

Supporting Information for

**Formal Synthesis of Aspidosperma Alkaloids via the Intramolecular [3 + 2]
Cycloadditions of 2-Azapentadienyllithiums**

William H. Pearson*[‡] and Aaron Aponick

*Department of Chemistry, The University of Michigan,
Ann Arbor, Michigan, 48109-1055*

wpearson@berryassoc.com

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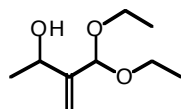
- General Experimental Methods. (S2)
- Full experimental section: (S2-S13)
- Photocopies of spectra for all new compounds: (S14-S26)
15-19, 2, 24, 25, 6b.

[‡] Current address: Berry & Associates, Inc., 2434 Bishop Circle East, Dexter, Michigan, 48130, USA.

Experimental Section

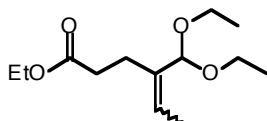
General. Unless otherwise noted, reactions were carried out under an atmosphere of dry nitrogen in flame dried glassware equipped with tightly fitted rubber septum. Toluene, triethylamine, pyridine, dichloromethane, diethylamine, and diisopropylamine were distilled from powdered calcium hydride. Dimethylformamide (DMF) was distilled at reduced pressure from barium oxide. Tetrahydrofuran (THF) and diethyl ether were distilled under nitrogen from sodium/benzophenone ketyl. Commercial *n*-butyllithium was titrated with diphenyl acetic acid prior to use. The aldehydes used in the preparation of tributylstannylimines were purified by distillation. Reagents which required preparation via literature procedures are referenced when described. All other reagents were obtained from the Aldrich Chemical Company, and used without further purification. Chromatography refers to liquid chromatography on silica gel.

Proton nuclear magnetic resonance (^1H NMR) spectra were recorded at 500, 400 or 300 MHz respectively, on Varian Unity INOVA 500, Varian Unity INOVA 400 or Varian Mercury 300 spectrometers. Chemical shift (δ) is reported in parts per million (ppm) downfield relative to tetramethylsilane (TMS). Coupling constants (J) are reported in Hz. Multiplicities are reported using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; app, apparent. ^{13}C NMR spectra were recorded on a Varian Unity INOVA 400 spectrometer at 100 MHz, and chemical shift is reported in ppm relative to the carbon resonance of CDCl_3 (77.06 ppm). Infrared spectra were obtained on a Perkin Elmer Spectrum BX FT-IR spectrometer at 2.0 cm^{-1} resolution and are reported in wavenumbers (signal intensity and shape). The following abbreviations are used in describing IR data: w, weak; m, medium; s, strong; br, broad. UV-VIS spectra were recorded on a Shimadzu UV160U spectrophotometer. Routine mass spectral data were obtained using a Hewlett Packard 6890 Gas Chromatograph equipped with an HP 5973 mass selective detector (GCMS) via electron impact (EI) at 70 eV. High resolution mass spectral (HRMS), X-ray crystallography, and elemental analyses were performed by the facilities operated by the University of Michigan.

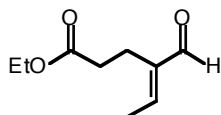


3-(Diethoxymethyl)-but-3-en-2-ol (12). *n*-BuLi (10.53 mL of a 2.5M solution in hexanes) was added to a $-78\text{ }^\circ\text{C}$ solution of the bromide **11** (5.0000 g, 23.923 mmol) in THF (150

mL) over 10 min in a dropwise fashion. After stirring for 1 h, acetaldehyde (10 mL, 178 mmol) was added, and the reaction mixture maintained at -78°C for 15 min before warming to rt. Saturated aqueous NaHCO_3 was then added, the mixture further diluted with water, extracted with CH_2Cl_2 , dried over MgSO_4 , and the solvent removed *in vacuo*. Flash chromatography (20% EtOAc/hexanes) afforded 4.1651 g (>99%) of a pale yellow oil: $R_f = 0.22$ (20% EtOAc/hexanes); ^1H NMR (CDCl_3 , 500MHz) δ 5.28 (s, 1H), 5.24 (s, 1H), 4.91 (s, 1H), 4.45 (q, 1H, $J = 6.5$ Hz), 3.73-3.61 (m, 2H), 3.55-3.45 (m, 2H), 2.80 (s, 1H), 1.35 (d, 3H, $J = 6.5$ Hz), 1.24 (app td, 6H, $J = 7.1, 3.5$ Hz); ^{13}C NMR (CDCl_3 , 125 MHz) δ 148.1, 113.1, 103.3, 66.9, 62.5, 62.1, 21.5, 15.1; IR (neat) 3437 (m) cm^{-1} ; LRMS (EI, 70 eV) m/z (rel intensity) 129(59), 113(15), 103(63), 83(100), 75(46), 55(64), 45(90).

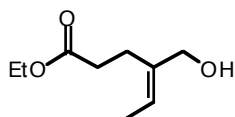


(Z)-4-(Diethoxymethyl)-hex-4-enoic acid ethyl ester and (E)-4-(diethoxymethyl)-hex-4-enoic acid ethyl ester (13). Triethyl orthoacetate (21.0020 g, 129.46 mmol) and propionic acid (0.3483 g, 4.71 mmol) were added to a solution of the allyl alcohol **12** (4.1130 g, 23.610 mmol) in toluene (85.0 mL). The solution was heated to reflux and maintained for 24 h before cooling to rt and removing most of the volatile organics by repeated co-distillation with benzene using a rotary evaporator. By this method, 6.1427 g of a crude oil containing a 1:1 mixture of diastereomers and small amounts of benzene and triethyl orthoacetate was obtained, and used without further purification: ^1H NMR (CDCl_3 , 500MHz) δ 5.67 (q, 1H, $J = 6.8$ Hz), 5.48 (q, 1H, $J = 7.1$ Hz), 5.17 (s, 1H), 4.63 (s, 1H), 4.12 (q, 2H, $J = 7.2$ Hz), 4.11 (q, 2H, $J = 7.2$ Hz), 3.66-3.56 (m, 4H), 3.47-3.38 (m, 4H), 2.51-2.39 (m, 8H), 1.70 (d, 3H, $J = 7.1$ Hz), 1.69 (d, 3H, $J = 6.8$ Hz), 1.23-1.18 (m, 8H).

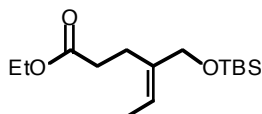


(E)-4-Formyl-hex-4-enoic acid ethyl ester (14). A 1 : 1 mixture of *E/Z* olefins **13** (6.1427 g of a crude oil containing small amounts of benzene and triethyl orthoacetate, 23.61 mmol) was dissolved in methanol and water (50 mL of a 9 : 1 mixture of MeOH : H_2O by

volume), oxalic acid (0.2126 g, 2.361 mmol) was added and the resulting solution was flushed with nitrogen and stirred at rt for 24 h. The reaction mixture was diluted with CH₂Cl₂ and washed once with NaHCO₃ (saturated aqueous solution), dried over MgSO₄, and the solvent removed *in vacuo* to yield 3.7293 g (93% of a yellow oil) of the *E*- α,β -unsaturated aldehyde which was used without further purification: R_f = 0.33 (20% EtOAc/hexanes); ¹H NMR (CDCl₃, 500MHz) δ 9.37 (s, 1H), 6.66 (q, 1H, J = 7.0 Hz), 4.11 (q, 2H, J = 7.0 Hz), 2.58 (t, 2H, J = 7.5 Hz), 2.41 (t, 2H, J = 7.5 Hz), 2.04 (d, 3H, J = 7.0 Hz), 1.25 (t, 3H, J = 7.0 Hz); ¹³C NMR (CDCl₃, 125 MHz) δ 194.7, 172.8, 151.0, 142.8, 60.4, 32.4, 19.3, 14.9, 14.2; IR (neat) 1733 (s), 1684(s) cm⁻¹; LRMS (EI, 70 eV) m/z (rel intensity) 142(76), 125(100), 113(73), 97(78), 67(56); HRMS (CI with NH₃) calcd for C₉H₁₅O₃ (M+H)⁺ 171.1021, found 171.1018.

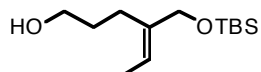


(*E*)-4-(Hydroxymethyl)-hex-4-enoic acid ethyl ester (15). Over a period of 1 min, solid NaBH₄ (0.9946 g, 26.2920 mmol) was added to a solution of the aldehyde **14** (3.7923 g, 21.9100 mmol) in dry MeOH (110 mL) at 0 °C. After 30 min, the solution was acidified with aqueous HCl (5 mL of a 1 M solution) and allowed to warm to rt. The reaction mixture was then diluted with water, extracted with CH₂Cl₂, and dried over MgSO₄. The solvent was removed *in vacuo* to yield 3.5594 g (94%) of a pale yellow oil which was used without further purification: R_f = 0.15 (20% EtOAc/ hexanes); ¹H NMR (CDCl₃, 500MHz) δ 5.56 (q, 1H, J = 7.0 Hz), 4.13 (q, 2H, J = 7.0 Hz), 4.03 (s, 2H), 2.48-2.42 (m, 4H), 1.65 (d, 3H, J = 7.0 Hz), 1.26 (t, 3H, J = 7.0 Hz); IR (neat) 3437 (s), 1734(s) cm⁻¹; LRMS (EI, CI with NH₃) m/z (rel intensity) 173(15), 155(100), 144(44), 127(54); HRMS (CI with NH₃) calcd for C₉H₁₇O₃ (M+H)⁺ 173.1178, found 173.1176.

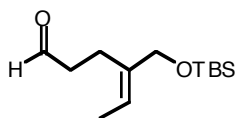


(*E*)-4-(*tert*-Butyldimethylsilyloxymethyl)-hex-4-enoic acid ethyl ester. Imadazole (2.7372 g, 40.2056 mmol) was added to a solution of the alcohol **15** (3.4621 g, 20.1028 mmol) in CH₂Cl₂ (100 mL) at 0 °C followed by *tert*-butyldimethylsilyl chloride (3.9389 g, 26.1336 mmol).

A white precipitate immediately formed, and after 1 h at 0 °C the reaction was diluted with water and allowed to warm to rt. The reaction mixture was washed with water and two portions of cold HCl (0.25 M aqueous solution), dried over MgSO₄, and the solvent removed *in vacuo*. Flash chromatography (5% EtOAc/hexanes) afforded 5.0310 g (87%) of a clear colorless oil: R_f = 0.61 (5% EtOAc/ hexanes); ¹H NMR (CDCl₃, 500MHz) δ 5.51 (q, 1H, J = 6.5 Hz), 4.12 (q, 2H, J = 7.0 Hz), 4.05 (s, 2H), 2.39 (app s, 4H), 1.64 (d, 3H, J = 6.5 Hz), 1.25 (t, 3H, J = 7.0 Hz), 0.90 (s, 9H), 0.06 (s, 6H); ¹³C NMR (CDCl₃, 125 MHz) δ 173.4, 137.5, 121.1, 67.0, 60.3, 33.1, 26.0, 23.1, 18.4, 14.3, 12.9, -5.3; IR (neat) 1738 (s) cm⁻¹; LRMS (CI with NH₃) m/z (rel intensity) 287(12), 229(47), 183(23), 155(100); HRMS (CI with NH₃) calcd for C₁₅H₃₁O₃Si (M+H)⁺ 287.2042, found 287.2040.

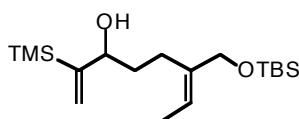


(E)-4-(tert-Butyldimethylsilyloxymethyl)-hex-4-en-1-ol. A solution of the ester (1.6983 g, 5.9282 mmol) in THF (3 mL) was added in a dropwise fashion to a suspension of lithium aluminum hydride (0.4737 g, 11.8564 mmol) in THF (27 mL) at -78 °C. The reaction was maintained at this temperature for 15 min before warming to 0 °C. After 30 min, water (0.47 mL), 15% NaOH solution in water (0.47 mL), and water (1.41 mL) were added sequentially in a dropwise fashion. After stirring for 5 min, the reaction mixture was filtered over a pad of celite with ether and the solvent removed *in vacuo*. Flash chromatography (10% EtOAc/hexanes) afforded 1.2944 g (89%) of a colorless oil: R_f = 0.08 (10% EtOAc/ hexanes); ¹H NMR (CDCl₃, 500MHz) δ 5.53 (q, 1H, J = 7.0 Hz), 4.07 (s, 2H), 3.66 (t, 2H, J = 6.3 Hz), 2.18 (t, 2H, J = 7.5 Hz), 1.72-1.67 (m, 3H), 1.65 (t, 3H, J = 7.0 Hz), 0.92 (s, 9H), -0.09 (s, 6H); ¹³C NMR (CDCl₃, 125 MHz) δ 138.6, 120.7, 67.7, 62.8, 31.2, 26.0, 24.0, 18.5, 13.1, -5.3; IR (neat) 3345 (m) cm⁻¹; LRMS (CI with NH₃) m/z (rel intensity) 245(100), 187(32), 130(53), 95(54); HRMS (CI with NH₃) calcd for C₁₃H₂₉O₂Si (M+H)⁺ 245.1937, found 245.1925.



(E)-4-(tert-Butyldimethylsilyloxymethyl)-hex-4-enoic acid carbaldehyde (16). Methylene chloride (1.8 mL) was added to oxalyl chloride (0.716 mL of a 2.0 M solution in

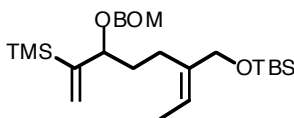
CH₂Cl₂, 1.432 mmol) and the resulting solution was cooled to -78 °C. A solution of dimethyl sulfoxide (0.2238 g, 2.864 mmol) in CH₂Cl₂ was added in a dropwise fashion and allowed to stir for 20 min. The alcohol (0.3183 g, 1.302 mmol) in CH₂Cl₂ (2 mL) was then added in a dropwise fashion and allowed to stir for 20 min. Triethylamine (0.90 mL, 6.51 mmol) was added, the reaction maintained at -78 ° for 20 min, warmed to rt and allowed to stir for an additional 15 min. The reaction was then diluted with CH₂Cl₂, and washed successively with two portions of aqueous HCl (1.0 M), H₂O, NaHCO₃ (saturated aqueous solution), H₂O, and brine. The organic extract was then dried over MgSO₄ and the solvent removed *in vacuo* to afford 0.3061 g (97%) of a colorless oil which was used without further purification: *R*_f = 0.47 (10% EtOAc/hexanes); ¹H NMR (CDCl₃, 500MHz) δ 9.78 (s, 1H), 5.52 (q, 1H, *J* = 7.0 Hz), 4.04 (s, 2H), 2.55 (t, 2H, *J* = 7.5 Hz), 2.39 (t, 2H, *J* = 7.5 Hz), 1.63 (d, 3H, *J* = 7.0 Hz), 0.90 (s, 9H), 0.05 (s, 6H); ¹³C NMR (CDCl₃, 125 MHz) δ 202.4, 137.4, 121.1, 67.1, 42.5, 25.8, 20.1, 18.2, 12.8, -5.3; IR (neat) 1727 (m) cm⁻¹; LRMS (CI with NH₃) *m/z* (rel intensity) 243(14), 185(34), 111(100); HRMS (CI with NH₃) calcd for C₁₃H₂₇O₂Si (M+H)⁺ 243.1780, found 243.1778.



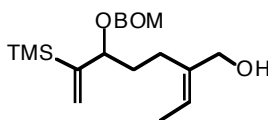
(E)-6-(*tert*-butyldimethylsilyloxymethyl)-3-hydroxy-2-trimethylsilyloct-1,6-diene.

tert-Butyllithium (4.71 mL of a 1.7 M solution in pentane, 8.000 mmol) was added in a dropwise fashion to a solution of bromovinyl trimethylsilane (0.7166 g, 4.000 mmol) in ether (9 mL) which had been cooled to -78 °C, and the solution maintained for 2.5 h. A solution of the aldehyde **16** (0.8057 g, 3.3234 mmol) in ether (3.3 mL) was then added and stirred for 15 min before warming the reaction mixture to 0 °C. After an additional 15 min, the reaction was quenched by the addition of saturated aqueous NH₄Cl and diluted with ether. The resulting biphasic mixture was washed twice with saturated aqueous NH₄Cl and once with brine, dried over magnesium sulfate, and the solvent removed *in vacuo* to obtain 1.2041 g of a pale yellow oil that was used without further purification. For characterization purposes a small sample was purified by flash chromatography (0-10% EtOAc/hexanes gradient): *R*_f = 0.48 (10% EtOAc/hexanes); ¹H NMR (CDCl₃, 500MHz) δ 5.80 (s, 1H), 5.51 (q, 1H, *J* = 6.5 Hz), 5.42 (d, 1H, *J* = 5.0 Hz), 4.30-4.24 (m, 1H), 4.07 (s, 2H), 2.24-2.11 (m, 2H), 1.86 (d, 1H, *J* = 4.0 Hz, -

OH), 1.73-1.53 [m, 5H containing 1.64 (d, $J = 6.5$ Hz)], 0.92 (s, 9H), 0.14 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 155.4, 138.8, 123.7, 120.2, 75.9, 67.4, 36.0, 26.0, 24.2, 18.5, 13.1, -0.53, -0.51, -5.3; IR (neat) 3454 (m), 1250 (m), 837 (s) cm^{-1} ; LRMS (EI, 70 eV) m/z (rel intensity) 211(1), 177(3), 147(20), 119(11), 93(10), 73(100); HRMS (electrospray) calcd for $\text{C}_{18}\text{H}_{38}\text{O}_2\text{Si}_2\text{Na}(\text{M}+\text{Na})^+$ 365.2308, found 365.2302.

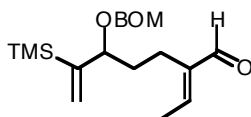


(*E*)-3-(benzyloxy)methoxy-6-(*tert*-butyldimethylsilyloxymethyl)-2-trimethylsilyl-octa-1,6-diene (17). The free alcohol (1.0989 g, 3.207 mmol) was dissolved in THF (16mL) and tetrabutylammonium iodide (0.5923 g, 1.604 mmol) and *N,N*-diisopropylethylamine (1.17 mL, 6.73 mmol) added. After brief stirring, chloromethyl benzyl ether (0.89 mL, 6.414 mmol) was added and the resulting mixture brought to reflux and maintained for 2 h before being cooled to rt. The reaction was then diluted with ether, washed with three portions saturated aqueous NH_4Cl and brine, and dried over magnesium sulfate. The solvent was removed *in vacuo*. Flash chromatography (0-5% EtOAc/hexanes gradient) afforded 1.273 g (86%) of a clear colorless oil: $R_f = 0.61$ (10% EtOAc/hexanes); ^1H NMR (CDCl_3 , 500MHz) δ 7.35 (app d, 4H, $J = 4.5$ Hz), 7.31-7.27 (m, 1H), 5.79 (d, 1H, $J = 2.5$ Hz), 5.51 (d, 1H, $J = 2.5$ Hz), 5.48 (q, 1H, $J = 6.5$ Hz), 4.64 (AB_q , $J = 11.5$ Hz, $\Delta\nu_{\text{AB}} = 92.3$ Hz, 2H), 4.69-4.66 (m, 2H), 4.25 (dd, 1H, $J = 8.0, 5.5$ Hz), 4.05 (s, 2H), 2.25 (td, 1H, $J = 13.0, 5.0$ Hz), 2.04 (td, 1H, $J = 13.0, 5.0$ Hz), 1.72-1.55 [m, 5H containing 1.63 (d, $J = 6.5$ Hz)], 0.91 (s, 9H), 0.13 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 152.1, 139.0, 138.1, 128.4, 127.9, 127.7, 127.0, 119.4, 92.0, 81.7, 69.5, 67.0, 35.0, 26.0, 24.5, 18.5, 13.0, -0.4, -5.2; IR (neat) 836 (s) cm^{-1} ; LRMS (EI, 70 eV) m/z (rel intensity) 324(4), 251(1), 195(7), 165(7), 147(18), 91(100), 73(92); HRMS (electrospray) calcd for $\text{C}_{26}\text{H}_{46}\text{O}_3\text{Si}_2\text{Na}(\text{M}+\text{Na})^+$ 485.2883, found 485.2882.



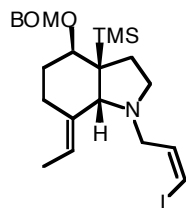
(*E*)-3-(benzyloxy)methoxy-6-hydroxymethyl-2-trimethylsilyl-octa-1,6-diene (18). *p*-Toluenesulfonic acid hydrate (8.2 mg, 0.04321 mmol) was added to a solution of the silyl ether

17 (0.2000 g, 0.4321 mmol) in dry methanol (4.3 mL). After 30 min, analysis of the reaction by TLC indicated that the starting material had been consumed. The reaction mixture was then diluted with ether and washed sequentially with saturated aqueous NaHCO₃ and two portions brine. The organic layer was dried over magnesium sulfate and the solvent removed *in vacuo*. Flash chromatography (10% EtOAc/hexanes) afforded 0.1232 g (82%) of a colorless oil: R_f = 0.19 (10% EtOAc/hexanes); ¹H NMR (CDCl₃, 500MHz) δ 7.36-7.34 (m, 4H), 7.32-7.27 (m, 1H), 5.80 (d, 1H, J = 2.5 Hz), 5.53 (d, 1H, J = 2.5 Hz), 5.51 (q, 1H, J = 7.0 Hz), 4.65 (AB_q, J = 12.0 Hz, $\Delta\nu_{AB}$ = 98.3 Hz, 2H), 4.70-4.67 (m, 2H), 4.28 (dd, 1H, J = 8.0, 5.0 Hz), 4.03 (s, 2H), 2.30 (td, 1H, J = 13.0, 5.0 Hz), 2.11 (td, 1H, J = 13.0, 5.0 Hz), 1.96 (br s, 1H), 1.75-1.59 [m, 5H containing 1.65 (d, J = 7.0 Hz)], 0.14 (s, 9H); ¹³C NMR (CDCl₃, 125 MHz) d 151.9, 139.6, 138.0, 128.4, 127.8, 127.6, 126.9, 121.2, 92.0, 81.5, 69.5, 67.2, 34.8, 24.5, 13.0, -0.6; IR (neat) 3415 (m), 1026 (s), 837 (s) cm⁻¹; LRMS (EI, 70 eV) m/z (rel intensity) 287(1), 219(4), 195(6), 127(8), 91(100), 73(35); HRMS (electrospray) calcd for C₂₀H₃₂O₃SiNa (M+Na)⁺ 371.2018, found 371.2012.



(E)-3-(benzyloxy)methoxy-6-formyl-2-trimethylsilyl-octa-1,6-diene (19). Solid Dess-Martin periodinane (1.1071 g, 2.610 mmol) was added to a solution of the alcohol **18** (0.6998 g, 2.008 mmol) in CH₂Cl₂ (100 mL) in one portion. After 30 min, sodium sulfite (100 mL of a saturated aqueous solution) was added to the reaction mixture, and allowed to react for 30 min. The reaction was then diluted with ether (200 mL) and washed sequentially with two portions of a saturated aqueous solution of NaHCO₃ and brine. The organic layer was then dried over MgSO₄ and the solvent removed *in vacuo* to obtain 0.6626 g (95%) of a clear colorless oil: R_f = 0.35 (10% EtOAc/hexanes); ¹H NMR (CDCl₃, 500MHz) δ 9.37 (s, 1H), 7.37-7.53 (m, 4H), 7.30-7.26 (m, 1H), 6.56 (q, 1H, J = 7.0 Hz), 5.81 (d, 1H, J = 3.0 Hz), 5.52 (d, 1H, J = 3.0 Hz), 4.65 (AB_q, J = 12.0 Hz, $\Delta\nu_{AB}$ = 85.7 Hz, 2H), 4.69 (app q, 2H, J = 7.0 Hz), 4.29 (dd, 1H, J = 8.0, 5.0 Hz), 2.44 (td, 1H, J = 11.5, 5.0 Hz), 2.27 (td, 1H, J = 11.5, 5.0 Hz), 1.99 (d, 3H, J = 7.0 Hz), 1.65-1.54 (m, 2H), 0.13 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz) δ 194.7, 151.8, 149.7, 144.6, 138.0, 128.4, 127.8, 127.6, 126.9, 92.1, 81.2, 69.5, 34.7, 20.5, 14.8, -0.6; IR (neat) 1686 (s), 1036

(s), 1026 (s), 838 (s) cm^{-1} ; LRMS (EI, 70 eV) m/z (rel intensity) 301(1), 225(6), 195(5), 165(5), 127(5), 105(4), 91(100), 73(26); HRMS (electrospray) calcd for $\text{C}_{20}\text{H}_{30}\text{O}_3\text{SiNa}$ ($\text{M}+\text{Na}$)⁺ 369.1862, found 369.1863.

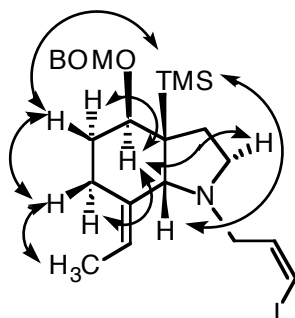


(3a*S,4*R**,7*R**)-4-(benzyloxy)methoxy-7-[(*E*)-ethylidene]-1-[(*Z*)-3-iodoprop-2-enyl]-3a-trimethylsilyl-octahydroindole (2).** A solution of the stannylamine **20** (0.1206 g, 0.3768 mmol) in ether (1 mL) was added to a solution of the aldehyde (0.1187 g, 0.3425 mmol) containing molecular sieves. After stirring for overnight, the reaction mixture was filtered over celite with ether to remove a fine particulate of crushed molecular sieves, and the solvent removed *in vacuo* to afford 0.2236 g of a colorless oil that was used without further purification.

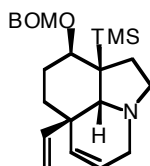
A solution of the crude oil in THF (5 mL) was added in a dropwise fashion to a solution of *n*-butyllithium (0.445 mL of a 1.54 M solution in hexanes, 0.6850 mmol) at -78 °C. After 30 min, the reaction was quenched with water and allowed to warm to rt. The biphasic mixture was then diluted with Na_2CO_3 (10% aqueous solution) and extracted with CH_2Cl_2 . The organic layer was dried over sodium sulfate and the solvent removed *in vacuo* to provide **22**, an extremely polar oil that was used without purification.

The cycloadduct **22** was dissolved in THF (2.4 mL) and solid K_2CO_3 (0.1893 g, 1.37 mmol) and the allyl bromide **23** (0.1015 g, 0.4110 g) added. The reaction mixture was heated to reflux and maintained for 1 h before being cooled to rt. A dark brown suspension resulted which was diluted with $\text{CH}_2\text{Cl}_2/\text{H}_2\text{O}$ and extracted with CH_2Cl_2 . Column chromatography (0-10% EtOAc/hexanes) afforded 0.1070 g of a pale yellow oil (59%) which was typically used without further purification. To obtain an analytically pure sample, a portion of the material was exposed to reverse phase chromatography using C_{18} silica that was eluted first with CH_3CN then 0.1% trifluoroacetic acid in CH_3CN : $R_f = 0.23$ (0.1 % TFA/ CH_3CN); $R_f = 0.21$ (10% EtOAc/hexanes); ^1H NMR (CDCl_3 , 400MHz) δ 7.36-7.34 (m, 4H), 7.32-7.28 (m, 1H), 6.27-6.21 (m, 2H), 5.38 (q, 1H, $J = 6.4$ Hz), 4.76 (AB_q, $J = 7.2$ Hz, $\Delta\nu_{\text{AB}} = 47.0$ Hz, 2H), 4.75-4.65 (m, 2H), 3.93 (dd, 1H, $J = 11.2, 4.4$ Hz), 3.26-3.17 (m, 2H), 2.69 (dd, 1H, $J = 15.6, 4.8$ Hz), 2.68 (s, 1H), 2.44-2.39 (m,

1H), 2.20-2.13 (m, 1H), 2.11-2.00 (m, 2H), 1.89-1.75 (m, 2H), 1.65 (td, 3H, $J = 6.4, 1.2$ Hz), 1.60-1.49 (m, 1H), 0.06 (s, 9H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 139.4, 138.1, 136.8, 128.5, 127.9, 127.6, 121.3, 93.7, 83.7, 81.8, 75.4, 69.6, 56.9, 51.8, 41.1, 31.9, 29.8, 21.7, 13.1, -0.4; IR (neat) 1026 (s), 836 (s) cm^{-1} ; LRMS (EI, 70 eV) m/z (rel intensity) 526(1), 510(6), 417(35), 400(25), 344(19), 314(48), 222(18), 209(30), 196(100), 149(31), 91(82), 73(64); HRMS (electrospray) calcd for $\text{C}_{24}\text{H}_{37}\text{INO}_2\text{Si}$ ($\text{M}+\text{H}$) $^+$ 526.1638, found 526.1630.

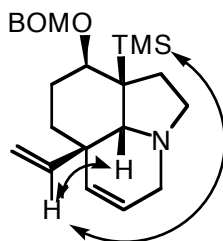


Assignment of the relative stereochemistry was made based on the observed NOE's illustrated above. Nearly all ^1H NMR signals for the compounds above were able to be assigned based on extensive two dimensional NMR studies including GCOSY and NOE experiments.

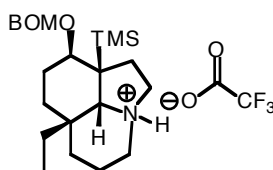


(6a*R,9*R**,9a*S**,9b*R**)-9-(benzyloxy)methoxy-9a-trimethylsilyl-6a-vinyl-1,2,6a,7,8,9,9a,9b-octahydro-4*H*-pyrrolo[3,2,1-*i,j*]-quinolin-9-one (24).** The vinyl iodide **2** (0.0260 g, 0.0495 mmol) was tared into a flask, and in the glovebox, tetrabutylammonium chloride (0.0206 g, 0.0742 mmol) was added. K_2CO_3 (0.0342 g, 0.247 mmol) and palladium acetate (0.0006 g, 0.003 mmol) were quickly added under ambient atmosphere and the flask flushed with N_2 . Degassed DMF (0.5 mL) was added and the flask immediately heated to 70 $^\circ\text{C}$ in a pre-heated oil bath. After 50 min, TLC analysis indicated that the starting material had been consumed. The reaction was cooled to rt, diluted with Na_2CO_3 (10% aqueous solution), and extracted with four portions ether. The combined organic extract was dried over sodium sulfate and the solvent removed *in vacuo*. Flash chromatography (0-100% ether hexanes gradient) afforded 0.0085 g (43%) of a yellow oil: $R_f = 0.50$ (50% EtOAc/hexanes); ^1H NMR (CDCl_3 ,

500MHz) δ 7.35-7.34 (m, 4H), 7.30-7.26 (m, 1H), 5.94 (dd, 1H, $J = 17.5, 10.5$ Hz), 5.61 (ddd, 1H, $J = 10.0, 5.0, 1.5$ Hz), 5.33 (dt, 1H, $J = 10.0, 2.0$ Hz), 5.20 (dd, 1H, $J = 10.5, 1.0$ Hz), 5.16 (dd, 1H, $J = 17.5, 1.0$ Hz), 4.77 (AB_q, $J = 7.0$ Hz, $\Delta\nu_{AB} = 65.6$ Hz, 2H), 4.65-4.60 (m, 2H), 3.79 (dd, 1H, $J = 11.5, 4.5$ Hz), 3.44 (ddd, 1H, $J = 16.5, 5.0, 1.5$ Hz), 3.31 (td, 1H, $J = 9.0, 4.0$ Hz), 2.68 (dt, 1H, $J = 16.5, 2.0$ Hz), 2.19 (s, 1H), 2.15 (ddd, 1H, $J = 11.0, 9.0, 7.0$ Hz), 1.96-1.63 (m, 6H), 0.12 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz) δ 144.3, 138.1, 135.4, 128.4, 127.8, 127.6, 122.9, 115.0, 93.5, 84.5, 72.2, 69.5, 53.7, 52.8, 43.0, 39.4, 32.7, 30.5, 26.6, 0.73; IR (neat) 1038 (s), 1026 (s), 835 (s) cm⁻¹; LRMS (EI, 70 eV) m/z (rel intensity) 397(2), 382(5), 352(2), 324(7), 276(100), 260(9), 186(31), 158(17), 91(84); HRMS (electrospray) calcd for C₂₄H₃₆NO₂Si (M+H)⁺ 398.2515, found 398.2518.

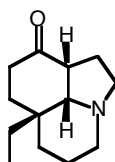


Assignment of the relative stereochemistry was made based on the observed NOE's illustrated above. Nearly all ¹H NMR signals for the compounds above were able to be assigned based on extensive two dimensional NMR studies including GCOSY and NOE experiments.



(6aR*,9R*,9aS*,9bR*)-9-(Benzyloxy)methoxy-6a-ethyl-9a-trimethylsilyl decahydro-pyrrolo[3,2,1-*i,j*]-quinolin-9-one trifluoroacetic acid salt (25). Trifluoroacetic acid (0.0165 mL, 0.214 mmol) was added to MeOH (5 mL) and 0.5 mL of the resulting solution was used to dissolve the diene **24** (0.0085 g, 0.021 mmol). To the solution was added 10% palladium on carbon (4.2 mg) and the reaction pressurized to 45 psi under an H₂ atmosphere using a Parr hydrogenation apparatus. The reaction mixture was shaken for 4 h at rt then filtered over celite with EtOAc. The solvent was removed *in vacuo* to afford 10.8 mg (98%) of a yellow oil: ¹H NMR (CDCl₃, 400MHz) δ 10.88 (br s, 1H), 7.34-7.32 (m, 4H), 7.30-7.27 (m, 1H), 4.78 (AB_q, J

= 6.6 Hz, $\Delta\nu_{AB}$ = 26.4 Hz, 2H), 4.61 (AB_q, J = 11.8 Hz, $\Delta\nu_{AB}$ = 38.6 Hz, 2H), 4.14-4.05 (m, 1H), 3.94 (dd, 1H, J = 11.8, 4.6 Hz), 3.83 (d, 1H, J = 10.8 Hz), 2.60-2.35 (m, 2H), 2.17-1.99 (m, 5H), 1.84 (d, 1H, J = 14.0 Hz), 1.73-1.69 (m, 2H), 1.63-1.43 (m, 3H), 1.27-1.06 (m, 2H), 0.88 (t, 3H, J = 7.6 Hz), 0.22 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz) δ 137.9, 128.4, 127.6, 127.5, 127.5, 94.4, 81.7, 78.1, 69.9, 53.1, 51.5, 38.4, 36.1, 33.1, 31.4, 30.7, 26.6, 23.4, 21.1, 19.3, 6.7, 0.7; IR (neat) 3378 (w), 1673 (s), 1455 (m), 1405 (m), 1382 (m), 1197 (s), 1130 (s) cm⁻¹; LRMS (EI, 70 eV) m/z (rel intensity) 328(9), 280(100), 264(9), 208(22), 190(29), 162(19), 84(88); HRMS (electrospray) calcd for C₂₄H₄₀NO₂Si (M+H)⁺ 402.2828, found 402.2835.



(6a*S,9a*R**,9b*R**)-6a-Ethyldecahydro-pyrrolo[3,2,1-*i,j*]-quinolin-9-one (6b).** The salt **25** (0.0329 g, 0.0638 mmol) was dissolved in THF (1 mL) and NH₃ (approximately 1 mL) was condensed into the flask at -78 °C. An argon balloon was then attached to the reaction vessel, and small pieces of lithium metal were added until a blue color persisted. The reaction was stirred at -78 °C for 2.5 h before it was allowed to slowly warm to rt and the NH₃ evaporate. Upon warming, a slurry resulted which was dissolved in water and stirred for 5 min before the addition of Na₂CO₃ (10% aqueous solution). The reaction mixture was extracted with 3 portions CH₂Cl₂, dried over sodium sulfate, and the solvent removed *in vacuo*.

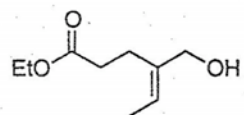
A mixture of the desired alcohol and what appears to be a somewhat stable hemiacetal was observed by ¹H NMR. To convert the undesired product into the alcohol, the crude products were dissolved in THF (0.3 mL), MeOH (0.9 mL), and HCl (0.1 mL of 0.25 M aqueous solution) and allowed to react for 1 h at rt. The reaction mixture was then made basic by the addition of Na₂CO₃ (10% aqueous solution), extracted with CH₂Cl₂, dried over sodium sulfate, and the solvent removed to afford 20.9 mg of an extremely polar yellow residue. To avoid loss of material, further purification was avoided.

The residue was dissolved in CH₂Cl₂ (3.19 mL), cooled to 0 °C, and solid Dess-Martin Periodinane (0.1082 g, 0.2552 mmol) was added in one portion. After 5 min, the bath was removed and the reaction mixture allowed to warm to rt. After stirring for 1 h total, sodium sulfite (5 mL of a saturated aqueous solution) was added to the reaction mixture, and allowed to

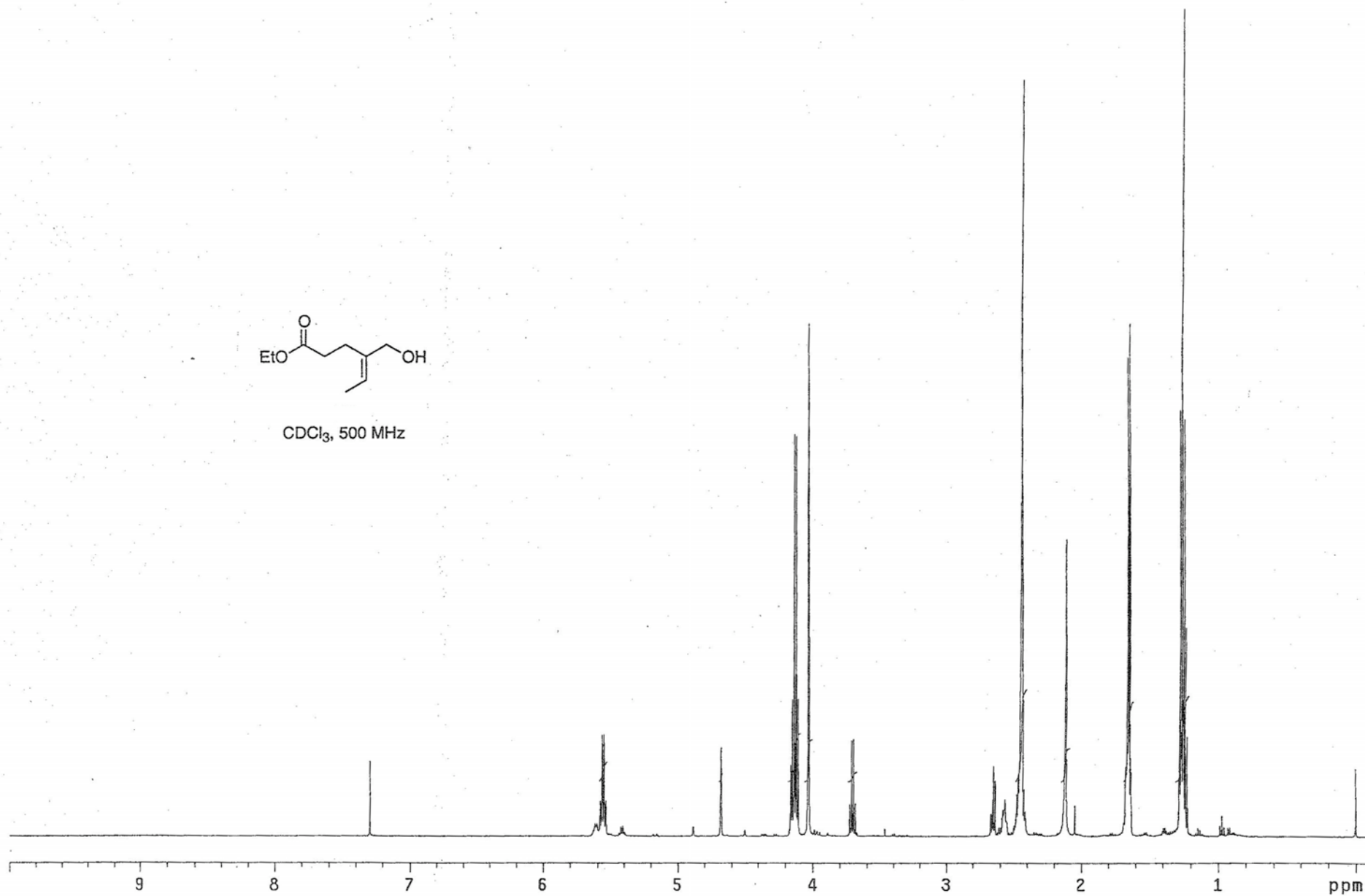
react for 30 min. The reaction was then diluted with ether and washed sequentially with two portions of a saturated aqueous solution of NaHCO_3 and brine. The solvent was then removed to give a mixture of the desired ketone **6** and the corresponding α -silylketone.

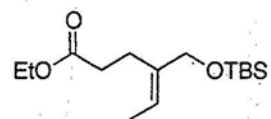
To fully eliminate the TMS group, the residue was dissolved in ether (2 mL), water (1.8 mL), and HCl (0.2 mL of a 1 M aqueous solution) and stirred for 1 h. The reaction was then made basic with K_2CO_3 (saturated aqueous solution), extracted with 3 portions ether, and the combined extract dried over sodium sulfate. Flash chromatography (0-60% EtOAc/hexanes gradient) afforded 0.0071 g (54%) of a pale yellow oil whose spectral characteristics are in full accord with spectra kindly provided by Professor Aube: $R_f = 0.30$ (50% EtOAc/hexanes); ^1H NMR (CDCl_3 , 500MHz) δ 3.03-2.99 (m, 2H), 2.66 (ddd, 1H, $J = 9.0, 5.0, 2.0$ Hz), 2.44-2.35 (m, 2H), 2.33-2.28 (m, 1H), 2.24 (td, 1H, $J = 13.5, 4.5$ Hz), 1.97-1.58 (m, 7H), 1.52-1.46 (m, 2H), 1.32 (app sextet, 1H, $J = 7.5$ Hz), 1.10 (td, 1H, $J = 13.3, 4.5$ Hz), 0.93 (t, 3H, $J = 7.5$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 211.6, 73.6, 53.3, 53.0, 48.2, 36.9, 34.8, 32.9, 30.1, 26.1, 21.4, 21.3, 7.2; IR (neat) 2932 (s), 2786 (m), 2726 (w), 1710 (s) cm^{-1} ; LRMS (EI, 70 eV) m/z (rel intensity) 207(57), 206(100), 178(59), 150(10), 124(18), 95(14), 82(31); HRMS (EI, 70 eV) calcd for $\text{C}_{13}\text{H}_{21}\text{NO}$ (M) $^+$ 207.1623, found 207.1618.

Compound 15

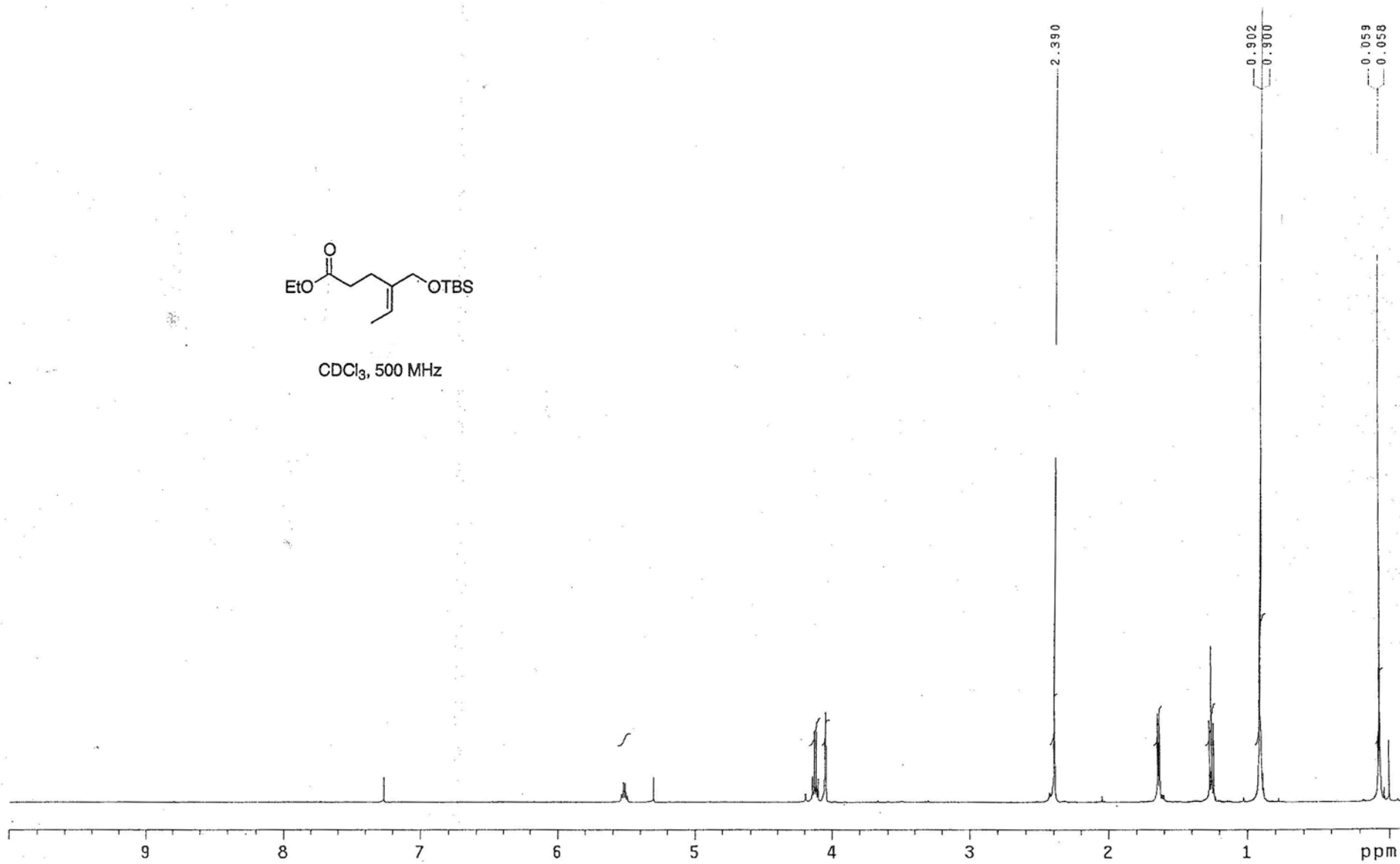


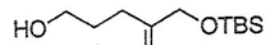
CDCl₃, 500 MHz



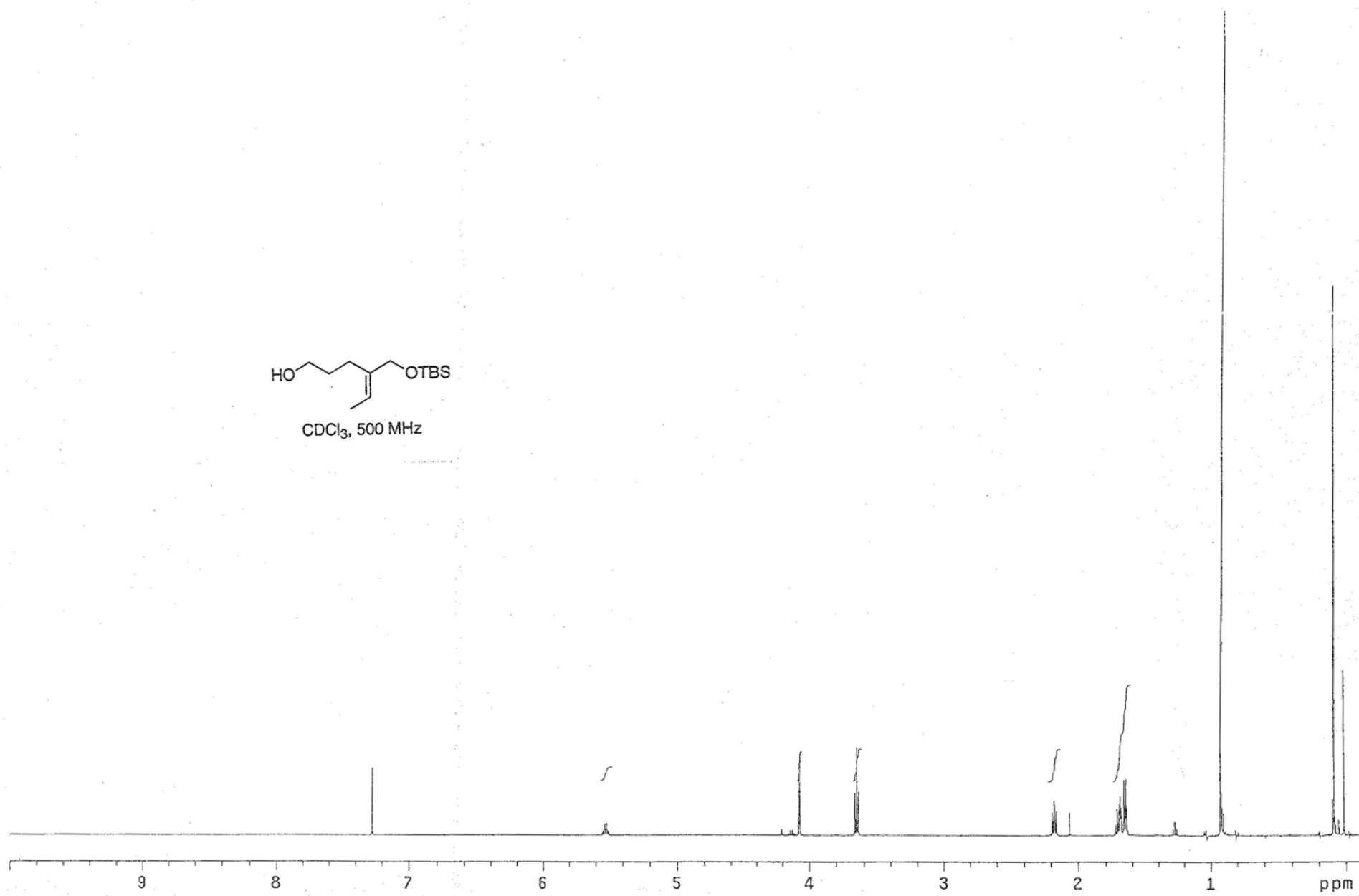


CDCl₃, 500 MHz

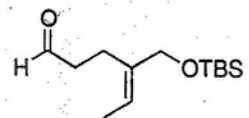




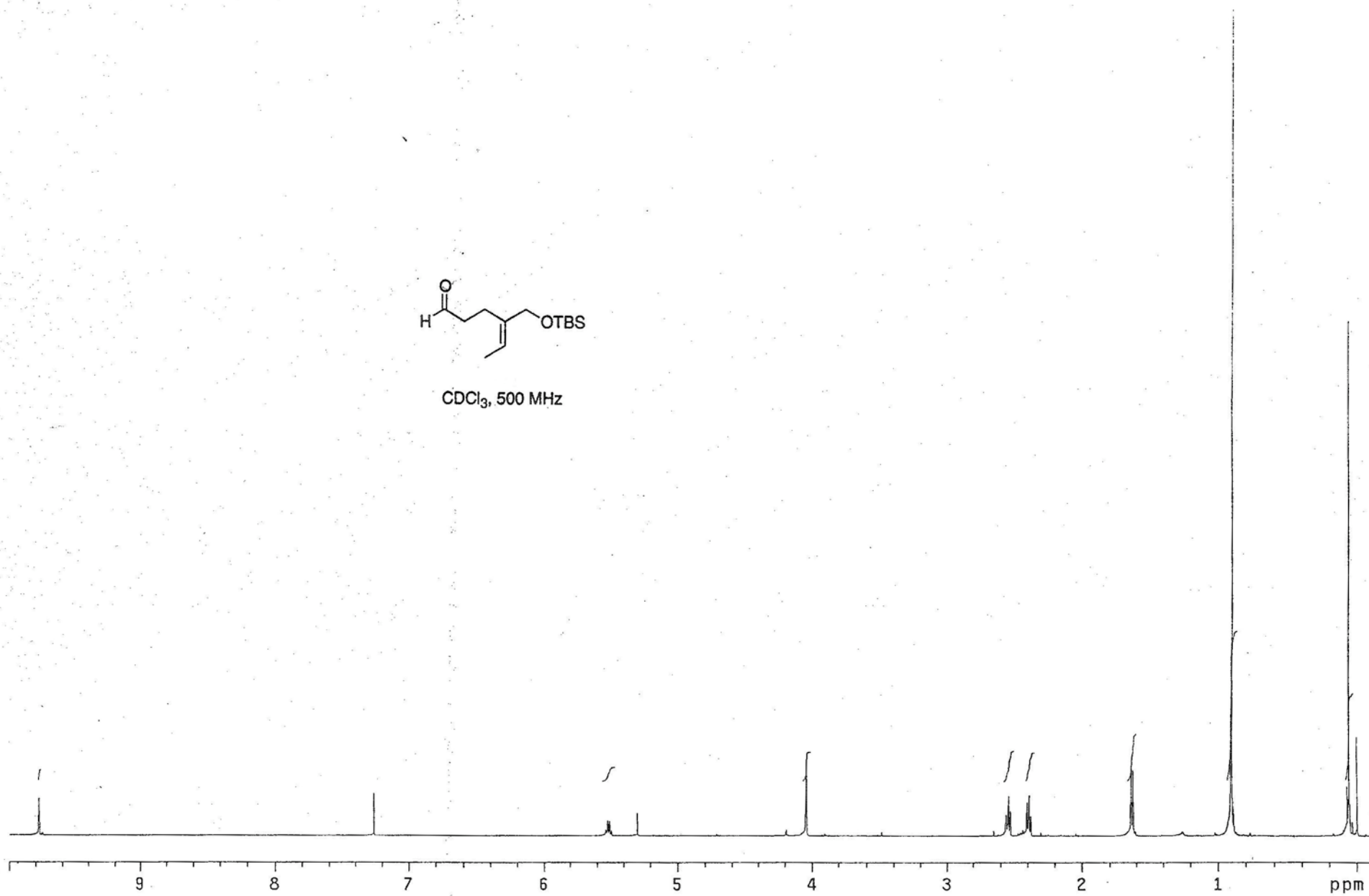
CDCl₃, 500 MHz

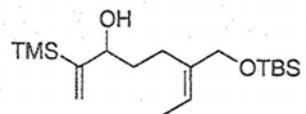


Compound 16

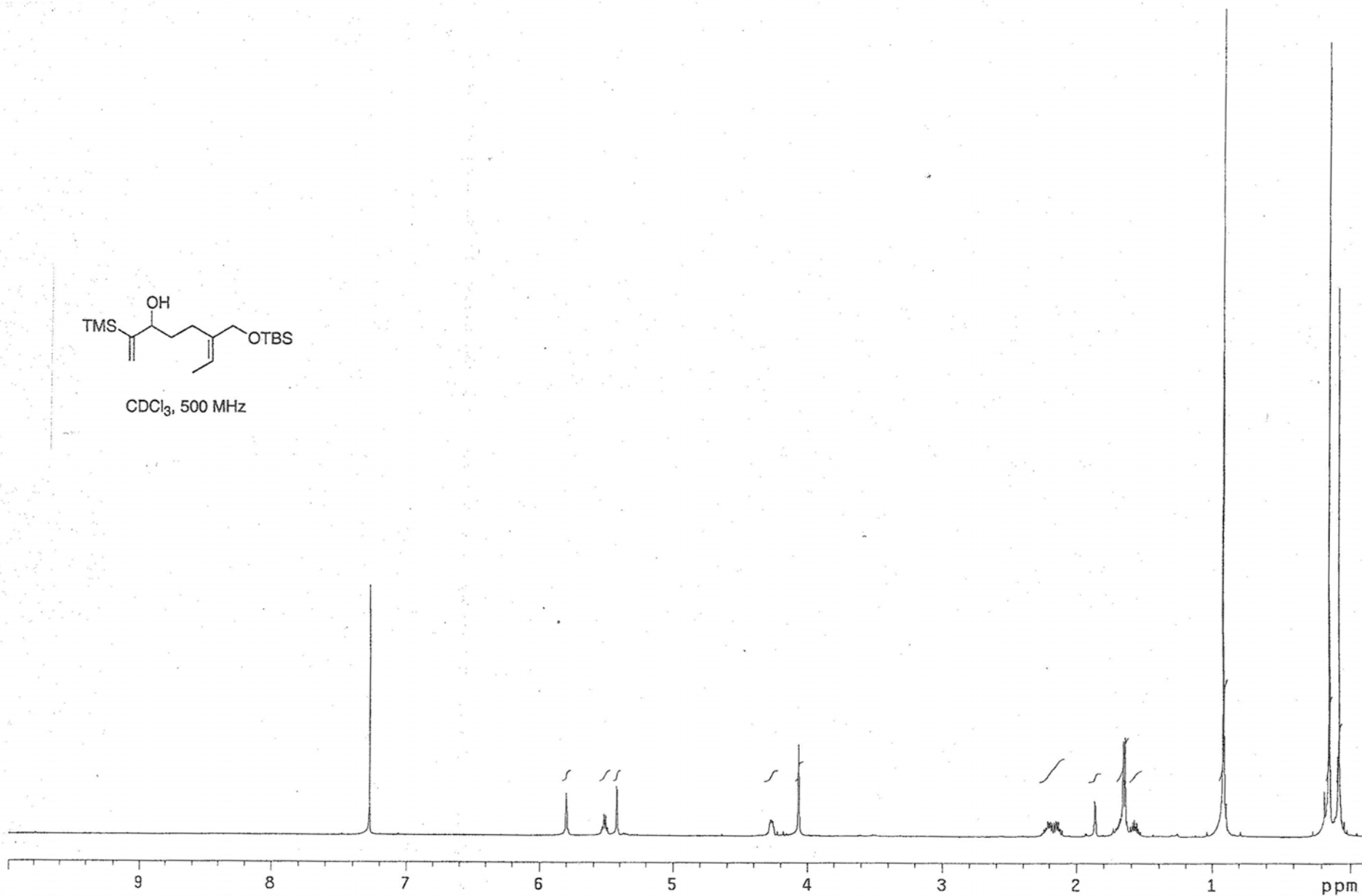


CDCl₃, 500 MHz

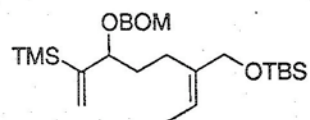




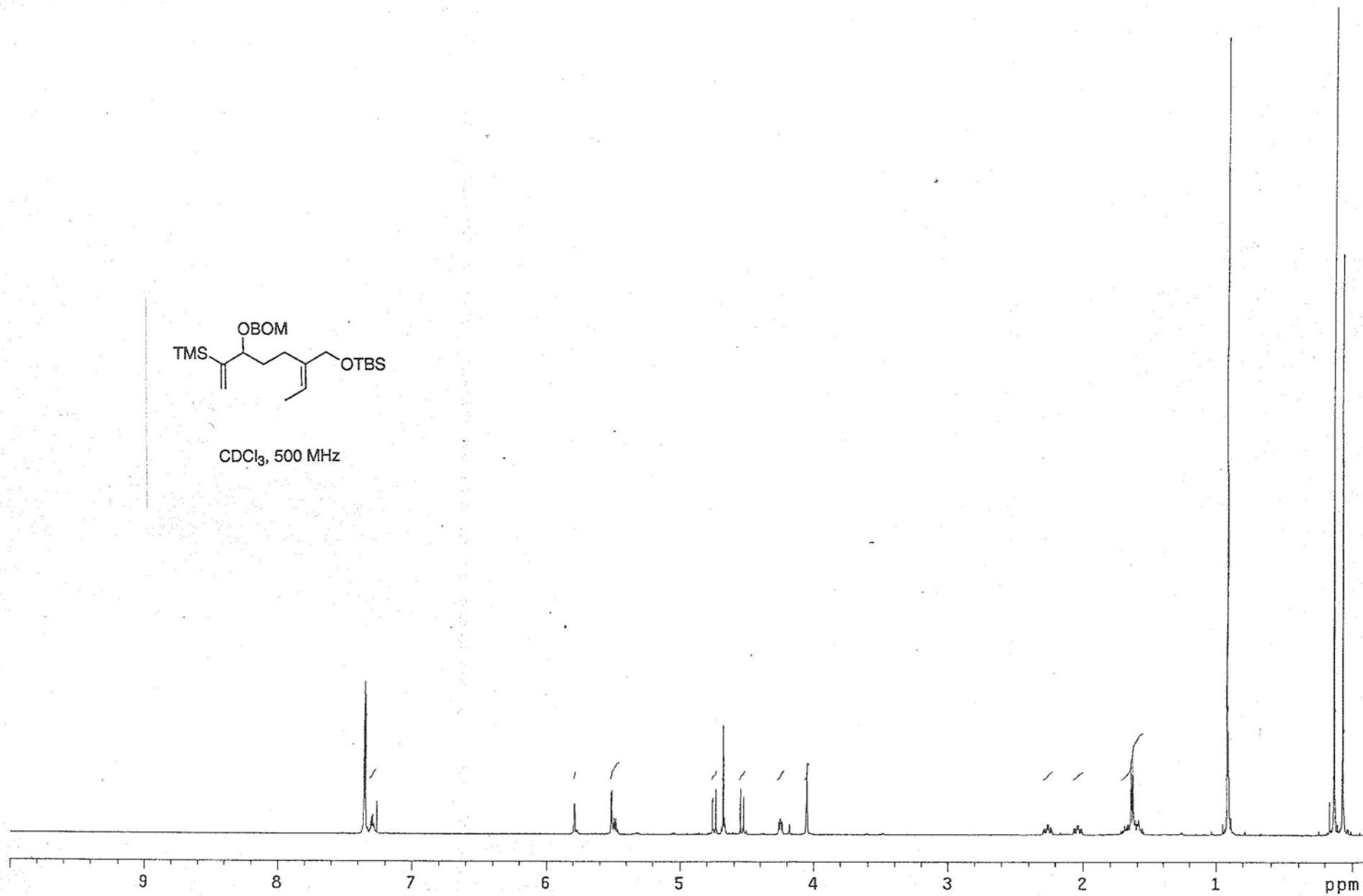
CDCl₃, 500 MHz



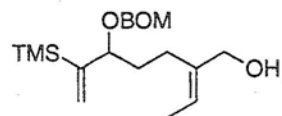
Compound 17



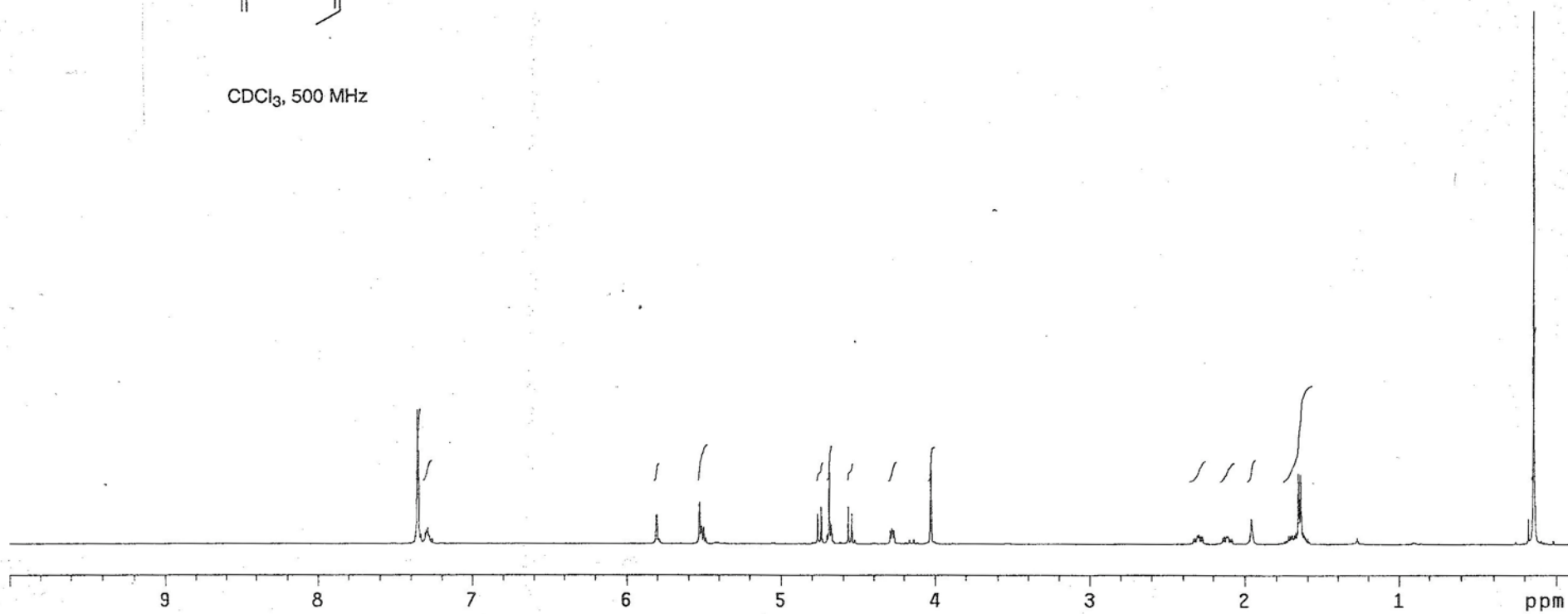
CDCl₃, 500 MHz



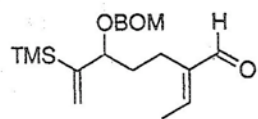
Compound 18



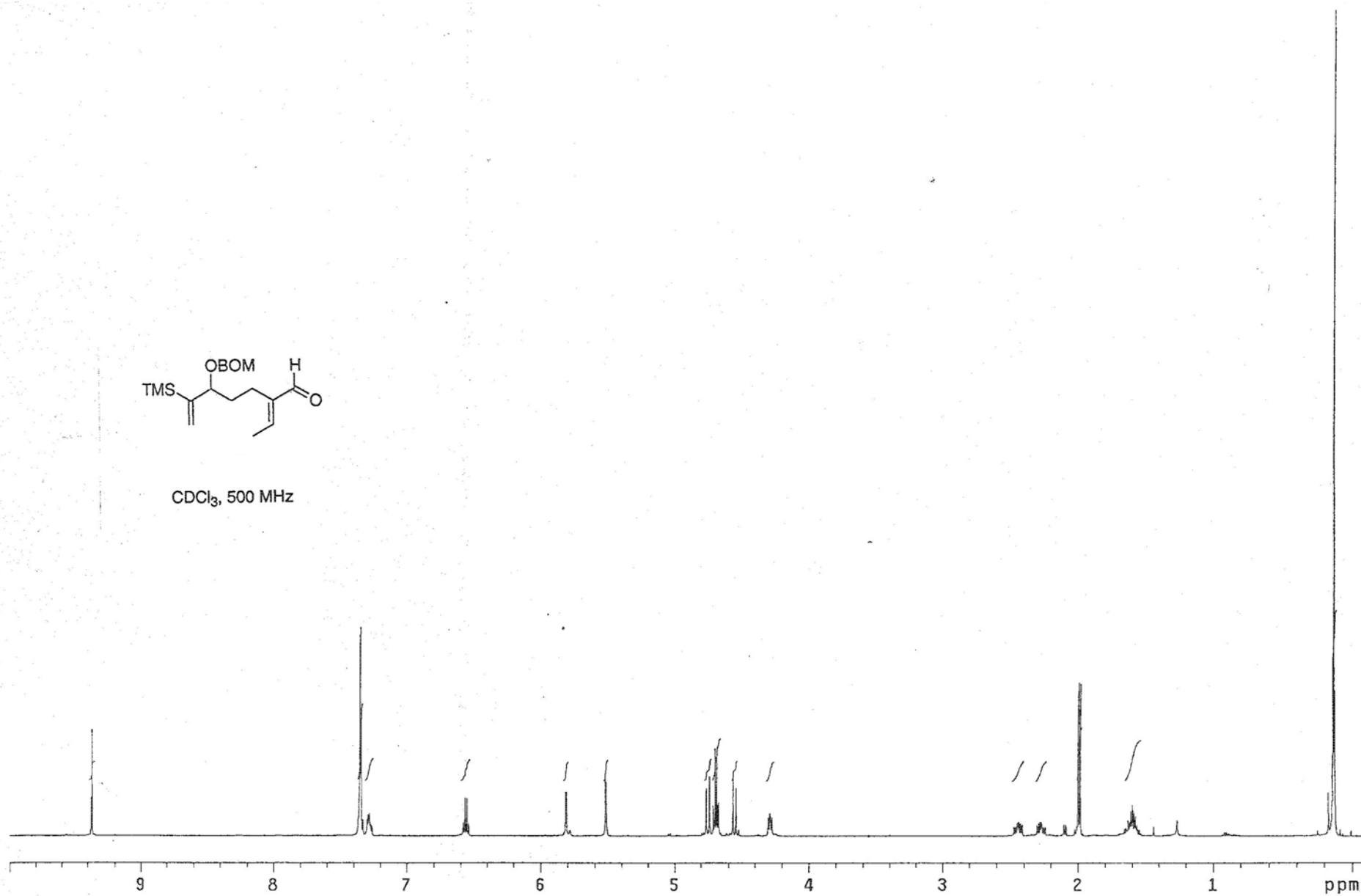
CDCl₃, 500 MHz



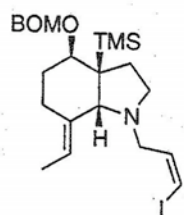
Compound 19



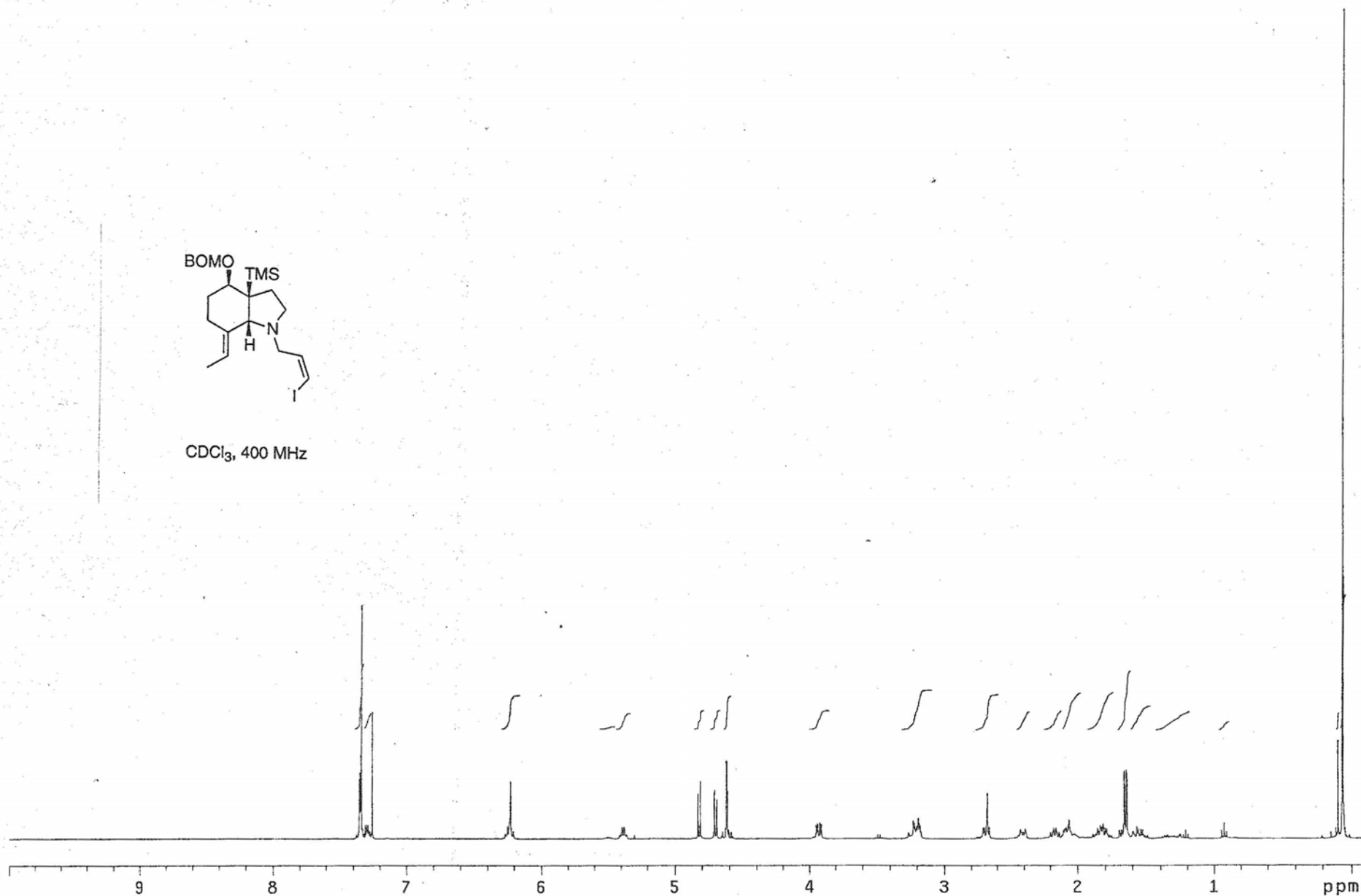
CDCl₃, 500 MHz



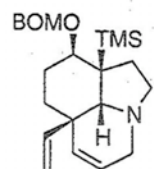
Compound 2



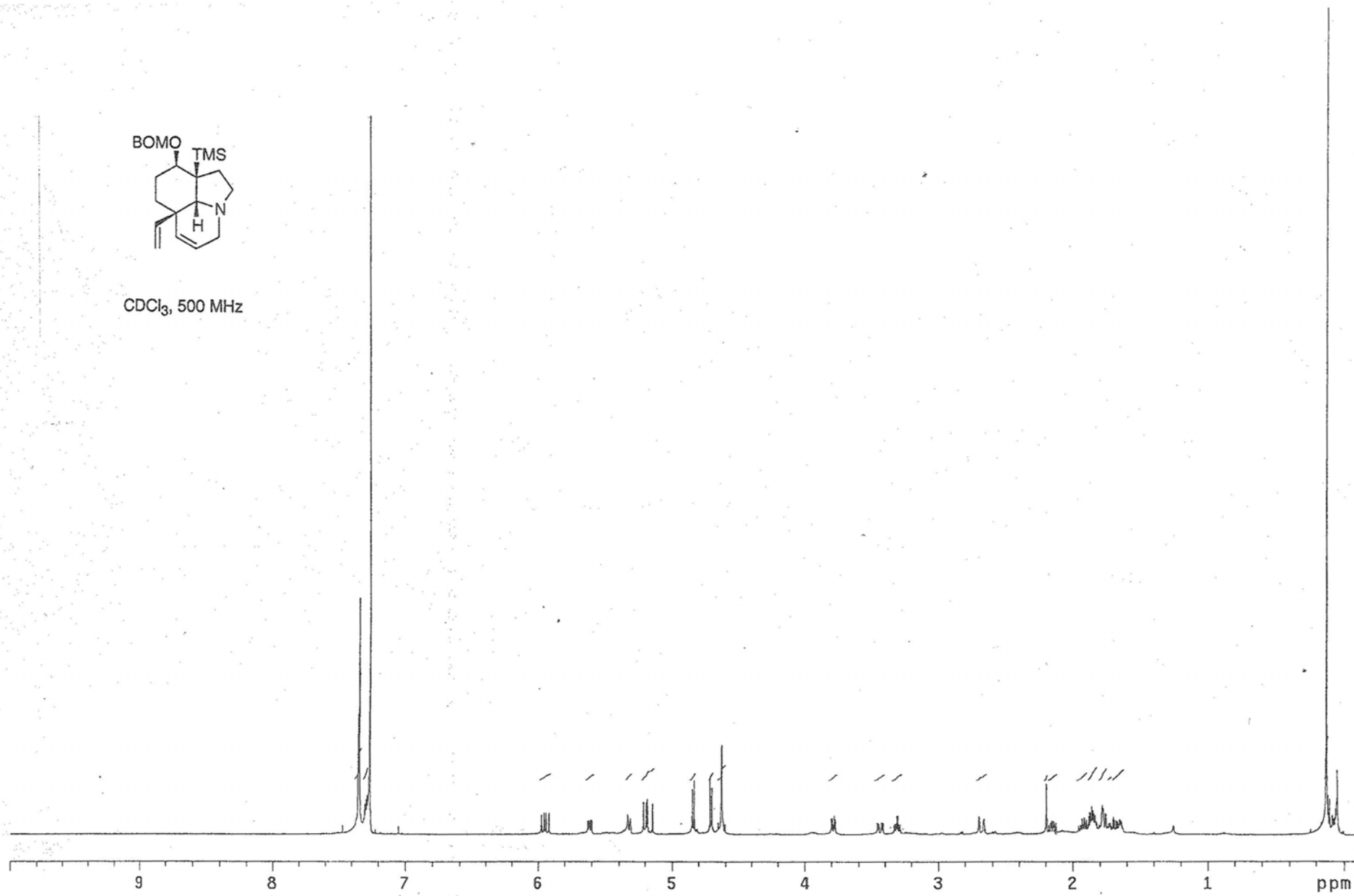
CDCl₃, 400 MHz



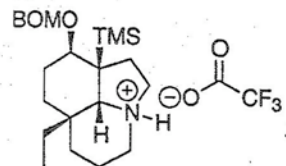
Compound 24



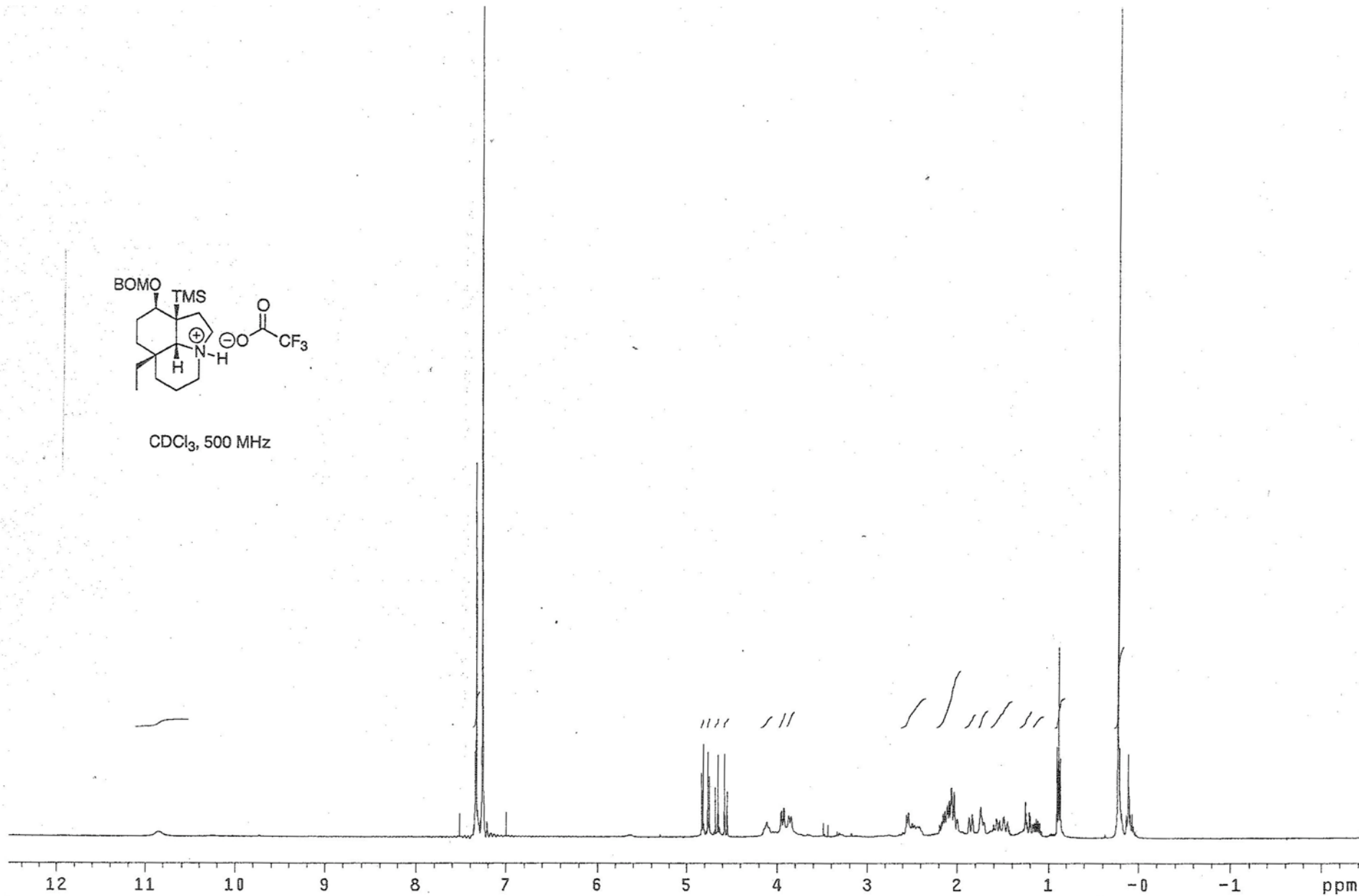
CDCl₃, 500 MHz



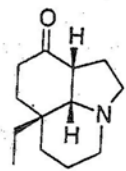
Compound 25



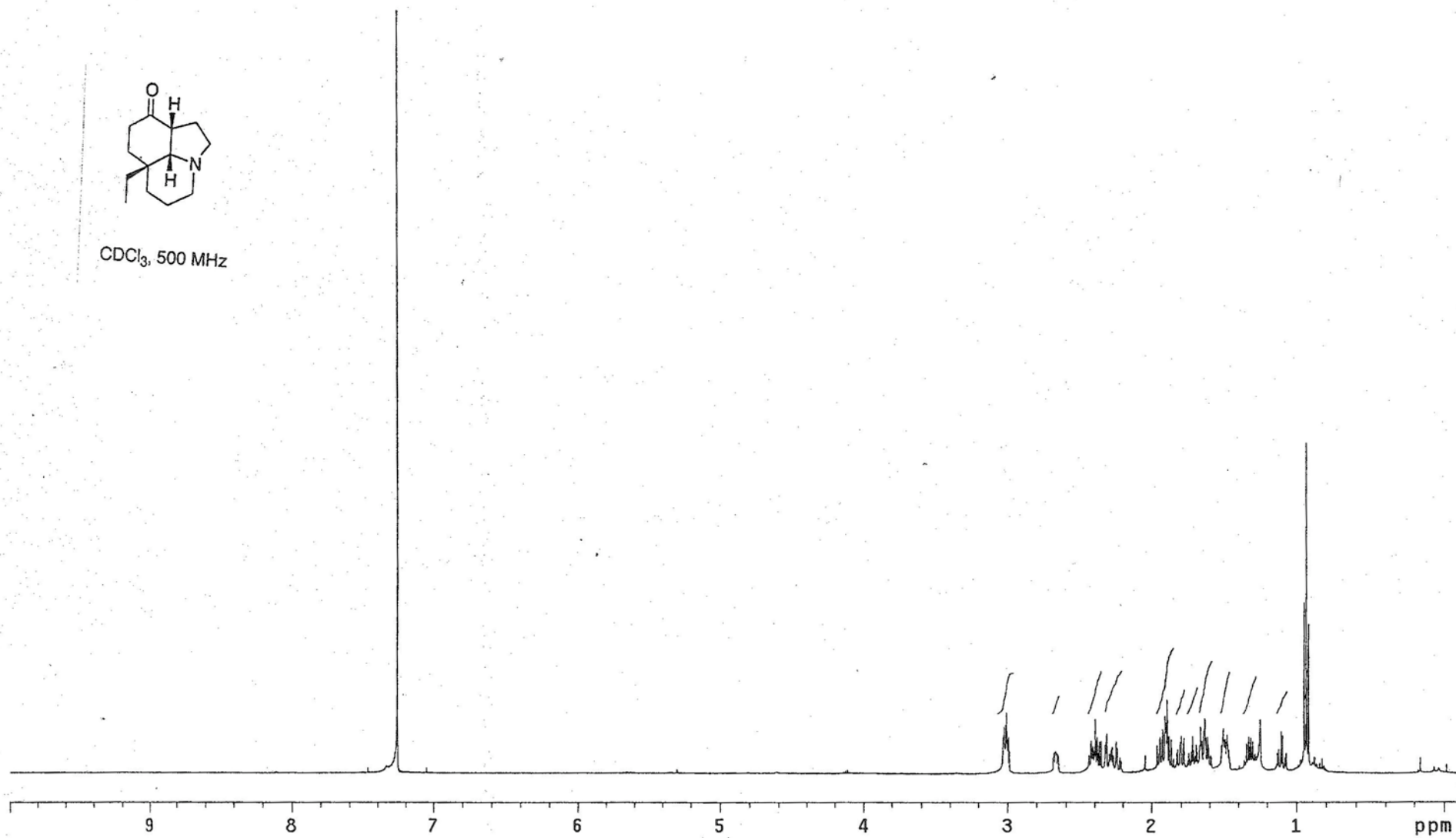
CDCl₃, 500 MHz



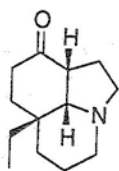
Compound **6b**



CDCl₃, 500 MHz



Compound **6b**



CDCl₃, 100 MHz

