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Supporting Information

Assessing Synthetic Strategies: Total Syntheses of (±)-Neodolabellane-Type Diterpenoids

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Supplementary Information

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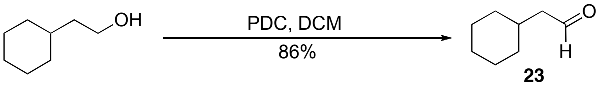
General Experimental:

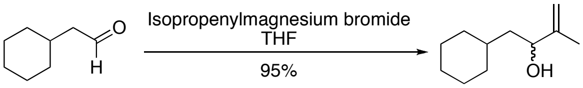
All reactions were carried out under an atmosphere of argon in flame-dried flasks using freshly distilled or anhydrous solvents, unless indicated otherwise. Tetrahydrofuran (THF) and diethyl ether were distilled over sodium benzophenone ketyl radical under an atmosphere of argon. Dichloromethane, toluene, acetonitrile, pyridine, triethylamine (TEA), diisopropylamine (DIPEA) and hexamethylphosphoramide (HMPA) were distilled over calcium hydride under an atmosphere of argon. Anhydrous 1,4-dioxane and 1-methyl-2-pyrrolidinone (NMP) were purchased from Fluka, stored over 4Å molecular sieves, and handled under an atmosphere of argon. Anhydrous benzene, dimethylsulfoxide (DMSO) and *N,N*-dimethylformamide (DMF) were purchased from Aldrich and handled under an atmosphere of argon. $CDCl_3$, C_6D_6, CD_2Cl_2 and DMSO-*d*6 were purchased from Cambridge Isotope Laboratories and used without further purification. All other reagents were purchased from commercial sources and were used without further purification, unless indicated otherwise. Thin layer chromatography (TLC) was performed on Whattman 60 F254 glass plates and was visualized using UV light (254nm) and/or potassium permanganate. Column chromatography purifications were carried out using the flash technique on Silicycle silica gel 60 (230-400 mesh). NMR spectra were recorded on a Bruker 600 AV, 400 AV or 300 AV spectrometer as indicated. The chemical shifts (δ) for ^{1}H spectra are given in ppm are referenced to the residual proton signal of the deuterated solvent. The chemical shifts (δ) for ^{13}C spectra are referenced relative to the signal from the carbon of the deuterated solvent. ^{13}C APT spectra represent a positive set of peaks (indicated by (+)) for quaternary carbons as well as carbon atoms with even number of protons and a negative set of peaks (indicated by (-)) for carbon atoms with odd number of protons. Abbreviations used to define multiplicies are as follows: s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet; br = broad. IR spectra were recorded on a Thermal Nicolet 380 FT-IR with an ATR germanium crystal spectrometer. Elemental analyses were performed by Chemisar Laboratories, Inc. in Guelph, Ontario. HRMS analyses were performed by McMaster Regional Centre for Mass Spectrometry in Hamilton, Ontario.

Synthetic Procedures:



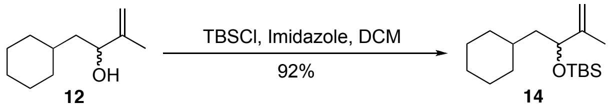
23

2-Cyclohexylethanal (23): To a solution of 2-cyclohexylethanol (6.0 g, 46.8 mmol) in CH_2Cl_2 (230 mL) was added PDC (26.4 g, 70.2 mmol) in one portion. The heterogeneous mixture was vigorously stirred until full consumption of starting material was observed (TLC, ~ 12 h). The solvent was removed under reduced pressure. To the solid residue was added ~ 200 mL pentane. The solid material was broken apart with a spatula and the mixture was sonicated before being passed through a thick, well-packed bed of celite. This procedure was repeated with ~ 100 mL of fresh pentane. The combined filtrates were concentrated under reduced pressure to give **23** (5.10 g, 86%) as an aromatic, colorless oil that required no further purification. Note: silica gel chromatography appears to polymerize the product. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.75 (t, *J* = 2.4 Hz, 1H), 2.29 (dd, *J* = 6.9, 2.4 Hz, 2H), 1.92-1.86 (m, 1H), 1.74-1.65 (m, 5H), 1.32-0.99 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 203.0 (-), 51.4 (+), 33.2 (+), 32.7 (-), 26.1 (+), 26.0 (+). IR (neat): 2919, 2853, 2714, 1725 cm^{-1}. The spectral data are in accordance with those reported in literature.[1]

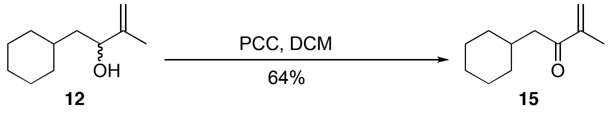


23 12

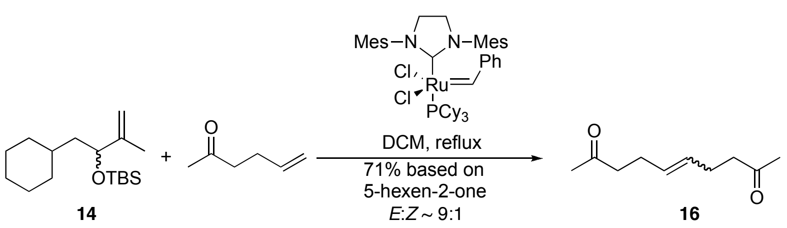
1-Cyclohexyl-3-methylbut-3-en-2-ol (12): To a solution of **23** (2.0 g, 15.8 mmol) in THF (35 mL) was added isopropenylmagnesium bromide (33.2 mL, 16.6 mmol, 0.5 M solution in THF) at 0 °C. The reaction was warmed to r.t. and stirred for 30 minutes before being quenched with 1 M HCl and diluted with Et_2O. The organic layer was extracted, separated, washed with brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (R_f = 0.30; 20% Et_2O in pentane) to give **12** (2.5 g, 95%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.95 (s, 1H), 4.82 (s, 1H), 4.15 (br. t, *J* = 9.6 Hz, 1H), 1.73 (s, 3H), 1.85-1.55 (m, 5H), 1.50-1.05 (m, 7H), 1.00-0.85 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.3 (+), 110.7 (+), 73.6 (-), 43.0 (+), 34.2 (-), 34.0 (+), 33.0 (+), 26.6 (+), 26.3 (+), 26.2 (+), 17.5 (-). Note: as with most compounds in this series, the hydroxyl centre renders the cyclohexyl carbons diastereotopic. IR (neat): 3360 (br), 2907, 2852, 1444 cm^{-1}. HRMS *m/e* calcd. for $C_{11}H_{20}O$ (M^+) 168.1514, found 168.1522.



***tert*-Butyl(1-cyclohexyl-3-methylbut-3-en-2-yloxy)dimethylsilane (14)**: To a suspension of imidazole (79 mg, 1.2 mmol) and TBSCl (200 mg, 1.3 mmol) in CH_2Cl_2 (4.0 mL) was added a solution of **12** (150 mg, 0.89 mmol) in CH_2Cl_2 (0.5 mL). The reaction mixture was stirred at r.t. for 18 h before being quenched with brine and diluted with Et_2O. The organic layer was separated and the aqueous layer extracted with Et_2O; the combined organic layers were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel ($R_f = 0.70$; pentane) to give 230 mg of **14** (92%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.83 (br. s, 1H), 4.74 (br. s, 1H), 4.13 (dd, *J* = 10.4, 7.2 Hz, 1H), 1.88-1.60 (m, 8H), 1.47-1.10 (m, 6H), 0.95-0.82 (m, 11H), 0.04 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.5 (+), 110.4 (+), 74.5 (-), 44.2 (+), 34.0 (+), 33.8 (-), 33.2 (+), 26.7 (+), 26.4 (+), 26.3 (+), 25.9 (-), 18.2 (+), 16.8 (-), -4.6 (-), -4.7 (-). IR (neat): 3071, 2953, 2927, 2854, 1472, 1462 cm^{-1}. HRMS *m/e* calcd. for $C_{13}H_{25}OSi$ $(M - C_4H_9)^+$ 225.1675, found 225.1680.



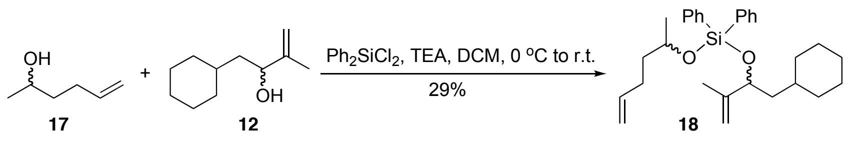
1-Cyclohexyl-3-methylbut-3-en-2-one (15): To a solution of **12** (200 mg, 1.2 mmol) in CH_2Cl_2 (6 mL) was added PCC (380 mg, 1.8 mmol) in one portion and the resulting heterogeneous mixture stirred vigorously at r.t. for 3h. The solvent was removed under reduced pressure and ~ 30 mL of pentane was added. The solid material was broken apart with a spatula and the mixture was sonicated before being passed through a thick, well-packed bed of celite. This procedure was repeated with additional pentane and the combined filtrates were concentrated under reduced pressure. The residue was purified by column chromatography on silica gel ($R_f = 0.30$; 1% Et_2O in pentane) to give **15** (127 mg, 64%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.94 (s, 1H), 5.76 (s, 1H), 2.54 (d, *J* = 7.2 Hz, 2H), 1.88 (s, 3H), 1.74 (m, 5H), 1.34-0.97 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 202.2 (+), 145.1 (+), 124.5 (+), 45.1 (+), 34.8 (-), 33.4 (+), 26.2 (+), 26.1 (+), 17.6 (-). IR (neat): 3095, 2924, 2851, 1676, 1449 cm^{-1}. HRMS *m/e* calcd. for $C_{11}H_{18}O$ (M^+) 166.1358, found 166.1351.



14

16

(*E*)-Dec-5-ene-2,9-dione (**16**, representative example): To a solution of 9.0 mg of tricyclohexylphosphine[1,3-*bis*(2,4,6-trimethylphenyl)-4,5-dihydroimidazole-2-ylidene]-benzylidine ruthemiun (IV) dichloride (9.0 mg, 0.01 mmol) in CH_2Cl_2 (1 mL) was added a solution of **14** (60 mg, 0.21 mmol) and 5-hexen-2-one (31 mg, 0.32 mmol) in CH_2Cl_2 (0.5 mL) at r.t. The reaction mixture was warmed to reflux and stirred for 14 h. After the reaction was judged complete, the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel ($R_f = 0.15$; 10% EtOAc in hexanes) to give a 9:1 *E*:*Z* mixture of **16** (19 mg, 71% based on 5-hexen-2-one) as a white solid. M.p. = 35-36 °C (Lit. m.p. = 36.8-37.6 °C).[2] Spectral data for *E* isomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.42 (t, *J* = 3.6 Hz, 2H), 2.47 (t, *J* = 7.5 Hz, 4H), 2.53 (m, 4H), 2.14 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 208.4 (+), 129.5 (-), 43.3 (+), 30.0 (-), 26.7 (+). The spectral data are in accordance with those reported in literature.[2]

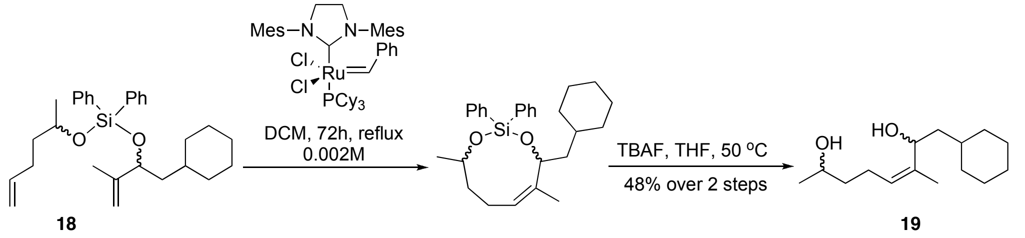


17

12

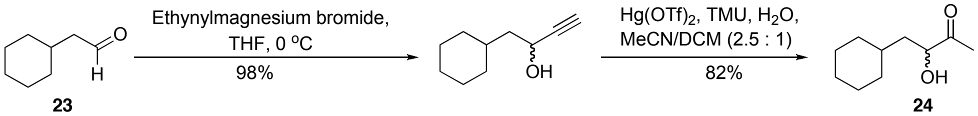
18

(1-Cyclohexyl-3-methylbut-3-en-2-yloxy)(hex-5-en-2-yloxy)diphenylsilane (**18**): To a solution of Ph_2SiCl_2 (250 mg, 1.00 mmol) and triethylamine (0.31 mL, 2.19 mmol) in CH_2Cl_2 (2.4 mL) was added a solution of 5-hexen-2-ol (100 mg, 1.00 mmol) and **12** (168 mg, 1.00 mmol) in CH_2Cl_2 (2 mL); the resultant mixture was stirred at 0 °C for 4 hours and then at r.t. for 12 h and then diluted with water and Et_2O. The organic layer was separated and the aqueous layer extracted with Et_2O; the combined organic layers were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel ($R_f = 0.30$; 2% EtOAc in hexanes) to give an equimolar mixture of diasteriomers of **18** (130 mg, 29%) as a viscous, colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65 (m, 4H), 7.39 (m, 6H), 5.74 (m, 1H), 4.94 (m, 2H), 4.79 (br. s, 1H), 4.73 (br. s, 1H), 4.34 (t, *J* = 6.6 Hz, 1H), 4.07 (m, 1H), 2.08 (m, 2H), 1.72-1.42 (m, 19H), 0.78 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.0 (+), 146.9 (+), 138.8 (-), 138.8 (-), 135.2 (-), 135.1 (-), 134.1 (+), 129.9 (-), 129.9 (-), 127.6 (-), 127.5 (-), 114.2 (+), 114.2 (+), 111.4 (+), 111.4 (+), 75.1 (-), 75.0 (-), 68.9 (-), 43.7 (+), 43.7 (+), 38.5 (+), 33.6 (-), 33.6 (-), 33.5 (+), 33.4 (+), 33.4 (+), 29.7 (+), 26.6 (+), 26.3 (+), 26.2 (+), 23.3 (-), 23.2 (-), 17.0 (-), 16.9 (-). HRMS *m/e* calcd. for $C_{29}H_{40}O_2Si$ $(M+H)^+$ 449.2876, found 449.2891.



(*Z*)-1-Cyclohexyl-3-methyloct-3-ene-2,7-diol (19): To a solution of tricyclohexylphosphine[1,3-*bis*(2,4,6-trimethylphenyl)-4,5-dihydroimidazole-2-ylidene]-benzylidineruthemiun (IV) dichloride (13 mg, 15 μmol) in CH_2Cl_2 (75 mL) was added **18** (66 mg, 0.18 mmol) and the reaction mixture stirred at 40 °C for 72 hours. The solvent was removed under reduced pressure and the residue taken up in pentane and passed through a bed of celite. The pentane was removed under reduced pressure and the residue was dissolved in THF (0.25 mL). To this solution was added TBAF (0.55 mL, 0.55 mmol, 1.0 M in THF) and the reaction mixture was stirred for 18 h at 50 °C at which point water and Et_2O were added. The organic layer was separated and the aqueous layer extracted with Et_2O; the combined organic layers were washed with brine and dried ($MgSO_4$). After filtering and concentrating under reduced pressure, the residue was purified by column chromatography on silica gel (R_f = 0.25; 40%

EtOAc in hexanes) to give **19** (17 mg, 48% from **18**) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.21 (t, *J* = 7.5 Hz, 1H), 4.72 (t, *J* = 6.0 Hz, 1H), 3.79 (m, 1H), 2.67 (br. s, 1H), 2.32 (m, 1H), 2.15-0.85 (m, 23 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.9 (+), 127.1 (-), 66.8 (-), 66.7 (-), 42.4 (+), 38.9 (+), 34.3 (-), 34.0 (+), 33.3 (+), 26.6 (+), 26.3 (+), 26.2 (+), 23.8 (-), 23.3 (+), 17.6 (-). HRMS *m/e* calcd. for $C_{15}H_{28}O_2$ $(M+NH_4-H_2O)^+$ 240.2327, found 240.2328.

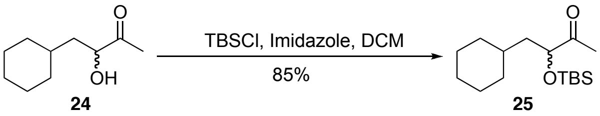


4-Cyclohexyl-3-hydroxybutan-2-one (24): To a solution of **23** (4.5 g, 35.7 mmol) in THF (100 mL) was added ethynylmagnesium chloride (74.9 mL, 37.4 mmol, 0.5 M solution in THF) at 0 °C. The reaction mixture was stirred for 10 minutes before warming to r.t., where it was allowed to stir for an additional 30 minutes after which 1M HCl (100 mL) was added. After separating the layers, the aqueous layer was extracted with Et_2O (2×) and the combined organic layers were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (R_f = 0.30; 20% Et_2O in pentane) to give the propargylic alcohol (5.3 g, 98%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.45 (m, 1H), 2.46 (d, *J* = 2.0 Hz, 1H), 1.81-1.53 (m, 9H), 1.27-1.13 (m, 3H), 0.98-0.95 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 85.4 (+), 72.7 (+), 60.3 (-), 34.0 (-), 33.3 (+), 33.0 (+), 26.5 (+), 26.2 (+), 26.1 (+). IR (neat): 3405 (br), 3303 (sharp), 2917, 2847, 2133 (weak) cm^{-1}. Anal. Calcd. for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 78.58; H, 10.21.

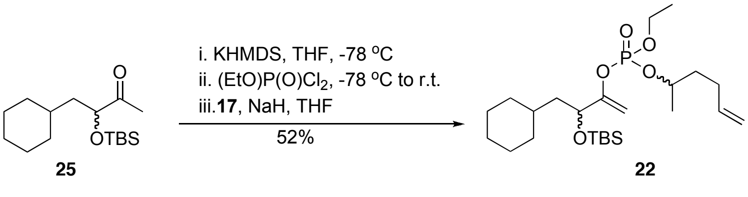
To a solution of the above propargylic alcohol (3.85 g, 25.29 mmol) in MeCN (125 mL) was added sequentially 1,1,3,3-tetramethylurea (435 mg, 5.06 mmol), distilled water (1.37 mL, 75.87 mmol) and mercury(II) triflate[a] (1.26 g, 2.53 mmol). CH_2Cl_2 (50 mL) was added and the resulting white suspension was stirred at r.t. for 24 hours after which it was diluted with HCl (1 M) and Et_2O. The organic layer was extracted, separated, washed with saturated $NaHCO_3$, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (R_f = 0.40; 3% Et_2O in pentane) to give **24** (3.51 g, 82%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.28-

4.00 (m, 1H), 3.44 (d, J = 4.8 Hz, 1H), 2.21 (s, 3H), 1.94 (d, J = 12.4 Hz, 1H), 1.80-1.55 (m, 6H), 1.45-1.10 (m, 4H), 1.05-0.85 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.6 (+), 75.0 (-), 41.3 (+), 34.3 (+), 33.9 (-), 32.2 (+), 26.5 (+), 26.3 (+), 26.0 (+), 25.2 (-). IR (neat): 3468 (br.), 2923, 2853, 1710 cm^{-1}.

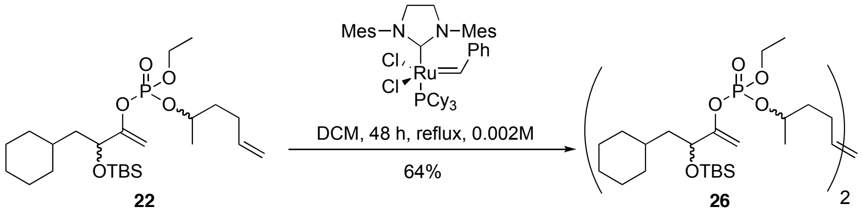
[a] Preparation of mercury(II) triflate[3]: To a suspension of mercury(II) oxide yellow (2.98 g, 13.75 mmol) in MeCN (70 mL) at r.t. was added triflic anhydride (3.88 g, 13.75 mmol) in one portion. The orange suspension gave way to a clear and colorless solution within 3 minutes. The solvent was removed under reduced pressure to give mercury(II) triflate (6.80 g, >99% yield) as a white solid (m.p. > 300 °C) that was used without further purification.



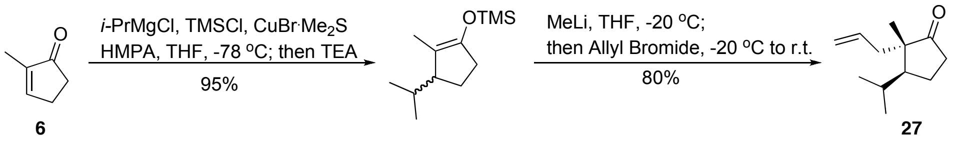
3-(*tert*-Butyldimethylsilyloxy)-4-cyclohexylbutan-2-one (25): To a solution of *t*-butyldimethylsilyl chloride (1.16 g, 7.68 mmol) in CH_2Cl_2 (26 mL) was added imidazole (453 mg, 6.66 mmol) and **24** (871 mg, 5.12 mmol) and the resulting mixture was stirred for 24 hours at r.t. The reaction mixture was diluted with Et_2O, washed with water, then brine, dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (R_f = 0.30; 2% Et_2O in pentane) to give **25** (1.24 g, 85%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.05 (m, 1H), 2.13 (s, 3H), 1.75-1.62 (m, 5H), 1.51-1.34 (m, 3H), 1.26-1.10 (m, 3H), 0.96-0.85 (m, 11H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 212.5 (+), 77.0 (+), 42.3 (+), 34.0 (+), 33.3 (-), 32.8 (+), 26.5 (+), 26.3 (+), 26.0 (+), 25.7 (-), 24.6 (-), 18.1 (+), -4.9 (-), -4.8 (-). IR (neat): 2927, 2855, 1719 cm^{-1}. HRMS *m/e* calcd. for $C_{16}H_{32}O_2Si$ $(M+H)^+$ 285.2250, found 285.2244.



3-(*tert*-Butyldimethylsilyloxy)-4-cyclohexylbut-1-en-2-yl ethyl hex-5-en-2-yl phosphate (22): To a solution of potassium bis(trimethylsilyl)amide (405 mg, 1.93 mmol) in THF (5.8 mL) at –78 °C was added drop-wise over 20 minutes a solution of **25** (500 mg, 1.76 mmol) in THF (0.5 mL) and the resulting mixture was stirred for an additional 60 minutes (Flask A). The contents of flask A were cannulated into a solution containing ethyl dichlorophosphate (328 mg, 1.93 mmol) in THF (6.2 mL) at –78 °C (Flask B, equipped with a relux condenser) and the resulting mixture was allowed to stir for 2 hours before warming to r.t. where it was stirred for an additional 60 minutes. In a separate flask (Flask C) was added 5-hexen-2-ol (352 mg, 3.52 mmol), THF (5.0 mL) and then 95% dry NaH (89 mg, 3.52 mmol). The resulting solution was stirred at r.t. for 60 minutes. The formed alkoxide was then cannulated into flask B and the resulting solution was warmed to reflux and allowed to stir for 2 hours. The reaction mixture was diluted with brine, the layers separated and the aqueous layer extracted with Et_2O (2×); the combined organic layers were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel ($R_f = 0.55$; 50% Et_2O in pentane) to give **22** (447 mg, 52%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.88-5.72 (m, 1H), 5.07-4.92 (m, 3H), 4.74 (br. s, 1H), 4.61-4.50 (m, 1H), 4.20-4.08 (m, 3H), 2.22-2.15 (m, 2H), 1.80-1.56 (m, 7H), 1.50-1.30 (m, 6H), 1.27-1.10 (m, 4H), 0.98-0.80 (m, 11H), 0.05 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.4 (+), 157.2 (+), 137.5 (-), 115.1 (+), 95.4 (+), 76.2 (-), 76.1 (-), 70.6 (-), 70.5 (-), 70.4 (-), 64.2 (+), 43.5 (+), 36.6 (+), 36.5 (+), 34.2 (+), 33.5 (-), 33.0 (+), 29.3 (+), 26.6 (+), 26.4 (+), 26.1 (+), 25.8 (-), 21.4 (-), 18.1 (+), 16.2 (-), 16.1 (-), -4.6 (-), -4.4 (-). HRMS *m/e* calcd. for $C_{24}H_{47}O_5PSi$ $(M+H)^+$ 475.3001, found 475.3000.



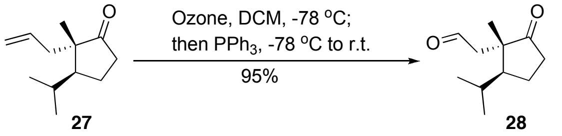
(*E*)-Bis(3-(*tert*-butyldimethylsilyloxy)-4-cyclohexylbut-1-en-2-yl) dec-5-ene-2,9-diyl diethyl diphosphate (26): To a solution of **22** (55 mg, 0.116 mmol) in CH_2Cl_2 (58 mL, 0.002M) was added tricyclohexylphosphine[1,3-*bis*(2,4,6-trimethylphenyl)-4,5-dihydroimidazole-2-ylidene]-benzylidine ruthemiun (IV) dichloride (9.8 mg, 0.012 mmol). The solution was warmed to reflux and stirred for 48 hours. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel ($R_f = 0.50$; 40% EtOAc in hexanes) to give **26** (34 mg, 64%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.45-5.35 (m., 2H), 4.94-4.90 (m, 2H), 4.77-4.73 (m, 2H), 4.59-4.50 (m, 2H), 4.17-4.05 (m, 6H), 2.15-2.00 (m, 4H), 1.80-1.55 (m, 14H), 1.50-1.40 (m, 4H), 1.39-1.30 (m, 12H), 1.30-1.10 (m, 8H), 0.95-0.82 (m, 22H), 0.07 (s, 6H), 0.06 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.4 (+), 157.3 (+), 129.7 (-), 95.4 (+), 76.3 (-), 70.6 (-), 70.5 (-), 70.4 (-), 64.2 (+), 43.5 (+), 43.5 (+), 37.2 (+), 34.2 (+), 33.5 (-), 33.0 (+), 28.2 (+), 26.6 (+), 26.4 (+), 26.1 (+), 25.8 (-), 21.5 (-), 18.1 (+), 16.1 (-), 16.0 (-), 4.60 (-), 4.50 (-). Anal. Calcd. for $C_{46}H_{90}O_{10}P_2Si_2$: C, 59.97; H, 9.85. Found: C, 60.35; H, 9.97.



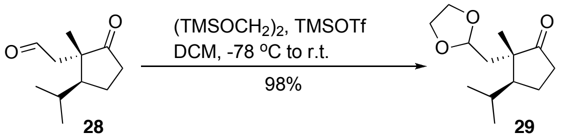
2-Allyl-3-isopropyl-2-methylcyclopentanone (27): To a solution of isopropylmagnesium chloride (23.4 mL, 46.8 mmol, 2.0 M solution in THF) in THF (95 mL) at –78 °C was added CuBr•Me_2S (450 mg, 2.19 mmol) under a cone of argon. The resulting solution was stirred for 15 minutes after which HMPA (10.9 mL, 62.4 mmol) was injected via syringe followed by 20 minutes of additional stirring. A solution of 2-methyl-2-cyclopenten-1-one (3.0 g, 31.2 mmol) and TMSCl (6.8 g, 62.4 mmol) in THF (10 mL) was added via syringe pump over 30 minutes and the resulting solution was stirred at –78 °C for 3 hours. TEA (9.2 mL, 6.54 mmol) was then added and the solution stirred for an additional 15 minutes before being diluted with pentane (~ 150 mL) and water (~ 400 mL). The layers were separated, and the aqueous layer extracted again with fresh pentane (~ 300 mL). The combined organic extracts were washed with ample water and brine, and then dried ($MgSO_4$), filtered and concentrated under reduced pressure to provide the silyl enol ether (6.30 g, 95% yield) as a colorless oil that required no further purification. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.40-2.48 (m, 1H), 2.27-2.19 (m, 2H), 1.95-1.85 (m, 1H), 1.78-1.70 (m, 1H), 1.60-1.50 (m, 1H), 1.47 (s, 3H), 0.89 (d, J = 7.2 Hz, 3H), 0.70 (d, J = 6.8 Hz, 3H), 0.18 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 147.1 (+), 115.6 (+), 50.5 (-), 33.0 (+), 28.9 (-), 20.6 (-

), 20.1 (+), 15.8 (-), 10.5 (-), 0.6 (-). IR (neat): 2950, 1695 cm^{-1}. The spectral data were in accordance with those reported in the literature.[4]

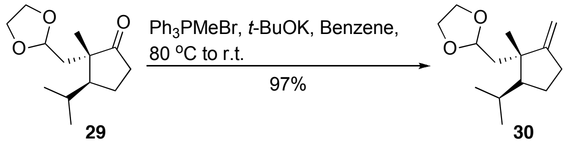
To a solution of the above silyl enol ether (400 mg, 1.88 mmol) in THF (19 mL) at -20 °C was added MeLi (1.41 mL, 1.97 mmol, 1.4 M solution in Et_2O) drop-wise over 20 minutes. The solution was stirred for an additional 10 minutes before adding freshly distilled allyl bromide (0.65 mL, 7.53 mmol) drop-wise over 15 minutes. The reaction was stirred at –20 °C for 1 hour and then at r.t. for 2 hours before being quenched with HCl (1 M) and diluted with Et_2O. The separated organic layer was washed with water and brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (R_f = 0.30; 4% Et_2O in pentane) to give **27** (272 mg, 80%) as a colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 5.60-5.52 (m, 1H), 5.05-4.98 (m, 2H), 2.53 (dd, *J* = 14.8, 6.0 Hz, 1H), 2.35-2.31 (m, 1H), 2.18 (dd, *J* = 13.6, 8.8 Hz, 1H), 2.08-1.98 (m, 2H), 1.85-1.80 (m, 1H), 1.72-1.64, (m, 1H), 1.49-1.40 (m, 1H), 1.04 (d, *J* = 6.4 Hz, 3H), 0.93 (d, *J* = 7.0 Hz, 3H), 0.92 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 223.8 (+), 134.6 (-), 118.2 (+), 52.1 (+), 48.0 (-), 42.1 (+), 37.8 (+), 29.5 (-), 23.8 (+), 22.3 (-), 21.4 (-), 17.9 (-). IR (neat): 3075, 2960, 1740 cm^{-1}. The spectral data were in accordance with those reported in the literature.[4]



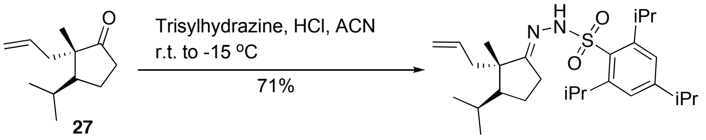
2-(-2-Isopropyl-1-methyl-5-oxocyclopentyl)ethanal (28): A vigorously stirred solution of **27** (1.10 g, 6.10 mmol) in CH_2Cl_2 (60 mL) was degassed with argon prior to being cooled to –78 °C. The argon inlet was replaced with an ozone inlet and the solution purged until the solution became indigo blue (approx. 15 min.). The solution was stirred for an additional 5 minutes before being purged with argon to remove the intense blue color after which PPh_3 (4.8 g, 18.3 mmol) was added. The reaction mixture was allowed to warm to r.t. over 30 minutes and was stirred for an additional 4 hours for complete destruction of the ozonide. The solvent was removed under reduced pressure and the resultant viscous liquid was triturated with hexanes, filtered and the filtrate was concentrated. The crude product was purified by column chromatography on silica gel ($R_f = 0.50$; 40% Et_2O in pentane) to give **28** (1.05 g, 95%) as a colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 9.60 (s, 1H), 2.96-2.83 (m, 2H), 2.50-2.35 (m, 2H), 2.23-2.10 (m, 1H), 1.96-1.85 (m, 1H), 1.70-1.58 (m, 1H), 1.52-1.40 (m, 1H), 0.98 (d, $J = 6.4$ Hz, 3H), 0.95 (d, $J = 6.8$ Hz, 3H), 0.94 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 222.7 (+), 200.3 (-), 52.1 (+), 49.4 (-), 49.0 (+), 36.4 (+), 29.7 (-), 24.7 (+), 22.5 (-), 21.7 (-), 17.3 (-). IR (neat): 2970, 2727, 1735 cm^{-1}. The spectral data were in accordance with those reported in the literature.[4]



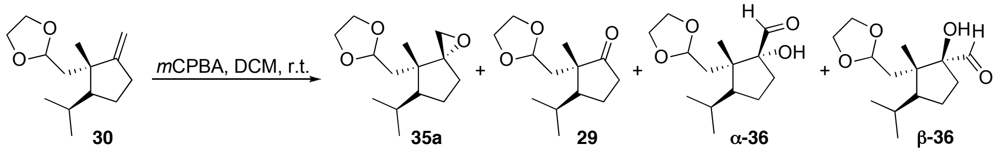
2-((1,3-Dioxolan-2-yl)methyl)-3-isopropyl-2-methylcyclopentanone (29): To a stirred solution of **28** (4.10 g, 22.5 mmol) in CH_2Cl_2 (70 mL) at r.t. was added 1,2-bis(trimethylsiloxy)ethane (5.52 mL, 22.5 mmol) after which the solution was cooled to -78 °C and TMSOTf (41 uL, 0.23 mmol) was added. The resulting mixture was stirred for 15 minutes before removing the dry ice/acetone bath and allowing the reaction to gradually warm to r.t. After 45 minutes the reaction was quenched with pyridine (3 mL) and diluted with pentane. The mixture was washed with water and brine and the organic layer dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography ($R_f = 0.35$; 40% Et_2O in pentane) to give **29** (5.0 g, 98%) as a colorless oil. ^1H NMR ($CDCl_3$, 300 MHz): δ 5.01 (dd, $J = 6.9, 3.9$ Hz, 1H), 3.95-3.65 (m, 4H), 2.35-1.90 (m, 5H), 1.83 (dd, $J = 14.4, 3.9$ Hz, 1H), 1.70-1.55 (m, 1H), 1.45-1.30 (m, 1H), 1.02 (d, $J = 6.6$ Hz, 3H), 0.94 (d, $J = 6.6$ Hz, 3H), 0.87 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 223.0 (+), 102.3 (-), 64.8 (+), 64.1 (+), 49.5 (+), 48.2 (-), 41.1 (+), 37.0 (+), 29.6 (-), 24.4 (+), 22.2 (-), 21.6 (-), 18.4 (-). IR (neat): 2961, 2879, 1739 cm^{-1}. Anal. Calcd. for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 69.28; H, 10.12.



2-((-2-Isopropyl-1-methyl-5-methylenecyclopentyl)methyl)-1,3-dioxolane (30): To a flask equipped with a reflux condenser was added Ph_3PMeBr (19.32 g, 53.0 mmol), *t*-BuOK (6.27 g, 53.0 mmol) and anhydrous benzene (260 mL) and the resulting mixture was stirred vigorously under reflux for 1 hour before being cooled to r.t. To the canary-yellow suspension was added a solution of **29** (8.00 g, 35.4 mmol) in anhydrous benzene (20 mL, 5 mL rinse) and the resulting mixture was stirred under reflux for 5 hours and then at r.t. overnight before being quenched with saturated $NaHCO_3$. The organic layer was diluted with pentane and the aqueous layer was extracted and separated. The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography ($R_f = 0.30$; 5% Et_2O in pentane) to give **30** (7.69 g, 97%) as a colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 4.91 (s, 1H), 4.80 (t, $J = 4.4$ Hz, 1H), 4.76 (s, 1H), 4.00-3.90 (m, 2H), 3.88-3.75 (m, 2H), 2.45-2.35 (m, 1H), 2.33-2.20 (m, 1H), 1.95-1.90 (m, 2H), 1.85-1.78 (m, 2H), 1.75-1.65 (m, 1H), 1.40-1.25 (m, 1H), 1.02 (s, 3H), 1.00 (d, $J = 6.4$ Hz, 3H), 0.89 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.3 (+), 104.1 (+), 103.6 (-), 64.7 (+), 64.1 (+), 52.2 (-), 45.6 (+), 44.6 (+), 32.5 (+), 28.6 (-), 26.3 (+), 23.9 (-), 23.1 (-), 21.4 (-). IR (neat): 3069, 2954, 2877, 1649, 1472 cm^{-1}. Anal. Calcd. for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 74.96; H, 10.95.



***N'*-2-Allyl-3-isopropyl-2-methylcyclopentylidene)-2,4,6-triisopropylbenzenesulfono-hydrazide (32):** To a suspension of **27** (200 mg, 1.11 mmol) and 2,4,6-triisopropylbenzenesulfonyl hydrazide (397 mg, 1.33 mmol) in acetonitrile (1.2 mL) was added drop-wise 12 N hydrochloric acid (0.10 mL) after which the solution became homogeneous. The round bottom flask was wrapped with aluminum foil so as to avoid exposure to light and was allowed to stir at r.t for 12 hours. The resulting heterogeneous solution was cooled to -15 °C (salt-ice bath) and the white precipitate was filtered and subsequently washed with ice-cold acetonitrile. The white solid was air-dried and collected to give the trisylhydrazone (364 mg, 71%) that required no further purification. M.p. = 118-120 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.17 (s, 2H), 6.97 (br. s, 1H), 5.20-5.08 (m, 1H), 4.69 (dd, $J = 10.4$, 1.6 Hz, 1H), 4.51 (d, *J* = 16.8 Hz, 1H), 4.22 (m, 2H), 2.89 (m, 1H), 2.34-2.23 (m, 2H), 2.07 (dd, *J* = 13.6, 8.0 Hz, 1H), 1.98-1.78 (m, 2H), 1.63-1.53 (m, 2H), 1.46-1.38 (m, 1H), 1.30 (d, *J* = 6.8 Hz, 6H), 1.26 (d, *J* = 6.8 Hz, 12H), 0.96 (d, *J* = 6.0 Hz, 3H), 0.92 (s, 3H), 0.85 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (CDCl$_3$, 100 MHz): δ 169.6 (+), 153.2 (+), 151.1 (+), 134.7 (-), 131.4 (+), 123.6 (-), 117.6 (+), 49.4 (-), 48.9 (+), 43.0 (+), 34.2 (-), 29.8 (-), 28.6 (-), 26.5 (+), 25.2 (+), 24.9 (-), 24.7 (-), 23.6 (-), 23.6 (-), 22.5 (-), 21.5 (-), 21.1 (-). IR (CDCl$_3$): 3242, 2963, 2872, 1600, 1462 cm^{-1}. Anal. Calcd. for $C_{27}H_{44}N_2O_2S$: C, 70.39; H, 9.63, found: C, 70.68; H, 9.68.



To a solution of **30** (1.00 g, 4.46 mmol) in CH_2Cl_2 (30 mL) was added *m*CPBA (1.50 g, 6.69 mmol, ~ 77% purity) in one portion and the reaction was stirred at r.t. for 3 hours. Starting material **30** was still present by TLC thus an additional 400 mg of *m*CPBA were added (1.78 mmol) and then again after 1 hour (500 mg, 2.23 mmol). After an additional 1 hour of stirring, the reaction was deemed complete (TLC) and the reaction was quenched with saturated Na_2CO_3 and diluted with pentane. The layers were separated and the organic layer was washed with additional saturated Na_2CO_3, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography (20% Et_2O in pentane) to give products **35a**, **29**, **α-36** and **β-36**.

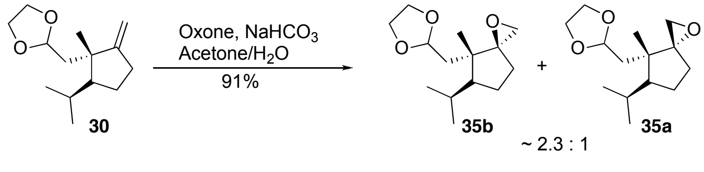
4-((1,3-Dioxolan-2-yl)methyl)-5-isopropyl-4-methyl-1-oxaspiro[2.4]heptane (35a): 468 mg (44%) was isolated (R_f = 0.45; 20% Et_2O in pentane) as a colorless oil. ^{1}H NMR (CDCl$_3$, 600 MHz): δ 4.94 (dd, *J* = 6.0, 3.0 Hz, 1H), 3.96-3.86 (m, 2H), 3.82-3.74 (m, 2H), 2.74 (d, *J* = 4.8 Hz, 1H), 2.64 (d, *J* = 4.8 Hz, 1H), 1.98-1.90 (m, 1H), 1.90-1.82 (m, 2H), 1.78-1.68 (m, 3H), 1.57 (dd, *J* = 15.0, 3.0 Hz, 1H), 1.42-1.35 (m, 1H), 0.98 (d, *J* = 7.2 Hz, 3H), 0.88 (d, *J* = 7.2 Hz, 3H), 0.87 (s, 3H); ^{13}C NMR (C_6D_6, 75 MHz): δ 103.4 (-), 69.7 (+), 64.5 (+), 63.9 (+), 51.6 (-), 49.9 (+), 42.3 (+), 40.7 (+), 31.0 (+), 28.6 (-), 24.2 (+), 23.1 (-), 21.0 (-), 19.4 (-). IR (neat): 2958, 2880, 1717 cm^{-1}. HRMS *m/e* calcd. for $C_{14}H_{24}O_3$ (M$^+$) 240.1725, found 240.1723.

Compound **29**: 117 mg (11%) was isolated (R_f = 0.30; 20% Et_2O in pentane) as a colorless oil. Spectral data was identical to that listed above.

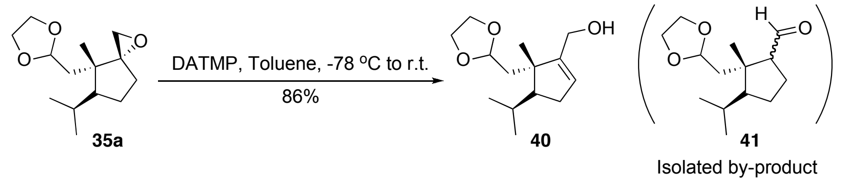
α-Hydroxyaldehydes **α-36** and **β-36** (307 mg combined, 27%) were isolated (R_f = 0.15; 20% Et_2O in pentane) as colorless oils. Test tube fractions containing pure diasteriomers were set aside for structure confirmation.

2-((1,3-Dioxolan-2-yl)methyl)-1-hydroxy-3-isopropyl-2-methylcyclopentanecarb-aldehyde (α-36): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.77 (s, 1H), 4.80 (t, J = 4.8 Hz, 1H), 4.02-3.90 (m, 3H), 4.88-4.75 (m, 2H), 2.28-2.15 (m, 1H), 2.14-2.00 (m, 2H), 1.99-1.90 (m, 2H), 1.75-1.65 (m, 1H), 1.63-1.45 (m, 2H), 1.16 (s, 3H), 1.00 (d, J = 6.4 Hz, 3H), 0.94 (d, J = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 204.2 (-), 102.2 (-), 89.4 (+), 64.4 (+), 64.3 (+), 55.3 (-), 51.7 (+), 40.1 (+), 32.5 (+), 28.4 (-), 26.1 (+), 23.6 (-), 22.6 (-), 16.2 (-). IR (neat): 3459 (br.), 2958, 2876, 1724 cm^{-1}. IR ($CHCl_3$): 3354 (br.), 2974, 2863, 1723 cm^{-1}. HRMS *m/e* calcd. for $C_{14}H_{24}O_4$ (M^+) 256.1675, found 256.1685.

2-((1,3-Dioxolan-2-yl)methyl)-1-hydroxy-3-isopropyl-2-methylcyclopentanecarb-aldehyde (β-36): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.85 (s, 1H), 5.07 (dd, J = 8.4, 2.0 Hz, 1H), 4.37 (s, 1H), 4.05-3.82 (m, 4H), 2.13 (dd, J = 14.4, 2.0 Hz, 1H), 1.95-1.48 (m, 6H), 1.09 (s, 3H), 1.00 (d, J = 6.4 Hz, 3H), 0.92 (d, J = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 205.7 (-), 102.5 (-), 88.5 (+), 64.9 (+), 64.8 (+), 52.9 (-), 48.4 (+), 40.1 (+), 31.0 (+), 29.7 (-), 24.1 (+), 23.7 (-), 22.0 (-), 14.6 (-). IR (neat): 3459 (br.), 2958, 2876, 1724 cm^{-1}. HRMS *m/e* calcd. for $C_{14}H_{24}O_4$ (M^+) 256.1675, found 256.1681.



4-((1,3-Dioxolan-2-yl)methyl)-5-isopropyl-4-methyl-1-oxaspiro[2.4]heptane (35a) and 4-((1,3-dioxolan-2-yl)methyl)-5-isopropyl-4-methyl-1-oxaspiro[2.4]heptane (35b): To a 100 mL round bottom flask charged with **30** (250 mg, 1.12 mmol) was added acetone (20 mL) and solid $NaHCO_3$ (1.40 g, 16.73 mmol). A solution of Oxone (6.85 g, 11.2 mmol) in water (20 mL) was added rapidly; to avoid spillage due to excessive effervescence, an oversized round bottom flask was used. The reaction was monitored by TLC and deemed complete within 10 minutes after which it was poured into a separatory funnel containing equal volumes of Et_2O and water (300 mL total). The layers were separated and the aqueous layer extracted a second time with additional Et_2O. The combined organic fractions were washed with water, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography (R_f = 0.4, 40% Et_2O in pentane) to give an inseparable mixture of diasteriomers **35a** and **35b** (244 mg, 91%) as a colorless oil contaminated with a trace amount (<5%) of ring-opened aldehyde **41**. The decomposition to the aldehyde occurs on silica-gel during purification. ^1H and ^{13}C NMR spectra are reported as a mixture of diasteriomers. Resonances from the major and minor diasteriomers that are discernable are reported as 'major' and 'minor', respectively, along with the sum of their integration. Resonances from the major and minor diasteriomers that are not discernable are reported as a mutliplet along with the sum of their integration. ^1H NMR (C_6D_6, 400 MHz): δ {(5.33 (dd, *J* = 6.0, 3.2 Hz, minor) & 4.98 (t, *J* = 4.8 Hz, major)), 1H}, 3.70-3.55 (m, 2H), 3.50-3.35 (m, 2H), {(2.82 (d, *J* = 4.4 Hz, major) & 2.59 (d, *J* = 4.8 Hz, minor) & 2.58 (d, *J* = 4.4 Hz, major) & 2.42 (d, *J* = 4.4 Hz, minor)), 2H}, 2.20-1.50 (m, 8H), {(1.19 (d, *J* = 6.8 Hz, minor) & 1.09 (d, *J* = 6.8 Hz, major) & 1.08 (s, major) & 1.01 (d, *J* = 6.8 Hz, major) & 0.96 (d, *J* = 6.8 Hz, minor) & 0.88 (s, minor)), 9H}. ^{13}C NMR (C_6D_6, 100 MHz): δ 103.4 (-, minor), 102.7 (-, major), 69.7 (+, minor), 68.9 (+, major), 64.5 (+, minor), 64.4 (+, major), 64.2 (+, major), 63.9 (+, minor), 52.2 (-, major), 51.6 (-, minor), 49.9 (+), 44.0 (+), 42.6 (+), 42.3 (+), 40.7 (+), 31.9 (+, major), 31.0 (+, minor), 28.6 (-, minor), 28.4 (+, major), 24.4 (+, major), 24.2 (+, minor), 23.4 (-, major), 23.1 (-, minor), 21.0 (-, minor), 20.4 (-, major), 19.4 (-, minor), 16.7 (-, major). HRMS *m/e* calcd. for $C_{14}H_{24}O_3$ (M^+) 240.1725, found 240.1723.

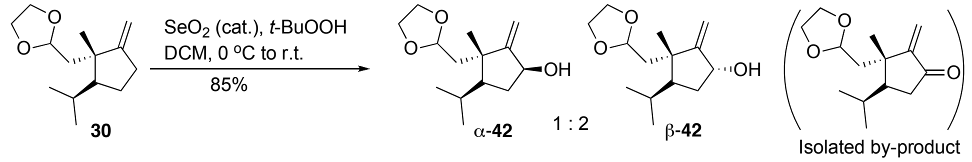


Preparation of DATMP:[5] To a solution of 2,2,6,6-tetramethylpiperidine (1.70 mL, 10.0 mmol) in anhydrous benzene (13.7 mL) at 0 °C was added *n*-BuLi (4.00 mL, 10.0 mmol, 2.5 M solution in hexanes). The resulting solution was stirred for 30 minutes before drop-wise addition of Et_2AlCl (5.56 mL, 10.0 mmol, 1.8 M solution in toluene), upon which LiCl precipitates. The heterogeneous mixture was stirred for 40 minutes and then warmed to r.t. Upon standing, LiCl deposits as sediment and the supernatant was used. No loss in activity was observed upon storage of this solution under argon for up to one week.

5-((1,3-Dioxolan-2-yl)methyl)-4-isopropyl-5-methylcyclopent-1-enyl)methanol (40): To a solution of **35a** (887 mg, 3.69 mmol) in toluene (13 mL) at -78 °C was added DATMP (13.9 mL, 5.54 mmol, ~ 0.4 M solution) drop-wise over 5 minutes. The resulting solution was stirred at -78 °C for 1 hour before slowly warming to r.t. where upon it was quenched with HCl (1M) and diluted with Et_2O. The layers were separated and the aqueous layer extracted once more with Et_2O; the combined organic layers were washed with saturated $NaHCO_3$, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography (R_f= 0.40; 75 % Et_2O in pentane) to give **40** (763 mg, 86%) as a colorless oil. ^1H NMR ($CDCl_3$, 400 MHz): δ 5.66 (s, 1H), 4.94 (t, *J* = 4.8 Hz, 1H), 4.20-4.10 (m, 2H), 4.00-3.90 (m, 2H), 3.87-3.80 (m, 2H), 2.55 (t, *J* = 5.6 Hz, 1H), 2.42-2.30 (m, 1H), 2.05-1.90 (m, 4H), 1.80-1.72 (m, 1H), 1.03 (d, *J* = 6.4 Hz, 3H), 1.01 (s, 3H), 0.92 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 150.4 (+), 126.2 (-), 103.0 (-), 64.6 (+), 64.5 (+), 59.4 (+), 51.7 (-), 48.5 (+), 42.1 (+), 34.7 (+), 29.3 (-), 22.7 (-), 22.3 (-), 20.7 (-). IR (neat): 3513, 2957, 2880 cm^{-1}. Anal. Calcd. for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07. Found: C, 69.65; H, 10.35.

2-((1,3-Dioxolan-2-yl)methyl)-3-isopropyl-2-methylcyclopentanecarbaldehyde (41) was an isolated by-product (70 mg, 8%). ^1H NMR ($CDCl_3$, 400 MHz): 9.85 (d, *J* = 3.0 Hz, 1H), 5.01 (t, *J* = 5.1 Hz, 1H), 4.00-3.75 (m, 4H), 2.70-2.60 (m, 1H), 2.05 (dd, *J* = 14.4, 4.2 Hz, 1H), 1.98-1.75 (m, 4 H), 1.72-1.45 (m, 3H), 1.09 (s, 3H), 0.96 (d, *J* = 6.6 Hz, 3H), 0.88 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 205.4 (-), 103.0 (-), 64.6 (+), 64.6 (+), 61.7 (-), 54.3 (-), 46.3 (+), 41.5 (+), 28.7 (-), 26.4 (+), 23.9 (-), 22.9 (+), 21.9 (-), 21.3 (-). IR (neat): 2958, 2879, 1714 cm^{-1}. HRMS *m*/*e* calcd. for $C_{14}H_{24}O_3$ (M^+)

240.1725, found 240.1727.



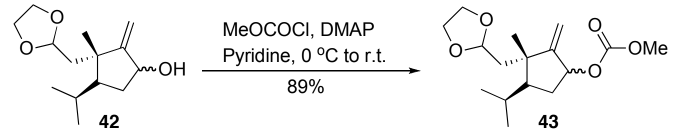
3-((1,3-Dioxolan-2-yl)methyl)-4-isopropyl-3-methyl-2-methylenecyclopentanol (**α-42**) and **3-((1,3-dioxolan-2-yl)methyl)-4-isopropyl-3-methyl-2-methylenecyclopentanol** (**β-42**): To a suspension of SeO_2 (644 mg, 5.80 mmol) in CH_2Cl_2 (290 mL) at 0 °C was added *t*-BuOOH (5.97 mL, 46.4 mmol, 70% w/w in water). The mixture was stirred for 45 minutes at 0 °C before adding a solution of **30** (6.5 g, 29.0 mmol) in CH_2Cl_2 (5 mL + 5 mL rinse). The reaction was warmed to r.t. and monitored by ^{1}H NMR spectroscopy (it was found that optimal yields of **42** were obtained when the amount of **30** and the amount of the over-oxidized enone were equivalent (~ 5 hours)). The reaction was quenched with saturated Na_2SO_3 and diluted with pentane. The organic layer was separated, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography (R_f = 0.35-0.40, step gradient, 50% Et_2O in pentane followed by 75% Et_2O in pentane) to give a 2:1 mixture of **α-42** and **β-42**, respectively (5.90 g combined, 85%). Fractions containing pure diasteriomers were independently collected for the purpose of analysis.

Compound α-42: (R_f = 0.40; 75% Et_2O in pentane) was collected as a white solid. M.p. = 39-43 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.16 (d, *J* = 2.4 Hz, 1H), 4.93 (d, *J* = 2.4 Hz, 1H), 4.76 (t, *J* = 4.8 Hz, 1H), 4.37 (br t, *J* = 7.5 Hz, 1H), 3.98-3.68 (m, 4H), 2.17 (quin., *J* = 5.7 Hz, 1H), 1.98-1.70 (m, 4H), 1.70-1.56 (m, 1H), 1.30-1.15 (m, 1H), 1.07 (s, 3H), 0.99 (d, *J* = 6.6 Hz, 3H), 0.90 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163.5 (+), 105.6 (+), 103.4 (-), 74.0 (-), 64.8 (+), 64.1 (+), 46.7 (-), 45.4 (+), 44.3 (+), 37.4 (+), 28.3 (-), 25.2 (-), 23.3 (-), 22.2 (-). IR (neat): 3367 (br.), 2961, 2879 cm^{-1}. Anal. Calcd. for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07. Found: C, 69.96; H, 10.33.

Compound β-42: (R_f = 0.35; 75% Et_2O in pentane) was collected as a colorless viscous oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.32 (s, 1H), 5.04 (t, *J* = 5.4 Hz, 1H), 4.98 (s, 1H), 4.36 (d, *J* = 4.8 Hz, 1H), 4.00-

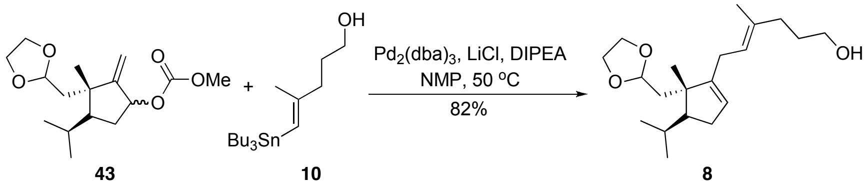
3.75 (m, 4H), 2.90 (br. s, 1H), 2.25-2.10 (m, 1H), 2.05 (apparent dd, *J* = 14.4, 5.1 Hz, 1H), 1.98-1.85 (m, 2H), 1.72-1.60 (m, 1H), 1.46 (dt, *J* = 12.6, 4.8 Hz, 1H), 1.03 (d, *J* = 6.6 Hz, 3H), 1.02 (s, 3H), 0.92 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163.4 (+), 110.1 (+), 103.2 (-), 74.2 (-), 64.5 (+), 64.2 (+), 48.7 (-), 44.5 (+), 44.3 (+), 37.4 (+), 28.7 (-), 25.4 (-), 22.9 (-), 22.1 (-). IR (neat): 3446 (br.), 2964, 2879 cm^{-1}. Anal. Calcd. for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07. Found: C, 70.12; H, 10.32.

3-((1,3-Dioxolan-2-yl)methyl)-4-isopropyl-3-methyl-2-methylenecyclopentanone (R_f = 0.40; 40% Et_2O in pentane) was collected as a colorless viscous oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.05 (s, 1H), 5.22 (s, 1H), 4.76 (t, *J* = 4.5 Hz, 1H), 4.00-3.90 (m, 2 H), 3.85-3.75 (m, 2H), 2.44 (apparent dd, *J* = 18.0, 7.8 Hz, 1H), 2.25-2.05 (m, 2H), 1.97 (d, *J* = 4.5 Hz, 2H), 2.00-1.85 (m, 1H), 1.22 (s, 3H), 1.00 (d, *J* = 6.6 Hz, 3H), 0.78 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 206.8 (+), 153.7 (+), 116.4 (+), 102.5 (-), 64.7 (+), 64.4 (+), 45.6 (-), 44.4 (+), 44.3 (+), 38.7 (+), 28.5 (-), 22.9 (-), 22.9 (-), 19.5 (-). IR (neat): 2961, 2879, 1726 cm^{-1}. Anal. Calcd. for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.24; H, 9.32.



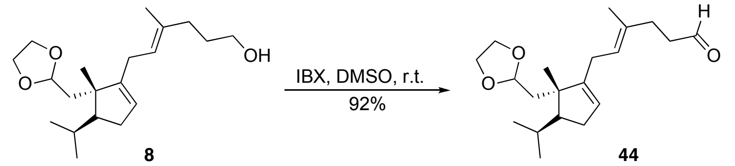
3-((1,3-Dioxolan-2-yl)methyl)-4-isopropyl-3-methyl-2-methylenecyclopentylmethylcarbon-ate (43): To a solution of **α,β-42** (2.1 g, 8.73 mmol), DMAP (54 mg, 0.44 mmol) and pyridine (3.46 mL, 34.92 mmol) in CH_2Cl_2 (45 mL) at 0 °C was added methyl chloroformate (2.70 mL, 34.92 mmol) drop-wise. The thick white suspension was then warmed to r.t. to provide a clear solution which was stirred for 4 hours. The reaction was quenched with saturated $NaHCO_3$ and diluted with pentane. The organic layer was separated and the aqueous layer was extracted a second time with pentane. The combined organic layers were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography (R_f = 0.40; 30% Et_2O in pentane) to give a 2:1 mixture of diasteriomers of **43** (2.31 g total, 89%) as a clear viscous oil. Resonances from the major and minor diasteriomers that are discernable are reported as 'major' and 'minor', respectively, along with the sum of their integration.

Resonances from the major and minor diasteriomers that are not discernable are reported as a mutliplet along with the sum of their integration. ^{1}H NMR ($CDCl_3$, 400 MHz): δ {5.45 (s, major) & 5.17 (d, *J* = 1.6 Hz, minor), 1H}, 5.40-5.30 (m, 1H), {5.14 (s, major) & 5.02 (d, *J* = 2.0 Hz, minor), 1H}, 4.00-3.88 (m, 2H), 3.87-3.72 (m, 2H), {3.82 (s, minor) & 3.79 (s, major), 3H}, {2.35 (quin., *J* = 6.0 Hz, minor) & 2.17 (dt, *J* = 11.6, 6.8 Hz, major), 1H}, 2.05-1.85 (m, 3H), {1.75-1.60 (m) & 1.41 (q, *J* = 10.4 Hz, major), 2H}, 1.10-1.0 (m, 6H), 0.93 (apparent t, *J* = 8.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.3 (+), 157.1 (+), 155.7 (+), 155.4 (+), 113.6 (+), 107.9 (+), 103.1 (-), 103.0 (-), 79.8 (-), 78.5 (-), 64.8 (+), 64.6 (+), 64.0 (+), 63.9 (+), 54.6 (-), 54.3 (-), 48.9 (-), 46.5 (-), 45.0 (+), 44.8 (+), 44.6 (+), 44.3 (+), 34.0 (+), 33.3 (+), 28.5 (-), 28.3 (-), 24.9 (-), 24.2 (-), 23.0 (-), 22.7 (-), 21.9 (-), 21.6 (-). IR (neat): 2958, 2876, 1742 cm^{-1}. Anal. Calcd. for $C_{16}H_{26}O_5$: C, 64.41; H, 8.78. Found: C, 64.72; H, 9.08.

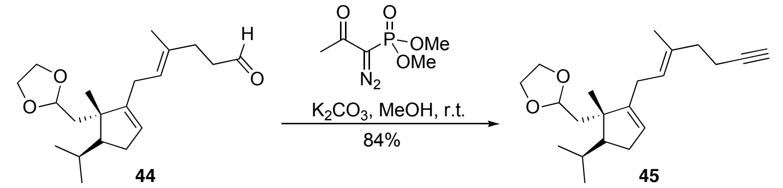


(*E*)-6-(5-((1,3-Dioxolan-2-yl)methyl)-4-isopropyl-5-methylcyclopent-1-enyl)-4-methylhex-4-en-1-ol (8): To a solution of $Pd_2(dba)_3$ (630 mg, 0.69 mmol) and LiCl (2.78 g, 64.77 mmol) in NMP (40 mL) was added a solution of **43** (4.11 g, 13.78 mmol) in NMP (5 mL + 2 mL rinse). To the dark-burgundy mixture was added a solution of **10** (~26.49 mmol) and DIPEA (4.81 mL, 27.56 mmol) in NMP (45 mL). The resulting dark-green solution was warmed to 50 °C and stirred for 5 hours before being quenched with saturated $NaHCO_3$ and diluted with Et_2O. The organic layer was separated, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography (R_f = 0.30; step gradient, 20% Et_2O in pentane gradually replaced by 50% Et_2O in pentane gradually replaced by 70% Et_2O in pentane) to give **8** (3.65 g, 82%) as a pale yellow oil. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 5.29 (t, *J* = 6.6 Hz, 1H), 5.26 (s, 1H), 4.75 (t, *J* = 4.2 Hz, 1H), 3.95 (q, *J* = 7.2 Hz, 1H), 3.90 (q, *J* = 7.2 Hz, 1H), 3.81 (q, *J* = 7.2 Hz, 1H), 3.75 (q, *J* = 7.2 Hz, 1H), 3.63 (t, *J* = 6.6 Hz, 2H), 2.67 (dd, *J* = 17.4, 6.6 Hz, 1H), 2.52 (dd, *J* = 17.4, 6.6 Hz, 1H), 2.27 (apparent dd, *J* = 15.6, 7.8

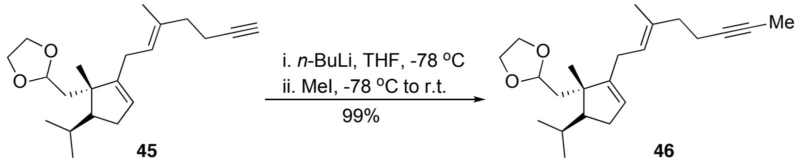
Hz, 1H), 2.09 (t, *J* = 7.2 Hz, 2H), 1.98 (q, *J* = 8.4 Hz, 1H), 1.90 (d, *J* = 4.2 Hz, 2H), 1.90-1.85 (m, 1H), 1.75-1.62 (m, 4H), 1.60 (s, 3H), 1.01 (d, *J* = 6.6 Hz, 3H), 0.92 (s, 3H), 0.88 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 149.6 (+), 135.4 (+), 122.5 (-), 122.3 (-), 103.4 (-), 64.7 (+), 64.2 (+), 62.7 (+), 51.1 (-), 49.0 (+), 41.7 (+), 35.9 (+), 34.5 (+), 30.8 (+), 29.3 (-), 25.5 (+), 22.6 (-), 22.3 (-), 19.8 (-), 15.7 (-). IR (neat): 3376 (br), 2951, 2929, 2882 cm^{-1}. HRMS *m/e* calcd. for $C_{20}H_{34}O_3$ (M+) 322.2508, found 322.2508. Anal. Calcd. for $C_{20}H_{34}O_3$: C, 74.49; H, 10.63. Found: C, 74.62; H, 10.62.



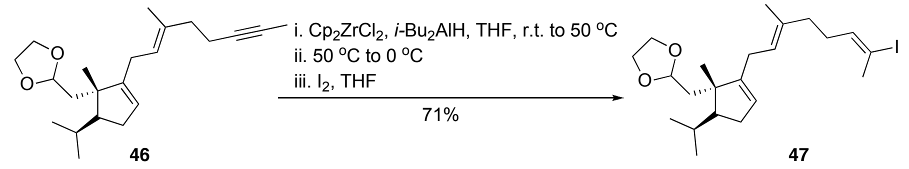
(*E*)-6-(-5-((1,3-Dioxolan-2-yl)methyl)-4-isopropyl-5-methylcyclopent-1-enyl)-4-methylhex-4-enal (44): To a solution of **8** (3.80 g, 11.80 mmol) in DMSO (50 mL) was added 2-iodoxybenzoic acid (9.91 g, 35.40 mmol) in one portion. The resulting solution was stirred for 1 hour before being quenched with saturated $NaHCO_3$ (upon which a thick precipitate forms) and diluted with pentane. The biphasic mixture was passed through a bed of celite to remove the precipitate, which was washed with fresh Et_2O. The organic layer was extracted, separated, dried ($MgSO_4$), filtered and concentrated under reduced pressure to give **44** (3.50 g, 92%) as a pale yellow oil that required no further purification. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.80 (s, 1H), 5.31 (t, *J* = 6.8 Hz, 1H), 5.25 (s, 1H), 4.78 (d, J = 4.2 Hz, 1H), 4.00-3.90 (m, 2H), 3.88-3.75 (m, 2H), 2.70 (dd, *J* = 17.2, 6.4 Hz, 1H), 2.60-2.50 (m, 3H), 2.39 (t, *J* = 7.2 Hz, 2H), 2.30 (apparent dd, *J* = 14.8, 7.2 Hz, 1H), 2.0 (q, *J* = 8.8 Hz, 1H), 1.94-1.88 (m, 3 H), 1.80-1.70 (m, 1H), 1.63 (s, 3H), 1.02 (d, *J* = 6.4 Hz, 3H), 0.94 (s, 3H), 0.90 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.6 (-), 149.3 (+), 133.8 (+), 122.9 (-), 122.7 (-), 103.4 (-), 64.7 (+), 64.2 (+), 51.2 (-), 49.0 (+), 42.1 (+), 41.7 (+), 34.6 (+), 31.8 (+), 29.4 (-), 25.6 (+), 22.6 (-), 22.4 (-), 19.9 (-), 16.0 (-). IR (neat): 2961, 2886, 2834, 2714, 1720 cm^{-1}. HRMS *m/e* calcd. for $C_{20}H_{32}O_3$ (M^+) 320.2351, found 320.2345.



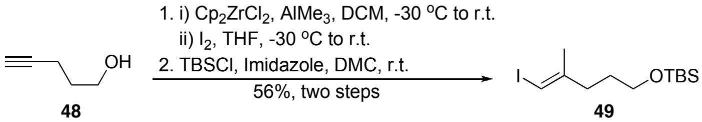
2-((-5-Isopropyl-1-methyl-2-((*E*)-3-methylhept-2-en-6-ynyl)cyclopent-2-enyl)methyl)-1,3-dioxolane (45): To a suspension of powdered K_2CO_3 (3.77 g, 27.25 mmol) in anhydrous MeOH (60 mL) was added the Bestmann–Ohira reagent[6] (3.78 g, 19.7 mmol) followed by a solution of **44** (3.50 g, 10.9 mmol) in anhydrous MeOH (15 mL + 5 mL rinse) at r.t. The mixture was stirred overnight before being quenched with water and diluted with Et_2O. The organic layer was separated, washed with brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography (R_f = 0.40; step gradient, 5% Et_2O in pentane gradually replaced by 10% Et_2O in pentane) to give **45** (2.90 g, 84%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 5.35-5.30 (m, 2H), 4.76 (t, *J* = 4.2 Hz, 1H), 3.97 (q, *J* = 7.2 Hz, 1H), 3.91 (q, *J* = 7.2 Hz, 1H), 3.81 (q, *J* = 7.2 Hz, 1H), 3.75 (q, *J* = 7.2 Hz, 1H), 2.68 (dd, *J* = 17.4, 6.6 Hz, 1H), 2.52 (dd, *J* = 17.4, 6.6 Hz, 1H), 2.33-2.20 (m, 5H), 1.98 (q, *J* = 8.4 Hz, 1H), 1.95 (t, *J* = 2.4 Hz, 1H), 1.90 (d, *J* = 4.2 Hz, 2H), 1.90-1.85 (m, 1H), 1.75-1.70 (m, 1H), 1.60 (s, 3H), 1.00 (d, *J* = 6.6 Hz, 3H), 0.93 (s, 3H), 0.88 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 149.3 (+), 134.0 (+), 123.1 (-), 122.7 (-), 103.4 (-), 84.4 (+), 68.4 (+), 64.7 (+), 64.2 (+), 51.2 (-), 48.9 (+), 41.7 (+), 38.4 (+), 34.5 (+), 29.4 (-), 25.6 (+), 22.6 (-), 22.3 (-), 19.9 (-), 17.5 (+), 15.6 (-). IR (neat): 3307, 2964, 2879, 2829, 2120 (weak) cm^{-1}.HRMS *m/e* calcd. for $C_{21}H_{32}O_2$ (M+) 316.2402, found 316.2413. Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.66; H, 9.82.



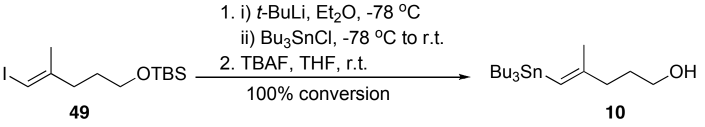
2-((-5-Isopropyl-1-methyl-2-((*E*)-3-methyloct-2-en-6-ynyl)cyclopent-2-enyl)methyl)-1,3-dioxolane (46): To a solution of **45** (2.67 g, 8.44 mmol) in THF (45 mL) at -78 °C was added *n*-BuLi (3.54 mL, 8.87 mmol, 2.5 M solution in hexane) drop-wise. The mixture was stirred for 45 minutes before adding iodomethane (11.9 g, 84.4 mmol, passed through a plug of K_2CO_3 before use). After stirring for 15 minutes, the dry ice bath was removed and the reaction was warmed to r.t. before being quenched with saturated $NaHCO_3$ and diluted with pentane. The organic layer was separated, washed with brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure to give **46** (2.76 g, 99%) as a colorless oil, which required no further purification. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 5.33 (s, 1H), 5.31 (t, *J* = 7.2 Hz, 1H), 4.76 (t, *J* = 4.8 Hz, 1H), 3.96 (q, *J* = 6.6 Hz, 1H), 3.91 (q, *J* = 6.6 Hz, 1H), 3.82 (q, *J* = 6.6 Hz, 1H), 3.76 (q, *J* = 6.6 Hz, 1H), 2.68 (dd, *J* = 17.4, 6.6 Hz, 1H), 2.52 (dd, *J* = 17.4, 6.6 Hz, 1H), 2.32-2.20 (m, 5H), 1.99 (q, *J* = 8.4 Hz, 1H), 1.91 (d, *J* = 4.2 Hz, 2H), 1.90-1.85 (m, 1H), 1.77 (s, 3H), 1.75-1.70 (m, 1H), 1.59 (s, 3H), 1.01 (d, *J* = 6.6 Hz, 3H), 0.93 (s, 3H), 0.89 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 149.5 (+), 134.5 (+), 122.8 (-), 122.7 (-), 103.5 (-), 79.0 (+), 75.6 (+), 64.7 (+), 64.2 (+), 51.2 (-), 48.9 (+), 41.7 (+), 39.0 (+), 34.5 (+), 29.4 (-), 25.5 (+), 22.6 (-), 22.3 (-), 19.8 (-), 17.8 (+), 15.5 (-), 3.43 (-). IR (neat): 2952, 2920, 2885 cm^{-1}. HRMS *m/e* calcd. for $C_{22}H_{34}O_2$ (M+) 330.2559, found 330.2553. Anal. Calcd. for $C_{22}H_{34}O_2$: C, 79.95; H, 10.37. Found: C, 79.69; H, 10.35.



2-((-2-((2*E*,6*E*)-7-Iodo-3-methylocta-2,6-dienyl)-5-isopropyl-1-methylcyclopent-2-enyl)methyl)-1,3-dioxolane (47): To a suspension of Cp_2ZrCl_2 (3.40 g, 11.62 mmol) in THF (11 mL) was added *i*-Bu_2AlH (11.1 mL, 11.1 mmol, 1.0 M solution in toluene) drop-wise at 0 °C. The mixture was stirred for 5 minutes before being warmed to r.t. and stirred for an additional 5 minutes. To the resultant white suspension was added a solution of **46** (800 mg, 2.42 mmol) in THF (10 mL). The flask wrapped with aluminum foil, placed in a 50 °C oil bath and stirred for 90 minutes before being cooled to 0 °C. A solution of iodine (1.84 g, 7.26 mmol) in THF (10 mL) was added over 2 minutes and stirring was continued for 15 minutes before being quenched with saturated Na_2SO_3. The mixture was diluted with Et_2O and saturated Rochelle's salt and vigorously stirred overnight. The organic layer was separated, washed with water and brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography ($R_f = 0.40$, 5% Et_2O in pentane) to give Compound **47** (787 mg, 71%) as a colorless oil (15:1 regioselectivity in preference of **47**). The product was contaminated with a small amount of an unidentified impurity (^1H NMR δ 3.21 (t, $J = 7.2$ Hz)) that was of no consequence in subsequent reactions. ^1H NMR ($CDCl_3$, 400 MHz): δ 6.16 (t, $J = 7.2$ Hz, 1H), 5.32 (s, 1H), 5.29 (t, $J = 7.2$ Hz, 1H), 4.79 (t, $J = 4.4$ Hz, 1H), 4.00-3.90 (m, 2H), 3.88-3.75 (m, 2H), 2.70 (dd, $J = 17.4$, 6.6 Hz, 1H), 2.53 (dd, $J = 17.4$, 6.6 Hz, 1H), 2.39 (s, 3H), 2.36-2.27 (m, 1H), 2.17 (t, $J = 7.2$ Hz, 2H), 2.07-2.13 (m, 2H), 2.01 (q, $J = 8.4$ Hz, 1H), 1.96-1.82 (m, 1H), 1.92 (d, $J = 4.4$ Hz, 2H), 1.80-1.70 (m, 1H), 1.59 (s, 3H), 1.03 (d, $J = 6.4$ Hz, 3H), 0.96 (s, 3H), 0.91 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 149.5 (+), 141.0 (-), 134.6 (+), 122.9 (-), 122.8 (-), 103.5 (-), 93.5 (+), 64.8 (+), 64.3 (+), 51.2 (-), 49.0 (+), 41.8 (+), 38.6 (+), 34.6 (+), 29.4 (-), 29.1 (+), 27.5 (-), 25.6 (+), 22.7 (-), 22.4 (-), 20.0 (-), 15.7 (-). HRMS *m/e* calcd. for $C_{22}H_{35}IO_2$ (M+) 458.1682, found 458.1682.

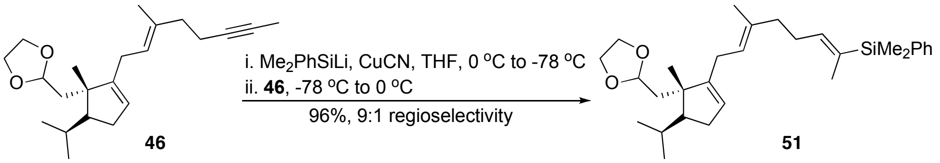


(*E*)-*tert*-Butyl(5-iodo-4-methylpent-4-enyloxy)dimethylsilane (49): To a suspension of Cp_2ZrCl_2 (14.6 g, 50 mmol) in CH_2Cl_2 (125 mL) at -20 °C was added Me_3Al (75 mL, 150 mmol, 2 M solution in hexane). The resulting solution was warmed to r.t. and stirred for 1 hour before being cooled to -30 °C. A solution of 4-pentyn-1-ol **48** (4.21 g, 50 mmol) in CH_2Cl_2 (5 mL) was added slowly and the reaction was warmed gradually to r.t. and stirred overnight before being cooled again to -30 °C. A solution of iodine (16.5 g, 65 mmol) in THF (40 mL) was added drop-wise and the resulting solution was warmed to r.t. and stirred for 2 hours and then cooled to -5 °C (ice/salt bath). The reaction was quenched with EXTREME CAUTION by the drop-wise addition of H_2O (~ 30 mL). The mixture was then diluted with Et_2O and HCl (1 M). The organic layer was separated and sequentially washed with saturated $NaHCO_3$, saturated potassium sodium tartrate, and brine after which it was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting inseparable mixture of product and 4-pentyn-1-ol was diluted with CH_2Cl_2 (160 mL) and imidazole (8.85 g, 130 mmol) and TBDMSCl (11.30 g, 75 mmol) were added. The resulting suspension was stirred overnight before being quenched with saturated $NaHCO_3$ and diluted with pentane. The organic layer was separated, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography ($R_f = 0.50$; 10% CH_2Cl_2 in pentane) to give **49** (9.45 g, 56%, two steps) as a colorless oil. If desired, additional product can be isolated by concentrating the subsequent fractions (containing a mixture of **46** and *t*-butyldimethyl(pent-4-ynyloxy)silane) under reduced pressure and repeating silica gel chromatography. ^1H NMR ($CDCl_3$, 400 MHz): δ 5.91 (s, 1H), 3.60 (t, J = 6.4 Hz, 2H), 2.29 (t, J = 7.6 Hz, 2H), 1.86 (s, 3H), 1.70-1.60 (m, 2H), 0.91 (s, 9H), 0.06 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.7 (+), 74.7 (-), 62.1 (+), 35.8 (+), 30.8 (+), 25.9 (-), 23.9 (-), 18.3 (+), -5.3 (-). The spectral data were in accordance with those reported in the literature.[7]



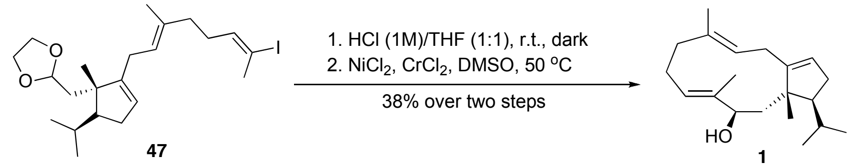
(*E*)-4-methyl-5-(tributylstannyl)pent-4-en-1-ol (10): To a solution of **49** (9.01 g, 26.49 mmol) in THF at -78 °C was added *t*-BuLi (34.3 mL, 58.29 mmol, 1.7 M solution in pentane). The reaction was stirred at this temperature for 15 minutes before adding Bu_3SnCl (7.34 g, 22.53 mmol) after which it was warmed to r.t and stirred for 1 hour before being quenched with water and diluted with pentane. The organic layer was separated, dried ($MgSO_4$), filtered and concentrated under reduced pressure to provide the silylated vinyl stannane **50** (100% conversion by ^1H NMR spectroscopy) as a colorless oil contaminated with uncharacterized organostannane by-product(s) (11.0 g combined mass). This mixture was used directly in the next reaction without consequence. To a solution of the impure silylated vinyl stannane in THF (100 mL) was added TBAF (27.7 mL, 27.7 mmol, 1 M solution in THF) at r.t. The reaction was monitored by ^1H NMR spectroscopy and deemed complete in approximately 1.5 hours at which time it was quenched with saturated $NaHCO_3$ and diluted with Et_2O. The organic layer was separated, dried ($MgSO_4$), filtered and concentrated under reduced pressure to provide **10** (100%

conversion by ^{1}H NMR) as a colorless oil contaminated with uncharacterized organostannane and organosilane by-product(s) (14.5g combined mass). This mixture was used directly in the next reaction without further purification.



((2*E*,6*E*)-8-(-5-((1,3-Dioxolan-2-yl)methyl)-4-isopropyl-5-methylcyclopent-1-enyl)-6-methylocta-2,6-dien-2-yl)dimethyl(phenyl)silane (51): Preparation of $Me_2PhSiLi$ (~ 0.5 M solution in THF): To a suspension of diced lithium wire (199 mg, 28.67 mmol) in THF (5.8 mL) was added $Me_2PhSiCl$ (500 mg, 2.93 mmol) at r.t. and the resulting mixture was stirred overnight to provide a dark red/brown solution which was used directly in the next step.[8]

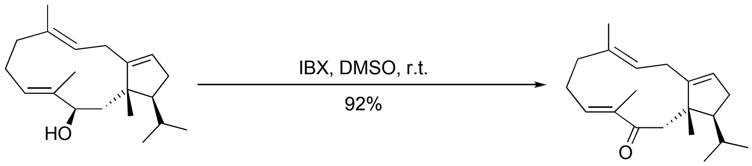
To a suspension of CuCN (112 mg, 1.25 mmol) in THF (1 mL) at 0 °C was added previously prepared $Me_2PhSiLi$ (5.0 mL, 2.50 mmol, ~ 0.5 M solution in THF) and the suspension was stirred for 20 minutes before being cooled to – 78 °C. A solution of **46** (83 mg, 0.25 mmol) in THF (1 mL) was added and the mixture was allowed to stir for 2 hours at -78 °C and then for 1 hour at 0 °C. The reaction was quenched with a mixture of NH_4OH:NH_4Cl (1:9) and then diluted with Et_2O. The organic layer was separated, washed with additional NH_4OH:NH_4Cl (1:9) and then brine, after which it was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography (R_f = 0.40; step gradient, 5% Et_2O in pentane) to give the vinyl silane (112 mg, 96%) as a colorless oil (9:1 regioselectivity). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.56-7.50 (m, 2H), 7.40-7.34 (m, 3H), 5.86 (dt, *J* = 6.3, 1.5 Hz, 1H), 5.35-5.28 (m, 2H), 4.80 (t, *J* = 4.8 Hz, 1H), 4.02-3.72 (m, 4H), 2.72 (dd, *J* = 17.7, 6.9 Hz, 1H), 2.55 (dd, *J* = 17.7, 6.9 Hz, 1H), 2.35-2.20 (m, 3H), 2.13 (apparent t, *J* = 7.8 Hz, 1H), 2.03 (q, *J* = 9.0 Hz, 1H), 1.95 (d, *J* = 4.2 Hz, 2H), 1.95-1.85 (m, 1H), 1.75 (q, *J* = 6.9 Hz, 1H), 1.70 (s, 3H), 1.64 (s, 3H), 1.05 (d, *J* = 6.6 Hz, 3H), 0.97 (s, 3H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.35 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 149.7 (+), 141.4 (-), 138.9 (+), 135.7 (+), 134.0 (-), 128.8 (-), 127.7 (-), 122.6 (-), 122.0 (-), 103.6 (-), 64.8 (+), 64.3 (+), 51.3 (-), 49.0 (+), 41.8 (+), 39.1 (+), 34.6 (+), 29.5 (-), 27.2 (+), 25.6 (+), 22.7 (-), 22.4 (-), 20.0 (-), 15.9 (-), 14.8 (-), -3.4 (-). Overlapping peaks account for the remaining ^{13}C resonance. HRMS *m/e* calcd. for $C_{30}H_{46}O_2Si$ (M+) 466.3267, found 466.3271.



(6*E*,10*E*)-3-isopropyl-3a,6,10-trimethyl-2,3,3a,4,5,8,9,12-octahydrocyclopenta[11]-annulen-5-ol (1): To a solution of **47** (614 mg, 1.34 mmol) in THF (220 mL) was added freshly prepared 1 M HCl (220 mL) and the reaction was vigorously stirred in the dark for 10 hours after which a portion of the reaction mixture (~150 mL) was poured into a 1 L separatory funnel charged with 500 mL of Et_2O. The aqueous layer was extracted and discarded. An additional portion of the reaction mixture (~150 mL) was added to the separatory funnel, extracted and discared (2×). The organic layer was then washed with saturated $NaHCO_3$ and brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The flask containing the residue was purged with argon and then the residue was taken up in anhydrous DMSO (535 mL). To this solution was added solid $CrCl_2$ (1.65g, 13.4 mmol) and $NiCl_2$ (17.4 mg, 0.134 mmol) in one portion. The reaction was warmed to 50 °C and stirred for 24 hours before being diluted with an equal volume of water. The aqueous layer was extracted with EtOAc (3×). The combined organic layers were washed with water (2×), then brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography (R_f = 0.25; 10% Et_2O in pentane) to provide **1** contaminated with trace amounts of unidentified impurities. The residue was taken up in a minimum amount of cold pentane and then decanted to provide pure **1** (134 mg, 37%) as a white solid. M.p. = 99-102 °C.[9] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.40 (br s, 1H), 4.98 (br s, 1H), 4.80 (br d, *J* = 8.0 Hz, 1H), 4.12 (br s, 1H), 2.72 (d, *J* = 12.8 Hz, 1H), 2.47 (dd, *J* = 13.6, 10.4 Hz, 1H), 2.40 (dd, *J* = 15.2, 7.6 Hz, 1H), 2.30-2.18 (m, 1H), 2.17-1.95 (m, 5H), 1.80-1.65 (m, 3H), 1.61 (s, 3H), 1.49 (s, 3H), 1.28 (s, 1H), 1.06 (d, *J* = 6.8 Hz, 3H), 0.95 (s, 3H), 0.93 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100

MHz): δ 149.9 (+), 137.7 (br, +), 131.9 (+), 128.5 (-), 127.7 (-), 125.7 (-), 75.9 (-), 51.0 (+), 49.2 (-), 45.9 (br, +), 38.5 (+), 35.7 (+), 30.2 (-), 26.5 (+), 23.0 (+), 22.9 (-), 22.4 (-), 21.8 (-) 15.5 (-), 10.3 (br, -). HRMS *m*/*e* calcd. for $C_{20}H_{32}O$ (M+) 288.2453, found 288.2445. The spectral data were in accordance with those reported in the literature.[10]

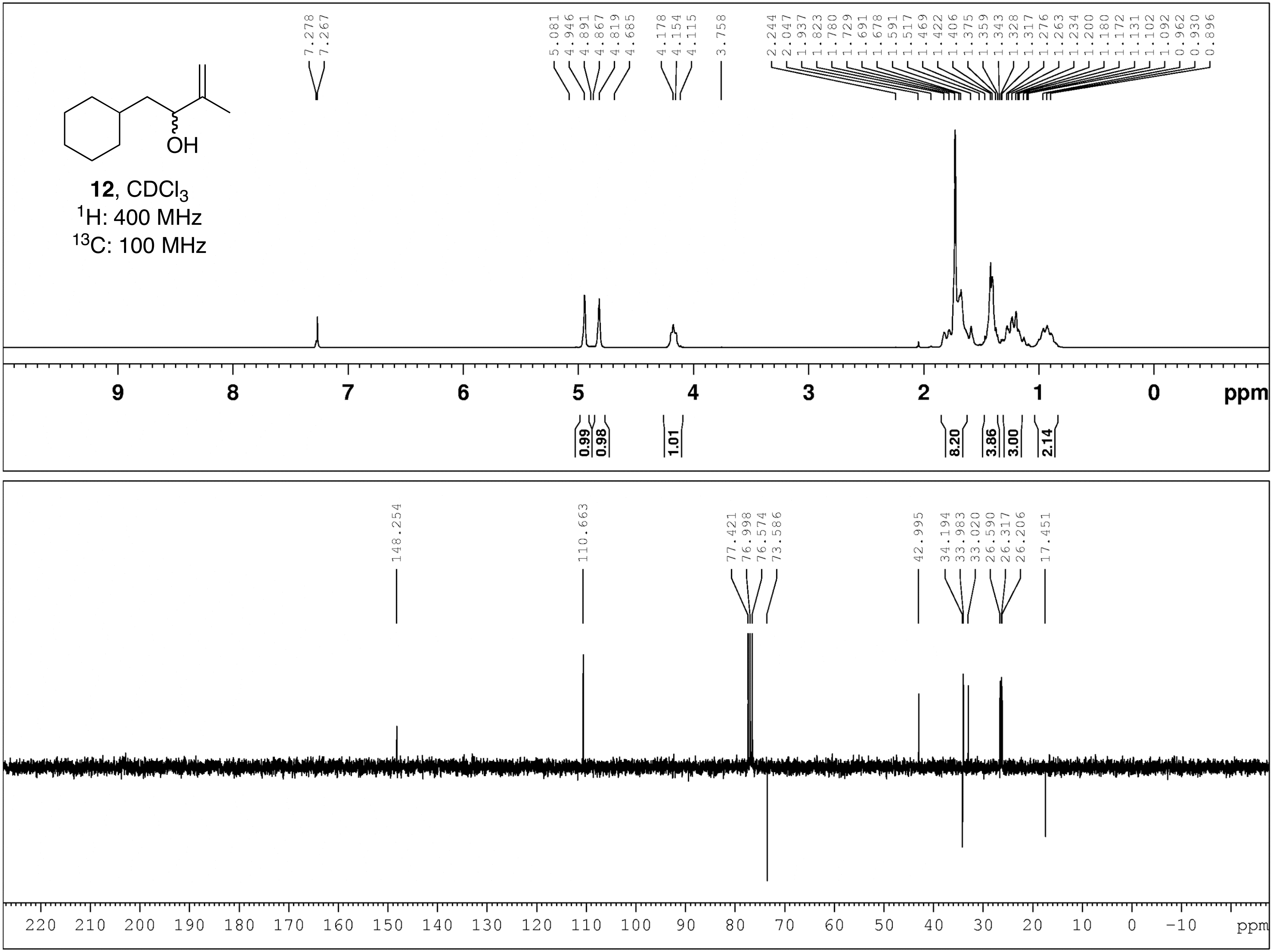
^{13}C NMR spectroscopy CDCl$_3$		^{1}H NMR spectroscopy CDCl$_3$	
Literature (**1**) (125 MHz)	Experimental (**1**) (100 MHz)	Literature (**1**) (500 MHz)	Experimental (**1**) (400 MHz)
150.0	149.9	5.38 (br s, 1H)	5.40 (br s, 1H)
138.6	138.4	4.96 (br s, 1H)	4.98 (br s, 1H),
131.9	131.9	4.77 (br d, *J* = 10.2 Hz, 1H)	4.80 (br d, *J* = 8.0 Hz, 1H)
128.4	128.5	4.11 (t, *J* = 3.8 Hz, 1H)	4.12 (br s, 1H),
127.6	127.7	2.70 (br d, *J* = 14.1 Hz, 1H)	2.72 (d, *J* = 12.8 Hz, 1H)
125.6	125.7	2.46 (dd, *J* = 14.1, 10.2 Hz, 1H)	2.47 (dd, *J* = 13.6, 10.4 Hz, 1H)
75.9	75.9	2.39 (ddd, *J* = 15.4, 7.9, 2.0 Hz, 1H)	2.40 (dd, *J* = 15.2, 7.6 Hz, 1H)
51.0	51.0	2.21 (br dd, J = 2.2, 11.0 Hz, 1H)	2.30-2.18 (m, 1H)
49.2	49.2	2.12 (m, 1H)	2.17-1.95 (m, 5H)
47.2	47.0	2.04 (m, 1H)	"
38.5	38.5	2.02 (m, 1H)	"
35.6	35.7	2.01 (m, 1H)	"
30.1	30.2	1.99 (m, 1H)	"
26.5	26.5	1.74 (m, 1H)	1.80-1.65 (m, 3H)
23.0	23.0	1.69 (m, 2H)	"
22.9	22.9	1.59 (br s, 3H)	1.61 (s, 3H)
22.3	22.4	1.46 (br s, 3H)	1.49 (s, 3H)
21.8	21.8	--	1.28 (s, 1H, O*H*)
15.4	15.5	1.05 (d, *J* = 6.6, 3H)	1.06 (d, *J* = 6.8 Hz, 3H)
11.2	11.0	0.94 (s, 3H)	0.95 (s, 3H)
		0.92 (d, *J* = 6.6, 3H)	0.93 (d, *J* = 7.2 Hz, 3H)



1 **2**

(6*E*,10*E*)-3-isopropyl-3a,6,10-trimethyl-2,3,3a,4,8,9-hexahydrocyclopenta[11]annulen-5(12*H*)-one (2): To a solution of **1** (50 mg, 0.173 mmol) in DMSO (2 mL) was added 2-iodoxybenzoic acid (252 mg, 0.9 mmol) at r.t. The mixture was stirred for 30 minutes before being diluted with water and Et_2O. The organic layer was separated, washed with brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography (R_f = 0.40; 10% Et_2O in pentane) to provide **2** (45 mg, 91%) as a white solid. M.p. = 105-108 °C.[9] ^{1}H NMR (C_6D_6, 400 MHz): δ 5.57 (br d, *J* = 10.4 Hz, 1H), 5.24 (br s, 1H), 5.12 (br t, *J* = 8.4 Hz, 1H), 3.15 (d, *J* = 11.2 Hz, 1H), 3.03 (dd, J = 13.2, 10.8 Hz, 1H), 2.90 (br d, *J* = 7.0 Hz, 1H), 2.52 (br dd, *J* = 13.2, 6.0 Hz, 1H), 2.41 (dd, *J* = 16.8, 7.6 Hz, 1H), 2.32-2.19 (m, 2H), 2.08-1.85 (m, 5H), 1.78 (s, 3H), 1.48 (s, 3H), 1.12 (s, 3H), 1.08 (d, *J* = 6.8 Hz, 3H), 0.81 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 205.4 (+), 147.2 (+), 140.1 (-), 137.9 (+), 134.8 (+), 127.7 (-), 124.8 (-), 52.5 (+, two overlapping peaks), 51.6 (-), 37.7 (+), 30.7 (+), 28.2 (-), 28.0 (+), 25.5 (+), 22.5 (-), 21.8 (-), 18.0 (-), 15.0 (-), 12.1 (-). The spectral data were in accordance with those reported in the literature.[10]

^{13}C NMR spectroscopy C_6D_6		^{1}H NMR spectroscopy C_6D_6	
Literature (**2**) (125 MHz)	Experimental (**2**) (100 MHz)	Literature (**2**) (500 MHz)	Experimental (**2**) (400 MHz)
205.6	205.4	5.50 (br d, *J* = 10.4 Hz, 1H)	5.57 (br d, *J* = 10.4 Hz, 1H)
147.5	147.2	5.17 (br s, 1H)	5.24 (br s, 1H)
140.3	140.1	5.04 (br dd, *J* = 10.2, 6.1 Hz, 1H)	5.12 (br t, *J* = 8.4 Hz, 1H)
138.2	137.9	3.08 (d, *J* = 11.1 Hz, 1H)	3.15 (d, *J* = 11.2 Hz, 1H)
134.9	134.8	2.97 (dd, *J* = 13.7, 10.2 Hz, 1H)	3.03 (dd, J = 13.2, 10.8 Hz, 1H)
127.9	127.7	2.84 (br d, *J* = 7.8, 1H)	2.90 (br d, *J* = 7.0 Hz, 1H)
125.2	124.8	2.46 (br dd, *J* = 13.7, 6.1 Hz, 1H)	2.52 (br dd, *J* = 13.2, 6.0 Hz, 1H)
52.8	52.5	2.35 (tdd, *J* = 16.9, 7.8, 1.9 Hz, 1H)	2.41 (dd, *J* = 16.8, 7.6 Hz, 1H)
52.7	"	2.13-2.25 (m, 1H)	2.32-2.19 (m, 2H)
51.9	51.6	2.22 (d, *J* = 11.1 Hz, 1H)	"
37.9	37.7	1.99-1.89 (m, 2H)	2.08-1.85 (m, 5H)
30.9	30.7	1.91 (m, 1H)	"
28.5	28.2	1.88 (m, 1H)	"
28.2	28	1.85 (qd, *J* = 16.9, 2.3 Hz, 1H)	"
25.7	25.5	1.72 (br s, 3H)	1.78 (s, 3H)
22.8	22.5	1.41 (br s, 3H)	1.48 (s, 3H)
22	21.8	1.05 (s, 3H)	1.12 (s, 3H)
18.2	18	1.02 (d, *J* = 6.8 Hz, 3H)	1.08 (d, *J* = 6.8 Hz, 3H)
15.2	15	0.75 (d, J = 6.6 Hz, 3H)	0.81 (d, *J* = 6.4 Hz, 3H)
12.3	12.1		


OH
12, CDCl$_3$
^{1}H: 400 MHz
^{13}C: 100 MHz
7.278
7.267
5.081
4.946
4.891
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4.819
4.685
4.178
4.154
4.115
3.758
2.244
2.047
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1.780
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1.591
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1.328
1.317
1.276
1.263
1.234
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1.131
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0.930
0.896
9
8
7
6
5
4
3
2
1
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ppm
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1.01
8.20
3.86
3.00
2.14
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73.586
42.995
34.194
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26.317
26.206
17.451
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210
200
190
180
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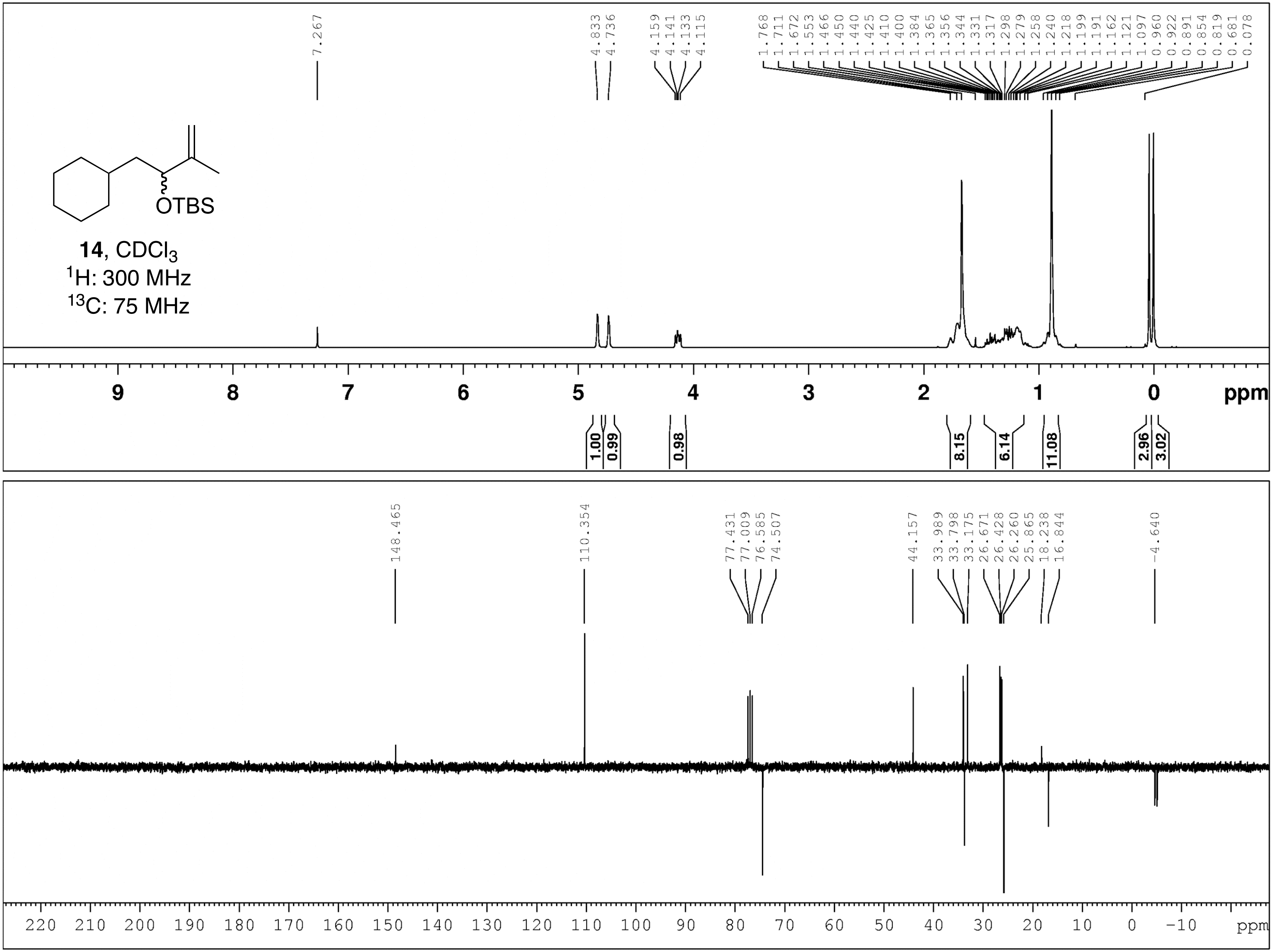
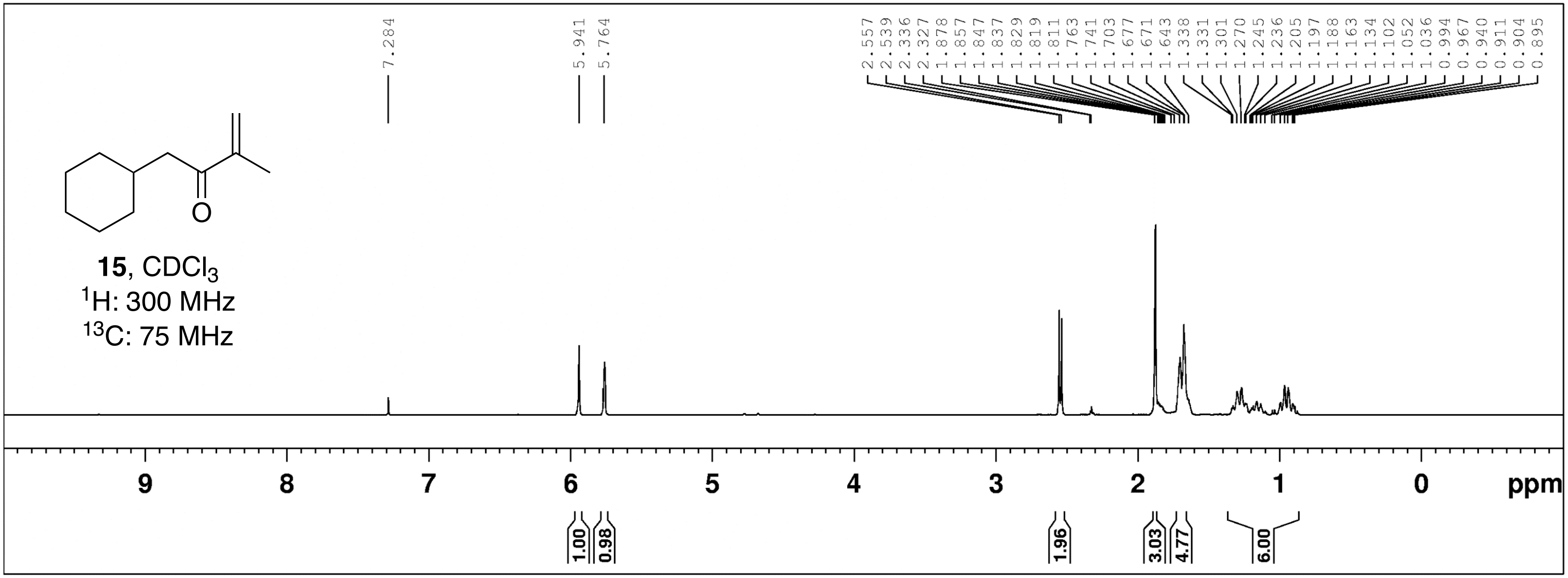
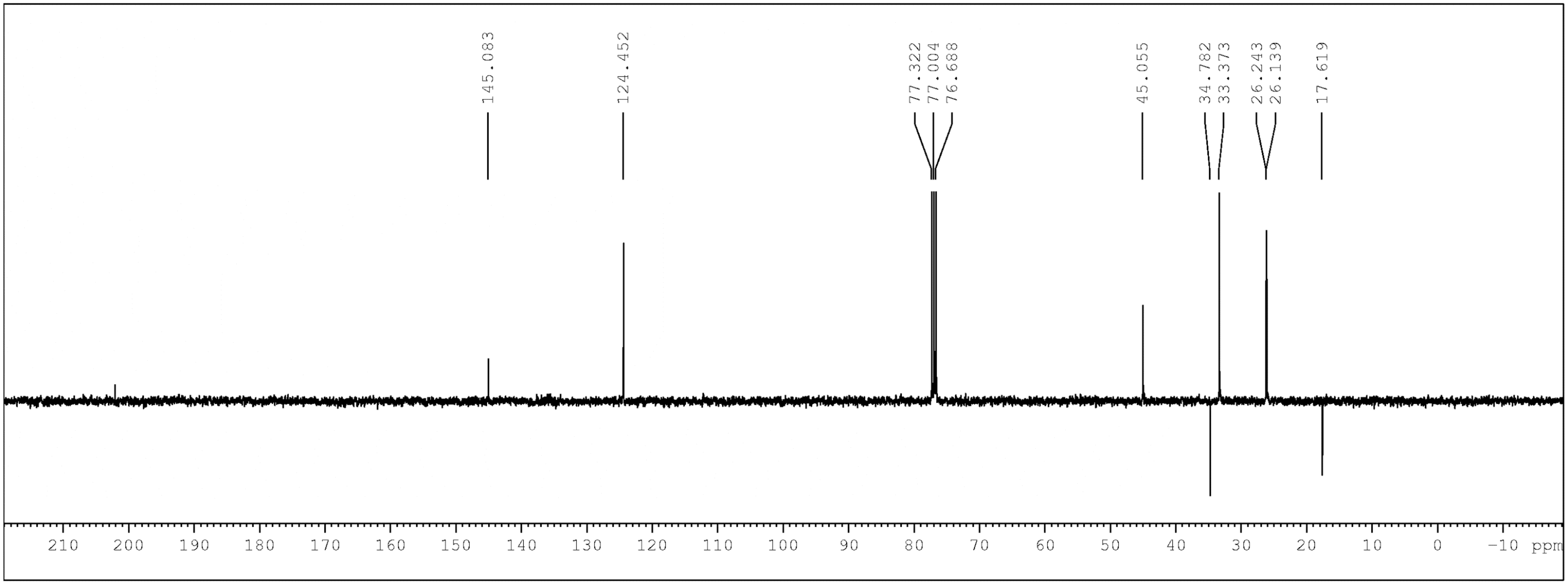
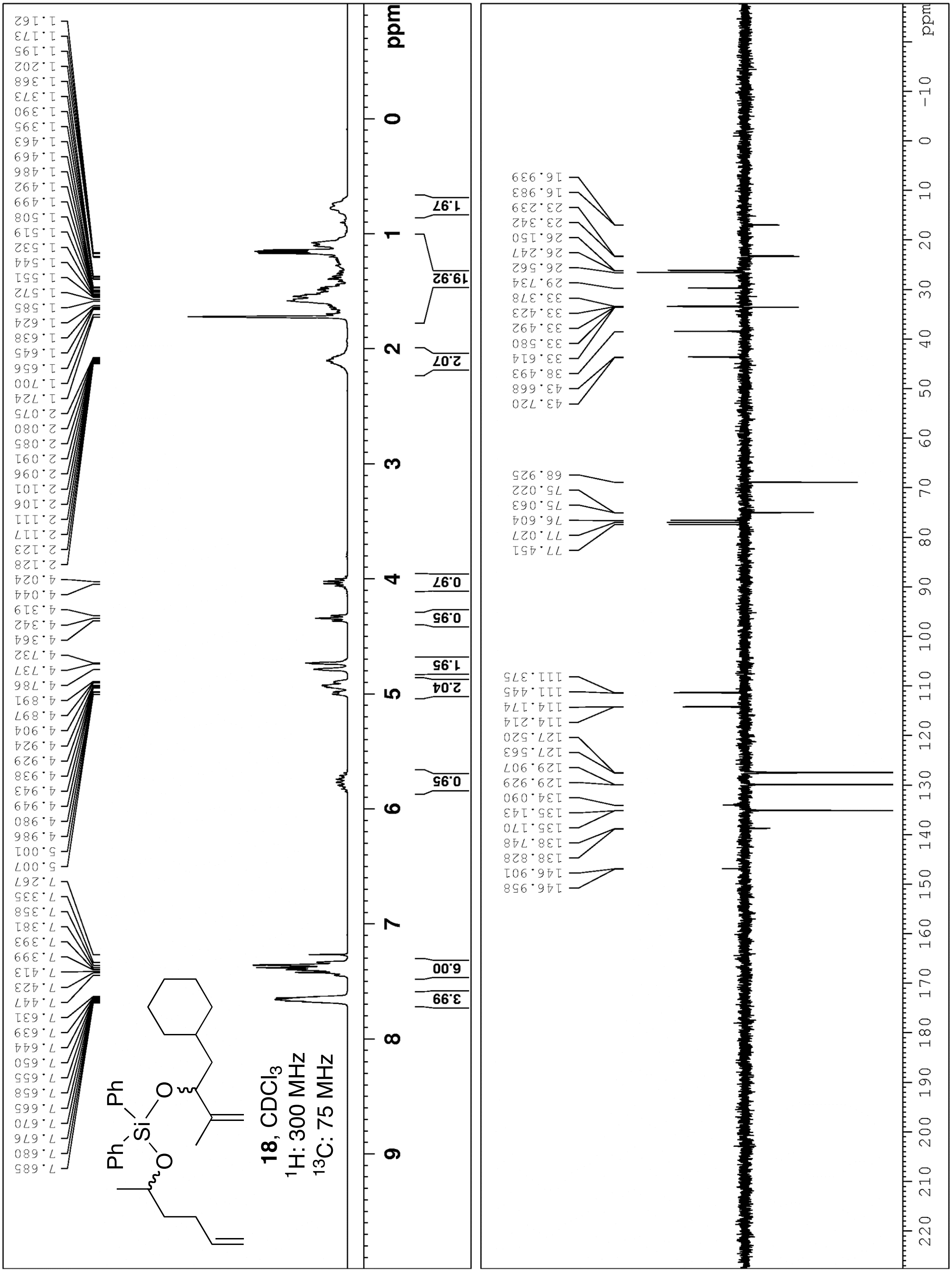


14, CDCl$_3$
^{1}H: 300 MHz
^{13}C: 75 MHz

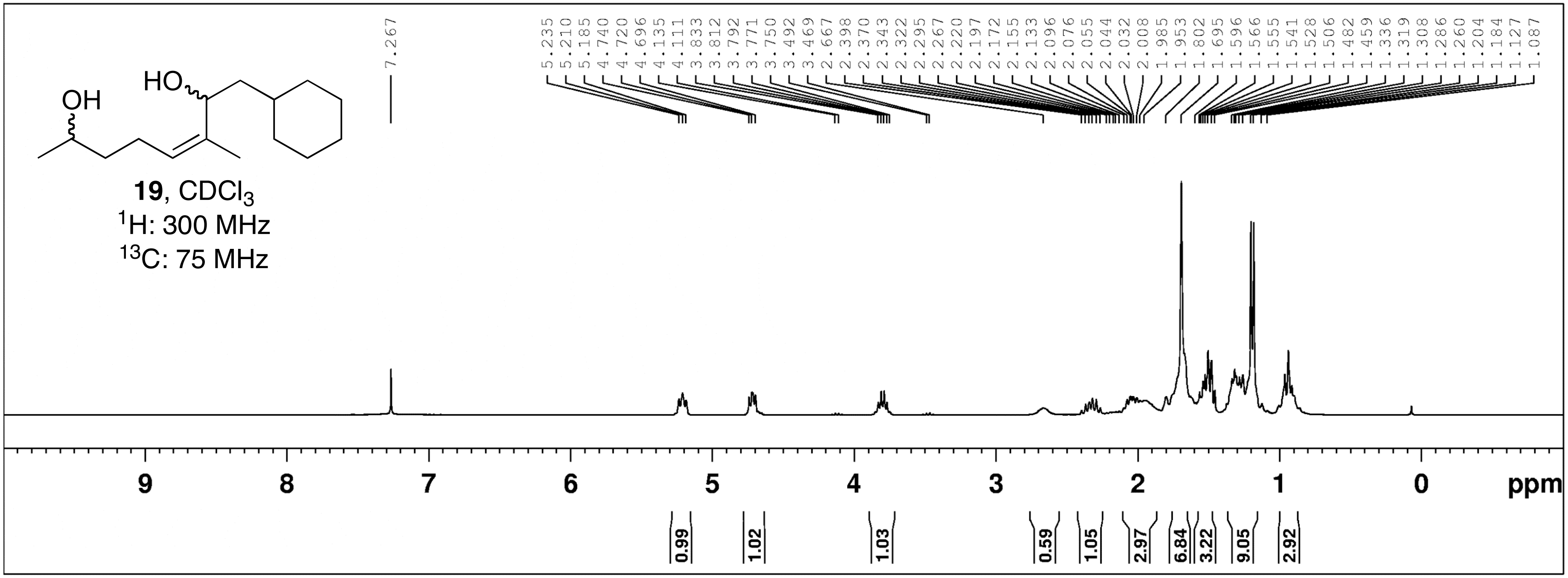


15, $CDCl_3$
^1H: 300 MHz
^{13}C: 75 MHz

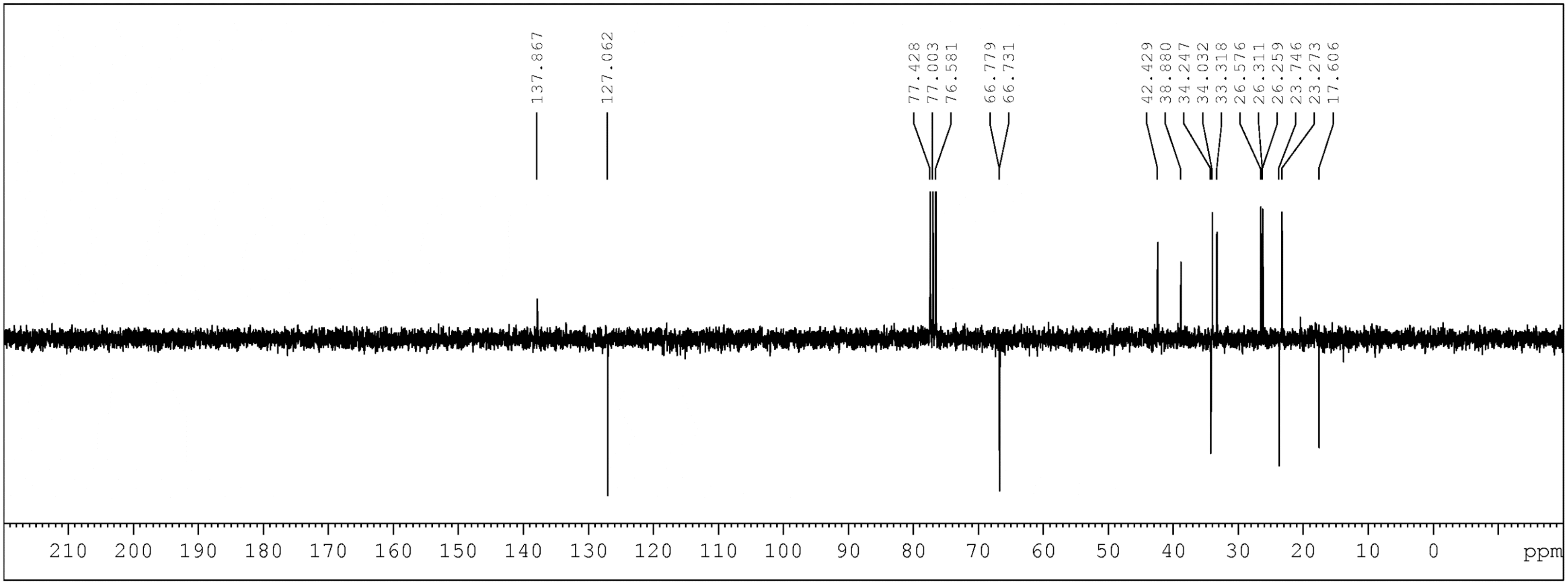


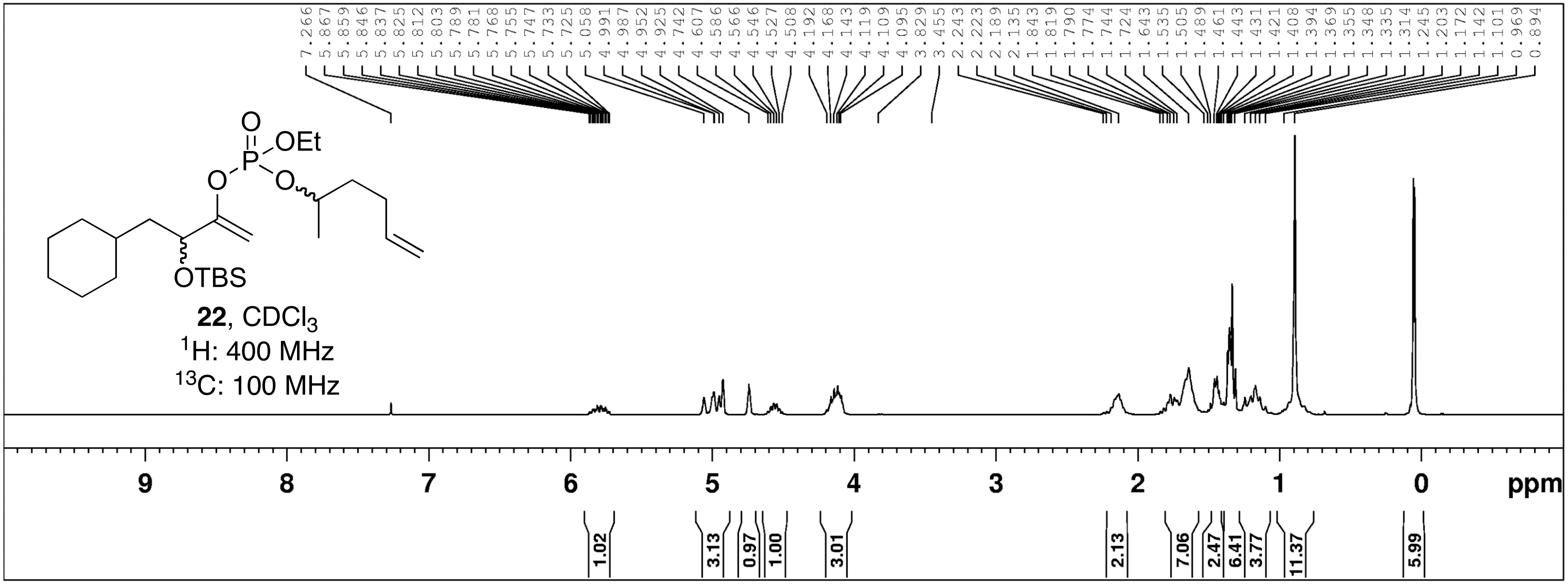


18, $CDCl_3$
^1H: 300 MHz
^{13}C: 75 MHz



19, $CDCl_3$
^1H: 300 MHz
^{13}C: 75 MHz

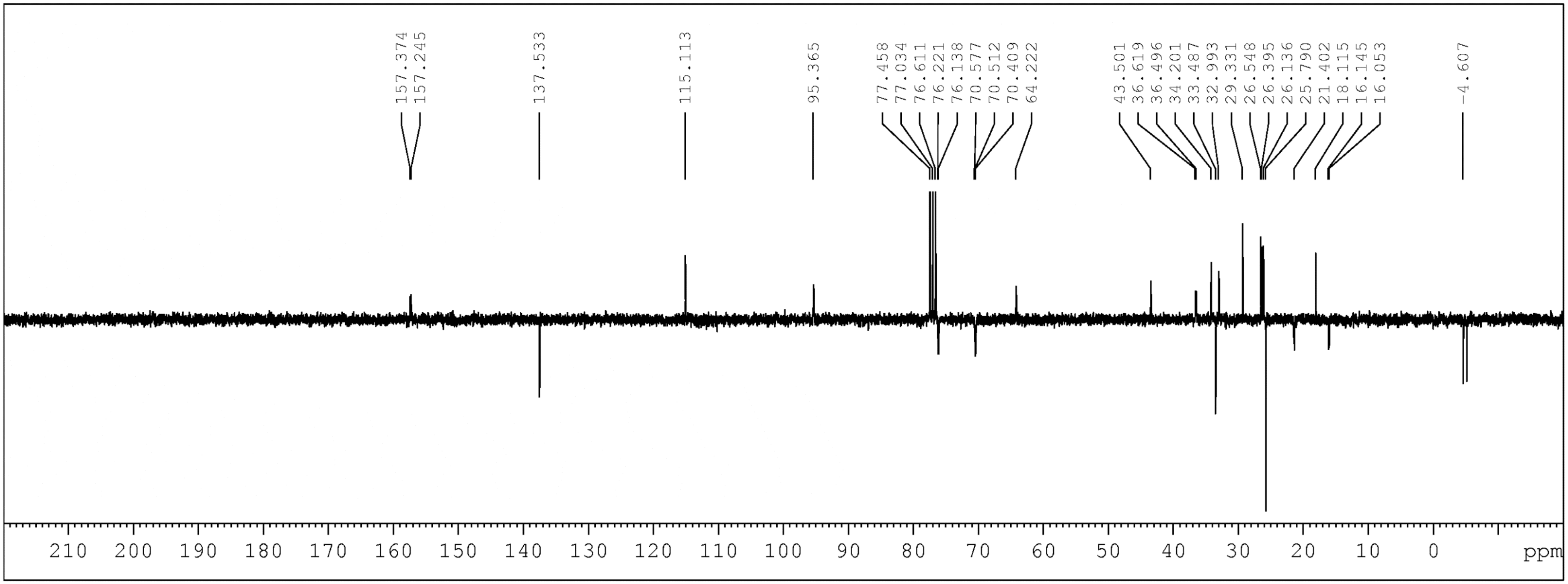


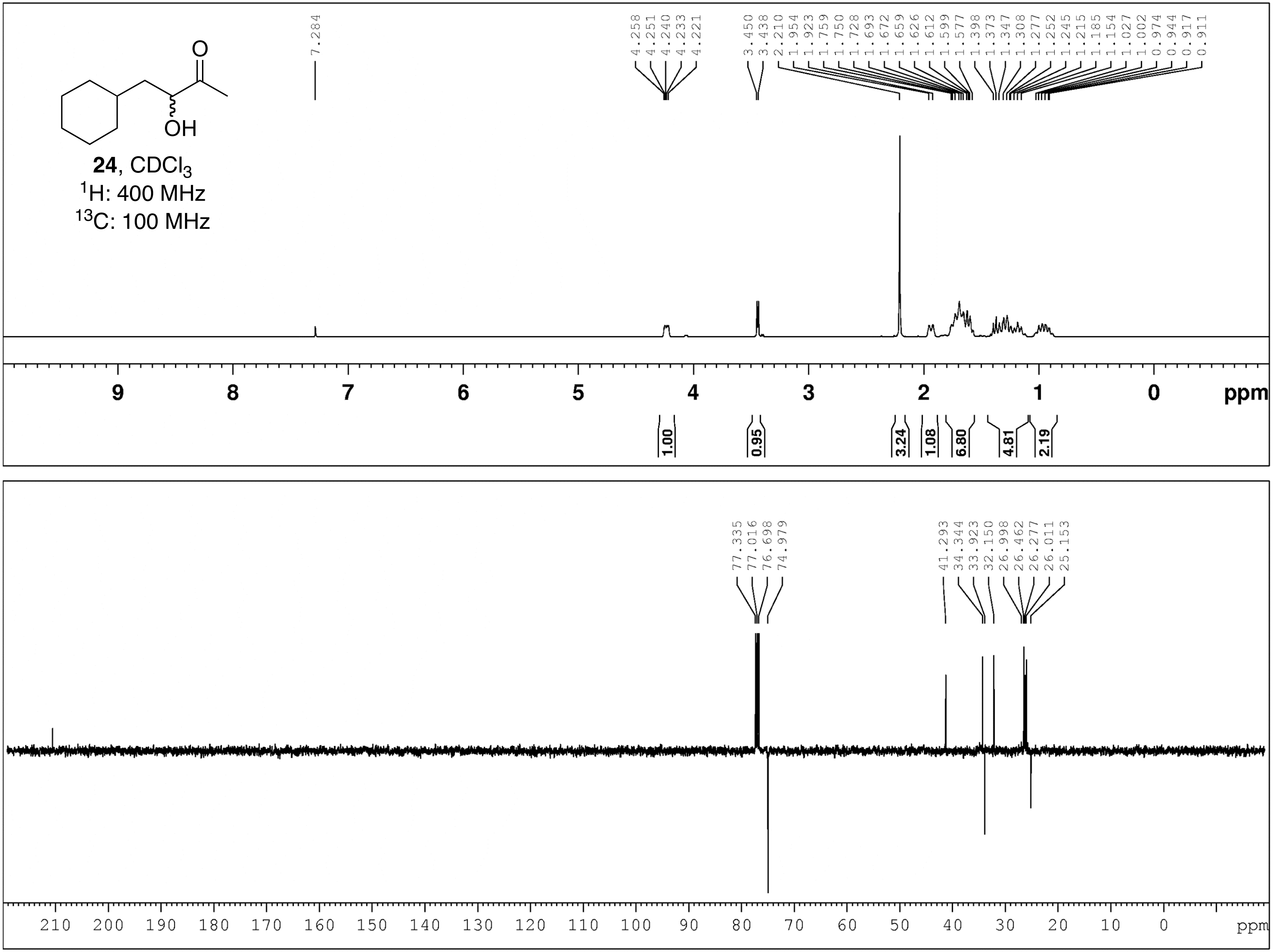


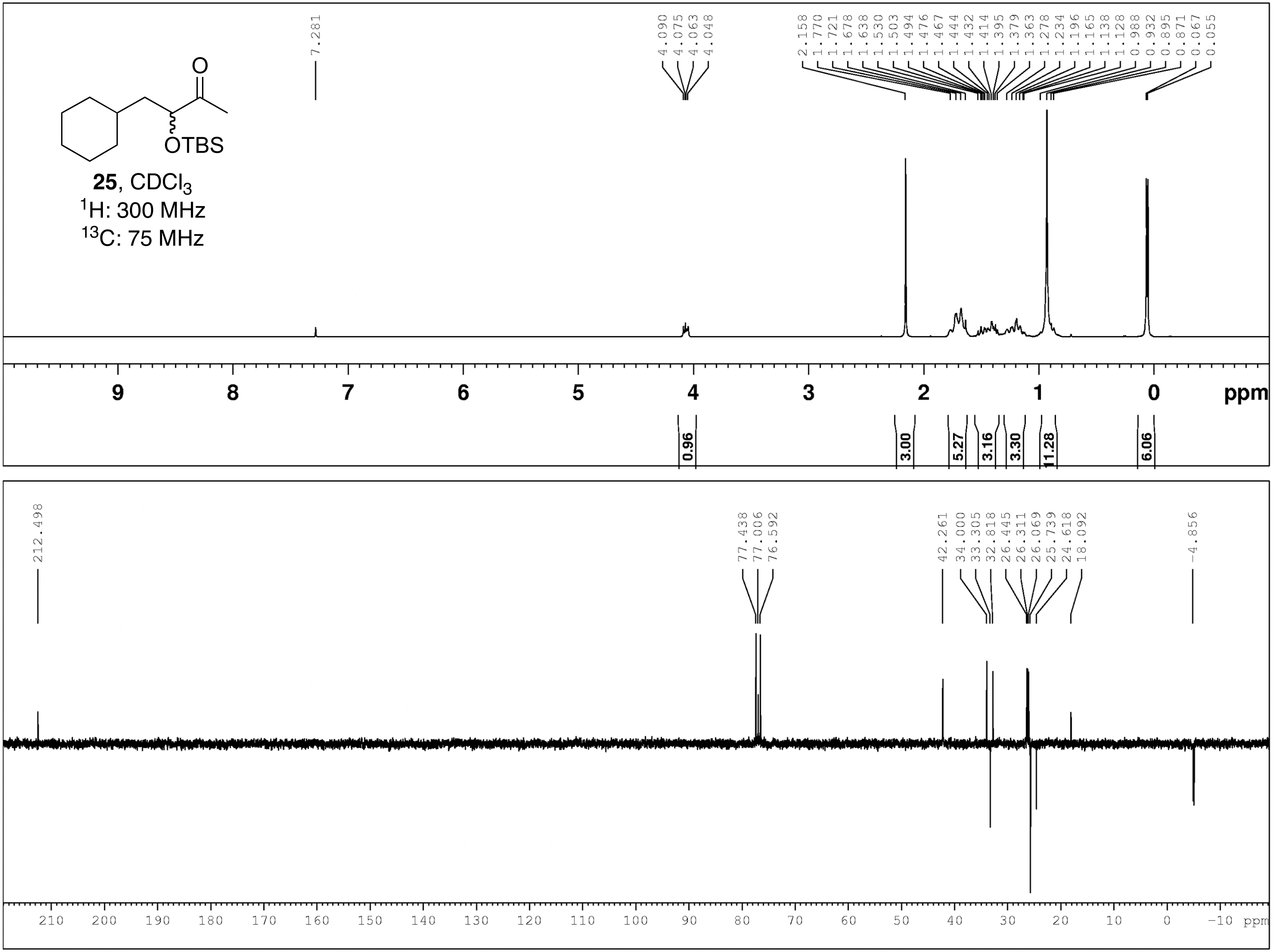
22, $CDCl_3$

^1H: 400 MHz

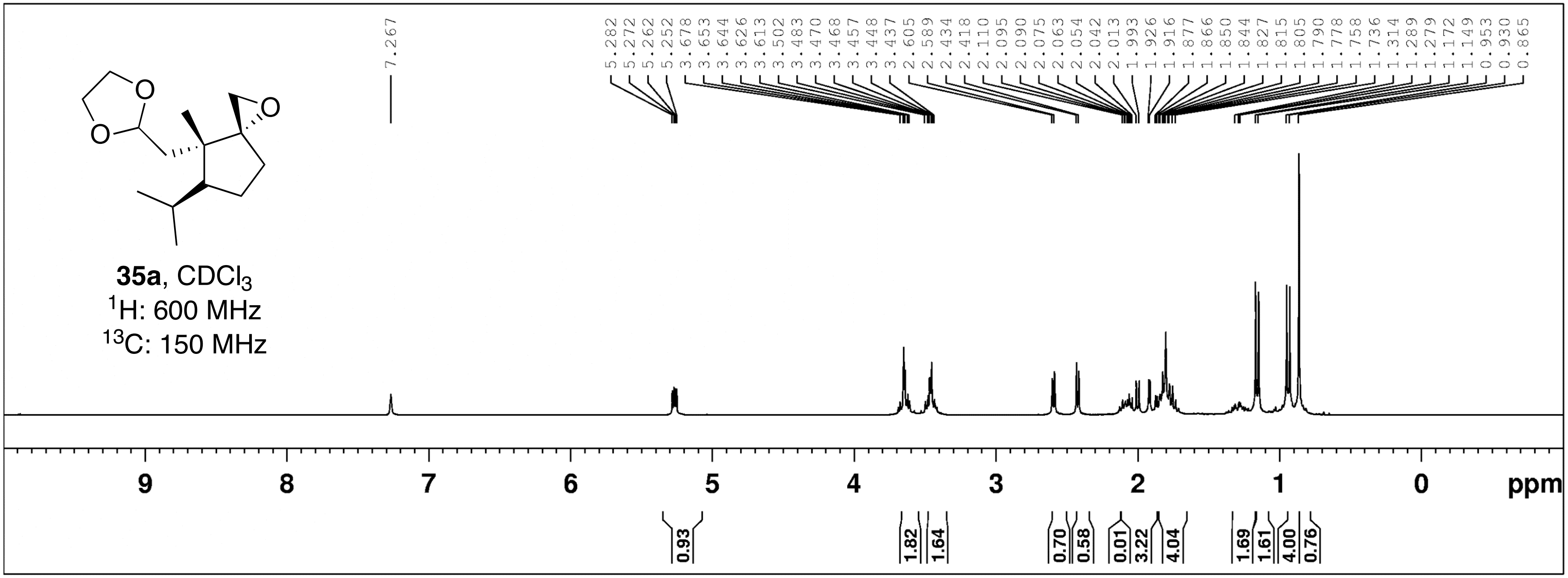
^{13}C: 100 MHz



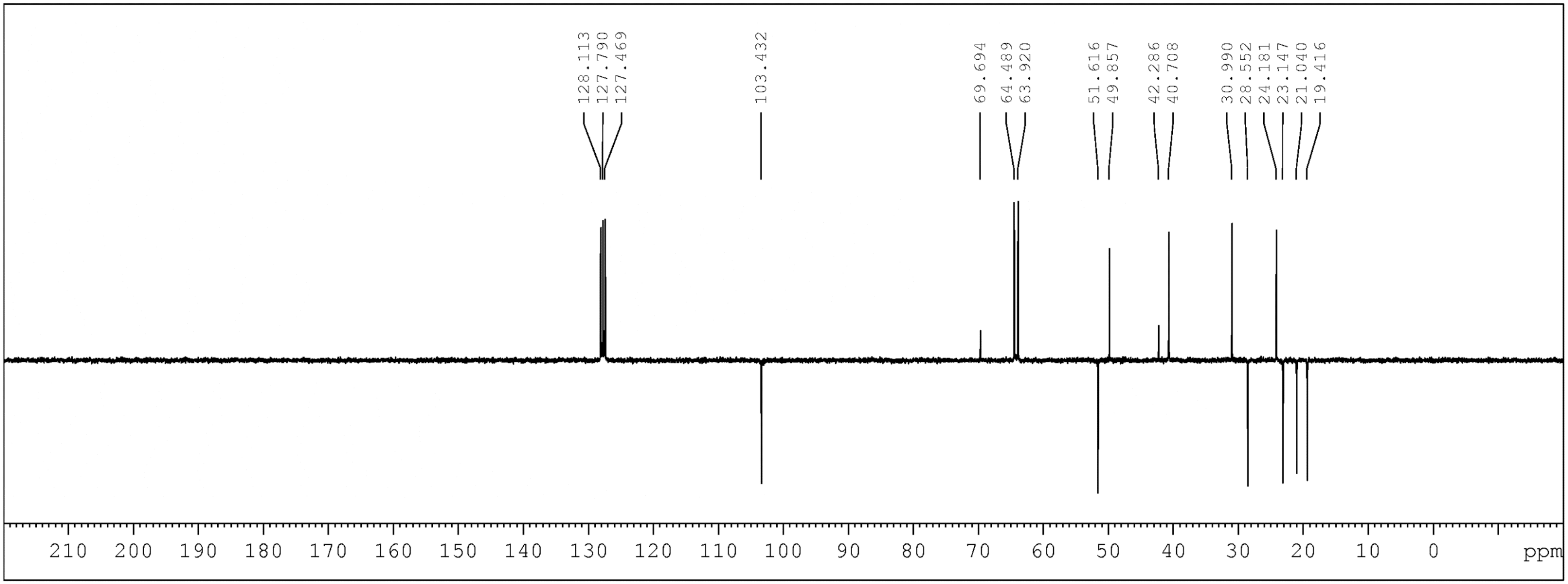

24, $CDCl_3$
^1H: 400 MHz
^{13}C: 100 MHz

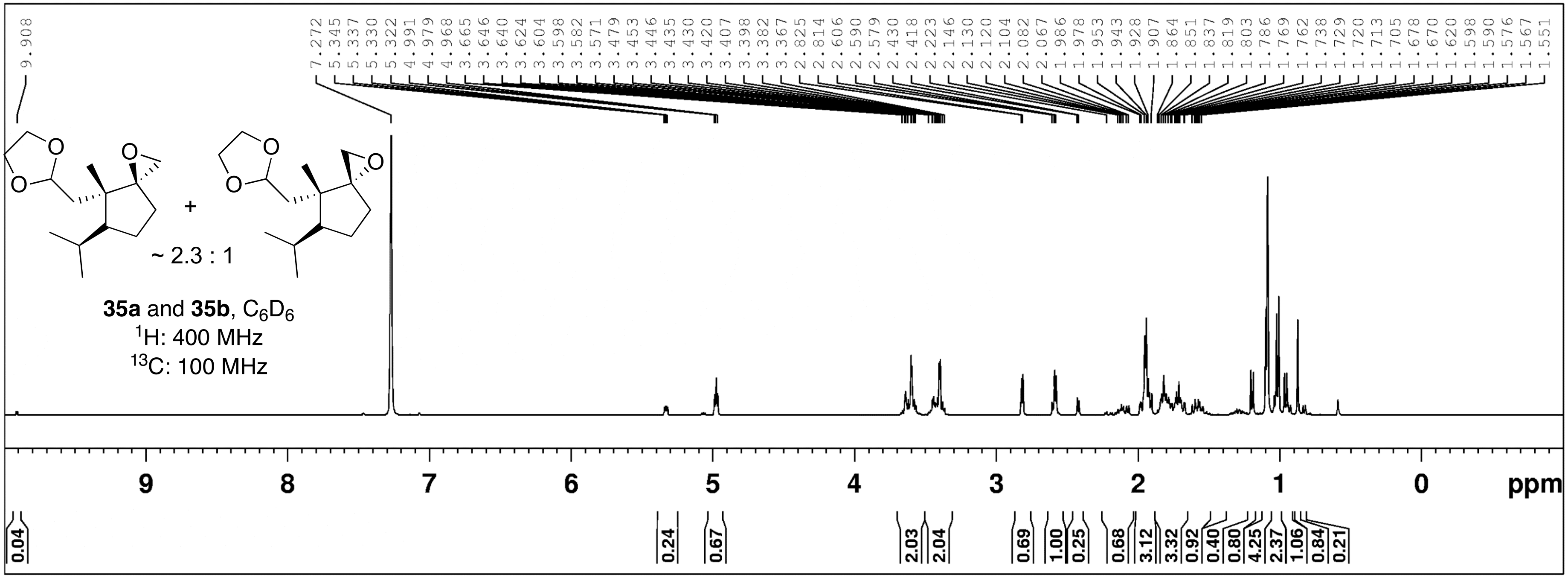


25, $CDCl_3$
^1H: 300 MHz
^{13}C: 75 MHz

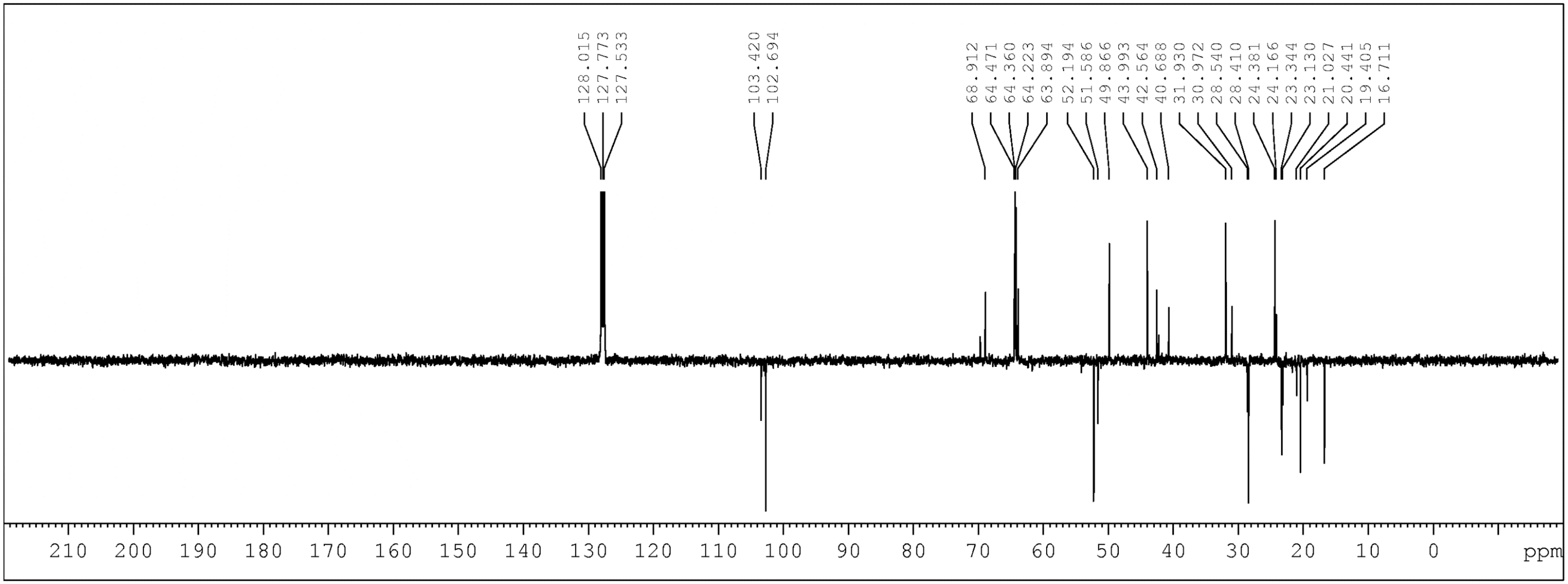


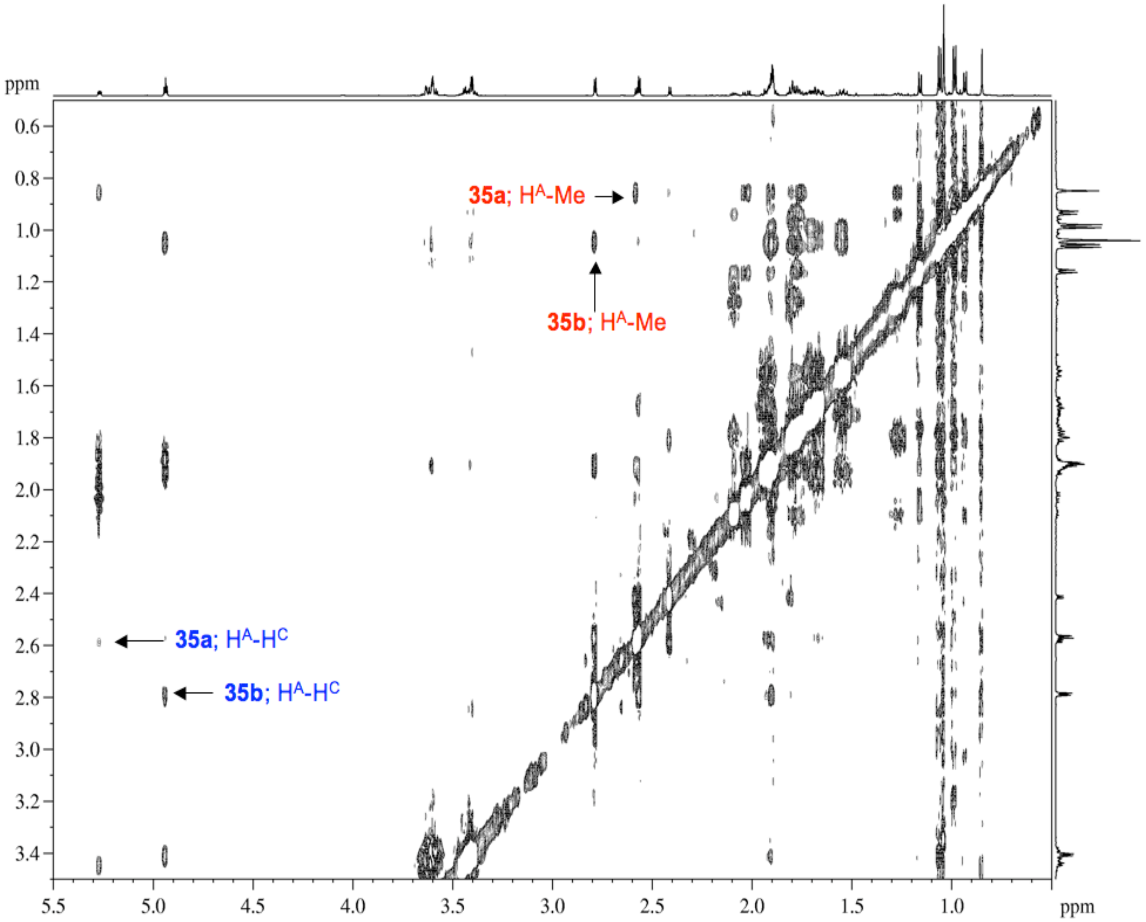
35a, $CDCl_3$
^1H: 600 MHz
^{13}C: 150 MHz

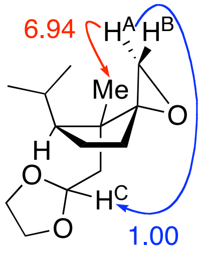




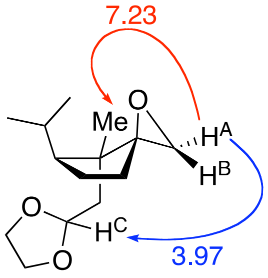
35a and **35b**, C_6D_6
^1H: 400 MHz
^{13}C: 100 MHz







35a 1 : 2.3 ratio



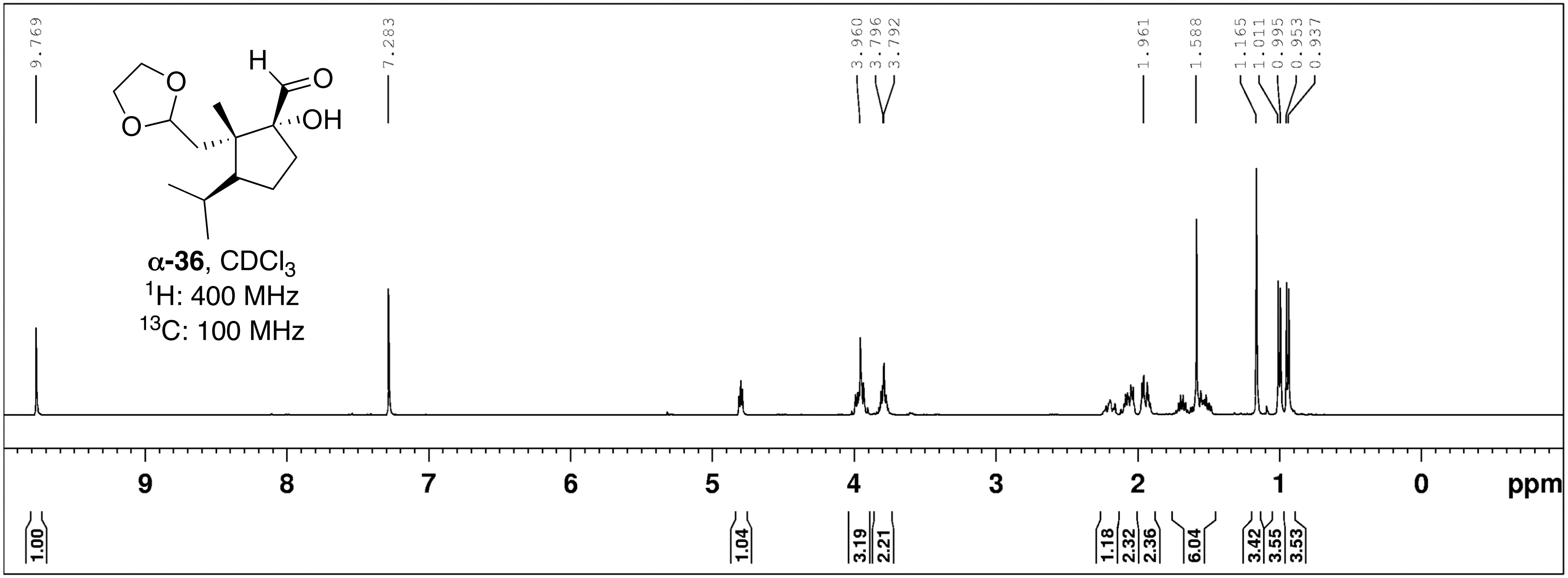
35b

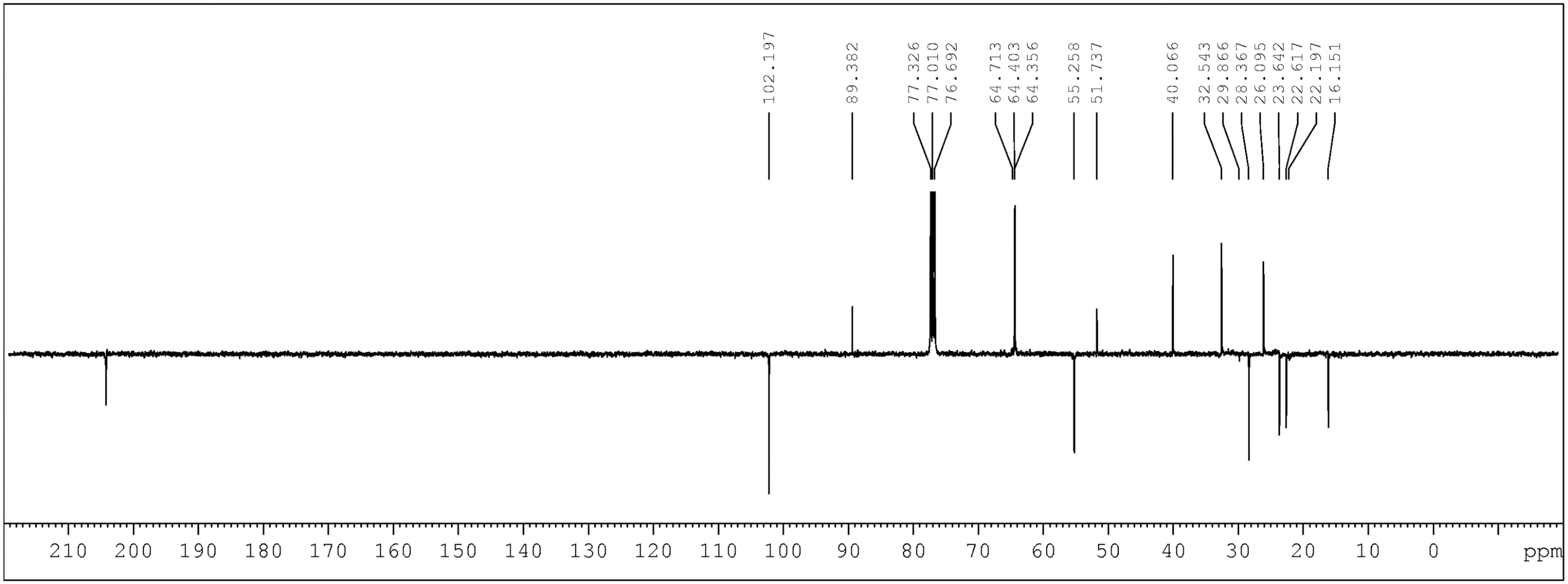
The numerical values represent the relative nOE volumes. Given there is H^A-Me, H^B-Me and H^A-H^C nOEs for both **35a** and **35b**, we cannot ascertain what ^{1}H NMR spectroscopy resonances correspond to each isomer based on the absence/presence of nOE interactions for the two diasteriomers. As such, relative nOE volumes were used to deduce their structures.

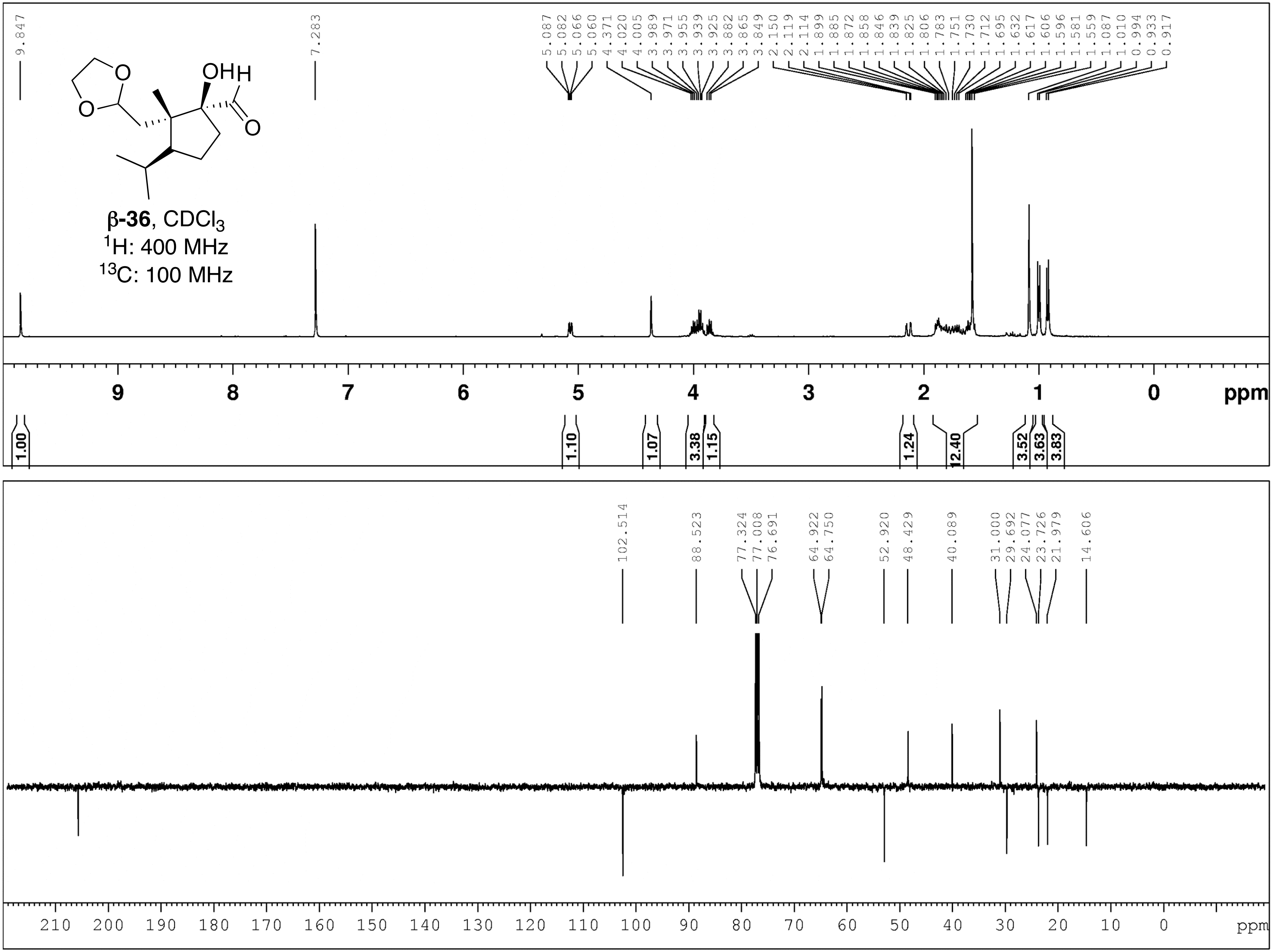
H^A-Me nOE: The relative volumes for **35a** and **35b** are 6.94 and 7.23 (or 1 : 1.04), respectively. Given the ratio of these two compounds is 1 : 2.3, the nOE of **35a** is much stronger than that of **35b**.

H^A-H^C: The relative volumes for **35a** and **35b** are 1 and 3.97, respectively. Given the ratio of these two compounds is 1 : 2.3, the nOE of **35b** is much stronger than that of **35a**.

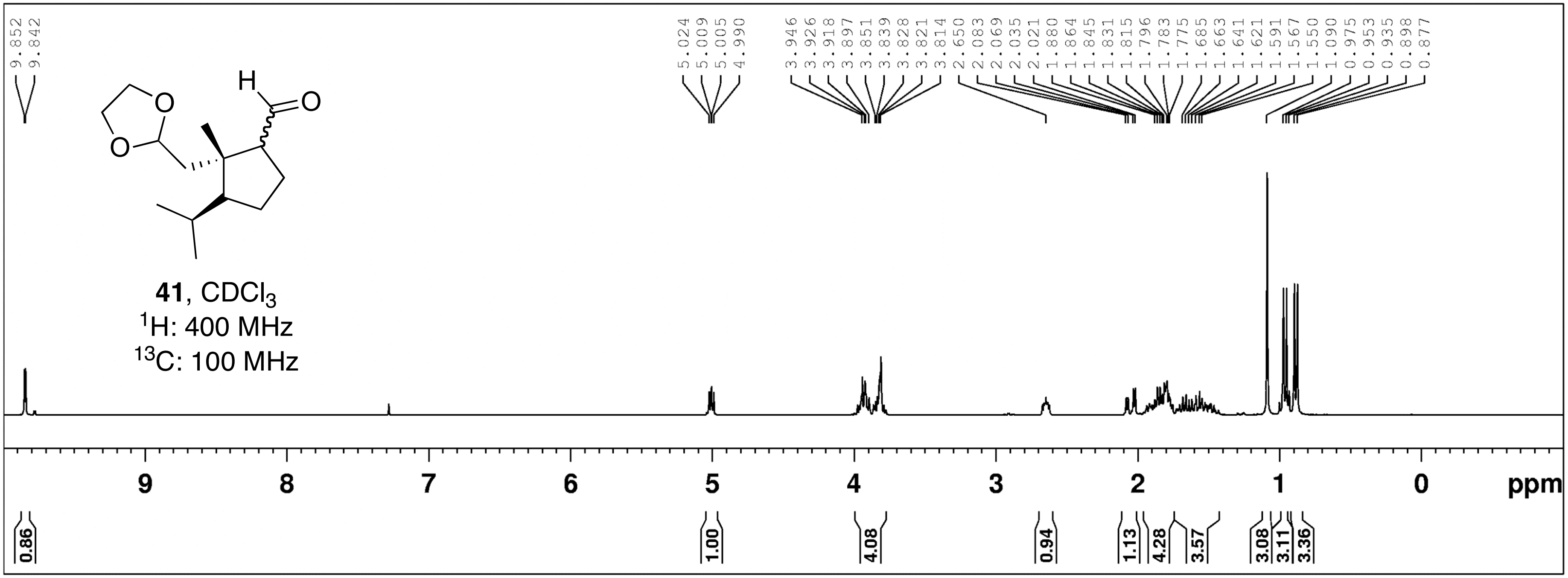
These two factors are consistent with the structures of **35a** and **35b** shown above.


α-36, $CDCl_3$
^1H: 400 MHz
^{13}C: 100 MHz

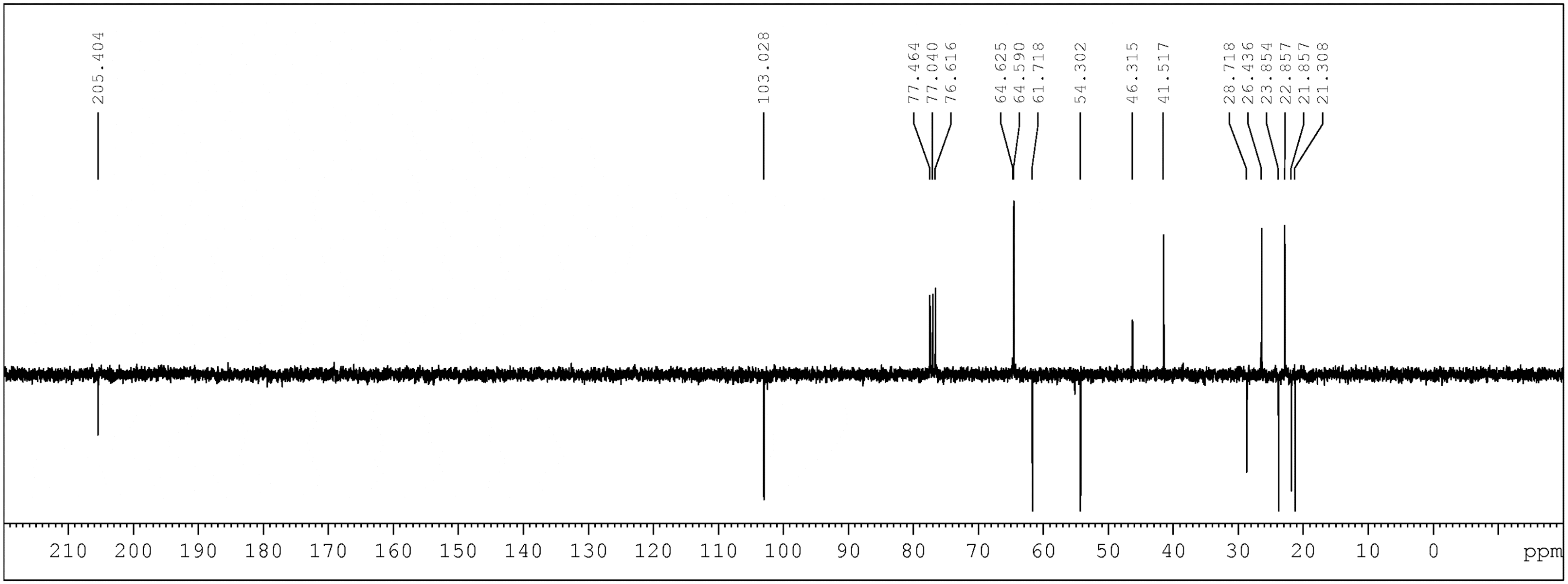


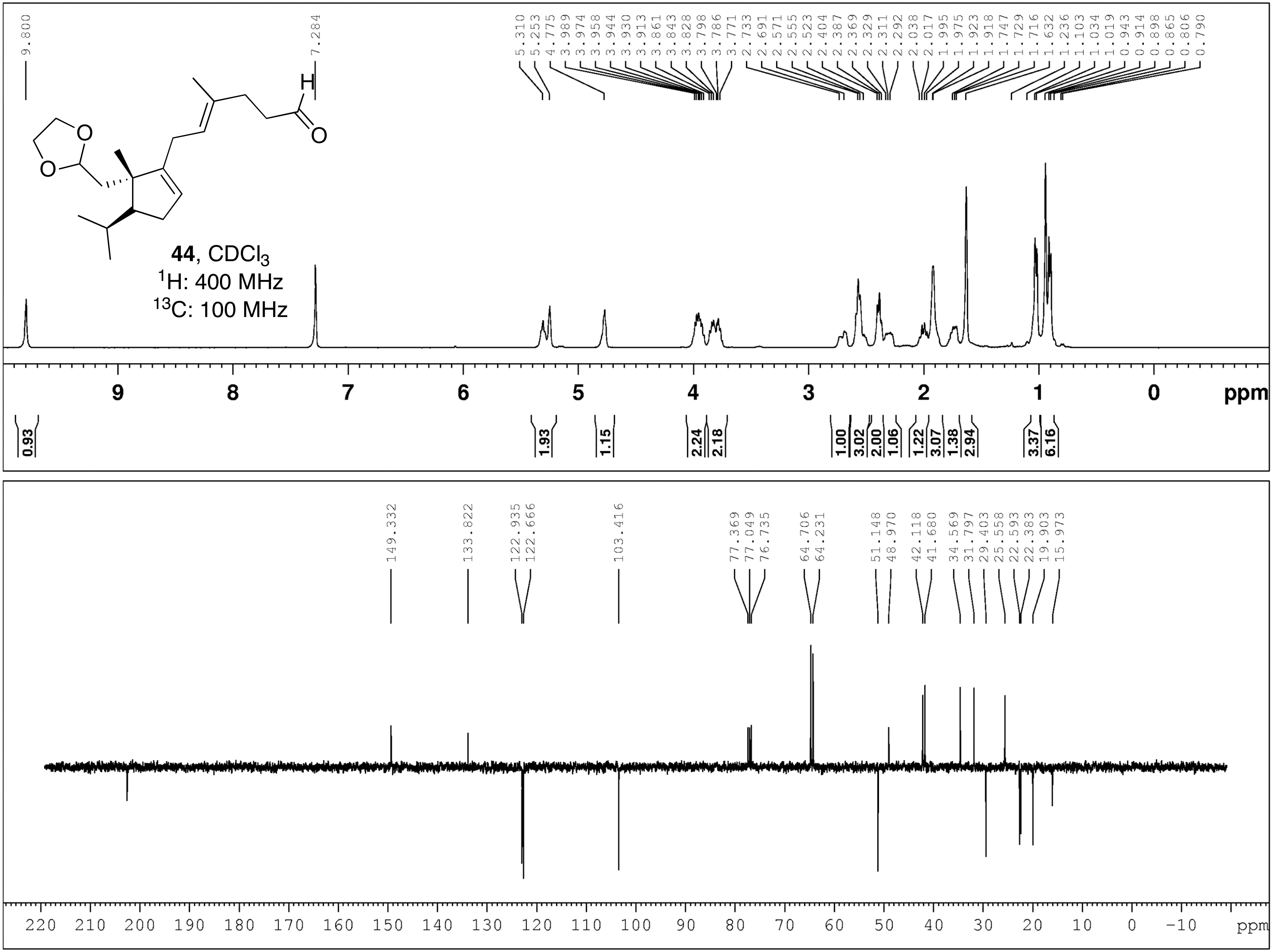


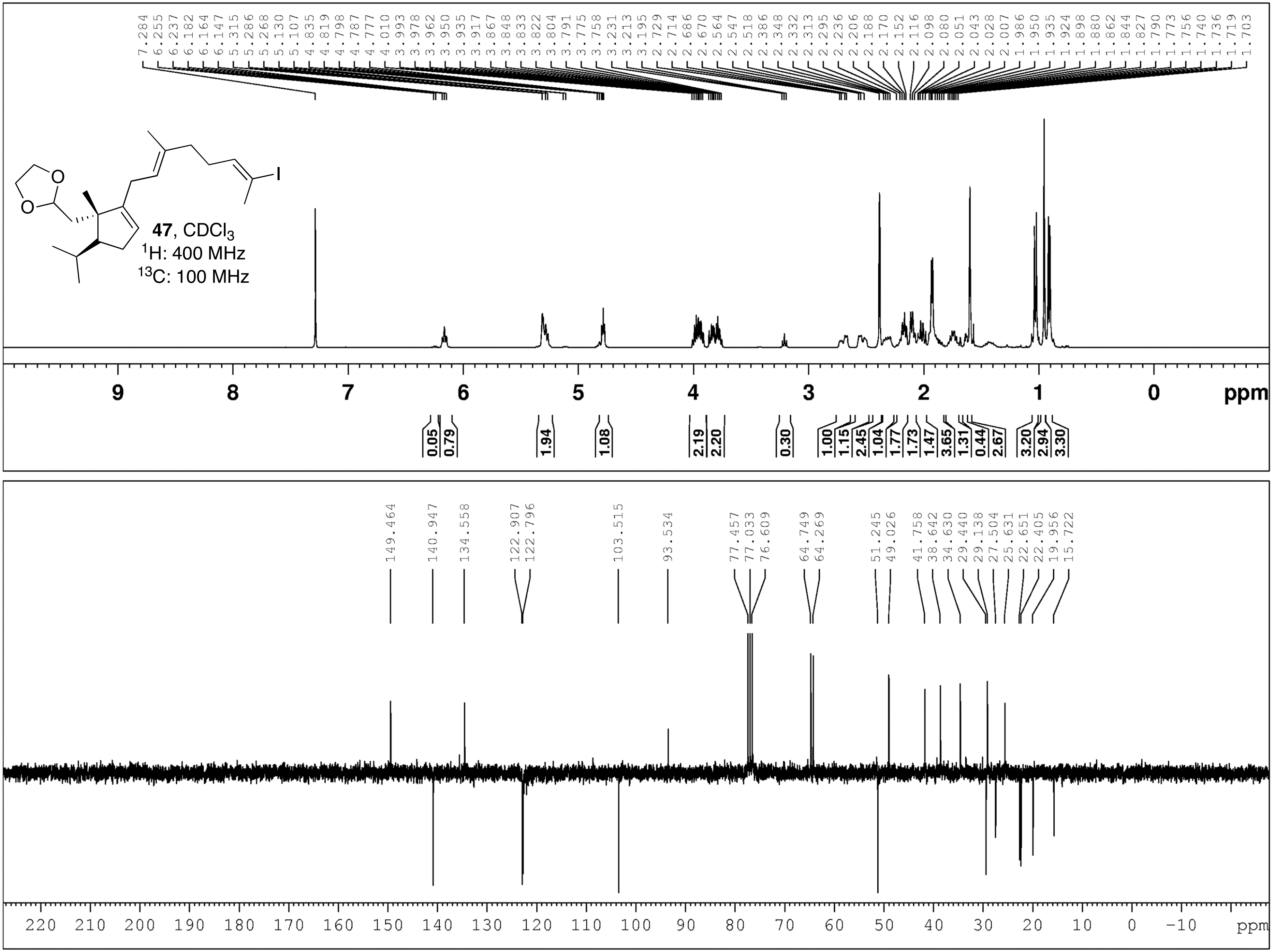
β-36, $CDCl_3$
^1H: 400 MHz
^{13}C: 100 MHz

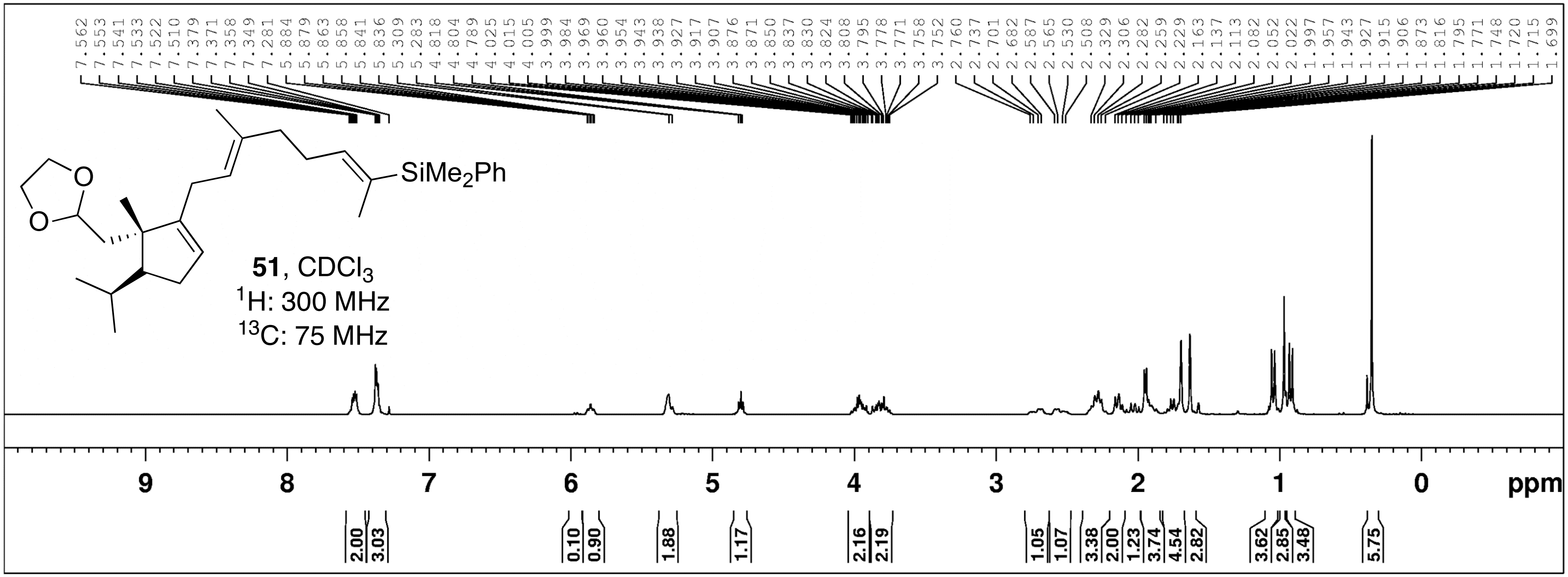


41, $CDCl_3$
^1H: 400 MHz
^{13}C: 100 MHz




44, CDCl$_3$
^{1}H: 400 MHz
^{13}C: 100 MHz
O
O
H
O
9.800
7.284
5.310 5.253 4.775 3.989 3.974 3.958 3.944 3.930 3.913 3.861 3.843 3.828 3.798 3.786 3.771 2.733 2.691 2.571 2.555 2.523 2.404 2.387 2.369 2.329 2.311 2.292 2.038 2.017 1.995 1.975 1.923 1.918 1.747 1.729 1.716 1.632 1.236 1.103 1.034 1.019 0.943 0.914 0.898 0.865 0.806 0.790
9 8 7 6 5 4 3 2 1 0 ppm
0.93 1.93 1.15 2.24 2.18 1.00 3.02 2.00 1.06 1.22 3.07 1.38 2.94 3.37 6.16
149.332 133.822 122.935 122.666 103.416 77.369 77.049 76.735 64.706 64.231 51.148 48.970 42.118 41.680 34.569 31.797 29.403 25.558 22.593 22.383 19.903 15.973
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 ppm

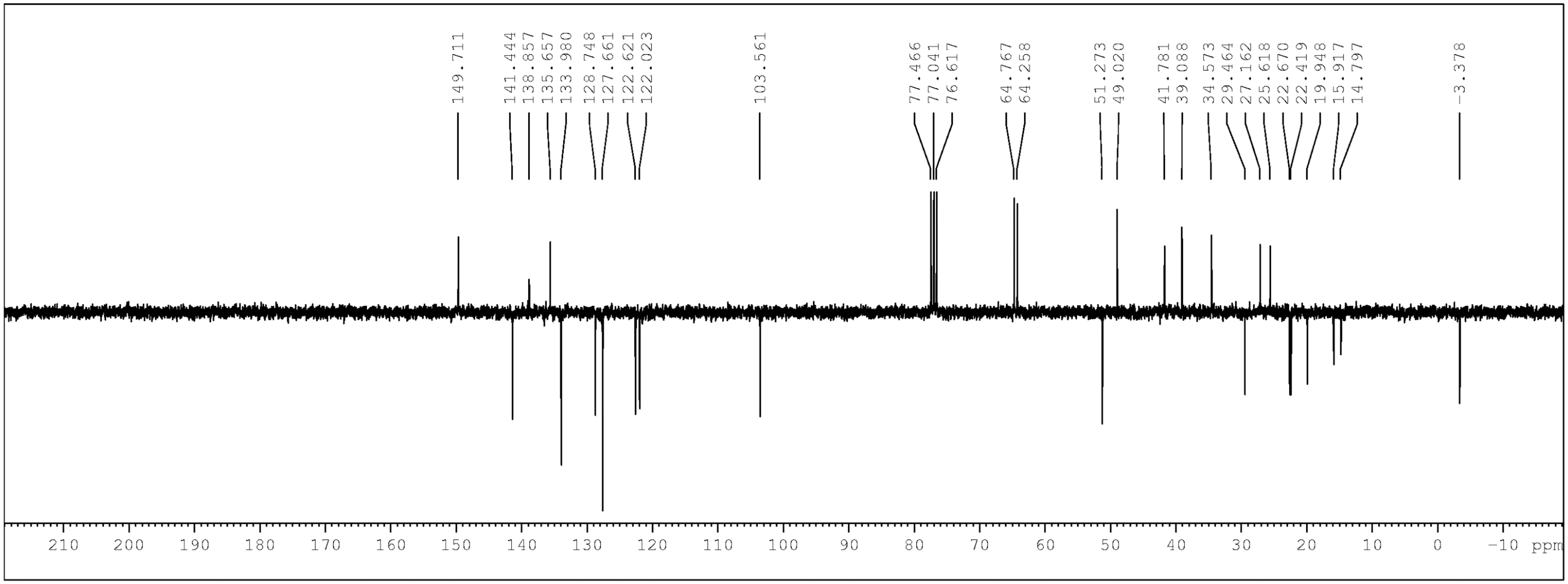

47, $CDCl_3$
^1H: 400 MHz
^{13}C: 100 MHz

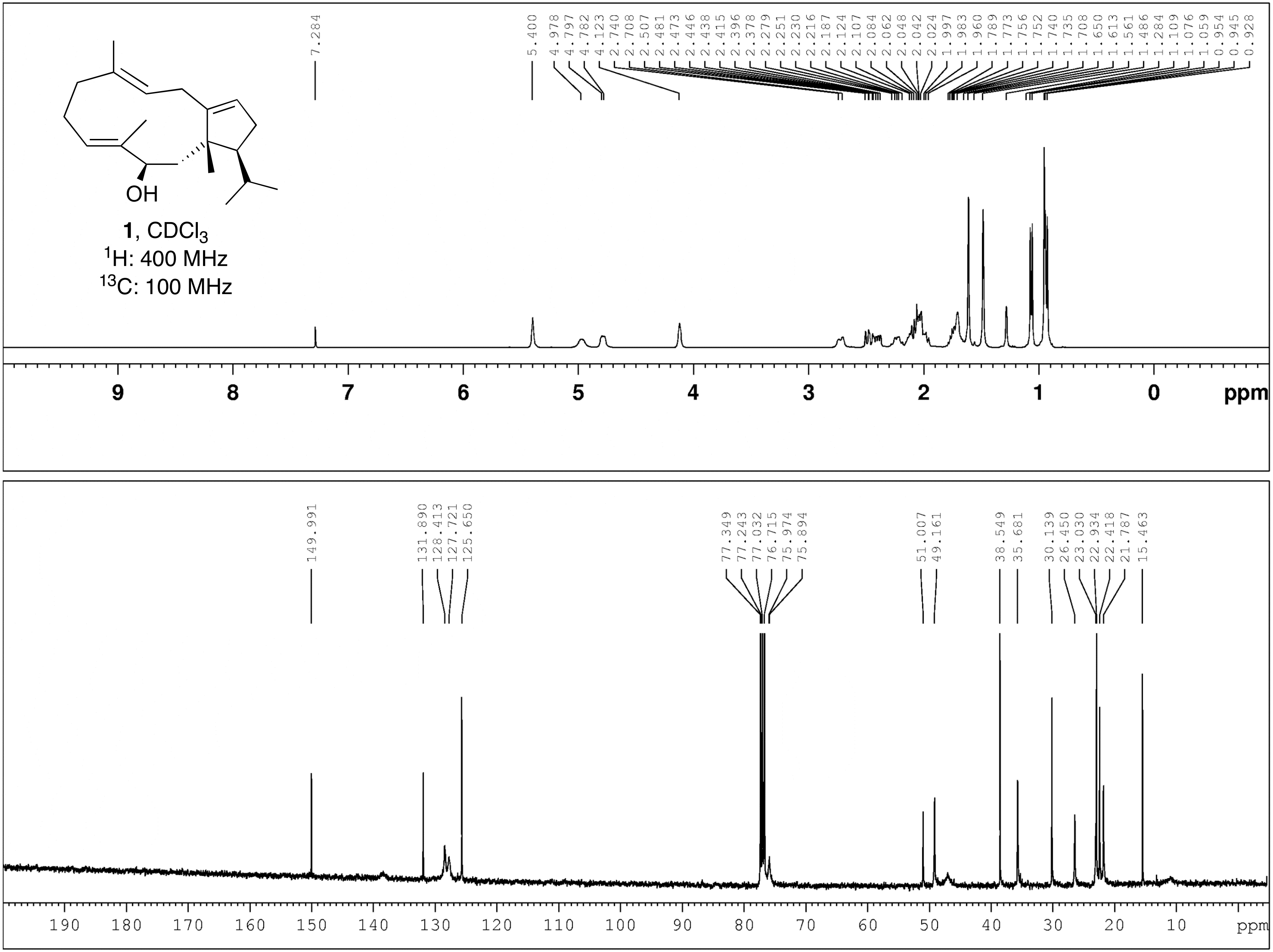


51, $CDCl_3$

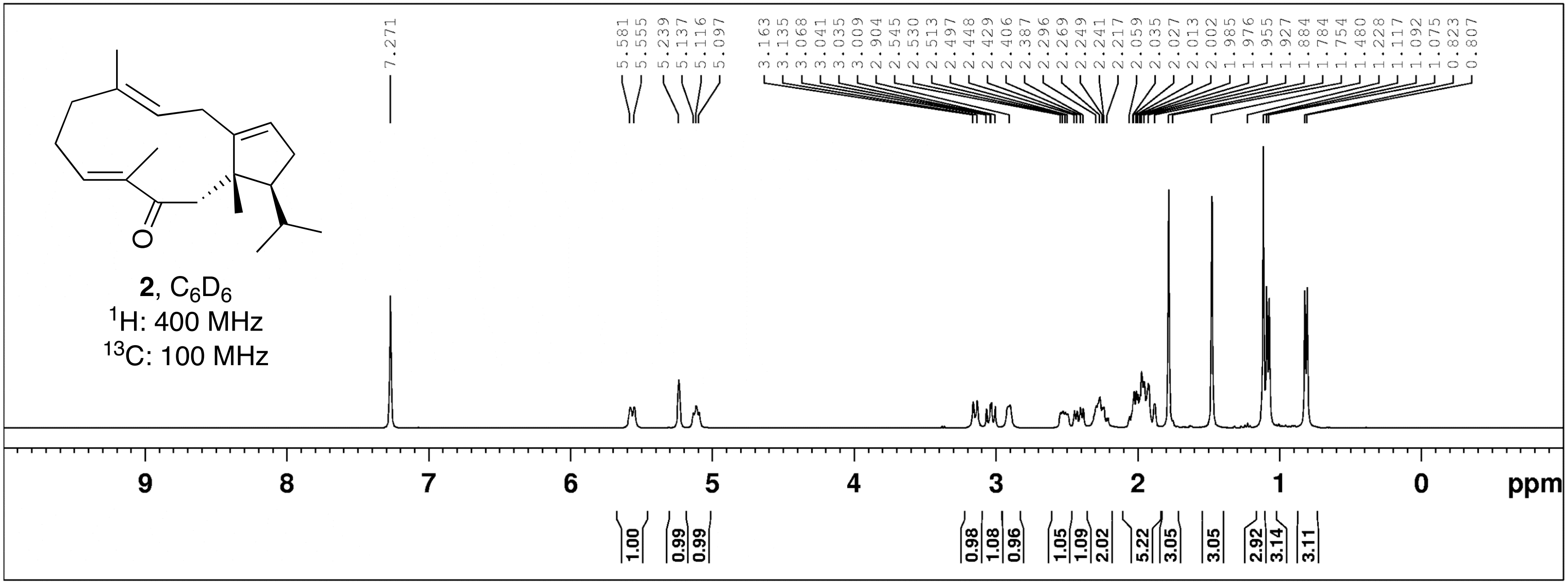
^1H: 300 MHz

^{13}C: 75 MHz

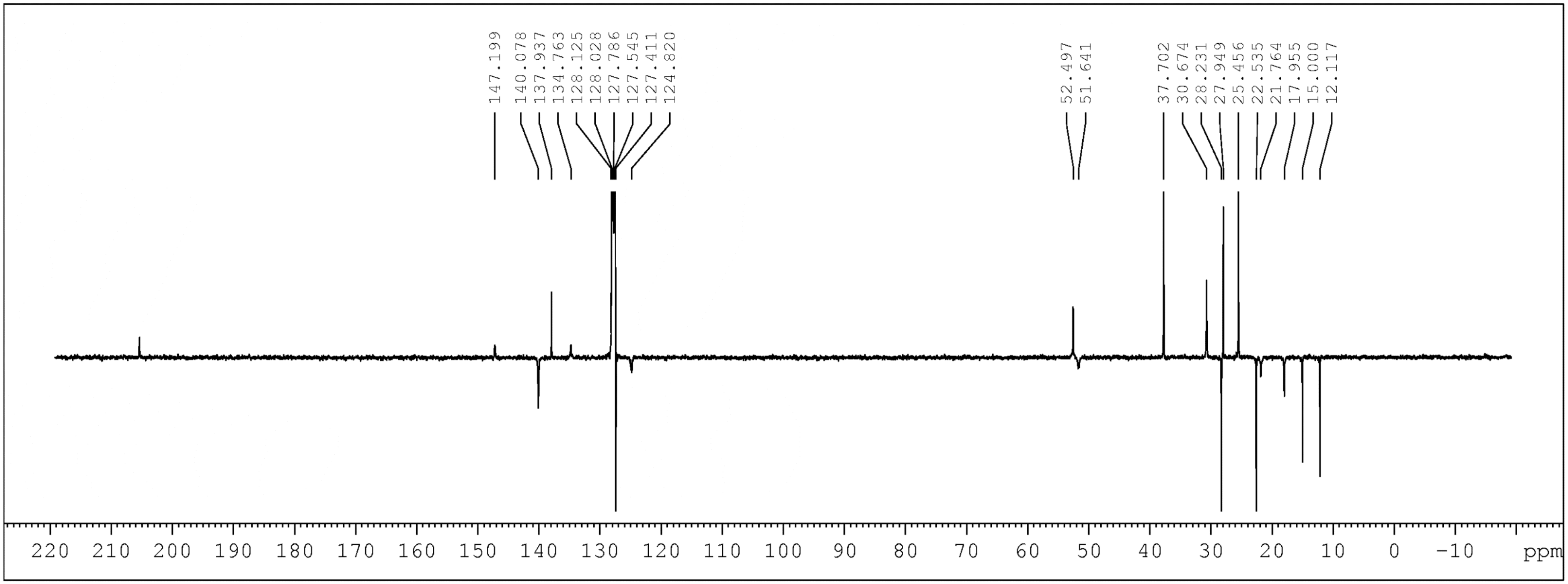




1, $CDCl_3$
^1H: 400 MHz
^{13}C: 100 MHz



2, C_6D_6
^{1}H: 400 MHz
^{13}C: 100 MHz



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[9] From ref 9: Naturally occurring neodolabellanes **1** and **2** were isolated as white solids, however their melting points were not reported.

[10] Iguchi, K.; Fukaya, T.; Yasumoto, A.; Watanabe, K. *J. Nat. Prod.* **2004**, *67*, 577-583.