Concise and Stereoselective Total Syntheses of Annotinolides C, D, and E

Pei Qu and Scott A. Snyder*

[1]Department of Chemistry, The University of Chicago, 5735 S. Ellis Avenue, Chicago, IL 60637

Supporting Information

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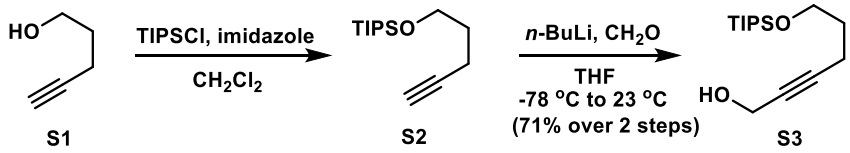
Experimental Data for Compounds

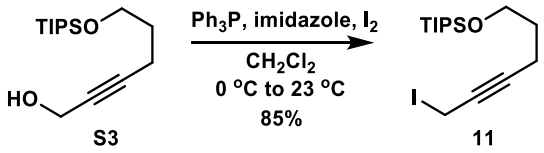
General Procedures. All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Dry tetrahydrofuran (THF), toluene, dimethylformamide (DMF), diethyl ether (Et_2O) and dichloromethane (CH_2Cl_2) were obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Yields refer to chromatographically and spectroscopically (^1H and ^{13}C NMR) homogeneous materials, unless otherwise stated. Steps refer to operations conducted in a single reaction flask; filtration, extraction, or other form of purification denotes the end of an individual step. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reactions were magnetically stirred and monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent, and an ethanolic solution of phosphomolybdic acid and cerium sulfate, and heat as developing agents. SiliCycle silica gel (60, academic grade, particle size 0.040–0.063 mm) was used for flash column chromatography. Preparative thin-layer chromatography separations were carried out on 0.50 mm E. Merck silica gel plates (60F-254). NMR spectra were recorded on Bruker 400, 500 and 700 MHz instruments and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet, app = apparent. IR spectra were recorded on a Perkin-Elmer 1000 series FT-IR spectrometer. High-resolution mass spectra (HRMS) were recorded on Agilent 6244 Tof-MS using ESI (Electrospray Ionization) at the University of Chicago Mass Spectroscopy Core Facility.

Abbreviations. TIPSCl = triisopropylsilyl chloride, MeOH = methanol, THF = tetrahydrofuran, EtOAc = ethyl acetate, *n*-BuLi = *n*-butyl lithium, Ph_3P = triphenyl phosphine, *i*-PrMgCl = isopropyl magnesium chloride, Et_3Al = triethyl aluminum, TMSCN = trimethylsilyl cyanide, LDA = lithium diisopropylamide, *i*-PrNH = diisopropyl amine, TBSOTf = tert-butyel dimethyl trifluoromethanesulfonate, *i*-Pr_2NEt = diisopropyl ethyl amine, $Ph_3PAuNTf_2$ = [bis(trifluoromethanesulfonyl)imidate] (triphenylphosphine)gold(I), AgOTf = silver trifluoromethanesulfonate, *t*-BuOH = tert-butyl alcohol, *i*-PrOH = isopropanol, $Pd(Ph_3P)_4$ = tetrakis(triphenylphosphine)palladium(0), MeCN = acetonitrile, DPPA = diphenylphosphoryl azide, Et_3N = triethyl amine, *t*-BuOK = potassium tert-butoxide, DIBAL-H = diisobutylaluminum hydride, NIS = *N*-iodosuccinimide, Et_3B = triethyl borane, *n*-Bu_3SnH = tributyltin hydride, TBAF = tetrabutylammonium fluoride, DMP = Dess–Martin periodinane, MsCl = methanesulfonyl chloride, TFA = trifluoroacetic acid, *t*-BuLi = tert-butyl lithium, MeONa = sodium methoxide, TBD = triazabicyclodecene, L-selectride = lithium tri-*sec*-butylborohydride, MTBE = Methyl-tert-butyl ether, MS = molecular sieves, Ac = acetyl, BzCl = benzoyl chloride, 4-DMAP = 4-(dimethylamino)pyridine, PCC = pyridinium chlorochromate, DMSO = dimethyl sulfoxide, LiHMDS = lithium hexamethyldisilazide, NaHMDS = sodium hexamethyldisilazide, KHMDS = potassium hexamethyldisilazide, LiTMP = lithium tetramethylpiperidide.

Synthesis of ketone 12

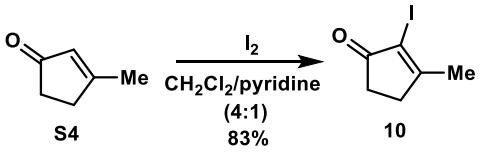


Propargyl alcohol S3. To a solution of 4-penty-1-ol (16.8 g, 0.200 mol, 1.0 equiv) in CH_2Cl_2 (400 mL) at 23 °C was sequentially added imidazole (20.4 g, 0.300 mol, 1.5 equiv) and TIPSCl (51.4 mL, 0.240 mol, 1.2 equiv), after which a white participate formed. The resultant suspension was then stirred at 23 °C for 4 h. Next, MeOH (1.72 mL, 1.36 g, 0.0400 mol) was added and the reaction contents were stirred for an additional 30 min. Upon completion, the reaction contents were filtered through a pad of Celite (eluting with hexanes) and concentrated directly. Pressing forward without any further purification, the so-obtained TIPS-protected alcohol was dissolved in THF (1.05 L) and the reaction contents were cooled to –78 °C. Next, *n*-BuLi (100 mL, 2.5 M in hexane, 0.250 mol, 1.25 equiv) was then added at –78 °C via cannula over the course of 5 min, during which time the solution turned bright yellow. The reaction contents were then stirred for an additional 30 min at –78 °C. Solid paraformaldehyde (12.7 g, 0.420 mol, 2.1 equiv) was then added to the solution in a single portion, and the resultant suspension was then slowly warmed to 23 °C and stirred for 12 h. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (600 mL) and poured into a seapratory funnel. After separating the layers, the aqueous phase was extracted with EtOAc (2 × 600 mL). The combined organic layers were then washed with brine (1 L), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash chromatography chromatography (silica gel, hexanes/EtOAc = 10:1) provided the desired propargyl alcohol (38.4 g, 71% yield over 2 steps) as a pale-yellow oil. Its spectral data matched that previously reported.[1]

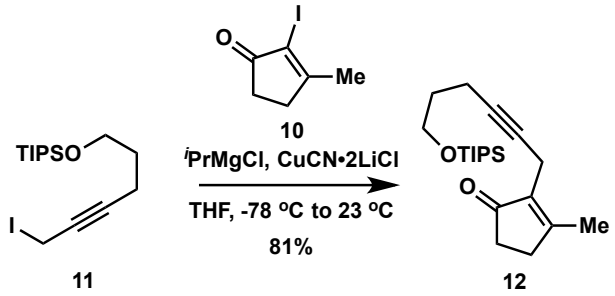


Propargyl iodide 11. To a flame-dried flask containing CH_2Cl_2 (800 mL) at 23 °C was sequentially added Ph_3P (45.86 g, 0.175 mol, 1.2 equiv) and imidazole (11.9 g, 0.175 mol, 1.2 equiv). The resultant solution was then cooled to 0 °C using an ice-water bath and I_2 (44.4 g, 0.175 mol, 1.2 equiv) was added in a single portion, forming an orange-brown suspension. The resultant suspension was then stirred at 0 °C for 30 min before a solution of propargyl alcohol (39.4 g, 0.146 mol, 1.0 equiv) in CH_2Cl_2 (200 mL) was added, rinse that flask with a minimal amount of CH_2Cl_2 to ensure a complete transfer. Next, the ice-water bath was removed, at which time the suspension turned bright yellow. After stirring the resultant suspension at 23 °C for 1 h, the reaction was filtered directly through Celite (eluting with hexanes) and concentrated. The resultant residue was redissolved in hexanes (600 mL) and filtered a second time through a pad of Celite (eluting with hexanes) again. The resultant filtrate was concentrated and purification of the resultant residue by flash chromatography chromatography (silica gel, hexanes/EtOAc = 50:1), provided the desired propargyl iodid**e** (47.0 g, 85% yield) as a yellow oil. **11**: R_f = 0.87

(silica gel, hexanes/EtOAc, 4:1); IR (film) ν_{max} 2930, 2892, 2866, 2361, 2339, 1464, 1171, 1109, 680 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.76 (t, J = 6.0 Hz, 2 H), 3.70 (t, J = 2.5 Hz, 2 H), 2.32 (tt, J = 7.1, 2.5 Hz, 2 H), 1.72 (p, J = 6.6 Hz, 2 H), 1.11–1.06 (m, 21 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 86.4, 77.1, 61.7, 31.6, 18.0, 15.6, 12.0, –16.9; HRMS (ESI) calcd for $C_{15}H_{30}IOSi^+$ [M + H^+] 380.1032, found 380.1030.



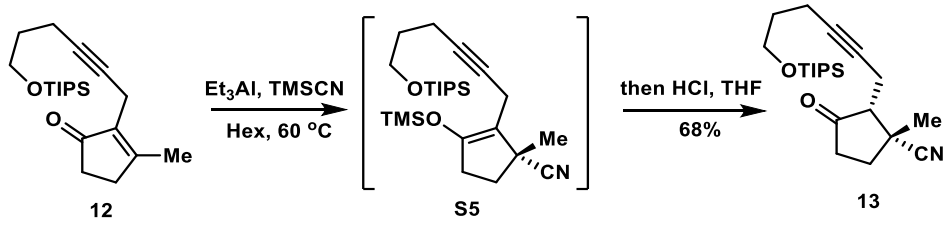
Iodide 10. A flame-dried flask at 23 °C was charged sequentially with 3-methyl-2-cyclopenten-1-one (9.81 mL, 9.61 g, 0.100 mol, 1.0 equiv), CH_2Cl_2 (800 mL), and pyridine (200 mL). Next, I_2 (55.9 g, 0.220 mol, 2.2 equiv) was added, forming a dark-brown solution. The resultant mixture was then stirred at 23 °C for 48 h. Upon completion, the reaction contents were quenched the addition of saturated aqueous $Na_2S_2O_3$ (600 mL) and poured into a separatory funnel. After separating the layers, the organic phase was washed with 3 N HCl (1 L), H_2O (600 mL), and brine (600 mL). The organic layer was then dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 4:1→2:1) afforded the desired iodide (18.5 g, 83% yield) as a pale-yellow solid. Its spectral data matched that previously reported.[2]



CuCN•2LiCl solution (1.0 M in THF). A round-bottom flask equipped with a stir bar at 23 °C was charged with LiCl (8.10 g, 0.191 mol, 3.0 equiv). Next, the flask and its contents were dried with a propane torch under vacuum until the appearance of the LiCl became a sand-like solid without chunks. The flask was then removed from the vacuum line, flushing with argon, and then THF (96 mL) was added followed by CuCN (8.56 g, 95.6 mmol, 1.5 equiv). The resultant cloudy green solution was stirred at 23 °C for 1 h, at which point it was ready for use.

Enone 12. Iodide **10** (21.2 g, 95.6 mmol, 1.5 equiv) was dissolved in THF (350 mL) in a flame-dried flask at 23 °C and then was cooled to –78 °C using a dry ice-acetone bath, forming a yellow suspension. Next, *i*-PrMgCl (2.0 M in THF, 47.8 mL, 95.6 mmol, 1.5 equiv) was added dropwise at –78 °C, during which time the yellow suspension turned into a pale brown solution. After stirring the resultant solution for 30 min at –78 °C, freshly prepared CuCN•2LiCl (1.0 M in

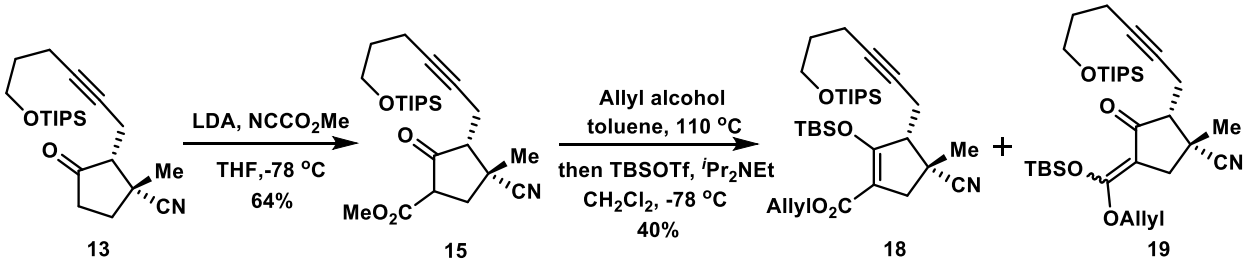
THF, 96 mL, 95.6 mmol, 1.5 equiv) was added, and the resultant gray/green suspension was stirred for a further 15 min at –78 °C. Next, a solution of propargyl iodide **11** (24.2 g, 63.7 mmol, 1.0 equiv) in THF (40 mL) was added to the suspension, rinsing the flask with additional THF (10 mL) to ensure a complete transfer. Once the transfer was complete, the cold bath was removed and the suspension was slowly warmed to 23 °C over the course of 30 min with stirring, during which time the suspension turned brown. Upon completion, the reaction contents were quenched by the sequential addition of saturated aqueous NH_4Cl (200 mL) and 3 M NaOH (200 mL) and poured into a separatory funnel. After separating the layers, the aqueous layer was extracted with EtOAc (2 × 400 mL). The combined organic layers were then washed with brine (800 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 10:1→4:1), providing the desired enone (17.9 g, 81% yield) as a yellow oil. **12**: R_f = 0.29 (silica gel, hexanes/EtOAc, 4:1); IR (film) ν_{max} 2942, 2865, 2360, 2339, 1700, 1653, 1457, 1107, 668 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.72 (t, *J* = 6.1 Hz, 2 H), 3.06 (s, 2 H), 2.58–2.47 (m, 2 H), 2.44–2.34 (m, 2 H), 2.23 (tt, *J* = 7.1, 2.5 Hz, 2 H), 2.17 (s, 3 H), 1.68 (p, *J* = 6.7 Hz, 2 H), 1.06–1.03 (m, 21 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.6, 171.8, 136.1, 79.7, 76.0, 61.8, 33.9, 32.0, 31.6, 17.9, 17.3, 15.1, 12.5, 11.8; HRMS (ESI) calcd for $C_{21}H_{37}O_2Si^+$ [M + H^+] 349.2558, found 349.2553.



Nitrile 13. Et_3Al (1.0 M in heptane, 40.4 mL, 40.4 mmol, 1.2 equiv) and hexanes (19 mL) were added sequentially to a flame-dried flask at 23 °C. Next, TMSCN (9.2 mL, 74.0 mmol, 2.2 equiv) was added and the resultant colorless solution was stirred for 15 min at 23 °C. A solution of enone **12** (11.7 g, 33.6 mmol, 1.0 equiv) in hexanes (200 mL) was then added, using an additional portion of hexanes (60 mL) to complete the transfer. The reaction solution turned a red-brown color and then was warmed to 60 °C using a pre-heated oil bath. After stirring the resultant solution at 60 °C for 1 h. Upon completion, the reaction contents were then cooled to 0 °C using an ice-water bath and quenched by the addition of H_2O until no bubble formation was observed from the solution. The reaction contents were then warmed to 23 °C and stirred for 30 min before being filtered through a pad of Na_2SO_4 (eluting with hexanes) and concentrated directly. The resultant crude silyl enol ether was then dissolved in THF (100 mL) and 3 M HCl (25 mL) was added at 23 °C. The resultant solution was stirred at 23 °C until the presence of the silyl enol ether had disappeared based on TLC monitoring (typically 10 min). Upon completion, the reaction contents were quenched by the addition of H_2O (25 mL) and poured into a separatory funnel. After separating the layers, the aqueous layer was extracted with EtOAc (2 × 100 mL). The combined organic layers were then washed with brine (300 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant crude product by flash column chromatography (silica gel, hexanes/EtOAc = 10:1→4:1) providing the desired nitrile (8.67 g, 68% yield) as a pale brown oil. [Note: this compound contains a minor impurity which produces

signals at 2.70 ppm as well as a few other sites; removal of these consistent impurities did not prove possible with several different developing solvents, even preparative TLC with different solvents and collecting different portions of the main band. In all cases, we observed no additional impurity by TLC but these signals are always present based on NMR analysis. We also attempted silyl deprotection/reprotection and reduction/oxidation to reform this compound without that impurity, but no fruitful results were obtained]. **13**: R_f = 0.29 (silica gel, hexanes/EtOAc, 4:1); IR (film) ν_{max} 2943, 2892, 2866, 2235, 1751, 1490, 1246, 1108 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.73 (t, *J* = 6.0 Hz, 2 H), 2.87 (ddq, *J* = 17.4, 4.1, 2.2 Hz, 1 H), 2.53 (ddt, *J* = 12.9, 8.0, 2.0 Hz, 1 H), 2.46–2.40 (m, 2 H), 2.35 (ddt, *J* = 19.6, 12.2, 2.6 Hz, 1 H), 2.25 (td, *J* = 7.2, 3.4 Hz, 2 H), 2.14 (dd, *J* = 10.1, 3.7 Hz, 1 H), 1.86 (ddd, *J* = 12.8, 11.2, 8.9 Hz, 1 H), 1.74 (d, *J* = 1.2 Hz, 3 H), 1.72–1.66 (m, 2 H), 1.09–1.00 (m, 21 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.6, 121.3, 82.3, 76.2, 61.8, 57.5, 41.7, 35.2, 34.2, 31.9, 25.3, 17.9, 16.7, 15.1, 11.9; HRMS (ESI) calcd for $C_{22}H_{38}NO_2Si^+$ [M + H^+] 376.2667, found 376.2667.

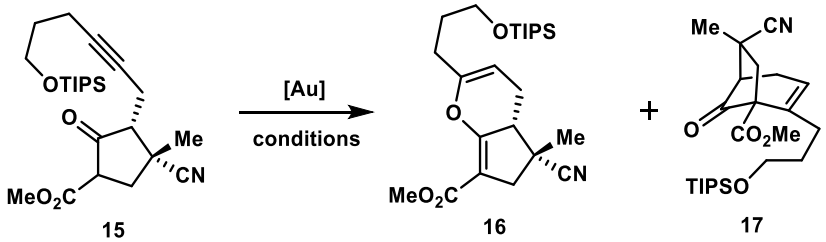
Exploration of Conia-ene reaction



Silyl enol ether 18 and 19. To a flame-dried flask at 23 °C was added *i*-Pr_2NH (3.71 mL, 26.5 mmol, 2.1 equiv) and THF (27 mL), and the resultant solution was cooled to 0 °C using an ice-water bath. Next, *n*-BuLi (1.6 M in hexanes, 16.6 mL, 26.5 mmol, 2.1 equiv) was added dropwise, generating a colorless solution. After stirring the reaction contents for 10 min at 0 °C, the ice-water bath was exchanged for a dry ice-acetone bath to cool the solution to –78 °C. A solution of nitrile **13** (4.74 g, 12.6 mmol, 1.0 equiv) in THF (90 mL) was then added quickly, using an additional portion of THF (10 mL) to complete the transfer. The reaction solution turned a red-brown color and was stirred for an additional 30 min at –78 °C before Mander's reagent (**14**, 1.52 mL, 18.9 mmol, 1.5 equiv) was added dropwise. The resultant solution was then stirred at –78 °C for another 1 h. Upon completion, the reaction contents were quenched at –78 °C by the addition of saturated aqueous NH_4Cl (100 mL) and warmed to 23 °C. The contents were then poured into a separatory funnel and the layers were separated. The aqueous layer was further extracted with EtOAc (2 × 100 mL). The combined organic layers were then washed with brine (300 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 8:1→4:1) provided the desired β-ketoester **15** (3.51 g, 64% yield) as a pale-yellow oil and as an inseparable mixture of diastereomers, also with enol form based on NMR analysis. **15**: R_f = 0.29 (silica gel, hexanes/EtOAc, 4:1); IR (film) ν_{max} 2943, 2893, 2865, 2230, 1734, 1717, 1705, 1635, 1464, 1386, 1254, 1124, 672 cm^{-1}; ^1H NMR (500 MHz, $CHCl_3$, list major two diastereomers) δ 3.79–

3.76 (m, 3 H), 3.76–3.72 (m, 2 H), 3.47 (dd, J = 12.2, 8.4 Hz, 0.71 H), 3.26 (dd, J = 11.4, 8.7 Hz, 0.28 H), 3.07 (dd, J = 14.0, 5.4 Hz, 0.28 H), 2.94–2.88 (m, 1 H), 2.88–2.80 (m, 0.28 H), 2.78–2.72 (m, 1 H), 2.72–2.67 (m, 0.28 H), 2.66–2.56 (m, 0.71 H), 2.55–2.49 (m, 0.56 H), 2.39 (ddt, J = 16.9, 10.1, 2.3 Hz, 1 H), 2.35–2.33 (m, 1 H), 2.30–2.23 (m, 3 H), 2.22–2.14 (m, 0.56 H), 1.81 (s, 2 H), 1.77–1.67 (m, 3 H), 1.08–1.01 (m, 21 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.3, 168.1, 120.8, 82.9, 75.6, 61.8, 57.4, 53.0, 52.3, 51.5, 51.2, 50.8, 39.8, 37.7, 32.1, 32.0, 31.7, 25.0, 19.2, 18.0, 16.8, 15.2, 15.1, 15.0, 12.2, 12.0; HRMS (ESI) calcd for $C_{24}H_{40}NO_4Si^+$ [M + H$^+$] 434.2721, found 434.2719.

Pushing forward, the newly formed β-ketoester **15** was dissolved in a mixture of toluene (40 mL) and allyl alcohol (10 mL), and the reaction contents were then heated directly to 110 °C using a pre-heated oil bath. After stirring at 110 °C for 3 h, the reaction contents were then cooled to 23 °C and concentrated directly. Finally, the resultant crude product was then dissolved in CH_2Cl_2 (81 mL) and *i*-Pr_2NEt (7.04 mL, 40.4 mmol, 5.0 equiv) was added at 23 °C. The resultant solution was then cooled to –78 °C using a dry ice-acetone bath and TBSOTf (3.72 mL, 16.2 mmol, 2.0 equiv) was added dropwise. After stirring the resultant solution for 30 min at –78 °C, the reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (60 mL). The reaction contents were then warmed to 23 °C, poured into a separatory funnel, and the layers were separated. The aqueous layer was further extracted with CH_2Cl_2 (2 × 60 mL). The combined organic layers were then washed with brine (150 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 20:1), providing a mixture of silyl enol ethers **18** and **19** (1.86 g, 40% yield) as a pale-yellow oil. **18** and **19**: R_f = 0.59 (silica gel, hexanes/EtOAc, 4:1); IR (film) ν_{max} 2942, 2893, 2865, 2232, 1720, 1703, 1635, 1463, 1390, 1251, 1231, 1133, 1108, 1067, 1057, 1013, 995, 841, 788 cm^{-1}; ^{1}H NMR (400 MHz, C_6D_6) δ 5.73 (ddtd, J = 18.0, 10.7, 5.6, 2.0 Hz, 1 H), 5.09 (ddt, J = 17.2, 3.6, 1.7 Hz, 1 H), 4.97 (ddt, J = 10.4, 2.7, 1.4 Hz, 1 H), 4.45 (dd, J = 5.6, 1.5 Hz, 2 H), 3.71–3.60 (m, 2 H), 3.24 (dd, J = 14.9, 1.9 Hz, 0.67 H), 2.98–2.87 (m, 0.67 H), 2.68 (ddt, J = 17.1, 4.5, 2.4 Hz, 0.67 H), 2.61–2.54 (m, 0.67 H), 2.51 (dd, J = 15.0, 1.6 Hz, 0.33 H), 2.40–2.31 (m, 1 H), 2.22 (tq, J = 6.9, 2.4 Hz, 2 H), 2.14 (ddd, J = 6.2, 4.0, 1.5 Hz, 0.67 H), 2.10 (dt, J = 9.2, 2.4 Hz, 0.33 H), 1.70–1.61 (m, 2 H), 1.17 (s, 1 H), 1.11–1.06 (m, 23 H), 0.95–0.90 (m, 9 H), 0.31 (d, J = 18.3 Hz, 3 H), 0.15 (d, J = 17.8 Hz, 3 H); ^{13}C NMR (100 MHz, C_6D_6) δ 163.70, 163.67, 163.65, 163.1, 133.64, 133.61, 125.9, 122.9, 118.2, 107.5, 106.5, 83.9, 83.7, 76.67, 76.65, 64.9, 62.8, 57.1, 55.2, 42.5, 42.2, 37.2, 36.5, 33.0, 32.9, 27.7, 26.5, 26.44, 21.1, 20.2, 19.29, 19.25, 18.89, 18.87, 18.7, 17.9, 16.2, 16.1, 12.9, –3.2, –3.3, –3.6, –3.8; HRMS (ESI) calcd for $C_{32}H_{55}NNaO_4Si_2^+$ [M + Na$^+$] 596.3562, found 596.3560.

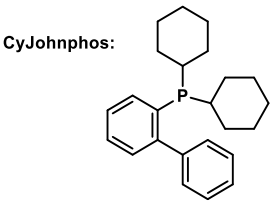


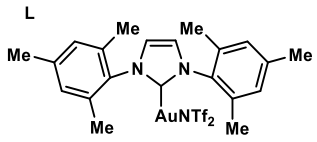
General procedure for Conia-ene reactions performed as part of condition screening: To a flame-dried flask at 23 °C was added a solution of substrate **15** (1.0 equiv) in the indicated solvent (at a final concentration of 0.10 M). The indicated gold salt (0.20 equiv) and (if applicable) silver salt (0.20 equiv) were then added subsequently, forming a pale-yellow suspension. If needed, the suspension was then directly placed in pre-heated oil bath, and the resultant solution was either stirred at 23 °C or 40 °C for 24 h. Upon completion, the reaction contents were filtered through a pad of Celite (eluting with CH_2Cl_2). The filtrate was then concentrated directly and characterized by NMR analysis. **16**: R_f = 0.33 (silica gel, hexanes/EtOAc, 4:1); IR (film) ν_{max} 2943, 2891, 2866, 2235, 1752, 1675, 1652, 1472, 1457, 1237, 1104, 882 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.91 (dd, *J* = 6.4, 2.3 Hz, 1 H), 3.77 (s, 3 H), 3.75 (t, *J* = 6.3 Hz, 2 H), 3.19 (dd, *J* = 15.0, 1.4 Hz, 1 H), 2.82–2.74 (m, 1 H), 2.65 (dd, *J* = 14.9, 2.2 Hz, 1 H), 2.50–2.43 (m, 1 H), 2.42–2.32 (m, 3 H), 1.81 (p, *J* = 6.8 Hz, 2 H), 1.59 (s, 3 H), 1.15–1.03 (m, 21 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.1, 159.0, 152.4, 122.7, 102.0, 95.9, 62.3, 51.2, 46.9, 41.2, 40.8, 29.2, 24.2, 21.8, 18.0, 12.0; HRMS (ESI) calcd for $C_{24}H_{39}NNaO_4Si^+$ [M + Na^+] 456.2541, found 456.2545. **17**: R_f = 0.31 (silica gel, hexanes/EtOAc, 4:1); IR (film) ν_{max} 2943, 2892, 2866, 2237, 1768, 1737, 1652, 1470, 1455, 1233, 1104, 882 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.51 (br s, 1 H), 3.82 (s, 3 H), 3.72 (t, *J* = 6.0 Hz, 2 H), 3.05 (d, *J* = 18.2 Hz, 1 H), 2.95 (d, *J* = 18.1 Hz, 1 H), 2.88 (d, *J* = 13.9 Hz, 1 H), 2.61 (d, *J* = 13.8 Hz, 1 H), 2.45 (t, *J* = 3.4 Hz, 1 H), 2.33–2.20 (m, 1 H), 2.15–2.04 (m, 1 H), 1.78–1.63 (m, 2 H), 1.51 (s, 3 H), 1.10–1.02 (m, 21 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.0, 168.2, 143.4, 122.7, 119.4, 62.5, 62.1, 53.1, 52.6, 46.5, 36.5, 34.0, 31.0, 29.9, 28.4, 18.0, 11.9; HRMS (ESI) calcd for $C_{24}H_{39}NNaO_4Si^+$ [M + Na^+] 456.2541, found 456.2542.

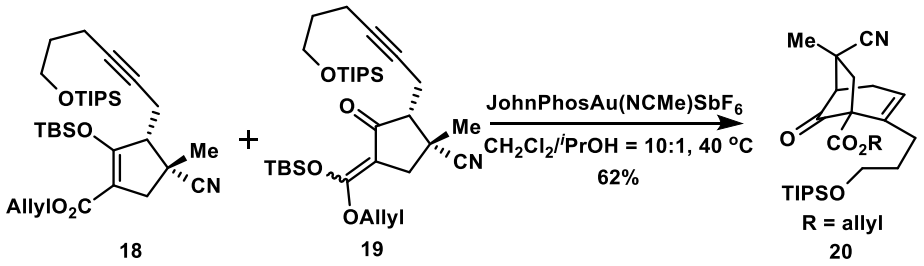
Table S1. Condition screening for Conia-ene reaction of **15**

Entry	Catalyst	Condition	Result
1	$Ph_3PAuNTf_2$	CH_2Cl_2, 23 °C	16:17 = 4:1
2	$Ph_3PAuCl/AgOTf$	CH_2Cl_2, 23 °C	Only 16
3	CyJohnPhosAuCl/AgOTf	CH_2Cl_2, 40 °C	16:17 = 2:1
4	CyJohnPhosAuCl/AgOTf	tol, 40 °C	16:17 = 1:1
5	CyJohnPhosAuCl/AgOTf	tol/^{t}BuOH, 40 °C	16:17 = 10:1
6	CyJohnPhosAuCl/AgOTf	acetone, 40 °C	Only 16
7	CyJohnPhosAuCl/AgOTf	CH_3CN, 40 °C	Unkown product
8	CyJohnPhosAuCl/$AgBF_4$	tol, 40 °C	16:17 = 8:1
9	CyJohnPhosAuCl/$AgSbF_6$	tol, 40 °C	16:17 = 10:1
10	L$AuNTf_2$ (0.2 eq.)	tol, 40 °C	NR

CyJohnphos:







β-ketoester 20. A mixture of silyl enol ethers **18** and **19** (2.98 g, 5.20 mmol, 1.0 equiv) were dissolved in CH_2Cl_2 (47 mL) and *i*-PrOH (4.7 mL) at 23 °C and then JohnPhosAu(NCMe)SbF_6 (1.20 g, 1.56 mmol, 0.30 equiv) was added. The resultant solution was then warmed to 40 °C using a pre-heated oil bath and stirred at that temperature for 48 h, during which time the original yellow solution gradually turned a dark brown and a participate formed. Once the reaction appeared complete, as judged by no obvious turnover based on TLC analysis, the reaction contents were cooled to 23 °C and concentrated directly. Purified the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 16:1→4:1), providing the desired β-ketoester (1.48 g, 62% yield) as a pale brown oil. **20**: R_f = 0.43 (silica gel, hexanes/EtOAc, 4:1); IR (film) ν_{max} 2943, 2892, 2867, 2238, 1768, 1734, 1652, 1463, 1386, 1248, 1106, 995, 882 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.93 (ddt, *J* = 17.3, 10.4, 5.9 Hz, 1 H), 5.50 (dd, *J* = 4.5, 2.3 Hz, 1 H), 5.38 (dq, *J* = 17.2, 1.5 Hz, 1 H), 5.27 (dt, *J* = 10.4, 1.3 Hz, 1 H), 4.74 (ddt, *J* = 13.1, 6.0, 1.4 Hz, 1 H), 4.66 (ddt, *J* = 13.1, 6.0, 1.4 Hz, 1 H), 3.69 (t, *J* = 6.0 Hz, 2 H), 3.03 (ddd, *J* = 18.1, 4.4, 2.2 Hz, 1 H), 2.98–2.90 (m, 1 H), 2.87 (d, *J* = 13.8 Hz, 1 H), 2.60 (d, *J* = 13.8 Hz, 1 H), 2.44 (dd, *J* = 4.4, 2.5 Hz, 1 H), 2.30–2.19 (m, 1 H), 2.17–2.06 (m, 1 H), 1.69 (dddd, *J* = 10.1, 7.8, 6.8, 3.7 Hz, 2 H), 1.50 (s, 3 H), 1.07–1.03 (m, 21 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.8, 167.4, 143.3, 131.4, 122.7, 119.5, 119.2, 66.4, 62.5, 62.0, 53.0, 46.5, 36.5, 33.9, 31.1, 29.9, 28.4, 25.9, 18.0, 12.0, 11.9; HRMS (ESI) calcd for $C_{26}H_{42}NO_4Si^+$ [M + H^+] 460.2878, found 460.2876.

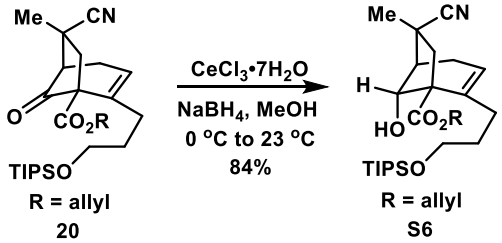
General procedure for Conia-ene reactions performed as part of condition screening: To a flame-dried flask at 23 °C was added a solution of substrate mixture **18** and **19** (1.0 equiv) in the indicated solvent (at a final concentration of 0.10 M). The indicated gold salt (0.20 equiv) and (if applicable) silver salt (0.20 equiv) were then added subsequently, forming a pale-yellow suspension. If needed, the suspension was then directly placed in pre-heated oil bath, and the resultant solution was either stirred at 23 °C or 40 °C for 48 h. Upon completion or no further conversion based on TLC analysis, the reaction contents were filtered through a pad of Celite (eluting with CH_2Cl_2). The filtrate was then concentrated and purified by flash column chromatography (silica gel, hexanes/EtOAc = 16:1→4:1).

Table S2. Condition screening for Conia-ene reaction of **18** and **19**

	Catalyst	Condition	Result
1	$Ph_3PAuNTf_2$ (0.2 eq.)	CH_2Cl_2, 40 °C	20% (42% brsm)
2	$Ph_3PAuCl/AgSbF_6$ (0.2 eq.)	CH_2Cl_2/^{i}PrOH, 40 °C	low conversion
3	JohnPhosAu(NCMe)SbF_6 (0.2 eq.)	acetone, 40 °C	50% (55% brsm)
4	$Ph_3PAuNTf_2$ (0.2 eq.)	tol/^{t}BuOH, 40 °C	22% (31% brsm)
5[a]	JohnPhosAu(NCMe)SbF_6 (0.2 eq.)	acetone, 40 °C	30% conversion
6[a]	JohnPhosAu(NCMe)SbF_6 (0.2 eq.)	acetone, 23 °C	N. R.
7[a]	$Ph_3PAuNTf_2$ (0.2 eq.)	CH_2Cl_2/^{i}PrOH, 23 °C	N. R.
8	JohnPhosAu(NCMe)SbF_6 (0.3 eq.)	CH_2Cl_2/^{i}PrOH, 40 °C	62%

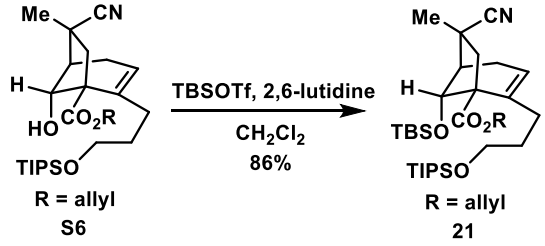
a: with additives 4 Å MS and 2,4,6-tri-tert-butylpyrimidine

Synthesis of key common intermediate ketone 7

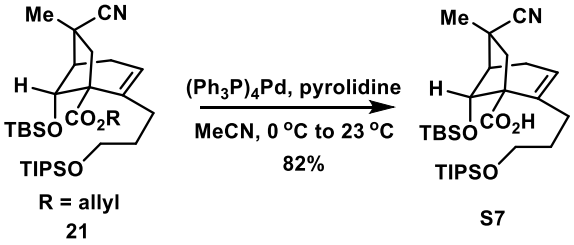


Alcohol S6. β-ketoester **20**(1.48 g, 3.22 mmol, 1.0 equiv) was dissolved in MeOH (32 mL) at 23 °C and then $CeCl_3$•$7H_2O$ (1.44 g, 3.86 mmol, 1.2 equiv) was added. After all the solids had dissolved, the resultant solution was then cooled to 0 °C using an ice-water bath and $NaBH_4$ (0.180 g, 4.83 mmol, 1.5 equiv) was added in a single portion. After the solution stopped bubbling, the reaction contents were stirred at 0 °C for another 5 min and then the ice-water bath was removed. The resultant contents were then stirred at 23 °C for 30 min. Upon completion, the reaction contents were diluted by the addition of CH_2Cl_2 (32 mL) and quenched with saturated aqueous NH_4Cl (60 mL). The reaction contents were the poured into a separatory funnel and the resultant layers were separated. The aqueous layer was then further extracted with CH_2Cl_2 (3 × 60 mL). The combined organic layers were then washed with brine (120 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 4:1→2:1) provided the desired alcohol (1.25 g, 84% yield) as a colorless oil. **S6**: R_f = 0.19 (silica gel, hexanes/EtOAc, 4:1); IR (film) ν_{max} 3527, 2942, 2892, 2866, 2235, 1734, 1717, 1669, 1457, 1437, 1382, 1292, 1248, 1105, 1072, 883 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.91 (ddt, *J* = 16.5, 10.3, 6.0 Hz, 1 H), 5.62–5.49 (m, 1 H), 5.35 (dq, *J* = 17.2, 1.5 Hz, 1 H), 5.30–5.24 (m, 1 H), 4.65 (ddt, *J* = 5.7, 2.6, 1.3 Hz, 2 H), 4.23 (dd, *J* = 5.5, 1.8 Hz, 1 H), 3.67 (t, *J* = 6.1 Hz, 2 H), 3.17 (d, *J* = 2.8 Hz, 1 H), 2.74–2.66 (m, 1 H), 2.63 (d, *J* = 13.9 Hz, 1 H), 2.41 (ddd, *J* = 18.4, 4.6, 2.2 Hz, 1 H), 2.25 (dt, *J* = 5.2, 2.6 Hz, 1 H), 2.17 (d, *J* = 13.8 Hz, 1 H), 2.02 (h, *J* = 5.4, 4.2 Hz, 2 H), 1.73–1.62 (m, 2 H), 1.50 (s, 3 H), 1.09–0.99 (m, 21 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 136.1, 131.2, 124.0, 120.6, 119.6, 71.7, 65.9, 62.6,

56.5, 47.6, 45.8, 35.9, 30.9, 29.8, 28.9, 27.7, 18.0, 11.9; HRMS (ESI) calcd for $C_{26}H_{44}NO_4Si^+$ [M + H^+] 462.3034, found 462.3032.



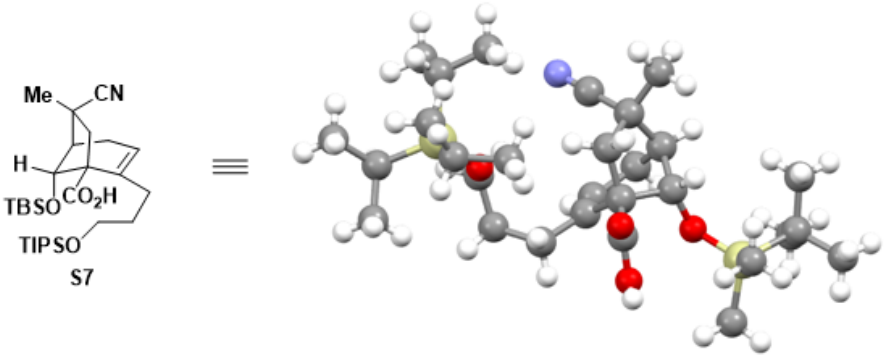
Silyl ether 21. Alcohol **S6** (1.25 g, 2.71 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (27 mL) and 2,6-lutidine (1.57 mL, 13.5 mmol, 5.0 equiv) was added at 23 °C. Next, TBSOTf (0.93 mL, 4.06 mmol, 1.5 equiv) was added dropwise. The resultant solution was then stirred for 4 h Stirred the reaction for 4 h at 23 °C. Upon completion, the reaction contents were quenched by the addition of saturated aqueous $NaHCO_3$ (25 mL), poured into a separatory funnel, and the resultant layers were separated. The aqueous layer was then further extracted with (2 × 30 mL). The combined organic layers were then washed with brine (90 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant crude residue by flash column chromatography (silica gel, hexanes/EtOAc = 16:1) provided the desired silyl ether (1.34 g, 86% yield) as a colorless oil. **21**: R_f = 0.69 (silica gel, hexanes/EtOAc, 4:1); IR (film) ν_{max} 2939, 2892, 2865, 2235, 1733, 1653, 1472, 1457, 1247, 1138, 1102, 873, 838 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.92 (ddt, *J* = 16.7, 10.3, 6.1 Hz, 1 H), 5.46 (br s, 1 H), 5.38–5.28 (m, 1 H), 5.24 (dq, *J* = 10.4, 1.3 Hz, 1 H), 4.66 (ddt, *J* = 13.1, 6.0, 1.4 Hz, 1 H), 4.50 (ddt, *J* = 13.0, 6.1, 1.4 Hz, 1 H), 4.20 (d, *J* = 5.3 Hz, 1 H), 3.71–3.62 (m, 2 H), 2.64 (d, *J* = 17.9 Hz, 1 H), 2.50 (d, *J* = 13.8 Hz, 1 H), 2.39–2.27 (m, 2 H), 2.23–2.13 (m, 1 H), 2.05 (s, 2 H), 1.66 (ddt, *J* = 24.6, 12.3, 6.1 Hz, 2 H), 1.52 (s, 3 H), 1.08–1.00 (m, 21 H), 0.87 (s, 9 H), 0.03 (d, *J* = 5.2 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 137.0, 131.8, 124.3, 119.7, 119.1, 73.5, 65.8, 62.9, 57.4, 48.1, 47.6, 35.7, 31.5, 31.2, 3.1, 29.1, 28.0, 26.0, 25.7, 18.0, 11.9, –5.0, –5.1; HRMS (ESI) calcd for $C_{32}H_{58}NO_4Si_2^+$ [M + H^+] 576.3899, found 576.3896.

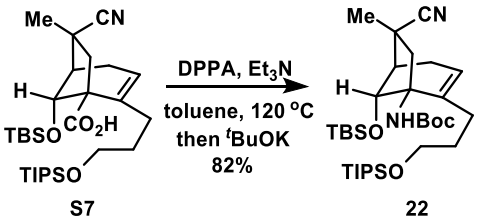


Carboxylic acid S7. Silyl ether **21** (1.34 g, 2.33 mmol, 1.0 equiv) was dissolved in MeCN (23 mL) and pyrrolidine (0.229 mL, 2.79 mmol, 1.2 equiv) was added at 23 °C. The resultant solution was then cooled to 0 °C using an ice-water bath, and $Pd(Ph_3P)_4$ (1.07 g, 0.930 mmol, 0.4 equiv) was added. After the reaction contents were stirred at 0 °C for 5 min, the ice-water bath was removed and the reaction contents were stirred at 23 °C for 1 h. Upon completion, the reaction contents were diluted with EtOAc (10 mL) and quenched by the addition of 3 M HCl (20 mL). The reaction contents were then poured into a separatory funnel

and the resultant layers were separated. The aqueous layer was further extracted with EtOAc (3 × 30 mL). The combined organic layers were then washed with brine (90 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 6:1→4:1) provided the desired carboxylic acid (1.03 g, 82% yield) as a white solid. **S7**: R_f = 0.57 (silica gel, hexanes/EtOAc, 4:1); IR (film) ν_{max} 2940, 2892, 2865, 2236, 1700, 1653, 1457, 1436, 1254, 1140, 1108, 872, 838 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.56 (s, 1 H), 4.24 (d, *J* = 5.3 Hz, 1 H), 3.69 (td, *J* = 6.3, 2.5 Hz, 2 H), 2.63–2.53 (m, 2 H), 2.45 (d, *J* = 18.4 Hz, 1 H), 2.21–1.98 (m, 4 H), 1.76–1.65 (m, 2 H), 1.52 (s, 3 H), 1.10–1.02 (m, 21 H), 0.92 (s, 9 H), 0.15 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 135.8, 123.8, 120.2, 72.8, 62.6, 57.2, 16.9, 46.7, 35.7, 31.17, 29.5, 29.0, 27.9, 25.6, 18, 11.9, –4.6, –5.3; HRMS (ESI) calcd for $C_{29}H_{54}NO_4Si_2^+$ [M + H^+] 536.3586, found 536.3587.

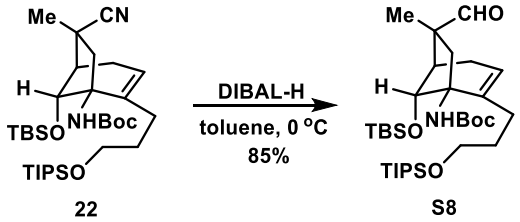
Figure S1. X-ray structure of carboxylic acid **S7**



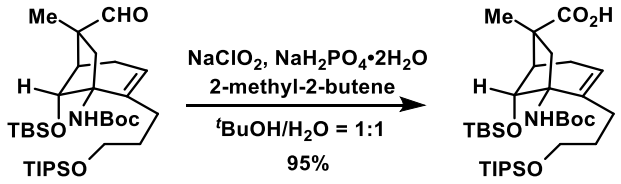


Boc amide 22. Carboxylic acid **S7** (1.03 g, 1.92 mmol, 1.0 equiv) was dissolved in toluene (20 mL) at 23 °C and then Et_3N (0.535 mL, 3.84 mmol, 2.0 equiv) and diphenyl phosphoryl azide (0.620 mL, 2.88 mmol, 1.5 equiv) were added sequentially. After stirring the resultant solution for 30 min at 23 °C, the reaction contents were heated at 120 °C using a pre-heated oil bath and stirred for an additional 1 h at that temperature. Upon completion, the reaction contents were cooled to 23 °C and *t*-BuOK (1.0 M in *t*-BuOH, 3.84 mL, 3.84 mmol, 2.0 equiv) was added and the reaction contents were stirred for another 1 h at 23 °C, during which time the color of the reaction solution transformed into a pale yellow suspension. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (20 mL). The reaction contents were then poured into a separatory funnel and the resultant layers were separated. The aqueous layer was further extracted with EtOAc (2 × 20 mL). The combined organic layers were then washed with brine (50 mL), dried (Na_2SO_4), filtered, and

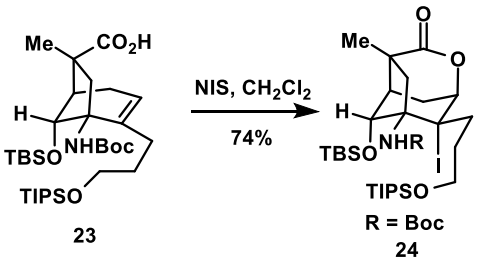
concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 10:1) provided the desired Boc amide intermediate (0.971 g, 82% yield) as a colorless oil. **22**: R_f = 0.62 (silica gel, hexanes/EtOAc, 4:1); IR (film) ν_{max} 3470, 3438, 2940, 2894, 2865, 2235, 1719, 1496, 1472, 1463, 1390, 1366, 1250, 1165, 1135, 1105, 1010, 880, 838 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.41–5.32 (m, 1 H), 4.68 (s, 1 H), 4.40 (d, *J* = 5.2 Hz, 1 H), 3.70 (t, *J* = 6.2 Hz, 2 H), 2.64 (d, *J* = 13.4 Hz, 1 H), 2.56–2.46 (m, 2 H), 2.32 (ddd, *J* = 18.0, 4.4, 2.2 Hz, 1 H), 2.14–2.06 (m, 2 H), 2.00–1.93 (m, 1 H), 1.67 (ddd, *J* = 14.0, 7.8, 6.2 Hz, 2 H), 1.54 (s, 3 H), 1.42 (s, 9 H), 1.05 (s, 21 H), 0.88 (s, 9 H), 0.08 (d, *J* = 7.5 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 139.4, 124.5, 119.8, 79.2, 72.0, 63.0, 62.7, 47.1, 45.9, 35.7, 32.1, 29.2, 28.4, 28.1, 27.5, 25.6, 18.0, 17.9, 11.9, –4.8, –5.0; HRMS (ESI) calcd for $C_{33}H_{62}N_2NaO_4Si_2^+$ [M + Na^+] 629.4140, found 629.4137.



Aldehyde S8. The Boc amide intermediate **22** (0.960 g, 1.58 mmol, 1.0 equiv) was dissolved in toluene (16 mL) and then the reaction solution was cooled to 0 °C using an ice-water bath. Next, DIBAL-H (20 wt % in toluene, 5.27 mL, 6.32 mmol, 4.0 equiv) was added dropwise, and then the reaction contents were stirred for an additional 15 min at 0 °C. Upon completion, the reaction contents were quenched by the addition of saturated aqueous Rochelle's salt (16 mL). The resultant biphasic reaction contents were then warmed to 23 °C and stirred for 40 min until both layers became clear. The reaction contents were then poured into a separatory funnel and the resultant layers were separated. The aqueous layer was further extracted with EtOAc (2 × 15 mL). The combined organic layers were then washed with brine (20 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 10:1), providing the desired aldehyde (0.828 g, 85% yield) as a colorless oil. **S8**: R_f = 0.65 (silica gel, hexanes/EtOAc, 4:1); IR (film) ν_{max} 3437, 2930, 2894, 2865, 2712, 1724, 1720, 1506, 1496, 1472, 1457, 1388, 1366, 1250, 1168, 1136, 1101, 884, 837 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.60 (s, 1H), 5.17 (dt, *J* = 3.9, 2.0 Hz, 1 H), 4.72 (s, 1 H), 4.42 (s, 1 H), 3.69 (t, *J* = 6.3 Hz, 2 H), 2.78 (d, *J* = 13.5 Hz, 1 H), 2.38 (dt, *J* = 18.0, 3.4 Hz, 1 H), 2.19–2.07 (m, 3 H), 2.04–1.99 (m, 1 H), 1.91 (ddd, *J* = 18.2, 4.6, 2.1 Hz, 1 H), 1.71–1.61 (m, 2 H), 1.43 (s, 9 H), 1.23 (s, 3H), 1.12–0.97 (m, 21 H), 0.88 (s, 9 H), 0.10 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.5, 155.0, 140.8, 118.6, 79.0, 74.0, 63.5, 62.9, 49.6, 46.7, 41.8, 32.3, 28.4, 27.6, 25.7, 25.6, 24.9, 18.0, 18.0, 12.0, –4.7, –4.9; HRMS (ESI) calcd for $C_{33}H_{63}NNaO_5Si_2^+$ [M + Na^+] 632.4137, found 632.4138.

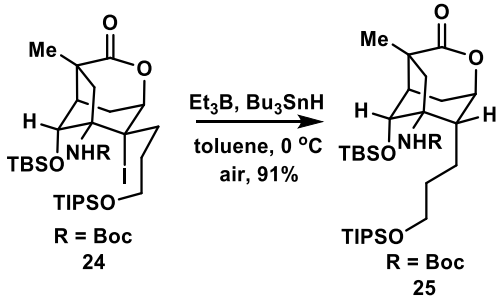


Carboxylic acid 23. Aldehyde **S8** (0.825 g, 1.35 mmol, 1.0 equiv) was dissolved in *t*-BuOH (13.5 mL) at 23 °C and then H_2O (13.5 mL), 2-methyl-2-butene (4.5 mL), and NaH_2PO_4•$2H_2O$ (4.21 g, 27.0 mmol, 20 equiv) were added sequentially. After all the solids had dissolved, $NaClO_2$ (1.22 g, 13.5 mmol, 10 equiv) was then added and the initially cloudy solution turned yellow in color. The resultant solution was stirred for an additional 40 min at 23 °C for 40 min during which time it became colorless. Upon completion, the reaction contents were diluted with EtOAc (15 mL), poured into a separatory funnel, and the layers were separated. The aqueous layer was further extracted with EtOAc (2 × 15 mL). The combined organic layers were then washed with brine (20 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 4:1) provided the desired carboxylic acid (0.801 g, 95% yield) as a colorless oil. **23**: R_f = 0.30 (silica gel, hexanes/EtOAc, 4:1); IR (film) ν_{max} 3470, 2940, 2893, 2865, 1718, 1654, 1496, 1463, 1390, 1251, 1165, 1127, 1104, 880, 837 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.14 (d, *J* = 3.8 Hz, 1 H), 4.71 (s, 1 H), 4.59 (s, 1 H), 3.67 (t, *J* = 6.3 Hz, 2 H), 2.89 (d, *J* = 13.4 Hz, 1 H), 2.37 (d, *J* = 17.8 Hz, 1 H), 2.20 (d, *J* = 13.4 Hz, 1 H), 2.09–1.95 (m, 4 H), 1.64 (p, *J* = 7.0 Hz, 2 H), 1.48 (s, 3 H), 1.42 (s, 9 H), 1.11–0.97 (m, 21 H), 0.86 (s, 9 H), 0.08 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.1, 154.8, 139.2, 119.0, 78.8, 73.0, 72.9, 68.0, 63.3, 62.9, 47.6, 46.9, 42.8, 32.1, 29.7, 29.5, 28.4, 27.7, 26.6, 25.7, 18.0, 17.9, 12.0, –4.7, –4.9; HRMS (ESI) calcd for $C_{33}H_{63}NNaO_6Si_2^+$ [M + Na^+] 648.4086, found 648.4086.

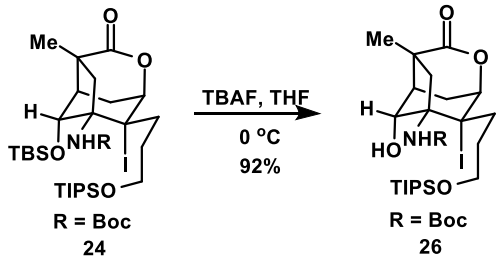


Iodolactone 24. Carboxylic acid **23** (0.800 g, 1.28 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (13 mL) at 23 °C and *N*-iodosuccinimide (1.44 g, 6.39 mmol, 5.0 equiv) was then added in a single portion, leading initially to the formation of a white participate and eventually a purple colored solution. The reaction contents were stirred at 23 °C for 6 h. Upon completion, the reaction was quenched by the addition of 3 M $Na_2S_2O_3$ (13 mL). The reaction contents were then poured into a separatory funnel and the resultant layers were separated. The aqueous layer was further extracted with CH_2Cl_2 (2 × 15 mL). The combined organic layers were then washed with brine (20 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 16:1), providing the iodolactone (0.712 g, 74% yield) as a colorless oil. **24**: R_f = 0.58 (silica gel, hexanes/EtOAc,

4:1); IR (film) ν_{max} 3362, 2941, 2880, 1735, 1700, 1653, 1472, 1455, 1367, 1167, 1110, 1012, 619 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.93 (s, 1 H), 4.86 (d, *J* = 3.0 Hz, 1 H), 4.46 (s, 1 H), 3.78 (dt, *J* = 10.9, 5.5 Hz, 1 H), 3.70 (dt, *J* = 9.9, 6.2 Hz, 1 H), 2.93 (dd, *J* = 14.2, 2.5 Hz, 1 H), 2.57 (d, *J* = 14.5 Hz, 1 H), 2.49–2.38 (m, 1 H), 2.04–1.88 (m, 4 H), 1.82–1.70 (m, 2 H), 1.41 (s, 9 H), 1.31 (s, 3 H), 1.03 (d, *J* = 5.1 Hz, 21 H), 0.95 (s, 9 H), 0.17 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.8, 154.1, 80.6, 64.1, 62.6, 60.6, 41.9, 41.5, 35.6, 34.6, 31.5, 29.2, 28.3, 25.9, 25.2, 24.6, 23.7, 22.6, 18.0, 11.9, –4.5, –5.2; HRMS (ESI) calcd for $C_{33}H_{63}INO_6Si_2^+$ [M + H^+] 752.3233, found 752.3232.

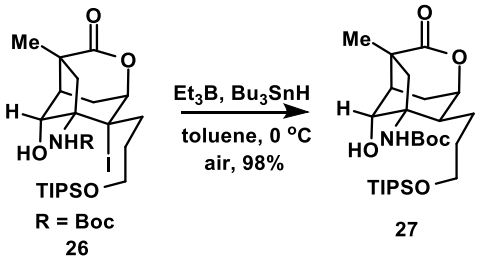


Lactone 25. Iodoalcohol **24** (0.270 g, 0.359 mmol, 1.0 equiv) was dissolved in toluene (7.2 mL) at 23 °C and then cooled to 0 °C with an ice-water bath. Next, *n*-Bu_3SnH (0.157 g, 0.538 mmol, 1.5 equiv) and Et_3B (1.0 M in hexane, 0.359 mL, 0.359 mmol, 1.0 equiv) were then added sequentially, and 1.0 mL of air from syringe was subsequently bubbled through the solution to initiate the reaction. The reaction contents were then stirred for 15 min at 0 °C. Upon completion, the reaction contents were quenched by the addition of saturated aqueous $NaHCO_3$ (5 mL). The reaction contents were then poured into a separatory funnel and the resultant layers were separated. The aqueous layer was further extracted with EtOAc (2 × 5 mL). The combined organic layers were then washed with brine (10 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 8:1) provided the desired lactone (0.201 g, 91% yield) as a colorless oil. **25**: R_f = 0.54 (silica gel, hexanes/EtOAc, 4:1); ^1H NMR (500 MHz, $CDCl_3$) δ 4.79 (s, 1 H), 4.43 (s, 1 H), 4.33–4.22 (m, 1 H), 3.68 (t, *J* = 6.5 Hz, 2 H), 2.45 (d, *J* = 14.0 Hz, 1 H), 2.38 (d, *J* = 13.4 Hz, 1 H), 2.34–2.29 (m, 1 H), 2.07–1.98 (m, 1 H), 1.95 (d, *J* = 6.2 Hz, 1 H), 1.87–1.77 (m, 1 H), 1.71–1.59 (m, 3 H), 1.42 (s, 9 H), 1.39–1.34 (m, 1 H), 1.31 (s, 3 H), 1.07–1.03 (m, 21 H), 0.92 (s, 9 H), 0.13 (s, 3 H), 0.08 (s, 3 H).

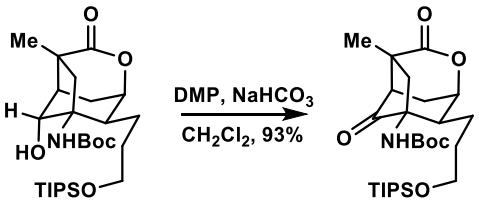


Iodoalcohol 26. Iodolactone **24** (0.340 g, 0.452 mmol, 1.0 equiv) was dissolved in THF (4.5 mL) at 23 °C and then was cooled to 0 °C with an ice-water bath. Next, TBAF (1.0 M in

THF, 0.452 mL, 0.452 mmol, 1.0 equiv) was added dropwise. The resultant pale-yellow solution was stirred for an additional 15 min at 0 °C. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (4 mL). The reaction contents were then poured into a separatory funnel and the resultant layers were separated. The aqueous layer was further extracted with EtOAc (2 × 6 mL). The combined organic layers were then washed with brine (10 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 8:1) provided the desired iodoalcohol (0.266 g, 92% yield) as a colorless oil. **26**: R_f = 0.34 (silica gel, hexanes/EtOAc, 4:1); IR (film) ν_{max} 3365, 2942, 2880, 2865, 1734, 1700, 1653, 1472, 1457, 1367, 1166, 1105, 1012, 622 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.41 (s, 1 H), 5.20 (s, 1 H), 4.86 (s, 1 H), 4.56 (s, 1 H), 3.82 (dt, *J* = 10.5, 5.1 Hz, 1 H), 3.71 (dt, *J* = 12.5, 6.2 Hz, 1 H), 3.10 (d, *J* = 14.4 Hz, 1 H), 2.47 (d, *J* = 14.0 Hz, 1 H), 2.25 (s, 1 H), 2.07 (q, *J* = 18.3, 16.3 Hz, 2 H), 1.87–1.74 (m, 4 H), 1.43 (s, 9 H), 1.31 (s, 3 H), 1.13–0.97 (m, 21 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.7, 154.9, 80.7, 74.6, 65.1, 62.3, 57.8, 45.4, 43.1, 42.0, 35.1, 29.6, 28.8, 28.2, 24.2, 24.1, 18.0, 11.9; HRMS (ESI) calcd for $C_{27}H_{48}INNaO_6Si^+$ [M + Na^+] 660.2188, found 660.2184.



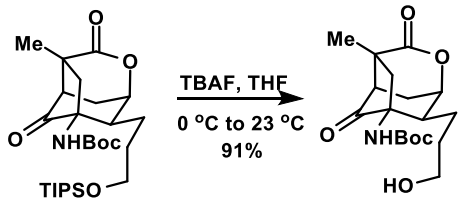
Lactone 27. Iodoalcohol **26** (0.260 g, 0.408 mmol, 1.0 equiv) was dissolved in toluene (8.2 mL) at 23 °C and then was cooled to 0 °C with an ice-water bath. Next, *n*-Bu_3SnH (0.178 g, 0.612 mmol, 1.5 equiv) and Et_3B (1.0 M in hexane, 0.41 mL, 0.408 mmol, 1.0 equiv) were then added sequentially and 1.0 mL of air from syringe was subsequently bubbled through the solution to initiate the reaction. The reaction contents were then stirred for 15 min at 0 °C. Upon completion, the reaction contents were quenched by the addition of saturated aqueous $NaHCO_3$ (6 mL). The reaction contents were then poured into a separatory funnel and the resultant layers were separated. The aqueous layer was further extracted with EtOAc (2 × 6 mL). The combined organic layers were then washed with brine (10 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (hexanes/EtOAc = 8:1) provided the desired lactone (0.205 g, 98% yield) as a colorless oil. **27**: R_f = 0.32 (silica gel, hexanes/EtOAc, 4:1); IR (film) ν_{max} 3335, 2942, 2881, 2865, 1734, 1700, 1653, 1473, 1457, 1367, 1168, 1100, 1009 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.09 (s, 1 H), 5.10–4.99 (m, 1 H), 4.62 (q, *J* = 2.8 Hz, 1 H), 4.28 (dd, *J* = 6.4, 2.7 Hz, 1 H), 3.71 (qd, *J* = 5.7, 2.5 Hz, 1 H), 3.66–3.55 (m, 1 H), 2.62 (d, *J* = 13.0 Hz, 2 H), 2.17 (q, *J* = 4.5 Hz, 1 H), 2.02 (d, *J* = 13.1 Hz, 1 H), 1.70 (tdd, *J* = 11.6, 6.3, 2.5 Hz, 1 H), 1.65–1.59 (m, 1 H), 1.55–1.46 (m, 3 H), 1.43–1.37 (m, 10 H), 1.27 (s, 3 H), 1.08–0.98 (m, 21 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.0, 156.6, 80.9, 76.6, 76.5, 63.7, 63.4, 44.6, 43.03, 42.96, 38.1, 30.3, 28.1, 26.8, 24.3, 21.7, 18.0, 11.8; HRMS (ESI) calcd for $C_{27}H_{49}NNaO_6Si^+$ [M + Na^+] 534.3221, found 534.3217.



27 7

Ketone 7. Lactone **27** (0.200 g, 0.391 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (7.8 mL) at 23 °C and then $NaHCO_3$ (0.328 g, 3.91 mmol, 10 equiv) and Dess–Martin periodinane (0.332 g, 0.782 mmol, 2.0 equiv) were added sequentially in single portions. The reaction contents were then stirred for 30 min at 23 °C. Upon completion, the reaction contents were quenched by the addition of saturated aqueous $Na_2S_2O_3$ (6 mL). The reaction contents were then poured into a separatory funnel and the resultant layers were separated. The aqueous layer was further extracted with EtOAc (2 × 6 mL). The combined organic layers were then washed with brine (10 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 8:1) provided the desired lactone (0.185 g, 93% yield) as a colorless oil. **7**: R_f = 0.32 (silica gel, hexanes/EtOAc, 4:1); IR (film) ν_{max} 3335, 2942, 2881, 2865, 1734, 1700, 1653, 1473, 1457, 1367, 1168, 1100, 1009 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.41 (s, 1 H), 5.20 (s, 1 H), 4.86 (s, 1 H), 4.56 (s, 1 H), 3.82 (dt, *J* = 10.5, 5.1 Hz, 1 H), 3.71 (dt, *J* = 12.5, 6.2 Hz, 1 H), 3.10 (d, *J* = 14.4 Hz, 1 H), 2.47 (d, *J* = 14.0 Hz, 1 H), 2.25 (s, 1 H), 2.07 (q, *J* = 18.3, 16.3 Hz, 2 H), 1.87–1.74 (m, 4 H), 1.43 (s, 9 H), 1.31 (s, 3 H), 1.13–0.97 (m, 21 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.7, 154.9, 80.7, 74.6, 65.1, 62.3, 57.8, 45.4, 43.1, 42.0, 35.1, 29.6, 28.8, 28.2, 24.2, 24.1, 18.0, 11.9; HRMS (ESI) calcd for $C_{27}H_{47}NNaO_6Si^+$ [M + Na^+] 532.3065, found 532.3059.

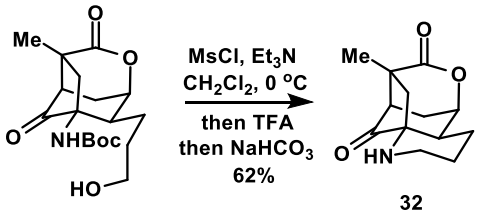
Syntheses of Annotinolide D and Annotinolide C



7 31

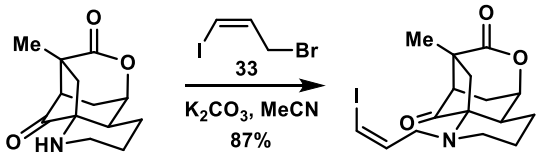
Alcohol 31. Ketone **7** (60.1 mg, 0.118 mmol, 1.0 equiv) was dissolved in THF (2.4 mL) at 23 °C and then was cooled to 0 °C with an ice-water bath. Next, TBAF (1.0 M in THF, 0.177 mL, 0.177 mmol, 1.5 equiv) was added dropwise. The resultant pale-yellow solution was stirred for an additional 1 h at 0 °C. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (2 mL). The reaction contents were then poured into a separatory funnel and the resultant layers were separated. The aqueous layer was further extracted with EtOAc (2 × 3 mL). The combined organic layers were then washed with brine (5 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/acetone = 2:1→1:1) provided the desired alcohol

(37.8 mg, 91% yield) as a colorless oil. **31**: R_f = 0.48 (silica gel, hexanes/acetone, 1:1); IR (film) ν_{max} 3362, 2973, 2934, 2872, 1734, 1700, 1457, 1387, 1367, 1165, 1131, 1007 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.27 (s, 1 H), 4.62 (dq, *J* = 4.2, 2.4 Hz, 1 H), 3.68 (dt, *J* = 11.8, 6.0 Hz, 1 H), 3.63 (dt, *J* = 10.9, 6.0 Hz, 1 H), 2.87 (d, *J* = 14.1 Hz, 1 H), 2.51–2.42 (m, 2 H), 2.24 (s, 1 H), 2.15 (td, *J* = 6.3, 3.0 Hz, 1 H), 2.12–1.98 (m, 1 H), 1.92 (d, *J* = 14.0 Hz, 1 H), 1.87–1.65 (m, 2 H), 1.51 (dtd, *J* = 12.3, 6.0, 3.0 Hz, 1 H), 1.41 (s, 9 H), 1.34 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.2, 174.8, 154.8, 80.1, 73.9, 66.7, 62.3, 52.1, 48.4, 40.8, 39.2, 37.0, 29.9, 28.2, 24.3, 21.5; HRMS (ESI) calcd for $C_{18}H_{27}NNaO_6^+$ [M + Na^+] 376.1731, found 376.1724.



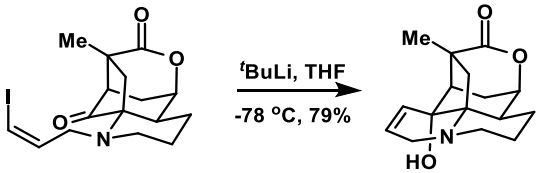
31 32

Amine 32. Alcohol **31** (35.2 mg, 0.099 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (2.0 mL) at 23 °C and then the reaction contents were cooled to 0 °C using an ice-water bath. Next, Et_3N (0.138 mL, 0.990 mmol, 10.0 equiv) and MsCl (0.026 mL, 0.297 mmol, 3.0 equiv) were added sequentially, affording a pale-yellow solution. The resultant solution was then stirred for 30 min at 0 °C. TFA (0.5 mL) was then added at 0 °C and the cold bath was removed. The resultant solution was then stirred for 1 h at 23 °C. Upon completion, the reaction contents were quenched by the portion-wise addition of saturated aqueous $NaHCO_3$ until the mixture stopped bubbling. Next, an additional aliquot of saturated aqueous $NaHCO_3$ (3 mL) and CH_2Cl_2 (4.0 mL) were then added and the resultant biphasic mixture was stirred vigorously for 30 min at 23 °C. The reaction contents were then poured into a separatory funnel and the resultant layers were separated. The aqueous layer was further extracted with CH_2Cl_2 (4 × 5 mL). The combined organic layers were then washed with brine (8 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, CH_2Cl_2/MeOH = 50:1→5:1) provided the desired amine (14.4 mg, 62% yield) as a white amorphous solid. **32**: R_f = 0.13 (silica gel, hexanes/acetone = 1:1); IR (film) ν_{max} 3333, 2924, 2865, 2844, 1751, 1735, 1457, 1134, 1025 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.38 (t, *J* = 2.4 Hz, 1 H), 3.04 (d, *J* = 13.2 Hz, 1 H), 2.85 (s, 1 H), 2.63 (t, *J* = 13.0 Hz, 1 H), 2.44–2.38 (m, 2 H), 2.26–2.19 (m, 1 H), 2.06 (dt, *J* = 12.4, 2.7 Hz, 1 H), 1.91 (qd, *J* = 13.0, 3.9 Hz, 1 H), 1.81 (dd, *J* = 13.7, 3.5 Hz, 1 H), 1.74 (d, *J* = 13.6 Hz, 1 H), 1.56 (dd, *J* = 13.4, 1.8 Hz, 1 H), 1.48 (dt, *J* = 13.1, 4.4 Hz, 1 H), 1.34 (d, *J* = 1.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.7, 175.4, 76.7, 67.1, 50.3, 49.1, 42.1, 40.6, 39.5, 37.9, 26.5, 24.4, 23.0; HRMS (ESI) calcd for $C_{13}H_{17}NNaO_3^+$ [M + Na^+] 258.1101, found 258.1100.



32 S9

Vinyl iodide S9. Amine **32** (13.2 mg, 0.0553 mmol, 1.0 equiv) was dissolved in MeCN (0.55 mL) at 23 °C and then K_2CO_3 (76.4 mg, 0.553 mmol, 10 equiv) and allylic bromide **33** (68.1 mg, 0.276 mmol, 5.0 equiv)[3] were added sequentially. The resultant white suspension was then stirred for 24 h at 23 °C. Upon completion, the reaction contents were filtered through Celite (eluting with EtOAc). The filtrate was then concentrated and the resultant residue was purified by flash column chromatography (silica gel, hexanes/acetone = 2:1) to provide the desired vinyl iodide (19.4 mg, 87% yield) as a white amorphous solid. **S9**: R_f = 0.70 (silica gel, hexanes/acetone = 1:1); IR (film) ν_{max} 2932, 2868, 2835, 1748, 1736, 1653, 1457, 1122, 1033, 667 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.41–6.37 (m, 1 H), 6.36–6.33 (m, 1 H), 4.40 (t, *J* = 2.8 Hz, 1 H), 3.22 (ddq, *J* = 14.2, 4.7, 2.1 Hz, 1 H), 2.92–2.84 (m, 1 H), 2.79 (d, *J* = 12.2 Hz, 1 H), 2.57–2.52 (m, 1 H), 2.40 (ddq, *J* = 14.4, 6.4, 2.2 Hz, 1 H), 2.33 (dt, *J* = 5.7, 2.5 Hz, 1 H), 2.27–2.14 (m, 3 H), 1.88–1.76 (m, 3 H), 1.72 (dt, *J* = 13.5, 2.9 Hz, 1 H), 1.65–1.57 (m, 1 H), 1.38 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.4, 175.3, 138.9, 83.6, 76.9, 72.7, 55.4, 50.7, 49.0, 48.4, 39.9, 38.8, 31.2, 24.8, 24.7, 23.0; HRMS (ESI) calcd for $C_{16}H_{21}INO_3^+$ [M + Na^+] 402.0561, found 402.0570.



S9 **2:** annotinolide D

Annotinolide D (2). Vinyl iodide **S9** (16.0 mg, 39.9 mmmol, 1.0 equiv) was dissolved in THF (0.79 mL) at 23 °C and then the reaction contents were cooled to –78 °C with a dry ice-acetone bath. Next, *t*-BuLi (1.7 M in pentanes, 0.049 mL, 83.7 mmol, 2.1 equiv) was added dropwise, during which time the solution turned a pale yellow color. The reaction contents were then stirred for 30 min at –78 °C. Upon completion, the reaction contents were quenched by the addition of H_2O (1.5 mL) and warmed to 23 °C with stirring. The reaction contents were then poured into a separatory funnel and the resultant layers were separated. The aqueous layer was further extracted with EtOAc (2 × 3 mL). The combined organic layers were then washed with brine (4 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, CH_2Cl_2/MeOH = 50:1→5:1) provided annotinolide D (**2**, 8.7 mg, 79% yield) as a white amorphous solid. **2**: R_f = 0.24 (silica gel, hexanes/acetone, 1:1); IR (film) ν_{max} 3245, 2930, 2869, 2837, 1734, 1653, 1473, 1457, 1383, 1288, 1125, 1071, 1017 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.82 (dt, *J* = 10.1, 1.9 Hz, 1 H), 5.78 (ddd, *J* = 9.9, 3.8, 1.9 Hz, 1 H), 4.36 (p, *J* = 2.7 Hz, 1 H), 3.33 (ddd, *J* = 18.3, 3.5, 1.5 Hz, 1 H), 2.85 (ddd, *J* = 18.3, 2.2, 2.2 Hz, 1 H), 2.71 (br d, *J* = 11.3 Hz, 1 H), 2.67 (ddd, *J* = 14.0, 3.0, 1.3 Hz, 1 H), 2.27 (m, 1 H), 2.24 (dd, *J* = 11.5, 3.1 Hz, 1 H), 2.05 (d, *J* = 13.3 Hz, 1 H), 1.93 (ddd, *J* = 5.0, 1.6, 1.6 Hz, 1 H),

1.75–1.67 (m, 6 H), 1.24 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.2, 130.6, 127.3, 79.1, 72.7, 65.8, 51.4, 49.8, 46.2, 42.6, 39.6, 31.5, 29.9, 25.0, 24.3, 23.6; HRMS (ESI) calcd for $C_{16}H_{22}NO_3^+$ [M + H^+] 276.1594, found 276.1579.

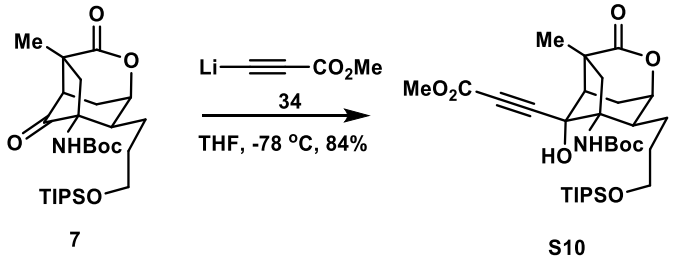
Table S3. ^{1}H NMR spectra comparison of natural and synthetic annotinolide D (**2**).

Natural **2** (^{1}H NMR, $CDCl_3$, 400 MHz) δ (*J* in Hz)	Synthetic **2** (^{1}H NMR, $CDCl_3$, 500 MHz) δ (*J* in Hz)	Δδ, ppm
5.83, ddd (9.8, 2.0, 1.2)	5.82, dt (10.1, 1.9)	-0.01
5.79, ddd (9.8, 3.7, 2.0)	5.78, ddd (9.9, 3.8, 1.9)	-0.01
4.36, dddd (5.1, 3.1, 2.8, 1.6)	4.36, p (2.7)	0.00
3.34, ddd (18.7, 3.7, 1.2)	3.33, ddd (18.3, 3.5, 1.5)	-0.01
2.86, ddd (18.7, 2.0, 2.0)	2.85, ddd (18.3, 2.2, 2.2)	-0.01
2.71, br d (11.3)	2.71, br d (11.3)	0.00
2.67, ddd (13.9, 3.1, 1.6)	2.67, ddd (14.0, 3.0, 1.3)	0.00
2.29, br d (13.6)	2.27, m	-0.02
2.24, ddd (11.3, 11.3, 1.3)	2.24, ddd (11.5, 11.5, 3.5)	0.00
2.04, d (13.3)	2.04, d (13.3)	0.00
1.92, ddd (5.0, 1.6, 1.6)	1.91, ddd (5.0, 1.6, 1.6)	-0.01
1.72 overlapped	1.75–1.67, m	
1.72 overlapped		
1.69 overlapped		
1.68 overlapped		
1.68 overlapped		
1.65, dd (13.3, 1.9)	1.65, dd (13.3, 1.9)	0.00
1.25, s	1.24, s	0.00

Table S4. ^{13}C NMR spectra comparison of natural and synthetic annotinolide D (**2**).

Natural **2** (^{13}C NMR, $CDCl_3$, 100 MHz) δ	Synthetic **2** (^{13}C NMR, $CDCl_3$, 126 MHz) δ	Δδ, ppm
178.2	178.2	0.0
130.6	130.6	0.0
127.5	127.3	-0.2
79.1	79.0	-0.1

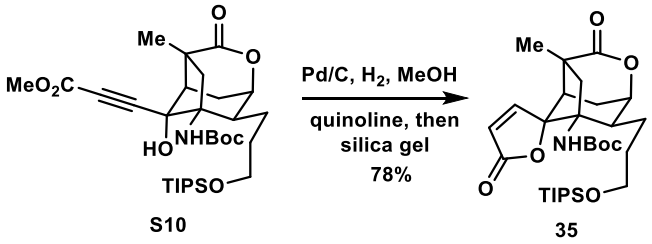
72.7	72.7	0.0
65.8	65.8	0.0
51.4	51.4	0.0
49.9	49.8	-0.1
46.2	46.2	0.0
42.6	42.6	0.0
39.7	39.7	0.0
31.4	31.4	0.0
29.9	29.9	0.0
25.1	25.0	-0.1
24.3	24.3	0.0
23.6	23.6	0.0



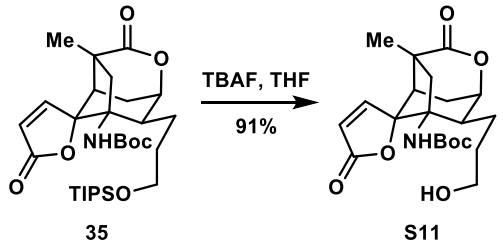
7 S10

Alkynyl ester S10. Methyl propiolate (0.022 mL, 0.250 mmol, 2.5 equiv) was dissolved in THF (0.75 mL) at 23 °C and then the reaction contents were cooled to –78 °C with a dry ice-acetone bath. Next, freshly prepared LDA (1.0 M in THF, 0.250 mL, 0.250 mmol, 2.5 equiv) was added and the resulting orange solution was stirred for an additional 30 min at –78 °C. A solution of ketone **7** (51.1 mg, 0.100 mmol, 1.0 equiv) in THF (0.90 mL) was then added, using another aliquot of THF (0.10 mL) to complete the transfer. The reaction contents were stirred for an additional 15 min at –78 °C. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (1.5 mL) and warmed to 23 °C. The reaction contents were then poured into a separatory funnel and the resultant layers were separated. The aqueous layer was further extracted with EtOAc (2 × 2 mL). The combined organic layers were then washed with brine (3 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexane/EtOAc= 4:1) to provide the desired alkynyl ester (50.1 mg, 84% yield) as a pale-yellow oil. **S10**: R_f = 0.65 (silica gel, hexanes/EtOAc, 2:1); IR (film) ν_{max} 3313, 2943, 2880, 2866, 2233, 1750, 1734, 1717, 1473, 1457, 1382, 1254, 1159, 1093 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.22 (s, 1 H), 5.02–4.95 (m, 1 H), 4.63 (q, *J* = 2.6 Hz, 1 H), 3.79–3.76 (m, 3 H), 3.74 (t, *J* = 5.3 Hz, 1 H), 3.66–3.61 (m, 1 H), 2.78–2.72 (m, 2 H), 2.45 (dt, *J* = 5.3, 1.7 Hz, 1 H), 2.10 (d, *J* = 13.4 Hz, 1 H), 1.96 (dd, *J* = 13.3, 2.0 Hz, 1 H), 1.77–1.67 (m, 3 H), 1.62–1.51 (m, 2 H), 1.44 (s, 3 H), 1.43 (s, 9 H), 1.06–1.00 (m, 21 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.3, 156.9, 153.5, 88.0, 81.9, 77.5, 77.2, 75.9, 67.0,

63.4, 52.8, 50.6, 43.5, 43.1, 38.5, 30.4, 28.3, 28.1, 24.1, 22.1, 18.0, 11.9; HRMS (ESI) calcd for $C_{31}H_{51}NNaO_8Si^+$ [M + Na^+] 616.3276, found 616.3273.

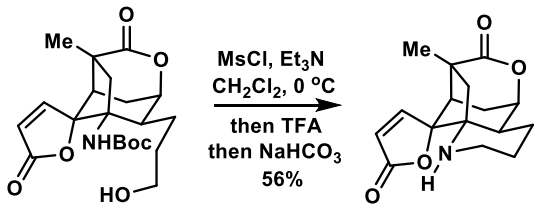


Butenolide 35. Alkynyl ester **S10** (50.1 mg, 0.842 mmol, 1.0 equiv) and quinoline (0.0030 mL, 0.253 mmol, 3.0 equiv) were sequentially dissolved in MeOH (1.68 mL) at 23 °C. Next, Pd/C (10% wt., 8.9 mg, 0.10 equiv based on Pd) was added, and the resulting black suspension was degassed with a H_2 atmosphere. The resultant suspension was then stirred for 1 h at 23 °C in the presence of a H_2 atmosphere (from a balloon). Upon completion, the reaction contents were filtered directly through a pad of Celite (eluting with EtOAc). The resultant filtrate was then washed with 3 M HCl (3 mL), poured into a separatory funnel, and the layers were separated. The aqueous layer was then further extracted with EtOAc (3 × 3 mL). The combined organic layers were then washed with brine (4 mL), dried (Na_2SO_4), filtered, and concentrated. The resultant crude residue was then dissolved in CH_2Cl_2 (0.84 mL) at 23 °C and silica gel (84.2 mg, 1.0 g/mmol substrate) was added. The resultant slurry was stirred for 30 min, before being loaded directly on a silica gel column and purified by flash column chromatography (silica gel, hexane/acetone= 4:1) to provide the desired butenolide (37.2 mg, 78% yield) as a white solid. **35**: R_f = 0.53 (silica gel, hexanes/acetone, 2:1); IR (film) ν_{max} 3342, 2941, 2878, 2866, 1772, 1748, 1715, 1464, 1457, 1388, 1255, 1245, 1165, 1099 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 5.9 Hz, 1 H), 6.04 (d, *J* = 5.7 Hz, 1 H), 4.65 (s, 1 H), 4.38 (s, 1 H), 3.77 (p, *J* = 5.7, 5.2 Hz, 1 H), 3.67 (td, *J* = 10.4, 8.7, 4.5 Hz, 1 H), 3.12 (d, *J* = 14.7 Hz, 1 H), 2.52 (dd, *J* = 14.4, 3.0 Hz, 1 H), 2.31 (d, *J* = 14.5 Hz, 1 H), 2.16 (t, *J* = 9.2 Hz, 2 H), 1.97 (ddd, *J* = 14.4, 5.2, 2.5 Hz, 1 H), 1.80–1.59 (m, 3 H), 1.56–1.47 (m, 1 H), 1.43 (s, 3 H), 1.33 (s, 9 H), 1.13–0.97 (m, 21 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.5, 170.8, 156.2, 154.5, 119.6, 95.0, 80.1, 74.5, 65.9, 62.9, 44.7, 44.2, 42.9, 36.6, 30.4, 30.0, 28.1, 24.5, 21.3, 18.0, 11.9; HRMS (ESI) calcd for $C_{30}H_{49}NNaO_7Si^+$ [M + Na^+] 586.3171, found 586.3165.



Alcohol S11. Butenolide **35** (35.5 mg, 0.0621 mmol, 1.0 equiv) was dissolved in THF (1.24 mL) at 23 °C and TBAF (1.0 M in THF, 0.093 mL, 0.0931 mmol, 1.5 equiv) was added dropwise. The resultant light brown solution was stirred for an additional 1 h at 23 °C. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (2

mL). The reaction contents were then poured into a separatory funnel and the resultant layers were separated. The aqueous layer was further extracted with EtOAc (2 × 3 mL). The combined organic layers were then washed with brine (5 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/acetone = 2:1→1:1), to provide the desired alcohol (23.0 mg, 91% yield) as a white solid. **S11**: R_f = 0.49 (silica gel, hexanes/acetone, 1:1); IR (film) ν_{max} 3335, 2975, 2936, 2873, 1771, 1744, 1717, 1472, 1457, 1388, 1367, 1270, 1247, 1165, 1096, 1050 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, *J* = 5.8 Hz, 1 H), 6.06 (d, *J* = 5.7 Hz, 1 H), 4.71 (d, *J* = 7.9 Hz, 1 H), 4.65 (t, *J* = 2.8 Hz, 1 H), 3.73 (dt, *J* = 10.9, 6.9 Hz, 1 H), 3.67 (dt, *J* = 10.8, 6.2 Hz, 1 H), 3.00 (d, *J* = 14.1 Hz, 1 H), 2.53 (dd, *J* = 14.6, 3.0 Hz, 1 H), 2.35 (d, *J* = 14.6 Hz, 1 H), 2.30–2.22 (m, 1 H), 2.18–2.15 (m, 1 H), 1.98 (ddd, *J* = 14.5, 5.1, 2.5 Hz, 1 H), 1.85–1.75 (m, 2 H), 1.72–1.61 (m, 2 H), 1.54 (ddt, *J* = 12.7, 8.8, 6.3 Hz, 1 H), 1.43 (s, 3 H), 1.35 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.5, 170.8, 156.2, 154.7, 119.8, 95.1, 80.2, 74.5, 69.5, 65.9, 62.3, 53.7, 43.0, 31.7, 30.5, 29.4, 28.1, 24.5, 21.2; HRMS (ESI) calcd for $C_{21}H_{29}NNaO_7^+$ [M + Na^+] 430.1836, found 430.1832.



S11 **1:** annotinolide C

Annotinolide C (1). Alcohol **S11** (17.5 mg, 0.0429 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (0.86 mL) at 23 °C and then the reaction contents were cooled to 0 °C using an ice-water bath. Next, Et_3N (0.062 mL, 0.429 mmol, 10 equiv) and MsCl (0.010 mL, 0.129 mmol, 3.0 equiv) were added sequentially, affording a pale-yellow solution. The resultant solution was then stirred for 30 min at 0 °C. TFA (0.22 mL) was then added at 0 °C and the cold bath was removed. The resultant solution was then stirred for 1 h at 23 °C. Upon completion, the reaction contents were quenched by the portion-wise addition of saturated aqueous $NaHCO_3$ until the mixture stopped bubbling. Next, an additional aliquot of saturated aqueous $NaHCO_3$ (3 mL) and CH_2Cl_2 (4.0 mL) were then added and the resultant biphasic mixture was stirred vigorously for 30 min at 23 °C. The reaction contents were then poured into a separatory funnel and the resultant layers were separated. The aqueous layer was further extracted with CH_2Cl_2 (4 × 5 mL). The combined organic layers were then washed with brine (8 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, CH_2Cl_2/MeOH = 50:1→5:1), provided the desired annotinolide C (**1**, 6.7 mg, 56% yield) as a white amorphous solid. **1**: R_f = 0.22 (silica gel, hexanes/acetone, 1:1); IR (film) ν_{max} 3306, 2933, 2887, 2860, 1762, 1734, 1653, 1465, 1457, 1248, 1220, 1128, 1097, 678 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 5.8 Hz, 1 H), 6.16 (d, *J* = 5.8 Hz, 1 H), 4.40 (p, *J* = 2.7 Hz, 1 H), 2.90 (ddt, *J* = 13.6, 4.1, 1.8 Hz, 1 H), 2.75 (d, *J* = 14.1 Hz, 1 H), 2.61 (ddd, *J* = 13.8, 3.0, 1.3 Hz, 1 H), 2.55 (br d, *J* = 12.5 Hz, 1 H), 2.25 (br d, *J* = 12.5 Hz, 1 H), 2.20–2.17 (m, 1 H), 1.96 (ddd, *J* = 14.1, 5.1, 2.5 Hz, 1 H), 1.83 (dddd, *J* = 12.9, 12.9, 12.9, 4.2 Hz, 1 H), 1.79–1.75 (m, 1 H), 1.74–1.70 (m, 1 H), 1.68 (dd, *J* = 14.1, 1.8 Hz, 1 H), 1.46–1.40 (m, 1 H), 1.43 (s, 3 H); ^{13}C NMR

(125 MHz, $CDCl_3$) δ 176.0, 170.6, 156.0, 121.3, 94.6, 77.9, 65.3, 47.3, 43.2 ,42.9, 42.2, 41.2, 31.5, 27.2, 24.2, 23.6; HRMS (ESI) calcd for $C_{16}H_{20}NO_4^+$ [M + H^+] 290.1387, found 290.1389.

Table S5. ^{1}H NMR spectra comparison of natural and synthetic annotinolide C (**1**).

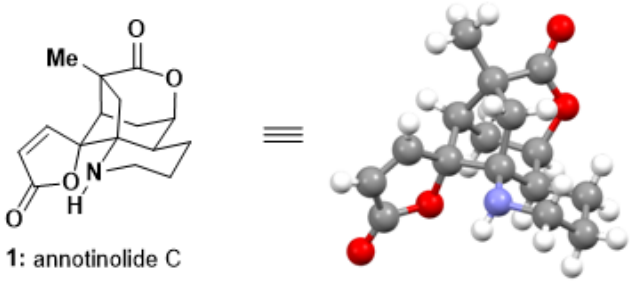
Natural **1** (^{1}H NMR, $CDCl_3$, 400 MHz) δ (*J* in Hz)	Synthetic **1** (^{1}H NMR, $CDCl_3$, 500 MHz) δ (*J* in Hz)	Δδ, ppm
7.60, d (5.8)	7.60, d (5.8)	0.00
6.16, d (5.8)	6.16, d (5.8)	0.00
4.40, br ddd (3.0, 2.5, 1.2)	4.40, p (2.7)	0.00
2.90, ddd (13.5, 3.8, 3.8)	2.90, ddt (13.6, 4.1, 1.8)	0.00
2.76, d (14.0)	2.75, d (14.1)	-0.01
2.61, ddd (13.0, 3.0, 1.2)	2.61, ddd (13.8, 3.0, 1.3)	0.00
2.56, ddd (13.5, 13.5, 2.8)	2.56, ddd (13.5, 13.5, 2.9)	0.00
2.25, br d (12.7)	2.25 br d (12.5)	0.00
2.19, ddd (5.1, 1.2, 1.2)	2.19, ddd (5.2, 1.3, 1.3)	0.00
1.96, ddd (13.1, 5.1, 2.5)	1.96, ddd (14.1, 5.1, 2.5)	0.00
1.83, dddd (12.7, 12.7, 12.7, 4.0)	1.83, dddd (12.9, 12.9, 12.9, 4.2)	0.00
1.75, m	1.75, m	0.00
1.72, m	1.73, m	0.01
1.68, dd (14.0, 1.9)	1.68, dd (14.1, 1.8)	0.00
1.43, m	1.43, m	0.00
1.43, s	1.43, s	0.00

Table S6. ^{13}C NMR spectra comparison of natural and synthetic annotinolide C (**1**).

Natural **1** (^{13}C NMR, $CDCl_3$, 100 MHz) δ	Synthetic **1** (^{13}C NMR, $CDCl_3$, 126 MHz) δ	Δδ, ppm
176.6	176.6	0.0
170.6	170.6	0.0
156.0	156.0	0.0
121.3	121.3	0.0
94.6	94.6	0.0
77.9	77.9	0.0
65.3	65.3	0.0

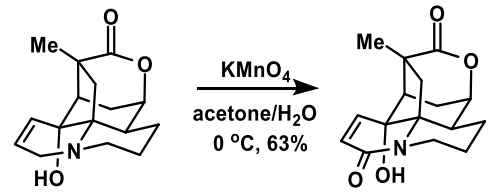
47.3	47.3	0.0
43.2	43.2	0.0
42.9	42.9	0.0
42.2	42.2	0.0
41.2	41.2	0.0
31.5	31.5	0.0
27.2	27.2	0.0
24.2	24.2	0.0
23.6	23.6	0.0

Figure S2. X-ray structure of annotinolide C (**1**).



1: annotinolide C

Transformations between annotinolides C, D and E



2: annotinolide D **3:** annotinolide E

Annotinolide E (3). Annotinolide D (**2**, 1.9 mg, 0.0069 mmol, 1.0 equiv) was dissolved in acetone (0.56 mL) and deionized water (0.14 mL) at 23 °C and then the resultant solution was cooled 0 °C using an ice-water bath. $KMnO_4$ (1.6 mg, 0.0104 mmol, 1.5 equiv) was then added in a single portion, leading to a purple-colored solution. The reaction contents were stirred for 15 min at 0 °C. Upon completion, the reaction contents were quenched by the addition of saturated $Na_2S_2O_3$ (0.50 mL) and warmed to 23 °C. The reaction contents were then poured into a separatory funnel and the resultant layers were separated. The aqueous layer was further extracted with EtOAc (3 × 3 mL). The combined organic layers were then washed with brine (4 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, CH_2Cl_2/MeOH = 50:1→5:1) to provide annotinolide E (**3**, 1.2 mg, 63% yield) as a white amorphous solid. **3**: R_f = 0.27 (silica gel, hexanes/acetone, 1:1); IR (film) ν_{max} 3312, 2931, 2865, 1734, 1653, 1602, 1436, 1383, 1127, 1059, 1021, 988 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.66 (d, J = 9.7 Hz, 1 H), 6.04 (d, J = 9.7 Hz, 1 H), 4.37 (p, J = 2.5

Hz, 1 H), 2.76 (ddd, J = 14.2, 3.2, 1.4 Hz, 1 H), 2.67 (ddd, J = 13.5, 13.5, 3.6 Hz, 1 H), 2.56 (br d, J = 12.4 Hz, 1 H), 2.50 (d, J = 13.7 Hz, 1 H), 2.18 (ddd, J = 5.1, 1.6, 1.6 Hz, 1 H), 1.94 (dp, J = 13.3, 3.4 Hz, 1 H), 1.85–1.78 (m, overlapping, 2 H), 1.76 (dddd, J = 13.2, 13.2, 13.2, 3.5 Hz, 1 H), 1.65 (dd, J = 13.7, 1.8 Hz, 1 H), 1.61–1.53 (m, 1 H), 1.25 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.9, 163.2, 142.7, 126.4, 78.0, 72.8, 66.1, 48.6, 42.8, 41.5, 39.9, 38.9, 30.3, 23.9, 22.7, 22.6; HRMS (ESI) calcd for $C_{16}H_{20}NO_4^+$ [M + H$^+$] 290.1387, found 290.1393.

Figure S3. X-ray structure of annotinolide E (**3**).

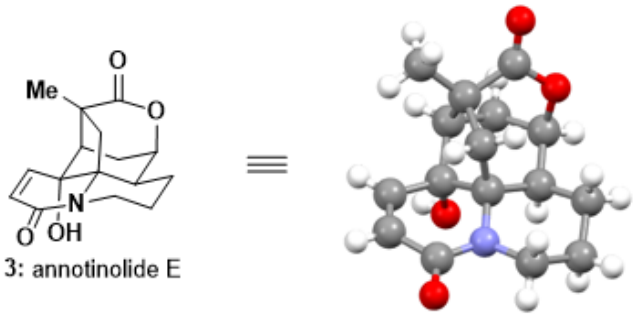
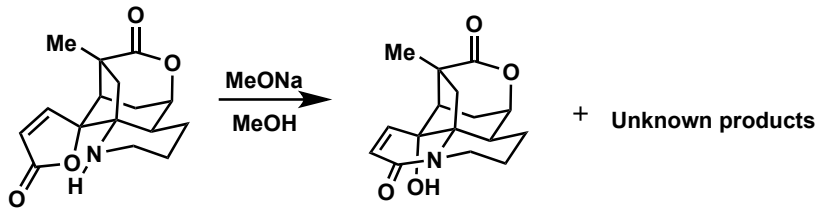


Table S7. ^{1}H NMR spectra comparison of natural and synthetic annotinolide E (**3**).

Natural **3** (^{1}H NMR, $CDCl_3$, 400 MHz) δ (J in Hz)	Synthetic **3** (^{1}H NMR, $CDCl_3$, 500 MHz) δ (J in Hz)	Δδ, ppm
6.66, d (9.7)	6.66, d (9.7)	0.00
6.03, d (9.7)	6.04, d (9.7)	0.01
4.47, dddd (5.1, 3.1, 2.8, 1.3)	4.47, p (2.5)	0.00
4.28, br d (13.4)	4.28, br d (12.7)	0.00
2.76, ddd (4.9, 1.3, 1.3)	2.76, ddd (14.2, 3.2, 1.4)	0.00
2.67, ddd (13.4, 13.4, 3.6)	2.67, ddd (13.5, 13.5, 3.6)	0.00
2.55, br d (13.4)	2.56, br d (12.4)	0.01
2.50, d (13.8)	2.50, d (13.7)	0.00
2.18, ddd (4.9, 1.3, 1.3)	2.18, ddd (5.1, 1.6, 1.6)	0.00
1.93, m	1.94, dp (13.3, 3.4)	0.01
1.80, overlapped	1.81, m, overlapped	0.01
1.79, overlapped	1.79, m, overlapped	0.00
1.76, dddd (13.4, 13.4, 13.4, 3.6)	1.76, dddd (13.2, 13.2, 13.2, 3.5)	0.00
1.65, dd (13.8, 1.8)	1.65, dd (13.7, 1.8)	0.00
1.55, m	1.56, m	0.01
1.25, s	1.25, s	0.00

Table S8. ^{13}C NMR spectra comparison of natural and synthetic annotinolide E (**3**).

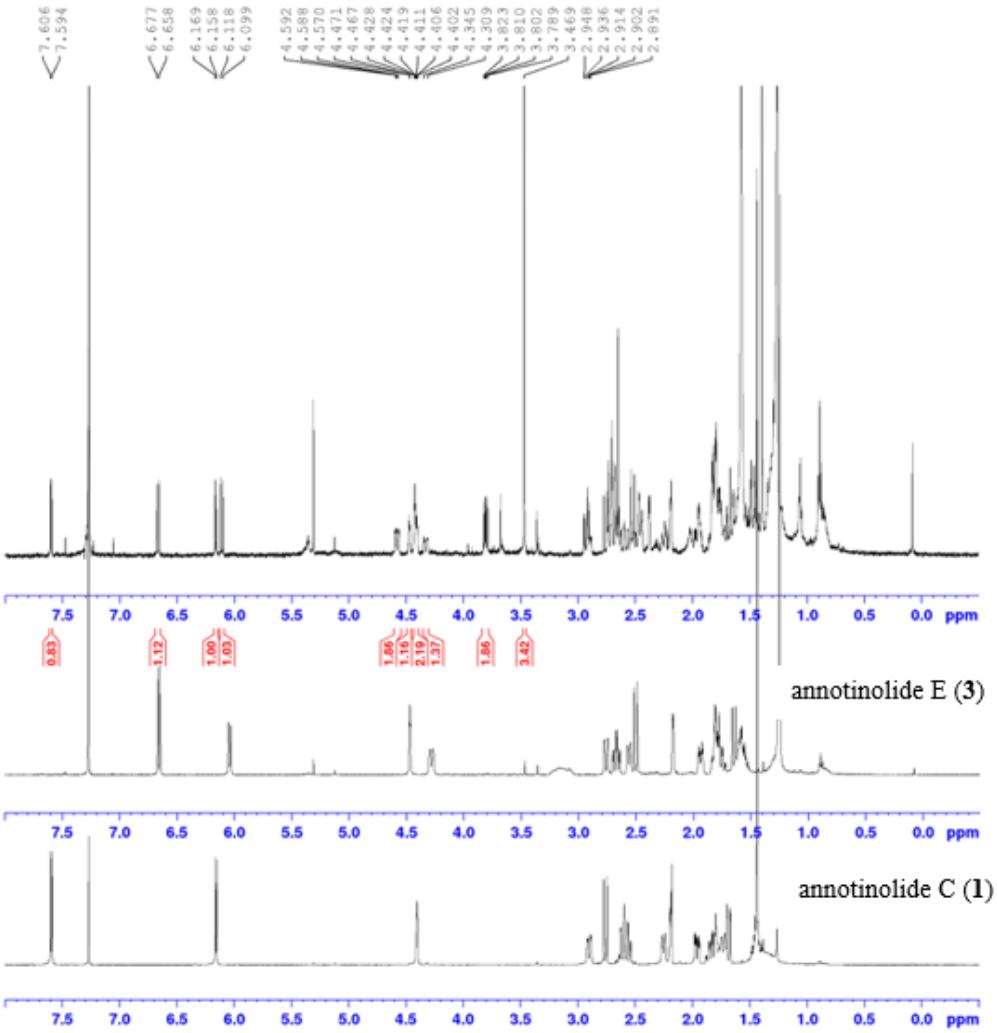
Natural **3** (^{13}C NMR, $CDCl_3$, 100 MHz) δ	Synthetic **3** (^{13}C NMR, $CDCl_3$, 126 MHz) δ	Δδ, ppm
176.9	176.8	-0.1
163.2	163.2	0.0
142.7	142.7	0.0
126.4	126.4	0.0
78.0	78.0	0.0
72.7	72.8	0.1
66.1	66.1	0.0
48.6	48.6	0.0
42.8	12.8	0.0
41.5	41.5	0.0
39.9	39.9	0.0
38.9	38.9	0.0
30.3	30.3	0.0
23.9	23.9	0.0
22.7	22.7	0.0
22.6	22.6	0.0

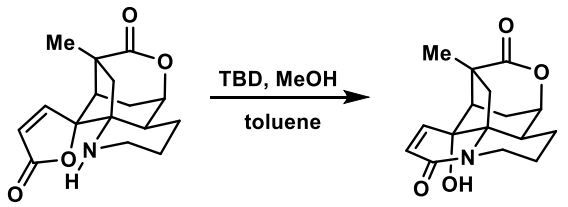


1: annotinolide C **3:** annotinolide E

Annotinolide E (3). Annotinolide C (**1**, 0.6 mg, 0.0021 mmol, 1.0 equiv) was dissolved in MeOH (0.30 mL) at 23 °C and NaOMe (0.6 mg, 0.01 mmol, 5.0 equiv) was added. The resultant solution was stirred for 1.5 h at 23 °C, at which point TLC analysis indicated no further change. The reaction contents were then diluted with EtOAc (1.0 mL) and quenched by the addition of saturated aqueous NH_4Cl (0.50 mL). The reaction contents were then poured into a separatory funnel and the resultant layers were separated. The aqueous layer was further extracted with EtOAc (3 × 1 mL). The combined organic layers were then washed with brine (2 mL), dried (Na_2SO_4), filtered, and concentrated. The resultant residue was then analyzed

directly by ^{1}H NMR, affording the result shown below indicating a mixture of annotinolide C (**1**), annotinolide E (**3**), and some unknown products in an approximate ratio of 1:1:1.

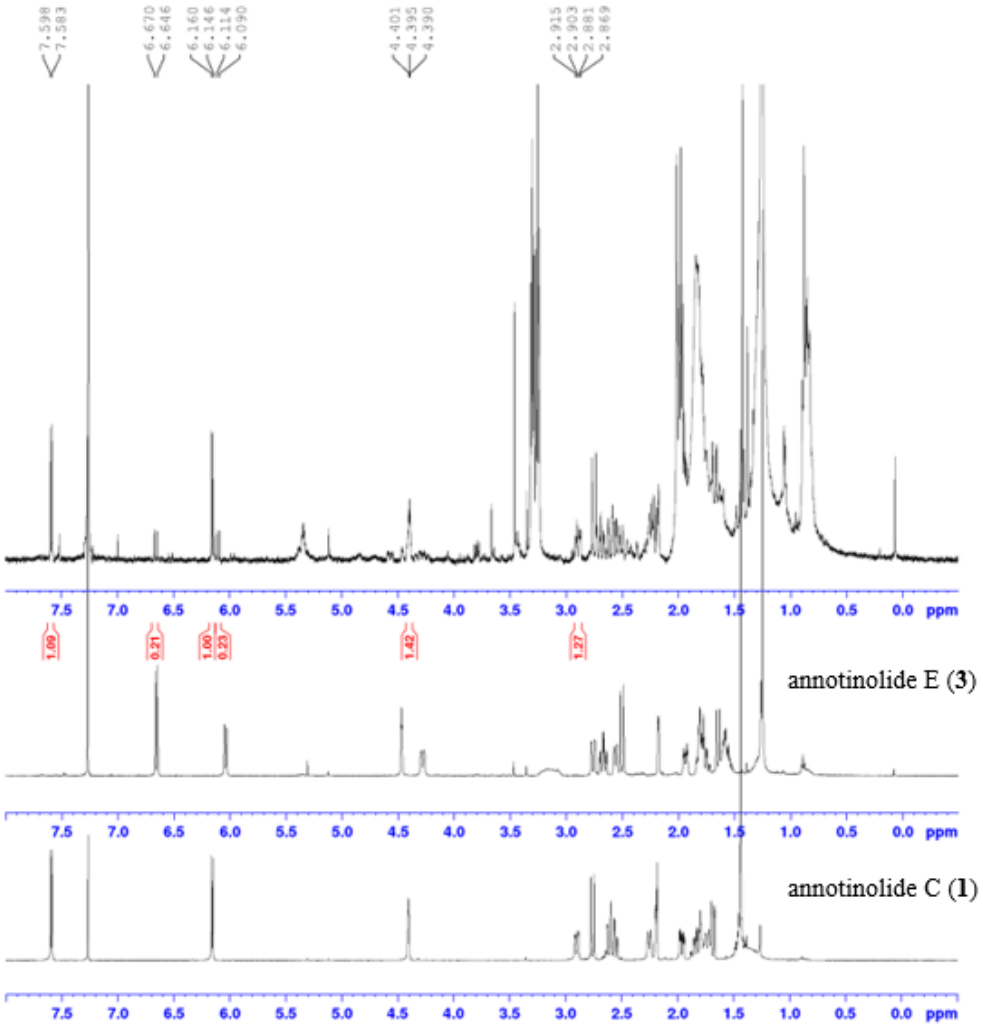




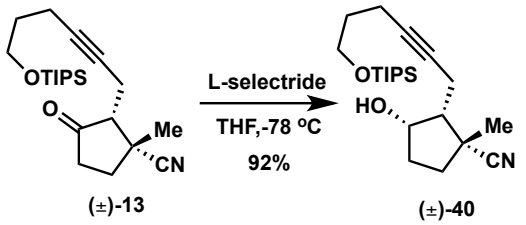
1: annotinolide C **3:** annotinolide E

Annotinolide E (3). Annotinolide C (**1**, 0.6 mg, 0.0021 mmol, 1.0 equiv) was dissolved in toluene (0.30 mL) and MeOH (0.030 mL) at 23 °C and triazabicyclo decene (0.3 mg, 0.0021 mmol, 1.0 equiv) was added in one portion. The reaction solution was stirred at 23 °C for 2 h, at which point TLC analysis indicated no further change. The reaction contents were diluted with EtOAc (1.0 mL) and quenched by saturated NH_4Cl solution (0.50 mL). The reaction contents

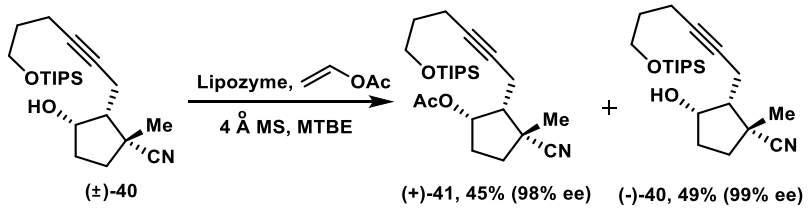
were then poured into a separatory funnel and the resultant layers were separated. The aqueous layer was further extracted with EtOAc (3 × 1 mL). The combined organic layers were then washed with brine (2 mL), dried (Na_2SO_4), filtered, and concentrated. The resultant residue was then analyzed directly by ^1H NMR, affording the result shown below indicating a mixture of annotinolide C (**1**) and annotinolide E (**3**) in an approximate ratio of 4:1.



Asymmetric synthesis of 15:

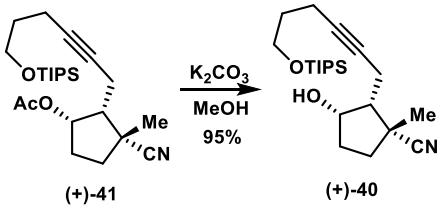


Alcohol 39. Ketone **13** (1.90 g, 5.06 mmol, 1.0 equiv) was dissolved in THF (51 mL) and then the reaction solution was cooled to –78 °C with a dry ice-acetone bath. Next, L-selectride (1.0 M in THF, 5.56 mL, 5.56 mmol, 1.1 equiv) was added dropwise, and the resulting pale-yellow solution was stirred at –78 °C for 30 min. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (40 mL) at –78 °C. After warming the reaction contents to 23 °C, they were poured into a separatory funnel and the resultant layers were separated. The aqueous layer was further extracted with EtOAc (2 × 40 mL). The combined organic layers were then washed with brine (100 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 6:1→3:1), providing desired alcohol (1.74 g, 92% yield) as a colorless oil. **39**: R_f = 0.26 (silica gel, hexanes/EtOAc = 4:1); IR (film) ν_{max} 3482, 2943, 2890, 2866, 2234, 1462, 1457, 1248, 1107, 1068 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.48–4.40 (m, 1 H), 3.74 (t, *J* = 6.1 Hz, 2 H), 2.65–2.57 (m, 1 H), 2.51–2.47 (m, 1 H), 2.47–2.40 (m, 1 H), 2.26 (tt, *J* = 7.1, 2.4 Hz, 2 H), 2.09–2.01 (m, 1 H), 1.91 (d, *J* = 4.2 Hz, 1 H), 1.86 (dddd, *J* = 14.5, 8.6, 6.4, 2.3 Hz, 1 H), 1.75 (dt, *J* = 10.4, 5.3 Hz, 1 H), 1.72–1.64 (m, 3 H), 1.43 (s, 3 H), 1.08–1.01 (m, 21 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 123.8, 84.7, 77.3, 73.9, 61.8, 54.7, 39.6, 38.1 ,32.4, 32.1, 25.45, 18.0, 15.8, 15.1, 11.9; HRMS (ESI) calcd for $C_{22}H_{40}NO_2Si^+$ [M + H^+] 378.2823, found 378.2819.

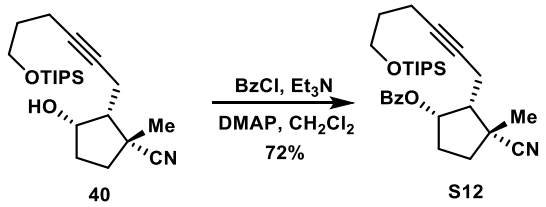


Acetate 40. 4 Å molecular sieves (4.05 g, 180 mg/mL solvent) were added to a round bottom flask and subsequently dried by flame heating under vacuum until any chunks in the original sample had disappeared to leave only a residual powder. The flask was then cooled to 23 °C under vacuum and charged with argon. A stir bar and a solution of alcohol **39** (1.65 g, 4.37 mmol, 1.0 equiv) in MTBE (20 mL) were then added at 23 °C. Another portion of MTBE (2.5 mL) was used to rinse the flask to complete the transfer of alcohol **39**. Finally, vinyl acetate (2.08 mL, 22.5 mmol, 5.0 equiv) and Lipozyme (0.450 g, 20 mg/mL solvent) were added and the resulting suspension was stirred at 23 °C for 24 h. Upon completion, the reaction suspension was filtered through a pad of Celite (eluting with EtOAc) and concentrated directly. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 8:1→4:1) provided desired acetate (0.826 g, 45% yield, 98% ee) as a colorless oil and unreacted alcohol (0.813 g, 49% yield, 99% ee) as a colorless oil. [Note: The ee values of (+)-**41** and (–)-**40** were

measured after they had been transformed separately into benzoate **S12** as delineated below]. **41**: R_f = 0.31 (silica gel, hexanes/EtOAc, 4:1); IR (film) ν_{max} 2943, 2893, 2866, 2234, 1740, 1464, 1457, 1239, 1107, 1067 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.31 (td, *J* = 5.3, 1.9 Hz, 1 H), 3.72 (t, *J* = 6.1 Hz, 2 H), 2.58–2.51 (m, 1 H), 2.47–2.38 (m, 2 H), 2.22 (tt, *J* = 7.2, 2.0 Hz, 2 H), 2.12 (ddd, *J* = 15.2, 9.7, 5.5 Hz, 1H), 2.07 (s, 3 H), 1.94–1.85 (m, 2 H), 1.76–1.70 (m, 1 H), 1.70–1.64 (m, 2 H), 1.52–1.48 (m, 3 H), 1.07–1.01 (m, 21 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.3, 123.1, 81.5, 76.7, 76.0, 61.9, 53.1, 40.4, 38.1, 32.1, 30.7, 25.6, 20.9, 18.0, 16.0, 15.1, 11.9; HRMS (ESI) calcd for $C_{24}H_{42}NO_3Si^+$ [M + H^+] 420.2928, found 420.2930. $[\alpha]_D^{23}$ = +22º (*c* = 1.0, $CHCl_3$). Alcohol (–)-**40**: $[\alpha]_D^{23}$ = –26º (*c* = 1.0, $CHCl_3$).



Alcohol 40. Acetate **41** (0.770 g, 1.83 mmol, 1.0 equiv) was dissolved in MeOH (92 mL) at 23 °C and then K_2CO_3 (2.54 g, 18.3 mmol, 10.0 equiv) was added. The reaction suspension was then vigorously stirred at 23 °C for 1 h. Upon completion, the reaction mixture was filtered through Celite (eluting with EtOAc) and concentrated directly. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 4:1) providing the desired alcohol (0.658 g, 95% yield) as a colorless oil. (+)-**40**: $[\alpha]_D^{23}$ = +25º (*c* = 1.0, $CHCl_3$)



General procedure to prepare benzoate S12 for ee measurement. Alcohol **40** (10.2 mg, 0.0270 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (0.54 mL) at 23 °C. Then Et_3N (13.7 mg, 0.135 mmol, 5.0 equiv), 4-DMAP (3.3 mg, 0.0270 mmol, 1.0 equiv), and BzCl (5.7 mg, 0.0405 mmol, 1.5 equiv) were added sequentially, forming a yellow solution. The reaction contents were then stirred at 23 °C for 24 h. Upon completion, the reaction solution was quenched by the addition of saturated $NaHCO_3$ solution (0.5 mL) and poured into a separatory funnel. After separating the layers, the aqueous layer was extracted further with CH_2Cl_2 (2 × 2 mL). The combined organic layers were then washed with brine (4 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 10:1) providing the desired benzoate **S12** (9.4 mg, 72% yield) as a colorless oil. IR (film) ν_{max} 2942, 2894, 2865, 2233, 1722, 1462, 1452, 1272, 1110, 1070, 711 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.15–8.11 (m, 2 H), 7.58–7.51 (m, 2 H), 7.48–7.43 (m, 1 H), 5.60 (td, *J* = 5.2, 1.9 Hz, 1 H), 3.68 (t, *J* = 6.0 Hz, 2 H), 2.68 (ddt, *J* = 16.7, 9.1, 2.5 Hz, 1 H), 2.54 (ddt, *J* = 14.8, 6.4, 4.1 Hz, 2 H), 2.28–2.16 (m, 3 H), 2.10–2.00 (m, 2 H), 1.83 (ddd, *J* = 13.7, 10.0, 6.1 Hz, 1 H), 1.64 (dddd, *J* = 13.3, 7.3, 6.1, 2.7 Hz, 2 H), 1.58 (s, 3 H), 1.06–0.99 (m, 21 H); ^{13}C NMR

(125 MHz, $CDCl_3$) δ 165.8, 133.1, 129.9, 128.5, 123.5, 81.8, 76.8, 76.7, 61.8, 53.8, 40.5, 38.3, 32.1, 30.8, 25.7, 18.0, 17.9, 16.1, 15.1, 11.9; HRMS (ESI) calcd for $C_{29}H_{43}NNaO_3Si^+$ [M + Na^+] 504.2904, found 504.2905. (+)-**S12**: $[\alpha]_D^{23}$ = +45° (*c* = 1.0, $CHCl_3$); (–)-**S12**: $[\alpha]_D^{23}$ = –43° (*c* = 1.0, $CHCl_3$). HPLC condition: OD-H column, 4.6 × 250 mm, hexanes/*i*-PrOH = 99:1, 1 mL/min, UV detector at 240 nm, R_T[(+)-**S12**] = 7.14 min, R_T[(–)-**S12**] = 8.13 min.

Racemic **S12**:

Analysis Report

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Date Processed	: 11/25/2020 6:08:39 PM	Processed by	: Snyder Group

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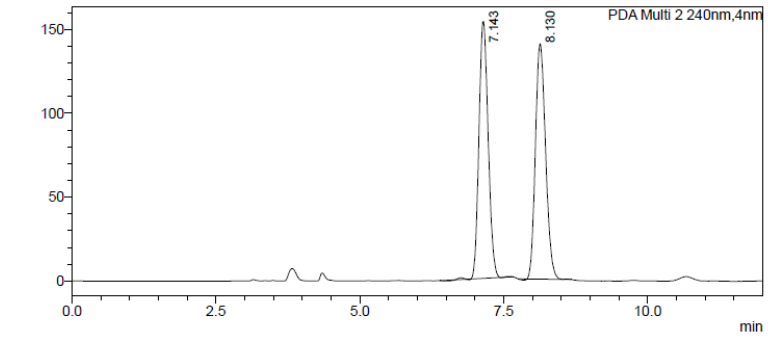

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(+)-**S12** (from resolution product **41**):

Analysis Report

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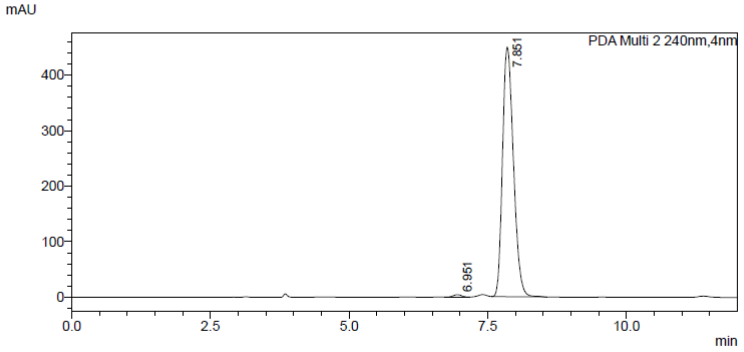

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(–)-**S12** (from resolution product **40**):

Analysis Report

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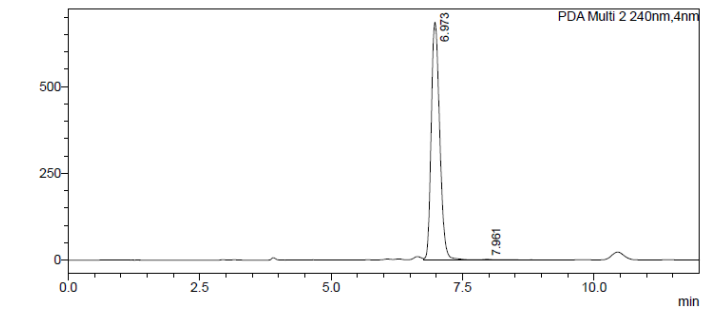

<Peak Table>

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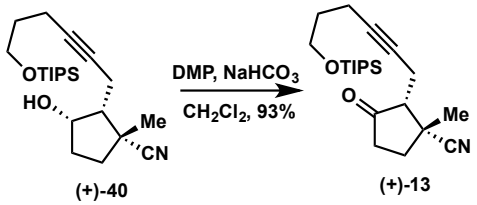
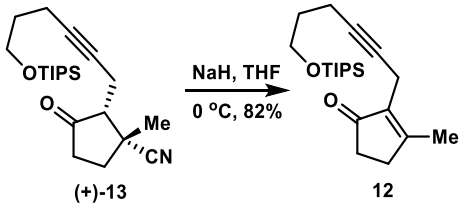


(+)-40 (+)-13

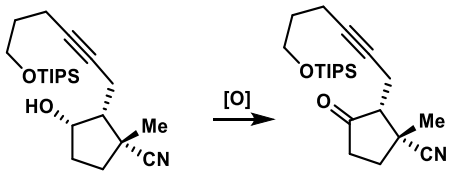
Ketone 13. Alcohol **40** (0.650 g, 1.72 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (17 mL) at 23 °C and then $NaHCO_3$ (1.44 g, 17.2 mmol, 10 equiv) and Dess–Martin periodinane (1.45 g, 34.4 mmol, 2.0 equiv) were added sequentially. The resultant suspension was then vigorously stirred at 23 °C for 45 min. Upon completion, the reaction contents were quenched by the addition of 3 M $Na_2S_2O_3$ (15 mL) and poured into a separatory funnel. After separating the layers, the aqueous layer was further extracted with CH_2Cl_2 (2 × 15 mL). The combined organic layers were then washed with brine (40 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 8:1) provided desired ketone (0.604 g, 93% yield) as a colorless oil. (+)-**13**: $[\alpha]_D^{23} = +81°$ (*c* = 1.0, $CHCl_3$).



(+)-13 12

Enone 12. Ketone **13** (0.550 g, 1.42 mmol, 1.0 equiv) was dissolved in THF (14 mL) at 23 °C and then the resultant solution was cooled to 0 °C using an ice-water bath. Then NaH (60% dispersion in mineral oil, 0.284 g, 7.10 mmol, 5.0 equiv) was added in a single portion, forming a pale yellow suspension. The reaction mixture was then stirred at 0 °C for 1 h. Upon completion, the reaction contents were quenched by the addition of H_2O (10 mL), warmed to 23 °C, and poured into a separatory funnel. After separating the layers, the aqueous layer was further extracted with EtOAc (2 × 10 mL). The combined organic layers were then washed with brine (30 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 10:1) provided desired enone (0.405 g, 82% yield) as a pale yellow oil whose spectral data fully matched that of previously characterized material.

Table S9. Condition screening for the oxidation of **40**



(-)-40 (-)-13

Entry	Condition	Result[a]
1	PCC (1.5 equiv), CH_2Cl_2, 23 °C	96% ee[b]
2	DMP (2.0 equiv), CH_2Cl_2, 23 °C	96%, 95% ee[c]
3	DMP (2.0 equiv), $NaHCO_3$ (10,0 equiv), CH_2Cl_2, 23 °C	88%, 91% ee[d]
4	$(COCl)_2$ (1.5 equiv), DMSO (5.0 equiv), Et_3N (10.0 equiv) CH_2Cl_2, -78 °C to -40 °C	87% ee[b]

a: ee value was measured after transforming **13** to benzoate **S12**
b: yield not determined
c: the reaction was perfomed on 0.2 g scale
d: the reaction was perfomed on 0.8 g scale

Procedure for entry 2. Alcohol **40** (0.181 g, 0.477 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (4.77 mL) at 23 °C and then Dess–Martin periodinane (0.404 g, 0.953 mmol, 2.0 equiv) was added. The resultant suspension was then vigorously stirred at 23 °C for 30 min. Upon completion, the reaction contents were quenched by the addition of 3 M $Na_2S_2O_3$ (5 mL) and poured into a separatory funnel. After separating the layers, the aqueous layer was further extracted with CH_2Cl_2 (2 × 5 mL). The combined organic layers were then washed with brine (10 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 8:1) provided desired ketone (0.173 g, 96% yield) as a colorless oil. (–)-**13**: $[\alpha]_D^{23} = -84°$ (*c* = 1.0, $CHCl_3$).

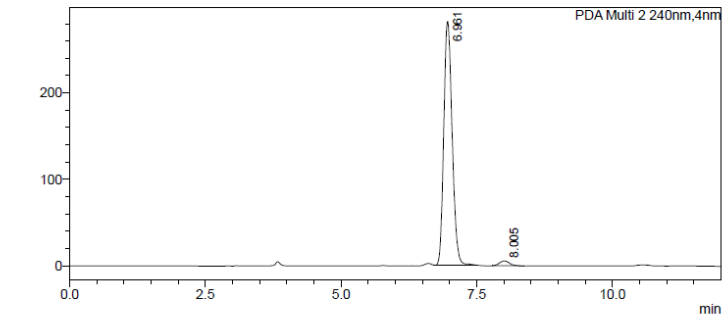
HPLC trace for entry 1:

Analysis Report

<Sample Information>

Sample Name	: PQ-1798-2		
Sample ID	: PQ-1798-2		
Data Filename	: PQ-1798-2.lcd		
Method Filename	: Default Method.lcm		
Batch Filename	:		
Vial #	: -1	Sample Type	: Unknown
Injection Volume	: 20 uL		
Date Acquired	: 3/18/2021 10:13:40 AM	Acquired by	: Snyder Group
Date Processed	: 3/18/2021 10:27:22 AM	Processed by	: Snyder Group

<Chromatogram>



<Peak Table>

PDA Ch2 240nm

Peak#	Ret. Time	Height	Area	Height%	Area%
1	6.961	281849	3019970	98.052	97.716
2	8.005	5600	70590	1.948	2.284
Total		287449	3090559	100.000	100.000

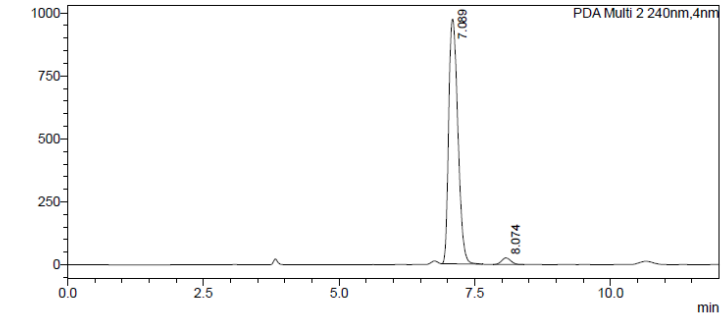
HPLC trace for entry 2:

Analysis Report

<Sample Information>

Sample Name	: PQ-1793		
Sample ID	: PQ-1793		
Data Filename	: PQ-1793.lcd		
Method Filename	: Default Method.lcm		
Batch Filename	:		
Vial #	: -1	Sample Type	: Unknown
Injection Volume	: 20 uL		
Date Acquired	: 3/6/2021 10:37:55 AM	Acquired by	: Snyder Group
Date Processed	: 3/17/2021 9:12:44 AM	Processed by	: Snyder Group

<Chromatogram>



<Peak Table>

PDA Ch2 240nm

Peak#	Ret. Time	Height	Area	Height%	Area%
1	7.089	971303	11454802	97.390	97.369
2	8.074	26032	309567	2.610	2.631
Total		997335	11764369	100.000	100.000

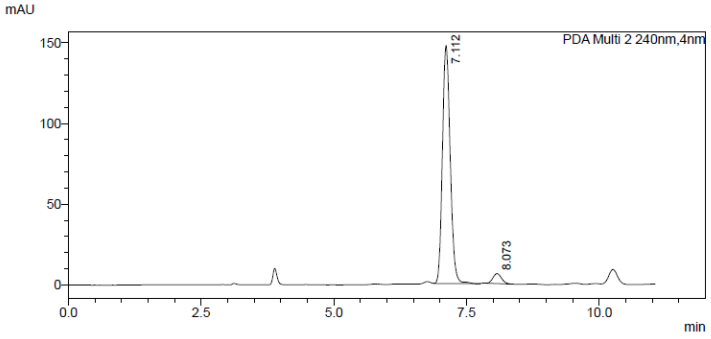
HPLC trace for entry 3:

Analysis Report

<Sample Information>

Sample Name	: PQ-1783		
Sample ID	: PQ-1783		
Data Filename	: PQ-1783.lcd		
Method Filename	: Default Method.lcm		
Batch Filename	:		
Vial #	: -1	Sample Type	: Unknown
Injection Volume	: 20 uL		
Date Acquired	: 2/28/2021 11:34:56 AM	Acquired by	: Snyder Group
Date Processed	: 3/17/2021 9:15:38 AM	Processed by	: Snyder Group

<Chromatogram>



<Peak Table>

PDA Ch2 240nm

Peak#	Ret. Time	Height	Area	Height%	Area%
1	7.112	147484	1503542	95.988	95.603
2	8.073	6164	69156	4.012	4.397
Total		153647	1572698	100.000	100.000

HPLC trace for entry 4:

Analysis Report

<Sample Information>

Sample Name	: PQ-1812		
Sample ID	: PQ-1812		
Data Filename	: PQ-1812.lcd		
Method Filename	: Default Method.lcm		
Batch Filename	:		
Vial #	: -1	Sample Type	: Unknown
Injection Volume	: 20 uL		
Date Acquired	: 3/17/2021 1:28:59 PM	Acquired by	: Snyder Group
Date Processed	: 3/17/2021 1:43:40 PM	Processed by	: Snyder Group

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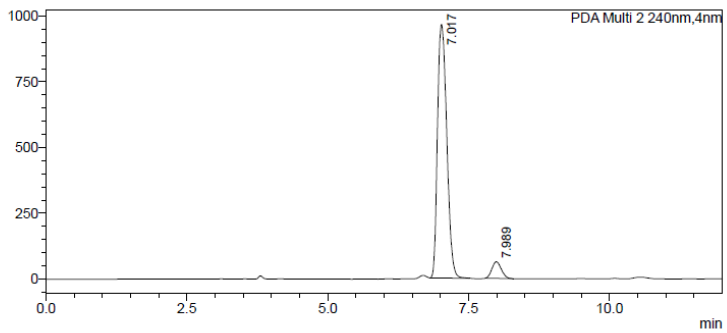
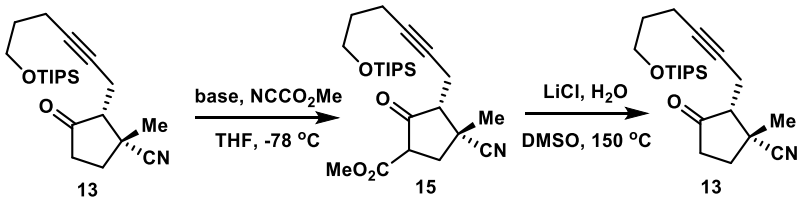


<Peak Table>

PDA Ch2 240nm

Peak#	Ret. Time	Height	Area	Height%	Area%
1	7.017	964041	11057125	93.857	93.795
2	7.989	63095	731494	6.143	6.205
Total		1027136	11788619	100.000	100.000

Table S10. Condition screening acylation of **13**



Entry[a]	Base	Variants	Result[b]
1	LDA (1.9 equiv)	none	72% ee[c]
2	LDA (1.9 equiv)	pre-mix 13 with $NCCO_2Me$	unkown product
3	LDA (1.9 equiv)	Et_2O as solvent	unkown product
4	LDA (1.9 equiv)	toluene as solvent	unkown product
5	LiHMDS (1.9 equiv)	none	unkown product
6	NaHMDS (1.9 equiv)	none	complex mixture
7	KHMDS (1.9 equiv)	none	69% ee[c]
8	LiTMP (1.9 equiv)	none	76% ee[c]
9[d]	LDA (1.9 equiv)	none	62%, 79% ee

a: ketone **13** was 91% ee and the reaction was perfomed on 50 mg scale. The procedures were kept the same as the recamic procdure except the base and variants in this table

b: ee value was measured after transforming **13** to benzoate **S12**

c: yield not determined

d: the reaction was perfomed on 0.2 g scale and keton **13** was 95% ee

General procedure for preparing ketone 13 from β-ketoester 15. β-ketoester **15** (16.1 mg, 0.0369 mmol, 1.0 equiv) was dissolved in DMSO (0.19 mL) at 23 °C, and then LiCl (3.1 mg, 0.0738 mmol, 2.0 equiv) and H_2O (3.3 mg, 0.184 mmol, 5.0 equiv) were added subsequently. The resultant reaction solution was then warmed to 150 °C using a pre-heated oil bath and stirred at that temperature for 2 h. Upon completion, the reaction contents were cooled to 23 °C and diluted by the addition of Et_2O (4 mL). The reaction contents were then poured into a separatory funnel, the layers were separated, and the organic layer was washed with 1:1 mixture of brine and water (2 × 2 mL). The organic layer was then dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes/EtOAc = 8:1) provided desired ketone (6.0 mg, 49% yield) as a colorless oil.

HPLC trace for entry 1:

Analysis Report

<Sample Information>

Sample Name	: PQ-1695-2		
Sample ID	: PQ-1695-2		
Data Filename	: PQ-1695-3.lcd		
Method Filename	: Default Method.lcm		
Batch Filename	:		
Vial #	: -1	Sample Type	: Unknown
Injection Volume	: 20 uL		
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Date Processed	: 3/17/2021 1:03:58 PM	Processed by	: Snyder Group

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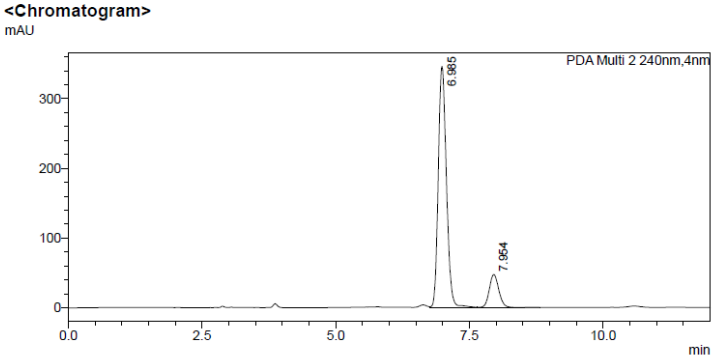

<Peak Table>

PDA Ch2 240nm

Peak#	Ret. Time	Height	Area	Height%	Area%
1	6.985	345925	3676198	87.924	85.961
2	7.954	47510	600400	12.076	14.039
Total		393435	4276597	100.000	100.000

HPLC trace for entry 7:

Analysis Report

<Sample Information>

Sample Name	: PQ-1706		
Sample ID	: PQ-1706		
Data Filename	: PQ-1706.lcd		
Method Filename	: Default Method.lcm		
Batch Filename	:		
Vial #	: -1	Sample Type	: Unknown
Injection Volume	: 20 uL		
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Date Processed	: 3/17/2021 9:00:03 AM	Processed by	: Snyder Group

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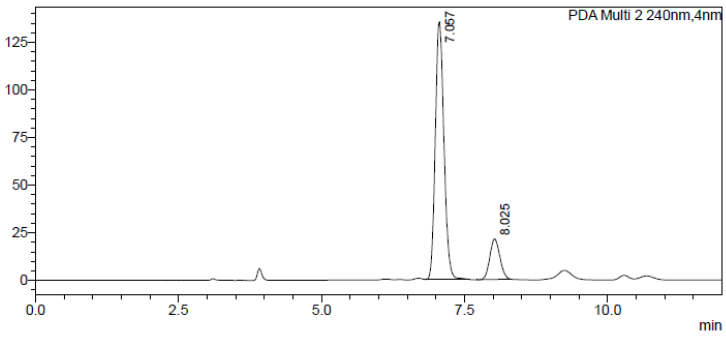

<Peak Table>

PDA Ch2 240nm

Peak#	Ret. Time	Height	Area	Height%	Area%
1	7.057	135380	1425525	86.440	84.523
2	8.025	21238	261035	13.560	15.477
Total		156618	1686560	100.000	100.000

HPLC trace for entry 8:

Analysis Report

<Sample Information>

Sample Name	: PQ-1700-2		
Sample ID	: PQ-1700-2		
Data Filename	: PQ-1700-2.lcd		
Method Filename	: Default Method.lcm		
Batch Filename	:		
Vial #	: -1	Sample Type	: Unknown
Injection Volume	: 20 uL		
Date Acquired	: 3/18/2021 9:57:45 AM	Acquired by	: Snyder Group
Date Processed	: 3/18/2021 10:30:32 AM	Processed by	: Snyder Group

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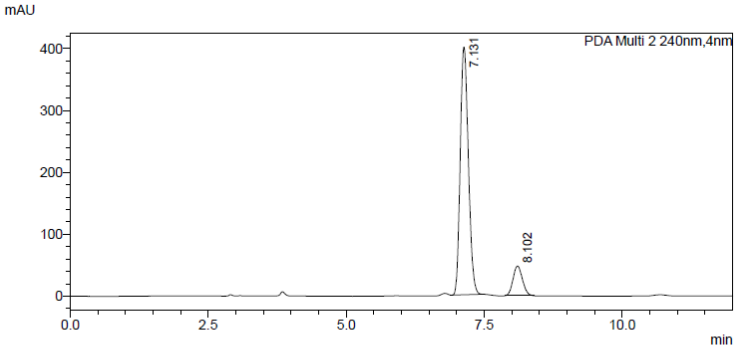


<Peak Table>

PDA Ch2 240nm

Peak#	Ret. Time	Height	Area	Height%	Area%
1	7.131	399781	4097706	89.327	87.850
2	8.102	47765	566708	10.673	12.150
Total		447546	4664414	100.000	100.000

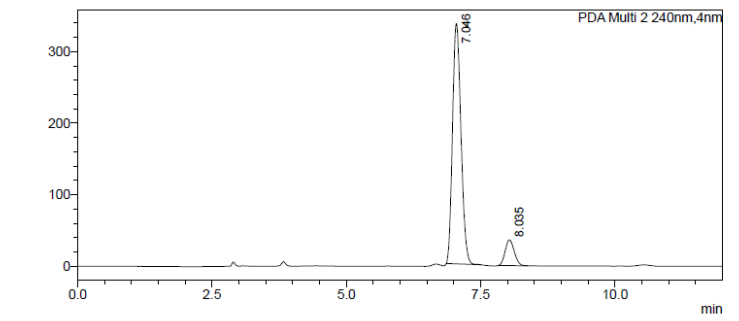
HPLC trace for entry 9:

Analysis Report

<Sample Information>

Sample Name	: PQ-1810-1		
Sample ID	: PQ-1810-1		
Data Filename	: PQ-1810-1.lcd		
Method Filename	: Default Method.lcm		
Batch Filename	:		
Vial #	: -1	Sample Type	: Unknown
Injection Volume	: 20 uL		
Date Acquired	: 3/17/2021 1:14:31 PM	Acquired by	: Snyder Group
Date Processed	: 3/17/2021 1:34:28 PM	Processed by	: Snyder Group

<Chromatogram>



<Peak Table>

PDA Ch2 240nm

Peak#	Ret. Time	Height	Area	Height%	Area%
1	7.046	335603	3677124	90.316	89.666
2	8.035	35984	423779	9.684	10.334
Total		371586	4100903	100.000	100.000

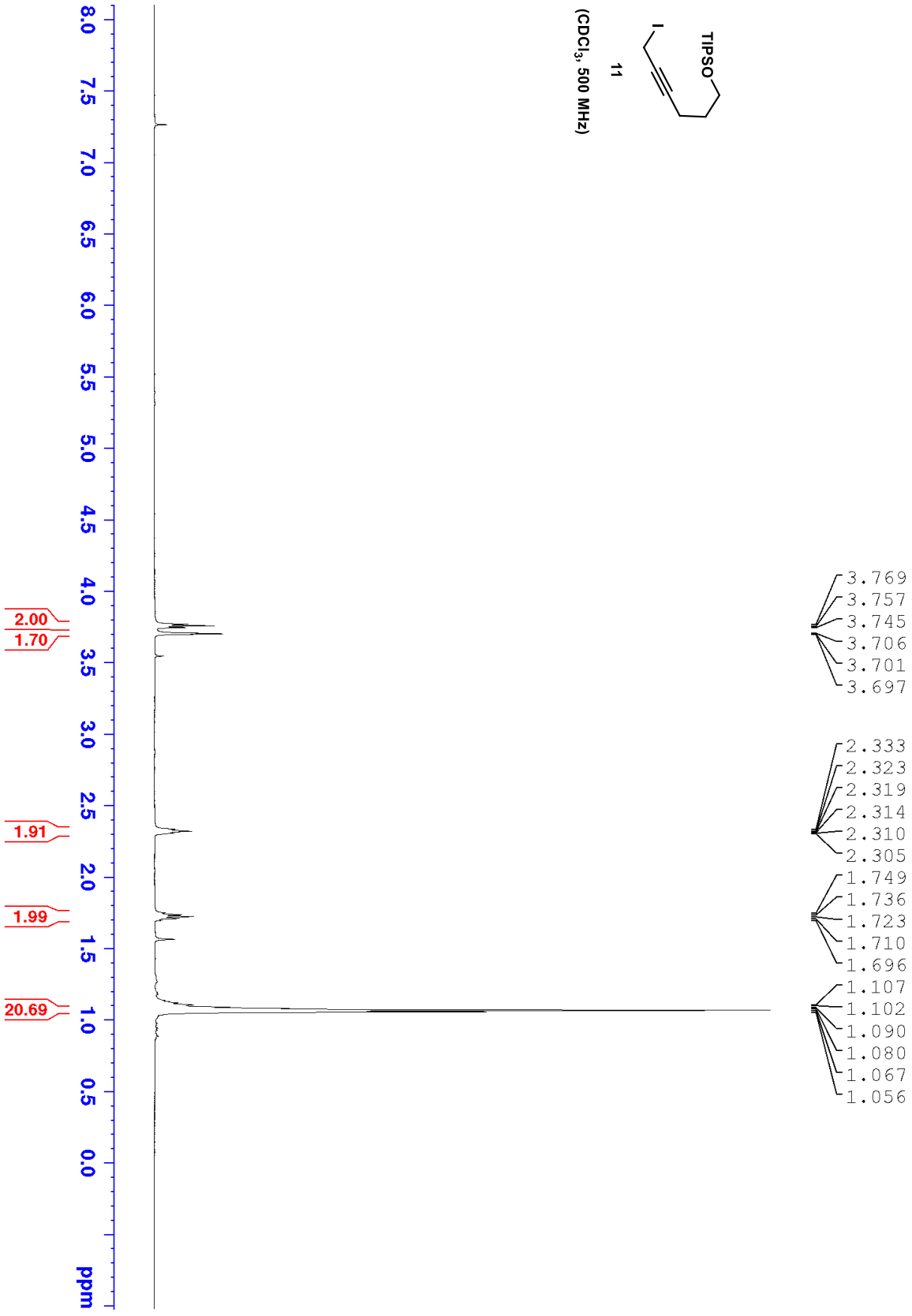
References

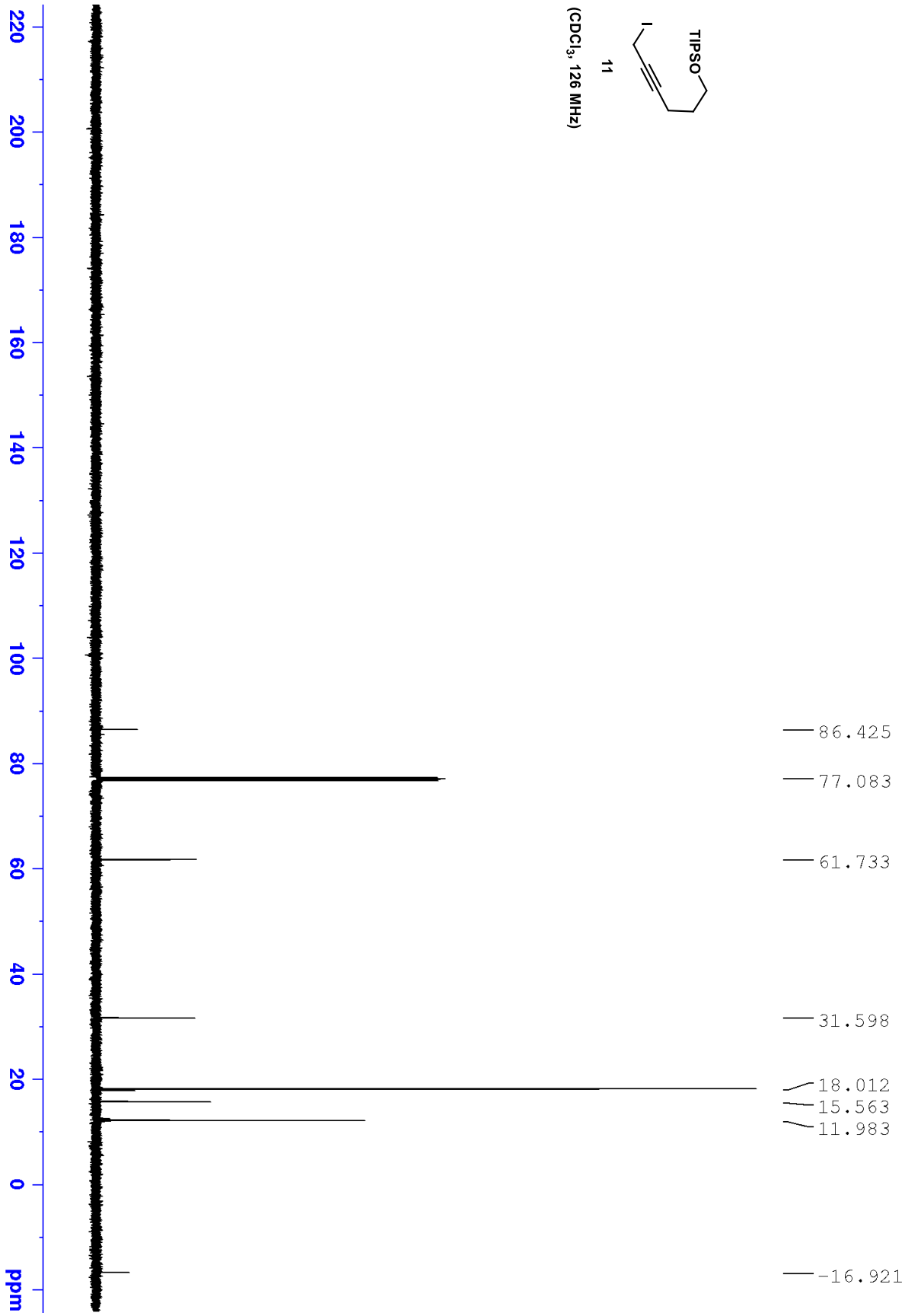
[1] Kippo, T.; Fukuyama, T.; Ryu, I. *Org. Lett.* **2011**, *13*, 3864.

[2] Johnson, C. R.; Adams, J. P.; Braun, M. P.; Senanayake, C. B. W.; Wovkulich, P, M.; Uskoković, M. R. *Tetrahedron Lett.* **1992**, *31*, 917.

[3] Piers, E.; Ranaud, J. *J. Org. Chem.* **1993**, *58*, 11.

^{1}H and ^{13}C NMR data for selected intermediates

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200
180
160
140
120
100
80
60
40
20
0
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61.733
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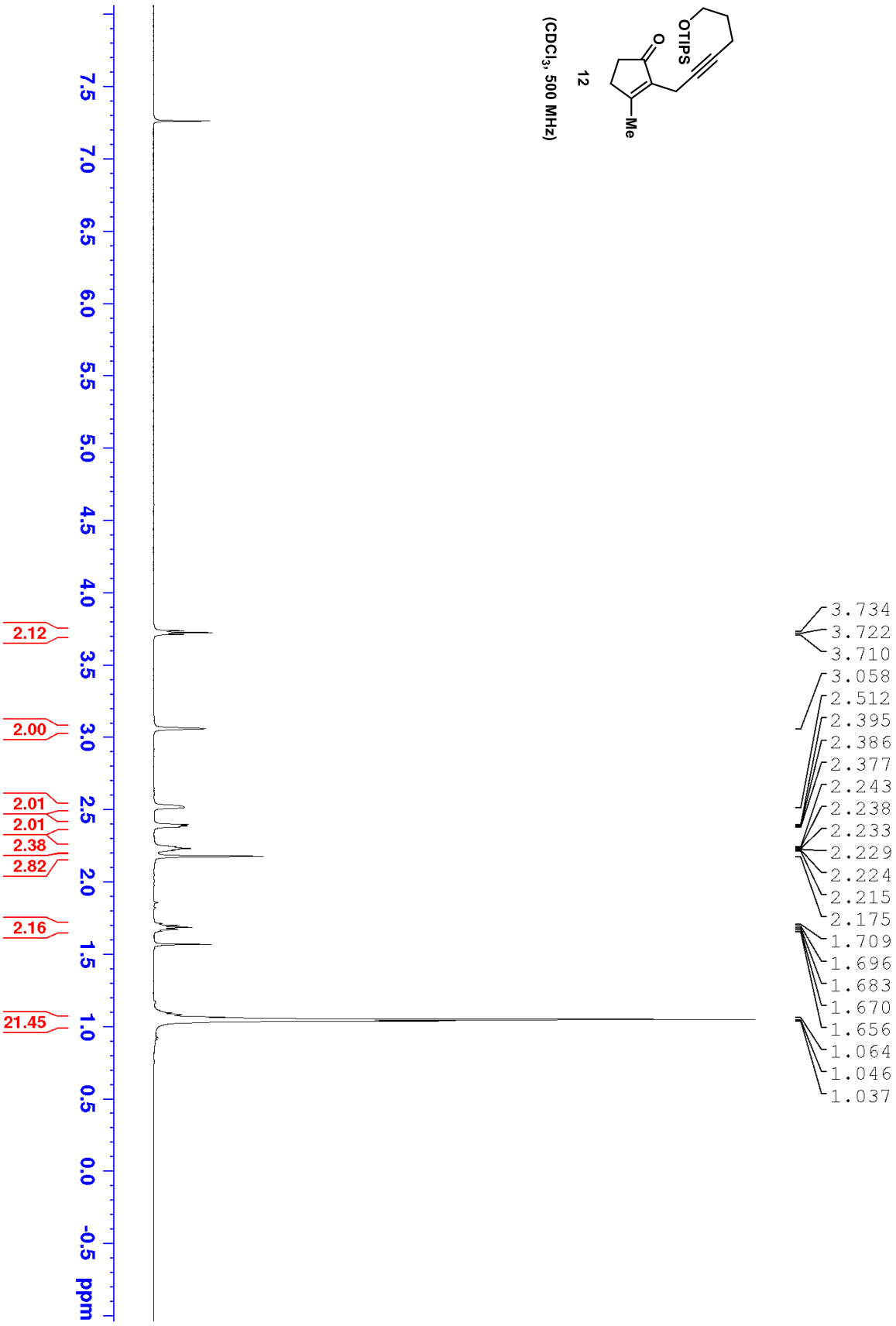
18.012
15.563
11.983
-16.921


12
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OTIPS
O
Me
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
ppm
2.12
2.00
2.01
2.01
2.38
2.82
2.16
21.45
3.734
3.722
3.710
3.058
2.512
2.395
2.386
2.377
2.243
2.238
2.233
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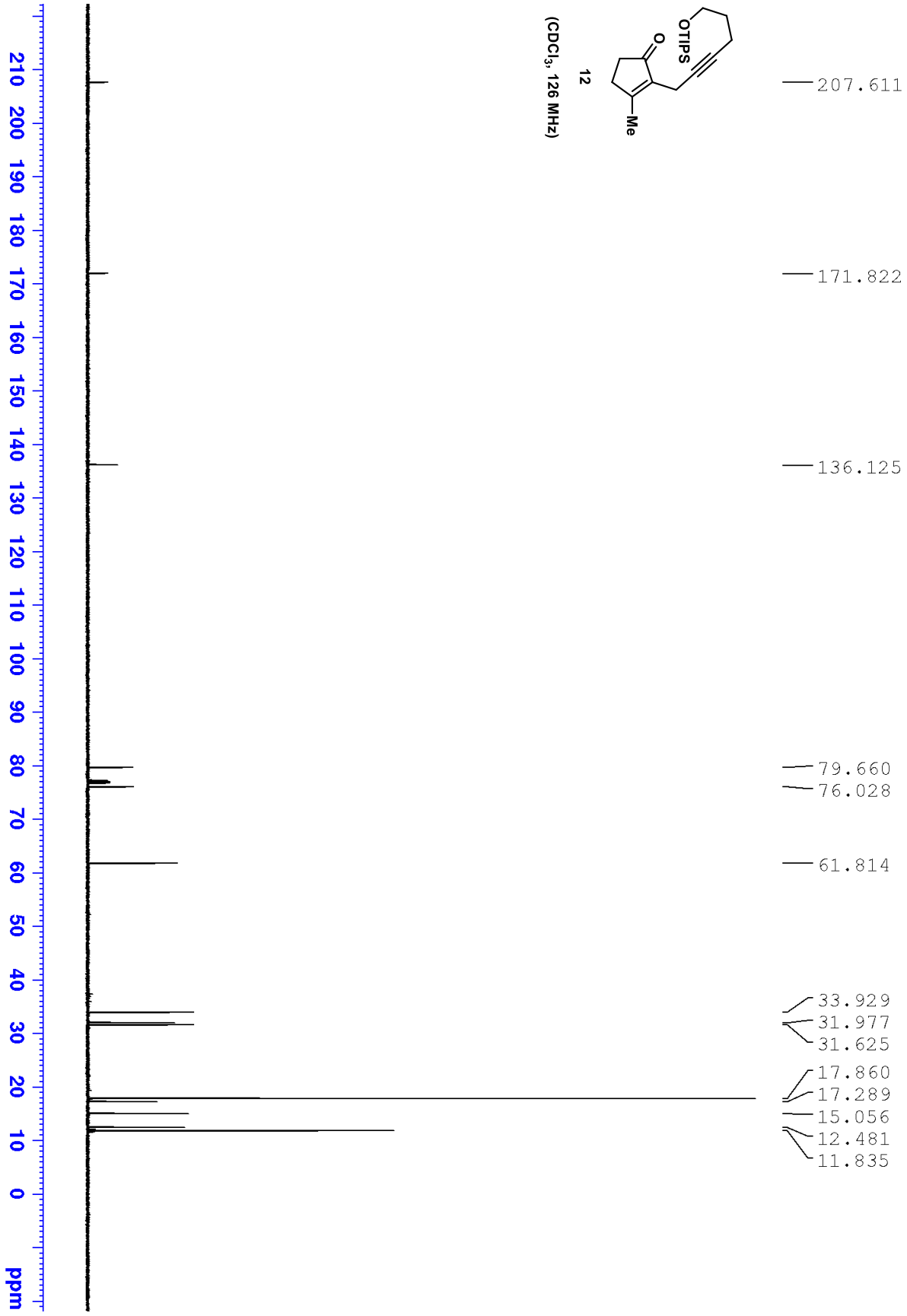
1.683
1.670
1.656
1.064
1.046
1.037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31.977
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17.289
15.056
12.481
11.835
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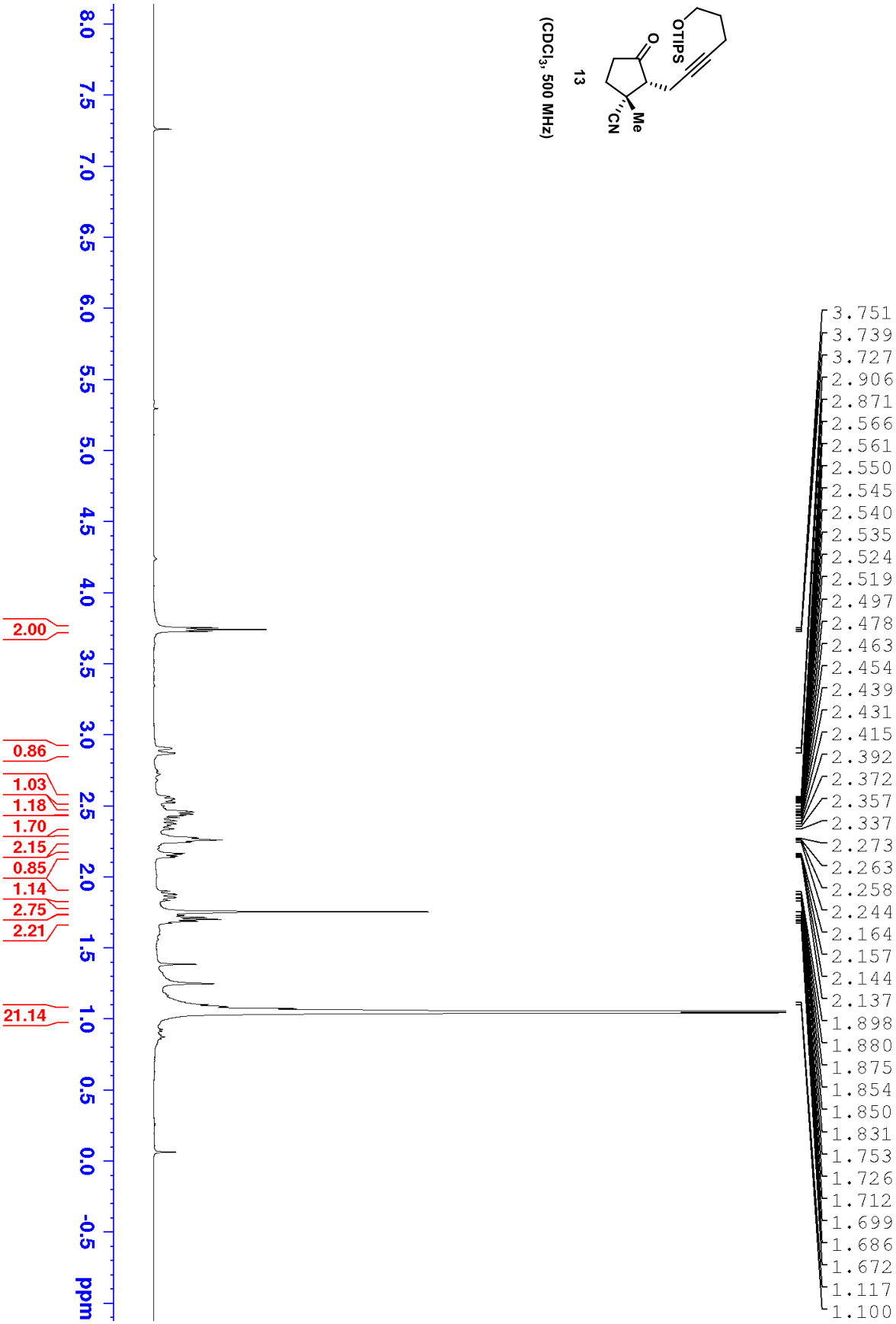
ppm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2.524
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2.454
2.439
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2.415
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2.357
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2.273
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1.854
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1.831
1.753
1.726
1.712
1.699
1.686
1.672
1.117
1.100
2.00
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1.03
1.18
1.70
2.15
0.85
1.14
2.75
2.21
21.14
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
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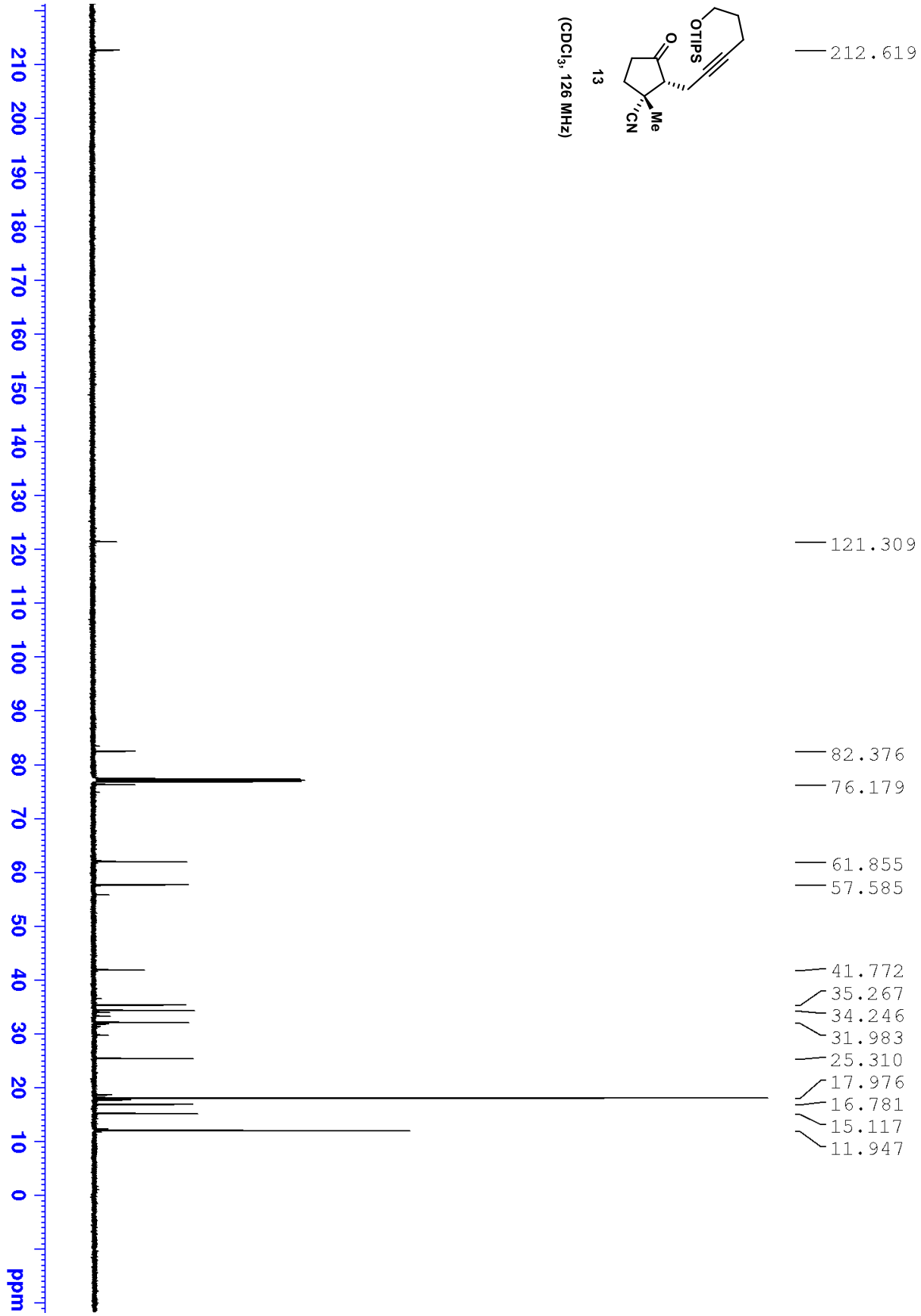
ppm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35.267
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17.976
16.781
15.117
11.947
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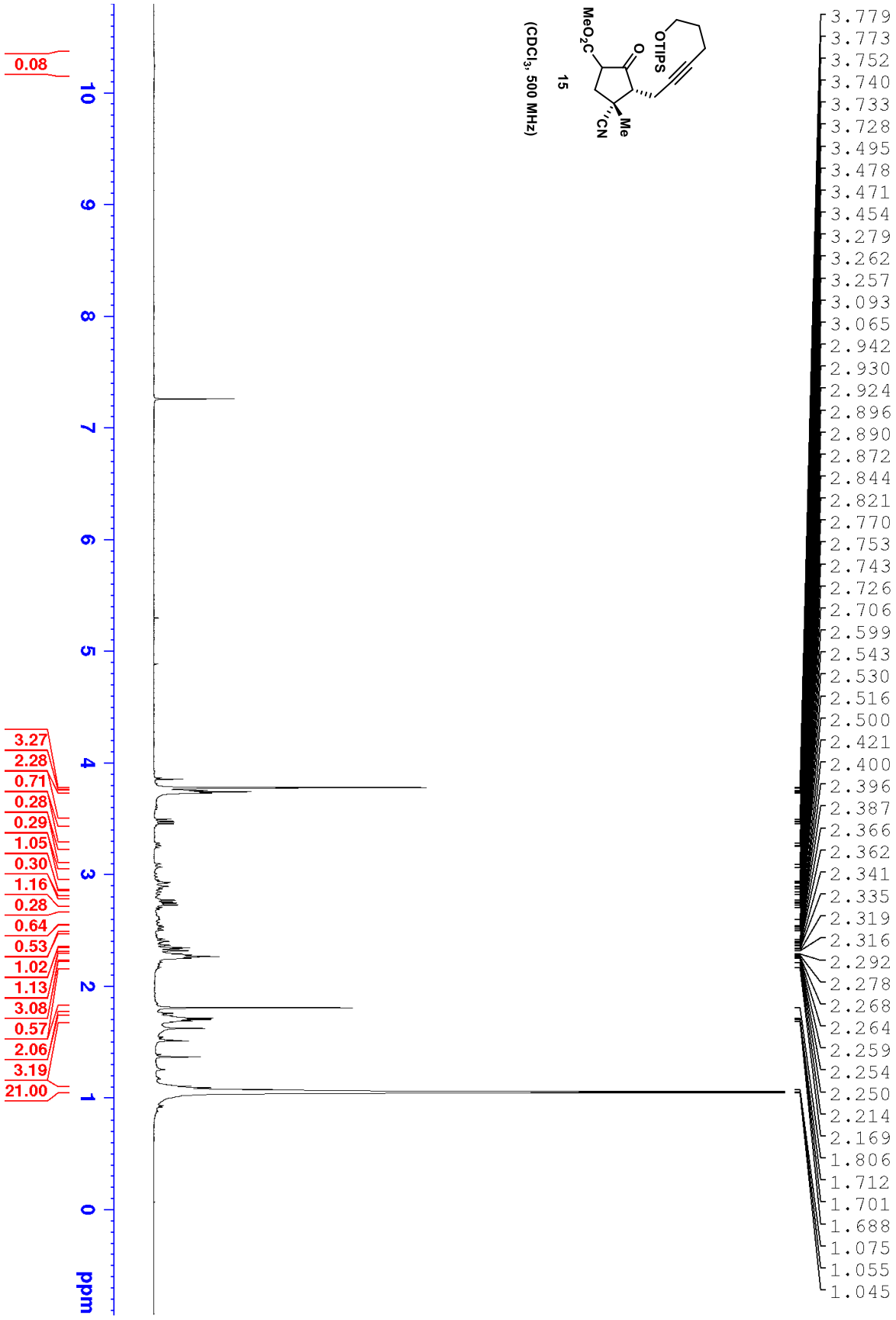
15
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O
OTIPS
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CN
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2.28
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0.29
1.05
0.30
1.16
0.28
0.64
0.53
1.02
1.13
3.08
0.57
2.06
3.19
21.00
ppm
3.779
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3.752
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3.478
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2.924
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2.821
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2.753
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2.706
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2.396
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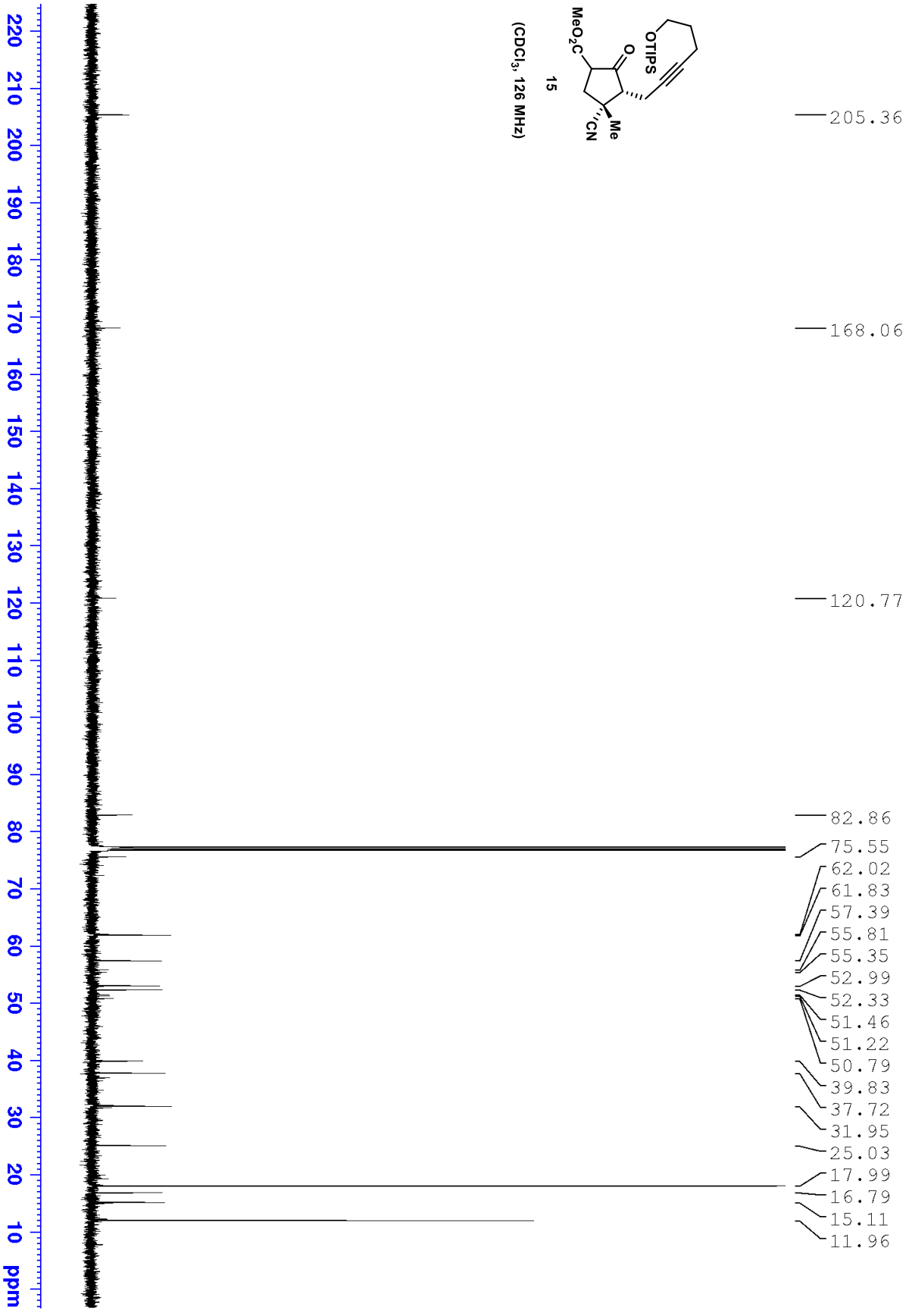
MeO2C
O
OTIPS
CN
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120.77
82.86
75.55
62.02
61.83
57.39
55.81
55.35
52.99
52.33
51.46
51.22
50.79
39.83
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25.03
17.99
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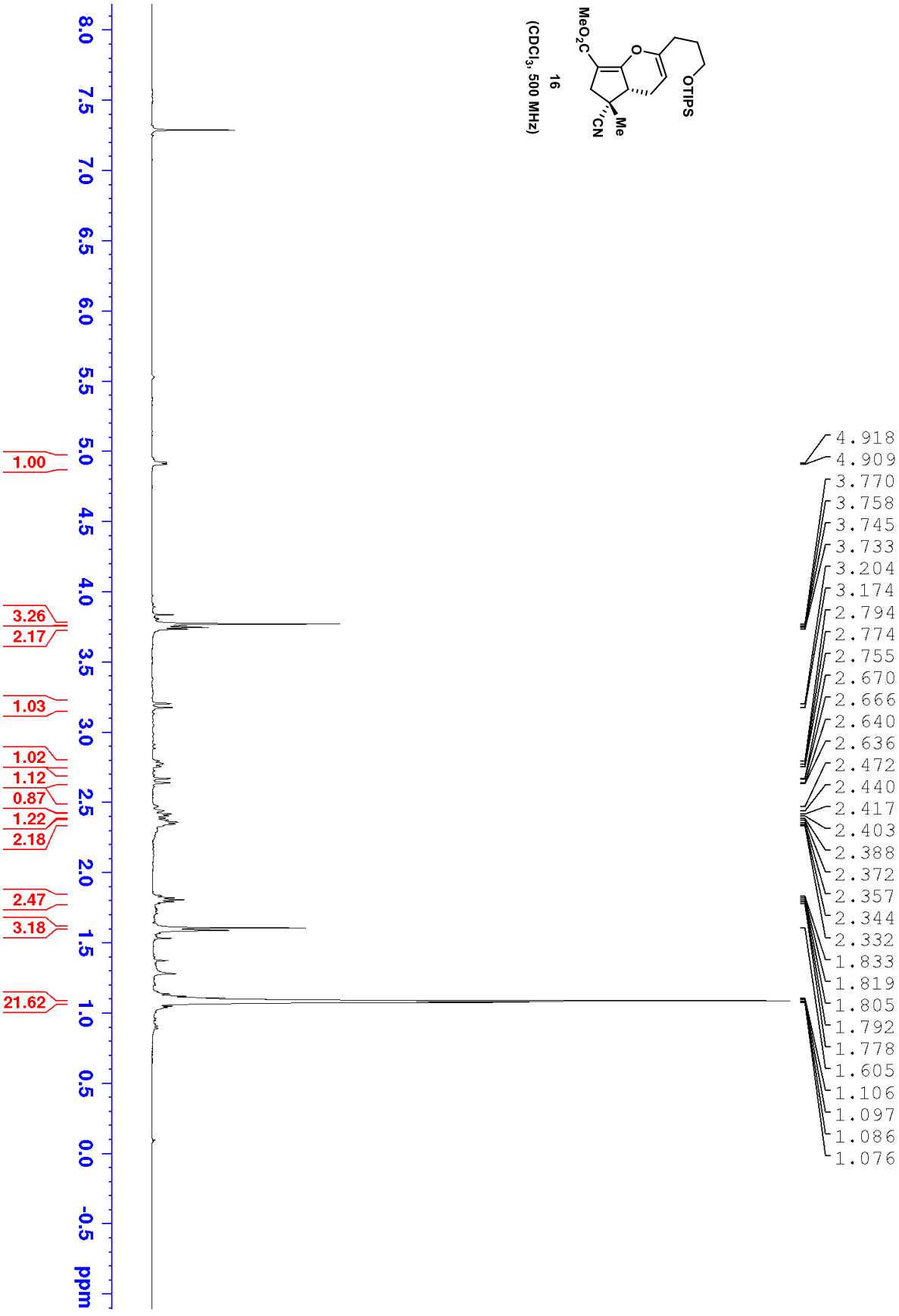
11.96
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
ppm
1.00
3.26
2.17
1.03
1.02
1.12
0.87
1.22
2.18
2.47
3.18
21.62
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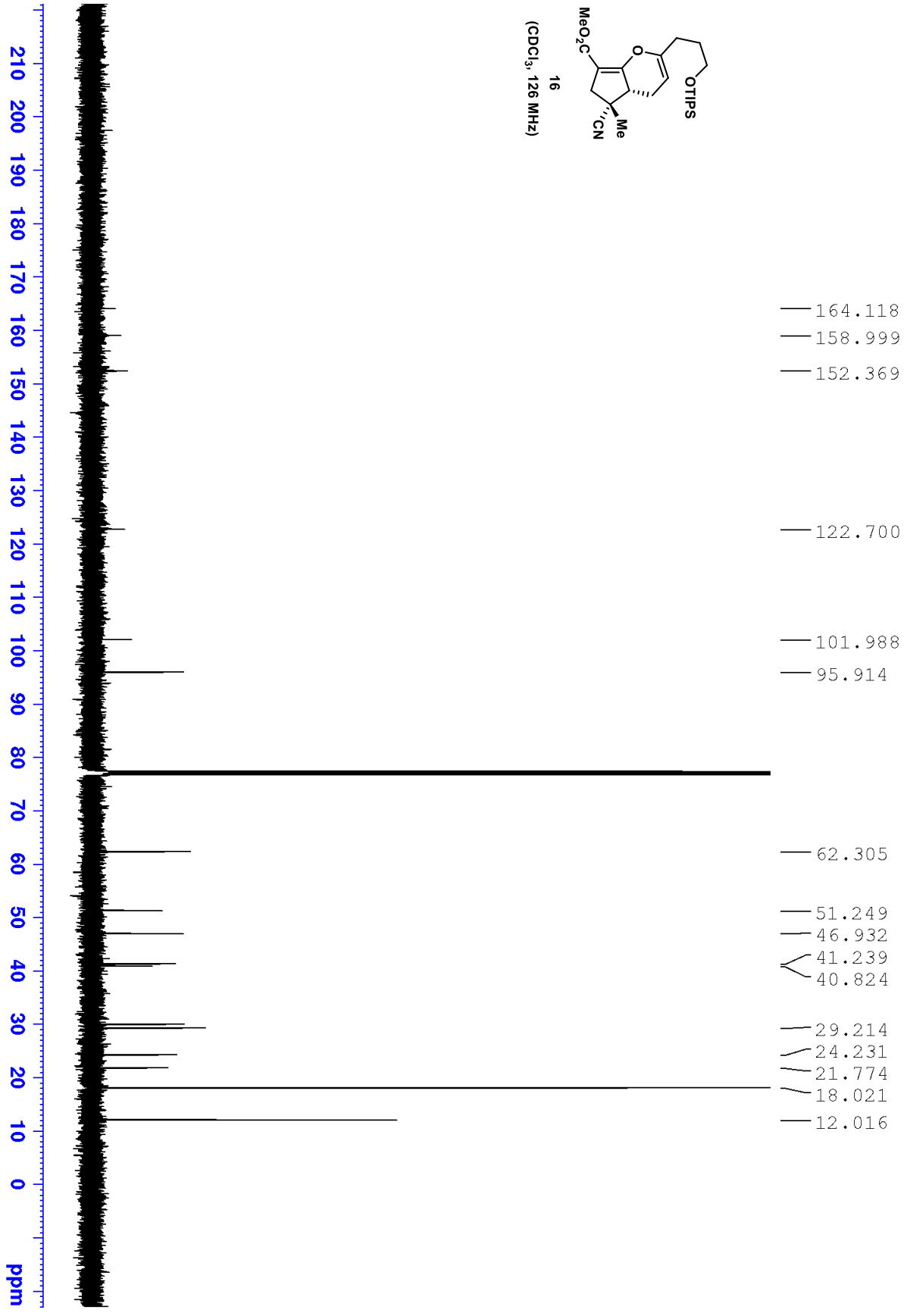
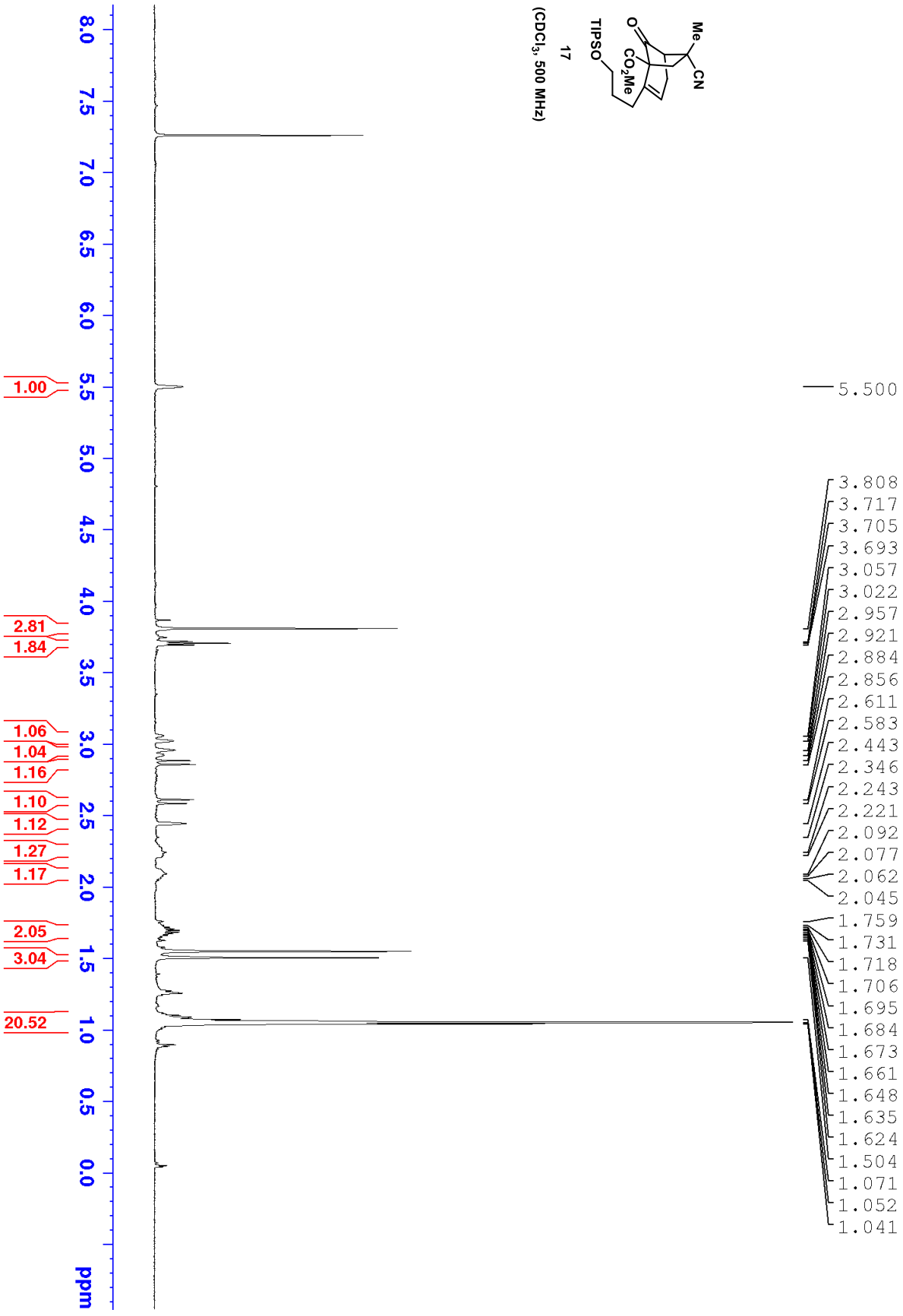
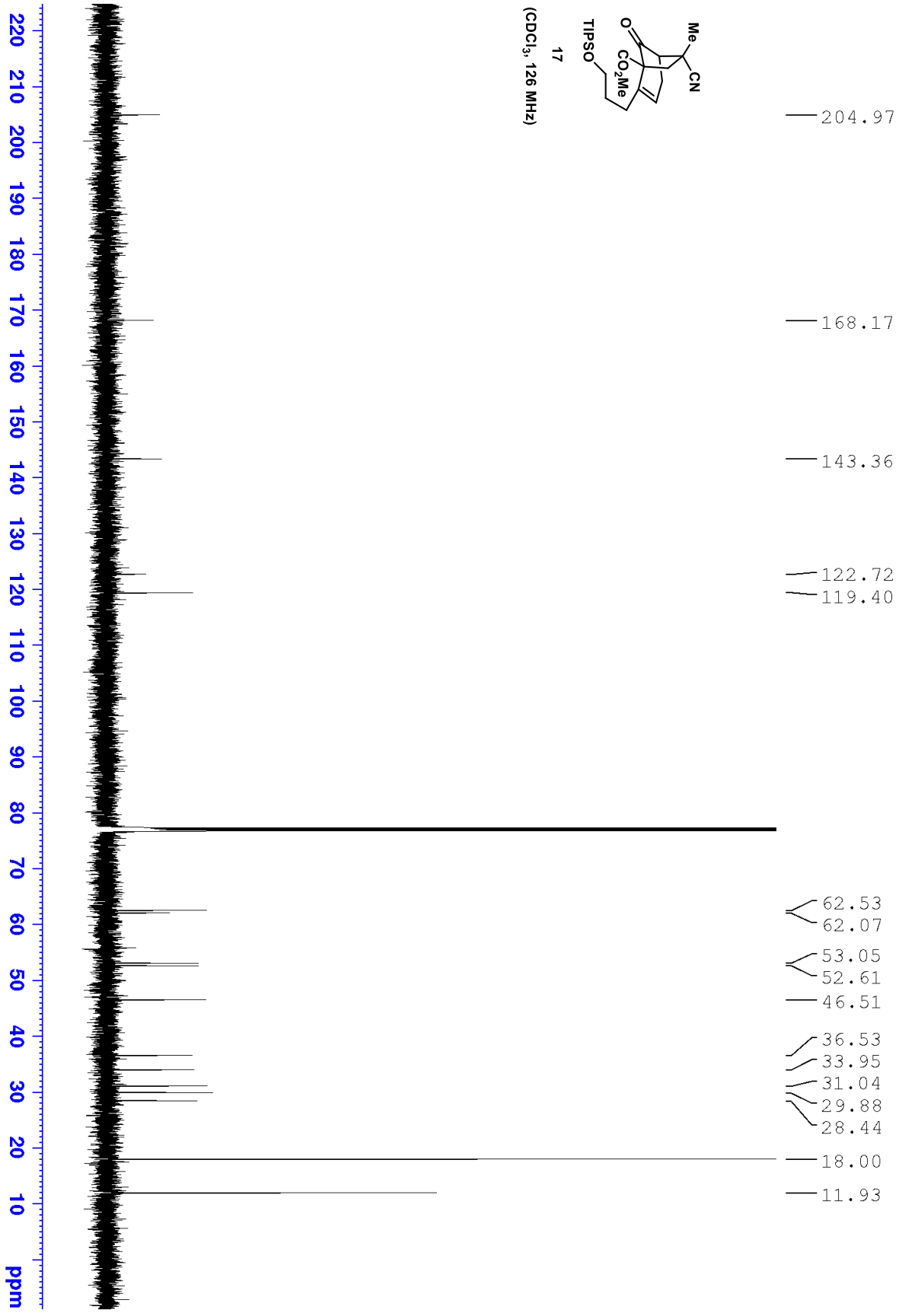
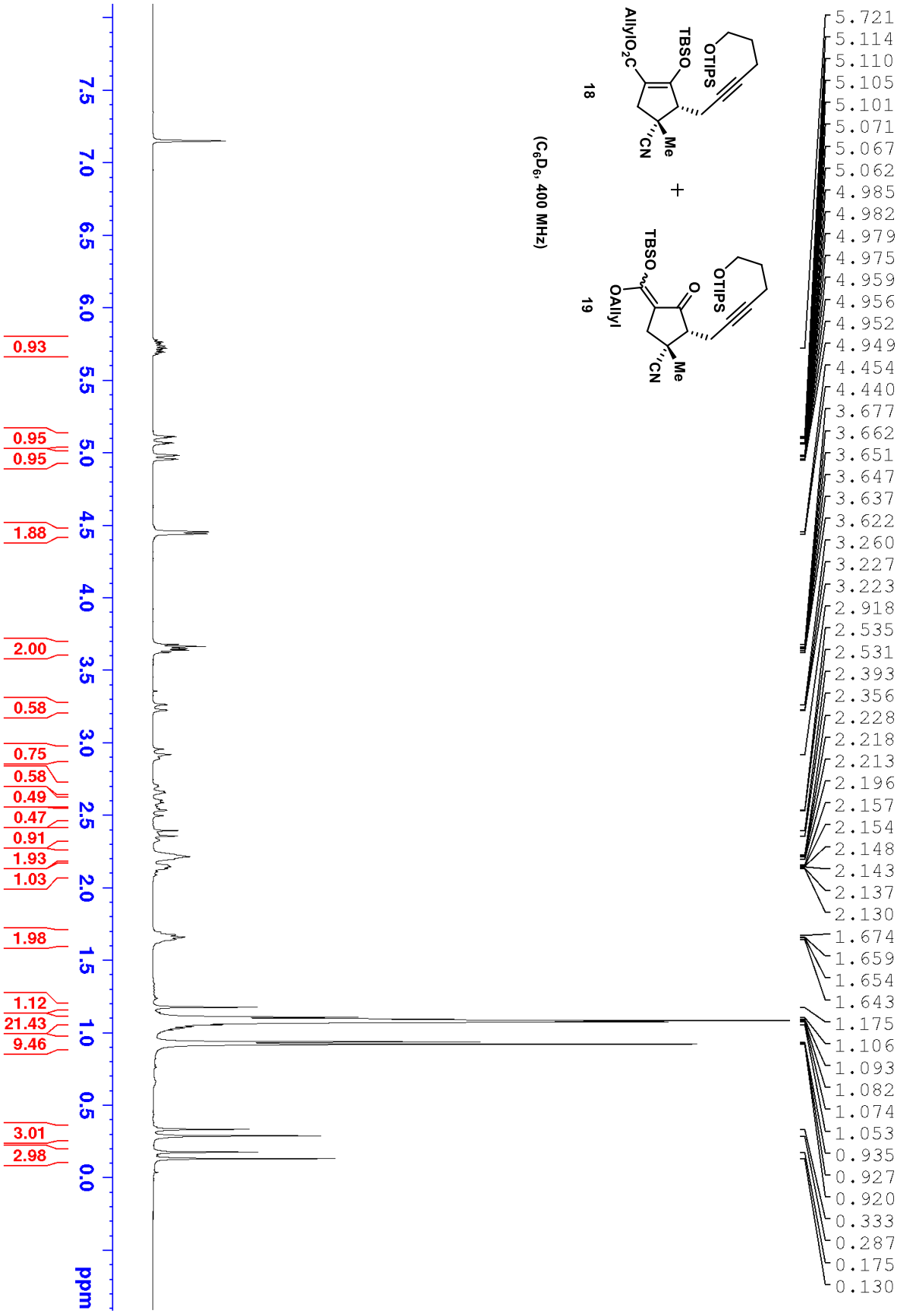
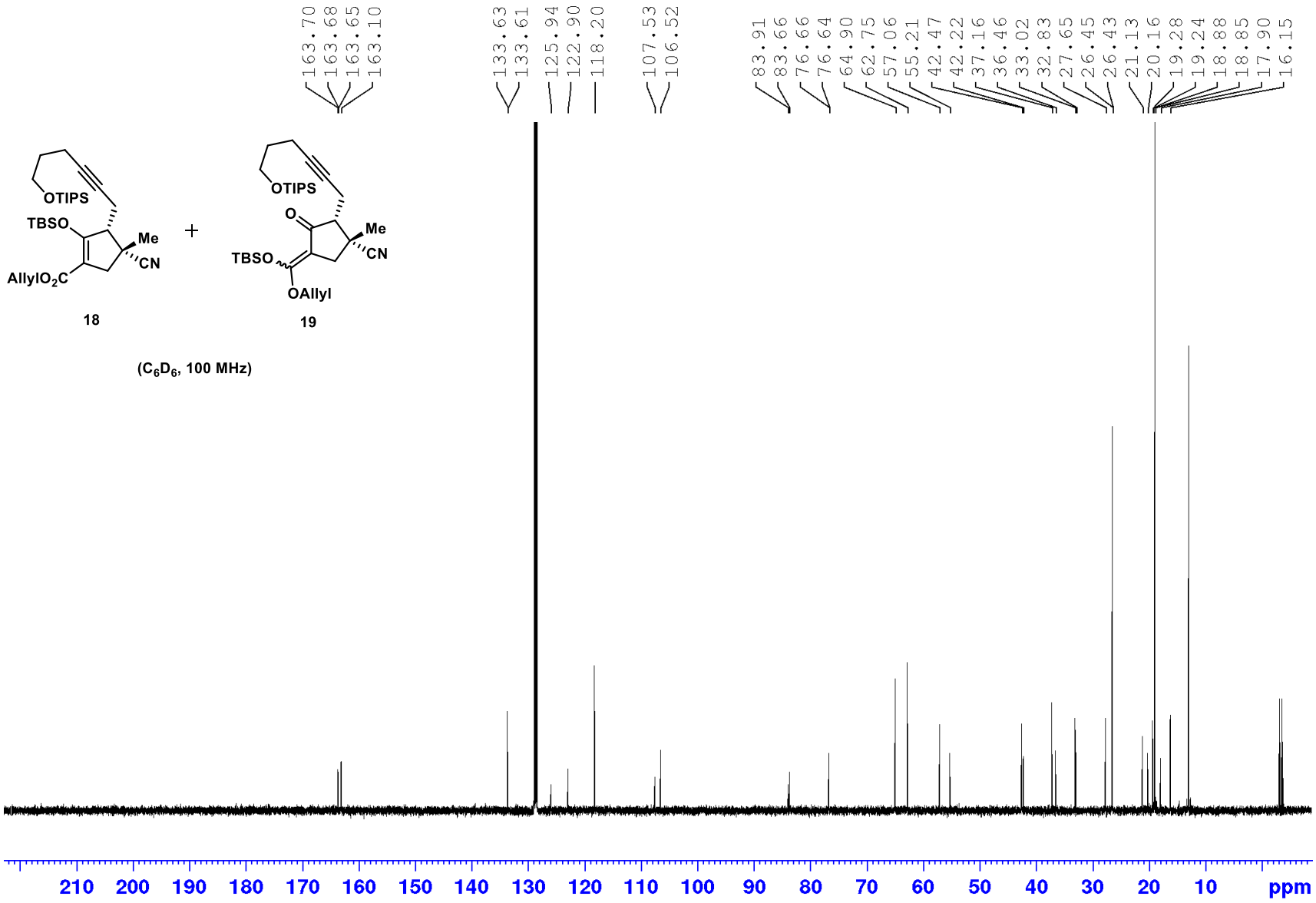
4.909
3.770
3.758
3.745
3.733
3.204
3.174
2.794
2.774
2.755
2.670
2.666
2.640
2.636
2.472
2.440
2.417
2.403
2.388
2.372
2.357
2.344
2.332
1.833
1.819
1.805
1.792
1.778
1.605
1.106
1.097
1.086
1.076

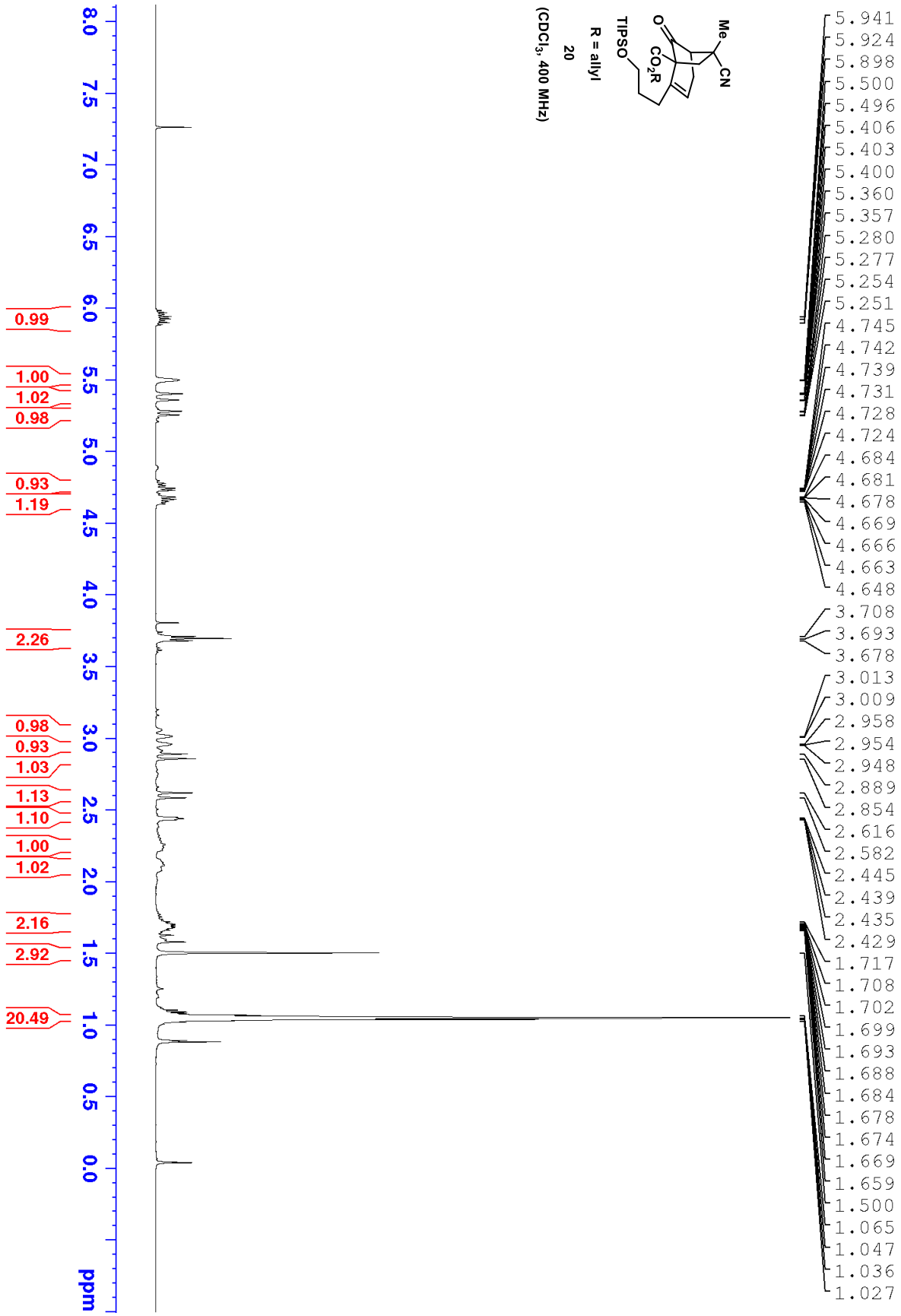

16
(CDCl3, 126 MHz)
MeO2C
O
OTIPS
Me
CN
164.118
158.999
152.369
122.700
101.988
95.914
62.305
51.249
46.932
41.239
40.824
29.214
24.231
21.774
18.021
12.016
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

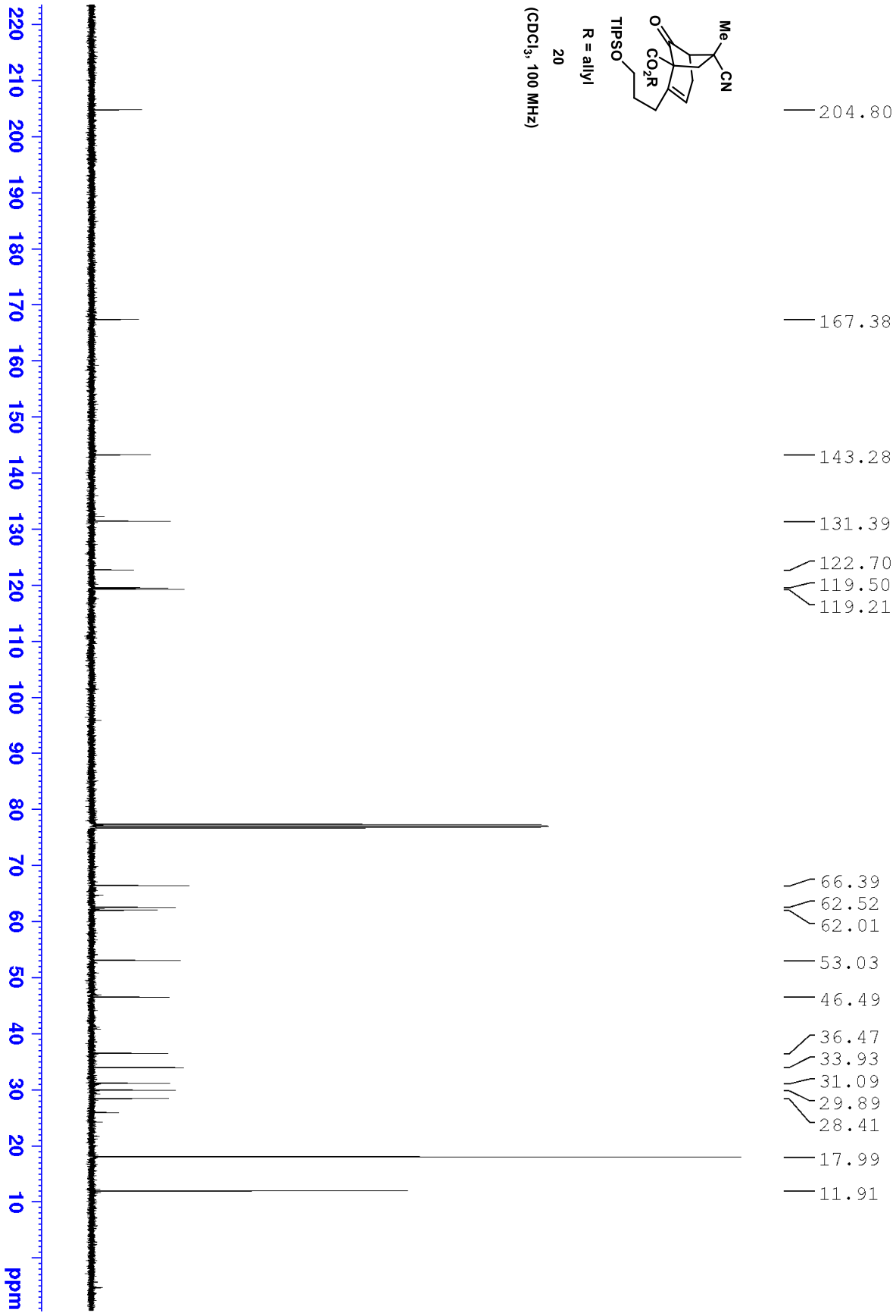

17
(CDCl3, 500 MHz)
TIPSO
CO2Me
O
Me
CN
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
2.81
1.84
1.06
1.04
1.16
1.10
1.12
1.27
1.17
2.05
3.04
20.52
5.500
3.808
3.717
3.705
3.693
3.057
3.022
2.957
2.921
2.884
2.856
2.611
2.583
2.443
2.346
2.243
2.221
2.092
2.077
2.062
2.045
1.759
1.731
1.718
1.706
1.695
1.684
1.673
1.661
1.648
1.635
1.624
1.504
1.071
1.052
1.041

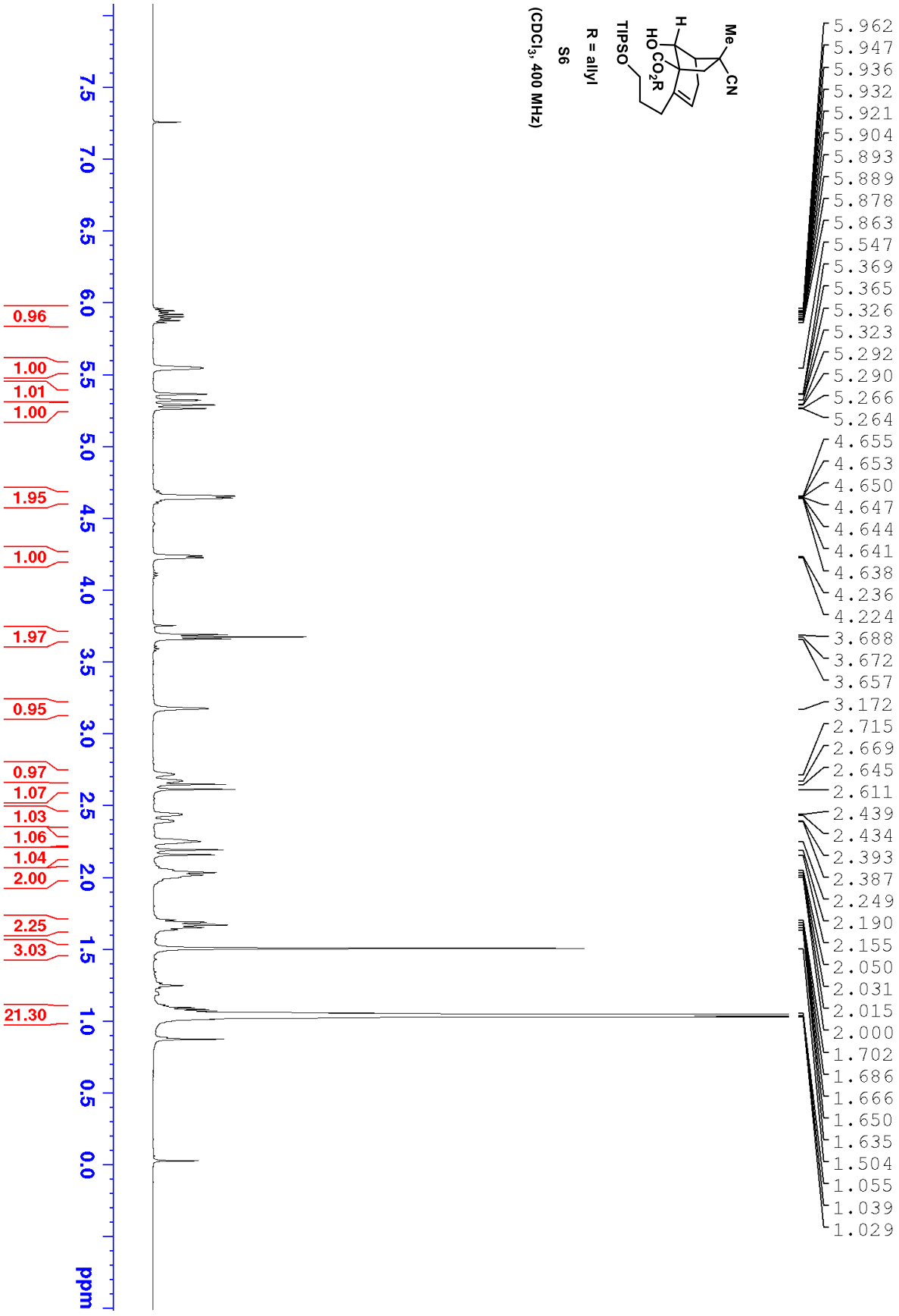

17
(CDCl3, 126 MHz)
TIPSO
CO2Me
O
Me
CN
204.97
168.17
143.36
122.72
119.40
62.53
62.07
53.05
52.61
46.51
36.53
33.95
31.04
29.88
28.44
18.00
11.93
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

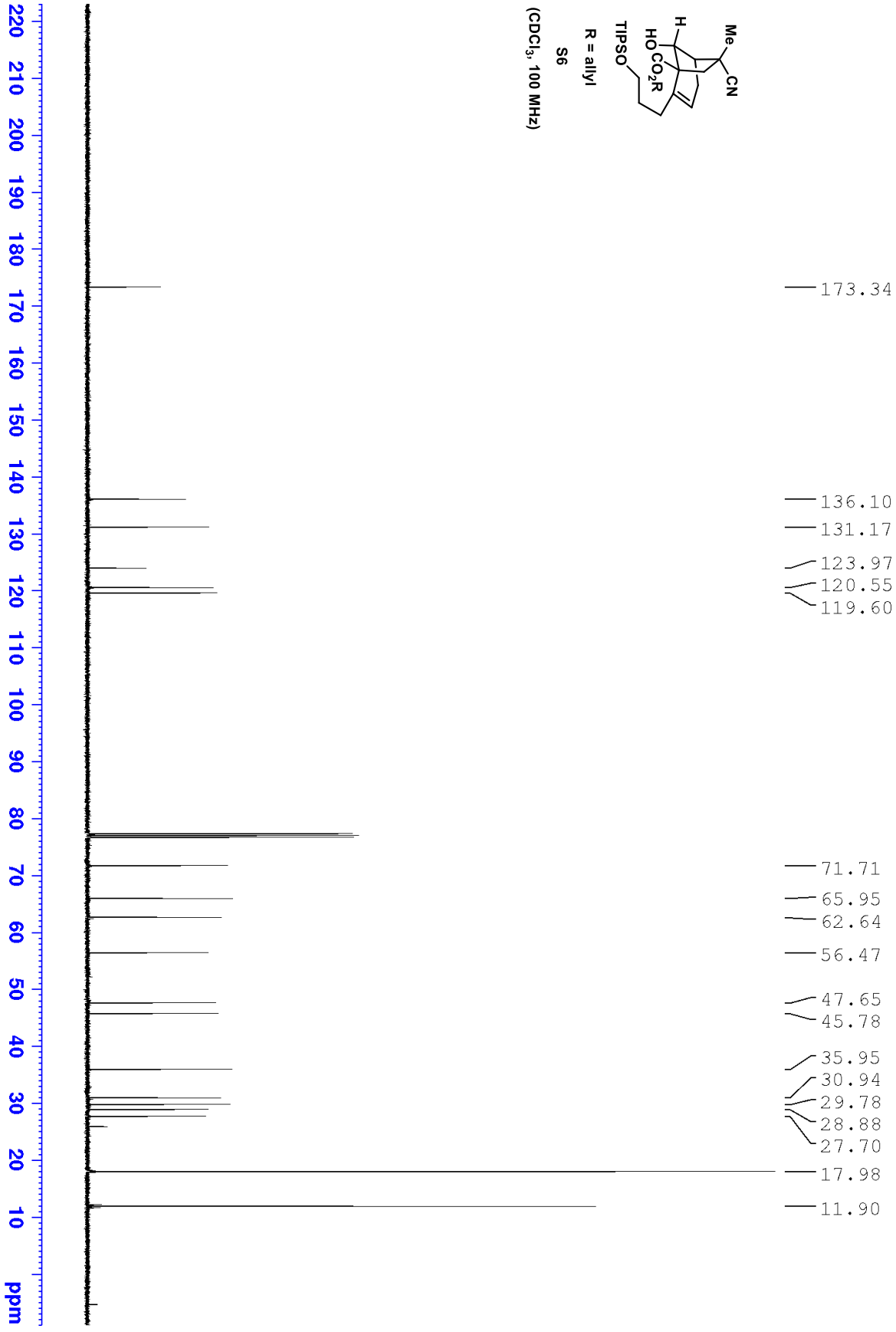

(C6D6, 400 MHz)
18
19
+
TBSO
OTIPS
AllylO2C
Me
CN
OAllyl
O
5.721
5.114
5.110
5.105
5.101
5.071
5.067
5.062
4.985
4.982
4.979
4.975
4.959
4.956
4.952
4.949
4.454
4.440
3.677
3.662
3.651
3.647
3.637
3.622
3.260
3.227
3.223
2.918
2.535
2.531
2.393
2.356
2.228
2.218
2.213
2.196
2.157
2.154
2.148
2.143
2.137
2.130
1.674
1.659
1.654
1.643
1.175
1.106
1.093
1.082
1.074
1.053
0.935
0.927
0.920
0.333
0.287
0.175
0.130
0.93
0.95
0.95
1.88
2.00
0.58
0.75
0.58
0.49
0.47
0.91
1.93
1.03
1.98
1.12
21.43
9.46
3.01
2.98
ppm

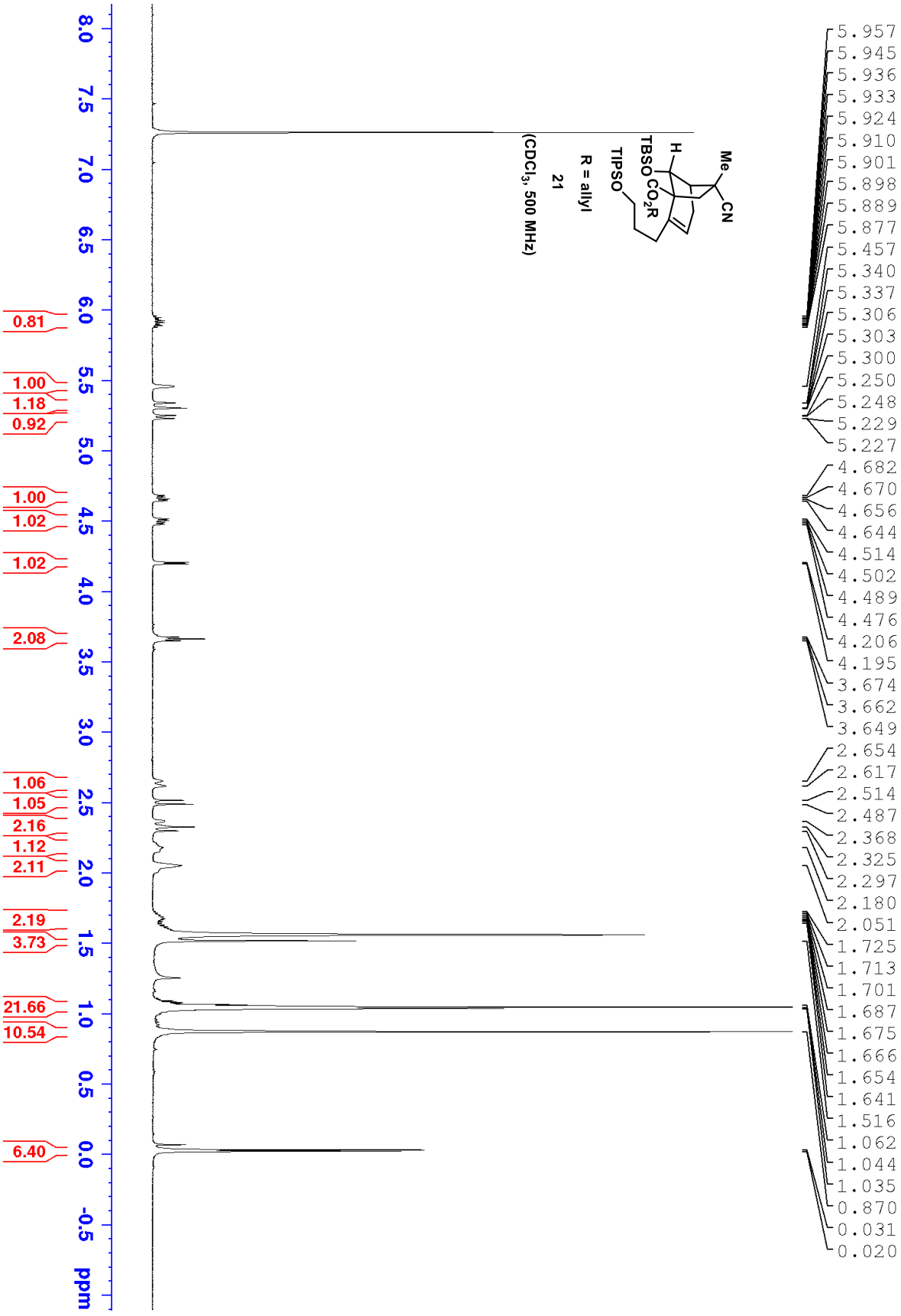

163.70
163.68
163.65
163.10
133.63
133.61
125.94
122.90
118.20
107.53
106.52
83.91
83.66
76.66
76.64
64.90
62.75
57.06
55.21
42.47
42.22
37.16
36.46
33.02
32.83
27.65
26.45
26.43
21.13
20.16
19.28
19.24
18.88
18.85
17.90
16.15
OTIPS
TBSO
Me
CN
AllylO2C
18
+
OTIPS
O
Me
CN
TBSO
OAllyl
19
(C6D6, 100 MHz)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

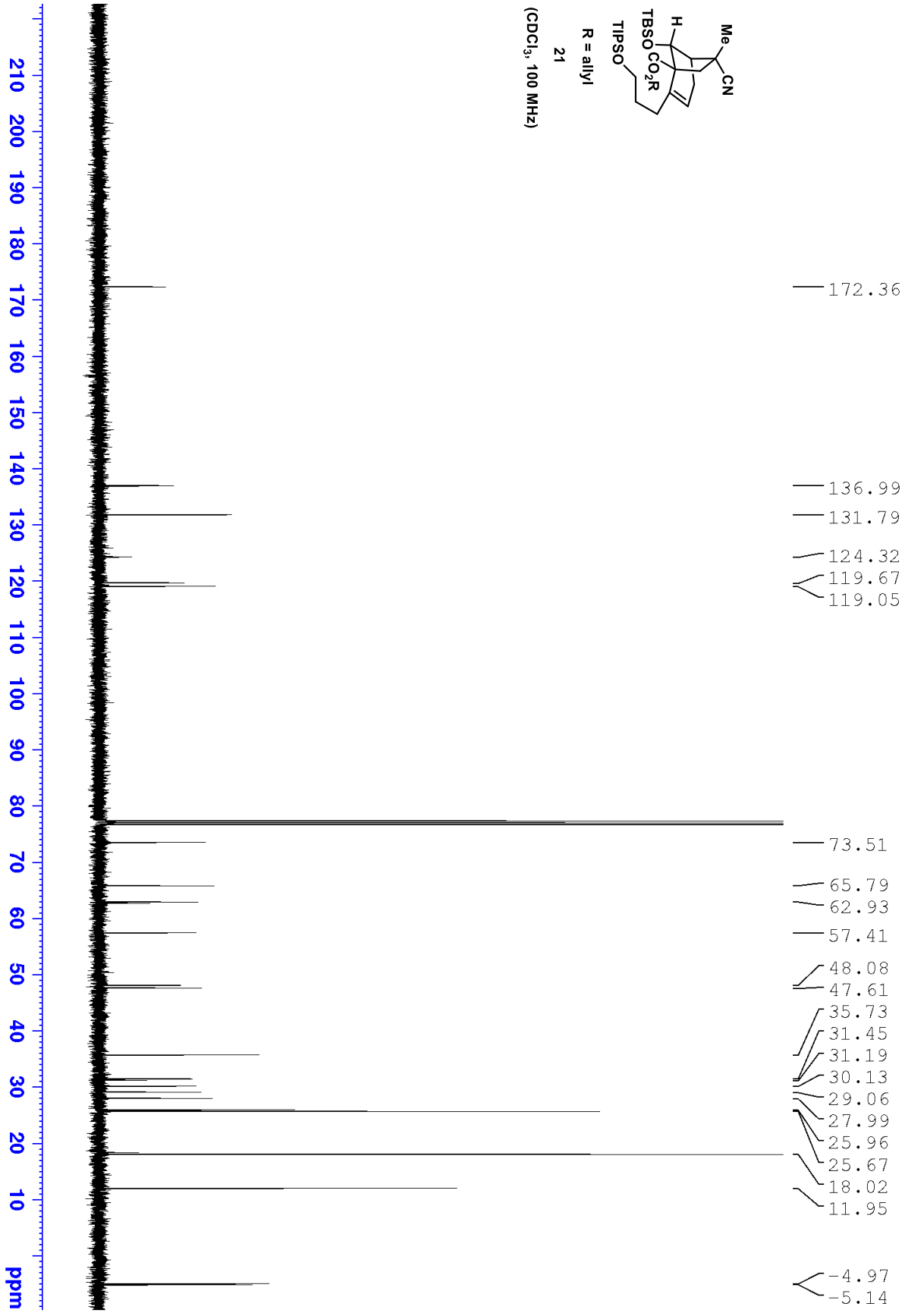

TIPSO
O
CO2R
Me
CN
R = allyl
20
(CDCl3, 400 MHz)
5.941
5.924
5.898
5.500
5.496
5.406
5.403
5.400
5.360
5.357
5.280
5.277
5.254
5.251
4.745
4.742
4.739
4.731
4.728
4.724
4.684
4.681
4.678
4.669
4.666
4.663
4.648
3.708
3.693
3.678
3.013
3.009
2.958
2.954
2.948
2.889
2.854
2.616
2.582
2.445
2.439
2.435
2.429
1.717
1.708
1.702
1.699
1.693
1.688
1.684
1.678
1.674
1.669
1.659
1.500
1.065
1.047
1.036
1.027
0.99
1.00
1.02
0.98
0.93
1.19
2.26
0.98
0.93
1.03
1.13
1.10
1.00
1.02
2.16
2.92
20.49
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

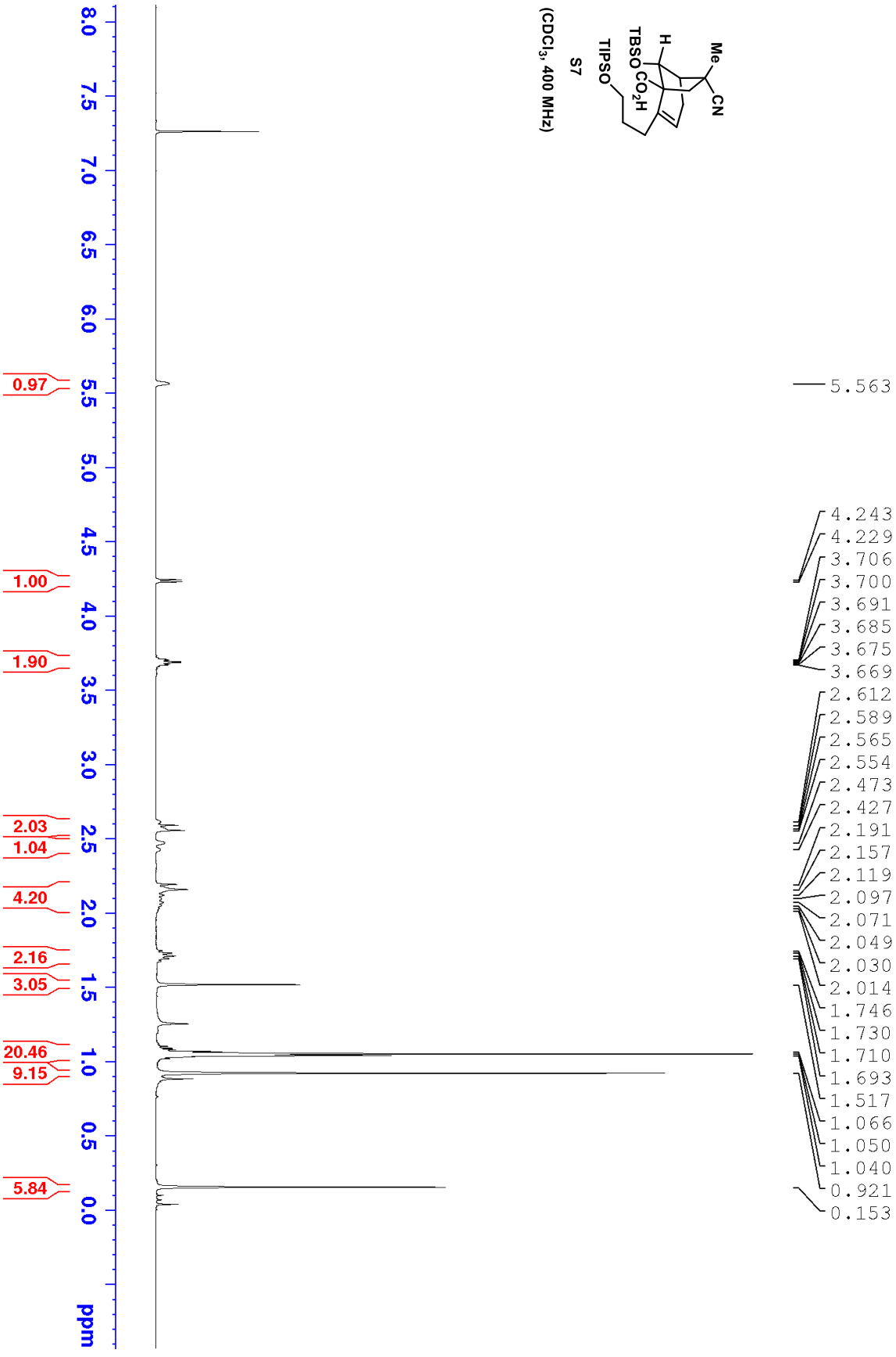

TIPSO
O
CO2R
Me
CN
R = allyl
20
(CDCl3, 100 MHz)
204.80
167.38
143.28
131.39
122.70
119.50
119.21
66.39
62.52
62.01
53.03
46.49
36.47
33.93
31.09
29.89
28.41
17.99
11.91
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

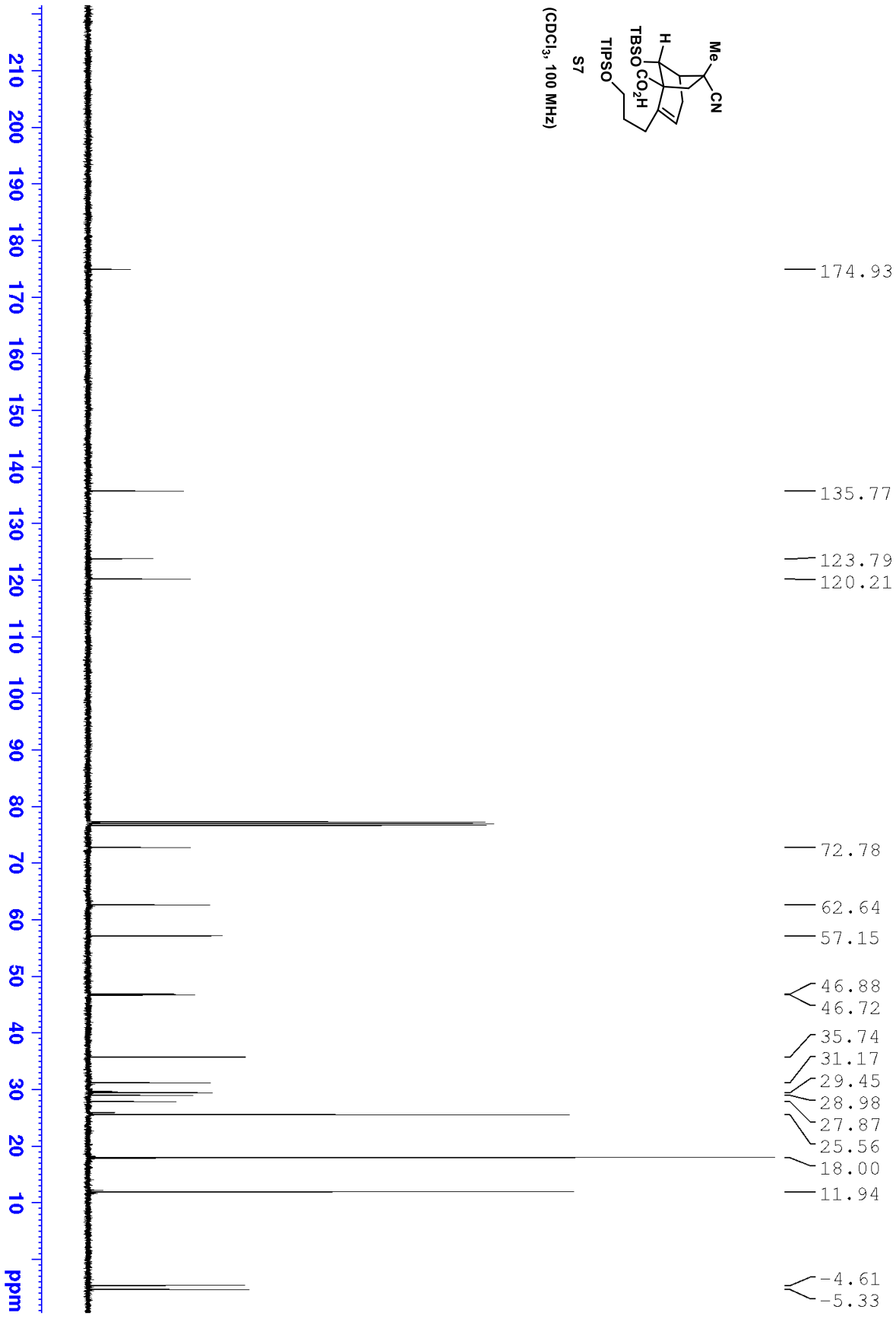

S6
R = allyl
(CDCl3, 400 MHz)
TIPSO
HO2CR
H
Me
CN
5.962
5.947
5.936
5.932
5.921
5.904
5.893
5.889
5.878
5.863
5.547
5.369
5.365
5.326
5.323
5.292
5.290
5.266
5.264
4.655
4.653
4.650
4.647
4.644
4.641
4.638
4.236
4.224
3.688
3.672
3.657
3.172
2.715
2.669
2.645
2.611
2.439
2.434
2.393
2.387
2.249
2.190
2.155
2.050
2.031
2.015
2.000
1.702
1.686
1.666
1.650
1.635
1.504
1.055
1.039
1.029
0.96
1.00
1.01
1.00
1.95
1.00
1.97
0.95
0.97
1.07
1.03
1.06
1.04
2.00
2.25
3.03
21.30
ppm

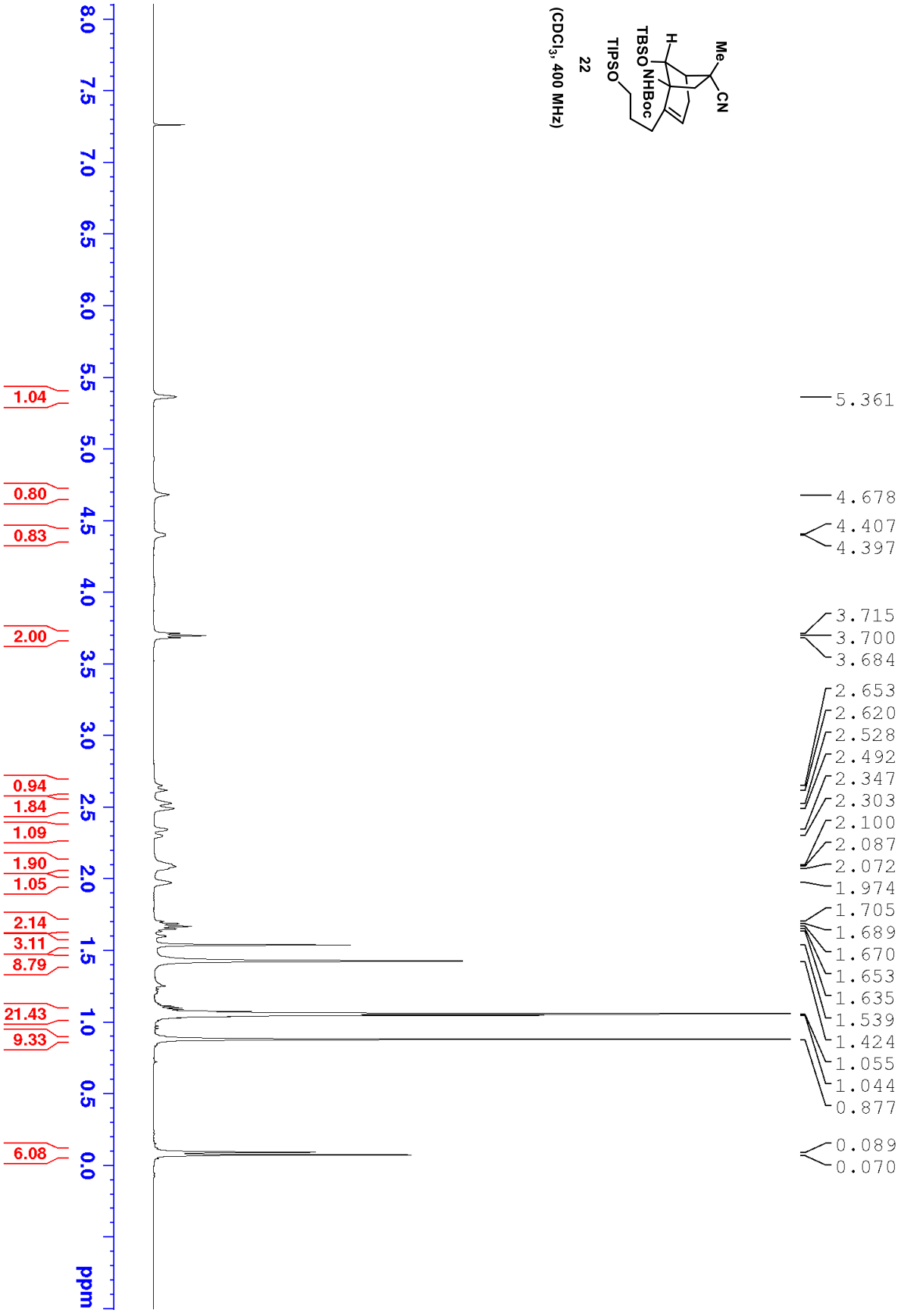

Me
CN
H
HO
CO2R
TIPSO
R = allyl
S6
(CDCl3, 100 MHz)
173.34
136.10
131.17
123.97
120.55
119.60
71.71
65.95
62.64
56.47
47.65
45.78
35.95
30.94
29.78
28.88
27.70
17.98
11.90
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

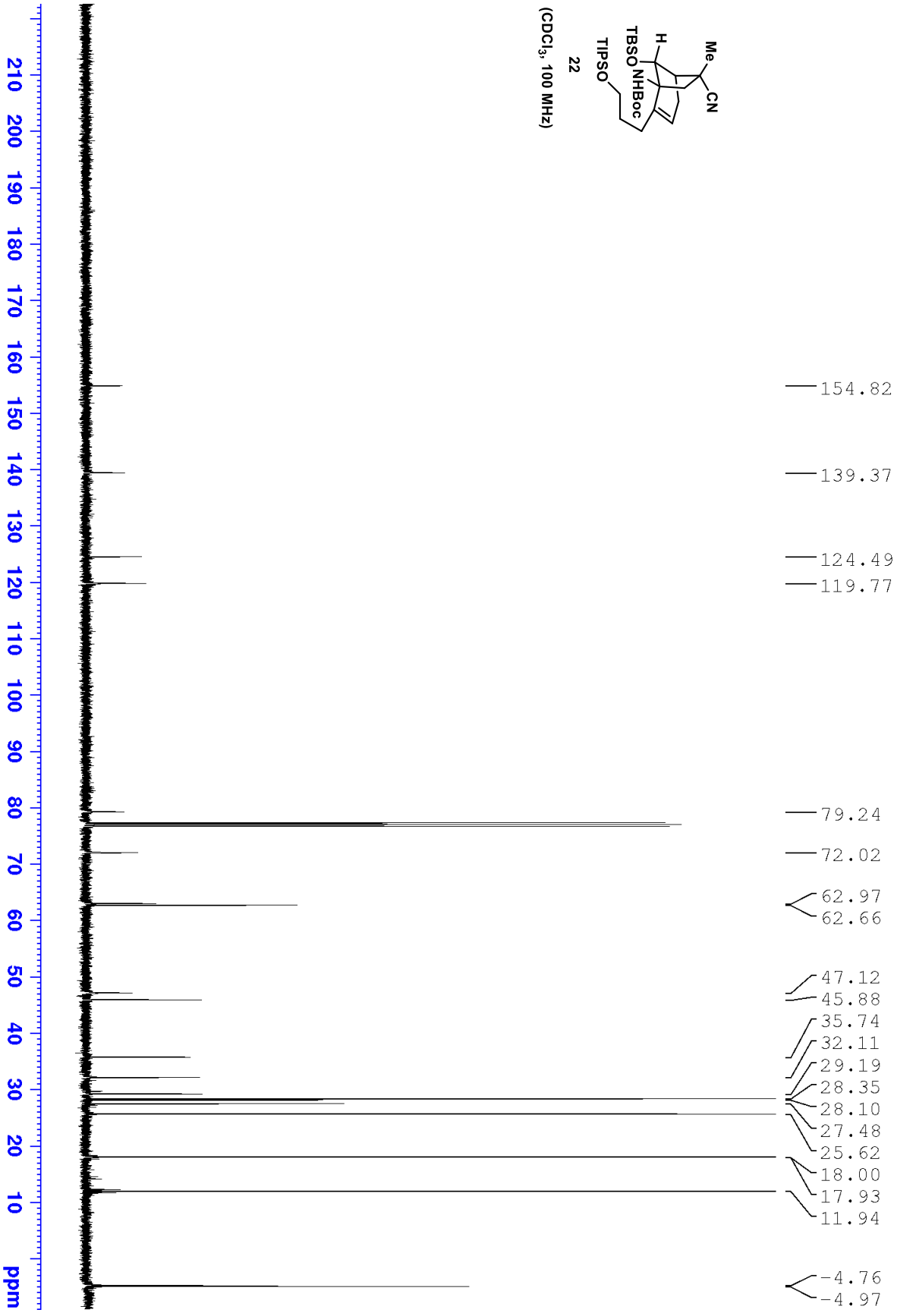

21
R = allyl
(CDCl3, 500 MHz)
TIPSO
TBSO
CO2R
H
Me
CN
0.81
1.00
1.18
0.92
1.00
1.02
1.02
2.08
1.06
1.05
2.16
1.12
2.11
2.19
3.73
21.66
10.54
6.40
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
ppm
5.957
5.945
5.936
5.933
5.924
5.910
5.901
5.898
5.889
5.877
5.457
5.340
5.337
5.306
5.303
5.300
5.250
5.248
5.229
5.227
4.682
4.670
4.656
4.644
4.514
4.502
4.489
4.476
4.206
4.195
3.674
3.662
3.649
2.654
2.617
2.514
2.487
2.368
2.325
2.297
2.180
2.051
1.725
1.713
1.701
1.687
1.675
1.666
1.654
1.641
1.516
1.062
1.044
1.035
0.870
0.031
0.020

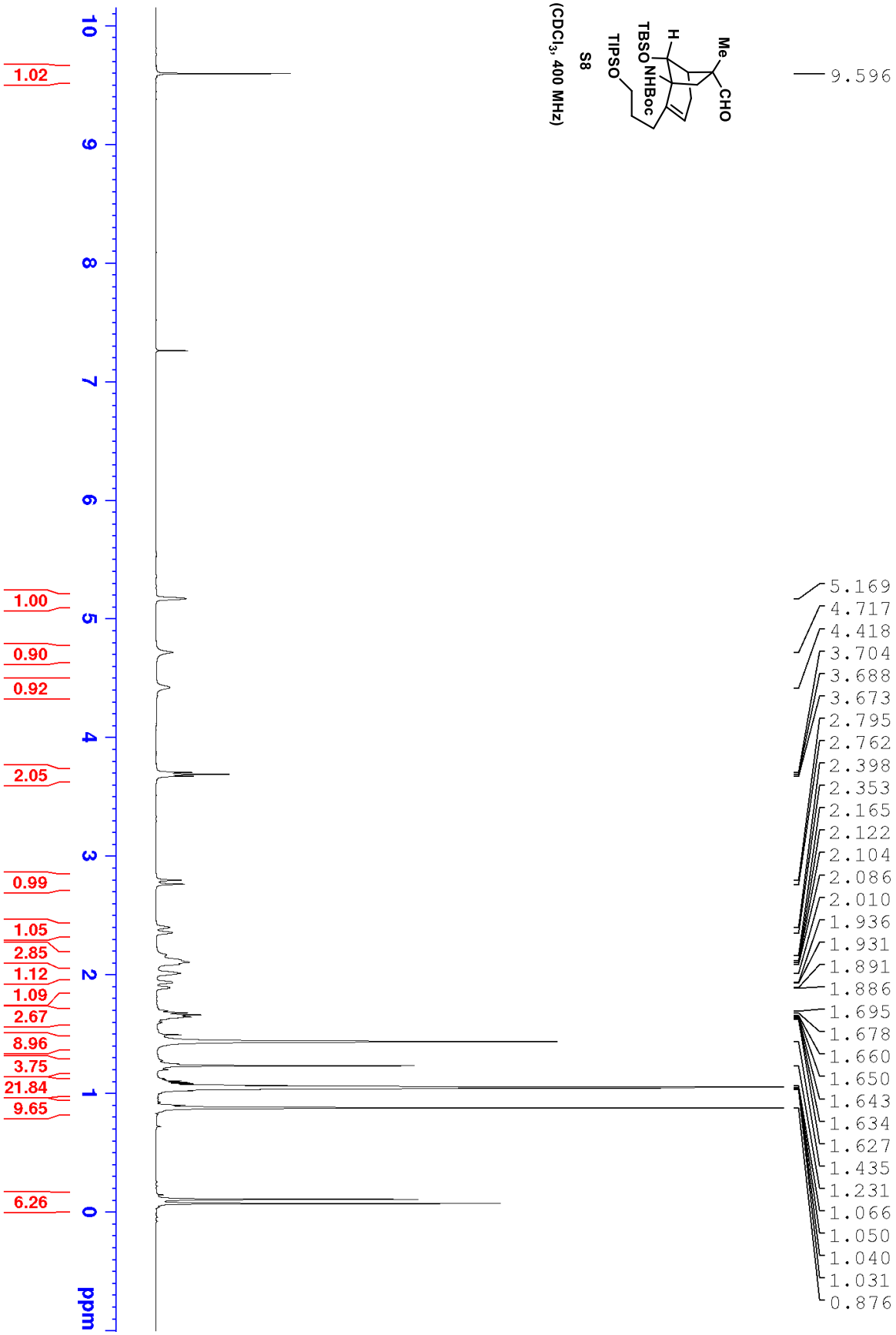

TIPSO
TBSO
CO2R
H
Me
CN
R = allyl
21
(CDCl3, 100 MHz)
172.36
136.99
131.79
124.32
119.67
119.05
73.51
65.79
62.93
57.41
48.08
47.61
35.73
31.45
31.19
30.13
29.06
27.99
25.96
25.67
18.02
11.95
-4.97
-5.14
ppm

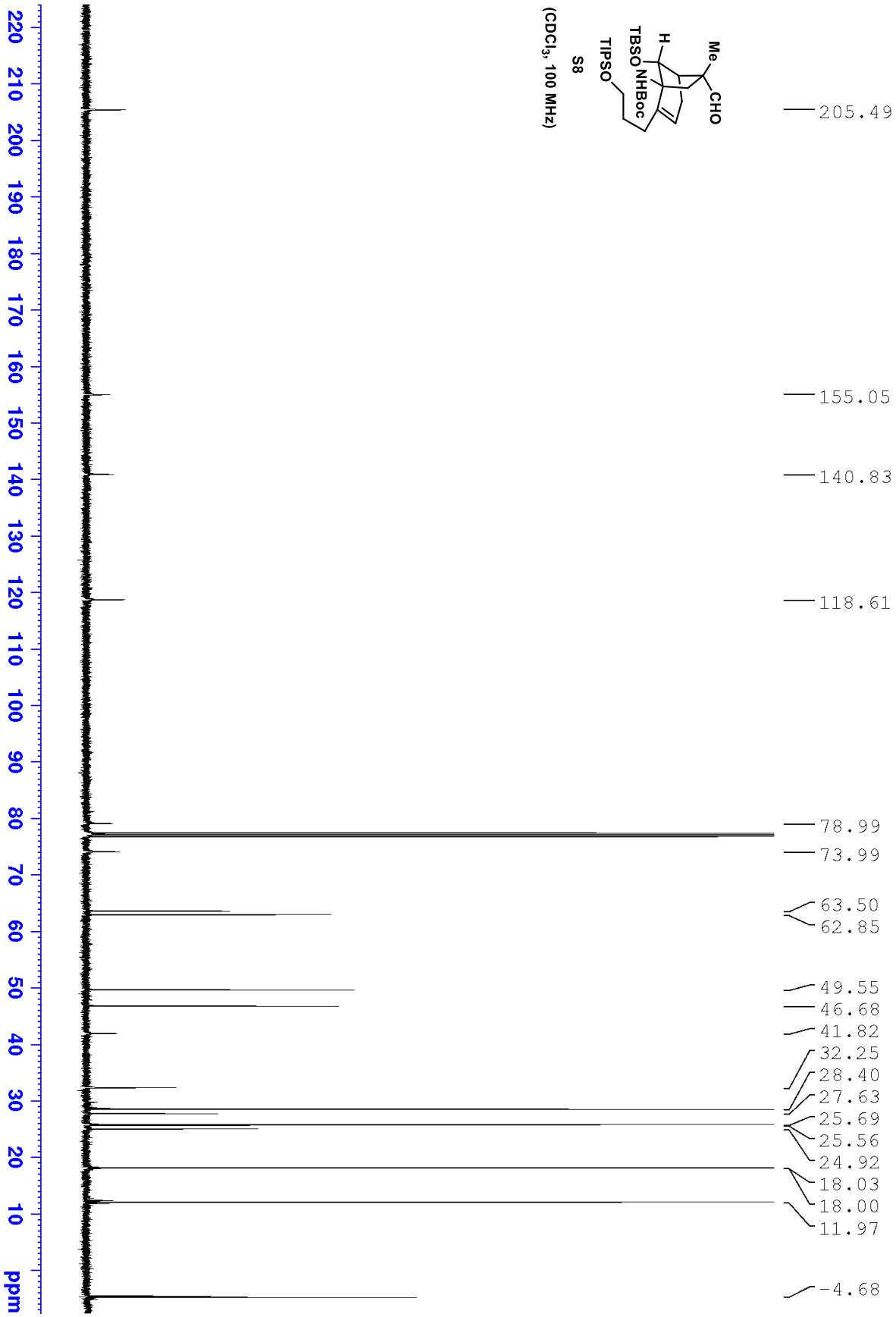

S7
(CDCl3, 400 MHz)
TIPSO
TBSO
CO2H
H
Me
CN
5.563
4.243
4.229
3.706
3.700
3.691
3.685
3.675
3.669
2.612
2.589
2.565
2.554
2.473
2.427
2.191
2.157
2.119
2.097
2.071
2.049
2.030
2.014
1.746
1.730
1.710
1.693
1.517
1.066
1.050
1.040
0.921
0.153
0.97
1.00
1.90
2.03
1.04
4.20
2.16
3.05
20.46
9.15
5.84
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

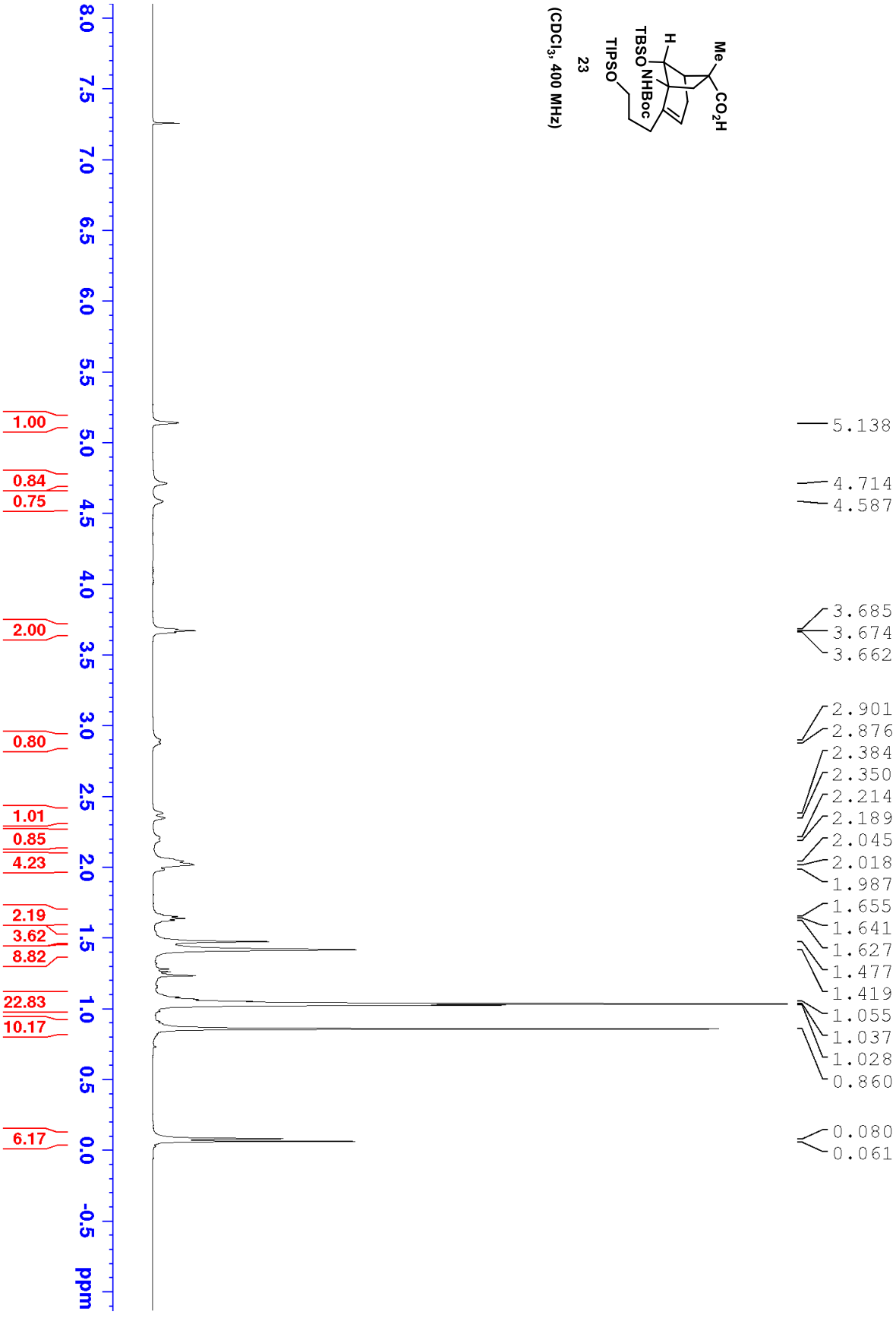

S7
(CDCl3, 100 MHz)
TIPSO
TBSO
CO2H
H
Me
CN
174.93
135.77
123.79
120.21
72.78
62.64
57.15
46.88
46.72
35.74
31.17
29.45
28.98
27.87
25.56
18.00
11.94
-4.61
-5.33
ppm

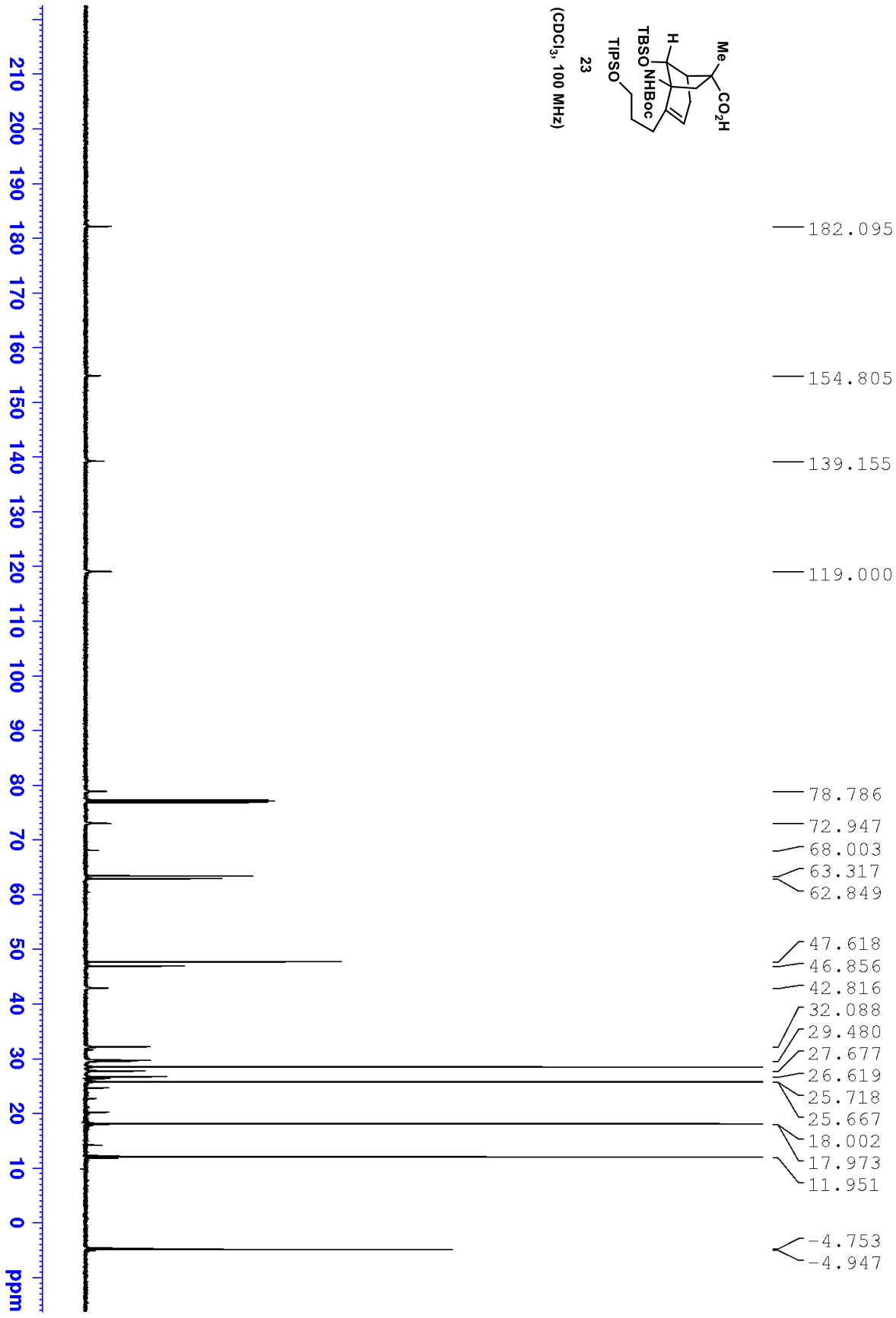

22
(CDCl3, 400 MHz)
TIPSO
TBSO
NHBoc
H
Me
CN
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.04
0.80
0.83
2.00
0.94
1.84
1.09
1.90
1.05
2.14
3.11
8.79
21.43
9.33
6.08
5.361
4.678
4.407
4.397
3.715
3.700
3.684
2.653
2.620
2.528
2.492
2.347
2.303
2.100
2.087
2.072
1.974
1.705
1.689
1.670
1.653
1.635
1.539
1.424
1.055
1.044
0.877
0.089
0.070

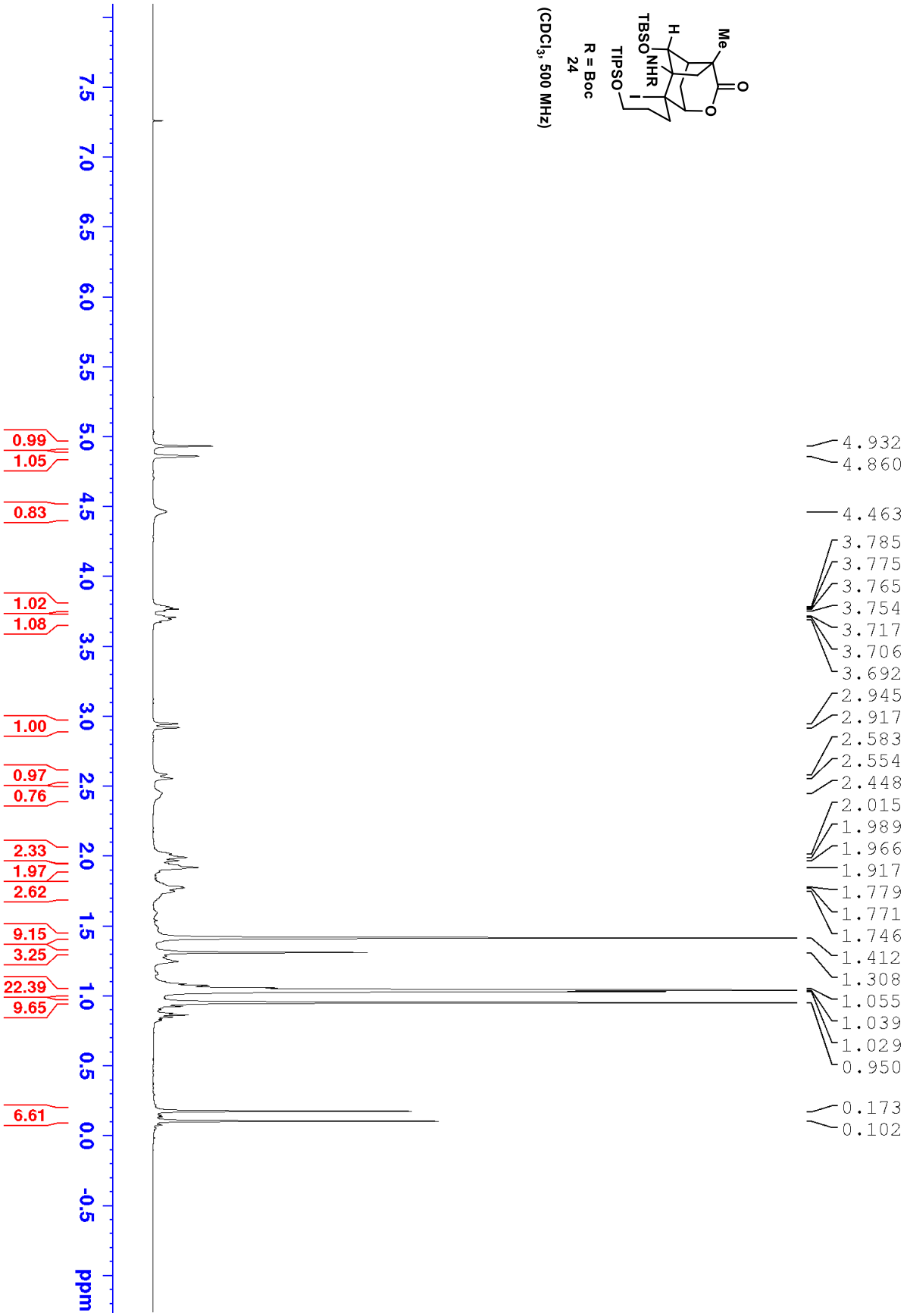

22
(CDCl3, 100 MHz)
TIPSO
TBSO
NHBoc
H
Me
CN
154.82
139.37
124.49
119.77
79.24
72.02
62.97
62.66
47.12
45.88
35.74
32.11
29.19
28.35
28.10
27.48
25.62
18.00
17.93
11.94
-4.76
-4.97
ppm

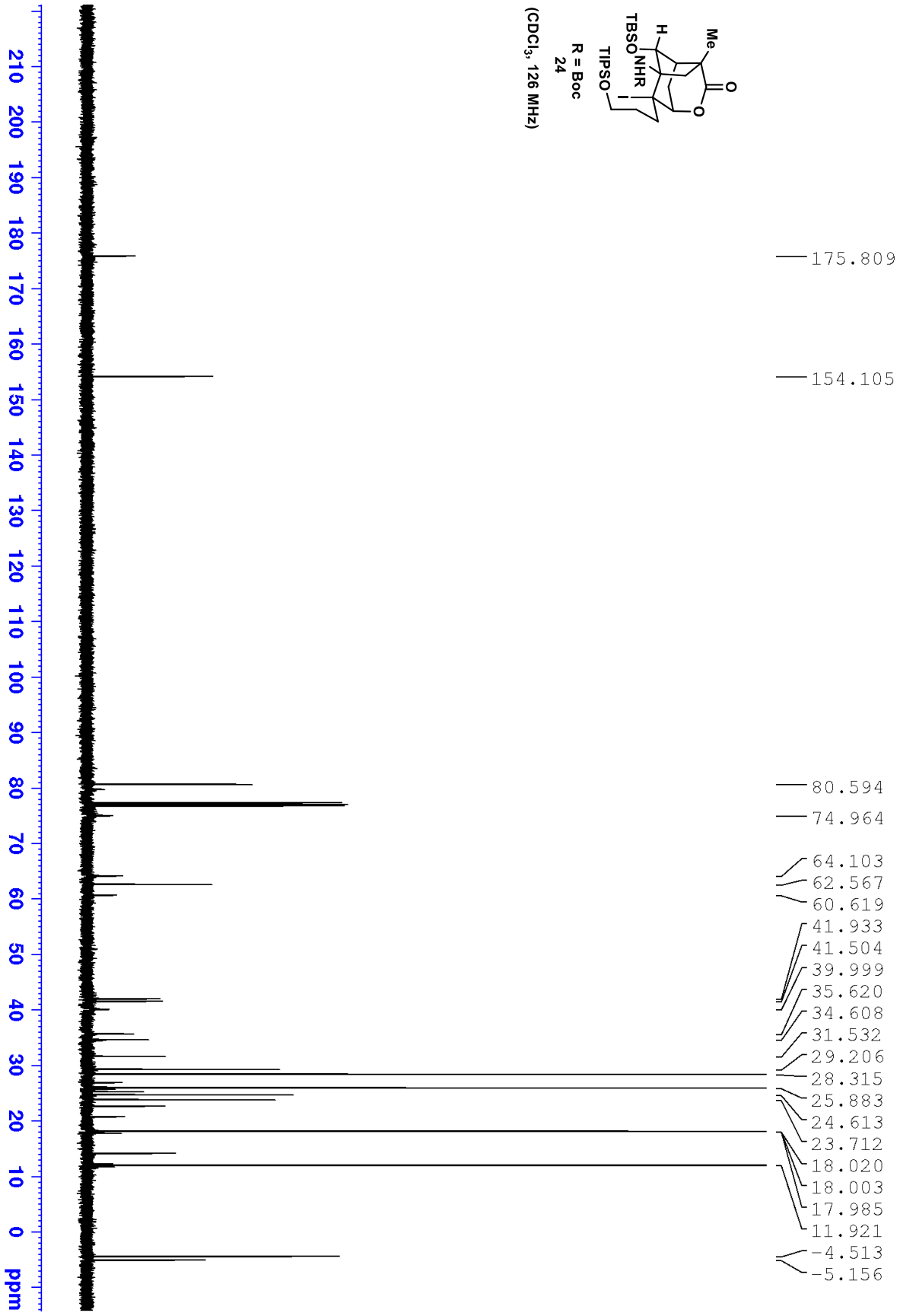

S8
(CDCl3, 400 MHz)
TIPSO
TBSO
NHBoc
H
Me
CHO
9.596
5.169
4.717
4.418
3.704
3.688
3.673
2.795
2.762
2.398
2.353
2.165
2.122
2.104
2.086
2.010
1.936
1.931
1.891
1.886
1.695
1.678
1.660
1.650
1.643
1.634
1.627
1.435
1.231
1.066
1.050
1.040
1.031
0.876
1.02
1.00
0.90
0.92
2.05
0.99
1.05
2.85
1.12
1.09
2.67
8.96
3.75
21.84
9.65
6.26
ppm

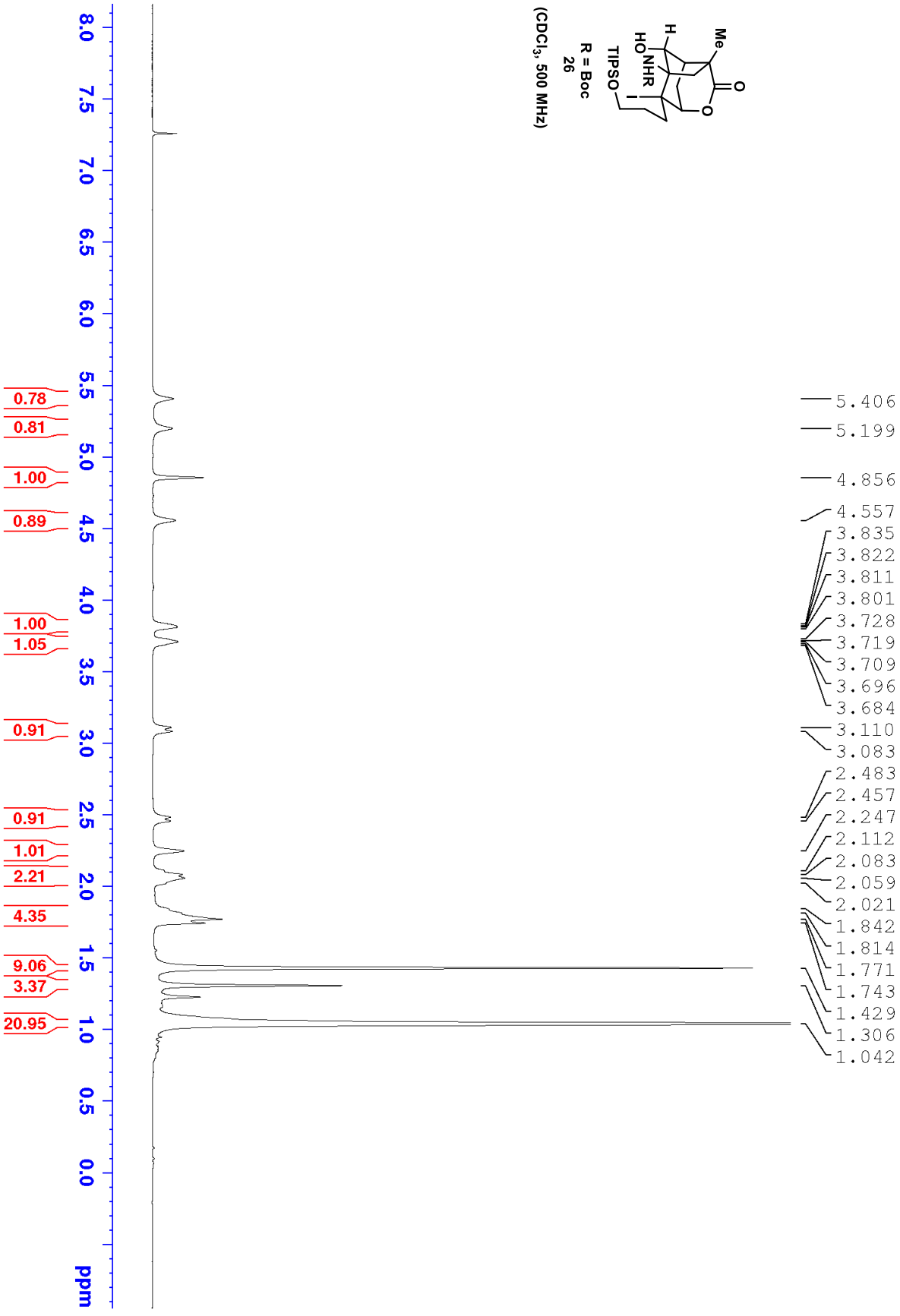

S8
(CDCl3, 100 MHz)
TIPSO
TBSO
NHBoc
H
Me
CHO
205.49
155.05
140.83
118.61
78.99
73.99
63.50
62.85
49.55
46.68
41.82
32.25
28.40
27.63
25.69
25.56
24.92
18.03
18.00
11.97
-4.68
ppm

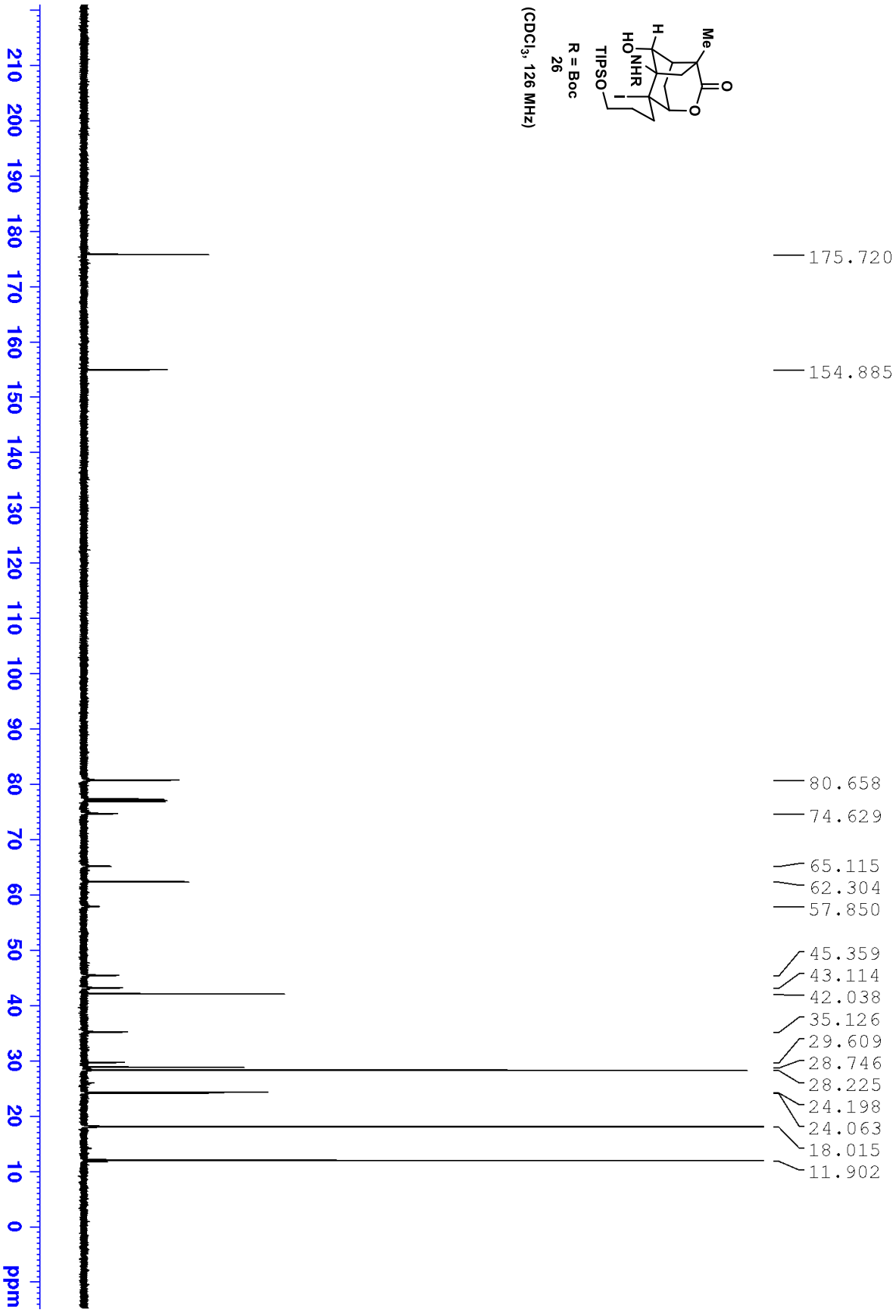

23
(CDCl3, 400 MHz)
TIPSO
TBSO
NHBoc
H
Me
CO2H
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
ppm
1.00
0.84
0.75
2.00
0.80
1.01
0.85
4.23
2.19
3.62
8.82
22.83
10.17
6.17
5.138
4.714
4.587
3.685
3.674
3.662
2.901
2.876
2.384
2.350
2.214
2.189
2.045
2.018
1.987
1.655
1.641
1.627
1.477
1.419
1.055
1.037
1.028
0.860
0.080
0.061

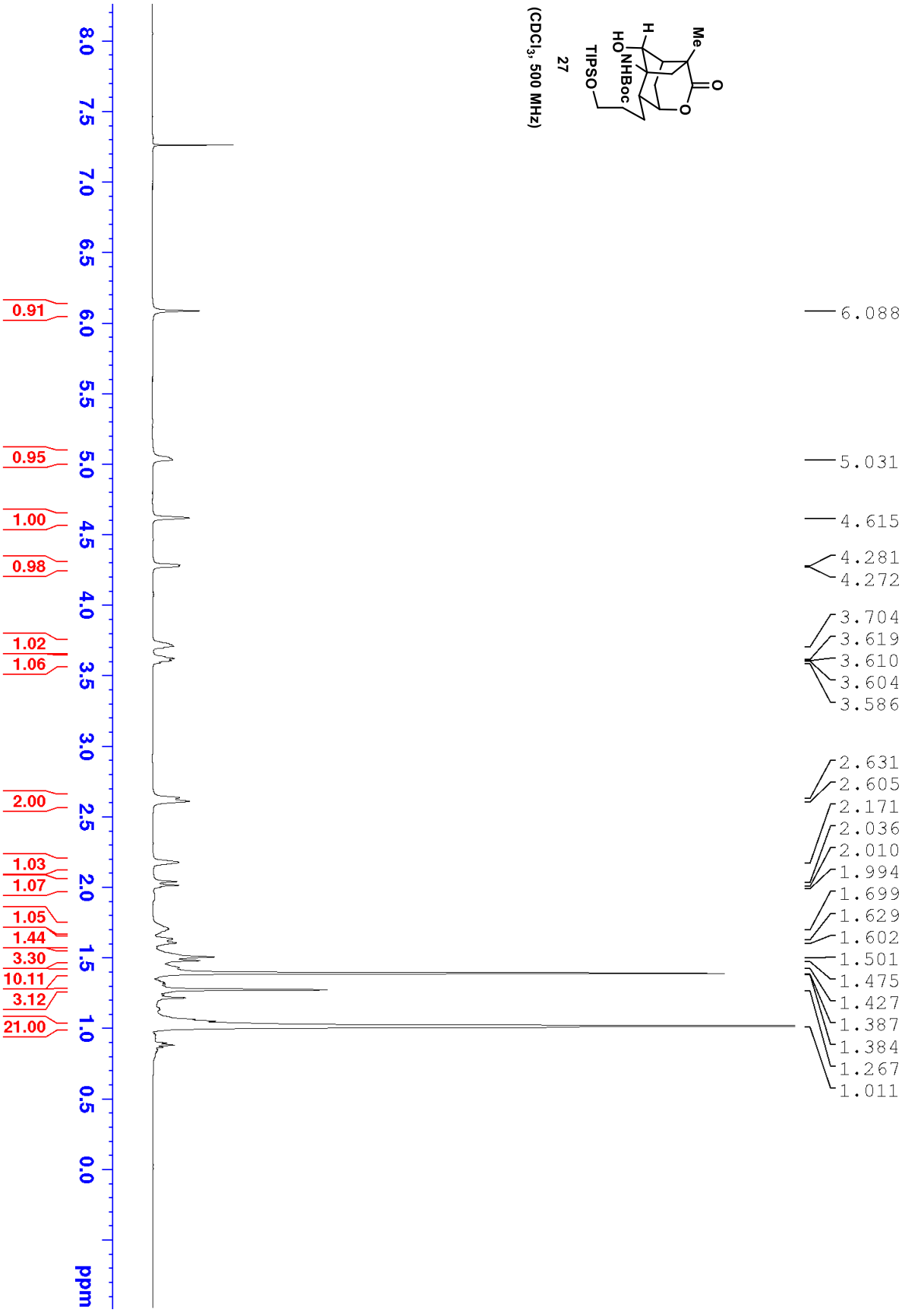

23
(CDCl3, 100 MHz)
TIPSO
TBSO
NHBoc
H
Me
CO2H
182.095
154.805
139.155
119.000
78.786
72.947
68.003
63.317
62.849
47.618
46.856
42.816
32.088
29.480
27.677
26.619
25.718
25.667
18.002
17.973
11.951
-4.753
-4.947
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

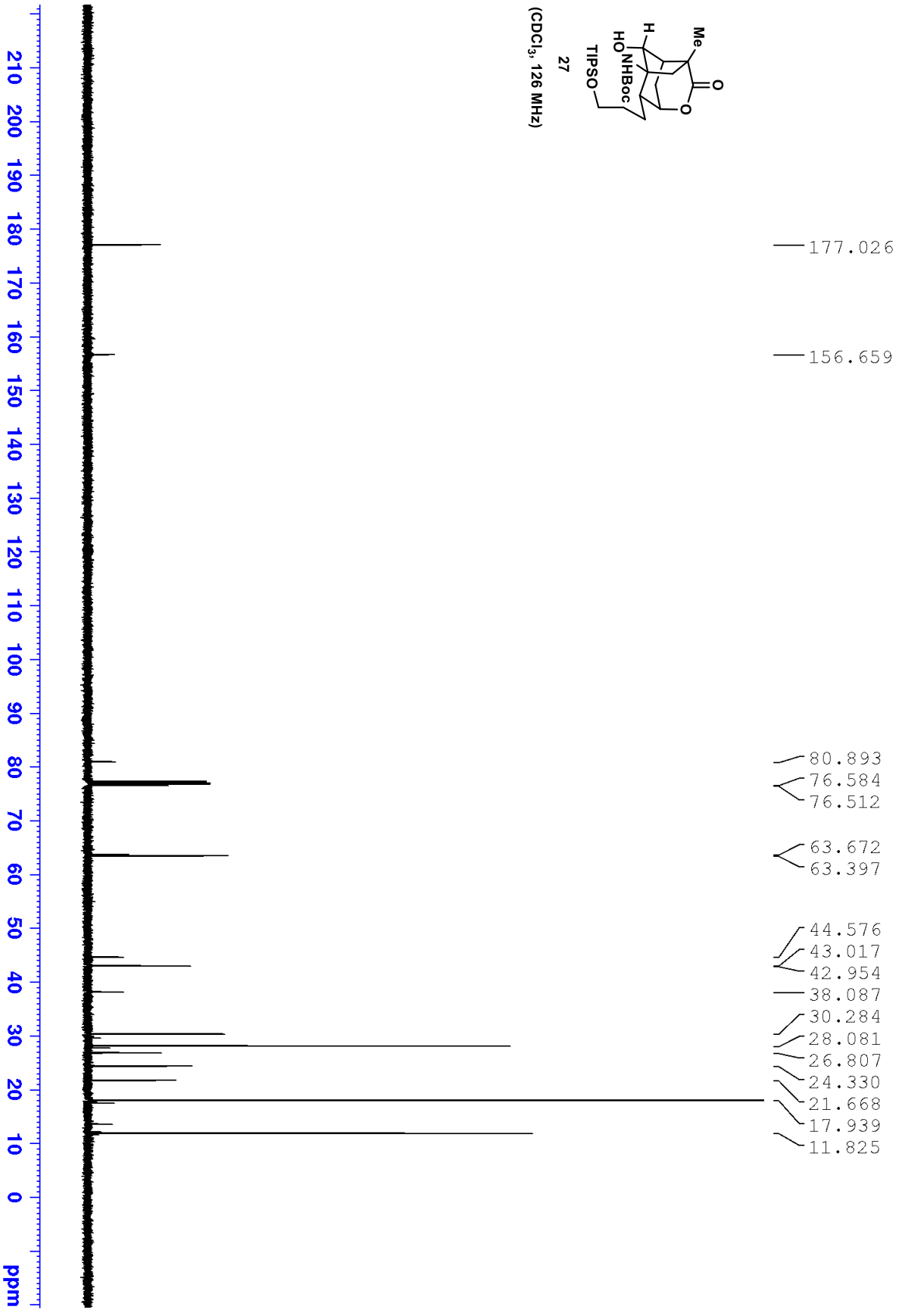

24
R = Boc
(CDCl3, 500 MHz)
TIPSO
TBSO
NHR
H
Me
O
O
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
ppm
0.99
1.05
0.83
1.02
1.08
1.00
0.97
0.76
2.33
1.97
2.62
9.15
3.25
22.39
9.65
6.61
4.932
4.860
4.463
3.785
3.775
3.765
3.754
3.717
3.706
3.692
2.945
2.917
2.583
2.554
2.448
2.015
1.989
1.966
1.917
1.779
1.771
1.746
1.412
1.308
1.055
1.039
1.029
0.950
0.173
0.102

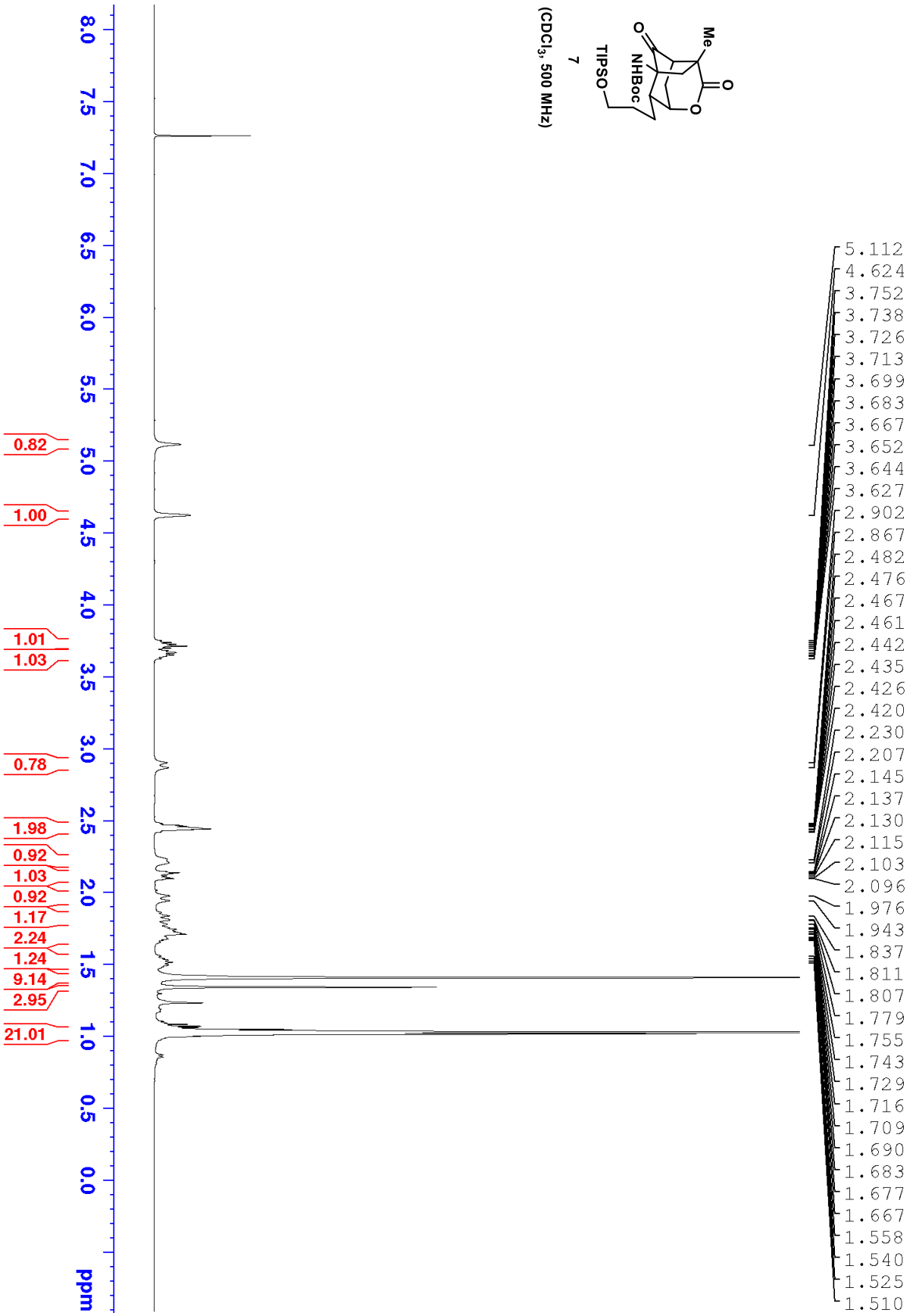

R = Boc
24
(CDCl3, 126 MHz)
TBSO
NHR
H
Me
TIPSO
O
O
175.809
154.105
80.594
74.964
64.103
62.567
60.619
41.933
41.504
39.999
35.620
34.608
31.532
29.206
28.315
25.883
24.613
23.712
18.020
18.003
17.985
11.921
-4.513
-5.156
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

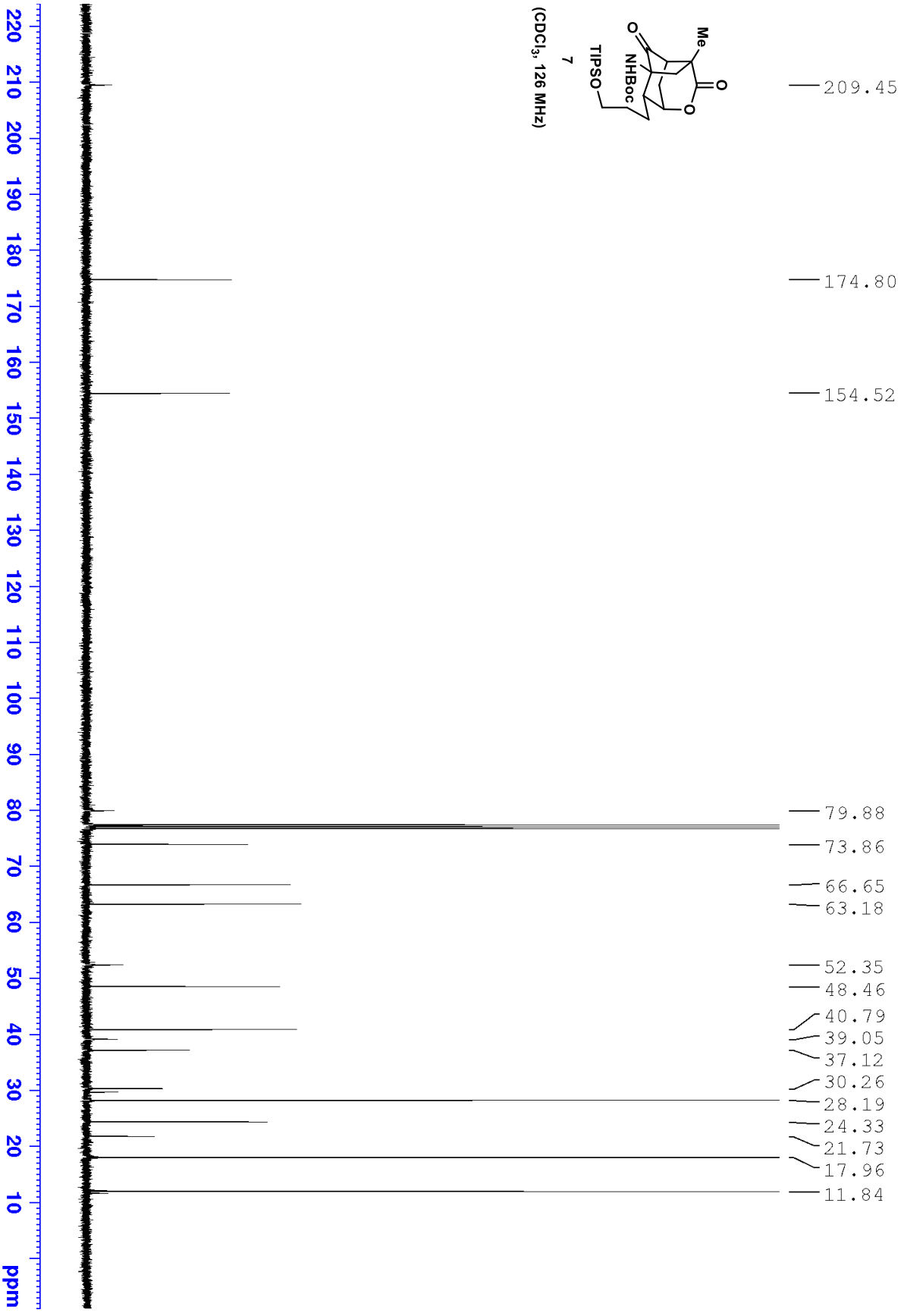

26
R = Boc
(CDCl3, 500 MHz)
TIPSO
HO
NHR
H
Me
O
O
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.78
0.81
1.00
0.89
1.00
1.05
0.91
0.91
1.01
2.21
4.35
9.06
3.37
20.95
5.406
5.199
4.856
4.557
3.835
3.822
3.811
3.801
3.728
3.719
3.709
3.696
3.684
3.110
3.083
2.483
2.457
2.247
2.112
2.083
2.059
2.021
1.842
1.814
1.771
1.743
1.429
1.306
1.042

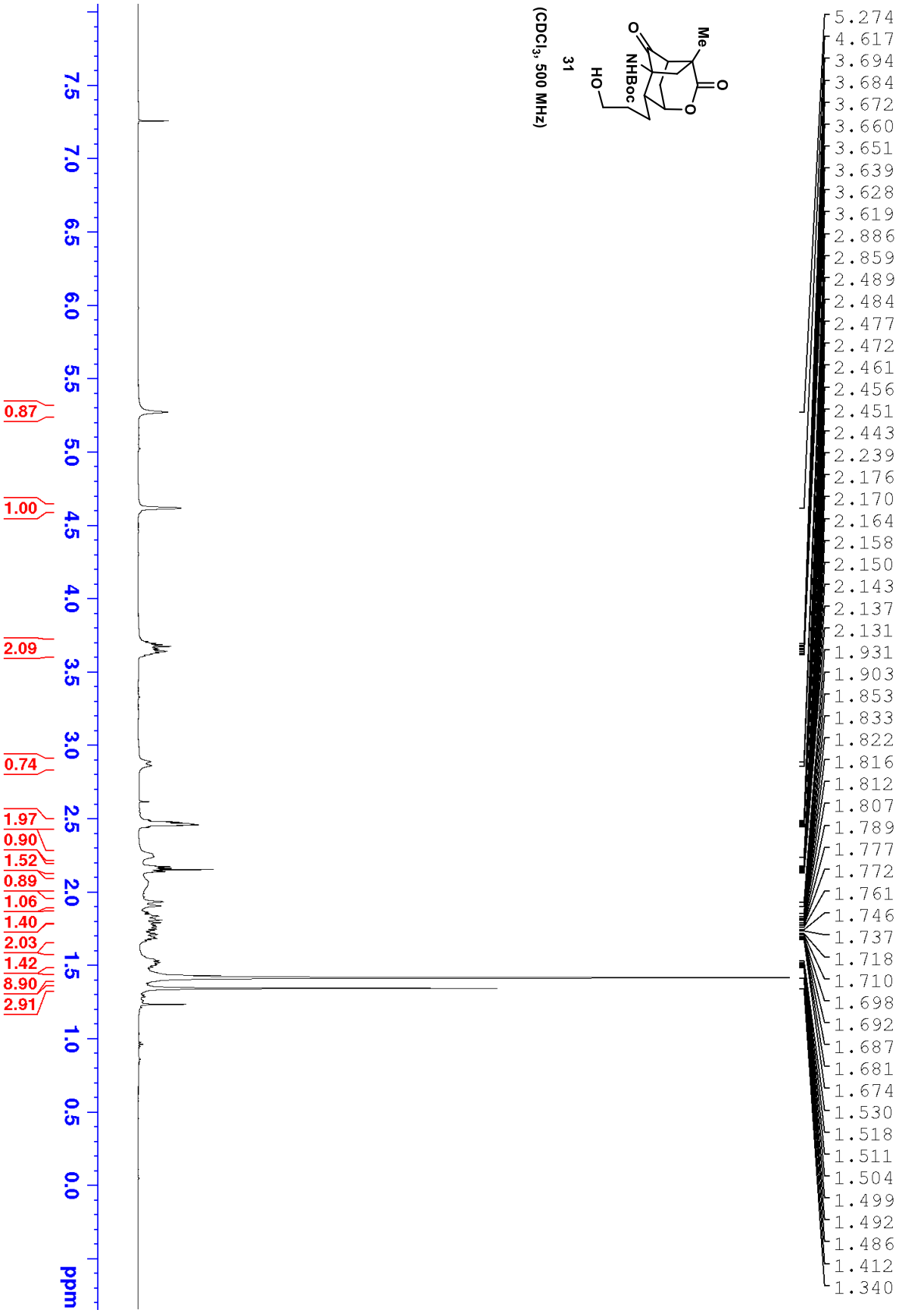

26
R = Boc
(CDCl3, 126 MHz)
TIPSO
HO
NHR
H
Me
O
O
175.720
154.885
80.658
74.629
65.115
62.304
57.850
45.359
43.114
42.038
35.126
29.609
28.746
28.225
24.198
24.063
18.015
11.902
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

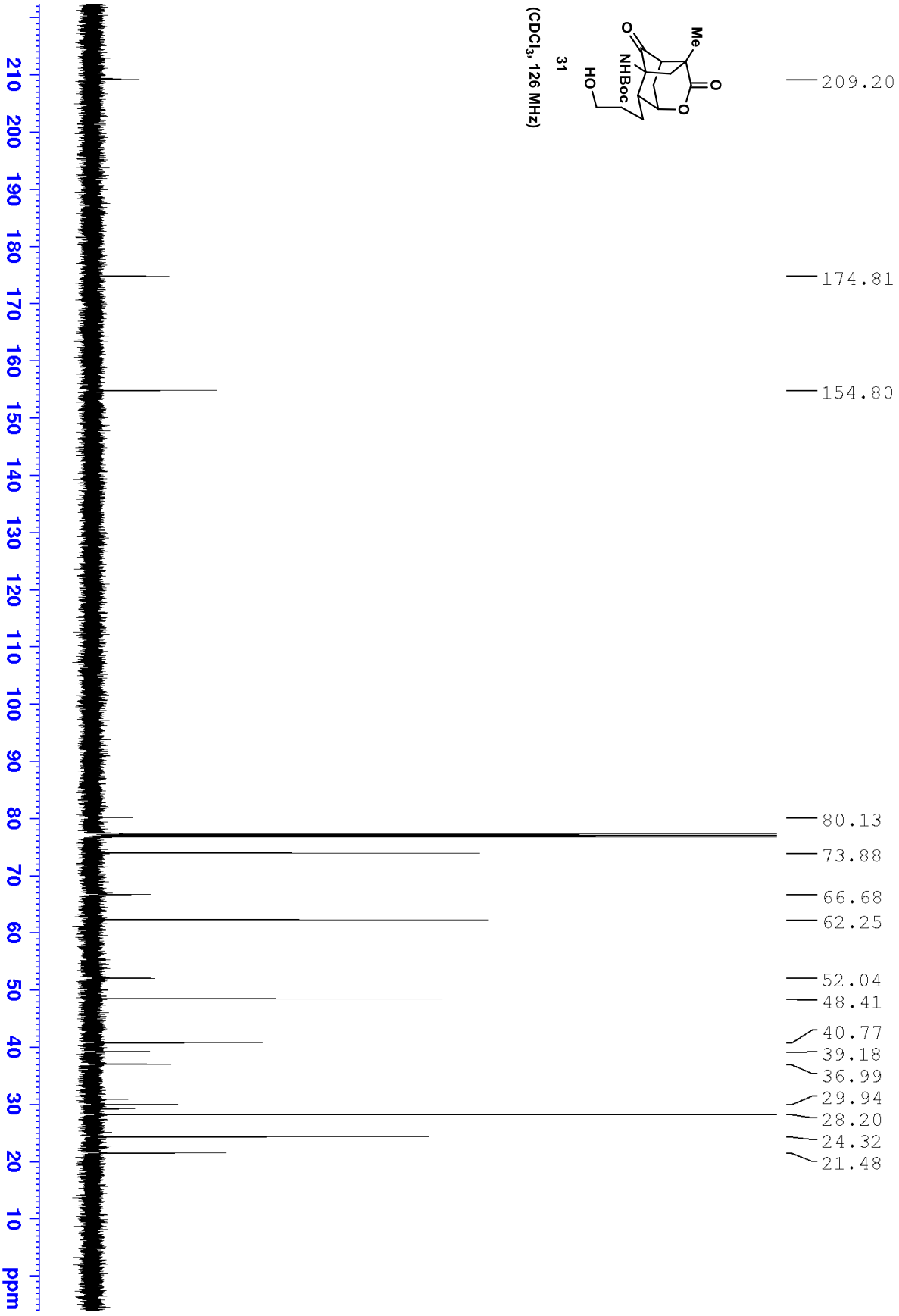

27
(CDCl3, 500 MHz)
TIPSO
HO
NHBoc
H
Me
O
O
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.91
0.95
1.00
0.98
1.02
1.06
2.00
1.03
1.07
1.05
1.44
3.30
10.11
3.12
21.00
6.088
5.031
4.615
4.281
4.272
3.704
3.619
3.610
3.604
3.586
2.631
2.605
2.171
2.036
2.010
1.994
1.699
1.629
1.602
1.501
1.475
1.427
1.387
1.384
1.267
1.011

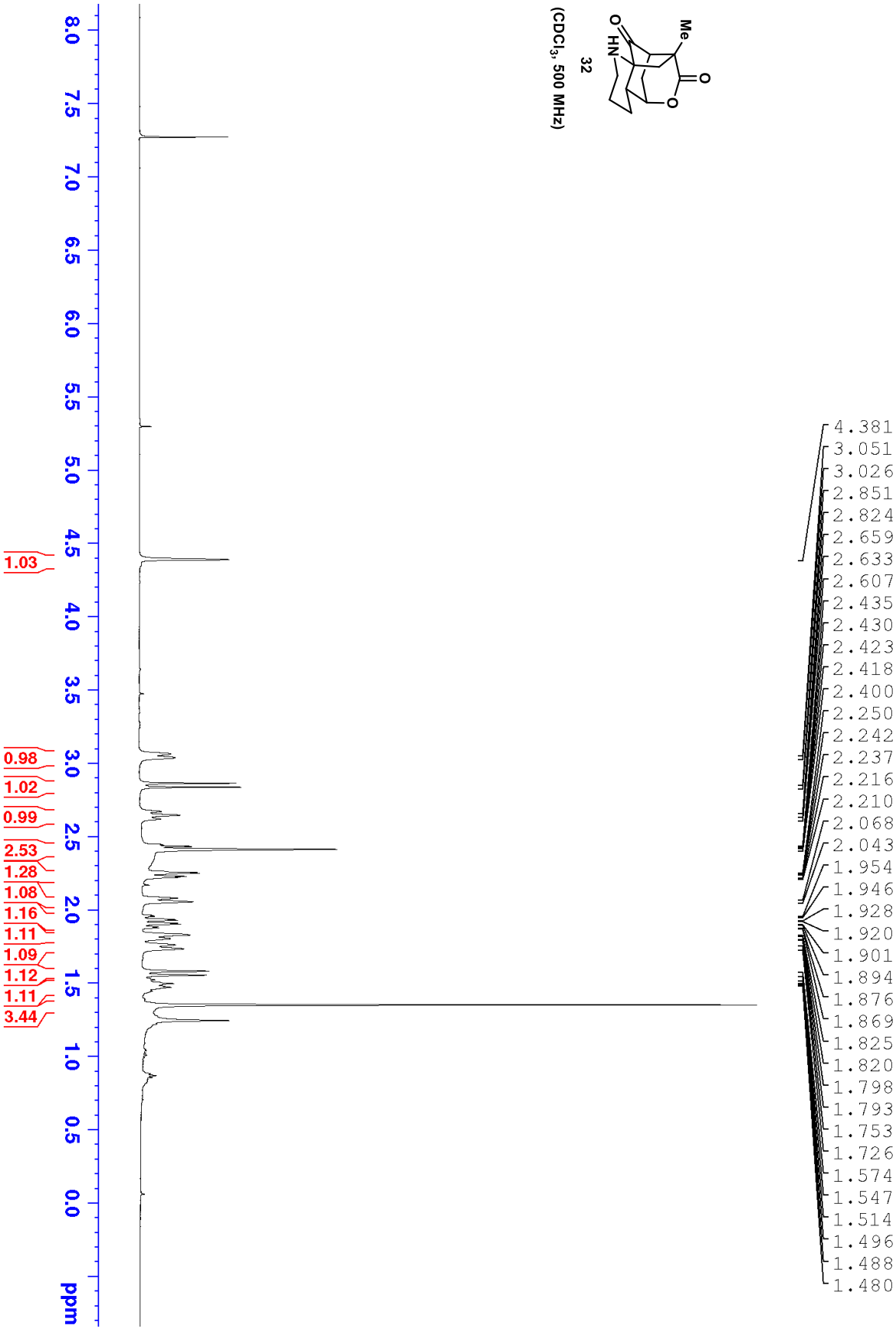

27
(CDCl3, 126 MHz)
TIPSO
HO
NHBoc
H
Me
O
O
177.026
156.659
80.893
76.584
76.512
63.672
63.397
44.576
43.017
42.954
38.087
30.284
28.081
26.807
24.330
21.668
17.939
11.825
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

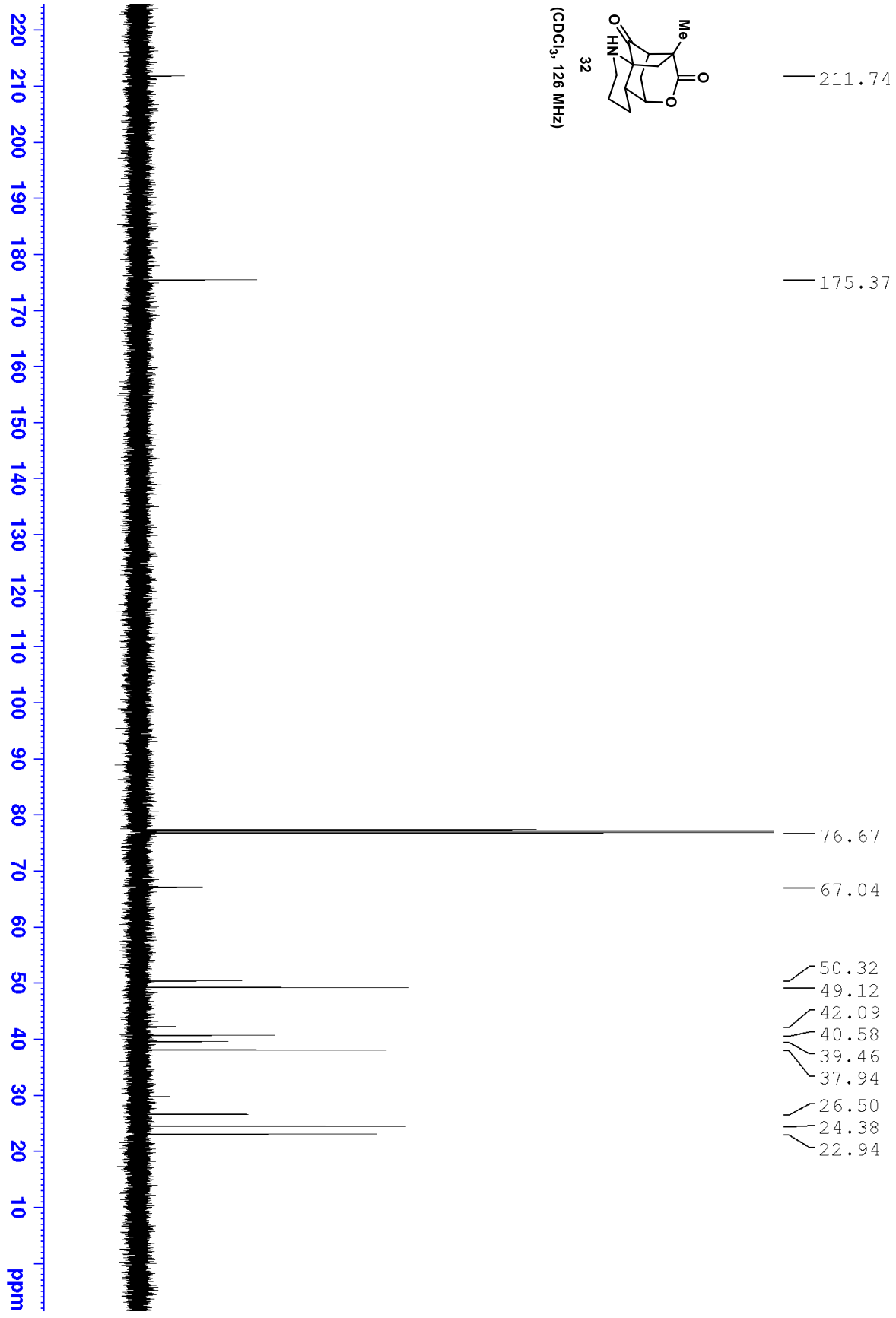

7
(CDCl3, 500 MHz)
TIPSO
NHBoc
Me
O
O
O
O
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.82
1.00
1.01
1.03
0.78
1.98
0.92
1.03
0.92
1.17
2.24
1.24
9.14
2.95
21.01
5.112
4.624
3.752
3.738
3.726
3.713
3.699
3.683
3.667
3.652
3.644
3.627
2.902
2.867
2.482
2.476
2.467
2.461
2.442
2.435
2.426
2.420
2.230
2.207
2.145
2.137
2.130
2.115
2.103
2.096
1.976
1.943
1.837
1.811
1.807
1.779
1.755
1.743
1.729
1.716
1.709
1.690
1.683
1.677
1.667
1.558
1.540
1.525
1.510

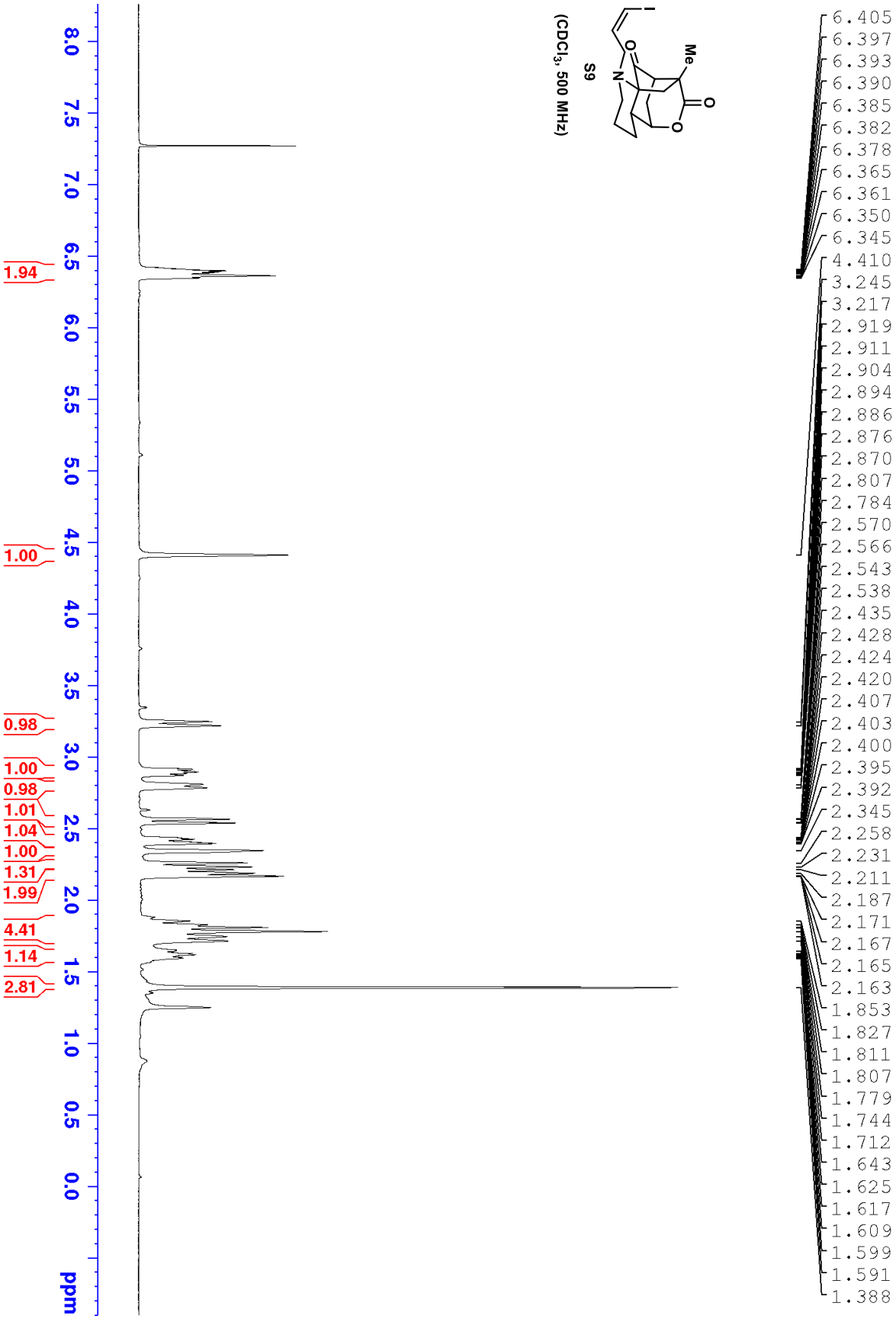

7
(CDCl3, 126 MHz)
TIPSO
NHBoc
Me
O
O
O
O
209.45
174.80
154.52
79.88
73.86
66.65
63.18
52.35
48.46
40.79
39.05
37.12
30.26
28.19
24.33
21.73
17.96
11.84
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

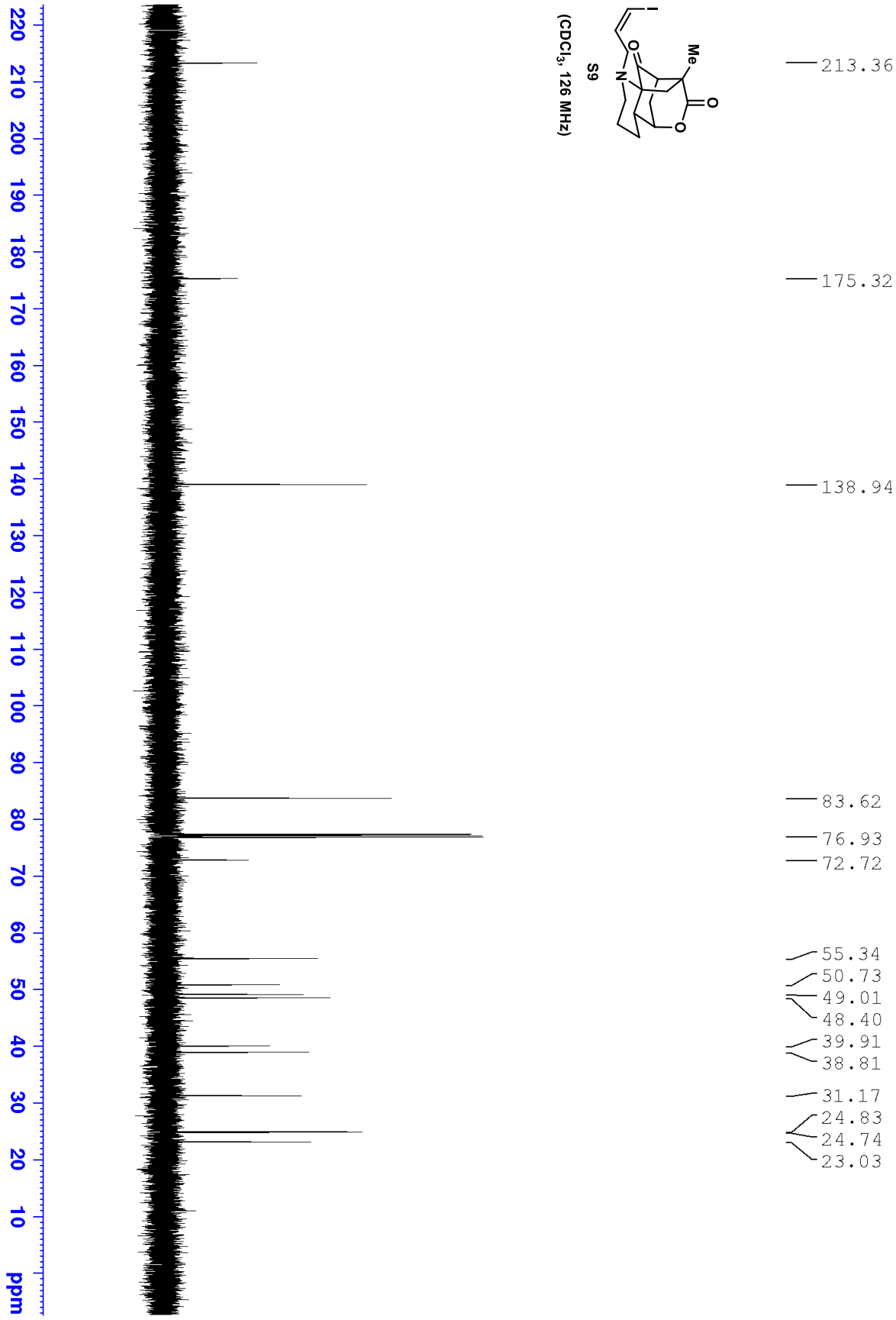

31
(CDCl3, 500 MHz)
Me
O
NHBoc
HO
O
O
5.274
4.617
3.694
3.684
3.672
3.660
3.651
3.639
3.628
3.619
2.886
2.859
2.489
2.484
2.477
2.472
2.461
2.456
2.451
2.443
2.239
2.176
2.170
2.164
2.158
2.150
2.143
2.137
2.131
1.931
1.903
1.853
1.833
1.822
1.816
1.812
1.807
1.789
1.777
1.772
1.761
1.746
1.737
1.718
1.710
1.698
1.692
1.687
1.681
1.674
1.530
1.518
1.511
1.504
1.499
1.492
1.486
1.412
1.340
0.87
1.00
2.09
0.74
1.97
0.90
1.52
0.89
1.06
1.40
2.03
1.42
8.90
2.91
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

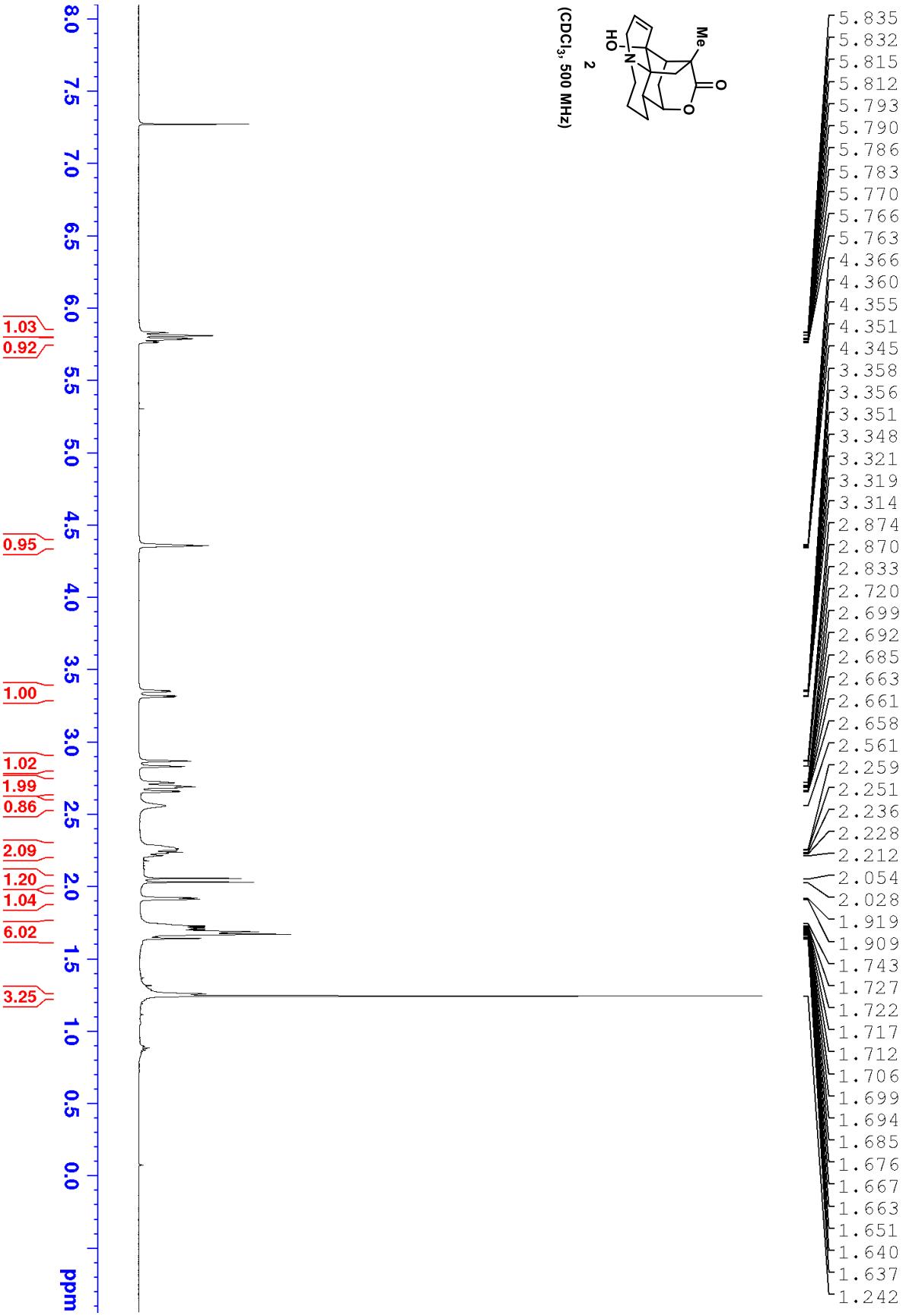

31
(CDCl3, 126 MHz)
HO
NHBoc
O
Me
O
O
209.20
174.81
154.80
80.13
73.88
66.68
62.25
52.04
48.41
40.77
39.18
36.99
29.94
28.20
24.32
21.48
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

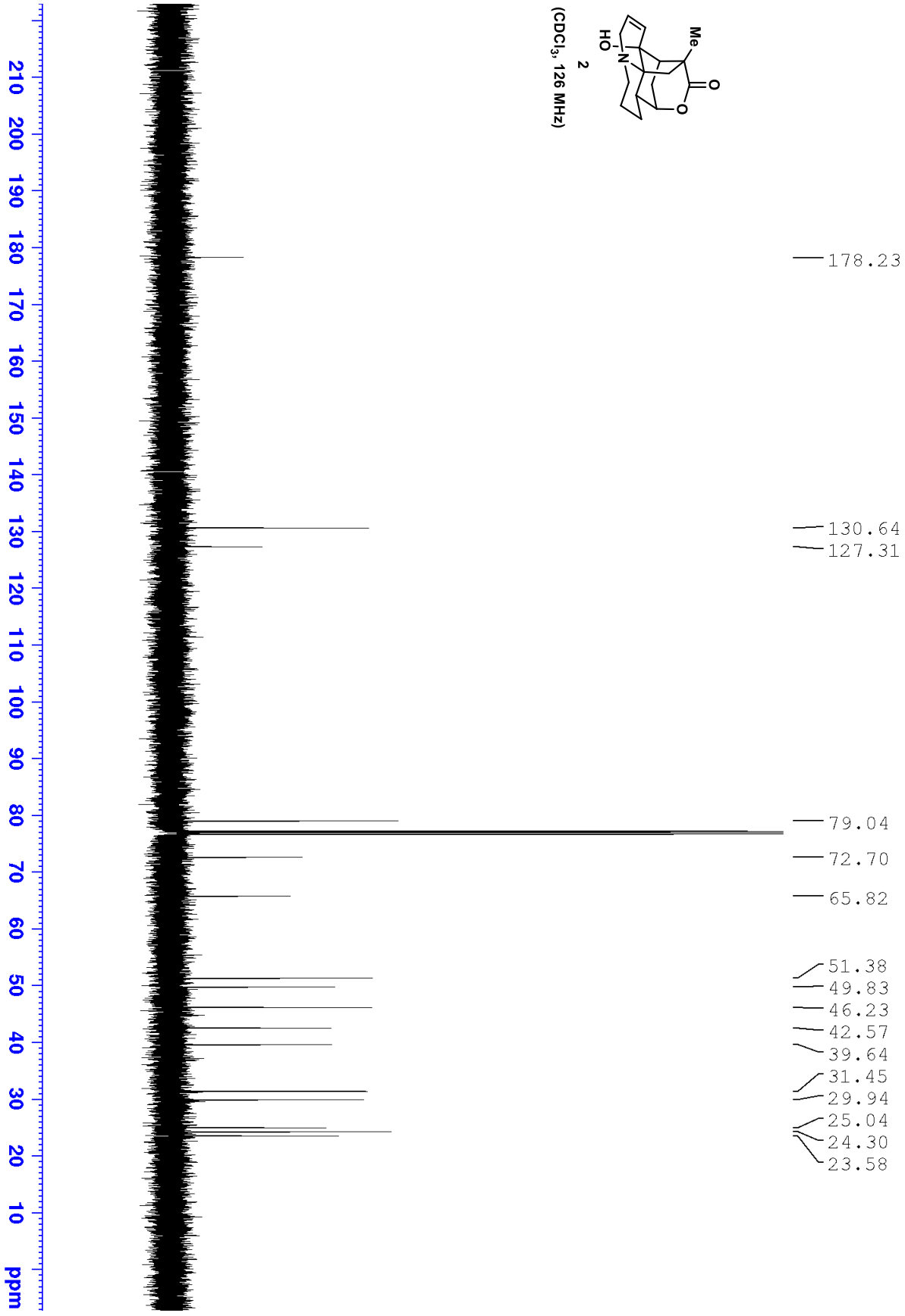

32
(CDCl3, 500 MHz)
HN
O
Me
O
O
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.03
0.98
1.02
0.99
2.53
1.28
1.08
1.16
1.11
1.09
1.12
1.11
3.44
4.381
3.051
3.026
2.851
2.824
2.659
2.633
2.607
2.435
2.430
2.423
2.418
2.400
2.250
2.242
2.237
2.216
2.210
2.068
2.043
1.954
1.946
1.928
1.920
1.901
1.894
1.876
1.869
1.825
1.820
1.798
1.793
1.753
1.726
1.574
1.547
1.514
1.496
1.488
1.480

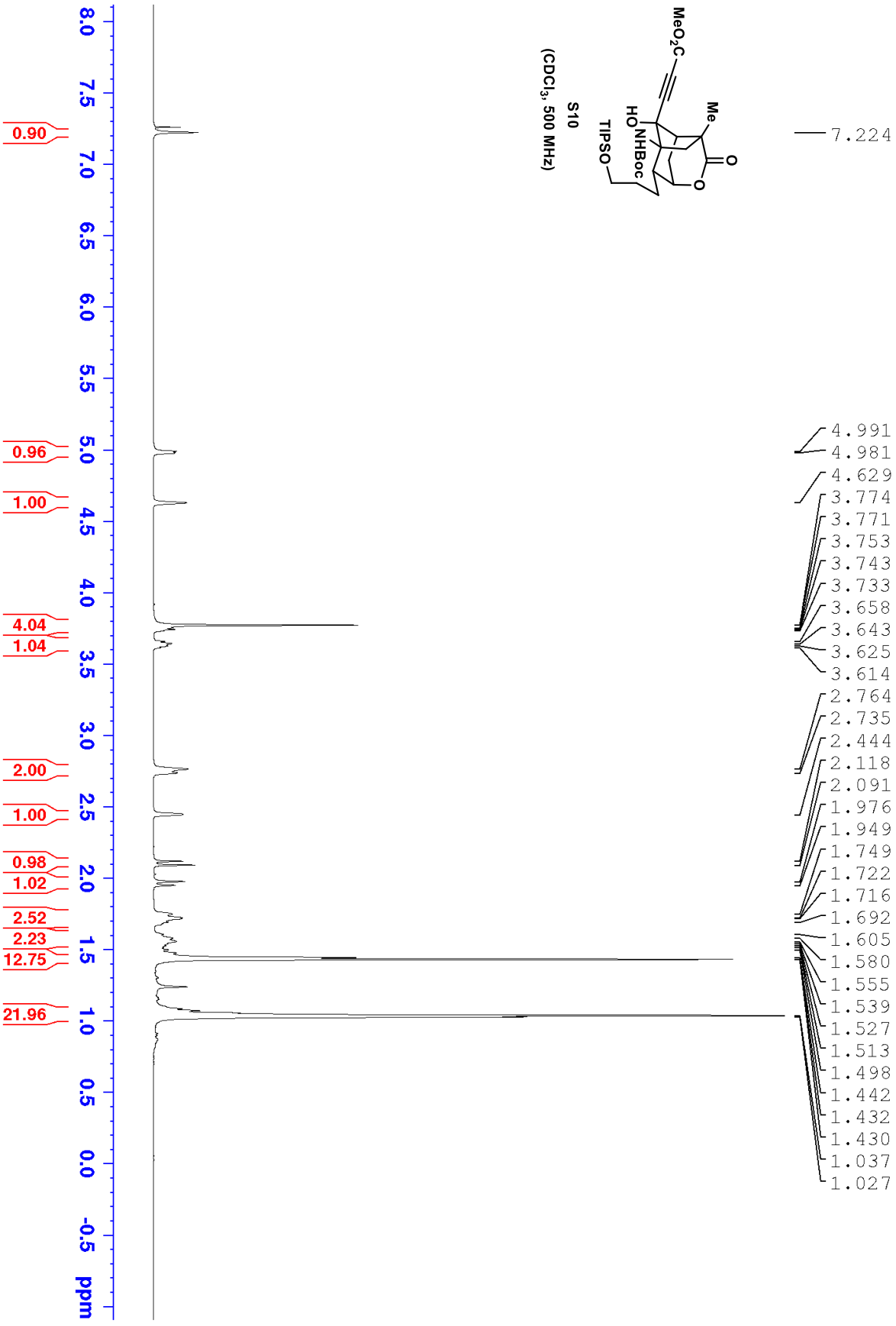

32
(CDCl3, 126 MHz)
Me
HN
O
O
O
211.74
175.37
76.67
67.04
50.32
49.12
42.09
40.58
39.46
37.94
26.50
24.38
22.94
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

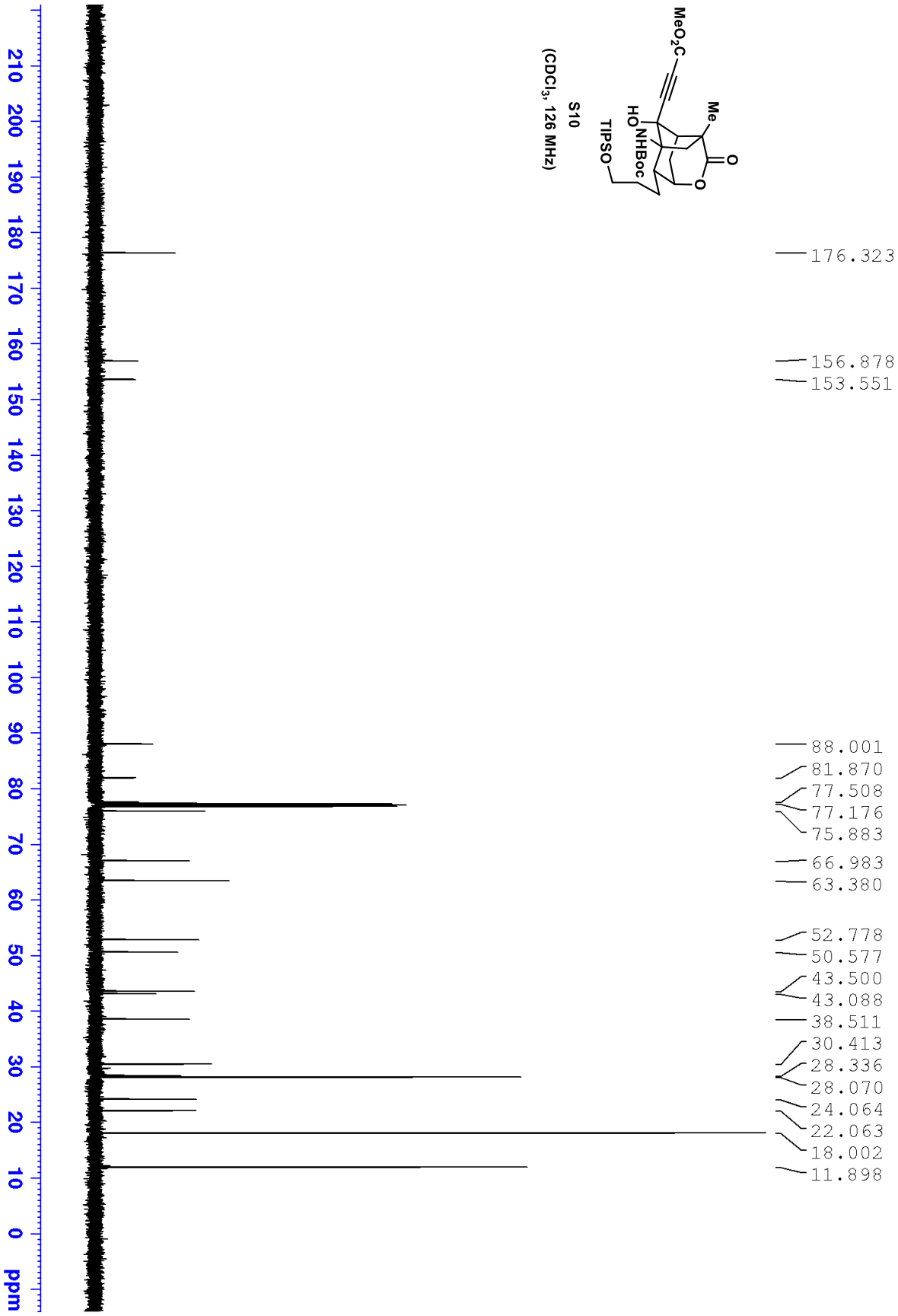

S9
(CDCl3, 500 MHz)
Me
O
N
O
O
O
I
6.405
6.397
6.393
6.390
6.385
6.382
6.378
6.365
6.361
6.350
6.345
4.410
3.245
3.217
2.919
2.911
2.904
2.894
2.886
2.876
2.870
2.807
2.784
2.570
2.566
2.543
2.538
2.435
2.428
2.424
2.420
2.407
2.403
2.400
2.395
2.392
2.345
2.258
2.231
2.211
2.187
2.171
2.167
2.165
2.163
1.853
1.827
1.811
1.807
1.779
1.744
1.712
1.643
1.625
1.617
1.609
1.599
1.591
1.388
1.94
1.00
0.98
1.00
0.98
1.01
1.04
1.00
1.31
1.99
4.41
1.14
2.81
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

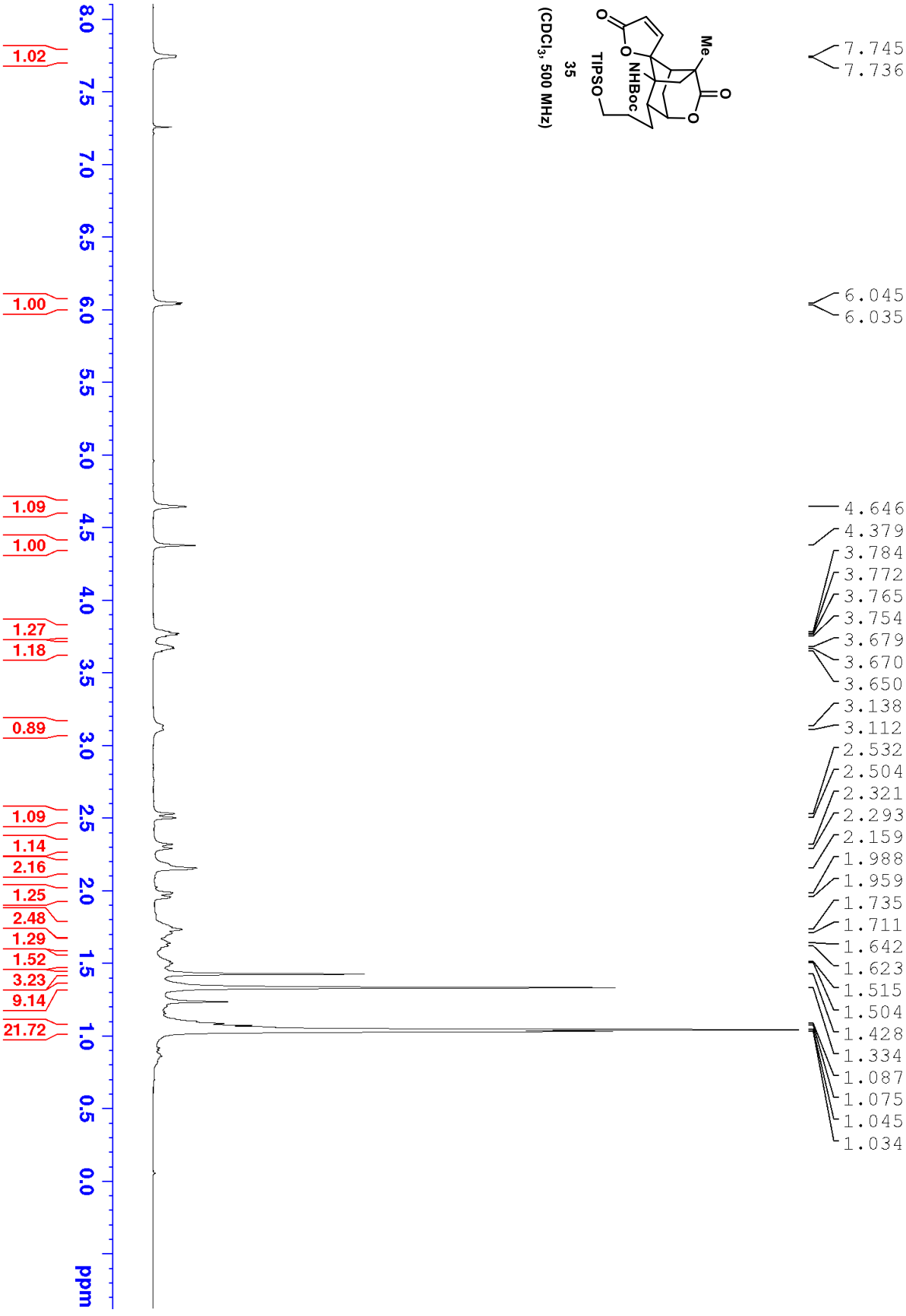

S9
(CDCl3, 126 MHz)
Me
O
N
O
O
O
213.36
175.32
138.94
83.62
76.93
72.72
55.34
50.73
49.01
48.40
39.91
38.81
31.17
24.83
24.74
23.03
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

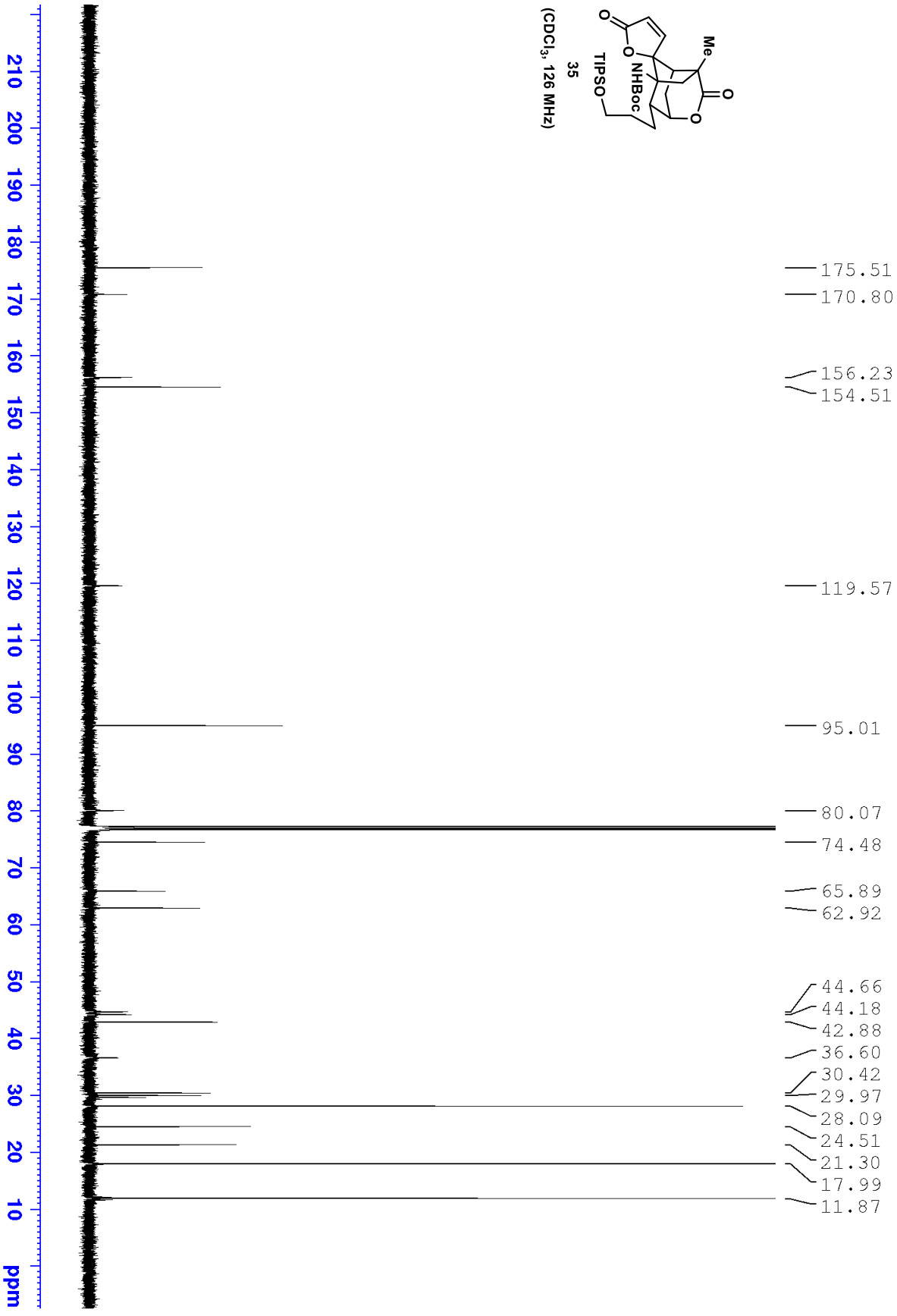

8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.03
0.92
0.95
1.00
1.02
1.99
0.86
2.09
1.20
1.04
6.02
3.25
2
(CDCl3, 500 MHz)
Me
HO
N
O
O
5.835
5.832
5.815
5.812
5.793
5.790
5.786
5.783
5.770
5.766
5.763
4.366
4.360
4.355
4.351
4.345
3.358
3.356
3.351
3.348
3.321
3.319
3.314
2.874
2.870
2.833
2.720
2.699
2.692
2.685
2.663
2.661
2.658
2.561
2.259
2.251
2.236
2.228
2.212
2.054
2.028
1.919
1.909
1.743
1.727
1.722
1.717
1.712
1.706
1.699
1.694
1.685
1.676
1.667
1.663
1.651
1.640
1.637
1.242


2
(CDCl3, 126 MHz)
HO
N
Me
O
O
178.23
130.64
127.31
79.04
72.70
65.82
51.38
49.83
46.23
42.57
39.64
31.45
29.94
25.04
24.30
23.58
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


S10
(CDCl3, 500 MHz)
MeO2C
Me
HO
NHBoc
TIPSO
O
O
7.224
4.991
4.981
4.629
3.774
3.771
3.753
3.743
3.733
3.658
3.643
3.625
3.614
2.764
2.735
2.444
2.118
2.091
1.976
1.949
1.749
1.722
1.716
1.692
1.605
1.580
1.555
1.539
1.527
1.513
1.498
1.442
1.432
1.430
1.037
1.027
0.90
0.96
1.00
4.04
1.04
2.00
1.00
0.98
1.02
2.52
2.23
12.75
21.96
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
ppm


S10
(CDCl3, 126 MHz)
MeO2C
Me
HO
NHBoc
TIPSO
O
O
176.323
156.878
153.551
88.001
81.870
77.508
77.176
75.883
66.983
63.380
52.778
50.577
43.500
43.088
38.511
30.413
28.336
28.070
24.064
22.063
18.002
11.898
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


35
(CDCl3, 500 MHz)
TIPSO
NHBoc
Me
7.745
7.736
6.045
6.035
4.646
4.379
3.784
3.772
3.765
3.754
3.679
3.670
3.650
3.138
3.112
2.532
2.504
2.321
2.293
2.159
1.988
1.959
1.735
1.711
1.642
1.623
1.515
1.504
1.428
1.334
1.087
1.075
1.045
1.034
1.02
1.00
1.09
1.00
1.27
1.18
0.89
1.09
1.14
2.16
1.25
2.48
1.29
1.52
3.23
9.14
21.72
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm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(CDCl3, 126 MHz)
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NHBoc
Me
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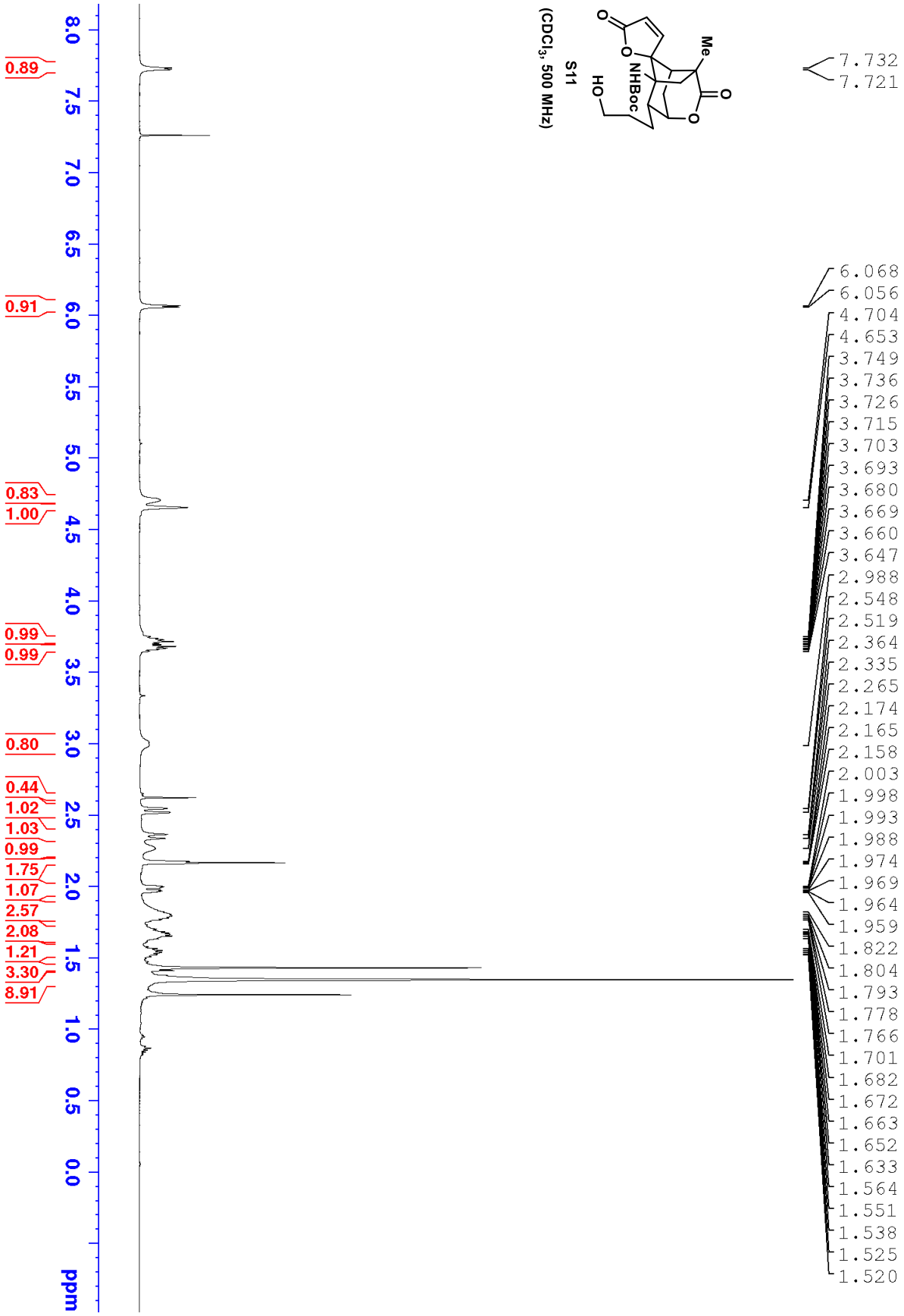
170.80
156.23
154.51
119.57
95.01
80.07
74.48
65.89
62.92
44.66
44.18
42.88
36.60
30.42
29.97
28.09
24.51
21.30
17.99
11.87
ppm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(CDCl3, 500 MHz)
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NHBoc
HO
O
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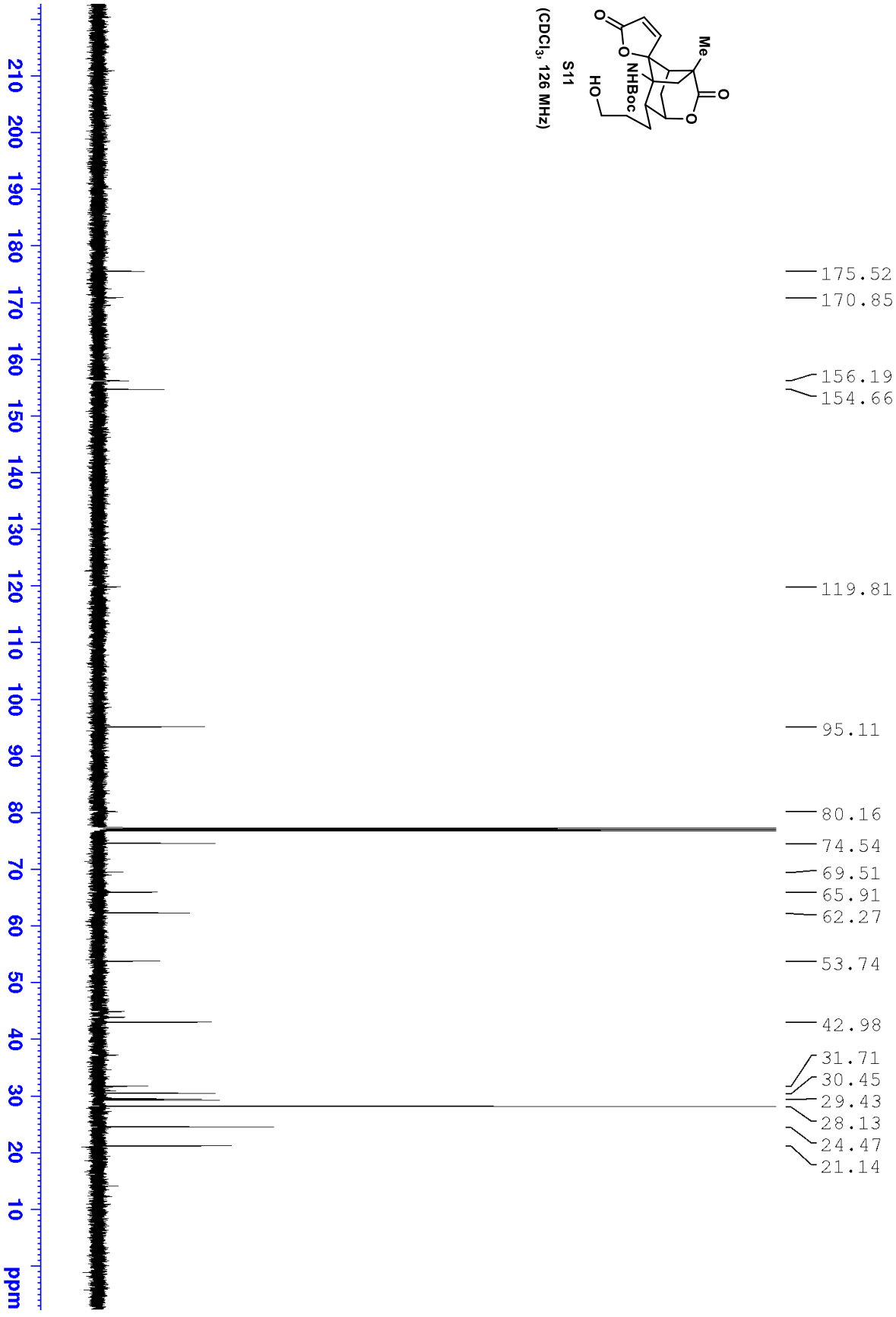
7.721
6.068
6.056
4.704
4.653
3.749
3.736
3.726
3.715
3.703
3.693
3.680
3.669
3.660
3.647
2.988
2.548
2.519
2.364
2.335
2.265
2.174
2.165
2.158
2.003
1.998
1.993
1.988
1.974
1.969
1.964
1.959
1.822
1.804
1.793
1.778
1.766
1.701
1.682
1.672
1.663
1.652
1.633
1.564
1.551
1.538
1.525
1.520
0.89
0.91
0.83
1.00
0.99
0.99
0.80
0.44
1.02
1.03
0.99
1.75
1.07
2.57
2.08
1.21
3.30
8.91
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


S11
(CDCl3, 126 MHz)
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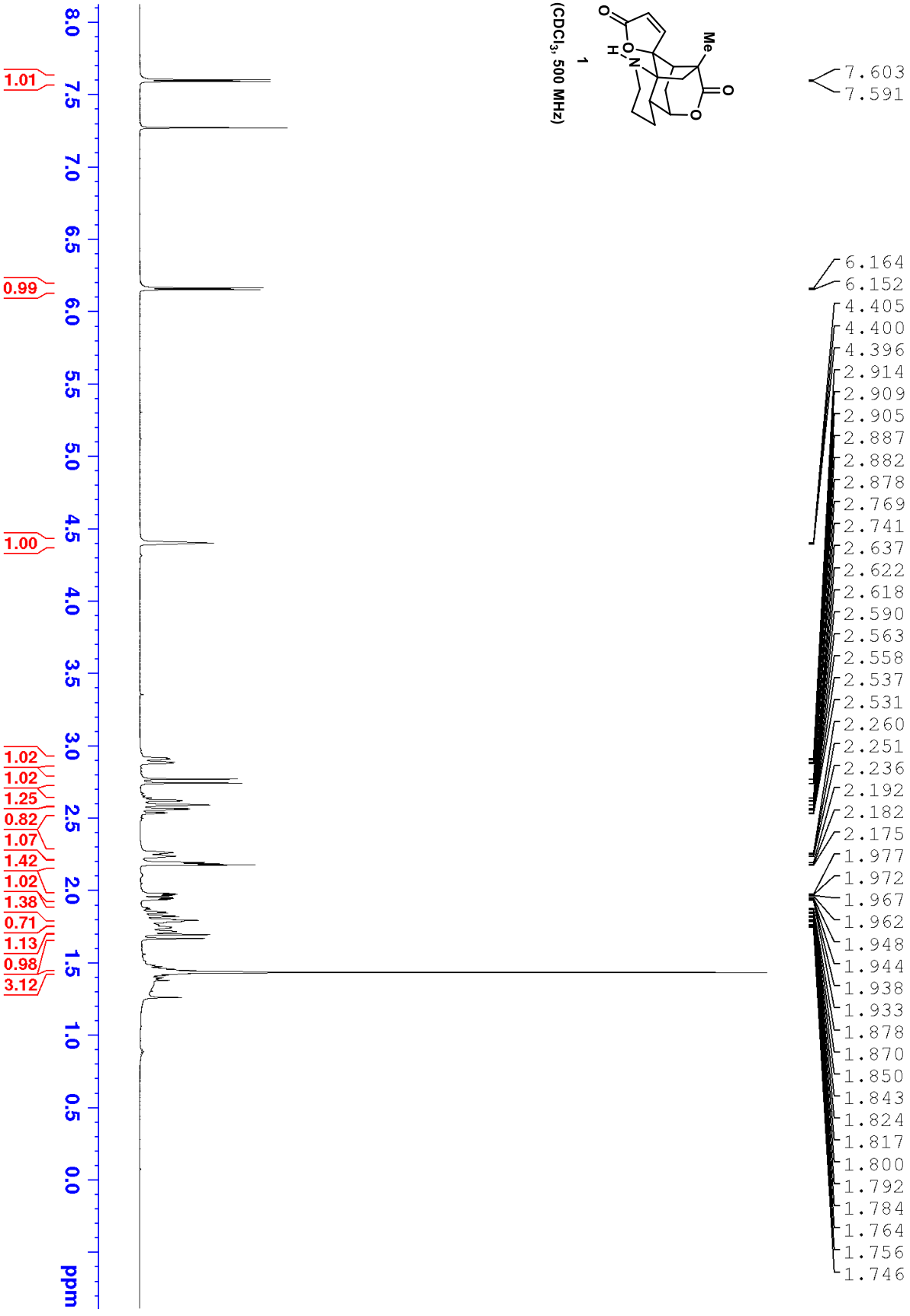
O
O
NHBoc
HO
O
O
175.52
170.85
156.19
154.66
119.81
95.11
80.16
74.54
69.51
65.91
62.27
53.74
42.98
31.71
30.45
29.43
28.13
24.47
21.14
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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7.591
6.164
6.152
4.405
4.400
4.396
2.914
2.909
2.905
2.887
2.882
2.878
2.769
2.741
2.637
2.622
2.618
2.590
2.563
2.558
2.537
2.531
2.260
2.251
2.236
2.192
2.182
2.175
1.977
1.972
1.967
1.962
1.948
1.944
1.938
1.933
1.878
1.870
1.850
1.843
1.824
1.817
1.800
1.792
1.784
1.764
1.756
1.746
1.01
0.99
1.00
1.02
1.02
1.25
0.82
1.07
1.42
1.02
1.38
0.71
1.13
0.98
3.12
8.0
7.5
7.0
6.5
6.0
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5.0
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4.0
3.5
3.0
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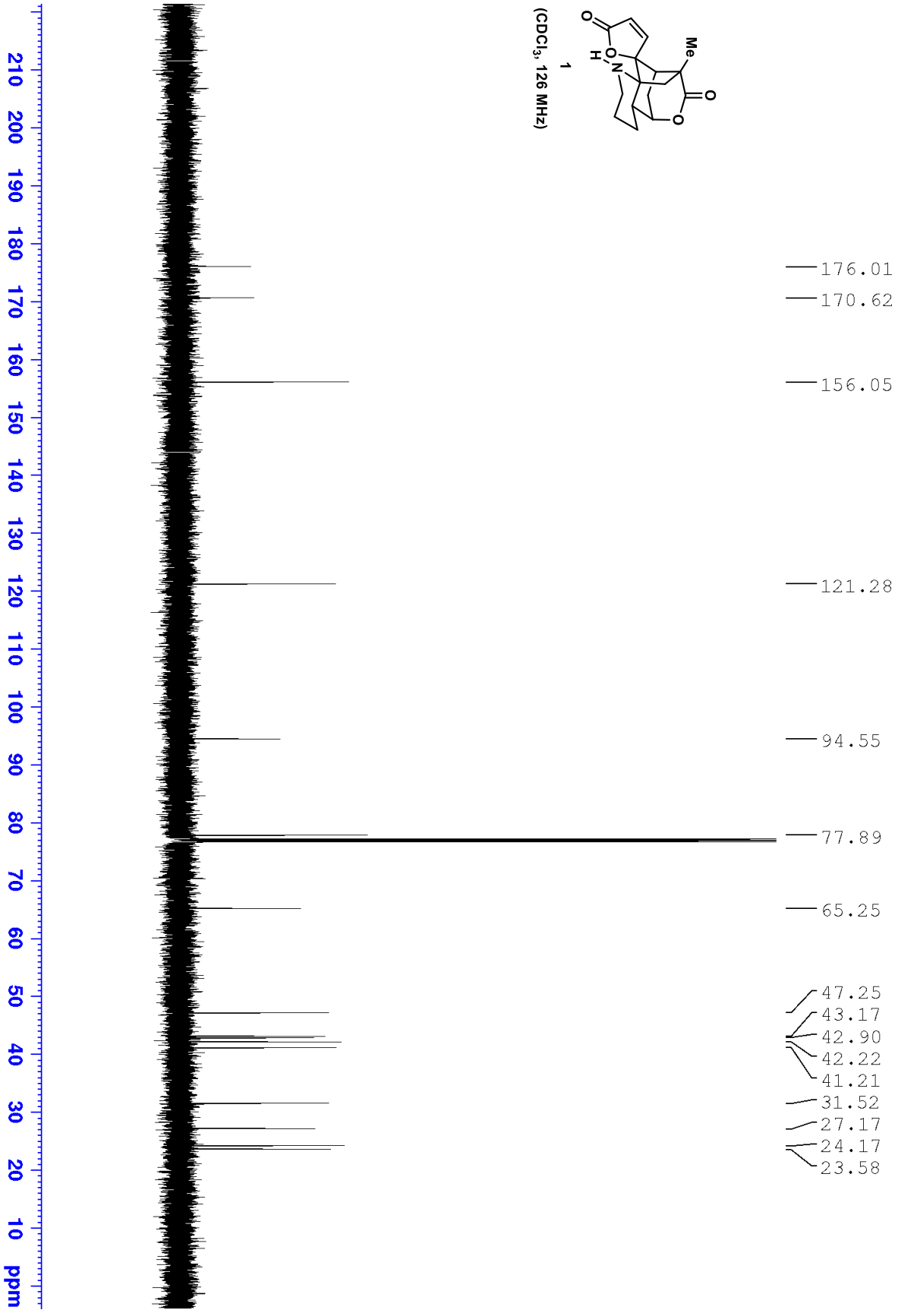
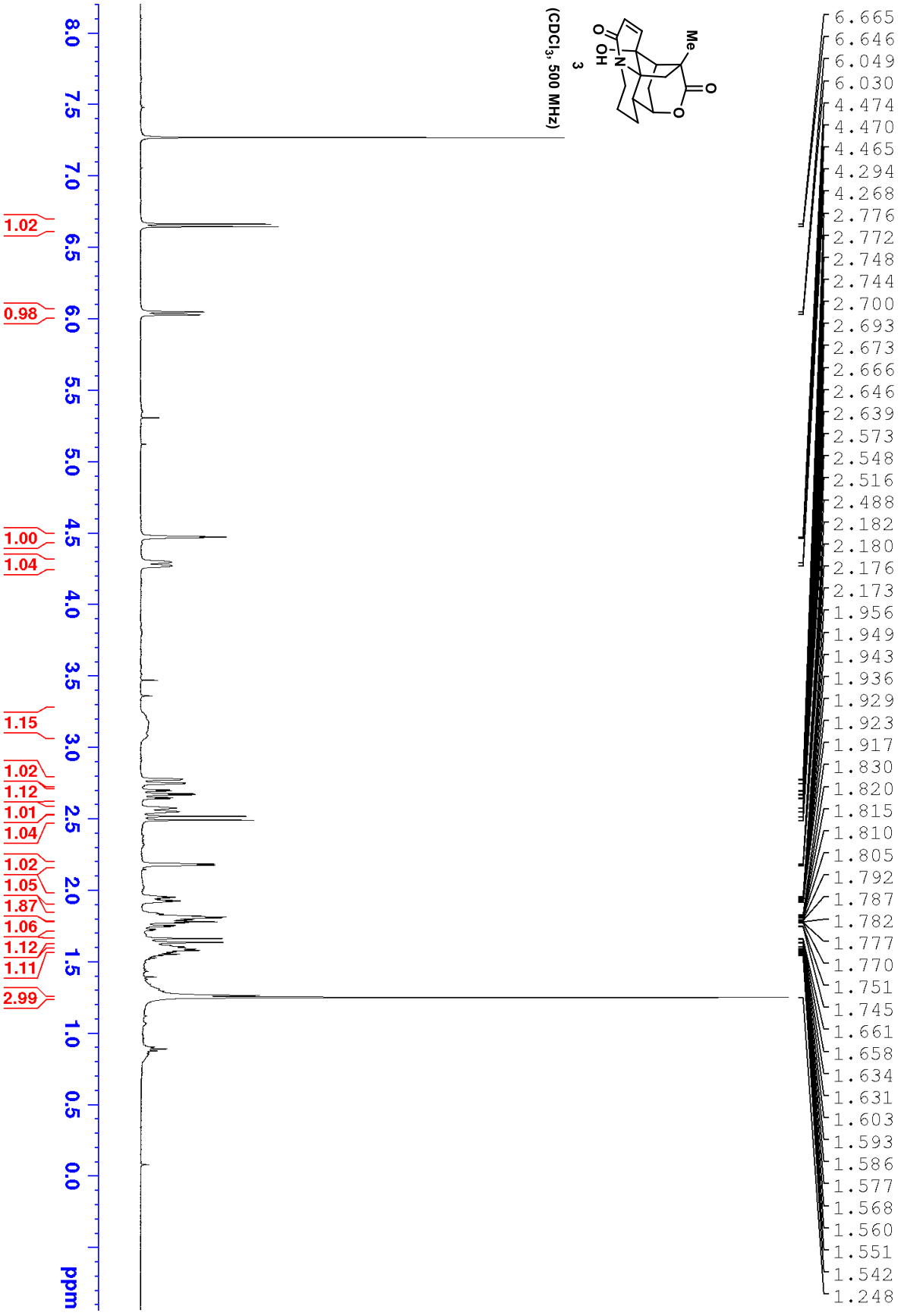
2.0
1.5
1.0
0.5
0.0
ppm


1
(CDCl3, 126 MHz)
Me
O
O
H
N
O
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
176.01
170.62
156.05
121.28
94.55
77.89
65.25
47.25
43.17
42.90
42.22
41.21
31.52
27.17
24.17
23.58


3
(CDCl3, 500 MHz)
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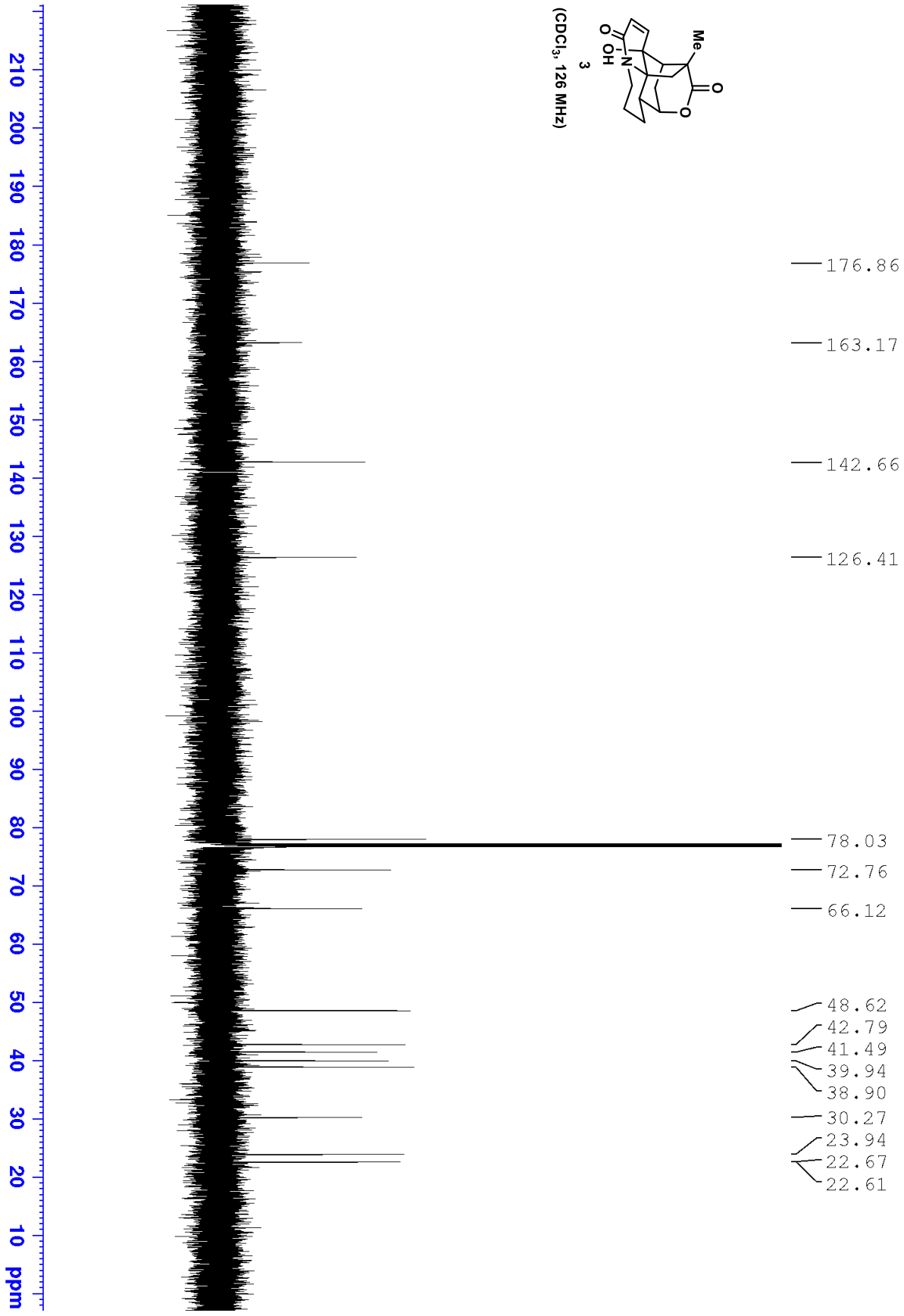
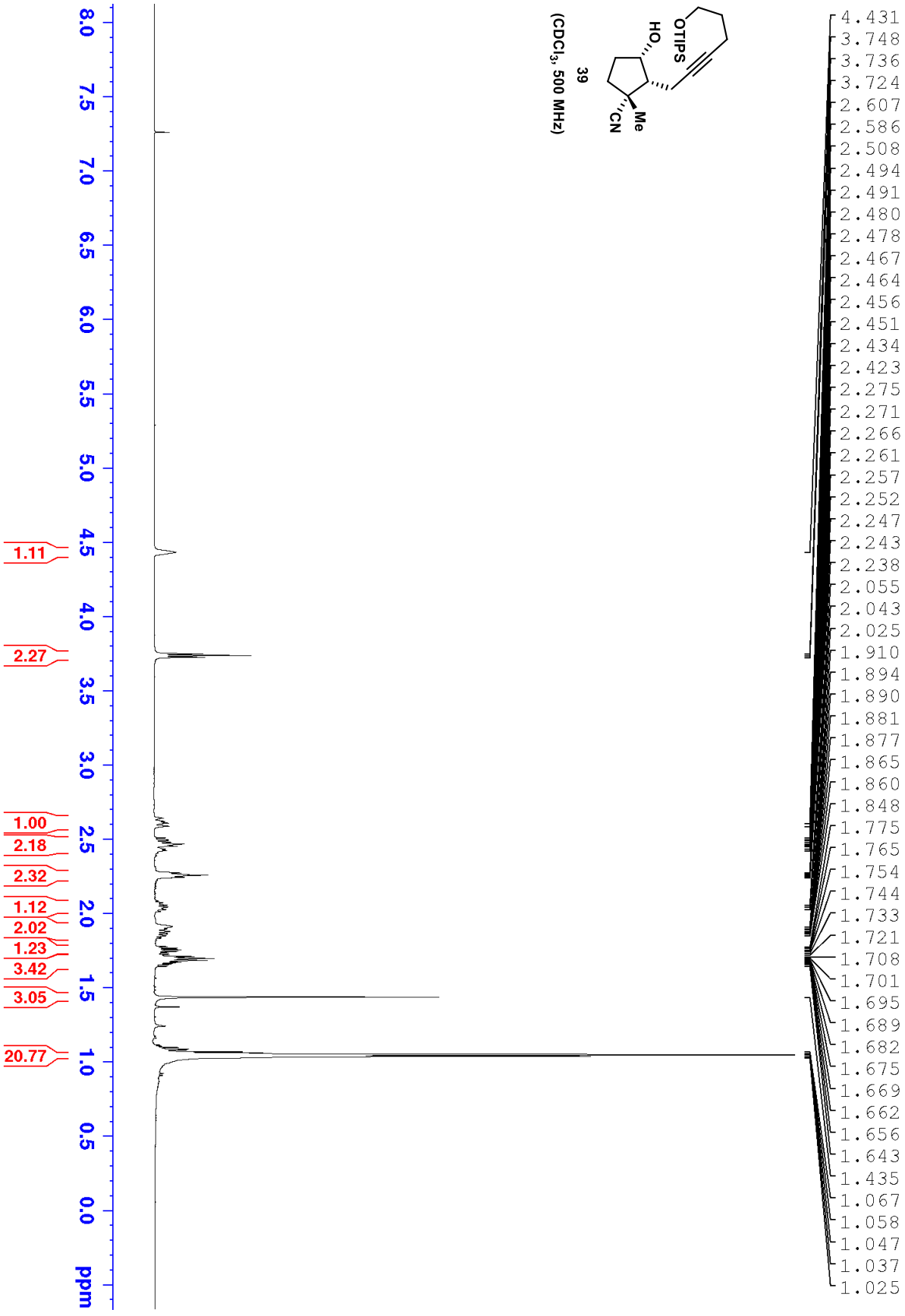
O
OH
N
O
O
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.02
0.98
1.00
1.04
1.15
1.02
1.12
1.01
1.04
1.02
1.05
1.87
1.06
1.12
1.11
2.99
6.665
6.646
6.049
6.030
4.474
4.470
4.465
4.294
4.268
2.776
2.772
2.748
2.744
2.700
2.693
2.673
2.666
2.646
2.639
2.573
2.548
2.516
2.488
2.182
2.180
2.176
2.173
1.956
1.949
1.943
1.936
1.929
1.923
1.917
1.830
1.820
1.815
1.810
1.805
1.792
1.787
1.782
1.777
1.770
1.751
1.745
1.661
1.658
1.634
1.631
1.603
1.593
1.586
1.577
1.568
1.560
1.551
1.542
1.248


3
(CDCl3, 126 MHz)
Me
O
O
N
OH
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
176.86
163.17
142.66
126.41
78.03
72.76
66.12
48.62
42.79
41.49
39.94
38.90
30.27
23.94
22.67
22.61


OTIPS
HO
Me
CN
39
(CDCl3, 500 MHz)
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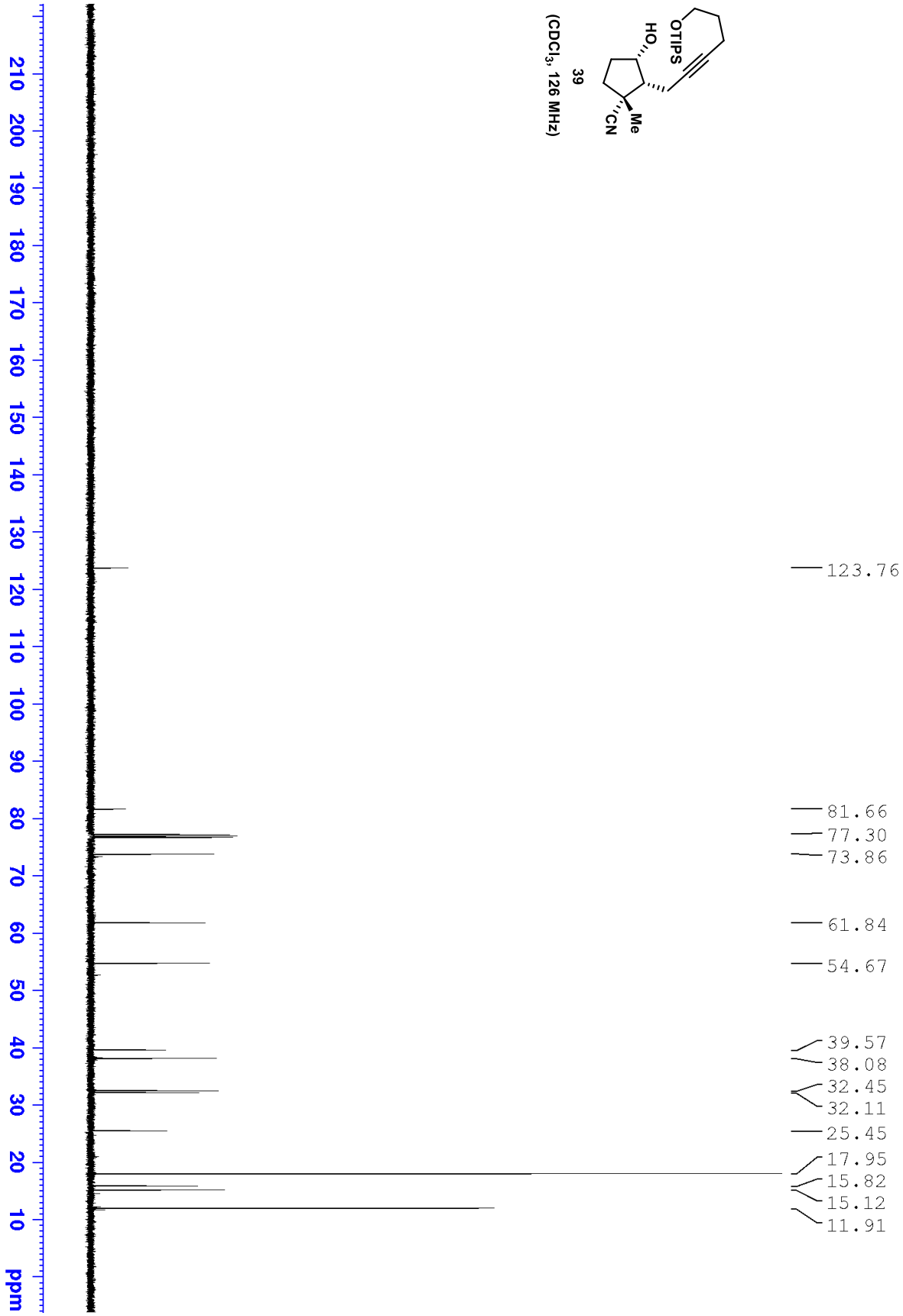
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.11
2.27
1.00
2.18
2.32
1.12
2.02
1.23
3.42
3.05
20.77
4.431
3.748
3.736
3.724
2.607
2.586
2.508
2.494
2.491
2.480
2.478
2.467
2.464
2.456
2.451
2.434
2.423
2.275
2.271
2.266
2.261
2.257
2.252
2.247
2.243
2.238
2.055
2.043
2.025
1.910
1.894
1.890
1.881
1.877
1.865
1.860
1.848
1.775
1.765
1.754
1.744
1.733
1.721
1.708
1.701
1.695
1.689
1.682
1.675
1.669
1.662
1.656
1.643
1.435
1.067
1.058
1.047
1.037
1.025


OTIPS
HO
Me
CN
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(CDCl3, 126 MHz)
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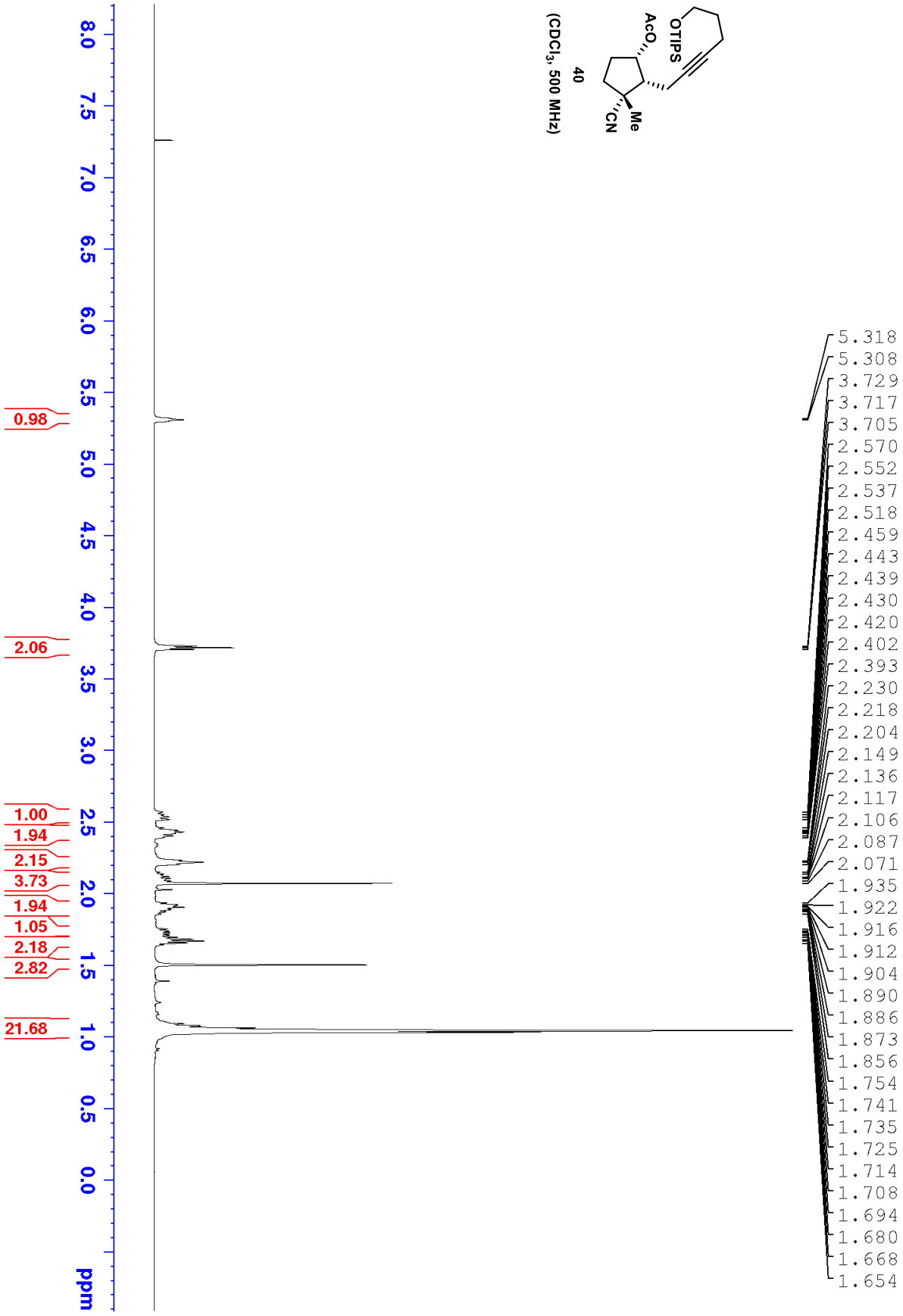
77.30
73.86
61.84
54.67
39.57
38.08
32.45
32.11
25.45
17.95
15.82
15.12
11.91
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


OTIPS
AcO
Me
CN
40
(CDCl3, 500 MHz)
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7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.98
2.06
1.00
1.94
2.15
3.73
1.94
1.05
2.18
2.82
21.68
5.318
5.308
3.729
3.717
3.705
2.570
2.552
2.537
2.518
2.459
2.443
2.439
2.430
2.420
2.402
2.393
2.230
2.218
2.204
2.149
2.136
2.117
2.106
2.087
2.071
1.935
1.922
1.916
1.912
1.904
1.890
1.886
1.873
1.856
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1.741
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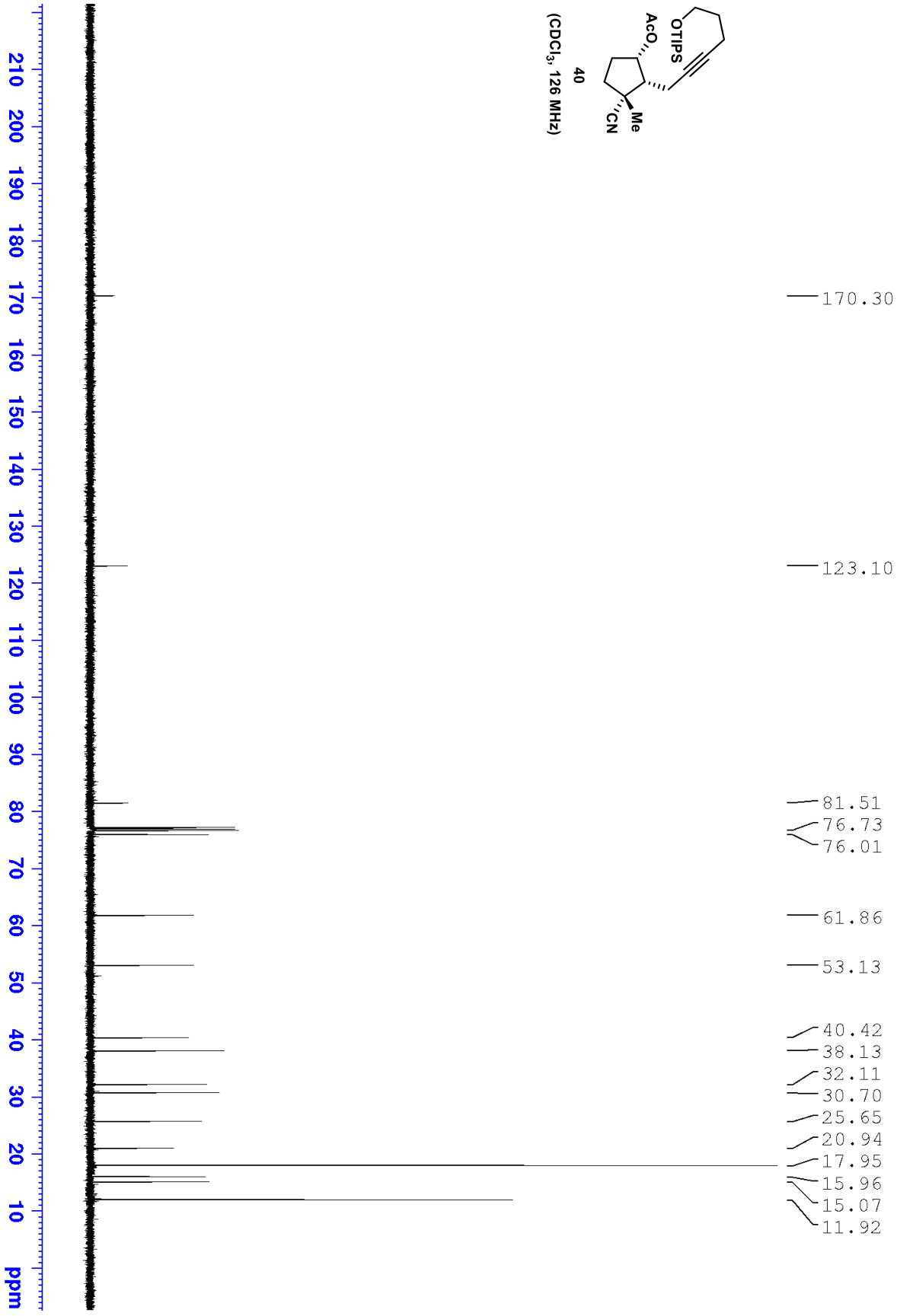
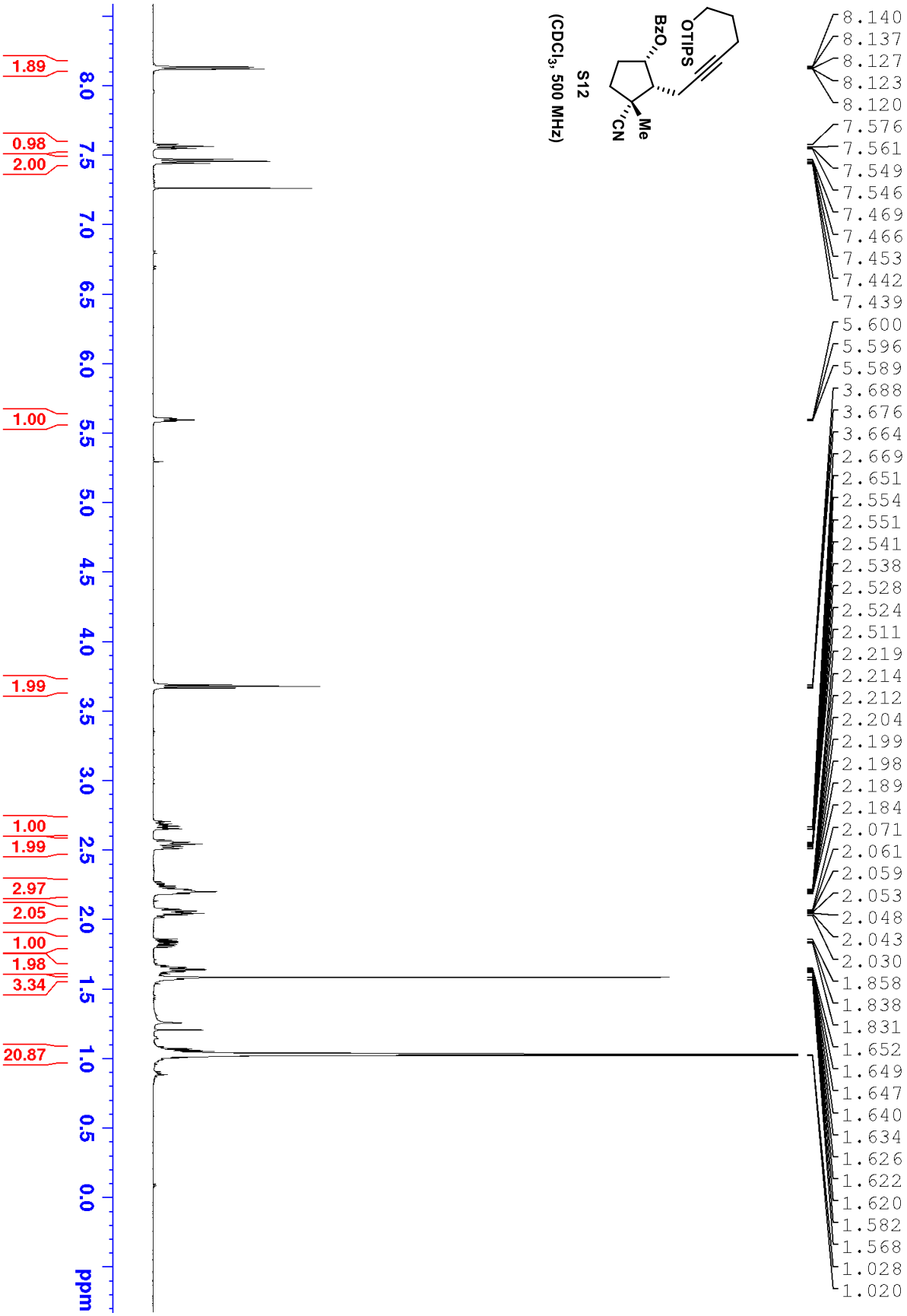
1.668
1.654


OTIPS
AcO
Me
CN
40
(CDCl3, 126 MHz)
170.30
123.10
81.51
76.73
76.01
61.86
53.13
40.42
38.13
32.11
30.70
25.65
20.94
17.95
15.96
15.07
11.92
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


S12
(CDCl3, 500 MHz)
OTIPS
BzO
Me
CN
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8.137
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8.123
8.120
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7.561
7.549
7.546
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7.466
7.453
7.442
7.439
5.600
5.596
5.589
3.688
3.676
3.664
2.669
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2.554
2.551
2.541
2.538
2.528
2.524
2.511
2.219
2.214
2.212
2.204
2.199
2.198
2.189
2.184
2.071
2.061
2.059
2.053
2.048
2.043
2.030
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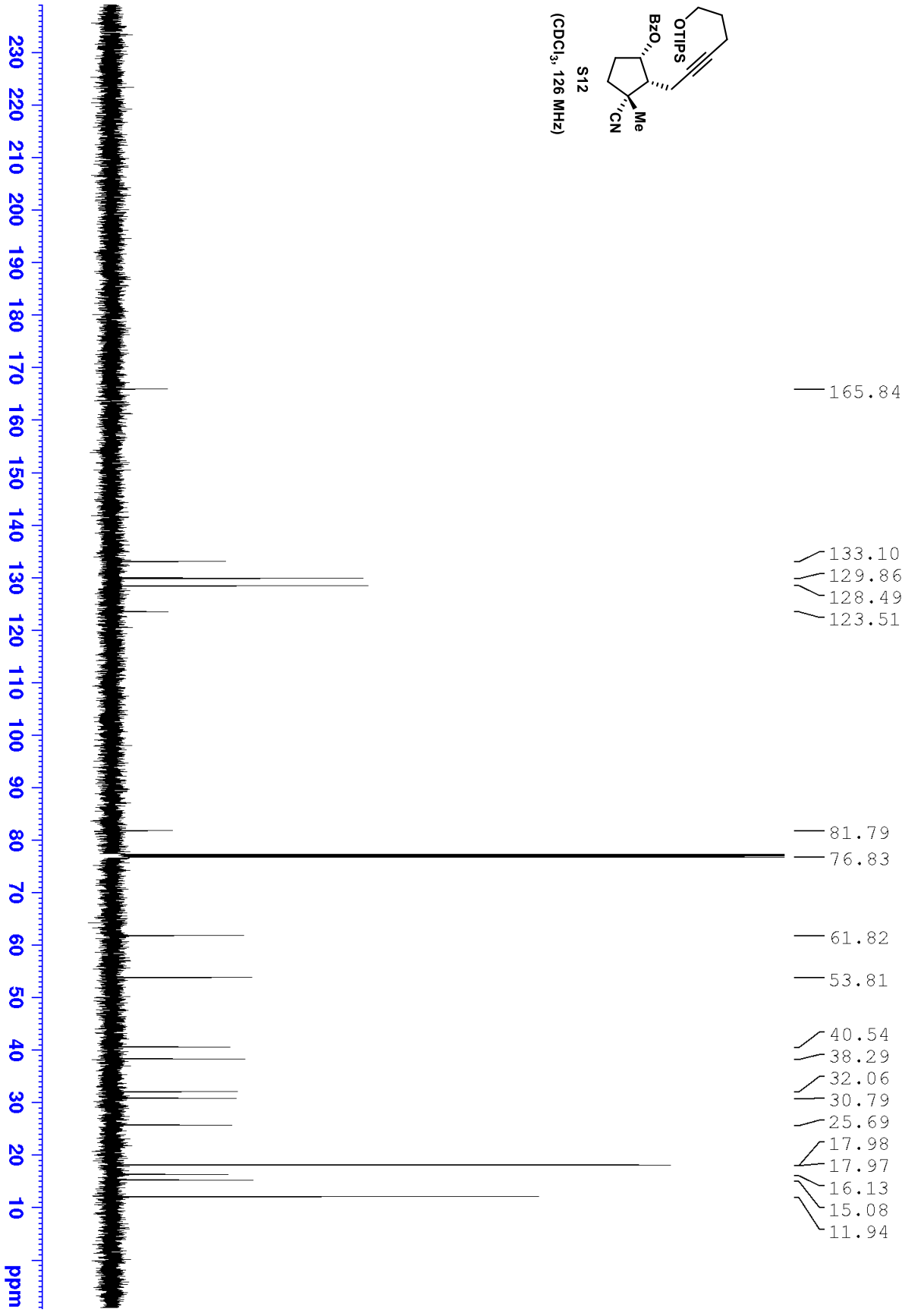
1.838
1.831
1.652
1.649
1.647
1.640
1.634
1.626
1.622
1.620
1.582
1.568
1.028
1.020
1.89
0.98
2.00
1.00
1.99
1.00
1.99
2.97
2.05
1.00
1.98
3.34
20.87
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


OTIPS
BzO
Me
CN
S12
(CDCl3, 126 MHz)
165.84
133.10
129.86
128.49
123.51
81.79
76.83
61.82
53.81
40.54
38.29
32.06
30.79
25.69
17.98
17.97
16.13
15.08
11.94
ppm

Crystal Experiment Section

Crystal growth of $C_{29}H_{53}NO_4Si_2$: Pei Qu (prof. Scott Snyder's group).

Data collected/reported: Andrew McNeece/Alexander S. Filatov, September/2019 (X-ray Laboratory, Searle B013, Department of Chemistry, the University of Chicago, Chicago, Il).

General information: A colorless block was selected and mounted on a Dual-Thickness MicroMount^{tm} (MiTeGen) with 30 μm sample aperture with Fluorolube™ oil. The diffraction data were measured at 100 K on a Bruker D8 VENTURE diffractometer equipped with a microfocus Mo-target X-ray tube (λ = 0.71073 Å) and PHOTON 100 CMOS detector. Data were collected using ϕ and ω scans to survey a hemisphere of reciprocal space. Data reduction and integration were performed with the Bruker APEX3 software package (Bruker AXS, version 2017.3-0, 2018). Data were scaled and corrected for absorption effects using the multi-scan procedure as implemented in SADABS (Bruker AXS, version 2014/5, Krause, Herbst-Irmer, Sheldrick & Stalke, *J. Appl. Cryst.* **2015**, *48*, 3-10). The structure was solved by SHELXT (Version 2018/2: Sheldrick, G. M. *Acta Crystallogr*. **2015**, ***A71***, 3-8) and refined by a full-matrix least-squares procedure using OLEX2 (O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann. J. Appl. Crystallogr. **2009**, *42*, 339-341) (XL refinement program version 2018/3, *Sheldrick, G. M. Acta Crystallogr.* **2015**, *C71*, 3-8). Crystallographic data and details of the data collection and structure refinement are listed in Table 1.

Specific details for structure refinement: All atoms were refined with anisotropic thermal parameters. Hydrogen atoms were included in idealized positions for structure factor calculations except those bound to oxygen atom of a carboxylic group which was located in the difference Fourier map. This hydrogen atom was fully independently refined. All structures are drawn with thermal ellipsoids at 50% probability.

Table 1 Crystal data and structure refinement for mo_0806_Snyder_0m.

Identification code	mo_0806_Snyder_0m
Empirical formula	$C_{29}H_{53}NO_4Si_2$
Formula weight	535.90
Temperature/K	100(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	16.2099(11)
b/Å	11.5462(8)
c/Å	17.8961(12)
α/°	90
β/°	106.578(2)
γ/°	90
Volume/Å^3	3210.3(4)
Z	4
ρ_{calc}g/cm^3	1.109
μ/mm^{-1}	0.142
F(000)	1176.0
Crystal size/mm^3	0.44 × 0.31 × 0.28
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.252 to 56.87
Index ranges	$-21 \leq h \leq 21$, $-15 \leq k \leq 15$, $-23 \leq l \leq 23$
Reflections collected	110805
Independent reflections	8064 [R_{int} = 0.0695, R_{sigma} = 0.0329]
Data/restraints/parameters	8064/0/340
Goodness-of-fit on F^2	1.071
Final R indexes [I>=2σ (I)]	R_1 = 0.0482, wR_2 = 0.1049
Final R indexes [all data]	R_1 = 0.0686, wR_2 = 0.1140
Largest diff. peak/hole / e Å^{-3}	0.58/-0.27

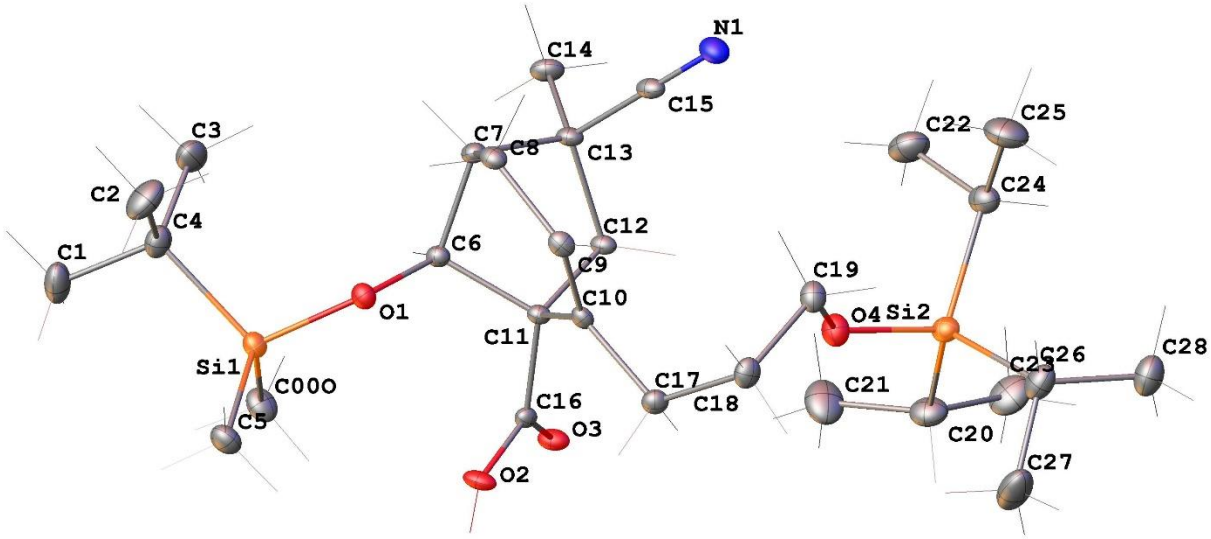
$R_{int} = \Sigma \mid F_o^2 - \langle F_o^2 \rangle \mid / \Sigma \mid F_o^2 \mid$

$R1 = \Sigma \mid \mid F_o \mid - \mid F_c \mid \mid / \Sigma \mid F_o \mid$

$wR2 = [\Sigma [w (F_o^2 - F_c^2)^2] / \Sigma [w (F_o^2)^2]]^{1/2}$

Goodness-of-fit = $[\Sigma [w (F_o^2 - F_c^2)^2] / (n-p)]^{1/2}$

n: number of independent reflections; p: number of refined parameters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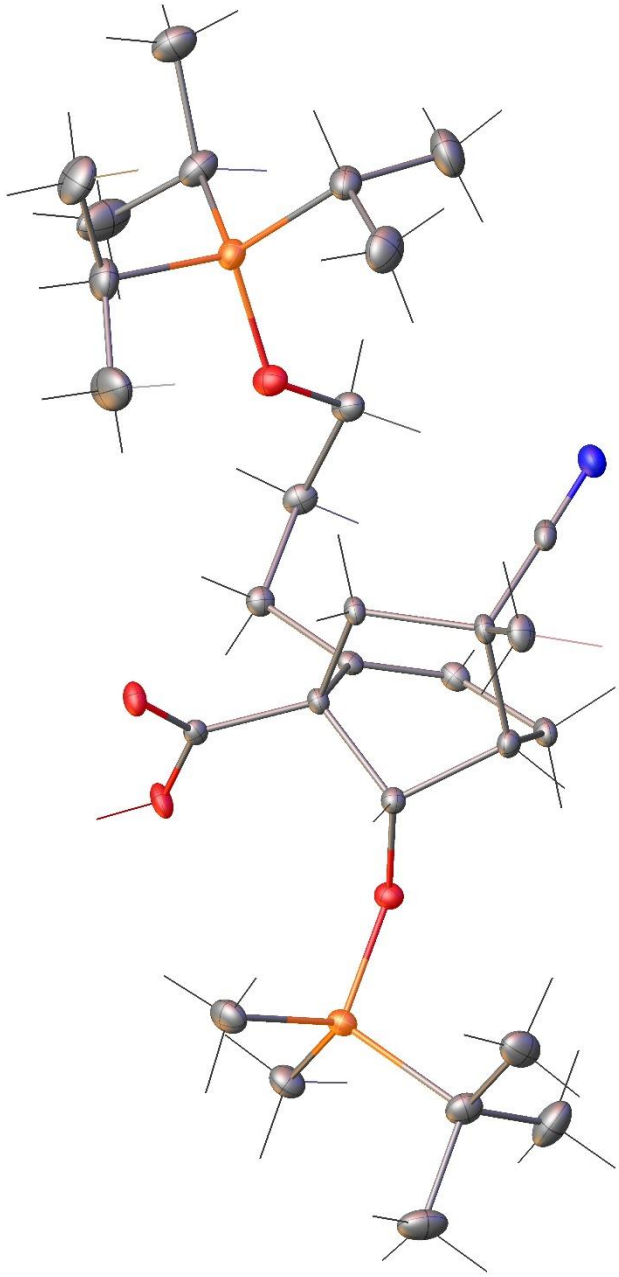
C14
C15
C3
C7
C8
C13
C22
C25
C2
C4
C12
C24
C1
C6
C9
C19
C10
O1
O4
Si2
C11
Si1
C26
C28
C17
C21
C000
C16
C18
C23
C5
O3
C20
O2
C27



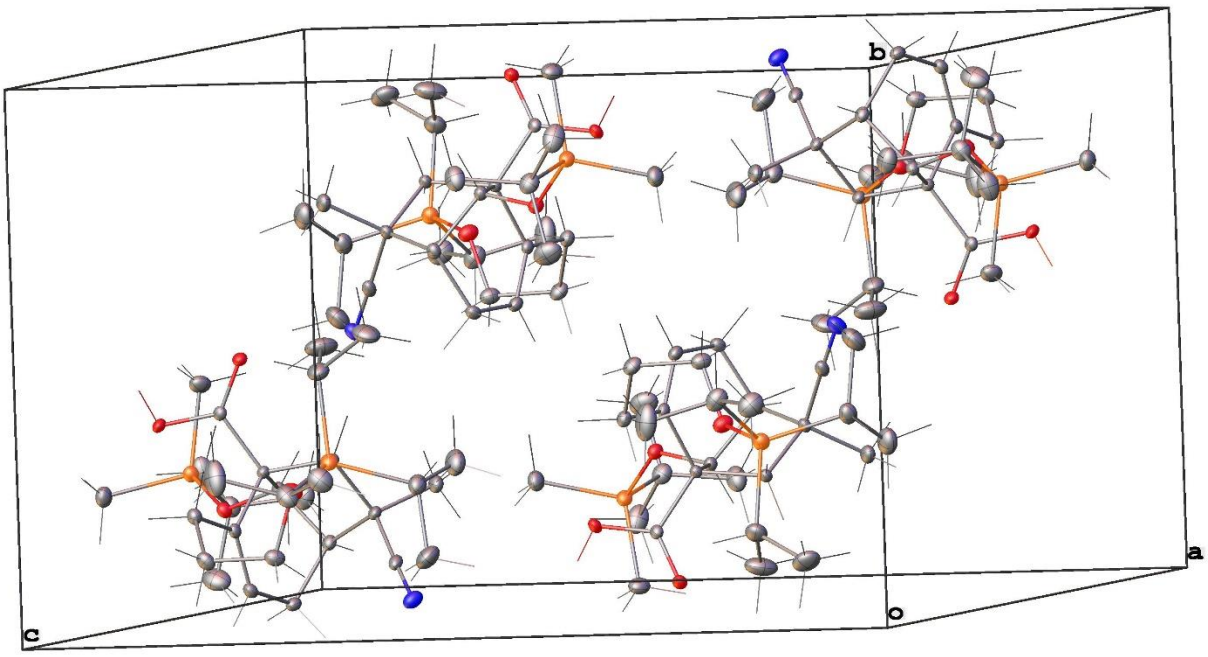

b
a
c
o

Table 2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for mo_0806_Snyder_0m. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
Si1	2605.0(3)	2186.7(4)	3896.5(2)	15.18(10)
Si2	8423.7(3)	2585.0(4)	4323.4(2)	17.51(10)
O1	3450.3(7)	2925.8(9)	3816.9(6)	15.0(2)
O2	4719.0(7)	1508.5(9)	4982.5(6)	17.2(2)
O3	5277.7(7)	412.1(9)	4219.5(6)	16.3(2)
O4	7494.0(7)	3005.2(10)	4432.8(7)	20.5(2)
N1	6032.0(9)	4852.7(12)	2572.3(8)	21.9(3)
C00O	2755.8(11)	600.9(14)	3810.9(10)	24.4(4)
C1	838.4(11)	1975.6(18)	3137.1(11)	32.3(4)
C2	1451.3(12)	3975.3(17)	3237.3(12)	35.0(4)
C3	1773.8(12)	2562.3(17)	2305.5(10)	28.9(4)
C4	1625.8(10)	2696.7(15)	3112.3(9)	22.2(3)
C5	2510.2(11)	2546.2(15)	4878.5(9)	22.8(3)
C6	4017.1(9)	2624.7(12)	3380.8(8)	12.5(3)
C7	4157.5(9)	3621.6(13)	2865.7(8)	14.0(3)
C8	4334.0(10)	4717.9(12)	3360.6(8)	15.0(3)
C9	5043.9(10)	4523.1(13)	4100.9(8)	14.9(3)
C10	5334.6(9)	3478.7(12)	4359.7(8)	12.1(3)
C11	4959.9(9)	2409.6(12)	3878.7(8)	11.3(3)
C12	5396.3(9)	2261.9(12)	3227.6(8)	12.6(3)
C13	4943.6(9)	3186.0(12)	2601.2(8)	13.6(3)
C14	4646.0(11)	2667.4(14)	1780.0(9)	19.9(3)
C15	5552.2(10)	4132.1(13)	2590.6(8)	15.8(3)
C16	5010.8(9)	1342.4(12)	4375.6(8)	11.5(3)
C17	6081.0(9)	3274.3(13)	5081.1(8)	15.6(3)
C18	6816.4(10)	4146.6(14)	5223.1(9)	18.5(3)
C19	7253.8(10)	4158.1(14)	4577.9(9)	19.5(3)
C20	8407.6(12)	964.1(15)	4408.9(11)	27.6(4)
C21	7508.3(14)	442.0(17)	4052.0(14)	41.8(5)
C22	7825.9(13)	2592.4(18)	2656.5(11)	34.9(4)
C23	9066.6(13)	371.9(17)	4070.0(12)	35.7(5)
C24	8546.0(11)	3035.8(15)	3352.1(10)	23.3(3)
C25	8628.9(15)	4350.0(17)	3288.7(12)	38.5(5)
C26	9305.4(11)	3267.1(16)	5127.8(10)	26.6(4)
C27	9261.7(13)	2904(2)	5937.2(11)	45.3(6)
C28	10215.5(11)	3075.5(18)	5055.2(11)	31.8(4)

Table 3 Anisotropic Displacement Parameters ($Å^2×10^3$) for mo_0806_Snyder_0m. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Si1	15.2(2)	15.3(2)	16.1(2)	-1.17(16)	6.01(15)	-2.10(16)
Si2	18.2(2)	16.9(2)	17.5(2)	1.62(16)	5.34(16)	3.59(17)
O1	15.6(5)	14.5(5)	16.2(5)	-1.5(4)	6.8(4)	0.1(4)
O2	28.5(6)	11.5(5)	15.0(5)	3.9(4)	11.6(5)	2.2(4)
O3	25.0(6)	11.1(5)	14.4(5)	2.1(4)	8.1(4)	2.8(4)
O4	19.6(6)	17.7(6)	25.5(6)	-3.4(5)	8.4(5)	0.5(4)
N1	23.6(7)	18.5(7)	25.6(7)	6.4(6)	10.2(6)	1.8(6)
C00O	26.9(9)	17.0(8)	31.8(9)	-1.8(7)	12.6(7)	-4.8(7)
C1	17.5(8)	49.9(12)	28.9(9)	-9.0(9)	5.5(7)	-6.3(8)
C2	29.2(10)	30.5(10)	37.8(11)	-1.0(8)	-2.5(8)	10.3(8)
C3	23.7(9)	39.7(11)	20.2(8)	0.5(7)	1.2(7)	-6.4(8)
C4	17.1(7)	26.2(9)	21.2(8)	-3.7(7)	2.1(6)	-1.4(6)
C5	25.6(8)	25.5(9)	20.2(8)	-0.1(7)	11.2(7)	-2.8(7)
C6	14.5(7)	12.2(7)	11.3(6)	0.1(5)	4.6(5)	1.0(5)
C7	15.1(7)	14.8(7)	11.8(7)	2.4(5)	3.5(5)	2.2(6)
C8	18.7(7)	11.1(7)	16.8(7)	2.4(5)	7.7(6)	1.8(6)
C9	18.8(7)	12.9(7)	14.6(7)	-3.3(5)	7.1(6)	-1.7(6)
C10	13.7(7)	13.1(7)	11.2(6)	-1.2(5)	6.2(5)	-1.0(5)
C11	14.3(6)	9.6(6)	10.6(6)	0.7(5)	4.6(5)	0.2(5)
C12	17.3(7)	10.2(7)	11.4(6)	1.6(5)	5.9(5)	2.0(5)
C13	18.8(7)	11.3(7)	11.5(7)	2.8(5)	5.8(5)	1.7(6)
C14	28.3(8)	19.0(8)	12.3(7)	1.2(6)	5.7(6)	2.5(6)
C15	20.5(7)	14.8(7)	13.9(7)	4.2(6)	7.7(6)	6.0(6)
C16	12.0(6)	12.4(7)	9.3(6)	-0.4(5)	1.5(5)	-1.4(5)
C17	17.7(7)	16.1(7)	12.9(7)	-1.2(6)	4.3(6)	0.0(6)
C18	16.8(7)	19.1(8)	18.1(7)	-5.7(6)	2.6(6)	-1.6(6)
C19	17.4(7)	16.1(7)	25.4(8)	-2.1(6)	6.6(6)	-0.4(6)
C20	35.2(10)	19.6(8)	27.9(9)	5.2(7)	8.9(7)	6.4(7)
C21	39.9(11)	20.2(9)	66.6(15)	5.8(9)	17.3(11)	-2.3(8)
C22	40.1(11)	41.9(11)	20.9(9)	3.5(8)	5.7(8)	6.9(9)
C23	39.6(11)	23.0(9)	41.5(11)	-1.8(8)	6.8(9)	12.6(8)
C24	24.6(8)	25.2(9)	22.2(8)	3.4(7)	10.0(7)	5.6(7)
C25	51.6(13)	30.8(11)	36.3(11)	12.4(9)	17.8(10)	0.4(9)
C26	21.2(8)	30.6(9)	25.6(9)	-3.3(7)	2.7(7)	5.4(7)
C27	28.4(10)	81.5(17)	22.2(9)	-1.5(10)	1.0(8)	7.8(11)
C28	21.1(9)	36.3(10)	35.2(10)	-5.3(8)	3.3(7)	0.9(8)

Table 4 Bond Lengths for mo_0806_Snyder_0m.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Si1	O1	1.6545(11)	C7	C13	1.564(2)
Si1	C00O	1.8594(17)	C8	C9	1.503(2)
Si1	C4	1.8879(17)	C9	C10	1.329(2)
Si1	C5	1.8543(16)	C10	C11	1.5282(19)
Si2	O4	1.6473(12)	C10	C17	1.515(2)
Si2	C20	1.8787(18)	C11	C12	1.5354(19)
Si2	C24	1.8784(17)	C11	C16	1.5081(19)
Si2	C26	1.8871(18)	C12	C13	1.5697(19)
O1	C6	1.4082(17)	C13	C14	1.532(2)
O2	C16	1.3164(17)	C13	C15	1.476(2)
O3	C16	1.2199(17)	C17	C18	1.525(2)
O4	C19	1.4313(19)	C18	C19	1.518(2)
N1	C15	1.146(2)	C20	C21	1.538(3)
C1	C4	1.535(2)	C20	C23	1.532(3)
C2	C4	1.532(3)	C22	C24	1.531(3)
C3	C4	1.538(2)	C24	C25	1.530(3)
C6	C7	1.532(2)	C26	C27	1.529(3)
C6	C11	1.5538(19)	C26	C28	1.534(2)
C7	C8	1.524(2)			

Table 5 Bond Angles for mo_0806_Snyder_0m.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
O1	Si1	C00O	111.67(7)	C17	C10	C11	116.53(12)
O1	Si1	C4	108.45(7)	C10	C11	C6	111.21(11)
O1	Si1	C5	105.12(7)	C10	C11	C12	108.79(11)
C00O	Si1	C4	110.38(8)	C12	C11	C6	99.98(11)
C5	Si1	C00O	110.29(8)	C16	C11	C6	110.37(11)
C5	Si1	C4	110.80(8)	C16	C11	C10	112.44(11)
O4	Si2	C20	104.43(7)	C16	C11	C12	113.41(11)
O4	Si2	C24	111.73(7)	C11	C12	C13	104.11(11)
O4	Si2	C26	107.81(7)	C7	C13	C12	104.94(11)
C20	Si2	C26	112.25(8)	C14	C13	C7	110.82(12)
C24	Si2	C20	111.04(8)	C14	C13	C12	112.00(12)
C24	Si2	C26	109.47(8)	C15	C13	C7	111.80(12)
C6	O1	Si1	127.42(9)	C15	C13	C12	109.53(12)
C19	O4	Si2	126.93(10)	C15	C13	C14	107.80(12)
C1	C4	Si1	109.82(12)	N1	C15	C13	178.55(16)
C1	C4	C3	109.04(14)	O2	C16	C11	113.29(12)

C2	C4	Si1	110.07(11)	O3	C16	O2	123.49(13)
C2	C4	C1	109.20(15)	O3	C16	C11	123.21(12)
C2	C4	C3	108.62(15)	C10	C17	C18	115.81(13)
C3	C4	Si1	110.07(11)	C19	C18	C17	113.04(12)
O1	C6	C7	112.37(11)	O4	C19	C18	109.88(13)
O1	C6	C11	114.34(11)	C21	C20	Si2	112.97(13)
C7	C6	C11	100.05(11)	C23	C20	Si2	112.64(13)
C6	C7	C13	102.38(11)	C23	C20	C21	110.25(16)
C8	C7	C6	108.05(11)	C22	C24	Si2	113.73(12)
C8	C7	C13	114.14(12)	C25	C24	Si2	112.21(12)
C9	C8	C7	110.93(12)	C25	C24	C22	109.50(15)
C10	C9	C8	123.30(13)	C27	C26	Si2	112.26(14)
C9	C10	C11	119.48(13)	C27	C26	C28	110.28(15)
C9	C10	C17	123.78(13)	C28	C26	Si2	114.38(12)

Crystal growth of $C_{16}H_{19}NO_4$: Pei Qu (prof. Scott Snyder's group).

Data collected/reported: Kate Jesse /Alexander S. Filatov, November / 2020 (X-ray Laboratory, Searle B013, Department of Chemistry, the University of Chicago, Chicago, Il).

General information: The diffraction data were measured at 100 K on a Bruker D8 VENTURE diffractometer equipped with a microfocus Mo-target X-ray tube (λ = 0.71073 Å) and PHOTON 100 CMOS detector. Data were collected using ω scans to survey a sphere of reciprocal space. Data reduction and integration were performed with the Bruker APEX3 software package (Bruker AXS, version 2017.3-0, 2018). Data were scaled and corrected for absorption effects using the multi-scan procedure as implemented in SADABS (Bruker AXS, version 2014/5, Krause, Herbst-Irmer, Sheldrick & Stalke, *J. Appl. Cryst.* **2015**, *48*, 3-10). The structure was solved by SHELXT (Version 2018/2: Sheldrick, G. M. *Acta Crystallogr*. **2015**, ***A71***, 3-8) and refined by a full-matrix least-squares procedure using OLEX2 (O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann. J. Appl. Crystallogr. **2009**, *42*, 339-341) (XL refinement program version 2018/3, Sheldrick, G. M. Acta Crystallogr. **2015**, *C71*, 3-8). Crystallographic data and details of the data collection and structure refinement are listed in Table 1.

Specific details for structure refinement: All atoms were refined with anisotropic thermal parameters. All hydrogen atoms were included in idealized positions for structure factor calculations except the hydrogen atom of the NH group. This atom was found in the difference Fourier map and refined without geometric restraints. All structures are drawn with thermal ellipsoids at 50% probability.

Table 1 Crystal data and structure refinement for 0957_PQ_Snyder_1.

Identification code	0957_PQ_Snyder_1
Empirical formula	$C_{16}H_{19}NO_4$
Formula weight	289.32
Temperature/K	100(2)
Crystal system	triclinic
Space group	P-1
a/Å	8.2800(6)
b/Å	8.7370(6)
c/Å	10.9196(8)
α/°	66.854(2)
β/°	72.523(2)
γ/°	70.057(2)
Volume/Å^3	670.06(8)
Z	2
ρ_{calc}g/cm^3	1.434
μ/mm^{-1}	0.103
F(000)	308.0
Crystal size/mm^3	0.245 × 0.124 × 0.111
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.134 to 60.026
Index ranges	$-10 \leq h \leq 11$, $-11 \leq k \leq 12$, $-15 \leq l \leq 15$
Reflections collected	13695
Independent reflections	3372 [R_{int} = 0.0367, R_{sigma} = 0.0475]
Data/restraints/parameters	3372/0/195
Goodness-of-fit on F^2	1.025
Final R indexes [I>=2σ (I)]	R_1 = 0.0463, wR_2 = 0.0972
Final R indexes [all data]	R_1 = 0.0741, wR_2 = 0.1072
Largest diff. peak/hole / e Å^{-3}	0.53/-0.26

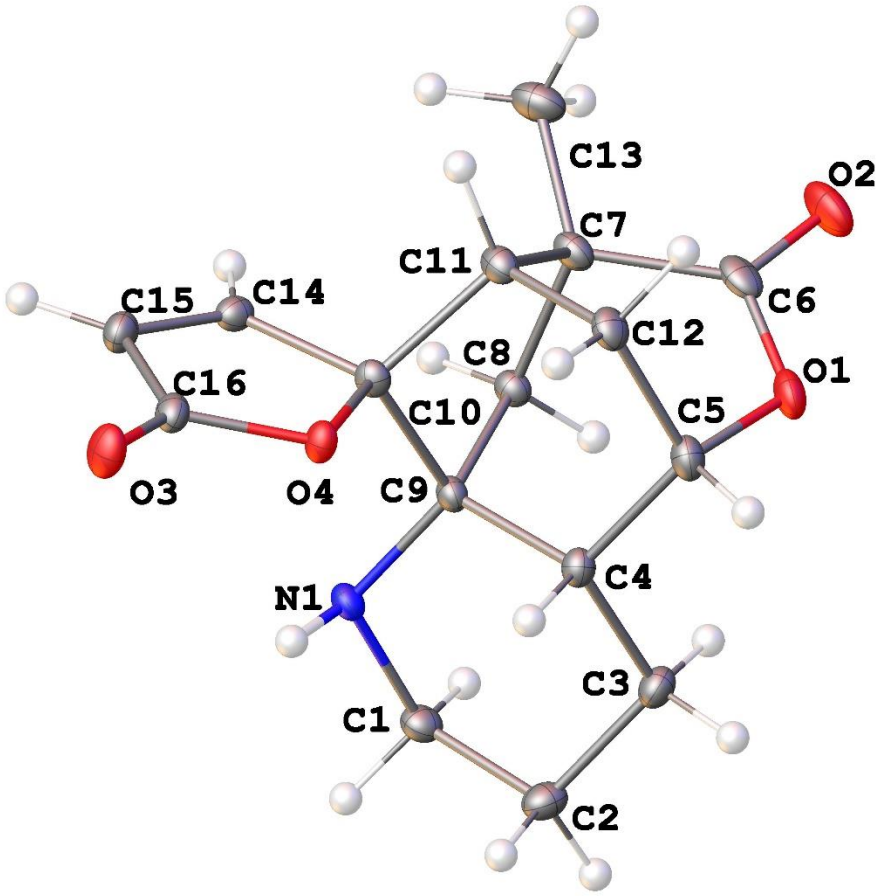
$R_{int} = \Sigma \mid F_o^2 - \langle F_o^2 \rangle \mid / \Sigma \mid F_o^2 \mid$

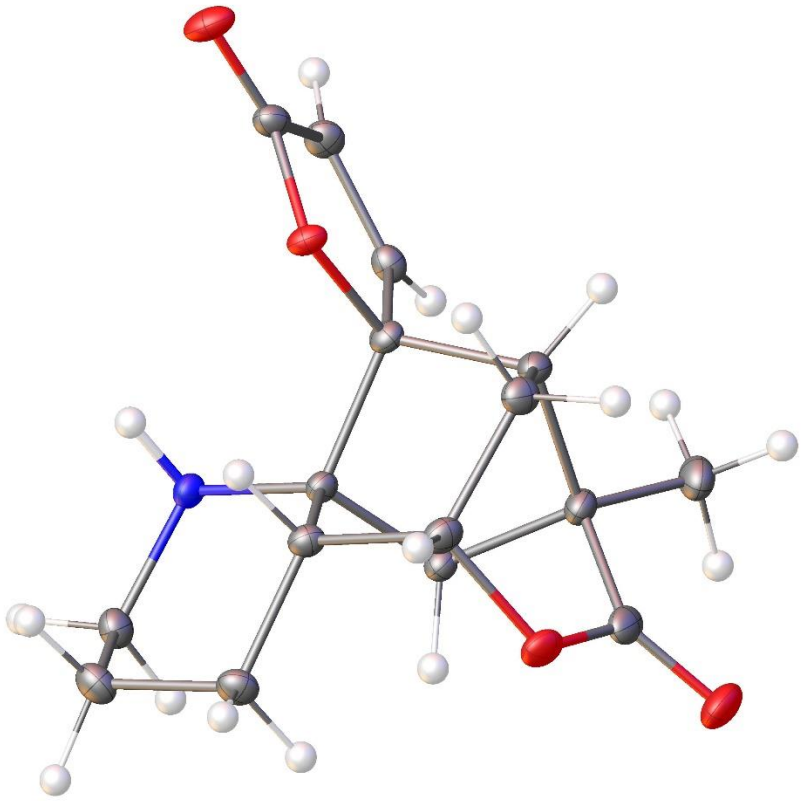
$R1 = \Sigma \mid \mid F_o \mid - \mid F_c \mid \mid / \Sigma \mid F_o \mid$

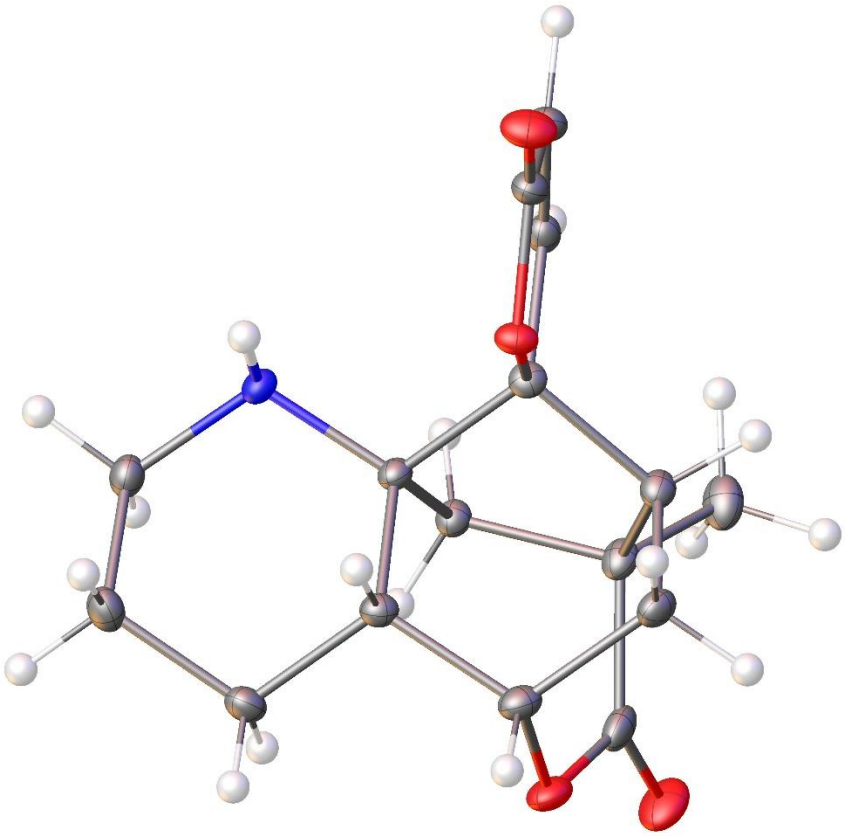
$wR2 = [\Sigma [w (F_o^2 - F_c^2)^2] / \Sigma [w (F_o^2)^2]]^{1/2}$

Goodness-of-fit = $[\Sigma [w (F_o^2 - F_c^2)^2] / (n-p)]^{1/2}$

n: number of independent reflections; p: number of refined parameters


C13
O2
C7
C11
C15
C14
C6
C12
C8
O1
C16
C10
C5
O3
O4
C9
C4
N1
C3
C1
C2





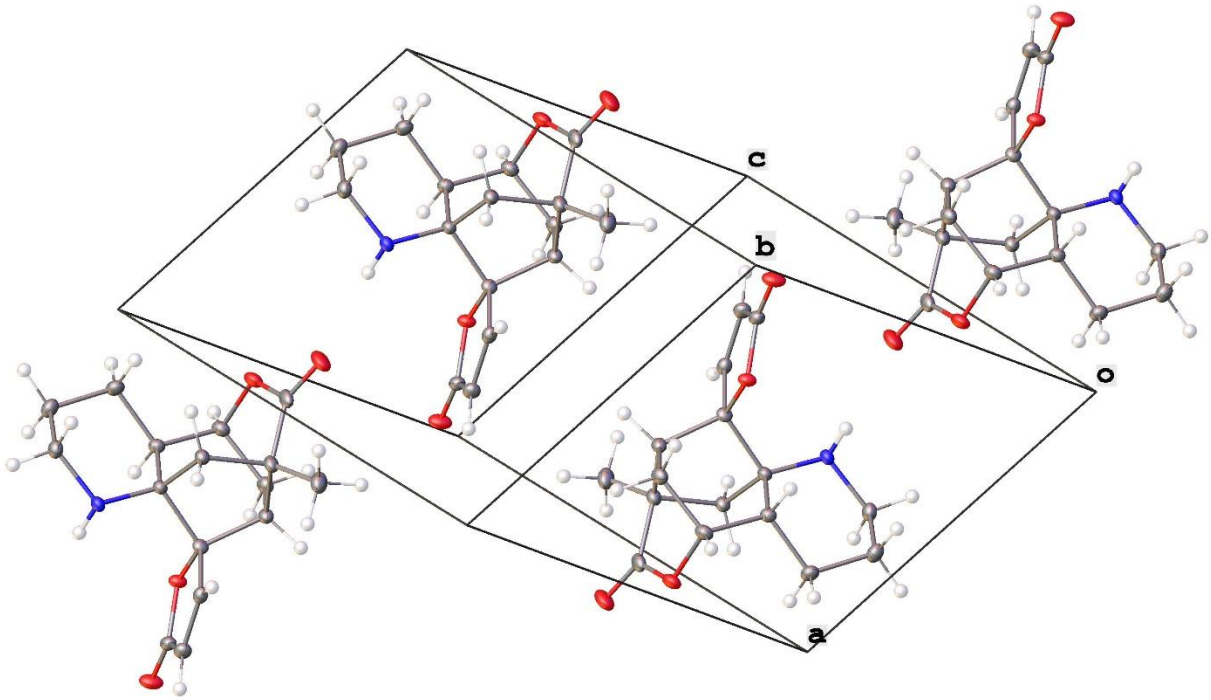

c
b
o
a

Table 2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for 0957_PQ_Snyder_1. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
O1	297.5(13)	6835.6(14)	8952.0(11)	17.4(3)
O2	-1260.9(14)	7811.5(15)	7362.8(13)	24.9(3)
O3	9122.6(13)	4210.9(14)	7139.5(11)	18.6(3)
O4	6233.3(12)	5383.5(13)	7623.0(10)	12.2(2)
N1	4863.2(16)	9240.9(16)	7284.6(12)	11.9(3)
C1	3970.2(19)	10508.8(19)	8000.6(15)	14.7(3)
C2	3261(2)	9736(2)	9505.0(15)	16.2(3)
C3	2095.6(19)	8602.4(19)	9703.3(15)	14.8(3)
C4	3095.3(18)	7229.5(18)	9023.9(14)	11.9(3)
C5	2038.5(18)	5959.6(19)	9297.1(16)	14.6(3)
C6	171.8(19)	7317.1(19)	7646.2(17)	16.5(3)
C7	1863.2(18)	7402.8(19)	6596.2(15)	13.9(3)
C8	2382.9(18)	8929.1(18)	6655.1(15)	11.9(3)
C9	3829.8(18)	8063.0(18)	7504.4(14)	10.8(3)
C10	4884.4(18)	6622.8(18)	6881.0(14)	11.2(3)
C11	3424.6(18)	5797.1(19)	7020.0(15)	13.0(3)
C12	2935.5(19)	4719.3(19)	8494.0(15)	14.4(3)
C13	1558(2)	7680(2)	5209.0(17)	20.0(4)
C14	5875.8(19)	7233.6(19)	5464.0(15)	12.6(3)
C15	7554.5(19)	6404.2(19)	5396.1(15)	14.5(3)
C16	7820.0(19)	5211.8(19)	6753.6(15)	13.4(3)

Table 3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for 0957_PQ_Snyder_1. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O1	9.2(5)	19.1(6)	23.8(6)	-8.3(5)	1.0(4)	-5.4(4)
O2	11.8(5)	25.6(6)	41.4(8)	-14.0(6)	-8.3(5)	-3.3(5)
O3	10.8(5)	20.3(6)	18.2(6)	-4.7(5)	-2.1(4)	1.4(4)
O4	8.6(5)	12.9(5)	11.6(5)	-3.0(4)	-1.1(4)	-0.6(4)
N1	9.6(6)	12.2(6)	15.2(7)	-4.8(5)	-2.0(5)	-4.1(5)
C1	15.9(7)	13.7(7)	16.8(8)	-6.0(6)	-3.4(6)	-5.3(6)
C2	20.3(8)	15.6(8)	14.4(8)	-6.9(6)	-2.5(6)	-4.7(6)
C3	14.7(7)	15.8(8)	13.0(8)	-6.2(6)	1.0(6)	-4.0(6)

Table 3 Anisotropic Displacement Parameters ($Å^2×10^3$) for 0957_PQ_Snyder_1. The Anisotropic displacement factor exponent takes the form: $-2π^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+…]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C4	10.3(7)	11.9(7)	12.3(7)	-3.7(6)	-1.2(5)	-2.5(5)
C5	10.7(7)	14.9(8)	16.7(8)	-4.3(6)	-0.6(6)	-4.1(6)
C6	13.5(7)	11.7(7)	27.8(9)	-8.4(7)	-4.7(6)	-4.3(6)
C7	10.9(7)	13.4(7)	19.4(8)	-6.2(6)	-5.1(6)	-2.3(6)
C8	10.5(7)	11.3(7)	14.3(7)	-4.4(6)	-3.3(6)	-2.2(6)
C9	8.6(6)	11.2(7)	13.0(7)	-4.4(6)	-1.3(5)	-2.9(5)
C10	9.7(7)	10.9(7)	12.0(7)	-2.6(6)	-3.9(5)	-1.0(5)
C11	10.5(7)	11.9(7)	17.4(8)	-6.4(6)	-3.1(6)	-1.6(6)
C12	13.3(7)	11.9(7)	17.9(8)	-4.2(6)	-1.2(6)	-5.3(6)
C13	19.1(8)	19.2(8)	26.7(9)	-10.1(7)	-11.2(7)	-1.7(6)
C14	15.2(7)	12.0(7)	11.5(7)	-3.9(6)	-1.9(6)	-5.1(6)
C15	13.9(7)	16.2(8)	12.7(8)	-5.2(6)	0.9(6)	-5.4(6)
C16	11.5(7)	13.7(7)	15.3(8)	-7.0(6)	0.7(6)	-3.6(6)

Table 4 Bond Lengths for 0957_PQ_Snyder_1.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C5	1.4673(17)	C5	C12	1.517(2)
O1	C6	1.3448(19)	C6	C7	1.524(2)
O2	C6	1.2064(18)	C7	C8	1.563(2)
O3	C16	1.2022(17)	C7	C11	1.570(2)
O4	C10	1.4510(16)	C7	C13	1.522(2)
O4	C16	1.3705(17)	C8	C9	1.5379(19)
N1	C1	1.4697(19)	C9	C10	1.541(2)
N1	C9	1.4602(18)	C10	C11	1.550(2)
C1	C2	1.523(2)	C10	C14	1.496(2)
C2	C3	1.522(2)	C11	C12	1.523(2)
C3	C4	1.526(2)	C14	C15	1.325(2)
C4	C5	1.527(2)	C15	C16	1.469(2)
C4	C9	1.549(2)			

Table 5 Bond Angles for 0957_PQ_Snyder_1.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C6	O1	C5	117.57(11)	N1	C9	C4	113.01(11)
C16	O4	C10	109.87(11)	N1	C9	C8	111.47(12)
C9	N1	C1	113.32(11)	N1	C9	C10	111.90(11)
N1	C1	C2	114.40(12)	C8	C9	C4	111.92(11)
C3	C2	C1	110.21(12)	C8	C9	C10	98.97(11)
C2	C3	C4	110.14(12)	C10	C9	C4	108.73(11)
C3	C4	C5	112.25(12)	O4	C10	C9	112.54(11)
C3	C4	C9	110.81(12)	O4	C10	C11	111.16(11)
C5	C4	C9	114.56(12)	O4	C10	C14	103.46(11)
O1	C5	C4	112.05(11)	C9	C10	C11	101.04(11)
O1	C5	C12	106.99(11)	C14	C10	C9	114.44(12)
C12	C5	C4	112.48(12)	C14	C10	C11	114.56(12)
O1	C6	C7	116.79(12)	C10	C11	C7	102.92(11)
O2	C6	O1	118.95(14)	C12	C11	C7	110.33(12)
O2	C6	C7	123.84(15)	C12	C11	C10	109.44(12)
C6	C7	C8	103.51(12)	C5	C12	C11	107.02(12)
C6	C7	C11	112.96(12)	C15	C14	C10	110.06(13)
C8	C7	C11	104.41(11)	C14	C15	C16	108.71(13)
C13	C7	C6	110.36(12)	O3	C16	O4	121.52(13)
C13	C7	C8	113.56(12)	O3	C16	C15	130.64(14)
C13	C7	C11	111.69(12)	O4	C16	C15	107.84(12)
C9	C8	C7	104.70(11)				

Data collected/reported: Kate Jesse /Alexander S. Filatov, December / 2020 (X-ray Laboratory, Searle B013, Department of Chemistry, the University of Chicago, Chicago, Il).

General information: The diffraction data were measured at 100 K on a Bruker D8 VENTURE diffractometer equipped with a microfocus Mo-target X-ray tube (λ = 0.71073 Å) and PHOTON 100 CMOS detector. Data were collected using ω scans to survey a sphere of reciprocal space. Data reduction and integration were performed with the Bruker APEX3 software package (Bruker AXS, version 2017.3-0, 2018). Data were scaled and corrected for absorption effects using the multi-scan procedure as implemented in SADABS (Bruker AXS, version 2014/5, Krause, Herbst-Irmer, Sheldrick & Stalke, *J. Appl. Cryst.* **2015**, *48*, 3-10). The structure was solved by SHELXT (Version 2018/2: Sheldrick, G. M. *Acta Crystallogr*. **2015**, ***A71***, 3-8) and refined by a full-matrix least-squares procedure using OLEX2 (O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann. J. Appl. Crystallogr. **2009**, *42*, 339-341) (XL refinement program version 2018/3, Sheldrick, G. M. Acta Crystallogr. **2015**, *C71*, 3-8). Crystallographic data and details of the data collection and structure refinement are listed in Table 1.

Specific details for structure refinement: All atoms were refined with anisotropic thermal parameters. All hydrogen atoms were included in idealized positions for structure factor calculations except the hydrogen atom of the OH group. This atom was found in the difference Fourier map and refined without any restraints. All structures are drawn with thermal ellipsoids at 50% probability.

Table 1 Crystal data and structure refinement for 0961_PQ_Snyder_2.

Identification code	0961_PQ_Snyder_2
Empirical formula	$C_{16}H_{19}NO_4$
Formula weight	289.32
Temperature/K	100(2)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	6.9925(5)
b/Å	22.6400(15)
c/Å	8.7190(6)
α/°	90
β/°	107.547(2)
γ/°	90
Volume/Å^3	1316.08(16)
Z	4
ρ_{calc}g/cm^3	1.460
μ/mm^{-1}	0.105
F(000)	616.0
Crystal size/mm^3	0.256 × 0.161 × 0.096
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.22 to 61.02
Index ranges	$-9 \le h \le 9$, $-30 \le k \le 31$, $-12 \le l \le 12$
Reflections collected	20251
Independent reflections	3851 [R_{int} = 0.0478, R_{sigma} = 0.0464]
Data/restraints/parameters	3851/0/195
Goodness-of-fit on F^2	1.044
Final R indexes [I>=2σ (I)]	R_1 = 0.0528, wR_2 = 0.1147
Final R indexes [all data]	R_1 = 0.0846, wR_2 = 0.1270
Largest diff. peak/hole / e Å^{-3}	0.49/-0.24

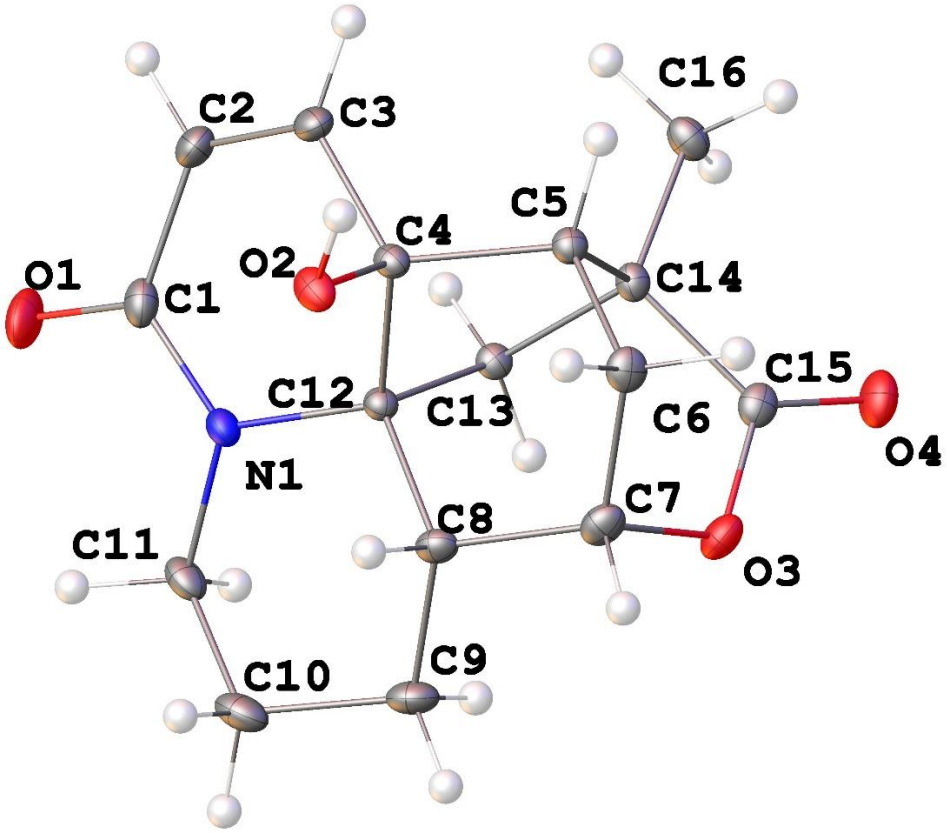
$R_{int} = \Sigma \mid F_o^2 - \langle F_o^2 \rangle \mid / \Sigma \mid F_o^2 \mid$

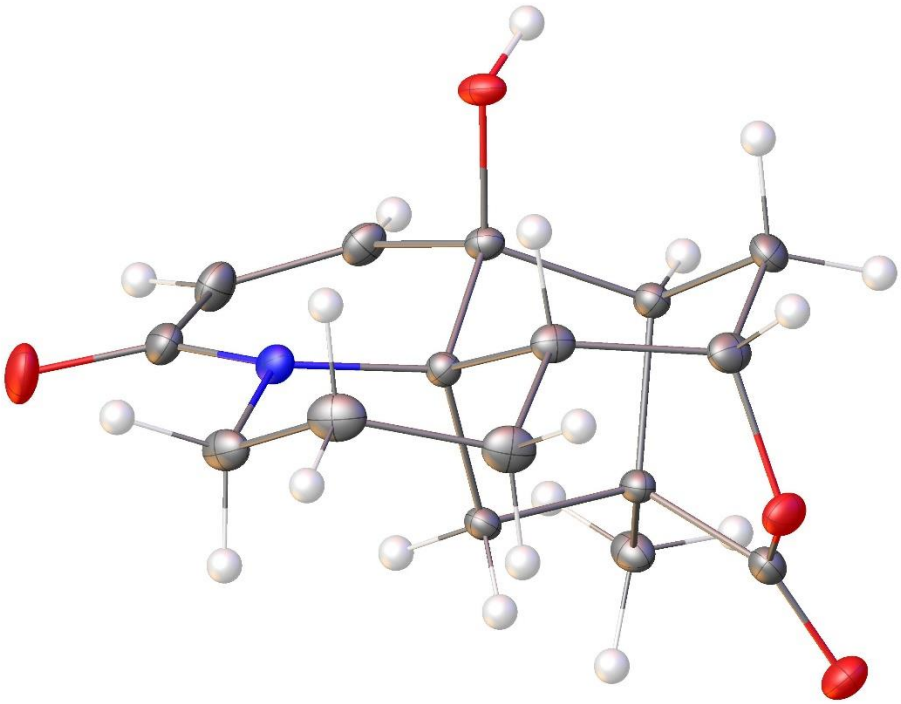
$R1 = \Sigma \mid \mid F_o \mid - \mid F_c \mid \mid / \Sigma \mid F_o \mid$

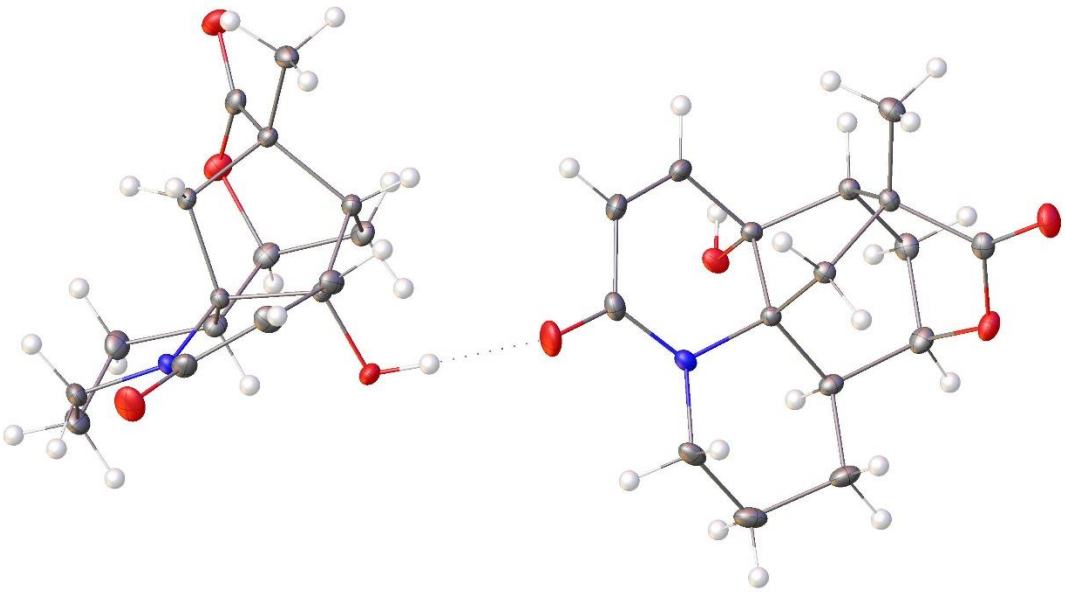
$wR2 = [\Sigma [w (F_o^2 - F_c^2)^2] / \Sigma [w (F_o^2)^2]]^{1/2}$

Goodness-of-fit = $[\Sigma [w (F_o^2 - F_c^2)^2] / (n-p)]^{1/2}$

n: number of independent reflections; p: number of refined parameters


C16
C2
C3
C5
C4
O1
O2
C14
C1
C15
C12
C13
C6
O4
N1
C7
C8
C11
O3
C10
C9





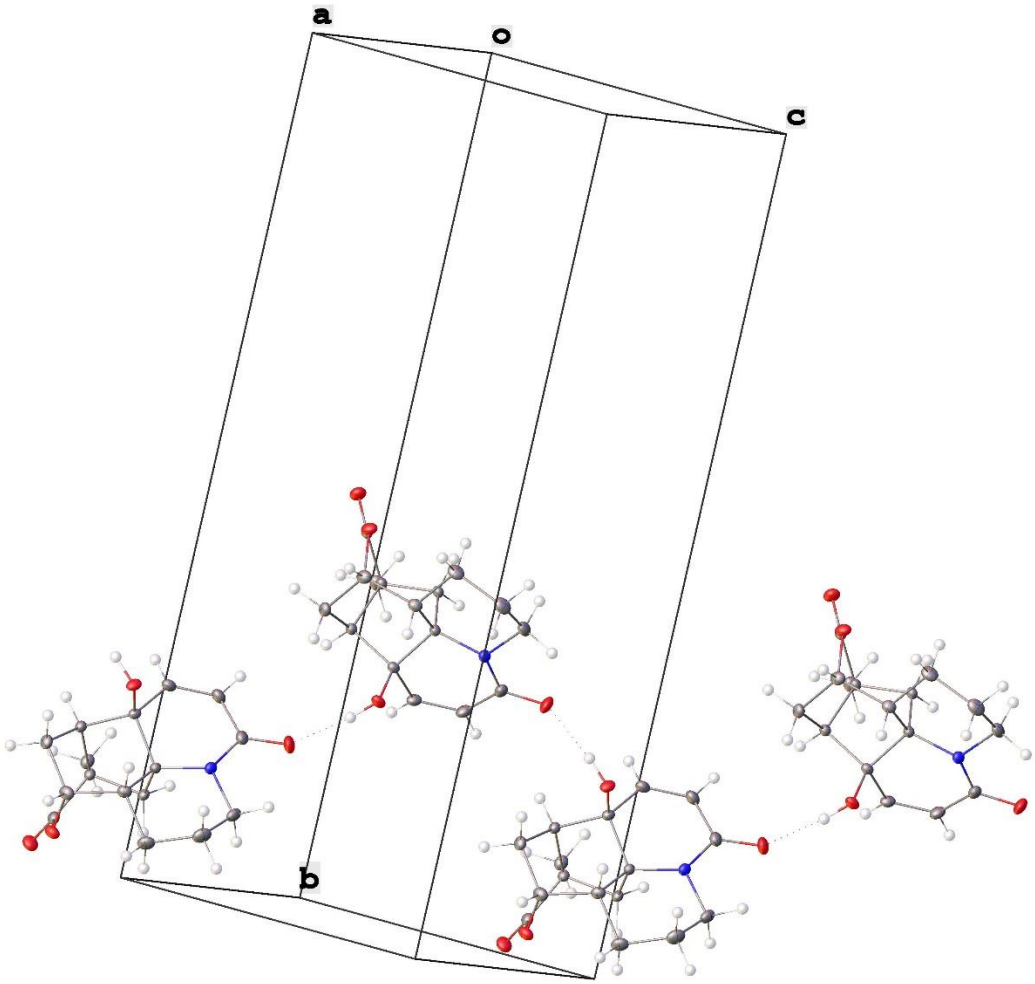

a
o
c
b

Table 2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for 0961_PQ_Snyder_2. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
O1	3938(2)	6965.3(6)	8801.5(15)	29.5(3)
O2	8423.6(17)	7299.0(5)	6039.3(13)	17.7(2)
O3	8312.5(17)	5405.2(5)	4428.6(14)	19.9(3)
O4	5812.3(19)	5132.9(5)	2344.0(14)	24.6(3)
N1	6245(2)	6537.0(6)	7822.2(14)	14.9(3)
C1	4733(3)	6922.3(7)	7713.0(19)	19.1(3)
C2	4028(3)	7289.8(7)	6252.3(19)	20.2(3)
C3	4901(2)	7286.8(7)	5096.1(19)	17.2(3)
C4	6768(2)	6926.4(6)	5302.6(17)	13.0(3)
C5	6894(2)	6622.2(6)	3749.9(17)	13.4(3)
C6	9049(2)	6416.3(7)	4028.0(19)	16.8(3)
C7	9409(2)	5922.3(7)	5255.3(19)	17.8(3)
C8	8866(2)	6097.0(7)	6772.7(18)	15.4(3)
C9	9118(2)	5597.8(7)	7983.9(19)	21.1(3)
C10	8735(3)	5841.0(8)	9487.1(19)	23.7(4)
C11	6657(3)	6098.0(7)	9133.2(18)	19.2(3)
C12	6772(2)	6385.3(6)	6360.8(17)	12.2(3)
C13	5153(2)	5998.0(6)	5231.0(17)	12.7(3)
C14	5480(2)	6070.8(6)	3555.6(17)	13.1(3)
C15	6527(2)	5508.4(7)	3327.1(18)	16.6(3)
C16	3511(2)	6143.3(7)	2227.1(18)	17.8(3)

Table 3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for 0961_PQ_Snyder_2. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O1	43.9(8)	27.0(7)	26.5(6)	-3.8(5)	24.0(6)	4.4(6)
O2	22.3(6)	13.9(5)	15.7(5)	-0.6(4)	4.1(5)	-7.1(4)
O3	19.4(6)	14.4(5)	26.6(6)	-3.3(4)	8.0(5)	2.1(4)
O4	31.2(7)	19.0(6)	25.6(6)	-8.6(5)	11.3(5)	-5.1(5)
N1	19.5(7)	14.4(6)	10.6(6)	0.1(5)	4.5(5)	-0.8(5)
C1	24.5(8)	17.1(8)	17.7(7)	-4.7(6)	9.6(6)	-2.4(6)
C2	23.3(8)	16.8(8)	20.8(8)	-2.0(6)	7.1(7)	5.8(6)
C3	20.3(8)	12.5(7)	17.0(7)	0.5(6)	3.1(6)	3.6(6)

Table 3 Anisotropic Displacement Parameters ($Å^2×10^3$) for 0961_PQ_Snyder_2. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C4	14.7(7)	11.1(7)	12.3(6)	0.7(5)	2.7(5)	-1.3(5)
C5	14.5(7)	12.8(7)	13.4(6)	0.3(5)	4.9(5)	-1.0(5)
C6	13.7(7)	19.2(8)	19.6(7)	-1.2(6)	8.0(6)	-2.7(6)
C7	12.1(7)	17.1(8)	23.9(8)	-1.1(6)	4.9(6)	0.6(6)
C8	12.6(7)	14.7(7)	17.1(7)	1.4(6)	1.4(6)	0.7(6)
C9	19.5(8)	18.0(8)	22.8(8)	6.7(6)	1.6(7)	3.8(6)
C10	26.1(9)	23.0(8)	16.9(8)	6.3(6)	-1.1(7)	-1.5(7)
C11	26.8(8)	18.5(8)	11.7(7)	2.0(6)	4.9(6)	-4.4(6)
C12	13.4(7)	11.7(7)	11.5(6)	0.9(5)	3.9(5)	-0.1(5)
C13	12.7(7)	12.5(7)	13.5(6)	0.7(5)	4.8(5)	-1.7(5)
C14	13.8(7)	13.2(7)	12.9(6)	-1.2(5)	4.8(5)	-2.5(5)
C15	18.4(8)	15.5(7)	18.6(7)	-0.3(6)	9.7(6)	-2.5(6)
C16	16.1(7)	21.8(8)	14.6(7)	-0.5(6)	3.3(6)	-3.8(6)

Table 4 Bond Lengths for 0961_PQ_Snyder_2.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C1	1.2402(19)	C5	C6	1.525(2)
O2	C4	1.4199(18)	C5	C14	1.570(2)
O3	C7	1.4644(19)	C6	C7	1.515(2)
O3	C15	1.3464(19)	C7	C8	1.534(2)
O4	C15	1.2037(19)	C8	C9	1.520(2)
N1	C1	1.352(2)	C8	C12	1.543(2)
N1	C11	1.4761(19)	C9	C10	1.518(2)
N1	C12	1.4699(18)	C10	C11	1.508(2)
C1	C2	1.476(2)	C12	C13	1.532(2)
C2	C3	1.327(2)	C13	C14	1.554(2)
C3	C4	1.504(2)	C14	C15	1.512(2)
C4	C5	1.545(2)	C14	C16	1.517(2)
C4	C12	1.533(2)			

Table 5 Bond Angles for 0961_PQ_Snyder_2.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C15	O3	C7	116.61(12)	C7	C8	C12	111.87(12)
C1	N1	C11	117.06(13)	C9	C8	C7	113.61(13)
C1	N1	C12	119.00(12)	C9	C8	C12	112.27(13)
C12	N1	C11	118.21(12)	C10	C9	C8	108.45(13)
O1	C1	N1	121.23(15)	C11	C10	C9	111.91(13)
O1	C1	C2	120.37(15)	N1	C11	C10	111.66(13)
N1	C1	C2	118.40(13)	N1	C12	C4	112.30(12)
C3	C2	C1	122.82(15)	N1	C12	C8	111.42(12)
C2	C3	C4	119.58(14)	N1	C12	C13	111.18(12)
O2	C4	C3	106.97(12)	C4	C12	C8	107.91(12)
O2	C4	C5	114.03(12)	C13	C12	C4	101.74(11)
O2	C4	C12	110.44(12)	C13	C12	C8	111.88(12)
C3	C4	C5	114.44(12)	C12	C13	C14	104.73(11)
C3	C4	C12	110.47(12)	C13	C14	C5	104.43(11)
C12	C4	C5	100.42(11)	C15	C14	C5	111.72(12)
C4	C5	C14	104.41(11)	C15	C14	C13	104.42(12)
C6	C5	C4	108.15(12)	C15	C14	C16	110.77(12)
C6	C5	C14	109.50(12)	C16	C14	C5	113.16(12)
C7	C6	C5	106.49(12)	C16	C14	C13	111.86(12)
O3	C7	C6	106.94(12)	O3	C15	C14	115.71(13)
O3	C7	C8	113.67(13)	O4	C15	O3	118.82(15)
C6	C7	C8	112.76(13)	O4	C15	C14	125.12(15)

Table 6 Torsion Angles for 0961_PQ_Snyder_2.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
O1	C1	C2	C3	175.92(16)	C6	C5	C14	C16	-138.46(13)
O2	C4	C5	C6	41.62(16)	C6	C7	C8	C9	177.11(13)
O2	C4	C5	C14	158.16(12)	C6	C7	C8	C12	48.71(17)
O2	C4	C12	N1	71.14(15)	C7	O3	C15	O4	161.41(14)
O2	C4	C12	C8	-52.05(15)	C7	O3	C15	C14	-25.02(18)
O2	C4	C12	C13	-169.90(11)	C7	C8	C9	C10	174.53(13)
O3	C7	C8	C9	55.17(17)	C7	C8	C12	N1	178.54(12)
O3	C7	C8	C12	-73.23(16)	C7	C8	C12	C4	-57.74(16)
N1	C1	C2	C3	-4.7(2)	C7	C8	C12	C13	53.37(16)

Table 6 Torsion Angles for 0961_PQ_Snyder_2.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
N1	C12	C13	C14	159.50(11)	C8	C9	C10	C11	59.28(18)
C1	N1	C11	C10	-160.51(14)	C8	C12	C13	C14	-75.20(14)
C1	N1	C12	C4	41.96(18)	C9	C8	C12	N1	49.44(17)
C1	N1	C12	C8	163.15(13)	C9	C8	C12	C4	173.16(12)
C1	N1	C12	C13	-71.29(17)	C9	C8	C12	C13	-75.72(15)
C1	C2	C3	C4	-4.0(2)	C9	C10	C11	N1	-53.07(18)
C2	C3	C4	O2	-90.57(17)	C11	N1	C1	O1	10.8(2)
C2	C3	C4	C5	142.10(15)	C11	N1	C1	C2	-168.53(14)
C2	C3	C4	C12	29.67(19)	C11	N1	C12	C4	-165.46(13)
C3	C4	C5	C6	165.24(12)	C11	N1	C12	C8	-44.26(17)
C3	C4	C5	C14	-78.21(15)	C11	N1	C12	C13	81.29(16)
C3	C4	C12	N1	-47.00(16)	C12	N1	C1	O1	163.72(15)
C3	C4	C12	C8	-170.19(12)	C12	N1	C1	C2	-15.6(2)
C3	C4	C12	C13	71.96(14)	C12	N1	C11	C10	46.38(18)
C4	C5	C6	C7	68.30(15)	C12	C4	C5	C6	-76.46(14)
C4	C5	C14	C13	-15.94(14)	C12	C4	C5	C14	40.08(14)
C4	C5	C14	C15	-128.23(12)	C12	C8	C9	C10	-57.29(17)
C4	C5	C14	C16	105.94(14)	C12	C13	C14	C5	-14.46(14)
C4	C12	C13	C14	39.76(14)	C12	C13	C14	C15	102.97(13)
C5	C4	C12	N1	-168.17(11)	C12	C13	C14	C16	-137.19(13)
C5	C4	C12	C8	68.64(13)	C13	C14	C15	O3	-60.53(16)
C5	C4	C12	C13	-49.21(13)	C13	C14	C15	O4	112.59(16)
C5	C6	C7	O3	73.38(14)	C14	C5	C6	C7	-44.89(16)
C5	C6	C7	C8	-52.27(16)	C15	O3	C7	C6	-36.99(17)
C5	C14	C15	O3	51.77(17)	C15	O3	C7	C8	88.12(16)
C5	C14	C15	O4	-135.12(16)	C16	C14	C15	O3	178.91(13)
C6	C5	C14	C13	99.66(13)	C16	C14	C15	O4	-8.0(2)
C6	C5	C14	C15	-12.62(16)					