

Enantioselective Lewis Base-Catalyzed Sulfenocyclization of Polyenes

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SUPPORTING INFORMATION

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General Experimental

Reaction solvents tetrahydrofuran (Fisher, HPLC grade, BHT stabilized), diethyl ether (Fisher, ACS grade, BHT stabilized), and dichloromethane (Fisher, HPLC grade, not stabilized) were dried by percolation through two columns packed with neutral alumina under positive pressure of argon. *N,N*-dimethylformamide (Fisher, ACS grade) was dried by percolation through two columns packed with molecular sieves. Methanol and ethanol were distilled from magnesium turnings under a nitrogen atmosphere. Pyridine and acetonitrile were distilled from calcium hydride under a nitrogen atmosphere. Solvents for filtration, transfers, chromatography, and recrystallizations were purchased from commercial sources and used as received. "Brine" refers to a saturated solution of sodium chloride in distilled water. Column chromatography was performed using Merck grade 9385, 60 Å silica gel. Visualization was accomplished by UV light, potassium permanganate solution, ceric ammonium molybdate solution, or phosphomolybdic acid solution. Analytical TLC was performed on Merck silica gel plates with F₂₅₄ indicator. R_f values reported were measured using a 10 x 2 cm plate.

¹H and ¹³C NMR spectra were recorded on a Carver-Bruker 500 MHz (500 MHz, ¹H; 126 MHz, ¹³C) spectrometer. Spectra are reference to residual chloroform ($\delta = 7.26$ ppm, ¹H; 77.16 ppm, ¹³C) or residual benzene ($\delta = 7.16$ ppm, ¹H; 128.06 ppm, ¹³C). Chemical shifts are reported in parts per million. Assignments were obtained by reference to COSY, HMQC, HMBC, and NOESY correlations. Elemental analysis was performed by the University of Illinois Microanalysis Laboratory. Mass spectrometry (MS) was performed by the University of Illinois Mass Spectrometry Laboratory. Electron Impact (EI) spectra were performed at 70 eV using methane as the carrier gas on a Finnagin-MAT C5 spectrometer. Electrospray Ionization (ESI) spectra were performed on a Micromass Q-ToF Ultima spectrometer. Data are reported in the form of m/z (intensity relative to the base peak = 100). Infrared spectra (IR) were recorded neat on a Perkin-Elmer FT-IR system and peaks were reported in cm⁻¹ with indicated relative intensities: s (strong, 0-33% T); m (medium, 34-66% T); w (weak, 67-100% T). Melting points (mp) were determined on a Thomas-Hoover capillary melting point apparatus in sealed tubes and are corrected.

The following commercial reagents were used as received: 1-(chloromethyl)-4-methylbenzene, 1-(chloromethyl)-4-methoxybenzene, magnesium turnings, geranyl acetate, copper(II) chloride (anhydrous), 2-isopropylphenol, methyl iodide, potassium carbonate

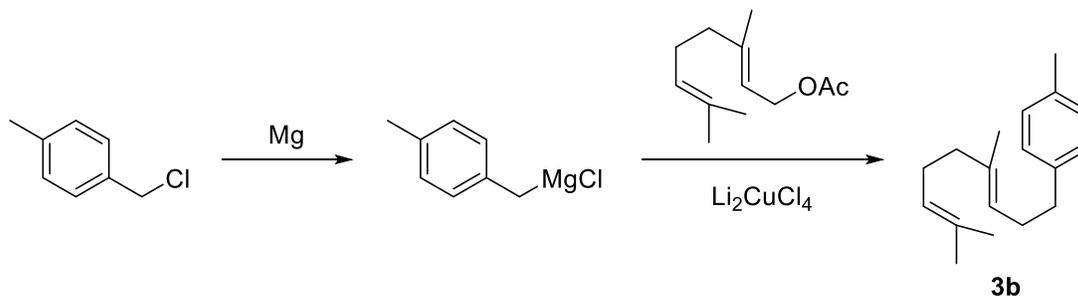
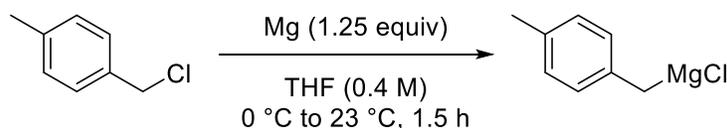
(anhydrous), potassium bromide, 18-Crown-6, *n*-butyllithium (solution in hexanes), sodium borohydride, thionyl chloride, potassium tert-butoxide, 1-octanethiol, tert-butyldimethylsilyl chloride, imidazole, sodium *p*-toluenesulfinate (hydrate), tetrabutylammonium bromide, sodium hexamethyldisilazide (1.0 M solution in THF), sodium dihydrogen phosphate (monohydrate), sodium amalgam (20% w/w sodium), hexafluoroisopropanol, tetra(*n*-butyl)ammonium fluoride trihydrate, hydrogen peroxide (30% w/w aq.), *n*-dodecane, trifluoroacetic anhydride, 2,6-lutidine, trifluoroacetic acid, chloriodomethane, isopropylmagnesium chloride (2.0 M solution in THF), lithium (granules), *N,N*-dimethyl-1-aminonaphthalene and boron tribromide.

1-Naphthaldehyde was purchased from commercial sources and purified as described by Denmark et al.¹ Lithium chloride was purchased from commercial sources and dried (130 °C, 0.1 torr) for 12 h before use.² *meta*-Chloroperbenzoic acid was purchased from commercial sources and washed with phosphate buffer before use.²

Literature Preparations

The following compounds were prepared by literature methods and characterization matched the data previously reported: *tert*-butyl (4-(hydroxymethyl)phenyl)carbamate,³ *tert*-butyl (4-(bromomethyl)phenyl)carbamate,⁴ *N*-((2,6-diisopropylphenyl)thio)-phthalimide **1**,⁵ (*R*)-4-(diisopropylamino)-3,5-dimethyl-4,5-dihydro-3H-dinaphtho[2,1-d:1',2'-f][1,3,2]diazaphosphepine-4-selenide (*R*)-**2**,⁶ and (*S*)-4-(diisopropylamino)-3,5-dimethyl-4,5-dihydro-3H-dinaphtho[2,1-d:1',2'-f][1,3,2]diazaphosphepine-4-selenide (*S*)-**2**.⁷ Geranyl bromide was prepared by a literature method⁸ and characterization matched the data previously reported.⁹

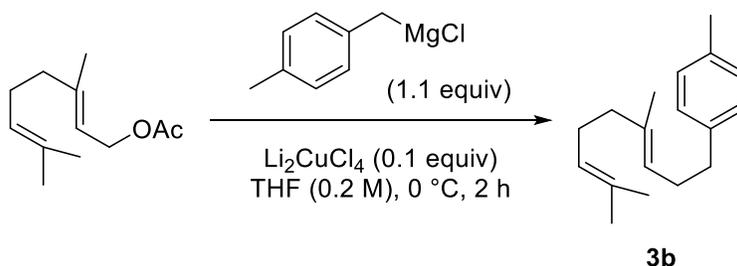
The following sulfenocyclization substrates were prepared by literature methods and characterization matched the data previously reported: (*E*)-(4,8-Dimethylnona-3,7-dien-1-yl)benzene **3a**,¹⁰ (*E*)-1-(4,8-dimethylnona-3,7-dienyl)-3,5-dimethoxybenzene **3d**,¹⁰ (*E*)-2-(3,7-dimethylocta-2,6-dien-1-yl)phenol **5a**,¹¹ (*E*)-2-(3,7-dimethylocta-2,6-dien-1-yl)-4-methylphenol **5b**,¹² (*E*)-2-(3,7-dimethylocta-2,6-dien-1-yl)-4-methoxyphenol **5c**,¹² (*E*)-1-(3,7-dimethylocta-2,6-dien-1-yl)naphthalen-2-ol **5d**,¹³ (*E*)-2-(3,7-dimethylocta-2,6-dien-1-yl)-4-fluorophenol **5e**,¹⁴ (*E*)-2-(3,7-dimethylocta-2,6-dien-1-yl)-4-chlorophenol **5f**,¹⁴ (*E*)-2-(3,7-dimethylocta-2,6-dien-1-yl)-4-bromophenol **5g**,¹⁵ and (*E*)-2-(3,7-dimethylocta-2,6-dien-1-yl)-4-(trifluoromethyl)phenol **5h**.¹⁶

Experimental Procedures: Synthesis of Substrates**(E)-1-(4,8-Dimethylnona-3,7-dien-1-yl)-4-methylbenzene (3b)****Preparation of (4-Methylbenzyl)magnesium Chloride**

A flame-dried, 50-mL, three-necked, round-bottomed flask equipped with a stir bar, argon inlet, two septa, and temperature probe was charged with magnesium turnings (182 mg, 7.50 mmol, 1.25 equiv). The turnings were mechanically activated immediately before use by grinding with a mortar and pestle for 10 min. The flask was again evacuated, flame-dried, and placed under argon. Once cool, the flask was charged with THF (10 mL) and a single drop of 1,2-dibromoethane. The mixture was stirred at 25 °C for 15 min and then cooled to 0 °C using an ice bath. A second, flame-dried flask was charged with 1-(chloromethyl)-4-methylbenzene (0.794 mL, 6.00 mmol) and THF (5 mL). The resulting solution was taken up in a 10-mL plastic Leur-Lock syringe and added dropwise to the reaction flask at 0 °C over 30 min using a syringe pump. The external ice bath is maintained throughout, but a slight exotherm (approx. 3 °C) is observed over the course of addition along with a slight darkening of the color. Once the addition was complete, the ice bath was removed and the mixture was allowed to warm to 25 °C. Stirring was continued for 1 h at 25 °C, and then the Grignard reagent was titrated in the following manner. An oven-dried, dram-sized vial equipped with a Teflon stir bar was charged with a small amount (roughly 1 mg) of 1,10-phenanthroline as an indicator. The vial was fitted with a Teflon-lined cap, evacuated, and placed under argon. A precise amount (300 μ L) of the Grignard reagent was added to the vial. The contents of the vial turned a deep purple color. A 1.0 M solution of *sec*-butanol in xylenes was added dropwise to the vial with a syringe with rapid stirring until a yellow endpoint was reached. The exact amount of *sec*-butanol solution added to

each vial was used to calculate the concentration of the Grignard reagent (the reaction is a 1:1 molar ratio). In this manner, the concentration of (4-methylbenzyl)magnesium chloride was determined to be 0.36 M (average of two runs; expected 0.40 M). The reagent was used immediately.

Preparation of (*E*)-1-(4,8-Dimethylnona-3,7-dien-1-yl)-4-methylbenzene (**3b**)



This compound was synthesized by an analogous procedure to the one described by Corey et al.¹⁰ A flame-dried, 5-mL, Schlenk flask was charged with anhydrous lithium chloride (38.8 mg, 0.92 mmol, 0.2 equiv) and anhydrous copper(II) chloride (61.6 mg, 0.46 mmol, 0.1 equiv) inside of the glove box. The flask was sealed, removed from the box, charged with THF (2.4 mL), and sonicated at 25 °C under argon for 15 min. An orange solution resulted, indicating formation of the desired Li_2CuCl_4 complex. A separate, flame-dried, 100-mL, three-necked, round-bottomed flask equipped with a stir bar, temperature probe, two septa, and argon inlet was charged with geranyl acetate (0.98 mL, 0.89 g, 4.58 mmol, $d = 0.916 \text{ g/mL}$) and THF (8.4 mL). The resulting clear, colorless solution was cooled to 0 °C using an ice bath. The orange solution of the Li_2CuCl_4 complex was added dropwise to the solution of geranyl acetate. The homogenous mixture was stirred at 0 °C for 10 min and then cooled to an internal temperature of -10 °C using an ice/salt bath. The Grignard solution prepared previously (14 mL, 0.36 M, 5.04 mmol, 1.1 equiv) was added dropwise to the reaction flask via cannula transfer over 20 min. The rate of addition was adjusted as needed such that the internal temperature did not exceed -3 °C. During the course of addition, the initially orange reaction mixture turned colorless, then yellow and eventually brown. Stirring was continued (below 0 °C) for 2 h. Full conversion was observed by TLC (hexanes/ CH_2Cl_2 , 90:10). The cold bath was removed, and the reaction was quenched by the addition of sat. aq. NH_4Cl (10 mL). The resulting biphasic mixture was stirred vigorously for 5 min and then partitioned between diethyl ether (50 mL) and water (50 mL). The layers were

separated, and the aqueous phase was extracted with diethyl ether (2 x 25-mL). The combined organic layers were washed with 1 M HCl (25 mL), sat. aq. NaHCO₃ (25 mL), and brine (25 mL), and then were dried over sodium sulfate, filtered, and concentrated (30 °C, 15 mmHg) to afford 1.1425 g of crude product as a hazy, pale yellow oil. The product was purified by chromatography (silica gel, 3 cm x 18 cm, dry load on Celite, 25 mL fractions, hexanes/CH₂Cl₂ gradient elution: 95:5 (300 mL) to 90:10 (300 mL)) to afford 887.9 mg (80%) of **3b** as a clear, colorless oil. Spectroscopic data for **3b** matched the literature values.¹⁷

Data for **3b**:

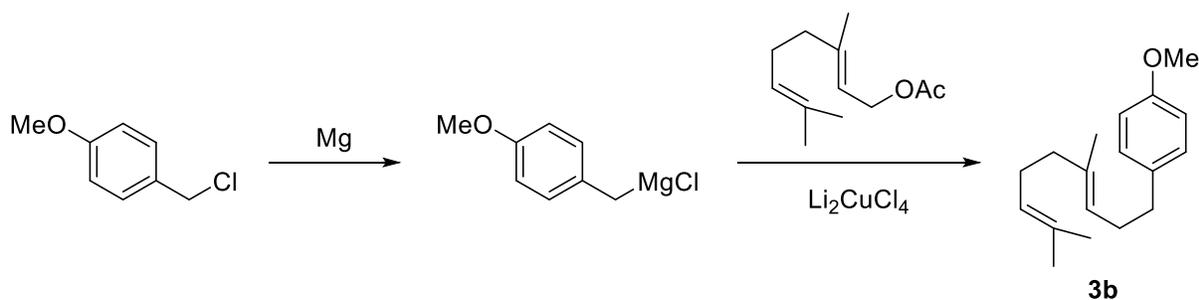
¹H NMR: (500 MHz, CDCl₃)

7.08 (app. s, 4H), 5.21-5.16 (m, 1H), 5.12-5.06 (m, 1H), 2.62-2.57 (m, 2H), 2.32 (s, 3H), 2.28 (q, *J* = 7.4 Hz, 2H), 2.06 (q, *J* = 7.0 Hz, 2H), 2.00-1.96 (m, 2H), 1.69 (s, 3H), 1.60 (s, 3H), 1.56 (s, 3H).

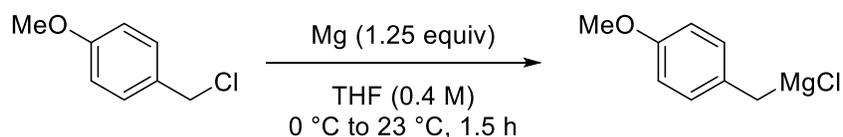
¹³C NMR: (126 MHz, CDCl₃)

139.50, 135.77, 135.19, 131.47, 129.04, 128.47, 124.50, 123.88, 39.86, 35.85, 30.25, 26.87, 25.85, 21.16, 17.84, 16.14.

(*E*)-1-(4,8-Dimethylnona-3,7-dien-1-yl)-4-methoxybenzene (3b**)**



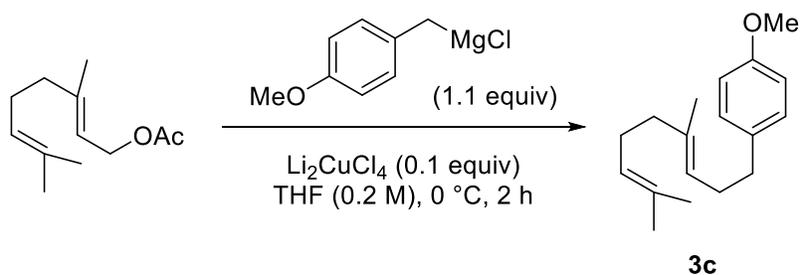
Preparation of (4-Methoxybenzyl)magnesium Chloride



A flame-dried, 100-mL, three-necked, round-bottomed flask equipped with a stir bar, argon inlet adapter, 25-mL addition funnel, temperature probe, and septum was charged with magnesium turnings (540.1 mg, 22.2 mmol, 1.25 equiv). The turnings were mechanically

activated immediately before use by grinding with a mortar and pestle for 10 min. The flask was again evacuated, flame-dried, and placed under argon. Once cool, the flask was charged with THF (30 mL) and a single drop of 1,2-dibromoethane. The mixture was stirred at 25 °C for 15 min and then cooled to 0 °C using an ice bath. The addition funnel was charged with 1-(chloromethyl)-4-methoxybenzene (2.41 mL, 2.78 g, 17.8 mmol) and THF (15 mL). This solution was added dropwise to the reaction flask at 0 °C over 30 min. The external ice bath was maintained throughout, but a slight exotherm (approx. 3 °C) was observed over the course of addition. The internal temperature was monitored, and it should not exceed 5 °C during the addition. A brown-black solution resulted over the course of addition. Once the addition was complete, the ice bath was removed and the mixture was allowed to warm to 25 °C. Stirring was continued for 1 h at 25 °C, and then the Grignard reagent was titrated in the manner described previously (pp. S4–S5). The concentration of (4-methoxybenzyl)magnesium chloride was determined to be 0.29 M (average of two runs; expected 0.40 M). The reagent was used immediately.

Preparation of (*E*)-1-(4,8-Dimethylnona-3,7-dien-1-yl)-4-methoxybenzene (**3c**)



This compound was synthesized by an analogous procedure to the one described by Corey et al.¹⁰ A flame-dried, 10-mL, Schlenk flask was charged with anhydrous lithium chloride (100.5 mg, 2.37 mmol, 0.2 equiv) and anhydrous copper(II) chloride (159.3 mg, 1.19 mmol, 0.1 equiv) inside a dry box. The flask was sealed, removed from the box, charged with THF (6 mL), and sonicated at 25 °C under argon for 15 min. An orange solution resulted, indicating formation of the desired Li_2CuCl_4 complex. A separate, flame-dried, 200-mL, Schlenk flask equipped with a stir bar and temperature probe was charged with geranyl acetate (2.54 mL, 2.33 g, 11.9 mmol, $D = 0.916 \text{ g/mL}$) and THF (20 mL). The resulting clear, colorless solution was cooled to 0 °C using an ice bath. The orange solution of the Li_2CuCl_4 complex was added dropwise to the

solution of geranyl acetate. The homogenous mixture was stirred at 0 °C for 10 min and then cooled to an internal temperature of -10 °C using an ice/salt bath. The Grignard solution prepared previously (43 mL, 0.29 M, 12.5 mmol, 1.05 equiv) was added dropwise to the reaction flask via cannula transfer over 20 min. The rate of addition was adjusted as needed such that the internal temperature did not exceed -3 °C. During the course of addition, the initially orange reaction mixture turned colorless, then yellow and eventually brown. Stirring was continued (below 0 °C) for 3 h. Full conversion was observed by TLC (hexanes/EtOAc, 80:20). The cold bath was removed, and the reaction was quenched by the addition of sat. aq. NH₄Cl (30 mL). The resulting biphasic mixture was stirred vigorously for 5 min and then partitioned between diethyl ether (100 mL) and water (100 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (2 x 50-mL). The combined organic layers were washed with 1 M HCl (50 mL), sat. aq. NaHCO₃ (50 mL), and brine (50 mL), and then were dried over sodium sulfate, filtered, and concentrated (30 °C, 15 mmHg) to afford 3.99 g of crude **3c**. The product was purified by chromatography (silica gel, 5 cm x 18 cm, 50-mL fractions, hexanes/Et₂O gradient elution: 98:2 (500 mL) to 96:4 (500 mL) to 94:6 (500 mL)) to afford **3c** contaminated with 4-methylanisole (from quenched Grignard reagent). This by-product was removed by drying the sample (120 °C, 0.1 mmHg) for 30 min to afford 2.9569 g (97%) of pure **3c** as a clear, colorless oil. Spectroscopic data for **3c** matched the literature values.¹⁷

Data for **3c**:

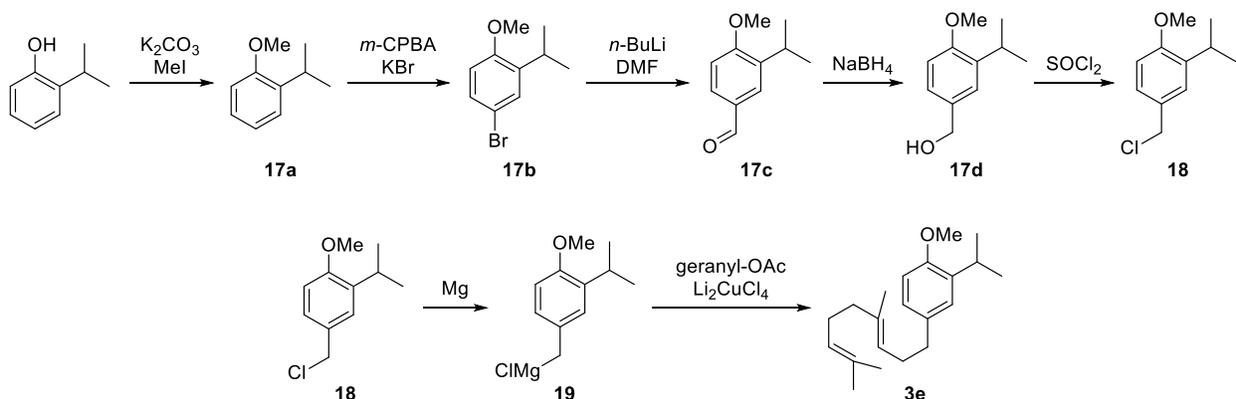
¹H NMR: (500 MHz, CDCl₃)

7.11 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 5.21-5.13 (m, 1H), 5.12-5.05 (m, 1H), 3.79 (s, 3H), 2.58 (app. t, 2H), 2.27 (q, *J* = 7.4 Hz, 2H), 2.10-2.03 (m, 2H), 2.01-1.94 (m, 2H), 1.69 (s, 3H), 1.61 (s, 3H), 1.55 (s, 3H).

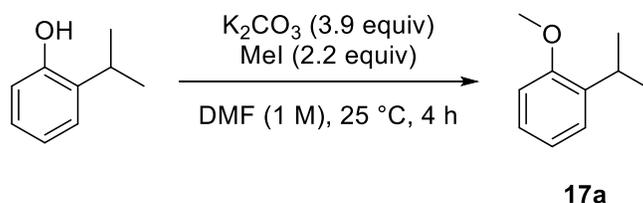
¹³C NMR: (126 MHz, CDCl₃)

157.66, 135.67, 134.55, 131.32, 129.33, 124.36, 123.67, 113.62, 55.26, 39.72, 35.21, 30.20, 26.72, 25.71, 17.70, 15.99.

Preparation of (*E*)-4-(4,8-Dimethylnona-3,7-dien-1-yl)-2-isopropyl-1-methoxybenzene (**3e**)



1-Isopropyl-2-methoxybenzene (**17a**)



The following is a modification of a published procedure.¹⁸ A 100-mL, round-bottomed flask equipped with a stir bar was charged with anhydrous K_2CO_3 (10.0 g, 72.4 mmol, 3.9 equiv) and DMF (20 mL). To the rapidly stirred suspension was added 2-isopropylphenol (2.5 mL, 2.5 g, 19 mmol) in one portion at 25 °C. A blue suspension was observed. Methyl iodide (2.5 mL, 5.7 g, 40 mmol, 2.2 equiv) was added in one portion at 25 °C and stirring was continued for 4 h at 25 °C under argon. A peach-yellow suspension was observed. Full conversion was observed by TLC (hexanes/EtOAc, 80:20). The mixture was diluted with hexanes (200 mL) and then washed with water (100 mL), 5% w/v aq. lithium chloride (3 x 100 mL), Claisen's alkali (2 x 100 mL), and brine (100 mL). The organic phase was dried over sodium sulfate, filtered, and concentrated (30 °C, 15 mmHg) to afford 2.56 g (92%) of **17a** as an orange oil requiring no further purification. Spectroscopic data matched those previously reported.¹⁸

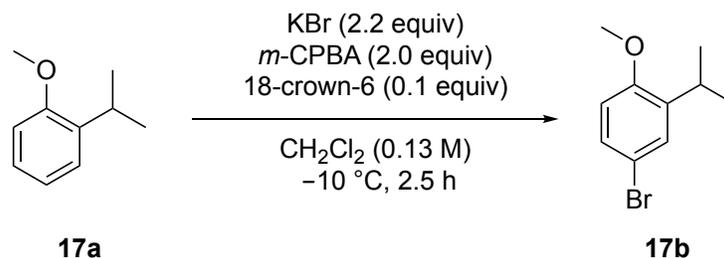
Data for **17a**:

¹H NMR: (500 MHz, CDCl_3)

7.21 (dd, $J = 7.5, 1.5$ Hz, 1H), 7.16 (td, $J = 8.0, 1.5$ Hz, 1H), 6.93 (t, $J = 7.5$ Hz,

1H), 6.85 (d, $J = 8.0$ Hz, 1H), 3.83 (s, 3H), 3.32 (hept, $J = 6.9$ Hz, 1H), 1.21 (d, $J = 6.9$ Hz, 6H).

4-Bromo-2-isopropyl-1-methoxybenzene (**17b**)

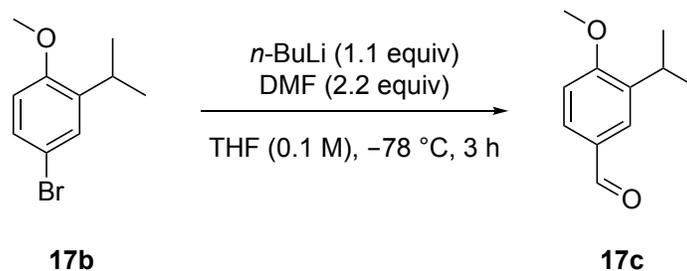


The following is a modification of a published procedure.^{18,19} A 300-mL, round-bottomed flask equipped with a stir bar was charged with potassium bromide (4.54 g, 38.2 mmol, 2.2 equiv) and CH₂Cl₂ (80 mL). The resulting colorless suspension was cooled to -10 °C with an ice/salt bath. To the flask were added 18-crown-6 (0.46 g, 1.7 mmol, 0.1 equiv) and *m*-CPBA (5.88 g, 34.1 mmol, 2.00 equiv), resulting in a bright orange suspension. The suspension was stirred for 1.5 h at -10 °C and developed a fine, thick consistency. An additional portion of CH₂Cl₂ (50 mL) was added to thin the suspension. 1-Isopropyl-2-methoxybenzene **17a** (2.56 g, 17.0 mmol) was added dropwise over 1 min at -10 °C. The resulting light yellow suspension was stirred for 1 h at -10 °C under argon. Full conversion was observed by TLC (hexanes/CH₂Cl₂, 90:10). The reaction was quenched by addition of sat. aq. Na₂S₂O₃ (80 mL) and sat. aq. NaHCO₃ (80 mL). The layers were separated, and the aqueous phase was extracted with CH₂Cl₂ (2 x 50 mL). The combined organic layers were washed with sat. aq. Na₂S₂O₃ (100 mL), sat. aq. NaHCO₃ (100 mL), and brine (100 mL), and then were dried over sodium sulfate, filtered, and concentrated (30 °C, 15 mmHg) to afford the crude product (5.16 g). The product was purified by column chromatography (silica gel, 5 x 13 cm, 50-mL fractions, hexanes/CH₂Cl₂ gradient elution: 95:5 (500 mL) to 90:10 (500 mL) to 85:15 (500 mL)) to afford 3.11 g (80%) of **17b** as a clear oil. Spectroscopic data matched those previously reported.^{18,19}

Data for **17b**:

¹H NMR: (500 MHz, CDCl₃)

7.28 (d, $J = 2.5$ Hz, 1H), 7.25 (dd, $J = 8.6, 2.5$ Hz, 1H), 6.71 (d, $J = 8.6$ Hz, 1H), 3.80 (s, 3H), 3.27 (hept, $J = 6.9$ Hz, 1H), 1.19 (d, $J = 6.9$ Hz, 6H).

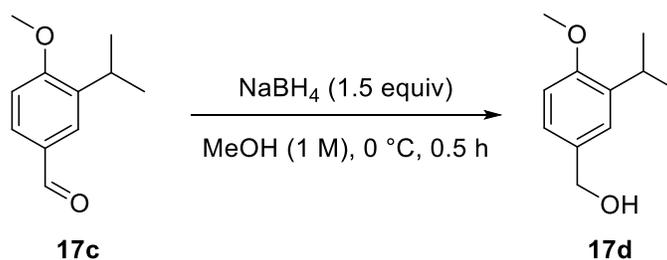
3-Isopropyl-4-methoxybenzaldehyde (17c)

The following is a modification of a published procedure.¹⁹ A flame-dried, 300-mL, two-necked, round-bottomed flask equipped with a stir bar, argon inlet adapter, temperature probe, and septum was charged with 4-bromo-2-isopropyl-1-methoxybenzene **17b** (3.11 g, 13.6 mmol) and THF (130 mL). The resulting colorless solution was cooled to -78 °C using a dry ice/acetone bath. A solution of *n*-butyllithium in hexanes (2.0 M, 7.2 mL, 1.1 equiv) was added dropwise over 5 min. The internal temperature did not exceed -70 °C. The resulting pale, yellow solution was stirred for 1 h at -78 °C. DMF (2.3 mL, 2.2 g, 29.8 mmol, 2.2 equiv) was added in one portion at -78 °C and stirring was continued for 2 h. A turbid, colorless solution resulted, and full conversion was observed by TLC (hexanes/EtOAc, 80:20). The mixture was warmed from -78 °C to -30 °C over 30 min and then quenched by pouring into ice-cold 5% (w/v) aq. NH₄Cl (200 mL). The mixture was diluted with Et₂O (100 mL) and the layers were separated. The aqueous phase was extracted with Et₂O (2 x 100 mL). The combined organic layers were washed with 5% w/v aq. lithium chloride (100 mL) and brine (100 mL), and then were dried over sodium sulfate, filtered, and concentrated (30 °C, 15 mmHg) to afford 2.575 g of the crude product as an orange oil. The product was purified by column chromatography (silica gel, 5 x 13 cm, 50-mL fractions, hexanes/EtOAc gradient elution: 95:5 (500 mL) to 90:10 (500 mL) to 85:15 (500 mL)) to afford 2.19 g (91%) of **17c** as a pale, yellow oil. Spectroscopic data matched those previously reported.¹⁹

Data for 17c:

¹H NMR: (500 MHz, CDCl₃)

9.88 (s, 1H), 7.77 (d, *J* = 2.0 Hz, 1H), 7.71 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 3.92 (s, 3H), 3.33 (hept, *J* = 6.9 Hz, 1H), 1.24 (d, *J* = 6.9 Hz, 6H).

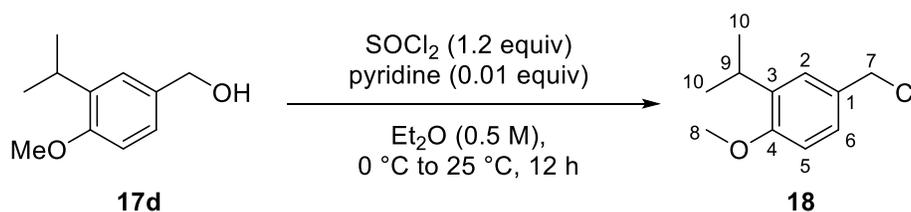
3-Isopropyl-4-methoxybenzyl alcohol (17d)

The following is a modification of a published procedure.¹⁹ A flame-dried, 100-mL, round-bottomed flask equipped with a stir bar was charged with 3-isopropyl-4-methoxybenzaldehyde **17c** (2.19 g, 12.3 mmol) and methanol (12.3 mL). The resulting pale, yellow solution was cooled to 0 °C. Sodium borohydride (0.68 g, 18.0 mmol, 1.5 equiv) was added in three portions over 1 min. Significant gas evolution was observed. The mixture was stirred at 0 °C for 30 min under argon. Full conversion was observed by TLC (hexanes/EtOAc, 80:20). The reaction was quenched by the cautious addition of sat. aq. NH₄Cl (12 mL). Methanol was removed by rotary evaporation (35 °C, 15 mmHg) and the residual aqueous phase was diluted with water (50 mL) and CH₂Cl₂ (50 mL). The layers were separated, and the aqueous phase was extracted with CH₂Cl₂ (2 x 50 mL). The combined organic layers were washed with brine (50 mL) and then were dried over sodium sulfate, filtered, and concentrated to afford 2.15 g (97%) of **17d** as a pale, yellow oil requiring no further purification. Spectroscopic data matched those previously reported.¹⁹

Data for 17d:

¹H NMR: (500 MHz, CDCl₃)

7.22 (d, *J* = 2.1 Hz, 1H), 7.16 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.83 (d, *J* = 8.3 Hz, 1H), 4.62 (d, *J* = 5.9 Hz, 2H), 3.83 (s, 3H), 3.32 (hept, *J* = 6.9 Hz, 1H), 1.49 (t, *J* = 5.9 Hz, 1H), 1.22 (d, *J* = 6.9 Hz, 6H).

3-Isopropyl-4-methoxybenzyl Chloride (18)

A flame-dried, 200-mL, three-necked, round-bottomed flask equipped with a stir bar, argon inlet adapter, temperature probe, and two septa was charged with benzylic alcohol **17d** (4.92 g, 27.3 mmol) and diethyl ether (55 mL, 0.5 M) to form a pale yellow solution. Pyridine (22 μL , 0.273 mmol, 0.01 equiv) was added to the flask, and the solution was cooled to an internal temperature of -3 °C using an ice/salt bath. Neat thionyl chloride (2.39 mL, 32.8 mmol, 1.2 equiv) was added dropwise to the flask over 15 min, making sure to maintain the internal temperature below 0 °C, resulting in a thin, white suspension. After addition was complete, the mixture was allowed to slowly warm to 25 °C, and then stirring was continued at 25 °C for 10 h. A turbid, colorless solution resulted. Full conversion was observed by TLC (hexanes/EtOAc, 80:20). The reaction was quenched by the addition of water (50 mL) and was stirred vigorously for 2 min. The resulting biphasic mixture was transferred to a 500-mL separatory funnel and the layers were separated. The aqueous layer was extracted with diethyl ether (2 x 50 mL). The combined organic layers were washed with sat. aq. sodium bicarbonate (1 x 100 mL – *caution* gas evolution observed) and brine (1 x 100 mL), then dried over sodium sulfate, filtered, and concentrated (30 °C, 15 mmHg) to afford a thin yellow oil (4.88 g). The product was further purified by Kugelrohr distillation (110 °C, 0.1 mmHg) to afford 4.34 g (80%) of **18** as a clear, colorless liquid.

Data for 18:

b.p.: 110 °C (ABT, 0.1 mmHg)

^1H NMR: (500 MHz, CDCl_3)

7.22 (d, $J = 2.3$ Hz, 1H, HC(2)), 7.19 (dd, $J = 8.3, 2.3$ Hz, 1H, HC(6)), 6.81 (d, $J = 8.3$ Hz, 1H, HC(5)), 4.58 (s, 2H, $\text{H}_2\text{C}(7)$), 3.83 (s, 3H, $\text{H}_3\text{C}(8)$), 3.30 (hept, $J = 6.9$ Hz, 1H, HC(9)), 1.21 (d, $J = 6.9$ Hz, 6H, $\text{H}_3\text{C}(10)$).

^{13}C NMR: (126 MHz, CDCl_3)

157.1 (C(4)), 137.6 (C(3)), 129.6 (C(1)), 127.2 (HC(6)), 126.9 (HC(2)), 110.5 (HC(5)), 55.6 ($\text{H}_3\text{C}(8)$), 47.0 ($\text{H}_2\text{C}(7)$), 26.9 (HC(9)), 22.7 ($\text{H}_3\text{C}(10)$).

IR: (neat)

2960 (w), 2869 (w), 2837 (w), 1608 (w), 1498 (m), 1463 (m), 1443 (w), 1383 (w), 1362 (w), 1348 (w), 1293 (w), 1246 (s), 1187 (w), 1171 (m), 1158 (w), 1116 (w), 1089 (m), 1032 (m), 941 (w), 893 (w), 866 (w), 812 (m), 750 (w), 688 (m), 597 (m), 472 (m)

LRMS: (EI, 70 eV)

51.0 (2), 74.0 (3), 77.0 (4), 78.0 (2), 79.0 (2), 91.0 (5), 103.0 (3), 105.0 (2), 115.0 (5), 116.0 (2), 117.0 (9), 131.0 (2), 133.0 (10), 134.0 (2), 147.0 (9), 148.0 (6), 149.0 (2), 163.0 (100), 164.1 (13), 183.0 (30), 184.0 (3), 185.0 (10), 198.0 (25), 199.0 (3), 200.0 (8).

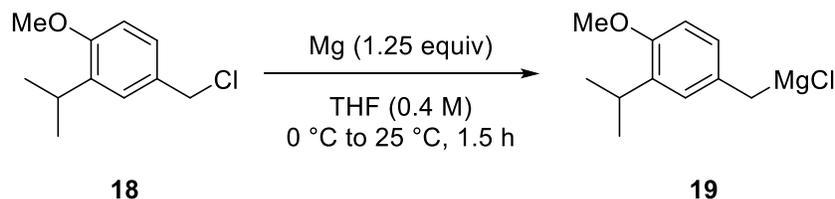
Analysis: C₁₁H₁₅ClO (198.69)

Calcd: C, 66.50%; H, 7.61%

Found: C, 66.41%; H, 7.43%

TLC: *R_f* 0.54 (silica gel, hexanes/EtOAc, 80:20, UV)

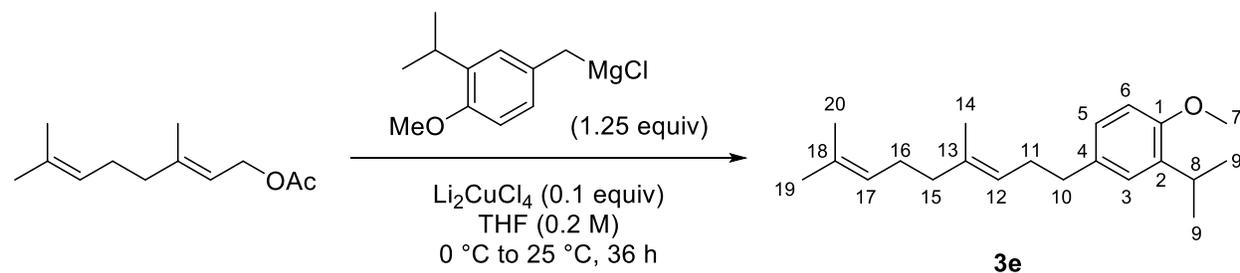
(3-Isopropyl-4-methoxybenzyl)magnesium Chloride (**19**)



A flame-dried, 50-mL, two-necked, round-bottomed flask equipped with a stir bar, temperature probe, septum, and argon inlet adapter was charged with magnesium turnings (177.8 mg, 7.32 mmol, 1.23 equiv). The turnings were mechanically activated immediately before use by grinding with a mortar and pestle for 10 min. The flask was charged with THF (10 mL) and 1 drop of 1,2-dibromoethane as initiator. The mixture was stirred at 25 °C for 15 min and then cooled to 0 °C. A flame-dried, 15-mL, tear-drop flask was charged with 4-(chloromethyl)-2-isopropyl-1-methoxybenzene (1.18 g, 5.93 mmol) and THF (5 mL) to form a colorless solution. The solution was taken up in a 10-mL Leur-Lock plastic syringe and added dropwise to the reaction flask over 30 min using a syringe pump. The internal temperature was monitored throughout, and the temperature was observed to rise from 0.5 °C to nearly 3.0 °C over the

course of addition (external ice bath was maintained throughout). A pale orange color resulted. The ice bath was removed and the mixture was stirred at 25 °C for 1 h. The Grignard reagent was titrated as described previously (pp. S4–S5). The concentration of (3-isopropyl-4-methoxybenzyl)magnesium chloride **19** was determined to be 0.33 M (average of two runs, theoretical = 0.395 M).

(E)-4-(4,8-Dimethylnona-3,7-dien-1-yl)-2-isopropyl-1-methoxybenzene (3e)



A flame-dried, 5-mL, Schlenk flask was charged with anhydrous lithium chloride (32.0 mg, 0.77 mmol, 0.2 equiv) and anhydrous copper(II) chloride (51.0 mg, 0.38 mmol, 0.1 equiv) inside of a glove box. The flask was sealed, removed from the glove box, and charged with THF (2 mL). The resulting mixture was sonicated for 15 min under argon at 25 °C, resulting in an orange solution indicative of the Li_2CuCl_4 complex. A separate, flame-dried, 100-mL, three-necked round-bottomed flask equipped with a stir bar, thermocouple probe, argon inlet adapter, and two septa was charged with geranyl acetate (0.82 mL, 0.75 g, 3.83 mmol) and THF (7 mL) and was cooled to 0 °C. The Li_2CuCl_4 solution prepared previously was added to the geranyl acetate solution at 0 °C in one portion. The orange solution was stirred at 0 °C for 10 min and then was cooled further to an internal temperature of –7 °C using an ice/salt bath. The previously prepared solution of (3-isopropyl-4-methoxybenzyl)magnesium chloride **19** (14 mL of 0.33 M solution, 4.6 mmol, 1.2 equiv) was added dropwise over 15 min to the reaction mixture via cannula transfer, taking care to maintain the internal temperature of the reaction flask below –5 °C. Over the course of the addition, the initially orange solution briefly became colorless, then gradually turned yellow and finally brown. Stirring was continued at 0 °C for 1 h, at which point the reaction was judged to be complete by TLC (hexanes/ Et_2O , 9:1). The reaction was quenched by the addition of sat. aq. ammonium chloride (approx. 25 mL) in one portion. The mixture was poured into a 125-mL separatory funnel (rinsing with small amounts of ether and water) and the layers were separated. The aqueous layer was extracted with ether (2 x 25 mL). The combined

organic layers were washed with 1 M aq. HCl (25 mL), sat. aq. NaHCO₃ (25 mL), and brine (25 mL), then dried over sodium sulfate, filtered, and concentrated (30 °C, 15 mmHg) to afford the crude product (1.39 g). The product was first purified by chromatography (silica gel, 4 x 18 cm, dry load on Celite, 25-mL fractions, hexanes/CH₂Cl₂ gradient elution: 97.5:2.5 (300 mL) to 95:5 (300 mL) to 92.5:7.5 (300 mL) to 90:10 (300 mL) to 87.5:12.5 (300 mL) to 85:15 (300 mL) to 82.5:17.5 (300 mL) to 80:20 (300 mL)) to afford **3e** as a clear oil (1.10 g) which is contaminated with 4-methyl-2-isopropylanisole (resulting from quenched Grignard reagent). The product was further purified by Kugelrohr distillation in two stages. Initially, the bulk material was heated to 95 °C (0.1 mmHg) without cooling for 30 min. All of the more volatile 4-methyl-2-isopropylanisole was removed under these conditions. Subsequently, the collection bulb was changed and the desired product was distilled at 180 °C (0.1 mmHg) to afford 1.00 g (87%) of analytically pure **3e** as a clear, colorless oil.

Data for 3e:

b.p.: 180 °C (ABT, 0.1 mmHg)

¹H NMR: (500 MHz, CDCl₃)

7.02 (d, *J* = 2.2 Hz, 1H, HC(3)), 6.97 (dd, *J* = 8.2, 2.2 Hz, 1H, HC(5)), 6.76 (d, *J* = 8.2 Hz, 1H, HC(6)), 5.24-5.16 (m, 1H, HC(12)), 5.15-5.05 (m, 1H, HC(17)), 3.80 (s, 3H, H₃C(7)), 3.29 (hept, *J* = 6.9 Hz, 1H, HC(8)), 2.63-2.53 (m, 2H, H₂C(10)), 2.28 (q, *J* = 7.4 Hz, 2H, H₂C(11)), 2.07 (q, *J* = 7.1 Hz, 2H, H₂C(16)), 2.01-1.93 (m, 2H, H₂C(15)), 1.69 (s, 3H, H₃C(19)), 1.60 (s, 3H, H₃C(20)), 1.56 (s, 3H, H₃C(14)), 1.21 (d, *J* = 6.9 Hz, 6H, H₃C(9)).

¹³C NMR: (126 MHz, CDCl₃)

155.02 (C(1)), 136.79 (C(2)), 135.67 (C(13)), 134.50 (C(4)), 131.46 (C(18)), 126.36 (HC(3)), 126.24 (HC(5)), 124.53 (HC(17)), 123.99 (HC(12)), 110.40 (HC(6)), 55.65 (H₃C(7)), 39.88 (H₂C(15)), 35.65 (H₂C(10)), 30.42 (H₂C(11)), 26.92 (H₂C(16)), 26.85 (HC(8)), 25.86 (H₃C(19)), 22.92 (H₃C(9)), 17.84 (H₃C(20)), 16.18 (H₃C(14)).

IR: (neat)

2961 (m), 2923 (m), 1609 (w), 1497 (s), 1443 (m), 1381 (w), 1361 (w), 1348 (w), 1290 (w), 1243 (s), 1170 (m), 1154 (w), 1090 (m), 1037 (m), 888 (w), 807 (m), 744 (w), 633 (w), 583 (w).

LRMS: (EI, 70 eV)

69.1 (7), 91.0 (4), 115.0 (3), 117.1 (5), 133.1 (8), 147.1 (4), 148.1 (7), 149.1 (4),
161.1 (3), 163.1 (100), 164.1 (35), 176.1 (20), 177.1 (4), 300.2 (12), 301.2 (3)

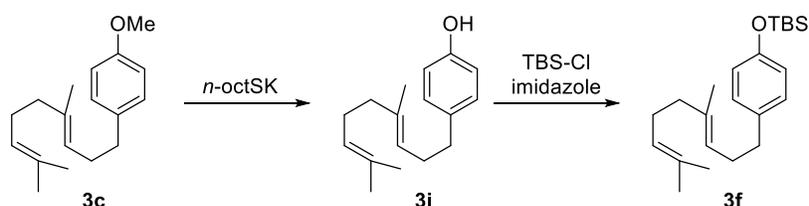
Analysis: C₂₁H₃₂O (300.49)

Calcd: C, 83.94%; H, 10.73%

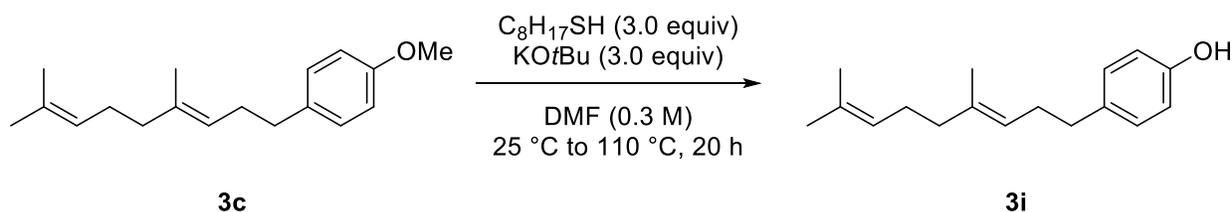
Found: C, 83.78%; H, 10.52%

TLC: *R_f* 0.29 (silica gel, hexanes/CH₂Cl₂, 90:10, UV/CAM)

(*E*)-tert-Butyl(4-(4,8-dimethylnona-3,7-dien-1-yl)phenoxy)dimethylsilane (3f)



(*E*)-4-(4,8-Dimethylnona-3,7-dien-1-yl)phenol (3i)



A flame-dried, 50-mL, two-necked, round-bottomed flask equipped with a stir bar and two septa was charged with potassium *tert*-butoxide (0.65 g, 5.82 mmol, 3.0 equiv) inside of a dry box and sealed with a septum. The flask was removed from the dry box and fitted with a reflux condenser and argon inlet adapter. The system was briefly evacuated and then placed under argon. The flask was charged with DMF (6.5 mL) through the septum. The potassium *tert*-butoxide dissolved with stirring to afford a pale yellow solution. To this solution, 1-octanethiol (1.0 mL, 0.85 g, 5.82 mmol, 3.0 equiv) was added dropwise over 5 min at 25 °C using a syringe. A thick, white suspension resulted, and a slight exotherm was observed. The suspension was stirred at 25 °C for 20 min. Next, (*E*)-4-homogeranylanisole **3c** (501.0 mg, 1.94 mmol) was added dropwise over 5 min at 25 °C using a syringe. The suspension was heated to 110 °C (oil

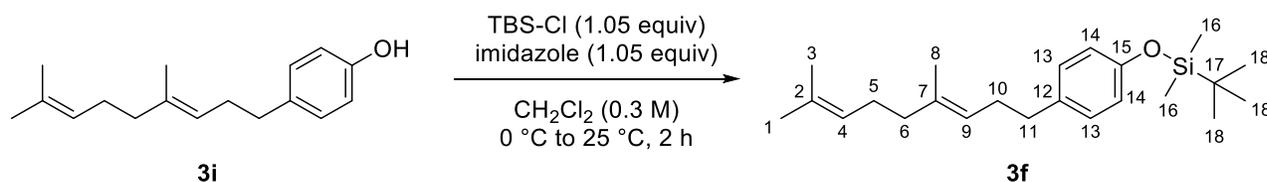
bath) for 20 h. Conversion was assessed periodically by TLC (hexanes/EtOAc, 80:20). Upon completion, the reaction mixture was cooled to 25 °C and poured into water (25 mL), which resulted in a white suspension. The mixture was acidified by the dropwise addition of 6 M HCl (1 mL), transferred to a 125-mL separatory funnel, and extracted ether (3 x 25 mL). The combined ethereal extracts were washed with a 5% (w/v) aq. lithium chloride solution (4 x 25 mL) and then dried over sodium sulfate, filtered, and concentrated (30 °C, 15 mmHg) to afford the crude product as a yellow liquid (1.28 g). The product was purified by chromatography (silica gel, 4 x 17 cm, dry load on Celite, 25-mL fractions, hexanes/EtOAc gradient elution: 95:5 (400 mL) to 90:10 (300 mL) to 85:15 (300 mL)) to afford 391.5 mg (83% yield) of **3i** as a pale yellow oil. Spectroscopic data were identical to those reported by Yamamoto et al. using sodium ethanethiolate for the demethylation.²⁰ The procedure described above, while slower, is preferred as 1-octanethiol is less odorous than ethanethiol and is more easily separated from the product.

Data for 3i:

¹H NMR: (500 MHz, CDCl₃)

7.05 (d, *J* = 8.5 Hz, 2H), 6.74 (d, *J* = 8.5 Hz, 2H), 5.19-5.14 (m, 1H), 5.11-5.06 (m, 1H), 4.51 (s, 1H), 2.59-2.54 (m, 2H), 2.26 (q, *J* = 7.5 Hz, 2H), 2.08-2.02 (m, 2H), 2.00-1.95 (m, 2H), 1.68 (s, 3H), 1.60 (s, 3H), 1.54 (s, 3H).

(*E*)-*tert*-Butyl(4-(4,8-dimethylnona-3,7-dien-1-yl)phenoxy)dimethylsilane (3f)



A flame-dried, two-necked, 25-mL, round-bottomed flask equipped with a stir bar, septum, and argon inlet adapter was charged with 4-homogeranylphenol **3i** (388.4 mg, 1.59 mmol) and dichloromethane (5 mL, 0.3 M). The resulting pale yellow solution was cooled to an internal temperature of 0 °C using an external ice bath. Imidazole (115.2 mg, 1.67 mmol, 1.05 equiv) was added as a solid all at once at 0 °C, immediately followed by *tert*-butyldimethylsilyl chloride (253.9 mg, 1.67 mmol, 1.05 equiv) as a solid all at once. The imidazole dissolved, but addition of *tert*-butyldimethylsilyl chloride resulted in a white/off-white suspension. The ice bath

was removed and the reaction was allowed to warm gradually to 25 °C. Stirring was continued for 2 h at 25 °C. Conversion was followed by TLC (hexanes/Et₂O, 90:10). After 2 h, essentially full conversion was observed, and the reaction was quenched by the addition of water (10 mL) which resulted in a clear biphasic mixture. The mixture was transferred to a 60-mL separatory funnel, and the layers were separated. The aqueous layer was extracted with dichloromethane (2 x 10 mL). The combined organic layers were washed with brine (1 x 20 mL), dried over sodium sulfate, filtered, and concentrated (30 °C, 15 mmHg) to afford the crude product (0.56 g) as a yellow oil. The product was purified by chromatography (silica gel, 3 x 18 cm, dry load on Celite, 25-mL fractions, hexanes/Et₂O gradient elution: 98:2 (300 mL) to 96:4 (300 mL)) to afford 490.9 mg (86%) of **3f** as a clear, colorless oil. The product was purified to an analytical standard by Kugelrohr distillation (180 °C ABT, 0.1 mmHg) to afford 470.8 mg (83%) of **3f** as a clear, colorless oil.

Data for 3f:

b.p.: 180 °C (ABT, 0.1 mmHg)

¹H NMR: (500 MHz, CDCl₃)

7.03 (d, *J* = 8.4 Hz, 2H, HC(13)), 6.74 (d, *J* = 8.4 Hz, 2H, HC(14)), 5.20-5.14 (m, 1H, HC(9)), 5.09 (tt, *J* = 7.0, 1.3 Hz, 1H, HC(4)), 2.56 (t, *J* = 7.4 Hz, 2H, H₂C(11)), 2.26 (q, *J* = 7.4 Hz, 2H, H₂C(10)), 2.05 (q, *J* = 7.0 Hz, 2H, H₂C(5)), 2.01-1.93 (m, 2H, H₂C(6)), 1.69 (s, 3H, H₃C(1)), 1.60 (s, 3H, H₃C(3)), 1.53 (s, 3H, H₃C(8)), 0.98 (s, 9H, H₃C(18)), 0.18 (s, 6H, H₃C(16)).

¹³C NMR: (125 MHz, CDCl₃)

153.7 (C(15)), 135.8 (C(7)), 135.3 (C(12)), 131.5 (C(2)), 129.4 (HC(13)), 124.5 (HC(4)), 123.8 (HC(9)), 119.9 (HC(14)), 39.9 (H₂C(6)), 35.4 (H₂C(11)), 30.3 (H₂C(10)), 26.9 (H₂C(5)), 25.9 (H₃C(18)), 25.8 (H₃C(1)), 18.4 (C(17)), 17.8 (H₃C(3)), 16.1 (H₃C(8)), -4.3 (H₃C(16)).

IR: (neat)

2958 (w), 2929 (m), 2857 (w), 1609 (w), 1509 (s), 1472 (w), 1463 (w), 1376 (w), 1362 (w), 1251 (s), 1168 (w), 1101 (w), 1006 (w), 913 (s), 836 (s), 809 (m), 779 (s), 688 (w), 657 (w), 546 (w)

LRMS: (EI, 70 eV)

69.1 (7), 73.1 (15), 91.1 (4), 107.1 (3), 149.0 (7), 163.1 (3), 164.1 (10), 165.1

(21), 166.1 (4), 177.1 (2), 205.1 (2), 221.1 (100), 222.1 (34), 223.1 (9), 234.1 (9), 235.1 (2), 358.3 (7), 359.3 (2)

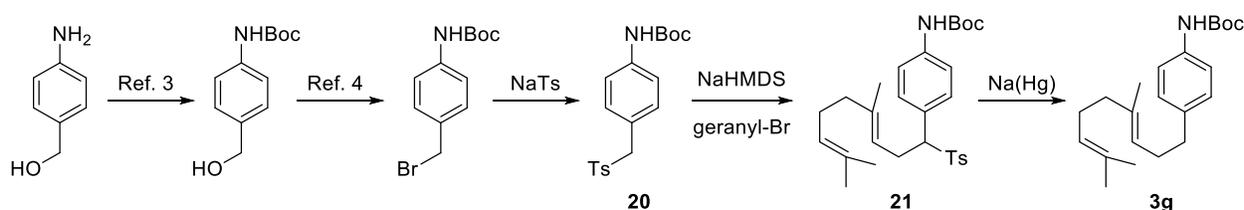
Analysis: C₂₃H₃₈OSi (358.64)

Calcd: C, 77.03%; H, 10.68%

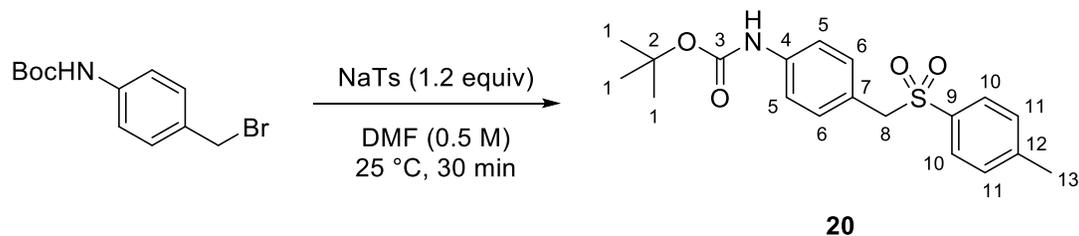
Found: C, 76.69%; H, 10.61%

TLC: R_f 0.82 (silica gel, hexanes/Et₂O, 90:10, KMnO₄)

***tert*-Butyl (*E*)-(4-(4,8-Dimethylnona-3,7-dien-1-yl)phenyl)carbamate (3g)**



***tert*-Butyl (4-(4-Methylphenylsulfonylmethyl)phenyl)carbamate (20)**



A flame-dried, 10-mL, round-bottomed flask equipped with a stir bar and argon inlet adapter was charged with *tert*-butyl 4-(bromomethyl)phenylcarbamate (429.5 mg, 1.50 mmol) and DMF (3 mL, 0.5 M). A pale-yellow solution resulted. Sodium *p*-toluenesulfinate (321.7 mg, 1.81 mmol, 1.2 equiv) was added in one portion at 25 °C. The heterogeneous mixture was stirred at 25 °C for 30 min, during which time most of the solid dissolved, ultimately resulting in a turbid, yellow solution. Consumption of starting material was confirmed by TLC (hexanes/EtOAc, 50:50). The solution was poured into a 125-mL separatory funnel containing water (50 mL). Residual material in the flask was rinsed in with ethyl acetate (25 mL). This initially resulted in an emulsion, but the layers separated upon standing. The aqueous phase was extracted with ethyl acetate (2 x 25 mL). The combined organic layers were washed with a 5% (w/v) aq. lithium chloride solution (3 x 25 mL), then dried over sodium sulfate, filtered, and

concentrated (30 °C, 15 mmHg) to afford the crude product (482.9 mg) as an off-white solid. The product was purified by trituration as follows. The crude material was suspended in a mixture of 1:1 EtOAc:hexanes (10 mL) and sonicated for 30 min at 25 °C. Vacuum filtration of this suspension yielded 225.5 mg (42%) of analytically pure **20** as a fine white solid. Yields are variable, ranging from 42% to 59%.

Data for **20**:

m.p.: 203–204 °C (d)

¹H NMR: (500 MHz, acetone-*d*₆)

8.44 (bs, 1H, NH), 7.57 (d, *J* = 8.2 Hz, 2H, HC(10)), 7.47 (d, *J* = 8.6 Hz, 2H, HC(5)), 7.37 (d, *J* = 8.2 Hz, 2H, HC(11)), 7.06 (d, *J* = 8.6 Hz, 2H, HC(6)), 4.40 (s, 2H, H₂C(8)), 2.42 (s, 3H, H₃C(13)), 1.48 (s, 9H, H₃C(1)).

¹³C NMR: (126 MHz, acetone-*d*₆)

153.58 (C(3)), 145.25 (C(12)), 140.87 (C(4)), 137.10 (C(9)), 132.24 (HC(6)), 130.30 (HC(11)), 129.38 (HC(10)), 123.52 (C(7)), 118.54 (HC(5)), 80.15 (C(2)), 62.15 (H₂C(8)), 28.50 (H₃C(1)), 21.49 (H₃C(13)).

IR: (neat)

3383 (w), 2982 (w), 1707 (m), 1615 (w), 1595 (w), 1522 (m), 1508 (m), 1416 (m), 1372 (w), 1314 (m), 1301 (m), 1259 (w), 1234 (m), 1146 (s), 1084 (m), 1056 (m), 1019 (w), 910 (w), 834 (m), 818 (m), 771 (w), 744 (m), 712 (m), 666 (s), 643 (m), 629 (w), 590 (w), 549 (s), 519 (s), 503 (w).

LRMS: (EI, 70 eV)

55.1 (11), 56.1 (6), 57.1 (39), 60.1 (8), 69.1 (18), 71.1 (8), 73.0 (10), 77.0 (7), 81.1 (8), 83.1 (7), 85.1 (6), 91.0 (14), 97.1 (6), 105.1 (6), 106.1 (73), 107.1 (6), 129.1 (8), 132.0 (36), 133.0 (6), 141.1 (8), 150.0 (100), 151.0 (10), 163.1 (65), 164.1 (7), 206.1 (66), 207.1 (11), 256.2 (7), 361.1 (2).

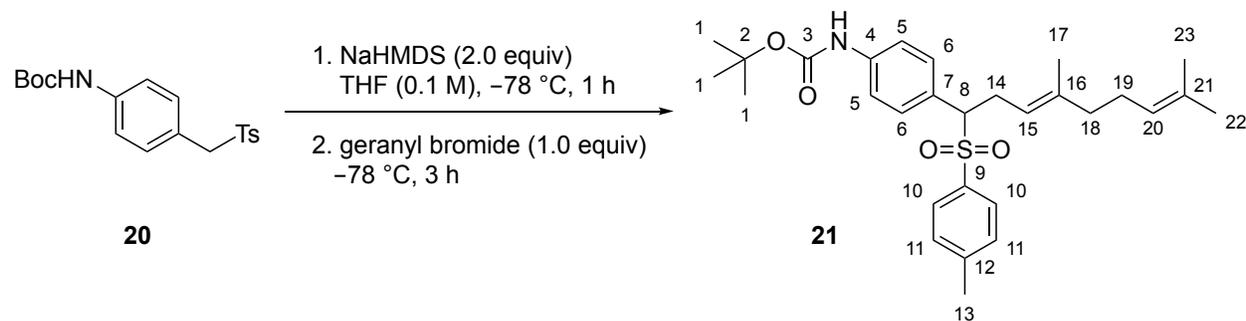
Analysis: C₁₉H₂₃NO₄S (361.46)

Calcd: C, 63.13%; H, 6.41%; N, 3.88%

Found: C, 62.80%; H, 6.38%; N, 3.90%

TLC: *R*_f 0.46 (silica gel, hexanes/EtOAc, 50:50, UV)

Preparation of *tert*-Butyl (*E*)-(4-(4,8-Dimethyl-1-(4-methylphenylsulfonyl) nona-3,7-dien-1-yl)phenyl)carbamate (21**)**



A flame-dried, 50-mL, three-necked, round-bottomed flask equipped with a stir bar, argon inlet adapter, temperature probe, and two septa was charged with *tert*-butyl (4-(4-methylphenylsulfonylmethyl)phenyl)carbamate **20** (452.0 mg, 1.25 mmol) and THF (12 mL). The resulting clear, colorless solution was cooled to $-78\text{ }^{\circ}\text{C}$ using a dry ice/acetone bath. Sodium hexamethyldisilazide (1.0 M solution in THF, 3.0 mL, 3.00 mmol, 2.40 equiv) was added dropwise over 5 min at $-78\text{ }^{\circ}\text{C}$. **Note:** Two equivalents of base are required in this case, due to the presence of the acidic N-H proton. The solution immediately turned bright yellow, and some orange precipitate was observed to form. Approximately halfway through the addition, more orange precipitate was observed, such that the appearance of the reaction was a bright-orange suspension. Stirring was continued at $-78\text{ }^{\circ}\text{C}$ for 1 h. Subsequently, a solution of geranyl bromide (333.6 mg, 1.54 mmol, 1.23 equiv) in THF (5 mL) was added dropwise at $-78\text{ }^{\circ}\text{C}$ over 20 min. The internal temperature was monitored throughout, and the rate of addition was maintained such that the internal temperature did not exceed $-70\text{ }^{\circ}\text{C}$. The reaction mixture lightened to an orange/yellow solution. Stirring was continued at $-78\text{ }^{\circ}\text{C}$ for 3 h. Full conversion was observed by TLC (hexanes/EtOAc, 80:20). The reaction was quenched by the addition of sat. aq. sodium bicarbonate (25 mL) all at once with rapid stirring. The cold bath was removed, and the resulting pale-yellow suspension was allowed to warm to $25\text{ }^{\circ}\text{C}$. The mixture was transferred to a 125-mL separatory funnel, rinsing with water (25 mL) and ethyl acetate (25 mL). The layers were separated, and the aqueous phase was extracted with ethyl acetate (2 x 25 mL). The combined organic phases were washed with brine (25 mL), dried over sodium sulfate, filtered, and concentrated ($30\text{ }^{\circ}\text{C}$, 15 mmHg) to afford the crude product (0.62 g). The crude mixture was purified by chromatography (silica gel, 3 x 17 cm, dry load on Celite, 25-mL fractions, hexanes/EtOAc gradient elution: 90:10 (300 mL) to 80:20 (300 mL) to 70:30 (300 mL)

to 60:40 (300 mL)) to afford 521.5 mg (84%) of **21** as an off-white solid. At this point, the level of purity is sufficient for the next step. But to obtain an analytically pure sample, the product was recrystallized from ethyl acetate/hexanes. The product was dissolved in a minimal amount of hot ethyl acetate (10 mL) and subsequently treated with hot hexanes (10 mL). The pale yellow solution was allowed to cool slowly to 25 °C. A seed crystal was added (these are typically obtained by allowing the column fractions to stand uncovered for several hours and then collecting the resulting crystals by vacuum filtration), and the flask was capped and placed in a –20 °C freezer for 12 h. The resulting white crystals were collected by vacuum filtration, rinsing with cold hexanes/EtOAc 50:50 (5 mL). The crystals were air-dried for 1 h and then dried under high vacuum (0.1 mmHg) for 12 h to afford 235.5 mg (38%) of analytically pure **21**.

Data for **21**:

m.p.: 145–146 °C (d)

¹H NMR: (500 MHz, CDCl₃)

7.43 (d, $J = 8.1$ Hz, 2H, HC(10)), 7.23 (d, $J = 8.6$ Hz, 2H, HC(5)), 7.18 (d, $J = 8.1$ Hz, 2H, HC(11)), 7.02 (d, $J = 8.6$ Hz, 2H, HC(6)), 6.47 (bs, 1H, NH), 4.92-4.86 (m, 1H, HC(20)), 4.84-4.75 (m, 1H, HC(15)), 3.95 (dd, $J = 11.7, 3.7$ Hz, 1H, HC(8)), 3.10 (ddd, $J = 14.4, 6.9, 3.7$ Hz, 1H, H₂C(14)), 2.76 (ddd, $J = 14.4, 11.7, 6.9$ Hz, 1H, H₂C(14)), 2.39 (s, 3H, H₃C(13)), 1.99-1.86 (m, 2H, H₂C(19)), 1.85-1.80 (m, 2H, H₂C(18)), 1.59 (s, 3H, H₃C(22)), 1.54 (s, 3H, H₃C(17)), 1.51 (s, 12H, H₃C(23) and H₃C(1)).

¹³C NMR: (126 MHz, CDCl₃)

152.58 (C(3)), 144.45 (C(12)), 138.84 (C(4)), 138.75 (C(16)), 134.65 (C(9)), 131.56 (C(21)), 130.83 (HC(6)), 129.43 (HC(11)), 129.22 (HC(10)), 126.68 (C(7)), 123.98 (HC(20)), 118.86 (HC(15)), 117.96 (HC(5)), 80.88 (C(2)), 71.01 (HC(8)), 39.66 (H₂C(18)), 28.47 (H₃C(1)), 26.59 (H₂C(14)), 26.51 (H₂C(19)), 25.76 (H₃C(22)), 21.77 (H₃C(13)), 17.79 (H₃C(23)), 16.38 (H₃C(17)).

IR: (neat)

3388 (w), 2983 (w), 2918 (w), 1698 (m), 1614 (w), 1592 (w), 1523 (m), 1507 (m), 1447 (w), 1417 (m), 1392 (w), 1367 (w), 1315 (m), 1299 (m), 1269 (w), 1235 (m), 1143 (s), 1084 (m), 1057 (m), 1020 (m), 945 (w), 902 (w), 841 (m), 814 (m), 776 (w), 754 (w), 732 (w), 711 (m), 667 (s), 598 (s), 572 (s), 554 (m),

517 (m).

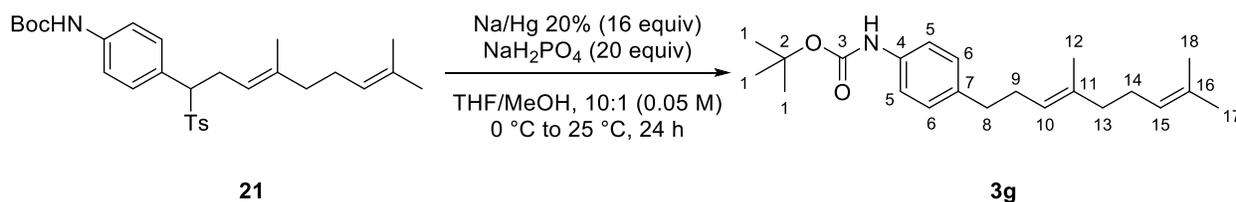
LRMS: (ESI, [M+Na]⁺)

138.6 (2), 235.8 (7), 285.9 (6), 342.0 (7), 498.0 (2), 515.1 (4), 520.0 (100), 521.0 (33), 522.0 (10), 536.0 (4), 577.9 (2).

Analysis: C₂₉H₃₉NO₄S (497.69)

Calcd: C, 69.99%; H, 7.90%; N, 2.81%

Found: C, 69.87%; H, 7.84%; N, 2.81%

TLC: R_f 0.22 (silica gel, hexanes/EtOAc 80:20, UV/CAM)***tert*-Butyl (*E*)-(4-(4,8-Dimethylnona-3,7-dien-1-yl)phenyl)carbamate (**3g**)**

A flame-dried, 100-mL, three-necked, round-bottomed flask equipped with a stir bar, argon inlet adapter, and two septa was charged with *tert*-butyl (*E*)-(4-(4,8-dimethyl-1-tosylnona-3,7-dien-1-yl)phenyl)carbamate **21** (1.01 g, 2.03 mmol), sodium dihydrogen phosphate (2.47 g, 20.3 mmol, 10.0 equiv), and THF (36 mL). A colorless suspension resulted, as the sodium dihydrogen phosphate is insoluble in THF. The suspension was cooled to 0 °C using an ice bath. Sodium amalgam (1.87 g, 16.2 mmol Na, 8.0 equiv Na) was added all at once. Immediately following, ethanol (4 mL) was added dropwise over 1 min resulting in a grayish suspension. The mixture was stirred at 0 °C for 3 h but was incomplete (monitored by TLC, hexanes/EtOAc, 80:20). The ice bath was removed and the mixture was stirred at 25 °C for 3 h but was still incomplete. The mixture was again cooled to 0 °C and an additional portion of sodium amalgam (1.87 g, 16.2 mmol Na, 8.0 equiv Na) was added all at once. The mixture was warmed to 25 °C and an additional portion of sodium dihydrogen phosphate (2.44 g, 20.3 mmol, 10.0 equiv) was added all at once. Stirring was continued for 18 h at 25 °C, over which time the mixture lightened to a very pale gray suspension. Full conversion was observed by TLC (hexanes/EtOAc, 80:20). The suspension was filtered through a pad of Celite (6 cm wide x 1 cm deep) to remove mercury, and the pad was rinsed with ethyl acetate (50 mL). The filtrate was transferred to a

separatory funnel along with water (75 mL) and additional ethyl acetate (75 mL). The layers were separated, and the aqueous phase was extracted with ethyl acetate (2 x 50 mL). The combined organic layers were washed with brine (50 mL), dried over sodium sulfate, filtered, and concentrated (30 °C, 15 mmHg) to afford the crude product (0.72 g). The product was purified by chromatography (silica gel, 3 x 15 cm, dry load on Celite, 25-mL fractions, hexanes/EtOAc gradient elution: 95:5 (300 mL) to 90:10 (300 mL) to 85:15 (300 mL) to 80:20 (300 mL)) to afford 644.0 mg (92% yield) of **3g** as a viscous oil, which crystallized to an analytically pure white solid upon standing.

Data for 3g:

m.p.: 50–52 °C

¹H NMR: (500 MHz, CDCl₃)

7.25 (d, *J* = 8.5 Hz, 2H, HC(5)), 7.10 (d, *J* = 8.5 Hz, 2H, HC(6)), 6.39 (bs, 1H, NH), 5.20-5.13 (m, 1H, HC(10)), 5.12-5.06 (m, 1H, HC(15)), 2.62-2.54 (m, 2H, H₂C(8)), 2.26 (q, *J* = 7.4 Hz, 2H, H₂C(9)), 2.05 (q, *J* = 7.0 Hz, 2H, H₂C(14)), 2.00-1.93 (m, 2H, H₂C(13)), 1.68 (s, 3H, H₃C(17)), 1.60 (s, 3H, H₃C(18)), 1.55 (s, 3H, H₃C(12)), 1.51 (s, 9H, H₃C(1)).

¹³C NMR: (126 MHz, CDCl₃)

153.00 (C(3)), 137.35 (C(7)), 136.12 (C(4) or C(11)), 135.87 (C(4) or C(11)), 131.46 (C(16)), 129.06 (HC(6)), 124.49 (HC(15)), 123.71 (HC(10)), 118.73 (HC(5)), 80.46 (C(2)), 39.85 (H₂C(13)), 35.58 (H₂C(8)), 30.16 (H₂C(9)), 28.52 (H₃C(1)), 26.86 (H₂C(14)), 25.85 (H₃C(17)), 17.85 (H₃C(18)), 16.14 (H₃C(12)).

IR: (neat)

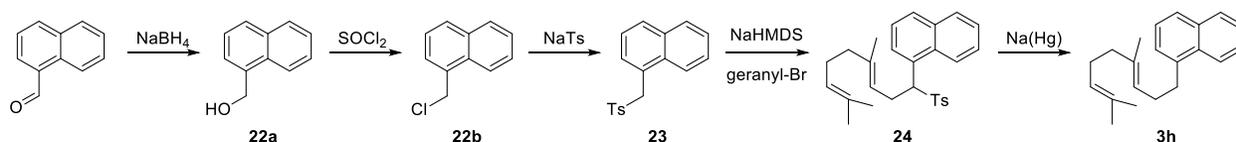
3385 (w), 2977 (w), 2923 (m), 2855 (w), 1700 (s), 1593 (m), 1523 (s), 1508 (s), 1444 (w), 1411 (m), 1384 (m), 1366 (m), 1319 (m), 1306 (m), 1232 (s), 1159 (s), 1110 (m), 1053 (s), 1019 (m), 930 (w), 907 (w), 848 (m), 822 (s), 796 (m), 771 (m), 748 (m), 605 (s), 516 (s), 494 (w).

LRMS: (ESI, [M+Na]⁺)

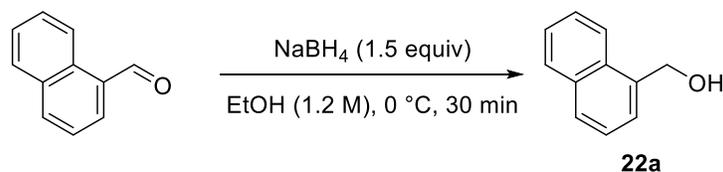
112.3 (2), 112.6 (2), 121.7 (2), 149.8 (16), 163.9 (4), 196.1 (3), 196.8 (2), 198.8 (2), 254.8 (3), 256.8 (4), 282.3 (3), 288.2 (12), 289.2 (2), 304.3 (4), 320.2 (15), 321.2 (3), 360.4 (3), 361.4 (3), 366.2 (100), 367.2 (36), 368.2 (6), 424.1 (2).

Analysis: C₂₂H₃₃NO₂ (343.51)
 Calcd: C, 76.92%; H, 9.68%; N, 4.08%
 Found: C, 76.65%; H, 9.51%; N, 4.25%
TLC: R_f 0.49 (silica gel, hexanes/EtOAc, 80:20, UV/CAM)

(E)-1-(4,8-Dimethylnona-3,7-dien-1-yl)naphthalene (3h)



Naphthalen-1-ylmethanol (22a)



A flame-dried, 200-mL, round-bottomed flask equipped with a stir bar and argon inlet adapter was charged with 1-naphthaldehyde (2.61 mL, 3.00 g, 19.2 mmol, D = 1.15 g/mL) and absolute ethanol (16 mL). The resulting solution was cooled to 0 °C using an ice bath. Sodium borohydride (1.09 g, 28.8 mmol, 1.50 equiv) was added in one portion at 0 °C. The resulting white suspension was stirred at 0 °C for 30 min. Full conversion was observed by TLC (hexanes/EtOAc, 80:20). The reaction was quenched at 0 °C by the *cautious* addition of sat. aq. NH₄Cl (16 mL) and the resulting mixture was allowed to warm to 25 °C. The biphasic mixture was concentrated (35 °C, 15 mmHg) to remove most of the ethanol, and the remaining aqueous layer was washed with CH₂Cl₂ (3 x 50 mL). The combined organic layers were washed with brine (50 mL), dried over sodium sulfate, filtered, and concentrated to afford 3.02 g (99%) of **22a** as a white solid requiring no further purification. Spectroscopic data match those reported previously for this compound accessed through a similar method.²¹

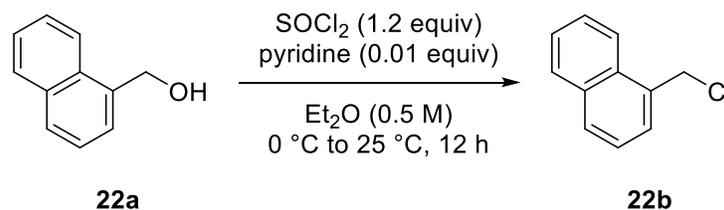
Data for 22a:

¹H NMR: (500 MHz, CDCl₃)

8.14 (d, *J* = 8.3 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.59-

7.49 (m, 3H), 7.49-7.43 (m, 1H), 5.17 (d, $J = 5.9$ Hz, 2H), 1.74 (t, $J = 5.9$ Hz, 1H).

1-(Chloromethyl)naphthalene (**22b**)

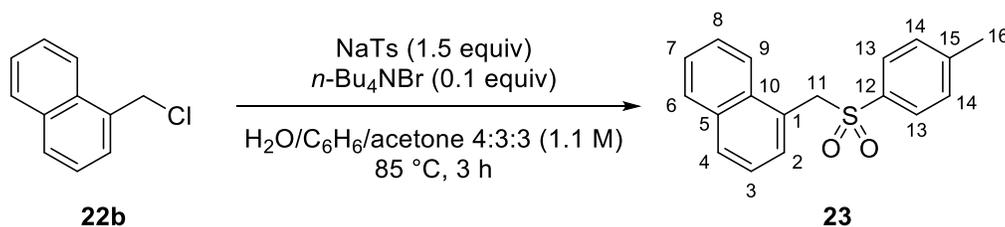


A flame-dried, 200-mL, two-necked, round-bottomed flask equipped with a stir bar, argon inlet adapter, temperature probe, and septum was charged with naphthalen-1-ylmethanol **22a** (3.02 g, 19.1 mmol) and diethyl ether (38 mL). Pyridine (15 μ L, 15.1 mg, 0.19 mmol, 0.01 equiv, $D = 0.98$ g/mL) was added, and the solution was cooled to an internal temperature of -5 °C using an ice/salt bath. Neat thionyl chloride (1.67 mL, 2.73 g, 22.9 mmol, 1.20 equiv, $d = 1.63$ g/mL) was added dropwise over 20 min. The rate of addition was closely monitored so that the internal temperature remained below 0 °C. The mixture was allowed to warm slowly to 25 °C over 4 h, and stirring was continued at 25 °C for 8 h. Full conversion was observed by TLC (hexanes/EtOAc, 80:20). The reaction was quenched by the addition of water (50 mL). The biphasic mixture was transferred to a 250-mL separatory funnel and the layers were separated. The aqueous layer was extracted with Et₂O (2 x 50 mL) and the combined organic layers were washed with sat. aq. NaHCO₃ (50 mL) and brine (50 mL), then dried over sodium sulfate, filtered, and concentrated to afford 3.31 g (98%) of **22b** as a turbid, pale-yellow oil requiring no further purification. Spectroscopic data matched those previously reported for this compound accessed through a different method.²²

Data for **22b**:

¹H NMR: (500 MHz, CDCl₃)

8.16 (d, $J = 8.4$ Hz, 1H), 7.90 (d, $J = 8.1$ Hz, 1H), 7.86 (d, $J = 8.2$ Hz, 1H), 7.64-7.58 (m, 1H), 7.57-7.51 (m, 2H), 7.46-7.41 (m, 1H), 5.07 (s, 2H).

1-(4-Methylphenylsulfonylmethyl)naphthalene (23)

A 25-mL, round-bottomed flask equipped with a stir bar and reflux condenser was charged with 1-(chloromethyl)naphthalene **22b** (2.17 g, 12.28 mmol), sodium *p*-toluenesulfinate (3.28 g, 18.43 mmol, 1.50 equiv), tetra-*n*-butylammonium bromide (0.40 g, 1.23 mmol, 0.10 equiv), water (4.4 mL), acetone (3.3 mL), and benzene (3.3 mL). The biphasic mixture was heated to 85 °C (oil bath temperature) with vigorous stirring for 3 h. The stir rate was set high enough such that the reaction appearance was that of a peach-colored suspension. After 3 h, the oil bath was removed, stirring was stopped, and the layers were allowed to separate. The upper layer (organic phase) had the appearance of an orange solution, while the lower layer (aqueous phase) had the appearance of a thin, cloudy, colorless suspension. Full consumption of starting material was observed by TLC (hexanes/EtOAc, 80:20). The reaction mixture was partitioned between water (25 mL) and diethyl ether (25 mL) in a 125-mL separatory funnel. The layers were separated, and the aqueous layer was extracted with diethyl ether (2 x 25-mL). The combined organic extracts were washed with brine (25 mL), dried over magnesium sulfate, filtered, and concentrated (30 °C, 15 mmHg) to afford 3.79 g of crude **23** as a yellow, oily solid. The product was purified by chromatography (silica gel, 5 cm x 16 cm, dry load on Celite, 50 mL fractions, hexanes/EtOAc gradient elution: 90:10 (500 mL) to 80:20 (500 mL) to 70:30 (500 mL) to 60:40 (500 mL) to 50:50 (500 mL)) to afford 3.31 g (91% yield) of **23** as an off-white solid. At this point, the level of purity of the bulk material is sufficient for the next reaction. An analytically pure sample was obtained by two recrystallizations from a minimal amount (20 mL) of hot diethyl ether (affording 818.5 mg, or 22% overall yield), followed by sublimation (90 °C, 0.1 mmHg). The product sublimes very slowly and this is not a practical method for harvesting large quantities of material. The product is soluble in chloroform-*d* but many of the ¹H-NMR signals overlap in this solvent. For this reason, the spectral data reported below were collected in benzene-*d*₆.

Data for **23**:

m.p.: 108–109 °C

¹H NMR: (500 MHz, C₆D₆)

7.80-7.71 (m, 1H, HC(9)), 7.55-7.50 (m, 1H, HC(6)), 7.48 (d, $J = 8.2$ Hz, 1H, HC(4)), 7.39 (d, $J = 8.2$ Hz, 2H, HC(13)), 7.19-7.16 (m, 1H, HC(8)), 7.16-7.13 (m, 1H, HC(7)), 7.03-6.97 (m, 1H, HC(3)), 6.97-6.90 (m, 1H, HC(2)), 6.51 (d, $J = 8.2$ Hz, 2H, HC(14)), 4.44 (s, 2H, H₂C(11)), 1.74 (s, 3H, H₃C(16)).

¹³C NMR: (126 MHz, C₆D₆)

143.9 (C(15)), 136.4 (C(12)), 134.2 (C(5)), 132.7 (C(10)), 130.7 (HC(2)), 129.5 (HC(4)), 129.3 (HC(14)), 129.1 (HC(13)), 128.7 (HC(6)), 126.5 (HC(8)), 126.03 (C(1)), 126.00 (HC(7)), 125.1 (HC(3)), 124.6 (HC(9)), 59.9 (H₂C(11)), 21.1 (H₃C(16)).

IR: (neat)

3050 (w), 2924 (w), 1597 (w), 1512 (w), 1494 (w), 1418 (w), 1398 (w), 1289 (m), 1216 (w), 1184 (w), 1155 (m), 1141 (m), 1129 (m), 1086 (m), 1018 (w), 946 (w), 890 (w), 855 (w), 803 (m), 774 (m), 746 (m), 728 (m), 672 (m), 643 (m), 626 (m), 561 (s), 515 (s), 498 (m), 486 (m), 460 (m)

LRMS: (EI, 70 eV)

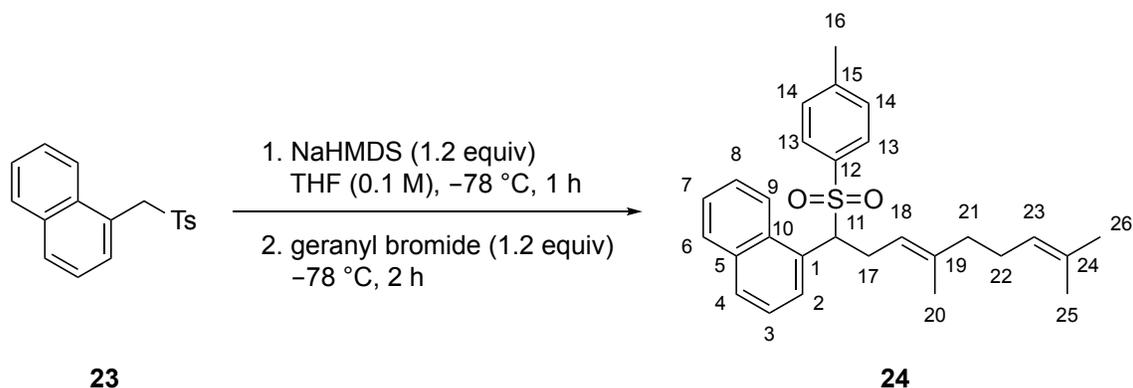
63.0 (2), 65.0 (4), 89.0 (3), 91.1 (10), 115.1 (21), 116.1 (2), 124.0 (3), 139.1 (8), 140.1 (2), 141.1 (100), 142.1 (13), 296.1 (9), 297.1 (2)

Analysis: C₁₈H₁₆O₂S (296.38)

Calcd: C, 72.94%; H, 5.44%

Found: C, 72.71%; H, 5.31%

TLC: R_f 0.20 (silica gel, hexanes/EtOAc, 80:20, UV)

(E)-1-(4,8-Dimethyl-1-(4-methylphenylsulfonyl)nona-3,7-dien-1-yl)naphthalene (24)

A flame-dried, 100-mL, three-necked, round-bottomed flask equipped with a stir bar, argon inlet adapter, temperature probe, and two septa was charged with 1-((4-methylphenylsulfonyl)methyl)naphthalene **23** (600.7 mg, 2.03 mmol) and THF (16.5 mL). The resulting colorless solution was cooled to an internal temperature of $-78\text{ }^\circ\text{C}$ using a dry ice/acetone bath. Sodium hexamethyldisilazide (1 M solution in THF, 2.43 mL, 2.43 mmol, 1.20 equiv) was added dropwise over 10 min at $-78\text{ }^\circ\text{C}$. Immediately, a bright yellow solution resulted. No significant exotherm was observed, and the internal temperature did not exceed $-70\text{ }^\circ\text{C}$ during the addition. The yellow solution was stirred at $-78\text{ }^\circ\text{C}$ for 1 h. A solution of geranyl bromide (530.3 mg, 2.43 mmol, 1.20 equiv) in THF (7.8 mL) was added dropwise at $-78\text{ }^\circ\text{C}$ over 20 min. Addition of this reagent does result in a slight exotherm, so the rate of addition was kept slow enough to maintain the internal temperature below $-70\text{ }^\circ\text{C}$. The solution remained yellow but did become somewhat turbid. Stirring was continued at $-78\text{ }^\circ\text{C}$ for 2 h, at which point full conversion was observed by TLC (hexanes/EtOAc, 80:20). The reaction was quenched at $-78\text{ }^\circ\text{C}$ by adding ($25\text{ }^\circ\text{C}$) sat. aq. sodium bicarbonate solution (40 mL). The cold bath was removed, and the off-white suspension was allowed to warm to $25\text{ }^\circ\text{C}$. The mixture was transferred to a 500-mL separatory funnel, rinsing with water (75 mL) and ethyl acetate (25 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic phases were washed with brine (50 mL), dried over sodium sulfate, filtered, and concentrated ($30\text{ }^\circ\text{C}$, 15 mmHg) to afford 0.99 g crude **24**. The product was purified by chromatography (silica gel, 4 cm x 20 cm, dry load on Celite, 25-mL fractions, hexanes/EtOAc gradient elution: 95:5 (300 mL) to 90:10 (300 mL) to 85:15 (300 mL) to 80:20 (300 mL)) to afford 737.0 mg (84% yield) of **24** as a highly-viscous, pale-yellow oil (analytically pure). The oil is not amenable to purification by distillation.

Data for 24:¹H NMR: (500 MHz, CDCl₃)

7.79 (d, $J = 8.1$ Hz, 1H, HC(4)), 7.76 (d, $J = 7.9$ Hz, 1H, HC(6)), 7.71-7.67 (m, 1H, HC(2)), 7.69-7.65 (m, 1H, HC(9)), 7.50-7.45 (m, 1H, HC(3)), 7.39-7.36 (m, 1H, HC(7)), 7.36 (d, $J = 8.1$ Hz, 2H, HC(13)), 7.34-7.29 (m, 1H, HC(8)), 6.99 (d, $J = 8.1$ Hz, 2H, HC(14)), 5.06 (dd, $J = 11.3, 4.0$ Hz, 1H, HC(11)), 4.80 (t, $J = 6.9$ Hz, 1H, HC(18)), 4.78-4.72 (m, 1H, HC(23)), 3.30 (ddd, $J = 14.5, 6.9, 4.0$ Hz, 1H, H₂C(17)), 2.99 (ddd, $J = 14.5, 11.3, 6.9$ Hz, 1H, H₂C(17)), 2.24 (s, 3H, H₃C(16)), 1.79-1.74 (m, 2H, H₂C(22)), 1.76-1.71 (m, 2H, H₂C(21)), 1.57 (s, 3H, H₃C(20)), 1.46 (s, 3H, H₃C(26)), 1.39 (s, 3H, H₃C(25)).

¹³C NMR: (126 MHz, CDCl₃)

144.35 (C(15)), 138.91 (C(19)), 134.65 (C(12)), 133.63 (C(5)), 133.02 (C(10)), 131.50 (C(24)), 129.32 (HC(4)), 129.18 (HC(14)), 129.16 (HC(13)), 128.90 (HC(6)), 128.76 (C(1)), 127.11 (HC(2)), 126.39 (HC(8)), 125.44 (HC(7)), 125.18 (HC(3)), 123.85 (HC(23)), 122.36 (HC(9)), 118.73 (HC(18)), 64.66 (HC(11)), 39.59 (H₂C(21)), 27.82 (H₂C(17)), 26.40 (H₂C(22)), 25.60 (H₃C(26)), 21.57 (H₃C(16)), 17.66 (H₃C(25)), 16.42 (H₃C(20)).

IR: (neat)

3050 (w), 2966 (w), 2917 (w), 1597 (w), 1513 (w), 1494 (w), 1445 (w), 1399 (w), 1376 (w), 1312 (m), 1300 (m), 1289 (m), 1214 (w), 1183 (w), 1142 (s), 1084 (s), 1019 (w), 982 (w), 948 (w), 801 (m), 778 (s), 762 (m), 728 (m), 716 (m), 666 (s), 645 (w), 576 (s), 520 (s)

LRMS: (EI, 70 eV)

115.0 (12), 123.1 (23), 128.0 (15), 135.1 (24), 139.0 (19), 141.1 (100), 142.1 (44), 152.0 (25), 153.1 (70), 154.1 (25), 165.1 (53), 166.1 (18), 167.1 (35), 178.1 (35), 179.1 (37), 180.1 (10), 181.1 (32), 191.1 (17), 192.1 (18), 193.1 (83), 194.1 (16), 195.1 (39), 207.1 (49), 208.1 (23), 209.1 (13), 221.1 (32), 235.1 (16), 276.2 (35), 277.2 (100), 278.2 (72), 432.2 (1), 433.2 (1).

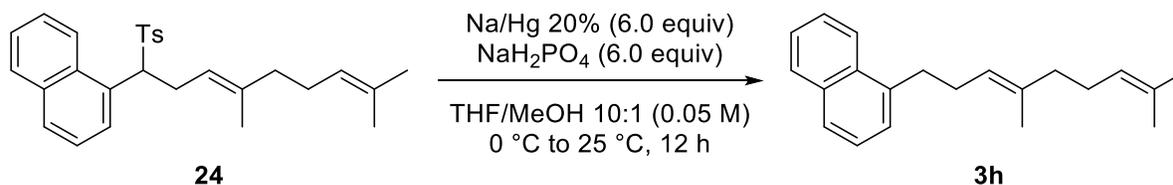
Analysis: C₂₈H₃₂O₂S (432.62)

Calcd: C, 77.74%; H, 7.46%;

Found: C, 77.38%; H, 7.21%

TLC: R_f 0.35 (silica gel, hexanes/EtOAc, 80:20, UV/CAM)

(E)-1-(4,8-Dimethylnona-3,7-dien-1-yl)naphthalene



A flame-dried, 100-mL, three-necked, round-bottomed flask equipped with a glass-coated stir bar, argon inlet adapter, and two septa was charged with (*E*)-1-(4,8-dimethyl-1-tosylnona-3,7-dien-1-yl)naphthalene **24** (509.4 mg, 1.18 mmol), sodium dihydrogen phosphate (0.85 g, 7.06 mmol, 6.0 equiv), and THF (24 mL). The resulting thin, white suspension was cooled to 0 °C using an ice bath. Sodium amalgam (20% w/w sodium, 0.42 g, 3.53 mmol, 3.0 equiv) was quickly added in one portion. Methanol (1.2 mL) was added dropwise at 0 °C over 1 min. The mixture was allowed to slowly warm to 25 °C over 3 h, and stirring was continued for 9 h at 25 °C. While the suspension did become thicker over time, the reaction appeared incomplete by TLC (hexanes/EtOAc, 80:20). The mixture was again cooled to 0 °C and another portion of sodium amalgam (20% w/w sodium, 0.42 g, 3.53 mmol, 3.0 equiv) was quickly added, followed by an additional portion of methanol (1.2 mL). The reaction was stirred for 3 h at 0 °C. Full conversion was observed by TLC (hexanes/EtOAc, 80:20). The mixture was filtered through Celite (to remove elemental mercury) and the filter case was rinsed with ethyl acetate. The filtrate was transferred to a separatory funnel with water (50 mL) and additional ethyl acetate (50 mL). The layers were separated, and the aqueous phase was extracted with ethyl acetate (2 x 50 mL). The combined organic layers were washed with brine (50 mL), dried over sodium sulfate, filtered, and concentrated (30 °C, 15 mmHg) to afford the crude product (324.9 mg). The product was purified by chromatography (silica gel, 2 x 16 cm, dry load on Celite, 10-mL fractions, hexanes/CH₂Cl₂ gradient elution: 97.5:2.5 (200 mL) to 95:5 (200 mL) to 92.5:7.5 (200 mL)) to afford **3h** as a clear, colorless oil (314.1 mg, 96%). Spectroscopic data matched those reported by Snyder et al. for this product accessed through a different method.²³

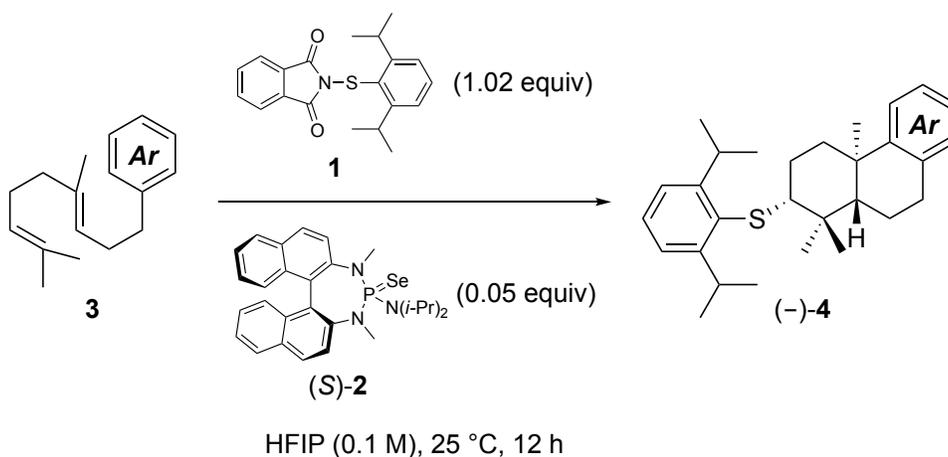
Data for 3h:¹H NMR: (500 MHz, CDCl₃)

8.07 (d, *J* = 8.4 Hz, 1H), 7.87-7.82 (m, 1H), 7.71 (d, *J* = 8.2 Hz, 1H), 7.53-7.44 (m, 2H), 7.40 (dd, *J* = 8.1, 7.1 Hz, 1H), 7.33 (d, *J* = 6.7 Hz, 1H), 5.31-5.26 (m, 1H), 5.14-5.08 (m, 1H), 3.10 (dd, *J* = 8.7, 7.1 Hz, 2H), 2.45 (q, *J* = 7.3 Hz, 2H), 2.07 (q, *J* = 7.3 Hz, 2H), 2.03-1.97 (m, 2H), 1.70 (s, 3H), 1.61 (s, 3H), 1.54 (s, 3H).

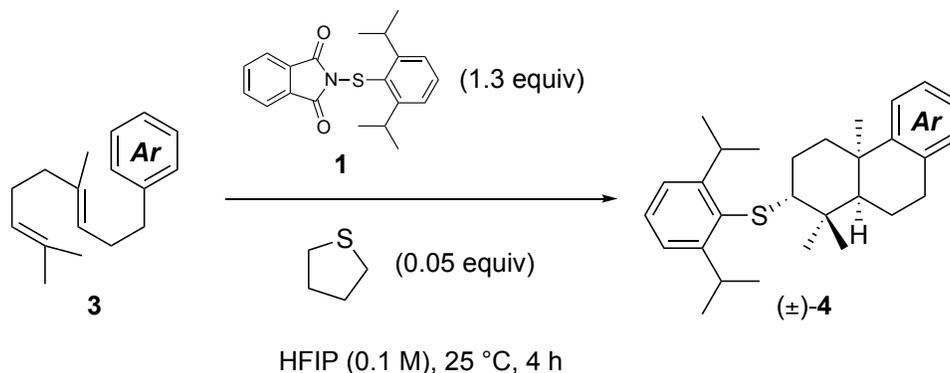
¹³C NMR: (126 MHz, CDCl₃)

138.6, 136.0, 134.0, 132.1, 131.5, 128.9, 126.6, 126.1, 125.8, 125.7, 125.5, 124.5, 124.0, 123.9, 39.9, 33.4, 29.4, 26.9, 25.9, 17.9, 16.2

General Procedure A: Enantioselective, Lewis Base-Catalyzed Sulfenocyclization of Homogeranylarenes

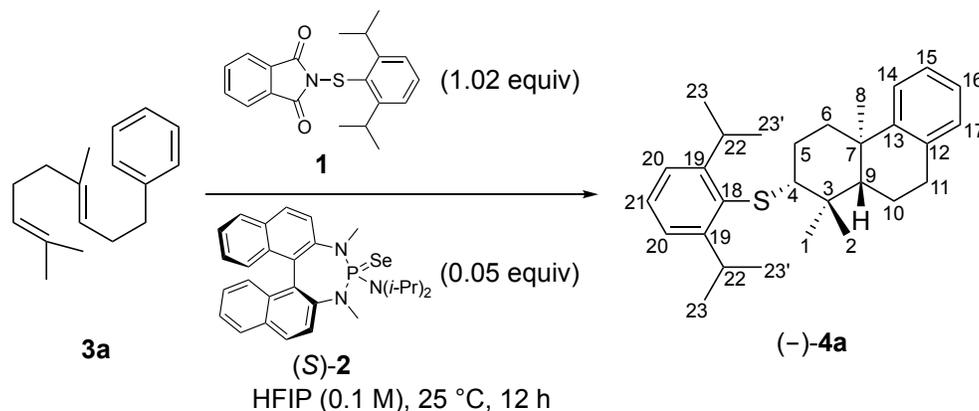


A 100-mL, round-bottomed flask equipped with a stir bar was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (1.02 mmol, 1.02 equiv), hexafluoroisopropyl alcohol (10 mL, 0.1 M), and **3** (1.00 mmol) resulting in a yellow solution. Catalyst (*S*)-**2** (0.05 equiv) was added in one portion and the mixture was stirred at 25 °C for 12 h. Conversion was monitored by TLC. Once full conversion was reached, the colored suspension was diluted with CH₂Cl₂ (10 mL). Volatiles were removed by rotary evaporation (30 °C, 15 mmHg) to afford crude (-)-**4**. Chromatography and subsequent recrystallization or trituration afforded pure (-)-**4**.

General Procedure B: Racemic, Lewis Base-Catalyzed Sulfenocyclization of Homogeranylarenes

A 100-mL, round-bottom flask equipped with a stir bar was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (1.10 mmol, 1.10 equiv), hexafluoroisopropyl alcohol (10 mL, 0.1 M), and **3** (1.00 mmol) resulting in a yellow solution. Tetrahydrothiophene (0.05 equiv) was added in one portion and the mixture was stirred at 25 °C. After 2 h, the reaction was charged with additional *N*-(2,6-diisopropylphenylthio)phthalimide **1** (0.20 mmol, 0.20 equiv) and stirring was continued for 2 h. [Note: unproductive consumption of **1** is observed as a minor reaction pathway, which necessitates the additional charge of **1** to reach full conversion.] Conversion was monitored by TLC. Once full conversion was reached, the colored suspension was diluted with CH₂Cl₂ (10 mL). Volatiles were removed by rotary evaporation (30 °C, 15 mmHg) to afford crude (±)-**4**. Chromatography and subsequent recrystallization or trituration afforded pure (±)-**4**.

Preparation of (–)-(2,6-Diisopropylphenyl) ((4*R*,7*R*,9*S*)-3,3,7-Trimethyl-3,4,5,6,7,9,10,11-octahydrophenanthren-4-yl) Sulfide ((–)-4a)



A 100-mL, round-bottomed flask equipped with a stir bar and argon inlet adapter was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (346.2 mg, 1.02 mmol, 1.02 equiv), hexafluoroisopropyl alcohol (10 mL, 0.1 M), and (*E*)-(4,8-dimethylnona-3,7-dien-1-yl)benzene **3a** (228.4 mg, 1.0 mmol, 1.0 equiv). A homogeneous, yellow solution resulted. Catalyst (*S*)-**2** (26.0 mg, 0.05 mmol, 0.05 equiv) was added in one portion and the mixture was stirred at 25 °C for 16 h. Full conversion was observed by TLC (hexanes/CH₂Cl₂, 90:10). The reaction mixture was diluted with CH₂Cl₂ (10 mL), and the volatiles were removed by rotary evaporation (30 °C, 15 mmHg) to afford crude (–)-**4a**. The crude product was purified by column chromatography (silica gel, 3 x 25 cm, dry load on Celite, 25-mL fractions, hexanes/CH₂Cl₂ gradient elution: 96:4 (300 mL) to 95:5 (300 mL) to 94:6 (300 mL)) to afford 317.1 mg (75%) of (–)-**4a** as a white solid. To obtain analytically pure material, the solid was dissolved in boiling abs. ethanol (3 mL) and allowed to cool slowly to 25 °C, followed by cooling in a –20 °C freezer for 12 h. The product was collected by vacuum filtration and rinsed with ice-cold hexanes (2 mL) to afford 254.5 mg (60%) of (–)-**4a** as white crystals. Spectroscopic data match those reported for (±)-**4a**.

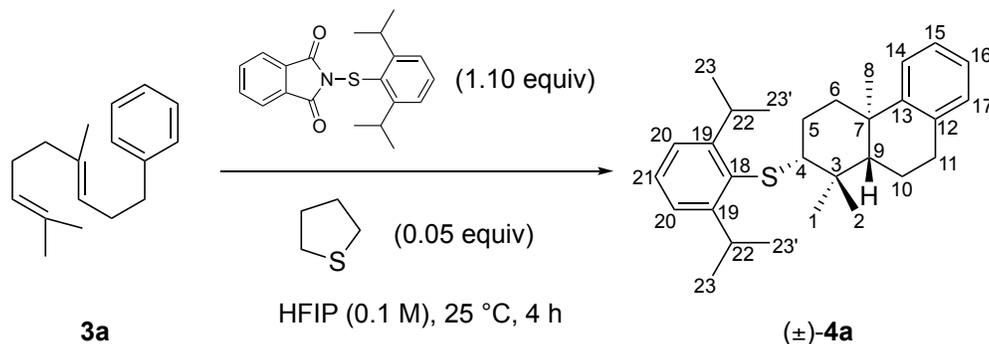
Data for (–)-**4a**:

- m.p.: 102–104 °C (ethanol)
- Analysis: C₂₉H₄₀S (420.70)
 Calcd: C, 82.79%; H, 9.58%;
 Found: C, 82.63%; H, 9.65%;
- HPLC: *t*_R 7.8 min (90%); *t*_R 10.6 min (10%) (Supelco Astec, hexanes/*i*-PrOH, 99:1, 0.5 mL/min, 220 nm, 24 °C)

after recrystallization: t_R 7.6 min (91%); t_R 9.7 min (9%)

Opt. Rot: $[\alpha]_D^{25} -10.2$ ($c = 1.06$ in CHCl_3)

Preparation of (±)-(2,6-Diisopropylphenyl) ((4*R,7*R**,9*S**)-3,3,7-Trimethyl-3,4,5,6,7,9,10,11-octahydro-phenanthren-4-yl) Sulfide ((±)-4a)**



A flame-dried, 100-mL, pear-shaped flask equipped with a stir bar and argon inlet adapter was charged with *N*-(2,6-diisopropylphenylthio)phthalimide (356.8 mg, 1.05 mmol, 1.05 equiv), hexafluoroisopropyl alcohol (10 mL, 0.1 M), and (*E*)-(4,8-dimethylnona-3,7-dien-1-yl)benzene **3a** (95.25% by mass, 239.9 mg, 1.00 mmol). [**Note:** the (*E*)-(4,8-dimethylnona-3,7-dien-1-yl)benzene is contaminated with 4.75% of 1,2-diphenylethane.] A homogeneous, yellow solution resulted. Tetrahydrothiophene (4.4 μL , 4.4 mg, 0.05 mmol, 0.05 equiv) was added to the solution at 25 $^\circ\text{C}$. The mixture was stirred at 25 $^\circ\text{C}$ for 3 h. Within 10 min, the yellow solution had turned pink, ultimately resulting in a magenta suspension with a white-colored precipitate. An additional portion of *N*-(2,6-diisopropylphenylthio)phthalimide (17.9 mg, 0.05 mmol, 0.05 equiv) was added and stirring was continued for 1 h. Full conversion was observed by TLC (hexanes/ CH_2Cl_2 , 90:10). The reaction mixture was diluted with CH_2Cl_2 (10 mL), and the volatiles were removed by rotary evaporation (30 $^\circ\text{C}$, 15 mmHg) to afford crude (\pm)-**4a**. [**Note:** ^1H NMR spectroscopy revealed approx. 10% of unreacted starting material remaining. Monitoring reaction progress by TLC may be misleading, and monitoring progress by ^1H NMR is recommended.] The crude product was purified by column chromatography (silica gel, 3 x 20 cm, dry load on Celite, 25-mL fractions, hexanes/ CH_2Cl_2 gradient elution: 97.5:2.5 (300 mL) to 95:5 (300 mL) to 92.5:7.5 (300 mL) to 90:10 (300 mL)) to afford 277.4 mg of (\pm)-**4a** as a white solid. The product was still contaminated with trace impurities which are not removable by chromatography. To obtain analytically pure material, the solid was dissolved in boiling hexanes

(3 mL) and allowed to cool slowly to 25 °C, whereupon the product crystallized as white prisms. The suspension was cooled in a -20 °C freezer for 4 h. The crystals were collected by vacuum filtration and rinsed with ice-cold hexanes (2 mL) to afford 199.9 mg (48%) of (\pm)-**4a** as flat, white crystals.

Data for (\pm)-**4a**:

m.p.: 160–162 °C (hexanes)

¹H NMR: (500 MHz, CDCl₃)

7.31 (t, $J = 7.7$ Hz, 1H, HC(21)), 7.16 (d, $J = 7.7$ Hz, 2H, HC(20)), 7.16-7.13 (m, 1H, HC(14)), 7.11-7.07 (m, 1H, HC(16) or HC(15)), 7.07-7.05 (m, 1H, HC(15) or HC(16)), 7.05-7.02 (m, 1H, HC(17)), 4.01 (hept, $J = 6.9$ Hz, 2H, HC(22)), 3.02-2.94 (m, 1H, H₂C(11^{eq})), 2.88 (ddd, $J = 17.5, 11.5, 7.3$ Hz, 1H, H₂C(11^{ax})), 2.62 (dd, $J = 12.5, 3.5$ Hz, 1H, HC(4)), 2.23 (dt, $J = 13.3, 3.4$ Hz, 1H, H₂C(6^{eq})), 2.01-1.93 (m, 1H, H₂C(10^{eq})), 1.93-1.84 (m, 1H, H₂C(5^{ax})), 1.84-1.74 (m, 1H, H₂C(10^{ax})), 1.57 (dq, $J = 10.2, 3.6$ Hz, 1H, H₂C(5^{eq})), 1.39 (s, 3H, H₃C(2)), 1.38 (dd, $J = 2.0$ Hz, 1H, HC(9)), 1.26 (d, $J = 6.9$ Hz, 6H, H₃C(23)), 1.28-1.23 (m, 1H, H₂C(6^{ax})), 1.22 (s, 3H, H₃C(8)), 1.18 (d, $J = 6.9$ Hz, 6H, H₃C(23')), 1.12 (s, 3H, H₃C(1)).

¹³C NMR: (126 MHz, CDCl₃)

154.18 (C(19)), 149.47 (C(13)), 135.09 (C(12)), 130.95 (C(18)), 129.11 (HC(17)), 128.91 (HC(21)), 125.91 (HC(16) or HC(15)), 125.54 (HC(15) or HC(16)), 124.48 (HC(14)), 123.70 (HC(20)), 61.89 (HC(4)), 52.44 (HC(9)), 39.27 (H₂C(6)), 39.05 (C(3)), 37.95 (C(7)), 31.49 (HC(22)), 30.85 (H₂C(11)), 29.77 (H₃C(2)), 26.20 (H₂C(5)), 25.04 (H₃C(23')), 24.98 (H₃C(8)), 24.13 (H₃C(23)), 19.68 (H₂C(10)), 17.75 (H₃C(1)).

IR: (neat)

2961 (m), 2864 (w), 2837 (w), 1575 (w), 1489 (w), 1449 (m), 1391 (w), 1375 (m), 1360 (m), 1307 (w), 1267 (w), 1245 (w), 1198 (w), 1160 (w), 1052 (m), 995 (w), 967 (w), 939 (w), 879 (w), 835 (w), 798 (s), 771 (m), 758 (s), 752 (s), 731 (m), 722 (s), 702 (w), 559 (w), 486 (w).

LRMS: (EI, 70 eV)

55.1 (36), 57.1 (22), 69.1 (62), 73.0 (11), 83.1 (25), 91.1 (24), 97.1 (23), 115.1

(23), 117.1 (43), 123.0 (12), 128.1 (27), 129.1 (42), 131.1 (100), 132.1 (11), 141.1 (15), 142.1 (12), 143.1 (67), 144.1 (16), 145.1 (20), 149.0 (22), 151.1 (25), 157.1 (44), 169.1 (13), 171.1 (22), 179.1 (12), 194.1 (52), 211.1 (30), 227.2 (62), 228.2 (12), 420.3 (61), 421.3 (20).

Analysis: C₂₉H₄₀S (420.70)

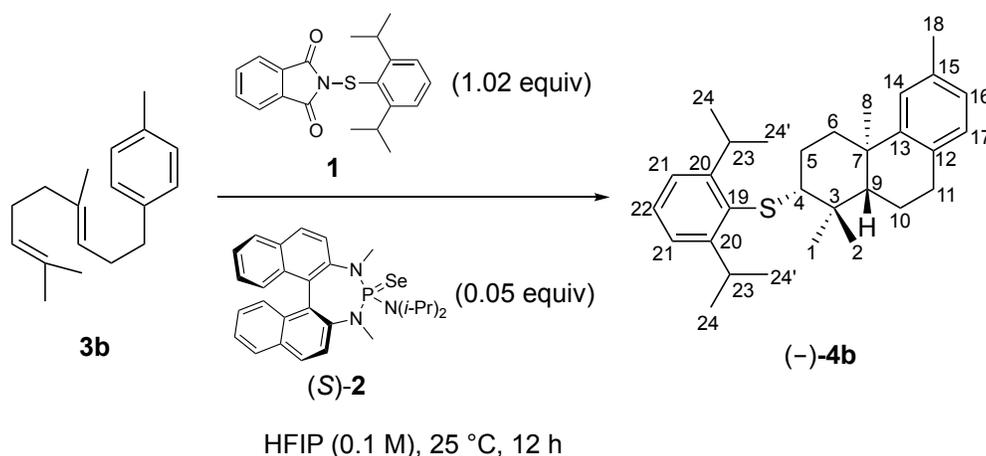
Calcd: C, 82.79%; H, 9.58%;

Found: C, 82.59%; H, 9.70%;

TLC: *R_f* 0.33 (silica gel, hexanes/CH₂Cl₂, 90:10, UV/CAM or PMA)

HPLC: *t_R* 7.4 min (50%); *t_R* 9.1 min (50%) (Supelco Astec, hexanes/*i*-PrOH, 99:1, 0.5 mL/min, 220 nm, 24 °C)

Preparation of (–)-(2,6-Diisopropylphenyl) ((4*R*,7*R*,9*S*)-3,3,7,15-Tetramethyl-3,4,5,6,7,9,10,11-octahydrophenanthren-4-yl) Sulfide ((–)-4b)



A 100-mL, round-bottomed flask equipped with a stir bar and argon inlet adapter was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (348.0 mg, 1.03 mmol, 1.02 equiv), hexafluoroisopropyl alcohol (10 mL, 0.1 M), and (*E*)-1-(4,8-dimethylnona-3,7-dien-1-yl)-4-methylbenzene **3b** (243.4 mg, 1.00 mmol). A homogeneous, yellow solution resulted. Catalyst (*S*)-**2** (26.5 mg, 0.05 mmol, 0.05 equiv) was added in one portion and the mixture was stirred at 25 °C for 5 h. Within 1 h, a beige suspension had formed, and a purple suspension was observed after 5 h. Full conversion was observed by TLC (hexanes/CH₂Cl₂, 90:10). The reaction mixture was diluted with CH₂Cl₂ (10 mL), and the volatiles were removed by rotary evaporation (30 °C, 15 mmHg) to afford crude (–)-**4b**. The crude product was purified by column chromatography

(silica gel, 3 x 25 cm, dry load on Celite, 25-mL fractions, hexanes/CH₂Cl₂ gradient elution: 97:3 (300 mL) to 94:6 (300 mL) to 91:9 (300 mL) to 88:12 (300 mL)) to afford 413.4 mg of (–)-**4b** as a white solid. The product was still contaminated with trace impurities which are not removable by chromatography. To obtain analytically pure material, the solid was dissolved in boiling abs. ethanol (3 mL) and allowed to cool slowly to 25 °C, followed by cooling in a –20 °C freezer for 12 h. The product was collected by vacuum filtration and rinsed with ice-cold hexanes (2 mL) to afford 261.3 mg (60%) of (–)-**4b** as small, white crystals. Spectroscopic data match those reported for (±)-**4b**.

Data for (–)-**4b**:

m.p.: 125–127 °C (ethanol)

Analysis: C₃₀H₄₂S (434.73)

Calcd: C, 82.89%; H, 9.74%

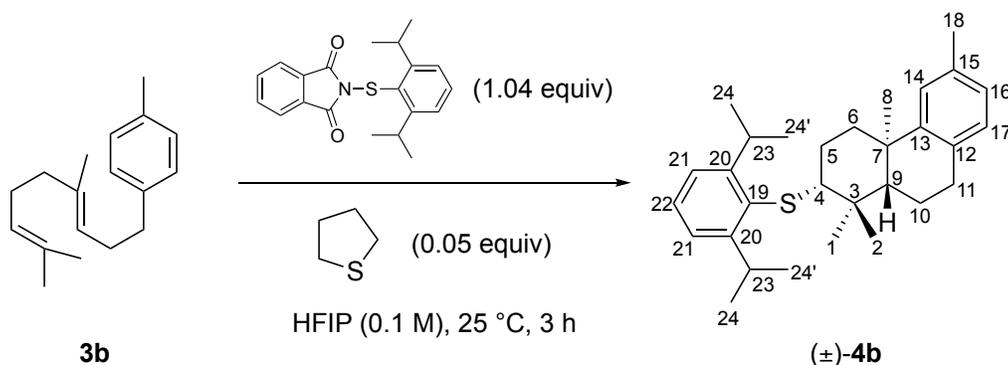
Found: C, 82.71%; H, 9.81%

HPLC: **Note:** The e.r. cannot be measured accurately prior to recrystallization due to overlapping signals arising from trace impurities. It is measured as 90:10 on either derivative (–)-**9b** or (–)-**13b** (*vide infra*).

After recrystallization: *t*_R 10.3 min (93%); *t*_R 11.5 min (7%) (Supelco Astec, hexanes/*i*-PrOH, 99:1, 0.3 mL/min, 220 nm, 24 °C)

Opt. Rot: [α]_D²⁵ –32.3 (*c* = 1.07 in CHCl₃)

Preparation of (±)-(2,6-Diisopropylphenyl) ((4*R,7*R**,9*S**)-3,3,7,15-Tetramethyl-3,4,5,6,7,9,10,11-octahydrophenanthren-4-yl) Sulfide ((±)-**4b**)**



A 50-mL, round-bottomed flask equipped with a stir bar and argon inlet adapter was charged with *N*-(2,6-diisopropylphenylthio)phthalimide (351.6 mg, 1.04 mmol, 1.04 equiv),

hexafluoroisopropyl alcohol (10 mL), and (*E*)-1-(4,8-dimethylnona-3,7-dien-1-yl)-4-methylbenzene **3b** (242.2 mg, 1.00 mmol). A homogeneous, yellow solution resulted. Tetrahydrothiophene (4.4 μ L, 0.05 mmol, 0.05 equiv) was added to the solution at 25 °C. The reaction was stirred at 25 °C for 3 h. Within 10 min, the yellow solution had turned pink, ultimately resulting in a purple suspension. Full conversion was observed by TLC (hexanes/ CH_2Cl_2 , 90:10). The reaction mixture was diluted with CH_2Cl_2 (10 mL), and the volatiles were removed by rotary evaporation (30 °C, 15 mmHg) to afford crude (\pm)-**4b**. [**Note:** ^1H NMR spectroscopy revealed approx. 10% of unreacted starting material remaining. Monitoring reaction progress by TLC may be misleading, and monitoring progress by ^1H NMR is recommended.] The crude product was purified by column chromatography (silica gel, 3 x 20 cm, dry load on Celite, 25-mL fractions, hexanes/ CH_2Cl_2 gradient elution: 97.5:2.5 (300 mL) to 95:5 (300 mL) to 92.5:7.5 (300 mL) to 90:10 (300 mL)) to afford 236.0 mg of (\pm)-**4b** as a white solid. The product was still contaminated with trace impurities which are not removable by chromatography. To obtain analytically pure material, the solid was dissolved in boiling hexanes (6 mL) and allowed to cool slowly to 25 °C, followed by cooling in a -20 °C freezer for 12 h. The product was collected by vacuum filtration and rinsed with ice-cold hexanes (2 mL) to afford 159.4 mg (37%) of (\pm)-**4b** as fluffy, white crystals.

Data for (\pm)-**4b**:

m.p.: 197–199 °C (hexanes)
 ^1H NMR: (500 MHz, CDCl_3)
7.30 (t, $J = 7.7$ Hz, 1H, HC(22)), 7.16 (d, $J = 7.7$ Hz, 2H, HC(21)), 6.96 (bs, 1H, HC(14)), 6.94 (d, $J = 7.7$ Hz, 1H, HC(17)), 6.91-6.86 (m, 1H, HC(16)), 4.01 (hept, $J = 6.8$ Hz, 2H, HC(23)), 2.93 (dd, $J = 16.9, 6.2$ Hz, 1H, $\text{H}_2\text{C}(11^{\text{eq}})$), 2.83 (ddd, $J = 17.5, 11.5, 7.4$ Hz, 1H, $\text{H}_2\text{C}(11^{\text{ax}})$), 2.61 (dd, $J = 12.5, 3.8$ Hz, 1H, HC(4)), 2.24 (s, 3H, $\text{H}_3\text{C}(18)$), 2.23 (dt, $J = 3.5$ Hz, 1H, $\text{H}_2\text{C}(6^{\text{eq}})$), 2.00-1.92 (m, 1H, $\text{H}_2\text{C}(10^{\text{eq}})$), 1.87 (qd, $J = 13.8, 3.4$ Hz, 1H, $\text{H}_2\text{C}(5^{\text{ax}})$), 1.83-1.72 (m, 1H, $\text{H}_2\text{C}(10^{\text{ax}})$), 1.56 (dq, $J = 14.0, 3.5$ Hz, 1H, $\text{H}_2\text{C}(5^{\text{eq}})$), 1.38 (s, 3H, $\text{H}_3\text{C}(2)$), 1.36 (dd, $J = 12.5, 2.0$ Hz, 1H, HC(9)), 1.26 (d, $J = 6.9$ Hz, 6H, $\text{H}_3\text{C}(24)$), 1.28-1.23 (m, 1H, $\text{H}_2\text{C}(6^{\text{ax}})$), 1.22 (s, 3H, $\text{H}_3\text{C}(8)$), 1.18 (d, $J = 6.9$ Hz, 6H, $\text{H}_3\text{C}(24')$), 1.11 (s, 3H, $\text{H}_3\text{C}(1)$).

¹³C NMR: (126 MHz, CDCl₃)
154.16 (C(20)), 149.34 (C(13)), 135.16 (C(15)), 131.94 (C(12)), 130.99 (C(19)),
129.02 (HC(17)), 128.88 (HC(22)), 126.44 (HC(16)), 125.04 (HC(14)), 123.69
(HC(21)), 61.94 (HC(4)), 52.55 (HC(9)), 39.31 (H₂C(6)), 39.07 (C(3)), 37.87
(C(7)), 31.48 (HC(23)), 30.44 (H₂C(11)), 29.79 (H₃C(2)), 26.19 (H₂C(5)), 25.04
(H₃C(24')), 24.94 (H₃C(8)), 24.12 (H₃C(24)), 21.39 (H₃C(18)), 19.75 (H₂C(10)),
17.75 (H₃C(1)).

IR: (neat)
2962 (s), 2929 (m), 2861 (m), 1573 (w), 1500 (m), 1457 (m), 1386 (m), 1375 (m),
1361 (m), 1305 (w), 1269 (w), 1248 (w), 1177 (m), 1161 (m), 1051 (m), 991 (w),
967 (m), 881 (m), 836 (w), 808 (s), 800 (s), 768 (m), 754 (s), 745 (m), 713 (w),
582 (w), 513 (w), 461 (s).

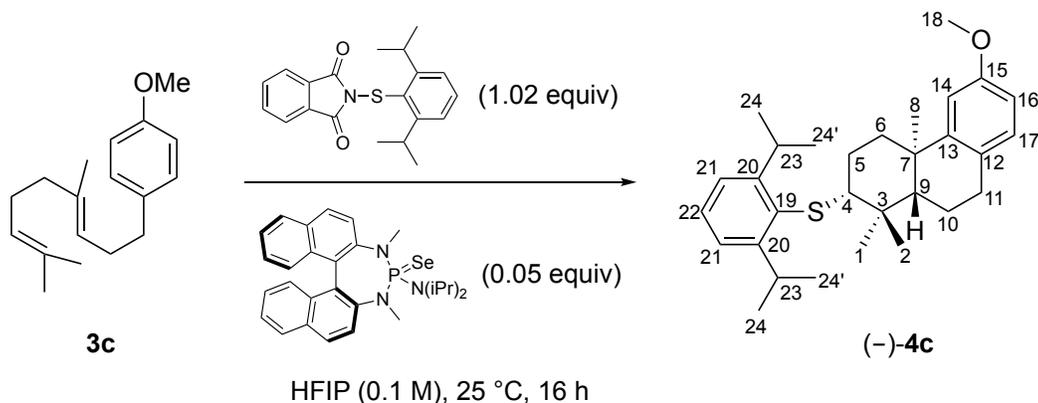
LRMS: (EI, 70 eV)
55.2 (16), 69.1 (46), 83.1 (14), 91.1 (15), 97.1 (13), 105.1 (15), 115.1 (17), 123.1
(11), 128.1 (18), 129.1 (19), 131.1 (40), 141.1 (16), 142.1 (17), 143.1 (33), 145.1
(100), 146.1 (12), 149.1 (19), 151.1 (28), 155.1 (12), 156.1 (11), 157.1 (68), 158.1
(17), 159.1 (21), 171.1 (48), 179.1 (12), 183.1 (11), 185.1 (23), 194.1 (38), 199.2
(11), 225.2 (34), 240.2 (11), 241.2 (97), 242.2 (19), 434.3 (66), 435.3 (24).

Analysis: C₃₀H₄₂S (434.73)
Calcd: C, 82.89%; H, 9.74%
Found: C, 82.55%; H, 9.82%

TLC: R_f 0.33 (silica gel, hexanes/CH₂Cl₂, 90:10, UV/CAM or PMA)

HPLC: 10.2 min (50%); t_R 11.3 min (50%) (Supelco Astec, hexanes/*i*-PrOH, 99:1, 0.3
mL/min, 220 nm, 24 °C)

Preparation of (–)-(2,6-Diisopropylphenyl) ((4*R*,7*R*,9*S*)-15-Methoxy-3,3,7-trimethyl-3,4,5,6,7,9,10,11-octahydrophenanthren-4-yl) Sulfide ((–)-4c)



A 100-mL, round-bottomed flask equipped with a stir bar and argon inlet adapter was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (346.2 mg, 1.02 mmol, 1.02 equiv), hexafluoroisopropyl alcohol (10 mL, 0.1 M), and (*E*)-1-(4,8-dimethylnona-3,7-dien-1-yl)-4-methoxybenzene **3c** (258.4 mg, 1.00 mmol). A homogeneous, yellow solution resulted. Catalyst (*S*)-**2** (26.0 mg, 0.05 mmol, 0.05 equiv) was added in one portion and the mixture was stirred at 25 °C for 16 h. Full conversion was observed by TLC (hexanes/CH₂Cl₂, 90:10). The reaction mixture was diluted with CH₂Cl₂ (10 mL), and the volatiles were removed by rotary evaporation (30 °C, 15 mmHg) to afford crude (–)-**4c**. The crude product was purified by column chromatography (silica gel, 3 x 25 cm, dry load on Celite, 25-mL fractions, hexanes/CH₂Cl₂ gradient elution: 83:17 (600 mL) to 80:20 (600 mL)) to afford crude (–)-**4c** as a sticky oil. To obtain analytically pure material, the compound was dissolved in boiling abs. ethanol (3 mL) and allowed to cool slowly to 25 °C, followed by cooling in a –20 °C freezer for 12 h. The product was collected by vacuum filtration and rinsed with ice-cold hexanes (2 mL) to afford 267.3 mg (59%) of (–)-**4c** as white crystals. Spectroscopic data match those reported for (±)-**4c**.

Data for (–)-**4c**:

m.p.: 119–120 °C (ethanol)

Analysis: C₃₀H₄₂OS (450.72)

Calcd: C, 79.94%; H, 9.39%

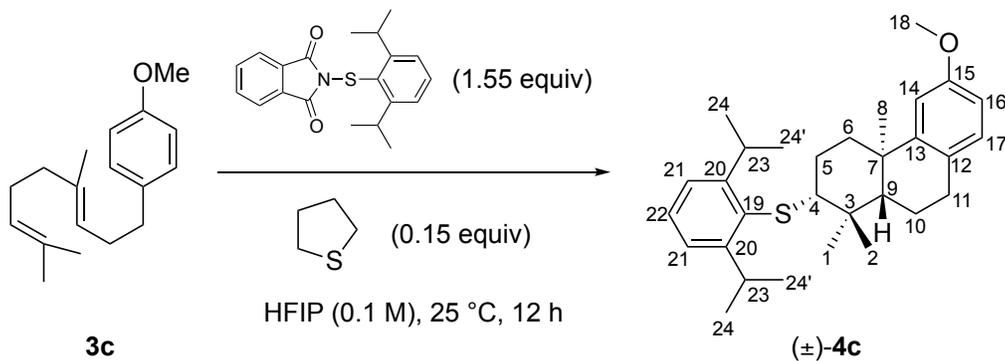
Found: C, 79.55%; H, 9.53%

HPLC: *t*_R 8.8 min (8%); *t*_R 9.5 min (92%) (Supelco Astec, hexanes/*i*-PrOH, 90:10, 0.5 mL/min, 220 nm, 24 °C)

after recrystallization: t_R 8.8 min (9%); t_R 9.7 min (91%)

Opt. Rot: $[\alpha]_D^{25} -29.5$ ($c = 1.05$ in CHCl_3)

Preparation of (\pm)-(2,6-Diisopropylphenyl) ((4*R,7*R**,9*S**)-15-Methoxy-3,3,7-trimethyl-3,4,5,6,7,9,10,11-octahydrophenanthren-4-yl) Sulfide ((\pm)-4c)**



A 50-mL pear-shaped flask equipped with a stir bar and argon inlet adapter was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (351.5 mg, 1.04 mmol, 1.03 equiv), hexafluoroisopropyl alcohol (10 mL, 0.1 M), and (*E*)-1-(4,8-dimethylnona-3,7-dien-1-yl)-4-methoxybenzene (259.7 mg, 1.01 mmol). A homogeneous, yellow solution resulted. Tetrahydrothiophene (4.4 μL , 0.05 mmol, 0.05 equiv) was added at 25 °C. The reaction was stirred at 25 °C for 4 h. Within 20 min, a red-purple solution was observed, ultimately resulting in a purple suspension. Incomplete conversion was observed by TLC (hexanes/ CH_2Cl_2 , 90:10). An additional portion of *N*-(2,6-diisopropylphenylthio)phthalimide **1** (180 mg, 0.53 mmol, 0.52 equiv) was added to the flask in one portion. The reaction was stirred at 25 °C under argon for 8 h. Full conversion was observed by TLC (hexanes/ CH_2Cl_2 , 90:10). The mixture was diluted with CH_2Cl_2 (10 mL) and the volatiles were removed by rotary evaporation (30 °C, 15 mmHg) to afford crude (\pm)-**4c**. The residue was purified by column chromatography (silica gel, 3 x 20 cm, dry load on Celite, 25-mL fractions, hexanes/ CH_2Cl_2 gradient elution: 90:10 (300 mL) to 85:15 (300 mL) to 80:20 (300 mL) to 75:25 (300 mL)) to afford 328.2 mg (73%) of (\pm)-**4c** as an off-white foam solid. The product was contaminated with trace impurities which cannot be removed by chromatography. To obtain analytically pure material, the solid was dissolved in boiling hexanes (10 mL) and the solution was allowed to cool first to 25 °C, followed by 8 h in a -20 °C freezer. The product was collected by vacuum filtration (rinsing with ice-cold hexanes) to afford 248.0 mg (55%) of analytically pure (\pm)-**4c** as white, cubic crystals.

Data for (±)-4c:

m.p.: 194–196 °C (hexanes)

¹H NMR: (500 MHz, CDCl₃)

7.31 (t, $J = 7.7$ Hz, 1H, HC(22)), 7.16 (d, $J = 7.7$ Hz, 2H, HC(21)), 6.96 (d, $J = 8.4$ Hz, 1H, HC(17)), 6.70 (d, $J = 2.6$ Hz, 1H, HC(14)), 6.65 (dd, $J = 8.4, 2.6$ Hz, 1H, HC(16)), 4.01 (hept, $J = 6.9$ Hz, 2H, HC(23)), 3.73 (s, 3H, H₃C(18)), 2.96-2.87 (m, 1H, H₂C(11^{eq})), 2.80 (ddd, $J = 17.0, 11.5, 7.0$ Hz, 1H, H₂C(11^{ax})), 2.62 (dd, $J = 12.5, 3.8$ Hz, 1H, HC(4)), 2.18 (dt, $J = 13.0, 3.3$ Hz, 1H, H₂C(6^{eq})), 1.98-1.92 (m, 1H, H₂C(10^{eq})), 1.92-1.83 (m, 1H, H₂C(5^{ax})), 1.82-1.72 (m, 1H, H₂C(10^{ax})), 1.56 (dq, $J = 13.5, 3.5$ Hz, 1H, H₂C(5^{eq})), 1.39 (s, 3H, H₃C(2)), 1.36 (dd, $J = 12.5, 2.0$ Hz, 1H, HC(9)), 1.29-1.23 (m, 1H, H₂C(6^{ax})), 1.26 (d, $J = 6.9$ Hz, 6H, H₃C(24)), 1.22 (s, 3H, H₃C(8)), 1.18 (d, $J = 6.9$ Hz, 6H, H₃C(24')), 1.11 (s, 3H, H₃C(1)).

¹³C NMR: (126 MHz, CDCl₃)

157.87 (C(15)), 154.16 (C(20)), 150.73 (C(13)), 130.93 (HC(19)), 129.89 (HC(17)), 128.92 (HC(22)), 127.27 (C(12)), 123.70 (HC(21)), 111.28 (HC(16)), 110.08 (HC(14)), 61.86 (HC(4)), 55.36 (H₃C(18)), 52.47 (HC(9)), 39.30 (H₂C(6)), 39.06 (C(3)), 38.15 (C(7)), 31.49 (HC(23)), 30.02 (H₂C(11)), 29.79 (H₃C(2)), 26.19 (H₂C(5)), 25.04 (H₃C(24')), 24.87 (H₃C(8)), 24.13 (H₃C(24)), 19.80 (H₂C(10)), 17.77 (H₃C(1)).

IR: (neat)

2963 (s), 2930 (m), 1607 (m), 1574 (w), 1494 (s), 1467 (m), 1386 (w), 1375 (m), 1361 (m), 1270 (m), 1254 (s), 1221 (m), 1192 (m), 1173 (m), 1088 (w), 1039 (s), 1007 (w), 992 (w), 968 (w), 879 (m), 806 (s), 770 (m), 755 (m), 745 (m), 736 (m), 712 (m), 638 (w), 581 (w), 471 (m).

LRMS: (EI, 70 eV)

55.1 (15), 69.1 (33), 83.1 (10), 91.1 (11), 115.1 (12), 121.1 (13), 128.1 (10), 147.1 (21), 151.1 (16), 159.1 (17), 161.1 (59), 173.1 (38), 174.1 (12), 175.1 (12), 187.1 (29), 201.1 (12), 241.2 (25), 256.2 (29), 257.2 (100), 258.2 (21), 450.3 (53), 451.3 (18).

Analysis: C₃₀H₄₂OS (450.73)

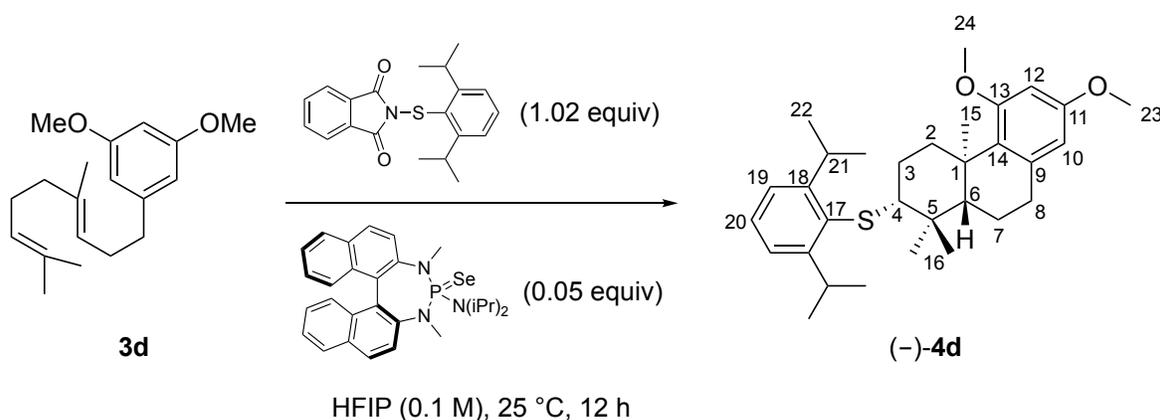
Calcd: C, 79.94%; H, 9.39%

Found: C, 79.75%; H, 9.45%

TLC: *R_f* 0.11 (silica gel, hexanes/CH₂Cl₂, 90:10, UV/CAM or PMA)

HPLC: *t_R* 8.9 min (50%); *t_R* 9.6 min (50%) (Supelco Astec, hexanes/*i*-PrOH, 90:10, 0.5 mL/min, 220 nm, 24 °C)

Preparation of (–)-(2,6-Diisopropylphenyl) ((1*R*,4*R*,6*S*)-11,13-Dimethoxy-1,5,5-trimethyl-1,2,3,4,5,6,7,8-octahydrophenanthren-4-yl) Sulfide (–)-4d****



A 100-mL, round-bottomed flask equipped with a stir bar and argon inlet adapter was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (346.2 mg, 1.02 mmol, 1.02 equiv), hexafluoroisopropyl alcohol (10 mL, 0.1 M), and (*E*)-1-(4,8-dimethylnona-3,7-dien-1-yl)-3,5-dimethoxybenzene **3d** (288.4 mg, 1.00 mmol). A homogeneous, yellow solution resulted. Catalyst (*S*)-**2** (26.0 mg, 0.05 mmol, 0.05 equiv) was added in one portion and the mixture was stirred at 25 °C for 16 h. Full conversion was observed by TLC (hexanes/CH₂Cl₂, 90:10). The reaction mixture was diluted with CH₂Cl₂ (10 mL), and the volatiles were removed by rotary evaporation (30 °C, 15 mmHg) to afford crude (–)-**4d**. The crude product was purified by column chromatography (silica gel, 3 x 25 cm, dry load on Celite, 25-mL fractions, hexanes/CH₂Cl₂ gradient elution: 83:17 (600 mL) to 80:20 (600 mL) to 67:33 (300 mL)) to afford crude (–)-**4d** (419.2 mg, 87%) as a white solid. To obtain analytically pure material, the compound was dissolved in boiling abs. ethanol (3 mL) and allowed to cool slowly to 25 °C, followed by cooling in a –20 °C freezer for 12 h. The product was collected by vacuum filtration and rinsed with ice-cold hexanes (2 mL) to afford 377.8 mg (78%) of (–)-**4d** as white crystals.

Data for (-)-4d:

m.p.: 139–141 °C (ethanol)

¹H NMR: (500 MHz, CDCl₃)

7.31 – 7.27 (m, 1H, HC(20)), 7.15 (d, J = 7.7 Hz, 2H, HC(19)), 6.25 (d, J = 2.6 Hz, 1H, HC(12)), 6.19 (d, J = 2.6 Hz, 1H, HC(10)), 4.02 (hept, J = 6.8 Hz, 2H, HC(21)), 3.74 (s, 3H, H₃C(23)), 3.69 (s, 3H, H₃C(24)), 3.02 (dt, J = 13.6, 3.5 Hz, 1H, H₂C(2)), 2.88 – 2.83 (m, 2H, H₂C(8)), 2.64 (dd, J = 12.6, 4.0 Hz, 1H, HC(4)), 1.92 – 1.76 (m, 2H, H₂C(7) and H₂C(3)), 1.68 – 1.58 (m, 1H, H₂C(7)), 1.44 (dq, J = 14.0, 3.7 Hz, 1H, H₂C(3)), 1.38 (s, 3H, H₃C(16)), 1.31 – 1.24 (m, 10H, H₃C(15), H₃C(22), and HC(6)), 1.18 (d, J = 6.9 Hz, 6H, H₃C(22)), 1.10 (s, 3H, H₃C(16)), 1.00 (td, J = 13.6, 3.2 Hz, 1H, H₂C(2)).

¹³C NMR: (126 MHz, CDCl₃)

159.5 (C(13)), 157.9 (C(11)), 154.0 (C(18)), 138.5 (C(9)), 131.0 (C(17)), 129.5 (C(14)), 128.6 (HC(20)), 123.5 (HC(19)), 104.7 (HC(10)), 97.6 (HC(12)), 61.8 (HC(4)), 55.4 (HC(6)), 55.1 (H₃C(23)), 54.9 (H₃C(24)), 39.2 (C(5)), 39.1 (C(1)), 37.2 (H₂C(2)), 33.6 (H₂C(8)), 31.3 (HC(21)), 30.1 (H₃C(16)), 26.3 (H₂C(3)), 24.9 (H₃C(22)), 24.0 (H₃C(22)), 19.8 (H₃C(15)), 19.5 (H₂C(7)), 18.1 (H₃C(16)).

IR: (neat)

2960 (w), 2866 (w), 2836 (w), 1604 (w), 1581 (w), 1461 (w), 1420 (w), 1390 (w), 1361 (w), 1350 (w), 1328 (w), 1307 (w), 1268 (w), 1246 (w), 1215 (w), 1201 (w), 1158 (m), 1095 (w), 1081 (w), 1053 (w), 1032 (w), 1020 (w), 998 (w), 974 (w), 939 (w), 909 (w), 883 (w), 826 (w), 802 (w), 767 (w), 753 (w), 732 (m), 649 (w), 632 (w), 568 (w), 463 (w).

LRMS: (EI, 70 eV)

57.1 (19), 69.1 (17), 83.1 (11), 191.1 (23), 203.1 (21), 271.2 (16), 287.2 (100), 446.2 (59), 480.3 (26).

HRMS: Calcd for C₃₁H₄₄O₂S ([M]⁺): 480.3062, Found: 480.3061

TLC: *R_f* 0.29 (silica gel, hexanes/CH₂Cl₂, 67:33, PMA)

HPLC: *t_R* 7.7 min (90%); *t_R* 8.9 min (10%) (Supelco Astec, hexanes/*i*-PrOH, 98:2, 0.5 mL/min, 220 nm, 24 °C)

After recrystallization: *t_R* 7.6 min (95%); *t_R* 8.6 min (5%)

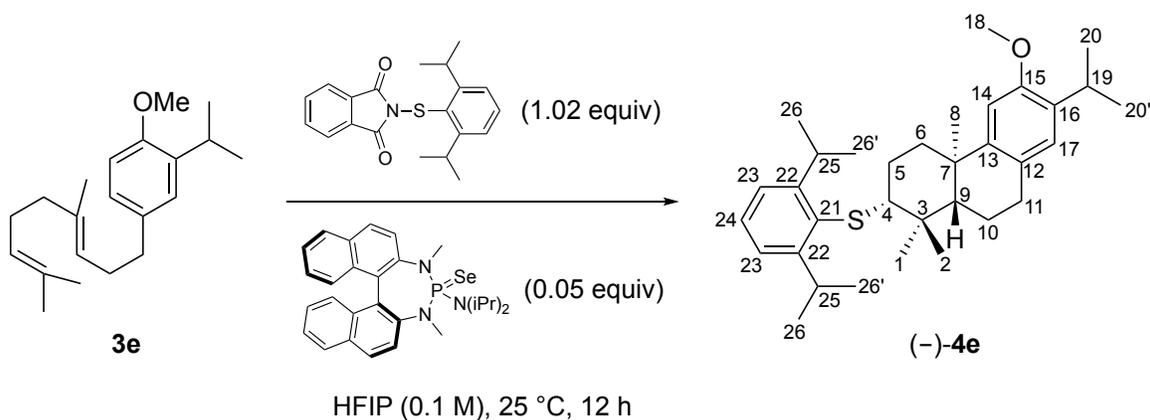
Opt. Rot.: $[\alpha]_D^{24} -33.7$ ($c = 1.10$ in CHCl_3)

Analysis: $\text{C}_{31}\text{H}_{44}\text{O}_2\text{S}$ (480.75)

Calcd: C, 77.45%; H, 9.23%

Found: C, 77.10%; H, 9.17%

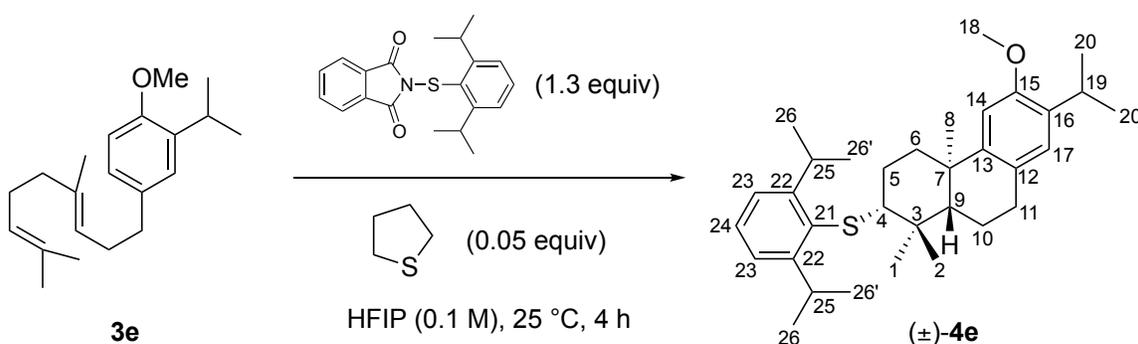
Preparation of (–)-(2,6-Diisopropylphenyl) ((4*R*,7*R*,9*S*)-16-Isopropyl-15-methoxy-3,3,7-trimethyl-3,4,5,6,7,9,10,11-octahydrophenanthren-4-yl) Sulfide ((–)-4e)



A 100-mL, round-bottomed flask equipped with a stir bar and argon inlet adapter was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (349.2 mg, 1.03 mmol, 1.03 equiv), hexafluoroisopropyl alcohol (10 mL, 0.1 M), and (*E*)-4-(4,8-dimethylnona-3,7-dien-1-yl)-2-isopropyl-1-methoxybenzene **3e** (301.4 mg, 1.00 mmol). A homogeneous, yellow solution resulted. Catalyst (*S*)-**2** (27.5 mg, 0.05 mmol, 0.05 equiv) was added in one portion and the mixture was stirred at 25 °C for 12 h. Full conversion was observed by TLC (hexanes/ CH_2Cl_2 , 90:10). The reaction mixture was diluted with CH_2Cl_2 (10 mL), and the volatiles were removed by rotary evaporation (30 °C, 15 mmHg) to afford crude (–)-**4e**. The crude product was purified by column chromatography (silica gel, 3 x 25 cm, dry load on Celite, 25-mL fractions, hexanes/ CH_2Cl_2 gradient elution: 92:8 (600 mL) to 91:9 (600 mL)) to afford (–)-**4e** (419.2 mg, 87%) as an oily solid. To obtain analytically pure material, the compound was dissolved in boiling abs. ethanol (3 mL) and allowed to cool slowly to 25 °C, followed by cooling in a –20 °C freezer for 12 h. The product was collected by vacuum filtration and rinsed with ice-cold hexanes (2 mL) to afford 336.7 mg (68%) of (–)-**4e** as white crystals. Spectroscopic data matched those for (±)-**4e**.

Data for (-)-4e:

- m.p.: 113–115 °C (ethanol)
Analysis: C₃₃H₄₈OS (492.81)
 Calcd: C, 80.43%; H, 9.82%
 Found: C, 80.57%; H, 10.01%
Opt. Rot.: [α]_D²⁴ -29.8 (*c* = 1.10 in CHCl₃) (82% ee)
HPLC: HPLC analysis is performed on derivative (-)-7e'

Preparation of (±)-(2,6-Diisopropylphenyl) ((4*R,7*R**,9*S**)-16-Isopropyl-15-methoxy-3,3,7-trimethyl-3,4,5,6,7,9,10,11-octahydrophenanthren-4-yl) Sulfide ((±)-4e)**

A 100-mL pear-shaped flask equipped with a stir bar and argon inlet adapter was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (365.2 mg, 1.08 mmol, 1.08 equiv), hexafluoroisopropyl alcohol (10 mL, 0.1 M), and (*E*)-4-(4,8-dimethylnona-3,7-dien-1-yl)-2-isopropyl-1-methoxybenzene **3e** (299.5 mg, 1.00 mmol). A homogeneous, yellow solution resulted. Tetrahydrothiophene (4.4 μ L, 4.4 mg, 0.050 mmol, 0.05 equiv) was added to the solution at 25 °C. The reaction was stirred at 25 °C under argon for 3 h. Within 10 min, a pink suspension resulted. After 3 h, incomplete conversion was observed by TLC analysis (hexanes/CH₂Cl₂, 90:10), and an additional portion of *N*-(2,6-diisopropylphenylthio)phthalimide **1** (70.2 mg, 0.21 mmol, 0.21 equiv) was added in one portion. Stirring was continued for 1 h at 25 °C, over which time a purple suspension resulted. At this point, TLC analysis showed full consumption of starting material. The mixture was diluted with CH₂Cl₂ (10 mL), and the volatiles were removed by rotary evaporation to afford crude (±)-**4e**. The residue was purified by column chromatography (silica gel, 3 x 20 cm, dry load on Celite, 25-mL fractions, hexanes/CH₂Cl₂ gradient elution: 95:5 (300 mL) to 90:10 (300 mL) to 85:15 (300 mL) to 80:20

(300 mL)) to afford 368.0 mg of (\pm)-**4e** as a white solid. The product was contaminated with trace impurities which are not removable by chromatography. To obtain analytically pure material, the solid was dissolved in boiling hexanes (2 mL) and allowed to cool slowly to 25 °C followed by 12 h in a -20 °C freezer. The product was collected by vacuum filtration and rinsed with ice-cold hexanes (2 mL), affording 172.4 mg (35%) of (\pm)-**4e** as fluffy, white crystals.

Data for (\pm)-**4e**:

m.p.: 143–145 °C (hexanes)

¹H NMR: (500 MHz, CDCl₃)

7.30 (t, $J = 7.7$ Hz, 1H, HC(24)), 7.15 (d, 7.7 Hz, 2H, HC(23)), 6.84 (s, 1H, HC(17)), 6.61 (s, 1H, HC(14)), 4.01 (hept, $J = 6.9$ Hz, 2H, HC(25)), 3.72 (s, 3H, H₃C(18)), 3.19 (hept, $J = 6.9$ Hz, 1H, HC(19)), 2.93-2.85 (m, 1H, H₂C(11^{eq})), 2.84-2.74 (m, 1H, H₂C(11^{ax})), 2.61 (dd, $J = 12.5, 3.8$ Hz, 1H, HC(4)), 2.20 (dt, $J = 13.1, 3.4$ Hz, 1H, H₂C(6^{eq})), 1.98-1.92 (m, 1H, H₂C(10^{eq})), 1.92-1.83 (m, 1H, H₂C(5^{ax})), 1.82-1.72 (m, 1H, H₂C(10^{ax})), 1.57 (dq, $J = 10.2, 3.6$ Hz, 1H, H₂C(5^{eq})), 1.39 (s, 3H, H₃C(2)), 1.38 (dd, $J = 12.0, 2.0$ Hz, 1H, HC(9)), 1.30 (dd, $J = 13.4, 3.5$ Hz, 1H, H₂C(6^{ax})), 1.26 (d, $J = 7.0$ Hz, 6H, H₃C(26)), 1.23 (s, 3H, H₃C(8)), 1.18 (d, $J = 7.0$ Hz, 3H, H₃C(20)), 1.17 (d, $J = 7.0$ Hz, 6H, H₃C(26')), 1.16 (d, $J = 7.0$ Hz, 3H, H₃C(20')), 1.11 (s, 3H, H₃C(1)).

¹³C NMR: (126 MHz, CDCl₃)

155.21 (C(15)), 154.16 (C(22)), 147.41 (C(13)), 134.59 (C(16)), 130.98 (C(21)), 128.89 (HC(24)), 126.68 (C(12)), 126.49 (HC(17)), 123.69 (HC(23)), 106.50 (HC(14)), 61.96 (HC(4)), 55.60 (H₃C(18)), 52.59 (HC(9)), 39.41 (H₂C(6)), 39.03 (C(3)), 37.96 (C(7)), 31.48 (HC(25)), 30.24 (H₂C(11)), 29.78 (H₃C(2)), 26.58 (HC(19)), 26.23 (H₂C(5)), 25.05 (H₃C(26')), 24.91 (H₃C(8)), 24.12 (H₃C(26)), 23.00 (H₃C(20') or H₃C(20)), 22.81 (H₃C(20) or H₃C(20')), 19.89 (H₂C(10)), 17.75 (H₃C(1)).

IR: (neat)

2965 (s), 2934 (s), 2868 (m), 1614 (w), 1574 (w), 1498 (s), 1463 (s), 1405 (m), 1383 (m), 1361 (m), 1303 (m), 1252 (s), 1235 (s), 1196 (s), 1166 (m), 1102 (m), 1074 (m), 1055 (s), 997 (m), 968 (m), 892 (m), 878 (m), 843 (s), 798 (s), 778 (s), 746 (s), 732 (m), 713 (w), 573 (w), 481 (m).

LRMS: (EI, 70 eV)

55.1 (13), 69.1 (23), 149.0 (11), 151.1 (16), 163.1 (16), 179.1 (10), 189.1 (17),
201.1 (14), 203.1 (39), 215.1 (30), 229.2 (18), 257.2 (16), 283.2 (20), 298.2 (27),
299.2 (100), 300.2 (29), 492.3 (62), 493.3 (23).

Analysis: C₃₃H₄₈OS (492.81)

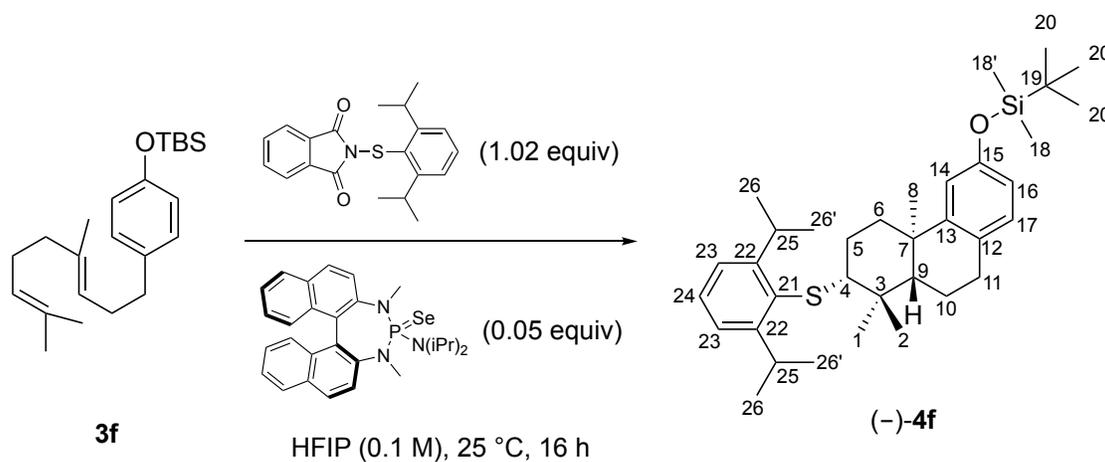
Calcd: C, 80.43%; H, 9.82%

Found: C, 80.76%; H, 9.99%

TLC: R_f 0.19 (silica gel, hexanes/CH₂Cl₂, 90:10, UV/CAM or PMA)

HPLC: HPLC analysis is performed on derivative (±)-**7e'**

Preparation of (–)-*tert*-Butyl(((4*R*,7*R*,9*S*)-4-(2,6-diisopropylphenylthio)-3,3,7-trimethyl-3,4,5,6,7,9,10,11-octahydrophenanthren-15-yl)oxy)dimethylsilane ((–)-4f**)**



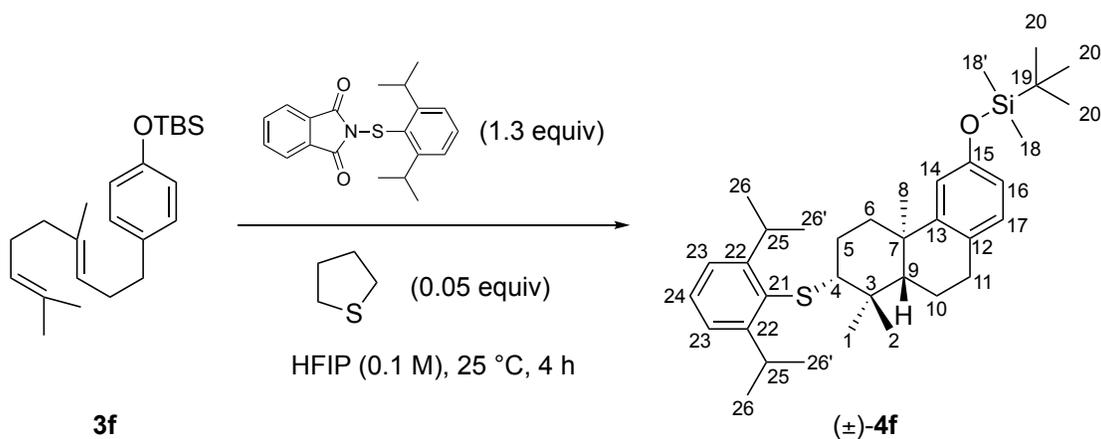
A 100-mL, round-bottomed flask equipped with a stir bar and argon inlet adapter was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (346.2 mg, 1.02 mmol, 1.02 equiv), hexafluoroisopropyl alcohol (10 mL, 0.1 M), and (*E*)-*tert*-butyl(4-(4,8-dimethylnona-3,7-dien-1-yl)phenoxy)dimethylsilane **3f** (358.6 mg, 1.00 mmol). A homogeneous, yellow solution resulted. Catalyst (*S*)-**2** (26.0 mg, 0.05 mmol, 0.05 equiv) was added in one portion and the mixture was stirred at 25 °C for 16 h. Full conversion was observed by TLC (hexanes/CH₂Cl₂, 90:10). The reaction mixture was diluted with CH₂Cl₂ (10 mL), and the volatiles were removed by rotary evaporation (30 °C, 15 mmHg) to afford crude (–)-**4f**. The crude product was purified by column chromatography (silica gel, 3 x 25 cm, dry load on Celite, 25-mL fractions, hexanes/CH₂Cl₂ gradient elution: 95:5 (600 mL) to 94:6 (600 mL)) to afford (–)-**4f** as an oily solid. To obtain

analytically pure material, the compound was dissolved in boiling abs. ethanol (3 mL) and allowed to cool slowly to 25 °C, followed by cooling in a –20 °C freezer for 12 h. The product was collected by vacuum filtration and rinsed with ice-cold hexanes (2 mL) to afford 389.1 mg (71%) of (–)-**4f** as white powder. Spectroscopic data matched those for (±)-**4f**.

Data for (–)-**4f**:

- m.p.: 122–124 °C (ethanol)
Analysis: C₃₅H₅₄OSSi (550.96)
 Calcd: C, 76.30%; H, 9.88%
 Found: C, 76.01%; H, 10.13%
Opt. Rot.: [α]_D²⁵ –40.4 (*c* = 1.06 in CHCl₃) (90% ee)
HPLC: HPLC analysis is performed on desilylated derivative (–)-**4i**.

Preparation of (±)-*tert*-Butyl(((4*R,7*R**,9*S**)-4-((2,6-diisopropylphenyl)thio)-3,3,7-trimethyl-3,4,5,6,7,9,10,11-octahydrophenanthren-15-yl)oxy)dimethylsilane ((±)-**4f**)**



A 100-mL, round-bottomed flask equipped with a stir bar and argon inlet adapter was charged with *N*-(2,6-diisopropylphenyl)thiophthalimide **1** (373.7 mg, 1.10 mmol, 1.11 equiv), hexafluoroisopropyl alcohol (10 mL, 0.1 M), and (*E*)-*tert*-butyl(4-(4,8-dimethylnona-3,7-dien-1-yl)phenoxy)dimethylsilane (354.6 mg, 0.99 mmol). A homogeneous, yellow solution resulted. Tetrahydrothiophene (4.4 μ L, 0.049 mmol, 0.05 equiv) was added in one portion at 25 °C. The reaction was stirred at 25 °C for 2 h under argon. Within 10 min, a turbid, salmon-colored solution was observed, ultimately resulting in a purple suspension. An additional portion of *N*-(2,6-diisopropylphenyl)thiophthalimide **1** (69.2 mg, 0.20 mmol, 0.21 equiv) was added in one portion as a solid. Stirring was continued for 2 h at 25 °C. Full conversion was observed by TLC

(hexanes/CH₂Cl₂, 90:10). The reaction mixture was diluted with CH₂Cl₂ (10 mL) and the volatiles were removed by rotary evaporation. The residue was purified by column chromatography (silica gel, 3 x 20 cm, dry load on Celite, 25-mL fractions, hexanes/CH₂Cl₂ gradient elution: 95:5 (300 mL) to 90:10 (300 mL) to 85:15 (300 mL) to 80:20 (300 mL)) to afford 349.5 mg (64% yield) of (±)-**4f** as a white solid. The solid was contaminated with trace impurities which cannot be removed by chromatography. To obtain analytically pure material, the solid was taken up in a minimal quantity of boiling abs. ethanol (8 mL) and the resulting solution was filtered and allowed to cool slowly to 25 °C followed by 12 h in a -20 °C freezer. The product was collected by vacuum filtration to afford 124.8 mg (23%) of (±)-**4f** as small, round, white crystals.

Data for (±)-**4f**:

m.p.: 93–98 °C (ethanol)

¹H NMR: (500 MHz, CDCl₃)

7.31 (t, *J* = 7.7 Hz, 1H, HC(24)), 7.16 (d, *J* = 7.7 Hz, 2H, HC(23)), 6.87 (d, *J* = 8.2 Hz, 1H, HC(17)), 6.61 (d, *J* = 2.5 Hz, 1H, HC(14)), 6.55 (dd, *J* = 8.2, 2.5 Hz, 1H, HC(16)), 4.01 (hept, *J* = 6.8 Hz, 2H, HC(25)), 2.93-2.84 (m, 1H, H₂C(11^{eq})), 2.83-2.74 (m, 1H, H₂C(11^{ax})), 2.60 (dd, *J* = 12.5, 3.8 Hz, 1H, HC(4)), 2.13 (dt, *J* = 13.3, 3.3 Hz, 1H, H₂C(6^{eq})), 1.97-1.91 (m, 1H, H₂C(10^{eq})), 1.91-1.82 (m, 1H, H₂C(5^{ax})), 1.80-1.70 (m, 1H, H₂C(10^{ax})), 1.56 (dq, *J* = 13.5, 3.6 Hz, 1H, H₂C(5^{eq})), 1.39 (s, 3H, H₃C(2)), 1.36-1.33 (m, 1H, HC(9)), 1.26 (d, *J* = 6.9 Hz, 6H, H₃C(26)), 1.24-1.21 (m, 1H, H₂C(6^{ax})), 1.20 (s, 3H, H₃C(8)), 1.18 (d, *J* = 6.9 Hz, 6H, H₃C(26')), 1.10 (s, 3H, H₃C(1)), 0.94 (s, 9H, H₃C(20)), 0.13 (s, 3H, H₃C(18)), 0.12 (s, 3H, H₃C(18')).

¹³C NMR: (126 MHz, CDCl₃)

154.21 (C(22)), 153.66 (C(15)), 150.53 (C(13)), 130.98 (C(21)), 129.72 (HC(17)), 128.93 (HC(24)), 127.66 (C(12)), 123.69 (HC(23)), 117.61 (HC(16)), 115.91 (HC(14)), 61.96 (HC(4)), 52.43 (HC(9)), 39.30 (H₂C(6)), 39.03 (C(3)), 37.94 (C(7)), 31.48 (HC(25)), 30.17 (H₂C(11)), 29.77 (H₃C(2)), 26.27 (H₂C(5)), 25.88 (H₃C(20)), 25.05 (H₃C(26')), 24.86 (H₃C(8)), 24.13 (H₃C(26)), 19.83 (H₂C(10)), 18.35 (C(19)), 17.78 (H₃C(1)), -4.24 (H₃C(18) or H₃C(18')), -4.28 (H₃C(18) or H₃C(18')).

IR: (neat)

2961 (m), 2858 (w), 1606 (w), 1573 (w), 1490 (m), 1470 (w), 1391 (w), 1376 (w), 1361 (w), 1288 (w), 1266 (m), 1252 (m), 1222 (w), 1188 (w), 1162 (w), 1054 (w), 1006 (w), 967 (m), 927 (w), 905 (m), 882 (w), 872 (w), 836 (s), 797 (m), 779 (s), 746 (m), 734 (w), 692 (w), 628 (w), 570 (w), 481 (w).

LRMS: (EI, 70 eV)

163.1 (21), 183.1 (10), 221.1 (50), 222.1 (11), 231.1 (11), 247.1 (33), 261.2 (55), 262.2 (12), 273.2 (17), 287.2 (12), 315.2 (14), 341.2 (21), 356.2 (27), 357.3 (100), 358.3 (31), 446.1 (41), 447.2 (14), 550.4 (26), 551.4 (12).

Analysis: C₃₅H₅₄OSSi (550.96)

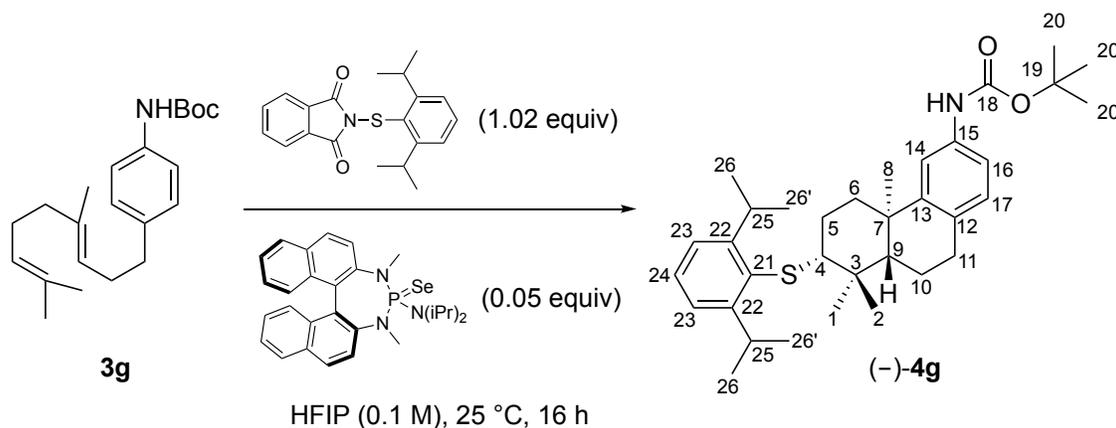
Calcd: C, 76.30% H, 9.88%

Found: C, 76.05% H, 9.95%

TLC: *R_f* 0.20 (silica gel, hexanes/CH₂Cl₂, 90:10, UV/CAM or PMA)

HPLC: Analysis performed on de-silylated compound (\pm)-**4i**.

Preparation of (-)-*tert*-Butyl ((4*R*,7*R*,9*S*)-4-(2,6-Diisopropylphenylthio)-3,3,7-trimethyl-3,4,5,6,7,9,10,11-octahydrophenanthren-15-yl)carbamate ((-)-4g**)**



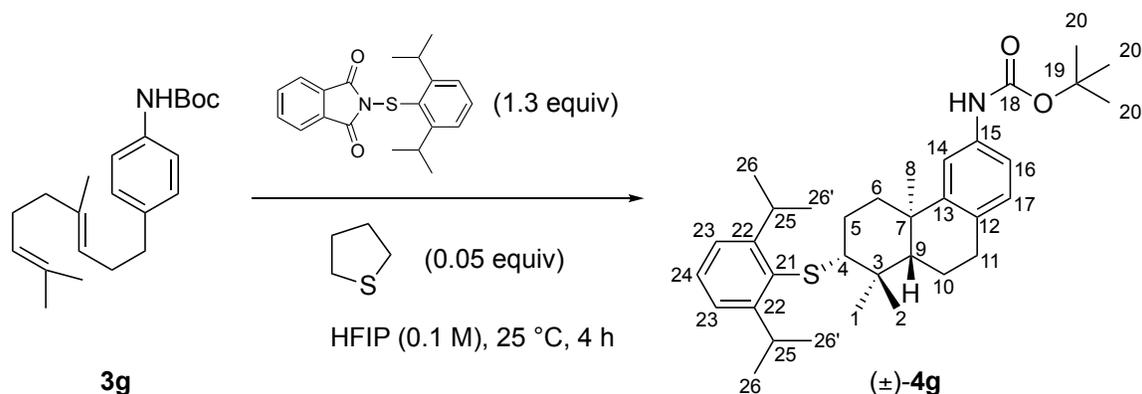
A 100-mL, round-bottomed flask equipped with a stir bar and argon inlet adapter was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (346.2 mg, 1.02 mmol, 1.02 equiv), hexafluoroisopropyl alcohol (10 mL, 0.1 M), and *tert*-butyl (*E*)-4-(4,8-dimethylnona-3,7-dien-1-yl)phenylcarbamate **3g** (343.5 mg, 1.00 mmol). A homogeneous, yellow solution resulted. Catalyst (*S*)-**2** (26.0 mg, 0.05 mmol, 0.05 equiv) was added in one portion and the mixture was stirred at 25 °C for 16 h. Full conversion was observed by TLC (hexanes/EtOAc, 80:20). The

reaction mixture was diluted with CH₂Cl₂ (10 mL), and the volatiles were removed by rotary evaporation (30 °C, 15 mmHg). The residue was purified by column chromatography (silica gel, 3 x 25 cm, dry load on Celite, 25-mL fractions, hexanes/EtOAc gradient elution: 25:1 (600 mL) to 20:1 (600 mL)) to afford a crude oily solid containing (–)-**4g** and (*S*)-**2**. The mixture was dissolved in methanol (15 mL) followed by addition of NiCl₂·6H₂O (237 mg). Sodium borohydride (114 mg) was added to the green solution, and the resulting jet-black suspension was stirred at 25 °C for 12 h under argon. The mixture was filtered through a pad of Celite and rinsed through with Et₂O (3 x 5 mL). The filtrate was concentrated (30 °C, 15 mmHg) and partitioned between Et₂O (25 mL) and brine (25 mL). The layers were separated, and the aqueous layer was extracted with Et₂O (3 x 25 mL). The combined organic layers were washed with brine (25 mL) and then dried over magnesium sulfate, filtered, and concentrated (30 °C, 15 mmHg). The resulting residue was purified by column chromatography (silica gel, 3 x 25 cm, dry load on Celite, 25-mL fractions, hexanes/EtOAc, 96:4 (1000 mL)) to afford (–)-**4g**. The product was contaminated with trace impurities which cannot be removed by chromatography. To obtain analytically pure material, the compound was dissolved in a hot methanol/ethanol 2:1 solution (3 mL) and allowed to cool slowly to 25 °C, followed by cooling in a –20 °C freezer for 12 h. The product was collected by vacuum filtration and rinsed with ice-cold ethanol (2 mL) to afford 419.0 mg (78%) of (–)-**4g** as white crystals. Spectroscopic data matched those for (±)-**4g**.

Data for (–)-**4g**:

- m.p.: 104-108 °C (methanol/ethanol)
- Analysis: C₃₄H₄₉NO₂S (535.83)
Calcd: C, 76.21% H, 9.22% N, 2.61%
Found: C, 76.03% H, 9.25% N, 2.74%
- Opt. Rot.: [α]_D²³ –61.8 (*c* = 1.30 in CHCl₃) (86% ee)
- HPLC: *t*_R 4.3 min (92%); *t*_R 12.6 min (8%) (Chiralpak IB-3, hexanes/*i*-PrOH, 90:10, 1.0 mL/min, 220 nm, 24 °C)
After recrystallization: *t*_R 4.3 min (93%); *t*_R 12.1 min (7%)

Preparation of (\pm)-*tert*-Butyl ((4*R,7*S**,9*S**)-4-(2,6-Diisopropylphenylthio)-3,3,7-trimethyl-3,4,5,6,7,9,10,11-octahydrophenanthren-15-yl)carbamate ((\pm)-**4g**)**



A 100-mL, round-bottomed flask equipped with a stir bar and argon inlet adapter was charged with *N*-(2,6-diisopropylphenyl)thiophthalimide **1** (359.4 mg, 1.06 mmol, 1.06 equiv), hexafluoroisopropyl alcohol (10 mL, 0.1 M), and *tert*-butyl (*E*)-(4-(4,8-dimethylnona-3,7-dien-1-yl)phenyl)carbamate **3g** (344.0 mg, 1.00 mmol). A homogeneous, yellow solution resulted. Tetrahydrothiophene (4.4 μ L, 0.050 mmol, 0.05 equiv) was added in one portion at 25 °C. Within 10 min, a purple suspension resulted. The mixture was stirred at 25 °C for 2 h under argon. An additional portion of *N*-(2,6-diisopropylphenyl)thiophthalimide **1** (74.7 mg, 0.22 mmol, 0.22 equiv) was added in one portion as a solid. Stirring was continued for 2 h at 25 °C. Full conversion was observed by TLC (hexanes/EtOAc, 80:20). The reaction mixture was diluted with CH₂Cl₂ (10 mL) and the volatiles were removed by rotary evaporation (30 °C, 15 mmHg). The residue was purified by column chromatography (silica gel, 3 x 20 cm, dry load on Celite, 25-mL fractions, hexanes/EtOAc gradient elution: 95:5 (300 mL) to 90:10 (300 mL) to 85:15 (300 mL)) to afford 438.9 mg (82%) of (\pm)-**4g** as a white solid. The product was contaminated with trace impurities which cannot be removed by chromatography. To obtain analytically pure material, the solid was dissolved in boiling methanol (20 mL) and the resulting solution was hot filtered and allowed to cool slowly to 25 °C followed by 12 h in a -20 °C freezer. The product was collected by vacuum filtration to afford 156.9 mg (29%) of (\pm)-**4g** as thin, white needles.

Data for (\pm)-**4g**:

- m.p.: 156-157 °C (methanol)
¹H NMR: (500 MHz, CDCl₃)
 7.30 (t, *J* = 7.7 Hz, 1H, HC(24)), 7.21 (bs, 1H, HC(14)), 7.16 (d, *J* = 7.7 Hz, 2H, HC(23)), 7.01-6.96 (m, 1H, HC(16)), 6.94 (d, *J* = 8.2 Hz, 1H, HC(17)), 6.30 (bs,

1H, NH), 4.00 (hept, $J = 6.8$ Hz, 2H, HC(25)), 2.95-2.87 (m, 1H, H₂C(11^{eq})), 2.85-2.75 (m, 1H, H₂C(11^{ax})), 2.59 (dd, $J = 12.5, 3.8$ Hz, 1H, HC(4)), 2.26-2.16 (m, 1H, H₂C(6^{eq})), 1.99-1.91 (m, 1H, H₂C(10^{eq})), 1.86 (qd, $J = 13.8, 3.3$ Hz, 1H, H₂C(5^{ax})), 1.81-1.72 (m, 1H, H₂C(10^{ax})), 1.56 (dq, $J = 13.5, 3.5$ Hz, 1H, H₂C(5^{eq})), 1.48 (s, 9H, H₃C(20)), 1.38 (s, 3H, H₃C(2)), 1.34 (dd, $J = 12.1, 2.0$ Hz, 1H, HC(9)), 1.26 (d, $J = 6.9$ Hz, 6H, H₃C(26)), 1.26-1.23 (m, 1H, H₂C(6^{ax})), 1.21 (s, 3H, H₃C(8)), 1.18 (d, $J = 6.9$ Hz, 6H, H₃C(26')), 1.10 (s, 3H, H₃C(1)).

¹³C NMR: (126 MHz, CDCl₃)
154.13 (C(22)), 152.93 (C(18)), 150.13 (C(13)), 136.16 (C(15)), 130.92 (C(21)), 129.86 (C(12)), 129.45 (HC(17)), 128.92 (HC(24)), 123.69 (HC(23)), 116.44 (HC(16)), 114.87 (HC(14)), 80.31 (C(19)), 61.93 (HC(4)), 52.43 (HC(9)), 39.26 (H₂C(6)), 39.05 (C(3)), 38.05 (C(7)), 31.48 (HC(25)), 30.18 (H₂C(11)), 29.78 (H₃C(2)), 28.51 (H₃C(20)), 26.12 (H₂C(5)), 25.04 (H₃C(26')), 24.85 (H₃C(8)), 24.13 (H₃C(26)), 19.69 (H₂C(10)), 17.77 (H₃C(1)).

IR: (neat)
3455 (w), 2965 (m), 1729 (m), 1705 (m), 1616 (w), 1586 (w), 1512 (m), 1461 (m), 1392 (m), 1366 (s), 1299 (w), 1222 (m), 1157 (s), 1054 (m), 1029 (w), 956 (w), 874 (w), 854 (w), 840 (w), 803 (m), 768 (w), 745 (w), 734 (w), 526 (m), 469 (w).

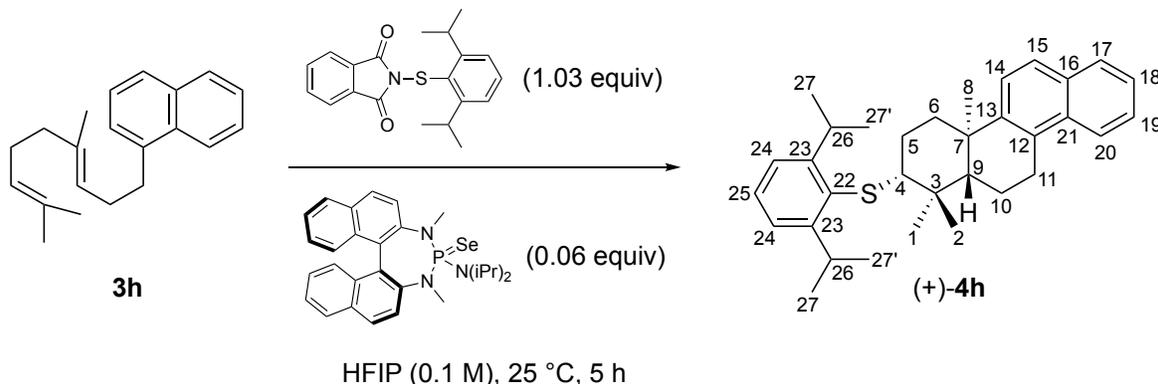
LRMS: (EI, 70 eV)
91.1 (14), 115.1 (16), 137.0 (31), 144.1 (16), 146.1 (21), 149.0 (18), 151.1 (20), 158.1 (19), 159.1 (15), 172.1 (14), 176.1 (13), 179.1 (63), 190.1 (39), 194.1 (82), 195.1 (14), 203.1 (27), 204.1 (15), 226.2 (13), 241.2 (30), 242.2 (40), 243.2 (38), 270.1 (22), 272.2 (14), 285.2 (52), 286.2 (40), 287.2 (100), 288.2 (25), 341.2 (21), 343.2 (28), 435.3 (39), 436.3 (14), 446.1 (28), 535.3 (19).

Analysis: C₃₄H₄₉NO₂S (535.83)
Calcd: C, 76.21% H, 9.22% N, 2.61%
Found: C, 76.01% H, 9.23% N, 2.78%

TLC: R_f 0.56 (silica gel, hexanes/EtOAc, 80:20, UV/CAM or PMA)

HPLC: t_R 4.3 min (50%); t_R 12.4 min (50%) (Chiralpak IB-3, hexanes/*i*-PrOH, 90:10, 1.0 mL/min, 220 nm, 24 °C)

Preparation of (+)-(2,6-Diisopropylphenyl) ((4*R*,7*R*,9*S*)-3,3,7-Trimethyl-3,4,5,6,7,9,10,11-octahydrochrysen-4-yl) Sulfide ((+)-4h**)**



A 100-mL, round-bottomed flask equipped with a stir bar and argon inlet adapter was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (347.0 mg, 1.02 mmol, 1.03 equiv), hexafluoroisopropyl alcohol (10 mL, 0.1 M), and (*E*)-1-(4,8-dimethylnona-3,7-dien-1-yl)naphthalene **3h** (277.4 mg, 1.00 mmol). A homogeneous, yellow solution resulted. Catalyst (*S*)-**2** (29.6 mg, 0.06 mmol, 0.06 equiv) was added in one portion and the mixture was stirred at 25 °C for 5 h. A yellow suspension with white precipitate was observed. Full conversion was observed by TLC (hexanes/CH₂Cl₂, 90:10). The reaction mixture was diluted with CH₂Cl₂ (10 mL), and the volatiles were removed by rotary evaporation (30 °C, 15 mmHg). The residue was purified by column chromatography (silica gel, 3 x 25 cm, dry load on Celite, 25-mL fractions, hexanes/CH₂Cl₂ gradient elution: 97:3 (300 mL) to 94:6 (300 mL) to 91:9 (300 mL) to 88:12 (300 mL)) to afford crude (+)-**4h** as a white solid. The product was contaminated with trace impurities which cannot be removed by chromatography. To obtain analytically pure material, the solid was triturated in boiling ethanol (3 mL) and allowed to cool slowly to 25 °C, followed by cooling in a -20 °C freezer for 12 h. The product was collected by vacuum filtration and rinsed with ice-cold ethanol (2 mL) to afford 277.6 mg (59%) of (+)-**4h** as a white solid. Spectroscopic data matched those for (±)-**4h**.

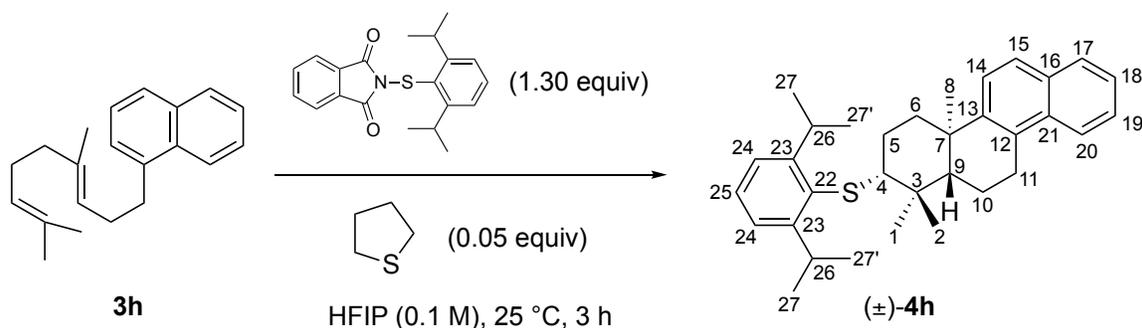
Data for (+)-**4h**:

<u>m.p.:</u>	136-138 °C (ethanol)
<u>Analysis:</u>	C ₃₃ H ₄₂ S (470.76)
	Calcd: C, 84.20% H, 8.99%
	Found: C, 84.15% H, 9.03%
<u>Opt. Rot.:</u>	[α] _D ²⁵ +69.8 (<i>c</i> = 1.29 in CHCl ₃) (84% ee)

HPLC: t_R 3.5 min (92%); t_R 4.5 min (8%) (Supelco Astec, hexanes/*i*-PrOH, 95:5, 1.0 mL/min, 254 nm, 24 °C)

After trituration: t_R 3.5 min (92%); t_R 4.5 min (8%)

Preparation of (±)-(2,6-Diisopropylphenyl) ((4*R,7*R**,9*S**)-3,3,7-Trimethyl-3,4,5,6,7,9,10,11-octahydrochrysen-4-yl) Sulfide ((±)-4h)**



A flame-dried, 100-mL, pear-shaped flask equipped with a stir bar and argon inlet adapter was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (372.4 mg, 1.10 mmol, 1.11 equiv), hexafluoroisopropyl alcohol (10 mL, 0.1 M), and (*E*)-1-(4,8-dimethylnona-3,7-dien-1-yl)naphthalene (275.7 mg, 0.99 mmol). A turbid, yellow solution resulted (the polyene is not fully soluble). Tetrahydrothiophene (4.4 μ L, 4.4 mg, 0.050 mmol, 0.05 equiv) was added to the solution at 25 °C. The mixture was stirred at 25 °C for 2 h. Within 10 min, the mixture changed from a yellow solution to a beige suspension. TLC analysis (hexanes/ CH_2Cl_2 90:10) showed incomplete consumption of starting material. An additional portion of *N*-(2,6-diisopropylphenylthio)phthalimide **1** (67.1 mg, 0.20 mmol, 0.20 equiv) was added to the flask, and stirring was continued for 1 h at 25 °C, over which time a darker brown suspension was observed. Full conversion was observed by TLC. The reaction mixture was diluted with CH_2Cl_2 (10 mL), and the volatiles were removed by rotary evaporation (30 °C, 15 mmHg) to afford crude (±)-**4h**. The crude product was purified by column chromatography (silica gel, 3 x 20 cm, dry load on Celite, 25-mL fractions, hexanes/ CH_2Cl_2 gradient elution: 95:5 (300 mL) to 90:10 (300 mL) to 85:15 (300 mL) to 80:20 (300 mL)) to afford 349.5 mg of (±)-**4h** as a beige solid. The product was still contaminated with trace impurities which are not removable by chromatography. To obtain analytically pure material, the solid was dissolved in boiling hexanes (10 mL) and allowed to cool slowly to 25 °C, whereupon white crystals deposited. The suspension was cooled further in a -20 °C freezer for 4 h. The crystals were collected by vacuum

filtration and rinsed with ice-cold hexanes (2 mL) to afford 235.5 mg (51%) of (\pm)-**4h** as white crystals.

Data for (\pm)-**4h**:

m.p.: 199–201 °C (hexanes)

$^1\text{H NMR}$: (500 MHz, CDCl_3)

7.96 (d, $J = 8.5$ Hz, 1H, HC(20)), 7.77-7.73 (m, 1H, HC(17)), 7.63 (d, $J = 8.8$ Hz, 1H, HC(15)), 7.48 (ddd, $J = 8.4, 6.8, 1.4$ Hz, 1H, HC(19)), 7.42 (ddd, $J = 7.9, 6.9, 1.1$ Hz, 1H, HC(18)), 7.36 (d, $J = 8.8$ Hz, 1H, HC(14)), 7.31 (t, $J = 7.7$ Hz, 1H, HC(25)), 7.17 (d, $J = 7.7$ Hz, 2H, HC(24)), 4.03 (hept, $J = 6.8$ Hz, 2H, HC(26)), 3.39 (dd, $J = 17.3, 6.0$ Hz, 1H, $\text{H}_2\text{C}(11^{\text{eq}})$), 3.15 (ddd, $J = 17.7, 11.8, 7.5$ Hz, 1H, $\text{H}_2\text{C}(11^{\text{ax}})$), 2.65 (dd, $J = 12.6, 3.9$ Hz, 1H, HC(4)), 2.34 (dt, $J = 13.1, 3.4$ Hz, 1H, $\text{H}_2\text{C}(6^{\text{eq}})$), 2.19 (dd, $J = 13.2, 7.5$ Hz, 1H, $\text{H}_2\text{C}(10^{\text{eq}})$), 2.01-1.93 (m, 1H, $\text{H}_2\text{C}(5^{\text{ax}})$), 1.92-1.85 (m, 1H, $\text{H}_2\text{C}(10^{\text{ax}})$), 1.61 (dq, $J = 13.7, 3.6$ Hz, 1H, $\text{H}_2\text{C}(5^{\text{eq}})$), 1.49 (dd, $J = 12.3, 1.6$ Hz, 1H, HC(9)), 1.45 (s, 3H, $\text{H}_3\text{C}(2)$), 1.33 (s, 3H, $\text{H}_3\text{C}(8)$), 1.27 (d, $J = 6.9$ Hz, 6H, $\text{H}_3\text{C}(27)$), 1.24 (dd, $J = 13.5, 3.4$ Hz, 1H, $\text{H}_2\text{C}(6^{\text{ax}})$), 1.18 (d, $J = 6.9$ Hz, 6H, $\text{H}_3\text{C}(27')$), 1.16 (s, 3H, $\text{H}_3\text{C}(1)$).

$^{13}\text{C NMR}$: (126 MHz, CDCl_3)

154.17 (C(23)), 146.14 (C(13)), 132.30 (C(21)), 131.67 (C(16)), 130.95 (C(22)), 129.63 (C(12)), 128.92 (HC(25)), 128.27 (HC(17)), 126.50 (HC(15)), 126.06 (HC(19)), 125.14 (HC(18)), 123.71 (HC(24)), 123.38 (HC(14)), 123.31 (HC(20)), 61.83 (HC(4)), 52.64 (HC(9)), 39.50 ($\text{H}_2\text{C}(6)$), 39.00 (C(3)), 38.33 (C(7)), 31.50 (HC(26)), 29.79 ($\text{H}_3\text{C}(2)$), 28.17 ($\text{H}_2\text{C}(11)$), 26.33 ($\text{H}_2\text{C}(5)$), 25.03 ($\text{H}_3\text{C}(27')$), 24.43 ($\text{H}_3\text{C}(8)$), 24.15 ($\text{H}_3\text{C}(27)$), 19.57 ($\text{H}_2\text{C}(10)$), 17.77 ($\text{H}_3\text{C}(1)$).

IR: (neat)

3051 (w), 2944 (w), 2863 (w), 1572 (w), 1508 (w), 1458 (m), 1436 (w), 1382 (w), 1362 (w), 1302 (w), 1201 (w), 1173 (w), 1158 (w), 1048 (w), 1037 (w), 991 (w), 974 (w), 956 (w), 923 (w), 883 (w), 858 (w), 806 (s), 778 (w), 744 (s), 688 (w), 668 (w), 618 (w), 544 (w), 529 (w).

LRMS: (EI, 70 eV)

69.1 (13), 141.1 (16), 149.0 (10), 151.1 (14), 165.1 (16), 167.1 (35), 178.1 (20), 179.1 (33), 181.1 (60), 191.1 (12), 192.1 (12), 193.1 (49), 194.1 (24), 195.1 (14),

207.1 (29), 221.1 (11), 261.2 (27), 276.2 (25), 277.2 (100), 278.2 (25), 470.3 (68), 471.3 (26).

Analysis: C₃₃H₄₂S (470.76)

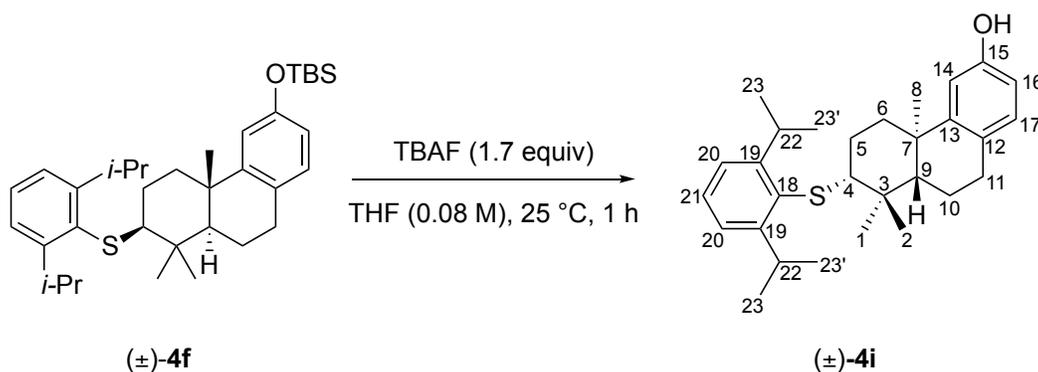
Calcd: C, 84.20% H, 8.99%

Found: C, 84.37% H, 9.18%

TLC: *R_f* 0.26 (silica gel, hexanes/CH₂Cl₂, 90:10, UV/CAM or PMA)

HPLC: *t_R* 3.5 min (50%); *t_R* 4.4 min (50%) (Supelco Astec, hexanes/*i*-PrOH, 95:5, 1.0 mL/min, 254 nm, 24 °C)

Preparation of (±)-(4*R,7*R**,9*S**)-4-(2,6-Diisopropylphenylthio)-3,3,7-trimethyl-3,4,5,6,7,9,10,11-octahydrophenanthren-15-ol ((±)-**4i**)**



To determine the enantiomeric composition of **4f** the compound is de-silylated to phenol **4i** for HPLC analysis. A racemic standard (±)-**4i** was prepared in the following manner. An oven-dried, dram-sized vial equipped with a stir bar and Teflon septum cap was charged with solid tetrabutylammonium fluoride trihydrate (25.2 mg, 0.080 mmol, 1.7 equiv) inside of a dry box. The vial was capped, removed from the dry box, and charged with tetrahydrofuran (0.6 mL) to form a colorless solution. Subsequently, the cap was briefly removed and (±)-**4f** (25.9 mg, 0.047 mmol) was added in one portion as a solid. The vial was capped and the reaction was stirred under argon for 1 h at 25 °C. The solution color turned pale yellow over time. Full conversion was observed by TLC (hexanes/EtOAc, 80:20). The reaction mixture was partitioned between ethyl acetate (5 mL) and water (3 mL) in a separatory funnel. The layers were separated, and the aqueous phase was extracted once more with ethyl acetate (3 mL). The combined organic layers were washed with brine (2 mL), dried over sodium sulfate, filtered, and concentrated (30 °C, 15 mmHg) to afford the crude product. The product was purified by column chromatography

(silica gel, 1 x 18 cm, dry load on Celite, 5-mL fractions, hexanes/EtOAc gradient elution: 95:5 (100 mL) to 90:10 (100 mL)) to afford phenol (\pm)-**4i** as a white solid (19.6 mg, 96%). The enantiomers of derivative (\pm)-**4i** were easily separated by chiral stationary phase HPLC.

Data for (\pm)-**4i**:

^1H NMR: (500 MHz, CDCl_3)

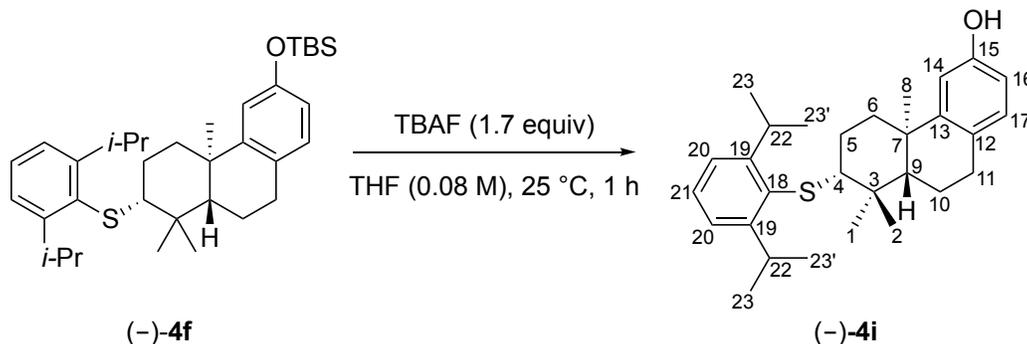
7.31 (t, $J = 7.7$ Hz, 1H, HC(21)), 7.16 (d, $J = 7.7$ Hz, 2H, HC(20)), 6.90 (d, $J = 8.2$ Hz, 1H, HC(17)), 6.61 (d, $J = 2.6$ Hz, 1H, HC(14)), 6.56 (dd, $J = 8.2, 2.6$ Hz, 1H, HC(16)), 4.38 (s, 1H, OH), 4.00 (hept, $J = 6.9$ Hz, 2H, HC(22)), 2.94-2.83 (m, 1H, $\text{H}_2\text{C}(11^{\text{eq}})$), 2.82-2.74 (m, 1H, $\text{H}_2\text{C}(11^{\text{ax}})$), 2.61 (dd, $J = 12.5, 3.8$ Hz, 1H, HC(4)), 2.13 (dt, $J = 13.3, 3.4$ Hz, 1H, $\text{H}_2\text{C}(6^{\text{eq}})$), 1.98-1.91 (m, 1H, $\text{H}_2\text{C}(10^{\text{eq}})$), 1.90-1.81 (m, 1H, $\text{H}_2\text{C}(5^{\text{ax}})$), 1.81-1.70 (m, 1H, $\text{H}_2\text{C}(10^{\text{ax}})$), 1.55 (dq, $J = 13.5, 3.5$ Hz, 1H, $\text{H}_2\text{C}(5^{\text{eq}})$), 1.38 (s, 3H, $\text{H}_3\text{C}(2)$), 1.35 (dd, $J = 12.2, 2.0$ Hz, 1H, HC(9)), 1.26 (d, $J = 6.8$ Hz, 6H, $\text{H}_3\text{C}(23)$), 1.26-1.22 (m, 1H, $\text{H}_2\text{C}(6^{\text{ax}})$), 1.20 (s, 3H, $\text{H}_3\text{C}(8)$), 1.18 (d, $J = 6.9$ Hz, 6H, $\text{H}_3\text{C}(23')$), 1.10 (s, 3H, $\text{H}_3\text{C}(1)$).

^{13}C NMR: (126 MHz, CDCl_3)

154.18 (C(19)), 153.59 (C(15)), 150.99 (C(13)), 130.92 (C(18)), 130.12 (HC(17)), 128.92 (HC(21)), 127.33 (C(12)), 123.71 (HC(20)), 112.97 (HC(16)), 111.06 (HC(14)), 61.80 (HC(4)), 52.40 (HC(9)), 39.25 ($\text{H}_2\text{C}(6)$), 39.05 (C(3)), 38.04 (C(7)), 31.50 (HC(22)), 30.05 ($\text{H}_2\text{C}(11)$), 29.78 ($\text{H}_3\text{C}(2)$), 26.19 ($\text{H}_2\text{C}(5)$), 25.04 ($\text{H}_3\text{C}(23')$), 24.86 ($\text{H}_3\text{C}(8)$), 24.13 ($\text{H}_3\text{C}(23)$), 19.79 ($\text{H}_2\text{C}(10)$), 17.77 ($\text{H}_3\text{C}(1)$).

HPLC: t_{R} 8.4 min (50%); t_{R} 15.8 min (50%) (Chiralpak IB-3, hexanes/*i*-PrOH, 95:5, 0.75 mL/min, 220 nm, 24 °C)

Preparation of (–)-(4*R*,7*R*,9*S*)-4-(2,6-Diisopropylphenylthio)-3,3,7-trimethyl-3,4,5,6,7,9,10,11-octahydrophenanthren-15-ol ((–)-4*i*)



To determine the enantiomeric composition of (–)-4*f* the compound is de-silylated to phenol (–)-4*i* for HPLC analysis. An oven-dried, dram-sized vial equipped with a stir bar and Teflon septum cap was charged with solid tetrabutylammonium fluoride trihydrate (31 mg, 0.1 mmol, 2.0 equiv) inside of a dry box. The vial was capped, removed from the dry box, and charged with tetrahydrofuran (0.6 mL) to form a colorless solution. Subsequently, the cap was briefly removed and (–)-4*f* (27.0 mg, 0.05 mmol) was added in one portion as a solid. The vial was capped and the reaction was stirred under argon for 1 h at 25 °C. The solution color turned pale yellow over time. Full conversion was observed by TLC (hexanes/EtOAc, 80:20). The reaction mixture was partitioned between ethyl acetate (5 mL) and water (3 mL) in a separatory funnel. The layers were separated, and the aqueous phase was extracted once more with ethyl acetate (3 mL). The combined organic layers were washed with brine (2 mL), dried over sodium sulfate, filtered, and concentrated (30 °C, 15 mmHg) to afford the crude product. The product was purified by column chromatography (silica gel, 1 x 18 cm, dry load on Celite, 5-mL fractions, hexanes/EtOAc gradient elution: 95:5 (100 mL) to 90:10 (100 mL)) to afford 18.7 mg (87%) of (–)-4*i* as a white solid. Spectroscopic data match those for (±)-4*i*.

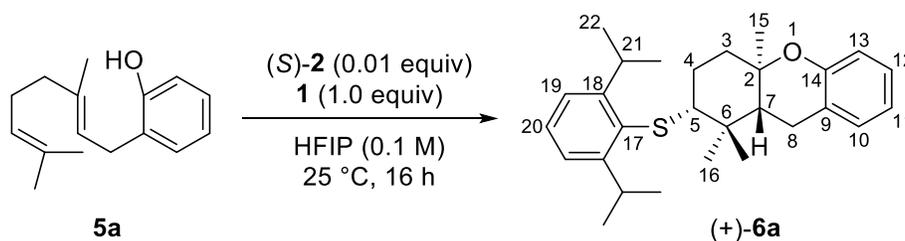
Data for (–)-4*i*:

HPLC: t_R 8.3 min (7%); t_R 15.6 min (93%) (Chiralpak IB-3, hexanes/*i*-PrOH, 95:5, 0.75 mL/min, 220 nm, 24 °C)

From recrystallized (–)-4*f*: t_R 8.3 min (5%); t_R 15.1 min (95%)

General Procedure: Enantioselective, Lewis Base-Catalyzed Sulfenocyclization of *ortho*-Geranylphenols

An oven-dried, 25-mL, Schlenk flask equipped with a stir bar was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (339.5 mg, 1.00 mmol, 1.00 equiv) and catalyst (*S*)-**2** (5.2 mg, 0.01 mmol, 0.01 equiv). The flask was fitted with a septum, evacuated, and back-filled with argon. Hexafluoroisopropyl alcohol (4 mL) was added to the flask, resulting in a yellow solution. A solution of *ortho*-geranylphenol **5** (1.00 mmol) in hexafluoroisopropyl alcohol (6 mL) was added to the flask using a syringe. The mixture was stirred at 25 °C for 16 h under argon. Conversion was assessed by TLC. Upon completion, the reaction was poured into Et₂O (100 mL) and the Schlenk flask was rinsed with Et₂O (2 x 5 mL). The combined solution was concentrated (40 °C, 50 mmHg) and the residue was purified by column chromatography to afford (+)-**6**. Analytically pure samples were obtained by recrystallization.

Preparation of (+)-(2*R*,5*R*,7*R*)-5-(2,6-Diisopropylphenylthio)-2,6,6-trimethyl-2,3,4,5,6,7-hexahydro-1*H*-xanthene ((+)-6a**)**

An oven-dried, 25-mL, Schlenk flask equipped with a stir bar was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (339.5 mg, 1.00 mmol, 1.00 equiv) and catalyst (*S*)-**2** (5.2 mg, 0.01 mmol, 0.01 equiv). The flask was fitted with a septum, evacuated, and back-filled with argon. Hexafluoroisopropyl alcohol (4 mL) was added to the flask, resulting in a yellow solution. A solution of (*E*)-2-(3,7-dimethylocta-2,6-dien-1-yl)phenol **5a** (230.4 mg, 1 mmol) in hexafluoroisopropyl alcohol (6 mL) was added to the flask using a syringe. The mixture was stirred at 25 °C for 16 h under argon. Conversion was assessed by TLC (hexanes/CH₂Cl₂, 80:20). Upon completion, the reaction was poured into Et₂O (100 mL) and the Schlenk flask was rinsed with Et₂O (2 x 5 mL). The combined solution was concentrated (40 °C, 50 mmHg) and the residue was purified by column chromatography (silica gel, 3 x 20 cm, dry load on Celite, 25-mL

fractions, hexanes/CH₂Cl₂ gradient elution: 8:1 (600 mL) to 6:1 (600 mL) to afford 368.8 mg (87%) of (+)-**6a** as a white solid. Recrystallization from methanol provided 305.1 mg (72%) of analytically pure (+)-**6a**.

Data for (+)-**6a**:

m.p.: 63–64 °C (methanol)

¹H NMR: (500 MHz, CDCl₃)

7.34 (t, *J* = 7.7 Hz, 1H, HC(20)), 7.19 (d, *J* = 7.7 Hz, 2H, HC(19)), 7.08 (t, *J* = 6.8 Hz, 2H, HC(10) and HC(12)), 6.84 (t, *J* = 7.4 Hz, 1H, HC(11)), 6.75 (d, *J* = 8.5 Hz, 1H, HC(13)), 3.99 (hept, *J* = 6.8 Hz, 2H, HC(21)), 2.86 – 2.64 (m, 3H, H₂C(8) and HC(5)), 1.97 – 1.88 (m, 1H, H₂C(3)), 1.76 (dd, *J* = 12.6, 5.4 Hz, 1H, HC(7)), 1.73 – 1.66 (m, 1H, H₂C(4)), 1.66 – 1.58 (m, 1H, H₂C(4)), 1.50 – 1.41 (m, 4H, H₂C(3) and H₃C(16)), 1.27 (d, *J* = 6.9 Hz, 6H, H₃C(22)), 1.24 (s, 3H, H₃C(15)), 1.21 (d, *J* = 6.9 Hz, 6H, H₃C(22)), 1.10 (s, 3H, H₃C(16)).

¹³C NMR: (126 MHz, CDCl₃)

153.9 (C(18)), 152.8 (C(14)), 130.3 (C(17)), 129.6 (HC(10)), 129.0 (HC(20)), 127.2 (HC(12)), 123.7 (HC(19)), 122.0 (C(9)), 119.8 (HC(11)), 116.9 (HC(13)), 76.3 (C(2)), 61.0 (HC(5)), 49.5 (HC(7)), 40.1 (H₂C(3)), 38.5 (C(6)), 31.4 (HC(21)), 28.8 (H₃C(16)), 26.6 (H₂C(4)), 24.9 (H₃C(22)), 23.9 (H₃C(22)), 23.5 (H₂C(8)), 19.8 (H₃C(15)), 16.5 (H₃C(16)).

IR: (neat)

2961 (w), 2866 (w), 1610 (w), 1584 (w), 1488 (w), 1454 (m), 1420 (w), 1390 (w), 1379 (w), 1361 (w), 1302 (w), 1281 (w), 1241 (m), 1203 (w), 1164 (w), 1147 (w), 1125 (w), 1108 (w), 1068 (w), 1052 (w), 1040 (w), 1003 (w), 983 (w), 953 (w), 927 (w), 908 (m), 881 (w), 866 (w), 856 (w), 800 (w), 751 (m), 731 (m), 648 (w), 563 (w), 538 (w), 511 (w), 478 (w).

LRMS: (EI, 70 eV)

69.1 (35), 91.1 (33), 107.1 (72), 123.1 (21), 131.1 (26), 145.1 (50), 149.0 (35), 185.1 (30), 229.2 (100), 422.3 (100).

HRMS: Calcd for C₂₈H₃₈OS ([M]⁺): 422.2643, Found: 422.2651

TLC: *R_f* 0.33 (hexanes/CH₂Cl₂, 80:20)

Opt. Rot.: [α]_D²⁴ +60.2 (*c* = 1.18 in CHCl₃)

HPLC: t_R 3.5 min (93%); t_R 6.4 min (7%) (Supelco Astec, hexanes/*i*-PrOH, 99:1, 1.0 mL/min, 220 nm, 24 °C)

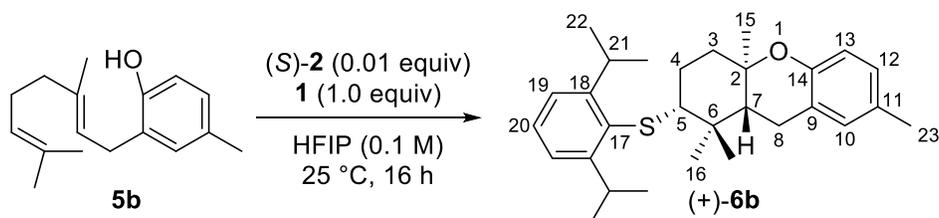
After recrystallization: t_R 3.6 min (93%); t_R 7.0 min (7%)

Analysis: C₂₈H₃₈OS (422.67)

Calcd: C, 79.57; H, 9.06%

Found: C, 79.47; H, 8.93%

Preparation of (+)-(2*R*,5*R*,7*R*)-5-(2,6-Diisopropylphenylthio)-2,6,6,11-tetramethyl-2,3,4,5,6,7-hexahydro-1*H*-xanthene ((+)-6b**)**



An oven-dried, 25-mL, Schlenk flask equipped with a stir bar was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (339.5 mg, 1.00 mmol, 1.00 equiv) and catalyst (*S*)-**2** (5.2 mg, 0.01 mmol, 0.01 equiv). The flask was fitted with a septum, evacuated, and back-filled with argon. Hexafluoroisopropyl alcohol (4 mL) was added to the flask, resulting in a yellow solution. A solution of (*E*)-2-(3,7-dimethylocta-2,6-dien-1-yl)-4-methylphenol **5b** (244.4 mg, 1 mmol) in hexafluoroisopropyl alcohol (6 mL) was added to the flask using a syringe. The mixture was stirred at 25 °C for 16 h under argon. Conversion was assessed by TLC (hexanes/CH₂Cl₂, 80:20). Upon completion, the reaction was poured into Et₂O (100 mL) and the Schlenk flask was rinsed with Et₂O (2 x 5 mL). The combined solution was concentrated (40 °C, 50 mmHg) and the residue was purified by column chromatography (silica gel, 3 x 20 cm, dry load on Celite, 25-mL fractions, hexanes/CH₂Cl₂ gradient elution: 7:1 (600 mL) to 5:1 (600 mL)) to afford 367.3 mg (84%) of (+)-**6b** as a white solid. Recrystallization from ethanol provided 309.9 mg (71%) of analytically pure (+)-**6b**.

Data for (+)-**6b**:

m.p.: 115–116 °C (ethanol)

¹H NMR: (500 MHz, CDCl₃)

7.34 (t, $J = 7.7$ Hz, 1H, HC(20)), 7.19 (d, $J = 7.7$ Hz, 2H, HC(19)), 6.89 (d, $J = 7.6$ Hz, 2H, HC(10) and HC(12)), 6.65 (d, $J = 8.3$ Hz, 1H, HC(13)), 3.99 (hept, J

= 6.6 Hz, 2H, HC(21)), 2.79 – 2.65 (m, 3H, H₂C(8) and HC(5)), 2.27 (s, 3H, H₃C(23)), 1.91 (dt, $J = 12.8, 3.3$ Hz, 1H, H₂C(3)), 1.77 – 1.65 (m, 2H, HC(7) and H₂C(4)), 1.62 (dq, $J = 13.9, 3.8$ Hz, 1H, H₂C(4)), 1.49 – 1.40 (m, 4H, H₃C(16) and H₂C(3)), 1.28 (d, $J = 6.9$ Hz, 6H, H₃C(22)), 1.23 (s, 3H, H₃C(15)), 1.21 (d, $J = 6.9$ Hz, 6H, H₃C(22)), 1.10 (s, 3H, H₃C(16))

¹³C NMR: (126 MHz, CDCl₃)
153.9 (C(18)), 150.5 (C(14)), 130.3 (C(17)), 129.9 (HC(10)), 129.0 (HC(20)), 128.9 (C(11)), 127.9 (HC(12)), 123.7 (HC(19)), 121.6 (C(9)), 116.6 (HC(13)), 76.1 (C(2)), 61.0 (HC(5)), 49.6 (HC(7)), 40.1 (H₂C(3)), 38.5 (C(6)), 31.4 (HC(21)), 28.8 (H₃C(16)), 26.6 (H₂C(4)), 24.9 (H₃C(22)), 23.9 (H₃C(22)), 23.5 (H₂C(8)), 20.5 (H₃C(23)), 19.7 (H₃C(15)), 16.5 (H₃C(16)).

IR: (neat)
2961 (w), 2866 (w), 1574 (w), 1498 (w), 1461 (w), 1390 (w), 1378 (w), 1361 (w), 1303 (w), 1281 (w), 1240 (w), 1205 (w), 1148 (w), 1127 (w), 1069 (w), 1042 (w), 953 (w), 935 (w), 910 (w), 868 (w), 814 (w), 800 (w), 783 (w), 756 (w), 733 (w), 699 (w), 649 (w), 546 (w), 513 (w).

LRMS: (EI, 70 eV)
105.1 (13), 121.1 (97), 123.1 (26), 145.1 (20), 149.0 (28), 159.1 (40), 179.1 (14), 199.1 (28), 243.2 (95), 436.3 (100)

HRMS: (ES⁺, TOF)
Calcd for C₂₉H₄₁OS ([M+H]⁺): 437.2878, Found: 437.2884

TLC: R_f 0.33 (hexanes/CH₂Cl₂, 80:20)

Opt. Rot.: $[\alpha]_D^{24} +73.3$ ($c = 1.01$ in CHCl₃)

HPLC: t_R 6.3 min (93%); t_R 8.4 min (7%) (Supelco Astec, hexanes/*i*-PrOH, 98:2, 0.5 mL/min, 220 nm, 24 °C)

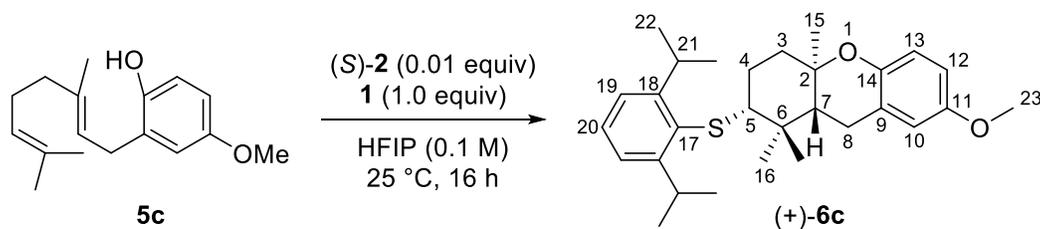
After recrystallization: t_R 6.5 min (93%); t_R 9.0 min (7%)

Analysis: C₂₉H₄₀OS (436.70)

Calcd: C, 79.76%; H, 9.23%

Found: C, 79.41%; H, 9.17%

Preparation of (+)-(2*R*,5*R*,7*R*)-5-(2,6-Diisopropylphenylthio)-11-methoxy-2,6,6-trimethyl-2,3,4,5,6,7-hexahydro-1*H*-xanthene ((+)-6*c*)



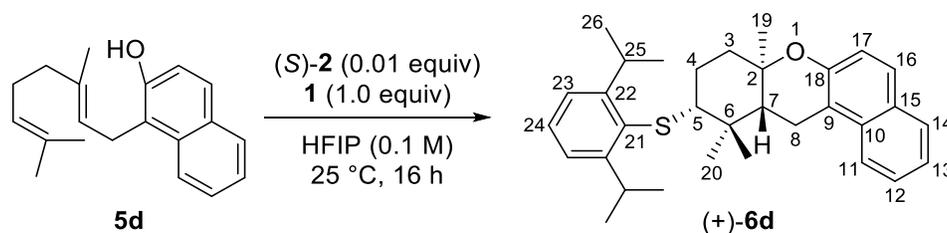
An oven-dried, 25-mL, Schlenk flask equipped with a stir bar was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (339.5 mg, 1.00 mmol, 1.00 equiv) and catalyst (*S*)-**2** (5.2 mg, 0.01 mmol, 0.01 equiv). The flask was fitted with a septum, evacuated, and back-filled with argon. Hexafluoroisopropyl alcohol (4 mL) was added to the flask, resulting in a yellow solution. A solution of (*E*)-2-(3,7-dimethylocta-2,6-dien-1-yl)-4-methoxyphenol **5c** (260.4 mg, 1 mmol) in hexafluoroisopropyl alcohol (6 mL) was added to the flask using a syringe. The mixture was stirred at 25 °C for 16 h under argon. Conversion was assessed by TLC (hexanes/CH₂Cl₂, 50:50). Upon completion, the reaction was poured into Et₂O (100 mL) and the Schlenk flask was rinsed with Et₂O (2 x 5 mL). The combined solution was concentrated (40 °C, 50 mmHg) and the residue was purified by column chromatography (silica gel, 3 x 20 cm, dry load on Celite, 25-mL fractions, hexanes/CH₂Cl₂ gradient elution: 3:1 (600 mL) to 2:1 (600 mL)) to afford 430.3 mg (94%) of (+)-**6c** as an oily solid. Recrystallization from ethanol provided 362.5 mg (80%) of analytically pure (+)-**6c**.

Data for (+)-6*c*:

- m.p.:** 136–137 °C (ethanol)
- ¹H NMR:** (500 MHz, CDCl₃)
 7.34 (t, *J* = 7.7 Hz, 1H, HC(20)), 7.19 (d, *J* = 7.7 Hz, 2H, HC(19)), 6.67 (d, *J* = 1.7 Hz, 2H, HC(12) and HC(13)), 6.64 (s, 1H, HC(10)), 3.98 (hept, *J* = 6.6 Hz, 2H, HC(21)), 3.76 (s, 3H, H₃C(23)), 2.81 – 2.65 (m, 3H, H₂C(8) and HC(5)), 1.89 (dt, *J* = 12.8, 3.3 Hz, 1H, H₂C(3)), 1.75 (dd, *J* = 12.4, 5.7 Hz, 1H, HC(7)), 1.69 (ddd, *J* = 13.9, 12.2, 3.2 Hz, 1H, H₂C(4)), 1.61 (dq, *J* = 13.9, 3.8 Hz, 1H, H₂C(4)), 1.48 – 1.40 (m, 4H, H₂C(3) and H₃C(16)), 1.27 (d, *J* = 6.9 Hz, 6H, H₃C(22)), 1.21 (s, 6H, H₃C(15) and H₃C(22)), 1.20 (s, 3H, H₃C(22)), 1.09 (s, 3H, H₃C(16)).

- ¹³C NMR: (126 MHz, CDCl₃)
153.9 (C(18)), 153.1 (C(11)), 146.8 (C(14)), 130.3 (C(17)), 129.0 (HC(20)), 123.7 (HC(19)), 122.6 (C(9)), 117.4 (HC(13)), 114.1 (HC(10)), 113.3 (HC(12)), 76.0 (C(2)), 61.0 (HC(5)), 55.7 (H₃C(23)), 49.5 (HC(7)), 40.0 (H₂C(3)), 38.5 (C(6)), 31.3 (HC(21)), 28.8 (H₃C(16)), 26.6 (H₂C(4)), 24.9 (H₃C(22)), 23.9 (H₃C(22)), 23.9 (H₂C(8)), 19.6 (H₃C(15)), 16.5 (H₃C(16)).
- IR: (neat)
2961 (w), 2866 (w), 1495 (m), 1462 (w), 1390 (w), 1378 (w), 1361 (w), 1304 (w), 1278 (w), 1225 (m), 1203 (w), 1146 (w), 1126 (w), 1069 (w), 1040 (w), 953 (w), 910 (w), 867 (w), 843 (w), 800 (w), 732 (w), 699 (w), 649 (w), 555 (w).
- LRMS: (EI, 70 eV)
123.1 (20), 137.1 (78), 149.0 (18), 175.1 (24), 194.1 (10), 215.1 (19), 259.2 (54), 452.2 (100).
- HRMS: (ES⁺, TOF)
Calcd for C₂₉H₄₁O₂S ([M+H]⁺): 453.2827, Found: 453.2829
- TLC: *R_f* 0.49 (hexanes/CH₂Cl₂, 50:50)
- Opt. Rot.: [α]_D²⁴ +86.0 (*c* = 0.94 in CHCl₃)
- HPLC: *t_R* 3.8 min (92%); *t_R* 8.0 min (8%) (Supelco Astec, hexanes/*i*-PrOH, 95:5, 1.0 mL/min, 220 nm, 24 °C)
After recrystallization: *t_R* 3.6 min (96%); *t_R* 7.0 min (4%)
- Analysis: C₂₉H₄₀O₂S (452.70)
Calcd: C, 76.94%; H, 8.91%
Found: C, 76.78%; H, 8.79%

Preparation of (+)-(2*R*,5*R*,7*R*)-5-(2,6-Diisopropylphenylthio)-2,6,6-trimethyl-2,3,4,5,6,7-hexahydro-9*H*-benzo[*a*]xanthene ((+)-6*d*)



An oven-dried, 25-mL, Schlenk flask equipped with a stir bar was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (339.5 mg, 1.00 mmol, 1.00 equiv) and catalyst (*S*)-**2** (5.2 mg, 0.01 mmol, 0.01 equiv). The flask was fitted with a septum, evacuated, and back-filled with argon. Hexafluoroisopropyl alcohol (4 mL) was added to the flask, resulting in a yellow solution. A solution of (*E*)-1-(3,7-dimethylocta-2,6-dien-1-yl)naphthalen-2-ol **5d** (280.4 mg, 1 mmol) in hexafluoroisopropyl alcohol (6 mL) was added to the flask using a syringe. The mixture was stirred at 25 °C for 16 h under argon. Conversion was assessed by TLC (hexanes/CH₂Cl₂, 80:20). Upon completion, the reaction was poured into Et₂O (100 mL) and the Schlenk flask was rinsed with Et₂O (2 x 5 mL). The combined solution was concentrated (40 °C, 50 mmHg) and the residue was purified by column chromatography (silica gel, 3 x 20 cm, dry load on Celite, 25-mL fractions, hexanes/CH₂Cl₂ gradient elution: 7:1 (600 mL) to 5:1 (600 mL)) to afford 393.8 mg (83%) of (+)-**6d** as a white solid. Recrystallization from ethanol provided 319.3 mg (67%) of analytically pure (+)-**6d**.

Data for (+)-**6d**:

m.p.: 136–137 °C (ethanol)

¹H NMR: (500 MHz, CDCl₃)

7.91 (d, *J* = 8.4 Hz, 1H, HC(11)), 7.79 (d, *J* = 8.1 Hz, 1H, HC(14)), 7.63 (d, *J* = 8.9 Hz, 1H, HC(16)), 7.54 (t, *J* = 7.6 Hz, 1H, HC(12)), 7.37 (t, *J* = 7.9 Hz, 2H, HC(24) and HC(13)), 7.23 (d, *J* = 7.7 Hz, 2H, HC(23)), 7.02 (d, *J* = 8.9 Hz, 1H, HC(17)), 4.04 (hept, *J* = 6.7 Hz, 2H, HC(25)), 3.25 – 3.16 (m, 1H, H₂C(8)), 2.94 – 2.83 (m, 1H, H₂C(8)), 2.78 (dd, *J* = 12.1, 3.3 Hz, 1H, HC(5)), 2.03 – 1.97 (m, 1H, H₂C(3)), 1.92 (dd, *J* = 12.8, 4.7 Hz, 1H, HC(7)), 1.79 (q, *J* = 13.8 Hz, 1H, H₂C(4)), 1.69 (dd, *J* = 13.8, 3.5 Hz, 1H, H₂C(4)), 1.60 – 1.52 (m, 4H, H₂C(3) and H₃C(20)), 1.31 (d, *J* = 6.8 Hz, 6H, H₃C(26)), 1.30 (s, 3H, H₃C(19)), 1.25 (d, *J* =

6.8 Hz, 6H, H₃C(26)), 1.23 (s, 3H, H₃C(20)).

¹³C NMR: (126 MHz, CDCl₃)
154.0 (C(22)), 150.2 (C(18)), 133.1 (C(10)), 130.3 (C(21)), 129.0 (HC(24)), 128.7 (C(15)), 128.5 (HC(14)), 127.8 (HC(16)), 126.2 (HC(12)), 123.7 (HC(23)), 123.0 (HC(13)), 121.7 (HC(11)), 119.3 (HC(17)), 113.3 (C(9)), 76.3 (C(2)), 61.0 (HC(5)), 49.5 (HC(7)), 39.9 (H₂C(3)), 38.7 (C(6)), 31.4 (HC(25)), 29.0 (H₃C(20)), 26.6 (H₂C(4)), 24.9 (H₃C(26)), 24.0 (H₃C(26)), 20.5 (H₂C(8)), 19.4 (H₃C(19)), 16.6 (H₃C(20)).

IR: (neat)
3057 (w), 2961 (w), 2865 (w), 1624 (w), 1599 (w), 1573 (w), 1515 (w), 1461 (w), 1433 (w), 1391 (w), 1379 (w), 1361 (w), 1301 (w), 1279 (w), 1259 (w), 1236 (m), 1204 (w), 1181 (w), 1148 (w), 1127 (w), 1070 (w), 1052 (w), 1042 (w), 1006 (w), 970 (w), 906 (m), 864 (w), 811 (m), 770 (w), 732 (m), 704 (w), 646 (w), 585 (w), 526 (w), 513 (w), 465 (w).

LRMS: (EI, 70 eV)
105.1 (25), 115.1 (42), 123.1 (43), 128.0 (39), 137.1 (39), 151.1 (63), 157.1 (100), 181.1 (25), 195.1 (56), 256.2 (15), 279.2 (30), 446.1 (48), 452.3 (22), 472.3 (81).

HRMS: (ES⁺, TOF)
Calcd for C₃₂H₄₁OS ([M+H]⁺): 473.2878, Found: 473.2870

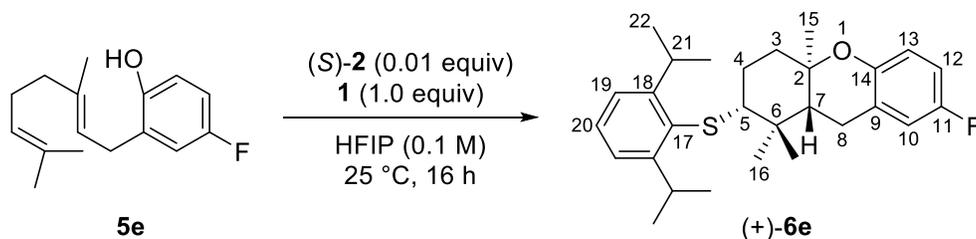
TLC: *R_f* 0.33 (hexanes/CH₂Cl₂, 80:20)

Opt. Rot.: [α]_D²⁴ +141.4 (*c* = 0.99 in CHCl₃)

HPLC: *t_R* 9.0 min (91%); *t_R* 10.8 min (9%) (Chiralpak-AD, hexanes/*i*-PrOH, 95:5, 0.5 mL/min, 254 nm, 24 °C)
t_R 13.6 min (89%); *t_R* 15.4 min (11%) (Supelco Astec, hexanes/*i*-PrOH, 99:1, 0.5 mL/min, 254 nm, 24 °C)

Analysis: C₃₂H₄₀OS (472.73)
Calcd: C, 81.30%; H, 8.53%
Found: C, 81.15%; H, 8.53%

Preparation of (+)-(2*R*,5*R*,7*R*)-5-((2,6-Diisopropylphenyl)thio)-11-fluoro-2,6,6-trimethyl-2,3,4,5,6,7-hexahydro-1*H*-xanthene ((+)-6*e*)



An oven-dried, 25-mL, Schlenk flask equipped with a stir bar was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (339.5 mg, 1.00 mmol, 1.00 equiv) and catalyst (*S*)-**2** (5.2 mg, 0.01 mmol, 0.01 equiv). The flask was fitted with a septum, evacuated, and back-filled with argon. Hexafluoroisopropyl alcohol (4 mL) was added to the flask, resulting in a yellow solution. A solution of (*E*)-2-(3,7-dimethylocta-2,6-dien-1-yl)-4-fluorophenol **5e** (248.4 mg, 1 mmol) in hexafluoroisopropyl alcohol (6 mL) was added to the flask using a syringe. The mixture was stirred at 25 °C for 16 h under argon. Conversion was assessed by TLC (hexanes/CH₂Cl₂, 80:20). Upon completion, the reaction was poured into Et₂O (100 mL) and the Schlenk flask was rinsed with Et₂O (2 x 5 mL). The combined solution was concentrated (40 °C, 50 mmHg) and the residue was purified by column chromatography (silica gel, 3 x 20 cm, dry load on Celite, 25-mL fractions, hexanes/CH₂Cl₂ gradient elution: 7:1 (600 mL) to 5:1 (600 mL)) to afford 389.8 mg (88%) of (+)-**6e** as a white solid. Recrystallization from ethanol provided 337.9 mg (77%) of analytically pure (+)-**6e**.

Data for (+)-**6e**:

m.p.: 121–122 °C (ethanol)

¹H NMR: (500 MHz, CDCl₃)

7.34 (t, *J* = 7.7 Hz, 1H, HC(20)), 7.19 (d, *J* = 7.7 Hz, 2H, HC(19)), 6.80 – 6.75 (m, 2H, HC(10) and HC(12)), 6.69 – 6.64 (m, 1H, HC(13)), 3.97 (hept, *J* = 6.6 Hz, 2H, HC(21)), 2.80 – 2.65 (m, 3H, H₂C(8) and HC(5)), 1.90 (dt, *J* = 12.9, 3.3 Hz, 1H, H₂C(3)), 1.76 – 1.65 (m, 2H, H₂C(4) and HC(7)), 1.61 (dq, *J* = 14.0, 3.9 Hz, 1H, H₂C(4)), 1.47 -1.39 (m, 4H, H₂C(3) and H₃C(16)), 1.27 (d, *J* = 6.9 Hz, 6H, H₃C(22)), 1.21 (s, 6H, H₃C(15) and H₃C(22)), 1.20 (s, 3H, H₃C(22)), 1.09 (s, 3H, H₃C(16)).

¹³C NMR: (126 MHz, CDCl₃)
156.6 (C(11)), 154.0 (C(18)), 148.8 (C(14)), 130.2 (C(17)), 129.0 (HC(20)), 123.7 (HC(19)), 123.1 (C(9)), 117.7 (HC(13)), 115.3 (HC(10)), 114.0 (HC(12)), 76.4 (C(2)), 60.9 (HC(5)), 49.2 (HC(7)), 40.0 (H₂C(3)), 38.5 (C(6)), 31.4 (HC(21)), 28.8 (H₃C(16)), 26.5 (H₂C(4)), 24.9 (H₃C(22)), 23.9 (H₃C(22)), 23.7 (H₂C(8)), 19.6 (H₃C(15)), 16.5 (H₃C(16)).

¹⁹F NMR: (470 MHz, CDCl₃)
-125.40 (q, *J* = 8.0 Hz).

IR: (neat)
2962 (w), 2866 (w), 1573 (w), 1492 (m), 1462 (w), 1431 (w), 1391 (w), 1380 (w), 1361 (w), 1304 (w), 1276 (w), 1243 (w), 1220 (m), 1201 (w), 1166 (w), 1148 (w), 1136 (w), 1127 (w), 1100 (w), 1069 (w), 1053 (w), 1042 (w), 1003 (w), 975 (w), 951 (w), 927 (w), 910 (m), 859 (w), 801 (w), 786 (w), 733 (m), 699 (w), 650 (w), 577 (w), 551 (w).

LRMS: (EI, 70 eV)
69.1 (21), 84.0 (100), 86.0 (65), 125.0 (40), 149.0 (34), 151.0 (30), 163.0 (30), 177.1 (14), 194.1 (22), 247.1 (76), 440.2 (56).

HRMS: (ES⁺, TOF)
Calcd for C₂₈H₃₈FOS ([M+H]⁺): 441.2622, Found: 441.2627

TLC: *R_f* 0.38 (hexanes/CH₂Cl₂, 80:20)

Opt. Rot.: [α]_D²⁴ +56.1 (*c* = 1.11 in CHCl₃)

HPLC: *t_R* 3.3 min (92%); *t_R* 6.9 min (8%) (Supelco Astec, hexanes/*i*-PrOH, 95:5, 1.0 mL/min, 220 nm, 24 °C)

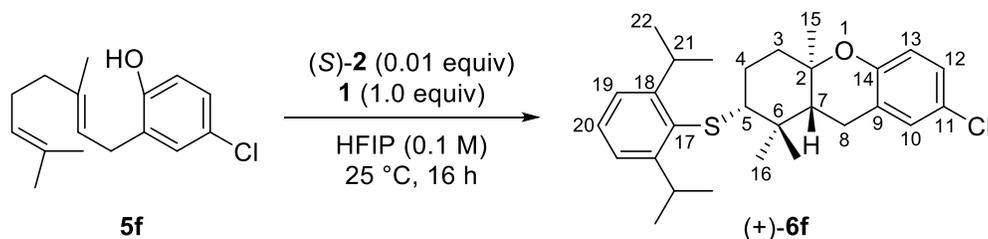
t_R 3.2 min (91%); *t_R* 6.2 min (9%)

Analysis: C₂₈H₃₇FOS (440.66)

Calcd: C, 76.32%; H, 8.46%

Found: C, 76.15%; H, 8.50%

Preparation of (+)-(2*R*,5*R*,7*R*)-11-Chloro-5-(2,6-diisopropylphenylthio)-2,6,6-trimethyl-2,3,4,5,6,7-hexahydro-1*H*-xanthene ((+)-6f**)**



An oven-dried, 25-mL, Schlenk flask equipped with a stir bar was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (339.5 mg, 1.00 mmol, 1.00 equiv) and catalyst (*S*)-**2** (5.2 mg, 0.01 mmol, 0.01 equiv). The flask was fitted with a septum, evacuated, and back-filled with argon. Hexafluoroisopropyl alcohol (4 mL) was added to the flask, resulting in a yellow solution. A solution of (*E*)-4-chloro-2-(3,7-dimethylocta-2,6-dien-1-yl)phenol **5f** (264.8 mg, 1 mmol) in hexafluoroisopropyl alcohol (6 mL) was added to the flask using a syringe. The mixture was stirred at 25 °C for 16 h under argon. Conversion was assessed by TLC (hexanes/CH₂Cl₂, 80:20). Upon completion, the reaction was poured into Et₂O (100 mL) and the Schlenk flask was rinsed with Et₂O (2 x 5 mL). The combined solution was concentrated (40 °C, 50 mmHg) and the residue was purified by column chromatography (silica gel, 3 x 20 cm, dry load on Celite, 25-mL fractions, hexanes/CH₂Cl₂ gradient elution: 7:1 (600 mL) to 5:1 (600 mL)) to afford 392.9 mg (86%) of (+)-**6f** as a white solid. Recrystallization from ethanol provided 361.8 mg (79%) of analytically pure (+)-**6f**.

Data for (+)-**6f**:

m.p.: 153–154 °C (ethanol)

¹H NMR: (500 MHz, CDCl₃)

7.33 (t, *J* = 7.7 Hz, 1H, HC(20)), 7.18 (d, *J* = 7.6 Hz, 2H, HC(19)), 7.05 (d, *J* = 2.5 Hz, 1H, HC(10)), 7.01 (dd, *J* = 8.6, 2.2 Hz, 1H, HC(12)), 6.65 (d, *J* = 8.4 Hz, 1H, HC(13)), 3.96 (hept, *J* = 6.6 Hz, 2H, HC(21)), 2.79 – 2.63 (m, 3H, H₂C(8) and HC(5)), 1.89 (dt, *J* = 12.8, 3.0 Hz, 1H, H₂C(3)), 1.74 – 1.56 (m, 3H, H₂C(4) and HC(7)), 1.46 – 1.38 (m, 4H, H₂C(3) and H₃C(16)), 1.26 (d, *J* = 6.9 Hz, 6H, H₃C(22)), 1.20 (s, 6H, H₃C(15) and H₃C(22)), 1.19 (s, 3H, H₃C(22)), 1.08 (s, 3H, H₃C(16)).

^{13}C NMR: (126 MHz, CDCl_3)
154.0 (C(18)), 151.5 (C(14)), 130.2 (C(17)), 129.1 (HC(10)), 129.1 (HC(20)),
127.2 (HC(12)), 124.5 (C(11)), 123.7 (C(9)), 123.6 (HC(19)), 118.2 (HC(13)),
76.7 (C(2)), 60.8 (HC(5)), 49.2 (HC(7)), 39.9 ($\text{H}_2\text{C}(3)$), 38.5 (C(6)), 31.4
(HC(21)), 28.8 ($\text{H}_3\text{C}(16)$), 26.5 ($\text{H}_2\text{C}(4)$), 24.9 ($\text{H}_3\text{C}(22)$), 23.9 ($\text{H}_3\text{C}(22)$), 23.5
($\text{H}_2\text{C}(8)$), 19.7 ($\text{H}_3\text{C}(15)$), 16.5 ($\text{H}_3\text{C}(16)$).

IR: (neat)
2962 (w), 2866 (w), 1575 (w), 1481 (w), 1413 (w), 1391 (w), 1380 (w), 1361 (w),
1296 (w), 1276 (w), 1243 (w), 1192 (w), 1148 (w), 1126 (w), 1071 (w), 1041 (w),
952 (w), 908 (w), 894 (w), 868 (w), 814 (w), 800 (w), 775 (w), 754 (w), 734 (w),
676 (w), 647 (w), 544 (w).

LRMS: (EI, 70 eV)
55.1 (60), 86.0 (62), 123.1 (31), 141.0 (57), 149.0 (45), 151.1 (39), 179.0 (27),
194.1 (46), 219.1 (23), 247.1 (19), 263.1 (100), 456.2 (71).

HRMS: (EI, 70 eV)
Calcd for $\text{C}_{28}\text{H}_{37}\text{ClOS}$ ($[\text{M}]^+$): 456.2254, Found: 456.2263

TLC: R_f 0.41 (hexanes/ CH_2Cl_2 , 80:20)

Opt. Rot.: $[\alpha]_D^{24} +97.0$ ($c = 1.11$ in CHCl_3)

HPLC: t_R 8.0 min (91%); t_R 12.9 min (9%) (Supelco Astec, hexanes/*i*-PrOH, 95:5 in
hexanes, 0.4 mL/min, 220 nm, 24 °C)

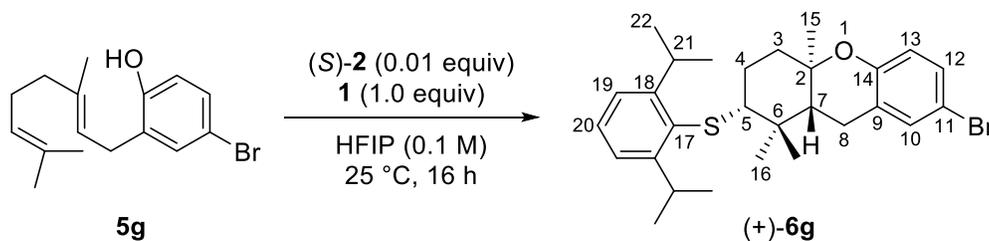
After recrystallization: t_R 7.9 min (94%); t_R 13.1 min (6%)

Analysis: $\text{C}_{28}\text{H}_{37}\text{ClOS}$ (457.11)

Calcd: C, 73.57%; H, 8.16%

Found: C, 73.51%; H, 8.25%

Preparation of (+)-(2*R*,5*R*,7*R*)-11-Bromo-5-((2,6-diisopropylphenyl)thio)-2,6,6-trimethyl-2,3,4,5,6,7-hexahydro-1*H*-xanthene ((+)-6g**)**



An oven-dried, 25-mL, Schlenk flask equipped with a stir bar was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (339.5 mg, 1.00 mmol, 1.00 equiv) and catalyst (*S*)-**2** (5.2 mg, 0.01 mmol, 0.01 equiv). The flask was fitted with a septum, evacuated, and back-filled with argon. Hexafluoroisopropyl alcohol (4 mL) was added to the flask, resulting in a yellow solution. A solution of (*E*)-4-bromo-2-(3,7-dimethylocta-2,6-dien-1-yl)phenol **5g** (309.3 mg, 1 mmol) in hexafluoroisopropyl alcohol (6 mL) was added to the flask using a syringe. The mixture was stirred at 25 °C for 16 h under argon. Conversion was assessed by TLC (hexanes/CH₂Cl₂, 80:20). Upon completion, the reaction was poured into Et₂O (100 mL) and the Schlenk flask was rinsed with Et₂O (2 x 5 mL). The combined solution was concentrated (40 °C, 50 mmHg) and the residue was purified by column chromatography (silica gel, 3 x 20 cm, dry load on Celite, 25-mL fractions, hexanes/CH₂Cl₂ gradient elution: 7:1 (600 mL) to 5:1 (600 mL)) to afford 414.4 mg (83%) of (+)-**6g** as a white solid. Recrystallization from ethanol provided 387.0 mg (77%) of analytically pure (+)-**6g**.

Data for (+)-**6g**:

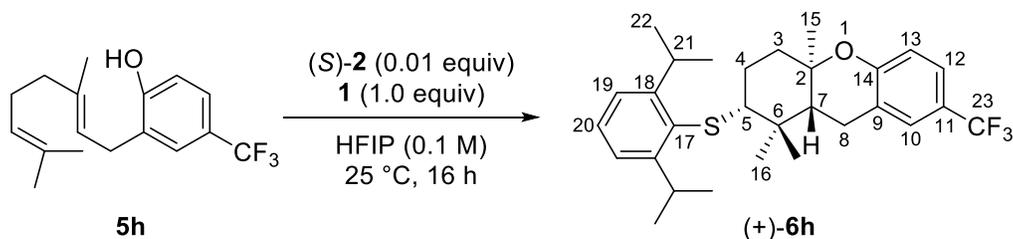
m.p.: 165–166 °C (ethanol)

¹H NMR: (500 MHz, CDCl₃)

7.33 (t, *J* = 7.7 Hz, 1H, HC(20)), 7.20 (d, *J* = 2.5 Hz, 1H, HC(10)), 7.18 (d, *J* = 7.7 Hz, 2H, HC(19)), 7.15 (dd, *J* = 8.6, 2.6 Hz, 1H, HC(12)), 6.61 (d, *J* = 8.6 Hz, 1H, HC(13)), 3.96 (hept, *J* = 6.6 Hz, 2H, HC(21)), 2.79 – 2.64 (m, 3H, H₂C(8) and HC(5)), 1.90 (dt, *J* = 12.9, 3.3 Hz, 1H, H₂C(3)), 1.74 – 1.58 (m, 3H, H₂C(4) and HC(7)), 1.47 – 1.39 (m, 4H, H₂C(3) and H₃C(16)), 1.26 (d, *J* = 6.9 Hz, 6H, H₃C(22)), 1.21 (s, 6H, H₃C(15) and H₃C(22)), 1.20 (s, 3H, H₃C(22)), 1.08 (s, 3H, H₃C(16)).

- ¹³C NMR: (126 MHz, CDCl₃)
153.9 (C(18)), 152.0 (C(14)), 132.1 (HC(10)), 130.2 (C(17)), 130.1 (HC(12)),
129.1 (HC(20)), 124.2 (C(9)), 123.7 (HC(19)), 118.7 (HC(13)), 111.8 (C(11)),
76.7 (C(2)), 60.8 (HC(5)), 49.2 (HC(7)), 39.9 (H₂C(3)), 38.5 (C(6)), 31.4
(HC(21)), 28.8 (H₃C(16)), 26.5 (H₂C(4)), 24.9 (H₃C(22)), 23.9 (H₃C(22)), 23.4
(H₂C(8)), 19.7 (H₃C(15)), 16.5 (H₃C(16)).
- IR: (neat)
2962 (w), 2866 (w), 1574 (w), 1480 (w), 1390 (w), 1380 (w), 1295 (w), 1243 (w),
1148 (w), 1126 (w), 1070 (w), 1041 (w), 952 (w), 910 (w), 886 (w), 867 (w), 812
(w), 772 (w), 734 (w), 662 (w).
- LRMS: (EI, 70 eV)
97.1 (33), 111.1 (29), 121.1 (64), 123.1 (60), 149.0 (70), 151.1 (61), 179.1 (29),
185.0 (61), 187.0 (60), 194.1 (65), 211.0 (26), 209.0 (19), 223.0 (28), 225.0 (30),
263.0 (25), 265.0 (26), 307.0 (100), 309.0 (100), 500.2 (66), 502.2 (68).
- HRMS: (EI, 70 eV)
Calcd for C₂₈H₃₇BrOS ([M]⁺): 500.1748, Found: 500.1751
- TLC: *R_f* 0.43 (hexanes/CH₂Cl₂, 80:20)
- Opt. Rot.: [α]_D²⁴ +92.7 (*c* = 0.94 in CHCl₃)
- HPLC: *t_R* 6.5 min (90%); *t_R* 9.6 min (10%) (Supelco Astec, hexanes/*i*-PrOH, 95:5, 0.5
mL/min, 220 nm, 24 °C)
After recrystallization: *t_R* 6.6 min (90%); *t_R* 9.7 min (10%)
- Analysis: C₂₈H₃₇BrOS (501.57)
Calcd: C, 67.05%; H, 7.44%
Found: C, 66.91%; H, 7.43%

Preparation of (+)-(2*R*,5*R*,7*R*)-5-((2,6-Diisopropylphenyl)thio)-2,6,6-trimethyl-11-(trifluoromethyl)-2,3,4,5,6,7-hexahydro-1*H*-xanthene ((+)-6h**)**



An oven-dried, 25-mL, Schlenk flask equipped with a stir bar was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (339.5 mg, 1.00 mmol, 1.00 equiv) and catalyst (*S*)-**2** (5.2 mg, 0.01 mmol, 0.01 equiv). The flask was fitted with a septum, evacuated, and back-filled with argon. Hexafluoroisopropyl alcohol (4 mL) was added to the flask, resulting in a yellow solution. A solution of (*E*)-2-(3,7-dimethylocta-2,6-dien-1-yl)-4-(trifluoromethyl)phenol **5h** (298.4 mg, 1 mmol) in hexafluoroisopropyl alcohol (6 mL) was added to the flask using a syringe. The mixture was stirred at 25 °C for 16 h under argon. Conversion was assessed by TLC (hexanes/CH₂Cl₂, 80:20). Upon completion, the reaction was poured into Et₂O (100 mL) and the Schlenk flask was rinsed with Et₂O (2 x 5 mL). The combined solution was concentrated (40 °C, 50 mmHg) and the residue was purified by column chromatography (silica gel, 3 x 20 cm, dry load on Celite, 25-mL fractions, hexanes/CH₂Cl₂ gradient elution: 12:1 (600 mL) to 10:1 (600 mL)) to afford 408.7 mg (83%) of (+)-**6h** as a white solid. Recrystallization from ethanol provided 373.9 mg (76%) of analytically pure (+)-**6h**.

Data for (+)-**6h**:

m.p.: 137–138 °C (ethanol)

¹H NMR: (500 MHz, CDCl₃)

7.37 – 7.30 (m, 3H, HC(10), HC(20) and HC(12)), 7.19 (d, *J* = 7.7 Hz, 1H, HC(19)), 6.79 (d, *J* = 8.5 Hz, 1H, HC(13)), 3.97 (hept, *J* = 6.9 Hz, 2H, HC(21)), 2.83 (dd, *J* = 16.5, 5.2 Hz, 1H, H₂C(8)), 2.76 (dd, *J* = 16.6, 12.7 Hz, 1H, H₂C(8)), 2.67 (dd, *J* = 12.0, 4.0 Hz, 1H, HC(5)), 1.93 (dt, *J* = 12.9, 3.3 Hz, 1H, H₂C(3)), 1.77 – 1.59 (m, 3H, HC(7) and H₂C(4)), 1.50 – 1.42 (m, 4H, H₂C(3) and H₃C(16)), 1.27 (d, *J* = 6.9 Hz, 3H, H₃C(22)), 1.24 (s, 3H, H₃C(15)), 1.20 (d, *J* = 6.9 Hz, 1H, H₃C(22)), 1.10 (s, 3H, H₃C(16)).

¹³C NMR: (126 MHz, CDCl₃)
155.7 (C(14)), 154.0 (C(18)), 130.2 (C(17)), 129.1 (HC(20)), 127.0 (HC(10)),
124.6 (C(23)), 124.5 (HC(12)), 123.7 (HC(19)), 122.3 (C(9)), 122.0 (C(11)),
117.2 (HC(13)), 77.4 (C(2)), 60.7 (HC(5)), 49.2 (HC(7)), 39.9 (H₂C(3)), 38.5
(C(6)), 31.4 (HC(21)), 28.8 (H₃C(16)), 26.5 (H₂C(4)), 24.9 (H₃C(22)), 24.0
(H₃C(22)), 23.5 (H₂C(8)), 19.8 (H₃C(15)), 16.5 (H₃C(16)).

¹⁹F NMR: (470 MHz, CDCl₃)
−61.36 (s).

IR: (neat)
2963 (w), 2867 (w), 1620 (w), 1593 (w), 1504 (w), 1461 (w), 1391 (w), 1381 (w),
1361 (w), 1329 (m), 1281 (w), 1258 (w), 1244 (w), 1187 (w), 1158 (m), 1117
(m), 1068 (m), 1041 (w), 1004 (w), 975 (w), 952 (w), 922 (w), 901 (w), 867 (w),
826 (w), 801 (w), 780 (w), 756 (w), 733 (m), 660 (w), 641 (w), 629 (w), 560 (w),
532 (w).

LRMS: (EI, 70 eV)
69.1 (24), 91.1 (14), 149.0 (27), 175.0 (40), 194.1 (100), 201.1 (24), 213.1 (28),
282.0 (23), 297.2 (49), 490.3 (83).

HRMS: (EI+, 70 eV)
Calcd for C₂₉H₃₇F₃OS ([M]⁺): 490.2517, Found: 490.2510

TLC: *R_f* 0.51 (hexanes/CH₂Cl₂, 80:20)

Opt. Rot.: [α]_D²⁴ +70.9 (*c* = 0.94 in CHCl₃)

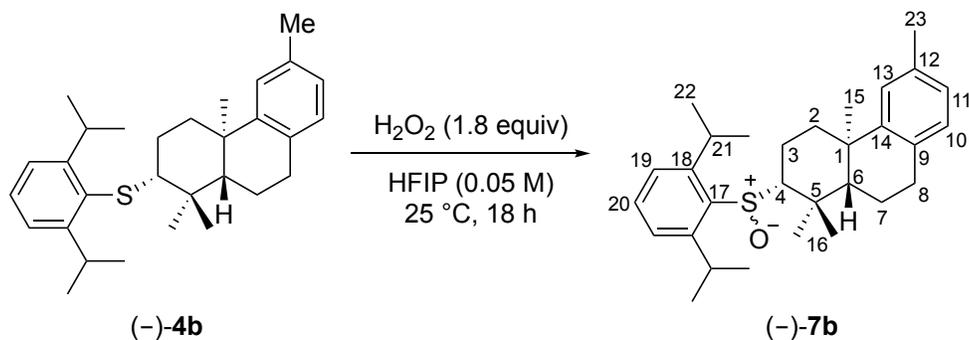
HPLC: *t_R* 7.1 min (92%); *t_R* 8.8 min (8%) (Chiralpak-AD, hexanes/*i*-PrOH, 99.5:0.5, 0.5
mL/min, 220 nm, 24 °C)

After recrystallization: *t_R* 7.4 min (92%); *t_R* 8.8 min (8%)

Analysis: C₂₉H₃₇F₃OS (490.67)

Calcd: C, 70.99%; H, 7.60%

Found: C, 70.84%; H, 7.74%

Product Derivatizations**Preparation of (–)-(1*R*,4*R*,6*S*)-4-(2,6-Diisopropylphenylsulfinyl)-1,5,5,12-tetramethyl-1,2,3,4,5,6,7,8-octahydrophenanthrene ((–)-7b)**

A 100-mL, round-bottomed flask equipped with a stir bar was charged with sulfide (–)-**4b** (1.3 g, 3.0 mmol, 91:9 e.r.) and hexafluoroisopropyl alcohol (60 mL, 0.05 M). The mixture was sonicated for 15 min at 25 °C, which resulted in a fine, white suspension. Hydrogen peroxide (30% w/w aq., 600 μ L, 1.8 equiv) was added to the reaction mixture by syringe at 25 °C. The flask was fitted with an argon inlet adapter, and the reaction was allowed to stir at 25 °C for 18 h under argon. A clear, colorless solution resulted. Full conversion was observed by TLC (hexanes/EtOAc, 90:10). The reaction was quenched with sat. aq. Na₂SO₃ (25 mL). Hexafluoroisopropyl alcohol was removed by rotary evaporation (40 °C, 50 mmHg). The residual aqueous phase was extracted with Et₂O (3 x 50 mL). The combined organic layers were washed with brine (25 mL) and then dried over MgSO₄, filtered, and concentrated (40 °C, 50 mmHg) to afford crude (–)-**7b**. The residue was purified by column chromatography (silica gel, 5 x 15 cm, dry load on Celite, 50-mL fractions, hexane/EtOAc, 10:1 (2000 mL)) to afford (–)-**7b** (1.3371 g, 99%) as a white solid. To obtain analytically pure material, the solid was recrystallized from hexanes to yield 1.1966 g (88%) of (–)-**7b** as a mixture of diastereomers. The diastereomers were separated on a small scale by preparative TLC (hexanes/EtOAc, 10:1).

Data for (–)-7b (mixture):

m.p.: 147–148 °C (hexanes)

IR: (neat)

2964 (w), 2868 (w), 2238 (w), 1578 (w), 1501 (w), 1461 (w), 1394 (w), 1378 (w), 1363 (w), 1311 (w), 1179 (w), 1161 (w), 1124 (w), 1060 (w), 1041 (w), 1023 (w), 968 (w), 907 (m), 836 (w), 802 (w), 727 (s), 645 (w), 618 (w), 586 (w), 538 (w),

523 (w), 461 (w).

LRMS: (ES⁺, TOF)

145.1 (13), 241.2 (95), 451.3 (100), 473.3 (23).

HRMS: (ES⁺, TOF)

Calcd for C₃₀H₄₃OS ([M+H]⁺): 451.3035; Found: 451.3029

Analysis: C₃₀H₄₂OS (450.73)

Calcd: C, 79.94%; H, 9.39%

Found: C, 79.97%; H, 9.33%

Data for (-)-7b'' (minor):

¹H NMR: (500 MHz, CDCl₃)

7.26 (t, *J* = 7.7 Hz, 1H, HC(20)), 7.11 (br s, 2H, HC(19)), 6.93 (s, 1H, HC(13)), 6.83 (d, *J* = 7.8 Hz, 1H, HC(10)), 6.81 – 6.76 (m, 1H, HC(11)), 4.48 (br s, 1H, HC(21)), 3.30 (br s, 1H, HC(21)), 2.83 (dd, *J* = 16.9, 6.0 Hz, 1H, H₂C(8)), 2.69 (ddd, *J* = 17.5, 11.7, 7.3 Hz, 1H, H₂C(8)), 2.50 – 2.39 (m, 2H, HC(4) and H₂C(2)), 2.30 (qd, *J* = 13.5, 3.5 Hz, 1H, H₂C(3)), 2.16 (s, 3H, H₃C(23)), 2.02 (dq, *J* = 13.7, 3.6 Hz, 1H, H₂C(3)), 1.85 – 1.78 (m, 1H, H₂C(7)), 1.67 (ddt, *J* = 18.5, 12.0, 6.5 Hz, 1H, H₂C(7)), 1.37 (td, *J* = 13.3, 3.6 Hz, 1H, H₂C(2)), 1.27 (dd, *J* = 12.0, 2.0 Hz, 1H, HC(6)), 1.21 – 1.14 (m, 15H, H₃C(22) and H₃C(15) and H₃C(16)), 1.11 (d, *J* = 6.4 Hz, 6H, H₃C(22)).

¹³C NMR: (126 MHz, CDCl₃)

148.7 (C(14)), 136.0 (C(17)), 135.1 (C(12)), 131.6 (C(9)), 130.9 (HC(20)), 128.8 (HC(10)), 126.4 (HC(11)), 125.0 (HC(13)), 73.1 (HC(4)), 52.6 (HC(6)), 38.6 (C(5)), 38.5 (H₂C(2)), 37.6 (C(1)), 30.3 (H₃C(16)), 30.2 (H₂C(8)), 24.7 (H₃C(15)), 21.2 (H₃C(23)), 18.9 (H₂C(7)), 18.7 (H₃C(22)), 16.7 (H₂C(3)).

TLC: *R_f* 0.40 (hexanes/EtOAc, 80:20, PMA)

Data for (-)-7b' (major):

¹H NMR: (500 MHz, CDCl₃)

7.43 (t, *J* = 7.8 Hz, 1H, HC(20)), 7.32 (dd, *J* = 7.8, 1.3 Hz, 1H, HC(19)), 7.20 (dd, *J* = 7.8, 1.3 Hz, 1H, HC(19')), 6.98 (d, *J* = 7.8 Hz, 1H, HC(10)), 6.96 (s, 1H,

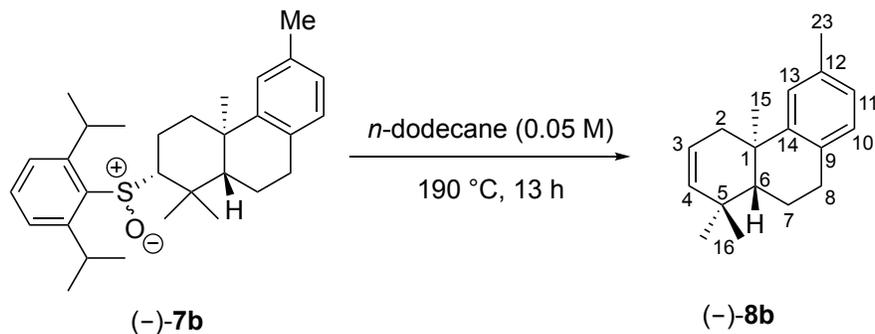
HC(13)), 6.92 (dd, $J = 7.7, 1.1$ Hz, 1H, HC(11)), 4.42 (hept, $J = 6.8$ Hz, 1H, HC(21)), 3.67 (hept, $J = 6.8$ Hz, 1H, HC(21')), 3.29 (dd, $J = 13.2, 3.6$ Hz, 1H, HC(4)), 2.98 (dd, $J = 17.0, 6.0$ Hz, 1H, H₂C(8)), 2.91 – 2.82 (m, 1H, H₂C(8)), 2.31 (dt, $J = 13.1, 3.5$ Hz, 1H, H₂C(2)), 2.27 (s, 3H, H₃C(23)), 2.07 (dd, $J = 13.2, 7.3$ Hz, 1H, H₂C(7)), 1.76 (ddt, $J = 18.6, 12.0, 6.5$ Hz, 1H, H₂C(7)), 1.67 – 1.56 (m, 4H, H₂C(3) and H₃C(16)), 1.47 (dd, $J = 12.0, 1.8$ Hz, 1H, HC(6)), 1.44 – 1.37 (m, 4H, H₂C(2) and H₃C(16)), 1.34 – 1.31 (m, 6H, H₃C(22) and H₃C(22')), 1.30 (d, $J = 6.9$ Hz, 3H, H₃C(22')), 1.26 (d, $J = 7.0$ Hz, 3H, H₃C(22)), 1.23 (s, 3H, H₃C(15)), 1.19 (dq, $J = 13.2, 3.6$ Hz, 1H, H₂C(3)).

¹³C NMR: (126 MHz, CDCl₃)

151.6 (C(18)), 149.5 (C(18')), 148.4 (C(14)), 136.6 (C(17)), 135.0 (C(12)), 131.7 (C(9)), 131.5 (HC(20)), 128.9 (HC(10)), 126.7 (HC(19)), 126.5 (HC(11)), 124.7 (HC(13)), 123.2 (HC(19')), 71.0 (HC(4)), 52.8 (HC(6)), 39.0 (C(5)), 38.2 (H₂C(2)), 37.3 (C(1)), 30.2 (H₂C(8)), 30.0 (H₃C(16)), 29.4 (HC(21')), 27.6 (HC(21)), 25.4 (H₃C(22')), 25.1 (H₃C(22)), 24.6 (H₃C(15)), 24.0 (H₃C(22)), 22.7 (H₃C(22')), 21.2 (H₃C(23)), 20.9 (H₂C(3)), 18.3 (H₂C(7)), 17.6 (H₃C(16')).

TLC: R_f 0.43 (hexanes/EtOAc, 80:20, PMA)

Preparation of (1*R*,6*R*)-1,5,5,12-tetramethyl-1,2,3,4,5,6,7,8-hexahydrophenanthrene ((-)-**8b**)



A 50-mL, round-bottomed flask equipped with a stir bar and reflux condenser was charged with sulfoxide (450.7 mg, 1.0 mmol, 91:9 e.r.). The flask was evacuated and back-filled with argon. *n*-Dodecane (20 mL) was added to the reaction via syringe. The solution was heated to 190 °C (oil bath temperature) and stirred for 13 h. Full conversion was observed by TLC

(hexanes). The reaction mixture was cooled to 25 °C, and *n*-dodecane was removed by vacuum distillation (45 °C, 0.05 mmHg). The residue was purified by column chromatography (silica gel, 3 x 25 cm, dry load on Celite, 25-mL fractions, hexanes) to afford (–)-**8b** (211.5 mg, 88%) as a colorless oil. Further purification via Kugelrohr distillation (85 °C, 0.05 mmHg) provided 205.7 mg (86%) of analytically pure (–)-**8b**.

Data for (–)-**8b**:

b.p.: 85 °C (ABT, 0.05 mmHg)

¹H NMR: (500 MHz, CDCl₃)

7.11 (s, 1H, HC(13)), 6.98 (d, *J* = 7.8 Hz, 1H, HC(10)), 6.94 (dd, *J* = 7.8, 1.3 Hz, 1H, HC(11)), 5.64 (ddd, *J* = 10.0, 6.1, 1.8 Hz, 1H, HC(3)), 5.52 (dd, *J* = 10.2, 2.5 Hz, 1H, HC(4)), 2.91 (dd, *J* = 16.2, 4.8 Hz, 1H, H₂C(8)), 2.83 (ddd, *J* = 16.8, 11.9, 6.7 Hz, 1H, H₂C(8)), 2.56 (dd, *J* = 16.8, 6.1 Hz, 1H, H₂C(2)), 2.34 (s, 3H, H₃C(23)), 2.14 (d, *J* = 16.8 Hz, 1H, H₂C(2)), 1.91 – 1.84 (m, 1H, H₂C(7)), 1.76 – 1.65 (m, 2H, HC(6) and H₂C(7)), 1.29 (s, 3H, H₃C(15)), 1.08 (s, 3H, H₃C(16)), 1.02 (s, 3H, H₃C(16)).

¹³C NMR: (126 MHz, CDCl₃)

147.7 (C(14)), 138.1 (HC(4)), 135.1 (C(12)), 132.3 (C(9)), 128.8 (HC(10)), 126.5 (HC(13)), 126.2 (HC(11)), 121.9 (HC(3)), 48.2 (HC(6)), 39.7 (H₂C(2)), 36.9 (C(1)), 35.1 (C(5)), 31.9 (H₃C(16)), 30.8 (H₂C(8)), 25.2 (H₃C(15)), 22.4 (H₃C(16)), 21.3 (H₃C(23)), 20.0 (H₂C(7)).

IR: (neat)

3009 (w), 2957 (w), 2934 (w), 2838 (w), 1612 (w), 1501 (w), 1468 (w), 1434 (w), 1394 (w), 1373 (w), 1359 (w), 1323 (w), 1305 (w), 1282 (w), 1261 (w), 1221 (w), 1169 (w), 1137 (w), 1091 (w), 1064 (w), 989 (w), 963 (w), 948 (w), 930 (w), 876 (w), 827 (w), 807 (m), 780 (w), 749 (w), 737 (m), 719 (m), 626 (w), 589 (w), 564 (w), 508 (w), 461 (w).

LRMS: (EI, 70 eV)

115.1 (15), 131.1 (29), 143.1 (51), 158.1 (100), 169.1 (16), 183.1 (16), 225.2 (30), 240.2 (45).

HRMS: Calcd for C₁₈H₂₄ ([M]⁺): 240.1878; Found: 240.1877

TLC: *R_f* 0.41 (silica gel, hexanes, UV)

Opt. Rot.: $[\alpha]_{\text{D}}^{24} -154.0$ ($c = 1.07$ in CHCl_3)

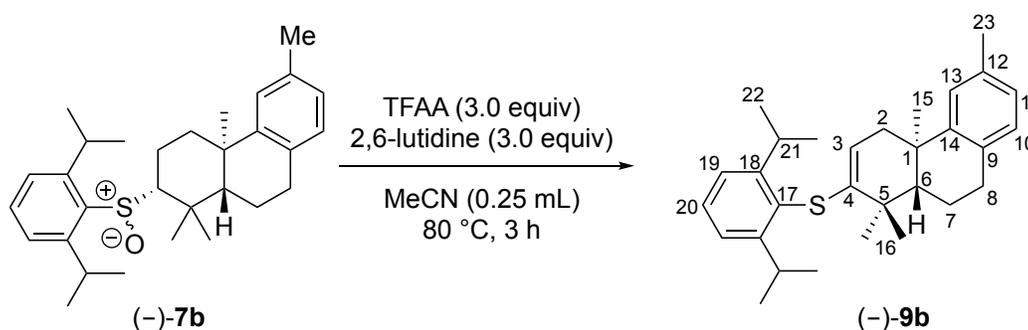
HPLC: t_{R} 8.7 min (9%); t_{R} 9.7 min (91%) (Chiralpak OJ-H, hexanes, 0.5 mL/min, 220 nm, 24°C)

Analysis: $\text{C}_{18}\text{H}_{24}$ (240.39)

Calcd: C, 89.94%; H, 10.06%

Found: C, 89.57%; H, 9.95%

Preparation of (2,6-Diisopropylphenyl) ((1*R*,6*S*)-1,5,5,12-Tetramethyl-1,2,5,6,7,8-hexahydrophenanthren-4-yl) Sulfide ((-)-9b**)**



An oven-dried, 5 mL, round-bottomed flask equipped with a stir bar was charged with sulfoxide (-)-**7b** (450.7 mg, 1.0 mmol, 91:9 e.r.) and acetonitrile (4 mL). Subsequently, 2,6-lutidine (349 μL , 3.0 mmol, 3.0 equiv) was added to the solution, followed by trifluoroacetic anhydride (416 μL , 3.0 mmol, 3.0 equiv). The flask was fitted with a reflux condenser and heated to 80 °C (oil bath temperature). The reaction was stirred at 80 °C under argon for 3 h. Full conversion was observed by TLC (hexanes). The mixture was cooled to 25 °C, and the volatiles were removed by rotary evaporation (50 °C, 50 mmHg). The residue was purified by column chromatography (silica gel, 3 x 20 cm, dry load on Celite, 25-mL fractions, hexanes/EtOAc, 99:1) to afford (-)-**9b** (397.3 mg, 92%) as a white solid. Recrystallization from a minimal amount of boiling ethanol provided 373.8 mg (86%) of analytically pure (-)-**9b**.

Data for (-)-**9b**:

m.p.: 128–130 °C (ethanol)

^1H NMR: (500 MHz, CDCl_3)

7.39 (t, $J = 7.7$ Hz, 1H, HC(20)), 7.24 (d, $J = 7.7$ Hz, 2H, HC(19)), 6.98 (s, 1H, HC(13)), 6.95 (d, $J = 7.8$ Hz, 1H, HC(10)), 6.90 (dd, $J = 7.8, 1.7$ Hz, 1H,

HC(11)), 4.56 (dd, $J = 6.7, 2.0$ Hz, 1H, HC(3)), 3.74 (hept, $J = 6.9$ Hz, 2H, HC(21)), 2.95 – 2.86 (m, 1H, H₂C(8)), 2.85 – 2.75 (m, 1H, H₂C(8)), 2.43 (dd, $J = 16.7, 6.7$ Hz, 1H, H₂C(2)), 2.26 (s, 3H, H₃C(23)), 2.03 (d, $J = 16.6$ Hz, 1H, H₂C(2)), 1.94 – 1.87 (m, 1H, H₂C(7)), 1.78 – 1.67 (m, 2H, H₂C(7) and HC(6)), 1.41 (s, 3H, H₃C(16)), 1.34 (s, 3H, H₃C(16)), 1.25 – 1.17 (m, 15H, H₃C(22) and H₃C(15)).

¹³C NMR: (126 MHz, CDCl₃)

154.2 (C(18)), 147.3 (C(14)), 144.4 (C(4)), 135.2 (C(12)), 132.2 (C(9)), 129.6 (HC(20)), 128.7 (HC(10)), 128.6 (C(17)), 126.4 (HC(13)), 126.3 (HC(11)), 123.7 (HC(19)), 114.9 (HC(3)), 50.3 (HC(6)), 41.1 (H₂C(2)), 39.6 (C(5)), 36.7 (C(1)), 31.6 (HC(21)), 31.1 (H₂C(8)), 30.7 (H₃C(16)), 24.8 (H₃C(15)), 24.3 (H₃C(22)), 24.3 (H₃C(22)), 21.2 (H₃C(23)), 21.1 (H₃C(16)), 20.6 (H₂C(7)).

IR: (neat)

2961 (w), 2865 (w), 1614 (w), 1574 (w), 1502 (w), 1462 (w), 1386 (w), 1372 (w), 1361 (w), 1313 (w), 1283 (w), 1246 (w), 1214 (w), 1177 (w), 1081 (w), 1054 (w), 956 (w), 926 (w), 908 (w), 836 (w), 813 (w), 800 (w), 790 (w), 732 (m), 649 (w), 604 (w), 511 (w), 462 (w).

LRMS: (EI, 70 eV)

57.1 (20), 69.0 (24), 91.0 (94), 131.0 (35), 149.0 (36), 185.0 (28), 201.1 (23), 231.1 (100), 432.2 (21).

HRMS: Calcd for C₃₀H₄₀O ([M]⁺): 432.2851; Found: 432.2850

TLC: R_f 0.27 (silica gel, hexanes, PMA)

Opt. Rot.: $[\alpha]_D^{24}$ –98.0 ($c = 0.95$ in CHCl₃)

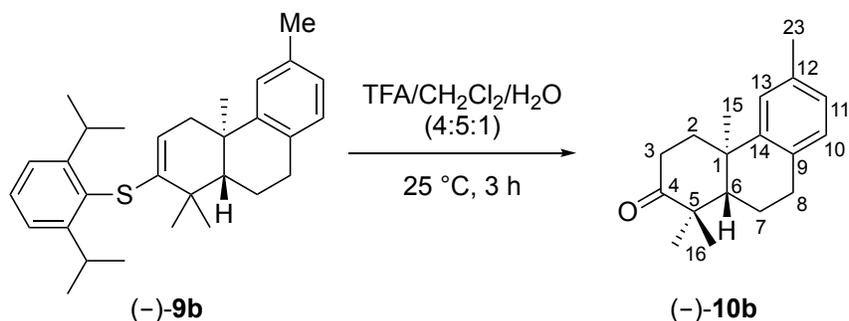
HPLC: t_R 9.0 min (90%); t_R 10.3 min (10%) (Supelco Astec, hexanes, 0.5 mL/min, 220 nm, 24 °C)

Analysis: C₃₀H₄₀S (432.71)

Calcd: C, 83.27%; H, 9.32%

Found: C, 83.01%; H, 9.37%

Preparation of (1*R*,6*S*)-1,5,5,12-Tetramethyl-1,2,3,6,7,8-hexahydrophenanthren-4(1*H*)-one ((-)-10b**)**



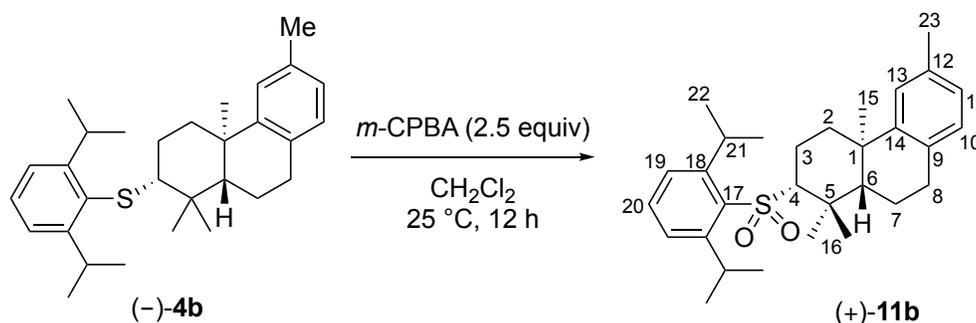
A 25-mL, round-bottomed flask equipped with a stir bar was charged with vinyl sulfide (–)-**9b** (432.7 mg, 1.0 mmol, 95:5 e.r.), CH₂Cl₂ (5 mL), water (1 mL) and TFA (4 mL). The resulting biphasic mixture was stirred rapidly at 25 °C for 3 h. Full conversion was observed by TLC (hexanes/EtOAc, 90:10). The reaction mixture was quenched by cautious, dropwise addition to a 125-mL Erlenmeyer flask sat. aq. NaHCO₃ (30 mL) at 0 °C. The mixture was diluted with CH₂Cl₂ (20 mL) and transferred to a 125-mL separatory funnel. The layers were separated, and the aqueous phase was extracted with CH₂Cl₂ (3 x 30 mL). The combined organic layers were washed with brine (30 mL), and then dried over anhydrous MgSO₄, filtered, and concentrated (35 °C, 50 mmHg) to afford crude (–)-**10b**. The product was purified by column chromatography (silica gel, 3 x 25 cm, dry load on Celite, 25-mL fractions, hexane/EtOAc, 96:4) to afford (–)-**10b** (254.3 mg, 97%) as a white solid. Recrystallization from a minimal amount of boiling hexanes provided 232.7 mg (91%) of analytically pure (–)-**10b**.

Data for (–)-**10b**:

m.p.: 77–78 °C (hexanes)
¹H NMR: (500 MHz, CDCl₃)
 7.06 (s, 1H, HC(13)), 6.97 (d, *J* = 7.8 Hz, 1H, HC(10)), 6.94 (dd, *J* = 7.8, 1.2 Hz, 1H, HC(11)), 2.94 (ddd, *J* = 16.8, 5.5, 1.6 Hz, 1H, H₂C(8)), 2.84 (ddd, *J* = 17.1, 11.7, 6.9 Hz, 1H, H₂C(8)), 2.71 (ddd, *J* = 15.8, 10.0, 7.5 Hz, 1H, H₂C(3)), 2.60 (ddd, *J* = 15.7, 7.6, 4.1 Hz, 1H, H₂C(3)), 2.50 (ddd, *J* = 13.1, 7.5, 4.2 Hz, 1H, H₂C(2)), 2.31 (s, 3H, H₃C(17)), 2.00 – 1.88 (m, 2H, H₂C(2) and HC(6)), 1.86 – 1.72 (m, 2H, H₂C(7)), 1.30 (s, 3H, H₃C(15)), 1.17 (s, 3H, H₃C(16)), 1.15 (s, 3H, H₃C(16)).

- ^{13}C NMR: (126 MHz, CDCl_3)
217.3 (C(4)), 147.2 (C(14)), 135.4 (C(12)), 131.7 (C(9)), 128.9 (HC(10)), 126.7 (HC(11)), 125.9 (HC(13)), 50.7 (HC(6)), 47.4 (C(5)), 37.5 (H_2C (2)), 37.3 (C(1)), 34.6 (H_2C (3)), 30.4 (H_2C (8)), 26.9 (H_3C (16)), 24.6 (H_3C (15)), 21.2 (H_3C (23)), 21.1 (H_3C (16)), 20.2 (H_2C (7)).
- IR: (neat)
2966 (w), 2940 (w), 2866 (w), 1703 (m), 1613 (w), 1501 (w), 1457 (w), 1434 (w), 1382 (w), 1362 (w), 1313 (w), 1269 (w), 1200 (w), 1140 (w), 1114 (w), 1046 (w), 1009 (w), 970 (w), 947 (w), 878 (w), 839 (w), 807 (w), 731 (w), 593 (w), 579 (w), 463 (w).
- LRMS: (EI, 70 eV)
91.1 (13), 115.1 (17), 128.1 (20), 143.1 (29), 157.1 (35), 171.1 (21), 199.1 (70), 241.2 (66), 256.2 (100).
- HRMS: Calcd for $\text{C}_{18}\text{H}_{24}\text{O}$ ($[\text{M}]^+$): 256.1827; Found: 256.1825
- TLC: R_f 0.39 (silica gel, hexanes/EtOAc, 91:9, PMA)
- Opt. Rot.: $[\alpha]_{\text{D}}^{24}$ -132.4 ($c = 0.94$ in CHCl_3)
- HPLC: t_{R} 12.1 min (95%); t_{R} 13.1 min (5%) (Supelco Astec, hexanes/*i*-PrOH 90:10, 0.5 mL/min, 220 nm, 24 °C)
- Analysis: $\text{C}_{18}\text{H}_{24}\text{O}$ (256.39)
Calcd: C, 84.32%; H, 9.43%
Found: C, 84.29%; H, 9.39%

Preparation of (+)-(1*R*,4*R*,6*S*)-2-((2,6-Diisopropylphenyl)sulfonyl)-1,5,5,12-tetramethyl-1,2,3,4,5,6,7,8-octahydrophenanthrene ((+)-11b)



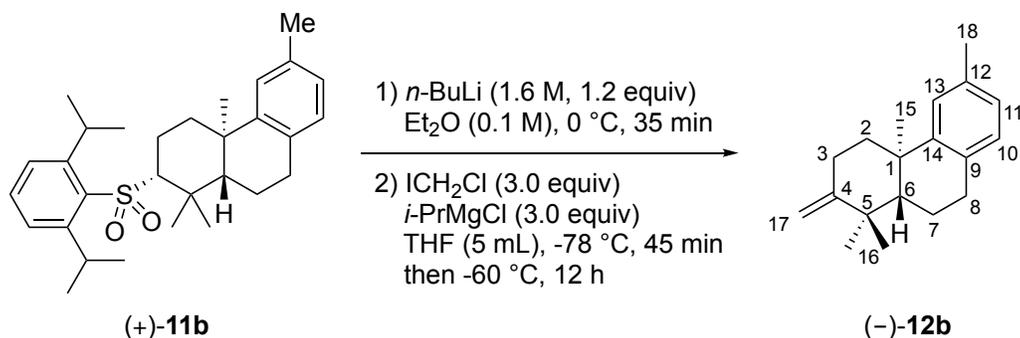
A 100-mL, round-bottomed flask equipped with a stir bar was charged with sulfide (–)-**4b** (652.1 mg, 1.5 mmol, 91:9 e.r.) and CH₂Cl₂ (30 mL). *m*-CPBA (647.1 mg, 3.75 mmol, 2.5 equiv) was added in one portion, and the solution was stirred at 25 °C for 12 h. Upon completion, the reaction was quenched by pouring into sat. aq. Na₂SO₃ (50 mL). The layers were separated, and the aqueous phase was extracted with CH₂Cl₂ (3 x 50 mL). The combined organic layers were washed with sat. aq. NaHCO₃ (50 mL), and then dried over anhydrous MgSO₄, filtered, and concentrated under reduced pressure (35 °C, 50 mmHg). The residue was purified by column chromatography (silica gel, 3 x 25 cm, dry load on Celite, 25-mL fractions, hexane/EtOAc, 98:2) afforded (+)-**11b** (692.9 mg, 98%) as a white solid. Recrystallization from a minimal amount of boiling hexanes provided 611.3 mg (87%) of analytically pure (+)-**11b**.

Data for (+)-11b:

- m.p.:** 163–164 °C (hexanes)
- ¹H NMR:** (500 MHz, CDCl₃)
- 7.51 (t, *J* = 7.8 Hz, 1H, HC(20)), 7.38 (d, *J* = 7.8 Hz, 2H, HC(19)), 7.01 (s, 1H, HC(13)), 6.99 (d, *J* = 7.8 Hz, 1H, HC(10)), 6.95 (d, *J* = 7.7 Hz, 1H, HC(11)), 4.54 – 4.19 (m, 2H, HC(21)), 3.04 – 2.96 (m, 2H, H₂C(8) and HC(4)), 2.86 (ddd, *J* = 17.6, 11.9, 7.2 Hz, 1H, H₂C(8)), 2.44 (dt, *J* = 13.1, 3.5 Hz, 1H, H₂C(2)), 2.37 (td, *J* = 13.4, 3.2 Hz, 1H, H₂C(3)), 2.28 (s, 3H, H₃C(23)), 2.03 (dd, *J* = 13.3, 7.2 Hz, 1H, H₂C(7)), 1.85 – 1.73 (m, 2H, H₂C(3) and H₂C(7)), 1.68 (s, 3H, H₃C(16)), 1.44 – 1.40 (m, 4H, HC(6) and H₃(16)), 1.39 – 1.33 (m, 7H, H₂C(2) and H₃C(22)), 1.32 (s, 3H, H₃C(15)), 1.29 (d, *J* = 6.8 Hz, 6H, H₃C(22)).

- ¹³C NMR: (126 MHz, CDCl₃)
151.0 (C(18)), 148.3 (C(14)), 136.1 (C(17)), 135.2 (C(12)), 132.6 (HC(20)), 131.7 (C(9)), 129.0 (HC(10)), 126.6 (HC(11)), 126.1 (HC(19)), 124.9 (HC(13)), 73.2 (HC(4)), 53.5 (HC(6)), 39.4 (C(5)), 38.1 (H₂C(2)), 37.6 (C(1)), 30.4 (H₂C(8)), 29.5 (H₃C(16)), 29.3 (HC(21)), 25.5 (H₃C(22)), 24.6 (H₃C(15)), 24.5 (H₃C(22)), 21.4 (H₂C(3)), 21.2 (H₃C(23)), 18.5 (H₃C(16)), 18.4 (H₂C(7)).
- IR: (neat)
2955 (w), 2869 (w), 2254 (w), 1578 (w), 1501 (w), 1463 (w), 1396 (w), 1379 (w), 1363 (w), 1292 (m), 1252 (w), 1225 (w), 1183 (w), 1155 (w), 1137 (m), 1052 (w), 995 (w), 968 (w), 908 (m), 836 (w), 805 (m), 769 (w), 728 (s), 665 (m), 648 (w), 633 (w), 597 (m), 576 (m), 535 (m), 515 (w), 499 (w), 485 (w), 463 (w).
- LRMS: (EI, 70 eV)
105.1 (13), 128.1 (11), 131.1 (43), 143.1 (25), 145.1 (81), 157.1 (62), 171.1 (37), 185.1 (27), 199.1 (11), 225.1 (21), 241.2 (100), 446.1 (11), 466.3 (4).
- HRMS: (ES⁺, TOF)
Calcd for C₃₀H₄₂O₂SNa ([M+Na]⁺): 489.2803; Found: 489.2793
- TLC: *R_f* 0.48 (silica gel, hexanes/EtOAc, 91:9, PMA)
- Opt. Rot.: [α]_D²⁴ +1.2 (c = 2.80, CHCl₃)
- HPLC: *t_R* 9.8 min (90%); *t_R* 10.5 min (10%) (Supelco Astec, hexanes/*i*-PrOH, 95:5, 0.4 mL/min, 220 nm, 24 °C)
- Analysis: C₃₀H₄₂O₂S (466.72)
Calcd: C, 77.20%; H, 9.07%
Found: C, 77.07%; H, 9.10%

Preparation of (1*R*,6*R*)-1,5,5,12-Tetramethyl-4-methylene-1,2,3,4,5,6,7,8-octahydrophenanthrene ((-)-12b)



A flame-dried, 25 mL, Schlenk flask ('A') equipped with a stir bar was charged with ClCH₂I (220 μL, 3.0 mmol, 3.0 equiv) and THF (5 mL), and then was cooled to -78 °C using a dry ice/acetone bath. The solution was stirred for 15 min to allow the internal temperature to equilibrate. A solution of *i*-PrMgCl (2 M, 1.5 mL, 3.0 equiv) was added dropwise and the solution was stirred at -78 °C for 45 min. A separate, flame-dried, 25 mL, Schlenk flask ('B') was charged with sulfone (-)-**11b** (466 mg, 1.0 mmol, 1.0 equiv, 90:10 e.r.) and Et₂O (10 mL), and then was cooled to 0 °C using an ice/water bath. A solution of *n*-butyllithium (1.6 M, 750 μL, 1.2 equiv) was added via syringe, and the resulting yellow solution was stirred at 0 °C for 35 min and then cooled to -78 °C for 10 min with a dry ice/acetone bath. The solution of α-lithiated sulfone 'B' was added dropwise to flask 'A' at -78 °C. Following this addition, flask 'A' was moved to a -60 °C cooling bath (maintained with a Cryo-Cool) and the reaction was stirred at this temperature for 12 h. Full conversion was observed by TLC (hexanes), and the reaction was quenched by addition of MeOH (0.2 mL) at -60 °C. The mixture was warmed to 25 °C and diluted with sat. aq. NH₄Cl (10 mL). The mixture was extracted with Et₂O (3 x 20 mL), and the combined organic layers were dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure (35 °C, 50 mmHg) to afford crude (-)-**12b**. The product was purified by column chromatography (silica gel, 3 x 25 cm, dry load on Celite, hexanes/EtOAc, 99:1) to afford (-)-**12b** (243.7 mg, 96%) as a colorless oil. Further purification via Kugelrohr distillation (85 °C, 0.05 mmHg) provided 240.1 mg (94%) of (-)-**12b**.

Data for (-)-12b:

b.p.: 85 °C (ABT, 0.05 mmHg)

¹H NMR: (500 MHz, CDCl₃)

7.05 (s, 1H, HC(13)), 6.95 (d, $J = 7.7$ Hz, 1H, HC(10)), 6.91 (d, $J = 7.7$ Hz, 1H, HC(11)), 4.75 (d, $J = 16.4$ Hz, 2H, H₂C(17)), 2.93 (dd, $J = 16.8, 6.2$ Hz, 1H, H₂C(8)), 2.82 (ddd, $J = 17.3, 11.5, 7.3$ Hz, 1H, H₂C(8)), 2.65 – 2.54 (m, 1H, H₂C(3)), 2.42 – 2.32 (m, 2H, H₂C(2) and H₂C(3)), 2.31 (s, 3H, H₃C(18)), 1.92 (ddt, $J = 12.7, 7.1, 1.9$ Hz, 1H, H₂C(7)), 1.78 (ddt, $J = 19.0, 12.5, 6.6$ Hz, 1H, H₂C(7)), 1.67-1.57 (m, 1H, H₂C(2)), 1.50 (dd, $J = 12.4, 2.4$ Hz, 1H, HC(6)), 1.30 (s, 3H, H₃C(15)), 1.17 (s, 3H, H₃C(16)), 1.10 (s, 3H, H₃C(16)).

¹³C NMR: (126 MHz, CDCl₃)

157.5 (C(4)), 149.6 (C(14)), 134.9 (C(12)), 131.8 (C(9)), 128.7 (HC(10)), 126.1 (HC(11)), 125.2 (HC(13)), 105.5 (H₂C(17)), 50.5 (HC(6)), 40.1 (H₂C(2)), 39.4 (C(5)), 38.0 (C(1)), 30.2 (H₂C(8)), 30.0 (H₂C(3)), 28.7 (H₃C(16)), 25.4 (H₃C(15)), 23.2 (H₃C(16)), 21.3 (H₃C(18)), 19.8 (H₂C(7)).

IR: (neat)

2931 (w), 2856 (w), 1636 (w), 1613 (w), 1501 (w), 1462 (w), 1436 (w), 1402 (w), 1373 (w), 1362 (w), 1307 (w), 1283 (w), 1201 (w), 1177 (w), 1150 (w), 1136 (w), 1025 (w), 994 (w), 969 (w), 938 (w), 888 (m), 844 (w), 828 (w), 804 (w), 727 (w), 676 (w), 618 (w), 590 (w), 461 (w).

LRMS: (EI, 70 eV)

115.1 (12), 131.1 (80), 143.1 (36), 158.1 (49), 171.1 (70), 183.1 (21), 239.2 (26), 254.2 (100).

HRMS: Calcd for C₁₉H₂₆ ([M]⁺): 254.2035, Found: 254.2035

TLC: R_f 0.34 (hexanes)

Opt. Rot.: $[\alpha]_D^{24} -67.3$ ($c = 1.45$ in CHCl₃)

HPLC: t_R 9.8 min (91%); t_R 10.4 min (9%) (Supelco Astec, hexanes, 0.5 mL/min, 220 nm, 24 °C)

Analysis: C₁₉H₂₆ (254.42)

Calcd: C, 89.70%; H, 10.30%

Found: C, 89.41%; H, 9.97%

fractions, hexanes) to afford (–)-**13b** (221.1 mg, 91%) as a colorless oil. Spectroscopic data match those previously reported.

Data for (–)-**13b**:

¹H NMR: (500 MHz, CDCl₃)

7.07 (s, 1H), 6.95 (d, $J = 7.7$ Hz, 1H), 6.90 (d, $J = 7.7$ Hz, 1H), 2.91 (dd, $J = 16.7$, 6.7 Hz, 1H), 2.82 (ddd, $J = 17.4$, 11.3, 7.5 Hz, 1H), 2.37 – 2.21 (m, 4H), 1.91 – 1.84 (m, $J = 13.2$, 7.5 Hz, 1H), 1.81 – 1.65 (m, 2H), 1.61 (dp, $J = 14.0$, 3.6 Hz, 1H), 1.51 – 1.46 (m, 1H), 1.40 (td, $J = 13.1$, 3.7 Hz, 1H), 1.34 (dd, $J = 12.5$, 2.3 Hz, 1H), 1.27 – 1.18 (m, 4H), 0.96 (s, 3H), 0.94 (s, 3H).

¹³C NMR: (126 MHz, CDCl₃)

150.0, 134.8, 132.1, 128.9, 126.0, 124.9, 50.4, 41.7, 38.8, 37.7, 33.5, 33.3, 30.0, 24.8, 21.6, 21.3, 19.3, 19.1.

IR: (neat)

2922 (w), 2865 (w), 1613 (w), 1500 (w), 1459 (w), 1440 (w), 1388 (w), 1374 (w), 1201 (w), 1144 (w), 1078 (w), 1040 (w), 995 (w), 971 (w), 946 (w), 874 (w), 833 (w), 804 (w), 732 (w), 461 (w).

LRMS: (EI, 70 eV)

69.1 (22), 115.1 (13), 131.1 (46), 145.1 (60), 157.1 (44), 171.1 (25), 227.2 (100), 242.2 (65).

HRMS: (EI, 70 eV)

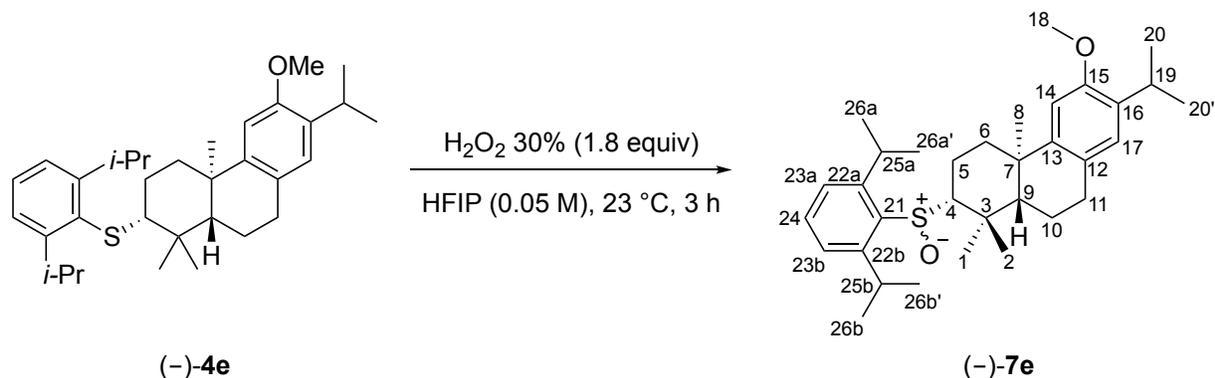
Calcd for C₁₈H₂₆ ([M]⁺): 242.2034, Found: 242.2031

TLC: R_f 0.46 (hexanes)

Opt. Rot.: $[\alpha]_D^{24}$ –62.7 ($c = 1.14$ in CHCl₃)

HPLC: t_R 8.2 min (90%); t_R 8.7 min (10%) (Supelco Astec, hexanes, 0.5 mL/min, 220 nm, 24 °C)

Preparation of (–)- (4*R*,7*R*,9*S*)-4-(2,6-Diisopropylphenylsulfinyl)-16-isopropyl-15-methoxy-3,3,7-trimethyl-3,4,5,6,7,9,10,11-octahydrophenanthrene ((–)-7e)



A dram-sized vial equipped with a stir bar was charged with (–)-4e (25.2 mg, 0.051 mmol) and hexafluoroisopropyl alcohol (1 mL). The mixture was sonicated for 5 min which resulted in a fine, white suspension. Hydrogen peroxide (aq., 30% w/w, 92 μ L, 10 mg, 1.8 equiv) was added at 25 °C. The white suspension was stirred at 25 °C for 3 h, over which time the suspension cleared to a nearly colorless solution. Full conversion was observed by TLC (hexanes/EtOAc, 9:1). The reaction was quenched by the addition of sat. aq. sodium thiosulfate (0.5 mL) and was stirred vigorously for 5 min. The mixture was diluted with water (3 mL) and extracted with CH₂Cl₂ (3 x 2 mL). The combined organic layers were washed with brine (3 mL), dried over sodium sulfate, filtered, and concentrated (30 °C, 15 mmHg) to afford crude (–)-7e. The product was purified by chromatography (silica gel, 1 x 20 cm, dry load on Celite, 5-mL fractions, hexanes/EtOAc gradient elution: 95:5 (100 mL) to 90:10 (100 mL) to 85:15 (100 mL)) to afford 24.5 mg (94%) of (–)-7e as a white solid (d.r. = 63:37). Prior to combining the fractions, an aliquot was taken from an earlier fraction containing only major diastereomer (–)-7e' and subjected to HPLC analysis to determine enantiomeric ratio of the compound. Spectroscopic data for combined (–)-7e matched those reported for (\pm)-7e (*vide infra*).

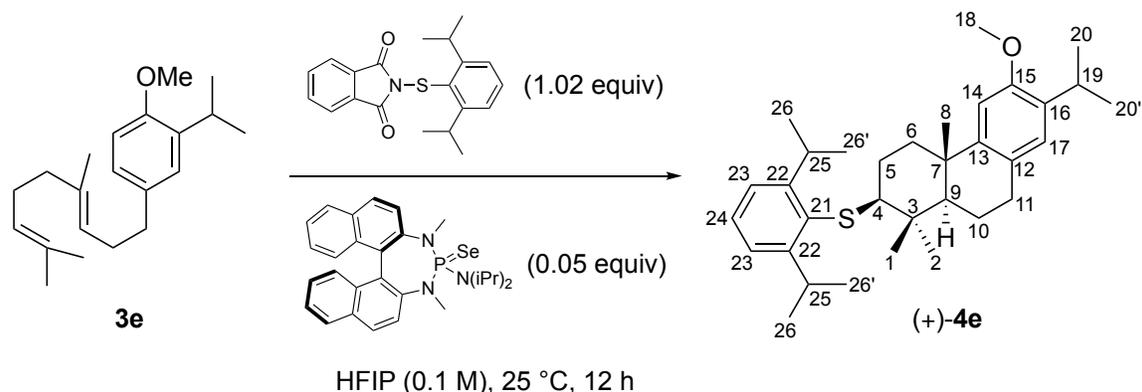
Data for (–)-7e:

d.r.: 63:37 7e':7e''

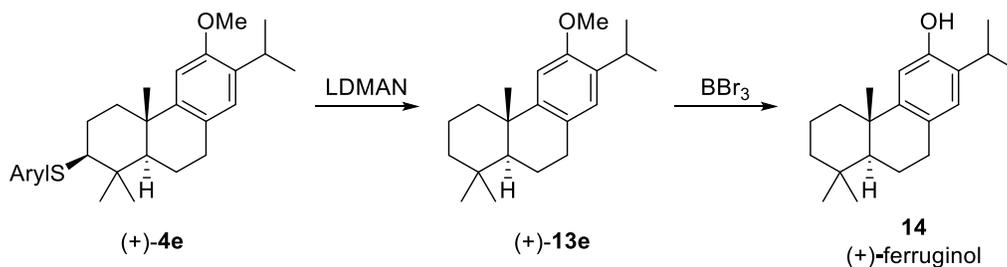
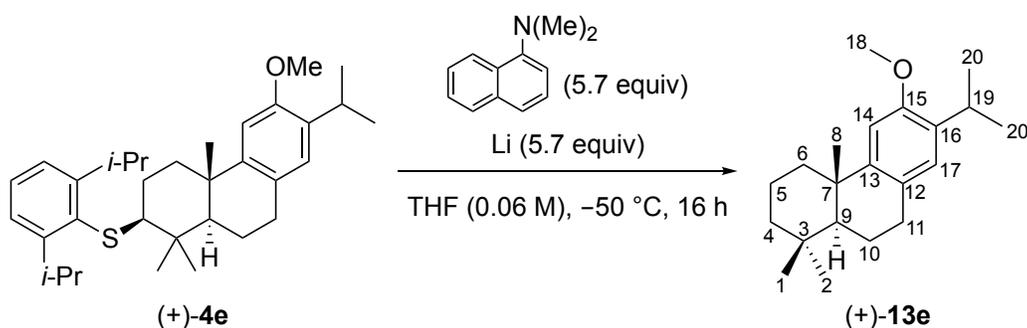
HPLC: (measured on major diastereomer (–)-7e')

From chromatographed (–)-4e: t_R 11.3 min (92%); t_R 13.6 min (8%) (Regis (*R,R*)-Whelk O1, hexanes/*i*-PrOH, 95:5, 0.8 mL/min, 220 nm, 24 °C)

From recrystallized (–)-4e: t_R 11.2 min (91%); t_R 13.6 min (9%)

Total Syntheses**Large-scale Preparation of (+)-4e**

A 250-mL, round-bottomed flask equipped with a stir bar and argon inlet adapter was charged with *N*-(2,6-diisopropylphenylthio)phthalimide **1** (1.0416 g, 3.07 mmol, 1.02 equiv), hexafluoroisopropyl alcohol (30 mL, 0.1 M), and (*E*)-4-(4,8-dimethylnona-3,7-dien-1-yl)-2-isopropyl-1-methoxybenzene **3e** (901.9 mg, 3.00 mmol). A homogeneous, yellow solution resulted. Catalyst (*R*)-**2** (78.0 mg, 0.15 mmol, 0.05 equiv, e.r. = 97:3) was added in one portion and the mixture was stirred at 25 °C for 12 h. Full conversion was observed by TLC (hexanes/CH₂Cl₂, 90:10). The reaction mixture was diluted with CH₂Cl₂ (30 mL), and the volatiles were removed by rotary evaporation (30 °C, 15 mmHg) to afford crude (+)-**4e**. The crude product was purified by column chromatography (silica gel, 5 x 20 cm, dry load on Celite, 50-mL fractions, hexanes/CH₂Cl₂ gradient elution, 95:5 (500 mL) to 90:10 (500 mL) to 85:15 (500 mL) to 80:20 (500 mL) to 75:15 (500 mL)) to afford (+)-**4e** (1.2321 g, 83%) as a white foam solid. The solid contained trace impurities which cannot be removed by chromatography. The compound was dissolved in a minimal amount of boiling abs. ethanol (9 mL) and the solution was allowed to cool slowly to 25 °C, followed by cooling in a -20 °C freezer for 12 h. The product was collected by vacuum filtration and rinsed with ice-cold hexanes (2 mL) to afford 820.8 (55%) of (+)-**4e** as white crystals. Spectroscopic data matched those reported for (±)-**4e**. Enantiomeric ratio was determined on derivative (+)-**7e'**. A second crop was obtained in the following manner. The mother liquor was concentrated (30 °C, 15 mmHg) and subjected to column chromatography (silica gel, 3 x 25 cm, dry load on Celite, 25-mL fractions, hexanes/CH₂Cl₂ gradient elution, 95:5 (300 mL) to 90:10 (300 mL) to 85:15 (300 mL) to 80:20 (300 mL)) to afford 257.4 mg of (+)-**4e**. The solid was recrystallized from ethanol (1 mL) as described previously to afford 108.9 mg (8%) of (+)-**4e**.

(+)-Ferruginol
Preparation of (+)-(7*S*,9*S*)-16-Isopropyl-15-methoxy-3,3,7-trimethyl-3,4,5,6,7,9,10,11-octahydrophenanthrene ((+)-13e)


A flame-dried, 25-mL, Schlenk flask equipped with a glass-coated stir bar was charged with lithium granules (21 mg, 3.0 mmol, 5.7 equiv) inside a glove box. The flask was removed from the glove box, placed under argon, and charged with THF (7.5 mL). The flask was fitted with a temperature probe and the mixture was cooled to an internal temperature of $-50\text{ }^\circ\text{C}$ (using a Cryo-Cool) and stirred for 1 h. *N,N*-Dimethyl-1-aminonaphthalene (495 μL , 3.0 mmol, 5.7 equiv) was added dropwise over 10 min. [Notes: This viscous amine should be added directly into the solution rather than dripped down the side of the flask, as it tends to adhere to the chilled walls of the flask. Also, if added too quickly, the amine may gel at the bottom of the flask and cause the stir bar to stick. If either of these problems are encountered, gently swirl the flask (while still submerged in the cold bath) until the amine is solubilized.] The resulting solution was allowed to stir for 12 h at $-50\text{ }^\circ\text{C}$. Generally within 1 h, a dark-green color is observed, but it takes several hours for the reagent to fully form. The temperature must be maintained at $-50\text{ }^\circ\text{C}$ or lower to prevent decomposition of the reagent (signaled by the solution turning brown). To the dark-green solution, sulfide (+)-4e (260.4 mg, 0.53 mmol) was added portionwise as a solid over 5-10 min. No change in solution color was observed. After addition, the walls of the flask were rinsed down (slowly, over 5 min) with THF (1.5 mL). The solution was stirred at $-50\text{ }^\circ\text{C}$ for 1 h,

at which point full conversion was observed by TLC (hexanes/CH₂Cl₂, 90:10). The reaction was quenched by the addition of methanol (1 mL) which caused the dark green color to immediately discharge. The cold bath was removed, and the clear, pale-yellow solution was allowed to warm to 25 °C. The mixture was partitioned between aq. 1 N HCl (25 mL) and diethyl ether (25 mL) in a 125-mL separatory funnel and the layers were separated. The aqueous phase was extracted with diethyl ether (2 x 25 mL) and the combined organic extracts were washed with brine (25 mL), dried over sodium sulfate, filtered, and concentrated (30 °C, 15 mmHg) to afford crude (+)-**13e** (304.1 mg) as a yellow oil. [**Note:** It is not necessary in this case to oxidize the thiol to remove it from the crude mixture. The thiol is easily separated from the desired product by chromatography.] The product was purified by chromatography (silica gel, 3 x 20 cm, dry load on Celite, 25-mL fractions, hexanes/CH₂Cl₂ gradient elution: 100:0 (300 mL) to 97.5:2.5 (300 mL) to 95:5 (300 mL) to 92.5:7.5 (300 mL)) which was then dried under high vacuum for 12 h (45 °C, 0.1 mmHg) to afford 145.3 mg (92%) of (+)-**13e** as a clear, colorless, highly viscous oil. The spectroscopic data for (+)-**13e** matched those reported previously.²⁴

Data for (+)-13e:

¹H NMR: (500 MHz, CDCl₃)

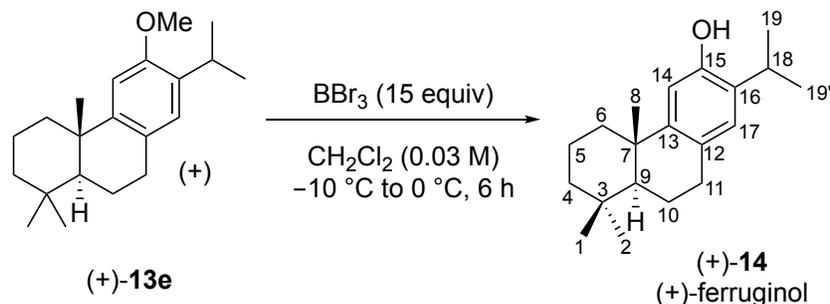
6.84 (s, 1H, HC(17)), 6.72 (s, 1H, HC(14)), 3.79 (s, 3H, H₃C(18)), 3.22 (hept, *J* = 6.9 Hz, 1H, HC(19)), 2.91-2.83 (m, 1H, H₂C(11^{eq})), 2.82-2.73 (m, 1H, H₂C(11^{ax})), 2.30-2.20 (m, 1H, H₂C(6^{eq})), 1.86 (ddt, *J* = 10.9, 7.2, 1.8 Hz, 1H, H₂C(10^{eq})), 1.82-1.71 (m, 1H, H₂C(5^{ax})), 1.71-1.63 (m, 1H, H₂C(10^{ax})), 1.60 (dq, *J* = 14.0, 3.6 Hz, 1H, H₂C(5^{eq})), 1.51-1.46 (m, 1H, H₂C(4^{eq})), 1.46-1.39 (m, 1H, H₂C(6^{ax})), 1.34 (dd, *J* = 12.4, 2.2 Hz, 1H, HC(9)), 1.23 (dd, *J* = 13.6, 4.1 Hz, 1H, H₂C(4^{ax})), 1.20 (s, 3H, H₃C(8)), 1.19 (d, *J* = 7.0 Hz, 3H, H₃C(20)), 1.18 (d, *J* = 7.0 Hz, 3H, H₃C(20')), 0.94 (s, 3H, H₃C(2)), 0.93 (s, 3H, H₃C(1)).

¹³C NMR: (126 MHz, CDCl₃)

155.14 (C(15)), 148.23 (C(13)), 134.27 (C(16)), 127.03 (C(12)), 126.52 (HC(17)), 106.71 (HC(14)), 55.74 (H₃C(18)), 50.64 (HC(9)), 41.86 (H₂C(4)), 39.08 (H₂C(6)), 38.00 (C(7)), 33.62 (C(3)), 33.49 (H₃C(2)), 29.98 (H₂C(11)), 26.59 (HC(19)), 24.97 (H₃C(8)), 23.06 (H₃C(20')), 22.85 (H₃C(20)), 21.78 (H₃C(1)), 19.51 (H₂C(5)), 19.39 (H₂C(10)).

Opt. Rot.: [α]_D²⁵ +49.1 (*c* = 1.38 in CHCl₃) (80% ee)

Preparation of (+)-Ferruginol: (+)-(7*S*,9*S*)-16-Isopropyl-3,3,7-trimethyl-3,4,5,6,7,9,10,11-octahydrophenanthren-15-ol ((+)-14)



A solution of boron tribromide in CH_2Cl_2 (1 M) was prepared as follows. A flame-dried, 10-mL, Schlenk flask equipped with a stir bar was charged with CH_2Cl_2 (5 mL) and cooled to -78°C using a dry ice/acetone bath. Boron tribromide (482 μL , 5 mmol) was injected quickly in one portion at -78°C . The cold bath was removed and the solution was allowed to warm to 25°C and then used immediately.

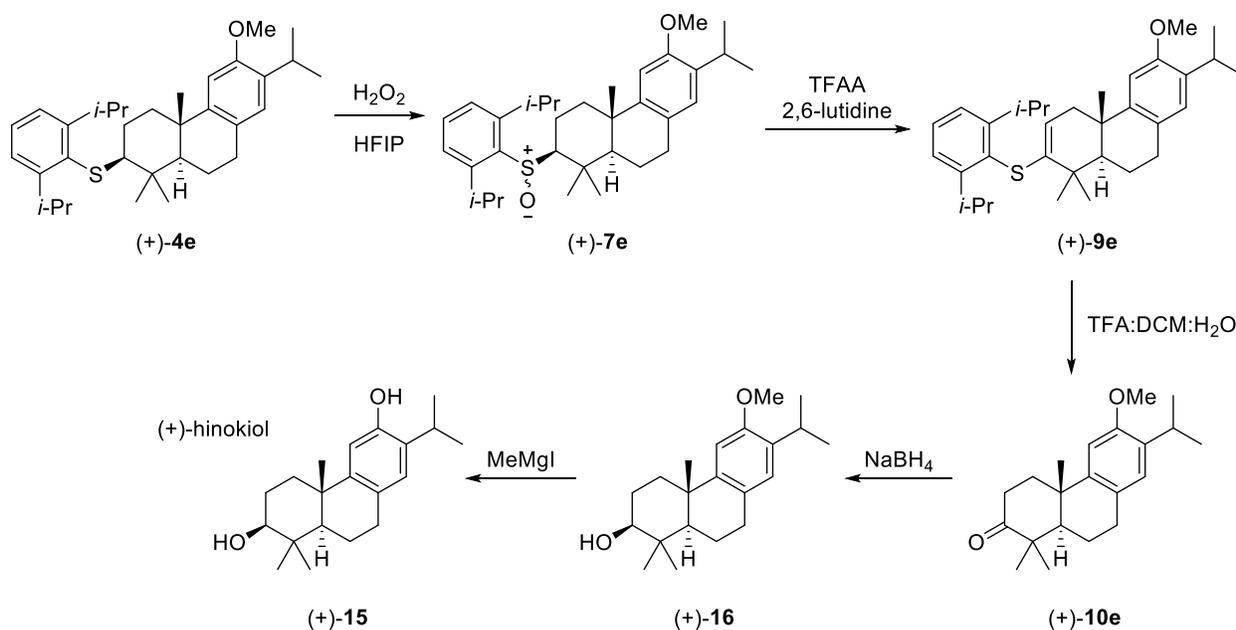
A flame-dried, 25-mL, Schlenk flask equipped with a stir bar was charged with a solution of ferruginyl methyl ether (+)-**13e** (102.1 mg, 0.34 mmol, 90:10 e.r.) in CH_2Cl_2 (8 mL). The pale, yellow solution was cooled to -10°C using an ice/salt bath. Freshly prepared BBr_3 solution (3.4 mL, 1.0 M, 3.4 mmol, 10 equiv) was added dropwise over 10 min. The resulting darker, yellow solution was stirred for 3 h and allowed to warm slowly to 0°C . Incomplete conversion was observed by TLC (hexanes/EtOAc, 90:10). An additional portion of BBr_3 solution (1.6 mL, 1.0 M, 1.6 mmol, 5 equiv) was added dropwise at 0°C and the reaction was stirred for an additional 3 h at 0°C . An orange solution was observed. Full conversion was observed by TLC. The reaction was quenched by the addition of water (10 mL). The resulting grey suspension was poured into a 125-mL separatory funnel. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine (25 mL), and then dried over sodium sulfate, filtered, and concentrated (30°C , 15 mmHg) to afford crude (+)-**14** (119.1 mg). The product was purified by column chromatography (silica gel, 2 x 15 cm, dry load on Celite, 10-mL fractions, hexanes/EtOAc gradient elution, 98:2 (200 mL) to 96:4 (200 mL) to 94:6 (200 mL) to 92:8 (200 mL)) and dried under vacuum (60°C , 0.1 mmHg, 12 h) to afford 88.6 mg (91%) of (+)-**14** as a beige solid. Spectroscopic data for (+)-**14** matched those previously reported.^{24,25}

Data for (+)-14:¹H NMR: (500 MHz, CDCl₃)

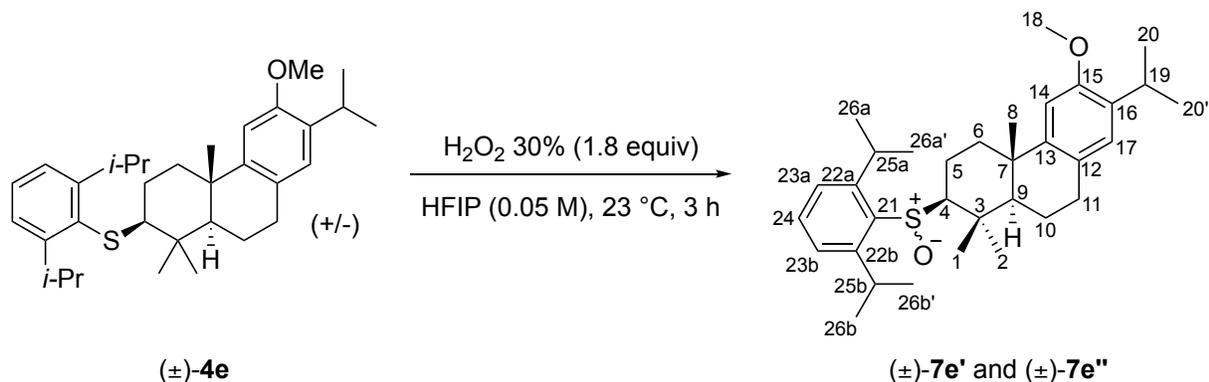
6.83 (s, 1H, HC(17)), 6.63 (s, 1H, HC(14)), 4.42 (s, 1H, OH), 3.11 (hept, $J = 6.9$ Hz, 1H, HC(18)), 2.91-2.82 (m, 1H, H₂C(11^{eq})), 2.81-2.72 (m, 1H, H₂C(11^{ax})), 2.17 (dtd, $J = 12.6, 3.3, 1.3$ Hz, 1H, H₂C(6^{eq})), 1.86 (ddt, $J = 12.7, 7.3, 1.8$ Hz, 1H, H₂C(10^{eq})), 1.78-1.70 (m, 1H, H₂C(5^{ax})), 1.69-1.62 (m, 1H, H₂C(10^{ax})), 1.62-1.55 (m, 1H, H₂C(5^{eq})), 1.47 (dtd, $J = 13.2, 3.2, 1.6$ Hz, 1H, H₂C(4^{eq})), 1.38 (td, $J = 13.0, 3.6$ Hz, 1H, H₂C(6^{ax})), 1.32 (dd, $J = 12.4, 2.3$ Hz, 1H, HC(9)), 1.24 (d, $J = 6.9$ Hz, 3H, H₃C(19)), 1.23 (d, $J = 6.9$ Hz, 3H, H₃C(19')), 1.23-1.19 (m, 1H, H₂C(4^{ax})), 1.17 (s, 3H, H₃C(8)), 0.94 (s, 3H, H₃C(2)), 0.92 (s, 3H, H₃C(1)).

¹³C NMR: (126 MHz, CDCl₃)

150.78 (C(15)), 148.83 (C(13)), 131.48 (C(16)), 127.47 (C(12)), 126.77 (HC(17)), 111.11 (HC(14)), 50.50 (HC(9)), 41.84 (H₂C(4)), 39.02 (H₂C(6)), 37.66 (C(7)), 33.59 (C(3)), 33.47 (H₃C(2)), 29.91 (H₂C(11)), 26.97 (HC(18)), 24.95 (H₃C(8)), 22.89 (H₃C(19')), 22.71 (H₃C(19)), 21.78 (H₃C(1)), 19.47 (H₂C(5)), 19.38 (H₂C(10)).

Opt. Rot.: $[\alpha]_D^{25} +41.5$ ($c = 0.98$ in CHCl₃) (80% ee)**(+)-Hinokiol**

Preparation of (\pm)- (2*S*,4*aS*,10*aR*)-2-(2,6-Diisopropylphenylsulfinyl)-16-isopropyl-15-methoxy-3,3,7-trimethyl-3,4,5,6,7,9,10,11-octahydrophenanthrene ((\pm)-7e'** and (\pm)-**7e''**)**



A 200-mL, round-bottomed flask equipped with a stir bar and argon inlet was charged with sulfide (\pm)-**4e** (1.08 g, 2.19 mmol) and hexafluoroisopropanol (43 mL). The mixture was sonicated for 10 min until a fine, white suspension was observed. Hydrogen peroxide (aq., 30% w/w, 0.40 mL, 0.45 g, 1.8 equiv) was added dropwise at 23 °C. The white suspension was stirred at 25 °C for 4 h, over which time the suspension cleared to a nearly colorless solution. Full conversion was observed by TLC (hexanes/EtOAc, 9:1). The reaction was quenched by the addition of sat. aq. sodium thiosulfate (10 mL) and was stirred vigorously for 5 min. The majority of the HFIP was removed by rotary evaporation (30 °C, 15 mmHg). The residue was diluted with water (30 mL) and extracted with CH₂Cl₂ (3 x 30 mL). The combined organic layers were washed with brine (30 mL), dried over sodium sulfate, filtered, and concentrated (30 °C, 15 mmHg) to afford 1.41 g of crude (\pm)-**7e** (sulfoxide d.r. = 64:36). The product was purified by chromatography (silica gel, 4 cm x 20 cm, dry load on Celite, 25 mL fractions, hexanes/EtOAc gradient elution: 19:1 (500 mL) to 9:1 (500 mL) to 5.67:1 (500 mL) to 4:1 (500 mL)). The two sulfoxide diastereomers (\pm)-**7e'** and (\pm)-**7e''** have similar *R_f* values but can be separated by multiple rounds of chromatography. It is not necessary to separate them, as they are both competent in the subsequent Pummerer rearrangement. The combined yield of both diastereomers after chromatography was 1.08 g (97%). Analytically pure samples were obtained in the following manner. The major diastereomer (less polar) was separated from most of the minor diastereomer by chromatography (silica gel, 4 cm x 20 cm, dry load on Celite, 25 mL fractions, hexanes/EtOAc gradient elution: 19:1 (500 mL) to 9:1 (500 mL) to 5.67:1 (500 mL) to 4:1 (500 mL)) to afford 364.1 mg (33%) of a white solid. The solid was recrystallized from boiling hexanes (6 mL) to afford 82.6 mg (7%) of white crystals. The product was again

chromatographed (silica gel, 2 cm x 22 cm, dry load on Celite, 10 mL fractions, hexanes/Et₂O gradient elution: 9:1 (200 mL) to 4:1 (200 mL) to 2.33:1 (200 mL) to 1.5:1 (200 mL)). The collected solid was chromatographed a third time (silica gel, 2 cm x 22 cm, dry load on Celite, 10 mL fractions, hexanes/EtOAc gradient elution: 19:1 (200 mL) to 9:1 (200 mL) to 5.67:1 (200 mL) to 4:1 (200 mL)) to afford 70.9 mg (6%) of analytically pure major diastereomer (\pm)-**7e'** as a white solid. The minor diastereomer (more polar) was separated from much of the major diastereomer by chromatography (silica gel, 4 cm x 20 cm, dry load on Celite, 25 mL fractions, hexanes/EtOAc gradient elution: 19:1 (500 mL) to 9:1 (500 mL) to 5.67:1 (500 mL) to 4:1 (500 mL)) followed by a second round of chromatography (silica gel, 3 cm x 20 cm, dry load on Celite, 25 mL fractions, hexanes/EtOAc gradient elution: 19:1 (300 mL) to 9:1 (300 mL) to 5.67:1 (300 mL) to 4:1 (300 mL)). This process afforded 324.2 mg (29%) of a white solid, which was recrystallized from boiling hexanes (3 mL) to afford 198.2 mg (18%) of white crystals. The product was again chromatographed (silica gel, 2 cm x 24 cm, dry load on Celite, 10 mL fractions, hexanes/Et₂O gradient elution: 9:1 (200 mL) to 4:1 (200 mL) to 2.33:1 (200 mL) to 1.5:1 (200 mL)) and then recrystallized again from hexanes to afford 74.4 mg (7%) of analytically pure minor diastereomer (\pm)-**7e''** as white crystals.

Data for (\pm)-**7e'** (major diastereomer):

m.p.: 188–190 °C

¹H NMR: (500 MHz, CDCl₃)

7.40 (t, $J = 7.8$ Hz, 1H, HC(24)), 7.30 (dd, $J = 7.8, 1.2$ Hz, 1H, HC(23a)), 7.17 (dd, $J = 7.8, 1.2$ Hz, HC(23b)), 6.86 (s, 1H, HC(17)), 6.58 (s, 1H, HC(14)), 4.40 (hept, $J = 6.7$ Hz, 1H, HC(25a)), 3.71 (s, 3H, H₃C(18)), 3.64 (hept, $J = 6.9$ Hz, 1H, HC(25b)), 3.27 (dd, $J = 13.2, 3.6$ Hz, 1H, HC(4)), 3.20 (hept, $J = 6.9$ Hz, 1H, HC(19)), 2.96-2.87 (m, 1H, H₂C(11^{eq})), 2.85-2.76 (m, 1H, H₂C(11^{ax})), 2.25 (dt, $J = 12.9, 3.4$ Hz, 1H, H₂C(6^{eq})), 2.08-2.00 (m, 1H, H₂C(10^{eq})), 1.72 (qd, $J = 12.1, 6.4$ Hz, 1H, H₂C(10^{ax})), 1.59 (qd, $J = 13.3, 3.3$ Hz, 1H, H₂C(5^{ax})), 1.56 (s, 3H, H₃C(2)), 1.47 (dd, $J = 12.0, 1.5$ Hz, 1H, HC(9)), 1.42 (td, $J = 13.3, 3.3$ Hz, 1H, H₂C(6^{ax})), 1.36 (s, 3H, H₃C(1)), 1.30 (d, $J = 6.5$ Hz, 3H, H₃C(26b)), 1.29 (d, $J = 6.5$ Hz, 3H, H₃C(26a)), 1.27 (d, $J = 6.5$ Hz, 3H, H₃C(26b')), 1.23 (d, $J = 6.5$ Hz, 3H, H₃C(26a')), 1.22 (s, 3H, H₃C(8)), 1.18 (d, $J = 7.0$ Hz, 3H, H₃C(20)), 1.19-1.14 (m, 1H, H₂C(5^{eq})), 1.16 (d, $J = 7.0$ Hz, 3H, H₃C(20')).

^{13}C NMR: (126 MHz, CDCl_3)
155.27 (C(15)), 151.85 (C(22a)), 149.69 (C(22b)), 146.63 (C(13)), 136.89 (C(21)), 134.90 (C(16)), 131.67 (HC(24)), 126.92 (HC(23a)), 126.77 (C(12)), 126.65 (HC(17)), 123.40 (HC(23b)), 106.37 (HC(14)), 70.92 (HC(4)), 55.60 ($\text{H}_3\text{C}(18)$), 53.12 (HC(9)), 39.16 (C(3)), 38.51 ($\text{H}_2\text{C}(6)$), 37.59 (C(7)), 30.31 ($\text{H}_2\text{C}(11)$), 30.18 ($\text{H}_3\text{C}(2)$), 29.61 (HC(25b)), 27.76 (HC(25a)), 26.60 (HC(19)), 25.66 ($\text{H}_3\text{C}(26\text{b})$), 25.24 ($\text{H}_3\text{C}(26\text{a})$), 24.74 ($\text{H}_3\text{C}(26\text{a}')$), 24.20 ($\text{H}_3\text{C}(8)$), 22.99 ($\text{H}_3\text{C}(20')$), 22.89 ($\text{H}_3\text{C}(26\text{b}')$), 22.79 ($\text{H}_3\text{C}(20)$), 21.12 ($\text{H}_2\text{C}(5)$), 18.66 ($\text{H}_2\text{C}(10)$), 17.75 ($\text{H}_3\text{C}(1)$).

IR: (neat)
2949 (m), 1614 (w), 1579 (w), 1500 (m), 1459 (m), 1382 (w), 1361 (w), 1328 (w), 1309 (w), 1254 (m), 1234 (m), 1200 (w), 1164 (w), 1119 (w), 1043 (m), 1027 (s), 974 (w), 883 (w), 840 (w), 801 (m), 733 (w), 716 (w), 681 (w), 620 (w), 504 (w), 476 (w).

LRMS: (ESI, $[\text{M}+\text{H}]^+$)
299.1 (16), 300.1 (3), 509.2 (100), 510.2 (36), 511.3 (11), 609.2 (2), 610.3 (5), 611.3 (2), 611.5 (2), 638.3 (12), 639.3 (5), 790.4 (3), 791.4 (2).

Analysis: $\text{C}_{33}\text{H}_{48}\text{O}_2\text{S}$ (508.81)
Calcd: C, 77.90% H, 9.51%
Found: C, 77.80% H, 9.55%

TLC: R_f 0.40 (silica gel, hexanes/diethyl ether, 50:50, UV/CAM)

HPLC: t_R 11.0 min (50%); t_R 13.2 min (50%) (Whelk, hexanes/*i*-PrOH, 95:5, 0.8 mL/min, 220 nm, 24 °C)

Data for (\pm)-7e'' (minor diastereomer):

Note: Some NMR signals are not well resolved at 23 °C, so ^1H and ^{13}C spectra were also collected at -50 °C. Both data sets are reported below.

m.p.: 163–165 °C

^1H NMR: (500 MHz, CDCl_3 , 23 °C)
7.37 (t, $J = 7.7$ Hz, 1H, HC(24)), 7.22 (bs, 2H, HC(23a) and HC(23b)), 6.84 (s, 1H, HC(17)), 6.68 (s, 1H, HC(14)), 4.61 (bs, 1H, HC(25a)), 3.76 (s, 3H,

H₃C(18)), 3.38 (bs, 1H, HC(25b)), 3.21 (hept, $J = 6.9$ Hz, 1H, HC(19)), 2.91 (dd, $J = 16.7, 5.6$ Hz, 1H, H₂C(11^{eq})), 2.82-2.73 (m, 1H, H₂C(11^{ax})), 2.55-2.48 (m, 2H, HC(4) and H₂C(6^{eq})), 2.42 (qd, $J = 13.3, 3.4$ Hz, 1H, H₂C(5^{ax})), 2.12 (dq, $J = 13.5, 3.3$ Hz, 1H, H₂C(5^{eq})), 1.97-1.89 (m, 1H, H₂C(10^{eq})), 1.77 (qd, $J = 12.2, 6.4$ Hz, 1H, H₂C(10^{ax})), 1.51 (td, $J = 13.1, 3.5$ Hz, 1H, H₂C(6^{ax})), 1.40 (dd, $J = 12.0, 1.7$ Hz, 1H, HC(9)), 1.30 (bd, 6H, H₃C(26a) and H₃C(26a')), 1.29 (s, 3H, H₃C(8)), 1.27 (s, 6H, H₃C(1) and H₃C(2)), 1.22 (bd, $J = 5.0$ Hz, 6H, H₃C(26b) and H₃C(26b')), 1.18 (d, $J = 7.0$ Hz, 3H, H₃C(20)), 1.16 (d, $J = 7.0$ Hz, 3H, H₃C(20')).

(600 MHz, CDCl₃, -50 °C)

7.40 (t, $J = 7.7$ Hz, 1H, HC(24)), 7.32 (d, $J = 7.2$ Hz, 1H, HC(23a)), 7.15 (d, $J = 7.2$ Hz, 1H, HC(23b)), 6.89 (s, 1H, HC(17)), 6.68 (s, 1H, HC(14)), 4.55 (hept, $J = 6.5$ Hz, 1H, HC(25a)), 3.76 (s, 3H, H₃C(18)), 3.24 (hept, $J = 6.5$ Hz, 1H, HC(25b)), 3.17 (hept, $J = 6.9$ Hz, 1H, HC(19)), 2.91 (dd, $J = 16.7, 5.6$ Hz, 1H, H₂C(11^{eq})), 2.81-2.71 (m, 1H, H₂C(11^{ax})), 2.56-2.49 (m, 1H, H₂C(6^{eq})), 2.48-2.37 (m, 2H, HC(4) and H₂C(5^{ax})), 2.11-2.02 (m, 1H, H₂C(5^{eq})), 1.94-1.90 (m, 1H, H₂C(10^{eq})), 1.74 (qd, $J = 12.3, 5.7$ Hz, 1H, H₂C(10^{ax})), 1.55-1.44 (m, 1H, H₂C(6^{ax})), 1.41 (d, $J = 11.6$ Hz, 1H, HC(9)), 1.30 (d, 3H, H₃C(26a)), 1.30 (s, 3H, H₃C(2)), 1.28 (s, 3H, H₃C(8)), 1.23 (s, 3H, H₃C(1)), 1.25-1.19 (m, 6H, H₃C(26a') and H₃C(26b)), 1.17 (d, $J = 6.9$ Hz, 3H, H₃C(20)), 1.13 (d, $J = 7.0$ Hz, 3H, H₃C(20')), 1.11 (d, $J = 7.0$ Hz, 3H, H₃C(26b')).

¹³C NMR:

(126 MHz, CDCl₃, 23 °C)

155.33 (C(15)), 146.94 (C(13)), 136.07 (C(21)), 134.79 (C(16)), 131.02 (HC(24)), 126.49 (C(12) and HC(17)), 106.54 (HC(14)), 73.26 (HC(4)), 55.68 (H₃C(18)), 52.86 (HC(9)), 38.82 (H₂C(6) or C(3)), 38.80 (H₂C(6) or C(3)), 37.90 (C(7)), 30.48 (H₃C(2)), 30.21 (H₂C(11)), 26.58 (HC(19)), 24.81 (H₃C(8)), 22.97 (H₃C(20')), 22.80 (H₃C(20)), 19.21 (H₂C(10)), 18.91 (H₃C(1)), 16.81 (H₂C(5)).

(151 MHz, CDCl₃, -50 °C)

154.65 (C(15)), 152.15 (C(22a)), 146.57 (C(22b) and C(13)), 134.76 (C(21)),

134.19 (C(16)), 130.94 (HC(24)), 126.47 (HC(23a)), 126.11 (HC(17) and C(12)), 124.05 (HC(23b)), 105.68 (HC(14)), 72.47 (HC(4)), 55.29 (H₃C(18)), 52.13 (HC(9)), 38.56 (C(3)), 38.14 (H₂C(6)), 37.58 (C(7)), 30.40 (H₃C(2)), 30.08 (H₂C(11)), 28.17 (HC(25b)), 26.65 (HC(25a)), 26.42 (H₃C(26a')), 26.03 (HC(19)), 25.05 (H₃C(26b)), 24.74 (H₃C(8)), 22.96 (H₃C(20')), 22.93 (H₃C(26a)), 22.84 (H₃C(26b')), 22.54 (H₃C(20)), 18.86 (H₂C(10) or H₃C(1)), 18.83 (H₂C(10) or H₃C(1)), 16.07 (H₂C(5)).

IR: (neat)

2964 (m), 1613 (w), 1577 (w), 1498 (s), 1463 (s), 1395 (w), 1373 (m), 1360 (m), 1328 (m), 1254 (m), 1235 (s), 1196 (m), 1166 (w), 1120 (w), 1101 (w), 1078 (s), 1067 (s), 1044 (s), 1000 (w), 969 (m), 892 (m), 880 (w), 844 (m), 800 (s), 768 (w), 745 (s), 618 (w), 573 (w), 540 (m), 477 (m).

LRMS: (ESI, [M+H]⁺)

163.1 (2), 189.1 (2), 203.1 (12), 204.2 (2), 215.1 (4), 229.2 (2), 243.2 (2), 257.2 (8), 258.2 (2), 297.2 (4), 298.2 (3), 299.2 (100), 300.2 (48), 301.2 (8), 313.2 (7), 314.2 (2), 355.2 (4), 491.3 (2), 509.3 (88), 510.4 (41), 511.4 (14), 512.4 (3), 531.3 (3).

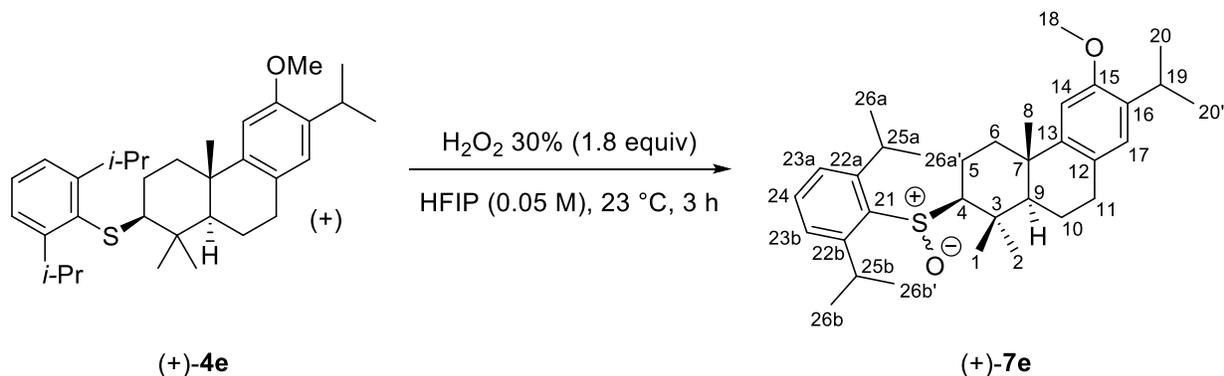
Analysis: C₃₃H₄₈O₂S (508.81)

Calcd: C, 77.90% H, 9.51%

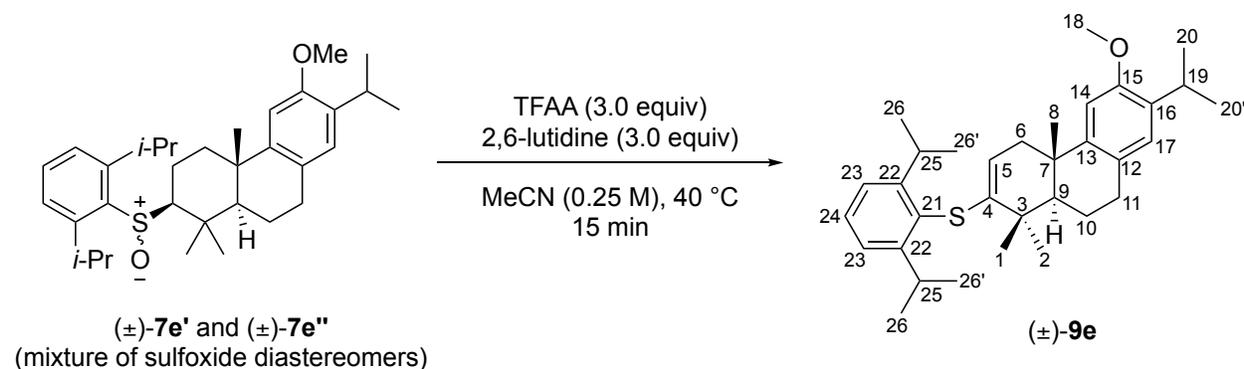
Found: C, 78.03% H, 9.69%

TLC: *R_f* 0.35 (silica gel, hexanes/diethyl ether, 50:50, UV/CAM)

Preparation of (+)- (4*S*,7*S*,9*R*)-4-(2,6-Diisopropylphenylsulfanyl)-16-isopropyl-15-methoxy-3,3,7-trimethyl-3,4,5,6,7,9,10,11-octahydrophenanthrene ((+)-7e)



A 200-mL, round-bottomed flask equipped with a stir bar and argon inlet was charged with sulfide (+)-4e (502.2 mg, 1.02 mmol) and hexafluoroisopropanol (20 mL). The mixture was sonicated for 2 min until a fine, white suspension was observed. Hydrogen peroxide (aq., 30% w/w, 0.19 mL, 0.21 g, 1.8 equiv) was added dropwise at 23 °C. The white suspension was stirred at 25 °C for 2.5 h, over which time the suspension cleared to a nearly colorless solution. Full conversion was observed by TLC (hexanes/EtOAc, 9:1). The reaction was quenched by the addition of sat. aq. sodium thiosulfate (5 mL) and was stirred vigorously for 5 min. The majority of the HFIP was removed by rotary evaporation (30 °C, 15 mmHg). The residue was diluted with water (30 mL) and extracted with CH₂Cl₂ (3 x 30 mL). The combined organic layers were washed with brine (30 mL), dried over sodium sulfate, filtered, and concentrated (30 °C, 15 mmHg) to afford crude (+)-7e as a white foam solid. The product was purified by chromatography (silica gel, 3 cm x 15 cm, dry load on Celite, 25 mL fractions, hexanes/EtOAc gradient elution: 19:1 (500 mL) to 9:1 (500 mL) to 5.67:1 (500 mL) to 4:1 (500 mL)). Since both diastereomers (+)-7e' and (+)-7e'' are competent in the Pummerer rearrangement, the fractions were combined, but prior to pooling the chromatography fractions, a small sample was removed from an early fraction (containing only major diastereomer) for HPLC analysis. After solvent removal, the combined yield of both diastereomers was 545.0 mg (>100%). The product was again chromatographed (silica gel, 3 cm x 15 cm, dry load on Celite, 25 mL fractions, hexanes/Et₂O gradient elution: 9:1 (300 mL) to 4:1 (300 mL) to 2.33:1 (300 mL) to 1.5:1 (300 mL)) to afford 494.3 mg (95%) of (+)-7e as a fluffy white foam solid. The d.r. of the isolated solid was 65:35 (measured by ¹H NMR integration).

Data for (+)-**7e**:d.r.: 65:35 **7e'**:**7e''**HPLC: (measured on major diastereomer (+)-**7e'**)From chromatographed (+)-**4e**: t_R 11.3 min (9%); t_R 13.5 min (91%) (Regis (*R,R*)-Whelk O1, hexanes/*i*-PrOH, 95:5, 0.8 mL/min, 220 nm, 24 °C)From recrystallized (+)-**4e**: t_R 11.3 min (10%); t_R 13.4 min (90%)**Preparation of (±)- (2,6-Diisopropylphenyl) ((7*S*,9*R*)-16-Isopropyl-15-methoxy-3,3,7-trimethyl-3,6,7,9,10,11-hexahydrophenanthren-4-yl) Sulfide ((±)-**9e**)**

A 25-mL, round-bottomed flask equipped with a stir bar was charged with sulfoxide (±)-**7e** (779.7 mg, 1.53 mmol, as a mixture of diastereomers (±)-**7e'** and (±)-**7e''**). Acetonitrile (6.2 mL) was added, resulting in a turbid, pale-yellow solution. To the flask was added 2,6-lutidine (0.54 mL, 493 mg, 4.60 mmol, 3.0 equiv) in one portion, followed by trifluoroacetic anhydride (0.64 mL, 966 mg, 4.60 mmol, 3.0 equiv) in one portion. A darker-yellow solution resulted. The mixture was heated to 45 °C in an oil bath and was maintained at this temperature for 10 min. Over this time, the yellow solution became slightly cloudy, then cleared again, then darkened to yellow-orange. At this point, full conversion was observed by TLC (hexanes/EtOAc, 90:10). The mixture was cooled to 25 °C and was diluted with CH₂Cl₂ (5 mL). The volatiles were removed by rotary evaporation (30 °C, 15 mmHg). The crude residue was directly subjected to chromatography (silica gel, 3 x 25 cm, dry load on Celite, 25-mL fractions, hexanes/CH₂Cl₂ gradient elution: 95:5 (300 mL) to 90:10 (300 mL) to 85:15 (300 mL) to 80:20 (300 mL)) to afford 604.1 mg (80%) of (±)-**9e** as a white solid. To obtain analytically pure material, the solid was dissolved in a minimal amount of boiling abs. ethanol (5 mL) and the solution was cooled in a -20 °C freezer for 12 h. The resulting white precipitate was collected by vacuum filtration and

dried in an Abderhalden (80 °C, 0.1 mmHg) for 12 h to afford 52.3 mg (7%) of (±)-**9e** as a white powder.

Data for (±)-**9e**:

m.p.: 114–116 °C (ethanol)

¹H NMR: (500 MHz, CDCl₃)

7.37 (t, $J = 7.7$ Hz, 1H, HC(24)), 7.22 (d, $J = 7.7$ Hz, 2H, HC(23)), 6.84 (s, 1H, HC(17)), 6.60 (s, 1H, HC(14)), 4.54 (dd, $J = 6.7, 2.1$ Hz, 1H, HC(5)), 3.72 (hept, $J = 6.8$ Hz, 2H, HC(25)), 3.72 (s, 3H, H₃C(18)), 3.20 (hept, $J = 6.9$ Hz, 1H, HC(19)), 2.91-2.82 (m, 1H, H₂C(11^{eq})), 2.81-2.69 (m, 1H, H₂C(11^{ax})), 2.39 (dd, $J = 16.7, 6.7$ Hz, 1H, H₂C(6^{eq})), 2.11-2.00 (m, 1H, H₂C(6^{ax})), 1.95-1.83 (m, 1H, H₂C(10^{eq})), 1.76-1.65 (m, 2H, H₂C(10^{ax}) and HC(9)), 1.39 (s, 3H, H₃C(2)), 1.32 (s, 3H, H₃C(1)), 1.23 (s, 3H, H₃C(8)), 1.22 (d, $J = 7.0$ Hz, 6H, H₃C(26)), 1.20 (d, $J = 6.5$ Hz, 6H, H₃C(26')), 1.19 (d, $J = 7.0$ Hz, 3H, H₃C(20)), 1.16 (d, $J = 6.9$ Hz, 3H, H₃C(20')).

¹³C NMR: (126 MHz, CDCl₃)

155.41 (C(15)), 154.31 (C(22)), 145.47 (C(13)), 144.73 (C(4)), 134.71 (C(16)), 129.74 (HC(24)), 128.79 (C(21)), 127.19 (C(12)), 126.28 (HC(17)), 123.91 (HC(23)), 115.01 (HC(5)), 107.71 (HC(14)), 55.60 (H₃C(18)), 50.45 (HC(9)), 41.40 (H₂C(6)), 39.73 (C(3)), 36.94 (C(7)), 31.71 (HC(25)), 30.91 (H₂C(11)), 30.85 (H₃C(2)), 26.62 (HC(19)), 24.88 (H₃C(8)), 24.51 (H₃C(26) or H₃C(26')), 24.42 (H₃C(26) or H₃C(26')), 23.00 (H₃C(20) or H₃C(20')), 22.80 (H₃C(20) or H₃C(20')), 21.24 (H₃C(1)), 20.89 (H₂C(10)).

IR: (neat)

2958 (s), 2863 (m), 1615 (w), 1576 (w), 1501 (s), 1464 (s), 1406 (w), 1373 (m), 1357 (m), 1323 (m), 1247 (s), 1205 (m), 1166 (m), 1122 (w), 1102 (m), 1073 (m), 1053 (s), 954 (m), 922 (m), 881 (m), 850 (m), 795 (s), 743 (s), 686 (w), 559 (w), 480 (w).

LRMS: (EI, 70 eV)

149.0 (18), 189.1 (54), 201.1 (31), 203.1 (25), 216.2 (49), 217.2 (17), 231.1 (49), 232.1 (10), 259.2 (100), 260.2 (33), 446.1 (26), 490.3 (43), 491.3 (16).

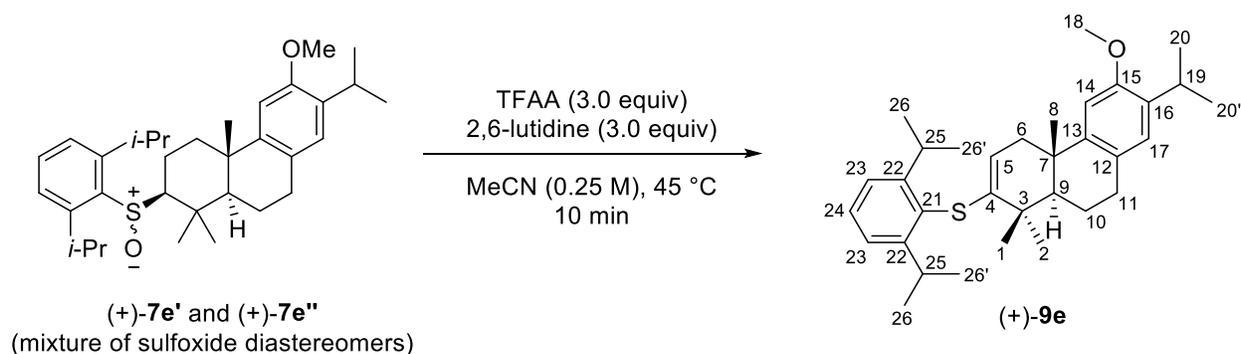
Analysis: C₃₃H₄₆OS (490.79)

Calcd: C, 80.76% H, 9.45%

Found: C, 80.51% H, 9.63%

TLC: R_f 0.19 (silica gel, hexanes/CH₂Cl₂, 90:10, UV/CAM)

Preparation of (+)- (2,6-Diisopropylphenyl) ((7*S*,9*R*)-16-Isopropyl-15-methoxy-3,3,7-trimethyl-3,6,7,9,10,11-hexahydrophenanthren-4-yl) Sulfide ((+)-9e**)**

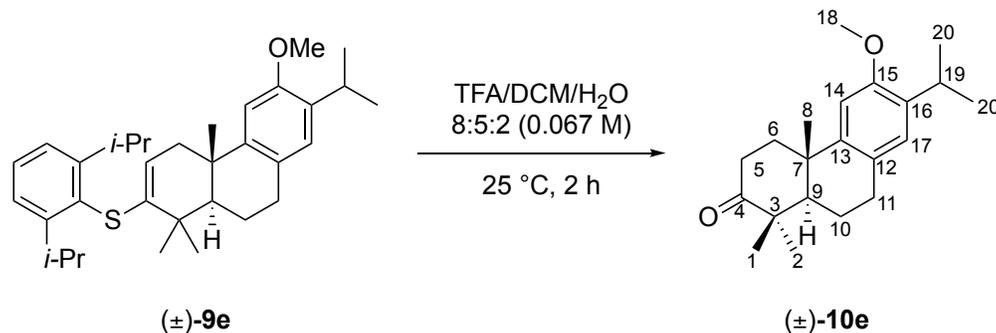


A flame-dried, 10-mL, Schlenk flask equipped with a stir bar was charged with sulfoxide (+)-**7e** (460.3 mg, 0.90 mmol, as a mixture of diastereomers (+)-**7e'** and (+)-**7e''**). Acetonitrile (4.0 mL) was added, resulting in a thin, white suspension. [Note: If needed, the suspension may be sonicated for 1 min to achieve a fine consistency.] To the flask was added 2,6-lutidine (0.32 mL, 291 mg, 2.71 mmol, 3.0 equiv) in one portion at 25 °C resulting in a pale-yellow suspension. Trifluoroacetic anhydride (0.38 mL, 570 mg, 2.71 mmol, 3.0 equiv) was added dropwise over 30 sec at 25 °C resulting in a bright-yellow suspension. Some thick, white vapor was observed in the headspace of the flask. The mixture was heated to 45 °C (pre-warmed oil bath) and was maintained at this temperature for 10 min. Within 1 min, a yellow solution was observed, which reverted to a thin, yellow suspension over time. Full conversion was observed by TLC (hexanes/EtOAc, 90:10). The mixture was cooled to 25 °C and transferred to a 100-mL recovery flask with CH₂Cl₂ (10 mL). The volatiles were removed by rotary evaporation (30 °C, 15 mmHg). The crude residue was directly subjected to chromatography (silica gel, 3 x 20 cm, dry load on Celite, 25-mL fractions, hexanes/CH₂Cl₂ gradient elution: 95:5 (300 mL) to 90:10 (300 mL) to 85:15 (300 mL) to 80:20 (300 mL)) to afford 415.6 mg (94%) of (+)-**9e** as a white solid. Spectroscopic data matched those reported for (±)-**9e**.

Data for (+)-**9e**:

Opt. Rot.: $[\alpha]_D + (c = 1.04 \text{ in } \text{CHCl}_3)$

Preparation of (\pm)-(**7S,9R**)-16-Isopropyl-15-methoxy-3,3,7-trimethyl-5,6,7,9,10,11-hexahydrophenanthren-4(**1H**)-one (\pm)-**10e**



A 50-mL, round-bottomed flask equipped with a stir bar was charged with vinyl sulfide (\pm)-**9e** (371.4 mg, 0.76 mmol) and CH_2Cl_2 (3.75 mL). Water (1.5 mL) and trifluoroacetic acid (6.0 mL) were added to the flask. The resulting, pink, biphasic mixture was stirred vigorously at 25 °C for 2 h. The mixture darkened to red-purple and full conversion was observed by TLC (hexanes/EtOAc, 80:20). [**Note:** Careful inspection of the TLC plate is required, as the 2,6-diisopropylthiophenol byproduct has nearly the same R_f value as (\pm)-**9e**.] The reaction was quenched by adding the mixture dropwise into a 250-mL Erlenmeyer flask containing sat. aq. NaHCO_3 (150 mL) cooled in an ice bath. Gas evolution was observed, and the red color disappeared. Additional CH_2Cl_2 (50 mL) was added to the flask, and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (2 x 50 mL), and the combined organic layers were washed with brine (50 mL), dried over Na_2SO_4 , filtered, and concentrated (30 °C, 15 mmHg) to afford 391.0 mg of crude (\pm)-**10e**. The product was purified by chromatography (silica gel, 3 x 20 cm, dry load on Celite, 25-mL fractions, hexanes/EtOAc gradient elution: 95:5 (300 mL) to 90:10 (300 mL) to 85:15 (300 mL) to 80:20 (300 mL)) to afford 220.7 mg (93%) of (\pm)-**10e** as a white solid, which is sufficiently pure to carry forward. To obtain analytically pure material, the product was dissolved in a minimal amount of boiling hexanes (approx. 4 mL) and the solution was cooled to 25 °C followed by 12 h in a -20 °C freezer. The product was collected by vacuum filtration and was rinsed with ice-cold hexanes to afford 163.2 mg (69%) of (\pm)-**10e** as colorless, cubic crystals.

Data for (±)-10e:

m.p.: 132–133 °C (hexanes)

¹H NMR: (500 MHz, CDCl₃)

6.87 (s, 1H, HC(17)), 6.69 (s, 1H, HC(14)), 3.80 (s, 3H, H₃C(18)), 3.23 (hept, *J* = 6.9 Hz, 1H, HC(19)), 2.90 (ddd, *J* = 16.5, 5.7, 1.9 Hz, 1H, H₂C(11^{eq})), 2.85-2.75 (m, 1H, H₂C(11^{ax})), 2.69 (ddd, *J* = 15.8, 9.8, 7.6 Hz, 1H, H₂C(5^{ax})), 2.60 (ddd, *J* = 15.8, 7.8, 4.2 Hz, 1H, H₂C(5^{eq})), 2.46 (ddd, *J* = 12.9, 7.6, 4.2 Hz, 1H, H₂C(6^{eq})), 2.05-1.95 (m, 1H, H₂C(6^{ax})), 1.92 (dd, *J* = 12.0, 2.5 Hz, 1H, HC(9)), 1.86-1.80 (m, 1H, H₂C(10^{eq})), 1.79-1.69 (m, 1H, H₂C(10^{ax})), 1.31 (s, 3H, H₃C(8)), 1.20 (d, *J* = 6.9 Hz, 3H, H₃C(20)), 1.18 (d, *J* = 6.9 Hz, 3H, H₃C(20')), 1.17 (s, 3H, H₃C(2)), 1.14 (s, 3H, H₃C(1)).

¹³C NMR: (126 MHz, CDCl₃)

217.55 (C(4)), 155.44 (C(15)), 145.33 (C(13)), 135.17 (C(16)), 126.73 (C(12)), 126.57 (HC(17)), 107.38 (HC(14)), 55.72 (H₃C(18)), 50.78 (HC(9)), 47.49 (C(3)), 37.75 (H₂C(6)), 37.54 (C(7)), 34.79 (H₂C(5)), 30.36 (H₂C(11)), 27.14 (H₃C(2)), 26.63 (HC(19)), 24.78 (H₃C(8)), 22.97 (H₃C(20) or H₃C(20')), 22.80 (H₃C(20) or H₃C(20')), 21.20 (H₃C(1)), 20.57 (H₂C(10)).

IR: (neat)

2932 (m), 2848 (w), 1699 (s), 1613 (w), 1502 (s), 1458 (m), 1442 (m), 1407 (m), 1384 (m), 1362 (m), 1322 (m), 1310 (m), 1247 (s), 1233 (m), 1206 (m), 1193 (m), 1163 (m), 1122 (m), 1099 (m), 1076 (w), 1058 (m), 1046 (s), 1013 (w), 969 (w), 926 (w), 888 (m), 866 (m), 763 (m), 706 (w), 580 (w).

LRMS: (EI, 70 eV)

125.1 (9), 201.1 (9), 213.1 (18), 215.1 (9), 257.2 (25), 299.2 (70), 300.2 (15), 314.2 (100), 315.2 (24).

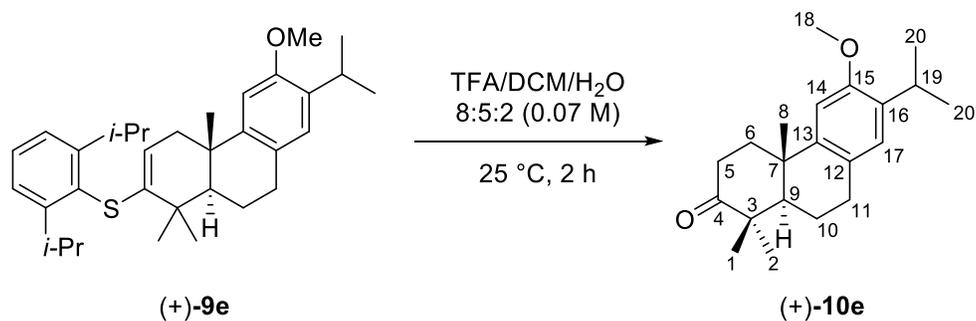
Analysis: C₂₁H₃₀O₂ (314.47)

Calcd: C, 80.21% H, 9.62%

Found: C, 80.13% H, 9.74%

TLC: *R_f* 0.38 (silica gel, hexanes/EtOAc, 80:20, UV/CAM)

Preparation of (+)-(7S,9R)-16-Isopropyl-15-methoxy-3,3,7-trimethyl-5,6,7,9,10,11-hexahydrophenanthren-4(1H)-one ((+)-10e)

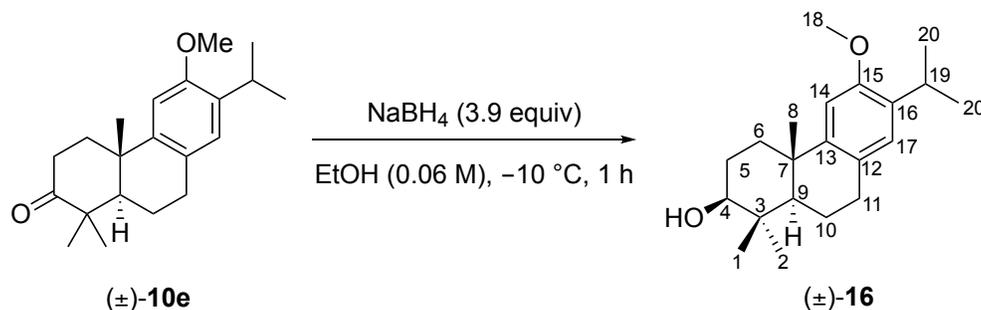


A 50-mL, round-bottomed flask equipped with a stir bar was charged with vinyl sulfide (+)-**9e** (380.3 mg, 0.77 mmol) and CH_2Cl_2 (3.75 mL). Water (1.5 mL) and trifluoroacetic acid (6.0 mL) were added to the flask. The resulting, yellow-pink, biphasic mixture was stirred vigorously at 25 °C for 2 h. Within 30 min, a pink-red homogeneous solution was observed. After 2 h, full conversion was observed by TLC (hexanes/EtOAc, 80:20). [Note: Careful inspection of the TLC plate is required, as the 2,6-diisopropylthiophenol byproduct has nearly the same R_f value as (+)-**9e**.] The reaction was quenched by adding the mixture dropwise into a 250-mL Erlenmeyer flask containing sat. aq. NaHCO_3 (150 mL) cooled in an ice bath. Gas evolution was observed, and the pink color disappeared. Additional CH_2Cl_2 (50 mL) was added to the flask, and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (2 x 50 mL), and the combined organic layers were washed with brine (50 mL), dried over Na_2SO_4 , filtered, and concentrated (30 °C, 15 mmHg) to afford crude (+)-**10e**. The product was purified by chromatography (silica gel, 3 x 20 cm, dry load on Celite, 25-mL fractions, hexanes/EtOAc gradient elution: 95:5 (300 mL) to 90:10 (300 mL) to 85:15 (300 mL) to 80:20 (300 mL)) to afford 225.4 mg (93%) of (+)-**10e** as a white solid. Spectroscopic data matched those reported for (\pm)-**10e**.

Data for (+)-10e:

Opt. Rot.: $[\alpha]_{\text{D}} +97.1$ ($c = 1.23$ in CHCl_3) (80% ee)

Preparation of (±)- (4*S*,7*S*,9*R*)-16-Isopropyl-15-methoxy-3,3,7-trimethyl-3,4,5,6,7,9,10,11-octahydrophenanthren-4-ol ((±)-16)



A 20-mL, round-bottomed flask equipped with a stir bar and argon inlet adapter was charged with ketone (±)-10e (117.5 mg, 0.37 mmol) and absolute ethanol (6 mL). The resulting thin, white suspension was cooled to $-10\text{ }^\circ\text{C}$ using an ice/salt bath. Sodium borohydride (55.4 mg, 1.46 mmol, 3.9 equiv) was added in one portion as a solid. The suspension was stirred at $-10\text{ }^\circ\text{C}$ for 1 h. A clear, colorless solution ultimately resulted. Full conversion was observed by TLC (hexanes/EtOAc, 80:20). The reaction was quenched by pouring the mixture into sat. aq. NH_4Cl (20 mL). Most of the ethanol was removed by rotary evaporation ($35\text{ }^\circ\text{C}$, 15 mmHg), and the residual aqueous phase was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine (20 mL) and then dried over sodium sulfate, filtered, and concentrated ($35\text{ }^\circ\text{C}$, 15 mmHg) to afford crude (±)-16. The product was purified by column chromatography (silica gel, 2 x 24 cm, dry load on Celite, 25-mL fractions, hexanes/EtOAc gradient elution, 95:5 (200 mL) to 90:10 (200 mL) to 85:15 (200 mL) to 80:20 (200 mL) to 75:25 (200 mL)) to afford 84.0 mg (71%) of (±)-16 in sufficient purity for the next step. To obtain analytically pure material, a portion of the product was chromatographed a second time (silica gel, 2 x 24 cm, dry load on Celite, 25-mL fractions, hexanes/EtOAc gradient elution, 95:5 (200 mL) to 90:10 (200 mL) to 85:15 (200 mL) to 80:20 (200 mL) to 75:25 (200 mL)) and dried in an Abderhalden ($80\text{ }^\circ\text{C}$, 0.1 mmHg, 8 h) to afford 43.5 mg (37%) of (±)-16 as a white solid.

Data for (±)-16:

- m.p.: 118–119 $^\circ\text{C}$ (ethyl acetate/hexanes)
- $^1\text{H NMR}$: (500 MHz, CDCl_3)
 6.85 (s, 1H, HC(17)), 6.70 (s, 1H, HC(14)), 3.79 (s, 3H, $\text{H}_3\text{C}(18)$), 3.34–3.27 (m, 1H, HC(4)), 3.22 (hept, $J = 6.9\text{ Hz}$, 1H, HC(19)), 2.95–2.85 (m, 1H, $\text{H}_2\text{C}(11^{\text{eq}})$), 2.84–2.73 (m, 1H, $\text{H}_2\text{C}(11^{\text{ax}})$), 2.29 (dt, $J = 13.0, 3.5\text{ Hz}$, 1H, $\text{H}_2\text{C}(6^{\text{eq}})$), 1.92–1.86

(m, 1H, H₂C(10^{eq})), 1.86-1.81 (m, 1H, H₂C(5^{ax})), 1.81-1.76 (m, 1H, H₂C(5^{eq})), 1.76-1.67 (m, 1H, H₂C(10^{ax})), 1.58 (td, $J = 13.0, 4.5$ Hz, 1H, H₂C(6^{ax})), 1.37 (d, $J = 5.9$ Hz, 1H, OH), 1.33 (dd, $J = 12.3, 2.1$ Hz, 1H, HC(9)), 1.21 (s, 3H, H₃C(8)), 1.19 (d, $J = 6.9$ Hz, 3H, H₃C(20)), 1.17 (d $J = 6.9$ Hz, 3H, H₃C(20')), 1.07 (s, 3H, H₃C(2)), 0.90 (s, 3H, H₃C(1)).

¹³C NMR: (126 MHz, CDCl₃)
155.23 (C(15)), 147.37 (C(13)), 134.63 (C(16)), 126.82 (C(12)), 126.52 (HC(17)), 106.68 (HC(14)), 78.91 (HC(4)), 55.72 (H₃C(18)), 50.06 (HC(9)), 39.15 (C(3)), 37.80 (C(7)), 37.19 (H₂C(6)), 30.24 (H₂C(11)), 28.33 (H₃C(2)), 28.19 (H₂C(5)), 26.60 (HC(19)), 24.99 (H₃C(8)), 23.03 (H₃C(20) or H₃C(20')), 22.82 (H₃C(20) or H₃C(20')), 19.17 (H₂C(10)), 15.54 (H₃C(1)).

IR: (neat)
3500 (wb), 2944 (m), 2868 (m), 2834 (w), 1613 (w), 1571 (w), 1498 (m), 1464 (m), 1403 (m), 1370 (m), 1359 (m), 1339 (w), 1323 (w), 1305 (w), 1250 (m), 1192 (m), 1164 (m), 1118 (w), 1076 (m), 1054 (w), 1028 (s), 1005 (m), 968 (m), 936 (m), 888 (m), 848 (m), 810 (w), 761 (m), 716 (w), 686 (w), 611 (w), 559 (w), 499 (w), 479 (m).

LRMS: (EI, 70 eV)
161.1 (13), 163.1 (13), 173.1 (11), 189.1 (15), 201.1 (14), 213.1 (17), 215.1 (17), 229.2 (15), 241.2 (19), 283.2 (64), 284.2 (14), 301.2 (42), 302.2 (10), 316.2 (100), 317.2 (37).

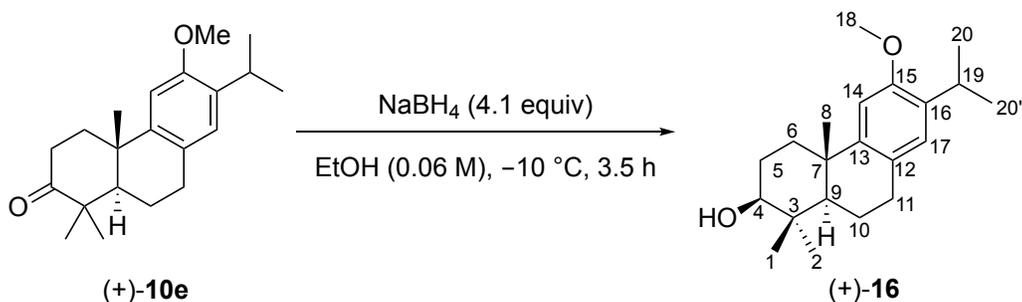
Analysis: C₂₁H₃₂O₂ (316.48)

Calcd: C, 79.70% H, 10.19%

Found: C, 79.35% H, 10.11%

TLC: R_f 0.14 (silica gel, hexanes/EtOAc, 80:20, UV/CAM)

Preparation of (+)-(4*S*,7*S*,9*R*)-16-Isopropyl-15-methoxy-3,3,7-trimethyl-3,4,5,6,7,9,10,11-octahydrophenanthren-4-ol ((+)-16)

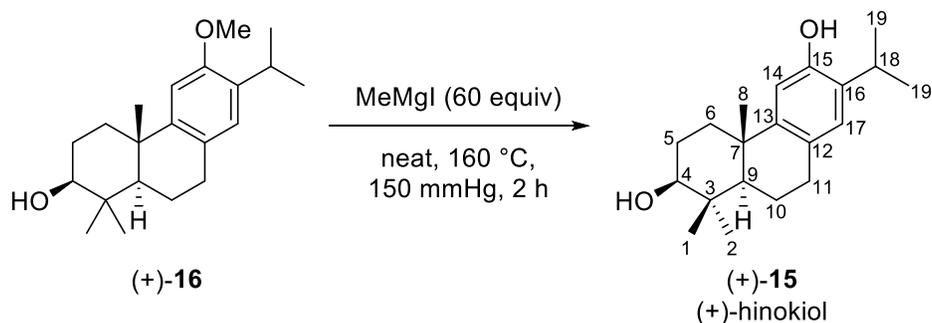


A flame-dried, 50-mL, round-bottomed flask equipped with a stir bar and argon inlet adapter was charged with ketone (+)-10e (190.1 mg, 0.60 mmol) and absolute ethanol (10 mL). The resulting white suspension was cooled to $-10\text{ }^\circ\text{C}$ using an ice/salt bath. Sodium borohydride (94.1 mg, 2.49 mmol, 4.1 equiv) was added in three portions within 1 min at $-10\text{ }^\circ\text{C}$. The reaction was stirred for 3.5 h at $-10\text{ }^\circ\text{C}$ under argon, over which time a clear, colorless solution resulted. Full conversion was observed by TLC (hexanes/EtOAc, 80:20). The reaction was quenched by the *cautious*, dropwise addition of sat. aq. NH_4Cl (10 mL). Ethanol was removed by rotary evaporation ($35\text{ }^\circ\text{C}$, 15 mmHg), and the remaining aqueous phase was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were washed with brine (25 mL) and then dried over sodium sulfate, filtered, and concentrated ($30\text{ }^\circ\text{C}$, 15 mmHg) to afford crude (+)-16 (0.19 g) as a white foam solid (d.r. = 93:7, determined from analysis of the crude ^1H NMR spectrum). The product was purified by column chromatography (silica gel, 2 x 22 cm, dry load on Celite, 10-mL fractions, hexanes/EtOAc gradient elution: 95:5 (200 mL) to 90:10 (200 mL) to 85:15 (200 mL) to 80:20 (200 mL) to 75:25 (200 mL)) to afford 168.3 mg (88%) of (+)-16 as a white solid (single diastereomer).

Data for (+)-16:

Opt. Rot.: $[\alpha]_{\text{D}} + 47.5$ ($c = 1.00$ in CHCl_3)

Preparation of (+)-Hinokiol, (+)-(4*S*,7*S*,9*R*)-16-Isopropyl-3,3,7-trimethyl-3,4,5,6,7,9,10,11-octahydrophenanthrene-4,15-diol ((+)-15)



A solution of methylmagnesium iodide in diethyl ether was prepared in the following manner.²⁶ A flame-dried, three-necked, 250-mL round-bottomed flask equipped with a stir bar, addition funnel, argon inlet adapter, temperature probe, and septum was charged with magnesium turnings (0.86 g, 35.3 mmol) and diethyl ether (50 mL). The turnings were mechanically activated immediately before use by grinding with a mortar and pestle for 10 min. The addition funnel was charged with a solution of methyl iodide (2.20 mL) in diethyl ether (15 mL). A portion of this solution (2 mL) was added quickly to the reaction flask, with rapid stirring. The mixture was brought just to the boiling point (40 °C) using a heat gun. The remaining methyl iodide solution was added dropwise over 15 min (the mixture maintained a gentle reflux without external heating, indicating that initiation had occurred). The resulting turbid, grey mixture was stirred for 1 h (without external heat input). The reagent was titrated (0.48 M; expected 0.54 M) as previously described (pp. *S4–S5*). [**Note:** In this case, the Grignard-phenanthroline complex turns only a light purple color even after stirring for several minutes (as opposed to the typical dark purple). For this reason, the yellow endpoint is more difficult to discern, but the cessation of methane gas generation also indicates that the endpoint has been reached.] The reagent may be stored in a Schlenk bottle for several weeks at 25 °C with no appreciable decrease in concentration.

A flame-dried, 20-mL, Schlenk flask equipped with a stir bar was attached via a three-way valve to both the Schlenk manifold and a diaphragm pump with programmable pressure control. The flask was charged with compound (+)-16 (84.5 mg, 0.27 mmol), evacuated, and placed under argon. Methylmagnesium iodide (0.48 M solution in diethyl ether, 33 mL, 16.0 mmol, 60 equiv) was added portionwise to the flask in the following manner. Approx. 10 mL of the reagent was added to the flask through the septum. Mild bubbling was observed upon contact

with (+)-**16**. The three-way valve was opened to the diaphragm pump, and the solution was concentrated to remove most of the diethyl ether. The pressure should be decreased slowly (760 mmHg to 150 mmHg over 15 min) and a rapid stir rate should be maintained in order to avoid excessive bumping of the solution. The flask was placed under argon, an additional portion of Grignard reagent (approx. 10 mL) was added, and this process was repeated until a total of 33 mL of (concentrated) reagent had been dispensed into the reaction flask. The resulting viscous, yellow mixture was heated under vacuum (160 °C, 150 mmHg) for 2 h. The mixture was allowed to cool to 25 °C and the pale, yellow solid was transferred to a 250-mL Erlenmeyer flask. This was accomplished by adding diethyl ether (10 mL) to the flask, sonicating for 5 min, transferring the resulting milky, white suspension to the Erlenmeyer flask, and repeating this process until all of the reaction mixture had been transferred. The suspension was cooled to 0 °C and quenched by the cautious addition of water (50 mL). The resulting biphasic mixture was acidified with 1 M HCl and transferred to a 250-mL separatory funnel. The layers were separated, and the aqueous phase was extracted with diethyl ether (3 x 50 mL). The combined organic layers were washed with brine (50 mL), and then dried over sodium sulfate, filtered, and concentrated to afford 280.4 mg of crude (+)-**15** as a white, oily solid. The product was purified by column chromatography (silica gel, 2 x 20 cm, dry load on Celite, 10-mL fractions, hexanes/EtOAc gradient elution, 90:10 (200 mL) to 80:20 (200 mL) to 70:30 (200 mL) to 60:40 (200 mL) to 50:50 (200 mL)) to afford 70.5 mg (85%) of (+)-**15** as a white solid. The compound contains 3% EtOAc by mass which cannot be purged even after extended drying times (90 °C, 0.1 mmHg, 24 h). Spectroscopic data for (+)-**15** matched those previously reported.²⁵ The compound is only sparingly soluble in CDCl₃, so the spectral data in DMSO-*d*₆ are also provided.

Data for (+)-**15**:

¹H NMR: (500 MHz, CDCl₃)

6.84 (s, 1H, HC(17)), 6.61 (s, 1H, HC(14)), 4.48 (s, 1H, phenolic OH), 3.29 (dd, *J* = 11.4, 4.8 Hz, 1H, HC(4)), 3.10 (hept, *J* = 6.9 Hz, 1H, HC(18)), 2.94-2.84 (m, 1H, H₂C(11^{eq})), 2.83-2.71 (m, 1H, H₂C(11^{ax})), 2.20 (dt, *J* = 13.0, 3.5 Hz, 1H, H₂C(6^{eq})), 1.88 (ddt, *J* = 13.1, 7.3, 1.8 Hz, 1H, H₂C(10^{eq})), 1.84-1.79 (m, 1H, H₂C(5^{ax})), 1.79-1.74 (m, 1H, H₂C(5^{eq})), 1.74-1.67 (m, 1H, H₂C(10^{ax})), 1.54 (td, *J* = 12.9, 4.3 Hz, 1H, H₂C(6^{ax})), 1.36 (bs, 1H, 2° OH), 1.31 (dd, *J* = 12.3, 2.2 Hz,

1H, HC(9)), 1.24 (d, $J = 6.9$ Hz, 3H, H₃C(19)), 1.22 (d, $J = 6.9$ Hz, 3H, H₃C(19')), 1.18 (s, 3H, H₃C(8)), 1.06 (s, 3H, H₃C(2)), 0.89 (s, 3H, H₃C(1)).

(500 MHz, DMSO-*d*₆)

8.75 (s, 1H, phenolic OH), 6.69 (s, 1H, HC(17)), 6.61 (s, 1H, HC(14)), 4.40 (d, $J = 5.1$ Hz, 1H, 2° OH), 3.15-3.00 (m, 2H, HC(18) and HC(4)), 2.76 (dd, $J = 16.5, 5.8$ Hz, 1H, H₂C(11^{eq})), 2.70-2.58 (m, 1H, H₂C(11^{ax})), 2.07 (dt, $J = 12.8, 3.1$ Hz, 1H, H₂C(6^{eq})), 1.82-1.72 (m, 1H, H₂C(10^{eq})), 1.69-1.54 (m, 3H, H₂C(5) and H₂C(10^{ax})), 1.41-1.30 (m, 1H, H₂C(6^{ax})), 1.15 (dd, $J = 12.1, 2.0$ Hz, 1H, HC(9)), 1.11 (d, $J = 7.0$ Hz, 3H, H₃C(19)), 1.09 (d, $J = 7.0$ Hz, 3H, H₃C(19')), 1.07 (s, 3H, H₃C(8)), 0.96 (s, 3H, H₃C(2)), 0.76 (s, 3H, H₃C(1)).

¹³C NMR: (126 MHz, CDCl₃)

150.90 (C(15)), 147.96 (C(13)), 131.84 (C(16)), 127.25 (C(12)), 126.76 (HC(17)), 111.16 (HC(14)), 78.90 (HC(4)), 49.92 (HC(9)), 39.13 (C(3)), 37.47 (C(7)), 37.13 (H₂C(6)), 30.16 (H₂C(11)), 28.31 (H₃C(2)), 28.16 (H₂C(5)), 26.97 (HC(18)), 24.98 (H₃C(8)), 22.88 (H₃C(19')), 22.69 (H₃C(19)), 19.17 (H₂C(10)), 15.53 (H₃C(1)).

(126 MHz, DMSO-*d*₆)

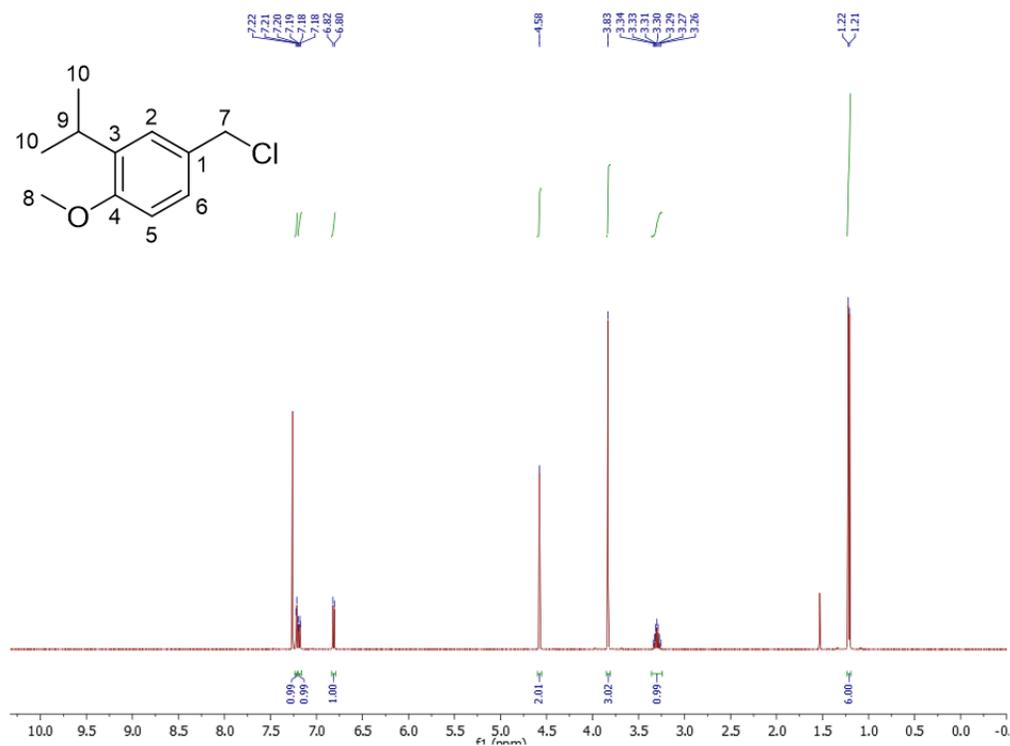
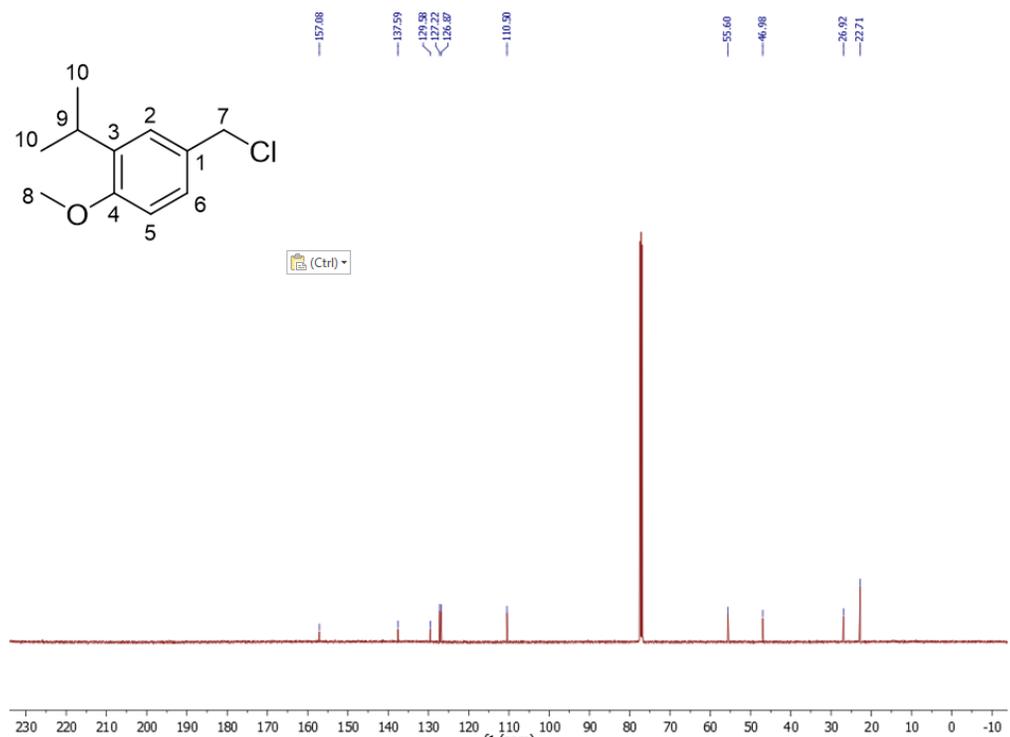
152.12 (C(15)), 147.15 (C(13)), 131.46 (C(16)), 125.76 (HC(17)), 124.50 (C(12)), 110.38 (HC(14)), 76.60 (HC(4)), 49.59 (HC(9)), 38.60 (C(3)), 36.81 (H₂C(6)), 29.63 (H₂C(11)), 28.25 (H₃C(2)), 27.83 (H₂C(5)), 26.06 (HC(18)), 24.78 (H₃C(8)), 22.65 (H₃C(19')), 22.50 (H₃C(19)), 18.74 (H₂C(10)), 15.78 (H₃C(1)).

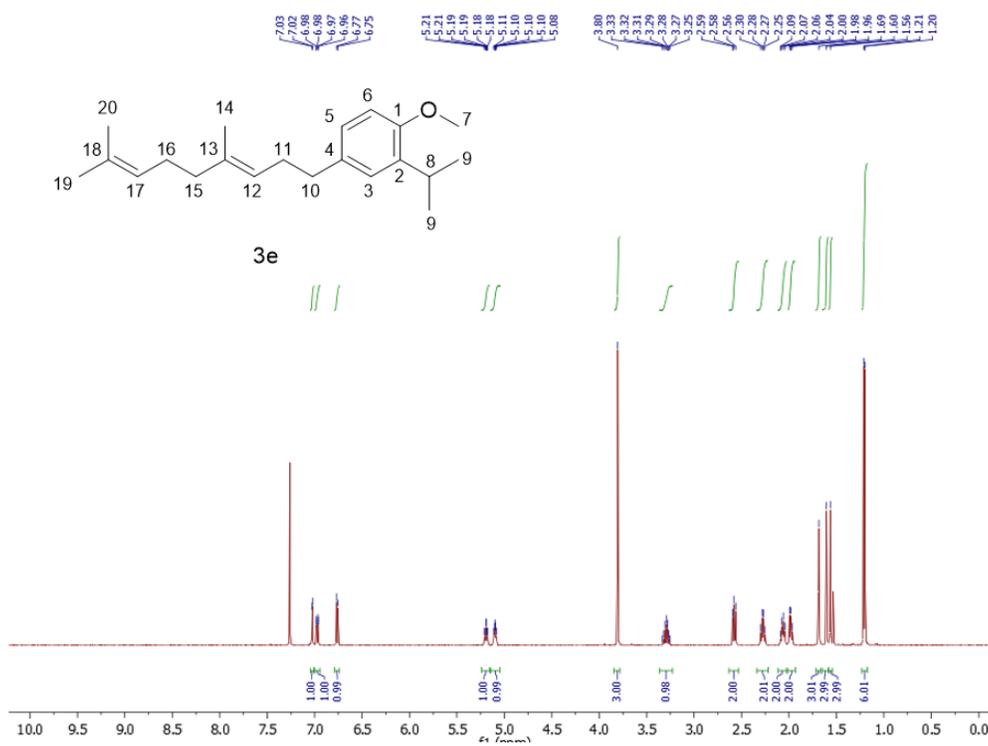
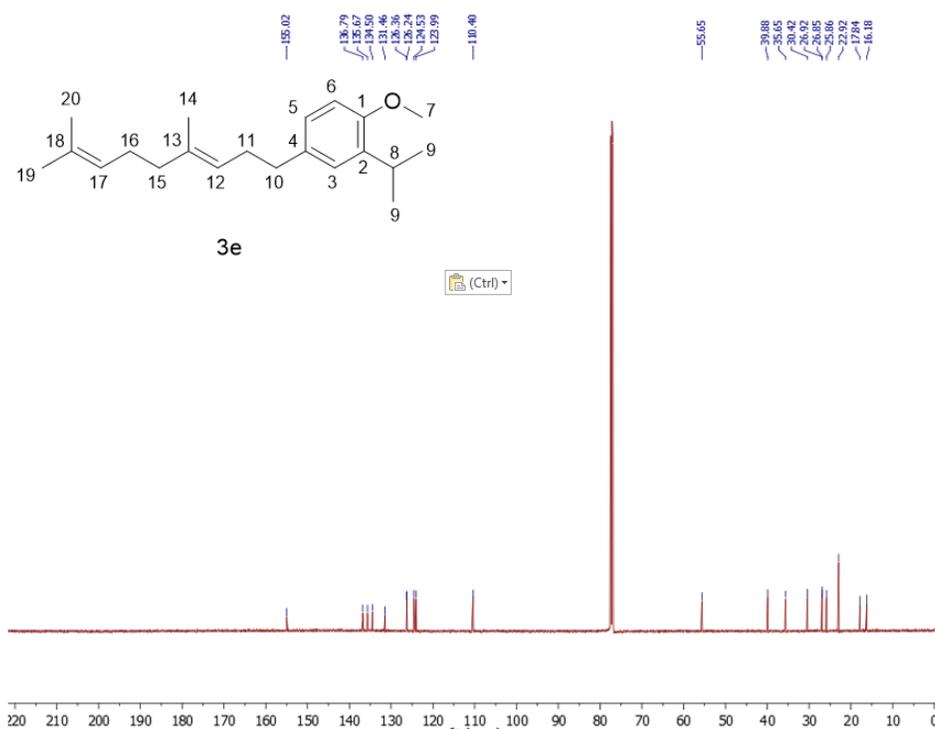
Opt. Rot.: $[\alpha]_{\text{D}}^{25} +47.9$ ($c = 0.92$ in 95% EtOH) (80% ee)

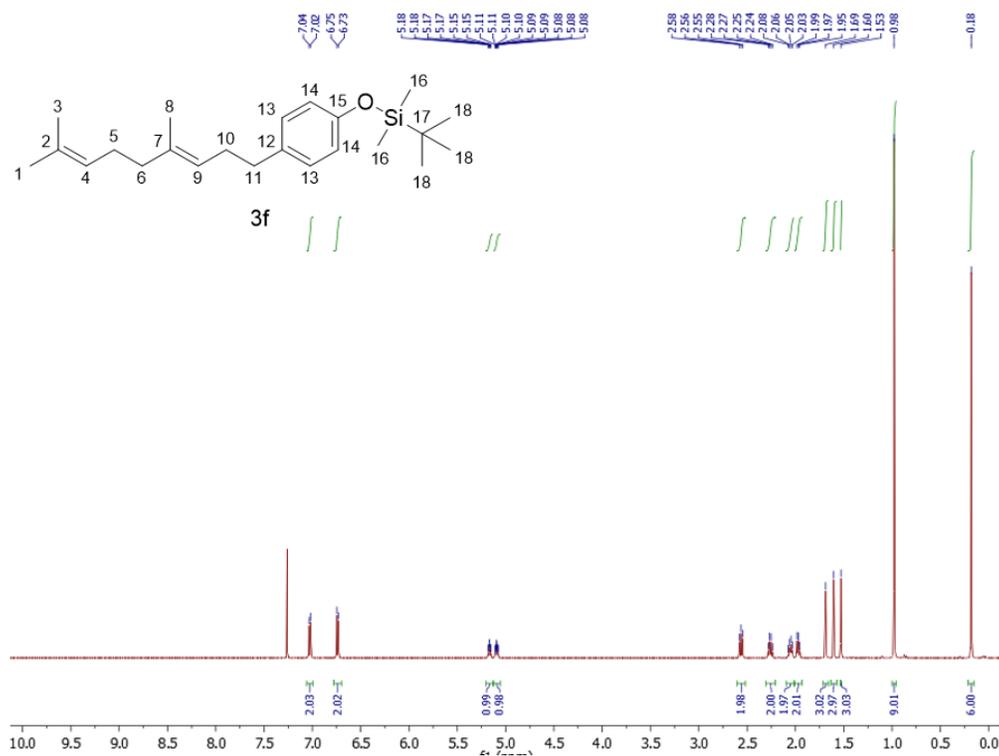
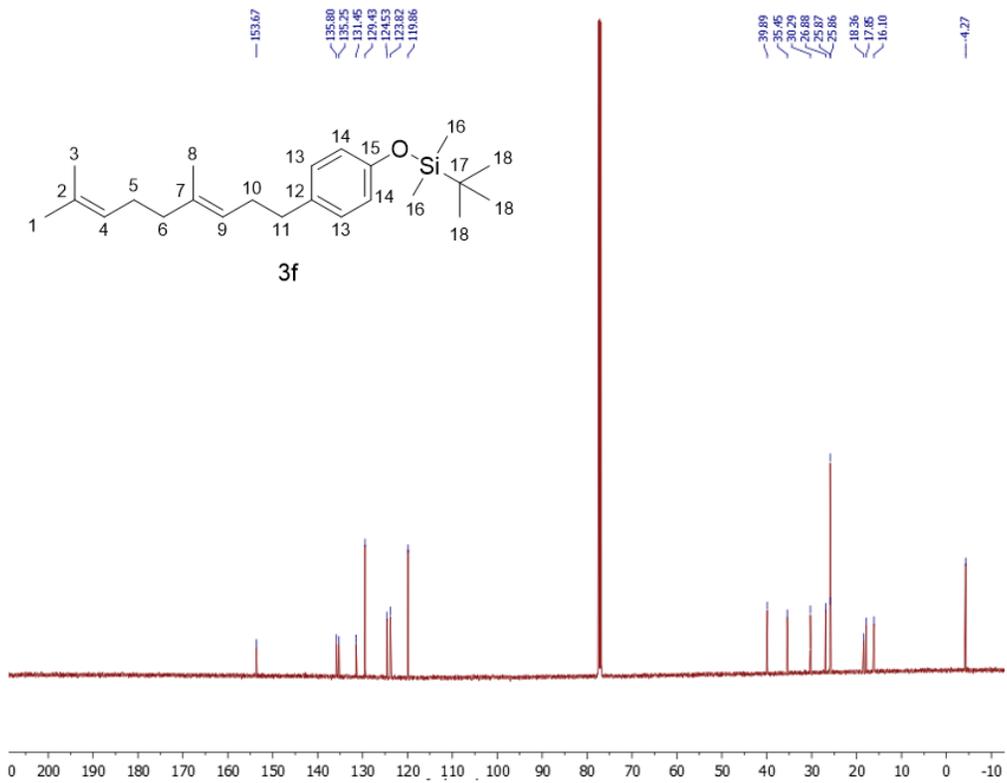
References

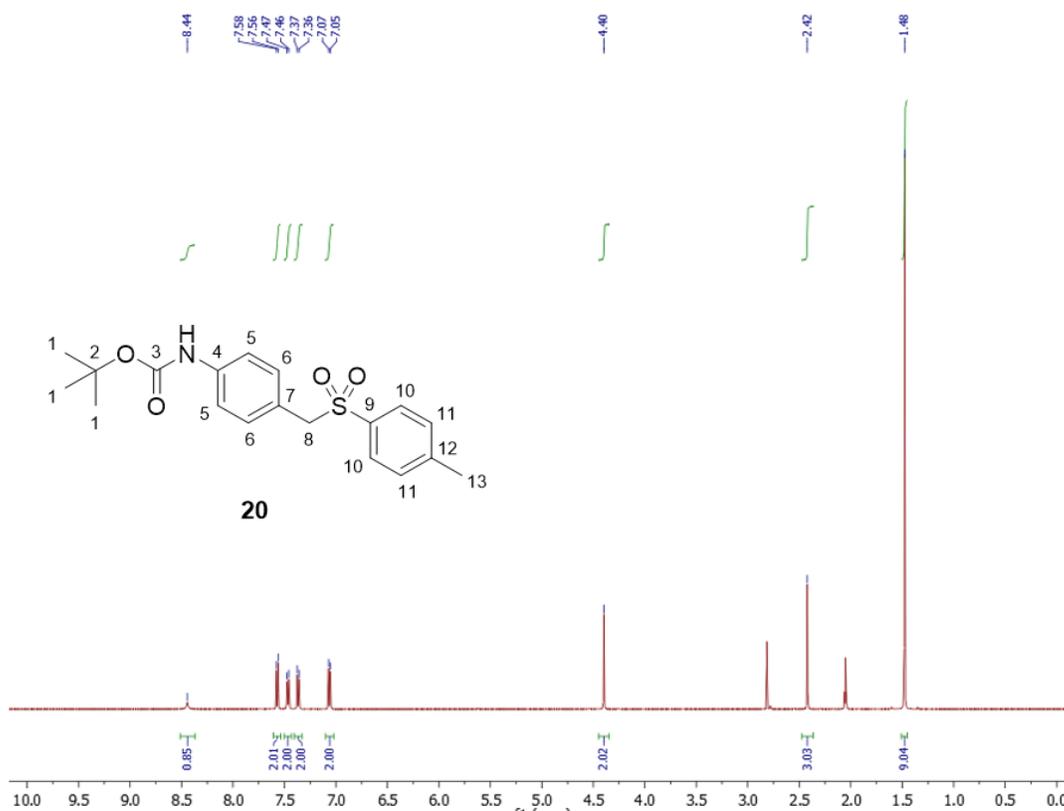
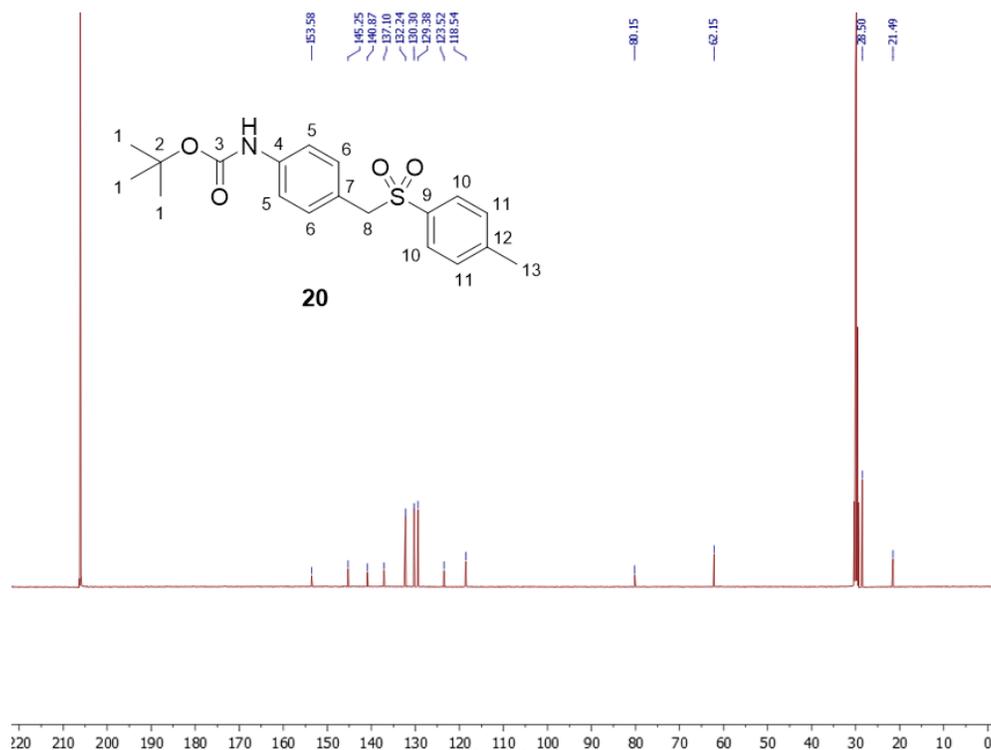
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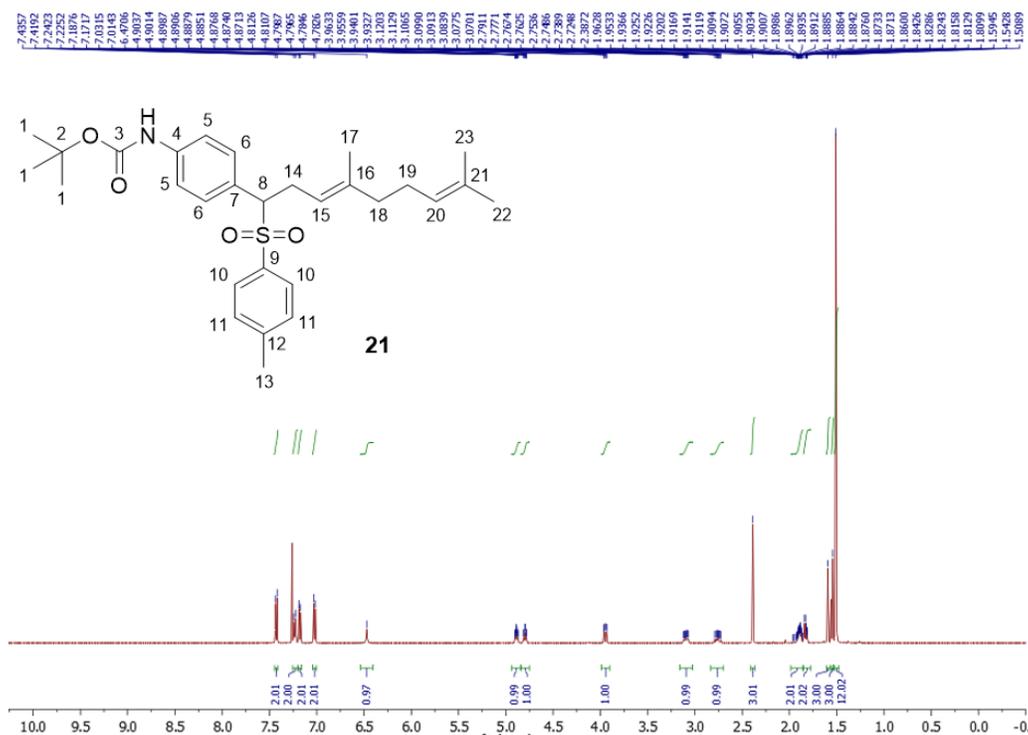
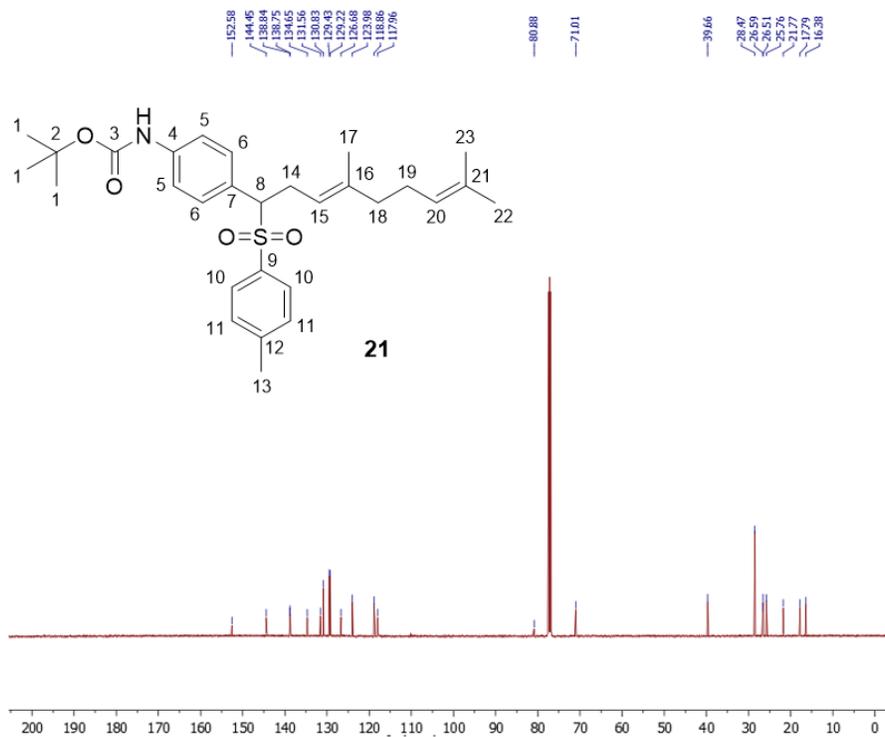
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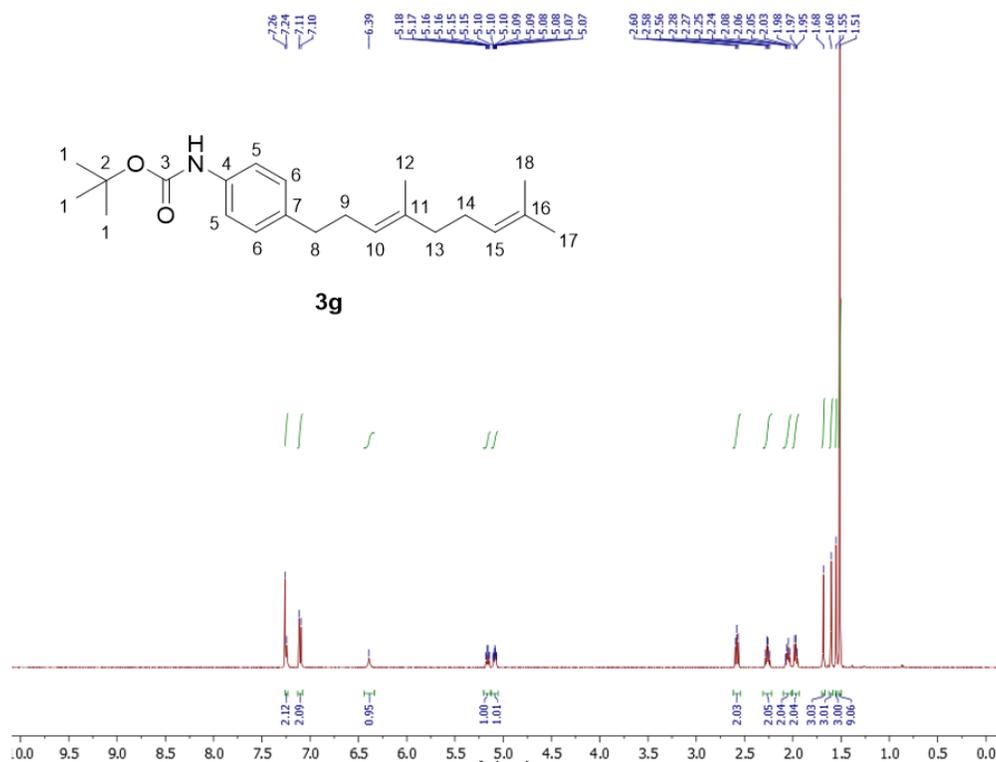
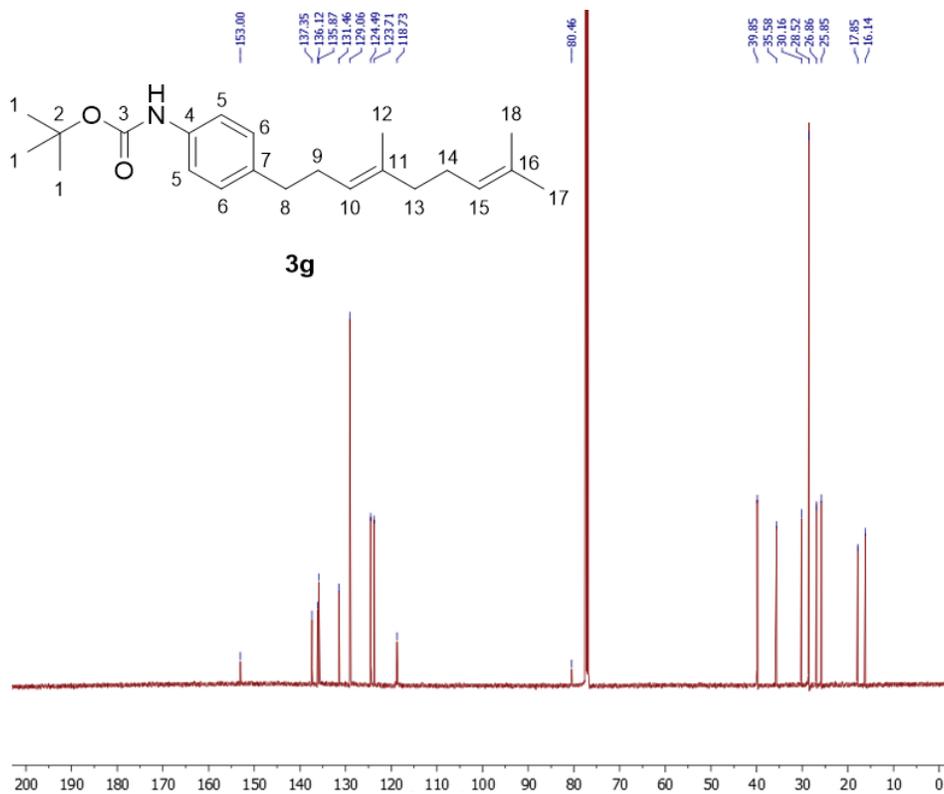
NMR Spectra and CSP-HPLC Traces**18** ^1H NMR (500 MHz, CDCl_3)**18** ^{13}C NMR (126 MHz, CDCl_3)

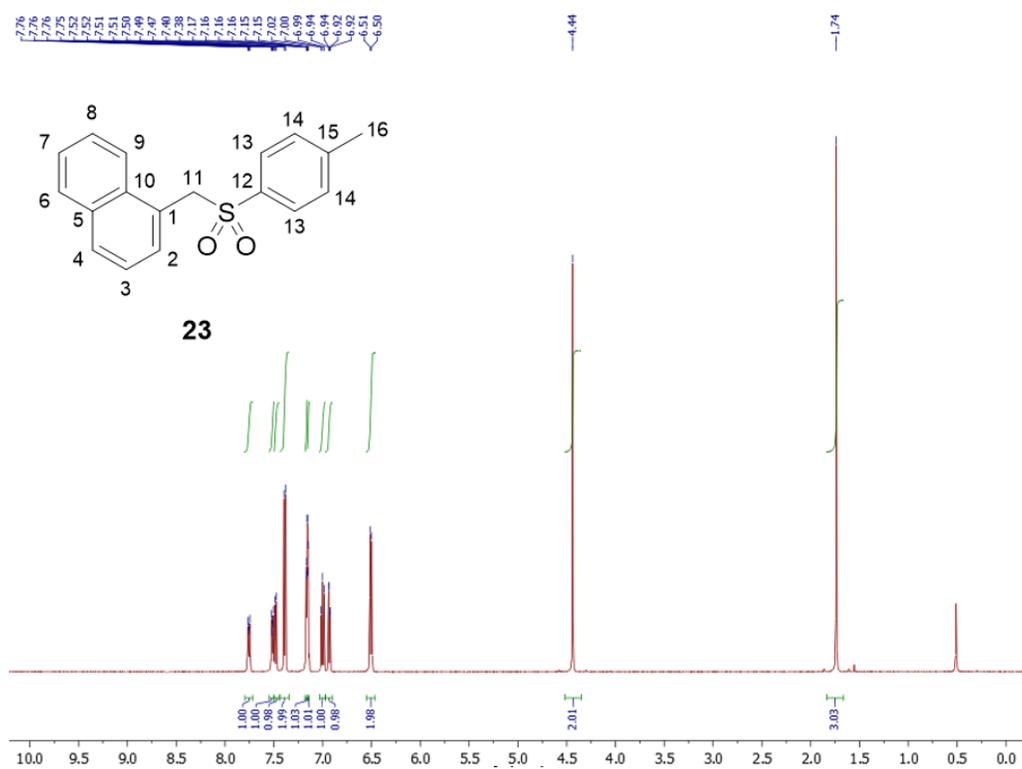
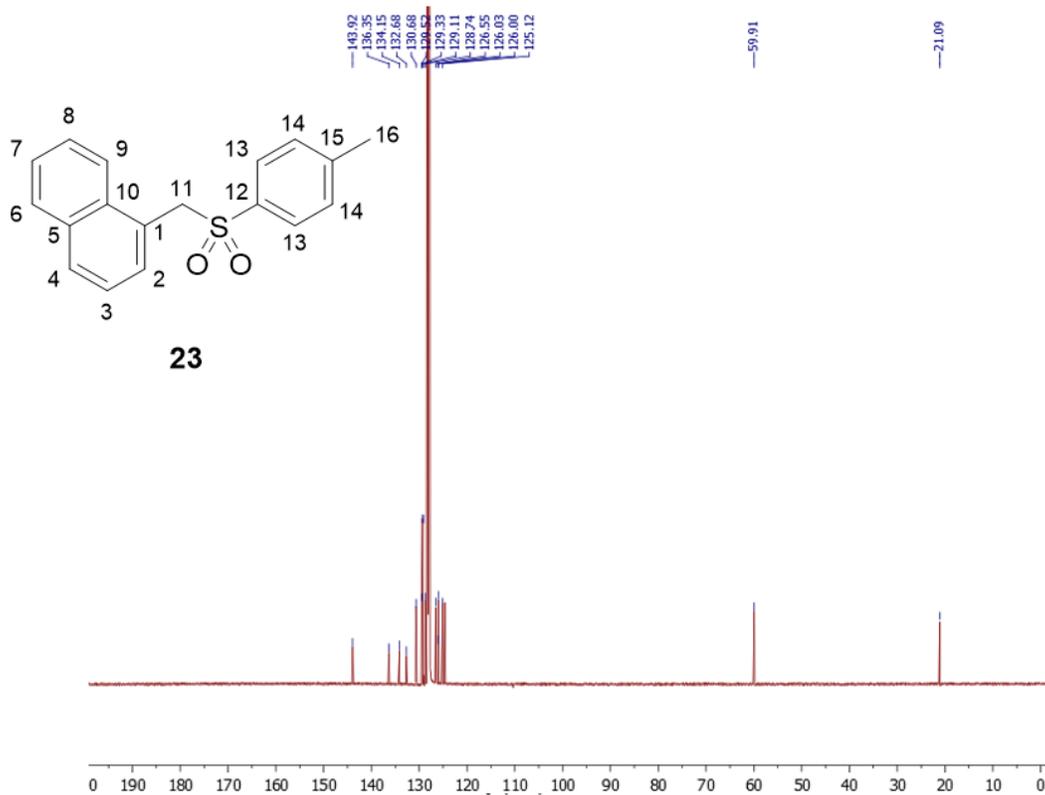
3e ^1H NMR (500 MHz, CDCl_3)**3e** ^{13}C NMR (126 MHz, CDCl_3)

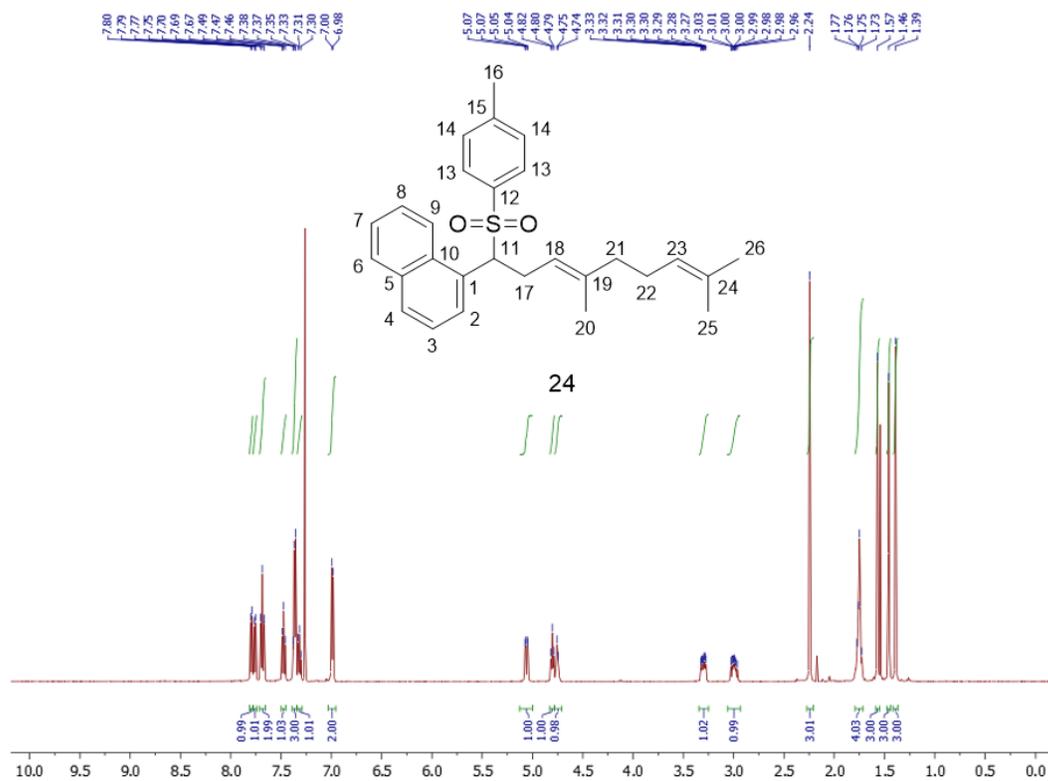
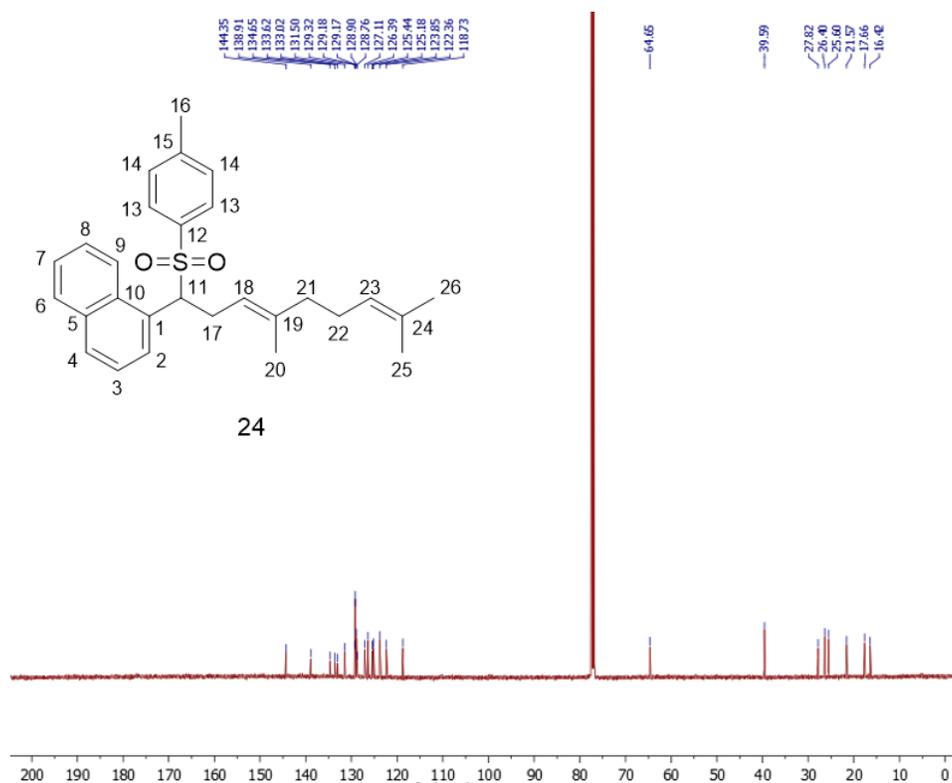
3f ^1H NMR (500 MHz, CDCl_3)**3f** ^{13}C NMR (126 MHz, CDCl_3)

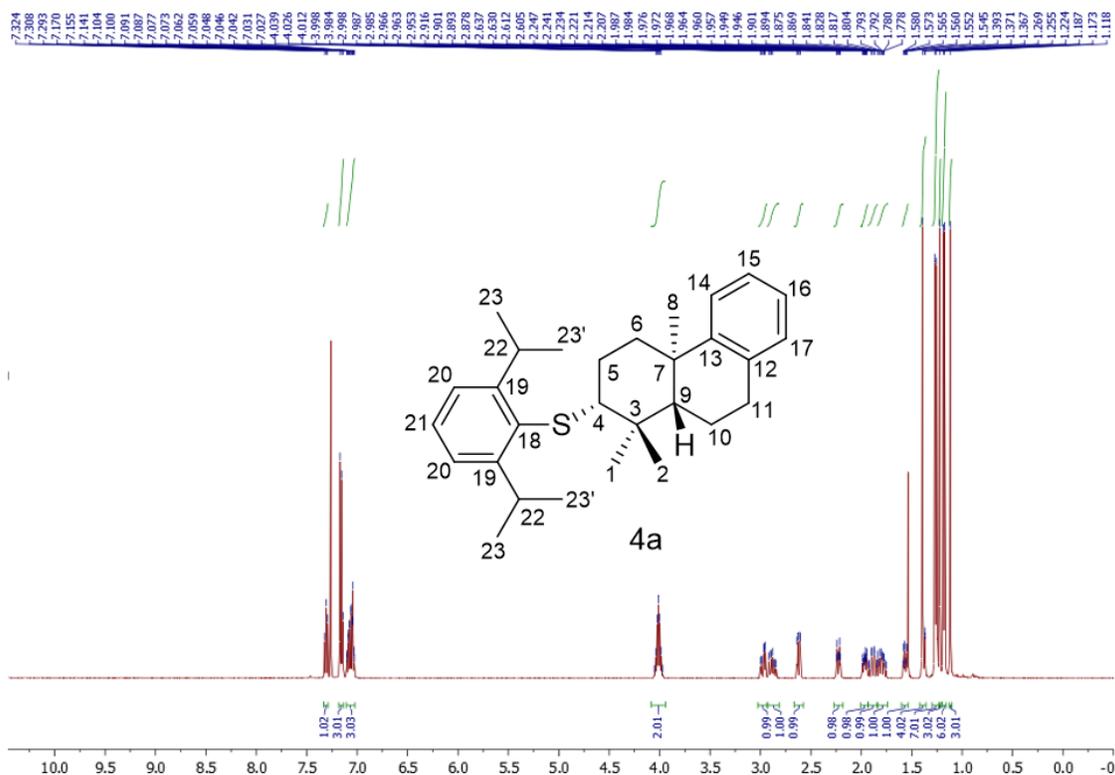
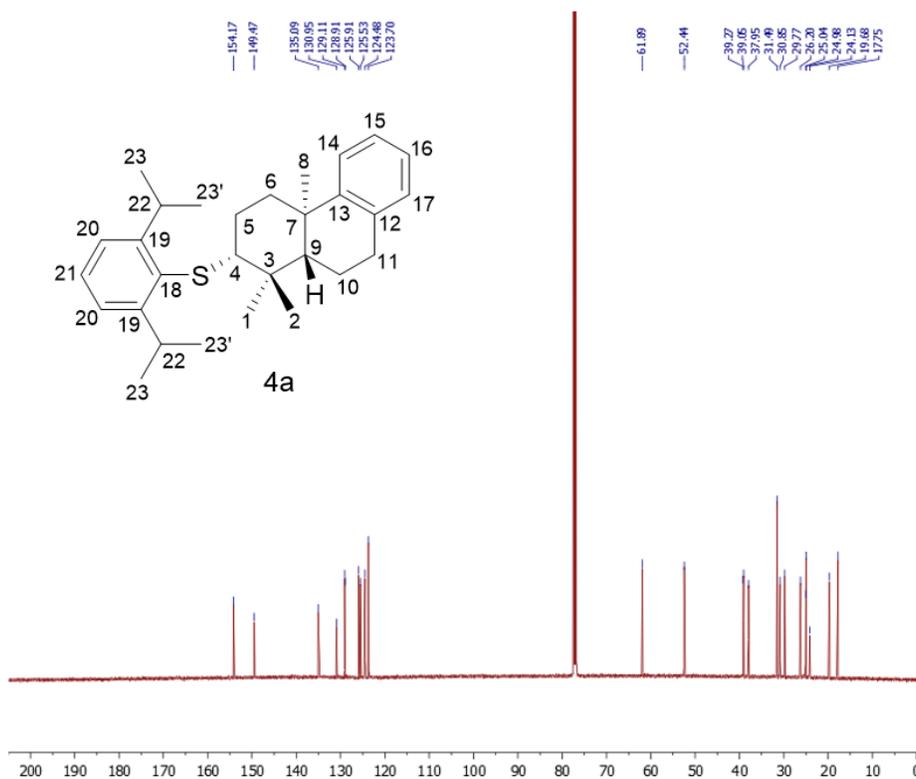
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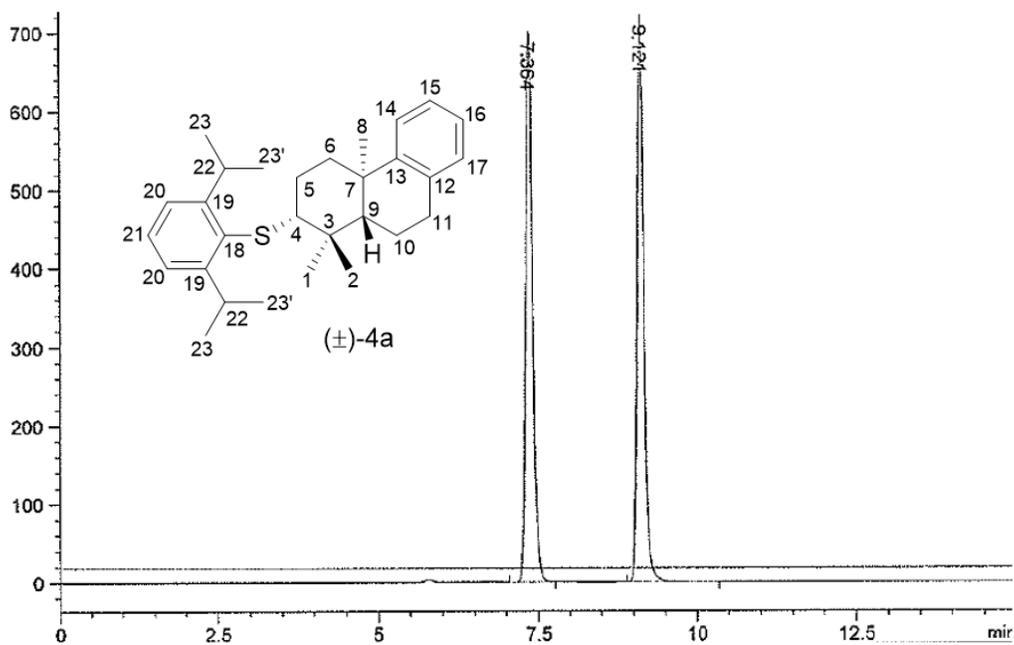
21 ^1H NMR (500 MHz, CDCl_3)**21** ^{13}C NMR (126 MHz, CDCl_3)

3g ^1H NMR (500 MHz, CDCl_3)**3g** ^{13}C NMR (126 MHz, CDCl_3)

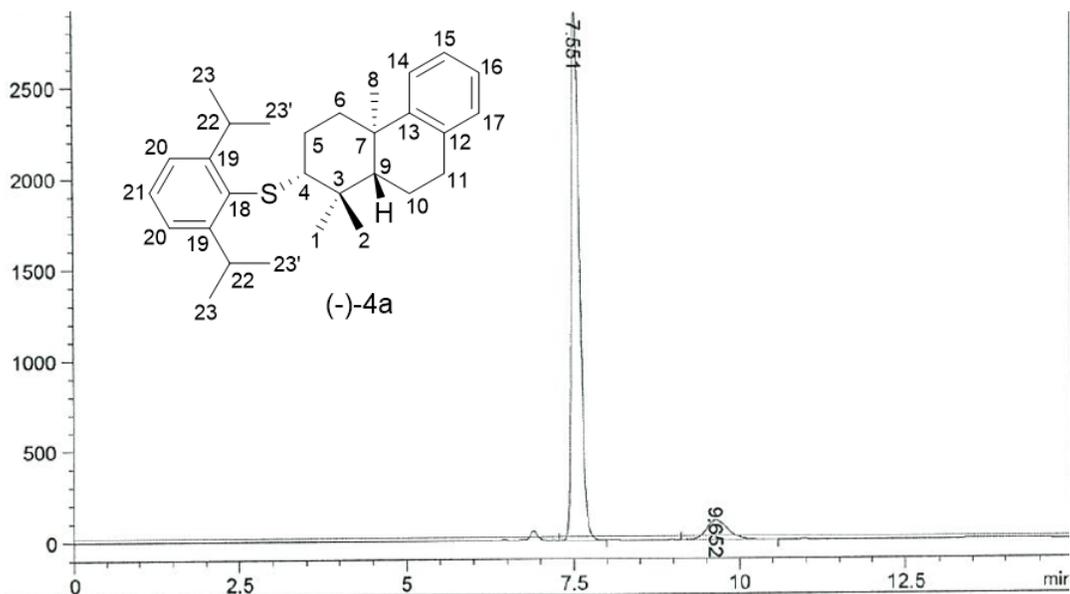
23 ^1H NMR (500 MHz, benzene- d_6)**23** ^{13}C NMR (126 MHz, benzene- d_6)

24 ^1H NMR (500 MHz, CDCl_3)**24** ^{13}C NMR (126 MHz, CDCl_3)

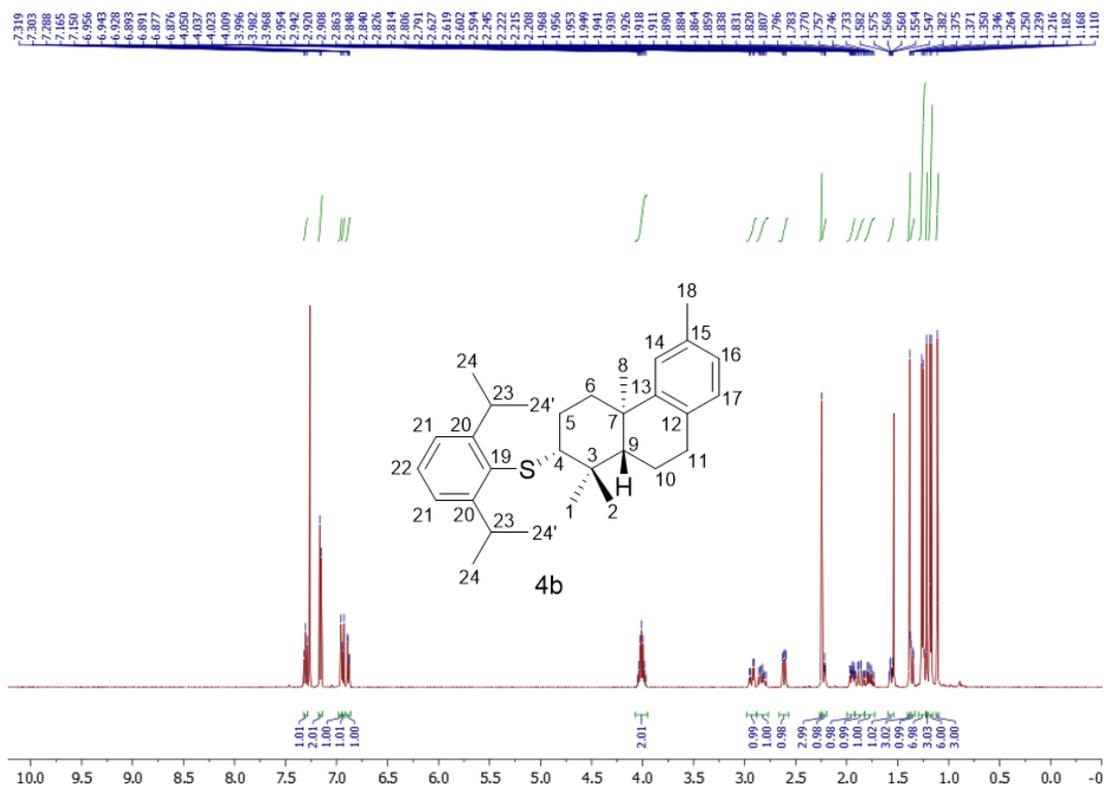
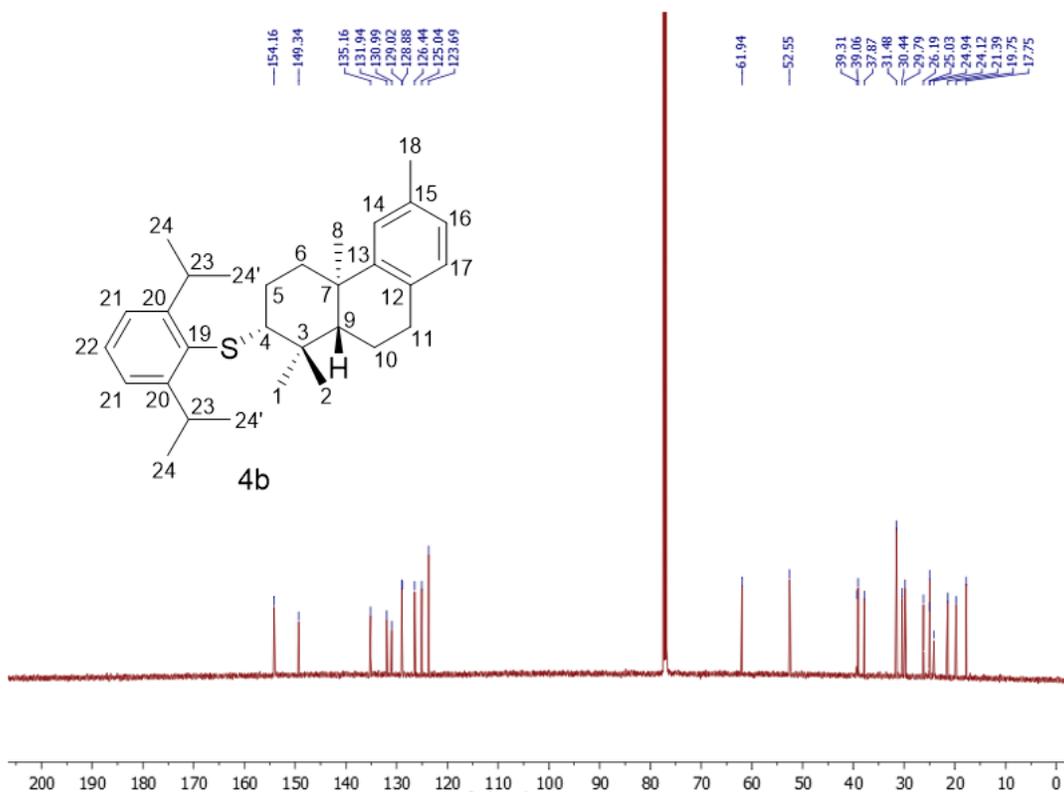
4a ^1H NMR (500 MHz, CDCl_3)**4a** ^{13}C NMR (126 MHz, CDCl_3)

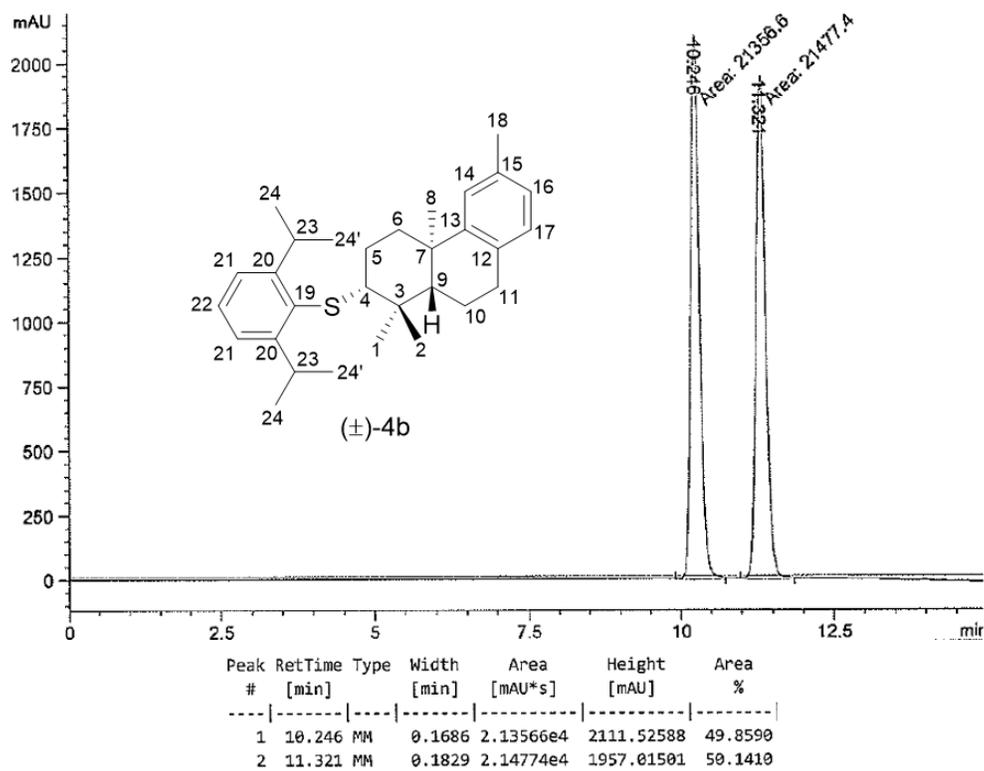
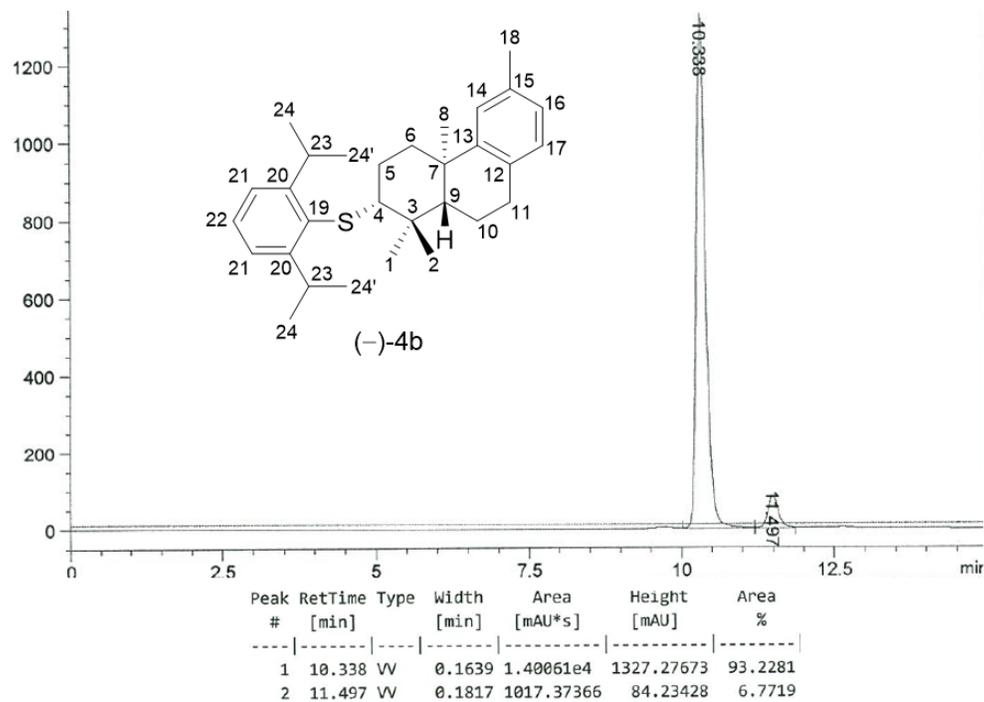
(±)-4a

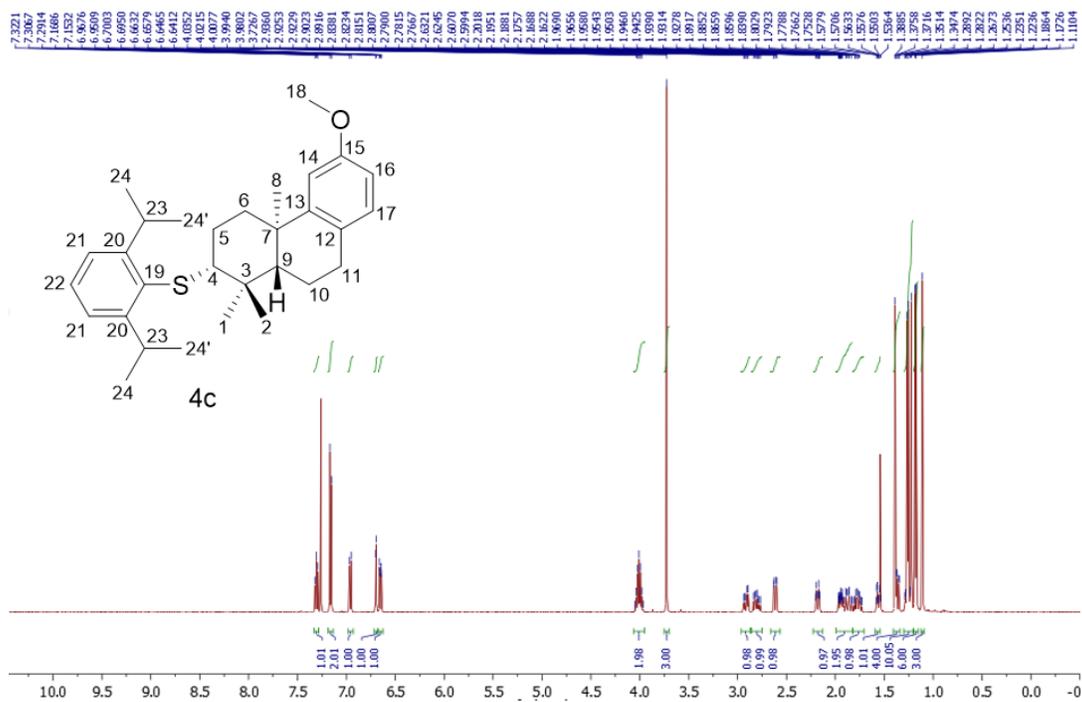
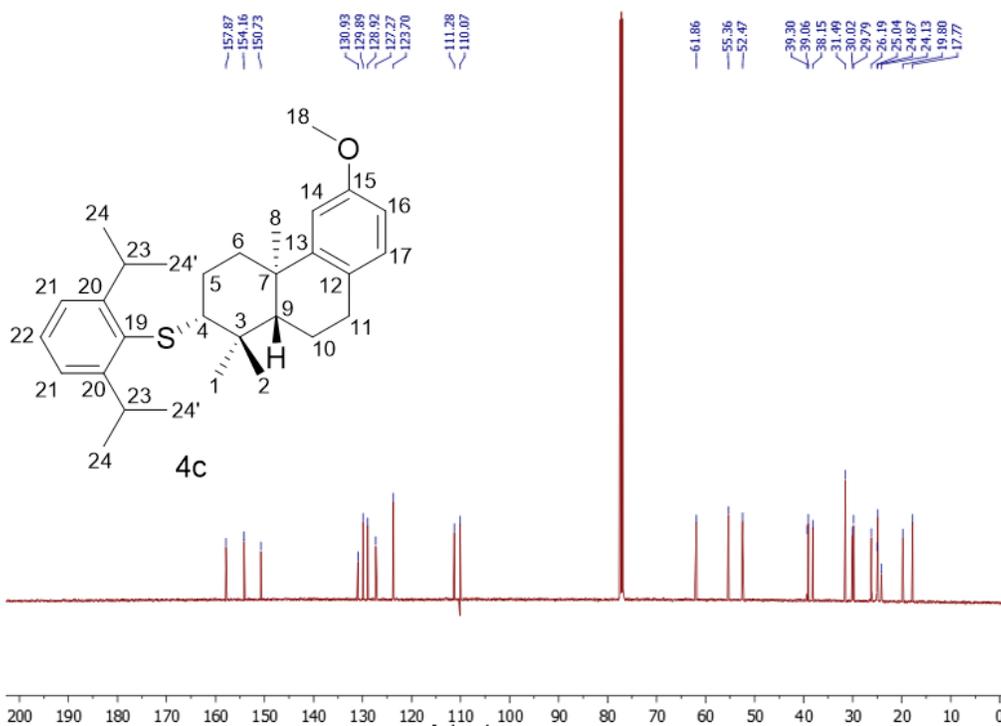
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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2	9.121	VB	0.1150	5266.99951	715.64038	49.9889

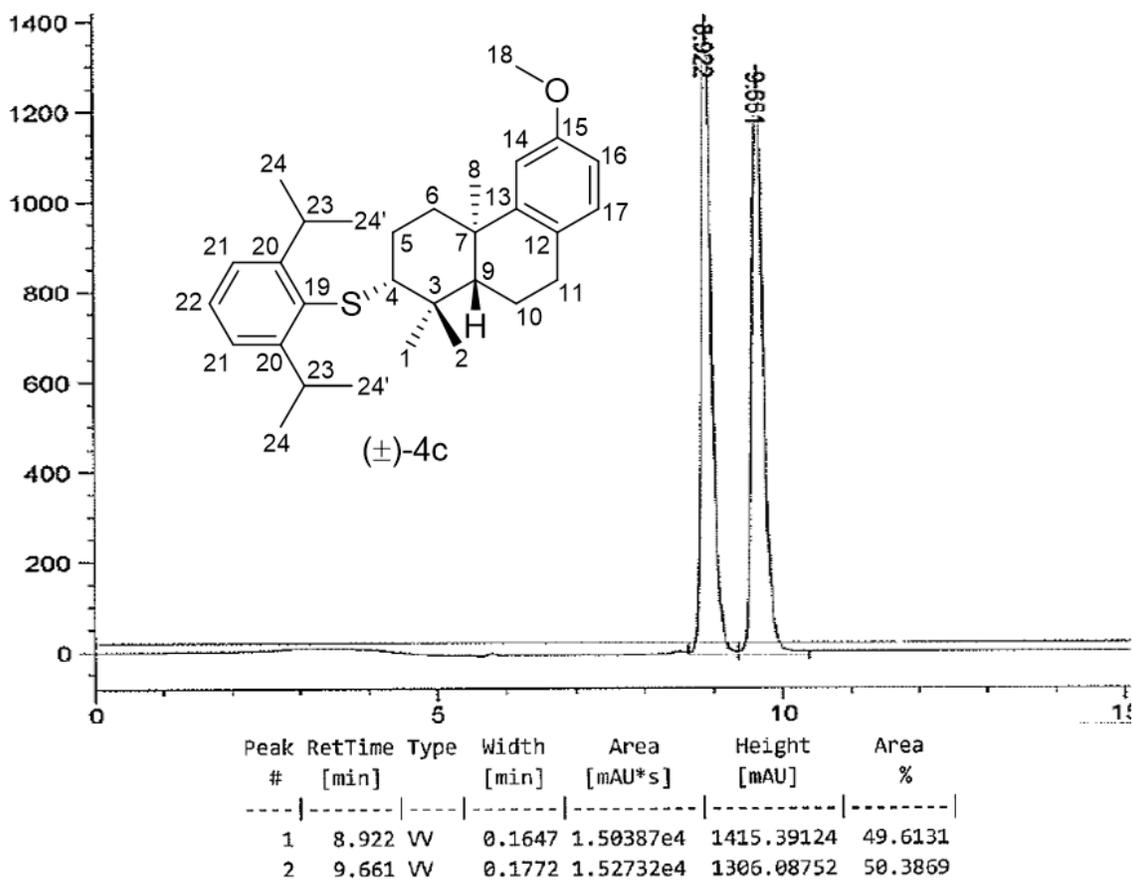
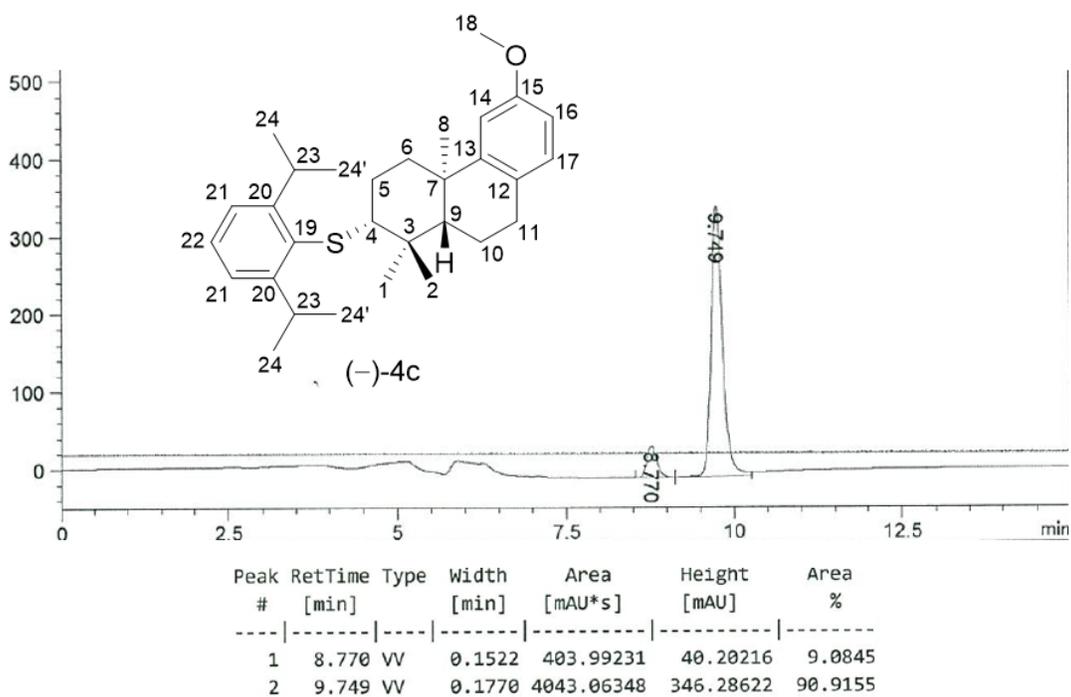
(-)-4a

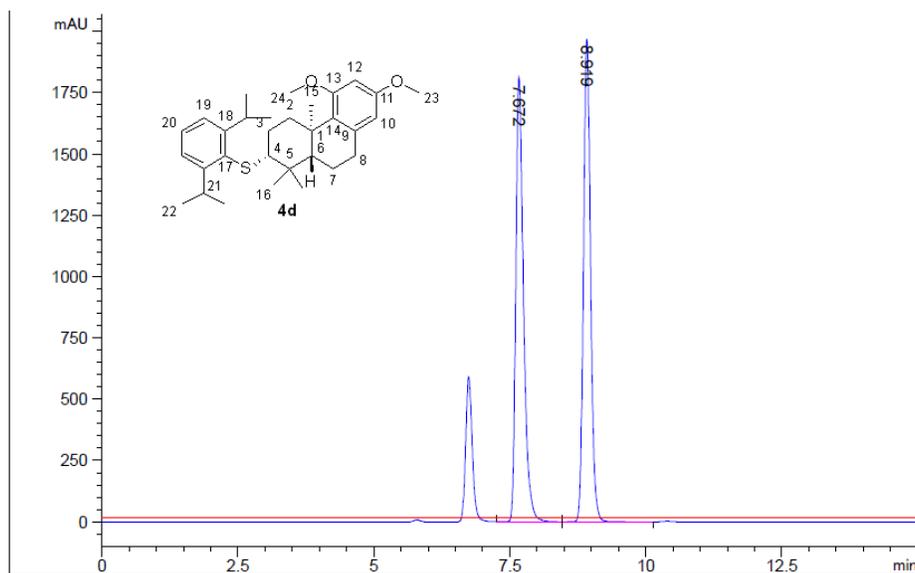
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1	7.551	VV	0.1374	2.54041e4	2892.53516	91.1593
2	9.652	VB	0.3570	2463.70630	106.58136	8.8407

4b ^1H NMR (500 MHz, CDCl_3)**4b** ^{13}C NMR (500 MHz, CDCl_3)

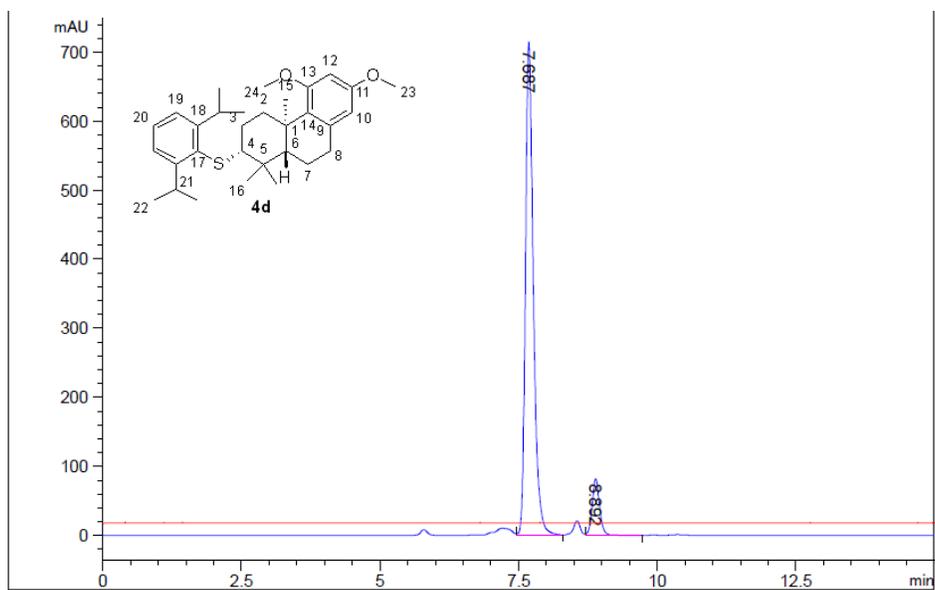
(±)-4b**(-)-4b**

4c ^1H NMR (500 MHz, CDCl_3)**4c** ^{13}C NMR (500 MHz, CDCl_3)

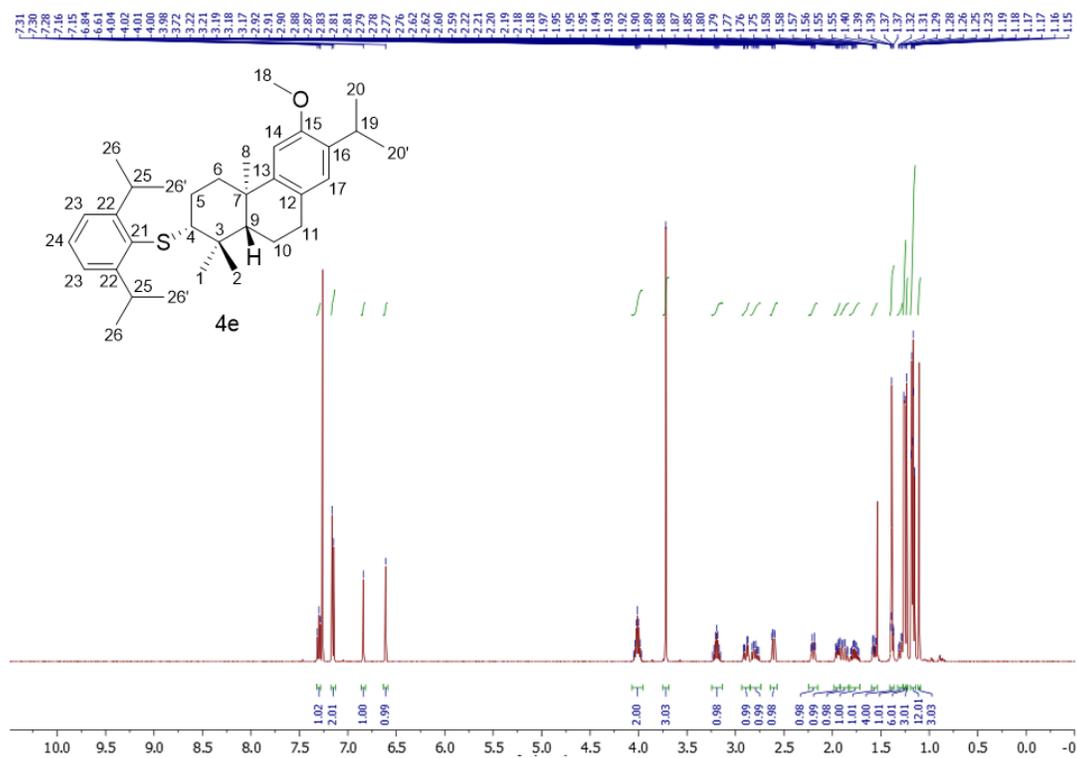
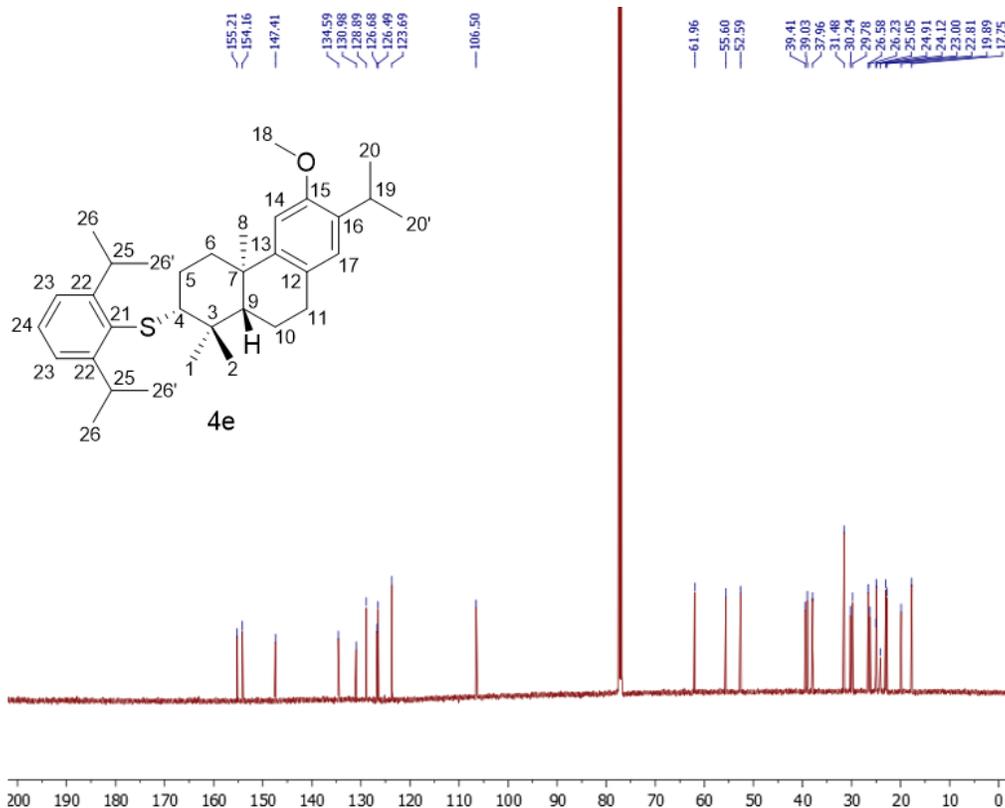
(±)-4c**(-)-4c**

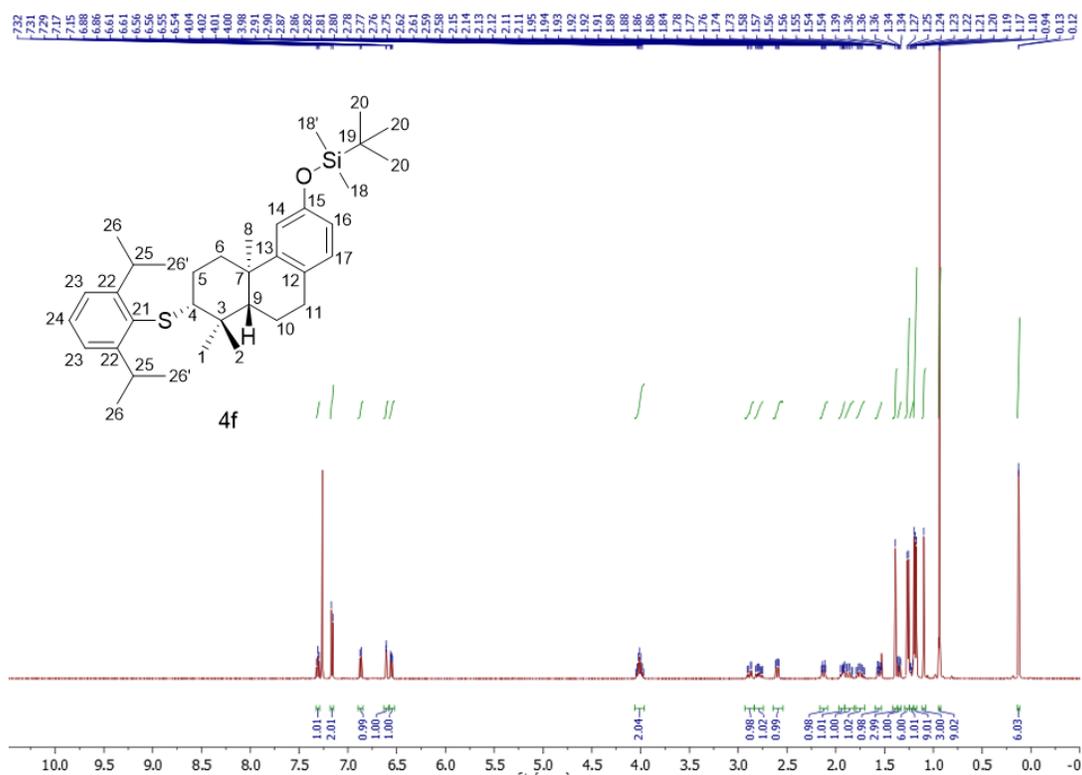
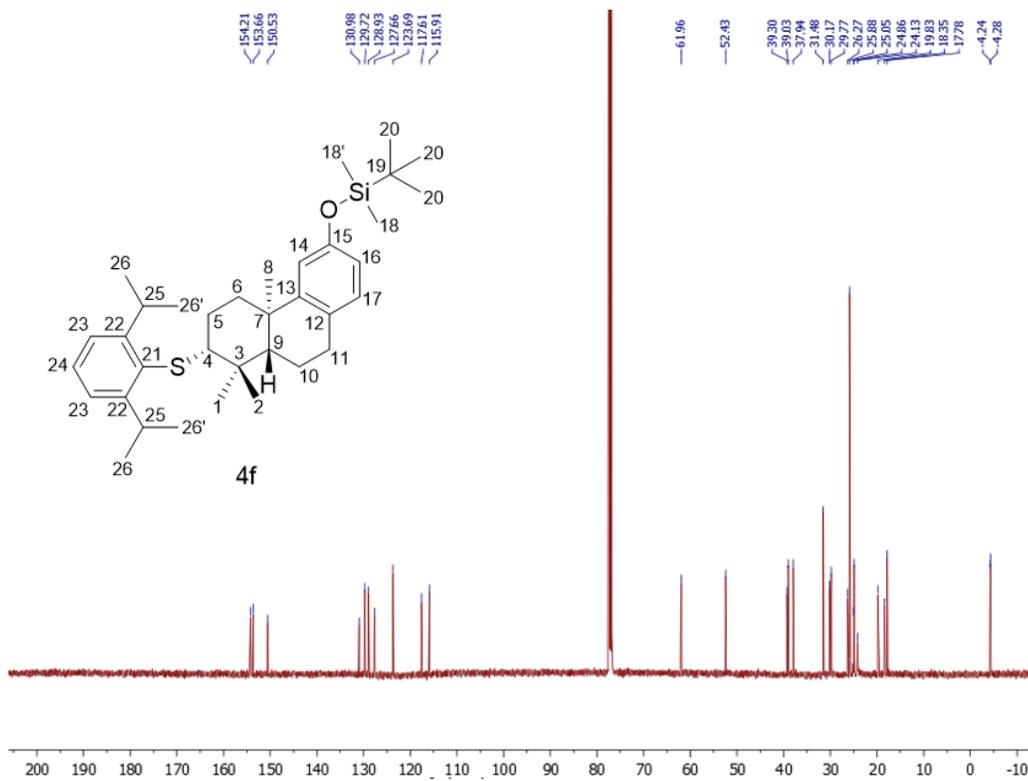
(±)-4d

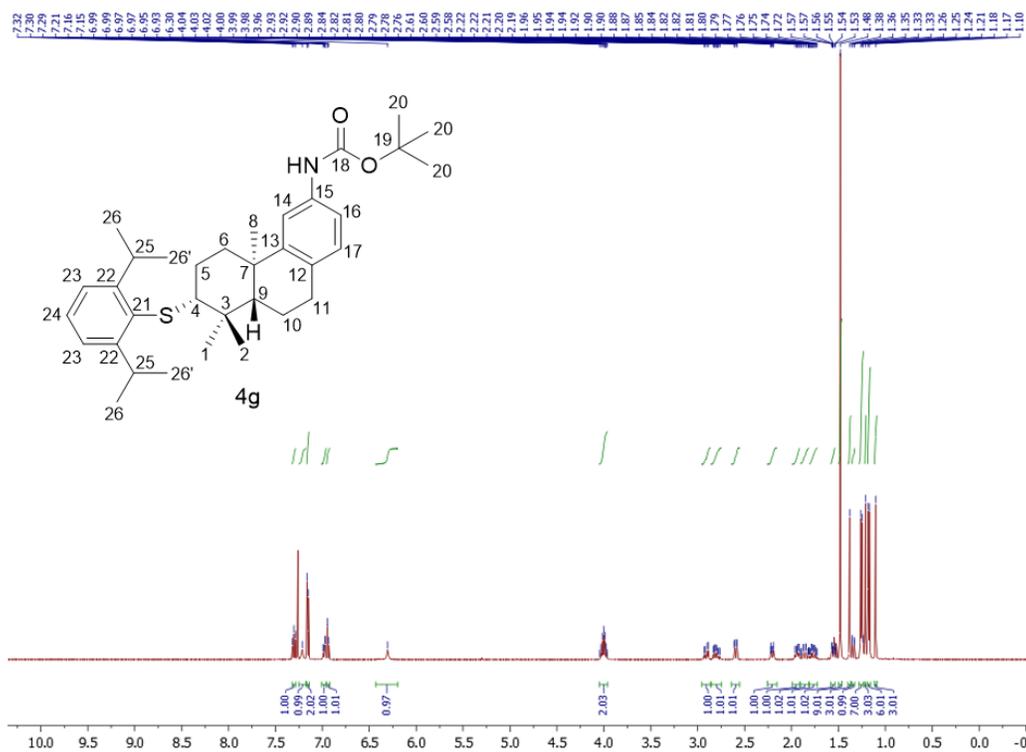
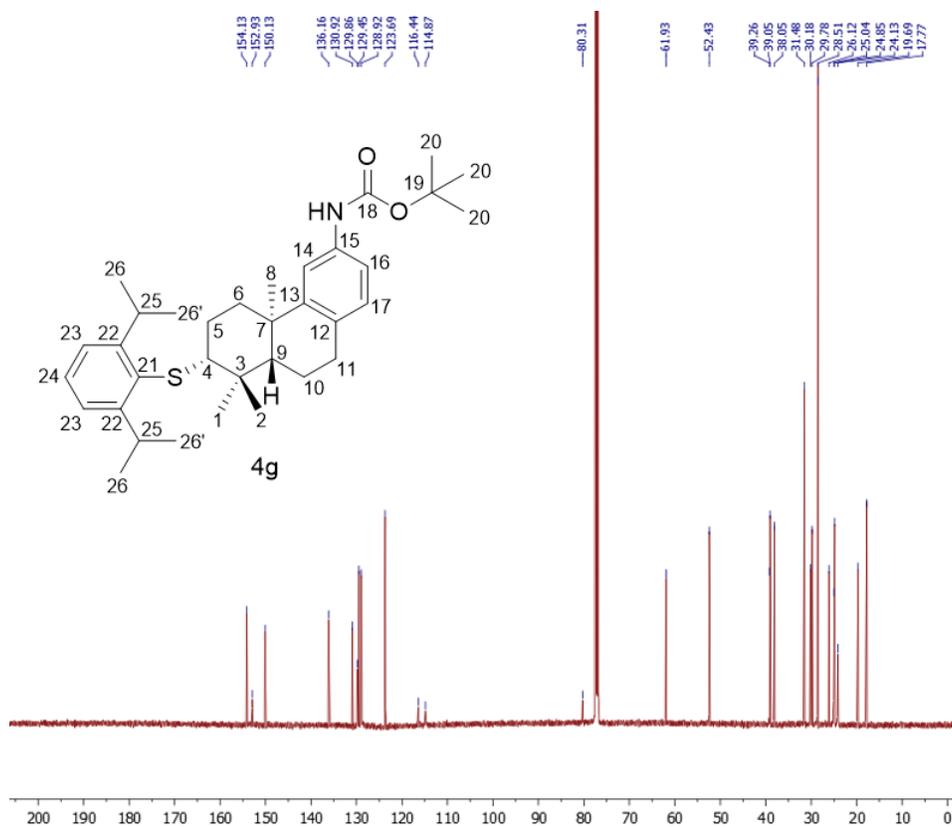
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.672	VV	0.1512	1.79360e4	1800.00439	50.1757
2	8.919	VV	0.1468	1.78104e4	1960.29248	49.8243

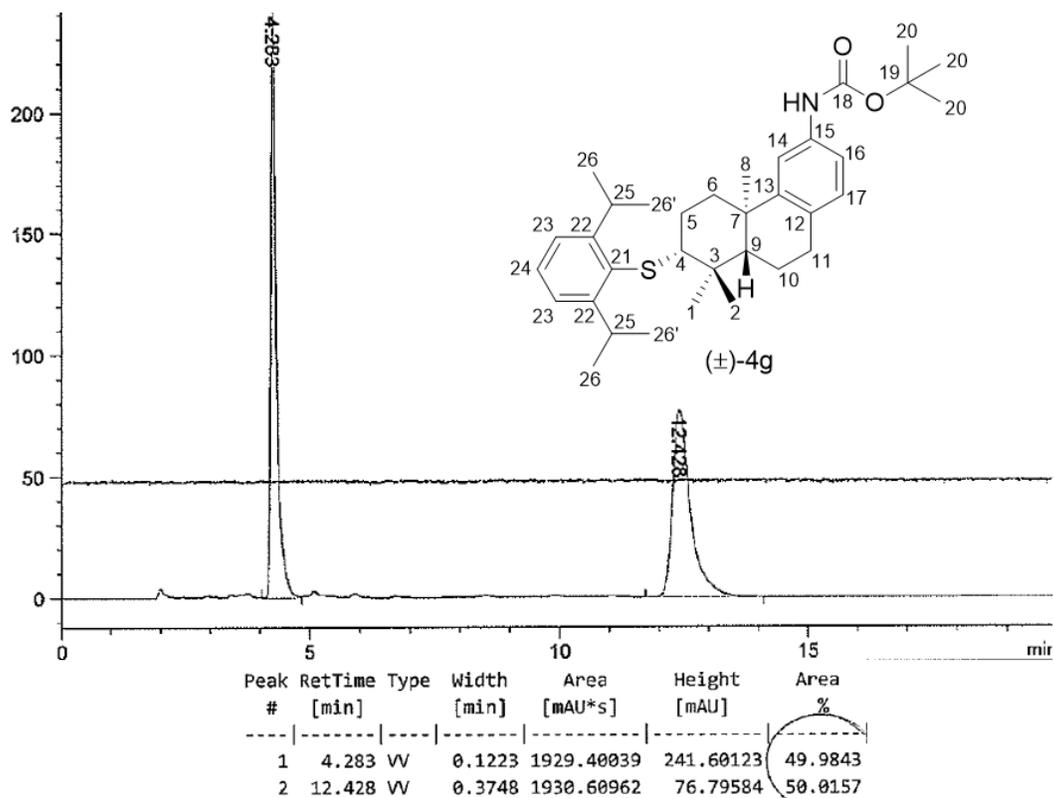
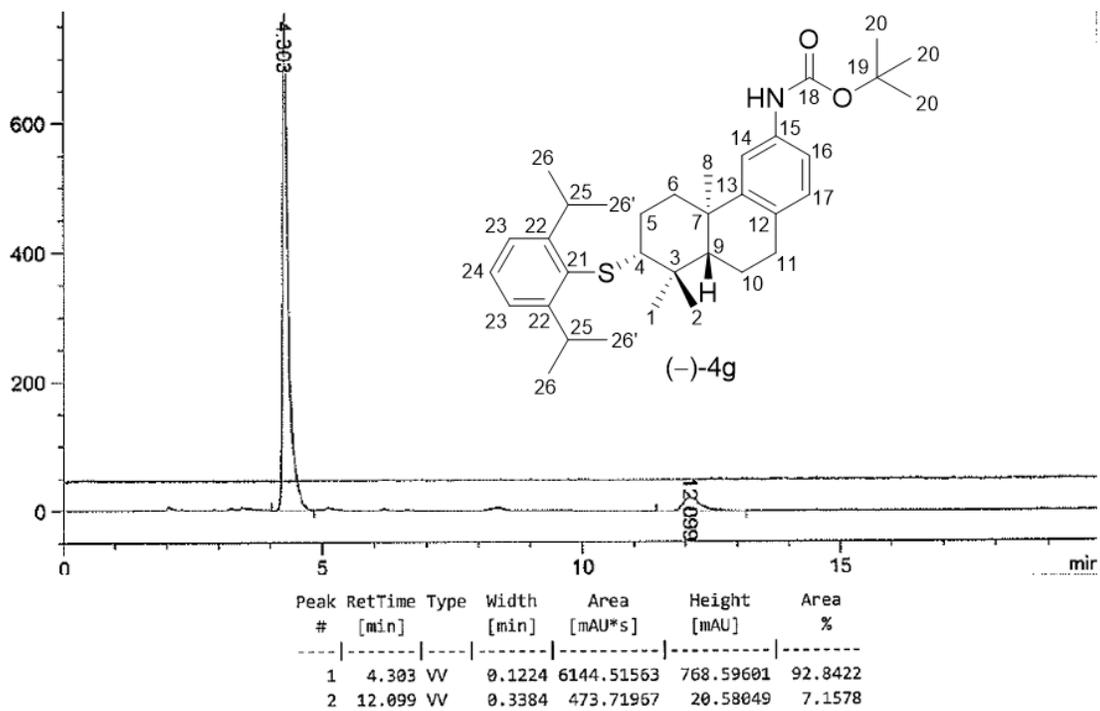
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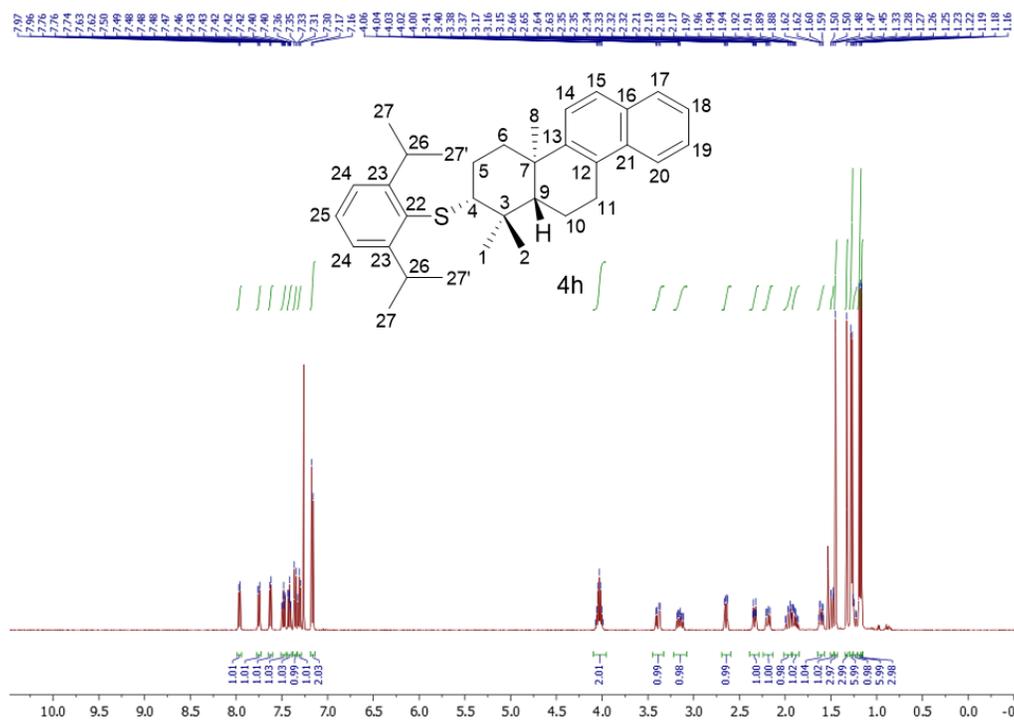
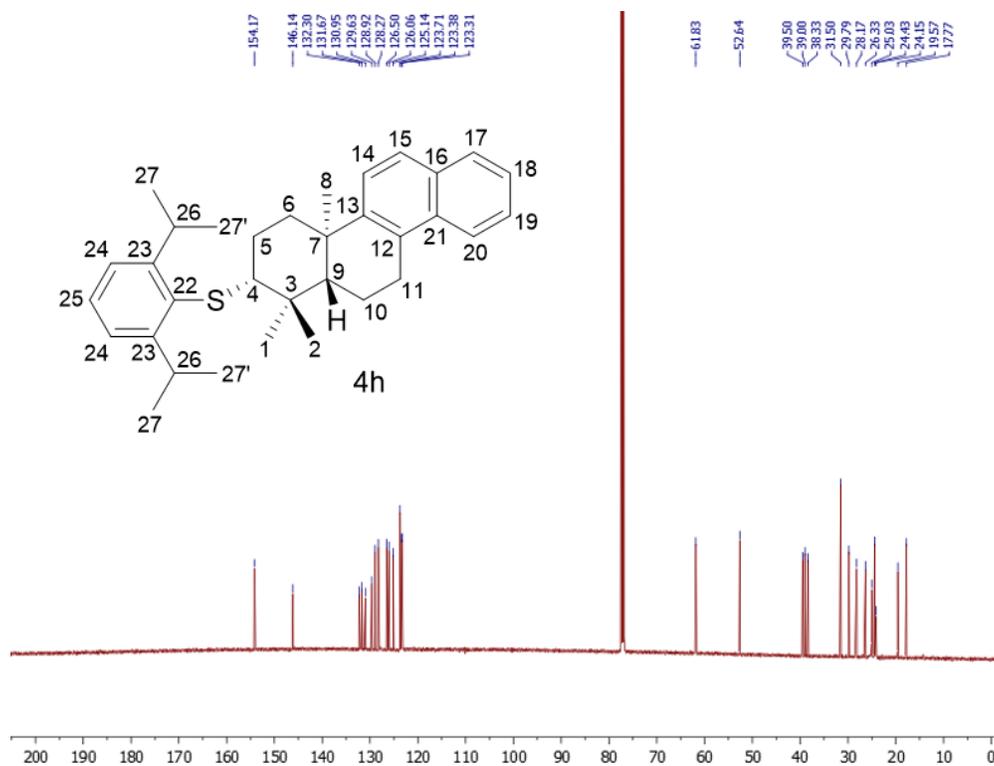
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1	7.687	VV	0.1520	7112.64209	708.93549	90.2965
2	8.892	VV	0.1442	764.34283	81.60392	9.7035

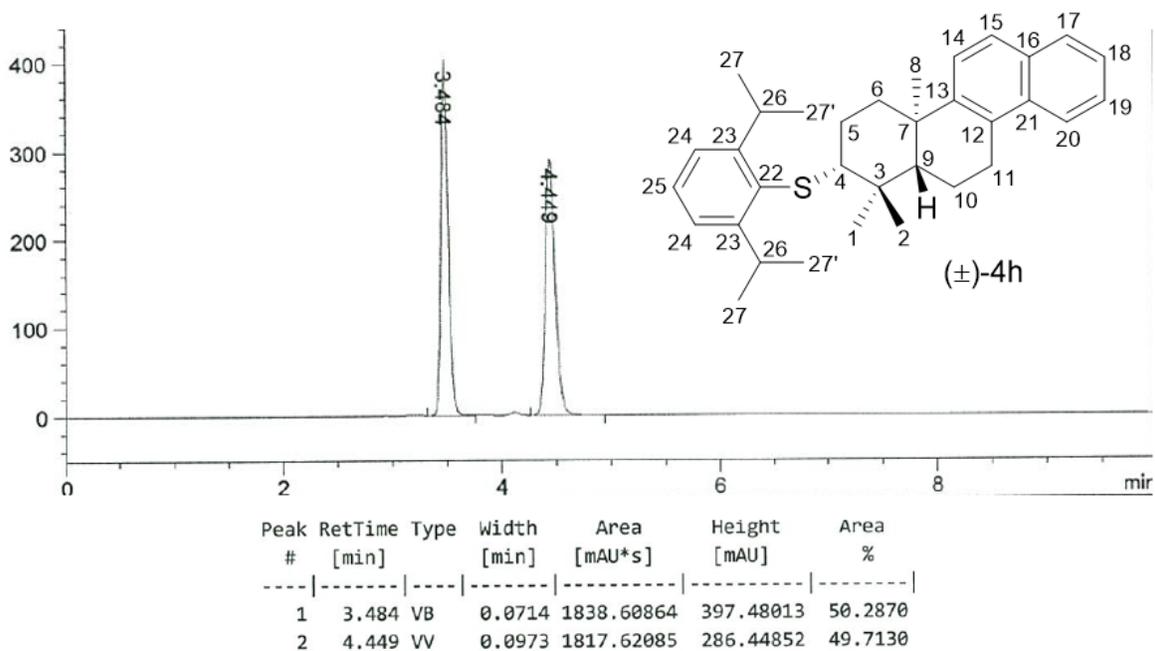
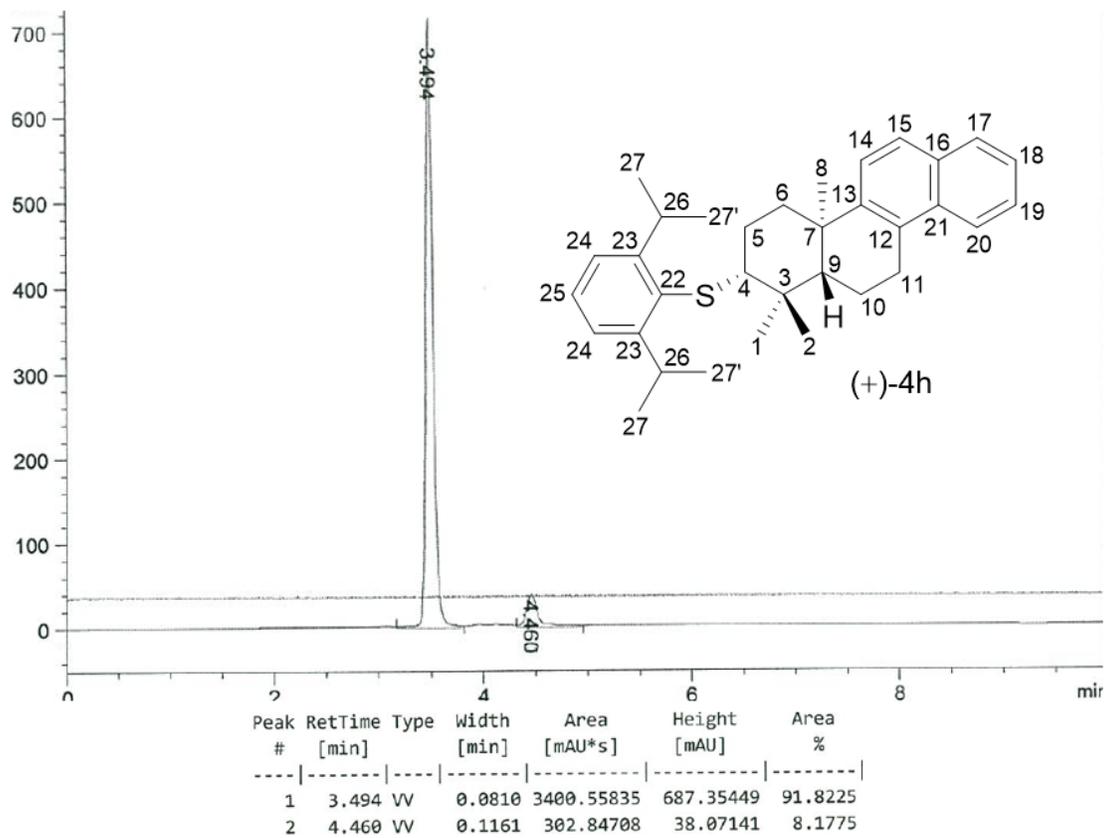
4e ^1H NMR (500 MHz, CDCl_3)**4e** ^{13}C NMR (126 MHz, CDCl_3)

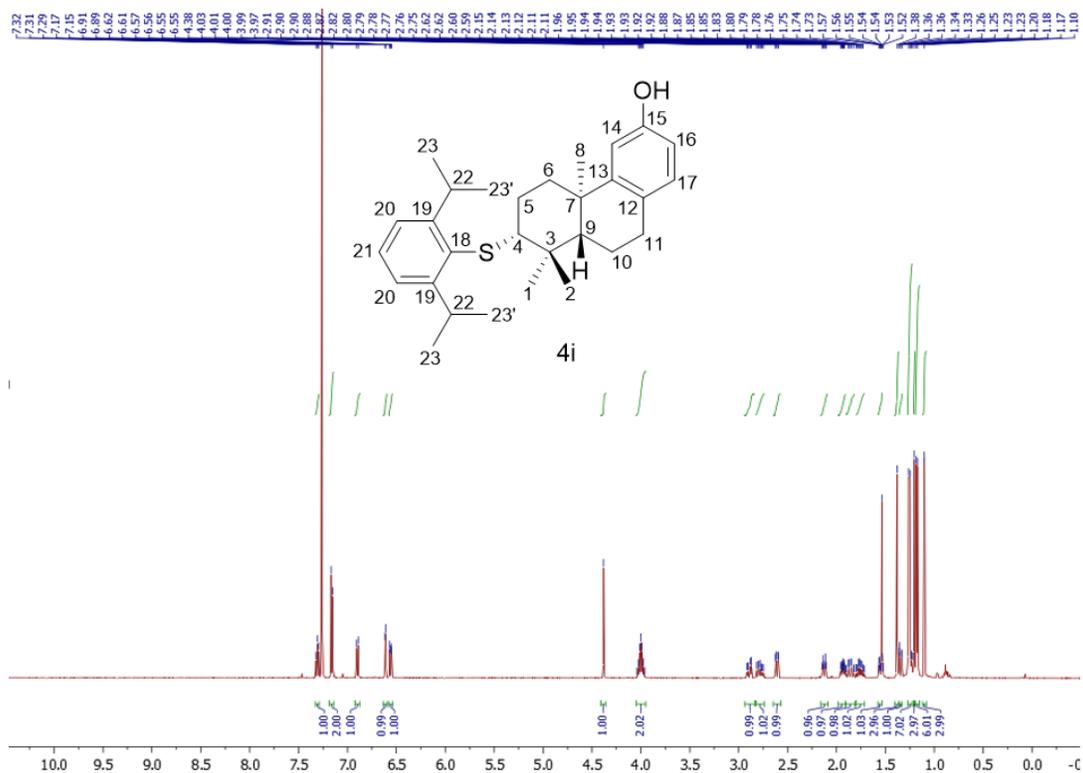
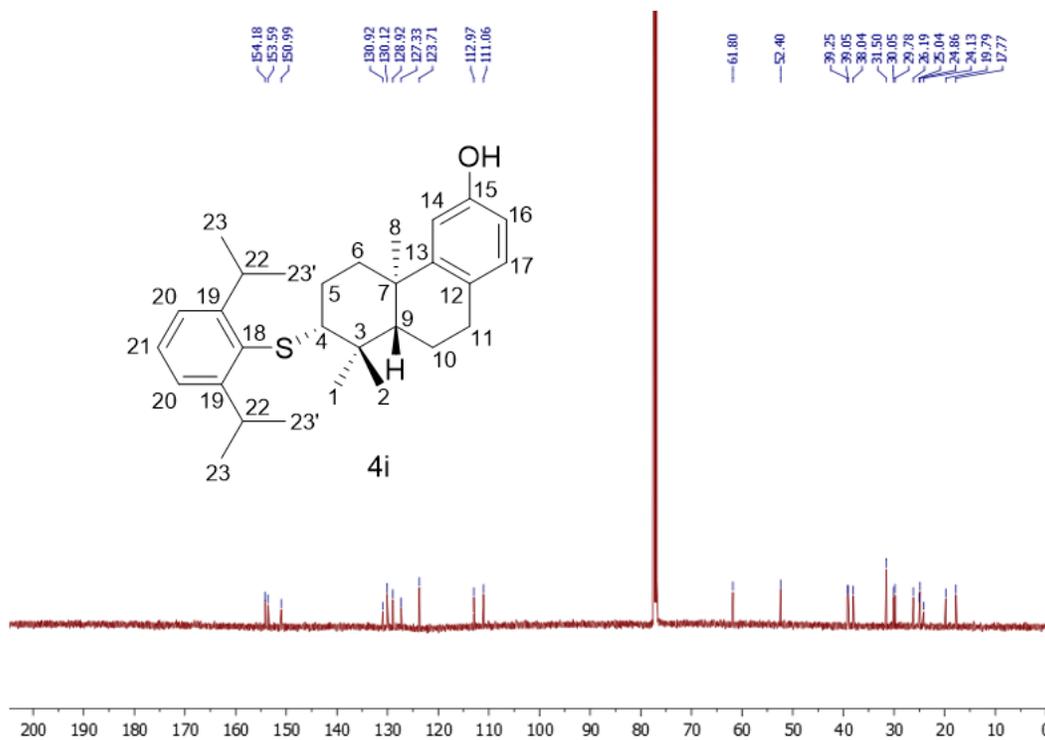
4f ^1H NMR (500 MHz, CDCl_3)**4f** ^{13}C NMR (126 MHz, CDCl_3)

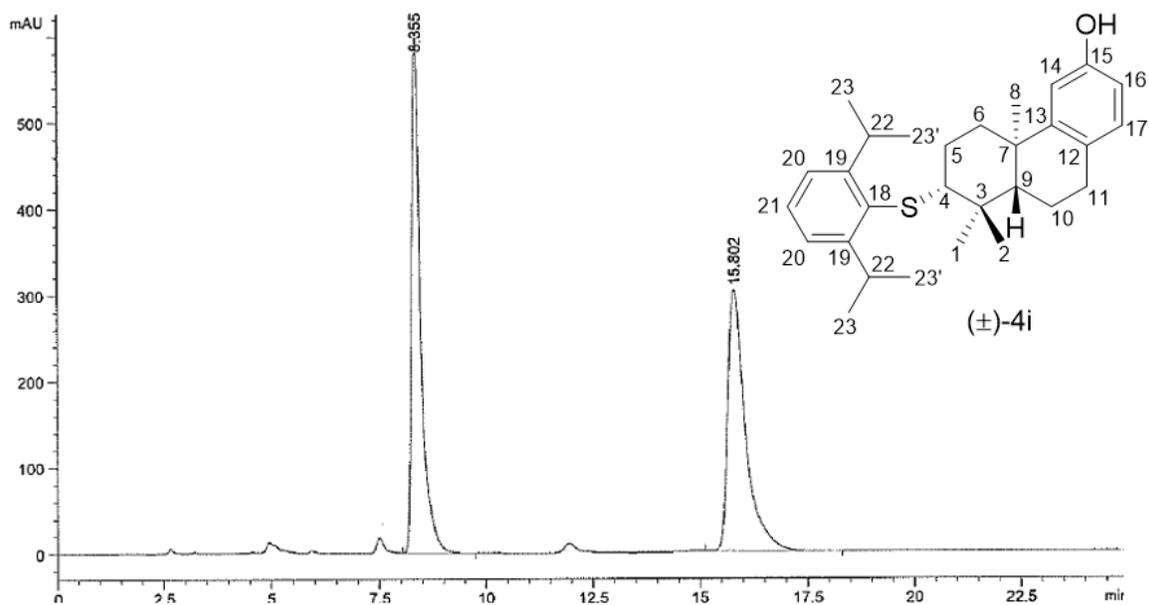
4g ^1H NMR (500 MHz, CDCl_3)**4g** ^{13}C NMR (126 MHz, CDCl_3)

(±)-4g**(-)-4g**

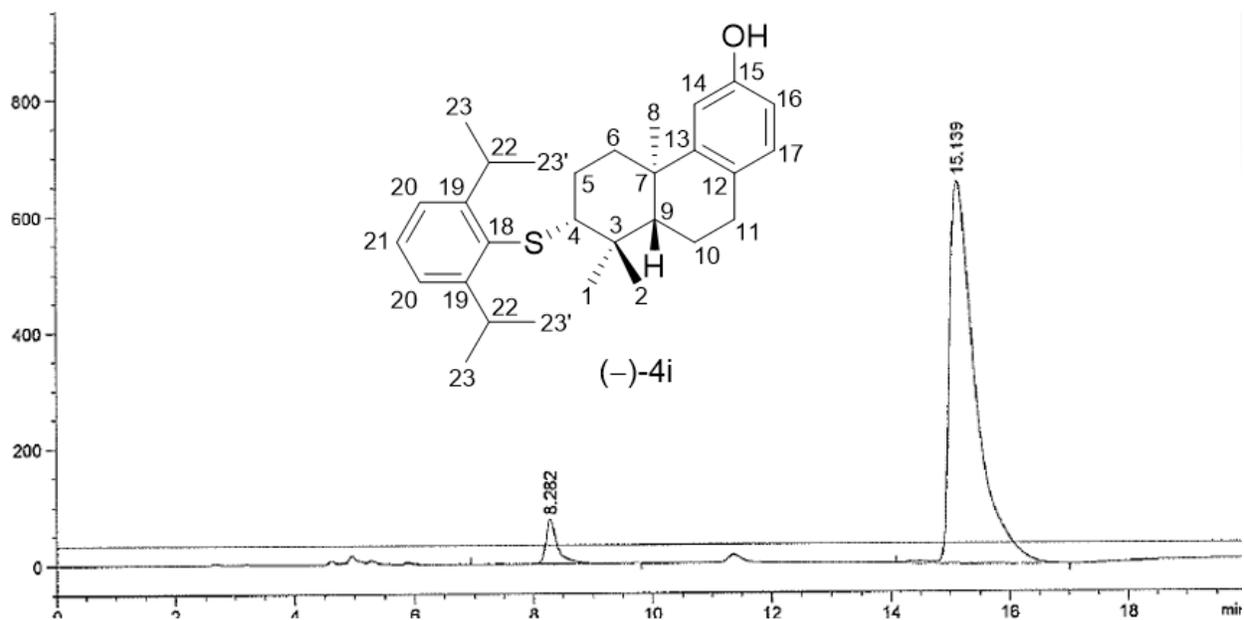
4h ^1H NMR (500 MHz, CDCl_3)**4h** ^{13}C NMR (126 MHz, CDCl_3)

(±)-4h**(+)-4h**

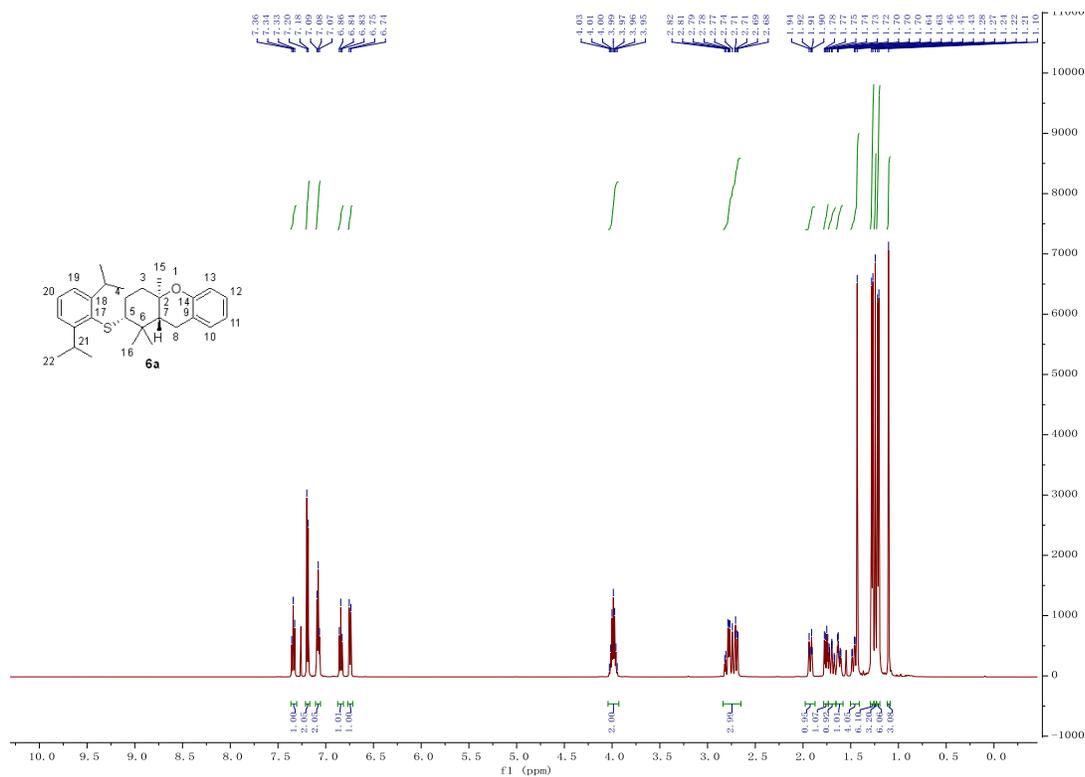
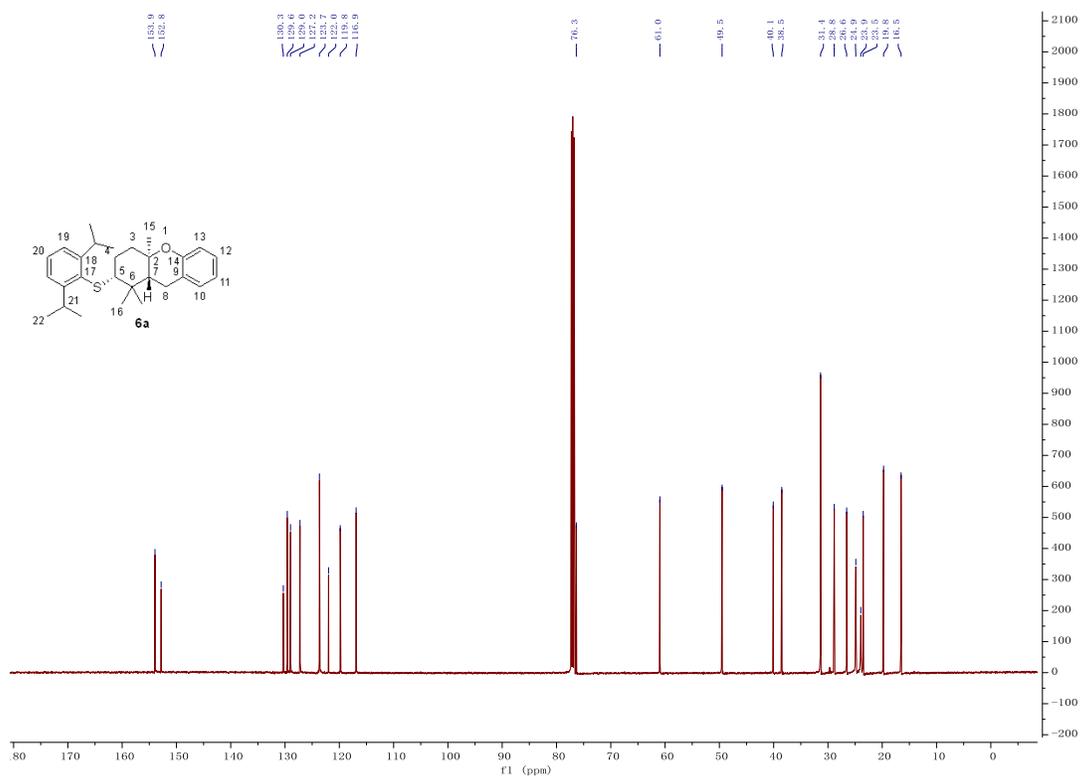
4i ^1H NMR (500 MHz, CDCl_3)**4i** ^{13}C NMR (126 MHz, CDCl_3)

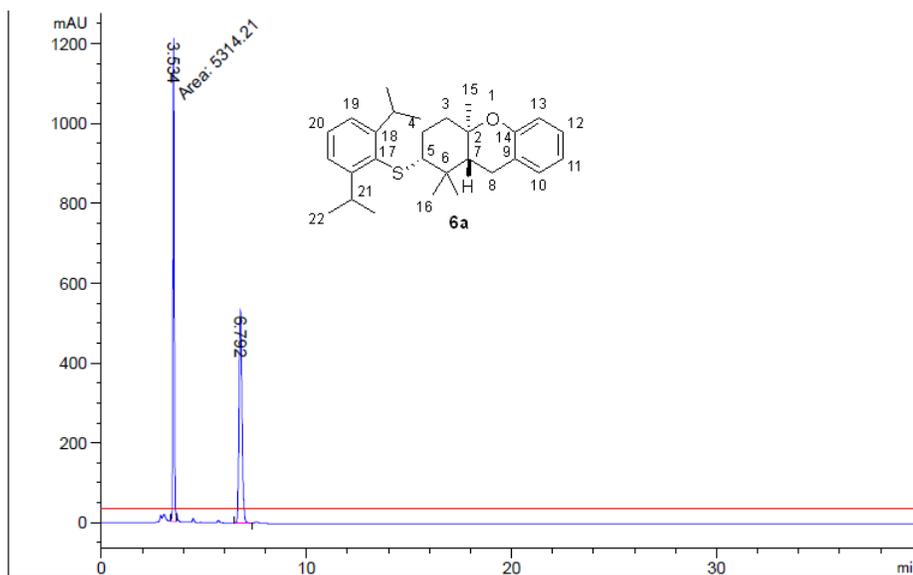
(±)-4i

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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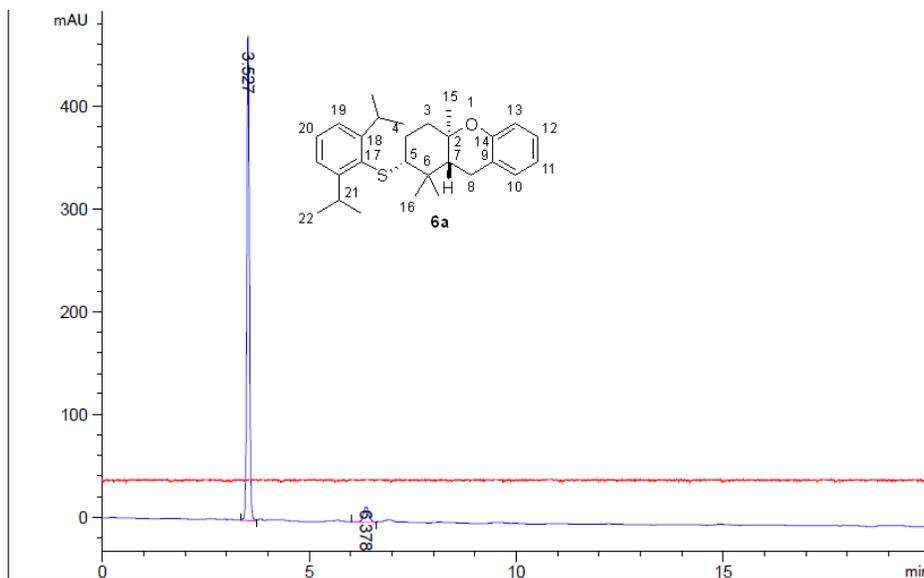
(-)-4i

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.282	VB R	0.1978	1014.95953	74.69286	4.8393
2	15.139	VB R	0.4549	1.99584e4	656.12268	95.1607

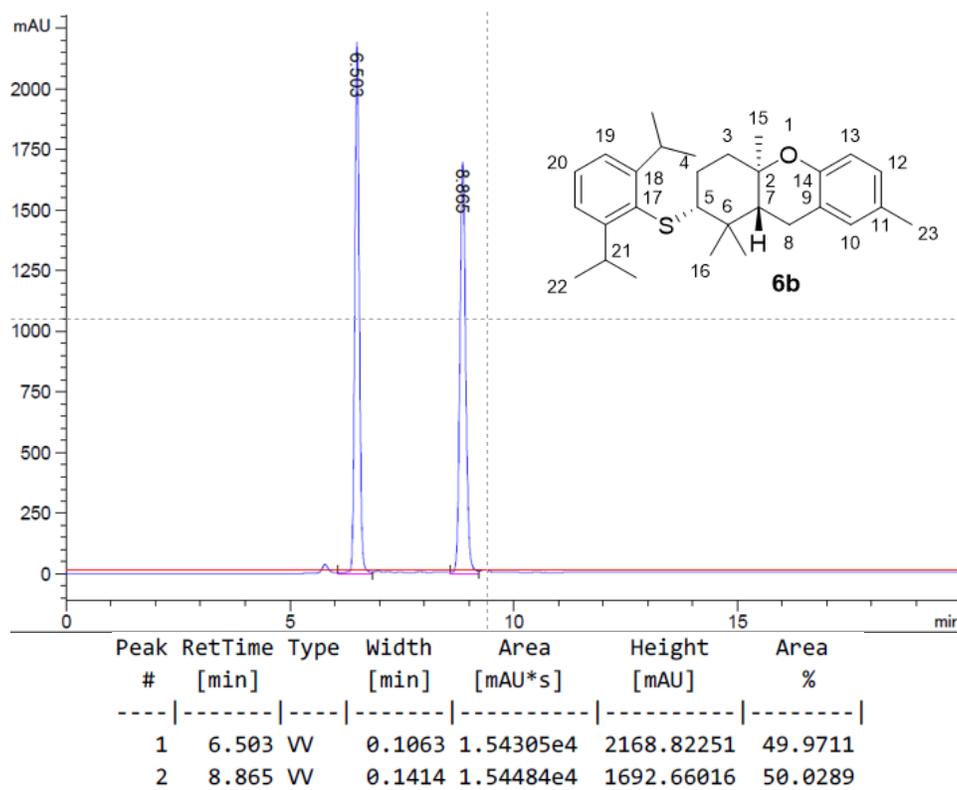
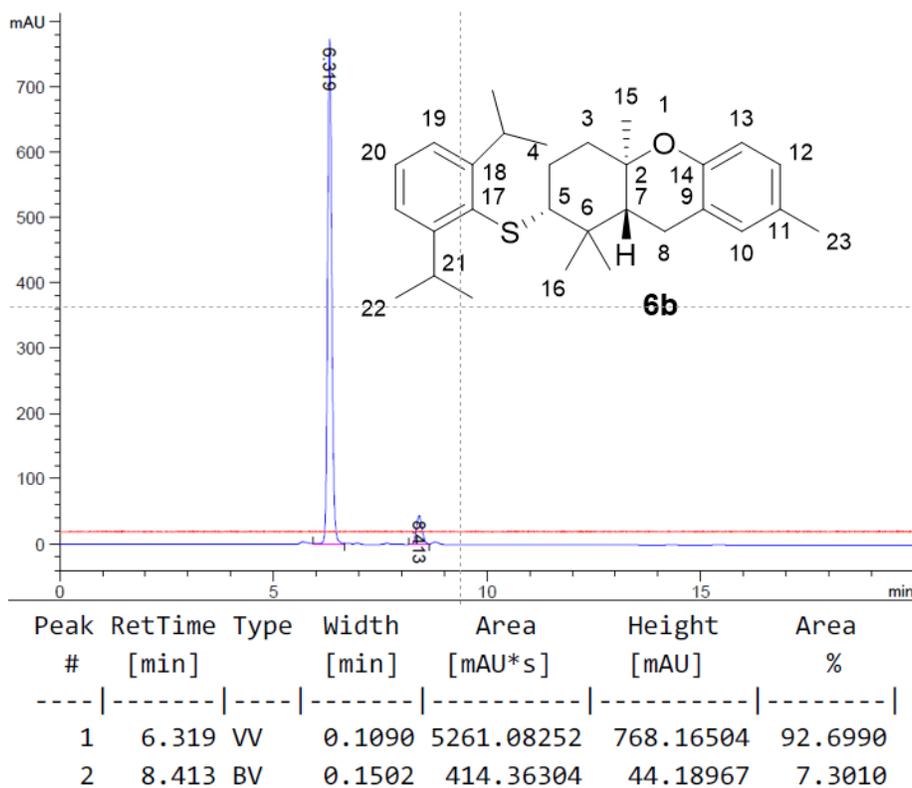
6a ^1H NMR (500 MHz, CDCl_3)**6a** ^{13}C NMR (126 MHz, CDCl_3)

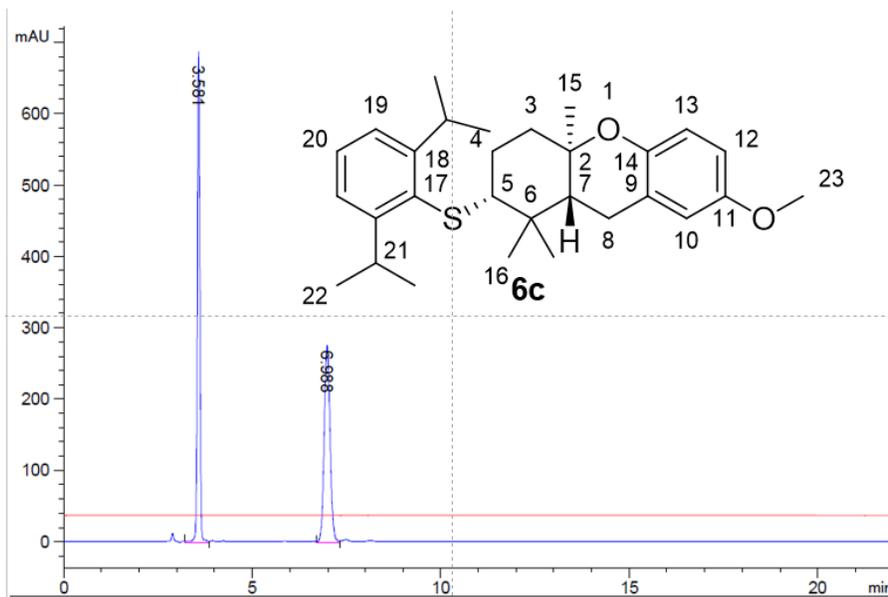
(±)-6a

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.534	MM	0.0731	5314.21338	1211.30981	49.8324
2	6.792	VV	0.1525	5349.96387	530.84662	50.1676

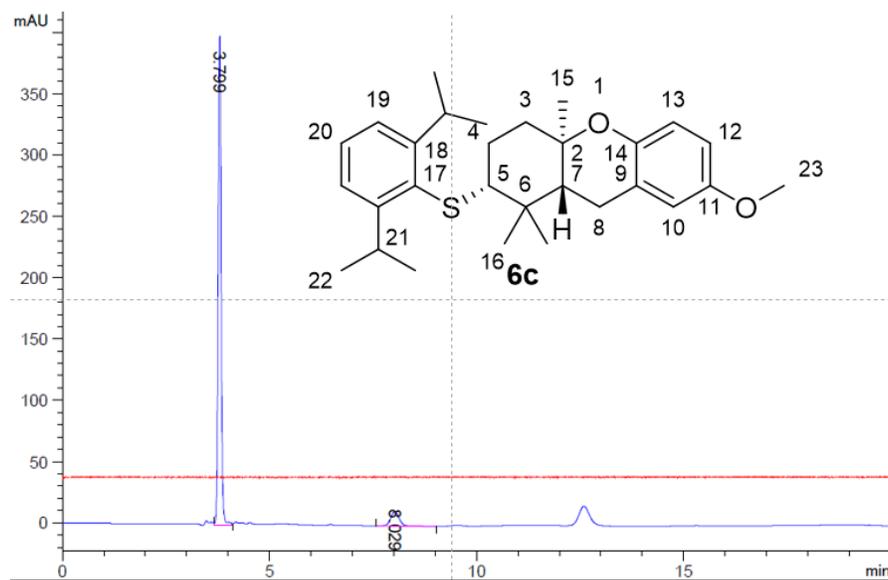
(+)-6a

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.527	VV	0.0757	2067.44141	460.38141	93.3990
2	6.378	VV	0.1484	146.11717	15.02727	6.6010

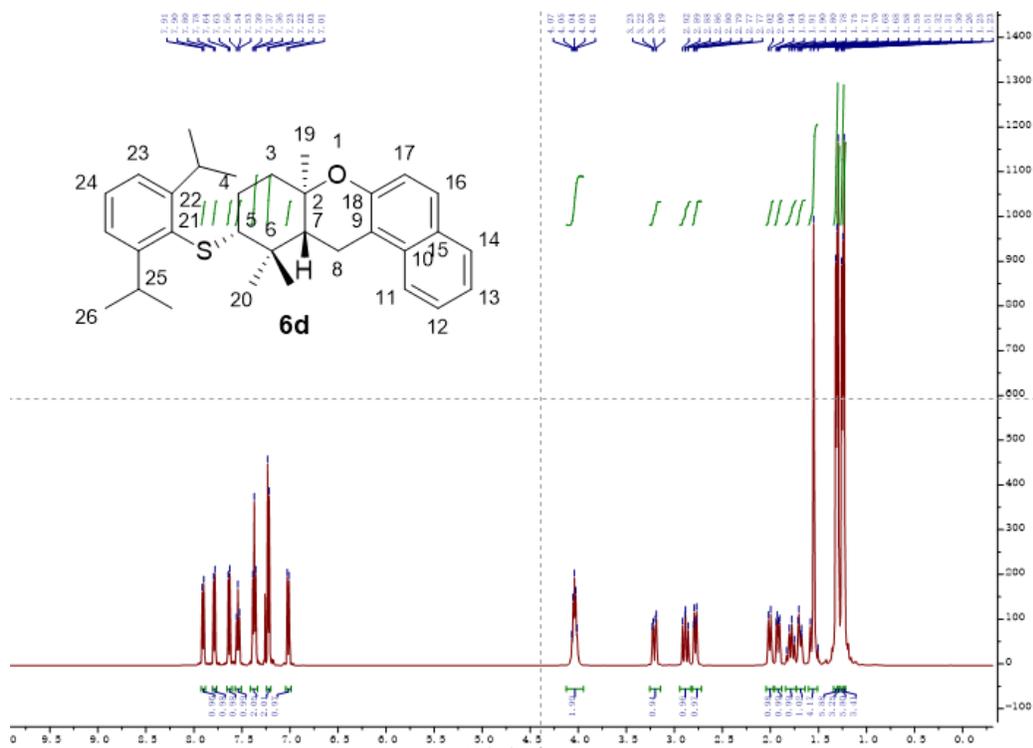
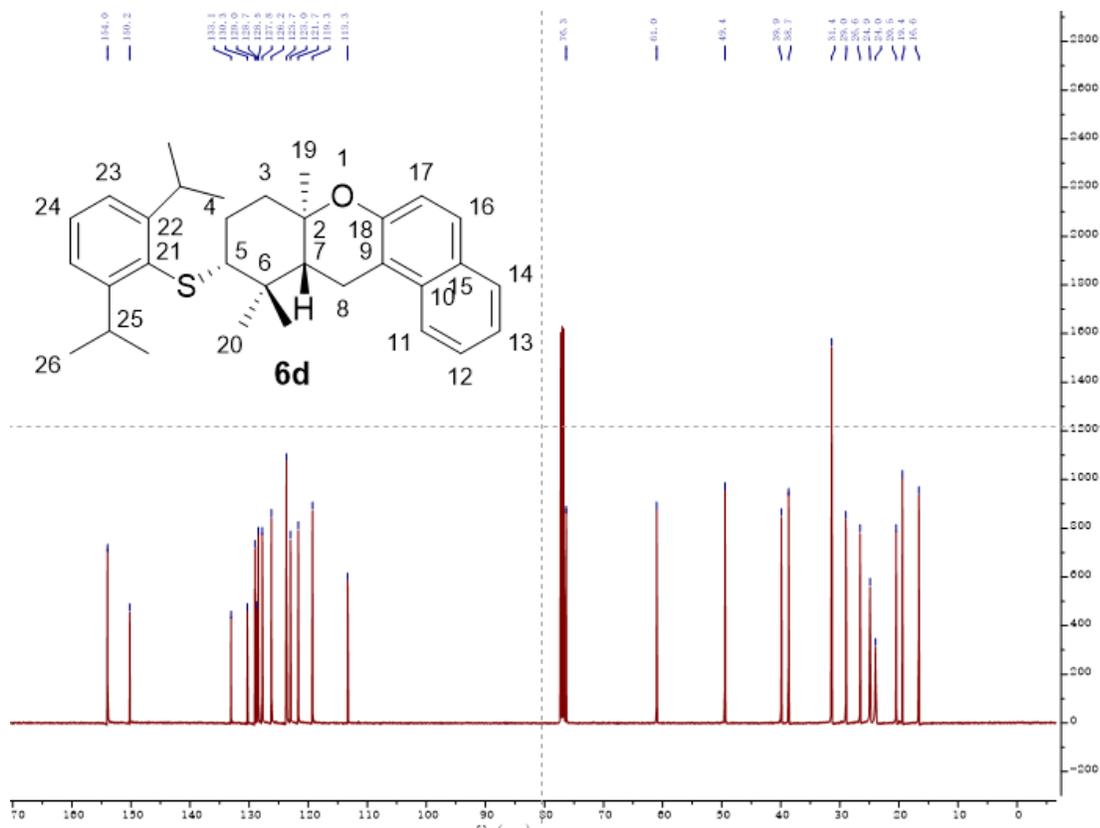
(±)-6b**(+)-6b**

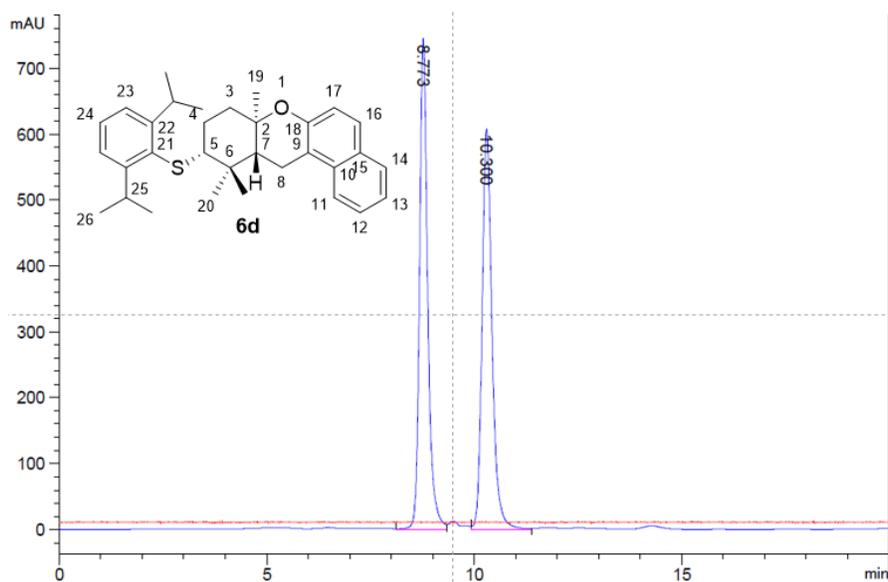
(±)-6c

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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2	6.988	VV	0.1736	2999.93433	275.56967	49.1542

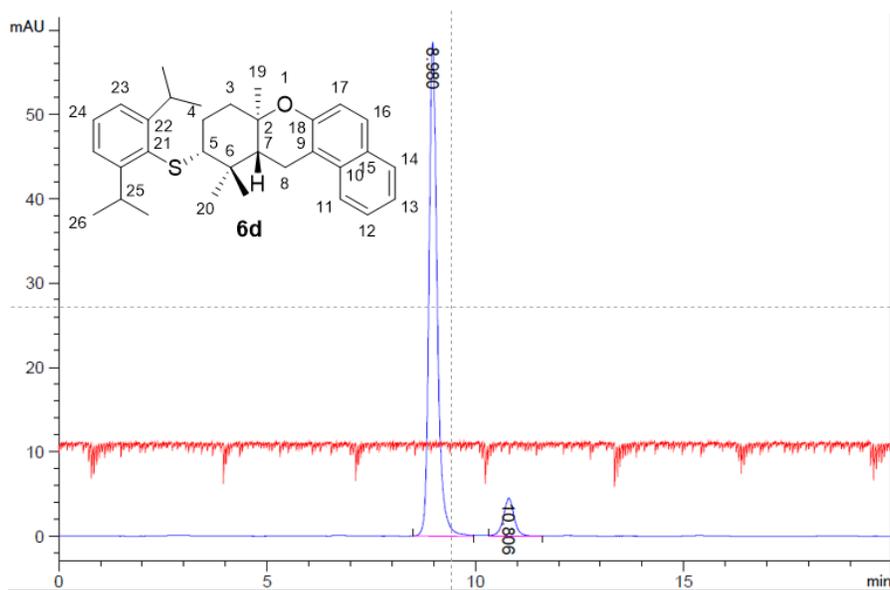
(+)-6c

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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2	8.029	VV	0.2248	177.93120	12.04333	8.3937

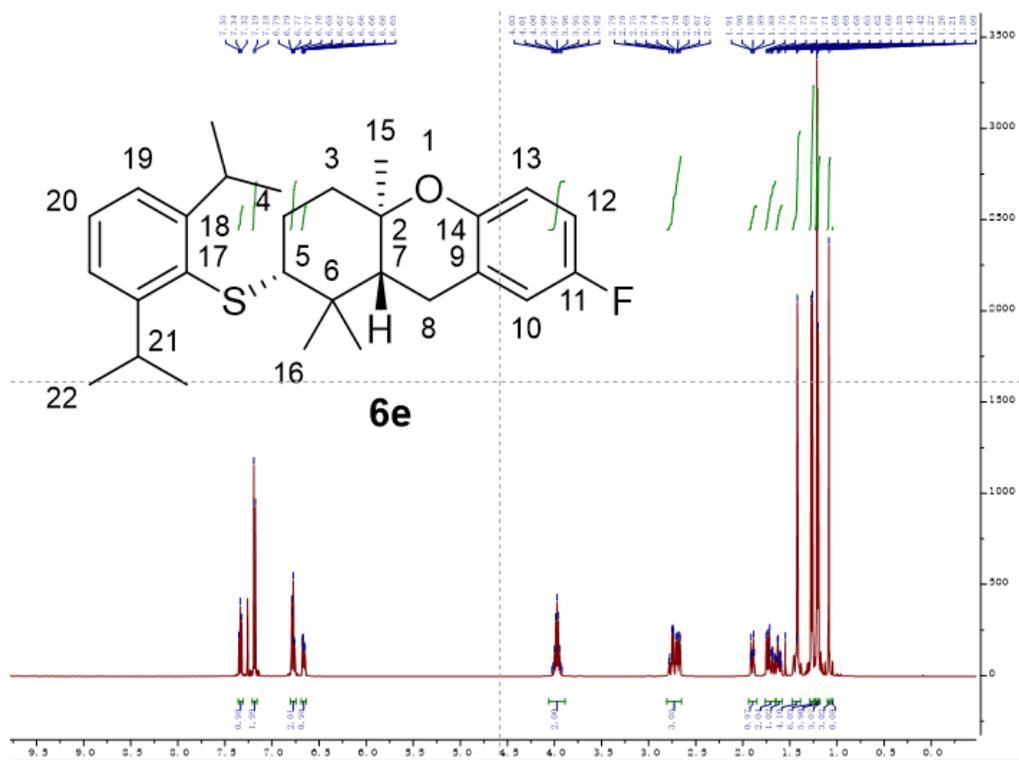
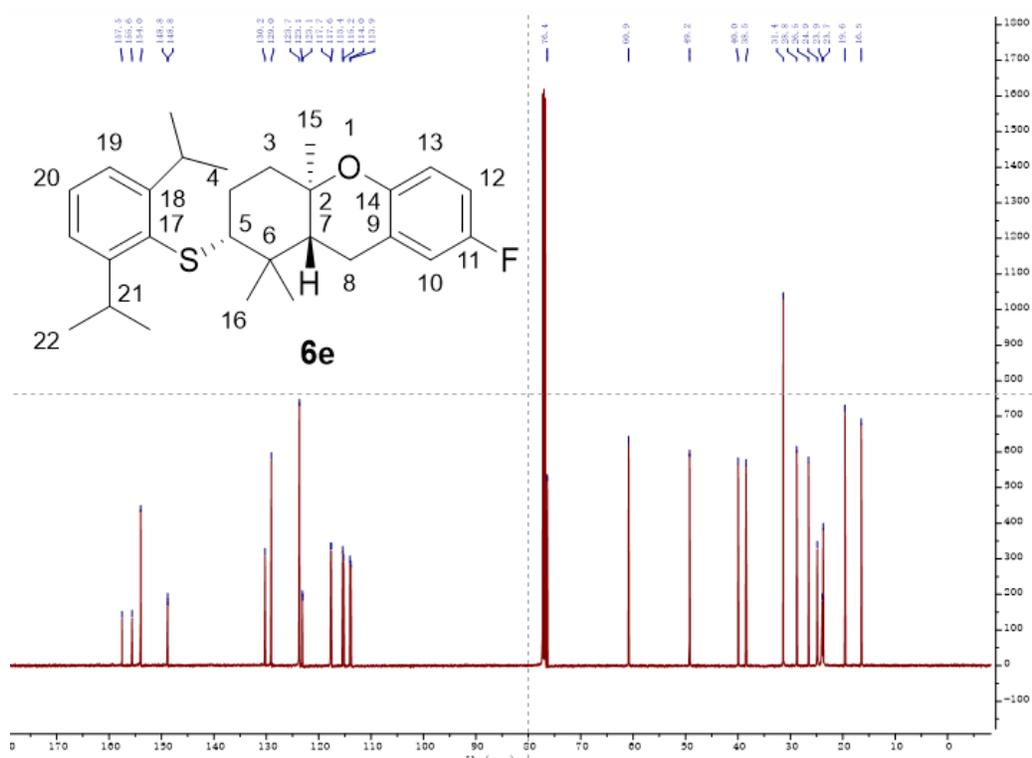
6d ^1H NMR (500 MHz, CDCl_3)**6d** ^{13}C NMR (126 MHz, CDCl_3)

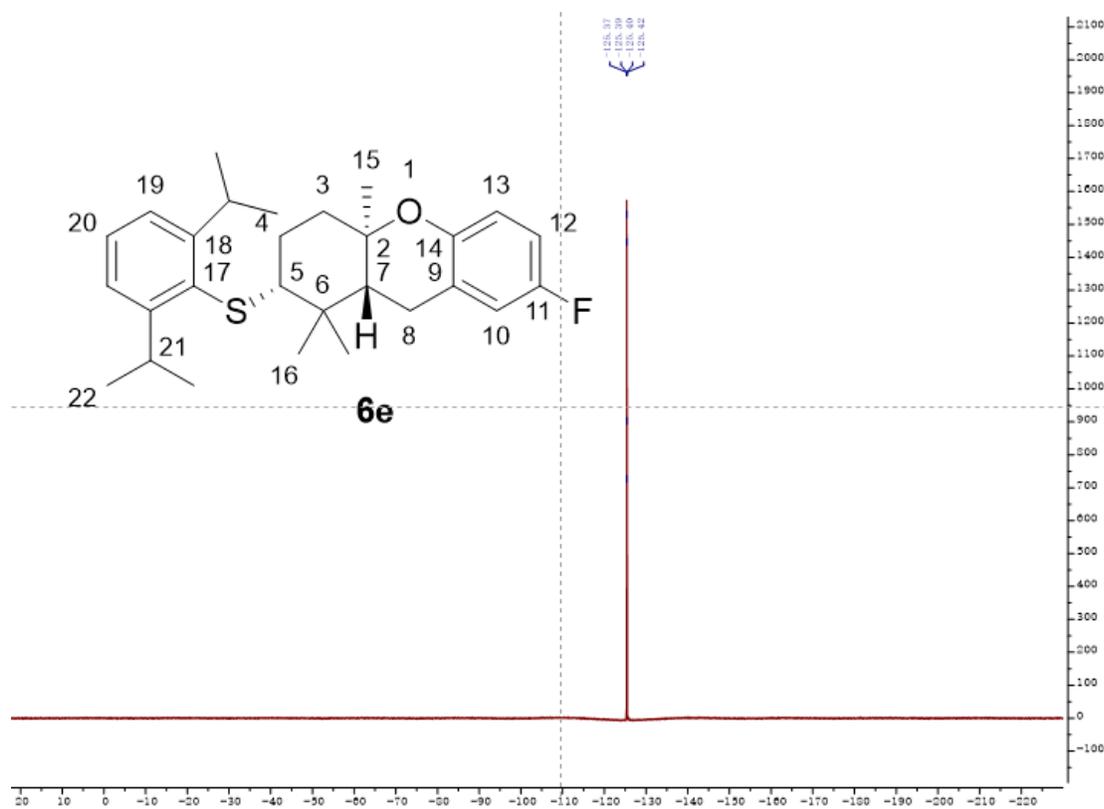
(±)-6d

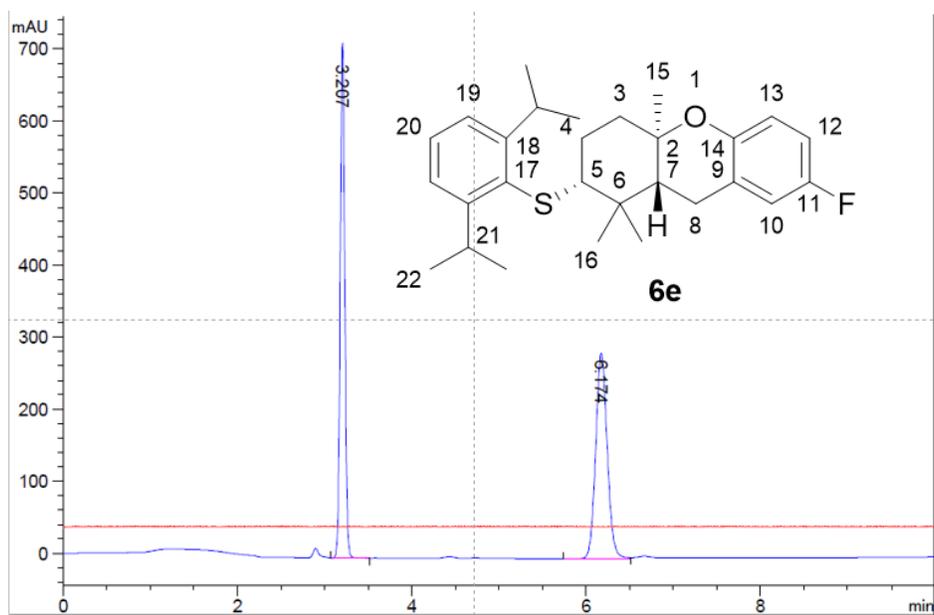
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.773	VV	0.2072	1.02190e4	742.49927	50.2334
2	10.300	VV	0.2530	1.01240e4	606.51965	49.7666

(+)-6d

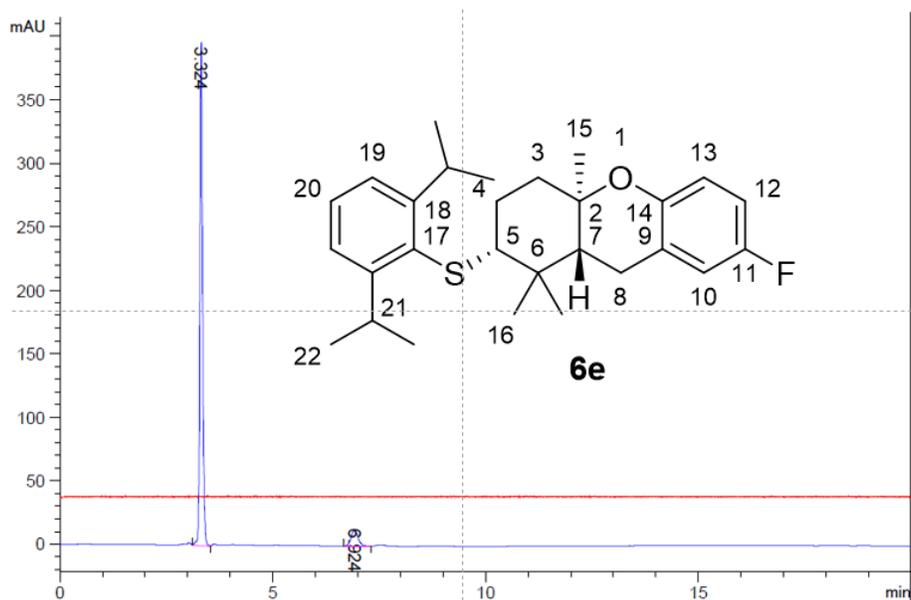
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.980	BV	0.2082	810.93048	58.55297	90.9057
2	10.806	VB	0.2747	81.12610	4.49412	9.0943

6e ^1H NMR (500 MHz, CDCl_3)**6e** ^{13}C NMR (126 MHz, CDCl_3)

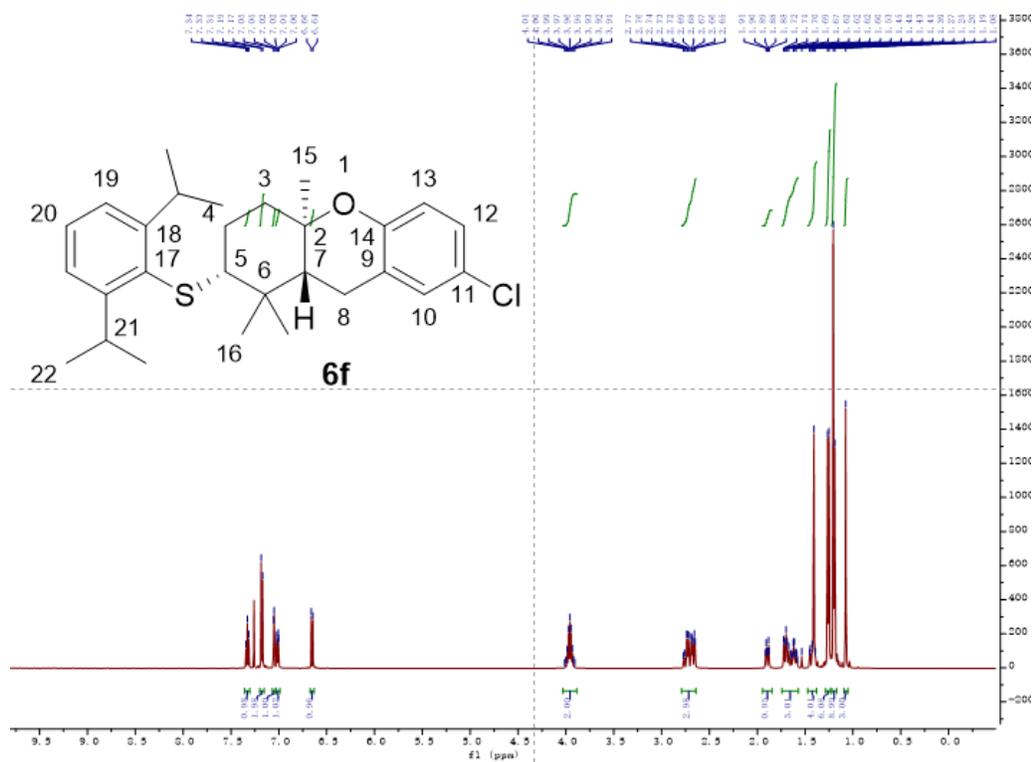
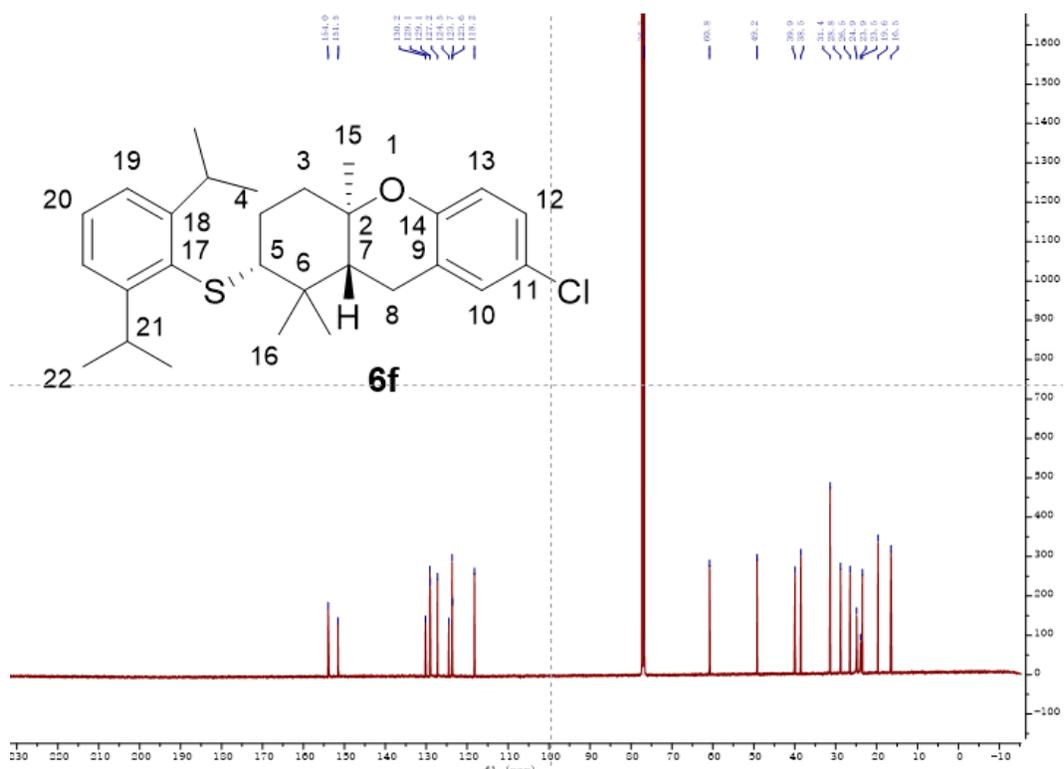
6e ^{19}F NMR (470 MHz, CDCl_3)

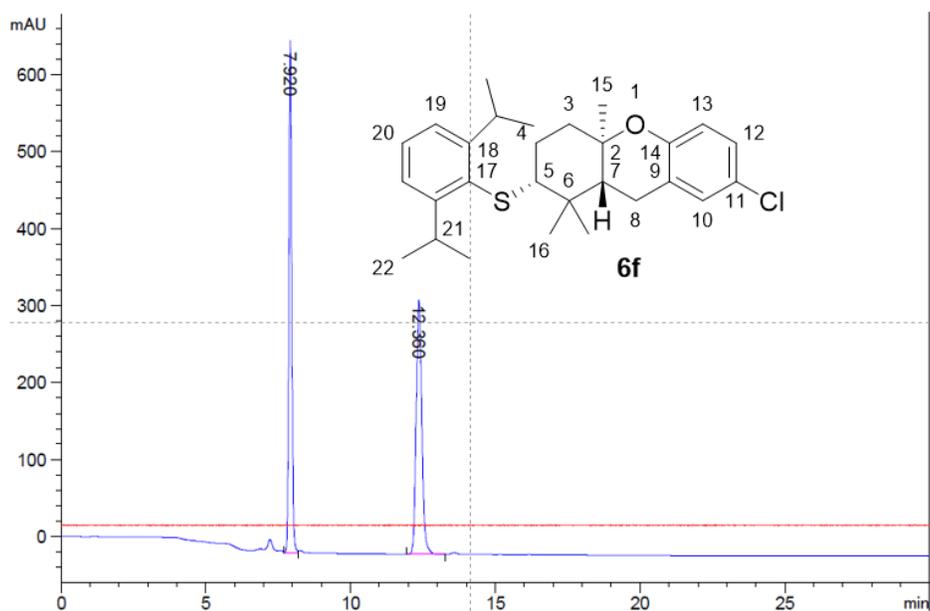
(±)-6e

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.207	VV	0.0615	2616.47559	693.19092	49.9111
2	6.174	VV	0.1431	2625.80005	283.18909	50.0889

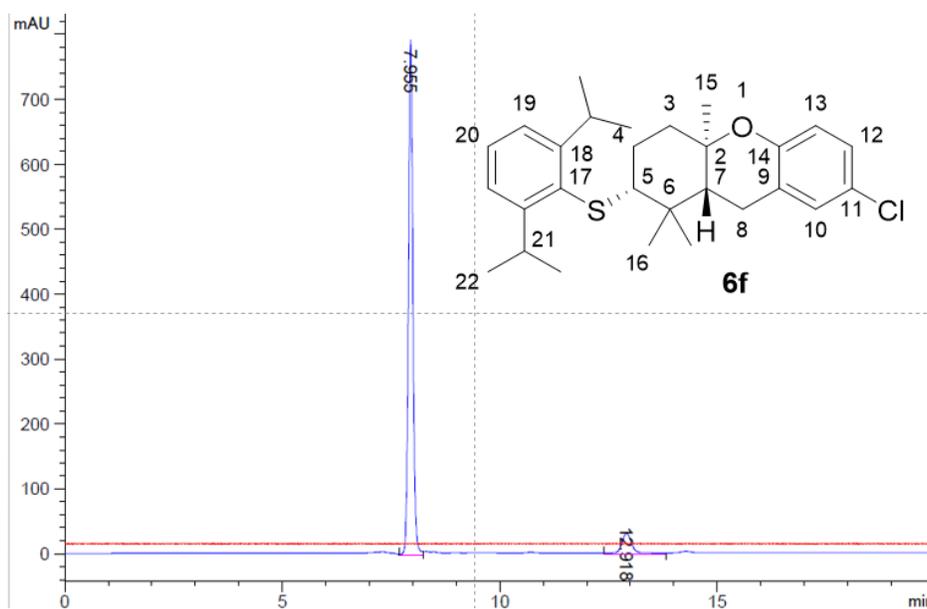
(+)-6e

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.324	VV	0.0704	1798.30688	396.50812	92.5075
2	6.924	BV	0.1750	145.65131	12.80092	7.4925

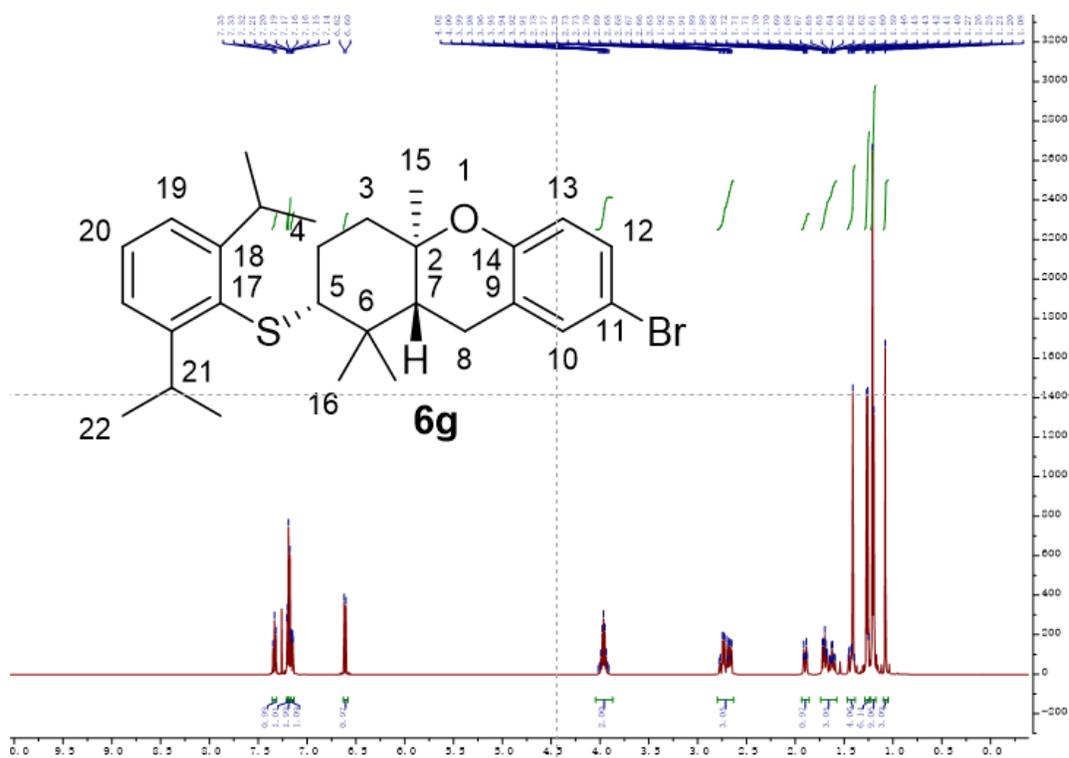
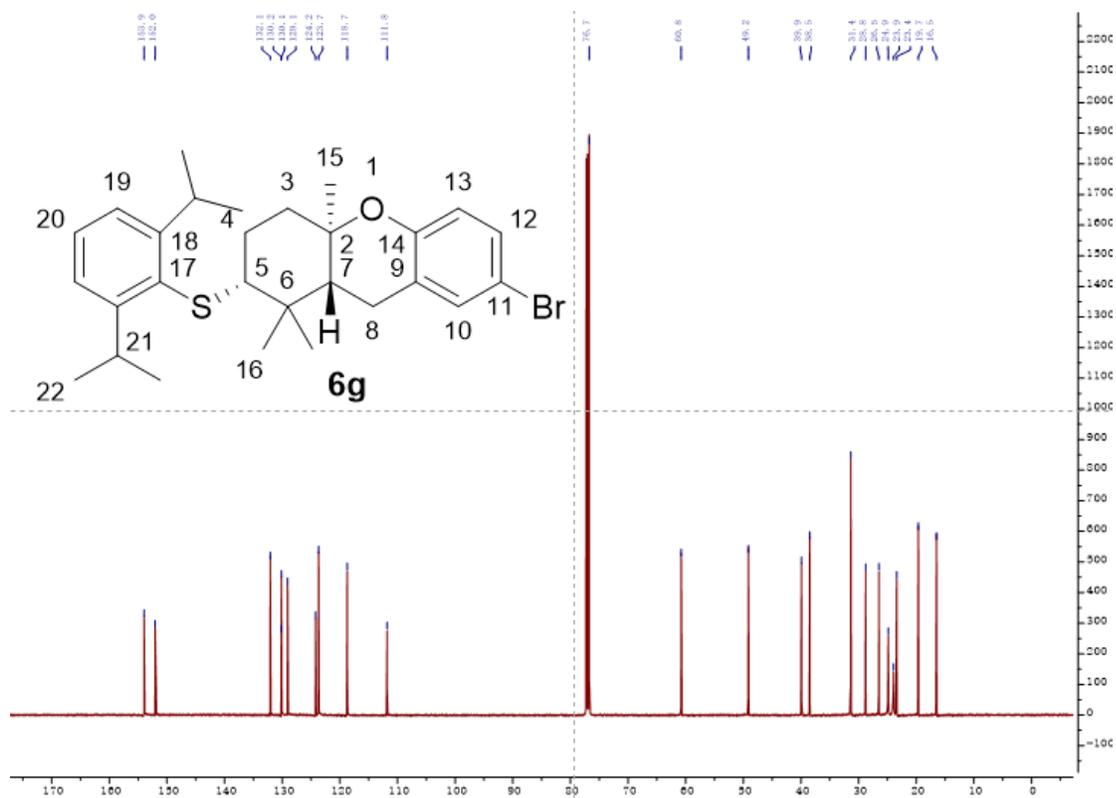
6f ^1H NMR (500 MHz, CDCl_3)**6f** ^{13}C NMR (126 MHz, CDCl_3)

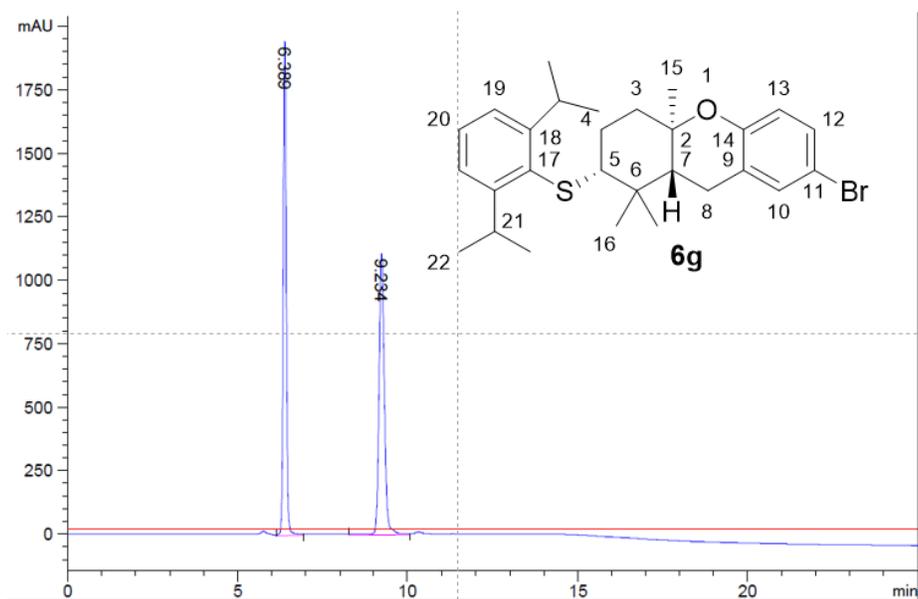
(±)-6f

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.920	VV	0.1044	4568.40332	657.46143	50.3245
2	12.360	VV	0.2118	4509.48291	330.18918	49.6755

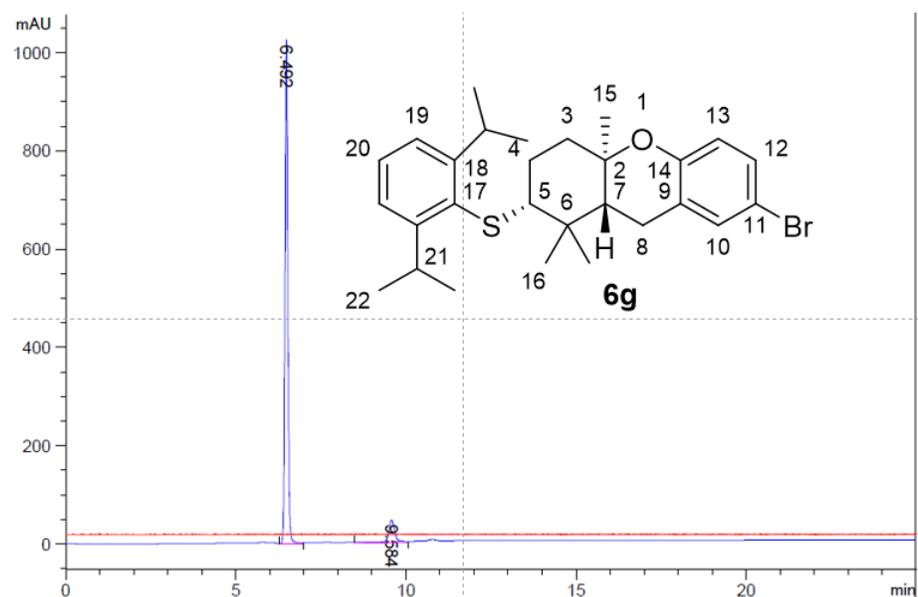
(+)-6f

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.955	VV	0.1127	5634.00684	786.25110	90.8464
2	12.918	VV	0.2597	567.67603	31.94572	9.1536

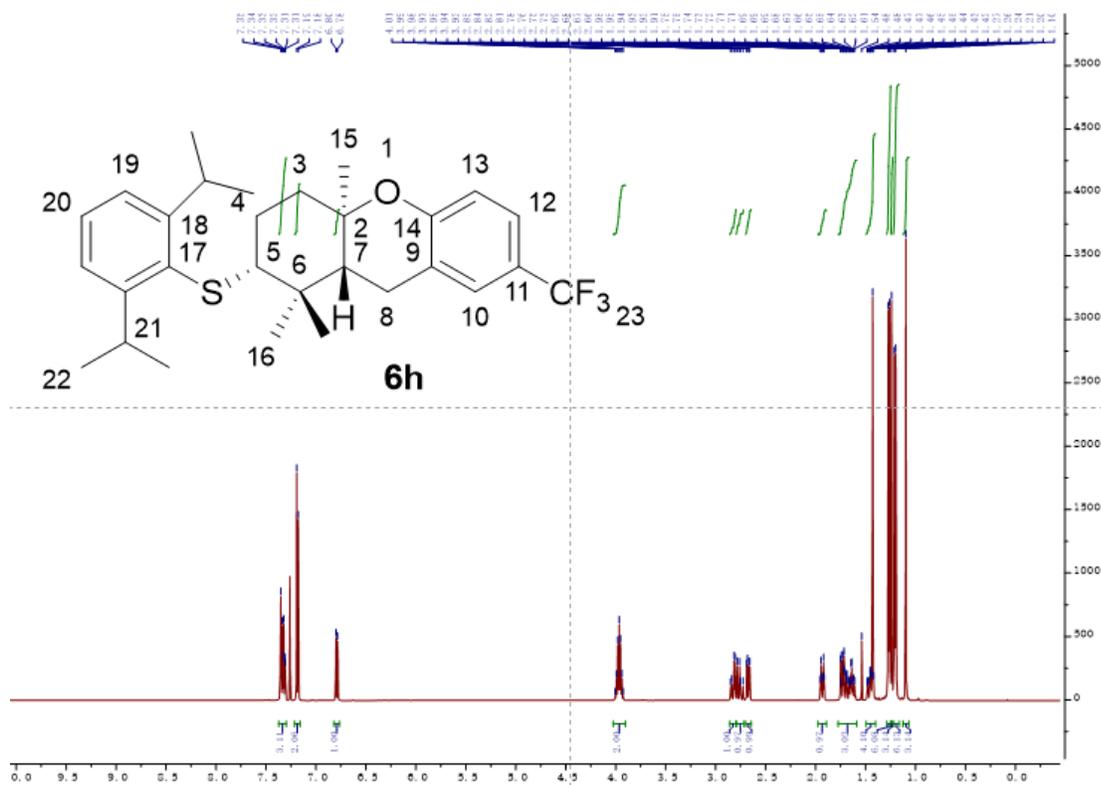
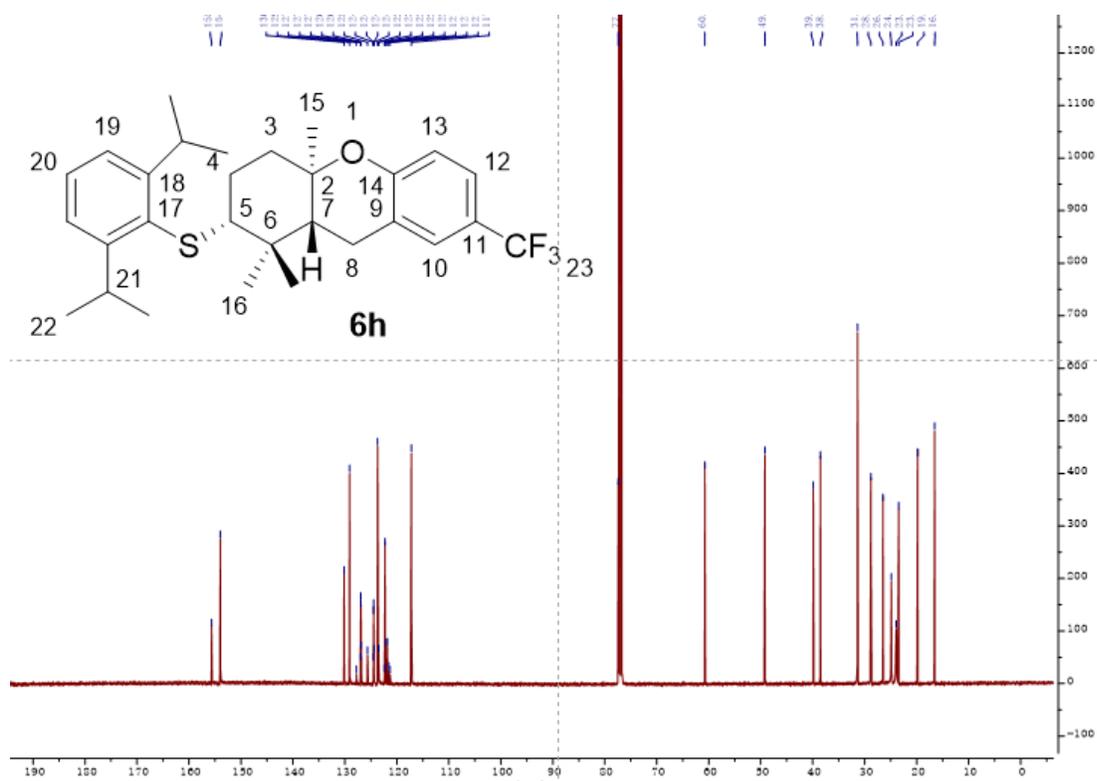
6g ^1H NMR (500 MHz, CDCl_3)**6g** ^{13}C NMR (126 MHz, CDCl_3)

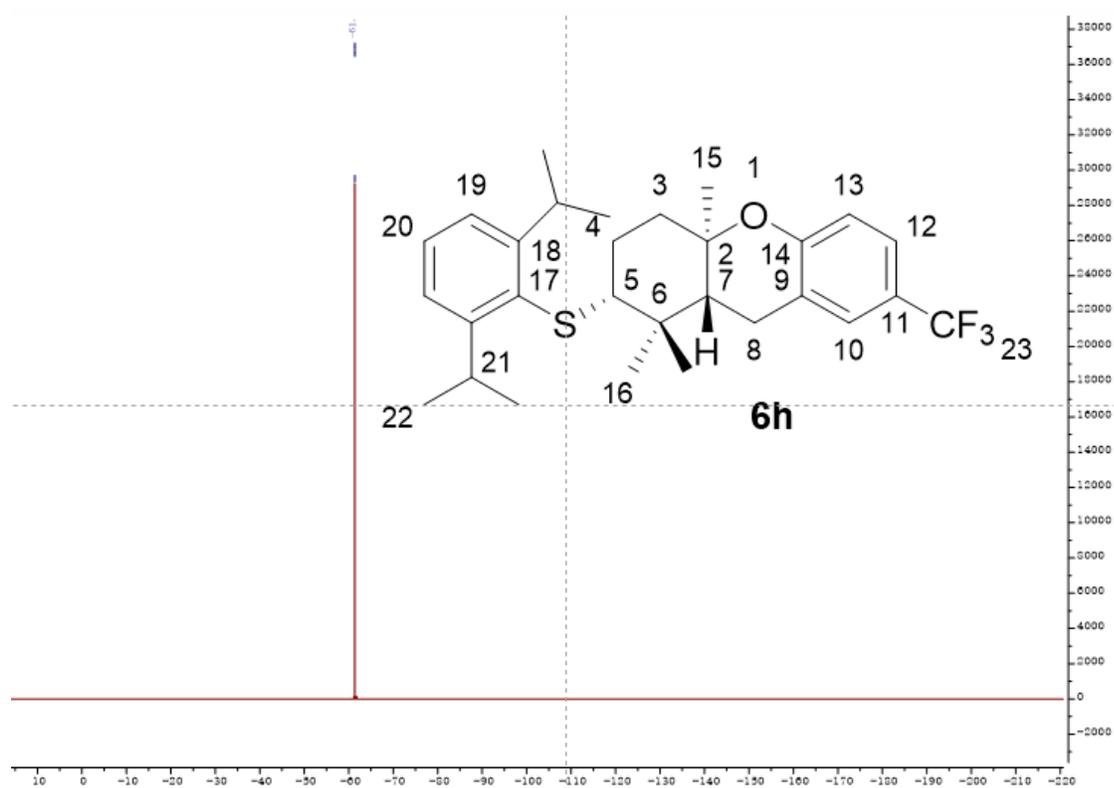
(±)-6g

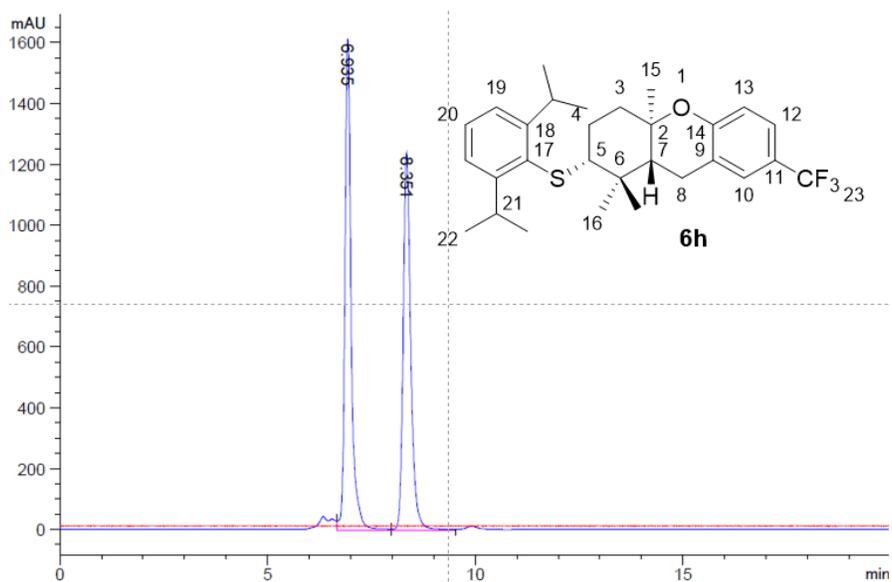
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.389	VB	0.0978	1.19253e4	1944.42639	49.3302
2	9.234	VV	0.1699	1.22491e4	1106.80811	50.6698

(+)-6g

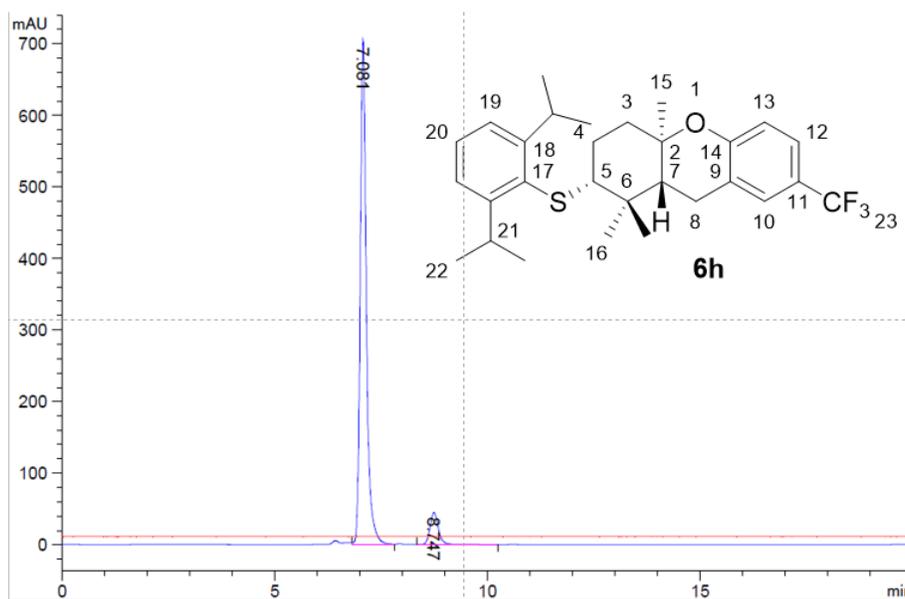
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.492	VV	0.0910	5948.37451	1024.39087	89.9027
2	9.584	VV	0.2125	668.08563	46.17598	10.0973

6h ^1H NMR (500 MHz, CDCl_3)**6h** ^{13}C NMR (126 MHz, CDCl_3)

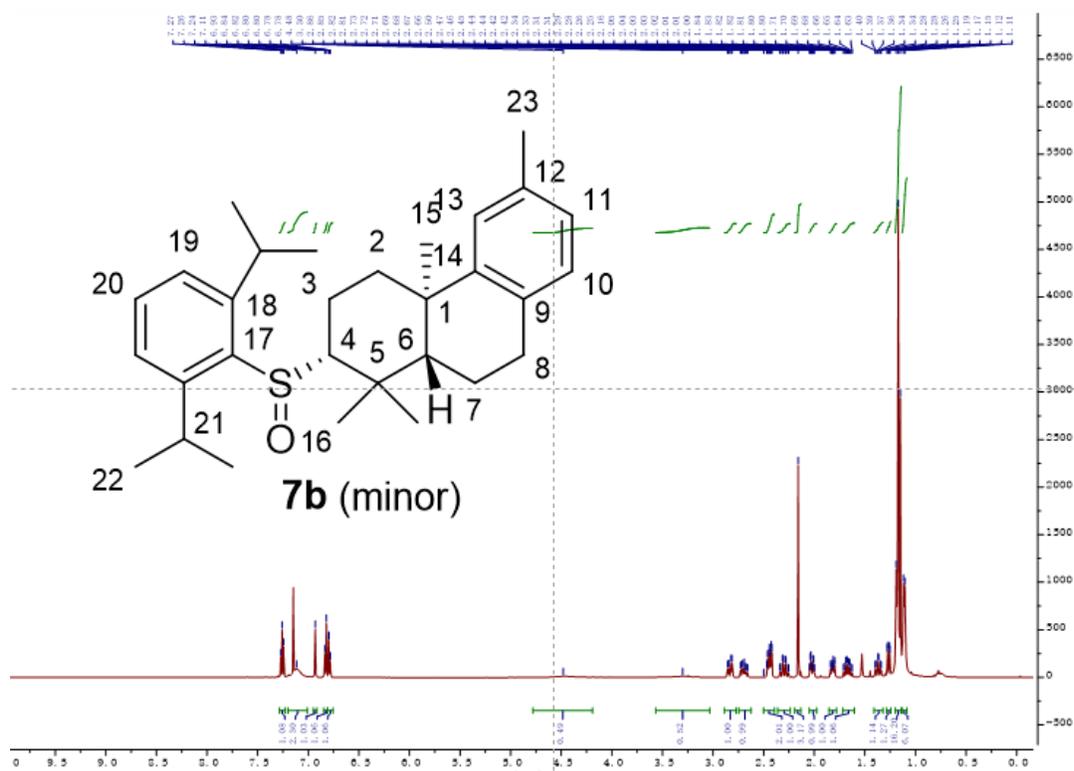
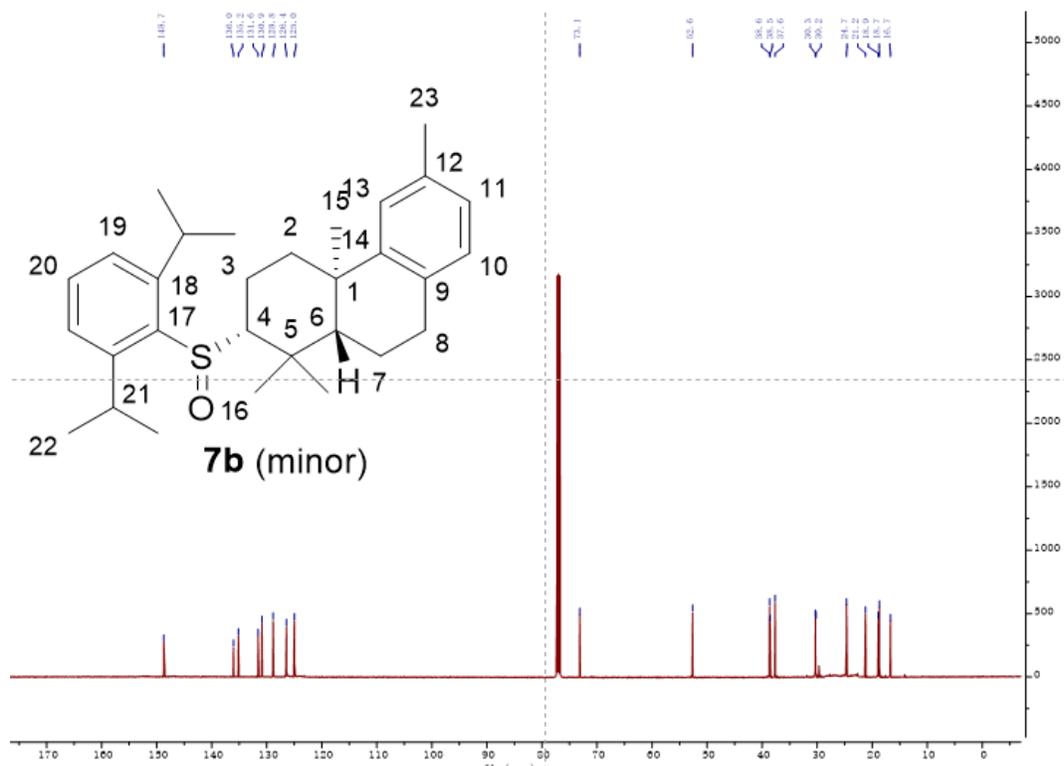
6h ^{19}F NMR (470 MHz, CDCl_3)

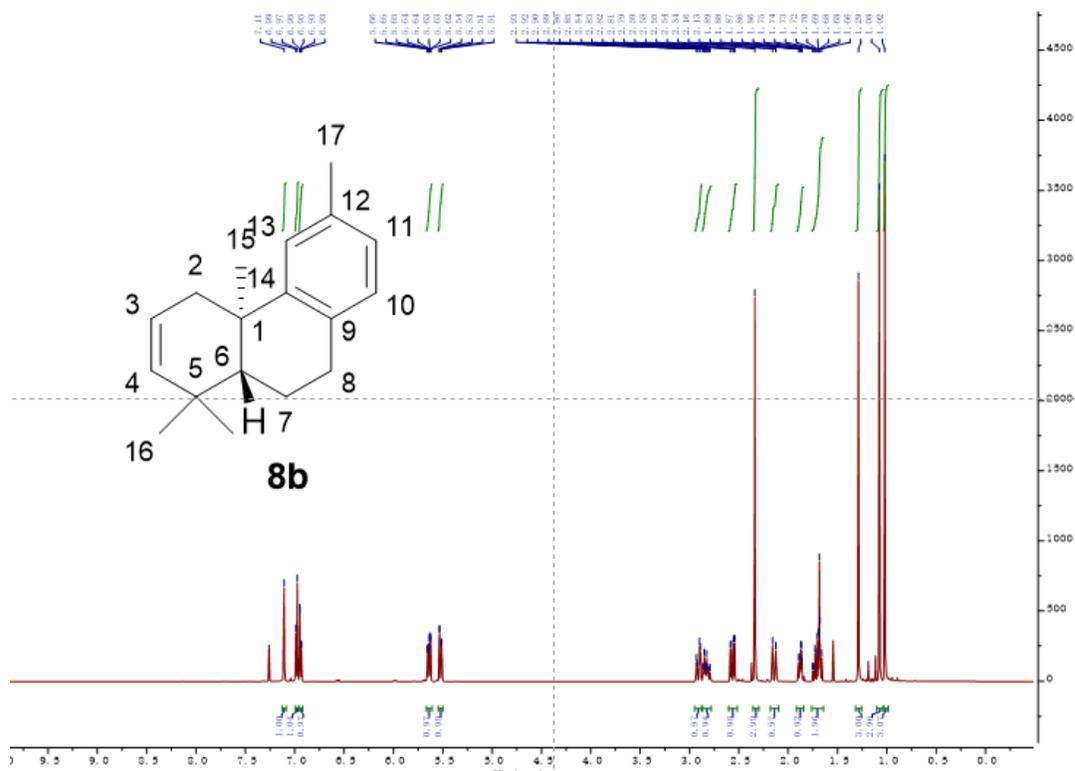
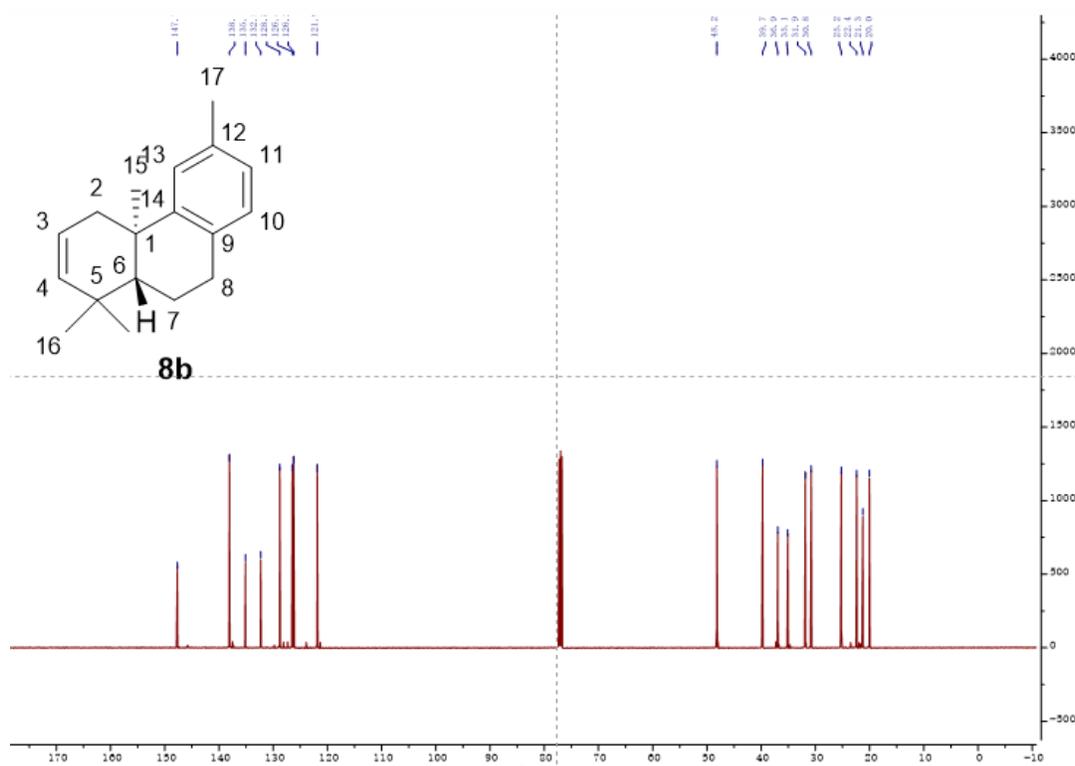
(±)-6h

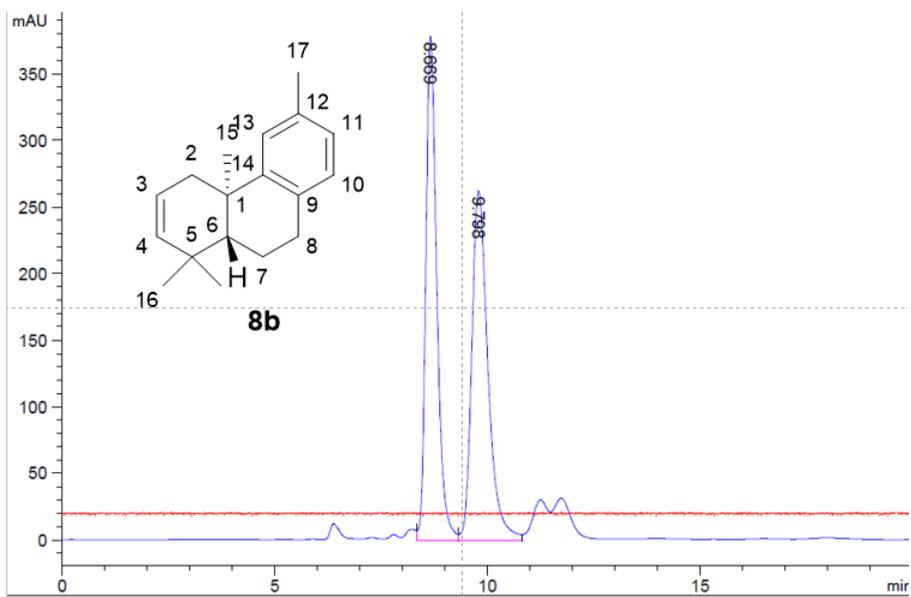
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.935	VV	0.1524	1.66398e4	1612.78931	51.3699
2	8.351	VV	0.1918	1.57523e4	1240.62512	48.6301

(+)-6h

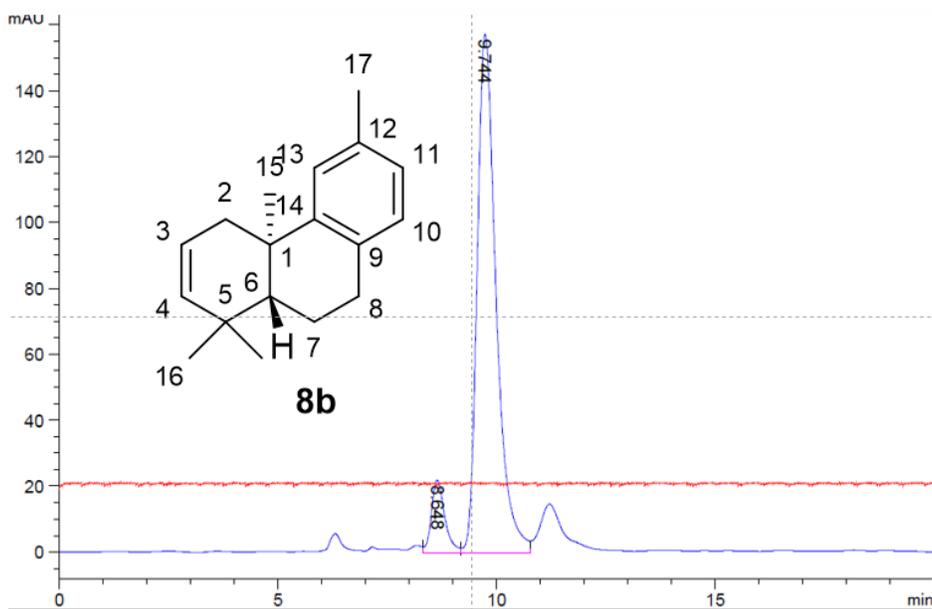
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.081	VV	0.1526	7081.84668	702.33289	91.6231
2	8.747	VB	0.2198	647.47888	45.13220	8.3769

7b'' (minor) ^1H NMR (500 MHz, CDCl_3)**7b''** (minor) ^{13}C NMR (126 MHz, CDCl_3)

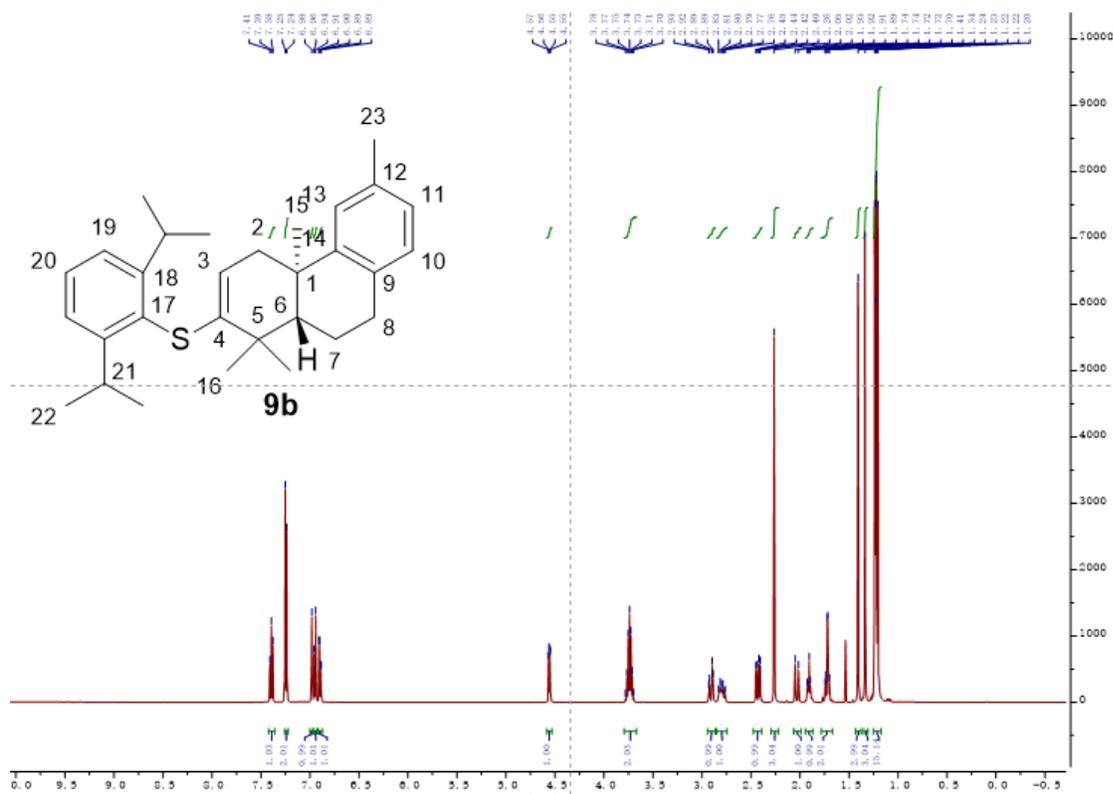
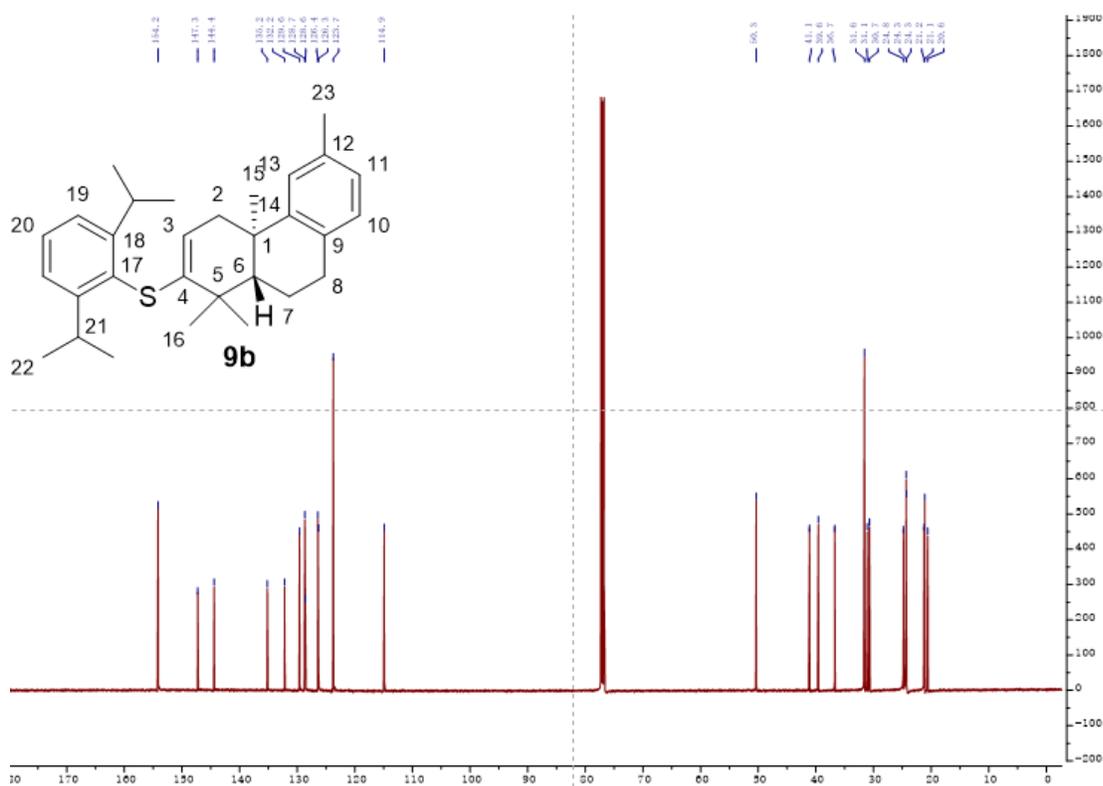
8b ^1H NMR (500 MHz, CDCl_3)**8b** ^{13}C NMR (126 MHz, CDCl_3)

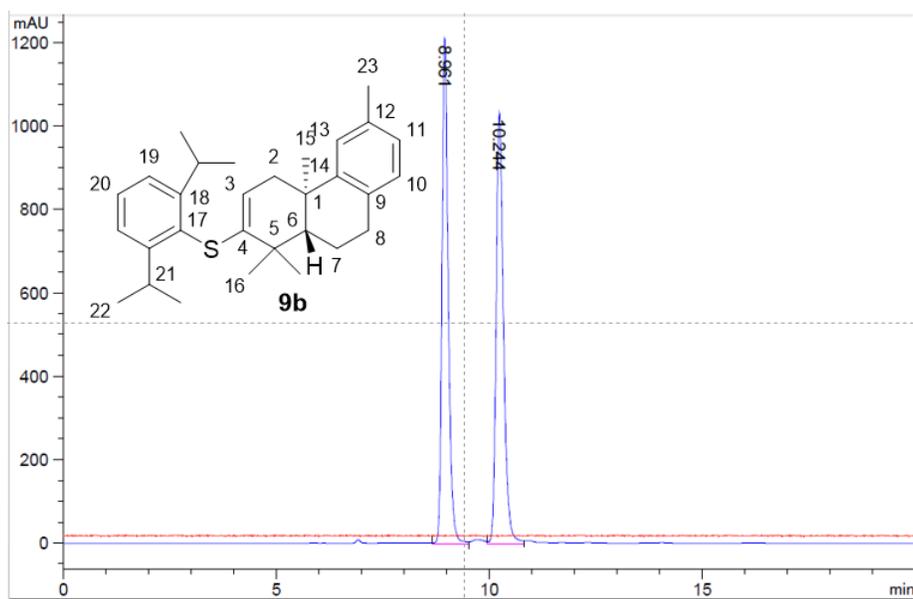
(±)-8b

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.669	VV	0.2734	6781.08740	377.87836	49.5233
2	9.798	VV	0.4009	6911.63525	262.01392	50.4767

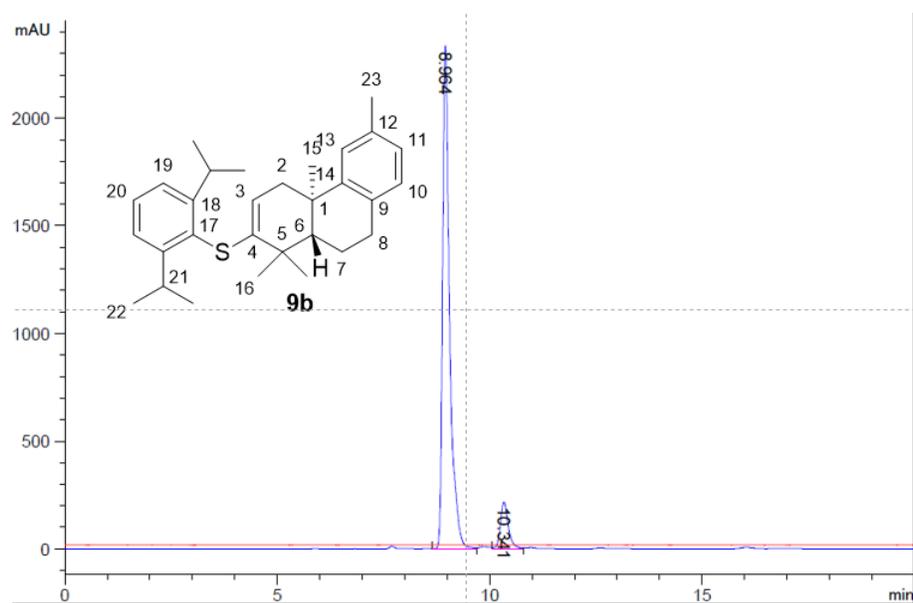
(-)-8b

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.648	VV	0.3234	465.70331	21.93658	8.9564
2	9.744	VV	0.4559	4733.97412	157.30193	91.0436

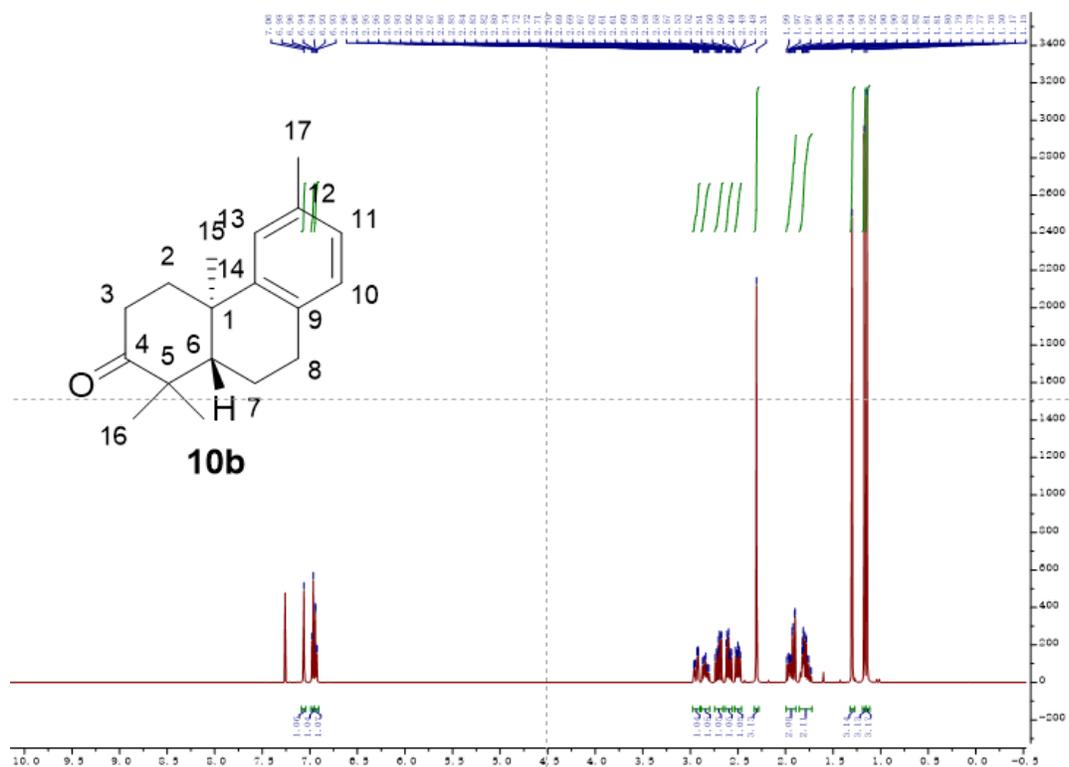
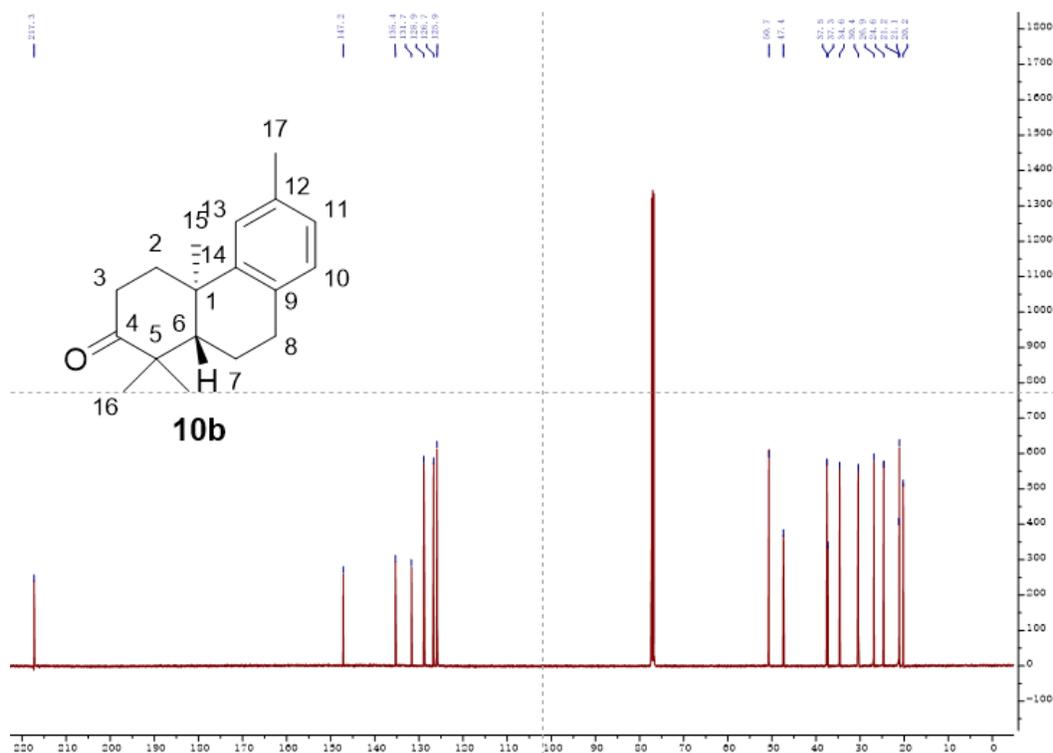
9b ^1H NMR (500 MHz, CDCl_3)**9b** ^{13}C NMR (126 MHz, CDCl_3)

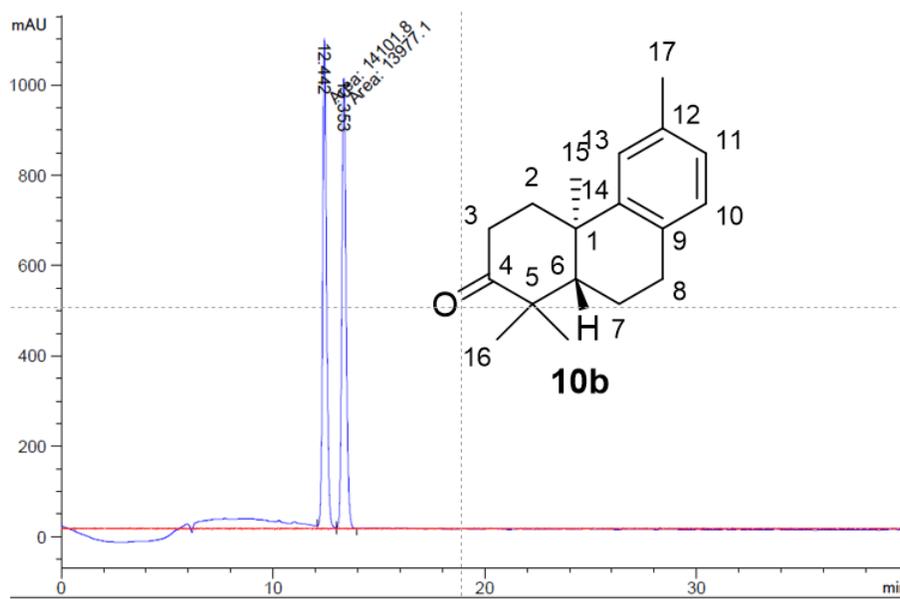
(±)-9b

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.961	VV	0.1599	1.23320e4	1207.27563	49.8707
2	10.244	VV	0.1809	1.23960e4	1031.72583	50.1293

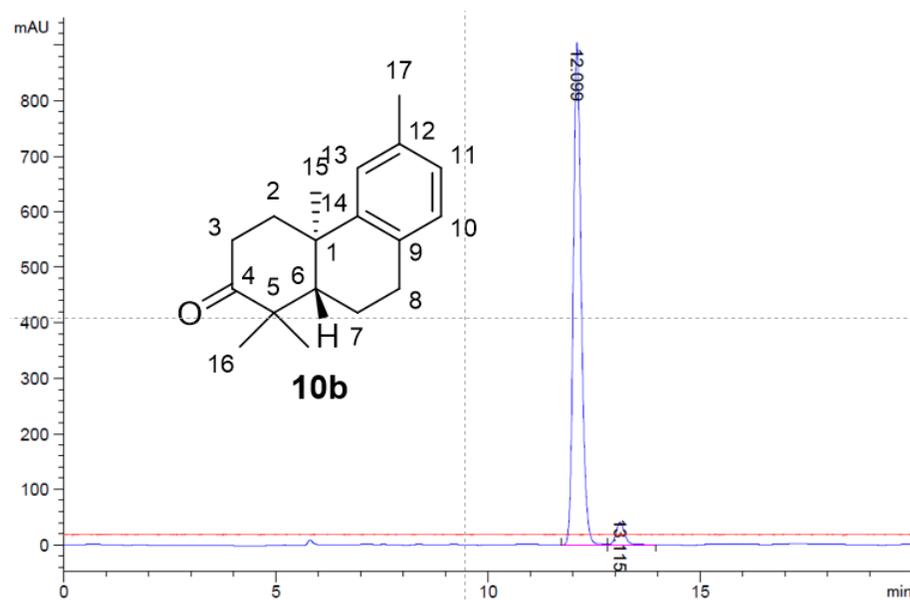
(-)-9b

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.964	VV	0.1692	2.68257e4	2331.97656	90.4003
2	10.341	VV	0.1998	2848.63989	216.90831	9.5997

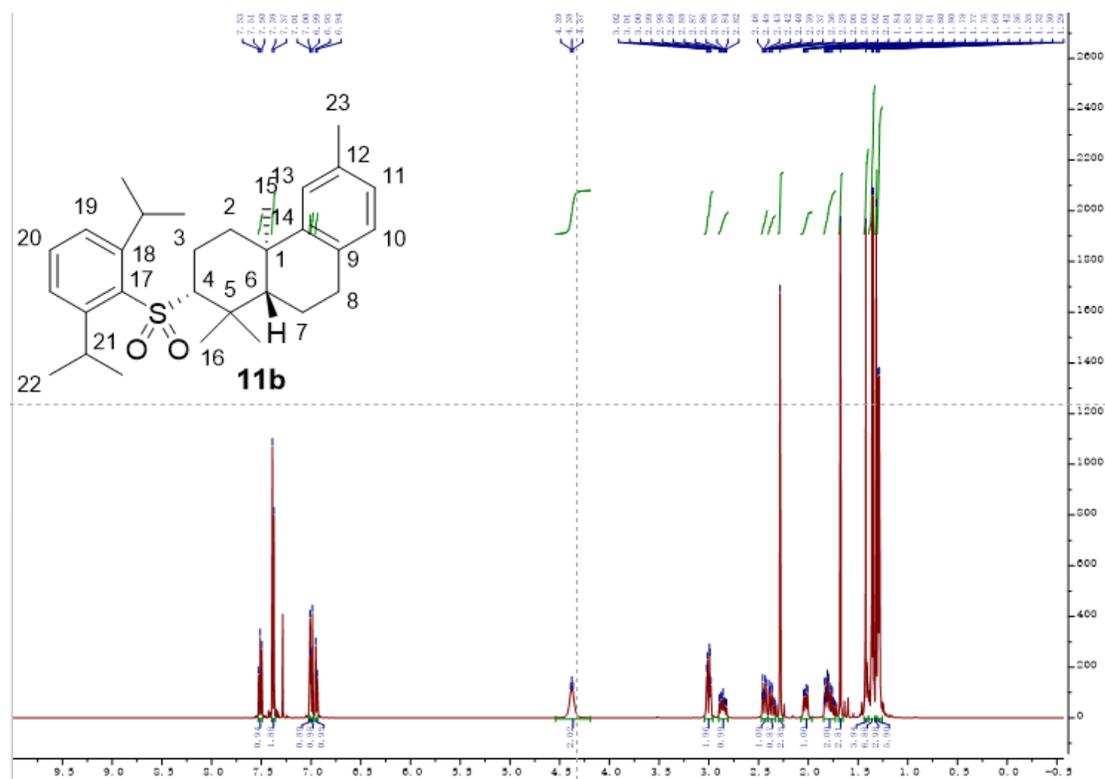
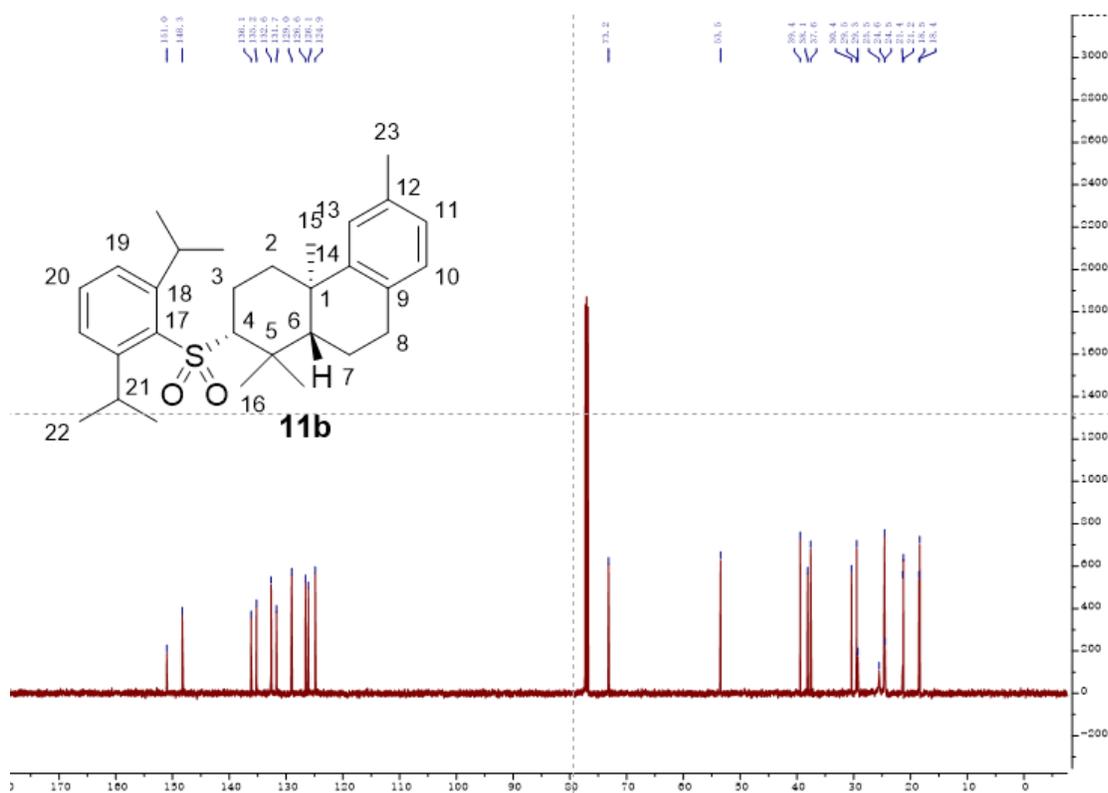
10b ^1H NMR (500 MHz, CDCl_3)**10b** ^{13}C NMR (126 MHz, CDCl_3)

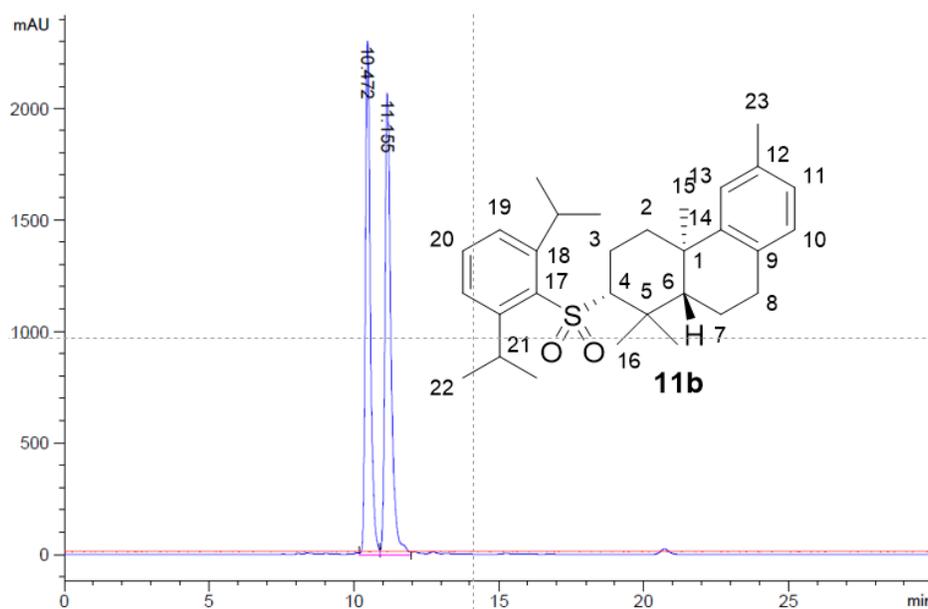
(±)-10b

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.442	MF	0.2161	1.41018e4	1087.49597	50.2222
2	13.353	FM	0.2319	1.39771e4	1004.59656	49.7778

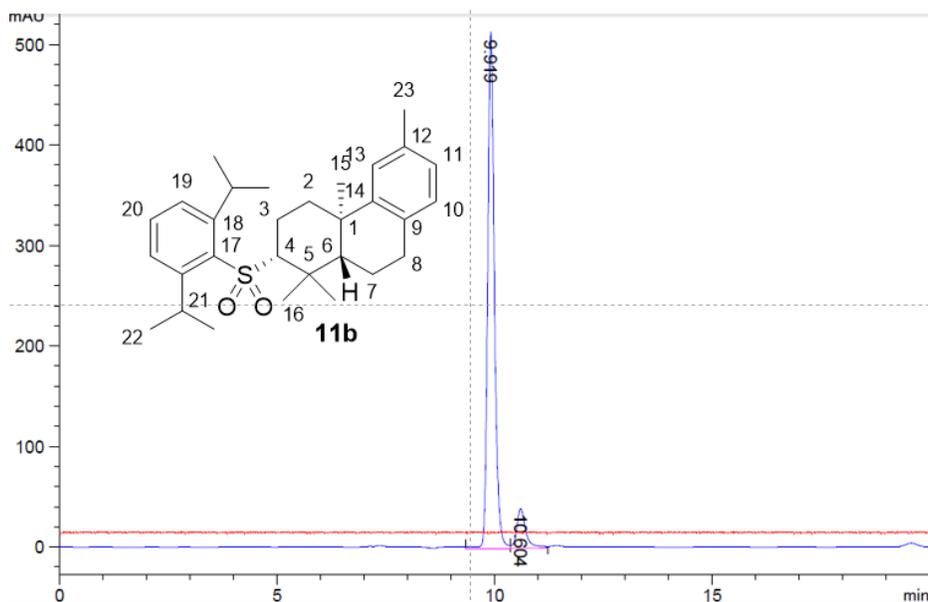
(-)-10b

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.099	VV	0.1991	1.18061e4	903.00348	94.7911
2	13.115	VV	0.2336	648.76794	41.76496	5.2089

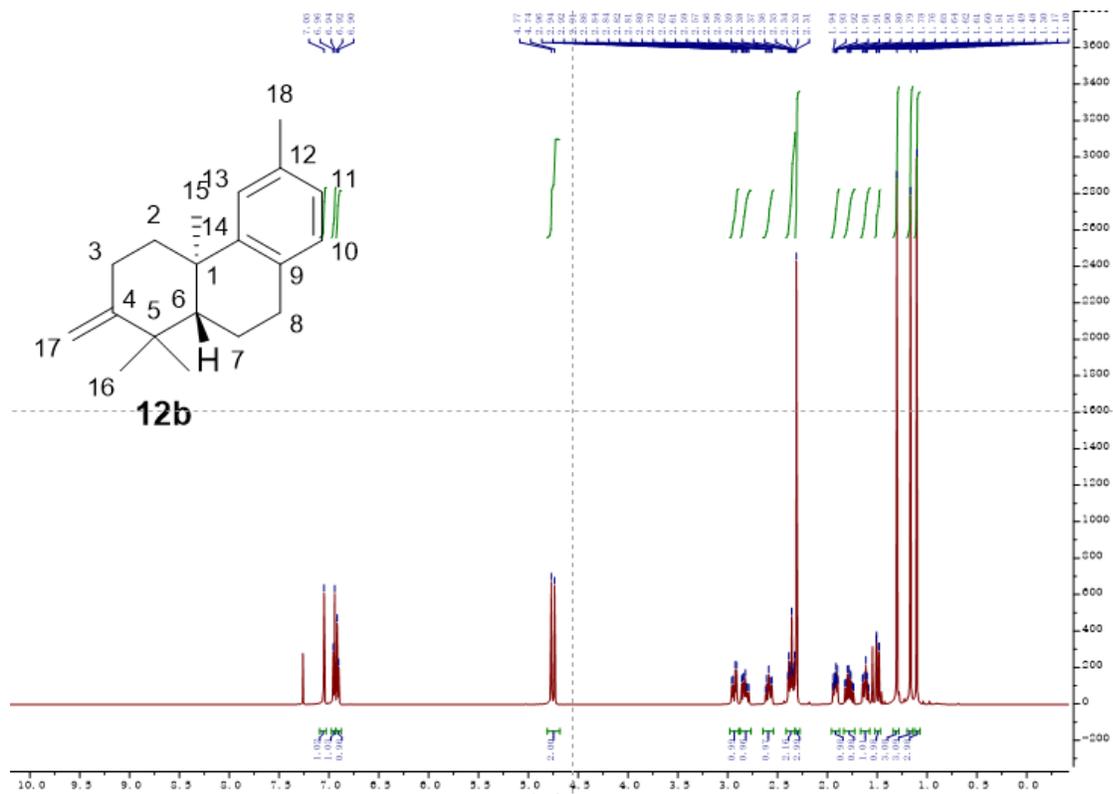
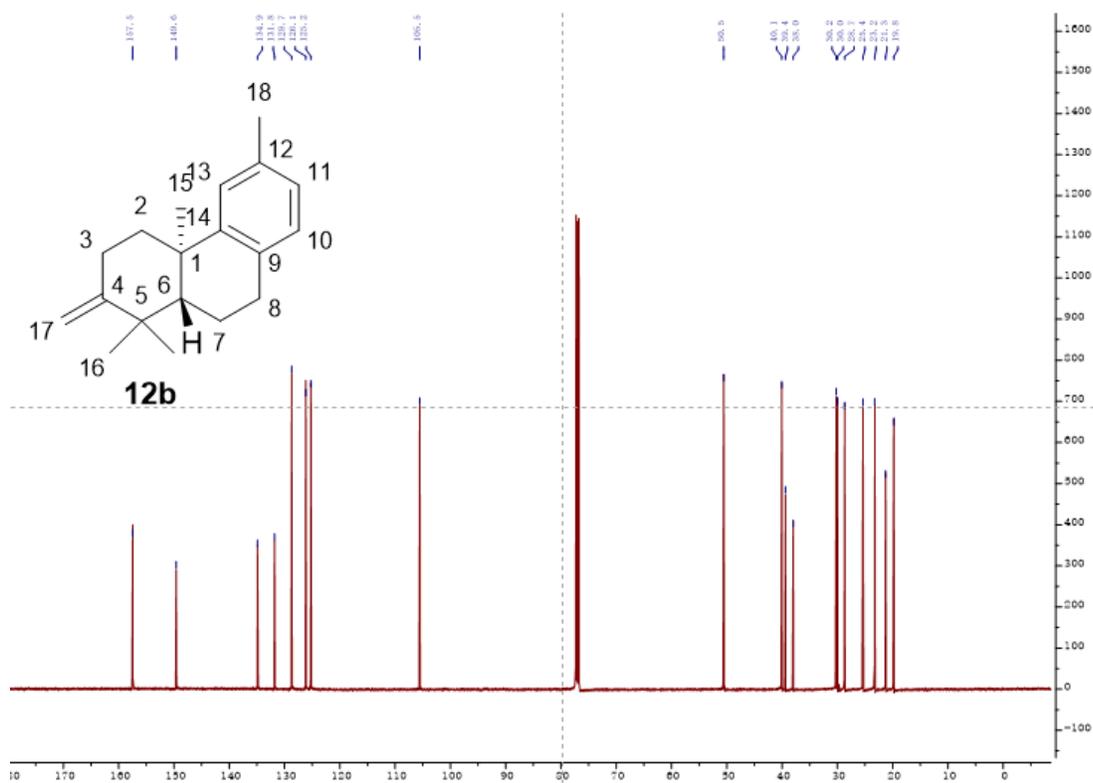
11b ^1H NMR (500 MHz, CDCl_3)**11b** ^{13}C NMR (126 MHz, CDCl_3)

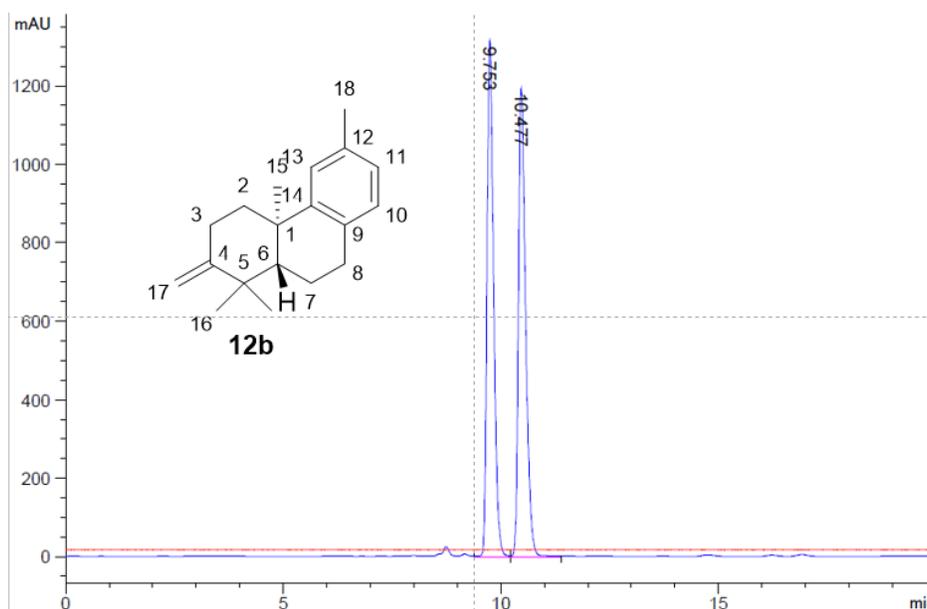
(±)-11b

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.472	VV	0.1891	2.81122e4	2301.87378	48.4818
2	11.155	VV	0.2185	2.98729e4	2062.57642	51.5182

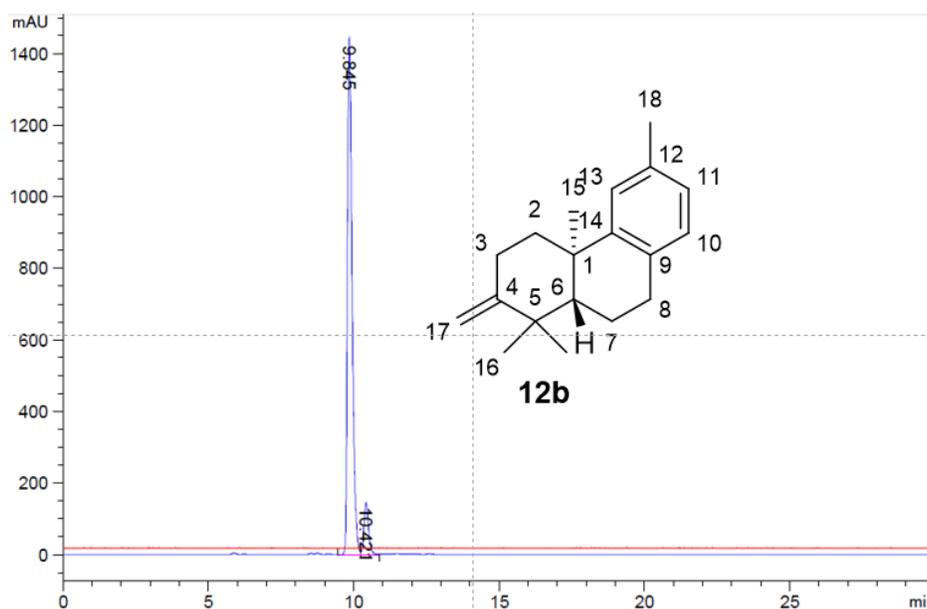
(-)-11b

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.919	VV	0.1604	5498.29150	511.47217	90.5783
2	10.604	VV	0.2160	571.91711	39.37973	9.4217

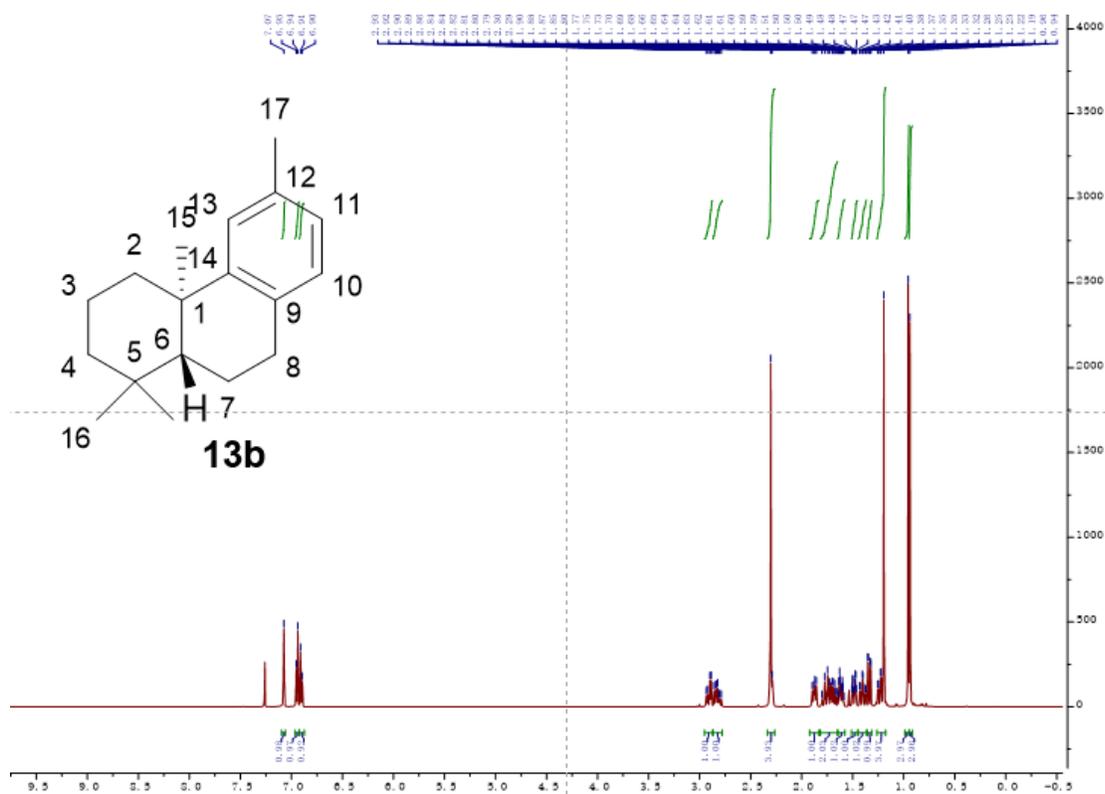
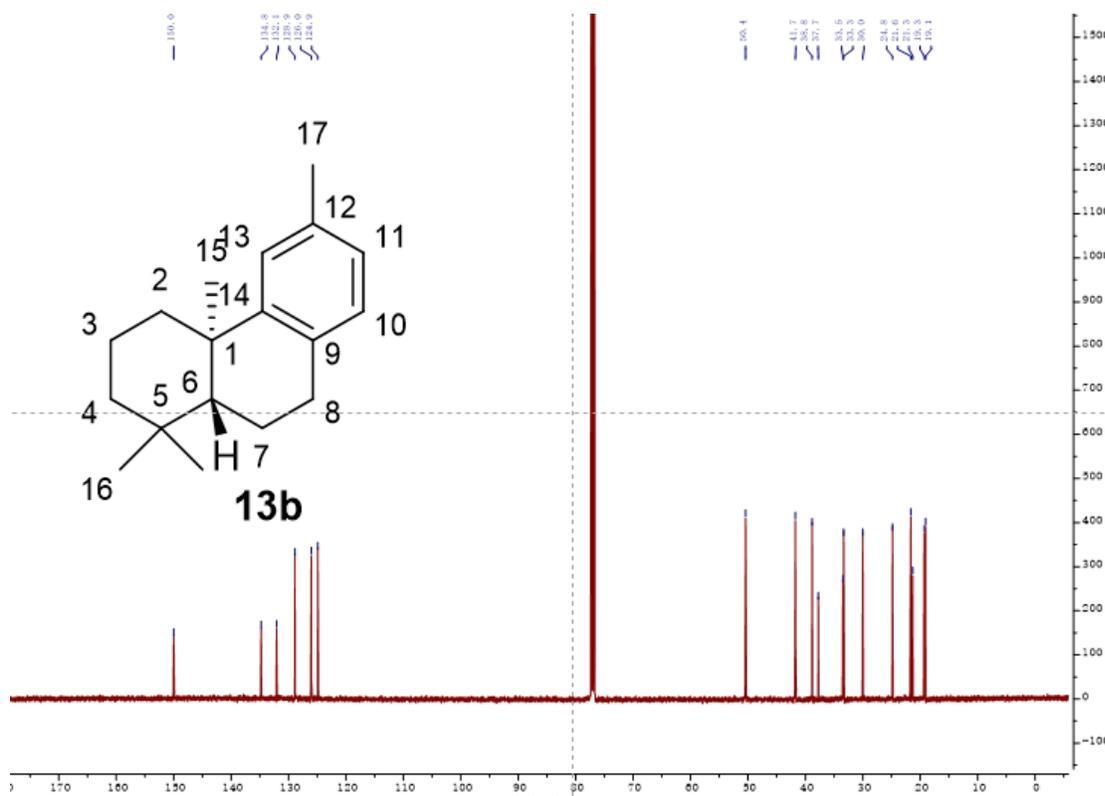
12b ^1H NMR (500 MHz, CDCl_3)**12b** ^{13}C NMR (126 MHz, CDCl_3)

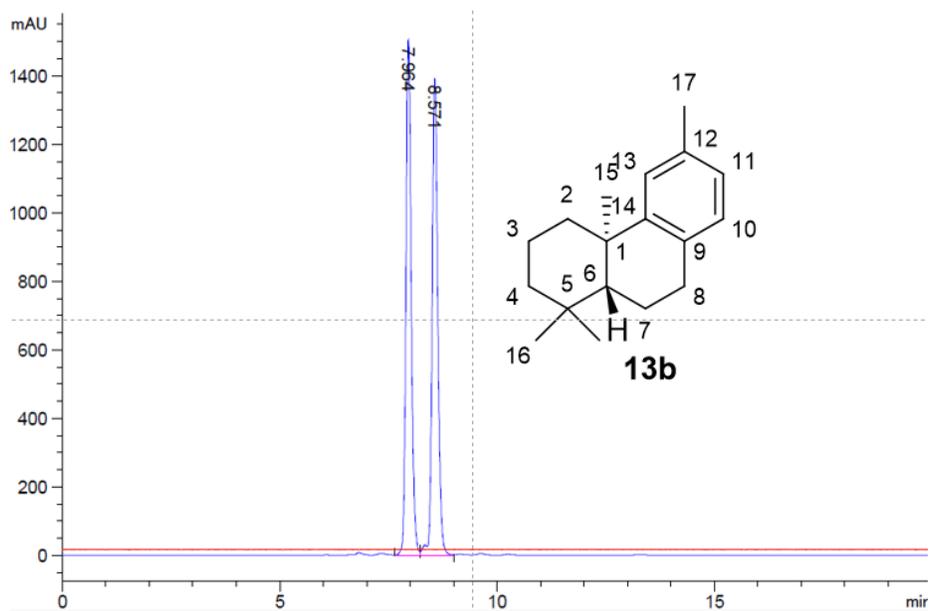
(±)-12b

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.753	VV	0.1637	1.38370e4	1313.35962	50.0046
2	10.477	VV	0.1758	1.38345e4	1195.11670	49.9954

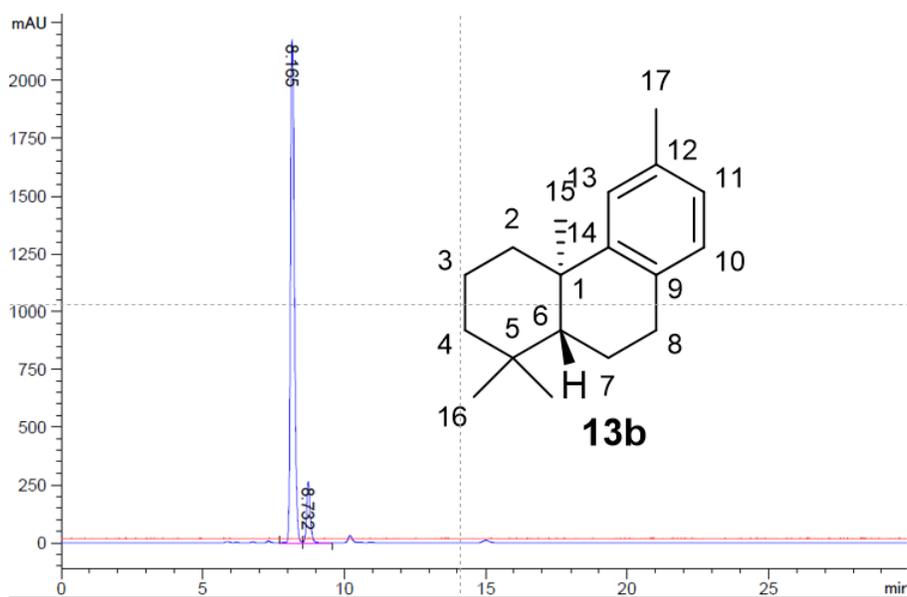
(-)-12b

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.845	VV	0.1715	1.60926e4	1435.67065	90.9088
2	10.421	VV	0.1696	1609.32727	145.76247	9.0912

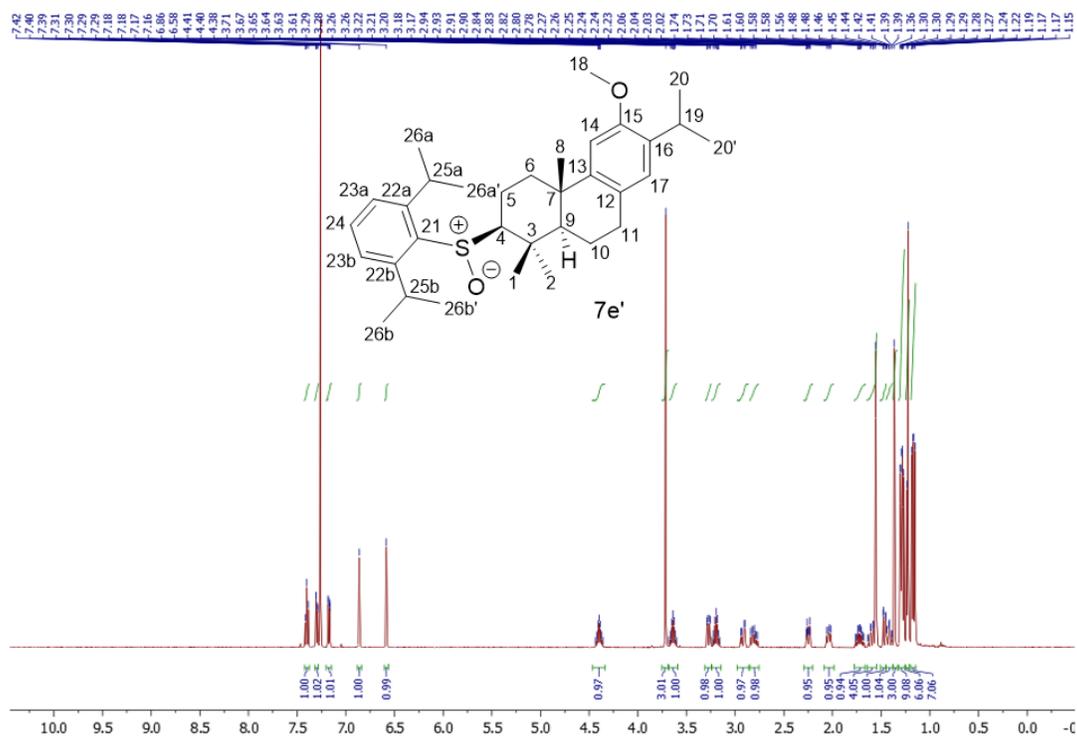
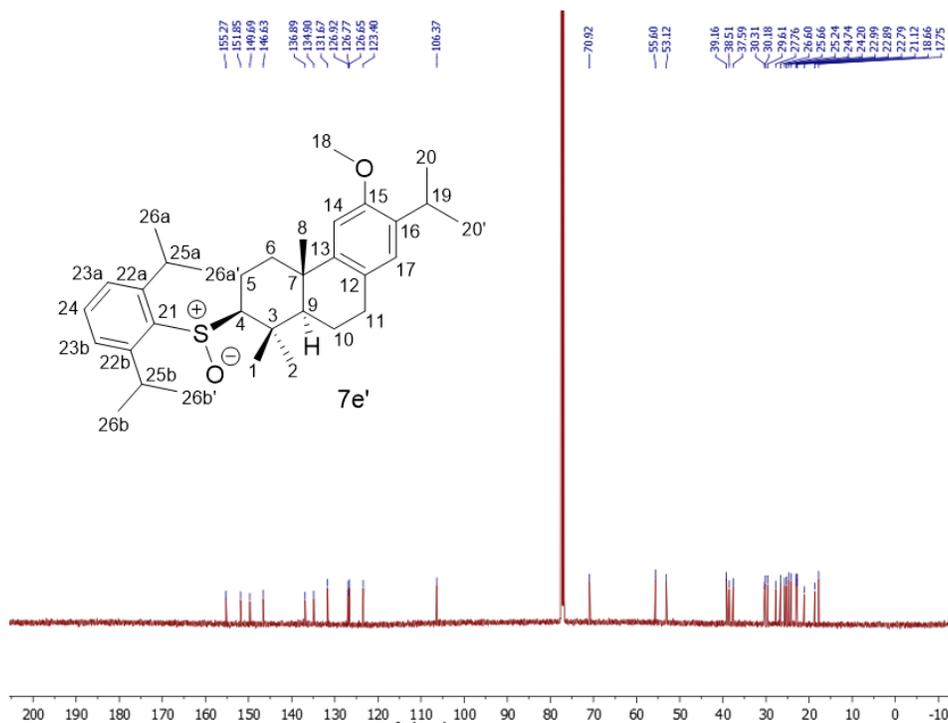
13b ^1H NMR (500 MHz, CDCl_3)**13b** ^{13}C NMR (126 MHz, CDCl_3)

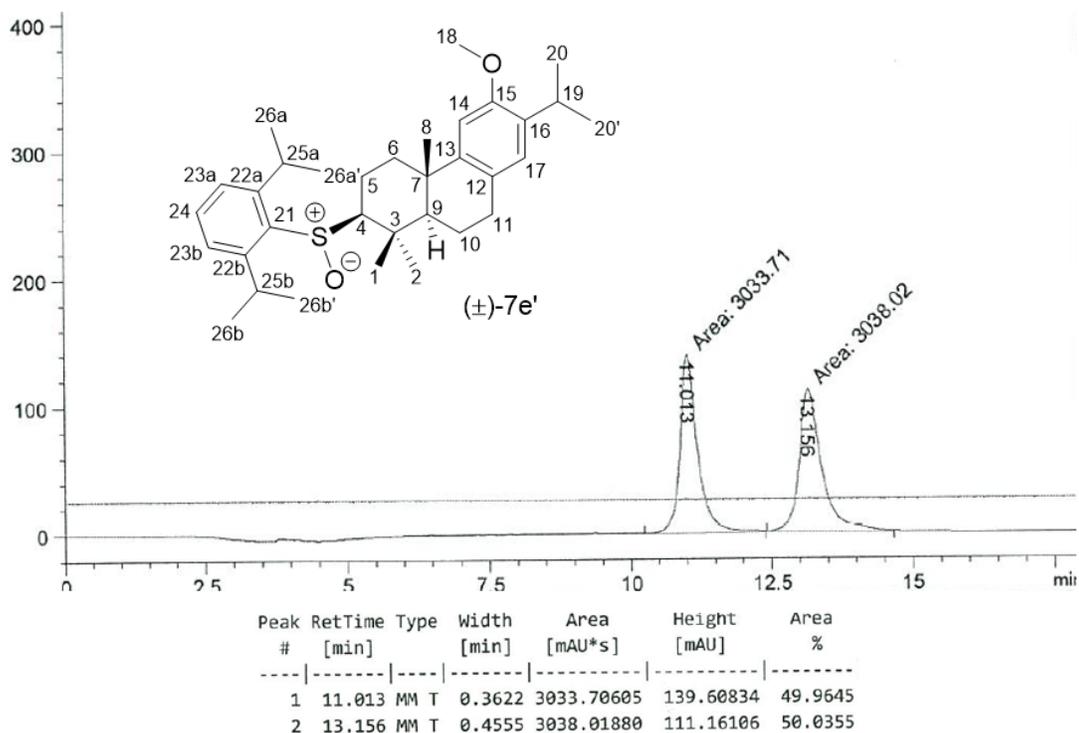
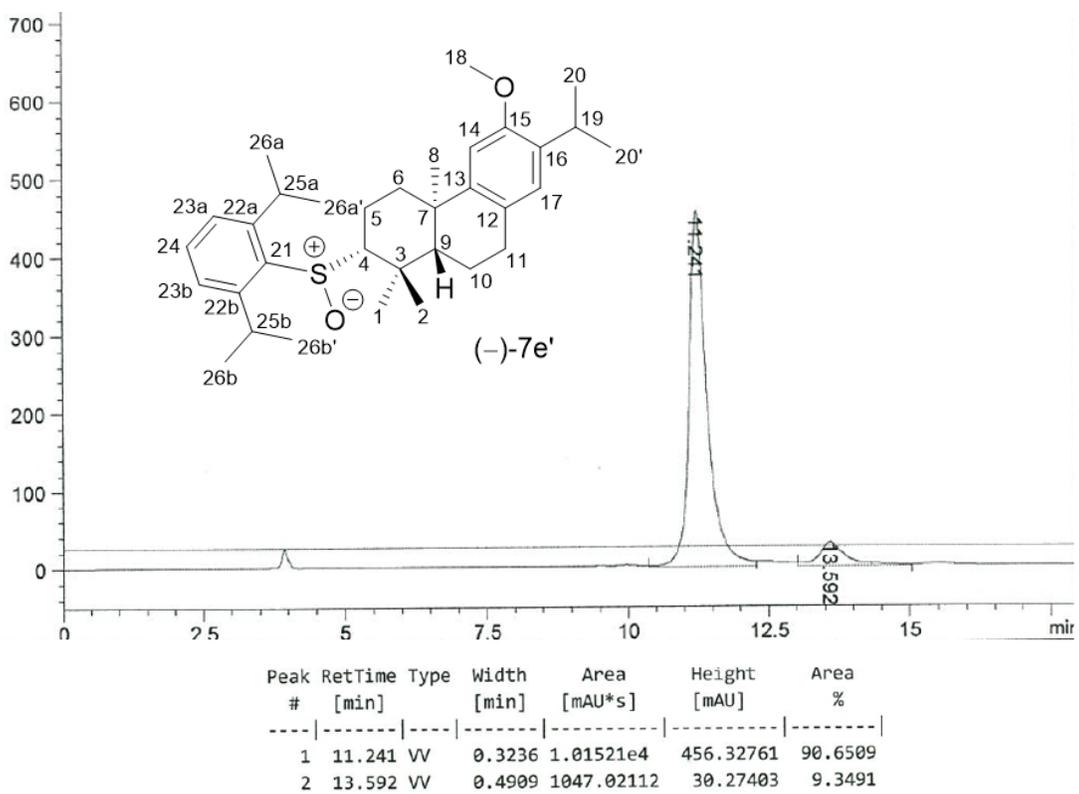
(±)-13b

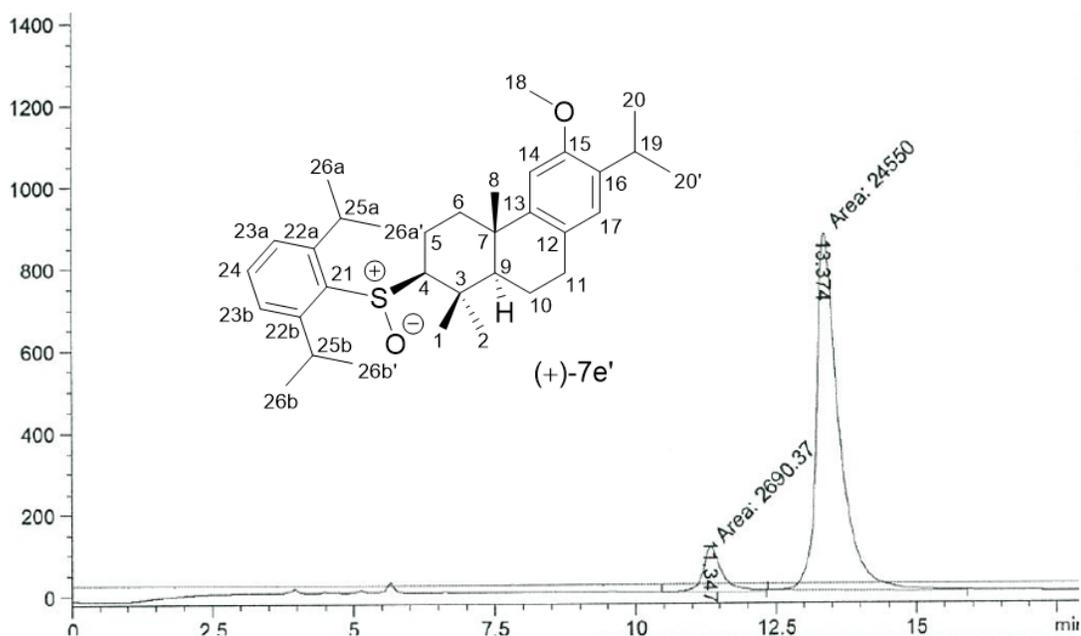
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.964	VV	0.1337	1.26733e4	1497.56982	50.2080
2	8.571	VV	0.1406	1.25683e4	1387.74463	49.7920

(-)-13b

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.165	VV	0.1547	2.12612e4	2177.34399	89.9508
2	8.732	VV	0.1402	2375.28491	263.20529	10.0492

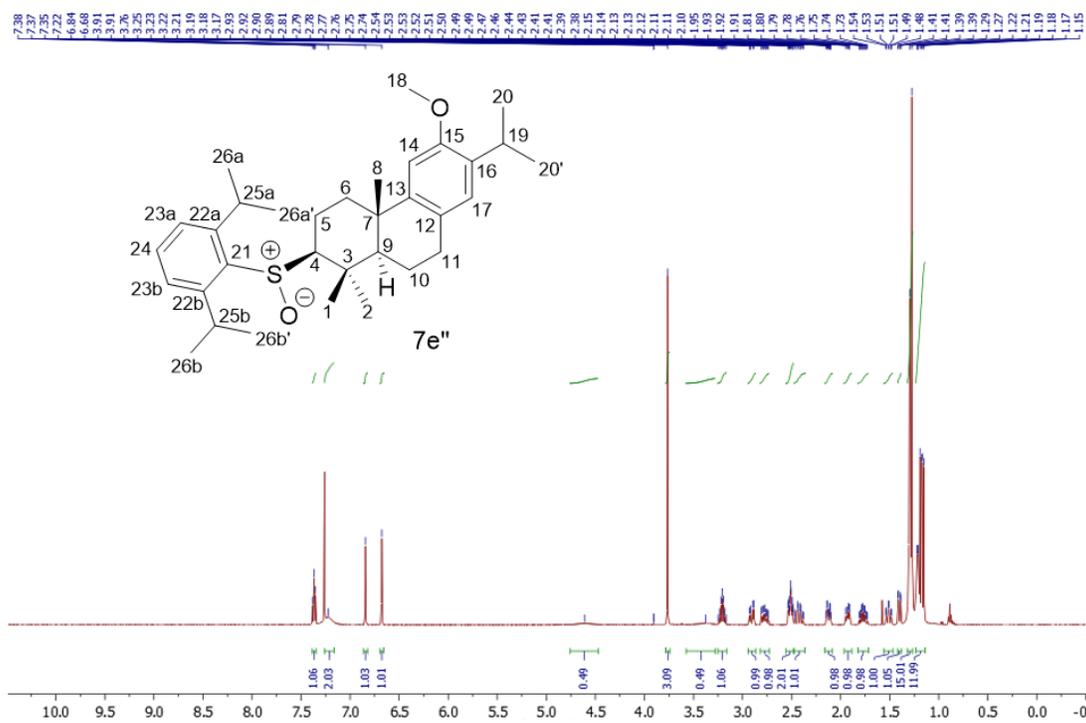
7e' (major) ^1H NMR (500 MHz, CDCl_3)**7e'** (major) ^{13}C NMR (126 MHz, CDCl_3)

(\pm) -7e' (major) $(-)$ -7e' (major)

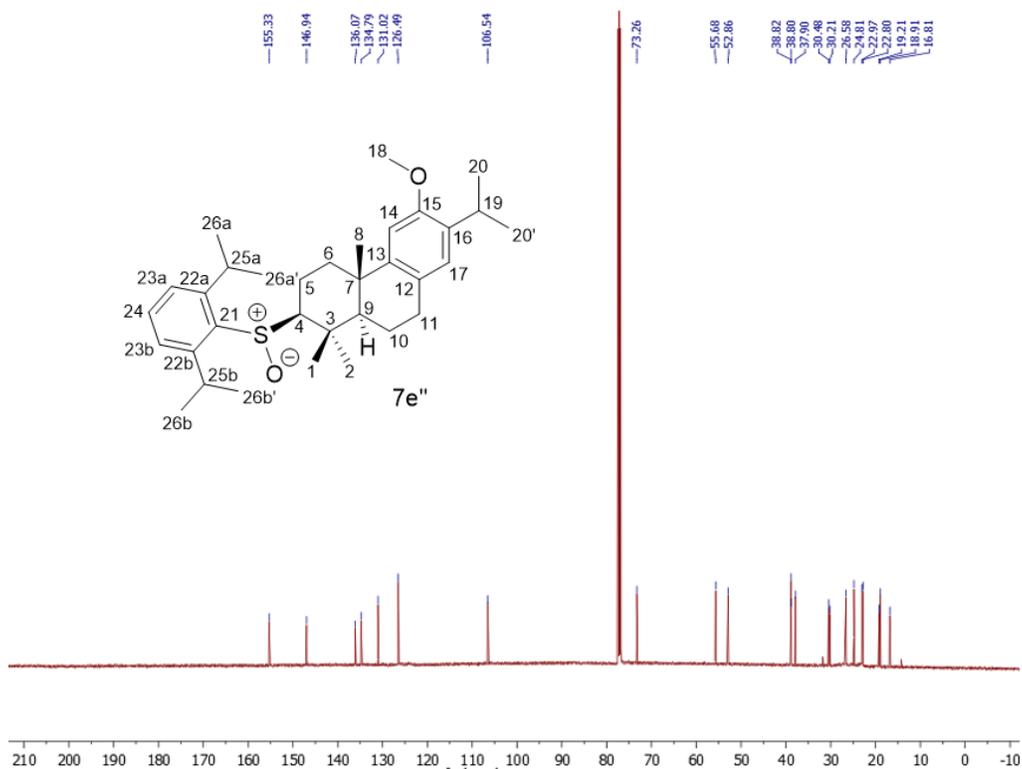
(+)-7e' (major)

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.347	MM T	0.5759	2690.37476	109.46920	9.8764
2	13.374	MM T	0.4695	2.45500e4	871.48932	90.1236

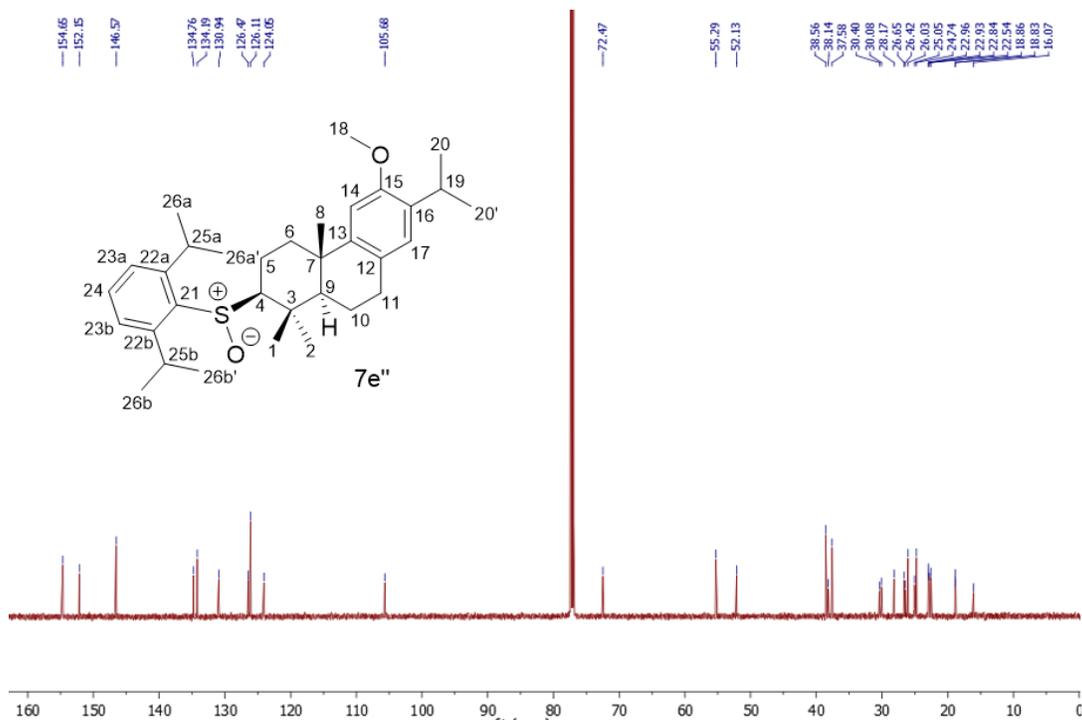
7e'' (minor) ¹H NMR (500 MHz, CDCl₃, 23 °C)

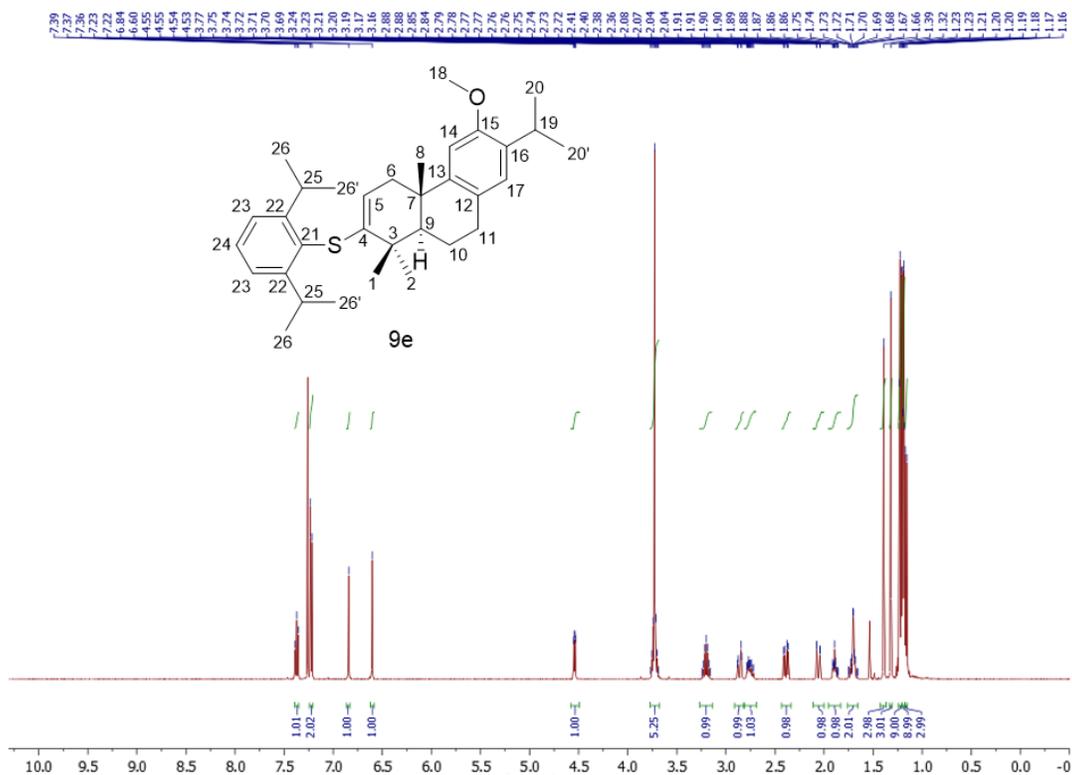
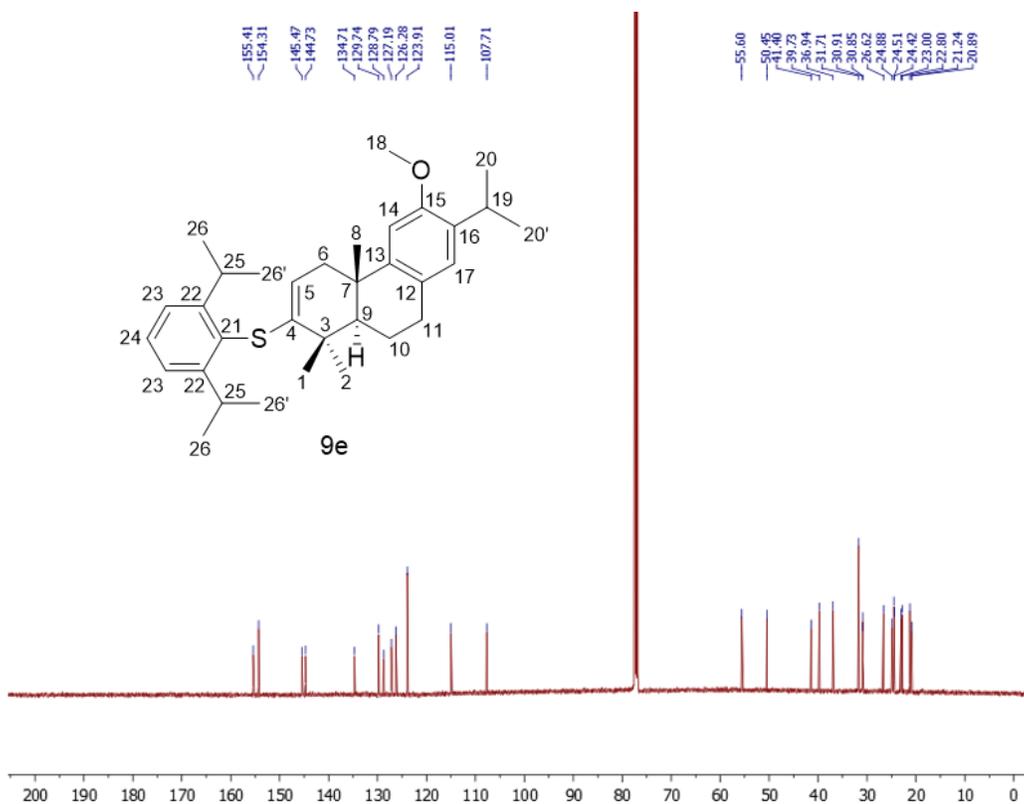


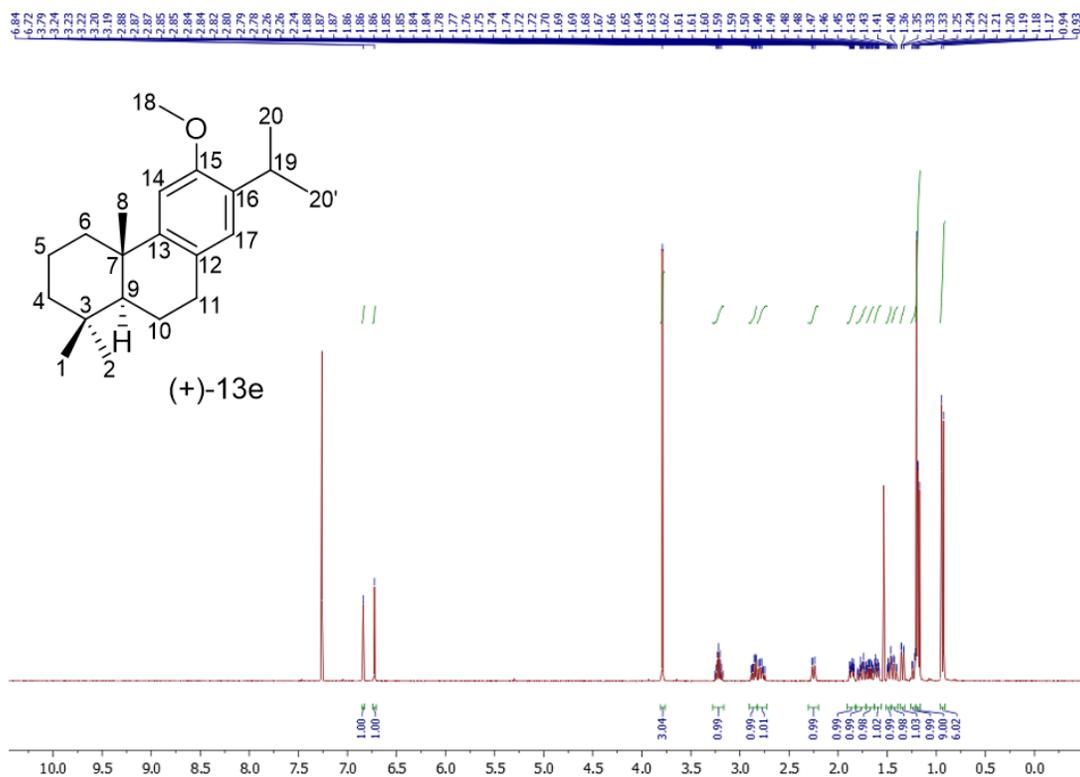
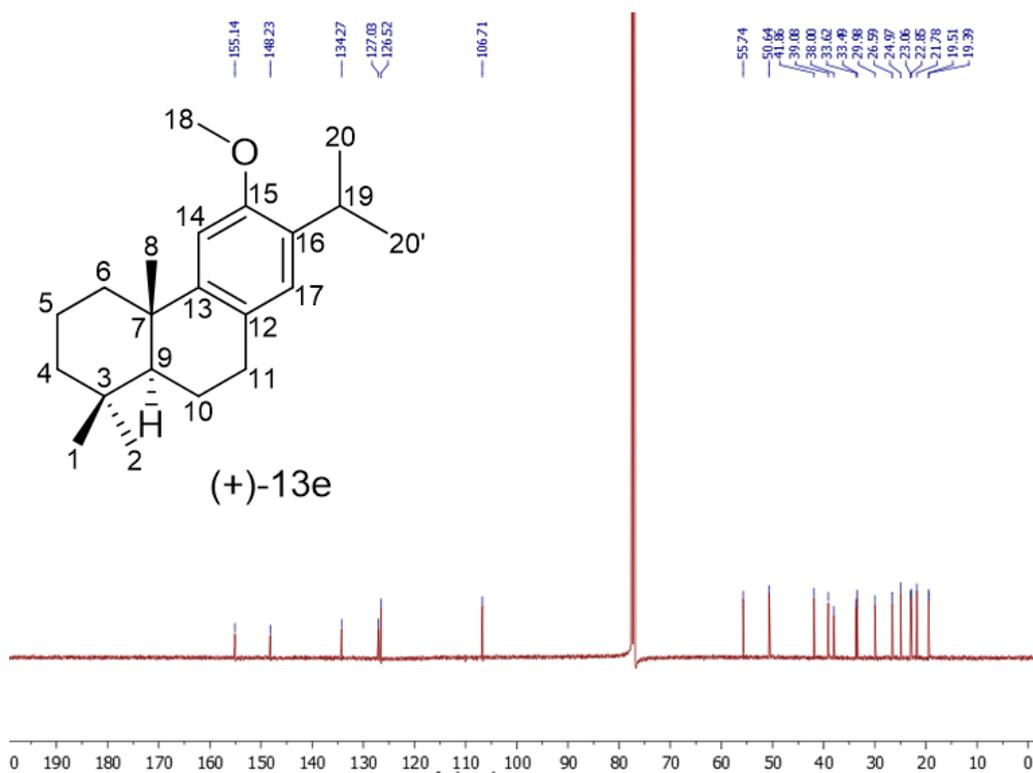
7e'' (minor) ^{13}C NMR (126 MHz, CDCl_3 , 23 °C)

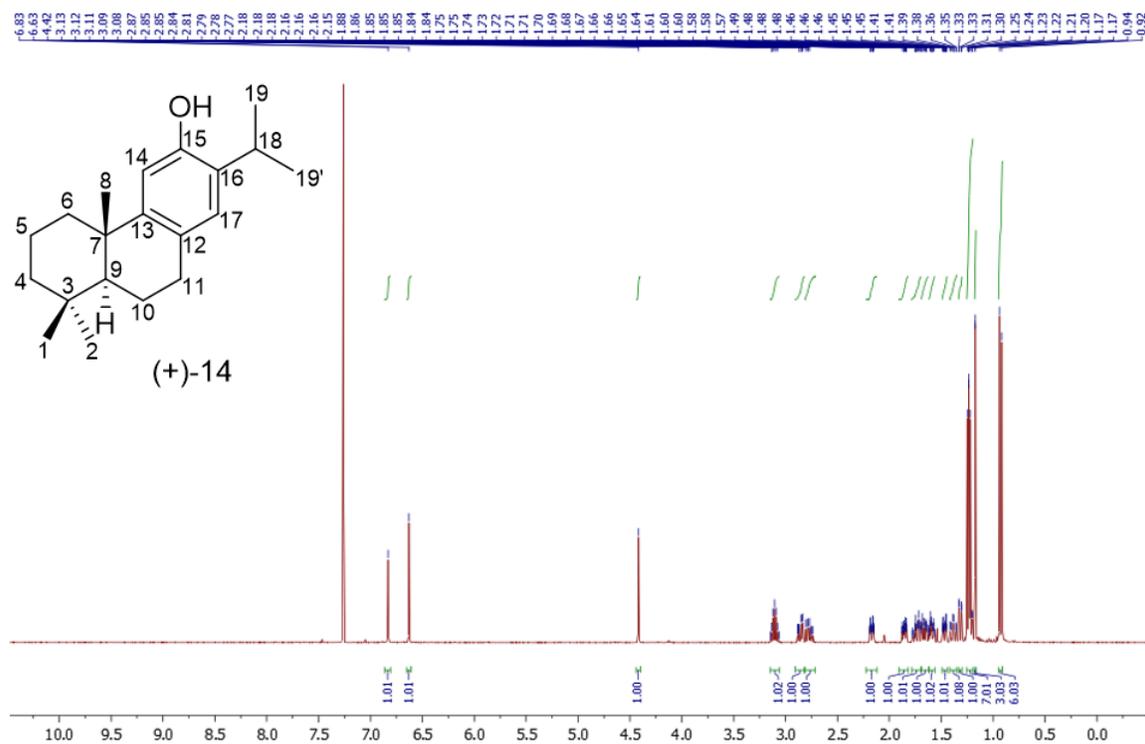
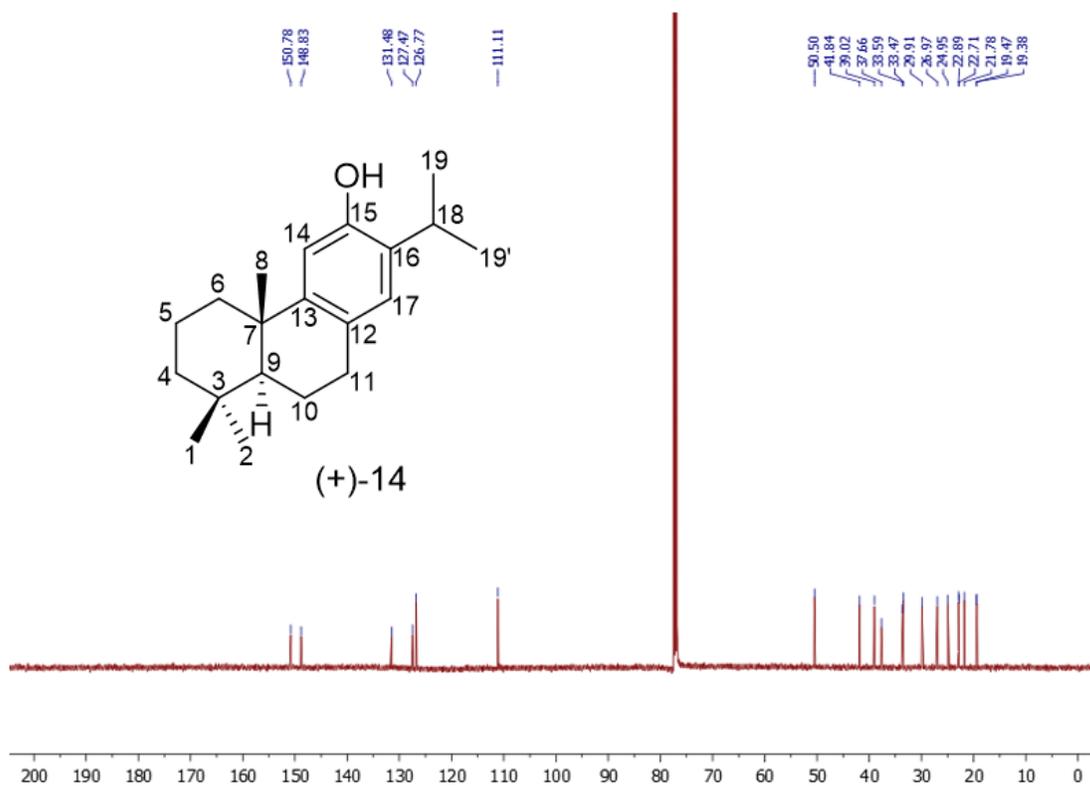


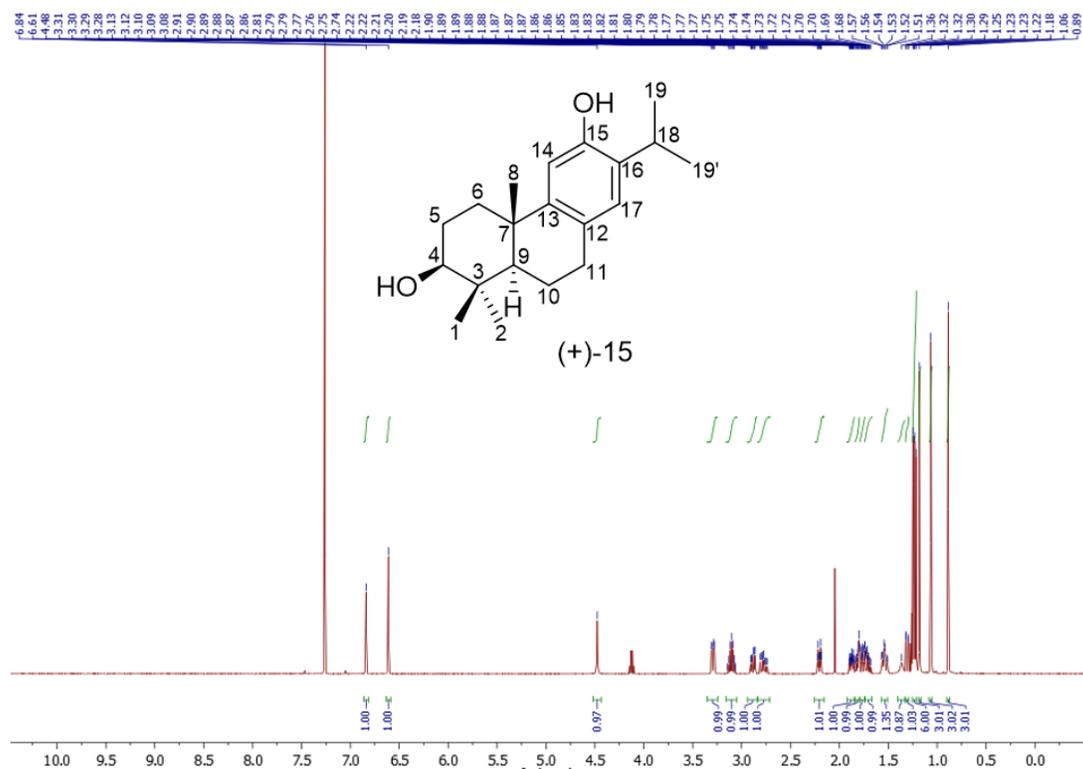
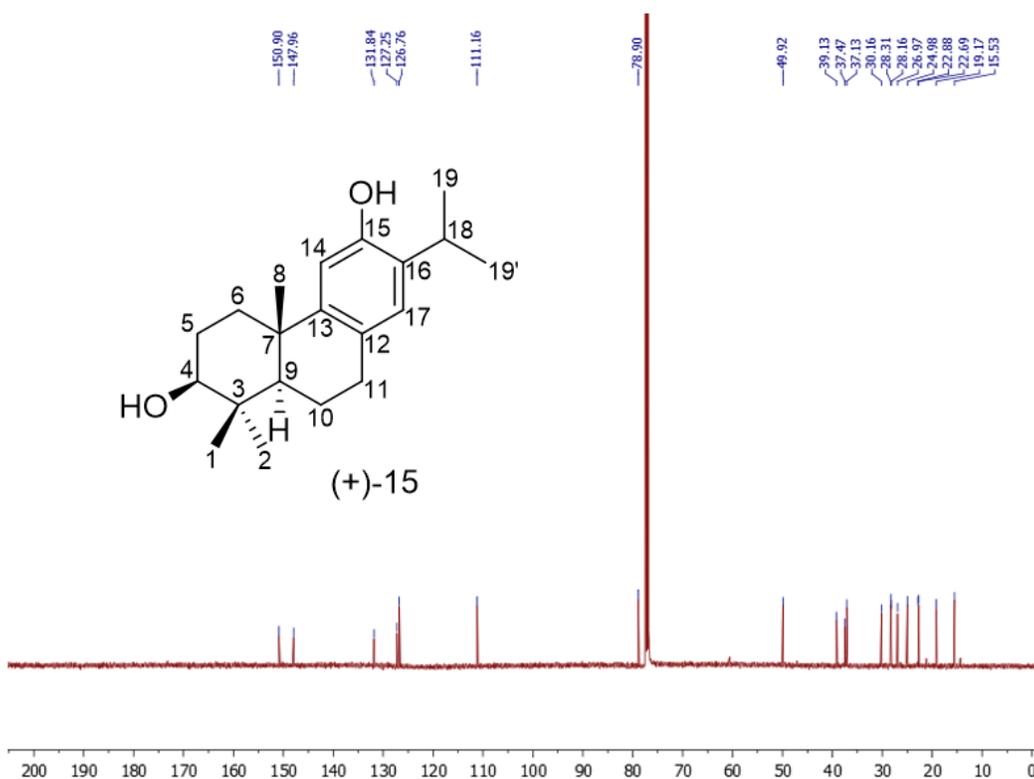
7e'' (minor) ^{13}C NMR (151 MHz, CDCl_3 , -50 °C)

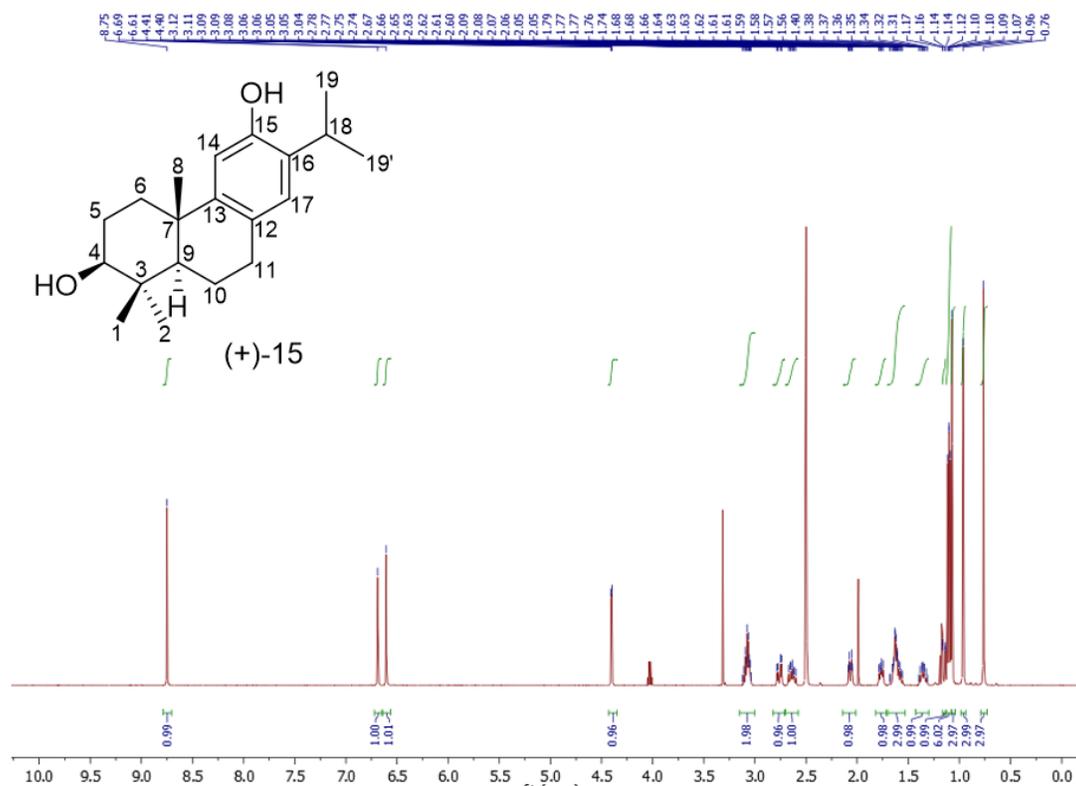


9e ^1H NMR (500 MHz, CDCl_3)**9e** ^{13}C NMR (126 MHz, CDCl_3)

(+)-13e ^1H NMR (500 MHz, CDCl_3)**(+)-13e** ^{13}C NMR (126 MHz, CDCl_3)

(+)-14 (+)-Ferruginol ^1H NMR (500 MHz, CDCl_3)**(+)-14 (+)-Ferruginol** ^{13}C NMR (126 MHz, CDCl_3)

(+)-15 (+)-Hinokiol ^1H NMR (500 MHz, CDCl_3)**(+)-15 (+)-Hinokiol** ^{13}C NMR (126 MHz, CDCl_3)

(+)-15 (+)-Hinokiol ^1H NMR (500 MHz, $\text{DMSO-}d_6$)**(+)-15 (+)-Hinokiol** ^{13}C NMR (126 MHz, $\text{DMSO-}d_6$)