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Supporting Information

A six-step total synthesis of α-thujone and d_6-α-thujone enabling facile access to isotopically labeled metabolites

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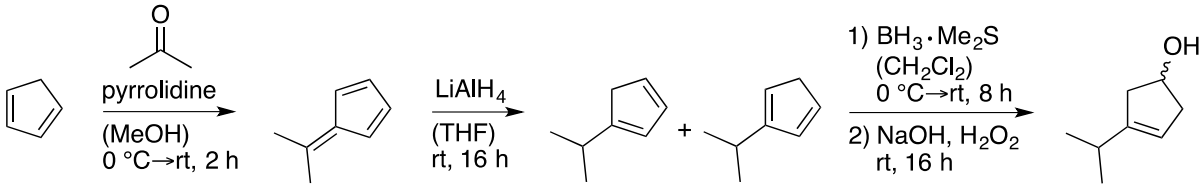
1 General information

Experimental: All reactions sensitive to air or moisture were carried out under an atmosphere of argon. Analytical thin-layer chromatography (TLC) was performed on Merck silica gel 60 F254 glass-baked plates, which were analysed after exposure to standard staining solutions: cerium ammonium molybdate solution [CAM] (2 g cerium(IV) sulfate, 50 g ammonium heptamolybdate and 50 mL H_2SO_4 in 300 mL water) or potassium permanganate solution [$KMnO_4$] (3 g potassium permanganate, 20 g potassium carbonate und 5 mL sodium hydroxide solution (5%) in 300 mL water). All solvents for chromatography were distilled prior to use. Column chromatography of crude products was performed with a hundredfold excess of silica gel (w/w). ^{1}H NMR spectra were recorded at 360 MHz or 500 MHz, using a Bruker AVHD 300 and AVHD 500 spectrometer, respectively. ^{13}C NMR spectra were recorded at 75, 91 or 126 MHz on a Bruker AVHD 300 and AVHD 500 spectrometer, respectivly. Chemical shifts of ^{1}H NMR and ^{13}C NMR (measured at 298 K) are given in ppm by using $CDCl_3$ as references (7.26 ppm and 77.16 ppm, respectively). Coupling constants (*J*) are reported in Hertz (Hz). Standard abbreviations indicating multiplicity were used as follows: s (singlet), d (doublet), dd (doublet of doublets), t (triplet), q (quartet), p (pentet), hept (heptet), m (multiplet). The degree of deuteration was determined by the integration of the signals in the ^{1}H NMR spectra. GC analyses were performed on an Agilent GC6890 instrument equipped with a HP-5 column (poly-dimethyl/diphenyl-siloxane, 95/5) and mass detector (Agilent 5973 Network). Hydrogen was used as the carrier gas and the constant-flow mode (flow rate = 1.8 mL/min) with a split ratio of 1:20 was used. The following temperature-program was used: 60 °C for 3 min, 15 °C/min to 250 °C, and 250 °C for 5 min. Enantiomeric excess (ee) were determined by chiral GC analysis on an Agilent GC6890 instrument equipped with an 2,3-dimethyl-6-TBDMS-β-cyclodextrine modified column and FID detector. The following temperature-program was used: 60 °C for 1 min, 15 °C/min to 220 °C. Infrared spectra were recorded on a JASCO FT/IR-4100 spectrometer. Standard abbreviations indicating signal intensity were used as followed: w (weak), m (medium), s (strong), br (broad). High-resolution mass spectra were obtained on a Thermo Finnigan MAT 95 mass spectrometer using the electron impact ionization (EI, 70 eV) technique the Specific rotations were measured on a 241 MC Perkin Elmer polarimeter with a 1 dm cuvette and are stated in ° mL dm^{-1} g^{-1} (c in g/100 mL).

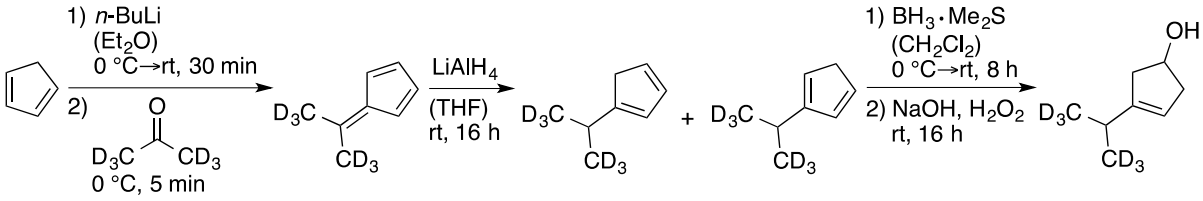
Sources of chemicals: Anhydrous dichloromethane, diethyl ether and tetrahydrofuran were taken from a solvent drying system (MBraun SPS-800). Tetrahydrofuran was further dried by distillation from sodium/benzophenone under argon atmosphere. Dry dichloromethane was stored over 4Å molecular sieves. $CDCl_3$ (99.8%) and d_6-acetone were purchased from Deutero GmbH. Filter agent (celite), lithium aluminium hydride, anhydrous chloroform, *n*-butyllithium solution in hexanes, borane dimethyl sulfide complex solution in dichloromethane, dimethyl sulfoxide, pyrrolidine, (–)-α-thujone. N,N'-dimethyl-N,N'-trimethyleneurea, isopropenyl acetate, *p*-toluenesulfonic acid, potassium bis(trimethylsilyl)amide, diiodomethane and vinyl acetate were purchased from Sigma-Aldrich. Silica gel (0.040-0.063 mm, 230-400 mesh ASTM), triethylamine and triphenyl phospine were purchased from Merck. Sodium sulfate and magnesium sulfate were purchased from AppliChem. Ammonium chloride and oxone were purchased from ABCR and Grüssing respectively. Dry acetone, sodium hydroxide and sodium thiosulfate were purchased from VWR. Pancreatin and diethyl zinc solution in hexane were purchased from TCI. Diisopropylazodicarboxylate was purchased from Carbolution. Hydrochloric acid (37%), cyclopentadiene, hydrogen peroxide, *o*-iodobenzoic acid, sodium methoxide, 3-chloroperoxybenzoic acide, acetic acid and methyl iodide were purchased from Acros Organics. Methanol, pentane and diethyl ether were purchased from Brenntag and distilled prior to use. Chemicals were used without further purification, unless stated otherwise.

2 Experimental procedures



8a **9a** **7a**

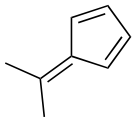
Scheme S1. Synthesis of 3-isopropylcyclopent-3-en-1-ol (7a)



8b **9b** **7b**

Scheme S2. Synthesis of 3-(propan-2-yl-1,1,1,3,3,3-*d*$_6$)cyclopent-3-en-1-ol (7b)

2.1 Synthesis of 6,6-dimethylfulvene (8a)



C_8H_{10}
106.17 g/mol

8a

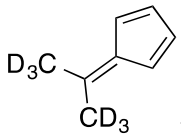
Fulvene **8a** was synthesized according to a modified literature procedure.[1] To a solution of freshly distilled cyclopentadiene (19.8 mL, 240 mmol, 1.20 eq.) and anhydrous acetone (14.7 mL, 200 mmol, 1.00 eq.) in dry methanol (50 mL) was added pyrrolidine (32.8 mL, 400 mmol, 2.00 eq.) at 0 °C. The mixture turned yellow while it was stirred at room temperature for 2 hours. After diluting with diethyl ether and water (100 mL each), the mixture was neutralised with acetic acid. The aqueous phase was extracted with ether (2 x 100 mL) and the combined organic layers were washed with water and brine (50 mL each), then dried over anhydrous magnesium sulfate and carefully concentrated (600 mbar, room temperature) to afford a yellow volatile oil, which was used without further purification in the next step as shown in Scheme S1.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.55 - 6.44 (m, 4H, CH), 2.21 (s, 6H, CH_3).

TLC: R_f = 0.59 (pentane, [CAM])

The spectroscopic data matched those reported in literature.[1]

2.2 Synthesis of 6,6-bis(trideuteriomethyl)fulvene (8b)



$C_8H_4D_6$
112.20 g/mol

8b

Fulvene **8b** was synthesized according to a modified literature procedure.[2] To a stirred solution of a *n*-butyllithium (2.5 M in hexane, 35.8 mL, 89.5 mmol, 1.15 eq.) in anhydrous diethyl ether (7 mL) was added freshly distilled cyclopentadiene (6.50 mL, 77.8 mmol, 1.00 eq.) over a period of 10 min at 0 °C. A white precipitate is formed immediately. After warming to room temperature the solution was stirred for an additional 30 min and then cooled again to 0 °C. A solution of d_6-acetone (17.2 mL, 234 mmol, 3.00 eq.) in anhydrous diethyl ether (6 mL) was added slowly. The white precipitate dissolved and the solution turned yellow. After stirring for an additional 5 min at 0 °C, the mixture was quenched by addition of ice water (10 mL) and pentane (70 mL). The organic layer was separated and extracted with ice water (70 mL) until the aqueous layer was neutral. The combined organic layers were then dried over anhydrous sodium sulfate and carefully concentrated (600 mbar, room temperature) to afford a yellow volatile oil, which was used without further purification in the next step as shown in Scheme S2. The degree of deuteration was calculated from the integrals of the proton signals at δ 6.60 – 6.40 and 2.20 ppm (95.5% d at the methyl groups).

^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 6.60 - 6.40 (m, 4H, CH).

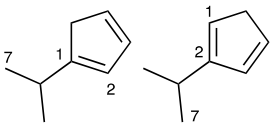
TLC: R_f = 0.59 (pentane, [CAM])

The spectroscopic data matched those reported in literature.[2]

2.3 General procedure for the reduction to 1- and 2-isopropylcyclopenta-1,3-diene (9a/9b)

To anhydrous tetrahydrofuran was added lithium aluminium hydride (0.50 eq.) at 0 °C (1.00 M). After stirring the suspension for 10 min, the fulvene (1.00 eq.) was added dropwise at 0 °C. The mixture was stirred at room temperature until complete conversion. The mixture was treated subsequently with ice water, 2 M NaOH and water. The resulting slurry was filtered through celite and washed with pentane. The aqueous layer was extracted with pentane (2 x) and the combined organic layers were dried over anhydrous sodium sulfate and concentrated (600 mbar, room temperature).

2.3.1 Synthesis of 1- and 2-isopropylcyclo-penta-1,3-diene (9a)



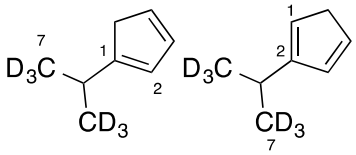
C_8H_{12}
108.18 g/mol

9a

Compound **9a** was prepared according to the general procedure (see 2.3) with fulvene **8a** (21.0 g, 197.8 mmol, 1.00 eq.) and lithium aluminium hydride (3.75 g, 98.9 mmol, 0.50 eq.) in tetrahydrofuran (98.9 mL), a modification of a published method.[3] The reaction mixture was stirred for 16 h and treated with ice water (4 mL), 2 M NaOH (4 mL) and water (12 mL). The resulting volatile, yellow oil was used without further purification in the next step as shown in Scheme S1.

^{1}H NMR (360 MHz, $CDCl_3$): δ [ppm] = 6.54 - 5.95 (m, 3H, H-1-4), 2.94 - 2.91 (m, 2H, H-5), 2.76 - 2.59 (m, 1H, H-6), 1.16 - 1.14 (m, 6H, H-7).
TLC: R_f = 0.86 (pentane, [CAM])
The spectroscopic data matched those reported in literature.[3]

2.3.2 Synthesis of 1- and 2-(propan-2-yl-1,1,1,3,3,3- *d*$_6$)cyclopenta-1,3-diene (9b)



$C_8H_6D_6$
114.22 g/mol

9b

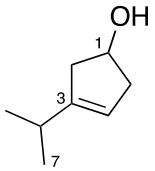
The reduction was carried out according to the general procedure (see 2.3) with fulvene **8b** (6.88 g, 61.3 mmol, 1.00 eq.) and lithium aluminium hydride (1.16 g, 30.6 mmol, 0.50 eq.) in tetrahydrofuran (31 mL). The reaction mixture was stirred for 16 h and treated with ice water (2 mL), 2 M NaOH (2 mL) and water (6 mL). The resulting volatile, yellow oil was used without further purification in the next step as shown in Scheme S2.

^{1}H NMR (360 MHz, $CDCl_3$): δ [ppm] = 6.54 - 5.95 (m, 3H, H-1-4), 2.96-2.89 (m, 1H, H-5), 2.64 (d, *J* = 19.6 Hz, 1H, H-6).
Degree of deuteration: >95%
TLC: R_f = 0.86 (pentane, [CAM])

2.4 General procedure for the hydroboration to 3-isopropylcyclopent-3-en-1-ol (7a/7b)

A solution of borane dimethyl sulfide complex (BDMS) (1 M in dichloromethane, 0.50 eq.) was added dropwise to the crude diene at 0 °C. After 1 h, the mixture was warmed to room temperature and stirred for 16 h. After addition of NaOH (2 M) and H_2O_2 (35%) stirring was continued for 24 h. The solid formed was removed by filtration and washed with diethyl ether. The organic phase was washed with water and dried over sodium sulfate. After removing the solvent under reduced pressure (600 mbar, room temperature), the crude product was purified *via* column chromatography (pentane/diethyl ether, 5:2).

2.4.1 Synthesis of 3-isopropylcyclopent-3-en-1-ol (7a)



$C_8H_{14}O$
126.20 g/mol

7a

The hydroboration was carried out according to the general procedure (see 2.4) with diene **9a** (1.01 g, 9.34 mmol, 1.00 eq.), BDMS (1 M in dichloromethane, 4.67 mL, 4.67 mmol, 0.50 eq.), NaOH (2 M, 7.5 mL), and H_2O_2 (35%, 7.5 mL). After column chromatography, cyclopentenol **7a** (590 mg, 4.67 mmol, 34% yield over three steps) was obtained as yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ [ppm] = 5.27 (s, 1H, H-4), 4.49 (tt, *J* = 6.2, 2.2 Hz, 1H, H-1), 2.73 - 2.52 (m, 2H, H-5), 2.34 (dt, *J* = 13.7, 6.9 Hz, 1H, H-6), 2.25 (t, *J* = 18.6 Hz, 2H, H-2), 1.04 (t, *J* = 7.0 Hz, 6H, H-7).

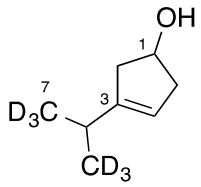
^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 148.7 (C, C-3), 118.4 (CH, C-4), 72.4 (CH-OH, C-1), 43.5 (CH_2, C-2), 42.8 (CH_2, C-5), 29.9 (CH, C-6), 21.5 (CH_3, C-7), 21.4 (CH_3, C-7).

HRMS (EI, 70 eV): calc. for $C_8H_{14}O_1^+$ [M^+]: 126.1039, found: 126.1042

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3347 (br, O-H), 3054(w, =C-H), 2959 (s, -CH_3), 2929 (s, -CH_2), 2872 (s, -CH_3), 2845 (s, -CH_2), 1711 (w, C=C), 1040 (m, C-OH).

TLC: R_f = 0.22 (pentane/diethyl ether, 5:2, [CAM])

2.4.2 Synthesis of 3-(propan-2-yl-1,1,1,3,3,3-*d*$_6$)cyclopent-3-en-1-ol (7b)



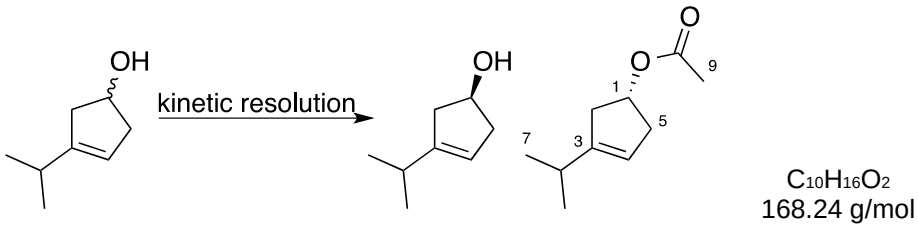
$C_8H_8D_6O$
132.24 g/mol

7b

The hydroboration was carried out according to the general procedure (see 2.4) with *d*$_6$-diene **9b** (4.11 g, 36.0 mmol, 1.00 eq.), BDMS (1 M in dichloromethane, 18.0 mL, 18.0 mmol, 0.50 eq.), NaOH (2 M, 30 mL), and H_2O_2 (35%, 30 mL). After column chromatography *d*$_6$-cyclopentenol **7b** (2.81 g, 21.2 mmol, 27% yield over three steps) was obtained as yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ [ppm] = 5.25 (s, 1H, H-4), 4.46 (tt, *J* = 6.1, 2.3 Hz, 1H, H-1), 2.66 – 2.54 (m, 2H, H-5), 2.28 (s, 1H, H-6), 2.21 (t, *J* = 18.6 Hz, 2H, H-2).
Degree of deuteration: >95%
^{13}C NMR (91 MHz, $CDCl_3$): δ [ppm] = 148.7 (C, C-3), 118.3 (CH, C-4), 72.3 (CH-OH, C-1), 43.4 (CH_2, C-2), 42.7 (CH_2, C-5), 29.4 (CH, C-6), 20.9 (br., CD_3, 2 C, C-7).
HRMS (EI, 70 eV): calc. for $C_8H_8D_6O_1^+$ [M^+]: 132.1416, found: 132.1417
IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3343 (br, O-H), 3055 (w, =C-H), 2925 (s, -CH_2), 2860 (m, -CH), 2846 (s, -CH_2), 2215 (s, -CD_3), 2126 (w, -CD_3), 2067 (w, -CD_3), 1708 (w, C=C), 1057 (s, C-OH), 833(w, C=C-H).
TLC: R_f = 0.22 (pentane/diethyl ether, 5:2, [CAM])

2.5 Kinetic resolution of 3-isopropylcyclopent-3-en-1-ol (7a) to produce (+)-3-isopropylcyclopent-3-en-1-yl acetate (+)-11a



$C_{10}H_{16}O_2$
168.24 g/mol

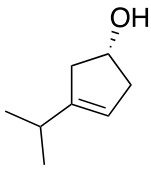
(+)-7a **(+)-11a**

A suspension of cyclopentenol **7a** (1.52 g, 12.0 mmol, 1.00 eq.), pancreatin (12.0 g), vinyl acetate (2.32 mL, 24.1 mmol, 2.00 eq.), and triethylamine (3.34 mL, 24.1 mmol, 2.00 eq.) in acetone (55 mL) was stirred at room temperature. After 3 d, the mixture was filtered through

celite. The filtrate was concentrated, taken up in diethyl ether and filtered through a silica-plug. The solvent was evaporated. After column chromatography (pentane/diethyl ether, 80:1, 1% triethylamine) the alcohol (35% ee) and the acetate (+)-**11a** (313 mg, 1.86 mmol, 95% ee, 31%) was isolated at 35% conversion.

^{1}H NMR (500 MHz, $CDCl_3$): δ [ppm] = 5.33 (tt, *J* = 7.0, 2.8 Hz, 1H, H-1), 5.27 (hept, *J* = 2.1 Hz, 1H, H-4), 2.78 - 2.65 (m, 2H, H-5), 2.39 - 2.27 (m, 3H, H-6, H-2), 2.03 (s, 3H, H-9), 1.04 (t, *J* = 6.7 Hz, 6H, H-7).
^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 171.3 (C=O, C-8), 148.6 (C, C-3), 118.5 (CH, C-4), 74.9 (CH, C-1), 40.4 (CH_2, C-5), 39.5 (CH_2, C-2), 29.7 (CH, C-6), 21.5 (CH_3, C-9), 21.4 (CH_3, C-7), 21.3 (CH_3, C-7').
TLC: R_f = 0.3 (pentane/diethyl ether, 20:1, [CAM])
Optical rotation: $[\alpha]_{546}^{23}$ = +5.1 (c = 1.28, $CHCl_3$, 95% ee)

2.6 Deacetylation of (+)-3-isopropylcyclopent-3-en-1-yl acetate ((+)-11a) to produce (–)-3-isopropylcyclopent-3-en-1-ol ((–)-7a)

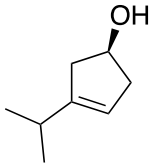


$C_8H_{14}O$
126.20 g/mol

(–)-7a

Acetate (+)-**11a** (560 mg, 3.33 mmol) was stirred in a solution of NaOH (2.5 M in methanol, 19.3 mL) at room temperature. After 2 h the reaction mixture was neutralized with HCl (2 M) and extracted with diethyl ether (3 x 20 mL). The combined organic layers were washed with water (20 mL) and dried over sodium sulfate. The solvent was removed under reduced pressure (600 mbar, 40 °C) and the crude product purified *via* column chromatography (pentane/diethyl ether, with 1% triethylamine) to obtain cyclopentenol (–)-**7a** (329 mg, 2.61 mmol, 78%). $[\alpha]_{546}^{23}$ = –3.6° (c = 0.83, $CHCl_3$, 95% ee), R_f = 0.13 (pentane/diethyl ether, 5:1).
The spectroscopic data match those reported in 2.4.1 for the racemic compound.

2.7 Mitsunobu reaction of (–)-3-isopropylcyclopent-3-en-1-ol ((–)-7a) to produce (+)-3-isopropylcyclopent-3-en-1-ol ((+)-7a)



$C_8H_{14}O$
126.20 g/mol

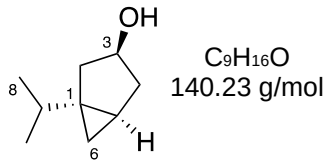
(+)-**7a**

Diisopropylazodicarboxylate (DIAD) (1.02 mL, 5.21 mmol, 2.00 eq.) was slowly added to a solution of triphenylphosphine (1.37 g, 5.21 mmol. 2.00 eq.) in anhydrous diethyl ether (15 mL) at 0 °C and stirred for 30 min. Then a solution of cyclopentenol (–)-**7a** (329 mg, 2.61 mmol, 1.00 eq.) and benzoic acid (636 mg, 5.21 mmol, 2.00 eq.) in anhydrous diethyl ether (15 mL) was slowly added. The reaction mixture was warmed to room temperature and stirred for 17 h. The mixture was filtered and concentrated. Then NaOH (2.5 M in methanol, 12 mL) was added to the residue and stirred overnight. After neutralization with HCl (2 M), the mixture was extracted with diethyl ether. The combined organic layers were washed with water and dried over sodium sulfate. The solvent was evaporated (600 mbar, 40 °C) and the crude product was purified by column chromatography (pentane/diethyl ether, 5:1 with 1% triethylamine) to yield cyclopentenol (+)-**7a** (234 mg, 1.85 mmol, 71 %) as yellow oil. $[\alpha]_{546}^{23}$= + 3.6 (c = 0.83, $CHCl_3$, 95% ee). R_f = 0.13 (pentane/diethyl ether, 5:1, [CAM]). The spectroscopic data match those reported in 2.4.1 for the racemic compound.

2.8 General procedure for the cyclopropanation

To a solution of the cyclopentenol **7a/7b** in anhydrous dichloromethane (0.1 M) was added diethyl zinc (1 M in hexane, 2.00 eq.) at 0 °C. After stirring for 10 min, diiodomethane (2.00 eq.) was added. A white precipitate formed while the mixture was allowed to warm to room temperature. After full conversion, the reaction mixture was diluted with ether and washed subsequently with a solution of saturated ammonium chloride and a solution of saturated sodium thiosulfate. The combined organic layers were dried over anhydrous magnesium sulfate and the solvent was removed under reduced pressure. The crude product was purified *via* column chromatography (pentane/diethyl ether, 5:2, [CAM]).

2.8.1 Synthesis of 1-isopropylbicyclo[3.1.0]hexan-3-ol (6a)



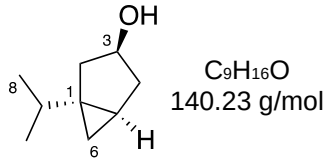
$C_9H_{16}O$
140.23 g/mol

6a

The reaction was performed as described in 2.8.1 with the use of cyclopentenol **7a** (1.27 g, 10.1 mmol, 1.00 eq.) in anhydrous dichloromethane (100 mL), 1 M diethyl zinc (20.1 mL, 20.1 mmol, 2.00 eq.) in hexane and diiodomethane (1.62 mL, 20.1 mmol, 2.00 eq.) The reaction mixture was stirred for 16 h. After purification *via* column chromatography cyclopropane **6a** (1.18 g, 8.48 mmol, 84%) was obtained as yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ [ppm] = 4.38 (t, *J* = 6.7 Hz, 1H, H-3), 2.13 (dt, *J* = 14.0, 5.5 Hz, 1H, H-4), 2.01 (ddd, *J* = 14.0, 6.8, 1.8 Hz, 1H, H-2) 1.67 (d, *J* = 14.0 Hz, 1H, H-4'), 1.63 (d, *J* = 14.0 Hz, 1H, H-2'), 1.35 (br. s, 1H, OH) 1.36 (dq, *J* = 13.5, 6.8 Hz, 1H, H-7), 1.04 (dt, *J* = 8.5, 4.4 Hz, 1H, H-5), 0.92 (d, *J* = 6.8 Hz, 3H, H-8), 0.87 (d, *J* = 6.8 Hz, 3H, H-8'), 0.69 (t, *J* = 4.2 Hz, 1H, H-6), 0.46 - 0.41 (m, 1H, H-6').
^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 73.9 (CH-OH, C-3), 39.1 (CH_2, C-4), 38.9 (CH_2, C-2), 34.9 (C, C-1), 33.0 (CH, C-7), 22.6 (CH, C-5), 20.2 (CH_3, C-8), 20.2 (CH_3, C-8'), 17.1 (CH_2, C-6).
HRMS (EI, 70 eV): calc. for $C_9H_{14}^+$ [$(M-H_2O)^+$]: 122.1090, found: 122.1085
IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3354 (br, -OH), 3072 (w, cyclopropane), 3010 (w, -CH), 2994 (m, -CH), 2955 (s, $-CH_3$), 2927 (s, $-CH_2$), 2871 (s, $-CH_3$), 2853 (s, $-CH_3$), 1454 (w, $-CH_2$), 1363, (m), 969 (m).
TLC: R_f = 0.24 (pentane/diethyl ether, 5:1, [$KMnO_4$])

2.8.2 Synthesis of (+)-1-isopropylbicyclo[3.1.0]hexan-3-ol ((+)-6a)



$C_9H_{16}O$
140.23 g/mol

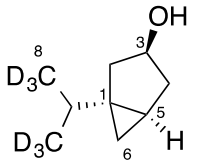
(+)-**6a**

The reaction was performed as described in the general procedure starting from the optically active cyclopentenol (+)-**7a** (223 mg, 1.77 mmol, 1.00 eq.) in anhydrous dichloromethane

(17 mL), 1 M diethyl zinc (3.54 mL, 3.54 mmol, 2.00 eq.) in hexane and diiodomethane (285 µL, 3.54 mmol, 2.00 eq.). The product cyclopropane (+)-**6a** (132 g, 941 µmol, 53%) was obtained as yellow oil. $[\alpha]_{546}^{23}$= +2.2 (c = 0.77, $CHCl_3$, 95% ee). The spectroscopic data for (+)-**6a** were identical to those described for **6a**.

R_f = 0.24 (pentane/diethyl ether, 5:1, [$KMnO_4$])

2.8.3 Synthesis of 1-(propan-2-yl-1,1,1,3,3,3-*d*$_6$)bicyclo[3.1.0]hexan-3-ol (6b)



$C_9H_{10}D_6O$
146.26 g/mol

6b

The reaction was performed as described in the general procedure starting from the cyclopentenol **7b** (588 mg, 4.45 mmol, 1.00 eq.) in dichloromethane (50 mL), 1 M diethyl zinc (8.90 mL, 8.90 mmol, 2.00 eq.) in hexane and diiodomethane (718 µL, 8.90 mmol, 2.00 eq.) The reaction mixture was stirred for 16 h. After purification *via* column chromatography cyclopropane **6b** (466 mg, 3.18 mmol, 72%) was obtained as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ [ppm] = 4.37 (t, *J* = 6.4 Hz, 1H, H-3), 2.15 - 2.08 (m, 1H, H-4), 1.99 (ddd, *J* = 14.0, 6.8, 1.6 Hz, 1H, H-2), 1.66 (dd, *J* = 14.2, 3.1 Hz, 1H, H-4'), 1.61 (d, *J* = 14.0 Hz, 1H, H-2'), 1.44 (s, 1H, OH), 1.32 (s, 1H, H-7), 1.02 (dt, *J* = 8.6, 4.4 Hz, 1H, H-5), 0.68 (t, *J* = 4.1 Hz, 1H, H-6), 0.44 - 0.40 (m, 1H, H-6').

Degree of deuteration: >95%

^{13}C NMR (126 MHz, $CDCl_3$): δ [ppm] = 73.9 (CHOH, C-3), 39.2 (CH_2, C-4), 38.9 (CH_2, C-2), 34.9 (C, C-1), 32.5 (CH, C-7), 22.6 (CH, C-5), 19.2 (br., CD_3, 2C, C-8/8'), 17.0 (CH_2, C-6).

HRMS (EI, 70 eV): calc. for $C_9H_8D_6^+$ [$(M\text{-}H_2O)^+$]: 128.1467, found: 128.1470

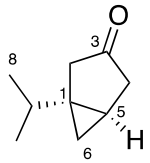
IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3344 (br, -OH), 3072 ($w, C\nabla C$), 3010 (w, -CH), 2994 (m, -CH), 2924 (s, -CH_2), 2877 (s, -CH), 2210 (s, -CD_3), 2126 (w, -CD_3), 2070 (m, -CD_3), 1433 (m, -CH_2), 1298 (m), 1056 (s, C-OH)

TLC: R_f = 0.24 (pentane/diethyl ether, 5:1, [$KMnO_4$])

2.9 General procedure for the oxidation to 1-isopropylbicyclo[3.1.0]hexan-3-one (10a/10b)

The reaction was carried out under air atmosphere. A suspension of *o*-iodoxybenzoic acid (IBX) (3.00 eq.) in dimethyl sulfoxide (approximately 1.0 M) was stirred at room temperature for 30 min, before the alcohol **6a/6b** (1.00 eq.) in dimethyl sulfoxide (approximately 1.5 M) was added. The reaction mixture was stirred at room temperature until full conversion. The reaction was quenched with saturated sodium thiosulfate and the phases were separated. The aqueous layer was extracted with diethyl ether. Then the combined organic layers were washed with brine and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure (300 mbar/ 40°C). Column chromatography (pentane/diethyl ether, 20:1) afforded the ketone.

2.9.1 Synthesis of 1-isopropylbicyclo[3.1.0]hexan-3-one (10a)



$C_9H_{14}O$
138.21 g/mol

10a

The reaction was performed according to the general procedure as described in 2.9 with the use of IBX (7.05 g, 25.2 mmol, 3.00 eq.) in dimethyl sulfoxide (25 mL) and alcohol **6a** (1.18 g, 8.39 mmol, 1.00 eq.) in dimethyl sulfoxide (6 mL). The reaction was stirred for 4 h. The reaction was quenched with sodium thiosulfate (10 mL). After column chromatography the ketone **10a** (897 mg, 6.49 mmol, 77%) was obtained as yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.62 (ddtd, *J* = 18.9, 5.6, 2.0, 1.2 Hz, 1H, H-4), 2.47 (dtd, *J* = 18.8, 2.3, 1.2 Hz, 1H, H-2), 2.20 (d, *J* = 18.9 Hz, 1H, H-4'), 2.12 (d, *J* = 18.8 Hz, 1H, H-2'), 1.46 - 1.39 (m, 1H, H-7), 1.34 (ddd, *J* = 9.6, 5.0, 3.3 Hz, 1H, H-5), 1.00 (d, *J* = 6.8 Hz, 3H, H-8), 0.92 (d, *J* = 6.9 Hz, 3H, H-8'), 0.76 (ddt, *J* = 7.8, 5.4, 2.1 Hz, 1H, H-6), 0.07 (dd, *J* = 5.6, 3.9 Hz, 1H, H-6').

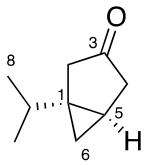
^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 218.6 (C=O, C-3), 42.6 (CH_2, C-4), 41.9 (CH_2, C-2), 33.1 (CH, C-7), 30.4 (C, C-1), 20.0 (CH_3, C-8), 20.0 (CH_3, C-8') 18.5 (CH_2, C-6), 18.1 (CH, C-5).

HRMS (EI, 70 eV): calc. for $C_9H_{14}O_1^+$ [M^+]: 138.1039, found: 138.1039

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3055 (w, -CH), 3031 (w, -CH), 2957 (s, -CH_3), 2903 (m, -CH_2), 2873 (m, -CH_3), 1744 (s, -C=O), 1465 (m, -CH_2), 1153 (m).

TLC: R_f = 0.26 (pentane/diethyl ether, 20:1, [$KMnO_4$])

2.9.2 Synthesis of (+)-1-isopropylbicyclo[3.1.0]hexan-3-one ((+)-10a)

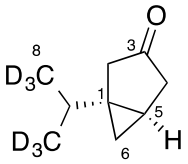


$C_9H_{14}O$
138.21 g/mol

(+)-**10a**

The reaction was performed according to the general procedure as described in 2.9 with the use of IBX (1.15 g, 4.09 mmol, 3.00 eq.) in dimethyl sulfoxide (4 mL) and alcohol (+)-**6a** (191 mg, 1.36 mmol, 1.00 eq.) in dimethyl sulfoxide (1 mL). The ketone (+)-**10a** (77.7 mg, 0.56 mmol, 41%) was obtained as yellow oil. $[\alpha]_{546}^{23}$= + 52.8 (c = 1.12, $CHCl_3$, 95% ee). The spectroscopic data for (+)-**10a** were identical to those described for **10a**.

2.9.3 Synthesis of 1-(propan-2-yl-1,1,1,3,3,3-*d*$_6$)bicyclo[3.1.0]hexan-3-one (10b)



$C_9H_8D_6O$
144.25 g/mol

10b

The reaction was performed according to the general procedure as described in 2.9.1 with the use of IBX (2.67 g, 9.54 mmol, 3.00 eq.) in dimethyl sulfoxide (10 mL) and the alcohol **6a** (465 mg, 3.18 mmol, 1.00 eq.) in dimethyl sulfoxide (2 mL). The reaction was stirred for 4 h. The reaction was quenched with sodium thiosulfate (5 mL). After column chromatography ketone **10b** (404 mg, 2.80 mmol, 88%) was obtained as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.61 (dd, *J* = 18.9, 4.6 Hz, 1H, H-4), 2.47 (d, *J* = 18.9 Hz, 1H, H-2), 2.19 (dd, *J* = 19.0, 2.3 Hz, 1H, H-4'), 2.12 (d, *J* = 18.9 Hz, 1H, H-2'), 1.38 (s, 1H, H-7), 1.34 (ddd, *J* = 8.1, 5.6, 4.0 Hz, 1H, H-5), 0.76 (t, *J* = 6.8 Hz, 1H, H-6), 0.06 (t, *J* = 4.9 Hz, 1H, H-6').

Degree of deuteration: >95%

^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 218.6 (C=O, C-3), 42.6 (CH_2, C-4), 41.9 (CH_2, C-2), 32.6 (CH, C-7), 30.3 (C, C-1), 18.5 (CH_2, C-6), 18.1 (CH, C-5).

HRMS (EI, 70 eV): calc. for $C_9H_8D_6O_1^+$ [M^+]: 144.1416, found: 144.1403

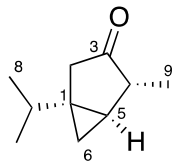
IR (ATR): $\tilde{\nu}$[cm^{-1}] =3055 (w, -CH), 2983, (w, -CH), 2933 (m, -CH_2), 2901 (w, -CH), 2879 (m, -CH_2), 2210 (m, -CD_3), 2129 (w, -CD_3), 2071 (w, -CD_3), 1742 (s, -C=O), 1409 (w), 1153 (m), 1055(m).

TLC: R_f = 0.26 (pentane/diethyl ether, 20:1, [$KMnO_4$])

2.10 General procedure for methylation to α-thujone (1a/1b)

To a stirred solution of ketone **10a/10b** (1.00 eq.) in anhydrous tetrahydrofuran (0.1 M) was slowly added potassium bis(trimethylsilyl)amide (KHMDS) (15% in toluene, 1.00 eq.) at –78 °C. After 30 min, N,N'-dimethyl-N,N'-trimethyleneurea (DMPU) (1.16 eq.) and methyl iodide (1.00 eq.) were added sequentially. Stirring was stopped 10 sec after complete addition. After 2 h at –78 °C, the reaction was directly quenched at 0 °C with saturated sodium hydrogen carbonate and the aqueous phase was extracted with diethyl ether (3x). The combined organic phase was washed subsequently with water (2x) and brine, dried over anhydrous magnesium sulfate and concentrated under vacuum. The toluene contained was removed *via* column chromatography (pentane/diethyl ether, 1:0→0:1). Afterwards, the crude product was purified *via* column chromatography (pentane/diethyl ether, 50:1→ 40:1).

2.10.1 Synthesis of α-thujone (1a)



$C_{10}H_{16}O$
152.24 g/mol

1a

The methylation was carried out according to the general procedure (see 2.10) with ketone **10a** (100 mg, 723 µmol, 1.00 eq.) in anhydrous tetrahydrofuran (7 mL), KHMDS (15% in toluene, 1.10 mL, 723 µmol, 1.00 eq.), DMPU (102 µL, 839 µmol, 1.16 eq.) and methyl iodide (45.2 µL, 723 µmol, 1.00 eq.). After column chromatography, α-thujone **1a** (82.6 mg, 543 µmol, 75%) was obtained as colourless oil.

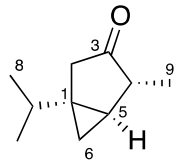
^{1}H NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.54 (ddd, *J* = 18.8, 2.3, 1.1 Hz, 1H, H-2), 2.21 (q, *J* = 7.2 Hz, 1H, H-4), 2.07 (d, *J* = 18.8 Hz, 1H, H-2'), 1.36 (hept, *J* = 6.8 Hz, 1H, H-7), 1.15 (d, *J* = 7.5 Hz, 3H, H-9), 1.08 (dd, *J* = 8.1, 4.0 Hz, 1H, H-5), 1.00 (d, *J* = 6.8 Hz, 3H, H-8), 0.95 (d, *J* = 6.8 Hz, 3H, H-8') 0.76 (ddd, *J* = 8.1, 5.6, 2.5 Hz, 1H, H-6), 0.12 (dd, *J* = 5.6, 4.1 Hz, 1H, H-6').

^{13}C NMR (91 MHz, $CDCl_3$): δ [ppm] = 221.7 (C=O, C-3), 47.5 (CH, C-4), 39.9 (CH_2, C-2), 33.1 (CH, C-7), 29.8 (C, C-1), 25.7 (CH, C-5), 20.1 (CH_3, C-8), 19.9 (CH_3, C-8') 18.9 (CH_3, C-9), 18.4 (CH_2, C-6).

The spectroscopic data matched to those reported in literature.[5]

TLC: R_f = 0.20 (pentane/diethyl ether, 40:1, [$KMnO_4$])

2.10.2 Synthesis of (–)-α-thujone (1a)

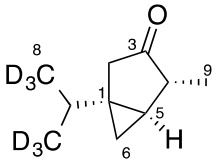


$C_{10}H_{16}O$
152.24 g/mol

(–)-**1a**

The reaction was performed according to the general procedure in 2.10 with the use of ketone (+)-**10a** (30 mg, 217 µmol, 1.00 eq.) in anhydrous tetrahydrofuran (3 mL), KHMDS (15% in toluene, 434 µL, 217 µmol, 1.00 eq.), DMPU (30.5 µL, 251 µmol, 1.16 eq.) and methyl iodide (13.6 µL, 217 µmol, 1.00 eq.). The product (–)-**1a** (12.6 mg, 82.8 µmol, 38%) was isolated as volatile liquid. $[\alpha]_D^{23}$ = –19.9 (c = 1.02, $CHCl_3$, 95% ee). The optical rotation matches with literature value of enantiomeric pure (–)-α-thujone **1a** $[\alpha]_D^{23}$ = –20.5 (c = 1.0, $CHCl_3$, 99% ee)/ $[\alpha]_{546}^{23}$ = –27.16.[6] The spectroscopic data for (–)-α-thujone **1a** were identical to those described for α-thujone **1a**.

2.10.3 Synthesis of d_6-thujone (1b)



$C_{10}H_{10}D_6O$
158.27 g/mol

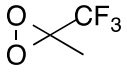
1b

The reaction was carried out as described in 2.10 with ketone **10b** (625 mg, 4.33 mmol, 1.00 eq.) in anhydrous tetrahydrofuran (28 mL), KHMDS (8.67 mL, 4.33 mmol, 1.00 eq.),

DMPU (608 µL, 5.03 mmol, 1.16 eq.) and methyl iodide (271 µL, 4.33 mmol, 1.00 eq.). After purification d_6-thujone **1b** (425 mg, 2.69 mmol, 62%) was obtained.

^{1}H NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.54 (d, *J* = 18.9 Hz, 1H, H-2), 2.21 (q, *J* = 7.5 Hz, 1H, H-4), 2.07 (d, *J* = 18.9 Hz, 1H, H-2'), 1.32 (s, 1H, H-7), 1.15 (d, *J* = 7.5 Hz, 3H, H-9), 1.08 (dd, *J* = 8.1, 4.0 Hz, 1H, H-5), 0.75 (ddd, *J* = 6.8, 5.7, 1.8 Hz, 1H, H-6), 0.11 (t, *J* = 5.0 Hz, 1H, H-6').
Degree of deuteration: >95%
^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 221.7 (C=O, C-3), 47.5 (CH_2, C-4), 39.9 (CH_2, C-2), 32.6 (CH, C-7), 29.6 (C, C-1), 25.6 (CH, C-5), 18.8 (CH_3, C-9), 18.4 (CH_2, C-6).
HRMS (EI, 70 eV): calc. for $C_{10}H_{10}D_6O_1^+$ [M^+]: 158.1572, found: 158.1573
IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3054 (w, -CH), 3017 (w, -CH), 2963 (m, -CH), 2929 (m, -CH_2), 2873 (m, -CH_2), 2210 (m, -CD_3), 2128 (w, -CD_3), 2071 (w, -CD_3), 1739 (s, -C=O), 1455 (m, -CH_2), 1056 (m).
TLC: R_f = 0.20 (pentane/diethyl ether, 40:1, [$KMnO_4$])

2.11 Preparation of methyl(trifluoromethyl)dioxirane (TFDO)



$C_3H_3F_2O_2$
128.05 g/mol

12

A 1 L, three-necked, round bottom flask, was equipped with over-head stirrer, a septum and a condenser which was attached to a 25 mL receiving flask by a distillation receiver with an argon balloon (see Figure S1). Prior to use all glassware was triple-rinsed with EDTA-solution (0.1 M), water and acetone. The condenser and the receiving flask were cooled at –78 °C by an *i*-propanol bath with dry ice. The set-up was then purged with argon, charged with a slurry of 26.0 g $NaHCO_3$ in 26 mL Millipore-water and cooled to 0 °C with an ice bath. Under vigorous stirring, freshly grinded 48 g Oxone was added in one portion under strong evolution of CO_2 gas. After 2 min 24.0 mL trifluoroacetone was added to the reaction mixture within 20 sec using a pre-cooled dropping funnel. After few seconds, the pale yellow solution of the methyl(trifluoromethyl)dioxirane in trifluoroacetone started to condense and within 20 min 8-10 mL liquid was collected in the cooled receiving flask.

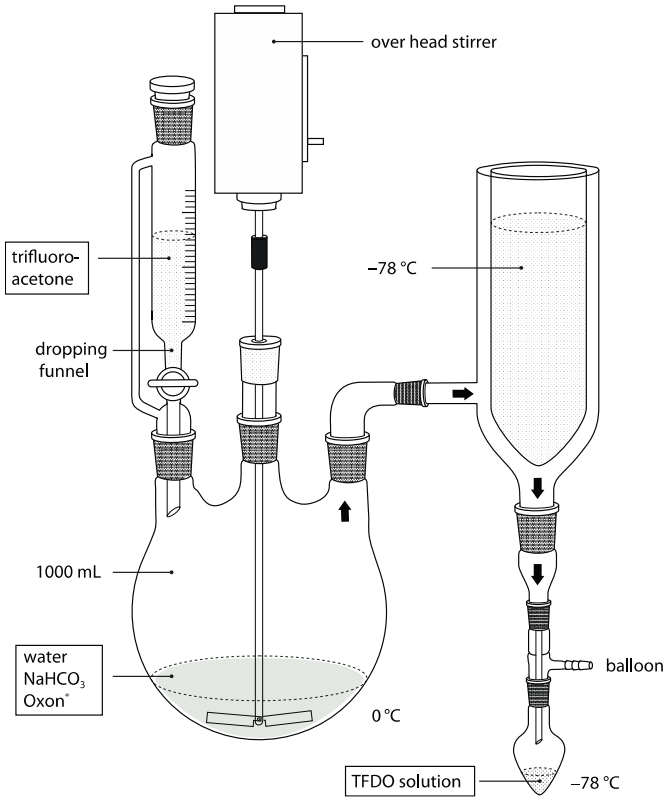


Figure S1: Set-up for the synthesis of TFDO.

The receiving flask was tightly closed with a septum, covered with aluminum foil and stored at –80 °C. The concentration of TFDO was determined iodometrically by the addition of 0.1 mL of the TFDO solution to a mixture of 0.25 mL saturated KI-solution and 1.0 mL glacial acetic acid. The resulting dark-red solution was titrated with a freshly prepared aqueous $Na_2S_2O_3$ solution (0.05 M), indicating a concentration of 0.7 M.

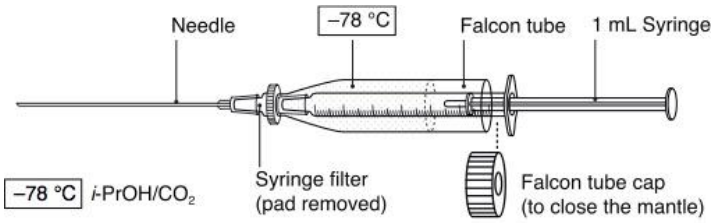
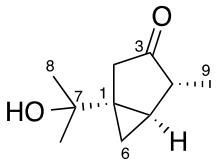


Figure S2: Mantle-cooled syringe for handling of volatile or reactive liquids and solutions.

Handling of the volatile liquid was performed at –78 °C with a mantle-cooled syringe, which was made from of a falcon tube, a syringe filter and a 1 mL syringe. A hole was cut into the tip of the falcon tube. The filter pad was removed from the syringe filter and then connected to the falcon tube with the help of a heat gun. The length of the falcon tube was adjusted to fit the 1 mL syringe (see Figure S2). Freshly crushed dry ice was added into the cooling mantle and mixed with *iso*-propanol. The needle was pre-cooled at –78 °C prior to use. The syringe was then used as usual to pull up and measure the volume of the TFDO-solution.

2.12 Synthesis of 7-hydroxy thujone (3a)



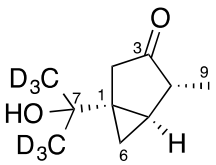
$C_{10}H_{16}O_2$
168.24 g/mol

3a

A solution of (–)-α-thujone **1a** (10.0 mg, 66.0 µmol, 1.00 eq.) in dry dichloromethane (0.7 mL) was cooled to –20 °C with a cryostate. A 0.7 M TFDO solution (~0.28 mL, 198 µmol, 3.00 eq.) was added using a mantle-cooled syringe. The reaction mixture was stirred at –20 °C until reaction control by GC-MS-analysis of an aliquot indicated clean conversion of the starting material to a single product (>90% conversion). The reaction was quenched after 3 h at –20 °C with saturated $Na_2S_2O_3$ solution (0.1 mL). After warming up to room temperature, water (5 mL) was added and the reaction mixture was extracted with dichloromethane (3 × 10 mL). All organic phases were combined, dried over Na_2SO_4, filtered and concentrated under reduced pressure to yield the product. To remove residual solvent traces a column chromatography (pentane/diethyl ether, 2:1, [$KMnO_4$]) was performed and an analytically pure sample of the volatile product was isolated as colorless oil.

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.78 (ddd, *J* = 18.8, 2.8, 1.3 Hz, 1H, H-2), 2.29 (qd, *J* = 7.5, 1.3 Hz, 1H, H-4), 2.18 (d, *J* = 18.8 Hz, 1H, H-2'), 1.34 (dd, *J* = 8.5, 4.3 Hz, 1H, H-5), 1.31 (s, 3H, H-8), 1.21 (s, 3H, H-8'), 1.18 (d, *J* = 7.5 Hz, 3H, H-9), 1.12 (ddd, *J* = 8.4, 5.7, 2.6 Hz, 1H, H-6), 0.11 (dd, *J* = 5.7, 4.3 Hz, 1H, H-6').
^{13}C-NMR (101 MHz, $CDCl_3$): δ [ppm] = 220.8 (C=O, C-3), 70.1 (C, C-7), 47.5 (CH, C-4), 41.3 (CH_2, C-2), 33.3 (C, C-1), 27.7 (CH_3, C-8), 27.5 (CH_3, C-8'), 23.6 (CH, C-5), 18.4 (CH_3, C-9), 16.4 (CH_2, C-6).
TLC: R_f = 0.2 (pentane/diethyl ether, 1:1, [$KMnO_4$])
The spectroscopic data matched those reported in literature.[5]

2.12.1 Synthesis of *d_6*-hydroxy thujone (3b)

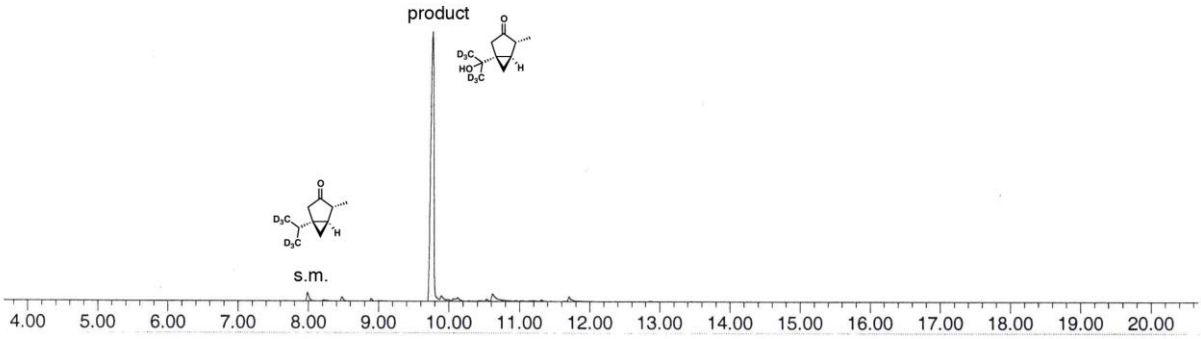


$C_{10}H_{10}D_6O_2$
174.15 g/mol

3b

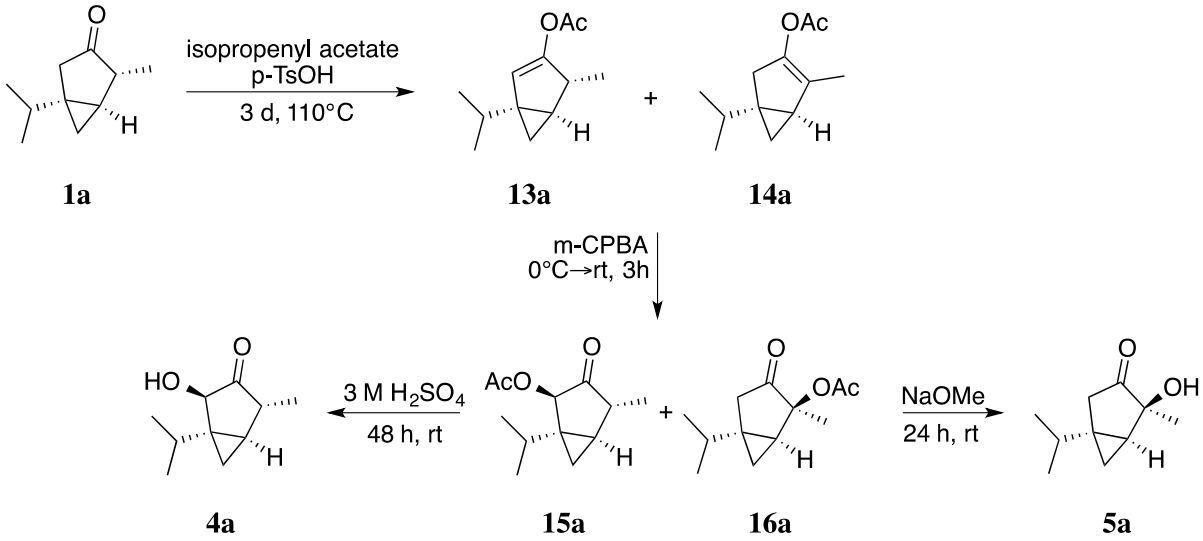
The reaction was carried out as described in 2.12 with the use of d_6-thujone **1b** (10.0 mg, 63.0 µmol, 1.00 eq.) 0.7 M TFDO solution (~0.27 mL, 189 µmol, 3.00 eq.) with >90% conversion (see Scheme S3). An analytically pure sample of the volatile title compound was obtained after column chromatography (pentane/diethyl ether, 2:1, [$KMnO_4$]) as colorless oil.

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.78 (ddd, *J* = 19.0, 2.9, 1.3 Hz, 1H, H-2), 2.29 (q, *J* = 7.5 Hz, 1H, H-4), 2.18 (d, *J* = 18.8 Hz, 1H, H-2'), 1.34 (dd, *J* = 8.5, 4.2 Hz, 1H, H-5), 1.18 (d, *J* = 7.5 Hz, 3H, CH_3), 1.14 - 1.10 (m, 2H, H-6), 0.11 (dd, *J* = 5.9, 4.7 Hz, 1H, H-6').
Degree of deuteration: >95%
^{13}C-NMR (126 MHz, $CDCl_3$): δ [ppm] = 220.8 (C=O, C-3), 69.9 (C, C-7), 47.5 (CH, C-4), 41.2 (CH_2, C-2), 33.2 (C, C-1), 26.7 (br., CD_3, 2C, C-8/8'), 23.6 (CH, C-5), 18.4 (CH_3, C-9), 16.4 (CH_2, C-6).
HR-MS (EI, 70 eV): calc. for $C_{10}H_{10}D_6O_2$: 174.1527, found: 174.1521.
IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3446 (br, OH), 2964 (w, CH), 2929 (w, CH), 2872(w, CH), 2227 (w), 1731 (s, C=O), 1455 (m, -CH_2), 1371 (w), 1264 (w), 1212 (w), 1156 (m), 1097 (m), 1051 (s), 811 (m), 700 (w).
TLC: R_f = 0.2 (pentane/diethyl ether, 1:1, [$KMnO_4$])



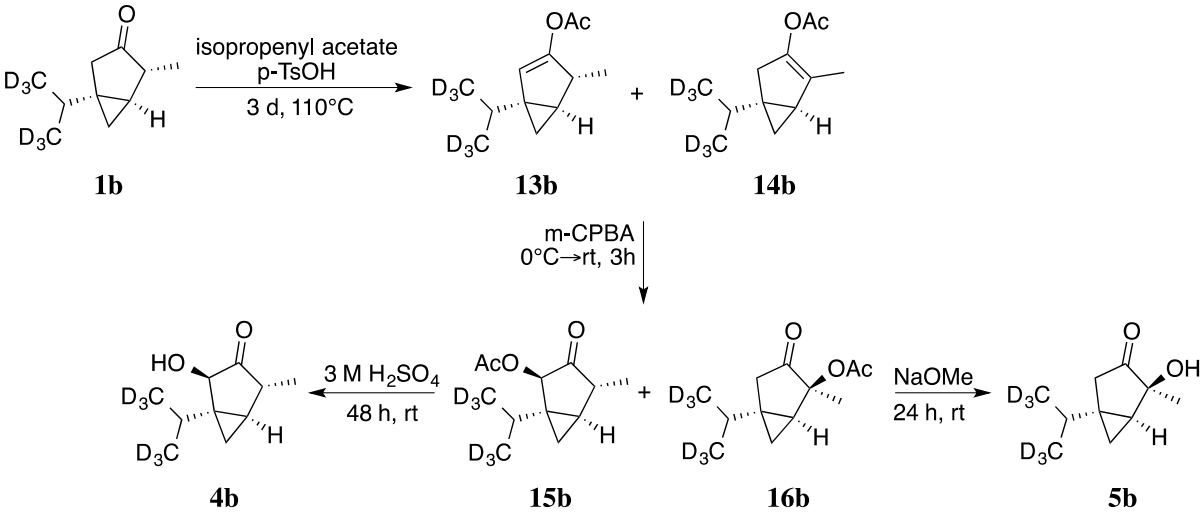
Scheme S3. GC-Analysis of the crude reaction mixture of the TFDO oxidation of 1b

2.13 Synthesis of (R)-2-hydroxythujone (4a/4b) and α-4-hydroxythujone (5a/5b)



1a **13a** **14a** **4a** **15a** **16a** **5a**

Scheme S4. Synthesis of (R)-2-hydroxythujone (4a) and α-4-hdroxythujone (5a)

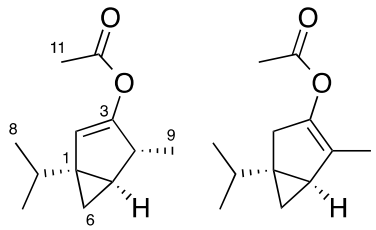


1b **13b** **14b** **4b** **15b** **16b** **5b**

Scheme S5. Synthesis of d_6-(R)-2-hydroxythujone (4b) and d_6-α-4-hydroxythujone (5b)

2.13.1 Synthesis of (1*S*,4*R*,5*R*)-1-isopropyl-4-methylbicyclo[3.1.0]hex-2-en-3-yl acetate (13a) and (1*S*,5*S*)-5-isopropyl-2-methylbicyclo[3.1.0]hex-2-en-3-yl acetate (14a)

$C_{12}H_{18}O_2$
194.27 g/mol



$C_{12}H_{18}O_2$
194.27 g/mol

13a **14a**

Compounds **13a/14a** were synthesized according to a modified literature procedure.[5] A solution of (–)-α-thujone **1a** (100 mg, 656 µmol, 1.00 eq.) in isopropenyl acetate (819 µL, 7.55 mmol, 11.5 eq.) was treated with *p*-toluenesulfonic acid (10.2 mg, 59.2 µmol, 0.09 eq.) and heated to 110 °C in a pressure vial for 3 d. The dark brown reaction mixture was purified *via* column chromatography (pentane/diethyl ether, 1:0 → 20:1). The nonresolved mixture (124 mg, 638 µmol, 97% yield) of the 3,4-enol acetate **14a** (25%) and the 2,3-enol acetate **13a** (75%) was used without further separation as shown in Scheme S4.

2,3-enol acetate 13a

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.64 (s, 1H, H-2), 2.59 (q, *J* = 7.08 Hz, 1H, H-4), 2.10 (s, 3H, H-11), 1.36 (dt, *J* = 13.6, 6.8 Hz, 1H, H-7), 1.08 (d, *J* = 7.0 Hz, 3H, H-9), 0.99 (d, *J* = 6.8 Hz, 3H, H-8), 0.93 (m, 1H, H-5), 0.91 (d, *J* = 6.8 Hz, 3H, H-8'), 0.75 (dd, *J* = 7.9, 4.1 Hz, 1H, H-6), 0.30 (t, *J* = 4.1 Hz, 1H, H-6').

TLC: R_f = 0.50 (pentane/diethyl ether, 10:1, [$KMnO_4$])

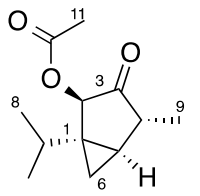
3,4-enol acetate 14a

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.66 (dq, *J* = 15.9, 2.3 Hz, 1H, H-2), 2.30 (d, *J* = 15.9 Hz, 1H, H-2'), 2.11 (s, 3H, H-11), 1.60 (t, *J* = 2.2 Hz, 3H, H-9), 1.44 - 1.30 (m, 2H, H-7/H-5), 0.96 (d, *J* = 6.9 Hz, 3H, H-8), 0.88 (d, *J* = 6.9 Hz, 3H, H-8'), 0.76 - 0.73 (m, 1H, H-6), 0.26 - 0.22 (m, 1H, H-6').

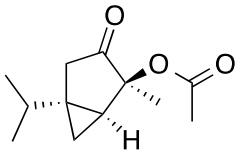
TLC: R_f = 0.42 (pentane/diethyl ether, 10:1, [$KMnO_4$])

2.13.2 Synthesis of 2-acetoxy-α-thujone (15a) and 4-acetoxy-α-thujone (16a)

$C_{12}H_{18}O_3$
210.27 g/mol



15a



16a

$C_{12}H_{18}O_3$
210.27 g/mol

To a solution of the enol acetate mixture **13a/14a** (124 mg, 638 µmol, 1.00 eq.) in dry chloroform (0.45 mL) was added a solution of *m*-chloroperoxybenzoic acid (82.6 mg, 479 µmol, 0.75 eq.) in dry chloroform (2.1 mL) at 0 °C and stirred for 30 min. Then the same amount of *m*-chloroperoxybenzoic acid (82.6 mg, 479 µmol, 0.75 eq.) was added. After the reaction mixture was warmed to room temperature and stirred for 3 h, the mixture was diluted with diethyl ether and subsequently washed with $NaHSO_3$ (3 mL), $NaHCO_3$ (3 mL) and brine

(3 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated under vacuum. The crude product mixture was purified *via* column chromatography (pentane/diethyl ether, 20:1) and 2-acetoxy-α-thujone **15a** (62.1 mg, 295 µmol, 45% over two steps) and 4-acetoxy-α-thujone **16a** (12.4 mg, 59.0 µmol, 9% over two steps) were obtained as oils.

2-acetoxy-α-thujone 15a:

^{1}H NMR (500 MHz, $CDCl_3$): δ [ppm] = 5.97 (s, 1H, H-2), 2.35 (q, *J* = 7.5 Hz, 1H, H-4), 2.14 (s, 3H, H-11), 1.42 (p, *J* = 6.9 Hz, 1H, H-7), 1.25 - 1.07 (m, 1H, H-5), 1.22 (d, *J* = 7.5 Hz, 3H, H-9), 1.07 (d, *J* = 6.9 Hz, 3H, H-8), 0.97 (d, *J* = 6.9 Hz, 3H, H-8'), 0.82 - 0.77 (m, 1H, H-6), 0.53 (dd, *J* = 6.2, 4.2 Hz, 1H, H-6').

^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 213.1 (C=O, C-3), 170.7 (C=O, C-10), 76.0 (CH, C-2), 44.9 (CH, C-4), 32.2 (CH, C-7), 31.5 (C, C-1), 24.3 (CH_3, C-9), 21.1 (CH_3, C-11), 20.1 (CH_3, C-8), 19.7 (CH_3, C-8'), 18.1 (CH, C-5), 15.6 (CH_2, C-6).

HRMS (EI, 70 eV): calc. for $C_{12}H_{18}O_3^+$ [M^+]: 210.1250, found: 210.1253

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 2960 (m, -CH_3), 2931 (w, -CH_2), 2873 (w, -CH_3), 1760 (s, -C=O), 1739 (s, -C=O), 1456 (w, -CH_2), 1369 (m, -CO-O-C), 1226 (s, -CO-O-C), 1172 (w), 1083, (w), 1060 (m), 1024 (s), 940 (w)

TLC: R_f = 0.29 (pentane/diethyl ether, 10:1, [$KMnO_4$])

Optical rotation: $[\alpha]_{546}^{23}$= +0.038 (c = 1.07, $CHCl_3$, >99% ee).

4-acetoxy-α-thujone 16a:

^{1}H NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.60 (dd, *J* = 18.8, 2.7 Hz, 1H, H-2), 2.25 (d, *J* = 18.8 Hz, 1H, H-2'), 2.06 (s, 3H, H-11), 2.02 (dd, *J* = 8.3, 4.0 Hz, 1H, H-5), 1.58 (s, 3H, H-9), 1.40 (p, *J* = 6.8 Hz, 1H, H-7), 1.00 (d, *J* = 6.8 Hz, 3H, H-8), 0.95 (d, *J* = 6.9 Hz, 3H, H-8'), 0.76 (ddd, *J* = 8.4, 6.0, 2.6 Hz, 1H, H-6), 0.49 (dd, *J* = 6.0, 4.0 Hz, 1H, H-6').

^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 211.7 (C=O, C-3), 170.5 (C=O, C-10), 86.7 (C, C-4), 38.0 (CH_2, C-2), 32.8 (CH, C-7), 29.0 (CH, C-5), 28.8 (C, C-1), 22.4 (CH_3, C-9), 21.8 (CH_3, C-11), 19.7 (CH_3, C-8), 19.6 (CH_3, C-8'), 16.3 (CH_2, C-6).

HRMS (EI, 70 eV): calc. for $C_{10}H_{15}O_2^+$ [$(M–C_2H_3O)^+$]: 167.1067, found: 167.1070

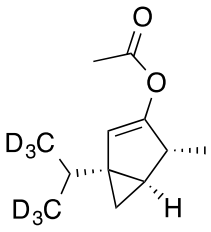
IR (ATR): $\tilde{\nu}$[cm^{-1}] = 2958 (m, -CH_3), 2933 (m, -CH_2), 2873 (w, -CH_3), 1763 (s, -C=O), 1735 (s, -C=O), 1464 (w, -CH_2), 1366 (s, -CO-O-C), 1245 (s, -CO-O-C), 1170 (w), 1078 (s), 1017 (w), 854 (w).

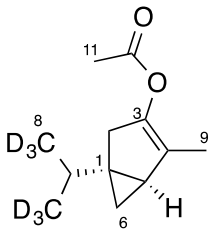
TLC: R_f = 0.16 (pentane/diethyl ether, 10:1, [$KMnO_4$])

Optical rotation: $[\alpha]_{546}^{23}$= + 0.562 (c = 0.67, $CHCl_3$, >99% ee).

2.13.3 Synthesis of 4-methyl-1-(propan-2-yl-1,1,1,3,3,3-d_6)bicyclo[3.1.0]hex-2-en-3-yl acetate (13b) and 2-methyl-5-(propan-2-yl-1,1,1,3,3,3-d_6)bicyclo[3.1.0]hex-2-en-3-yl acetate (14b)

$C_{12}H_{12}D_6O_2$
200.31 g/mol





$C_{12}H_{12}D_6O_2$
200.31 g/mol

13b **14b**

The reaction was performed as described in 2.13.1 with the use of d_6-α-thujone **1b** (158 mg, 1.00 mmol, 1.00 eq.), isopropenyl acetate (1.53 mL, 14.0 mmol, 14.00 eq.) and *p*-toluenesulfonic acid (19.0 mg, 110 µmol, 0.11 eq.). After purification via column chromatography a mixture (166 mg, 830 µmol, 83% yield) of the 3,4-enol acetate **14b** (10%) and the 2,3-enol acetate **13b** (90%) was obtained and used without further separation as shown in Scheme S4

2,3-enol acetate 13b

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.64 (s, 1H, H-2), 2.59 (q, *J* = 7.08 Hz, 1H, H-4), 2.10 (s, 3H, H-11), 1.31 (s, 1H, H-7), 1.08 (d, *J* = 7.0 Hz, 3H, H-9), 0.93 (m, 1H, H-5), 0.75 (dd, *J* = 7.9, 4.1 Hz, 1H, H-6), 0.30 (t, *J* = 4.1 Hz, 1H, H-6').

TLC: R_f = 0.50 (pentane/diethyl ether, 10:1)

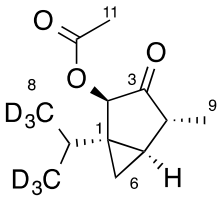
3,4-enol acetate 14b

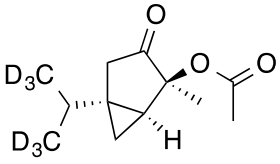
^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.66 (dq, *J* = 15.9, 2.3 Hz, 1H, H-2), 2.30 (d, *J* = 15.9 Hz, 1H, H-2'), 2.11 (s, 3H, H-11), 1.60 (t, *J* = 2.2 Hz, 3H, H-9), 1.39 (d, *J* = 7.6 Hz, 1H, H-5), 1.33 (s, 1H, H-7), 0.76 - 0.73 (m, 1H, H-6), 0.26 - 0.22 (m, 1H, H-6').

TLC: R_f = 0.42 (pentane/diethyl ether, 10:1, [$KMnO_4$])

2.13.4 Synthesis of 4-methyl-3-oxo-1-(propan-2-yl-1,1,1,3,3,3-d_6)bicyclo[3.1.0]hexan-2-yl acetate (15b) and 2-methyl-3-oxo-5-(propan-2-yl-1,1,1,3,3,3-d_6)bicyclo[3.1.0]hexan-2-yl acetate (16b)

$C_{12}H_{12}D_6O_3$
216.31 g/mol





$C_{12}H_{12}D_6O_3$
216.31 g/mol

15b **16b**

The reaction was performed as described in 2.13.2 with the use of enol acetate mixture **13b**/**14b** (160 mg, 800 µmol, 1.00 eq.) in dry chloroform (0.70 mL) and *m*-chloroperoxybenzoic acid (2x 103 mg, 599 µmol, 0.75 eq.). After purification *via* column chromatography 2-acetoxy-α-thujone **15b** (121 mg, 559 µmol, 56% over two steps) and 4-acetoxy-α-thujone **16b** (28.1 mg, 130 µmol, 13% over two steps) were obtained as oils.

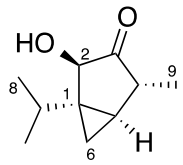
2-acetoxy-α-thujone 15b:

^{1}H NMR (500 MHz, $CDCl_3$): δ [ppm] = 5.97 (s, 1H, H-2), 2.34 (q, *J* = 7.5 Hz, 1H, H-4), 2.13 (s, 3H, H-11), 1.39 (br. s, 1H, H-7) 1.25 (dd, *J* = 10.7, 7.6 Hz, 1H, H-5) 1.21 (d, *J* = 7.5 Hz, 3H, H-9), 0.79 (ddd, *J* = 8.0, 6.2, 2.0 Hz, 1H, H-6), 0.52 (dd, *J* = 6.2, 4.1 Hz, 1H, H-6').
Degree of deuteration: >95%
^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 213.1 (C=O, C-3), 170.7 (C=O, C-10), 76.0 (CH, C-2), 45.0 (CH, C-4), 31.7 (CH, C-7), 31.4 (C, C-1), 24.2 (CH_3, C-9), 21.1 (CH_3, C-11), 18.1 (CH, C-5), 15.6 (CH_2, C-6).
HRMS (EI, 70 eV): calc. for $C_{10}H_9D_6O_2^+$ [$(M–C_2H_3O)^+$]: 173.1443, found: 173.1457
IR (ATR): $\tilde{\nu}$[cm^{-1}] = 2966 (m, -CH_3), 2930 (m, -CH_3), 2874 (m, -CH_3), 2215 (m, -CD_3), 2133 (w, -CD_3), 2072 (w, -CD_3), 1760 (s, -C=O), 1739 (s, -C=O), 1455 (m, -CH_2), 1370 (s, -CO-O-C), 1227 (s, -CO-O-C), 1057 (s), 1036 (m), 939 (m), 887 (w).
TLC: R_f = 0.29 (pentane/diethyl ether, 10:1, [$KMnO_4$])

4-acetoxy-α-thujone 16b:

^{1}H NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.60 (dd, *J* = 18.8, 2.7 Hz, 1H, H-2), 2.25 (d, *J* = 19.0 Hz, 1H, H-2'), 2.06 (s, 3H, H-11), 2.02 (dd, *J* = 8.2, 4.0 Hz, 1H, H-5), 1.58 (s, 3H, H-9), 1.37 (s, 1H, H-7), 0.76 (t, *J* = 6.0 Hz, 1H, H-6), 0.49 (dd, *J* = 5.9, 4.3 Hz, 1H, H-6').
Degree of deuteration: >95%
^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 211.4 (C=O, C-3), 170.4 (C=O, C-10), 86.7 (C, C-4), 38.1 (CH_2, C-2), 32.2 (CH, C-7), 29.0 (CH, C-5), 28.7 (C, C-1), 22.4 (CH_3, C-9), 21.8 (CH_3, C-11), 16.3 (CH_2, C-6).
HRMS (EI, 70 eV): calc. for $C_{10}H_9D_6O_2^+$ [$(M–C_2H_3O)^+$]: 173.1443, found: 173.1445
IR (ATR): $\tilde{\nu}$[cm^{-1}] = 2975 (w, -CH_3), 2931 (w, -CH_2), 2875 (w, -CH_3), 2213 (m, -CD_3), 2128 (w, -CD_3), 2071 (w, -CD_3), 1760 (s, -C=O), 1736 (s, -C=O), 1454 (m, -CD_3), 1368 (s, -CO-O-C), 1244 (s, -CO-O-C), 1080 (s), 1048 (s), 1020 (s), 956 (w), 734 (w).
TLC: R_f = 0.16 (pentane/diethyl ether, 10:1, [$KMnO_4$])

2.13.5 Synthesis of (R)-2-hydroxythujone 4a



$C_{10}H_{16}O_2$
168.23 g/mol

4a

To a solution of 2-acetoxy-α-thujone **15a** (49.0 mg, 233 µmol, 1.00 eq.) in methanol (3.5 mL) was added H_2SO_4 (3 M, 777 µL) at room temperature and stirred for 3 d. Then the reaction mixture was diluted with water and extracted with diethyl ether (3x). The combined organic layers were extracted with water until the aqueous phase was pH-neutral and dried over anhydrous $MgSO_4$. The crude product was purified *via* column chromatography (pentane/diethyl ether, 20:1→10:1) to obtain (R)-2-hydroxythujone **4a** (26.9 mg, 160 µmol, 69% yield) as colourless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ [ppm] = 4.63 (br. s, 1H, H-2), 2.36 (q, *J* = 7.5 Hz, 1H, H-4), 1.49 (hept, *J* = 6.8 Hz, 1H, H-7), 1.20 (d, *J* = 7.5 Hz, 3H, H-9), 1.25 - 1.14 (m, 1H, H-5), 1,10 (d, *J* = 5.3 Hz, 3H, H-8), 1.08 (d, *J* = 5.4 Hz, 3H, H-8'), 0.71 (ddd, *J* = 7.8, 6.3, 2.1 Hz, 1H, H-6), 0.32 (dd, *J* = 6.2, 4.1 Hz, 1H, H-6').

^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 219.2 (C=O, C-3), 74.9 (CH, C-2), 44.7 (CH, C-4), 33.4 (C, C-1), 32.5 (CH, C-7), 23.4 (CH, C-5), 20.4 (CH_3, C-8), 19.9 (CH_3, C-8'), 18.2 (CH_3, C-9), 14.6 (CH_2, C-6).

The spectroscopic data matched those reported in literature.[5]

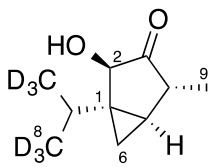
HRMS (EI, 70 eV): calc. for $C_{10}H_6O_2^+$ [M^+]: 168.1145, found: 168.1145

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3457 (br., -OH), 3062 (w, cyclopropane), 2961 (s, -CH_3), 2932 (m, -CH_2), 2873 (m, -CH_3), 1751 (s, -C=O), 1456 (m, -CH_2), 1367 (w), 1097 (m), 1006 (m), 808 (w).

TLC: R_f = 0.22 (pentane/diethyl ether, 5:2, [$KMnO_4$])

Optical rotation: $[\alpha]_{546}^{23}$ = –0.269 (c = 1.17, $CHCl_3$, >99% ee).

2.13.6 Synthesis of *d*$_6$-(R)-2-hydroxythujone (4b)



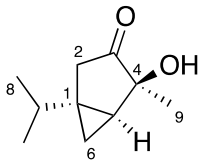
$C_{10}H_{10}D_6O_2$
174.27 g/mol

4b

The reaction was performed as described in 2.13.5 with the use of 2-acetoxy-α-thujone **15b** (32.0 mg, 148 µmol, 1.00 eq.) in methanol (2 mL) and H_2SO_4 (3 M, 493 µL). After purification *via* column chromatography a colourless oil of **4b** (10.6 mg, 61.0 µmol, 41% yield) was obtained.

^{1}H NMR (500 MHz, $CDCl_3$): δ [ppm] = 4.62 (t, *J* = 1.6 Hz, 1H, H-2), 2.36 (qt, *J* = 7.5, 1.4 Hz, 1H, H-4), 1.48 (br. s, 1H, H-7), 1.20 (dd, *J* = 6.7, 1.9 Hz, 3H, H-9), 1.19 - 1.17 (m, 1H, H-5), 0.71 (ddd, *J* = 7.9, 6.3, 1.9 Hz, 1H, H-6), 0.35 - 0.28 (m, 1H, H-6').
Degree of deuteration: >95%
^{13}C NMR (126 MHz, $CDCl_3$): δ [ppm] = 219.2 (C=O, C-3), 75.0 (CH, C-2), 44.7 (CH, C-4), 32.0 (C, C-1), 31.9 (CH, C-7), 23.4 (CH, C-5), 18.1 (CH_3, C-9), 14.5 (CH_2, C-6).
HRMS (EI, 70 eV): calc. for $C_{10}H_{10}D_6O_2^+$ [M^+]: 174.1521, found: 174.1518
IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3464 (br, -OH), 3059 (w, cyclopropane), 2965 (m, -CH_3), 2929 (m, -CH_2), 2872 (s, -CH_3), 2214 (s, -CD_3), 2129 (w, -CD_3), 2072 (w, -CD_3), 1750 (s, -C=O), 1456 (m, -CH_2), 1372 (w), 1277 (w), 1091 (m), 990 (w).
TLC: R_f = 0.22 (pentane/diethyl ether, 5:2, [$KMnO_4$])

2.13.7 Synthesis of α-4-hydroxythujone (5a)



$C_{10}H_{16}O_2$
168.23 g/mol

5a

To a solution of 4-acetoxy-α-thujone **16a** (15.0 mg, 71.0 µmol, 1.00 eq.) in methanol (4 mL) was added sodium methoxide (1.93 mg, 36.0 µmol, 0.5 eq.) at room temperature. After 14 h the same amount of sodium methoxide was added and stirred futher for 10 h. Then the reaction mixture was diluted with water (5 mL) and extracted with diethyl ether (3x5 mL). The combined organic layers were extracted with water and brine and dried over anhydrous $MgSO_4$. The crude product was purified *via* column chromatography (pentane/diethyl ether, 20:1→10:1) to obtain α-4-Hydroxythujone **5a** (7.07 mg, 42.0 µmol, 59% yield) as colourless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.68 (dd, *J* = 18.1, 2.5 Hz, 1H, H-2), 2.22 (d, *J* = 18.1 Hz, 1H, H-2'), 1.47 (dd, *J* = 8.0, 3.9 Hz, 1H, H-5), 1.42 (p, *J* = 6.8 Hz, 1H, H-7), 1.37 (s, 3H,

H-9), 1.03 (d, *J* = 6.8 Hz, 3H, H-8), 0.96 (d, *J* = 6.9 Hz, 3H, H-8'), 0.74 (s, 1H, H-6), 0.34 (dd, *J* = 6.2, 4.0 Hz, 1H, H-6').

^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 217.7 (C=O, C-3), 79.8 (C-OH, C-4), 38.1 (CH_2, C-2), 30.5 (C, C-1), 32.2 (CH, C-7), 29.1 (CH, C-5), 26.0 (CH_3, C-9), 19.7 (CH_3, C-8), 19.6 (CH_3, C-8'), 15.6 (CH_2, C-6).

The spectroscopic data matched those reported in literature.[5]

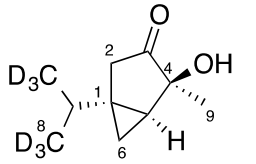
HRMS (EI, 70 eV): calc. for $C_{10}H_{14}O_1^+$ [$(M–H_2O)^+$]: 150.1039, found: 150.1033

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3442 (br, -OH), 3059 (w, cyclopropane), 2958 (s, -CH_3), 2928 (s, -CH_2), 2872 (m, -CH_3), 1751 (s, -C=O), 1457 (m, -CH_2), 1365 (m), 1184 (m), 1075 (m), 948 (w).

TLC: R_f = 0.15 (pentane/diethyl ether, 5:2, [$KMnO_4$])

Optical rotation: $[\alpha]_{546}^{23}$ = –0.421 (c = 0.45, $CHCl_3$, >99% ee).

2.13.8 Synthesis of d_6-α-4-hydroxythujone (5b)



$C_{10}H_{10}D_6O_2$
174.27 g/mol

5b

The reaction was performed as described in 2.13.7 with the use of 4-acetoxy-α-thujone **16b** (17.2 mg, 79.5 µmol, 1.00 eq.) in methanol (4 mL) and two times sodium methoxide (2.15 mg, 39.8 µmol, 0.50 eq.). After purification *via* column chromatography a colourless oil of **5b** (7.6 mg, 43.6 µmol, 55% yield) was obtained.

^{1}H NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.67 (dd, *J* = 18.1, 2.6 Hz, 1H, H-2), 2.22 (d, *J* = 18.1 Hz, 1H, H-2'), 1.46 (dd, *J* = 8.0, 4.0 Hz, 1H, H-5), 1.37 (s, 3H, H-9), 1.25 (s, 1H, H-7), 0.74 (ddd, *J* = 8.2, 6.1, 2.5 Hz, 1H, H-6), 0.33 (dd, *J* = 6.1, 3.9 Hz, 1H, H-6').

Degree of deuteration: >95%

^{13}C NMR (126 MHz, $CDCl_3$): δ [ppm] = 217.7 (C=O, C-3), 79.9 (C-OH, C-4), 38.1 (CH_2, C-2), 32.2 (CH, C-7), 30.4 (C, C-1), 29.0 (CH, C-5), 26.0 (CH_3, C-9), 15.6 (CH_2, C-6).

IR (ATR): $\tilde{\nu}$[cm^{-1}] = 3457 (br, -OH), 3059 (w, cyclopropane), 2967 (m, -CH_3), 2925 (s, -CH_2), 2211 (s, -CD_3), 2133 (w, -CD_3), 2070 (w, -CD_3), 1751 (s, -C=O), 1455 (m, -CH_2), 1361 (m), 1175 (m), 1079 (m), 973 (w).

TLC: R_f = 0.15 (pentane/diethyl ether, 5:2, [$KMnO_4$])

3 References

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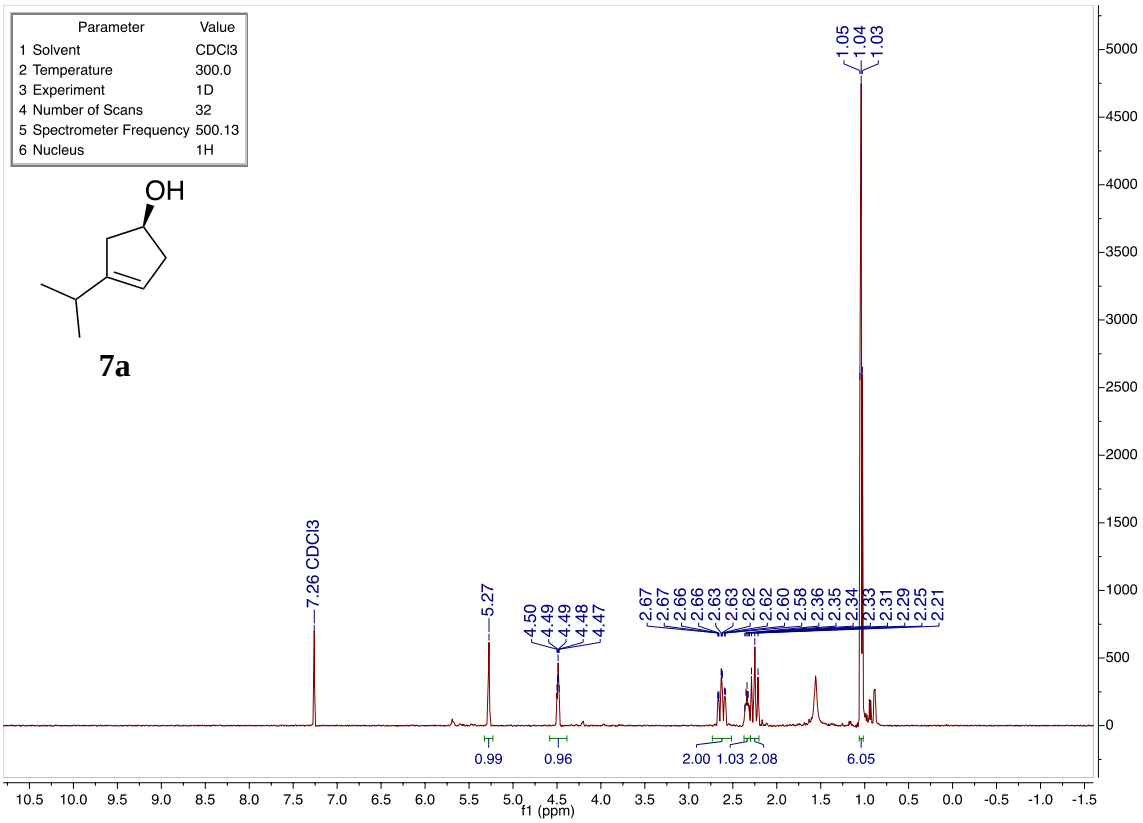
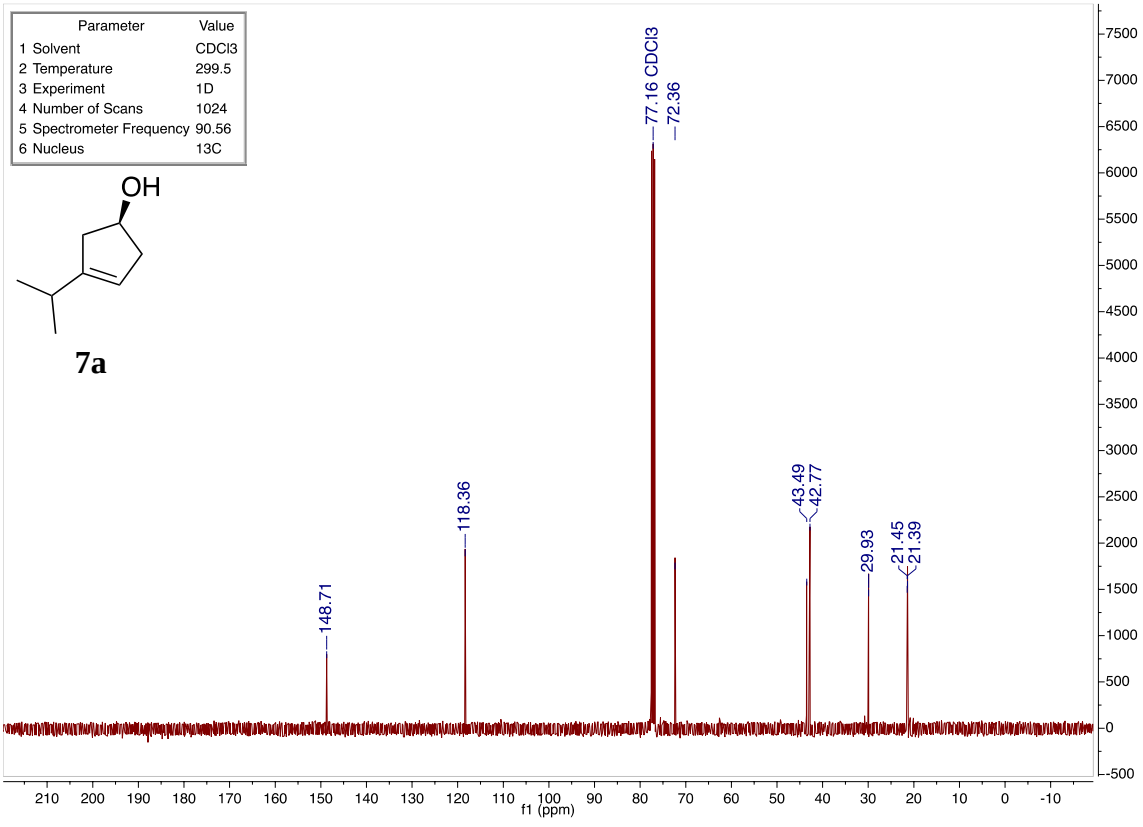
4 ^{1}H and ^{13}C NMR Spectra





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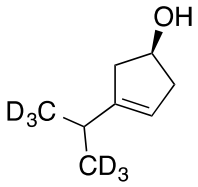
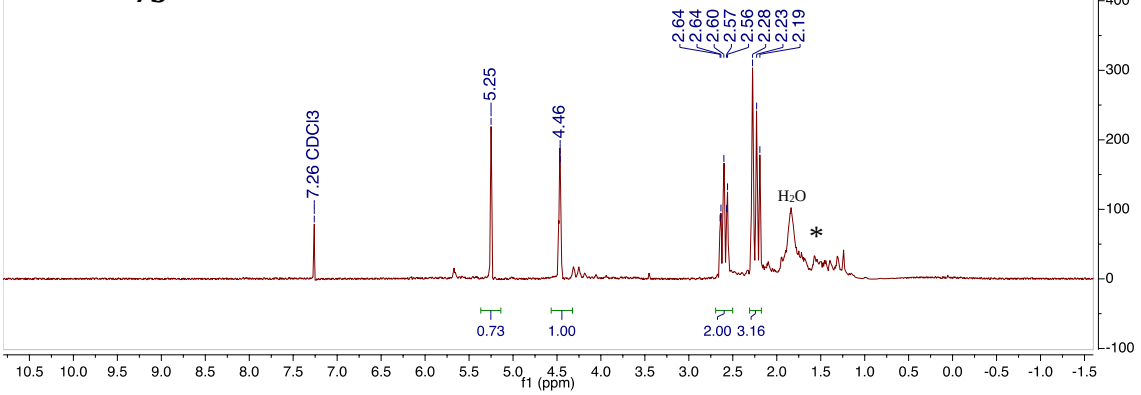
5 Spectrometer Frequency	500.13
6 Nucleus	1H

*residual non-deuterated methyl groups



7b



Parameter	Value
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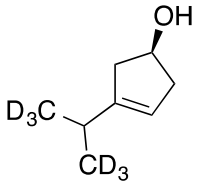
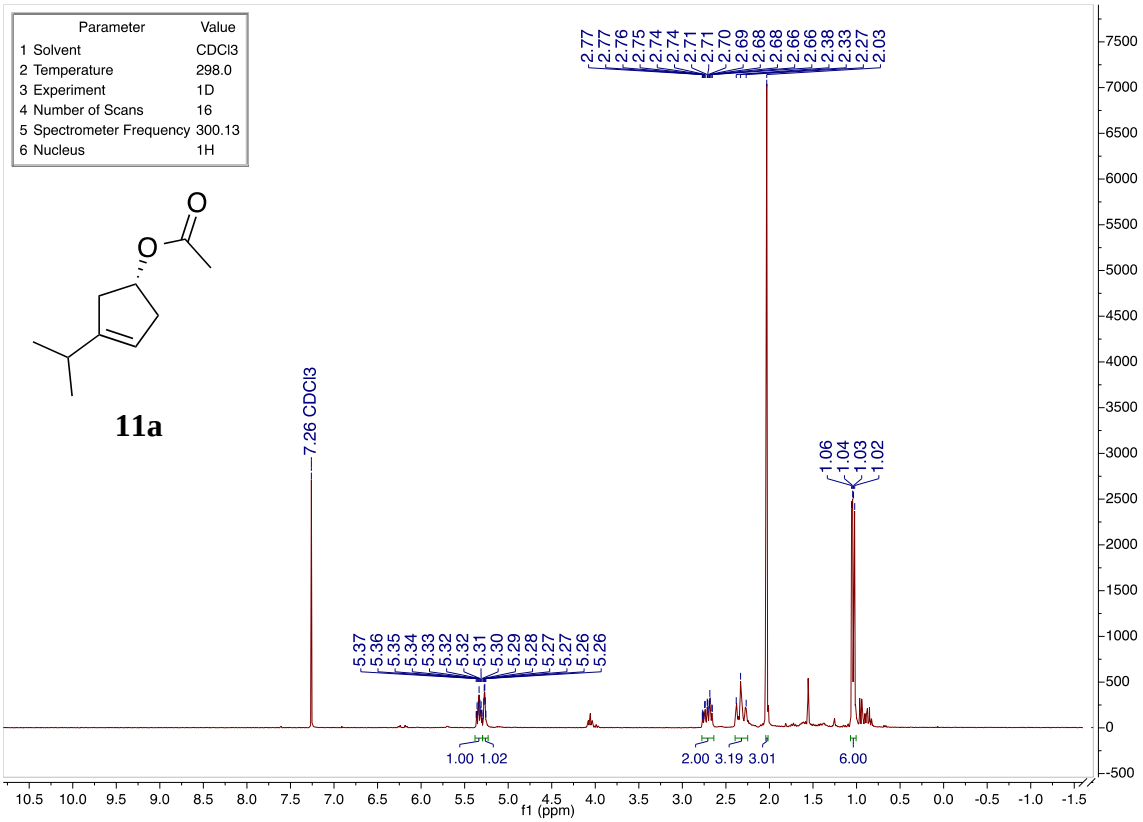
3 Experiment	1D
4 Number of Scans	1024
5 Spectrometer Frequency	90.56
6 Nucleus	13C

° loss in intensity due to CD_3 mulitpett



7b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3 Experiment 1D
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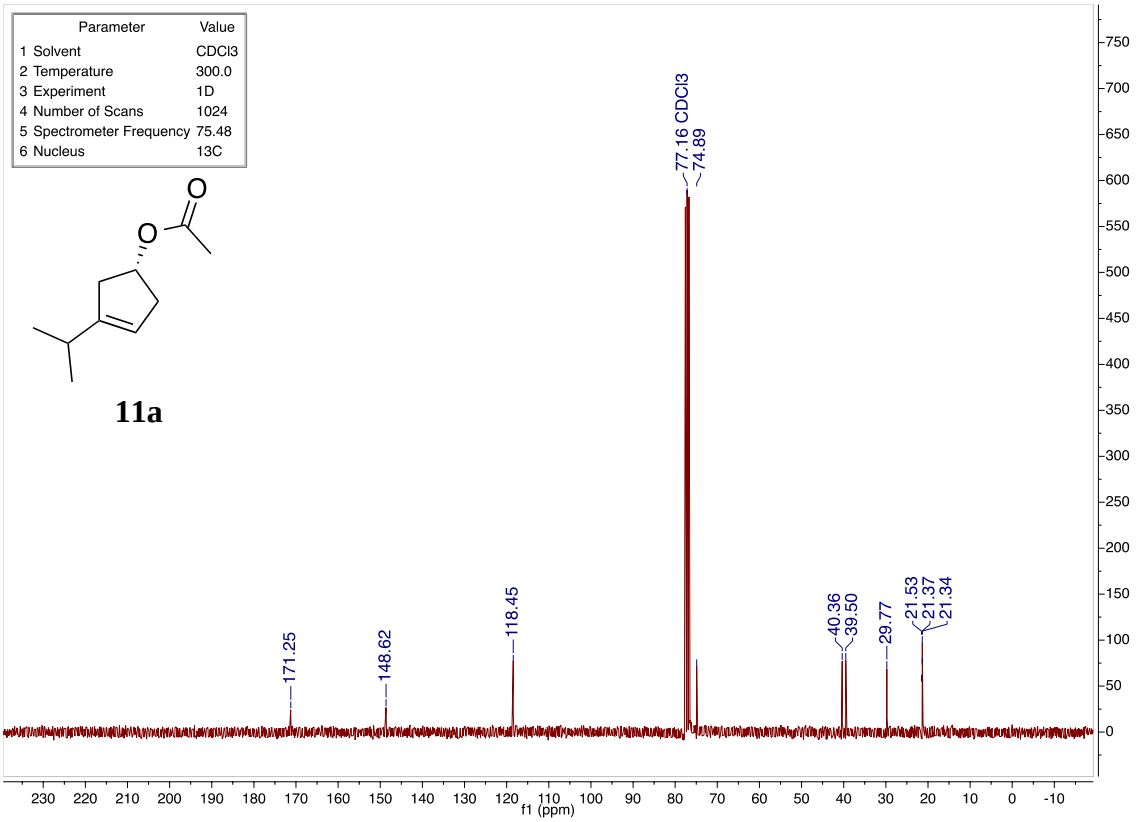
6 Nucleus 1H
11a
7.26 CDCl3
2.77 2.77 2.76 2.75 2.74 2.74 2.71 2.71 2.70 2.69 2.68 2.68 2.66 2.66 2.38 2.33 2.27 2.03
1.06 1.04 1.03 1.02
5.37 5.36 5.35 5.34 5.33 5.32 5.32 5.31 5.30 5.29 5.28 5.27 5.27 5.26 5.26
1.00 1.02
2.00 3.19 3.01
6.00
f1 (ppm)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6 Nucleus 13C
11a
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40.36
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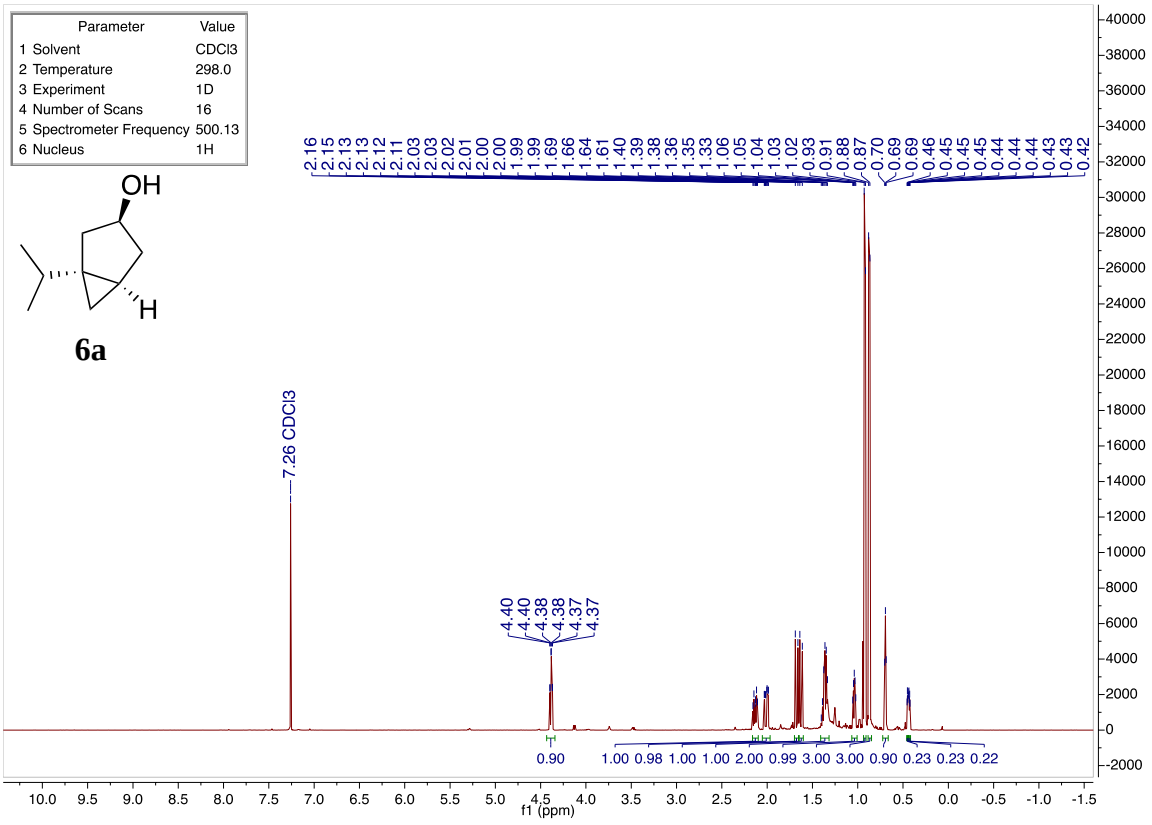
29.77
21.53
21.37
21.34
f1 (ppm)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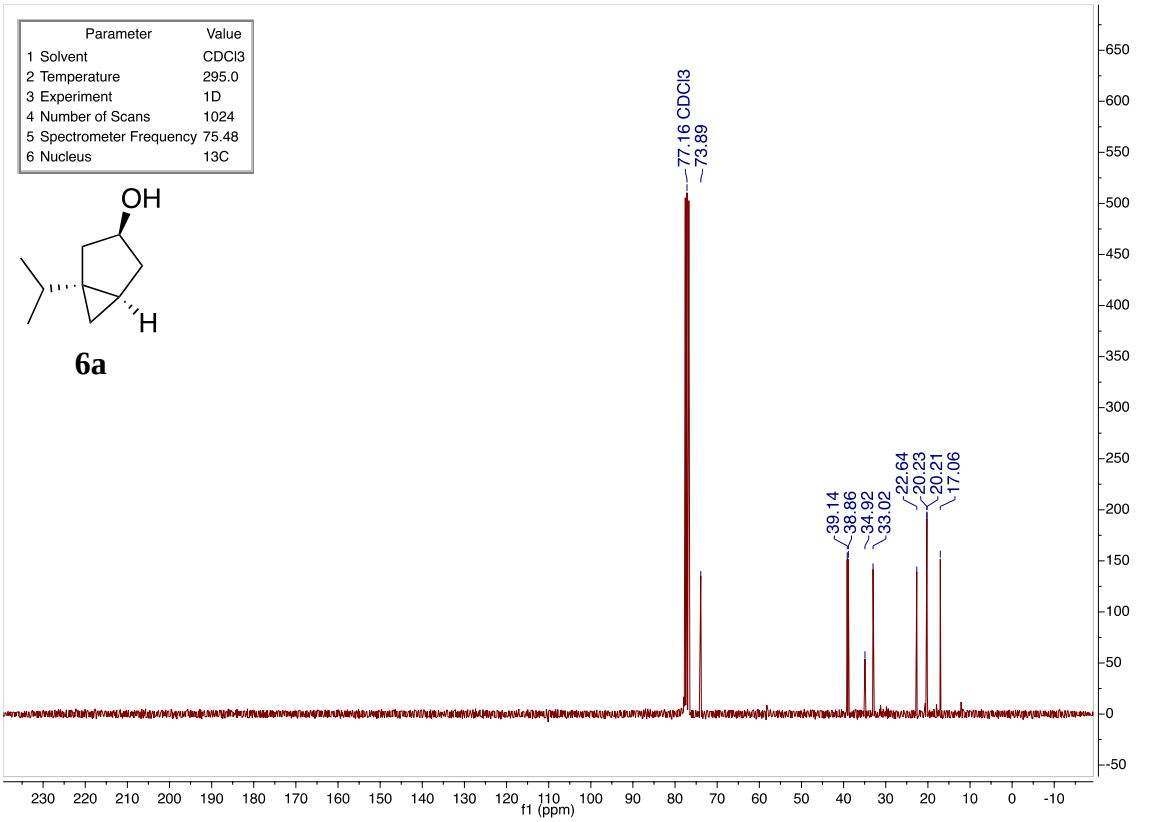
6 Nucleus 1H
OH
H
6a
7.26 CDCl3
2.16 2.15 2.13 2.13 2.12 2.11 2.03 2.03 2.02 2.01 2.00 2.00 1.99 1.99 1.69 1.66 1.64 1.61 1.40 1.39 1.38 1.36 1.35 1.33 1.06 1.05 1.04 1.03 1.02 0.93 0.91 0.88 0.87 0.70 0.69 0.69 0.46 0.45 0.45 0.44 0.44 0.44 0.43 0.43 0.42
4.40 4.40 4.38 4.38 4.37 4.37
0.90 1.00 0.98 1.00 1.00 2.00 0.99 3.00 3.00 0.90 0.23 0.23 0.22
f1 (ppm)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5 Spectrometer Frequency 75.48
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OH
H
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73.89
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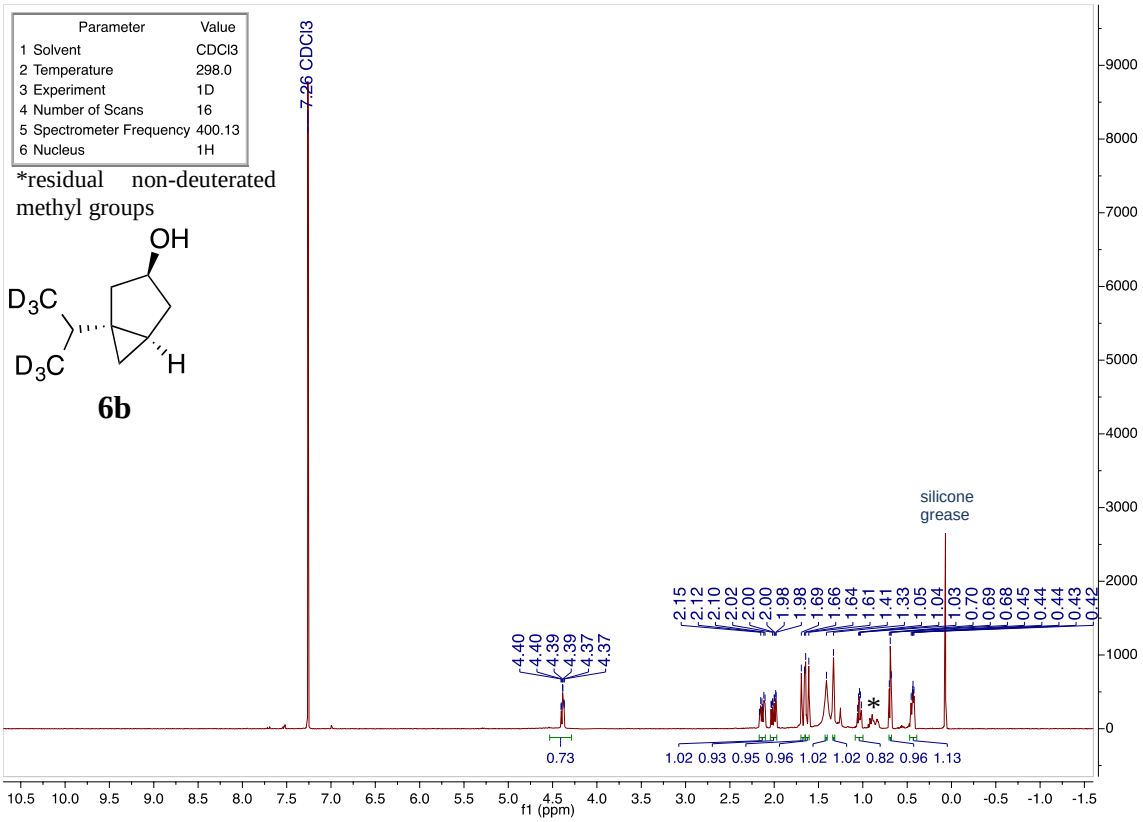
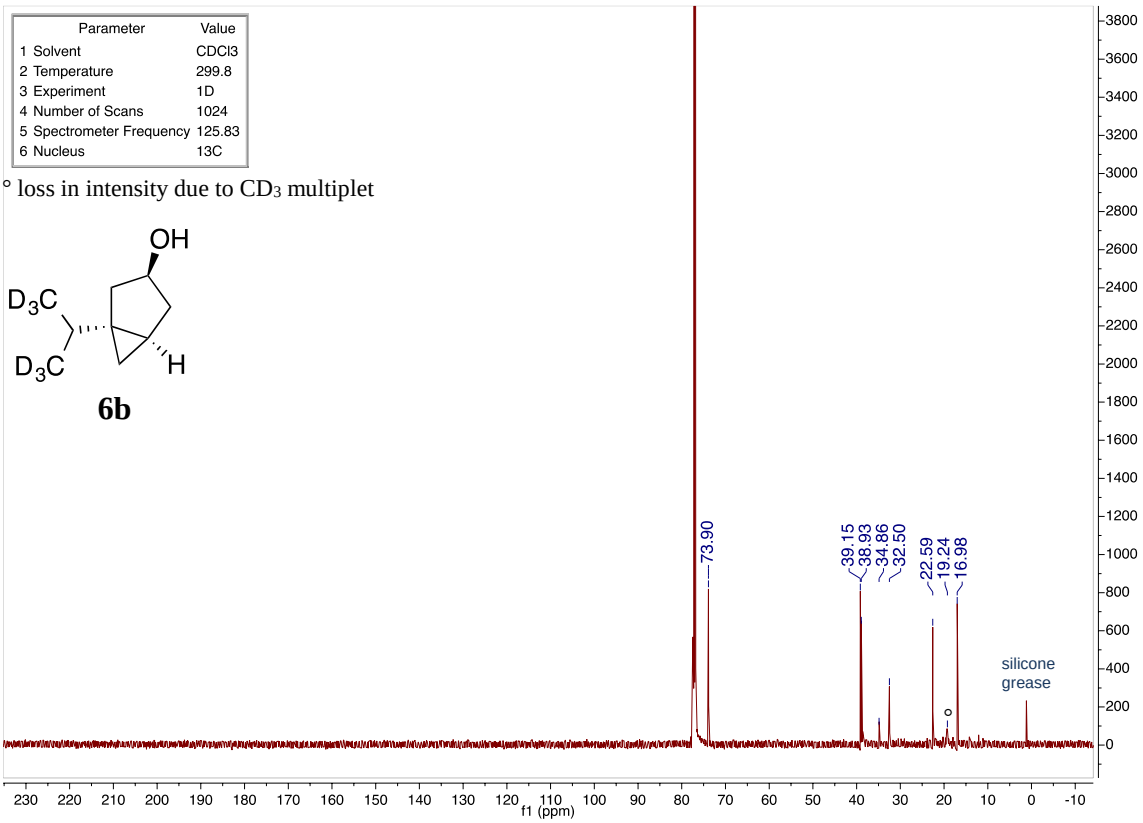
f1 (ppm)



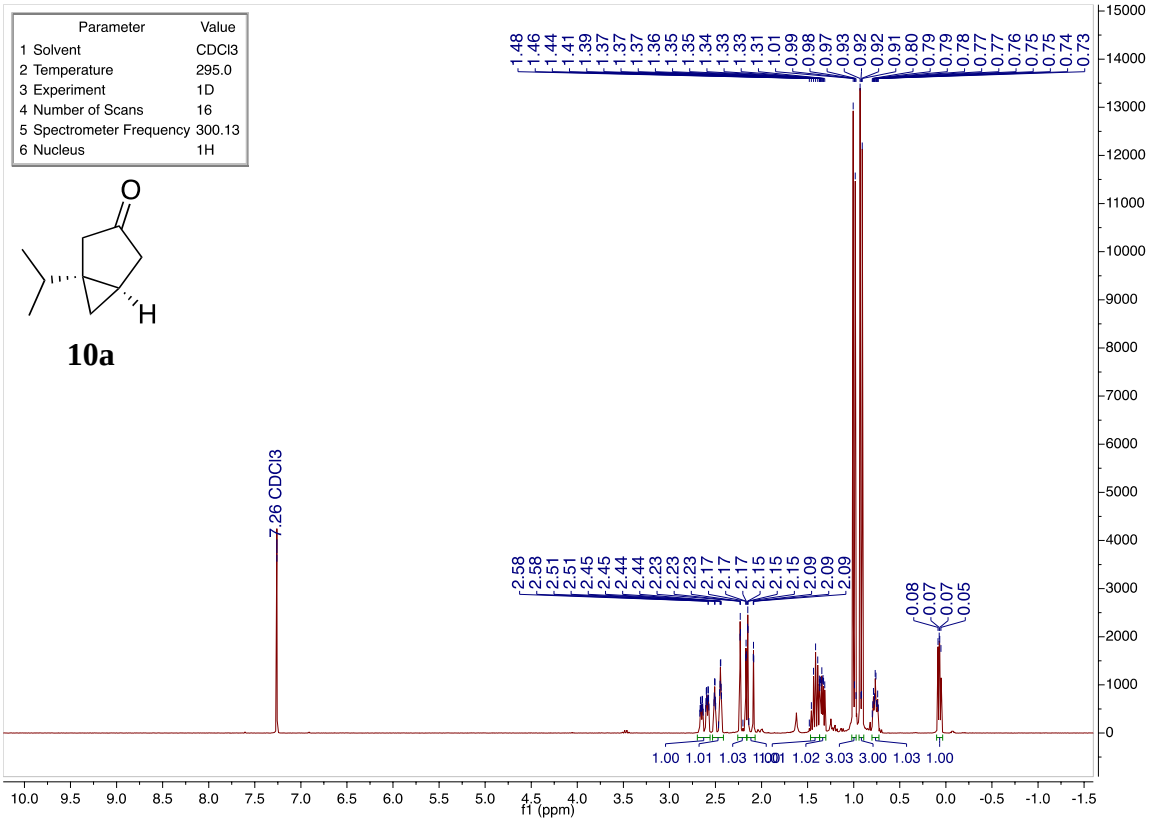
*residual non-deuterated methyl groups

6b



° loss in intensity due to CD_3 multiplet

6b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O
H
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7.26 CDCl3
1.48 1.46 1.44 1.41 1.39 1.37 1.37 1.37 1.36 1.35 1.35 1.34 1.33 1.33 1.31 1.01 0.99 0.98 0.97 0.93 0.92 0.92 0.91 0.80 0.79 0.79 0.78 0.77 0.77 0.76 0.75 0.75 0.74 0.73
2.58 2.58 2.51 2.51 2.45 2.45 2.44 2.44 2.23 2.23 2.23 2.17 2.17 2.17 2.15 2.15 2.15 2.09 2.09 2.09
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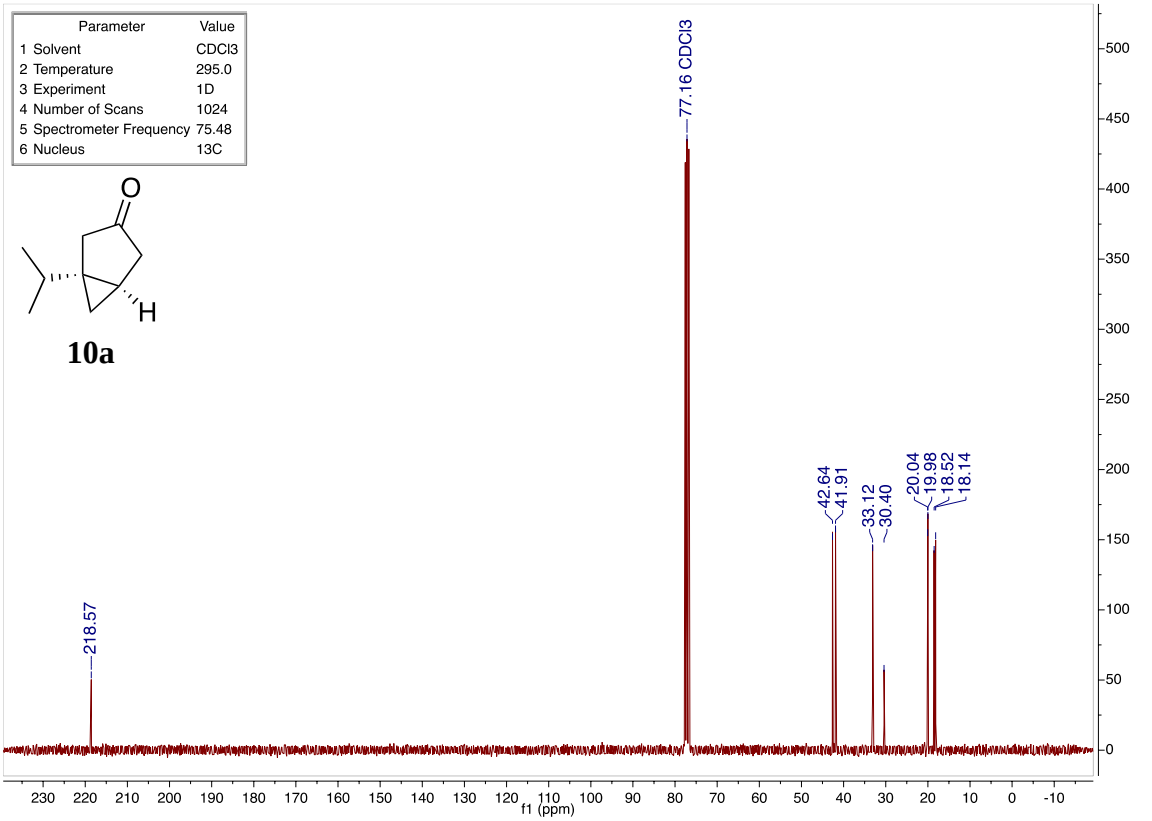
f1 (ppm)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H
10a
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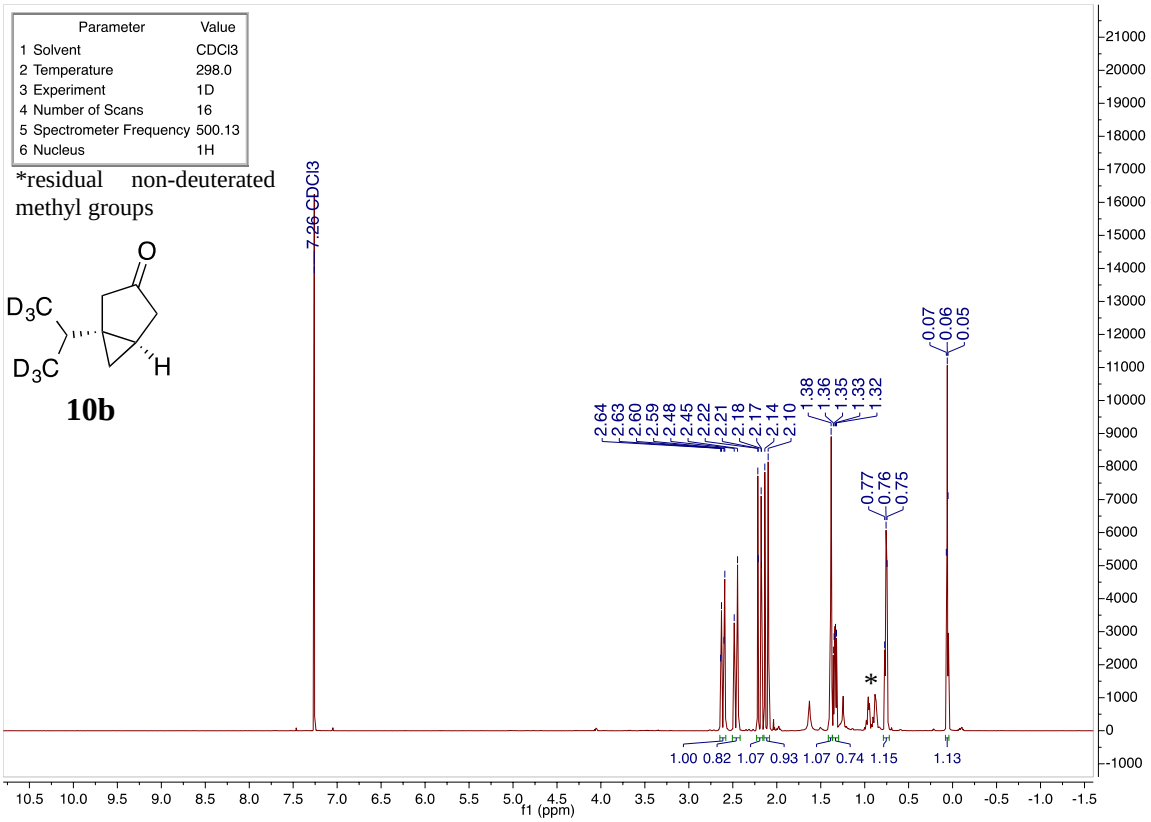
18.14
218.57
f1 (ppm)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6 Nucleus 1H
*residual non-deuterated methyl groups
10b
7.26 CDCl3
2.64 2.63 2.60 2.59 2.48 2.45 2.22 2.21 2.18 2.17 2.14 2.10
1.38 1.36 1.35 1.33 1.32
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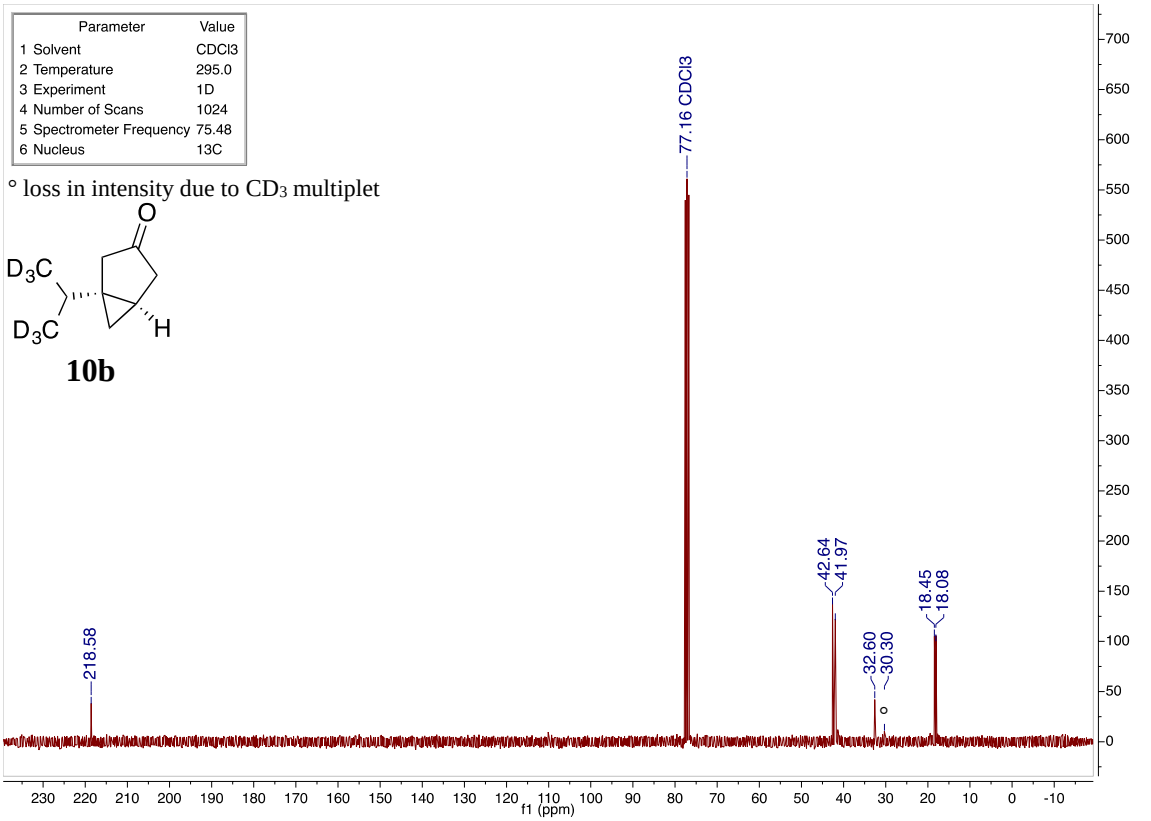
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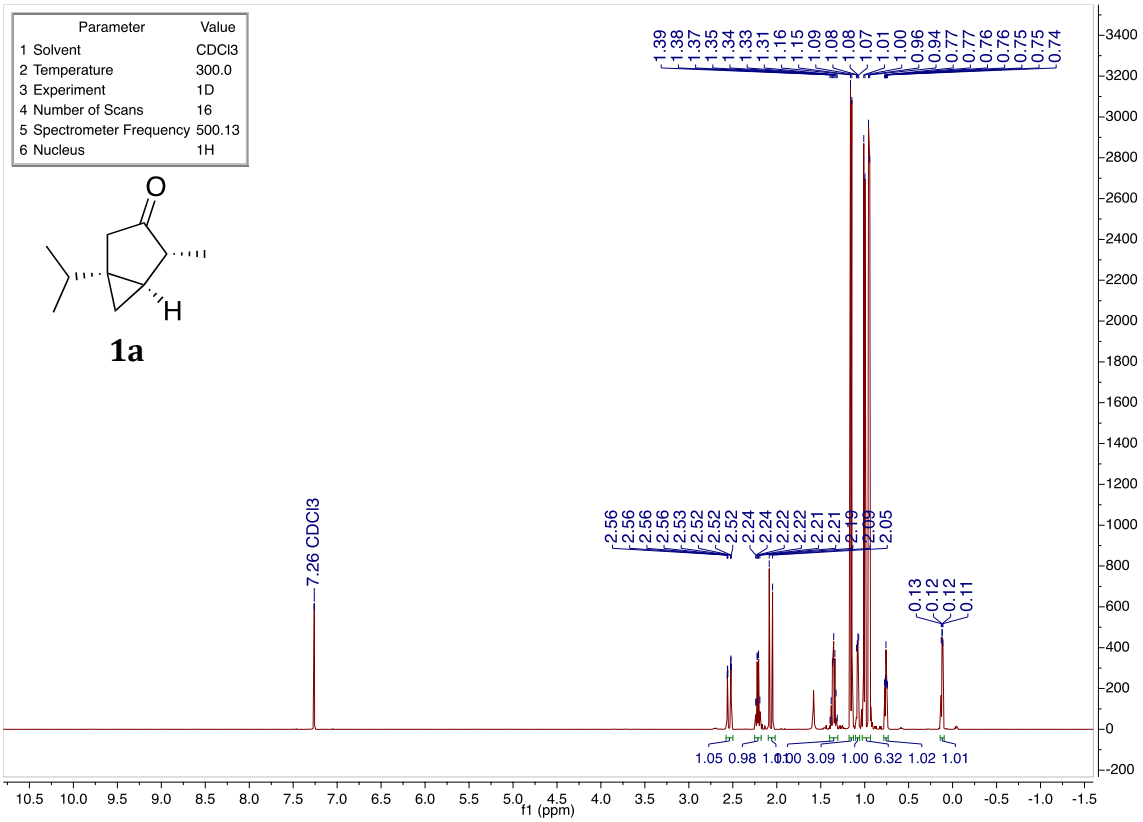
42.64 41.97
32.60 30.30
18.45 18.08
f1 (ppm)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O
H
1a
7.26 CDCl3
1.39 1.38 1.37 1.35 1.34 1.33 1.31 1.16 1.15 1.09 1.08 1.08 1.07 1.01 1.00 0.96 0.94 0.77 0.76 0.76 0.75 0.74
2.56 2.56 2.56 2.56 2.53 2.52 2.52 2.52 2.24 2.24 2.22 2.22 2.21 2.21 2.19 2.09 2.05
0.13 0.12 0.12 0.11
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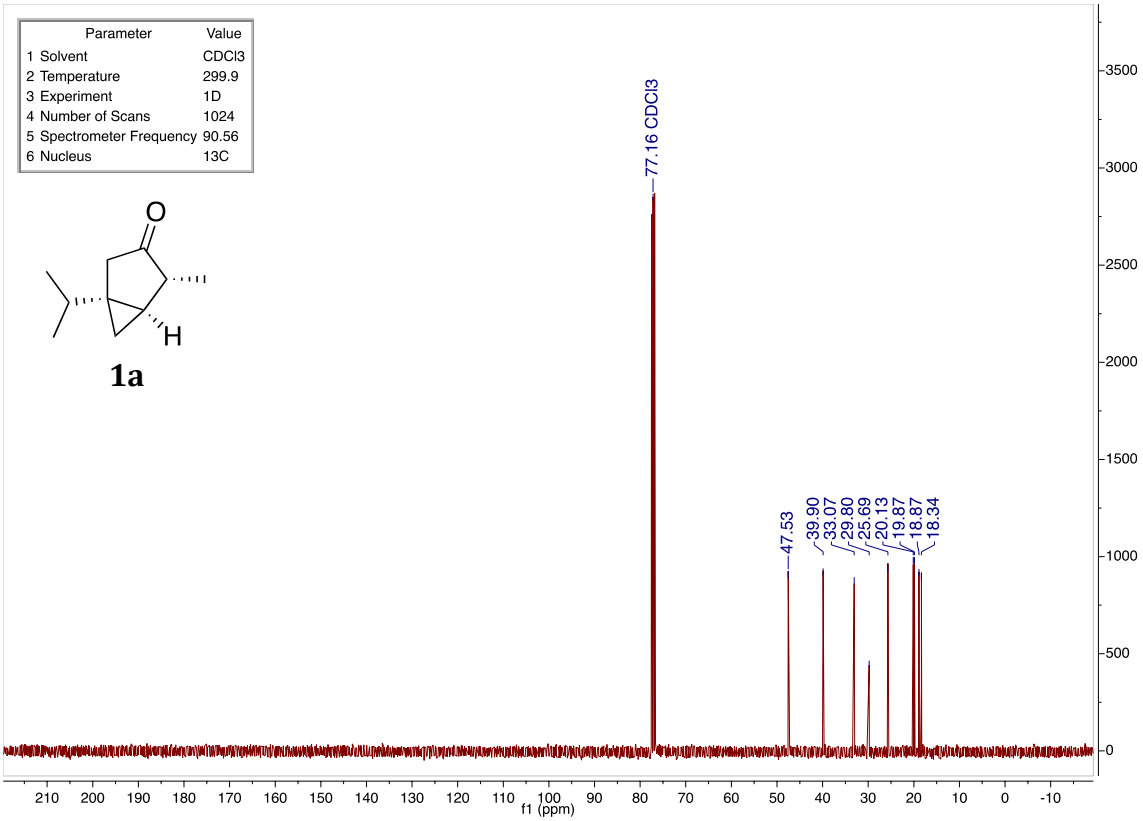
f1 (ppm)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H
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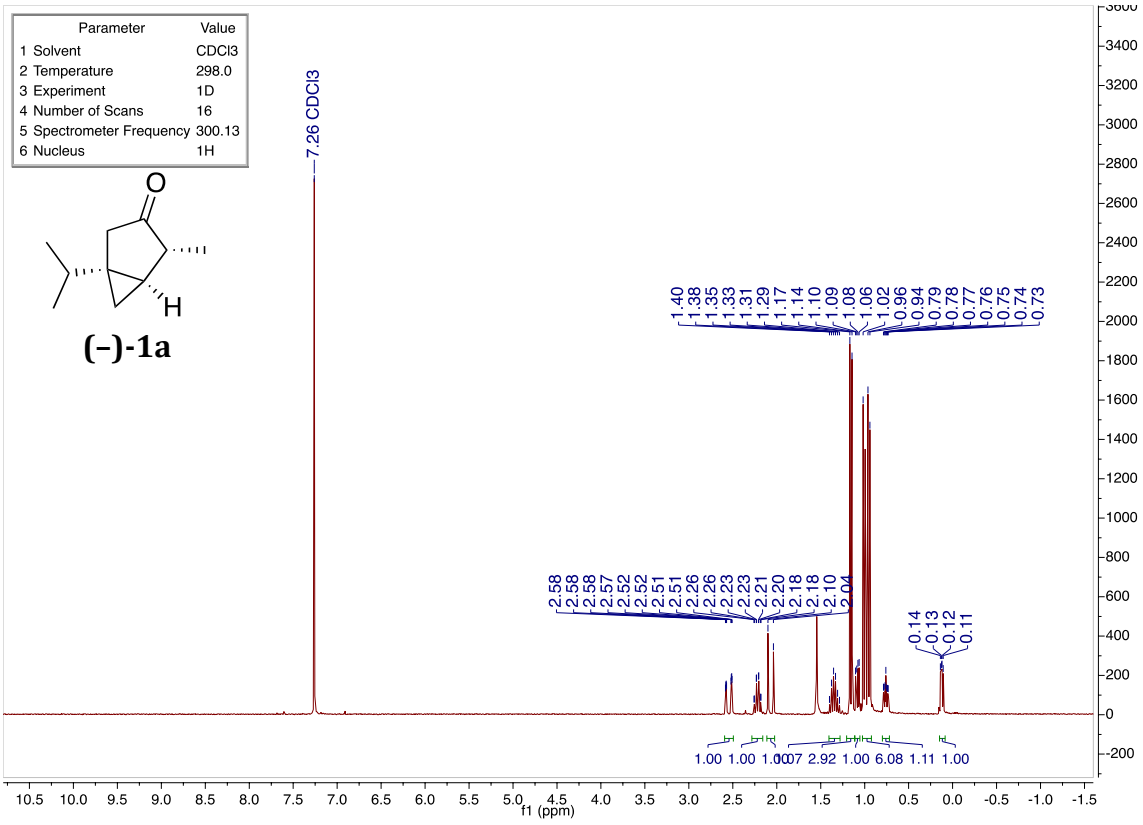
f1 (ppm)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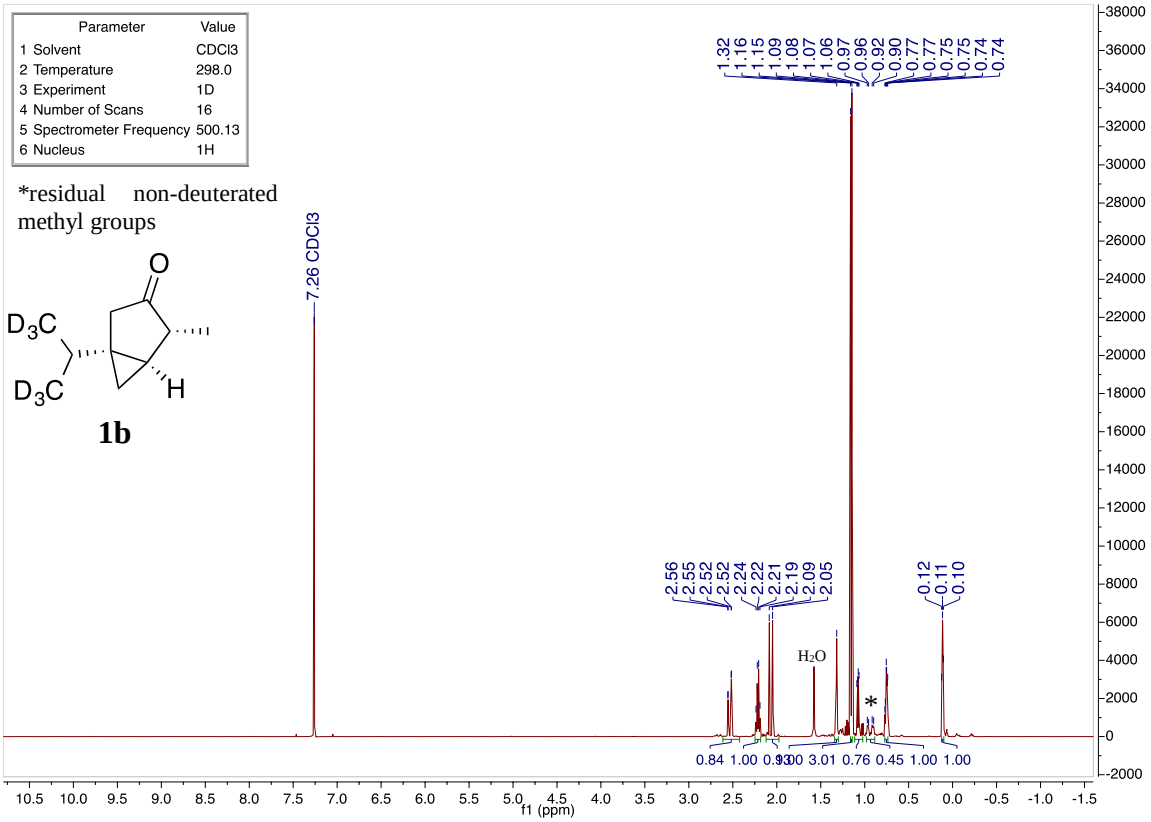
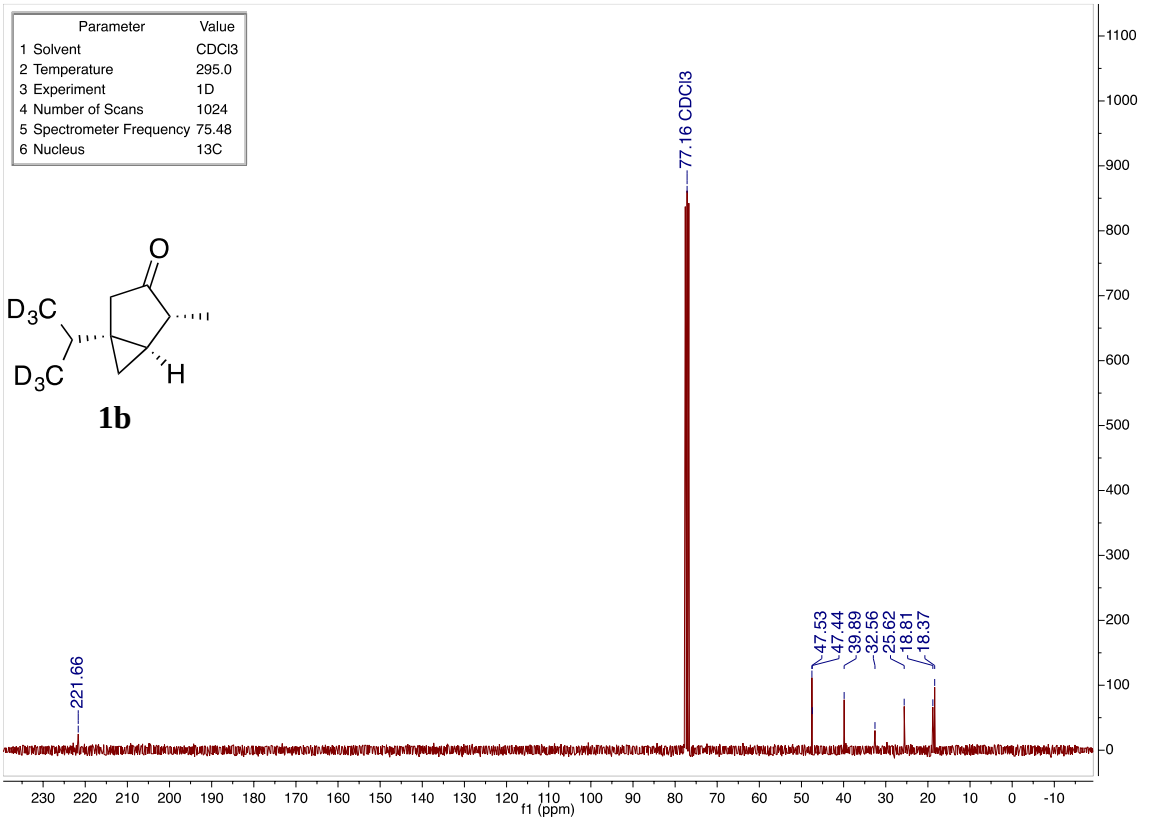
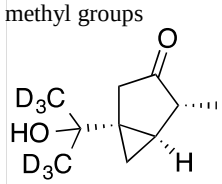
O
H
(–)-1a
7.26 CDCl3
1.40 1.38 1.35 1.33 1.31 1.29 1.17 1.14 1.10 1.09 1.08 1.06 1.02 0.96 0.94 0.79 0.78 0.77 0.76 0.75 0.74 0.73
2.58 2.58 2.58 2.57 2.52 2.52 2.51 2.51 2.26 2.26 2.23 2.23 2.21 2.20 2.18 2.10 2.04
0.14 0.13 0.12 0.11
1.00 1.00 1.00 2.92 1.00 6.08 1.11 1.00
f1 (ppm)


Parameter Value
1 Solvent CDCl3
2 Temperature 298.0
3 Experiment 1D
4 Number of Scans 16
5 Spectrometer Frequency 500.13
6 Nucleus 1H
*residual non-deuterated methyl groups
1b
7.26 CDCl3
1.32 1.16 1.15 1.09 1.08 1.07 1.06 0.97 0.96 0.92 0.90 0.77 0.77 0.75 0.75 0.74 0.74
2.56 2.55 2.52 2.52 2.24 2.22 2.21 2.19 2.09 2.05
0.12 0.11 0.10
H2O
*
0.84 1.00 0.93 3.00 3.01 0.76 0.45 1.00 1.00
f1 (ppm)


Parameter Value
1 Solvent CDCl3
2 Temperature 295.0
3 Experiment 1D
4 Number of Scans 1024
5 Spectrometer Frequency 75.48
6 Nucleus 13C
1b
77.16 CDCl3
221.66
47.53 47.44 39.89 32.56 25.62 18.81 18.37
f1 (ppm)

Parameter	Value
1 Solvent	CDCl3
2 Temperature	298.0
3 Experiment	1D
4 Number of Scans	16
5 Spectrometer Frequency	500.13
6 Nucleus	1H

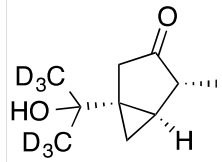
*residual non-deuterated methyl groups



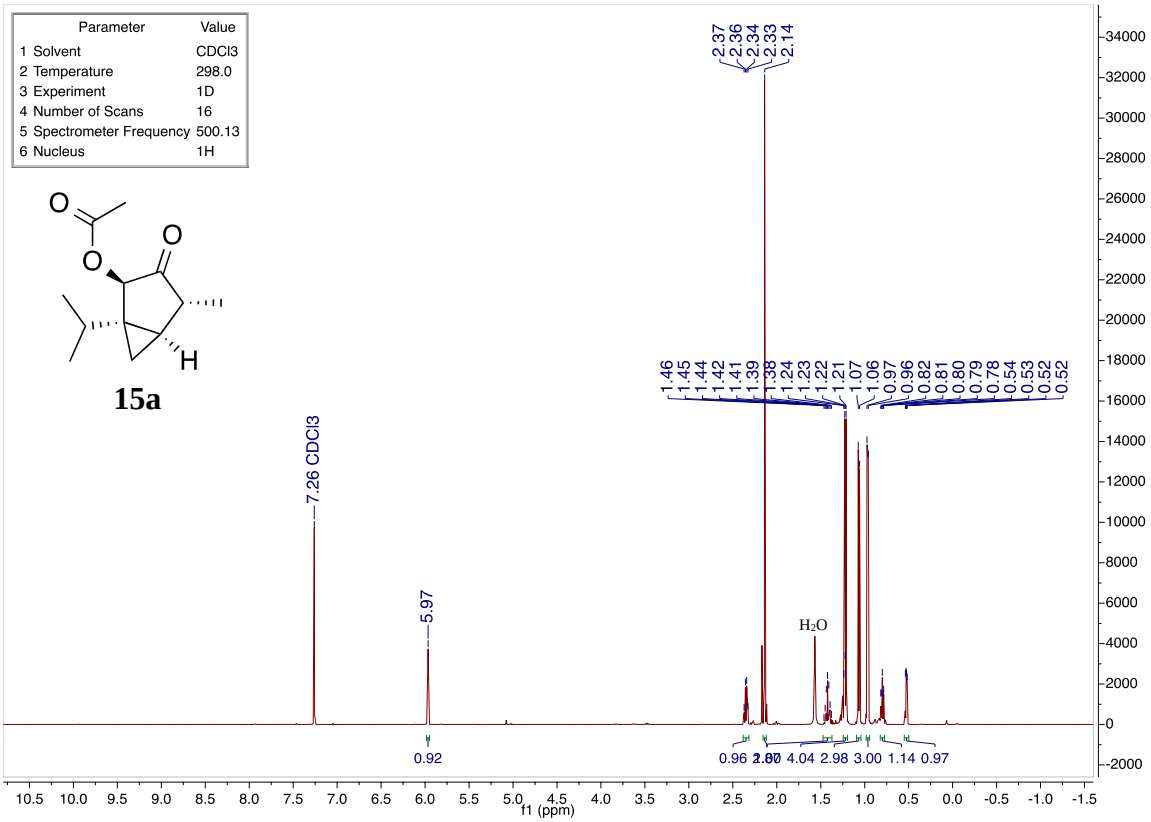
3b

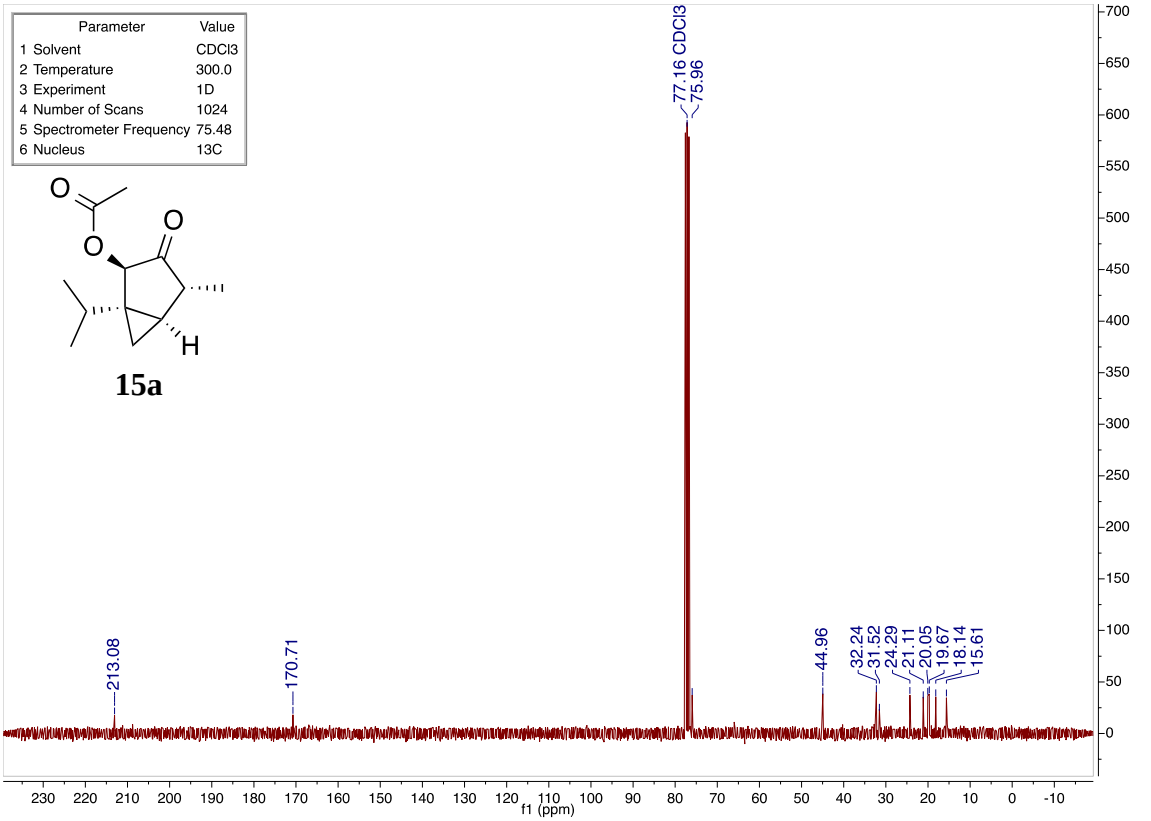
Parameter	Value
1 Solvent	CDCl3
2 Temperature	299.9
3 Experiment	1D
4 Number of Scans	256
5 Spectrometer Frequency	125.83
6 Nucleus	13C

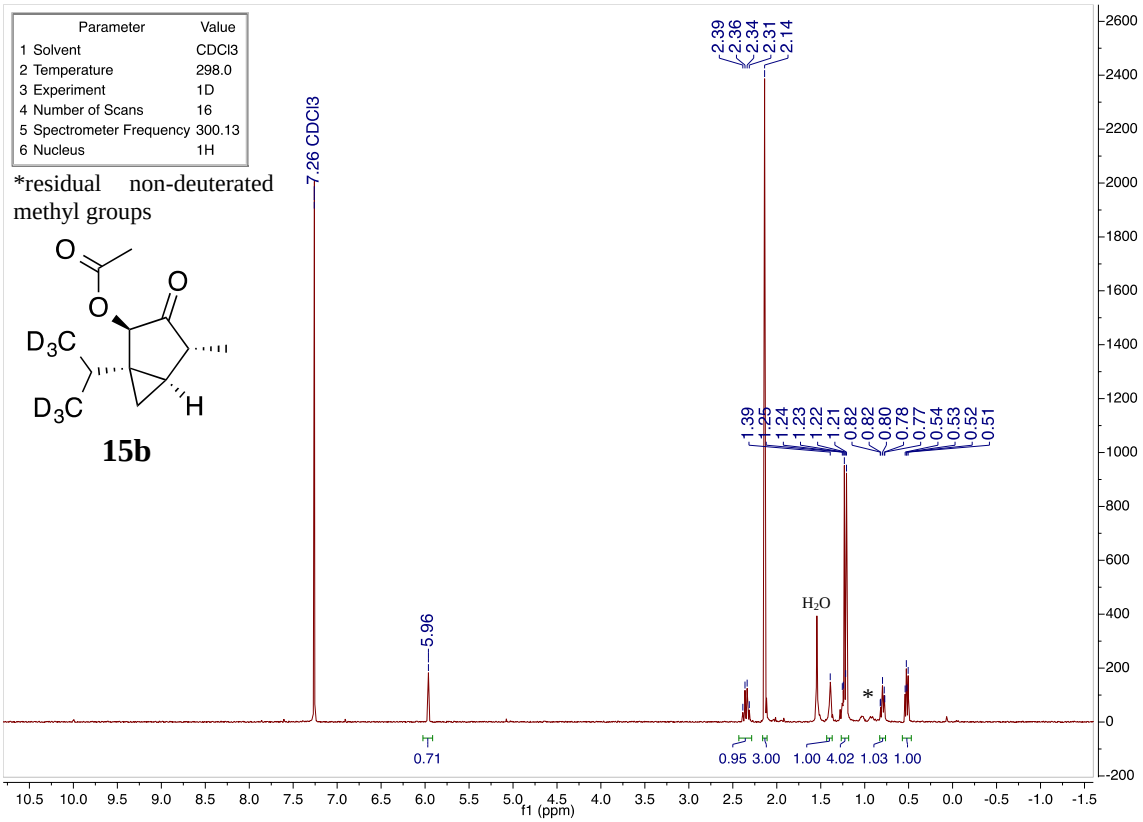
° loss in intensity due to CD_3 multiplet



3b

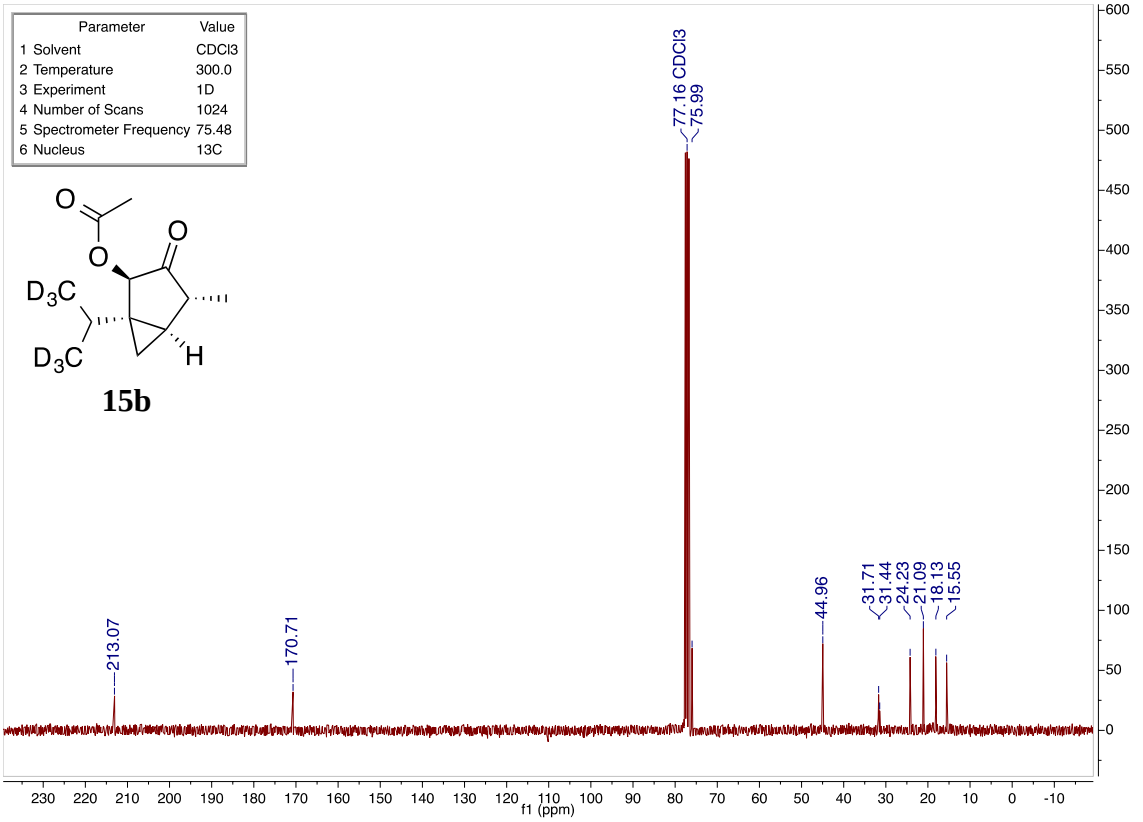

Parameter Value
1 Solvent CDCl3
2 Temperature 298.0
3 Experiment 1D
4 Number of Scans 16
5 Spectrometer Frequency 500.13
6 Nucleus 1H
15a
7.26 CDCl3
5.97
H2O
0.92
f1 (ppm)


Parameter Value
1 Solvent CDCl3
2 Temperature 300.0
3 Experiment 1D
4 Number of Scans 1024
5 Spectrometer Frequency 75.48
6 Nucleus 13C
15a
77.16 CDCl3
75.96
213.08
170.71
44.96
f1 (ppm)

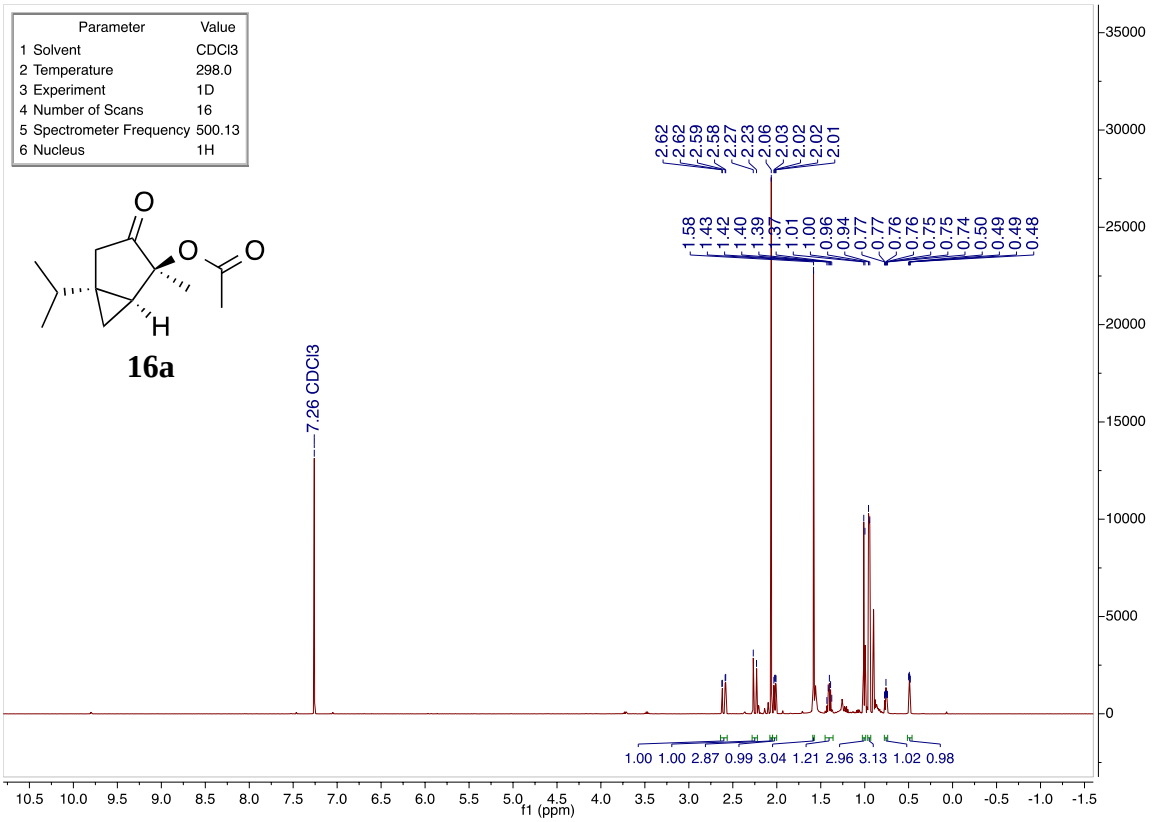


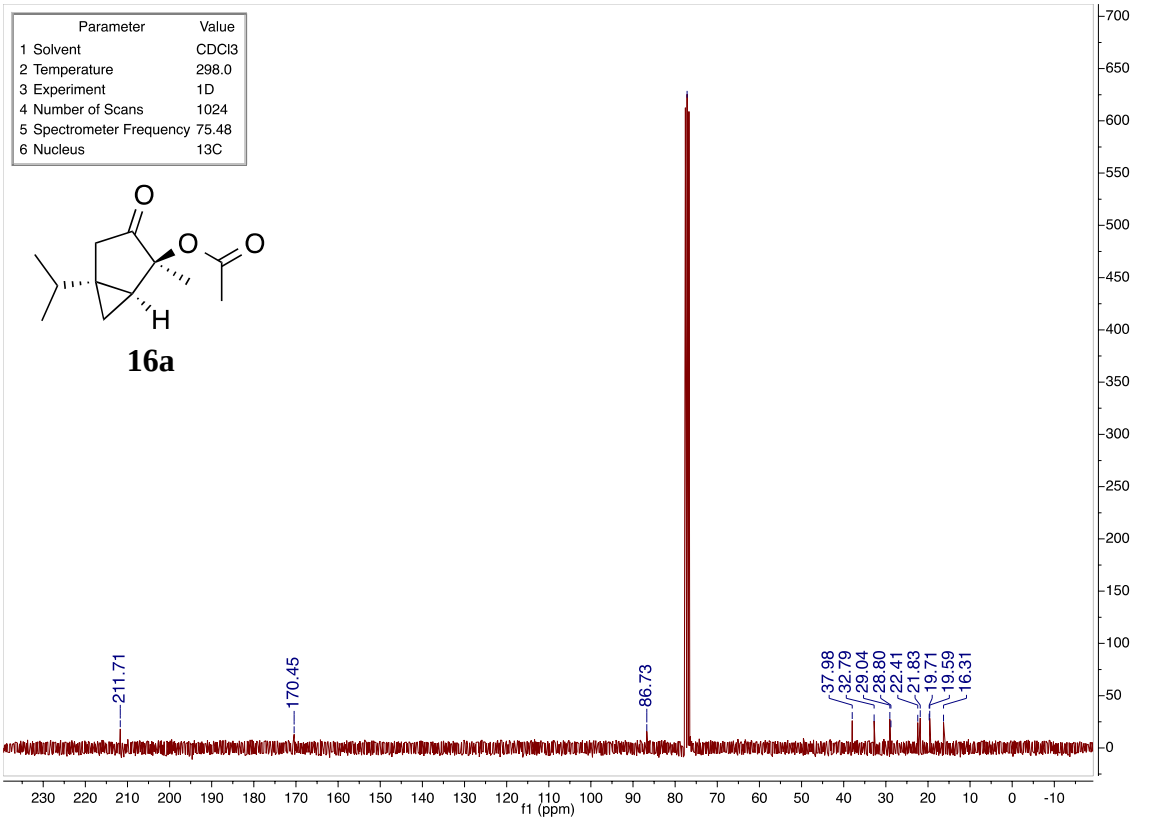
*residual non-deuterated methyl groups

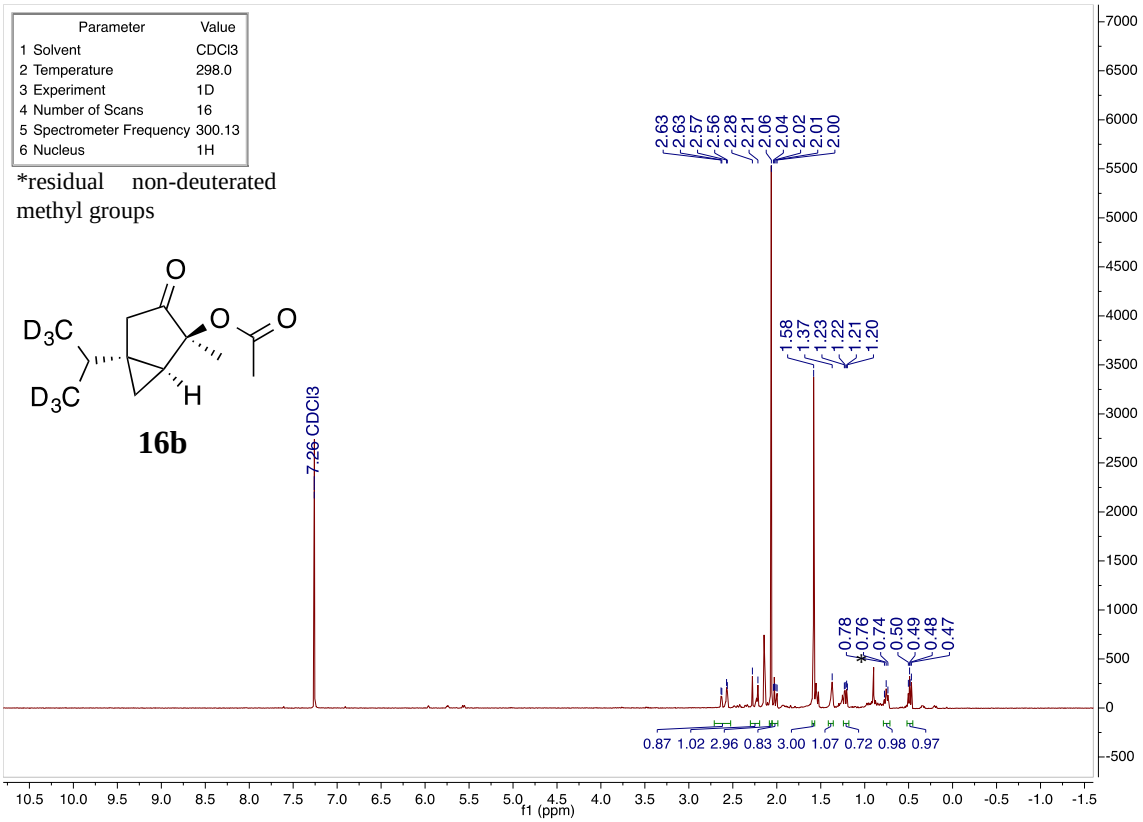
15b

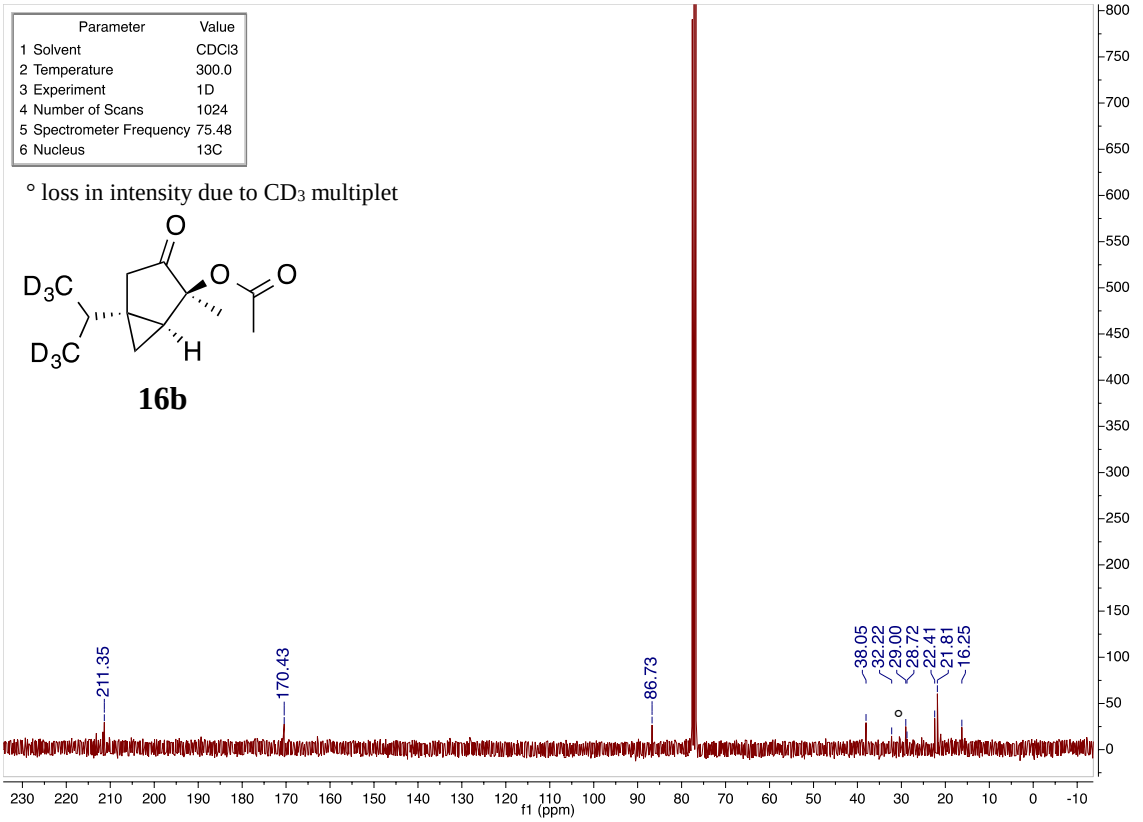


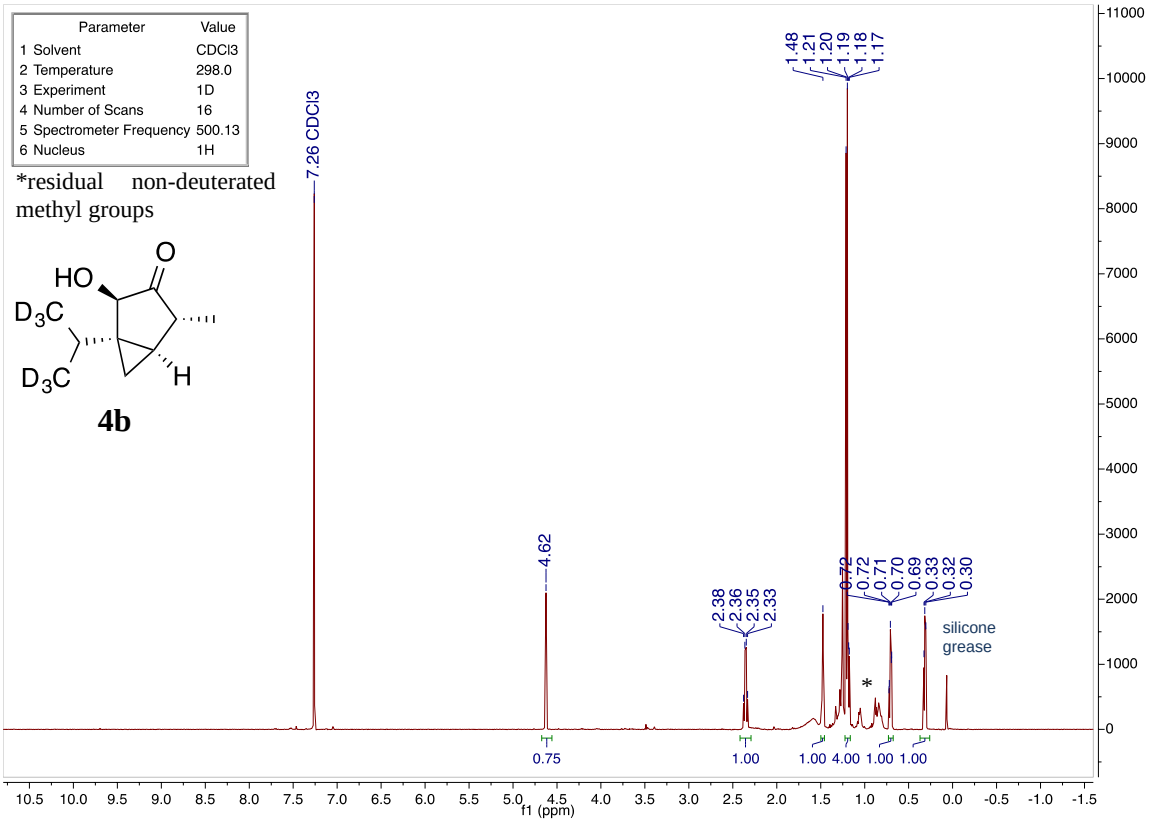
15b


Parameter Value
1 Solvent CDCl3
2 Temperature 298.0
3 Experiment 1D
4 Number of Scans 16
5 Spectrometer Frequency 500.13
6 Nucleus 1H
16a
7.26 CDCl3
2.62 2.62 2.59 2.58 2.27 2.23 2.06 2.03 2.02 2.02 2.01
1.58 1.43 1.42 1.40 1.39 1.37 1.01 1.00 0.96 0.94 0.77 0.77 0.76 0.76 0.75 0.75 0.74 0.50 0.49 0.49 0.48
1.00 1.00 2.87 0.99 3.04 1.21 2.96 3.13 1.02 0.98
f1 (ppm)


Parameter Value
1 Solvent CDCl3
2 Temperature 298.0
3 Experiment 1D
4 Number of Scans 1024
5 Spectrometer Frequency 75.48
6 Nucleus 13C
16a
211.71
170.45
86.73
37.98 32.79 29.04 28.80 22.41 21.83 19.71 19.59 16.31
f1 (ppm)

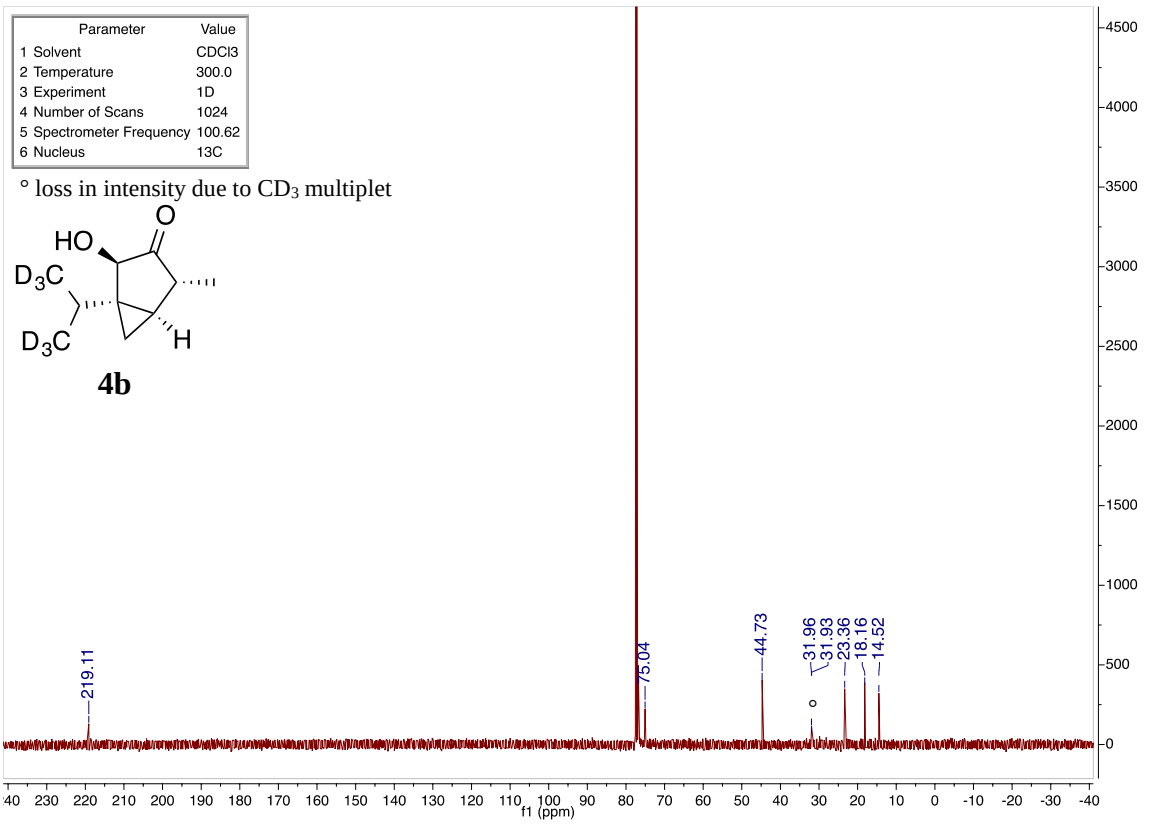

Parameter Value
1 Solvent CDCl3
2 Temperature 298.0
3 Experiment 1D
4 Number of Scans 16
5 Spectrometer Frequency 300.13
6 Nucleus 1H
*residual non-deuterated methyl groups
16b
7.26 CDCl3
2.63 2.63 2.57 2.56 2.28 2.21 2.06 2.04 2.02 2.01 2.00
1.58 1.37 1.23 1.22 1.21 1.20
0.78 0.76 0.74 0.50 0.49 0.48 0.47
0.87 1.02 2.96 0.83 3.00 1.07 0.72 0.98 0.97
f1 (ppm)


Parameter Value
1 Solvent CDCl3
2 Temperature 300.0
3 Experiment 1D
4 Number of Scans 1024
5 Spectrometer Frequency 75.48
6 Nucleus 13C
° loss in intensity due to CD3 multiplet
16b
211.35
170.43
86.73
38.05
32.22
29.00
28.72
22.41
21.81
16.25
f1 (ppm)



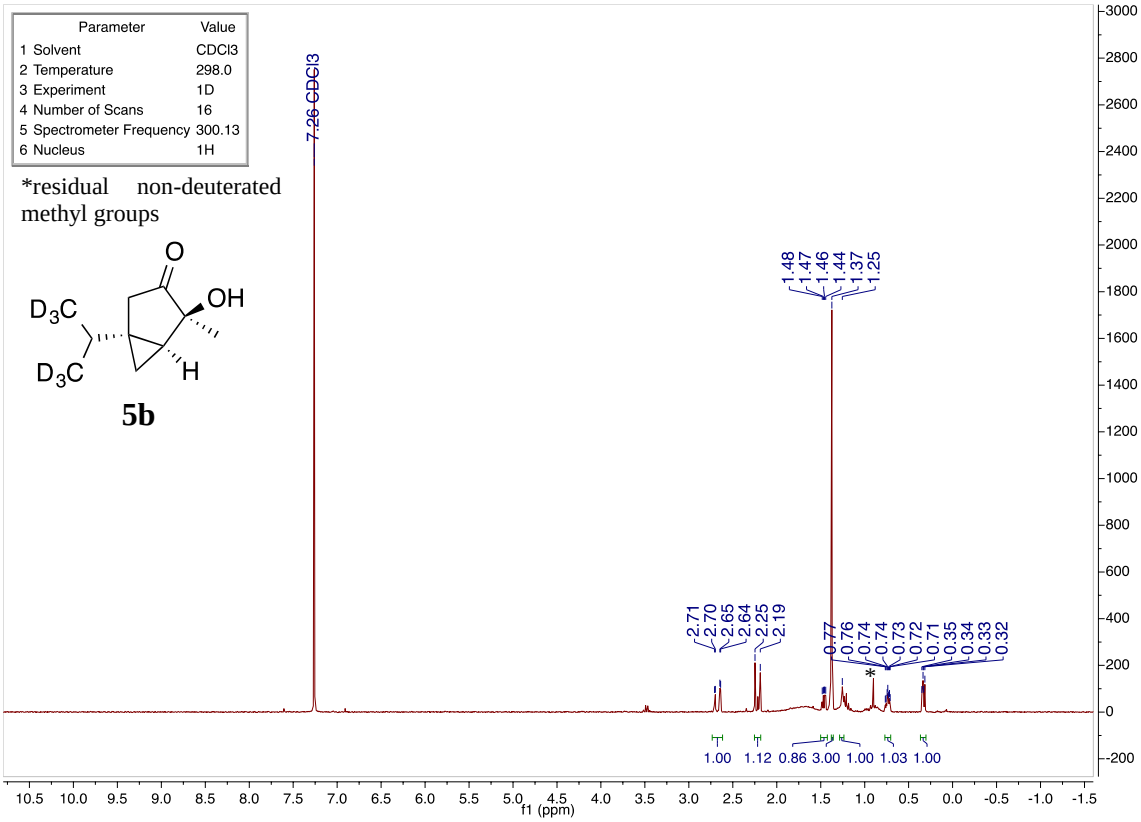
*residual non-deuterated methyl groups

4b



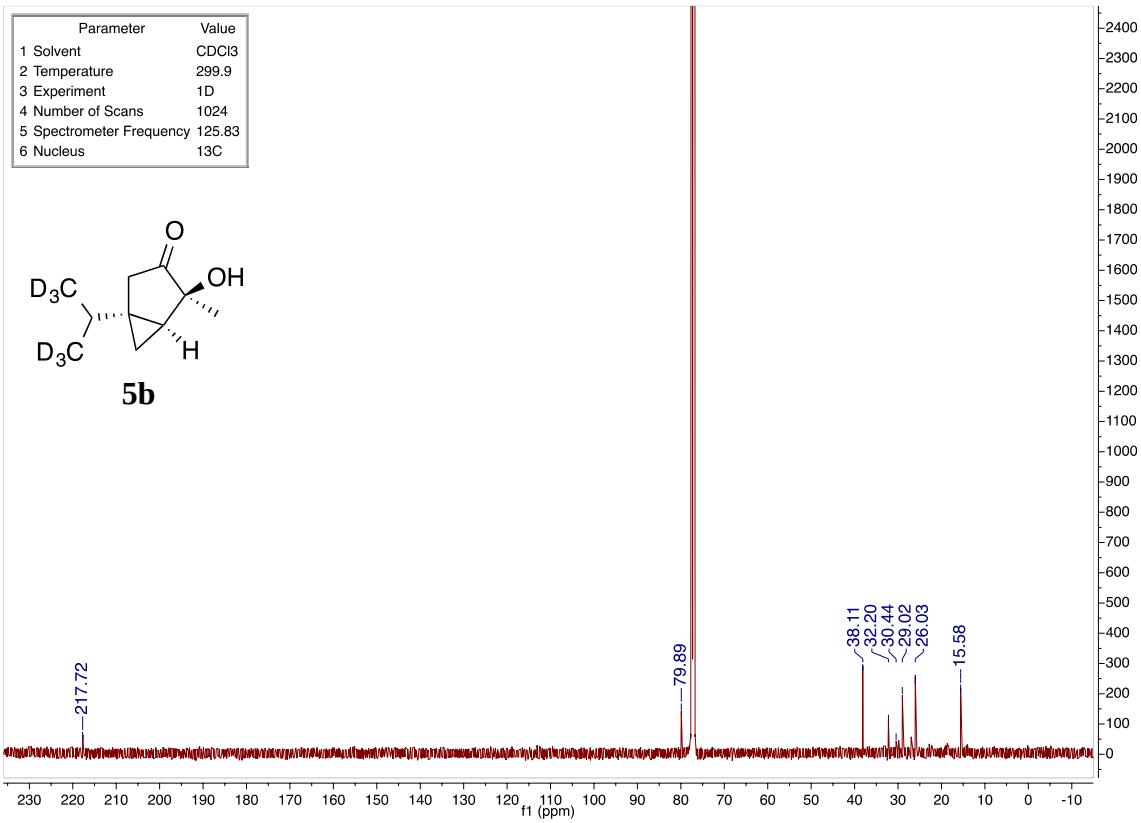
° loss in intensity due to CD_3 multiplet

4b



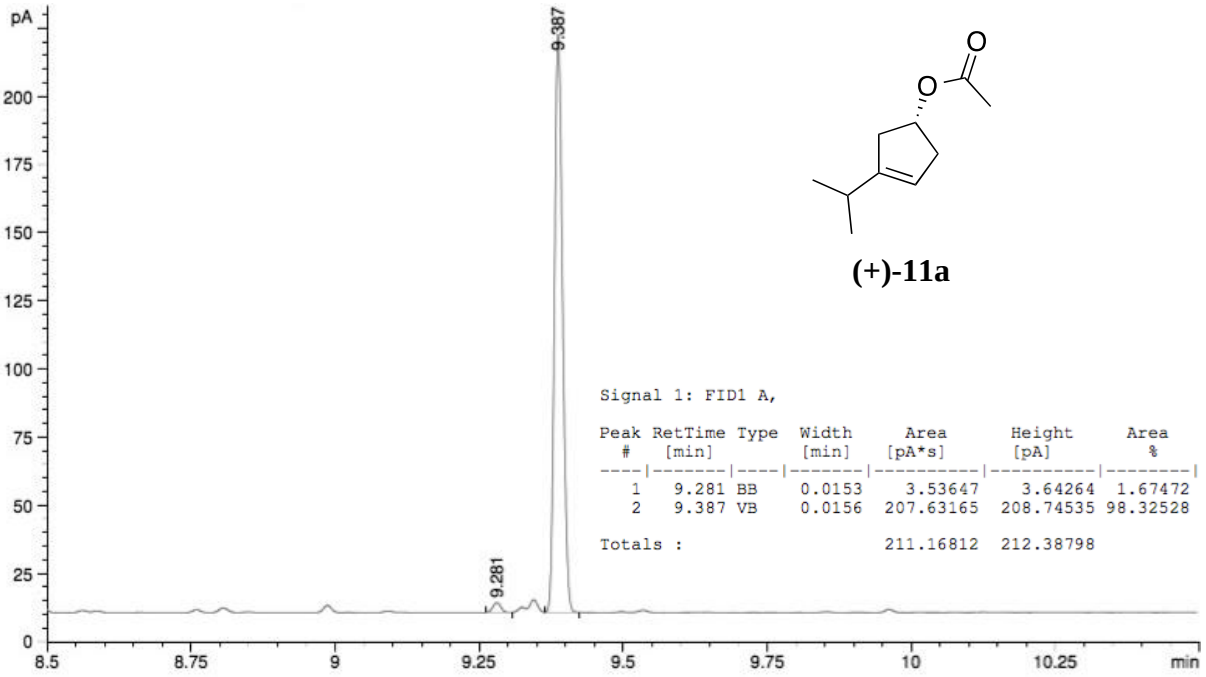
*residual non-deuterated methyl groups

5b



5b

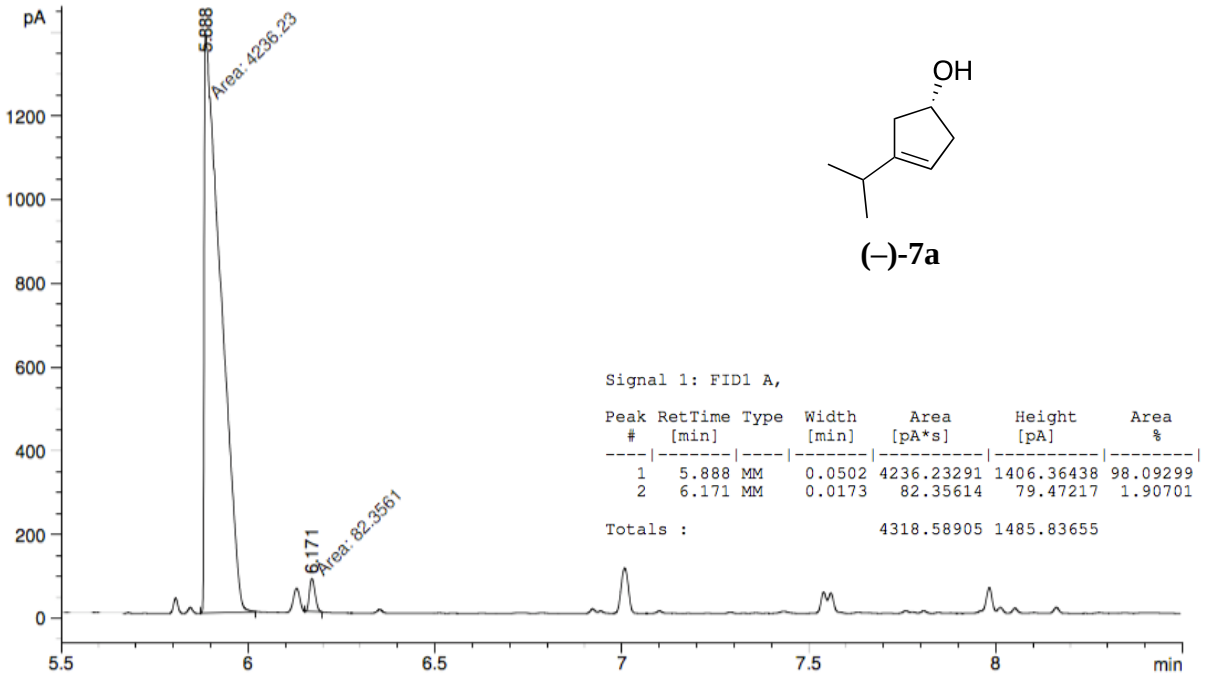
5 Chiral GC Spectra



(+)-11a

Signal 1: FID1 A,

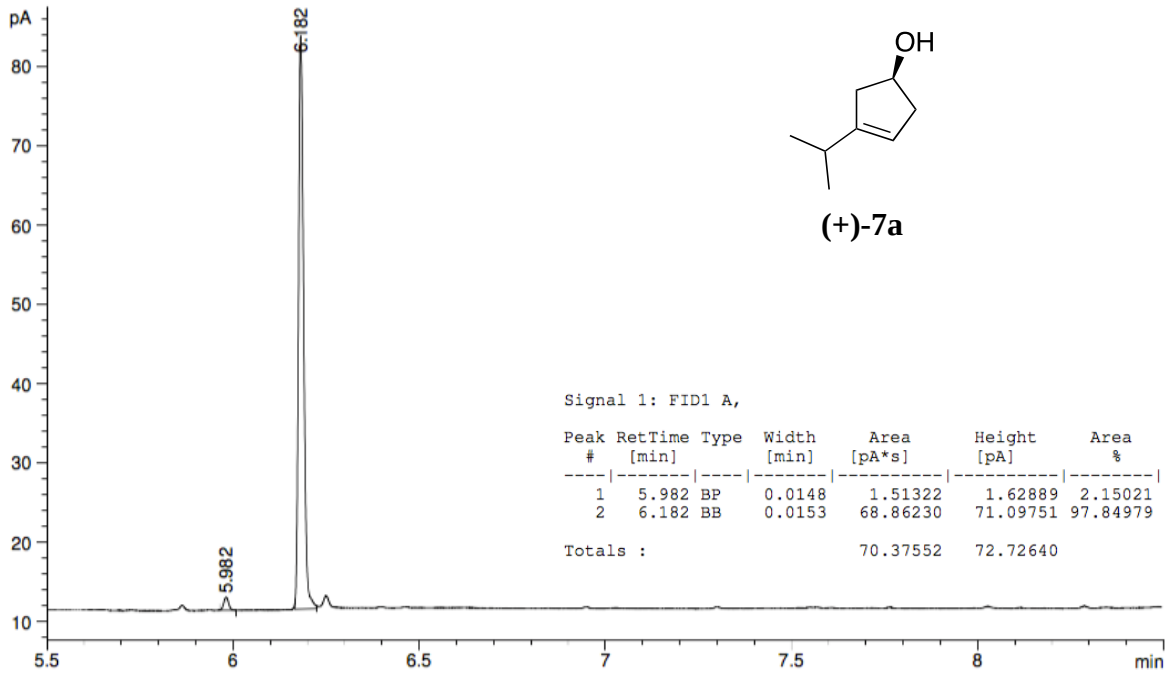
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	9.281	BB	0.0153	3.53647	3.64264	1.67472
2	9.387	VB	0.0156	207.63165	208.74535	98.32528
Totals :				211.16812	212.38798	



(–)-7a

Signal 1: FID1 A,

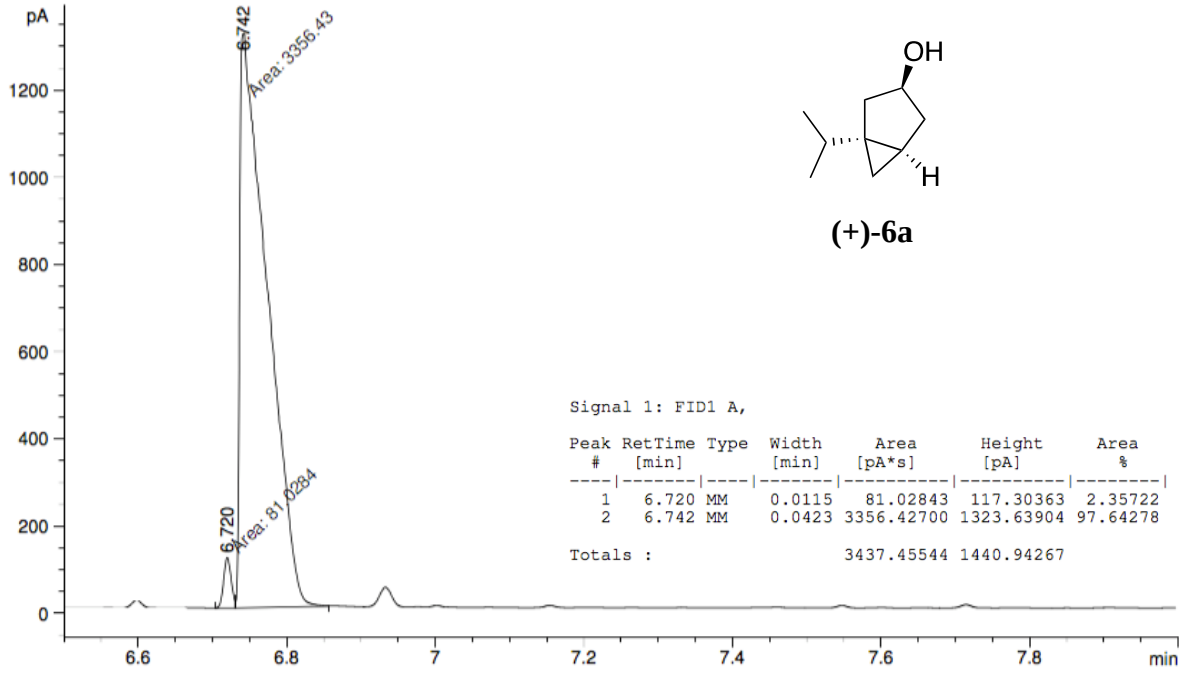
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.888	MM	0.0502	4236.23291	1406.36438	98.09299
2	6.171	MM	0.0173	82.35614	79.47217	1.90701
Totals :				4318.58905	1485.83655	



(+)-7a

Signal 1: FID1 A,

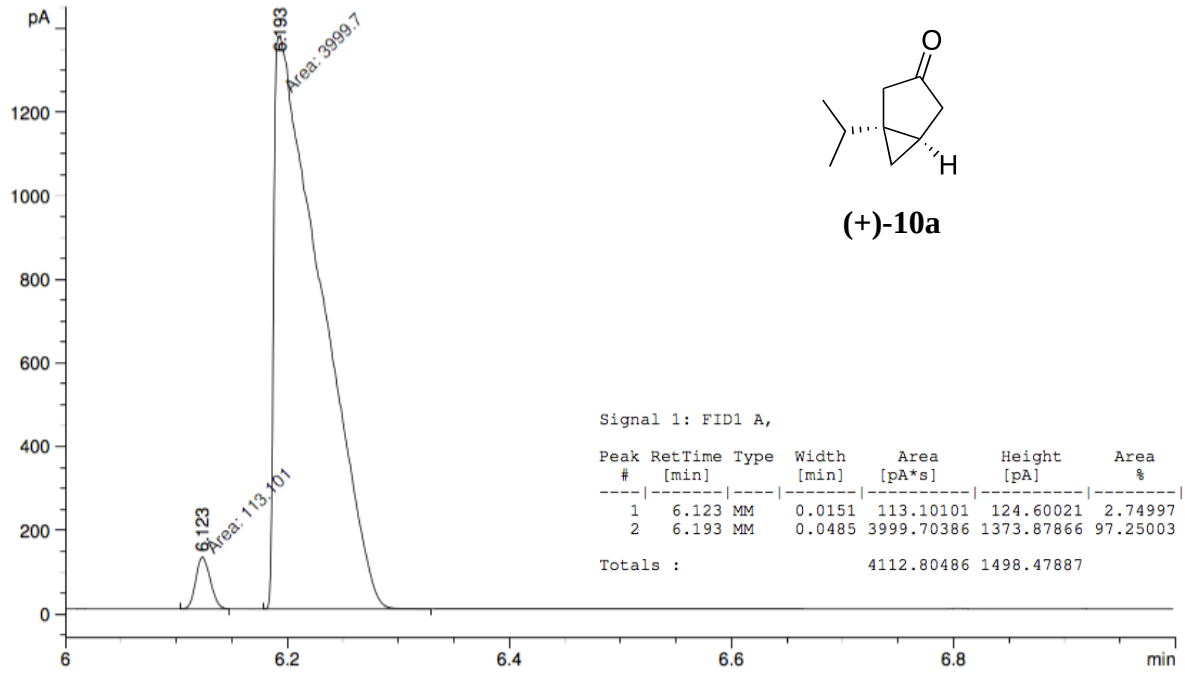
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.982	BP	0.0148	1.51322	1.62889	2.15021
2	6.182	BB	0.0153	68.86230	71.09751	97.84979
Totals :				70.37552	72.72640	



(+)-6a

Signal 1: FID1 A,

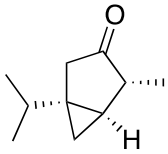
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	6.720	MM	0.0115	81.02843	117.30363	2.35722
2	6.742	MM	0.0423	3356.42700	1323.63904	97.64278
Totals :				3437.45544	1440.94267	



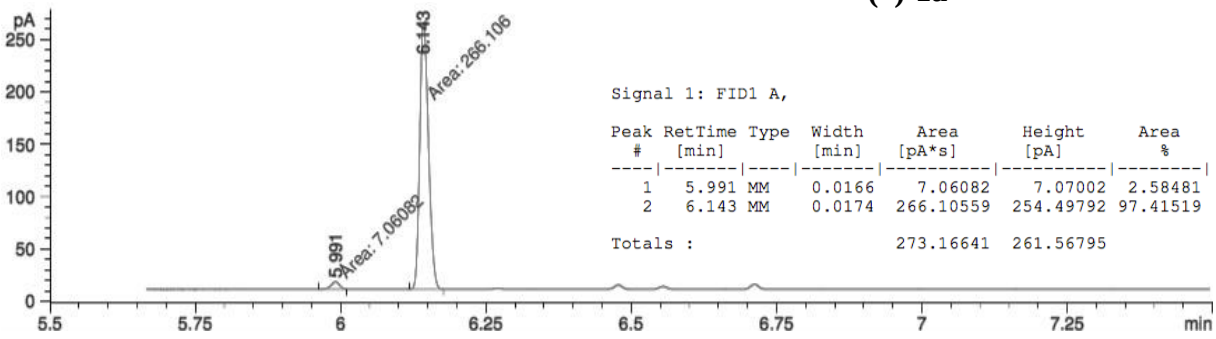
Signal 1: FID1 A,

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	6.123	MM	0.0151	113.10101	124.60021	2.74997
2	6.193	MM	0.0485	3999.70386	1373.87866	97.25003
Totals :				4112.80486	1498.47887	

(+)-10a

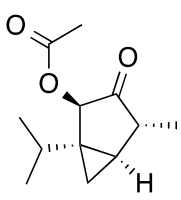


(–)-1a



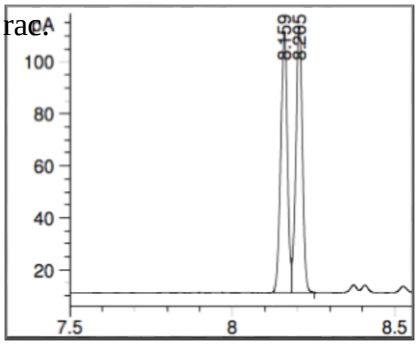
Signal 1: FID1 A,

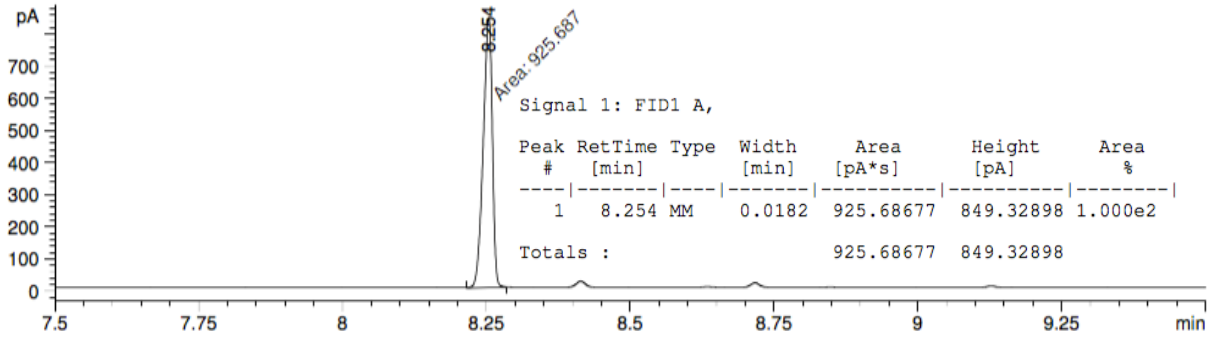
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	5.991	MM	0.0166	7.06082	7.07002	2.58481
2	6.143	MM	0.0174	266.10559	254.49792	97.41519
Totals :				273.16641	261.56795	



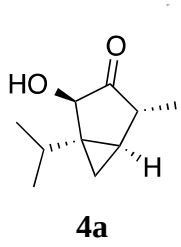
15a

rac.

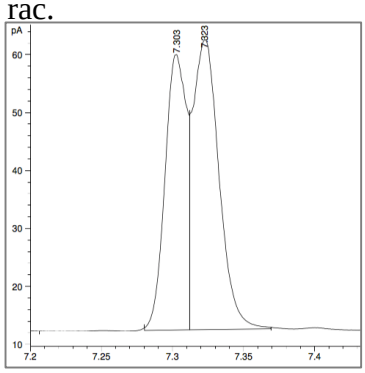


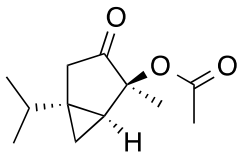


rac.



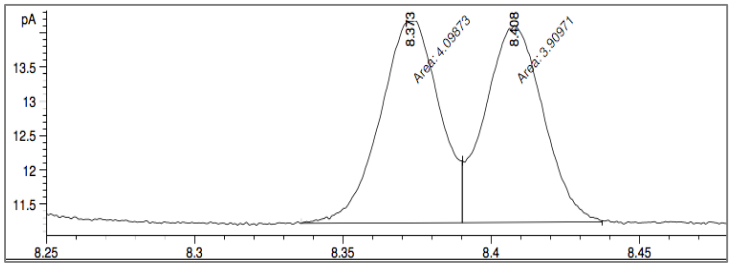
4a

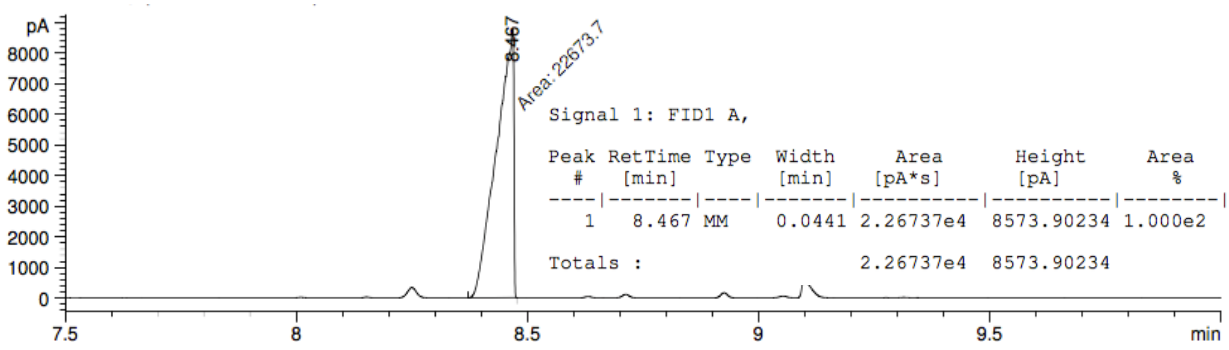




16a

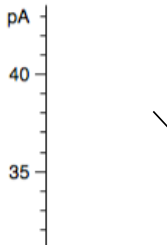
rac.





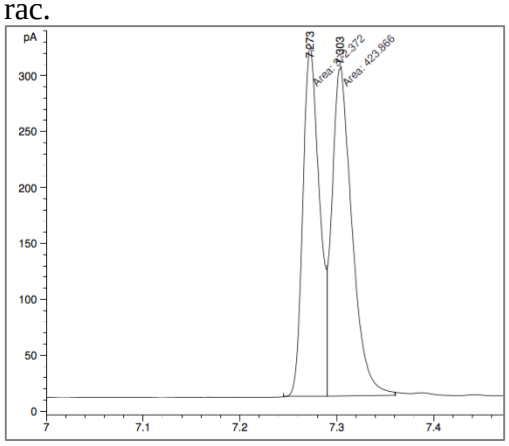
Signal 1: FID1 A,

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	8.467	MM	0.0441	2.26737e4	8573.90234	1.000e2
Totals :				2.26737e4	8573.90234	



5a

rac.



Signal 1: FID1 A,

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	7.321	MM	0.0169	30.49021	30.12832	1.000e2
Totals :				30.49021	30.12832	