The Supporting Information was replaced on October 3, 2011: see the Note Added after ASAP for details.

Total Synthesis of Echinopines A and B: Exploiting a Bio-inspired Late-Stage Intramolecular Cyclopropanation

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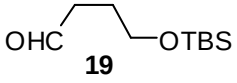
Supporting Information Available

I) Experimental Section

Experimental Data for Compounds

General Procedures. All reactions were carried out under a nitrogen or argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Dry tetrahydrofuran (THF), hexane, diethyl ether (Et_2O), methylene chloride (CH_2Cl_2), and toluene were obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Methanol (MeOH), benzene, *N*,*N*'-dimethylformamide (DMF), and 1-methyl-2-pyrrolidinone (NMP) were purchased in anhydrous form and used without further purification. Water, ethyl acetate (EtOAc), diethyl ether (Et_2O), methylene chloride (CH_2Cl_2), and hexanes were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Yields refer to chromatographically and spectroscopically (^{1}H 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 visualizing agent and an ethanolic solution of ammonium molybdate, anisaldehyde, potassium permanganate and heat as developing agents. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. NMR spectra were recorded on a Bruker AV-600 instrument 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, quint = quintet, m = multiplet, pent = pentet, hex = hexet, br = broad. IR

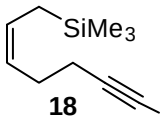
spectra were recorded on a Perkin-Elmer Spectrum One FTIR spectrometer with diamond ATR accessory. Optical rotation ($[\alpha]_D^{25}$) were recorded on a Perkin-Elmer Model 341 polarimeter at 25 °C using thermostable optical glass cell (100mm path length). Melting points (m.p.) are uncorrected, and recorded on a Buchi B-540 melting point apparatus. High-resolution mass spectra (HRMS) were recorded on an Agilent ESI TOF (time of flight) mass spectrometer at 3500 V emitter voltage.



19

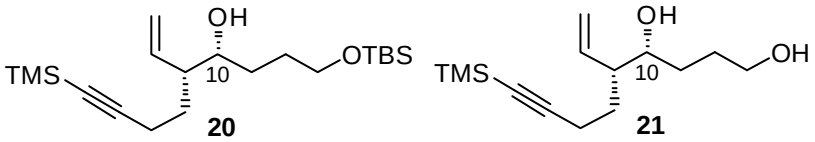
Aldehyde 19: To a stirred solution of 1,4-butanediol (26.0 g, 288.5 mmol) in CH_2Cl_2 (500 mL) at room temperature was added TBSCl (21.7 g, 144.0 mmol). The resulting mixture was cooled to 0 °C before Et_3N (20.0 mL, 144.0 mmol) was slowly added. The resulting mixture was warmed to room temperature and stirred for 3 h before it was quenched with NH_4Cl (250 mL, sat. aq.). The layers were separated and the organic layer was washed with H_2O (200 mL), dried (Na_2SO_4) and concentrated in *vacuo* to afford the corresponding mono-protected alcohol (27.4 g, 93%) as a light yellow oil, which was used directly without further purification.

To a stirred solution of $(COCl)_2$ (8.07 mL, 95.4 mmol) in CH_2Cl_2 (400 mL) at −78 °C was added DMSO (13.6 mL, 190.8 mmol). The resulting mixture was stirred for 15 min before a solution of the mono-protected alcohol (obtained above, 13.0 g, 63.6 mmol) in CH_2Cl_2 (100 mL) was added. The resulting mixture was stirred for 30 min before Et_3N (53.2 mL, 381.6 mmol) was added. The resulting mixture was warmed to room temperature before it was quenched with H_2O (250 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were washed with brine (2 × 200 mL), dried (Na_2SO_4) and concentrated in *vacuo* to afford aldehyde **19** (12.51 g, 97%) as a light yellow oil, which was used directly without further purification. All physical characteristics of aldehyde **19** were identical to those reported in literature.[1]



18

Allyl silane 18: To a stirred suspension of freshly prepared $Ph_3P^+CH_3I^-$ (23.4 g, 60 mmol)[2] in THF (120 mL) at 0 °C was added *n*-BuLi (2.0 M in cyclohexane, 33 mL, 66 mmol). The resulting mixture was stirred for 30 min before $TMSCH_2I$ (10.8 mL, 72 mmol) was added. The resulting mixture was warmed to room temperature and stirred for 10 h before it was cooled to 0 °C and *n*-BuLi (2.0 M in cyclohexane, 27 mL, 54 mmol) was added. The resulting mixture was stirred for 1 h before it was cooled to −78 °C and a solution of 5-(trimethylsilyl)pent-4-ynal[3] (7.5 g, 49 mmol) in THF (10 mL) was added. The resulting mixture was warmed to room temperature over a period of 30 min and stirred for 90 min before it was quenched with pH7 buffer (100 mL, aq.). The resulting mixture was diluted with EtOAc (200 mL), the layers were separated and the aqueous layer was extracted with EtOAc (2 × 100 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexane) afforded allyl silane **18** (7.18 g, 62%) as a colorless oil. All physical characteristics of allyl silane **18** were identical to those reported in literature.[4]

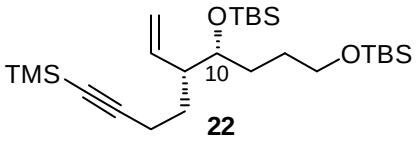


20 **21**

Sakurai products 20 and 21: To a stirred solution of allyl silane **18** (8.4 g, 35.2 mmol) and aldehyde **19** (6.5 g, 32.1 mmol) in CH_2Cl_2 (400 mL) at −78 °C was added $TiCl_4$ dropwise (3.7 mL, 33.7 mmol). The initial light yellow solution slowly turned bright orange was stirred for 1 h before it was warmed to room temperature and quenched with HCl (1.0 N aq., 200 mL). The resulting mixture was diluted with Et_2O (800 mL), the layers were separated and the aqueous layer was extracted with Et_2O (2 × 100 mL). The combined organic layers were washed with H_2O (300 mL), dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 95:05, 80:20, then 10:90) afforded the Sakurai product **20** (4.67 g, 40%, ca. 3:1 mixture of C_{10} epimers by ^1H NMR) and Sakurai product **21** (2.74 g, 34%, ca. 3:1 mixture of C_{10} epimers by ^1H NMR) as colorless oils.

20: R_f = 0.35 (silica gel, hexanes:EtOAc 90:10); IR (film) ν_{max} 3438, 2955, 2929, 2858, 2174, 1472, 1463, 1423, 1388, 1361, 1249, 1096, 1033, 998, 916, 835774, 759 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$, ca. 3:1 mixture of C_{10} epimers) δ = 5.67–5.54 (m, 1 H), 5.26–5.00 (m, 2 H), 3.65 (t, *J* = 5.7 Hz, 2 H), 3.57–3.52 (m, 0.3 H), 3.49 (dd, *J* = 11.3, 4.6 Hz, 0.7 H), 2.60 (s, 0.7 H), 2.39 (s, 0.3 H), 2.28 (ddt, *J* = 12.8, 7.3, 3.6 Hz, 1 H), 2.20–2.06 (m, 2 H), 1.96–1.85 (m, 1 H), 1.73–1.59 (m, 3 H), 1.54–1.43 (m, 1 H), 1.38 (ddd, *J* = 9.4, 8.3, 3.7 Hz, 1 H), 0.89 (s, 9 H), 0.13 (s, 9 H), 0.09 (s, 1 H), 0.06 ppm (s, 5 H); ^{13}C NMR (151 MHz, $CDCl_3$, ca. 3:1 mixture of C_{10} epimers) δ = 138.8, 138.0, 118.5, 117.5, 107.9, 107.7, 85.0, 84.8, 74.1, 73.6, 63.8, 50.2, 49.7, 32.3, 32.0, 30.3, 29.5(3), 29.4(7), 29.4, 26.3 (3C), 26.0, 18.6, 18.2, 0.5(3C), –3.2, –5.0(3C) ppm; HRMS (ESI): calcd for $C_{20}H_{40}NaO_2Si_2^+$ [M + Na^+]: 391.2465, found 391.2447.

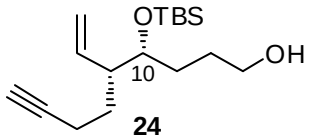
21: R_f = 0.3 (silica gel, hexanes:EtOAc 60:40); IR (film) ν_{max} 3322, 2955, 2896, 2173, 1639, 1422, 1339, 1248, 1053, 996, 916, 838, 759 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$, ca. 3:1 mixture of C_{10} epimers) δ = 5.70–5.48 (m, 1 H), 5.33–4.99 (m, 2 H), 3.77–3.60 (m, 2 H), 3.57–3.48 (m, 1 H), 2.84 (s, 1 H), 2.41 (dd, *J* = 8.7, 5.7 Hz, 0.3 H), 2.37–2.06 (m, 2.7 H), 1.92–1.78 (m, 1 H), 1.69 (s, 3 H), 1.58–1.44 (m, 1 H), 1.44–1.32 (m, 1 H), 0.88 (s, 1 H), 0.13 ppm (s, 9 H); ^{13}C NMR (151 MHz, $CDCl_3$, ca. 3:1 mixture of C_{10} epimers) δ = 119.1, 118.3, 107.7, 107.5, 85.2, 85.0, 74.4, 73.7, 63.2, 62.6, 50.2, 49.9, 32.1, 31.8, 31.1, 30.1, 29.7, 29.5, 29.3, 28.0, 26.2, 18.1(4), 18.0(7), 0.5(3C); HRMS (ESI): calcd for $C_{14}H_{26}NaO_2Si^+$ [M + Na^+]: 277.1600, found 277.1588.



22

TBS ether 22: To a stirred solution of alcohol **20** (7.55 g, 20.5 mmol), diol **21** (3.79 g, 14.9 mmol) and Et_3N (22.0 mL, 157.8 mmol) in CH_2Cl_2 (300 mL) at 0 °C was added TBSOTf (16.3 mL, 70.9 mmol). The resulting mixture was stirred for 1 h before it was quenched with $NaHCO_3$ (150 mL, sat. aq.). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were washed with brine (200 mL), dried (Na_2SO_4) and

concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 98:02 → 90:10) afforded the TBS ether **22** (15.18 g, 89%, ca. 3:1 mixture of C_{10} epimers by ^{1}H NMR) as a colorless oil. **22**: R_f = 0.55 (silica gel, hexanes:EtOAc 98:02); IR (film) ν_{max} 2955, 2929, 2895, 2857, 2175, 1472, 1463, 1388, 1361, 1250, 1096, 1073, 1053, 1004, 938, 916 834, 773, 760 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$, ca. 3:1 mixture of C_{10} epimers) δ = 5.62 (ddd, *J* = 17.2, 10.3, 9.0 Hz, 1 H), 5.16–4.95 (m, 2 H), 3.59 (dt, *J* = 9.8, 6.1 Hz, 3 H), 2.36–2.21 (m, 2 H), 2.17–2.03 (m, 1 H), 1.73 (tdd, *J* = 11.4, 8.5, 3.5 Hz, 1 H), 1.62–1.54 (m, 1 H), 1.53–1.32 (m, 4 H), 0.89 (s, 18 H), 0.14 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H), 0.04 ppm (s, 6 H); ^{13}C NMR (151 MHz, $CDCl_3$, ca. 3:1 mixture of C_{10} epimers) δ = 139.1, 138.3, 117.5, 116.9, 107.9, 84.9, 75.4, 75.3, 63.7, 63.5, 48.5, 48.5, 31.0, 30.5, 29.8, 29.4, 28.8, 28.7, 26.3 (6C), 18.6(8), 18.6(6), 18.5(1), 18.4(7), 18.2, 0.5(3C), –3.9, –4.0, –4.9(2C) ppm; HRMS (ESI): calcd for $C_{26}H_{54}NaO_2Si_3^+$ [M + Na^+]: 505.3329, found 505.3337.

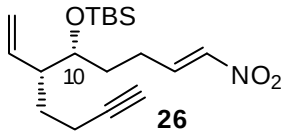


24

Alcohol 24: To a stirred solution of TBS ether **22** (15.18 g, 31.4 mmol) in CH_2Cl_2/MeOH (5:1, 300 mL) at –10 °C was added *p*-TsOH (479 mg, 2.52 mmol). The temperature of the resulting mixture was maintained between –10 °C and 0 °C and stirred for 3 h before it was quenched with $NaHCO_3$ (200 mL, sat. aq.). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were washed with brine (200 mL), dried (Na_2SO_4) and concentrated in *vacuo* to afford crude alcohol **23** as a yellow oil, which was used directly without further purification.

To a stirred solution of alcohol **23** (obtained above) in MeOH (300 mL) at room temperature was added K_2CO_3 (21.6 g, 156.5 mmol). The resulting mixture was stirred for 3 h before it was quenched with H_2O (200 mL) and diluted with CH_2Cl_2 (500 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 150 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 80:20) afforded alkyne

24 (6.38 g, 69% over the two steps, ca. 3:1 mixture of C_{10} epimers by ^{1}H NMR) as a colorless oil. **24**: R_f = 0.30 (silica gel, hexanes:EtOAc 80:20); IR (film) ν_{max} 3312, 2952, 2929, 2886, 2857, 1639, 1472, 1463, 1431, 1361, 1254, 1099, 1057, 1005, 915, 834, 811, 773 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$, ca. 3:1 mixture of C_{10} epimers) δ = 5.60 (tdd, *J* = 17.3, 10.3, 9.3 Hz, 1 H), 5.16–4.99 (m, 2 H), 3.62 (dd, *J* = 10.7, 5.4 Hz, 3 H), 2.31 (ddt, *J* = 10.8, 8.7, 4.3 Hz, 1 H), 2.23 (ddd, *J* = 16.8, 7.7, 5.0, Hz, 1 H), 2.11–2.02 (m, 1 H), 1.93 (dd, *J* = 4.6, 2.0 Hz, 1 H), 1.78 (dtd, *J* = 13.2, 8.3, 3.6 Hz, 1 H), 1.69–1.64 (m, 2 H), 1.62–1.57 (m, 1 H), 1.55–1.48 (m, 2 H), 1.39 (ddd, *J* = 13.1, 10.6, 7.9, Hz, 1 H), 0.90 (s, 9 H), 0.07 (s, 3 H), 0.06 ppm (s, 3 H); ^{13}C NMR (151 MHz, $CDCl_3$, ca. 3:1 mixture of C_{10} epimers) δ = 138.8, 138.2, 117.8, 117.2, 84.9, 75.3, 75.1, 68.9, 68.6, 63.5, 63.4, 48.7, 48.5, 30.9, 30.8, 29.5, 29.3, 29.1, 28.4, 26.3(3C), 18.4(9), 18.4(5), 16.8, 16.7, –3.9, –4.1 ppm; HRMS (ESI): calcd for $C_{17}H_{32}NaO_2Si^+$ [M + Na^+]: 319.2069, found 319.2066.



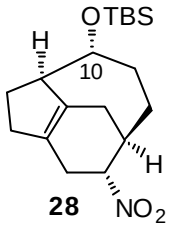
26

Nitroolefin 26: To a stirred solution of $(COCl)_2$ (2.06 mL, 24.3 mmol) in CH_2Cl_2 (120 mL) at −78 °C was added DMSO (3.45 mL, 48.6 mmol). The resulting mixture was stirred for 15 min before a solution of alcohol **24** (4.81 g, 16.2 mmol) in CH_2Cl_2 (120 mL) was added. The resulting mixture was stirred for 30 min before Et_3N (13.6 mL, 97.6 mmol) was added. The resulting mixture was warmed to room temperature over 30 min before it was quenched with H_2O (100 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (100 mL). The combined organic layers were washed with brine (200 mL), dried (Na_2SO_4) and concentrated in *vacuo* to afford aldehyde **25** as a light yellow oil, which was used directly without further purification.

To a stirred solution of aldehyde **25** (obtained above) in nitromethane (200 mL) at room temperature was added TMG (1.0 mL, 7.97 mmol). The resulting mixture was stirred for 5 min before it was quenched with NH_4Cl (100 mL, sat. aq.) and diluted with Et_2O (200 mL). The layers were separated and the aqueous layer was extracted with Et_2O (2 × 100 mL). The combined organic layers

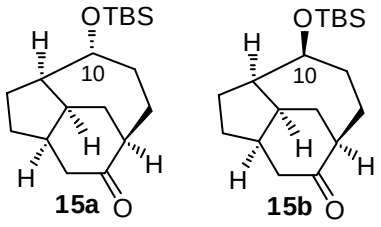
were washed with H_2O (200 mL), dried (Na_2SO_4) and concentrated in *vacuo* to afford the corresponding nitro alcohol as a light yellow oil, which was used directly without further purification.

To a stirred solution of the nitro alcohol (obtained above) in CH_2Cl_2 (200 mL) at room temperature were added pyridine (26 mL, 322 mmol) and acetic anhydride (7.7 mL, 81.6 mmol). The resulting mixture was stirred for 20 h before it was diluted with CH_2Cl_2 (200 mL), washed with HCl (1.0 N aq., 3 × 150 mL), $NaHCO_3$ (100 mL, sat. aq.) and H_2O (100 mL). The organic layer was dried (Na_2SO_4) and concentrated in *vacuo* to afford a mixture of nitroolefin **26** and its acetylated precursor. The crude mixture was dissolved in CH_2Cl_2 (200 mL) and DMAP (990 mg, 8.11 mmol) was added. The resulting mixture was stirred for 3.5 h before it was quenched with citric acid (10% wt/wt aq., 100 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (100 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 95:05) afforded nitroolefin **26** (4.1 g, 75% over 3 steps, ca. 3:1 mixture of C_{10} epimers by ^{1}H NMR) as a colorless oil. **26**: R_f = 0.45 (silica gel, hexanes:EtOAc 95:05); IR (film) ν_{max} 3310, 2954, 2929, 2857, 1650, 1525, 1472, 1463, 1432, 1351, 1255, 1094, 1073, 1004, 958, 937, 919, 832, 813, 774 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$, ca. 3:1 mixture of C_{10} epimers) δ = 7.29 (dq, *J* = 16.4, 7.5 Hz, 1 H), 6.99 (ddd, *J* = 13.4, 3.5, 1.9 Hz, 1 H), 5.61 (m, 1 H), 5.23–5.06 (m, 2 H), 3.71–3.64 (m, 1 H), 2.42–2.24 (m, 3 H), 2.16–2.04 (m, 1 H), 1.96 (s, 1 H), 1.87–1.77 (m, 1 H), 1.75–1.58 (m, 2 H), 1.58–1.48 (m, 1 H), 1.45–1.37 (m, 1 H), 0.93 (s, 9 H), 0.11 (s, 3 H), 0.08 ppm (s, 3 H); ^{13}C NMR (151 MHz, $CDCl_3$, ca. 3:1 mixture of C_{10} epimers): δ = 143.1, 142.7, 140.0, 139.9, 138.0, 137.7, 118.3, 117.8, 84.5, 74.6, 74.2, 68.9(4), 68.8(7), 48.6, 48.5, 32.5, 32.4, 29.2, 29.0, 26.3, 26.1(3C), 25.2, 24.1, 18.5, 18.4, 16.7, –4.0(2C) ppm; HRMS (ESI): calcd for $C_{18}H_{31}NNaO_3Si^+$ [M + Na^+]: 360.1971, found 360.1965.



28

Tricycle 28: To a stirred solution of $Pd(OAc)_2$ (32 mg, 0.14 mmol) in toluene (10 mL) at room temperature was added PPh_3 (77 mg, 0.28 mmol). The resulting mixture was stirred for 30 min before an aliquot (2 mL) was added to a solution of ene-yne nitroolefin **26** (95 mg, 0.28 mmol) in toluene (8 mL). The resulting mixture was heated to 80 °C and stirred for 2.5 h before it was cooled to room temperature and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 98:02 → 95:05) afforded tricycle **28** (69 mg, 73%, ca. 3:1 mixture of C_{10} epimers by ^{1}H NMR) as a light yellow oil. **28**: R_f = 0.50 (hexanes:EtOAc 95:05); IR (film) ν_{max} 2952, 2929, 2856, 1546, 1471, 1461, 1442, 1376, 1349, 1253, 1082, 1044, 1006, 991, 956, 912, 877, 835, 774 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$, ca. 3:1 mixture of C_{10} epimers) δ = 4.23–4.13 (m, 0.75 H), 4.12–4.06 (m, 0.25 H), 3.90–3.82 (m, 0.25 H), 3.78 (m, 0.75 H), 3.06 (s, 0.25 H), 2.85 (s, 0.75 H), 2.80 (dd, *J* = 13.8, 6.6 Hz, 1 H), 2.70 (s, 1 H), 2.66–2.59 (m, 1 H), 2.51 (m, 2 H), 2.35 (m, 1 H), 2.29–2.00 (m, 2 H), 1.85–1.65 (m, 2 H), 1.48 (dd, *J* = 12.1, 9.8 Hz, 1 H), 1.38 (d, *J* = 14.6 Hz, 1 H), 0.91 (s, 7 H), 0.89 (s, 2 H), 0.76 (t, *J* = 13.5 Hz, 1 H), 0.07 (s, 2 H), 0.05 (s, 2 H), 0.03 ppm (s, 2 H); ^{13}C NMR (151 MHz, $CDCl_3$, ca. 3:1 mixture of C_{10} epimers): δ = 144.4, 142.8, 135.7, 133.6, 88.4, 88.1, 76.3, 74.6, 54.9, 51.4, 41.2, 40.2, 36.1, 35.1, 34.1, 32.1, 31.7, 30.9, 29.7, 29.5, 28.8, 28.5, 28.1, 27.1, 25.8(3C), 21.8, 18.2, 18.1, –4.8, –4.8(6), –4.8(8), –5.0 ppm; HRMS (ESI): calcd for $C_{18}H_{31}NNaO_3Si^+$ [M + Na^+]: 360.1971, found 360.1963.



15a **15b**

Ketones 15a and 15b: To a stirred solution of tricycle **28** (2.05 g, 6.07 mmol) in CH_2Cl_2 (250 mL) at room temperature were added freshly prepared *o*-nitrobenzenesulfonylhydrazide (13.2 g, 60.8 mmol)[5] and Et_3N (25.3 mL, 181.5 mmol). The resulting

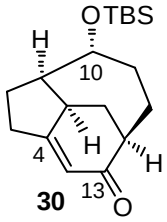
suspension was stirred for 7 h before the bright orange solution obtained was diluted with CH_2Cl_2 (150 mL) and washed with $NaHCO_3$ (3 × 200 mL, sat. aq.). The organic layer was dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 95:05) afforded the reduced tricycle **28'** (1.75 g, 85%, ca. 3:1 mixture of C_{10} epimers by ^1H NMR) as a colorless oil.

To a stirred solution of the reduced tricycle **28'** (obtained above, 507 mg, 1.50 mmol) in THF (60 mL) was added *t*-BuOK (1.0 g, 9 mmol). The resulting red solution was stirred for 5 min before a solution of Na_2HPO_4 (1.0 N aq., 45 mL) and Oxone® (2.8 g, 4.5 mmol) in H_2O (15 mL) was added. The resulting suspension was stirred for 30 min before H_2O (30 mL) was added and the solution was extracted with EtOAc (3 × 50 mL). The organic layer was dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 95:05) afforded ketone **15** (396 mg, 86%, ca. 3:1 mixture of C_{10} epimers by ^1H NMR) as a colorless oil. For analytical purpose the C_{10} epimers could be separated and fully characterized.

15a: R_f = 0.60 (silica gel, hexanes:EtOAc 80:20); IR (film) ν_{max} 2950, 2927, 2856, 1707, 1471, 1462, 1380, 1360, 1253, 1167, 1077, 1027, 1006, 979, 940, 895, 862, 835, 773 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 3.87–3.84 ppm (m, 1 H), 2.63–2.57 (m, 2 H), 2.53–2.45 (m, 2 H), 2.42 (dd, *J* = 2.2, 14.3 Hz, 1 H), 2.38–2.31 (m, 1 H), 2.20–2.14 (m, 1 H), 2.02–1.93 (m, 2 H), 1.79–1.60 (m, 5 H), 0.04 (s, 3 H), 1.42–1.27 (m, 2 H), 0.90 (s, 9 H), 0.05 (s, 3 H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 217.1, 73.7, 48.6, 46.3, 44.7, 40.0, 37.5, 32.9, 29.3, 29.0, 28.9, 25.9(3C), 25.2, 18.0, –4.8, –5.0 ppm; HRMS (ESI): calcd for $C_{18}H_{33}O_2Si^+$ [M + H^+]: 309.2250, found 309.2240.

15b: R_f = 0.55 (silica gel, hexanes:EtOAc 80:20); IR (film) ν_{max} 2926, 2855, 1707, 1471, 1462, 1385, 1360, 1254, 1175, 1136, 1067, 1005, 940, 901, 866, 835, 773 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 3.93 ppm (ddd, *J* = 2.0, 4.8, 11.3 Hz, 1 H), 2.63–2.47 (m, 2 H), 2.44–2.38 (m, 1 H), 2.28–2.22 (m, 1 H), 2.06–2.00 (m, 2 H), 1.89–1.85 (m, 1 H), 1.85–1.77 (m, 1 H), 1.74–1.60 (m, 4 H), 1.57–1.54 (m, 2 H), 1.44–1.29 (m, 2 H), 0.87 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 216.2, 73.6, 47.1,

46.3, 44.5, 40.6, 35.1, 33.0, 31.7, 29.7, 29.0, 25.8(3C), 25.0, 18.1, –4.8, –4.9 ppm; HRMS (ESI): calcd for $C_{18}H_{33}O_2Si^+$ [M + H^+]: 309.2250, found 309.2240.

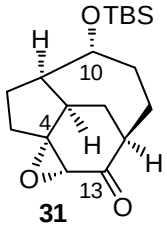


30

Enone 30: To a stirred solution of ketone **15** (612 mg, 1.99 mmol) in THF (70 mL) at –78 °C was added LDA (0.5 M in THF, 12 mL, 6.0 mmol). The resulting mixture was stirred for 30 min before a solution of PhSeBr (720 mg, 3.06 mmol) in THF (5 mL) was added. The resulting mixture was stirred for 1 h before it was quenched with NH_4Cl (60 mL, sat. aq.) and diluted with EtOAc (120 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 × 40 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in *vacuo*.

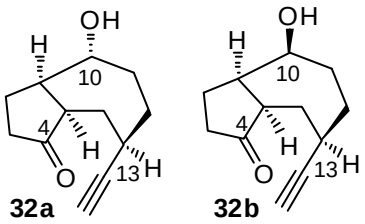
To a stirred solution of the crude residue (obtained above) in CH_2Cl_2 (36 mL) at 0 °C was added pyridine (4.0 mL) followed by H_2O_2 (40 mL, 18% aq.). The resulting mixture was stirred for 15 min before it was diluted with H_2O (50 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 70 mL). The combined organic layers were quickly washed with HCl (1.0 N aq., 50 mL), dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 90:10) afforded enone **30** (362 mg, 59%, ca. 3:1 mixture of C_{10} epimers by ^{1}H NMR) as a colorless oil. **30**: R_f = 0.45 (hexanes:EtOAc 80:20); IR (film) ν_{max} 2950, 2926, 2855, 1666, 1471, 1461, 1444, 1379, 1359, 1307, 1250, 1183, 1159, 1075, 1000, 894, 835, 774 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$, ca. 3:1 mixture of C_{10} epimers) δ = 6.00 ppm (s, 0.3 H), 5.96 (s, 0.7 H), 3.89 (dd, *J* = 6.1, 10.3 Hz, 0.3 H), 3.67 (dd, *J* = 2.1, 7.1 Hz, 0.7 H), 2.74–2.66 (m, 1 H), 2.64–2.56 (m, 1 H), 2.55–2.47 (m, 3 H), 2.47–2.26 (m, 2 H), 2.03–1.90 (m, 1 H), 1.81–1.63 (m, 2 H), 1.60–1.48 (m, 2 H), 1.36–1.28 (m, 1 H), 0.91 (s, 6.7 H), 0.86 (s, 2.3 H), 0.06 (s, 2.2 H), 0.03 (s, 0.8 H), 0.03 (s, 0.8 H), 0.02 (s, 2.2 H); ^{13}C NMR (151 MHz, $CDCl_3$, ca. 3:1 mixture of C_{10} epimers): δ = 203.6, 202.5, 172.1, 170.6, 123.6, 123.2, 77.2, 74.8, 44.4, 44.4, 44.1, 40.8, 40.0, 37.8, 31.2, 31.0, 30.9, 30.8, 29.7, 27.8, 26.3, 25.9(6C), 25.7,

23.1, 22.6, 22.2, 18.1, –4.8, –4.8, –4.9, –4.9 ppm; HRMS (ESI): calcd for $C_{18}H_{31}O_2Si^+$ [M + H^+]: 307.2093, found 307.2091.



31

Epoxy ketone 31: To a stirred solution of enone **30** (362 mg, 1.18 mmol) in MeOH (70 mL) at 0 °C was added a solution of NaOH (10% wt/wt aq., 9.6 mL, 24 mmol) followed by H_2O_2 (18% aq., 11 mL, 58.2 mmol). The resulting mixture was stirred for 20 min before it was quenched with NH_4Cl (100 mL, sat. aq.) and diluted with EtOAc (280 mL). The layers were separated and the organic layer was thoroughly washed with NH_4Cl (100 mL, sat. aq.) and H_2O (3 × 100 mL), then dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 90:10) afforded the epoxy ketone **31** (351 mg, 92%, ca. 3:1 mixture of C_{10} epimers by ^{1}H NMR) as a colorless oil. **31**: R_f = 0.55 (silica gel, hexanes:EtOAc 80:20); IR (film) ν_{max} 2926, 2855, 1705, 1462, 1450, 1255, 1077, 1044, 1002, 869, 834, 771 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$, ca. 4:1 mixture of C_{10} epimers): δ = 3.93 ppm (dd, *J* = 5.8, 9.3 Hz, 0.2 H), 3.78 (dd, *J* = 3.0, 7.3 Hz, 0.8 H), 2.69–2.46 (m, 2 H), 2.17–2.04 (m, 2 H), 1.97–1.88 (m, 1 H), 1.67 (m, 2 H), 1.61–1.47 (m, 4 H), 1.35–1.27 (m, 2 H), 0.91 (s, 7.2 H), 0.87 (s, 1.8 H), 0.07 (s, 2.4 H), 0.05 (s, 0.6 H), 0.04 (d, *J* = 1.8 Hz, 0.6 H), 0.04 (s, 2.4 H); ^{13}C NMR (151 MHz, $CDCl_3$, ca. 4:1 mixture of C_{10} epimers): δ = 210.5, 209.5, 74.7, 74.7, 70.0, 69.6, 59.8, 59.6, 44.0, 44.0, 43.5, 41.6, 36.4, 34.6, 33.0, 31.3, 28.8, 28.4, 28.4, 27.4, 25.9(3C), 25.8(3C), 24.9, 22.5, 21.8, 21.5, 18.1, 17.9, –4.8, –4.9, –4.9, –5.0 ppm; HRMS (ESI): calcd for $C_{18}H_{31}O_3Si^+$ [M + H^+] 323.2042, found 323.2032.



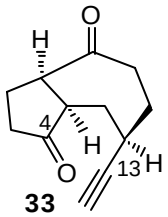
32a **32b**

Keto alkynes 32a and 32b: To a stirred solution of epoxy ketone **31** (70 mg, 0.22 mmol) in CH_2Cl_2 (14 mL) at room temperature were added TFA (84 μL, 1.1 mmol), silica gel (196 mg) and *p*-toluenesulfonylhydrazide (207 mg, 1.1 mmol). The resulting mixture was stirred for 20 min before it was filtered, diluted with CH_2Cl_2 (30 mL) and washed with $NaHCO_3$ (15 mL, sat. aq.). The organic layer was dried (Na_2SO_4) and concentrated in *vacuo* to afford the fragmentation product in its hydrazone form. The desired keto-alkyne **32** was obtained by dissolving the hydrazone in a mixture of acetone (2 mL) and THF/HCl (1.0 N aq., 1:1, 10 mL). The solution was stirred at room temperature for 4 h before it was extracted with EtOAc (3 × 10 mL), dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 50:50) afforded the keto-alkyne **32a** (33 mg, 78%) and **32b** (7 mg, 17%) as colorless oils.

32a: R_f = 0.25 (silica gel, hexanes:EtOAc 40:60); IR (film) ν_{max} 3430, 2927, 1733, 1666, 1453, 1406, 1336, 1164, 1042, 813, 675 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 3.72 (dt, *J* = 8.8, 5.8 Hz, 1 H), 2.93–2.78 (m, 1 H), 2.48–2.37 (m, 2 H), 2.37–2.32 (m, 2 H), 2.29–2.23 (m, 1 H), 2.21–2.11 (m, 1 H), 2.09 (d, *J* = 2.6 Hz, 1 H), 2.08–2.02 (m, 1 H), 1.97–1.82 (m, 2 H), 1.72–1.58 (m, 2 H), 1.58–1.48 ppm (m, 2 H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 219.1, 87.1, 76.7, 69.9, 50.8, 48.0, 37.4, 34.4(4), 34.4(1), 28.2, 27.5, 26.6 ppm; HRMS (ESI): calcd for $C_{12}H_{16}NaO_2^+$ [M + Na^+] 215.1048, found 215.1046.

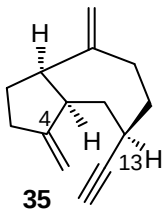
32b: R_f = 0.45 (silica gel, hexanes:EtOAc 40:60); IR (film) ν_{max} 3445, 3298, 2918, 2850, 1724, 1454, 1406, 1359, 1285, 1261, 1156, 1060, 1013, 915, 730, 630 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 4.08 (s, 1 H), 2.84–2.78 (m, 1 H), 2.53 (tdd, *J* = 11.4, 5.1, 1.4 Hz, 1 H), 2.47–2.37 (m, 1 H), 2.34–2.26 (m, 1 H), 2.19 (d, *J* = 2.6 Hz, 1 H), 2.16 (ddd, *J* = 18.8, 9.7, 5.6 Hz, 1 H), 2.07–1.88 (m, 5 H), 1.70 (ddd, *J* = 11.2, 6.5, 2.5 Hz, 2 H), 1.54 ppm (ddd, *J* = 14.2, 11.0, 5.6 Hz, 2 H); ^{13}C NMR (151 MHz, $CDCl_3$): δ =

220.7, 87.9, 71.1, 69.4, 48.1, 45.5, 38.0, 34.9, 34.5, 29.1, 28.5, 23.9 ppm; HRMS (ESI): calcd for $C_{12}H_{16}NaO_2^+$ [M + Na^+] 215.1048, found 215.1050.

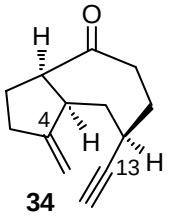


33

Diketone 33: To a stirred solution of keto alkyne **32** (53 mg, 0.28 mmol) in CH_2Cl_2 (20 mL) at room temperature were added $NaHCO_3$ (235 mg, 2.8 mmol) and DMP (237 mg, 0.56 mmol). The resulting mixture was stirred for 2 h before it was diluted with CH_2Cl_2 (20 mL) and quenched with $Na_2S_2O_3$ (20 mL, sat. aq.). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic layers were washed with $NaHCO_3$ (50 mL), dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 70:30 → 50:50) afforded diketone **33** (47 mg, 89%) as a colorless oil. **33**: R_f = 0.50 (silica gel, hexanes:EtOAc 40:60); IR (film) ν_{max} 3230, 2925, 2853, 1737, 1700, 1455, 1364, 1166, 674 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 3.22 (td, *J* = 4.1, 2.0 Hz, 1 H), 2.97 (ddd, *J* = 18.9, 13.1, 3.6 Hz, 1 H), 2.90 (ddd, *J* = 12.4, 10.8, 6.6 Hz, 1 H), 2.59–2.50 (m, 2 H), 2.49–2.43 (m, 1 H), 2.38–2.30 (m, 1 H), 2.27–2.07 (m, 4 H), 2.07–2.00 (m, 1 H), 1.96–1.84 (m, 1 H), 1.50 ppm (ddd, *J* = 13.9, 12.0, 4.0 Hz, 1 H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 217.2, 210.7, 83.3, 73.4, 54.7, 47.4, 38.9, 36.9, 35.8, 28.5, 26.4, 21.2 ppm; HRMS (EI): calcd for $C_{12}H_{14}O_2$, 190.0994, found 190.0989.



35



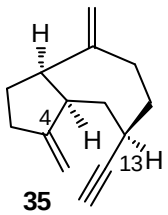
34

Diene-yne 35 and ene-yne 34: To a stirred suspension of freshly prepared $Ph_3P^+CH_3I^-$ (1.45 g, 3.6 mmol)[2] in THF (80 mL) at 0 °C was added *n*-BuLi (2.0 M in cyclohexane, 1.76 mL, 3.53 mmol). The resulting mixture was stirred for 30 min before it was cooled to –20 °C and diketone **33** (136 mg, 0.72 mmol) in THF (5 mL) was added. The resulting mixture was

warmed to 0 °C and stirred for 6 h before it was quenched with NH_4Cl (50 mL, sat. aq.). The layers were separated and the aqueous layer was extracted with Et_2O (2 × 50 mL). The combined organic layers were washed with H_2O (50 mL), dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, 100% hexane, then hexanes:EtOAc 95:05 → 90:10) afforded diene-yne **35** (74 mg, 55%) and ene-yne **34** (41 mg, 30%) as colorless oils.

35: R_f = 0.60 (silica gel, 100% hexanes); IR (film) ν_{max} 3311, 3075, 2925, 2854, 1650, 1631, 1438, 1376, 1309, 1248, 1159, 1096, 1025, 947, 885, 805 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 4.94 (d, *J* = 2.1 Hz, 1 H), 4.85–4.82 (m, 1 H), 4.81 (d, *J* = 2.1 Hz, 1 H), 4.76 (d, *J* = 1.6 Hz, 1 H), 3.04 (dd, *J* = 4.7, 2.5 Hz, 1 H), 2.93–2.77 (m, 1 H), 2.58–2.45 (m, 1 H), 2.44–2.31 (m, 2 H), 2.28–2.22 (m, 1 H), 2.11 (d, *J* = 2.6 Hz, 1 H), 2.03–1.95 (m, 1 H), 1.94–1.85 (m, 1 H), 1.80–1.70 (m, 1 H), 1.68–1.52 (m, 2 H), 0.99–0.84 ppm (m, 2 H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 156.6, 151.8, 108.4, 105.1, 87.1, 69.1, 51.4, 44.9, 40.6, 32.5, 32.4, 30.6, 30.3, 29.7 ppm; HRMS (EI): calcd for $C_{14}H_{18}$, 186.1409, found 186.1384.

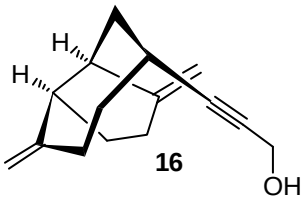
34: R_f = 0.40 (silica gel, hexanes:EtOAc 95:05); IR (film) ν_{max} 3292, 3077, 2933, 2856, 1737, 1634, 1450, 1438, 1406, 1361, 1279, 1241, 1208, 1145, 1039, 994, 935, 891, 635 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 4.94–4.90 (m, 1 H), 4.85–4.80 (m, 1 H), 3.03 (dd, *J* = 4.7, 2.6 Hz, 1 H), 2.92–2.78 (m, 1 H), 2.63–2.52 (m, 1 H), 2.51–2.35 (m, 3 H), 2.24 (m, 3 H), 2.08 (d, *J* = 2.4 Hz, 1 H), 1.93 (m, 1 H), 1.85–1.73 (m, 1 H), 1.69–1.62 (m, 1 H), 1.37 ppm (ddd, *J* = 13.9, 11.2, 4.6 Hz, 1 H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 219.6, 151.1, 109.9, 86.3, 71.1, 51.1, 48.4, 38.2, 35.9, 32.6, 31.5, 29.4, 27.0 ppm; HRMS (ESI): calcd for $C_{13}H_{16}NaO^+$ [M + Na^+] 211.1099, found 211.1095.



35

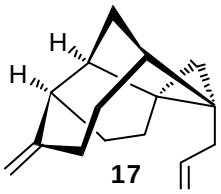
Diene-yne 35: To a stirred solution of ene-yne **34** (16 mg, 0.085 mmol) in THF (8 mL) at −78 °C were added pyridine (137 μL, 1.7 mmol) and Tebbe reagent (0.5 M in toluene, 0.68 mL, 0.34 mmol). The resulting mixture was stirred at −78 °C for 15 min, then at 0 °C for 15 min and 5 h at room

temperature before it was cooled to 0 °C and quenched with HCl (1.0 N aq., 10 mL). The resulting mixture was diluted with Et_2O (15 mL), the layers were separated and the aqueous layer was extracted with Et_2O (20 mL). The combined organic layers were washed with H_2O (20 mL), dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, 100% hexanes) afforded diene-yne **35** (12 mg, 76%) as a colorless oil and whose analytical data are identical those described above.



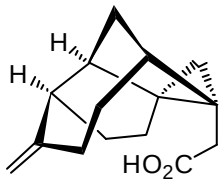
16

Propargyl alcohol 16: To a stirred solution of diene-yne **35** (20 mg, 0.107 mmol) in THF (18 mL) at −78 °C was added *n*-BuLi (2.0 M in cyclohexane, 0.55 mL, 1.1 mmol). The resulting mixture was warmed to −20 °C and stirred for 30 min before paraformaldehyde (89 mg, 2.97 mmol) was added. The resulting mixture was stirred for 20 min at room temperature before it was quenched with H_2O (15 mL) and diluted with EtOAc (20 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 90:10 → 80:20) afforded propargyl alcohol **16** (20 mg, 86%) as a colorless oil. **16**: R_f = 0.40 (silica gel, hexanes:EtOAc 80:20); IR (film) ν_{max} 3340, 3075, 2930, 2867, 1651, 1631, 1434, 1357, 1225, 1121, 1018, 975, 881 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 4.96–4.89 (m, 1 H), 4.82–4.79 (m, 1 H), 4.77 (d, *J* = 2.0 Hz, 1 H), 4.73 (d, *J* = 1.1 Hz, 1 H), 4.27 (dd, *J* = 5.7, 1.8 Hz, 2 H), 3.06–3.00 (m, 1 H), 2.92–2.71 (m, 1 H), 2.47 (dd, *J* = 16.2, 8.2 Hz, 1 H), 2.42–2.26 (m, 3 H), 2.24–2.16 (m, 1 H), 1.99–1.91 (m, 1 H), 1.91–1.85 (m, 1 H), 1.71 (ddt, *J* = 14.0, 11.4, 2.4 Hz, 1 H), 1.64–1.57 (m, 1 H), 1.51 (ddd, *J* = 13.8, 11.2, 4.7 Hz, 1 H), 1.45 (t, *J* = 6.0 Hz, 1 H), 0.88 ppm (t, *J* = 7.0 Hz, 1 H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 156.7, 151.9, 108.3, 105.1, 88.9, 80.2, 51.5, 51.2, 45.1, 40.6, 32.7, 32.4, 30.6, 30.4, 29.8 ppm; HRMS (EI): calcd for $C_{15}H_{20}O$, 216.1514, found 216.1500.



17

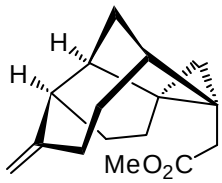
Aldehyde 17: To a stirred solution of propargyl alcohol **16** (9 mg, 0.042 mmol) in freshly distilled acetone (4 mL) at room temperature was added a stock solution (1.0 mL) containing $CpRu(PPh_3)_2Cl$ (36.3 mg, 0.05 mmol in 5 mL of acetone) and CSA (8.7 mg, 0.037 mmol in 5 mL of acetone). The resulting mixture was heated at 56 °C for 5 min in a sealed tube before $In(OTf)_3$ (1.0 mL from a stock solution containing 28.1 mg, 0.05 mmol in 5 mL of acetone) was added. The resulting mixture was stirred at 56 °C for 20 h before it was quenched with $NaHCO_3$ (5 mL, sat. aq.), and diluted with Et_2O (10 mL). The layers were separated and the aqueous layer was extracted with Et_2O (2 × 10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in *vacuo*. Preparative TLC purification (silica gel, hexanes:CH_2Cl_2 60:40) afforded aldehyde **17** (2.9 mg, 32%) as a colorless oil. **17**: R_f = 0.40 (silica gel, hexanes:EtOAc 90:10); IR (film) 3063, 2924, 2866, 1723, 1635, 1455, 1437, 1197, 1119, 1053, 968, 887, 799, 721, 694 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 9.84 (dd, *J* = 3.0, 1.8 Hz, 1 H), 4.67 (d, *J* = 3.0 Hz, 1 H), 4.64 (d, *J* = 2.4 Hz, 1 H), 2.85 (td, *J* = 9.6, 2.4 Hz, 1 H), 2.68 (dq, *J* = 16.2, 1.8 Hz, 1 H), 2.38–2.37 (m, 1 H), 2.32 (t, *J* = 8.1 Hz, 1 H), 2.23–2.13 (m, 2 H), 2.01–1.96 (m, 1 H), 1.88–1.80 (m, 3 H), 1.73–1.67 (m, 1 H), 1.61–1.54 (m, 1 H), 1.53–1.48 (m, 1 H), 1.41 (d, *J* = 13.8 Hz, 1 H), 1.33–1.27 (m, 1 H), 0.82 (dd, *J* = 5.4, 1.8 Hz, 1 H), 0.50 ppm (d, *J* = 5.4 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 203.1, 154.2, 112.3, 48.7, 48.4, 44.7, 40.6, 40.4, 32.8, 31.1, 30.8, 29.5, 28.5, 25.8, 15.9 ppm.



Echinopine A (**1**)

Echinopine A (1): To a stirred solution of aldehyde **17** (11.3 mg, 0.052 mmol) and 2-methyl-2-butene (55 μL, 0.52 mmol) in *t*-BuOH/pH 7 phosphate buffer (1:1, 0.8 mL) at room temperature was added $NaClO_2$ (0.3 M aq., 349 μL, 0.105 mmol). The resulting mixture was stirred for

1 h before it was filtered through a short pad of anhydrous Na_2SO_4/SiO_2 and concentrated in vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 4:1) afforded echinopine A (**1**) (11.4 mg, 94%) as a white solid. **1**: R_f = 0.25 (silica gel, hexanes:EtOAc 3:1); m.p. = 104–105 °C (EtOAc) [Lit.[6] m.p. = 99–102 °C]; IR (film) 2935, 2866, 1703, 1636, 1453, 1410, 1299, 1231, 948, 886, 666 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 10.69 (br s, 1 H), 4.64 (d, *J* = 2.4 Hz, 1 H), 4.61 (d, *J* = 2.4 Hz, 1 H), 2.81 (td, *J* = 9.0, 1.8 Hz, 1 H), 2.66 (dd, *J* = 15.0, 1.2 Hz, 1 H), 2.44 (m, 1 H), 2.27 (t, *J* = 8.0 Hz, 1 H), 2.16 (m, 1 H), 2.14 (dt, *J* = 13.8, 4.5 Hz, 1 H), 1.95 (m, 1 H), 1.94 (m, 1 H), 1.82 (td, *J* = 13.2, 4.2 Hz, 1 H), 1.76 (d, *J* = 15.0 Hz, 1 H), 1.69 (dddd, *J* = 13.8, 9.6, 6.6, 2.4 Hz, 1 H), 1.52 (ddd, *J* = 13.2, 9.6, 3.8 Hz, 1 H), 1.44 (dtd, *J* = 13.8, 7.2, 1.2 Hz, 1 H), 1.36 (d, *J* = 13.8 Hz, 1 H), 1.27 (tdd, *J* = 13.8, 4.2, 3.0 Hz, 1 H), 0.73 (dd, *J* = 5.4, 1.2 Hz, 1 H), 0.50 ppm (d, *J* = 4.8 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 178.7, 154.3, 112.1, 48.7, 48.5, 41.4, 40.5, 35.2, 32.7, 31.0, 30.5, 29.9, 29.4, 25.7, 16.1 ppm; HRMS (ESI): calcd for $C_{15}H_{20}O_2Na^+$ [M + Na^+] 255.1356, found 255.1357.

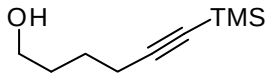


Echinopine B (**2**)

Echinopine B (2): To a stirred solution of echinopine A (**1**) (4.1 mg, 0.018 mmol) in benzene/MeOH (4:1, 1.5 mL) at room temperature was added $TMSCHN_2$ (2.0 M in Et_2O, 13.3 µL, 0.027 mmol). The resulting mixture was stirred for 0.5 h before it was concentrated in vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 200:1) afforded echinopine B (**2**) (4.0 mg, 92%) as a white amorphous solid. **2**: R_f = 0.40 (silica gel, hexanes:EtOAc 95:5); IR (film) 3064, 2933, 2866, 1740, 1636, 1456, 1434, 1270, 1221, 1165, 1075, 1009, 885 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 4.63 (d, *J* = 3.0 Hz, 1 H), 4.60 (d, *J* = 3.0 Hz, 1 H), 3.68 (s, 3 H), 2.80 (td, *J* = 9.0, 1.8 Hz, 1 H), 2.64 (dd, *J* = 15.0, 1.2 Hz, 1 H), 2.39 (m, 1 H), 2.25 (t, *J* = 8.1 Hz, 1 H), 2.14 (m, 1 H), 2.12 (m, 1 H), 1.93 (m, 2 H), 1.82 (td, *J* = 13.2, 4.2 Hz, 1 H), 1.72 (d, *J* = 15.0 Hz, 1 H), 1.65 (m, 1 H), 1.51 (m, 1 H), 1.44 (m, 1 H), 1.35 (d, *J* = 13.8 Hz, 1 H), 1.26 (m, 1 H), 0.69 (dd, *J* = 5.1, 1.5 Hz, 1 H), 0.47 ppm (d, *J* = 5.4

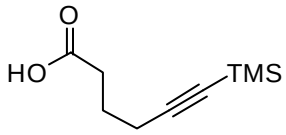
Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 173.6, 154.3, 111.8, 51.4, 48.5, 48.4, 41.2, 40.5, 35.2, 32.6, 30.9, 30.3, 30.0, 29.3, 25.6, 15.9 ppm; HRMS (ESI): calcd for $C_{16}H_{22}O_2Na^+$ [M + Na^+] 269.1512, found 269.1514.

Asymmetric Synthesis of (–)-22:



37

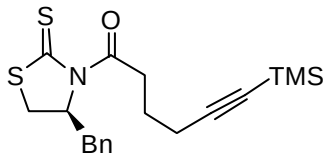
TMS alcohol 37: To a stirred solution of 5-hexyne-1-ol (5.7 mL, 50 mmol) in THF (150 mL) at –78 °C were added *n*-BuLi (1.55 M in hexane, 71 mL, 110 mmol) and DMAP (1.31 g, 10.6 mmol). The resulting mixture was stirred for 1 h before TMSCl (19.0 mL, 180 mmol) was added. The resulting mixture was warmed to room temperature and stirred for 2 h before it was quenched with HCl (1.0 N aq., 50 mL). The resulting mixture was stirred for 30 min before EtOAc (200 mL) was added. The layers were separated and the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with $NaHCO_3$ (100 mL, sat. aq.), brine (30 mL), dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 80:20) afforded TMS alcohol **37** (7.60 g, 99%) as a colorless oil. **37**: R_f = 0.38 (silica gel, hexanes:EtOAc 80:20). The ^{1}H and ^{13}C NMR spectroscopic data were identical to those reported in literature.[7]



38

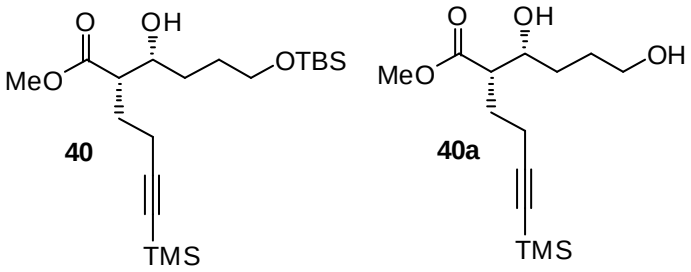
Acid 38: To a stirred solution of alcohol **37** (6.34 g, 41 mmol) in DMF (82 mL) at 0 °C was added PDC (54.2 g, 144 mmol). The resulting mixture was stirred for 15 min before it was warmed to room temperature and stirred for 12 h. Silica gel (100 g) and EtOAc (100 mL) were added and the resulting mixture was stirred for 10 min before it was filtered through a pad of silica gel and washed through with EtOAc (3 × 150 mL). The combined filtrate was concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 90:10 → 70:30) afforded acid **38** (4.34 g, 56%) as a colorless oil. **38**: R_f = 0.28 (silica gel, hexanes:EtOAc 70:30); IR (film) ν_{max} 3006, 2989, 2960, 2902,

2175, 1708, 1411, 1275, 1260, 1046, 836, 750, 698, 637 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 2.50 ppm (t, *J* = 7.2 Hz, 2 H), 2.32 (t *J* = 6.6 Hz, 2 H), 1.84 (q, *J* = 7.1 Hz, 2 H), 0.15 (s, 9 H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 178.7, 105.7, 85.7, 32.5, 23.4, 19.2, 0.1 ppm (3C); HRMS (ESI): calcd for $C_9H_{15}O_2Si^-$ [M – H^+] 183.0841, found 183.0846.



39

Thiazolidinethione 39: To a stirred solution of DCC (5.67 g, 27.2 mmol) in CH_2Cl_2 (100 mL) at −15 °C was added acid **38** (5 g, 27.2 mmol). The resulting mixture was stirred for 30 min before thiazolidinethione[8] (5.69 g, 27.2 mmol) was added followed by DMAP (3.69 g, 29.2 mmol). The resulting mixture was warmed to room temperature over a period of 1 h before it was filtered through a pad of Celite® and washed through with CH_2Cl_2 (200 mL). The combined filtrate was concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 90:10) afforded thiazolidinethione **39** (5.74 g, 56%) as a yellow oil. **39**: R_f = 0.42 (silica gel, hexanes:EtOAc 80:20); $[\alpha]_D^{25}$ = +109.3 (*c* = 1.00, $CHCl_3$); IR (film) ν_{max} 3029, 2958, 2173, 1695, 1496, 1454, 1363, 1341, 1318, 1292, 1265, 1248, 1192, 1155, 1136, 1039, 842, 702, 639 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 7.36–7.33 ppm (m, 2 H), 7.30–7.27 (m, 3 H), 5.40–5.36 (m, 1 H), 3.51 (ddd, *J* = 17.7, 8.4, 6.0 Hz, 1 H), 1.15 (s, 9 H), 3.39 (ddd, *J* = 11.5, 7.2, 0.8 Hz, 1 H), 3.23 (ddd, *J* = 17.7, 8.4, 6.0 Hz, 1 H), 3.23 (dd, *J* = 13.2, 3.9 Hz, 1 H), 3.21 (dd, *J* = 13.1, 10.5 Hz, 1 H), 2.88 (d, *J* = 11.5 Hz, 1 H), 2.34 (td, *J* = 7.0, 1.3 Hz, 2 H), 1.98–1.83 (m, 2 H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 201.0, 173.5, 136.5, 129.4 (2C), 128.9 (2C), 127.2, 106.1, 85.7, 68.5, 37.3, 36.8, 31.9, 23.6, 19.1, 0.1 ppm (3C); HRMS (ESI): calcd for $C_{19}H_{25}NOS_2SiNa^+$ [M + Na^+] 398.1045, found 398.1050.



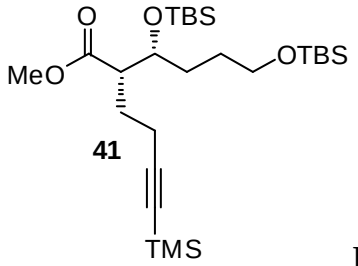
Methyl esters 40 and 40a: To a stirred solution of thiazolidinethione **39** (4.62 g, 12.3 mmol) in CH_2Cl_2 (130 mL) at –78 °C was added $TiCl_4$ (1.42 mL, 12.9 mmol). The resulting mixture was stirred for 15 min before *i*-Pr_2NEt (2.25 mL, 12.9 mmol) was added, and the resulting mixture was stirred for 45 min before NMP (2.49 mL, 25.8 mmol) was added. The resulting mixture was stirred for 15 min before a solution of aldehyde **19** (3.0 g, 14.8 mmol) in CH_2Cl_2 (3 mL) was added. The resulting mixture was warmed to –40 °C before it was warmed to –20 °C over a period of 1.5 h and then quenched with HCl (1.0 N aq., 100 mL). The resulting mixture was diluted with Et_2O (300 mL) and warmed to room temperature. The layers were separated and the aqueous layer was extracted with Et_2O (2 × 100 mL). The combined organic layers were washed with H_2O (80 mL), dried (Na_2SO_4) and concentrated in *vacuo*. The aldol product appeared to be unstable on silica gel and was therefore used directly without further purification.

To a stirred solution of the crude aldol product (obtained above) in MeOH (120 mL) at room temperature were added imidazole (8.2 g, 120.6 mmol) and DMAP (1.50 g, 12.3 mmol). The resulting mixture was stirred for 12 h before it was quenched with NH_4Cl (200 mL, sat. aq.) and diluted with EtOAc (200 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 150 mL). The combined organic layers were washed with brine (100 mL), dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 95:05 → 30:70) afforded methyl esters **40** (377 mg, 8%) and **40a** (1.96 g, 56%) as a colorless oils and recovered thiazolidinethione (2.25 g, 87%) as a white solid.

40: R_f = 0.50 (silica gel, hexanes:EtOAc 75:25); $[\alpha]_D^{25}$ = –22.4 (*c* = 1.0, $CHCl_3$); IR (film) ν_{max} 3427, 2953, 2929, 2898, 2857, 2175, 1735, 1472, 1463, 1436, 1388, 1361, 1249, 1204, 1162, 1097, 1040,

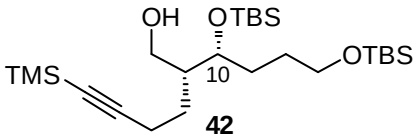
1005, 938, 835, 775, 760 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 3.84 (ddd, *J* = 10.1, 7.3, 2.8 Hz, 1 H), 3.70 (s, 3 H), 3.67–3.63 (m, 2 H), 3.20 (d, *J* = 4.5 Hz, 1 H), 2.60 (ddd, *J* = 9.6, 5.3, 4.0 Hz, 1 H), 2.35–2.16 (m, 2 H), 1.98–1.84 (m, 2 H), 1.72–1.63 (m, 2 H), 1.62–1.57 (m, 1 H), 1.50 (ddt, *J* = 13.9, 9.1, 6.8 Hz, 1 H), 0.89 (s, 9 H), 0.14 (s, 9 H), 0.06 ppm (s, 6 H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 175.0, 106.4, 85.1, 71.8, 63.2, 51.7, 50.2, 31.8, 29.1, 26.4, 25.9(3C), 18.2(8), 18.2(6), 0.1(3C), –5.40(2C) ppm; HRMS (ESI): calcd for $C_{20}H_{40}NaO_4Si_2^+$ [M + Na^+] 423.2363, found 423.2359.

40a: R_f = 0.30 (silica gel, hexanes:EtOAc 75:25); $[\alpha]_D^{25}$ = +40.2 (*c* = 1.0, $CHCl_3$); IR (film) ν_{max} 3365, 2954, 2174, 1717, 1436, 1365, 1249, 1205, 1163, 1108, 1042, 912, 838, 759, 732, 698, 639 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 3.94–3.83 (m, 1 H), 3.71 (s, 3 H), 3.77–3.59 (m, 2 H), 2.67–2.55 (m, 1 H), 2.37–2.15 (m, 2 H), 1.94 (ddd, *J* = 13.4, 9.8, 7.4 Hz, 1 H), 1.85 (dtd, *J* = 13.8, 7.9, 3.8 Hz, 1 H), 1.77–1.68 (m, 2 H), 1.64–1.46 (m, 2 H), 0.13 ppm (s, 9 H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 175.2, 106.2, 85.4, 71.8, 62.7, 51.8, 50.0, 31.6, 29.4, 26.1, 18.2, 0.1(3C) ppm; HRMS (ESI): calcd for $C_{14}H_{26}NaO_4Si^+$ [M + Na^+] 309.1498, found 309.1505.



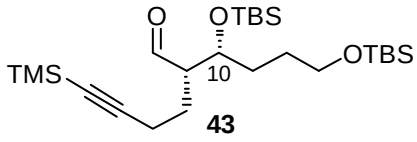
Bis-TBS ether 41: To a stirred solution of diol **40a** (2.32 g, 8.1 mmol) in CH_2Cl_2 (80 mL) at 0 °C were added Et_3N (6.8 mL, 48.8 mmol) and TBSOTf (5.6 mL, 24.3 mmol). The resulting mixture was stirred for 30 min before it was quenched with $NaHCO_3$ (100 mL, sat. aq.) and diluted with CH_2Cl_2 (100 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with NH_4Cl (2 × 100 mL, sat. aq.), brine (50 mL), dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 95:05 → 90:10) afforded bis-TBS ether **41** (3.76 g, 90%) as a colorless oil. **41**: R_f = 0.80 (silica gel, hexanes:EtOAc 90:10); $[\alpha]_D^{25}$ = +39.5 (*c* = 1.0, $CHCl_3$); IR (film) ν_{max} 2954, 2929, 2895,

2857, 2175, 1737, 1472, 1463, 1435, 1388, 1361, 1275, 1250, 1200, 1164, 1083, 1044, 1005, 939, 833, 772 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 3.98 (q, *J* = 4.9 Hz, 1 H), 3.67 (s, 3 H), 3.59 (dd, *J* = 5.5, 3.3 Hz, 2 H), 2.69 (ddd, *J* = 10.6, 4.8, 3.3 Hz, 1 H), 2.37–2.14 (m, 2 H), 1.90 (ddd, *J* = 13.5, 10.8, 6.8 Hz, 1 H), 1.77–1.68 (m, 1 H), 1.59–1.47 (m, 4 H), 0.89 (s, 9 H), 0.87 (s, 9 H), 0.13 (s, 9 H), 0.04 ppm (s, 12 H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 174.3, 106.6, 85.1, 73.1, 63.0, 51.4, 49.3, 31.1, 28.3, 25.9(3C), 25.8(3C), 25.8, 18.3, 18.0(2C), 0.1(3C), –4.3, –4.8, –5.3(2C) ppm; HRMS (ESI): calcd for $C_{26}H_{54}NaO_4Si_3^+$ [M + Na^+] 537.3228, found 537.3240.



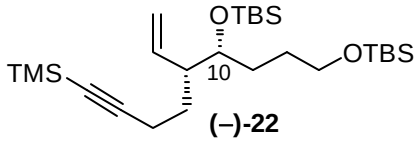
42

Alcohol 42: To a stirred solution of methyl ester **41** (3.64 g, 7.06 mmol) in CH_2Cl_2 (70 mL) at –78 °C was added Dibal-H (1.0 M in toluene, 21.0 mL, 21.0 mmol). The resulting mixture was stirred for 1 h before it was warmed to 0 °C, quenched with HCl (1.0 N aq., 100mL) and diluted with EtOAc (100 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with brine (50 mL), dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc 95:05 → 80:20) afforded alcohol **42** (3.38 g, 96%) as a colorless oil. **42**: R_f = 0.35 (silica gel, hexanes:EtOAc 90:10); $[\alpha]_D^{25}$ = +35.2 (*c* = 1.0, $CHCl_3$); IR (film) ν_{max} 3447, 2954, 2929, 2896, 2857, 2174, 1472, 1463, 1387, 1361, 1249, 1096, 1033, 1005, 939, 832, 773, 760 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 3.91–3.83 (m, 1 H), 3.75 (ddd, *J* = 11.8, 8.7, 3.4 Hz, 1 H), 3.67–3.57 (m, 3 H), 2.92 (dd, *J* = 6.9, 3.4 Hz, 1 H), 2.36–2.21 (m, 2 H), 2.08–1.97 (m, 1 H), 1.71–1.60 (m, 1 H), 1.58–1.51 (m, 2 H), 1.48–1.35 (m, 3 H), 0.89 (s, 18 H), 0.14 (s, 9 H), 0.13 (s, 3 H), 0.09 (s, 3 H), 0.04 ppm (s, 6 H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 106.8, 85.1, 75.7, 63.9, 63.0, 43.4, 29.7, 28.4, 26.4, 25.9(4)(3C), 25.8(5)(3C), 18.3, 18.1, 17.9, 0.1(3C), –4.2, –4.5, –5.3(2C) ppm; HRMS (ESI): calcd for $C_{25}H_{54}NaO_3Si_3^+$ [M + Na^+] 509.3278, found 509.3297.



43

Aldehyde 43: To a stirred solution of alcohol **42** (3.34 g, 6.86 mmol) in CH_2Cl_2 (70 mL) at room temperature was added $NaHCO_3$ (11.51 g, 137.0 mmol) followed by DMP (5.8 g, 13.7 mmol). The resulting mixture was stirred for 90 min before it was quenched with $Na_2S_2O_3$ (100 mL, sat. aq.). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with $NaHCO_3$ (100 mL), dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (silica gel, hexanes:EtOAc from 95:05 → 90:10) afforded aldehyde **43** (2.97 g, 89%) as a colorless oil. **43**: R_f = 0.70 (silica gel, hexanes:EtOAc 90:10); $[\alpha]_D^{25}$ = +46.0 (*c* = 1.0, $CHCl_3$); IR (film) ν_{max} 2954, 2929, 2896, 2857, 2174, 1725, 1472, 1463, 1434, 1407, 1388, 1361, 1250, 1096, 1048, 1005, 968, 938, 833, 773, 760 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 9.84 (s, 1 H), 4.09 (s, 1 H), 3.60 (s, 2 H), 2.74–2.62 (m, 1 H), 2.40–2.22 (m, 2 H), 1.98 (td, *J* = 15.0, 6.3 Hz, 1 H), 1.66–1.39 (m, 5 H), 0.89 (s, 9 H), 0.88 (s, 9 H), 0.13 (s, 9 H), 0.08 (s, 6 H), 0.04 ppm (s, 6 H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 204.9, 106.4, 85.5, 72.3, 62.7, 55.5, 30.8, 29.1, 25.9(3C), 25.8(3C), 22.9, 18.3, 18.1, 18.0, 0.1(3C), –4.4, –4.5, –5.1(2C) ppm; HRMS (ESI): calcd for $C_{25}H_{52}NaO_3Si_3^+$ [M + Na^+] 507.3122, found 507.3132.

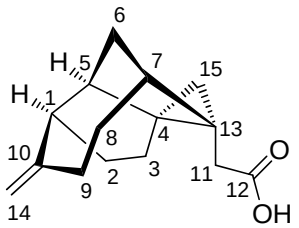


(–)-22

Alkene (–)-**22**: To a stirred solution of $Ph_3P^+CH_3I^-$ (4.92 g, 12.2 mmol) in THF (100 mL) at 0 °C was added *n*-BuLi (1.6 M in hexane, 7.5 mL, 12.0 mmol). The resulting homogeneous solution was cooled to –40 °C before a solution of aldehyde **43** (2.95 g, 6.08 mmol) in THF (10 mL) was added. The resulting mixture was warmed to 5 °C over a period of 1.5 h before it was quenched with NH_4Cl (100 mL, sat. aq.) and diluted with EtOAc (100 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 × 100 mL). The combined organic layers were washed with brine (100 mL), dried (Na_2SO_4) and concentrated in *vacuo*. Flash column

chromatography (silica gel, hexanes:EtOAc from 98:02 → 95:05) afforded alkene (–)-**22** (1.34 g, 46%) as a colorless oil. (–)-**22**: R_f = 0.55 (silica gel, hexanes:EtOAc 98:02); $[\alpha]_D^{25}$ = –13.7 (*c* = 1.0, $CHCl_3$); IR (film) ν_{max} 2955, 2929, 2896, 2857, 2176, 1472, 1463, 1406, 1387, 1361, 1249, 1096, 1004, 938, 916, 832, 772, 760 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 5.64 (ddd, *J* = 17.2, 10.3, 9.0 Hz, 1 H), 5.14–5.02 (m, 2 H), 3.74–3.52 (m, 3 H), 2.39–2.24 (m, 2 H), 2.17–2.05 (m, 1 H), 1.75 (tdd, *J* = 11.4, 8.5, 3.5 Hz, 1 H), 1.66–1.36 (m, 5 H), 0.92 (m, 9 H), 0.91 (s, 9 H), 0.17 (s, 9 H), 0.08 (s, 3 H), 0.07 ppm (s, 9 H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 138.7, 116.5, 107.6, 84.5, 74.9, 63.3, 48.2, 30.2, 28.4(3), 28.3(5), 26.0(6C), 18.3, 18.1, 17.8, 0.2(3C), –4.3, –4.4, –5.3(2C) ppm; HRMS (ESI): calcd for $C_{26}H_{54}NaO_2Si_3^+$ [M + Na^+] 505.3329, found 505.3336.

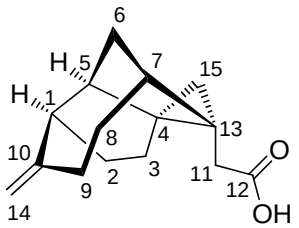
Table 1. ^{1}H NMR Spectroscopic (600 MHz, $CDCl_3$, 25 °C) Comparison of Synthetic and Natural[9] Echinopine A (**1**)



Echinopine A (**1**)

No.	**Synthetic** δ ^{1}H [ppm, mult, *J* (Hz)]	**Natural**[9] δ ^{1}H [ppm, mult, *J* (Hz)]
1	2.81 (td, *J* = 9.0, 1.8 Hz)	2.81 (td, *J* = 9.1, 2.1 Hz)
2a	2.16 (m)	2.16 (m)
2b	1.69 (dddd, *J* = 13.8, 9.6, 6.6, 2.4 Hz)	1.65 (dddd, *J* = 14.0, 9.7, 6.7, 2.6 Hz)
3a	1.95 (m)	1.95 (m)
3b	1.52 (ddd, *J* = 13.2, 9.6, 3.8 Hz)	1.52 (ddd, *J* = 13.5, 9.7, 4.0 Hz)
4	--	--
5	2.27 (t, *J* = 8.0 Hz)	2.26 (~t, *J* = ~8.0 Hz)
6a	1.44 (dtd, *J* = 13.8, 7.2, 1.2 Hz)	1.44 (dtd, *J* = 13.7, 7.4, 0.9 Hz)
6b	1.36 (d, *J* = 13.8 Hz)	1.36 (d, *J* = 13.7 Hz)
7	2.44 (m)	2.43 (m)
8a	1.94 (m)	1.93 (m)
8b	1.27 (tdd, *J* = 13.8, 4.2, 3.0 Hz)	1.27 (tdd, *J* = 13.6, 4.0, 3.0 Hz)
9a	2.14 (dt, *J* = 13.8, 4.5 Hz)	2.12 (dt, *J* = 13.3, ~4.7 Hz)
9b	1.82 (td, *J* = 13.2, 4.2 Hz)	1.82 (td, *J* = 13.3, 4.2 Hz)
10	--	--
11a	2.66 (dd, *J* = 15.0, 1.2 Hz)	2.66 (dd, *J* = 15.3, 1.3 Hz)
11b	1.76 (d, *J* = 15.0 Hz)	1.75 (d, *J* = 15.3 Hz)
12	--	--
13	--	--
14a	4.64 (d, *J* = 2.4 Hz)	4.63 (d, *J* = 2.6 Hz)
14b	4.61 (d, *J* = 2.4 Hz)	4.60 (d, *J* = 2.6 Hz)
15a	0.73 (dd, *J* = 5.4, 1.2 Hz)	0.73 (dd, *J* = 5.3, 1.3 Hz)
15b	0.50 (d, *J* = 4.8 Hz)	0.50 (d, *J* = 5.3 Hz)
OH	10.69 (br s)	10.53 (br s)

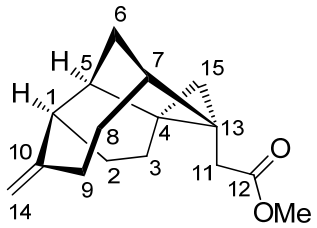
Table 2. ^{13}C NMR Spectroscopic (150 MHz, $CDCl_3$, 25 °C) Comparison of Synthetic and Natural[9] Echinopine A (**1**)



Echinopine A (**1**)

No.	**Synthetic** $\delta\ ^{13}C$ (ppm)	**Natural**[9] $\delta\ ^{13}C$ (ppm)
1	48.7	48.7
2	31.0	31.1
3	25.7	25.7
4	41.4	41.5
5	48.5	48.6
6	30.5	30.5
7	40.5	40.6
8	32.7	32.8
9	29.4	29.4
10	154.3	154.3
11	35.2	35.2
12	178.7	178.2
13	29.9	29.9
14	112.1	112.1
15	16.1	16.1

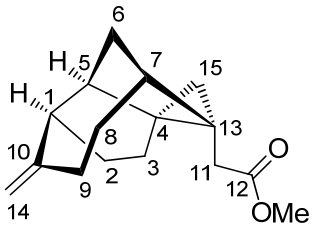
Table 3. ^{1}H NMR Spectroscopic (600 MHz, $CDCl_3$, 25 °C) Comparison of Synthetic and Natural[9] Echinopine B (**2**)



Echinopine B (**2**)

No.	**Synthetic** δ ^{1}H [ppm, mult, *J* (Hz)]	**Natural**[9] δ ^{1}H [ppm, mult, *J* (Hz)]
1	2.80 (td, *J* = 9.0, 1.8 Hz)	2.80 (br t, *J* = ~10.0 Hz)
2a	2.14 (m)	2.14 (m)
2b	1.65 (m)	1.65 (m)
3a	1.93 (m)	1.93 (m)
3b	1.51 (m)	1.51 (m)
4	--	--
5	2.25 (t, *J* = 8.1 Hz)	2.25 (~t, *J* = ~9.0 Hz)
6a	1.44 (m)	1.44 (m)
6b	1.35 (d, *J* = 13.8 Hz)	1.35 (d, *J* = 13.8 Hz)
7	2.39 (m)	2.39 (m)
8a	1.93 (m)	1.93 (m)
8b	1.26 (m)	1.26 (m)
9a	2.12 (m)	2.11 (m)
9a	1.82 (td, *J* = 13.2, 4.2 Hz)	1.82 (td, *J* = 13.2, 4.0 Hz)
10	--	--
11a	2.64 (dd, *J* = 15.1, 1.2 Hz)	2.65 (dd, *J* = 15.1, 1.3 Hz)
11b	1.72 (d, *J* = 15.0 Hz)	1.72 (d, *J* = 15.1 Hz)
12	--	--
13	--	--
14a	4.63 (d, *J* = 3.0 Hz)	4.63 (d, *J* = 2.6 Hz)
14b	4.60 (d, *J* = 3.0 Hz)	4.60 (d, *J* = 2.6 Hz)
15a	0.69 (dd, *J* = 5.1, 1.5 Hz)	0.69 (dd, *J* = 5.1, 1.3 Hz)
15b	0.47 (d, *J* = 4.0 Hz)	0.47 (d, *J* = 5.1 Hz)
OMe	3.68 (s)	3.68 (s)

Table 4. ^{13}C NMR Spectroscopic (150 MHz, $CDCl_3$, 25 °C) Comparison of Synthetic and Natural[9] Echinopine B (**2**)



Echinopine B (**2**)

No.	**Synthetic** $\delta\ ^{13}C$ (ppm)	**Natural**[9] $\delta\ ^{13}C$ (ppm)
1	48.5	48.5
2	30.9	30.9
3	25.6	25.4
4	30.0	29.8
5	48.4	48.4
6	30.3	30.3
7	40.5	40.4
8	32.6	32.5
9	29.3	29.3
10	154.3	154.3
11	35.2	35.1
12	173.6	173.7
13	41.2	41.0
14	111.8	111.9
15	15.9	15.7
OMe	51.4	51.3

II) Abbreviations

TBS = *tert*-butyldimethylsilyl

TMS = trimethylsilyl

DMSO = dimethyl sulfoxide

OTf = trifluoromethanesulfonate

p-TsOH = *p*-toluenesulfonic acid

DMP = Dess-Martin periodinane

Dibal-H = diisobutylaluminium hydride

DMF = *N*,*N*'-dimethylformamide

LDA = lithium diisopropylamide

PDC = pyridinium dichromate

DCC = dicyclohexylcarbodiimide

DMAP = 4-dimethylaminopyridine

NMP = *N*-methylpyrrolidone

TMG = 1,1,3,3-tetramethylguanidine

CSA = camphorsulfonic acid

III) References

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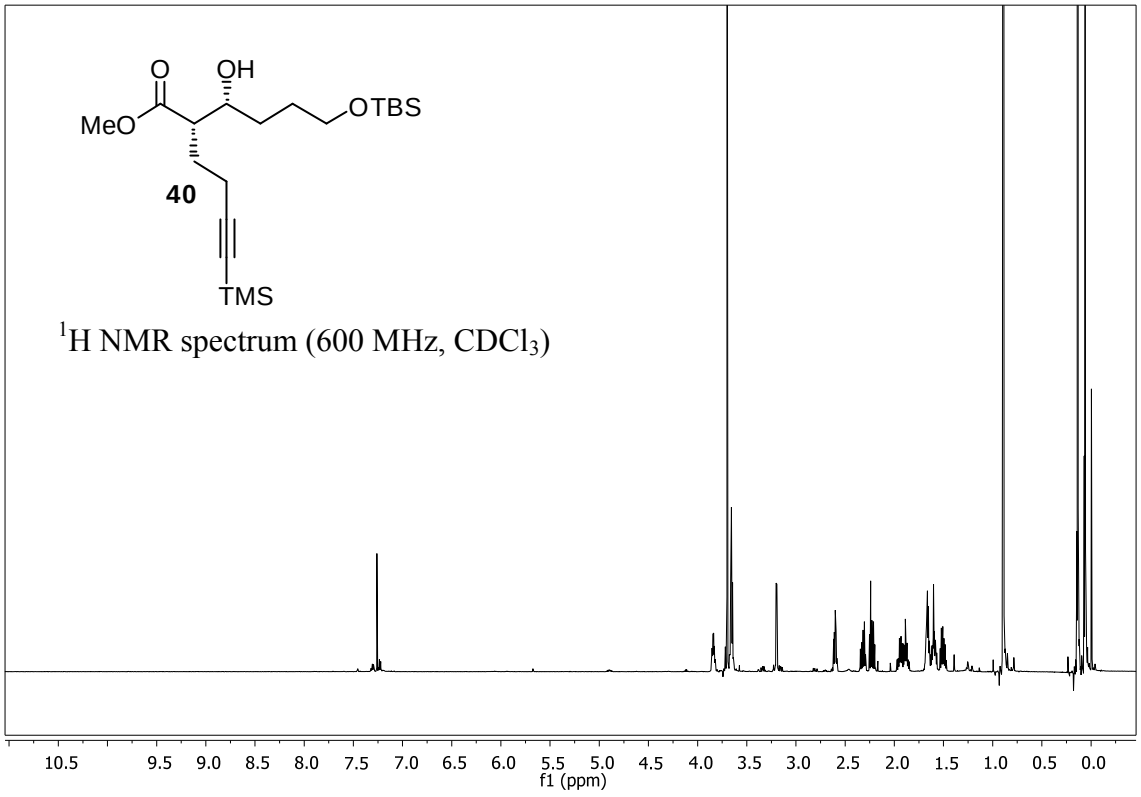
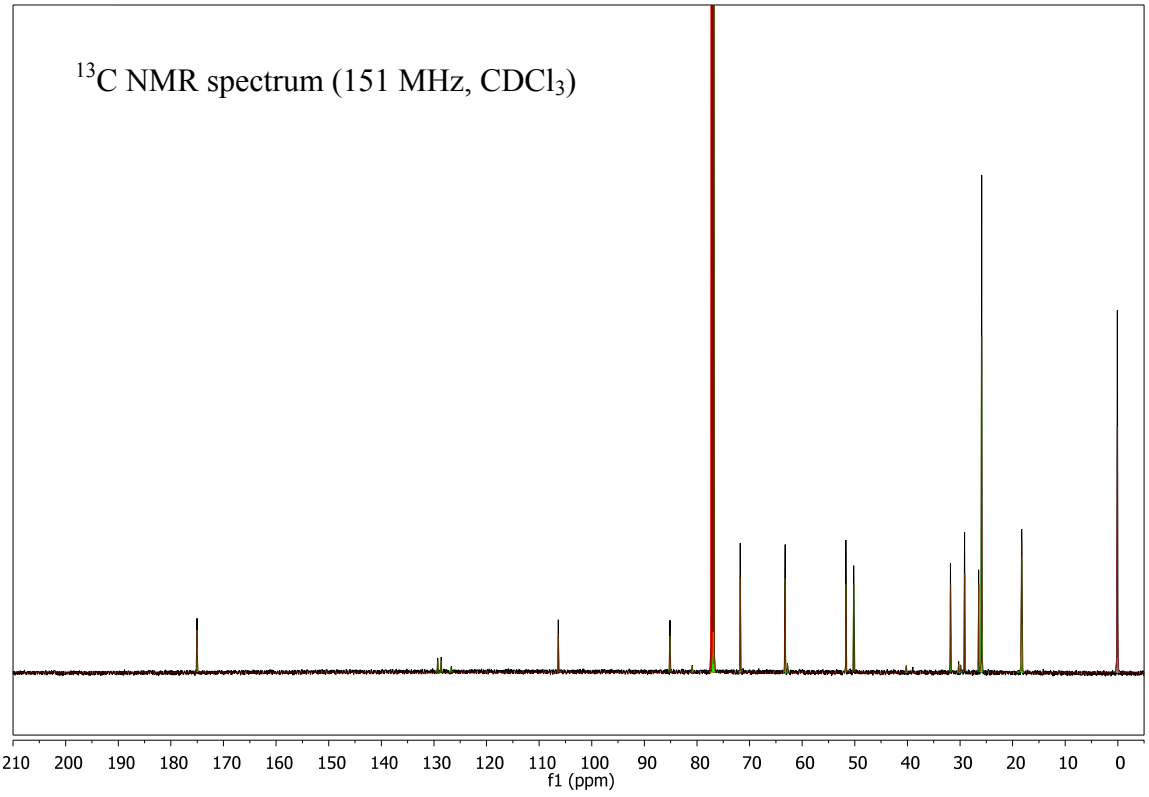
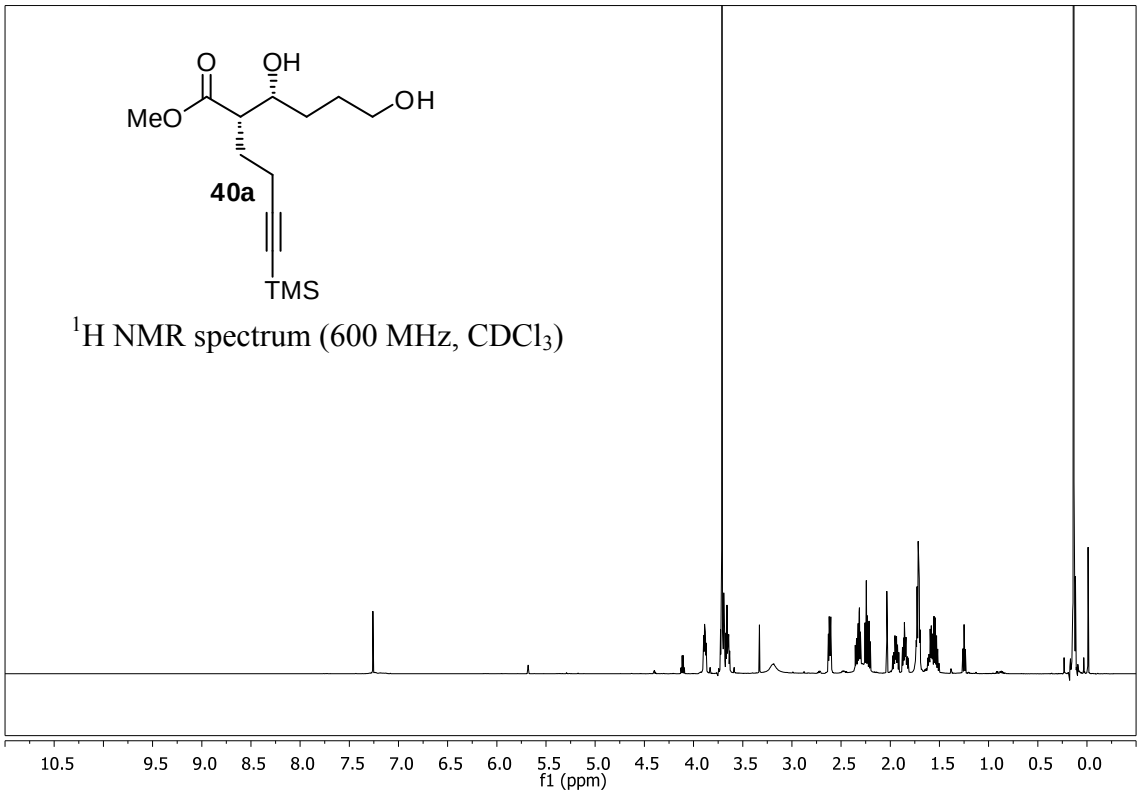
IV) ^{1}H and ^{13}C NMR Spectra of Compounds



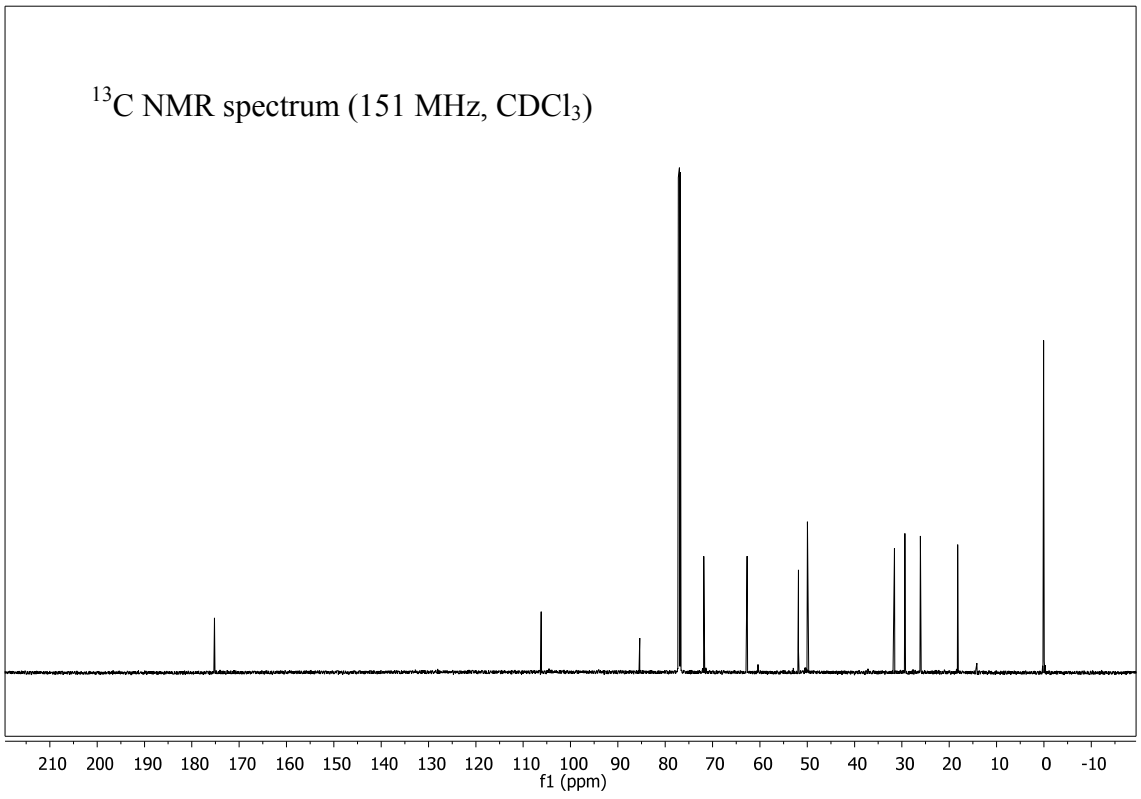
^{1}H NMR spectrum (600 MHz, $CDCl_3$)



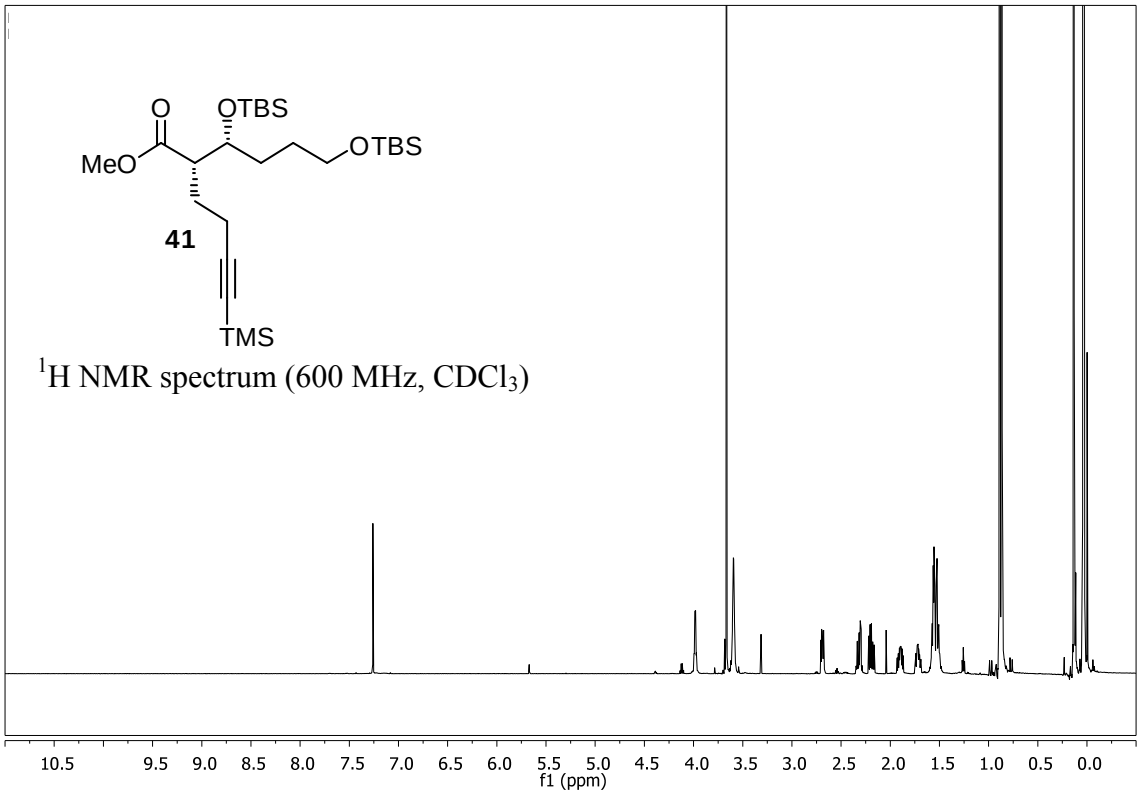
^{13}C NMR spectrum (151 MHz, $CDCl_3$)



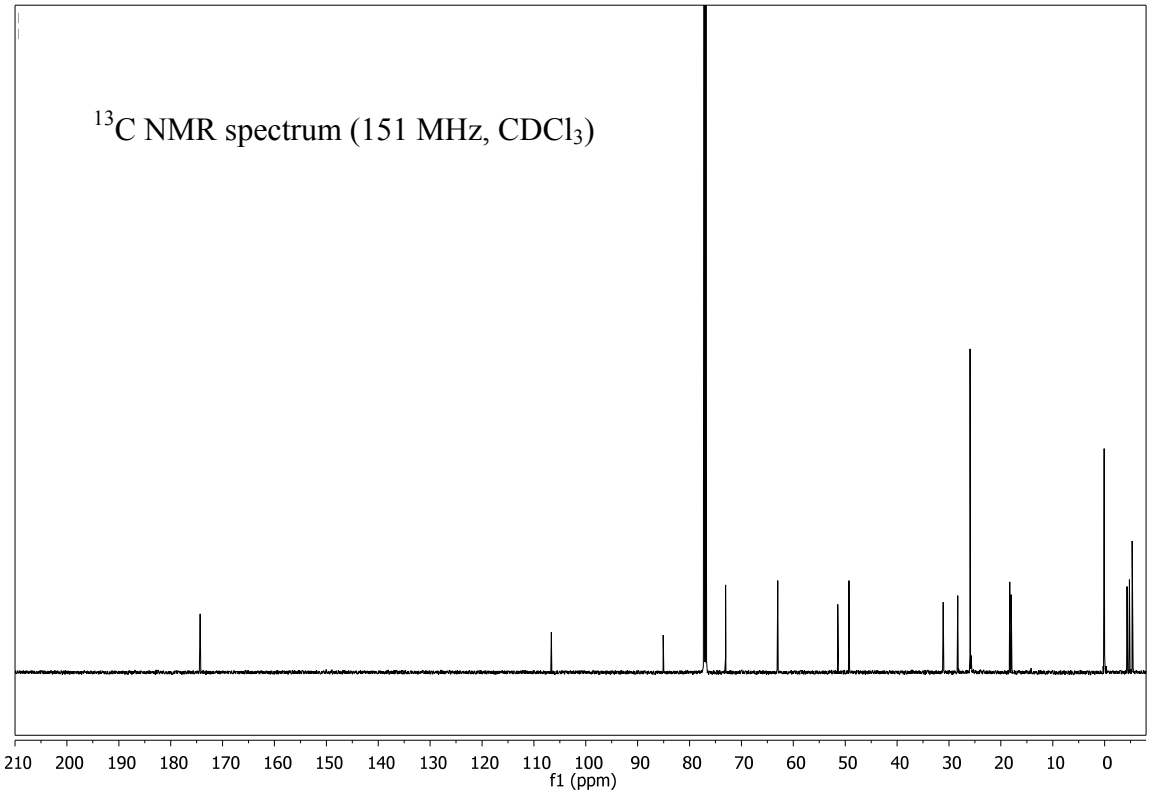
^{1}H NMR spectrum (600 MHz, $CDCl_3$)



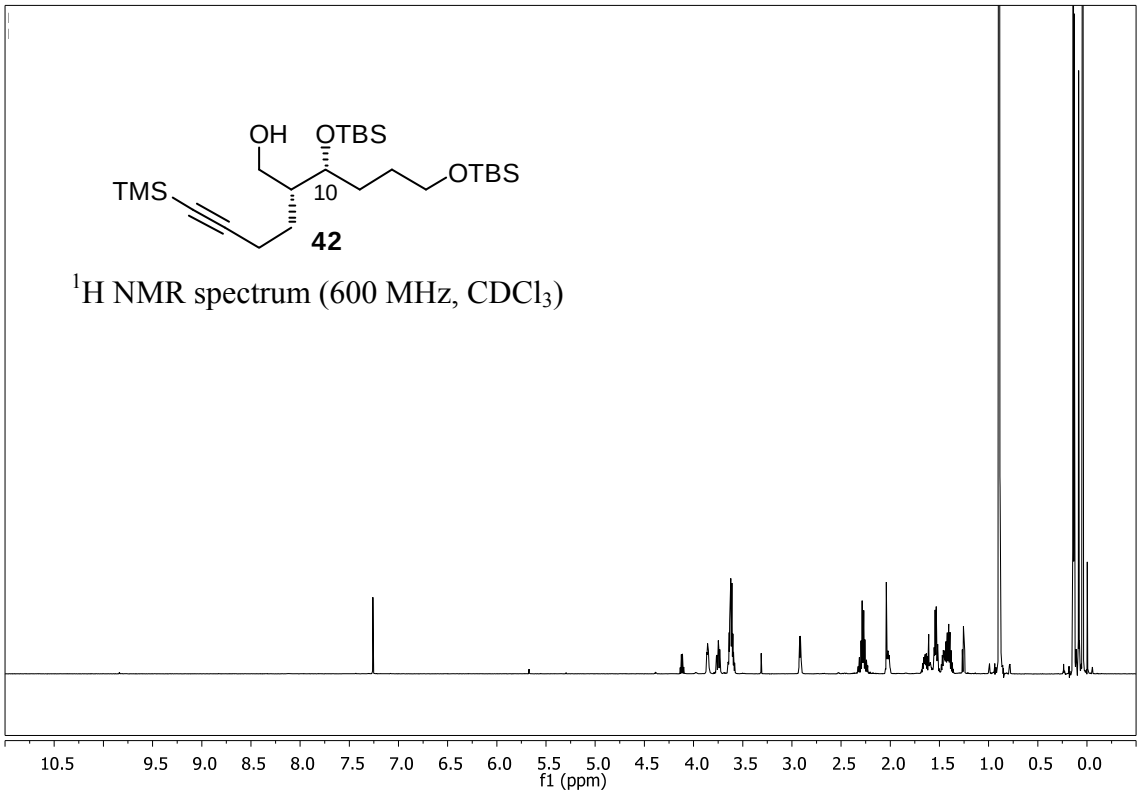
^{13}C NMR spectrum (151 MHz, $CDCl_3$)



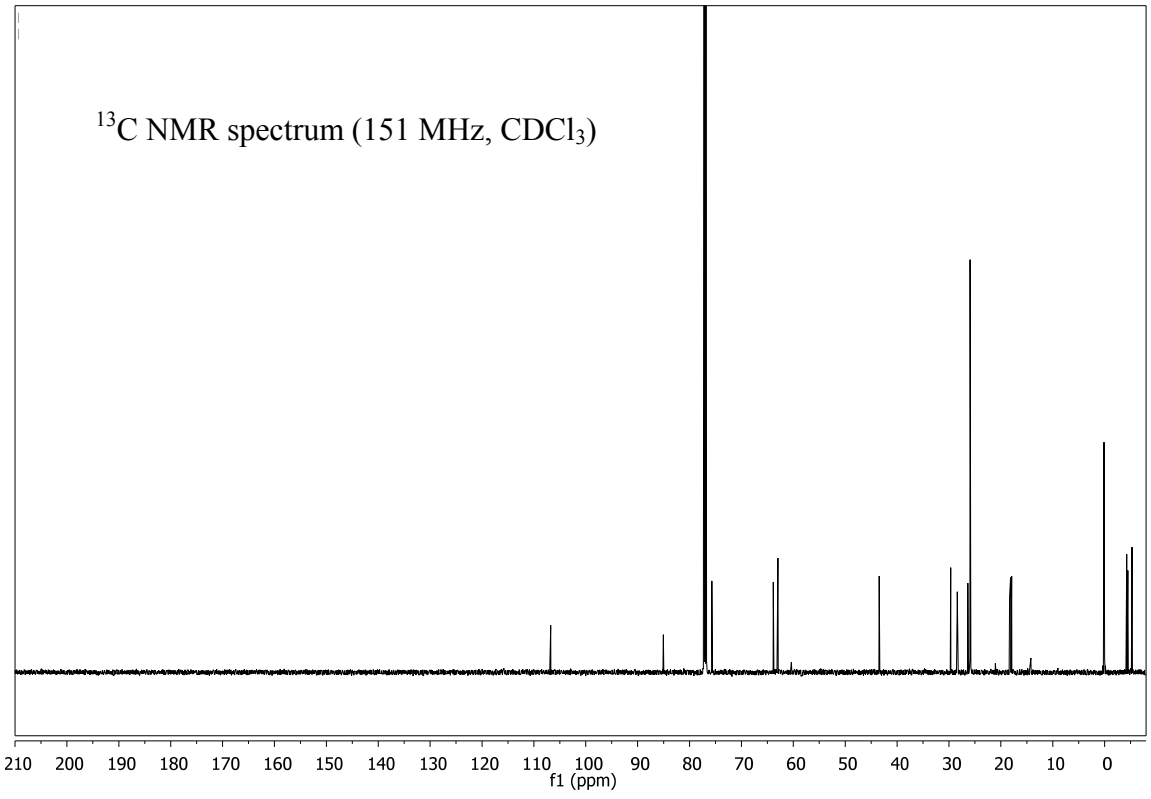
^{1}H NMR spectrum (600 MHz, $CDCl_3$)



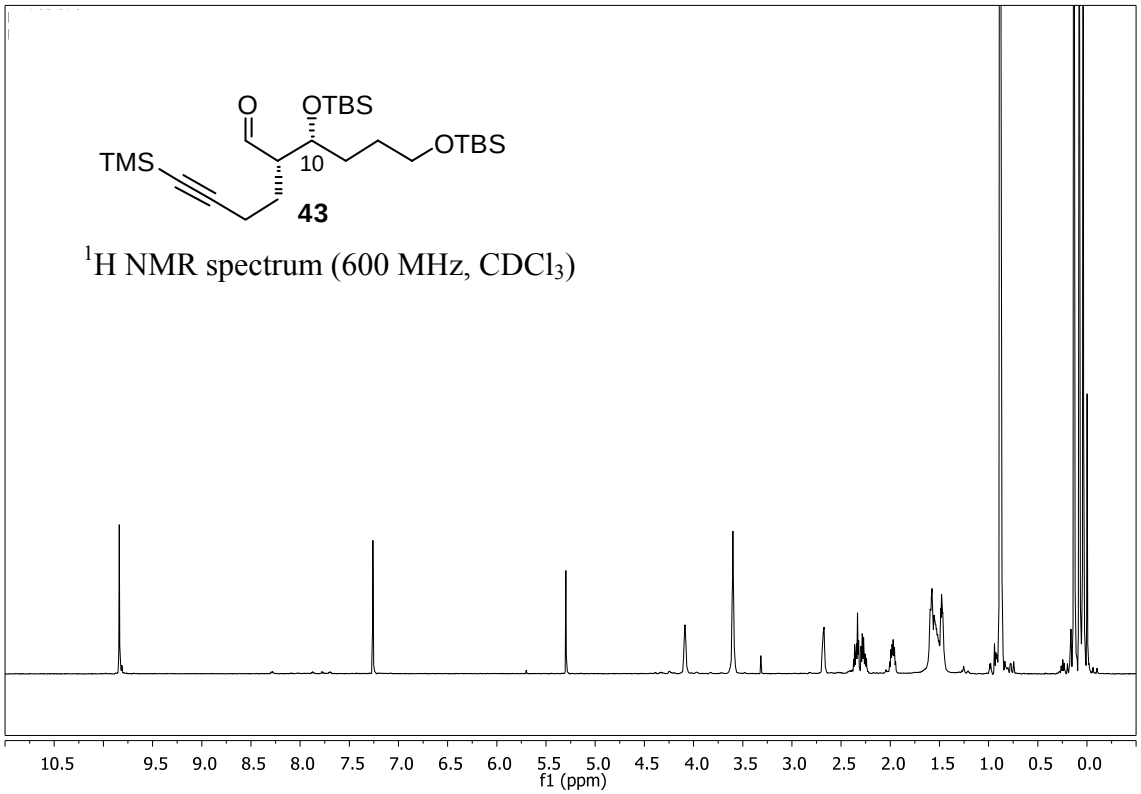
^{13}C NMR spectrum (151 MHz, $CDCl_3$)



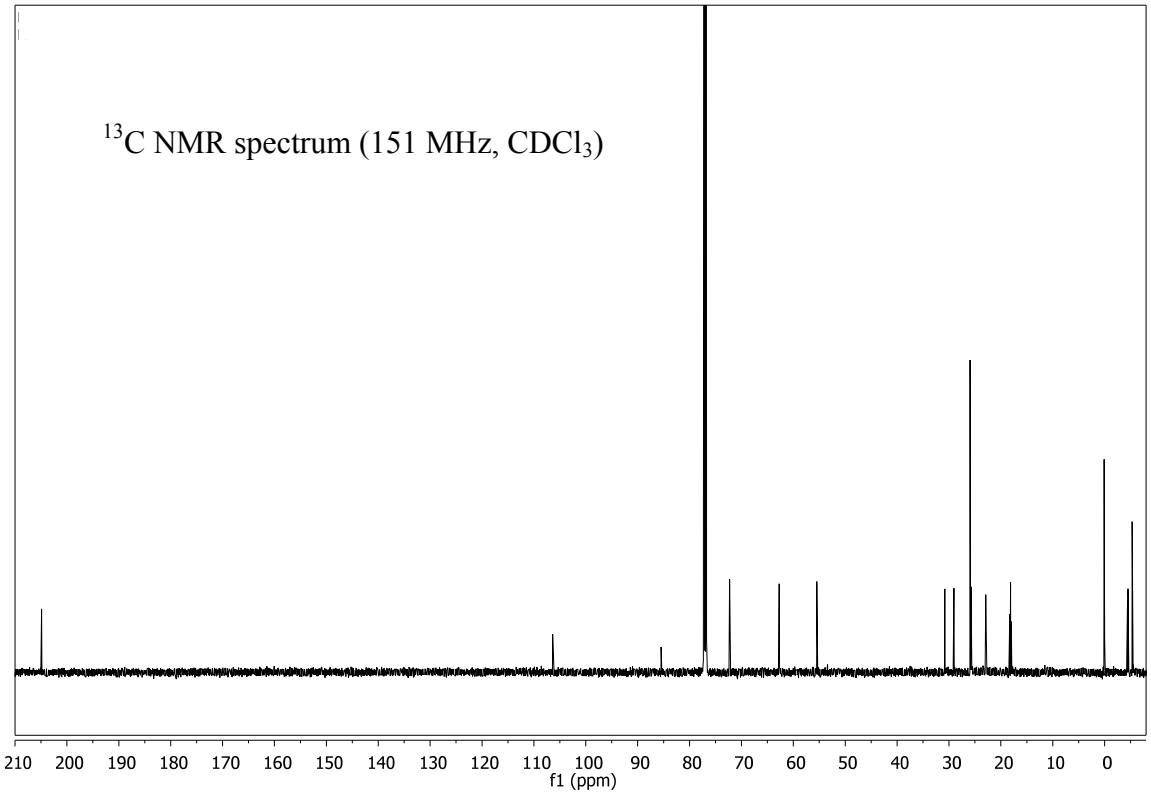
^{1}H NMR spectrum (600 MHz, $CDCl_3$)



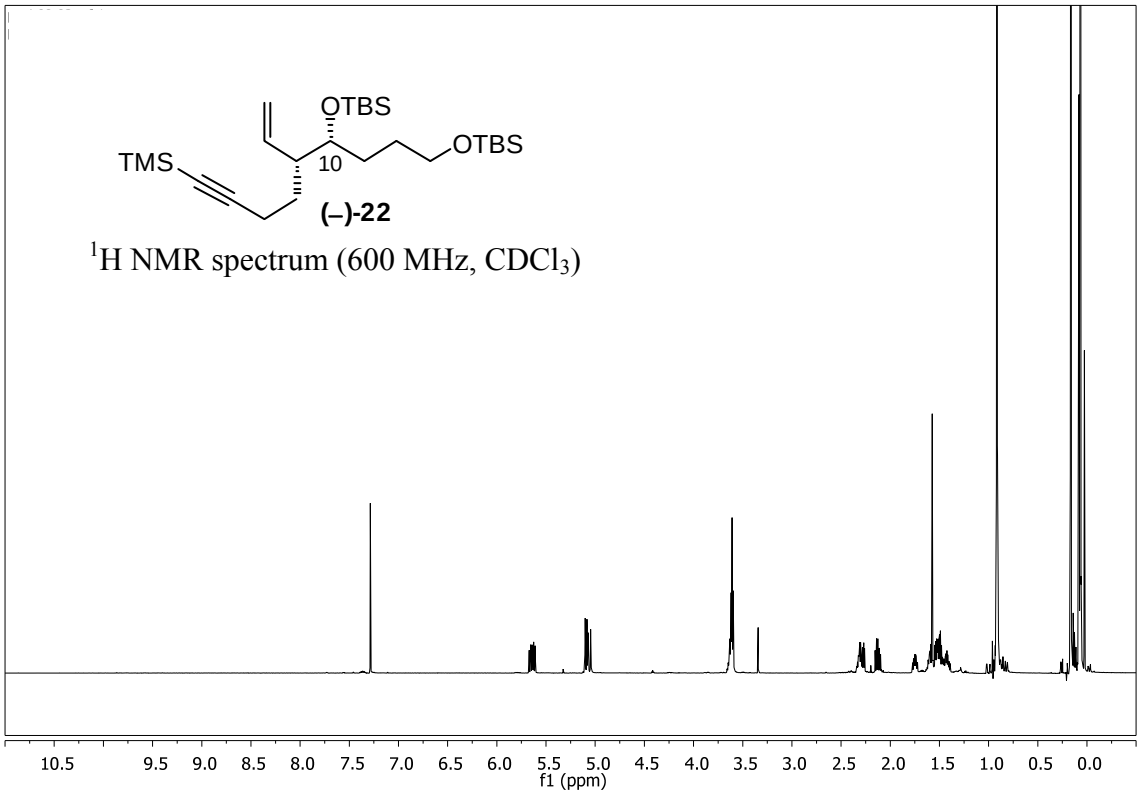
^{13}C NMR spectrum (151 MHz, $CDCl_3$)

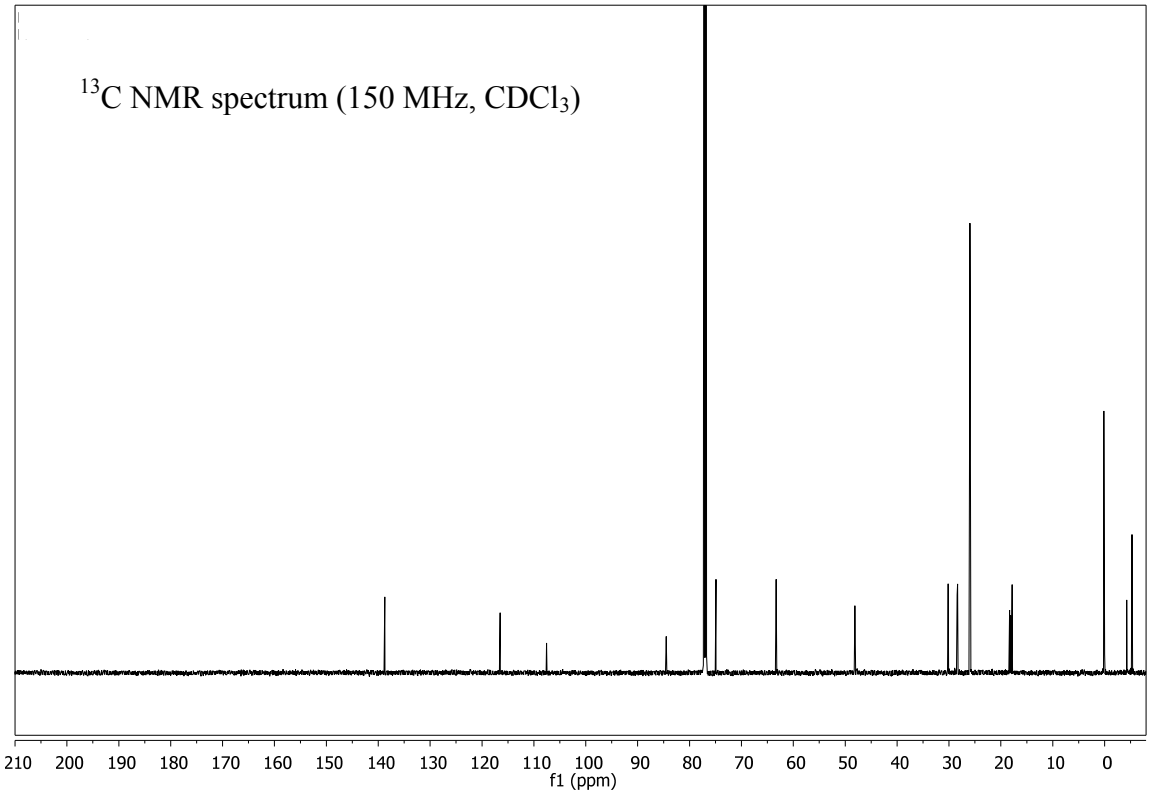


^{1}H NMR spectrum (600 MHz, $CDCl_3$)



^{13}C NMR spectrum (151 MHz, $CDCl_3$)


OTBS
OTBS
TMS
10
(–)-22
^{1}H NMR spectrum (600 MHz, $CDCl_3$)
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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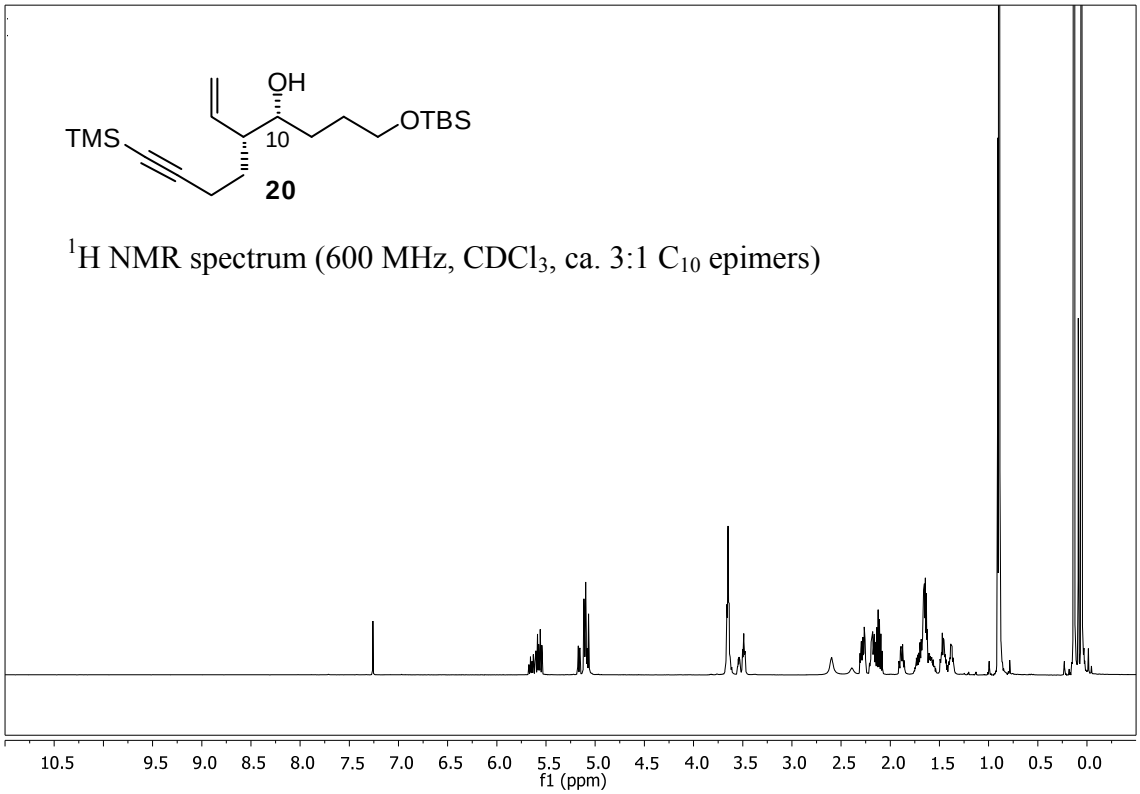
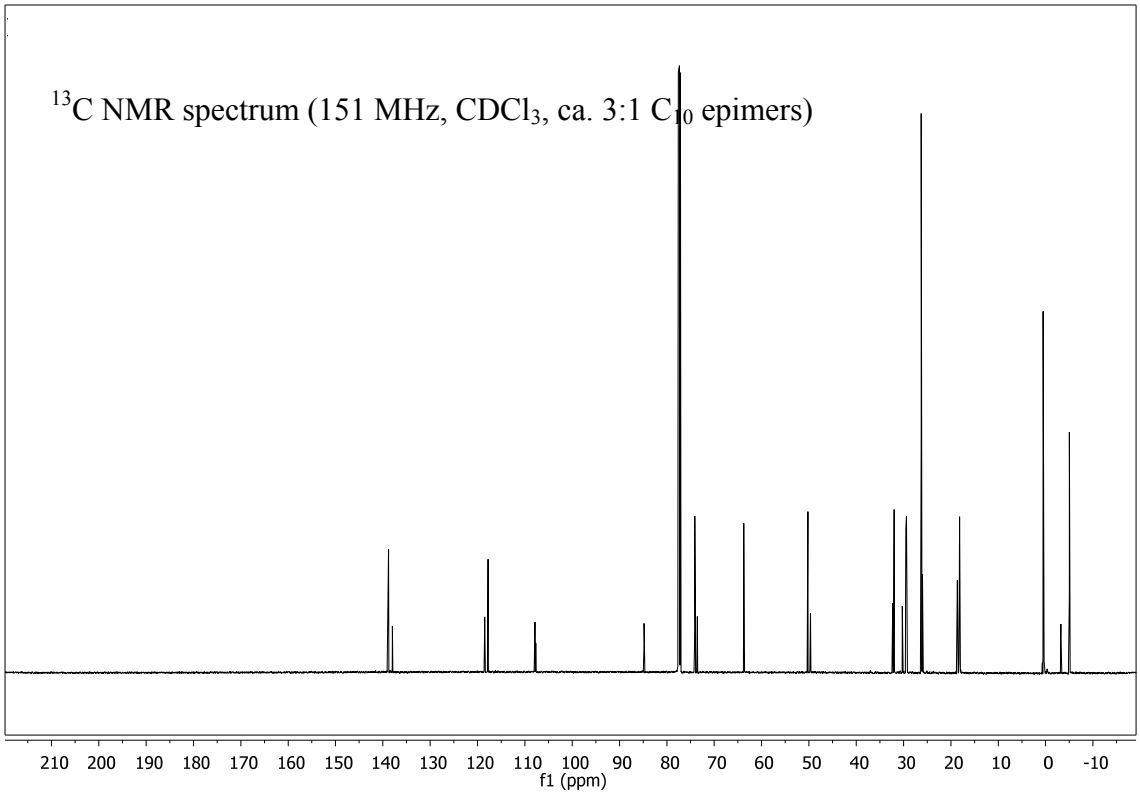
f1 (ppm)


OH
TMS
10
OTBS
20
^{1}H NMR spectrum (600 MHz, $CDCl_3$, ca. 3:1 C_{10} epimers)
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


^{13}C NMR spectrum (151 MHz, $CDCl_3$, ca. 3:1 C_{10} epimers)
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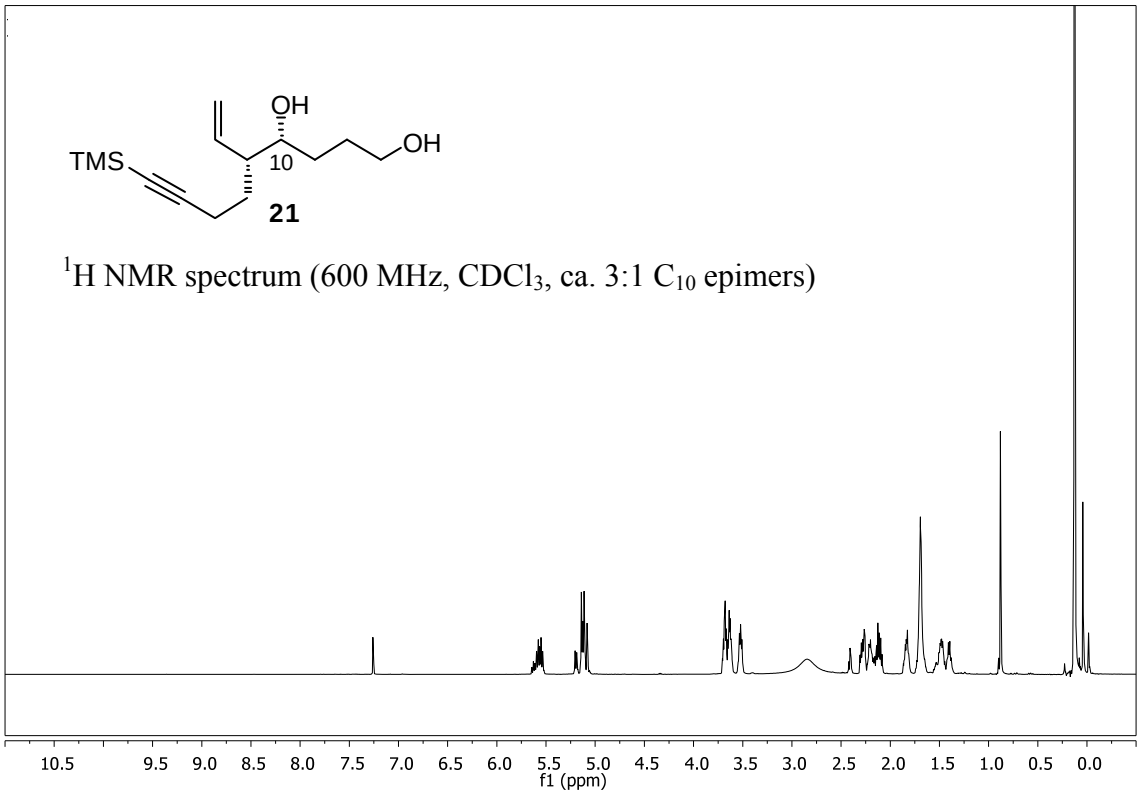
f1 (ppm)


OH
OH
TMS
10
21
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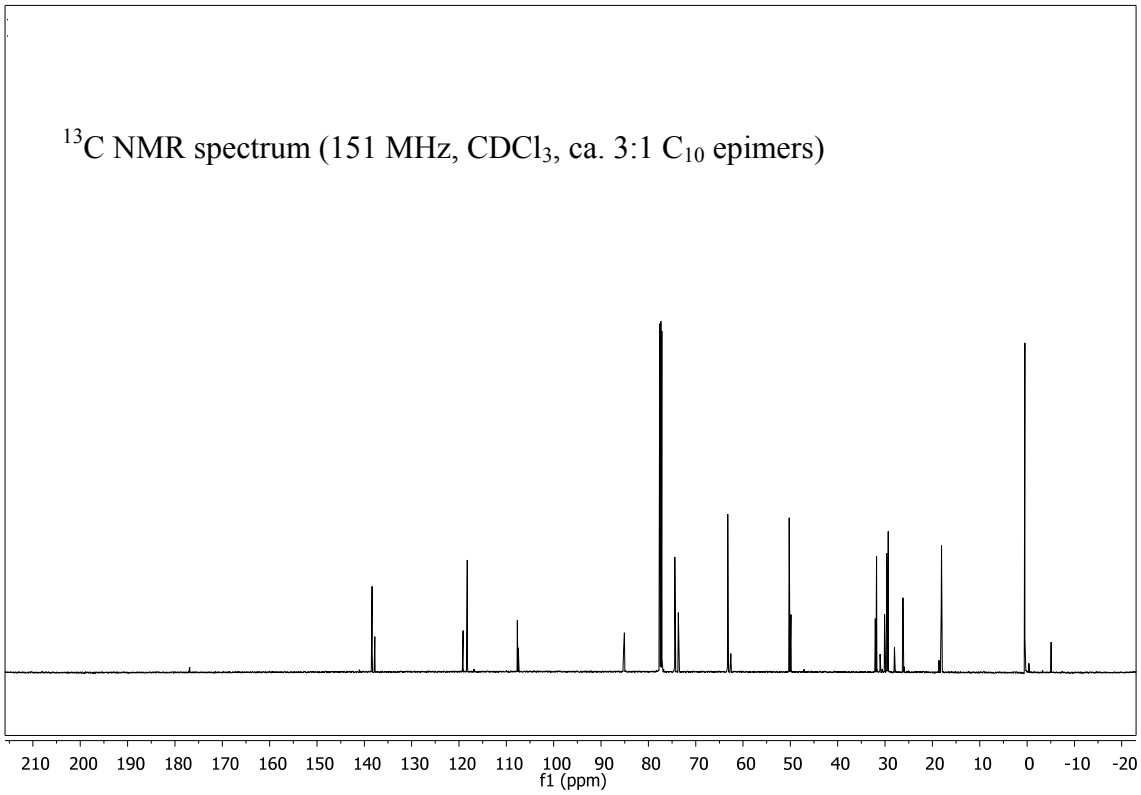
f1 (ppm)


^{13}C NMR spectrum (151 MHz, $CDCl_3$, ca. 3:1 C_{10} epimers)
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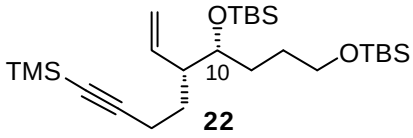
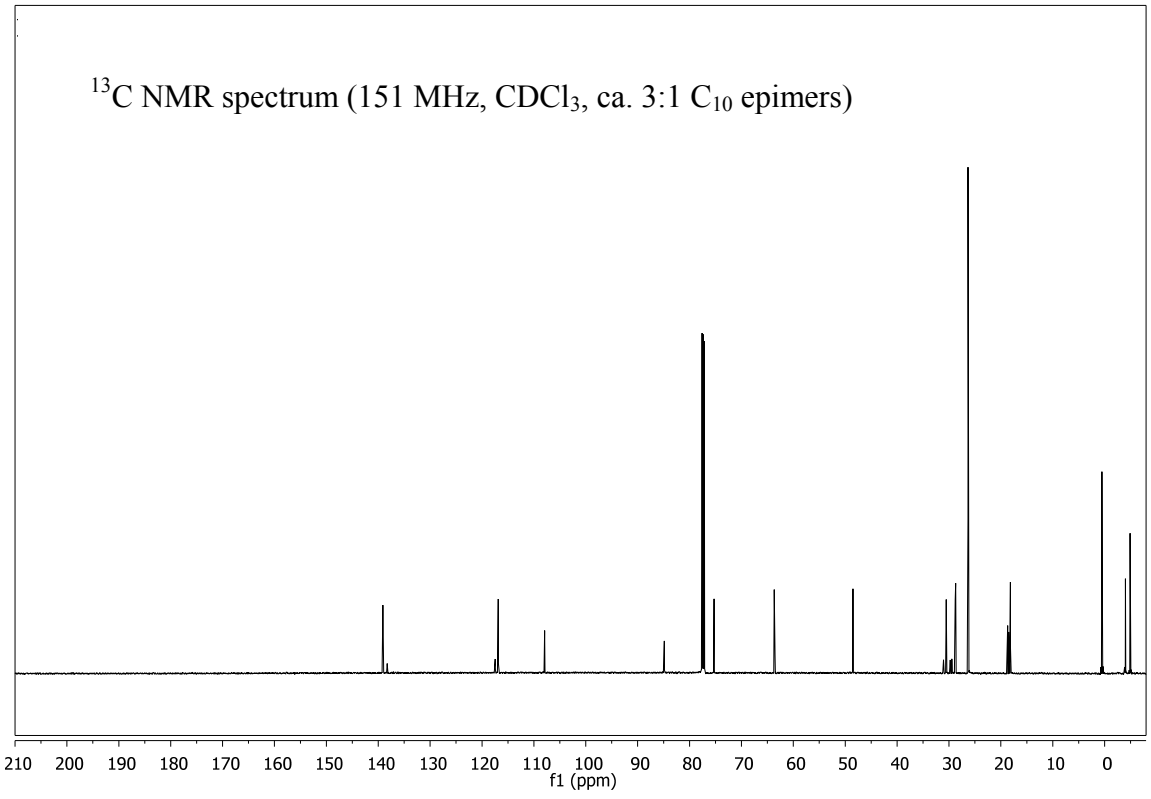
f1 (ppm)

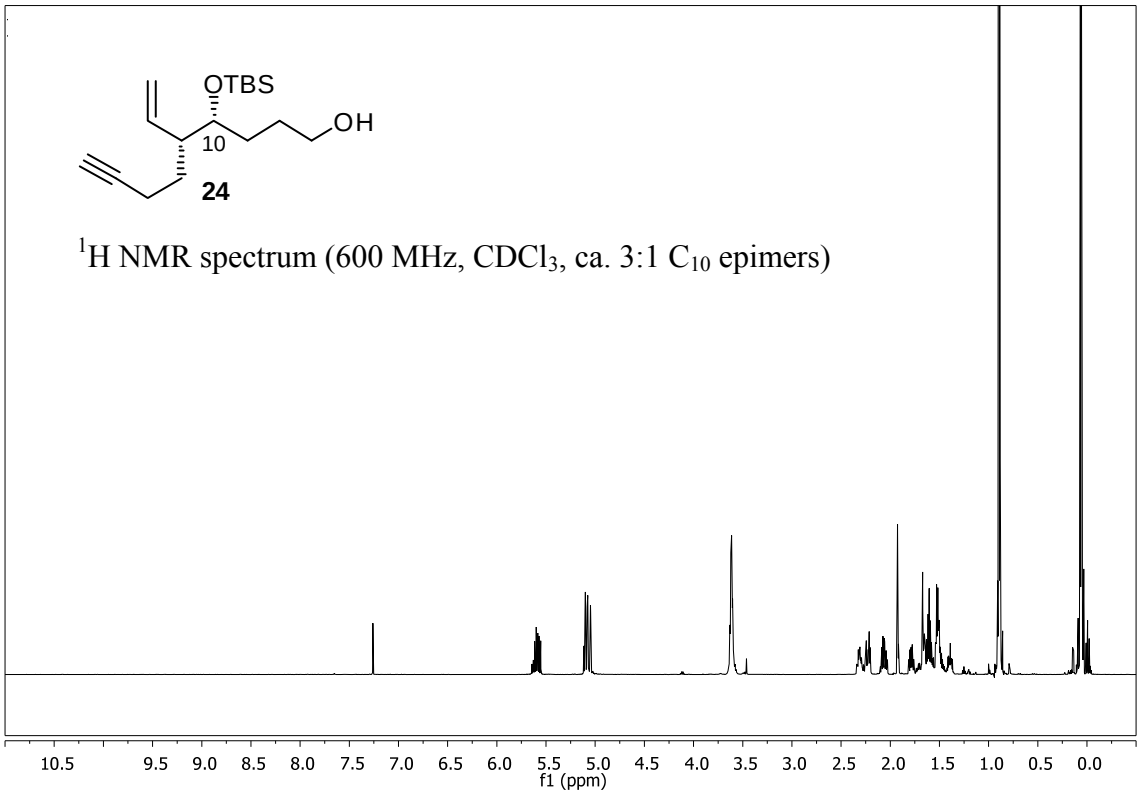


22

^{1}H NMR spectrum (600 MHz, $CDCl_3$, ca. 3:1 C_{10} epimers)

^{13}C NMR spectrum (151 MHz, $CDCl_3$, ca. 3:1 C_{10} epimers)

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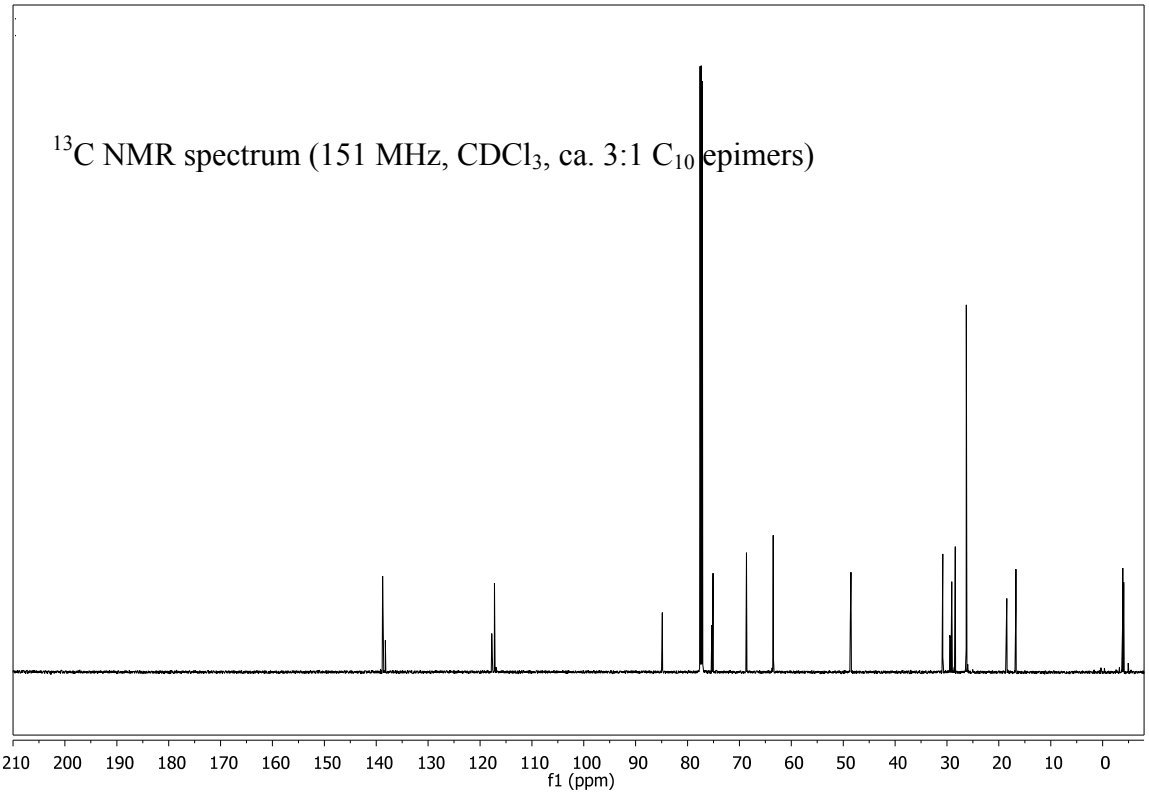
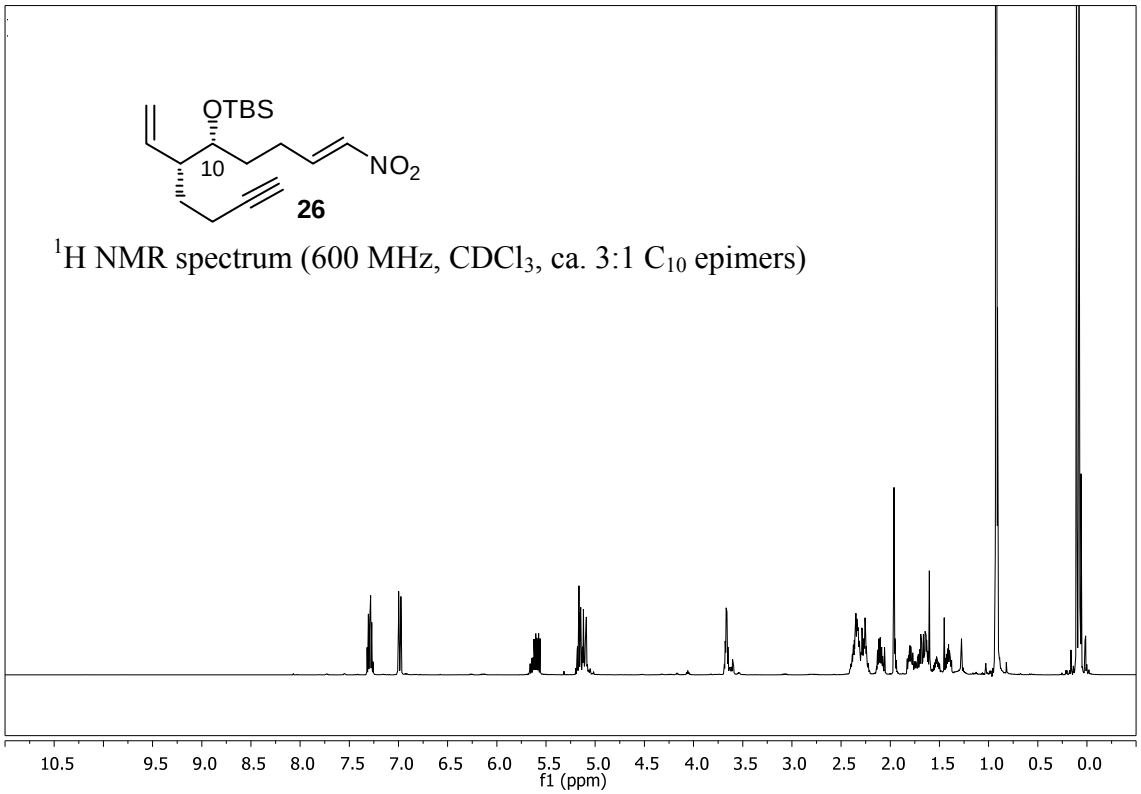
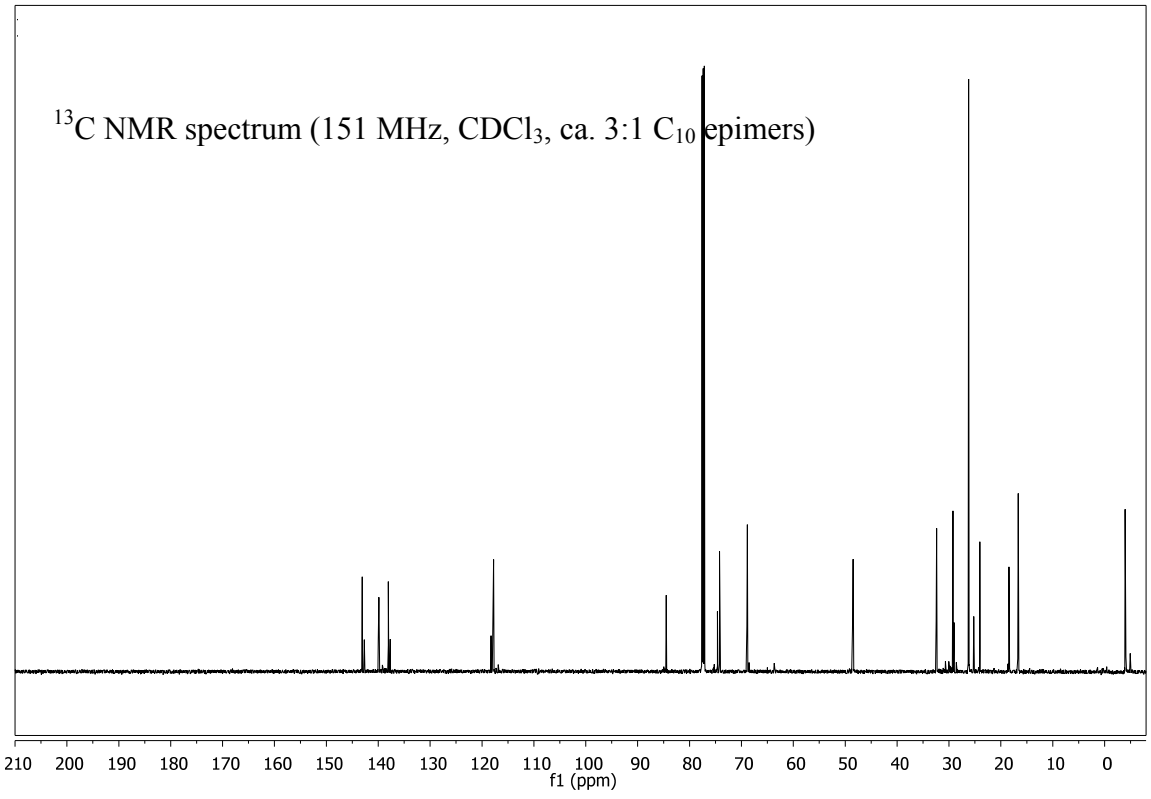
10
24
^{1}H NMR spectrum (600 MHz, $CDCl_3$, ca. 3:1 C_{10} epimers)
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


^{13}C NMR spectrum (151 MHz, $CDCl_3$, ca. 3:1 C_{10} epimers)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

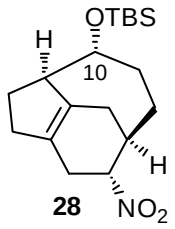


^{1}H NMR spectrum (600 MHz, $CDCl_3$, ca. 3:1 C_{10} epimers)



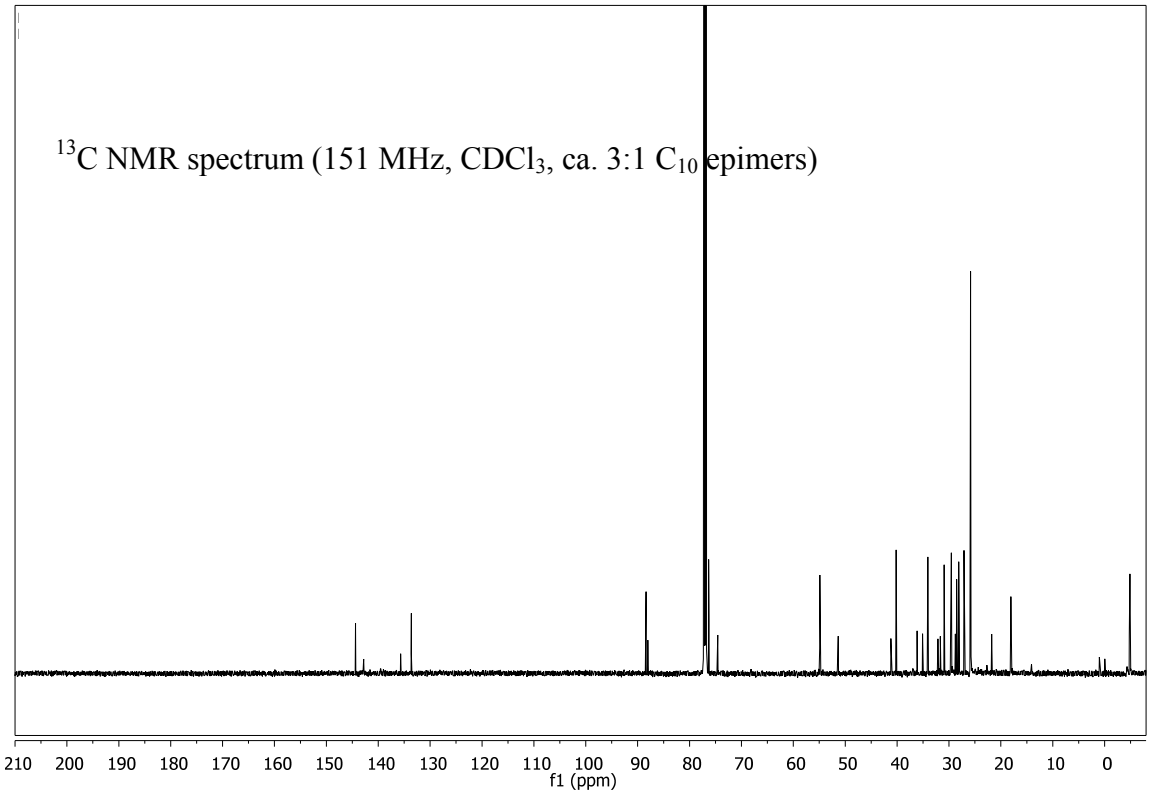
^{13}C NMR spectrum (151 MHz, $CDCl_3$, ca. 3:1 C_{10} epimers)

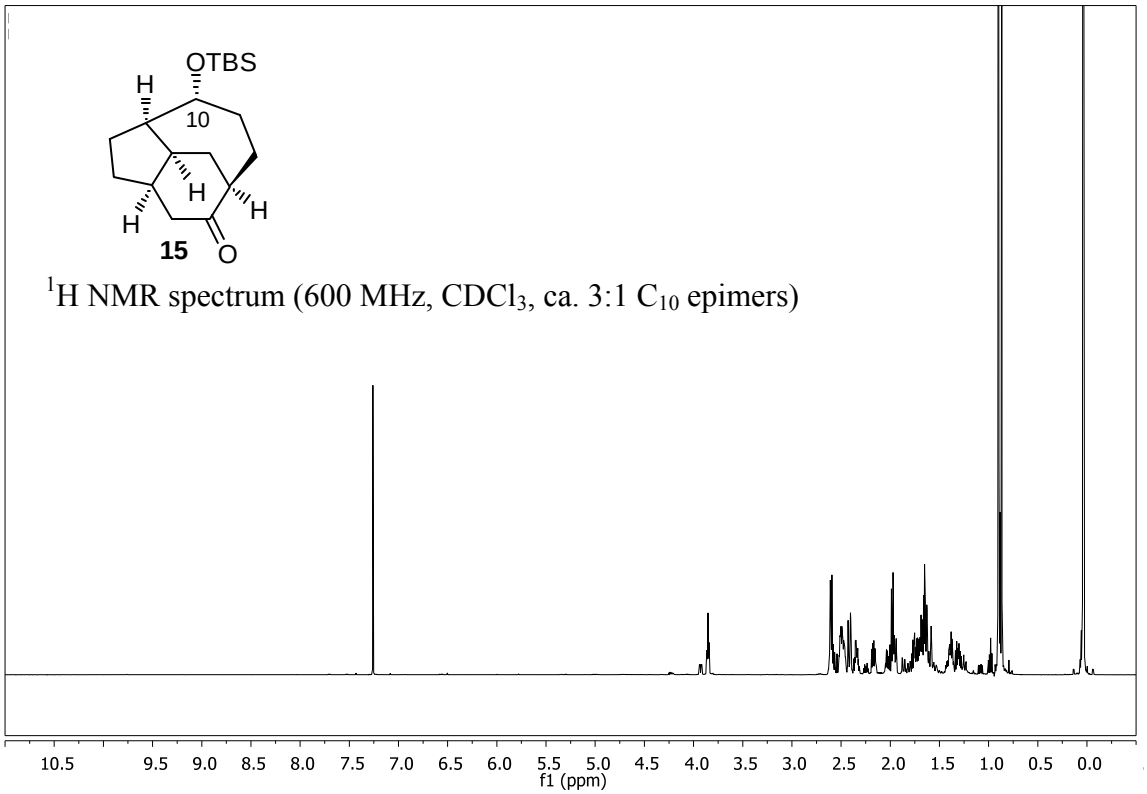
^{1}H NMR spectrum (600 MHz, $CDCl_3$, ca. 3:1 C_{10} epimers)



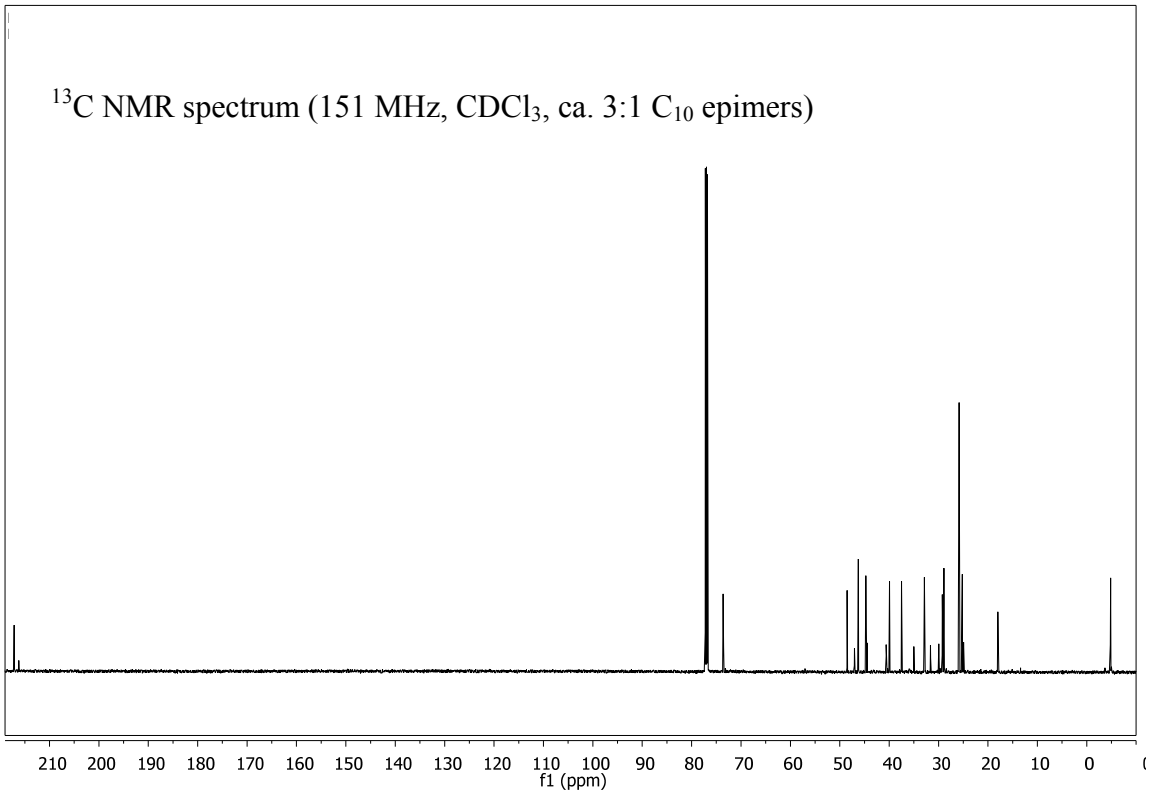
28

^{13}C NMR spectrum (151 MHz, $CDCl_3$, ca. 3:1 C_{10} epimers)

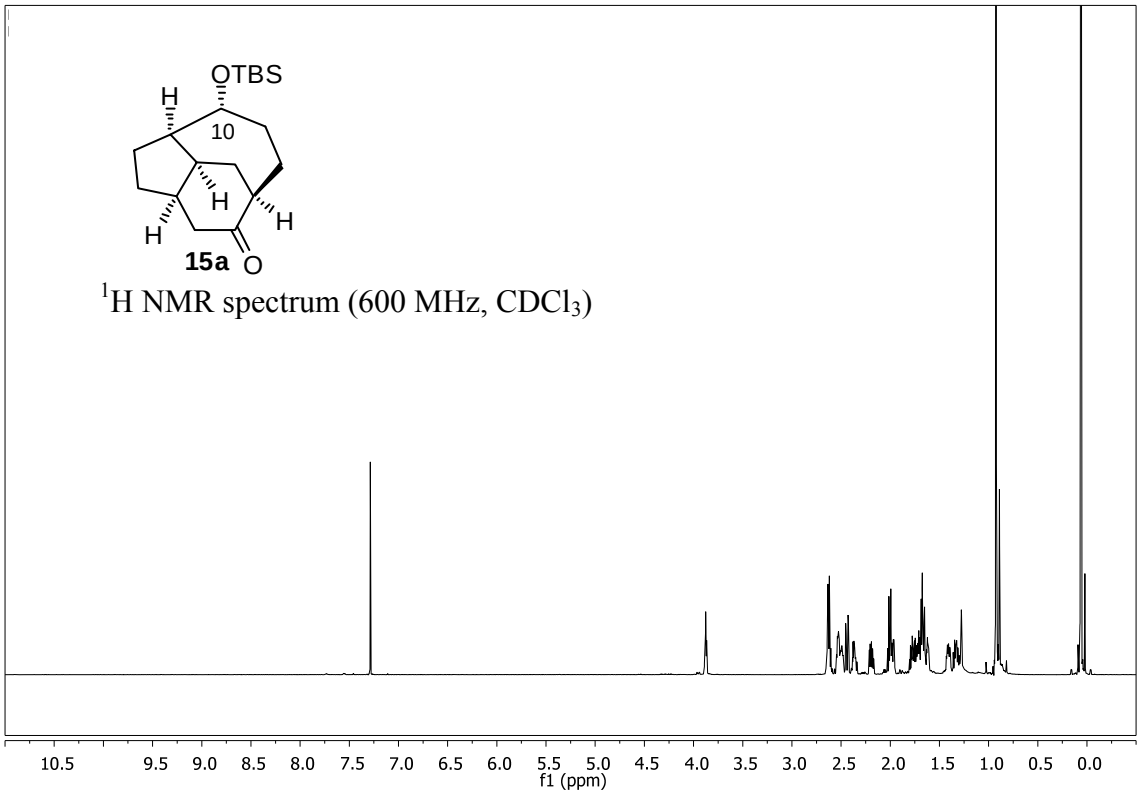




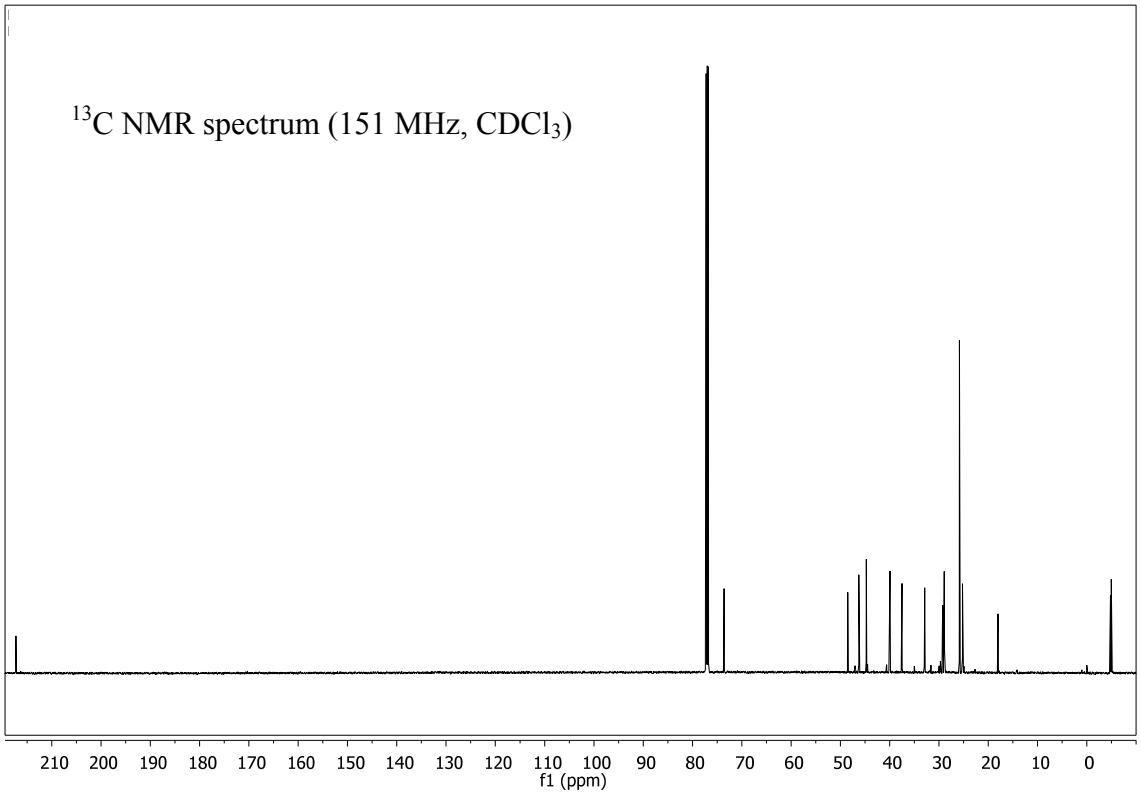
^{1}H NMR spectrum (600 MHz, $CDCl_3$, ca. 3:1 C_{10} epimers)



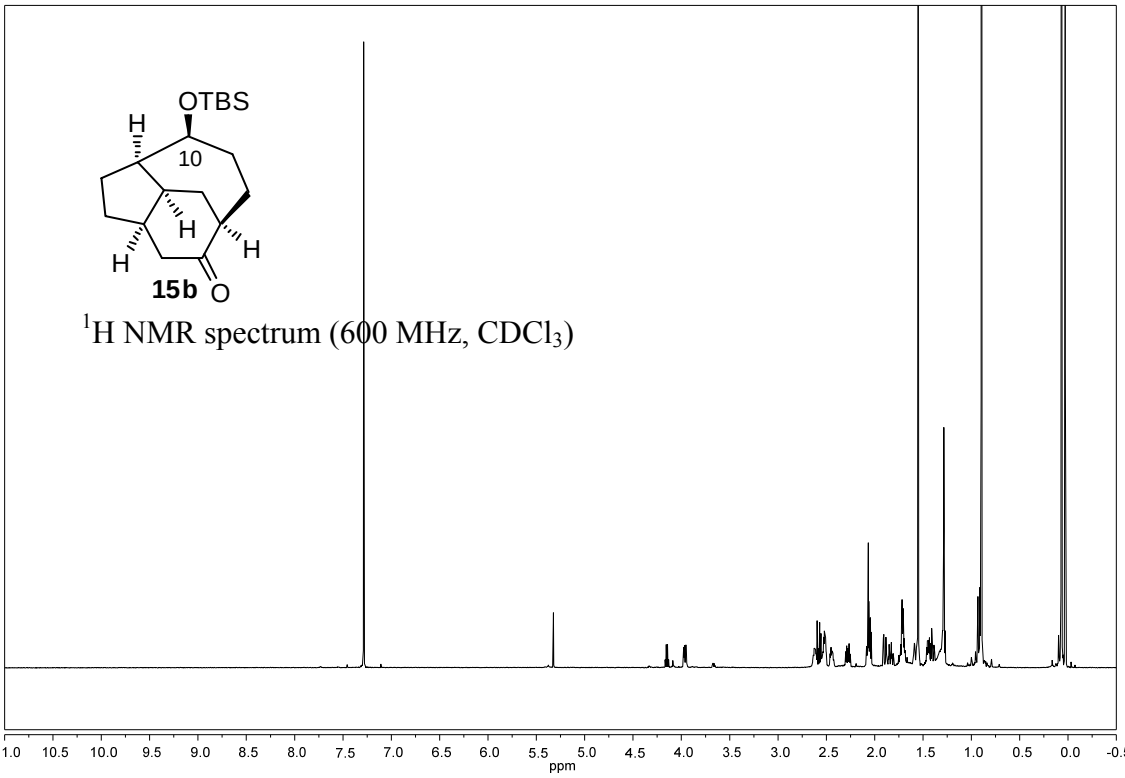
^{13}C NMR spectrum (151 MHz, $CDCl_3$, ca. 3:1 C_{10} epimers)



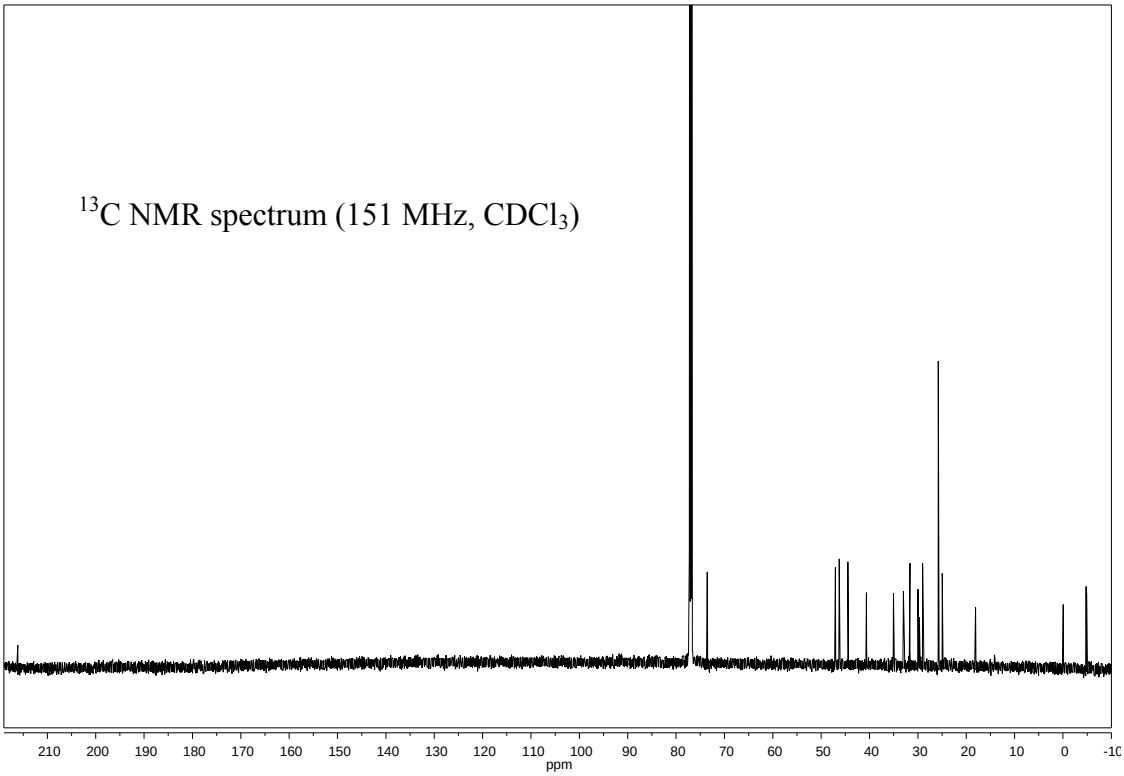
^{1}H NMR spectrum (600 MHz, $CDCl_3$)



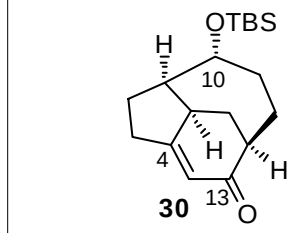
^{13}C NMR spectrum (151 MHz, $CDCl_3$)



^{1}H NMR spectrum (600 MHz, $CDCl_3$)



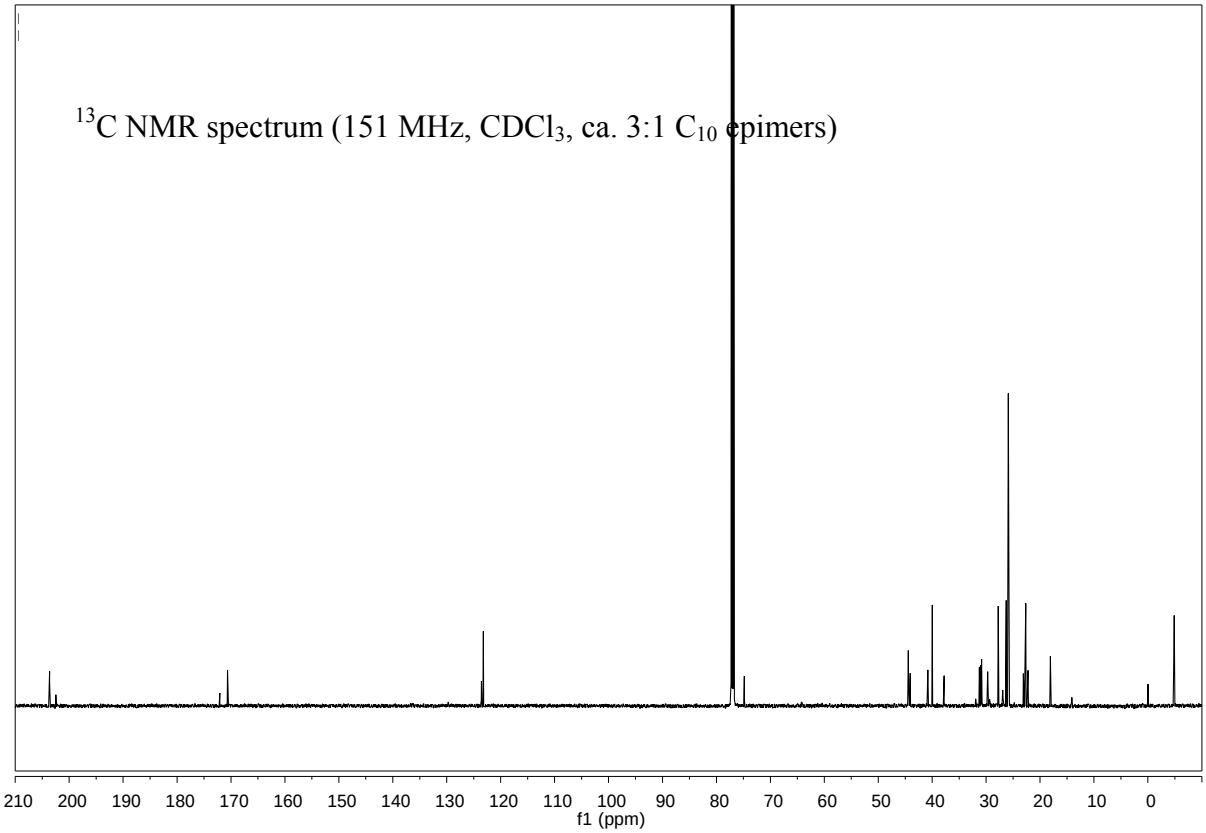
^{13}C NMR spectrum (151 MHz, $CDCl_3$)

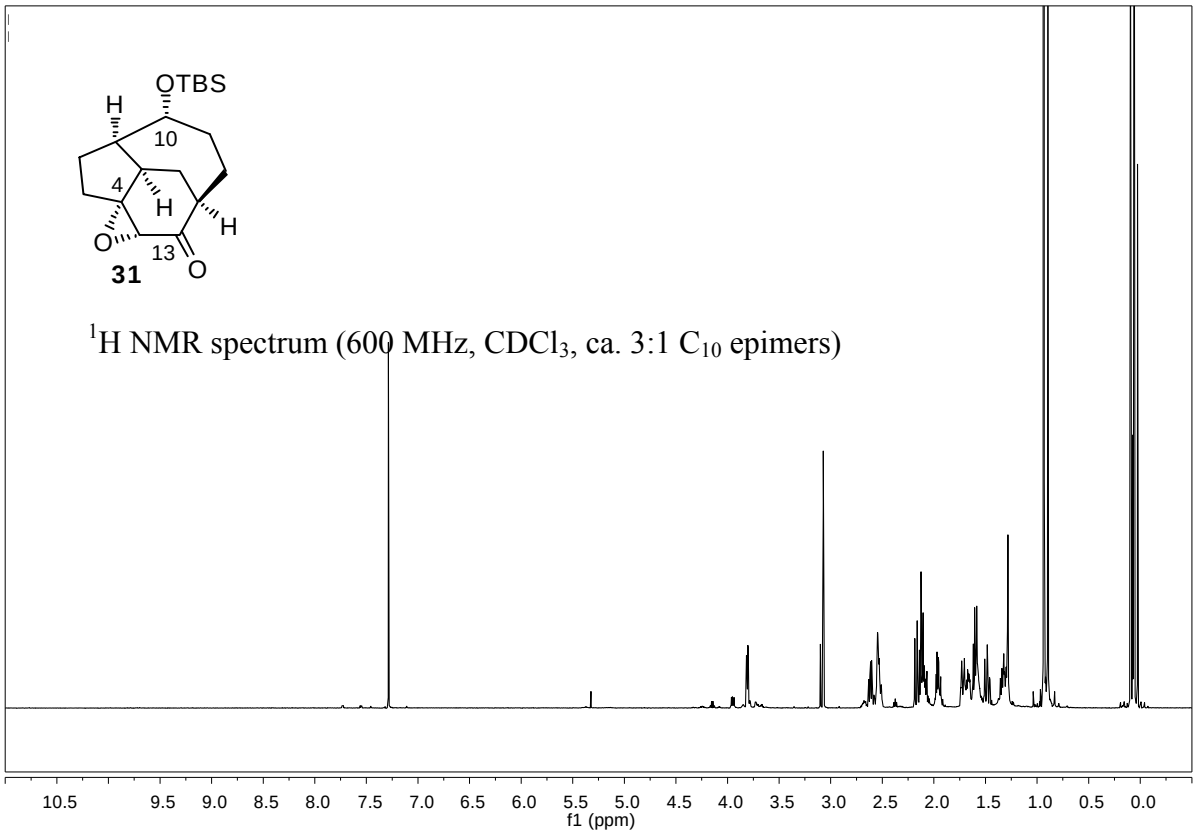


30

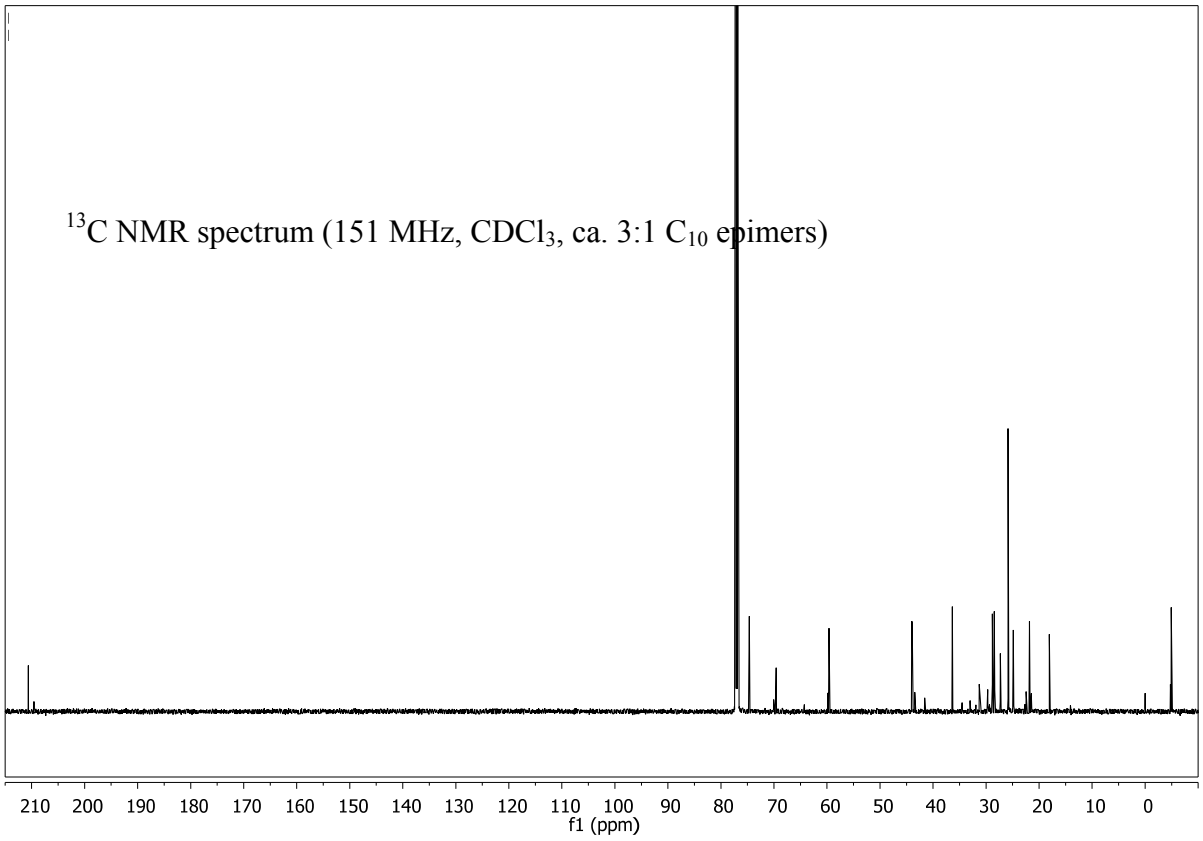
^{1}H NMR spectrum (600 MHz, $CDCl_3$, ca. 3:1 C_{10} epimers)

^{13}C NMR spectrum (151 MHz, $CDCl_3$, ca. 3:1 C_{10} epimers)

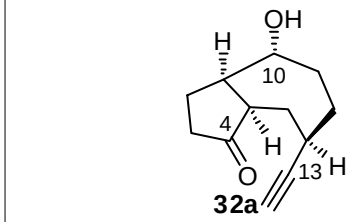




^{1}H NMR spectrum (600 MHz, $CDCl_3$, ca. 3:1 C_{10} epimers)

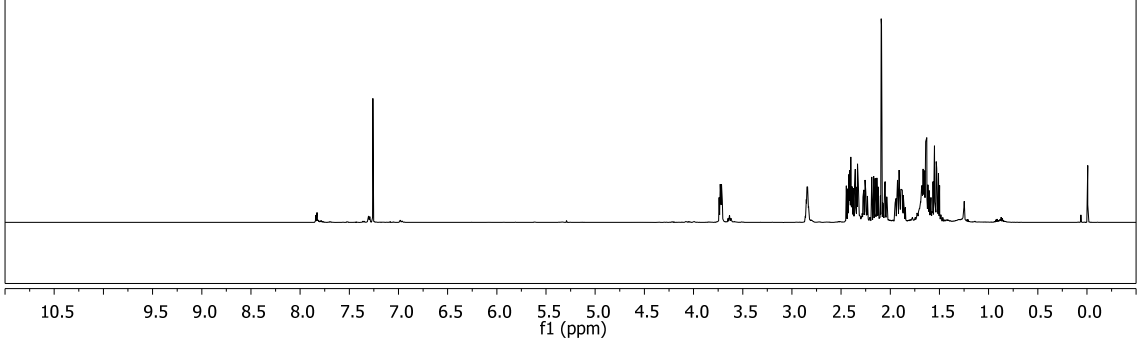


^{13}C NMR spectrum (151 MHz, $CDCl_3$, ca. 3:1 C_{10} epimers)

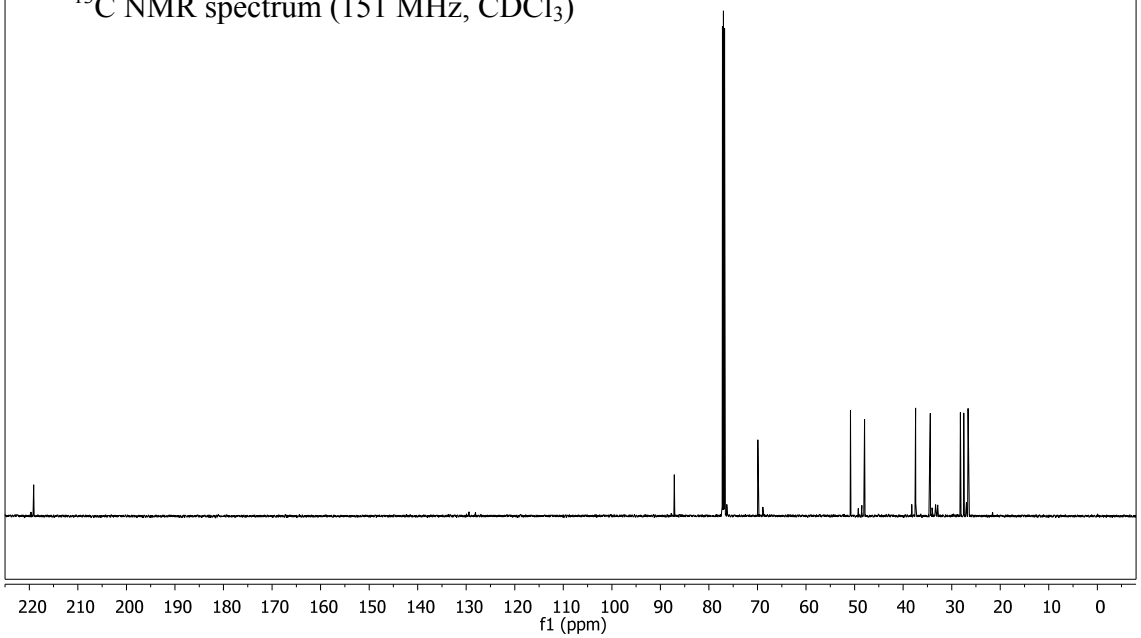


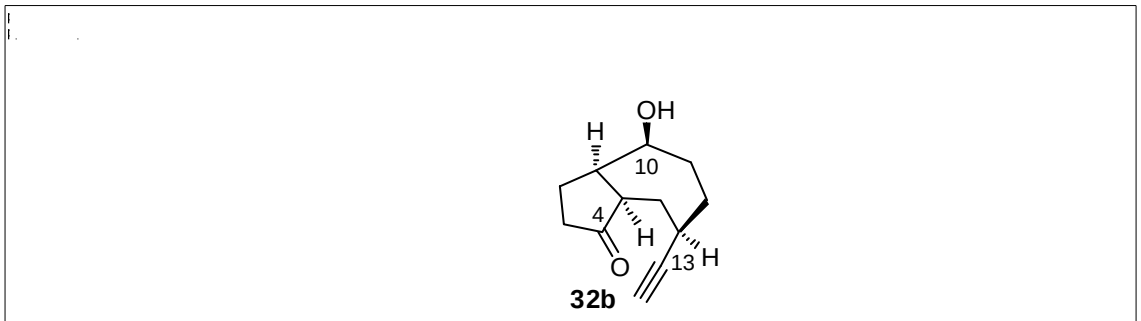
32a

^{1}H NMR spectrum (600 MHz, $CDCl_3$)



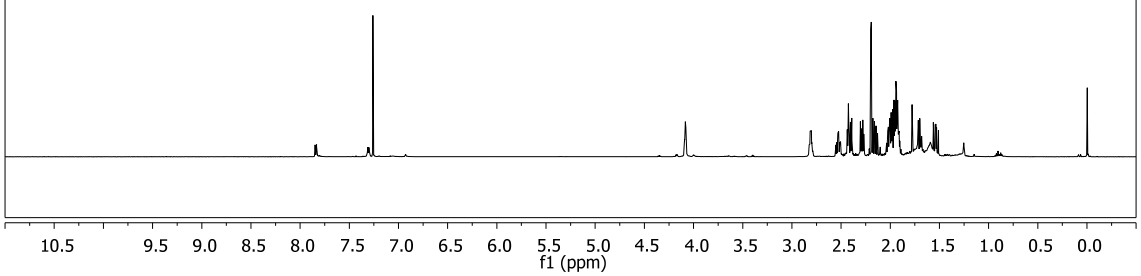
^{13}C NMR spectrum (151 MHz, $CDCl_3$)



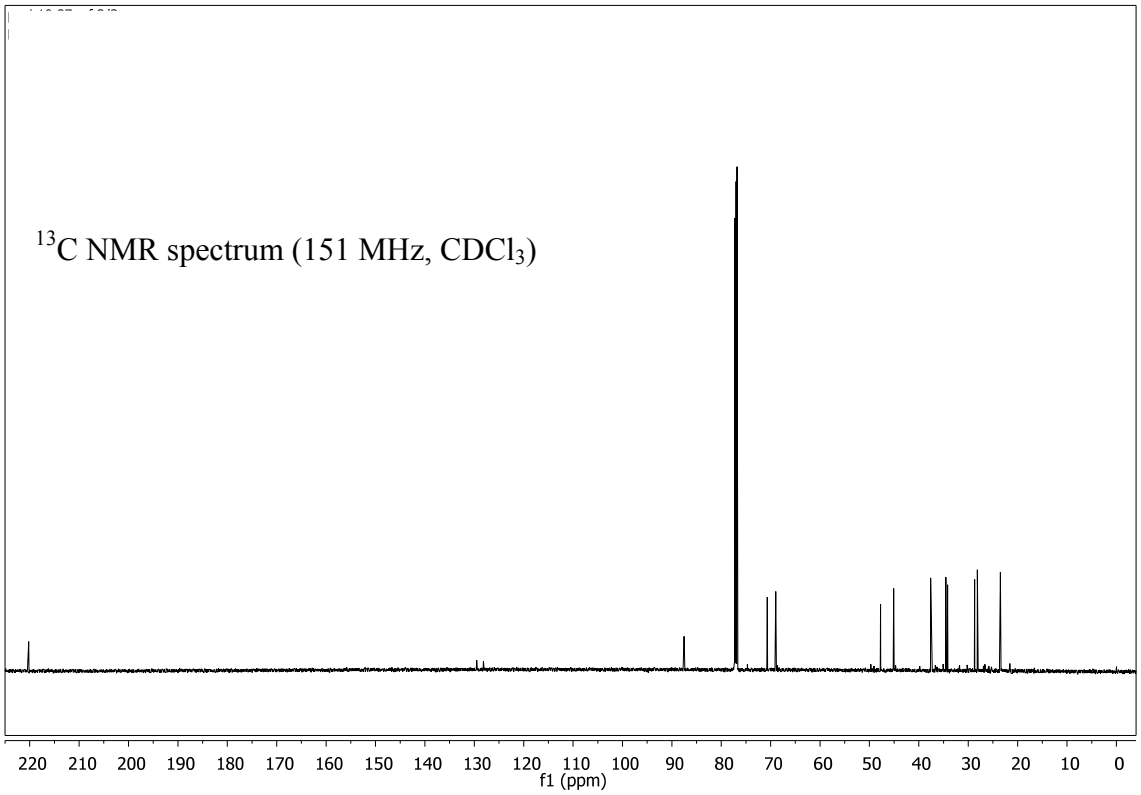


32b

^{1}H NMR spectrum (600 MHz, $CDCl_3$)

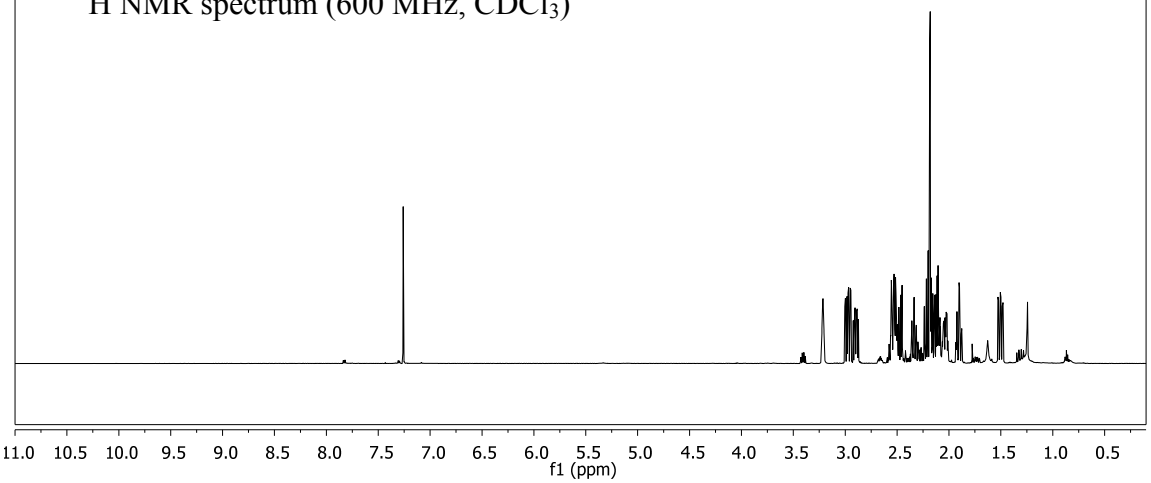


^{13}C NMR spectrum (151 MHz, $CDCl_3$)

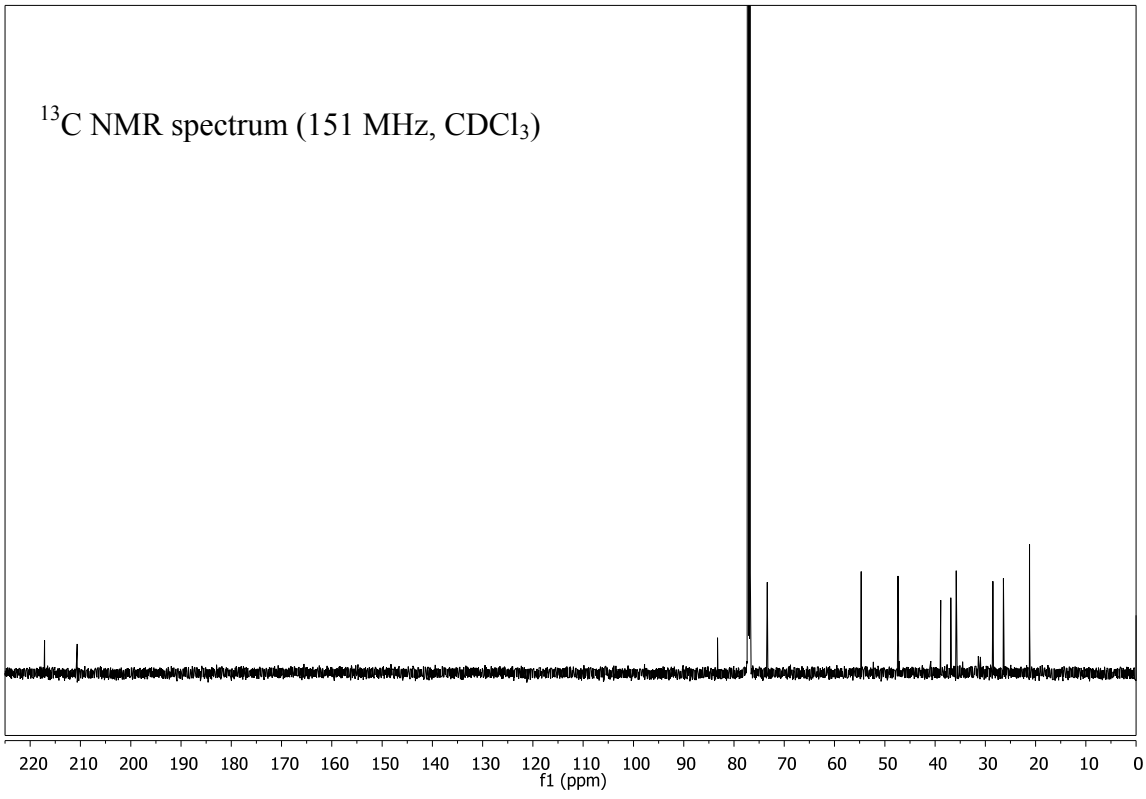


33

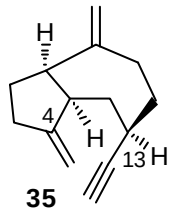
^{1}H NMR spectrum (600 MHz, $CDCl_3$)



^{13}C NMR spectrum (151 MHz, $CDCl_3$)

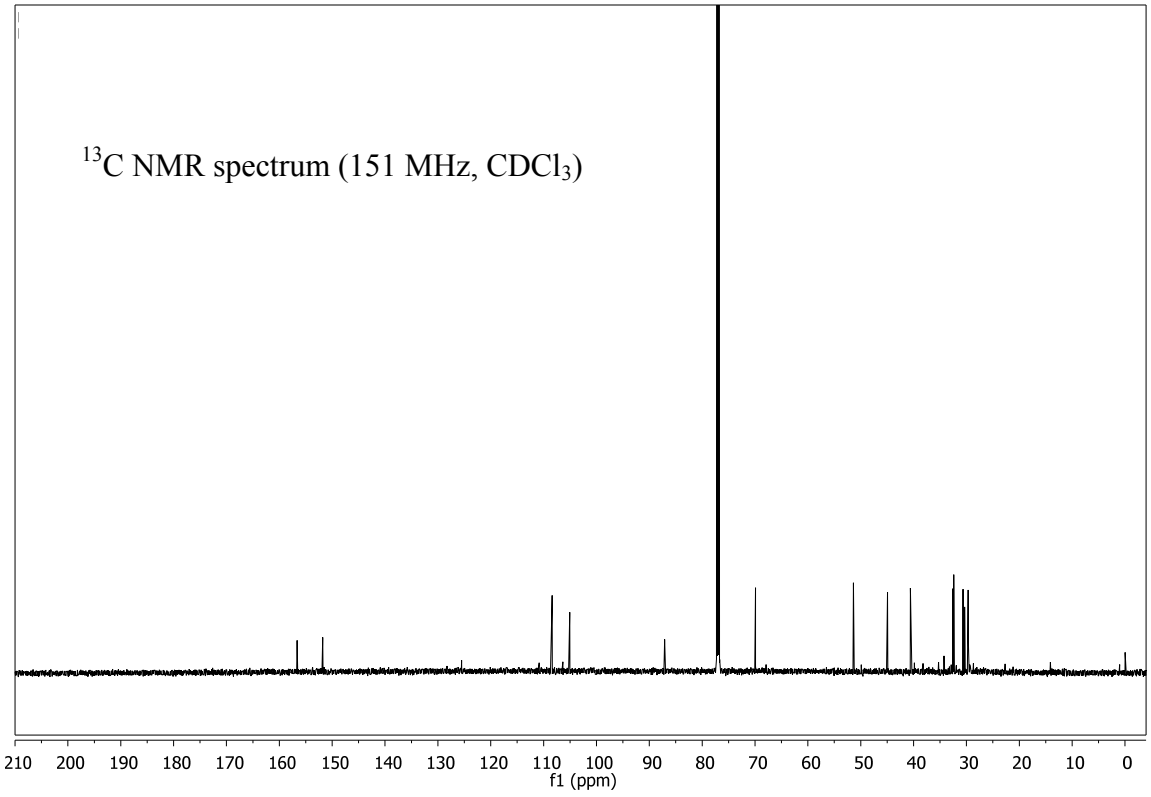


^{1}H NMR spectrum (600 MHz, $CDCl_3$)

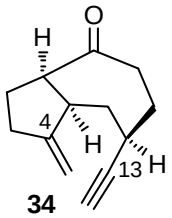


35

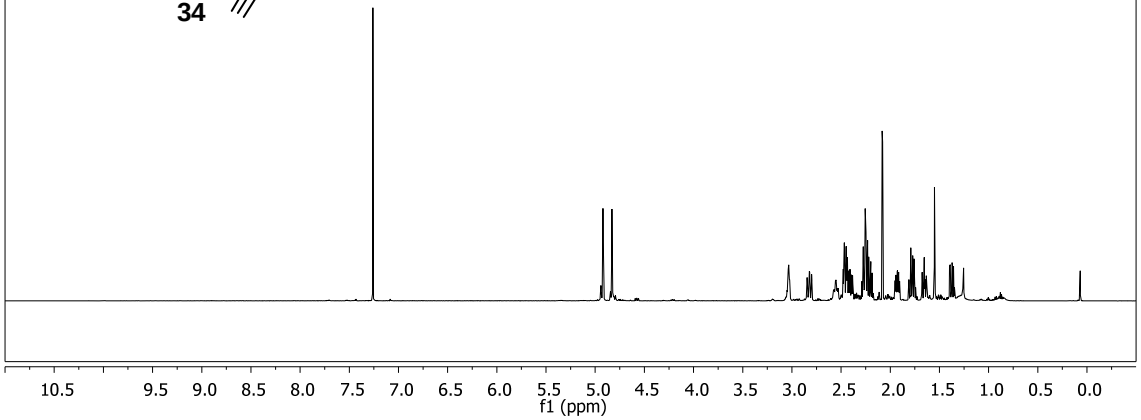
^{13}C NMR spectrum (151 MHz, $CDCl_3$)



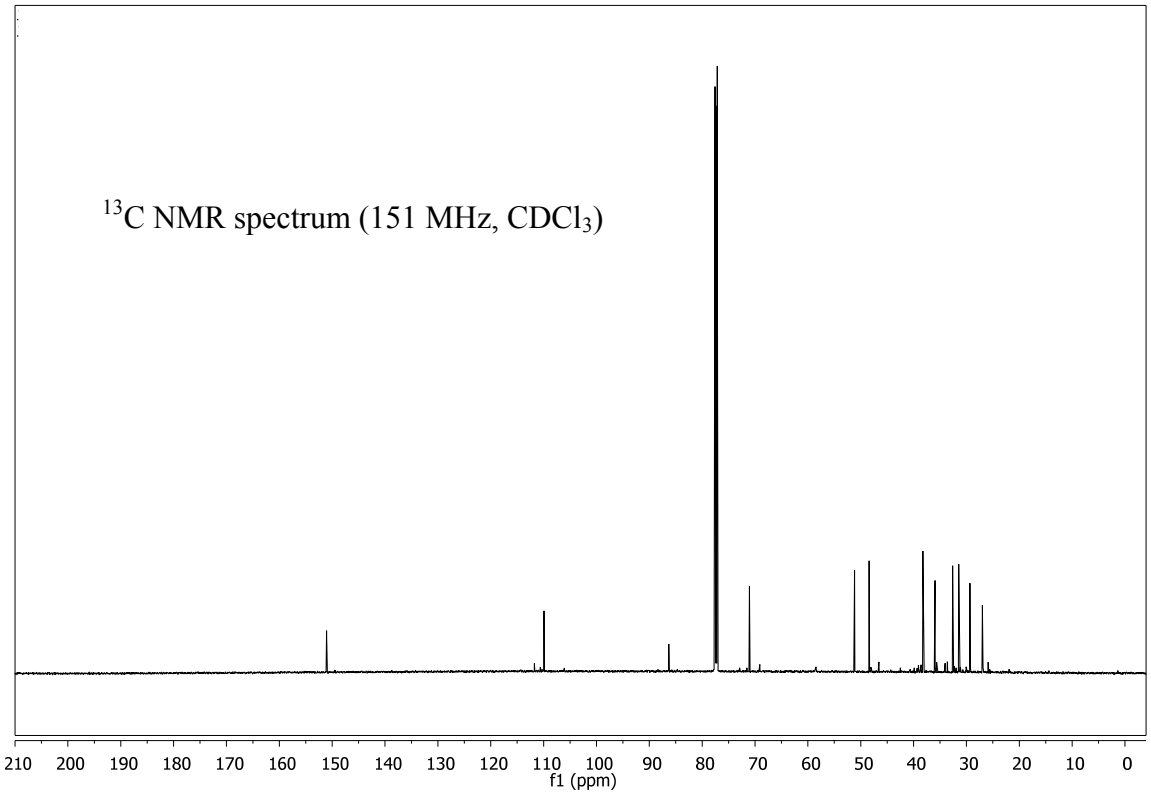
^{1}H NMR spectrum (600 MHz, $CDCl_3$)



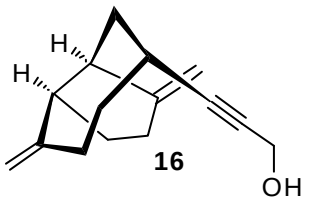
34

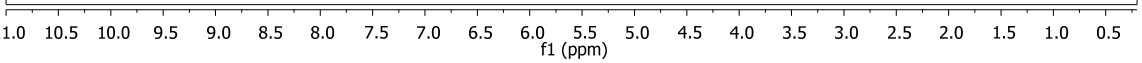


^{13}C NMR spectrum (151 MHz, $CDCl_3$)

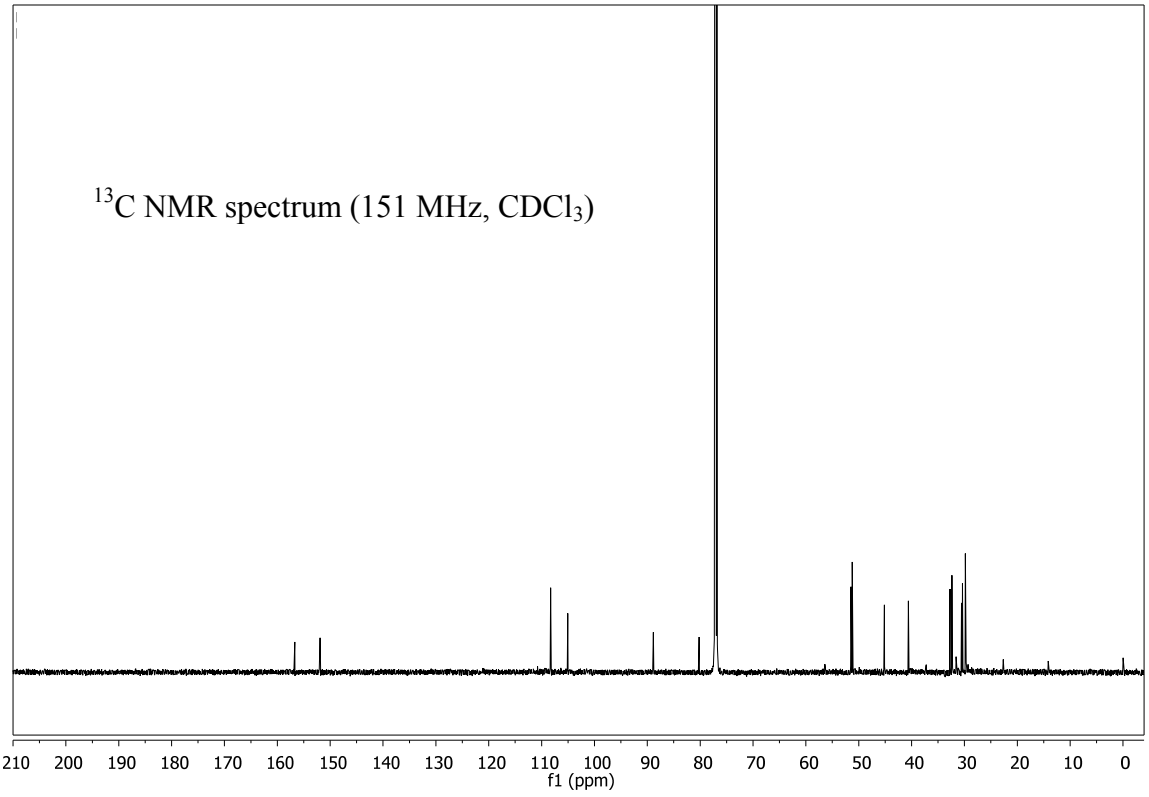


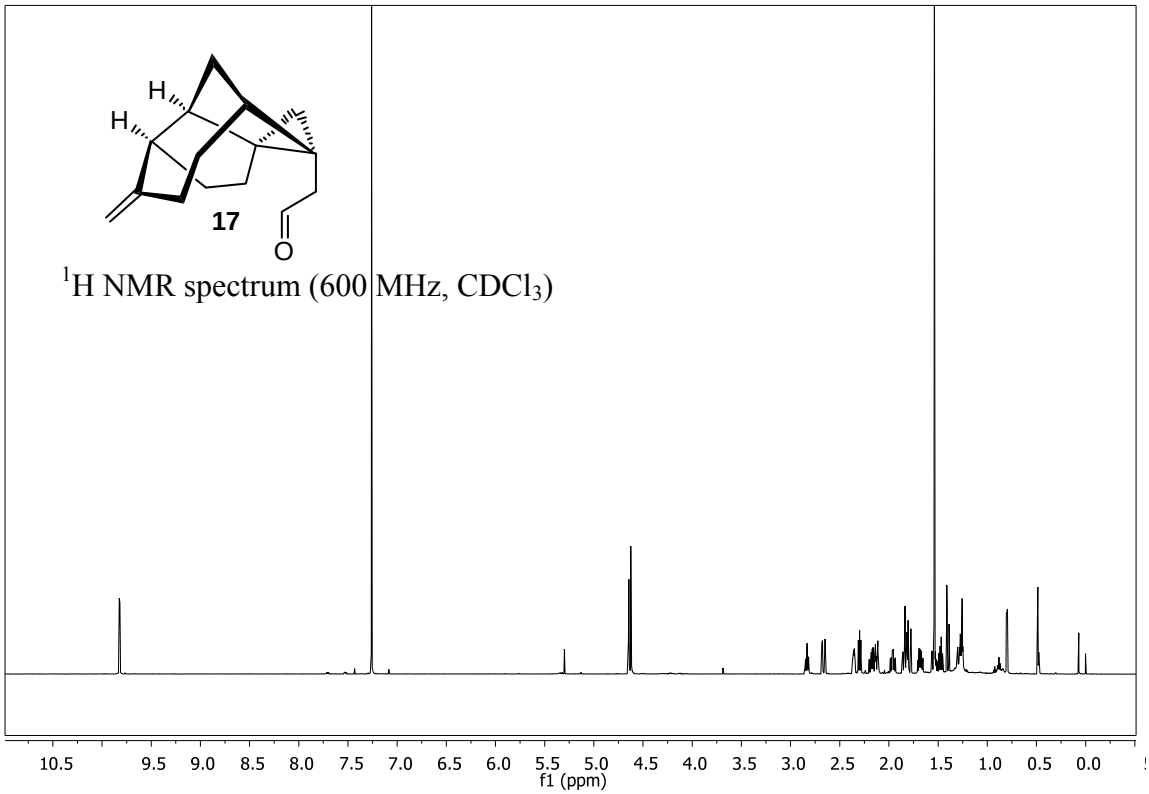
^{1}H NMR spectrum (600 MHz, $CDCl_3$)





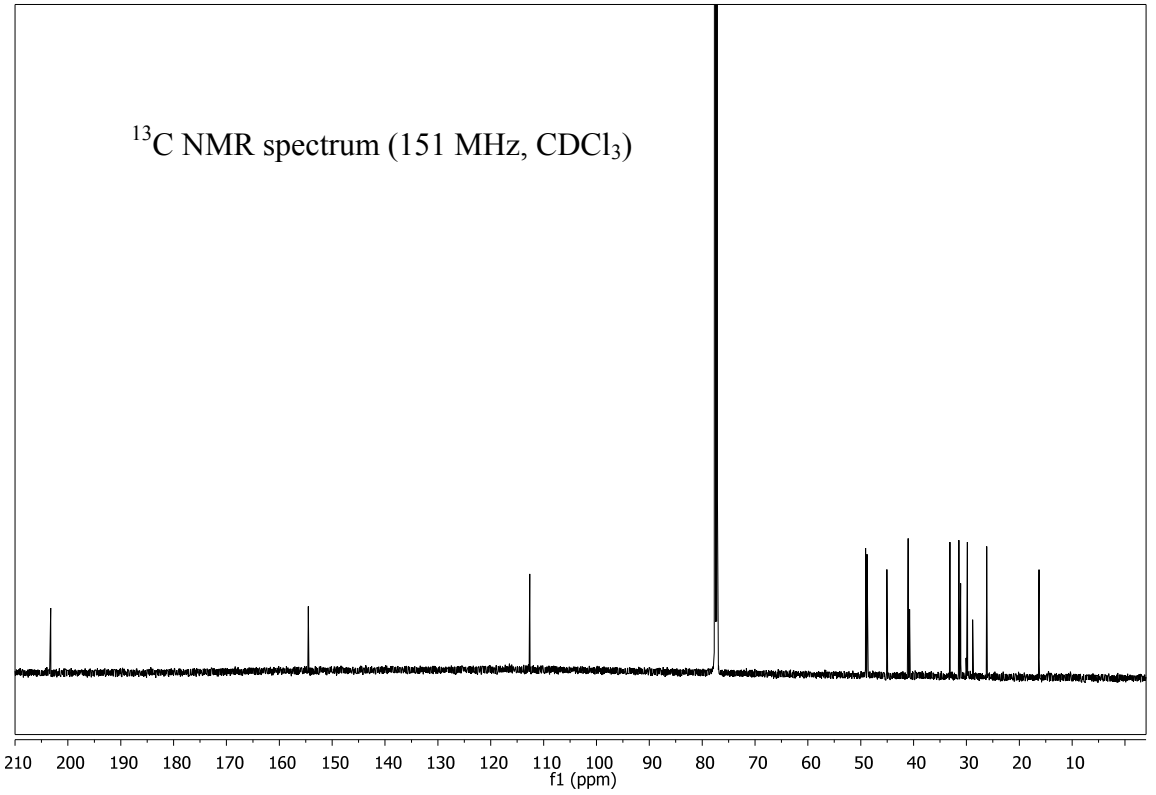
^{13}C NMR spectrum (151 MHz, $CDCl_3$)



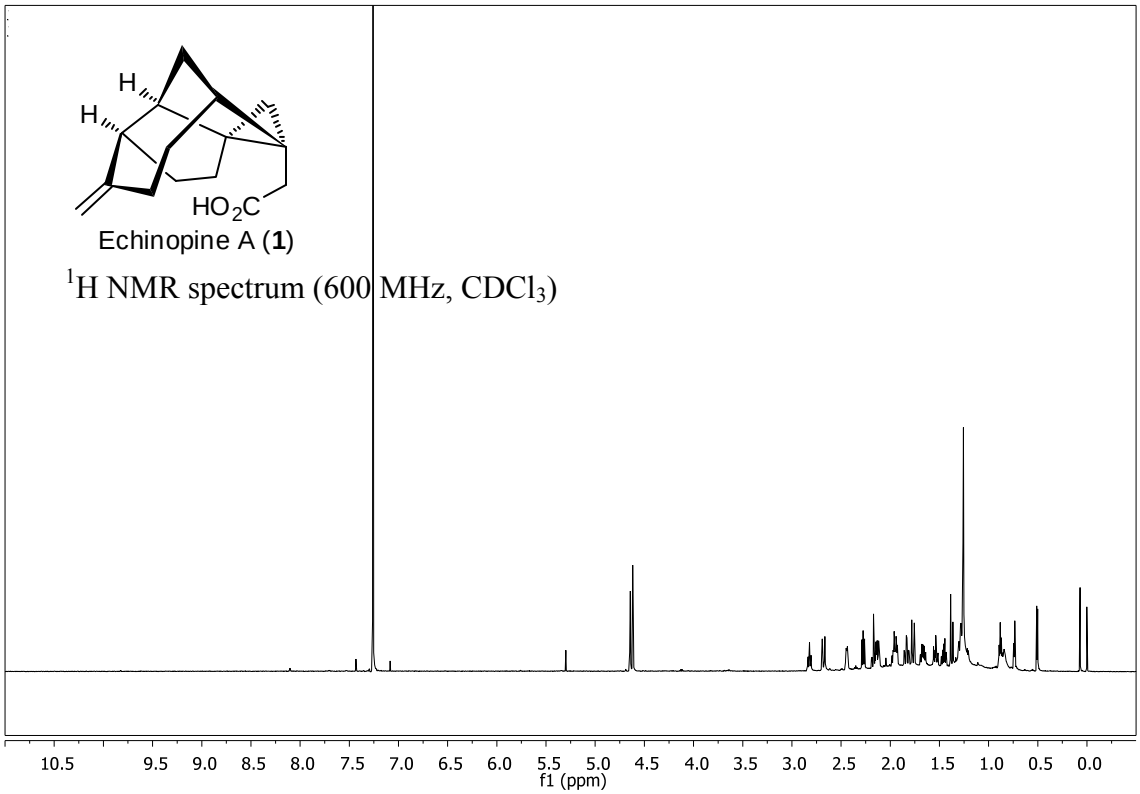


17

^{1}H NMR spectrum (600 MHz, $CDCl_3$)

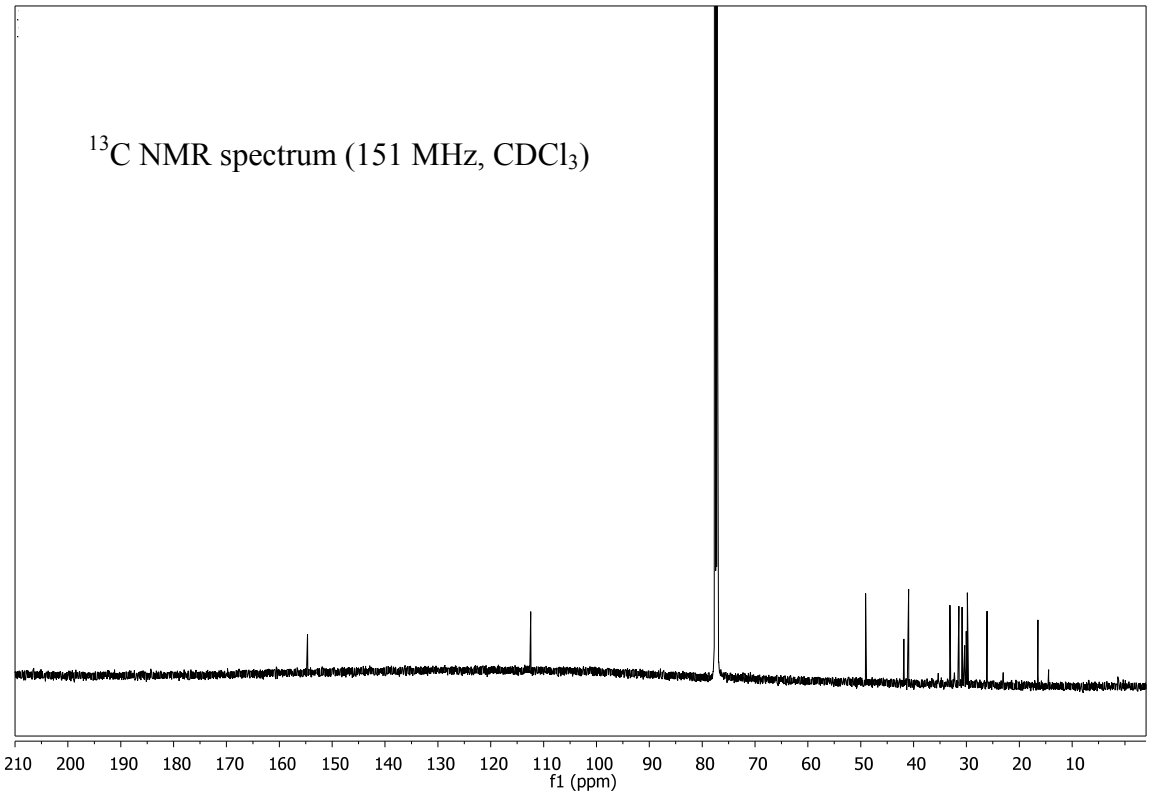


^{13}C NMR spectrum (151 MHz, $CDCl_3$)

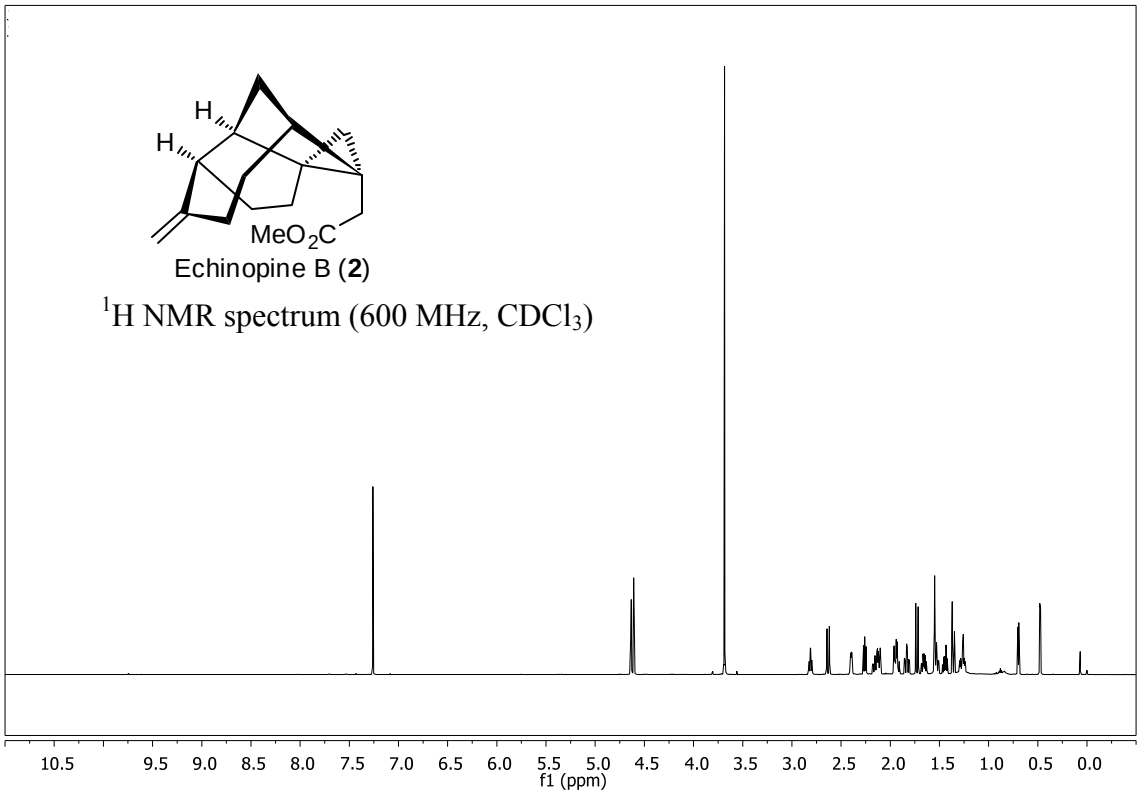


Echinopine A (**1**)

^{1}H NMR spectrum (600 MHz, $CDCl_3$)

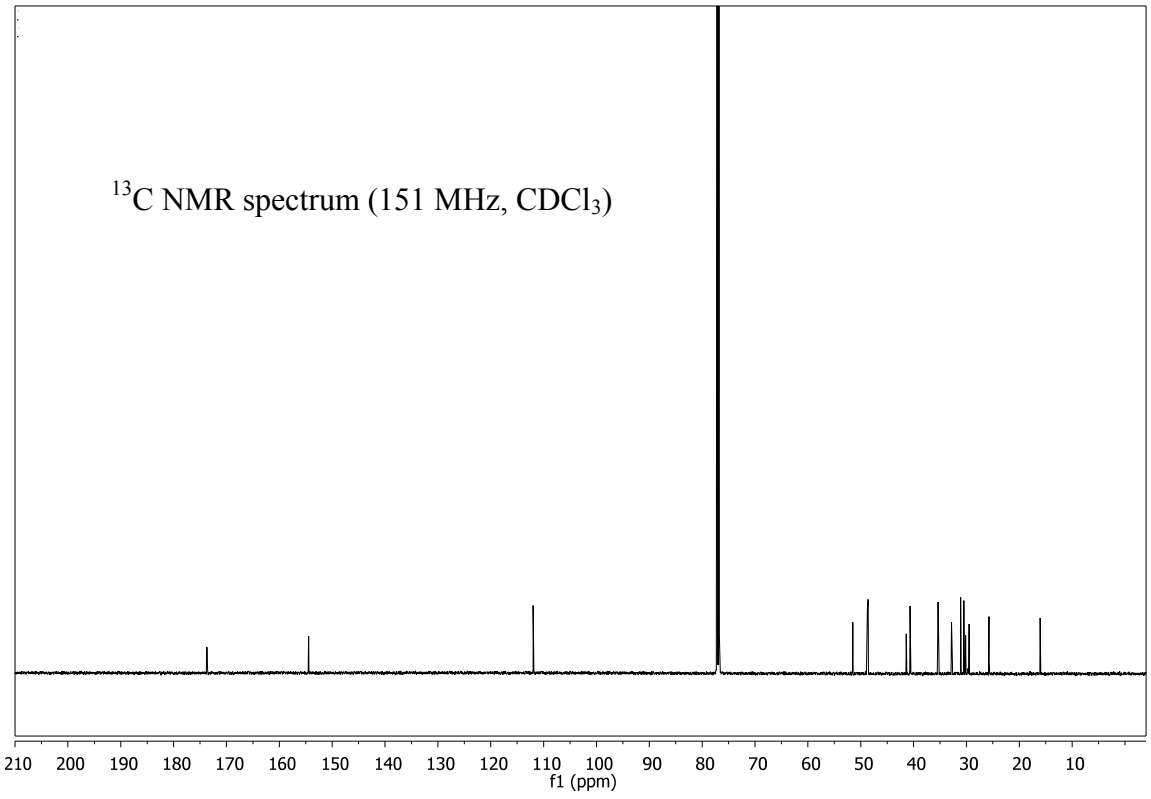


^{13}C NMR spectrum (151 MHz, $CDCl_3$)



Echinopine B (**2**)

^{1}H NMR spectrum (600 MHz, $CDCl_3$)



^{13}C NMR spectrum (151 MHz, $CDCl_3$)