

Enantioselective Construction of the Tricyclic Core of Curcusones A–D via a Cross-Electrophile Coupling Approach

Austin C. Wright and Brian M. Stoltz*

Warren and Katharine Schlinger Laboratory for Chemistry and Chemical Engineering, Division of Chemistry and Chemical Engineering, California Institute of Technology, MC 101-20, Pasadena, California 91125, United States

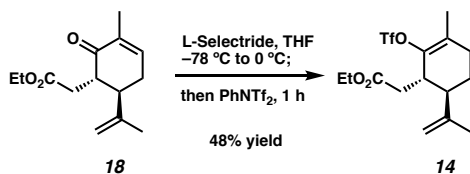
Table of Contents

1. Materials and Methods.....	S2
2. Procedural Information	S2
3. NMR and IR Spectra of New Compounds.....	S8
4. X-Ray Crystal Structure Analysis of 24	S26

Materials and Methods

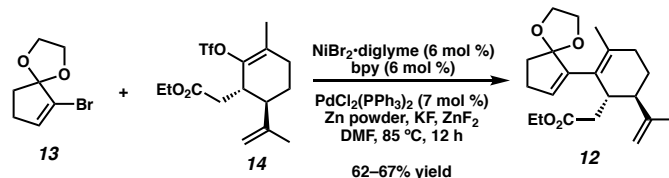
Unless otherwise stated, reactions were performed in oven-dried glassware under a nitrogen atmosphere using dry, deoxygenated solvents (passed over a column of activated alumina under argon). Commercially obtained reagents were used as received. Reactions requiring external heat were modulated to the specified temperatures using an IKAmag temperature controller. Reaction progress was monitored by thin-layer chromatography (TLC), which was performed using E. Merck silica gel 60 F254 precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching, potassium permanganate, or *p*-anisaldehyde staining. Silicycle SiliaFlash® P60 Academic Silica gel (particle size 40-63 nm) was used for column chromatography. ¹H and ¹³C NMR spectra were recorded on Varian Inova 500 (500 MHz and 126 MHz, respectively) and Bruker 400 (400 MHz and 101 MHz, respectively) spectrometers. Data for ¹H NMR are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, m = multiplet. Infrared (IR) spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer using thin films deposited on NaCl plates and are reported in frequency of absorption (cm⁻¹). Optical rotations were measured with a Jasco P-2000 polarimeter operating on the sodium D-line (589 nm), using a 100 mm path-length cell and are reported as: [α]_D²⁵ (concentration in g/100 mL, solvent). High Resolution Mass Spectrometer in an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI+).

Procedural Information



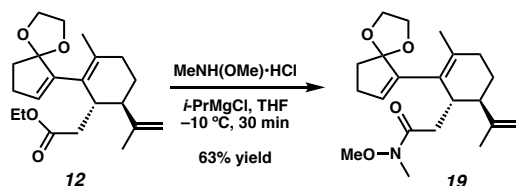
Ethyl 2-((1*S*,6*R*)-3-methyl-6-(prop-1-en-2-yl)-2-(((trifluoromethyl)sulfonyl)oxy)cyclohex-2-en-1-yl)acetate (**14**)

To a solution of **18** (8.00 g, 33.86 mmol) in THF (113 mL, 0.3M) at -78 °C was added a 1M solution of L-Selectride in THF (33.9 mL, 1.0 equiv) over 1 min. The solution was stirred at -78 °C for an additional 30 min. The septum was briefly removed, and solid *N*-phenyltriflimide (12.1 g, 33.9 mmol, 1.0 equiv) was quickly added in one portion. The resulting mixture was warmed to 0 °C. After stirring for an additional 30 min, the reaction was poured into sat. aq. NH₄Cl (300 mL) and extracted with Et₂O (3 X 500 mL). The combined organic layers were dried (Na₂SO₄), concentrated *in vacuo*, and purified by *careful* column chromatography (3% EtOAc in hexanes) to afford vinyl triflate **14** as a colorless oil (6.43 g, 48% yield); $R_f = 0.6$ (5% EtOAc in hexanes); [α]_D²⁵ -27.6 (*c* 1, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 4.83–4.81 (m, 2H), 4.10–4.06 (m, 2H), 2.92–2.87 (m, 1H), 2.63–2.60 (m, 1H), 2.44–2.36 (m, 2H), 2.16–2.13 (m, 2H), 1.77 (s, 3H), 1.69 (s, 3H), 1.70–1.69 (m, 2H), 1.66–1.62 (m, 4H), 1.22 (t, $J = 7.1$ Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 171.2, 145.5, 143.4, 128.8, 118.4 (q, $J = 321$ Hz, CF₃) 112.6, 60.4, 47.5, 37.8, 35.0, 29.6, 25.2, 19.7, 17.3, 14.0; IR (Neat Film, NaCl) 2981.4, 2936.9, 1738.2, 1732.2, 1415.6, 1377.8, 1247.2, 1209.3, 1158.3, 1142.6, 1036.0, 947.8, 890.0, 813.3 cm⁻¹; HRMS (ESI-TOF) m/z calc'd for C₁₅H₂₁F₃O₅SNa [M+Na]⁺: 393.0954, found 393.0947.



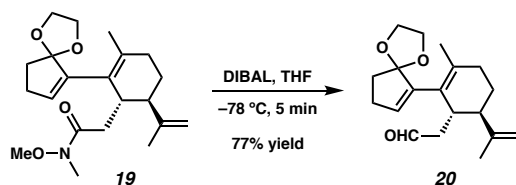
Ethyl 2-((1*S*,6*R*)-3-methyl-6-(prop-1-en-2-yl)-2-(1,4-dioxaspiro[4.4]non-6-en-6-yl)cyclohexan-1-yl)acetate (**12**)

In a nitrogen-filled glovebox, a solution of NiBr₂·diglyme (169.3 mg, 6 mol %) precatalyst and bpy (75.0 mg, 6 mol %) in DMF (5 mL) was prepared and stirred vigorously for 10 min. Meanwhile, Zn⁰ dust (2.09 g, 32.0 mmol, 4 equiv), KF (464.2 mg, 8.00 mmol, 1 equiv), PdCl₂(PPh₃)₂ (393.4 mg, 7 mol %), and ZnF₂ (1.65 g, 16.00 mmol, 2 equiv) were added to a 100 mL vial equipped with a cross-shaped stir bar. These solids were diluted with DMF (43 mL), and the resulting suspension was treated with a solution of vinyl bromide **13** (328.1 mg, 1.60 mmol, 0.2 equiv) and vinyl triflate **14** (2.96 g, 8.00 mmol, 1.0 equiv) in DMF (10 mL). The light green Ni(II)bpy solution was added to the vial, and the vial was capped with a septum and removed from the glove box. The reaction mixture was placed under a N₂ atmosphere and heated to 85 °C under vigorous stirring. Next, a pre-made solution of bromide **13** (1.97 g, 9.6 mmol, 1.2 equiv) in DMF (8 mL) was added to the heated mixture over 2 h via syringe pump. The reaction was stirred vigorously at 85 °C for an additional 12 h, after which it was allowed to cool to 23 °C. The resulting black slurry was poured into sat. aq. LiCl (500 mL), and it was extracted with Et₂O (500 mL x 4) until TLC confirmed no product remained in the aqueous layer. The combined organic layers were again extracted with brine (1 L), dried (Na₂SO₄), and concentrated *in vacuo*. (Note during extraction: The border between the organic and aqueous layers may be readily determined by olfactory analysis; If Zn(II) salts remain in the organic layer following extraction, they can be easily removed by passage through a plug of silica (Et₂O as eluent).) The crude mixture was purified by column chromatography (15% EtOAc in hexanes) to afford bicycle **12** as a colorless oil (1.72 g, 62% yield); R_f = 0.55 (20% EtOAc in hexanes); [α]_D²⁵ –122.8 (*c* 1, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 5.71 (t, *J* = 2.5 Hz, 1H), 4.82–4.75 (m, 2H), 4.05 (q, *J* = 7.1 Hz, 2H), 3.97–3.91 (m, 4H), 2.80–2.76 (m, 1H), 2.62–2.58 (m, 1H), 2.38–2.36 (m, 2H), 2.27–2.22 (m, 2H), 2.08–1.95 (m, 5H), 1.71 (s, 3H), 1.65–1.63 (m, 4H), 1.24–1.21 (m, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 147.8, 141.8, 136.1, 132.7, 127.9, 120.8, 110.9, 65.0, 64.4, 59.8, 45.5, 37.9, 37.4, 36.0, 30.0, 27.9, 25.0, 21.6, 20.4, 14.2; IR (Neat Film, NaCl) 2974.0, 2922.1, 2884.9, 1735.7, 1449.8, 1373.1, 1373.1, 1317.0, 1171.1, 1149.4, 1039.9, 1028.2, 946.5, 923.9, 888.5, 856.6, 850.4 cm⁻¹; HRMS (ESI-TOF) *m/z* calc'd for C₂₁H₃₀O₄ [M+H]⁺: 347.2222, found 347.2215.



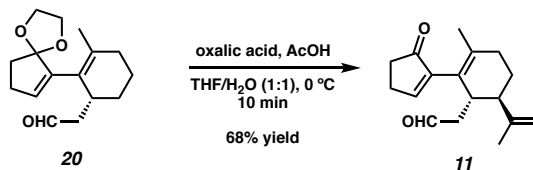
N-methoxy-*N*-methyl-2-((1*S*,6*R*)-3-methyl-6-(prop-1-en-2-yl)-2-(1,4-dioxaspiro[4.4]non-6-en-6-yl)cyclohexan-1-yl)acetamide (**19**)

To a $-10\text{ }^{\circ}\text{C}$ solution of ester **12** (1.72 g, 4.96 mmol) and $\text{MeNH}(\text{OMe})\cdot\text{HCl}$ (1.07 g, 10.92 mmol, 2.2 equiv) in THF (50 mL) was slowly added a 2M solution of *i*-PrMgCl in THF (10 mL, 4.0 equiv) over several minutes. The reaction was stirred at $-10\text{ }^{\circ}\text{C}$ for 30 min then poured into sat. aq. NH_4Cl (50 mL), extracted with Et_2O (50 mL X 3), dried (Na_2SO_4) and concentrated *in vacuo*. The crude residue was purified by column chromatography (50% EtOAc in hexanes), concentrated, and stripped twice with hexanes (5 mL X 2) to provide amide **19** as a viscous clear oil (1.11 g, 63% yield); $R_f = 0.40$ (50% EtOAc in hexanes); $[\alpha]_{\text{D}}^{25} -118.5$ (*c* 1, CHCl_3); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 5.75 (t, $J = 2.5$, 1H), 4.87 (s, 1H), 4.80 (s, 1H), 4.04–3.90 (m, 4H), 3.67 (s, 3H), 3.15 (s, 3H), 2.70 (m, 2.71–2.68, 1H), 2.42–2.38 (m, 1H), 2.35–2.33 (m, 4H), 2.11–2.01 (m, 4H), 1.76 (s, 3H), 1.71–1.64 (m, 5H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 174.4, 147.9, 142.3, 135.8, 132.3, 128.3, 120.7, 110.2, 64.9, 64.4, 61.1, 44.3, 36.7, 36.1, 35.1, 29.5, 27.9, 24.0, 21.6 (two resolved signals), 21.1; IR (Neat Film, NaCl) 2932.6, 1669.5, 1451.9, 1405.9, 1377.1, 1317.0, 1217.2, 1198.3, 1140.9, 1102.9, 1043.4, 1024.0, 1005.4, 948.9, 927.1, 890.5, 858.4 cm^{-1} ; HRMS (ESI-TOF) m/z calc'd for $\text{C}_{21}\text{H}_{31}\text{NO}_4$ $[\text{M}+\text{H}]^+$: 362.2326, found 362.2314.



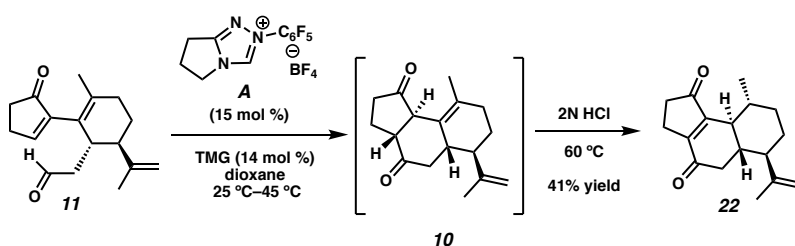
2-((1*S*,6*R*)-3-methyl-6-(prop-1-en-2-yl)-2-(1,4-dioxaspiro[4.4]non-6-en-6-yl)cyclohexan-1-yl)acetaldehyde (20**)**

To a $-78\text{ }^{\circ}\text{C}$ solution of amide **19** (1.13 g, 3.11 mmol) in THF (31 mL) was added a 1M solution of DIBAL (3.72 mmol, 1.2 equiv) over 1 min. The solution was stirred at $-78\text{ }^{\circ}\text{C}$ for 5 min after which it was poured into a combined solution of aq. NaHCO_3 (2 M, 100 mL) and sat. aq. Rochelle's salt (100 mL). The biphasic mixture was vigorously stirred for 30 min, extracted with Et_2O (100 mL X 3), dried (Na_2SO_4), and concentrated *in vacuo*. The crude residue was purified by column chromatography (15% EtOAc in hexanes) to provide aldehyde **20** as a pale yellow oil (729 mg, 77% yield); $R_f = 0.35$ (5% EtOAc in hexanes); $[\alpha]_{\text{D}}^{25} -118.5$ (*c* 1, CHCl_3); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 9.60 (s, 1H), 5.66 (t, $J = 2.5$ Hz, 1H), 4.79–4.78 (m, 2H), 3.92–3.88 (m, 4H), 2.88–2.83 (m, 1H), 2.49–2.48 (m, 1H), 2.40–2.34 (m, 3H), 2.08–2.03 (m, 5H), 1.68 (s, 3H), 1.67–1.64 (s, 5H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 204.2, 147.5, 141.7, 136.8, 133.4, 127.7, 120.9, 111.7, 64.9, 64.5, 47.3, 47.2, 36.4, 35.9, 30.7, 27.9, 26.6, 20.1 (2 resolved signals); IR (Neat Film, NaCl) 2967.8, 2919.9, 2857.8, 2831.6, 2716.8, 1721.1, 1644.3, 1449.7, 1376.7, 1317.6, 1216.6, 1142.2, 1088.5, 1044.2, 1025.3, 948.2, 926.2, 892.1, 855.7 cm^{-1} ; HRMS (ESI-TOF) m/z calc'd for $\text{C}_{19}\text{H}_{26}\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$: 325.1774, found 325.1764.



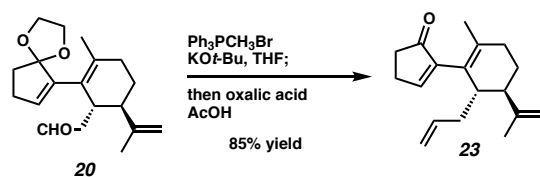
2-((1*S*,6*R*)-3-methyl-2-(5-oxocyclopent-1-en-1-yl)-6-(prop-1-en-2-yl)cyclohex-2-en-1-yl)acetaldehyde (11**)**

To a 0 °C solution of ketal **20** (345 mg, 1.34 mmol) in THF (10 mL) were sequentially added a pre-made solution of AcOH (0.8 mL, 13.40 mmol, 10 equiv) and H₂O (1 mL) followed by solid oxalic acid•dihydrate (169 mg, 1.0 equiv). The reaction was religiously monitored by TLC until deemed complete (ca. 5–10 min) after which it was quickly poured into ice-cold sat. aq. Na₂CO₃ (30 mL). (Note: prolonged reaction times result in rapid product decomposition.) The mixture was extracted with Et₂O (3 X 30 mL), dried (Na₂SO₄) and concentrated *in vacuo*. The crude residue was purified by column chromatography (20% EtOAc in hexanes) to provide enone **11** as a pale yellow oil (234.3 mg, 68% yield); *R*_f = 0.55 (30% EtOAc in hexanes); [α]_D²⁵ 1.5 (*c* 1, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 9.52 (s, 1H), 7.34 (t, *J* = 2.8 Hz, 1H), 4.82 (s, 2H), 3.00–2.93 (m, 1H), 2.65–2.63 (m, 2H), 2.43–2.41 (m, 2H), 2.31–2.23 (m, 2H), 2.17–2.09 (m, 2H), 2.03–2.01 (m, 1H), 1.70–1.67 (m, 5H), 1.50 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 209.0, 202.8, 161.9, 147.1, 146.5, 134.1, 124.9, 112.2, 47.3, 47.1, 36.2, 34.5, 30.7, 26.8, 26.1, 21.1, 19.9; IR (Neat Film, NaCl) 3071.3, 2920.7, 2715.1, 1697.5, 1644.9, 1436.1, 1407.7, 1377.7, 1297.7, 1267.7, 1195.4, 1092.7, 1054.5, 1010.1, 928.3, 896.8, 790.2 cm⁻¹; HRMS (ESI-TOF) *m/z* calc'd for C₁₇H₂₂O₂Na [M+Na]⁺: 281.1512, found 281.1504.



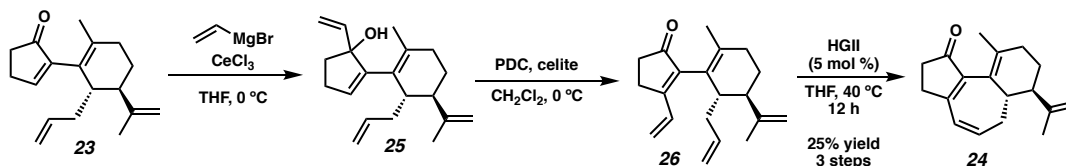
(5*aS*,6*R*,9*R*,9*aS*)-9-methyl-6-(prop-1-en-2-yl)-3,5,5*a*,6,7,8,9,9*a*-octahydro-1*H*-cyclopenta[*a*]naphthalene-1,4(2*H*)-dione (22**)**

To a vial containing catalyst **A** (16 mg, 15 mol %) under N₂ was added a solution of enone **11** (75 mg, 0.29 mmol) in dioxane (5 mL). To the stirring reaction was added catalytic 1,1,3,3-tetramethylguanidine (TMG, 5 μL, 14 mol %). The resulting yellow solution was stirred at 23 °C for 1 h after which it was heated to 35 °C and stirred for an additional 1 h. The solution was further heated to 45 °C and stirred for 12 h. Upon completion, the diastereomeric mixture was treated with 2N aq. HCl (5 mL) and heated to 60 °C until deemed complete by TLC (ca. 48 h). The reaction was diluted with H₂O (20 mL) and extracted with EtOAc (3 X 20 mL). (Note: the product will remain in the aqueous layer if neutralized with base). The combined organic layers were dried (MgSO₄), concentrated *in vacuo*, and purified by column chromatography (15% EtOAc in hexanes) to afford ene-dione **22** as a viscous yellow oil (31 mg, 41% yield); *R*_f = 0.65 (20% EtOAc in hexanes); [α]_D²⁵ -111.5 (*c* 0.5, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 4.81 (s, 1H), 4.76 (s, 1H), 2.93–2.58 (m, 6H), 2.28–1.98 (m, 4H), 1.84 (s, 3H), 1.71–1.54 (m, 7H); ¹³C NMR (126 MHz, CDCl₃) δ 207.4, 199.5, 157.6, 151.6, 146.3, 142.6, 121.4, 112.3, 50.1, 45.6, 40.9, 36.0, 33.8, 27.1, 23.3, 22.2, 15.3; IR (Neat Film, NaCl) 2919.9, 2891.1, 1715.8, 1677.2, 1642.8, 1438.0, 1251.6, 1200.2, 114.3, 893.0 cm⁻¹; HRMS (ESI-TOF) *m/z* calc'd for C₁₇H₂₂O₂ [M+H]⁺: 259.1698, found 259.1686.



2-((5*R*,6*S*)-6-allyl-2-methyl-5-(prop-1-en-2-yl)cyclohex-1-en-1-yl)cyclopent-2-en-1-one (**23**)

To a 0 °C mixture of methyltriphenylphosphonium bromide (429 mg, 1.20 mmol, 1.5 equiv) in THF (4 mL) was added 1M $\text{KO}t\text{-Bu}$ in THF (1.0 mL, 1.3 equiv). The reagent mixture was stirred for 10 min after which a solution of aldehyde **20** (242 mg, 0.8 mmol) in THF (4 mL) was added dropwise over 1 min. The reaction was stirred at 0 °C until deemed complete by TLC (ca. 1 h). Subsequently, a solution of AcOH in H_2O (1:1, 2 mL) was added, followed by solid oxalic acid·dihydrate (100 mg, 1.0 equiv). The resulting mixture was stirred at 0 °C until deemed complete by TLC (ca. 1 h) after which it was poured into 2N Na_2CO_3 (20 mL), extracted with Et_2O (3 X 20 mL), dried (MgSO_4) and concentrated *in vacuo*. The crude product was purified by column chromatography (15%–20% EtOAc in hexanes) to provide enone **23** as a pale yellow oil (174.1 mg, 85% yield); $R_f = 0.50$ (20% EtOAc in hexanes); $[\alpha]_D^{25} -31.9$ (c 1, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.31 (s, 1H), 5.61–5.51 (m, 1H), 4.90–4.75 (m, 4H), 2.63–2.61 (m, 2H), 2.50–2.42 (m, 1H), 2.41–2.40 (m, 2H), 2.20–2.13 (m, 1H), 2.05–2.00 (m, 3H), 1.68 (s, 3H), 1.67–1.60 (m, 2H), 1.48 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 208.7, 160.4, 147.8, 146.8, 136.9, 133.3, 125.9, 115.9, 110.9, 43.9, 39.7, 36.2, 34.6, 30.2, 26.6, 25.1, 21.0, 20.4; IR (Neat Film, NaCl) 3071.6, 2974.8, 2924.2, 2859.1, 1703.5, 1642.8, 1440.1, 1406.5, 1375.8, 1297.7, 1255.9, 1195.0, 1093.5, 1001.1, 908.5, 889.4, 790.9 cm^{-1} ; HRMS (ESI-TOF) m/z calc'd for $\text{C}_{18}\text{H}_{25}\text{O}$ $[\text{M}+\text{H}]^+$: 257.1905, found 257.1899.

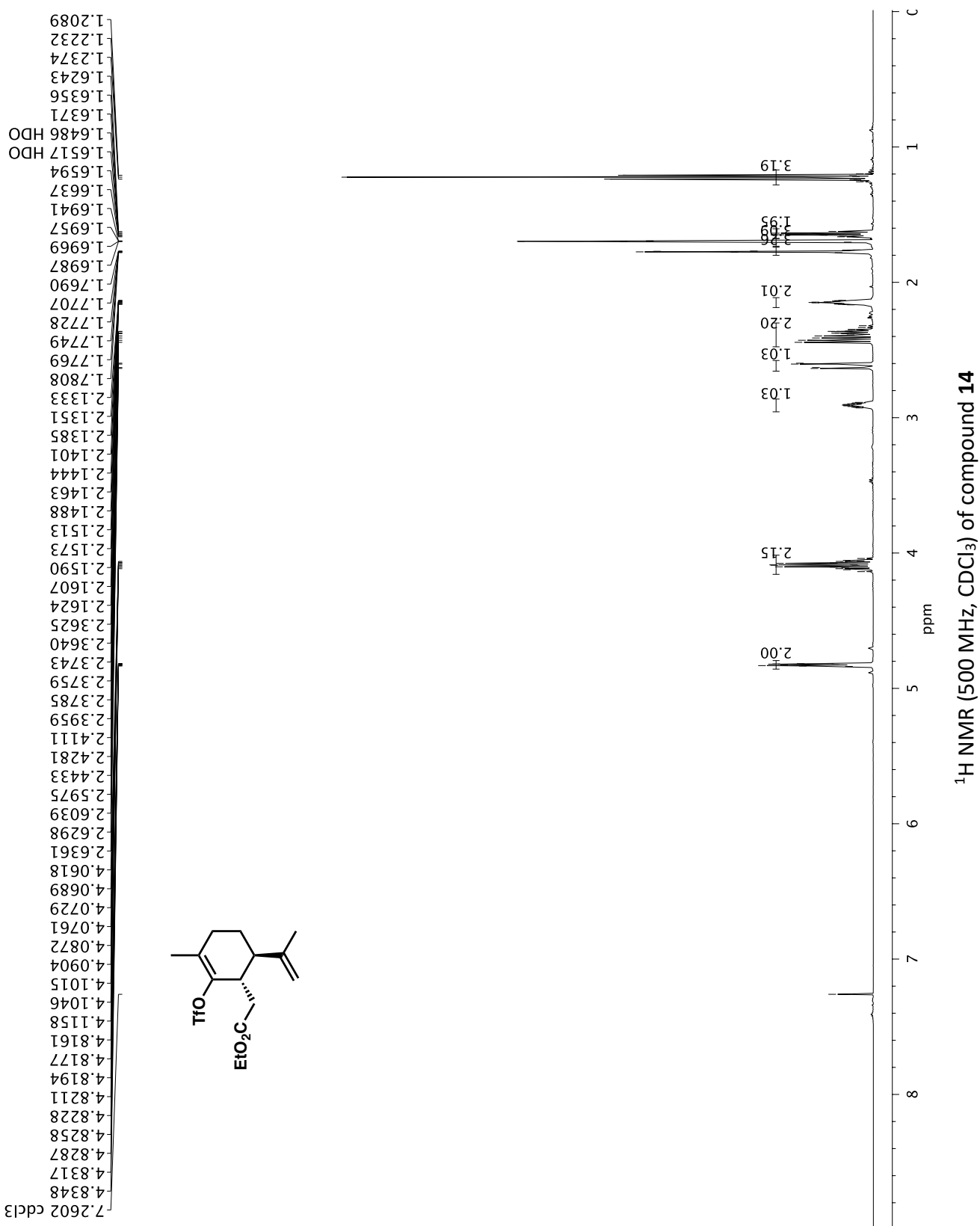


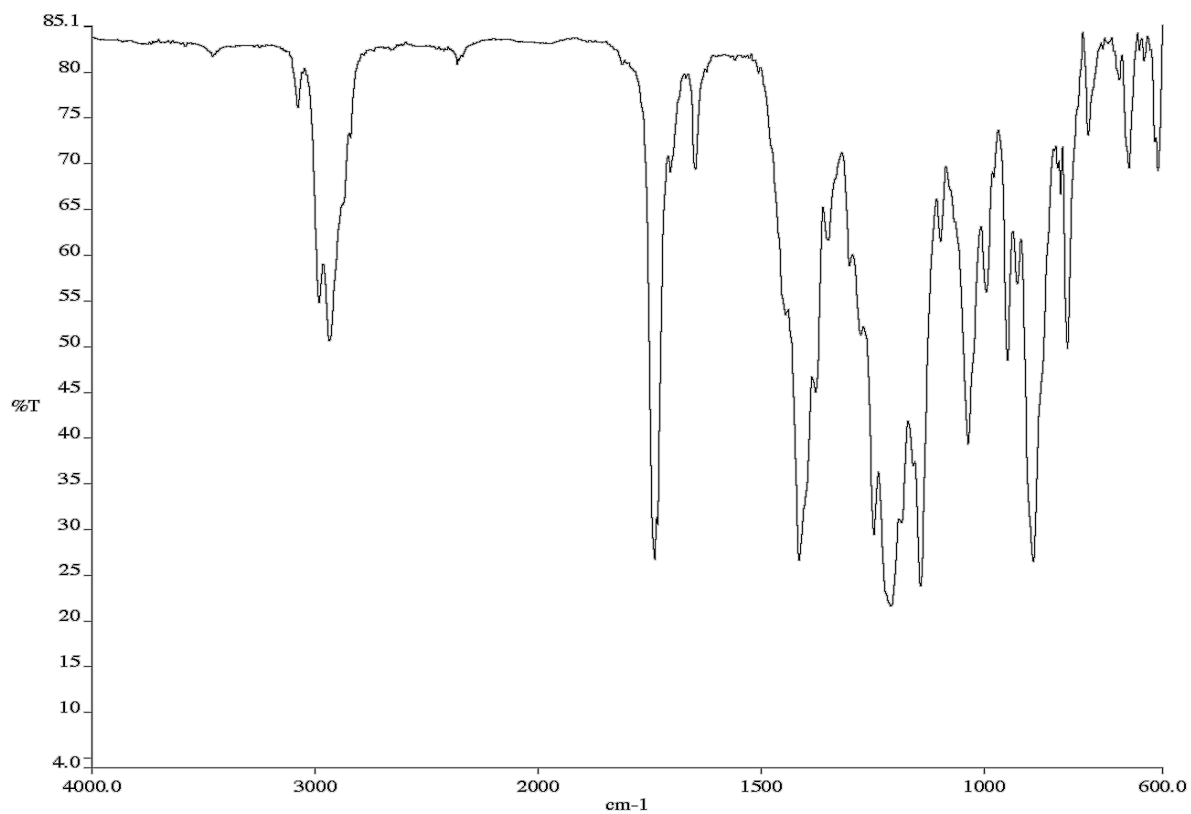
(6*aS*,7*R*)-10-methyl-7-(prop-1-en-2-yl)-3,6,6*a*,7,8,9-hexahydrobenzo[*e*]azulen-1(2*H*)-one (**24**)

In a nitrogen-filled glovebox, anhydrous CeCl_3 (149 mg, 1.0 equiv) was added to the reaction vessel. The vessel was sealed, removed from the glove box, and placed under a N_2 atmosphere. To the solid CeCl_3 was added a solution of enone **23** (183 mg, 0.61 mmol) in THF (6 mL, 0.1M). The reaction was cooled to 0 °C and stirred for several min, after which it was treated with 1M vinylmagnesium bromide in THF (1.2 mL, 3 equiv). The reaction was stirred at the designated temperature until deemed complete by TLC (ca. 30 min). (Note: In cases where the reaction remained incomplete, an additional 1 equiv of vinyl Grignard solution was added). Upon completion, the reaction was quenched by addition of sat. aq. NH_4Cl , extracted with Et_2O (3 X 30 mL), dried (Na_2SO_4), and concentrated *in vacuo*. The crude residue was partially purified by passing through a plug of silica (20% EtOAc in hexanes) to provide *bis*-allyl alcohol **25** as a 1:1 mixture of diastereomers. The mixture was committed to the next reaction without further purification. The crude mixture was dissolved in benchtop CH_2Cl_2 (6 mL) and cooled to 0 °C. Under air, the reaction was treated with PDC (451 mg, 1.20 mmol, 2 equiv) and celite (100 mg), and the mixture was allowed to warm to 23 °C over 2 h. Upon completion, the black mixture was passed through a plug of silica (CH_2Cl_2), concentrated *in vacuo*, and subjected to column

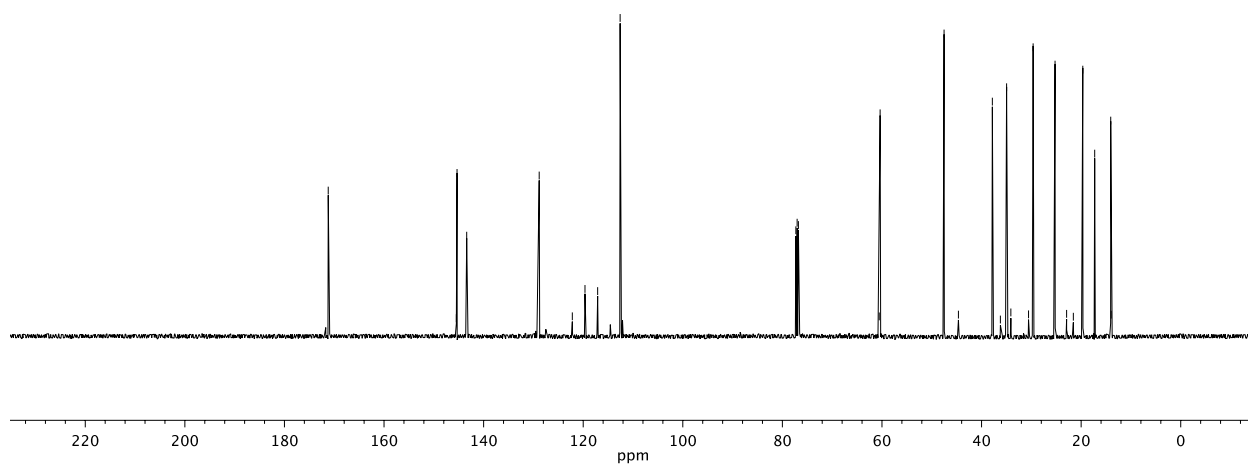
chromatography (15% EtOAc in hexanes) to provide dienone **26** as a pale yellow oil (82 mg) that was satisfactorily pure for the next reaction. A reaction vessel was charged with Hoveyda–Grubbs II catalyst (6.9 mg, 5 mol %). Upon purging with N₂, a solution of semi-pure dienone **26** (82 mg) in THF (10 mL) was added, and the resulting solution was heated to 40 °C for 12 h. Upon completion, the solution was allowed to cool to 23 °C, and the catalyst was quenched by addition of ethyl vinyl ether (2 drops). After stirring for 5 min, the solution was concentrated *in vacuo*, and the resulting residue was purified by column chromatography (10%–20% EtOAc in hexanes) to provide tricycle **24** as a pale yellow oil (39 mg, 25% yield over 3 steps), which could be crystallized from hexanes (35 °C to 4 °C); $R_f = 0.40$ (20% EtOAc in hexanes); $[\alpha]_D^{25} -168.5$ (*c* 1, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 6.27–6.23 (m, 1H), 6.07–6.04 (m, 1H), 4.81–4.73 (m, 2H), 2.62–2.50 (m, 2H), 2.49–2.40 (m, 5H), 2.17–2.14 (m, 2H), 1.97–1.93 (m, 1H), 1.78–1.62 (m, 5H), 1.52 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 206.3, 165.7, 147.3, 142.4, 141.2, 133.9, 125.7, 124.6, 111.2, 46.2, 41.6, 39.6, 35.3, 31.8, 30.0, 23.6, 22.8, 21.3; IR (Neat Film, NaCl) 3009.8, 2912.5, 1696.9, 1585.0, 1430.0, 1318.2, 1295.2, 1112.2, 894.9 cm⁻¹; HRMS (ESI-TOF) *m/z* calc'd for C₁₈H₂₂ONa [M+Na]⁺: 277.1563, found 277.1572.

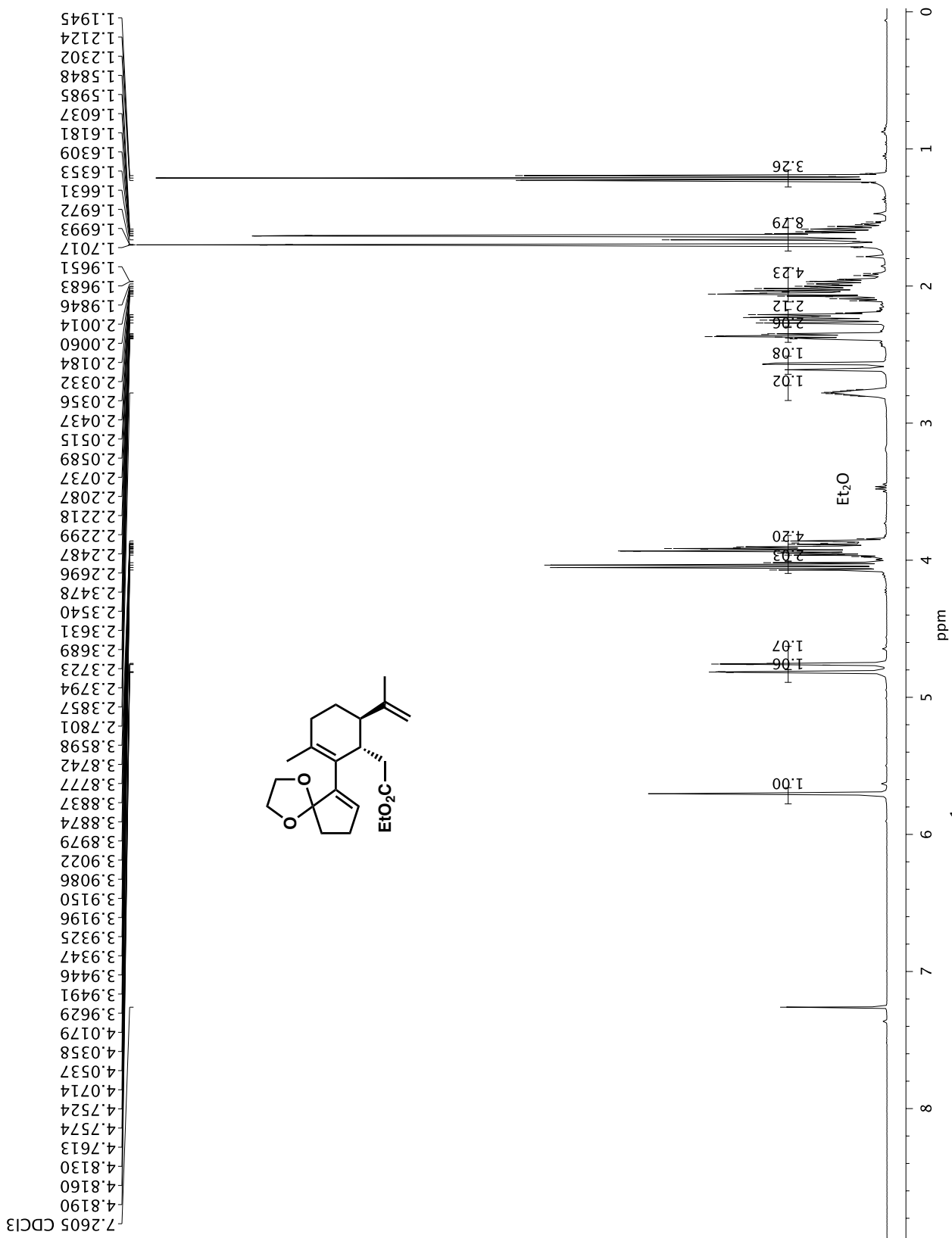
NMR and IR Spectra of New Compounds

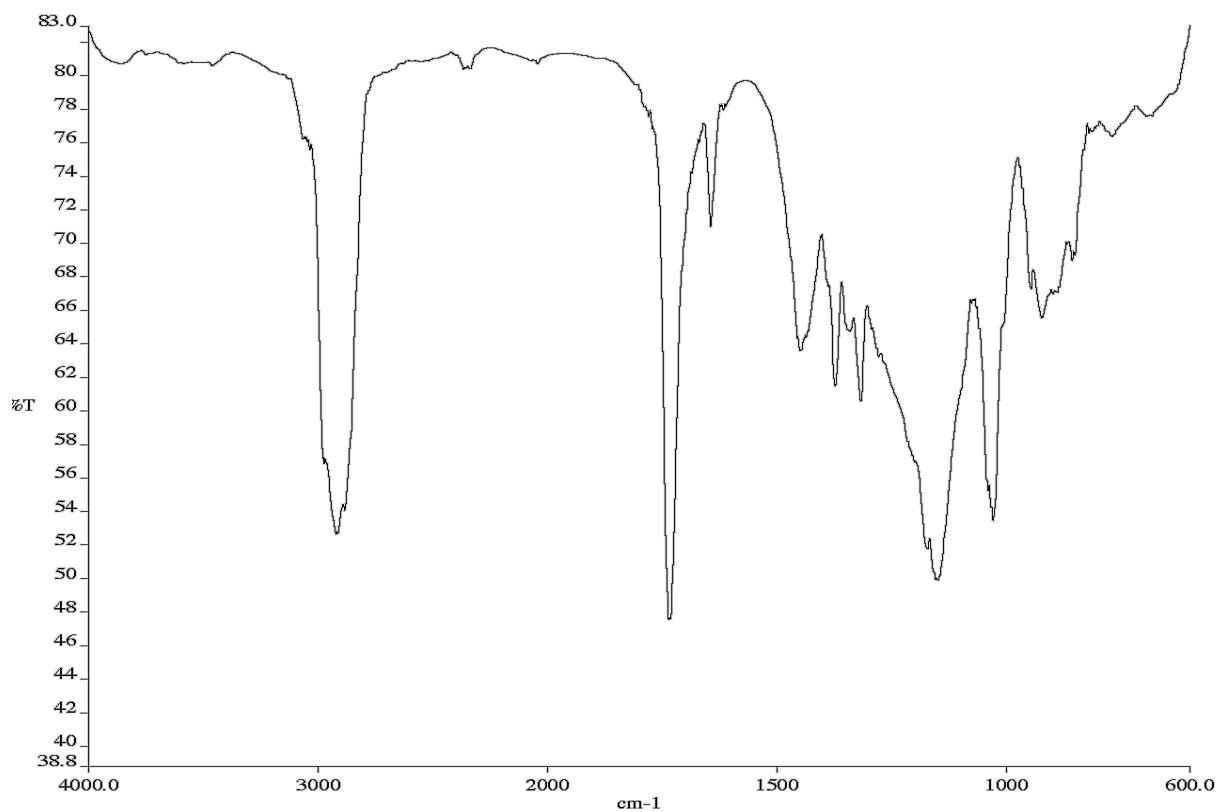
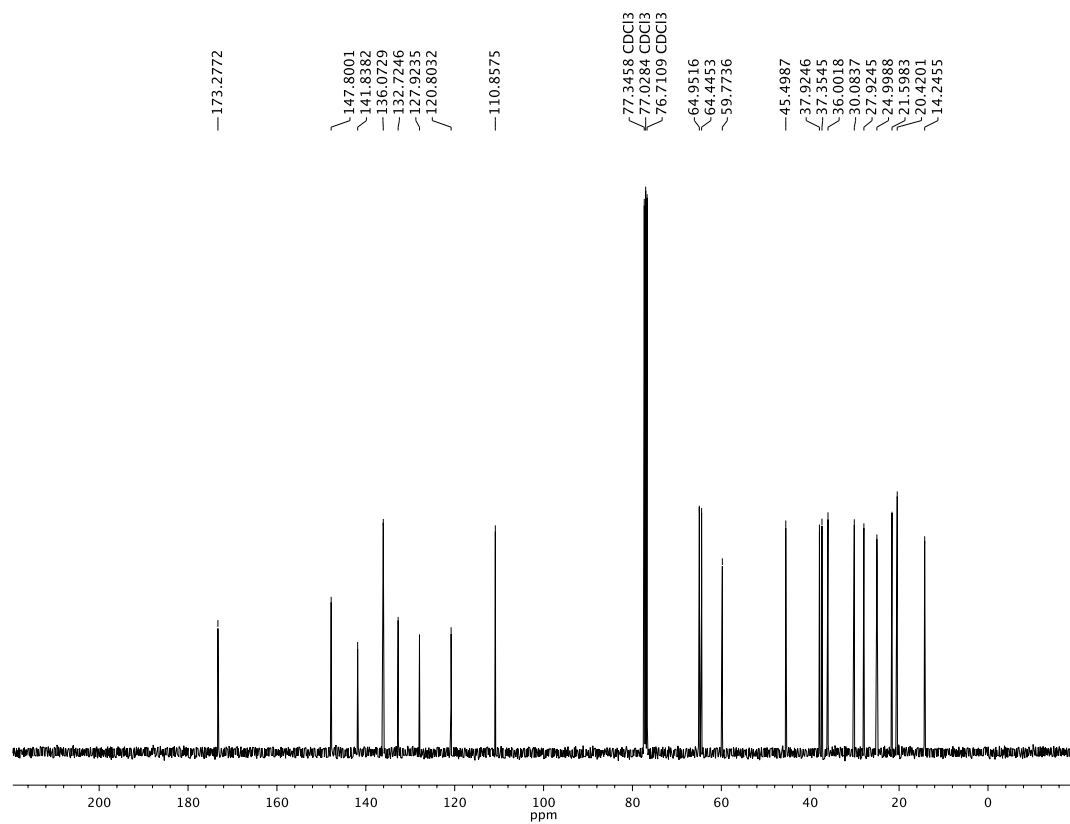


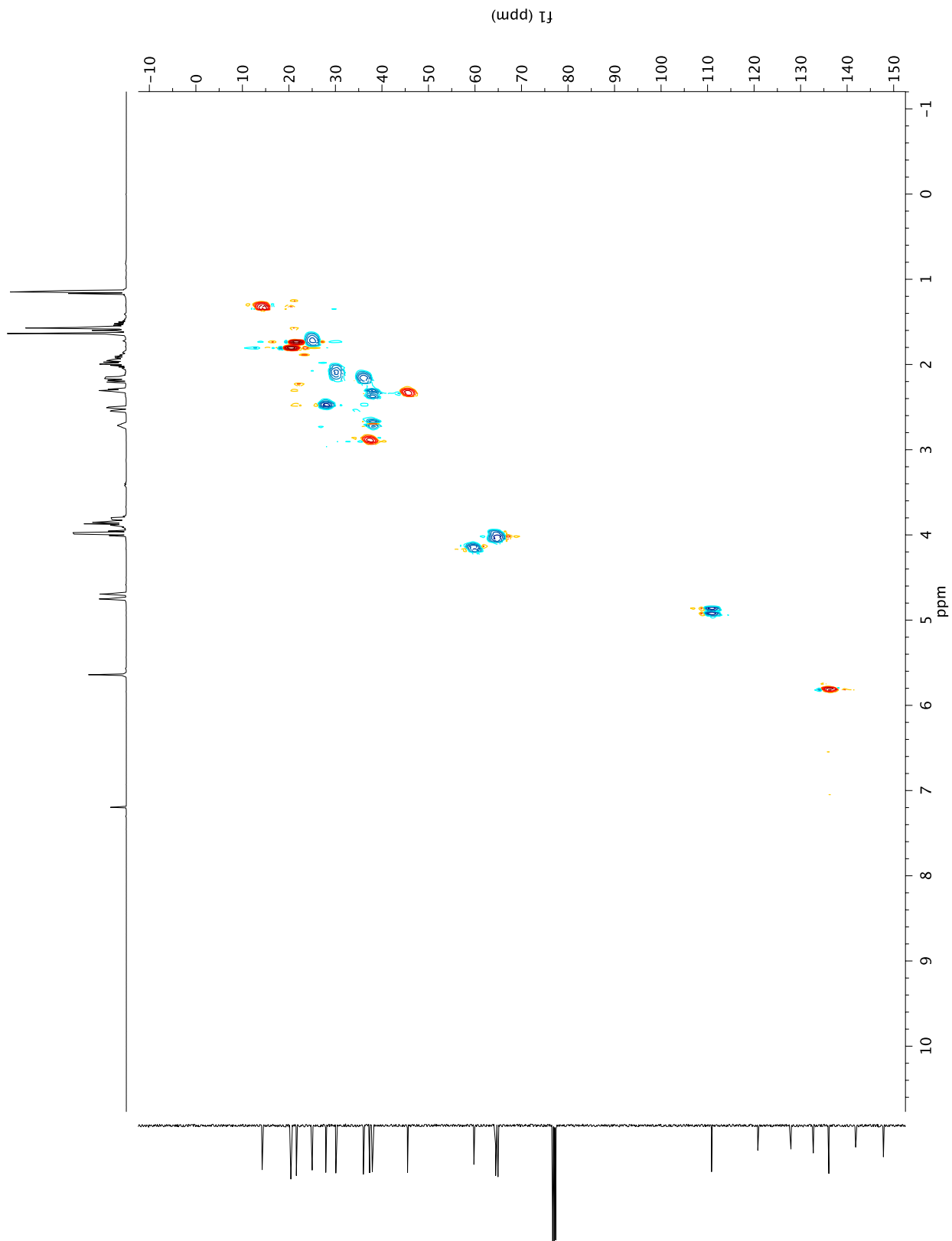


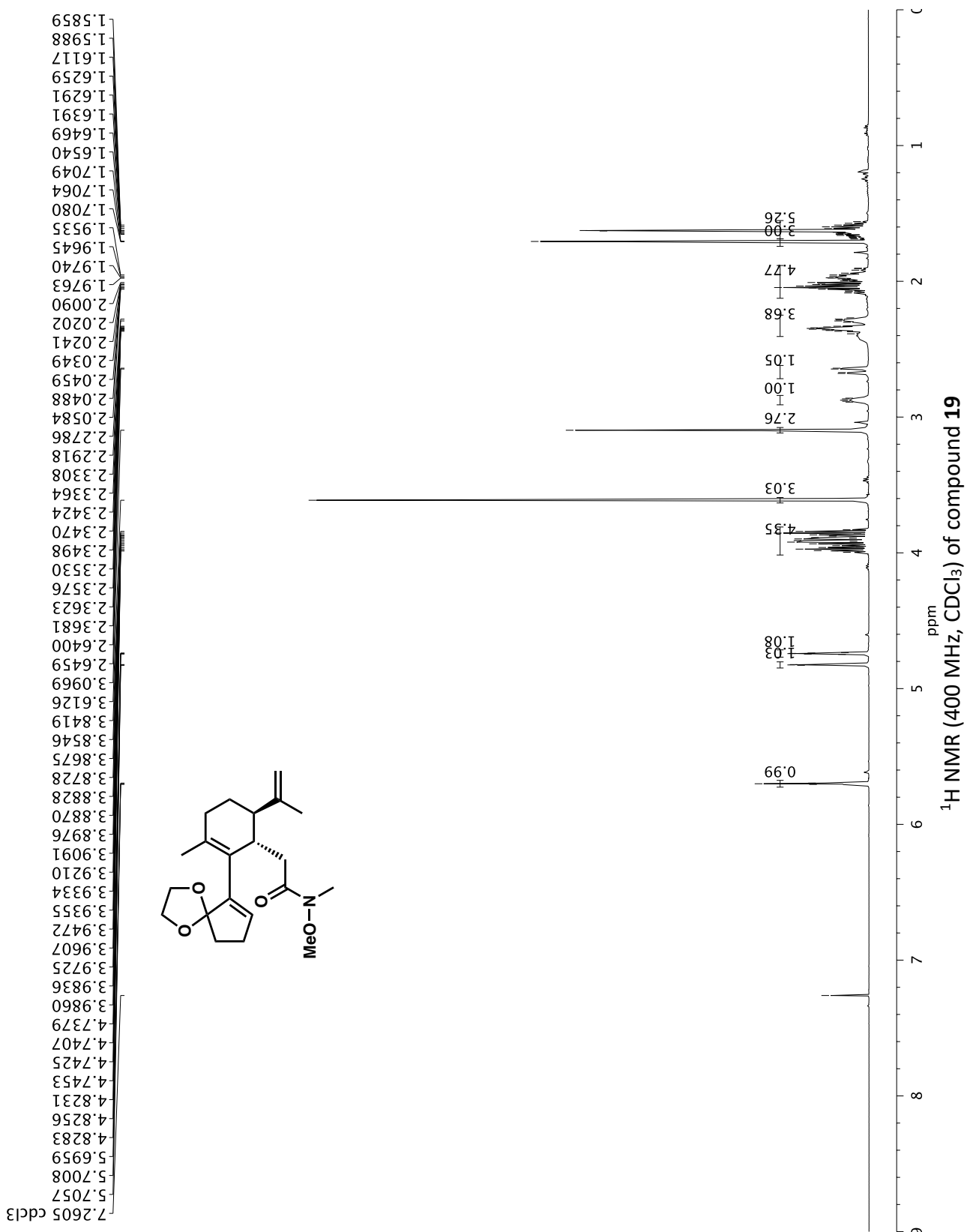
— 171.2071
/ 145.4787
/ 145.3381
/ 143.3982
— 128.8389
/ 122.1869
/ 119.6431
/ 117.0995
/ 112.5852
/ 77.2936 cdd13
/ 77.0375 cdd13
/ 76.7822 cdd13
/ 60.5545
/ 60.3718
/ 47.5277
/ 44.6454
/ 37.8318
/ 36.2187
/ 34.9705
/ 34.1159
/ 30.5646
/ 29.6432
/ 25.2400
/ 22.9187
/ 21.5664
/ 19.6688
/ 17.2790
/ 14.0587
/ 13.9700

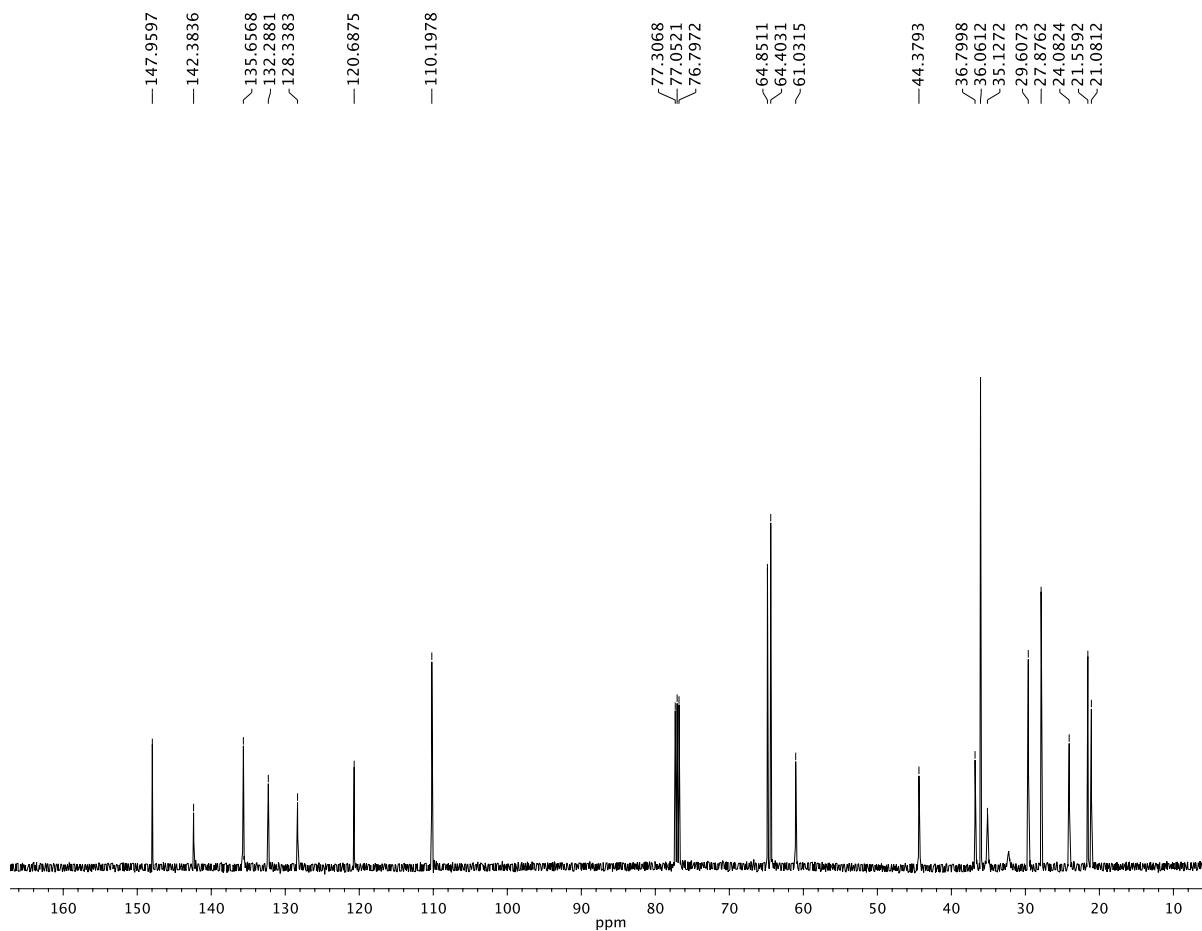
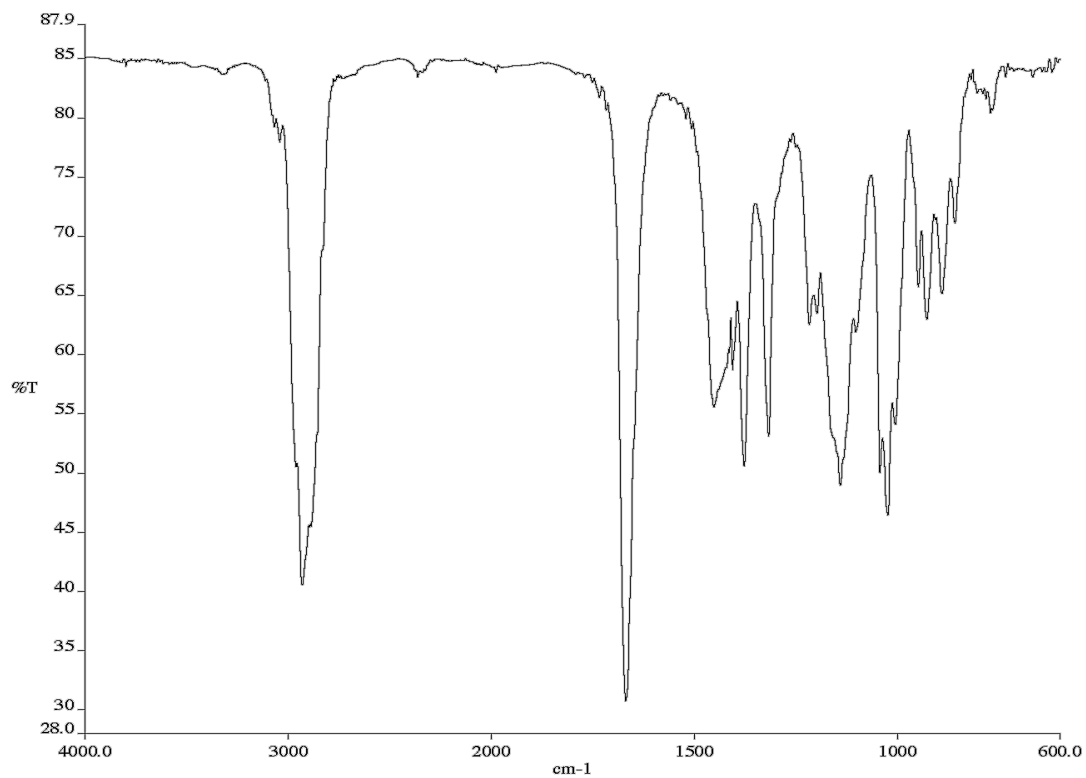




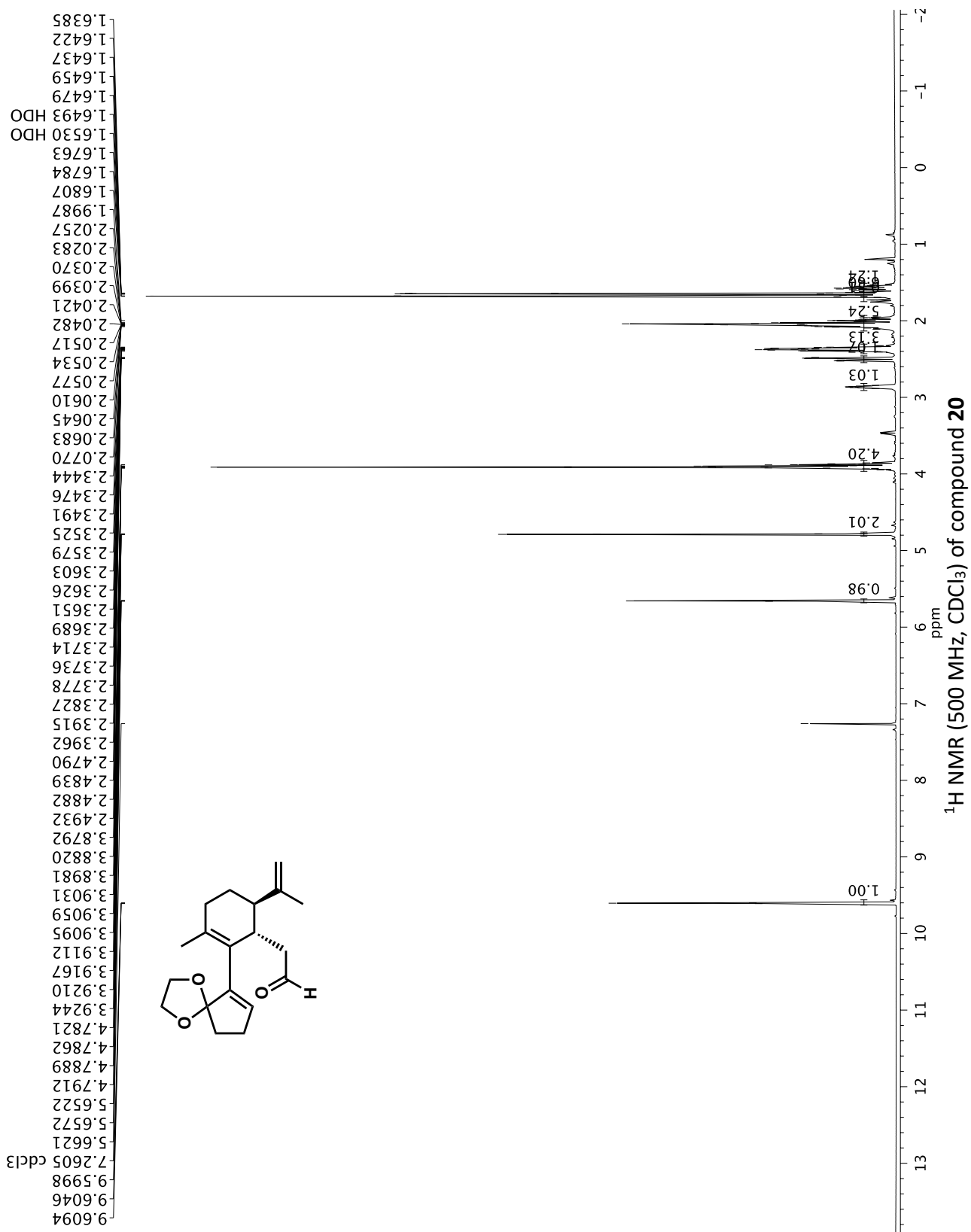
Infrared spectrum (Thin Film, NaCl) of compound **12**¹³C NMR (101 MHz, CDCl₃) of compound **12**

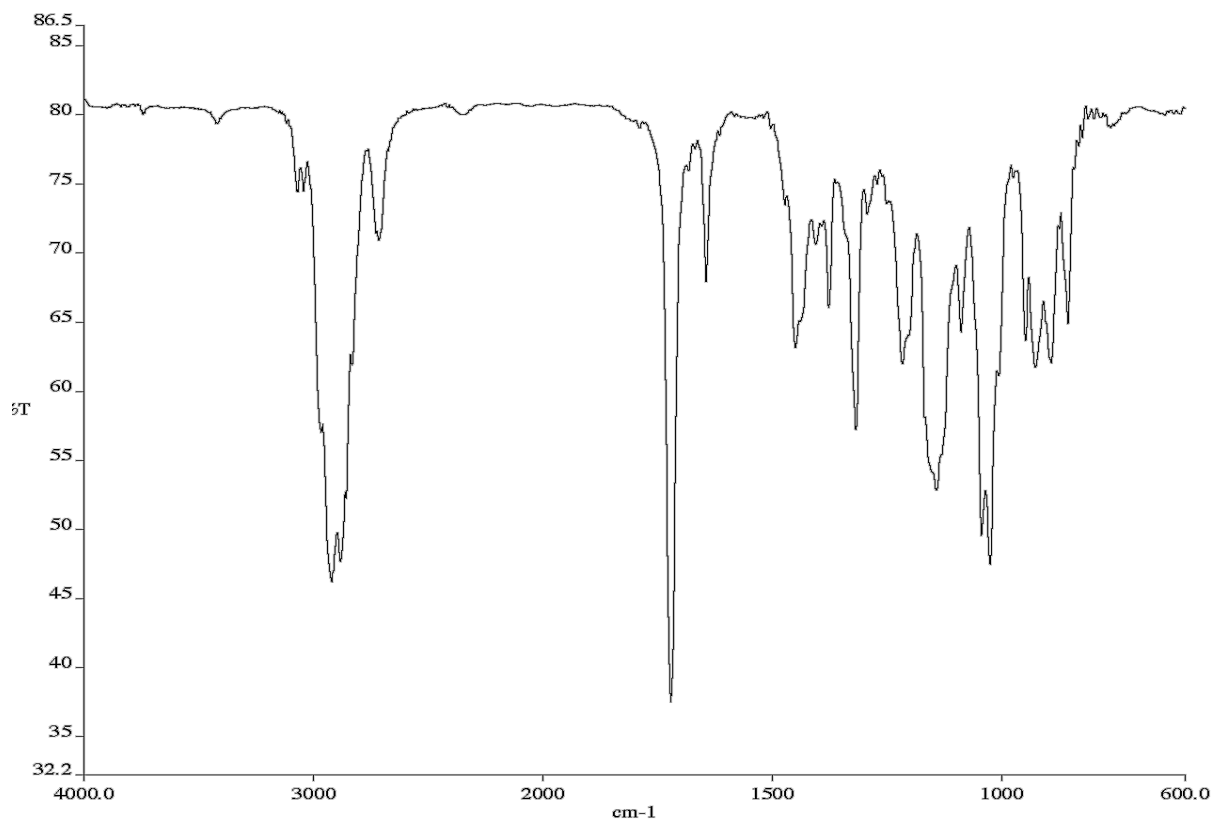






¹³C NMR (101 MHz, CDCl₃) of compound **19**





— 204.1678

— 147.5099

— 141.6537

— 136.7585

— 133.3950

— 127.6970

— 120.9256

— 111.7066

— 77.3110 cdc13

— 77.0568 cdc13

— 76.8017 cdc13

— 64.9310

— 64.5454

— 64.5377

— 47.2914

— 47.1892

— 36.3692

— 35.8879

— 30.6818

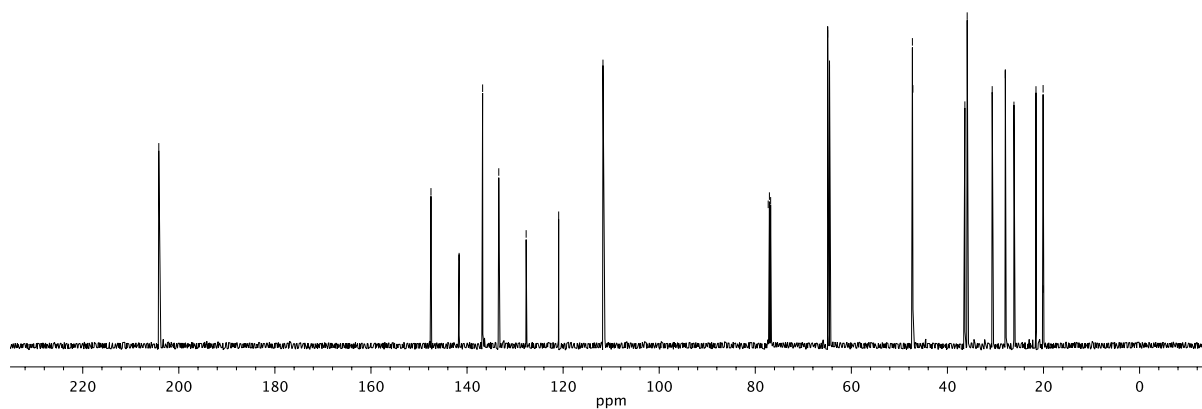
— 27.9439

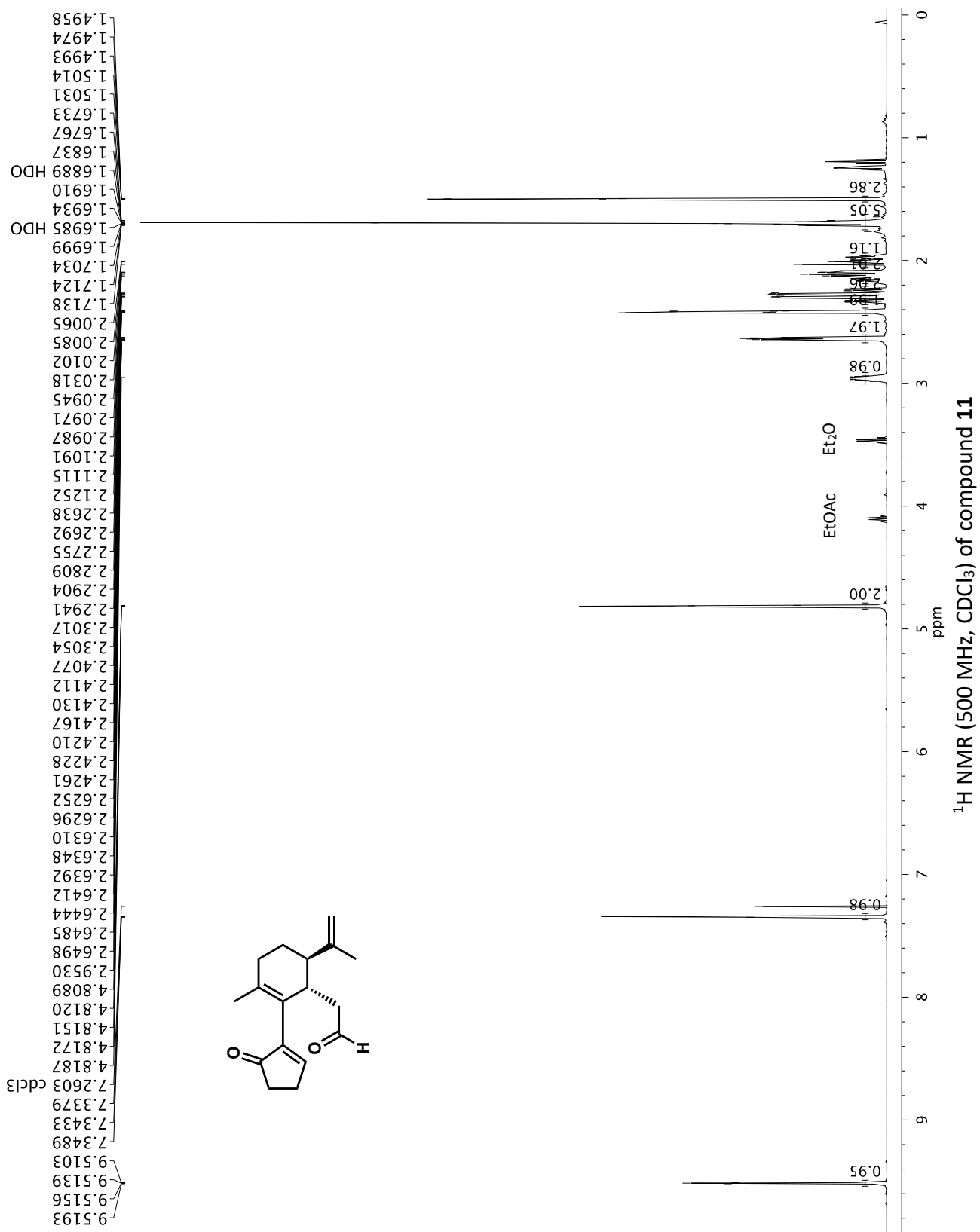
— 26.1528

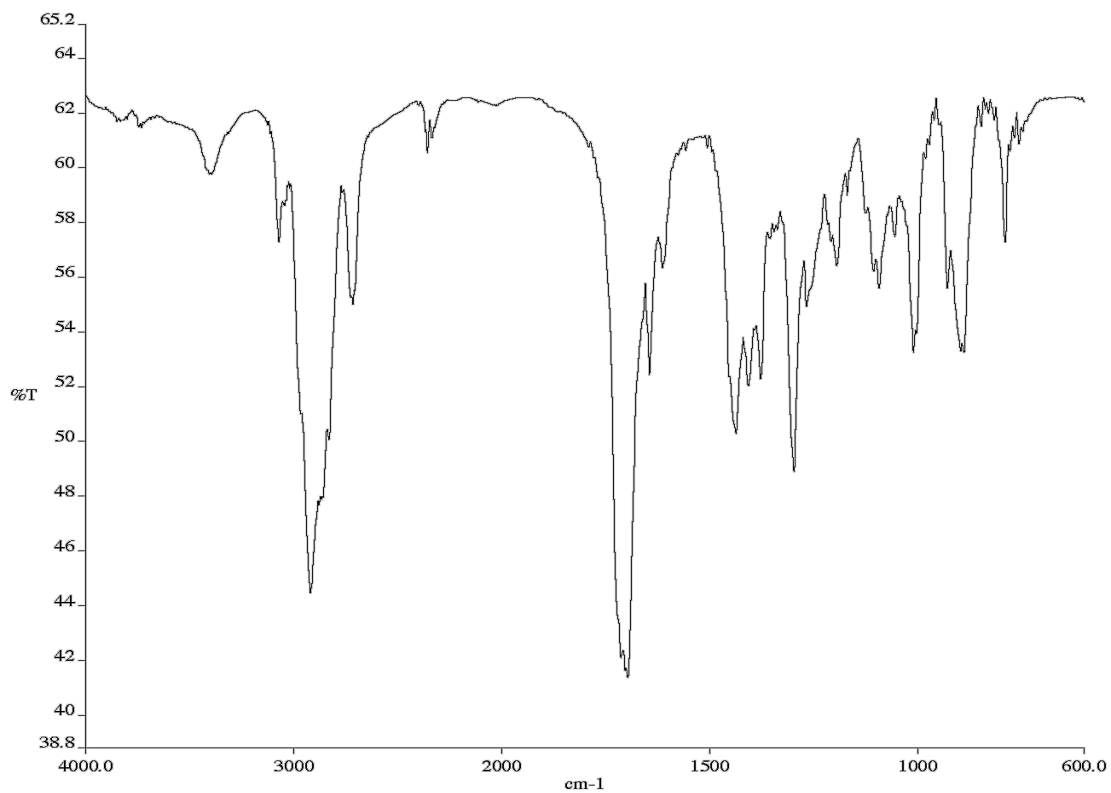
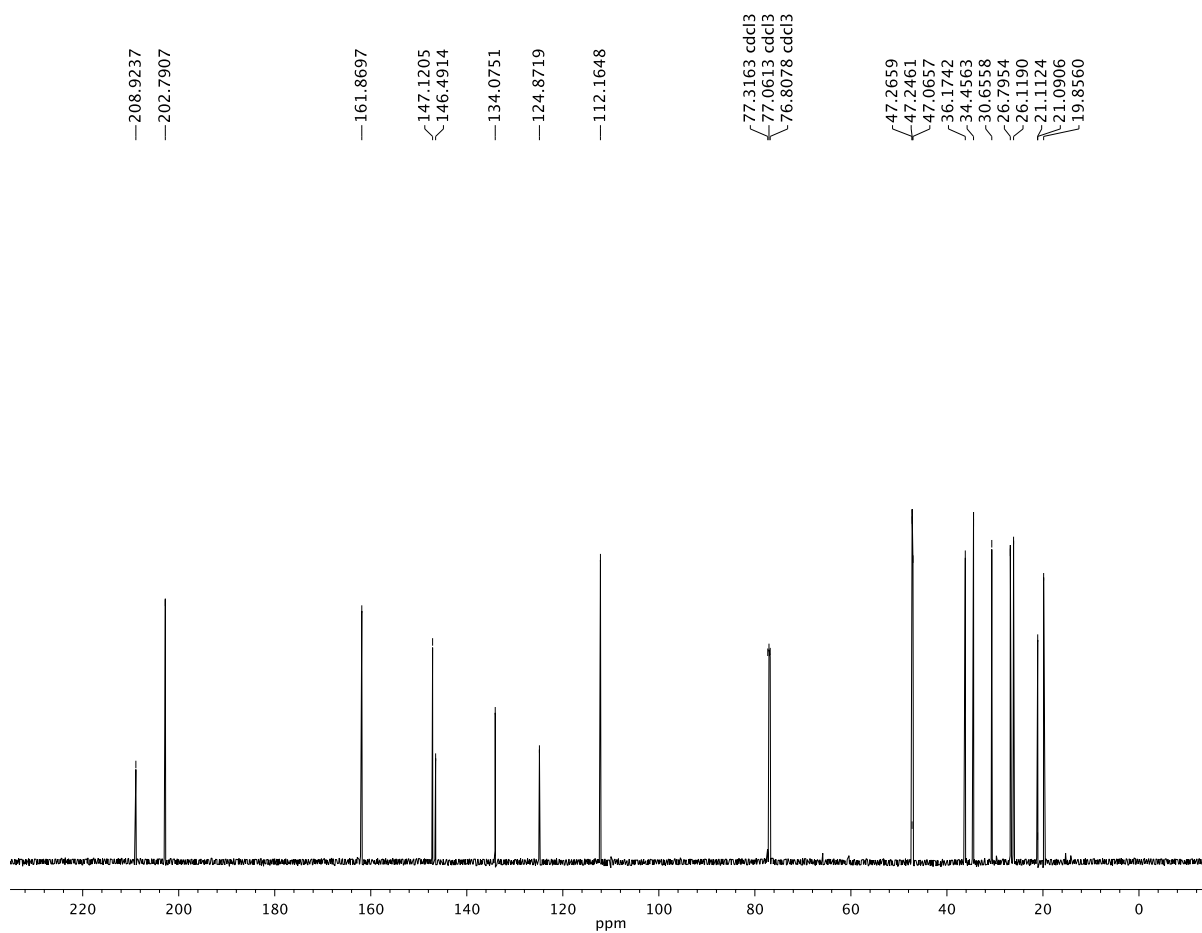
— 21.5664

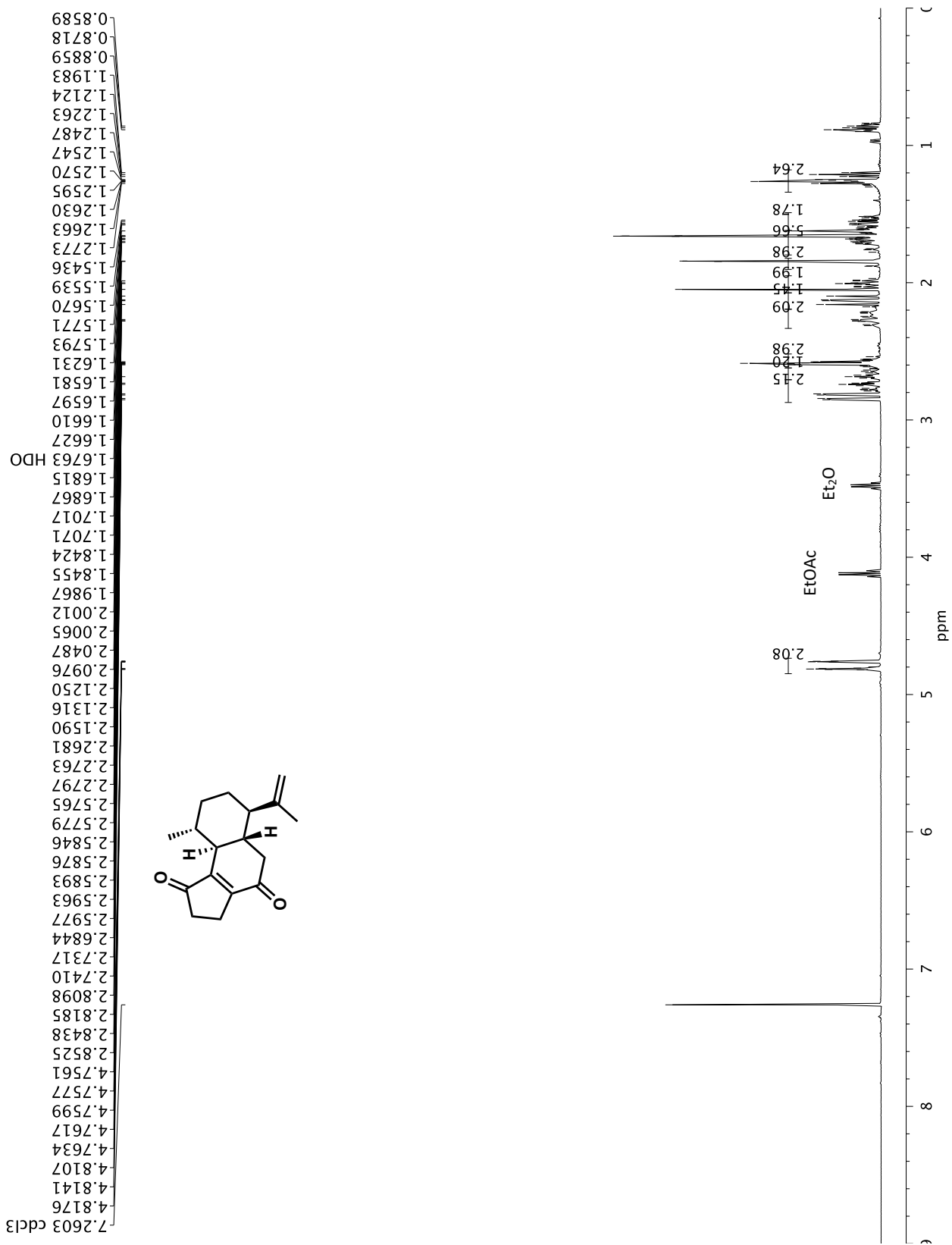
— 20.0848

— 20.0757

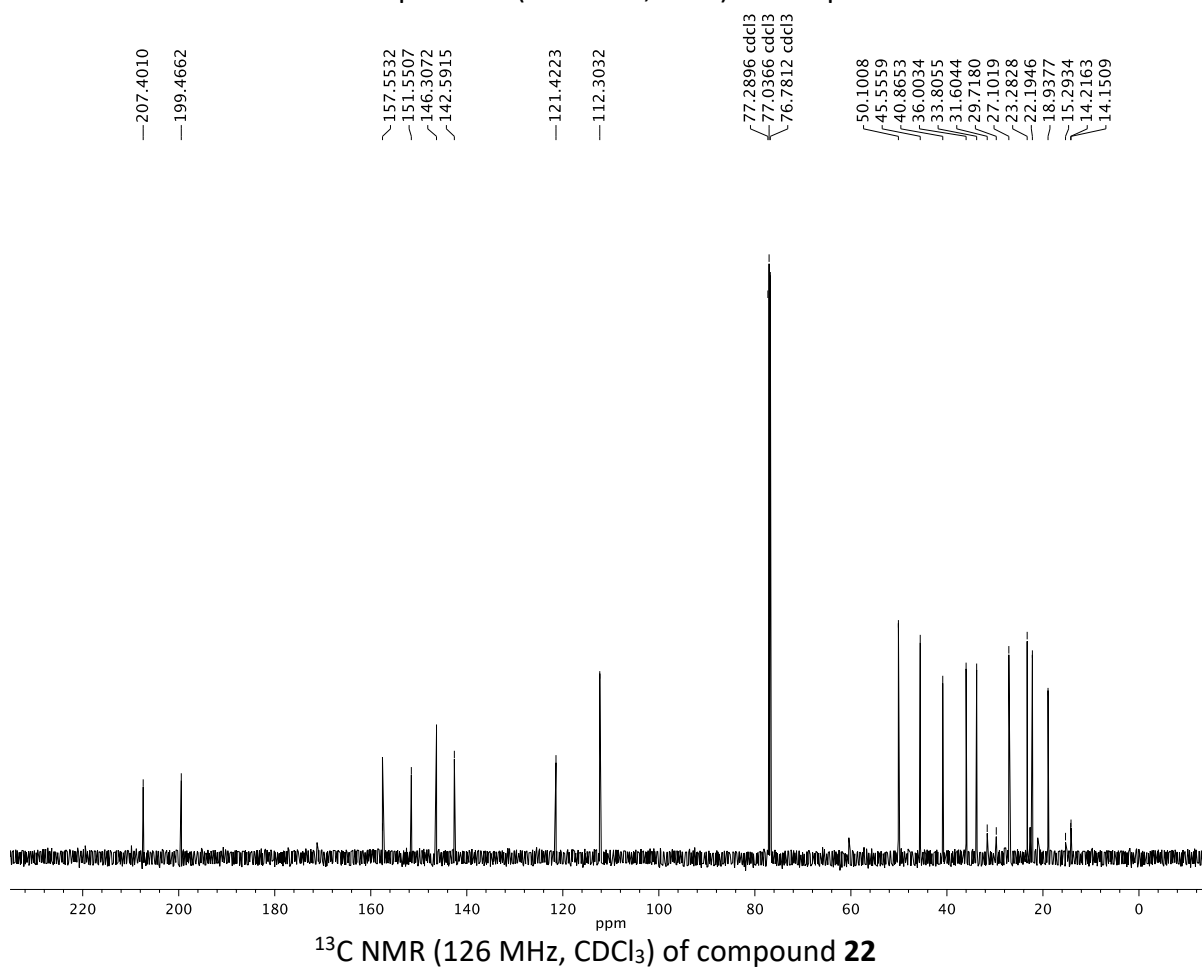
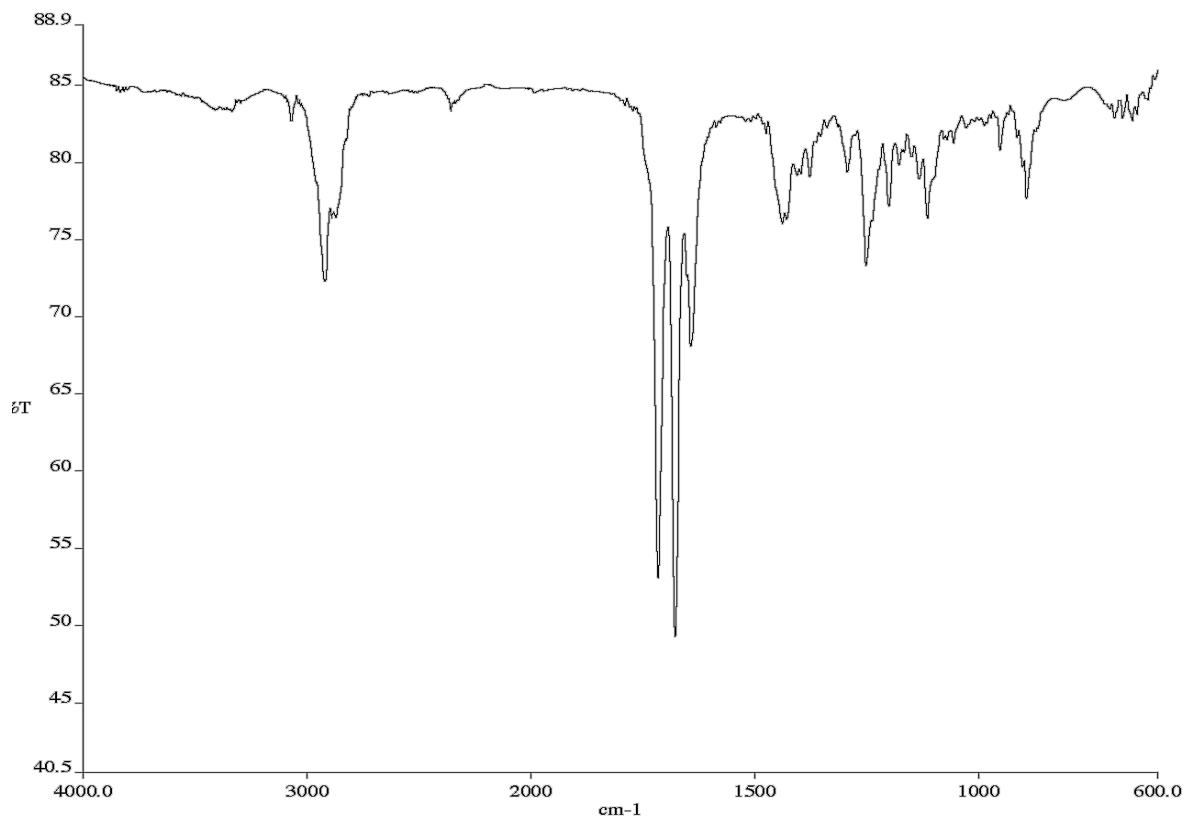
¹³C NMR (126 MHz, CDCl₃) of compound **20**

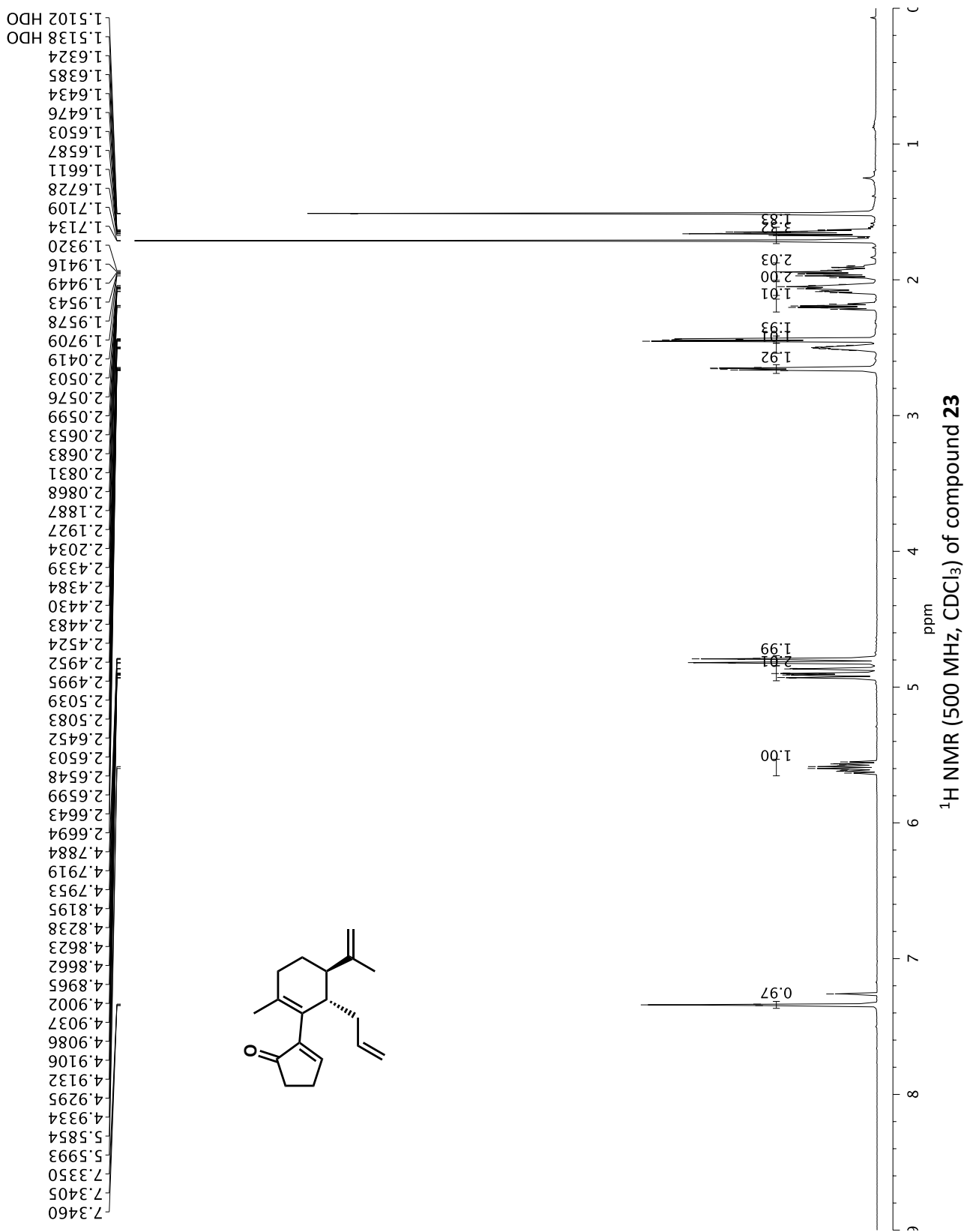


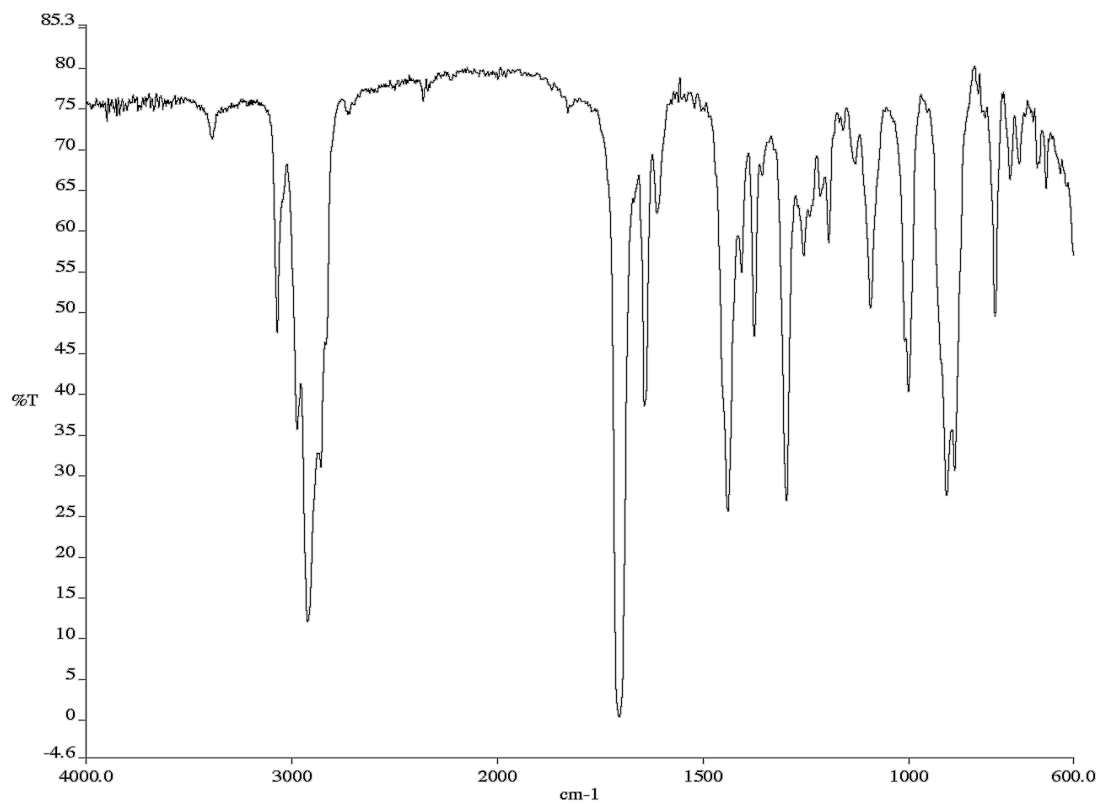
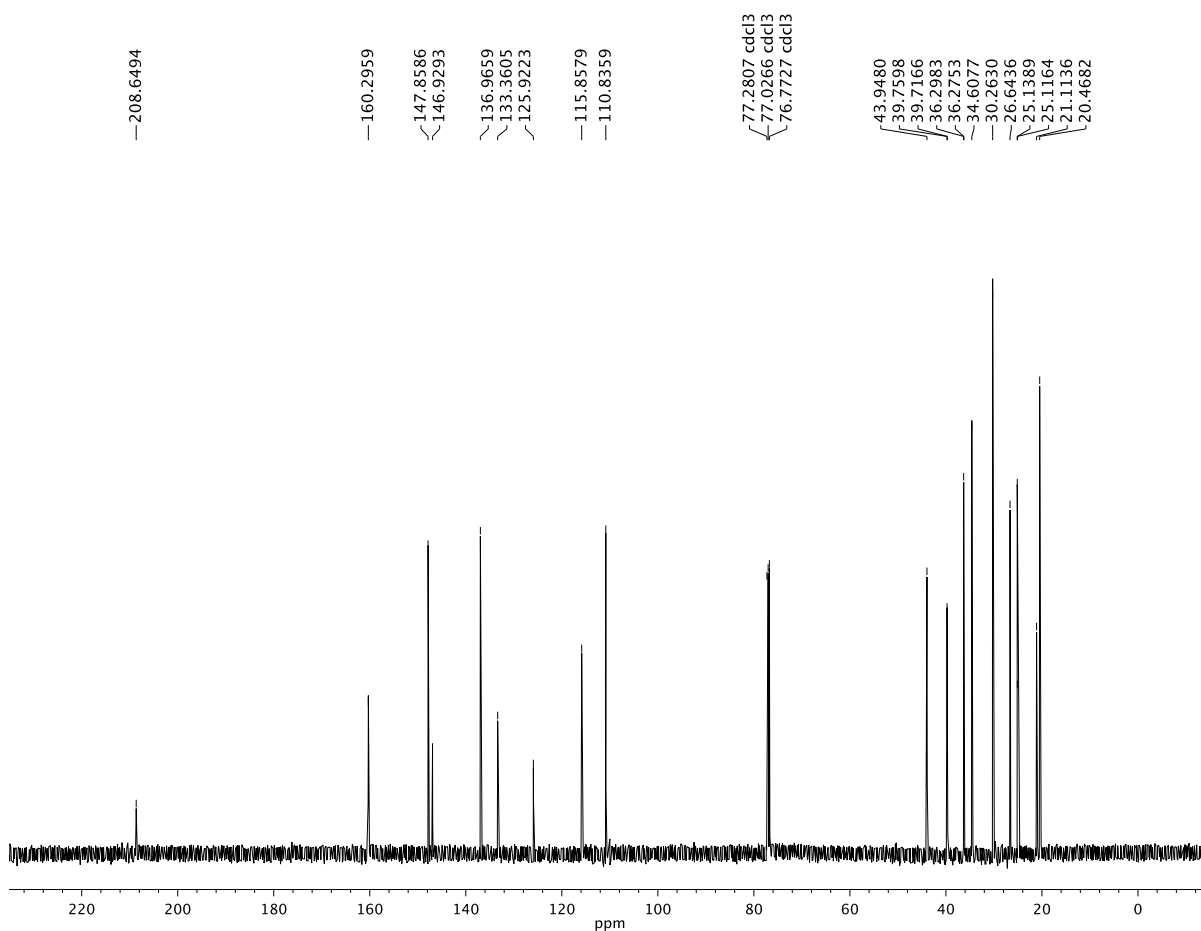
Infrared spectrum (Thin Film, NaCl) of compound **11**¹³C NMR (126 MHz, CDCl₃) of compound **11**



7.2603 cdc13
4.8176
4.8141
4.8107
4.7634
4.7617
4.7599
4.7577
4.7561
2.8525
2.8438
2.8185
2.8098
2.7410
2.7317
2.6844
2.5977
2.5963
2.5893
2.5876
2.5846
2.5779
2.5765
2.2797
2.2763
2.2681
2.1590
2.1316
2.1250
2.0976
2.0487
2.0065
2.0012
1.9867
1.8455
1.8424
1.7071
1.7017
1.6867
1.6815
1.6763 H₂O
1.6627
1.6610
1.6597
1.6581
1.6231
1.5793
1.5771
1.5670
1.5539
1.5436
1.2773
1.2663
1.2630
1.2595
1.2570
1.2547
1.2487
1.2263
1.2124
1.1983
0.8859
0.8718
0.8589





Infrared spectrum (Thin Film, NaCl) of compound **23**¹³C NMR (126 MHz, CDCl₃) of compound **23**

— 208.6494

— 160.2959

— 147.8586

— 146.9293

— 136.9659

— 133.3605

— 125.9223

— 115.8579

— 110.8359

77.2807 cdcl3

77.0266 cdcl3

76.7727 cdcl3

43.9480

39.7598

39.7166

36.2983

36.2753

34.6077

30.2630

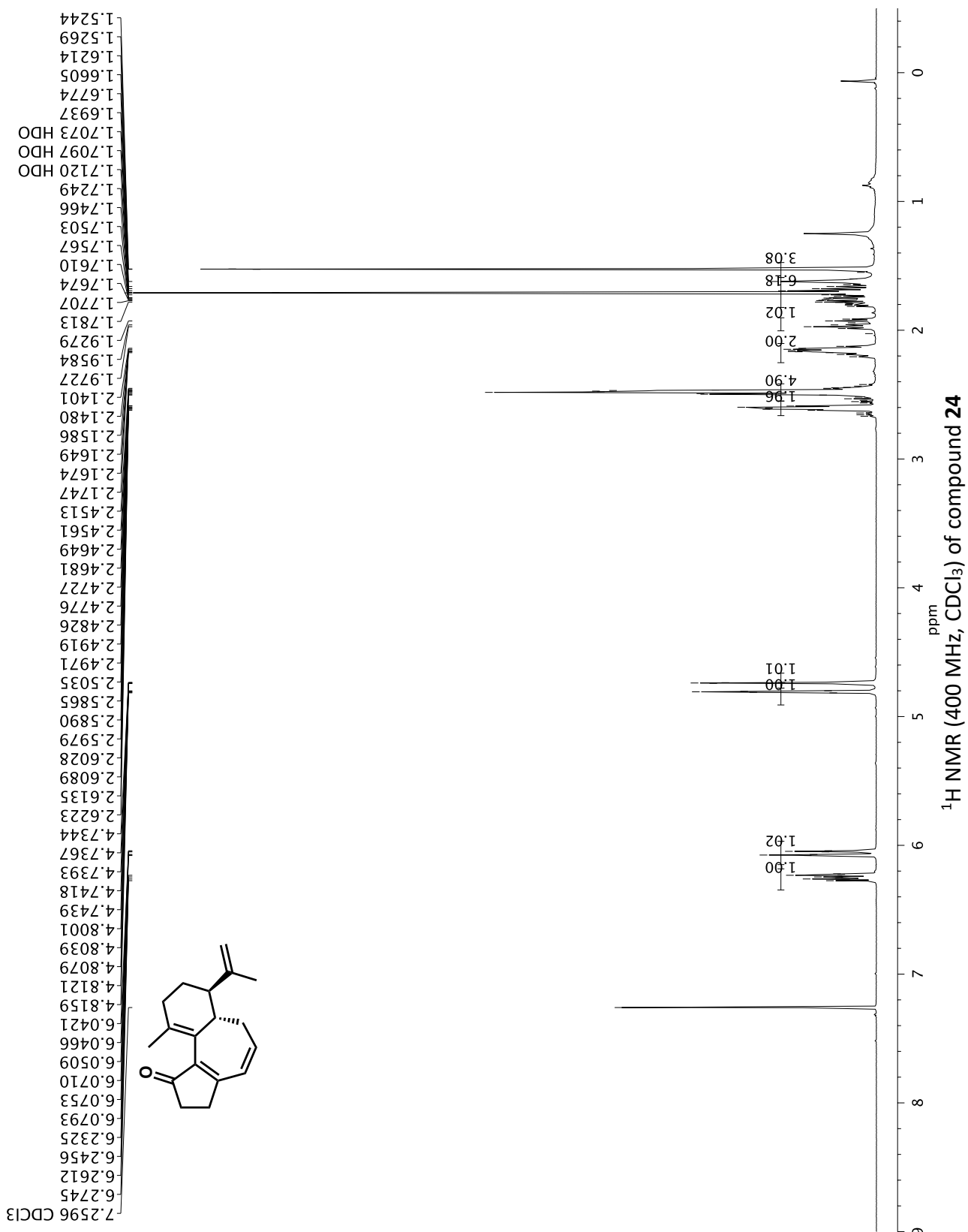
26.6436

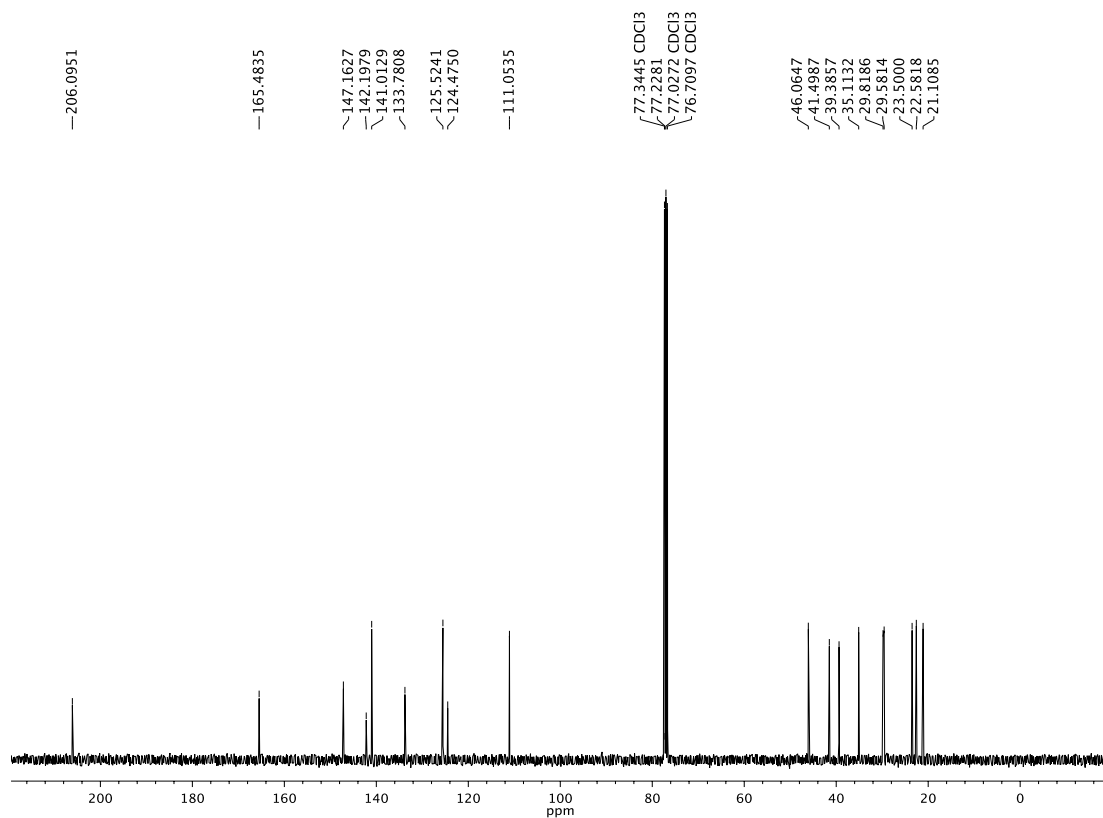
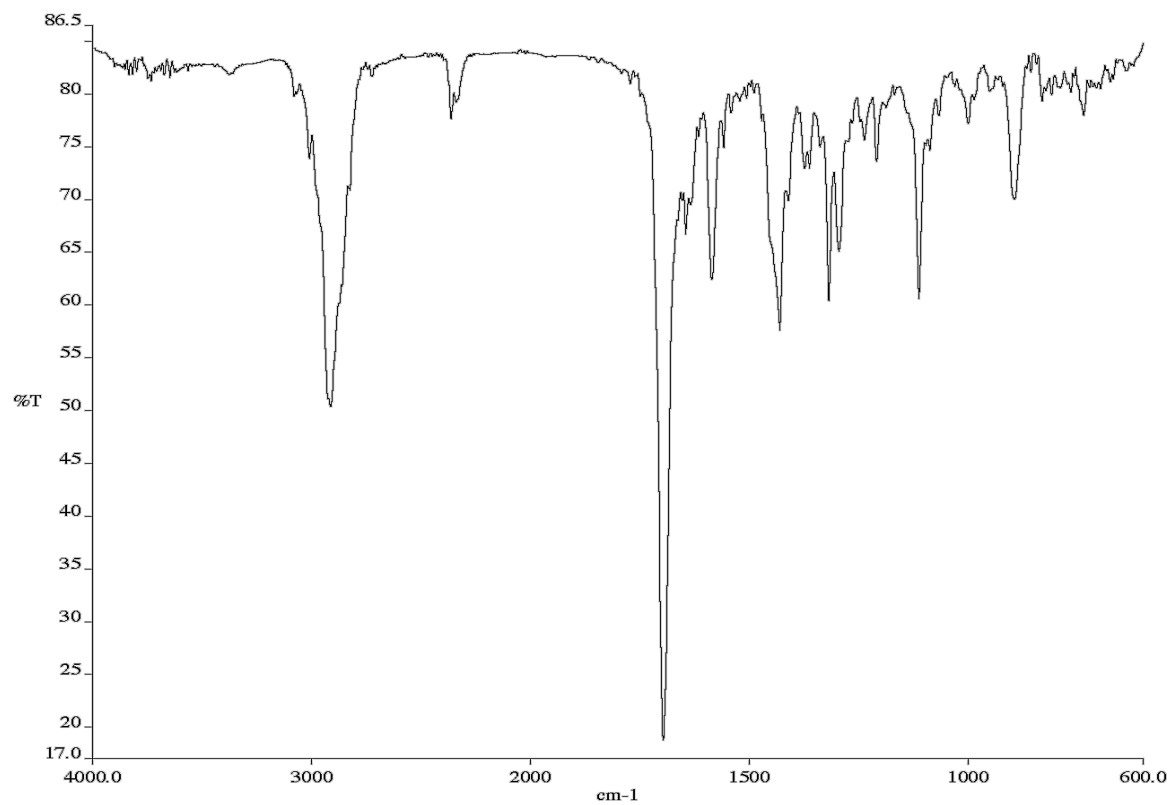
25.1389

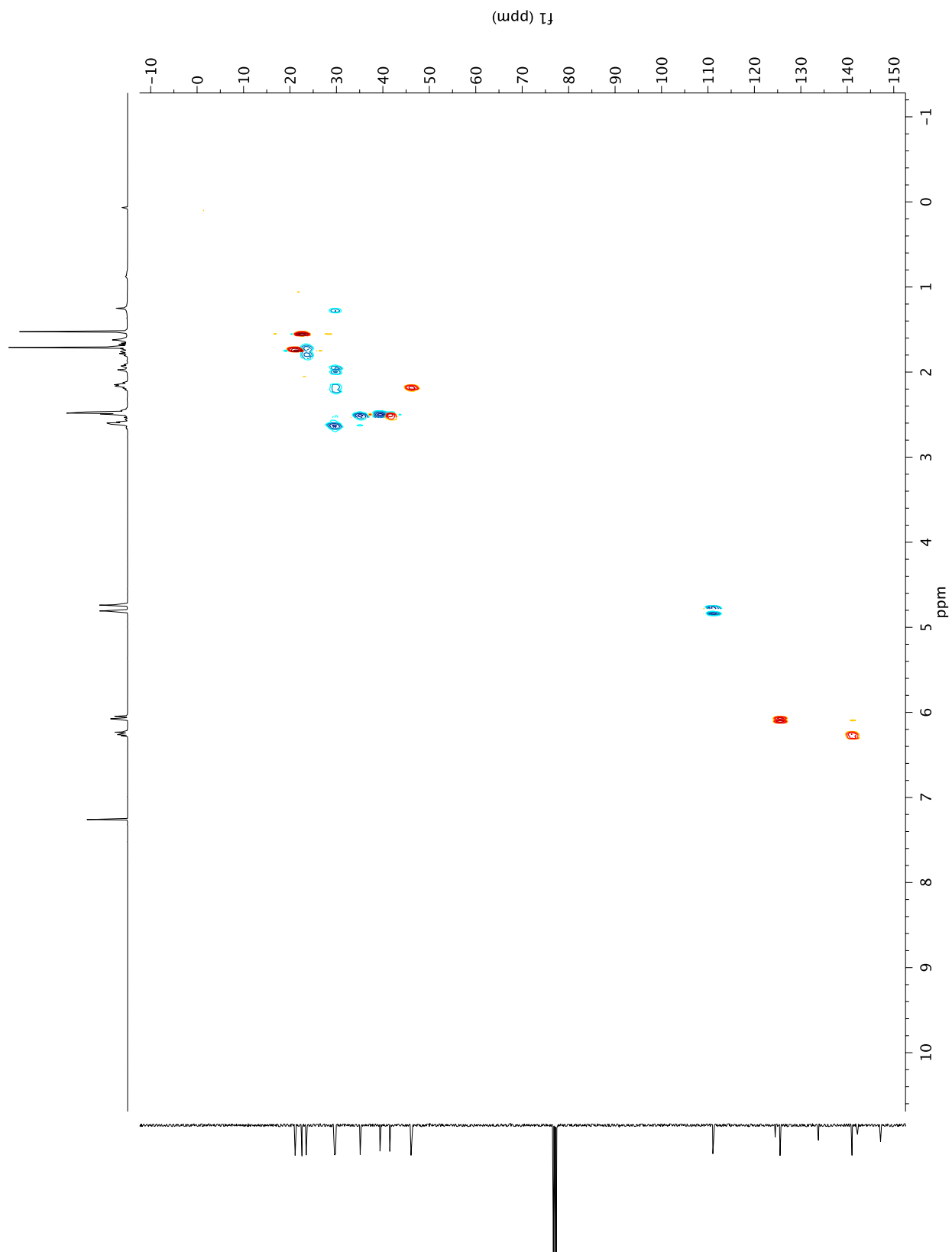
25.1164

21.1136

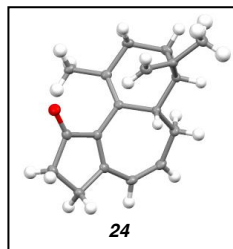
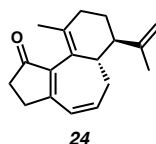
20.4682







X-Ray Crystal Structure Analysis of 24 (V19305)



X-Ray Structure Determination

Low-temperature diffraction data (ϕ - and ω -scans) were collected on a Bruker AXS D8 VENTURE KAPPA diffractometer coupled to a PHOTON II CPAD detector with Cu K_{α} radiation ($\lambda = 1.54178 \text{ \AA}$) from an $I\mu\text{S}$ micro-source for the structure of compound V19305. The structure was solved by direct methods using SHELXS

¹ and refined against F^2 on all data by full-matrix least squares with SHELXL-2017² using established refinement techniques.³ All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were included into the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the U value of the atoms they are linked to (1.5 times for methyl groups).

Compound V19305 crystallizes in the orthorhombic space group $P2_12_12_1$ with one molecule in the asymmetric unit.

Table 1. Crystal data and structure refinement for V19305.

Identification code	V19305	
Empirical formula	C ₁₈ H ₂₂ O	
Formula weight	254.35	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2 ₁ 2 ₁ 2 ₁	
Unit cell dimensions	a = 6.7708(6) Å	a = 90°.
	b = 10.8979(10) Å	b = 90°.
	c = 19.414(2) Å	g = 90°.
Volume	1432.5(2) Å ³	
Z	4	
Density (calculated)	1.179 Mg/m ³	
Absorption coefficient	0.541 mm ⁻¹	
F(000)	552	

Crystal size	0.350 x 0.300 x 0.150 mm ³
Theta range for data collection	4.555 to 74.559°.
Index ranges	-8<=h<=8, -13<=k<=13, -24<=l<=24
Reflections collected	48838
Independent reflections	2938 [R(int) = 0.0345]
Completeness to theta = 67.679°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7538 and 0.6977
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	2938 / 0 / 174
Goodness-of-fit on F ²	1.059
Final R indices [I>2sigma(I)]	R1 = 0.0282, wR2 = 0.0699
R indices (all data)	R1 = 0.0283, wR2 = 0.0700
Absolute structure parameter	0.10(4)
Extinction coefficient	n/a
Largest diff. peak and hole	0.172 and -0.158 e.Å ⁻³

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for V19305. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	$U(\text{eq})$
C(1)	7111(2)	2852(1)	6676(1)	16(1)
C(2)	5291(2)	2699(1)	7094(1)	18(1)
O(1)	4865(2)	1814(1)	7449(1)	25(1)
C(3)	4012(2)	3832(1)	6999(1)	23(1)
C(4)	5034(2)	4576(1)	6436(1)	22(1)
C(5)	6946(2)	3901(1)	6303(1)	17(1)
C(6)	8389(2)	4420(1)	5831(1)	20(1)
C(7)	9894(2)	3860(1)	5516(1)	21(1)
C(8)	10489(2)	2534(1)	5518(1)	22(1)
C(9)	9146(2)	1577(1)	5867(1)	16(1)
C(10)	10099(2)	302(1)	5786(1)	18(1)
C(15)	8664(2)	-766(1)	5788(1)	18(1)
C(16)	6898(2)	-743(1)	6084(1)	22(1)
C(17)	9404(3)	-1896(1)	5419(1)	27(1)
C(11)	11718(2)	133(1)	6336(1)	21(1)
C(12)	10898(2)	276(1)	7063(1)	20(1)
C(13)	9533(2)	1357(1)	7152(1)	17(1)
C(18)	9244(2)	1734(1)	7891(1)	21(1)
C(14)	8673(2)	1915(1)	6613(1)	15(1)

Table 3. Bond lengths [\AA] and angles [$^\circ$] for V19305.

C(1)-C(5)	1.3575(18)
C(1)-C(14)	1.4751(18)
C(1)-C(2)	1.4843(18)
C(2)-O(1)	1.2201(18)
C(2)-C(3)	1.5198(19)
C(3)-C(4)	1.526(2)
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(4)-C(5)	1.5119(19)
C(4)-H(4A)	0.9900
C(4)-H(4B)	0.9900
C(5)-C(6)	1.454(2)
C(6)-C(7)	1.335(2)
C(6)-H(6)	0.9500
C(7)-C(8)	1.500(2)
C(7)-H(7)	0.9500
C(8)-C(9)	1.5408(18)
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(9)-C(14)	1.5278(18)
C(9)-C(10)	1.5411(17)
C(9)-H(9)	1.0000
C(10)-C(15)	1.5166(19)
C(10)-C(11)	1.5414(19)
C(10)-H(10)	1.0000
C(15)-C(16)	1.327(2)
C(15)-C(17)	1.5105(19)
C(16)-H(16A)	0.9500
C(16)-H(16B)	0.9500
C(17)-H(17A)	0.9800
C(17)-H(17B)	0.9800
C(17)-H(17C)	0.9800
C(11)-C(12)	1.524(2)
C(11)-H(11A)	0.9900

C(11)-H(11B)	0.9900
C(12)-C(13)	1.5073(19)
C(12)-H(12A)	0.9900
C(12)-H(12B)	0.9900
C(13)-C(14)	1.3436(18)
C(13)-C(18)	1.5048(19)
C(18)-H(18A)	0.9800
C(18)-H(18B)	0.9800
C(18)-H(18C)	0.9800
C(5)-C(1)-C(14)	126.68(12)
C(5)-C(1)-C(2)	108.52(12)
C(14)-C(1)-C(2)	124.24(11)
O(1)-C(2)-C(1)	126.43(13)
O(1)-C(2)-C(3)	125.18(13)
C(1)-C(2)-C(3)	108.39(11)
C(2)-C(3)-C(4)	105.08(12)
C(2)-C(3)-H(3A)	110.7
C(4)-C(3)-H(3A)	110.7
C(2)-C(3)-H(3B)	110.7
C(4)-C(3)-H(3B)	110.7
H(3A)-C(3)-H(3B)	108.8
C(5)-C(4)-C(3)	104.58(11)
C(5)-C(4)-H(4A)	110.8
C(3)-C(4)-H(4A)	110.8
C(5)-C(4)-H(4B)	110.8
C(3)-C(4)-H(4B)	110.8
H(4A)-C(4)-H(4B)	108.9
C(1)-C(5)-C(6)	127.50(13)
C(1)-C(5)-C(4)	112.91(12)
C(6)-C(5)-C(4)	119.56(12)
C(7)-C(6)-C(5)	128.54(13)
C(7)-C(6)-H(6)	115.7
C(5)-C(6)-H(6)	115.7
C(6)-C(7)-C(8)	130.09(13)
C(6)-C(7)-H(7)	115.0

C(8)-C(7)-H(7)	115.0
C(7)-C(8)-C(9)	119.62(12)
C(7)-C(8)-H(8A)	107.4
C(9)-C(8)-H(8A)	107.4
C(7)-C(8)-H(8B)	107.4
C(9)-C(8)-H(8B)	107.4
H(8A)-C(8)-H(8B)	106.9
C(14)-C(9)-C(8)	112.21(11)
C(14)-C(9)-C(10)	113.70(11)
C(8)-C(9)-C(10)	108.55(11)
C(14)-C(9)-H(9)	107.4
C(8)-C(9)-H(9)	107.4
C(10)-C(9)-H(9)	107.4
C(15)-C(10)-C(9)	115.06(11)
C(15)-C(10)-C(11)	111.22(11)
C(9)-C(10)-C(11)	109.56(11)
C(15)-C(10)-H(10)	106.9
C(9)-C(10)-H(10)	106.9
C(11)-C(10)-H(10)	106.9
C(16)-C(15)-C(17)	121.35(13)
C(16)-C(15)-C(10)	124.36(13)
C(17)-C(15)-C(10)	114.29(12)
C(15)-C(16)-H(16A)	120.0
C(15)-C(16)-H(16B)	120.0
H(16A)-C(16)-H(16B)	120.0
C(15)-C(17)-H(17A)	109.5
C(15)-C(17)-H(17B)	109.5
H(17A)-C(17)-H(17B)	109.5
C(15)-C(17)-H(17C)	109.5
H(17A)-C(17)-H(17C)	109.5
H(17B)-C(17)-H(17C)	109.5
C(12)-C(11)-C(10)	111.74(11)
C(12)-C(11)-H(11A)	109.3
C(10)-C(11)-H(11A)	109.3
C(12)-C(11)-H(11B)	109.3
C(10)-C(11)-H(11B)	109.3

H(11A)-C(11)-H(11B)	107.9
C(13)-C(12)-C(11)	114.21(11)
C(13)-C(12)-H(12A)	108.7
C(11)-C(12)-H(12A)	108.7
C(13)-C(12)-H(12B)	108.7
C(11)-C(12)-H(12B)	108.7
H(12A)-C(12)-H(12B)	107.6
C(14)-C(13)-C(18)	124.23(12)
C(14)-C(13)-C(12)	122.00(12)
C(18)-C(13)-C(12)	113.77(12)
C(13)-C(18)-H(18A)	109.5
C(13)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(13)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(13)-C(14)-C(1)	124.00(12)
C(13)-C(14)-C(9)	122.59(12)
C(1)-C(14)-C(9)	113.32(11)

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for V19305. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2}U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	19(1)	14(1)	14(1)	-3(1)	-2(1)	-2(1)
C(2)	20(1)	18(1)	17(1)	-3(1)	-1(1)	0(1)
O(1)	25(1)	23(1)	28(1)	5(1)	6(1)	-2(1)
C(3)	24(1)	21(1)	24(1)	-3(1)	2(1)	5(1)
C(4)	26(1)	18(1)	22(1)	-2(1)	-2(1)	5(1)
C(5)	22(1)	14(1)	15(1)	-4(1)	-3(1)	0(1)
C(6)	28(1)	14(1)	18(1)	2(1)	-4(1)	-3(1)
C(7)	26(1)	18(1)	19(1)	4(1)	1(1)	-6(1)
C(8)	26(1)	18(1)	21(1)	2(1)	7(1)	-1(1)
C(9)	17(1)	14(1)	16(1)	2(1)	1(1)	0(1)
C(10)	18(1)	16(1)	18(1)	0(1)	4(1)	2(1)
C(15)	23(1)	16(1)	17(1)	1(1)	-2(1)	2(1)
C(16)	21(1)	19(1)	27(1)	-1(1)	-2(1)	-3(1)
C(17)	34(1)	18(1)	30(1)	-4(1)	2(1)	2(1)
C(11)	14(1)	19(1)	30(1)	1(1)	0(1)	2(1)
C(12)	19(1)	18(1)	24(1)	4(1)	-5(1)	0(1)
C(13)	16(1)	16(1)	19(1)	1(1)	-2(1)	-4(1)
C(18)	28(1)	19(1)	17(1)	2(1)	-5(1)	-3(1)
C(14)	15(1)	13(1)	16(1)	1(1)	0(1)	-3(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for V19305.

	x	y	z	U(eq)
H(3A)	3934	4309	7432	28
H(3B)	2659	3601	6856	28
H(4A)	4214	4607	6015	26
H(4B)	5293	5425	6594	26
H(6)	8241	5270	5734	24
H(7)	10716	4384	5250	25
H(8A)	11803	2480	5739	26
H(8B)	10660	2280	5032	26
H(9)	7869	1565	5608	19
H(10)	10775	294	5328	21
H(16A)	6071	-1447	6066	27
H(16B)	6461	-23	6314	27
H(17A)	8433	-2558	5465	41
H(17B)	10662	-2156	5622	41
H(17C)	9599	-1708	4930	41
H(11A)	12311	-693	6287	25
H(11B)	12773	747	6261	25
H(12A)	10176	-482	7187	24
H(12B)	12017	364	7387	24
H(18A)	8262	2394	7915	32
H(18B)	10501	2027	8080	32
H(18C)	8782	1029	8159	32

Table 6. Torsion angles [°] for V19305.

C(5)-C(1)-C(2)-O(1)	173.96(14)
C(14)-C(1)-C(2)-O(1)	2.0(2)
C(5)-C(1)-C(2)-C(3)	-5.26(15)
C(14)-C(1)-C(2)-C(3)	-177.21(12)
O(1)-C(2)-C(3)-C(4)	-172.03(14)
C(1)-C(2)-C(3)-C(4)	7.20(14)
C(2)-C(3)-C(4)-C(5)	-6.34(14)
C(14)-C(1)-C(5)-C(6)	-9.2(2)
C(2)-C(1)-C(5)-C(6)	179.09(13)
C(14)-C(1)-C(5)-C(4)	172.73(12)
C(2)-C(1)-C(5)-C(4)	1.03(15)
C(3)-C(4)-C(5)-C(1)	3.51(15)
C(3)-C(4)-C(5)-C(6)	-174.72(12)
C(1)-C(5)-C(6)-C(7)	20.2(2)
C(4)-C(5)-C(6)-C(7)	-161.89(14)
C(5)-C(6)-C(7)-C(8)	4.0(3)
C(6)-C(7)-C(8)-C(9)	6.5(2)
C(7)-C(8)-C(9)-C(14)	-53.97(17)
C(7)-C(8)-C(9)-C(10)	179.52(12)
C(14)-C(9)-C(10)-C(15)	81.49(14)
C(8)-C(9)-C(10)-C(15)	-152.87(11)
C(14)-C(9)-C(10)-C(11)	-44.68(15)
C(8)-C(9)-C(10)-C(11)	80.97(14)
C(9)-C(10)-C(15)-C(16)	-24.94(19)
C(11)-C(10)-C(15)-C(16)	100.38(16)
C(9)-C(10)-C(15)-C(17)	155.08(12)
C(11)-C(10)-C(15)-C(17)	-79.61(15)
C(15)-C(10)-C(11)-C(12)	-70.33(14)
C(9)-C(10)-C(11)-C(12)	58.00(14)
C(10)-C(11)-C(12)-C(13)	-44.76(16)
C(11)-C(12)-C(13)-C(14)	18.31(18)
C(11)-C(12)-C(13)-C(18)	-161.66(12)
C(18)-C(13)-C(14)-C(1)	-9.3(2)
C(12)-C(13)-C(14)-C(1)	170.73(12)

C(18)-C(13)-C(14)-C(9)	174.39(13)
C(12)-C(13)-C(14)-C(9)	-5.6(2)
C(5)-C(1)-C(14)-C(13)	138.53(14)
C(2)-C(1)-C(14)-C(13)	-51.01(19)
C(5)-C(1)-C(14)-C(9)	-44.87(18)
C(2)-C(1)-C(14)-C(9)	125.60(13)
C(8)-C(9)-C(14)-C(13)	-104.09(14)
C(10)-C(9)-C(14)-C(13)	19.59(18)
C(8)-C(9)-C(14)-C(1)	79.25(14)
C(10)-C(9)-C(14)-C(1)	-157.07(11)

[1] Sheldrick, G. M. *Acta Cryst.* **1990**, A46, 467-473.

[2] Sheldrick, G. M. *Acta Cryst.* **2015**, C71, 3-8.

[3] Müller, P. *Crystallography Reviews* **2009**, 15, 57-83.