Total Synthesis of Norcembrenolide B and Scabrolide D

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Supporting Information

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General Techniques

All reagents were commercially obtained (Aldrich, Acros, Strem) at highest commercial quality and used without further purification except where noted. Air- and moisture-sensitive liquids and solutions were transferred via syringe or stainless steel cannula. Organic solutions were concentrated by rotary evaporation below 40 °C at approximately 15 mmHg. All non-aqueous reactions were carried out under anhydrous conditions using flame-dried glassware within an argon atmosphere in dry, freshly distilled solvents, unless otherwise noted. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (CH_2Cl_2), toluene ($PhCH_3$) and benzene (PhH) were purified by passage through a bed of activated alumina.[1] Dimethylformamide (DMF) were distilled from calcium hydride under reduced pressure (20 mmHg) and stored over 4Å molecular sieves until needed. Yields refer to chromatographically and spectroscopically (^{1}H NMR, ^{13}C NMR) homogeneous materials, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as the visualizing agent and 10% ethanolic phosphomolybdic acid (PMA) or Potassium Permanganate solution ($KMnO_4$) in water and heat as developing agents. E. Merck silica gel (60, particle size 0.040-0.063 mm) was used for flash chromatography. Preparative thin-layer chromatography separations were carried out on 0.25 or 0.50 mm E. Merck silica gel plates (60F-254). NMR spectra were recorded on Varian Mercury 300, 400 and/or Jeol Unity 500 MHz instruments and calibrated using the residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad, dd = doublet of doublet, dt = doublet of triplet. Optical rotations were recorded on a Jasco P-1010 polarimeter and values are reported as follows: $[\alpha]T\lambda$ (c: g/100mL, solvent). High resolution mass spectra (HRMS) were recorded on a VG 7070 HS or on a VG ZAB-ZSE mass spectrometers. X-ray data were recorded on a Bruker SMART APEX 3kW Sealed Tube X-ray diffraction system.

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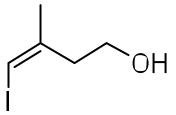
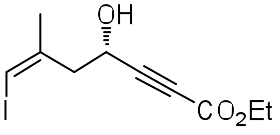
[1] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15,* 1518-1520.

Experimental Procedures

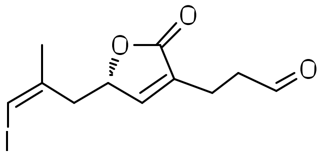


Vinyl-iodo alcohol (i): To a solution of $ZrCp_2Cl_2$ (5.00 g, 17.12 mmol, 0.2 eq) in 1,2-dichloroethane (140 mL) at 0 °C was added a solution of trimethylaluminum (2M, 107 mL, 214 mmol, 2.5 eq) in hexanes dropwise. A solution of but-3-yn-1-ol (6.49 mL, 86 mmol) in 1,2-dichloroethane (20 mL) was then added dropwise. The solution was stirred at rt for 24h. The solution was then warmed to 86 °C and gently refluxed for 4 days. The reaction was then cooled to -40 °C and a solution of iodine (43.5 g, 171 mmol, 2 eq) in 100 mL of dry THF was added via cannula. The solution turned black and was stirred for 30 minutes. The reaction was warmed up to 0 °C and a solution of sat. K_2CO_3 was added very slowly (the solution frothed and bubbled) until eventually turning yellow with aluminum gel precipitate. Ether (250 mL) was added and the solution was filtered through fritted funnel. The gel was extracted with a large amount of ether to remove all organics. 200 mL of water was added to the organic layer which was separated. The aqueous layer was then extracted 3x with ether. The combined organic layers were washed once with brine, dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (up to 20% EtOAc in hexanes) of the crude mixture gave alcohol **i** (9.3 g, 43.9 mmol, 51% yield) as a light brown oil. R_f=0.30 (20% EtOAc in hexanes), ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.01 (d, 1H, *J*=1.4 Hz), 3.78 (t, 2H, *J*=6.7 Hz), 2.53 (t, 2H, *J*=6.7 Hz), 1.94 (d, 3H, *J*=1.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.3, 76.3, 60.1, 41.6, 23.8.

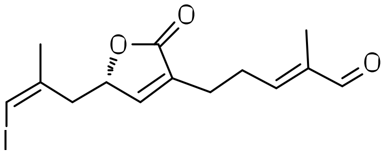


Alkyne (ii): To an oven-dried flask was added dry HMDS (bis(trimethylsilyl)amine) (19.93 mL, 94 mmol, 3 eq) and THF (95 mL). The solution was cooled to -78 °C and n-BuLi (1.6M in hexanes, 56.7 mL, 91 mmol, 2.9 eq) was added dropwise. The solution turned yellow and was then warmed up to 0 °C and stirred for 20 minutes. The reaction was cooled back down to -78 °C and a solution of ethyl propiolate (9.51 mL, 94 mmol, 3 eq) in THF (60 mL) was added dropwise over 30 minutes. The solution remained pale yellow. The reaction was stirred at -78 °C for 1 hour. During this time, to a solution of the alcohol **i**

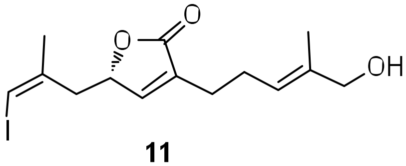
(6.63 g, 31.3 mmol) in CH_2Cl_2 (156 mL) at rt was added $NaHCO_3$ (15.76 g, 188 mmol, 6 eq) followed by Dess-Martin periodinate (17.24 g, 40.7 mmol, 1.3 eq) in one portion. After 15 minutes, the reaction was completed. A 1:1:1 mixture of aq. sat. $Na_2S_2O_3$, aq. sat. $NaHCO_3$ and water (160 mL) was added slowly to the CH_2Cl_2 solution and was stirred vigorously for 20 minutes. Layers were separated and the aqueous layer was extracted 3x with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure at rt to yield aldehyde which was used without further purification. The aldehyde was then taken up in dry THF (50 mL) and was cooled to -78 °C in a separate cooling bath. The cold aldehyde solution was added via cannula quickly to the solution of the alkyne at -78 °C. The solution turned dark red and was stirred for 30 minutes at -78 °C. The reaction was then quenched with sat. NH_4Cl solution (100 mL). The organic layer was separated, and the aqueous layer was extracted 3x with ether. The combined organic layers were washed once with Brine, dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (up to 18% EtOAc in hexanes) of the crude mixture gave alkyne **iii** (5.54 g, 17.98 mmol, 65% yield over 2 steps) as a light red oil. R_f=0.34 (silica, 20% EtOAc in hexanes),^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.13 (d, 1H, *J*=1.4 Hz), 4.72 (td, 1H, *J*=6.1 Hz, *J*=8.3 Hz), 4.25 (q, 2H, *J*=7.1 Hz), 2.80 (dd, 1H, *J*=8.3 Hz, *J*= 13.6Hz), 2.65 (dd, 1H, *J*=6.0 Hz, *J*=13.6 Hz), 2.00 (d, 3H, *J*=1.4 Hz), 1.32 (t, 3H, *J*=7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.3, 142.4, 86.9, 78.4, 76.7, 62.2, 60.1, 45.3, 24.6, 13.9; HRMS calcd. for (M+Na$^+$) 330.9802, found 330.9803.



Aldehyde (iii): To a solution of the alkyne **ii** (0.592 g, 1.921 mmol) in dry DMF (3.84 mL) was added allyl alcohol (0.261 mL, 3.84 mmol), CSA (0.112 g, 0.480 mmol) under an argon atmosphere. The reaction mixture was sparged with argon for 15 minutes before adding Tris(acetonitrile)cyclopentadienylruthenium (II) hexafluorophosphate (0.042 g, 0.096 mmol). The reaction was heated to 50 °C for 1.5 hrs. The reaction mixture was then quenched with saturated $NaHCO_3$ solution and extracted 4x with diethyl ether. Organics were combined dried and concentrated. Flash chromatography (up to 40% EtOAc in hexanes) of the crude mixture gave aldehyde **iv** (0.314 g, 0.98 mmol, 51% yield) as a dark orange oil, R_f=0.32 (silica, 40% EtOAc in hexanes),^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.73 (s, 1H), 7.11 (q, 1H, *J*=1.4 Hz), 6.06 (d, 1H, *J*=1.4 Hz), 5.01 (qdd, 1H, *J*=1.6 Hz, *J*=6.1 Hz, *J*=7.7 Hz), 2.73 (t, 2H, *J*=7.0 Hz), 2.57 (m, 3H), 2.49 (dd, 1H, *J*=7.5 Hz, *J*=13.6 Hz), 1.92 (d, 3H, *J*=1.5 Hz) ;^{13}C NMR (100 MHz, $CDCl_3$) δ: 200.3, 172.7, 148.6, 142.0, 132.4,79.3, 78.6, 42.2, 40.9, 24.6, 17.8; HRMS calcd. for ($M+H^+$) 320.9982, found 320.9884.



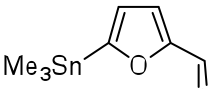
Alpha-Beta Unsaturated Aldehyde (iv): To a solution of aldehyde **iii** (0.680 g, 2.124 mmol) in dry benzene (14.16 mL) was added 2-(triphenylphosphoranylidene) propanal (1.352 g, 4.25 mmol, 2eq) in a microwave tube. The reaction mixture was sparged with argon for 10 minutes. The reaction was then microwaved for 40 minutes at 120 °C. The reaction was quenched with sat. NH_4Cl solution (10 mL), the organic layer was separated and the aqueous layer was extracted 3x with ethyl acetate. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (up to 30% EtOAc in hexanes) of the crude mixture gave aldehyde **v** (0.513 g, 1.423 mmol, 67% yield) as a yellow oil.R_f=0.52 (silica, 50% EtOAc in hexanes),^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.36 (s, 1H), 7.14 (d, 1H, *J*=1.3 Hz), 6.42 (dt, 1H, *J*=1.2 Hz, *J*=7.1 Hz), 6.08 (d, 1H, *J*=1.4 Hz), 5.05 (dt, 1H, *J*=1.6 Hz, *J*=7.1 Hz), 2.57 (m, 6H), 1.94 (d, 3H, *J*=1.3 Hz), 1.71 (d, 3H, *J*=0.6 Hz);^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.8, 172.8, 151.7, 148.2, 142.1, 140.2, 132.9, 79.4, 78.7, 42.2, 26.5, 24.7, 24.0, 9.3; HRMS calcd. for ($M+Na^+$) 383.0112, found 383.0115.



11

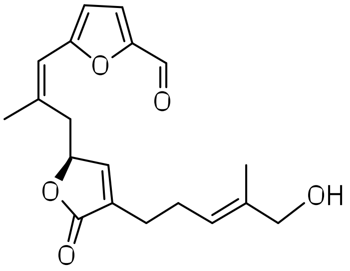
Allyl Alcohol 11: To a solution of aldehyde **iv** (1.58 g, 4.39 mmol) in MeOH (88 mL) at -20 °C was added sodium borohydride (0.183 g, 4.83 mmol, 1.1eq) in one portion. The solution went from orange-red to yellow. The reaction was stirred at -20 °C for 15 minutes. The reaction was quenched with sat.

NH_4Cl solution (50 mL), the organic layer was separated and the aqueous layer was extracted 3x with ethyl acetate. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (up to 55% EtOAc in hexanes) of the crude mixture gave alcohol **11** (1.589 g, 4.39 mmol, 100% yield), as a pale yellow oil, R_f= 0.30 (silica, 50% EtOAc in hexanes), ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.08 (d, 1H, *J*=1.4 Hz), 6.07 (d, 1H, *J*=1.4 Hz), 5.35 (m, 1H), 5.02 (ddd, 1H, *J*=1.5 Hz, *J*=6.1 Hz, *J*=7.5 Hz), 3.94 (s, 2H), 2.61 (dd, 1H, *J*=6.0 Hz, *J*=13.6 Hz), 2.50 (dd, 1H, *J*=7.5 Hz, *J*=13.6 Hz), 2.29 (m, 4H), 2.12 (s, 1H), 1.94 (d, 3H, *J*=1.4 Hz), 1.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ:173.7, 148.2, 142.6, 136.5, 134.1, 123.9, 79.7, 78.8, 68.5, 42.6, 25.6, 25.3, 25.0, 14.0; HRMS calcd. for ($M+Na^+$) 385.0271, found 385.0273.



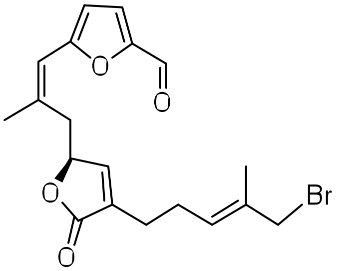
10

Furfural Stannane 10: To a suspension of N,O-dimethylhydroxylammonium chloride (3.62 g, 37.1 mmol, 1.3 eq) in THF (190 mL) was added the first amount of butylithium (46.3 mL, 74.1 mmol, 2.6eq) at -40 °C over 15 minutes. After 30 minutes stirring, furan-2-carbaldehyde (2.362 mL, 28.5 mmol) was added dropwise over 10 minutes. The reaction was stirred at -40 °C for 45 minutes. The second amount of butylithium (26.7 mL, 42.8 mmol, 1.5 eq) was added dropwise over 10 minutes. The reaction was stirred at -40 °C for 1 hour. Then a solution of the chlorotrimethylstannane (6.82 g, 34.2 mmol, 1.2 eq) in 20 mL of dry THF was added over 5 minutes. The reaction was stirred for 30 minutes then was quenched with sat. NH_4Cl solution (150 mL), the organic layer was separated and the aqueous layer was extracted 3x with ether. The combined organic layers were washed once with brine, dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (up to 10% EtOAc in hexanes) of the crude oil yielded stannane **10** (5.32 g, 20.53 mmol, 72% yield) as a pale yellow oil, R_f= 0.33 (silica, 10% EtOAc in hexanes), ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.64 (s, 1H), 7.22 (d, 1H, *J*=3.5 Hz), 6.71 (d, 1H, *J*=3.4 Hz), 0.38 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 177.3, 171.3 157.5, 123.1, 121.4, -9.1; HRMS calcd. for ($M+H^+$) 252.9958, found 252.9961.



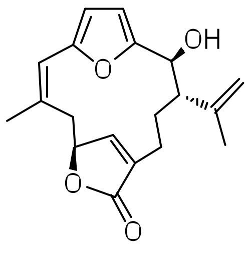
12

Carbaldehyde 12: To a solution of alcohol **11** (1.59 g, 4.39 mmol) in DMF (29.3 mL) was added stannane **10** (1.364g, 5.27 mmol, 1.2 eq). The solution was sparged with argon for 15 minutes. To this solution was added $Pd(PPh_3)_4$ (0.203 g, 0.176 mmol, 0.04 eq), copper iodide (0.067 g, 0.351 mmol, 0.08 eq) and cesium fluoride (1.334 g, 8.78 mmol, 2 eq) in one portion at rt. The solution went from yellow to brownish-grey and became heterogeneous. After 10 minutes of stirring, the reaction was quenched with sat. NH_4Cl solution (10 ml), the organic layer was separated and the aqueous layer was extracted 3x with ether. The combined organic layers were washed once with brine, dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (up to 70% EtOAc in hexanes) of the crude mixture gave carbaldehyde **12** (1.13 g, 3.42 mmol, 78% yield) as a yellow oil, R_f=0.23 (silica, 60% EtOAc in hexanes), ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.48 (s, 1H), 7.32 (d, 1H, *J*=1.4 Hz), 7.22 (d, 1H, *J*=3.7 Hz), 6.35 (d, 1H, *J*=3.7 Hz), 6.23 (s, 1H), 5.39 (ddd, 1H, *J*=1.3 Hz, *J*=5.5 Hz, *J*=7.9 Hz), 5.13 (qdd, 1H, *J*=1.6 Hz, *J*=3.5 Hz, *J*=8.6 Hz), 3.98 (s, 2H), 3.24 (dd, 1H, *J*=3.5 Hz, *J*=13.8 Hz), 2.44 (dd, 1H, *J*=8.6 Hz, *J*=13.8 Hz), 2.33 (m, 4H), 2.06 (d, 3H, *J*=1.4 Hz), 1.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 176.4, 173.8, 157.9, 151.2, 148.9, 141.8, 136.4, 133.4, 124.4, 123.6, 115.4, 111.2, 81.4, 68.3, 38.2, 26.6, 25.2, 24.8, 13.6; HRMS calcd. for $(M+Na^+)$ 353.1359, found 353.1356.



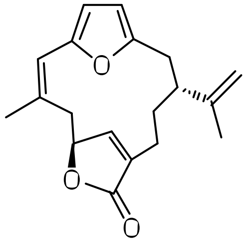
13

Allyl Bromide 13: To a solution of carbaldehyde **12** (1.13 g, 3.42 mmol) in dry CH_2Cl_2 (86 mL) at -20 °C was added triphenylphosphine (0.987 g, 3.76 mmol, 1.1 eq), the reaction mixture was stirred until it dissolved. N-bromosuccinimide (0.670 g, 3.76 mmol, 1.1 eq) was then added. After 15 minutes the reaction was complete. The reaction was diluted with water (50 mL), the organic layer was separated and the aqueous layer was extracted 3x with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (up to 30% EtOAc in hexanes) of the crude mixture gave allyl bromide **13** (1.264 g, 3.22 mmol, 94% yield) as a pale yellow oil, R_f=0.49 (silica, 40% EtOAc in hexanes), ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.52 (s, 1H), 7.26 (s, 1H), 7.20 (d, 1H, *J*=3.7 Hz), 6.35 (d, 1H, *J*=3.7 Hz), 6.24 (s, 1H), 5.54 (t, 1H, *J*=6.8 Hz), 5.13 (ddd, 1H, *J*=1.7 Hz, *J*=3.9 Hz, *J*=8.3 Hz), 3.93 (s, 2H), 3.19 (dd, 1H, *J*=4.0 Hz, *J*=13.8 Hz), 2.53 (dd, 1H, *J*=8.4 Hz, *J*=13.8 Hz), 2.36 (m, 2H), 2.28 (m, 2H), 2.05 (d, 3H, *J*=1.3 Hz), 1.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 176.3, 173.5, 157.8, 151.4, 148.9, 141.3, 133.5, 133.2, 129.3, 123.9, 123.8, 115.6, 111.2, 81.2, 41.2, 38.2, 26.7, 25.9, 24.6, 14.7; HRMS calcd. for ($M+Na^+$) 415.0515, found 415.0516.



6

Norbipinnatin J 6: Under an argon atmosphere, to dry THF (399 mL) were added powdered molecular sieves (11 g), $CrCl_2$ (3.24 g, 26.4 mmol, 12 eq) and $Ni(DME)_2Cl_2$ (1.448 g, 6.59 mmol, 3 eq. The reaction was stirred vigorously and sparged with argon for 10 minutes. The amount of allyl bromide **13** (0.864 g, 2.197 mmol) was taken up in dry THF (50 mL) and added to the stirring mixture via syringe pump over 1.5 Hrs at rt. The reaction was left to stir at rt overnight. 100 mL of water was then added and the solution and was diluted in 300 mL of ether. The organic layer was separated and the aqueous layer was extracted 3x with ether. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (up to 25% EtOAc in hexanes) of the crude mixture gave norbipinnatin J **6** (0.566 g, 1.80 mmol, 82% yield) as a white solid. R_f=0.21 (silica, 30% EtOAc in hexanes) ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.82 (t, 1H, *J*=1.6 Hz), 6.36 (d, 1H, *J*=3.2 Hz), 6.16 (s, 1H), 6.14 (d, 1H, *J*=3.2 Hz), 5.15 (m, 1H), 5.05 (s, 1H), 4.99 (m, 1H), 4.46 (dd, 1H, *J*=2.3 Hz, *J*=11.0 Hz), 3.22 (t, 1H, *J*=11.9 Hz), 2.74 (dd, 1H, *J*=4.4 Hz, *J*=11.8Hz), 2.40 (dt, 1H, *J*=3.1 Hz, *J*=14.5 Hz), 2.35 (t, 1H, *J*=10.9 Hz), 2.09 (m, 1H), 2.00 (d, 3H, *J*=1.2 Hz), 1.97 (d, 1H, *J*=2.6 Hz), 1.77 (d, 3H, *J*=0.6 Hz), 1.67 (tdd, 1H, *J*=3.4 Hz, *J*=10.9 Hz, *J*=13.9 Hz), 0.88 (dt, 1H, *J*=3.6 Hz, *J*=13.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 174.3, 153.8, 152.3, 152.1, 141.9, 132.6, 129.2, 118.7, 117.4, 112.0, 111.0, 78.6, 67.4, 51.2, 39.6, 30.0, 25.9, 19.6, 17.4; HRMS calcd. for (M+Na$^+$) 337.1410, found 337.1414.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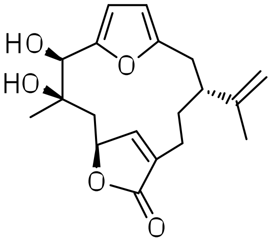
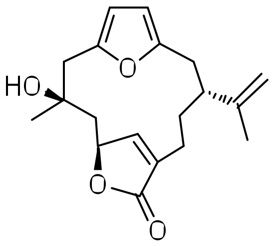
Norrubifolide 4: To a solution of Norbipinnatin J **6** (0.456 g, 1.450 mmol) in dry CH_2Cl_2 (58.0 mL) was first added triethylsilane (1.019 mL, 6.38 mmol, 4.4 eq), then trifluoroacetic acid (0.246 mL, 3.19 mmol, 2.2 eq) dropwise. After 15 minutes, the reaction was quenched with sat. $NaHCO_3$ solution (25 mL), the organic layer was separated and the aqueous layer was extracted 3x with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (up to 15% EtOAc in hexanes) of the crude mixture gave Rubifolide **4** (0.407 g, 1.407 mmol, 97% yield) as a white solid, R_f=0.70 (silica, 30% EtOAc in hexanes), ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.88 (s, 1H), 6.11 (s, 1H), 6.09 (d, 1H, *J*=3.2 Hz), 6.03 (dd, 1H, *J*=1.4 Hz, *J*=3.1 Hz), 4.97 (tdd, 1H, *J*=1.8 Hz, *J*=4.0 Hz, *J*=11.8 Hz), 4.90 (m, 1H), 4.88 (s, 1H), 3.25 (t, 1H, *J*=11.8 Hz), 2.69 (m, 2H), 2.58 (dd, 1H, *J*=12.5 Hz, *J*=15.3 Hz), 2.39 (m, 2H), 2.09 (m, 1H), 1.99 (s, 3H), 1.72 (s, 3H), 1.65 (tdd, 1H, *J*=3.4 Hz, *J*=10.8 Hz, *J*=14.0 Hz), 1.18 (ddt, 1H, *J*=0.9 Hz, *J*=3.5 Hz, *J*=13.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ; 174.5, 154.1, 152.0, 151.2, 145.2, 132.9, 127.3, 117.5, 113.2, 111.1, 108.7, 78.7, 43.4, 39.6, 32.9, 31.1, 25.8, 20.0, 19.1; HRMS calcd. for (M+Na$^+$) 321.1461, found 321.1460.

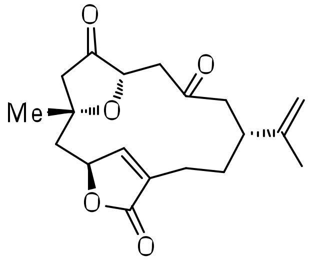

14

Diol 14: To a solution of norrubifolide **4** (0.064 g, 0.214 mmol) in a 1:1:1 ratio of water (0.298 mL), THF (0.298 mL) and acetone (0.298 mL) was added NMO (0.030 g, 0.257 mmol, 1.2 eq). The mixture was cooled to 0 °C and treated with osmium tetroxide 4% solution in water (0.136 mL, 0.021 mmol, 0.1eq) added dropwise. The reaction went from light yellow to brown and then turned dark green. It was stirred at 0 °C for 1.5h and then warmed up to rt and stirred for an additional 1.5h. The solution was quenched with sat. Na_2SO_3 solution, the organic layer was separated and the aqueous layer was extracted 3x with EtOAc. The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure. Flash chromatography (up to 80% EtOAc in hexanes) of the crude mixture gave diol **14** (0.046 g, 0.137 mmol, 64% yield) as a white solid, R_f=0.20 (silica, 50% Ethyl acetate in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.24 (d, 1H, *J*=3.0 Hz), 6.12 (d, 1H, *J*=3.0 Hz), 5.74 (s, 1H), 4.94 (d, 1H, *J*=11.4 Hz), 4.81 (s, 1H), 4.77 (s, 1H), 4.55 (s, 1H), 2.70 (d, 1H, *J*=13.3 Hz), 2.51 (dd, 1H, *J*=12.3 Hz, *J*=14.3 Hz), 2.34 (m, 2H), 2.24 (dd, 1H, *J*=11.5 Hz, *J*=14.4 Hz), 2.11 (m, 2H), 1.73 (s, 3H), 1.70 (m, 2H), 1.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ:173.7, 154.4, 149.8, 148.7, 146.3, 133.3, 112.4, 109.4, 108.7, 79.2, 75.7, 73.3, 43.9, 40.0, 33.1, 27.8, 23.4, 21.6, 18.9; HRMS calcd. for (M+Na$^+$) 355.1516, found 355.1518.



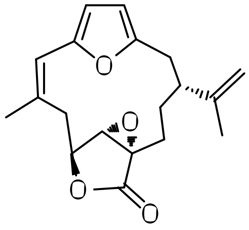
15

Teriary Alcohol 15: To a solution of diol **14** (0.0496 g, 0.149 mmol) in CH_2Cl_2 (9.95 mL) at - 40 °C was added boron trifluoride diethyl etherate (0.057 mL, 0.448 mmol, 3 eq) and triethylsilane (0.143 mL, 0.895 mmol, 6 eq). After 10 minutes, the reaction was quenched with sat. NH_4Cl solution (3 mL), the organic layer was separated and the aqueous layer was extracted 3x with CH_2Cl_2. The combined organic layers were washed once with brine, dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (up to 60% EtOAc in hexanes) of the crude mixture gave tertiary alcohol **15** (0.024 g, 0.075 mmol, 51% yield) as clear crystals, R_f=0.29 (silica, 50% EtOAc in hexanes), ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.08 (m, 2H), 6.02 (d, 1H, *J*=3.0 Hz), 4.88 (d, 1H, *J*=11.3 Hz), 4.79 (m, 1H), 4.77 (s, 1H), 2.88 (q, 2H, *J*=14.7 Hz), 2.65 (dd, 1H, *J*=1.5 Hz, *J*=14.7 Hz), 2.49 (dd, 1H, *J*=11.6 Hz, *J*=14.7 Hz), 2.42 (dd, 1H, *J*=4.0 Hz, *J*=14.0 Hz), 2.33 (ddd, 1H, *J*=4.2 Hz, *J*=11.5 Hz, *J*=15.9 Hz), 2.13 (m, 2H), 1.93 (bs, 1H), 1.85 (dd, 1H, *J*=11.4 Hz, *J*=14.0 Hz), 1.77 (m, 2H), 1.72 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.7, 153.9, 149.7, 149.3, 146.5, 133.0, 112.2, 108.9, 108.2, 79.1, 71.2, 45.6, 44.3, 43.2, 33.0, 28.4, 26.6, 21.6, 18.8; HRMS calcd. for (M+Na$^+$) 339.1567, found 339.1565.



7

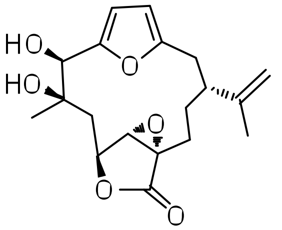
Norcembrenolide B 8: To a solution of alcohol **15** (0.124 g, 0.392 mmol) in acetone (1.3 mL) at 0 °C was added Jones reagent (0.161 mL, 0.431 mmol, 1.1 eq) dropwise. After 20 minutes, the reaction was quenched with sat. $NaHCO_3$ solution (100 mL), the organic layer was separated and the aqueous layer was extracted 3x with ethyl acetate. The combined organic layers were washed once with brine, dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (up to 6% Acetone in CH_2Cl_2) of the crude mixture gave Norcembrenolide B **8** (0.0646 g, 0.194 mmol, 50% yield) as a white solid, R_f: 0.30 (silica, 5% Acetone in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.21 (s, 1H), 5.13 (bs, 1H), 4.80 (s, 1H), 4.68 (s, 1H), 4.15 (dd, 1H, *J*=3.5 Hz, *J*=8.3 Hz), 2.97 (dd, 1H, *J*=3.4 Hz, *J*=15.3 Hz), 2.59 (dd, 1H, *J*=6.8 Hz, *J*=16.9 Hz), 2.53 (dd, 1H, *J*=10.7 Hz, *J*=24.6 Hz), 2.50 (m, 1H) 2.44 (d, 1H, *J*=18.1 Hz), 2.39 (m, 2H), 2.35 (dd, 1H, *J*=5.9 Hz, *J*=12.8 Hz), 2.22 (m, 3H), 1.94 (ddd, 1H, *J*=2.4 Hz, *J*=4.7 Hz, *J*=14.6 Hz), 1.76 (m, 1H), 1.66 (s, 3H), 1.31 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ: 211.6, 206.5, 173.4, 150.3, 146.1, 127.6, 112.9, 78.2, 77.8, 74.6, 47.8, 46.1, 45.6, 42.7, 40.8, 27.8, 24.6, 21.1, 18.0; HRMS calcd. for (M+Na$^+$) 355.1516, found 355.1514.



5

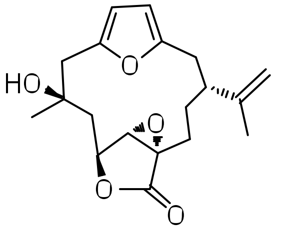
Norcoralloidolide 5: To a solution of norrubifolide **4** (0.288 g, 0.965 mmol) in dry THF (3.11 mL) at 0 °C was added tBuOOH (0.241 mL, 1.448 mmol, 1.5 eq) dropwise. The reaction was stirred for 5 minutes at 0 °C. triton B (4.39 µl, 9.65 µmol, 0.01 eq) was then immediately added dropwise. The reaction was then stirred at 0 °C and monitored by TLC. The reaction completed within 10 minutes. The reaction was quenched by adding solid Na_2SO_3 and stirred for 30 minutes.

The reaction was then diluted with dry ether and filtered over celite. The reaction was concentrated under reduced pressure and yielded Norcoralloidolide **5** (0.300 g, 0.956 mmol, 99% yield) as a white solid which was used without further purification. R_f=0.55 (silica, 20% EtOAc in hexanes), ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.18 (s, 1H), 6.11 (d, 1H, *J*=3.1 Hz), 6.04 (dd, 1H, *J*=1.5 Hz, *J*=3.1 Hz), 4.96 (m, 1H), 4.87 (s, 1H), 4.56 (dd, 1H, *J*=4.3 Hz, *J*=12.7 Hz), 3.76 (s, 1H), 3.68 (t, 1H, *J*=12.7 Hz), 2.78 (d, 1H, *J*=14.8 Hz), 2.60 (m, 1H), 2.55 (m, 3H), 1.98 (s, 3H), 1.73 (s, 3H), 1.55 (m, 2H), 1.03 (dd, 1H, *J*=12.3 Hz, *J*=14.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.3, 152.9, 150.7, 144.5, 127.0, 117.9, 113.4, 110.8, 108.4, 77.1, 61.3, 60.7, 44.1, 36.1, 32.9, 27.6, 25.0, 21.5, 19.1; HRMS calcd. for (M+Na$^+$) 337.1410, found 337.1408.



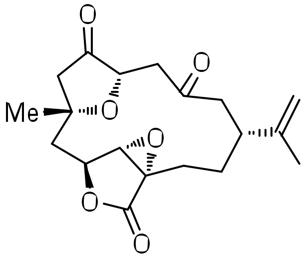
16

Diol 16: Norcoralloidolide **5** (0.059 g, .188 mmol) was subjected to identical conditions found for diol **14**. Flash chromatography (up to 80% EtOAc in hexanes) of the crude mixture gave diol **16** (0.027 g, 0.076 mmol, 42% yield) as a white solid, R_f=0.20 (silica, 50% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.24 (d, 1H, *J*=3.1 Hz), 6.04 (dd, 1H, *J*=1.1 Hz, *J*=3.1 Hz), 4.92 (s, 2H), 4.67 (dd, 1H, *J*=6.9 Hz, *J*=8.9 Hz), 4.53 (s, 1H), 3.54 (s, 1H), 2.77 (d, 1H, *J*=13.7 Hz), 2.62 (m, 2H), 2.40 (m, 1H), 2.00 (dd, 1H, *J*=9.0 Hz, *J*=15.1 Hz), 1.81 (dd, 1H, *J*=6.9 Hz, *J*=15.1 Hz), 1.74 (s, 3H), 1.55 (m, 2H), 1.38 (s, 3H), 1.34 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.5, 153.8, 150.4, 145.3, 112.8, 109.6, 107.9, 75.4, 75.3, 73.1, 62.6, 60.5, 43.2, 39.8, 32.0, 27.2, 25.9, 21.3, 19.3; HRMS calcd. for (M+Na$^+$) 371.1465, found 371.1463.



17

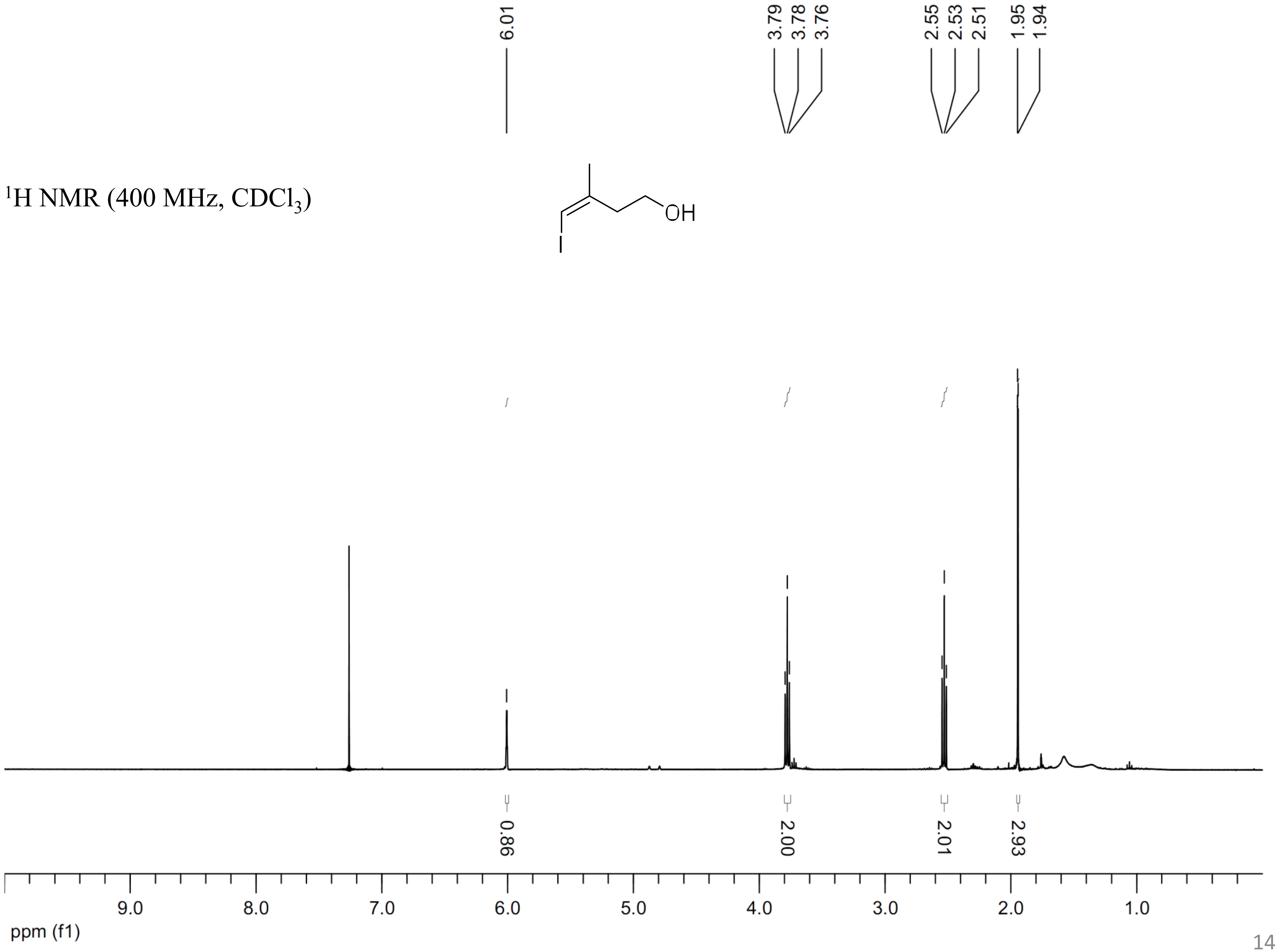
Tertiary alcohol 17: Diol **16** (0.0245 g, 0.070 mmol) was subjected to identical conditions found for tertiary alcohol to afford compound **17** (0.014g, 0.042mmol, 60% yield) as clear crystals, R_f=0.32 (silica, 50% EtOAc in hexanes), ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.06 (d, 1H, *J*=3.0 Hz), 5.96 (d, 1H, *J*=2.9 Hz), 4.99 (s, 1H), 4.90 (m, 1H), 4.71 (t, 1H, *J*=8.1 Hz), 3.83 (s, 1H), 3.20 (d, 1H, *J*=14.7 Hz), 2.93 (m, 1H), 2.81 (d, 1H, *J*=14.7 Hz), 2.72 (dd, 1H, *J*=2.1 Hz, *J*=15.7 Hz), 2.59 (dd, 1H, *J*=11.8 Hz, *J*=15.8 Hz), 2.44 (m, 1H), 1.73 (s, 3H), 1.66 (dd, 2H, *J*=5.1 Hz, *J*=8.1 Hz), 1.62 (dd, 1H, *J*=3.9 Hz, *J*=8.1 Hz), 1.45 (m, 3H), 1.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.8, 152.9, 149.8, 145.7, 112.7, 108.9, 107.4, 75.3, 71.6, 62.7, 60.9, 42.1, 41.9, 41.0, 31.7, 29.1, 27.7, 22.0, 19.1; HRMS calcd. for ($M+Na^+$) 355.1516, found 355.1511.



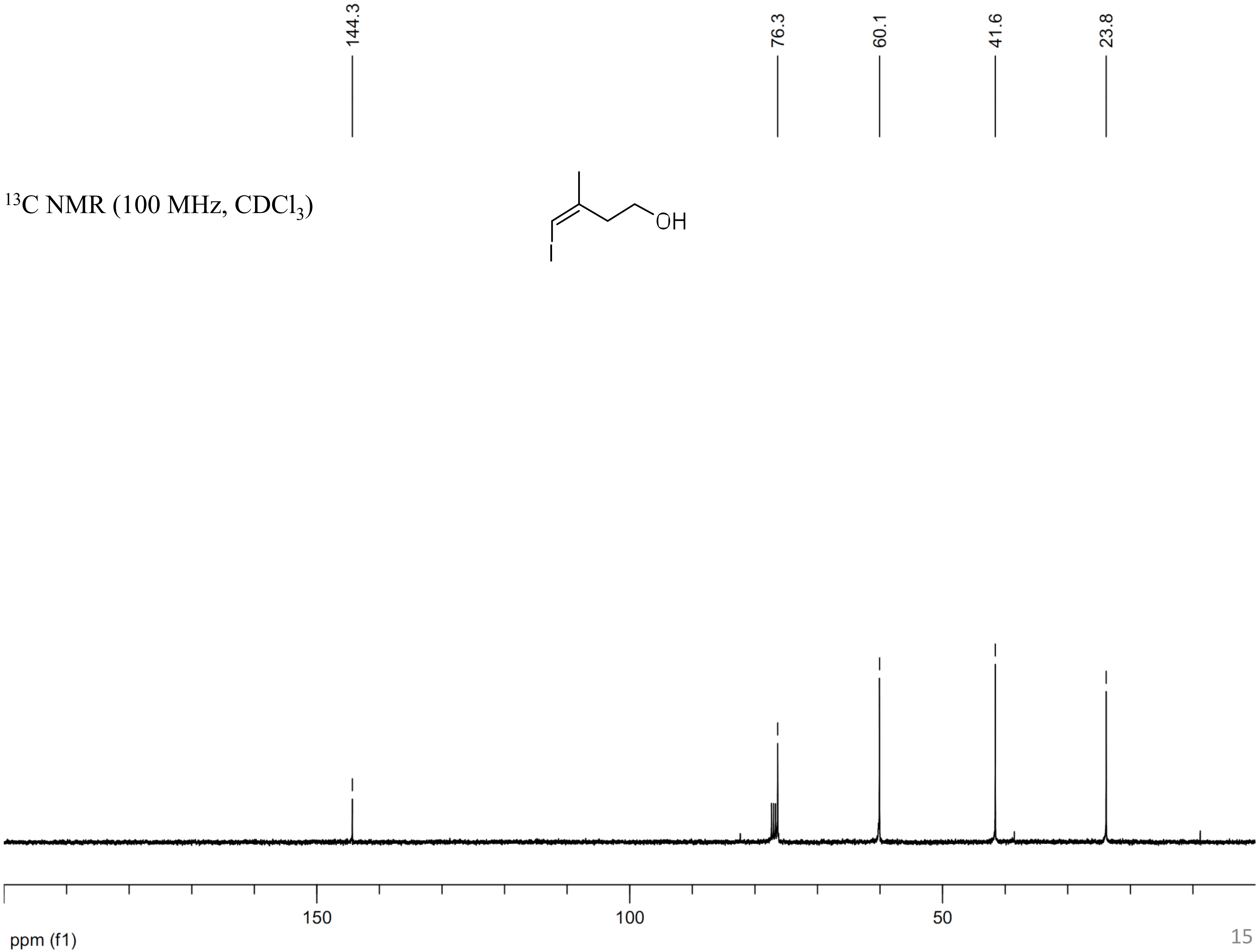
8

Scabrolide D (Norcembrenolide C) 9: Tertiary alcohol **17** (0.0363 g, 0.109mmol) was subjected to identical conditions as Norcembrenolide A **7**. Flash chromatography (up to 4% Acetone in CH_2Cl_2) of the crude mixture gave Scabrolide D **9** (0.019 g, 0.055 mmol, 51% yield) as a white solid, Rf=0.45 (silica, 5% Acetone in CH_2Cl_2);^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.93 (s, 1H), 4.86 (s, 1H), 4.74 (t, 1H, *J*=6.6 Hz), 4.20 (dd, 1H, *J*=4.0 Hz, *J*=5.7 Hz), 3.95 (s, 1H), 3.09 (dd, 1H, *J*=4.0 Hz, *J*=16.4 Hz), 2.73 (dd, 1H, *J*=5.8 Hz, *J*=16.4 Hz), 2.63 (d, 1H, *J*=18.2 Hz), 2.61 (m, 1H), 2.52 (dd, 1H, *J*=2.4 Hz, *J*=12.0 Hz), 2.49 (d, 1H, *J*=18.2 Hz), 2.31 (dd, 1H, *J*=7.0 Hz, *J*=14.9 Hz), 2.20 (m, 2H), 2.11 (dd, 1H, *J*=6.2 Hz, *J*=14.9 Hz), 1.75 (m, 1H), 1.68 (s, 3H), 1.65 (dd, 1H, *J*=3.5 Hz, *J*=8.2 Hz), 1.47 (s, 3H), 1.35 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 213.8, 207.6, 172.3, 145.7, 112.7, 79.1, 75.8, 75.0, 62.7, 60.7, 49.7, 48.3, 44.7, 42.4, 40.7, 26.9, 25.6, 21.3, 18.7; HRMS calcd. for ($M+Na^+$) 371.1465, found 371.1466.

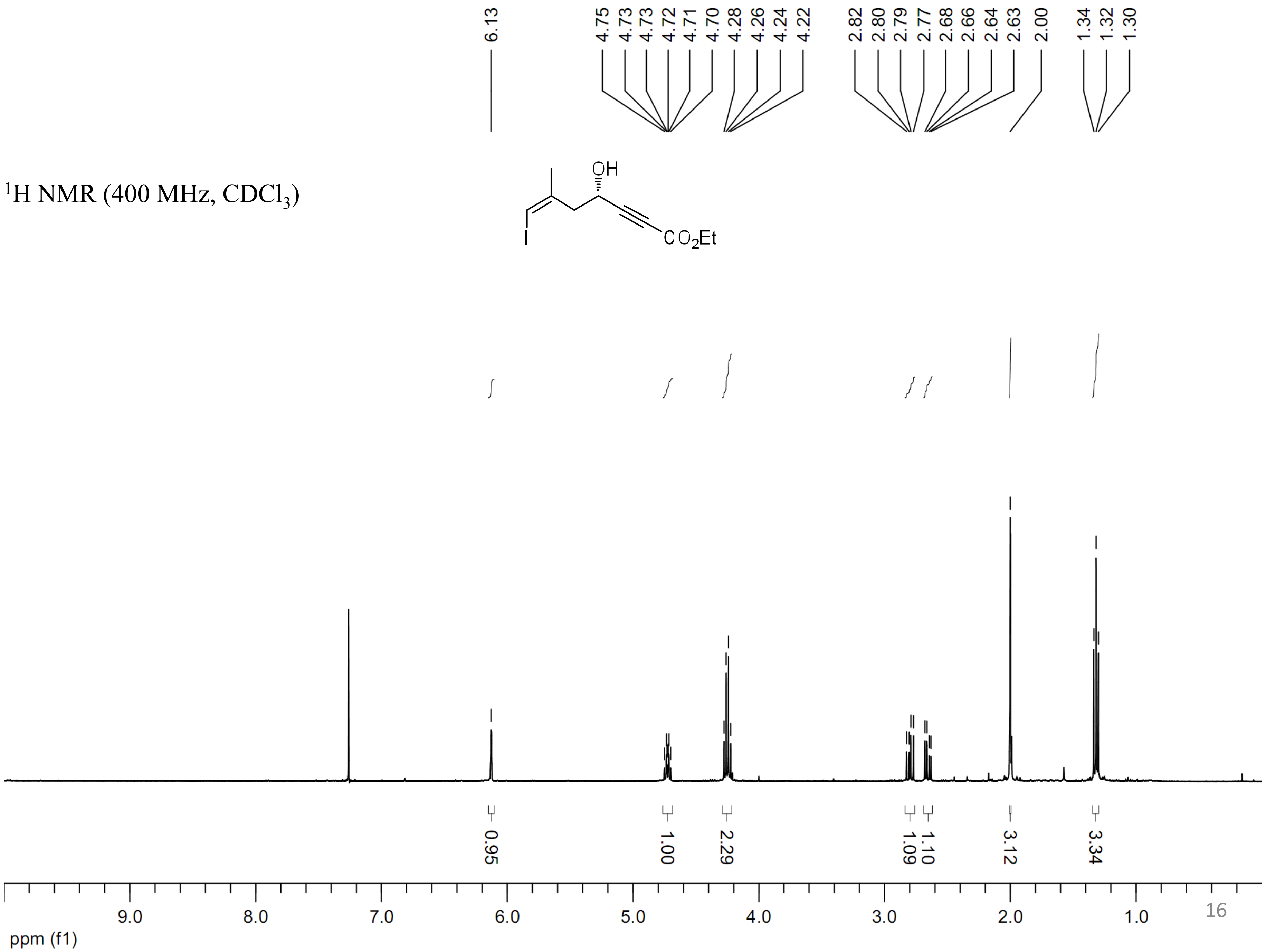
^{1}H NMR (400 MHz, CDCl$_3$)



^{13}C NMR (100 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, $CDCl_3$)



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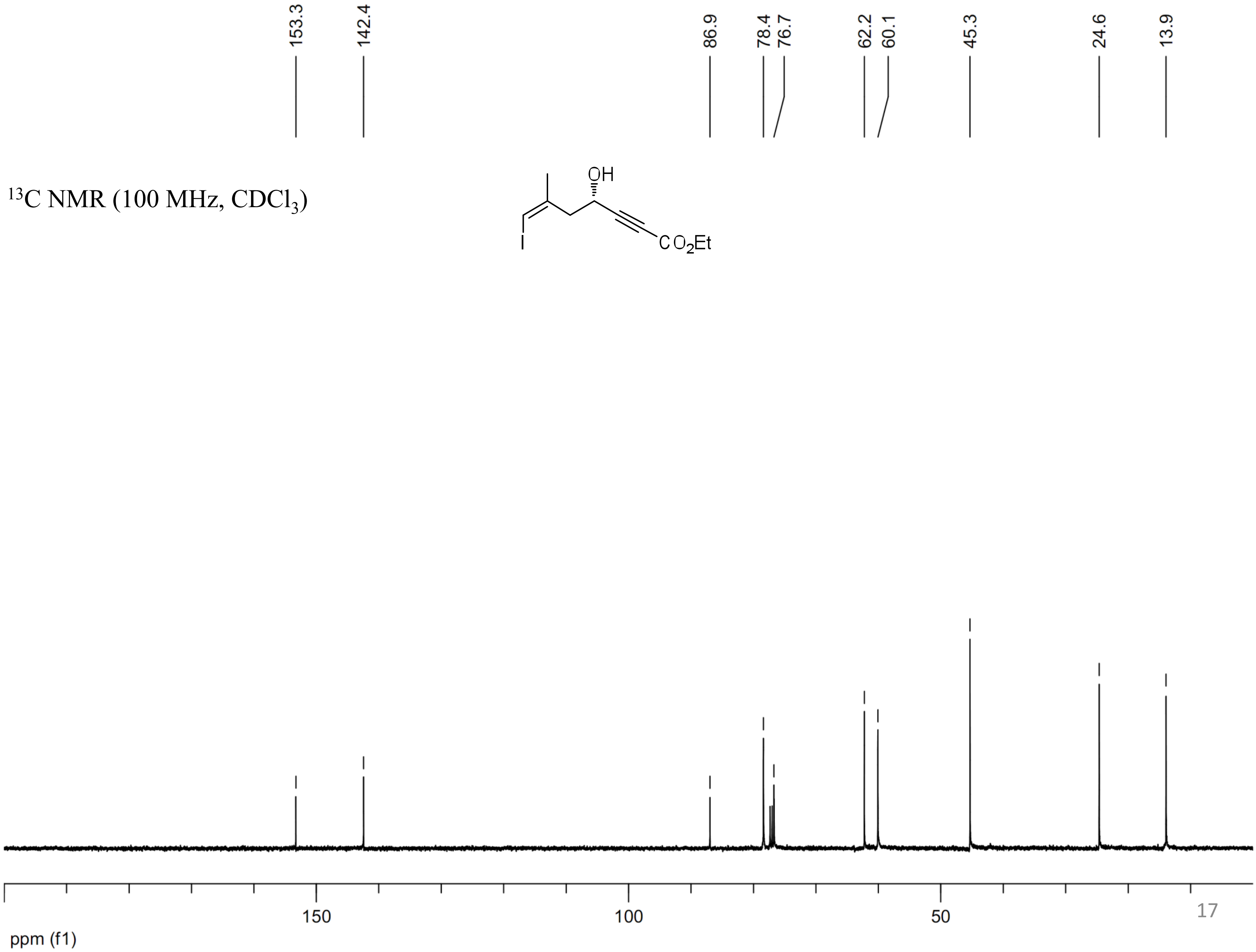

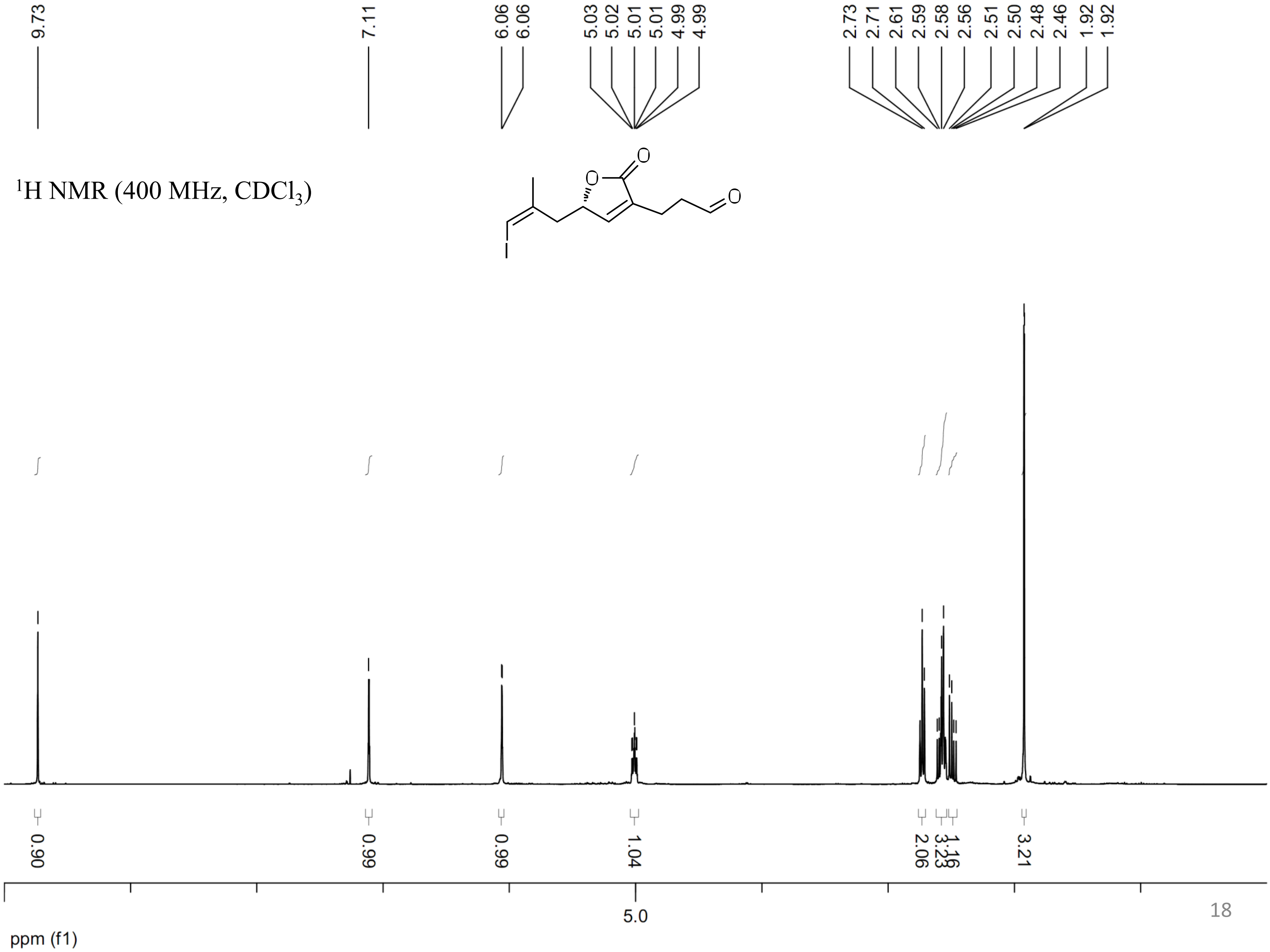

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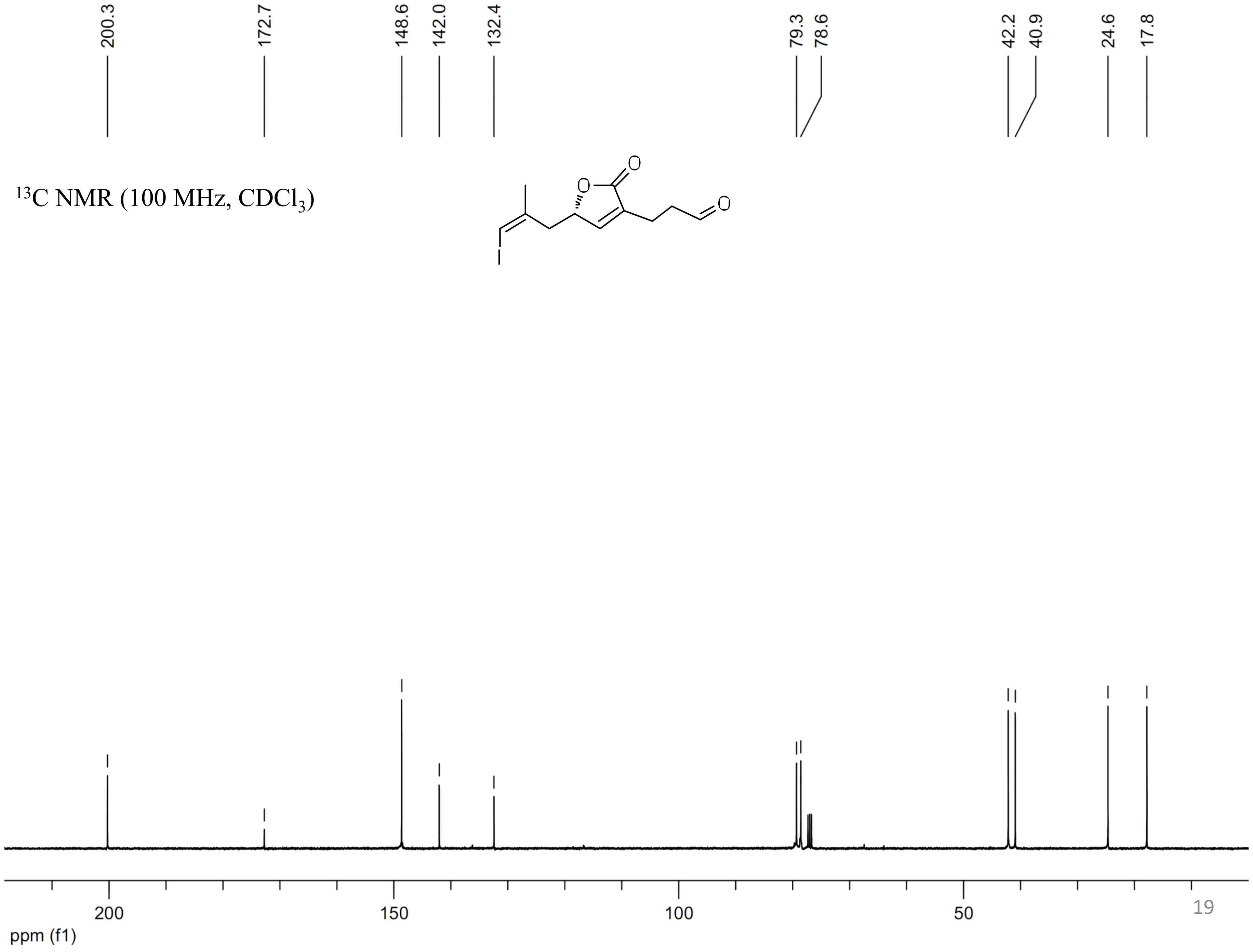

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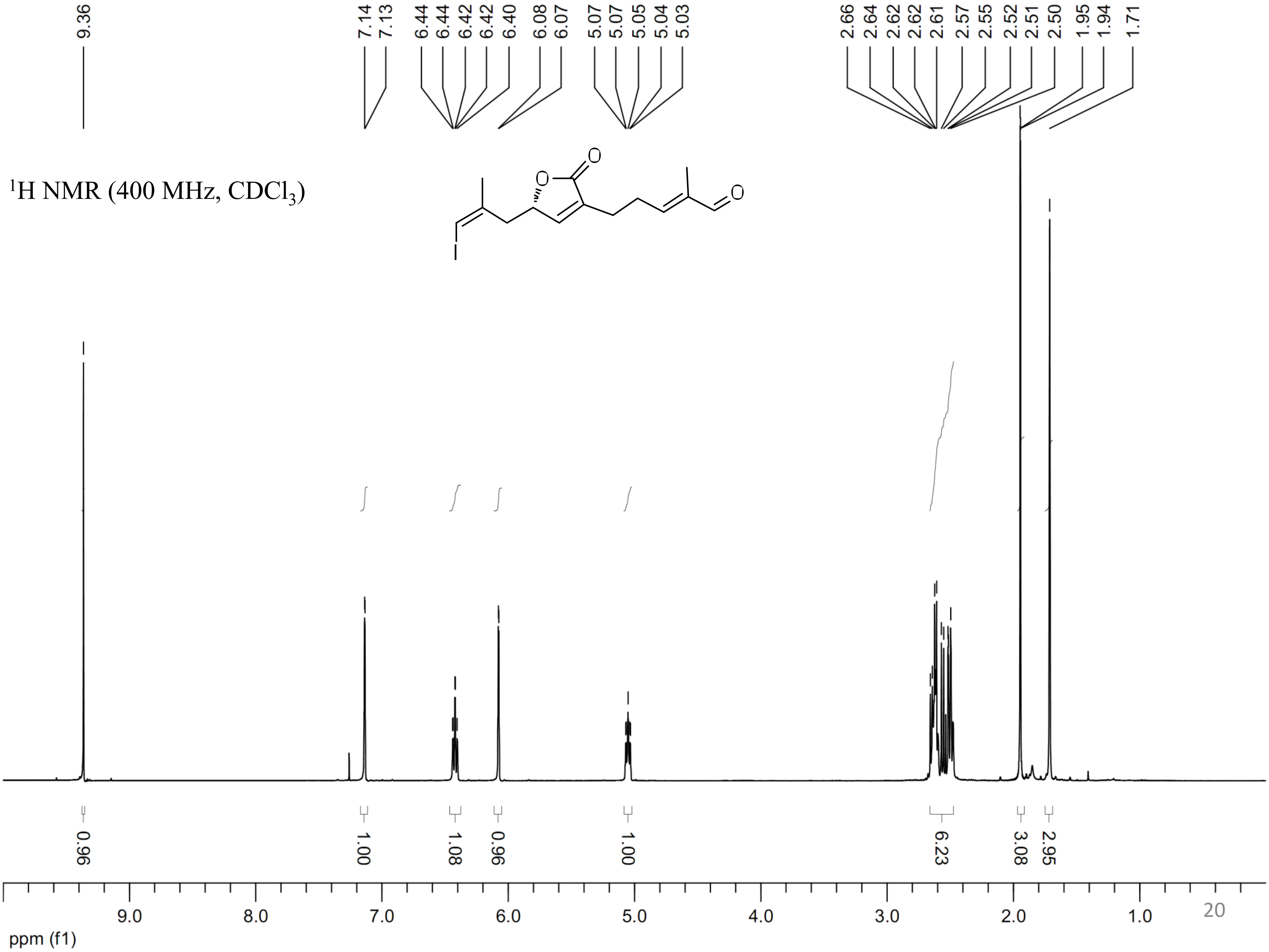
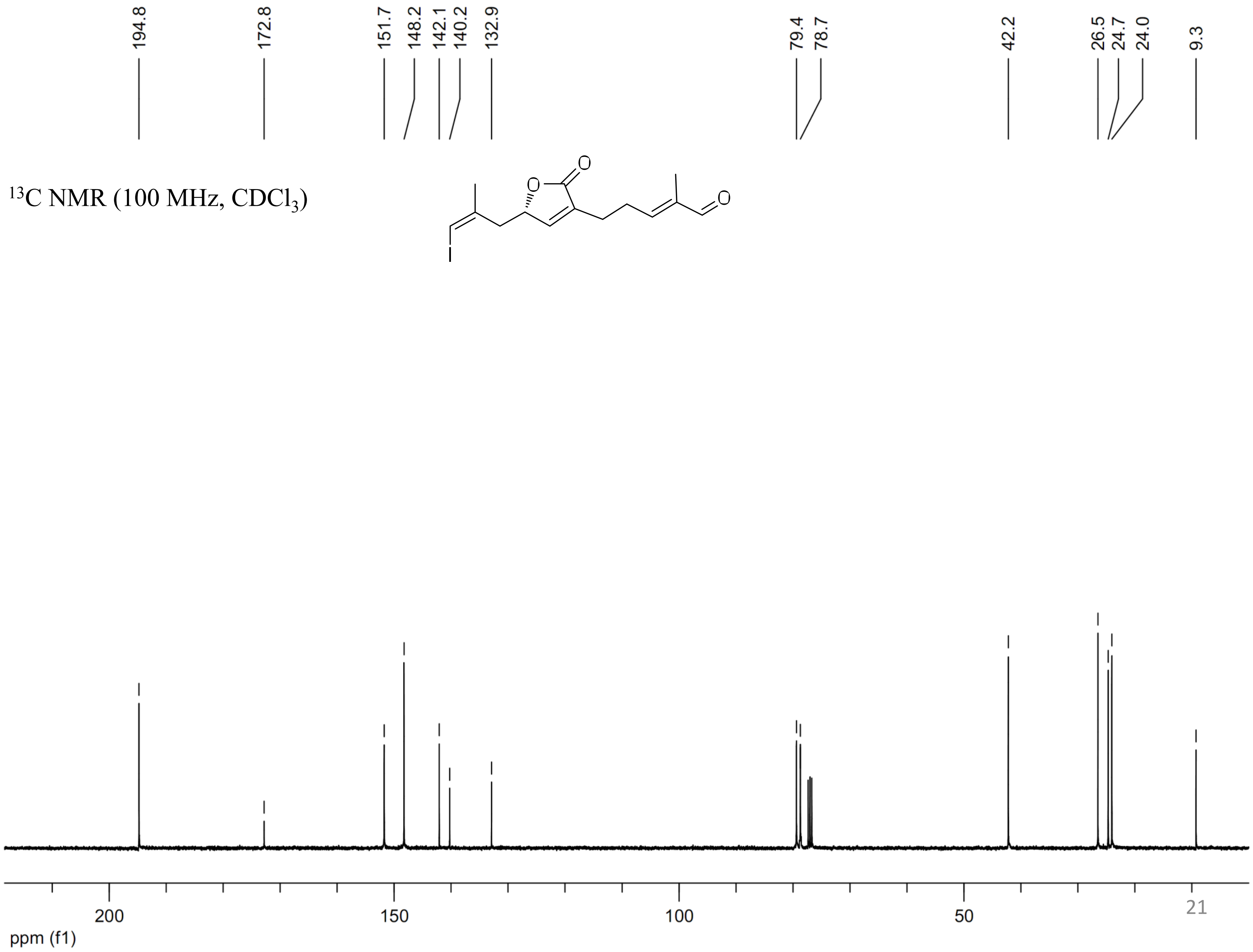
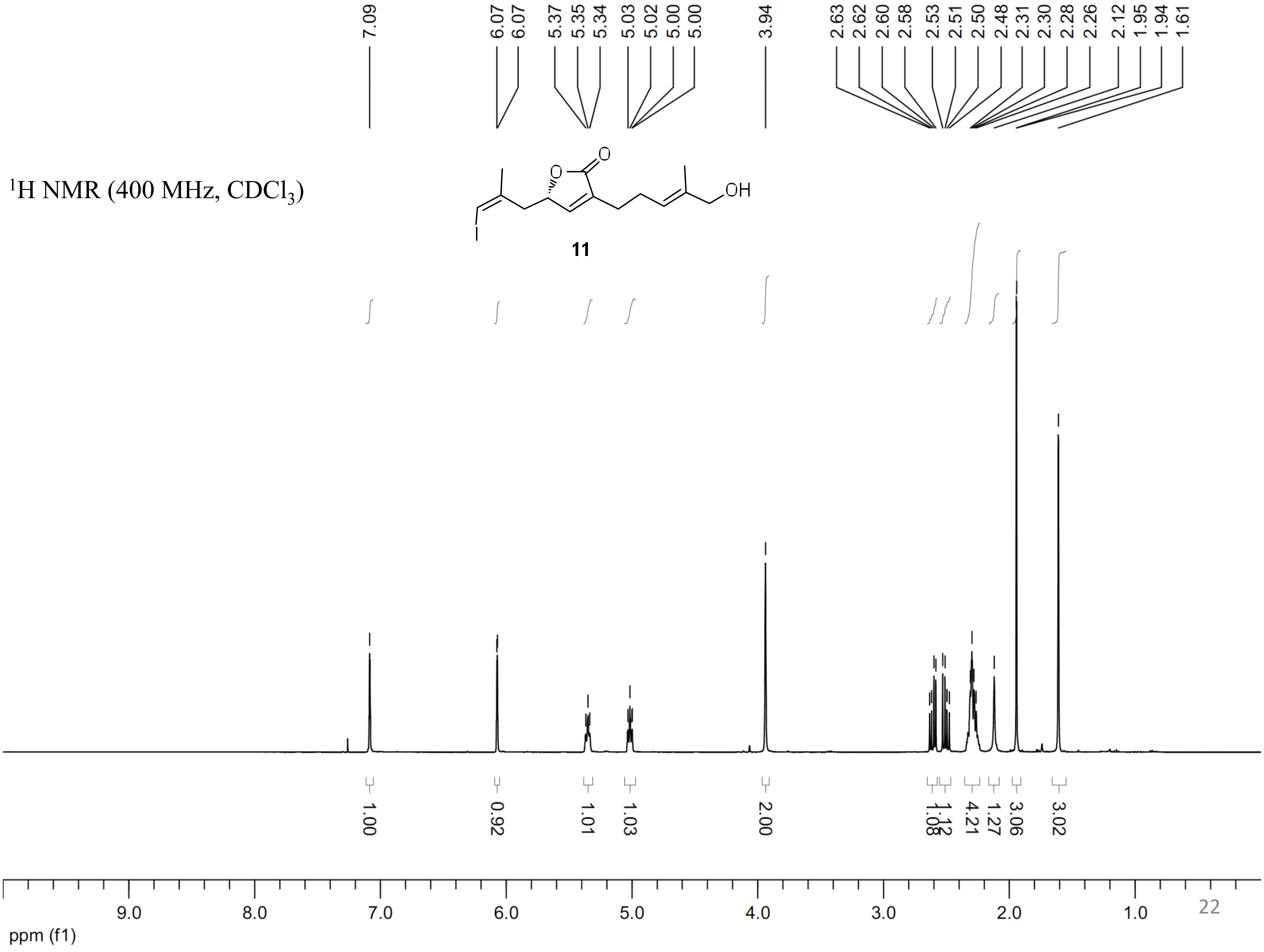


^{1}H NMR (400 MHz, $CDCl_3$)

^{13}C NMR (100 MHz, CDCl$_3$)

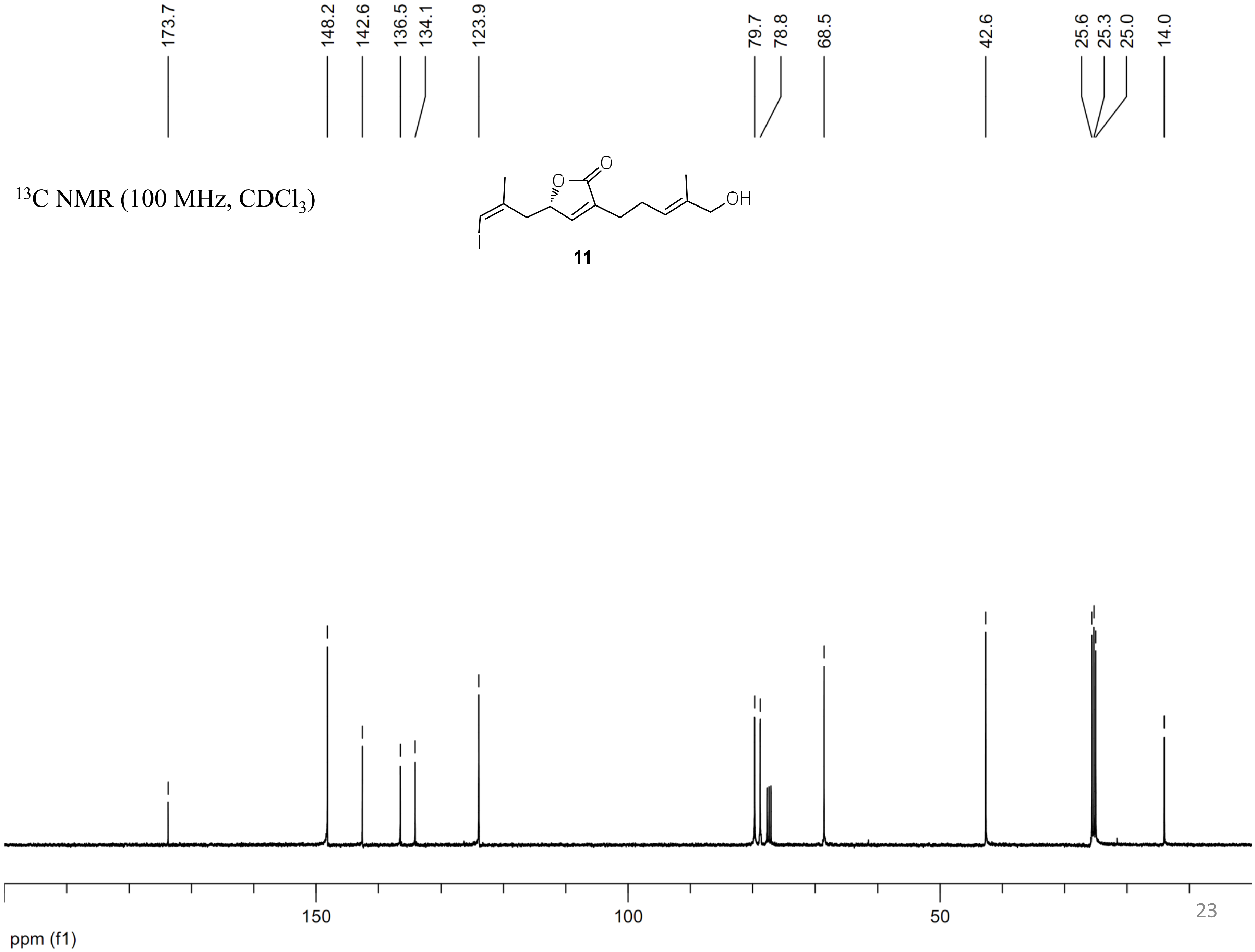


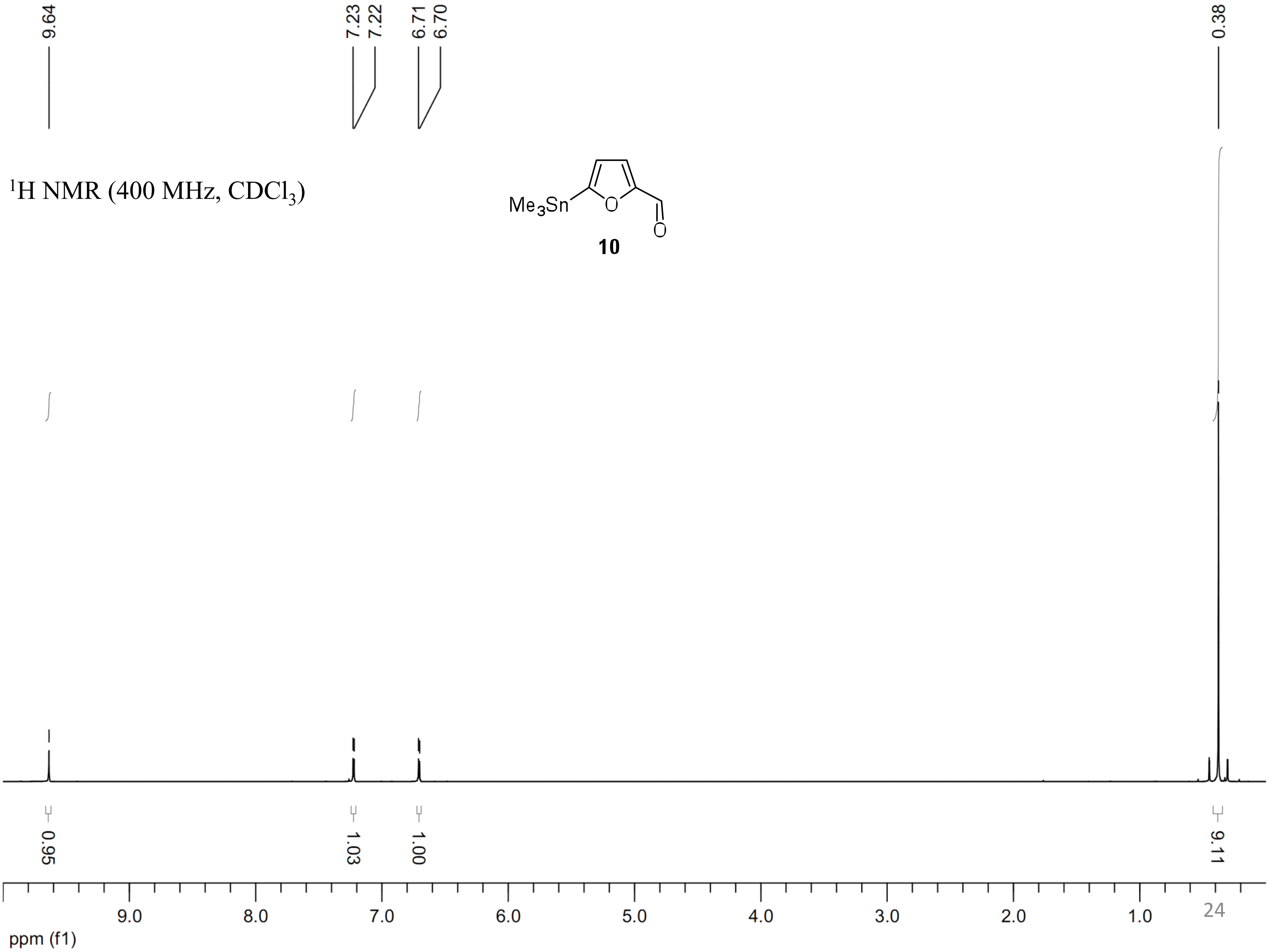
^{1}H NMR (400 MHz, $CDCl_3$)



11

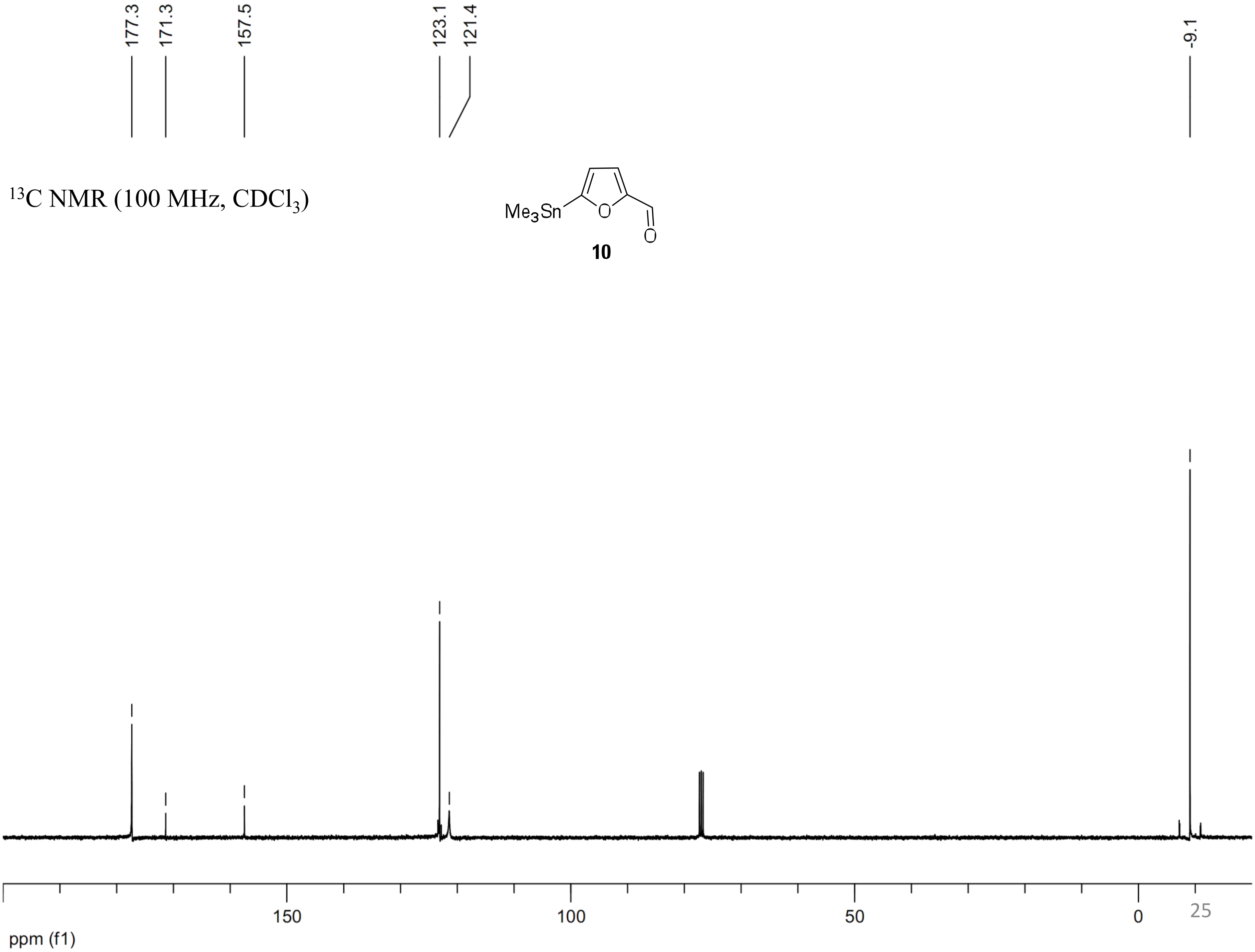
^{13}C NMR (100 MHz, CDCl$_3$)





^{1}H NMR (400 MHz, $CDCl_3$)

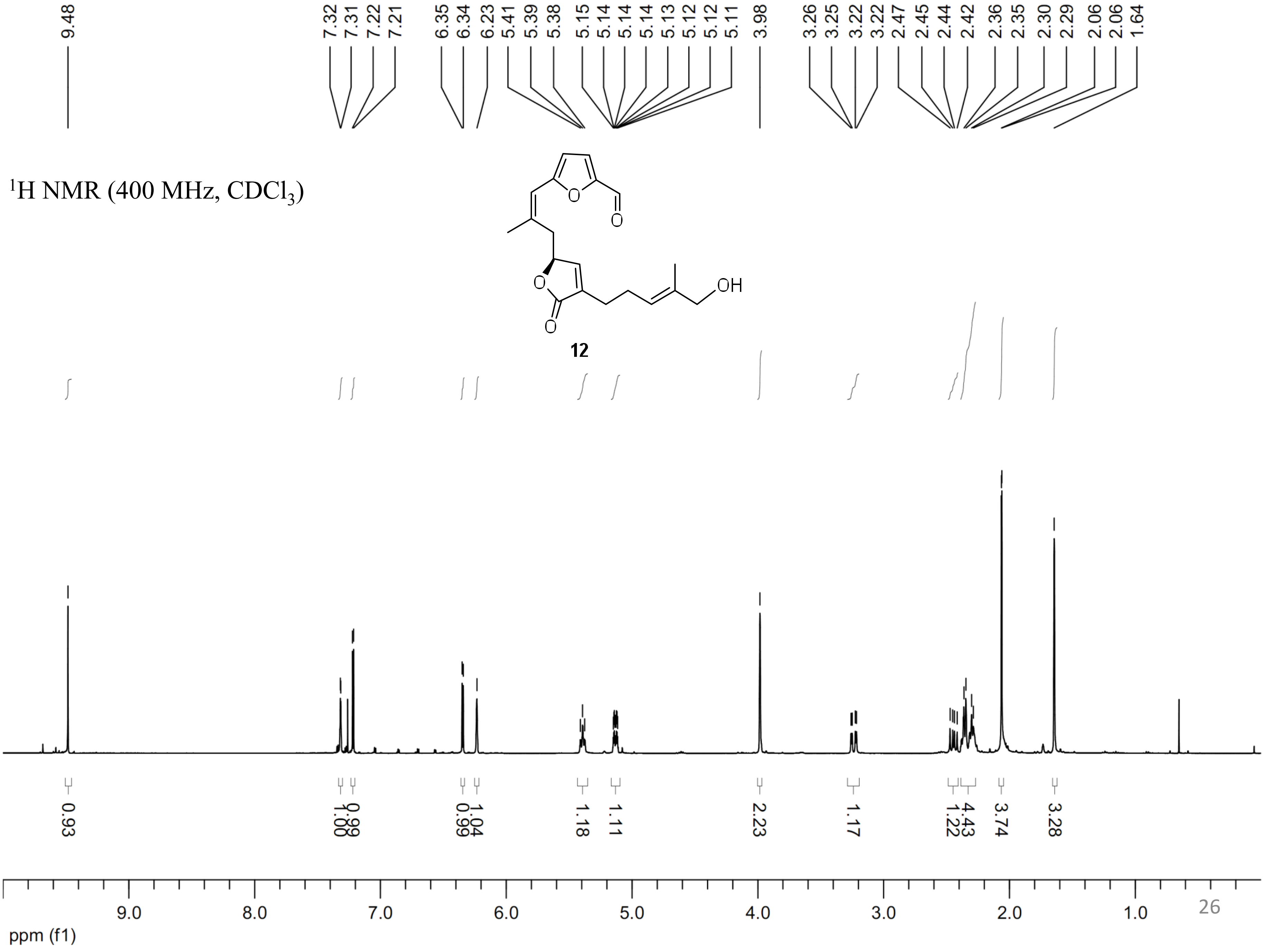
10



^{13}C NMR (100 MHz, CDCl$_3$)

10

^{1}H NMR (400 MHz, $CDCl_3$)



12

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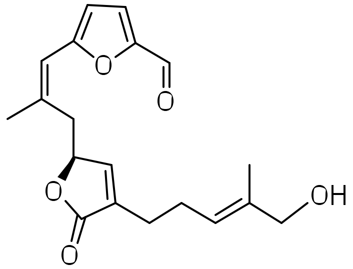

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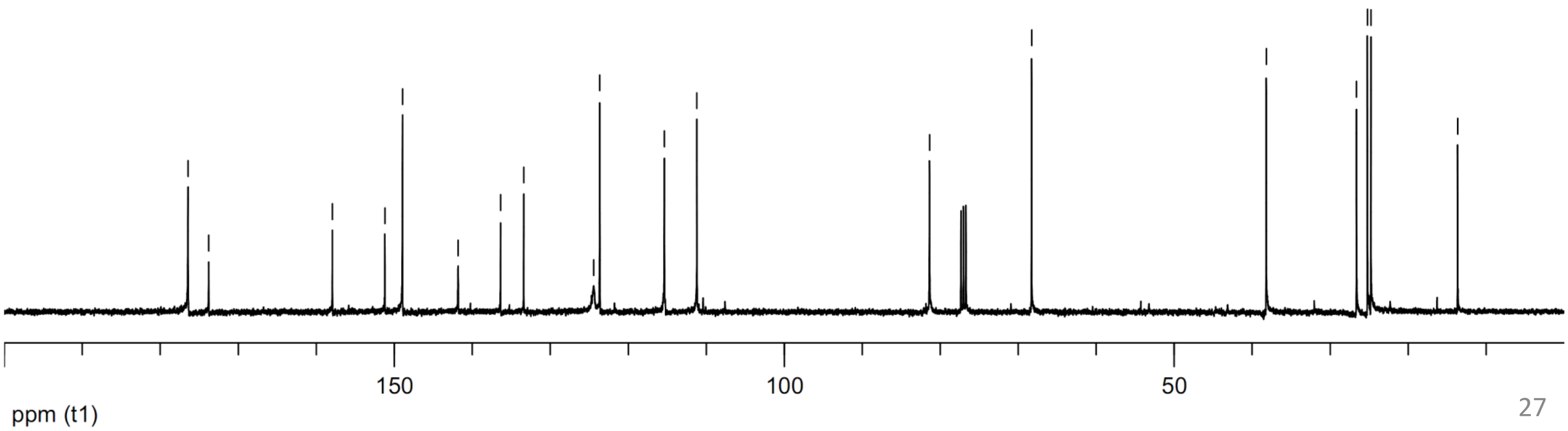
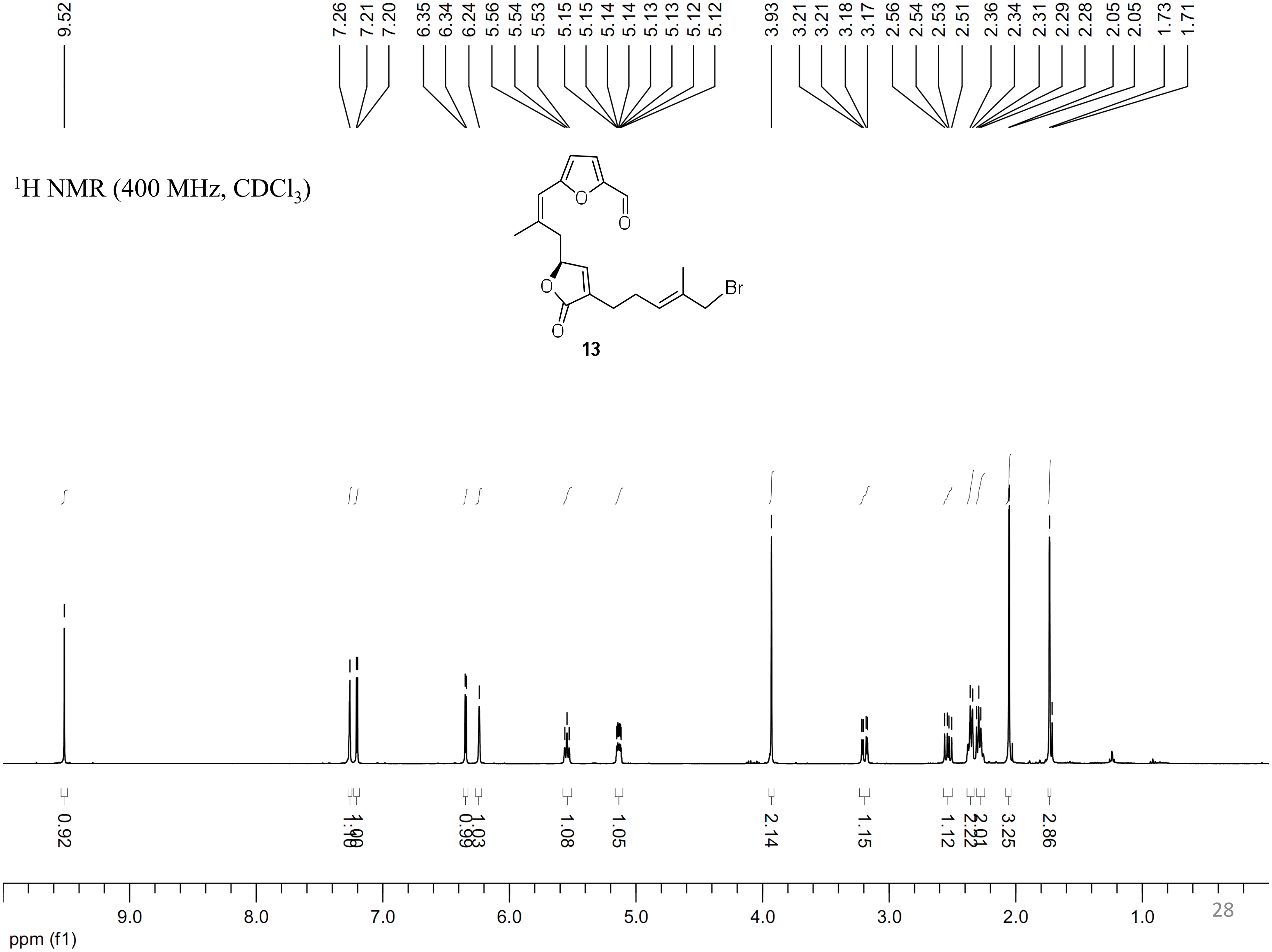
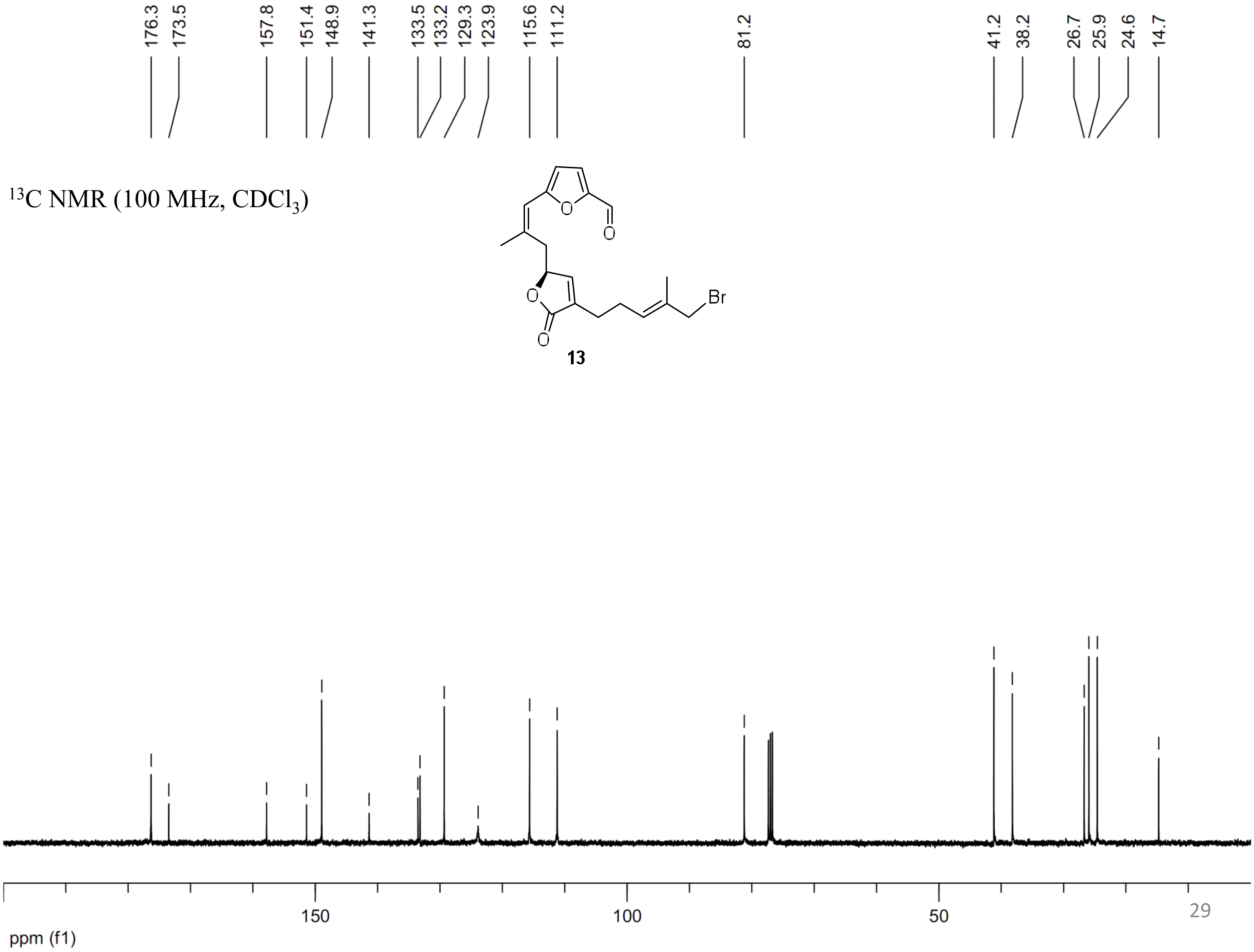




^{1}H NMR (400 MHz, CDCl$_3$)

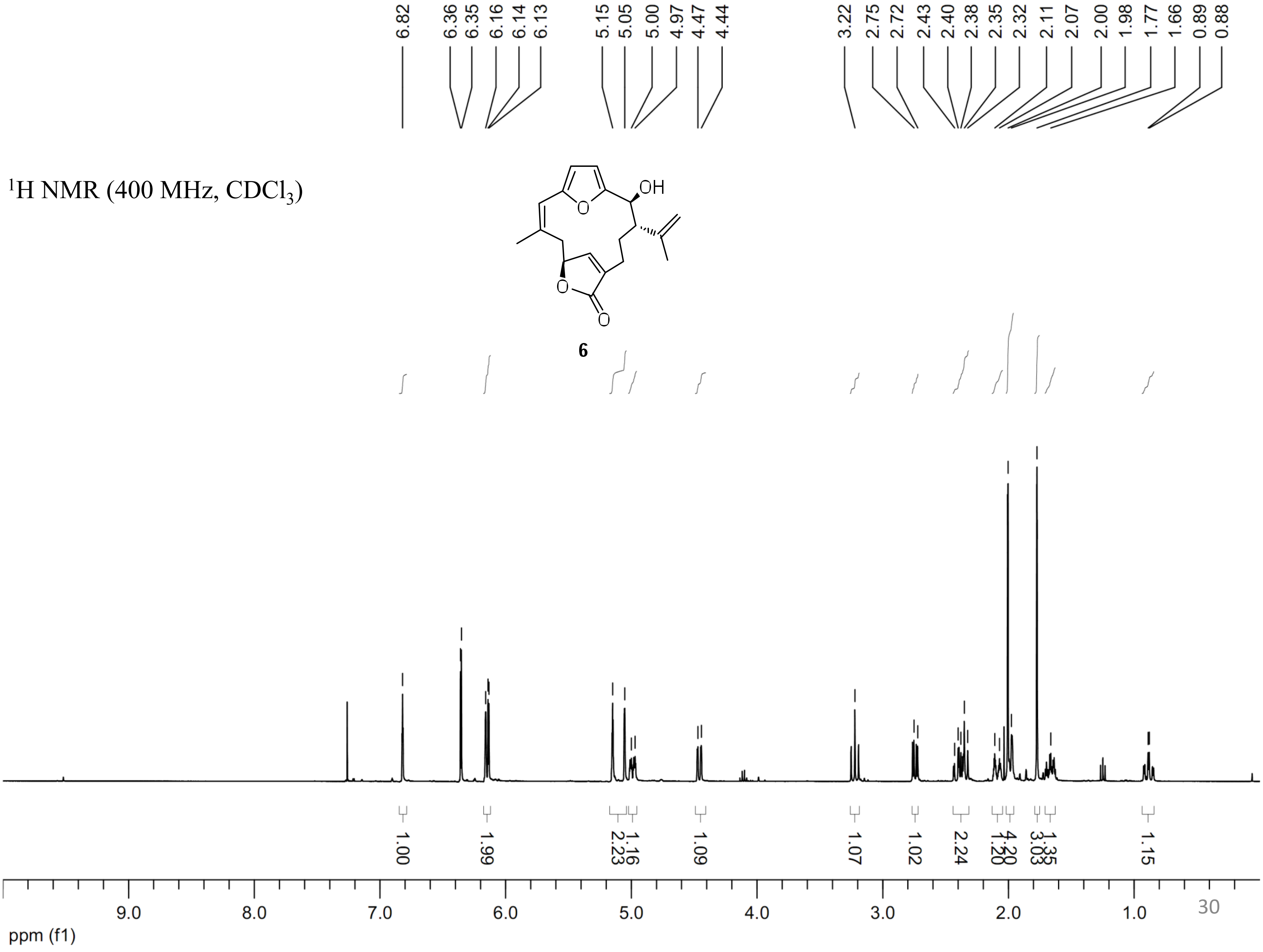
13



^{13}C NMR (100 MHz, $CDCl_3$)

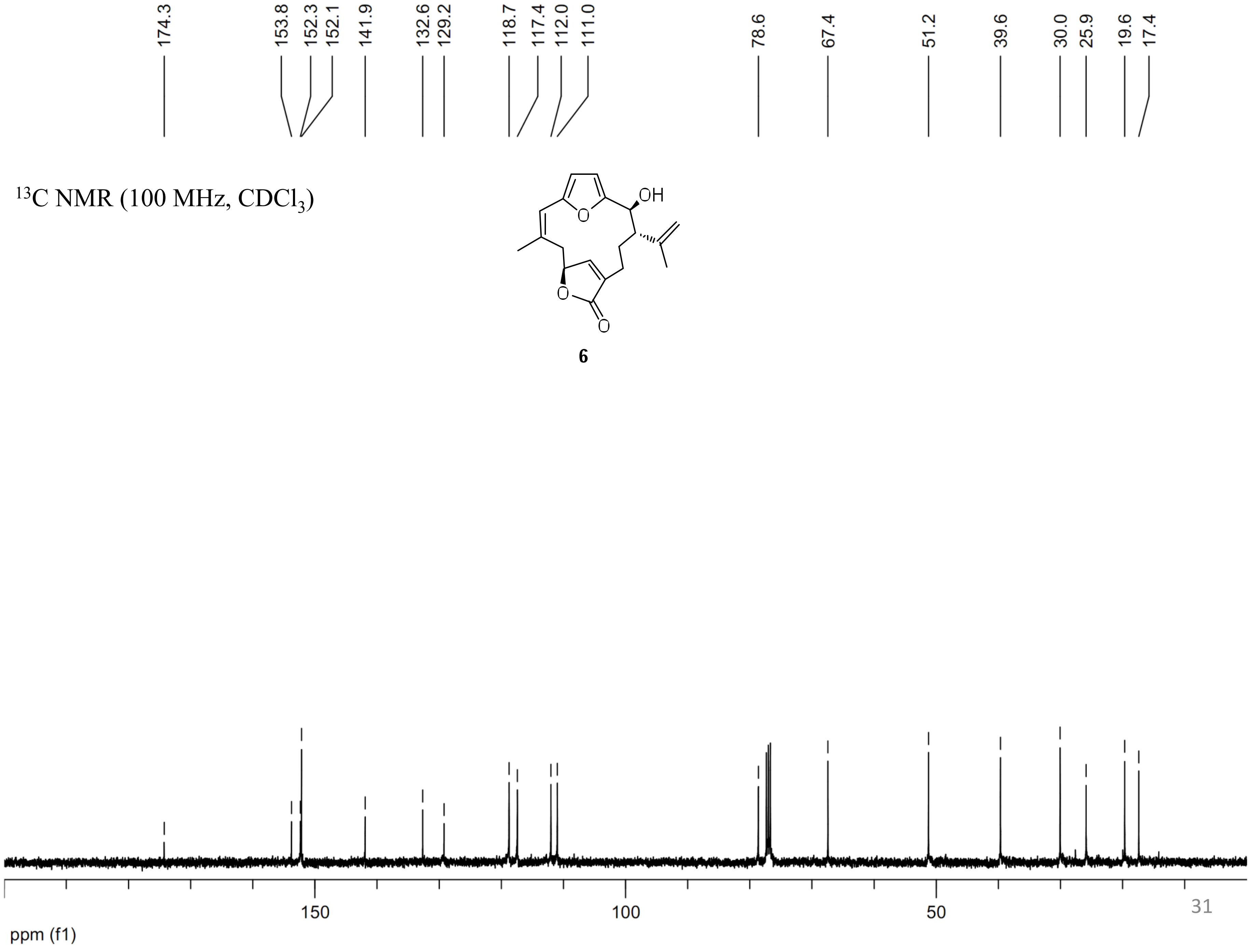
13

^{1}H NMR (400 MHz, $CDCl_3$)



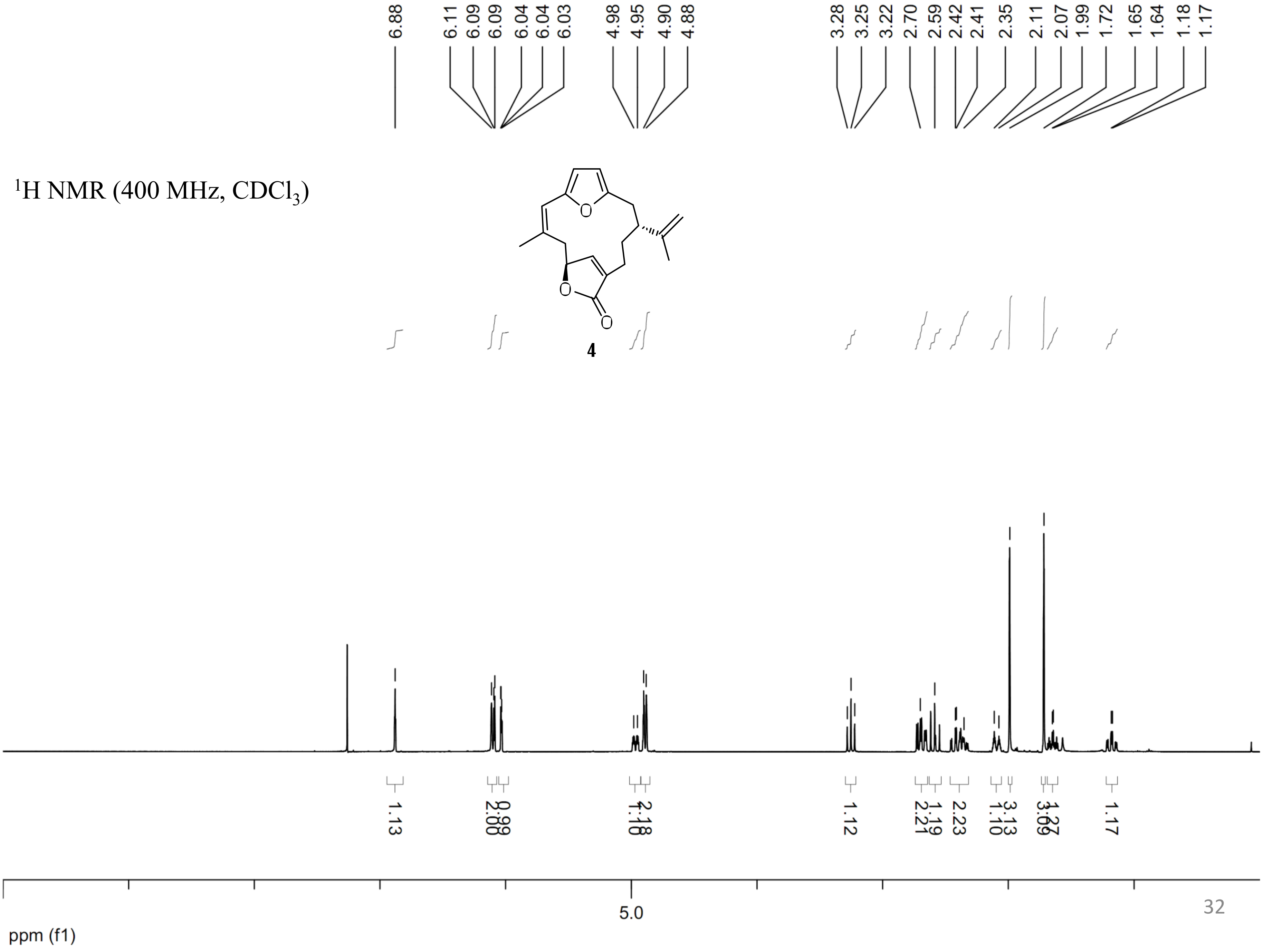
6

^{13}C NMR (100 MHz, CDCl$_3$)



6

^{1}H NMR (400 MHz, CDCl$_3$)



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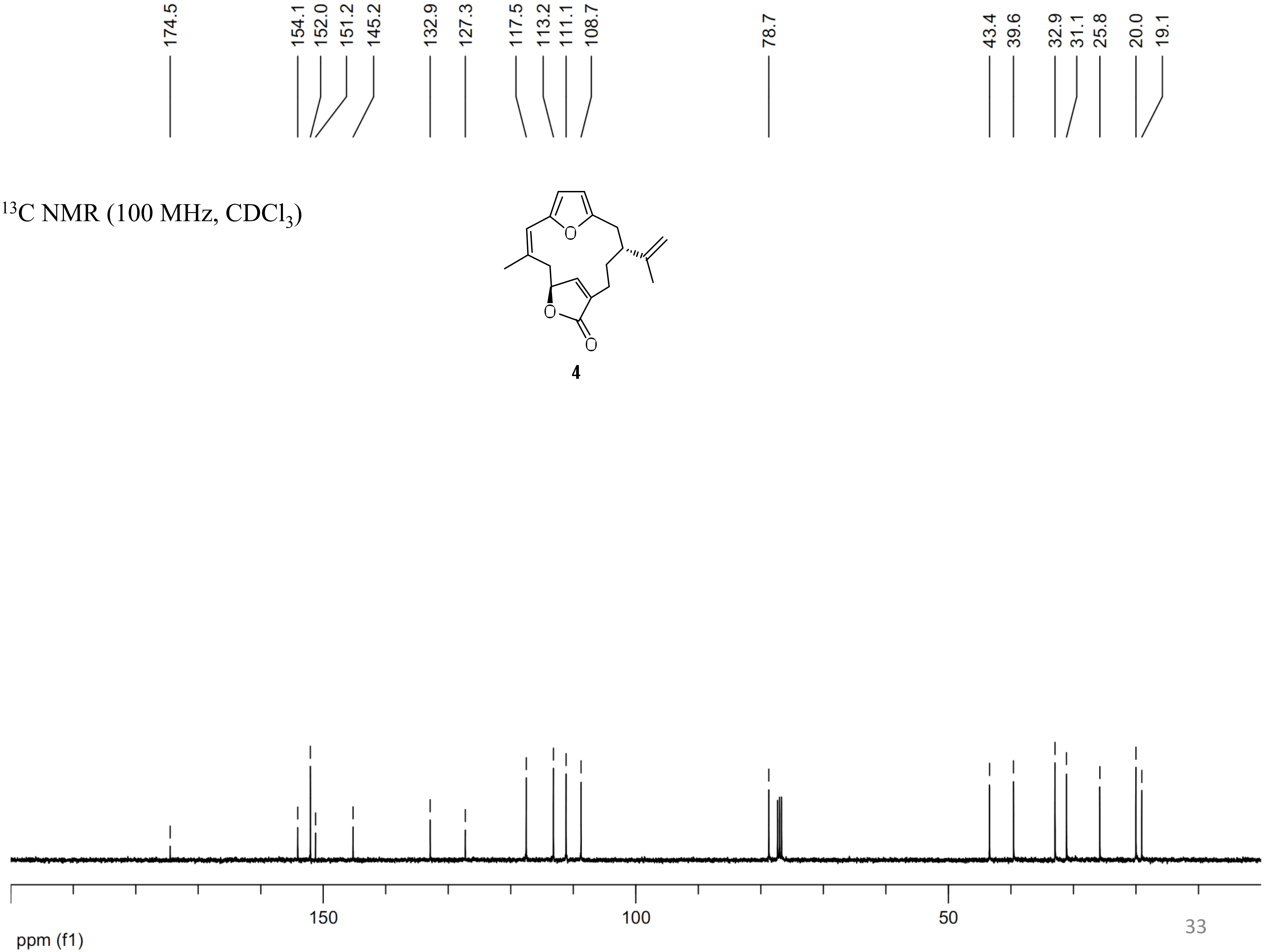
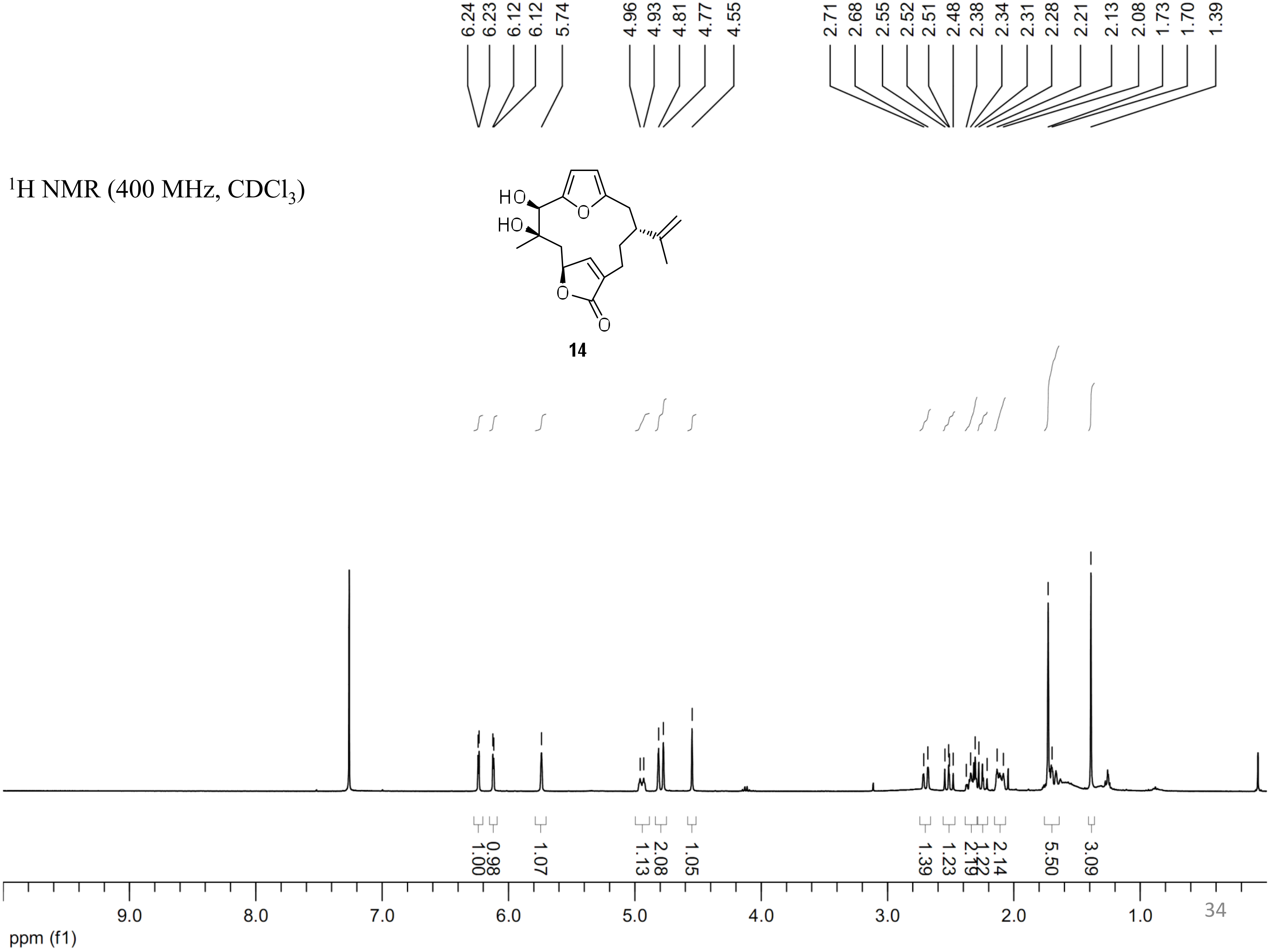


^{13}C NMR (100 MHz, CDCl$_3$)

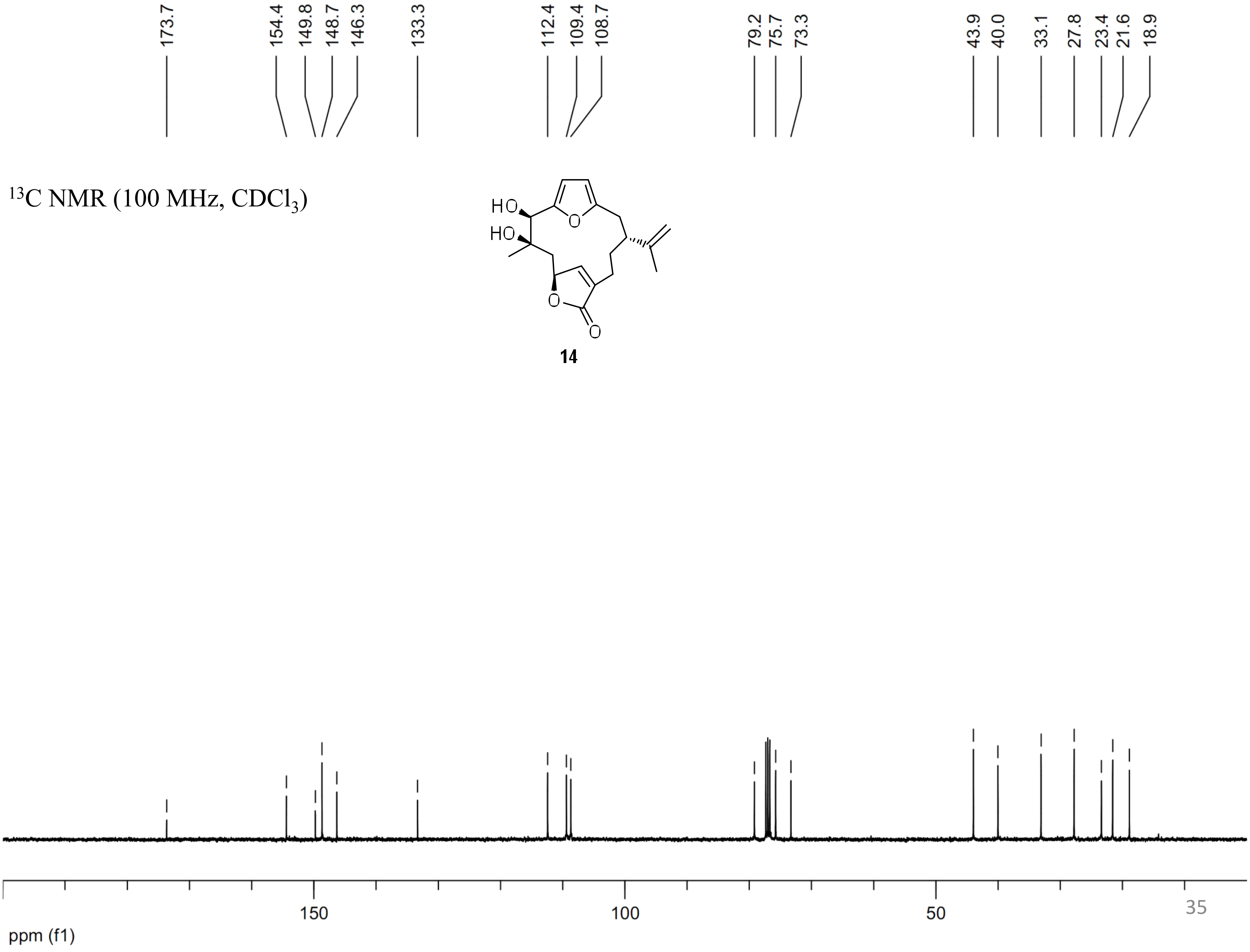
4

^{1}H NMR (400 MHz, $CDCl_3$)



14

^{13}C NMR (100 MHz, CDCl$_3$)



14

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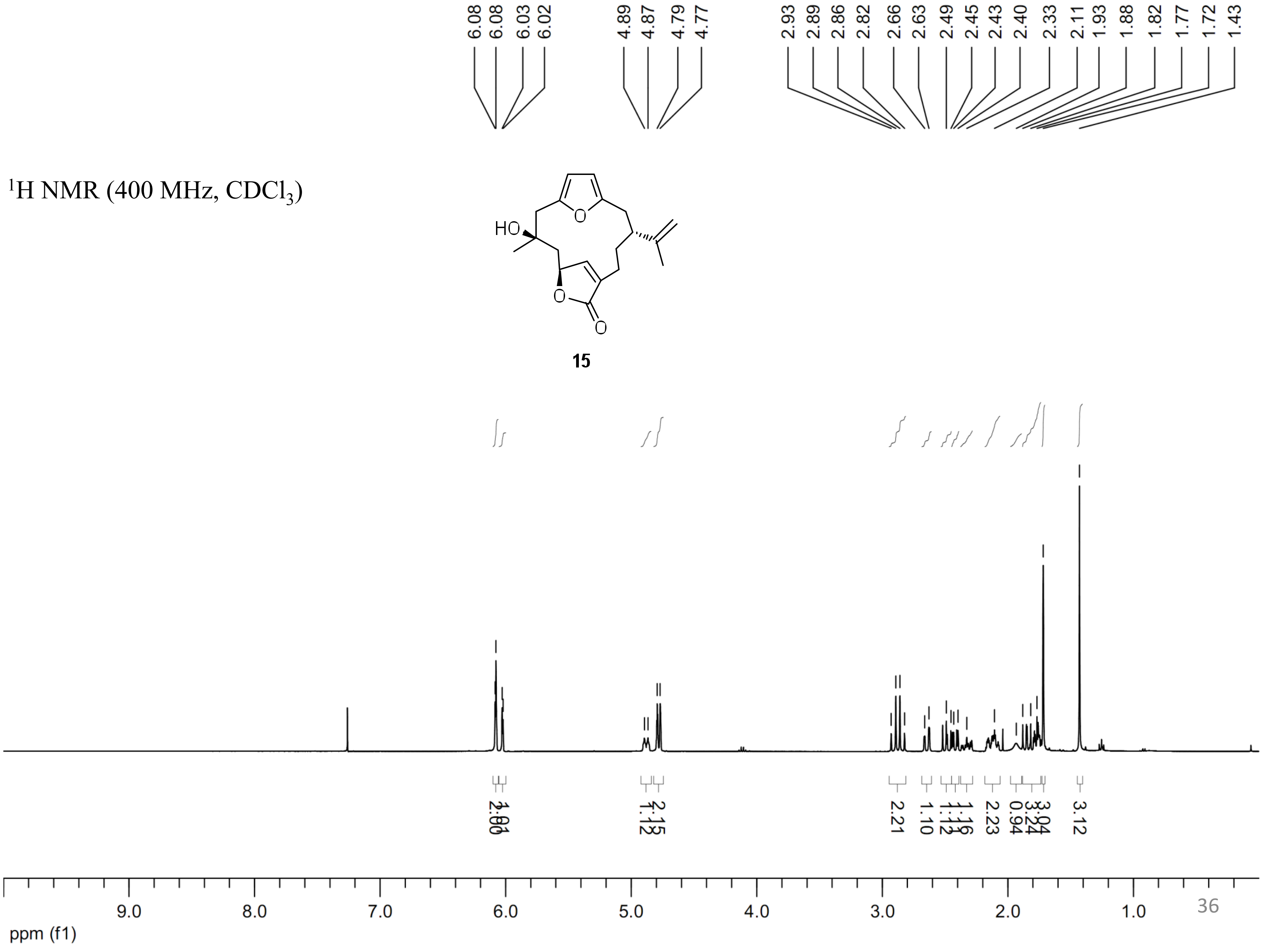

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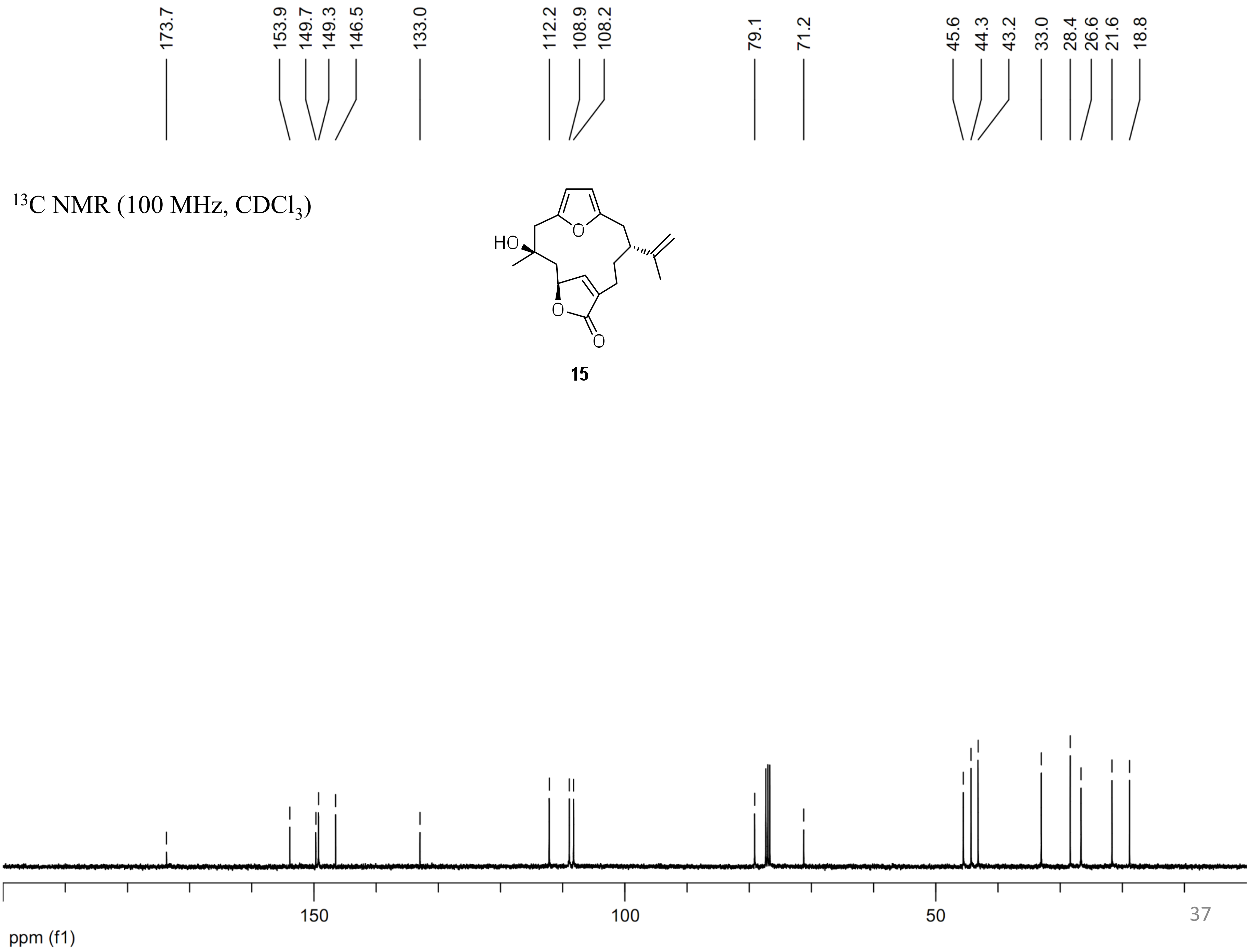
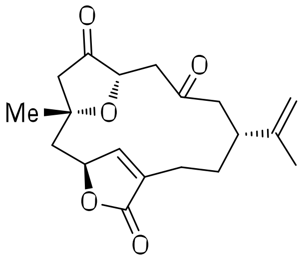
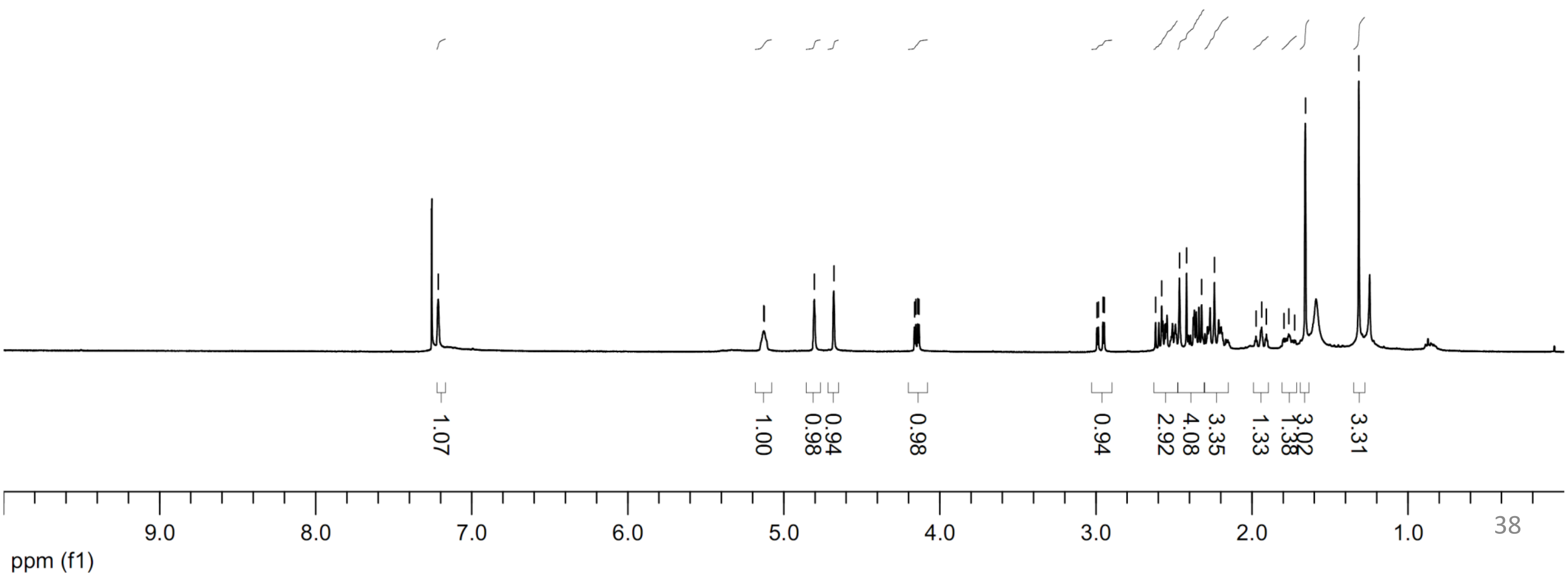


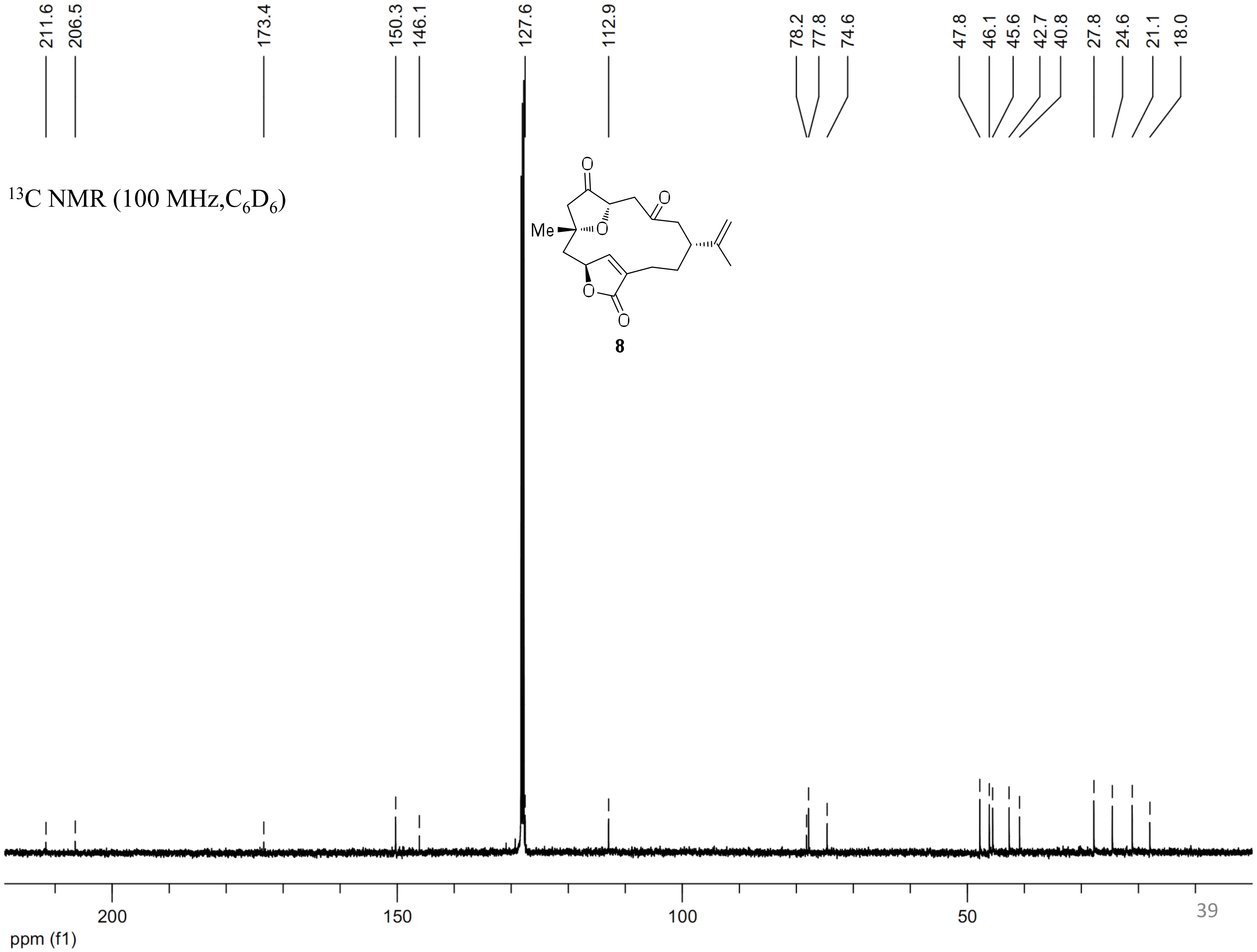
15

^{1}H NMR (400 MHz, CDCl$_3$)



8

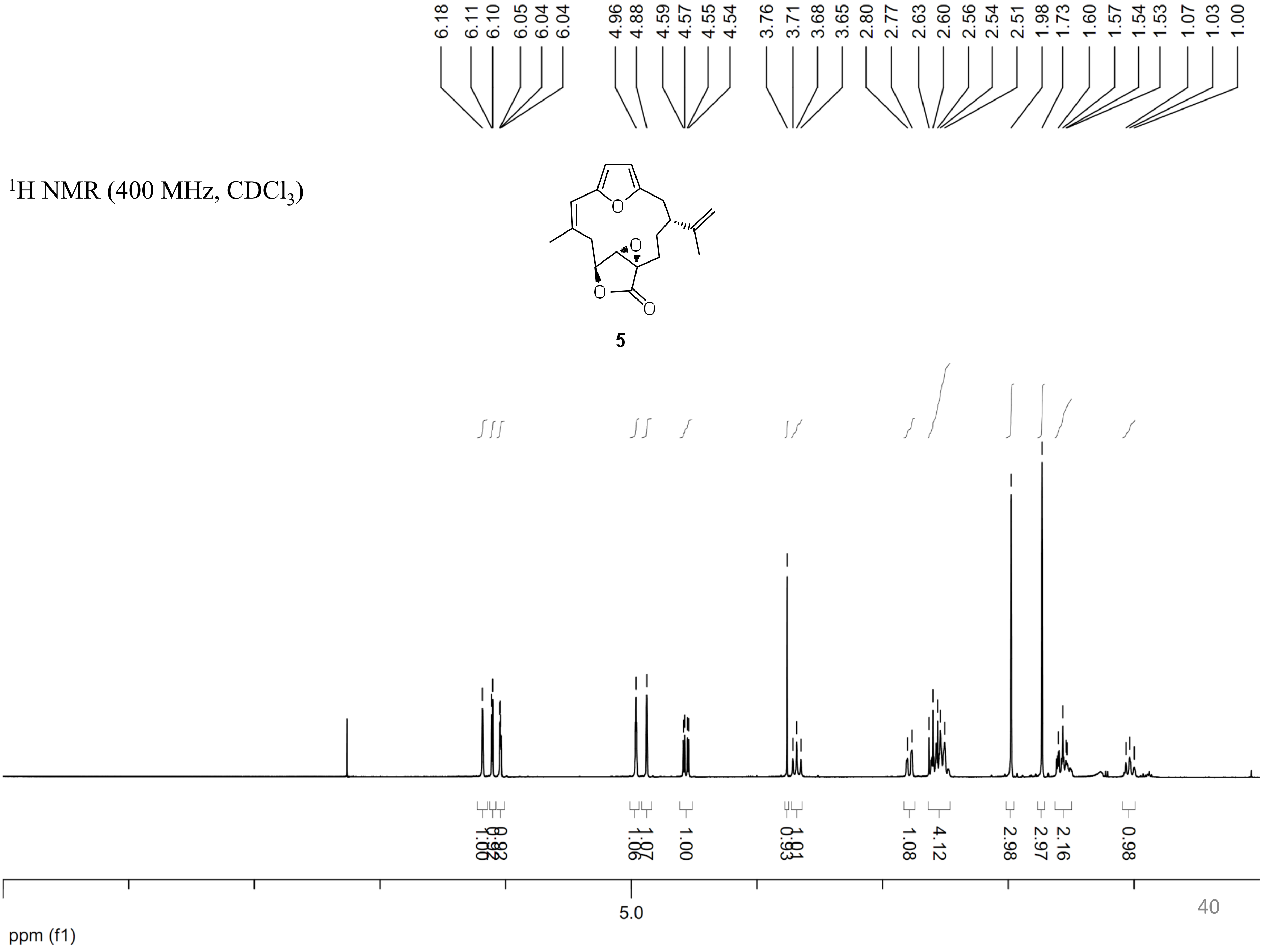




^{13}C NMR (100 MHz,C_6D_6)

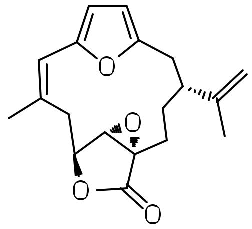
8

^{1}H NMR (400 MHz, $CDCl_3$)



5

^{13}C NMR (100 MHz, $CDCl_3$)



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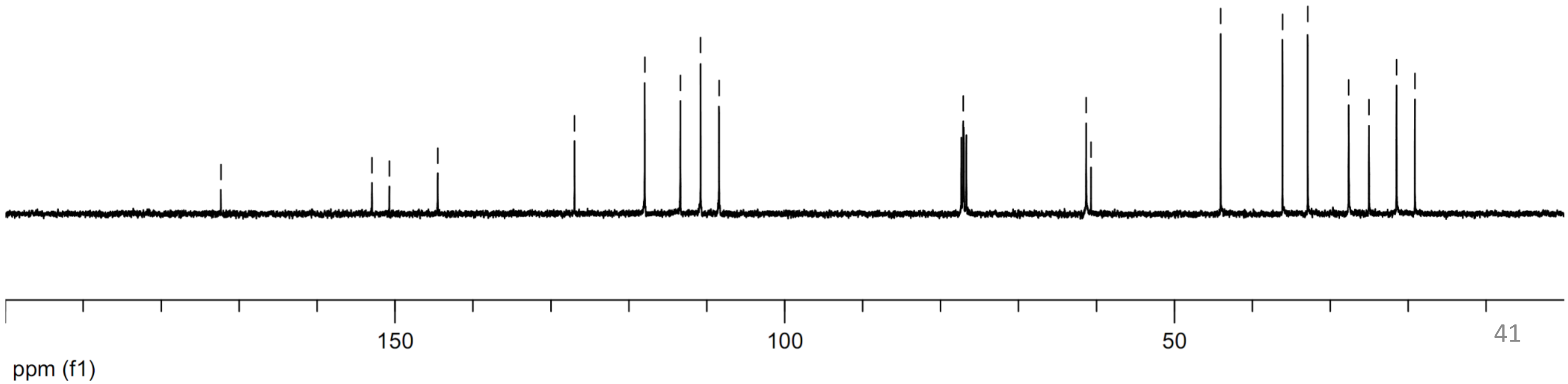
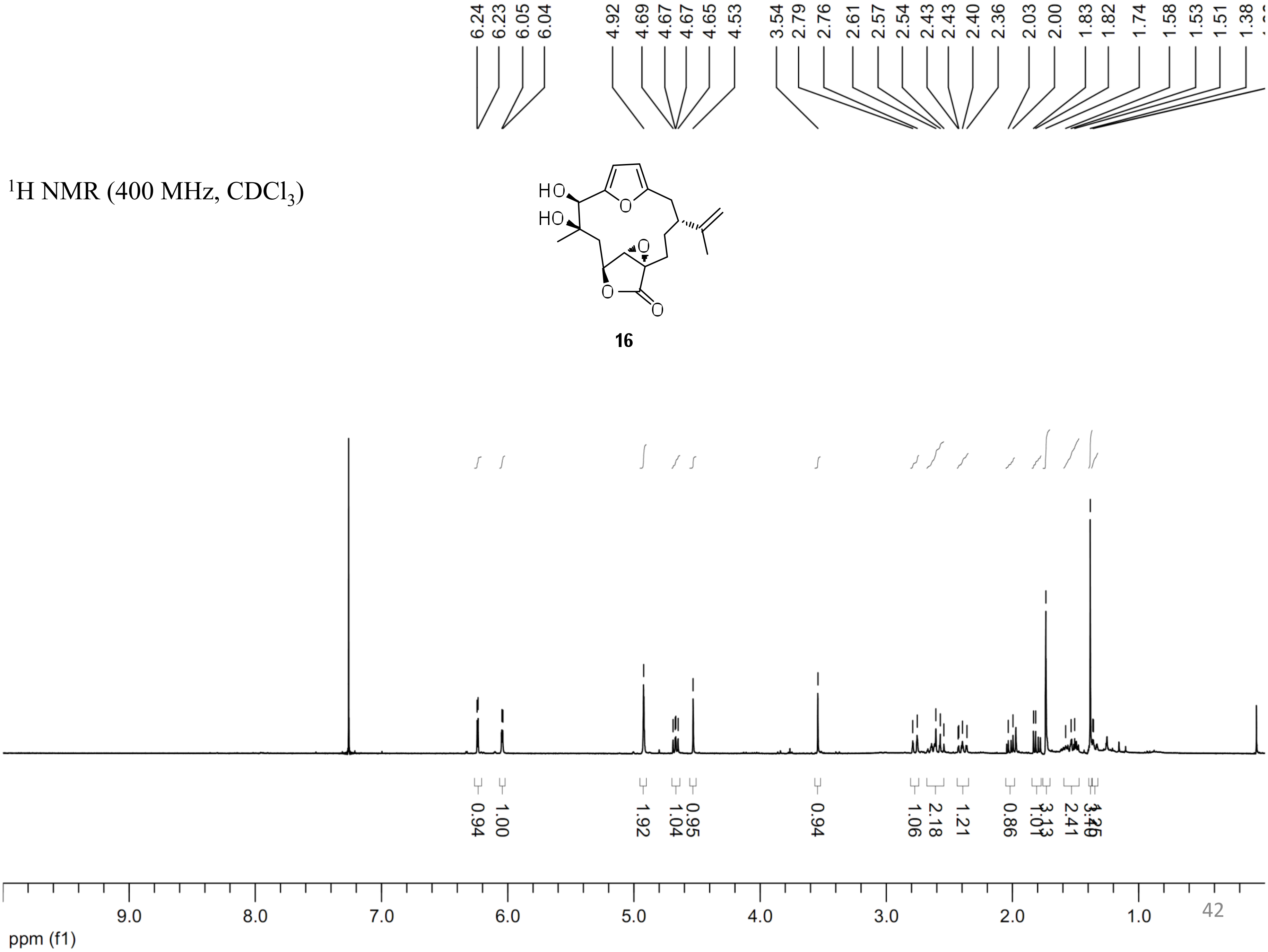
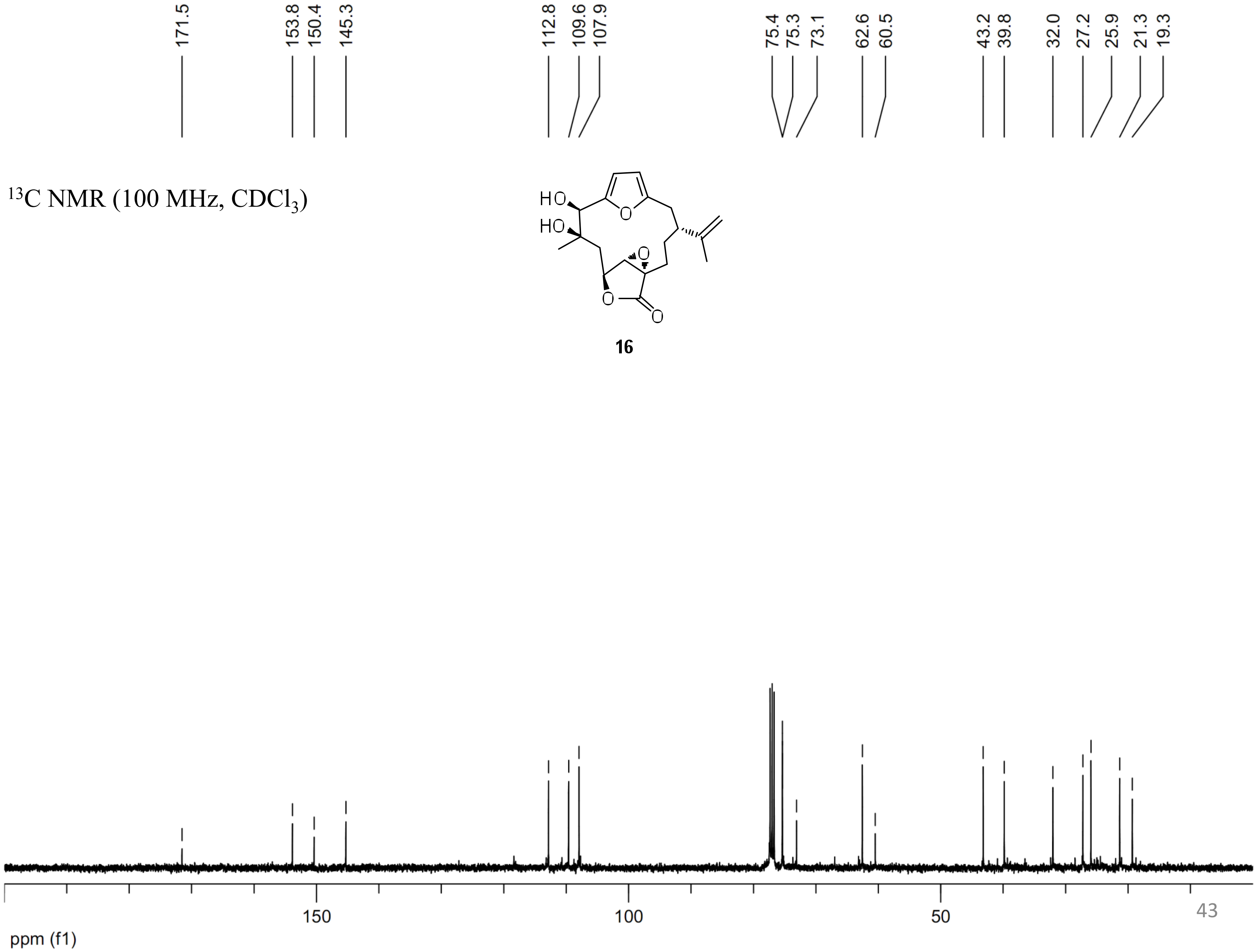


^{1}H NMR (400 MHz, $CDCl_3$)



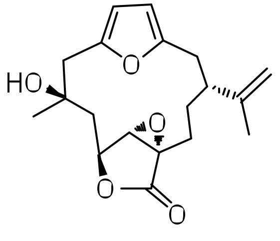
16



^{13}C NMR (100 MHz, $CDCl_3$)

16

^{1}H NMR (400 MHz, $CDCl_3$)



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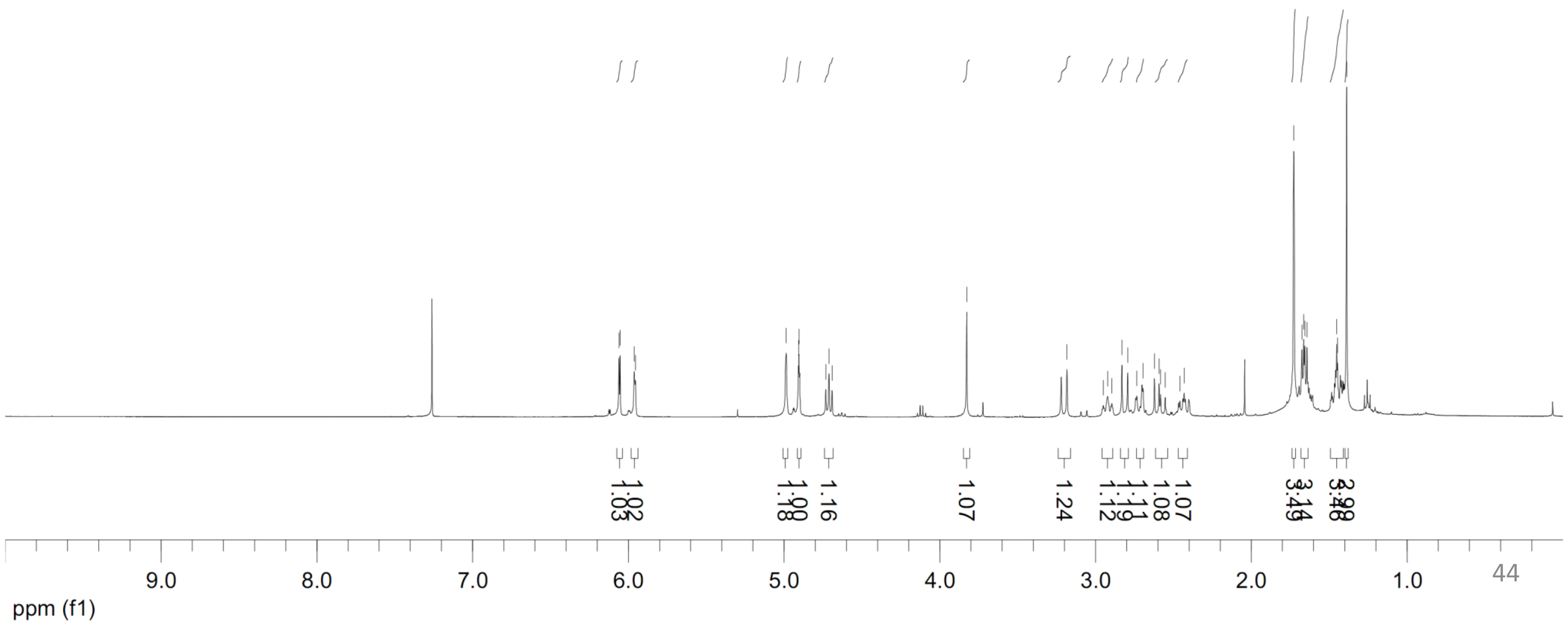
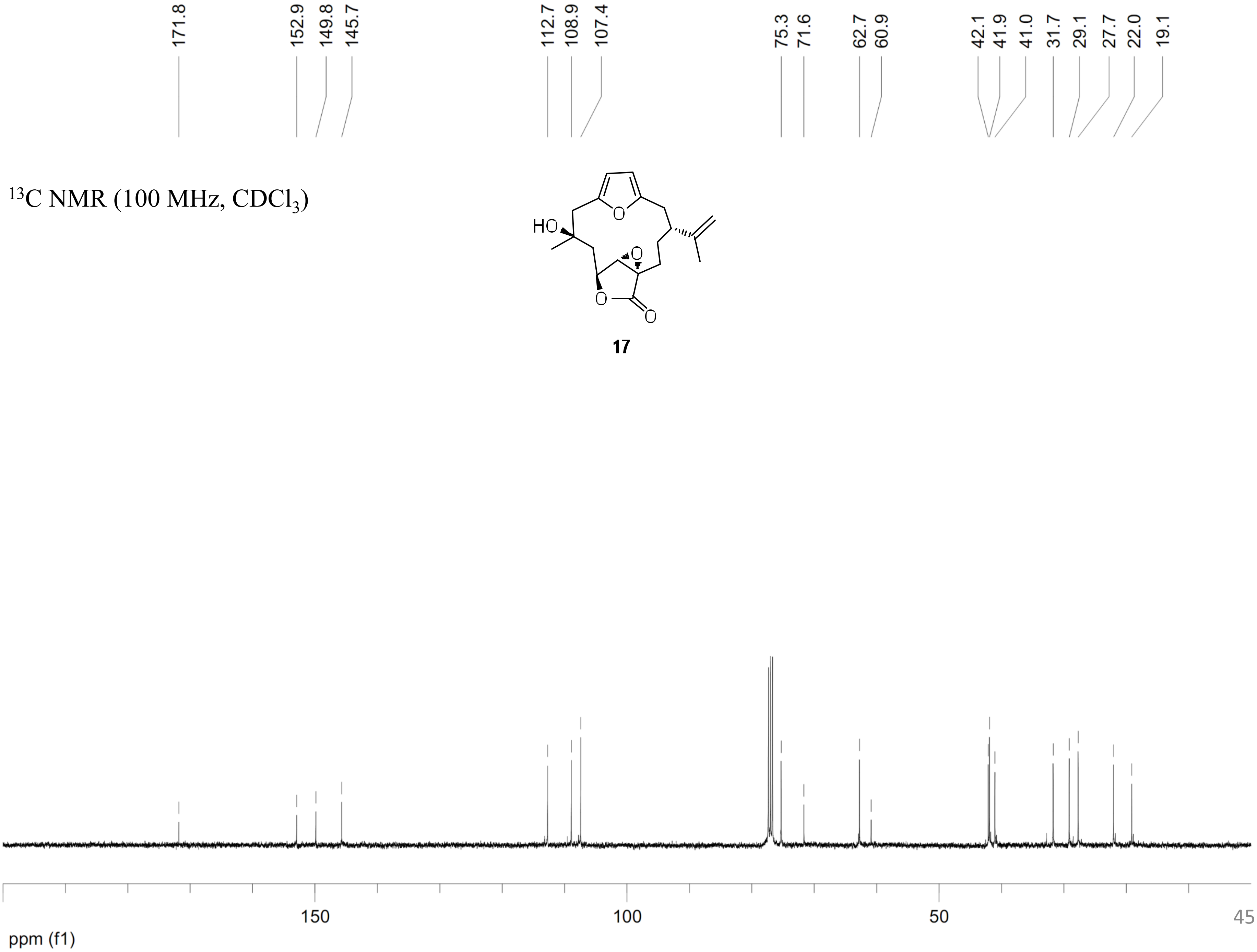
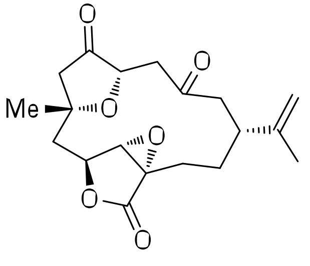


^{13}C NMR (100 MHz, CDCl$_3$)

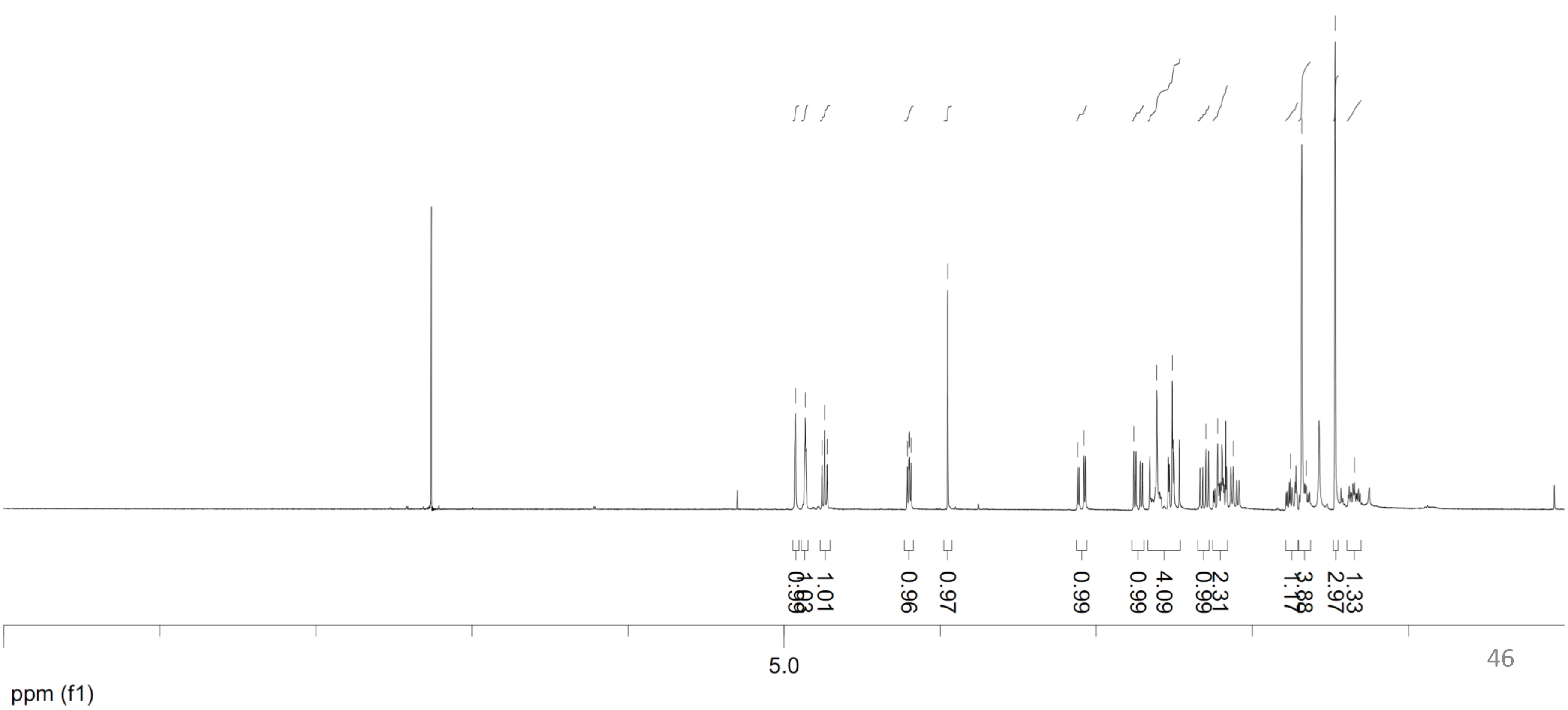


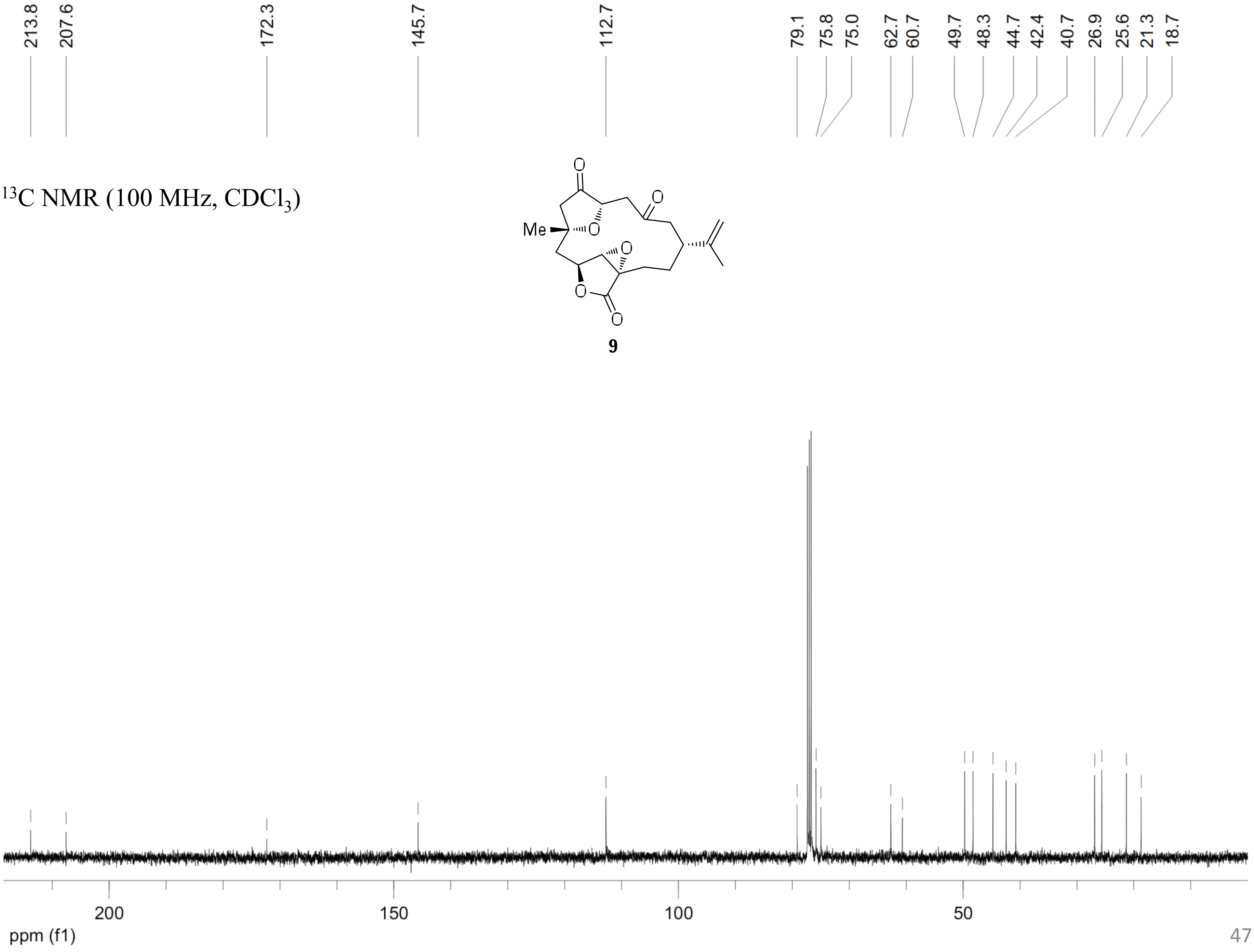
17

^{1}H NMR (400 MHz, CDCl$_3$)



9





^{13}C NMR (100 MHz, CDCl$_3$)

9