Electronic Supplementary Material (ESI) for Chemical Communications.

SUPPORTING INFORMATION

Enantioselective halogenative semi-pinacol rearrangement: a stereodivergent reaction on a racemic mixture

Fedor Romanov-Michailidis, Marion Pupier, Laure Guénée, and Alexandre Alexakis

University of Geneva, Quai Ernest Ansermet 30, CH-1211 Geneva 4, Switzerland

Table of Contents

GENERAL METHODS **2**
PREPARATION OF SUBSTRATES **3**
GENERAL PROCEDURE FOR THE SYNTHESIS OF SUBSTRATES: HWE REACTION 3
GENERAL PROCEDURE FOR THE SYNTHESIS OF SUBSTRATES: HYDROGENATION REACTION 6
GENERAL PROCEDURE FOR THE SYNTHESIS OF SUBSTRATES: $LiAlH_4$ REDUCTION 9
GENERAL PROCEDURE FOR THE SYNTHESIS OF SUBSTRATES: TOSYLATION REACTION 12
GENERAL PROCEDURE FOR THE SYNTHESIS OF SUBSTRATES: CYANIDE S_N2 SUBSTITUTION 15
GENERAL PROCEDURE FOR THE SYNTHESIS OF SUBSTRATES: SAPONIFICATION OF THE NITRILE 18
GENERAL PROCEDURE FOR THE SYNTHESIS OF SUBSTRATES: CYCLIZATION TO METHYL-TETRALONE 21
GENERAL PROCEDURE FOR THE SYNTHESIS OF SUBSTRATES: VINYLIC BROMIDES 24
GENERAL PROCEDURE FOR THE SYNTHESIS OF SUBSTRATES: CYCLOBUTANOLS 28
GENERAL PROCEDURE FOR THE SYNTHESIS OF SUBSTRATES: CYCLOPROPANOLS 33
GENERAL PROCEDURE FOR THE STEREODIVERGENT FLUORINATION/SEMI-PINACOL REACTION: RACEMATES **36**
GENERAL PROCEDURE FOR THE STEREODIVERGENT FLUORINATION/SEMI-PINACOL REACTION: ENANTIOSELECTIVE VERSION **37**
CHARACTERIZATION OF FLUORINATED PRODUCTS 37
GENERAL PROCEDURE FOR THE STEREODIVERGENT BROMINATION/SEMI-PINACOL REACTION: RACEMATES **50**
GENERAL PROCEDURE FOR THE STEREODIVERGENT BROMINATION/SEMI-PINACOL REACTION: ENANTIOSELECTIVE VERSION **50**
CHARACTERIZATION OF BROMINATED PRODUCTS 50
NOE STUDIES **62**
X-RAY CRYSTAL STRUCTURES OF PRODUCTS **63**
SYNTHETIC DERIVATIZATIONS **63**
BAEYER-VILLIGER OXIDATION 63
DIASTEREOSELECTIVE REDUCTION 64
REFERENCES AND NOTES **66**
NMR SPECTRA **66**
FLUORINATED COMPOUNDS 66
BROMINATED COMPOUNDS 138
HPLC TRACES **166**
FLUORINATED COMPOUNDS 166
BROMINATED COMPOUNDS 180

General Methods

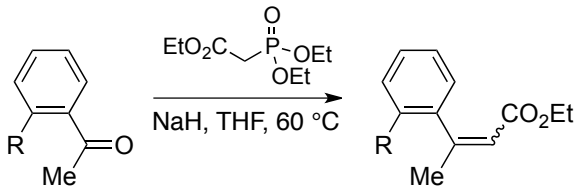
^1H, ^{13}C, ^{19}F and ^{31}P NMR spectra were recorded on a Bruker (^1H, 300 MHz), a Bruker (^1H, 400 MHz), or a Bruker (^1H, 500 MHz) spectrometers, using deuterated solvents $CDCl_3$, CD_2Cl_2 or C_6D_6. Chemical shifts (δ) are reported in ppm downfield from Me_4Si by using the residual solvent peak as an internal standard. Scalar coupling constants (J) are reported in hertz (Hz). All reactions were carried out in heat-gun dried glassware equipped with magnetic stirrer bars under an inert atmosphere of dry nitrogen or argon. ^1H NMR, TLC or GC-MS control of the crude reaction mixtures was routinely performed to ensure complete conversions of the starting material. 3 Å and 4 Å molecular sieves were powdered and heated under high vacuum at 260 °C during overnight prior to use. DMF was distilled over CaH_2 and stored over activated 4 Å molecular sieves. 1,2-Dichloroethane, 1-chlorobenzene and chloroform were distilled over P_2O_5 and stored over activated 4 Å molecular sieves. MeOH and EtOH were distilled over CaH_2 under argon, and stored over activated 4 Å molecular sieves. *N*,*N*-

Diisopropylethylamine and 1,1,1,3,3,3-hexamethyldisilazane were distilled over CaH_2 and stored over activated 4 Å molecular sieves. Acrylonitrile, 1-fluorobenzene and hexafluorobenzene were distilled over P_2O_5 and stored over activated 4 Å molecular sieves. Benzene and 1,4-dioxane were distilled over Na/benzophenone under argon, and stored over activated 4 Å molecular sieves. Toluene, THF, Et_2O, CH_2Cl_2 and CH_3CN were dried by passage through a column of activated alumina, under nitrogen atmosphere. KHMDS and KO*t*-Bu were sublimed under high vacuum prior to use. NaH (60% *w/w* suspension in mineral oils) was washed with anhydrous *n*-hexane prior to use. Neutralized silica gel was prepared by suspending silica gel in EtOAc containing Et_3N (1 mL / 50 g of silica gel) followed by concentration of the solvents and drying under high vacuum for overnight. Imidazolium salts **A** and **B** were prepared according to known literature procedures. Triazolium salts **E** and **H** were purchased from Sigma-Aldrich. All other chemical reagents were purchased from commercial suppliers and used as such without further purification. Toluene, THF, Et_2O, CH_2Cl_2 and CH_3CN were dried by passage through a column of activated alumina, under nitrogen atmosphere. C_6H_5F, *c*-Hex, and $^iPr_2O$ were distilled over CaH_2 and stored over activated 4 Å molecular sieves. Selectfluor™, Na_2CO_3, and Na_3PO_4 were finely powdered and dried under high vacuum (10^{-2} mbar) at 80 °C for 2 h prior to use. LiCl was dried under high vacuum (10^{-2} mbar) at 140 °C for 4 h prior to use. Mg^0 was activated by heating at 200 °C under high vacuum (10^{-2} mbar) for overnight, followed by sublimation of a seed of iodine prior to use. Grignard solutions were titrated according to the method of Knochel *et al.*[1] Electrospray-ionization high-resolution mass (ESI-HRMS) spectra were recorded on a QSTAR Pulsar (AB/MDS Sciex) apparatus. Electron-impact high-resolution mass (EI-HRMS) spectra were recorded on a DFS-Thermofischer instrument. Racemic β-fluoro spiroketones $\mathbf{B_x}$ were obtained by carrying out the fluoro-semipinacol rearrangement in acetonitrile at 0 °C, in the absence of the phosphoric acid catalyst. Racemic β-iodo spiroketones $\mathbf{D_x}$ were obtained by carrying out the iodo-semipinacol rearrangement with iodonium salts $\mathbf{S_0}$ or $\mathbf{S_2}$ in acetonitrile at ambient temperature, in the absence of the phosphoric acid catalyst. Chiral separations were performed on Agilent 1290 Infinity HPLC or Waters TharSFC SFC instruments. *n*-Hexane/isopropanol or CO_2/methanol eluents. Retention times are cited in minutes. Iodinating reagents $\mathbf{S_0}$[2] and $\mathbf{S_{1\text{-}4}}$[3] were prepared according to literature methods. Iodinating reagents $\mathbf{S_{1\text{-}9}}$ were re-precipitated from nitromethane and stored at -20 °C in the dark in tightly sealed containers. X-ray data were measured using Cu radiation on a SuperNova Dual source equipped with an Atlas detector.

(1) A. Krasovskiy, P. Knochel, *Synthesis* **2006**, *5*, 890-891.

Preparation of Substrates

General Procedure for the Synthesis of Substrates: HWE Reaction

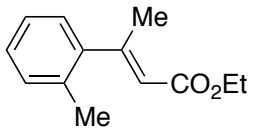


R = Me, OMe, F, Cl

To a cooled (0 °C, ice/water bath) solution of *n*-hexane-washed NaH (60% *w/w* suspension in mineral oil, 1.5 equiv.) in anhydrous THF (0.30 M) was added triethyl phosphonoacetate (1.8 equiv.) dropwise over a period of 5 min (*caution! vigorous gas evolution*). The resultant suspension was then stirred at

0 °C for 2 h. A solution of the required acetophenone (1.0 equiv.) in anhydrous THF (0.75 M) was then added and the resultant mixture was heated at reflux (*ca.* 60 °C) for overnight. Upon cooling down to ambient temperature, the reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used in the next step as such, without further purification.

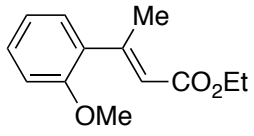
(*E*)-ethyl 3-(*o*-tolyl)but-2-enoate



(*E*)-ethyl 3-(*o*-tolyl)but-2-enoate
Chemical Formula: $C_{13}H_{16}O_2$
Molecular Weight: 204.26

To a cooled (0 °C, ice/water bath) solution of NaH (60% *w/w* suspension in mineral oil, 1.64 g, 34.2 mmol, 1.5 equiv.) in anhydrous THF (120 mL) was added triethyl phosphonoacetate (8.22 mL, 41.0 mmol, 1.8 equiv.) dropwise over a period of 5 min (*caution! vigorous gas evolution*). The resultant suspension was then stirred at 0 °C for 2 h. A solution of 2-methylacetophenone (3.0 mL, 22.8 mmol, 1.0 equiv.) in anhydrous THF (30 mL) was then added and the resultant mixture was heated at reflux for overnight. Upon cooling down to ambient temperature, the reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 9:1) 0.57. Pale-yellow oil.

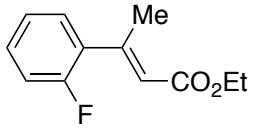
(*E*)-ethyl 3-(2-methoxyphenyl)but-2-enoate



(*E*)-ethyl 3-(2-methoxyphenyl) but-2-enoate
Chemical Formula: $C_{13}H_{16}O_3$
Molecular Weight: 220.26

To a cooled (0 °C, ice/water bath) solution of NaH (60% *w/w* suspension in mineral oil, 1.64 g, 34.2 mmol, 1.5 equiv.) in anhydrous THF (120 mL) was added triethyl phosphonoacetate (8.22 mL, 41.0 mmol, 1.8 equiv.) dropwise over a period of 5 min (*caution! vigorous gas evolution*). The resultant suspension was then stirred at 0 °C for 2 h. A solution of 2-methoxyacetophenone (3.14 mL, 22.8 mmol, 1.0 equiv.) in anhydrous THF (30 mL) was then added and the resultant mixture was heated at reflux for overnight. Upon cooling down to ambient temperature, the reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.39. Colorless oil.

(*E*)-ethyl 3-(2-fluorophenyl)but-2-enoate

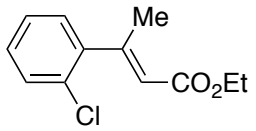


(*E*)-ethyl 3-(2-fluorophenyl) but-2-enoate
Chemical Formula: $C_{12}H_{13}FO_2$
Molecular Weight: 208.23

To a cooled (0 °C, ice/water bath) solution of NaH (60% *w/w* suspension in mineral oil, 1.64 g, 34.2 mmol, 1.5 equiv.) in anhydrous THF (120 mL) was added triethyl phosphonoacetate (8.22 mL, 41.0 mmol, 1.8 equiv.) dropwise over a period of 5 min (*caution! vigorous gas evolution*). The resultant suspension was then stirred at 0 °C for 2 h. A solution of 2-fluoroacetophenone (2.77 mL, 22.8 mmol, 1.0 equiv.) in anhydrous THF (30 mL) was then added and the resultant mixture was heated at reflux for overnight. Upon cooling down to ambient temperature, the reaction mixture was quenched with saturated aqueous

NH_4Cl and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 9:1) 0.62. Colorless oil.

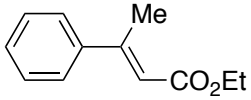
(*E*)-ethyl 3-(2-chlorophenyl)but-2-enoate



(*E*)-ethyl 3-(2-chlorophenyl) but-2-enoate
Chemical Formula: $C_{12}H_{13}ClO_2$
Molecular Weight: 224.68

To a cooled (0 °C, ice/water bath) solution of NaH (60% *w/w* suspension in mineral oil, 1.64 g, 34.2 mmol, 1.5 equiv.) in anhydrous THF (120 mL) was added triethyl phosphonoacetate (8.22 mL, 41.0 mmol, 1.8 equiv.) dropwise over a period of 5 min (*caution! vigorous gas evolution*). The resultant suspension was then stirred at 0 °C for 2 h. A solution of 2-chloroacetophenone (2.94 mL, 22.8 mmol, 1.0 equiv.) in anhydrous THF (30 mL) was then added and the resultant mixture was heated at reflux for overnight. Upon cooling down to ambient temperature, the reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.49. Pale-yellow oil.

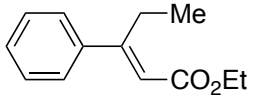
(*E*)-ethyl 3-phenylbut-2-enoate



(*E*)-ethyl 3-phenylbut-2-enoate
Chemical Formula: $C_{12}H_{14}O_2$
Molecular Weight: 190.24

To a cooled (0 °C, ice/water bath) solution of NaH (60% *w/w* suspension in mineral oil, 1.64 g, 34.2 mmol, 1.5 equiv.) in anhydrous THF (120 mL) was added triethyl phosphonoacetate (8.22 mL, 41.0 mmol, 1.8 equiv.) dropwise over a period of 5 min (*caution! vigorous gas evolution*). The resultant suspension was then stirred at 0 °C for 2 h. A solution of acetophenone (2.73 mL, 22.8 mmol, 1.0 equiv.) in anhydrous THF (30 mL) was then added and the resultant mixture was heated at reflux for overnight. Upon cooling down to ambient temperature, the reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.55. Faint-yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.45-7.49 (2H, *m*, $C^{ar}H$), 7.32-7.40 (3H, *m*, $C^{ar}H$), 6.13 (1H, *q*, *J* 1.3, olefinic C=C*H*), 4.22 (2H, *q*, *J* 7.1, ethoxy CH_2-O), 2.58 (3H, *d*, *J* 1.3, allylic CH_3), 1.32 (3H, *t*, *J* 7.1, ethoxy CH_3) ppm.

(*E*)-ethyl 3-phenylpent-2-enoate

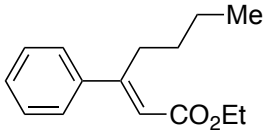


(*E*)-ethyl 3-phenylpent-2-enoate
Chemical Formula: $C_{13}H_{16}O_2$
Molecular Weight: 204.26

To a cooled (0 °C, ice/water bath) solution of NaH (60% *w/w* suspension in mineral oil, 1.64 g, 34.2 mmol, 1.5 equiv.) in anhydrous THF (120 mL) was added triethyl phosphonoacetate (8.22 mL, 41.0 mmol, 1.8 equiv.) dropwise over a period of 5 min (*caution! vigorous gas evolution*). The resultant suspension was then stirred at 0 °C for 2 h. A solution of propiophenone (3.06 mL, 22.8 mmol, 1.0 equiv.) in anhydrous THF (30 mL) was then added and the resultant mixture was heated at reflux for overnight. Upon cooling down to ambient temperature, the reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude

residue was used as such, without further purification. $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.55. Colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.45-7.49 (2H, *m*, $C^{ar}H$), 7.32-7.40 (3H, *m*, $C^{ar}H$), 6.13 (1H, *q*, *J* 1.3, olefinic C=C*H*), 4.22 (2H, *q*, *J* 7.1, ethoxy CH_2-O), 2.58 (3H, *d*, *J* 1.3, allylic CH_3), 1.32 (3H, *t*, *J* 7.1, ethoxy CH_3) ppm.

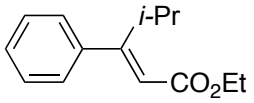
(*E*)-ethyl 3-phenylhept-2-enoate



(*E*)-ethyl 3-phenylhept-2-enoate
Chemical Formula: $C_{15}H_{20}O_2$
Molecular Weight: 232.32

To a cooled (0 °C, ice/water bath) solution of NaH (60% *w/w* suspension in mineral oil, 1.64 g, 34.2 mmol, 1.5 equiv.) in anhydrous THF (120 mL) was added triethyl phosphonoacetate (8.22 mL, 41.0 mmol, 1.8 equiv.) dropwise over a period of 5 min (*caution! vigorous gas evolution*). The resultant suspension was then stirred at 0 °C for 2 h. A solution of valerophenone (3.80 mL, 22.8 mmol, 1.0 equiv.) in anhydrous THF (30 mL) was then added and the resultant mixture was heated at reflux for overnight. Upon cooling down to ambient temperature, the reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.66. Colorless oil.

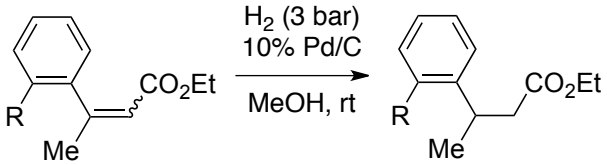
(*E*)-ethyl 4-methyl-3-phenylpent-2-enoate



(*E*)-ethyl 4-methyl-3-phenylpent-2-enoate
Chemical Formula: $C_{14}H_{18}O_2$
Molecular Weight: 218.29

To a cooled (0 °C, ice/water bath) solution of NaH (60% *w/w* suspension in mineral oil, 1.64 g, 34.2 mmol, 1.5 equiv.) in anhydrous THF (120 mL) was added triethyl phosphonoacetate (8.22 mL, 41.0 mmol, 1.8 equiv.) dropwise over a period of 5 min (*caution! vigorous gas evolution*). The resultant suspension was then stirred at 0 °C for 2 h. A solution of isobutyrophenone (3.41 mL, 22.8 mmol, 1.0 equiv.) in anhydrous THF (30 mL) was then added and the resultant mixture was heated at reflux for overnight. Upon cooling down to ambient temperature, the reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.64. Colorless oil.

General Procedure for the Synthesis of Substrates: Hydrogenation Reaction

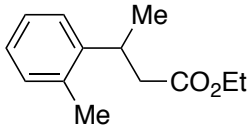


R = Me, OMe, F, Cl

A solution composed of the required alkene (1.0 equiv.) and Pd/C (10% *w/w*, 50 mg/mmol) in absolute MeOH (0.20 M) was pressurized with H_2 gas (*ca.* 3-4 bar) and stirred at ambient temperature for 16-24 h. The solvent was removed *in vacuo* and the product was re-dissolved in diethyl ether. Filtration

through a plug of Celite, followed by evaporation of solvent under reduced pressure afforded the crude material, which was used in the next step as such without further purification.

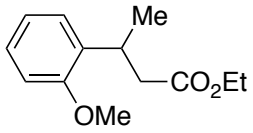
Ethyl 3-(*o*-tolyl)butanoate



ethyl 3-(*o*-tolyl)butanoate
Chemical Formula: $C_{13}H_{18}O_2$
Molecular Weight: 206.28

A solution composed of ethyl 3-(*o*-tolyl)but-2-enoate (4.66 g, 22.8 mmol, 1.0 equiv.) and Pd/C (10% *w/w*, 1.14 g, 50 mg/mmol) in absolute MeOH (114 mL) was pressurized with H_2 gas (*ca.* 3-4 bar) and stirred at ambient temperature for 16 h. The solvent was removed *in vacuo* and the product was re-dissolved in diethyl ether. Filtration through a plug of Celite, followed by evaporation of solvent under reduced pressure afforded the crude material that was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 9:1). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 9:1) 0.48. Colorless oil. Isolated yield 88% (4.15 g, 20.1 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.06-7.18 (4H, *m*, C^{ar}*H*), 4.08 (2H, *q*, *J* 7.1, ethoxy CH_2-O), 3.54 (1H, *sext.*, *J* 6.9, benzylic C*H*), 2.62 (1H, *dd*, J_1 15.2, J_2 6.6, ABX spin-system, diastereotopic CH_2), 2.53 (1H, *dd*, J_1 15.2, J_2 8.5, ABX spin-system, diastereotopic CH_2), 2.38 (3H, *s*, CH_3), 1.26 (3H, *d*, *J* 6.9, CH_3), 1.17 (3H, *t*, *J* 7.1, ethoxy CH_3) ppm.

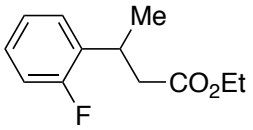
Ethyl 3-(2-methoxyphenyl)butanoate



ethyl 3-(2-methoxyphenyl)butanoate
Chemical Formula: $C_{13}H_{18}O_3$
Molecular Weight: 222.28

A solution composed of ethyl 3-(2-methoxyphenyl)but-2-enoate (5.02 g, 22.8 mmol, 1.0 equiv.) and Pd/C (10% *w/w*, 1.14 g, 50 mg/mmol) in absolute MeOH (114 mL) was pressurized with H_2 gas (*ca.* 3-4 bar) and stirred at ambient temperature for 16 h. The solvent was removed *in vacuo* and the product was re-dissolved in diethyl ether. Filtration through a plug of Celite, followed by evaporation of solvent under reduced pressure afforded the crude material that was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 9:1). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 4:1) 0.43. Colorless oil. Isolated yield 99% (5.07 g, 22.8 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.06-7.18 (4H, *m*, C^{ar}*H*), 4.08 (2H, *q*, *J* 7.1, ethoxy CH_2-O), 3.54 (1H, *sext.*, *J* 6.9, benzylic C*H*), 2.62 (1H, *dd*, J_1 15.2, J_2 6.6, ABX spin-system, diastereotopic CH_2), 2.53 (1H, *dd*, J_1 15.2, J_2 8.5, ABX spin-system, diastereotopic CH_2), 2.38 (3H, *s*, CH_3), 1.26 (3H, *d*, *J* 6.9, CH_3), 1.17 (3H, *t*, *J* 7.1, ethoxy CH_3) ppm.

Ethyl 3-(2-fluorophenyl)butanoate

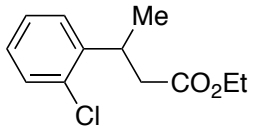


ethyl 3-(2-fluorophenyl)butanoate
Chemical Formula: $C_{12}H_{15}FO_2$
Molecular Weight: 210.24

A solution composed of ethyl 3-(2-fluorophenyl)butanoate (4.75 g, 22.8 mmol, 1.0 equiv.) and Pd/C (10% *w/w*, 1.14 g, 50 mg/mmol) in absolute MeOH (114 mL) was pressurized with H_2 gas (*ca.* 3-4 bar) and stirred at ambient temperature for 16 h. The solvent was removed *in vacuo* and the product was re-dissolved in diethyl ether. Filtration through a plug of Celite, followed by evaporation of solvent under reduced pressure afforded the crude material that was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 9:1). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 9:1) 0.55. Pale-yellow oil. Isolated yield 99% (4.79 g, 22.8 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.06-7.18 (4H, *m*, C^{ar}*H*), 4.08 (2H, *q*, *J* 7.1, ethoxy CH_2-O), 3.54 (1H, *sext.*, *J* 6.9, benzylic C*H*), 2.62 (1H, *dd*, J_1 15.2, J_2 6.6, ABX spin-system, diastereotopic CH_2), 2.53 (1H, *dd*, J_1 15.2, J_2 8.5,

ABX spin-system, diastereotopic CH_2), 2.38 (3H, *s*, CH_3), 1.26 (3H, *d*, *J* 6.9, CH_3), 1.17 (3H, *t*, *J* 7.1, ethoxy CH_3) ppm.

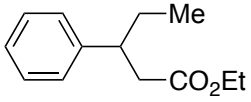
Ethyl 3-(2-chlorophenyl)butanoate



ethyl 3-(2-chlorophenyl)butanoate
Chemical Formula: $C_{12}H_{15}ClO_2$
Molecular Weight: 226.70

A solution composed of ethyl 3-(2-chlorophenyl)butanoate (5.12 g, 22.8 mmol, 1.0 equiv.) and Pd/C (10% *w/w*, 1.14 g, 50 mg/mmol) in absolute MeOH (114 mL) was pressurized with H_2 gas (*ca.* 3-4 bar) and stirred at ambient temperature for 16 h. The solvent was removed *in vacuo* and the product was re-dissolved in diethyl ether. Filtration through a plug of Celite, followed by evaporation of solvent under reduced pressure afforded the crude material that was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 9:1). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 9:1) 0.38. Pale-yellow oil. Isolated yield 99% (5.17 g, 22.8 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.06-7.18 (4H, *m*, C^{ar}H), 4.08 (2H, *q*, *J* 7.1, ethoxy CH_2-O), 3.54 (1H, *sext.*, *J* 6.9, benzylic C*H*), 2.62 (1H, *dd*, J_1 15.2, J_2 6.6, ABX spin-system, diastereotopic CH_2), 2.53 (1H, *dd*, J_1 15.2, J_2 8.5, ABX spin-system, diastereotopic CH_2), 2.38 (3H, *s*, CH_3), 1.26 (3H, *d*, *J* 6.9, CH_3), 1.17 (3H, *t*, *J* 7.1, ethoxy CH_3) ppm.

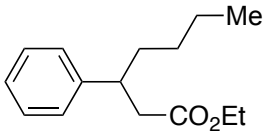
Ethyl 3-phenylpentanoate



ethyl 3-phenylpentanoate
Chemical Formula: $C_{13}H_{18}O_2$
Molecular Weight: 206.28

A solution composed of ethyl 3-phenylpent-2-enoate (4.66 g, 22.8 mmol, 1.0 equiv.) and Pd/C (10% *w/w*, 1.14 g, 50 mg/mmol) in absolute MeOH (114 mL) was pressurized with H_2 gas (*ca.* 3-4 bar) and stirred at ambient temperature for 16 h. The solvent was removed *in vacuo* and the product was re-dissolved in diethyl ether. Filtration through a plug of Celite, followed by evaporation of solvent under reduced pressure afforded the crude material that was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 9:1). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 9:1) 0.58. Pale-yellow oil. Isolated yield 99% (4.79 g, 22.8 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.06-7.18 (4H, *m*, C^{ar}H), 4.08 (2H, *q*, *J* 7.1, ethoxy CH_2-O), 3.54 (1H, *sext.*, *J* 6.9, benzylic C*H*), 2.62 (1H, *dd*, J_1 15.2, J_2 6.6, ABX spin-system, diastereotopic CH_2), 2.53 (1H, *dd*, J_1 15.2, J_2 8.5, ABX spin-system, diastereotopic CH_2), 2.38 (3H, *s*, CH_3), 1.26 (3H, *d*, *J* 6.9, CH_3), 1.17 (3H, *t*, *J* 7.1, ethoxy CH_3) ppm.

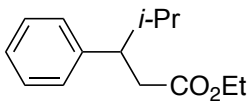
Ethyl 3-phenylheptanoate



ethyl 3-phenylheptanoate
Chemical Formula: $C_{15}H_{22}O_2$
Molecular Weight: 234.33

A solution composed of ethyl 3-phenylhept-2-enoate (5.34 g, 22.8 mmol, 1.0 equiv.) and Pd/C (10% *w/w*, 1.14 g, 50 mg/mmol) in absolute MeOH (114 mL) was pressurized with H_2 gas (*ca.* 3-4 bar) and stirred at ambient temperature for 16 h. The solvent was removed *in vacuo* and the product was re-dissolved in diethyl ether. Filtration through a plug of Celite, followed by evaporation of solvent under reduced pressure afforded the crude material that was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 9:1). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 9:1) 0.60. Pale-yellow oil. Isolated yield 99% (4.79 g, 22.8 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.06-7.18 (4H, *m*, C^{ar}H), 4.08 (2H, *q*, *J* 7.1, ethoxy CH_2-O), 3.54 (1H, *sext.*, *J* 6.9, benzylic C*H*), 2.62 (1H, *dd*, J_1 15.2, J_2 6.6, ABX spin-system, diastereotopic CH_2), 2.53 (1H, *dd*, J_1 15.2, J_2 8.5, ABX spin-system, diastereotopic CH_2), 2.38 (3H, *s*, CH_3), 1.26 (3H, *d*, *J* 6.9, CH_3), 1.17 (3H, *t*, *J* 7.1, ethoxy CH_3) ppm.

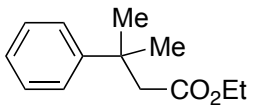
Ethyl 4-methyl-3-phenylpentanoate



ethyl 4-methyl-3-phenylpentanoate
Chemical Formula: $C_{14}H_{20}O_2$
Molecular Weight: 220.31

A solution composed of ethyl 4-methyl-3-phenylpent-2-enoate (4.98 g, 22.8 mmol, 1.0 equiv.) and Pd/C (10% *w/w*, 1.14 g, 50 mg/mmol) in absolute MeOH (114 mL) was pressurized with H_2 gas (*ca.* 3-4 bar) and stirred at ambient temperature for 16 h. The solvent was removed *in vacuo* and the product was re-dissolved in diethyl ether. Filtration through a plug of Celite, followed by evaporation of solvent under reduced pressure afforded the crude material that was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 9:1). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 9:1) 0.59. Pale-yellow oil. Isolated yield 99% (4.79 g, 22.8 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.06-7.18 (4H, *m*, C^{ar}*H*), 4.08 (2H, *q*, *J* 7.1, ethoxy C*H*$_2$-O), 3.54 (1H, *sext.*, *J* 6.9, benzylic C*H*), 2.62 (1H, *dd*, J_1 15.2, J_2 6.6, ABX spin-system, diastereotopic C*H*$_2$), 2.53 (1H, *dd*, J_1 15.2, J_2 8.5, ABX spin-system, diastereotopic C*H*$_2$), 2.38 (3H, *s*, C*H*$_3$), 1.26 (3H, *d*, *J* 6.9, C*H*$_3$), 1.17 (3H, *t*, *J* 7.1, ethoxy C*H*$_3$) ppm.

Ethyl 3-methyl-3-phenylbutanoate

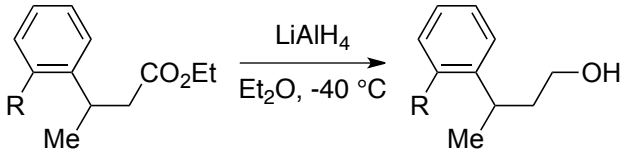


ethyl 3-methyl-3-phenylbutanoate
Chemical Formula: $C_{13}H_{18}O_2$
Molecular Weight: 206.28

<u>*Preparation of the cuprate:*</u> To a cooled (0 °C, ice/water bath) solution of CuI (2.0 g, 10.5 mmol, 2.0 equiv.) in anhydrous Et_2O (10 mL) was added MeLi (1.6 M solution in Et_2O, 13.1 mL, 21.0 mmol, 4.0 equiv.) dropwise *via* syringe. The resultant suspension was stirred at 0 °C until complete dissolution of the precipitate (*ca.* 15 min). Solvent was removed *in vacuo* at 0 °C, and anhydrous CH_2Cl_2 (10 mL) was added. After stirring for an additional 10 min, the solvent was once more evaporated under reduced pressure, and the resultant pale-yellow residue was suspended in pre-cooled anhydrous CH_2Cl_2 (60 mL).

<u>*Conjugate addition reaction*</u>: To a cooled (0 °C, ice/water bath) solution of the above-prepared Me_2CuLi solution (10.5 mmol, 2.0 equiv.) was added Me_3SiCl (1.35 mL, 10.5 mmol, 2.0 equiv.) followed by a pre-cooled solution of ethyl 3-phenylbut-2-enoate (1.0 g, 5.25 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (10 mL). The resultant mixture was stirred at 0 °C for 2 h, upon which a 1:1 (*v/v*) mixture of saturated aqueous NH_4Cl and 23% (*w/w*) aqueous NH_4OH was added to quench the reaction. The layers were separated, and the aqueous layer was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude residue was used in the next step as such, without further purification. $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 4:1) 0.57. Colorless liquid. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.37 (2H, *dd*, J_1 8.6, J_2 1.4, C^{ar}*H*), 7.31 (2H, *t*, *J* 7.4, C^{ar}*H*), 7.19 (1H, *td*, J_1 7.2, J_2 1.3, C^{ar}*H*), 3.98 (2H, *q*, *J* 7.1, ethoxy C*H*$_2$-O), 2.61 (2H, *s*, α-carbonyl C*H*$_2$), 1.46 (6H, *s*, *gem*-dimethyl C*H*$_3$), 1.09 (3H, *t*, *J* 7.1, ethoxy C*H*$_3$) ppm.

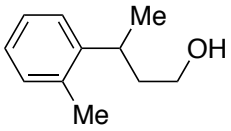
General Procedure for the Synthesis of Substrates: $LiAlH_4$ Reduction



R = Me, OMe, F, Cl

To a cooled (-40 °C, dry ice/acetonitrile bath) slurry of $LiAlH_4$ (2.0 equiv.) in anhydrous Et_2O (0.20 M) was added the required ester (1.0 equiv.) dropwise as a solution in anhydrous Et_2O (0.40 M). The resultant mixture was stirred at -40 °C for 6-8 h, upon which EtOAc was added to quench the reaction. Methanol was then added, followed by water, and the layers were separated. The aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used in the next step as such, without further purification.

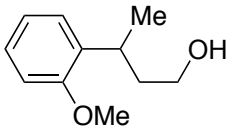
3-(*o*-tolyl)butan-1-ol



3-(*o*-tolyl)butan-1-ol
Chemical Formula: $C_{11}H_{16}O$
Molecular Weight: 164.24

To a cooled (-40 °C, dry ice/acetonitrile bath) slurry of $LiAlH_4$ (1.53 g, 40.2 mmol, 2.0 equiv.) in anhydrous Et_2O (200 mL) was added ethyl 3-(*o*-tolyl)butanoate (4.15 g, 20.1 mmol, 1.0 equiv.) dropwise as a solution in anhydrous Et_2O (50 mL). The resultant mixture was stirred at -40 °C for 2 h, upon which EtOAc was added to quench the reaction. Water was then added, and the layers were separated. The aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used in the next step as such, without further purification. Quantitative yield (3.36 g, 20.1 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.15. Colorless oil.

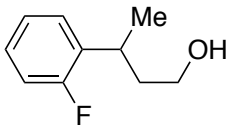
3-(2-methoxyphenyl)butan-1-ol



3-(2-methoxyphenyl)butan-1-ol
Chemical Formula: $C_{11}H_{16}O_2$
Molecular Weight: 180.24

To a cooled (-40 °C, dry ice/acetonitrile bath) slurry of $LiAlH_4$ (1.73 g, 45.6 mmol, 2.0 equiv.) in anhydrous Et_2O (200 mL) was added ethyl 3-(2-methoxyphenyl)butanoate (4.79 g, 22.8 mmol, 1.0 equiv.) dropwise as a solution in anhydrous Et_2O (50 mL). The resultant mixture was stirred at -40 °C for 2 h, upon which EtOAc was added to quench the reaction. Water was then added, and the layers were separated. The aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used in the next step as such, without further purification. Quantitative yield (4.11 g, 22.8 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.07. Colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.14-7.19 (2H, *m*, C^{ar}*H*), 6.92 (1H, *td*, J_1 7.4, J_2 1.0, C^{ar}*H*), 6.85 (1H, *d*, *J* 8.6, C^{ar}*H*), 3.94-4.05 (2H, *m*, diastereotopic CH_2-O), 3.81 (3H, *s*, CH_3-O), 3.30 (1H, *sext.*, *J* 7.1, benzylic C*H*), 2.00 (1H, *brs*, hydroxylic O*H*), 1.82-1.99 (2H, *m*, CH_2), 1.24 (3H, *d*, *J* 7.0, CH_3) ppm.

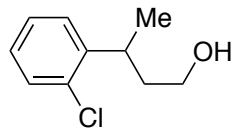
3-(2-fluorophenyl)butan-1-ol



3-(2-fluorophenyl)butan-1-ol
Chemical Formula: $C_{10}H_{13}FO$
Molecular Weight: 168.21

To a cooled (-40 °C, dry ice/acetonitrile bath) slurry of $LiAlH_4$ (1.73 g, 45.6 mmol, 2.0 equiv.) in anhydrous Et_2O (200 mL) was added ethyl 3-(2-fluorophenyl)butanoate (4.79 g, 22.8 mmol, 1.0 equiv.) dropwise as a solution in anhydrous Et_2O (50 mL). The resultant mixture was stirred at -40 °C for 2 h, upon which EtOAc was added to quench the reaction. Water was then added, and the layers were separated. The aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used in the next step as such, without further purification. Quantitative yield (3.84 g, 22.8 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.17. Colorless oil.

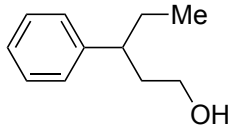
3-(2-chlorophenyl)butan-1-ol



3-(2-chlorophenyl)butan-1-ol
Chemical Formula: $C_{10}H_{13}ClO$
Molecular Weight: 184.66

To a cooled (-40 °C, dry ice/acetonitrile bath) slurry of $LiAlH_4$ (1.73 g, 45.6 mmol, 2.0 equiv.) in anhydrous Et_2O (200 mL) was added ethyl 3-(2-chlorophenyl)butanoate (5.17 g, 22.8 mmol, 1.0 equiv.) dropwise as a solution in anhydrous Et_2O (50 mL). The resultant mixture was stirred at -40 °C for 2 h, upon which EtOAc was added to quench the reaction. Water was then added, and the layers were separated. The aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used in the next step as such, without further purification. Quantitative yield (4.21 g, 22.8 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.10. Colorless oil.

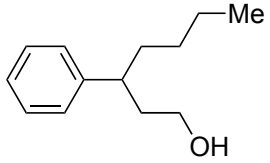
3-phenylpentan-1-ol



3-phenylpentan-1-ol
Chemical Formula: $C_{11}H_{16}O$
Molecular Weight: 164.24

To a cooled (-40 °C, dry ice/acetonitrile bath) slurry of $LiAlH_4$ (1.73 g, 45.6 mmol, 2.0 equiv.) in anhydrous Et_2O (200 mL) was added ethyl 3-phenylpentanoate (4.70 g, 22.8 mmol, 1.0 equiv.) dropwise as a solution in anhydrous Et_2O (50 mL). The resultant mixture was stirred at -40 °C for 2 h, upon which EtOAc was added to quench the reaction. Water was then added, and the layers were separated. The aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used in the next step as such, without further purification. Quantitative yield (3.74 g, 22.8 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.11. Colorless liquid.

3-phenylheptan-1-ol

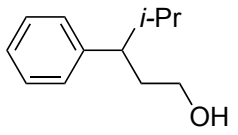


3-phenylheptan-1-ol
Chemical Formula: $C_{13}H_{20}O$
Molecular Weight: 192.30

To a cooled (-40 °C, dry ice/acetonitrile bath) slurry of $LiAlH_4$ (1.73 g, 45.6 mmol, 2.0 equiv.) in anhydrous Et_2O (200 mL) was added ethyl 3-phenylheptanoate (5.34 g, 22.8 mmol, 1.0 equiv.) dropwise as a solution in anhydrous Et_2O (50 mL). The resultant mixture was stirred at -40 °C for 2 h, upon which EtOAc was added to quench the reaction. Water was then added, and the layers were separated. The aqueous layer was extracted with diethyl ether. The combined organic

layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used in the next step as such, without further purification. Quantitative yield (4.38 g, 22.8 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.22. Colorless liquid.

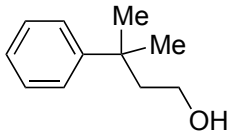
4-methyl-3-phenylpentan-1-ol



4-methyl-3-phenylpentan-1-ol
Chemical Formula: $C_{12}H_{18}O$
Molecular Weight: 178.27

To a cooled (-40 °C, dry ice/acetonitrile bath) slurry of $LiAlH_4$ (1.73 g, 45.6 mmol, 2.0 equiv.) in anhydrous Et_2O (200 mL) was added ethyl 4-methyl-3-phenylpentanoate (5.02 g, 22.8 mmol, 1.0 equiv.) dropwise as a solution in anhydrous Et_2O (50 mL). The resultant mixture was stirred at -40 °C for 2 h, upon which EtOAc was added to quench the reaction. Water was then added, and the layers were separated. The aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used in the next step as such, without further purification. Quantitative yield (4.06 g, 22.8 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.19. Colorless liquid.

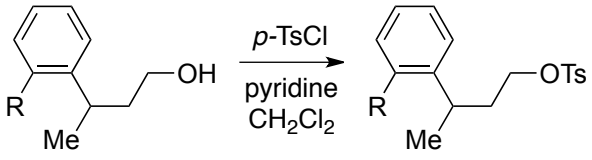
3-methyl-3-phenylbutan-1-ol



3-methyl-3-phenylbutan-1-ol
Chemical Formula: $C_{11}H_{16}O$
Molecular Weight: 164.24

To a cooled (-40 °C, dry ice/acetonitrile bath) slurry of $LiAlH_4$ (440 mg, 10.5 mmol, 2.0 equiv.) in anhydrous Et_2O (30 mL) was added ethyl 3-methyl-3-phenylbutanoate (1.09 g, 5.25 mmol, 1.0 equiv.) dropwise as a solution in anhydrous Et_2O (20 mL). The resultant mixture was stirred at -40 °C for 2 h, upon which EtOAc was added to quench the reaction. Water was then added, and the layers were separated. The aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used in the next step as such, without further purification. Quantitative yield (864 mg, 5.25 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.14. Colorless liquid.

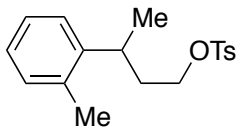
General Procedure for the Synthesis of Substrates: Tosylation Reaction



R = Me, OMe, F, Cl

To a well-stirred solution of the required homobenzylic alcohol (1.0 equiv.) and anhydrous pyridine (2.5 equiv.) in anhydrous CH_2Cl_2 (0.33 M) was added TsCl (2.0 equiv.). The resultant homogeneous mixture was stirred at ambient temperature for 12-24 h. Upon completion, the reaction mixture was concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel, using an adequate *n*-hexane/Et_2O mixture as eluent.

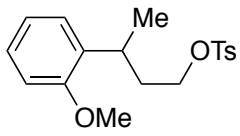
3-(*o*-tolyl)butyl 4-methylbenzenesulfonate



3-(*o*-tolyl)butyl 4-methyl benzenesulfonate
Chemical Formula: $C_{18}H_{22}O_3S$
Molecular Weight: 318.43

To a well-stirred solution of 3-(*o*-tolyl)butan-1-ol (3.56 g, 20.1 mmol, 1.0 equiv.) and anhydrous pyridine (4.06 mL, 50.3 mmol, 2.5 equiv.) in anhydrous CH_2Cl_2 (60 mL) was added TsCl (7.66 g, 40.2 mmol, 2.0 equiv.). The resultant mixture was stirred at ambient temperature for 24 h. Upon completion, the reaction mixture was concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5 → *n*-hexane/Et_2O 9:1). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.39. Colorless oil. Isolated yield 87% (5.59 g, 17.5 mmol).

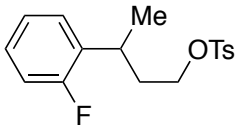
3-(2-methoxyphenyl)butyl 4-methylbenzenesulfonate



3-(2-methoxyphenyl)butyl 4-methylbenzenesulfonate
Chemical Formula: $C_{18}H_{22}O_4S$
Molecular Weight: 334.43

To a well-stirred solution of 3-(2-methoxyphenyl)butan-1-ol (4.11 g, 22.8 mmol, 1.0 equiv.) and anhydrous pyridine (4.65 mL, 57.0 mmol, 2.5 equiv.) in anhydrous CH_2Cl_2 (60 mL) was added TsCl (8.69 g, 45.6 mmol, 2.0 equiv.). The resultant mixture was stirred at ambient temperature for 24 h. Upon completion, the reaction mixture was concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5 → *n*-hexane/Et_2O 9:1). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.30. Colorless oil. Isolated yield 49% (3.74 g, 11.2 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.73 (2H, *d*, *J* 8.3, $C^{ar}H$), 7.30 (2H, *d*, *J* 8.3, $C^{ar}H$), 7.16 (1H, *td*, J_1 7.4, J_2 1.7, $C^{ar}H$), 7.04 (1H, *dd*, J_1 7.6, J_2 1.7, $C^{ar}H$), 6.86 (1H, *dd*, J_1 7.4, J_2 1.0, $C^{ar}H$), 6.83 (1H, *t*, *J* 8.2, $C^{ar}H$), 3.91-4.00 (2H, *m*, diastereotopic CH_2-O), 3.78 (3H, *s*, CH_3-O), 3.23 (1H, *sext.*, *J* 7.0, benzylic C*H*), 2.44 (3H, *s*, arylic CH_3), 1.85-2.03 (2H, *m*, CH_2), 1.17 (3H, *d*, *J* 7.0, CH_3) ppm.

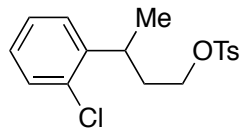
3-(2-fluorophenyl)butyl 4-methylbenzenesulfonate



3-(2-fluorophenyl)butyl 4-methyl benzenesulfonate
Chemical Formula: $C_{17}H_{19}FO_3S$
Molecular Weight: 322.39

To a well-stirred solution of 3-(2-fluorophenyl)butan-1-ol (3.84 g, 22.8 mmol, 1.0 equiv.) and anhydrous pyridine (4.65 mL, 57.0 mmol, 2.5 equiv.) in anhydrous CH_2Cl_2 (60 mL) was added TsCl (8.69 g, 45.6 mmol, 2.0 equiv.). The resultant mixture was stirred at ambient temperature for 24 h. Upon completion, the reaction mixture was concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5 → *n*-hexane/Et_2O 9:1). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.43. Pale-yellow oil. Isolated yield 61% (4.45 g, 13.8 mmol).

3-(2-chlorophenyl)butyl 4-methylbenzenesulfonate

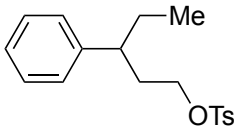


3-(2-chlorophenyl)butyl 4-methylbenzenesulfonate
Chemical Formula: $C_{17}H_{19}ClO_3S$
Molecular Weight: 338.85

To a well-stirred solution of 3-(2-chlorophenyl)butan-1-ol (4.21 g, 22.8 mmol, 1.0 equiv.) and anhydrous pyridine (4.65 mL, 57.0 mmol, 2.5 equiv.) in anhydrous CH_2Cl_2 (60 mL) was added TsCl (8.69 g, 45.6 mmol, 2.0 equiv.). The resultant mixture was stirred at ambient temperature for 24 h. Upon completion, the reaction mixture was concentrated under reduced pressure. The crude

residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5 → *n*-hexane/Et_2O 9:1). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.43. Pale-yellow oil. Isolated yield 64% (4.92 g, 14.5 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.74 (2H, *d*, *J* 8.3, C^{ar}*H*), 7.30 (2H, *d*, *J* 8.3, C^{ar}*H*), 7.29 (1H, *d*, *J* 7.8, C^{ar}*H*), 7.08-7.21 (3H, *m*, C^{ar}*H*), 3.92-4.04 (2H, *m*, diastereotopic CH_2-O), 3.36 (1H, *sext.*, *J* 7.1, benzylic C*H*), 2.44 (3H, *s*, arylic CH_3), 1.88-2.06 (2H, *m*, CH_2), 1.19 (3H, *d*, *J* 7.0, CH_3) ppm.

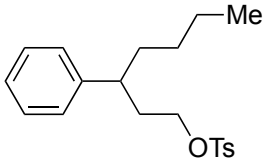
3-phenylpentyl 4-methylbenzenesulfonate



3-phenylpentyl 4-methyl benzenesulfonate
Chemical Formula: $C_{18}H_{22}O_3S$
Molecular Weight: 318.43

To a well-stirred solution of 3-phenylpentan-1-ol (3.74 g, 22.8 mmol, 1.0 equiv.) and anhydrous pyridine (4.65 mL, 57.0 mmol, 2.5 equiv.) in anhydrous CH_2Cl_2 (60 mL) was added TsCl (8.69 g, 45.6 mmol, 2.0 equiv.). The resultant mixture was stirred at ambient temperature for 24 h. Upon completion, the reaction mixture was concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5 → *n*-hexane/Et_2O 9:1). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.39. Colorless oil. Isolated yield 70% (5.08 g, 16.0 mmol).

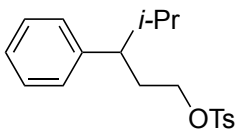
3-phenylpentyl 4-methylbenzenesulfonate



3-phenylheptyl 4-methyl benzenesulfonate
Chemical Formula: $C_{20}H_{26}O_3S$
Molecular Weight: 346.48

To a well-stirred solution of 3-phenylheptan-1-ol (4.38 g, 22.8 mmol, 1.0 equiv.) and anhydrous pyridine (4.65 mL, 57.0 mmol, 2.5 equiv.) in anhydrous CH_2Cl_2 (60 mL) was added TsCl (8.69 g, 45.6 mmol, 2.0 equiv.). The resultant mixture was stirred at ambient temperature for 24 h. Upon completion, the reaction mixture was concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5 → *n*-hexane/Et_2O 9:1). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.39. Colorless oil. Isolated yield 68% (5.37 g, 15.5 mmol).

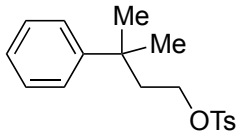
4-methyl-3-phenylpentyl 4-methylbenzenesulfonate



4-methyl-3-phenylpentyl 4-methylbenzenesulfonate
Chemical Formula: $C_{19}H_{24}O_3S$
Molecular Weight: 332.46

To a well-stirred solution of 4-methyl-3-phenylpentan-1-ol (4.06 g, 22.8 mmol, 1.0 equiv.) and anhydrous pyridine (4.65 mL, 57.0 mmol, 2.5 equiv.) in anhydrous CH_2Cl_2 (60 mL) was added TsCl (8.69 g, 45.6 mmol, 2.0 equiv.). The resultant mixture was stirred at ambient temperature for 24 h. Upon completion, the reaction mixture was concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5 → *n*-hexane/Et_2O 9:1). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.39. Colorless oil. Isolated yield 75% (5.69 g, 17.1 mmol).

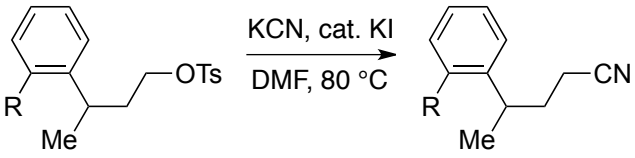
3-methyl-3-phenylbutyl 4-methylbenzenesulfonate



3-methyl-3-phenylbutyl 4-methylbenzenesulfonate
Chemical Formula: $C_{18}H_{22}O_3S$
Molecular Weight: 318.43

To a well-stirred solution of 3-methyl-3-phenylbutan-1-ol (864 mg, 5.25 mmol, 1.0 equiv.) and anhydrous pyridine (1.08 mL, 13.1 mmol, 2.5 equiv.) in anhydrous CH_2Cl_2 (15 mL) was added TsCl (2.0 g, 10.5 mmol, 2.0 equiv.). The resultant mixture was stirred at ambient temperature for 24 h. Upon completion, the reaction mixture was concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5 → *n*-hexane/Et_2O 9:1). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.43. Colorless oil. Isolated yield 21% (330 mg, 1.1 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.68 (2H, *d*, *J* 8.3, C^{ar}*H*), 7.19-7.30 (6H, *m*, C^{ar}*H*), 7.17 (1H, *td*, J_1 7.0, J_2 1.7, C^{ar}*H*), 3.85 (2H, *t*, *J* 7.4, CH_2-O), 2.44 (3H, *s*, *p*-toluenesulfonyl CH_3), 2.02 (2H, *t*, *J* 7.4, CH_2), 1.29 (6H, *s*, *gem*-dimethyl CH_3) ppm.

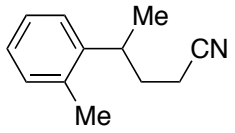
General Procedure for the Synthesis of Substrates: Cyanide S_N2 Substitution



R = Me, OMe, F, Cl

A solution composed of the required tosylate (1.0 equiv.), KCN (2.0 equiv.), and KI (0.5 equiv.) in anhydrous DMF (0.40 M) was heated at 60 °C for 24-48 h. Upon completion, the reaction mixture was diluted with water and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used in the next step as such, without further purification.

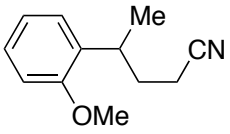
4-(*o*-tolyl)pentanenitrile



4-(*o*-tolyl)pentanenitrile
Chemical Formula: $C_{12}H_{15}N$
Molecular Weight: 173.25

A solution composed of 3-(*o*-tolyl)butyl 4-methylbenzenesulfonate (5.59 g, 17.5 mmol, 1.0 equiv.), KCN (2.28 g, 35.0 mmol, 2.0 equiv.), and KI (1.45 g, 8.75 mmol, 0.5 equiv.) in anhydrous DMF (45 mL) was heated at 60 °C for 24 h. Upon completion, the reaction mixture was diluted with water and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 9:1) 0.47. Colorless oil. Isolated yield 99% (3.03 g, 17.5 mmol).

4-(2-methoxyphenyl)pentanenitrile

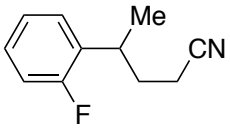


4-(2-methoxyphenyl)pentanenitrile
Chemical Formula: $C_{12}H_{15}NO$
Molecular Weight: 189.25

A solution composed of 3-(2-methoxyphenyl)butyl 4-methylbenzenesulfonate (3.73 g, 11.2 mmol, 1.0 equiv.), KCN (1.46 g, 22.4 mmol, 2.0 equiv.), and KI (930 mg, 5.60 mmol, 0.5 equiv.) in anhydrous DMF (30 mL) was heated at 60 °C for 24 h. Upon completion, the reaction mixture was diluted with water

and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.29. Colorless oil. Isolated yield 99% (2.12 g, 11.2 mmol).

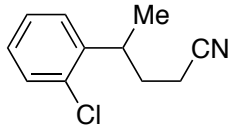
4-(2-fluorophenyl)pentanenitrile



4-(2-fluorophenyl)pentanenitrile
Chemical Formula: $C_{11}H_{12}FN$
Molecular Weight: 177.22

A solution composed of 3-(2-fluorophenyl)butyl 4-methylbenzenesulfonate (4.45 g, 13.8 mmol, 1.0 equiv.), KCN (1.80 g, 27.6 mmol, 2.0 equiv.), and KI (1.15 g, 6.90 mmol, 0.5 equiv.) in anhydrous DMF (35 mL) was heated at 60 °C for 24 h. Upon completion, the reaction mixture was diluted with water and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 9:1) 0.51. Colorless oil. Isolated yield 99% (2.45 g, 13.8 mmol).

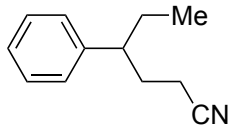
4-(2-chlorophenyl)pentanenitrile



4-(2-chlorophenyl)pentanenitrile
Chemical Formula: $C_{11}H_{12}ClN$
Molecular Weight: 193.67

A solution composed of 3-(2-chlorophenyl)butyl 4-methylbenzenesulfonate (4.92 g, 14.5 mmol, 1.0 equiv.), KCN (1.89 g, 29.0 mmol, 2.0 equiv.), and KI (1.20 g, 7.25 mmol, 0.5 equiv.) in anhydrous DMF (40 mL) was heated at 60 °C for 24 h. Upon completion, the reaction mixture was diluted with water and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 9:1) 0.51. Colorless oil. Isolated yield 99% (2.45 g, 13.8 mmol).

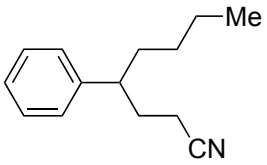
4-phenylhexanenitrile



4-phenylhexanenitrile
Chemical Formula: $C_{12}H_{15}N$
Molecular Weight: 173.25

A solution composed of 3-phenylpentyl 4-methylbenzenesulfonate (5.10 g, 16.0 mmol, 1.0 equiv.), KCN (2.08 g, 32.0 mmol, 2.0 equiv.), and KI (1.33 g, 8.0 mmol, 0.5 equiv.) in anhydrous DMF (45 mL) was heated at 60 °C for 24 h. Upon completion, the reaction mixture was diluted with water and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 9:1) 0.48. Pale-yellow oil. Isolated yield 99% (2.77 g, 16.0 mmol).

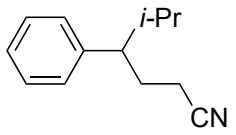
4-phenyloctanenitrile



4-phenyloctanenitrile
Chemical Formula: $C_{14}H_{19}N$
Molecular Weight: 201.31

A solution composed of 3-phenylheptyl 4-methylbenzenesulfonate (4.38 g, 12.6 mmol, 1.0 equiv.), KCN (1.64 g, 25.3 mmol, 2.0 equiv.), and KI (1.05 g, 6.3 mmol, 0.5 equiv.) in anhydrous DMF (40 mL) was heated at 60 °C for 24 h. Upon completion, the reaction mixture was diluted with water and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 9:1) 0.48. Pale-yellow oil. Isolated yield 99% (2.77 g, 16.0 mmol).

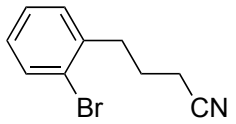
5-methyl-4-phenylhexanenitrile



5-methyl-4-phenylhexanenitrile
Chemical Formula: $C_{13}H_{17}N$
Molecular Weight: 187.28

A solution composed of 4-methyl-3-phenylpentyl 4-methylbenzenesulfonate (5.0 g, 15.0 mmol, 1.0 equiv.), KCN (1.95 g, 30.0 mmol, 2.0 equiv.), and KI (1.25 g, 7.50 mmol, 0.5 equiv.) in anhydrous DMF (45 mL) was heated at 60 °C for 24 h. Upon completion, the reaction mixture was diluted with water and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 9:1) 0.48. Pale-yellow oil. Isolated yield 99% (2.77 g, 16.0 mmol).

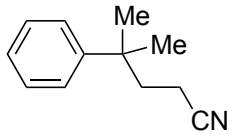
4-(2-bromophenyl)butanenitrile



4-(2-bromophenyl)butanenitrile
Chemical Formula: $C_{10}H_{10}BrN$
Molecular Weight: 224.10

A solution composed of 3-(2-bromophenyl)propyl 4-methylbenzenesulfonate (1.81 g, 4.90 mmol, 1.0 equiv.), KCN (638 mg, 9.80 mmol, 2.0 equiv.), and KI (407 mg, 2.45 mmol, 0.5 equiv.) in anhydrous DMF (15 mL) was heated at 60 °C for 24 h. Upon completion, the reaction mixture was diluted with water and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 9:1) 0.54. Pale-yellow oil. Isolated yield 99% (1.10 g, 4.90 mmol).

4-methyl-4-phenylpentanenitrile

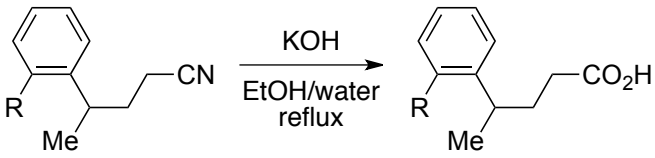


4-methyl-4-phenylpentanenitrile
Chemical Formula: $C_{12}H_{15}N$
Molecular Weight: 173.25

A solution composed of 3-methyl-3-phenylbutyl 4-methylbenzenesulfonate (330 mg, 1.1 mmol, 1.0 equiv.), KCN (143 mg, 2.2 mmol, 2.0 equiv.), and KI (100 mg, 0.55 mmol, 0.5 equiv.) in anhydrous DMF (5.0 mL) was heated at 60 °C for 24 h. Upon completion, the reaction mixture was diluted with water and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-

hexane/Et_2O 95:5). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 9:1) 0.48. Pale-yellow oil. Isolated yield 99% (2.77 g, 16.0 mmol).

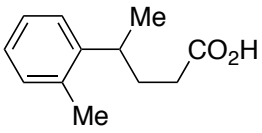
General Procedure for the Synthesis of Substrates: Saponification of the Nitrile



R = Me, OMe, F, Cl

A solution composed of the required nitrile (1.0 equiv.) and anhydrous KOH (4.0 equiv.) in EtOH/water (1:1 *v/v*, 0.20 M) was heated at reflux for 48-72 h. Upon cooling down to ambient temperature, the reaction mixture was washed with diethyl ether. The aqueous layer was separated and acidified with concentrated HCl (0 °C, ice/water bath cooling). The acidified aqueous layer was then extracted with dithyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used in the next step as such, without further purification.

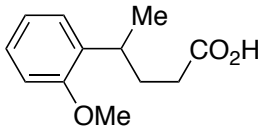
4-(*o*-tolyl)pentanoic acid



4-(*o*-tolyl)pentanoic acid
Chemical Formula: $C_{12}H_{16}O_2$
Molecular Weight: 192.25

A solution composed of 4-(*o*-tolyl)pentanenitrile (3.03 g, 17.5 mmol, 1.0 equiv.) and anhydrous KOH (3.93 g, 70.0 mmol, 4.0 equiv.) in EtOH/water (1:1 *v/v*, 100 mL) was heated at reflux for 48 h. Upon cooling down to ambient temperature, the reaction mixture was washed with diethyl ether. The aqueous layer was separated and acidified with concentrated HCl (0 °C, ice/water bath cooling). The acidified aqueous layer was then extracted with dithyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. Pale-orange oil. Isolated yield 87% (2.92 g, 15.2 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.02 (1H, *brs*, carboxylic CO_2H), 7.16-7.19 (2H, *m*, $C^{ar}H$), 7.07-7.14 (2H, *m*, $C^{ar}H$), 3.05 (1H, *sext.*, *J* 7.0, benzylic C*H*), 2.31 (3H, *s*, CH_3), 2.27 (2H, *t*, *J* 7.7, α-carbonyl CH_2), 1.87-2.01 (2H, *m*, diastereotopic CH_2), 1.23 (3H, *d*, *J* 6.9, CH_3) ppm.

4-(2-methoxyphenyl)pentanoic acid

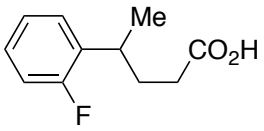


4-(2-methoxyphenyl)pentanoic acid
Chemical Formula: $C_{12}H_{16}O_3$
Molecular Weight: 208.25

A solution composed of 4-(2-methoxyphenyl)pentanenitrile (2.12 g, 11.2 mmol, 1.0 equiv.) and anhydrous KOH (2.52 g, 44.9 mmol, 4.0 equiv.) in EtOH/water (1:1 *v/v*, 70 mL) was heated at reflux for 48 h. Upon cooling down to ambient temperature, the reaction mixture was washed with diethyl ether. The aqueous layer was separated and acidified with concentrated HCl (0 °C, ice/water bath cooling). The acidified aqueous layer was then extracted with dithyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. Colorless oil. Isolated yield 85% (1.98 g, 9.52 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.02 (1H, *brs*, carboxylic CO_2H), 7.16-7.19 (2H, *m*, $C^{ar}H$), 7.07-7.14 (2H, *m*,

$C^{ar}H$), 3.05 (1H, *sext.*, *J* 7.0, benzylic C*H*), 2.31 (3H, *s*, CH_3), 2.27 (2H, *t*, *J* 7.7, α-carbonyl CH_2), 1.87-2.01 (2H, *m*, diastereotopic CH_2), 1.23 (3H, *d*, *J* 6.9, CH_3) ppm.

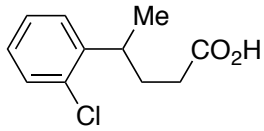
4-(2-fluorophenyl)pentanoic acid



4-(2-fluorophenyl)pentanoic acid
Chemical Formula: $C_{11}H_{13}FO_2$
Molecular Weight: 196.22

A solution composed of 4-(2-fluorophenyl)pentanenitrile (2.45 g, 13.8 mmol, 1.0 equiv.) and anhydrous KOH (3.10 g, 55.2 mmol, 4.0 equiv.) in EtOH/water (1:1 *v/v*, 80 mL) was heated at reflux for 48 h. Upon cooling down to ambient temperature, the reaction mixture was washed with diethyl ether. The aqueous layer was separated and acidified with concentrated HCl (0 °C, ice/water bath cooling). The acidified aqueous layer was then extracted with dithyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. Pale-yellow oil. Isolated yield 80% (2.15 g, 11.0 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 8.02 (1H, *brs*, carboxylic CO_2H), 7.16-7.19 (2H, *m*, $C^{ar}H$), 7.07-7.14 (2H, *m*, $C^{ar}H$), 3.05 (1H, *sext.*, *J* 7.0, benzylic C*H*), 2.31 (3H, *s*, CH_3), 2.27 (2H, *t*, *J* 7.7, α-carbonyl CH_2), 1.87-2.01 (2H, *m*, diastereotopic CH_2), 1.23 (3H, *d*, *J* 6.9, CH_3) ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): *δ* -118.3 (1F, *s*, $C^{ar}F$) ppm.

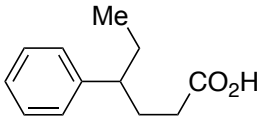
4-(2-chlorophenyl)pentanoic acid



4-(2-chlorophenyl)pentanoic acid
Chemical Formula: $C_{11}H_{13}ClO_2$
Molecular Weight: 212.67

A solution composed of 4-(2-chlorophenyl)pentanenitrile (2.45 g, 13.8 mmol, 1.0 equiv.) and anhydrous KOH (3.10 g, 55.2 mmol, 4.0 equiv.) in EtOH/water (1:1 *v/v*, 80 mL) was heated at reflux for 48 h. Upon cooling down to ambient temperature, the reaction mixture was washed with diethyl ether. The aqueous layer was separated and acidified with concentrated HCl (0 °C, ice/water bath cooling). The acidified aqueous layer was then extracted with dithyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. Pale-yellow oil. Isolated yield 80% (2.15 g, 11.0 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 8.02 (1H, *brs*, carboxylic CO_2H), 7.16-7.19 (2H, *m*, $C^{ar}H$), 7.07-7.14 (2H, *m*, $C^{ar}H$), 3.05 (1H, *sext.*, *J* 7.0, benzylic C*H*), 2.31 (3H, *s*, CH_3), 2.27 (2H, *t*, *J* 7.7, α-carbonyl CH_2), 1.87-2.01 (2H, *m*, diastereotopic CH_2), 1.23 (3H, *d*, *J* 6.9, CH_3) ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): *δ* -118.3 (1F, *s*, $C^{ar}F$) ppm.

4-phenylhexanoic acid

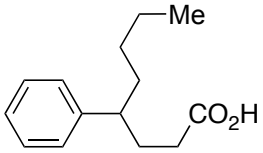


4-phenylhexanoic acid
Chemical Formula: $C_{12}H_{16}O_2$
Molecular Weight: 192.25

A solution composed of 4-phenylhexanenitrile (2.77 g, 16.0 mmol, 1.0 equiv.) and anhydrous KOH (3.59 g, 64.0 mmol, 4.0 equiv.) in EtOH/water (1:1 *v/v*, 100 mL) was heated at reflux for 48 h. Upon cooling down to ambient temperature, the reaction mixture was washed with diethyl ether. The aqueous layer was separated and acidified with concentrated HCl (0 °C, ice/water bath cooling). The acidified aqueous layer was then extracted with dithyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. Colorless oil. Isolated yield 90% (2.77 g, 14.4 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 8.02 (1H, *brs*, carboxylic CO_2H), 7.16-7.19

(2H, *m*, C^{ar}*H*), 7.07-7.14 (2H, *m*, C^{ar}*H*), 3.05 (1H, *sext.*, *J* 7.0, benzylic C*H*), 2.31 (3H, *s*, CH_3), 2.27 (2H, *t*, *J* 7.7, α-carbonyl CH_2), 1.87-2.01 (2H, *m*, diastereotopic CH_2), 1.23 (3H, *d*, *J* 6.9, CH_3) ppm.

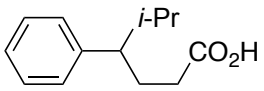
4-phenyloctanoic acid



4-phenyloctanoic acid
Chemical Formula: $C_{14}H_{20}O_2$
Molecular Weight: 220.31

A solution composed of 4-phenylhexanenitrile (2.77 g, 16.0 mmol, 1.0 equiv.) and anhydrous KOH (3.59 g, 64.0 mmol, 4.0 equiv.) in EtOH/water (1:1 *v/v*, 100 mL) was heated at reflux for 48 h. Upon cooling down to ambient temperature, the reaction mixture was washed with diethyl ether. The aqueous layer was separated and acidified with concentrated HCl (0 °C, ice/water bath cooling). The acidified aqueous layer was then extracted with dithyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. Colorless oil. Isolated yield 90% (2.77 g, 14.4 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 8.02 (1H, *brs*, carboxylic CO_2H), 7.16-7.19 (2H, *m*, C^{ar}*H*), 7.07-7.14 (2H, *m*, C^{ar}*H*), 3.05 (1H, *sext.*, *J* 7.0, benzylic C*H*), 2.31 (3H, *s*, CH_3), 2.27 (2H, *t*, *J* 7.7, α-carbonyl CH_2), 1.87-2.01 (2H, *m*, diastereotopic CH_2), 1.23 (3H, *d*, *J* 6.9, CH_3) ppm.

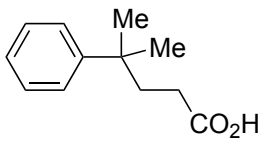
5-methyl-4-phenylhexanoic acid



5-methyl-4-phenylhexanoic acid
Chemical Formula: $C_{13}H_{18}O_2$
Molecular Weight: 206.28

A solution composed of 4-phenylhexanenitrile (2.77 g, 16.0 mmol, 1.0 equiv.) and anhydrous KOH (3.59 g, 64.0 mmol, 4.0 equiv.) in EtOH/water (1:1 *v/v*, 100 mL) was heated at reflux for 48 h. Upon cooling down to ambient temperature, the reaction mixture was washed with diethyl ether. The aqueous layer was separated and acidified with concentrated HCl (0 °C, ice/water bath cooling). The acidified aqueous layer was then extracted with dithyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. Colorless oil. Isolated yield 90% (2.77 g, 14.4 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 8.02 (1H, *brs*, carboxylic CO_2H), 7.16-7.19 (2H, *m*, C^{ar}*H*), 7.07-7.14 (2H, *m*, C^{ar}*H*), 3.05 (1H, *sext.*, *J* 7.0, benzylic C*H*), 2.31 (3H, *s*, CH_3), 2.27 (2H, *t*, *J* 7.7, α-carbonyl CH_2), 1.87-2.01 (2H, *m*, diastereotopic CH_2), 1.23 (3H, *d*, *J* 6.9, CH_3) ppm.

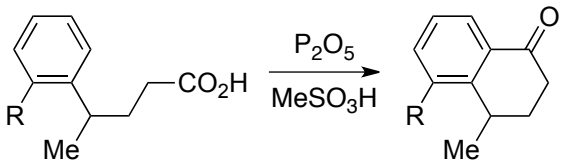
4-methyl-4-phenylpentanoic acid



4-methyl-4-phenylpentanoic acid
Chemical Formula: $C_{12}H_{16}O_2$
Molecular Weight: 192.25

A solution composed of 4-methyl-4-phenylpentanenitrile (2.77 g, 16.0 mmol, 1.0 equiv.) and anhydrous KOH (3.59 g, 64.0 mmol, 4.0 equiv.) in EtOH/water (1:1 *v/v*, 100 mL) was heated at reflux for 48 h. Upon cooling down to ambient temperature, the reaction mixture was washed with diethyl ether. The aqueous layer was separated and acidified with concentrated HCl (0 °C, ice/water bath cooling). The acidified aqueous layer was then extracted with dithyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. Colorless oil. Isolated yield 90% (2.77 g, 14.4 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 8.02 (1H, *brs*, carboxylic CO_2H), 7.16-7.19 (2H, *m*, C^{ar}*H*), 7.07-7.14 (2H, *m*, C^{ar}*H*), 3.05 (1H, *sext.*, *J* 7.0, benzylic C*H*), 2.31 (3H, *s*, CH_3), 2.27 (2H, *t*, *J* 7.7, α-carbonyl CH_2), 1.87-2.01 (2H, *m*, diastereotopic CH_2), 1.23 (3H, *d*, *J* 6.9, CH_3) ppm.

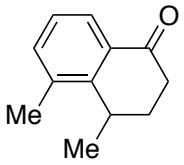
General Procedure for the Synthesis of Substrates: Cyclization to Methyl-Tetralone



R = Me, OMe, F, Cl $\mathbf{X_y}$

To a cooled (0 °C, ice/water bath) solution of the required carboxylic acid (1.0 equiv.) in methanesulfonic acid (0.35 M) was added P_2O_5 (2.5 equiv.). The resultant solution was stirred at ambient temperature for 24-48 h, and then poured over crushed ice. The mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel, unsing an adequate *n*-hexane/Et_2O mixture as eluent.

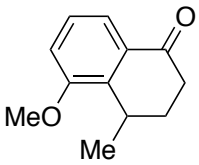
4,5-dimethyl-3,4-dihydronaphthalen-1(2*H*)-one (X_2)



4,5-dimethyl-3,4-dihydro naphthalen-1(2*H*)-one
Chemical Formula: $C_{12}H_{14}O$
Molecular Weight: 174.24

To a cooled (0 °C, ice/water bath) solution of 4-(*o*-tolyl)pentanoic acid (2.92 g, 15.2 mmol, 1.0 equiv.) in methanesulfonic acid (41 mL, 578 mmol, 38 equiv.) was added P_2O_5 (5.40 g, 38.0 mmol, 2.5 equiv.). The resultant solution was stirred at ambient temperature for 16 h, and then poured over crushed ice. The mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 98:2). Light-yellow crystalline solid. Isolated yield 86% (2.27 g, 13.0 mmol). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 4:1) 0.66. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.91 (1H, *d*, *J* 7.7, C^{ar}*H*), 7.35 (1H, *d*, *J* 7.4, C^{ar}*H*), 7.20 (1H, *t*, *J* 7.6, C^{ar}*H*), 3.29 (1H, broad *quin.*, *J* 6.9, benzylic C*H*), 2.85 (1H, *ddd*, J_1 12.6, J_2 9.4, J_3 3.2, α-carbonyl CH_2), 2.58 (1H, *ddd*, J_1 12.7, J_2 4.3, J_3 2.2, α-carbonyl CH_2), 2.38 (3H, *s*, CH_3), 2.29 (1H, *tt*, J_1 13.6, J_2 3.9, CH_2), 2.01 (1H, *dquin.*, J_1 13.6, J_2 2.7, CH_2), 1.32 (3H, *d*, *J* 7.1, CH_3) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 198.8 (ketone C*q*), 147.8 (C*q*), 135.7 (*C*H), 131.9 (C*q*), 126.3 (*C*H), 125.6 (*C*H), 33.2 (*C*H_2), 29.12 (*C*H), 29.09 (*C*H_2), 18.9 (*C*H_3), 18.6 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{12}H_{14}O$, expected $(M+NH_4)^+$ *m/z* 192.1383, observed $(M+NH_4)^+$ *m/z* 192.1386.

5-methoxy-4-methyl-3,4-dihydronaphthalen-1(2*H*)-one (X_3)

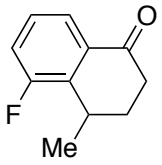


5-methoxy-4-methyl-3,4-di hydronaphthalen-1(2*H*)-one
Chemical Formula: $C_{12}H_{14}O_2$
Molecular Weight: 190.24

To a cooled (0 °C, ice/water bath) solution of 4-(2-methoxyphenyl)pentanoic acid (2.0 g, 9.60 mmol, 1.0 equiv.) in methanesulfonic acid (30 mL, 418 mmol, 38 equiv.) was added P_2O_5 (3.41 g, 24.0 mmol, 2.5 equiv.). The resultant solution was stirred at ambient temperature for 16 h, and then poured over crushed ice. The mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5 → 9:1). Colorless crystalline solid. Isolated yield 46% (840 mg, 4.42 mmol). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 4:1)

0.51. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.64 (1H, *dd*, J_1 8.6, J_2 0.7, $C^{ar}H$), 7.26 (1H, *d*, J 7.3, $C^{ar}H$), 7.03 (1H, *dd*, J_1 8.9, J_2 0.8, $C^{ar}H$), 3.87 (3H, *s*, methoxy CH_3-O), 3.42-3.49 (1H, *m*, benzylic C*H*), 2.82 (1H, *ddd*, J_1 17.6, J_2 15.0, J_3 5.2, α-carbonyl CH_2), 2.57 (1H, *dt*, J_1 17.6, J_2 1.2, α-carbonyl CH_2), 2.26 (1H, *tt*, J_1 13.6, J_2 5.1, CH_2), 1.99 (1H, *dquin.*, J_1 13.7, J_2 1.2, CH_2), 1.31 (3H, *d*, J 7.0, CH_3) ppm. **ESI-HRMS (positif)** M = $C_{12}H_{14}O_2$, expected $(M+H)^+$ *m/z* 191.1067, observed $(M+H)^+$ *m/z* 191.1066.

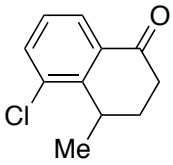
5-fluoro-4-methyl-3,4-dihydronaphthalen-1(2*H*)-one (X_4)



5-fluoro-4-methyl-3,4-dihydro naphthalen-1(2*H*)-one
Chemical Formula: $C_{11}H_{11}FO$
Molecular Weight: 178.20

To a cooled (0 °C, ice/water bath) solution of 4-(2-fluorophenyl)pentanoic acid (2.15 g, 11.0 mmol, 1.0 equiv.) in methanesulfonic acid (30 mL, 418 mmol, 38 equiv.) was added P_2O_5 (3.90 g, 27.5 mmol, 2.5 equiv.). The resultant solution was stirred at ambient temperature for 16 h, and then poured over crushed ice. The mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 98:2). Pale-yellow waxy solid. Isolated yield 91% (1.79 g, 10.0 mmol). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 4:1) 0.70. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.80 (1H, *dd*, J_1 7.6, J_2 1.4, $C^{ar}H$), 7.17-7.27 (2H, *m*, $C^{ar}H$), 3.42 (1H, broad *quin.*, J 7.0, benzylic C*H*), 2.80 (1H, *ddd*, J_1 17.6, J_2 14.6, J_3 5.2, α-carbonyl CH_2), 2.58 (1H, *dt*, J_1 17.5, J_2 3.8, α-carbonyl CH_2), 2.28 (1H, *tt*, J_1 14.0, J_2 4.6, CH_2), 1.99 (1H, *dquin.*, J_1 13.7, J_2 2.8, CH_2), 1.35 (3H, *d*, J 7.1, CH_3) ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -118.3 (1F, *s*, $C^{ar}F$) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 197.3 (*d*, J^{C-F} 3.3, ketone C*q*), 160.2 (*d*, J^{C-F} 245, *ipso*(F)-C*q*), 136.3 (*d*, J^{C-F} 16.4, *ortho*(F)-C*q*), 133.4 (*d*, J^{C-F} 3.8, *meta*(F)-C*q*), 127.5 (*d*, J^{C-F} 8.2, *meta*(F)-*C*H), 123.0 (*d*, J^{C-F} 3.4, *para*(F)-*C*H), 120.3 (*d*, J^{C-F} 22.1, *ortho*(F)-*C*H), 33.6 (CH_2), 28.8 (CH_2), 26.1 (*d*, J^{C-F} 2.3, *C*H), 19.2 (CH_3) ppm. **ESI-HRMS (positif)** M = $C_{11}H_{11}FO$, expected $(M+NH_4)^+$ *m/z* 196.1133, observed $(M+NH_4)^+$ *m/z* 196.1135.

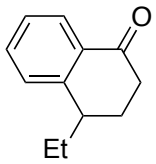
5-chloro-4-methyl-3,4-dihydronaphthalen-1(2*H*)-one (X_5)



5-chloro-4-methyl-3,4-dihydro naphthalen-1(2*H*)-one
Chemical Formula: $C_{11}H_{11}ClO$
Molecular Weight: 194.66

To a cooled (0 °C, ice/water bath) solution of 4-(2-chlorophenyl)pentanoic acid (2.15 g, 11.0 mmol, 1.0 equiv.) in methanesulfonic acid (30 mL, 418 mmol, 38 equiv.) was added P_2O_5 (3.90 g, 27.5 mmol, 2.5 equiv.). The resultant solution was stirred at ambient temperature for 16 h, and then poured over crushed ice. The mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 98:2). Pale-yellow waxy solid. Isolated yield 91% (1.79 g, 10.0 mmol). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 4:1) 0.70. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.97 (1H, *dd*, J_1 7.8, J_2 1.2, $C^{ar}H$), 7.55 (1H, *dd*, J_1 7.9, J_2 1.3, $C^{ar}H$), 7.25 (1H, *t*, J 7.8, $C^{ar}H$), 3.52 (1H, broad *quin.*, J 5.3, benzylic C*H*), 2.86 (1H, *ddd*, J_1 18.0, J_2 15.0, J_3 5.4, α-carbonyl CH_2), 2.62 (1H, *ddd*, J_1 18.0, J_2 4.4, J_3 2.2, α-carbonyl CH_2), 2.31 (1H, *tt*, J_1 13.8, J_2 4.6, CH_2), 2.05 (1H, *ddt*, J_1 13.6, J_2 5.4, J_3 2.3, CH_2), 1.38 (3H, *d*, J 7.1, CH_3) ppm. **ESI-HRMS (positif)** M = $C_{11}H_{11}FO$, expected $(M+NH_4)^+$ *m/z* 196.1133, observed $(M+NH_4)^+$ *m/z* 196.1135.

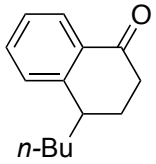
4-ethyl-3,4-dihydronaphthalen-1(2*H*)-one (X_{11})



4-ethyl-3,4-dihydro naphthalen-1(2*H*)-one
Chemical Formula: $C_{12}H_{14}O$
Molecular Weight: 174.24

To a cooled (0 °C, ice/water bath) solution of 4-phenylhexanoic acid (2.77 g, 14.4 mmol, 1.0 equiv.) in methanesulfonic acid (40 mL, 547 mmol, 38 equiv.) was added P_2O_5 (5.11 g, 36 mmol, 2.5 equiv.). The resultant solution was stirred at ambient temperature for 16 h, and then poured over crushed ice. The mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5). Light-orange viscous oil. Isolated yield 85% (2.14 g, 12.3 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.66. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.02 (1H, *dd*, J_1 7.8, J_2 1.4, C^{ar}*H*), 7.49 (1H, *td*, J_1 7.5, J_2 1.5, C^{ar}*H*), 7.27-7.33 (2H, *m*, C^{ar}*H*), 2.83-2.87 (1H, broad *m*, benzylic C*H*), 2.72-2.82 (1H, *m*, diastereotopic CH_2), 2.58 (1H, *dt*, J_1 17.8, J_2 5.2, α-carbonyl CH_2), 2.20-2.29 (1H, *m*, CH_2), 2.07 (1H, *dq*, J_1 13.6, J_2 5.1, CH_2), 1.02 (3H, *t*, *J* 7.4, CH_3) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 198.6 (ketone C*q*), 148.4 (C*q*), 133.5 (*C*H), 132.1 (C*q*), 128.4 (*C*H), 127.5 (*C*H), 126.7 (*C*H), 39.7 (α-carbonyl *C*H_2), 35.1 (benzylic *C*H), 27.5 (*C*H_2), 26.5 (*C*H_2), 12.3 (*C*H_3) ppm.

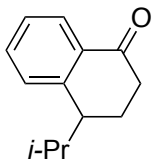
4-butyl-3,4-dihydronaphthalen-1(2*H*)-one (X_{12})



4-butyl-3,4-dihydro naphthalen-1(2*H*)-one
Chemical Formula: $C_{14}H_{18}O$
Molecular Weight: 202.29

To a cooled (0 °C, ice/water bath) solution of 4-phenyloctanoic acid (3.17 g, 14.4 mmol, 1.0 equiv.) in methanesulfonic acid (40 mL, 547 mmol, 38 equiv.) was added P_2O_5 (5.11 g, 36 mmol, 2.5 equiv.). The resultant solution was stirred at ambient temperature for 16 h, and then poured over crushed ice. The mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5). Light-orange viscous oil. Isolated yield 88% (2.57 g, 12.7 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.78. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.02 (1H, *dd*, J_1 7.8, J_2 1.4, C^{ar}*H*), 7.49 (1H, *td*, J_1 7.5, J_2 1.5, C^{ar}*H*), 7.27-7.33 (2H, *m*, C^{ar}*H*), 2.83-2.87 (1H, broad *m*, benzylic C*H*), 2.72-2.82 (1H, *m*, diastereotopic CH_2), 2.58 (1H, *dt*, J_1 17.8, J_2 5.2, α-carbonyl CH_2), 2.20-2.29 (1H, *m*, CH_2), 2.07 (1H, *dq*, J_1 13.6, J_2 5.1, CH_2), 1.02 (3H, *t*, *J* 7.4, CH_3) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 198.6 (ketone C*q*), 148.4 (C*q*), 133.5 (*C*H), 132.1 (C*q*), 128.4 (*C*H), 127.5 (*C*H), 126.7 (*C*H), 39.7 (α-carbonyl *C*H_2), 35.1 (benzylic *C*H), 27.5 (*C*H_2), 26.5 (*C*H_2), 12.3 (*C*H_3) ppm.

4-isopropyl-3,4-dihydronaphthalen-1(2*H*)-one (X_{13})

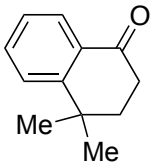


4-isopropyl-3,4-dihydro naphthalen-1(2*H*)-one
Chemical Formula: $C_{13}H_{16}O$
Molecular Weight: 188.27

To a cooled (0 °C, ice/water bath) solution of 5-methyl-4-phenylhexanoic acid (2.97 g, 14.4 mmol, 1.0 equiv.) in methanesulfonic acid (40 mL, 547 mmol, 38 equiv.) was added P_2O_5 (5.11 g, 36 mmol, 2.5 equiv.). The resultant solution was stirred at ambient temperature for 16 h, and then poured over crushed ice. The mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5). Light-orange viscous oil. Isolated yield 82% (2.22 g, 11.8 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.70. **^{1}H NMR**

(400 MHz, $CDCl_3$): δ 8.02 (1H, *dd*, J_1 7.8, J_2 1.4, $C^{ar}H$), 7.49 (1H, *td*, J_1 7.5, J_2 1.5, $C^{ar}H$), 7.27-7.33 (2H, *m*, $C^{ar}H$), 2.83-2.87 (1H, broad *m*, benzylic C*H*), 2.72-2.82 (1H, *m*, diastereotopic CH_2), 2.58 (1H, *dt*, J_1 17.8, J_2 5.2, α-carbonyl CH_2), 2.20-2.29 (1H, *m*, CH_2), 2.07 (1H, *dq*, J_1 13.6, J_2 5.1, CH_2), 1.02 (3H, *t*, *J* 7.4, CH_3) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 198.6 (ketone C*q*), 148.4 (C*q*), 133.5 (*C*H), 132.1 (C*q*), 128.4 (*C*H), 127.5 (*C*H), 126.7 (*C*H), 39.7 (α-carbonyl CH_2), 35.1 (benzylic *C*H), 27.5 (CH_2), 26.5 (CH_2), 12.3 (CH_3) ppm.

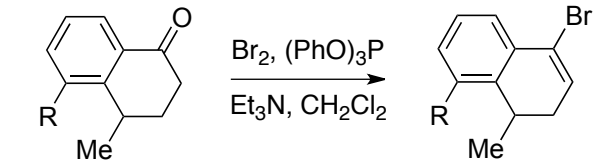
4,4-dimethyl-3,4-dihydronaphthalen-1(2*H*)-one (X_{10})



4,4-dimethyl-3,4-dihydro naphthalen-1(2*H*)-one
Chemical Formula: $C_{12}H_{14}O$
Molecular Weight: 174.24

To a cooled (0 °C, ice/water bath) solution of 4-methyl-4-phenylpentanoic acid (2.77 g, 14.4 mmol, 1.0 equiv.) in methanesulfonic acid (40 mL, 547 mmol, 38 equiv.) was added P_2O_5 (5.11 g, 36 mmol, 2.5 equiv.). The resultant solution was stirred at ambient temperature for 16 h, and then poured over crushed ice. The mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 95:5). Pale yellow oil. Isolated yield 60% (1.51 g, 8.67 mmol). **R_f** (silica gel, *n*-Hex/Et_2O 4:1) 0.70. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.02 (1H, *ddd*, J_1 7.8, J_2 1.4, J_3 0.3, $C^{ar}H$), 7.53 (1H, *td*, J_1 7.2, J_2 1.6, $C^{ar}H$), 7.42 (1H, *dd*, J_1 7.9, J_2 0.8, $C^{ar}H$), 7.30 (1H, *td*, J_1 7.2, J_2 1.2, $C^{ar}H$), 2.73 (2H, *t*, *J* 6.7, α-carbonyl CH_2), 2.03 (2H, *t*, *J* 6.9, CH_2), 1.40 (6H, *s*, *gem*-dimethyl CH_3) ppm.

General Procedure for the Synthesis of Substrates: Vinylic Bromides

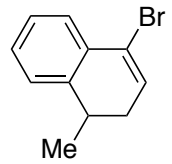


R = H, Me, OMe, F

X_y^{KR} **Y_y^{KR}**

To a cooled (-78 °C, dry ice/acetone bath) solution of $(PhO)_3P$ (1.1 equiv.) in anhydrous CH_2Cl_2 (0.33 M with respect to **X_y^{KR}**) was added Br_2 (1.2 equiv.). Anhydrous Et_3N (1.3 equiv.) and **X_y^{KR}** (1.0 equiv.) were then added to the faint orange solution. The resultant mixture was stirred for 18 h, while slowly warming up to ambient temperature. The mixture was then heated to reflux for a further 2 h. Upon cooling down to ambient temperature, 10% (*w/w*) aqueous Na_2SO_3 was added and the mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was then purified by flash chromatography on silica gel using an adequate *n*-hexane/Et_2O mixture as eluent.

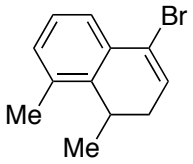
4-bromo-1-methyl-1,2-dihydronaphthalene (Y_1)



4-bromo-1-methyl-1,2-dihydronaphthalene
Chemical Formula: $C_{11}H_{11}Br$
Molecular Weight: 223.11

To a cooled (-78 °C, dry ice/acetone bath) solution of $(PhO)_3P$ (2.35 mL, 8.93 mmol, 1.1 equiv.) in anhydrous CH_2Cl_2 (35 mL) was added Br_2 (500 μL, 9.73 mmol, 1.2 equiv.). Anhydrous Et_3N (1.48 mL, 10.5 mmol, 1.3 equiv.) and 4-methyl-1-tetralone (**X_1**) (1.30 mL, 8.11 mmol, 1.0 equiv.) were then added to the faint orange solution. The resultant mixture was stirred for 18 h, while slowly warming up to ambient temperature. The mixture was then heated to reflux for a further 2 h. Upon cooling down to ambient temperature, 10% (*w/w*) aqueous Na_2SO_3 was added and the mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane). Light-yellow oil. Isolated yield 58% (1.05 g, 4.71 mmol). **R_f** (silica gel, *n*-Hex) 0.55. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.55-7.59 (1H, *m*, C^{ar}*H*), 7.21-7.27 (2H, *m*, C^{ar}*H*), 7.12-7.16 (1H, *m*, C^{ar}*H*), 6.38 (1H, *t*, *J* 4.9, olefinic C=C*H*), 2.98 (1H, *sext.*, *J* 7.0, benzylic C*H*), 2.53 (1H, *ddd*, J_1 16.8, J_2 6.7, J_3 4.4, diastereotopic CH_2), 2.18 (1H, *ddd*, J_1 16.9, J_2 7.2, J_3 5.3, diastereotopic CH_2), 1.27 (3H, *d*, *J* 7.0, CH_3) ppm.

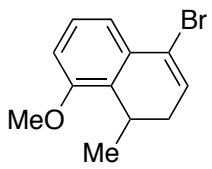
4-bromo-1,8-dimethyl-1,2-dihydronaphthalene (Y_2)



4-bromo-1,8-dimethyl-1,2-dihydronaphthalene
Chemical Formula: $C_{12}H_{13}Br$
Molecular Weight: 237.14

To a cooled (-78 °C, dry ice/acetone bath) solution of $(PhO)_3P$ (997 μL, 3.79 mmol, 1.1 equiv.) in anhydrous CH_2Cl_2 (12 mL) was added Br_2 (212 μL, 4.13 mmol, 1.2 equiv.). Anhydrous Et_3N (628 μL, 4.47 mmol, 1.3 equiv.) and 4,5-dimethyl-3,4-dihydronaphthalen-1(2*H*)-one (**X_2**) (600 mg, 3.44 mmol, 1.0 equiv.) were then added to the faint orange solution. The resultant mixture was stirred for 18 h, while slowly warming up to ambient temperature. The mixture was then heated to reflux for a further 2 h. Upon cooling down to ambient temperature, 10% (*w/w*) aqueous Na_2SO_3 was added and the mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane). Colorless oil. Isolated yield 71% (581 mg, 2.45 mmol). **R_f** (silica gel, *n*-Hex) 0.62. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.52 (1H, *d*, *J* 8.6, C^{ar}*H*), 7.17-7.26 (2H, *m*, C^{ar}*H*), 7.11 (1H, *d*, *J* 5.8, C^{ar}*H*), 6.46 (1H, *t*, *J* 4.8, olefinic C=C*H*), 2.84 (2H, *t*, *J* 7.9, benzylic CH_2), 2.36 (2H, *td*, J_1 8.4, J_2 4.8, allylic CH_2) ppm.

4-bromo-8-methoxy-1-methyl-1,2-dihydronaphthalene (Y_3)

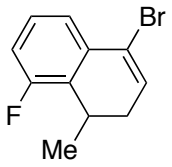


4-bromo-8-methoxy-1-methyl-1,2-dihydronaphthalene
Chemical Formula: $C_{12}H_{13}BrO$
Molecular Weight: 253.14

To a cooled (-78 °C, dry ice/acetone bath) solution of $(PhO)_3P$ (140 μL, 0.53 mmol, 1.1 equiv.) in anhydrous CH_2Cl_2 (4.0 mL) was added Br_2 (30 μL, 0.58 mmol, 1.2 equiv.). Anhydrous Et_3N (88 μL, 0.62 mmol, 1.3 equiv.) and 5-methoxy-4-methyl-3,4-dihydronaphthalen-1(2*H*)-one (**X_3**) (92 mg, 0.48 mmol, 1.0 equiv.) were then added to the faint orange solution. The resultant mixture was stirred for 18 h, while slowly warming up to ambient temperature. The mixture was then heated to reflux for a further 2 h.

Upon cooling down to ambient temperature, 10% (*w/w*) aqueous Na_2SO_3 was added and the mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane). Colorless oil. Isolated yield 65% (80 mg, 0.31 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 9:1) 0.37. **^{1}H NMR** (400 MHz, C_6D_6): δ 7.53 (1H, *d*, *J* 7.8, C^{ar}*H*), 7.02 (1H, *t*, *J* 8.1, C^{ar}*H*), 6.46 (1H, *d*, *J* 8.2, C^{ar}*H*), 6.09 (1H, *dd*, J_1 7.1, J_2 2.4, olefinic C=C*H*), 3.37 (1H, *quint.*, *J* 7.0, benzylic C*H*), 3.28 (3H, *s*, methoxy CH_3-O), 2.24 (1H, *ddd*, J_1 17.2, J_2 9.8, J_3 2.5, allylic CH_2), 1.75 (1H, *ddd*, J_1 17.2, J_2 7.1, J_3 1.2, allylic CH_2), 1.08 (3H, *d*, *J* 7.1, CH_3) ppm.

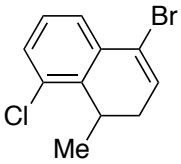
4-bromo-8-fluoro-1-methyl-1,2-dihydronaphthalene (Y_4)



4-bromo-8-fluoro-1-methyl-1,2-dihydronaphthalene
Chemical Formula: $C_{11}H_{10}BrF$
Molecular Weight: 241.10

To a cooled (-78 °C, dry ice/acetone bath) solution of $(PhO)_3P$ (997 µL, 3.79 mmol, 1.1 equiv.) in anhydrous CH_2Cl_2 (12 mL) was added Br_2 (212 µL, 4.13 mmol, 1.2 equiv.). Anhydrous Et_3N (628 µL, 4.47 mmol, 1.3 equiv.) and 5-fluoro-4-methyl-3,4-dihydronaphthalen-1(2*H*)-one ($\mathbf{X_4}$) (613 mg, 3.44 mmol, 1.0 equiv.) were then added to the faint orange solution. The resultant mixture was stirred for 18 h, while slowly warming up to ambient temperature. The mixture was then heated to reflux for a further 2 h. Upon cooling down to ambient temperature, 10% (*w/w*) aqueous Na_2SO_3 was added and the mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane). White crystalline solid. Isolated yield 59% (486 mg, 2.02 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex) 0.59. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.52 (1H, *d*, *J* 8.6, C^{ar}*H*), 7.17-7.26 (2H, *m*, C^{ar}*H*), 7.11 (1H, *d*, *J* 5.8, C^{ar}*H*), 6.46 (1H, *t*, *J* 4.8, olefinic C=C*H*), 2.84 (2H, *t*, *J* 7.9, benzylic CH_2), 2.36 (2H, *td*, J_1 8.4, J_2 4.8, allylic CH_2) ppm.

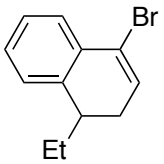
4-bromo-8-chloro-1-methyl-1,2-dihydronaphthalene (Y_5)



4-bromo-8-chloro-1-methyl-1,2-dihydronaphthalene
Chemical Formula: $C_{11}H_{10}BrCl$
Molecular Weight: 257.55

To a cooled (-78 °C, dry ice/acetone bath) solution of $(PhO)_3P$ (997 µL, 3.79 mmol, 1.1 equiv.) in anhydrous CH_2Cl_2 (12 mL) was added Br_2 (212 µL, 4.13 mmol, 1.2 equiv.). Anhydrous Et_3N (628 µL, 4.47 mmol, 1.3 equiv.) and 5-chloro-4-methyl-3,4-dihydronaphthalen-1(2*H*)-one ($\mathbf{X_5}$) (671 mg, 3.44 mmol, 1.0 equiv.) were then added to the faint orange solution. The resultant mixture was stirred for 18 h, while slowly warming up to ambient temperature. The mixture was then heated to reflux for a further 2 h. Upon cooling down to ambient temperature, 10% (*w/w*) aqueous Na_2SO_3 was added and the mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane). Colorless oil. Isolated yield 71% (630 mg, 2.45 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex) 0.62. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.52 (1H, *d*, *J* 8.6, C^{ar}*H*), 7.17-7.26 (2H, *m*, C^{ar}*H*), 7.11 (1H, *d*, *J* 5.8, C^{ar}*H*), 6.46 (1H, *t*, *J* 4.8, olefinic C=C*H*), 2.84 (2H, *t*, *J* 7.9, benzylic CH_2), 2.36 (2H, *td*, J_1 8.4, J_2 4.8, allylic CH_2) ppm.

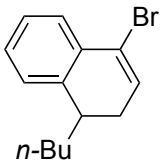
4-bromo-1-ethyl-1,2-dihydronaphthalene (Y_{11})



4-bromo-1-ethyl-1,2-dihydronaphthalene
Chemical Formula: $C_{12}H_{13}Br$
Molecular Weight: 237.14

To a cooled (-78 °C, dry ice/acetone bath) solution of $(PhO)_3P$ (997 μL, 3.79 mmol, 1.1 equiv.) in anhydrous CH_2Cl_2 (12 mL) was added Br_2 (212 μL, 4.13 mmol, 1.2 equiv.). Anhydrous Et_3N (628 μL, 4.47 mmol, 1.3 equiv.) and 4-ethyl-3,4-dihydronaphthalen-1(2*H*)-one (**X_{11}**) (600 mg, 3.44 mmol, 1.0 equiv.) were then added to the faint orange solution. The resultant mixture was stirred for 18 h, while slowly warming up to ambient temperature. The mixture was then heated to reflux for a further 2 h. Upon cooling down to ambient temperature, 10% (*w/w*) aqueous Na_2SO_3 was added and the mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane). Colorless oil. Isolated yield 75% (610 mg, 2.57 mmol). **R_f** (silica gel, *n*-Hex) 0.62. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.52 (1H, *d*, *J* 8.6, $C^{ar}H$), 7.17-7.26 (2H, *m*, $C^{ar}H$), 7.11 (1H, *d*, *J* 5.8, $C^{ar}H$), 6.46 (1H, *t*, *J* 4.8, olefinic C=C*H*), 2.84 (2H, *t*, *J* 7.9, benzylic CH_2), 2.36 (2H, *td*, J_1 8.4, J_2 4.8, allylic CH_2) ppm.

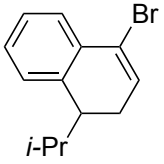
4-bromo-1-butyl-1,2-dihydronaphthalene (Y_{12})



4-bromo-1-butyl-1,2-dihydronaphthalene
Chemical Formula: $C_{14}H_{17}Br$
Molecular Weight: 265.19

To a cooled (-78 °C, dry ice/acetone bath) solution of $(PhO)_3P$ (997 μL, 3.79 mmol, 1.1 equiv.) in anhydrous CH_2Cl_2 (12 mL) was added Br_2 (212 μL, 4.13 mmol, 1.2 equiv.). Anhydrous Et_3N (628 μL, 4.47 mmol, 1.3 equiv.) and 4-butyl-3,4-dihydronaphthalen-1(2*H*)-one (**X_{12}**) (696 mg, 3.44 mmol, 1.0 equiv.) were then added to the faint orange solution. The resultant mixture was stirred for 18 h, while slowly warming up to ambient temperature. The mixture was then heated to reflux for a further 2 h. Upon cooling down to ambient temperature, 10% (*w/w*) aqueous Na_2SO_3 was added and the mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane). Colorless oil. Isolated yield 74% (676 mg, 2.55 mmol). **R_f** (silica gel, *n*-Hex) 0.62. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.52 (1H, *d*, *J* 8.6, $C^{ar}H$), 7.17-7.26 (2H, *m*, $C^{ar}H$), 7.11 (1H, *d*, *J* 5.8, $C^{ar}H$), 6.46 (1H, *t*, *J* 4.8, olefinic C=C*H*), 2.84 (2H, *t*, *J* 7.9, benzylic CH_2), 2.36 (2H, *td*, J_1 8.4, J_2 4.8, allylic CH_2) ppm.

4-bromo-1-butyl-1,2-dihydronaphthalene (Y_{13})

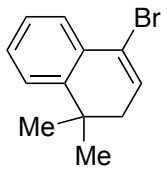


4-bromo-1-isopropyl-1,2-dihydronaphthalene
Chemical Formula: $C_{13}H_{15}Br$
Molecular Weight: 251.16

To a cooled (-78 °C, dry ice/acetone bath) solution of $(PhO)_3P$ (997 μL, 3.79 mmol, 1.1 equiv.) in anhydrous CH_2Cl_2 (12 mL) was added Br_2 (212 μL, 4.13 mmol, 1.2 equiv.). Anhydrous Et_3N (628 μL, 4.47 mmol, 1.3 equiv.) and 4-isopropyl-3,4-dihydronaphthalen-1(2*H*)-one (**X_{13}**) (648 mg, 3.44 mmol, 1.0 equiv.) were then added to the faint orange solution. The resultant mixture was stirred for 18 h, while slowly warming up to ambient temperature. The mixture was then heated to reflux for a further 2 h. Upon cooling down to ambient temperature, 10% (*w/w*) aqueous Na_2SO_3 was added and the mixture

was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane). Colorless oil. Isolated yield 74% (676 mg, 2.55 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex) 0.62. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.52 (1H, *d*, *J* 8.6, C^{ar}*H*), 7.17-7.26 (2H, *m*, C^{ar}*H*), 7.11 (1H, *d*, *J* 5.8, C^{ar}*H*), 6.46 (1H, *t*, *J* 4.8, olefinic C=C*H*), 2.84 (2H, *t*, *J* 7.9, benzylic CH_2), 2.36 (2H, *td*, J_1 8.4, J_2 4.8, allylic CH_2) ppm.

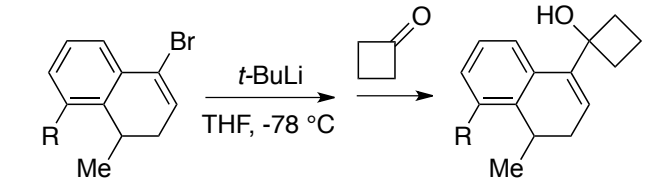
4-bromo-1,1-dimethyl-1,2-dihydronaphthalene ($\mathbf{Y_{10}}$)



4-bromo-1,1-dimethyl-1,2-dihydronaphthalene
Chemical Formula: $C_{12}H_{13}Br$
Molecular Weight: 237.14

To a cooled (-78 °C, dry ice/acetone bath) solution of $(PhO)_3P$ (997 μL, 3.79 mmol, 1.1 equiv.) in anhydrous CH_2Cl_2 (12 mL) was added Br_2 (212 μL, 4.13 mmol, 1.2 equiv.). Anhydrous Et_3N (628 μL, 4.47 mmol, 1.3 equiv.) and 4,4-dimethyl-3,4-dihydronaphthalen-1(2*H*)-one ($\mathbf{X_{10}}$) (600 mg, 3.44 mmol, 1.0 equiv.) were then added to the faint orange solution. The resultant mixture was stirred for 18 h, while slowly warming up to ambient temperature. The mixture was then heated to reflux for a further 2 h. Upon cooling down to ambient temperature, 10% (*w/w*) aqueous Na_2SO_3 was added and the mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane). Colorless oil. Isolated yield 77% (632 mg, 2.67 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex) 0.60. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.52 (1H, *d*, *J* 8.6, C^{ar}*H*), 7.17-7.26 (2H, *m*, C^{ar}*H*), 7.11 (1H, *d*, *J* 5.8, C^{ar}*H*), 6.46 (1H, *t*, *J* 4.8, olefinic C=C*H*), 2.84 (2H, *t*, *J* 7.9, benzylic CH_2), 2.36 (2H, *td*, J_1 8.4, J_2 4.8, allylic CH_2) ppm.

General Procedure for the Synthesis of Substrates: Cyclobutanols

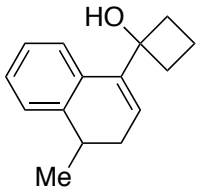


R = H, Me, OMe, F

$\mathbf{Y_y^{KR}}$ $\mathbf{A_y^{KR}}$

^{t}BuLi (1.9 M solution in pentane, 2.0 equiv.) was slowly added to a solution of $\mathbf{Y_y^{KR}}$ (1.0 equiv.) in anhydrous THF (0.4 M with respect to $\mathbf{Y_y^{KR}}$) at -78 °C over a period of 10 min. The resultant colorless solution was stirred at -78 °C for 0.5 h. Cyclobutanone (1.0 equiv.) was then added and the mixture was stirred at -78 °C for 0.5 h. The mixture was allowed to slowly reach ambient temperature. Water was added to quench the reaction, and the aqueous layer was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was then purified by flash chromatography on silica gel using an adequate *n*-hexane/Et_2O mixture as eluent.

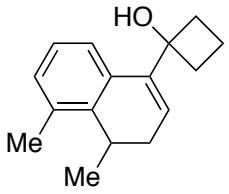
1-(4-methyl-3,4-dihydronaphthalen-1-yl)cyclobutanol (*rac*-$\mathbf{A_1}$)



1-(4-methyl-3,4-dihydro naphthalen-1-yl)cyclobutanol
Chemical Formula: $C_{15}H_{18}O$
Molecular Weight: 214.30

^{t}BuLi (1.9 M solution in pentane, 4.96 mL, 9.42 mmol, 2.0 equiv.) was slowly added to a solution of 4-bromo-1-methyl-1,2-dihydronaphthalene ($\mathbf{Y_1^{KR}}$) (1.05 g, 4.71 mmol, 1.0 equiv.) in anhydrous THF (16 mL) at -78 °C over a period of 10 min. The resultant colorless solution was stirred at -78 °C for 0.5 h. Cyclobutanone (355 μL, 4.71 mmol, 1.0 equiv.) was then added and the mixture was stirred at -78 °C for 0.5 h. The mixture was allowed to slowly reach ambient temperature. Water was added to quench the reaction, and the aqueous layer was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). White waxy solid. Isolated yield 89% (898 mg, 4.19 mmol). $\mathbf{R_f}$ (silica gel, *n*-Hex/EtOAc 9:1) 0.46. **^{1}H NMR** (500 MHz, C_6D_6): δ 7.81 (1H, *dd*, J_1 8.2, J_2 1.5, C^{ar}*H*), 7.08-7.14 (3H, *m*, C^{ar}*H*), 5.77 (1H, *t*, *J* 4.7, olefinic C=C*H*), 2.68 (1H, *sext.*, *J* 6.9, benzylic C*H*), 2.36-2.46 (2H, *m*, allylic CH_2), 2.16-2.29 (3H, *m*, cyclobutylic CH_2), 1.81-1.91 (2H, *m*, cyclobutylic CH_2), 1.51 (1H, *brs*, hydroxylic O*H*), 1.39-1.52 (1H, *m*, cyclobutylic CH_2), 1.12 (3H, *d*, *J* 7.0, CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 142.4 (C*q*), 139.7 (C*q*), 131.9 (C*q*), 127.4 (*C*H), 126.7 (*C*H), 126.5 (*C*H), 126.3 (*C*H), 123.2 (*C*H), 77.3 (O-C*q*), 36.2 (*C*H_2), 36.0 (*C*H_2), 32.5 (*C*H), 31.2 (*C*H_2), 20.2 (*C*H_3), 14.3 (*C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{15}H_{18}O$, expected (M-H_2O+H)$^+$ *m/z* 197.1325, observed (M-H_2O+H)$^+$ *m/z* 197.1325.

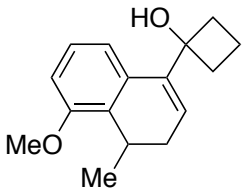
1-(4,5-dimethyl-3,4-dihydronaphthalen-1-yl)cyclobutanol (*rac*-$\mathbf{A_2}$)



1-(4,5-dimethyl-3,4-dihydro naphthalen-1-yl)cyclobutanol
Chemical Formula: $C_{16}H_{20}O$
Molecular Weight: 228.33

^{t}BuLi (1.9 M solution in pentane, 2.58 mL, 4.90 mmol, 2.0 equiv.) was slowly added to a solution of 4-bromo-1,8-dimethyl-1,2-dihydronaphthalene ($\mathbf{Y_2^{KR}}$) (581 mg, 2.45 mmol, 1.0 equiv.) in anhydrous THF (15 mL) at -78 °C over a period of 10 min. The resultant colorless solution was stirred at -78 °C for 0.5 h. Cyclobutanone (185 μL, 2.45 mmol, 1.0 equiv.) was then added and the mixture was stirred at -78 °C for 0.5 h. The mixture was allowed to slowly reach ambient temperature. Water was added to quench the reaction, and the aqueous layer was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 9:1). White amorphous solid. Isolated yield 79% (442 mg, 1.94 mmol). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 4:1) 0.47. **^{1}H NMR** (400 MHz, C_6D_6): δ 7.74 (1H, *d*, *J* 7.8, C^{ar}*H*), 7.07 (1H, *t*, *J* 7.6, C^{ar}*H*), 6.96 (1H, *d*, *J* 7.4, C^{ar}*H*), 5.74 (1H, *dd*, J_1 6.9, J_2 1.8, olefinic C=C*H*), 2.90 (1H, *quin.*, *J* 7.0, benzylic C*H*), 2.28-2.53 (4H, *m*, CH_2), 2.15-2.23 (1H, *m*, CH_2), 2.15 (3H, *s*, CH_3), 1.82-2.00 (2H, *m*, CH_2), 1.58 (1H, *brs*, hydroxylic O*H*), 1.42-1.58 (1H, *m*, CH_2), 1.01 (3H, *d*, *J* 7.0, CH_3) ppm. **^{13}C NMR** (100 MHz, C_6D_6): δ 140.7 (C*q*), 139.8 (C*q*), 134.4 (C*q*), 131.2 (C*q*), 129.7 (*C*H), 125.9 (*C*H), 124.7 (*C*H), 121.8 (*C*H), 77.6 (O-C*q*), 36.9 (*C*H_2), 35.7 (*C*H_2), 30.5 (*C*H_2), 28.2 (*C*H), 19.2 (*C*H_3), 18.3 (*C*H_3), 14.4 (*C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{16}H_{20}O$, expected (M-H_2O+H)$^+$ *m/z* 211.1482, observed (M-H_2O+H)$^+$ *m/z* 211.1485.

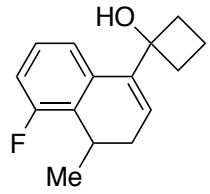
1-(5-methoxy-4-methyl-3,4-dihydronaphthalen-1-yl)cyclobutanol (*rac*-$\mathbf{A_3}$)



1-(5-methoxy-4-methyl-3,4-dihydro naphthalen-1-yl)cyclobutanol
Chemical Formula: $C_{16}H_{20}O_2$
Molecular Weight: 244.33

^{t}BuLi (1.9 M solution in pentane, 210 µL, 0.40 mmol, 2.0 equiv.) was slowly added to a solution of 4-bromo-8-methoxy-1-methyl-1,2-dihydronaphthalene ($\mathbf{Y_4^{KR}}$) (50 mg, 0.20 mmol, 1.0 equiv.) in anhydrous THF (2.5 mL) at -78 °C over a period of 10 min. The resultant colorless solution was stirred at -78 °C for 0.5 h. Cyclobutanone (15 µL, 0.20 mmol, 1.0 equiv.) was then added and the mixture was stirred at -78 °C for 0.5 h. The mixture was allowed to slowly reach ambient temperature. Water was added to quench the reaction, and the aqueous layer was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 7:3). White waxy solid. Isolated yield 84% (395 mg, 1.70 mmol). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 4:1) 0.23. **^{1}H NMR** (500 MHz, C_6D_6): δ 7.56 (1H, *d*, *J* 7.9, C^{ar}*H*), 7.10 (1H, *t*, *J* 8.1, C^{ar}*H*), 6.53 (1H, *dd*, J_1 8.2, J_2 0.5, C^{ar}*H*), 5.76 (1H, *dd*, J_1 6.9, J_2 1.6, olefinic C=C*H*), 3.59 (1H, *quin.*, *J* 7.1, benzylic C*H*), 3.38 (3H, *s*, methoxy CH_3-O), 2.46-2.52 (1H, *m*, diastereotopic CH_2), 2.31-2.43 (3H, *m*, diastereotopic CH_2), 2.14-2.22 (1H, *m*, CH_2), 2.03 (1H, *ddd*, J_1 16.9, J_2 6.9, J_3 1.3, CH_2), 1.84-1.92 (1H, *m*, CH_2), 1.58 (1H, *brs*, hydroxylic O*H*), 1.44-1.51 (1H, *m*, CH_2), 1.21 (3H, *d*, *J* 7.1, CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 156.4 (C*q*), 139.3 (C*q*), 132.5 (C*q*), 130.7 (C*q*), 126.5 (*C*H), 122.6 (*C*H), 119.5 (*C*H), 109.8 (*C*H), 77.6 (C*q*-O), 55.1 (*C*H_3-O), 36.7 (*C*H_2), 35.7 (*C*H_2), 30.3 (*C*H_2), 24.8 (benzylic *C*H), 18.9 (*C*H_3), 14.4 (*C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{16}H_{20}O_2$, expected $(M\text{-}H_2O+H)^+$ *m/z* 227.1431, observed $(M\text{-}H_2O+H)^+$ *m/z* 227.1432.

1-(5-fluoro-4-methyl-3,4-dihydronaphthalen-1-yl)cyclobutanol (*rac*-$\mathbf{A_4}$)

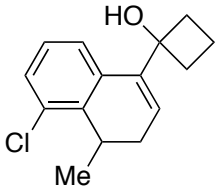


1-(5-fluoro-4-methyl-3,4-dihydro naphthalen-1-yl)cyclobutanol
Chemical Formula: $C_{15}H_{17}FO$
Molecular Weight: 232.29

^{t}BuLi (1.9 M solution in pentane, 2.13 mL, 4.04 mmol, 2.0 equiv.) was slowly added to a solution of 4-bromo-8-fluoro-1-methyl-1,2-dihydronaphthalene ($\mathbf{Y_5^{KR}}$) (487 mg, 2.02 mmol, 1.0 equiv.) in anhydrous THF (14 mL) at -78 °C over a period of 10 min. The resultant colorless solution was stirred at -78 °C for 0.5 h. Cyclobutanone (152 µL, 2.02 mmol, 1.0 equiv.) was then added and the mixture was stirred at -78 °C for 0.5 h. The mixture was allowed to slowly reach ambient temperature. Water was added to quench the reaction, and the aqueous layer was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 7:3). White waxy solid. Isolated yield 84% (395 mg, 1.70 mmol). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 4:1) 0.42. **^{1}H NMR** (400 MHz, C_6D_6): δ 7.55 (1H, *d*, *J* 7.8, C^{ar}*H*), 6.90 (1H, *dd*, J_1 8.1, J_2 6.1, C^{ar}*H*), 6.78 (1H, *td*, J_1 9.3, J_2 1.1, C^{ar}*H*), 5.65 (1H, *dd*, J_1 6.9, J_2 1.9, olefinic C=C*H*), 3.30 (1H, *quin.*, *J* 7.0, benzylic C*H*), 2.34-2.41 (1H, *m*, diastereotopic CH_2), 2.18-2.31 (3H, *m*, diastereotopic CH_2), 2.05-2.12 (1H, *m*, CH_2), 1.78-1.89 (2H, *m*, CH_2), 1.36-1.46 (1H, *m*, CH_2), 1.40 (1H, *brs*, hydroxylic O*H*), 1.07 (3H, *d*, *J* 7.1, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -117.6 (1F, *s*, C^{ar}*F*) ppm. **^{13}C NMR** (100 MHz, C_6D_6): δ 160.3 (*d*, $J^{C\text{-}F}$ 240, *ipso*(F)-C*q*), 138.6 (*d*, $J^{C\text{-}F}$ 3.2, olefinic C*q*), 133.5 (*d*, $J^{C\text{-}F}$ 4.9, *meta*(F)-C*q*), 129.0 (*d*, $J^{C\text{-}F}$ 16.4, *ortho*(F)-C*q*), 127.1 (*d*, $J^{C\text{-}F}$ 8.5, *meta*(F)-*C*H), 123.2 (olefinic *C*H), 122.5 (*d*, $J^{C\text{-}F}$ 3.0, *para*(F)-*C*H), 114.2 (*d*, $J^{C\text{-}F}$ 22.4, *ortho*(F)-*C*H),

77.3 (O-C*q*), 36.4 (*C*H_2), 35.6 (*C*H_2), 29.8 (*C*H_2), 24.6 (*d*, $J^{C\text{-}F}$ 3.2, benzylic *C*H), 19.4 (*C*H_3), 14.3 (*C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{15}H_{17}FO$, expected $(M\text{-}H_2O+H)^+$ *m/z* 215.1231, observed $(M\text{-}H_2O+H)^+$ *m/z* 215.1234.

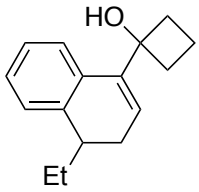
1-(5-chloro-4-methyl-3,4-dihydronaphthalen-1-yl)cyclobutanol (*rac*-$\mathbf{A_5}$)



1-(5-chloro-4-methyl-3,4-dihydro naphthalen-1-yl)cyclobutanol
Chemical Formula: $C_{15}H_{17}ClO$
Molecular Weight: 248.75

^{t}BuLi (1.9 M solution in pentane, 2.50 mL, 4.74 mmol, 2.0 equiv.) was slowly added to a solution of 4-bromo-8-chloro-1-methyl-1,2-dihydronaphthalene ($\mathbf{Y_6^{KR}}$) (610 mg, 2.37 mmol, 1.0 equiv.) in anhydrous THF (15 mL) at -78 °C over a period of 10 min. The resultant colorless solution was stirred at -78 °C for 0.5 h. Cyclobutanone (180 µL, 2.37 mmol, 1.0 equiv.) was then added and the mixture was stirred at -78 °C for 0.5 h. The mixture was allowed to slowly reach ambient temperature. Water was added to quench the reaction, and the aqueous layer was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 4:1). Colorless oil. Isolated yield 87% (530 mg, 2.13 mmol). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 4:1) 0.37. **^{1}H NMR** (500 MHz, C_6D_6): δ 7.68 (1H, *d*, *J* 7.8, C^{ar}*H*), 7.14 (1H, *dd*, J_1 8.0, J_2 1.1, C^{ar}*H*), 6.83 (1H, *t*, *J* 8.0, C^{ar}*H*), 5.64 (1H, *dd*, J_1 7.0, J_2 1.8, olefinic C=C*H*), 3.42 (1H, *quint.*, *J* 7.1, benzylic C*H*), 2.33-2.39 (1H, *m*, diastereotopic CH_2), 2.17-2.27 (3H, *m*, CH_2), 2.03-2.09 (1H, *m*, CH_2), 1.80-1.90 (2H, *m*, CH_2), 1.37-1.44 (1H, *m*, CH_2), 1.36 (1H, *brs*, hydroxylic O*H*), 1.07 (3H, *d*, *J* 7.1, CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 139.8 (*ipso*(Cl)-C*q*), 138.7 (olefinic C*q*), 133.6 (C*q*), 133.2 (C*q*), 128.4 (*C*H), 127.1 (*C*H), 125.3 (*C*H), 123.4 (olefinic *C*H), 77.3 (O-C*q*), 36.5 (*C*H_2), 35.6 (*C*H_2), 29.9 (*C*H_2), 29.0 (benzylic *C*H), 18.1 (*C*H_3), 14.3 (*C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{15}H_{17}ClO$, expected $(M\text{-}H_2O+H)^+$ *m/z* 231.0936, observed $(M\text{-}H_2O+H)^+$ *m/z* 231.0939.

1-(4-ethyl-3,4-dihydronaphthalen-1-yl)cyclobutanol (*rac*-$\mathbf{A_{11}}$)

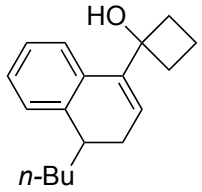


1-(4-ethyl-3,4-dihydro naphthalen-1-yl)cyclobutanol
Chemical Formula: $C_{16}H_{20}O$
Molecular Weight: 228.33

^{t}BuLi (1.9 M solution in pentane, 2.71 mL, 5.15 mmol, 2.0 equiv.) was slowly added to a solution of 4-bromo-1-ethyl-1,2-dihydronaphthalene ($\mathbf{Y_7^{KR}}$) (610 mg, 2.57 mmol, 1.0 equiv.) in anhydrous THF (18 mL) at -78 °C over a period of 10 min. The resultant colorless solution was stirred at -78 °C for 0.5 h. Cyclobutanone (192 µL, 2.57 mmol, 1.0 equiv.) was then added and the mixture was stirred at -78 °C for 0.5 h. The mixture was allowed to slowly reach ambient temperature. Water was added to quench the reaction, and the aqueous layer was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 4:1). Colorless viscous oil. Isolated yield 90% (528 mg, 2.31 mmol). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 4:1) 0.40. **^{1}H NMR** (400 MHz, C_6D_6): δ 7.81 (1H, *dd*, J_1 7.8, J_2 1.2, C^{ar}*H*), 7.03-7.14 (3H, *m*, C^{ar}*H*), 5.75 (1H, *dd*, J_1 6.2, J_2 3.1, olefinic C=C*H*), 2.15-2.48 (6H, *m*, diastereotopic CH_2 + C*H*), 2.05 (1H, *ddd*, J_1 16.6, J_2 6.2, J_3 3.5, CH_2), 1.80-1.90 (1H, *m*, CH_2), 1.53 (1H, *brs*, hydroxylic O*H*), 1.39-1.62 (3H, *m*, CH_2), 0.82 (3H, *t*, *J* 7.4, CH_3) ppm. **^{13}C NMR** (100 MHz, C_6D_6): δ 141.3 (C*q*), 139.7 (olefinic C*q*), 131.9 (C*q*), 128.2 (*C*H), 127.0 (*C*H), 126.5 (*C*H), 126.4 (*C*H), 122.9 (olefinic *C*H), 77.4 (O-C*q*), 39.8 (*C*H_2), 36.5 (*C*H_2), 35.8 (*C*H_2), 28.3 (benzylic *C*H), 27.0 (*C*H_2), 14.4

(CH_2), 12.3 (CH_3) ppm. **ESI-HRMS (positif)** M = $C_{16}H_{20}O$, expected $(M\text{-}H_2O+H)^+$ *m/z* 211.1482, observed $(M\text{-}H_2O+H)^+$ *m/z* 211.1485.

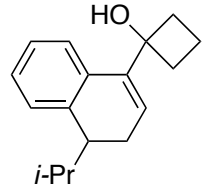
1-(4-butyl-3,4-dihydronaphthalen-1-yl)cyclobutanol (*rac*-A_{12})



1-(4-butyl-3,4-dihydrona phthalen-1-yl)cyclobutanol
Chemical Formula: $C_{18}H_{24}O$
Molecular Weight: 256.38

^{t}BuLi (1.9 M solution in pentane, 2.68 mL, 5.10 mmol, 2.0 equiv.) was slowly added to a solution of 4-bromo-1-butyl-1,2-dihydronaphthalene ($\mathbf{Y_7^{KR}}$) (676 mg, 2.55 mmol, 1.0 equiv.) in anhydrous THF (18 mL) at -78 °C over a period of 10 min. The resultant colorless solution was stirred at -78 °C for 0.5 h. Cyclobutanone (190 µL, 2.55 mmol, 1.0 equiv.) was then added and the mixture was stirred at -78 °C for 0.5 h. The mixture was allowed to slowly reach ambient temperature. Water was added to quench the reaction, and the aqueous layer was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 4:1). Colorless viscous oil. Isolated yield 90% (528 mg, 2.31 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.40. **^{1}H NMR** (500 MHz, C_6D_6): δ 7.82 (1H, *d*, *J* 7.5, C^{ar}*H*), 7.07-7.14 (3H, *m*, C^{ar}*H*), 5.78 (1H, *dd*, J_1 6.2, J_2 3.1, olefinic C=C*H*), 2.24-2.55 (5H, *m*, diastereotopic CH_2 + C*H*), 2.08 (1H, *ddd*, J_1 16.8, J_2 6.2, J_3 3.6, CH_2), 1.81-1.89 (1H, *m*, CH_2), 1.42-1.60 (4H, *m*, CH_2 + hydroxylic O*H*), 1.15-1.28 (3H, *m*, CH_2), 0.84 (3H, *t*, *J* 7.0, CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 141.3 (C*q*), 139.7 (olefinic C*q*), 131.9 (C*q*), 128.2 (*C*H), 127.0 (*C*H), 126.5 (*C*H), 126.4 (*C*H), 122.9 (olefinic *C*H), 77.4 (O-C*q*), 39.8 (*C*H_2), 36.5 (*C*H_2), 35.8 (*C*H_2), 28.3 (benzylic *C*H), 27.0 (*C*H_2), 14.4 (*C*H_2), 12.3 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{18}H_{24}O$, expected $(M\text{-}H_2O+H)^+$ *m/z* 239.1795, observed $(M\text{-}H_2O+H)^+$ *m/z* 239.1795.

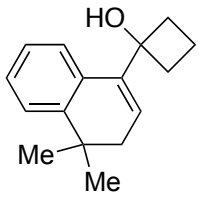
1-(4-isopropyl-3,4-dihydronaphthalen-1-yl)cyclobutanol (*rac*-A_{13})



1-(4-isopropyl-3,4-dihydro naphthalen-1-yl)cyclobutanol
Chemical Formula: $C_{17}H_{22}O$
Molecular Weight: 242.36

^{t}BuLi (1.9 M solution in pentane, 2.42 mL, 4.60 mmol, 2.0 equiv.) was slowly added to a solution of 4-bromo-1-isopropyl-1,2-dihydronaphthalene ($\mathbf{Y_6^{KR}}$) (578 mg, 2.30 mmol, 1.0 equiv.) in anhydrous THF (15 mL) at -78 °C over a period of 10 min. The resultant colorless solution was stirred at -78 °C for 0.5 h. Cyclobutanone (173 µL, 2.30 mmol, 1.0 equiv.) was then added and the mixture was stirred at -78 °C for 0.5 h. The mixture was allowed to slowly reach ambient temperature. Water was added to quench the reaction, and the aqueous layer was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 4:1). Colorless oil. Isolated yield 87% (530 mg, 2.13 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.37. **^{1}H NMR** (500 MHz, C_6D_6): δ 7.82 (1H, *dd*, J_1 7.8, J_2 1.0, C^{ar}*H*), 7.14 (1H, *td*, J_1 7.7, J_2 1.6, C^{ar}*H*), 7.07 (1H, *td*, J_1 7.4, J_2 1.4, C^{ar}*H*), 7.03 (1H, *dd*, J_1 7.5, J_2 1.3, C^{ar}*H*), 5.74 (1H, *dd*, J_1 6.8, J_2 3.9, olefinic C=C*H*), 2.36-2.47 (2H, *m*, diastereotopic CH_2), 2.14-2.31 (5H, *m*, CH_2), 1.81-1.89 (2H, *m*, CH_2), 1.48 (1H, *brs*, hydroxylic O*H*), 1.41-1.50 (1H, *m*, CH_2), 0.85 (3H, *d*, *J* 6.7, isopropylic CH_3), 0.79 (3H, *d*, *J* 6.8, isopropylic CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 140.3 (C*q*), 140.0 (olefinic C*q*), 132.5 (C*q*), 129.3 (*C*H), 126.6 (*C*H), 126.5 (*C*H), 126.3 (*C*H), 123.3 (olefinic *C*H), 77.3 (O-C*q*), 44.7 (isopropylic *C*H), 36.6 (*C*H_2), 35.7 (*C*H_2), 30.6 (benzylic *C*H), 25.9 (*C*H_2), 21.6 (*C*H_3), 20.7 (*C*H_3), 14.3 (*C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{17}H_{22}O$, expected $(M\text{-}H_2O+H)^+$ *m/z* 225.1638, observed $(M\text{-}H_2O+H)^+$ *m/z* 225.1642.

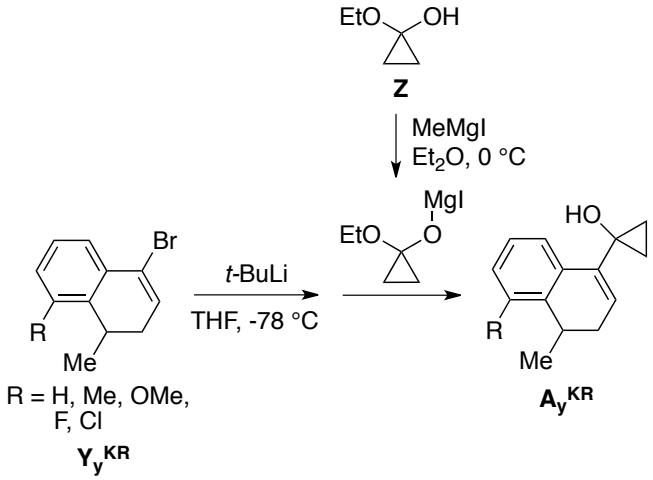
1-(4,4-dimethyl-3,4-dihydronaphthalen-1-yl)cyclobutanol (A_{10})



1-(4,4-dimethyl-3,4-dihydro naphthalen-1-yl)cyclobutanol
Chemical Formula: $C_{16}H_{20}O$
Molecular Weight: 228.33

^{t}BuLi (1.9 M solution in pentane, 2.81 mL, 5.34 mmol, 2.0 equiv.) was slowly added to a solution of 4-bromo-1,1-dimethyl-1,2-dihydronaphthalene ($\mathbf{Y_{13}^{KR}}$) (632 mg, 2.67 mmol, 1.0 equiv.) in anhydrous THF (20 mL) at -78 °C over a period of 10 min. The resultant colorless solution was stirred at -78 °C for 0.5 h. Cyclobutanone (200 μL, 2.67 mmol, 1.0 equiv.) was then added and the mixture was stirred at -78 °C for 0.5 h. The mixture was allowed to slowly reach ambient temperature. Water was added to quench the reaction, and the aqueous layer was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 4:1). White amorphous solid. Isolated yield 91% (555 mg, 2.43 mmol). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 4:1) 0.44. **^{1}H NMR** (500 MHz, C_6D_6): δ 7.82-7.85 (1H, *m*, C^{ar}*H*), 7.23-7.25 (1H, *m*, C^{ar}*H*), 7.11-7.13 (2H, *m*, C^{ar}*H*), 5.77 (1H, *t*, *J* 4.7, olefinic C=C*H*), 2.39-2.45 (2H, *m*, cyclobutylic CH_2), 2.20-2.26 (2H, *m*, cyclobutylic CH_2), 2.04 (2H, *d*, *J* 4.7, allylic CH_2), 1.82-1.90 (1H, *m*, cyclobutylic CH_2), 1.50 (1H, *brs*, hydroxylic O*H*), 1.43-1.49 (1H, *m*, cyclobutylic CH_2), 1.18 (6H, *s*, *gem*-dimethyl CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 145.8 (C*q*), 139.7 (olefinic C*q*), 131.5 (C*q*), 128.4 (*C*H), 126.7 (*C*H), 126.0 (*C*H), 124.3 (*C*H), 123.4 (olefinic *C*H), 77.5 (O-C*q*), 38.7 (*C*H_2), 36.2 (*C*H_2), 33.6 (C*q*), 28.4 (*gem*-dimethyl *C*H_3), 14.4 (*C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{16}H_{20}O$, expected (M-H_2O+H)$^+$ *m/z* 211.1482, observed (M-H_2O+H)$^+$ *m/z* 211.1484.

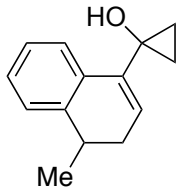
General Procedure for the Synthesis of Substrates: Cyclopropanols



^{t}BuLi (1.9 M solution in pentane, 2.0 equiv.) was slowly added to a solution of $\mathbf{Y_y^{KR}}$ (1.0 equiv.) in anhydrous THF (0.4 M with respect to $\mathbf{Y_y^{KR}}$) at -78 °C over a period of 10 min. The resultant blood-red solution was stirred at -78 °C for 0.5 h. Concurrently, to a cooled (0 °C, ice/water bath) solution of 1-ethoxycyclopropanol (**Z**) (1.1 equiv.) in anhydrous Et_2O (0.5 M with respect to **Z**) was added MeMgI (3.0 M solution in Et_2O, 1.1 equiv.) dropwise *via* syringe. The resultant white suspension was stirred at 0 °C for 10 min. The above organolithium solution was then cannulated into this suspension. The resultant reaction mixture was stirred at ambient temperature for 30 min, followed by stirring at 40 °C for overnight. The reaction mixture was then cooled down to 0 °C (ice/water bath) and

quenched with saturated aqueous NH_4Cl. The separated aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was then purified by flash chromatography on silica gel using an adequate *n*-hexane/Et_2O mixture as eluent.

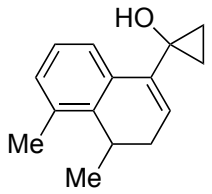
1-(4-methyl-3,4-dihydronaphthalen-1-yl)cyclopropanol (*rac*-$\mathbf{A_6}$)



1-(4-methyl-3,4-dihydro naphthalen-1-yl)cyclopropanol
Chemical Formula: $C_{14}H_{16}O$
Molecular Weight: 200.28

^{t}BuLi (1.9 M solution in pentane, 4.39 mL, 8.34 mmol, 2.0 equiv.) was slowly added to a solution of 4-bromo-1-methyl-1,2-dihydronaphthalene ($\mathbf{Y_1^{KR}}$) (930 mg, 4.17 mmol, 1.0 equiv.) in anhydrous THF (15 mL) at -78 °C over a period of 10 min. The resultant colorless solution was stirred at -78 °C for 0.5 h. Concurrently, to a cooled (0 °C, ice/water bath) solution of 1-ethoxycyclopropanol (**Z**) (469 mg, 4.59 mmol, 1.1 equiv.) in anhydrous Et_2O (8.0 mL) was added MeMgI (3.0 M solution in Et_2O, 1.53 mL, 4.59 mmol, 1.1 equiv.) dropwise *via* syringe. The resultant white suspension was stirred at 0 °C for 10 min. The above organolithium solution was then cannulated into this suspension. The resultant reaction mixture was stirred at ambient temperature for 30 min, followed by stirring at 40 °C for overnight. The reaction mixture was then cooled down to 0 °C (ice/water bath) and quenched with saturated aqueous NH_4Cl. The separated aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 9:1). Colorless oil. Isolated yield 92% (768 mg, 3.84 mmol). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 4:1) 0.19. **^{1}H NMR** (400 MHz, C_6D_6): δ 8.00 (1H, *dd*, J_1 7.7, J_2 1.2, C^{ar}*H*), 7.08-7.14 (3H, *m*, C^{ar}*H*), 5.71 (1H, *t*, *J* 4.5, olefinic C=C*H*), 2.70 (1H, *sext.*, *J* 7.0, benzylic C*H*), 2.18 (1H, *ddd*, J_1 16.8, J_2 7.2, J_3 1.8, allylic CH_2), 1.84 (1H, *ddd*, J_1 16.8, J_2 7.0, J_3 2.2, allylic CH_2), 1.65 (1H, *brs*, hydroxylic O*H*), 1.11 (3H, *d*, *J* 7.0, CH_3), 0.92-0.98 (2H, *m*, cyclopropylic CH_2), 0.66-0.69 (2H, *m*, cyclopropylic CH_2) ppm. **^{13}C NMR** (100 MHz, C_6D_6): δ 141.6 (C*q*), 138.0 (C*q*), 133.1 (C*q*), 127.7 (*C*H), 126.7 (*C*H), 126.5 (*C*H), 125.5 (*C*H), 124.6 (*C*H), 56.4 (O-C*q*), 32.2 (*C*H_2), 31.1 (benzylic *C*H), 20.4 (cyclopropylic *C*H_2), 13.6 (*C*H_3), 13.0 (cyclopropylic *C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{14}H_{16}O$, expected $(M\text{-}H_2O+H)^+$ *m/z* 183.1169, observed $(M\text{-}H_2O+H)^+$ *m/z* 183.1170.

1-(4,5-dimethyl-3,4-dihydronaphthalen-1-yl)cyclopropanol (*rac*-$\mathbf{A_7}$)

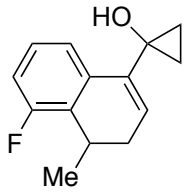


1-(4,5-dimethyl-3,4-dihydro naphthalen-1-yl)cyclopropanol
Chemical Formula: $C_{15}H_{18}O$
Molecular Weight: 214.30

^{t}BuLi (1.9 M solution in pentane, 2.75 mL, 5.22 mmol, 2.0 equiv.) was slowly added to a solution of 4-bromo-1,8-dimethyl-1,2-dihydronaphthalene ($\mathbf{Y_2^{KR}}$) (618 mg, 2.61 mmol, 1.0 equiv.) in anhydrous THF (10 mL) at -78 °C over a period of 10 min. The resultant colorless solution was stirred at -78 °C for 0.5 h. Concurrently, to a cooled (0 °C, ice/water bath) solution of 1-ethoxycyclopropanol (**Z**) (293 mg, 2.87 mmol, 1.1 equiv.) in anhydrous Et_2O (5.0 mL) was added MeMgI (3.0 M solution in Et_2O, 960 µL, 2.87 mmol, 1.1 equiv.) dropwise *via* syringe. The resultant white suspension was stirred at 0 °C for 10 min. The above organolithium solution was then cannulated into this suspension. The resultant reaction mixture was stirred at ambient temperature for 30 min, followed by stirring at 40 °C for overnight. The reaction mixture was then cooled down to 0 °C (ice/water bath) and quenched with saturated aqueous NH_4Cl. The separated aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered

and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 9:1). Colorless viscous oil. Isolated yield 88% (492 mg, 2.30 mmol). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 4:1) 0.26. **^{1}H NMR** (500 MHz, C_6D_6): δ 7.92 (1H, *d*, *J* 7.7, C^{ar}*H*), 7.14 (1H, *t*, *J* 7.7, C^{ar}*H*), 7.00 (1H, *d*, *J* 7.5, C^{ar}*H*), 5.68 (1H, *ddd*, J_1 6.1, J_2 2.3, J_3 1.6, olefinic C=C*H*), 2.88 (1H, *quint.*, *J* 7.0, benzylic C*H*), 2.31 (1H, *ddd*, J_1 17.0, J_2 7.1, J_3 2.4, allylic CH_2), 2.15 (3H, *s*, CH_3), 1.92 (1H, *ddd*, J_1 17.0, J_2 6.8, J_3 1.4, allylic CH_2), 1.63 (1H, *brs*, hydroxylic O*H*), 1.04 (1H, *ddd*, J_1 10.3, J_2 6.2, J_3 4.1, cyclopropylic CH_2), 0.99 (3H, *d*, *J* 7.1, CH_3), 0.91 (1H, *ddd*, J_1 11.4, J_2 6.6, J_3 4.9, cyclopropylic CH_2), 0.74 (1H, *ddd*, J_1 10.5, J_2 6.6, J_3 4.9, cyclopropylic CH_2), 0.68 (1H, *ddd*, J_1 10.7, J_2 6.4, J_3 4.1, cyclopropylic CH_2) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 139.9 (C*q*), 137.9 (C*q*), 134.2 (C*q*), 132.4 (C*q*), 129.9 (*C*H), 126.3 (*C*H), 123.8 (*C*H), 123.2 (*C*H), 56.6 (O-C*q*), 30.4 (*C*H_2), 28.0 (benzylic *C*H), 19.1 (*C*H_3), 18.7 (*C*H_3), 15.4 (cyclopropylic *C*H_2), 11.6 (cyclopropylic *C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{15}H_{18}O$, expected (M-H_2O+H)$^+$ *m/z* 197.1325, observed (M-H_2O+H)$^+$ *m/z* 197.1322.

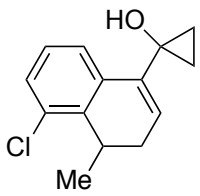
1-(5-fluoro-4-methyl-3,4-dihydronaphthalen-1-yl)cyclopropanol (*rac*-$\mathbf{A_8}$)



1-(5-fluoro-4-methyl-3,4-dihydro naphthalen-1-yl)cyclopropanol
Chemical Formula: $C_{14}H_{15}FO$
Molecular Weight: 218.27

^{t}BuLi (1.9 M solution in pentane, 2.41 mL, 4.58 mmol, 2.0 equiv.) was slowly added to a solution of 4-bromo-8-fluoro-1-methyl-1,2-dihydronaphthalene ($\mathbf{Y_5^{KR}}$) (553 mg, 2.29 mmol, 1.0 equiv.) in anhydrous THF (10 mL) at -78 °C over a period of 10 min. The resultant colorless solution was stirred at -78 °C for 0.5 h. Concurrently, to a cooled (0 °C, ice/water bath) solution of 1-ethoxycyclopropanol (**Z**) (258 mg, 2.52 mmol, 1.1 equiv.) in anhydrous Et_2O (4.5 mL) was added MeMgI (3.0 M solution in Et_2O, 840 μL, 2.52 mmol, 1.1 equiv.) dropwise *via* syringe. The resultant white suspension was stirred at 0 °C for 10 min. The above organolithium solution was then cannulated into this suspension. The resultant reaction mixture was stirred at ambient temperature for 30 min, followed by stirring at 40 °C for overnight. The reaction mixture was then cooled down to 0 °C (ice/water bath) and quenched with saturated aqueous NH_4Cl. The separated aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 9:1). Colorless viscous oil. Isolated yield 88% (492 mg, 2.30 mmol). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 4:1) 0.26. **^{1}H NMR** (500 MHz, C_6D_6): δ 7.73 (1H, *d*, *J* 7.8, C^{ar}*H*), 6.96 (1H, *td*, J_1 8.1, J_2 6.0, C^{ar}*H*), 6.83 (1H, *t*, *J* 9.4, C^{ar}*H*), 5.58 (1H, *dd*, J_1 6.7, J_2 1.8, olefinic C=C*H*), 3.28 (1H, *quint.*, *J* 7.2, benzylic C*H*), 2.20 (1H, *ddd*, J_1 17.4, J_2 7.6, J_3 2.4, diastereotopic CH_2), 1.81 (1H, *ddd*, J_1 17.4, J_2 6.7, J_3 1.4, diastereotopic CH_2), 1.46 (1H, *brs*, hydroxylic O*H*), 1.07 (3H, *d*, *J* 7.2, CH_3), 0.94-0.99 (1H, *m*, cyclopropylic CH_2), 0.81-0.86 (1H, *m*, cyclopropylic CH_2), 0.56-0.65 (2H, *m*, cyclopropylic CH_2) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -117.6 (1F, *s*, C^{ar}*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 160.3 (*d*, $J^{C\text{-}F}$ 240, *ipso*(F)-C*q*), 136.8 (*d*, $J^{C\text{-}F}$ 3.4, olefinic C*q*), 134.7 (*d*, $J^{C\text{-}F}$ 5.0, *meta*(F)-C*q*), 128.2 (*d*, $J^{C\text{-}F}$ 16.0, *ortho*(F)-C*q*), 127.5 (*d*, $J^{C\text{-}F}$ 8.5, *meta*(F)-*C*H), 124.7 (olefinic *C*H), 121.5 (*d*, $J^{C\text{-}F}$ 2.9, *para*(F)-*C*H), 114.4 (*d*, $J^{C\text{-}F}$ 22.4, *ortho*(F)-*C*H), 56.4 (O-C*q*), 29.7 (*C*H_2), 24.4 (*d*, $J^{C\text{-}F}$ 2.8, benzylic *C*H), 19.9 (*C*H_3), 14.9 (*C*H_2), 11.8 (*C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{14}H_{15}FO$, expected (M-H_2O+H)$^+$ *m/z* 201.1075, observed (M-H_2O+H)$^+$ *m/z* 201.1077.

1-(5-fluoro-4-methyl-3,4-dihydronaphthalen-1-yl)cyclopropanol (*rac*-$\mathbf{A_9}$)



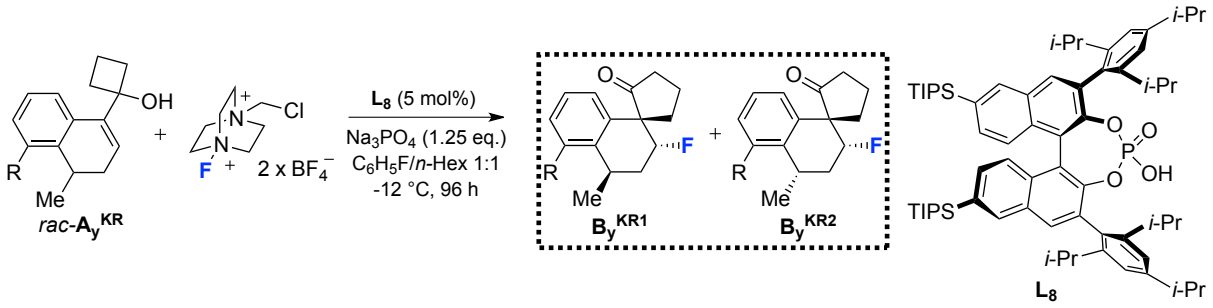
1-(5-chloro-4-methyl-3,4-dihydro naphthalen-1-yl)cyclopropanol
Chemical Formula: $C_{14}H_{15}ClO$
Molecular Weight: 234.72

^{t}BuLi (1.9 M solution in pentane, 2.50 mL, 4.74 mmol, 2.0 equiv.) was slowly added to a solution of 4-bromo-8-chloro-1-methyl-1,2-dihydronaphthalene ($\mathbf{Y_6^{KR}}$) (610 mg, 2.37 mmol, 1.0 equiv.) in anhydrous THF (15 mL) at -78 °C over a period of 10 min. The resultant colorless solution was stirred at -78 °C for 0.5 h. Concurrently, to a cooled (0 °C, ice/water bath) solution of 1-ethoxycyclopropanol (**Z**) (266 mg, 2.61 mmol, 1.1 equiv.) in anhydrous Et_2O (5.0 mL) was added MeMgI (3.0 M solution in Et_2O, 870 μL, 2.61 mmol, 1.1 equiv.) dropwise *via* syringe. The resultant white suspension was stirred at 0 °C for 10 min. The above organolithium solution was then cannulated into this suspension. The resultant reaction mixture was stirred at ambient temperature for 30 min, followed by stirring at 40 °C for overnight. The reaction mixture was then cooled down to 0 °C (ice/water bath) and quenched with saturated aqueous NH_4Cl. The separated aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 9:1). Colorless viscous oil. Isolated yield 88% (492 mg, 2.30 mmol). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 4:1) 0.26. **^{1}H NMR** (500 MHz, C_6D_6): δ 7.85 (1H, *d*, *J* 7.8, C^{ar}*H*), 7.16 (1H, *dd*, J_1 7.8, J_2 0.7, C^{ar}*H*), 6.89 (1H, *t*, *J* 7.9, C^{ar}*H*), 5.57 (1H, *dd*, J_1 6.7, J_2 2.1, olefinic C=C*H*), 3.39 (1H, *quint.*, *J* 7.2, benzylic C*H*), 2.20 (1H, *ddd*, J_1 17.3, J_2 7.4, J_3 2.4, diastereotopic CH_2), 1.82 (1H, *ddd*, J_1 17.3, J_2 6.8, J_3 1.2, CH_2), 1.43 (1H, *brs*, hydroxylic O*H*), 1.06 (3H, *d*, *J* 7.1, CH_3), 0.96 (1H, *ddd*, J_1 9.8, J_2 5.8, J_3 3.8, cyclopropylic CH_2), 0.82 (1H, *ddd*, J_1 11.2, J_2 6.5, J_3 4.8, cyclopropylic CH_2), 0.54-0.64 (2H, *m*, cyclopropylic CH_2) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 139.1 (*ipso*(Cl)-C*q*), 136.9 (olefinic C*q*), 134.7 (C*q*), 133.1 (C*q*), 128.6 (*C*H), 127.5 (*C*H), 124.8 (*C*H), 124.5 (olefinic *C*H), 56.3 (O-C*q*), 29.9 (*C*H_2), 28.8 (benzylic *C*H), 18.6 (*C*H_3), 15.1 (*C*H_2), 11.8 (*C*H_2) ppm.

General Procedure for the Stereodivergent Fluorination/Semi-Pinacol Reaction: Racemates

To a well-stirred solution of chiral, racemic allylic alcohol $\mathbf{A_y^{KR}}$ (0.20 mmol, 1.0 equiv.) and a 1:1 (*w/w*) mixture of (R_a/S_a)-TRIP ($\mathbf{L_4}$) (7.5 mg of each, 0.02 mmol, 10 mol%) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M) were added powdered Selectfluor^{TM} (106 mg, 0.30 mmol, 1.5 equiv.) and anhydrous Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.). The resultant heterogeneous mixture was stirred at -12 °C for 96 h. Saturated aqueous $Na_2S_2O_3$ was then added to quench the reaction. The layers were separated and the aqueous layer was extracted with methyl *tert*-butyl ether. The combined organic extracts were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Conversions and diastereomer ratios (*d.r.*) were determined by ^{1}H and ^{19}F NMR analysis of the crude compounds. Pure diastereomers ($\mathbf{B_y^{KR1}}$ and $\mathbf{B_y^{KR2}}$) were obtained after purification by flash chromatography on silica gel, using an adequate *n*-hexane/Et_2O mixture as eluent.

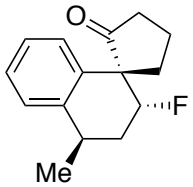
General Procedure for the Stereodivergent Fluorination/Semi-Pinacol Reaction: Enantioselective Version



To a well-stirred solution of chiral, racemic allylic alcohol $\mathbf{A_y^{KR}}$ (0.20 mmol, 1.0 equiv.) and (R_a)-TIPS-TRIP (**L_8**) (12 mg, 0.01 mmol, 5 mol%) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M) were added powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.) and anhydrous Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.). The resultant heterogeneous mixture was stirred at -12 °C for 96 h. Saturated aqueous $Na_2S_2O_3$ was then added to quench the reaction. The layers were separated and the aqueous layer was extracted with methyl *tert*-butyl ether. The combined organic extracts were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Conversions and diastereomer ratios (*d.r.*) were determined by ^{1}H and ^{19}F NMR analysis of the crude compounds. Pure diastereomers ($\mathbf{B_y^{KR1}}$ and $\mathbf{B_y^{KR2}}$) were obtained after purification by flash chromatography on silica gel, using an adequate *n*-hexane/Et_2O mixture as eluent. Enantiomer ratios (*e.r.*) were determined by chiral HPLC analysis of purified compounds.

Characterization of Fluorinated Products

β-Fluoro Spiroketone ($\mathbf{B_1^R}$)

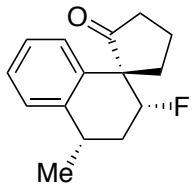


diastereomer 1
Chemical Formula: $C_{15}H_{17}FO$
Molecular Weight: 232.29

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A_1**) (43 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L_8**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 40% (19 mg, 0.08 mmol). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 9:1) 0.74. > 20:1 *d.r.* (^{1}H NMR). 96:4 *e.r.* Chiral HPLC. Chiralpak IC. *n*-Hex/*i*-PrOH 99.5:0.5. 1.0 mL/min. t_R 22.2 (major), 31.2 (minor). **^{1}H NMR** (400 MHz, C_6D_6): δ 7.10 (1H, *dd*, J_1 7.6, J_2 1.0, C^{ar}*H*), 7.04 (1H, *td*, J_1 7.1, J_2 1.4, C^{ar}*H*), 6.99 (1H, *td*, J_1 7.8, J_2 1.6, C^{ar}*H*), 6.80 (1H, *dd*, J_1 7.7, J_2 1.1, C^{ar}*H*), 4.41 (1H, *ddd*, $J_1^{H\text{-}F}$ 49.6, J_2 11.7, J_3 4.1, α-fluoro C*H*), 2.50-2.62 (2H, *m*, CH_2), 1.99-2.12 (3H, *m*, CH_2), 1.78-1.90 (1H, *m*, CH_2), 1.65-1.72 (2H, *m*, CH_2), 1.55-1.64 (1H, *m*, CH_2), 2.00-2.11 (1H, *m*, CH_2), 1.19 (3H, *d*, *J* 5.6, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -181.0 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (100 MHz, C_6D_6): δ 215.3 (*d*, $J^{C\text{-}F}$ 4.8, ketone C*q*), 141.7 (*d*, $J^{C\text{-}F}$ 2.3, C*q*), 138.5 (*d*, $J^{C\text{-}F}$ 8.0, C*q*), 127.3 (*d*, $J^{C\text{-}F}$ 2.3, *C*H), 127.1 (*C*H), 127.0 (*C*H), 126.8 (*d*, $J^{C\text{-}F}$ 0.7, *C*H), 96.7 (*d*, $J^{C\text{-}F}$ 174.2, *C*H-F), 56.2 (*d*, $J^{C\text{-}F}$ 19.8, α-carbonyl C*q*), 39.6 (CH_2), 38.4 (CH_2), 33.9 (*d*, $J^{C\text{-}F}$ 18.2, CH_2), 32.0 (*d*, $J^{C\text{-}F}$ 11.8, *C*H), 21.7 (CH_3), 20.6 (*d*, $J^{C\text{-}F}$ 1.8, CH_2) ppm. **ESI-HRMS (positif)** M =

$C_{15}H_{17}FO$, expected $(M+NH_4)^+$ *m/z* 250.1602, observed $(M+NH_4)^+$ *m/z* 250.1606. $[\alpha]^{20}_D$ +49.9 (*c* = 1.00, acetone).

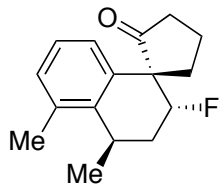
β-Fluoro Spiroketone (B_1^S)



diastereomer 2
Chemical Formula: $C_{15}H_{17}FO$
Molecular Weight: 232.29

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A$_1$**) (43 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L$_8$**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 43% (20 mg, 0.09 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 4:1) 0.48. > 20:1 *d.r.* (^{1}H NMR). 96.5:3.5 *e.r.* Chiral HPLC. Chiralpak IC. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 17.5 (minor), 23.7 (major). **^{1}H NMR** (400 MHz, C_6D_6): δ 6.98-7.04 (2H, *m*, C^{ar}*H*), 6.91 (1H, *dd*, J_1 6.9, J_2 2.3, C^{ar}*H*), 6.79 (1H, *dd*, J_1 7.1, J_2 2.0, C^{ar}*H*), 4.71 (1H, *ddd*, J_1^{H-F} 49.2, J_2 11.3, J_3 3.8, α-fluoro C*H*), 2.88-2.97 (1H, *m*, CH_2), 2.75-2.84 (1H, *m*, CH_2), 2.21-2.30 (1H, *m*, CH_2), 2.14 (2H, *t*, *J* 7.4, CH_2), 2.02 (1H, *ddd*, J_1 18.2, J_2 8.9, J_3 7.4, CH_2), 1.74-1.86 (1H, *m*, CH_2), 1.51-1.67 (2H, *m*, CH_2), 0.96 (3H, *d*, *J* 7.3, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -187.2 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (100 MHz, C_6D_6): δ 214.9 (*d*, J^{C-F} 5.1, ketone C*q*), 142.1 (*d*, J^{C-F} 2.1, C*q*), 137.6 (*d*, J^{C-F} 6.7, C*q*), 128.8 (*d*, J^{C-F} 0.9, *C*H), 127.6 (*d*, J^{C-F} 1.9, *C*H), 127.0 (*C*H), 126.8 (*d*, J^{C-F} 0.6, *C*H), 94.2 (*d*, J^{C-F} 173.0, *C*H-F), 56.1 (*d*, J^{C-F} 19.7, α-carbonyl C*q*), 39.3 (*C*H$_2$), 38.8 (*C*H$_2$), 32.5 (*d*, J^{C-F} 11.7, *C*H), 32.3 (*d*, J^{C-F} 18.8, *C*H$_2$), 24.0 (*C*H$_3$), 20.3 (*C*H$_2$) ppm. **ESI-HRMS (positif)** M = $C_{15}H_{17}FO$, expected $(M+NH_4)^+$ *m/z* 250.1602, observed $(M+NH_4)^+$ *m/z* 250.1603. $[\alpha]^{20}_D$ +8.7 (*c* = 1.00, acetone).

β-Fluoro Spiroketone (B_2^R)

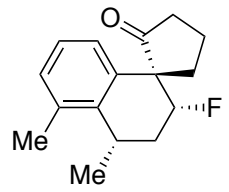


diastereomer 1
Chemical Formula: $C_{16}H_{19}FO$
Molecular Weight: 246.32

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A$_2$**) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L$_8$**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). White crystalline solid. Isolated yield 42% (21 mg, 0.08 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.77. > 20:1 *d.r.* (^{1}H NMR). 95:5 *e.r.* Chiral HPLC. Chiralcel OD-H. *n*-Hex/*i*-PrOH 99.5:0.5. 1.0 mL/min. t_R 14.9 (minor), 25.3 (major).**^{1}H NMR** (500 MHz, C_6D_6): δ 6.96 (1H, *t*, *J* 7.7, C^{ar}*H*), 6.88 (1H, *d*, *J* 7.1, C^{ar}*H*), 6.69 (1H, *d*, *J* 7.9, C^{ar}*H*), 4.87 (1H, *ddd*, J_1^{H-F} 49.8, J_2 12.7, J_3 4.5, α-fluoro C*H*), 2.90-2.96 (1H, *m*, diastereotopic CH_2), 2.88 (1H, *sext.*, *J* 6.0, benzylic C*H*), 2.23-2.33 (3H, *m*, CH_2), 2.01-2.08 (1H, *m*, CH_2), 1.99 (3H, *s*, CH_3), 1.90-1.97 (1H, *m*, CH_2), 1.72-1.78 (1H, *m*, CH_2), 1.60-1.68 (1H, *m*, CH_2), 0.84 (3H, *d*, *J* 7.2, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -187.3 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 215.3 (*d*, J^{C-F} 6.6, ketone C*q*), 140.5 (*d*, J^{C-F} 2.0, C*q*), 138.5 (*d*, J^{C-F} 7.8, C*q*), 135.9 (C*q*), 129.4 (*C*H), 126.9 (*C*H), 125.8 (*d*, J^{C-F} 1.8, *C*H), 95.8 (*d*, J^{C-F} 170.6, *C*H-F), 56.3 (*d*, J^{C-F} 19.7, α-carbonyl C*q*), 39.9 (*C*H$_2$), 39.5 (*C*H$_2$), 32.7 (*d*, J^{C-F} 18.1, *C*H$_2$), 30.7 (*d*, J^{C-F} 13.0, benzylic *C*H), 21.1 (*C*H$_3$), 20.8

(CH_2), 19.3 (CH_3) ppm. **ESI-HRMS (positif)** M = $C_{16}H_{19}FO$, expected $(M+NH_4)^+$ *m/z* 264.1759, observed $(M+NH_4)^+$ *m/z* 264.1762. $[\alpha]^{20}_D$ +61.3 (*c* = 1.00, acetone).

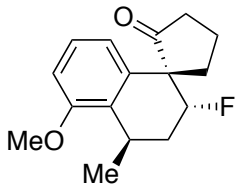
β-Fluoro Spiroketone (B_2^S)



diastereomer 2
Chemical Formula: $C_{16}H_{19}FO$
Molecular Weight: 246.32

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A₂**) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L₈**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless amorphous solid. Isolated yield 44% (22 mg, 0.09 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.49. > 20:1 *d.r.* (^{1}H NMR). 95.5:4.5 *e.r.* Chiral HPLC. Chiralpak IC. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 8.0 (minor), 13.1 (major). **^{1}H NMR** (400 MHz, C_6D_6): δ 6.99 (1H, *t*, *J* 7.5, $C^{ar}H$), 6.93 (1H, *d*, *J* 7.0, $C^{ar}H$), 6.71 (1H, *d*, *J* 7.7, $C^{ar}H$), 4.43 (1H, *ddd*, J_1^{H-F} 49.6, J_2 7.2, J_3 3.4, α-fluoro C*H*), 2.79-2.88 (1H, *m*, benzylic C*H*), 2.19-2.28 (1H, *m*, diastereotopic CH_2), 2.08-2.17 (1H, *m*, diatereotopic CH_2), 2.11 (3H, *s*, CH_3), 1.96-2.02 (1H, *m*, CH_2), 1.75-1.89 (3H, *m*, CH_2), 1.42-1.60 (2H, *m*, CH_2), 1.33 (3H, *dd*, J_1 7.0, J_2 1.8, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -178.0 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (100 MHz, C_6D_6): δ 214.6 (*d*, J^{C-F} 3.9, ketone C*q*), 140.4 (*d*, J^{C-F} 1.0, C*q*), 137.1 (*d*, J^{C-F} 2.5, C*q*), 135.7 (C*q*), 129.6 (*C*H), 126.7 (*C*H), 126.4 (*C*H), 92.1 (*d*, J^{C-F} 177.3, *C*H-F), 57.4 (*d*, J^{C-F} 19.2, α-carbonyl C*q*), 39.4 (*d*, J^{C-F} 5.3, *C*H_2), 38.7 (*C*H_2), 32.3 (*d*, J^{C-F} 18.6, *C*H_2), 29.2 (*d*, J^{C-F} 4.8, *C*H), 22.7 (*d*, J^{C-F} 4.0, *C*H), 19.8 (*C*H_3), 19.2 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{16}H_{19}FO$, expected $(M+NH_4)^+$ *m/z* 264.1759, observed $(M+NH_4)^+$ *m/z* 264.1760. $[\alpha]^{20}_D$ +16.5 (*c* = 1.00, acetone).

β-Fluoro Spiroketone (B_3^R)

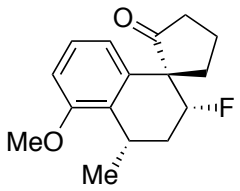


diastereomer 1
Chemical Formula: $C_{16}H_{19}FO_2$
Molecular Weight: 262.32

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A₃**) (49 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L₈**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 9:1). White crystalline solid. Isolated yield 41% (22 mg, 0.08 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.57. > 20:1 *d.r.* (^{1}H NMR). 96:4 *e.r.* Chiral HPLC. Chiralpak IC. *n*-Hex/*i*-PrOH 98:2. 1.0 mL/min. t_R 11.6 (major), 16.1 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.99 (1H, *t*, *J* 8.1, $C^{ar}H$), 6.50 (1H, *d*, *J* 7.8, $C^{ar}H$), 6.37 (1H, *dd*, J_1 8.1, J_2 0.6, $C^{ar}H$), 4.88 (1H, *ddd*, J_1^{H-F} 49.5, J_2 12.7, J_3 4.2, α-fluoro C*H*), 3.48-3.55 (1H, broad *m*, diastereotopic CH_2), 3.25 (3H, *s*, methoxy CH_3-O), 2.94 (1H, *sept.*, *J* 6.2, benzylic C*H*), 2.25-2.36 (3H, *m*, CH_2), 2.03-2.10 (1H, *m*, CH_2), 1.88-1.97 (1H, *m*, CH_2), 1.77-1.82 (1H, *m*, CH_2), 1.61-1.69 (1H, *m*, CH_2), 1.14 (3H, *d*, *J* 7.1, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -187.6 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 215.1 (*d*, J^{C-F} 5.9, ketone C*q*), 157.3 (methoxy C*q*-O), 139.5 (*d*, J^{C-F} 7.9, C*q*), 131.3 (*d*, J^{C-F} 2.4, C*q*), 127.7 (*C*H), 119.6 (*d*, J^{C-F} 2.1, *C*H), 108.6 (*C*H), 95.7 (*d*, J^{C-F} 171.2, *C*H-F), 56.0 (*d*, J^{C-F} 19.9, α-carbonyl C*q*), 54.9 (methoxy *C*H_3-O), 39.6 (*C*H_2), 39.2 (*C*H_2), 32.2 (*d*, J^{C-F} 18.1, *C*H_2), 28.3 (*d*, J^{C-F} 13.2, benzylic

*C*H), 21.3 (*C*H_2), 20.8 (*d*, $J^{C\text{-}F}$ 1.9, *C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{16}H_{19}FO_2$, expected $(M+H)^+$ *m/z* 263.1442, observed $(M+H)^+$ *m/z* 263.1443. $[\alpha]^{20}_D$ +47.5 (*c* = 1.00, acetone).

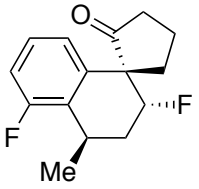
β-Fluoro Spiroketone (B_3^S)



diastereomer 2
Chemical Formula: $C_{16}H_{19}FO_2$
Molecular Weight: 262.32

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A$_3$**) (49 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L$_8$**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 9:1). White crystalline solid. Isolated yield 43% (23 mg, 0.09 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.24. > 20:1 *d.r.* (^{1}H NMR). 95.5:4.5 *e.r.* Chiral HPLC. Chiralcel OJ-H. *n*-Hex/*i*-PrOH 95:5. 1.0 mL/min. t_R 10.0 (minor), 18.3 (major). **^{1}H NMR** (500 MHz, C_6D_6): δ 7.02 (1H, *t*, *J* 8.0, C^{ar}*H*), 6.55 (1H, *dd*, J_1 8.0, J_2 0.8, C^{ar}*H*), 6.44 (1H, *dd*, J_1 8.1, J_2 0.8, C^{ar}*H*), 4.40 (1H, *ddd*, $J_1^{H\text{-}F}$ 49.4, J_2 8.9, J_3 3.7, α-fluoro C*H*), 3.31 (3H, *s*, methoxy CH_3-O), 3.27 (1H, *sext.*, *J* 7.9, benzylic C*H*), 2.19-2.33 (2H, *m*, CH_2), 1.89-2.08 (4H, *m*, CH_2), 1.62 (3H, *dd*, J_1 6.8, J_2 1.5, CH_3), 1.56-1.65 (1H, *m*, CH_2), 1.46-1.54 (1H, *m*, CH_2) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -177.7 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 214.6 (*d*, $J^{C\text{-}F}$ 3.3, ketone C*q*), 157.6 (methoxy C*q*-O), 138.5 (*d*, $J^{C\text{-}F}$ 4.1, C*q*), 131.1 (*d*, $J^{C\text{-}F}$ 1.6, C*q*), 127.2 (*C*H), 120.2 (*d*, $J^{C\text{-}F}$ 0.9, *C*H), 108.8 (*C*H), 93.0 (*d*, $J^{C\text{-}F}$ 177.6, *C*H-F), 56.7 (*d*, $J^{C\text{-}F}$ 19.2, α-carbonyl C*q*), 54.8 (methoxy *C*H_3-O), 39.1 (*C*H_2), 38.2 (*d*, $J^{C\text{-}F}$ 4.1, *C*H_2), 32.3 (*d*, $J^{C\text{-}F}$ 18.5, *C*H_2), 27.7 (*d*, $J^{C\text{-}F}$ 7.3, benzylic *C*H), 22.6 (*d*, $J^{C\text{-}F}$ 2.6, *C*H_2), 19.7 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{16}H_{19}FO_2$, expected $(M+H)^+$ *m/z* 263.1442, observed $(M+H)^+$ *m/z* 263.1443. $[\alpha]^{20}_D$ +47.5 (*c* = 1.00, acetone). **ESI-HRMS (positif)** M = $C_{16}H_{19}FO_2$, expected $(M+H)^+$ *m/z* 263.1442, observed $(M+H)^+$ *m/z* 263.1440. $[\alpha]^{20}_D$ +7.8 (*c* = 1.00, acetone).

β-Fluoro Spiroketone (B_4^R)

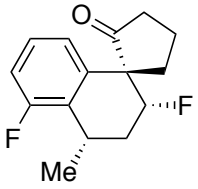


diastereomer 1
Chemical Formula: $C_{15}H_{16}F_2O$
Molecular Weight: 250.28

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A$_4$**) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L$_8$**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Pale-yellow crystalline solid. Isolated yield 43% (22 mg, 0.09 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 9:1) 0.80. > 20:1 *d.r.* (^{1}H NMR). 94.5:5.5 *e.r.* Chiral HPLC. Chiralcel OJ-H. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 13.0 (major), 15.3 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.75 (1H, *td*, J_1 8.0, J_2 5.9, C^{ar}*H*), 6.69 (1H, *td*, J_1 8.4, J_2 1.2, C^{ar}*H*), 6.47 (1H, *d*, *J* 7.8, C^{ar}*H*), 4.69 (1H, *ddd*, $J_1^{H\text{-}F}$ 49.1, J_2 12.6, J_3 4.1, α-fluoro C*H*), 2.80 (1H, *sept.*, *J* 6.3, benzylic C*H*), 2.09-2.27 (3H, *m*, diastereotopic CH_2), 1.99 (1H, *ddd*, J_1 15.9, J_2 8.8, J_3 7.2, diatereotopic CH_2), 1.81-1.90 (1H, *m*, CH_2), 1.49-1.66 (2H, *m*, CH_2), 1.16-1.24 (1H, *m*, CH_2), 1.00 (3H, *d*, *J* 7.2, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -116.7 (1F, *s*, C^{ar}*F*), -188.2 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 214.6 (*d*, $J^{C\text{-}F}$ 5.5, ketone C*q*), 161.2 (*d*, $J^{C\text{-}F}$ 244, *ipso*(F)-C*q*), 140.6 (*dd*, $J_1^{C\text{-}F}$ 8.2, $J_2^{C\text{-}F}$ 4.4, *meta*(F)-C*q*), 130.1 (*dd*, $J_1^{C\text{-}F}$ 16.4, $J_2^{C\text{-}F}$ 2.4, *ortho*(F)-C*q*), 128.0

(*para*(F)-*C*H), 122.9 (*t*, $J^{C\text{-}F}$ 2.6, *meta*(F)-*C*H), 113.7 (*d*, $J^{C\text{-}F}$ 22.3, *ortho*(F)-*C*H), 94.9 (*d*, $J^{C\text{-}F}$ 172, *C*H-F), 55.7 (*dd*, $J_1^{C\text{-}F}$ 20.6, $J_2^{C\text{-}F}$ 1.9, α-carbonyl C*q*), 39.4 (CH_2), 38.6 (CH_2), 31.5 (*d*, $J^{C\text{-}F}$ 18.7, benzylic *C*H), 30.2 (CH_3), 21.8 (CH_2), 20.6 (*d*, $J^{C\text{-}F}$ 2.1, CH_2) ppm. **ESI-HRMS (positif)** M = $C_{15}H_{16}F_2O$, expected $(M+NH_4)^+$ *m/z* 268.1508, observed $(M+NH_4)^+$ *m/z* 268.1507. $[\alpha]^{20}_D$ +62.6 (*c* = 1.00, acetone).

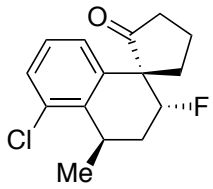
β-Fluoro Spiroketone (B_4^S)



diastereomer 2
Chemical Formula: $C_{15}H_{16}F_2O$
Molecular Weight: 250.28

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A₄**) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L₈**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). White crystalline solid. Isolated yield 43% (22 mg, 0.09 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.58. > 20:1 *d.r.* (^{1}H NMR). 98:2 *e.r.* Chiral HPLC. Chiralpak IC. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 17.3 (minor), 26.0 (major). **^{1}H NMR** (500 MHz, C_6D_6): *δ* 6.70-6.81 (2H, *m*, $C^{ar}H$), 6.52 (1H, *dd*, J_1 7.4, J_2 1.1, $C^{ar}H$), 4.24 (1H, *ddd*, $J_1^{H\text{-}F}$ 49.0, J_2 10.0, J_3 3.9, α-fluoro C*H*), 2.99 (1H, *sext.*, *J* 7.1, benzylic C*H*), 2.13-2.29 (2H, *m*, diastereotopic CH_2), 1.94-2.06 (2H, *m*, diatereotopic CH_2), 1.75-1.91 (2H, *m*, CH_2), 1.56-1.67 (1H, *m*, CH_2), 1.50 (3H, *dt*, J_1 6.8, $J_2^{H\text{-}F}$ 1.4, CH_3), 1.40-1.52 (1H, *m*, CH_2) ppm. **^{19}F NMR** (376 MHz, C_6D_6): *δ* -112.9 (1F, *s*, $C^{ar}F$), -181.5 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): *δ* 214.3 (*d*, $J^{C\text{-}F}$ 3.2, ketone C*q*), 161.7 (*d*, $J^{C\text{-}F}$ 244, *ipso*(F)-C*q*), 139.9 (*t*, $J^{C\text{-}F}$ 5.2, *meta*(F)-C*q*), 129.8 (*dd*, $J_1^{C\text{-}F}$ 15.0, $J_2^{C\text{-}F}$ 1.8, *ortho*(F)-C*q*), 128.1 (*para*(F)-*C*H), 123.2 (*d*, $J^{C\text{-}F}$ 1.3, *meta*(F)-*C*H), 114.0 (*d*, $J^{C\text{-}F}$ 22.9, *ortho*(F)-*C*H), 93.3 (*d*, $J^{C\text{-}F}$ 176, *C*H-F), 56.2 (*dd*, $J_1^{C\text{-}F}$ 19.9, $J_2^{C\text{-}F}$ 2.1, α-carbonyl C*q*), 39.1 (CH_2), 37.6 (*d*, $J^{C\text{-}F}$ 3.1, CH_2), 32.1 (*d*, $J^{C\text{-}F}$ 18.9, CH_2), 27.7 (*d*, $J^{C\text{-}F}$ 8.9, CH_3), 22.5 (*dd*, $J_1^{C\text{-}F}$ 6.2, $J_2^{C\text{-}F}$ 1.6, benzylic *C*H), 19.8 (CH_2) ppm. **ESI-HRMS (positif)** M = $C_{15}H_{16}F_2O$, expected $(M+NH_4)^+$ *m/z* 268.1508, observed $(M+NH_4)^+$ *m/z* 268.1508. $[\alpha]^{20}_D$ +23.9 (*c* = 1.00, acetone).

β-Fluoro Spiroketone (B_5^R)

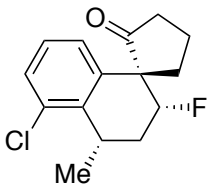


diastereomer 1
Chemical Formula: $C_{15}H_{16}ClFO$
Molecular Weight: 266.74

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A₅**) (50 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L₈**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 41% (22 mg, 0.08 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.68. > 20:1 *d.r.* (^{1}H NMR). 94.5:5.5 *e.r.* Chiral HPLC. Chiralcel OJ-H. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 7.5 (major), 10.1 (minor). **^{1}H NMR** (500 MHz, C_6D_6): *δ* 7.05 (1H, *dd*, J_1 7.9, J_2 1.2, $C^{ar}H$), 6.64 (1H, *t*, *J* 7.9, $C^{ar}H$), 6.36 (1H, *dd*, J_1 7.9, J_2 1.0, $C^{ar}H$), 5.42 (1H, *ddd*, $J_1^{H\text{-}F}$ 48.6, J_2 12.3, J_3 4.3, α-fluoro C*H*), 3.13-3.21 (1H, *m*, benzylic C*H*), 2.36-2.42 (1H, *m*, diastereotopic CH_2), 2.19-2.26 (1H, *m*, CH_2), 2.02-2.10 (1H, *m*, CH_2), 1.65-1.81 (3H, *m*, CH_2), 1.45-1.57 (2H, *m*, CH_2), 1.07 (3H, *d*, *J* 7.1, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): *δ* -190.2 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): *δ* 220.1 (ketone C*q*), 142.6 (*d*, $J^{C\text{-}F}$ 8.4,

C*q*), 138.5 (*d*, $J^{C\text{-}F}$ 2.4, C*q*), 134.2 (C*q*), 128.6 (*C*H), 128.2 (*C*H), 127.3 (*d*, $J^{C\text{-}F}$ 2.3, *C*H), 91.8 (*d*, $J^{C\text{-}F}$ 176.3, *C*H-F), 58.6 (*d*, $J^{C\text{-}F}$ 19.6, α-carbonyl C*q*), 40.4 (*C*H_2), 35.9 (*d*, $J^{C\text{-}F}$ 5.0, *C*H_2), 33.1 (*d*, $J^{C\text{-}F}$ 18.2, *C*H_2), 31.9 (*d*, $J^{C\text{-}F}$ 12.5, benzylic *C*H), 21.0 (*C*H_3), 20.0 (*d*, $J^{C\text{-}F}$ 3.0, *C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{15}H_{16}ClFO$, expected $(M+NH_4)^+$ *m/z* 284.1212, observed $(M+NH_4)^+$ *m/z* 284.1209. $[\alpha]^{20}_D$ +61.7 (*c* = 1.00, acetone).

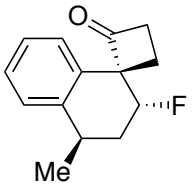
β-Fluoro Spiroketone (B_5^S)



diastereomer 2
Chemical Formula: $C_{15}H_{16}ClFO$
Molecular Weight: 266.74

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A$_5$**) (50 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L$_8$**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). White crystalline solid. Isolated yield 45% (21 mg, 0.09 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 4:1) 0.20. > 20:1 *d.r.* (^{1}H NMR). 96:4 *e.r.* Chiral HPLC. Chiralpak IC. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 20.1 (minor), 23.0 (major). **^{1}H NMR** (500 MHz, C_6D_6): δ 7.07 (1H, *d*, *J* 7.9, C^{ar}*H*), 6.67 (1H, *d*, *J* 7.9, C^{ar}*H*), 6.54 (1H, *d*, *J* 7.9, C^{ar}*H*), 4.73 (1H, *ddd*, $J_1^{H\text{-}F}$ 49.5, J_2 12.8, J_3 4.1, α-fluoro C*H*), 3.34-3.37 (1H, *m*, diastereotopic C*H*$_2$), 2.75 (1H, *sept.*, *J* 5.8, benzylic C*H*), 2.21-2.28 (1H, *m*, C*H*$_2$), 2.07-2.17 (2H, *m*, C*H*$_2$), 1.93-2.00 (1H, *m*, C*H*$_2$), 1.84-1.90 (1H, *m*, C*H*$_2$), 1.65-1.70 (1H, *m*, C*H*$_2$), 1.51-1.59 (1H, *m*, C*H*$_2$), 0.99 (3H, *d*, *J* 7.2, C*H*$_3$) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -188.0 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 214.6 (*d*, $J^{C\text{-}F}$ 6.6, ketone C*q*), 140.7 (*d*, $J^{C\text{-}F}$ 8.0, C*q*), 140.0 (*d*, $J^{C\text{-}F}$ 2.2, C*q*), 134.5 (C*q*), 128.5 (*C*H), 128.2 (*C*H), 126.5 (*d*, $J^{C\text{-}F}$ 1.8, *C*H), 95.4 (*d*, $J^{C\text{-}F}$ 171.4, *C*H-F), 56.1 (*d*, $J^{C\text{-}F}$ 20.4, α-carbonyl C*q*), 39.6 (*C*H_2), 39.3 (*C*H_2), 32.2 (*d*, $J^{C\text{-}F}$ 18.5, *C*H_2), 31.6 (*d*, $J^{C\text{-}F}$ 13.3, benzylic *C*H), 20.61 (*d*, $J^{C\text{-}F}$ 2.4, *C*H_2), 20.59 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{15}H_{16}ClFO$, expected $(M+NH_4)^+$ *m/z* 284.1212, observed $(M+NH_4)^+$ *m/z* 284.1215. $[\alpha]^{20}_D$ +15.0 (*c* = 1.00, acetone).

β-Fluoro Spiroketone (B_6^R)

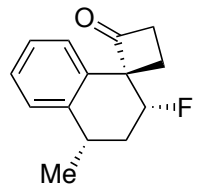


diastereomer 1
Chemical Formula: $C_{14}H_{15}FO$
Molecular Weight: 218.27

According to the General Procedure: chiral, racemic allylic cyclopropanol (*rac*-**A$_6$**) (40 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L$_8$**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 46% (20 mg, 0.09 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.67. > 20:1 *d.r.* (^{1}H NMR). 96:4 *e.r.* Chiral HPLC. Chiralcel OJ-H. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 13.7 (major), 18.4 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.96-7.06 (3H, *m*, C^{ar}*H*), 6.88 (1H, *d*, *J* 7.5, C^{ar}*H*), 4.34 (1H, *ddd*, $J_1^{H\text{-}F}$ 50.7, J_2 12.1, J_3 4.0, α-fluoro C*H*), 2.88 (1H, *dddd*, J_1 18.2, J_2 11.3, J_3 6.5, J_4 1.8, diastereotopic C*H*$_2$), 2.63 (1H, *ddd*, J_1 18.0, J_2 10.6, J_3 7.3, C*H*$_2$), 2.49 (1H, *sept.*, *J* 6.5, benzylic C*H*), 2.36 (1H, *td*, J_1 12.0, J_2 5.7, C*H*$_2$), 2.27 (1H, *dddd*, J_1 18.1, J_2 11.0, J_3 6.3, J_4 1.6, C*H*$_2$), 1.88-2.02 (2H, *m*, C*H*$_2$), 1.08 (3H, *dd*, J_1 6.8, J_2 0.9, C*H*$_3$) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -185.0 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 206.3 (*d*, $J^{C\text{-}F}$ 4.7, ketone C*q*), 140.6 (*d*, $J^{C\text{-}F}$ 2.4, C*q*), 133.5 (*d*, $J^{C\text{-}F}$ 8.7, C*q*), 127.50 (*C*H), 127.49 (*C*H), 127.0 (*d*, $J^{C\text{-}F}$

1.7, *C*H), 126.3 (*d*, $J^{C\text{-}F}$ 1.7, *C*H), 92.7 (*d*, $J^{C\text{-}F}$ 173, *C*H-F), 73.4 (*d*, $J^{C\text{-}F}$ 21.3, α-carbonyl C*q*), 44.2 (*C*H_2), 35.0 (*d*, $J^{C\text{-}F}$ 17.7, *C*H_2), 32.2 (*d*, $J^{C\text{-}F}$ 11.5, benzylic *C*H), 22.2 (*C*H_2), 21.7 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{14}H_{15}FO$, expected $(M+NH_4)^+$ *m/z* 236.1446, observed $(M+NH_4)^+$ *m/z* 236.1449. $[\alpha]^{20}_D$ +18.9 (*c* = 1.00, acetone).

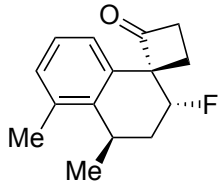
β-Fluoro Spiroketone (B_6^S)



diastereomer 2
Chemical Formula: $C_{14}H_{15}FO$
Molecular Weight: 218.27

According to the General Procedure: chiral, racemic allylic cyclopropanol (*rac*-**A$_6$**) (40 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L$_8$**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 44% (19 mg, 0.09 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 4:1) 0.59. > 20:1 *d.r.* (^{1}H NMR). 95:5 *e.r.* Chiral HPLC. Chiralpak IC. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 15.9 (minor), 17.9 (major). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.96-7.02 (2H, *m*, C^{ar}*H*), 6.86-6.89 (2H, *m*, C^{ar}*H*), 4.68 (1H, *ddd*, $J_1^{H\text{-}F}$ 50.3, J_2 11.3, J_3 3.9, α-fluoro C*H*), 2.83-2.93 (2H, *m*, benzylic C*H* + diastereotopic CH_2), 2.60-2.69 (2H, *m*, diastereotopic CH_2), 2.20 (1H, *ddd*, J_1 18.9, J_2 13.0, J_3 11.9, CH_2), 2.00 (1H, *ddd*, J_1 18.0, J_2 11.3, J_3 6.8, CH_2), 1.66 (1H, *tt*, J_1 13.0, J_2 3.7, CH_2), 0.89 (3H, *d*, *J* 7.3, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -187.0 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 205.9 (*d*, $J^{C\text{-}F}$ 5.4, ketone C*q*), 141.0 (*d*, $J^{C\text{-}F}$ 2.2, C*q*), 132.9 (*d*, $J^{C\text{-}F}$ 7.9, C*q*), 129.1 (*C*H), 127.5 (*C*H), 127.0 (*C*H), 126.4 (*d*, $J^{C\text{-}F}$ 2.0, *C*H), 90.9 (*d*, $J^{C\text{-}F}$ 172, *C*H-F), 73.1 (*d*, $J^{C\text{-}F}$ 21.3, α-carbonyl C*q*), 44.2 (*C*H_2), 33.2 (*d*, $J^{C\text{-}F}$ 18.3, *C*H_2), 32.7 (*d*, $J^{C\text{-}F}$ 11.2, benzylic *C*H), 23.8 (*C*H_3), 22.5 (*d*, $J^{C\text{-}F}$ 1.1, *C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{14}H_{15}FO$, expected $(M+NH_4)^+$ *m/z* 236.1446, observed $(M+NH_4)^+$ *m/z* 236.1443. $[\alpha]^{20}_D$ +13.3 (*c* = 1.00, acetone).

β-Fluoro Spiroketone (B_7^R)

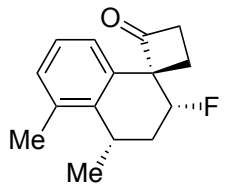


diastereomer 1
Chemical Formula: $C_{15}H_{17}FO$
Molecular Weight: 232.29

According to the General Procedure: chiral, racemic allylic cyclopropanol (*rac*-**A$_7$**) (43 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L$_8$**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). White amorphous solid. Isolated yield 43% (20 mg, 0.09 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.74. > 20:1 *d.r.* (^{1}H NMR). 95.5:4.5 *e.r.* Chiral HPLC. Chiralcel OJ-H. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 10.3 (major), 12.5 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.97 (1H, *t*, *J* 7.5, C^{ar}*H*), 6.92 (1H, *d*, *J* 6.7, C^{ar}*H*), 6.86 (1H, *d*, *J* 7.7, C^{ar}*H*), 4.32 (1H, *ddd*, $J_1^{H\text{-}F}$ 50.8, J_2 9.5, J_3 4.3, α-fluoro C*H*), 2.75-2.83 (2H, *m*, diastereotopic CH_2 + benzylic C*H*), 2.05 (3H, *s*, CH_3), 1.94-2.03 (2H, *m*, CH_2), 1.85-1.91 (1H, *m*, CH_2), 1.23 (3H, *dd*, J_1 7.0, J_2 1.3, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -179.2 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 206.3 (*d*, $J^{C\text{-}F}$ 4.1, ketone C*q*), 139.3 (*d*, $J^{C\text{-}F}$ 1.8, C*q*), 136.5 (C*q*), 133.1 (*d*, $J^{C\text{-}F}$ 5.4, C*q*), 130.4 (*C*H), 126.7 (*C*H), 124.8 (*d*, $J^{C\text{-}F}$ 1.0, *C*H), 92.3 (*d*, $J^{C\text{-}F}$ 176, *C*H-F), 73.4 (*d*, $J^{C\text{-}F}$ 20.3, α-carbonyl C*q*), 43.6 (*C*H_2), 33.1 (*d*, $J^{C\text{-}F}$ 18.2, *C*H_2), 29.8 (*d*, $J^{C\text{-}F}$ 8.1, benzylic *C*H), 23.4 (*d*, $J^{C\text{-}F}$ 2.1, *C*H_3), 23.1 (*d*, $J^{C\text{-}F}$ 5.0, *C*H_2), 19.9 (*C*H_3) ppm. **ESI-**

HRMS (positif) M = $C_{15}H_{17}FO$, expected $(M+NH_4)^+$ *m/z* 250.1602, observed $(M+NH_4)^+$ *m/z* 250.1606. $[\alpha]^{20}_D$ +27.8 (*c* = 1.00, acetone).

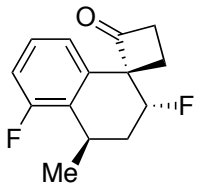
β-Fluoro Spiroketone (B_7^S)



diastereomer 2
Chemical Formula: $C_{15}H_{17}FO$
Molecular Weight: 232.29

According to the General Procedure: chiral, racemic allylic cyclopropanol (*rac*-**A$_7$**) (43 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L$_8$**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 44% (20 mg, 0.09 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 4:1) 0.65. > 20:1 *d.r.* (^{1}H NMR). 94.5:5.5 *e.r.* Chiral HPLC. Chiralpak IC. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 7.6 (major), 8.6 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.97 (1H, *t*, *J* 7.7, C^{ar}*H*), 6.88 (1H, *d*, *J* 7.1, C^{ar}*H*), 6.80 (1H, *d*, *J* 7.8, C^{ar}*H*), 4.86 (1H, *ddd*, J_1^{H-F} 50.6, J_2 12.7, J_3 4.0, α-fluoro C*H*), 2.96 (1H, *dddd*, J_1 18.2, J_2 11.3, J_3 6.5, J_4 2.0, diastereotopic CH_2), 2.81-2.87 (1H, *m*, benzylic C*H*), 2.65-2.70 (2H, *m*, CH_2), 2.34 (1H, *tdd*, J_1 12.3, J_2 7.3, J_3 1.6, CH_2), 2.11 (1H, *ddd*, J_1 12.0, J_2 10.7, J_3 6.5, CH_2), 1.95 (3H, *s*, CH_3), 1.78-1.84 (1H, *m*, CH_2), 0.77 (3H, *d*, *J* 7.2, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -189.1 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 206.2 (*d*, J^{C-F} 6.1, ketone C*q*), 139.3 (*d*, J^{C-F} 2.3, C*q*), 136.5 (C*q*), 133.3 (*d*, J^{C-F} 8.9, C*q*), 130.0 (*C*H), 127.1 (*d*, J^{C-F} 0.8, *C*H), 124.5 (*d*, J^{C-F} 2.1, *C*H), 91.0 (*d*, J^{C-F} 169, *C*H-F), 73.6 (*d*, J^{C-F} 21.2, α-carbonyl C*q*), 44.5 (*C*H_2), 33.6 (*d*, J^{C-F} 17.6, *C*H_2), 30.9 (*d*, J^{C-F} 12.5, benzylic *C*H), 22.8 (*C*H_2), 21.1 (*C*H_3), 19.2 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{15}H_{17}FO$, expected $(M+NH_4)^+$ *m/z* 250.1602, observed $(M+NH_4)^+$ *m/z* 250.1604. $[\alpha]^{20}_D$ +10.0 (*c* = 1.00, acetone).

β-Fluoro Spiroketone (B_8^R)

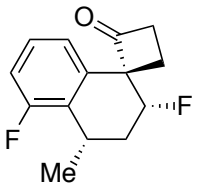


diastereomer 1
Chemical Formula: $C_{14}H_{14}F_2O$
Molecular Weight: 236.26

According to the General Procedure: chiral, racemic allylic cyclopropanol (*rac*-**A$_8$**) (44 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L$_8$**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). White crystalline solid. Isolated yield 41% (19 mg, 0.08 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.80. > 20:1 *d.r.* (^{1}H NMR). 95.5:4.5 *e.r.* Chiral HPLC. Chiralpak IC. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 8.0 (minor), 13.1 (major). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.70-6.79 (2H, *m*, C^{ar}*H*), 6.59 (1H, *d*, *J* 7.6, C^{ar}*H*), 4.16 (1H, *ddd*, J_1^{H-F} 50.3, J_2 10.9, J_3 4.0, α-fluoro C*H*), 2.89 (1H, *sext.*, *J* 7.3, benzylic C*H*), 2.78 (1H, *ddd*, J_1 18.2, J_2 11.2, J_3 6.8, J_4 1.2, diastereotopic CH_2), 2.12-2.20 (1H, *m*, CH_2), 2.04-2.09 (1H, *m*, CH_2), 1.78-1.91 (2H, *m*, CH_2), 1.37 (3H, *dt*, J_1 6.9, J_2 1.3, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -112.0 (1F, *s*, C^{ar}*F*), -181.6 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 205.6 (*d*, J^{C-F} 3.7, ketone C*q*), 162.0 (*d*, J^{C-F} 245.3, *ipso*(F)-C*q*), 135.7 (*dd*, J_1^{C-F} 6.8, J_2^{C-F} 4.9, *ortho*(F)-C*q*), 128.4 (*para*(F)-*C*H), 125.9 (*meta*(F)-C*q*), 122.1 (*dd*, J_1^{C-F} 2.9, J_2^{C-F} 1.9, *meta*(F)-*C*H), 114.5 (*d*, J^{C-F} 22.9, *ortho*(F)-*C*H), 91.7 (*d*, J^{C-F} 174.7, *C*H-F), 72.6 (*dd*, J_1^{C-F} 21.2, J_2^{C-F} 1.9, α-carbonyl C*q*), 43.9 (*C*H_2), 33.1 (*d*, J^{C-F} 18.3, *C*H_2), 30.5 (*C*H_2), 28.2 (*d*, J^{C-F} 10.0, benzylic *C*H), 22.5 (*dd*, J_1^{C-F} 6.7, J_2^{C-F} 0.8, *C*H_3), 22.2 (*d*, J^{C-F} 3.3, *C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{14}H_{14}F_2O$,

expected $(M+NH_4)^+$ *m/z* 254.1351, observed $(M+NH_4)^+$ *m/z* 254.1360. $[\alpha]^{20}_D$ +33.3 (*c* = 1.00, acetone).

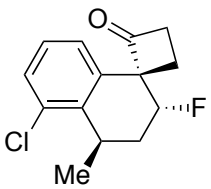
β-Fluoro Spiroketone (B_8^S)



diastereomer 2
Chemical Formula: $C_{14}H_{14}F_2O$
Molecular Weight: 236.26

According to the General Procedure: chiral, racemic allylic cyclopropanol (*rac*-**A$_8$**) (44 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L$_8$**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 42% (19 mg, 0.08 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.68. > 20:1 *d.r.* (^{1}H NMR). 96:4 *e.r.* Chiral HPLC. Chiralcel OJ-H. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 10.7 (major), 24.5 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.74 (1H, *q*, *J* 8.0, C^{ar}*H*), 6.66 (1H, *t*, *J* 10.1, C^{ar}*H*), 6.58 (1H, *d*, *J* 7.8, C^{ar}*H*), 5.04 (1H, *ddd*, $J_1^{H\text{-}F}$ 48.9, J_2 11.7, J_3 3.4, α-fluoro C*H*), 2.97-3.04 (1H, *m*, benzylic C*H*), 2.86 (1H, *dddd*, J_1 23.2, J_2 13.7, J_3 9.6, J_4 1.9, diastereotopic CH_2), 2.65 (1H, *ddd*, J_1 23.1, J_2 13.2, J_3 7.7, CH_2), 2.34 (1H, *tdd*, J_1 14.2, J_2 7.7, J_3 1.8, CH_2), 1.66-1.74 (1H, *m*, CH_2), 1.56-1.64 (1H, *m*, CH_2), 0.95 (3H, *dd*, J_1 7.2, J_2 2.6, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -112.0 (1F, *s*, C^{ar}*F*), -181.6 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 210.0 (ketone C*q*), 161.1 (*d*, $J^{C\text{-}F}$ 244.7, *ipso*(F)-C*q*), 138.3 (*dd*, $J_1^{C\text{-}F}$ 7.6, $J_2^{C\text{-}F}$ 4.4, *ortho*(F)-C*q*), 128.7 (*d*, $J^{C\text{-}F}$ 9.0, *para*(F)-*C*H), 123.3 (*t*, $J^{C\text{-}F}$ 2.1, *meta*(F)-*C*H), 114.3 (*d*, $J^{C\text{-}F}$ 22.3, *ortho*(F)-*C*H), 88.2 (*d*, $J^{C\text{-}F}$ 176.3, *C*H-F), 73.2 (*dd*, $J_1^{C\text{-}F}$ 20.4, $J_2^{C\text{-}F}$ 1.6, α-carbonyl C*q*), 45.8 (*C*H$_2$), 32.5 (*d*, $J^{C\text{-}F}$ 18.5, *C*H$_2$), 27.7 (*dd*, $J_1^{C\text{-}F}$ 11.1, $J_2^{C\text{-}F}$ 1.6, benzylic *C*H), 24.8 (*d*, $J^{C\text{-}F}$ 5.2, *C*H$_2$), 21.4 (*d*, $J^{C\text{-}F}$ 2.7, *C*H$_3$) ppm. **ESI-HRMS (positif)** M = $C_{14}H_{14}F_2O$, expected $(M+NH_4)^+$ *m/z* 254.1351, observed $(M+NH_4)^+$ *m/z* 254.1355. $[\alpha]^{20}_D$ +7.9 (*c* = 1.00, acetone).

β-Fluoro Spiroketone (B_9^R)

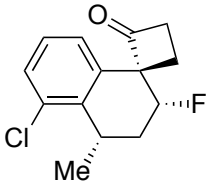


diastereomer 1
Chemical Formula: $C_{14}H_{14}ClFO$
Molecular Weight: 252.71

According to the General Procedure: chiral, racemic allylic cyclopropanol (*rac*-**A$_9$**) (47 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L$_8$**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Pale-yellow amorphous solid. Isolated yield 40% (20 mg, 0.08 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.55. > 20:1 *d.r.* (^{1}H NMR). 96:4 *e.r.* Chiral HPLC. Chiralpak IA. *n*-Hex/*i*-PrOH 98:2. 1.0 mL/min. t_R 5.3 (major), 12.4 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.97 (1H, *t*, *J* 7.5, C^{ar}*H*), 6.92 (1H, *d*, *J* 6.7, C^{ar}*H*), 6.86 (1H, *d*, *J* 7.7, C^{ar}*H*), 4.32 (1H, *ddd*, $J_1^{H\text{-}F}$ 50.8, J_2 9.5, J_3 4.3, α-fluoro C*H*), 2.75-2.83 (2H, *m*, diastereotopic CH_2 + benzylic C*H*), 2.05 (3H, *s*, CH_3), 1.94-2.03 (2H, *m*, CH_2), 1.85-1.91 (1H, *m*, CH_2), 1.23 (3H, *dd*, J_1 7.0, J_2 1.3, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -179.2 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 206.3 (*d*, $J^{C\text{-}F}$ 4.1, ketone C*q*), 139.3 (*d*, $J^{C\text{-}F}$ 1.8, C*q*), 136.5 (C*q*), 133.1 (*d*, $J^{C\text{-}F}$ 5.4, C*q*), 130.4 (*C*H), 126.7 (*C*H), 124.8 (*d*, $J^{C\text{-}F}$ 1.0, *C*H), 92.3 (*d*, $J^{C\text{-}F}$ 176, *C*H-F), 73.4 (*d*, $J^{C\text{-}F}$ 20.3, α-carbonyl C*q*), 43.6 (*C*H$_2$), 33.1 (*d*, $J^{C\text{-}F}$ 18.2, *C*H$_2$), 29.8 (*d*, $J^{C\text{-}F}$ 8.1, benzylic *C*H), 23.4 (*d*, $J^{C\text{-}F}$ 2.1,

CH_3), 23.1 (*d*, $J^{C\text{-}F}$ 5.0, CH_2), 19.9 (CH_3) ppm. **ESI-HRMS (positif)** M = $C_{14}H_{14}ClFO$, expected $(M+NH_4)^+$ *m/z* 270.1056, observed $(M+NH_4)^+$ *m/z* 270.1059. $[\alpha]^{20}_D$ +24.2 (*c* = 1.00, acetone).

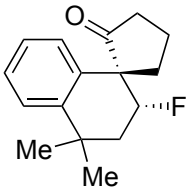
β-Fluoro Spiroketone (B_9^S)



diastereomer 2
Chemical Formula: $C_{14}H_{14}ClFO$
Molecular Weight: 252.71

According to the General Procedure: chiral, racemic allylic cyclopropanol (*rac*-**A$_9$**) (47 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L$_8$**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor^{TM} (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 45% (23 mg, 0.09 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.53. > 20:1 *d.r.* (^{1}H NMR). 96:4 *e.r.* Chiral HPLC. Chiralpak IC. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 11.0 (minor), 13.7 (major). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.97 (1H, *t*, *J* 7.7, $C^{ar}H$), 6.88 (1H, *d*, *J* 7.1, $C^{ar}H$), 6.80 (1H, *d*, *J* 7.8, $C^{ar}H$), 4.86 (1H, *ddd*, $J_1^{H\text{-}F}$ 50.6, J_2 12.7, J_3 4.0, α-fluoro C*H*), 2.96 (1H, *dddd*, J_1 18.2, J_2 11.3, J_3 6.5, J_4 2.0, diastereotopic CH_2), 2.81-2.87 (1H, *m*, benzylic C*H*), 2.65-2.70 (2H, *m*, CH_2), 2.34 (1H, *tdd*, J_1 12.3, J_2 7.3, J_3 1.6, CH_2), 2.11 (1H, *ddd*, J_1 12.0, J_2 10.7, J_3 6.5, CH_2), 1.95 (3H, *s*, CH_3), 1.78-1.84 (1H, *m*, CH_2), 0.77 (3H, *d*, *J* 7.2, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -189.1 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 206.2 (*d*, $J^{C\text{-}F}$ 6.1, ketone C*q*), 139.3 (*d*, $J^{C\text{-}F}$ 2.3, C*q*), 136.5 (C*q*), 133.3 (*d*, $J^{C\text{-}F}$ 8.9, C*q*), 130.0 (*C*H), 127.1 (*d*, $J^{C\text{-}F}$ 0.8, *C*H), 124.5 (*d*, $J^{C\text{-}F}$ 2.1, *C*H), 91.0 (*d*, $J^{C\text{-}F}$ 169, *C*H-F), 73.6 (*d*, $J^{C\text{-}F}$ 21.2, α-carbonyl C*q*), 44.5 (CH_2), 33.6 (*d*, $J^{C\text{-}F}$ 17.6, CH_2), 30.9 (*d*, $J^{C\text{-}F}$ 12.5, benzylic *C*H), 22.8 (CH_2), 21.1 (CH_3), 19.2 (CH_3) ppm. **ESI-HRMS (positif)** M = $C_{14}H_{14}ClFO$, expected $(M+NH_4)^+$ *m/z* 270.1056, observed $(M+NH_4)^+$ *m/z* 270.1058. $[\alpha]^{20}_D$ +19.1 (*c* = 1.00, acetone).

β-Fluoro Spiroketone (B_{10})

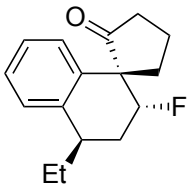


Chemical Formula: $C_{16}H_{19}FO$
Molecular Weight: 246.32

According to the General Procedure: allylic cyclobutanol (**A$_{10}$**) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L$_8$**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor^{TM} (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). White amorphous solid. Isolated yield 87% (43 mg, 0.17 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.56. > 20:1 *d.r.* (^{1}H NMR). 94.5:5.5 *e.r.* Chiral HPLC. Chiralpak IC. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 11.2 (major), 15.1 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 7.12 (1H, *dd*, J_1 8.0, J_2 1.4, $C^{ar}H$), 7.04 (1H, *td*, J_1 7.1, J_2 1.4, $C^{ar}H$), 6.97 (1H, *td*, J_1 8.1, J_2 1.3, $C^{ar}H$), 6.80 (1H, *dd*, J_1 7.9, J_2 1.2, $C^{ar}H$), 4.71 (1H, *ddd*, $J_1^{H\text{-}F}$ 49.3, J_2 12.4, J_3 4.2, α-fluoro C*H*), 2.82 (1H, *td*, J_1 12.5, J_2 7.2, diastereotopic CH_2), 2.18-2.31 (3H, *m*, CH_2), 2.04 (1H, *ddd*, J_1 18.0, J_2 8.7, J_3 6.6, CH_2), 1.81-1.90 (1H, *m*, CH_2), 1.72 (1H, *ddd*, J_1 14.8, J_2 10.7, J_3 4.2, CH_2), 1.55-1.64 (1H, *m*, CH_2), 1.27 (3H, *s*, diastereotopic *gem*-dimethyl CH_3), 1.00 (3H, *s*, diastereotopic *gem*-dimethyl CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -185.6 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 215.1 (*d*, $J^{C\text{-}F}$ 5.0, ketone C*q*), 145.8 (*d*, $J^{C\text{-}F}$ 2.4, C*q*), 137.3 (*d*, $J^{C\text{-}F}$ 7.9, C*q*), 127.28 (*C*H), 127.25 (*C*H), 126.8 (*C*H), 126.7 (*C*H), 95.1 (*d*, $J^{C\text{-}F}$ 172, *C*H-F), 56.3 (*d*, $J^{C\text{-}F}$ 19.9, α-carbonyl C*q*), 39.7 (*d*, $J^{C\text{-}F}$ 17.2, CH_2), 39.6 (CH_2), 38.3 (CH_2), 35.7 (*d*, $J^{C\text{-}F}$ 12.2, CH_2), 32.7 (diastereotopic *gem*-dimethyl CH_3), 31.8 (diastereotopic *gem*-dimethyl CH_3), 20.7 (*d*, $J^{C\text{-}F}$ 1.6, CH_2)

ppm. **ESI-HRMS (positif)** M = $C_{16}H_{19}FO$, expected $(M+NH_4)^+$ *m/z* 264.1759, observed $(M+NH_4)^+$ *m/z* 264.1763. $[\alpha]^{20}_D$ +29.9 (*c* = 1.00, acetone).

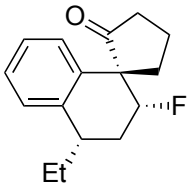
β-Fluoro Spiroketone (B_{11}^R)



diastereomer 1
Chemical Formula: $C_{16}H_{19}FO$
Molecular Weight: 246.32

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A$_{11}$**) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L$_8$**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 45% (22 mg, 0.09 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.39. > 20:1 *d.r.* (^{1}H NMR). 96.5:3.5 *e.r.* Chiral HPLC. Chiralcel OD-H. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 10.0 (minor), 11.8 (major). **^{1}H NMR** (500 MHz, C_6D_6): δ 7.10 (1H, *d*, *J* 7.7, C^{ar}*H*), 7.05 (1H, *td*, J_1 8.4, J_2 1.3, C^{ar}*H*), 6.99 (1H, *t*, *J* 7.9, C^{ar}*H*), 6.83 (1H, *dd*, J_1 8.5, J_2 0.7, C^{ar}*H*), 4.43 (1H, *ddd*, J_1^{H-F} 49.3, J_2 11.5, J_3 4.1, α-fluoro C*H*), 2.53-2.64 (2H, *m*, benzylic C*H* + diastereotopic CH_2), 2.14-2.31 (3H, *m*, diastereotopic CH_2), 2.05 (1H, *ddd*, J_1 15.7, J_2 8.9, J_3 6.9, CH_2), 1.55-1.95 (5H, *m*, CH_2), 0.83 (3H, *t*, *J* 7.5, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -180.6 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 215.3 (*d*, J^{C-F} 4.3, ketone C*q*), 140.3 (*d*, J^{C-F} 2.3, C*q*), 138.8 (*d*, J^{C-F} 7.9, C*q*), 127.4 (*C*H), 127.3 (*d*, J^{C-F} 2.2, *C*H), 127.0 (*C*H), 126.7 (*C*H), 96.9 (*d*, J^{C-F} 174, *C*H-F), 56.0 (*d*, J^{C-F} 19.9, α-carbonyl C*q*), 39.7 (*C*H$_2$), 37.9 (*d*, J^{C-F} 12.1, *C*H$_2$), 29.9 (*d*, J^{C-F} 18.5, benzylic *C*H), 28.4 (*C*H$_2$), 20.6 (*d*, J^{C-F} 1.5, *C*H$_2$), 10.5 (*C*H$_3$) ppm. **ESI-HRMS (positif)** M = $C_{16}H_{19}FO$, expected $(M+H)^+$ *m/z* 247.1493, observed $(M+H)^+$ *m/z* 247.1497. $[\alpha]^{20}_D$ +35.7 (*c* = 1.00, acetone).

β-Fluoro Spiroketone (B_{11}^S)

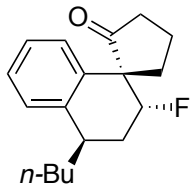


diastereomer 2
Chemical Formula: $C_{16}H_{19}FO$
Molecular Weight: 246.32

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A$_{11}$**) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L$_8$**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 46% (23 mg, 0.09 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.66. > 20:1 *d.r.* (^{1}H NMR). 95:5 *e.r.* Chiral HPLC. Chiralcel OJ-H. *n*-Hex/*i*-PrOH 99.5:0.5. 1.0 mL/min. t_R 22.8 (major), 32.1 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.98-7.03 (2H, *m*, C^{ar}*H*), 6.90 (1H, *dd*, J_1 6.6, J_2 2.7, C^{ar}*H*), 6.79 (1H, *dd*, J_1 6.9, J_2 2.3, C^{ar}*H*), 4.73 (1H, *ddd*, J_1^{H-F} 49.5, J_2 11.9, J_3 4.0, α-fluoro C*H*), 2.76 (1H, *sept.*, *J* 5.8, diastereotopic CH_2), 2.62-2.67 (1H, *m*, benzylic C*H*), 2.27 (1H, *ddd*, J_1 14.8, J_2 5.6, J_3 1.0, CH_2), 2.16-2.19 (2H, *m*, CH_2), 2.03 (1H, *ddd*, J_1 16.6, J_2 8.9, J_3 7.7, CH_2), 1.82-1.92 (2H, *m*, CH_2), 1.56-1.65 (1H, *m*, CH_2), 1.33-1.42 (1H, *m*, CH_2), 1.17-1.26 (1H, *m*, CH_2), 0.73 (3H, *t*, *J* 7.5, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -186.4 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 215.0 (*d*, J^{C-F} 5.7, ketone C*q*), 141.3 (*d*, J^{C-F} 2.0, C*q*), 138.1 (*d*, J^{C-F} 7.1, C*q*), 129.3 (*C*H), 127.7 (*d*, J^{C-F} 1.7, *C*H), 126.9 (*C*H), 126.8 (*C*H), 94.9 (*d*, J^{C-F} 172, *C*H-F), 56.2 (*d*, J^{C-F} 19.8, α-carbonyl C*q*), 40.0 (*d*, J^{C-F} 11.7, *C*H$_2$), 39.2 (*d*, J^{C-F} 18.8, *C*H$_2$), 30.7 (*C*H$_2$), 28.8 (*d*, J^{C-}

^{F} 18.8, benzylic *C*H), 20.5 (*d*, $J^{C\text{-}F}$ 1.4, *C*H_2), 12.5 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{16}H_{19}FO$, expected $(M+H)^+$ *m/z* 247.1493, observed $(M+H)^+$ *m/z* 247.1495. $[\alpha]^{20}_D$ +9.9 (*c* = 1.00, acetone).

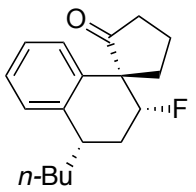
β-Fluoro Spiroketone (B_{12}^R)



diastereomer 1
Chemical Formula: $C_{18}H_{23}FO$
Molecular Weight: 274.37

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A$_{12}$**) (51 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L$_8$**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 42% (22 mg, 0.09 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.73. > 20:1 *d.r.* (^{1}H NMR). 95:5 *e.r.* Chiral HPLC. Chiralcel OJ-H. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 16.6 (major), 19.2 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.99-7.05 (2H, *m*, C^{ar}*H*), 6.94 (1H, *dd*, J_1 8.9, J_2 2.1, C^{ar}*H*), 6.80 (1H, *dd*, J_1 7.2, J_2 1.9, C^{ar}*H*), 4.79 (1H, *ddd*, $J_1^{H\text{-}F}$ 49.5, J_2 11.5, J_3 3.8, α-fluoro C*H*), 2.74-2.85 (2H, *m*, benzylic C*H* + diastereotopic CH_2), 2.29 (1H, *ddd*, J_1 15.3, J_2 9.0, J_3 6.2, CH_2), 2.21 (2H, *t*, *J* 7.5, CH_2), 2.04 (1H, *ddd*, J_1 18.0, J_2 16.6, J_3 7.8, CH_2), 1.83-1.94 (2H, *m*, CH_2), 1.57-1.65 (1H, *m*, CH_2), 1.06-1.39 (6H, *m*, CH_2), 0.82 (3H, *t*, *J* 6.9, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -186.4 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 215.1 (*d*, $J^{C\text{-}F}$ 5.7, ketone C*q*), 141.6 (*d*, $J^{C\text{-}F}$ 2.1, C*q*), 138.1 (*d*, $J^{C\text{-}F}$ 7.3, C*q*), 129.3 (*C*H), 127.6 (*C*H), 127.5 (*C*H), 126.9 (*d*, $J^{C\text{-}F}$ 13.9, *C*H), 95.1 (*d*, $J^{C\text{-}F}$ 172, *C*H-F), 56.1 (*d*, $J^{C\text{-}F}$ 19.8, α-carbonyl C*q*), 39.3 (*d*, $J^{C\text{-}F}$ 25.5, *C*H_2), 38.5 (*d*, $J^{C\text{-}F}$ 11.9, benzylic *C*H), 37.9 (*C*H_2), 30.3 (*C*H_2), 29.2 (*d*, $J^{C\text{-}F}$ 18.7, *C*H_2), 23.0 (*C*H_2), 20.5 (*C*H_2), 14.2 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{18}H_{23}FO$, expected $(M+NH_4)^+$ *m/z* 292.2072, observed $(M+NH_4)^+$ *m/z* 292.2075. $[\alpha]^{20}_D$ +39.5 (*c* = 1.00, acetone).

β-Fluoro Spiroketone (B_{12}^S)

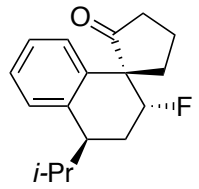


diastereomer 2
Chemical Formula: $C_{18}H_{23}FO$
Molecular Weight: 274.37

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A$_{12}$**) (51 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP (**L$_8$**) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 43% (23 mg, 0.09 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.51. > 20:1 *d.r.* (^{1}H NMR). 95.5:4.5 *e.r.* Chiral HPLC. Chiralpak IC. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 8.7 (minor), 13.0 (major). **^{1}H NMR** (500 MHz, C_6D_6): δ 7.16 (1H, *d*, *J* 7.6, C^{ar}*H*), 7.07 (1H, *td*, J_1 7.3, J_2 1.4, C^{ar}*H*), 7.00 (1H, *td*, J_1 7.9, J_2 0.7, C^{ar}*H*), 6.84 (1H, *dd*, J_1 7.9, J_2 1.1, C^{ar}*H*), 4.44 (1H, *ddd*, $J_1^{H\text{-}F}$ 49.4, J_2 11.4, J_3 4.0, α-fluoro C*H*), 2.56-2.67 (2H, *m*, benzylic C*H* + diastereotopic CH_2), 2.15-2.32 (3H, *m*, CH_2), 1.95-2.08 (2H, *m*, CH_2), 1.74-1.88 (2H, *m*, CH_2), 1.56-1.71 (2H, *m*, CH_2), 1.16-1.31 (3H, *m*, CH_2), 0.84 (3H, *t*, *J* 7.0, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -180.6 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 215.3 (*d*, $J^{C\text{-}F}$ 4.3, ketone C*q*), 140.7 (*d*, $J^{C\text{-}F}$ 2.4, C*q*), 138.7 (*d*, $J^{C\text{-}F}$ 7.9, C*q*), 127.4 (*C*H), 127.3 (*d*, $J^{C\text{-}F}$ 2.2, *C*H), 127.0 (*C*H), 126.7 (*C*H), 96.9 (*d*, $J^{C\text{-}F}$ 174, *C*H-F), 56.1 (*d*, $J^{C\text{-}F}$ 19.9, α-carbonyl C*q*), 39.7 (*C*H_2), 38.0 (*C*H_2), 36.8 (*d*, $J^{C\text{-}F}$ 11.2, benzylic *C*H), 35.8 (*C*H_2), 30.5 (*d*, $J^{C\text{-}F}$ 18.4, *C*H_2), 28.6 (*C*H_2),

23.3 (CH_2), 20.6 (*d*, $J^{C\text{-}F}$ 1.5, CH_2), 14.3 (CH_3) ppm. **ESI-HRMS (positif)** M = $C_{18}H_{23}FO$, expected $(M+NH_4)^+$ *m/z* 292.2072, observed $(M+NH_4)^+$ *m/z* 292.2074. $[\alpha]^{20}_D$ +7.8 (*c* = 1.00, acetone).

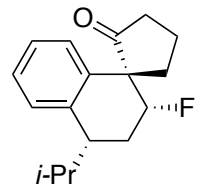
β-Fluoro Spiroketone (B_{13}^R)



diastereomer 1
Chemical Formula: $C_{17}H_{21}FO$
Molecular Weight: 260.35

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-$\mathbf{A_{13}}$) (48 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP ($\mathbf{L_8}$) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 44% (23 mg, 0.09 mmol). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 9:1) 0.79. > 20:1 *d.r.* (^{1}H NMR). 97:3 *e.r.* Chiral HPLC. Chiralcel OJ-H. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 15.9 (major), 18.4 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 7.00-7.04 (2H, *m*, $C^{ar}H$), 6.94-6.96 (1H, *m*, $C^{ar}H$), 6.79 (1H, *dd*, J_1 15.8, J_2 7.1, $C^{ar}H$), 4.80 (1H, *ddd*, $J_1^{H\text{-}F}$ 49.9, J_2 10.9, J_3 3.9, α-fluoro C*H*), 2.58-2.63 (1H, *m*, benzylic C*H*), 2.50-2.57 (1H, *m*, diastereotopic CH_2), 2.26 (1H, *ddd*, J_1 18.3, J_2 9.1, J_3 5.5, CH_2), 1.89-2.16 (4H, *m*, CH_2), 1.75-1.85 (1H, *m*, CH_2), 1.69 (1H, *oct.*, *J* 6.8, CH_2), 1.53-1.61 (1H, *m*, CH_2), 0.77 (3H, *d*, *J* 6.8, isopropylic CH_3), 0.62 (3H, *d*, *J* 6.8, isopropylic CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -183.7 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 214.7 (*d*, $J^{C\text{-}F}$ 6.2, ketone C*q*), 140.0 (*d*, $J^{C\text{-}F}$ 1.7, C*q*), 138.7 (*d*, $J^{C\text{-}F}$ 5.9, C*q*), 129.4 (*C*H), 126.9 (*C*H), 126.4 (*C*H), 94.5 (*d*, $J^{C\text{-}F}$ 172, *C*H-F), 56.4 (*d*, $J^{C\text{-}F}$ 19.3, α-carbonyl C*q*), 43.5 (*d*, $J^{C\text{-}F}$ 10.3, benzylic *C*H), 39.7 (CH_2), 39.1 (CH_2), 32.7 (isopropylic *C*H), 27.1 (*d*, $J^{C\text{-}F}$ 19.3, CH_2), 21.7 (isopropylic CH_3), 20.1 (*d*, $J^{C\text{-}F}$ 1.2, CH_2), 19.2 (isopropylic CH_3) ppm. **ESI-HRMS (positif)** M = $C_{17}H_{21}FO$, expected $(M+NH_4)^+$ *m/z* 278.1915, observed $(M+NH_4)^+$ *m/z* 278.1915. $[\alpha]^{20}_D$ +42.2 (*c* = 1.00, acetone).

β-Fluoro Spiroketone (B_{13}^S)



diastereomer 2
Chemical Formula: $C_{17}H_{21}FO$
Molecular Weight: 260.35

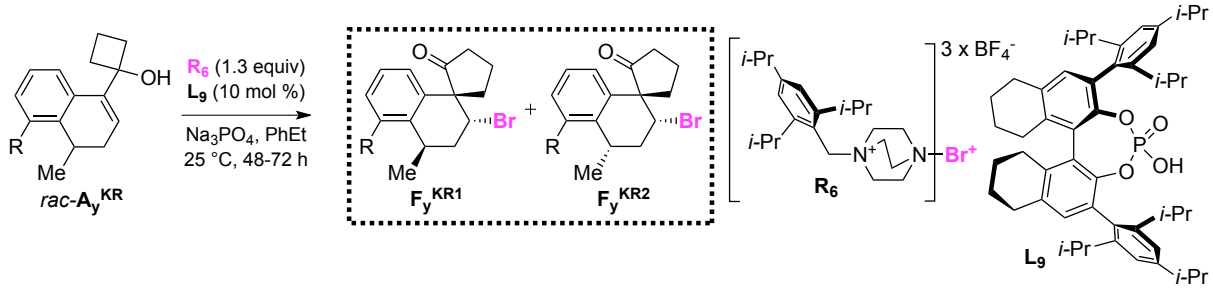
According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-$\mathbf{A_{13}}$) (48 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-TIPS-TRIP ($\mathbf{L_8}$) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na_3PO_4 (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_6H_5F/*n*-Hex 1:1 (*v/v*) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 44% (23 mg, 0.09 mmol). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 9:1) 0.49. > 20:1 *d.r.* (^{1}H NMR). 95.5:4.5 *e.r.* Chiral HPLC. Chiralcel OD-H. *n*-Hex/*i*-PrOH 98.5:1.5. 1.0 mL/min. t_R 7.6 (minor), 8.5 (major). **^{1}H NMR** (500 MHz, C_6D_6): δ 7.14 (1H, *d*, *J* 8.1, $C^{ar}H$), 7.06 (1H, *td*, J_1 7.2, J_2 1.3, $C^{ar}H$), 6.99 (1H, *t*, *J* 7.8, $C^{ar}H$), 6.83 (1H, *d*, *J* 7.8, $C^{ar}H$), 4.43 (1H, *ddd*, $J_1^{H\text{-}F}$ 49.5, J_2 12.0, J_3 4.7, α-fluoro C*H*), 2.59-2.68 (2H, *m*, benzylic C*H* + diastereotopic CH_2), 2.15-2.39 (4H, *m*, diastereotopic CH_2), 2.05 (1H, *ddd*, J_1 17.9, J_2 8.7, J_3 6.4, CH_2), 1.81-1.90 (2H, *m*, CH_2), 1.55-1.65 (1H, *m*, isopropylic C*H*), 0.88 (3H, *d*, *J* 6.9, isopropylic CH_3), 0.83 (3H, *d*, *J* 6.9, isopropylic CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -183.7 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 215.4 (*d*, $J^{C\text{-}F}$ 4.4, ketone C*q*), 139.8 (*d*, $J^{C\text{-}F}$ 2.2, C*q*), 139.5 (*d*, $J^{C\text{-}F}$ 8.2, C*q*), 127.4 (*d*, $J^{C\text{-}F}$ 2.2, *C*H), 126.99 (*C*H), 126.95 (*C*H), 126.71 (*C*H), 97.8 (*d*, $J^{C\text{-}F}$ 174, *C*H-F), 55.8 (*d*, $J^{C\text{-}F}$ 19.9, α-carbonyl C*q*), 42.3 (*d*, $J^{C\text{-}F}$ 11.0, benzylic *C*H), 39.8 (CH_2), 38.2

(CH_2), 30.2 (isopropylic *C*H), 24.3 (*d*, $J^{C\text{-}F}$ 18.8, CH_2), 21.0 (isopropylic CH_3), 20.7 (*d*, $J^{C\text{-}F}$ 0.8, CH_2), 15.8 (isopropylic CH_3) ppm. **ESI-HRMS (positif)** M = $C_{17}H_{21}FO$, expected $(M+NH_4)^+$ *m/z* 278.1915, observed $(M+NH_4)^+$ *m/z* 278.1919. $[\alpha]^{20}_D$ +11.1 (*c* = 1.00, acetone).

General Procedure for the Stereodivergent Bromination/Semi-Pinacol Reaction: Racemates

To a well-stirred solution of chiral, racemic allylic alcohol $\mathbf{A_y^{KR}}$ (0.20 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (3.0 mL, 0.07 M) was added $(collidine)_2Br^+PF_6^-$ (126 mg, 0.26 mmol, 1.3 equiv.) at -20 °C. The resultant homogeneous reaction mixture was stirred at -20 °C for 12-24 h. Saturated aqueous $Na_2S_2O_3$ was then added to quench the reaction. The layers were separated and the aqueous layer was extracted with methyl *tert*-butyl ether. The combined organic extracts were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Conversions and diastereomer ratios (*d.r.*) were determined by ^1H NMR analysis of the crude compounds. Pure diastereomers ($\mathbf{F_y^{KR1}}$ and $\mathbf{F_y^{KR2}}$) were obtained after purification by flash chromatography on silica gel, using an adequate *n*-hexane/Et_2O mixture as eluent.

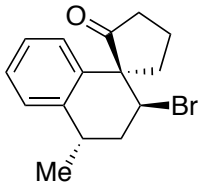
General Procedure for the Stereodivergent Bromination/Semi-Pinacol Reaction: Enantioselective Version



To a well-stirred solution of chiral, racemic allylic alcohol $\mathbf{A_y^{KR}}$ (0.20 mmol, 1.0 equiv.) and chiral phosphoric acid $\mathbf{L_9}$ (15 mg, 0.02 mmol, 10 mol%) in anhydrous ethylbenzene (4.0 mL, 0.05 M) were added brominating reagent $\mathbf{R_6}$ (260 mg, 0.26 mmol, 1.3 equiv.) and powdered anhydrous Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.). The resultant heterogeneous mixture was stirred at ambient temperature for 48-72 h. Saturated aqueous $Na_2S_2O_3$ was then added to quench the reaction. The layers were separated and the aqueous layer was extracted with methyl *tert*-butyl ether. The combined organic extracts were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Conversions and diastereomer ratios (*d.r.*) were determined by ^1H NMR analysis of the crude compounds. Pure diastereomers ($\mathbf{F_y^{KR1}}$ and $\mathbf{F_y^{KR2}}$) were obtained after purification by flash chromatography on silica gel, using an adequate *n*-hexane/Et_2O mixture as eluent. Enantiomer ratios (*e.r.*) were determined by chiral HPLC or chiral SFC analysis of purified compounds.

Characterization of Brominated Products

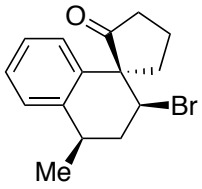
β-Bromo Spiroketone (C_1^S)



diastereomer 1
Chemical Formula: $C_{15}H_{17}BrO$
Molecular Weight: 293.20

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A$_1$**) (43 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L$_9$**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T$_3$**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Pale-yellow oil. Isolated yield 42% (25 mg, 0.08 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.75. > 20:1 *d.r.* (^{1}H NMR). 95:5 *e.r.* Chiral HPLC. Chiralcel OJ-H. *n*-Hex/*i*-PrOH 99.5:0.5. 1.0 mL/min. t_R 21.7 (major), 41.4 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 7.01 (1H, *td*, J_1 8.1, J_2 1.3, C^{ar}*H*), 6.88-6.93 (2H, *m*, C^{ar}*H*), 6.66 (1H, *dd*, J_1 6.7, J_2 1.2, C^{ar}*H*), 4.83 (1H, *dd*, J_1 10.1, J_2 3.3, α-bromo C*H*), 2.76 (1H, *sext.*, *J* 6.8, benzylic C*H*), 2.36 (1H, *dt*, J_1 13.6, J_2 6.9, diastereotopic CH_2), 2.11-2.29 (3H, *m*, CH_2), 1.99-2.07 (1H, *m*, CH_2), 1.86-1.93 (1H, *m*, CH_2), 1.49-1.64 (2H, *m*, CH_2), 1.04 (3H, *d*, *J* 7.1, CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 216.6 (ketone C*q*), 140.0 (C*q*), 138.4 (C*q*), 129.2 (*C*H), 127.2 (*C*H), 126.8 (*C*H), 126.4 (*C*H), 58.5 (α-carbonyl C*q*), 40.1 (α-bromo *C*H), 39.4 (*C*H_2), 38.6 (*C*H_2), 35.8 (*C*H_2), 34.1 (benzylic *C*H), 23.5 (*C*H_3), 18.7 (*C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{15}H_{17}BrO$, expected $(M+NH_4)^+$ *m/z* 310.0802, 312.0781; observed $(M+NH_4)^+$ *m/z* 310.0805, 312.0784. **[α]$^{20}_D$** -38.6 (*c* = 1.00, acetone).

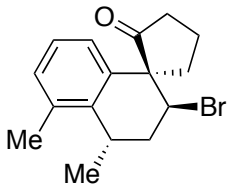
β-Bromo Spiroketone (C_1^R)



diastereomer 2
Chemical Formula: $C_{15}H_{17}BrO$
Molecular Weight: 293.20

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A$_1$**) (43 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L$_9$**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T$_3$**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 43% (25 mg, 0.09 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.52. > 20:1 *d.r.* (^{1}H NMR). 95:5 *e.r.* Chiral HPLC. Chiralcel OD-H. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 14.5 (minor), 19.0 (major). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.92-7.00 (2H, *m*, C^{ar}*H*), 6.85 (1H, *dd*, J_1 7.4, J_2 1.6, C^{ar}*H*), 6.80 (1H, *dd*, J_1 7.6, J_2 1.3, C^{ar}*H*), 4.29 (1H, *dd*, J_1 12.4, J_2 3.6, α-bromo C*H*), 3.34 (1H, *td*, J_1 12.8, J_2 6.0, diastereotopic CH_2), 2.81 (1H, *quin.d*, J_1 7.1, J_2 2.7, benzylic C*H*), 2.31-2.45 (2H, *m*, CH_2), 2.04-2.16 (2H, *m*, CH_2), 1.93 (1H, *dt*, J_1 13.2, J_2 2.9, CH_2), 1.79-1.88 (1H, *m*, CH_2), 1.55-1.64 (1H, *m*, CH_2), 0.92 (3H, *d*, *J* 7.3, CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 214.9 (ketone C*q*), 141.4 (C*q*), 138.5 (C*q*), 129.5 (*C*H), 127.3 (*C*H), 127.0 (*C*H), 126.9 (*C*H), 55.8 (α-carbonyl C*q*), 55.5 (α-bromo *C*H), 39.5 (*C*H_2), 38.7 (*C*H_2), 37.4 (*C*H_2), 34.3 (benzylic *C*H), 24.1 (*C*H_3), 20.1 (*C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{15}H_{17}BrO$, expected $(M+NH_4)^+$ *m/z* 310.0802, 312.0781; observed $(M+NH_4)^+$ *m/z* 310.0803, 312.0782. **[α]$^{20}_D$** -17.2 (*c* = 1.00, acetone).

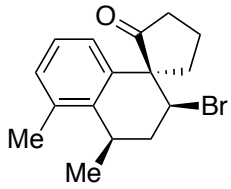
β-Bromo Spiroketone (C_2^S)



diastereomer 1
Chemical Formula: $C_{16}H_{19}BrO$
Molecular Weight: 307.23

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A₂**) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L₉**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T₃**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless crystalline solid. Isolated yield 40% (25 mg, 0.08 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 9:1) 0.77. > 20:1 *d.r.* (^{1}H NMR). 96:4 *e.r.* Chiral HPLC. Chiralpak IC. *n*-Hex/*i*-PrOH 99.5:0.5. 1.0 mL/min. t_R 15.6 (major), 22.9 (minor). **^{1}H NMR** (400 MHz, C_6D_6): δ 6.90-6.92 (2H, *m*, C^{ar}*H*), 6.79-6.83 (1H, *m*, C^{ar}*H*), 3.77 (1H, *dd*, J_1 13.2, J_2 4.8, α-bromo C*H*), 3.02 (1H, *td*, J_1 13.4, J_2 8.4, diastereotopic CH_2), 2.74-2.83 (1H, *m*, CH_2), 2.57 (1H, *dt*, J_1 14.3, J_2 9.4, diastereotopic CH_2), 2.38-2.47 (2H, *m*, CH_2), 2.01-2.18 (2H, *m*, CH_2), 2.06 (3H, *s*, CH_3), 1.69-1.85 (1H, *m*, CH_2), 1.55-1.75 (1H, *m*, CH_2), 1.25 (3H, *d*, *J* 6.7, CH_3) ppm. **^{13}C NMR** (100 MHz, C_6D_6): δ 215.2 (ketone C*q*), 140.1 (C*q*), 139.1 (C*q*), 136.9 (C*q*), 130.1 (*C*H), 126.2 (*C*H), 124.8 (*C*H), 58.7 (α-bromo *C*H), 55.9 (α-carbonyl C*q*), 39.6 (benzylic *C*H), 39.4 (*C*H_2), 38.8 (*C*H_2), 32.3 (*C*H_3), 23.1 (*C*H_2), 20.6 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{16}H_{19}BrO$, expected $(M+NH_4)^+$ *m/z* 324.0958, 326.0938; observed $(M+NH_4)^+$ *m/z* 324.0958, 326.0938. $[\alpha]^{20}_D$ -44.6 (*c* = 1.00, acetone).

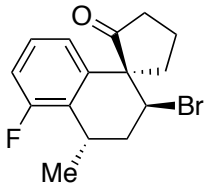
β-Bromo Spiroketone (C_2^R)



diastereomer 2
Chemical Formula: $C_{16}H_{19}BrO$
Molecular Weight: 307.23

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A₂**) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L₉**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T₃**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). White crystalline solid. Isolated yield 44% (27 mg, 0.09 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.57. > 20:1 *d.r.* (^{1}H NMR). 96:4 *e.r.* Chiral HPLC. Chiralcel OD-H. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 14.7 (minor), 17.3 (major). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.92 (1H, *t*, *J* 7.6, C^{ar}*H*), 6.85 (1H, *d*, *J* 7.4, C^{ar}*H*), 6.72 (1H, *d*, *J* 7.8, C^{ar}*H*), 4.44 (1H, *dd*, J_1 13.4, J_2 3.6, α-bromo C*H*), 3.44 (1H, *td*, J_1 13.1, J_2 5.4, diastereotopic CH_2), 2.76-2.83 (1H, *m*, CH_2), 2.36-2.52 (2H, *m*, CH_2), 2.24-2.31 (1H, *m*, CH_2), 2.08-2.16 (1H, *m*, CH_2), 1.91-2.02 (2H, *m*, CH_2), 1.94 (3H, *s*, CH_3), 1.60-1.72 (1H, *m*, CH_2), 0.81 (3H, *d*, *J* 7.1, CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 215.2 (ketone C*q*), 139.9 (C*q*), 139.4 (C*q*), 136.4 (C*q*), 129.4 (*C*H), 126.8 (*C*H), 125.4 (*C*H), 56.2 (α-bromo *C*H), 55.9 (α-carbonyl C*q*), 39.8 (benzylic *C*H), 38.7 (*C*H_2), 38.1 (*C*H_2), 32.2 (*C*H_3), 21.0 (*C*H_2), 20.4 (*C*H_3), 19.2 (*C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{16}H_{19}BrO$, expected $(M+NH_4)^+$ *m/z* 324.0958, 326.0938; observed $(M+NH_4)^+$ *m/z* 324.0956, 326.0936. $[\alpha]^{20}_D$ -12.5 (*c* = 1.00, acetone).

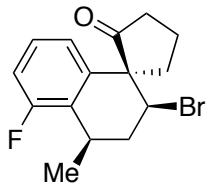
β-Bromo Spiroketone (C_3^S)



diastereomer 1
Chemical Formula: $C_{15}H_{16}BrFO$
Molecular Weight: 311.19

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A$_3$**) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L$_9$**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T$_3$**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 41% (26 mg, 0.08 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.80. > 20:1 *d.r.* (^{1}H NMR). 96.5:3.5 *e.r.* Chiral HPLC. Chiralpak IC. *n*-Hex/*i*-PrOH 99.5:0.5. 1.0 mL/min. t_R 13.2 (major), 19.9 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.68-6.74 (2H, *m*, C^{ar}*H*), 6.54-6.58 (1H, *m*, C^{ar}*H*), 3.63 (1H, *dd*, J_1 12.7, J_2 4.0, α-bromo C*H*), 2.83-2.97 (2H, *m*, diastereotopic CH_2 + benzylic C*H*), 2.47 (1H, *dt*, J_1 14.4, J_2 9.3, CH_2), 2.39 (1H, *dt*, J_1 18.3, J_2 10.1, CH_2), 2.17-2.24 (1H, *m*, CH_2), 2.08 (1H, *ddd*, J_1 18.3, J_2 9.0, J_3 4.0, CH_2), 1.98 (1H, *ddd*, J_1 12.5, J_2 8.8, J_3 3.7, CH_2), 1.74-1.82 (1H, *m*, CH_2), 1.52-1.61 (1H, *s*, CH_2), 1.43 (3H, *dd*, J_1 6.5, J_2 1.9, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -110.6 (1F, *s*, C^{ar}*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 214.6 (ketone C*q*), 162.2 (*d*, $J^{C\text{-}F}$ 245, *ipso*(F)-C*q*), 141.4 (*d*, $J^{C\text{-}F}$ 4.7, *meta*(F)-C*q*), 129.5 (*d*, $J^{C\text{-}F}$ 14.6, *ortho*(F)-C*q*), 127.6 (*d*, $J^{C\text{-}F}$ 9.5, *meta*(F)-*C*H), 122.4 (*d*, $J^{C\text{-}F}$ 3.1, *para*(F)-*C*H), 114.2 (*d*, $J^{C\text{-}F}$ 23.1, *ortho*(F)-*C*H), 57.5 (α-bromo *C*H), 55.3 (*d*, $J^{C\text{-}F}$ 1.8, α-carbonyl C*q*), 39.3 (*C*H_2), 38.8 (*C*H_2), 38.2 (*C*H_2), 30.4 (*C*H_3), 22.0 (*d*, $J^{C\text{-}F}$ 8.0, benzylic *C*H), 20.5 (*C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{15}H_{16}BrFO$, expected $(M+NH_4)^+$ *m/z* 328.0707, 330.0687; observed $(M+NH_4)^+$ *m/z* 328.0709, 330.0689. **[α]$^{20}_D$** -51.1 (*c* = 1.00, acetone).

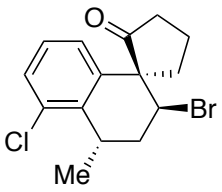
β-Bromo Spiroketone (A_3^R)



diastereomer 2
Chemical Formula: $C_{15}H_{16}BrFO$
Molecular Weight: 311.19

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A$_3$**) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L$_9$**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T$_3$**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Faint-orange oil. Isolated yield 42% (26 mg, 0.08 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.56. > 20:1 *d.r.* (^{1}H NMR). 95.5:4.5 *e.r.* Chiral HPLC. Chiralcel OD-H. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 13.9 (minor), 24.7 (major). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.64-6.73 (2H, *m*, C^{ar}*H*), 6.50 (1H, *d*, *J* 7.6, C^{ar}*H*), 4.23 (1H, *dd*, J_1 13.3, J_2 3.6, α-bromo C*H*), 3.33 (1H, *td*, J_1 13.2, J_2 6.0, diastereotopic CH_2), 3.14 (1H, *quin.*, *J* 7.1, benzylic C*H*), 2.31-2.45 (2H, *m*, CH_2), 2.03-2.13 (2H, *m*, CH_2), 1.83-1.92 (2H, *m*, CH_2), 1.52-1.62 (1H, *m*, CH_2), 0.97 (3H, *d*, *J* 7.2, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -116.5 (1F, *s*, C^{ar}*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 214.5 (ketone C*q*), 161.3 (*d*, $J^{C\text{-}F}$ 244, *ipso*(F)-C*q*), 141.4 (*d*, $J^{C\text{-}F}$ 4.4, *meta*(F)-C*q*), 129.5 (*d*, $J^{C\text{-}F}$ 16.6, *ortho*(F)-C*q*), 125.9 (*para*(F)-*C*H), 122.7 (*d*, $J^{C\text{-}F}$ 3.4, *meta*(F)-*C*H), 113.7 (*d*, $J^{C\text{-}F}$ 22.3, *ortho*(F)-*C*H), 55.4 (*d*, $J^{C\text{-}F}$ 1.9, α-carbonyl C*q*), 55.0 (α-bromo *C*H), 39.2 (*C*H_2), 38.7 (*C*H_2), 37.0 (*C*H_2), 30.4 (*C*H_3), 29.0 (*d*, $J^{C\text{-}F}$ 2.9, benzylic *C*H), 20.3 (*C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{15}H_{16}BrFO$, expected $(M+NH_4)^+$ *m/z* 328.0707, 330.0687; observed $(M+NH_4)^+$ *m/z* 328.0708, 330.0688. **[α]$^{20}_D$** -20.3 (*c* = 1.00, acetone).

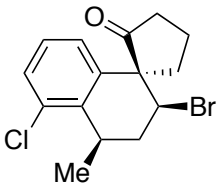
β-Bromo Spiroketone (C_4^S)



diastereomer 1
Chemical Formula: $C_{15}H_{16}BrClO$
Molecular Weight: 327.64

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A$_4$**) (48 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L$_9$**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T$_3$**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). White crystalline solid. Isolated yield 44% (29 mg, 0.09 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.62. > 20:1 *d.r.* (^{1}H NMR). 95.5:4.5 *e.r.* Chiral HPLC. Chiralcel OJ-H. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 12.2 (major), 15.9 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 7.05 (1H, *dd*, J_1 9.6, J_2 1.4, C^{ar}*H*), 6.63 (1H, *t*, *J* 9.9, C^{ar}*H*), 6.57 (1H, *d*, *J* 10.0, C^{ar}*H*), 4.27 (1H, *dd*, J_1 16.5, J_2 4.4, α-bromo C*H*), 3.19-3.35 (2H, *m*, benzylic C*H* + diastereotopic CH_2), 2.39-2.48 (1H, *m*, CH_2), 2.25-2.34 (1H, *m*, CH_2), 2.00-2.13 (2H, *m*, CH_2), 1.84-1.95 (2H, *m*, CH_2), 1.50-1.62 (1H, *m*, CH_2), 0.97 (3H, *d*, *J* 8.8, CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 214.6 (ketone C*q*), 141.6 (C*q*), 139.3 (C*q*), 135.0 (C*q*), 128.6 (*C*H), 127.8 (*C*H), 126.1 (*C*H), 55.7 (α-carbonyl C*q*), 55.1 (α-bromo *C*H), 39.5 (*C*H_2), 38.7 (*C*H_2), 37.5 (*C*H_2), 32.9 (benzylic *C*H), 20.5 (*C*H_3), 20.3 (*C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{15}H_{16}BrClO$, expected $(M+NH_4)^+$ *m/z* 344.0412, 346.0391; observed $(M+NH_4)^+$ *m/z* 344.0416, 346.0395. **[α]$^{20}_D$** -38.7 (*c* = 1.00, acetone).

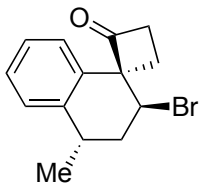
β-Bromo Spiroketone (C_4^R)



diastereomer 2
Chemical Formula: $C_{15}H_{16}BrClO$
Molecular Weight: 327.64

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A$_4$**) (48 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L$_9$**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T$_3$**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). White crystalline solid. Isolated yield 42% (28 mg, 0.08 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.31. > 20:1 *d.r.* (^{1}H NMR). 96.5:3.5 *e.r.* Chiral HPLC. Chiralcel OD-H. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 11.7 (major), 17.0 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 7.12 (1H, *dd*, J_1 7.5, J_2 1.6, C^{ar}*H*), 6.63-6.69 (2H, *m*, C^{ar}*H*), 3.47 (1H, *dd*, J_1 13.1, J_2 4.9, α-bromo C*H*), 3.09 (1H, *sext.*, *J* 6.7, benzylic C*H*), 2.87 (1H, *td*, J_1 13.6, J_2 8.2, diastereotopic CH_2), 2.49 (1H, *td*, J_1 14.5, J_2 9.4, CH_2), 2.31-2.40 (2H, *m*, CH_2), 2.07 (1H, *ddd*, J_1 18.2, J_2 8.9, J_3 3.6, CH_2), 1.86-1.91 (1H, *m*, CH_2), 1.68-1.75 (1H, *m*, CH_2), 1.53 (3H, *d*, *J* 6.7, CH_3), 1.47-1.54 (1H, *m*, CH_2) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 214.4 (ketone C*q*), 141.0 (C*q*), 139.7 (C*q*), 135.0 (C*q*), 129.3 (*C*H), 127.1 (*C*H), 125.5 (*C*H), 57.3 (α-bromo *C*H), 55.7 (α-carbonyl C*q*), 39.5 (*C*H_2), 38.9 (*C*H_2), 37.9 (*C*H_2), 32.7 (benzylic *C*H), 22.8 (*C*H_3), 20.5 (*C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{15}H_{16}BrClO$, expected $(M+NH_4)^+$ *m/z* 344.0412, 346.0391; observed $(M+NH_4)^+$ *m/z* 344.0415, 346.0394. **[α]$^{20}_D$** -19.5 (*c* = 1.00, acetone).

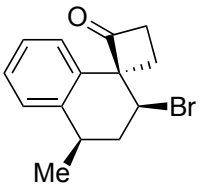
β-Bromo Spiroketone (C_5^S)



diastereomer 1
Chemical Formula: $C_{14}H_{15}BrO$
Molecular Weight: 279.17

According to the General Procedure: chiral, racemic allylic cyclopropanol (*rac*-**A$_5$**) (40 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L$_9$**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T$_3$**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 43% (24 mg, 0.09 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.70. > 20:1 *d.r.* (^{1}H NMR). 95:5 *e.r.* Chiral HPLC. Chiralcel OJ-H. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 8.9 (minor), 10.3 (major). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.99 (1H, *td*, J_1 7.3, J_2 1.5, C^{ar}*H*), 6.94 (1H, *td*, J_1 7.5, J_2 1.3, C^{ar}*H*), 6.89 (1H, *dd*, J_1 7.9, J_2 1.3, C^{ar}*H*), 6.83 (1H, *dd*, J_1 8.2, J_2 0.8, C^{ar}*H*), 4.31 (1H, *dd*, J_1 11.3, J_2 3.2, α-bromo C*H*), 3.03 (1H, *ddd*, J_1 18.6, J_2 11.1, J_3 6.5, diastereotopic CH_2), 2.90 (1H, *ddd*, J_1 13.5, J_2 11.3, J_3 5.9, diastereotopic CH_2), 2.62-2.68 (1H, *m*, benzylic C*H*), 2.59 (1H, *ddd*, J_1 17.9, J_2 10.6, J_3 7.3, CH_2), 2.08 (1H, *ddd*, J_1 12.4, J_2 11.1, J_3 7.3, CH_2), 1.91-1.98 (2H, *m*, CH_2), 0.89 (3H, *d*, *J* 7.3, CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 206.0 (ketone C*q*), 140.5 (C*q*), 133.2 (C*q*), 129.5 (*C*H), 127.5 (*C*H), 127.01 (*C*H), 126.98 (*C*H), 73.2 (α-carbonyl C*q*), 43.7 (α-bromo *C*H), 40.6 (benzylic *C*H), 34.8 (*C*H_2), 29.9 (*C*H_2), 27.9 (*C*H_2), 23.2 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{14}H_{15}BrO$, expected $(M+NH_4)^+$ *m/z* 296.0645, 298.0625; observed $(M+NH_4)^+$ *m/z* 296.0645, 298.0625. **[α]$^{20}_D$** -19.6 (*c* = 1.00, acetone).

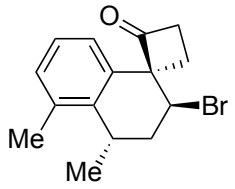
β-Bromo Spiroketone (C_5^R)



diastereomer 2
Chemical Formula: $C_{14}H_{15}BrO$
Molecular Weight: 279.17

According to the General Procedure: chiral, racemic allylic cyclopropanol (*rac*-**A$_5$**) (40 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L$_9$**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T$_3$**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Faint-yellow oil. Isolated yield 40% (22 mg, 0.08 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.49. > 20:1 *d.r.* (^{1}H NMR). 94.5:5.5 *e.r.* Chiral HPLC. Chiralpak IC. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 12.1 (major), 15.0 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.94-7.01 (2H, *m*, C^{ar}*H*), 6.89 (1H, *dd*, J_1 7.2, J_2 1.9, C^{ar}*H*), 6.83 (1H, *dd*, J_1 7.0, J_2 2.0, C^{ar}*H*), 4.24 (1H, *dd*, J_1 12.7, J_2 3.4, α-bromo C*H*), 3.00 (1H, *ddd*, J_1 18.4, J_2 11.1, J_3 6.4, diastereotopic CH_2), 2.90 (1H, *ddd*, J_1 13.2, J_2 12.0, J_3 6.0, diastereotopic CH_2), 2.62-2.75 (2H, *m*, CH_2 + benzylic C*H*), 2.23 (1H, *ddd*, J_1 12.3, J_2 11.2, J_3 7.3, CH_2), 1.89-1.99 (2H, *m*, CH_2), 0.86 (3H, *d*, *J* 7.2, CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 205.3 (ketone C*q*), 140.6 (C*q*), 133.6 (C*q*), 129.5 (*C*H), 127.5 (*C*H), 127.0 (*C*H), 126.7 (*C*H), 73.4 (α-carbonyl C*q*), 51.4 (α-bromo *C*H), 44.4 (benzylic *C*H), 38.4 (*C*H_2), 34.0 (*C*H_2), 25.5 (*C*H_2), 23.5 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{14}H_{15}BrO$, expected $(M+NH_4)^+$ *m/z* 296.0645, 298.0625; observed $(M+NH_4)^+$ *m/z* 296.0646, 298.0627. **[α]$^{20}_D$** -11.7 (*c* = 1.00, acetone).

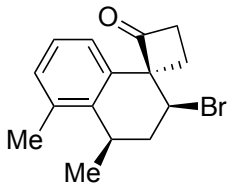
β-Bromo Spiroketone (C_6^S)



diastereomer 1
Chemical Formula: $C_{15}H_{17}BrO$
Molecular Weight: 293.20

According to the General Procedure: chiral, racemic allylic cyclopropanol (*rac*-**A$_6$**) (43 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L$_9$**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T$_3$**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Pale-yellow oil. Isolated yield 43% (25 mg, 0.09 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.73. > 20:1 *d.r.* (^{1}H NMR). 96:4 *e.r.* Chiral HPLC. Chiralcel OJ-H. *n*-Hex/*i*-PrOH 98:2. 1.0 mL/min. t_R 8.2 (major), 9.0 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.91 (1H, *t*, *J* 7.6, C^{ar}*H*), 6.86 (1H, *d*, *J* 6.8, C^{ar}*H*), 6.82 (1H, *d*, *J* 7.9, C^{ar}*H*), 4.54 (1H, *dd*, J_1 13.5, J_2 3.3, α-bromo C*H*), 3.19 (1H, *ddd*, J_1 18.7, J_2 11.1, J_3 5.9, diastereotopic CH_2), 3.14 (1H, *td*, J_1 13.3, J_2 5.3, diastereotopic CH_2), 2.65 (1H, *ddd*, J_1 18.6, J_2 10.8, J_3 7.8, CH_2), 2.50-2.56 (1H, *m*, benzylic C*H*), 2.19-2.28 (2H, *m*, CH_2), 2.04 (1H, *ddd*, J_1 12.5, J_2 10.8, J_3 5.9, CH_2), 1.90 (3H, *s*, CH_3), 0.75 (3H, *d*, *J* 7.1, CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 206.0 (ketone C*q*), 139.3 (C*q*), 136.9 (C*q*), 132.9 (C*q*), 129.8 (*C*H), 126.9 (*C*H), 125.0 (*C*H), 73.6 (α-carbonyl C*q*), 43.9 (α-bromo *C*H), 41.9 (benzylic *C*H), 33.1 (*C*H_2), 30.1 (*C*H_2), 26.9 (*C*H_2), 20.5 (*C*H_3), 19.1 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{15}H_{17}BrO$, expected $(M+NH_4)^+$ *m/z* 310.0802, 312.0781; observed $(M+NH_4)^+$ *m/z* 310.0805, 312.0784. **[α]$^{20}_D$** -33.7 (*c* = 1.00, acetone).

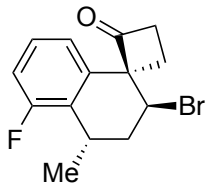
β-Bromo Spiroketone (C_6^R)



diastereomer 2
Chemical Formula: $C_{15}H_{17}BrO$
Molecular Weight: 293.20

According to the General Procedure: chiral, racemic allylic cyclopropanol (*rac*-**A$_6$**) (43 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L$_9$**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T$_3$**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). White crystalline solid. Isolated yield 43% (25 mg, 0.09 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.52. > 20:1 *d.r.* (^{1}H NMR). 96.5:3.5 *e.r.* Chiral HPLC. Chiralpak IC. *n*-Hex/*i*-PrOH 99.5:0.5. 1.0 mL/min. t_R 18.6 (major), 23.8 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.93 (1H, *t*, *J* 7.7, C^{ar}*H*), 6.86 (1H, *d*, *J* 7.9, C^{ar}*H*), 6.80 (1H, *d*, *J* 7.8, C^{ar}*H*), 4.42 (1H, *dd*, J_1 13.4, J_2 3.4, α-bromo C*H*), 3.10 (1H, *ddd*, J_1 18.7, J_2 11.2, J_3 6.0, diastereotopic CH_2), 3.02 (1H, *td*, J_1 13.1, J_2 5.4, diastereotopic CH_2), 2.64-2.75 (2H, *m*, CH_2 + benzylic C*H*), 2.37 (1H, *ddd*, J_1 12.5, J_2 11.3, J_3 7.7, CH_2), 2.01-2.06 (2H, *m*, CH_2), 1.90 (3H, *s*, CH_3), 0.74 (3H, *d*, *J* 7.1, CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 205.3 (ketone C*q*), 139.2 (C*q*), 136.7 (C*q*), 133.8 (C*q*), 129.9 (*C*H), 127.0 (*C*H), 124.7 (*C*H), 73.8 (α-carbonyl C*q*), 51.4 (α-bromo *C*H), 44.7 (benzylic *C*H), 39.3 (*C*H_2), 32.2 (*C*H_2), 25.0 (*C*H_2), 20.7 (*C*H_3), 19.1 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{15}H_{17}BrO$, expected $(M+NH_4)^+$ *m/z* 310.0802, 312.0781; observed $(M+NH_4)^+$ *m/z* 310.0808, 312.0787. **[α]$^{20}_D$** -12.0 (*c* = 1.00, acetone).

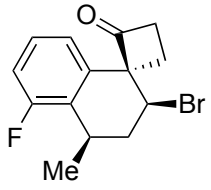
β-Bromo Spiroketone (C_7^S)



diastereomer 1
Chemical Formula: $C_{14}H_{14}BrFO$
Molecular Weight: 297.16

According to the General Procedure: chiral, racemic allylic cyclopropanol (*rac*-**A$_7$**) (44 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L$_9$**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T$_3$**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). White crystalline solid. Isolated yield 45% (27 mg, 0.09 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.75. > 20:1 *d.r.* (^{1}H NMR). 94.5:5.5 *e.r.* Chiral HPLC. Chiralpak IC. *n*-Hex/*i*-PrOH 99.5:0.5. 1.0 mL/min. t_R 12.0 (minor), 14.0 (major). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.64-6.72 (2H, *m*, C^{ar}*H*), 6.57 (1H, *d*, *J* 8.5, C^{ar}*H*), 4.28 (1H, *dd*, J_1 12.9, J_2 3.2, α-bromo C*H*), 3.10 (1H, *ddd*, J_1 18.8, J_2 11.1, J_3 6.0, diastereotopic CH_2), 2.96 (1H, *td*, J_1 13.2, J_2 5.9, CH_2), 2.86 (1H, broad *quint.*, *J* 6.1, benzylic C*H*), 2.58 (1H, *ddd*, J_1 18.6, J_2 10.7, J_3 7.7, CH_2), 2.15 (1H, *ddd*, J_1 12.6, J_2 11.1, J_3 7.7, CH_2), 2.05 (1H, *dt*, J_1 12.9, J_2 3.1, CH_2), 1.88 (1H, *ddd*, J_1 12.6, J_2 10.8, J_3 6.0, CH_2), 0.92 (3H, *d*, *J* 6.8, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -116.1 (1F, *s*, C^{ar}*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 205.1 (ketone C*q*), 161.6 (*d*, $J^{C\text{-}F}$ 244, *ipso*(F)-C*q*), 135.3 (*d*, $J^{C\text{-}F}$ 4.5, *meta*(F)-C*q*), 128.0 (*d*, $J^{C\text{-}F}$ 25.0, *ortho*(F)-C*q*), 125.9 (*para*(F)-*C*H), 122.4 (*d*, $J^{C\text{-}F}$ 3.2, *meta*(F)-*C*H), 114.0 (*d*, $J^{C\text{-}F}$ 22.4, *ortho*(F)-*C*H), 72.8 (*d*, $J^{C\text{-}F}$ 1.8, α-carbonyl C*q*), 44.0 (α-bromo *C*H), 40.6 (*C*H_2), 30.5 (*C*H_2), 29.9 (*d*, $J^{C\text{-}F}$ 2.3, benzylic *C*H), 26.9 (*C*H_2), 21.3 (*d*, $J^{C\text{-}F}$ 1.7, *C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{14}H_{14}BrFO$, expected $(M+NH_4)^+$ *m/z* 314.0551, 316.0530; observed $(M+NH_4)^+$ *m/z* 314.0555, 316.0533. **$[\alpha]^{20}_D$** -16.9 (*c* = 1.00, acetone).

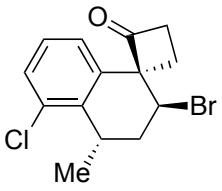
β-Bromo Spiroketone (C_7^R)



diastereomer 2
Chemical Formula: $C_{14}H_{14}BrFO$
Molecular Weight: 297.16

According to the General Procedure: chiral, racemic allylic cyclopropanol (*rac*-**A$_7$**) (44 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L$_9$**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T$_3$**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 41% (24 mg, 0.08 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.55. > 20:1 *d.r.* (^{1}H NMR). 96:4 *e.r.* Chiral HPLC. Chiralcel OJ-H. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 14.3 (major), 19.1 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.72 (1H, *td*, J_1 8.0, J_2 6.0, C^{ar}*H*), 6.66 (1H, *td*, J_1 9.6, J_2 2.2, C^{ar}*H*), 6.56 (1H, *d*, *J* 7.8, C^{ar}*H*), 4.18 (1H, *dd*, J_1 13.1, J_2 3.4, α-bromo C*H*), 2.96-3.07 (2H, *m*, CH_2 + benzylic C*H*), 2.89 (1H, *td*, J_1 13.1, J_2 5.8, diastereotopic CH_2), 2.64 (1H, *ddd*, J_1 18.4, J_2 10.7, J_3 7.6, CH_2), 2.26 (1H, *ddd*, J_1 12.5, J_2 11.2, J_3 7.6, CH_2), 1.85-1.93 (2H, *m*, CH_2), 0.90 (3H, *d*, *J* 7.2, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -116.9 (1F, *s*, C^{ar}*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 204.5 (ketone C*q*), 161.5 (*d*, $J^{C\text{-}F}$ 245, *ipso*(F)-C*q*), 136.1 (*d*, $J^{C\text{-}F}$ 4.5, *meta*(F)-C*q*), 128.4 (*d*, $J^{C\text{-}F}$ 24.8, *ortho*(F)-C*q*), 128.1 (*para*(F)-*C*H), 122.1 (*d*, $J^{C\text{-}F}$ 3.2, *meta*(F)-*C*H), 114.1 (*d*, $J^{C\text{-}F}$ 22.2, *ortho*(F)-*C*H), 73.0 (*d*, $J^{C\text{-}F}$ 1.6, α-carbonyl C*q*), 50.3 (α-bromo *C*H), 44.7 (*C*H_2), 38.1 (*C*H_2), 29.1 (*d*, $J^{C\text{-}F}$ 2.5, benzylic *C*H), 24.8 (*C*H_2), 21.1 (*d*, $J^{C\text{-}F}$ 1.9, *C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{14}H_{14}BrFO$, expected $(M+NH_4)^+$ *m/z* 314.0551, 316.0530; observed $(M+NH_4)^+$ *m/z* 314.0552, 316.0532. **$[\alpha]^{20}_D$** -12.0 (*c* = 1.00, acetone).

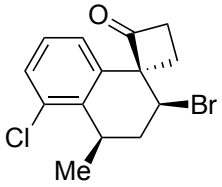
β-Bromo Spiroketone (C_8^S)



diastereomer 1
Chemical Formula: $C_{14}H_{14}BrClO$
Molecular Weight: 313.62

According to the General Procedure: chiral, racemic allylic cyclopropanol (*rac*-**A$_8$**) (47 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L$_9$**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T$_3$**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). White crystalline solid. Isolated yield 43% (26 mg, 0.08 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.60. > 20:1 *d.r.* (^{1}H NMR). 95:5 *e.r.* Chiral HPLC. Chiralcel OJ-H. *n*-Hex/*i*-PrOH 98:2. 1.0 mL/min. t_R 13.1 (major), 15.7 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 7.02-7.06 (1H, *m*, C^{ar}*H*), 6.63-6.67 (2H, *m*, C^{ar}*H*), 4.25 (1H, *dd*, J_1 13.4, J_2 3.4, α-bromo C*H*), 3.03-3.10 (2H, *m*, CH_2 + benzylic C*H*), 2.87 (1H, *td*, J_1 13.2, J_2 5.5, diastereotopic CH_2), 2.63 (1H, *ddd*, J_1 18.5, J_2 10.7, J_3 7.6, CH_2), 2.24-2.30 (1H, *m*, CH_2), 1.94-1.97 (1H, *m*, CH_2), 1.83-1.89 (1H, *m*, CH_2), 0.91 (3H, *d*, *J* 7.1, CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 204.4 (ketone C*q*), 138.5 (C*q*), 136.1 (C*q*), 135.2 (C*q*), 129.0 (*C*H), 128.0 (*C*H), 125.4 (*C*H), 73.3 (α-carbonyl C*q*), 50.3 (α-bromo *C*H), 44.9 (*C*H_2), 38.6 (*C*H_2), 33.0 (benzylic *C*H), 24.8 (*C*H_2), 20.2 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{14}H_{14}BrClO$, expected $(M+NH_4)^+$ *m/z* 330.0255, 332.0235; observed $(M+NH_4)^+$ *m/z* 330.0256, 332.0237. **$[\alpha]^{20}_D$** -32.6 (*c* = 1.00, acetone).

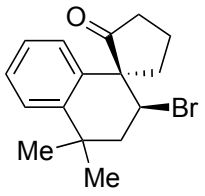
β-Bromo Spiroketone (C_8^R)



diastereomer 2
Chemical Formula: $C_{14}H_{14}BrClO$
Molecular Weight: 313.62

According to the General Procedure: chiral, racemic allylic cyclopropanol (*rac*-**A$_8$**) (47 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L$_9$**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T$_3$**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). White crystalline solid. Isolated yield 42% (26 mg, 0.08 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.46. > 20:1 *d.r.* (^{1}H NMR). 96.5:3.5 *e.r.* Chiral HPLC. Chiralcel OD-H. *n*-Hex/*i*-PrOH 98:2. 1.0 mL/min. t_R 7.9 (minor), 11.5 (major). **^{1}H NMR** (500 MHz, C_6D_6): δ 7.02-7.06 (1H, *m*, C^{ar}*H*), 6.63-6.67 (2H, *m*, C^{ar}*H*), 4.25 (1H, *dd*, J_1 13.4, J_2 3.4, α-bromo C*H*), 3.03-3.10 (2H, *m*, CH_2 + benzylic C*H*), 2.87 (1H, *td*, J_1 13.2, J_2 5.5, diastereotopic CH_2), 2.63 (1H, *ddd*, J_1 18.5, J_2 10.7, J_3 7.6, CH_2), 2.24-2.30 (1H, *m*, CH_2), 1.94-1.97 (1H, *m*, CH_2), 1.83-1.89 (1H, *m*, CH_2), 0.91 (3H, *d*, *J* 7.1, CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 204.4 (ketone C*q*), 138.5 (C*q*), 136.1 (C*q*), 135.2 (C*q*), 129.0 (*C*H), 128.0 (*C*H), 125.4 (*C*H), 73.3 (α-carbonyl C*q*), 50.3 (α-bromo *C*H), 44.9 (*C*H_2), 38.6 (*C*H_2), 33.0 (benzylic *C*H), 24.8 (*C*H_2), 20.2 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{14}H_{14}BrClO$, expected $(M+NH_4)^+$ *m/z* 330.0255, 332.0235; observed $(M+NH_4)^+$ *m/z* 330.0259, 332.0239. **$[\alpha]^{20}_D$** -22.2 (*c* = 1.00, acetone).

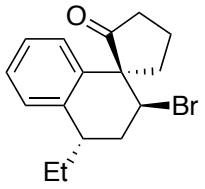
β-Bromo Spiroketone (C_9)



Chemical Formula: $C_{16}H_{19}BrO$
Molecular Weight: 307.23

According to the General Procedure: allylic cyclobutanol (**A_9**) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L_9**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T_3**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). White crystalline solid. Isolated yield 88% (54 mg, 0.18 mmol). **R_f** (silica gel, *n*-Hex/Et_2O 9:1) 0.50. > 20:1 *d.r.* (^{1}H NMR). 94.5:5.5 *e.r.* Chiral HPLC. Chiralpak IA. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 8.4 (minor), 10.9 (major). **^{1}H NMR** (500 MHz, C_6D_6): δ 7.09 (1H, *dd*, J_1 8.0, J_2 1.4, C^{ar}*H*), 7.01 (1H, *td*, J_1 7.1, J_2 1.3, C^{ar}*H*), 6.93 (1H, *td*, J_1 7.8, J_2 1.5, C^{ar}*H*), 6.83 (1H, *dd*, J_1 8.0, J_2 1.1, C^{ar}*H*), 4.32 (1H, *dd*, J_1 13.5, J_2 3.7, α-bromo C*H*), 3.38 (1H, *t*, *J* 13.5, diastereotopic CH_2), 2.43-2.50 (2H, *m*, CH_2), 2.16-2.22 (1H, *m*, CH_2), 2.07-2.14 (1H, *m*, CH_2), 1.99 (1H, *dd*, J_1 13.1, J_2 3.7, CH_2), 1.85-1.93 (1H, *m*, CH_2), 1.58-1.68 (1H, *m*, CH_2), 1.20 (3H, *s*, diastereotopic CH_3), 0.96 (3H, *s*, diastereotopic CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 215.0 (ketone C*q*), 145.3 (C*q*), 138.4 (C*q*), 127.24 (*C*H), 127.16 (*C*H), 127.0 (*C*H), 126.8 (*C*H), 56.9 (α-carbonyl C*q*), 56.0 (α-bromo *C*H), 45.2 (*C*H_2), 39.3 (*C*H_2), 39.0 (*C*H_2), 37.0 (benzylic C*q*), 32.4 (*C*H_2), 31.2 (*C*H_3), 20.5 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{16}H_{19}BrO$, expected $(M+NH_4)^+$ *m/z* 324.0958, 326.0938; observed $(M+NH_4)^+$ *m/z* 324.0962, 326.0942. **$[\alpha]^{20}_D$** -24.6 (*c* = 1.00, acetone).

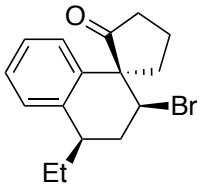
β-Bromo Spiroketone (C_{10}^S)



diastereomer 1
Chemical Formula: $C_{16}H_{19}BrO$
Molecular Weight: 307.23

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A_{10}**) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L_9**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T_3**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Pale-yellow oil. Isolated yield 42% (26 mg, 0.08 mmol). **R_f** (silica gel, *n*-Hex/Et_2O 9:1) 0.70. > 20:1 *d.r.* (^{1}H NMR). 94.5:5.5 *e.r.* Chiral HPLC. Chiralcel OD-H. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 7.4 (minor), 10.5 (major). **^{1}H NMR** (500 MHz, C_6D_6): δ 7.01 (1H, *td*, J_1 6.9, J_2 1.3, C^{ar}*H*), 6.89-6.94 (2H, *m*, C^{ar}*H*), 6.66 (1H, *dd*, J_1 7.7, J_2 1.2, C^{ar}*H*), 4.87 (1H, *dd*, J_1 10.5, J_2 3.1, α-bromo C*H*), 2.54-2.59 (1H, *m*, benzylic C*H*), 2.35-2.43 (2H, *m*, CH_2), 2.18-2.26 (2H, *m*, CH_2), 2.04 (1H, *ddd*, J_1 18.8, J_2 8.8, J_3 4.9, diastereotopic CH_2), 1.92 (1H, *ddd*, J_1 12.9, J_2 7.8, J_3 4.8, diastereotopic CH_2), 1.45-1.67 (4H, *m*, CH_2), 0.74 (3H, *t*, *J* 7.4, CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 216.8 (ketone C*q*), 139.1 (C*q*), 138.9 (C*q*), 129.5 (*C*H), 127.1 (*C*H), 126.8 (*C*H), 126.5 (*C*H), 58.4 (α-carbonyl C*q*), 40.9 (α-bromo *C*H), 39.6 (*C*H_2), 38.7 (*C*H_2), 36.5 (benzylic *C*H), 36.1 (*C*H_2), 30.3 (*C*H_2), 18.8 (*C*H_3), 12.0 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{16}H_{19}BrO$, expected $(M+NH_4)^+$ *m/z* 324.0958, 326.0938; observed $(M+NH_4)^+$ *m/z* 324.0962, 326.0940. **$[\alpha]^{20}_D$** -39.5 (*c* = 1.00, acetone).

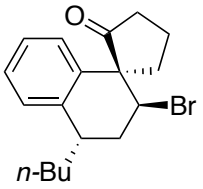
β-Bromo Spiroketone (C_{10}^{R})



diastereomer 2
Chemical Formula: $C_{16}H_{19}BrO$
Molecular Weight: 307.23

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A$_{10}$**) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L$_9$**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T$_3$**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 43% (26 mg, 0.09 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.50. > 20:1 *d.r.* (^{1}H NMR). 96:4 *e.r.* Chiral HPLC. Chiralpak IC. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 9.4 (minor), 12.4 (major). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.94-7.01 (2H, *m*, C^{ar}*H*), 6.80-6.86 (2H, *m*, C^{ar}*H*), 4.29 (1H, *dd*, J_1 12.7, J_2 3.5, α-bromo C*H*), 3.30 (1H, *td*, J_1 13.0, J_2 5.8, diastereotopic CH_2), 2.30-2.54 (3H, *m*, CH_2 + benzylic C*H*), 2.05-2.21 (3H, *m*, CH_2), 1.83-1.94 (1H, *m*, CH_2), 1.56-1.68 (1H, *m*, CH_2), 1.28-1.38 (1H, *m*, CH_2), 1.15-1.26 (1H, *m*, CH_2), 0.70 (3H, *t*, *J* 7.4, CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 214.9 (ketone C*q*), 140.7 (C*q*), 139.1 (C*q*), 129.9 (*C*H), 127.3 (*C*H), 127.0 (*C*H), 126.8 (*C*H), 55.8 (α-carbonyl C*q*), 55.7 (α-bromo *C*H), 41.7 (benzylic *C*H), 39.5 (*C*H_2), 38.7 (*C*H_2), 33.8 (*C*H_2), 30.8 (*C*H_2), 20.2 (*C*H_2), 12.5 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{16}H_{19}BrO$, expected $(M+NH_4)^+$ *m/z* 324.0958, 326.0938; observed $(M+NH_4)^+$ *m/z* 324.0959, 326.0939. **[α]$^{20}_D$** -15.3 (*c* = 1.00, acetone).

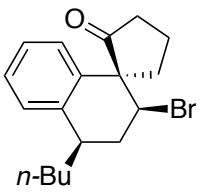
β-Bromo Spiroketone (C_{11}^{S})



diastereomer 1
Chemical Formula: $C_{18}H_{23}BrO$
Molecular Weight: 335.28

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A$_{11}$**) (51 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L$_9$**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T$_3$**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Pale-yellow oil. Isolated yield 44% (30 mg, 0.09 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.81. > 20:1 *d.r.* (^{1}H NMR). 95.5:4.5 *e.r.* Chiral HPLC. Chiralcel OJ-H. *n*-Hex/*i*-PrOH 99.5:0.5. 1.0 mL/min. t_R 15.6 (major), 18.6 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 7.14 (1H, *d*, *J* 8.0, C^{ar}*H*), 7.04 (1H, *t*, *J* 8.3, C^{ar}*H*), 6.96 (1H, *t*, *J* 7.8, C^{ar}*H*), 6.85 (1H, *d*, *J* 9.1, C^{ar}*H*), 3.95 (1H, *dd*, J_1 13.1, J_2 3.8, α-bromo C*H*), 3.15 (1H, *q*, *J* 13.0, benzylic C*H*), 2.59-2.65 (1H, *m*, diastereotopic CH_2), 2.41-2.51 (2H, *m*, CH_2), 2.24-2.29 (1H, *m*, CH_2), 2.08-2.18 (2H, *m*, CH_2), 1.83-1.92 (1H, *m*, CH_2), 1.58-1.73 (3H, *m*, CH_2), 1.12-1.24 (3H, *m*, CH_2), 0.82 (3H, *t*, *J* 7.0,2 CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 215.3 (ketone C*q*), 140.0 (C*q*), 139.8 (C*q*), 127.7 (*C*H), 127.1 (*C*H), 127.0 (*C*H), 126.6 (*C*H), 59.3 (α-bromo *C*H), 55.7 (α-carbonyl C*q*), 39.3 (*C*H_2), 39.14 (*C*H_2), 39.08 (benzylic *C*H), 36.2 (*C*H_2), 35.7 (*C*H_2), 28.3 (*C*H_2), 23.4 (*C*H_2), 20.5 (*C*H_2), 14.2 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{18}H_{23}BrO$, expected $(M+NH_4)^+$ *m/z* 352.1271, 354.1251; observed $(M+NH_4)^+$ *m/z* 352.1274, 354.1254. **[α]$^{20}_D$** -30.1 (*c* = 1.00, acetone).

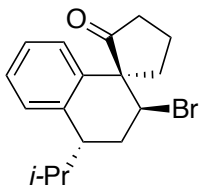
β-Bromo Spiroketone (C_{11}^{R})



diastereomer 2
Chemical Formula: $C_{18}H_{23}BrO$
Molecular Weight: 335.28

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A$_{11}$**) (51 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L$_9$**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T$_3$**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 40% (26 mg, 0.08 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.63. > 20:1 *d.r.* (^{1}H NMR). 96:4 *e.r.* Chiral HPLC. Chiralpak IC. *n*-Hex/*i*-PrOH 99.5:0.5. 0.8 mL/min. t_R 16.8 (minor), 21.2 (major). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.95-7.02 (2H, *m*, C^{ar}*H*), 6.89 (1H, *dd*, J_1 7.3, J_2 1.7, C^{ar}*H*), 6.83 (1H, *dd*, J_1 7.7, J_2 1.4, C^{ar}*H*), 4.36 (1H, *dd*, J_1 12.8, J_2 3.5, α-bromo C*H*), 3.36 (1H, *td*, J_1 13.1, J_2 5.8, diastereotopic CH_2), 2.62-2.67 (1H, *m*, benzylic C*H*), 2.33-2.48 (2H, *m*, CH_2), 2.16-2.23 (2H, *m*, CH_2), 2.10 (1H, *ddd*, J_1 15.2, J_2 6.4, J_3 2.3, C^{ar}*H*), 1.85-1.94 (1H, *m*, CH_2), 1.58-1.68 (1H, *m*, CH_2), 1.24-1.36 (3H, *m*, CH_2), 1.03-1.17 (4H, *m*, CH_2), 0.80 (3H, *t*, *J* 6.9, CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 215.0 (ketone C*q*), 140.9 (C*q*), 139.1 (C*q*), 129.9 (*C*H), 127.3 (*C*H), 126.9 (*C*H), 126.8 (*C*H), 55.86 (α-bromo *C*H), 55.76 (α-carbonyl C*q*), 40.1 (benzylic *C*H), 39.5 (*C*H_2), 38.7 (*C*H_2), 38.0 (*C*H_2), 34.4 (*C*H_2), 30.3 (*C*H_2), 23.0 (*C*H_2), 20.3 (*C*H_2), 14.2 (*C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{18}H_{23}BrO$, expected $(M+NH_4)^+$ *m/z* 352.1271, 354.1251; observed $(M+NH_4)^+$ *m/z* 352.1273, 354.1253. **[α]$^{20}_D$** -17.4 (*c* = 1.00, acetone).

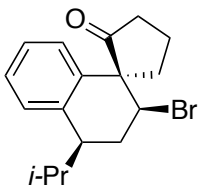
β-Bromo Spiroketone (C_{12}^{S})



diastereomer 1
Chemical Formula: $C_{17}H_{21}BrO$
Molecular Weight: 321.25

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A$_{12}$**) (49 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L$_9$**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T$_3$**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Pale-yellow oil. Isolated yield 45% (29 mg, 0.09 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.79. > 20:1 *d.r.* (^{1}H NMR). 94:6 *e.r.* Chiral HPLC. Chiralpak IC. *n*-Hex/*i*-PrOH 99:1. 1.0 mL/min. t_R 7.9 (minor), 9.3 (major). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.97-7.01 (2H, *m*, C^{ar}*H*), 6.91-6.94 (1H, *m*, C^{ar}*H*), 6.81-6.84 (1H, *m*, C^{ar}*H*), 4.36 (1H, *dd*, J_1 11.8, J_2 3.6, α-bromo C*H*), 3.05 (1H, *ddd*, J_1 14.7, J_2 11.8, J_3 6.2, diastereotopic CH_2), 2.53 (1H, *dq*, J_1 6.8, J_2 5.2, benzylic C*H*), 2.40 (1H, *ddd*, J_1 18.2, J_2 9.8, J_3 7.4, CH_2), 2.22-2.28 (2H, *m*, CH_2), 2.12-2.18 (1H, *m*, CH_2), 2.03-2.10 (1H, *m*, CH_2), 1.78-1.86 (1H, *m*, CH_2), 1.68 (1H, *oct.*, *J* 6.8, isopropylic C*H*), 1.53-1.62 (1H, *m*, CH_2), 0.75 (3H, *d*, *J* 6.8, isopropylic CH_3), 0.60 (3H, *d*, *J* 6.8, isopropylic CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 214.6 (ketone C*q*), 139.5 (C*q*), 139.3 (C*q*), 130.0 (*C*H), 127.6 (*C*H), 126.9 (*C*H), 126.4 (*C*H), 56.1 (α-carbonyl C*q*), 55.7 (α-bromo *C*H), 45.2 (benzylic *C*H), 39.9 (*C*H_2), 38.5 (*C*H_2), 33.3 (isopropylic *C*H), 32.1 (*C*H_2), 21.6 (isopropylic *C*H_3), 19.9 (*C*H_2), 19.5 (isopropylic *C*H_3) ppm. **ESI-HRMS (positif)** M = $C_{17}H_{21}BrO$, expected $(M+NH_4)^+$ *m/z* 338.1115, 340.1094; observed $(M+NH_4)^+$ *m/z* 338.1118, 340.1097. **[α]$^{20}_D$** -28.3 (*c* = 1.00, acetone).

β-Bromo Spiroketone (C_{12}^{R})



diastereomer 2
Chemical Formula: $C_{17}H_{21}BrO$
Molecular Weight: 321.25

According to the General Procedure: chiral, racemic allylic cyclobutanol (*rac*-**A$_{12}$**) (49 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_a)-H_8-TRIP (**L$_9$**) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (**T$_3$**) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na_3PO_4 (131 mg, 0.80 mmol, 4.0 equiv.) in anhydrous ethylbenzene (4.0 mL, 0.05 M). Purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 95:5). Colorless oil. Isolated yield 44% (28 mg, 0.09 mmol). **R$_f$** (silica gel, *n*-Hex/Et_2O 9:1) 0.58. > 20:1 *d.r.* (^{1}H NMR). 97:3 *e.r.* Chiral HPLC. Chiralcel OJ-H. *n*-Hex/*i*-PrOH 99.5:0.5. 0.8 mL/min. t_R 15.6 (major), 20.0 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.96-7.02 (2H, *m*, C^{ar}*H*), 6.93 (1H, *dd*, J_1 6.9, J_2 1.9, C^{ar}*H*), 6.82 (1H, *dd*, J_1 7.4, J_2 1.6, C^{ar}*H*), 4.42 (1H, *dd*, J_1 11.1, J_2 3.4, α-bromo C*H*), 3.05 (1H, *ddd*, J_1 13.9, J_2 11.1, J_3 6.1, diastereotopic CH_2), 2.50 (1H, broad *q*, *J* 6.1, benzylic C*H*), 2.43 (1H, *ddd*, J_1 17.9, J_2 8.5, J_3 7.8, CH_2), 2.29 (1H, *dt*, J_1 13.9, J_2 3.8, CH_2), 2.08-2.15 (2H, *m*, CH_2), 2.01 (1H, *ddd*, J_1 18.1, J_2 8.0, J_3 7.6, CH_2), 1.70-1.80 (2H, *m*, CH_2 + isopropylic C*H*), 1.51-1.58 (1H, *m*, CH_2), 0.75 (3H, *d*, *J* 6.8, isopropylic CH_3), 0.61 (3H, *d*, *J* 6.8, isopropylic CH_3) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 215.4 (ketone C*q*), 139.2 (C*q*), 138.8 (C*q*), 129.9 (*C*H), 127.8 (*C*H), 126.8 (*C*H), 126.4 (*C*H), 56.1 (α-carbonyl C*q*), 45.9 (α-bromo *C*H), 40.8 (benzylic *C*H), 37.6 (*C*H$_2$), 34.9 (*C*H$_2$), 34.1 (*C*H$_2$), 32.9 (isopropylic *C*H), 30.5 (*C*H$_2$), 21.5 (isopropylic *C*H$_3$), 19.5 (*C*H$_2$), 19.4 (isopropylic *C*H$_3$) ppm. **ESI-HRMS (positif)** M = $C_{17}H_{21}BrO$, expected $(M+NH_4)^+$ *m/z* 338.1115, 340.1094; observed $(M+NH_4)^+$ *m/z* 338.1117, 340.1096. **[α]$^{20}_D$** -28.3 (*c* = 1.00, acetone).

NOE Studies

Importantly, the stereodivergent nature of the title transformation originates from two salient features of the enantioselective process: (i) similar reaction rates of the two enantiomers of the starting material (as evidenced from Table 1, entry 4), and (ii) high steric tolerance of the catalyst's chiral pocket with respect to substitution at the benzylic position of the substrate (as evidenced from the control experiment of Scheme 4, see main text article). Taken together, these observations might explain why the pre-existing stereogenic center in the chiral, racemic substrates has little-to-zero influence on reaction stereochemistry, which is consequently dominated by the absolute configuration of the chiral, enantiopure phosphate anion (Scheme 5). Furthermore, the relative configuration of products in solution was confirmed from a set of homo- and hetero- nuclear Overhauser enhancement experiments.

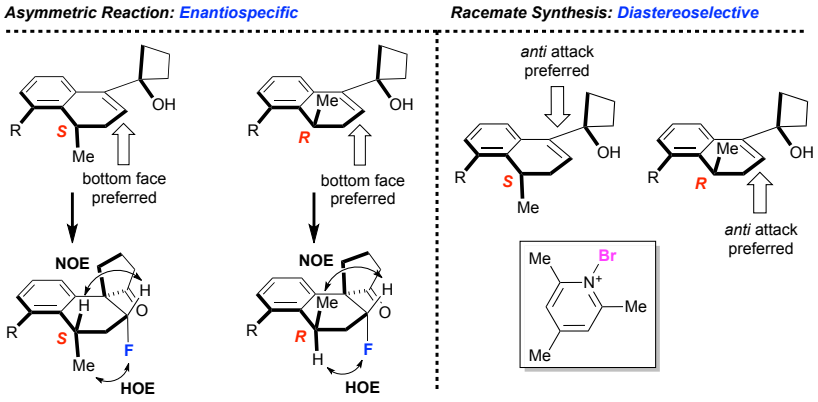


Figure 1. The origins of stereodivergency, and structural confirmation in solution from Overhauser enhancement spectroscopy.

X-Ray Crystal Structures of Products

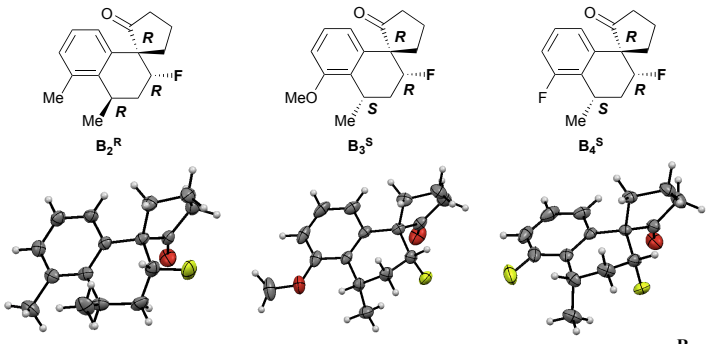


Figure 2. X-ray crystal structures of β-fluoro spiroketones $\mathbf{B_2}^{\mathbf{R}}$, $\mathbf{B_3}^{\mathbf{S}}$ and $\mathbf{B_4}^{\mathbf{S}}$. Thermal ellipsoids are set at 50% probability level.

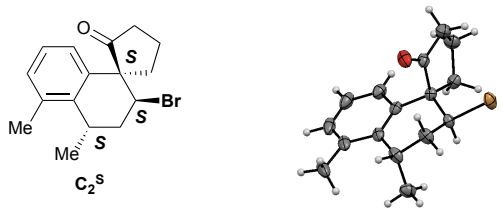


Figure 3. X-ray crystal structures of β-bromo spiroketone $\mathbf{C_2}^{\mathbf{S}}$. Thermal ellipsoids are set at 50% probability level.

Synthetic Derivatizations

Synthetic manipulations of products involved a Baeyer-Villiger oxidation of spiroketone $\mathbf{B_8}^{\mathbf{R}}$ and diastereoselective reduction of spiroketones $\mathbf{B_2}^{\mathbf{R}}$, $\mathbf{B_5}^{\mathbf{R}}$ and $\mathbf{C_4}^{\mathbf{S}}$.

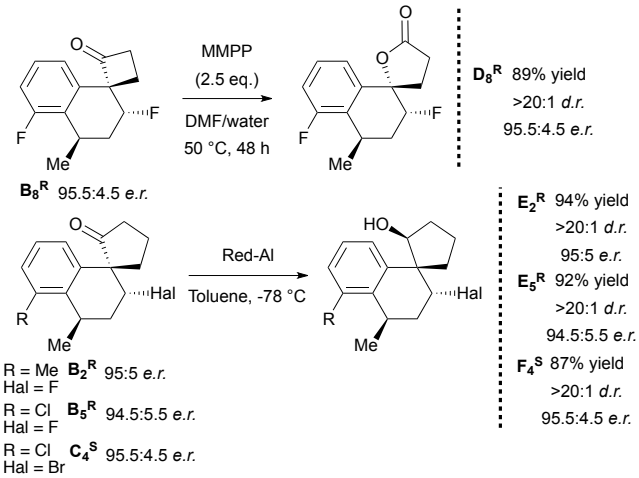
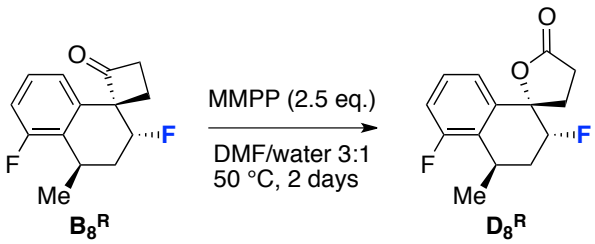
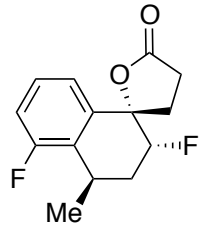


Figure 4. Synthetic manipulations of the product optically active β-halo spiroketones.

Baeyer-Villiger Oxidation



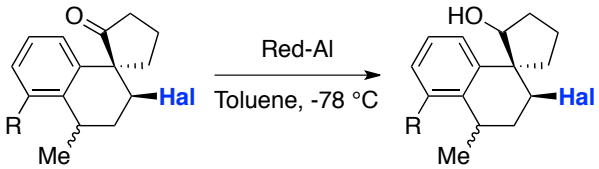
Spiro γ-Lactone (D_8^R)



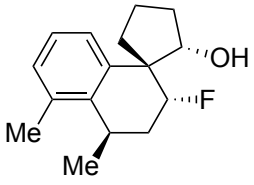
Chemical Formula: $C_{14}H_{14}F_2O_2$
Molecular Weight: 252.26

To a solution of β-fluoro spiroketone $\mathbf{B_8^R}$ (> 20:1 *d.r.*, 95.5:4.5 *e.r.*) (20 mg, 0.08 mmol, 1.0 equiv.) in DMF/water (3:1 *v/v*, 400 μL) was added MMPP (*ca.* 90% purity, 100 mg, 0.20 mmol, 2.5 equiv.), and the reaction mixture was heated at 50 °C for 48 h. The solution was cooled down to ambient temperature, and treated with saturated aqueous $Na_2S_2O_3$ followed by saturated aqueous $NaHCO_3$. The mixture was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude residue was purified by flash chromatography on silica gel (*n*-hexane/Et_2O 9:1 → 3:2). Colorless oil. Isolated yield 89% (18 mg, 0.07 mmol). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 1:1) 0.17. > 20:1 *d.r.* (^{1}H NMR). 95.5:4.5 *e.r.* Chiral HPLC. Chiralpak IC. ^{n}Hex/^{i}PrOH 90:10; 1.0 mL/min. t_R 18.9 (major), 24.2 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 6.69-6.75 (3H, *m*, C^{ar}*H*), 4.00 (1H, *ddd*, $J_1^{H\text{-}F}$ 48.7, J_2 8.7, J_3 3.1, α-fluoro C*H*), 2.86 (1H, *sext.*, *J* 7.0, benzylic C*H*), 2.07-2.19 (2H, *m*, diastereotopic β-fluoro CH_2), 1.75-1.83 (1H, *m*, CH_2), 1.44-1.65 (3H, *m*, CH_2), 1.31 (3H, *dt*, J_1 7.0, J_2 1.3, CH_3) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -113.0 (1F, *s*, C^{ar}*F*), -188.3 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 174.9 (γ-lactone C*q*), 161.3 (*d*, $J^{C\text{-}F}$ 245, *ipso*(F)-C*q*), 137.8 (*dd*, $J_1^{C\text{-}F}$ 4.3, $J_2^{C\text{-}F}$ 3.4, *meta*(F)-C*q*), 129.0 (*d*, $J^{C\text{-}F}$ 15.3, *ortho*(F)-C*q*), 121.9 (*d*, $J^{C\text{-}F}$ 3.1, *meta*(F)-*C*H), 115.7 (*d*, $J^{C\text{-}F}$ 22.6, *ortho*(F)-*C*H), 91.9 (*d*, $J^{C\text{-}F}$ 183, *C*H-F), 83.2 (*dd*, $J_1^{C\text{-}F}$ 17.0, $J_2^{C\text{-}F}$ 2.9, C*q*-O), 31.5 (*d*, $J^{C\text{-}F}$ 3.4, *C*H$_2$), 31.2 (*d*, $J^{C\text{-}F}$ 18.6, benzylic *C*H), 28.5 (*d*, $J^{C\text{-}F}$ 1.3, *C*H$_2$), 27.0 (*d*, $J^{C\text{-}F}$ 6.7, *C*H$_3$), 22.8 (*dd*, $J_1^{C\text{-}F}$ 5.4, $J_2^{C\text{-}F}$ 2.3, *C*H$_2$) ppm. **ESI-HRMS (positif)** M = $C_{14}H_{14}F_2O_2$, expected $(M+H)^+$ *m/z* 253.1035, observed $(M+H)^+$ *m/z* 253.1035. **$[\alpha]^{20}_D$** +75.9 (*c* = 1.00, CH_2Cl_2).

Diastereoselective Reduction



Spirocyclic Fluoro-Alcohol (E_2^R)

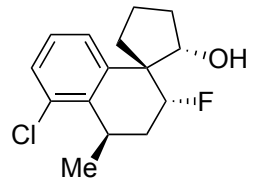


Chemical Formula: $C_{16}H_{21}FO$
Molecular Weight: 248.34

To a cooled (-78 °C, dry ice/acetone bath) solution of β-fluoro spiroketone $\mathbf{B_2^R}$ (> 20:1 *d.r.*, 95:5 *e.r.*) (20 mg, 0.08 mmol, 1.0 equiv.) in anhydrous toluene (2.5 mL) was added Red-Al^{TM} (3.5 M solution in toluene, 35 μL, 0.12 mmol, 1.5 equiv.) dropwise *via* syringe. The resultant colorless solution was stirred at -78 °C for 4 h. Saturated aqueous NH_4Cl was then added to quench the reaction. The layers were separated, and the aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 4:1). Colorless crystalline solid.

Isolated yield 94% (19 mg, 0.075 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.49. > 20:1 *d.r.* (^{1}H NMR). 95:5 *e.r.* Chiral HPLC. Chiralpak IC. ^{n}Hex/^{i}PrOH 95:5; 1.0 mL/min. t_R 12.0 (minor), 18.9 (major). **^{1}H NMR** (500 MHz, C_6D_6): δ 7.10 (1H, *d*, *J* 7.8, C^{ar}*H*), 7.02 (1H, *t*, *J* 7.6, C^{ar}*H*), 6.94 (1H, *d*, *J* 7.4, C^{ar}*H*), 4.45 (1H, broad *q*, *J* 6.0, C*H*-O), 4.34 (1H, *ddd*, $J_1^{H\text{-}F}$ 49.4, J_2 9.3, J_3 5.4, α-fluoro C*H*), 2.86 (1H, *sext.*, *J* 7.1, benzylic C*H*), 2.12 (3H, *s*, CH_3), 2.07-2.14 (2H, *m*, diastereotopic CH_2), 1.96-2.05 (2H, *m*, CH_2), 1.82-1.88 (1H, *m*, CH_2), 1.61-1.75 (2H, *m*, CH_2), 1.45-1.53 (1H, *m*, CH_2), 1.29-1.38 (1H, *m*, CH_2), 1.20 (3H, *dd*, J_1 6.9, J_2 1.4, CH_3), 0.72 (1H, *d*, *J* 5.8, hydroxylic O*H*) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -184.9 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 140.8 (*d*, $J^{C\text{-}F}$ 1.7, C*q*), 138.0 (*d*, $J^{C\text{-}F}$ 5.1, C*q*), 136.0 (C*q*), 129.8 (*C*H), 127.4 (*d*, $J^{C\text{-}F}$ 0.8, *C*H), 126.1 (*C*H), 95.0 (*d*, $J^{C\text{-}F}$ 176, *C*H-F), 75.4 (*d*, $J^{C\text{-}F}$ 5.2, *C*H-O), 53.9 (*d*, $J^{C\text{-}F}$ 17.3, α-carbonyl C*q*), 37.4 (*d*, $J^{C\text{-}F}$ 4.9, CH_2), 36.0 (CH_2), 33.6 (*d*, $J^{C\text{-}F}$ 18.7, CH_2), 30.1 (*d*, $J^{C\text{-}F}$ 9.5, benzylic *C*H), 23.2 (*d*, $J^{C\text{-}F}$ 1.7, CH_3), 21.3 (CH_2), 20.3 (CH_3) ppm. **ESI-HRMS (positif)** M = $C_{16}H_{21}FO$, expected $(M+H)^+$ *m/z* 249.1650, observed $(M+H)^+$ *m/z* 249.1650. **$[\alpha]^{20}_D$** -15.8 (*c* = 1.00, CH_2Cl_2).

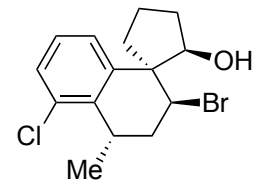
Spirocyclic Fluoro-Alcohol (E_5^R)



Chemical Formula: $C_{15}H_{18}ClFO$
Molecular Weight: 268.75

To a cooled (-78 °C, dry ice/acetone bath) solution of β-fluoro spiroketone $\mathbf{B}_5^R$ (> 20:1 *d.r.*, 94.5:5.5 *e.r.*) (20 mg, 0.07 mmol, 1.0 equiv.) in anhydrous toluene (2.5 mL) was added Red-Al^{TM} (3.5 M solution in toluene, 32 μL, 0.11 mmol, 1.5 equiv.) dropwise *via* syringe. The resultant colorless solution was stirred at -78 °C for 4 h. Saturated aqueous NH_4Cl was then added to quench the reaction. The layers were separated, and the aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 4:1). Colorless crystalline solid. Isolated yield 92% (17 mg, 0.06 mmol). $\mathbf{R}_f$ (silica gel, *n*-Hex/Et_2O 4:1) 0.39. > 20:1 *d.r.* (^{1}H NMR). 94.5:5.5 *e.r.* Chiral HPLC. Chiralpak IC. ^{n}Hex/^{i}PrOH 95:5; 1.0 mL/min. t_R 18.8 (major), 25.4 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 7.13 (1H, *dd*, J_1 7.9, J_2 1.2, C^{ar}*H*), 6.99 (1H, *dd*, J_1 8.0, J_2 1.1, C^{ar}*H*), 6.76 (1H, *t*, *J* 7.9, C^{ar}*H*), 4.58 (1H, *ddd*, $J_1^{H\text{-}F}$ 48.7, J_2 8.8, J_3 3.2, α-fluoro C*H*), 3.91 (1H, broad *q*, *J* 7.4, C*H*-O), 3.30-3.36 (1H, *m*, benzylic C*H*), 2.09-2.14 (1H, *m*, diastereotopic CH_2), 1.95-2.03 (1H, *m*, CH_2), 1.85-1.91 (1H, *m*, CH_2), 1.71-1.81 (2H, *m*, CH_2), 1.43-1.61 (3H, *m*, CH_2), 1.24 (3H, *d*, *J* 7.0, CH_3), 0.69 (1H, broad *d*, *J* 7.7, hydroxylic O*H*) ppm. **^{19}F NMR** (376 MHz, C_6D_6): δ -185.3 (1F, *s*, C(sp^3)-*F*) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 140.9 (*d*, $J^{C\text{-}F}$ 4.6, C*q*), 139.9 (*d*, $J^{C\text{-}F}$ 1.2, C*q*), 134.5 (C*q*), 128.5 (*C*H), 128.1 (*C*H), 127.1 (*C*H), 94.1 (*d*, $J^{C\text{-}F}$ 175, *C*H-F), 78.6 (*d*, $J^{C\text{-}F}$ 3.3, *C*H-O), 54.3 (*d*, $J^{C\text{-}F}$ 17.6, α-carbonyl C*q*), 37.0 (*d*, $J^{C\text{-}F}$ 5.5, CH_2), 35.6 (CH_2), 33.5 (*d*, $J^{C\text{-}F}$ 19.5, CH_2), 30.1 (*d*, $J^{C\text{-}F}$ 7.7, benzylic *C*H), 21.5 (CH_3), 21.4 (CH_2) ppm. **ESI-HRMS (positif)** M = $C_{15}H_{18}ClFO$, expected $(M+H)^+$ *m/z* 269.1103, observed $(M+H)^+$ *m/z* 269.1107. **$[\alpha]^{20}_D$** -19.9 (*c* = 1.00, CH_2Cl_2).

Spirocyclic Bromo-Alcohol (F_4^S)



Chemical Formula: $C_{15}H_{18}BrClO$
Molecular Weight: 329.66

To a cooled (-78 °C, dry ice/acetone bath) solution of β-bromo spiroketone $\mathbf{C}_4^S$ (> 20:1 *d.r.*, 95.5:4.5 *e.r.*) (25 mg, 0.08 mmol, 1.0 equiv.) in anhydrous toluene (2.5 mL) was added Red-Al^{TM} (3.5 M solution in toluene, 35 μL, 0.12 mmol, 1.5 equiv.) dropwise *via* syringe. The resultant colorless solution was stirred at -78 °C for 4 h. Saturated aqueous NH_4Cl was then added to quench the

reaction. The layers were separated, and the aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (*n*-hexane → *n*-hexane/Et_2O 4:1). Colorless oil. Isolated yield 87% (23 mg, 0.07 mmol). $\mathbf{R_f}$ (silica gel, *n*-Hex/Et_2O 4:1) 0.43. > 20:1 *d.r.* (^{1}H NMR). 95.5:4.5 *e.r.* Chiral HPLC. Chiralpak IC. ^{n}Hex/^{i}PrOH 95:5; 1.0 mL/min. t_R 12.2 (major), 15.4 (minor). **^{1}H NMR** (500 MHz, C_6D_6): δ 7.14 (1H, *dd*, J_1 7.8, J_2 1.2, C^{ar}*H*), 6.67 (1H, *td*, J_1 7.9, J_2 0.3, C^{ar}*H*), 6.56 (1H, *dd*, J_1 8.0, J_2 1.0, C^{ar}*H*), 4.26-4.29 (2H, *m*, α-bromo C*H*-Br + C*H*-O), 3.20-3.27 (1H, *m*, benzylic C*H*), 2.51 (1H, broad *d*, *J* 4.3, hydroxylic O*H*), 2.29 (1H, *ddd*, J_1 15.1, J_2 8.8, J_3 3.6, diastereotopic CH_2), 2.07 (1H, *ddd*, J_1 15.1, J_2 6.1, J_3 2.5, diastereotopic CH_2), 1.96-2.03 (1H, *m*, CH_2), 1.81-1.88 (1H, *m*, CH_2), 1.69-1.76 (1H, *m*, CH_2), 1.64 (3H, *d*, *J* 7.2, CH_3), 1.57-1.62 (1H, *m*, CH_2), 1.12-1.27 (2H, *m*, CH_2) ppm. **^{13}C NMR** (125 MHz, C_6D_6): δ 142.5 (C*q*), 137.8 (C*q*), 135.3 (C*q*), 128.9 (*C*H), 126.7 (*C*H), 124.9 (*C*H), 80.1 (*C*H-O), 57.4 (α-bromo *C*H-Br), 57.1 (α-carbonyl C*q*), 39.1 (*C*H_2), 37.1 (*C*H_2), 35.4 (*C*H_2), 30.6 (benzylic *C*H), 23.9 (*C*H_3), 22.9 (*C*H_2) ppm. **ESI-HRMS (positif)** M = $C_{15}H_{18}BrClO$, expected $(M+H)^+$ *m/z* 329.0303, 331.0282; observed $(M+H)^+$ *m/z* 329.0308, 331.0287. **$[\alpha]^{20}_D$** +17.4 (*c* = 1.00, CH_2Cl_2).

References and Notes

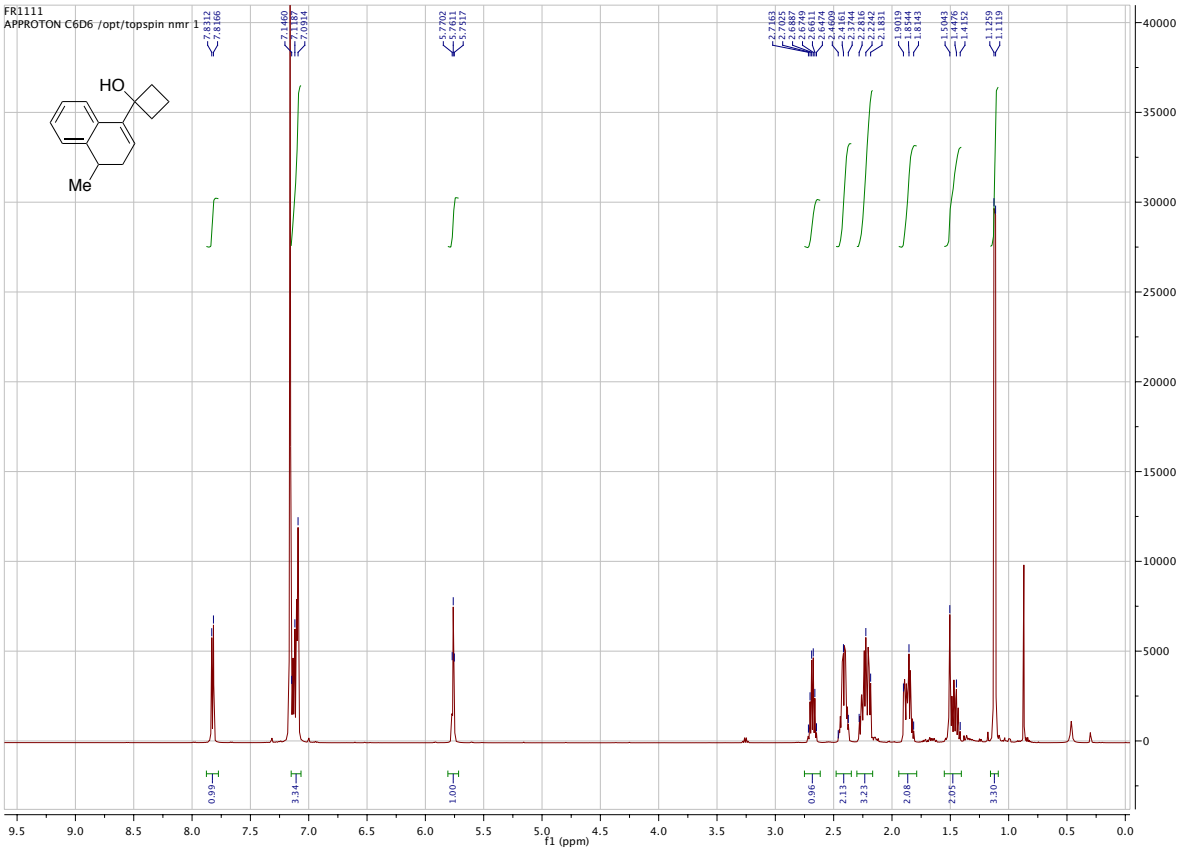
(1) A. Krasovskiy, P. Knochel, *Synthesis* **2006**, *5*, 890-891.
(2) F. Homsi, S. Robin, G. Rousseau, *Org. Synth.* **2000**, *77*, 206-208.
(3) Y.-M. Wang, J. Wu, C. Hoong, V. Rauniyar, F. D. Toste, *J. Am. Chem. Soc*. **2012**, *134*, 12928-12931.
(4) F. Romanov-Michailidis, L. Guénée, A. Alexakis, *Angew. Chem., Int. Ed.* **2013**, *52*, 9266-9270.
(5) Z. Chai, T. J. Rainey, *J. Am. Chem. Soc.* **2012**, *134*, 3615-3618.

NMR Spectra

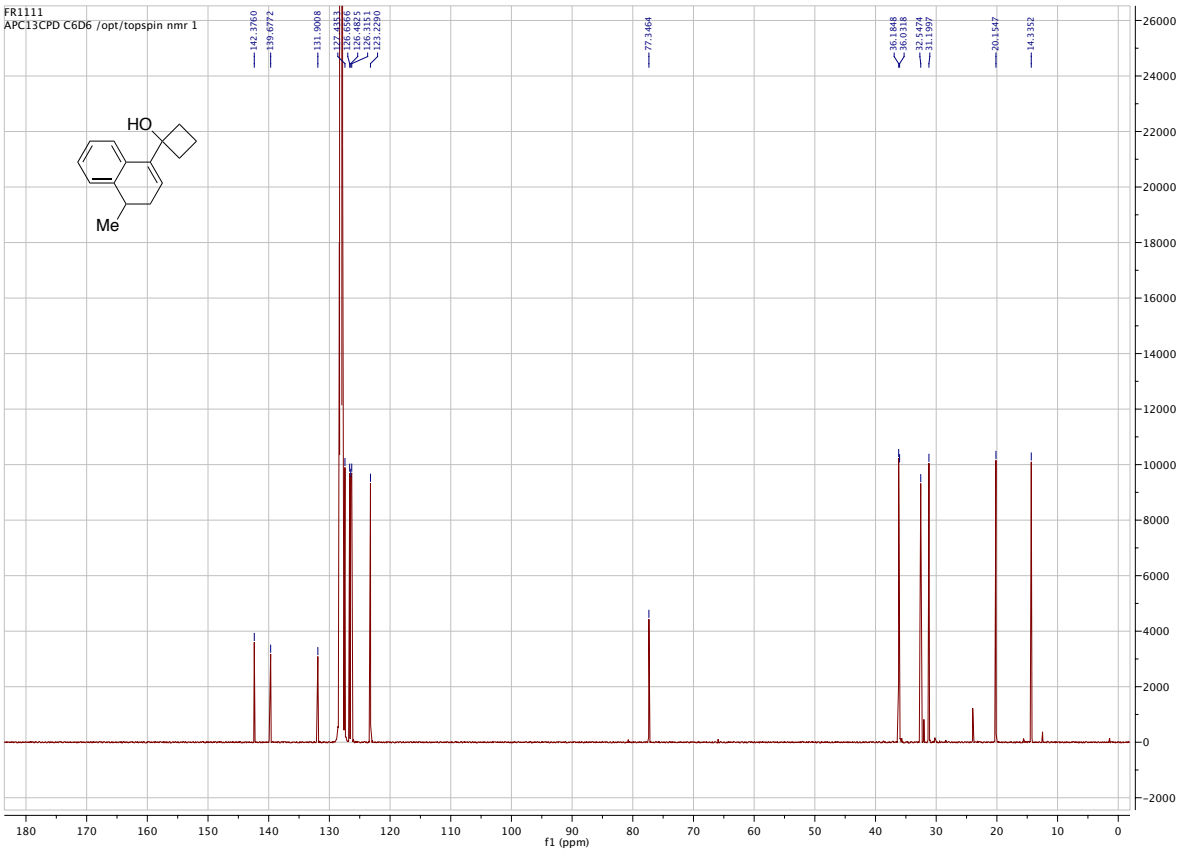
Fluorinated Compounds

Substrate *rac*-$\mathbf{A_1}$

^{1}H NMR 400 MHz, C_6D_6

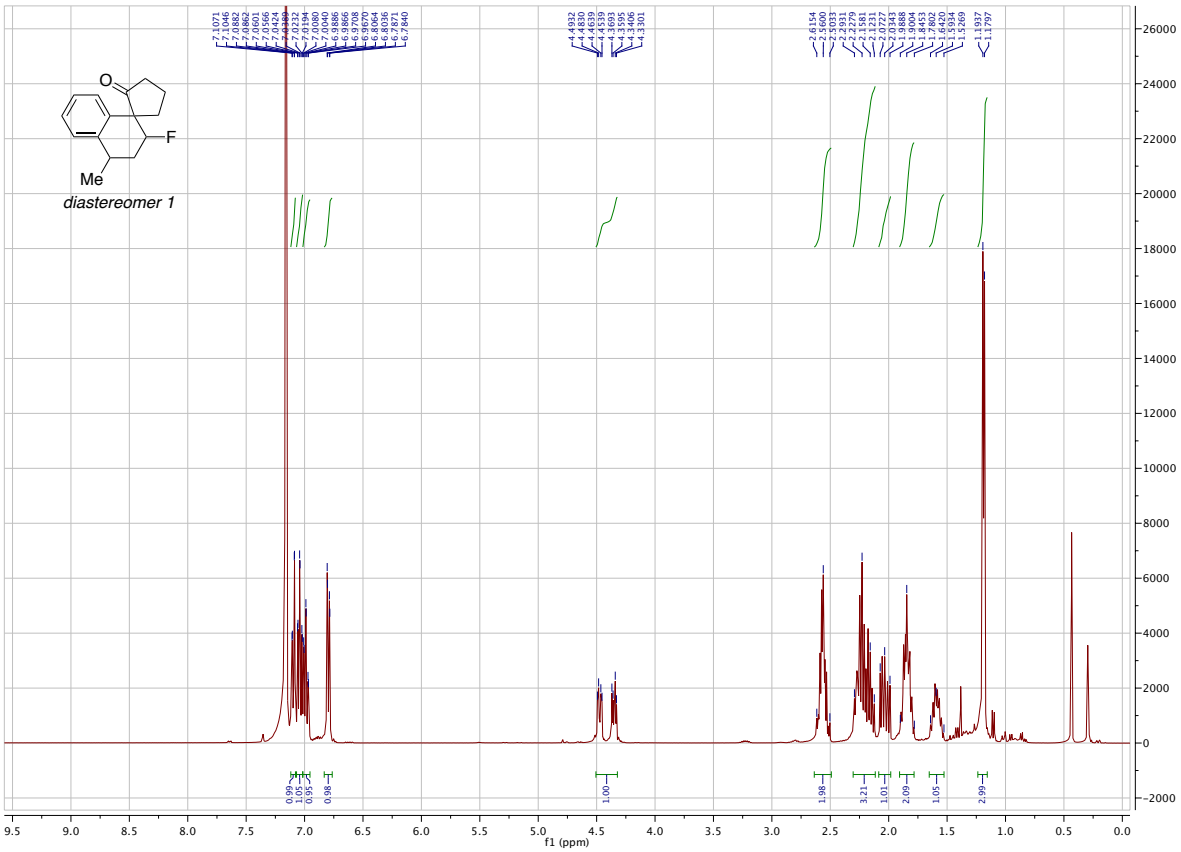


^{13}C NMR 125 MHz, C_6D_6

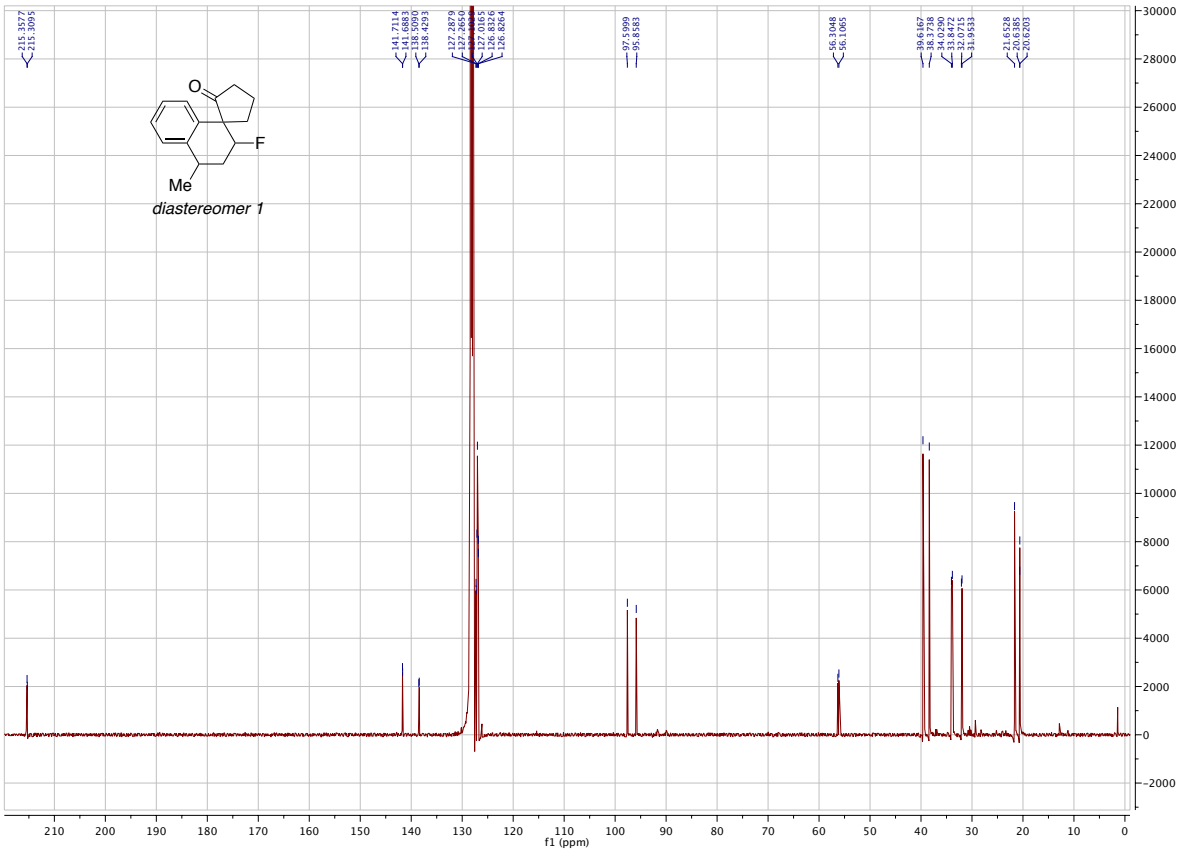


β-Fluoro Spiroketone B_1^R

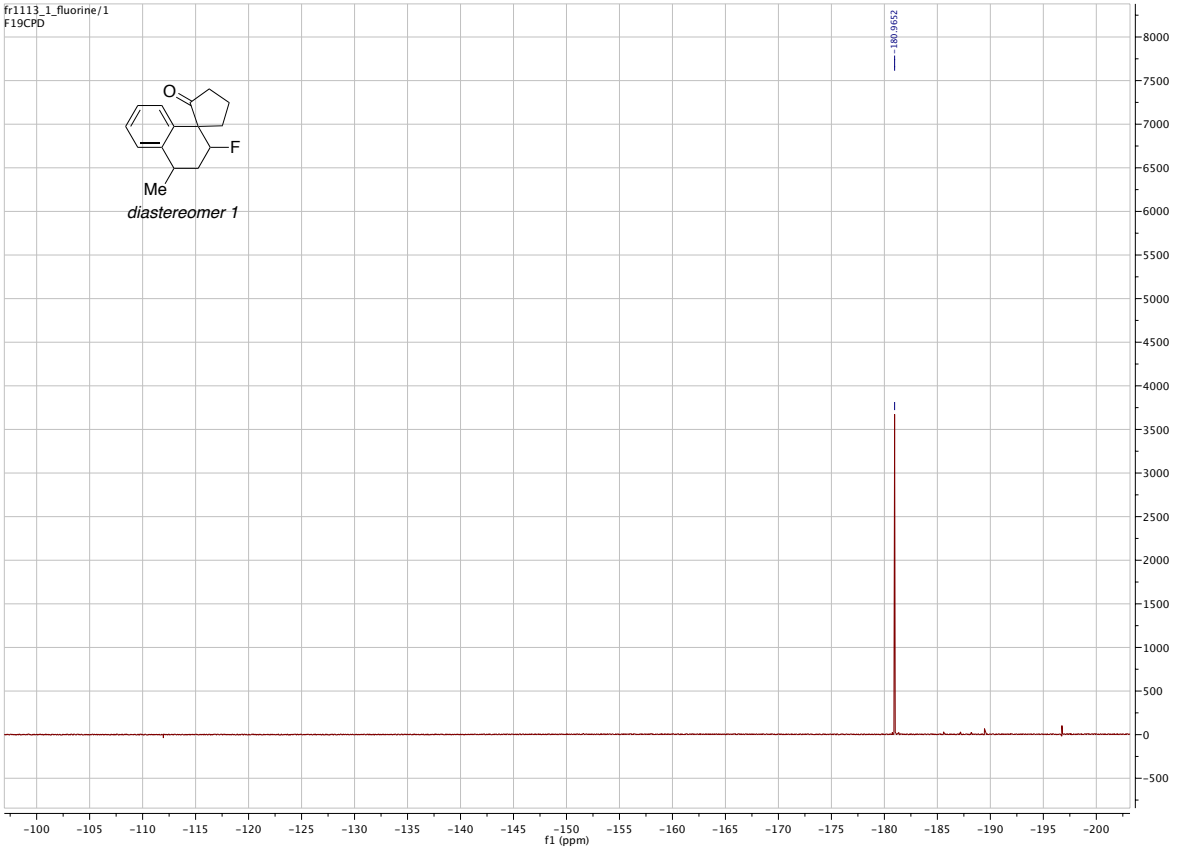
^{1}H NMR 400 MHz, C_6D_6



^{13}C NMR 100 MHz, C_6D_6

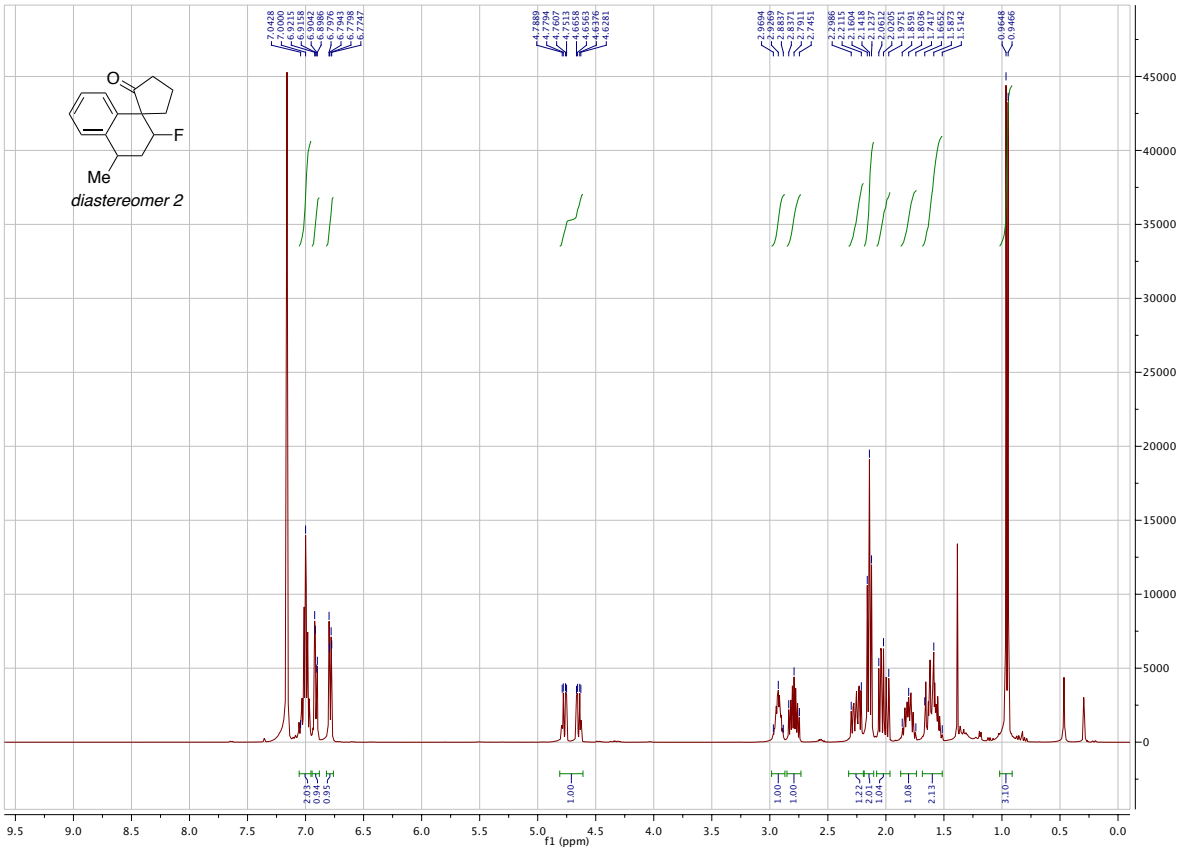


^{19}F NMR 375 MHz, C_6D_6

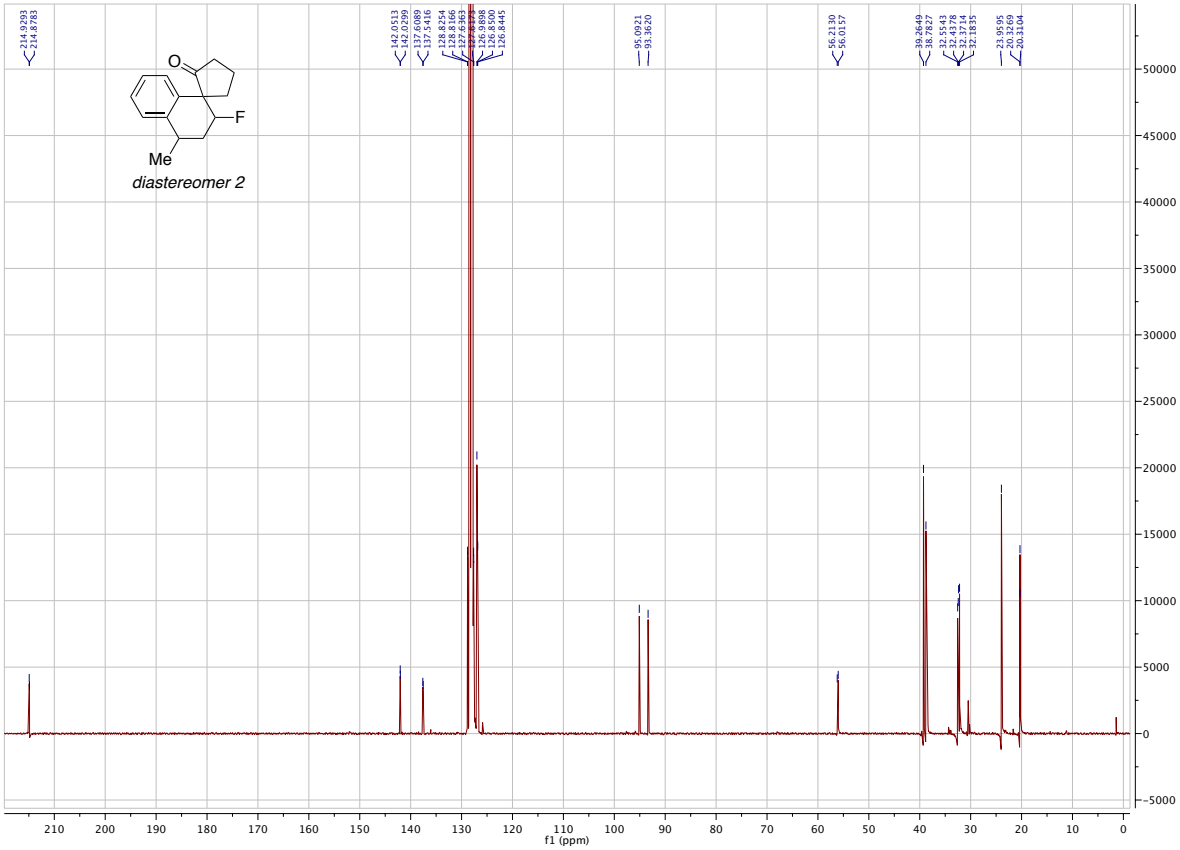


β-Fluoro Spiroketone B_1^S

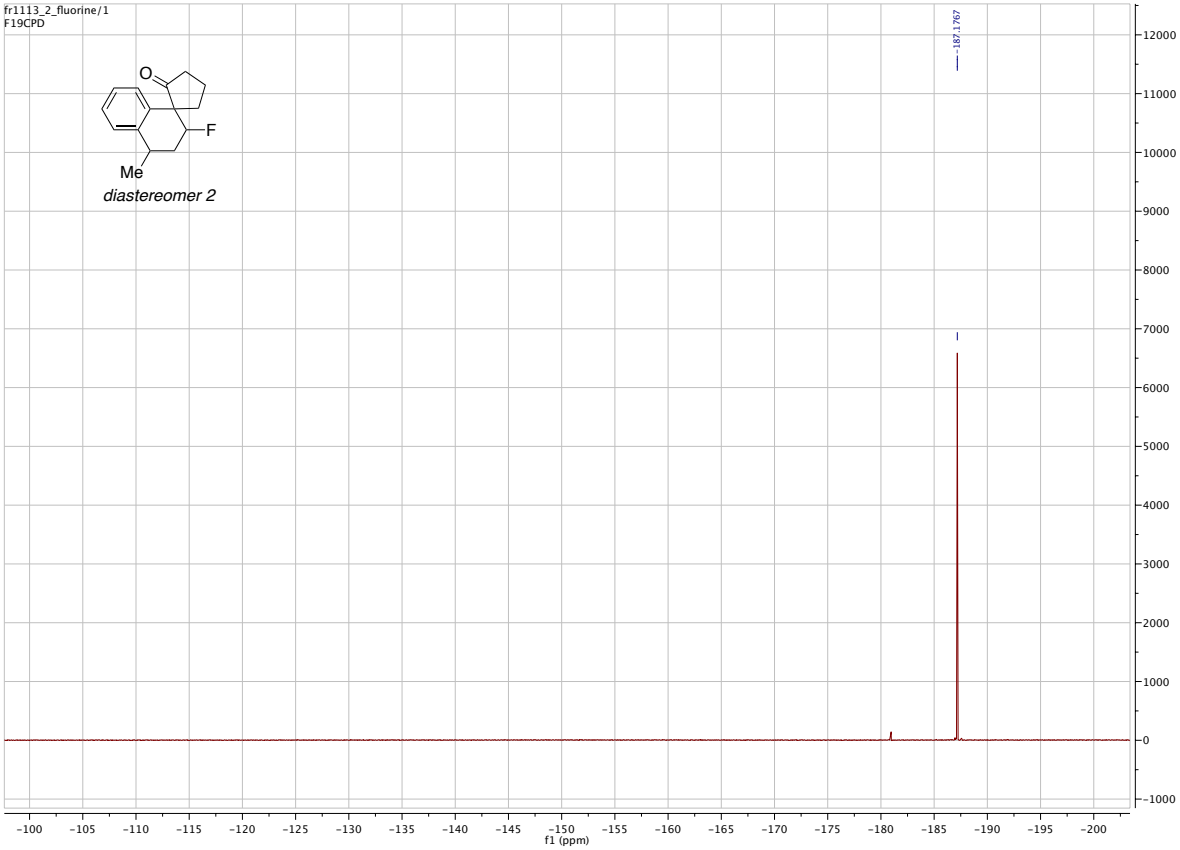
^{1}H NMR 400 MHz, C_6D_6



^{13}C NMR 100 MHz, C_6D_6

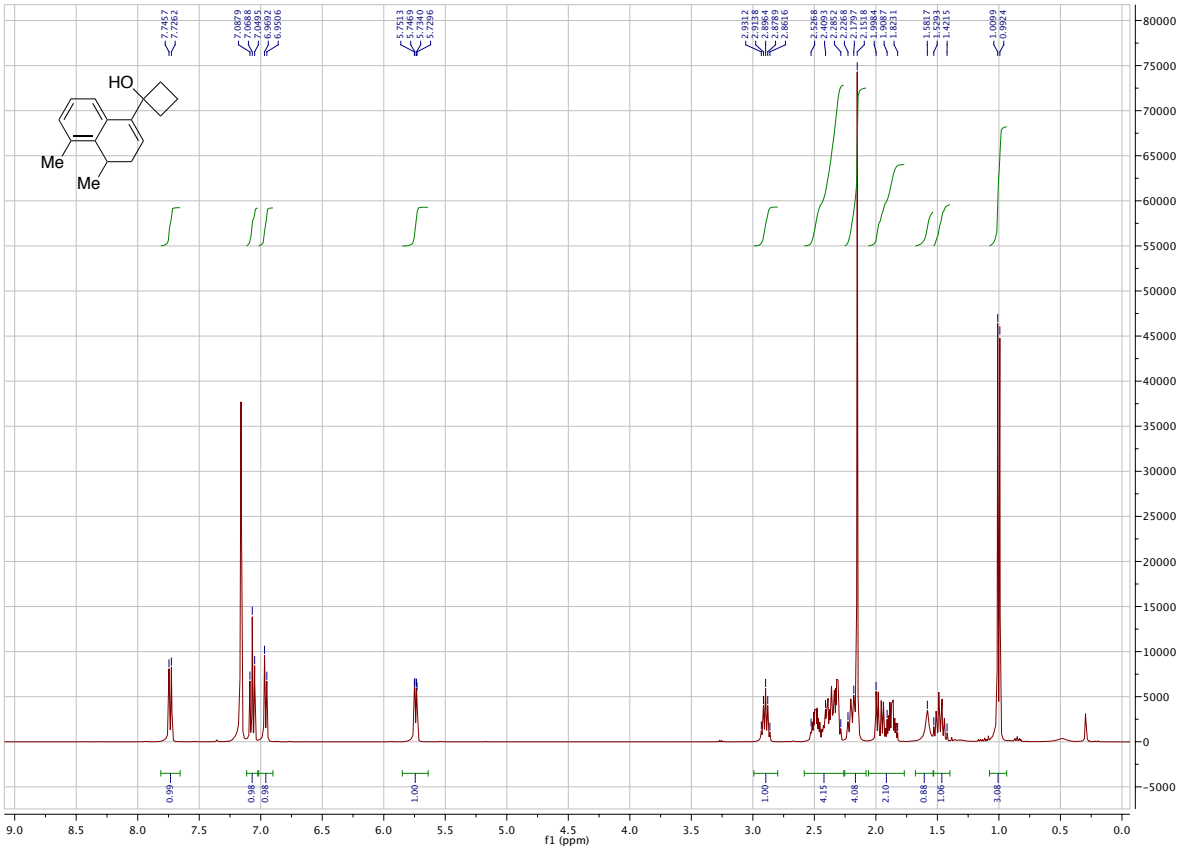


^{19}F NMR 375 MHz, C_6D_6

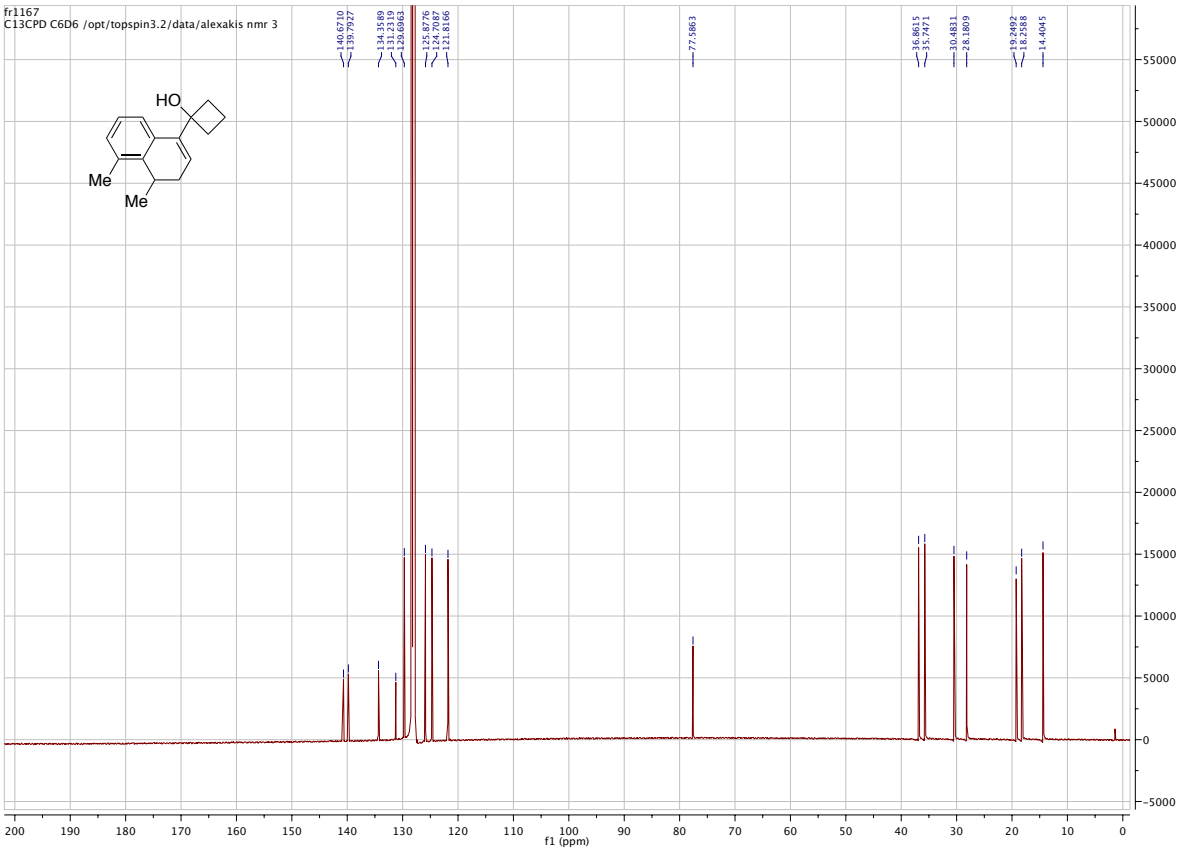


Substrate *rac*-A_2

^{1}H NMR 400 MHz, C_6D_6

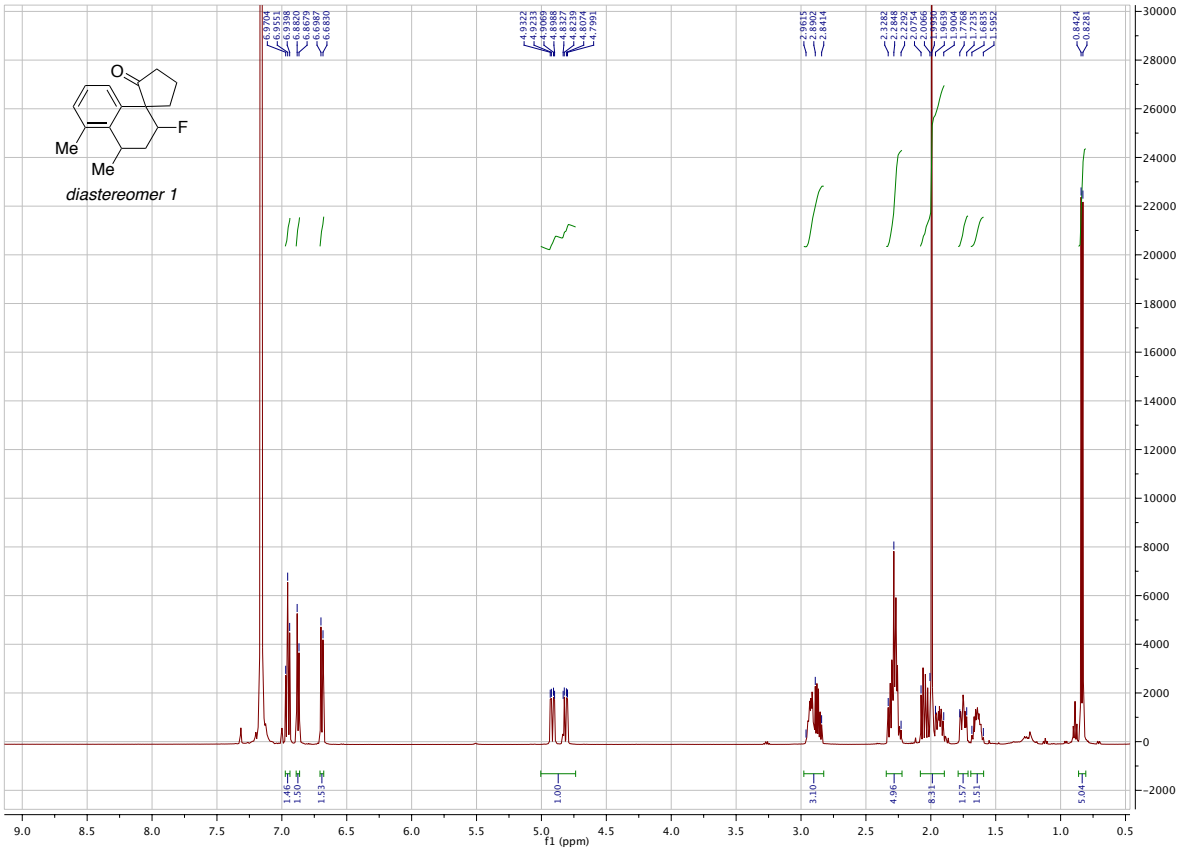


^{13}C NMR 100 MHz, C_6D_6

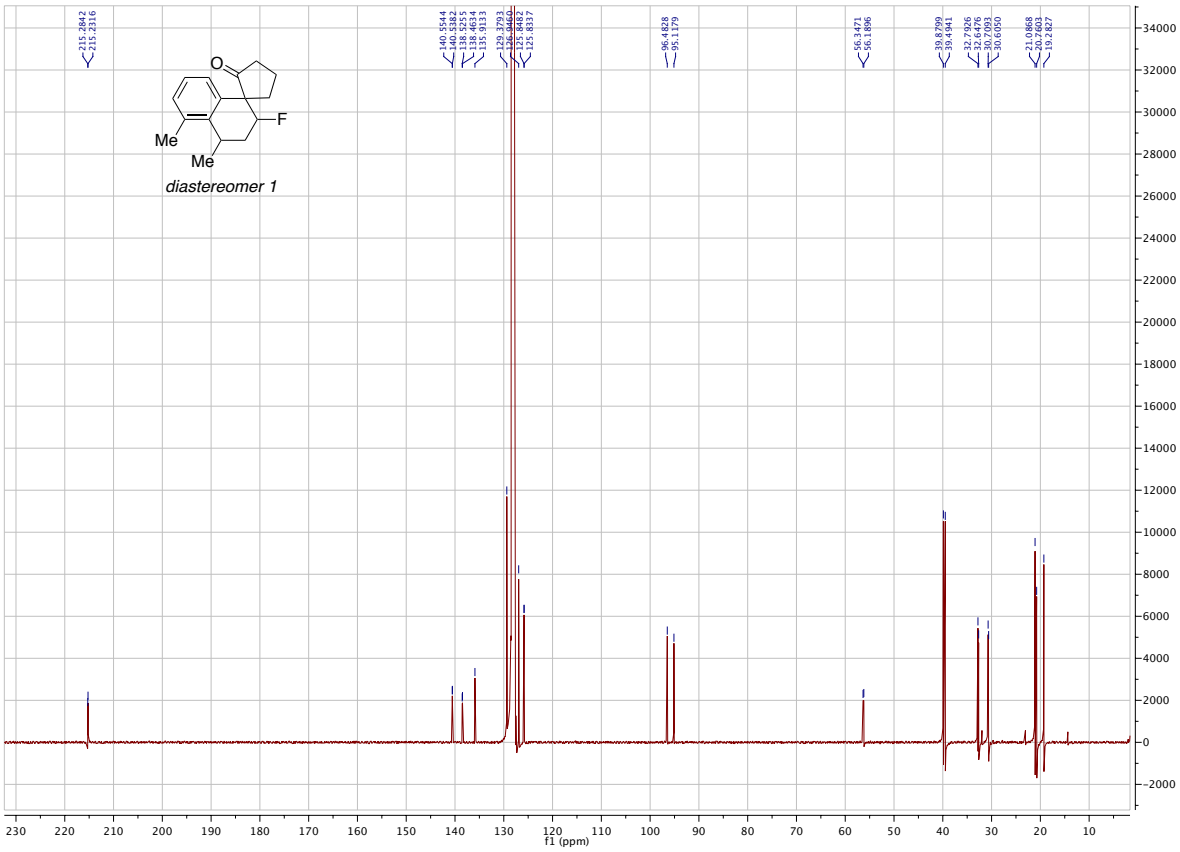


β-Fluoro Spiroketone B_2^R

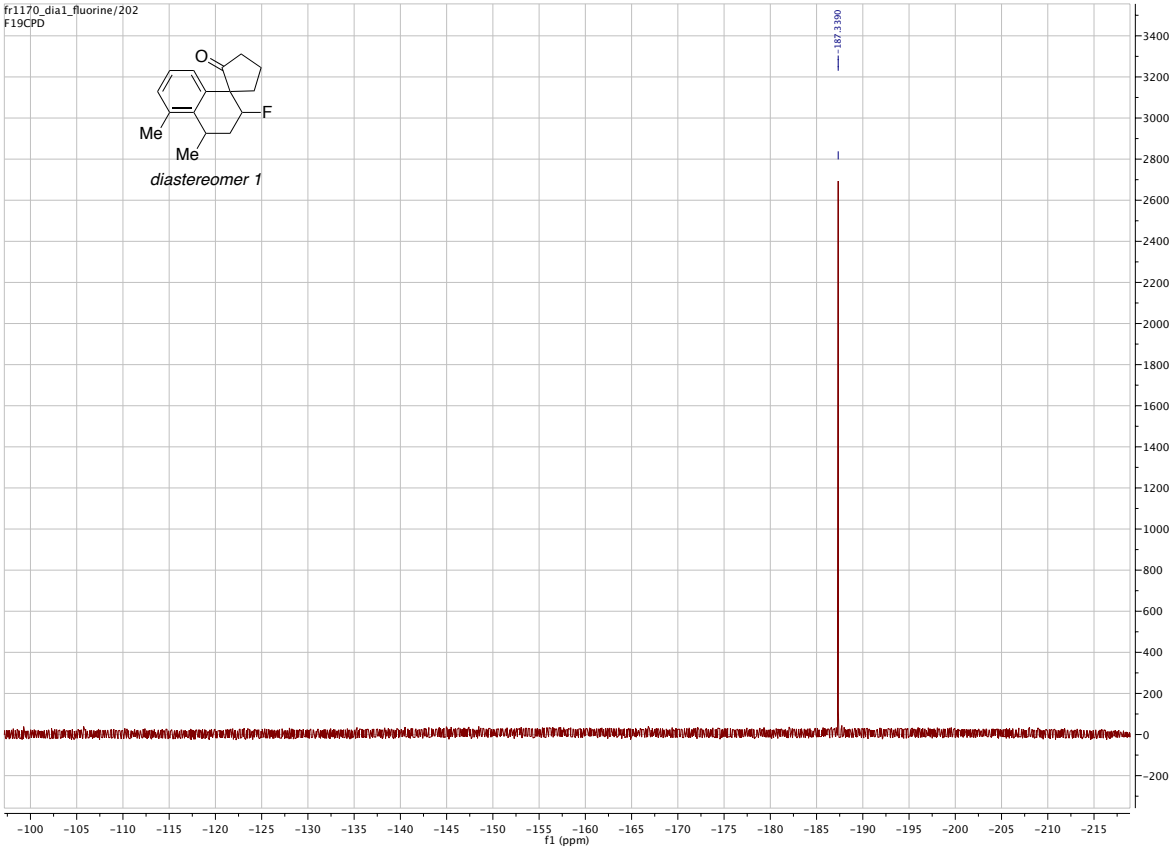
^{1}H NMR 500 MHz, C_6D_6



^{13}C NMR 125 MHz, C_6D_6

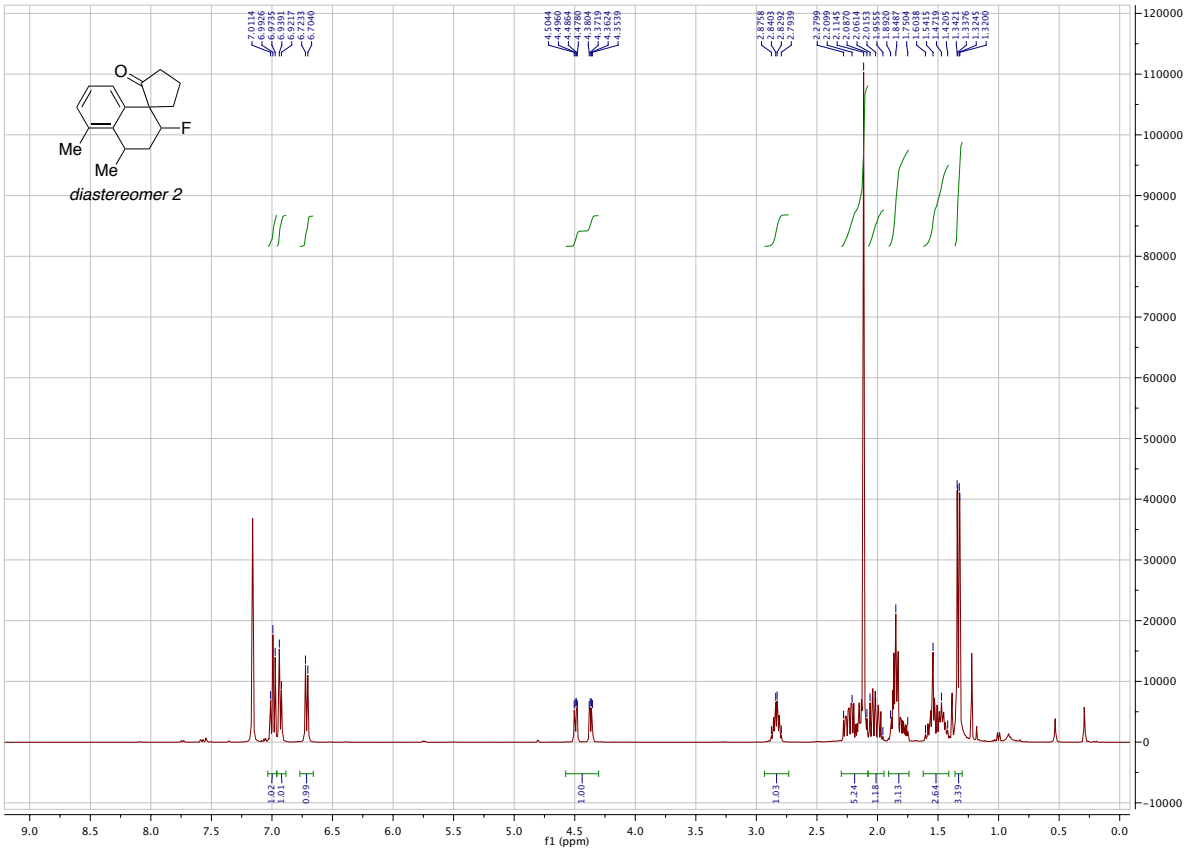


^{19}F NMR 375 MHz, C_6D_6

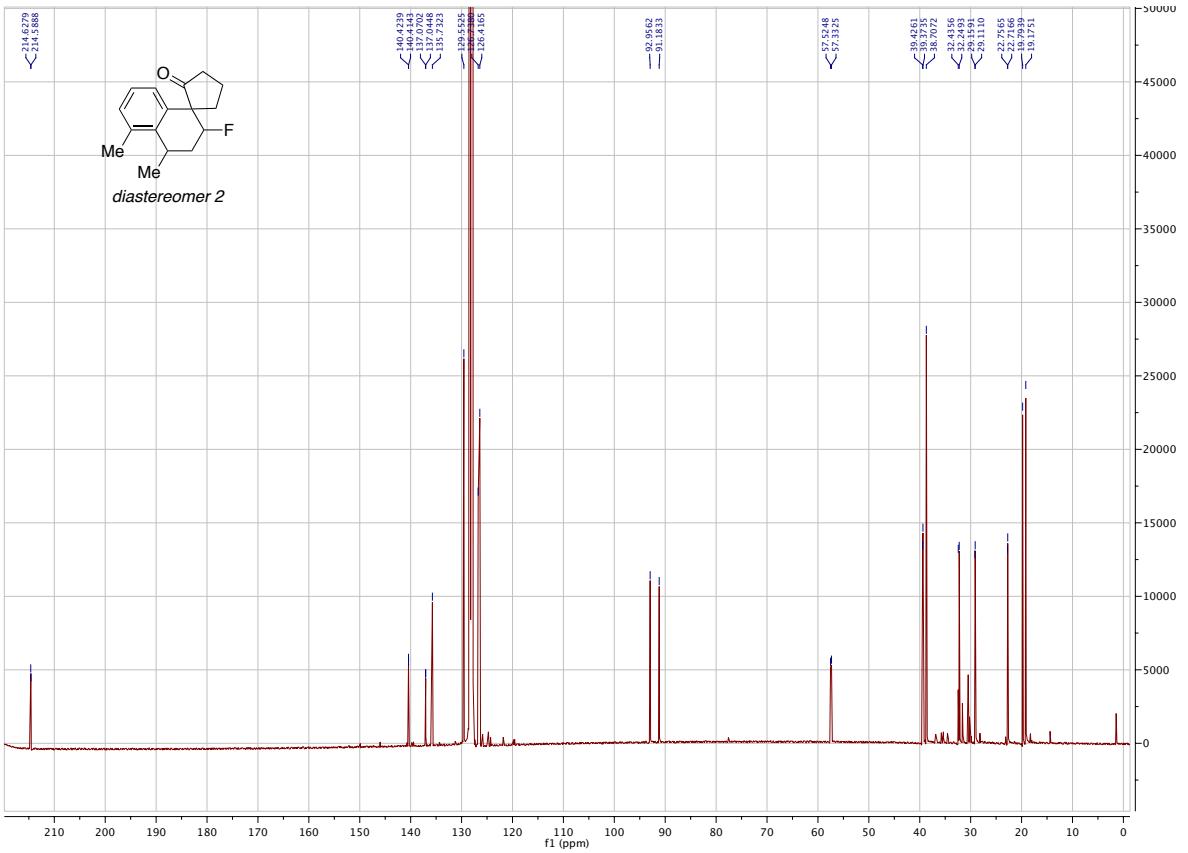


β-Fluoro Spiroketone B_2^S

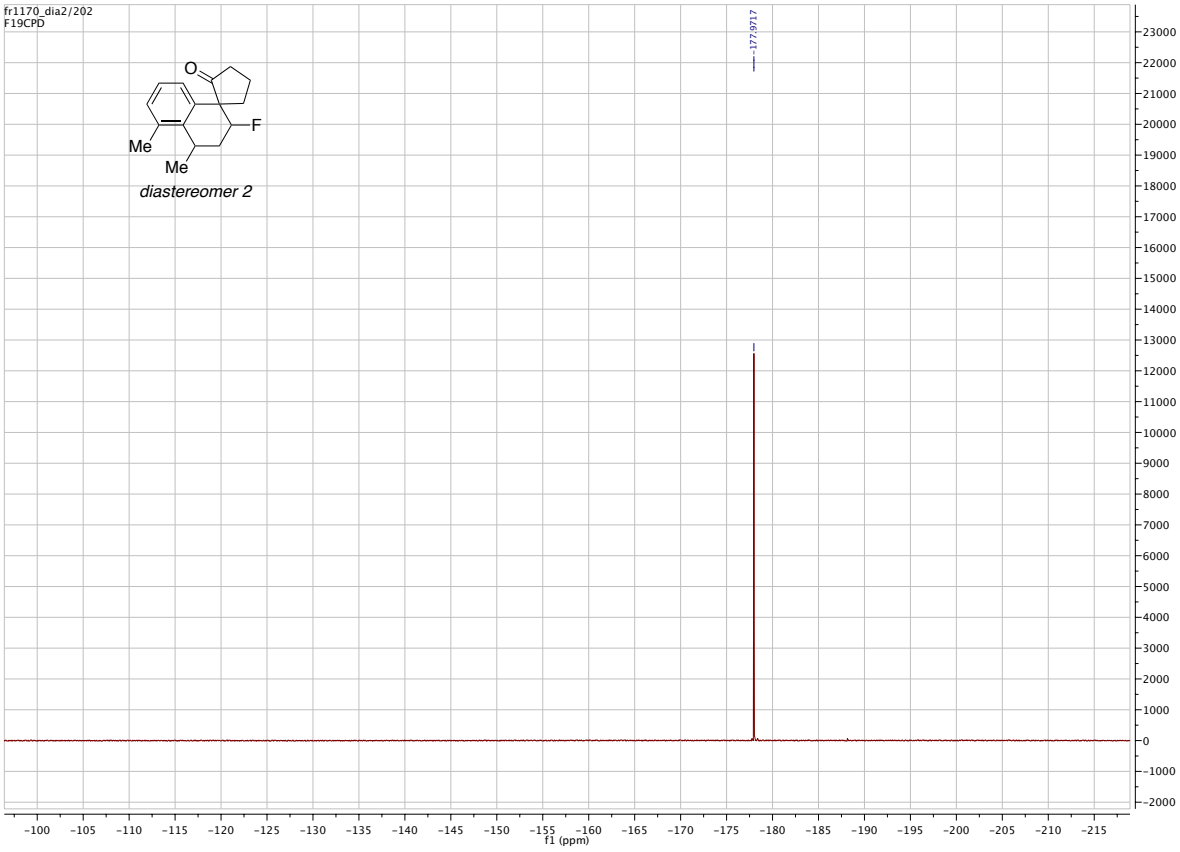
^{1}H NMR 400 MHz, C_6D_6



^{13}C NMR 100 MHz, C_6D_6

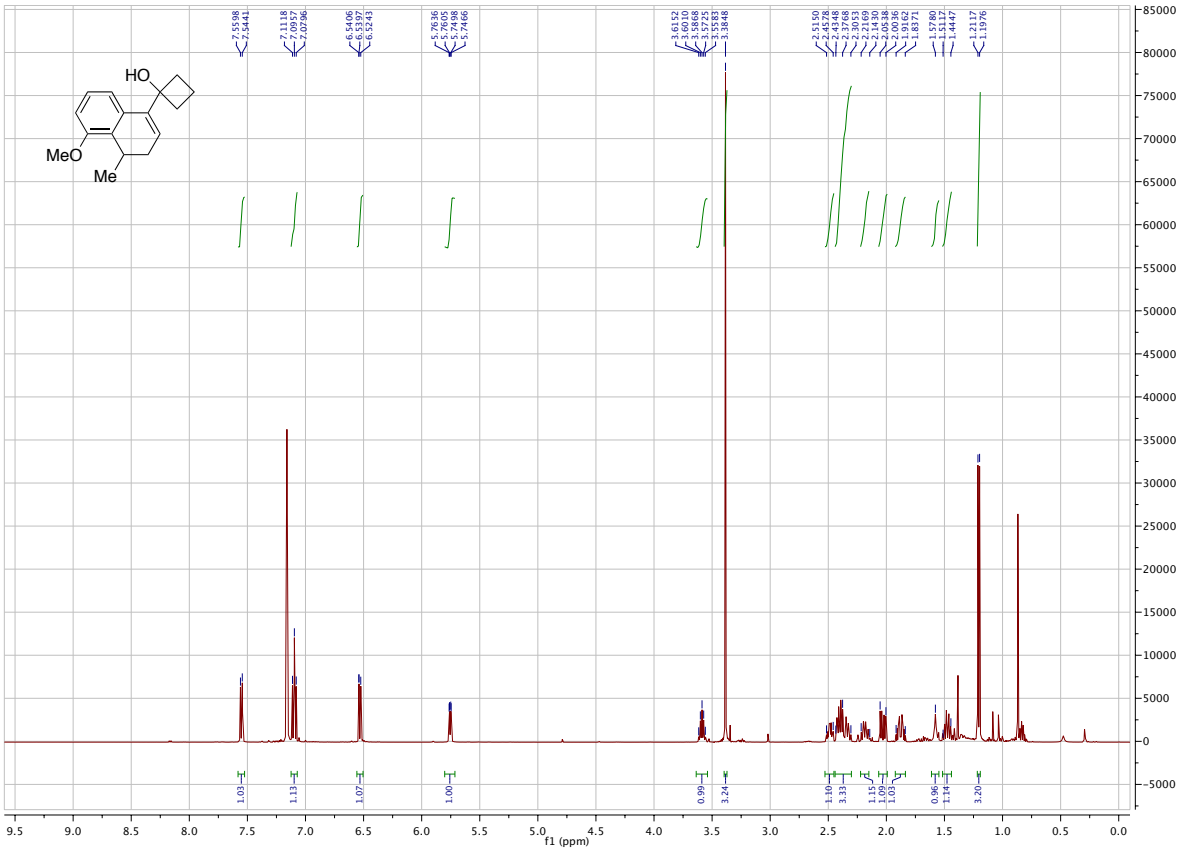


^{19}F NMR 375 MHz, C_6D_6

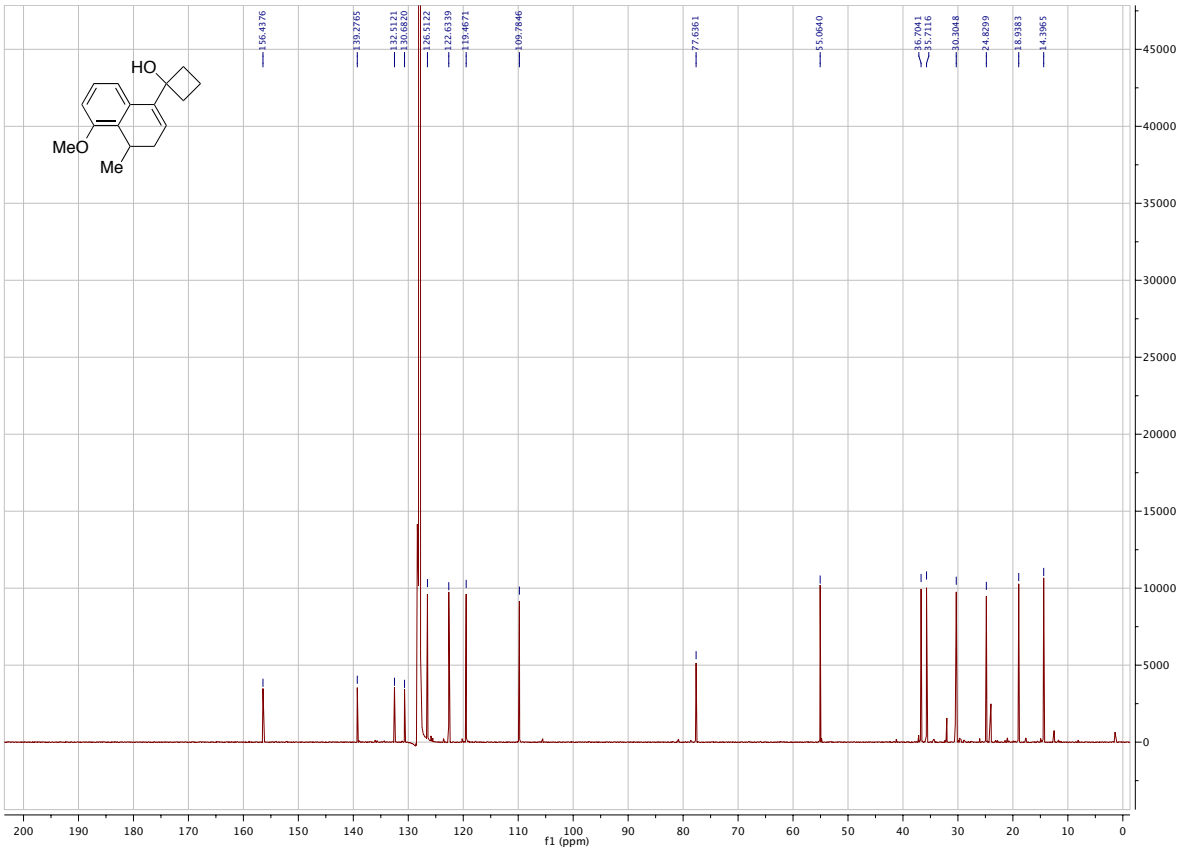


Substrate *rac*-A_3

^{1}H NMR 500 MHz, C_6D_6

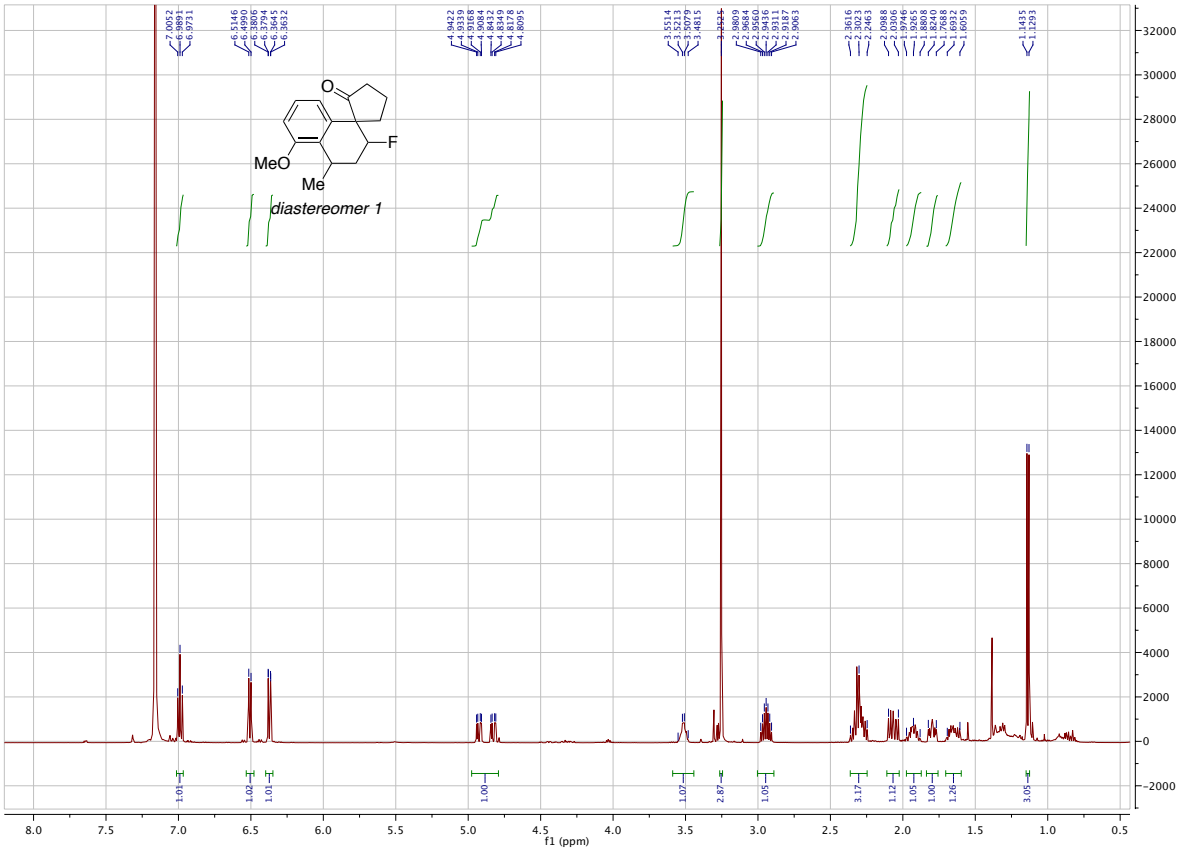


^{13}C NMR 125 MHz, C_6D_6

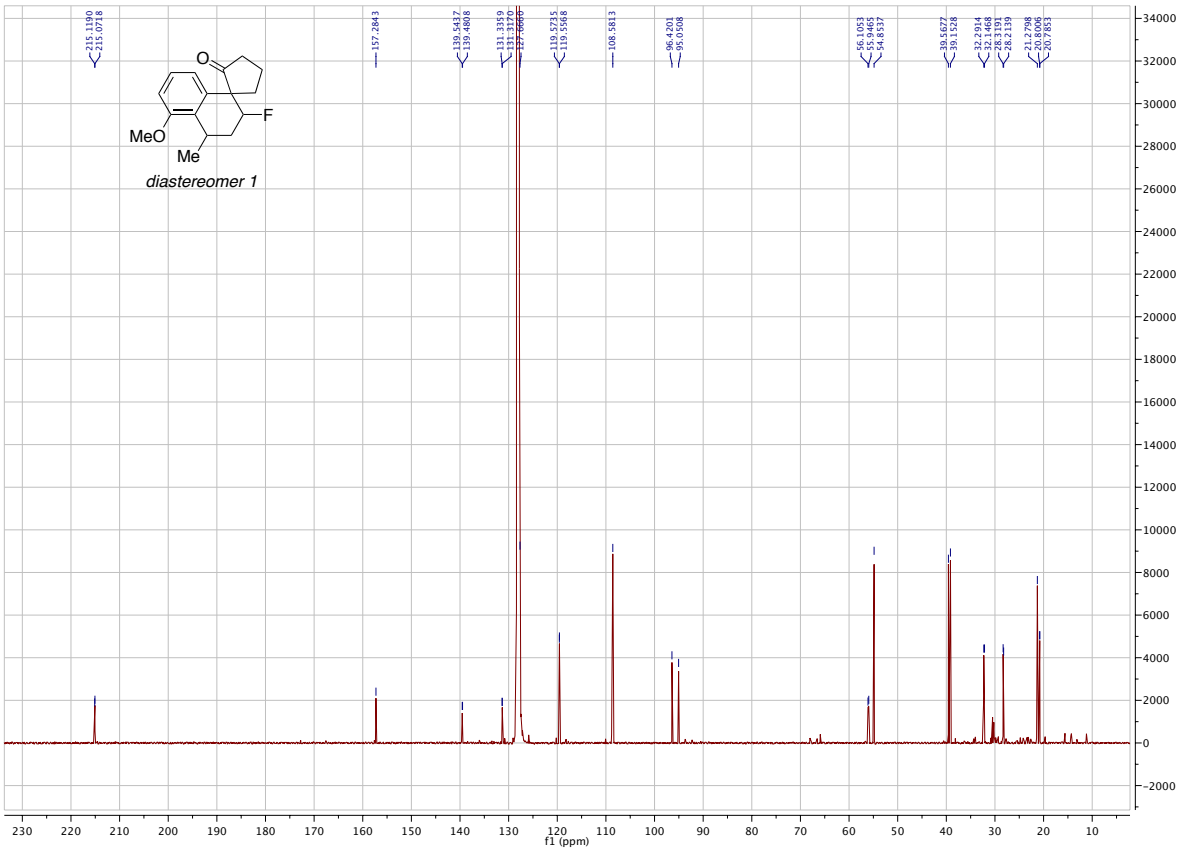


β-Fluoro Spiroketone B_3^R

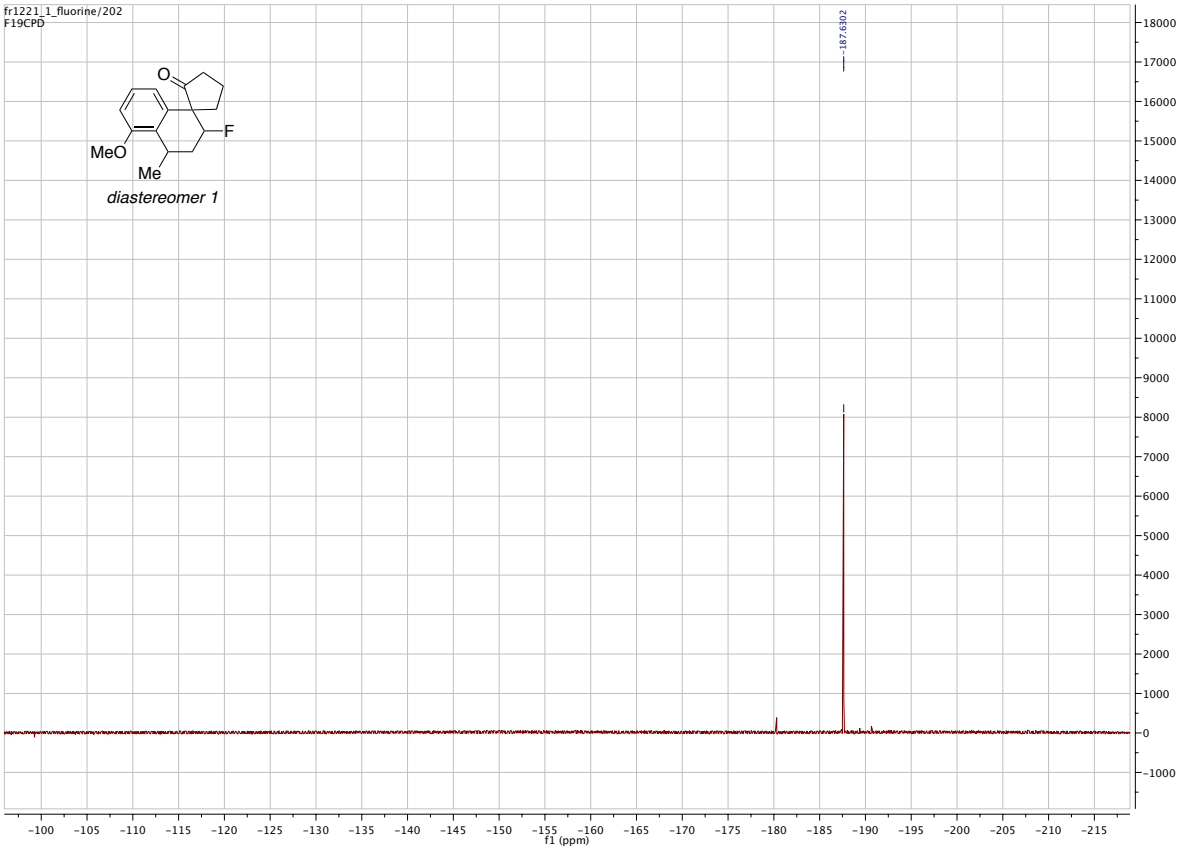
^{1}H NMR 500 MHz, C_6D_6



^{13}C NMR 125 MHz, C_6D_6

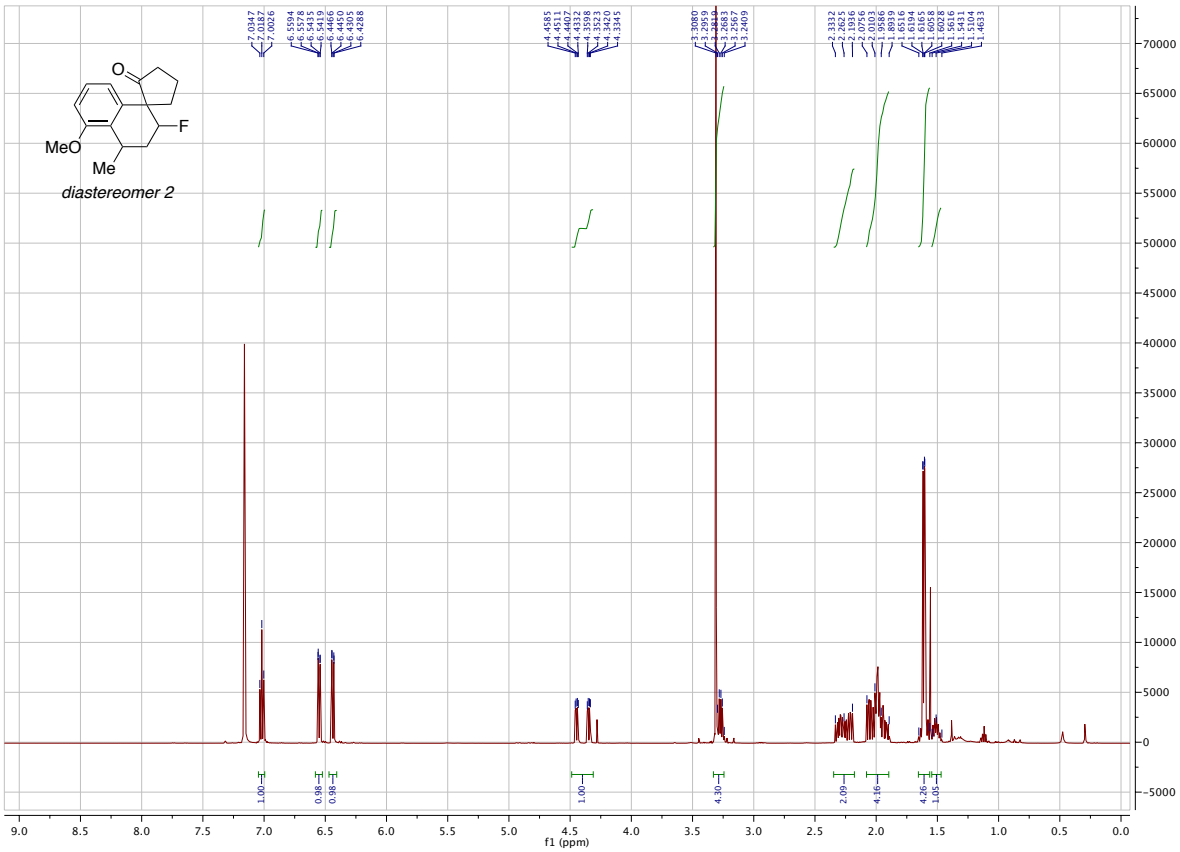


^{19}F NMR 375 MHz, C_6D_6

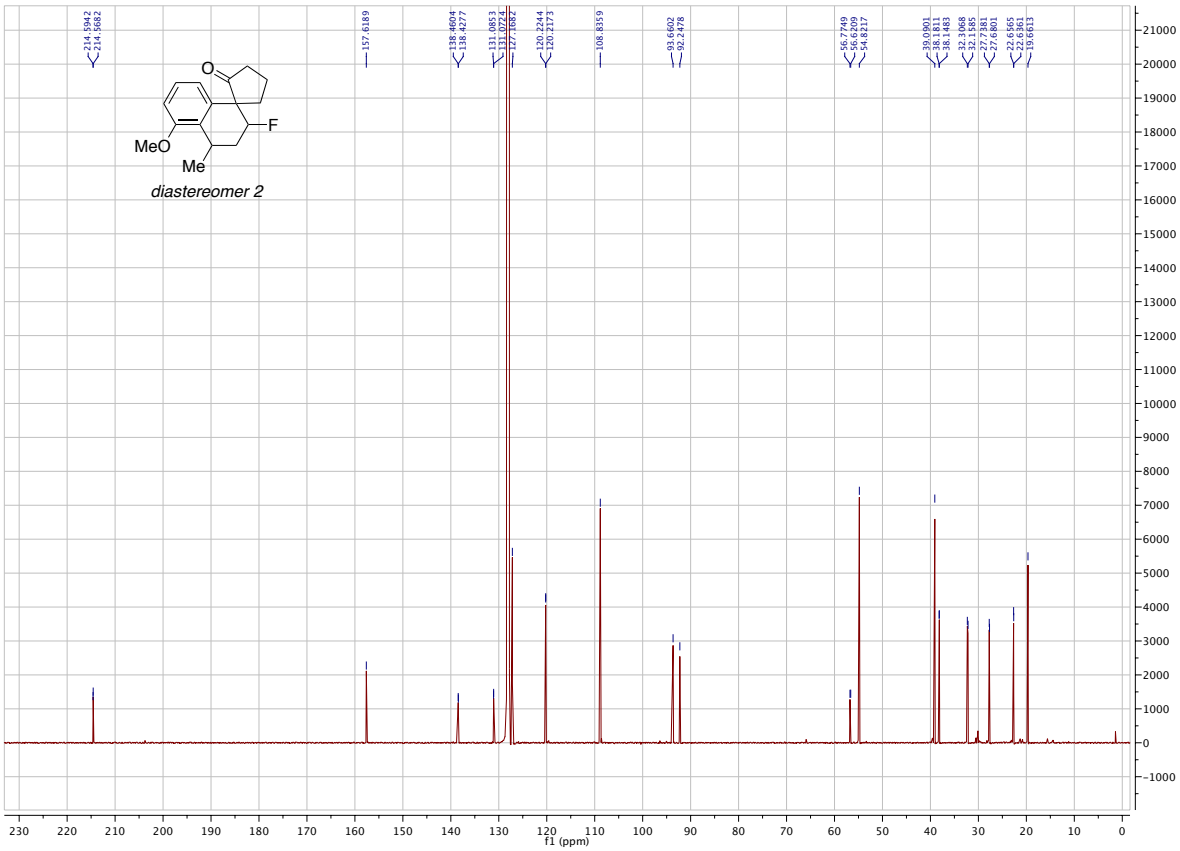


β-Fluoro Spiroketone B_3^S

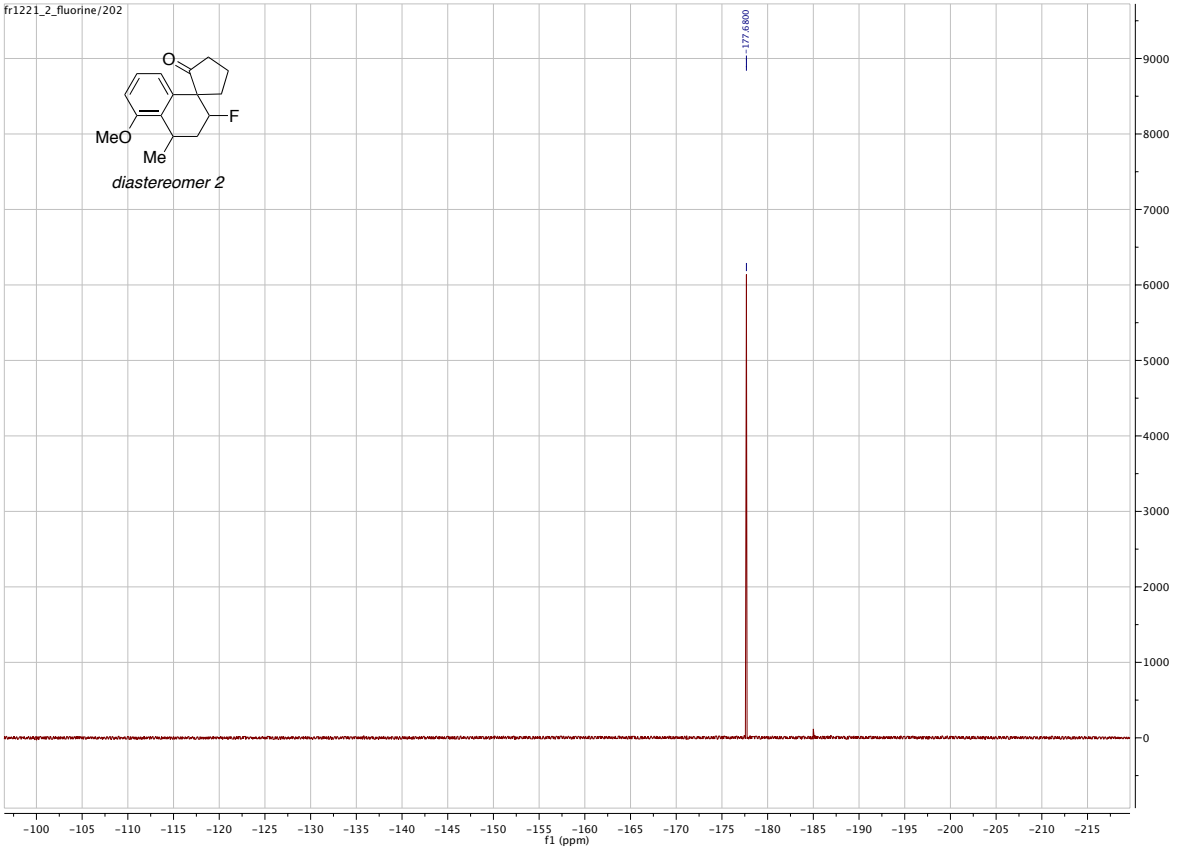
^{1}H NMR 500 MHz, C_6D_6



^{13}C NMR 125 MHz, C_6D_6

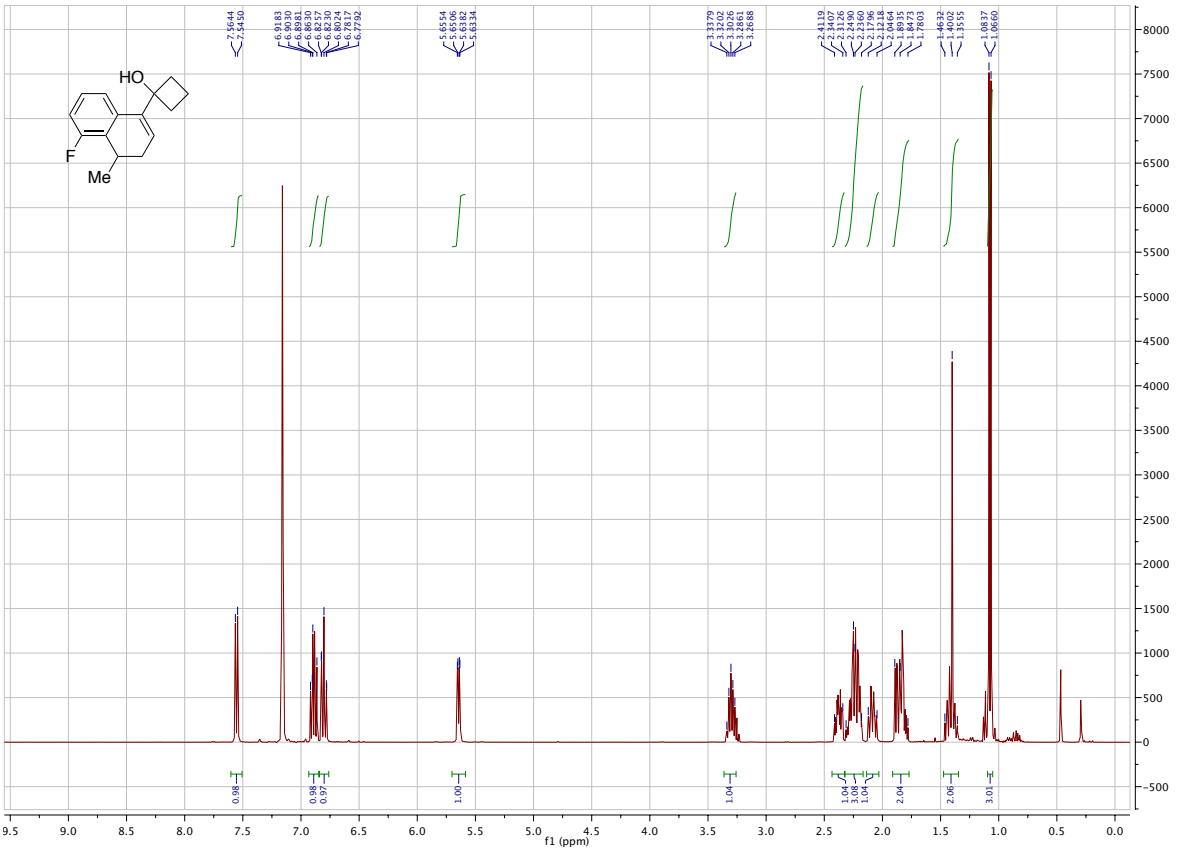


^{19}F NMR 375 MHz, C_6D_6

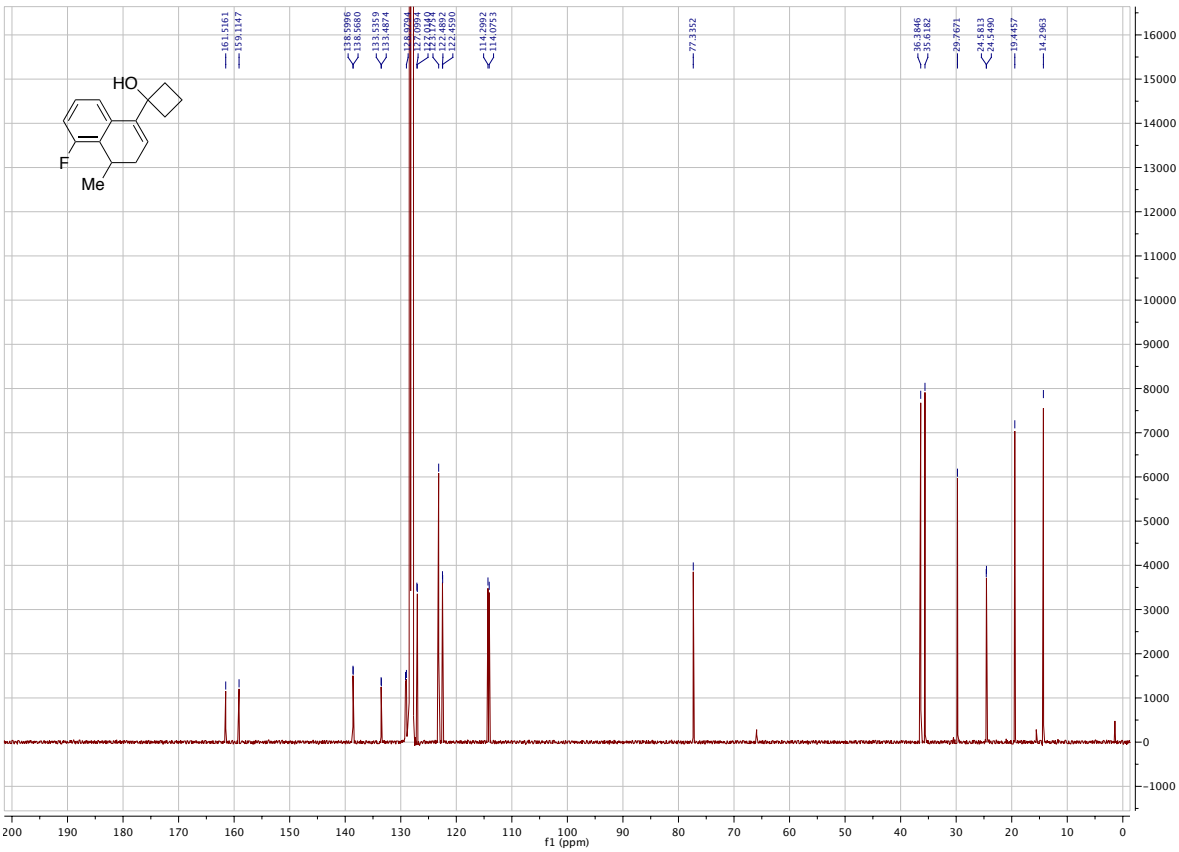


Substrate *rac*-A_4

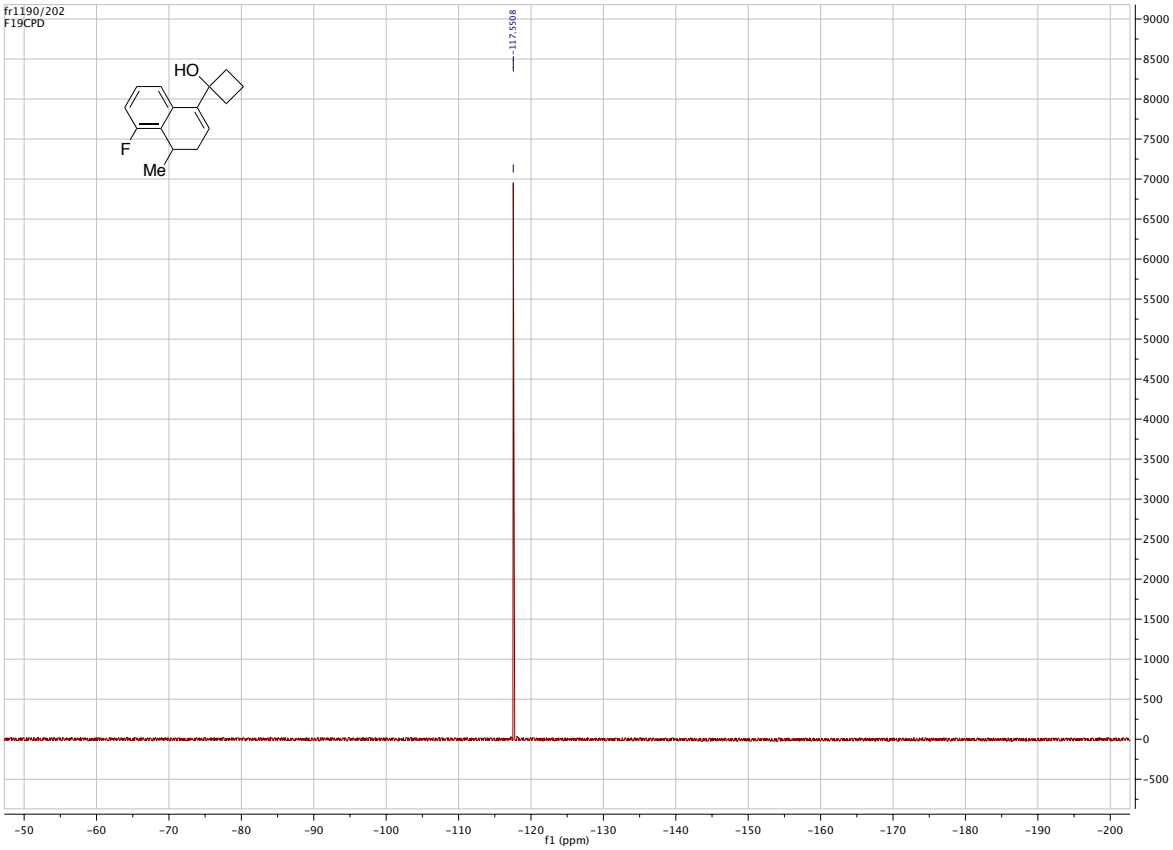
^{1}H NMR 400 MHz, C_6D_6



^{13}C NMR 100 MHz, C_6D_6

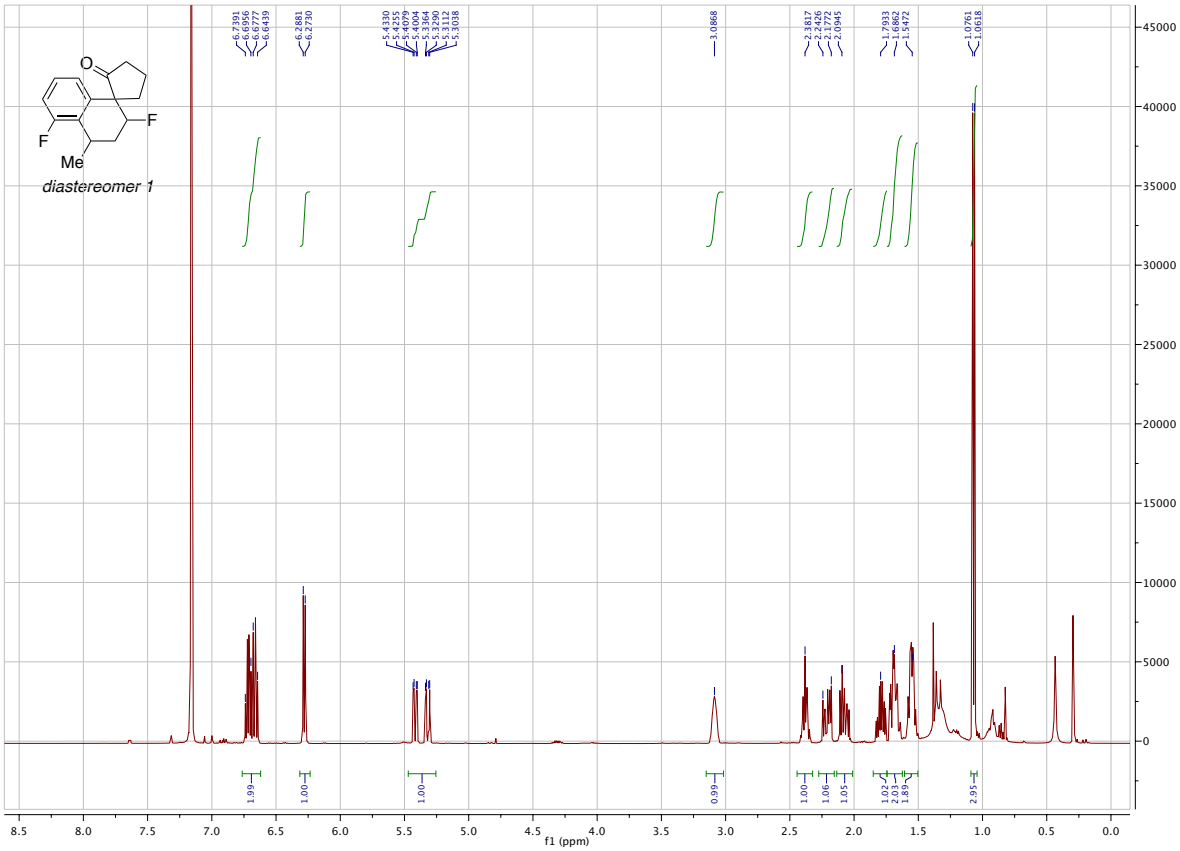


^{19}F NMR 375 MHz, C_6D_6

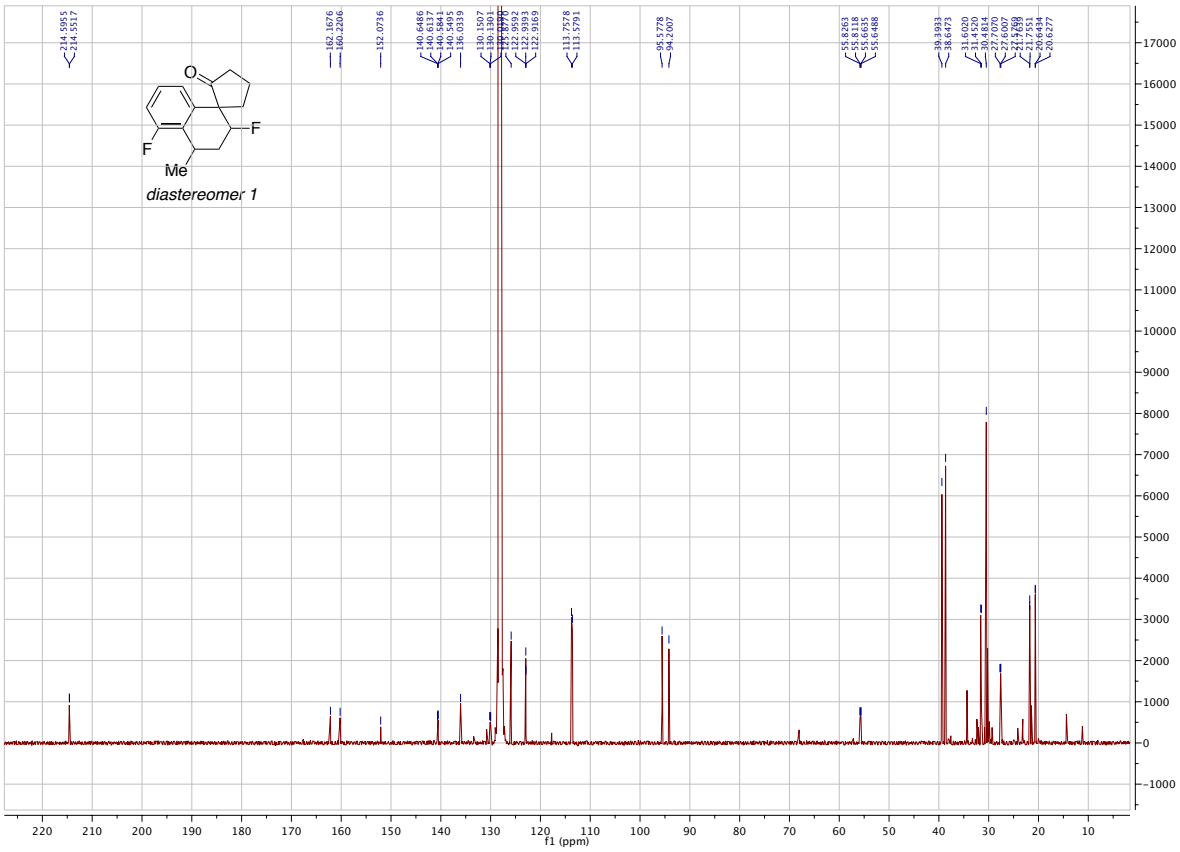


β-Fluoro Spiroketone B_4^R

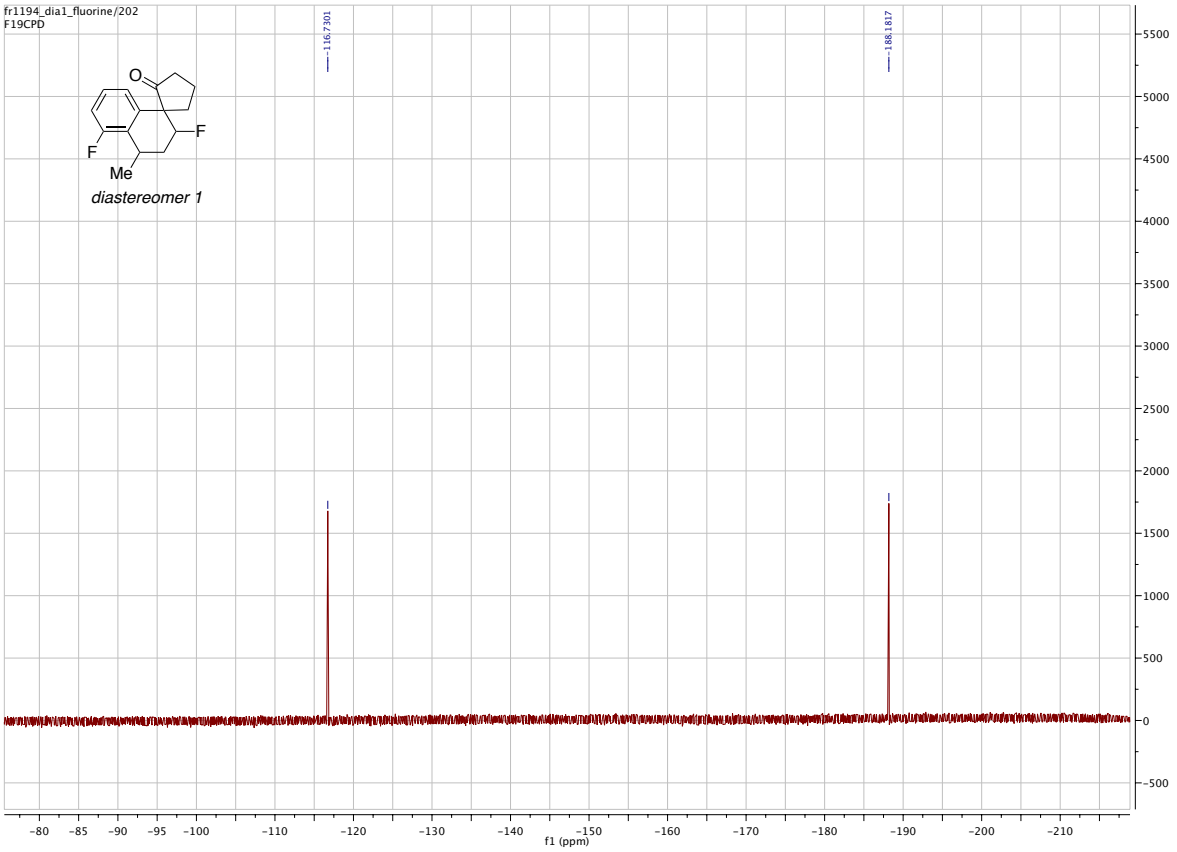
^{1}H NMR 500 MHz, C_6D_6



^{13}C NMR 125 MHz, C_6D_6



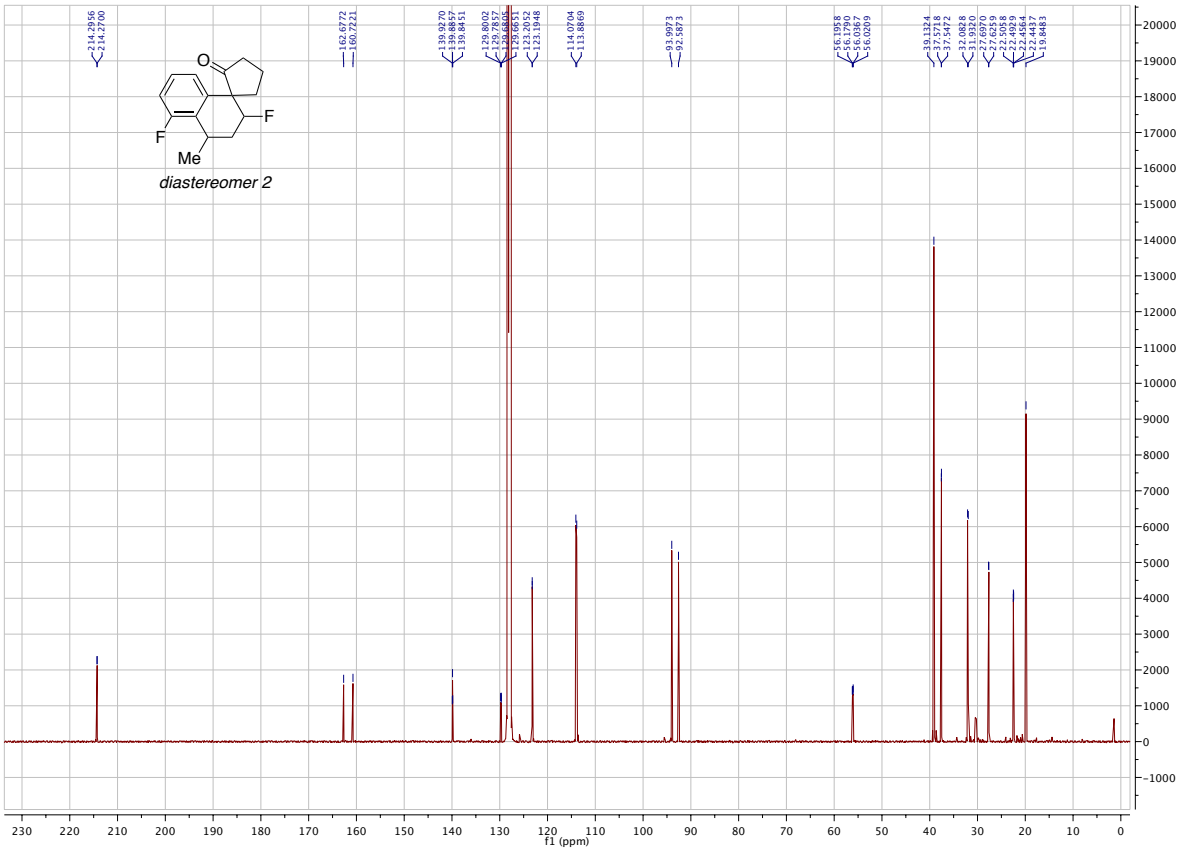
^{19}F NMR 375 MHz, C_6D_6



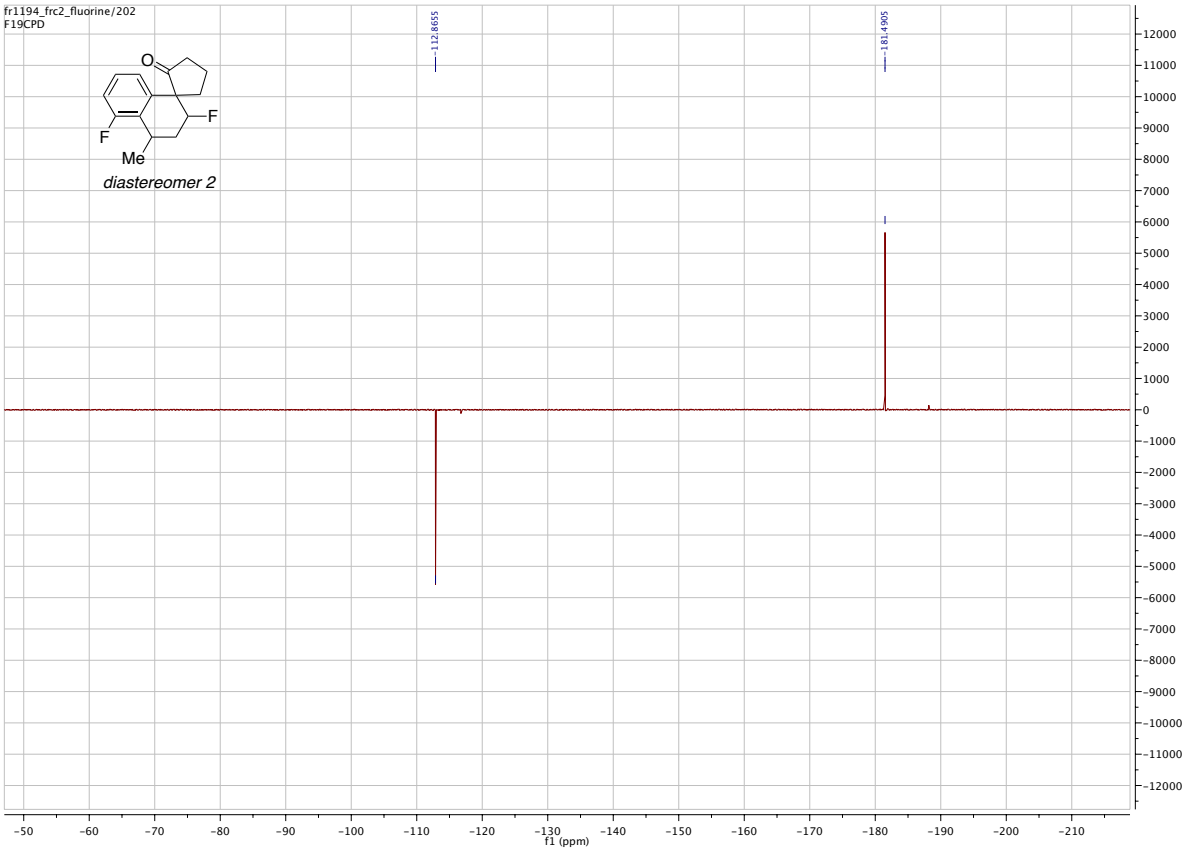
β-Fluoro Spiroketone B_4^S

^{1}H NMR 500 MHz, C_6D_6

^{13}C NMR 125 MHz, C_6D_6

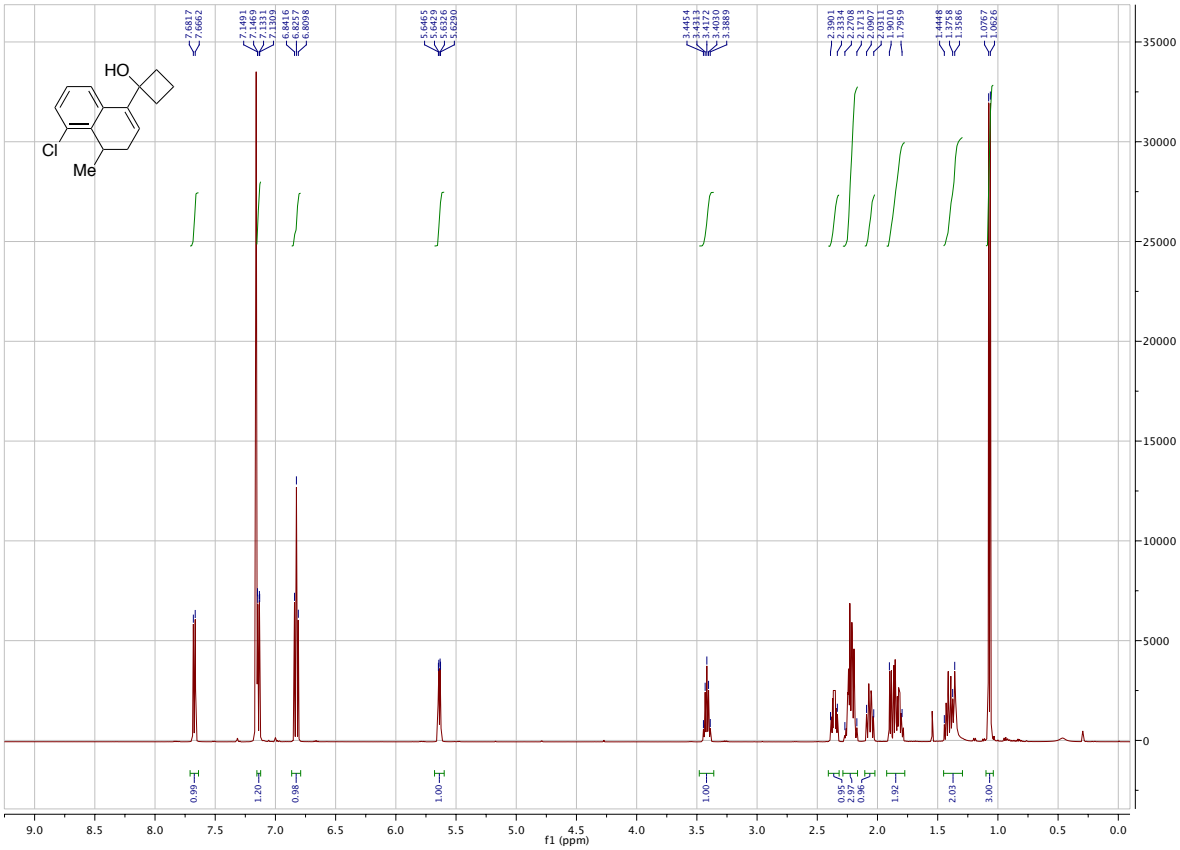


^{19}F NMR 375 MHz, C_6D_6

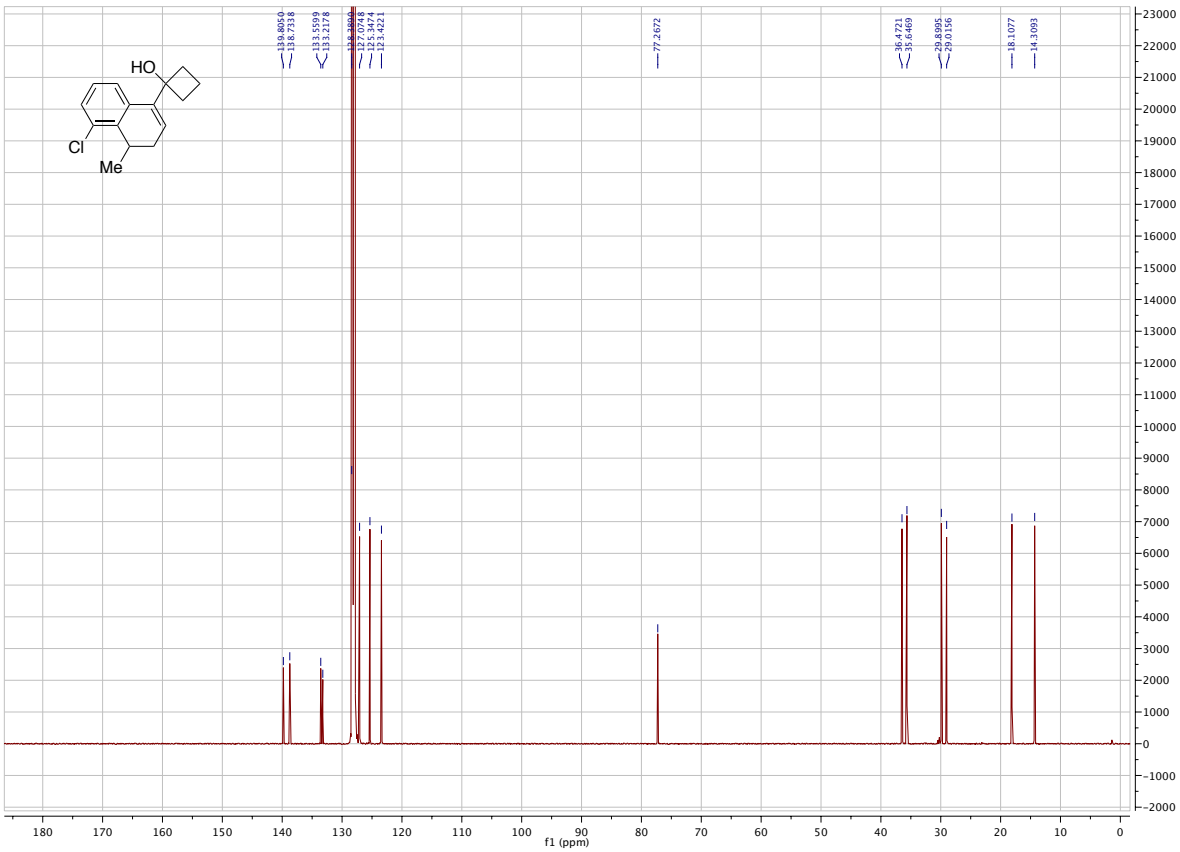


Substrate *rac*-A_5

^{1}H NMR 500 MHz, C_6D_6

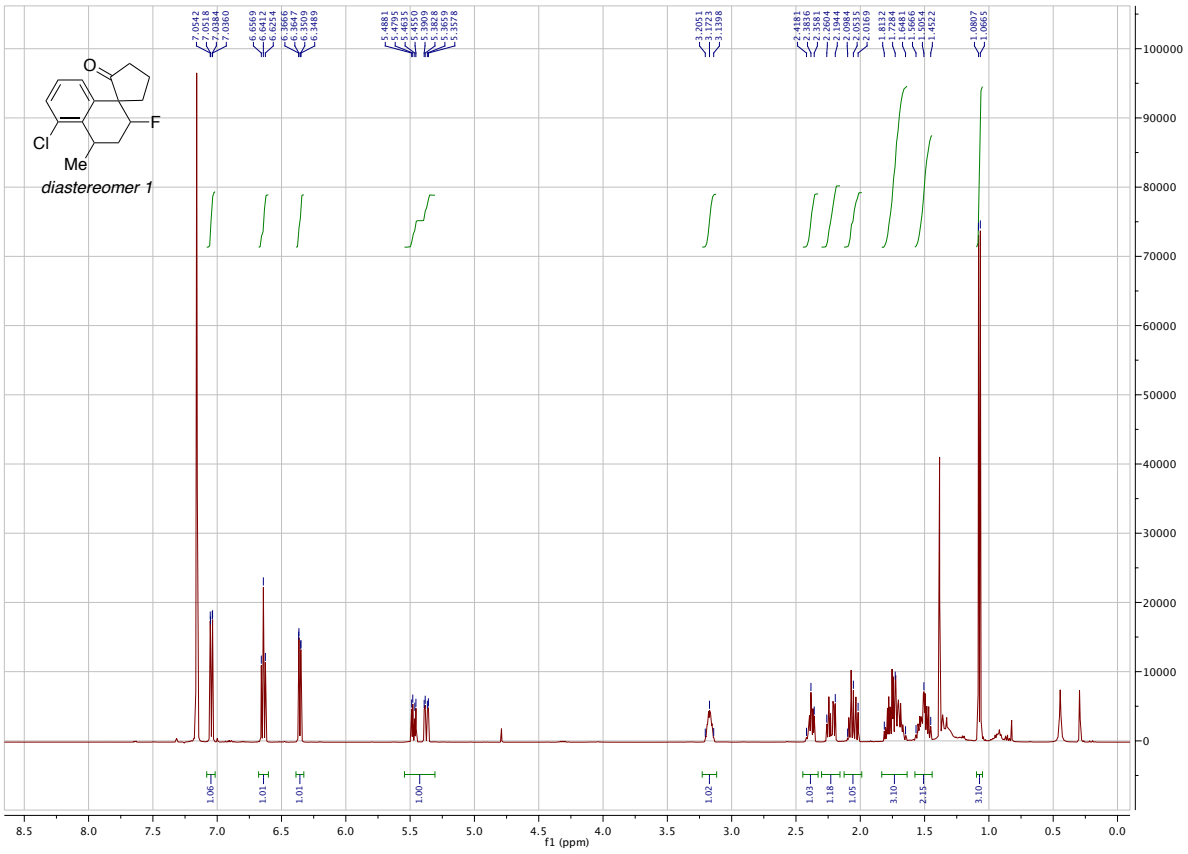


^{13}C NMR 125 MHz, C_6D_6

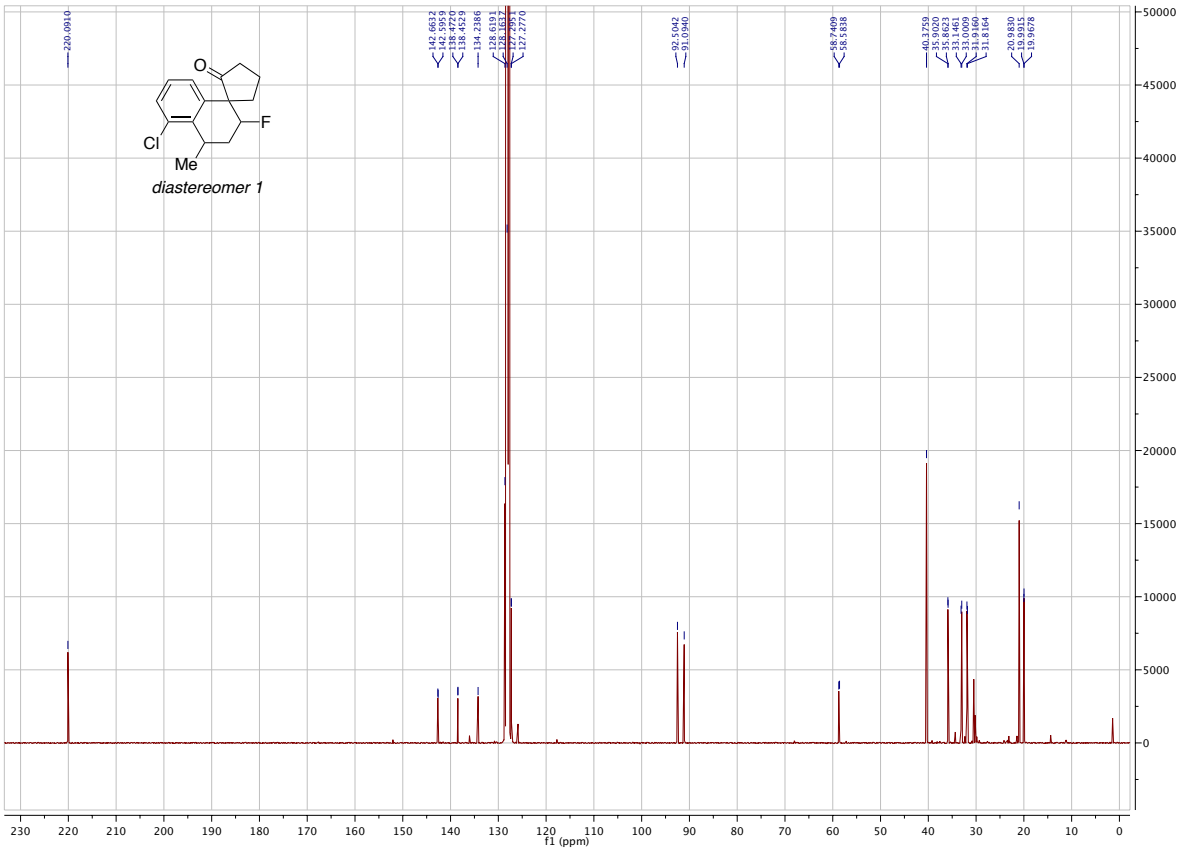


β-Fluoro Spiroketone B_5^R

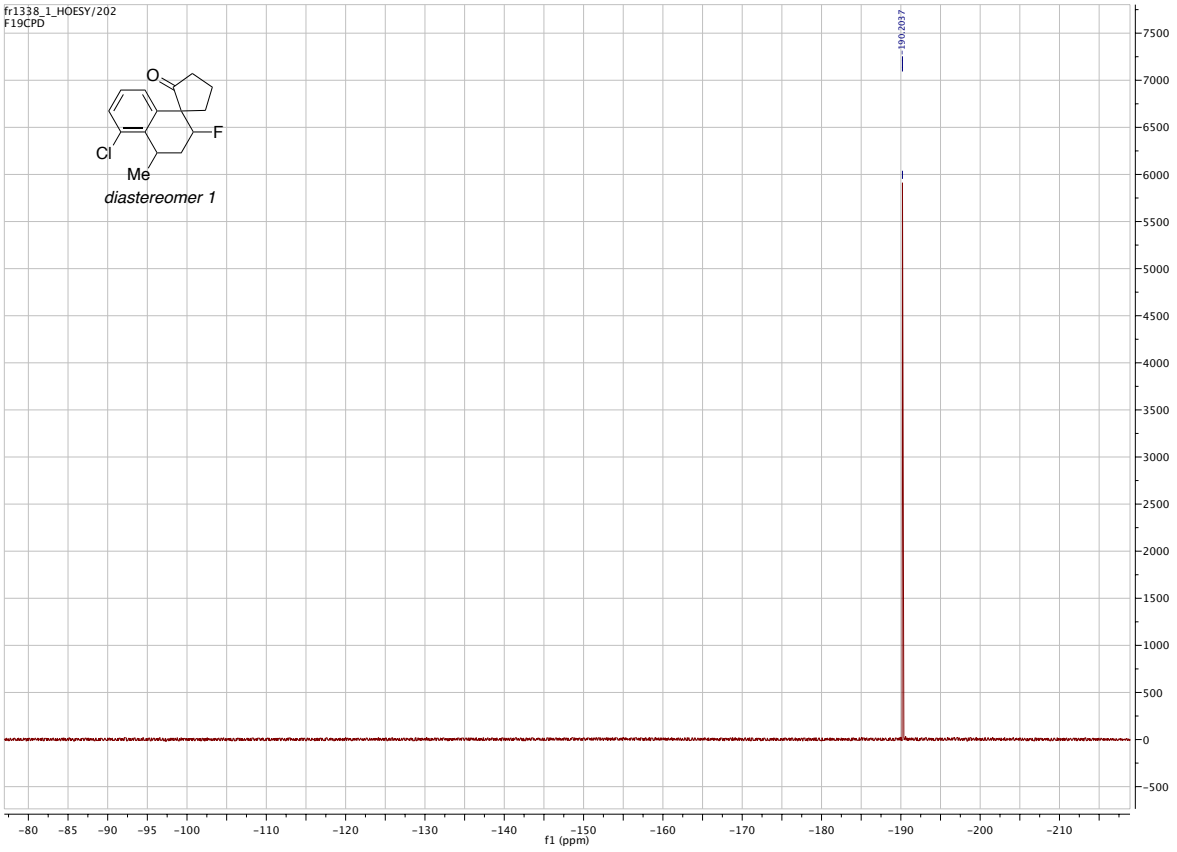
^{1}H NMR 500 MHz, C_6D_6



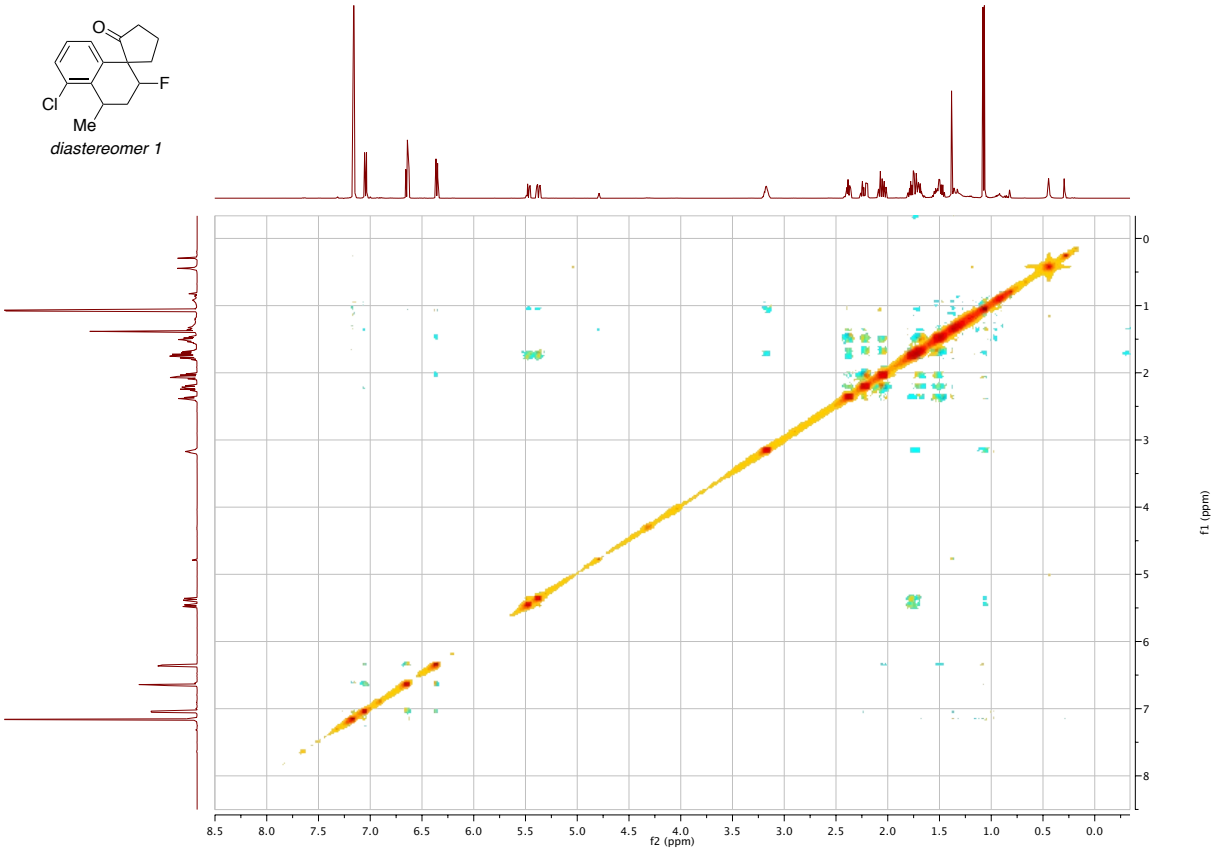
^{13}C NMR 125 MHz, C_6D_6



^{19}F NMR 375 MHz, C_6D_6

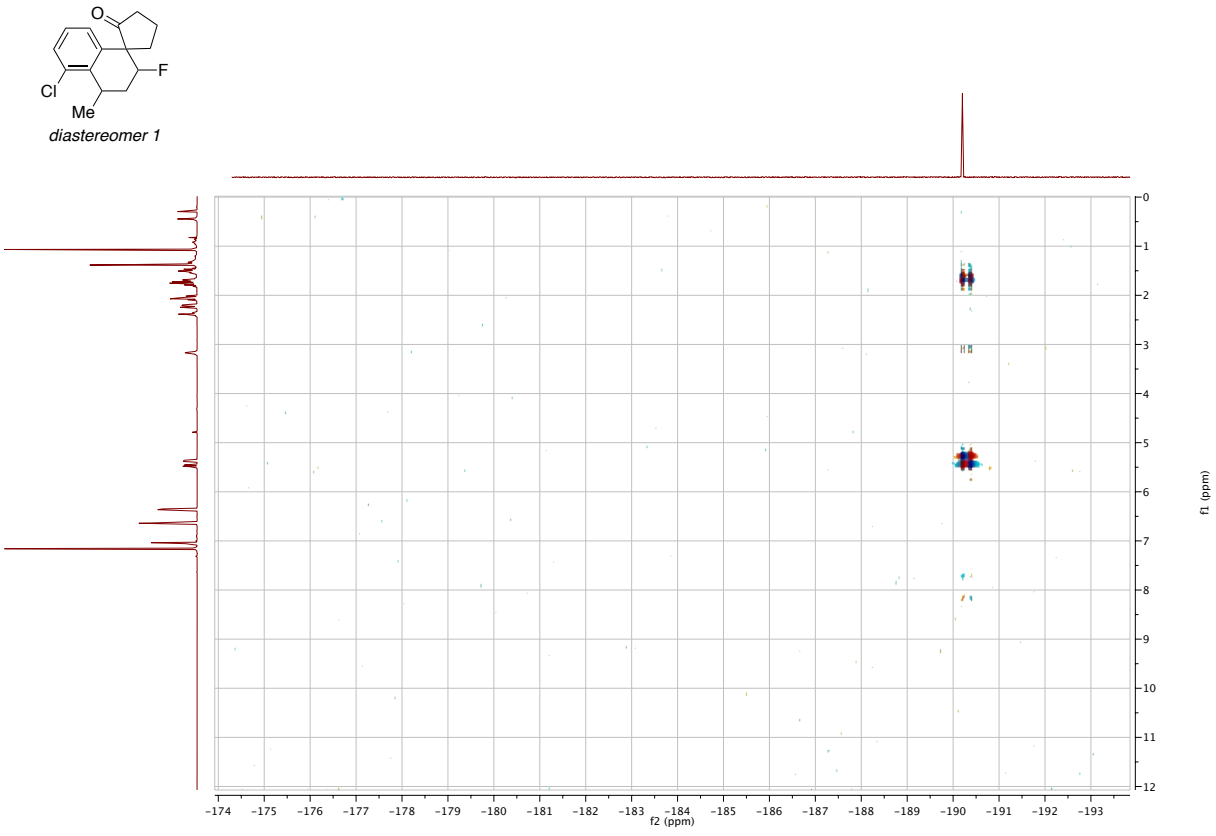


^{1}H-^{1}H NOESY 500 MHz, C_6D_6



diastereomer 1

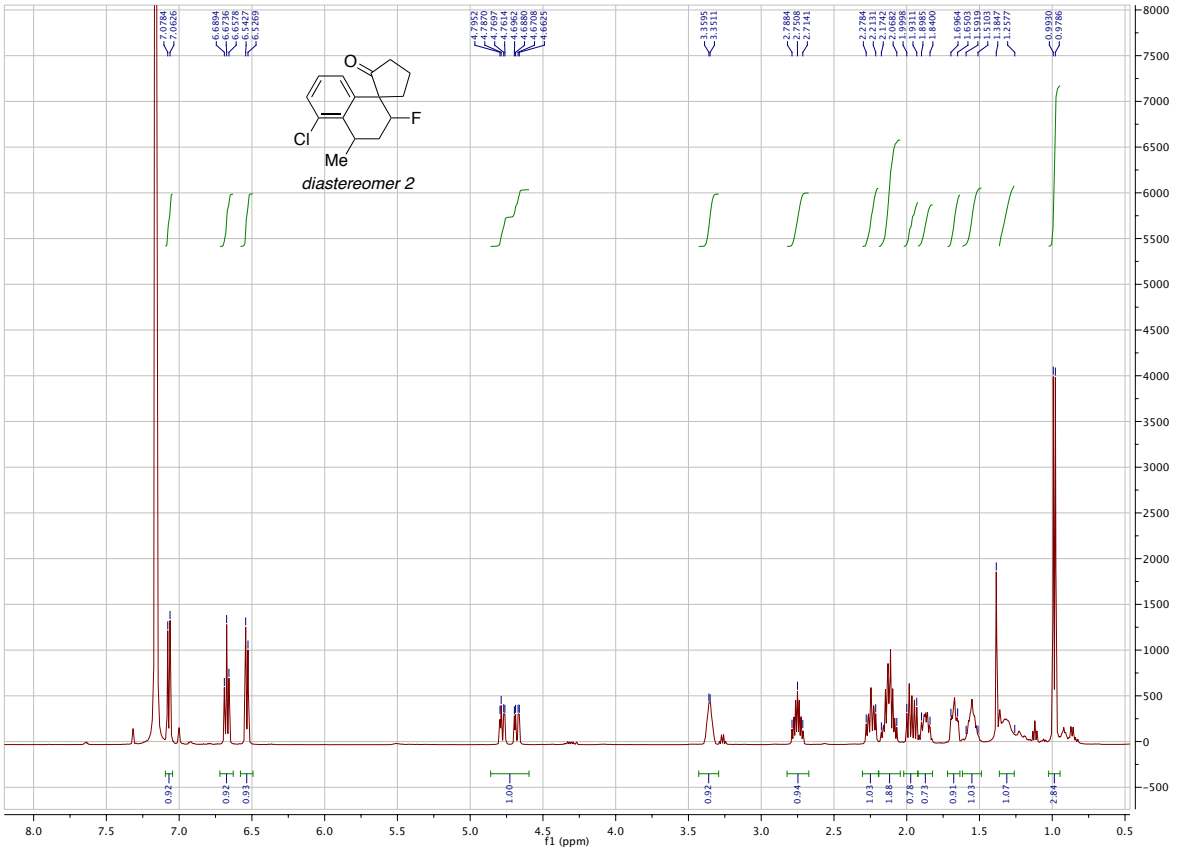
^{1}H-^{19}F HOESY 300 MHz, C_6D_6



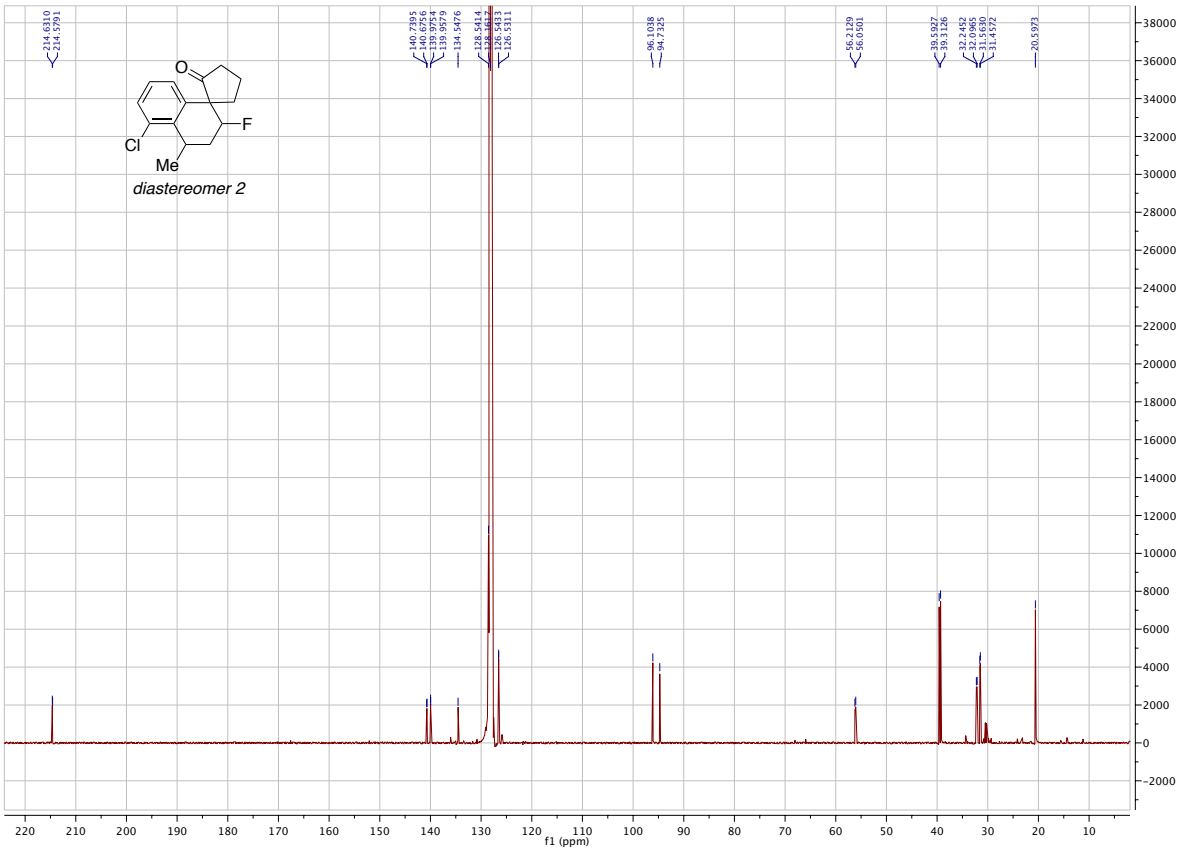
diastereomer 1

β-Fluoro Spiroketone B_5^S

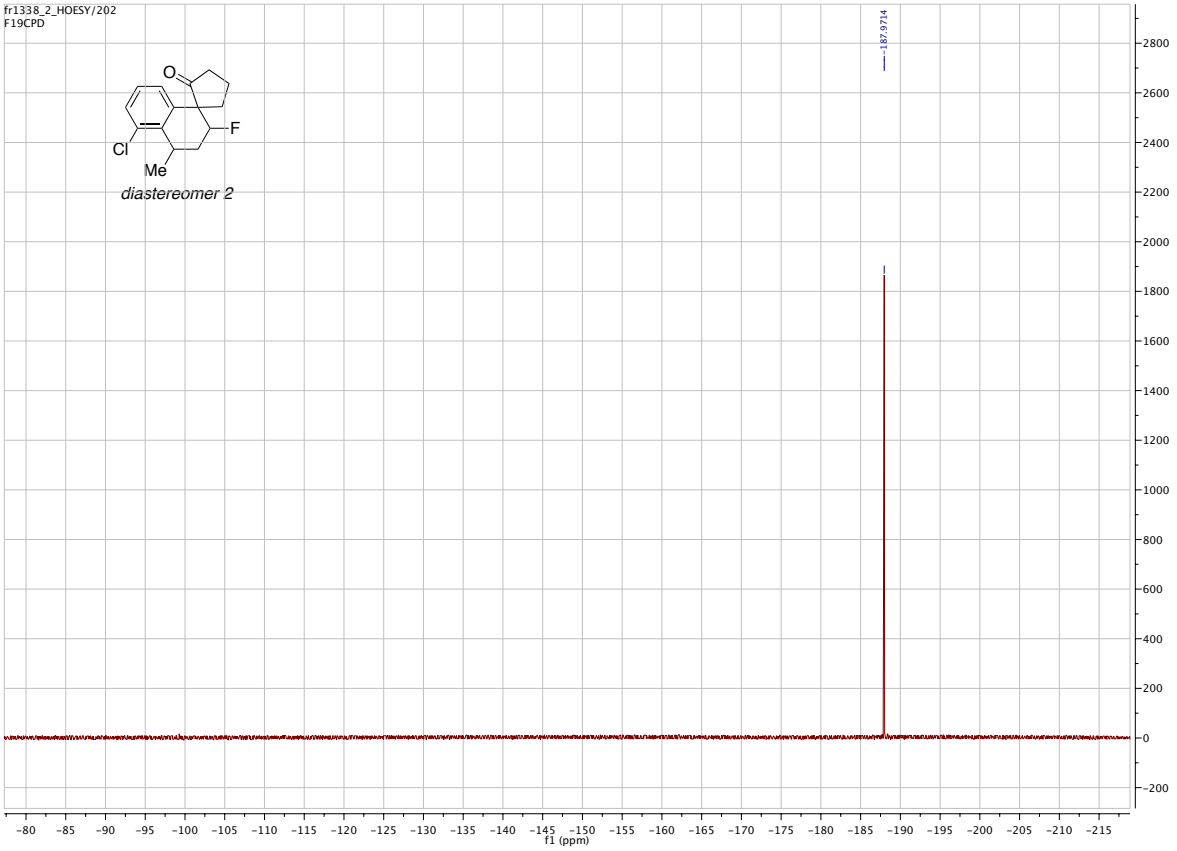
^{1}H NMR 500 MHz, C_6D_6



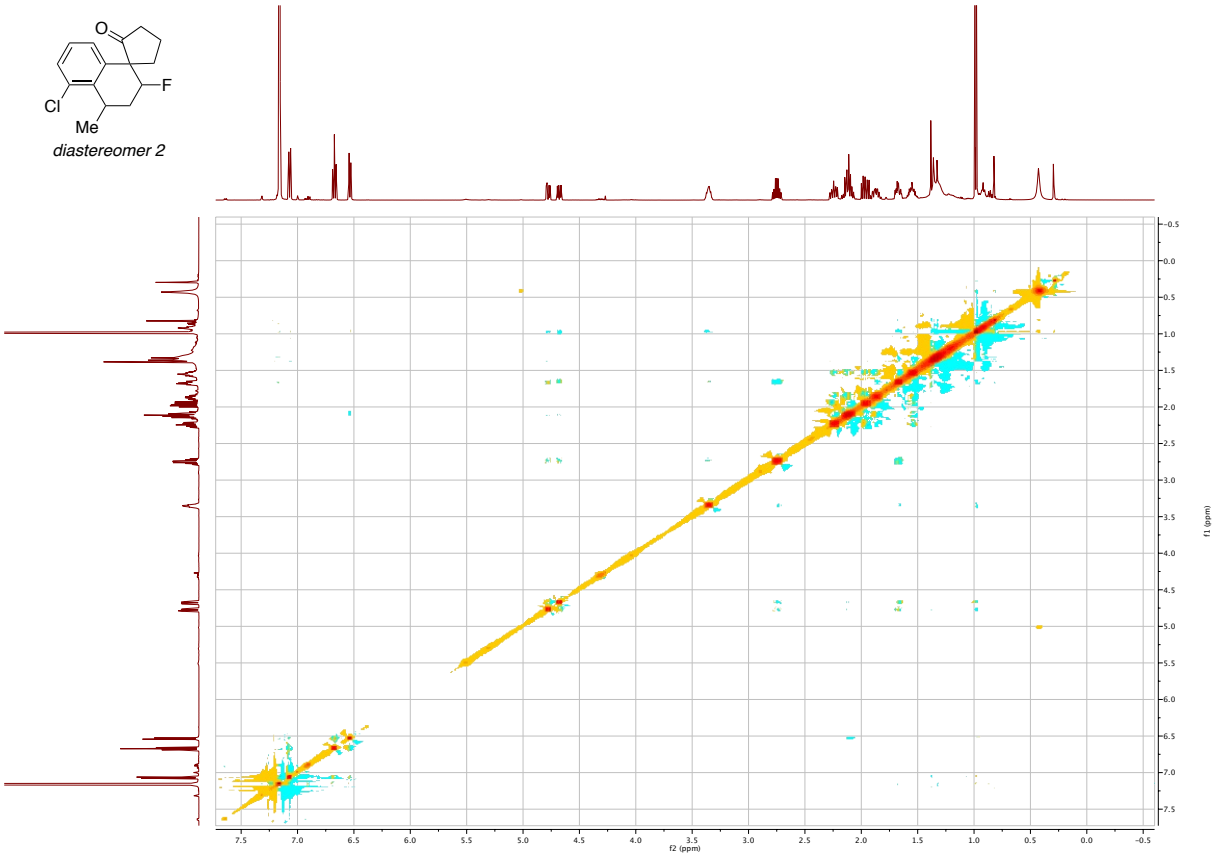
^{13}C NMR 125 MHz, C_6D_6



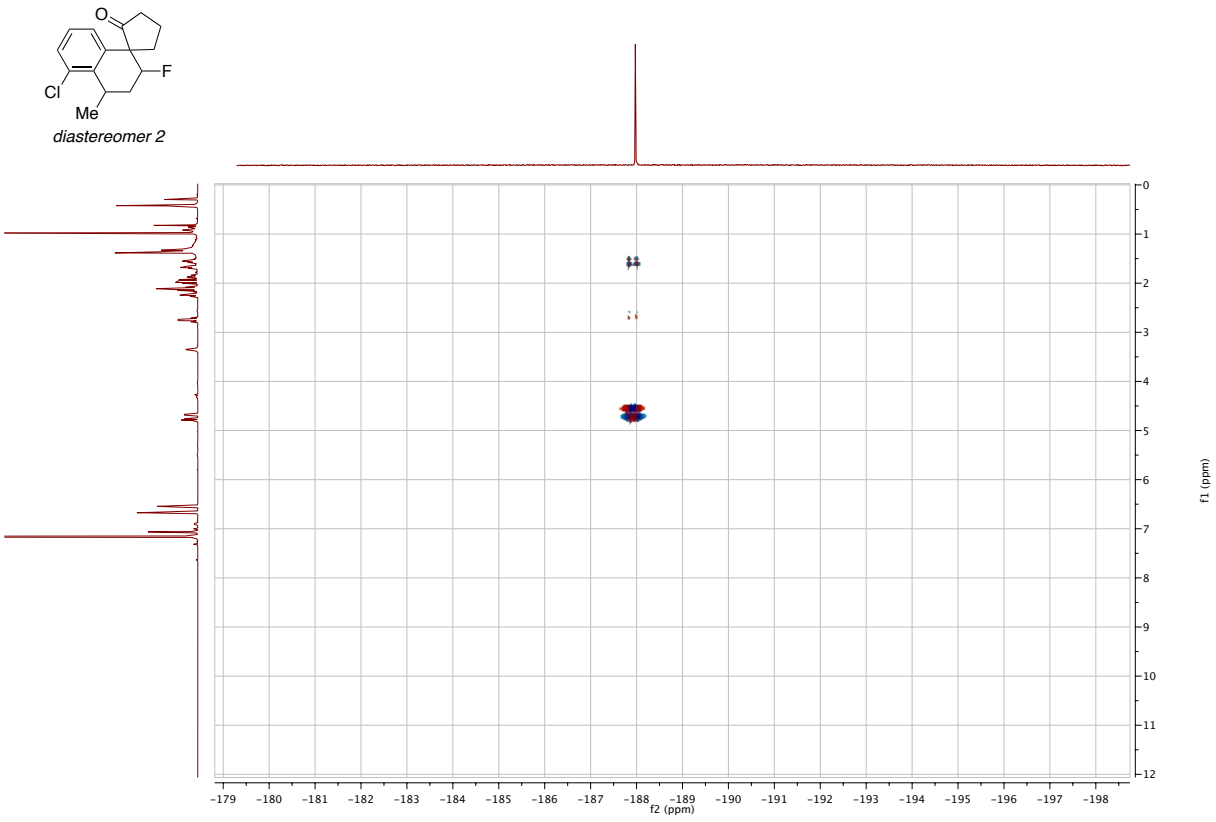
^{19}F NMR 375 MHz, C_6D_6



^{1}H-^{1}H NOESY 500 MHz, C_6D_6

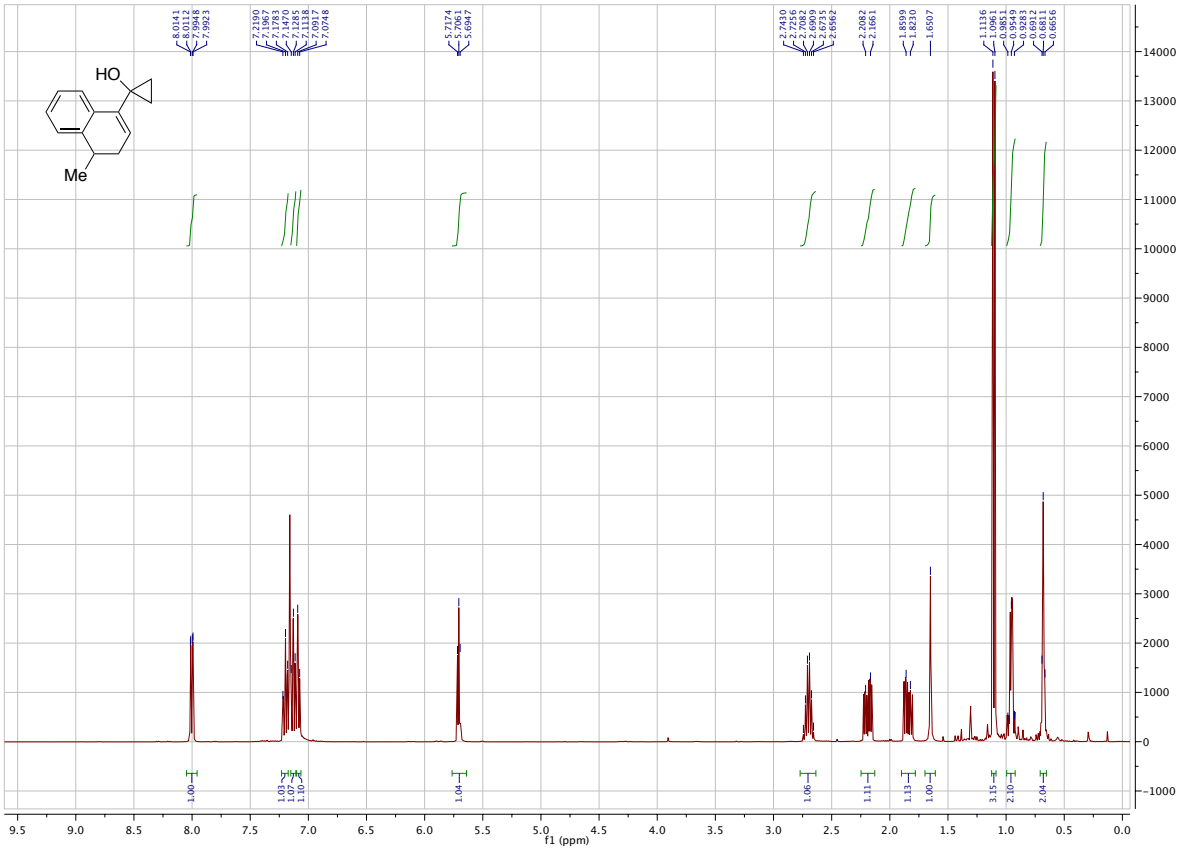


^{1}H-^{19}F HOESY 300 MHz, C_6D_6

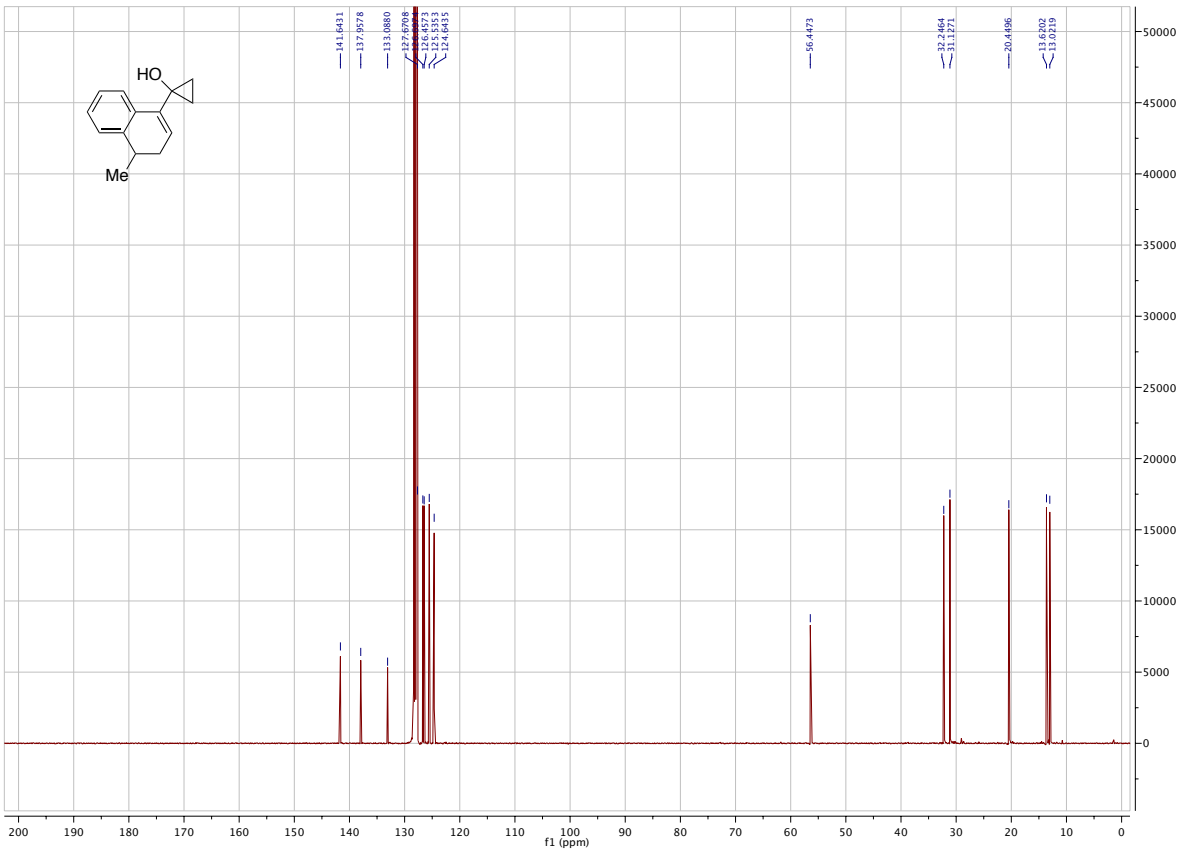


Substrate *rac*-A_6

^{1}H NMR 400 MHz, C_6D_6

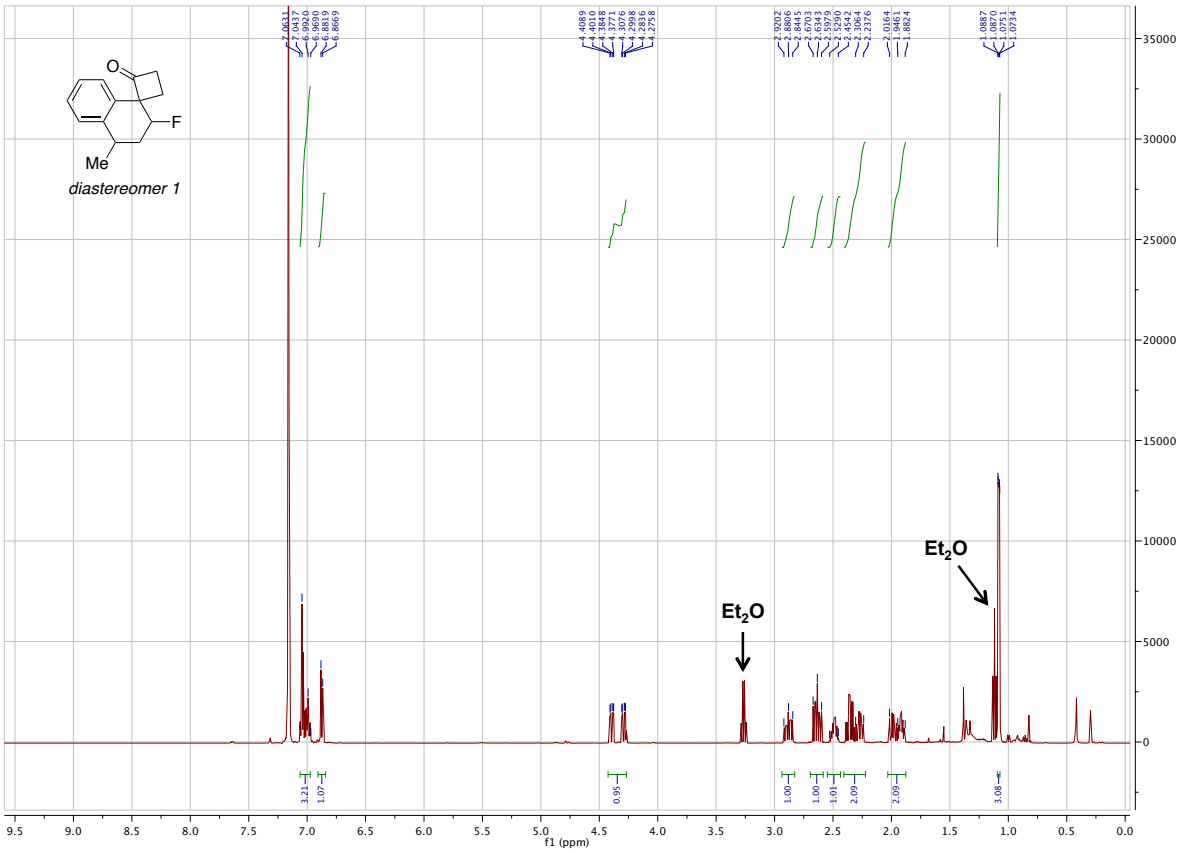


^{13}C NMR 100 MHz, C_6D_6

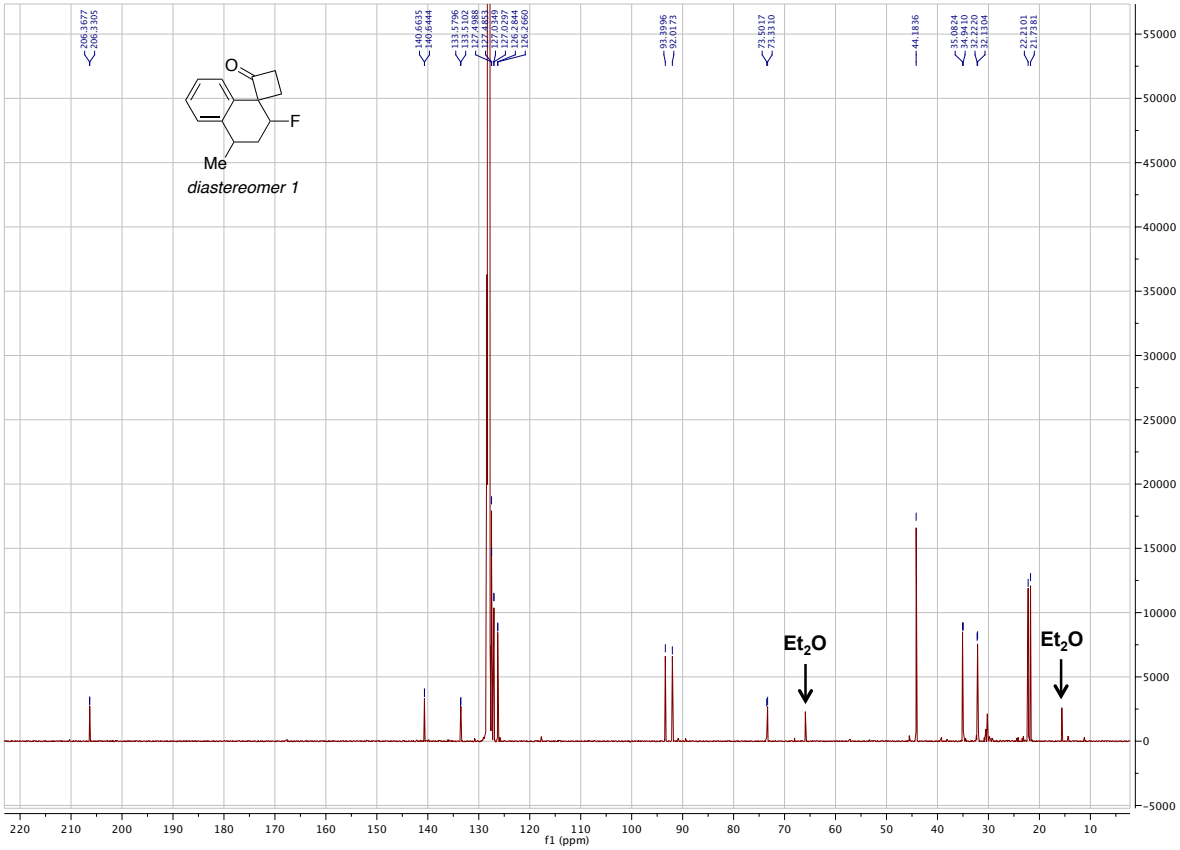


β-Fluoro Spiroketone B_6^R

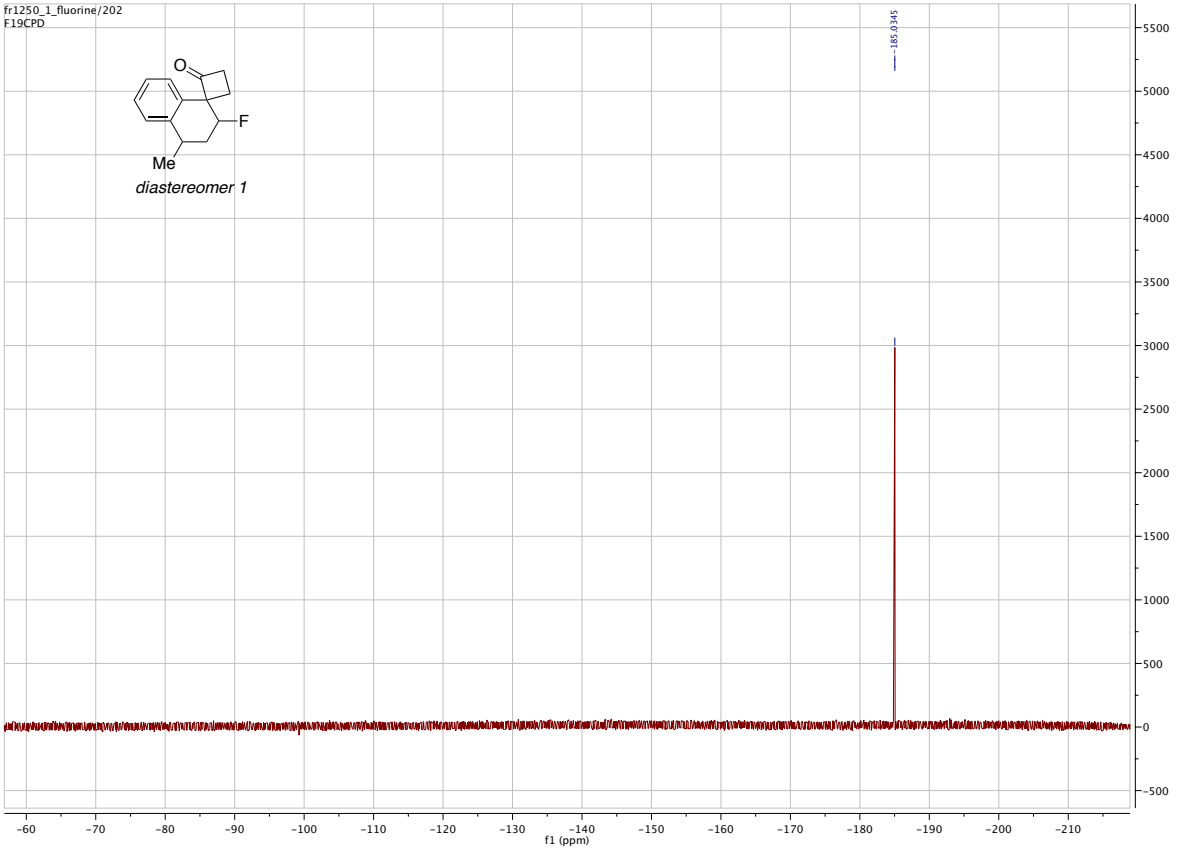
^{1}H NMR 500 MHz, C_6D_6



^{13}C NMR 125 MHz, C_6D_6

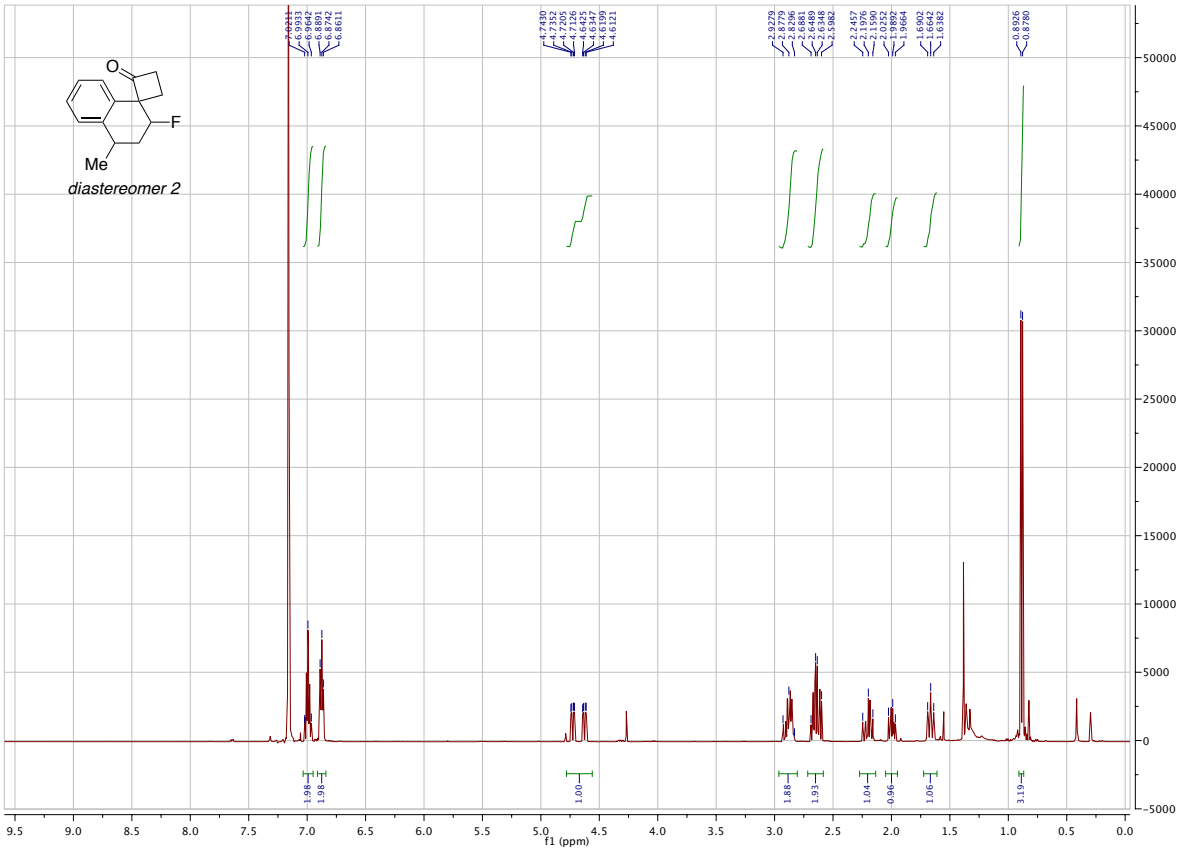


^{19}F NMR 375 MHz, C_6D_6

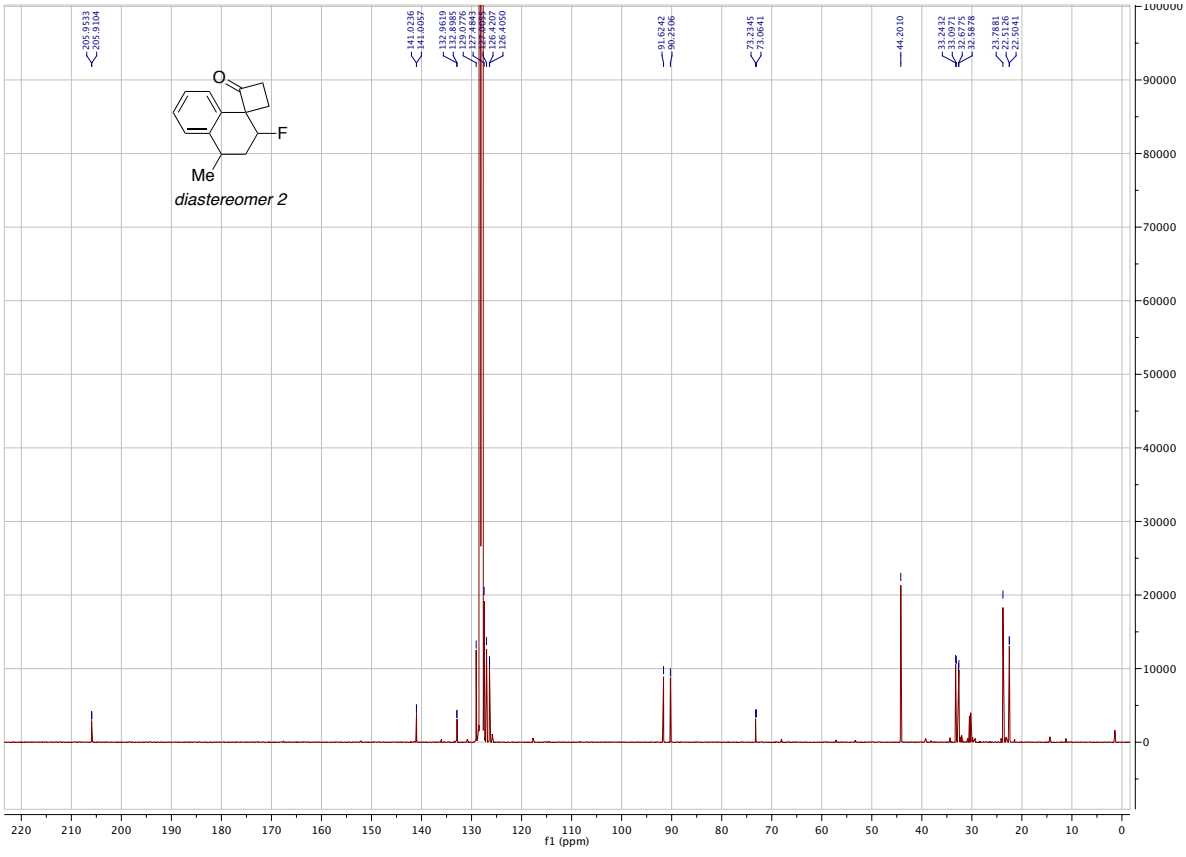


β-Fluoro Spiroketone B_6^S

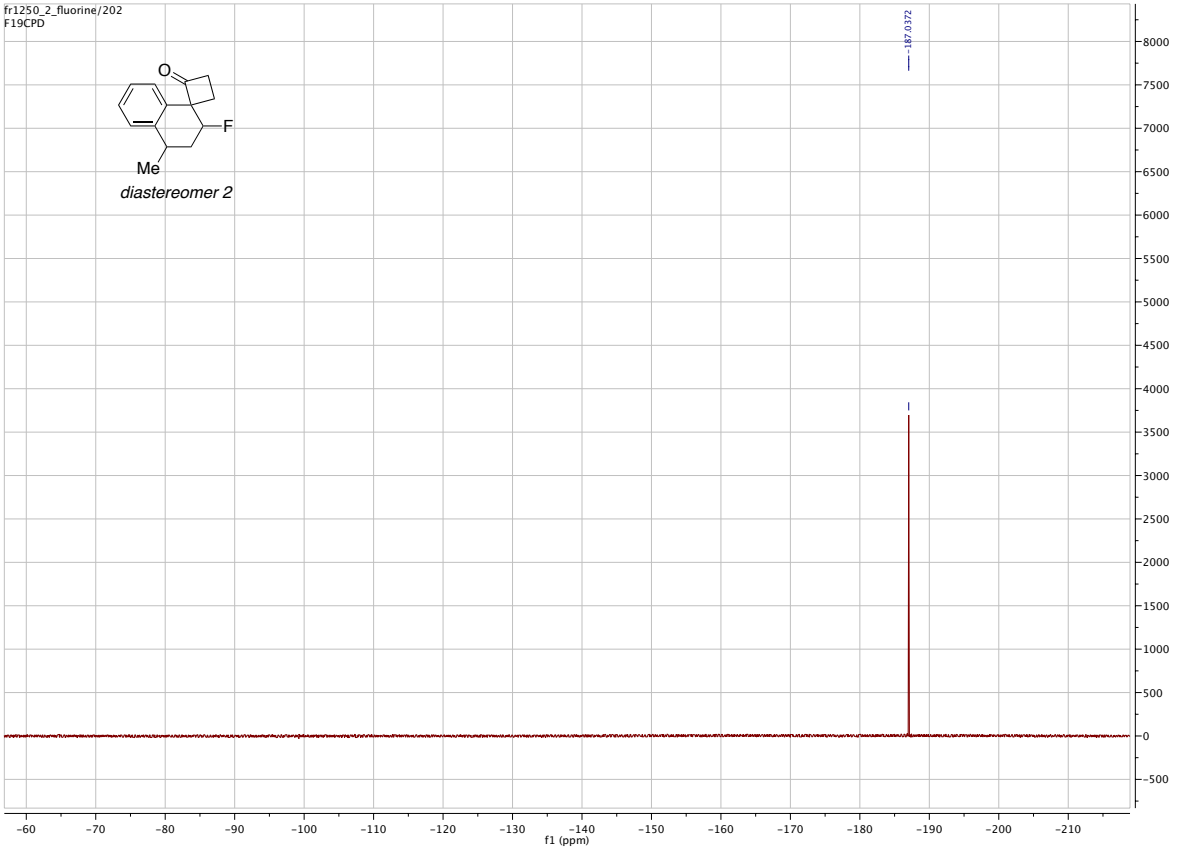
^{1}H NMR 500 MHz, C_6D_6



^{13}C NMR 125 MHz, C_6D_6

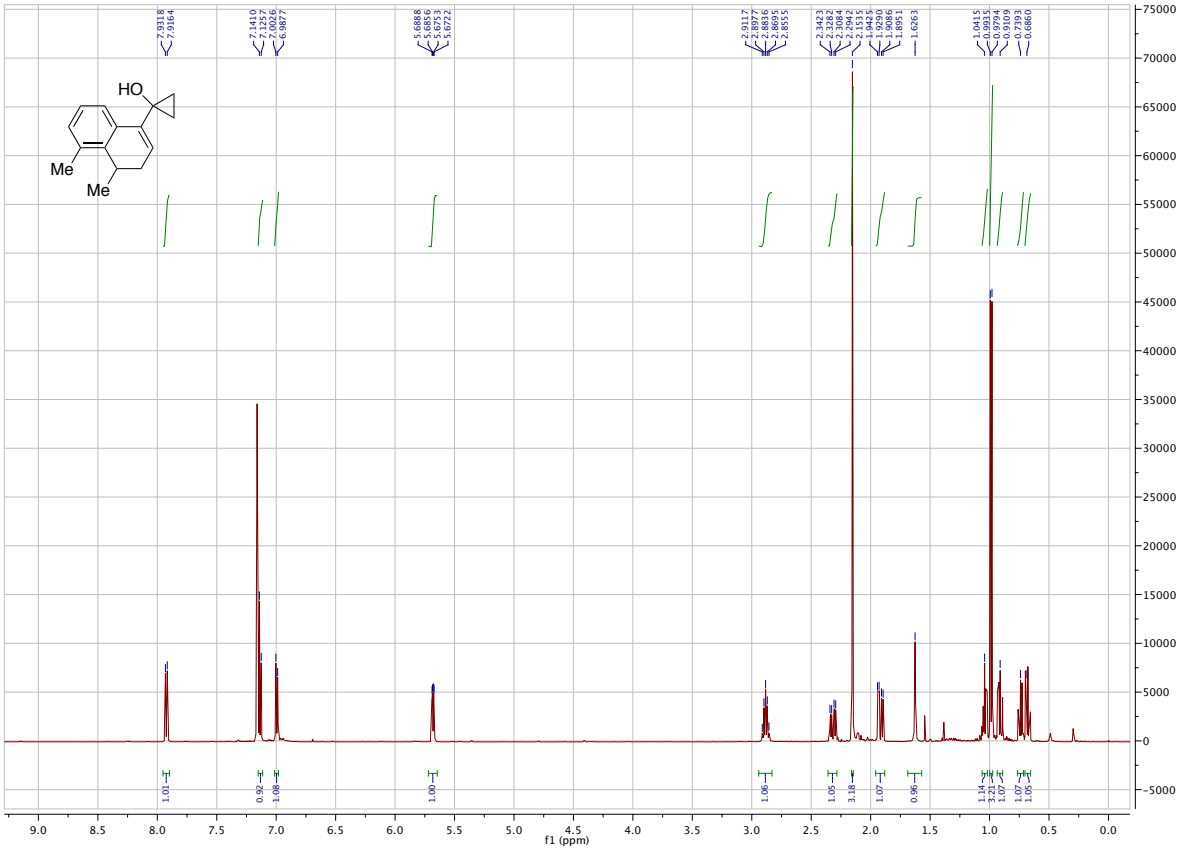


^{19}F NMR 375 MHz, C_6D_6

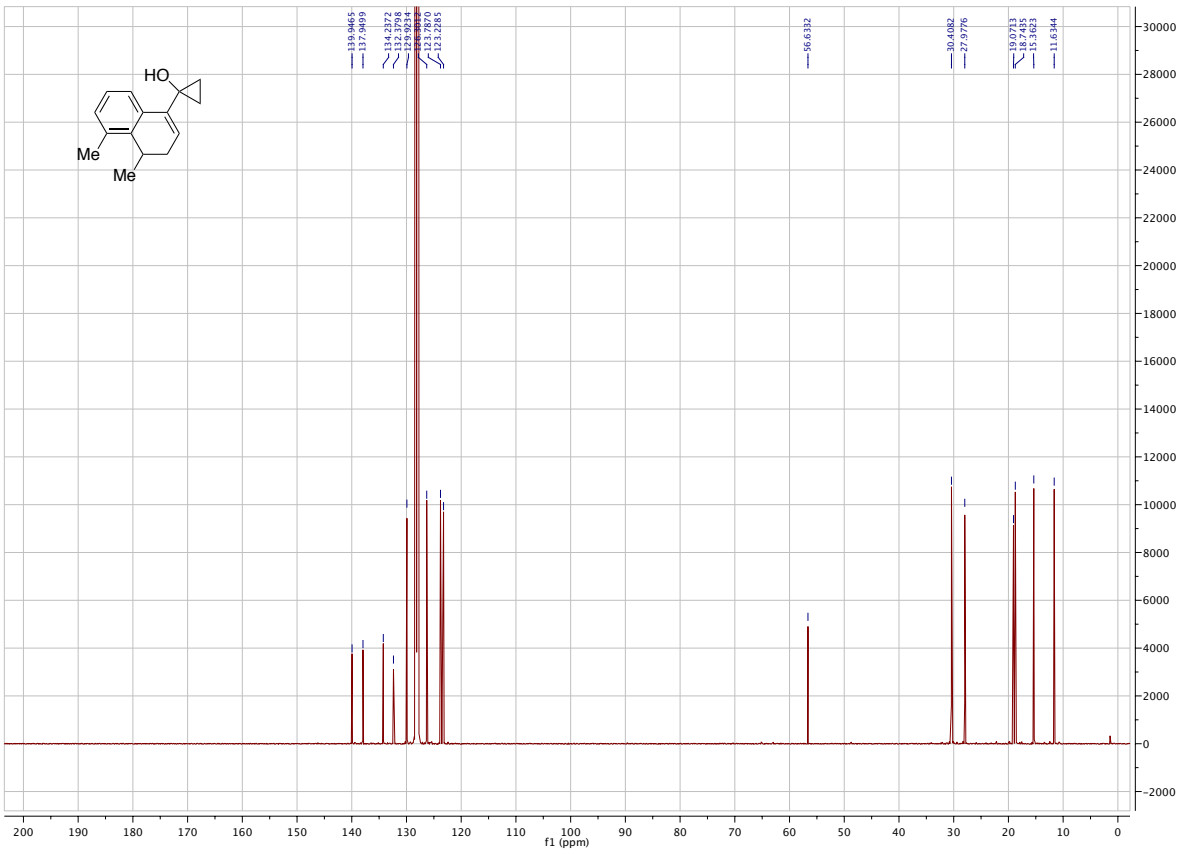


Substrate *rac*-A_7

^{1}H NMR 500 MHz, C_6D_6



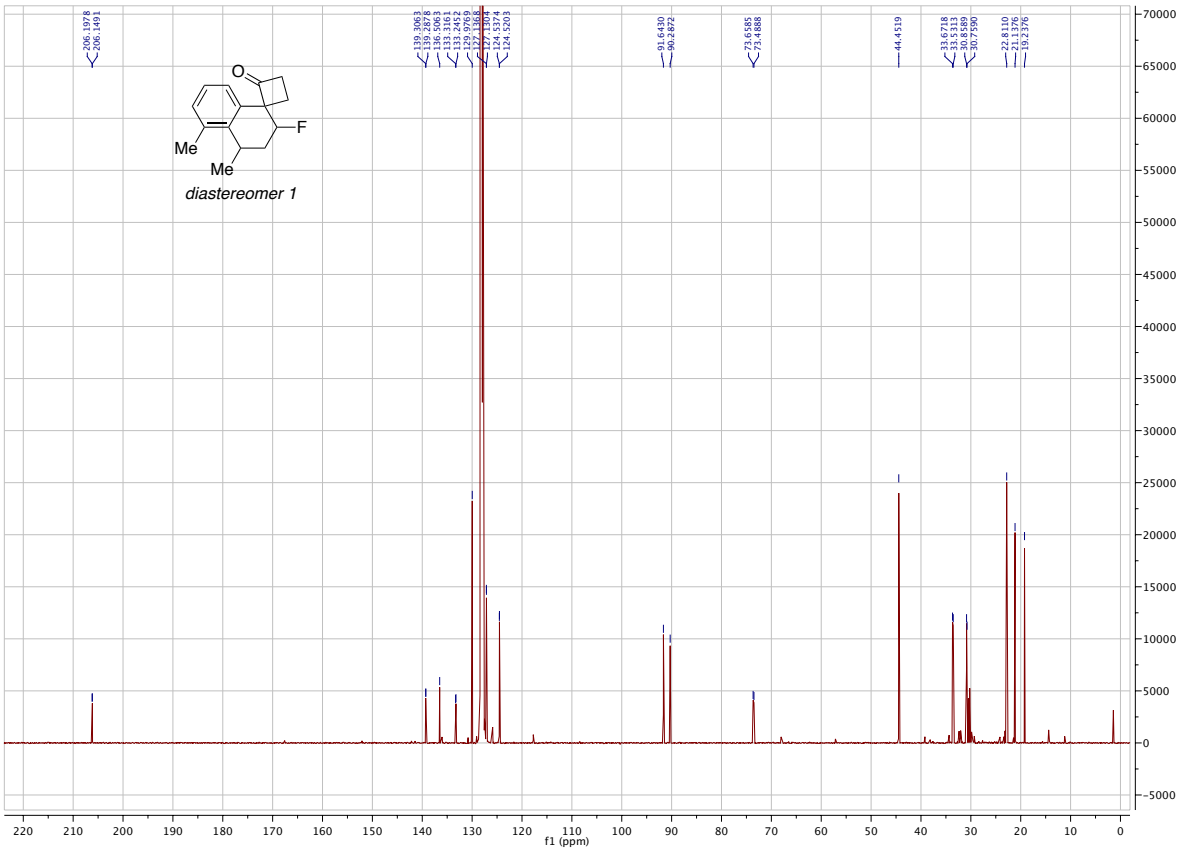
^{13}C NMR 125 MHz, C_6D_6



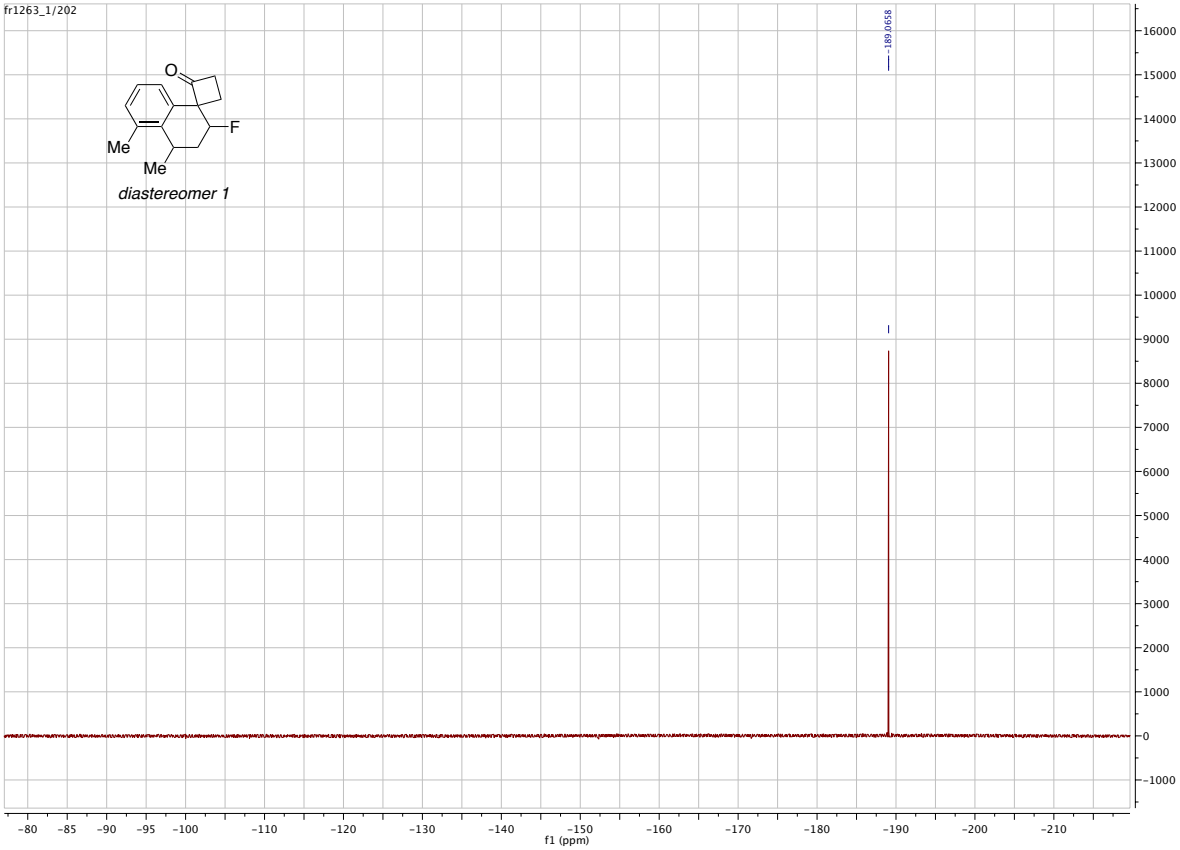
β-Fluoro Spiroketone B_7^R

^{1}H NMR 500 MHz, C_6D_6

^{13}C NMR 125 MHz, C_6D_6

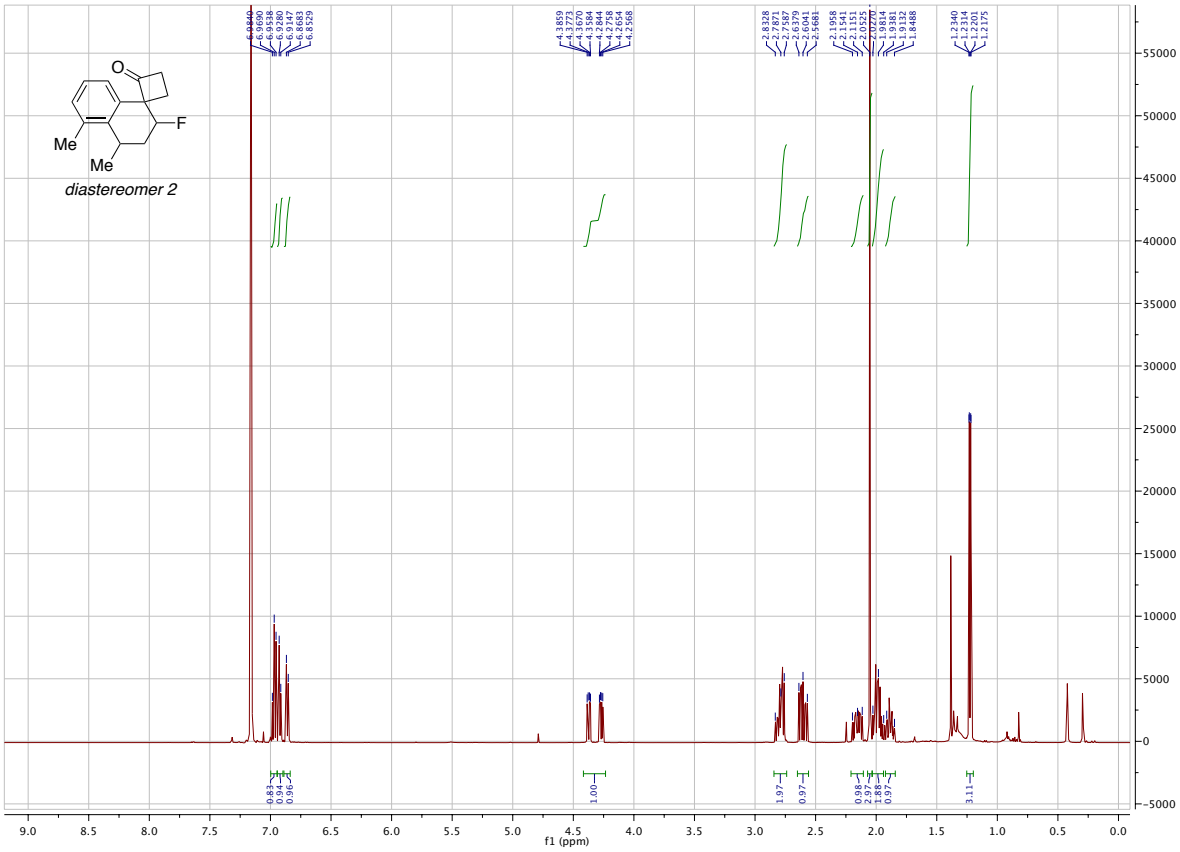


^{19}F NMR 375 MHz, C_6D_6

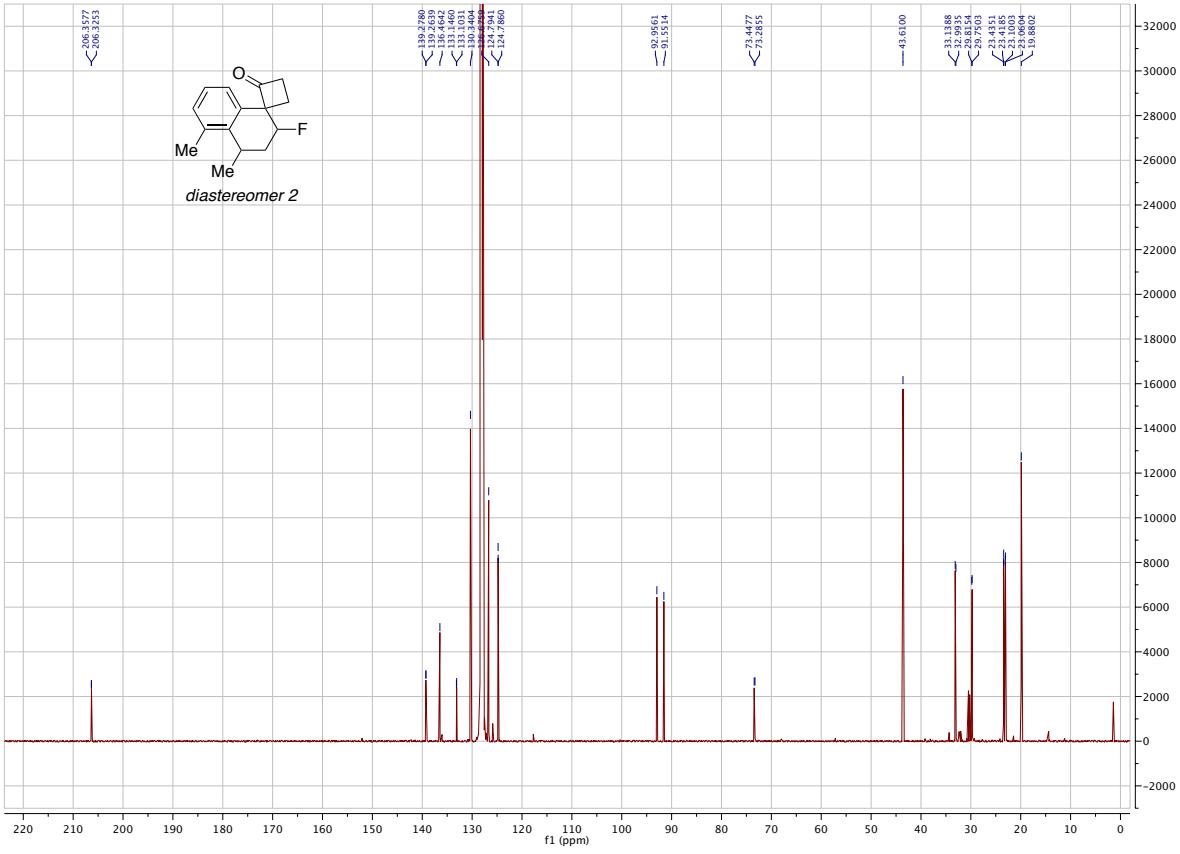


β-Fluoro Spiroketone B_7^S

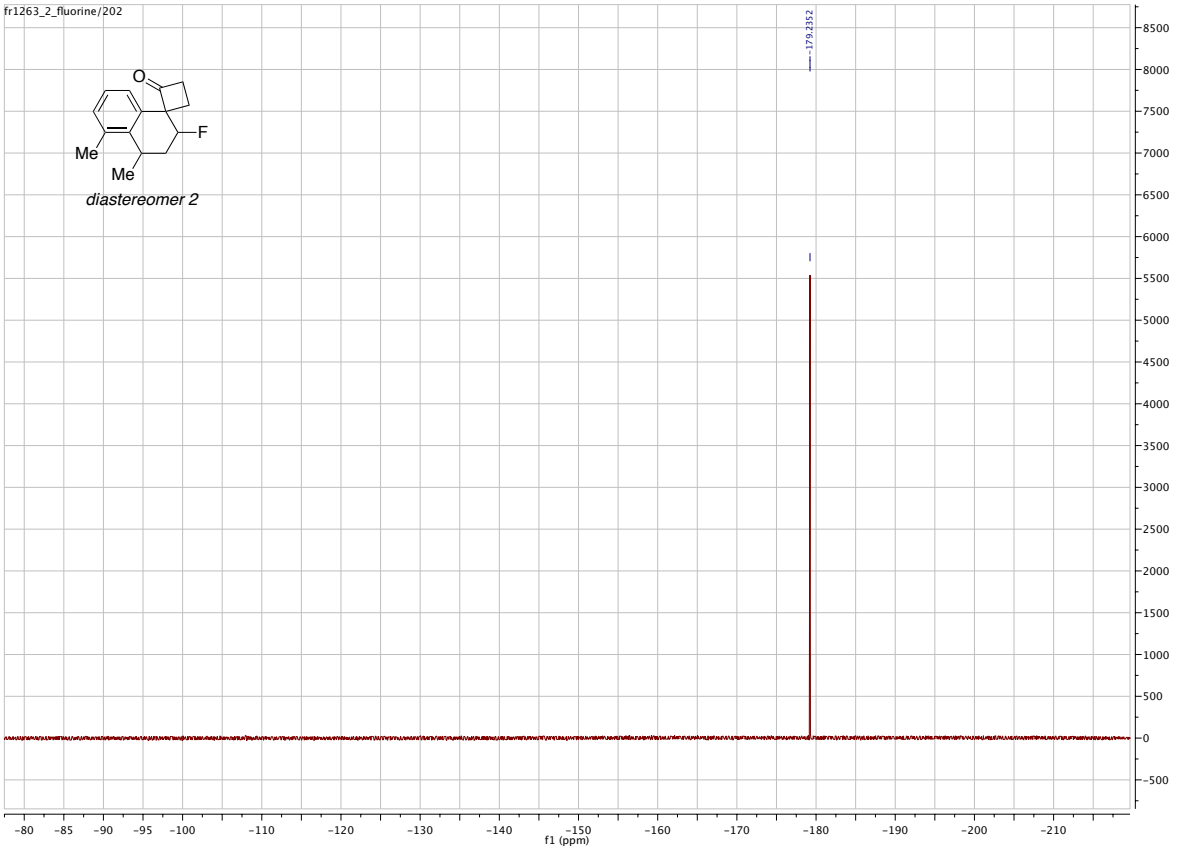
^{1}H NMR 500 MHz, C_6D_6



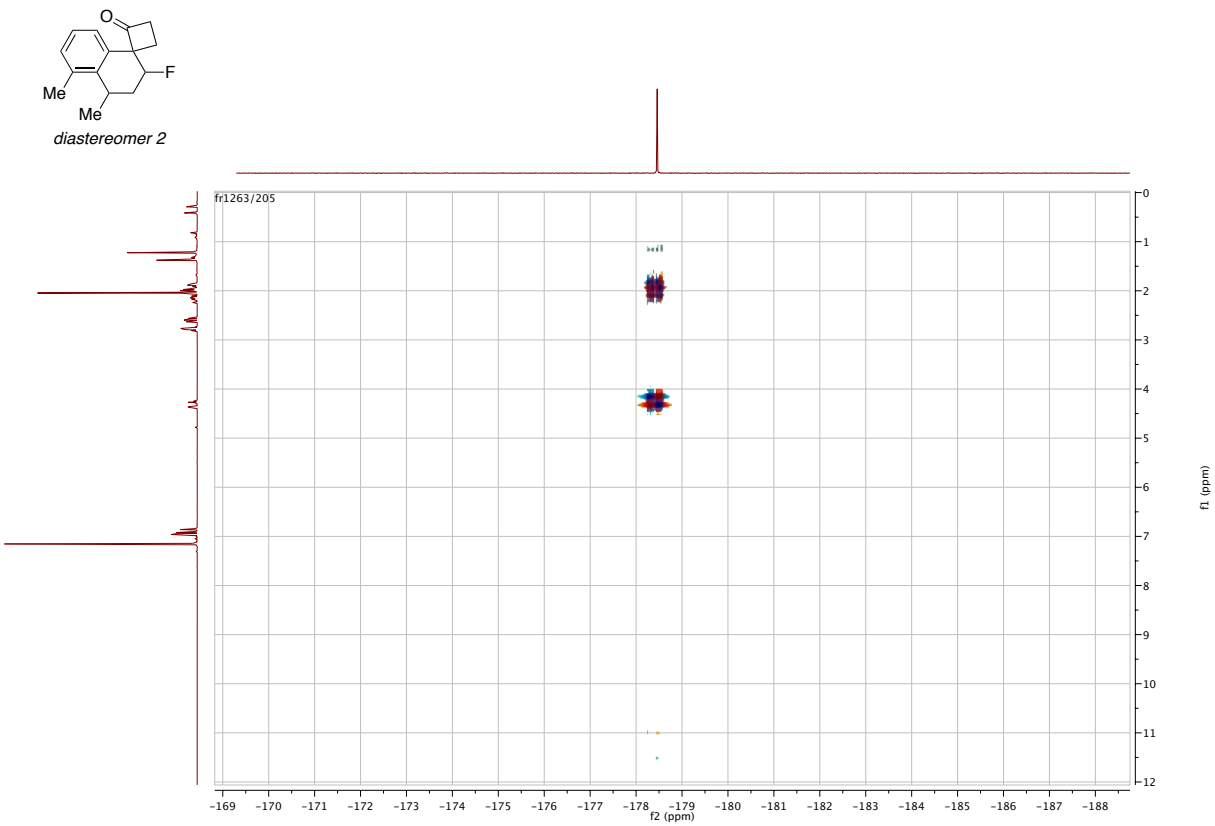
^{13}C NMR 125 MHz, C_6D_6



^{19}F NMR 375 MHz, C_6D_6



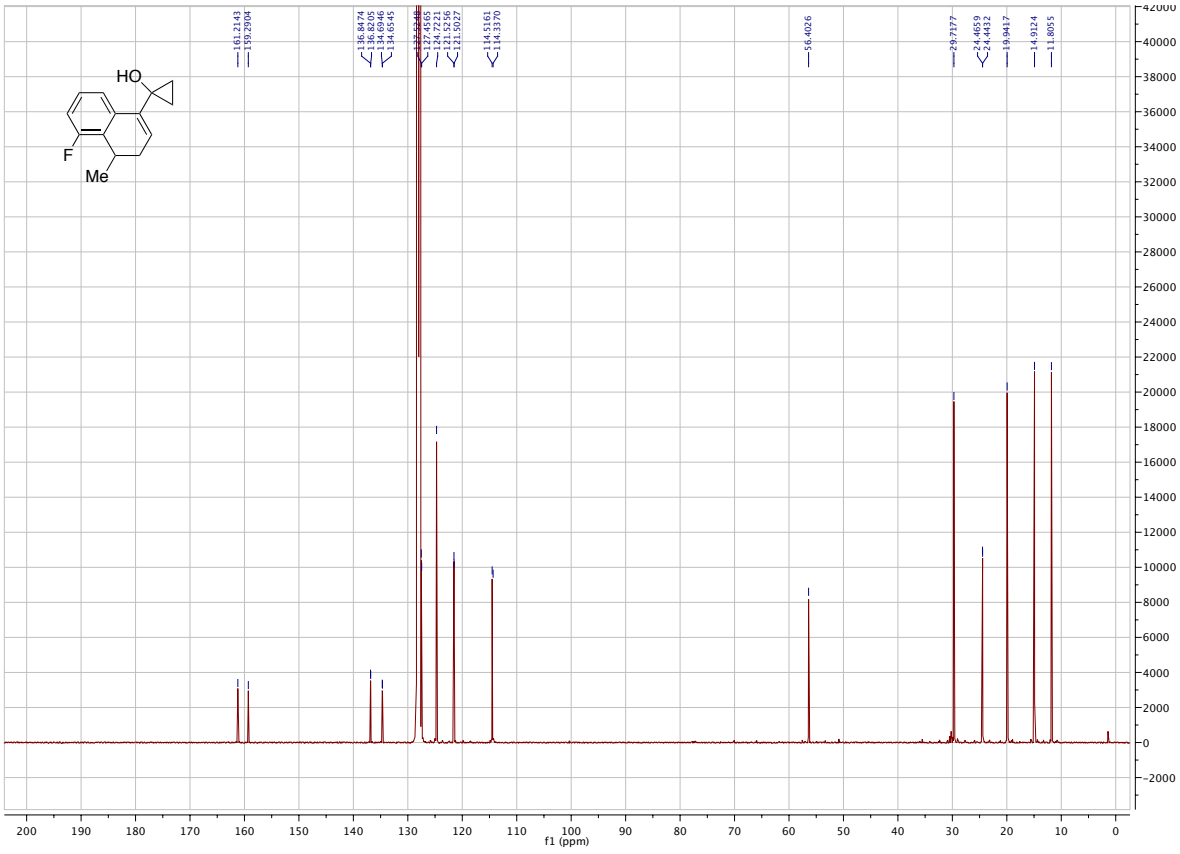
^{1}H-^{19}F HOESY 300 MHz, C_6D_6



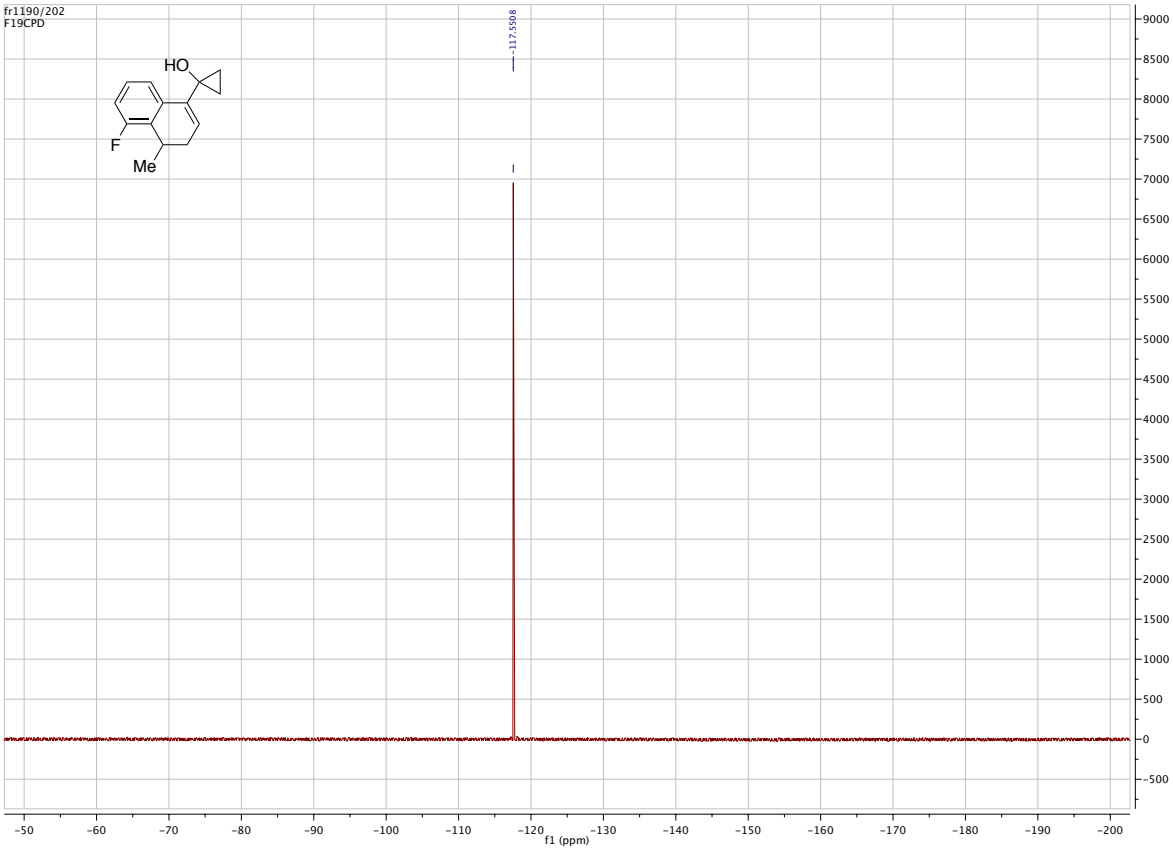
Substrate *rac*-A_8

^{1}H NMR 500 MHz, C_6D_6

^{13}C NMR 125 MHz, C_6D_6

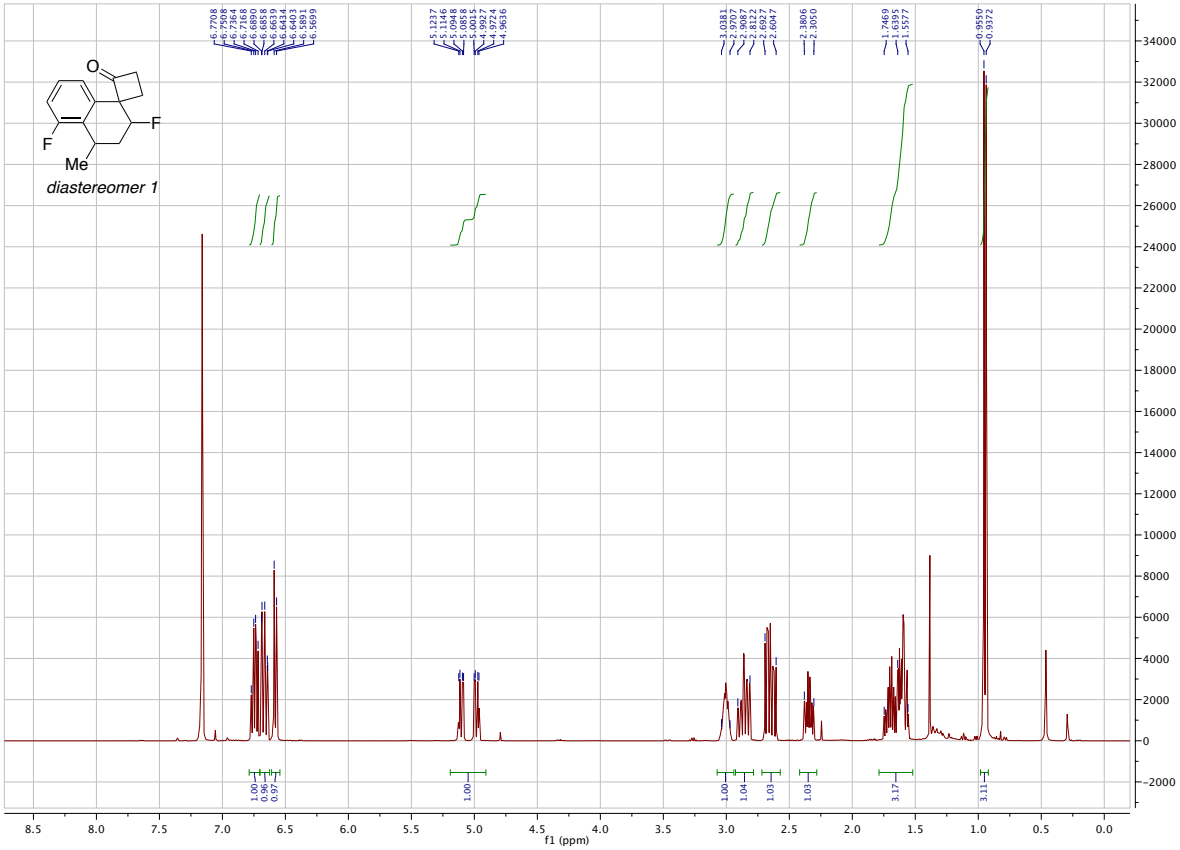


^{19}F NMR 375 MHz, C_6D_6

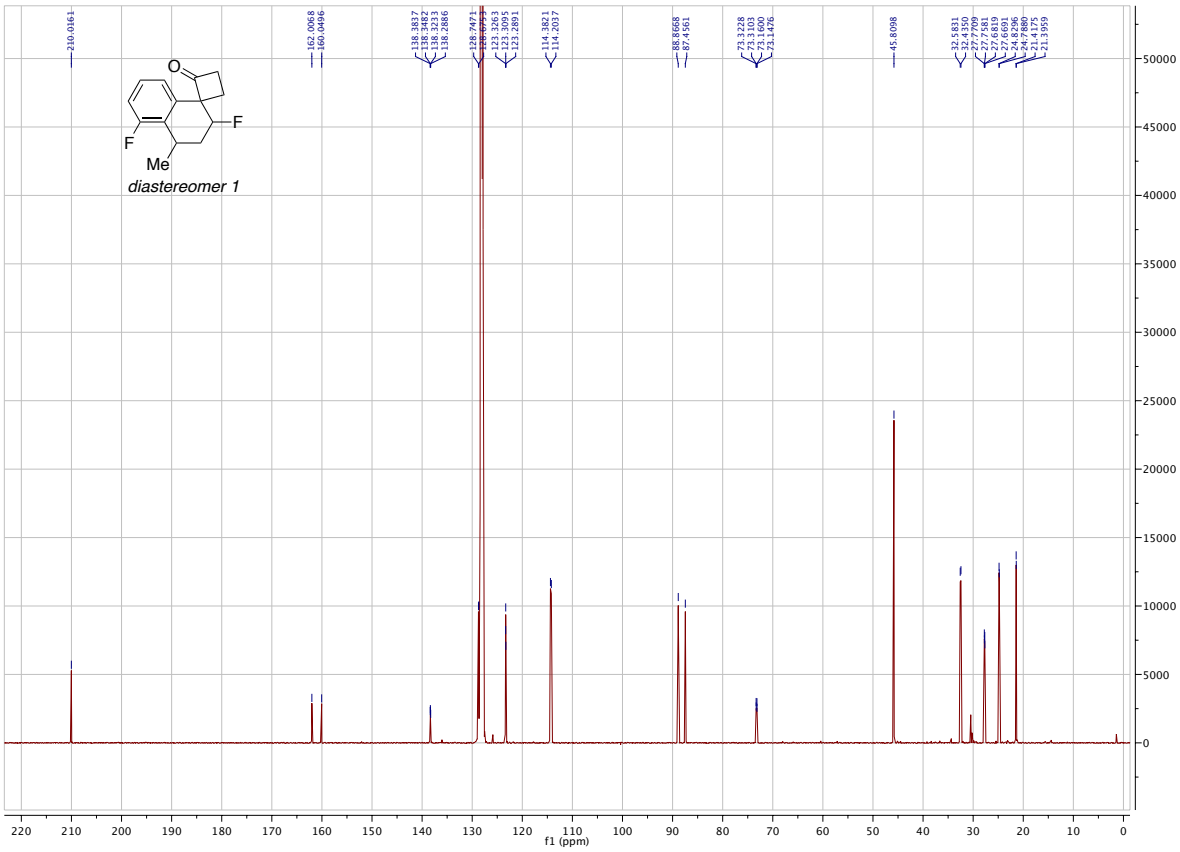


β-Fluoro Spiroketone B_8^R

^{1}H NMR 500 MHz, C_6D_6

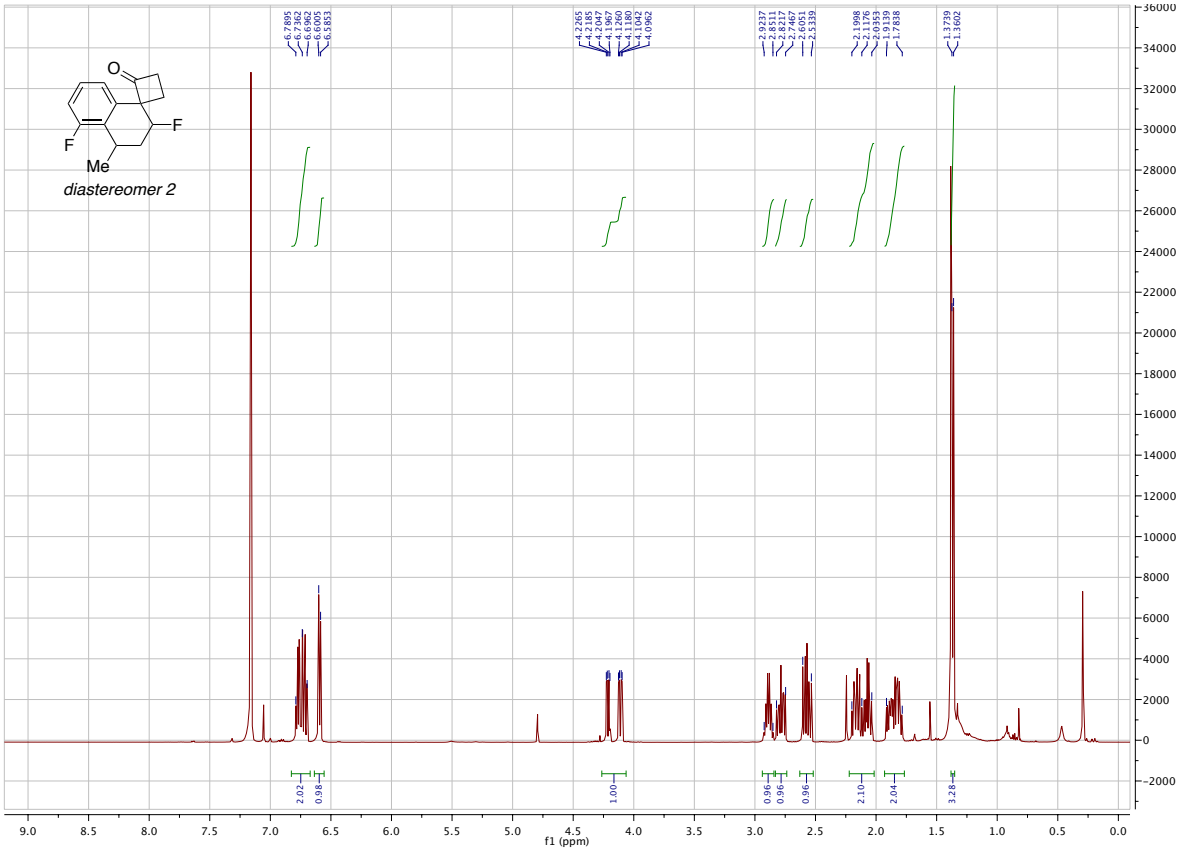


^{13}C NMR 125 MHz, C_6D_6

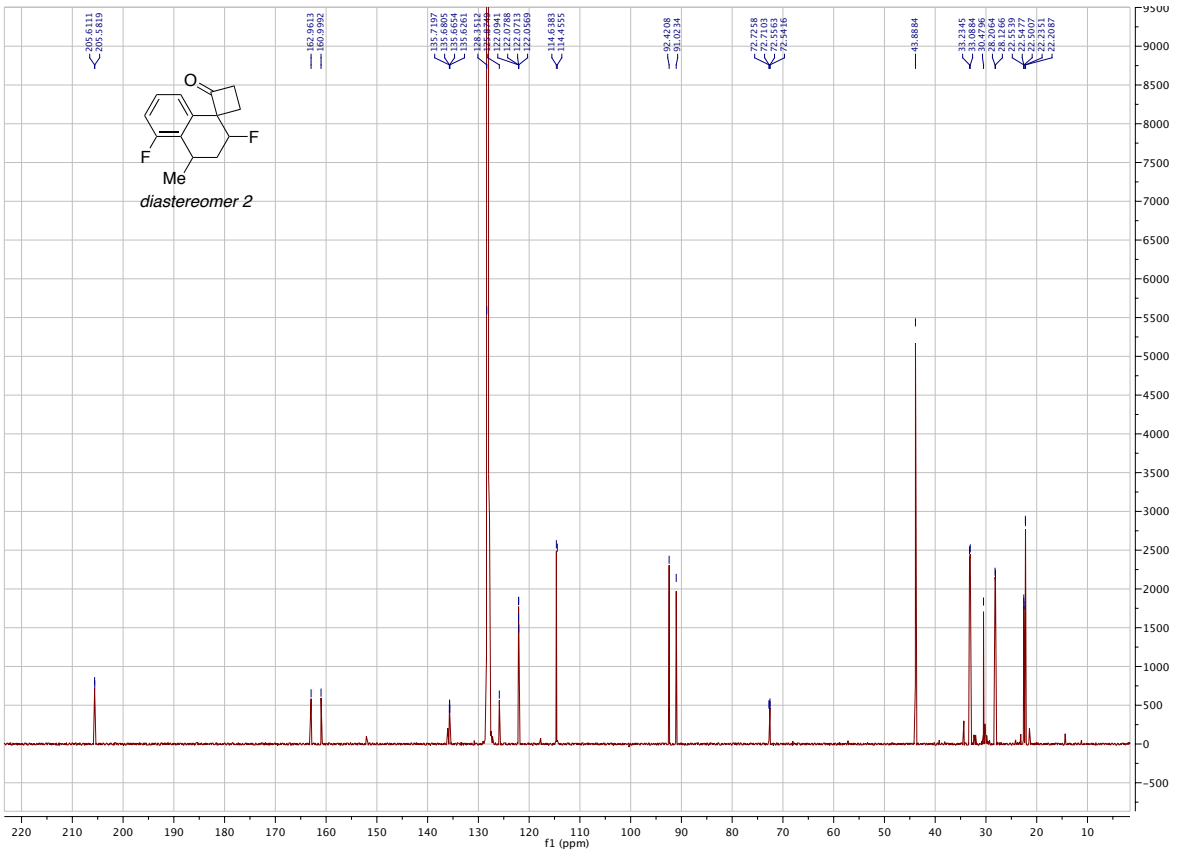


β-Fluoro Spiroketone B_8^S

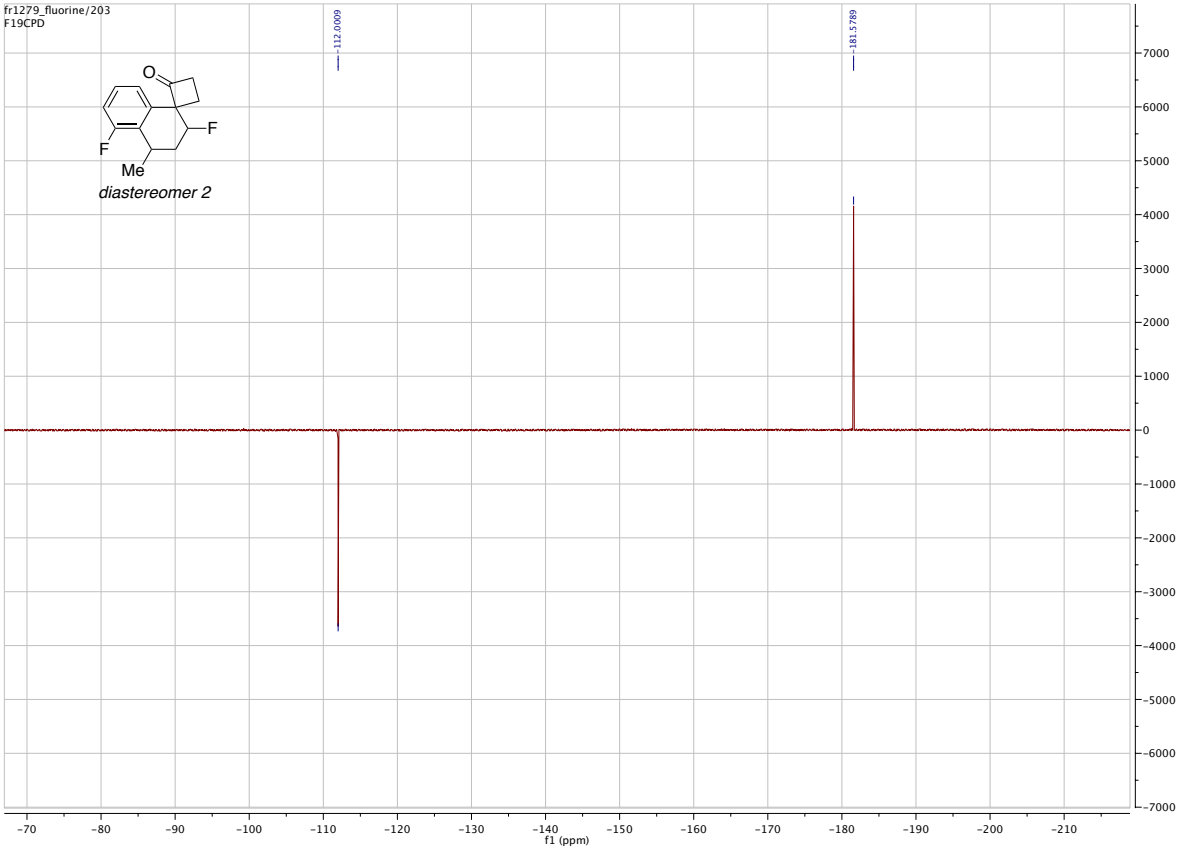
^{1}H NMR 500 MHz, C_6D_6



^{13}C NMR 125 MHz, C_6D_6

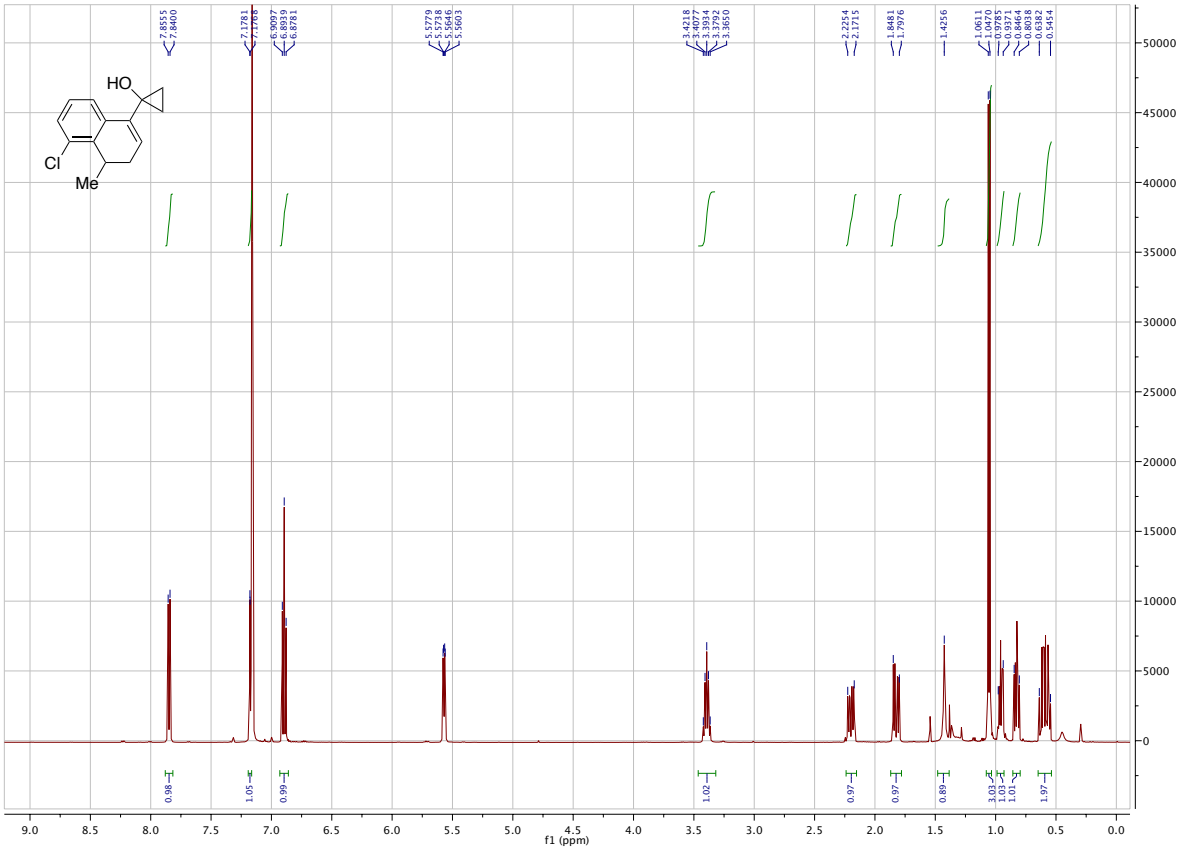


^{19}F NMR 375 MHz, C_6D_6

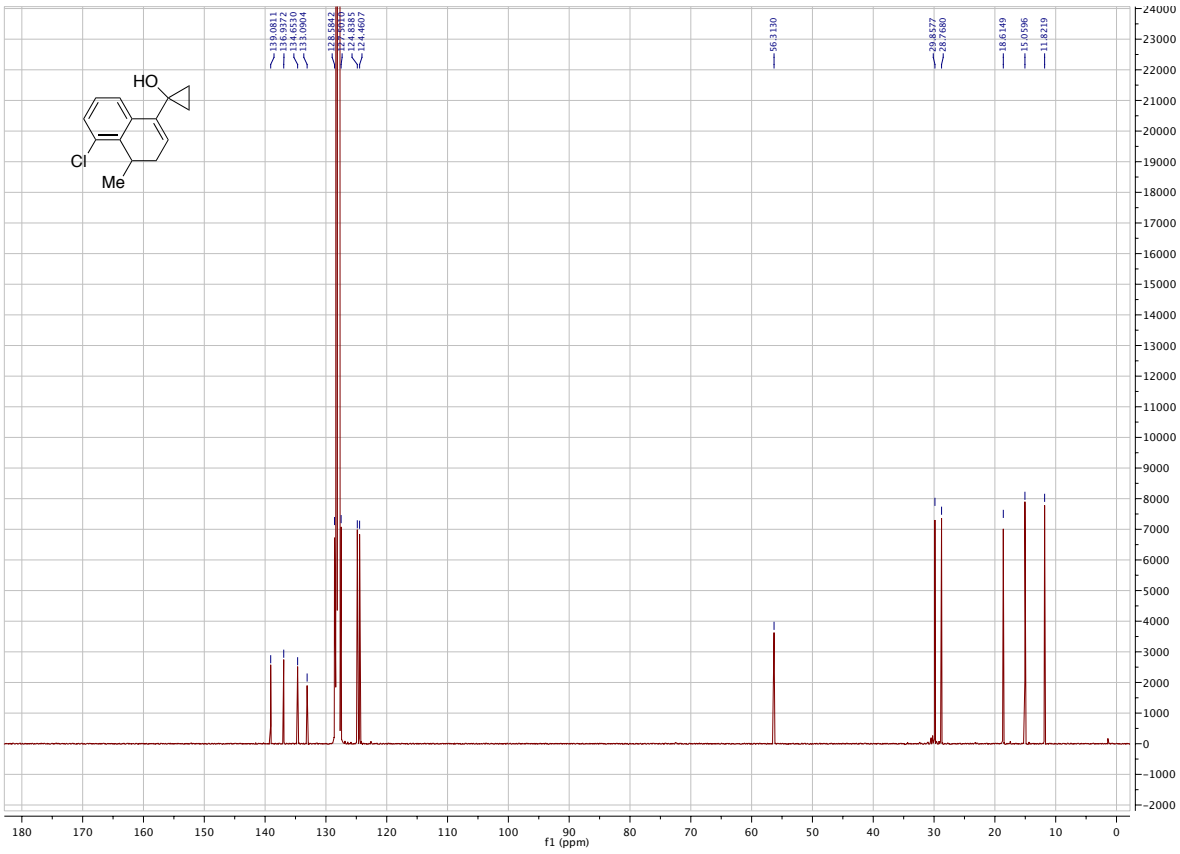


Substrate *rac*-A_9

^{1}H NMR 500 MHz, C_6D_6

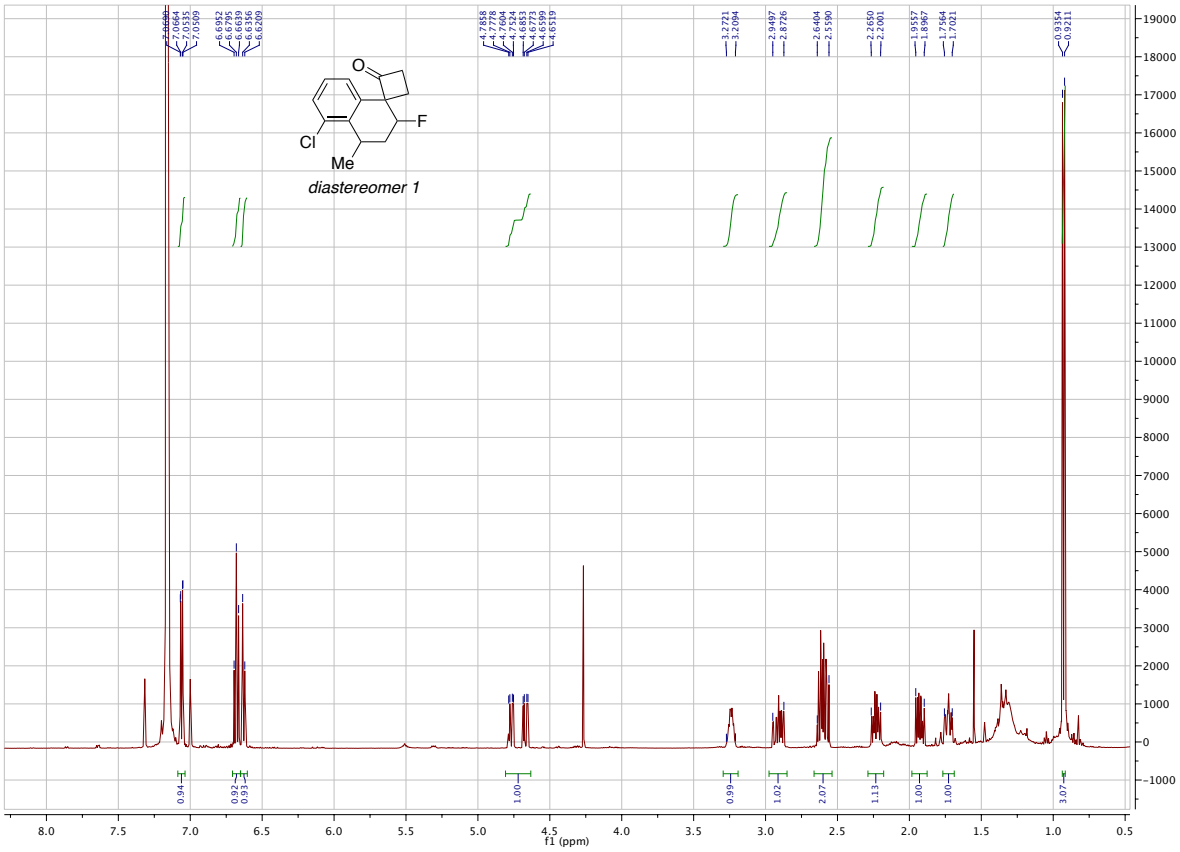


^{13}C NMR 125 MHz, C_6D_6

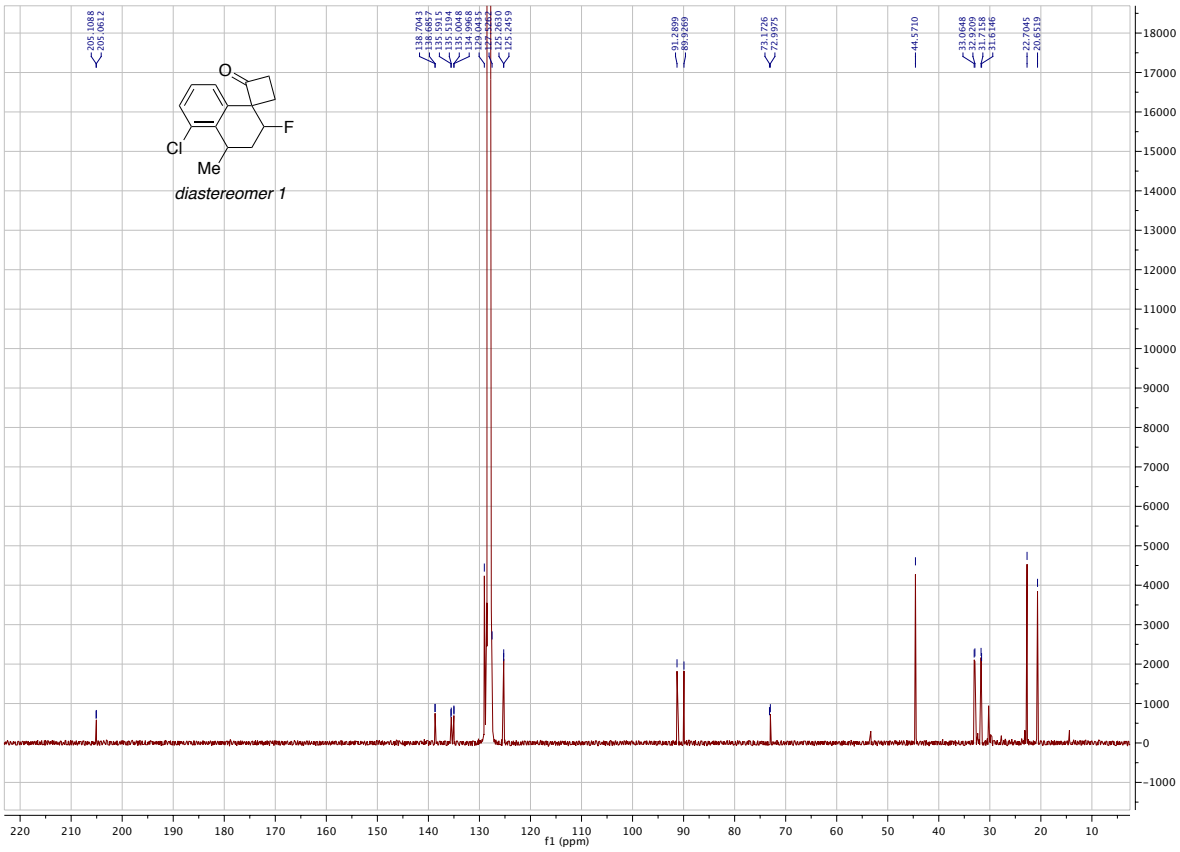


β-Fluoro Spiroketone B_9^R

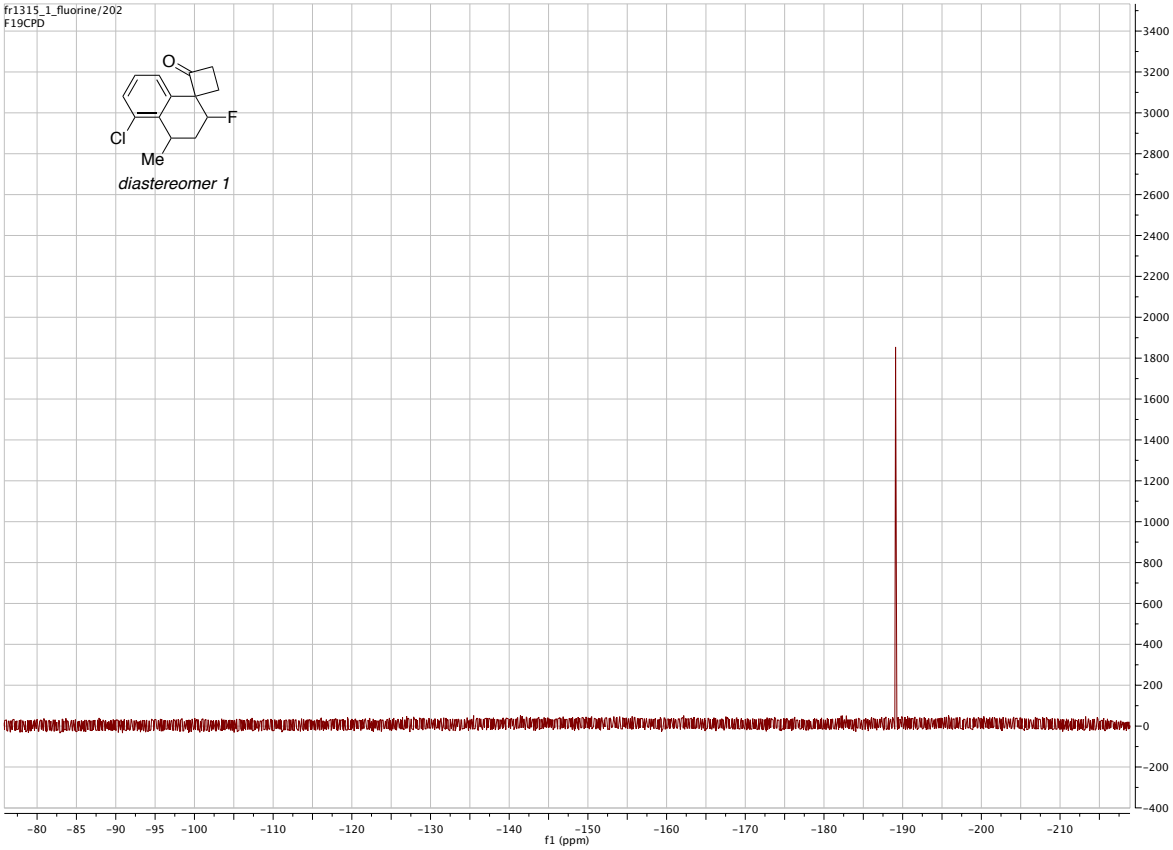
^{1}H NMR 500 MHz, C_6D_6



^{13}C NMR 125 MHz, C_6D_6

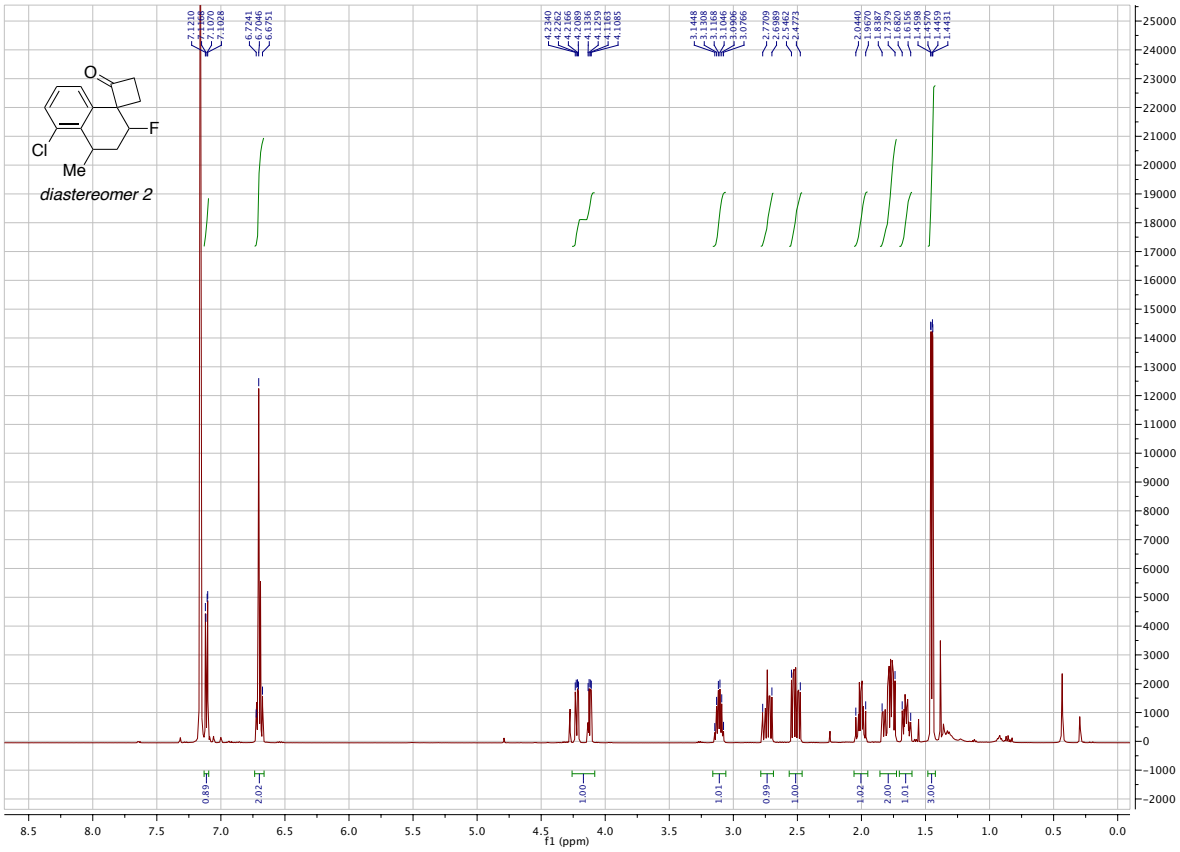


^{19}F NMR 375 MHz, C_6D_6

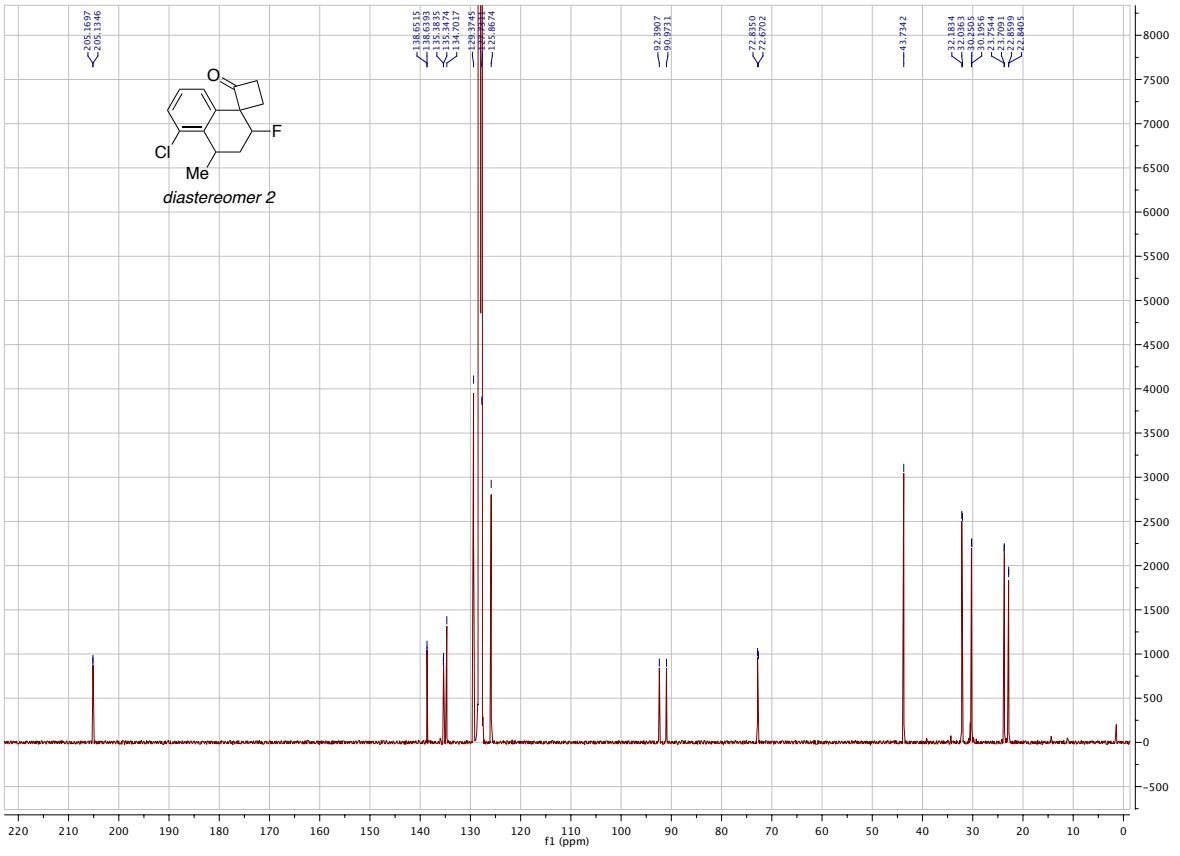


β-Fluoro Spiroketone B_9^S

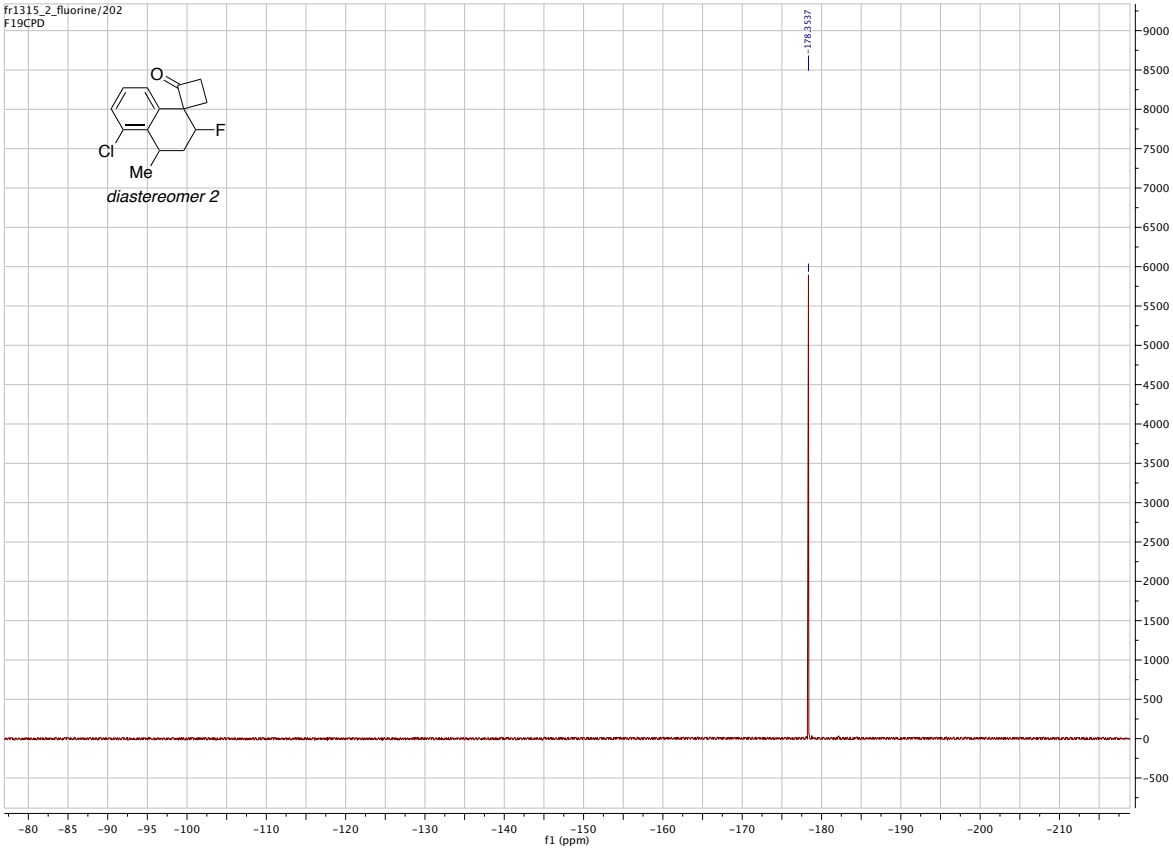
^{1}H NMR 500 MHz, C_6D_6



^{13}C NMR 125 MHz, C_6D_6

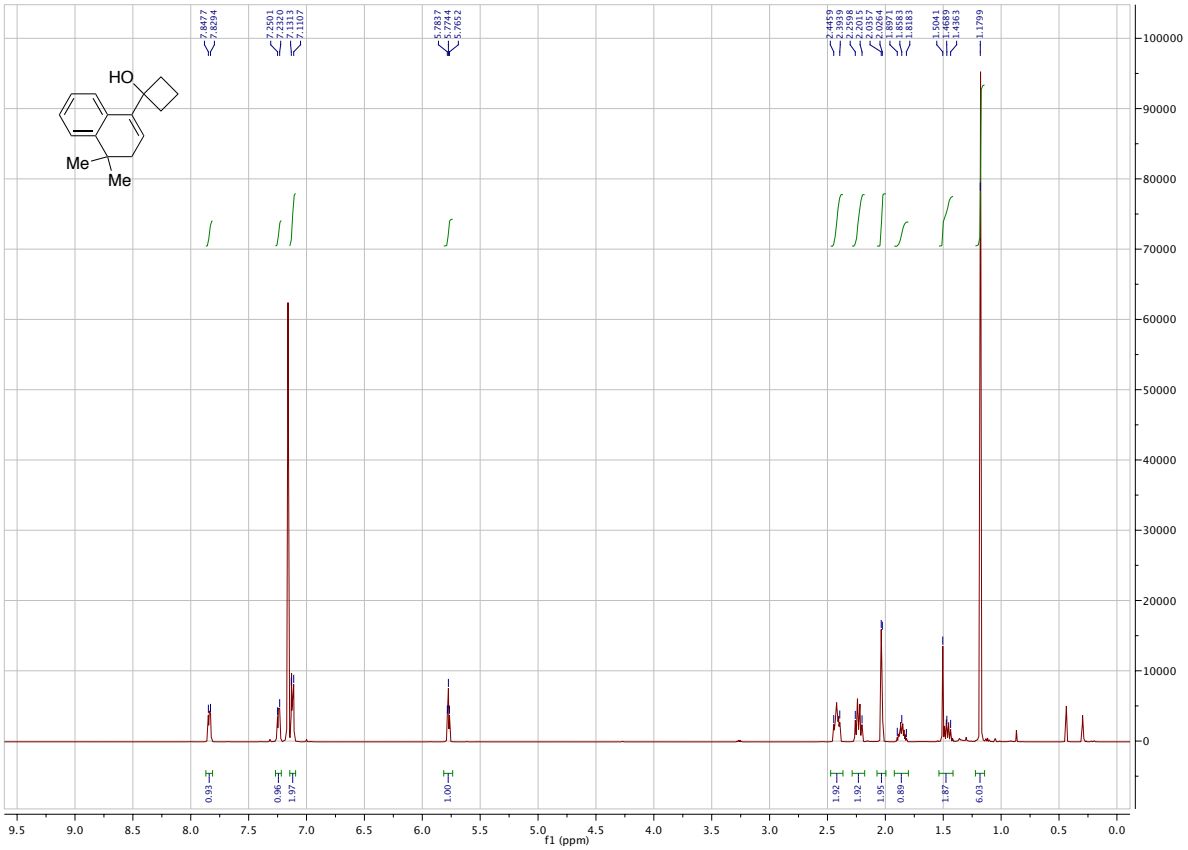


^{19}F NMR 375 MHz, C_6D_6

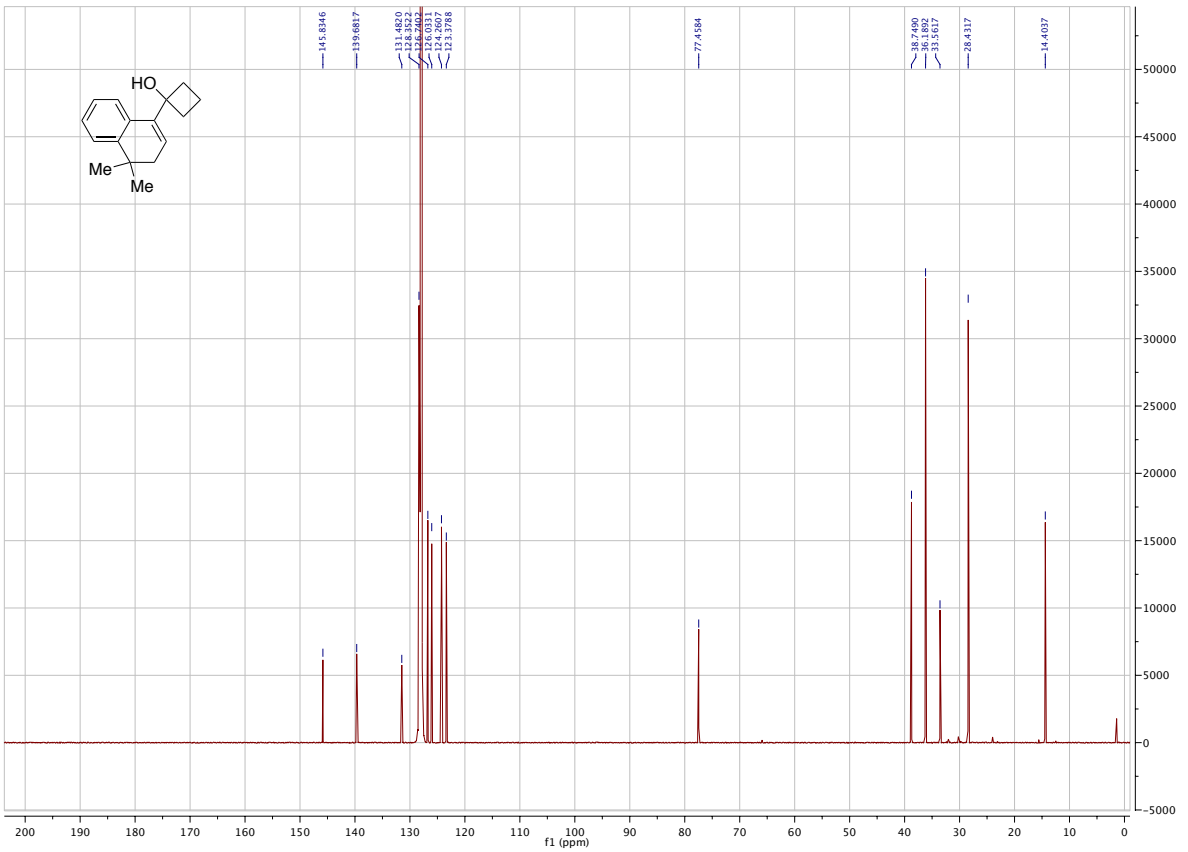


Substrate A_{10}

^{1}H NMR 500 MHz, C_6D_6

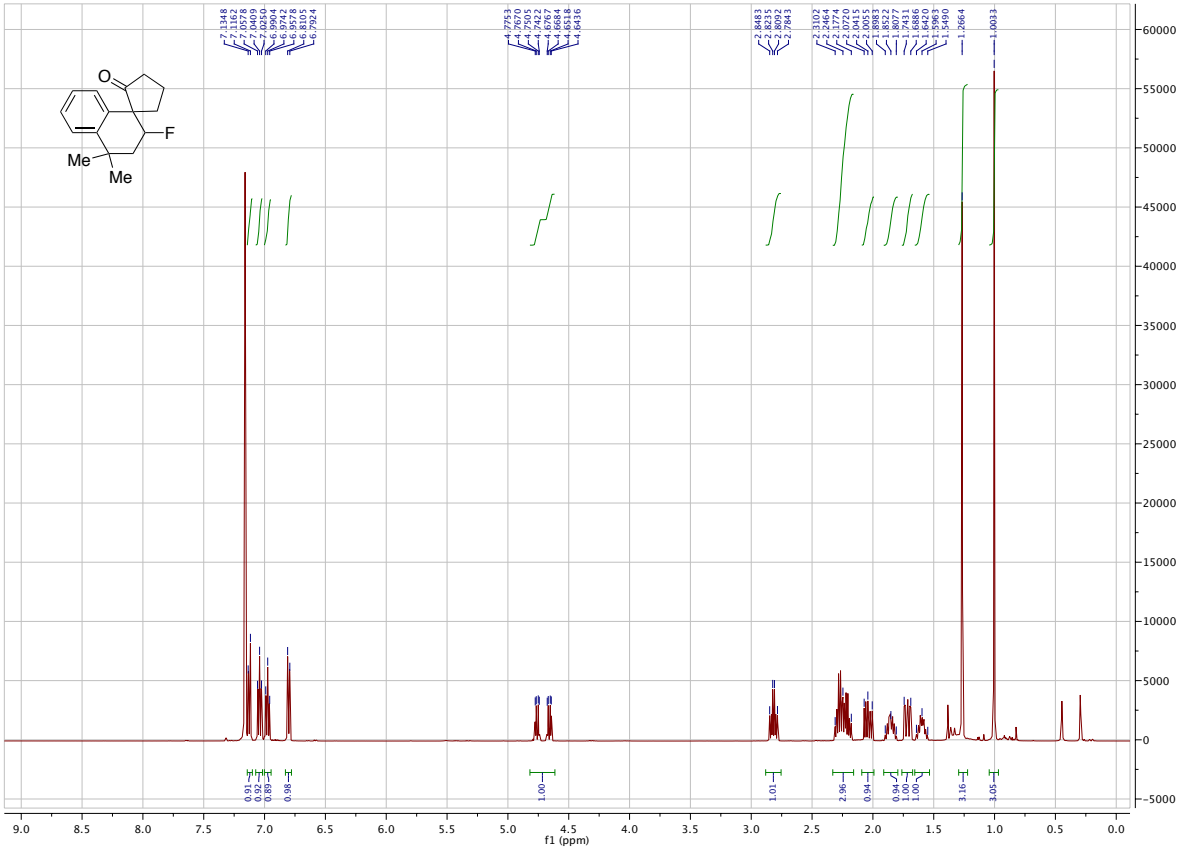


^{13}C NMR 125 MHz, C_6D_6

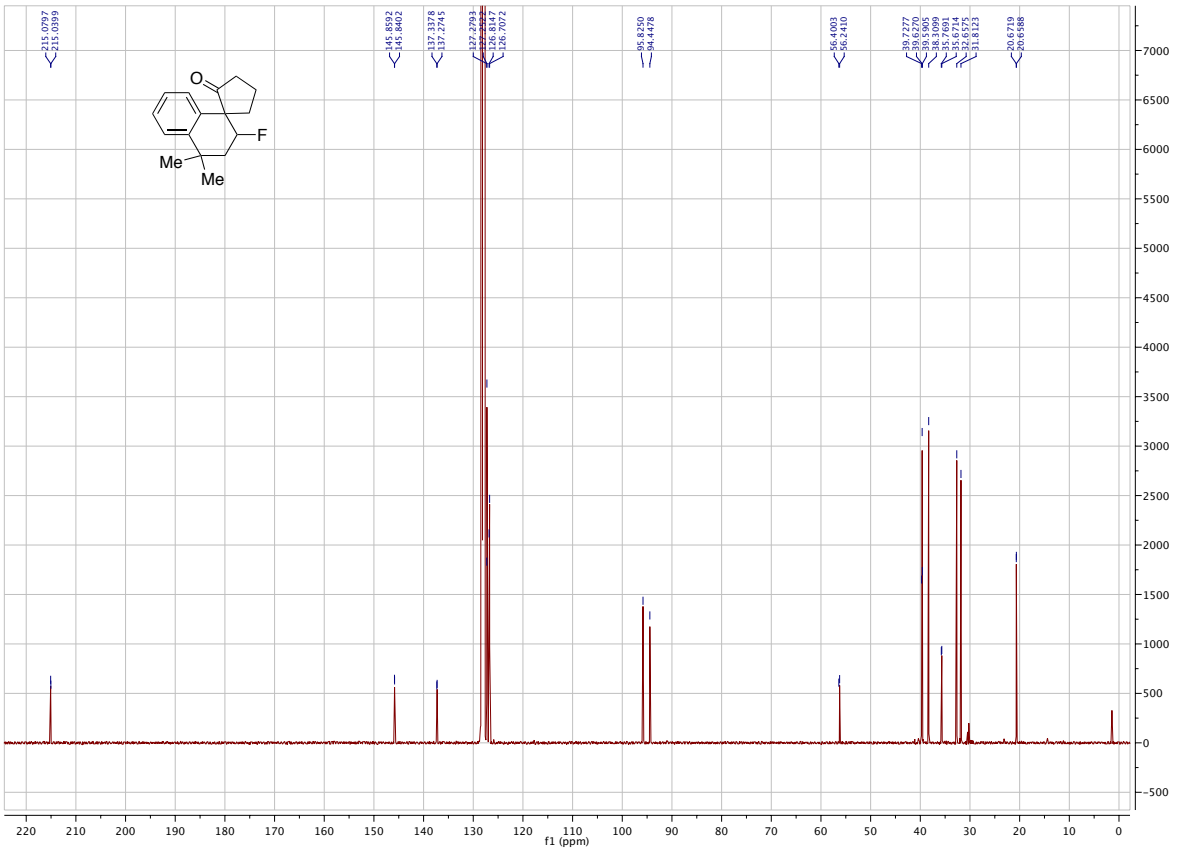


β-Fluoro Spiroketone B_{10}

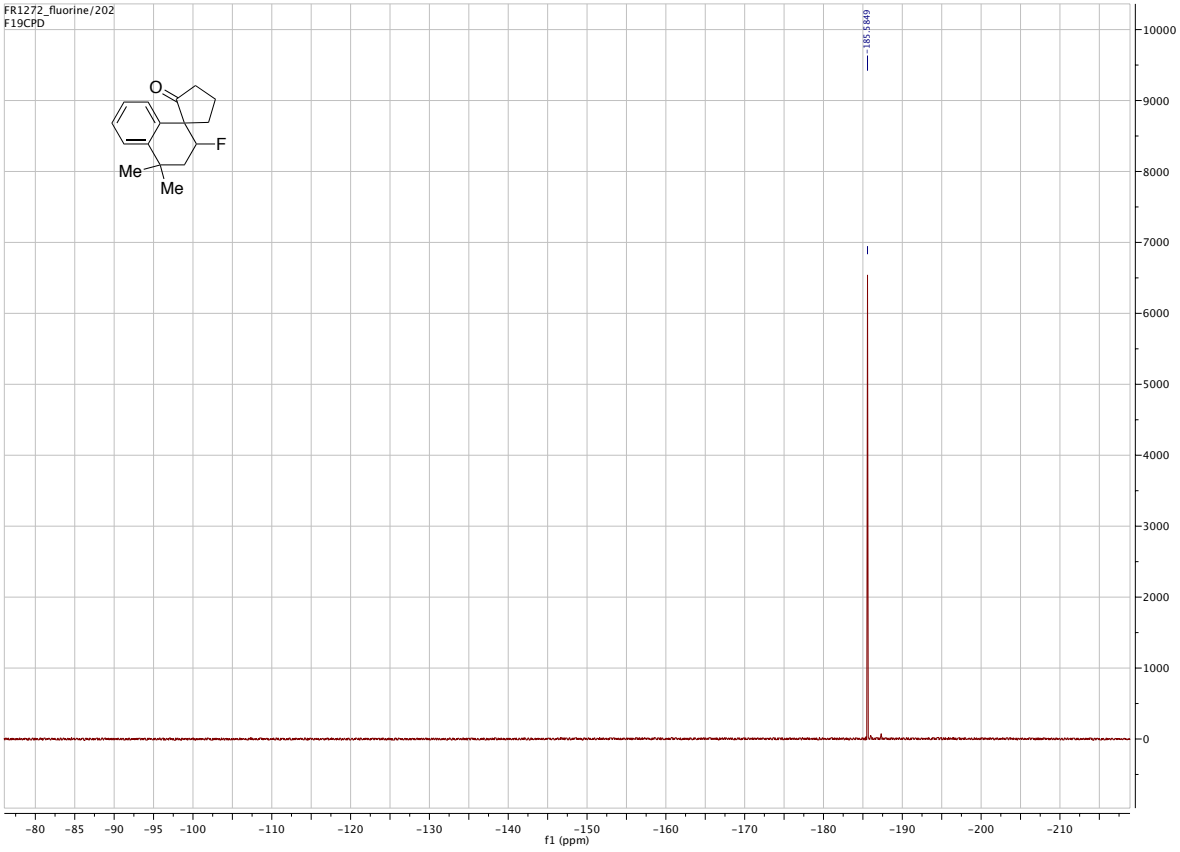
^{1}H NMR 500 MHz, C_6D_6



^{13}C NMR 125 MHz, C_6D_6

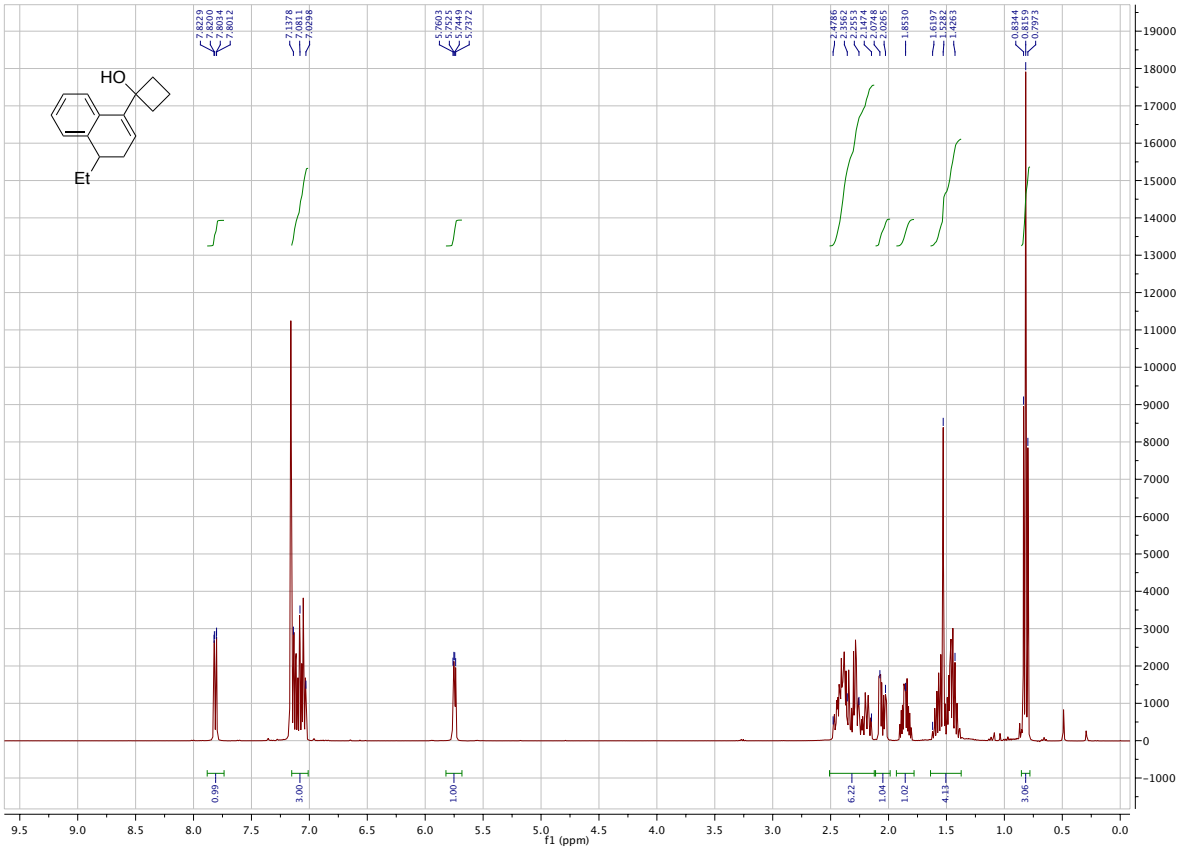


^{19}F NMR 375 MHz, C_6D_6

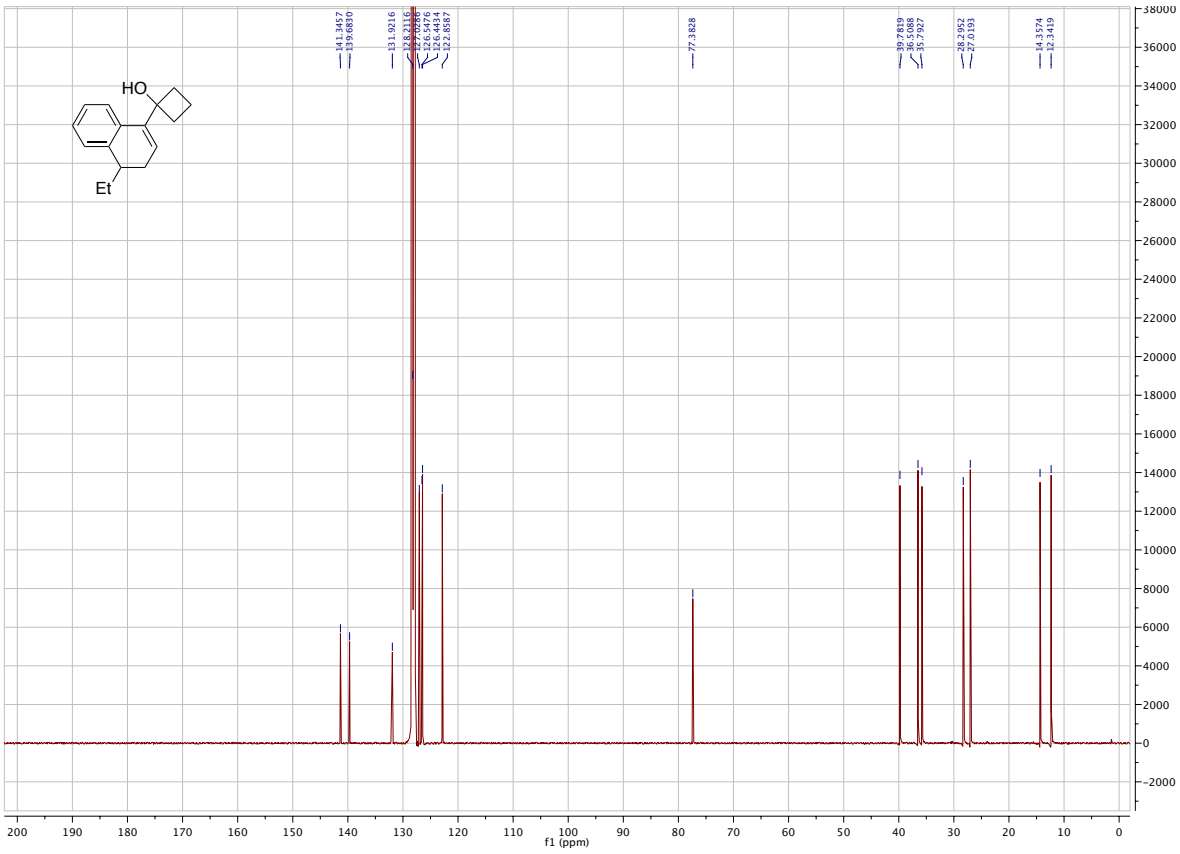


Substrate *rac*-A_{11}

^{1}H NMR 400 MHz, C_6D_6

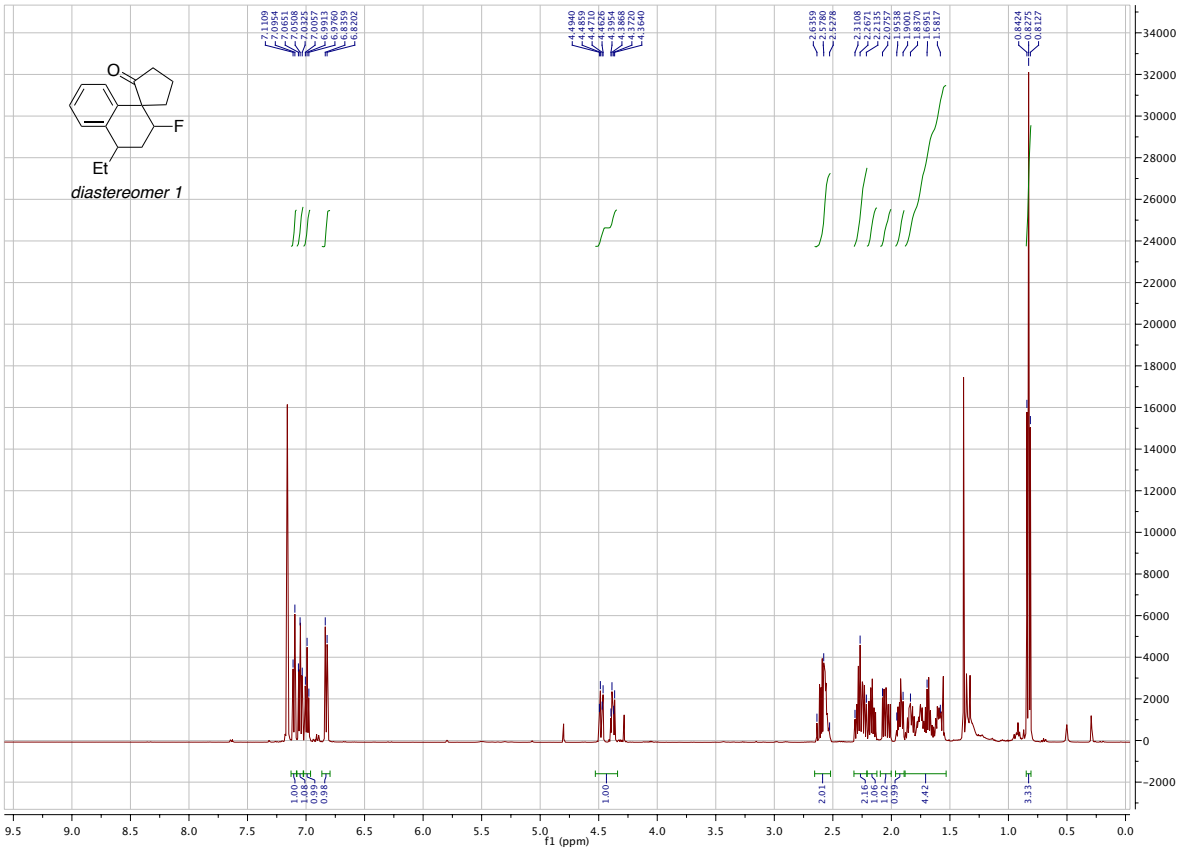


^{13}C NMR 100 MHz, C_6D_6

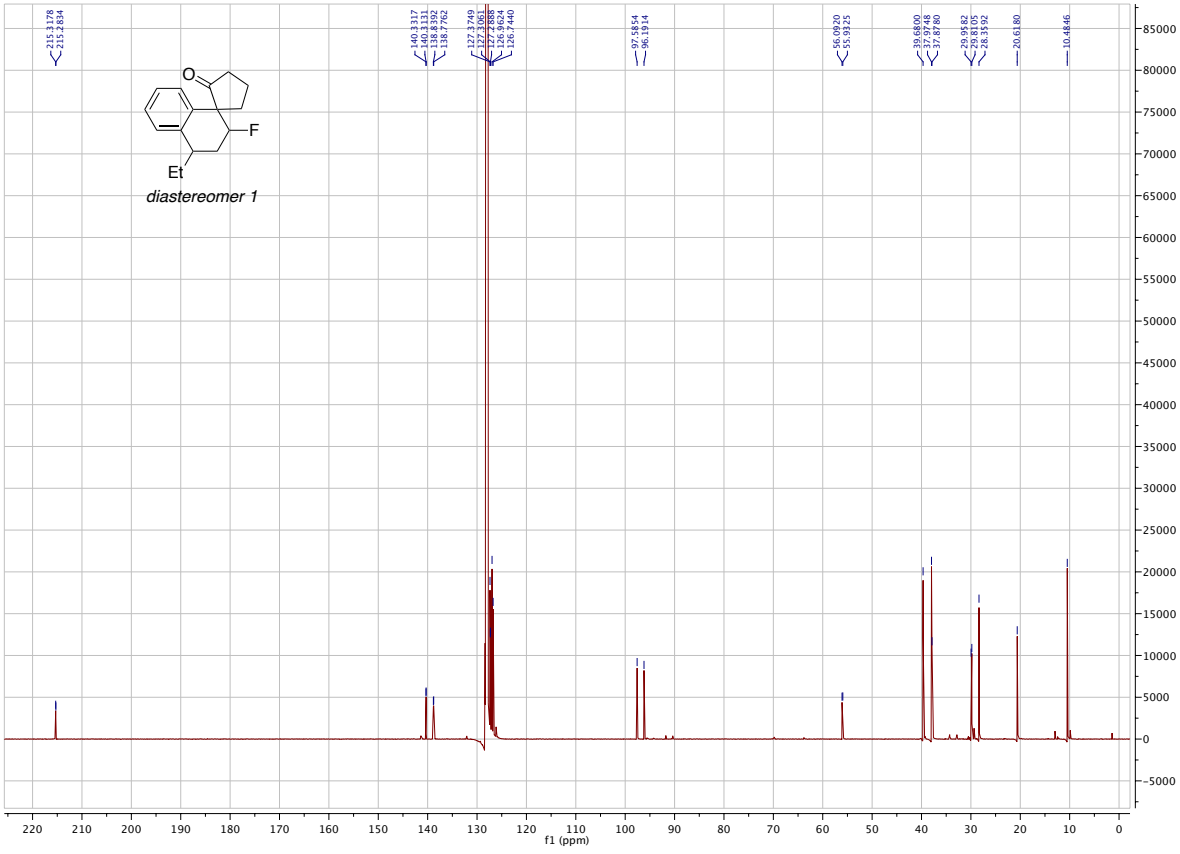


β-Fluoro Spiroketone B_{11}^{R}

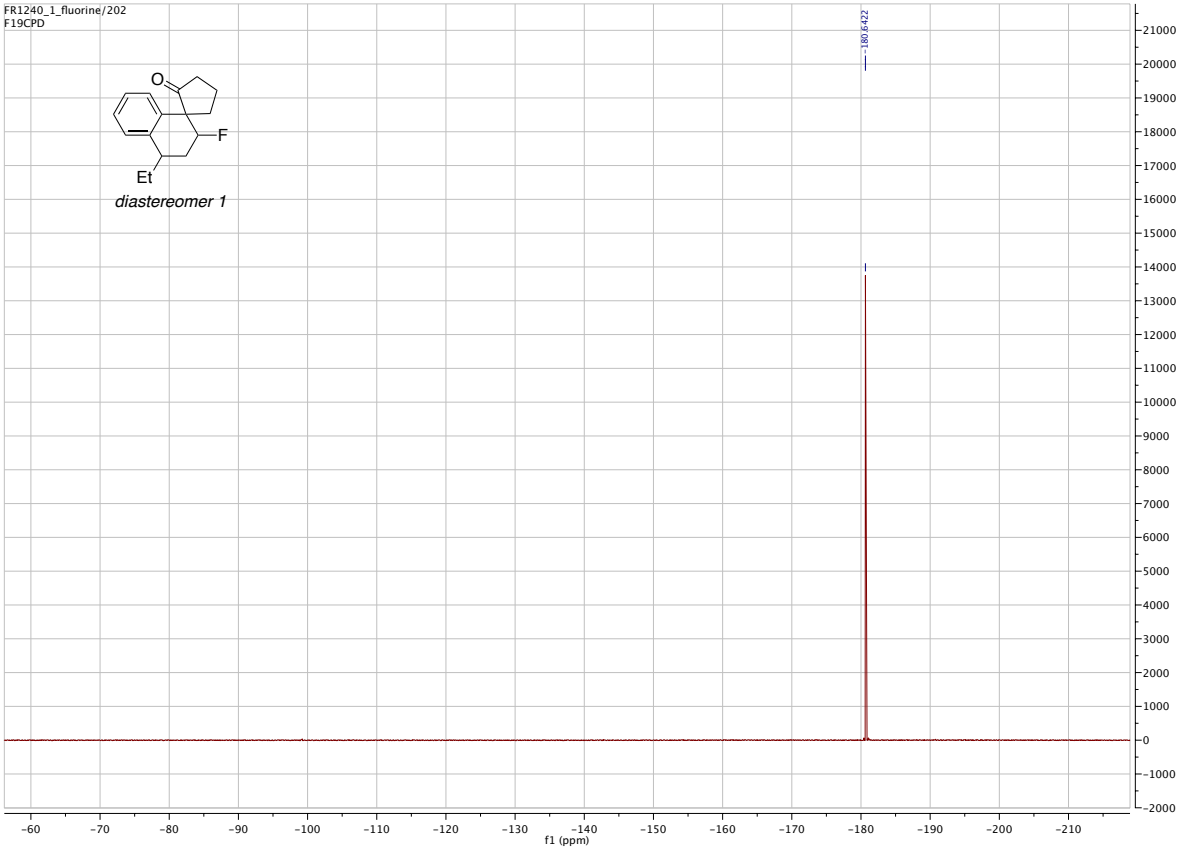
^{1}H NMR 500 MHz, C_6D_6



^{13}C NMR 125 MHz, C_6D_6

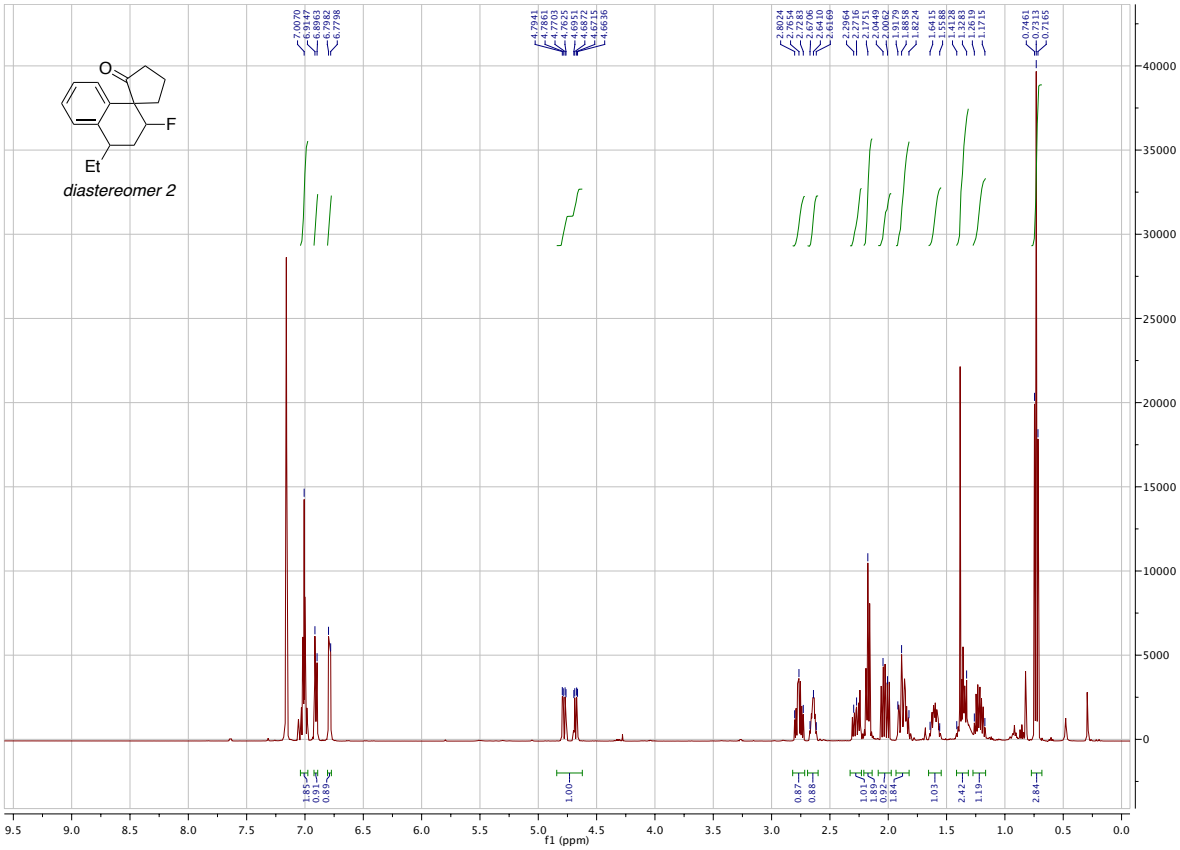


^{19}F NMR 375 MHz, C_6D_6

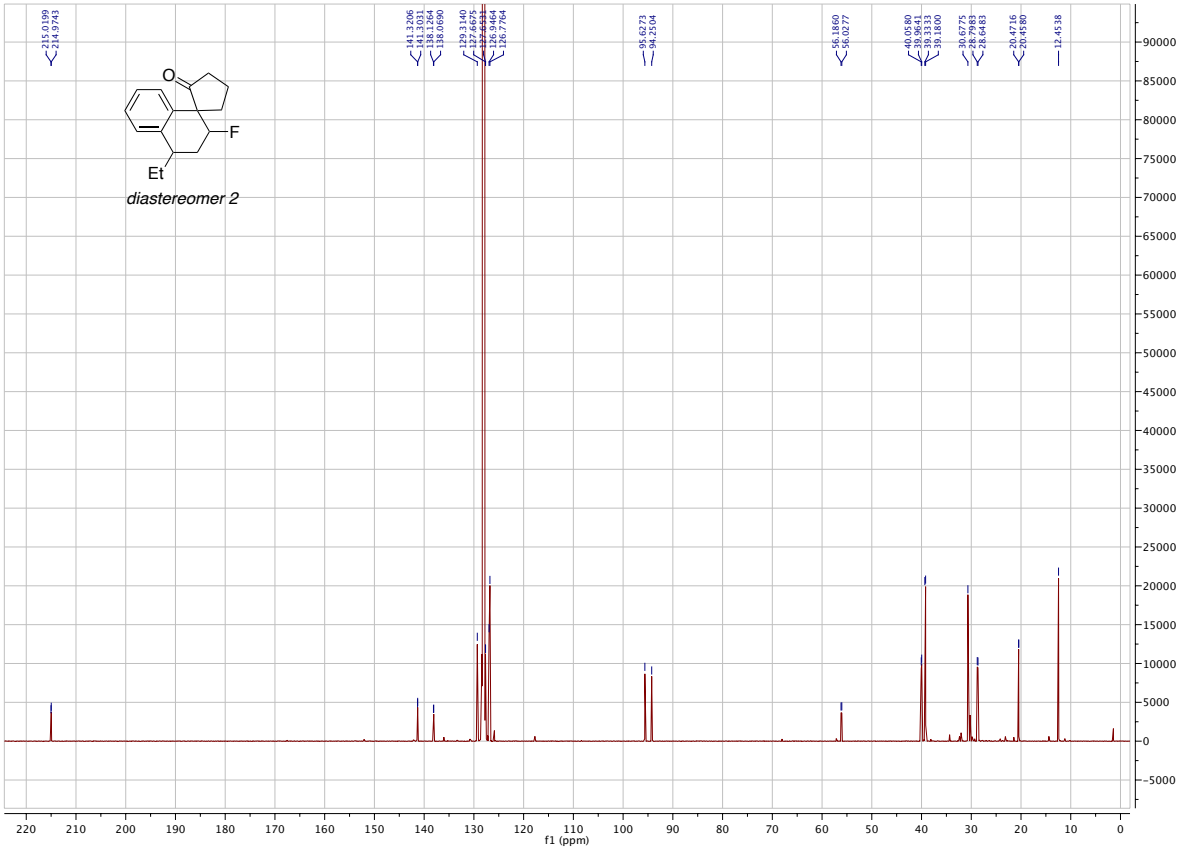


β-Fluoro Spiroketone B_{11}^{S}

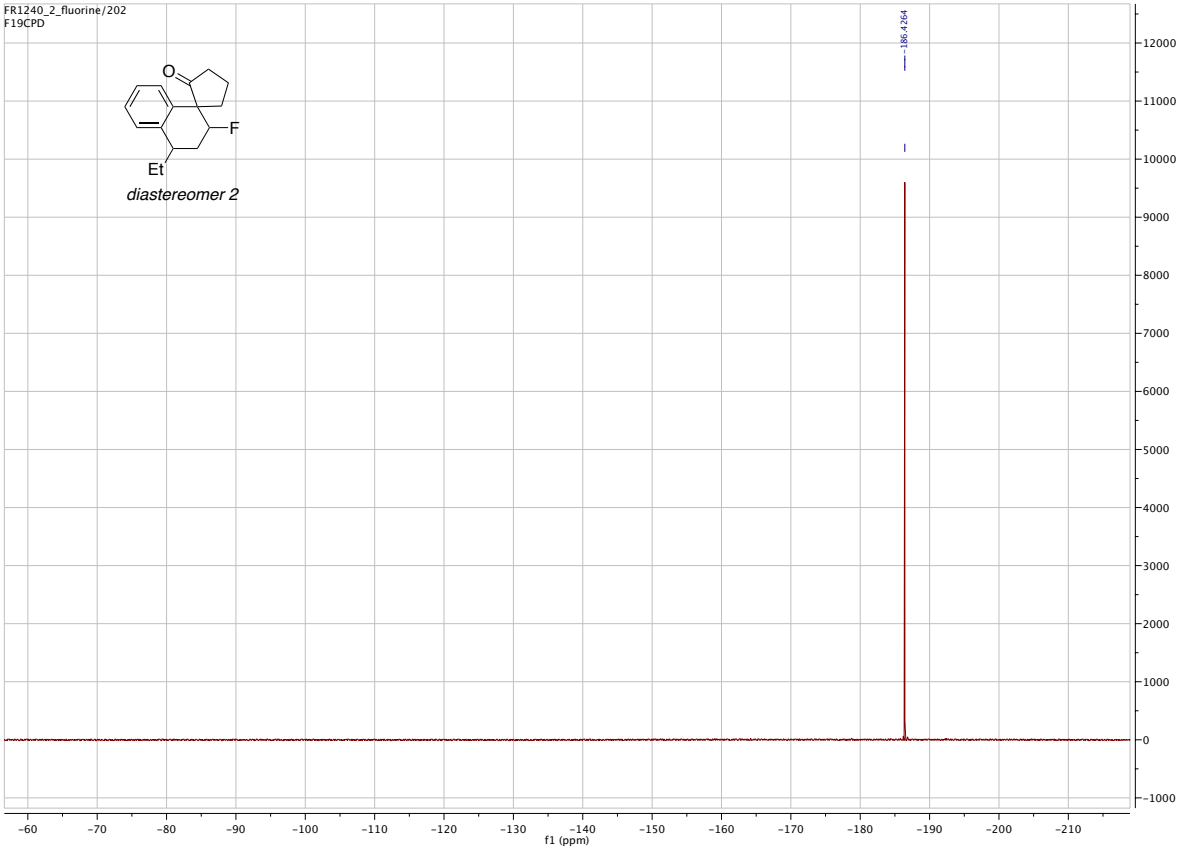
^{1}H NMR 500 MHz, C_6D_6



^{13}C NMR 125 MHz, C_6D_6

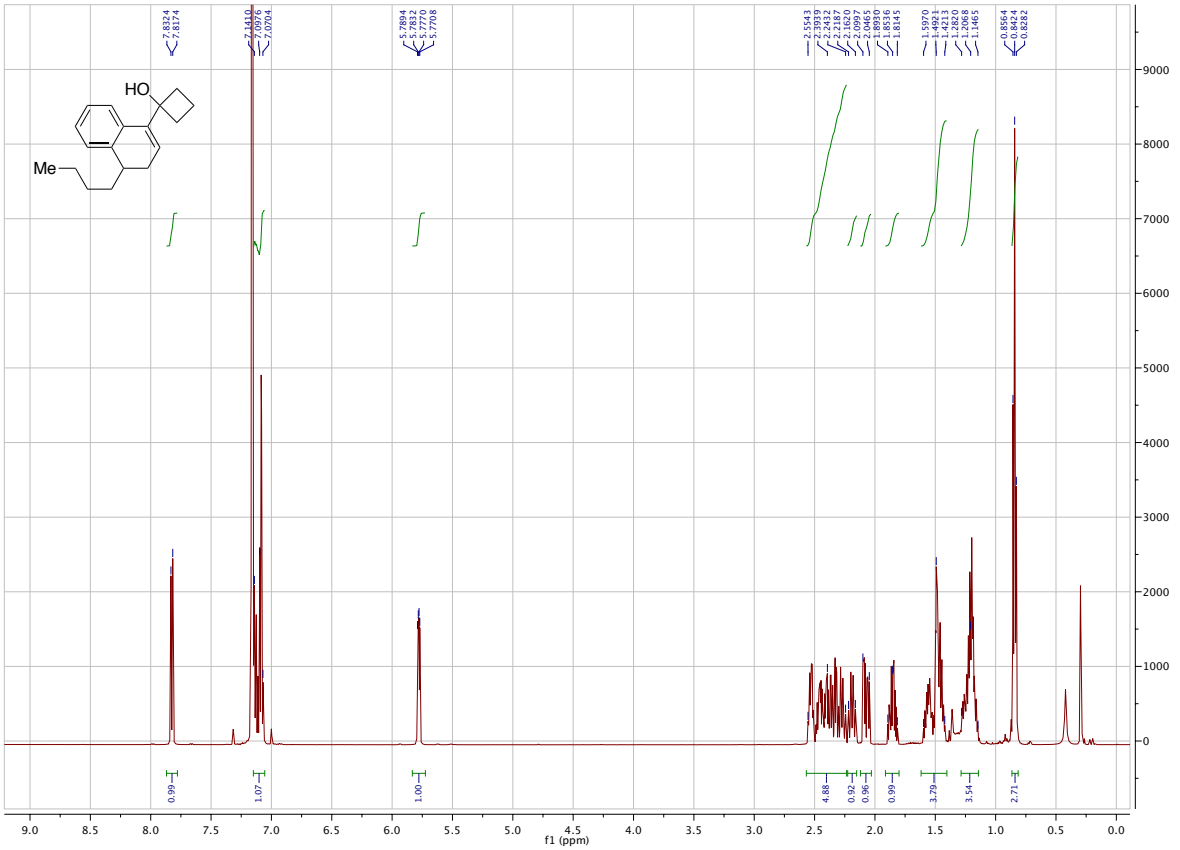


^{19}F NMR 375 MHz, C_6D_6

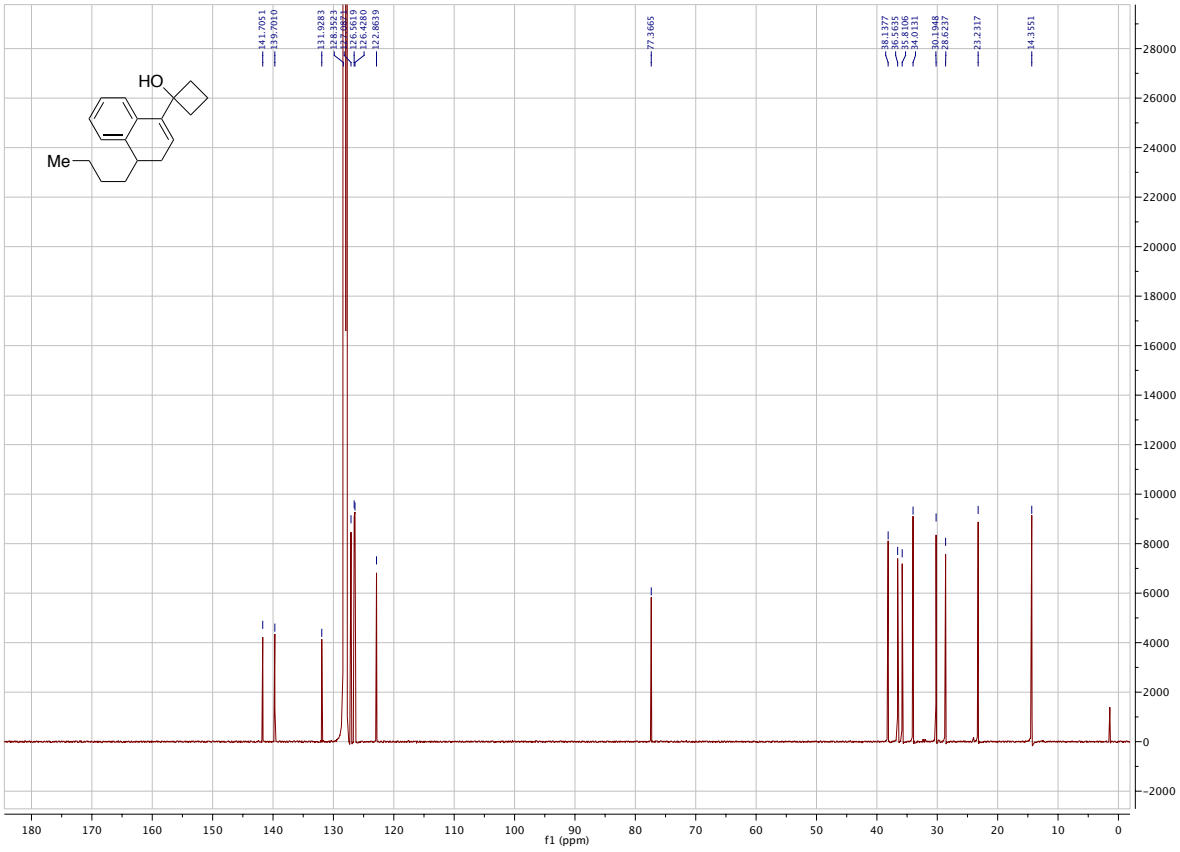


Substrate *rac*-A_{12}

^{1}H NMR 500 MHz, C_6D_6



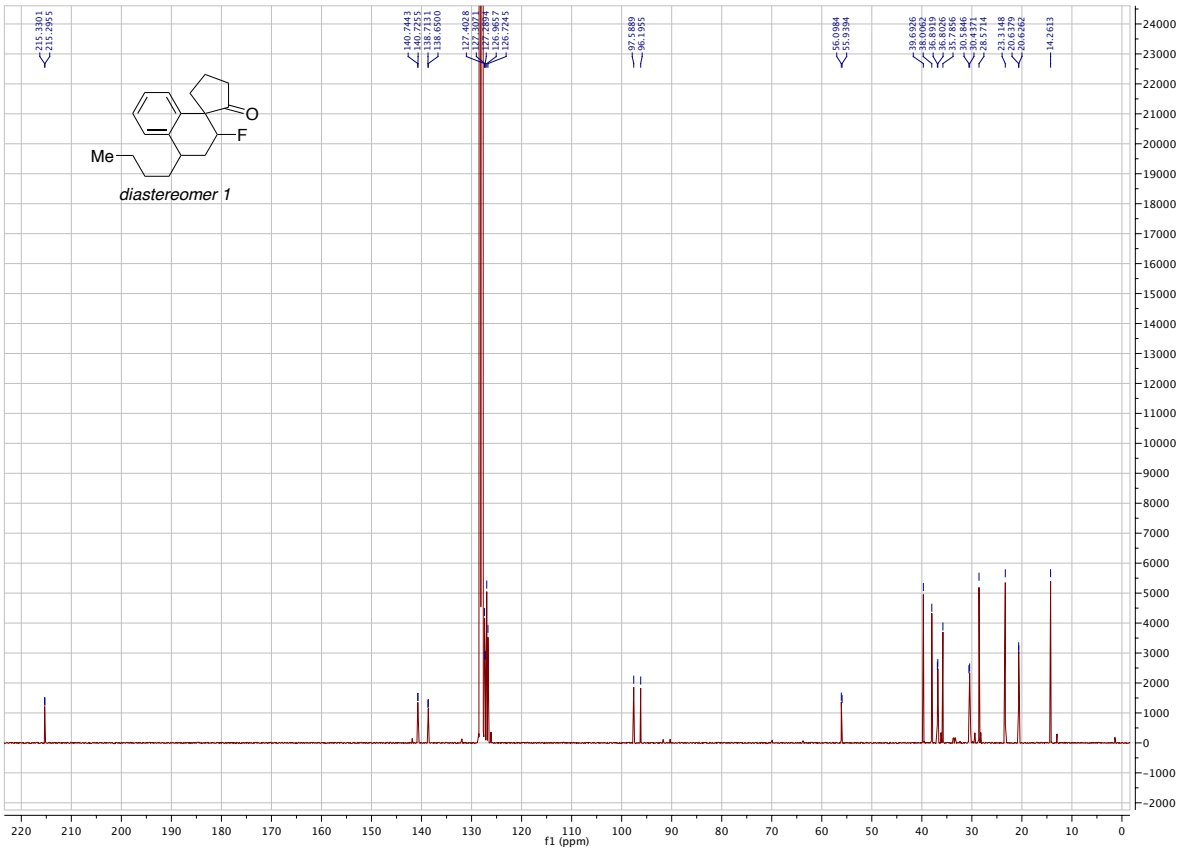
^{13}C NMR 125 MHz, C_6D_6



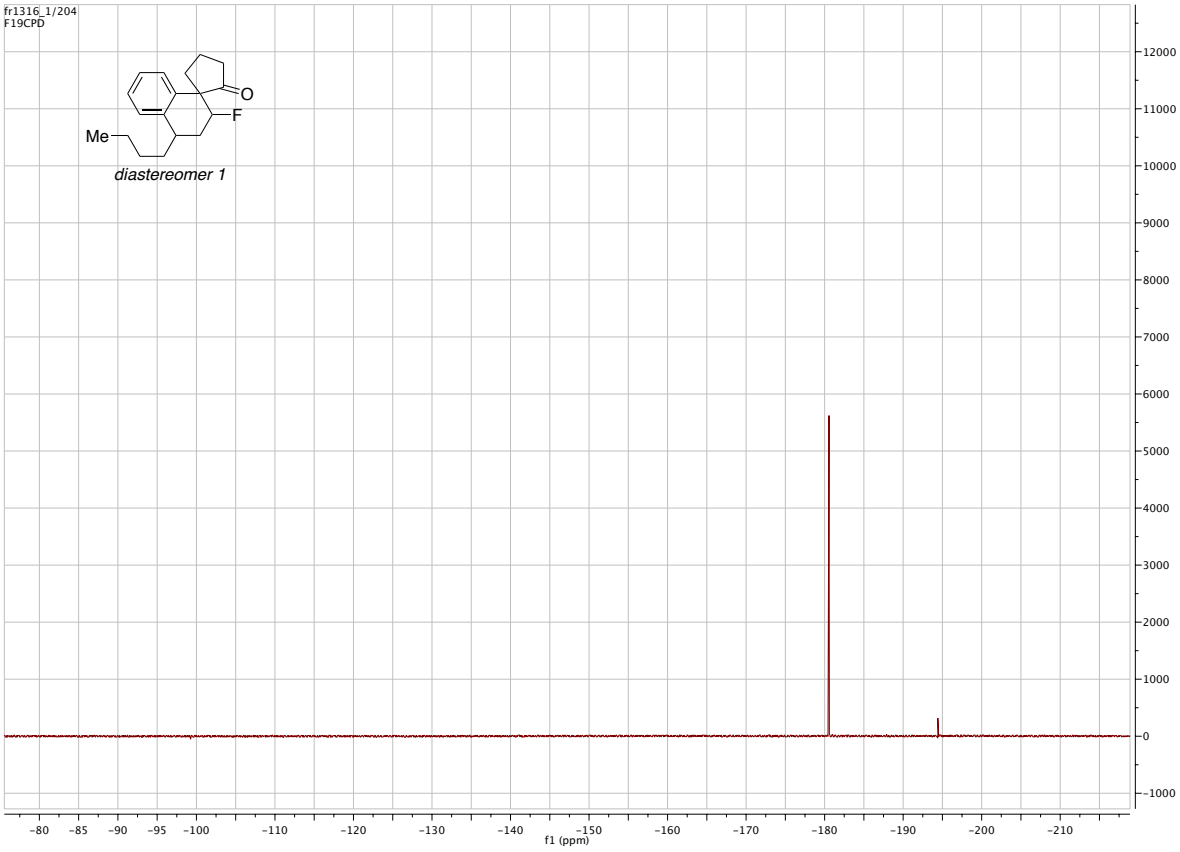
β-Fluoro Spiroketone B_{12}^{R}

^{1}H NMR 500 MHz, C_6D_6

^{13}C NMR 125 MHz, C_6D_6

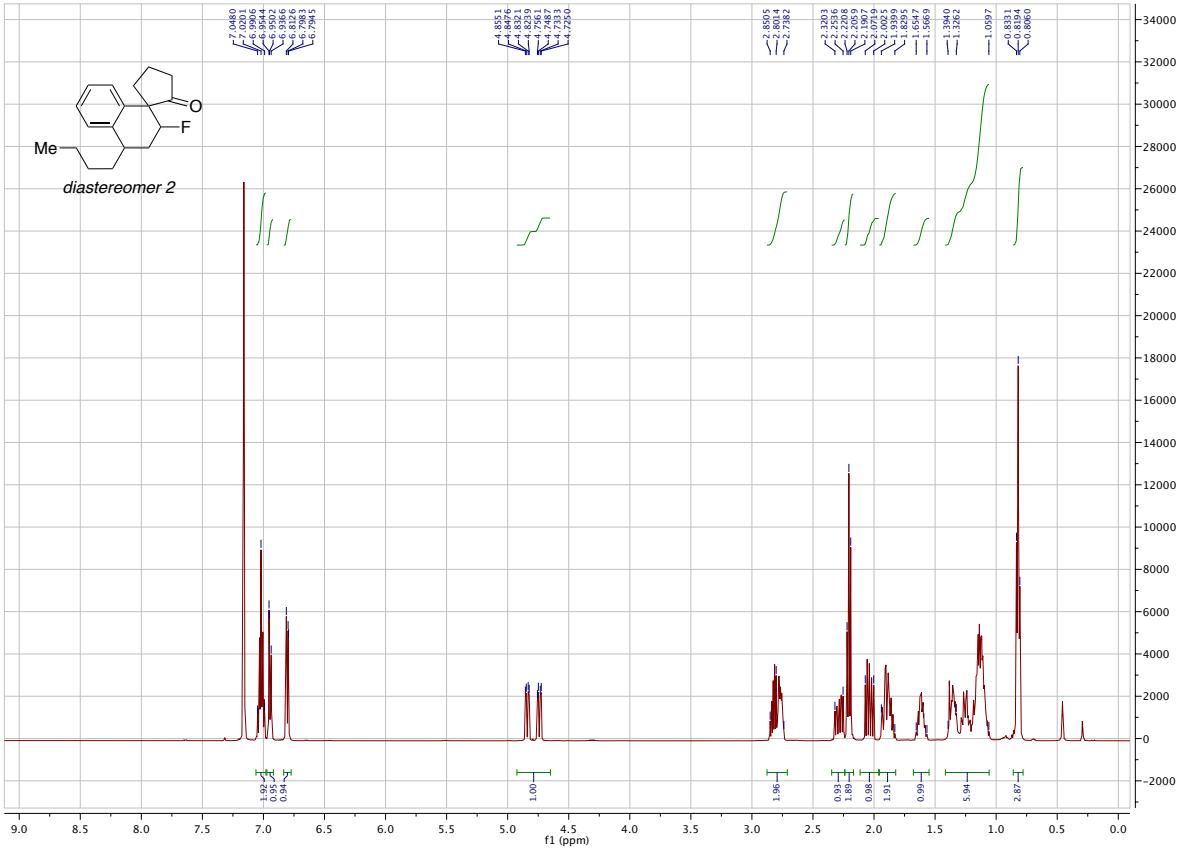


^{19}F NMR 375 MHz, C_6D_6

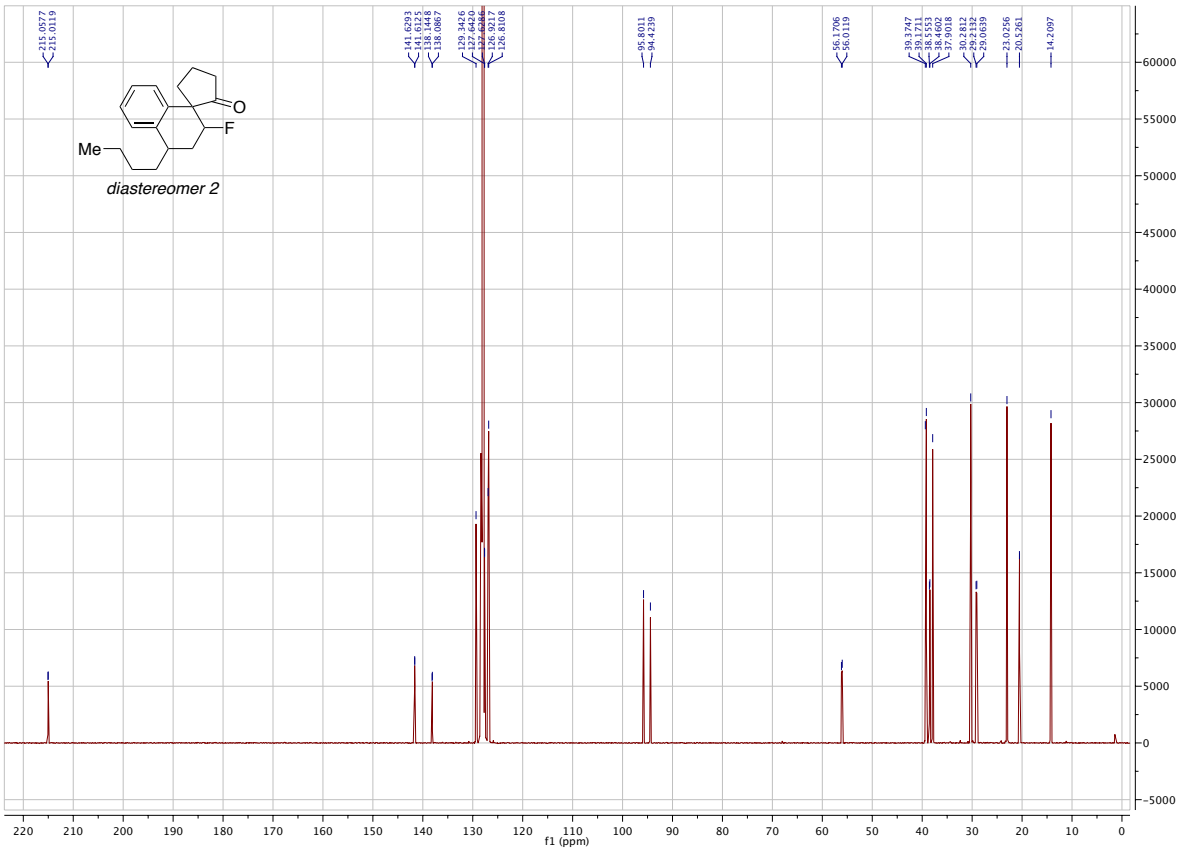


β-Fluoro Spiroketone B_{12}^{S}

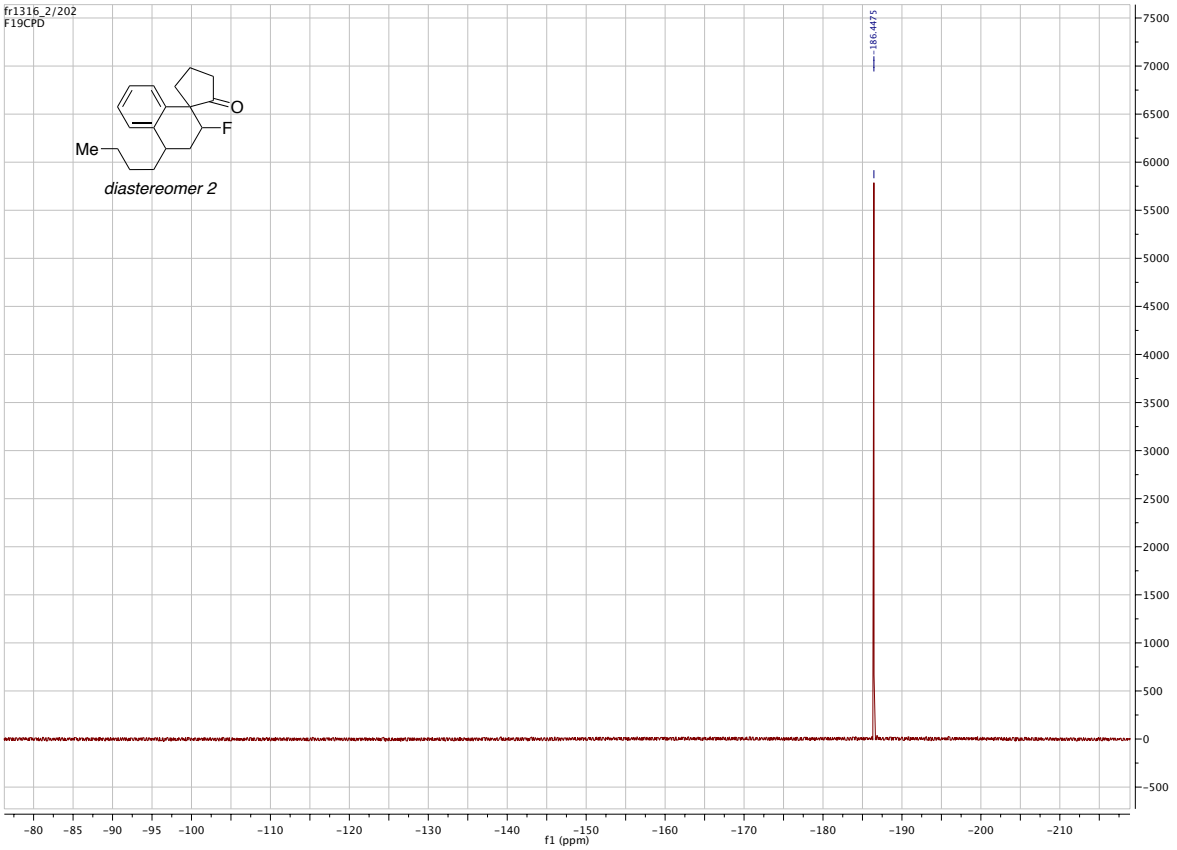
^{1}H NMR 500 MHz, C_6D_6



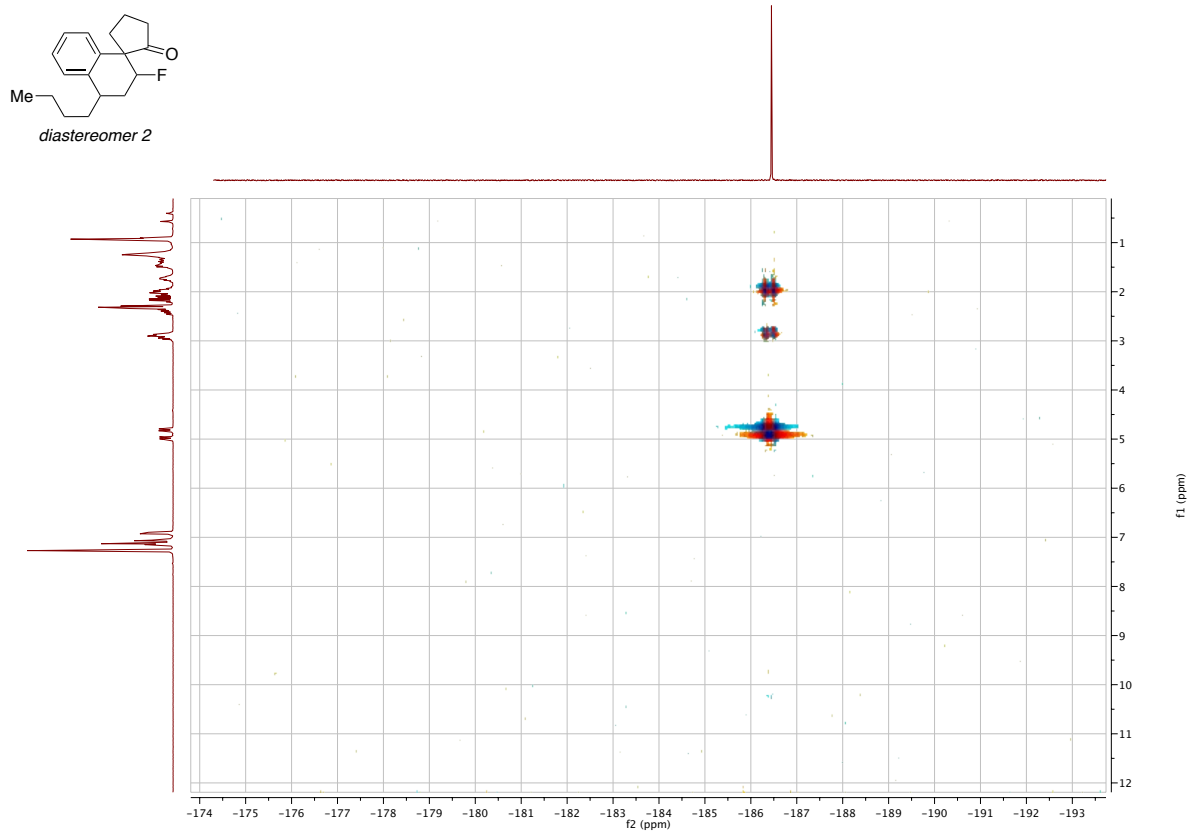
^{13}C NMR 125 MHz, C_6D_6



^{19}F NMR 375 MHz, C_6D_6

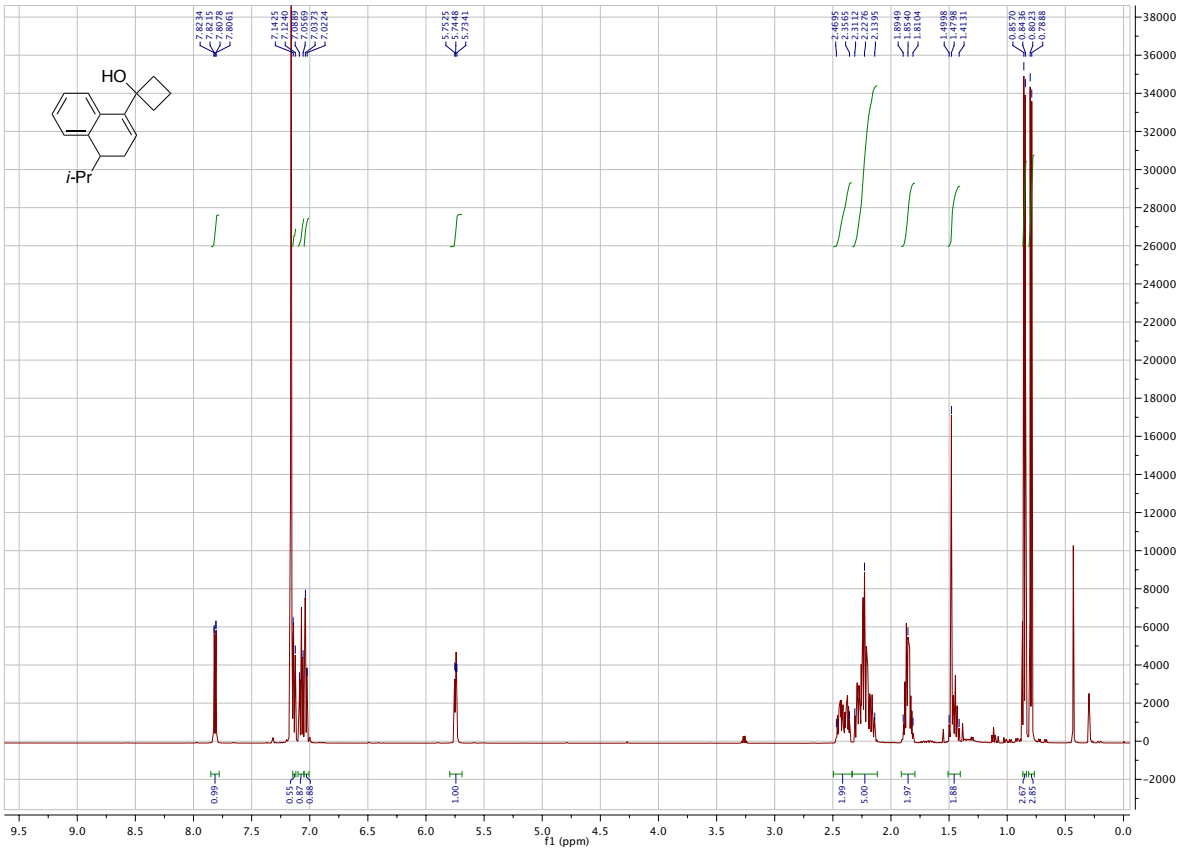


^{1}H-^{19}F HOESY 300 MHz, C_6D_6

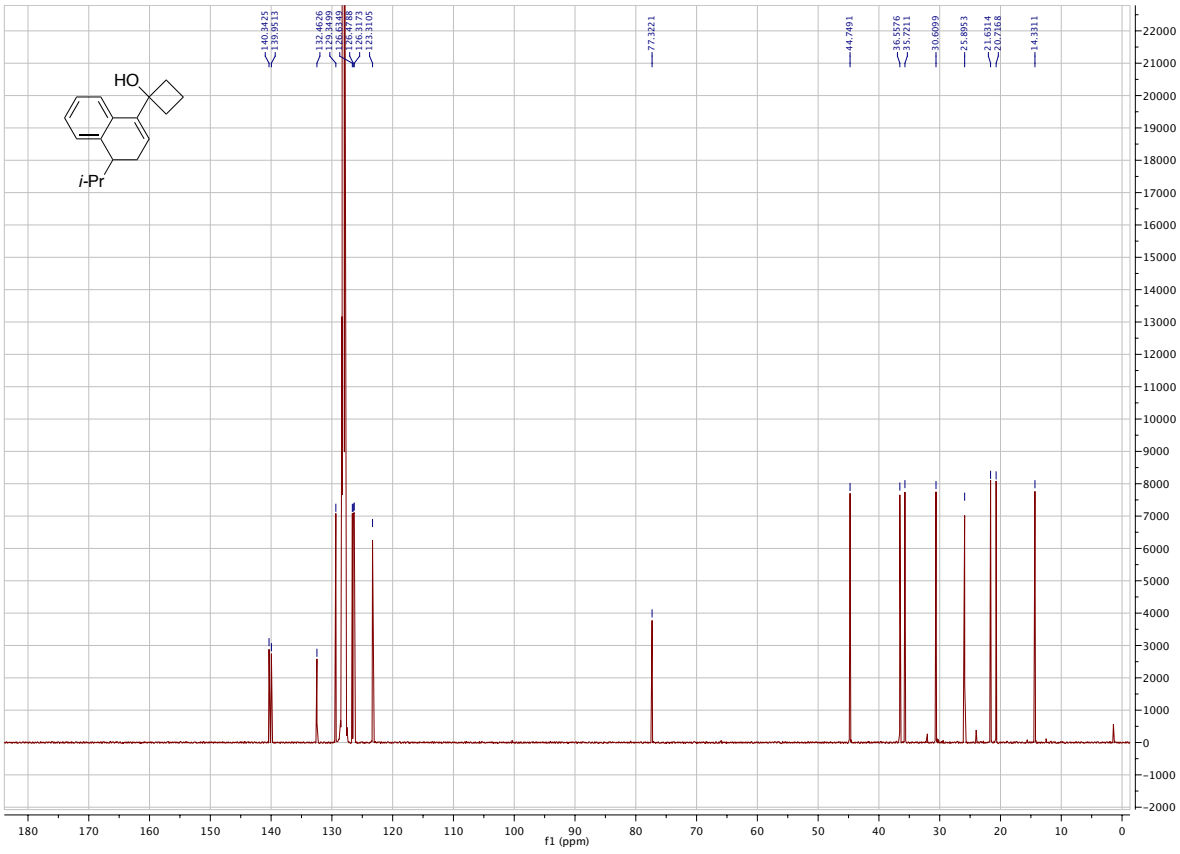


Substrate *rac*-A_{13}

^{1}H NMR 500 MHz, C_6D_6



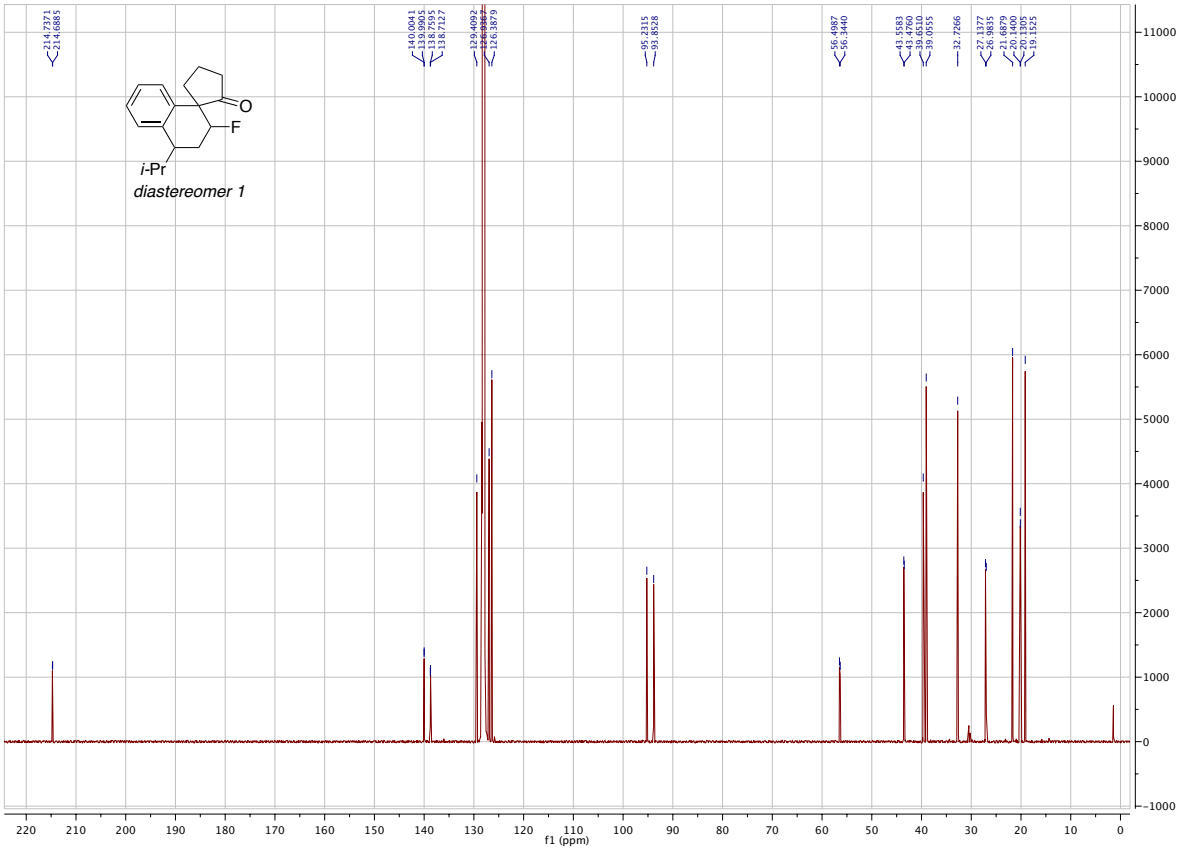
^{13}C NMR 125 MHz, C_6D_6



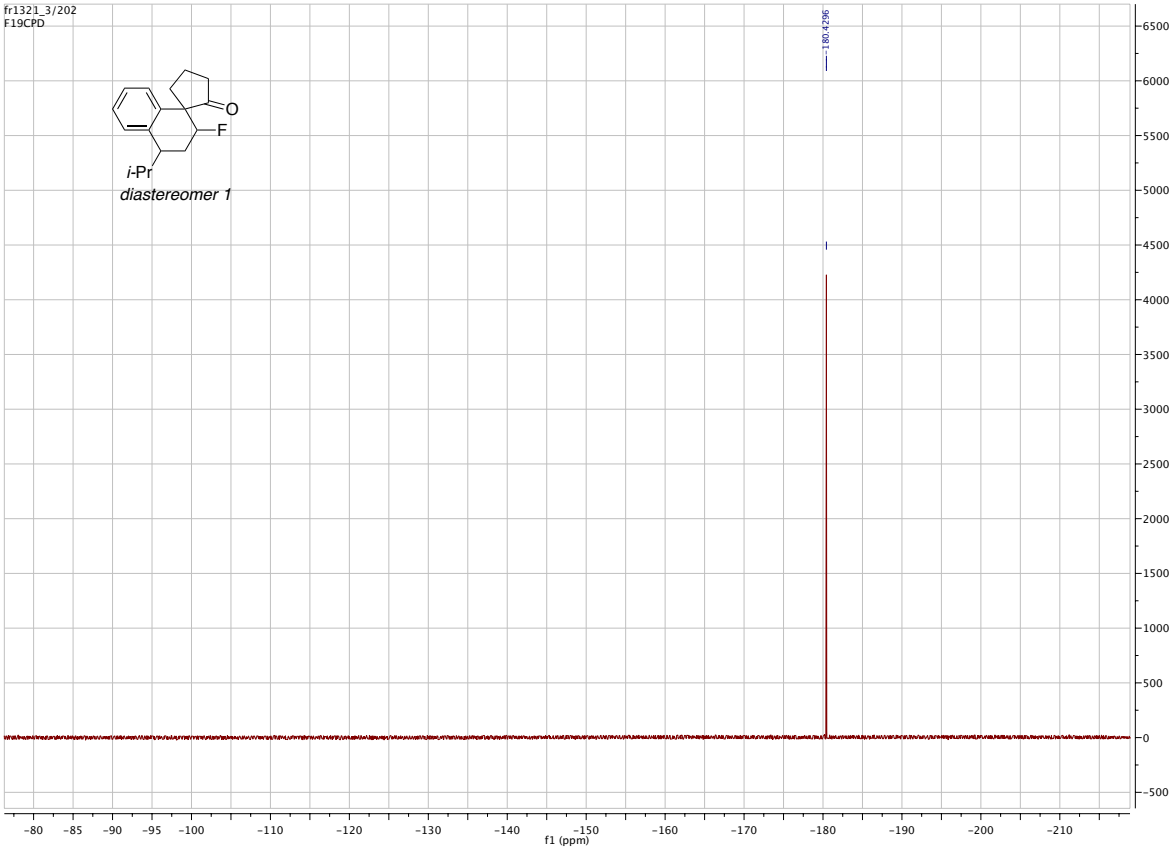
β-Fluoro Spiroketone B_{13}^{R}

^{1}H NMR 500 MHz, C_6D_6

^{13}C NMR 125 MHz, C_6D_6

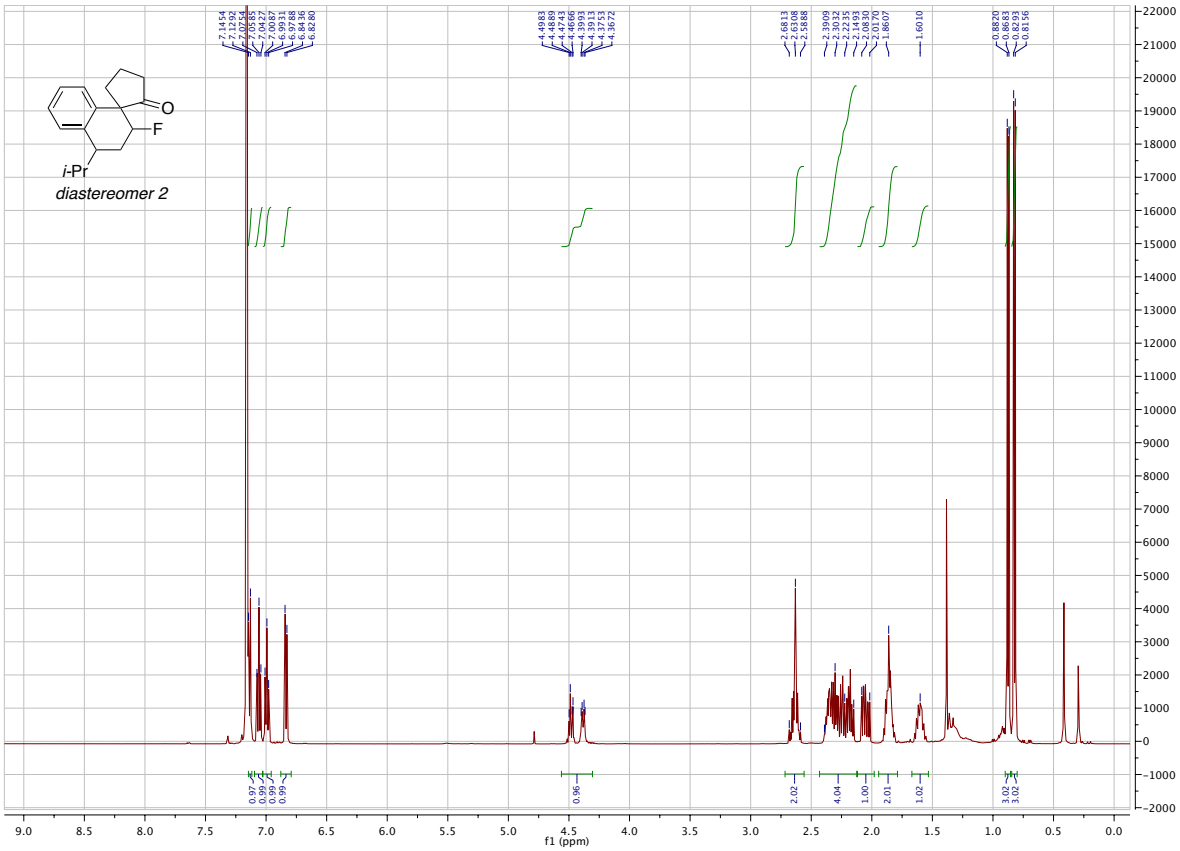


^{19}F NMR 375 MHz, C_6D_6

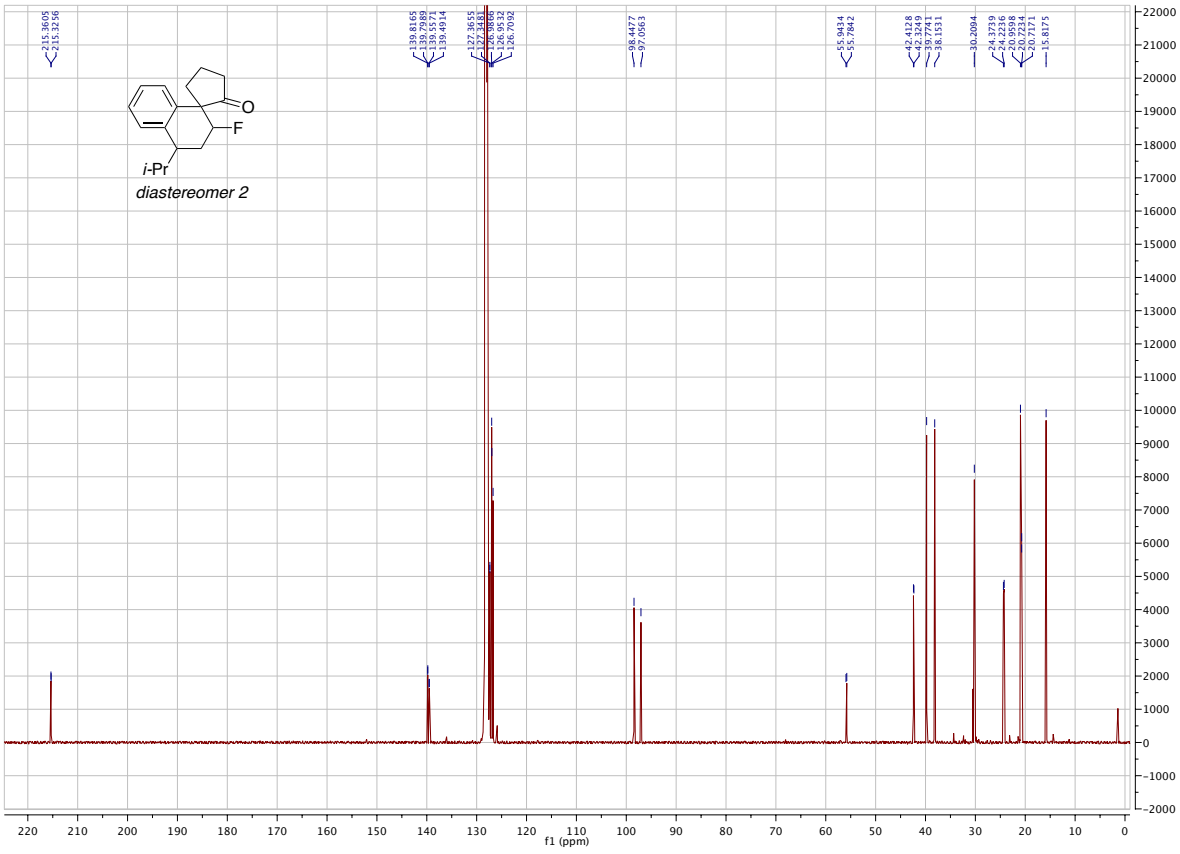


β-Fluoro Spiroketone B_{13}^{S}

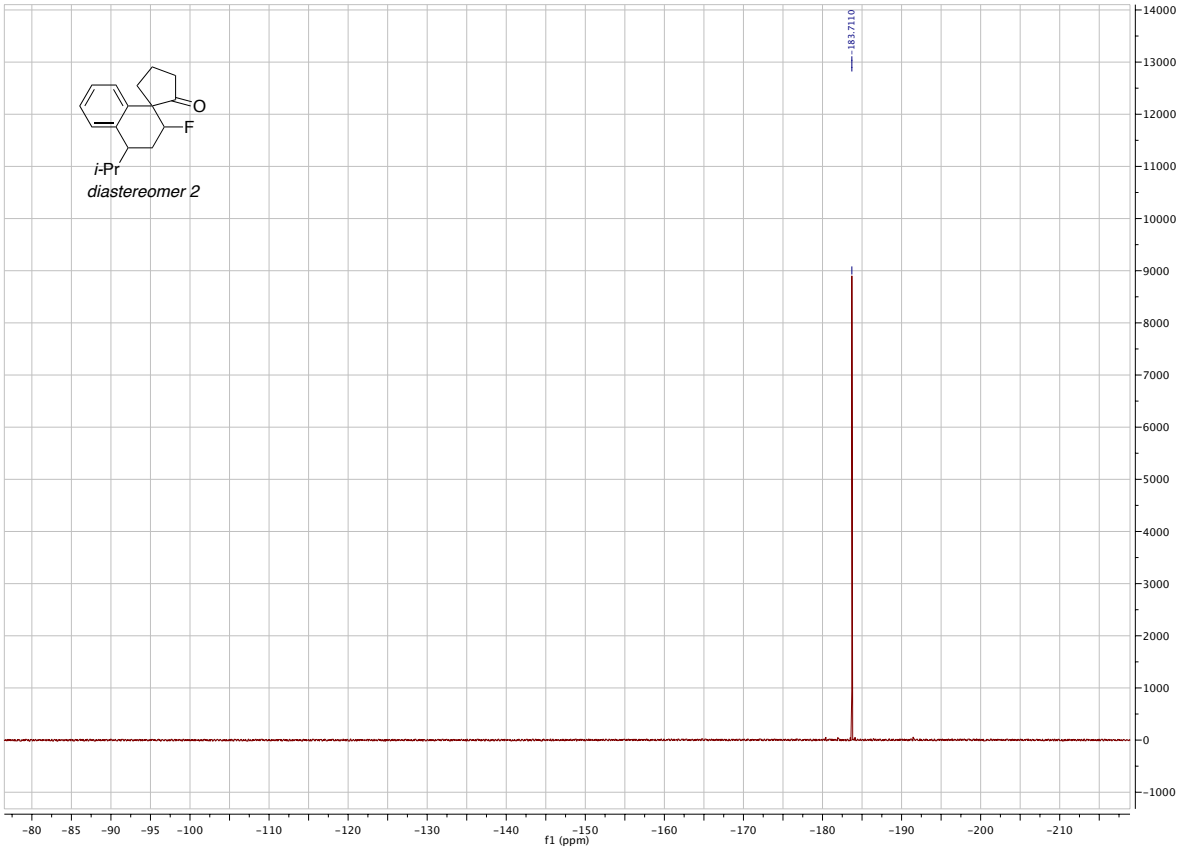
^{1}H NMR 500 MHz, C_6D_6



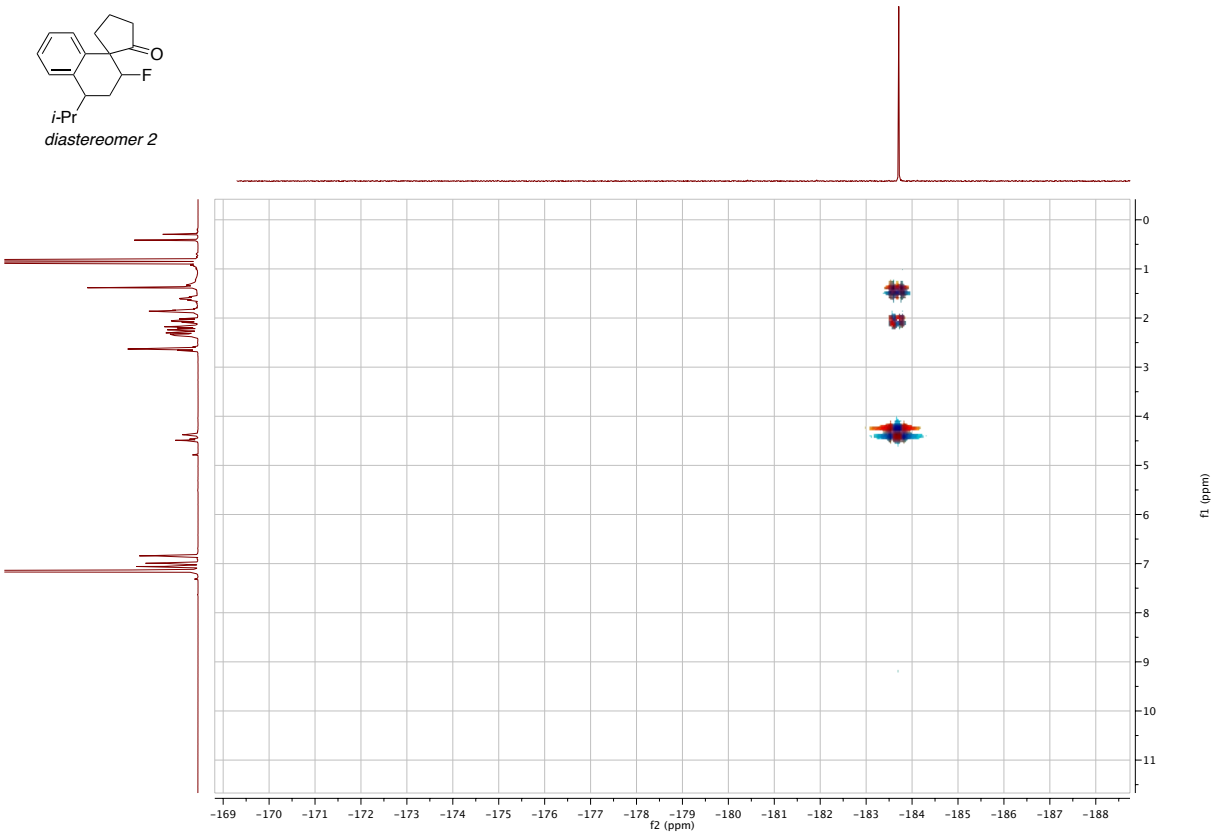
^{13}C NMR 125 MHz, C_6D_6



^{19}F NMR 375 MHz, C_6D_6

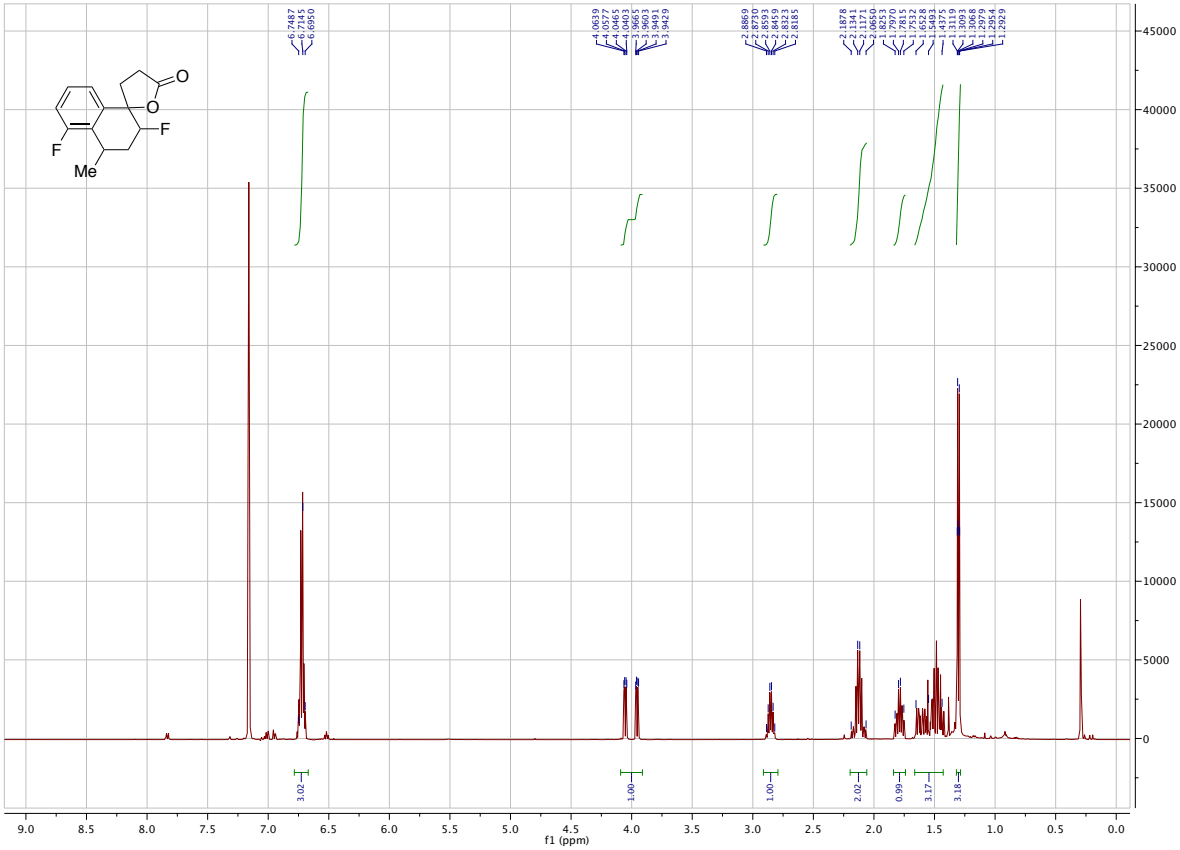


^{1}H-^{19}F HOESY 300 MHz, C_6D_6

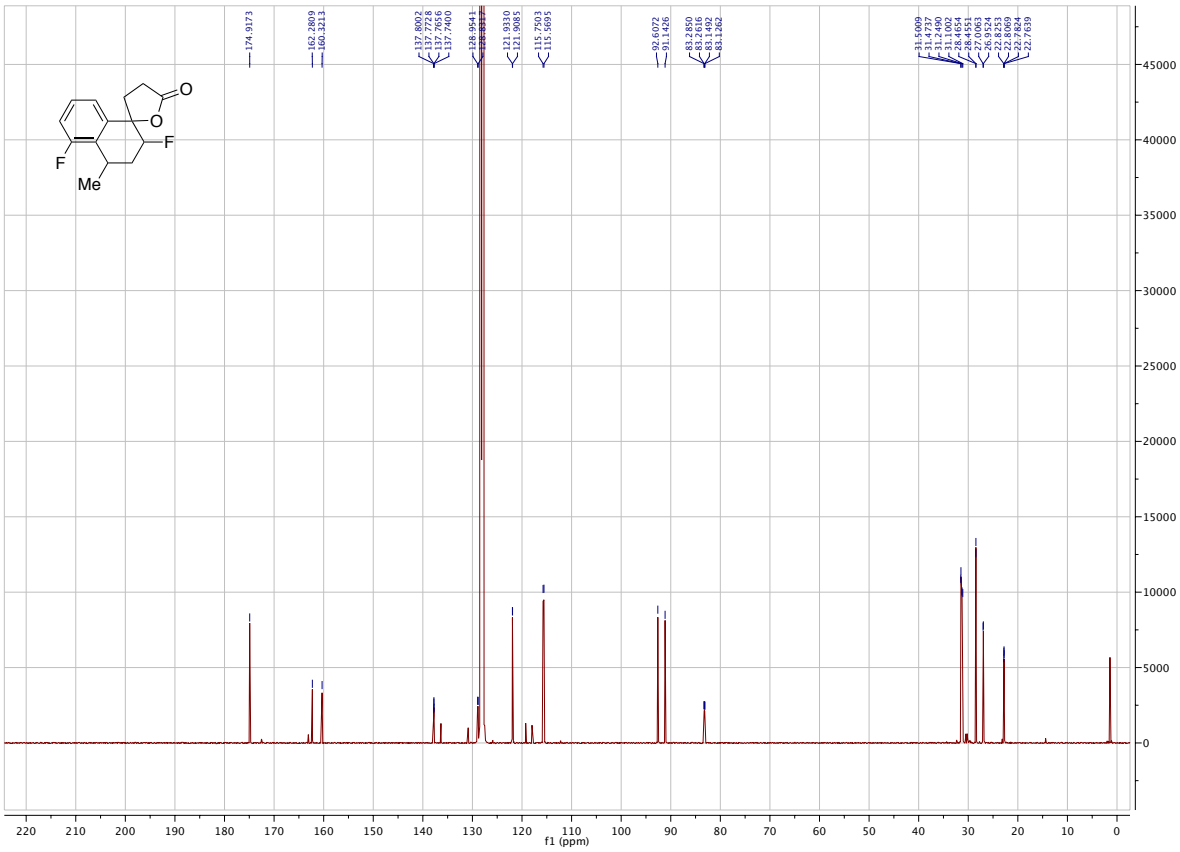


γ-Lactone D_8^R

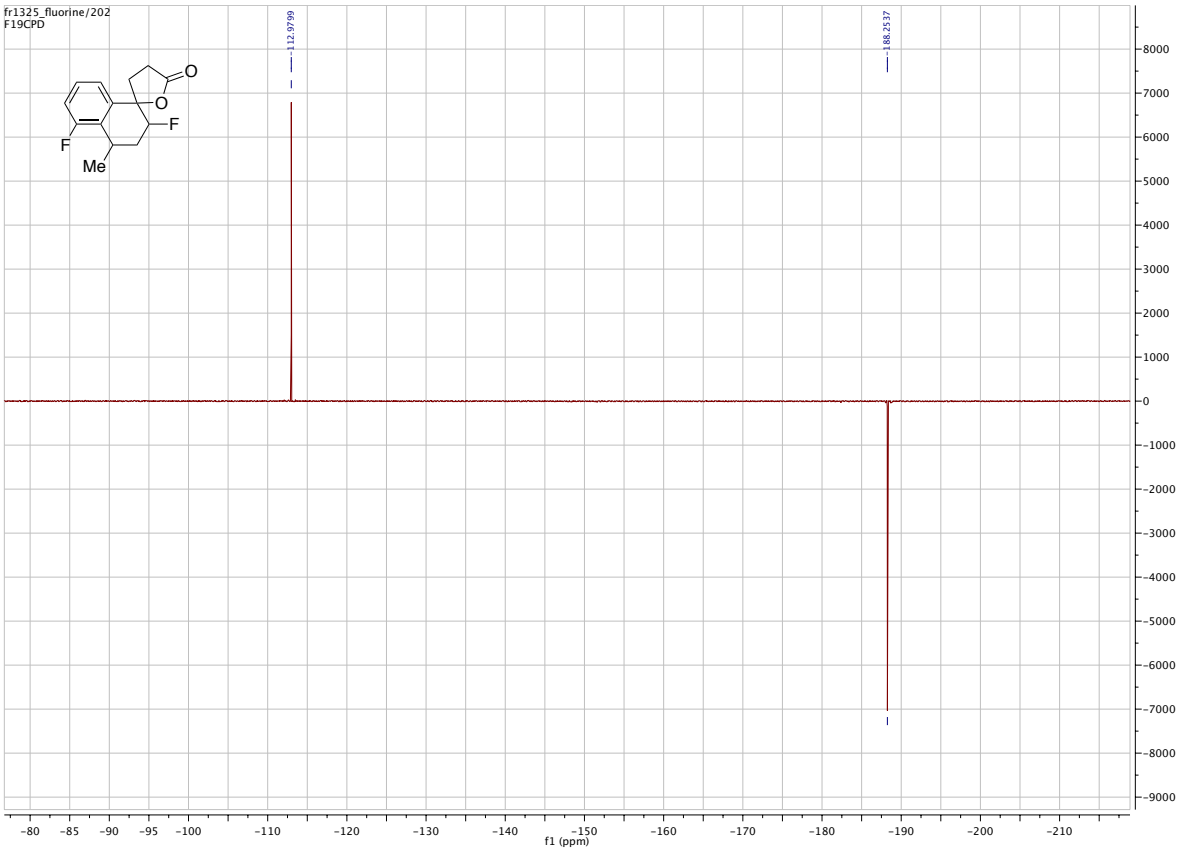
^{1}H NMR 500 MHz, C_6D_6



^{13}C NMR 125 MHz, C_6D_6



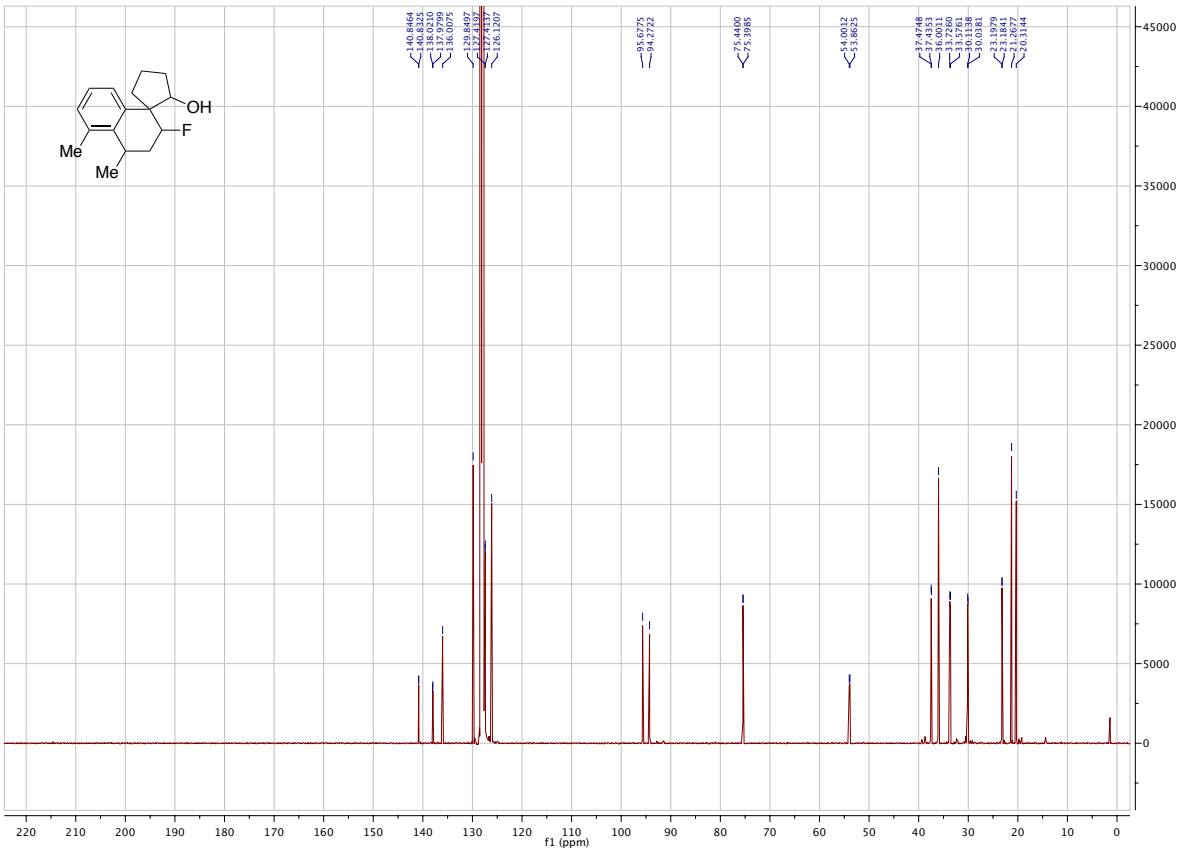
^{19}F NMR 375 MHz, C_6D_6



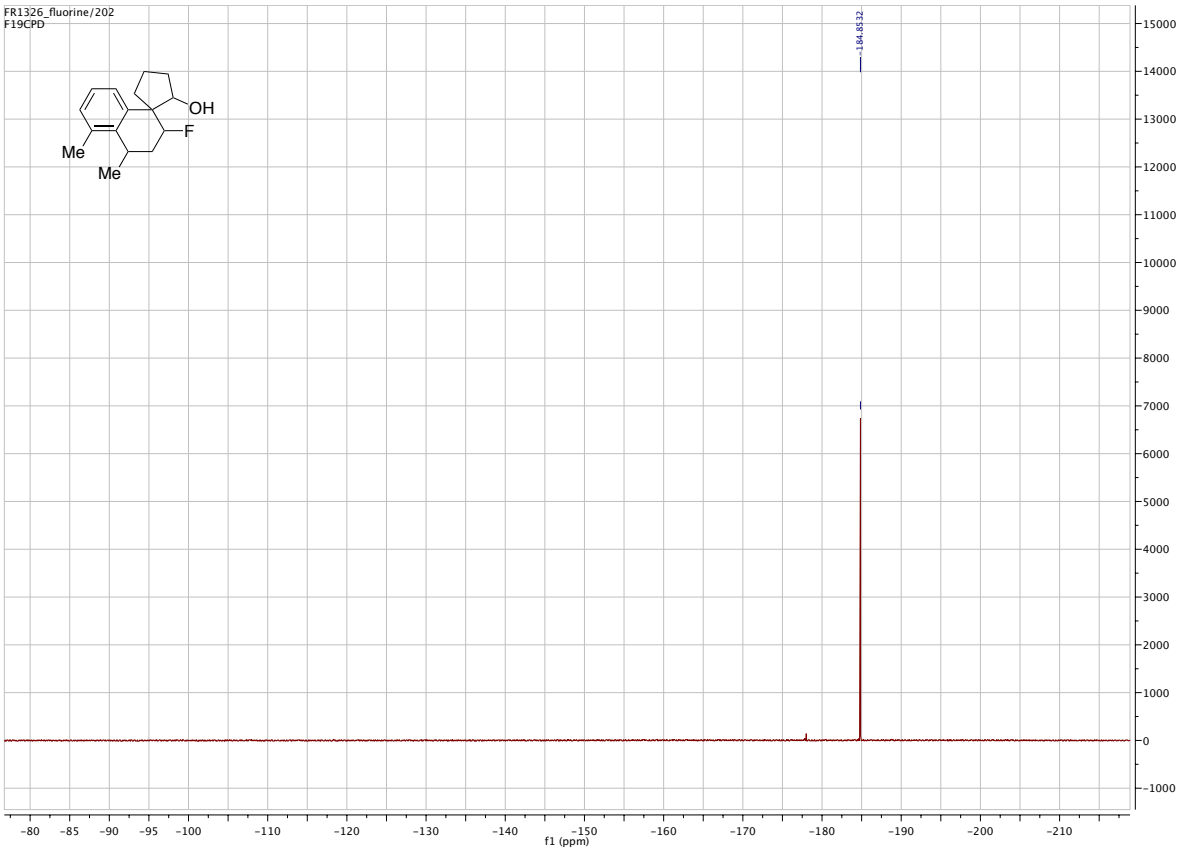
Fluoro Alcohol E_2^R

^{1}H NMR 500 MHz, C_6D_6

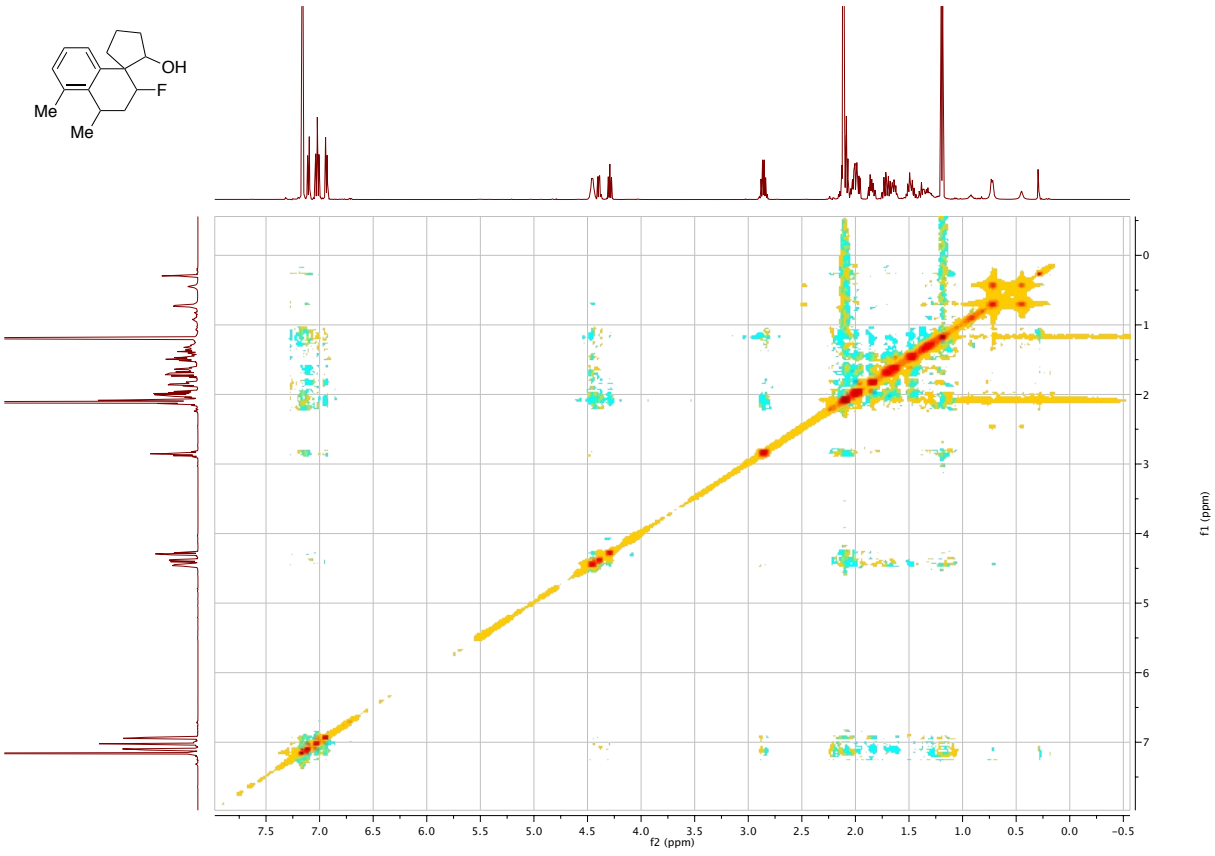
^{13}C NMR 125 MHz, C_6D_6



^{19}F NMR 375 MHz, C_6D_6

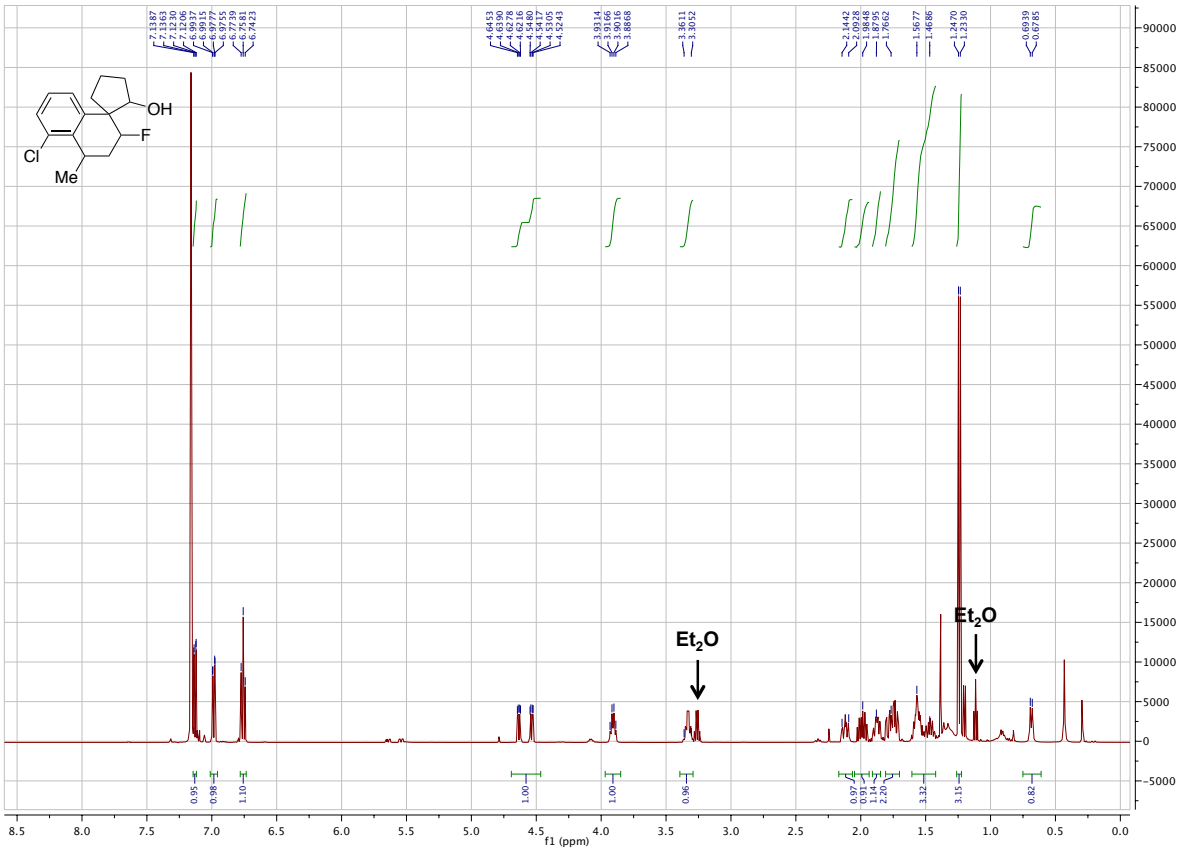


^{1}H-^{1}H NOESY 500 MHz, C_6D_6

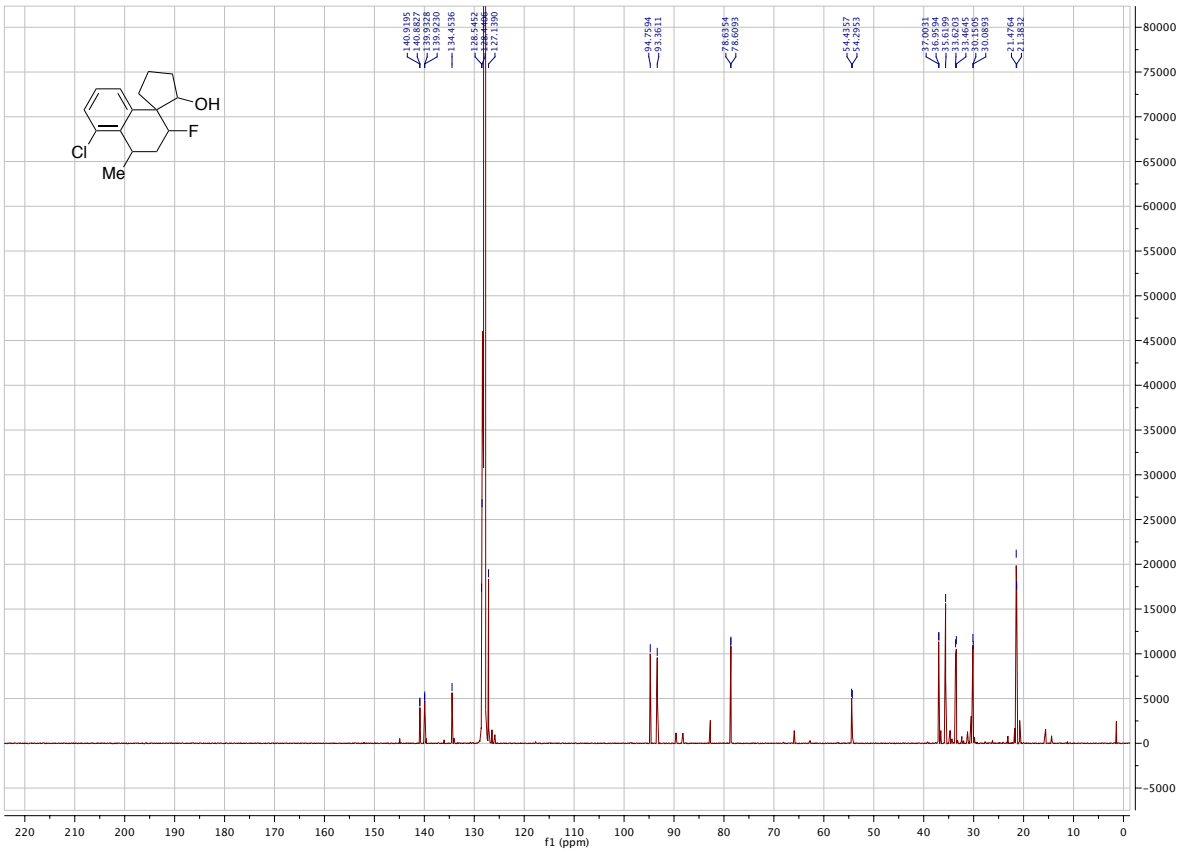


Fluoro Alcohol E_5^R

^{1}H NMR 500 MHz, C_6D_6



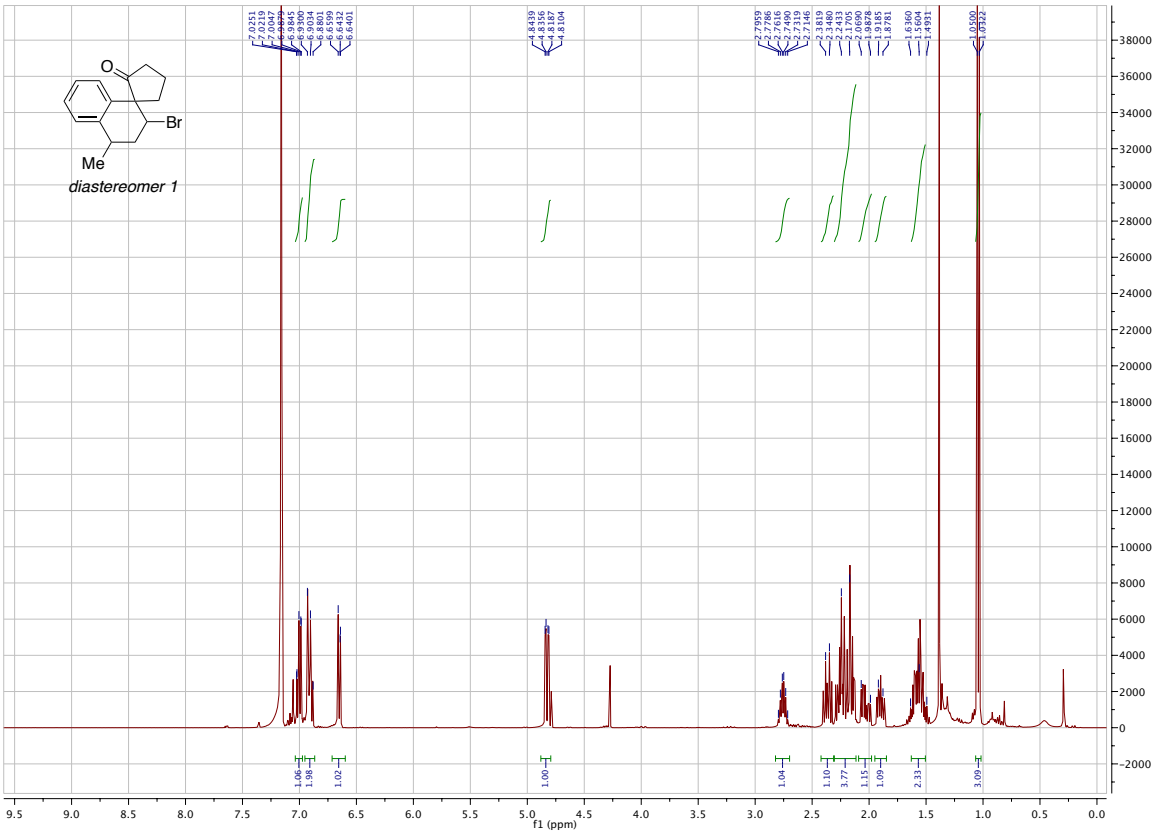
^{13}C NMR 125 MHz, C_6D_6



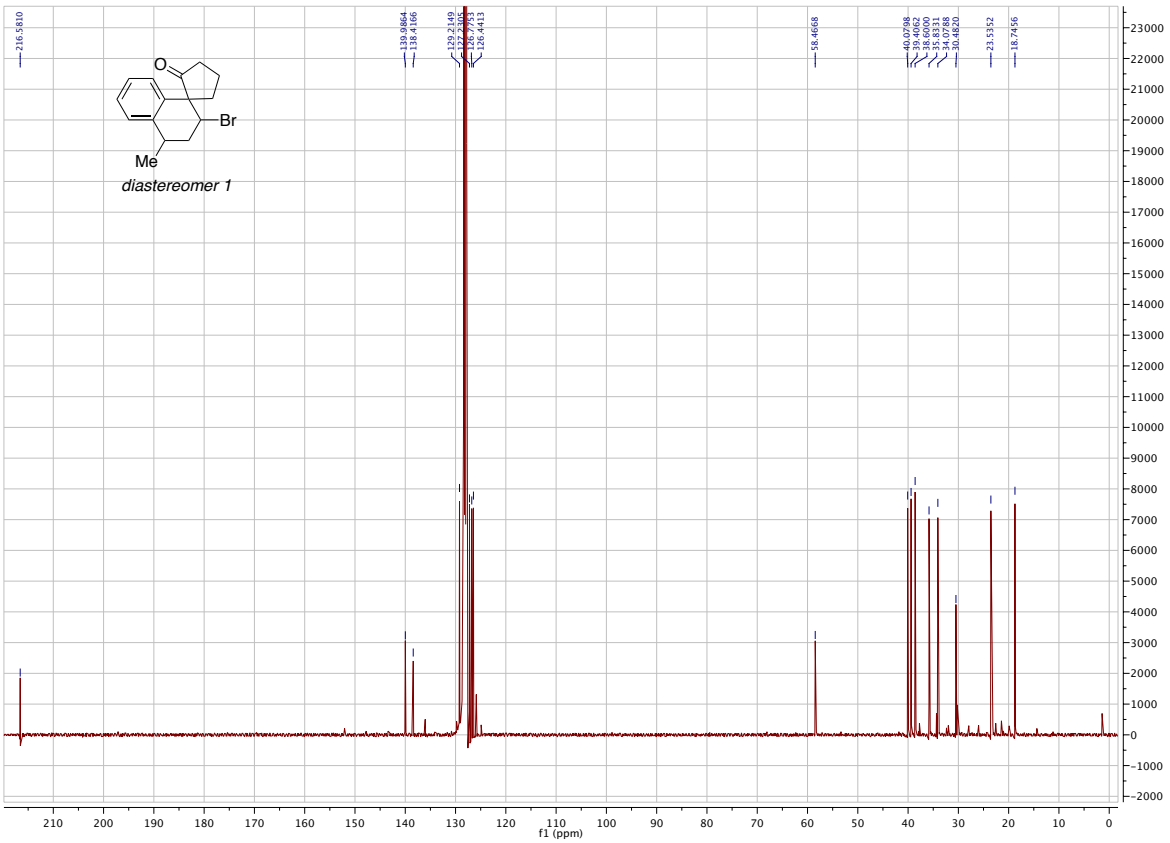
Brominated Compounds

β-Bromo Spiroketone C_1^R

^{1}H NMR 500 MHz, C_6D_6

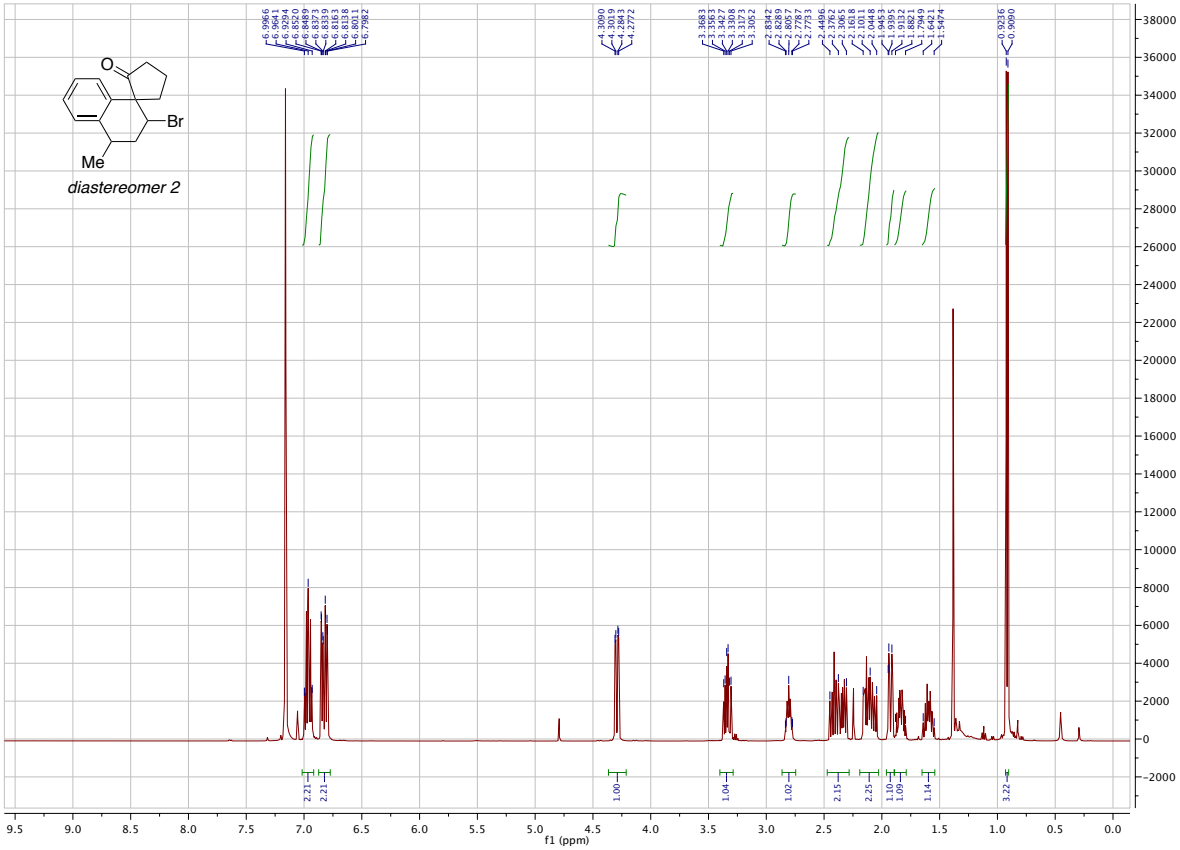


^{13}C NMR 125 MHz, C_6D_6

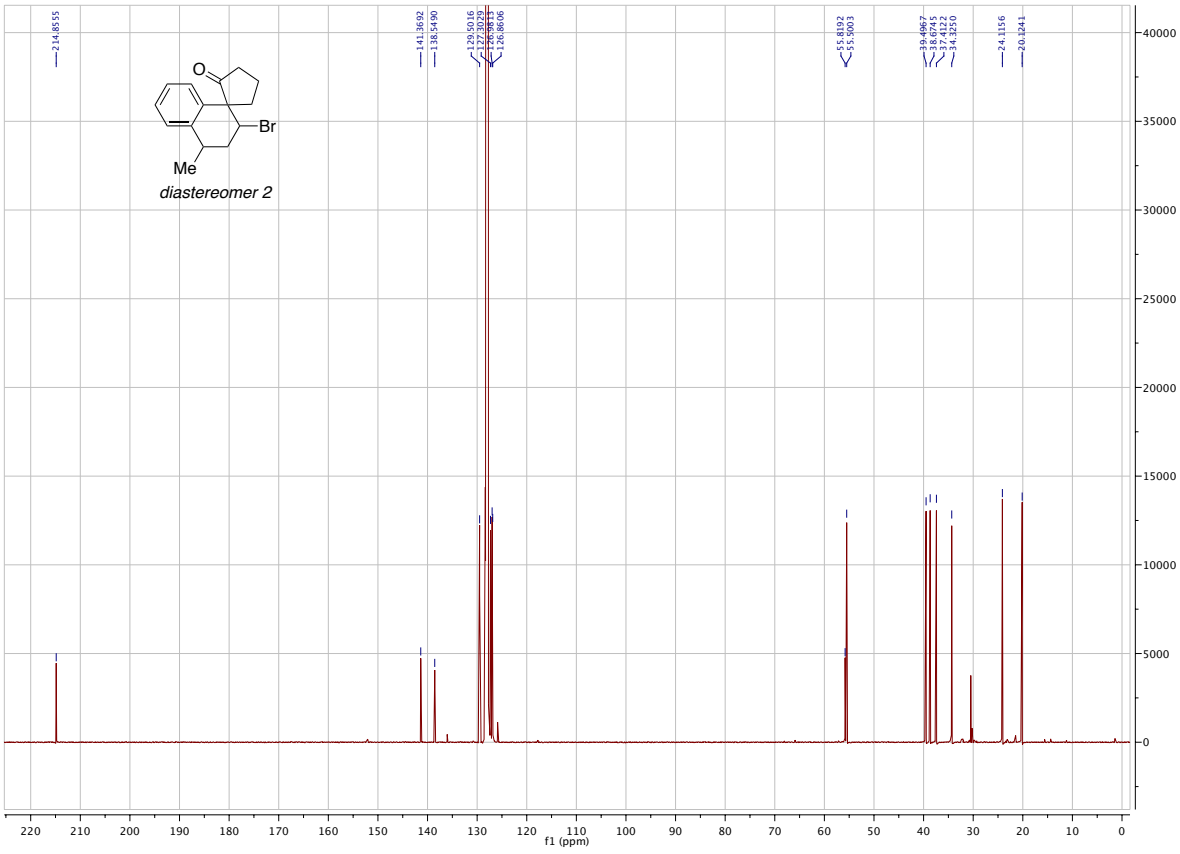


β-Bromo Spiroketone C_1^S

^{1}H NMR 500 MHz, C_6D_6

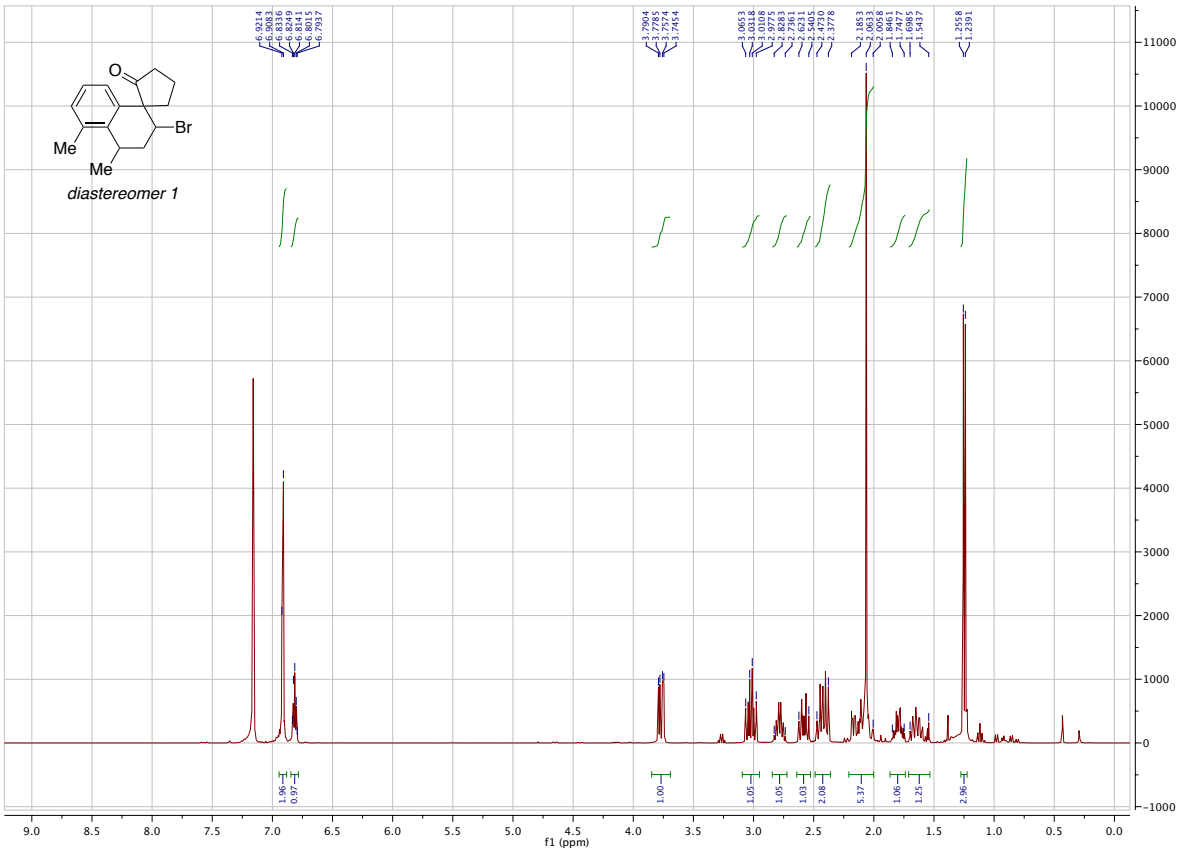


^{13}C NMR 125 MHz, C_6D_6

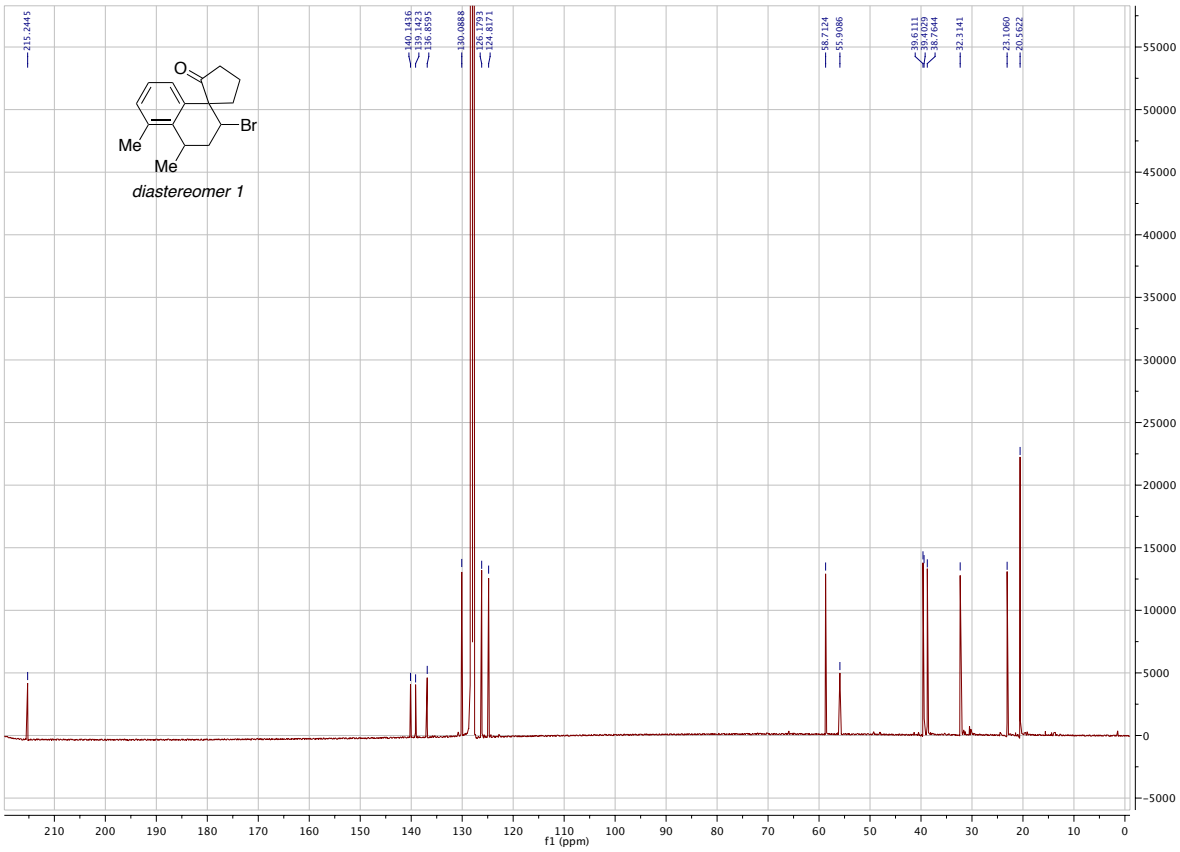


β-Bromo Spiroketone C_2^R

^{1}H NMR 400 MHz, C_6D_6

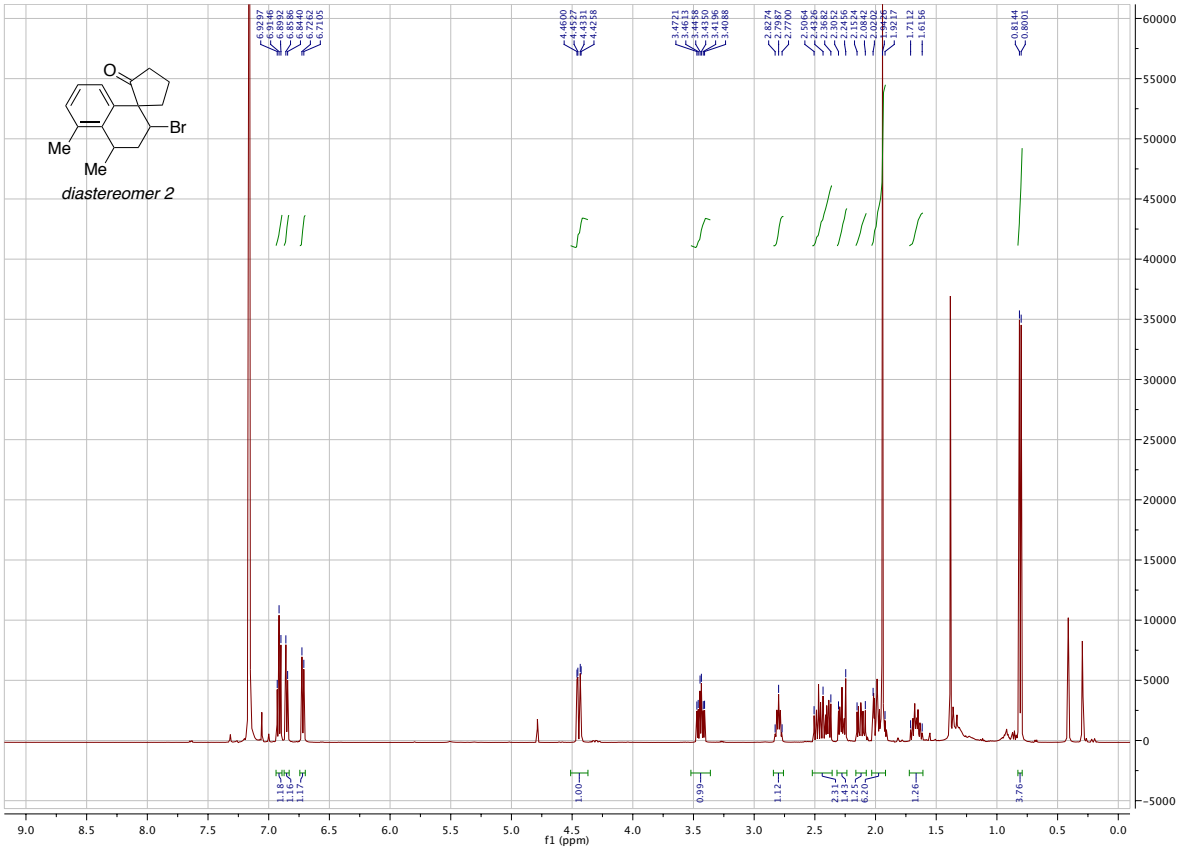


^{13}C NMR 100 MHz, C_6D_6

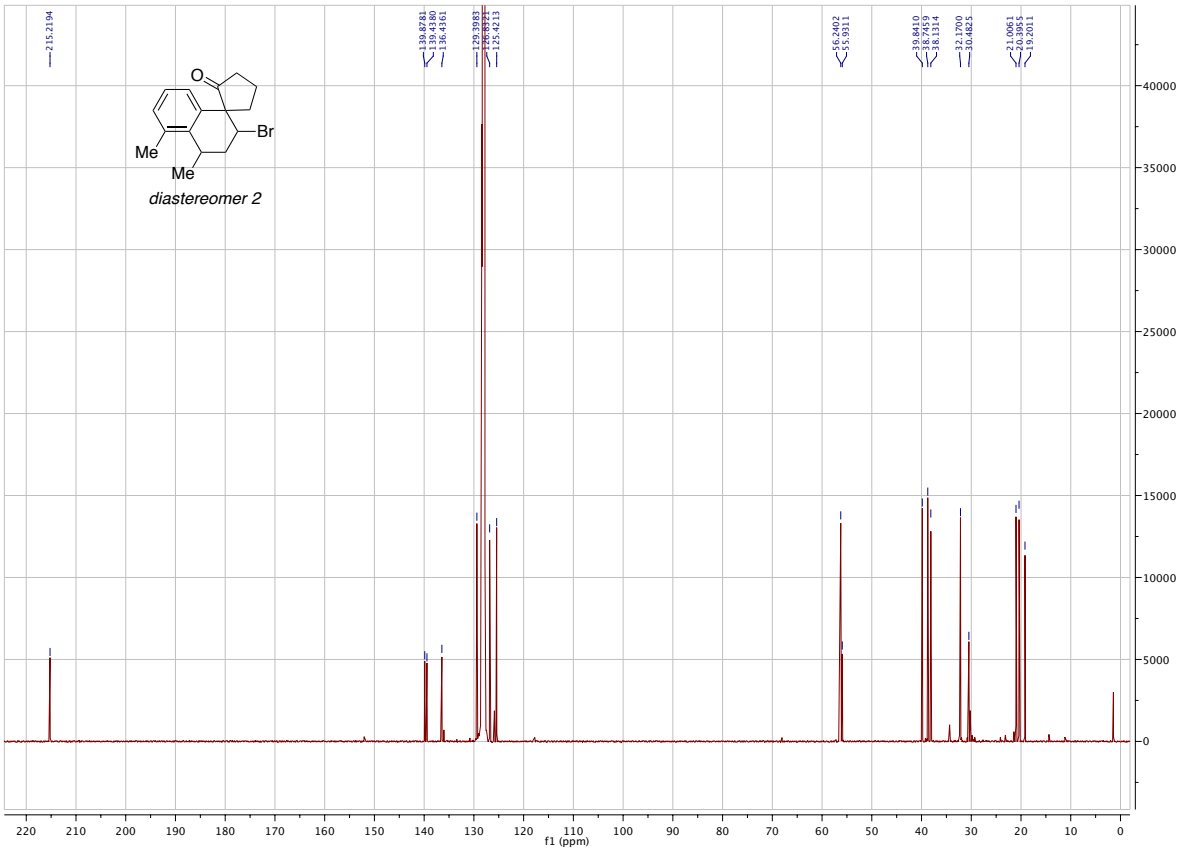


β-Bromo Spiroketone C_2^S

^{1}H NMR 500 MHz, C_6D_6

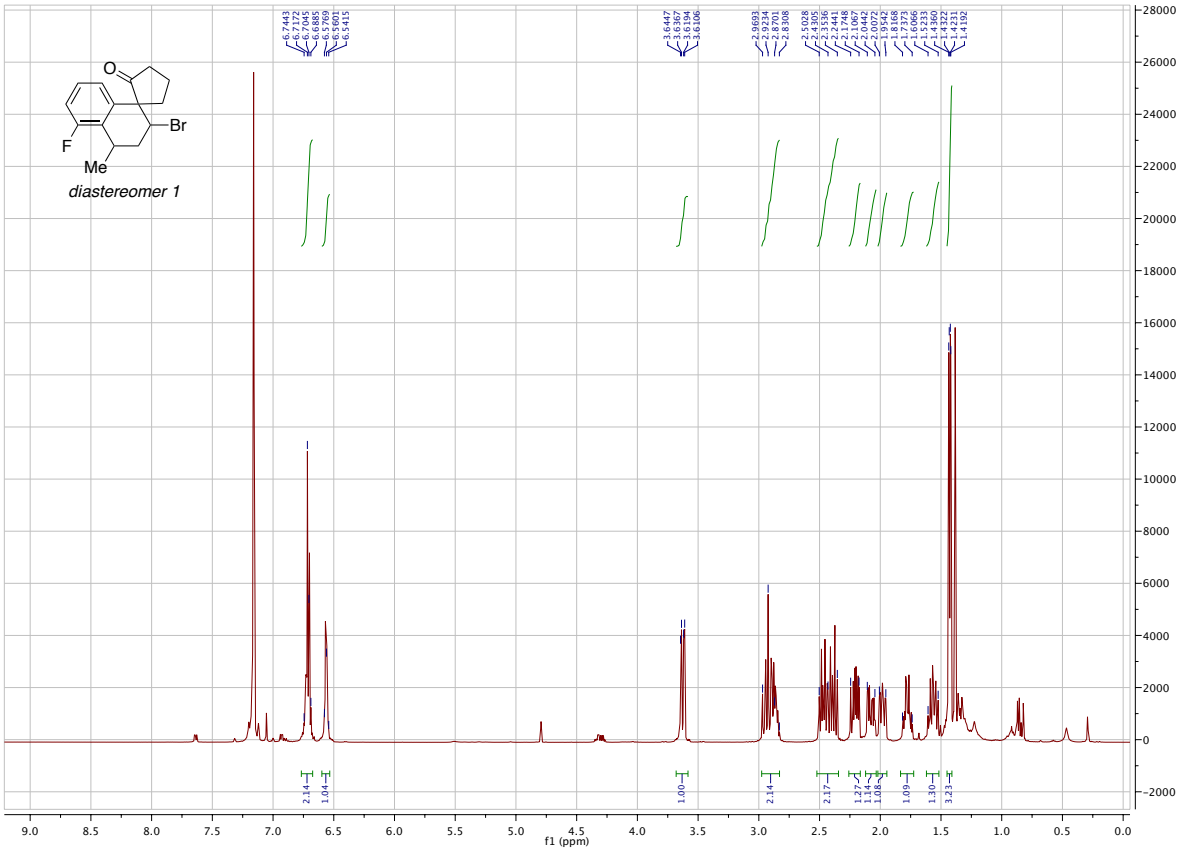


^{13}C NMR 125 MHz, C_6D_6

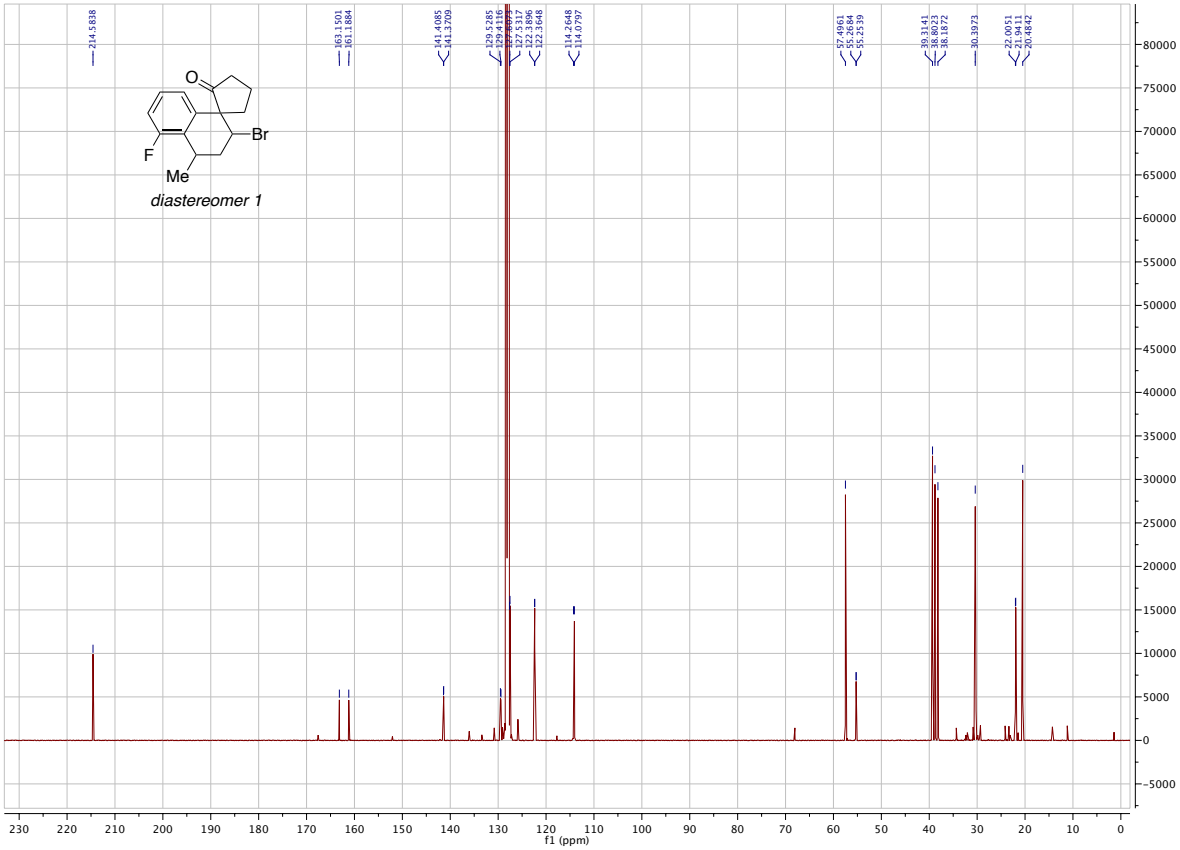


β-Bromo Spiroketone C_3^R

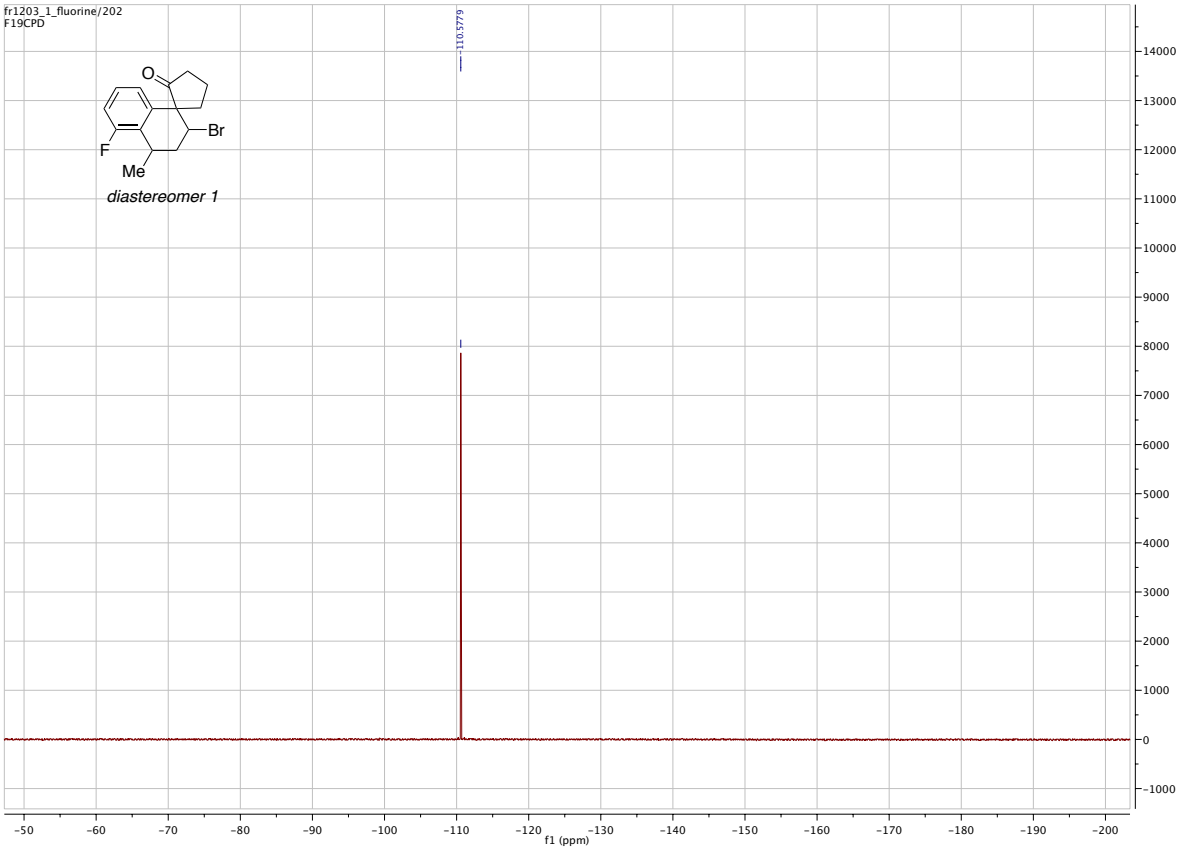
^{1}H NMR 500 MHz, C_6D_6



^{13}C NMR 125 MHz, C_6D_6

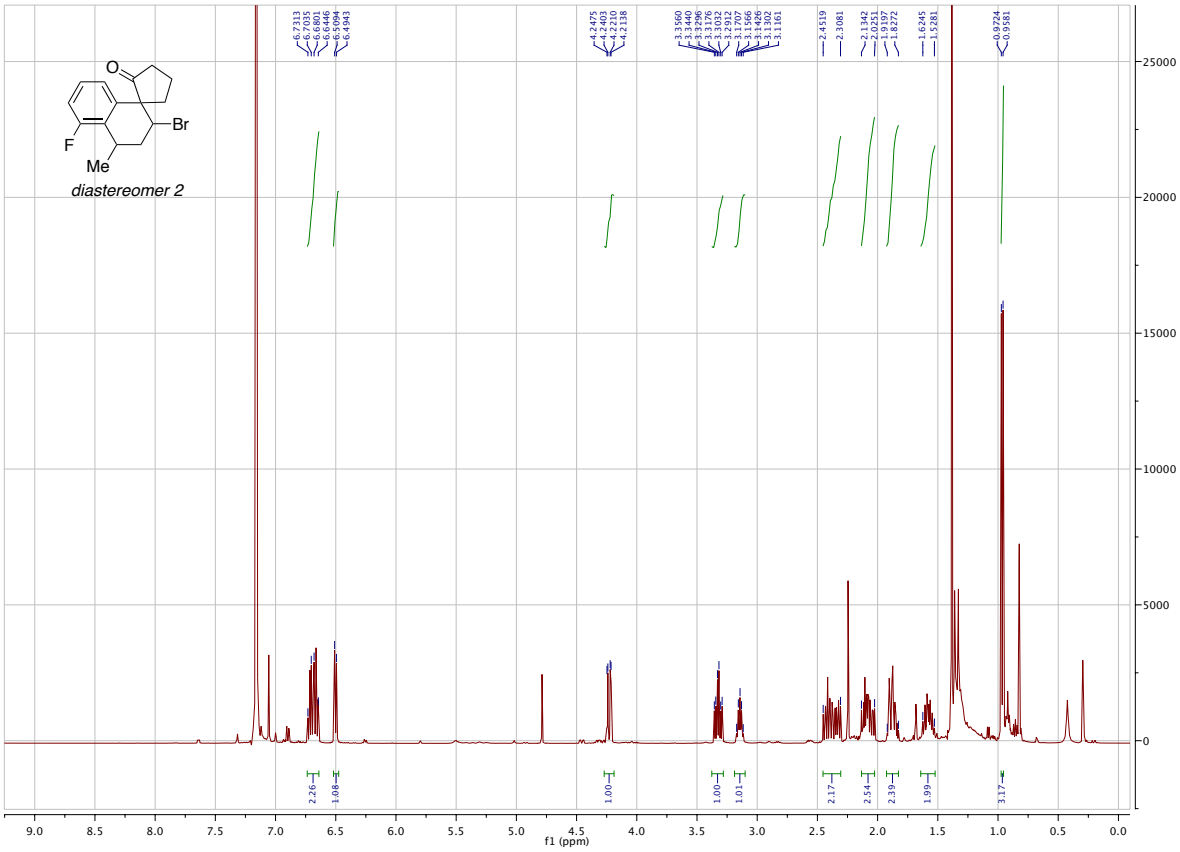


^{19}F NMR 375 MHz, C_6D_6

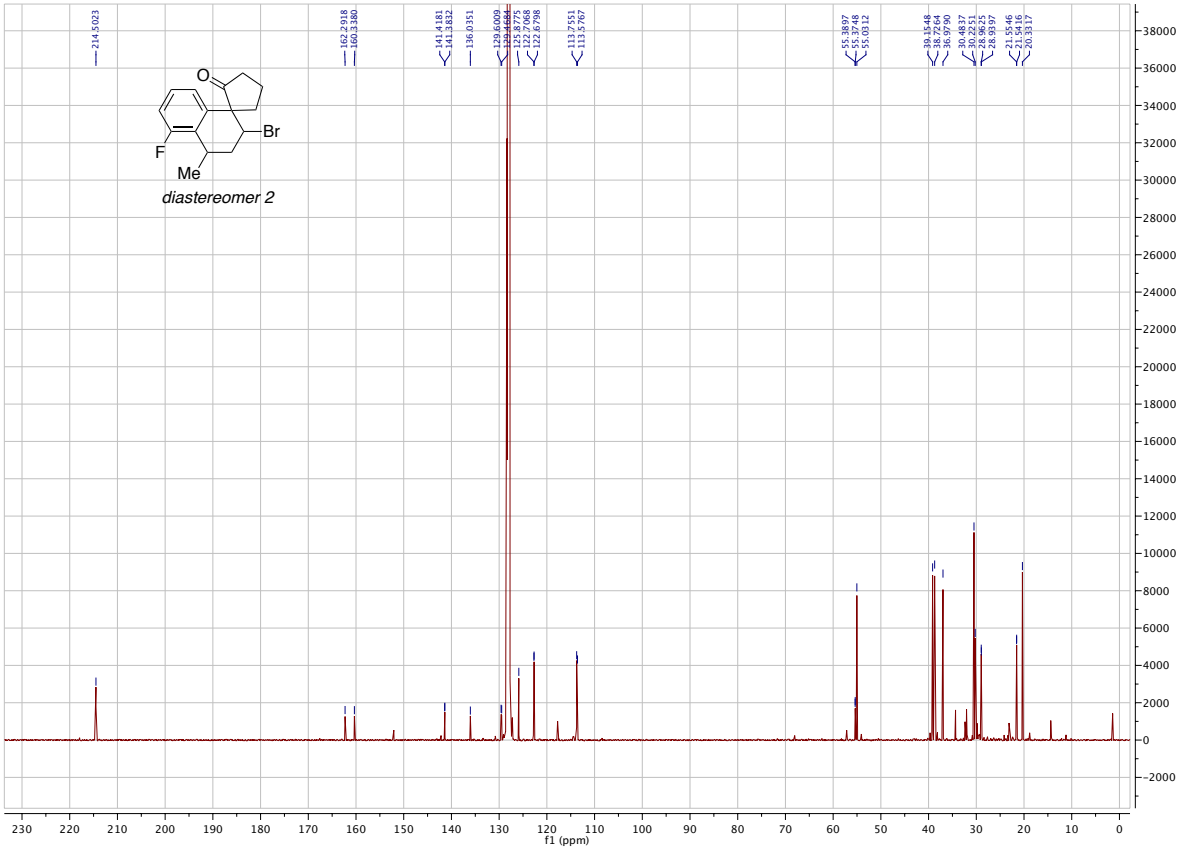


β-Bromo Spiroketone C_3^S

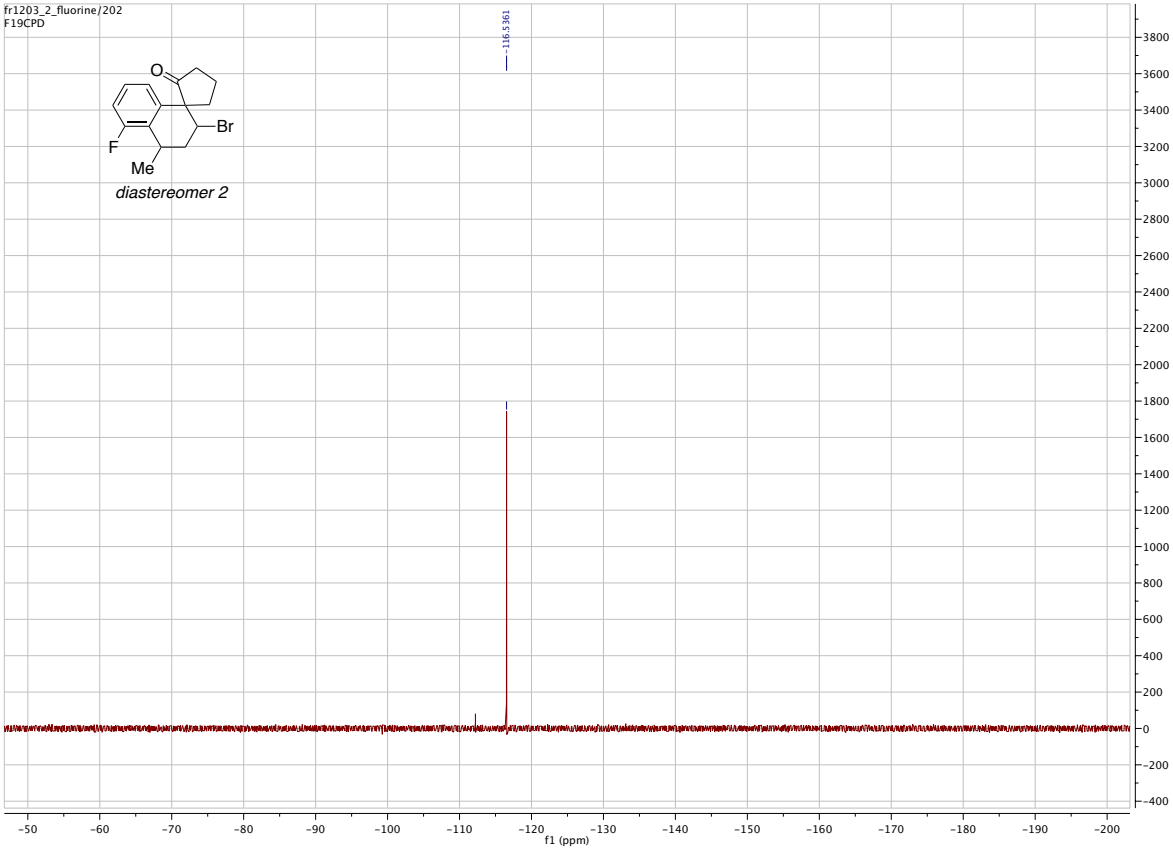
^{1}H NMR 500 MHz, C_6D_6



^{13}C NMR 125 MHz, C_6D_6

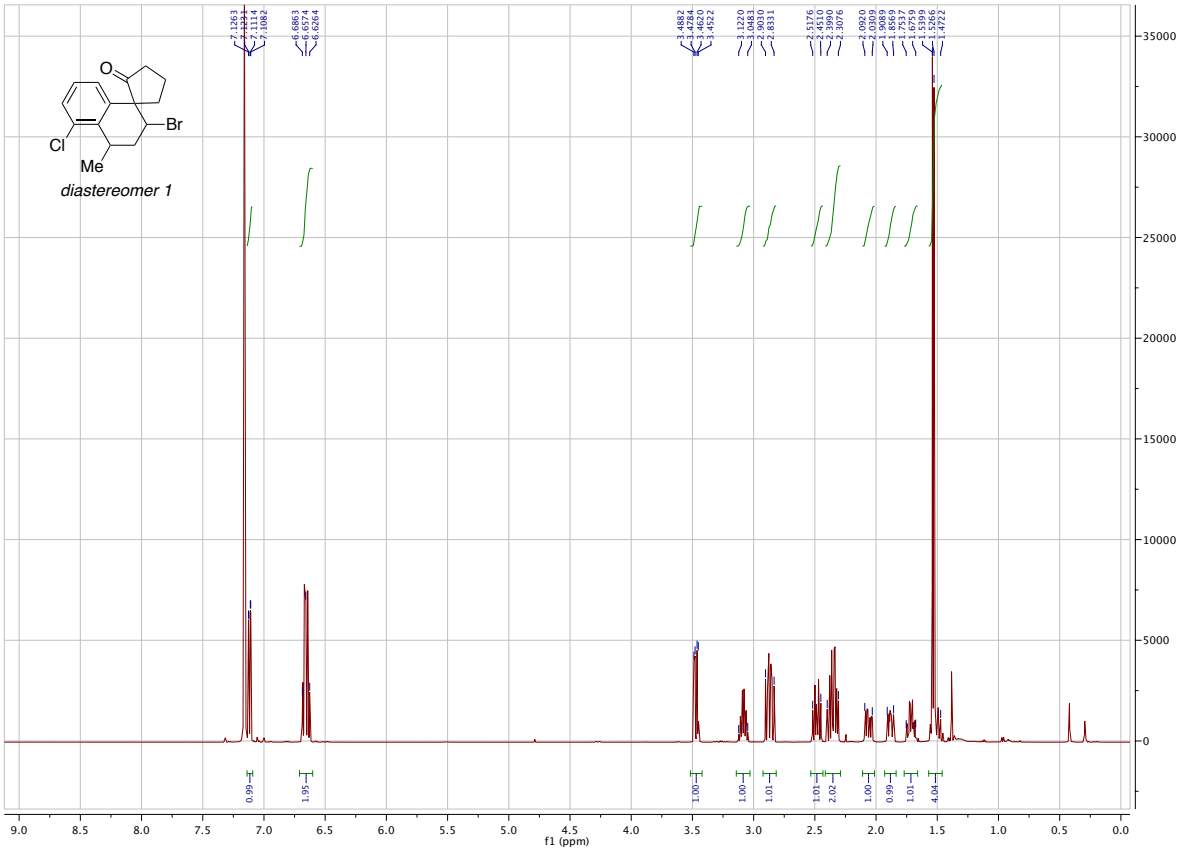


^{19}F NMR 375 MHz, C_6D_6

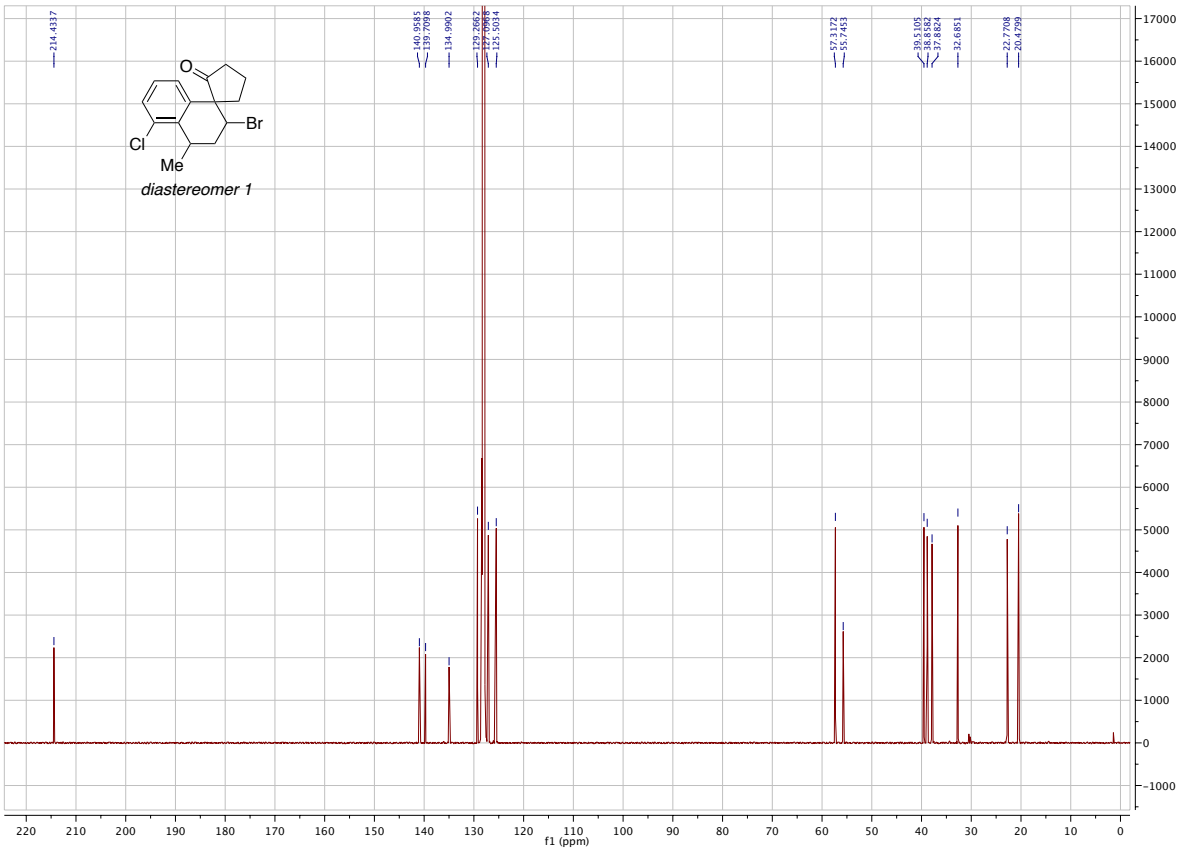


β-Bromo Spiroketone C_4^R

^{1}H NMR 500 MHz, C_6D_6

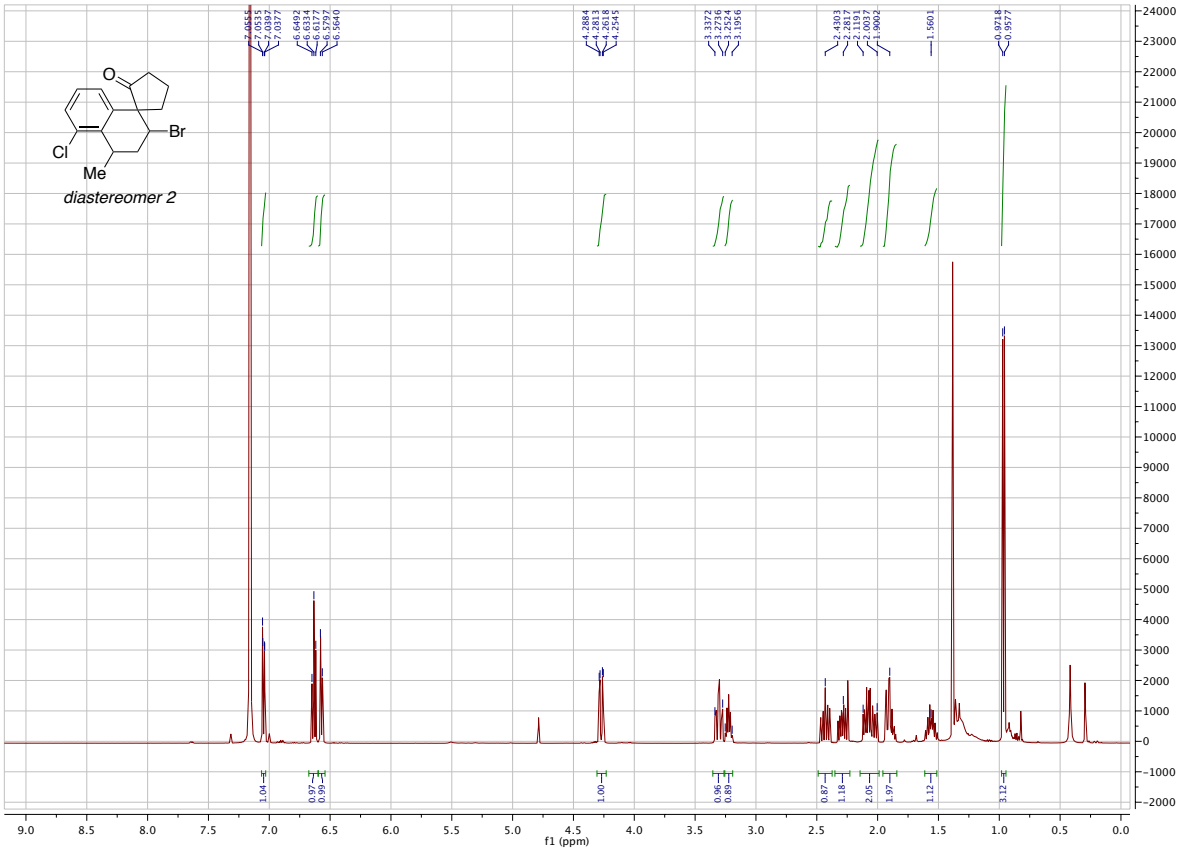


^{13}C NMR 125 MHz, C_6D_6

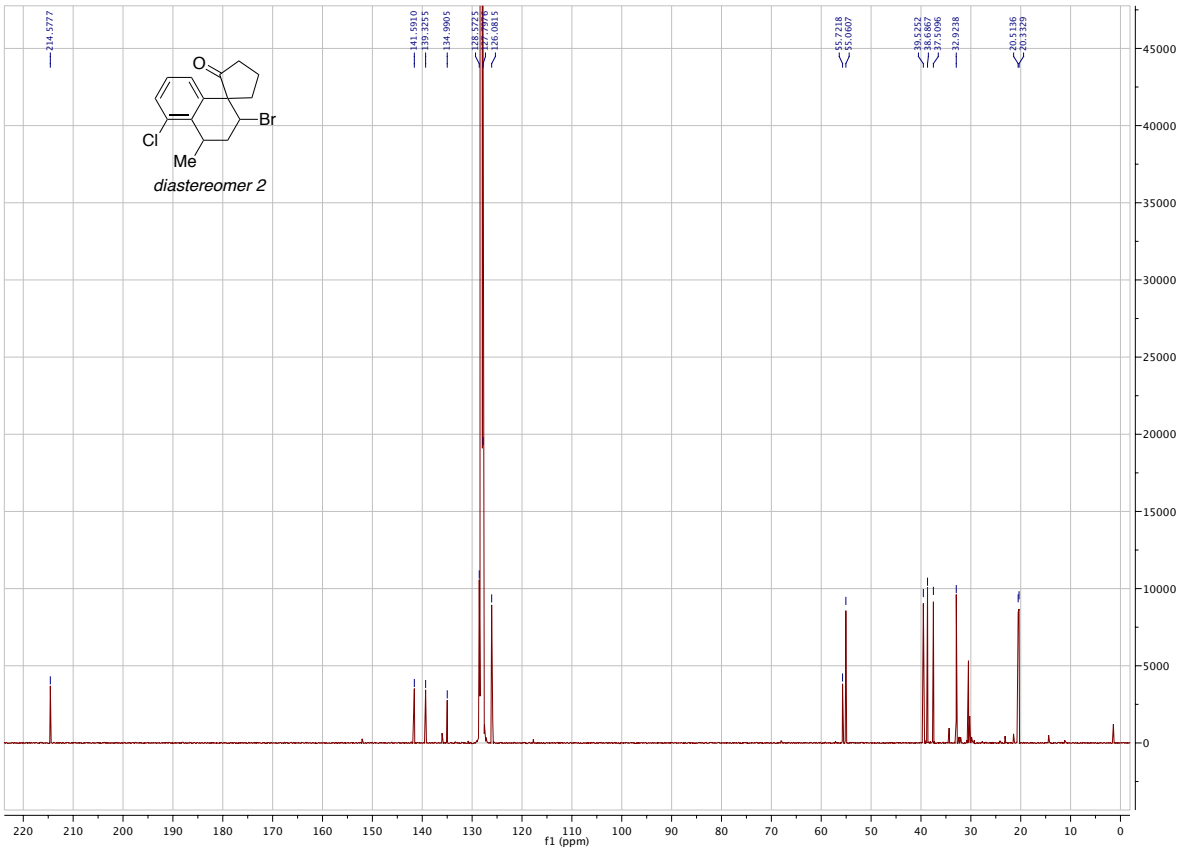


β-Bromo Spiroketone C_4^S

^{1}H NMR 500 MHz, C_6D_6

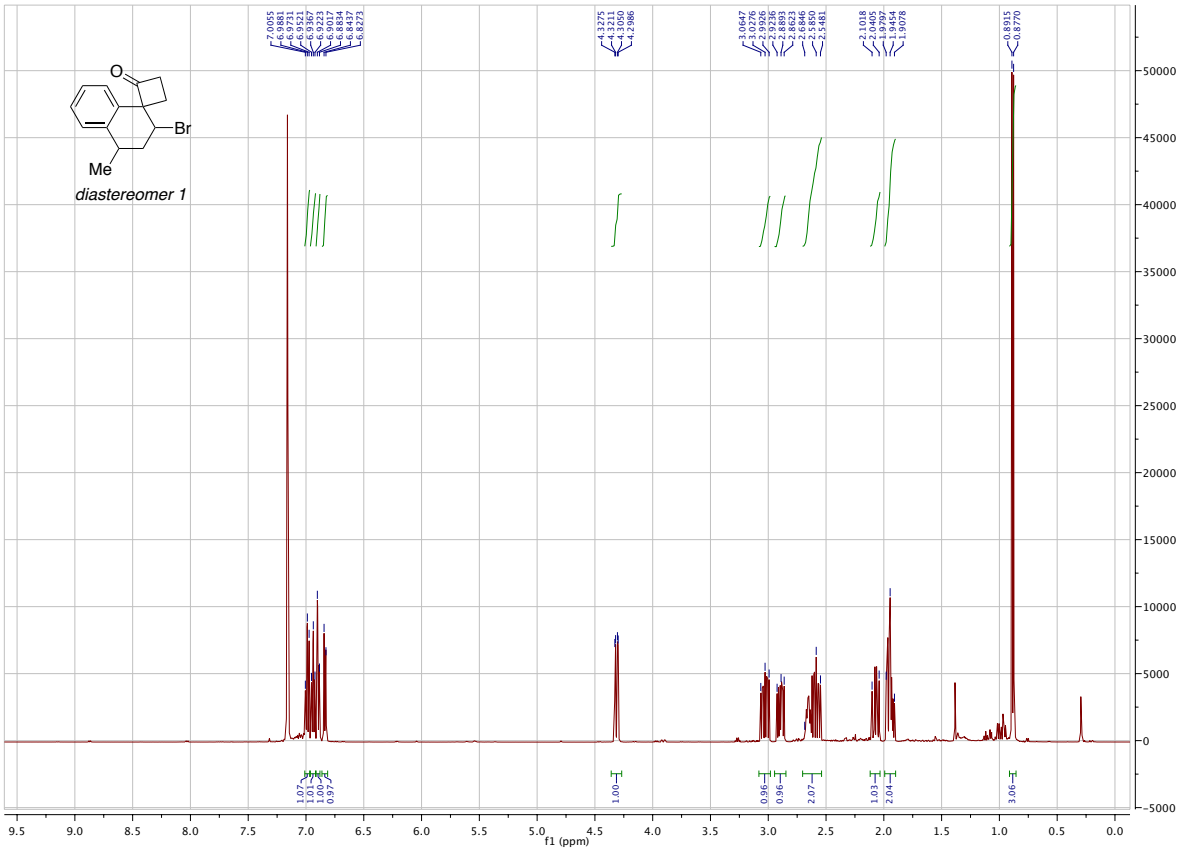


^{13}C NMR 125 MHz, C_6D_6

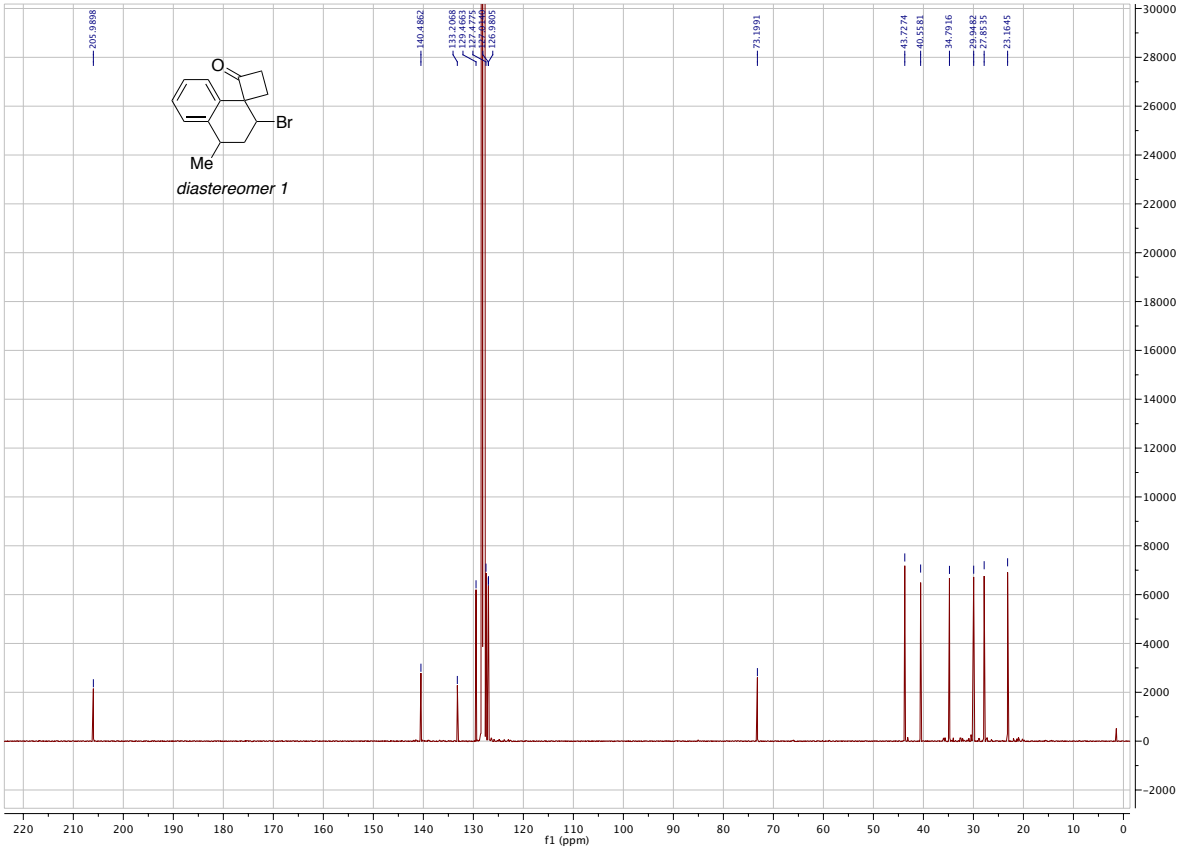


β-Bromo Spiroketone C_5^R

^{1}H NMR 500 MHz, C_6D_6

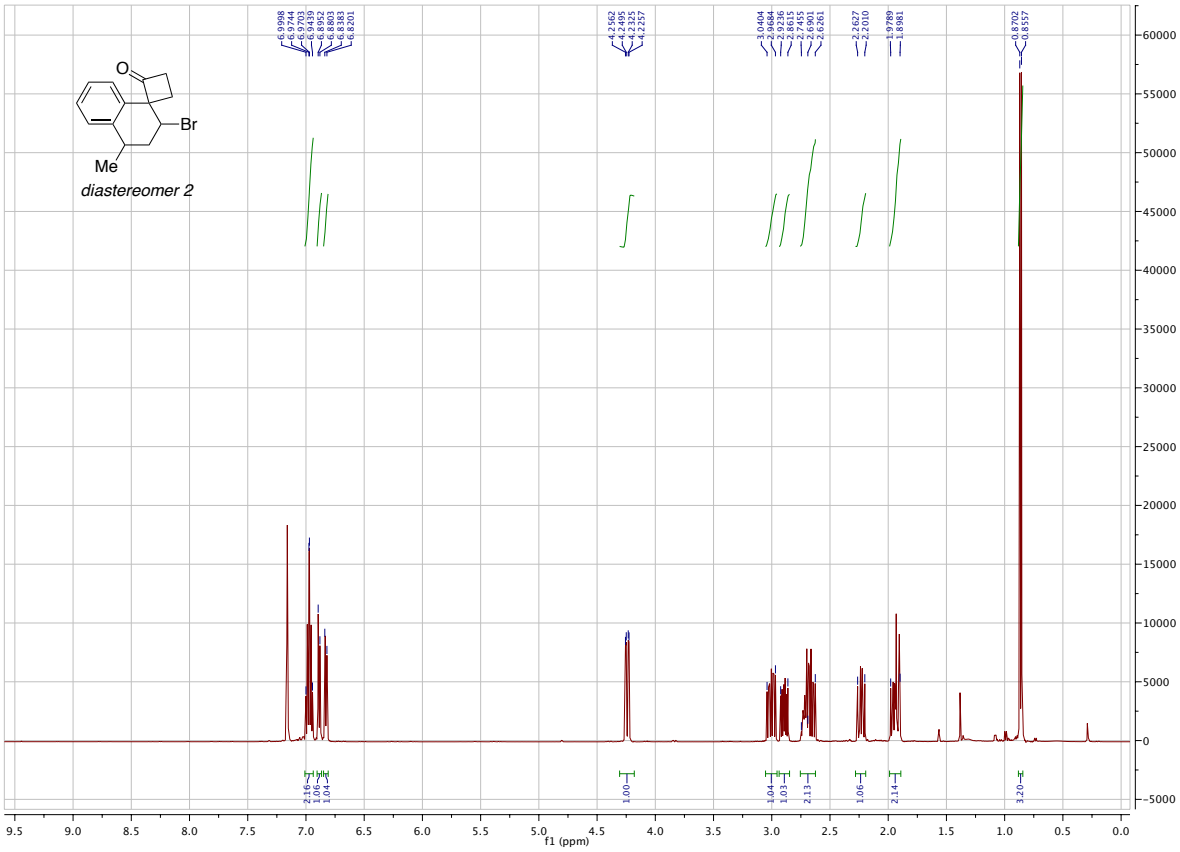


^{13}C NMR 125 MHz, C_6D_6

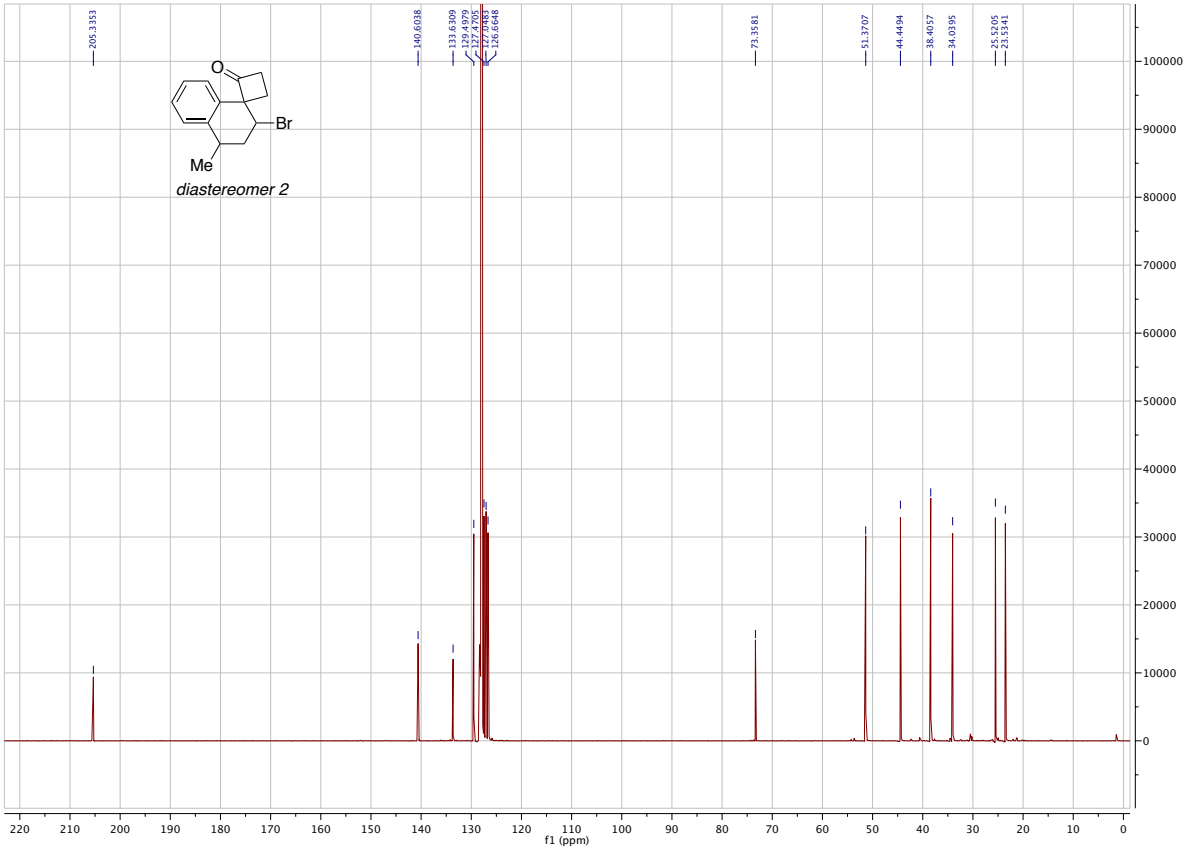


β-Bromo Spiroketone C_5^S

^{1}H NMR 400 MHz, C_6D_6



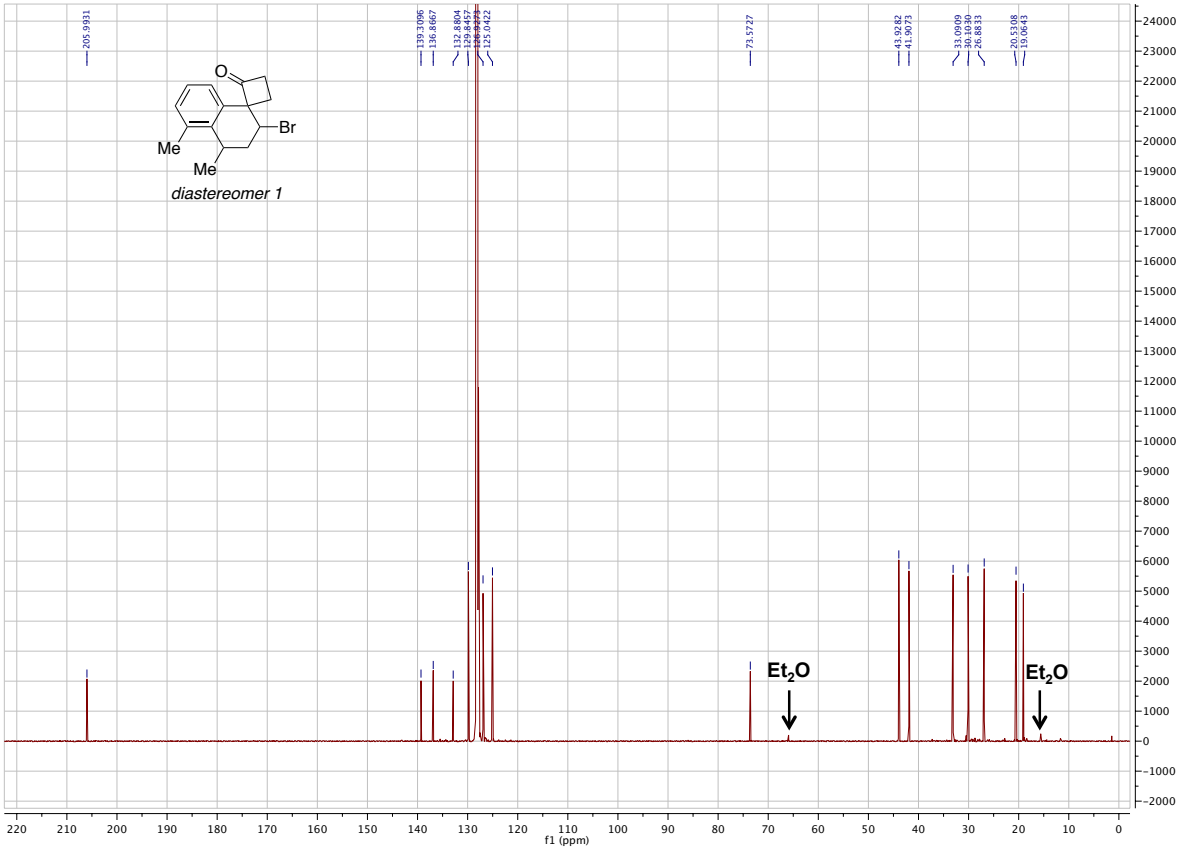
^{13}C NMR 100 MHz, C_6D_6



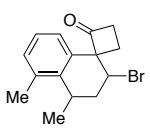
β-Bromo Spiroketone C_6^R

^{1}H NMR 500 MHz, C_6D_6

^{13}C NMR 125 MHz, C_6D_6



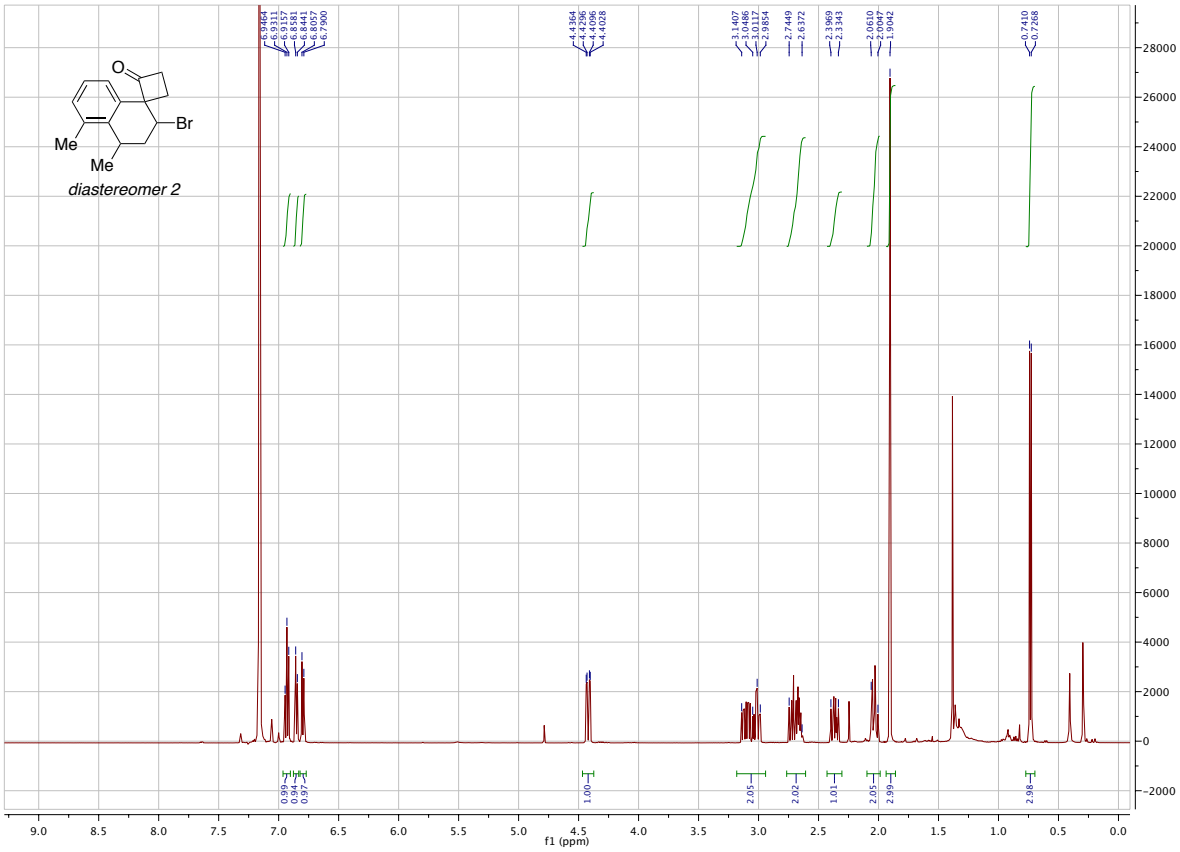
^{1}H-^{1}H NOESY 500 MHz, C_6D_6



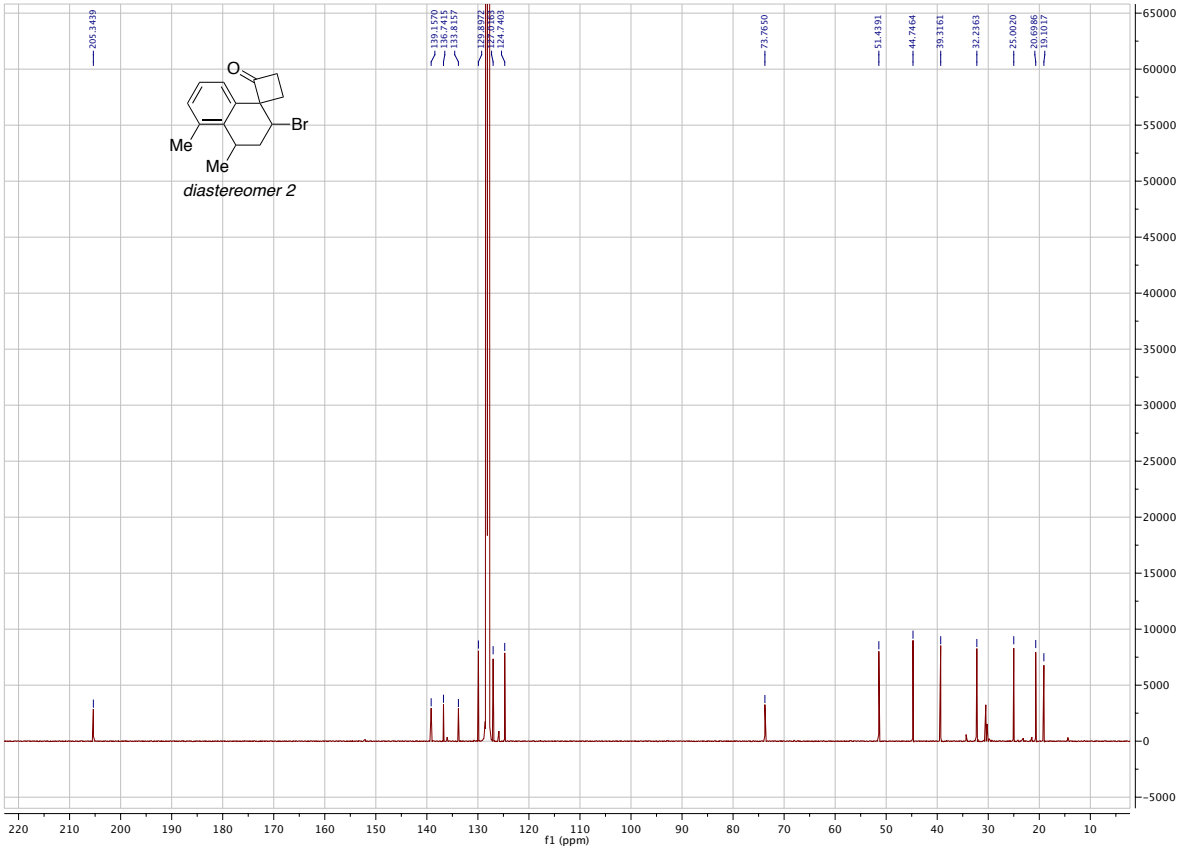
diastereomer 1

β-Bromo Spiroketone C_6^S

^{1}H NMR 500 MHz, C_6D_6

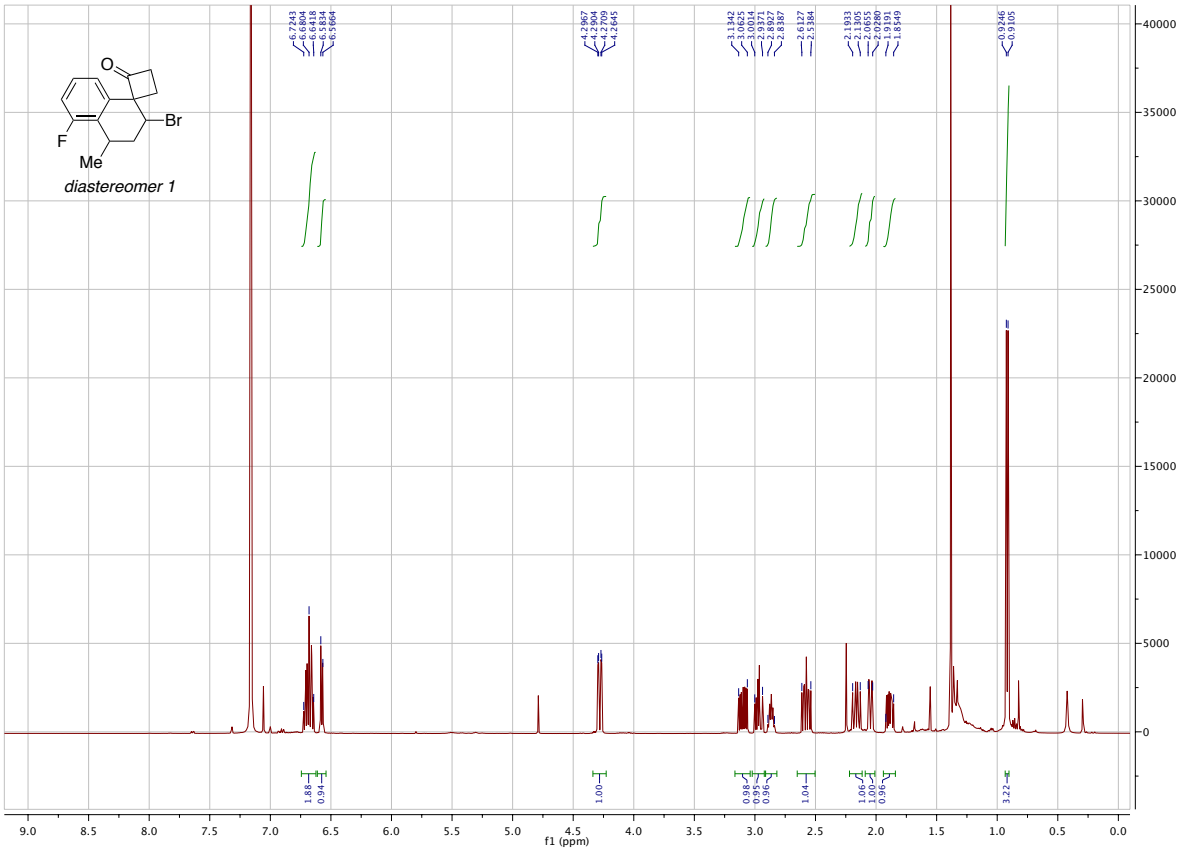


^{13}C NMR 125 MHz, C_6D_6

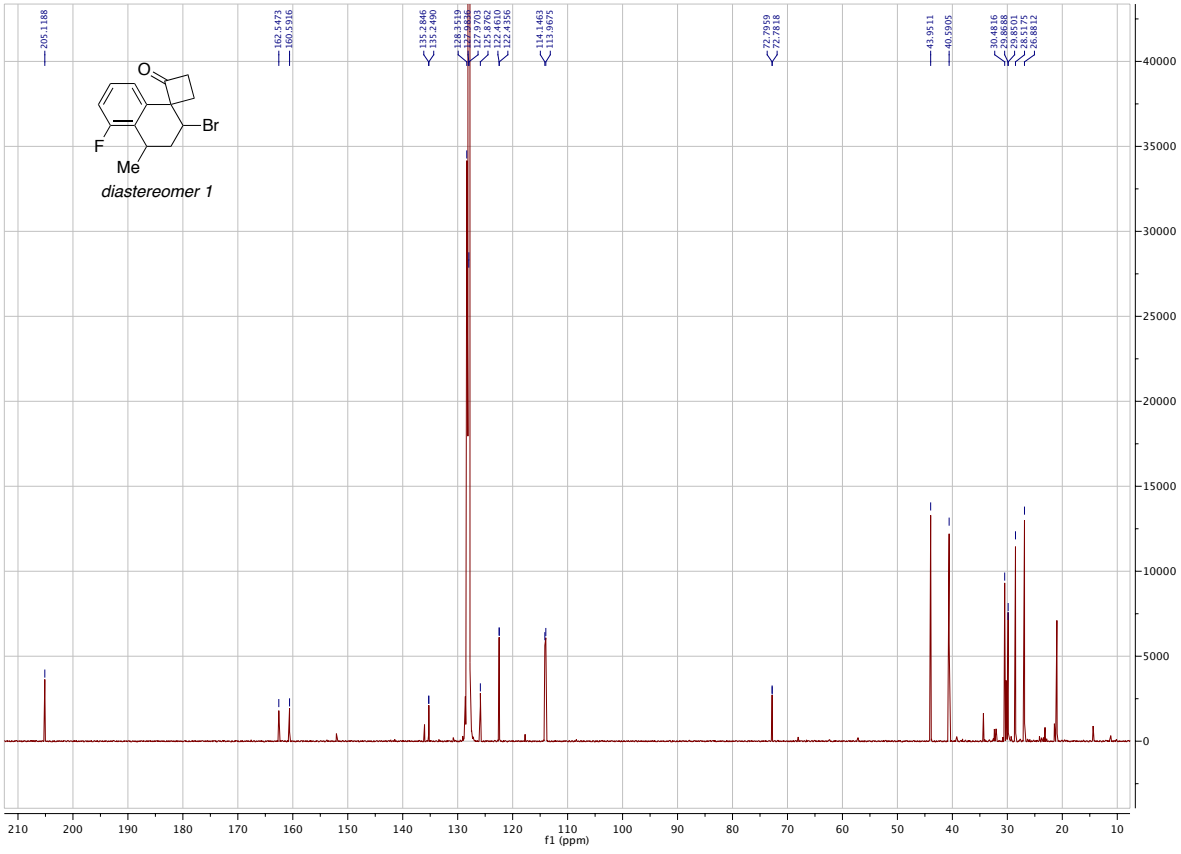


β-Bromo Spiroketone C_7^R

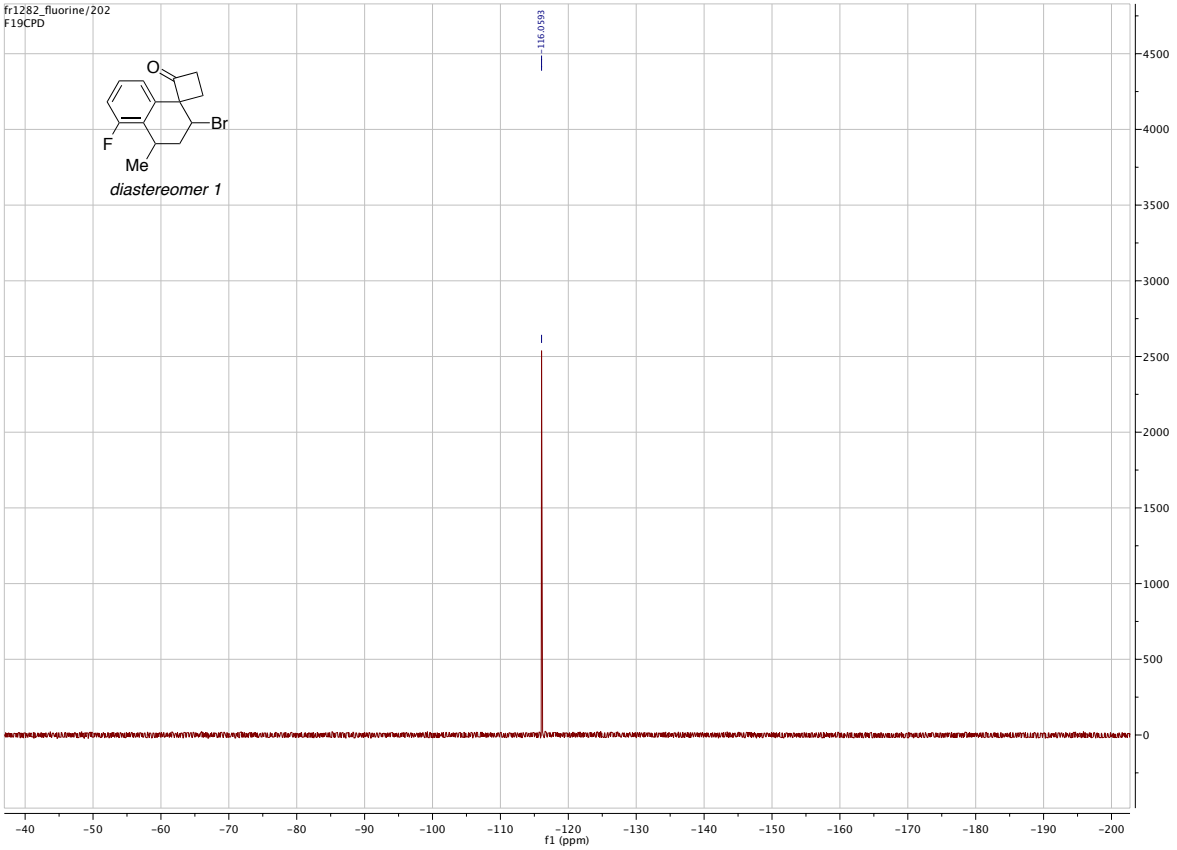
^{1}H NMR 500 MHz, C_6D_6



^{13}C NMR 125 MHz, C_6D_6



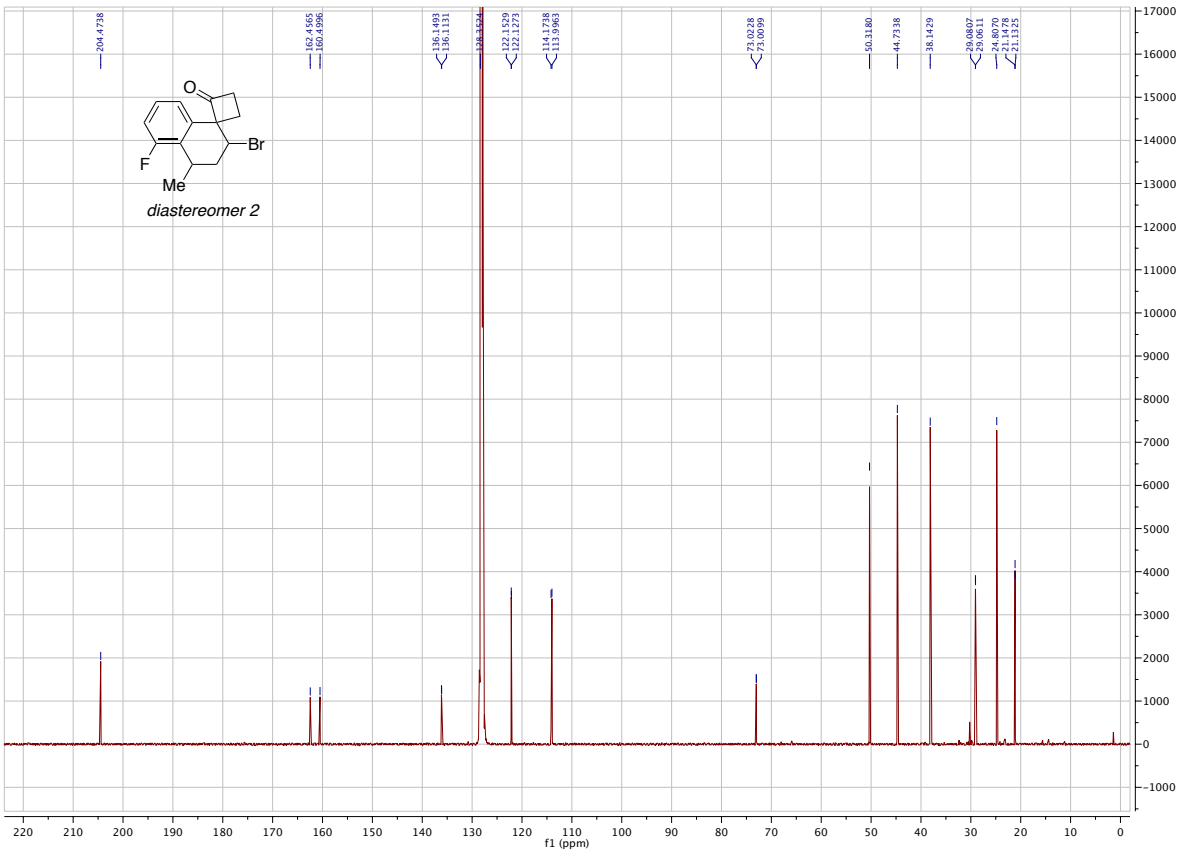
^{19}F NMR 375 MHz, C_6D_6



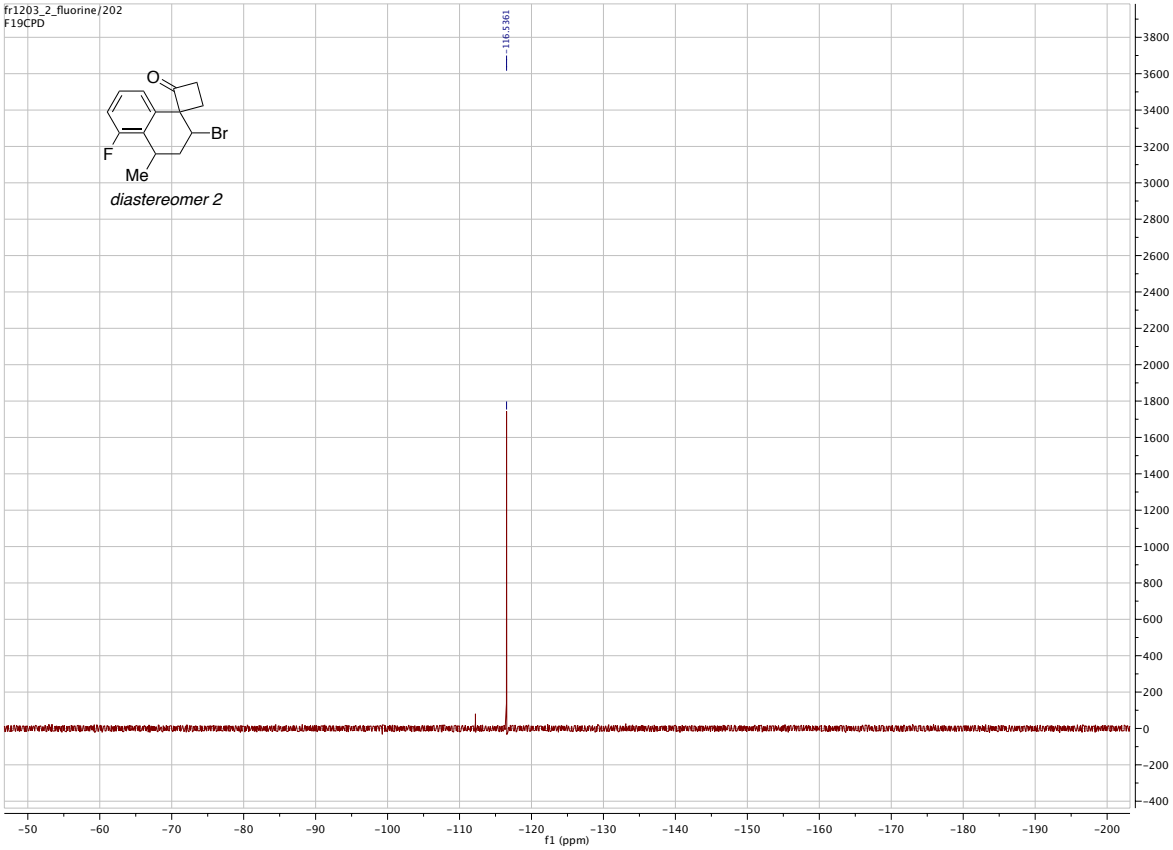
β-Bromo Spiroketone C_7^S

^{1}H NMR 500 MHz, C_6D_6

^{13}C NMR 125 MHz, C_6D_6

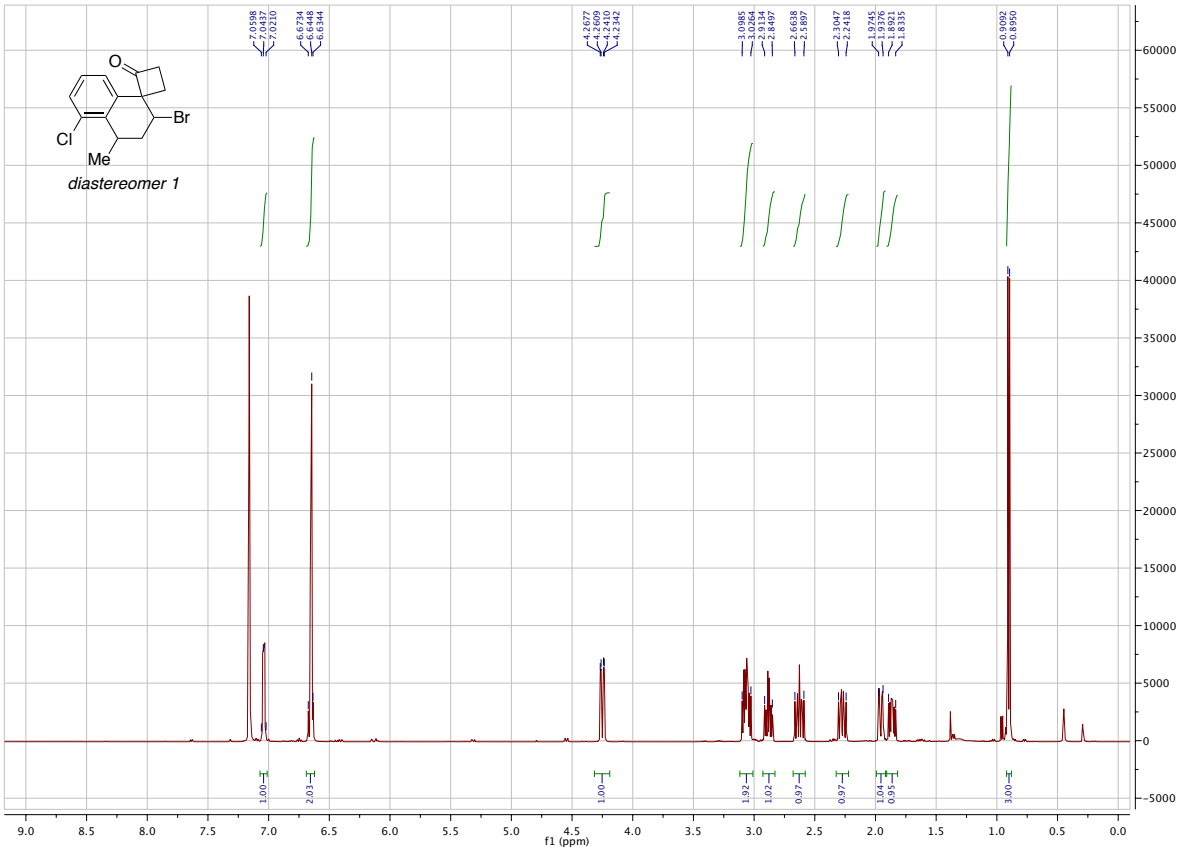


^{19}F NMR 375 MHz, C_6D_6

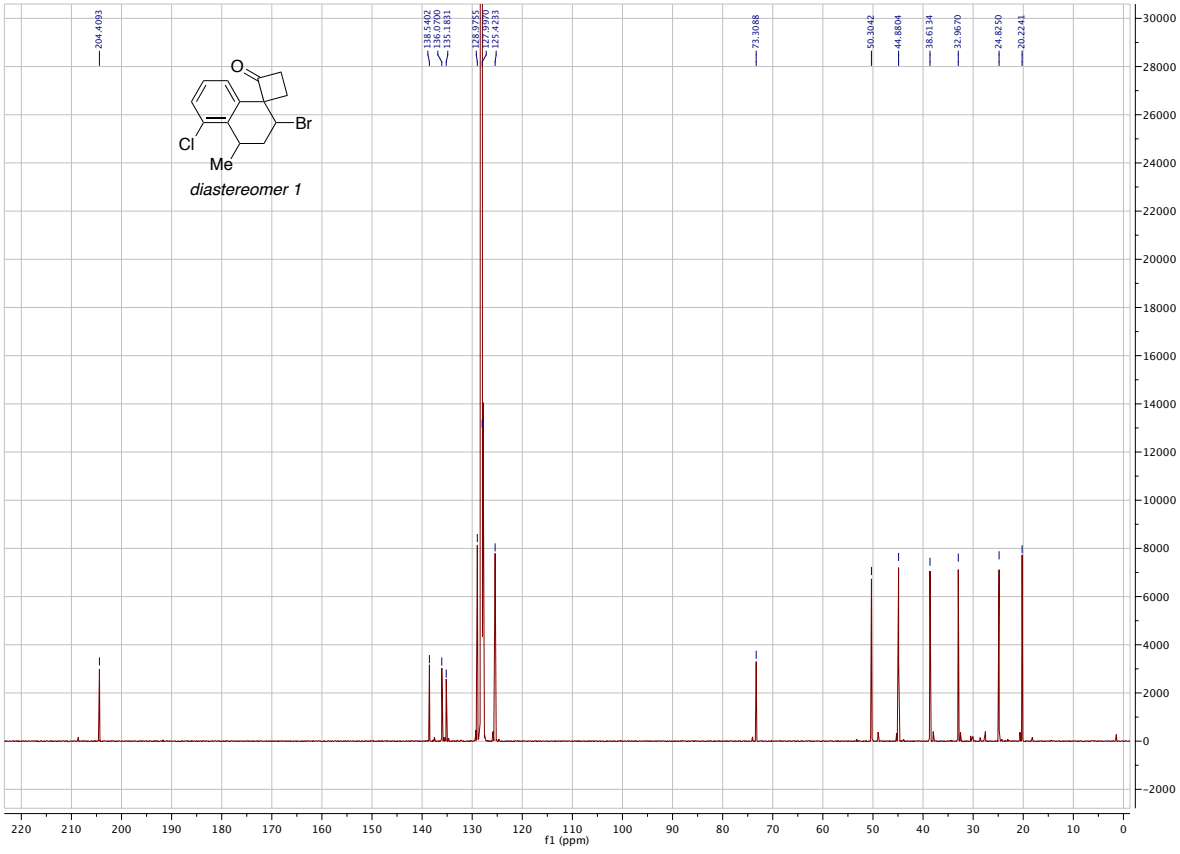


β-Bromo Spiroketone C_8^R

^{1}H NMR 500 MHz, C_6D_6

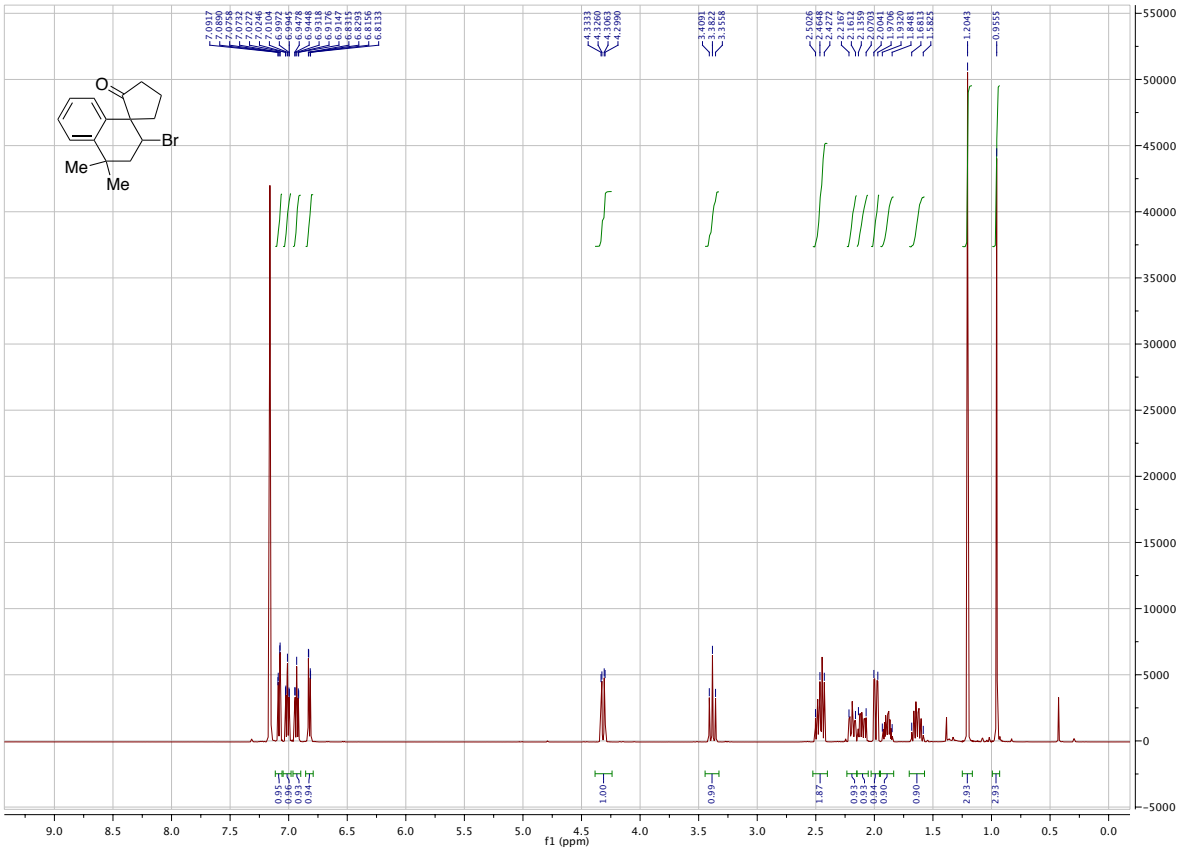


^{13}C NMR 125 MHz, C_6D_6

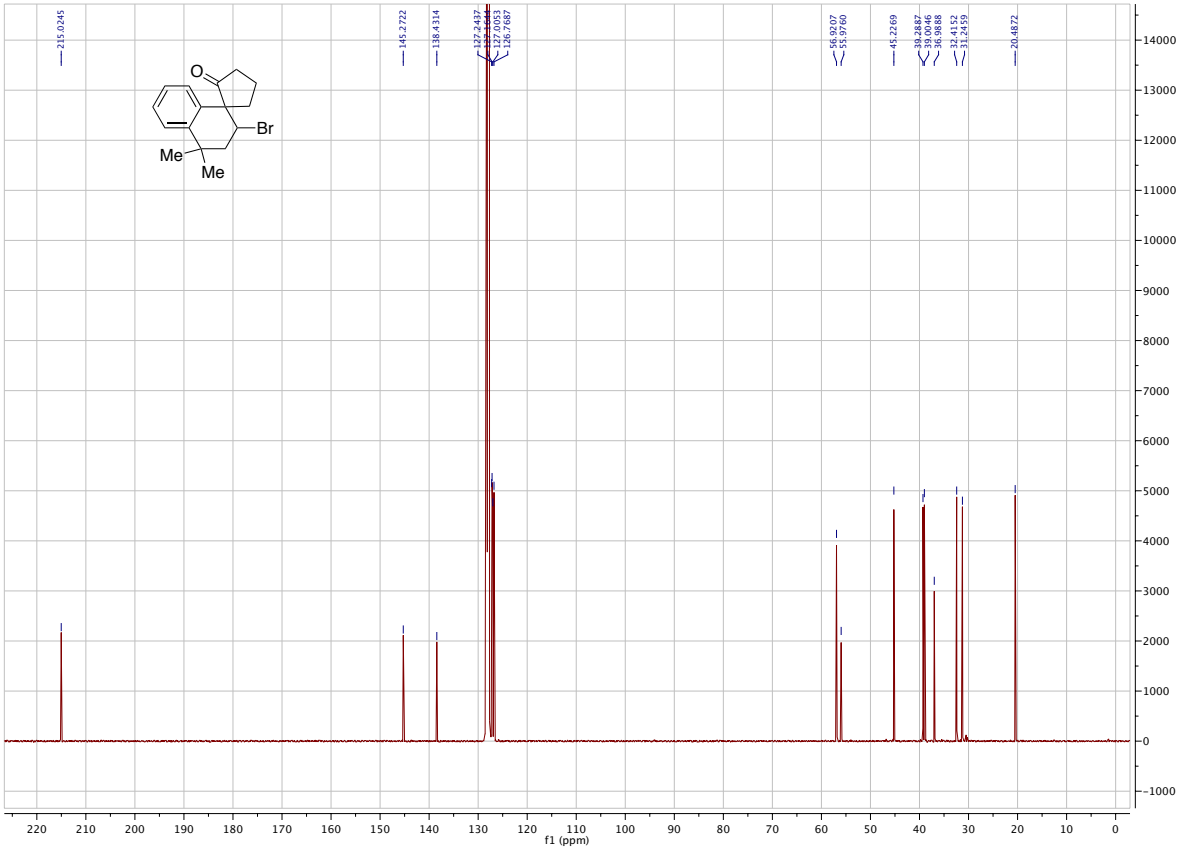


β-Bromo Spiroketone C_9

^{1}H NMR 500 MHz, C_6D_6

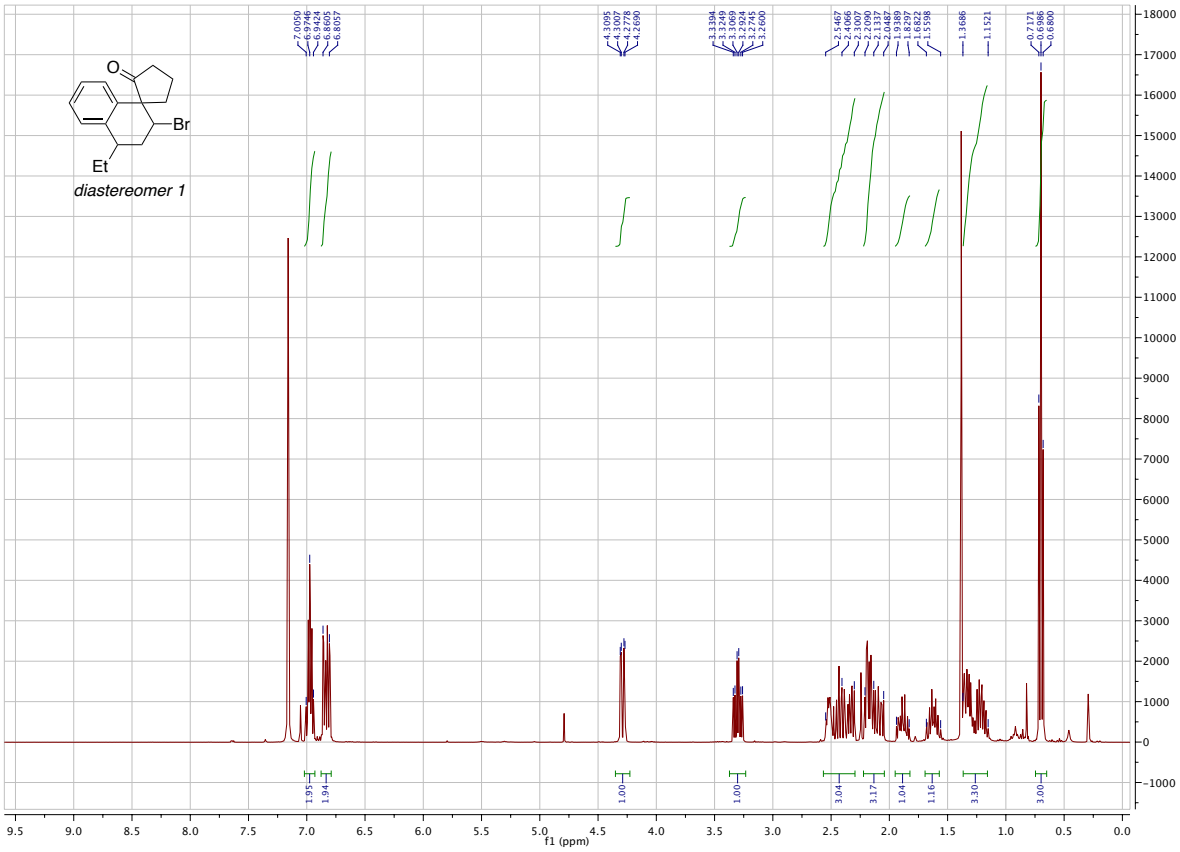


^{13}C NMR 125 MHz, C_6D_6

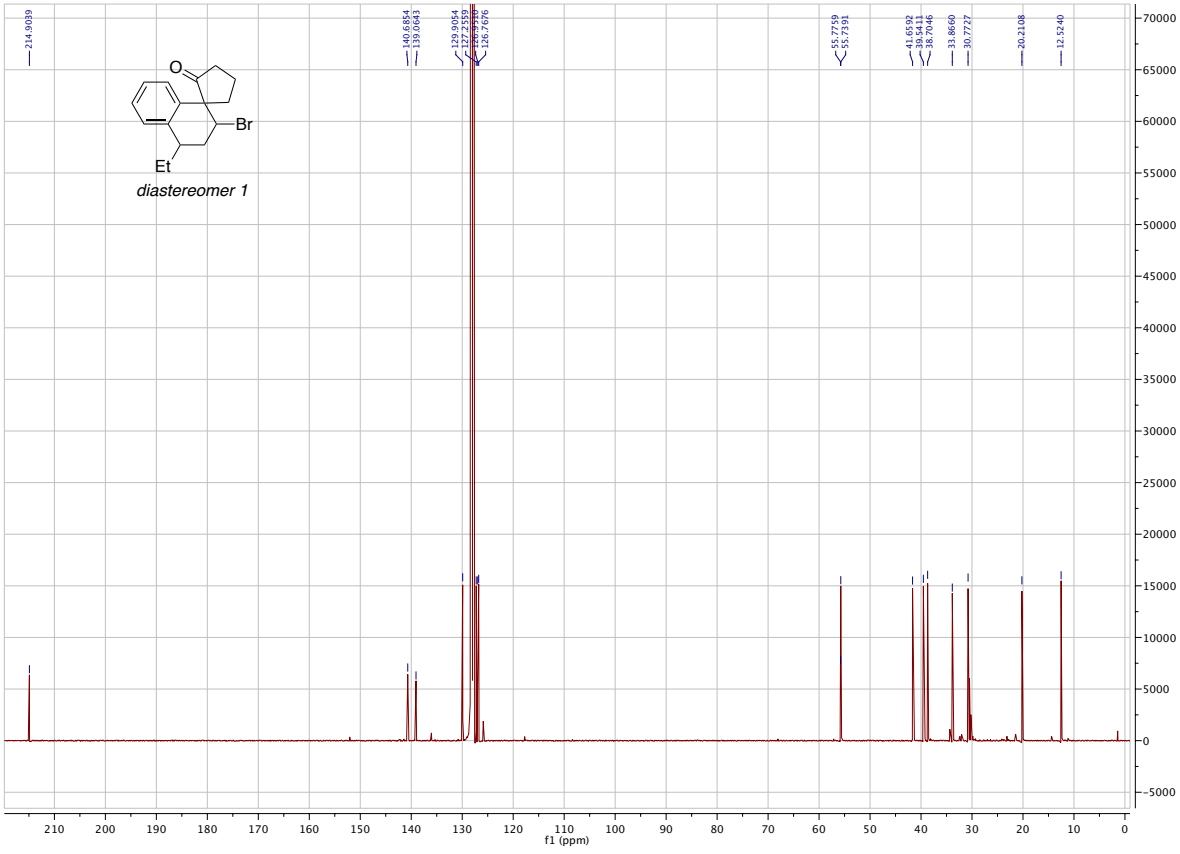


β-Bromo Spiroketone C_{10}^{R}

^{1}H NMR 500 MHz, C_6D_6

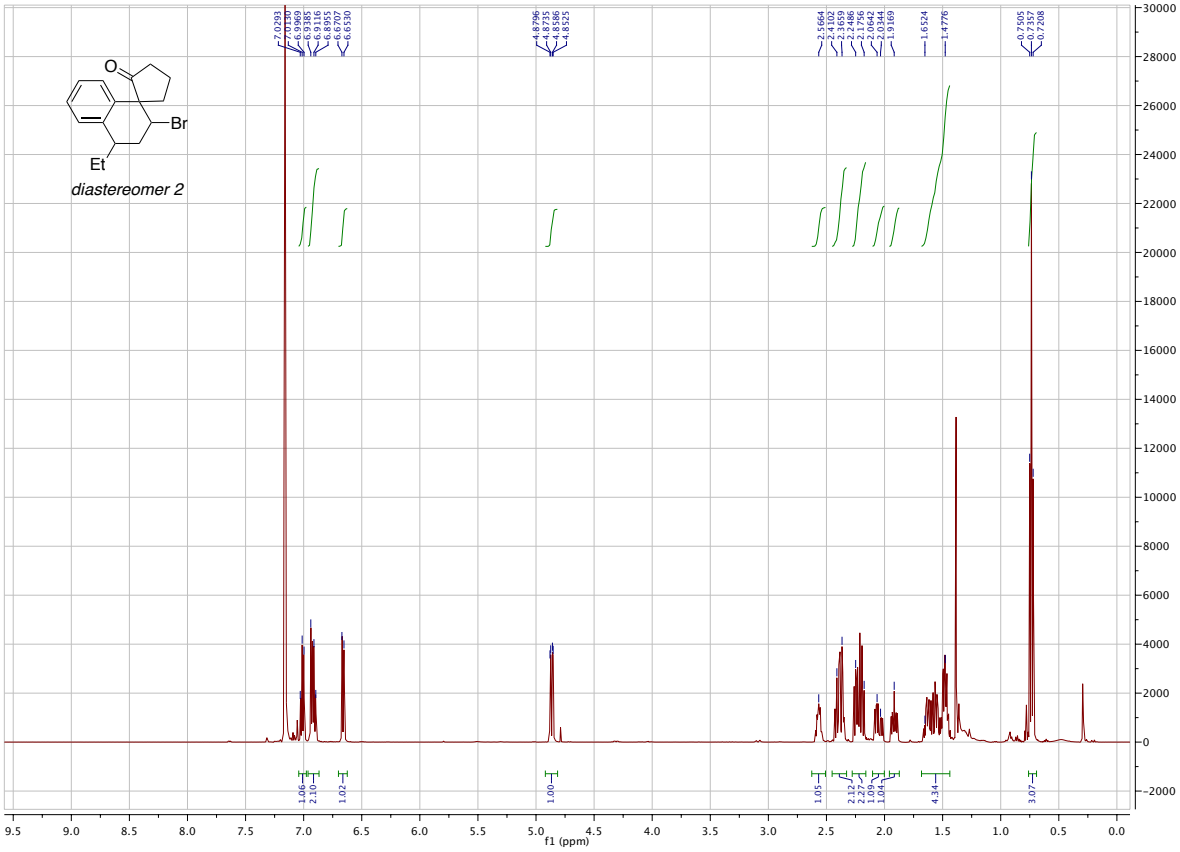


^{13}C NMR 125 MHz, C_6D_6

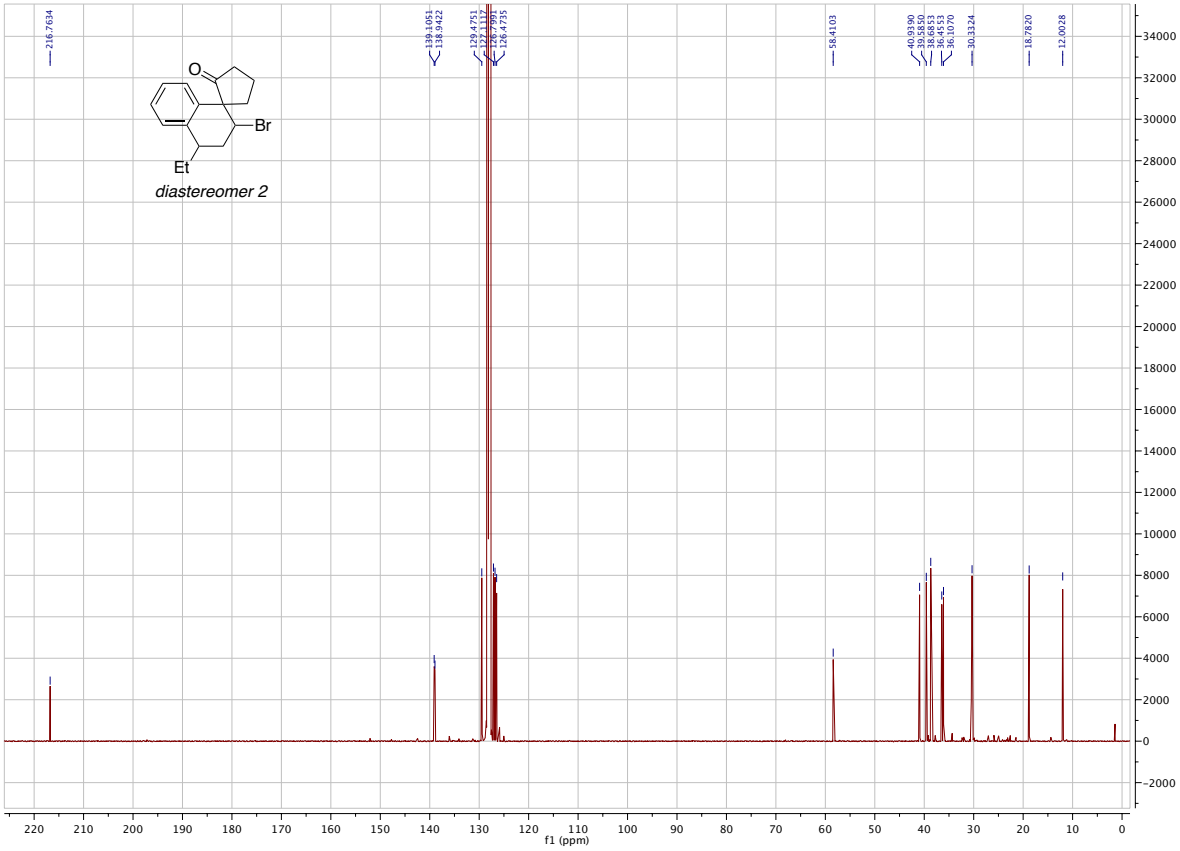


β-Bromo Spiroketone C_{10}^{S}

^{1}H NMR 500 MHz, C_6D_6

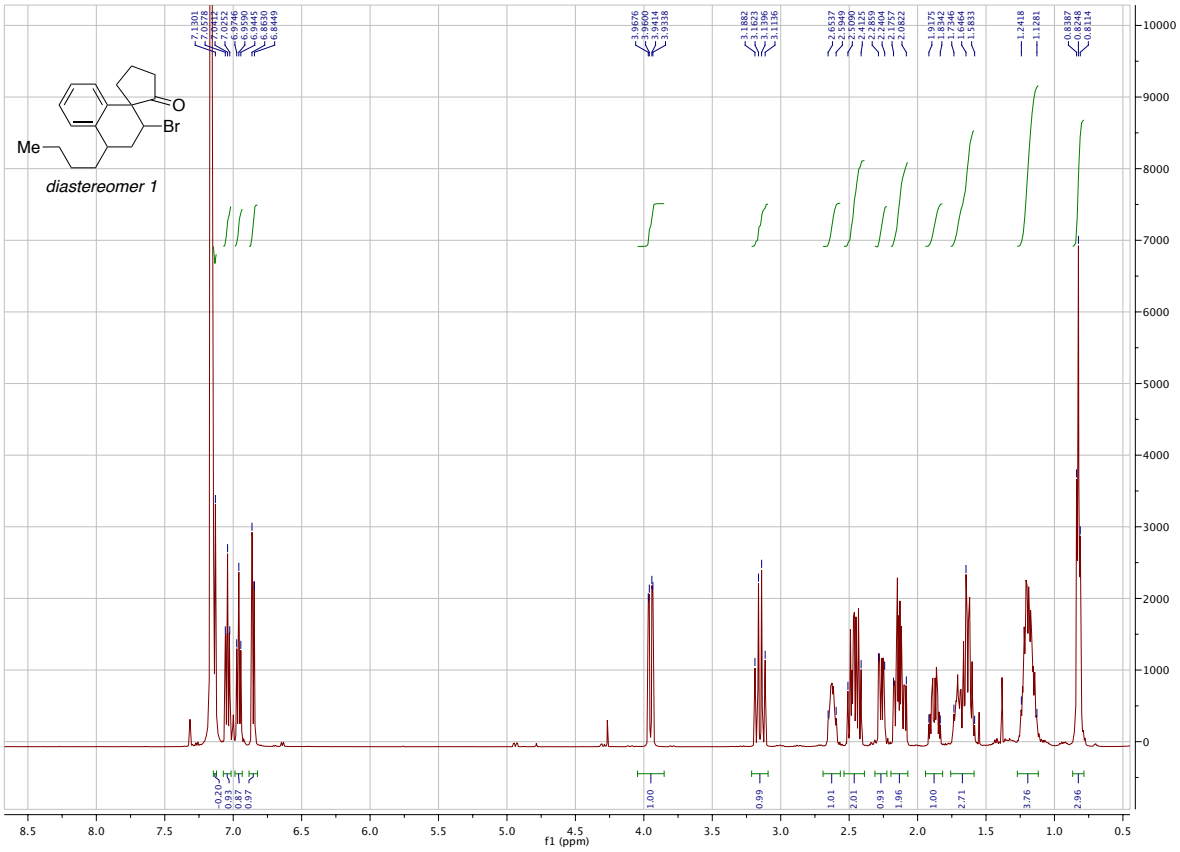


^{13}C NMR 125 MHz, C_6D_6

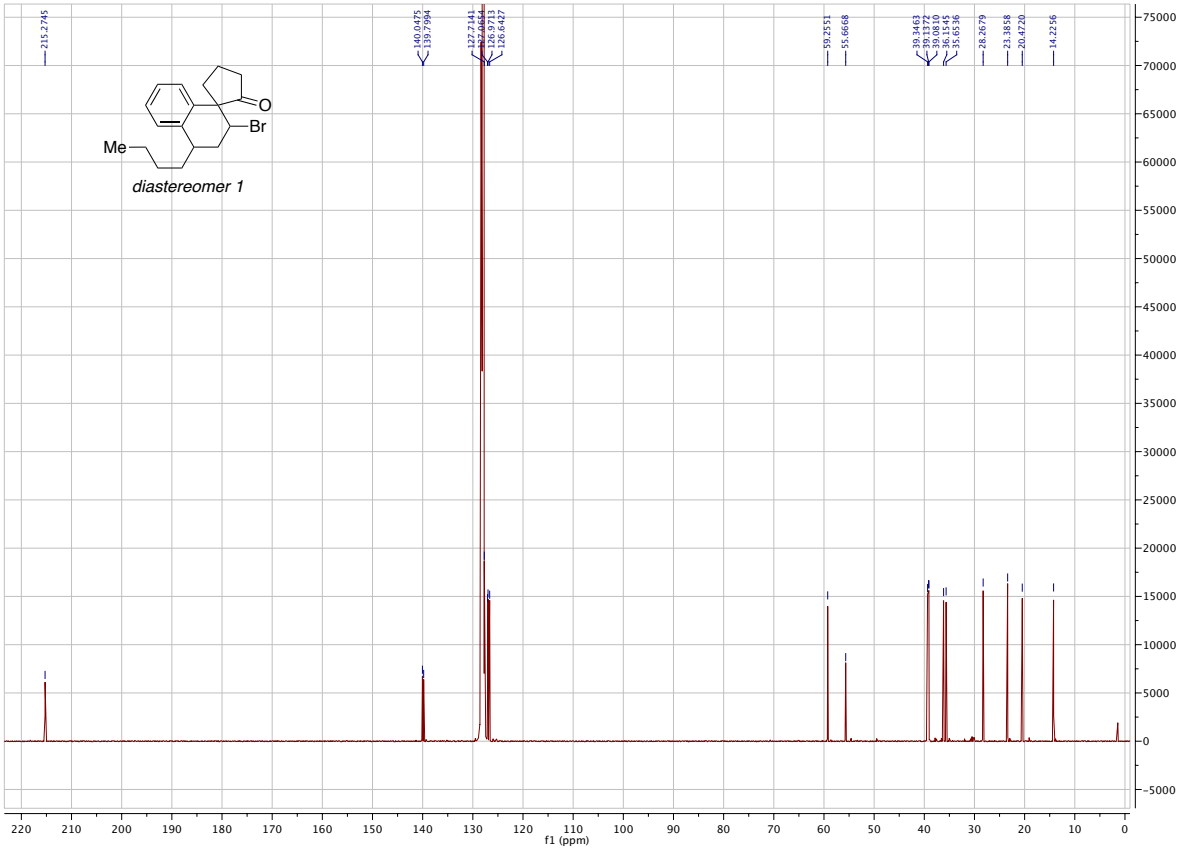


β-Bromo Spiroketone C_{11}^{R}

^{1}H NMR 500 MHz, C_6D_6

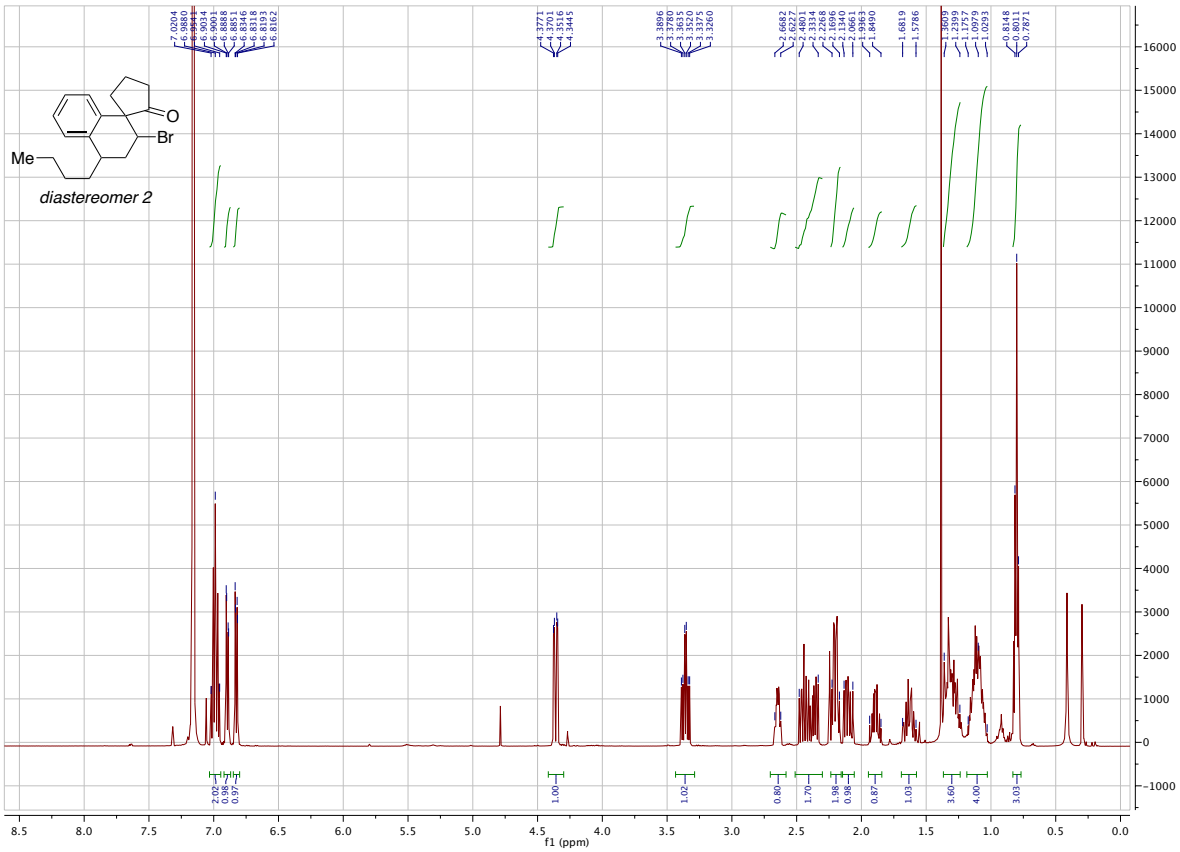


^{13}C NMR 125 MHz, C_6D_6

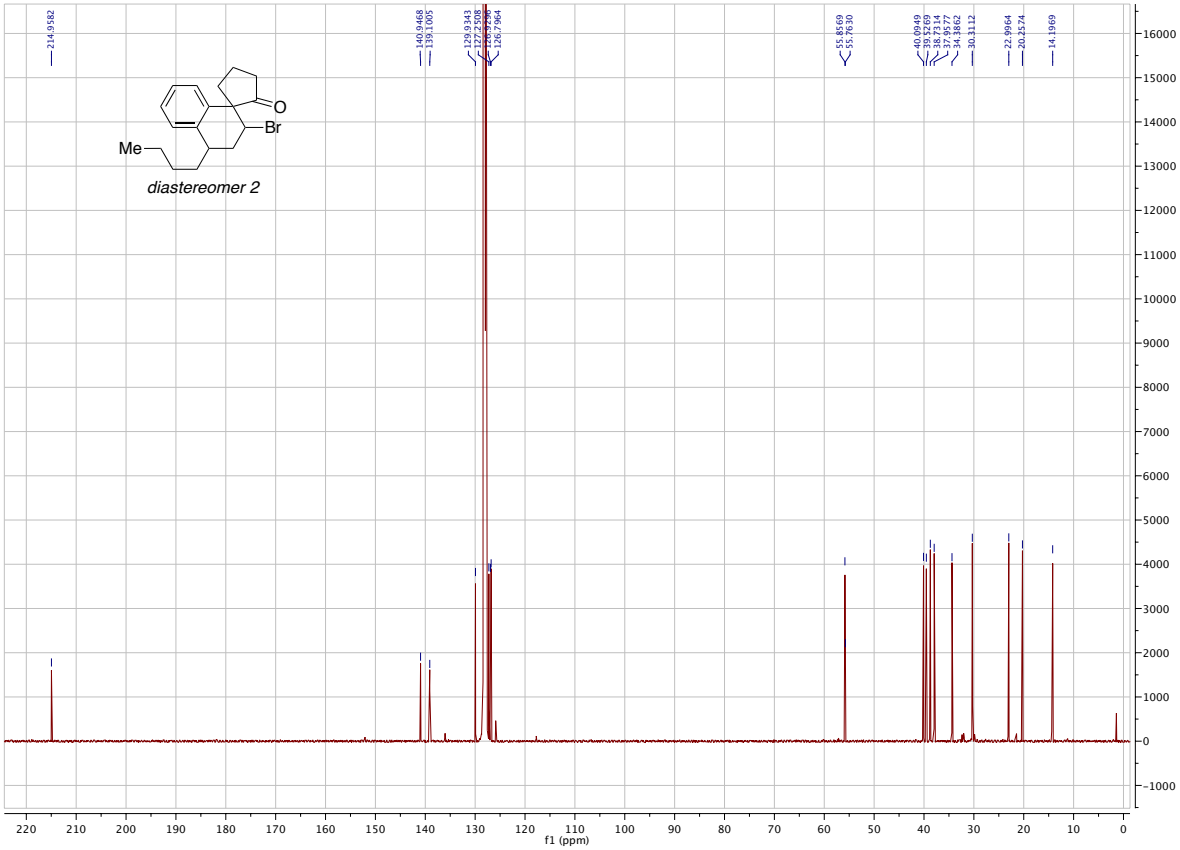


β-Bromo Spiroketone C_{11}^{S}

^{1}H NMR 500 MHz, C_6D_6



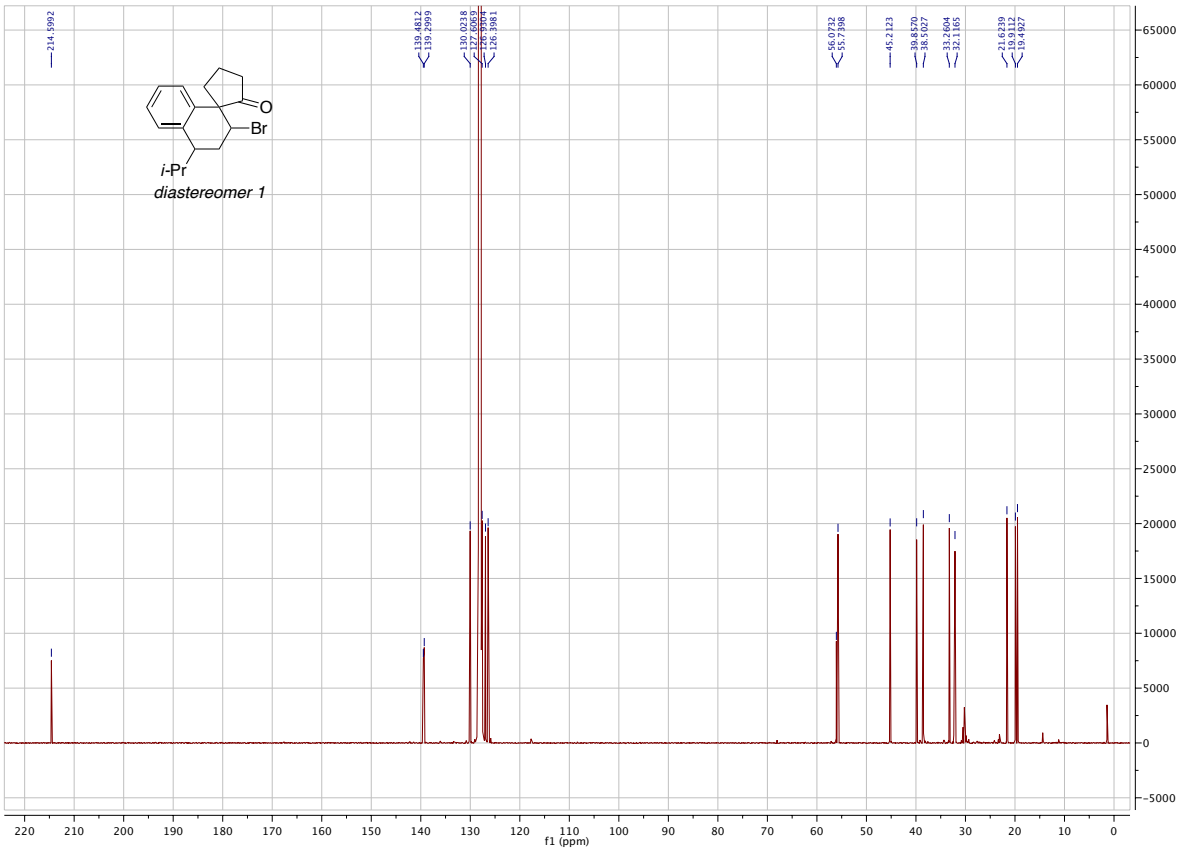
^{13}C NMR 125 MHz, C_6D_6



β-Bromo Spiroketone C_{12}^{R}

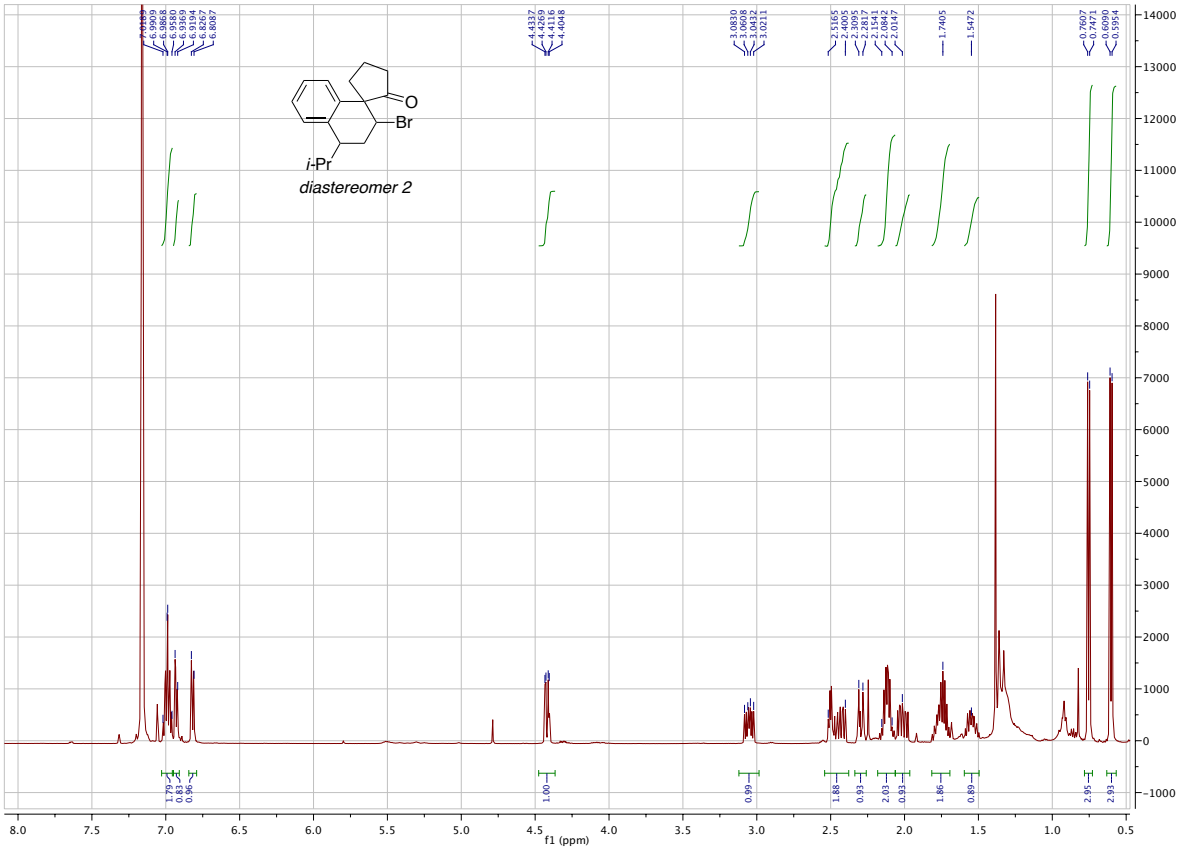
^{1}H NMR 500 MHz, C_6D_6

^{13}C NMR 125 MHz, C_6D_6

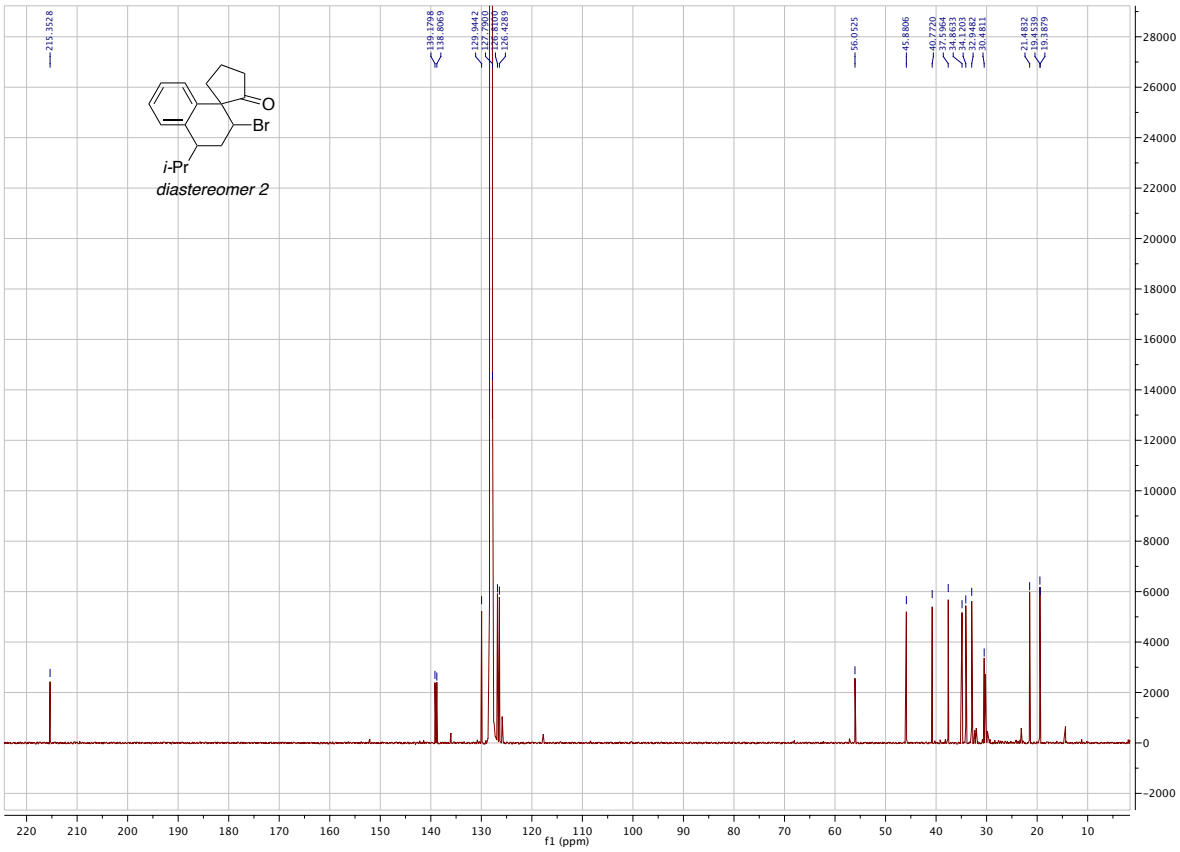


β-Bromo Spiroketone C_{12}[S]

^{1}H NMR 500 MHz, C_6D_6

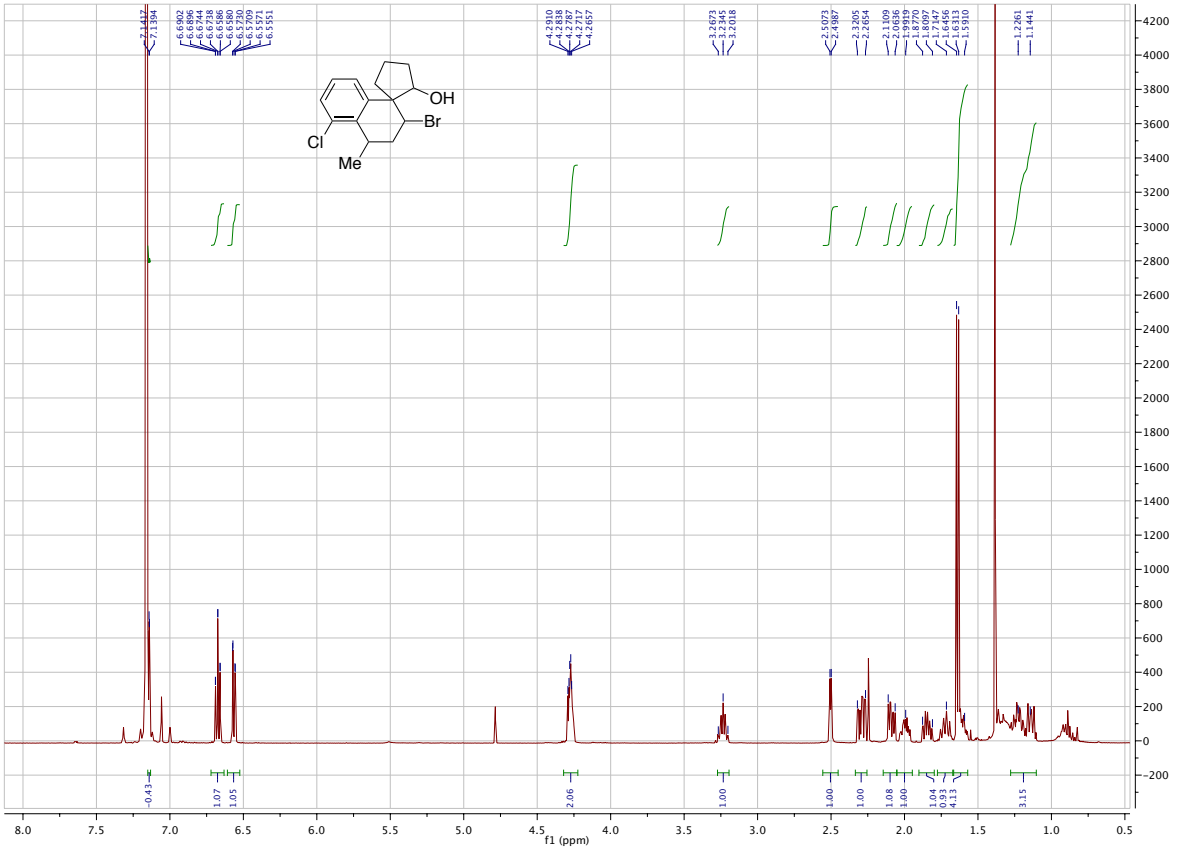


^{13}C NMR 125 MHz, C_6D_6

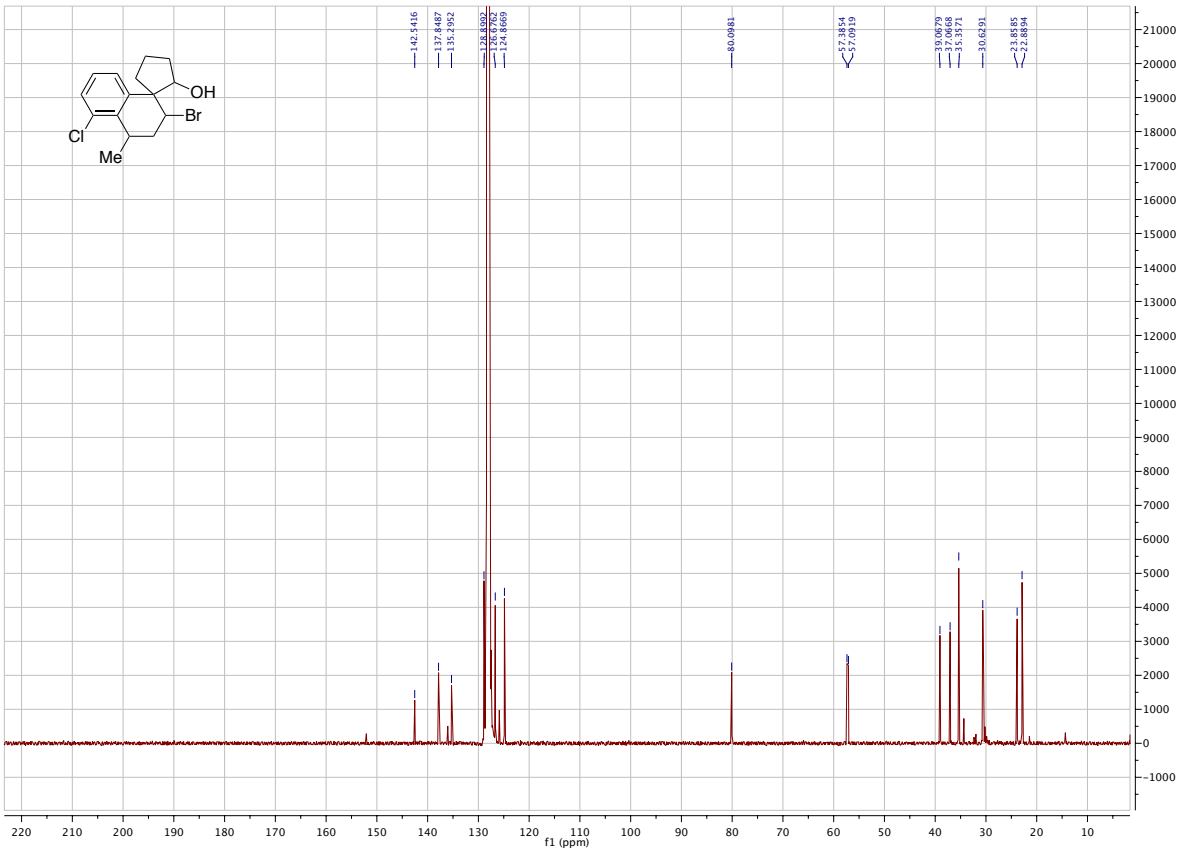


Bromo Alcohol F_4^S

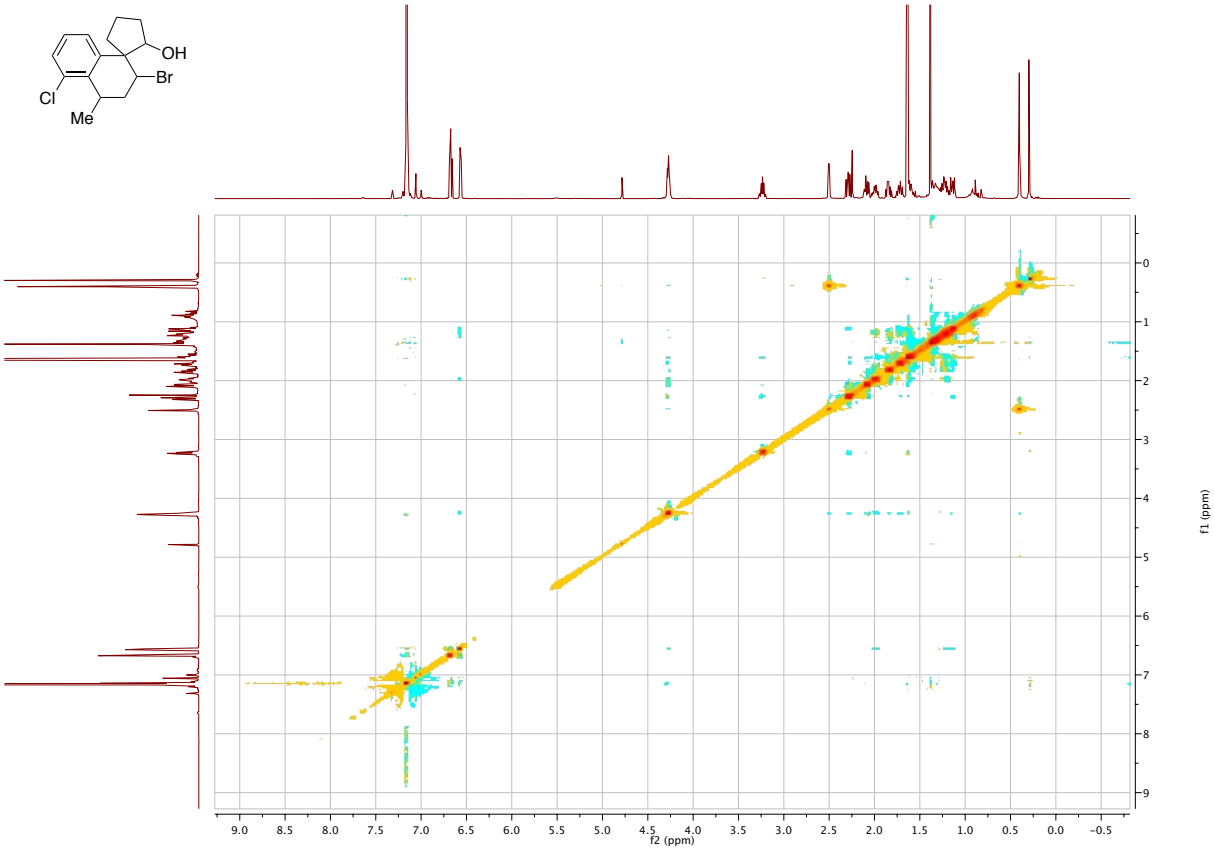
^{1}H NMR 500 MHz, C_6D_6



^{13}C NMR 125 MHz, C_6D_6



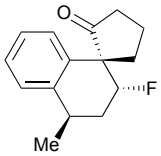
^{1}H-^{1}H NOESY 500 MHz, C_6D_6



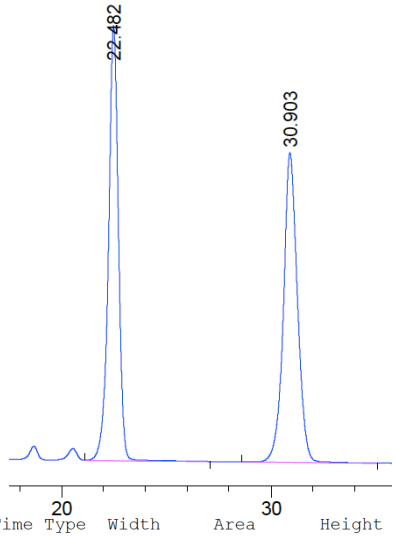
HPLC Traces

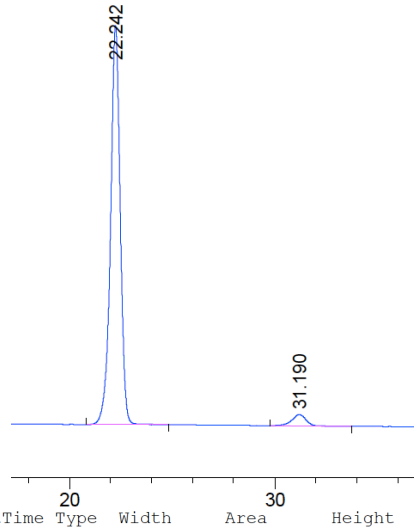
Fluorinated Compounds

β-Fluoro Spiroketone B_1^R



B_1^R

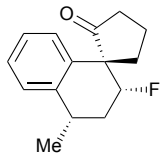




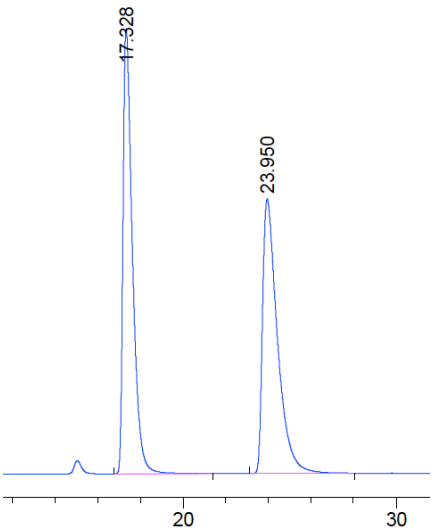
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.482	VB	0.4974	9035.70996	273.54648	49.8604
2	30.903	BV	0.6961	9086.30371	194.83844	50.1396

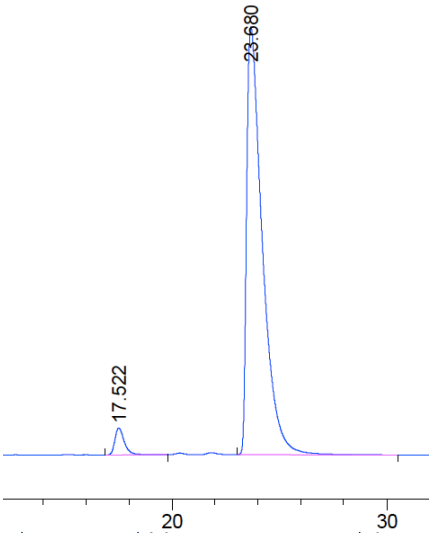
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.242	BB	0.4957	9539.63477	290.07578	95.9186
2	31.190	BB	0.7241	405.91302	8.27736	4.0814

β-Fluoro Spiroketone B_1^S



B_1^S

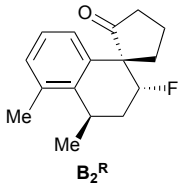




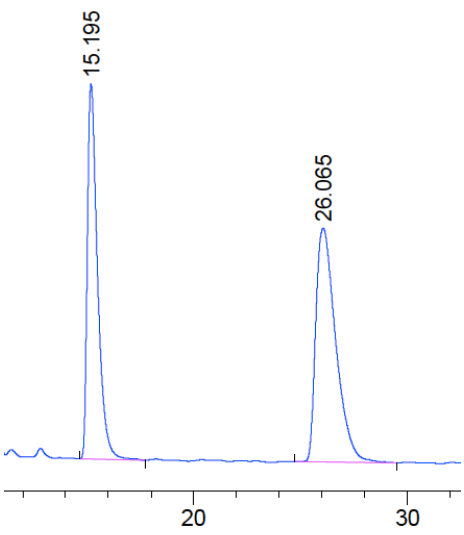
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.328	BB	0.4601	1.03980e4	336.85147	50.7118
2	23.950	BB	0.7282	1.01061e4	207.49112	49.2882

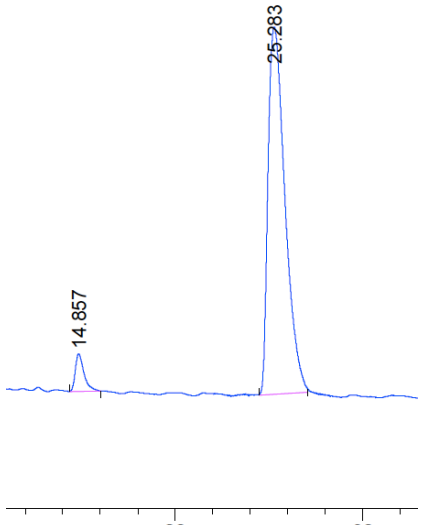
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.522	BB	0.4623	755.07147	24.86391	3.6252
2	23.680	BB	0.7487	2.00735e4	395.11212	96.3748

β-Fluoro Spiroketone B_2^R



B_2^R

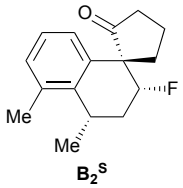




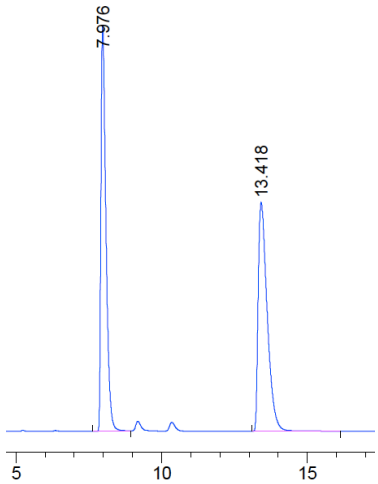
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.195	BV	0.4993	2403.30933	72.39978	45.0763
2	26.065	BB	0.9859	2928.33569	45.07901	54.9237

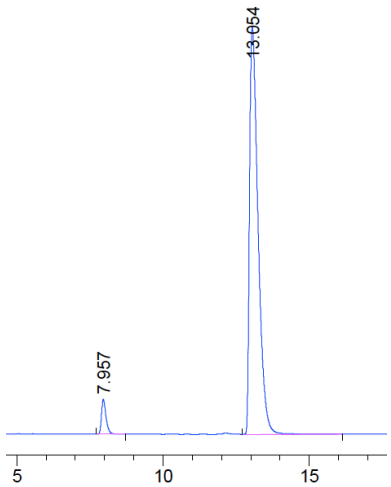
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.857	BB	0.4604	455.40961	14.22760	4.9158
2	25.283	BV	0.7801	8808.74609	140.19252	95.0842

β-Fluoro Spiroketone B_2^S



B_2^S

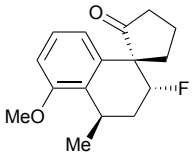




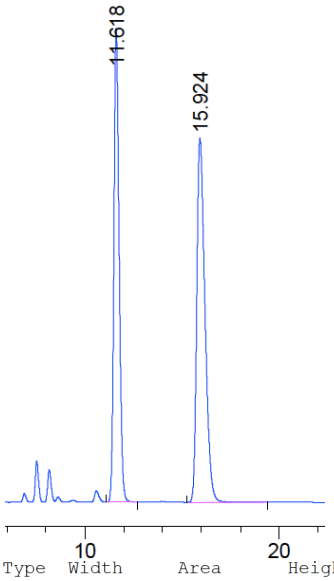
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.976	BV	0.1852	8866.37891	732.77325	49.7064
2	13.418	BV	0.3323	8971.13770	414.78665	50.2936

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.957	BV	0.1675	382.06720	34.95509	4.4386
2	13.054	BB	0.3089	8225.67773	405.12045	95.5614

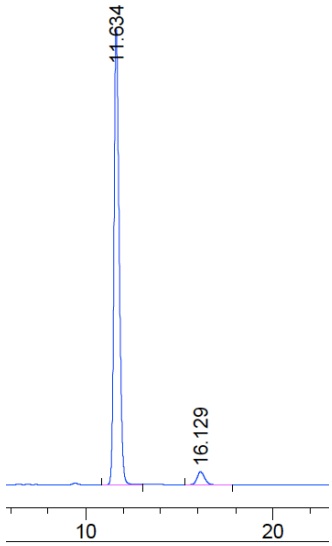
β-Fluoro Spiroketone B_3^R



B_3^R

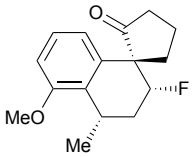


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.618	BV	0.2898	7773.49219	416.39566	45.2906
2	15.924	BB	0.4499	9390.10449	320.45029	54.7094

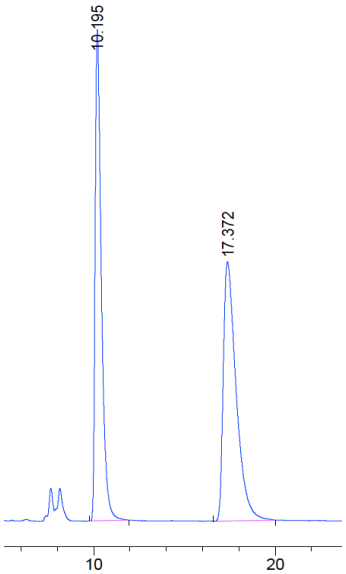


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.634	BV	0.2955	1.52373e4	795.35815	96.0420
2	16.129	BB	0.4264	627.94501	22.72341	3.9580

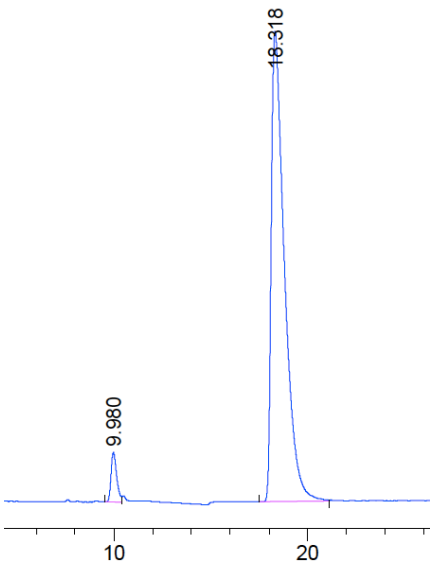
β-Fluoro Spiroketone B_3^S



B_3^S

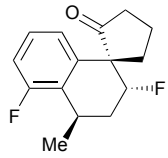


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.195	BB	0.3581	9020.09473	378.43790	47.8906
2	17.372	BB	0.7347	9814.70313	199.58249	52.1094

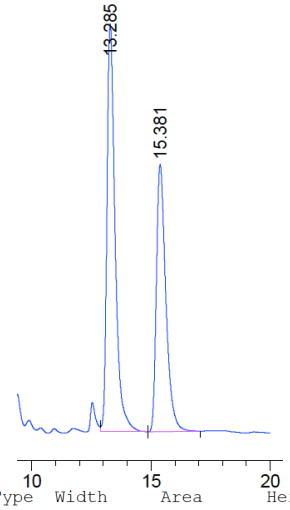


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.980	BV	0.3128	694.24371	34.20577	4.3601
2	18.318	BV	0.6944	1.52286e4	322.80643	95.6399

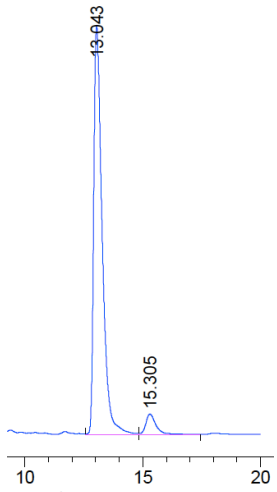
β-Fluoro Spiroketone B_4^R



B_4^R

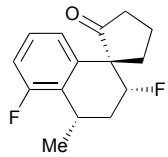


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.285	VB	0.3623	2209.88721	92.62593	56.8878
2	15.381	BB	0.4177	1674.75720	60.73676	43.1122

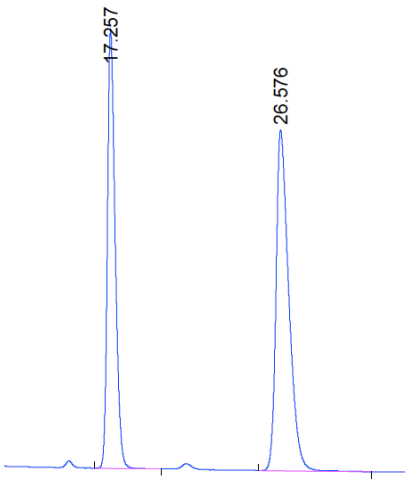


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.043	VV	0.3780	7406.30176	297.94452	94.3127
2	15.305	VB	0.4464	446.62259	14.87118	5.6873

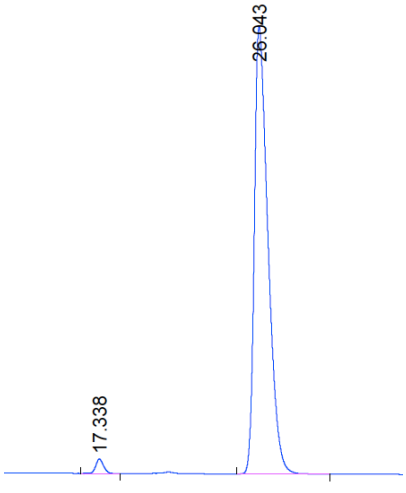
β-Fluoro Spiroketone B_4^S



B_4^S

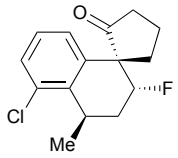


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.257	BV	0.4463	1.10257e4	375.78247	43.8244
2	26.576	BB	0.7297	1.41331e4	291.45602	56.1756

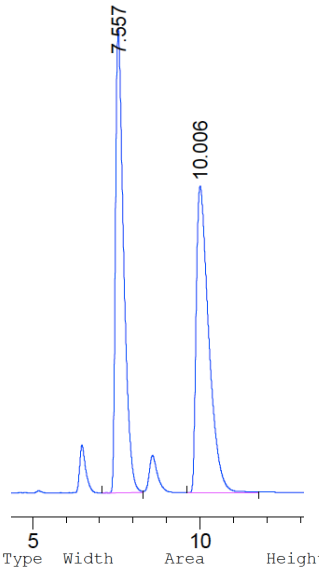


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.338	BB	0.4469	335.16025	11.40410	1.8011
2	26.043	BB	0.7811	1.82735e4	354.67810	98.1989

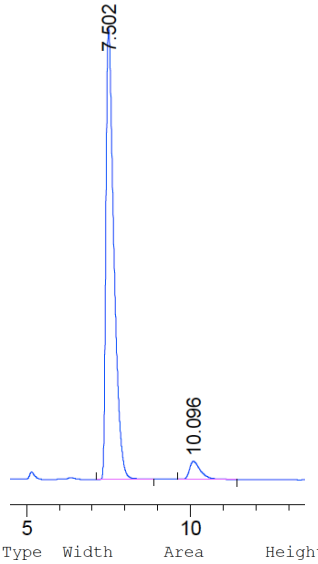
β-Fluoro Spiroketone B_5^R



B_5^R

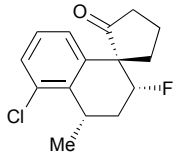


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.557	BV	0.2551	1.05014e4	615.35358	49.6995
2	10.006	BV	0.3978	1.06284e4	405.46109	50.3005

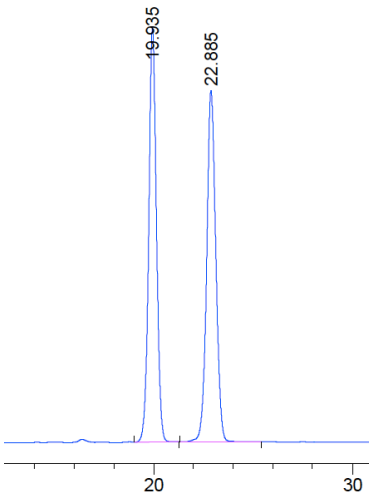


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.502	BV	0.2538	9436.61426	556.51764	94.6428
2	10.096	VB	0.3544	534.15802	22.38280	5.3572

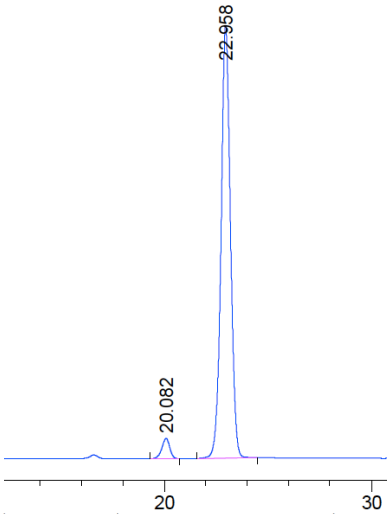
β-Fluoro Spiroketone B_5^S



B_5^S

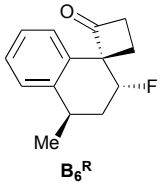


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.935	VB	0.4082	1.27215e4	475.38623	49.8246
2	22.885	BB	0.4873	1.28111e4	402.56671	50.1754

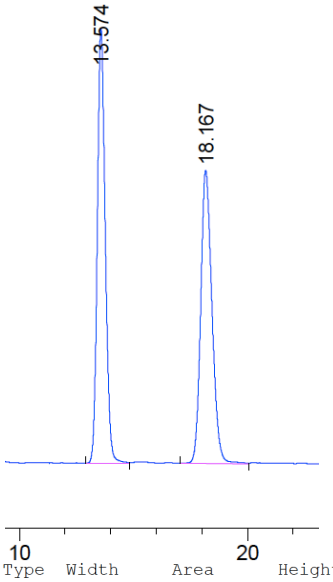


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.082	VB	0.4092	391.89233	14.78512	3.8202
2	22.958	BB	0.4796	9866.52832	313.17319	96.1798

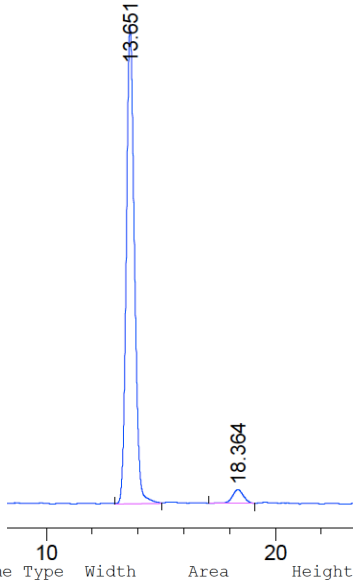
β-Fluoro Spiroketone B_6^R



B_6^R

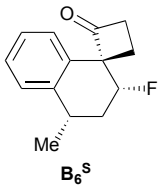


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.574	BV	0.3651	5565.57129	231.02536	51.0732
2	18.167	BV	0.5240	5331.66504	155.49635	48.9268

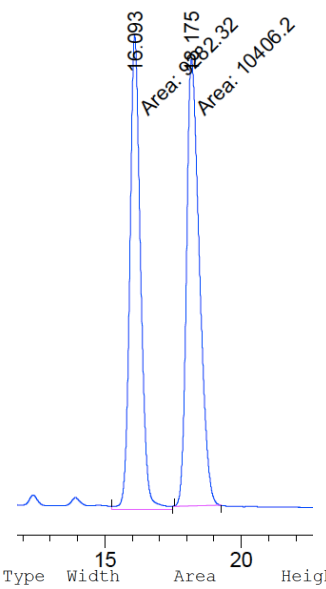


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.651	BV	0.3751	3960.15649	160.92087	96.2545
2	18.364	BB	0.5156	154.09985	4.59048	3.7455

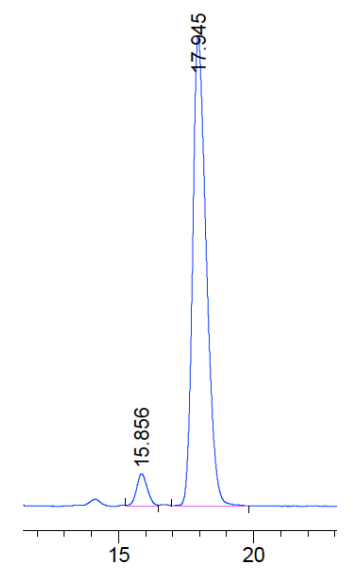
β-Fluoro Spiroketone B_6^S



B_6^S

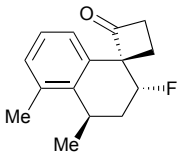


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.093	MM	0.4575	9282.32227	338.17816	47.1459
2	18.175	MM	0.5451	1.04062e4	318.16687	52.8541

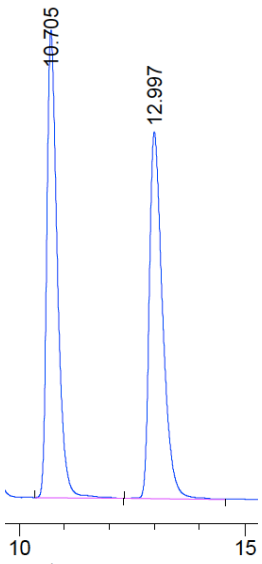


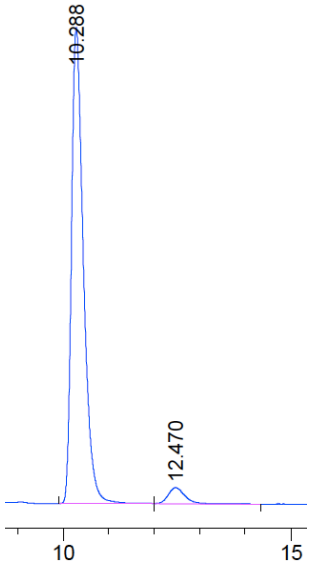
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.856	VV	0.4190	413.16928	14.92501	5.1406
2	17.945	BV	0.5385	7624.14063	216.68707	94.8594

β-Fluoro Spiroketone B_7^R



B_7^R

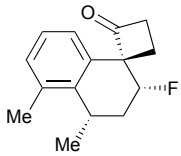




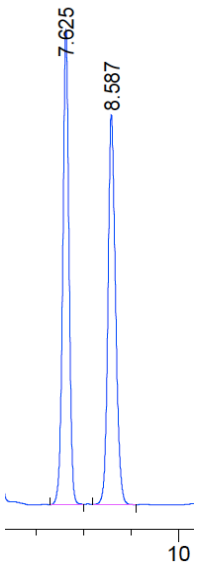
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.705	VB	0.2499	6865.88281	421.73056	50.2935
2	12.997	BV	0.3145	6785.74268	331.92365	49.7065

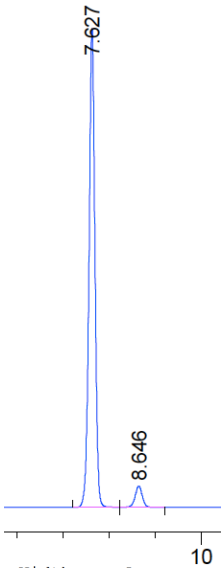
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.288	BV	0.2768	1.00537e4	551.21716	95.3402
2	12.470	VB	0.3988	491.38504	18.68739	4.6598

β-Fluoro Spiroketone B_7^S



B_7^S

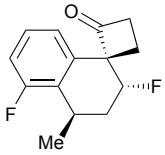




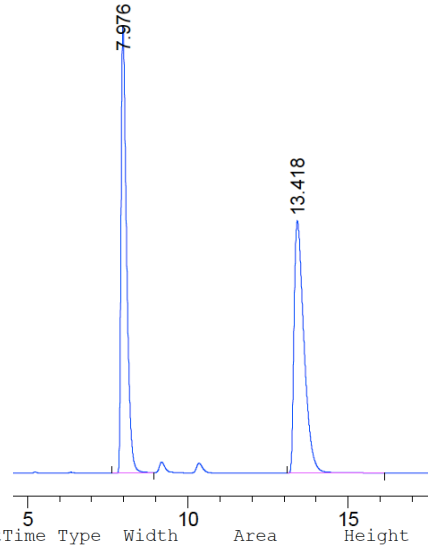
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.625	BV	0.1476	6734.02246	730.37201	49.9775
2	8.587	VV	0.1751	6740.08887	599.63495	50.0225

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.627	BV	0.1416	4637.22168	512.50665	94.6816
2	8.646	VB	0.1750	260.48154	23.19332	5.3184

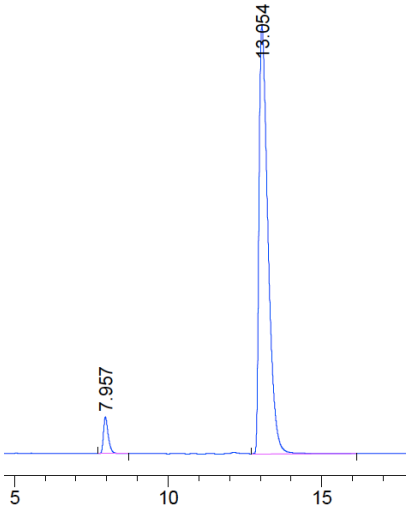
β-Fluoro Spiroketone B_8^R



B_8^R

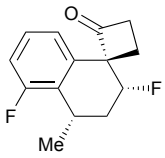


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.976	BV	0.1852	8866.37891	732.77325	49.7064
2	13.418	BV	0.3323	8971.13770	414.78665	50.2936

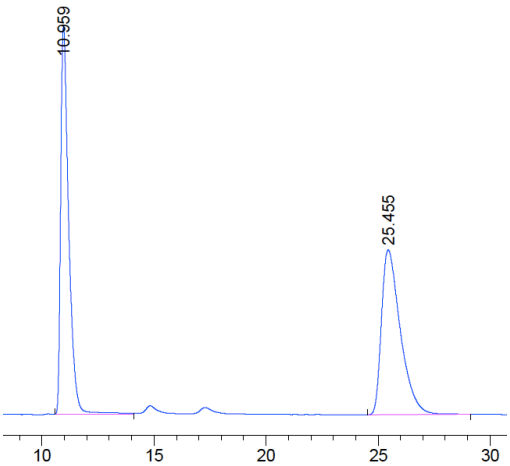


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.957	BV	0.1675	382.06720	34.95509	4.4386
2	13.054	BB	0.3089	8225.67773	405.12045	95.5614

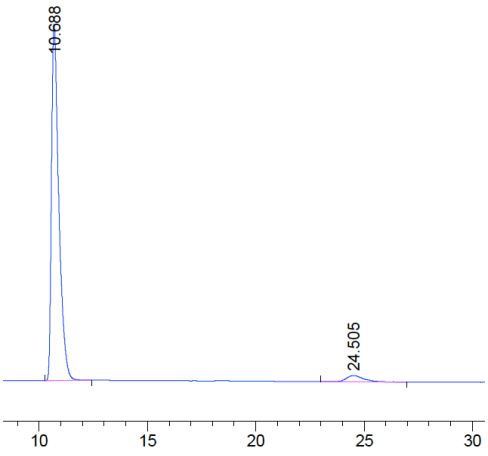
β-Fluoro Spiroketone B_8^S



B_8^S

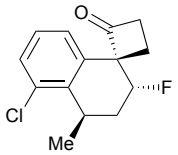


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.959	BV	0.3742	9173.53320	363.79477	50.2842
2	25.455	BB	0.8974	9069.82617	154.39218	49.7158

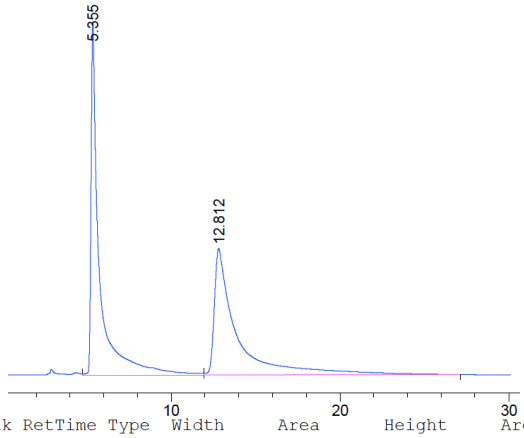


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.688	BB	0.3498	8862.10156	377.60336	95.9864
2	24.505	BB	0.7990	370.56635	6.72398	4.0136

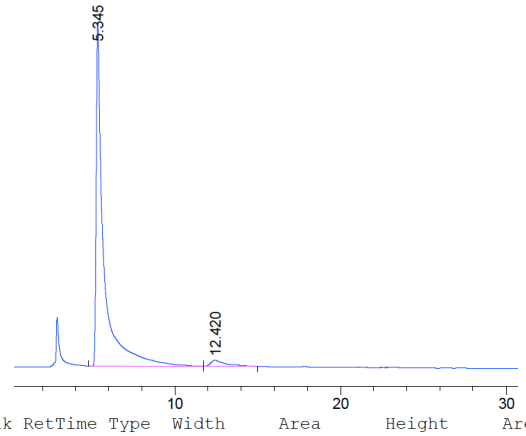
β-Fluoro Spiroketone B_9^R



B_9^R

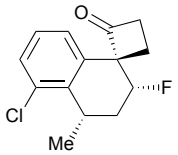


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.355	VV	0.4557	7057.31299	205.99309	50.8682
2	12.812	VB	1.1991	6816.40381	73.69560	49.1318

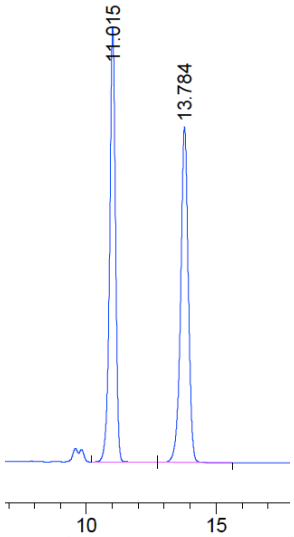


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.345	BV	0.4223	3731.19580	117.55669	96.1966
2	12.420	VB	0.8983	147.52357	2.16688	3.8034

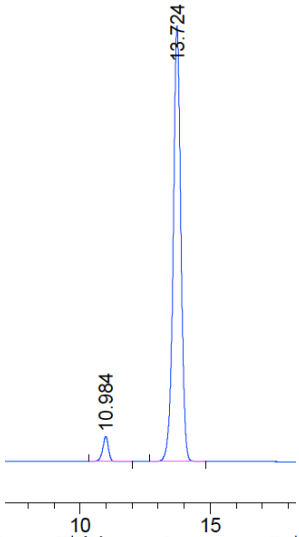
β-Fluoro Spiroketone B_9^S



B_9^S

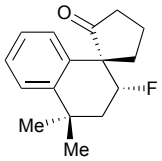


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.015	VB	0.2435	7560.95850	480.74316	49.9287
2	13.784	BB	0.3146	7582.55127	370.76709	50.0713

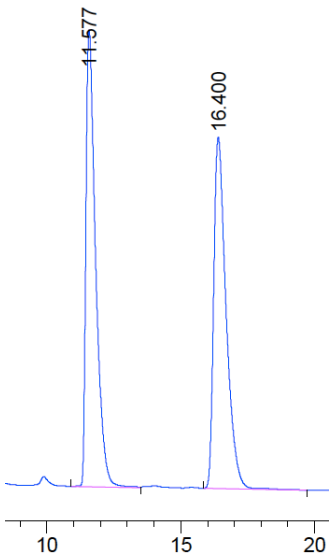


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.984	BB	0.2370	568.44934	36.64627	4.1980
2	13.724	BB	0.3117	1.29726e4	631.36194	95.8020

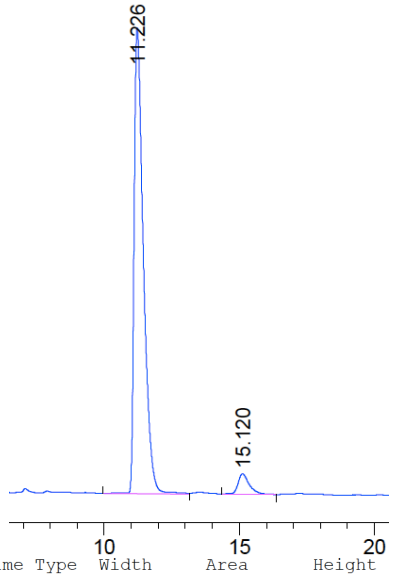
β-Fluoro Spiroketone B_{10}



B_{10}

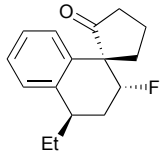


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.577	BV	0.3823	5383.80713	213.41173	50.4084
2	16.400	VB	0.4840	5296.57324	164.33920	49.5916

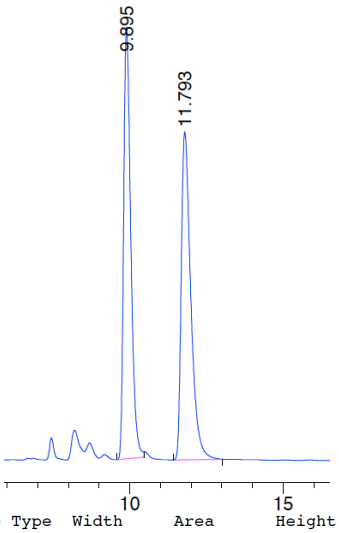


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.226	BV	0.3590	4428.68213	185.17812	94.6182
2	15.120	VV	0.4402	251.89738	8.34377	5.3818

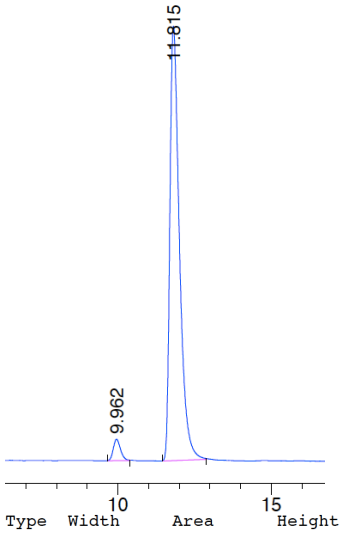
β-Fluoro Spiroketone B_{11}^{R}



B_{11}^{R}

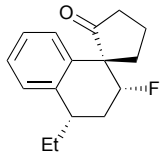


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.895	BB	0.2481	8848.36328	548.66522	49.5209
2	11.793	BB	0.3326	9019.56836	416.58359	50.4791

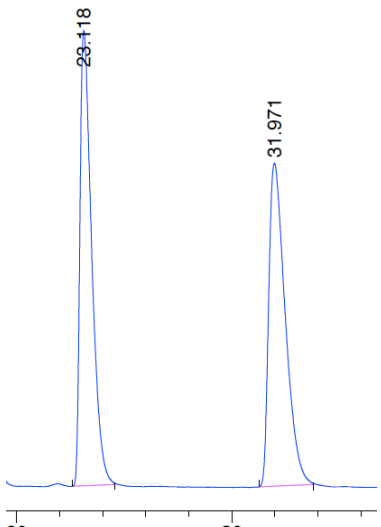


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.962	BB	0.2544	292.20447	17.90661	3.5871
2	11.815	BB	0.3308	7853.76563	362.46780	96.4129

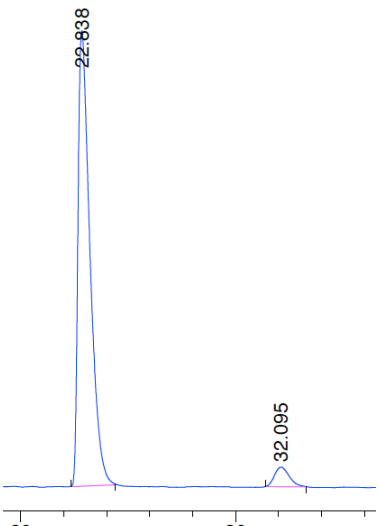
β-Fluoro Spiroketone B_{11}^{S}



B_{11}^{S}

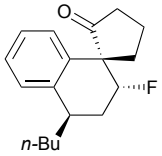


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.118	BB	0.5683	7545.93457	199.92696	50.0483
2	31.971	BB	0.7874	7531.36719	141.85916	49.9517

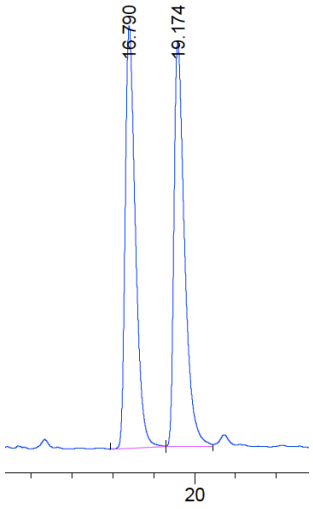


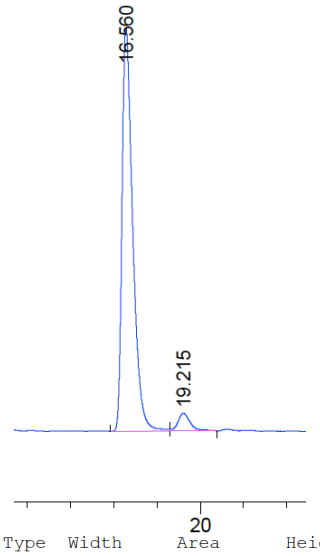
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.838	BB	0.5866	8244.26465	213.47922	94.9031
2	32.095	BB	0.6041	442.77069	9.18959	5.0969

β-Fluoro Spiroketone B_{12}^{R}



B_{12}^{R}

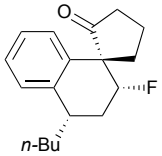




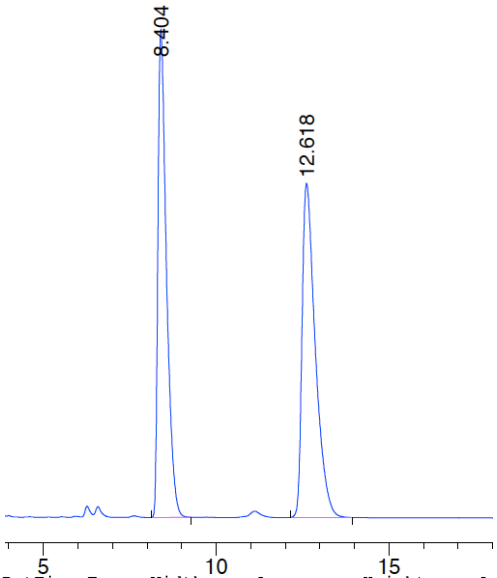
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.790	BB	0.5289	4671.51855	134.61131	50.0800
2	19.174	BV	0.5413	4656.59326	128.95334	49.9200

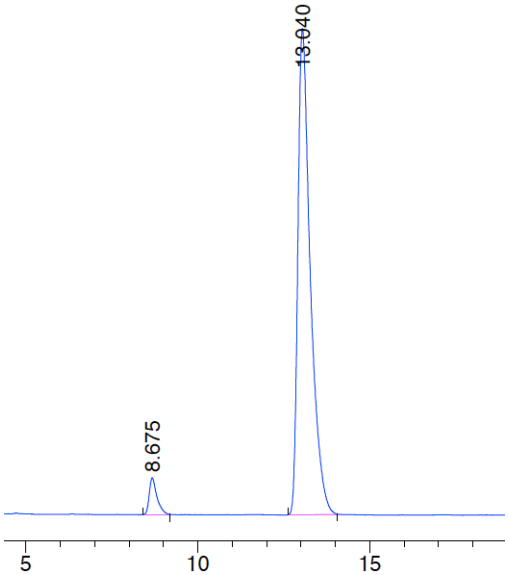
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.560	BV	0.5214	6055.37744	175.98755	95.2075
2	19.215	VV	0.5936	304.81207	7.77069	4.7925

β-Fluoro Spiroketone B_{12}^{S}



B_{12}^{S}

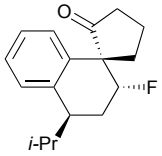




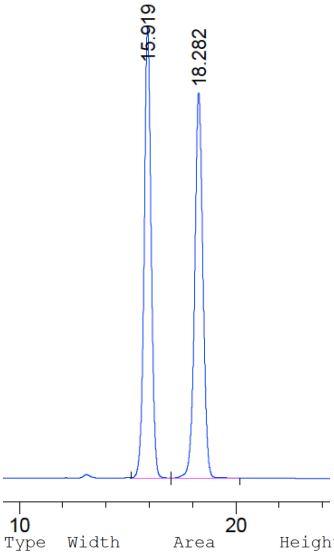
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.404	BB	0.2569	1.83972e4	1068.28918	48.5742
2	12.618	BB	0.4007	1.94772e4	731.46216	51.4258

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.675	BB	0.2305	344.39267	22.01178	4.5148
2	13.040	BB	0.3711	7283.65186	289.87540	95.4852

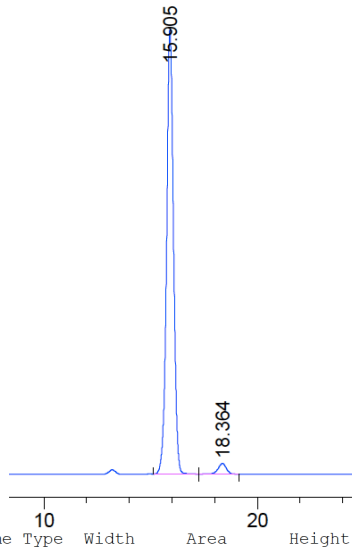
β-Fluoro Spiroketone B_{13}^{R}



B_{13}^{R}

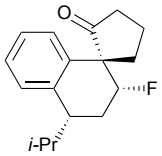


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.919	VB	0.3425	1.01769e4	452.29510	49.8022
2	18.282	BV	0.4060	1.02578e4	386.05777	50.1978

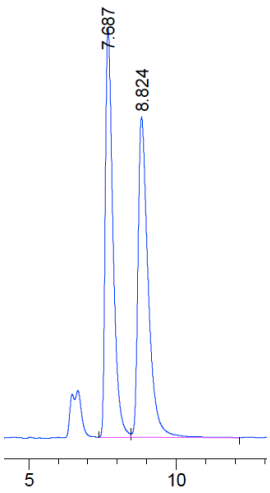


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.905	VV	0.3452	9334.23047	416.97638	96.9833
2	18.364	VB	0.4233	290.34012	10.22419	3.0167

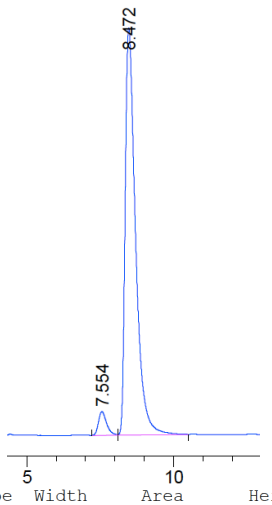
β-Fluoro Spiroketone B_{13}^{S}



B_{13}^{S}



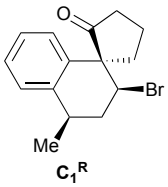
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.687	BV	0.2766	1.01892e4	559.17365	49.2387
2	8.824	VV	0.3602	1.05043e4	437.37979	50.7613



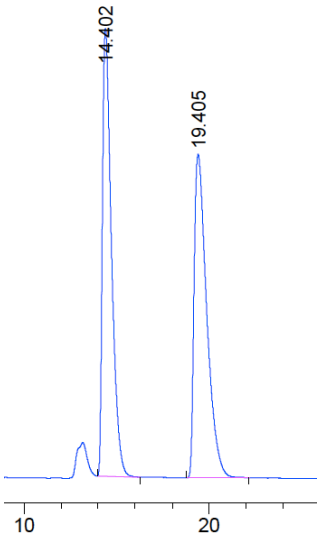
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.554	BV	0.2914	552.45728	28.85462	4.3564
2	8.472	VV	0.3668	1.21290e4	493.41730	95.6436

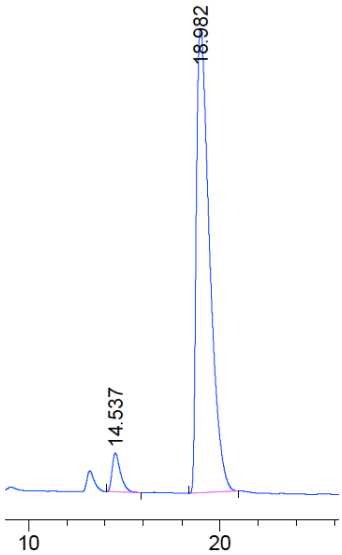
Brominated Compounds

β-Bromo Spiroketone C_1^R



C_1^R

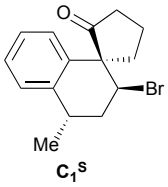




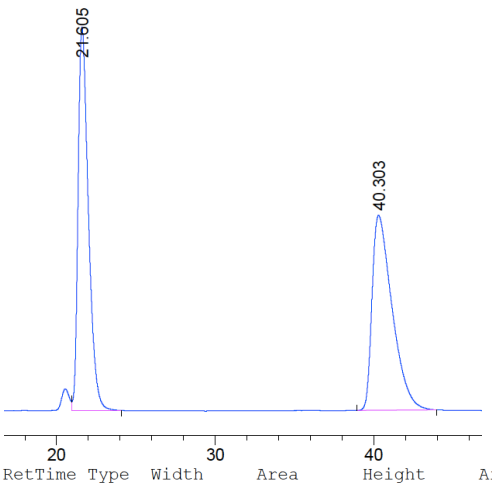
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.402	BB	0.5125	6435.13037	189.82944	49.7446
2	19.405	BB	0.7142	6501.22119	137.09613	50.2554

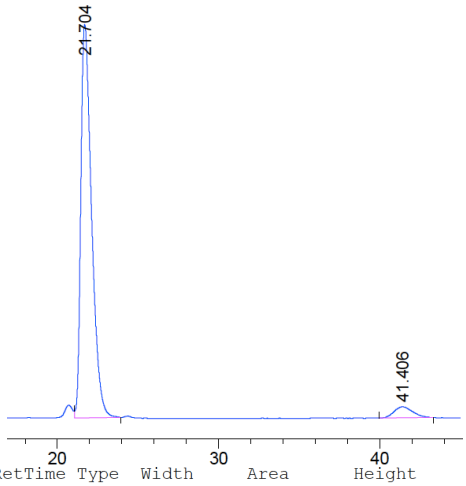
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.537	BB	0.4563	501.46869	16.51081	5.0412
2	18.982	BB	0.7330	9445.92285	196.09216	94.9588

β-Bromo Spiroketone C_1^S



C_1^S

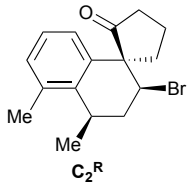




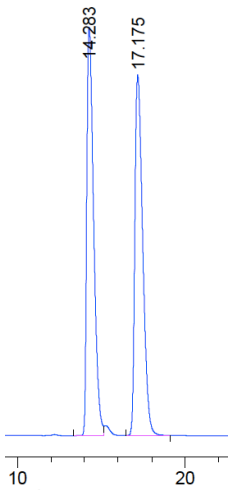
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.605	VB	0.6908	6475.93018	143.13416	50.2137
2	40.303	BB	1.2532	6420.81543	72.78189	49.7863

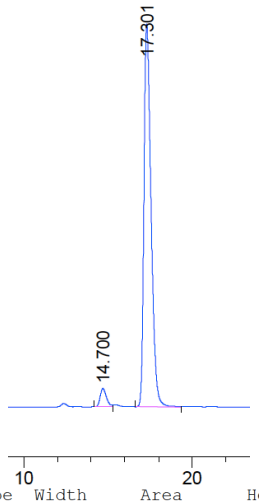
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.704	VB	0.7058	9456.06934	204.35506	95.2260
2	41.406	BB	0.9679	474.06393	5.79191	4.7740

β-Bromo Spiroketone C_2^R



C_2^R

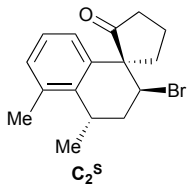




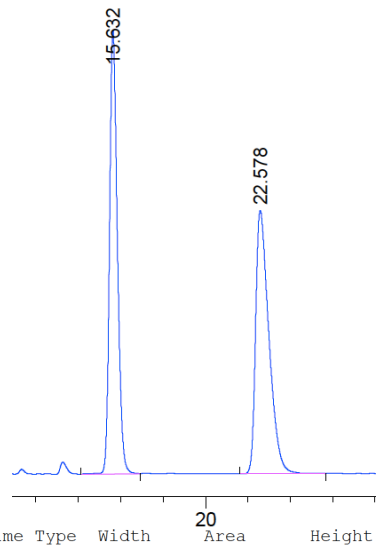
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.283	BV	0.4409	1.44801e4	507.51505	49.7701
2	17.175	VV	0.5086	1.46139e4	447.96729	50.2299

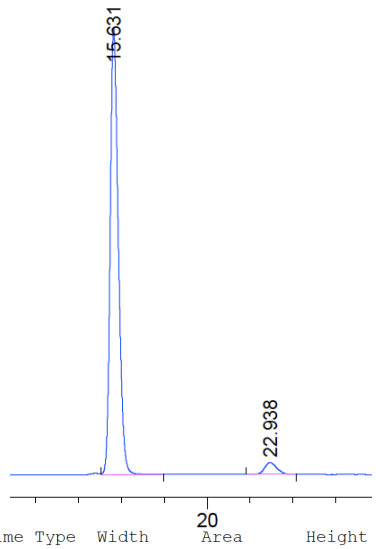
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.700	BV	0.3983	330.96542	12.77251	4.0797
2	17.301	BV	0.4483	7781.57617	266.75378	95.9203

β-Bromo Spiroketone C_2^S



C_2^S

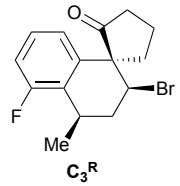




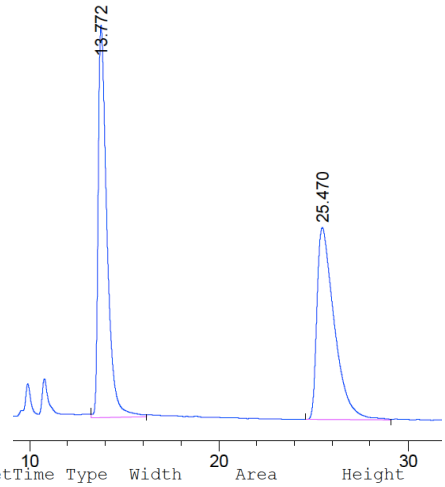
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.632	BV	0.3959	7874.45410	306.32892	49.9359
2	22.578	BB	0.6553	7894.65674	181.56534	50.0641

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.631	VV	0.4039	1.50583e4	570.49146	96.0248
2	22.938	BV	0.6254	623.38617	15.23562	3.9752

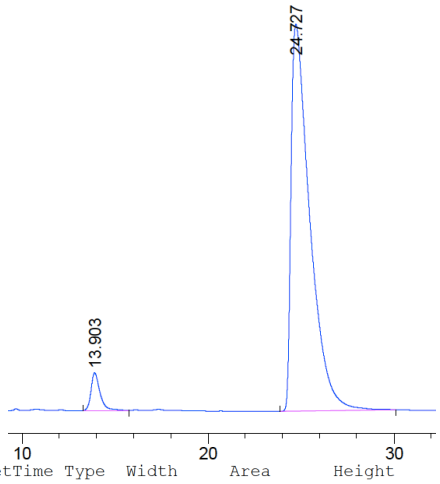
β-Bromo Spiroketone C_3^R



C_3^R

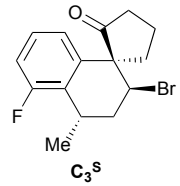


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.772	VV	0.4821	9071.35645	279.90497	50.8917
2	25.470	BV	0.9530	8753.46777	137.07603	49.1083

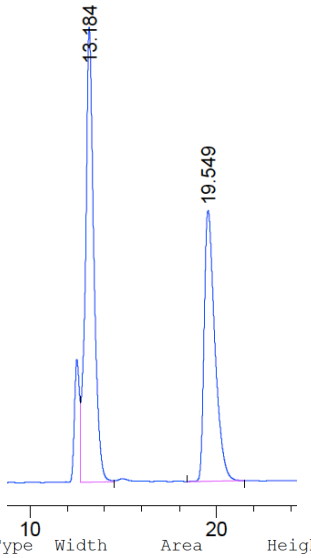


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.903	BV	0.5124	872.94611	25.43756	4.5671
2	24.727	BB	1.0387	1.82411e4	259.93356	95.4329

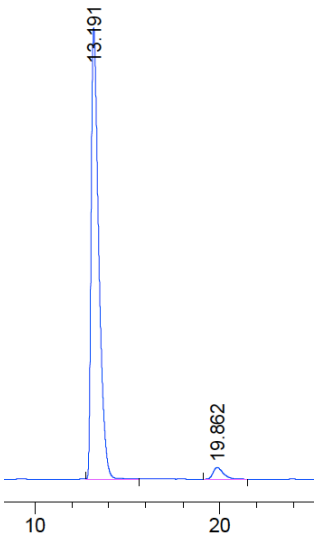
β-Bromo Spiroketone C_3^S



C_3^S

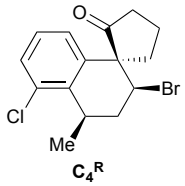


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.184	VV	0.4528	4249.86963	135.90485	56.8046
2	19.549	BB	0.6017	3231.69043	80.96684	43.1954

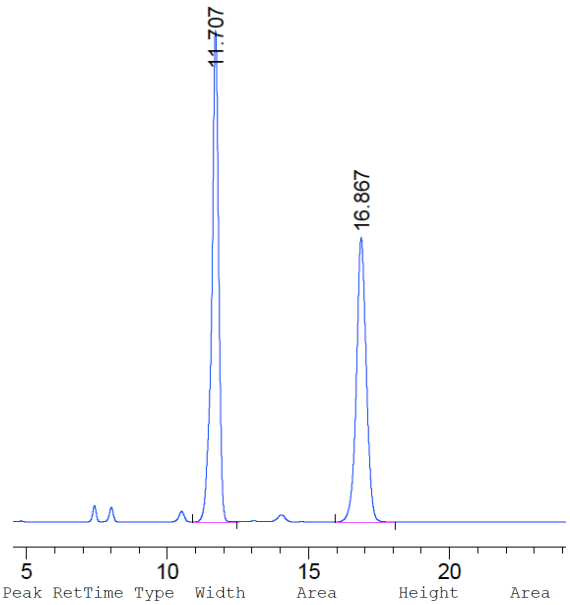


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.191	VV	0.4305	1.33961e4	467.25974	96.5995
2	19.862	BB	0.5754	471.57126	12.29781	3.4005

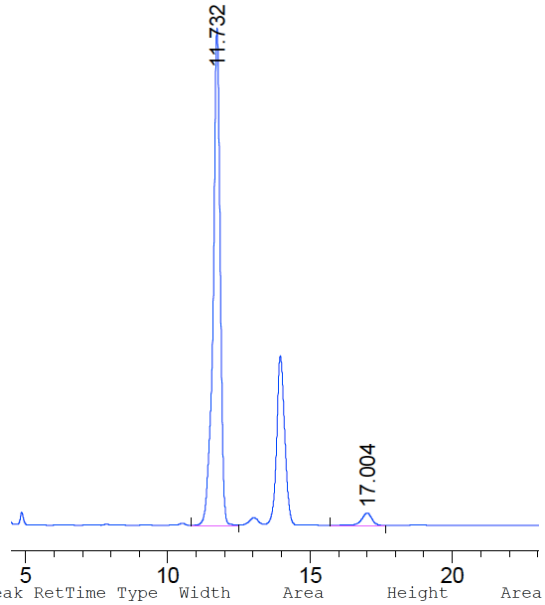
β-Bromo Spiroketone C_4^R



C_4^R

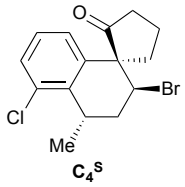


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.707	BV	0.2563	7899.74707	460.17453	54.9550
2	16.867	BV	0.3680	6475.20361	265.96622	45.0450

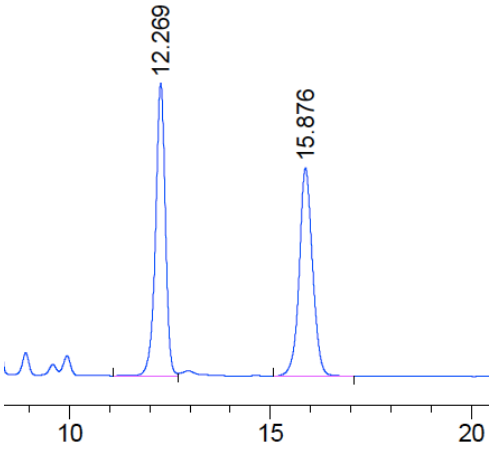


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.732	BV	0.2628	6181.84473	355.67166	96.4878
2	17.004	BB	0.3769	225.02065	8.96172	3.5122

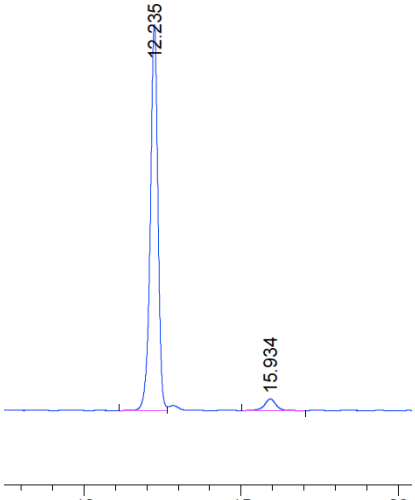
β-Bromo Spiroketone C_4^S



C_4^S

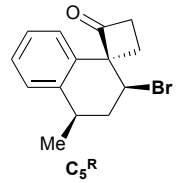


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.269	BV	0.2578	2311.99121	136.37790	50.7888
2	15.876	VB	0.3533	2240.17554	97.05193	49.2112

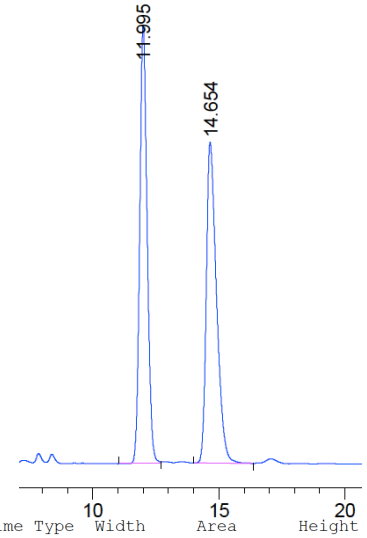


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.235	BV	0.2605	2526.27612	149.98247	95.3361
2	15.934	VV	0.3938	123.58751	4.59543	4.6639

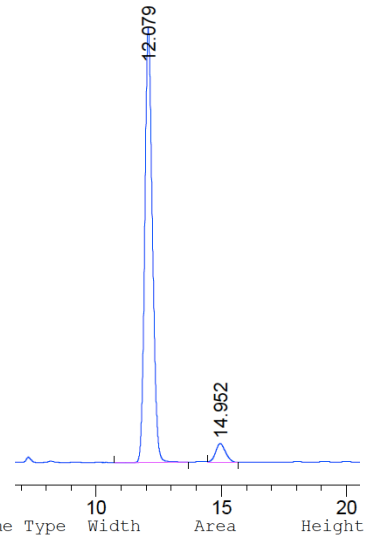
β-Bromo Spiroketone C_5^R



C_5^R

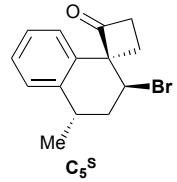


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.995	BV	0.3119	4704.57471	228.81064	50.0201
2	14.654	BV	0.4235	4700.80176	167.44551	49.9799

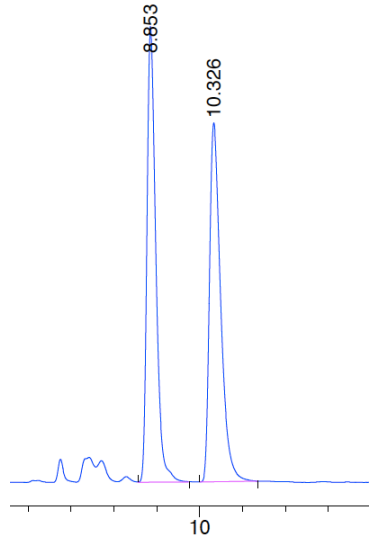


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.079	BV	0.3244	4995.44531	234.63078	94.6634
2	14.952	VB	0.4288	281.61520	10.11448	5.3366

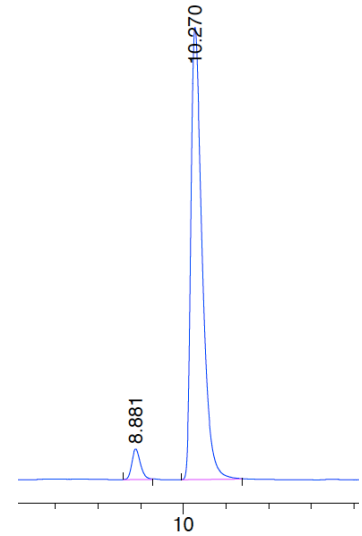
β-Bromo Spiroketone C_5^S



C_5^S

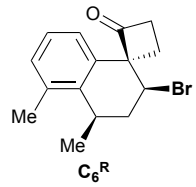


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.853	VB	0.2217	9407.46582	654.58569	50.2782
2	10.326	BB	0.2765	9303.34180	515.69385	49.7218

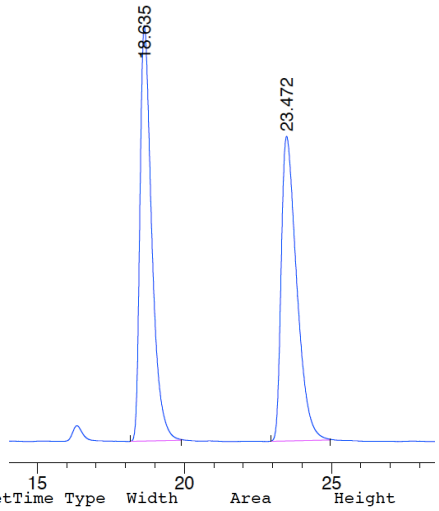


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.881	BB	0.2149	693.53278	49.68323	4.9046
2	10.270	BB	0.2794	1.34470e4	735.24915	95.0954

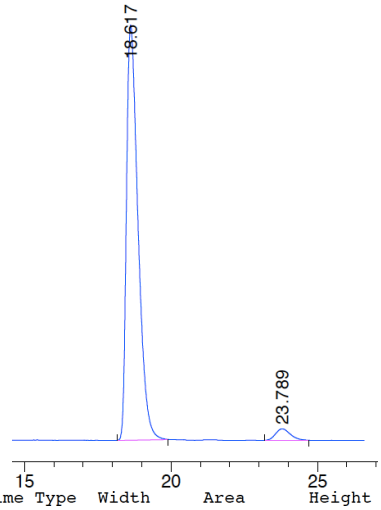
β-Bromo Spiroketone C_6^R



C_6^R

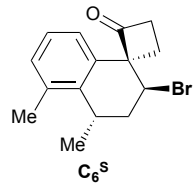


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.635	BB	0.4210	9280.13672	333.13126	50.9109
2	23.472	BB	0.5613	8948.03809	244.33542	49.0891

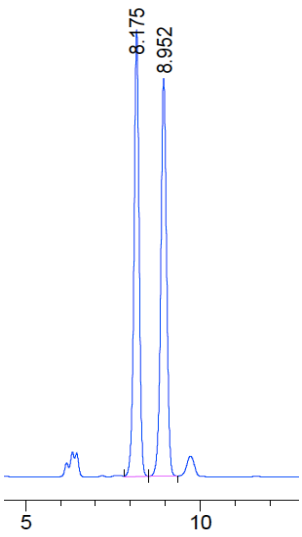


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.617	BB	0.4215	1.22278e4	446.47739	96.5313
2	23.789	BB	0.5307	439.38953	12.42018	3.4687

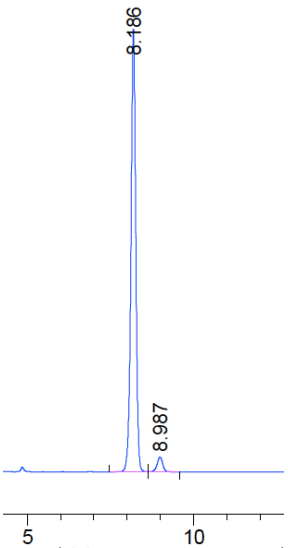
β-Bromo Spiroketone C_6^S



C_6^S

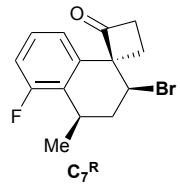


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.175	VB	0.1595	6573.97510	641.73877	49.9518
2	8.952	BV	0.1784	6586.67188	571.85956	50.0482

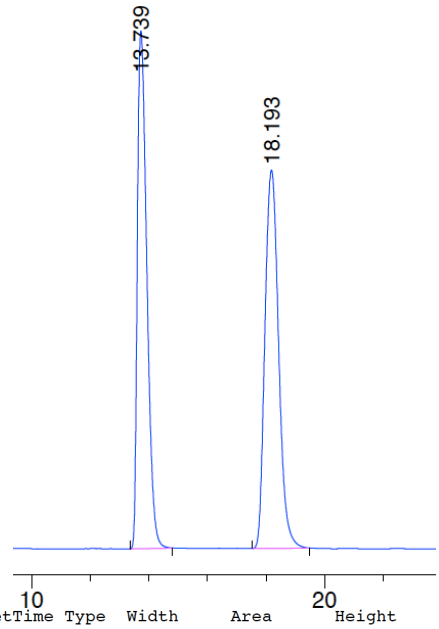


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.186	VV	0.1583	5262.87256	519.10120	96.1481
2	8.987	VB	0.1817	210.84341	17.86059	3.8519

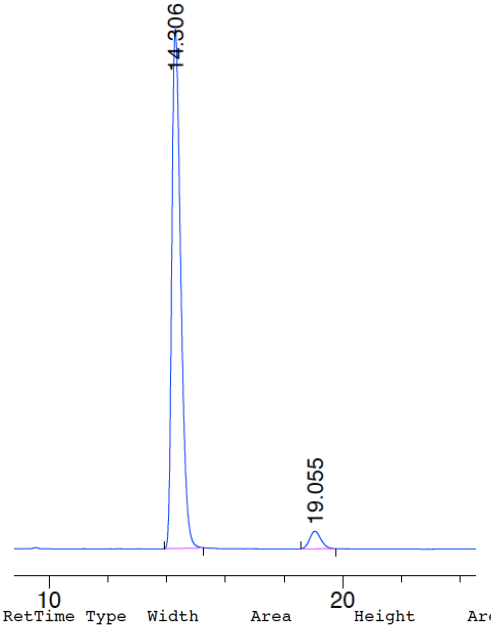
β-Bromo Spiroketone C_7^R



C_7^R

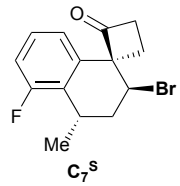


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.739	BB	0.3566	2.08683e4	927.00372	48.7442
2	18.193	BB	0.5199	2.19435e4	677.49371	51.2558

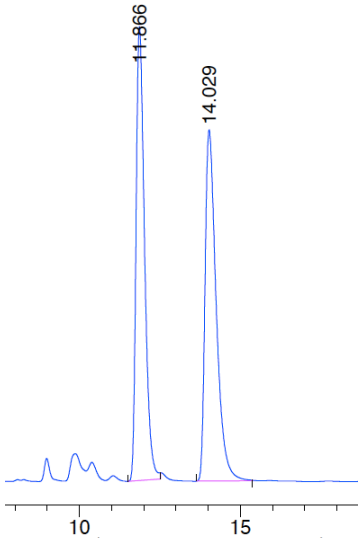


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.306	BB	0.3315	1.34900e4	635.88617	95.8597
2	19.055	BB	0.4200	582.64484	21.64547	4.1403

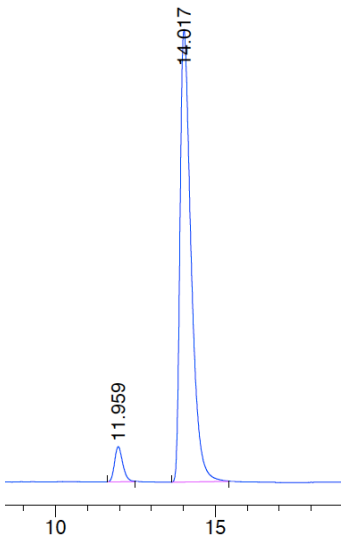
β-Bromo Spiroketone C_7^S



C_7^S

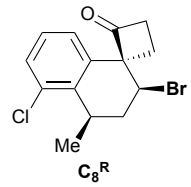


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.866	VB	0.2836	1.12928e4	616.69049	49.6135
2	14.029	BB	0.3662	1.14688e4	477.49319	50.3865

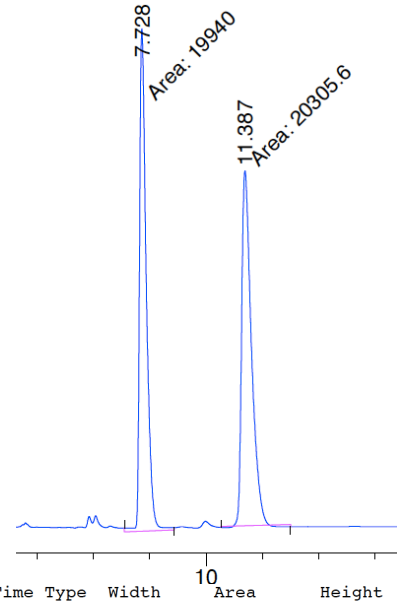


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.959	BB	0.2703	862.68878	48.32224	5.4437
2	14.017	BB	0.3668	1.49848e4	622.60999	94.5563

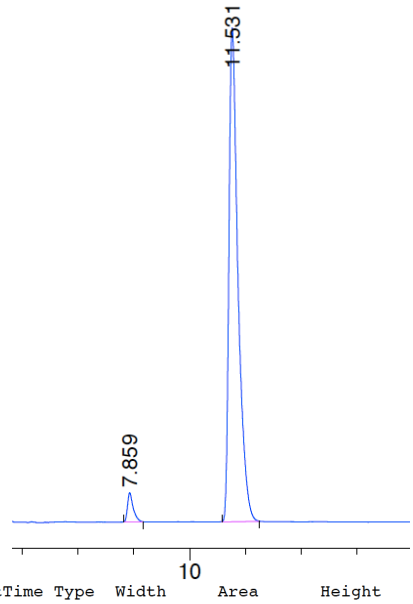
β-Bromo Spiroketone C_8^R



C_8^R

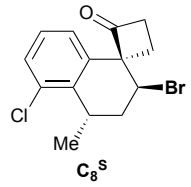


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.728	MM	0.2783	1.99400e4	1194.31445	49.5458
2	11.387	MM	0.4011	2.03056e4	843.70038	50.4542

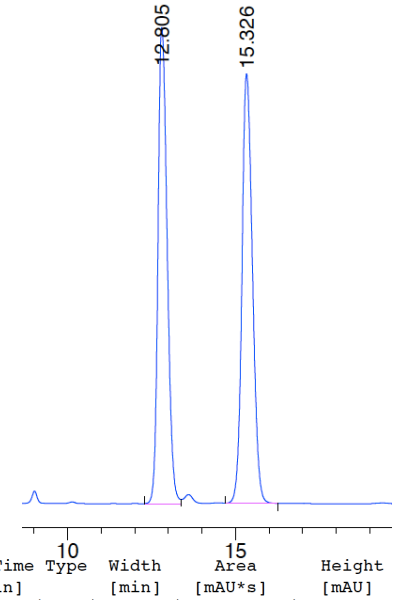


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.859	BB	0.2100	360.50809	25.33295	3.6171
2	11.531	BB	0.3347	9606.16211	426.58621	96.3829

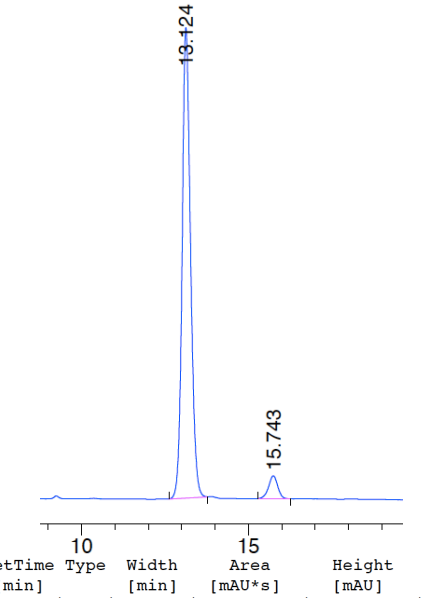
β-Bromo Spiroketone C_8^S



C_8^S

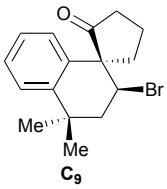


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.805	BV	0.2980	2.51964e4	1324.22937	49.2339
2	15.326	VB	0.3375	2.59805e4	1195.58179	50.7661

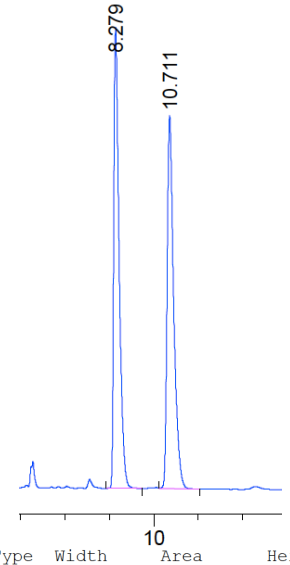


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.124	BB	0.2658	9736.18262	557.35156	94.8441
2	15.743	BB	0.2982	529.27704	27.30240	5.1559

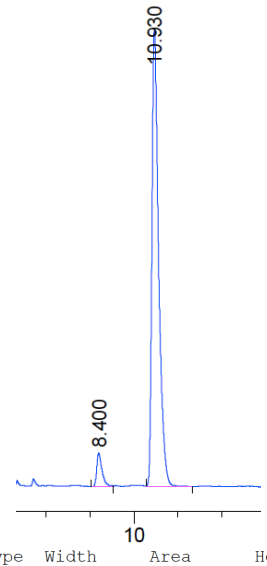
β-Bromo Spiroketone C_9



C_9

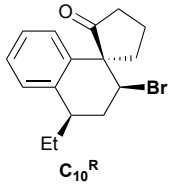


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.279	VB	0.2527	4796.59668	284.56424	50.3438
2	10.711	VB	0.3070	4731.08301	230.90935	49.6562

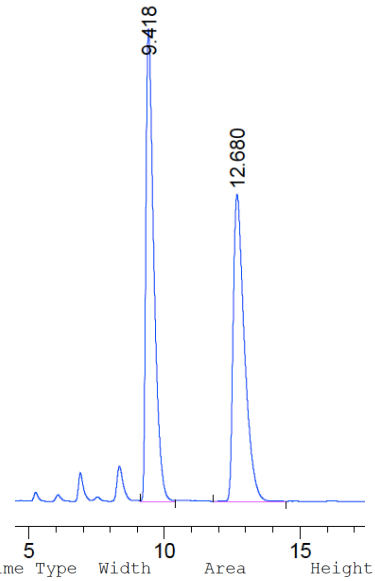


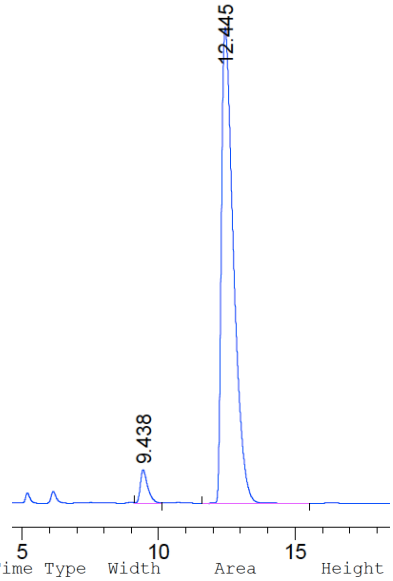
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.400	BV	0.2478	253.25462	15.08726	5.5022
2	10.930	VB	0.3134	4349.50732	206.78595	94.4978

β-Bromo Spiroketone C_{10}^{R}



C_{10}^{R}

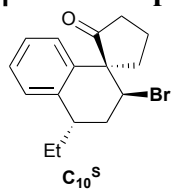




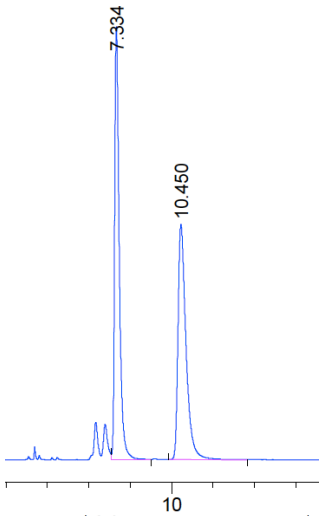
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.418	VV	0.3076	9389.01758	457.23148	52.1786
2	12.680	BV	0.4378	8604.97559	297.21582	47.8214

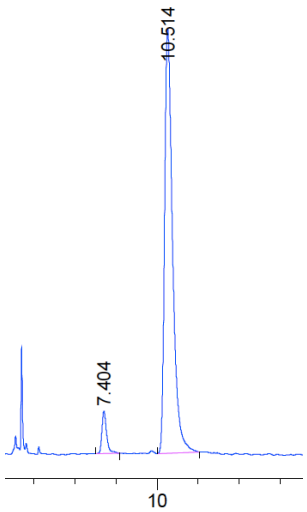
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.438	VV	0.2841	801.30457	42.47490	4.1327
2	12.445	BB	0.4670	1.85883e4	603.99847	95.8673

β-Bromo Spiroketone C_{10}^{S}



C_{10}^{S}

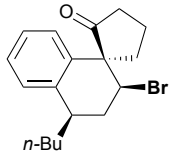




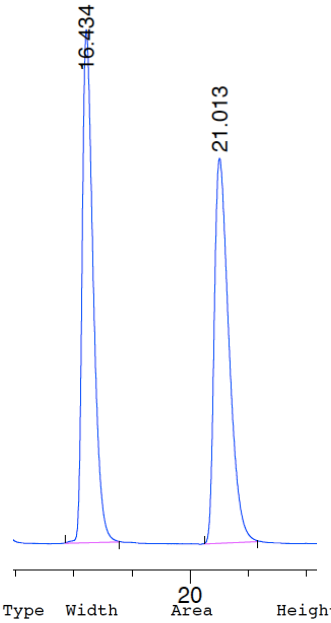
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.334	VB	0.2318	5531.32324	358.96432	51.1691
2	10.450	BV	0.4027	5278.57568	195.68085	48.8309

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.404	BB	0.2420	305.64920	19.07179	5.6303
2	10.514	BB	0.4075	5122.98633	189.44563	94.3697

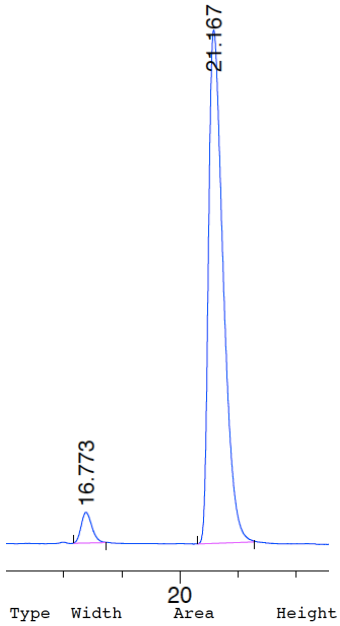
β-Bromo Spiroketone C_{11}^{R}



C_{11}^{R}

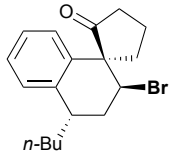


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.434	BB	0.4050	7589.78223	288.47427	49.9973
2	21.013	BB	0.5412	7590.60156	216.43394	50.0027

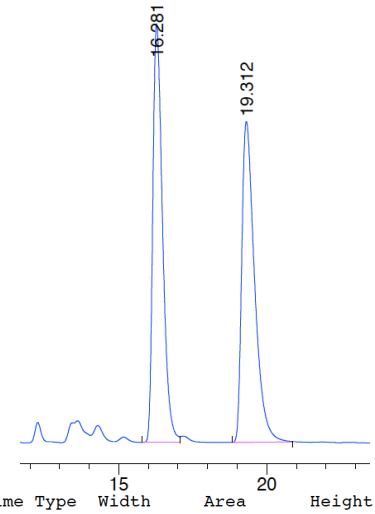


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.773	BB	0.3733	370.76306	14.45383	4.1901
2	21.167	BB	0.5284	8477.78906	241.00252	95.8099

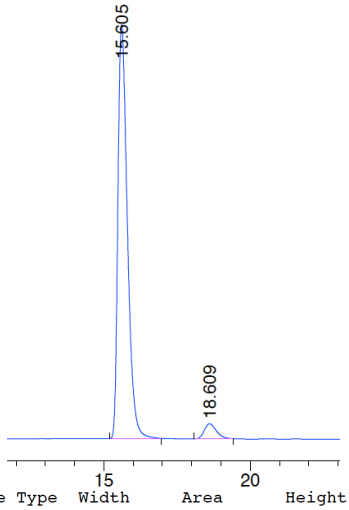
β-Bromo Spiroketone C_{11}^{S}



C_{11}^{S}

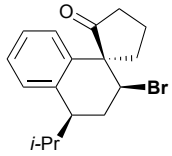


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.281	VV	0.3525	1.57470e4	689.35126	49.7025
2	19.312	BB	0.4557	1.59355e4	528.54242	50.2975

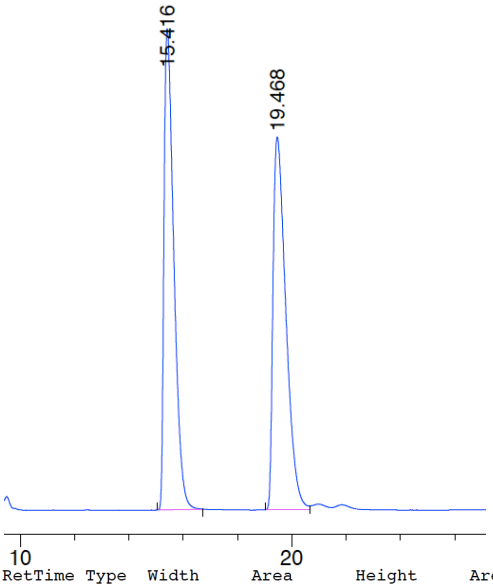


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.605	BB	0.3463	1.78716e4	794.81152	95.4301
2	18.609	BB	0.4468	855.82227	29.29772	4.5699

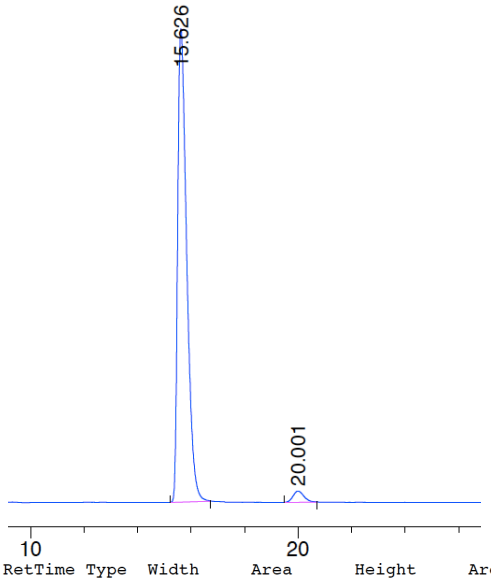
β-Bromo Spiroketone C_{12}^{R}



C_{12}^{R}

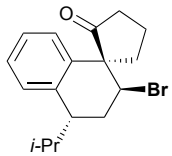


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.416	BB	0.3877	2.06065e4	818.53601	49.6198
2	19.468	BB	0.5028	2.09224e4	634.33051	50.3802

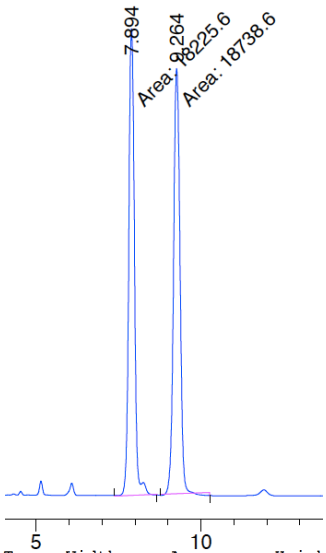


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.626	BB	0.3591	1.17143e4	500.51410	97.2072
2	20.001	BB	0.4152	336.55707	11.85508	2.7928

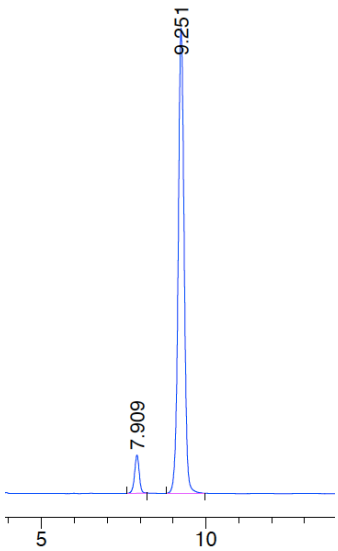
β-Bromo Spiroketone C_{12}^{S}



C_{12}^{S}

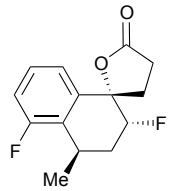


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.894	MM	0.1992	1.82256e4	1524.80249	49.3060
2	9.264	MM	0.2248	1.87386e4	1389.29285	50.6940

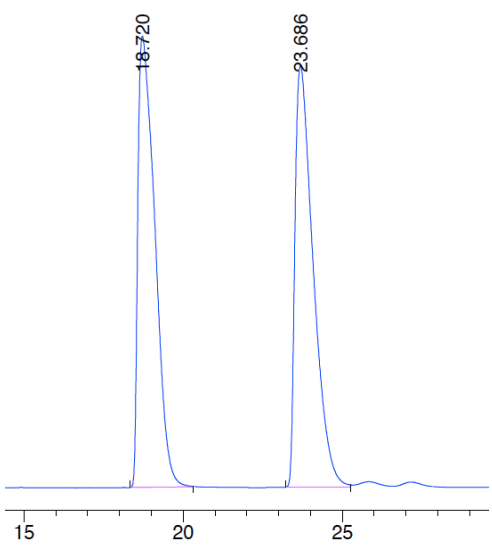


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.909	BB	0.1490	845.46582	85.79994	6.0693
2	9.251	BB	0.1924	1.30848e4	1042.98059	93.9307

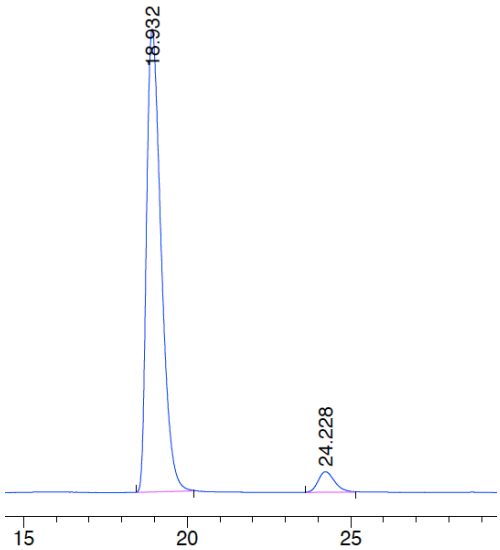
Spiro γ-Lactone (D_8^R)



D_8^R

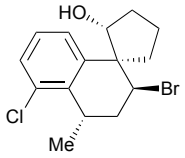


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.720	BB	0.6128	2.14635e4	578.60938	49.8481
2	23.686	BB	0.5859	2.15943e4	540.79346	50.1519

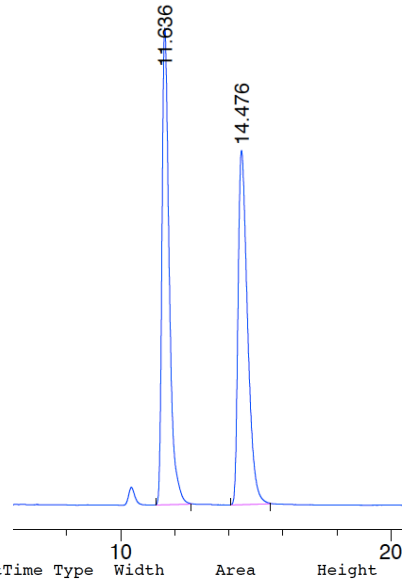


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.932	BB	0.4809	1.19352e4	385.85699	95.2437
2	24.228	BB	0.4766	596.02618	17.10369	4.7563

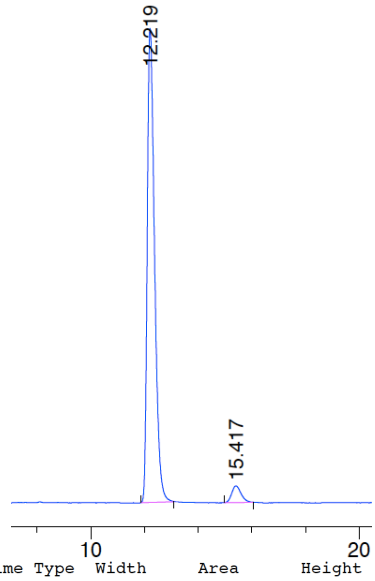
Spirocyclic Bromo-Alcohol (F_4^S)



F_4^S

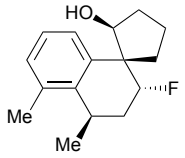


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.636	BB	0.2851	6585.98730	350.65170	50.9540
2	14.476	BB	0.3720	6339.37012	260.46445	49.0460

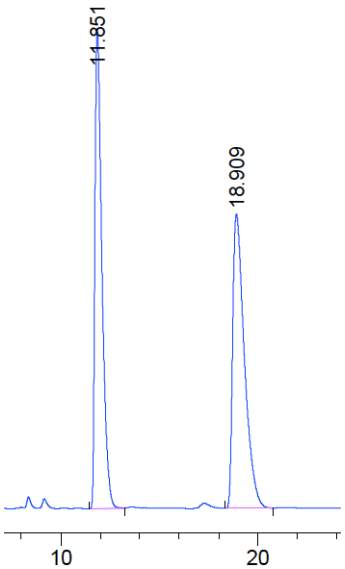


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.219	BB	0.2927	7150.37061	377.90396	95.6153
2	15.417	BB	0.3733	327.90054	13.31764	4.3847

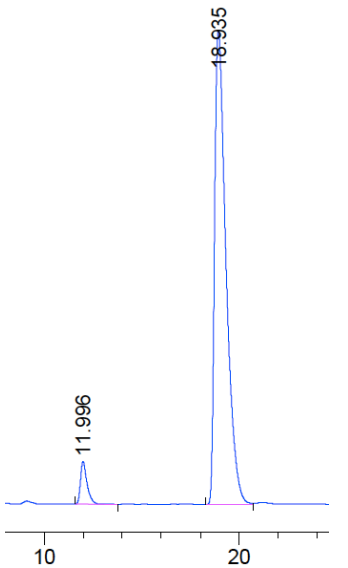
Spirocyclic Fluoro-Alcohol (E_2^R)



E_2^R

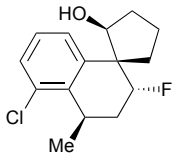


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.851	BV	0.3720	1.45466e4	589.31293	49.3663
2	18.909	BV	0.6225	1.49200e4	360.73105	50.6337

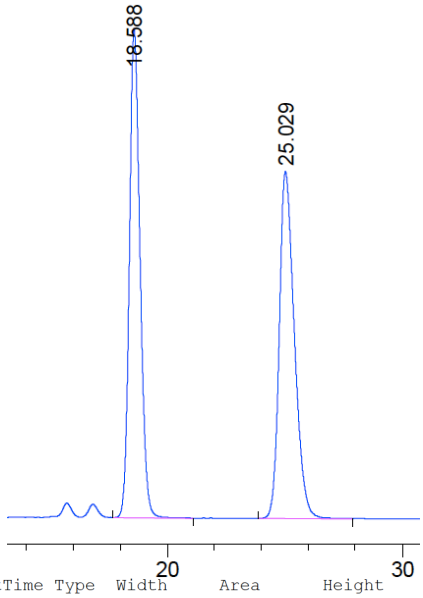


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.996	VB	0.3503	632.19293	26.88546	4.9737
2	18.935	BV	0.6109	1.20786e4	296.70810	95.0263

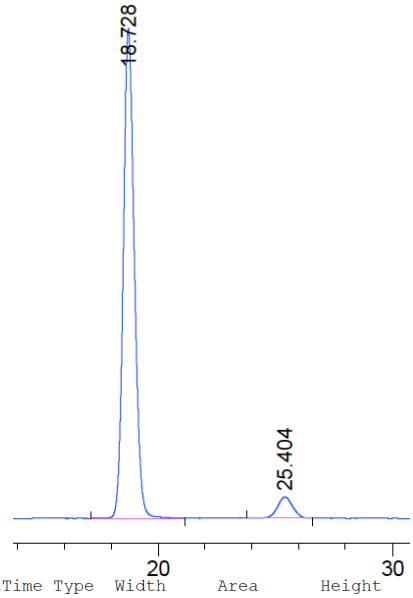
Spirocyclic Fluoro-Alcohol (E_5^R)



E_5^R



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.588	BB	0.4867	1.62045e4	515.52667	49.8245
2	25.029	VV	0.6806	1.63187e4	365.68851	50.1755



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.728	BV	0.5017	7788.62744	238.04538	94.2686
2	25.404	BB	0.7175	473.53558	10.35631	5.7314