Stereoselective synthesis of (–)-lepadins A–C

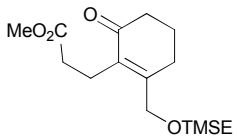
Mercedes Amat,* Alexandre Pinto, Rosa Griera, and Joan Bosch

Laboratory of Organic Chemistry, Faculty of Pharmacy and Institute of Biomedicine (IBUB), University of Barcelona, 08028-Barcelona, Spain,

Supporting Information Available

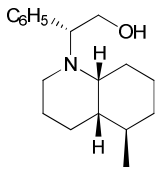
Experimental procedures and spectroscopic data

General Procedures: All air sensitive manipulations were carried out under a dry argon or nitrogen atmosphere. THF was carefully dried and distilled from sodium/benzophenone prior to use. CH_2Cl_2 was dried and distilled from CaH_2. Other solvents and all standard reagents were purchased from Aldrich, Fluka or Alfa Aesar and were used without further purification. Drying of organic extracts during the work-up of reactions was performed over anhydrous Na_2SO_4. Evaporation of solvent was accomphished with a rotatory evaporator. Analytical thin-layer chromatography was performed on SiO_2 (Merck silica gel 60 F_{254}), and the spots were located with 1% aqueous $KMnO_4$. Chromatography refers to flash chromatography and was carried out on SiO_2 (SDS silica gel 60 ACC, 35-75 mm, 230-240 mesh ASTM). NMR spectra were recorded at 400 MHz (^{1}H) and 100.6 MHz (^{13}C), and chemical shifts are reported in δ values downfield from TMS or relative to residual chloroform (7.26 ppm, 77.0 ppm) as an internal standard. Data are reported in the following manner: chemical shift, integrated intensity, multiplicity, coupling constant (J) in hertz (Hz), and assignment (when possible). Assignments and stereochemical determinations are given only when they are derived from definitive two-dimensional NMR experiments (HSQC-COSY). IR spectra were performed in a spectrophotometer Nicolet Avantar 320 FT-IR and only noteworthy IR absorptions (cm^{-1}) are listed. Optical rotations were measured on Perkin-Elmer 241 polarimeter. $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. High resolution mass spectra (HMRS) were performed by Centres Científics i Tecnològics de la Universitat de Barcelona.



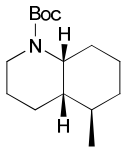
Methyl 6-oxo-2-[2-(trimethylsilyl)ethoxymethyl]cyclohexene-propionate (7): *First step*: EDIPA (0.22 mL, 1.25 mmol) and trifluoromethanesulfonic anhydride (0.21 mL, 1.25 mmol) were added to a solution of methyl 2,6-dioxocyclohexanepropionate (250 mg, 1.25 mmol) in CH_2Cl_2 (10 mL) at –78 ºC, and the mixture was stirred for 45 min. Then CH_2Cl_2 (10 mL) was added, and the resulting mixture was washed with H_2O. The organic layer were dried, and concentrated. Flash chromatography (4:1 hexane-EtOAc) afforded the triflate derivative (260 mg, 65%) as a yellow oil: δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.05-2.14 (2 H, m), 2.42-2.51 (4 H, m), 2.64-2.70 (2 H, m), 2.76-2.80 (2 H, m), 3.67 (3 H, s); δ_C (75.4 MHz; $CDCl_3$; Me_4Si) 19.3 (CH_2), 20.4 (CH_2), 28.7 (CH_2), 32.0 (CH_2), 36.6 (CH_2), 51.6 (CH_3O), 118.1 (CF_3), 130.0 (C), 162.4 (C), 172.4 (COO), 197.0 (CO).

Second step: Degassed toluene (2.7 mL) and degassed H_2O (0.9 mL) were added *via* syringe to a sealed tube containing the above vinyl triflate (100 mg, 0.3 mmol), Cs_2CO_3 (296 mg, 0.9 mmol), $Pd(dppf)Cl_2{\cdot}CH_2Cl_2$ (24.6 mg, 0.03 mmol), and potassium trimethylsilylethoxymethyltrifluoroborate[11b] (108 mg, 0.45 mmol), and the vessel was purged with nitrogen. The reaction mixture was stirred at 100 ºC for 24 h. After cooling to room temperature, EtOAc was added, the resulting suspension was filtered over Celite®, and the filtrate was concentrated. Flash chromatography (7:3 hexane–EtOAc) afforded compound **7** (80 mg, 94%) as a colourless oil: ν = 1739, 1670 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 0.01 (9 H, s, $(CH_3)_3Si$), 0.93-0.97 (2 H, m, CH_2Si), 1.90-1.97 (2 H, m, CH_2), 2.33-2.40 (4 H, m, CH_2), 2.45 (2 H, t, J = 6 Hz, CH_2), 2.59 (2 H, t, J = 7.6 Hz,), 3.49-3.54 (2 H, m, OCH_2), 3.64 (3 H, s, OCH_3), 4.16 (2 H, s, OCH_2); δ_C (100.6 MHz; $CDCl_3$) –1.39 ($3CH_3Si$), 18.2 (CH_2Si), 20.7 (CH_2), 22.2 (CH_2), 28.0 (CH_2), 33.3 (CH_2), 37.9 (CH_2), 51.5 (OCH_3), 68.5 (OCH_2), 69.9 (OCH_2), 134.3 (C=C), 156.0 (C=C), 173.5 (COO), 198.9 (CO); HRMS calcd for [$C_{16}H_{29}O_4Si$ [M + H^+]: 313.183, found 313.1824.

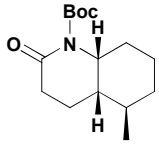


(4a*S*,5*R*,8a*R*)-1-[(1*R*)-2-Hydroxy-1-phenylethyl]-5-methyldecahydroquinoline (2b): $LiAlH_4$ (1.10 g, 28.93 mmol) was slowly added to a suspension of $AlCl_3$ (1.19 g, 8.94 mmol) in THF (94 mL) at 0 ºC. After the mixture was stirred at this temperature for 30 min and cooled to –78 ºC, a solution of lactam **1** (1.27g, 4.45 mmol) in THF (5 mL) was added dropwise. The stirring was continued at –78 ºC for 90 min and at room temperature for 3 h. Water was slowly added, the resulting mixture was filtered over Celite®, and the filtrate was

washed with EtOAc. The organic extracts were dried and concentrated. Flash chromatography (hexane to 8:2 hexane–EtOAc) afforded **2b** (960 mg, 79%) as a colourless oil: $[\alpha]^{22}_{D}$ −41.4 (*c* 0.9 in MeOH); IR (film): ν = 3429 cm^{-1}; δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.85 (3 H, d, *J* = 6.8 Hz, CH_3), 1.01-1.17 (2 H, m, H-4, H-8), 1.25-1.30 (2 H, m, H-4a, H-6), 1.34-1.50 (2 H, m, H-3, H-7), 1.56-1.88 (6 H, m, H-2, H-3, H-4, H-6, H-7, H-8), 2.04-2.08 (1 H, m, H-5), 2.46-2.53 (1 H, m, H-8a), 2.96 (1 H, d, *J* = 10.4 Hz, H-2), 3.60 (1 H, dd, *J* = 10.4, 5.0 Hz, H-2'), 4.03 (1 H, t, *J* = 10.4 Hz, H-2'), 4.24-4.28 (1 H, m, H-1'), 7.20-7.35 (5 H, m, Ar-H); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 19.7 (CH_3), 20.6 (C-7), 21.6 (C-3), 27.0 (C-4), 28.7 (C-5), 29.2 (C-6), 35.4 (C-8), 44.4 (C-4a), 46.1 (C-2), 57.6 (C-8a), 59.9 (C-1' and C-2'), 127.5 (C-*o, m*), 128.1 (C-*p*), 128.9 (C-*o, m*), 135.9 (C-*i*); HMRS calcd for $[C_{18}H_{27}NO + H]^+$: 274.2165, found: 274.2168.

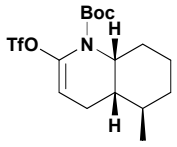


(4a*S*,5*R*,8a*R*)-1-(*tert*-Butoxycarbonyl)-5-methyldecahydroquinoline (3): A solution of **2b** (960 mg, 3.52 mmol) and di-*tert*-butyl dicarbonate (1.0 g, 4.58 mmol) in MeOH (50 mL) containing 40% $Pd(OH)_2$ (380 mg) was stirred under hydrogen at room temperature for 24 h. The catalyst was removed by filtration, and the filtrate was concentrated. Flash chromatography (8:2 hexane–Et_2O) afforded **3** (640 mg, 72%) as an oil: $[\alpha]^{22}_{D}$ –37.3 (*c* 1.1 in MeOH); IR (film): ν = 1693 cm^{-1}; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.76 (3 H, d, *J* = 7.6 Hz, CH_3), 1.19-1.26 (1 H, m, H-6), 1.34-1.43 (3 H, m, H-3, H-4, H-8), 1.45 [9 H, s, $C(CH_3)_3$], 1.51-1.58 (4 H, m, H-4a, H-6, H-7), 1.60-1.77 (4 H, m, H-3, H-4, H-5, H-8), 2.76 (1 H, td, *J* = 13.0, 2.8 Hz, H-2), 3.90 (1 H, d, *J* = 12.0 Hz, H-2), 4.23-4.30 (1H, m, H-8a); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 19.0 (CH_3), 20.1 (C-7), 24.0 (C-4), 25.7 (C-8), 25.9 (C-3), 26.3 (C-6), 28.5 [(CH_3)$_3$C], 34.2 (C-5), 39.5 (C-2), 41.0 (C-4a), 49.5 (C-8a), 79.0 [$(CH_3)_3C$], 155.0 (NCOO); HMRS calcd for $[C_{15}H_{27}NO_2 + H]^+$: 254.1958, found: 254.1970.

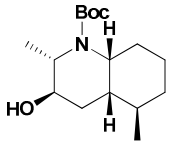


(4a*S*,5*R*,8a*R*)-1-(*tert*-Butoxycarbonyl)-5-methyl-2-oxodecahydroquinoline (4): $NaIO_4$ (1.79 g, 8.37 mmol) and $RuCl_3 \cdot nH_2O$ (17.4 mg, 0.08 mmol) were added to a heterogenous solution of **3** (212 mg, 0.84 mmol) in CCl_4–MeCN–H_2O (6 mL, 3:3:4) at 0 ºC. The mixture was stirred at 0 ºC for 5 min and at room temperature for 1 h. Then, EtOAc was added, the resulting mixture was filtered through Celite®, and the filtrate was concentrated. Flash chromatography (7:3 hexane–EtOAc) afforded **4** (164 mg, 73%) as a white solid: mp 99–102 ºC; $[\alpha]^{23}_{D}$ = – 23.92 (*c* 1.0 in $CHCl_3$); IR (film): ν = 1765, 1712 cm^{-1}; δ_H (400 MHz; $CDCl_3$;

Me_4Si) 1.08 (3 H, d, J = 7.3 Hz, CH_3), 1.20-1.28 (1 H, m, H-7), 1.45-1.68 (5 H, m, H-4, H-6, H-7, H-8), 1.51 [9 H, s, $C(CH_3)_3$], 1.76-1.93 (3 H, m, H-4a, H-5, H-6), 2.05-2.17 (1 H, m, H-4), 2.39-2.59 (2 H, m, H-3), 4.13-4.21 (1H, m, H-8a); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 19.0 (CH_3), 19.8 (C-7), 23.0 (C-4), 27.2 (C-7), 27.9 [(CH_3)$_3$C], 28.7 (C-6), 32.6 (C-5), 33.4 (C-3), 39.3 (C-4a), 54.6 (C-8a), 82.7 [(CH_3)$_3C$], 153.3 (CO), 171.4 (C-2); HRMS calcd for $[C_{15}H_{25}NO_3 + Na]^+$: 290.1727, found 290.1723.



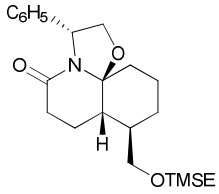
(4a*S*,5*R*,8a*R*)-1-(*tert*-Butoxycarbonyl)-2-(trifluoromethylsulfonyloxy)-5-methyl- 1,4,4a,5,6,7,8,8a-octahydroquinoline: A solution of LiHMDS (1.7 mL of a 1 M solution in THF, 1.7 mmol) in THF (1.7 mL) was added to a solution of lactam **4** (300 mg, 1.12 mmol) in THF (3.8 mL) at –78 ºC, and the mixture was stirred at this temperature for 2 h. Then, a solution of Comins' reagent (880 mg, 2.24 mmol) in THF (3.7 mL) was added, and the reaction mixture was allowed to reach room temperature. After 1.5 h of stirring, the reaction was quenched by addition of 10% aqueous NaOH (6 mL), and the mixture was extracted with Et_2O. The combined organic extracts were dried and concentrated. Flash chromatography with SiO_2 previously deactivated with Et_3N (7:3 hexane–EtOAc) afforded the title vinyl triflate (425 mg, 95%) as a white solid: mp 52-55 ºC; $[\alpha]^{23}_D$ = –62.13 (*c* 1.0 in $CHCl_3$); IR (film): ν = 1675, 1168 cm^{-1}; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.12 (3 H, d, J = 7.2 Hz, CH_3), 1.22-1.29 (2 H, m, H-7), 1.49 [9 H, br s, $C(CH_3)_3$], 1.54-1.62 (4 H, m, H-6, H-8), 1.76-1.86 (2 H, m, H-4a, H-5), 2.21 (2 H, dt, J = 9.2, 3.6 Hz, H-4), 4.47 (1 H, dt, J = 12.4, 3.8 Hz, H-8a), 5.22 (1 H, t, J = 3.8 Hz, H-3); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 18.8 (CH_3), 20.2 (C-6), 24.5 (C-8), 25.3, (C-4), 25.4 (C-7), 28.0 [(CH_3)$_3$C], 32.1 (C-5), 37.2 (C-4a), 52.3 (C-8a), 82.7 [(CH_3)$_3C$], 105.8 (C-3), 118.4 (CF_3), 138.5 (C-2), 152.6 (CO); HRMS calcd for $[C_{16}H_{24}F_3NO_5S + Na]^+$: 422.1219, found 422.1222.



(2*S*,3*R*,4a*S*,5*R*,8a*R*)-1-(*tert*-Butoxycarbonyl)-3-hydroxy-2,5-dimethyldecahydroquinoline (6): *First step*: MeLi (1.56 mL, of a 1.6 M solution in Et_2O, 2.50 mmol) was added to a suspension of CuI (238 mg, 1.25 mmol) in THF (6.3 mL) at –20 ºC, and the mixture was stirred at this temperature for 30 min. After cooling to –78 ºC, the above vinyl triflate (100 mg, 0.25 mmol) in THF (1 mL) was added dropwise. Stirring was continued overnight, allowing the mixture to slowly reach room temperature. Hexane was added, and the

resulting suspension was filtered over Celite®, which was then washed with EtOAc. The filtrates were concentrated, and the resulting residue was dissolved in Et_2O. The solution was filtered through 0.45 μm HPLC filters and concentrated to afford enecarbamate **5**, which was used without further purification in the next step.

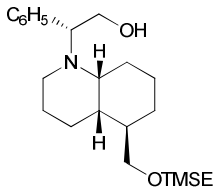
Second step: $BH_3{\cdot}SMe_2$ (1.25 mL of a 2.0 M solution in THF, 2.50 mmol) was added to a solution of the above crude **5** in dry THF (23 mL) at –78 ºC. The mixture was stirred overnight and allowed to slowly warm to room temperature. Then, $Me_3NO{\cdot}2H_2O$ (417 mg, 3.75 mmol) was added, and the mixture was heated at reflux for 45 min. After cooling to room temperature, the solution was concentrated, water was added, and the resulting mixture was extracted with CH_2Cl_2. The combined organic extracts were dried and concentrated. Flash chromatography (hexane to 8:2 hexane–EtOAc) afforded alcohol **6** (55 mg, 78%) as a white solid: mp 133-36 ºC $[\alpha]^{23}_D$ = +7.96 (*c* 0.7 in MeOH); *v* = 3430, 1682 cm^{-1}; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.10 (3 H, d, *J* = 7.6 Hz, CH_3), 1.17 (3 H, d, *J* = 7.2 Hz, CH_3), 1.24-1.32 (2 H, m, H-7), 1.40-1.81 (7 H, m, H-3', H-4, H-5, H-6, H-8), 1.46 [9 H, s, $C(CH_3)_3$], 1.96-2.12 (2 H, m, H-4a, H-4), 3.81 (1 H, br s, H-3), 4.13 (1 H, q, *J* = 7.2 Hz, H-2), 4.21 (1 H, br s, H-8a); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 19.4 (C-5), 20.1 (C-7), 20.3 (CH_3), 26.7, 28.1, 28.5 [$(CH_3)_3C$], 33.1, 33.7, 49.4 (C-8a), 53.5 (C-2), 69.5 (C-3), 79.4 [$(CH_3)_3C$], 155.8 (NCOO); HRMS calcd for $[C_{16}H_{29}NO_3 + H]^+$: 284.2220, found 284.2214.



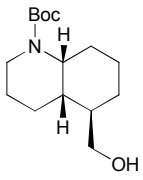
(3*R*,7a*S*,8*R*,11a*S*)-5-Oxo-3-phenyl-8-{[2-(trimethylsilyl)ethoxy]methyl}decahydrooxazolo[2,3-*j*]quinoline (8): *Fisrt step:* (*R*)-Phenylglycinol (878 mg, 6.4 mmol) was added to a solution of ketoester **7** (1.0 g, 3.2 mmol) and AcOH (370 μL, 6.4 mmol) in benzene (40 mL). The mixture was heated at reflux with azeotropic elimination of water by a Dean-Stark system. Additional 1.0 equiv of (*R*)-phenylglycinol and AcOH were added every 24 h to the reaction mixture, until all starting material was consumed. After 72 h, the mixture was cooled and concentrated, and the resulting oil was taken up in EtOAc. The organic solution was washed with saturated aqueous $NaHCO_3$ and brine, dried and concentrated.

Second step: A solution of the above residue in methanol (20 mL) containing 20% Pt_2O (288 mg) was stirred under hydrogen at room temperature for 5 h. The catalyst was removed by filtration, and the solvent was evaporated. Flash chromatography (hexane to 6:4 hexane–EtOAc) afforded compound **8** (860 mg, 67%) as a colourless oil: $[\alpha]_D^{22}$ = –65.1 (*c* 1.0 in MeOH); IR

(film): ν = 1244, 1659 cm^{-1}; δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.01 [9 H, s, $Si(CH_3)_3$], 0.94 (2 H, dd, J = 7.2, 2.4 Hz, CH_2Si), 1.39-1.44 (1 H, m, H-9), 1.52-1.70 (4 H, m, H-9, H-10, H-11), 1.72-1.93 (3 H, m, H-7, H-7a, H-11), 1.97-2.04 (1 H, m, H-8), 2.10-2.23 (1 H, m, H-7), 2.48 (1 H, ddd, J = 18.4, 10.8, 8.0 Hz, H-6), 2.64 (1 H, dd, J = 18.4, 6.8 Hz, H-6), 3.48-3.54 (2 H m, OCH_2), 3.56 (2 H d, J = 7.6 Hz, CH_2O), 3.82 (1 H, t, J = 8.4 Hz, H-2), 4.49 (1 H, t, J = 8.4 Hz, H-2), 5.31 (1 H, t, J = 8.4 Hz, H-3), 7.13-7.34 (5 H, m, Ar-H); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) –1.4, [$Si(CH_3)_3$], 18.2 (CH_2TMS), 18.2 (C-9), 21.8 (C-10), 24.2 (C-7), 30.3 (C-11), 31.0 (C-6), 40.0 (C-8), 40.8 (C-7a), 58.1 (C-3), 68.0 (OCH_2), 69.5 (C-2), 72.2 (CH_2O), 95.0 (C-11a), 125.3, 127.0 (C-*o, m*), 128.4 (C-*p*), 140.2 (C-*i*), 169.3 (C-5); HRMS calcd for $[C_{23}H_{35}NO_3Si + H]^+$: 402.2459, found 402.2455.



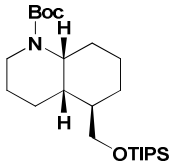
(4a*S*,5*R*,8a*R*)-1-[(1*R*)-2-Hydroxy-1-phenylethyl]-5-{[2-(trimethylsilyl)ethoxy]methyl}decahydroquinoline: Operating as in the above preparation of **2**, from $LiAlH_4$ (844 mg, 22.23 mmol) and $AlCl_3$ (912 mg, 6.84 mmol) in THF (70 mL), and a solution of lactam **8** (1.37g, 3.42 mmol) in THF (5 mL), the title decahydroquinoline (1.01 g, 76%) was obtained as a colourless oil after flash chromatography (6:4 hexane–EtOAc): $[\alpha]_D^{22}$ = –10.08 (*c* 1.25 in MeOH); IR (film): ν = 3438, 1248 cm^{-1}; δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.01 [9 H, s, $Si(CH_3)_3$], 0.94 (2 H, dd, J = 7.2, 2.4 Hz, CH_2Si), 1.14-1.44 (8 H, m), 1.65-1.68 (3 H, m), 1.80-1.85 (2 H, m), 2.38 (1 H, br s), 2.40 (1 H, br s), 2.57 (1 H, br s), 2.93 (1 H, br s), 3.26 (1 H, dd, J = 8.8, 6.4 Hz, OCH_2), 3.32 (1 H, m, OCH_2), 3.63 (1 H, br s, CH_2O), 4.01 (1 H, br s), 4.21 (1 H, br s), 7.21-7.35 (5 H, m, Ar-H). Several of the signals in the ^{13}C NMR spectrum at 25 ºC were broad and ill-defined, even not observed, thus indicating the existence of a slow conformational equilibrium. δ_C (100.6 MHz; $CDCl_3$; Me_4Si) –1.3 [$Si(CH_3)_3$], 18.1 (CH_2), 20.4 (CH_2), 29.7 (CH_2), 30.9 (CH_2), 68.3 (OCH_2), 73.0 (CH_2O), 127.6 (C-*p*), 128.1 (C-*o, m*), 128.9 (C-*o, m*); HRMS calcd for $[C_{23}H_{39}NO_2Si + H]^+$: 390.2823, found 390.2817.



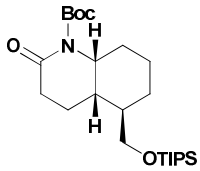
(4a*S*,*5R*,8a*R*)-1-(*tert*-Butoxycarbonyl)-5-(hydroxymethyl)decahydroquinoline (9): *Fisrt step:* $BF_3.Et_2O$ (970 µL, 7.85 mmol) was added to a solution of the above decahydroquinoline (610 mg, 1.57 mmol) in CH_2Cl_2 (11 mL) at 0 ºC. The mixture was allowed

to warm to room temperature and stirred for 2 h. Then, saturated aqueous $NaHCO_3$ was added, the phases were separated, and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried and concentrated to afford the desilylated product (445 mg, 99%) as a white foam.

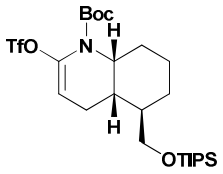
Second step: A solution of the above crude alcohol (690 mg, 2.39 mmol) and di-*tert*-butyl dicarbonate (565 mg, 2.58 mmol) in MeOH (20 mL) was hydrogenated at room temperature for 20 h in the presence of 40% $Pd(OH)_2$ (290 mg). The catalyst was removed by filtration, and the solvent was evaporated. Flash chromatography (7:3 hexane–EtOAc) afforded compound **9** (510 mg, 79%) as a colourless oil: $[\alpha]^{23}_D = -6.7$ (*c* 1.0 in $CHCl_3$); IR (film): ν = 3435, 1693 cm^{-1}; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.13-1.26 (1 H, m), 1.30-1.48 (6 H, m), 1.45 [9 H, s, $C(CH_3)_3$], 1.49-1.57 (1 H, m), 1.58-1.82 (5 H, m), 2.73 (1 H, d, *J* = 8.6 Hz, H-2), 3.58 (1 H, t, *J* = 9.2 Hz, CH_2OH), 3.68 (1 H, t, *J* = 9.2 Hz, CH_2OH), 3.84 (1 H, d, *J* = 8.4 Hz, H-2), 4.11 (1 H, br s, H-8a); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 20.8 (CH_2), 21.8 (CH_2), 23.8 (CH_2), 25.3 (CH_2), 25.9 (CH_2), 28.3 [(CH_3)$_3$C], 35.4 (C-4a), 39.1 (C-2), 42.6 (C-5), 63.5 (CH_2OH), 79.2 [(CH_3)$_3$*C*], 155.1 (NCOO); HRMS calcd for $[C_{15}H_{27}NO_3 + H]^+$: 270.2064, found 270.2061.



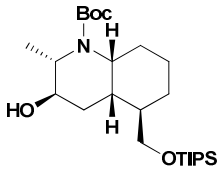
(4a*S*,5*R*,8a*R*)-1-(*tert*-Butoxycarbonyl)-5-(triisopropylsilyloxymethyl)decahydroquinoline: Imidazole (259 mg, 3.80 mmol) and TIPSCl (270 µL, 1.27 mmol) were added to a solution of alcohol **9** (170 mg, 0.63 mmol) in DMF (3.3 mL), and the mixture was stirred at room temperature overnight. Saturated aqueous $NaHCO_3$ was added, and the resulting mixture was extracted with EtOAc. The combined organic extracts were washed with brine, dried, and concentrated. Flash chromatography (9:1 hexane-EtOAc) afforded the TIPS derivative (250 mg, 93%) as a colourless oil: $[\alpha]^{23}_D = +3.24$ (*c* 1.0 in $CHCl_3$); IR (film): ν = 1695 cm^{-1}; δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.99-1.11 [21 H, m, Si(*i*Pr)$_3$)], 1.34-1.83 (9 H, m, H-3, H-4, H-6, H-7, H-8), 1.43 [9 H, s, $C(CH_3)_3$], 1.83-1.92 (3 H, m, H-4a, H-5, H-8), 2.75 (1 H, td, *J* = 12.4, 2.8 Hz, H-2), 3.67-3.78 (2 H, m, CH_2OTIPS), 3.90 (1 H, d, *J* = 12.4 Hz, H-2), 4.12 (1 H, d, *J* = 12.4 Hz, H-8a); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 12.0 [(CH_3-*C*H)$_3$Si], 18.0 [(*C*H$_3$-CH)$_3$Si], 20.8 (CH_2), 21.5 (CH_2), 23.9 (CH_2), 25.5 (CH_2), 26.0 (CH_2), 28.4 [(CH_3)$_3$C], 35.9 (C-4a), 39.0 (C-2), 43.0 (C-5), 49.8 (C-8a), 64.4 (CH_2OTIPS), 79.0 [(CH_3)$_3$*C*], 155.0 (NCOO); HRMS calcd for $[C_{24}H_{47}NO_3Si + H]^+$: 426.3398, found 426.3392.



(4a*S*,5*R*,8a*R*)-1-(*tert*-Butoxycarbonyl)-2-oxo-5-(triisopropylsilyloxymethyl)decahydroquinoline (10): Operating as described for the preparation of **4**, from the above decahydroquinoline (200 mg, 0.47 mmol), $NaIO_4$ (1.81 g, 4.7 mmol), and $RuCl_3{\cdot}nH_2O$ (9.7 mg, 0.05 mmol) in CCl_4–MeCN–H_2O (6 mL, 3:3:4), lactam **10** (200 mg, 97%) was obtained as a colourless oil after flash chromatography (9:1 hexane–EtOAc): $[\alpha]^{23}_D = -3.95$ (*c* 1.0 in $CHCl_3$); IR (film): ν = 1773, 1724, 1246 cm^{-1}; δ_H (400 MHz; $CDCl_3$; Me_4Si) – 0.99-1.15 [21 H, m, Si(*i*Pr)$_3$)], 1.42-1.62 [6 H, m, H-4, H-6, H-7, H-8], 1.50 [9 H, s, C(CH$_3$)$_3$], 1.83-1.92 (2 H, m, H-5, H-8), 2.12-2.24 (2 H, m, H-4, H-4a), 2.44-2.61 (2 H, m, H-3), 3.73 (2 H, td, *J* = 10.6, 7.2, 2.6 Hz, CH_2OTIPS), 4.13 (1 H, ddd, *J* = 10.0, 3.8 Hz, H-8a); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 11.9 [(CH$_3$-*C*H)$_3$Si], 18.0 [(*C*H$_3$-CH)$_3$Si], 20.7 (C-6), 22.4 (C-7), 22.9 (C-4), 27.9 [(*C*H$_3$)$_3$C], 28.4 (C-8), 33.8 (C-3), 33.9 (C-4a), 41.4 (C-5), 54.9 (C-8a), 64.5 (CH_2OTIPS), 82.7 [(CH$_3$)$_3$*C*], 153.1 (NCOO), 171.4 (C-2); HRMS calcd for [$C_{24}H_{45}NO_4Si$ – BOC + H]$^+$: 340.2666, found 340.2661.

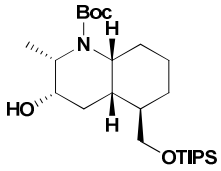


(4a*S*,5*R*,8a*R*)-*1*-(*tert*-Butoxycarbonyl)-2-(trifluoromethylsulfonyloxy)-5-(triisopropylsilyloxymethyl)-1,4,4a,5,6,7,8,8a-octahydroquinoline: Operating as described for the preparation of the vinyl triflate derived from **4,** from lactam **10** (170 mg, 0.39 mmol), LiHMDS (580 µL of a 1 M solution in THF, 0.58 mmol), and Comins' reagent (304 mg, 0.774 mmol) in THF for 2.5 h at room temperature, the title vinyl triflate (198 mg, 90%) was obtained as a yellowish oil after flash chromatograpy (SiO_2 pre-treated with Et_3N; 9:1 hexane–EtOAc): $[\alpha]^{23}_D = -30.32$ (*c* 1.0 in $CHCl_3$); IR (film): ν = 1724, 1688, 1137 cm^{-1}; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.01-1.14 [21 H, m, Si(*i*Pr)$_3$)], 1.41-1.66 [6 H, m, H-6, H-7, H-8], 1.47 [9 H, s, C(CH$_3$)$_3$], 1.77-1.84 (1 H, m, H-5), 2.14-2.20 (1 H, m, H-4a), 2.27-2.21 (2 H, m, H-4), 3.74 (2 H, td, *J* = 10.6, 7.4, 3.6 Hz, CH_2OTIPS), 4.39 (1 H, ddd, *J* = 11.6, 4.2 Hz, H-8a), 5.23 (1 H, t, *J* = 4.2 Hz, H-3); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 12.0 [(CH$_3$-*C*H)$_3$Si], 18.0 [(*C*H$_3$-CH)$_3$Si], 21.1 (CH_2), 21.2 (CH_2), 24.3 (CH_2), 25.2 (C-4), 27.9 [(*C*H$_3$)$_3$C], 31.8 (C-4a), 41.1 (C-5), 52.8 (C-8a), 64.1 (CH_2OTIPS), 82.6 [(CH$_3$)$_3$*C*], 105.6 (C-3), 118.4 (q, CF_3), 138.4 (C-2), 152.4 (NCOO); HRMS calcd for [$C_{25}H_{44}F_3NO_6SSi + NH_4$]$^+$: 589.2943, found 589.2949.



(2*S*,3*R*,4a*S*,5*R*,8a*R*)-1-(*tert*-Butoxycarbonyl)-3-hydroxy-2-methyl-5-(triisopropylsilyloxymethyl)decahydroquinoline (12): *First step*: Operating as in the preparation of **5**, from a solution of the above triflate (770 mg, 1.35 mmol) in THF (6 mL), MeLi (8.44 mL, of a 1.6 M solution in Et_2O, 13.5 mmol), and CuI (1.29 g, 6.75 mmol) in THF (35 mL), enecarbamate **11** was obtained.

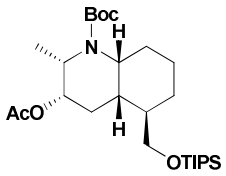
Second step: Operating as in the preparation of **6**, from a solution of the above crude **11** in THF (135 mL), $BH_3{\cdot}SMe_2$ (6.75 mL of a 2.0 M solution in THF, 13.5 mmol), and $Me_3NO{\cdot}2H_2O$ (2.25 g, 20.25 mmol), alcohol **12** (500 mg, 81%) was obtained as a yellowish oil after flash chromatography (9.5:0.5 CH_2Cl_2–MeOH): $[\alpha]^{23}_D = +19.45$ (*c* 0.6 in $CHCl_3$); IR (film): ν = 3432, 1687, 1662, 1245 cm^{-1}; δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.99-1.14 [21 H, m, Si(*i*Pr)$_3$)], 1.15 (3 H, d, *J* = 13.2 Hz, CH_3), 1.34-1.79 (8 H, m, H-4, H-5, H-6, H-7, H-8), 1.45 [9 H, s, C$(CH_3)_3$], 1.77-1.84 (1 H, m, H-5), 2.06-2.16 (1 H, m, H-4), 2.20-2.27 (1 H, m, H-4a), 3.65-3.79 (2 H, m, CH_2OTIPS), 3.82 (1 H, br s, H-3), 4.04-4.19 (2 H, m, H-2, H-8a); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 12.0 [(CH_3-*C*H)$_3$Si], 18.0 [(*C*H_3-CH)$_3$Si], 20.0 (CH_3), 21.0 (CH_2), 21.7 (CH_2), 27.9 (2 carbons), 28.4 [(*C*H_3)$_3$C and CH_2], 42.4 (C-5), 50.2 (C-2), 53.4 (C-8a), 64.5 (CH_2OTIPS), 69.4 (C-3), 79.4 [(CH_3)$_3$*C*], 155.7 (NCOO); HRMS calculated for$[C_{25}H_{49}NO_4Si + H]^+$: 456.3504, found 456.3497.



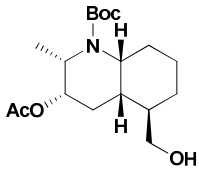
(2*S*,3*S*,4a*S*,5*R*,8a*R*)-1-(*tert*-Butoxycarbonyl)-3-hydroxy-2-methyl-5-(triisopropylsilyloxymethyl)decahydroquinoline (13): *Fisrt step*: Dess-Martin periodinane (1.05 g, 2.48 mmol) was added to a solution of alcohol **12** (750 mg, 1.65 mmol) in CH_2Cl_2 (118 mL). The resulting white suspension was stirred at room temperature for 2.5 h. Then, the mixture was filtered through Celite® and the filtrate was concentrated.

Second step: $NaBH_4$ (250 mg, 6.6 mmol) was added to a solution of the above residue in MeOH (24 mL) at –55 ºC, and the mixture was stirred overnight at –40 ºC. Then, the mixture was filtered and the filtrate was concentrated. Flash chromatography (7:3 hexane–EtOAc) afforded alcohol **13** (630 mg, 84%) as a colourless oil: $[\alpha]^{23}_D = -30.32$ (*c* 1.0 in $CHCl_3$); IR (NaCl): 3432, 1665 cm^{-1} δ_H (400 MHz; $CDCl_3$; Me_4Si, amide rotamers) 1.04 [21 H, br s, Si(*i*Pr)$_3$)], 1.15 (3 H, d, *J* = 6.8 Hz, CH_3), 1.33-2.06 (10 H, m, H-4, H-5, H-6, H-7, H-8), 1.44 [9 H, s, C$(CH_3)_3$], 3.59 (2 H, m, CH_2OTIPS), 3.80-3.88 (1 H, m, H-3), 3.96 and 4.02 (1 H, br, H-8a), 4.30 and 4.43 (1

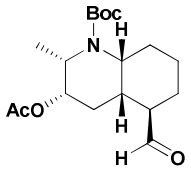
H, br s, H-2); δ_C (100.6 MHz; $CDCl_3$; Me_4Si, amide rotamers) 12.0 [$(CH_3$-*C*H$)_3Si$], 14.8 and 14.6 (1 carbon in 2:1 ratio, CH_3), 18.0 [(*C*H_3-CH$)_3Si$], 21.6 and 21.0 (1 carbon in 2:1 ratio, CH_2), 22.7 and 22.1 (1 carbon in 2:1 ratio, CH_2), 28.4 [(*C*$H_3)_3$C], 28.8 and 28.2 (1 carbon in 2:1 ratio, CH_2), 30.1 and 29.7 (1 carbon in 2:1 ratio, C-4), 35.3 and 34.5 (1 carbon in 2:1 ratio, C-4a), 43.1 and 42.6 (1 carbon in 2:1 ratio, C-5), 49.9 and 49.3 (1 carbon in 2:1 ratio, C-8a), 50.7 and 50.0 (1 carbon in 2:1 ratio, C-2), 64.6 (CH_2OTIPS), 70.1 (C-3), 79.4 [$(CH_3)_3$*C*], 155.1 (NCOO); HRMS calcd for $[C_{25}H_{49}NO_4Si + H]^+$: 456.3504, found 456.3497.



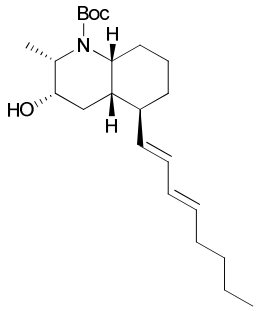
(2*S*,3*S*,4a*S*,5*R*,8a*R*)-3-Acetoxy-1-(*tert*-butoxycarbonyl)-2-methyl-5-(triisopropylsilyloxymethyl)decahydroquinoline: Et_3N (620 μL, 4.44 mmol) and DMAP (18 mg, 0.15 mmol) were added to a solution of **13** (675 mg, 1.48 mmol) in CH_2Cl_2 (36 mL). The resulting solution was cooled to 0 ºC, Ac_2O (210 μL, 2.22 mmol) was added dropwise, and stirring was continued at room temperature for 3 h. The reaction mixture was diluted with CH_2Cl_2 and quenched with saturated aqueous $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried, and concentrated. Flash chromatography (7:3 hexane–EtOAc) afforded the acetyl derivative (670 mg, 91%) as a colourless oil: $[\alpha]^{23}_D$ = +4.33 (*c* 2.0 in $CHCl_3$); IR (NaCl): 1740, 1687, 1238 cm^{-1}; δ_H (400 MHz; $CDCl_3$; Me_4Si, amide rotamers) 0.91-1.11 [21 H, br s, Si(*i*Pr)$_3$)], 1.13 (3 H, d, *J* = 6.8 Hz, CH_3), 1.30-1.94 (10 H, m, H-4, H-4a, H-5, H-6, H-7, H-8), 1.44 [9 H, s, C$(CH_3)_3$], 2.05 (3 H, s, CH_3CO_2), 3.61-3.78 (2 H, m, CH_2OTIPS), 4.0 and 4.05 (1 H, br s, H-8a), 4.38 and 4.50 (1 H, br s, H-2), 4.88 (1 H, ddd, *J* = 11.2, 4.6 Hz, H-3); δ_C (100.6 MHz; $CDCl_3$; Me_4Si, amide rotamers) 12.0 [$(CH_3$-*C*H$)_3Si$], 15.4 and 15.7 (CH_3), 17.7 and 18.0 [(*C*H_3-CH$)_3Si$], 20.9 and 21.4, 21.2 (CH_2), 21.8 (CH_2), 24.3 (CH_2), 25.2 (C-4), 26.5, 28.1 [(*C*$H_3)_3$C], 28.4 (CH_2), 35.0 (C-4a), 43.0 (C-5), 48.0 (C-2), 49.4 (C-8a), 64.4 (CH_2OTIPS), 71.9 (C-3), 79.7 [$(CH_3)_3$*C*], 154.8 (NCOO), 170.1 (COO); HRMS calcd for $[C_{27}H_{51}NO_5Si + H]^+$: 498.3609, found 498.3611.



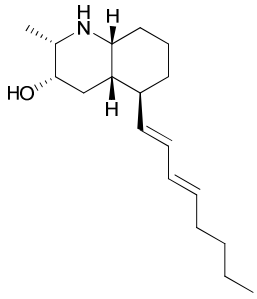
(2*S*,3*S*,4a*S*,5*R*,8a*R*)-3-Acetoxy-1-(*tert*-butoxycarbonyl)-5-(hydroxymethyl) -2-methyldecahydroquinoline: TBAF (7.6 mL of a 1 M solution in THF, 7.6 mmol) and AcOH (440 μL, 7.6 mmol) were added to a solution of the above acetate (750 mg, 1.51 mmol) in THF (25 mL), and the mixture was stirred at 30-40 ºC for 24 h. The reaction was quenched with saturated aqueous NH_4Cl and extracted with Et_2O. The combined organic extracts were washed with brine, dried, and concentrated. Flash chromatography (7:3 to 1:1 hexane–EtOAc) afforded the title alcohol (430 mg, 83%) as a yellowish oil: $[\alpha]^{23}_D$ = +7.17 (*c* 1.0 in $CHCl_3$); IR (film): ν = 3309, 1740, 1683 cm^{-1}; δ_H (400 MHz; $CDCl_3$; Me_4Si, amide rotamers) 1.13 (3 H, d, *J* = 6.8 Hz, CH_3), 1.19-1.34 (4 H, m), 1.37-1.90 (6 H, m), 1.44 [9 H, s, $C(CH_3)_3$], 1.92-2.11 (5 H, m, CH_3, H-4, H-4a), 3.60-3.79 (2 H, m, CH_2OH), 4.11 (1 H, ddd, *J* = 10.8, 7.4, 3.0Hz, H-8a), 4.37 and 4.47 (1 H, br s, 2:1 ratio, H-2) 4.84-4.95 (1 H, m, H-3); δ_C (100.6 MHz; $CDCl_3$; Me_4Si, amide rotamers) 15.8 (CH_3), 21.1 (2 carbons CH_2, CH_3COO), 22.4 (CH_2), 22.6 (CH_2), 26.4 (C-4), 28.0 and 28.4 [$(CH_3)_3C$], 31.6 (CH_2), 34.6 (C-4a), 42.6 (C-5), 48.0 (C-2), 49.0 (C-8a), 64.1 (CH_2OH), 71.7 (C-3), 79.8 [$(CH_3)_3C$], 154.9 (NCOO), 170.1 (COO); HRMS calcd for $[C_{18}H_{31}NO_5 + H]^+$: 342.2275, found 342.227.



(2*S*,3*S*,4a*S*,5*R*,8a*R*)-3-Acetoxy-1-(*tert*-butoxycarbonyl)-5-formyl-2-methyl decahydroquinoline (14): Dess-Martin periodinane (1.34 g, 3.15 mmol) was added to a solution of the above alcohol (430 mg, 1.26 mmol) in CH_2Cl_2 (92 mL), and the mixture was stirred at room temperature for 3 h. Then, saturated aqueous $Na_2S_2O_3$ (20 mL) and saturated aqueous $NaHCO_3$ (20mL) were added, and the resulting mixture was stirred for 1 h. The phases were separated, and the aqueous phase was extracted with Et_2O. The combined organic extracts were dried and concentrated to afford crude aldehyde **14**, which was used without further purification in the next step.

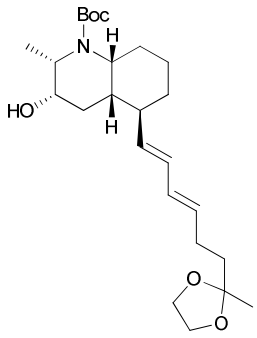


(2*S*,3*S*,4a*S*,5*R*,8a*R*)-1-(*tert*-Butoxycarbonyl)-3-hydroxy-2-methyl-5-[(1'*E*,3'*E*)-1,3-octadienyl]decahydroquinoline (16): KHMDS (570 μL of a 0.5 M solution in toluene, 0.28 mmol) was slowly added at –78 ºC to a solution of phosphonate **15** (67 mg, 0.24 mmol) in THF (1 mL). After the addition was complete, the solution was stirred for 30 min. Then, a solution of the above crude aldehyde **14** (0.06 mmol) in THF (1 mL) was slowly added (10 min), and the resulting mixture was stirred at –78 ºC overnight. The mixture was slowly warmed to room temperature (5 h) and stirred at this temperature for an additional 30 min. Saturated aqueous NH_4Cl was added, and the resulting mixture was extracted with Et_2O. The organic extracts were dried and concentrated. Flash chromatography (9:1 to 7:3 hexane–EtOAc) afforded compound **16** (15 mg, 68%) as a yellowish oil: $[\alpha]^{23}_D = -1.29$ (*c* 1.0 in $CHCl_3$); δ_H (400 MHz; $CDCl_3$; Me_4Si, amide rotamers) 0.89 (3 H, t, *J* = 6.4 Hz, CH_3), 1.15 (3 H, d, *J* = 6.8 Hz, CH_3), 1.21-1.99 (13 H, m, H-4, H-4a, H-6, H-7, H-8, $2CH_2$), 1.45 [9 H, s, $C(CH_3)_3$], 2.06 (2 H, br s), 2.35 (1 H, br s, H-5), 3.77-3.90 (1 H, m, H-3), 4.02 and 4.16 (1 H, br s, 2:1 ratio, H-8a), 4.31 and 4.43 (1 H, br s, 2:1 ratio, H-2), 5.47-5.65 (1 H, m), 5.67-5.85 (1 H, m), 5.90-6.11 (2 H, m); δ_C (100.6 MHz; $CDCl_3$; Me_4Si, amide rotamers) 13.9 (CH_3), 14.7 and 14.9 (1 carbon), 21.1, 22.2 (CH_2), 26.1, 28.0, 28.4 [$(CH_3)_3C$], 29.7 and 29.9 (1 carbon), 31.5 (CH_2), 32.3, 39.4 and 39.8 (1 carbon), 42.5 and 42.8 (1 carbon), 49.0, 50.0 and 50.8, (1 carbon), 70.1 (C-3), 79.5 [$(CH_3)_3C$], 130.2 (CH=), 130.3 (CH=), 133.4 (CH=), 134.7 (CH=), 155.1 (NCOO).

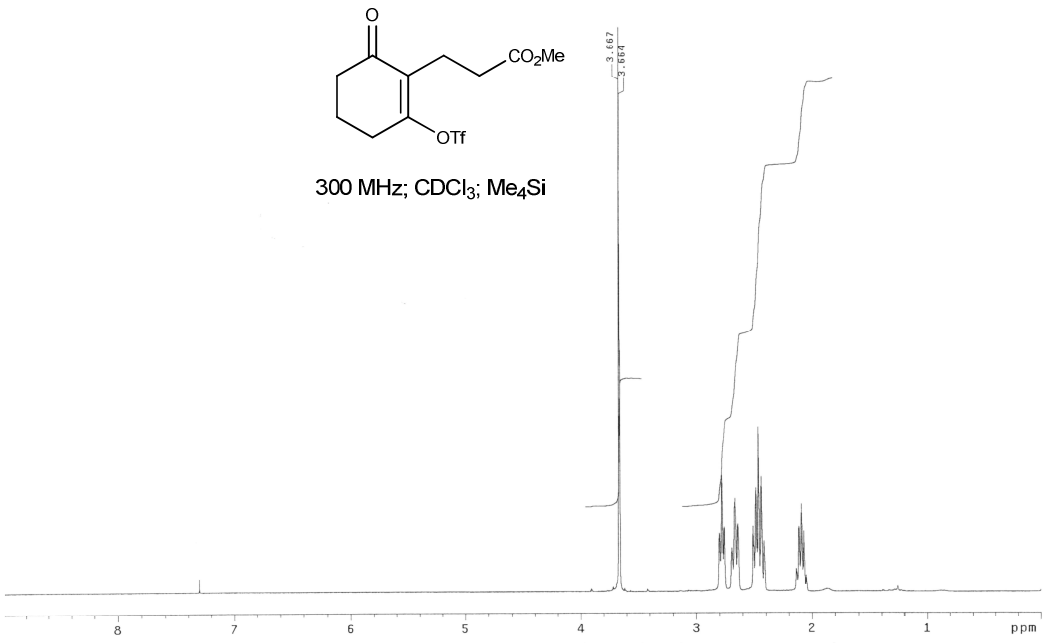


(–)-Lepadin B: TFA (280 μL) was slowly added to a solution of compound **16** (24 mg, 0.06 mmol) in CH_2Cl_2 (2.8 mL) at 0 ºC, and the resulting solution was stirred at room temperature for 1 h. The mixture was concentrated, and the residue was taken up with $CHCl_3$ (11 mL). K_2CO_3 (224 mg) was added, and the resulting suspension was stirred at room temperature for 1 h. The mixture was filtered and concentrated to afford (–)-**lepadin B** (17.6 mg, 99%) as a white solid: $[\alpha]^{23}_D = -74.8$ (*c* 0.55 in MeOH); δ_H (400 MHz; $CDCl_3$;

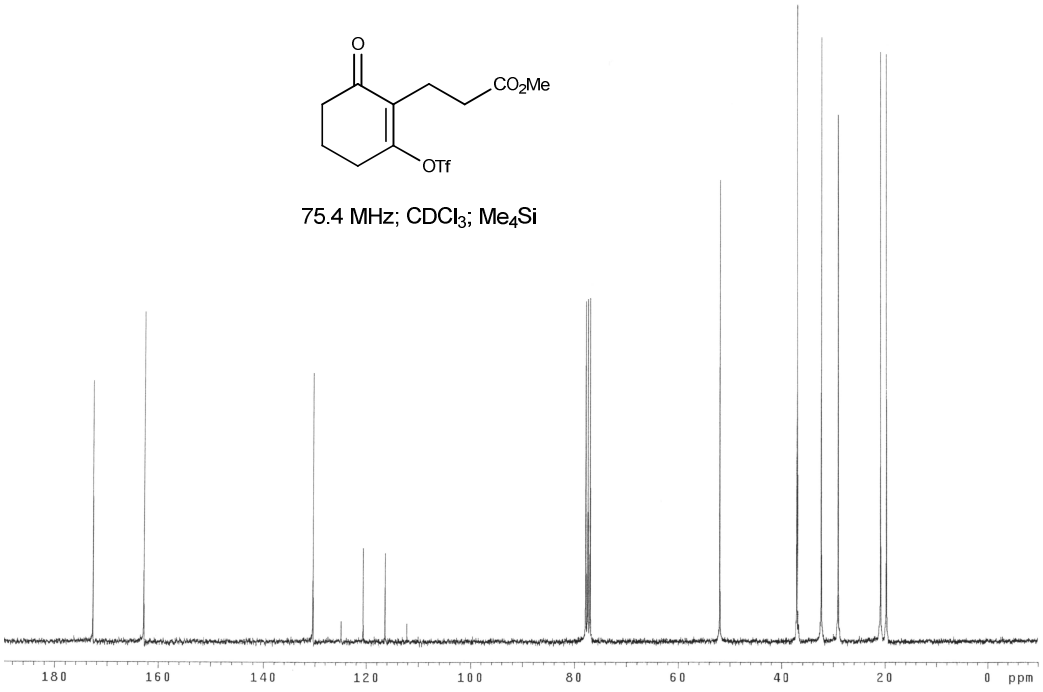
Me_4Si) 0.89 (3 H, t, J = 7.2 Hz, CH_3), 1.13 (3 H, d, J = 6.8 Hz, CH_3), 1.24-1.78 (12 H, m, C-4, C-4a, C-6, C-7, C-8, CH_2), 2.05 (2 H, q, J = 6.8 Hz, CH_2), 2.12 (1 H, ddd, J = 14.4, 2.4 Hz, H-4) 2.61 (1 H, qd, J = 11.6, 3.8 Hz, H-5), 2.79 (1 H, qd, J = 5.1, 1.2 Hz, H-2), 2.96 (1 H, br s, H-8a), 3.54 (1 H, d, J = 1.6 Hz, H-3), 5.37 (1 H, dd, J = 8.8, 2.4 Hz), 5.59 (1 H, dt, J = 14.8, 6.8 Hz), 6.00 (1 H, dt, J = 14.8, 10.0 Hz), 6.08 (1 H, dd, J = 14.8, 10.0 Hz); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 13.9 (CH_3), 18.4 (CH_3), 20.8 (CH_2), 22.3 (CH_2), 31.5 (CH_2), 32.3 (CH_2), 33.0 (C-8), 34.1 (C-4), 34.2 (C-6), 38.7 (C-4a), 41.1 (C-5), 56.2 (C-8a), 56.7 (C-2), 68.8 (C-3), 130.3 (CH=), 130.9 (CH=), 132.8 (CH=), 137.1 (CH=); HRMS calcd for $[C_{18}H_{31}NO + H]^+$: 278.2478, found 278.2473.



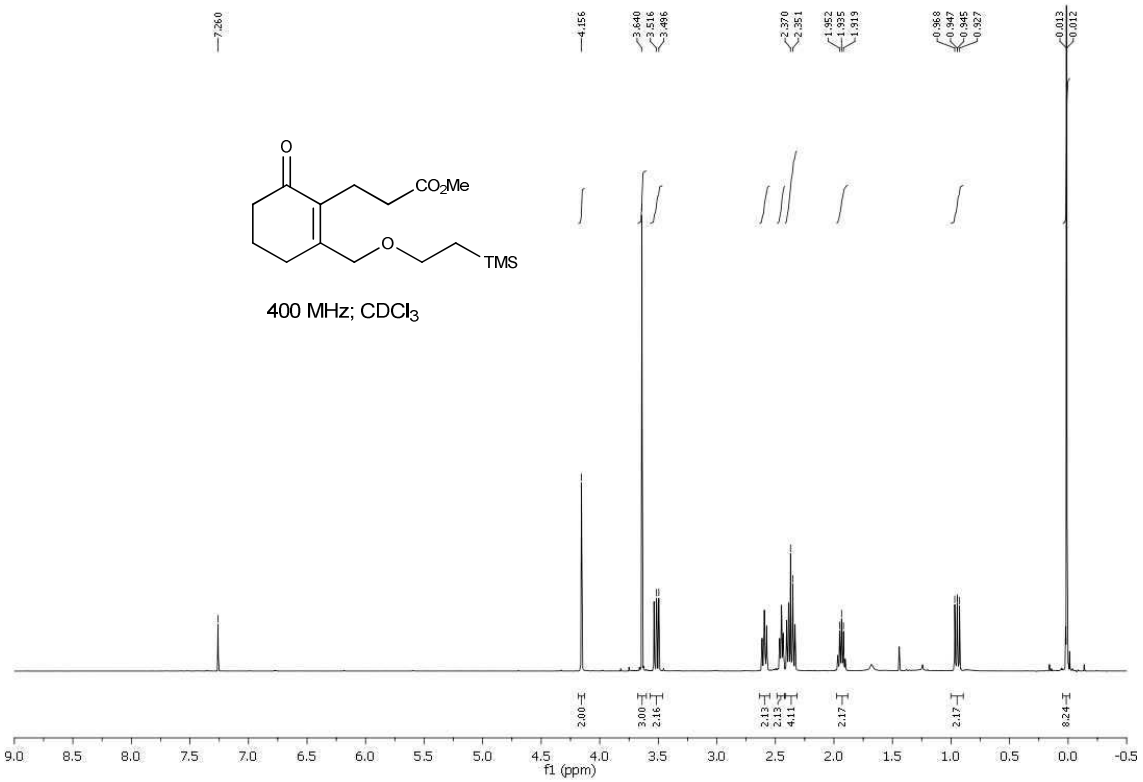
(2*S*,3*S*,4a*S*,5*R*,8a*R*)-1-(*tert*-Butoxycarbonyl)-3-hydroxy-2-methyl-5-[(1'*E*,3'*E*)-7,7-(ethylenedioxy)-1,3-octadienyl]decahydroquinoline (18): NaHMDS (210 µL of a 1.0 M solution in THF, 0.21 mmol) was slowly added at –78 ºC to a solution of phosphonate **17** (62 mg, 0.21 mmol) in DME (1 mL). After the addition was complete, the solution was stirred for 1 h. Then, a solution of the crude aldehyde **14** (0.05 mmol) in DME (1 mL) was slowly added (10 min), and the resulting mixture was stirred at –78 ºC and slowly warmed to room temperature overnight. Saturated aqueous NH_4Cl was added, and the resulting mixture was extracted with EtOAc. The organic extracts were dried and concentrated. Flash chromatography (9:1 to 7:3 hexane–EtOAc) afforded compound **18** (13 mg, 57%) as a colorless oil: $[\alpha]^{23}_D$ = –2.2 (*c* 1.1 in $CHCl_3$); δ_H (400 MHz; $CDCl_3$; Me_4Si, amide rotamers) 1.15 (3 H, d, J = 7.2 Hz, CH_3), 1.32 (3 H, s, CH_3), 1.40-1.97 (13 H, m), 1.45 (9 H, br s), 2.17 (2 H, br s), 2.35 (1 H, br s), 3.80-3.89 (1 H, m), 3.94 (4 H, dd like, J = 4.0 Hz), 4.03 and 4.15 (1 H, br s, 2:1 ratio), 4.31 and 4.43 (1 H, br s, 2:1 ratio), 5.50-5.65 (1 H, m), 5.70- 5.85 (1 H, m), 5.91-6.10 (2 H, m); δ_C (100.6 MHz; $CDCl_3$; Me_4Si, amide rotamers) 21.1 (CH_3), 23.9 (CH_3), 26.0 (CH_2), 27.2 (CH_2), 27.9 (CH_2), 28.4 ($3CH_3$-*t*Bu), 29.7 and 29.9 (1 carbon in 2:1 ratio), 38.6 (CH, 2 carbons), 39.4 and 39.7 (1 carbon in 2:1 ratio), 49.0 and 49.8 (1 carbon in 2:1 ratio), 50.0 and 50.7 (1 carbon in 2:1 ratio), 64.7 (OCH_2, 2 carbons), 70.1 (C-3), 79.5 (Cq-*t*Bu), 109.8 (Cq), 130.0 (C=C), 130.4 (C=C), 132.5 (C=C), 135.0 (C=C), 155.1 (COO).

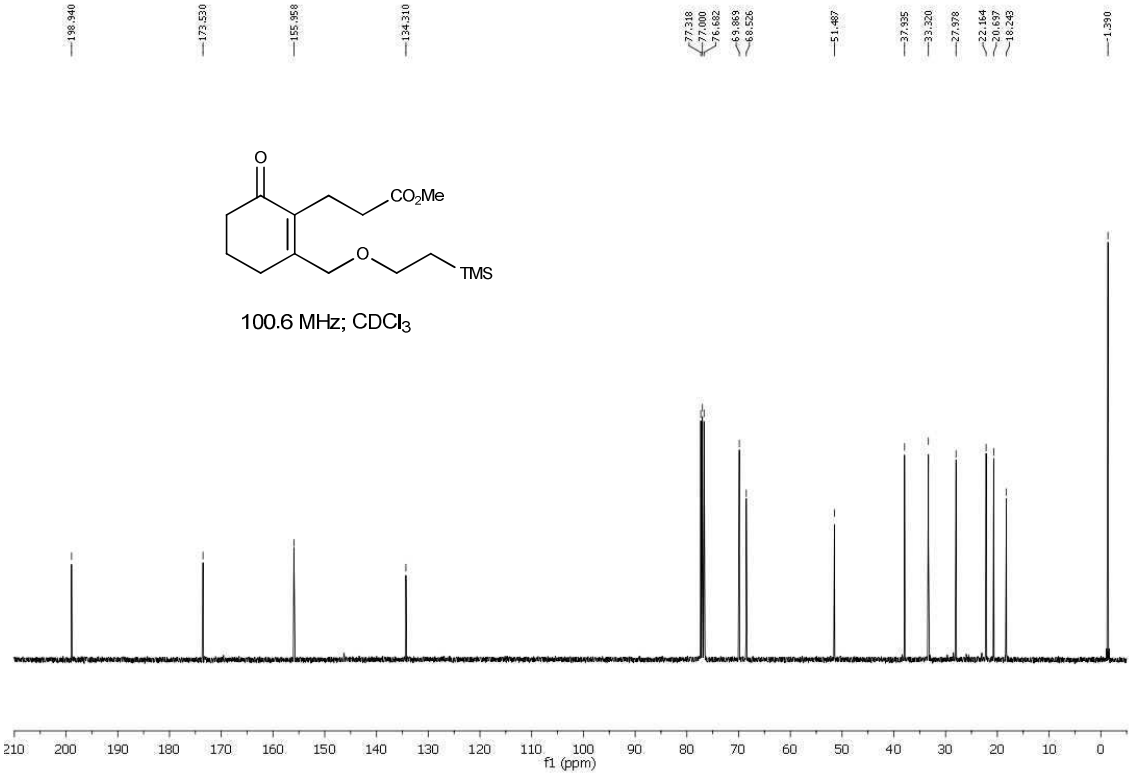


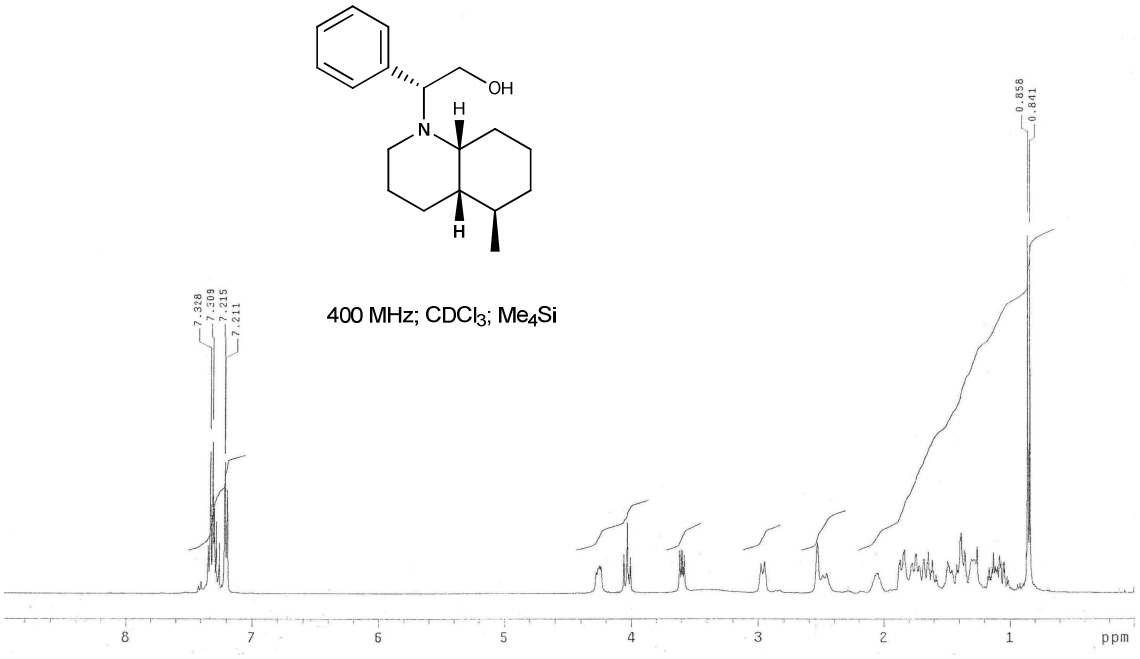
300 MHz; $CDCl_3$; Me_4Si

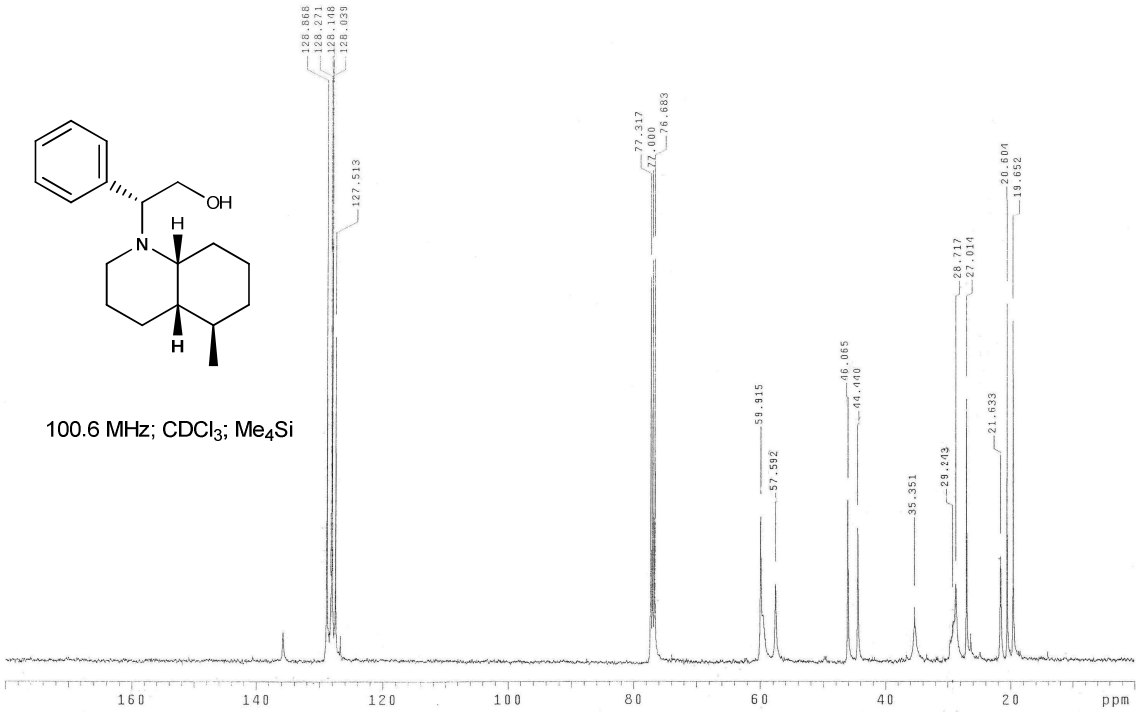


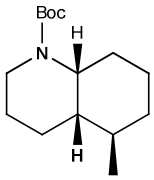
75.4 MHz; $CDCl_3$; Me_4Si


7.260
4.456
3.640
3.516
3.496
2.370
2.351
1.952
1.935
1.919
0.968
0.947
0.945
0.927
0.013
0.012
O
CO2Me
O
TMS
400 MHz; CDCl3
2.00
3.00
2.16
2.13
2.13
4.11
2.17
2.17
8.24
f1 (ppm)

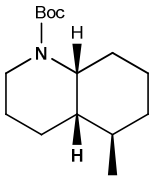

198.940
173.530
155.958
134.310
77.318
77.000
76.682
69.889
68.526
51.487
37.935
33.320
27.978
22.164
20.697
18.243
1.390
O
CO2Me
O
TMS
100.6 MHz; CDCl3
f1 (ppm)


OH
H
N
H
400 MHz; CDCl3; Me4Si
7.328
7.309
7.215
7.211
0.858
0.841
8
7
6
5
4
3
2
1
ppm

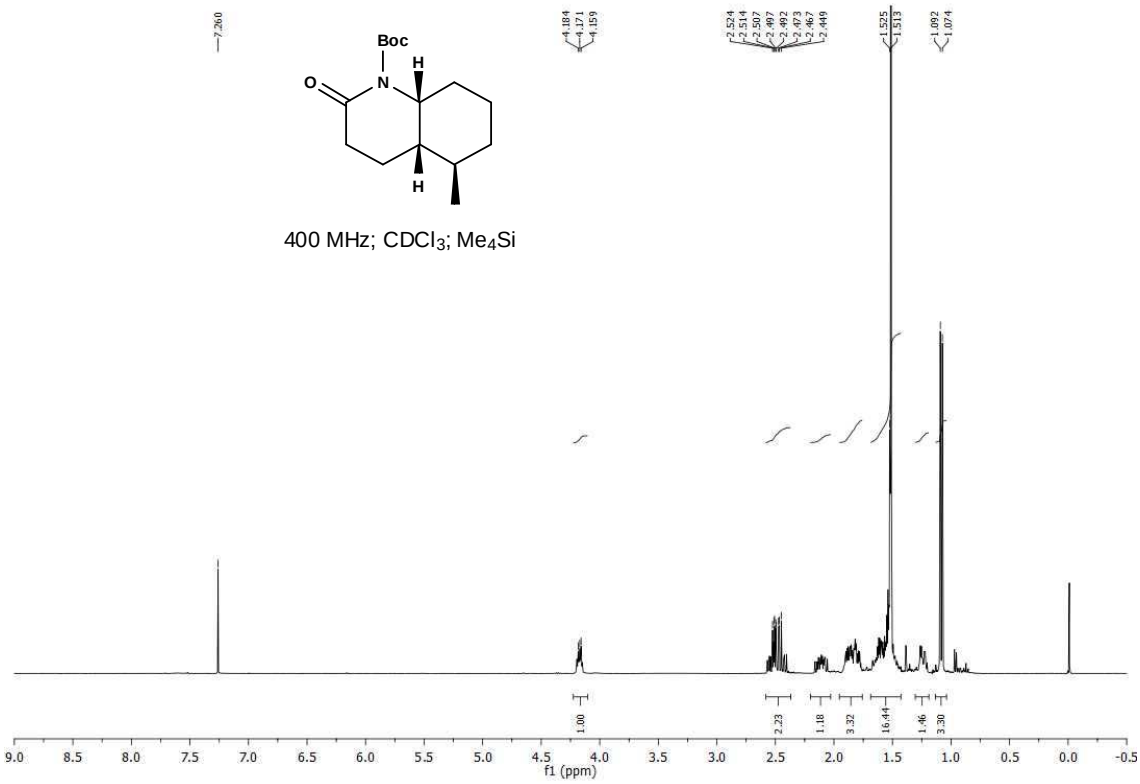

OH
H
N
H
100.6 MHz; CDCl3; Me4Si
128.868
128.271
128.148
128.039
127.513
77.317
77.000
76.683
59.915
57.592
46.065
44.440
35.351
29.243
28.717
27.014
21.633
20.604
19.652
160
140
120
100
80
60
40
20
ppm



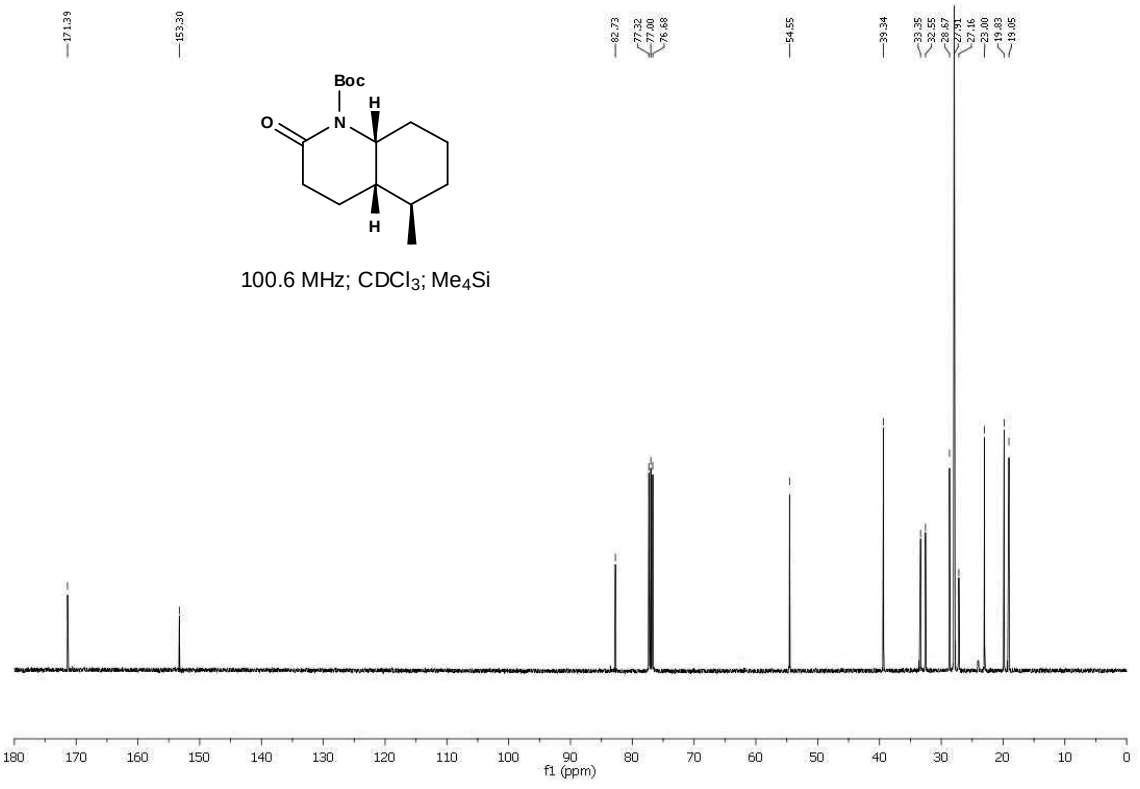
400 MHz; $CDCl_3$; Me_4Si



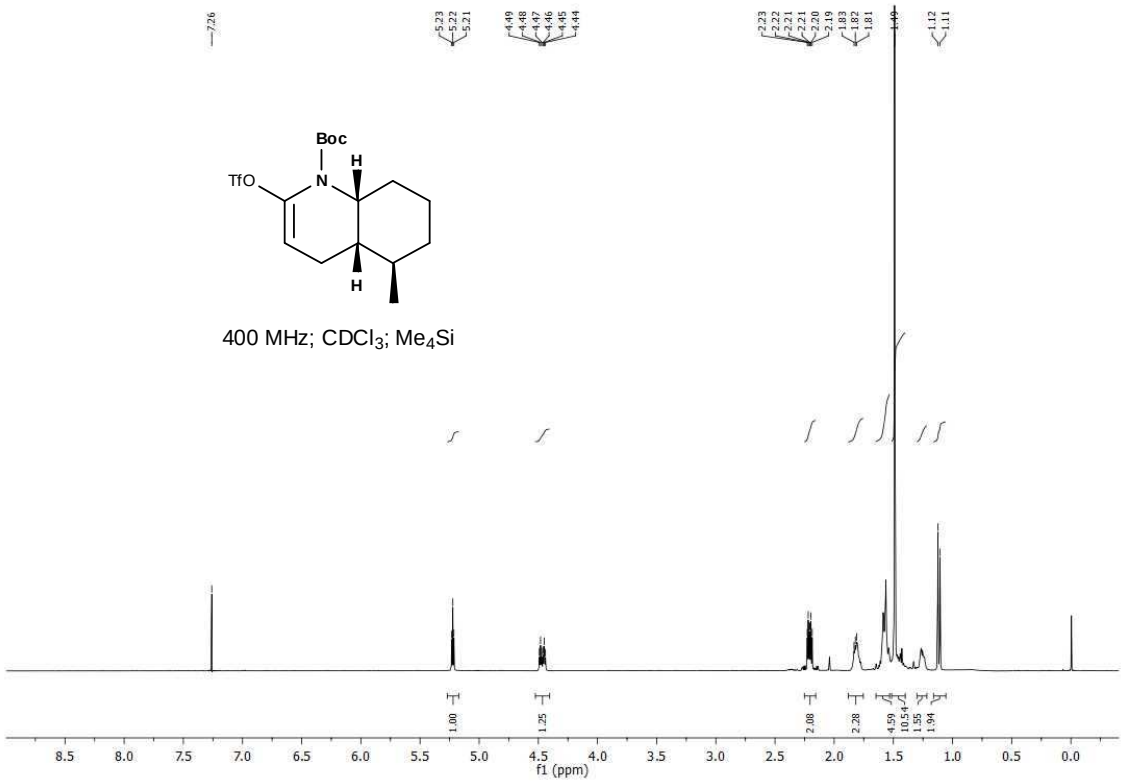
100.6 MHz; $CDCl_3$; Me_4Si



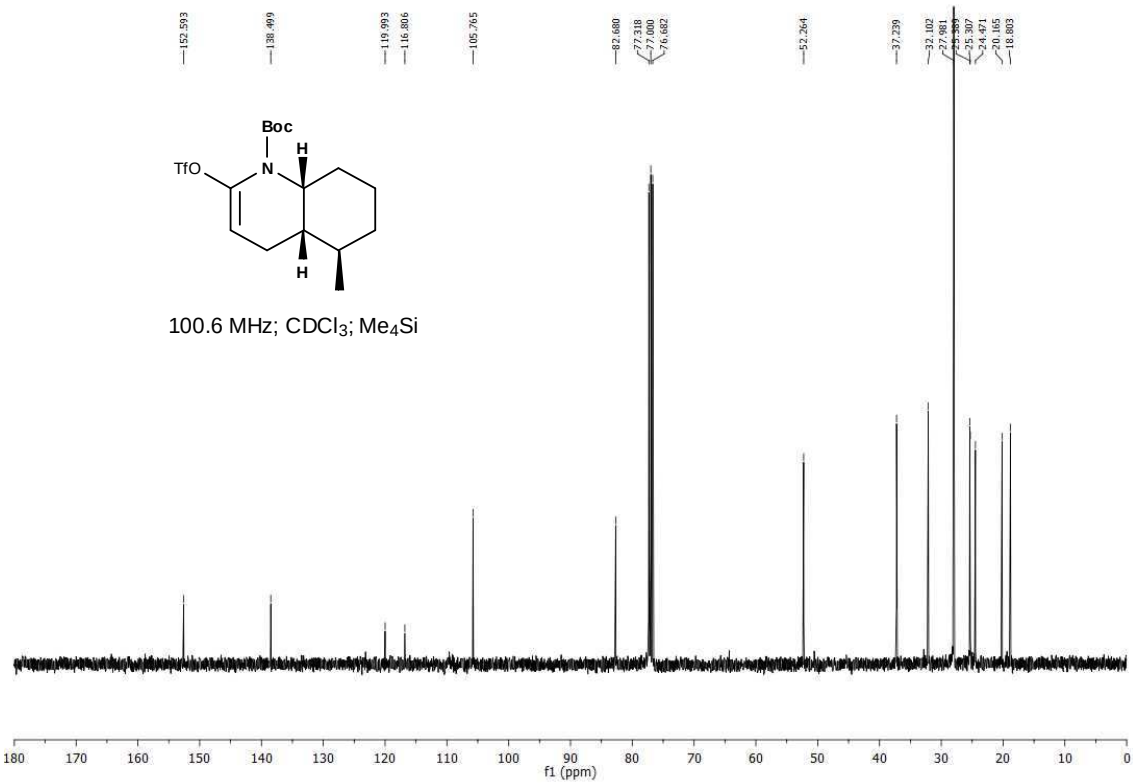
400 MHz; $CDCl_3$; Me_4Si



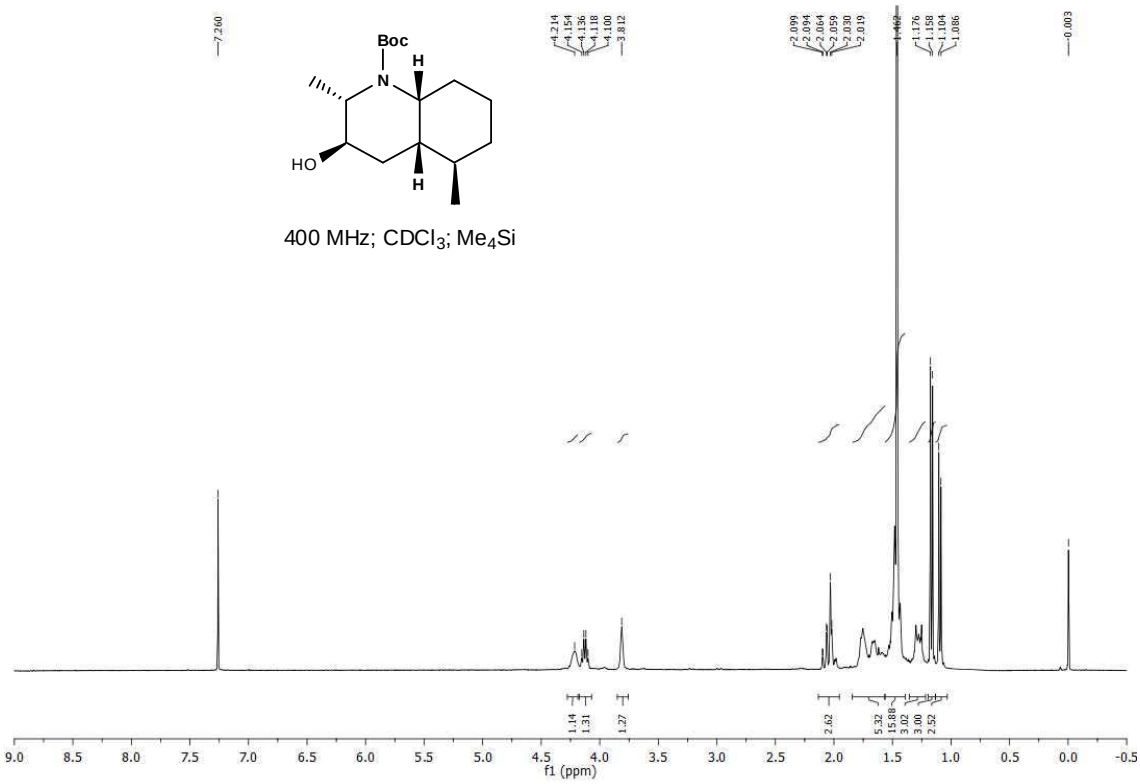
100.6 MHz; $CDCl_3$; Me_4Si



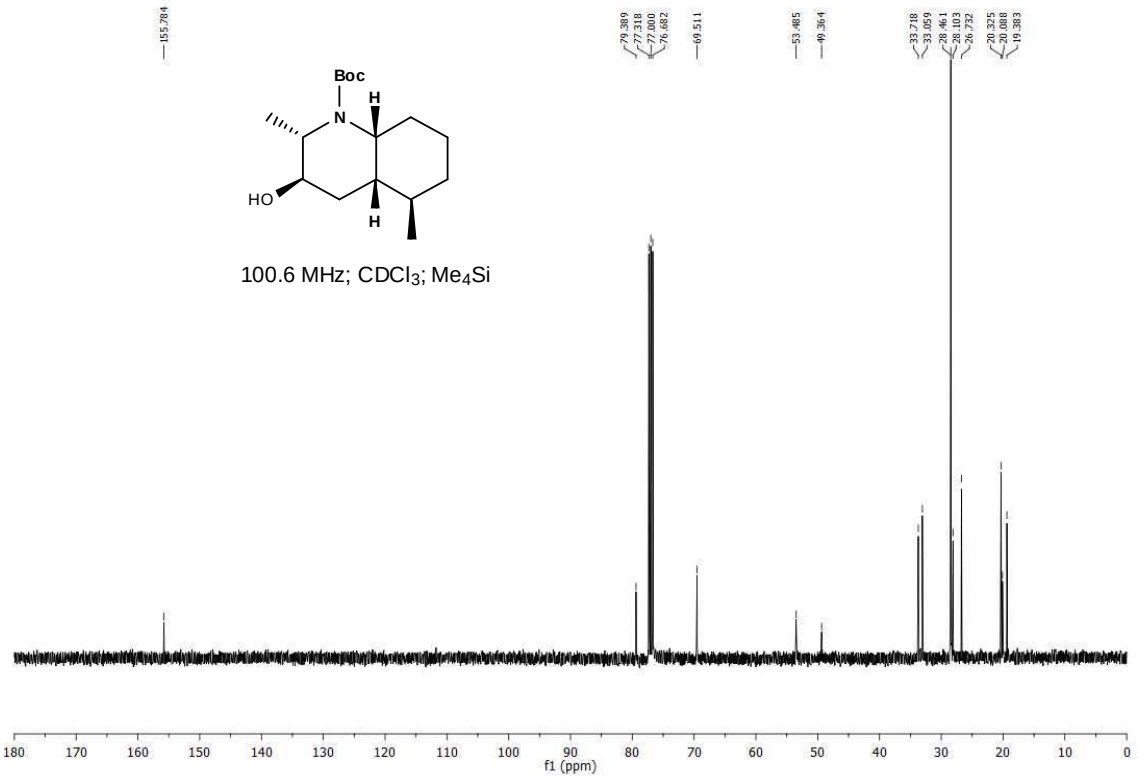
400 MHz; $CDCl_3$; Me_4Si



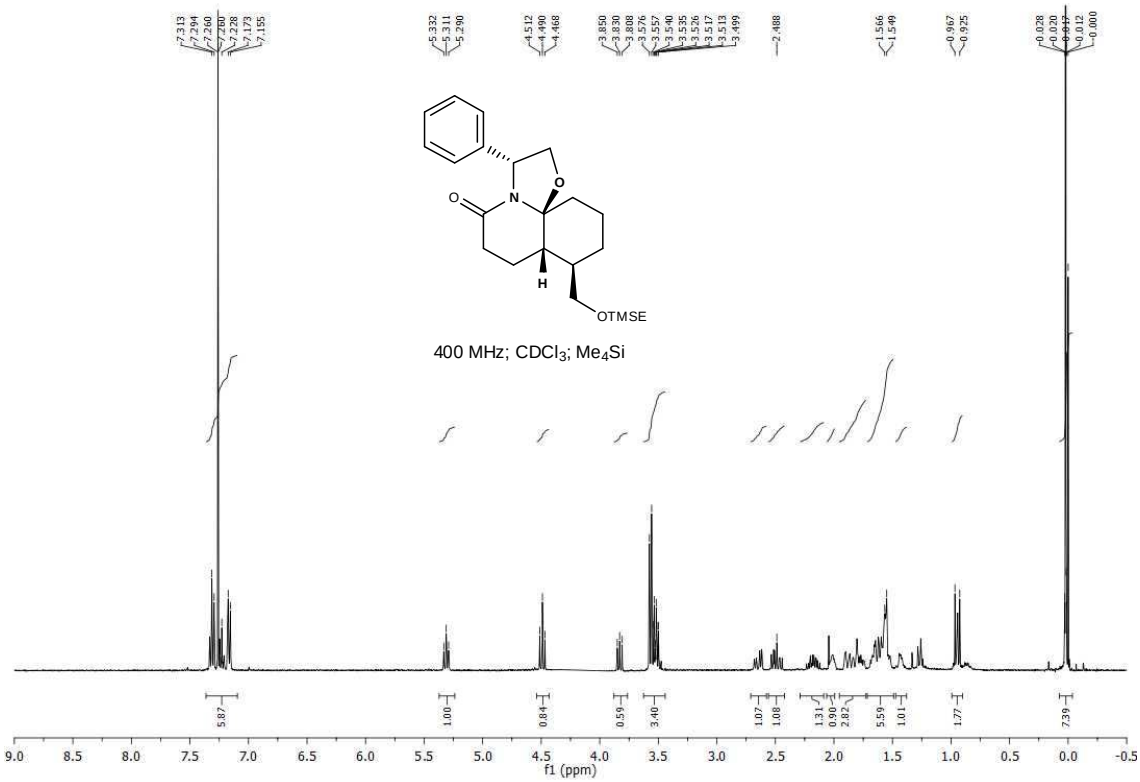
100.6 MHz; $CDCl_3$; Me_4Si



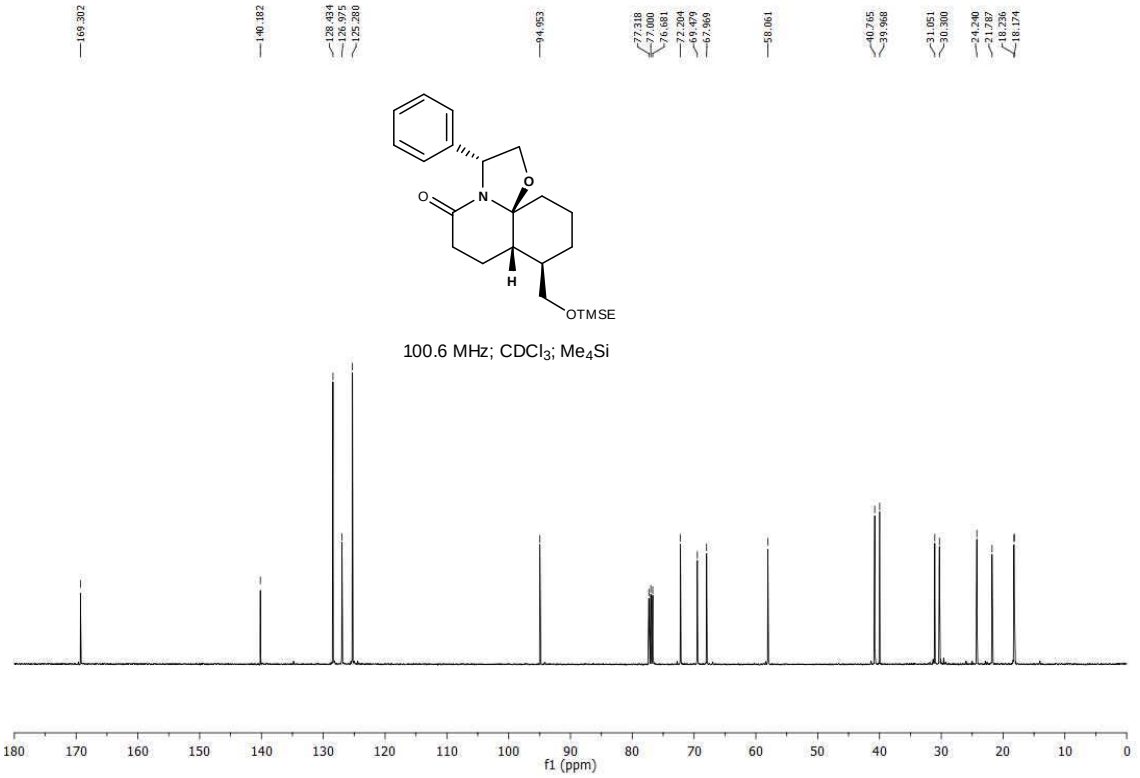
400 MHz; $CDCl_3$; Me_4Si



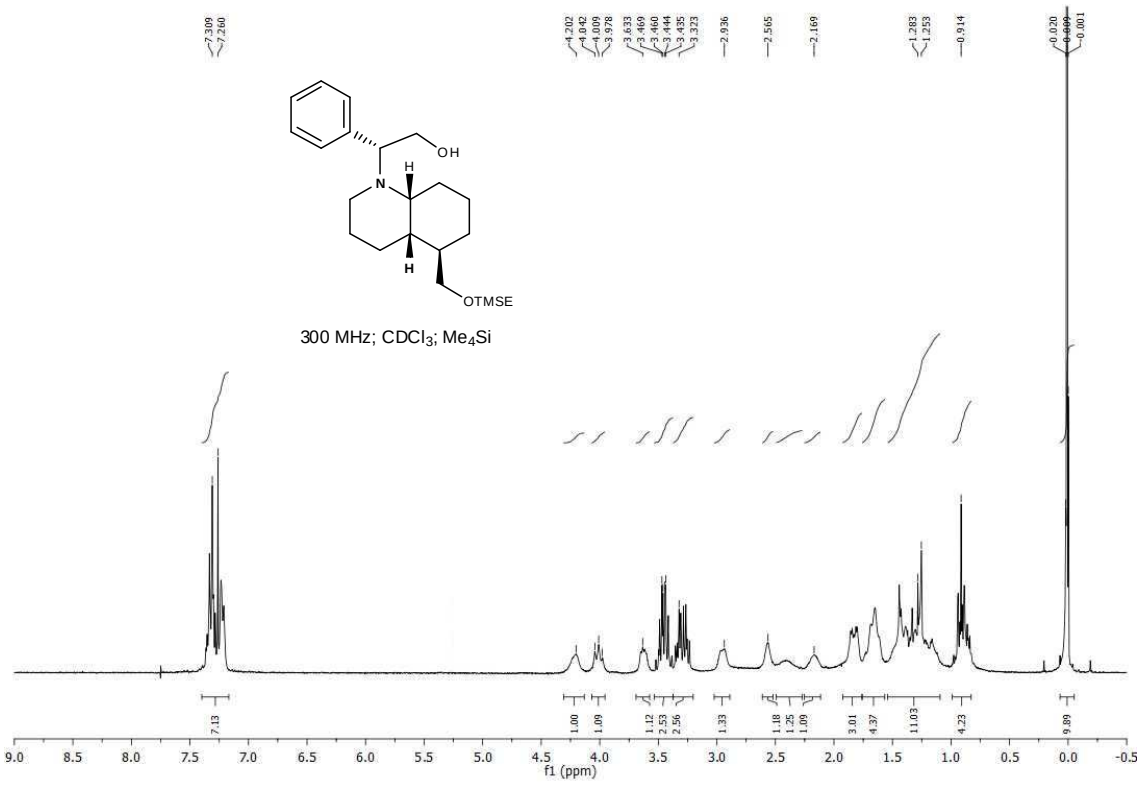
100.6 MHz; $CDCl_3$; Me_4Si

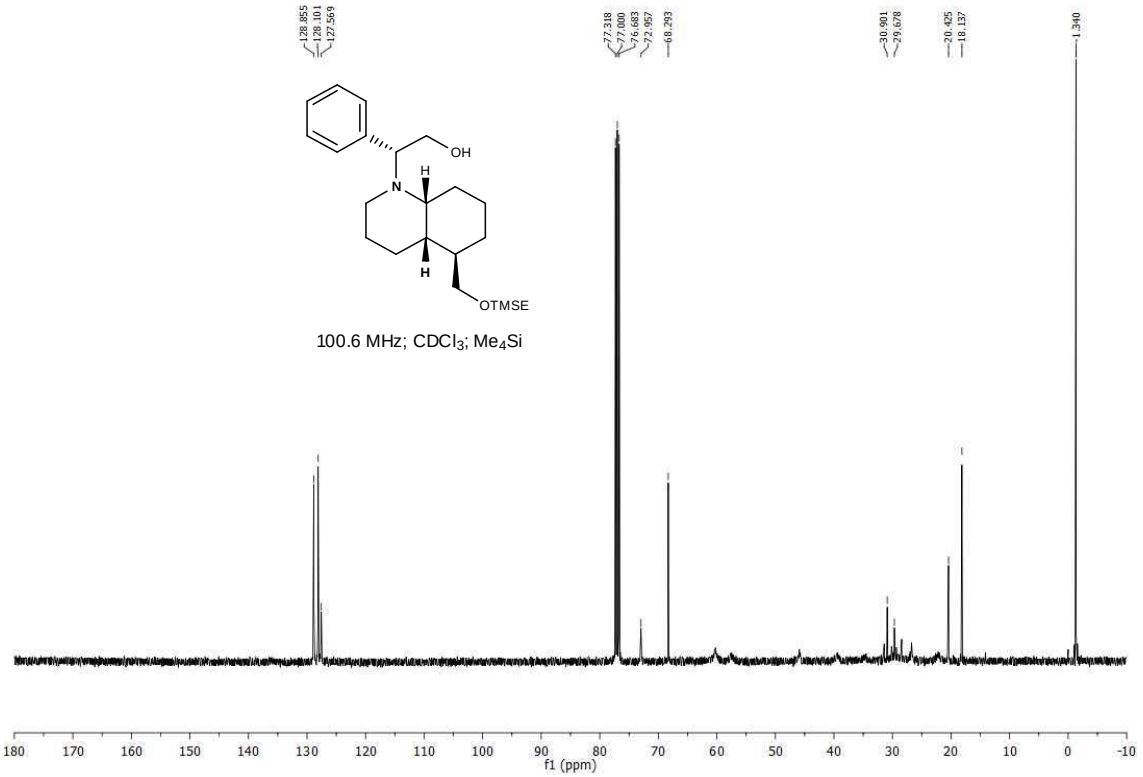


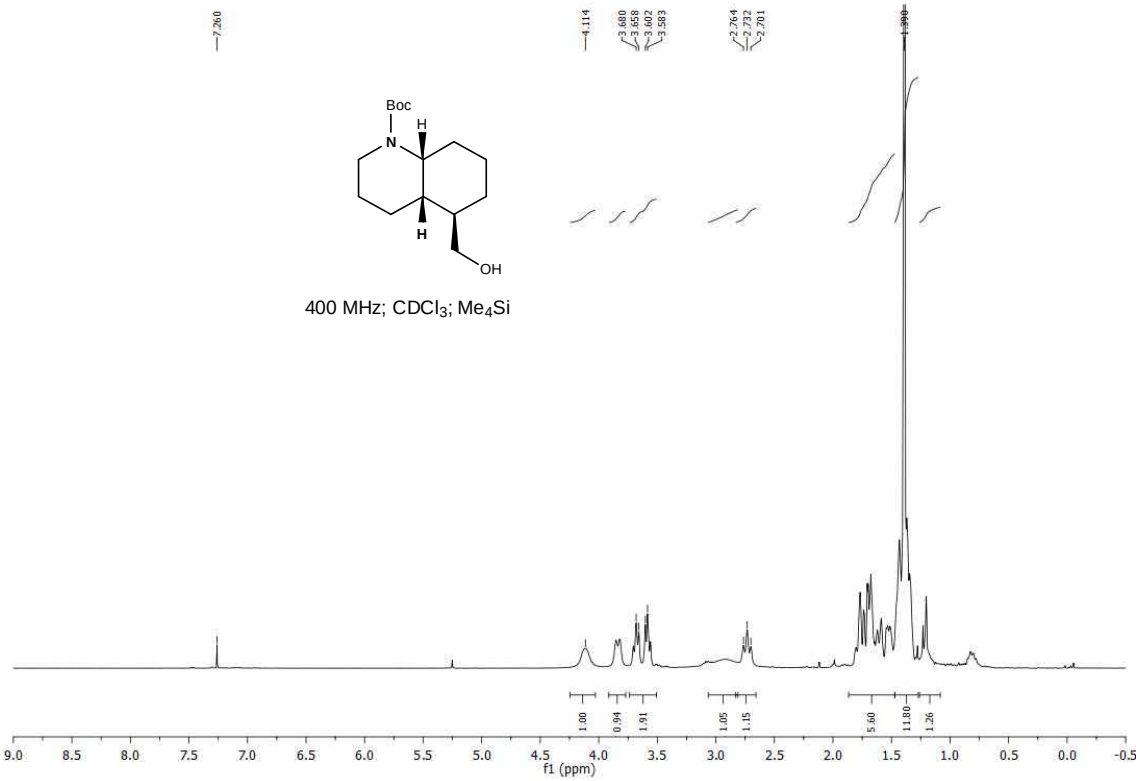
400 MHz; $CDCl_3$; Me_4Si



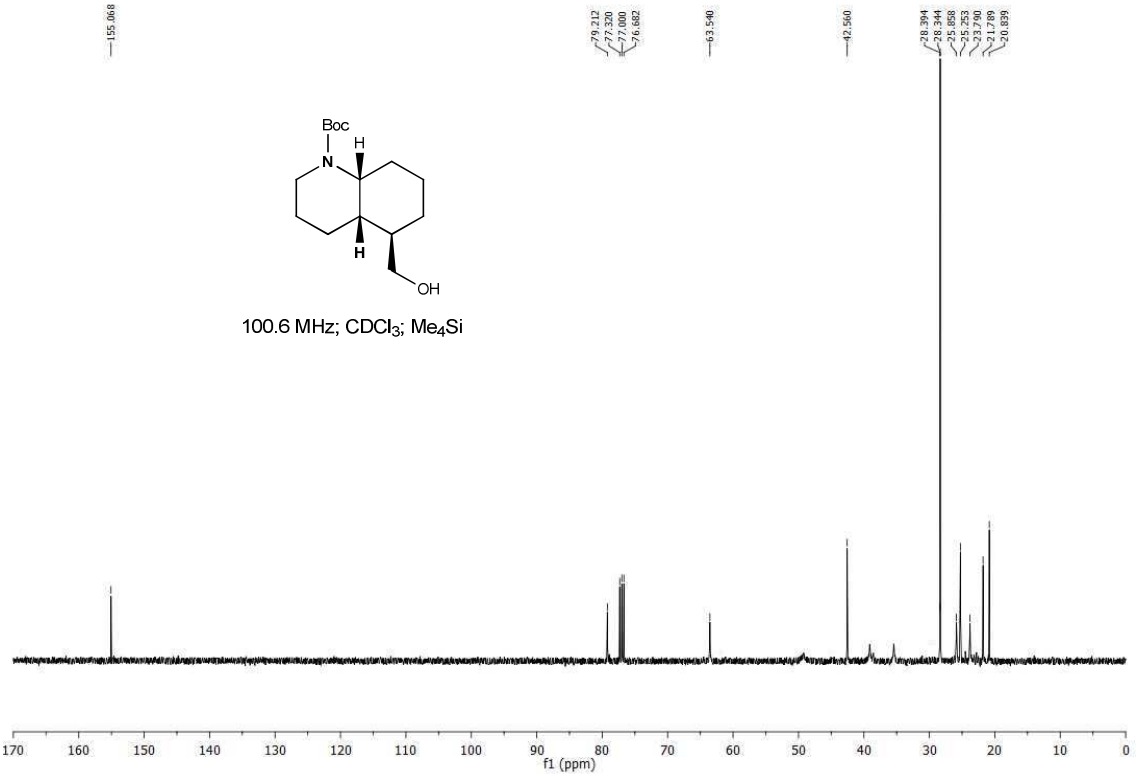
100.6 MHz; $CDCl_3$; Me_4Si


OH
H
N
H
OTMSE
300 MHz; CDCl3; Me4Si
f1 (ppm)

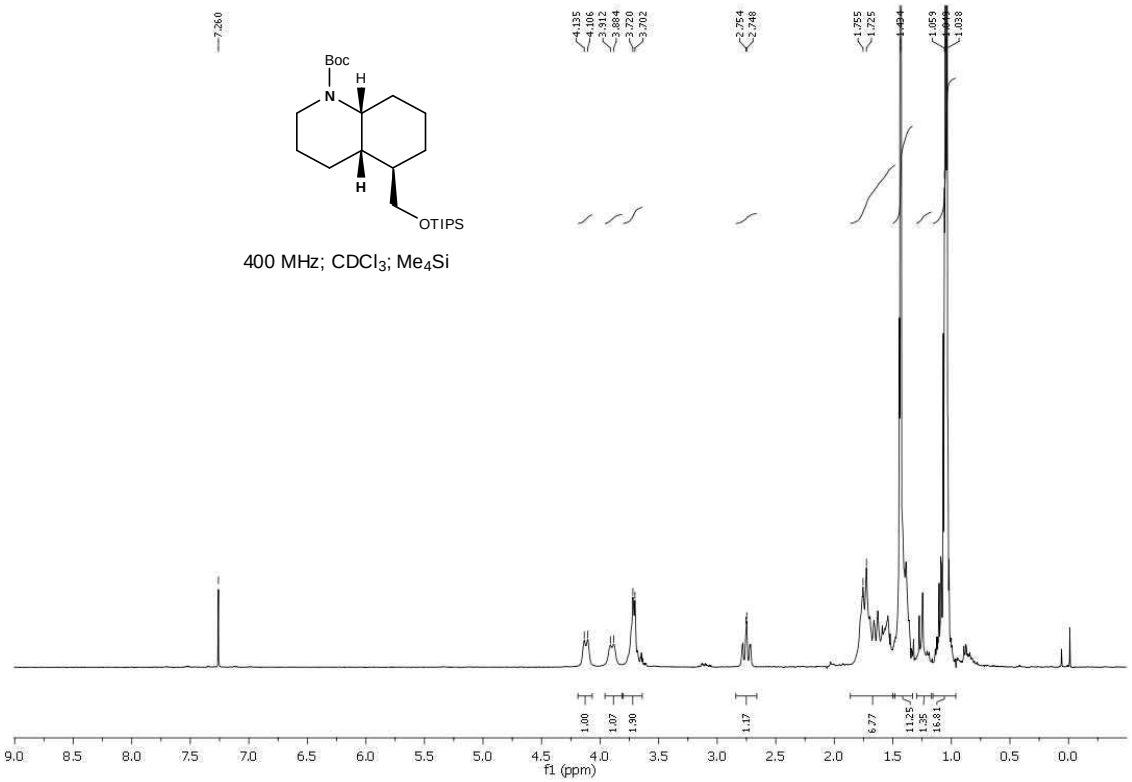

OH
H
N
H
OTMSE
100.6 MHz; CDCl3; Me4Si
f1 (ppm)

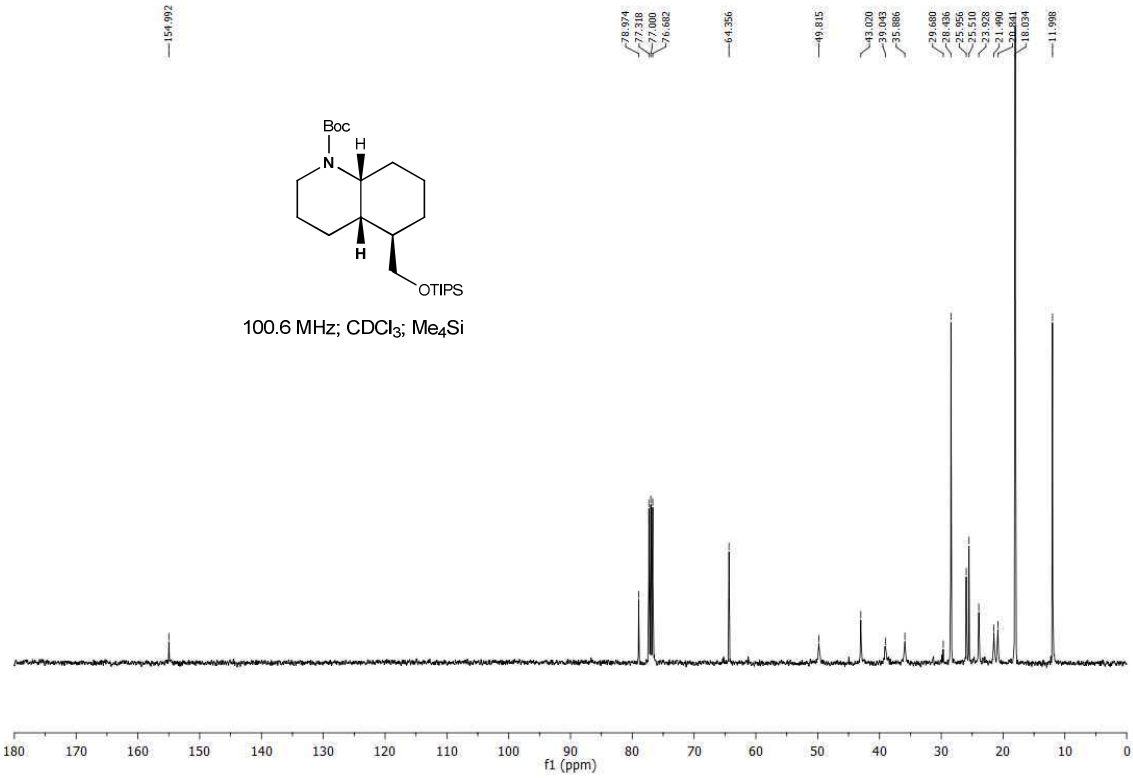


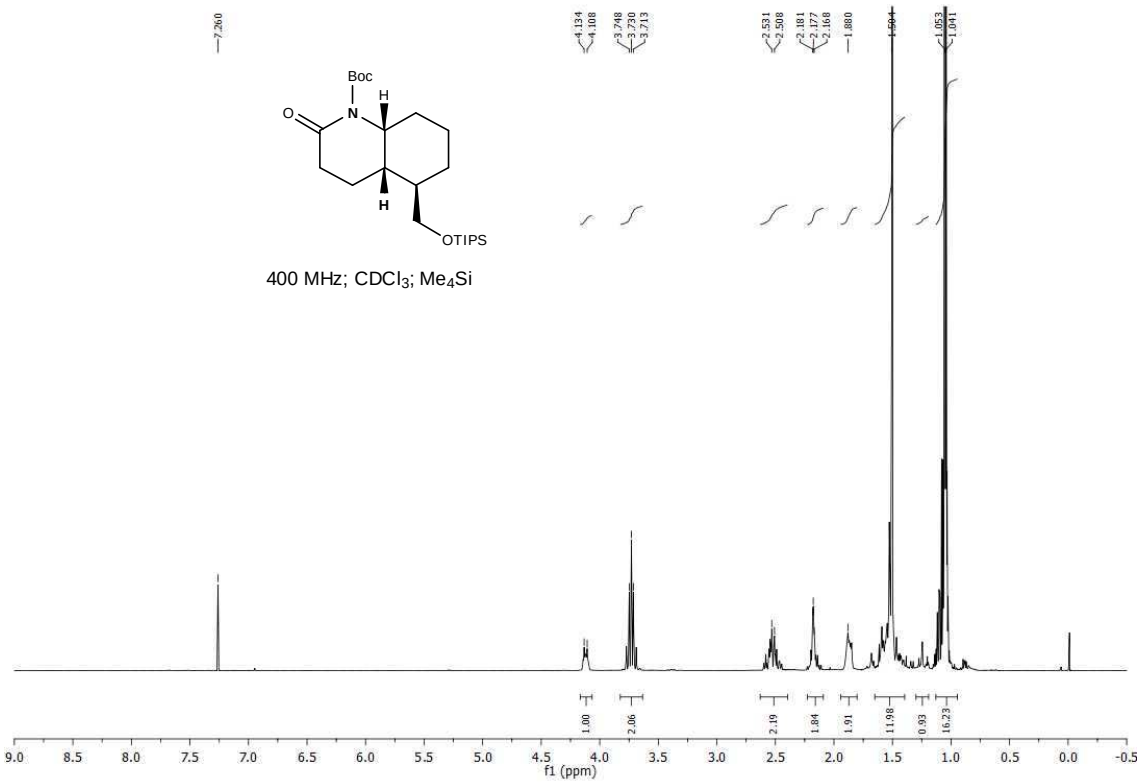
400 MHz; $CDCl_3$; Me_4Si



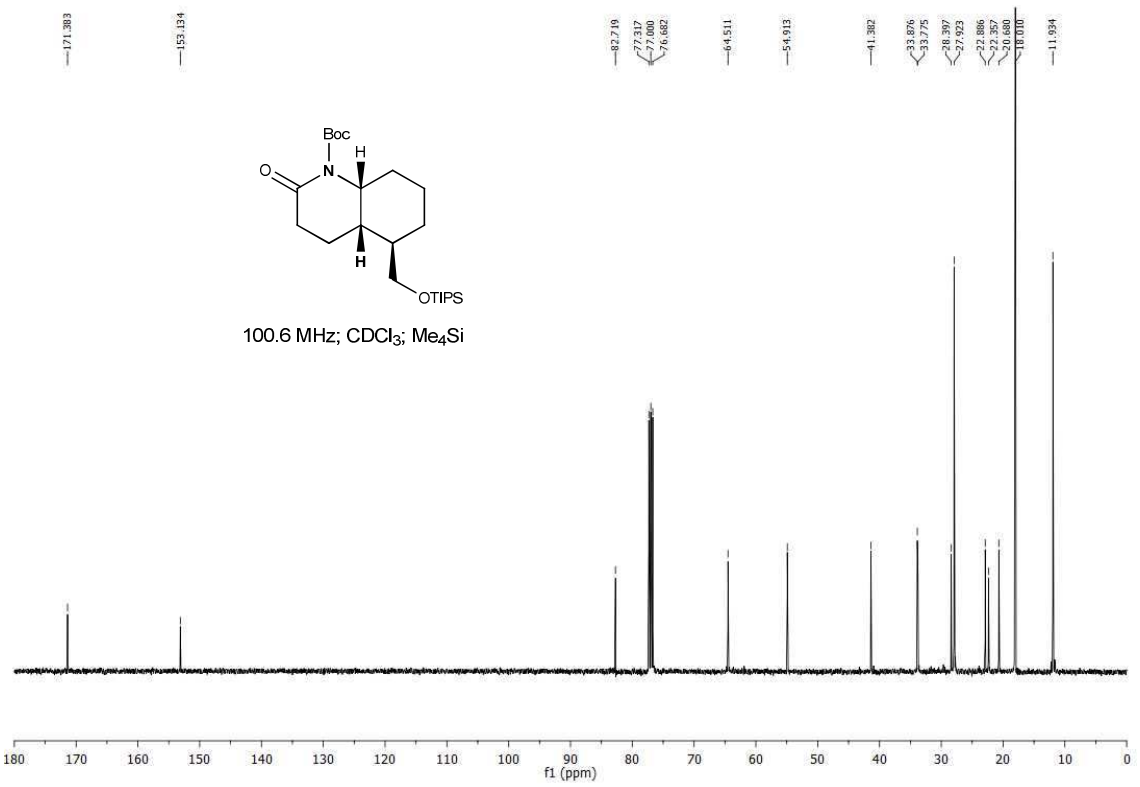
100.6 MHz; $CDCl_3$; Me_4Si


Boc
N
H
H
OTIPS
400 MHz; CDCl3; Me4Si
f1 (ppm)

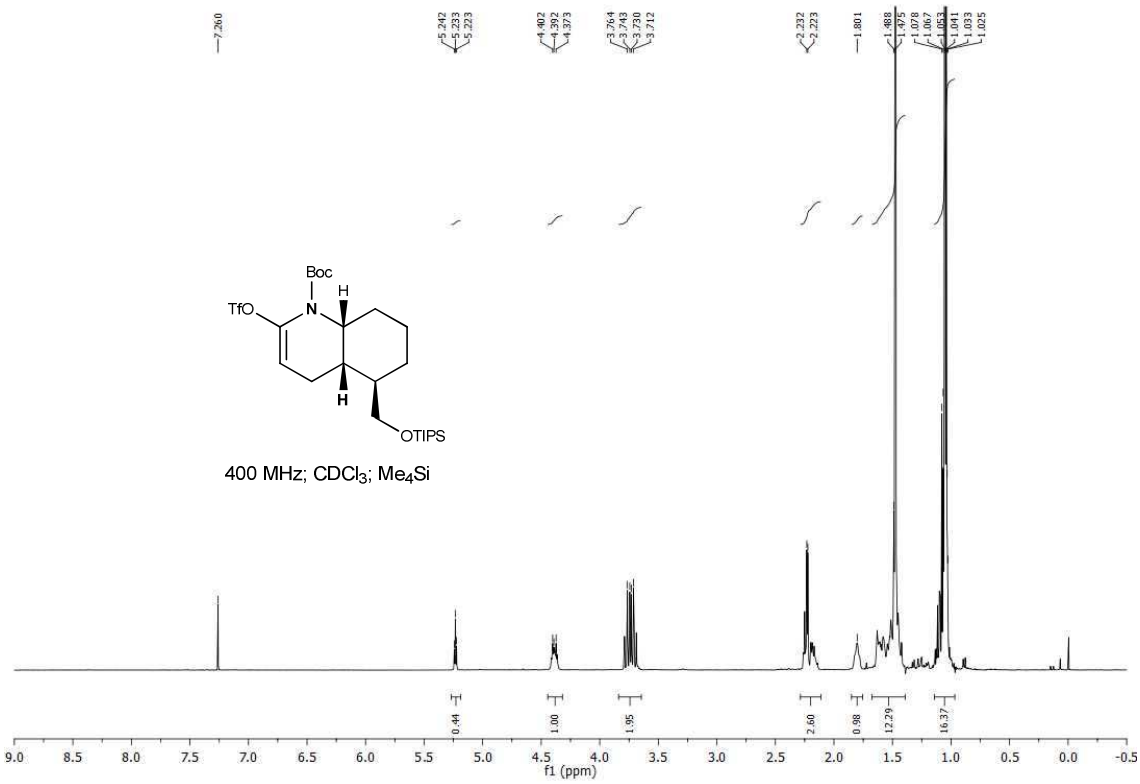

Boc
N
H
H
OTIPS
100.6 MHz; CDCl3; Me4Si
f1 (ppm)

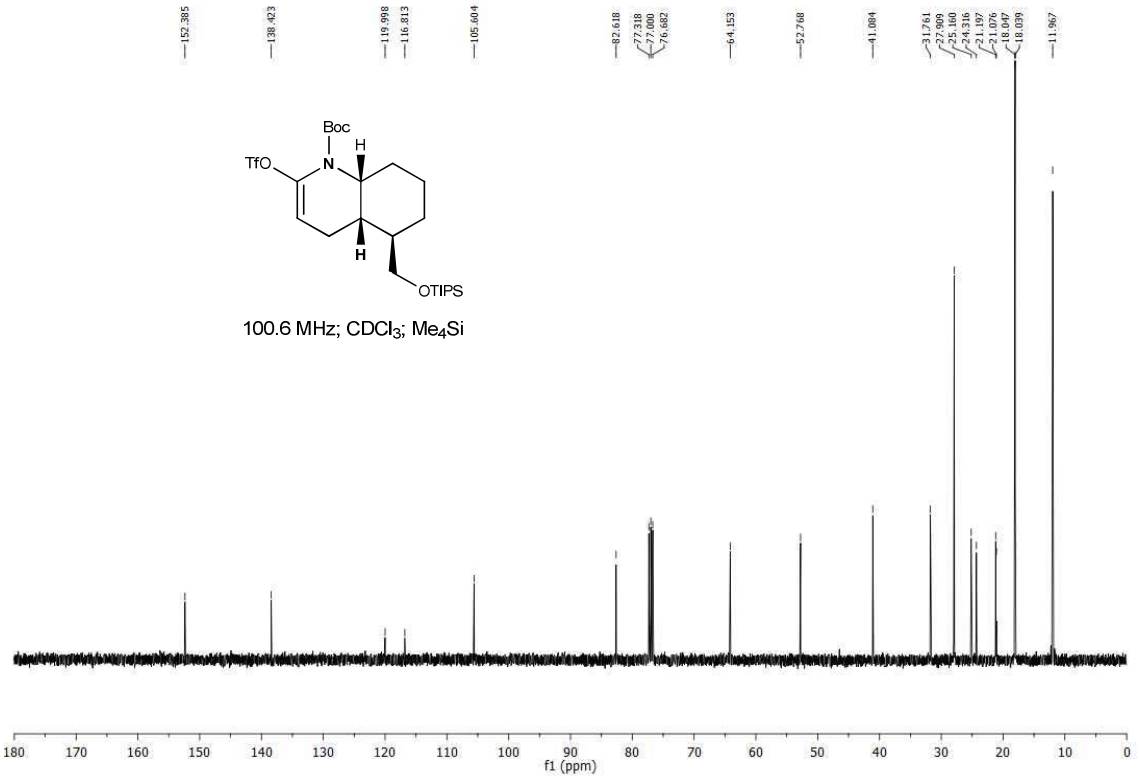


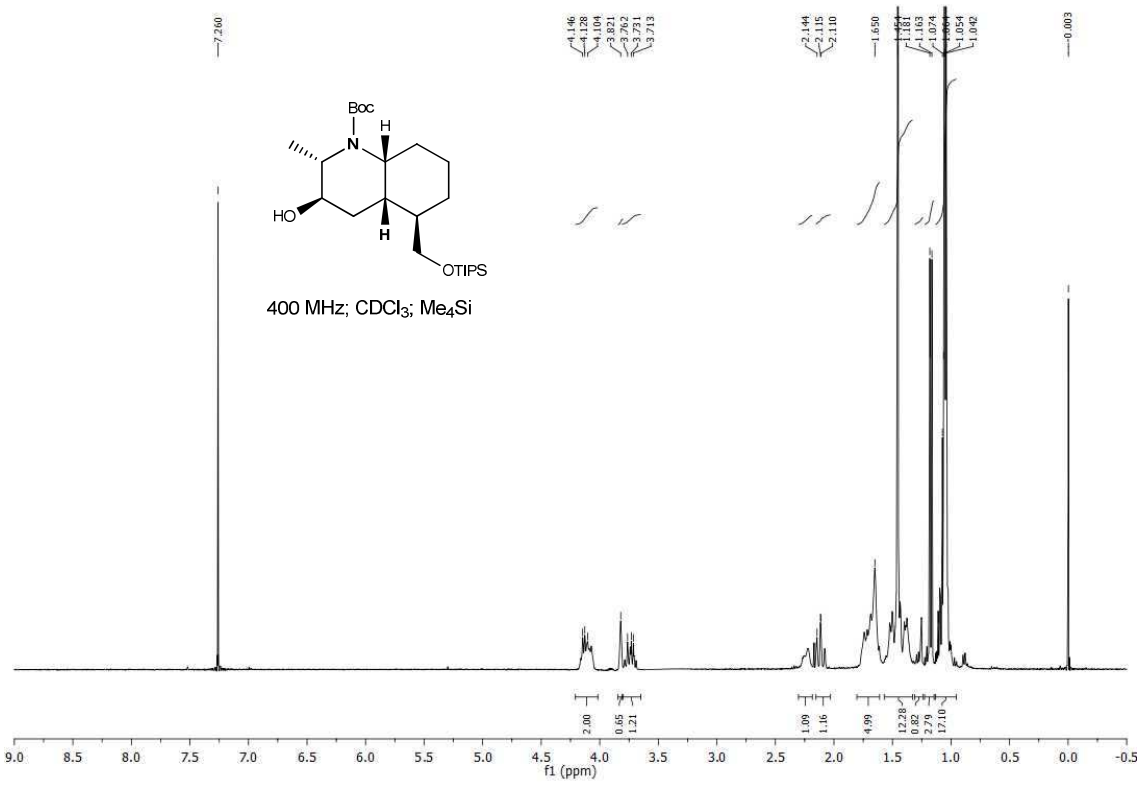
400 MHz; $CDCl_3$; Me_4Si

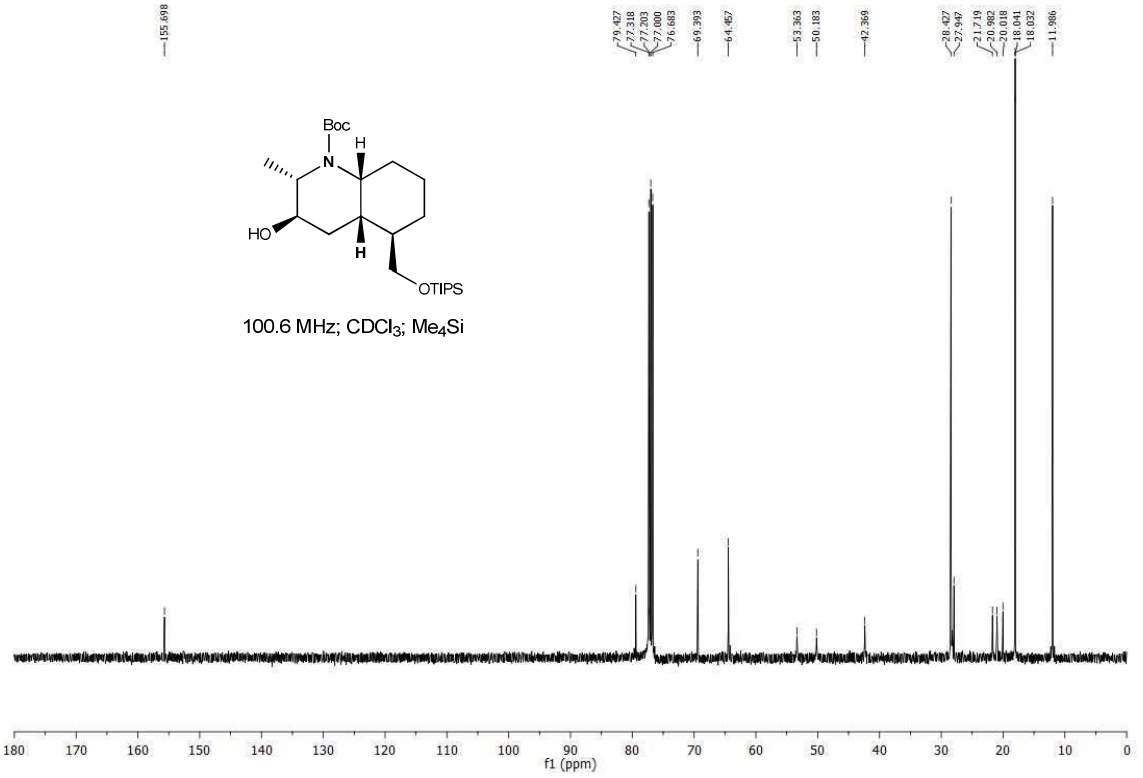


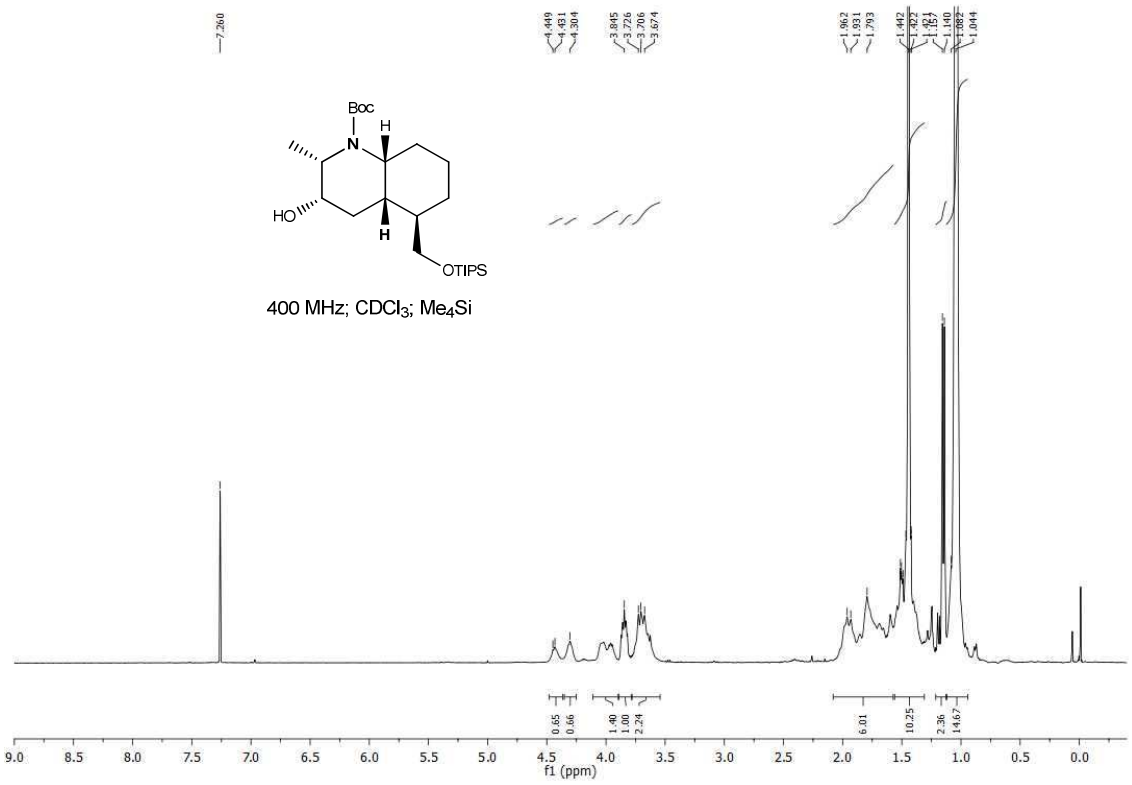
100.6 MHz; $CDCl_3$; Me_4Si


Boc
H
TfO
N
H
OTIPS
400 MHz; CDCl3; Me4Si
f1 (ppm)

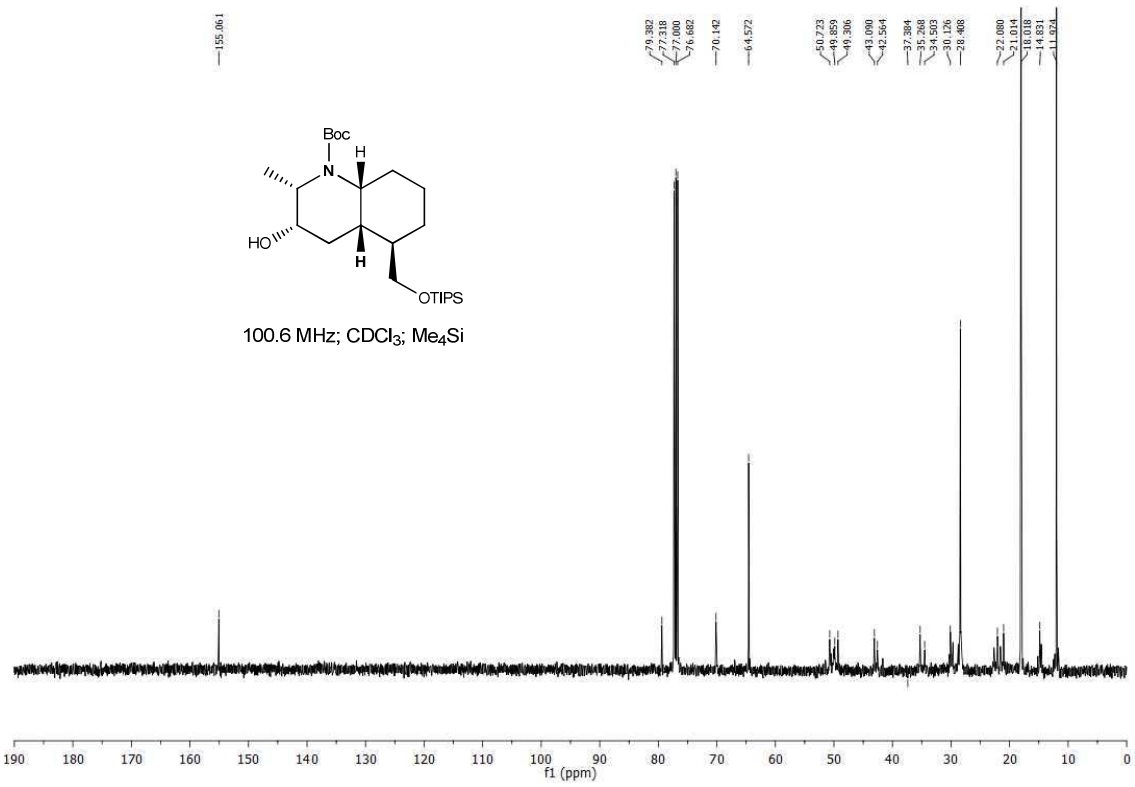

Boc
H
TfO
N
H
OTIPS
100.6 MHz; CDCl3; Me4Si
f1 (ppm)


Boc
H
N
HO
H
OTIPS
400 MHz; CDCl3; Me4Si
f1 (ppm)

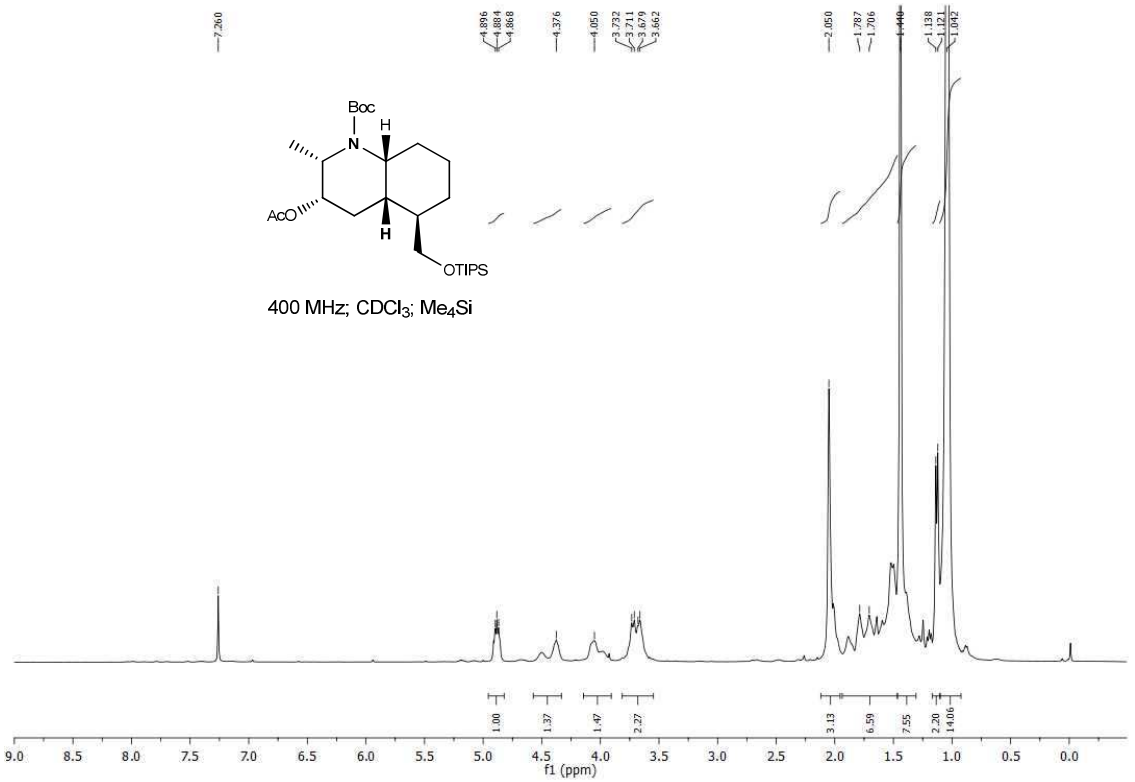

Boc
H
N
HO
H
OTIPS
100.6 MHz; CDCl3; Me4Si
f1 (ppm)



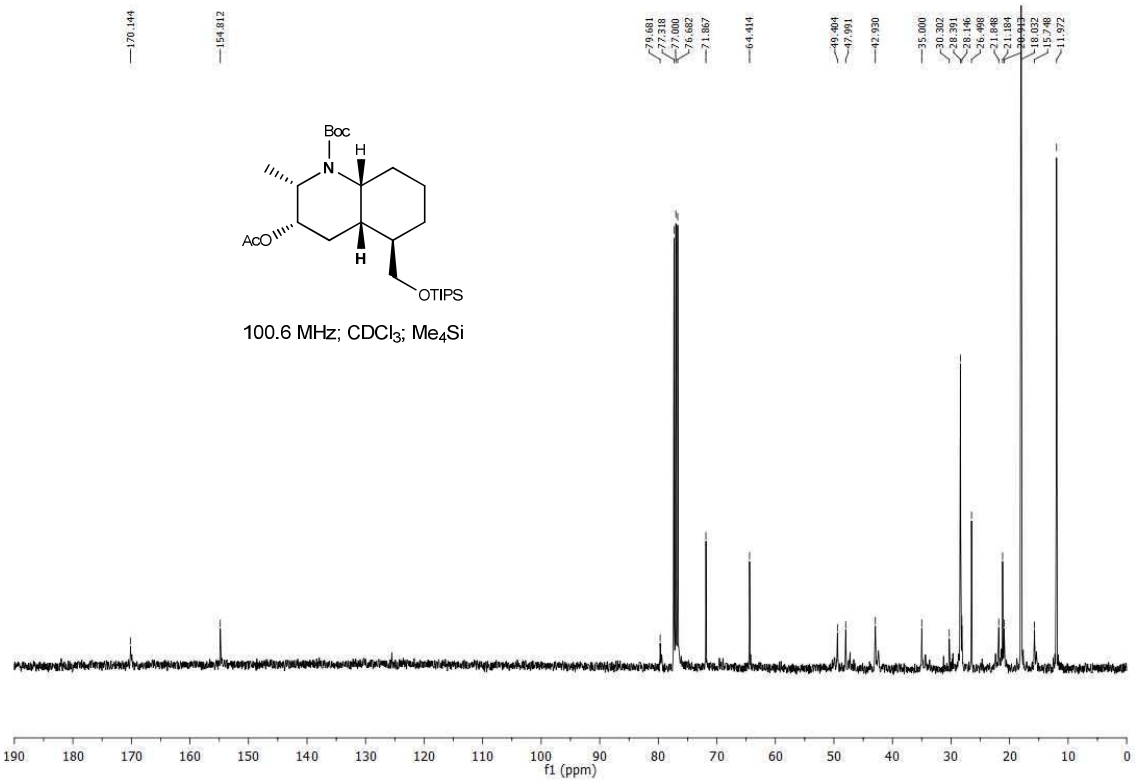
400 MHz; $CDCl_3$; Me_4Si



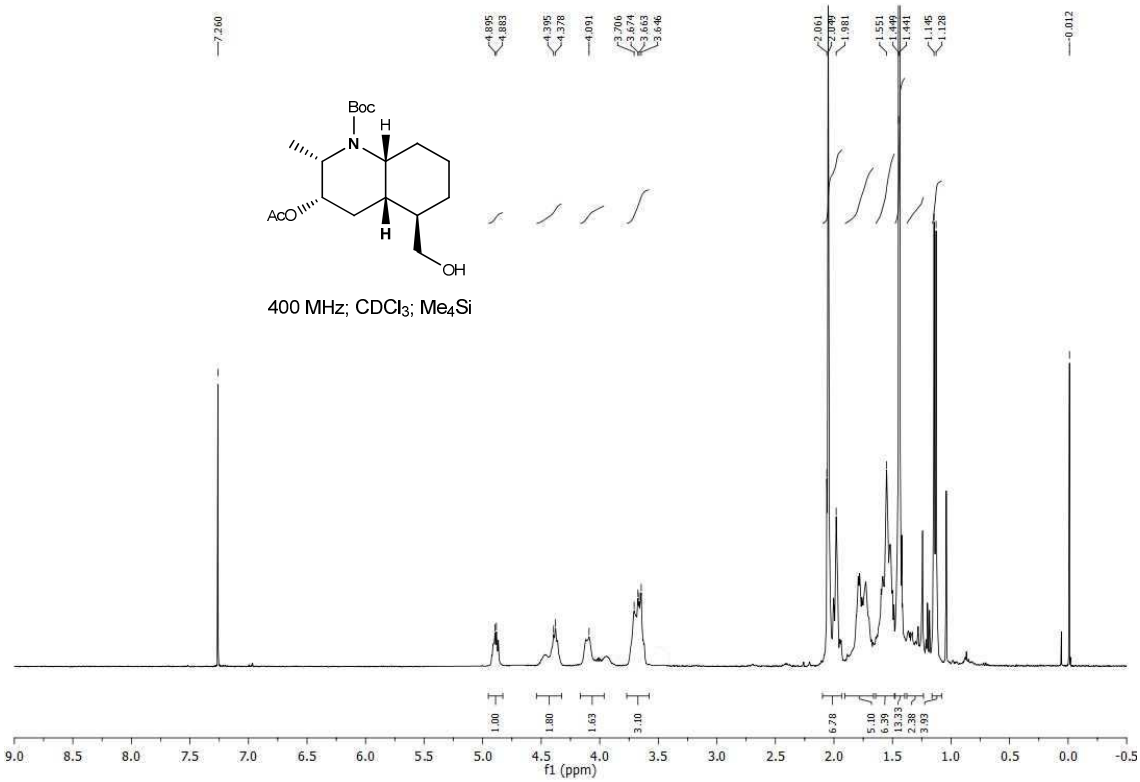
100.6 MHz; $CDCl_3$; Me_4Si

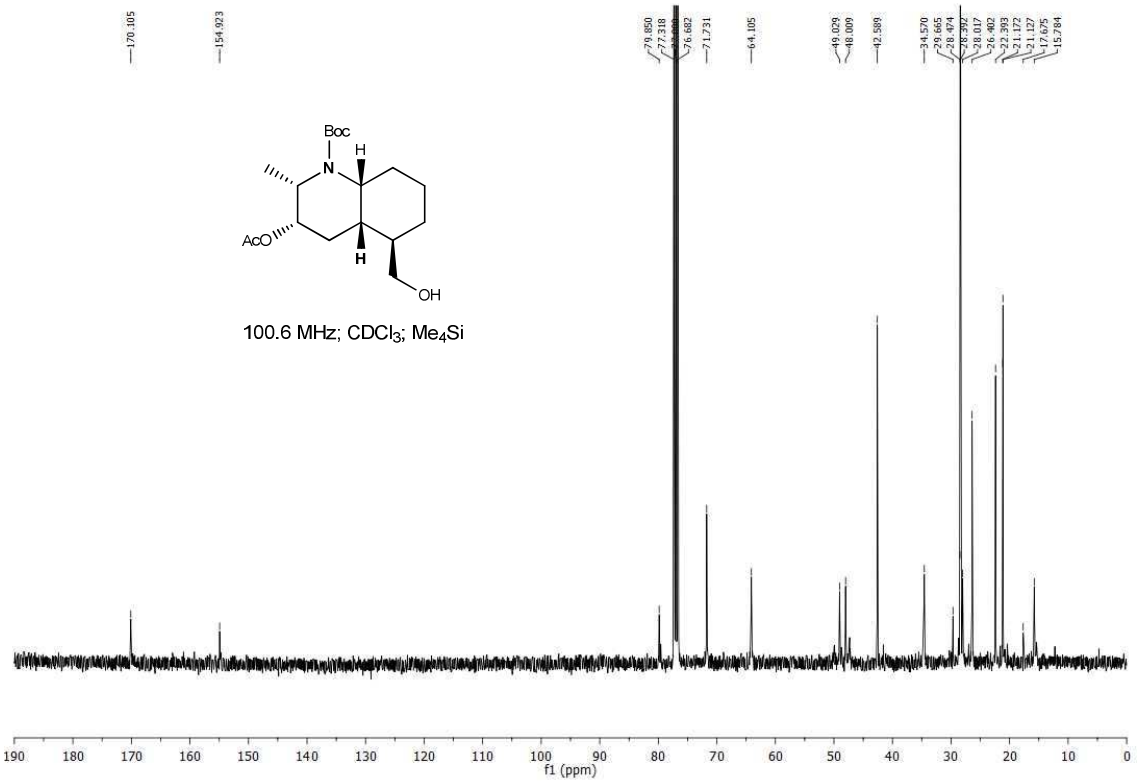


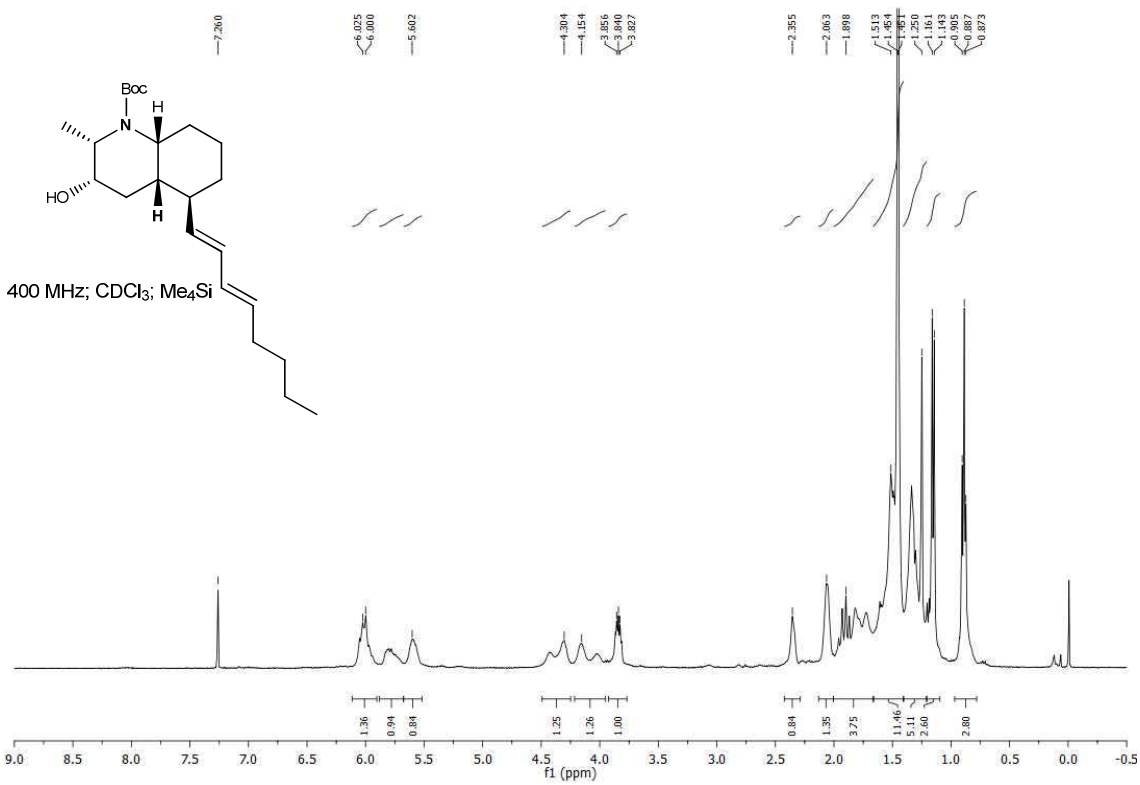
400 MHz; $CDCl_3$; Me_4Si

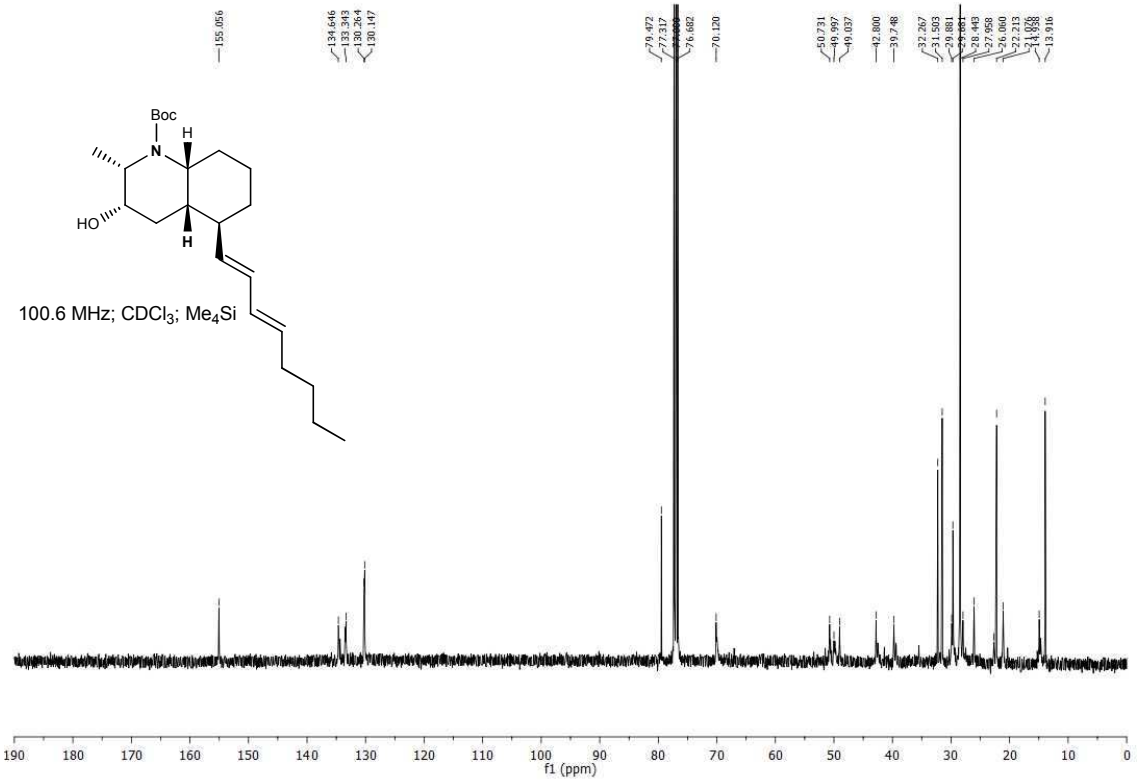


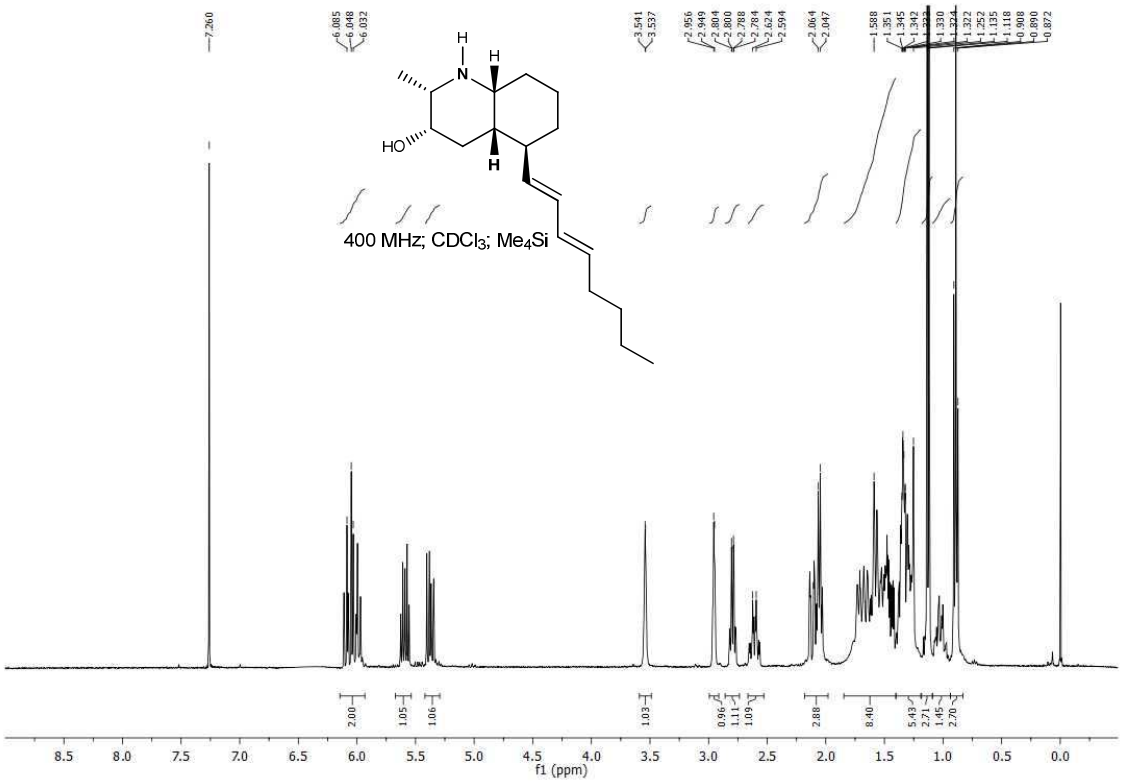
100.6 MHz; $CDCl_3$; Me_4Si

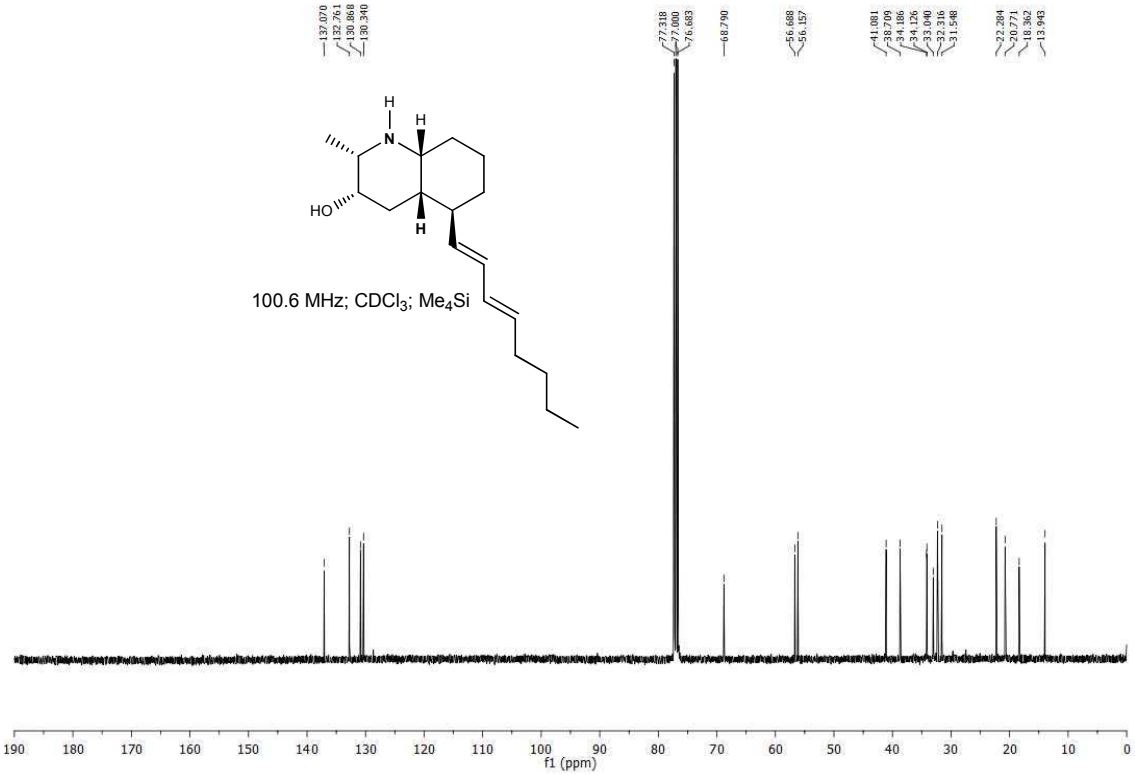

Boc
H
N
AcO
H
OH
400 MHz; CDCl3; Me4Si
f1 (ppm)

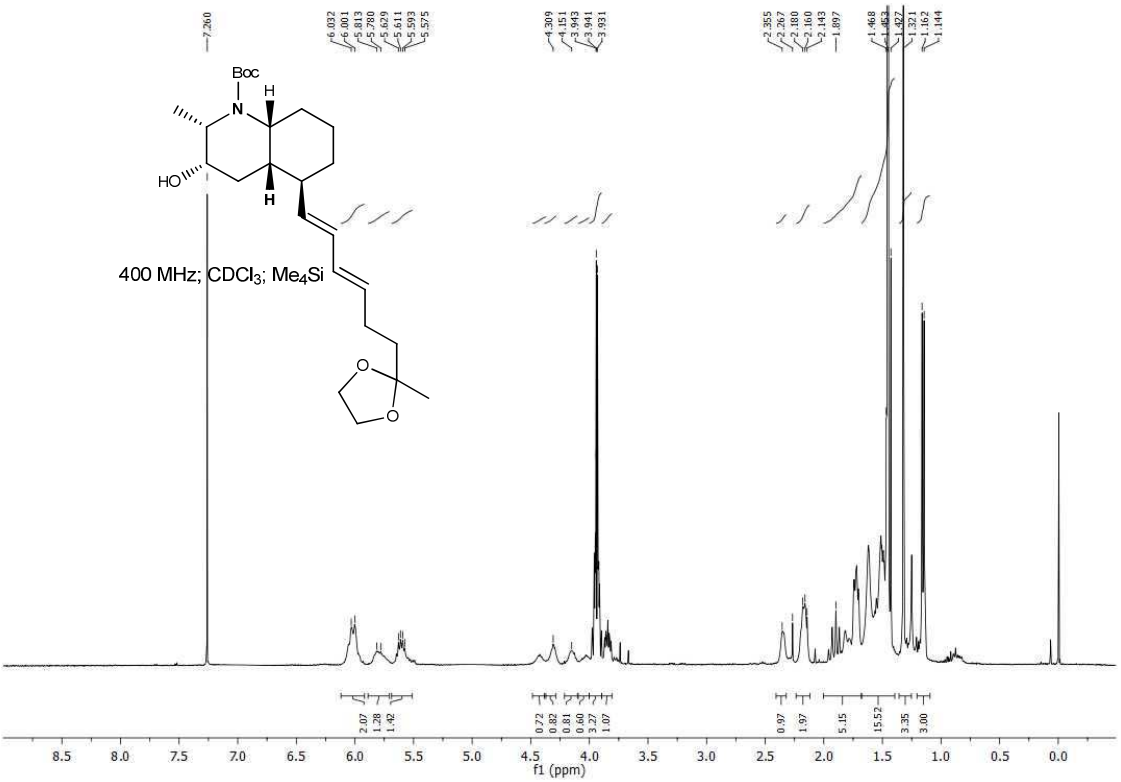

Boc
H
N
AcO
H
OH
100.6 MHz; CDCl3; Me4Si
f1 (ppm)

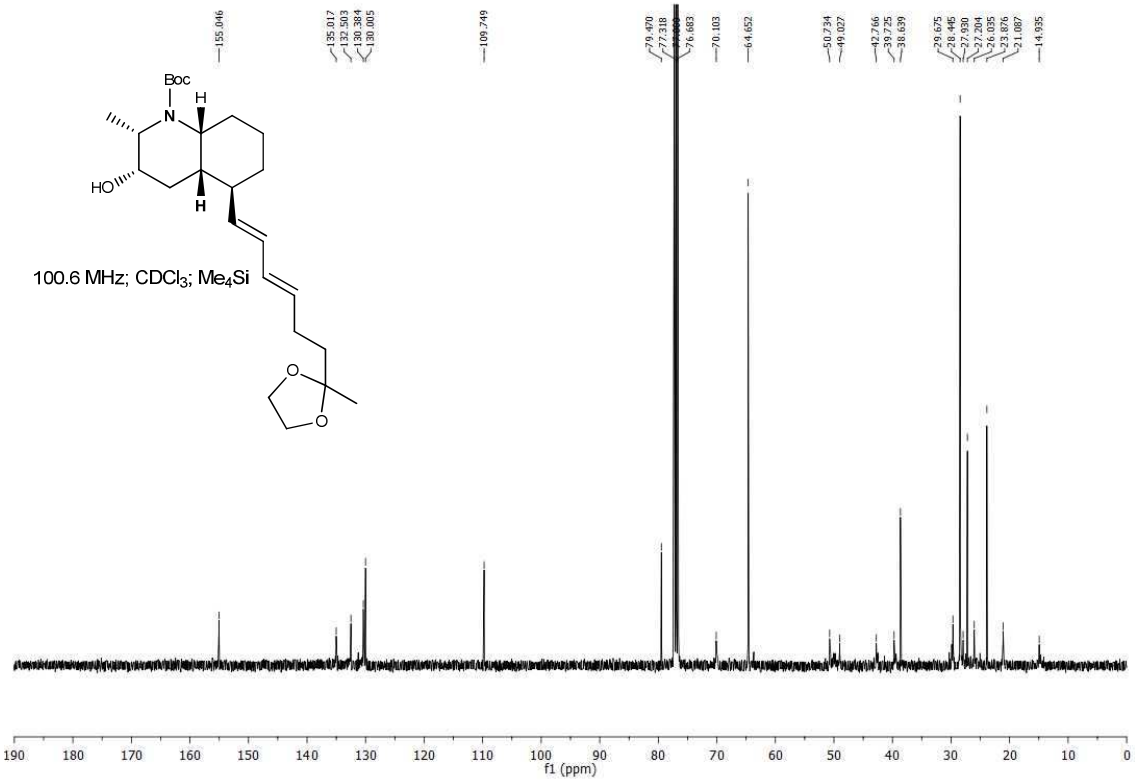

Boc
H
N
HO
H
400 MHz; CDCl3; Me4Si
f1 (ppm)


Boc
H
N
HO
H
100.6 MHz; CDCl3; Me4Si
f1 (ppm)


400 MHz; CDCl3; Me4Si
f1 (ppm)


100.6 MHz; CDCl3; Me4Si
f1 (ppm)


Boc
N
H
HO
H
O
O
400 MHz; CDCl3; Me4Si
f1 (ppm)


Boc
N
H
HO
H
O
O
100.6 MHz; CDCl3; Me4Si
f1 (ppm)