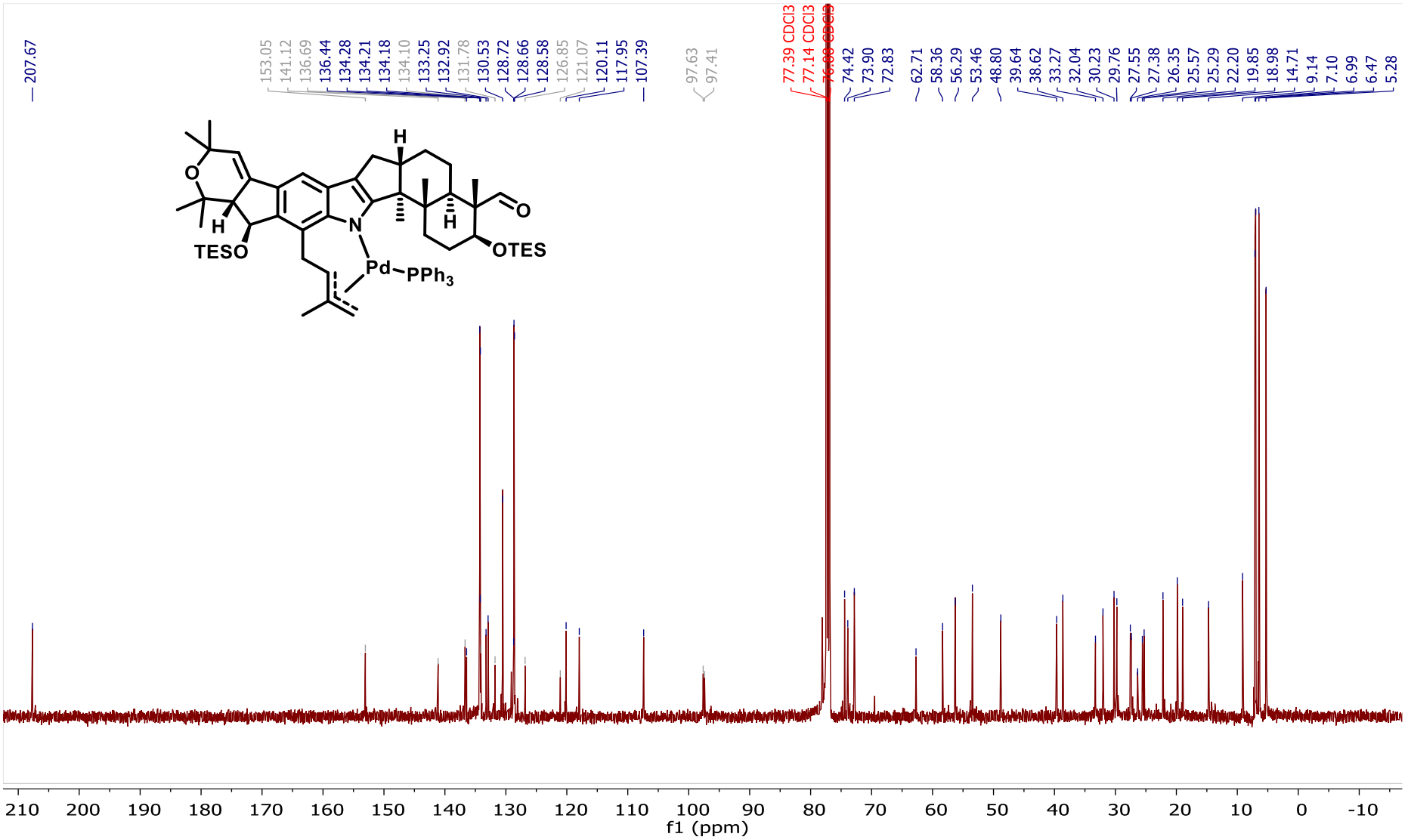
^{13}C NMR (126 MHz) Spectrum of Compound **(+)-84** in $CDCl_3$



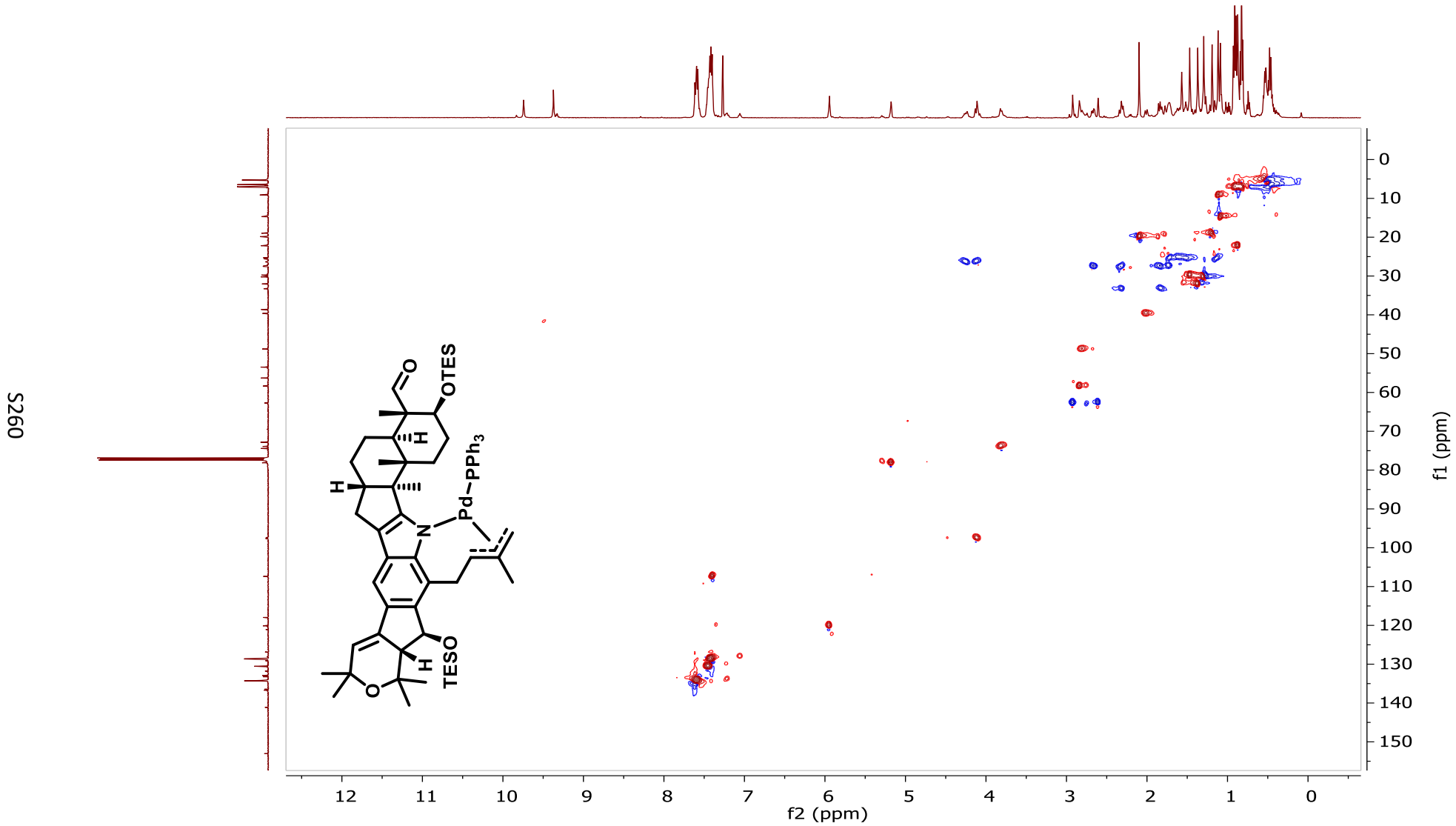
IR Spectrum of Compound **(+)-84**



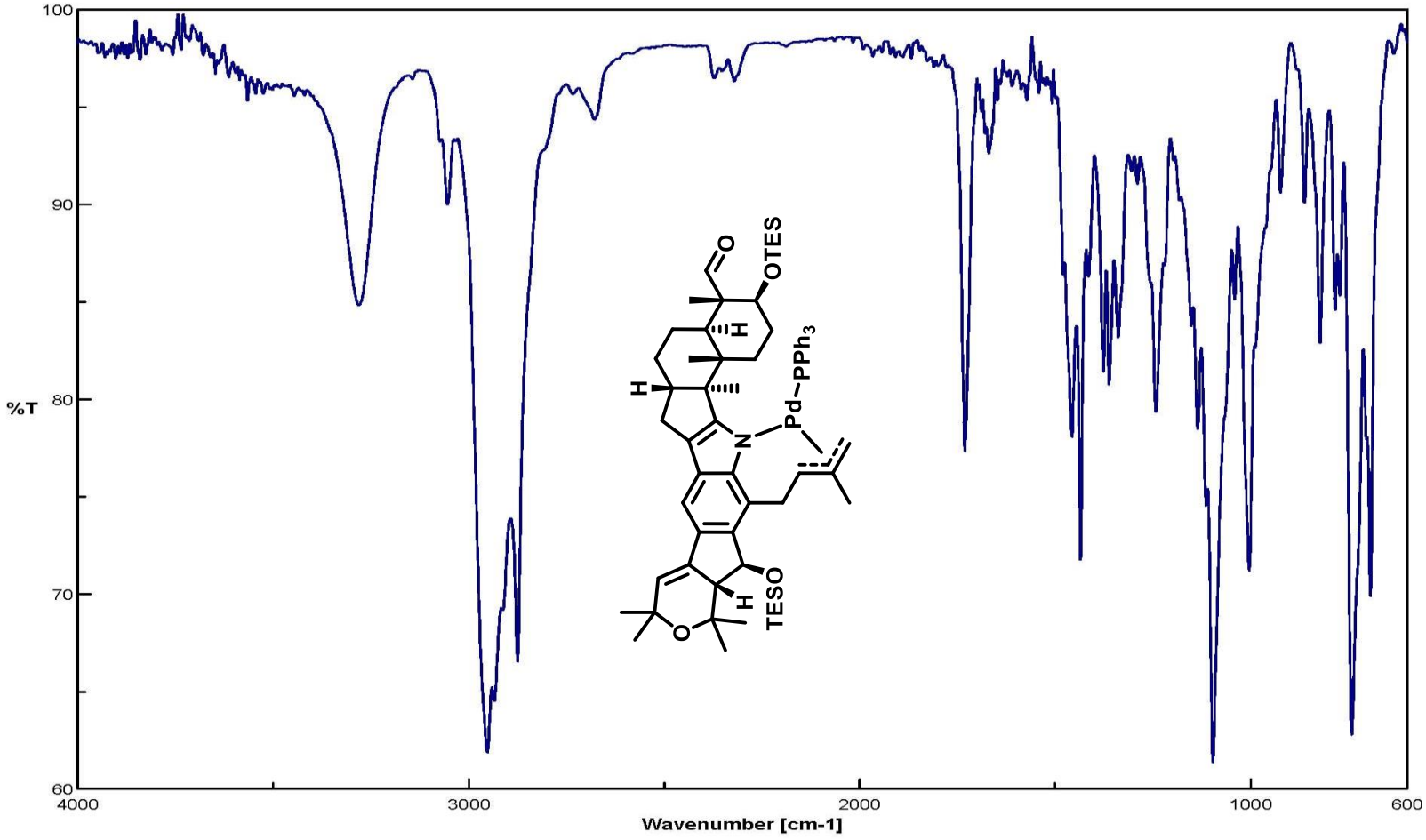
^{1}H NMR (500 MHz) Spectrum of Compound **(+)-85** in $CDCl_3$



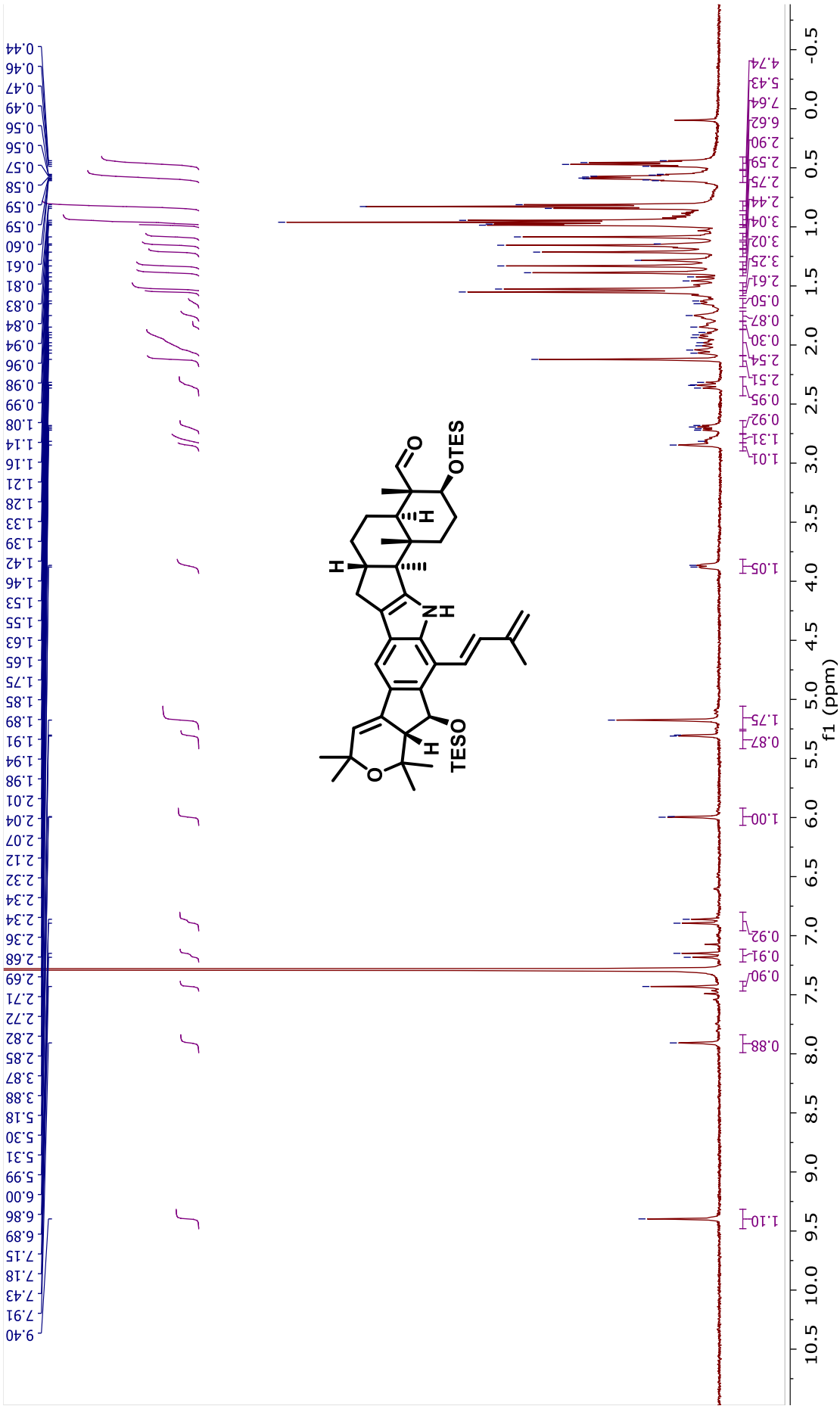
^{13}C NMR (126 MHz) Spectrum of Compound **(+)-85** in $CDCl_3$



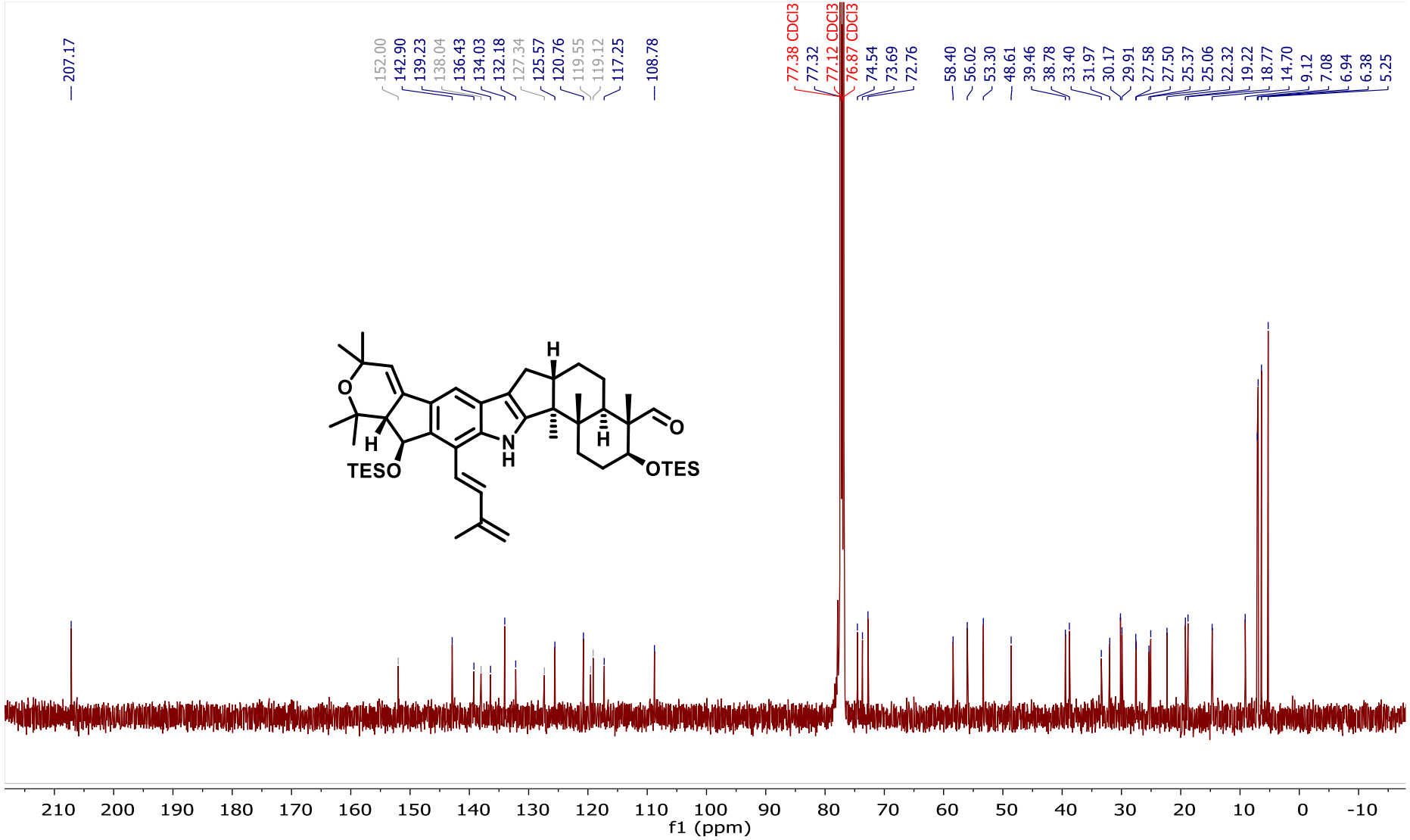
HSQC Spectrum of Compound **(+)-85** in CDCl3



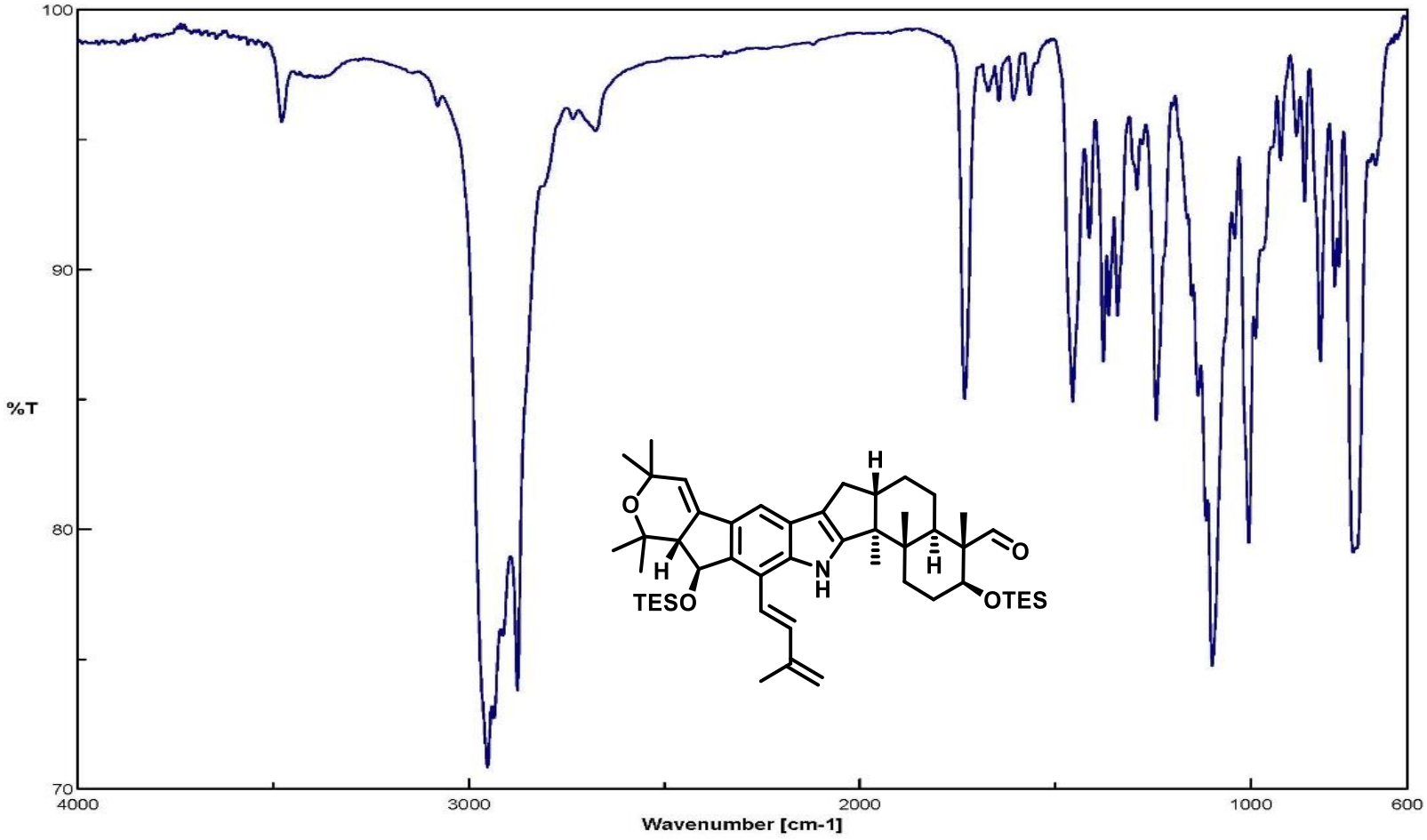
IR Spectrum of Compound **(+)-85**



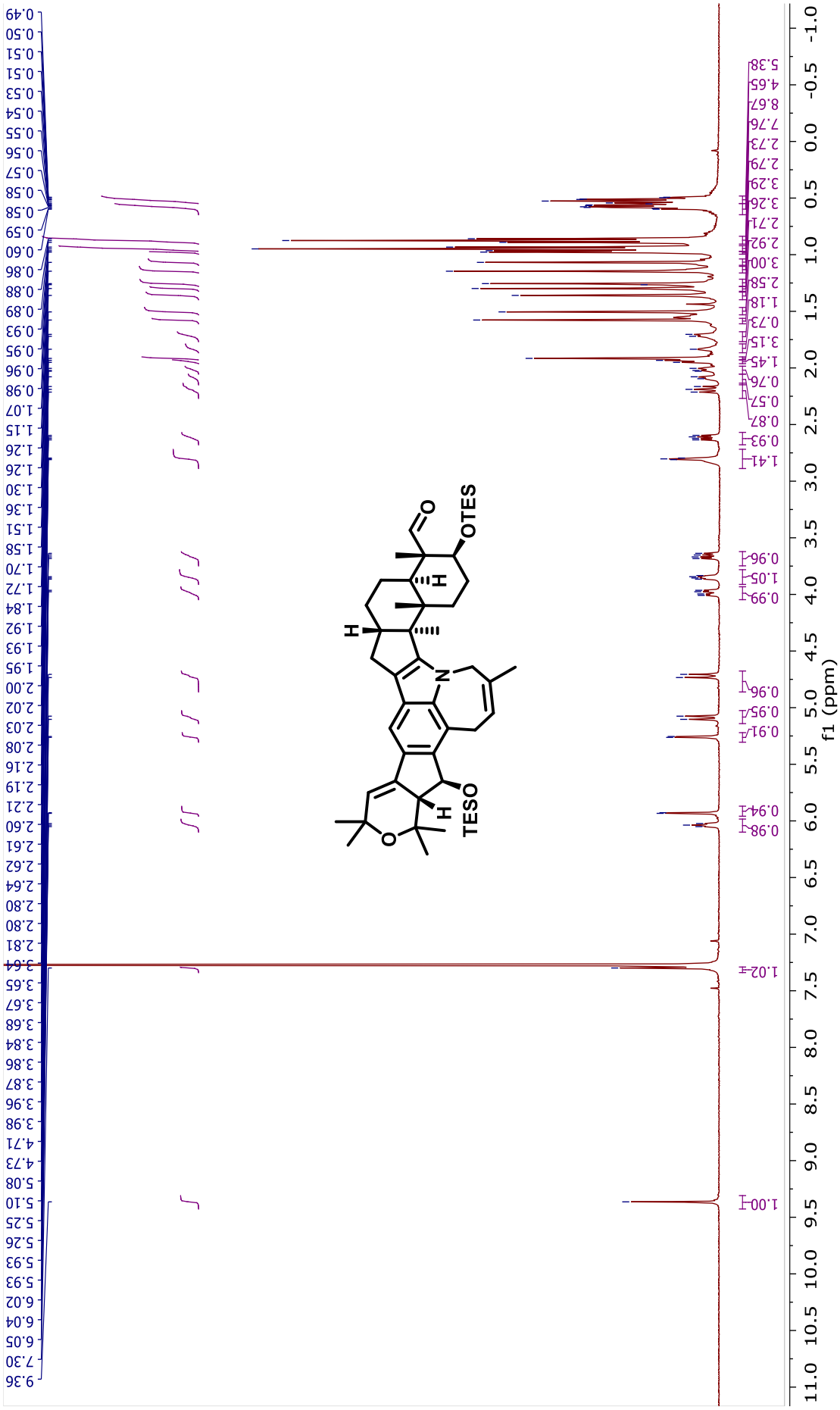
^{1}H NMR (500 MHz) Spectrum of Compound **(+)-86** in $CDCl_3$



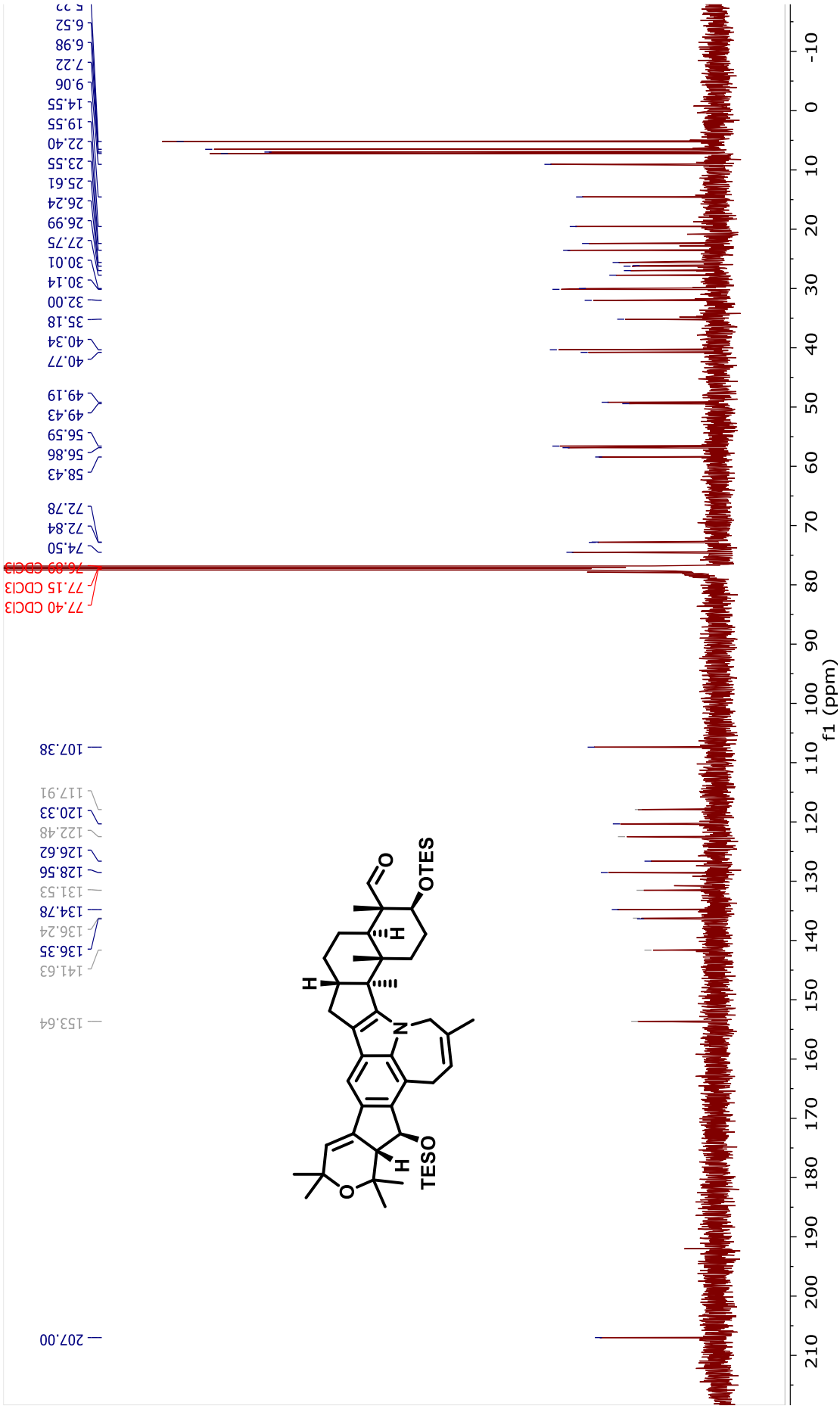
^{13}C NMR (126 MHz) Spectrum of Compound **(+)-86** in $CDCl_3$



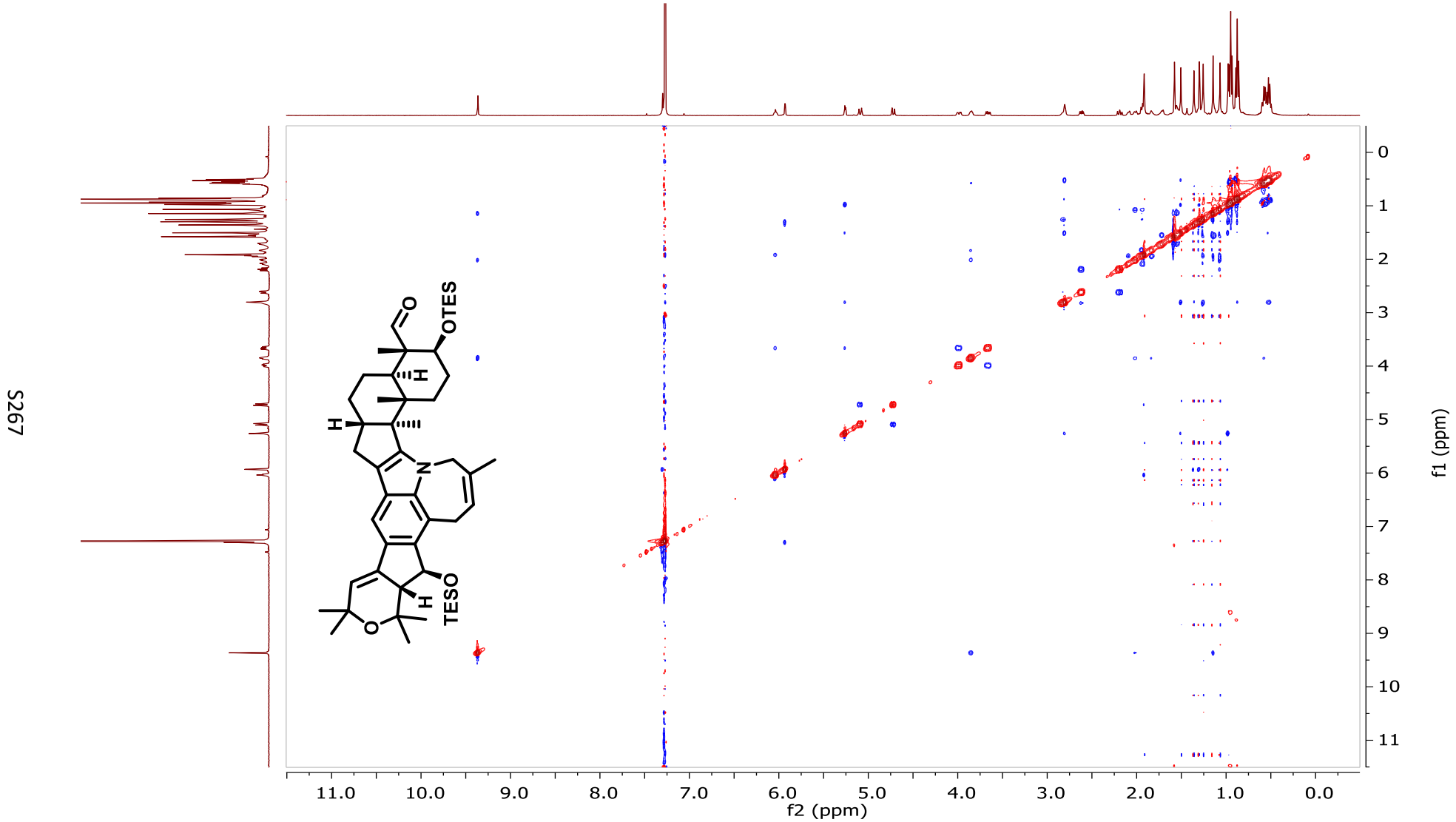
IR Spectrum of Compound **(+)-86**



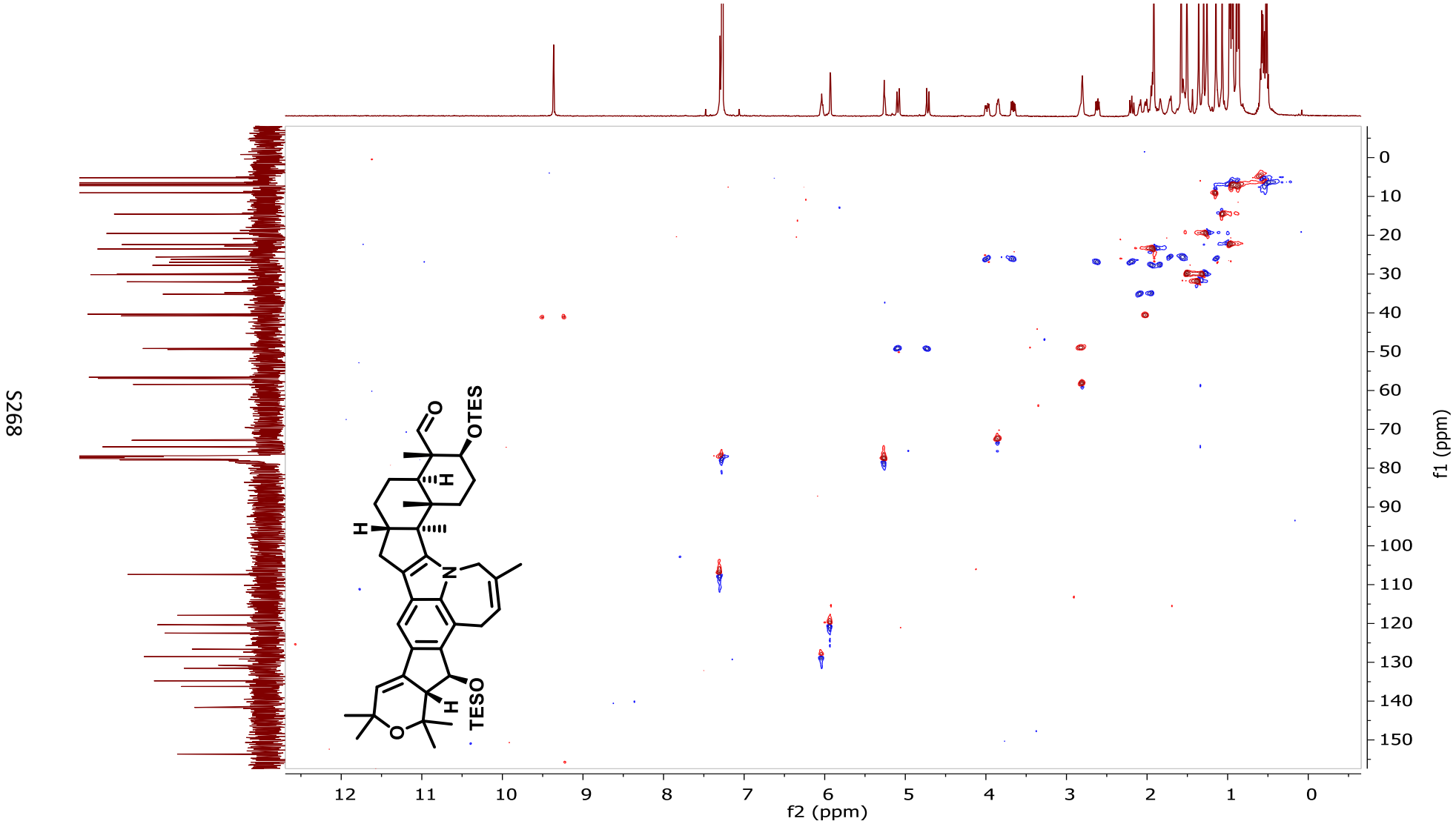
^{1}H NMR (500 MHz) Spectrum of Compound **(+)-90** in $CDCl_3$



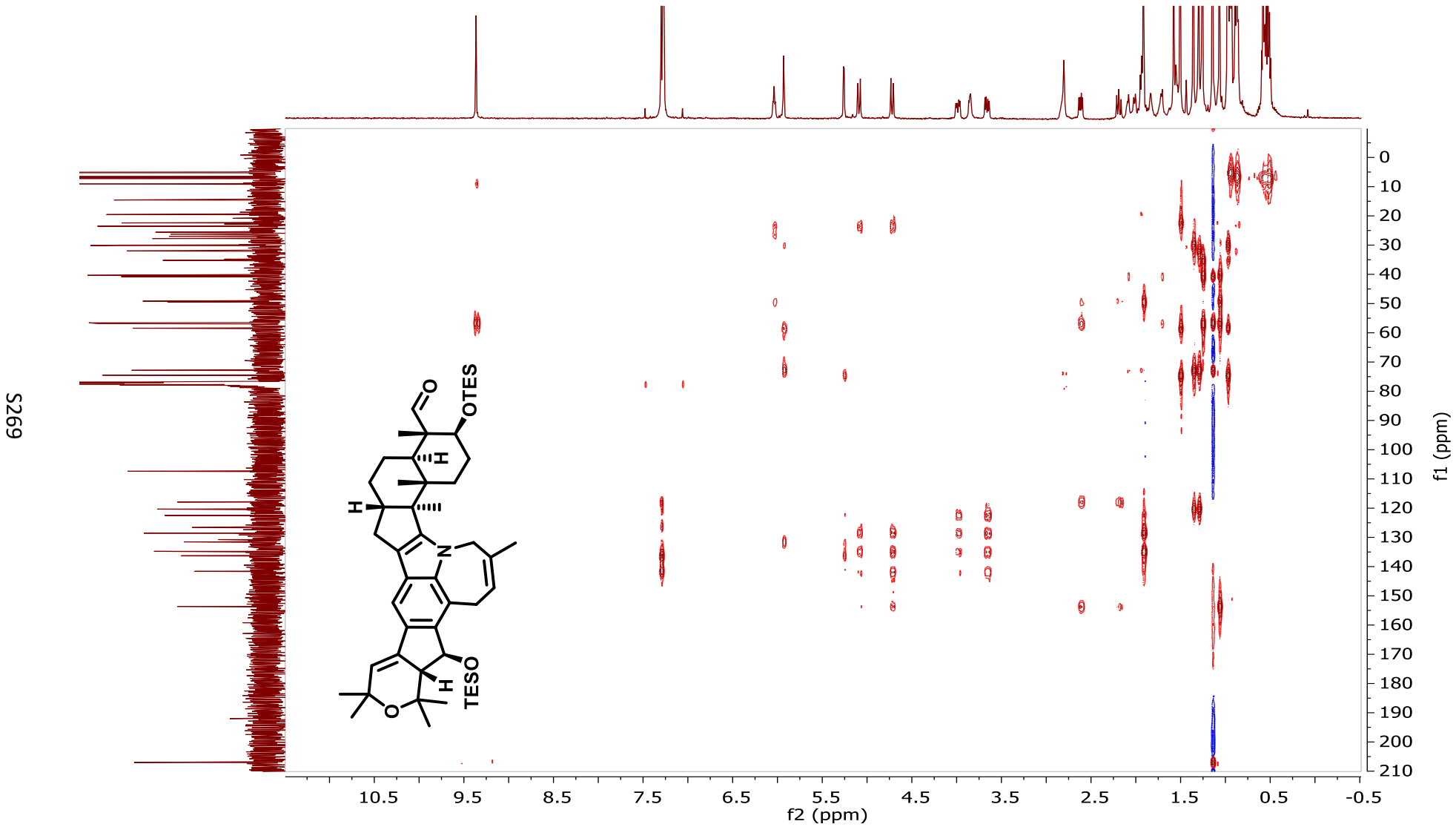
^{13}C NMR (126 MHz) Spectrum of Compound **(+)-90** in $CDCl_3$



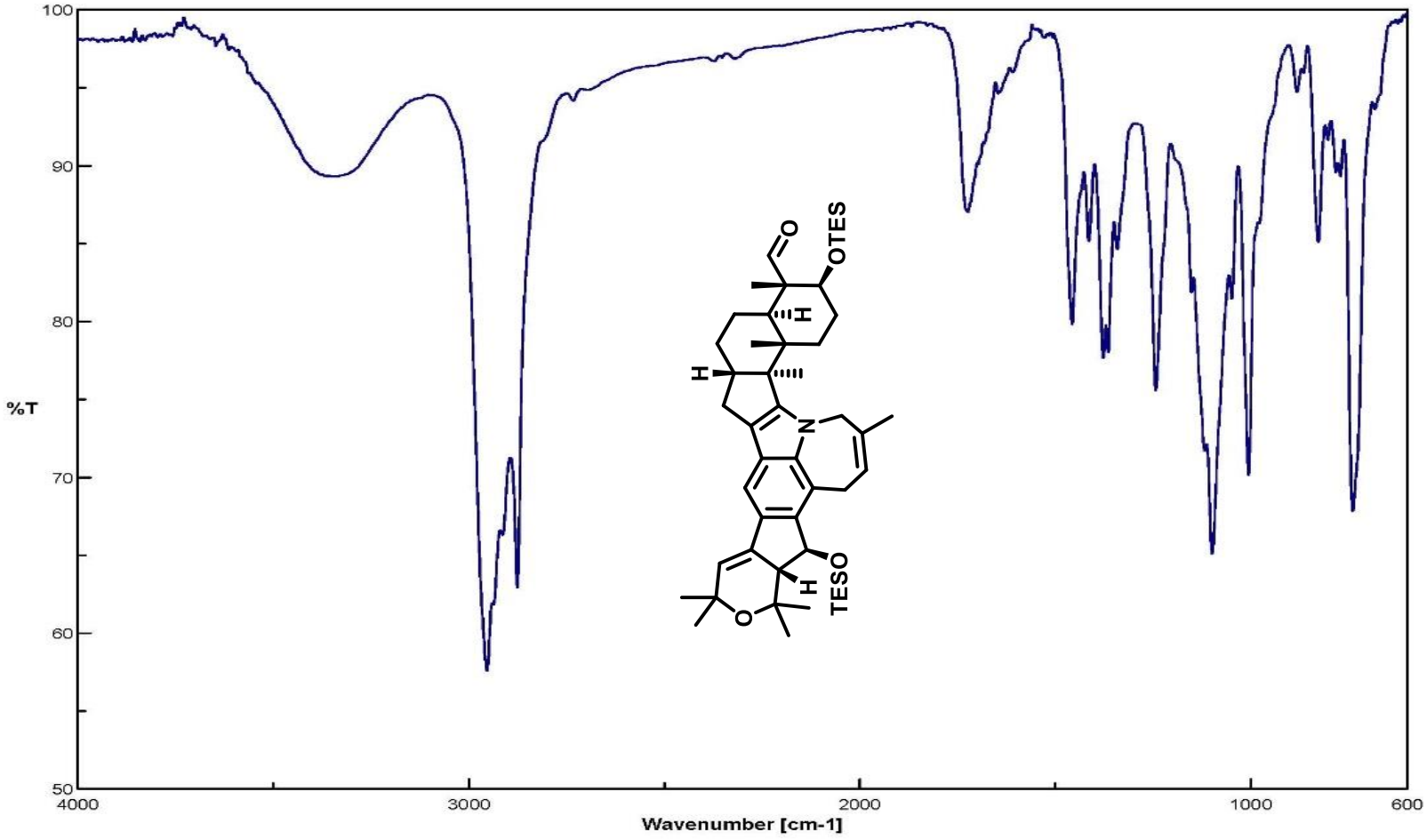
NOESY Spectrum of Compound **(+)-90** in $CDCl_3$



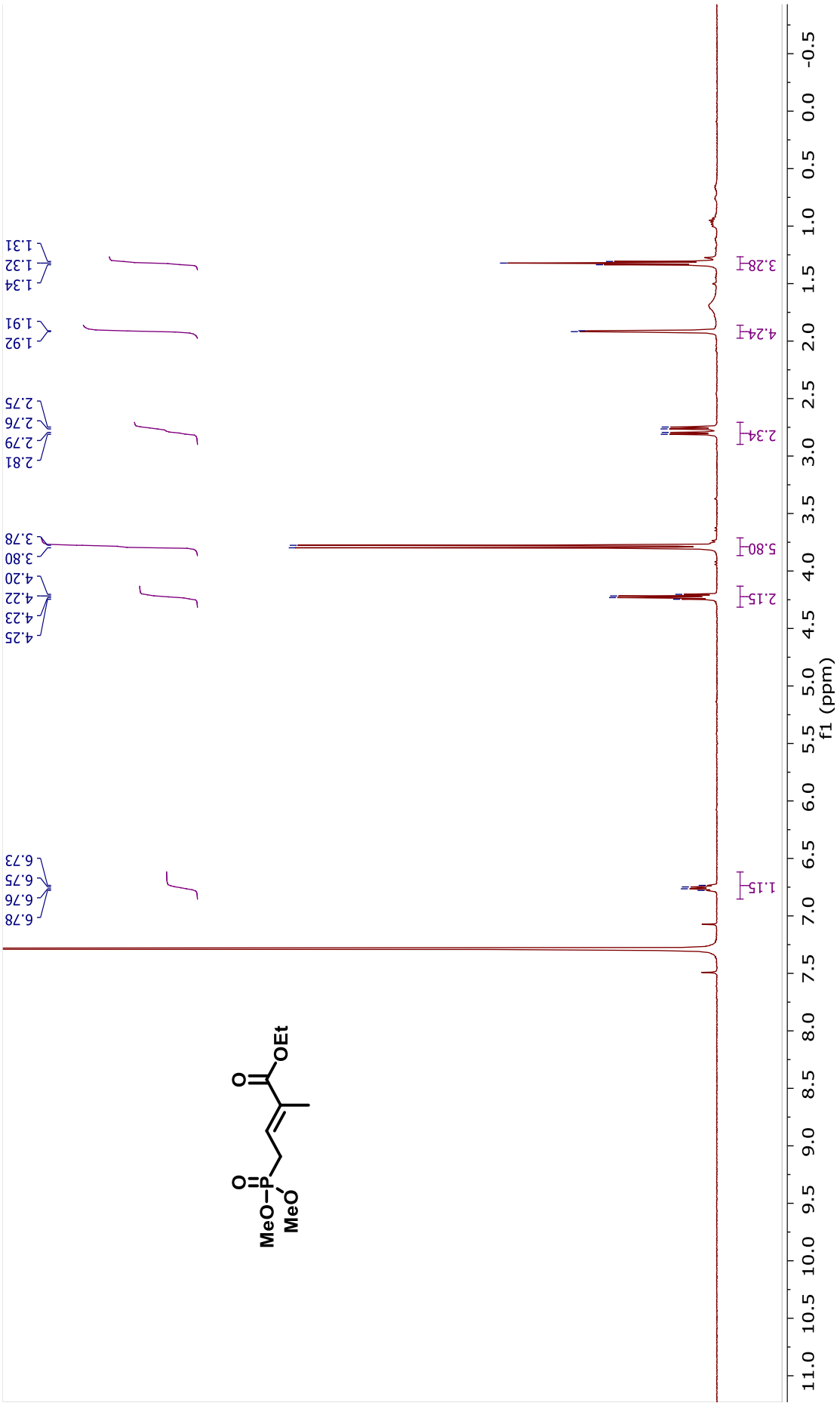
HSQC Spectrum of Compound **(+)-90** in $CDCl_3$



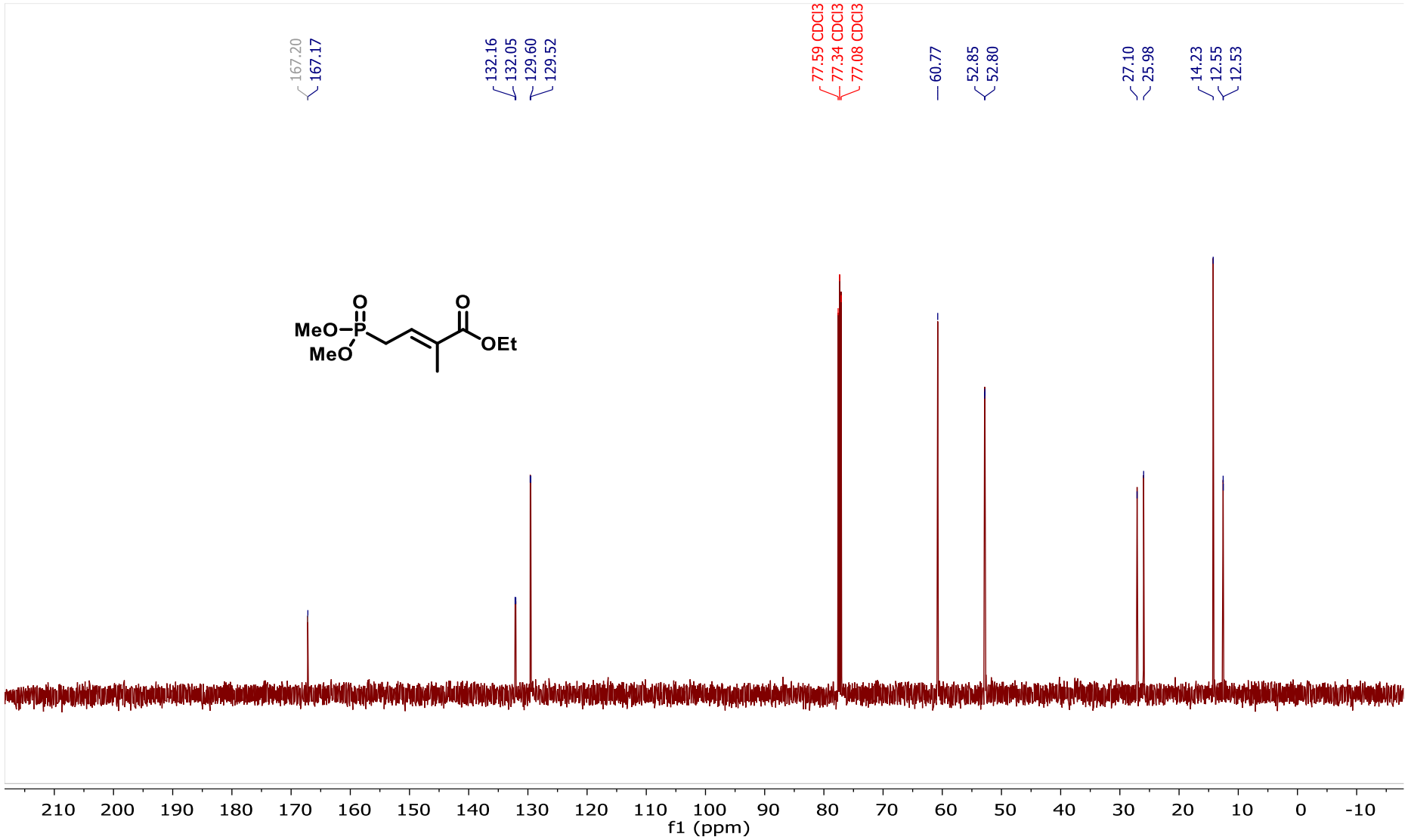
HMBC Spectrum of Compound **(+)-90** in $CDCl_3$



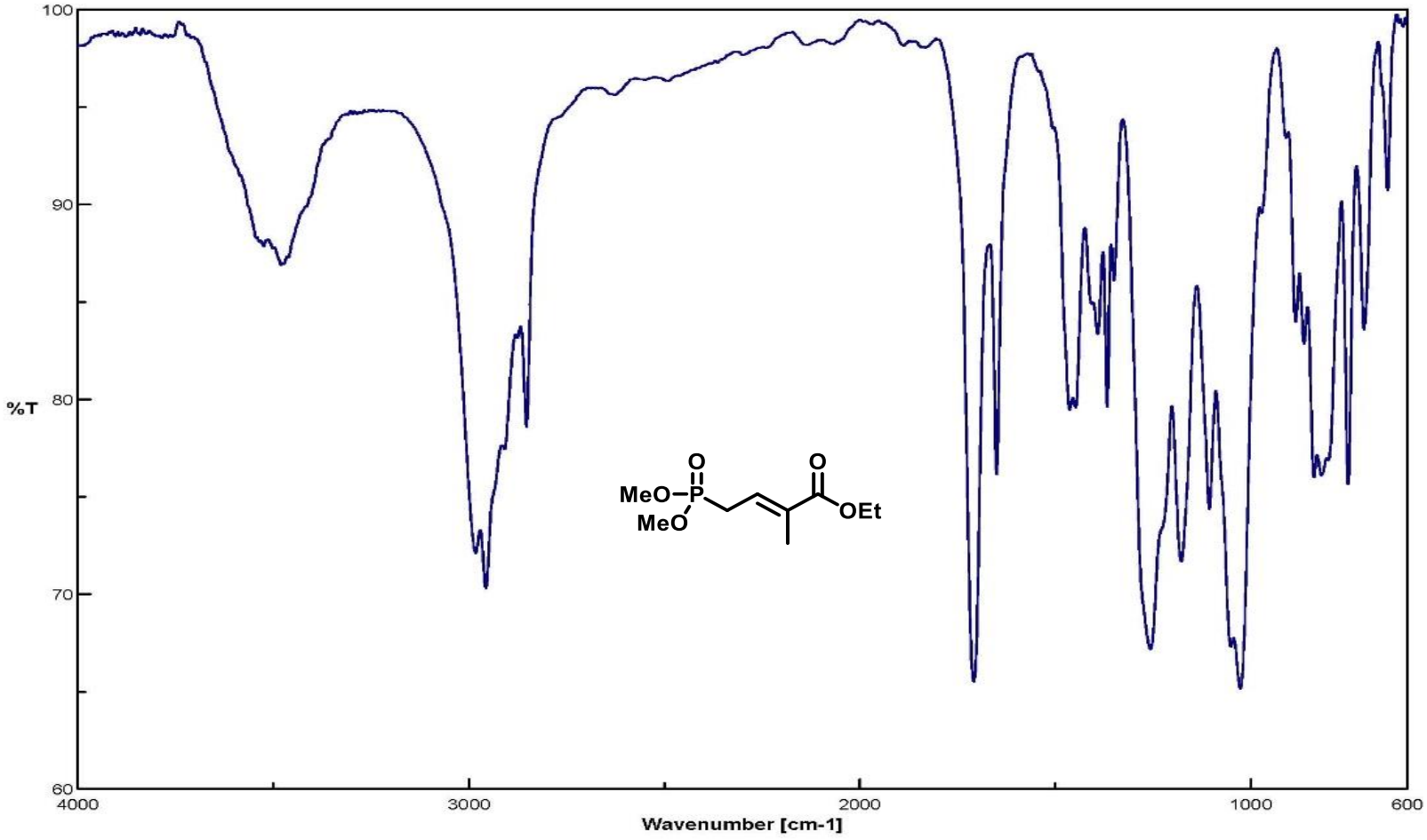
IR Spectrum of Compound **(+)-90**



^{1}H NMR (500 MHz) Spectrum of Compound **92** in $CDCl_3$

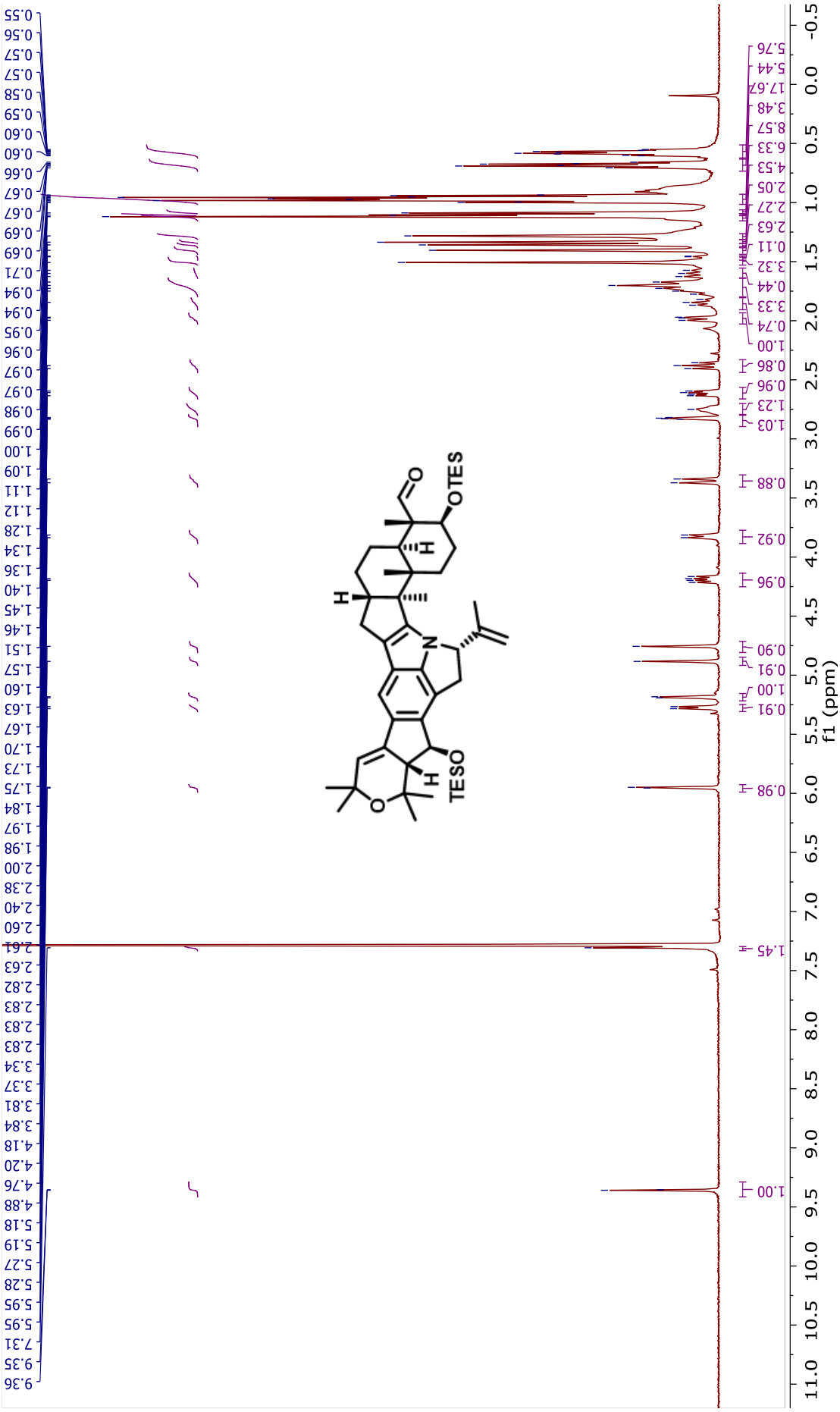


^{13}C NMR (126 MHz) Spectrum of Compound **92** in $CDCl_3$

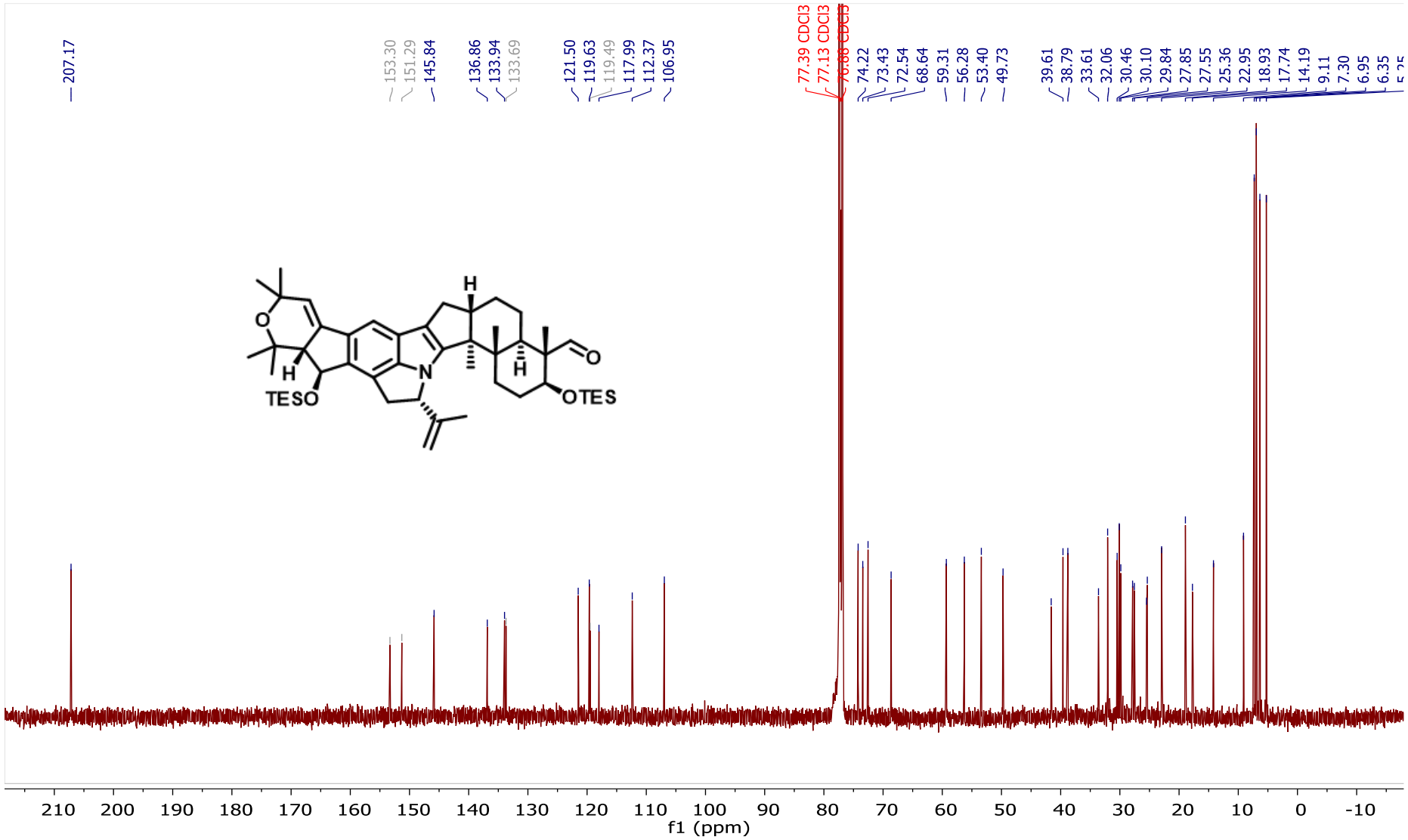


IR Spectrum of Compound **92**

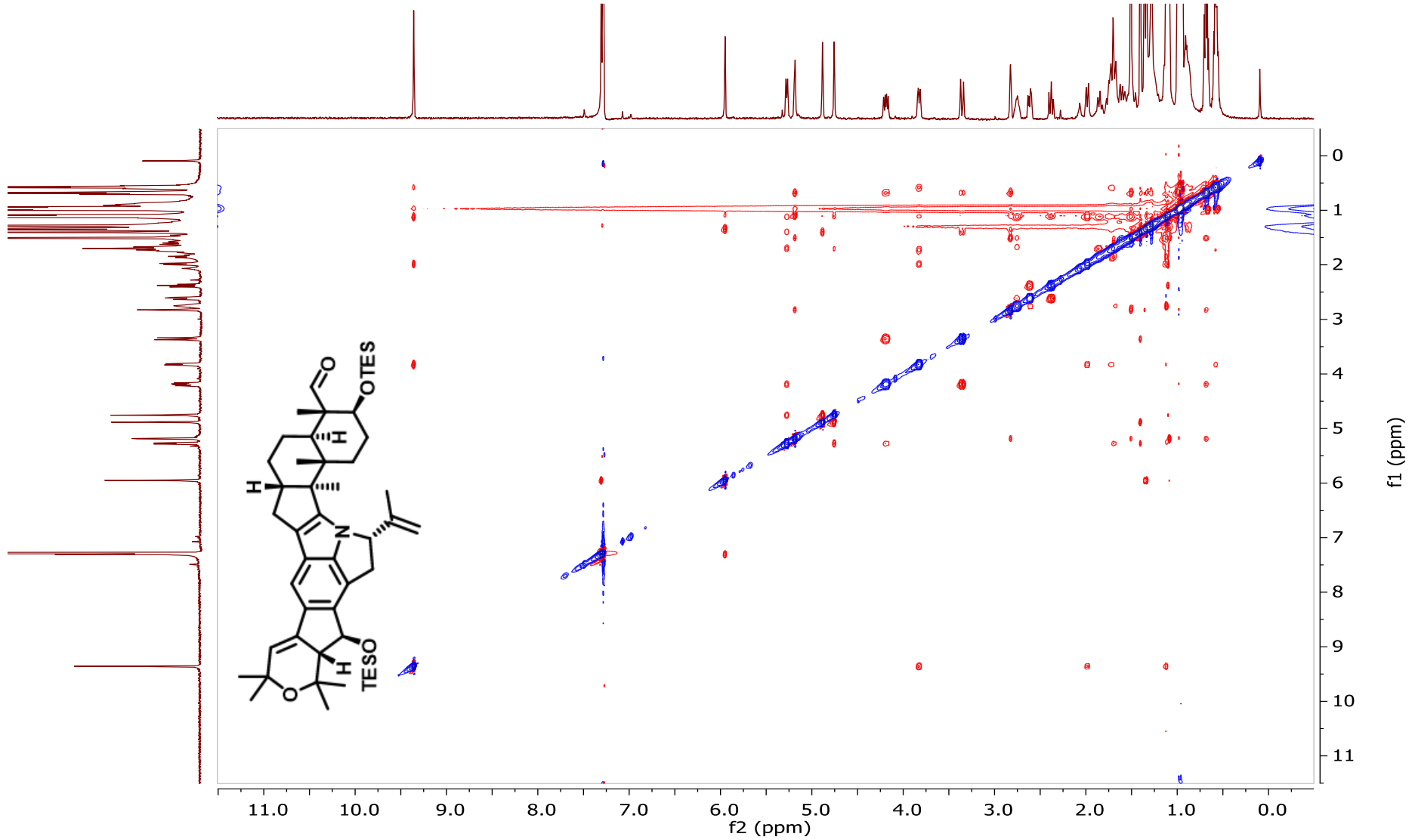
Note: due to the extremely unstable nature of the tricyclic indole core toward air, the spectra of late-stage intermediates possessing the tricyclic indole-indoline core contained different degree of decomposition appeared as tiny peaks on baseline.



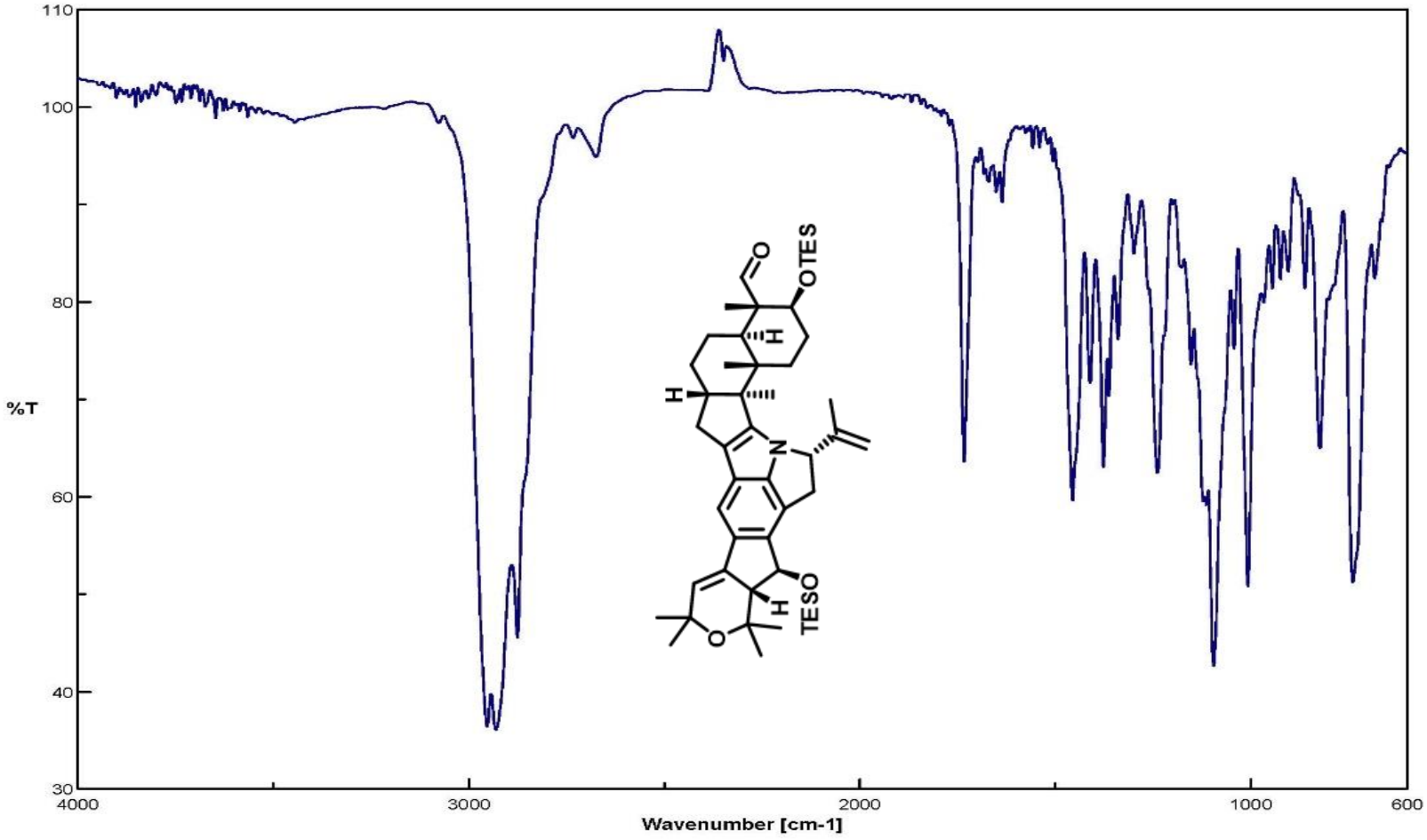
^{1}H NMR (500 MHz) Spectrum of Compound **(+)-88** in $CDCl_3$



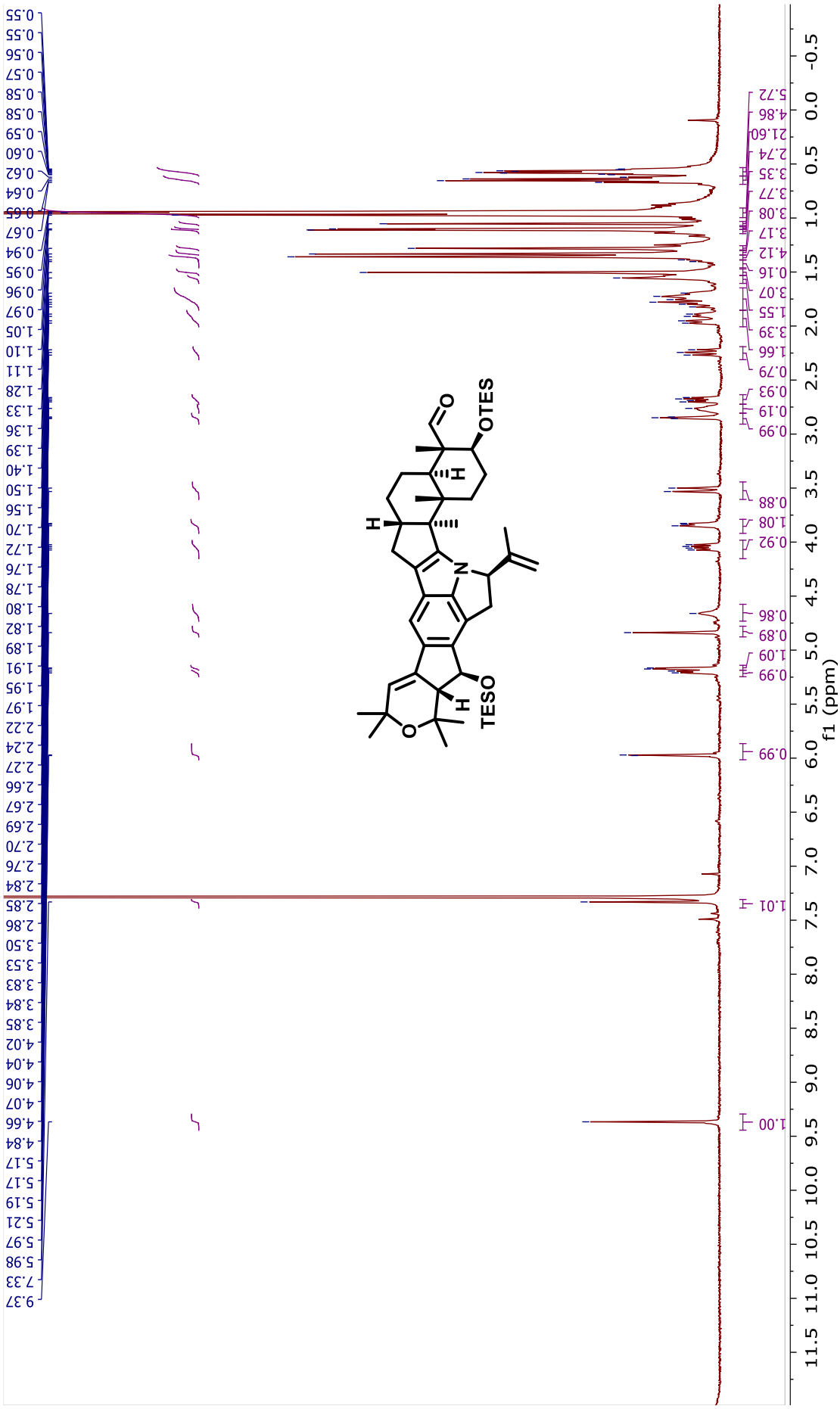
^{13}C NMR (126 MHz) Spectrum of Compound **(+)-88** in $CDCl_3$



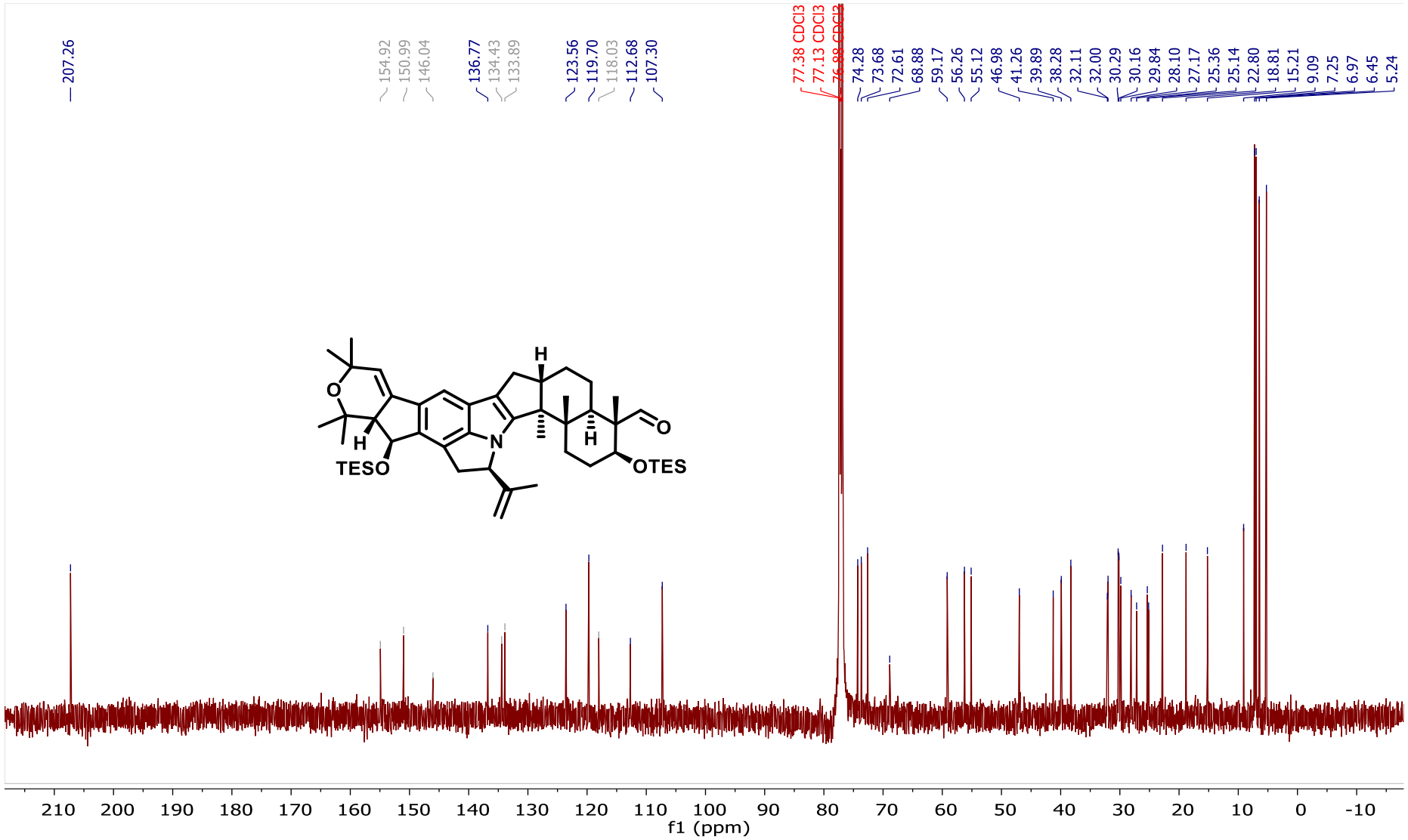
NOESY Spectrum of Compound **(+)-88** in $CDCl_3$



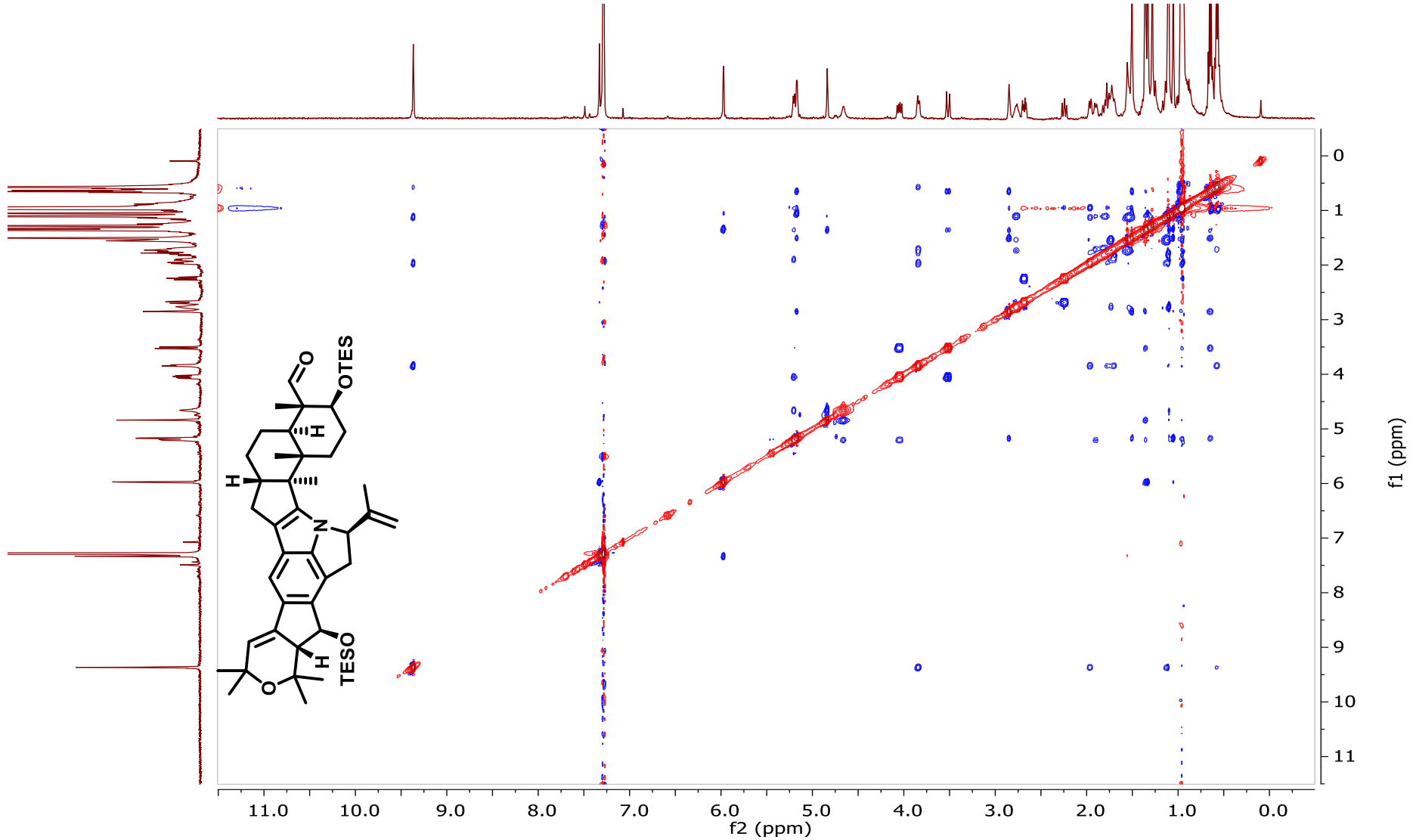
IR Spectrum of Compound **(+)-88**



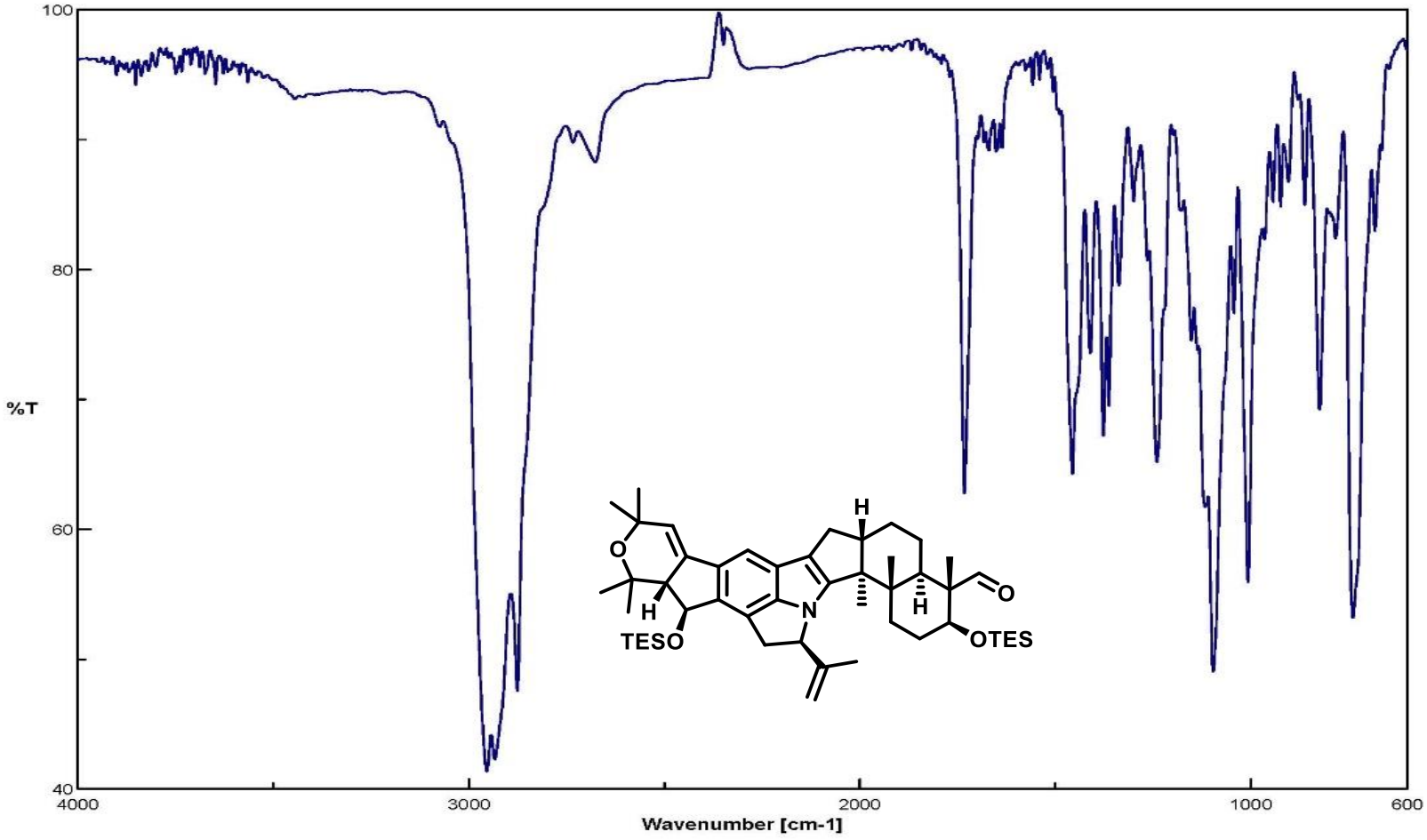
^{1}H NMR (500 MHz) Spectrum of Compound **(+)-89** in $CDCl_3$



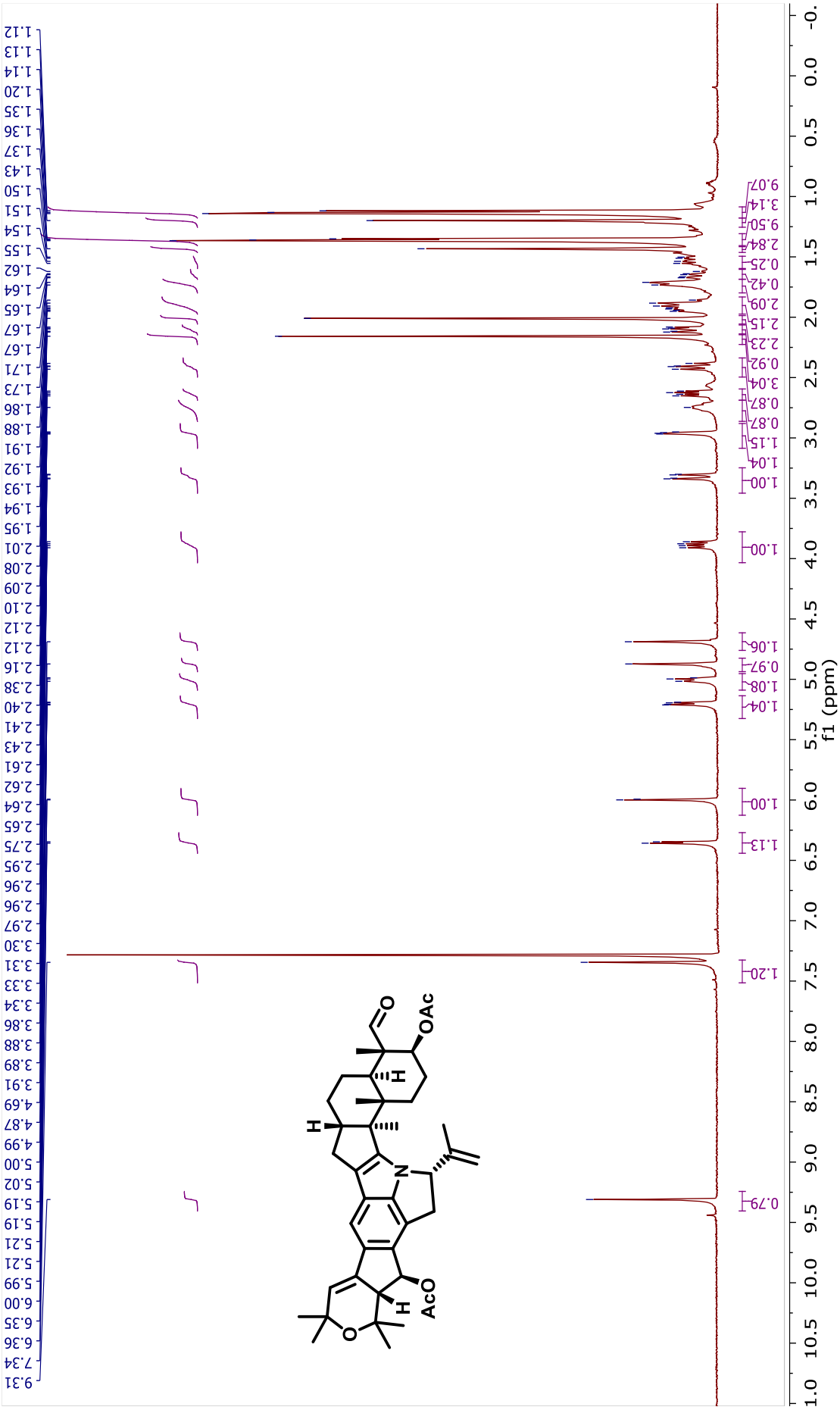
^{13}C NMR (126 MHz) Spectrum of Compound **(+)-89** in $CDCl_3$



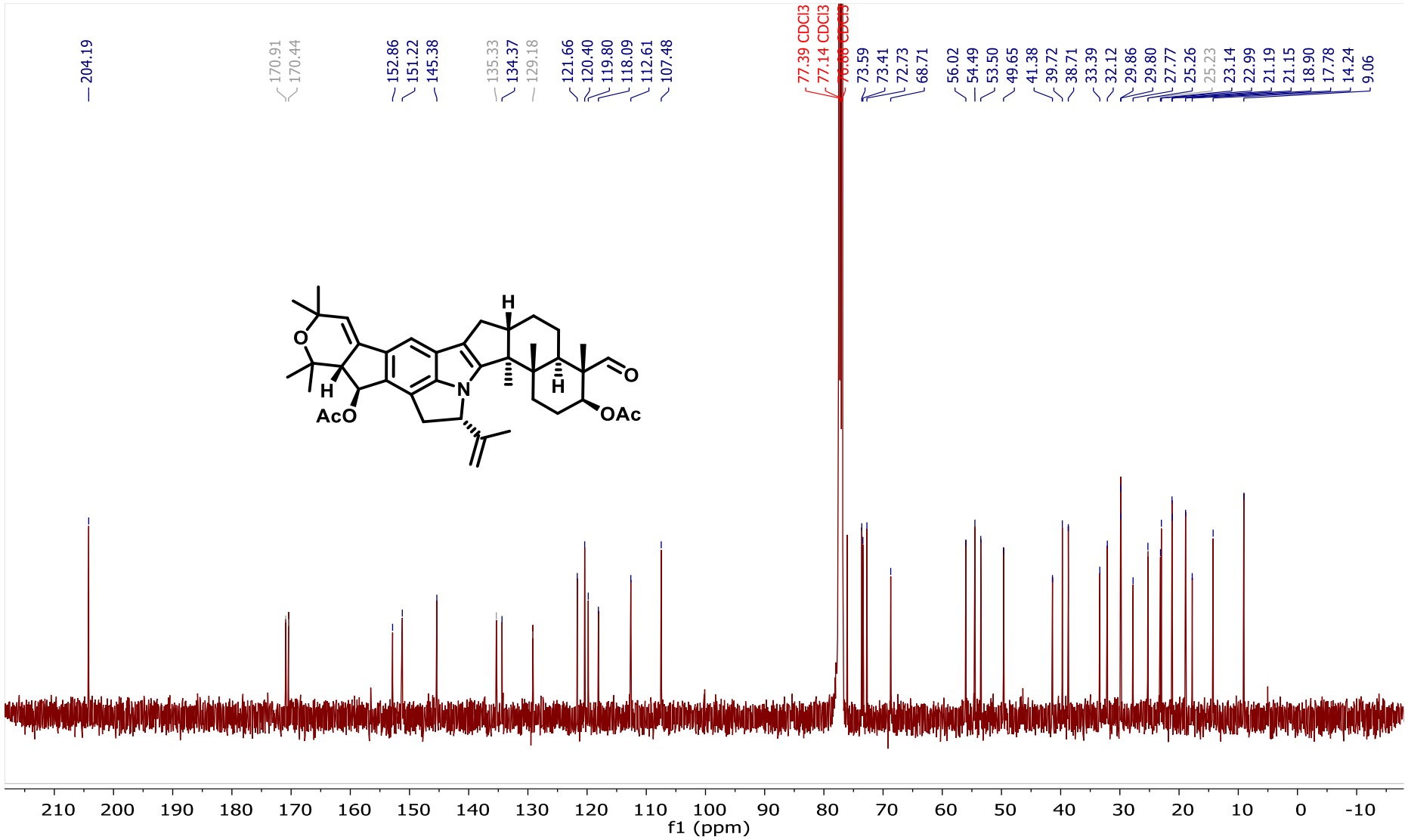
NOESY Spectrum of Compound **(+)-89** in $CDCl_3$



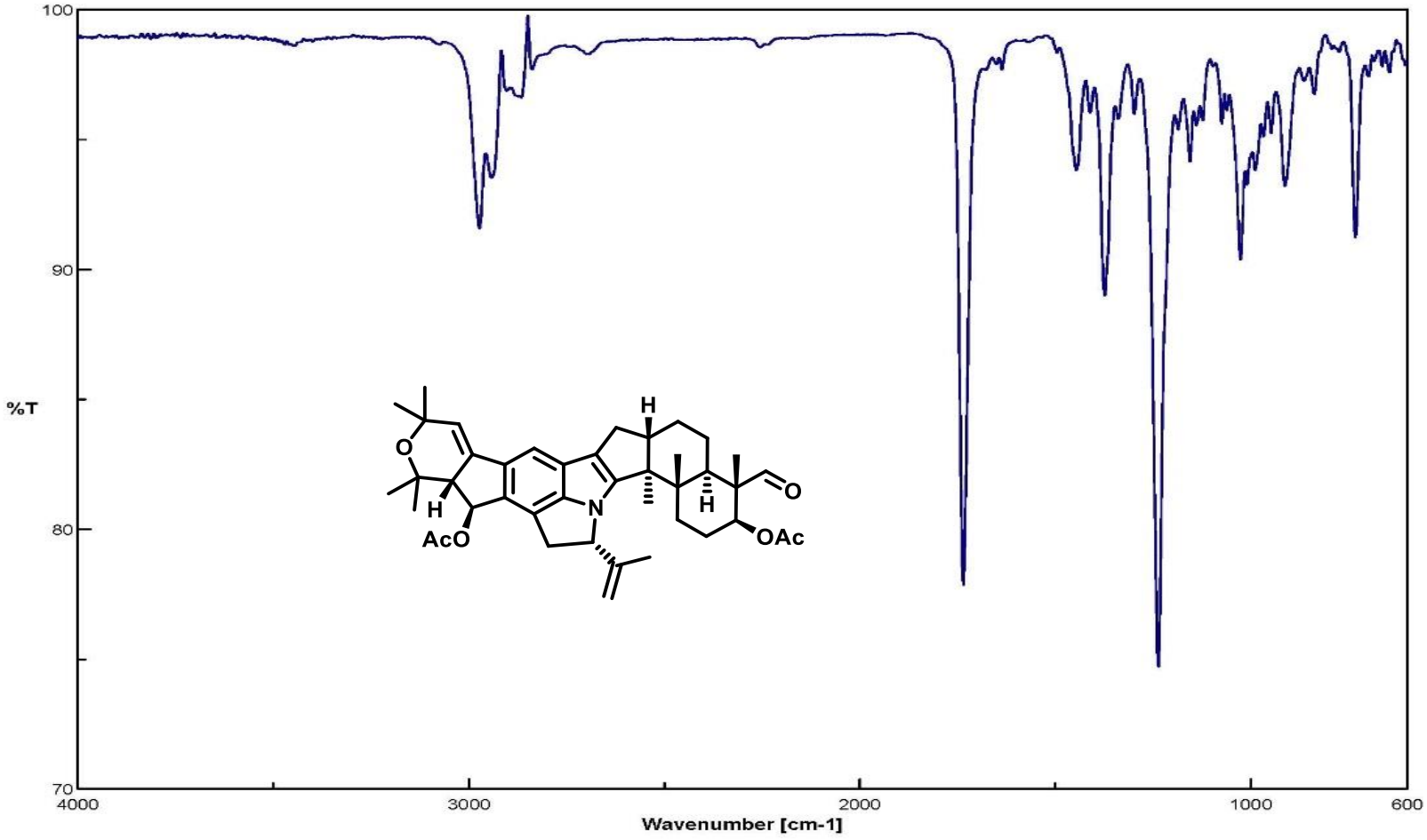
IR Spectrum of Compound **(+)-89**



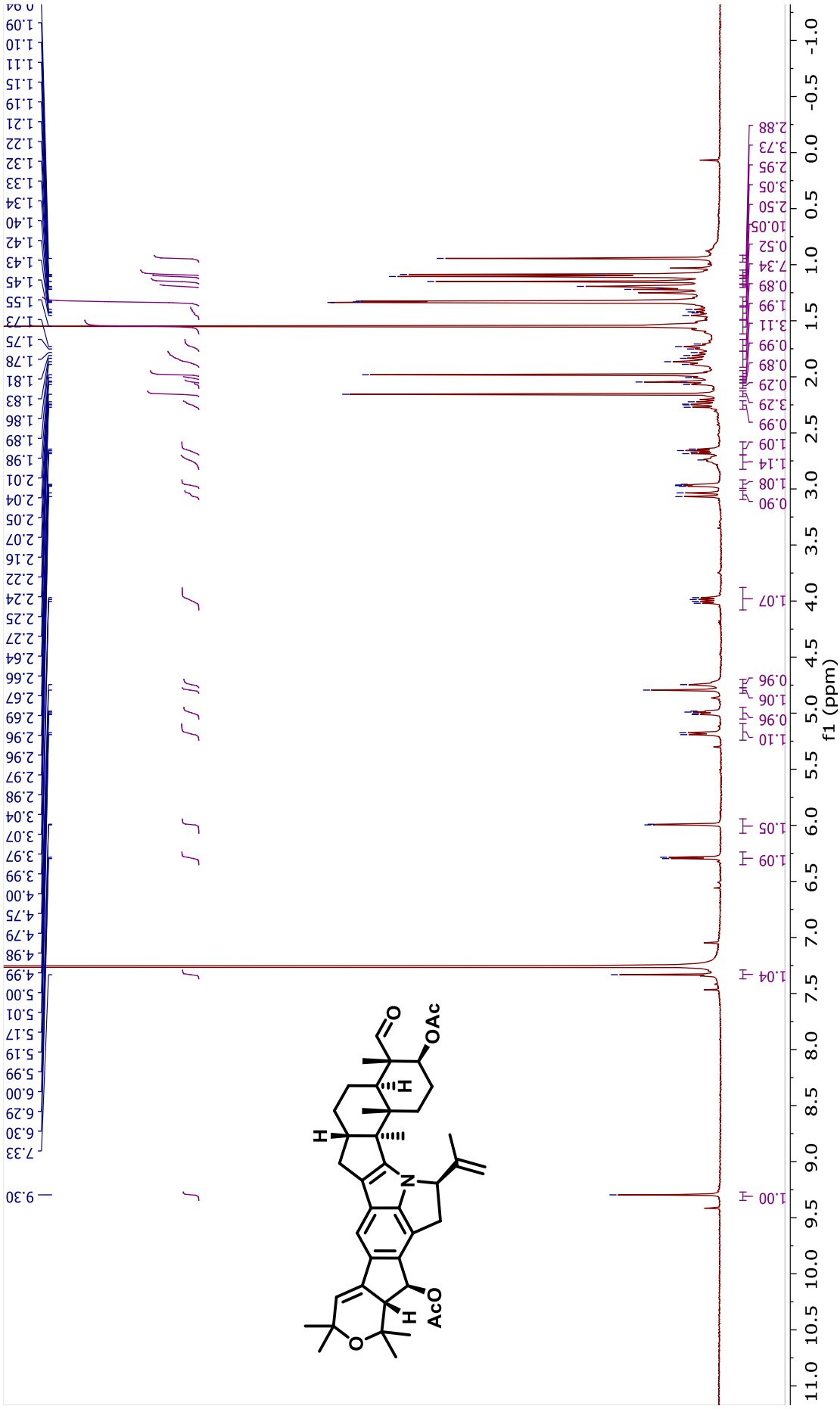
^{1}H NMR (500 MHz) Spectrum of Compound **(–)-91** in $CDCl_3$



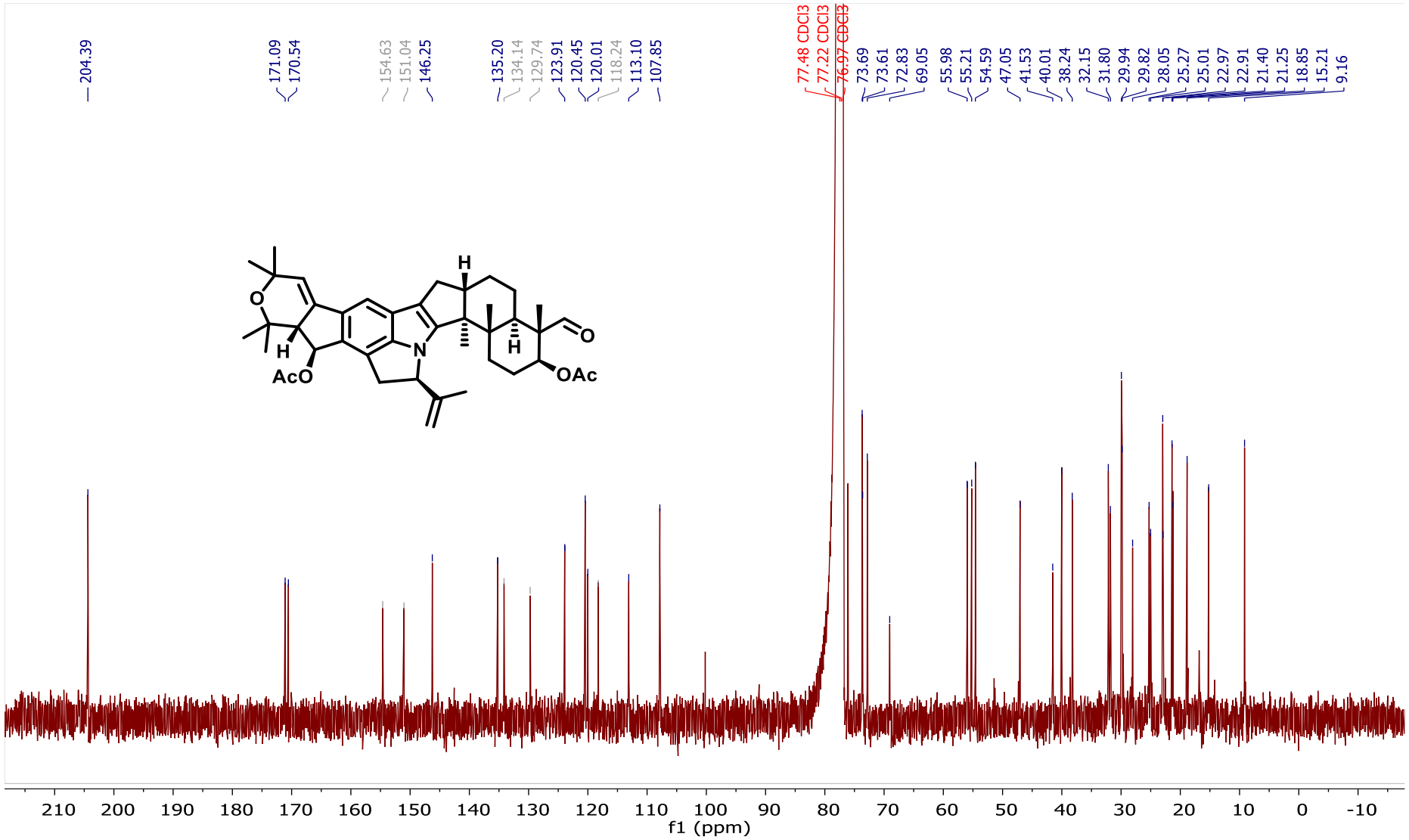
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-91** in $CDCl_3$



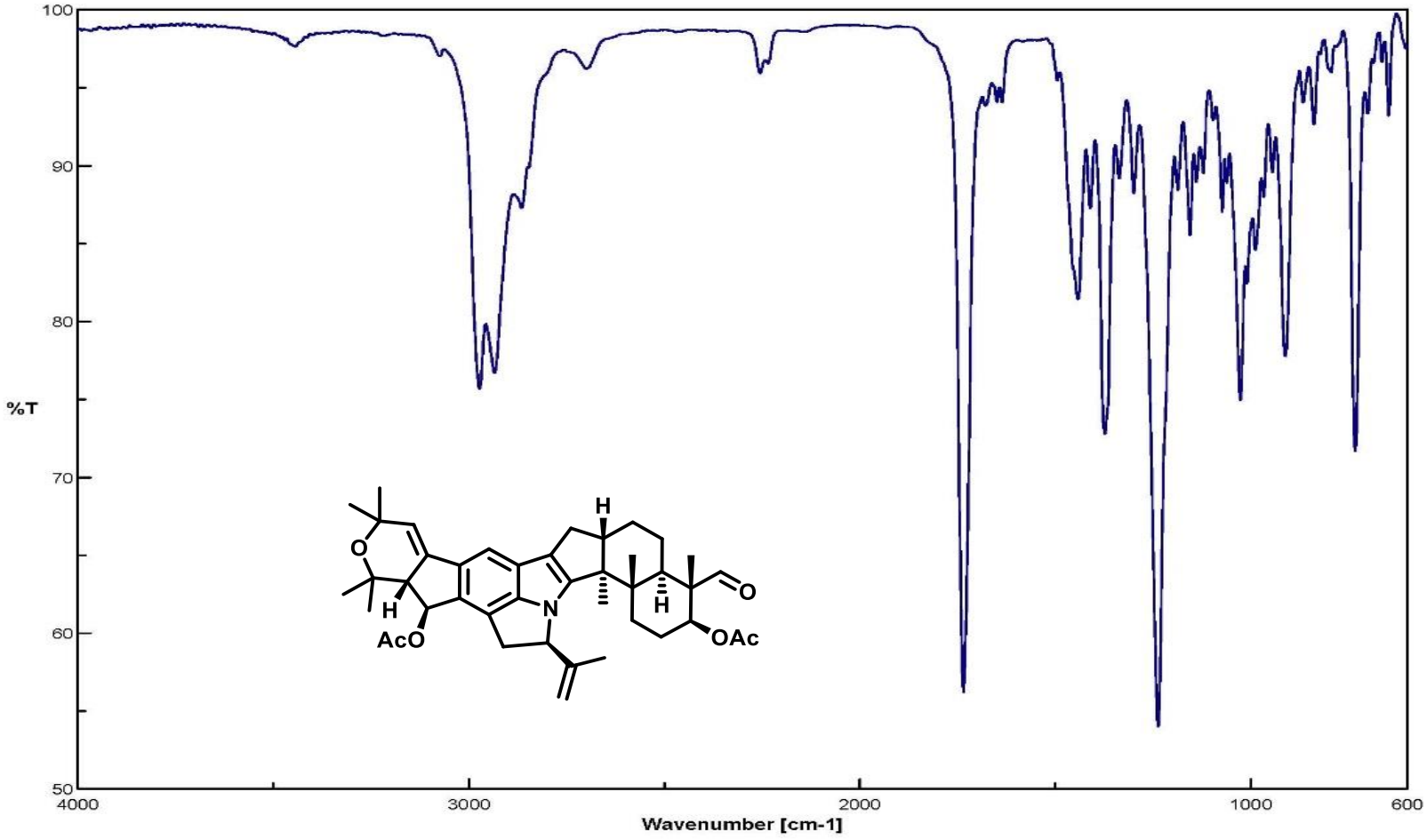
IR Spectrum of Compound (–)-**91**



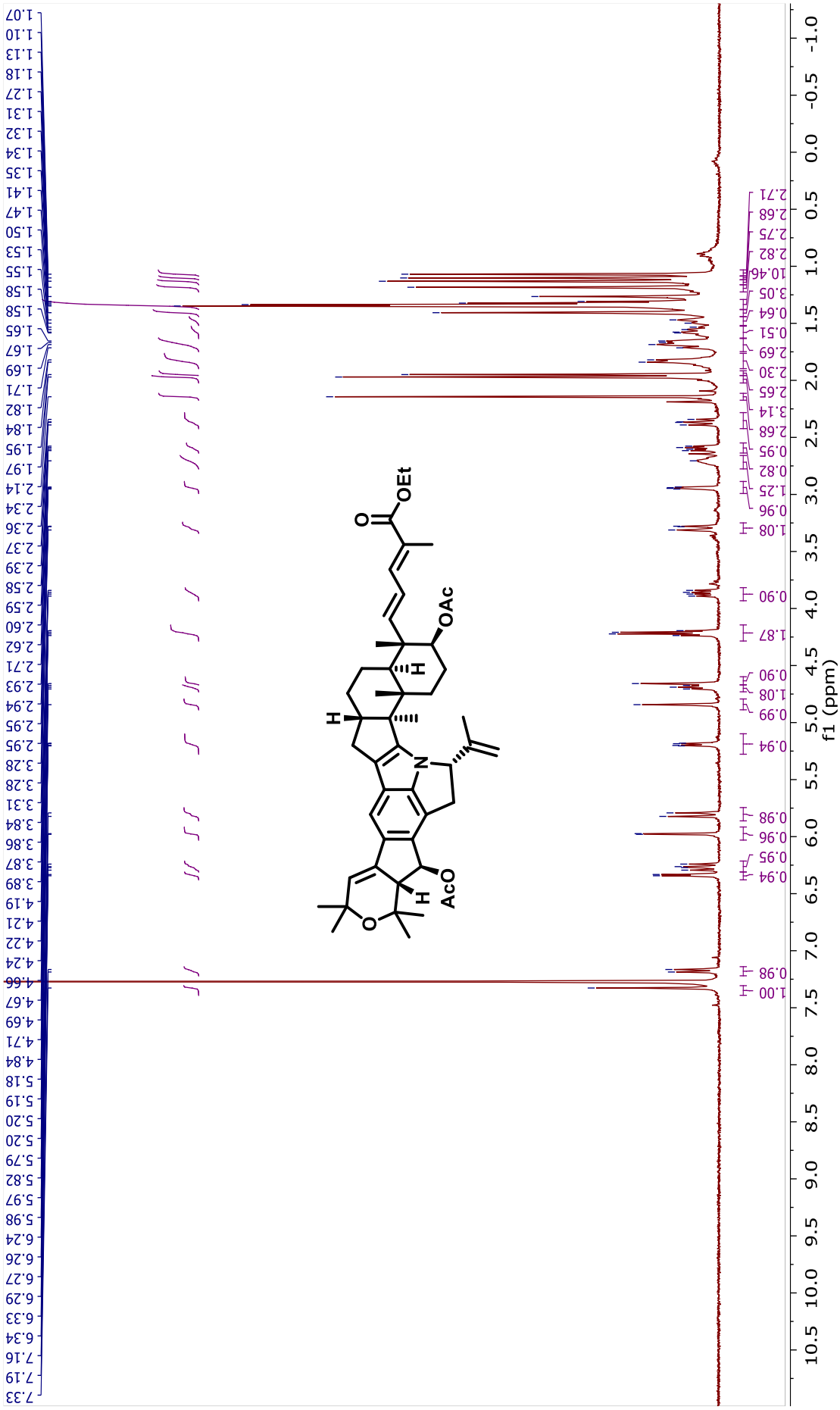
^{1}H NMR (500 MHz) Spectrum of Compound (–)-**95** in $CDCl_3$



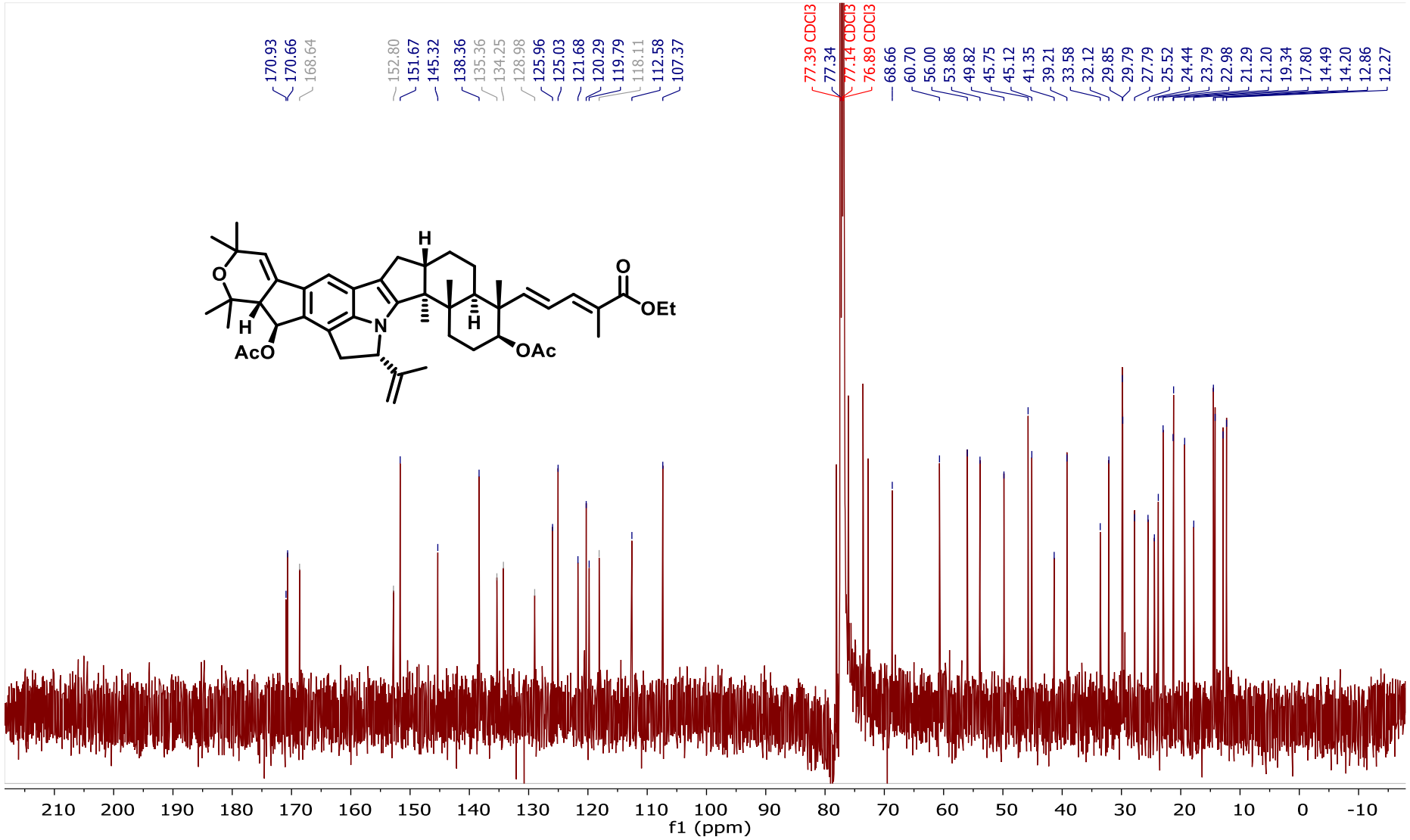
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-95** in $CDCl_3$



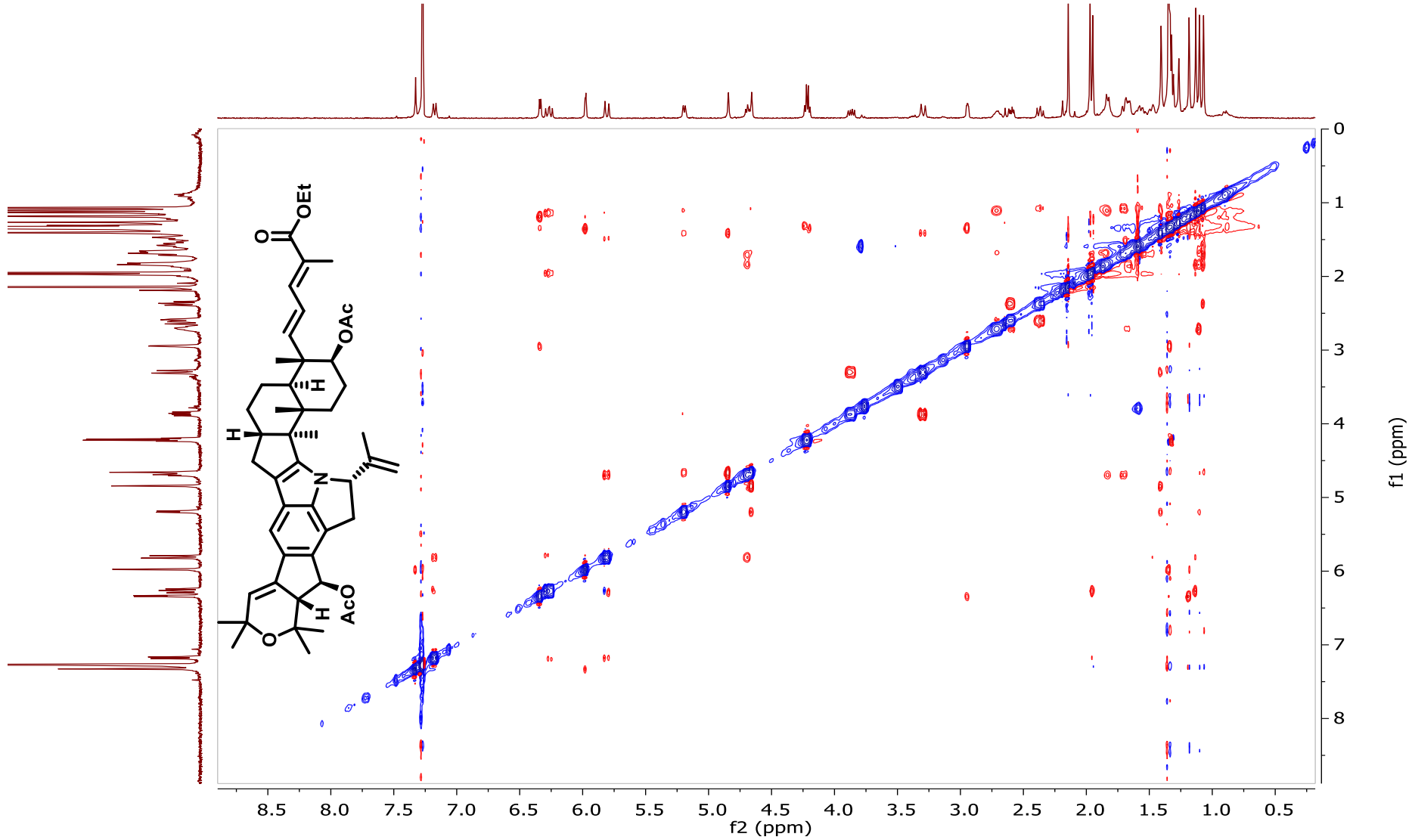
IR Spectrum of Compound (−)-95



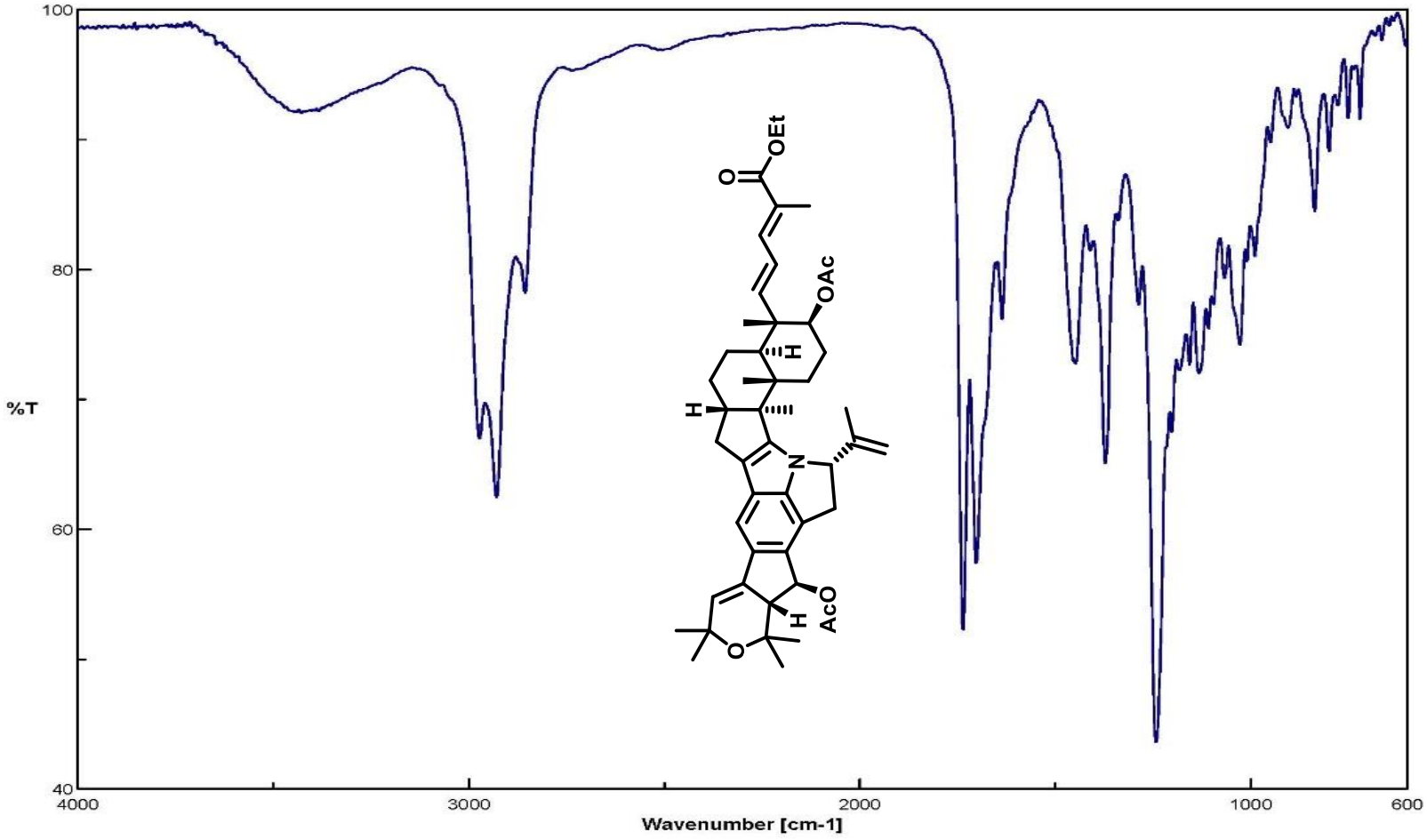
^{1}H NMR (500 MHz) Spectrum of Compound (–)-**93** in $CDCl_3$



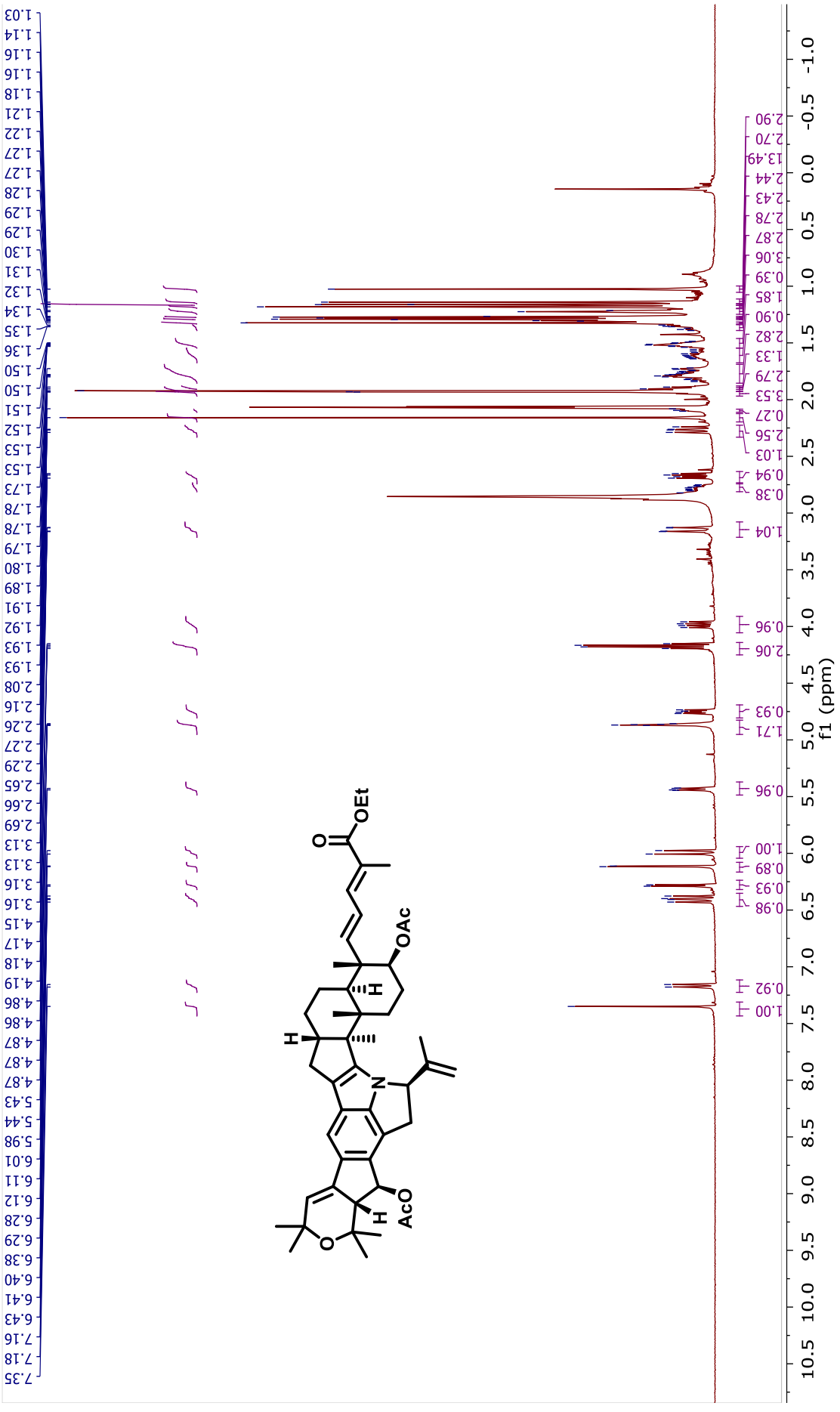
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-93** in $CDCl_3$



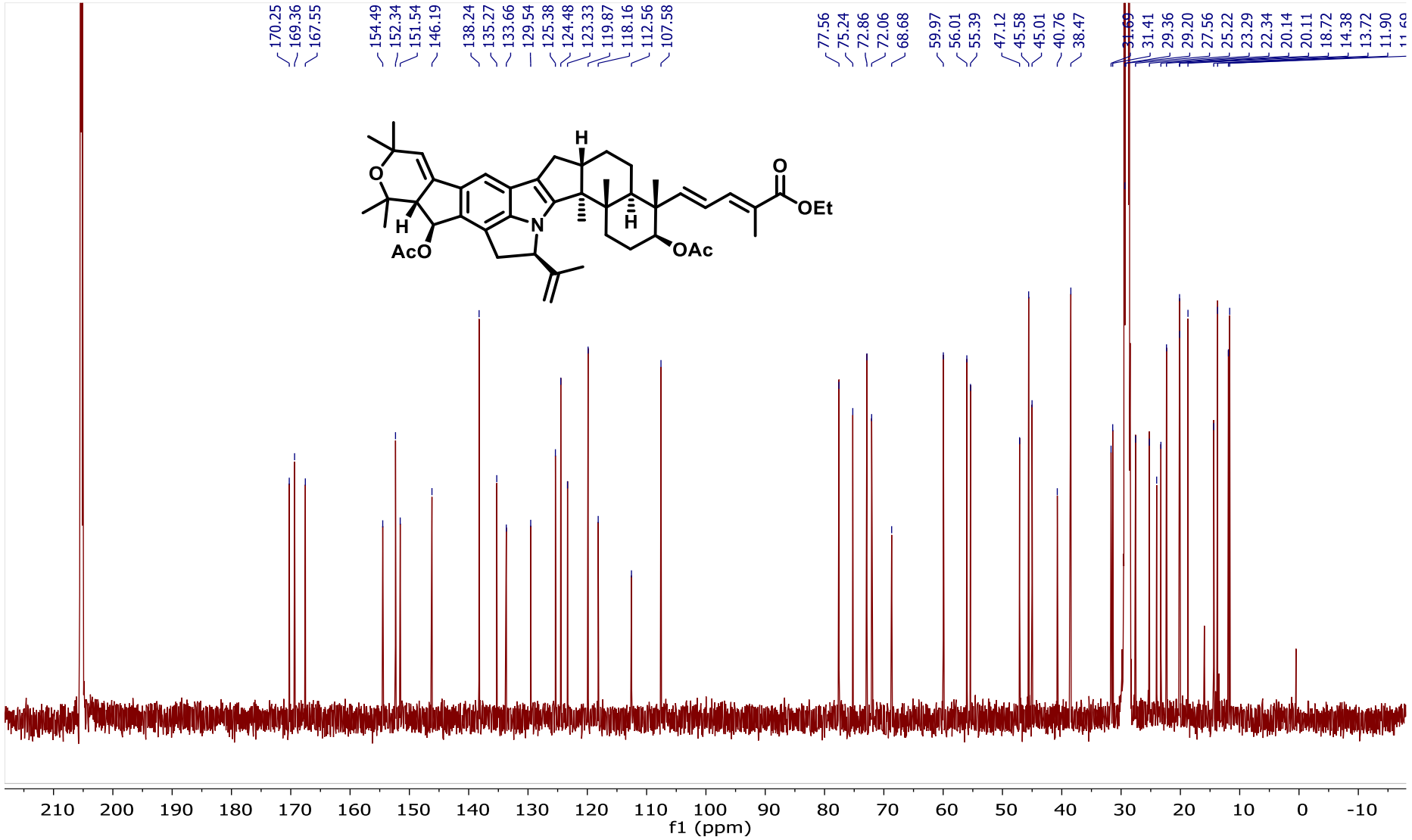
NOESY Spectrum of Compound (–)-**93** in $CDCl_3$



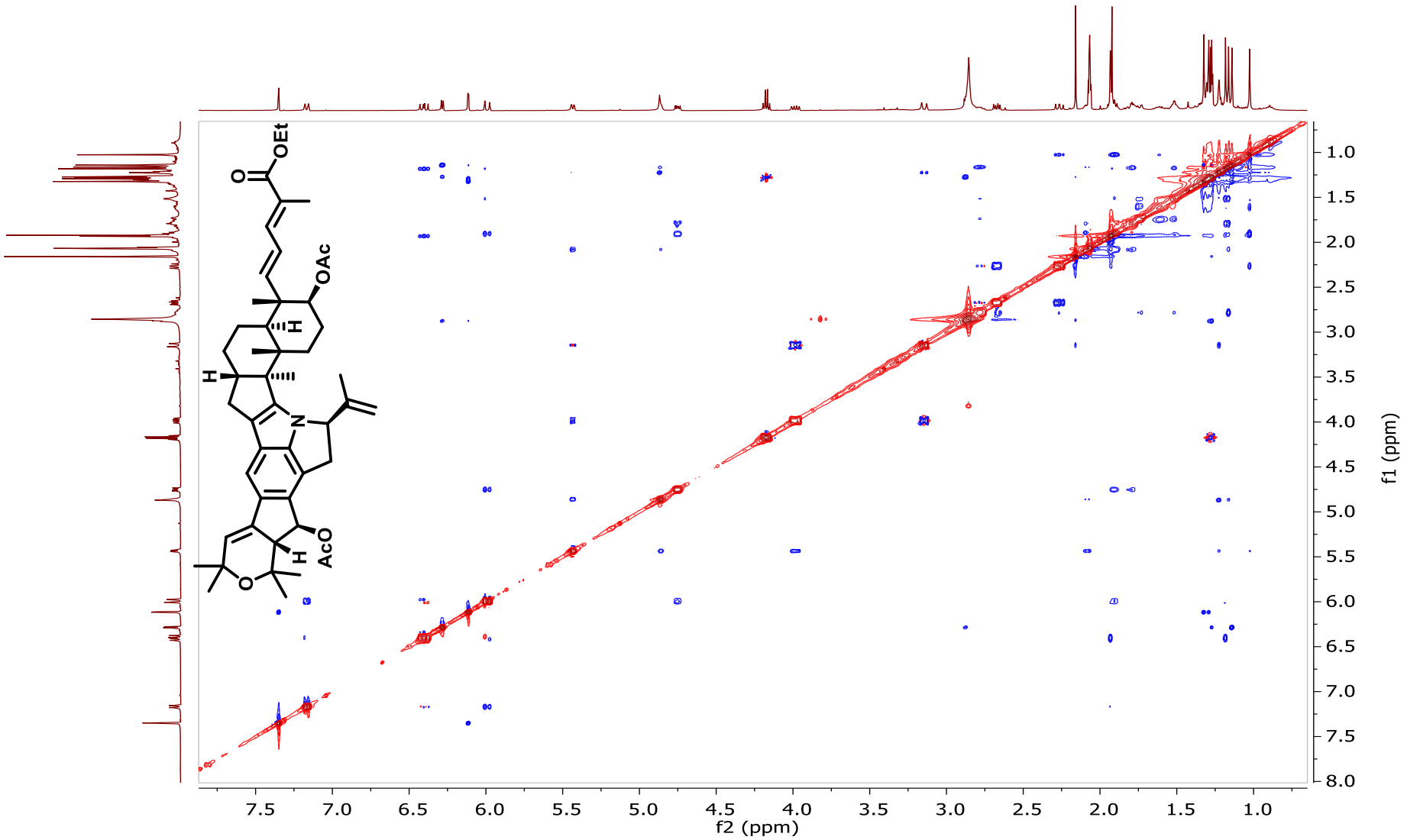
IR Spectrum of Compound (–)-**93**



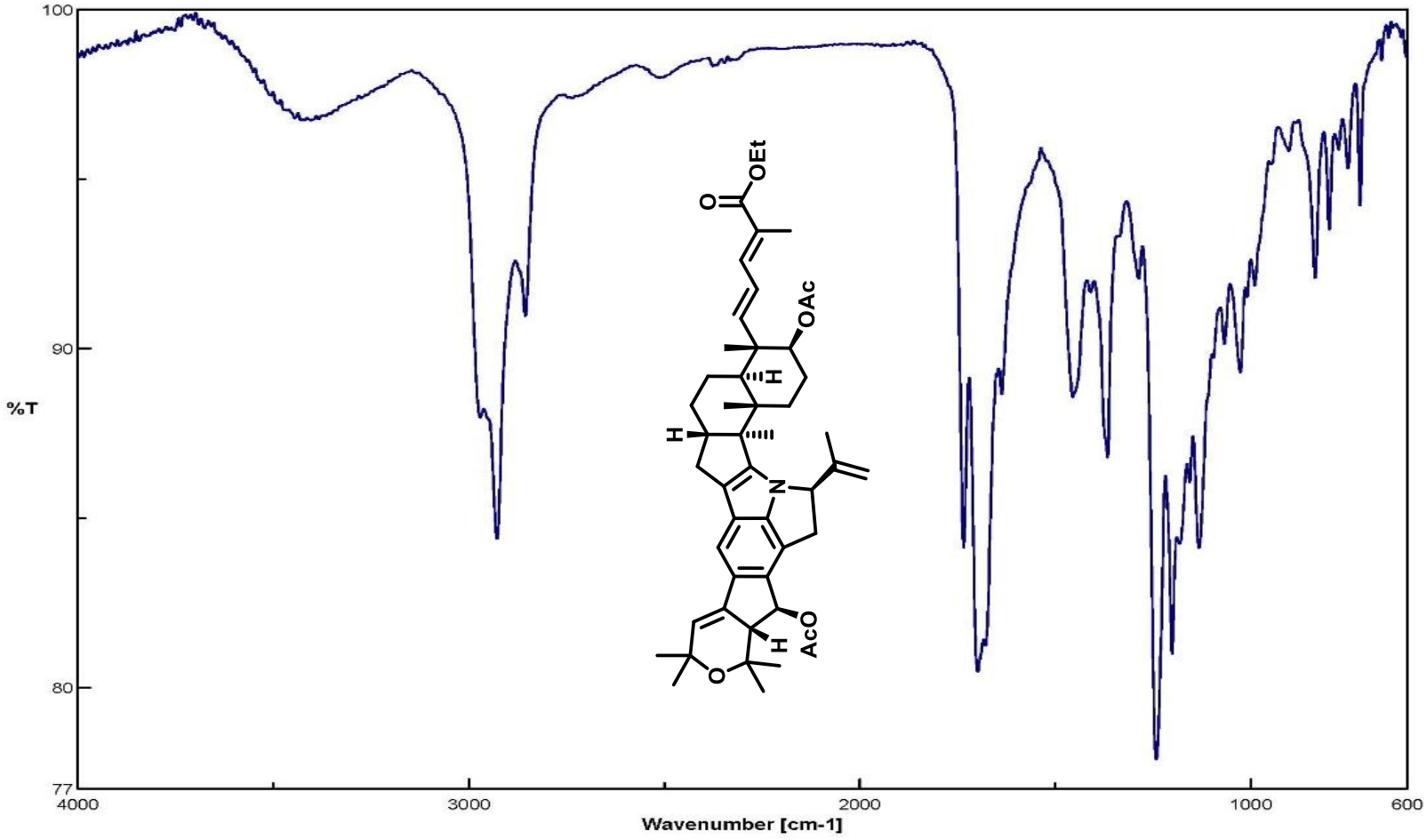
^{1}H NMR (500 MHz) Spectrum of Compound **(–)-96** in $(CD_3)_2CO$



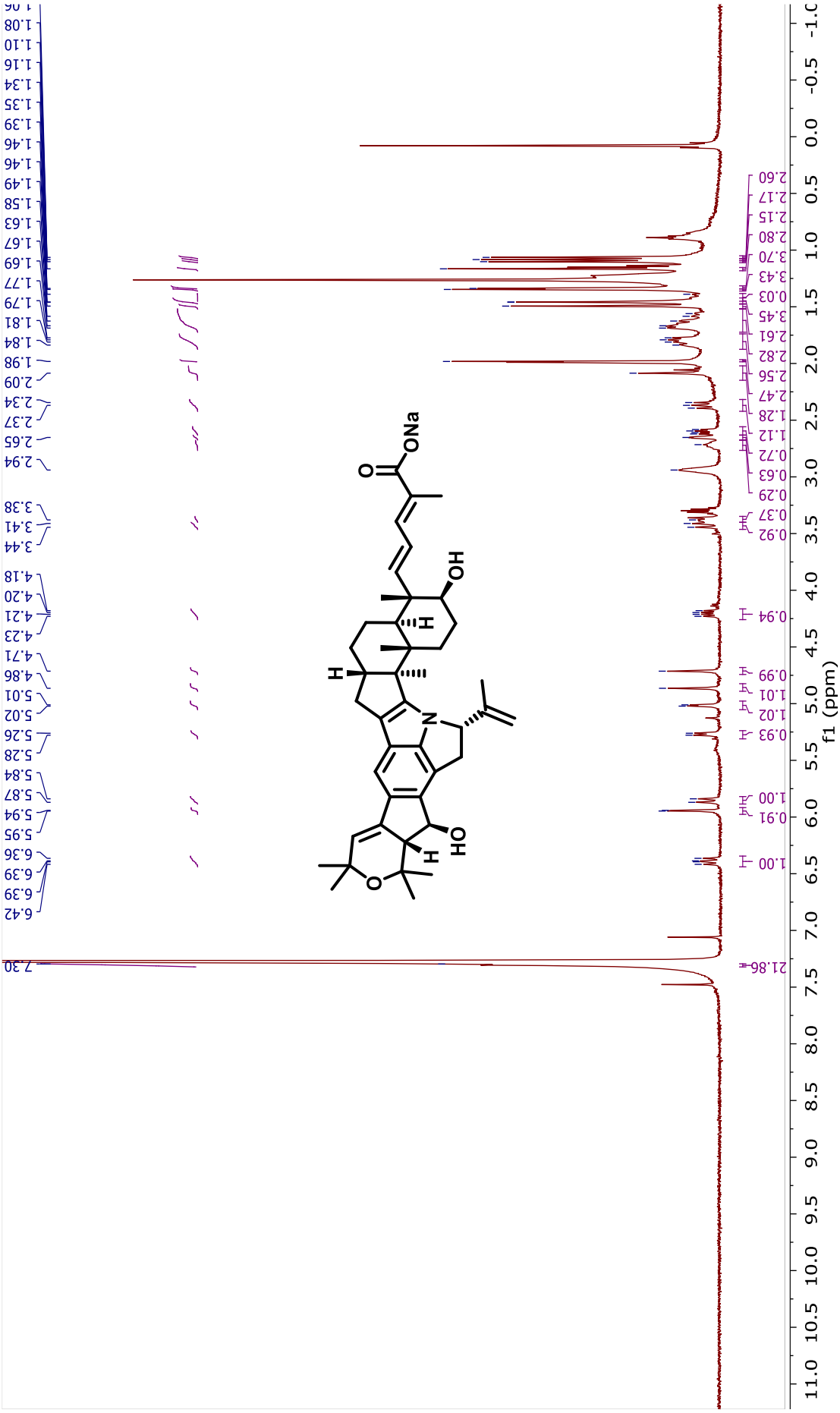
^{13}C NMR (126 MHz) Spectrum of Compound **(–)-96** in $(CD_3)_2CO$



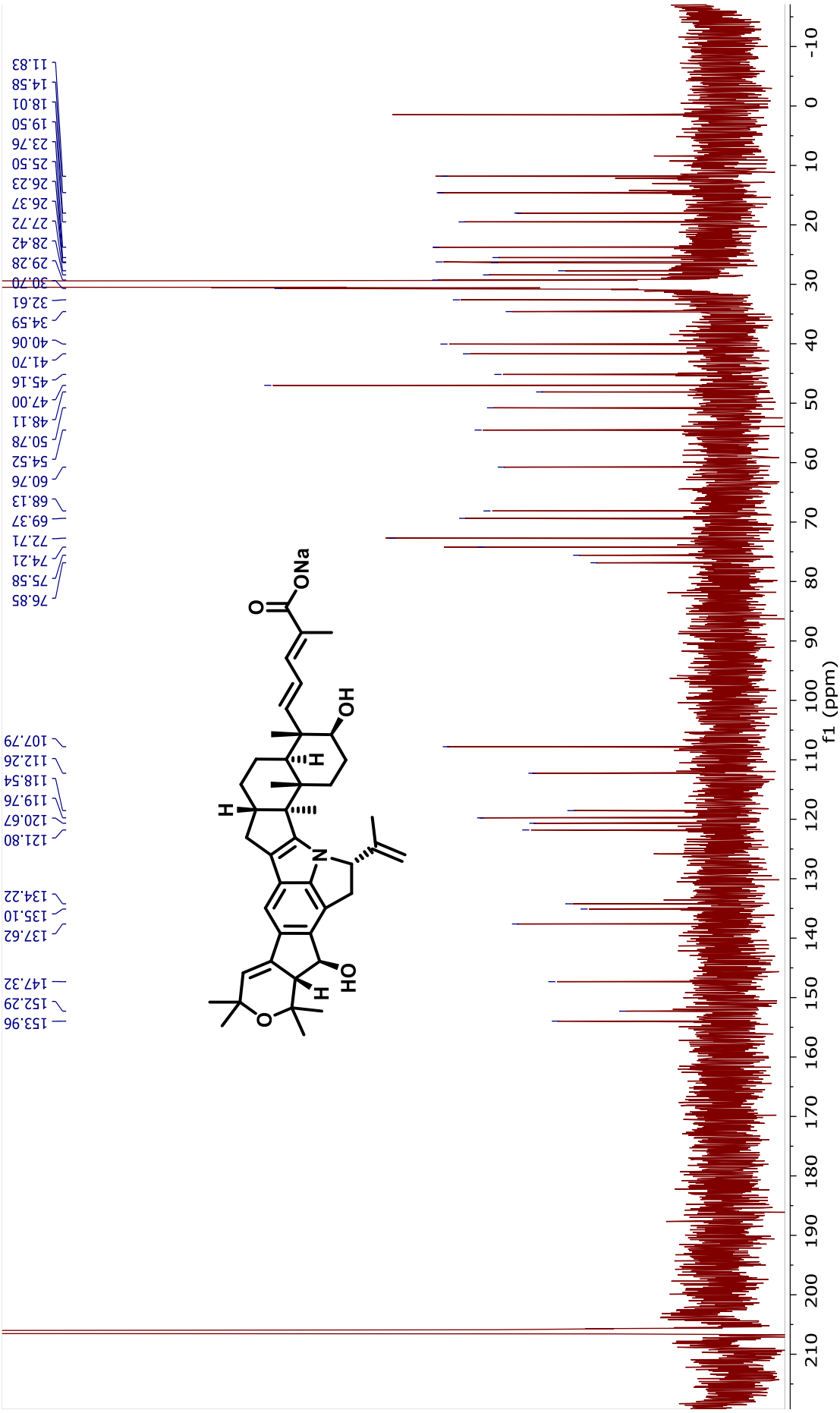
NOESY Spectrum of Compound **(–)-96** in $(CD_3)_2CO$



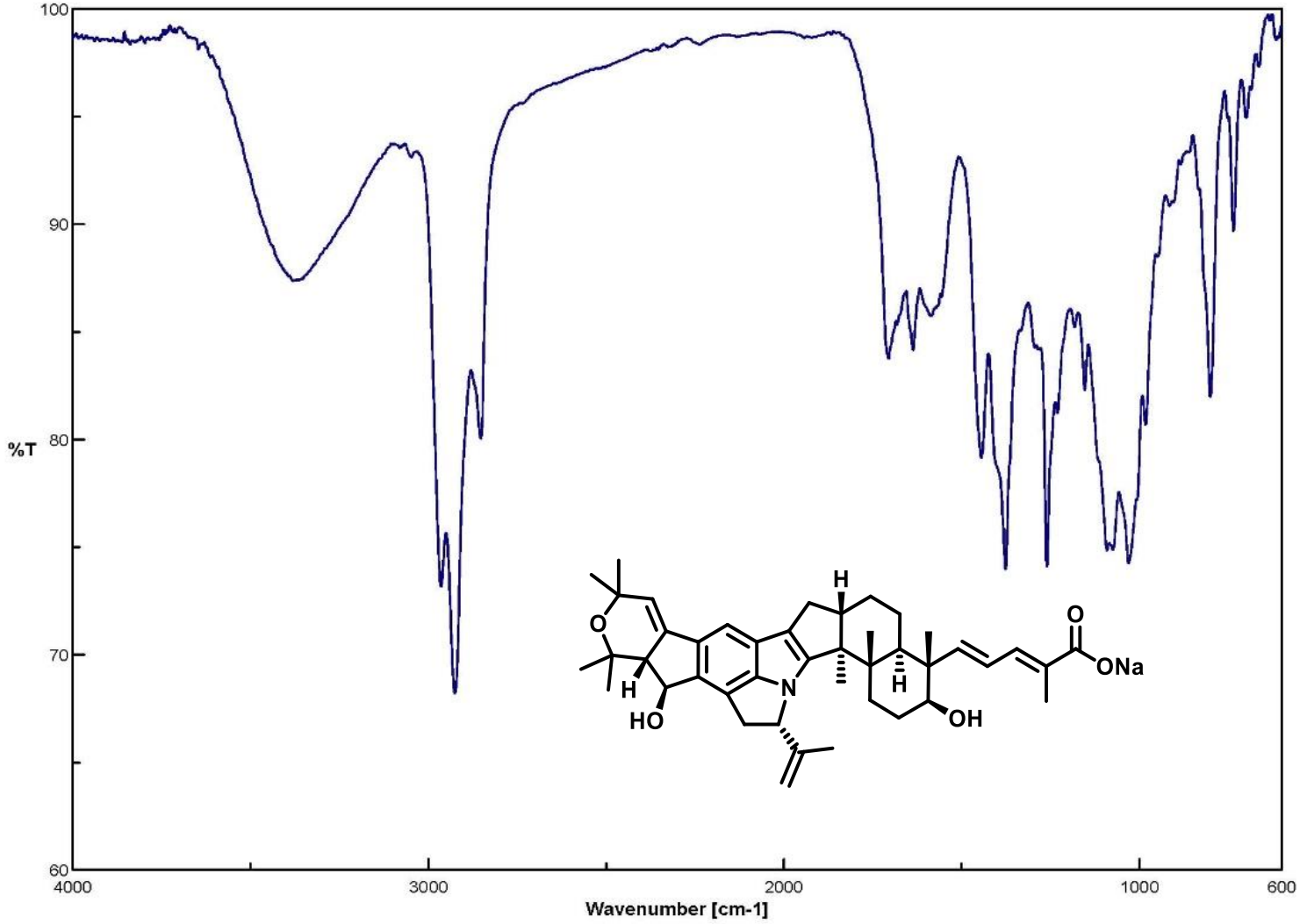
IR Spectrum of Compound (–)-**96**



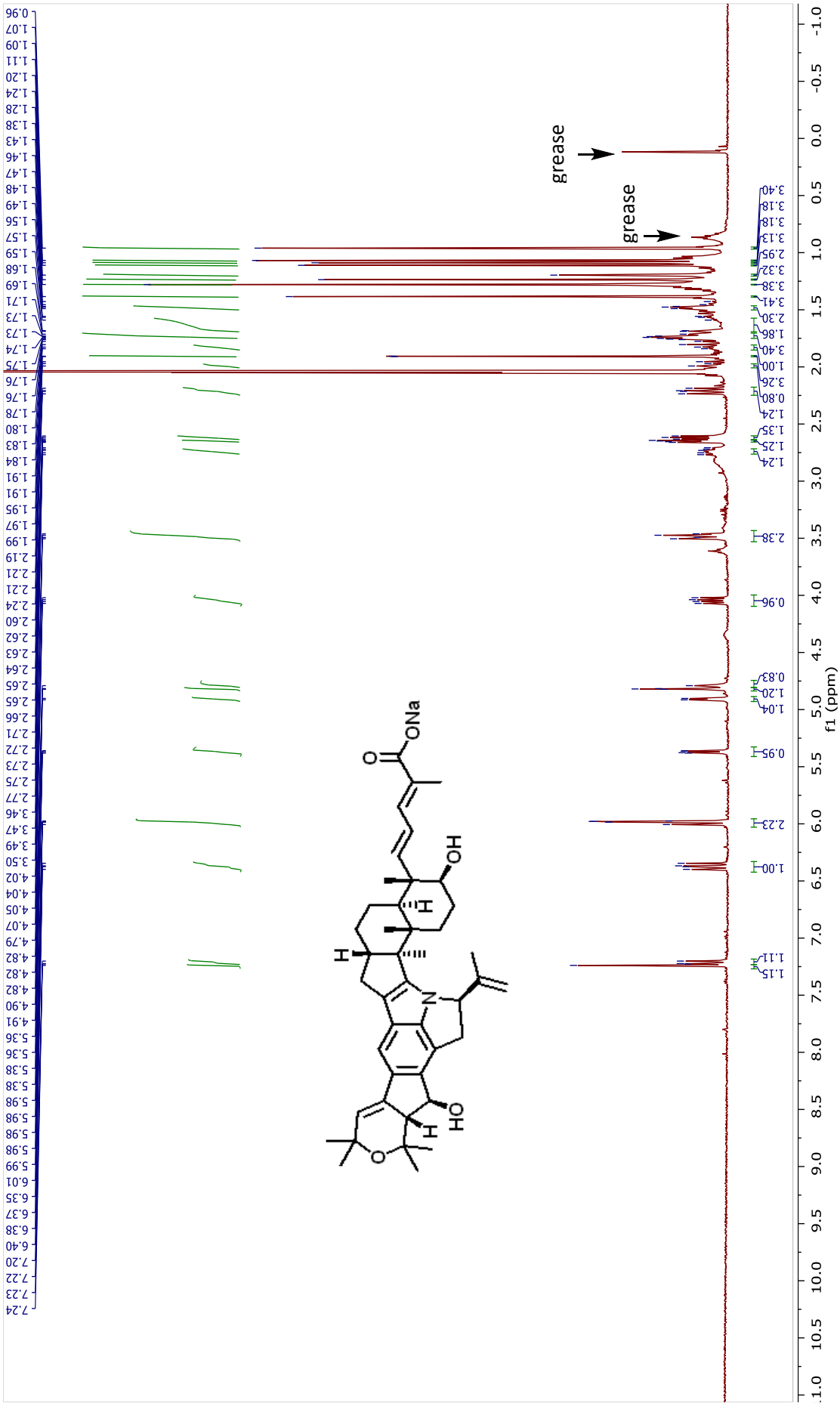
^{1}H NMR (500 MHz) Spectrum of Compound (–)- **94-Sodium Salt** in $CDCl_3$



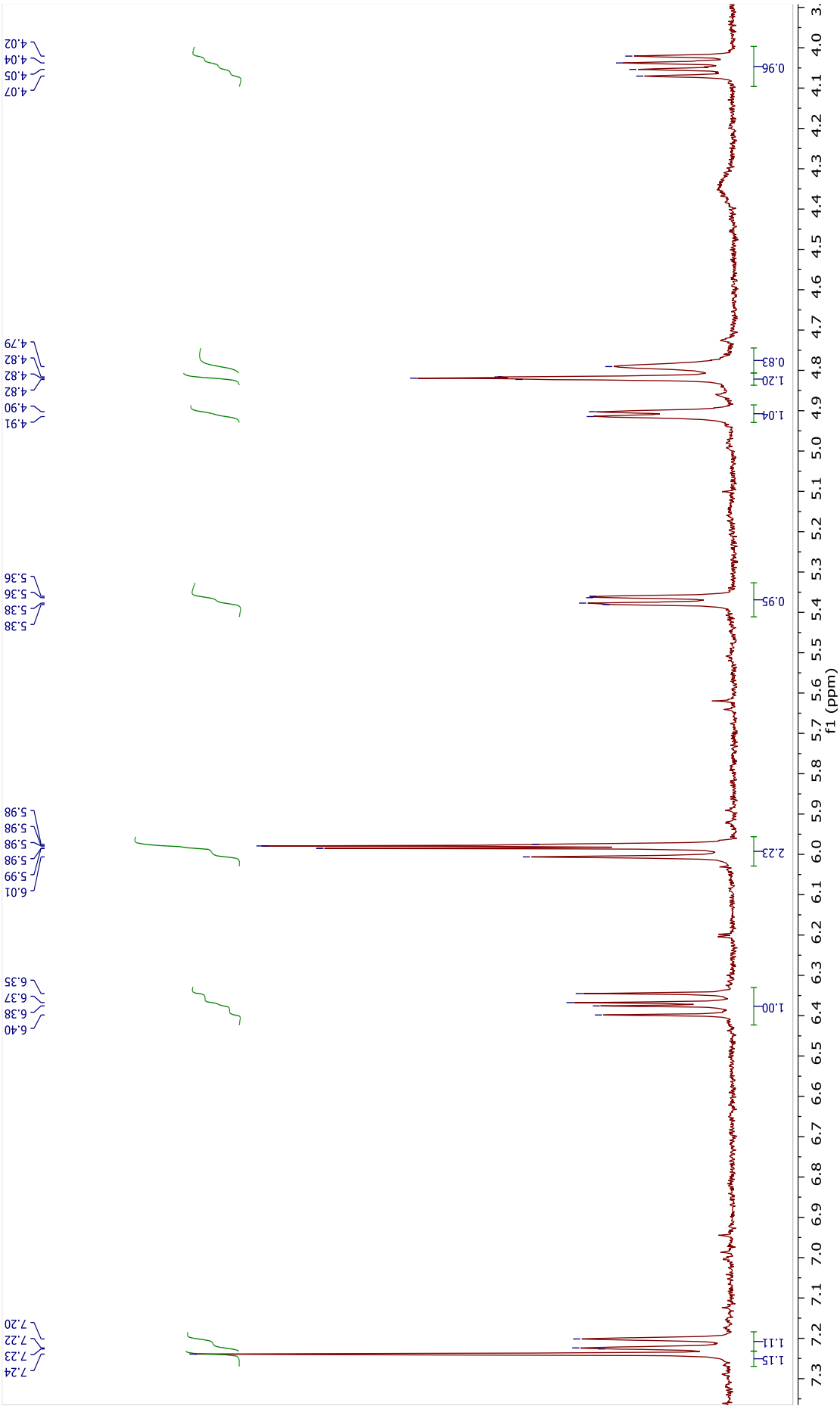
^{13}C NMR (126 MHz) Spectrum of Compound **(–)- 94-Sodium Salt** in $(CD_3)_2CO$



IR Spectrum of Compound (–)- **94-Sodium Salt**

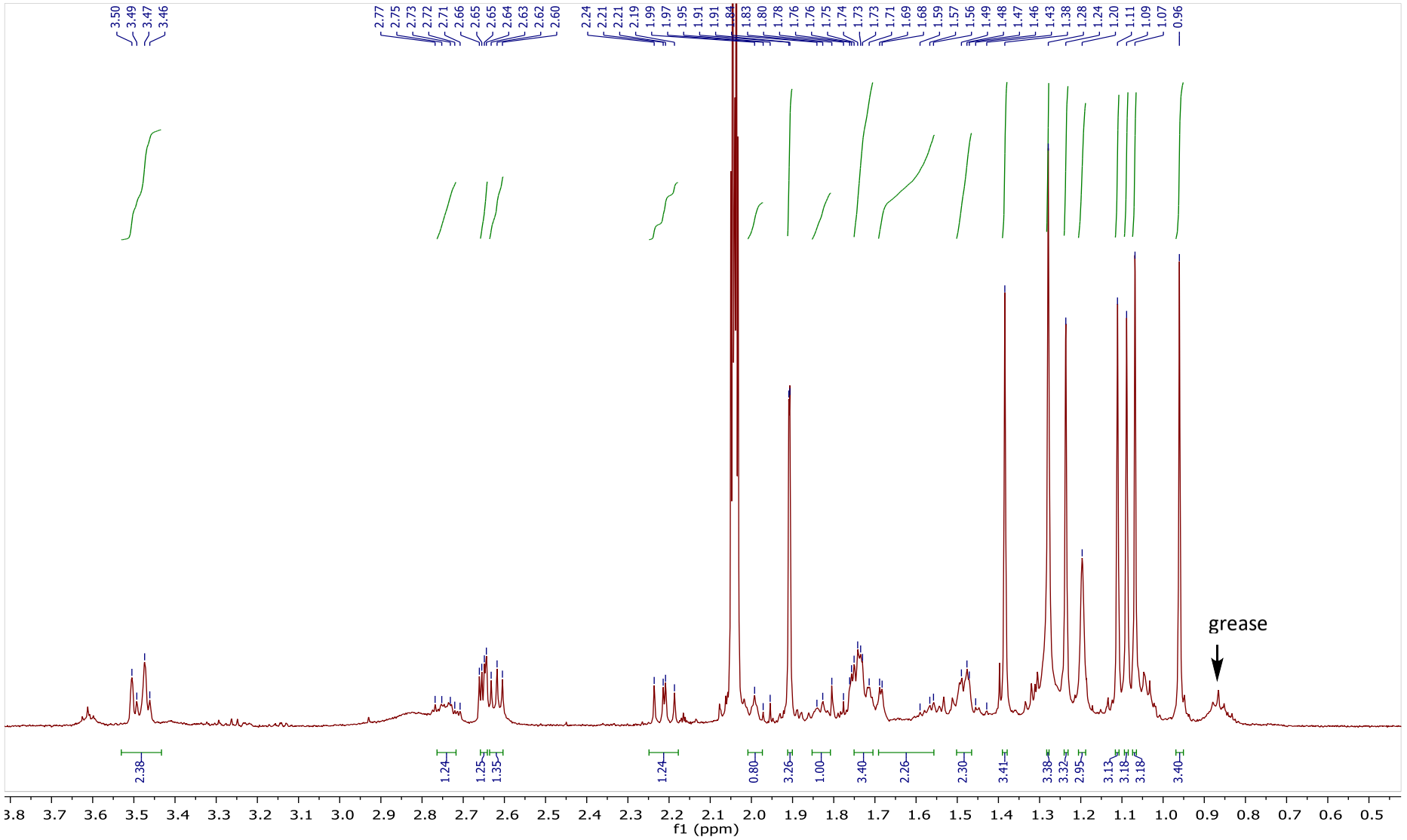


^{1}H NMR (500 MHz) Spectrum of Compound **(–)- 2-Sodium Salt** in $(CD_3)_2CO$



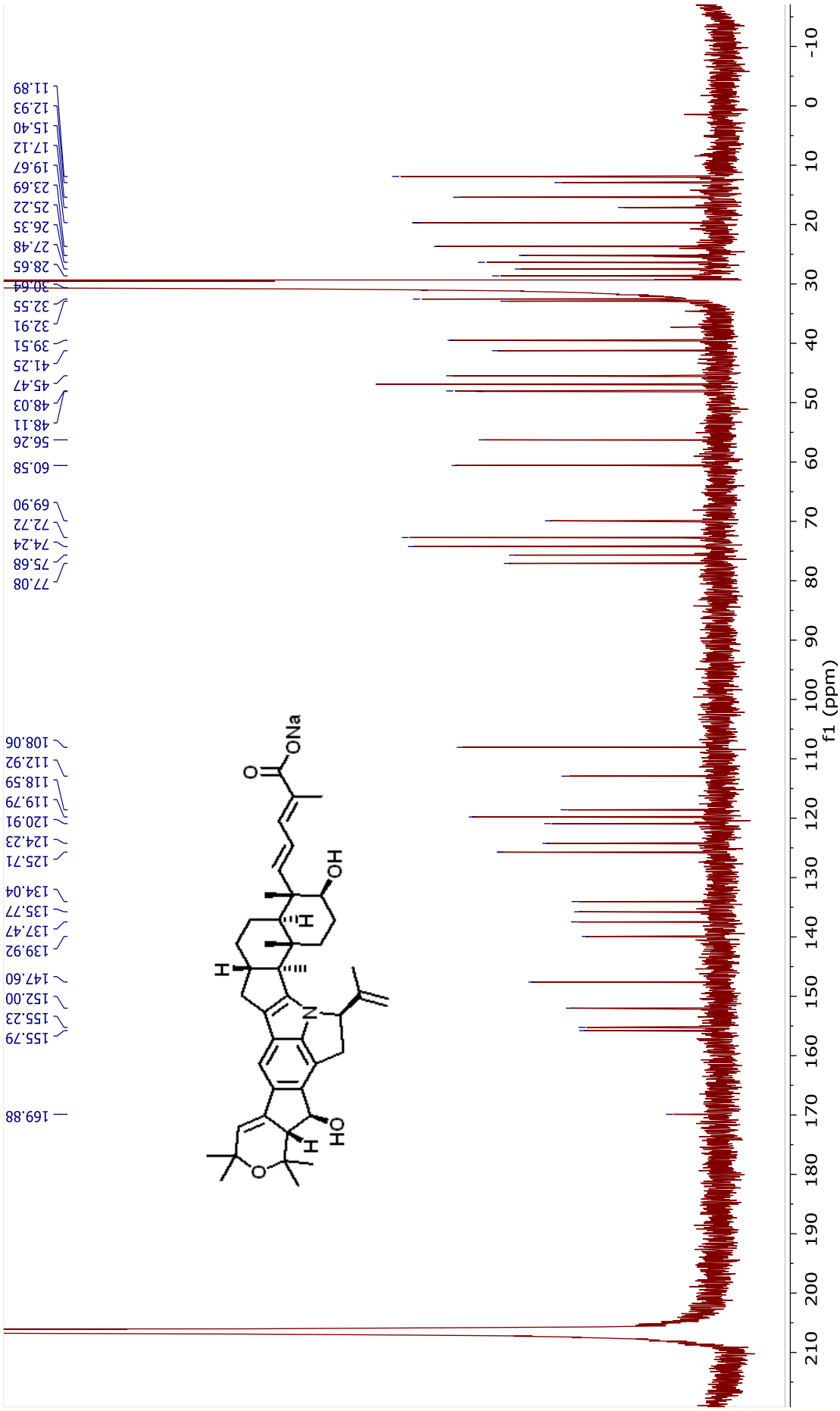
^{1}H NMR (500 MHz) Spectrum of Compound (–)- **2-Sodium Salt** in $(CD_3)_2CO$

(7.3 ppm to 3.9 ppm Expanded View)

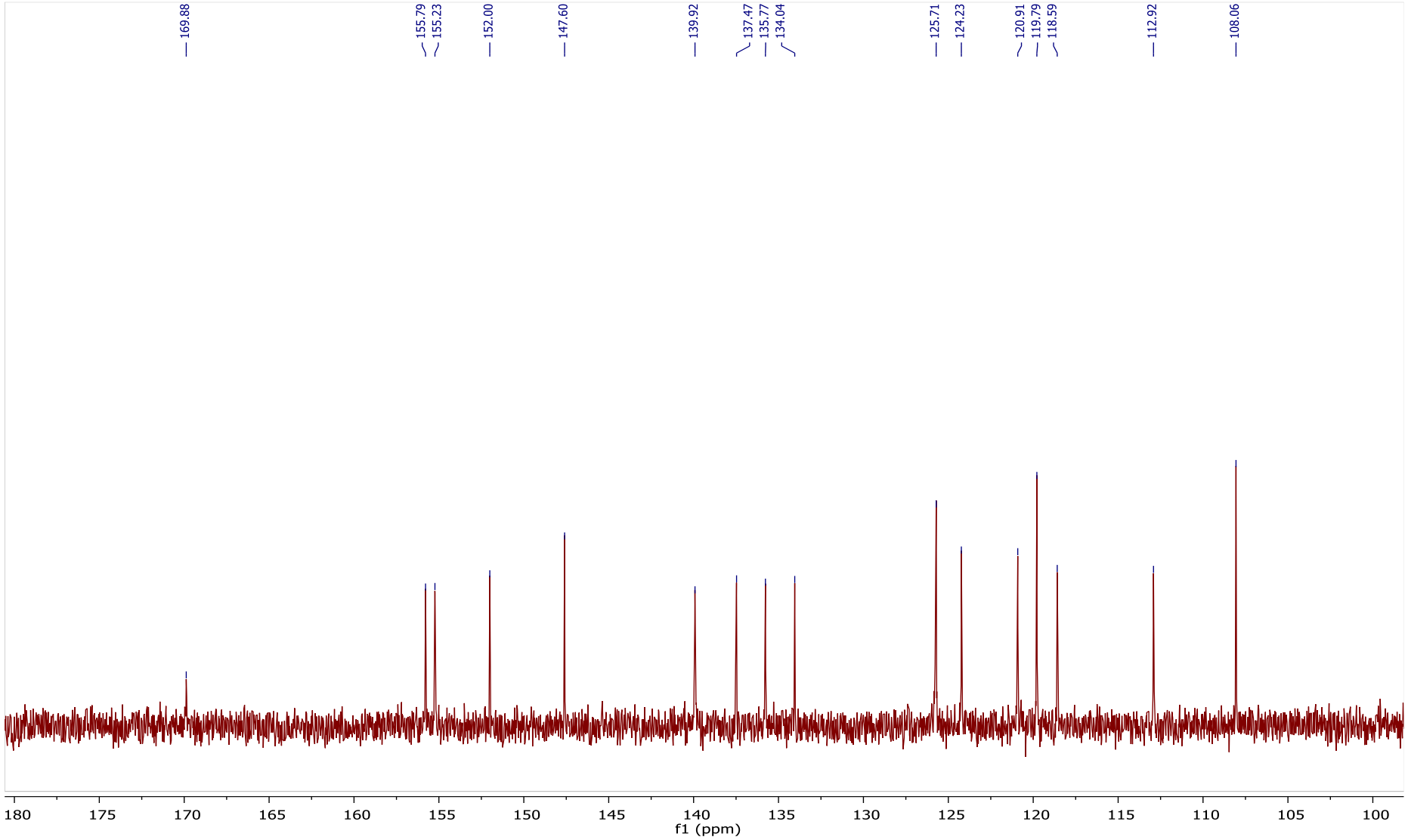


^{1}H NMR (500 MHz) Spectrum of Compound **(–)- 2-Sodium Salt** in $(CD_3)_2CO$

(3.8 ppm to 0.4 ppm Expanded View)

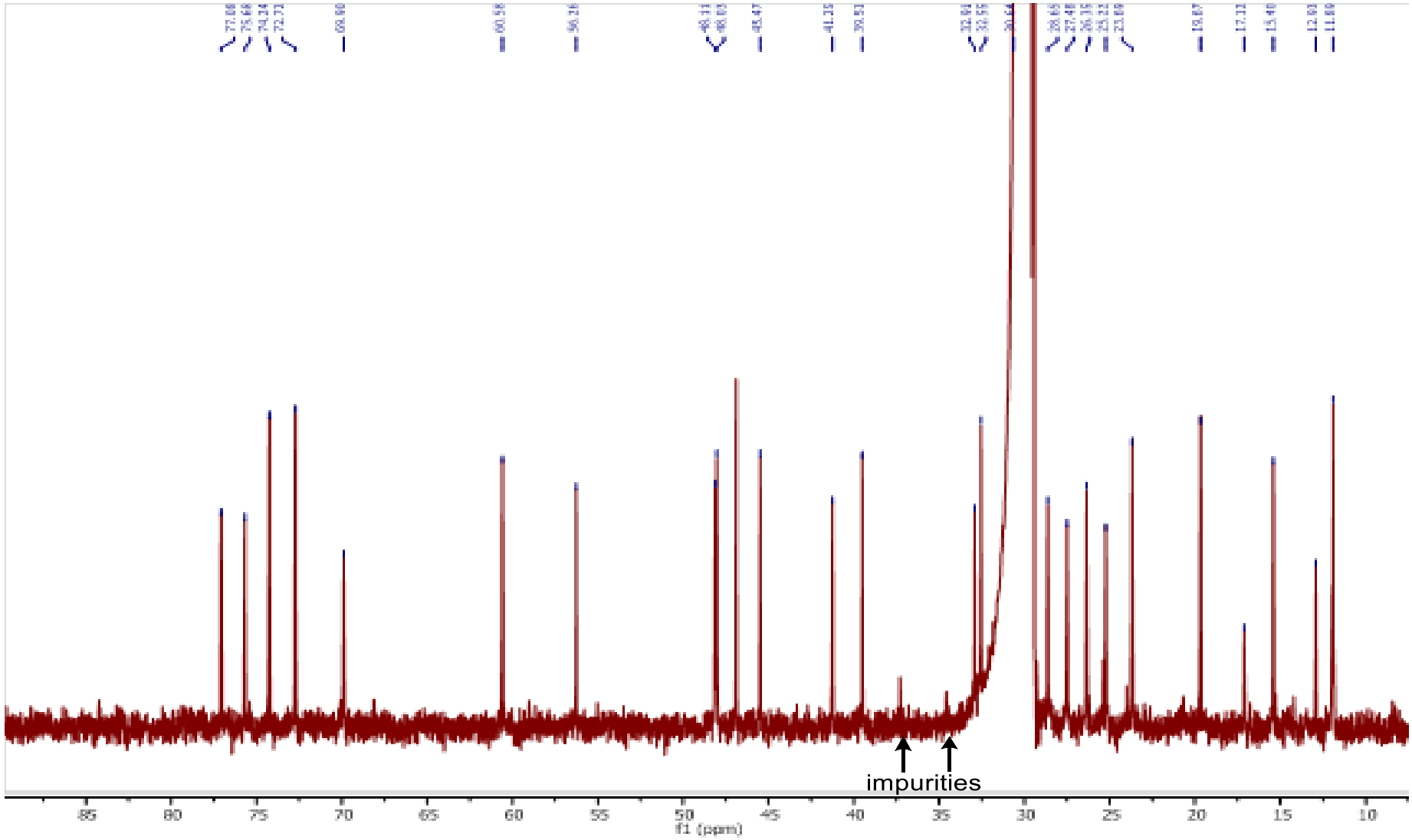


^{13}C NMR (126 MHz) Spectrum of Compound **(–)- 2-Sodium Salt** in $(CD_3)_2CO$



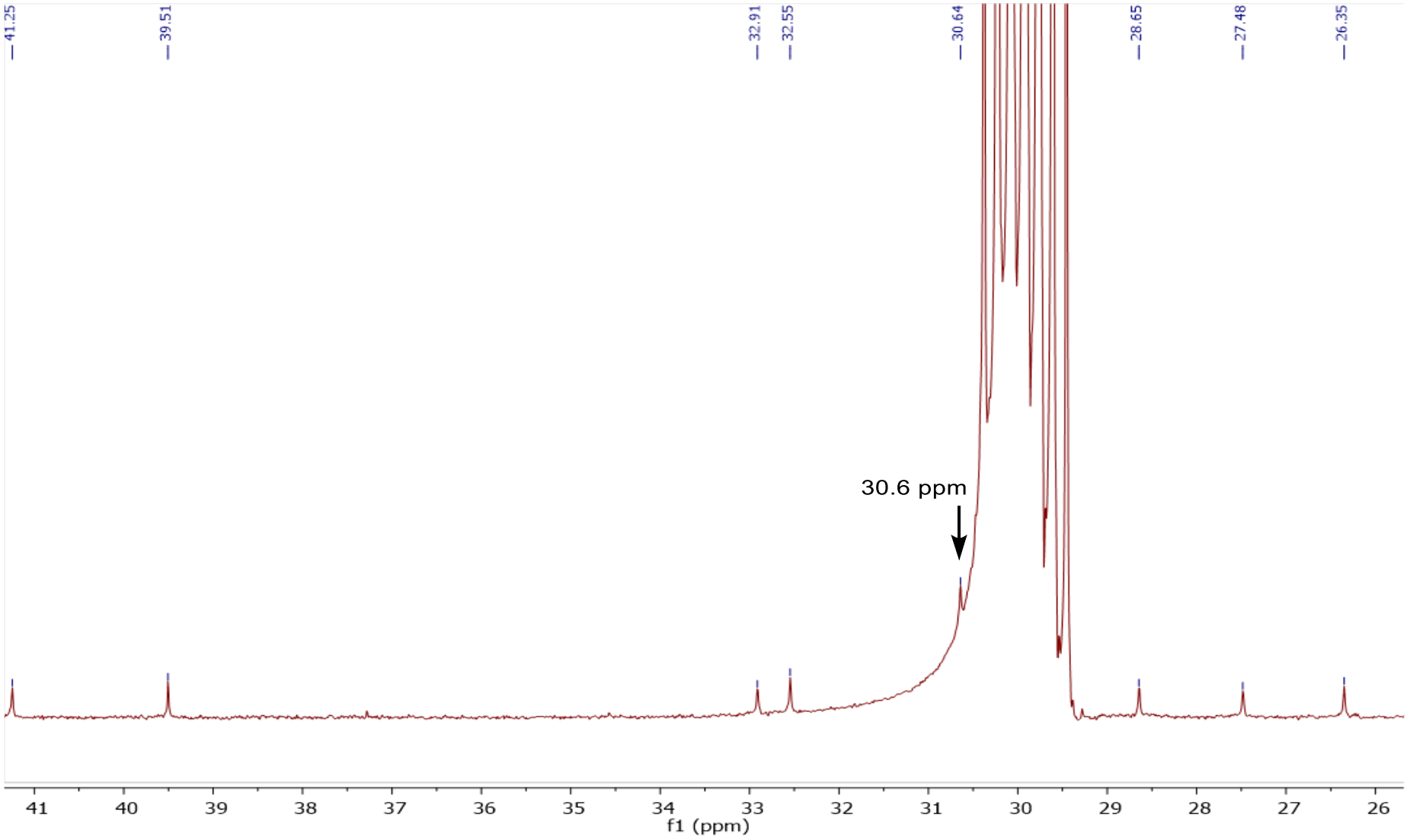
^{13}C NMR (126 MHz) Spectrum of Compound **(–)- 2-Sodium Salt** in $(CD_3)_2CO$

(180 ppm to 100 ppm Expanded View)



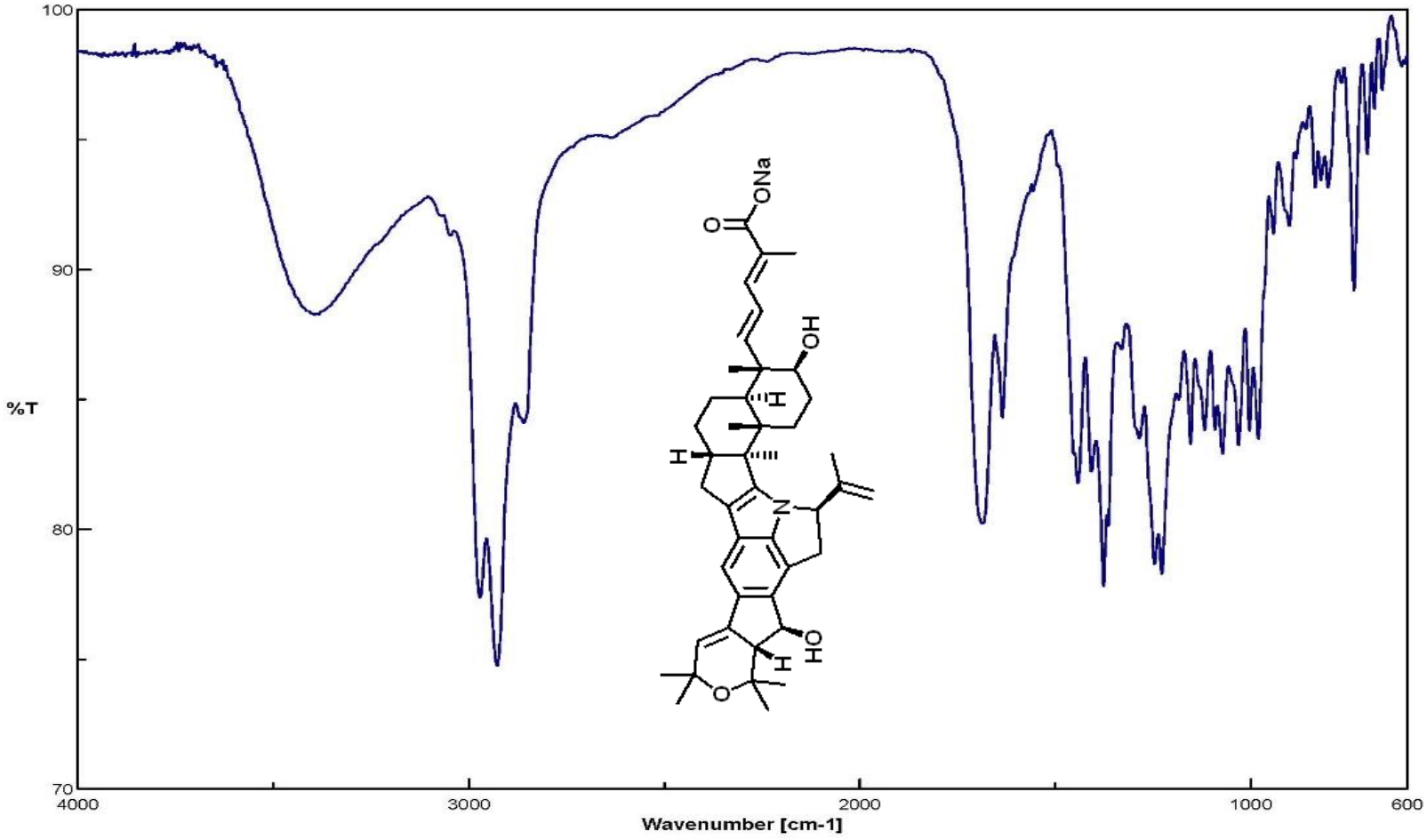
^{13}C NMR (126 MHz) Spectrum of Compound **(–)- 2-Sodium Salt** in $(CD_3)_2CO$

(87 ppm to 8 ppm Expanded View)



^{13}C NMR (126 MHz) Spectrum of Compound **(–)- 2-Sodium Salt** in

$(CD_3)_2CO$ (41 ppm to 26 ppm Expanded View)



IR Spectrum of Compound (–)- **2-Sodium Salt**