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
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General Methods

1H, 13C, 19F and 31P 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 CDCl3, CD2Cl2 or C6D6. Chemical shifts (δ) are reported in ppm downfield from Me2Si 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 CaH2 and stored over activated 4 Å molecular sieves. 1,2-Dichloroethane, 1-chlorobenzene and chloroform were distilled over P2O5 and stored over activated 4 Å molecular sieves. MeOH and EtOH were distilled over CaH2 under argon, and stored over activated 4 Å molecular sieves. N,N-
Diusopropylethylamine and 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$_2$O$_5$ 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$_2$O, CH$_2$Cl$_2$ and CH$_3$CN were dried by passage through a column of activated alumina, under nitrogen atmosphere. KHMDS and KOr-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$_3$N (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$_2$O, CH$_2$Cl$_2$ and CH$_3$CN were dried by passage through a column of activated alumina, under nitrogen atmosphere. Selectfluor$^\text{TM}$, Na$_2$CO$_3$, and Na$_3$PO$_4$ 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 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 D$_x$ were obtained by carrying out the iodo-semipinacol rearrangement with iodonium salts S$_0$ or 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 S$_0^2$ and S$_{1,4}^3$ were prepared according to literature methods. Iodinating reagents S$_{1,9}$ 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.


**Preparation of Substrates**

**General Procedure for the Synthesis of Substrates: HWE Reaction**

\[
\begin{align*}
\text{O} & \quad \text{PO} & \quad \text{OEt} \\
\text{OEt} & \quad \text{PO} & \quad \text{OEt}
\end{align*}
\]

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 NH₄Cl and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was used in the next step as such, without further purification.

\( \text{(E)-ethyl 3-((o-tolyl)but-2-enoate} \)

\[
\begin{align*}
\text{Chemical Formula: } & \text{C}_{13}\text{H}_{16}\text{O}_{2} \\
\text{Molecular Weight: } & 204.26
\end{align*}
\]

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 NH₄Cl and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. Rf (silica gel, n-Hex/Et₂O 9:1) 0.57. Pale-yellow oil.

\( \text{(E)-ethyl 3-((2-methoxyphenyl)but-2-enoate} \)

\[
\begin{align*}
\text{Chemical Formula: } & \text{C}_{13}\text{H}_{16}\text{O}_{3} \\
\text{Molecular Weight: } & 220.26
\end{align*}
\]

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 NH₄Cl and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. Rf (silica gel, n-Hex/Et₂O 4:1) 0.39. Colorless oil.

\( \text{(E)-ethyl 3-((2-fluorophenyl)but-2-enoate} \)

\[
\begin{align*}
\text{Chemical Formula: } & \text{C}_{12}\text{H}_{13}\text{FO}_{2} \\
\text{Molecular Weight: } & 208.23
\end{align*}
\]

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
NH₄Cl and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. Rₚ (silica gel, n-Hex/Et₂O 9:1) 0.62. Colorless oil.

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

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 NH₄Cl and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. Rₚ (silica gel, n-Hex/Et₂O 4:1) 0.49. Pale yellow oil.

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

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 NH₄Cl and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. Rₚ (silica gel, n-Hex/Et₂O 4:1) 0.55. Faint yellow oil.

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

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 NH₄Cl and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. Rₚ (silica gel, n-Hex/Et₂O 4:1) 0.49. Pale-yellow oil.

1H NMR (400 MHz, CDCl₃): δ 7.45-7.49 (2H, m, CarH), 7.32-7.40 (3H, m, CarH), 6.13 (1H, q, J 1.3, olefinic C=C), 4.22 (2H, q, J 7.1, ethoxy CH₂-O), 2.58 (3H, d, J 1.3, allylic CH₃), 1.32 (3H, t, J 7.1, ethoxy CH₃) ppm.
residue was used as such, without further purification. \( R_f \) (silica gel, \( n\)-Hex/Et\(_2\)O 4:1) 0.55. Colorless oil. \( ^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 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=CH\(_2\)), 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**

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 valeronaphthon (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\(_4\)Cl and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na\(_2\)SO\(_4\), filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. \( R_f \) (silica gel, \( n\)-Hex/Et\(_2\)O 4:1) 0.66. Colorless oil.

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

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 isobutyronaphthon (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\(_4\)Cl and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na\(_2\)SO\(_4\), filtered and concentrated under reduced pressure. The crude residue was used as such, without further purification. \( R_f \) (silica gel, \( n\)-Hex/Et\(_2\)O 4:1) 0.64. Colorless oil.

**General Procedure for the Synthesis of Substrates: Hydrogenation Reaction**

\[
\text{R}^\text{Me}\text{CO}_2\text{Et} \xrightarrow{\text{H}_2 (3 \text{ bar})} \text{R} \text{Me} \text{CO}_2\text{Et}
\]

\( R = \text{Me, OMe, F, Cl} \)

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**

![Chemical Structure of Ethyl 3-(o-tolyl)butanoate](image)

**Chemical Formula:** C$_{13}$H$_{18}$O$_2$

**Molecular Weight:** 206.28

A solution composed of ethyl 3-(o-tolyl)but-2-enolate (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$_2$O 9:1). R$_f$ (silica gel, n-Hex/Et$_2$O 9:1) 0.48. Colorless oil. Isolated yield 88% (4.15 g, 20.1 mmol). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.06-7.18 (4H, m, C$_6^\equiv$H), 4.08 (2H, q, J 7.1, ethoxy CH$_2$-O), 3.54 (1H, sext., J 6.9, benzylic CH), 2.62 (1H, dd, J 15.2, J 6.6, ABX spin-system, diastereotopic CH$_2$), 2.53 (1H, dd, J 15.2, J 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**

![Chemical Structure of Ethyl 3-(2-methoxyphenyl)butanoate](image)

**Chemical Formula:** C$_{13}$H$_{18}$O$_3$

**Molecular Weight:** 222.28

A solution composed of ethyl 3-(2-methoxyphenyl)but-2-enolate (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$_2$O 4:1). R$_f$ (silica gel, n-Hex/Et$_2$O 4:1) 0.43. Colorless oil. Isolated yield 99% (5.07 g, 22.8 mmol). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.06-7.18 (4H, m, C$_6^\equiv$H), 4.08 (2H, q, J 7.1, ethoxy CH$_2$-O), 3.54 (1H, sext., J 6.9, benzylic CH), 2.62 (1H, dd, J 15.2, J 6.6, ABX spin-system, diastereotopic CH$_2$), 2.53 (1H, dd, J 15.2, J 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**

![Chemical Structure of Ethyl 3-(2-fluorophenyl)butanoate](image)

**Chemical Formula:** C$_{12}$H$_{15}$FO$_2$

**Molecular Weight:** 210.24

A solution composed of ethyl 3-(2-fluorophenyl)but-2-enolate (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$_2$O 9:1). R$_f$ (silica gel, n-Hex/Et$_2$O 9:1) 0.55. Pale-yellow oil. Isolated yield 99% (4.79 g, 22.8 mmol). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.06-7.18 (4H, m, C$_6^\equiv$H), 4.08 (2H, q, J 7.1, ethoxy CH$_2$-O), 3.54 (1H, sext., J 6.9, benzylic CH), 2.62 (1H, dd, J 15.2, J 6.6, ABX spin-system, diastereotopic CH$_2$), 2.53 (1H, dd, J 15.2, J 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.
ABX spin-system, diastereotopic CH₂, 2.38 (3H, s, CH₃), 1.26 (3H, d, J 6.9, CH₃), 1.17 (3H, t, J 7.1, ethoxy CH₃) ppm.

**Ethyl 3-(2-chlorophenyl)butanoate**

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 H₂ 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/Et₂O 9:1). Rₛ (silica gel, n-Hex/Et₂O 9:1) 0.38. Pale-yellow oil. Isolated yield 99% (5.17 g, 22.8 mmol). **¹H NMR (400 MHz, CDCl₃): δ 7.06-7.18 (4H, m, CCH₂), 4.08 (2H, q, J 7.1, ethoxy CH₂-O), 3.54 (1H, sext., J 6.9, benzylic CH), 2.62 (1H, dd, J₁ 15.2, J₂ 6.6, ABX spin-system, diastereotopic CH₂), 2.53 (1H, dd, J₁ 15.2, J₂ 8.5, ABX spin-system, diastereotopic CH₂), 2.38 (3H, s, CH₃), 1.26 (3H, d, J 6.9, CH₃), 1.17 (3H, t, J 7.1, ethoxy CH₃) ppm.

**Ethyl 3-phenylpentanoate**

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 H₂ 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/Et₂O 9:1). Rₛ (silica gel, n-Hex/Et₂O 9:1) 0.58. Pale-yellow oil. Isolated yield 99% (4.79 g, 22.8 mmol). **¹H NMR (400 MHz, CDCl₃): δ 7.06-7.18 (4H, m, CCH₂), 4.08 (2H, q, J 7.1, ethoxy CH₂-O), 3.54 (1H, sext., J 6.9, benzylic CH), 2.62 (1H, dd, J₁ 15.2, J₂ 6.6, ABX spin-system, diastereotopic CH₂), 2.53 (1H, dd, J₁ 15.2, J₂ 8.5, ABX spin-system, diastereotopic CH₂), 2.38 (3H, s, CH₃), 1.26 (3H, d, J 6.9, CH₃), 1.17 (3H, t, J 7.1, ethoxy CH₃) ppm.

**Ethyl 3-phenylheptanoate**

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 H₂ 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/Et₂O 9:1). Rₛ (silica gel, n-Hex/Et₂O 9:1) 0.60. Pale-yellow oil. Isolated yield 99% (4.79 g, 22.8 mmol). **¹H NMR (400 MHz, CDCl₃): δ 7.06-7.18 (4H, m, CCH₂), 4.08 (2H, q, J 7.1, ethoxy CH₂-O), 3.54 (1H, sext., J 6.9, benzylic CH), 2.62 (1H, dd, J₁ 15.2, J₂ 6.6, ABX spin-system, diastereotopic CH₂), 2.53 (1H, dd, J₁ 15.2, J₂ 8.5, ABX spin-system, diastereotopic CH₂), 2.38 (3H, s, CH₃), 1.26 (3H, d, J 6.9, CH₃), 1.17 (3H, t, J 7.1, ethoxy CH₃) ppm.
Ethyl 4-methyl-3-phenylpentanoate

![Chemical Structure](image)

**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/mmoll) 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 redissolved 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$_2$O 9:1). $R_f$ (silica gel, n-Hex/Et$_2$O 9:1) 0.59. Pale-yellow oil. Isolated yield 99% (4.79 g, 22.8 mmol). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 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 CH), 2.62 (1H, dd, J1 15.2, J2 6.6, ABX spin-system, diastereotopic CH$_2$), 2.53 (1H, dd, J1 15.2, J2 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-methyl-3-phenylbutanoate

![Chemical Structure](image)

**Chemical Formula:** $C_{13}H_{18}O_2$

**Molecular Weight:** 206.28

Preparation of the cuprate: To a cooled (0 °C, ice/water bath) solution of CuI (2.0 g, 10.5 mmol, 2.0 equiv.) in anhydrous Et$_2$O (10 mL) was added MeLi (1.6 M solution in Et$_2$O, 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$_2$Cl$_2$ (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$_2$Cl$_2$ (60 mL).

Conjugate addition reaction: To a cooled (0 °C, ice/water bath) solution of the above-prepared Me$_2$CuLi solution (10.5 mmol, 2.0 equiv.) was added Me$_2$SiCl (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$_2$Cl$_2$ (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$_4$Cl and 23% (w/w) aqueous NH$_4$OH 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$_2$SO$_4$, filtered and concentrated in vacuo. The crude residue was used in the next step as such, without further purification. $R_f$ (silica gel, n-Hex/Et$_2$O 4:1) 0.57. Colorless liquid. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.37 (2H, dd, J1 8.6, J2 1.4, C"ar'H), 7.31 (2H, t, J 7.4, C"ar'H), 7.19 (1H, td, J1 7.2, J2 1.3, C"ar'H), 3.98 (2H, q, J 7.1, ethoxy CH$_2$-O), 2.61 (2H, s, $\alpha$-carbonyl CH$_2$), 1.46 (6H, s, gem-dimethyl CH$_3$), 1.09 (3H, t, J 7.1, ethoxy CH$_3$) ppm.

General Procedure for the Synthesis of Substrates: LiAlH$_4$ Reduction
To a cooled (-40 °C, dry ice/acetonitrile bath) slurry of LiAlH₄ (2.0 equiv.) in anhydrous Et₂O (0.20 M) was added the required ester (1.0 equiv.) dropwise as a solution in anhydrous Et₂O (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 Na₂SO₄, 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

To a cooled (-40 °C, dry ice/acetonitrile bath) slurry of LiAlH₄ (1.53 g, 40.2 mmol, 2.0 equiv.) in anhydrous Et₂O (200 mL) was added ethyl 3-(o-tolyl)butanoate (4.15 g, 20.1 mmol, 1.0 equiv.) dropwise as a solution in anhydrous Et₂O (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 Na₂SO₄, 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). R_f (silica gel, n-Hex/Et₂O 4:1) 0.15. Colorless oil.

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

To a cooled (-40 °C, dry ice/acetonitrile bath) slurry of LiAlH₄ (1.73 g, 45.6 mmol, 2.0 equiv.) in anhydrous Et₂O (200 mL) was added ethyl 3-(2-methoxyphenyl)butanoate (4.79 g, 22.8 mmol, 1.0 equiv.) dropwise as a solution in anhydrous Et₂O (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 Na₂SO₄, 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). R_f (silica gel, n-Hex/Et₂O 4:1) 0.07. Colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 7.14-7.19 (2H, m, C"H), 6.92 (1H, td, J₁, 7.4, J₂ 1.0, C"H), 6.85 (1H, d, J 8.6, C"H), 3.94-4.05 (2H, m, diastereotopic CH₂-O), 3.81 (3H, s, CH₃-O), 3.30 (1H, sext., J 7.1, benzylic CH), 2.00 (1H, brs, hydroxylic OH), 1.82-1.99 (2H, m, CH₂), 1.24 (3H, d, J 7.0, CH₃) ppm.
3-(2-fluorophenyl)butan-1-ol

To a cooled (-40 °C, dry ice/acetonitrile bath) slurry of LiAlH₄ (1.73 g, 45.6 mmol, 2.0 equiv.) in anhydrous Et₂O (200 mL) was added ethyl 3-(2-fluorophenyl)butanoate (4.79 g, 22.8 mmol, 1.0 equiv.) dropwise as a solution in anhydrous Et₂O (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 Na₂SO₄, 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). RF (silica gel, n-Hex/Et₂O 4:1) 0.17. Colorless oil.

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

To a cooled (-40 °C, dry ice/acetonitrile bath) slurry of LiAlH₄ (1.73 g, 45.6 mmol, 2.0 equiv.) in anhydrous Et₂O (200 mL) was added ethyl 3-(2-chlorophenyl)butanoate (5.17 g, 22.8 mmol, 1.0 equiv.) dropwise as a solution in anhydrous Et₂O (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 Na₂SO₄, 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). RF (silica gel, n-Hex/Et₂O 4:1) 0.10. Colorless oil.

3-phenylpentan-1-ol

To a cooled (-40 °C, dry ice/acetonitrile bath) slurry of LiAlH₄ (1.73 g, 45.6 mmol, 2.0 equiv.) in anhydrous Et₂O (200 mL) was added ethyl 3-phenylpentanoate (4.70 g, 22.8 mmol, 1.0 equiv.) dropwise as a solution in anhydrous Et₂O (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 Na₂SO₄, 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). RF (silica gel, n-Hex/Et₂O 4:1) 0.11. Colorless liquid.

3-phenylheptan-1-ol

To a cooled (-40 °C, dry ice/acetonitrile bath) slurry of LiAlH₄ (1.73 g, 45.6 mmol, 2.0 equiv.) in anhydrous Et₂O (200 mL) was added ethyl 3-phenylheptanoate (5.34 g, 22.8 mmol, 1.0 equiv.) dropwise as a solution in anhydrous Et₂O (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 Na₂SO₄, 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). RF (silica gel, n-Hex/Et₂O 4:1) 0.11. Colorless liquid.
layers were dried over anhydrous Na₂SO₄, 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). \( R_f \) (silica gel, n-Hex/Et₂O 4:1) 0.22. Colorless liquid.

**4-methyl-3-phenylpentan-1-ol**

To a cooled (-40 °C, dry ice/acetonitrile bath) slurry of LiAlH₄ (1.73 g, 45.6 mmol, 2.0 equiv.) in anhydrous Et₂O (200 mL) was added ethyl 4-methyl-3-phenylpentanoate (5.02 g, 22.8 mmol, 1.0 equiv.) dropwise as a solution in anhydrous Et₂O (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 Na₂SO₄, 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). \( R_f \) (silica gel, n-Hex/Et₂O 4:1) 0.19. Colorless liquid.

**3-methyl-3-phenylbutan-1-ol**

To a cooled (-40 °C, dry ice/acetonitrile bath) slurry of LiAlH₄ (440 mg, 10.5 mmol, 2.0 equiv.) in anhydrous Et₂O (30 mL) was added ethyl 3-methyl-3-phenylbutanoate (1.09 g, 5.25 mmol, 1.0 equiv.) dropwise as a solution in anhydrous Et₂O (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 Na₂SO₄, 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). \( R_f \) (silica gel, n-Hex/Et₂O 4:1) 0.14. Colorless liquid.

**General Procedure for the Synthesis of Substrates: Tosylation Reaction**

\[
\begin{align*}
&\text{R} = \text{Me, OMe, F, Cl} \\
&\text{p-TsCl}\quad \text{pyridine} \quad \text{CH}_2\text{Cl}_2 \\
&\text{Me} \quad \text{OH} \quad \text{OTs} \quad \text{R} \\
\end{align*}
\]

To a well-stirred solution of the required homobenzylic alcohol (1.0 equiv.) and anhydrous pyridine (2.5 equiv.) in anhydrous CH₂Cl₂ (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/Et₂O mixture as eluent.
3-[(o-tolyl)butyl 4-methylbenzenesulfonate

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 CH2Cl2 (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/Et2O 95:5 → n-hexane/Et2O 9:1). Rf (silica gel, n-Hex/Et2O 4:1) 0.39. Colorless oil. Isolated yield 87% (5.59 g, 17.5 mmol).

3-(2-methoxyphenyl)butyl 4-methylbenzenesulfonate

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 CH2Cl2 (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/Et2O 95:5 → n-hexane/Et2O 9:1). Rf (silica gel, n-Hex/Et2O 4:1) 0.30. Colorless oil. Isolated yield 49% (3.74 g, 11.2 mmol). 1H NMR (400 MHz, CDCl3): δ 7.73 (2H, d, J 8.3, C′H), 7.30 (2H, d, J 8.3, C′H), 7.16 (1H, td, J 7.4, J 1.7, C′H), 7.04 (1H, dd, J 7.6, J 1.7, C′H), 6.86 (1H, dd, J 7.4, J 1.0, C′H), 6.83 (1H, t, J 8.2, C′H), 3.91-4.00 (2H, m, dia stereotopic CH2-O), 3.78 (3H, s, CH3-O), 3.23 (1H, sext., J 7.0, benzylic CH), 2.44 (3H, s, aryl CH3), 1.85-2.03 (2H, m, CH2), 1.17 (3H, d, J 7.0, CH3) ppm.

3-(2-fluorophenyl)butyl 4-methylbenzenesulfonate

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 CH2Cl2 (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/Et2O 95:5 → n-hexane/Et2O 9:1). Rf (silica gel, n-Hex/Et2O 4:1) 0.43. Pale-yellow oil. Isolated yield 61% (4.45 g, 13.8 mmol).

3-(2-chlorophenyl)butyl 4-methylbenzenesulfonate

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 CH2Cl2 (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$_2$O 95:5 → $n$-hexane/Et$_2$O 9:1). $R_f$ (silica gel, $n$-Hex/Et$_2$O 4:1) 0.43. Pale-yellow oil. Isolated yield 64% (4.92 g, 14.5 mmol).

### 1H NMR (400 MHz, CDCl$_3$):

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<th>J (Hz)</th>
<th>Multiplicity</th>
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<td>7.0</td>
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3-phenylpentyl 4-methylbenzenesulfonate

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$_2$Cl$_2$ (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$_2$O 95:5 → $n$-hexane/Et$_2$O 9:1). $R_f$ (silica gel, $n$-Hex/Et$_2$O 4:1) 0.39. Colorless oil. Isolated yield 70% (5.08 g, 16.0 mmol).

3-phenylheptyl 4-methylbenzenesulfonate

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$_2$Cl$_2$ (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$_2$O 95:5 → $n$-hexane/Et$_2$O 9:1). $R_f$ (silica gel, $n$-Hex/Et$_2$O 4:1) 0.39. Colorless oil. Isolated yield 68% (5.37 g, 15.5 mmol).

4-methyl-3-phenylpentyl 4-methylbenzenesulfonate

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$_2$Cl$_2$ (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$_2$O 95:5 → $n$-hexane/Et$_2$O 9:1). $R_f$ (silica gel, $n$-Hex/Et$_2$O 4:1) 0.39. Colorless oil. Isolated yield 75% (5.69 g, 17.1 mmol).
3-methyl-3-phenylbutyl 4-methylbenzenesulfonate

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 CH₂Cl₂ (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/Et₂O 95:5 → n-hexane/Et₂O 9:1). Rᵣ (silica gel, n-Hex/Et₂O 4:1) 0.43. Colorless oil. Isolated yield 21% (330 mg, 1.1 mmol).

1H NMR (400 MHz, CDCl₃): δ 7.68 (2H, d, J 8.3, C₅H₃), 7.19-7.30 (6H, m, C₅H₃), 7.17 (1H, td, J₁ 7.0, J₂ 1.7, C₅H₃), 3.85 (2H, t, J 7.4, CH₂), 2.44 (3H, s, p-toluenesulfonyl CH₃), 2.02 (2H, t, J 7.4, CH₂), 1.29 (6H, s, gem-dimethyl CH₃) ppm.

General Procedure for the Synthesis of Substrates: Cyanide S₂N₂ Substitution

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 Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was used in the next step as such, without further purification.

4-(o-tolyl)pentanenitrile

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 Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane/Et₂O 95:5). Rᵣ (silica gel, n-Hex/Et₂O 9:1) 0.47. Colorless oil. Isolated yield 99% (3.03 g, 17.5 mmol).

4-(2-methoxyphenyl)pentanenitrile

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$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel ($n$-hexane/Et$_2$O 95:5). $R_f$ (silica gel, $n$-Hex/Et$_2$O 4:1) 0.29. Colorless oil. Isolated yield 99% (2.12 g, 11.2 mmol).

**4-(2-fluorophenyl)pentanenitrile**

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$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel ($n$-hexane/Et$_2$O 95:5). $R_f$ (silica gel, $n$-Hex/Et$_2$O 9:1) 0.51. Colorless oil. Isolated yield 99% (2.45 g, 13.8 mmol).

**4-(2-chlorophenyl)pentanenitrile**

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$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel ($n$-hexane/Et$_2$O 95:5). $R_f$ (silica gel, $n$-Hex/Et$_2$O 9:1) 0.51. Colorless oil. Isolated yield 99% (2.45 g, 13.8 mmol).

**4-phenylhexanenitrile**

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$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel ($n$-hexane/Et$_2$O 95:5). $R_f$ (silica gel, $n$-Hex/Et$_2$O 9:1) 0.48. Pale-yellow oil. Isolated yield 99% (2.77 g, 16.0 mmol).
4-phenyloctanenitrile

A solution composed of 3-phenylethyl 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$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel ($n$-hexane/Et$_2$O 95:5). $R_f$ (silica gel, $n$-Hex/Et$_2$O 9:1) 0.48. Pale-yellow oil. Isolated yield 99% (2.77 g, 16.0 mmol).

5-methyl-4-phenylhexanenitrile

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$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel ($n$-hexane/Et$_2$O 95:5). $R_f$ (silica gel, $n$-Hex/Et$_2$O 9:1) 0.48. Pale-yellow oil. Isolated yield 99% (2.77 g, 16.0 mmol).

4-(2-bromophenyl)butanenitrile

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$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel ($n$-hexane/Et$_2$O 95:5). $R_f$ (silica gel, $n$-Hex/Et$_2$O 9:1) 0.54. Pale-yellow oil. Isolated yield 99% (1.10 g, 4.90 mmol).

4-methyl-4-phenylpentanenitrile

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$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel ($n$-hexane/Et$_2$O 95:5). $R_f$ (silica gel, $n$-Hex/Et$_2$O 9:1) 0.48. Pale-yellow oil. Isolated yield 99% (2.77 g, 16.0 mmol).
hexane/Et$_2$O 95:5). $R_f$ (silica gel, $n$-Hex/Et$_2$O 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**

\[
\begin{array}{c}
\text{R} \quad \text{CN} \\
\text{Me} \\
\downarrow \quad \text{KOH} \\
\text{EtOH/water} \\
\text{reflux} \\
\text{R} \quad \text{CO}_2\text{H} \\
\text{Me}
\end{array}
\]

\(R = \text{Me, OMe, F, Cl}\)

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$_2$SO$_4$, 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**

\[
\text{Me} \\
\text{CO}_2\text{H} \\
\text{4-(o-tolyl)pentanoic acid} \\
\text{Chemical Formula: C}_{12}\text{H}_{16}\text{O}_2} \\
\text{Molecular Weight: 192.25}
\]

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$_2$SO$_4$, 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$_3$): $\delta$ 8.02 (1H, brs, carboxylic CO$_2$H), 7.16-7.19 (2H, m, C$_\text{ar}$H), 7.07-7.14 (2H, m, C$_\text{ar}$H), 3.05 (1H, sext., $J$ 7.0, benzylic C$_\text{H}$), 2.31 (3H, s, C$_\text{H}_3$), 2.27 (2H, t, $J$ 7.7, $\alpha$-carbonyl C$_\text{H}_2$), 1.87-2.01 (2H, m, diastereotopic C$_\text{H}_2$), 1.23 (3H, d, $J$ 6.9, C$_\text{H}_3$) ppm.

**4-(2-methoxyphenyl)pentanoic acid**

\[
\text{OMe} \\
\text{CO}_2\text{H} \\
\text{4-(2-methoxyphenyl)pentanoic acid} \\
\text{Chemical Formula: C}_{12}\text{H}_{16}\text{O}_3} \\
\text{Molecular Weight: 208.25}
\]

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$_2$SO$_4$, 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$_3$): $\delta$ 8.02 (1H, brs, carboxylic CO$_2$H), 7.16-7.19 (2H, m, C$_\text{ar}$H), 7.07-7.14 (2H, m, C$_\text{ar}$H), 3.05 (1H, sext., $J$ 7.0, benzylic C$_\text{H}$), 2.31 (3H, s, C$_\text{H}_3$), 2.27 (2H, t, $J$ 7.7, $\alpha$-carbonyl C$_\text{H}_2$), 1.87-2.01 (2H, m, diastereotopic C$_\text{H}_2$), 1.23 (3H, d, $J$ 6.9, C$_\text{H}_3$) ppm.
C\textsuperscript{ar}H), 3.05 (1H, sext., J 7.0, benzylic CH), 2.31 (3H, s, CH\textsubscript{3}), 2.27 (2H, t, J 7.7, \(\alpha\)-carbonyl CH\textsubscript{2}), 1.87-2.01 (2H, m, diastereotopic CH\textsubscript{2}), 1.23 (3H, d, J 6.9, CH\textsubscript{3}) ppm.

4-(2-fluorophenyl)pentanoic acid

\[
\begin{array}{c}
\text{C}_1\text{H}_3\text{F}_2\text{O}_2 \\
\text{Me} \longleftarrow \text{CO}_2\text{H}
\end{array}
\]

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\textsubscript{2}SO\textsubscript{4}, filtered, and concentrated under reduced pressure. Colorless oil. Isolated yield 80% (2.15 g, 11.0 mmol). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \(\delta\) 8.02 (1H, brs, carboxylic CO\textsubscript{H}), 7.16-7.19 (2H, m, C\textsuperscript{ar}H), 7.07-7.14 (2H, m, C\textsuperscript{ar}H), 3.05 (1H, sext., J 7.0, benzylic CH\textsubscript{2}), 2.31 (3H, s, CH\textsubscript{3}), 2.27 (2H, t, J 7.7, \(\alpha\)-carbonyl CH\textsubscript{2}), 1.87-2.01 (2H, m, diastereotopic CH\textsubscript{2}), 1.23 (3H, d, J 6.9, CH\textsubscript{3}) ppm. \textsuperscript{19}F NMR (376 MHz, CDCl\textsubscript{3}): \(\delta\) -118.3 (1F, s, C\textsuperscript{ar}F) ppm.

4-(2-chlorophenyl)pentanoic acid

\[
\begin{array}{c}
\text{C}_1\text{H}_3\text{Cl}_2\text{O}_2 \\
\text{Me} \longleftarrow \text{CO}_2\text{H}
\end{array}
\]

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\textsubscript{2}SO\textsubscript{4}, filtered, and concentrated under reduced pressure. Pale-yellow oil. Isolated yield 80% (2.15 g, 11.0 mmol). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \(\delta\) 8.02 (1H, brs, carboxylic CO\textsubscript{H}), 7.16-7.19 (2H, m, C\textsuperscript{ar}H), 7.07-7.14 (2H, m, C\textsuperscript{ar}H), 3.05 (1H, sext., J 7.0, benzylic CH\textsubscript{2}), 2.31 (3H, s, CH\textsubscript{3}), 2.27 (2H, t, J 7.7, \(\alpha\)-carbonyl CH\textsubscript{2}), 1.87-2.01 (2H, m, diastereotopic CH\textsubscript{2}), 1.23 (3H, d, J 6.9, CH\textsubscript{3}) ppm. \textsuperscript{19}F NMR (376 MHz, CDCl\textsubscript{3}): \(\delta\) -118.3 (1F, s, C\textsuperscript{ar}F) ppm.

4-phenylhexanoic acid

\[
\begin{array}{c}
\text{C}_9\text{H}_8\text{O}_2 \\
\text{Me} \longleftarrow \text{CO}_2\text{H}
\end{array}
\]

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\textsubscript{2}SO\textsubscript{4}, filtered, and concentrated under reduced pressure. Colorless oil. Isolated yield 90% (2.77 g, 14.4 mmol). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \(\delta\) 8.02 (1H, brs, carboxylic CO\textsubscript{H}), 7.16-7.19
(2H, \(m, C^\beta H\)), 7.07-7.14 (2H, \(m, C^\alpha H\)), 3.05 (1H, sext., \(J 7.0\), benzylic \(CH\)), 2.31 (3H, \(s, CH_3\)), 2.27 (2H, \(t, J 7.7, \alpha\)-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**

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 diethyl ether. The combined organic layers were dried over anhydrous Na$_2$SO$_4$, 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$_3$): \(\delta\) 8.02 (1H, brs, carboxylic CO$_2$H), 7.16-7.19 (2H, \(m, C^\alpha H\)), 7.07-7.14 (2H, \(m, C^\alpha H\)), 3.05 (1H, sext., \(J 7.0\), benzylic \(CH\)), 2.31 (3H, \(s, CH_3\)), 2.27 (2H, \(t, J 7.7, \alpha\)-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-phenyloctanoic acid**

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 diethyl ether. The combined organic layers were dried over anhydrous Na$_2$SO$_4$, 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$_3$): \(\delta\) 8.02 (1H, brs, carboxylic CO$_2$H), 7.16-7.19 (2H, \(m, C^\alpha H\)), 7.07-7.14 (2H, \(m, C^\alpha H\)), 3.05 (1H, sext., \(J 7.0\), benzylic \(CH\)), 2.31 (3H, \(s, CH_3\)), 2.27 (2H, \(t, J 7.7, \alpha\)-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**

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 diethyl ether. The combined organic layers were dried over anhydrous Na$_2$SO$_4$, 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$_3$): \(\delta\) 8.02 (1H, brs, carboxylic CO$_2$H), 7.16-7.19 (2H, \(m, C^\alpha H\)), 7.07-7.14 (2H, \(m, C^\alpha H\)), 3.05 (1H, sext., \(J 7.0\), benzylic \(CH\)), 2.31 (3H, \(s, CH_3\)), 2.27 (2H, \(t, J 7.7, \alpha\)-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

\[ \text{R} = \text{Me, OMe, F, Cl} \]

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 \( \text{P}_2\text{O}_5 \) (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 \( \text{Na}_2\text{SO}_4 \), filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel, using an adequate \( n \)-hexane/\( \text{Et}_2\text{O} \) mixture as eluent.

4,5-dimethyl-3,4-dihyronaphthalen-1(2H)-one (X₁)

\[ \begin{array}{c}
\text{Me} \\
\text{Me} \\
\text{O}
\end{array} \]

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 \( \text{P}_2\text{O}_5 \) (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 \( \text{Na}_2\text{SO}_4 \), filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (\( n \)-hexane/\( \text{Et}_2\text{O} \) 98:2). Light-yellow crystalline solid. Isolated yield 86% (2.27 g, 13.0 mmol). \( R_f \) (silica gel, \( n \)-Hex/\( \text{Et}_2\text{O} \) 4:1) 0.66. \(^1\)H NMR (400 MHz, \( \text{CDCl}_3 \)): \( \delta \) 7.91 (1H, d, J 7.7, \( C^\text{ar} \text{H} \)), 7.35 (1H, d, J 7.4, \( C^\text{ar} \text{H} \)), 7.20 (1H, t, J 7.6, \( C^\text{ar} \text{H} \)), 3.29 (1H, broad quin., J 6.9, benzylic CH), 2.85 (1H, ddd, J 12.6, J 9.4, J 3.2, \( \alpha \)-carbonyl CH₂), 2.58 (1H, ddd, J 12.7, J 4.3, J 2.2, \( \alpha \)-carbonyl CH₂), 2.38 (3H, s, CH₃), 2.29 (1H, tt, J 13.6, J 3.9, CH₂), 2.01 (1H, dquin., J 13.6, J 2.7, CH₂), 1.32 (3H, d, J 7.1, CH₃) ppm. \(^{13}\)C NMR (100 MHz, \( \text{CDCl}_3 \)): \( \delta \) 198.8 (ketone Cq), 147.8 (Cq), 135.7 (CH), 131.9 (Cq), 126.3 (CH), 125.6 (CH), 33.2 (CH₂), 29.12 (CH), 29.09 (CH₃), 18.9 (CH₃), 18.6 (CH₃) ppm. ESI-HRMS (positive) \( M = C_{12}H_{14}O \), expected (M+\( \text{NH}_3 \)) \( m/z \) 192.1383, observed (M+\( \text{NH}_3 \)) \( m/z \) 192.1386.

5-methoxy-4-methyl-3,4-dihyronaphthalen-1(2H)-one (X₂)

\[ \begin{array}{c}
\text{MeO} \\
\text{Me} \\
\text{O}
\end{array} \]

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 \( \text{P}_2\text{O}_5 \) (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 \( \text{Na}_2\text{SO}_4 \), filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (\( n \)-hexane/\( \text{Et}_2\text{O} \) 95:5 → 9:1). Colorless crystalline solid. Isolated yield 46% (840 mg, 4.42 mmol). \( R_f \) (silica gel, \( n \)-Hex/\( \text{Et}_2\text{O} \) 4:1)
0.51. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 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 CH), 2.82 (1H, dddd, $J_1$ 17.6, $J_2$ 15.0, $J_3$ 5.2, $\alpha$-carbonyl CH$_2$), 2.57 (1H, dt, $J_1$ 17.6, $J_2$ 1.2, $\alpha$-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$_5$, expected (M+H)$^+$ m/z 191.1067, observed (M+H)$^+$ m/z 191.1066.

5-fluoro-4-methyl-3,4-dihydronaphthalen-1(2H)-one (X$_4$)

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$_2$O$_5$ (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$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane/EtO 98:2). Pale-yellow waxy solid. Isolated yield 91% (1.79 g, 10.0 mmol). R$_f$ (silica gel, n-Hex/EtO 4:1) 0.70. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 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 CH), 2.80 (1H, dddd, $J_1$ 17.6, $J_2$ 14.6, $J_3$ 5.2, $\alpha$-carbonyl CH$_2$), 2.58 (1H, dt, $J_1$ 17.5, $J_2$ 3.8, $\alpha$-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$_3$): $\delta$ -118.3 (1F, s, C$_{ar}$F) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 197.3 (d, $f^C$ 3.3, ketone C$_q$), 160.2 (d, $f^C$ 245, ipso(F)-C$_q$), 136.3 (d, $f^C$ 16.4, ortho(F)-C$_q$), 133.4 (d, $f^C$ 3.8, meta(F)-C$_q$), 127.5 (d, $f^C$ 8.2, para(F)-C$_q$), 123.0 (d, $f^C$ 3.4, para(F)-C$_q$), 120.3 (d, $f^C$ 22.1, ortho(F)-C$_q$), 33.6 (CH$_2$), 28.8 (CH$_2$), 26.1 (d, $f^C$ 2.3, CH), 19.2 (CH$_3$) ppm. ESI-HRMS (positif) M = C$_{12}$H$_{14}$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(2H)-one (X$_5$)

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$_2$O$_5$ (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$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane/EtO 98:2). Pale-yellow waxy solid. Isolated yield 91% (1.79 g, 10.0 mmol). R$_f$ (silica gel, n-Hex/EtO 4:1) 0.70. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 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 CH), 2.86 (1H, dddd, $J_1$ 18.0, $J_2$ 15.0, $J_3$ 5.4, $\alpha$-carbonyl CH$_2$), 2.62 (1H, dddd, $J_1$ 18.0, $J_2$ 4.4, $J_3$ 2.2, $\alpha$-carbonyl CH$_2$), 2.31 (1H, tt, $J_1$ 13.8, $J_2$ 4.6, CH$_2$), 2.05 (1H, dddd, $J_1$ 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$_{12}$H$_{14}$FO, expected (M+NH$_4^+$) m/z 196.1133, observed (M+NH$_4^+$) m/z 196.1135.
4-ethyl-3,4-dihydronaphthalen-1(2H)-one (X_{11})

![Chemical structure](image)

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_{2}O_{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_{2}SO_{4}, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane/Et_{2}O 95:5). Light-orange viscous oil. Isolated yield 82% (2.22 g, 11.8 mmol). \( R_{f} \) (silica gel, n-Hex/Et_{2}O 4:1) 0.66. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 8.02 (1H, dd, J = 7.8, J = 2.29 mol, 1.0 equiv.) in methanesulfonic acid (40 mL, 547 mmol, 38 equiv.) was added P_{2}O_{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_{2}SO_{4}, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane/Et_{2}O 95:5). Light-orange viscous oil. Isolated yield 88% (2.57 g, 12.3 mmol). \( R_{f} \) (silica gel, n-Hex/Et_{2}O 4:1) 0.78. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 8.02 (1H, dd, J = 7.8, J = 2.29 mol, 1.0 equiv.) in methanesulfonic acid (40 mL, 547 mmol, 38 equiv.) was added P_{2}O_{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_{2}SO_{4}, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane/Et_{2}O 95:5). Light-orange viscous oil. Isolated yield 82% (2.22 g, 11.8 mmol). \( R_{f} \) (silica gel, n-Hex/Et_{2}O 4:1) 0.70. \(^1\)H NMR
(400 MHz, CDCl$_3$): $\delta$ 8.02 (1H, $dd$, $J_1$ 7.8, $J_2$ 1.4, C$_{\alpha}$H), 7.49 (1H, $td$, $J_1$ 7.5, $J_2$ 1.5, C$_{\alpha}$H), 7.27-7.33 (2H, $m$, C$_{\alpha}$H), 2.83-2.87 (1H, broad $m$, benzylic CH), 2.72-2.82 (1H, $m$, diastereotopic CH$_2$), 2.58 (1H, $dt$, $J_1$ 17.8, $J_2$ 5.2, $\alpha$-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$_3$): $\delta$ 198.6 (ketone C$q$), 148.4 (C$q$), 133.5 (CH), 132.1 (C$q$), 128.4 (CH), 127.5 (CH), 126.7 (CH), 39.7 ($\alpha$-carbonyl CH$_2$), 35.1 (benzylic CH), 27.5 (CH$_2$), 26.5 (CH$_2$), 12.3 (CH$_3$) ppm.

4,4-dimethyl-3,4-dihydronaphthalen-1(2$H$)-one (X$_{10}$)

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$_2$O$_5$ (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$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane/Et$_2$O 95:5). Pale yellow oil. Isolated yield 60% (1.51 g, 8.67 mmol). $R_f$ (silica gel, n-Hex/Et$_2$O 4:1) 0.70. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.02 (1H, $ddd$, $J_1$ 7.8, $J_2$ 1.4, $J_3$ 0.3, C$_{\alpha}$H), 7.53 (1H, $td$, $J_1$ 7.2, $J_2$ 1.6, C$_{\alpha}$H), 7.42 (1H, $dd$, $J_1$ 7.9, $J_2$ 0.8, C$_{\alpha}$H), 7.30 (1H, $td$, $J_1$ 7.2, $J_2$ 1.2, C$_{\alpha}$H), 2.73 (2H, $t$, $J$ 6.7, $\alpha$-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: Vinlyic Bromides**

![Diagram](image)

To a cooled (-78 °C, dry ice/acetone bath) solution of (PhO)$_2$P (1.1 equiv.) in anhydrous CH$_2$Cl$_2$ (0.33 M with respect to X$_y^{KR}$) was added Br$_2$ (1.2 equiv.). Anhydrous Et$_3$N (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$_2$SO$_3$ was added and the mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude residue was then purified by flash chromatography on silica gel using an adequate n-hexane/Et$_2$O mixture as eluent.
4-bromo-1-methyl-1,2-dihydronaphthalene (Y₁)

To a cooled (-78 °C, dry ice/acetone bath) solution of (PhO)₃P (2.35 mL, 8.93 mmol, 1.1 equiv.) in anhydrous CH₂Cl₂ (35 mL) was added Br₂ (500 µL, 9.73 mmol, 1.2 equiv.). Anhydrous Et₃N (1.48 mL, 10.5 mmol, 1.3 equiv.) and 4-methyl-1-tetralone (X₁) (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 Na₂SO₃ was added and the mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na₂SO₄, 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). Rf (silica gel, n-Hex) 0.55. ¹H NMR (400 MHz, CDCl₃): δ 7.55-7.59 (1H, m, C₆H₄), 7.21-7.27 (2H, m, C₆H₄), 7.12-7.16 (1H, m, C₆H₄), 6.38 (1H, t, J 4.9, olefinic C=CH₂), 2.98 (1H, sext., J 7.0, benzylic CH₂), 2.53 (1H, ddd, J₁ 16.8, J₂ 6.7, J₢ 4.4, diastereotopic CH₂), 2.18 (1H, ddd, J₁ 16.9, J₂ 7.2, J₢ 5.3, diastereotopic CH₂), 1.27 (3H, d, J 7.0, CH₃) ppm.

4-bromo-1,8-dimethyl-1,2-dihydronaphthalene (Y₂)

To a cooled (-78 °C, dry ice/acetone bath) solution of (PhO)₃P (997 µL, 3.79 mmol, 1.1 equiv.) in anhydrous CH₂Cl₂ (12 mL) was added Br₂ (212 µL, 4.13 mmol, 1.2 equiv.). Anhydrous Et₃N (628 µL, 4.47 mmol, 1.3 equiv.) and 4,5-dimethyl-3,4-dihydropyridine-1(2H)-one (X₂) (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 Na₂SO₃ was added and the mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na₂SO₄, 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). Rf (silica gel, n-Hex) 0.62. ¹H NMR (400 MHz, CDCl₃): δ 7.52 (1H, d, J 8.6, C₆H₄), 7.17-7.26 (2H, m, C₆H₄), 7.11 (1H, d, J 5.8, C₆H₄), 6.46 (1H, t, J 4.8, olefinic C=CH₂), 2.84 (2H, t, J 7.9, benzylic CH₂), 2.36 (2H, td, J 8.4, J 4.8, allylic CH₂) ppm.

4-bromo-8-methoxy-1-methyl-1,2-dihydronaphthalene (Y₃)

To a cooled (-78 °C, dry ice/acetone bath) solution of (PhO)₃P (140 µL, 0.53 mmol, 1.1 equiv.) in anhydrous CH₂Cl₂ (4.0 mL) was added Br₂ (30 µL, 0.58 mmol, 1.2 equiv.). Anhydrous Et₃N (88 µL, 0.62 mmol, 1.3 equiv.) and 5-methoxy-4-methyl-3,4-dihydropyridine-1(2H)-one (X₃) (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$_2$SO$_3$ was added and the mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na$_2$SO$_4$, 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). $R_f$ (silica gel, n-Hex/Et$_2$O 9:1) 0.37. $^1$H NMR (400 MHz, CD$_2$Cl$_2$): $\delta$ 7.53 (1H, $d$, $J$ 7.8, C$^a$H), 7.02 (1H, $t$, $J$ 8.1, C$^a$H), 6.46 (1H, $d$, $J$ 8.8, C$^a$H), 6.09 (1H, $dd$, $J_1$ 7.1, $J_2$ 2.4, olefinic C=CH), 3.37 (1H, quint., $J$ 7.0, benzylic CH$_2$), 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](image)

To a cooled (-78 °C, dry ice/acetone bath) solution of (PhO)$_3$P (997 µL, 3.79 mmol, 1.1 equiv.) in anhydrous CH$_2$Cl$_2$ (12 mL) was added Br$_2$ (212 µL, 4.13 mmol, 1.2 equiv.). Anhydrous Et$_3$N (628 µL, 4.47 mmol, 1.3 equiv.) and 5-fluoro-4-methyl-3,4-dihydronaphthalen-1(2H)-one (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$_2$SO$_3$ was added and the mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na$_2$SO$_4$, 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, 3.44 mmol, 1.0 equiv.). $R_f$ (silica gel, n-Hex) 0.59. $^1$H NMR (400 MHz, CD$_2$Cl$_2$): $\delta$ 7.52 (1H, $d$, $J$ 8.6, C$^a$H), 7.17-7.26 (2H, $m$, C$^a$H), 7.11 (1H, $d$, $J$ 5.8, C$^a$H), 6.46 (1H, $t$, $J$ 4.8, olefinic C=CH), 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$_2$)

![4-bromo-8-chloro-1-methyl-1,2-dihydronaphthalene](image)

To a cooled (-78 °C, dry ice/acetone bath) solution of (PhO)$_3$P (997 µL, 3.79 mmol, 1.1 equiv.) in anhydrous CH$_2$Cl$_2$ (12 mL) was added Br$_2$ (212 µL, 4.13 mmol, 1.2 equiv.). Anhydrous Et$_3$N (628 µL, 4.47 mmol, 1.3 equiv.) and 5-chloro-4-methyl-3,4-dihydronaphthalen-1(2H)-one (X$_2$) (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$_2$SO$_3$ was added and the mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na$_2$SO$_4$, 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). $R_f$ (silica gel, n-Hex) 0.62. $^1$H NMR (400 MHz, CD$_2$Cl$_2$): $\delta$ 7.52 (1H, $d$, $J$ 8.6, C$^a$H), 7.17-7.26 (2H, $m$, C$^a$H), 7.11 (1H, $d$, $J$ 5.8, C$^a$H), 6.46 (1H, $t$, $J$ 4.8, olefinic C=CH), 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 (Y₁₁)

To a cooled (-78 °C, dry ice/acetone bath) solution of (PhO)₃P (997 µL, 3.79 mmol, 1.1 equiv.) in anhydrous CH₂Cl₂ (12 mL) was added Br₂ (212 µL, 4.13 mmol, 1.2 equiv.). Anhydrous Et₃N (628 µL, 4.47 mmol, 1.3 equiv.) and 4-ethyl-3,4-dihydronaphthalen-1(2H)-one (X₁₁) (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 Na₂SO₄ was added and the mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na₂SO₄, 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). Rₛ (silica gel, n-Hex) 0.62. ¹H NMR (400 MHz, CDCl₃): δ 7.52 (1H, d, J 8.6, CαH), 7.17-7.26 (2H, m, CαH), 7.11 (1H, d, J 5.8, CαH), 6.46 (1H, t, J 4.8, olefinic C=CH₂), 2.84 (2H, t, J 7.9, benzylic CH₂), 2.36 (2H, td, J 8.4, J 4.8, allylic CH₂) ppm.

4-bromo-1-butyl-1,2-dihydronaphthalene (Y₁₂)

To a cooled (-78 °C, dry ice/acetone bath) solution of (PhO)₃P (997 µL, 3.79 mmol, 1.1 equiv.) in anhydrous CH₂Cl₂ (12 mL) was added Br₂ (212 µL, 4.13 mmol, 1.2 equiv.). Anhydrous Et₃N (628 µL, 4.47 mmol, 1.3 equiv.) and 4-butyl-3,4-dihydronaphthalen-1(2H)-one (X₁₂) (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 Na₂SO₄ was added and the mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na₂SO₄, 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). Rₛ (silica gel, n-Hex) 0.62. ¹H NMR (400 MHz, CDCl₃): δ 7.52 (1H, d, J 8.6, CαH), 7.17-7.26 (2H, m, CαH), 7.11 (1H, d, J 5.8, CαH), 6.46 (1H, t, J 4.8, olefinic C=CH₂), 2.84 (2H, t, J 7.9, benzylic CH₂), 2.36 (2H, td, J 8.4, J 4.8, allylic CH₂) ppm.

4-bromo-1-isopropyl-1,2-dihydronaphthalene (Y₁₃)

To a cooled (-78 °C, dry ice/acetone bath) solution of (PhO)₃P (997 µL, 3.79 mmol, 1.1 equiv.) in anhydrous CH₂Cl₂ (12 mL) was added Br₂ (212 µL, 4.13 mmol, 1.2 equiv.). Anhydrous Et₃N (628 µL, 4.47 mmol, 1.3 equiv.) and 4-isopropyl-3,4-dihydronaphthalen-1(2H)-one (X₁₃) (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 Na₂SO₄ was added and the mixture
was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na$_2$SO$_4$, 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$_3$): $\delta$ 7.52 (1H, d, $J$ 8.6, Car H), 7.17-7.26 (2H, m, Car H), 7.11 (1H, d, $J$ 5.8, Car H), 6.46 (1H, t, $J$ 4.8, olefinic C=CH), 2.84 (2H, t, $J$ 7.9, benzylic CH$_2$), 2.36 (2H, td, $J$ 8.4, J$_2$ 4.8, allylic CH$_2$) ppm.

4-bromo-1,1-dimethyl-1,2-dihydronaphthalene (Y$_{10}$)

To a cooled (-78 °C, dry ice/acetone bath) solution of (PhO)$_3$P (997 µL, 3.79 mmol, 1.1 equiv.) in anhydrous CH$_2$Cl$_2$ (12 mL) was added Br$_2$ (212 µL, 4.13 mmol, 1.2 equiv.). Anhydrous Et$_3$N (628 µL, 4.47 mmol, 1.3 equiv.) and 4,4-dimethyl-3,4-dihydronaphthalen-1(2H)-one (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$_2$SO$_3$ was added and the mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na$_2$SO$_4$ and the mixture was extracted with methylene chloride. The combined organic layers were dried over anhydrous Na$_2$SO$_4$, 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). R$_f$ (silica gel, n-Hex) 0.60. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.52 (1H, d, $J$ 8.6, Car H), 7.17-7.26 (2H, m, Car H), 7.11 (1H, d, $J$ 5.8, Car H), 6.46 (1H, t, $J$ 4.8, olefinic C=CH), 2.84 (2H, t, $J$ 7.9, benzylic CH$_2$), 2.36 (2H, td, $J$ 8.4, J$_2$ 4.8, allylic CH$_2$) ppm.

General Procedure for the Synthesis of Substrates: Cyclobutans

$^1$BuLi (1.9 M solution in pentane, 2.0 equiv.) was slowly added to a solution of Y$_{yKR}$ (1.0 equiv.) in anhydrous THF (0.4 M with respect to Y$_{yKR}$) 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$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude residue was then purified by flash chromatography on silica gel using an adequate n-hexane/Et$_2$O mixture as eluent.
1-(4-methyl-3,4-dihydronaphthalen-1-yl)cyclobutanol (rac-A₁)

\[ \text{Chemical Formula: } C_{15}H_{18}O \]
\[ \text{Molecular Weight: 214.30} \]

\[ ^{1} \text{BuLi} \] (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 (Y₁KR) (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 Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane → n-hexane/Et₂O 9:1). White waxy solid. Isolated yield 89% (898 mg, 4.19 mmol). \( R_f \) (silica gel, n-Hex/EtOAc 9:1) 0.46. \(^1\)H NMR (500 MHz, \( C_6D_6 \)): \( \delta \) 7.81 (1H, dd, J₁ 8.2, J₂ 1.5, C\( ^{11}H \)), 7.08-7.14 (3H, m, C\( ^{13}H \)), 5.77 (1H, t, J 4.7, olefinic C=CH₂), 2.68 (1H, sext., J 6.9, benzyl CH), 2.36-2.46 (2H, m, allylic CH₂), 2.16-2.29 (3H, m, cyclobutyl CH₂), 1.81-1.91 (2H, m, cyclobutyl CH₂), 1.51 (1H, brs, hydroxyl OH), 1.39-1.52 (1H, m, cyclobutyl CH₂), 1.12 (3H, d, J 7.0, CH₃) ppm. \(^{13}\)C NMR (125 MHz, \( C_6D_6 \)): \( \delta \) 142.4 (Cq), 139.7 (Cq), 131.9 (Cq), 127.4 (CH), 126.7 (CH), 126.5 (CH), 126.3 (CH), 123.2 (CH), 77.3 (O-Cq), 36.2 (CH₂), 36.0 (CH₂), 32.5 (CH), 31.2 (CH₂), 20.2 (CH₃), 14.3 (CH₃) ppm. ESI-HRMS (positif) \( M = C_{15}H_{17}O \), expected (M+H²O+H)\(^+\) m/z 197.1325, observed (M+H²O+H)\(^+\) m/z 197.1325.

1-(4,5-dimethyl-3,4-dihydronaphthalen-1-yl)cyclobutanol (rac-A₂)

\[ \text{Chemical Formula: } C_{18}H₂O \]
\[ \text{Molecular Weight: 228.33} \]

\[ ^{1} \text{BuLi} \] (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 (Y₂KR) (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 Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane → n-hexane/Et₂O 9:1). White amorphous solid. Isolated yield 79% (442 mg, 1.94 mmol). \( R_f \) (silica gel, n-Hex/EtOAc 4:1) 0.47. \(^1\)H NMR (400 MHz, \( C_6D_6 \)): \( \delta \) 7.74 (1H, d, J 7.8, C\( ^{11}H \)), 7.07 (1H, t, J 7.6, C\( ^{13}H \)), 6.96 (1H, d, J 7.4, C\( ^{15}H \)), 5.74 (1H, dd, J₃ 6.9, J₄ 1.8, olefinic C=CH), 2.90 (1H, quin., J 7.0, benzyl CH), 2.28-2.53 (4H, m, CH₂), 2.15-2.23 (1H, m, CH₂), 2.15 (3H, s, CH₃), 1.82-2.00 (2H, m, CH₂), 1.58 (1H, brs, hydroxyl OH), 1.42-1.58 (1H, m, CH₂), 1.01 (3H, d, J 7.0, CH₃) ppm. \(^{13}\)C NMR (100 MHz, \( C_6D_6 \)): \( \delta \) 140.7 (Cq), 139.8 (Cq), 134.4 (Cq), 131.2 (Cq), 129.7 (CH), 125.9 (CH), 124.7 (CH), 121.8 (CH), 77.6 (O-Cq), 36.9 (CH₂), 35.7 (CH₂), 30.5 (CH₂), 28.2 (CH), 19.2 (CH₃), 18.3 (CH₃), 14.4 (CH₂) ppm. ESI-HRMS (positif) \( M = C_{18}H_{20}O \), expected (M+H²O+H)\(^+\) m/z 211.1482, observed (M+H²O+H)\(^+\) m/z 211.1485.
1-(5-methoxy-4-methyl-3,4-dihyronaphthalen-1-yl)cyclobutanol (rac-A₃)

'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-dihyronaphthalene (Y₄KR) (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 Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane → n-hexane/Et₂O 7:3). White waxy solid. Isolated yield 84% (395 mg, 1.70 mmol). Rₚ (silica gel, n-Hex/Et₂O 4:1) 0.23. ¹H NMR (500 MHz, C₆D₆): δ 7.56 (1H, d, J 7.9, C₆H), 7.10 (1H, t, J 8.1, C₆H), 6.53 (1H, dd, J 8.2, J 3, C₆H), 5.76 (1H, dd, J 6.9, J 1.6, olefinic C=CH), 3.59 (1H, quin., J 7.1, benzylic CH), 3.38 (3H, s, methoxy CH₃-O), 2.46-2.52 (1H, m, diastereotopic CH₂), 2.31-2.43 (3H, m, diastereotopic CH₂), 2.14-2.22 (1H, m, CH₃), 2.03 (1H, ddd, J 1.69, J 6.9, J 1.3, CH₂), 1.84-1.92 (1H, m, CH₂), 1.58 (1H, brs, hydroxyl OH), 1.44-1.51 (1H, m, CH₂), 1.21 (3H, d, J 7.1, CH₃) ppm. ¹³C NMR (125 MHz, C₆D₆): δ 156.4 (Cq), 139.3 (Cq), 132.5 (Cq), 130.7 (Cq), 126.5 (CH), 122.6 (CH), 119.5 (CH), 109.8 (CH), 77.6 (Cq-O), 55.1 (CH₃-O), 36.7 (CH₂), 35.7 (CH₂), 30.3 (CH₂), 24.8 (benzylic CH), 18.9 (CH₃), 14.4 (CH₃) ppm. ESI-HRMS (positive) M = C₁₈H₂₀O₂, expected (M+H²⁺) m/z 227.1431, observed (M+H₂O⁺H⁺) m/z 227.1432.

1-(5-fluoro-4-methyl-3,4-dihyronaphthalen-1-yl)cyclobutanol (rac-A₄)

'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-dihyronaphthalene (Y₅KR) (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 Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane → n-hexane/Et₂O 7:3). White waxy solid. Isolated yield 84% (395 mg, 1.70 mmol). Rₚ (silica gel, n-Hex/Et₂O 4:1) 0.42. ¹H NMR (400 MHz, C₆D₆): δ 7.55 (1H, d, J 7.8, C₆H), 6.90 (1H, dd, J 8.1, J 6.1, C₆H), 6.78 (1H, td, J 9.3, J 1.1, C₆H), 5.65 (1H, dd, J 6.9, J 1.9, olefinic C=CH), 3.30 (1H, quin., J 7.0, benzylic CH), 2.34-2.41 (1H, m, diastereotopic CH₂), 2.18-2.31 (3H, m, diastereotopic CH₂), 2.05-2.12 (1H, m, CH₂), 1.78-1.89 (2H, m, CH₂), 1.36-1.46 (1H, m, CH₂), 1.40 (1H, brs, hydroxyl OH), 1.07 (3H, d, J 7.1, CH₃) ppm. ¹⁹F NMR (376 MHz, C₆D₆): δ -117.6 (1F, s, C₆F) ppm. ¹³C NMR (100 MHz, C₆D₆): δ 160.3 (d, J₉⁻F 240, ipso(F)-Cq), 138.6 (d, J₉⁻F 3.2, olefinic Cq), 133.5 (d, J₉⁻F 4.9, meta(F)-Cq), 129.0 (d, J₉⁻F 16.4, ortho(F)-Cq), 127.1 (d, J₉⁻F 8.5, meta(F)-CH), 123.2 (olefinic CH), 122.5 (d, J₉⁻F 3.0, para(F)-CH), 114.2 (d, J₉⁻F 22.4, ortho(F)-CH),
1-(5-chloro-4-methyl-3,4-dihydronaphthalen-1-yl)cyclobutanol (rac-A_3)

'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-1-ethyl-1,2-dihydronaphthalene (Y^KR _6) (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.

Cyclobutanol (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 Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane → n-hexane/Et₂O 4:1). Colorless oil. Isolated yield 87% (530 mg, 2.13 mmol). Rf (silica gel, n-Hex/Et₂O 4:1) 0.37. ^1H NMR (500 MHz, C₆D₆): δ 7.68 (1H, d, J 7.8, C=C), 7.14 (1H, dd, J₁ 8.0, J₂ 1.1, C=C), 6.83 (1H, t, J 8.0, C=C), 5.64 (1H, dd, J₁ 7.0, J₂ 1.8, olefinic C=CH), 3.42 (1H, quint., J 7.1, benzylic CH), 2.33-2.39 (1H, m, diastereotopic CH₂), 2.17-2.27 (3H, m, CH₃), 2.03-2.09 (1H, m, CH₂), 1.80-1.90 (2H, m, CH₂), 1.25-1.37 (1H, m, CH₂), 1.36 (1H, brs, hydroxylic OH), 1.07 (3H, d, J 7.1, CH₃) ppm. ^13C NMR (125 MHz, C₆D₆): δ 139.8 (ipso(C)-C), 138.7 (olefinic Cq), 133.6 (Cq), 133.2 (Cq), 128.4 (CH), 127.1 (CH), 125.3 (CH), 123.4 (olefinic CH), 77.3 (O=Cq), 36.5 (CH₂), 35.6 (CH₂), 29.9 (CH₂), 29.0 (benzylic CH), 18.1 (CH₃), 14.3 (CH₂) ppm. ESI-HRMS (positif) M = C_{15}H_{17}ClO, expected (M-H₂O+H)^+ m/z 231.0936, observed (M-H₂O+H)^+ m/z 231.0939.

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

'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 (Y^KR _6) (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.

Cyclobutanolone (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 Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane → n-hexane/Et₂O 4:1). Colorless viscous oil. Isolated yield 90% (528 mg, 2.31 mmol). Rf (silica gel, n-Hex/Et₂O 4:1) 0.40. ^1H NMR (400 MHz, C₆D₆): δ 7.81 (1H, dd, J₁ 7.8, J₂ 1.2, C=C), 7.03-7.14 (3H, m, C=C), 5.75 (1H, dd, J₁ 6.2, J₂ 3.1, olefinic C=CH), 2.15-2.48 (6H, m, diastereotopic CH₂ + CH₃), 2.05 (1H, ddd, J₁ 16.6, J₂ 6.2, J₃ 3.5, CH₂), 1.80-1.90 (1H, m, CH₂), 1.53 (1H, brs, hydroxylic OH), 1.39-1.62 (3H, m, CH₂), 0.82 (3H, t, J 7.4, CH₃) ppm. ^13C NMR (100 MHz, C₆D₆): δ 141.3 (Cq), 139.7 (olefinic Cq), 131.9 (Cq), 128.2 (CH), 127.0 (CH), 126.5 (CH), 126.4 (CH), 122.9 (olefinic CH), 77.4 (O=Cq), 39.8 (CH₂), 36.5 (CH₂), 35.8 (CH₂), 28.3 (benzylic CH), 27.0 (CH₂), 14.4
(CH₂), 12.3 (CH₃) ppm. **ESI-HRMS (positif)** M = C₁₆H₂₀O, expected (M-H₂O+H)⁺ m/z 211.1482, observed (M-H₂O+H)⁺ m/z 211.1485.

1-(4-butyl-3,4-dihydronaphthalen-1-yl)cyclobutanol (rac-A₁₂)

![Image of 1-(4-butyl-3,4-dihydronaphthalen-1-yl)cyclobutanol]

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 (Y₄KR) (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 Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane → n-hexane/Et₂O 4:1). Colorless viscous oil. Isolated yield 90% (528 mg, 2.31 mmol). Rf (silica gel, n-Hex/Et₂O 4:1) 0.40. **¹H NMR** (500 MHz, C₆D₆): δ 7.82 (1H, d, J 7.5, C"H), 7.07-7.14 (3H, m, C"H), 5.78 (1H, dd, J 6.2, J 3.1, olefinic C=CH₂), 2.24-2.55 (5H, m, diastereotopic C₂H₂ + CH₂), 2.08 (1H, ddd, J 16.8, J 6.2, J 3.6, CH₂), 1.81-1.89 (1H, m, CH₂), 1.42-1.60 (4H, m, C₂H₂ + hydroxyl OH), 1.15-1.28 (3H, m, CH₃), 0.84 (3H, t, J 7.0, CH₃) ppm. **¹³C NMR** (125 MHz, C₆D₆): δ 141.3 (Cq), 139.7 (olefinic Cq), 131.9 (Cq), 128.2 (CH), 127.0 (CH), 126.5 (CH), 126.4 (CH), 122.9 (olefinic CH), 77.4 (O-Cq), 39.8 (CH₂), 36.5 (CH₂), 35.8 (CH₂), 28.3 (benzylic CH), 27.0 (CH₂), 14.4 (CH₂), 12.3 (CH₃) ppm. **ESI-HRMS (positif)** M = C₁₆H₂₀O, expected (M-H₂O+H)⁺ m/z 239.1795, observed (M-H₂O+H)⁺ m/z 239.1795.

1-(4-isopropyl-3,4-dihydronaphthalen-1-yl)cyclobutanol (rac-A₁₃)

![Image of 1-(4-isopropyl-3,4-dihydronaphthalen-1-yl)cyclobutanol]

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 (Y₆KR) (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 Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane → n-hexane/Et₂O 4:1). Colorless oil. Isolated yield 87% (530 mg, 2.13 mmol). Rf (silica gel, n-Hex/Et₂O 4:1) 0.37. **¹H NMR** (500 MHz, C₆D₆): δ 7.82 (1H, dd, J 7.8, J 1.0, C"H), 7.14 (1H, d, J 7.7, J 1.6, C"H), 7.07 (1H, td, J 7.4, J 1.4, C"H), 7.03 (1H, dd, J 7.5, J 1.3, C"H), 5.74 (1H, dd, J 6.8, J 3.9, olefinic C=CH₂), 2.36-2.47 (2H, m, diastereotopic CH₂), 2.14-2.31 (5H, m, CH₂), 1.81-1.89 (2H, m, CH₂), 1.48 (1H, brs, hydroxyl OH), 1.41-1.50 (1H, m, CH₃), 0.85 (3H, d, J 6.7, isopropyl CH₃), 0.79 (3H, d, J 6.8, isopropyl CH₃) ppm. **¹³C NMR** (125 MHz, C₆D₆): δ 140.3 (Cq), 140.0 (olefinic Cq), 132.5 (Cq), 129.3 (CH), 126.6 (CH), 126.5 (CH), 126.3 (CH), 123.3 (olefinic CH), 77.3 (O-Cq), 44.7 (isopropyl CH), 36.6 (CH₂), 35.7 (CH₂), 30.6 (benzyl CH), 25.9 (CH₂), 21.6 (CH₃), 20.7 (CH₃), 14.3 (CH₂) ppm. **ESI-HRMS (positif)** M = C₁₇H₂₂O, expected (M-H₂O+H)⁺ m/z 225.1638, observed (M-H₂O+H)⁺ m/z 225.1642.
1-(4,4-dimethyl-3,4-dihyronaphthalen-1-yl)cyclobutanol \((\text{A}_{10})\)

\[ \text{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-dihyronaphthalene (Y}_{13}^{\text{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 Na2SO4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane → n-hexane/EtO 4:1). White amorphous solid. Isolated yield 91% (555 mg, 2.43 mmol). \( R_f \) (silica gel, n-Hex/EtO 4:1) 0.44. \( ^1\text{H NMR} \) (500 MHz, \( \text{C}_6\text{D}_6 \)): \( \delta \) 7.82-7.85 (1H, \( m \), C\( ^{13}\text{H} \)), 7.23-7.25 (1H, \( m \), C\( ^{13}\text{H} \)), 7.11-7.13 (2H, \( m \), C\( ^{13}\text{H} \)), 5.77 (1H, \( t \), J 4.7, olefinic C=CH\(_2\)), 2.39-2.45 (2H, \( m \), cyclobutyl CH\(_2\)), 2.20-2.26 (2H, \( m \), cyclobutyl CH\(_2\)), 2.04 (2H, \( d \), J 4.7, allylic CH\(_2\)), 1.82-1.90 (1H, \( m \), cyclobutyl CH\(_2\)), 1.50 (1H, \( brs \), hydroxylic OH), 1.43-1.49 (1H, \( m \), cyclobutyl CH\(_2\)), 1.18 (6H, \( s \), gem-dimethyl CH\(_3\)) ppm. \( ^{13}\text{C NMR} \) (125 MHz, \( \text{C}_6\text{D}_6 \)): \( \delta \) 145.8 (C\( q \)), 139.7 (olefinic Cq), 131.5 (Cq), 128.4 (CH), 126.7 (CH), 126.0 (CH), 124.3 (CH), 123.4 (olefinic CH), 77.5 (O-Cq), 38.7 (CH\(_2\)), 36.2 (CH\(_2\)), 33.6 (Cq), 28.4 (gem-dimethyl CH\(_3\)), 14.4 (CH\(_3\)) ppm. \text{ESI-HRMS (positif)} \) M = C\(_{10}\)H\(_{20}\)O, expected (M-H\(_2\)O+H\(^+\)) \( m/z \) 211.1482, observed (M-H\(_2\)O+H\(^+\)) \( m/z \) 211.1484.

**General Procedure for the Synthesis of Substrates: Cyclopropanols**

\[ \text{BuLi (1.9 M solution in pentane, 2.0 equiv.) was slowly added to a solution of Y}_{y}^{\text{KR}} \) (1.0 equiv.) in anhydrous THF (0.4 M with respect to Y}_{y}^{\text{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\(_2\)O (0.5 M with respect to Z) was added MeMgl (3.0 M solution in Et\(_2\)O, 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 NH₄Cl. The separated aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was then purified by flash chromatography on silica gel using an adequate n-hexane/Et₂O mixture as eluent.

1-(4-methyl-3,4-dihydropnaphthalen-1-yl)cyclopropanol (rac-A₄)

\[
\text{BuLi (1.9 M solution in pentane, 4.39 mL, 8.34 mmol, 2.0 equiv.)}
\]
was slowly added to a solution of 4-bromo-1-methyl-1,2-dihydropnaphthalene (Y₁KR) (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 Et₂O (8.0 mL) was added MeMgI (3.0 M solution in Et₂O, 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 NH₄Cl. The separated aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane → n-hexane/Et₂O 9:1). Colorless oil. Isolated yield 92% (768 mg, 3.84 mmol). Rₜ (silica gel, n-Hex/Et₂O 4:1) 0.19. \(^1\)H NMR (400 MHz, C₆D₆): \(\delta\) 8.00 (1H, dd, \(J_1\) 7.7, \(J_2\) 1.2, C\(^{6H}\)), 7.08-7.14 (3H, \(m, C^{\text{mH}}\)), 5.71 (1H, \(t, J_4\) 4.5, olefinic C=CH\(^1\)), 2.70 (1H, sext., \(J_7\) 7.0, benzylic CH\(^1\)), 2.18 (1H, \(dd, J_1\) 16.8, \(J_2\) 7.2, \(J_3\) 1.8, allylic CH\(^2\)), 1.84 (1H, \(dd, J_1\) 16.8, \(J_2\) 7.0, \(J_3\) 2.2, allylic CH\(^3\)), 1.65 (1H, brs, hydroxylc OH\(^1\)), 1.11 (3H, \(d, J_7\) 7.0, CH\(^3\)), 0.92-0.98 (2H, \(m\), cyclopropyl CH\(^2\)), 0.66-0.69 (2H, \(m\), cyclopropyl CH\(^3\)) ppm. \(^13\)C NMR (100 MHz, C₆D₆): \(\delta\) 141.6 (C\(^q\)), 138.0 (C\(^q\)), 133.1 (C\(^q\)), 127.7 (CH), 126.7 (CH), 126.5 (CH), 125.5 (CH), 124.6 (CH), 56.4 (O-C\(^q\)), 32.2 (CH\(^2\)), 31.1 (benzylic CH), 20.4 (cyclopropyl CH\(^2\)), 13.6 (CH\(^3\)), 13.0 (cyclopropyl CH\(^3\)) ppm. ESI-HRMS (positive) \(M = C_{14}H_{16}O\), expected (M-H₂O+H\(^+\)) \(m/z\) 183.1169, observed (M-H₂O+H\(^+\)) \(m/z\) 183.1170.

1-(4,5-dimethyl-3,4-dihydropnaphthalen-1-yl)cyclopropanol (rac-A₅)

\[
\text{BuLi (1.9 M solution in pentane, 2.75 mL, 5.22 mmol, 2.0 equiv.)}
\]
was slowly added to a solution of 4-bromo-1,8-dimethyl-1,2-dihydropnaphthalene (Y₂KR) (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 Et₂O (5.0 mL) was added MeMgI (3.0 M solution in Et₂O, 960 \(\mu\)L, 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 NH₄Cl. The separated aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na₂SO₄, filtered
and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane → n-hexane/Et₂O 9:1). Colorless viscous oil. Isolated yield 88% (492 mg, 2.30 mmol). Rf (silica gel, n-Hex/Et₂O 4:1) 0.26. ¹H NMR (500 MHz, C₆D₆): δ 7.92 (1H, d, J 7.7, C²H), 7.14 (1H, t, J 7.7, C³H), 7.00 (1H, d, J 7.5, C⁴H), 5.68 (1H, ddd, J 1.1, J 2.3, J 1.6, olefinic C=CH), 2.88 (1H, quint., J 7.0, benzylic CH), 2.31 (1H, ddd, J 17.0, J 7.1, J 2.4, allylic CH₂), 2.15 (3H, s, CH₃), 1.92 (1H, ddd, J 17.0, J 6.8, J 1.4, allylic CH₂), 1.63 (1H, brs, hydroxyl CH), 1.04 (1H, ddd, J 10.3, J 6.2, J 4.1, cyclopropyl CCH₂), 0.99 (3H, d, J 7.1, CH₃), 0.91 (1H, ddd, J 11.4, J 6.6, J 4.9, cyclopropyl CH₂), 0.74 (1H, ddd, J 10.5, J 6.6, J 4.9, cyclopropyl CH₂), 0.68 (1H, ddd, J 10.7, J 6.4, J 4.1, cyclopropyl CH₂) ppm. ¹³C NMR (125 MHz, C₆D₆): δ 139.9 (Cq), 137.9 (Cq), 134.2 (Cq), 132.4 (Cq), 129.9 (CH), 126.3 (CH), 123.8 (CH), 32.4 (CCH₂), 28.0 (benzylic CH), 19.1 (CH₃), 18.7 (CH₃), 15.4 (cyclopropyl CH₂), 11.6 (cyclopropyl CH₂) ppm.

ESI-HRMS (positif) M = C₁₅H₁₈O, expected (M-H₂O+H)⁺ m/z 197.1325, observed (M-H₂O+H)⁺ m/z 197.1322.

1-(5-fluoro-4-methyl-3,4-dihyronaphthalen-1-yl)cyclopropanol (rac-A₈)

¹BuLi (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-dihyronaphthalene (Y₅KR) (553 mg, 2.29 mmol, 1.0 equiv.) in anhydrous THF (10 mL) at -78 °C over a period of 10 min. The result 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 Et₂O (4.5 mL) was added MeMgI (3.0 M solution in Et₂O, 840 µL, 2.29 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 NH₄Cl. The separated aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane → n-hexane/Et₂O 9:1). Colorless viscous oil. Isolated yield 88% (492 mg, 2.30 mmol). Rf (silica gel, n-Hex/Et₂O 4:1) 0.26. ¹H NMR (500 MHz, C₆D₆): δ 7.73 (1H, d, J 7.8, C²H), 6.96 (1H, td, J 8.1, J 6.0, C³H), 6.83 (1H, t, J 9.4, C⁴H), 5.58 (1H, ddd, J 6.7, J 2.4, olefinic C=CH), 3.28 (1H, quint., J 7.2, benzylic CH), 2.20 (1H, ddd, J 17.4, J 7.6, J 2.4, diastereotopic CH₂), 1.81 (1H, ddd, J 17.4, J 6.7, J 1.4, diastereotopic CH₂), 1.46 (1H, brs, hydroxyl CH), 1.07 (3H, d, J 7.2, CH₃), 0.94-0.99 (1H, m, cyclopropyl CH₂), 0.81-0.86 (1H, m, cyclopropyl CH₂), 0.56-0.65 (2H, m, cyclopropyl CH₂) ppm. ¹⁹F NMR (376 MHz, C₆D₆): δ -17.6 (1F, s, C⁻F) ppm.

¹³C NMR (125 MHz, C₆D₆): δ 160.3 (d, J⁻⁵F 240, ipso-F-Cq), 136.8 (d, J⁻⁵F 3.4, olefinic Cq), 134.7 (d, J⁻⁵F 5.0, meta(F)-Cq), 128.2 (d, J⁻⁵F 16.0, ortho(F)-Cq), 127.5 (d, J⁻⁵F 8.5, meta(F)-CH), 124.7 (olefinic CH), 121.5 (d, J⁻⁵F 2.9, para(F)-CH), 114.4 (d, J⁻⁵F 22.4, ortho(F)-CH), 56.4 (O-Cq), 29.7 (CH₂), 24.4 (d, J⁻⁵F 2.8, benzylic CH), 19.9 (CH₃), 14.9 (CH₂), 11.8 (CH₂) ppm. ESI-HRMS (positif) M = C₁₅H₁₃FO, expected (M-H₂O+H)⁺ m/z 201.1075, observed (M-H₂O+H)⁺ m/z 201.1077.
1-(5-fluoro-4-methyl-3,4-dihyronaphthalen-1-yl)cyclopropanol (rac-A₉)

\[ \text{BuLi (1.9 M solution in pentane, 2.50 mL, 4.74 mmol, 2.0 equiv.)} \]

was slowly added to a solution of 4-bromo-8-chloro-1-methyl-1,2-
dihyronaphthalene (Y₆ 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-
ethoxyecyclopropanol (Z) (266 mg, 2.61 mmol, 1.1 equiv.) in anhydrous Et₂O (5.0 mL) was added MeMgl (3.0 M solution in
Et₂O, 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 NH₄Cl. The separated aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane \( \rightarrow \) n-hexane/Et₂O 9:1). Colorless viscous oil. Isolated yield 88% (492 mg, 2.30 mmol). \( R_f \) (silica gel, n-Hex/Et₂O 4:1) 0.26. \( ^1 \text{H NMR} \) (500 MHz, CD₃OD): \( \delta 7.85 (1H, d, J 7.8, C\text{-H}), \)

7.16 (1H, dd, J 7.8, J 2 0.7, C\text{-H}), 6.89 (1H, t, J 7.9, C\text{-H}), 5.57 (1H, dd, J 6.7, J 2 2.1, olefinic C=CH), 3.39 (1H, quint., J 7.2, benzylic CH), 2.20 (1H, ddd, J 17.3, J 7.4, J 2 2.4, diastereotopic CH₂), 1.82 (1H, ddd, J 17.3, J 6.8, J 2 1.2, CH₂), 1.43 (1H, brs, hydroxylly OH), 1.06 (3H, d, J 7.1, CH₃), 0.96 (1H, ddd, J 9.8, J 5.8, J 3.8, cyclopropyl CH₂), 0.82 (1H, ddd, J 11.2, J 6.5, J 3 4.8, cyclopropyl CH₂), 0.54-0.64 (2H, m, cyclopropyl CH₂) ppm. \( ^{13} \text{C NMR} \) (125 MHz, CD₃OD): \( \delta 139.1 \) (ipsos(Cl)-Cq), 136.9 (olefinic Cq), 134.7 (Cq), 133.1 (Cq), 128.6 (CH), 127.5 (CH), 124.8 (CH), 124.5 (olefinic CH), 56.3 (O-Cq), 29.9 (CH₂), 28.8 (benzylic CH), 18.6 (CH₃), 15.1 (CH₂), 11.8 (CH₂) ppm.

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

**Racemates**

To a well-stirred solution of chiral, racemic allylic alcohol A₉ KR (0.20 mmol, 1.0 equiv.) and a 1:1 \( (\text{w/w}) \) mixture of \( (R\text{-})\text{TRIP (L₄)} \) (7.5 mg of each, 0.02 mmol, 10 mol%) in anhydrous CD₃HSF/n-Hex 1:1 \( (\text{v/v}) \) (total volume: 3.0 mL, 0.07 M) were added powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.) and anhydrous Na₂PO₄ (41 mg, 0.25 mmol, 1.25 equiv.). The resultant heterogeneous mixture was stirred at -12 °C for 96 h. Saturated aqueous Na₂S₂O₃ 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 Na₂SO₄, filtered and concentrated in vacuo. Conversions and diastereomer ratios \( (d.r.) \) were determined by \( ^1 \text{H and } ^{19} \text{F NMR analysis of the crude compounds. Pure diastereomers (B KR1 and B KR2) were obtained after purification by flash chromatography on silica gel, using an adequate n-hexane/Et₂O mixture as eluent.} \)
General Procedure for the Stereodivergent Fluorination/Semi-Pinacol Reaction: Enantioselective Version

To a well-stirred solution of chiral, racemic allylic alcohol \( \text{A}_y^\text{KR} \) (0.20 mmol, 1.0 equiv.) and \( \{\text{R}_x\}\)-TIPS-TRIP (\( \text{L}_4 \)) (12 mg, 0.01 mmol, 5 mol%) in anhydrous \( \text{C}_6\text{H}_5\text{F}/\text{Hex} \) 1:1 (v/v) (total volume: 3.0 mL, 0.07 M) were added powdered SelectfluorTM (106 mg, 0.30 mmol, 1.5 equiv.) and anhydrous \( \text{Na}_2\text{PO}_4 \) (41 mg, 0.25 mmol, 1.25 equiv.). The resultant heterogeneous mixture was stirred at -12 °C for 96 h. Saturated aqueous \( \text{Na}_2\text{SO}_4 \) 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 \( \text{Na}_2\text{SO}_4 \), filtered and concentrated in vacuo. Conversions and diastereomer ratios \( \{d.r.\} \) were determined by \( ^1\text{H} \) and \( ^19\text{F} \) NMR analysis of the crude compounds. Pure diastereomers \( \{\text{B}_y^\text{KR} \} \) were obtained after purification by flash chromatography on silica gel, using an adequate \( \text{n-hexane/Et}_2\text{O} \) mixture as eluent. Enantiomer ratios \( \{\text{e.r.}\} \) were determined by chiral HPLC analysis of purified compounds.

Characterization of Fluorinated Products

\( \beta \)-Fluoro Spiroketone \( \{\text{B}_1^\text{R}\} \)

According to the General Procedure: chiral, racemic allylic cyclobutanol \( \{\text{rac-A}_4\} \) (43 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid \( \{\text{R}_x\}\)-TIPS-TRIP (\( \text{L}_4 \)) (12 mg, 0.01 mmol, 5 mol%), powdered SelectfluorTM (106 mg, 0.30 mmol, 1.5 equiv.), and dried \( \text{Na}_2\text{PO}_4 \) (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous \( \text{C}_6\text{H}_5\text{F}/\text{Hex} \) 1:1 (v/v) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (n-hexane \( \rightarrow \) n-hexane/Et}_2\text{O} 95:5). Colorless oil. Isolated yield 40% (19 mg, 0.08 mmol). \( \text{R}_f \) (silica gel, n-Hex/Et}_2\text{O 9:1) 0.74. > 20:1 \( \{d.r.\} \). \( ^1\text{H} \) NMR. 96:4 e.r. Chiral HPLC. Chiralpak IC. n-Hex/i-PrOH 99.5:0.5. 1.0 mL/min. \( t_{\text{R}} \) 22.2 (major), 31.2 (minor). \( ^1\text{H} \) NMR (400 MHz, \( \text{C}_6\text{D}_6 \)): \( \delta \) 7.10 (1H, \( dd \), \( J = 7.6, J = 7.6 \)), 7.04 (1H, \( td \), \( J = 7.1, J = 1.4 \)), 6.99 (1H, \( td \), \( J = 7.6, J = 1.6 \)), 6.80 (1H, \( dd \), \( J = 7.0, J = 1.1 \)), 4.41 (1H, \( ddd \), \( J = 12.9 \)), 4.11 (1H, \( d \), \( J = 11.7 \)), 1.88 (1H, \( m \), \( CH_2 \)), 1.62-1.56 (1H, \( m \), \( CH_2 \)). 1H NMR (376 MHz, \( \text{C}_6\text{D}_6 \)): \( \delta \) 181.0 (1F, \( s \), C(sp^3)-F) ppm. \( ^1\text{F} \) NMR (376 MHz, \( \text{C}_6\text{D}_6 \)): \( \delta \) -181.0 (1F, \( s \), C(sp^3)-F) ppm. ESI-HRMS (positif) M =
β-Fluoro Spiroketone (B₁)⁸

![Chemical Structure](image)

**diastereomer 2**  
Chemical Formula: C₁₂H₁₇FO  
Molecular Weight: 232.29

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A₁) (43 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₃)-TIPS-TRIP (L₈) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na₂PO₄ (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C₆H₅F/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/Et₂O 95:5).  

Colorless oil. Isolated yield 43% (20 mg, 0.09 mmol). R₉ (silica gel, n-Hex/Et₂O 4:1) 0.48. > 20:1 d.r. (¹H NMR). 96.5:3.5 e.r. Chiral HPLC. Chiralpak IC. n-Hex/i-PrOH 99:1. 1.0 mL/min. tᵣ 17.5 (minor), 23.7 (major). ¹H NMR (400 MHz, C₆D₆): δ 6.98-7.04 (2H, m, C⁺⁺H), 6.91 (1H, dd, J = 6.9, J = 2.3, C⁺⁺H), 6.79 (1H, dd, J = 7.1, J = 2.0, C⁺⁺H), 4.71 (1H, dd, J₁₁=₂₂F 49.2, J₁₁ = 11.3, J₁₂ = 3.8, α-fluoro CH₂), 2.88-2.97 (1H, m, CH₂), 2.75-2.84 (1H, m, CH₂), 2.21-2.30 (1H, m, CH₂), 2.14 (2H, t, J = 7.4, CH₂), 2.02 (1H, ddd, J₁₂ = 18.2, J₁₂ = 8.9, J₁₂ = 7.4, CH₂), 1.74-1.86 (1H, m, CH₂), 1.51-1.67 (2H, m, CH₂), 0.96 (3H, d, J = 7.3, CH₃) ppm. ¹³C NMR (100 MHz, C₆D₆): δ 214.9 (d, J₁₃⁻⁻F 5.1, ketone Cq), 142.1 (d, J₁₃⁻⁻F 2.1, Cq), 137.6 (d, J₁₃⁻⁻F 6.7, Cq), 128.8 (d, J₁₃⁻⁻F 0.9, CH), 127.6 (d, J₁₃⁻⁻F 1.9, CH), 127.0 (CH), 126.8 (d, J₁₃⁻⁻F 0.6, CH), 94.2 (d, J₁₃⁻⁻F 173.0, CH-F), 56.1 (d, J₁₃⁻⁻F 19.7, α-carbonyl Cq), 39.3 (CH₂), 38.8 (CH₂), 32.5 (d, J₁₃⁻⁻F 11.7, CH), 32.3 (d, J₁₃⁻⁻F 18.8, CH₂), 24.0 (CH₂), 20.3 (CH₂) ppm. ESI-HRMS (positif) M = C₁₂H₁₇FO, expected (M+NH₄)⁺ m/z 250.1602, observed (M+NH₄)⁺ m/z 250.1603. [α]²⁰₀ ±49.9 (c = 1.00, acetone).

β-Fluoro Spiroketone (B₂)⁸

![Chemical Structure](image)

**diastereomer 1**  
Chemical Formula: C₁₈H₁₉FO  
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 (R₃)-TIPS-TRIP (L₈) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na₂PO₄ (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C₆H₅F/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/Et₂O 95:5).  

White crystalline solid. Isolated yield 42% (21 mg, 0.08 mmol). R₉ (silica gel, n-Hex/Et₂O 9:1) 0.77. > 20:1 d.r. (¹H NMR). 95.5:4 e.r. Chiral HPLC. Chiralcel OD-H. n-Hex/i-PrOH 99:0.5. 1.0 mL/min. tᵣ 14.9 (minor), 25.3 (major). ¹H NMR (500 MHz, C₆D₆): δ 6.96 (1H, t, J = 7.7, C⁺⁺H), 6.88 (1H, d, J = 7.1, C⁺⁺H), 6.69 (1H, d, J = 7.9, C⁺⁺H), 4.87 (1H, dddd, J₁₁=₂₂F 49.8, J₁₂ = 12.7, J₁₂ = 4.5, α-fluoro CH₂), 2.90-2.96 (1H, m, diastereotopic CH₂), 2.88 (1H, sext, J = 6.0, benzylic CH), 2.23-2.33 (3H, m, CH₃), 2.01-2.08 (1H, m, CH₂), 1.99 (3H, s, CH₃), 1.90-1.97 (1H, m, CH₂), 1.72-1.78 (1H, m, CH₂), 1.60-1.68 (1H, m, CH₂), 0.84 (3H, d, J = 7.2, CH₃) ppm. ¹³C NMR (376 MHz, C₆D₆): δ 215.3 (d, J₁₃⁻⁻F 6.6, ketone Cq), 140.5 (d, J₁₃⁻⁻F 2.0, Cq), 138.5 (d, J₁₃⁻⁻F 7.8, Cq), 135.9 (Cq), 129.4 (CH), 126.9 (CH), 125.8 (d, J₁₃⁻⁻F 1.8, CH), 95.8 (d, J₁₃⁻⁻F 170.6, CH-F), 56.3 (d, J₁₃⁻⁻F 19.7, α-carbonyl Cq), 39.9 (CH₂), 39.5 (CH₂), 32.7 (d, J₁₃⁻⁻F 18.1, CH₂), 30.7 (d, J₁₃⁻⁻F 13.0, benzylic CH), 21.1 (CH₂), 20.8
(CH₂), 19.3 (CH₃) ppm. **ESI-HRMS (positif)** Μ = C_{16}H_{19}FO, expected (M+NH₄)⁺ m/z 264.1759, observed (M+NH₄)⁺ m/z 264.1762. [α]²⁰₀ β +61.3 (ε = 1.00, acetone).

**β-Fluoro Spiroketone (B₂⁵)**

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A₃) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₃)-TIPS-TRIP (L₂) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na₂PO₄ (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C₂H₂F/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/Et₂O 95:5). Colorless amorphous solid. Isolated yield 44% (22 mg, 0.09 mmol).

**Rᵣ (silica gel, n-Hex/Et₂O 4:1) 0.49. > 20:1 d.r. (¹H NMR).** 95.5:4.5 e.r. Chiral HPLC. Chiralpak IC. n-Hex/i-PrOH 99:1. 1.0 mL/min. tᵣ 8.0 (minor), 13.1 (major). **¹H NMR** (400 MHz, C₆D₆): δ 6.99 (1H, t, J 7.5, C(sp³)H), 6.93 (1H, d, J 7.0, C(sp³)H), 6.71 (1H, d, J 7.7, C(sp²)H), 4.43 (1H, ddd, J₁₋₂F 49.6, J₂₋₃ 3.4, α-fluoro CH₂), 2.79-2.88 (1H, m, benzylic CH), 2.19-2.28 (1H, m, diastereotopic CH₂), 2.08-2.17 (1H, m, diastereotopic CH₂), 2.11 (3H, s, CH₃), 1.96-2.02 (1H, m, CH₂), 1.75-1.89 (3H, m, CH₃), 1.42-1.60 (2H, m, CH₂), 1.13 (3H, dd, J₁₋₂ 7.0, J₂₋₃ 1.8, CH₃) ppm. **¹⁹F NMR** (376 MHz, C₆D₆): δ -178.0 (1F, s, C(sp³)-F) ppm. **¹³C NMR** (100 MHz, C₆D₆): δ 214.6 (δ₁₋₂F 3.9, ketone Cq), 140.4 (δ₂₋₃ 1.0, Cq), 137.1 (δ₃₋₄ 2.5, Cq), 135.7 (Cq), 129.6 (CH), 126.7 (CH), 126.4 (CH), 92.1 (d, J₁₋₂F 177.3, CH-F), 57.4 (d, J₁₋₂F 19.2, α-carbonyl Cq), 39.4 (d, J₁₋₂F 5.3, CH₃), 38.7 (CH₂), 32.3 (d, J₁₋₂F 18.6, CH₂), 29.2 (d, J₁₋₂F 4.8, CH), 22.7 (d, J₁₋₂F 4.0, CH), 19.8 (CH₃), 19.2 (CH₂) ppm. **ESI-HRMS (positif)** Μ = C₁₆H₁₉FO, expected (M+NH₄)⁺ m/z 264.1759, observed (M+NH₄)⁺ m/z 264.1760. [α]²⁰₀ β +16.5 (ε = 1.00, acetone).

**β-Fluoro Spiroketone (B₂⁶)**

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A₃) (49 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₃)-TIPS-TRIP (L₂) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na₂PO₄ (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C₂H₂F/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/Et₂O 93:1). White crystalline solid. Isolated yield 41% (22 mg, 0.08 mmol).

**Rᵣ (silica gel, n-Hex/Et₂O 4:1) 0.57. > 20:1 d.r. (¹H NMR).** 96:4 e.r. Chiral HPLC. Chiralpak IC. n-Hex/i-PrOH 98:2. 1.0 mL/min. tᵣ 11.6 (major), 16.1 (minor). **¹H NMR** (500 MHz, C₆D₆): δ 6.99 (1H, t, J 8.1, C(sp³)H), 6.50 (1H, d, J 7.8, C(sp³)H), 6.37 (1H, dd, J₁₋₂ 8.1, J₂₋₃ 0.6, C(sp³)H), 4.88 (1H, ddd, J₁₋₂F 49.5, J₂₋₃ 12.7, J₃₋₄ 4.2, α-fluoro CH₂), 3.48-3.55 (1H, broad m, diastereotopic CH₂), 3.25 (3H, s, methoxy CH₃-O), 2.94 (1H, sept., J 6.2, benzylic CH₂), 2.25-2.36 (3H, m, CH₂), 2.03-2.10 (1H, m, CH₂), 1.88-1.97 (1H, m, CH₂), 1.77-1.82 (1H, m, CH₂), 1.61-1.69 (1H, m, CH₂), 1.14 (3H, d, J 7.1, CH₃) ppm. **¹⁹F NMR** (376 MHz, C₆D₆): δ -187.6 (1F, s, C(sp³)-F) ppm. **¹³C NMR** (125 MHz, C₆D₆): δ 215.1 (d, J₁₋₂F 5.9, ketone Cq), 157.3 (methoxy Cq-O), 139.5 (d, J₁₋₂F 7.9, Cq), 131.3 (d, J₁₋₂F 2.4, Cq), 127.7 (CH), 119.6 (d, J₁₋₂F 2.1, CH), 108.6 (CH), 95.7 (d, J₁₋₂F 171.2, CH-F), 56.0 (d, J₁₋₂F 19.9, α-carbonyl Cq), 54.9 (methoxy CH₃-O), 39.6 (CH₂), 39.2 (CH₂), 32.2 (d, J₁₋₂F 18.1, CH₂), 28.3 (d, J₁₋₂F 13.2, benzylic...
According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-\(\text{A}_{3}\)) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (\(\text{R}_{3}\))-TIPPS-TRIP (\(\text{L}_{8}\)) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor\textsuperscript{TM} (106 mg, 0.30 mmol, 1.5 equiv.), and dried \(\text{Na}_{2}\text{PO}_{4}\) (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous \(\text{C}_{6}\text{H}_{5}\text{F}\)/n-Hex 1:1 (\(\nu/\nu\)) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (\(n\)-hexane \(\rightarrow\) \(n\)-hexane/Et\(_2\)O 9:1).

White crystalline solid. Isolated yield 43% (23 mg, 0.09 mmol). \(\text{R}_{f}\) (silica gel, \(n\)-Hex/Et\(_2\)O 4:1) 0.24. > 20:1 d.r. (\(\text{H}^\text{NMR}\)). 95.5:4.5 e.r.

\(\text{Chiral HPLC. Chiralcel OJ-H. n-Hex/i-PrOH 95:5. 1.0 mL/min.} \text{t}_{\text{R}} 10.0\) (minor), 18.3 (major). \(\text{^1H NMR (500 MHz, C}_{6}\text{D}_{5}: \delta 7.02 (1\text{H, s, } \text{J} 8.0, \text{C}^{\text{Cw}}), 6.55 (1\text{H, dd, } \text{J} 8.0, \text{J} 8.6, \text{J} ^{\text{Cw}}), 6.44 (1\text{H, dd, } \text{J} 8.1, \text{J} 8.0, \text{C}^{\text{Cw}}), 4.40 (1\text{H, dd, } \text{J} ^{\text{Cw}} - 4.9, \text{J} 8.9, \text{J} 3.7, \text{J} \alpha-\text{fluoro CH}), 3.31 (3\text{H, s, methoxy CH-3O}), 3.27 (1\text{H, sext. }, \text{J} 7.9, \text{benzyl CH}), 2.19-2.33 (2\text{H, m, CH2}), 1.89-2.08 (4\text{H, m, CH2}), 1.62 (3\text{H, dd, } \text{J} 6.8, \text{J} 1.5, \text{CH})), 1.56-1.65 (1\text{H, m, CH2}), 1.46-1.54 (1\text{H, m, CH2}) \text{ppm.} \text{^19F NMR (376 MHz, C}_{6}\text{D}_{5}: \delta -177.7 (1\text{F, s, C(sp\textsuperscript{3})-F}) \text{ppm.} \text{^13C NMR (125 MHz, C}_{6}\text{D}_{5}: \delta 214.6 (2\text{F, J}^{\text{Cw}} 3.3, \text{ketone Cq}), 157.6 (\text{methoxy Cq-O}), 138.5 (2\text{F, J}^{\text{Cw}} 4.1, \text{Cq}), 131.1 (2\text{F, J}^{\text{Cw}} 1.6, \text{Cq}), 127.2 (\text{CH}), 120.2 (2\text{F, J}^{\text{Cw}} 0.9, \text{CH}), 108.8 (\text{CH}), 93.0 (2\text{F, J}^{\text{Cw}} 177.6, \text{CH-F}), 56.7 (2\text{F, J}^{\text{Cw}} 19.2, \text{J} \alpha-\text{carbonyl Cq}), 54.8 (\text{methoxy CH3O}), 39.1 (\text{CH3}), 38.2 (2\text{F, J}^{\text{Cw}} 4.1, \text{CH2}), 32.3 (2\text{F, J}^{\text{Cw}} 18.5, \text{CH2}), 27.7 (2\text{F, J}^{\text{Cw}} 7.3, \text{benzyl CH}), 22.6 (2\text{F, J}^{\text{Cw}} 2.6, \text{CH2}), 19.7 (\text{CH2}) \text{ppm.} \text{ESI-HRMS (positif) M} = \text{C}_{16}\text{H}_{19}\text{F}_{2}\text{O}, \text{expected (M+H})^\text{+) m/z 263.1442, observed (M+H})^\text{+) m/z 263.1443.} \text{[\alpha]^{20}_D +47.5 (c = 1.00, acetone).} \text{ESI-HRMS (positif) M} = \text{C}_{16}\text{H}_{19}\text{F}_{2}\text{O}, \text{expected (M+H})^\text{+) m/z 263.1442, observed (M+H})^\text{+) m/z 263.1440.} \text{[\alpha]^{20}_D +7.8 (c = 1.00, acetone).}
(para(F)-CH), 122.9 (t, J\textsuperscript{CF} 2.6, meta(F)-CH), 113.7 (d, J\textsuperscript{CF} 22.3, ortho(F)-CH), 94.9 (d, J\textsuperscript{CF} 172, CH-F), 55.7 (dd, J\textsuperscript{CF} 20.6, J\textsuperscript{CF} 1.9, α-carbonyl Cq), 39.4 (CH\textsubscript{3}), 38.6 (CH\textsubscript{3}), 31.5 (d, J\textsuperscript{CF} 18.7, benzylic CH), 30.2 (CH\textsubscript{3}), 21.8 (CH\textsubscript{2}), 20.6 (d, J\textsuperscript{CF} 2.1, CH\textsubscript{2}) ppm. ESI-HRMS (positif) M = C\textsubscript{15}H\textsubscript{16}F\textsubscript{2}O, expected (M+NH\textsubscript{4})\textsuperscript{+} m/z 268.1508, observed (M+NH\textsubscript{4})\textsuperscript{+} m/z 268.1507. [α]\textsuperscript{D}	extsuperscript{20} +62.6 (c = 1.00, acetone).

\textbf{β-Fluoro Spiroketone (B\textsubscript{4}\textsuperscript{(S)})}

According to the General Procedure: chiral, racemic allylic cyclobutanol \textit{rac-A\textsubscript{4}} (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R\textsubscript{a})-TIPS-TRIP (L\textsubscript{9}) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor\textsuperscript{TM} (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na\textsubscript{3}PO\textsubscript{4} (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C\textsubscript{6}H\textsubscript{6}/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\textsubscript{2}O 95:5).

White crystalline solid. Isolated yield 43% (22 mg, 0.09 mmol). R\textsubscript{f} (silica gel, n-Hex/Et\textsubscript{2}O 4:1) 0.58. > 20:1 d.r. \textit{\textit{1H} NMR} 98:2 e.r. Chiral HPLC. Chiralpak IC. n-Hex/i-PrOH 99:1. 1.0 mL/min. t\textsubscript{R} 17.3 (minor), 26.0 (major). \textit{\textit{1H} NMR} (500 MHz, C\textsubscript{6}D\textsubscript{6}): δ 6.70-6.81 (2H, m, C=CH), 6.52 (1H, dd, J\textsubscript{H-H} 7.4, J\textsubscript{1.1, C=CH} 4.24 (1H, J\textsubscript{dd, J\textsuperscript{H-H} 1.5, J\textsubscript{1.1, C=CH} 4.90, J\textsubscript{10.0, J\textsubscript{2.3, C=CH} 10.9, J\textsubscript{3.9, α-fluoro CH} 2.99 (1H, sext, J\subscript{7.1, benzylic CH} 2.13-2.29 (2H, m, diastereotopic CH\textsubscript{2}), 1.94-2.06 (2H, m, diastereotopic CH\textsubscript{2}), 1.75-1.91 (2H, m, CH\textsubscript{2}), 1.56-1.67 (1H, m, CH\textsubscript{2}, 1.50 (3H, dt, J\textsubscript{H-H} 6.8, J\textsuperscript{H-H} 1.4, CH\textsubscript{3}), 1.40-1.52 (1H, m, CH\textsubscript{2}) ppm. \textit{\textit{19F} NMR} (376 MHz, C\textsubscript{6}D\textsubscript{6}): δ -112.9 (1F, s, C=CH), -181.5 (1F, s, C(sp\textsuperscript{3})-F) ppm. \textit{\textit{13C} NMR} (125 MHz, C\textsubscript{6}D\textsubscript{6}): δ 214.3 (d, J\textsuperscript{CF} 3.2, ketone Cq), 161.7 (d, J\textsuperscript{CF} 244, ipso(F)-Cq), 139.9 (t, J\textsuperscript{CF} 5.2, meta(F)-Cq), 129.8 (dd, J\textsuperscript{CF} 15.0, J\textsuperscript{CF} 1.8, ortho(F)-Cq), 128.1 (para(F)-CH), 123.2 (d, J\textsuperscript{CF} 1.3, meta(F)-CH), 114.0 (d, J\textsuperscript{CF} 22.9, ortho(F)-CH), 93.3 (d, J\textsuperscript{CF} 176, CH-F), 56.2 (dd, J\textsuperscript{CF} 19.9, J\textsuperscript{CF} 2.1, α-carbonyl Cq), 39.1 (CH\textsubscript{3}), 37.6 (d, J\textsuperscript{CF} 3.1, CH\textsubscript{2}), 32.1 (d, J\textsuperscript{CF} 18.9, CH\textsubscript{3}), 27.7 (d, J\textsuperscript{CF} 8.9, CH\textsubscript{3}), 22.5 (dd, J\textsuperscript{CF} 6.2, J\textsuperscript{CF} 1.6, benzylic CH), 19.8 (CH\textsubscript{3}) ppm. ESI-HRMS (positif) M = C\textsubscript{15}H\textsubscript{16}F\textsubscript{2}O, expected (M+NH\textsubscript{4})\textsuperscript{+} m/z 268.1508, observed (M+NH\textsubscript{4})\textsuperscript{+} m/z 268.1508. [α]\textsuperscript{D}	extsuperscript{20} +23.9 (c = 1.00, acetone).

\textbf{β-Fluoro Spiroketone (B\textsubscript{5}\textsuperscript{(R)})}

According to the General Procedure: chiral, racemic allylic cyclobutanol \textit{rac-A\textsubscript{5}} (50 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R\textsubscript{a})-TIPS-TRIP (L\textsubscript{9}) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor\textsuperscript{TM} (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na\textsubscript{3}PO\textsubscript{4} (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C\textsubscript{6}H\textsubscript{6}/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\textsubscript{2}O 95:5).

Colorless oil. Isolated yield 41% (22 mg, 0.08 mmol). R\textsubscript{f} (silica gel, n-Hex/Et\textsubscript{2}O 4:1) 0.68. > 20:1 d.r. \textit{\textit{1H} NMR} 94:5.5 e.r. Chiral HPLC. Chiralcel OJ-H. n-Hex/i-PrOH 99:1. 1.0 mL/min. t\textsubscript{R} 7.5 (major), 10.1 (minor). \textit{\textit{1H} NMR} (500 MHz, C\textsubscript{6}D\textsubscript{6}): δ 7.05 (1H, dd, J\textsubscript{H-H} 7.9, J\textsubscript{1.2, C=CH} 6.64 (1H, t, J\textsubscript{H-H} 7.9, J\textsubscript{1.0, C=CH} 5.42 (1H, dd, J\textsuperscript{H-H} 48.6, J\textsubscript{1.2, C=CH} 12.3, J\textsubscript{1.0, C=CH} 4.3, α-fluoro CH), 3.13-3.21 (1H, m, benzylic CH), 2.36-2.42 (1H, m, diastereotopic CH\textsubscript{2}), 2.19-2.26 (1H, m, CH\textsubscript{2}), 2.02-2.10 (1H, m, CH\textsubscript{2}), 1.65-1.81 (3H, m, CH\textsubscript{2}), 1.45-1.57 (2H, m, CH\textsubscript{2}), 1.07 (3H, d, J\textsubscript{H-H} 7.1, CH\textsubscript{3}) ppm. \textit{\textit{19F} NMR} (376 MHz, C\textsubscript{6}D\textsubscript{6}): δ -190.2 (1F, s, C(sp\textsuperscript{3})-F) ppm. \textit{\textit{13C} NMR} (125 MHz, C\textsubscript{6}D\textsubscript{6}): δ 220.1 (ketone Cq), 142.6 (d, J\textsuperscript{CF} 8.4,
C<sub>q</sub>), 138.5 (d, J<sup>CF</sup> 2.4, C<sub>q</sub>), 134.2 (C<sub>q</sub>), 128.6 (CH), 128.2 (CH), 127.3 (d, J<sup>CF</sup> 2.3, CH), 91.8 (d, J<sup>CF</sup> 176.3, CH-F), 58.6 (d, J<sup>CF</sup> 19.6, α-carbonyl C<sub>q</sub>), 40.4 (CH<sub>3</sub>), 35.9 (d, J<sup>CF</sup> 5.0, CH<sub>2</sub>), 33.1 (d, J<sup>CF</sup> 18.2, CH<sub>3</sub>), 31.9 (d, J<sup>CF</sup> 12.5, benzylic CH), 21.0 (CH<sub>3</sub>), 20.0 (d, J<sup>CF</sup> 3.0, CH<sub>2</sub>) ppm. **ESI-HRMS (positive)** M = C<sub>15</sub>H<sub>16</sub>CIF<sub>4</sub>, expected (M+NH<sub>4</sub>)<sup>+</sup> m/z 284.1212, observed (M+NH<sub>4</sub>)<sup>+</sup> m/z 284.1209. [α]<sup>20</sup><sub>β</sub> +61.7 (c = 1.00, acetone).

**β-Fluoro Spiroketone (B<sub>6</sub>)**

![Structure of β-Fluoro Spiroketone (B<sub>6</sub>)]

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A<sub>6</sub>) (50 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R<sub>6</sub>)-TIPS-TRIP (L<sub>6</sub>) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor<sup>TM</sup> (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na<sub>2</sub>P<sub>2</sub>O<sub>7</sub> (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C<sub>15</sub>H<sub>16</sub>F<sub>n</sub>-Hex:1:1 (<i>v/v</i>) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (n-hexane → n-hexane/EtO<sub>2</sub> 95:5). White crystalline solid. Isolated yield 45% (21 mg, 0.09 mmol). R<sub>f</sub> (silica gel, n-hexane/EtO<sub>2</sub> 4:1) 0.20 > 20:1 d.r. (1<sup>1</sup>H NMR).

96:4 e.r. Chiral HPLC. Chiralpak IC. n-Hex/i-PrOH 99:1. 1.0 mL/min. <i>t</i><sub>f</sub> 20.1 (minor), 23.0 (major).

**1<sup>1</sup>H NMR** (500 MHz, C<sub>6</sub>D<sub>6</sub>): δ 7.07 (1H, d, J 7.9, C<sup>αH</sup>), 6.67 (1H, d, J 7.9, C<sup>αH</sup>), 6.54 (1H, d, J 7.9, C<sup>αH</sup>), 4.73 (1H, ddd, J<sup>CF</sup> 6.6, J<sup>CF</sup> 1.8, J<sup>CF</sup> 1.8), 1.25 (6H, ddd, J<sup>CF</sup> 1.8, J<sup>CF</sup> 1.8, J<sup>CF</sup> 1.8), 1.51 (6H, ddd, J<sup>CF</sup> 1.8, J<sup>CF</sup> 1.8, J<sup>CF</sup> 1.8), 0.99 (3H, d, J 7.2, CH<sub>3</sub>) ppm. **19<sup>F</sup>NMR** (376 MHz, C<sub>6</sub>D<sub>6</sub>): δ -188.0 (1F, s, C(s)+<sup>3</sup>F) ppm. **13<sup>C</sup>NMR** (125 MHz, C<sub>6</sub>D<sub>6</sub>): δ 214.6 (d, J<sup>CF</sup> 1.9, ketone C<sub>q</sub>), 140.7 (d, J<sup>CF</sup> 8.0, C<sub>q</sub>), 140.0 (d, J<sup>CF</sup> 2.2, C<sub>q</sub>), 134.5 (C<sub>q</sub>) ppm. 128.5 (C<sub>q</sub>), 126.5 (d, J<sup>CF</sup> 1.8, CH<sub>3</sub>), 95.4 (d, J<sup>CF</sup> 171.4, CH-F), 56.1 (d, J<sup>CF</sup> 20.4, α-carbonyl C<sub>q</sub>), 39.6 (CH<sub>3</sub>) ppm. **ESI-HRMS (positive)** M = C<sub>15</sub>H<sub>16</sub>CIF<sub>4</sub>, expected (M+NH<sub>4</sub>)<sup>+</sup> m/z 284.1212, observed (M+NH<sub>4</sub>)<sup>+</sup> m/z 284.1215. [α]<sup>20</sup><sub>β</sub> +15.0 (c = 1.00, acetone).

**β-Fluoro Spiroketone (B<sub>6</sub>)**

![Structure of β-Fluoro Spiroketone (B<sub>6</sub>)]

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A<sub>6</sub>) (40 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R<sub>6</sub>)-TIPS-TRIP (L<sub>6</sub>) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor<sup>TM</sup> (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na<sub>2</sub>P<sub>2</sub>O<sub>7</sub> (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C<sub>15</sub>H<sub>16</sub>F<sub>n</sub>-Hex:1:1 (<i>v/v</i>) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (n-hexane → n-hexane/EtO<sub>2</sub> 95:5). Colorless oil. Isolated yield 46% (20 mg, 0.09 mmol). R<sub>f</sub> (silica gel, n-Hex/EtO<sub>2</sub> 9:1) 0.67 > 20:1 d.r. (1<sup>1</sup>H NMR). 96:4 e.r. Chiral HPLC. Chiralcel OJ-H. n-Hex/i-PrOH 99:1. 1.0 mL/min. <i>t</i><sub>f</sub> 13.7 (major), 18.4 (minor). **1<sup>1</sup>H NMR** (500 MHz, C<sub>6</sub>D<sub>6</sub>): δ 6.96-7.06 (3H, m, C<sup>αH</sup>), 6.88 (1H, d, J 7.5, C<sup>αH</sup>), 4.34 (1H, ddd, J<sup>CF</sup> 50.7, J<sub>2</sub> 12.1, J<sub>3</sub> 4.0, α-fluoro CH), 2.88 (1H, ddd, J<sub>2</sub> 18.2, J<sub>3</sub> 11.3, J<sub>4</sub> 6.5, J<sub>5</sub> 1.8, diastereotopic CH<sub>2</sub>), 2.63 (1H, ddd, J<sub>2</sub> 18.2, J<sub>3</sub> 10.6, J<sub>4</sub> 7.3, CH<sub>2</sub>), 2.49 (1H, sept, J 6.5, benzylic CH), 2.36 (1H, td, J<sub>2</sub> 12.0, J<sub>3</sub> 5.7, CH<sub>2</sub>), 2.27 (1H, ddd, J<sub>2</sub> 18.1, J<sub>3</sub> 11.0, J<sub>4</sub> 6.3, J<sub>5</sub> 1.6, CH<sub>2</sub>), 1.88-2.02 (2H, m, CH<sub>2</sub>), 1.08 (3H, dd, J<sub>2</sub> 6.8, J<sub>3</sub> 0.9, CH<sub>3</sub>) ppm. **19<sup>F</sup>NMR** (376 MHz, C<sub>6</sub>D<sub>6</sub>): δ -185.0 (1F, s, C(s)+<sup>3</sup>F) ppm. **13<sup>C</sup>NMR** (125 MHz, C<sub>6</sub>D<sub>6</sub>): δ 206.3 (d, J<sup>CF</sup> 4.7, ketone C<sub>q</sub>), 140.6 (d, J<sup>CF</sup> 2.4, C<sub>q</sub>), 133.5 (d, J<sup>CF</sup> 8.7, C<sub>q</sub>), 127.50 (CH), 127.49 (CH), 127.0 (d, J<sup>CF</sup>
According to the General Procedure: chiral, racemic allylic cyclopropanol (rac-\(A_8\)) (40 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R\(_3\))-TIPS-TRIP (L\(_4\)) (12 mg, 0.01 mmol, 5 mol\%), powdered Selectfluor\(^\text{TM}\) (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na\(_3\)PO\(_4\) (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C\(_6\)H\(_5\)/n-Hex 1:1 (v/v) (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (n-hexane \(\rightarrow\) n-hexane/Et\(_2\)O 95:5). Colorless oil. Isolated yield 44\% (19 mg, 0.09 mmol). \(R_f\) (silica gel, n-Hex/Et\(_2\)O 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. \(R_t\) 15.9 (minor), 17.9 (major). \(^1\)H NMR (500 MHz, C\(_6\)D\(_6\)): \(\delta\) 6.96-7.02 (2H, m, C\(=\)H), 6.88-6.93 (2H, m, C\(=\)H), 4.68 (1H, ddd, J\(^{13}C\)\(-H\) 50.3, J\(_{12}\) 11.3, J\(_{3}\) 3.9, \(\alpha\)-fluoro CH), 2.83-2.93 (2H, m, benzylic CH + diastereotopic CH\(_2\)), 2.60-2.69 (2H, m, diastereotopic CH\(_2\)), 2.20 (1H, ddd, J\(_{12}\) 18.9, J\(_{3}\) 13.0, J\(_{1}\) 11.9, CH\(_2\)), 2.00 (1H, ddd, J\(_{12}\) 18.0, J\(_{3}\) 11.3, J\(_{1}\) 6.8, CH\(_2\)), 1.66 (1H, t, J\(_{1}\) 13.0, J\(_{3}\) 3.7, CH\(_2\)), 0.89 (3H, d, J 7.3, CH\(_3\)) ppm. \(^{19}\)F NMR (376 MHz, C\(_6\)D\(_6\)): \(\delta\) -187.0 (1F, s, C(sp\(^3\))-F) ppm. \(^{13}\)C NMR (125 MHz, C\(_6\)D\(_6\)): \(\delta\) 207.9 (d, J\(_{CF}\) 5.4, ketone C\(_q\)), 141.0 (d, J\(_{CF}\) 2.2, C\(_q\)), 132.9 (d, J\(_{CF}\) 7.9, C\(_q\)), 129.1 (CH), 127.5 (CH), 127.0 (CH), 126.4 (d, J\(_{CF}\) 2.0, CH), 90.9 (d, J\(_{CF}\) 172, CH-F), 73.1 (d, J\(_{CF}\) 21.3, \(\alpha\)-carbonyl C\(_q\)), 44.2 (CH\(_2\)), 33.2 (d, J\(_{CF}\) 18.3, CH\(_2\)), 32.7 (d, J\(_{CF}\) 11.2, benzylic CH), 23.8 (CH\(_3\)), 22.5 (d, J\(_{CF}\) 1.1, CH\(_3\)) ppm. ESI-HRMS (positive) M = C\(_{14}\)H\(_{15}\)FO, expected (M+NH\(_4\))\(^+\) m/z 236.1446, observed (M+NH\(_4\))\(^+\) m/z 236.1449. [\(|\alpha|\)\(^{19}\)F\(d\) +18.9 (c = 1.00, acetone).
**HRMS (positif)** $M = C_{13}H_{17}FO$, expected (M+NH$_4$)$^+$ m/z 250.1602, observed (M+NH$_4$)$^+$ m/z 250.1604. [α]$^{20}$D +27.8 ($c = 1.00$, acetone).

**β-Fluoro Spiroketone (B$_{7}^{\*}$)**

![diastereomer 2](image1)

**Chemical Formula:** C$_{13}$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$_A$) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor$^{\text{TM}}$ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na$_3$PO$_4$ (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$_2$O 95:5).

Colorless oil. Isolated yield 44% (20 mg, 0.09 mmol). R$_f$ (silica gel, n-Et$_2$O 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. $t_f$ 7.6 (major), 8.6 (minor). $^1$H NMR (500 MHz, $C_6D_6$): $\delta$ 6.97 (1H, $t$, $J = 7.7$, C$_{\text{ar}}$H), 6.88 (1H, $d$, $J = 7.1$, C$_{\text{ar}}$H), 6.80 (1H, $d$, $J = 7.8$, C$_{\text{ar}}$H), 4.86 (1H, $d$, $J = 6$, C$_{\text{ar}}$H), 4.78 (1H, $d$, $J = 4.0$, $\alpha$-fluoro CH)$_2$, 2.96 (1H, $d$, $J = 12.8$, J, $J = 1.95$, CH$_2$), 2.35 (1H, $dd$, $J = 12.3$, J, $J = 6.5$, CH$_2$), 2.11 (1H, $dd$, $J = 12.0$, J, $J = 10.7$, CH$_2$), 1.95 (3H, s, CH$_3$), 1.78-1.84 (1H, $m$, CH$_3$), 0.77 (3H, $m$, J, $J = 7.2$, CH$_3$) ppm. $^{19}$F NMR (376 MHz, $C_6D_6$): $\delta$ -189.1 (1F, s, C(sp$^3$)-F) ppm. $^{13}$C NMR (125 MHz, $C_6D_6$): $\delta$ 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, $C_{\text{ar}}$F), 130.0 (CH), 127.1 (d, $J_{C-F}$ = 0.8, CH), 124.5 (d, $J_{C-F}$ = 2.1, CH), 91.0 (d, $J_{C-F}$ = 169, CH-F), 73.6 (d, $J_{C-F}$ = 21.2, $\alpha$-carbonyl C$_q$), 44.5 (CH$_2$), 33.6 (d, $J_{C-F}$ = 17.6, CH$_2$), 30.9 (d, $J_{C-F}$ = 12.5, benzylic CH), 22.8 (CH$_2$), 21.1 (CH$_3$), 19.2 (CH$_3$) ppm. ESI-HRMS (positif) $M = C_{13}H_{17}FO$, expected (M+NH$_4$)$^+$ m/z 250.1602, observed (M+NH$_4$)$^+$ m/z 250.1604. [α]$^{20}$D +10.0 ($c = 1.00$, acetone).

**β-Fluoro Spiroketone (B$_{8}^{\*}$)**

![diastereomer 1](image2)

**Chemical Formula:** C$_{13}$H$_{14}$F$_2$O$_2$  
**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$^{\text{TM}}$ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na$_3$PO$_4$ (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$_2$O 95:5).

White crystalline solid. Isolated yield 41% (19 mg, 0.08 mmol). R$_f$ (silica gel, n-Hex/Et$_2$O 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. $t_f$ 8.0 (major), 13.1 (major). $^1$H NMR (500 MHz, $C_6D_6$): $\delta$ 6.70-6.79 (2H, $m$, C$_{\text{ar}}$H), 6.59 (1H, $d$, $J = 7.6$, C$_{\text{ar}}$H), 4.16 (1H, $dd$, $J = 1.95$, CH$_2$), 2.89 (1H, sext., $J = 7.3$, benzylic CH), 2.78 (1H, $dd$, $J = 18.2$, J, $J = 11.2$, J, $J = 6.8$, J, $J = 1.2$, 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, $J = 6.9$, J, $J = 1.3$, CH$_3$), 1.37 (3H, dt, $J = 6.6$, J, $J = 1.3$, CH$_3$) ppm. $^{19}$F NMR (376 MHz, $C_6D_6$): $\delta$ -112.0 (1F, s, C$_{\text{ar}}$F), -181.6 (1F, s, C(sp$^3$)-F) ppm. $^{13}$C NMR (125 MHz, $C_6D_6$): $\delta$ 205.6 (d, $J_{C-F}$ = 3.7, ketone C$_q$), 162.0 (d, $J_{C-F}$ = 245.3, ipso(C)-C$_q$), 135.7 (dd, $J_{C-F}$ = 6.8, J, $J_{C-F}$ = 4.9, ortho(F)-C$_q$), 128.4 (para(F)-CH), 125.9 (meta(F)-C$_q$), 122.1 (dd, $J_{C-F}$ = 2.9, $J_{C-F}$ = 1.9, meta(F)-CH), 114.5 (d, $J_{C-F}$ = 22.9, ortho(F)-CH), 91.7 (d, $J_{C-F}$ = 174.7, CH-F), 72.6 (dd, $J_{C-F}$ = 21.2, $J_{C-F}$ = 1.9, $\alpha$-carbonyl C$_q$), 43.9 (CH$_2$), 33.1 (d, $J_{C-F}$ = 18.3, CH$_2$), 30.5 (CH$_2$), 28.2 (d, $J_{C-F}$ = 10.0, benzylic CH), 22.5 (dd, $J_{C-F}$ = 6.7, $J_{C-F}$ = 3.3, CH$_3$), 22.2 (d, $J_{C-F}$ = 3.3, CH$_2$) ppm. ESI-HRMS (positif) $M = C_{13}H_{14}F_2O_2$, expected (M+NH$_4$)$^+$ m/z 250.1602, observed (M+NH$_4$)$^+$ m/z 250.1607. [α]$^{20}$D +10.0 ($c = 1.00$, acetone).
expected (M+NH₄)⁺ m/z 254.1351, observed (M+NH₄)⁺ m/z 254.1360. [α]²⁰_D +33.3 (c = 1.00, acetone).

**β-Fluoro Spiroketone (B₈⁻)**

According to the General Procedure: chiral, racemic allylic cyclopropanol (rac-A₈) (44 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₈)-TIPS-TRIP (L₈) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na₃PO₄ (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C₆H₅F/n-Hex:1:v/v (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (n-hexane → n-hexane/Et₂O 95:5). Colorless oil. Isolated yield 42% (19 mg, 0.08 mmol). R_F (silica gel, n-Hex/Et₂O 9:1) 0.68. > 20:1 d.r. ¹H NMR: 96.4 e.r. Chiral HPLC. Chiralcel OJ-H. n-Hex/d-PrOH 99:1. 1.0 mL/min. t_R 10.7 (major), 24.5 (minor). ¹H NMR (500 MHz, C₆D₆): δ 6.74 (1H, q, J 8.0, C₆H), 6.66 (1H, t, J 10.1, C₆H), 6.58 (1H, d, J 7.8, C₆H), 5.04 (1H, ddd, J = 5.5, 7.6, 14.3, α-fluoro CH₂), 2.97-3.04 (1H, m, benzylic CH), 2.86 (1H, dddd, J = 23.2, J = 13.7, J = 9.6, J = 1.9, diastereotropic CH₂), 2.65 (1H, dddd, J = 23.1, J = 13.2, J = 7.7, CH₂), 2.34 (1H, dddd, J = 14.2, J = 7.7, J = 1.8, CH₂), 1.66-1.74 (1H, m, CH₂), 1.56-1.64 (1H, m, CH₂), 0.95 (3H, dd, J = 7.2, J = 2.6, CH₃) ppm. ¹⁹F NMR (376 MHz, C₆D₆): δ -112.0 (1F, s, C₆F), -181.6 (1F, s, C(sp³)-F) ppm. ¹³C NMR (125 MHz, C₆D₆): δ 210.0 (ketone C), 161.1 (d, J = 244.7, ipsoF-C), 138.3 (d, J = 7.6, J = 4.4, orthoF-C), 128.7 (d, J = 9.0, paraF-CH), 123.3 (t, J = 2.1, metaF-CH), 114.3 (d, J = 22.3, orthoF-CH), 88.2 (d, J = 176.3, CH-F), 73.2 (dd, J = 24.0, J = 1.6, α-carbonyl C), 45.8 (CH₂), 32.5 (d, J = 18.5, CH₂), 27.7 (dd, J = 11.1, J = 1.6, benzylic CH), 24.8 (d, J = 5.2, CH₃), 21.4 (d, J = 2.7, CH₃) ppm. ESI-HRMS (positif) M = C₁₄H₁₄F₂O, expected (M+NH₄)⁺ m/z 254.1351, observed (M+NH₄)⁺ m/z 254.1355. [α]²⁰_D +7.9 (c = 1.00, acetone).

**β-Fluoro Spiroketone (B₈⁺)**

According to the General Procedure: chiral, racemic allylic cyclopropanol (rac-A₈) (47 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₈)-TIPS-TRIP (L₈) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor™ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na₃PO₄ (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C₆H₅F/n-Hex:1:v/v (total volume: 3.0 mL, 0.07 M). Purified by flash chromatography on silica gel (n-hexane → n-hexane/Et₂O 95:5). Pale-yellow amorphous solid. Isolated yield 40% (20 mg, 0.08 mmol). R_F (silica gel, n-Hex/Et₂O 9:1) 0.55. > 20:1 d.r. ¹H 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). ¹H NMR (500 MHz, C₆D₆): δ 6.97 (1H, t, J = 7.5, C₆H), 6.92 (1H, d, J = 6.7, C₆H), 6.86 (1H, d, J = 7.7, C₆H), 4.32 (1H, dddd, J = 50.8, 9.5, 4.3, α-fluoro CH₂), 2.75-2.83 (2H, m, diastereotropic CH₂ + benzylic CH₂), 2.05 (3H, s, CH₃), 1.94-2.03 (2H, m, CH₂), 1.85-1.91 (1H, m, CH₂), 1.23 (3H, dddd, J = 7.0, J = 1.3, CH₃) ppm. ¹⁹F NMR (376 MHz, C₆D₆): δ -179.2 (1F, s, C(sp³)-F) ppm. ¹³C NMR (125 MHz, C₆D₆): δ 206.3 (d, J = 4.1, ketone C), 139.3 (d, J = 18.8, C), 136.5 (C), 133.1 (d, J = 5.4, C), 130.4 (CH), 126.7 (CH), 124.8 (d, J = 1.0, CH), 92.3 (d, J = 176, CH-F), 73.4 (d, J = 20.3, α-carbonyl C), 43.6 (CH₂), 33.1 (d, J = 18.2, CH₂), 29.8 (d, J = 8.1, benzylic CH), 23.4 (d, J = 2.1,
According to the General Procedure: chiral, racemic allylic cyclopropanol (rac-A\textsubscript{40}) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R\textsubscript{a})-TIPS-TRIP (L\textsubscript{a}) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor\textsuperscript{TM} (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na\textsubscript{3}PO\textsubscript{4} (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C\textsubscript{6}H\textsubscript{5}F/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\textsubscript{2}O 95:5). Colorless oil. Isolated yield 45% (23 mg, 0.09 mmol). R\textsubscript{f} (silica gel, n-Hex/Et\textsubscript{2}O 4:1) 0.53. > 20:1 d.r. (\textsuperscript{1}H NMR). 96:4 e.r.

**\textbf{β-Fluoro Spiroketone (B\textsubscript{5})}**

According to the General Procedure: chiral, racemic allylic cyclopropanol (rac-A\textsubscript{40}) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R\textsubscript{a})-TIPS-TRIP (L\textsubscript{a}) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor\textsuperscript{TM} (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na\textsubscript{3}PO\textsubscript{4} (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C\textsubscript{6}H\textsubscript{5}F/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\textsubscript{2}O 95:5). White amorphous solid. Isolated yield 87% (43 mg, 0.17 mmol). R\textsubscript{f} (silica gel, n-Hex/Et\textsubscript{2}O 4:1) 0.56. > 20:1 d.r. (\textsuperscript{1}H NMR). 94.5:5.5 e.r. Chiral HPLC. Chiralpak IC. n-Hex/i-PrOH 99:1. 1.0 mL/min. t\textsubscript{R} 11.2 (major), 15.1 (minor). \textsuperscript{1}H NMR (500 MHz, C\textsubscript{6}D\textsubscript{6}): δ 7.12 (1H, dd, J = 8.0, J = 7.4), 6.91 (1H, dd, J = 8.0, J = 7.4), 4.51 (1H, dd, J = 8.0, J = 7.4). 6.97 (1H, td, J = 5.0, J = 1.4), 6.80 (1H, dd, J = 7.9, J = 1.2), 4.71 (1H, dd, J = 11.3), 49.3, J = 12.4, J = 4.2, α-fluoro CH\textsubscript{2}), 2.82 (1H, td, J = 12.5, J = 7.2, diastereotopic CH\textsubscript{2}), 2.18-2.31 (3H, m, CH\textsubscript{2}), 2.04 (1H, dd, J = 18.0, J = 8.7, J = 6.6, CH\textsubscript{2}), 1.81-1.90 (1H, m, CH\textsubscript{2}), 1.72 (1H, dd, J = 14.8, J = 10.7, J = 4.2, CH\textsubscript{2}), 1.55-1.64 (1H, m, CH\textsubscript{2}), 1.27 (3H, s, diastereotopic gem-dimethyl CH\textsubscript{3}), 1.00 (3H, s, diastereotopic gem-dimethyl CH\textsubscript{3}) ppm. 1\textsuperscript{3}F NMR (376 MHz, C\textsubscript{6}D\textsubscript{6}): δ -185.6 (1F, s, C(sp\textsuperscript{3})-F) ppm. 1\textsuperscript{3}C NMR (125 MHz, C\textsubscript{6}D\textsubscript{6}): δ 215.1 (d, J = 5.0, ketone C\textsubscript{q}), 145.8 (d, J = 2.4, C\textsubscript{q}), 137.3 (d, J = 7.9, C\textsubscript{q}), 127.28 (CH), 127.25 (CH), 126.8 (CH), 126.7 (CH), 95.1 (d, J = 172, CH-F), 56.3 (d, J = 19.9, α-carbonyl C\textsubscript{q}), 39.7 (d, J = 17.2, CH\textsubscript{3}), 39.6 (CH\textsubscript{3}), 38.3 (CH\textsubscript{3}), 35.7 (d, J = 12.2, CH\textsubscript{3}), 32.7 (diastereotopic gem-dimethyl CH\textsubscript{3}), 31.8 (diastereotopic gem-dimethyl CH\textsubscript{3}), 20.7 (d, J = 1.6, CH\textsubscript{2})
ppm. **ESI-HRMS (positif)** M = C₁₆H₁₉FO, expected (M+NH₄)⁺ m/z 264.1759, observed (M+NH₄)⁺ m/z 264.1763. [α]²⁰D +29.9 (c = 1.00, acetone).

**β-Fluoro Spiroketone (B₁₁⁻)**

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A₁₁) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (Rₐ)-TIPS-TRIP (L₈) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluorᵀᴹ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na₂PO₄ (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C₆H₆/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/Et₂O 95:5).

Colorless oil. Isolated yield 45% (22 mg, 0.09 mmol). Rₐ (silica gel, n-Hex/Et₂O 9:1) 0.39. > 20:1 d.r. (¹H NMR). 96.5:3.5 e.r. Chiral HPLC. Chiralcel OD-H. n-Hex/i-PrOH 99:1. 1.0 mL/min. tᵣ 10.0 (minor), 11.8 (major). **¹H NMR** (500 MHz, C₆D₆): δ 7.10 (1H, d, 7.7, C=H), 7.05 (1H, td, J = 8.4, J = 1.3, C=H), 6.99 (1H, t, J = 7.9, C=H), 6.83 (1H, dd, J = 8.5, J = 0.7, C=H), 4.43 (1H, add, J= J=H 49.3, J = 11.5, J = 4.1, α-fluoro CH), 2.53-2.64 (2H, m, benzylic CH + diastereotopic CH₂), 2.14-2.31 (3H, m, diastereotopic CH₂), 2.05 (1H, add, J = 15.7, J = 8.9, J = 6.9, CH₂), 1.55-1.95 (5H, m, CH₂), 0.83 (3H, t, J = 7.5, CH₃) ppm. **¹⁹F NMR** (376 MHz, C₆D₆): δ -180.6 (1F, s, C(sp³)-F) ppm. **¹³C NMR** (125 MHz, C₆D₆): δ 121.5 (3 (d, J=J= 4.3, ketone Cq), 140.3 (d, J=J=2.3, Cq), 138.8 (d, J=J=7.9, Cq), 127.4 (CH), 127.3 (d, J=J=2.2, CH), 127.0 (CH), 126.7 (CH), 96.9 (d, J=J=174, CH-F), 56.0 (d, J=J=19.9, α-carbonyl Cq), 39.7 (CH₂), 37.9 (d, J=J=12.1, CH₂), 29.9 (d, J=J=18.5, benzylic CH), 28.4 (CH₂), 20.6 (d, J=J=1.5, CH₂), 10.5 (CH₃) ppm. **ESI-HRMS (positif)** M = C₁₀H₁₉FO, expected (M+H)⁺ m/z 247.1493, observed (M+H)⁺ m/z 247.1497. [α]²⁰D +35.7 (c = 1.00, acetone).

**β-Fluoro Spiroketone (B₁₁⁻)**

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A₁₁) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (Rₐ)-TIPS-TRIP (L₈) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluorᵀᴹ (106 mg, 0.30 mmol, 1.5 equiv.), and dried Na₂PO₄ (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C₆H₆/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/Et₂O 95:5).

Colorless oil. Isolated yield 46% (23 mg, 0.09 mmol). Rₐ (silica gel, n-Hex/Et₂O 9:1) 0.66. > 20:1 d.r. (¹H NMR). 95.5 e.r. Chiral HPLC. Chiralcel OJ-H. n-Hex/i-PrOH 99.5:0.5. 1.0 mL/min. tᵣ 22.8 (major), 32.1 (minor). **¹H NMR** (500 MHz, C₆D₆): δ 6.98-7.03 (2H, m, C=H), 6.90 (1H, dd, J = 6.6, J = 2.7, C=H), 6.79 (1H, dd, J = 6.9, J = 2.3, C=H), 4.73 (1H, add, J= J=H 49.5, J = 11.9, J = 4.0, α-fluoro CH), 2.76 (1H, sept., J = 5.8, diastereotopic CH₂), 2.62-2.67 (1H, m, benzylic CH), 2.27 (1H, add, J = 14.8, J = 5.6, J = 1.0, CH₂), 1.64-1.89 (2H, m, CH₂), 1.03 (1H, add, J = 16.6, J = 8.9, J = 7.7, CH₂), 1.82-1.92 (2H, m, CH₂), 1.56-1.65 (1H, m, CH₂), 1.33-1.42 (1H, m, CH₂), 1.17-1.26 (1H, m, CH₂), 0.73 (3H, t, J = 7.5, CH₃) ppm. **¹³C NMR** (125 MHz, C₆D₆): δ -186.4 (1F, s, C(sp³)-F) ppm. **¹⁹F NMR** (376 MHz, C₆D₆): δ -180.6 (1F, s, C(sp³)-F) ppm. **¹³C NMR** (125 MHz, C₆D₆): δ 215.0 (d, J=J=5.7, ketone Cq), 141.3 (d, J=J=2.0, Cq), 138.1 (d, J=J=7.1, Cq), 129.3 (CH), 127.7 (d, J=J=1.7, CH), 126.9 (CH), 126.8 (CH), 94.9 (d, J=J=172, CH-F), 56.2 (d, J=J=19.8, α-carbonyl Cq), 40.0 (d, J=J=11.7, CH₂), 39.2 (d, J=J=18.8, CH₂), 30.7 (CH₂), 28.8 (d, J=J=
According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A_{12}) (51 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R)_{1}-TIPS-TRIP (L_{9}) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor\textsuperscript{TM} (106 mg, 0.30 mmol, 1.5 equiv.), and dried NaPO_{4} (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_{6}H_{6}/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_{2}O 95:5). Colorless oil. Isolated yield 42% (22 mg, 0.09 mmol). R_{f} (silica gel, n-Hex/Et_{2}O 9:1) 0.73. > 20:1 d.r. \textsuperscript{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). \textsuperscript{1}H NMR (500 MHz, C_{6}D_{6}): δ 6.99-7.05 (2H, m, C=H), 6.94 (1H, dd, J_{d-H} 8.9, J_{d-2} 2.1, C=H), 6.80 (1H, dd, J_{d-2} 7.2, J_{d-3} 1.9, C=H), 4.79 (1H, ddd, J_{d-H} 49.5, J_{d-C} 11.5, J_{d-C} 3.8, ω-fluoro CH), 2.74-2.85 (2H, m, benzylic CH + diastereotopic CH_{2}), 2.29 (1H, ddd, J_{d-2} 15.3, J_{d-7} 9.0, J_{d-6} 6.2, CH_{2}), 2.21 (2H, t, J_{d-7} 7.5, CH_{2}), 2.04 (1H, ddd, J_{d-7} 18.0, J_{d-6} 16.6, J_{d-5} 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_{3}), 0.82 (3H, m, J_{d-6} 6.9, CH_{3}) ppm. \textsuperscript{19}F NMR (367 MHz, C_{6}D_{6}): δ -186.4 (1F, s, C(sp\textsuperscript{3})-F) ppm. \textsuperscript{13}C NMR (125 MHz, C_{6}D_{6}): δ 215.1 (d, J_{C-F} 5.7, ketone Cq), 141.6 (d, J_{C-F} 2.1, Cq), 138.1 (d, J_{C-F} 7.3, Cq), 129.3 (CH), 127.6 (CH), 127.5 (CH), 126.9 (d, J_{C-F} 13.9, CH), 95.1 (d, J_{C-F} 172, CH-F), 56.1 (d, J_{C-F} 19.8, α-carbonyl Cq), 39.3 (d, J_{C-F} 25.5, CH_{2}), 38.5 (d, J_{C-F} 11.9, benzylic CH), 37.9 (CH_{3}), 30.3 (CH_{2}), 29.2 (d, J_{C-F} 18.7, CH_{2}), 23.0 (CH_{3}), 20.5 (CH_{2}), 14.2 (CH_{3}) ppm. ESI-HRMS (positif) M = C_{18}H_{23}FO, expected (M+NH\textsubscript{4})\textsuperscript{+} m/z 292.2072, observed (M+NH\textsubscript{4})\textsuperscript{+} m/z 292.2075. [α]_{D}^{20} +39.5 (c = 1.00, acetone).

\textbf{β-Fluoro Spiroketone (B_{12}^8)}

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A_{12}) (51 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R)_{1}-TIPS-TRIP (L_{9}) (12 mg, 0.01 mmol, 5 mol%), powdered Selectfluor\textsuperscript{TM} (106 mg, 0.30 mmol, 1.5 equiv.), and dried NaPO_{4} (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C_{6}H_{6}/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_{2}O 95:5). Colorless oil. Isolated yield 43% (23 mg, 0.09 mmol). R_{f} (silica gel, n-Hex/Et_{2}O 9:1) 0.51. > 20:1 d.r. \textsuperscript{1}H NMR (95:5 e.r. Chiral HPLC. Chiralpak IC. n-Hex/i-PrOH 99:1. 1.0 mL/min. t_{R} 8.7 (minor), 13.0 (major). \textsuperscript{1}H NMR (500 MHz, C_{6}D_{6}): δ 7.16 (1H, d, J_{7-H} 7.6, C=H), 7.07 (1H, dd, J_{d-H} 7.3, J_{d-J} 1.4, C=H), 7.00 (1H, dd, J_{d-J} 7.9, J_{d-C} 0.7, C=H), 6.84 (1H, dd, J_{d-H} 11.4, J_{d-3} 1.1, C=H), 4.44 (1H, ddd, J_{d-H} 49.4, J_{d-2} 11.4, J_{d-3} 4.0, ω-fluoro CH), 2.56-2.67 (2H, m, benzylic CH + 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_{d-7} 7.0, CH_{3}) ppm. \textsuperscript{19}F NMR (367 MHz, C_{6}D_{6}): δ -180.6 (1F, s, C(sp\textsuperscript{3})-F) ppm. \textsuperscript{13}C NMR (125 MHz, C_{6}D_{6}): δ 215.3 (d, J_{C-F} 4.3, ketone Cq), 140.7 (d, J_{C-F} 2.4, Cq), 138.7 (d, J_{C-F} 7.9, Cq), 127.4 (CH), 127.3 (d, J_{C-F} 2.2, CH), 127.0 (CH), 126.7 (CH), 96.9 (d, J_{C-F} 174, CH-F), 56.1 (d, J_{C-F} 19.9, α-carbonyl Cq), 39.7 (CH_{2}), 38.0 (CH_{2}), 36.8 (d, J_{C-F} 11.2, benzylic CH), 35.8 (CH_{2}), 30.5 (d, J_{C-F} 18.4, CH_{2}), 28.6 (CH_{2}), 20.5 (CH_{2}), 14.2 (CH_{3}) ppm. ESI-HRMS (positif) M = C_{18}H_{23}FO, expected (M+H\textsuperscript{+}) m/z 292.2072, observed (M+H\textsuperscript{+}) m/z 292.2075. [α]_{D}^{20} +39.5 (c = 1.00, acetone).
According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A13) (48 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R,R)-TIPS-TRIP (Lq) (12 mg, 0.01 mmol, 5 mol%), powdered SelectfluorTM (106 mg, 0.30 mmol, 1.5 equiv.), and dried NaPO₄ (41 mg, 0.25 mmol, 1.25 equiv.) in anhydrous C₆H₅F/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/EtOAc 95:5). Colorless oil. Isolated yield 44% (23 mg, 0.09 mmol). Rf (silica gel, n-Hex/EtOAc 9:1) 0.79. > 20:1 d.r. (1H NMR). 97:3 e.r. Chiral HPLC.

Chiralcel OD-H. n-Hex/i-PrOH 98.5:1.5. 1.0 mL/min. tr 7.6 (minor), 11.3 (major). ¹H NMR (500 MHz, C₆D₆): δ 7.14 (1H, d, J 8.1, C₆H₅), 7.06 (1H, td, J 7.2, J 1.3, C₆H₅), 6.99 (1H, t, J 7.8, C₆H₅), 6.83 (1H, d, J 7.8, C₆H₅), 4.43 (1H, ddd, J 10.6, J 4.9, J 12.0, J 4.7, α-fluoro CH₂), 2.59-2.68 (2H, m, benzylic CH + diastereotopic CH₂), 2.15-2.39 (4H, m, diastereotopic CH₂), 2.05 (1H, ddd, J 17.9, J 8.7, J 6.4, CH₂), 1.81-1.90 (2H, m, CH₂), 1.55-1.65 (1H, m, isopropyl CH), 0.88 (3H, d, J 6.9, isopropyl CH₃), 0.83 (3H, d, J 6.9, isopropyl CH₃) ppm. ¹³C NMR (376 MHz, C₆D₆): δ -183.7 (1F, s, C(sp³)-F) ppm. ³¹P NMR (167 MHz, C₆D₆) 28.9 (major), 55.1 (minor).

β-Fluoro Spiroketone (B₁₃)
(CH₂), 30.2 (isopropyl CH), 24.3 (d, J<sup>CF</sup> 18.8, CH₂), 21.0 (isopropyl CH₂), 20.7 (d, J<sup>CF</sup> 0.8, CH₂), 15.8 (isopropyl CH₃) ppm. **ESI-HRMS (positif)** M = C₁₇H₂₁FO, expected (M+NH₄)<sup>⁺</sup> m/z 278.1915, observed (M+NH₄)<sup>⁺</sup> m/z 278.1919. [α]<sub>D</sub> +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 A<sup>KR</sup> (0.20 mmol, 1.0 equiv.) in anhydrous CH₂Cl₂ (3.0 mL, 0.07 M) was added (collidine)_2Br<PF₆⁻> (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 Na₂S₂O₃ 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 Na₂SO₄, filtered and concentrated in vacuo. Conversions and diastereomer ratios (d.r.) were determined by <sup>1</sup>H NMR analysis of the crude compounds. Pure diastereomers (F<sub>KR1</sub> and F<sub>KR2</sub>) were obtained after purification by flash chromatography on silica gel, using an adequate n-hexane/Et₂O mixture as eluent.

**Enantioselective Version**

To a well-stirred solution of chiral, racemic allylic alcohol A<sup>KR</sup> (0.20 mmol, 1.0 equiv.) and chiral phosphoric acid L₉ (15 mg, 0.02 mmol, 10 mol%) in anhydrous ethylbenzene (4.0 mL, 0.05 M) were added brominating reagent R₆ (260 mg, 0.26 mmol, 1.3 equiv.) and powdered anhydrous Na₃PO₄ (131 mg, 0.80 mmol, 4.0 equiv.). The resultant heterogeneous mixture was stirred at ambient temperature for 48-72 h. Saturated aqueous Na₂S₂O₃ 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 Na₂SO₄, filtered and concentrated in vacuo. Conversions and diastereomer ratios (d.r.) were determined by <sup>1</sup>H NMR analysis of the crude compounds. Pure diastereomers (F<sub>KR1</sub> and F<sub>KR2</sub>) were obtained after purification by flash chromatography on silica gel, using an adequate n-hexane/Et₂O 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 (C₁)**

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A₁) (43 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₉)-H₅-TRIP (L₉) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T₃) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na₂PO₄ (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/Et₂O 95:5). Pale-yellow oil. Isolated yield 42% (25 mg, 0.08 mmol). Rₛ (silica gel, n-Hex/Et₂O 9:1) 0.75. > 20:1 d.r. (¹H NMR). 95:5 e.r. Chiral HPLC. Chiralcel OJ-H. n-Hex/i-PrOH 99:5.0:5. 1.0 mL/min. tᵣ 21.7 (major), 41.4 (minor). ¹H NMR (500 MHz, CD₃OD): δ 7.01 (1H, nd, J₁ 8.1, J₂ 1.3, C₃H₅), 6.88-6.93 (2H, m, C₆H), 6.66 (1H, dd, J₁ 6.7, J₂ 1.2, C₃H₅), 4.83 (1H, dd, J₁ 10.1, J₂ 3.3, α-bromo CH), 2.76 (1H, sext., J 6.8, benzylic CH), 2.36 (1H, dt, J₁ 13.6, J₂ 6.9, diastereotopic CH₃), 2.11-2.29 (3H, m, CH₃), 1.99-2.07 (1H, m, CH₂), 1.86-1.93 (1H, m, CH₂), 1.49-1.64 (2H, m, CH₂), 1.04 (3H, d, J 7.1, CH₃) ppm. ¹³C NMR (125 MHz, CD₃OD): δ 216.6 (ketone Cq), 140.0 (Cq), 138.4 (Cq), 129.2 (CH), 127.2 (CH), 126.8 (CH), 126.4 (CH), 58.5 (α-carbonyl Cq), 40.1 (α-bromo CH), 39.4 (CH₂), 38.6 (CH₂), 35.8 (CH₃), 34.1 (benzylic CH), 23.5 (CH₃), 18.7 (CH₂) ppm. ESI-HRMS (positif) M = C₁₃H₁₇BrO, expected (M+NH₄)⁺ m/z 310.0802, 312.0781; observed (M+NH₄)⁺ m/z 310.0805, 312.0784. [α]²⁰D -38.6 (c = 1.00, acetone).

**β-Bromo Spiroketone (C₁)**

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A₁) (43 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₉)-H₅-TRIP (L₉) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T₃) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na₂PO₄ (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/Et₂O 95:5). Colorless oil. Isolated yield 43% (25 mg, 0.09 mmol). Rₛ (silica gel, n-Hex/Et₂O 9:1) 0.52. > 20:1 d.r. (¹H NMR). 95:5 e.r. Chiral HPLC. Chiralcel OJ-H. n-Hex/i-PrOH 99:1: 1.0 mL/min. tᵣ 14.5 (minor), 19.0 (major). ¹H NMR (500 MHz, CD₃OD): δ 6.92-7.00 (2H, m, C₆H), 6.85 (1H, dd, J₁ 7.4, J₂ 1.6, C₃H₅), 6.80 (1H, dd, J₁ 7.6, J₂ 1.3, C₃H₅), 4.29 (1H, dd, J₁ 12.4, J₂ 3.6, α-bromo CH), 3.34 (1H, id, J₁ 12.8, J₂ 6.0, diastereotopic CH₂), 2.81 (1H, quin.d, J₁ 7.1, J₂ 2.7, benzylic CH), 2.31-2.45 (2H, m, CH₂), 2.04-2.16 (2H, m, CH₂), 1.93 (1H, dt, J₁ 13.2, J₂ 2.9, CH₂), 1.79-1.88 (1H, m, CH₂), 1.55-1.64 (1H, m, CH₂), 0.92 (3H, d, J 7.3, CH₃) ppm. ¹³C NMR (125 MHz, CD₃OD): δ 214.9 (ketone Cq), 141.4 (Cq), 138.5 (Cq), 129.5 (CH), 127.3 (CH), 127.0 (CH), 126.9 (CH), 55.8 (α-carbonyl Cq), 55.5 (α-bromo CH), 39.5 (CH₂), 38.7 (CH₂), 37.4 (CH₂), 34.3 (benzylic CH), 24.1 (CH₃), 20.1 (CH₂) ppm. ESI-HRMS (positif) M = C₁₃H₁₇BrO, expected (M+NH₄)⁺ m/z 310.0802, 312.0781; observed (M+NH₄)⁺ m/z 310.0803, 312.0782. [α]²⁰D -17.2 (c = 1.00, acetone).
**β-Bromo Spiroketone (C₂)**

![Chemical Structure](https://example.com/structure)

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A₂) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₉)-H₈-TRIP (L₉) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T₃) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na₂PO₄ (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/Et₂O 95:5). Colorless crystalline solid. Isolated yield 40% (25 mg, 0.08 mmol). Rᵣ (silica gel, n-Hex/Et₂O 9:1) 0.77. > 20:1 d.r. (¹H NMR). 96:4 e.r. Chiral HPLC. Chiralpak IC. n-Hex/i-PrOH 99:5:0.5. 1.0 mL/min. tᵣ 15.6 (major), 22.9 (minor). ¹H NMR (400 MHz, C₆D₆): δ 6.90-6.92 (2H, m, C₆H), 6.79-6.83 (1H, m, C₆H), 3.77 (1H, dd, J₁ 13.2, J₂ 4.8, α-bromo CH), 3.02 (1H, td, J₁ 13.4, J₂ 8.4, diastereotropic CH₂), 2.74-2.83 (1H, m, CH₂), 2.57 (1H, dt, J₁ 14.3, J₂ 9.4, diastereotropic CH₂), 2.38-2.47 (2H, m, CH₂), 2.01-2.18 (2H, m, CH₂), 2.06 (3H, s, CH₃), 1.69-1.85 (1H, m, CH₂), 1.55-1.75 (1H, m, CH₂), 1.25 (3H, d, J 6.7, CH₃) ppm. ¹³C NMR (100 MHz, C₆D₆): δ 215.2 (ketone Cq), 140.1 (Cq), 139.1 (Cq), 136.9 (Cq), 130.1 (CH), 126.2 (CH), 124.8 (CH), 58.7 (α-bromo CH), 55.9 (α-carbonyl Cq), 39.6 (benzylic CH), 39.4 (CH₂), 38.8 (CH₂), 32.3 (CH₃), 23.1 (CH₂), 20.6 (CH₃) ppm. ESI-HRMS (positif) M = C₁₈H₁₉BrO, expected (M+NH₄)⁺ m/z 324.0958, 326.0938; observed (M+NH₄)⁺ m/z 324.0958, 326.0938. [α]²⁰D -44.6 (c = 1.00, acetone).

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**β-Bromo Spiroketone (C₂)**

![Chemical Structure](https://example.com/structure)

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A₂) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₉)-H₈-TRIP (L₉) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T₃) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na₂PO₄ (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/Et₂O 95:5). White crystalline solid. Isolated yield 44% (27 mg, 0.09 mmol). Rᵣ (silica gel, n-Hex/Et₂O 4:1) 0.57. > 20:1 d.r. (¹H NMR). 96:4 e.r. Chiral HPLC. Chiralcel OD-H. n-Hex/i-PrOH 99:1. 1.0 mL/min. tᵣ 14.7 (minor), 17.3 (major). ¹H NMR (500 MHz, C₆D₆): δ 6.92 (1H, t, J 7.6, C₆H), 6.85 (1H, d, J 7.4, C₆H), 6.72 (1H, d, J 7.8, C₆H), 4.44 (1H, dd, J₁ 13.4, J₂ 3.6, α-bromo CH), 3.44 (1H, td, J₁ 13.1, J₂ 5.4, diastereotropic CH₂), 2.76-2.83 (1H, m, CH₂), 2.36-2.52 (2H, m, CH₂), 2.24-2.31 (1H, m, CH₂), 2.08-2.16 (1H, m, CH₂), 1.91-2.02 (2H, m, CH₂), 1.94 (3H, s, CH₃), 1.60-1.72 (1H, m, CH₂), 0.81 (3H, d, J 7.1, CH₃) ppm. ¹³C NMR (125 MHz, C₆D₆): δ 215.2 (ketone Cq), 139.9 (Cq), 139.4 (Cq), 136.4 (Cq), 129.4 (Cq), 126.8 (CH), 125.4 (CH), 56.2 (α-bromo CH), 55.9 (α-carbonyl Cq), 39.8 (benzylic CH), 38.7 (CH₂), 38.1 (CH₂), 32.2 (CH₃), 21.0 (CH₂), 20.4 (CH₃), 19.2 (CH₃) ppm. ESI-HRMS (positif) M = C₁₈H₁₉BrO, expected (M+NH₄)⁺ m/z 324.0958, 326.0938; observed (M+NH₄)⁺ m/z 324.0956, 326.0936. [α]²⁰D -12.5 (c = 1.00, acetone).
β-Bromo Spiroketone (C₃)

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A₃) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₅)-H₂-TRIP (L₅) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T₃) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na₂PO₄ (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/Et₂O 95:5). Colorless oil. Isolated yield 41% (26 mg, 0.08 mmol). Rₛ (silica gel, n-Hex/Et₂O 9:1) 0.80. > 20:1 d.r. (¹H NMR). 96.5:3.5 e.r. Chiral HPLC. Chiralpak IC. n-Hex/i-PrOH 99:5:0.5. 1.0 mL/min. tᵣ 13.2 (major), 19.9 (minor). ¹H NMR (500 MHz, C₆D₆): δ 6.68-6.74 (2H, m, C₆H), 6.54-6.58 (1H, m, C₆H), 3.63 (1H, dd, J₆ 12.7, J₆ 4.0, α-bromo CH₂), 2.83-2.97 (2H, m, diastereotopic CH₂ + benzylic CH), 2.47 (1H, dt, J₆ 14.4, J₆ 9.3, CH₂), 2.39 (1H, dt, J₆ 18.3, J₆ 10.1, CH₂), 2.17-2.24 (1H, m, CH₂), 2.08 (1H, dd, J₆ 18.3, J₆ 9.0, J₆ 4.0, CH₂), 1.98 (1H, dd, J₆ 12.5, J₆ 8.8, J₆ 3.7, CH₂), 1.74-1.82 (1H, m, CH₂), 1.52-1.61 (1H, s, CH₂), 1.43 (3H, dd, J₆ 6.5, J₆ 1.9, CH₃) ppm. ¹³C NMR (376 MHz, C₆D₆): δ -110.6 (1F, s, C₆H) ppm. ¹⁹F NMR (125 MHz, C₆D₆): δ 214.6 (ketone C₆H), 162.2 (d, Jₖ-F 245, ipso(F)-C₆H), 141.4 (d, Jₖ-F 4.7, meta(F)-C₆H), 129.5 (d, Jₖ-F 14.6, ortho(F)-C₆H), 127.6 (d, Jₖ-F 9.5, meta(F)-C₆H), 122.4 (d, Jₖ-F 3.1, para(F)-C₆H), 114.2 (d, Jₖ-F 23.1, ortho(F)-C₆H), 57.5 (α-bromo CH), 55.3 (d, Jₖ-F 1.8, α-carbonyl C₆H), 39.3 (CH₂), 38.8 (CH₂), 38.2 (CH₂), 30.4 (CH₂), 22.0 (d, Jₖ-F 8.0, benzylic CH), 20.5 (CH₂) ppm. ESI-HRMS (positif) M = C₁₃H₁₆BrFO, expected (M+NH₄)⁺ m/z 328.0707, 330.0687; observed (M+NH₄)⁺ m/z 328.0709, 330.0689. [α]²⁰ₛ -51.1 (c = 1.00, acetone).

β-Bromo Spiroketone (A₅)

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A₅) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₅)-H₂-TRIP (L₅) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T₃) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na₂PO₄ (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/Et₂O 95:5). Faint-orange oil. Isolated yield 42% (26 mg, 0.08 mmol). Rₛ (silica gel, n-Hex/Et₂O 9:1) 0.56. > 20:1 d.r. (¹H NMR). 95:5:4 e.r. Chiral HPLC. Chiralcel OD-H. n-Hex/i-PrOH 99:1. 1.0 mL/min. tᵣ 13.9 (minor), 24.7 (major). ¹H NMR (500 MHz, C₆D₆): δ 6.64-6.73 (2H, m, C₆H), 6.50 (1H, d, J₆ 7.6, C₆H), 4.23 (1H, dd, J₆ 13.3, J₆ 3.6, α-bromo CH₂), 3.33 (1H, td, J₆ 13.2, J₆ 6.0, diastereotopic CH₂), 3.14 (1H, quin., J₆ 7.1, benzylic CH₂), 2.31-2.45 (2H, m, CH₂), 2.03-2.13 (2H, m, CH₂), 1.83-1.92 (2H, m, CH₂), 1.52-1.62 (1H, m, CH₂), 0.97 (3H, d, J₆ 7.2, CH₃) ppm. ¹⁹F NMR (376 MHz, C₆D₆): δ -116.5 (1F, s, C₆H) ppm. ¹³C NMR (125 MHz, C₆D₆): δ 214.5 (ketone C₆H), 161.3 (d, Jₖ-F 244, ipso(F)-C₆H), 141.4 (d, Jₖ-F 4.4, meta(F)-C₆H), 129.5 (d, Jₖ-F 16.6, ortho(F)-C₆H), 122.7 (d, Jₖ-F 3.4, meta(F)-C₆H), 113.7 (d, Jₖ-F 22.3, ortho(F)-C₆H), 55.4 (d, Jₖ-F 1.9, α-carbonyl C₆H), 55.0 (α-bromo CH₂), 39.2 (CH₂), 38.7 (CH₂), 37.0 (CH₂), 30.4 (CH₂), 29.0 (d, Jₖ-F 2.9, benzylic CH), 20.3 (CH₂) ppm. ESI-HRMS (positif) M = C₁₅H₁₄BrFO, expected (M+NH₄)⁺ m/z 328.0707, 330.0687; observed (M+NH₄)⁺ m/z 328.0708, 330.0688. [α]²⁰ₛ -20.3 (c = 1.00, acetone).
β-Bromo Spiroketone (C₄ᵢ)

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A₄) (48 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₉)-H₂-TRIP (L₄) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T₃) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na₃PO₄ (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/Et₂O 95:5). White crystalline solid. Isolated yield 44% (29 mg, 0.09 mmol). Rₛ (silica gel, n-Hex/Et₂O 9:1) 0.62. 1H NMR (95.5:4.5 e.r. Chiral HPLC. Chiralcel OJ-H. n-Hex/i-PrOH 99:1. 1.0 mL/min. tᵣ 12.2 (major), 15.9 (minor). ESI-HRMS (positif) M = C₁₅H₁₅BrClO, expected (M+NH₄)⁺ m/z 344.0412, 346.0391; observed (M+NH₄)⁺ m/z 344.0416, 346.0395. [α]²⁰ₒᵤ -38.7 (c = 1.00, acetone).

β-Bromo Spiroketone (C₄ᵢ)

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A₄) (48 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₉)-H₂-TRIP (L₄) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T₃) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na₃PO₄ (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/Et₂O 95:5). White crystalline solid. Isolated yield 42% (28 mg, 0.08 mmol). Rₛ (silica gel, n-Hex/Et₂O 9:1) 0.31. > 20:1 d.r. (1H NMR). 96.5:3.5 e.r. Chiral HPLC. Chiralcel OD-H. n-Hex/i-PrOH 99:1. 1.0 mL/min. tᵣ 11.7 (major), 17.0 (minor). ESI-HRMS (positif) M = C₁₅H₁₅BrClO, expected (M+NH₄)⁺ m/z 344.0412, 346.0391; observed (M+NH₄)⁺ m/z 344.0415, 346.0394. [α]²⁰ₒᵤ -19.5 (c = 1.00, acetone).
β-Bromo Spiroketone (C₅)

According to the General Procedure: chiral, racemic allylic cyclopropanol (rac-A₃) (40 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₃)-H₃-TRIP (L₃) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T₃) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na₂PO₄ (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/Et₂O 95:5). Colorless oil. Isolated yield 43% (24 mg, 0.09 mmol). Rₚ (silica gel, n-Hex/Et₂O 9:1) 0.70. > 20:1 d.r. (¹H NMR). 95:5 e.r. Chiral HPLC. Chiralcel OJ-H. n-Hex/i-PrOH 99:1. 1.0 mL/min. tᵣ 8.9 (minor), 10.3 (major). ¹H NMR (500 MHz, CDCl₃): δ 6.99 (1H, td, J = 7.3, J = 1.5, C₅H), 6.94 (1H, td, J = 7.5, J = 1.3, C₅H), 6.89 (1H, dd, J = 7.9, J = 1.3, C₅H), 6.83 (1H, dd, J = 8.2, J = 0.8, C₅H), 4.31 (1H, dd, J = 11.3, J = 3.2, α-bromo CH), 3.03 (1H, ddd, J = 18.6, J = 6.5, diastereotopic CH₂), 2.90 (1H, ddd, J = 13.5, J = 11.3, J = 5.9, diastereotopic CH₂), 2.62-2.68 (1H, m, benzyl CH), 2.59 (1H, ddd, J = 17.9, J = 10.6, J = 7.3, CH₂), 2.08 (1H, ddd, J = 12.4, J = 11.1, J = 7.3, CH₂), 1.91-1.98 (2H, m, CH₂), 0.89 (3H, d, J = 7.3, CH₃) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 206.0 (ketone Cq), 140.5 (Cq), 133.2 (Cq), 129.5 (CH), 127.5 (CH), 127.01 (CH), 126.98 (CH), 126.95 (CH), 73.2 (α-carbonyl Cq), 43.7 (α-bromo CH), 40.6 (benzyl CH), 34.8 (CH₂), 29.9 (CH₂), 27.9 (CH₂), 23.2 (CH₂) ppm. ESI-HRMS (positif) M = C₁₄H₁₅BrO, expected (M+NH₄)⁺ m/z 296.0645, 298.0625; observed (M+NH₄)⁺ m/z 296.0645, 298.0625. [α]²⁰D -19.6 (c = 1.0, acetone).

β-Bromo Spiroketone (C₅)

According to the General Procedure: chiral, racemic allylic cyclopropanol (rac-A₃) (40 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₃)-H₃-TRIP (L₃) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T₃) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na₂PO₄ (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/Et₂O 95:5). Faint-yellow oil. Isolated yield 40% (22 mg, 0.08 mmol). Rₚ (silica gel, n-Hex/Et₂O 9:1) 0.49. > 20:1 d.r. (¹H NMR). 94.5:5.5 e.r. Chiral HPLC. Chiralpack IC. n-Hex/i-PrOH 99:1. 1.0 mL/min. tᵣ 12.1 (major), 15.0 (minor). ¹H NMR (500 MHz, CDCl₃): δ 6.94-7.01 (2H, m, C₅H), 6.89 (1H, dd, J = 7.2, J = 1.9, C₅H), 6.83 (1H, dd, J = 7.0, J = 2.0, C₅H), 4.24 (1H, dd, J = 12.7, J = 3.4, α-bromo CH), 3.00 (1H, ddd, J = 18.4, J = 7.2, J = 6.4, diastereotopic CH₂), 2.90 (1H, ddd, J = 13.2, J = 12.0, J = 6.0, diastereotopic CH₂), 2.62-2.75 (2H, m, CH₂ + benzyl CH), 2.23 (1H, ddd, J = 12.3, J = 11.2, J = 7.3, CH₂), 1.89-1.99 (2H, m, CH₂), 0.86 (3H, d, J = 7.2, CH₃) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 205.3 (ketone Cq), 140.6 (Cq), 133.6 (Cq), 129.5 (CH), 127.5 (CH), 127.0 (CH), 126.7 (CH), 73.4 (α-carbonyl Cq), 51.4 (α-bromo CH), 44.4 (benzyl CH), 38.4 (CH₂), 34.0 (CH₂), 25.5 (CH₂), 23.5 (CH₃) ppm. ESI-HRMS (positif) M = C₁₄H₁₅BrO, expected (M+NH₄)⁺ m/z 296.0645, 298.0625; observed (M+NH₄)⁺ m/z 296.0645, 298.0627. [α]²⁰D -11.7 (c = 1.0, acetone).
**β-Bromo Spiroketone (C₆^⁺)**

According to the General Procedure: chiral, racemic allylic cyclopropanol (rac-A₆) (43 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₆)-H₈-TRIP (L₈) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T₃) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na₂PO₄ (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/Et₂O 95:5). Pale-yellow oil. Isolated yield 43% (25 mg, 0.09 mmol). Rₚ (silica gel, n-Hex/Et₂O 9:1) 0.73. > 20:1 d.r. (¹H NMR). 96.4 e.r. Chiral HPLC. Chiralcel OJ-H. n-Hex/i-PrOH 98:2. 1.0 mL/min. tᵣ 8.2 (major), 9.0 (minor). **¹H NMR** (500 MHz, C₆D₆): δ 6.91 (1H, t, J 7.6, C₆H), 6.86 (1H, d, J 6.8, C₆H), 6.82 (1H, d, J 7.9, C₆H), 4.54 (1H, dd, J 13.5, J 3.3, α-bromo CH), 3.19 (1H, dd, J 18.7, J 11.1, J 3.9, diastereotopic CH₂), 3.14 (1H, td, J 13.3, J 5.3, diastereotopic CH₂), 2.65 (1H, ddd, J 13.5, J 10.8, J 7.8, CH₂), 2.50-2.56 (1H, m, benzylic CH), 2.19-2.28 (2H, m, CH₂), 2.04 (1H, ddd, J 12.5, J 10.8, J 5.9, CH₂), 1.90 (3H, s, CH₃), 0.75 (3H, d, J 7.1, CH₃) ppm. **¹³C NMR** (125 MHz, C₆D₆): δ 206.0 (ketone Cq), 139.3 (Cq), 136.9 (Cq), 129.2 (Cq), 129.8 (CH), 125.9 (CH), 73.6 (α-carbonyl Cq), 43.9 (α-bromo CH), 41.9 (benzylic CH), 33.1 (CH₂), 30.1 (CH₂), 26.9 (CH₂), 20.5 (CH₃), 19.1 (CH₃) ppm. **ESI-HRMS (positif)** M = C₁₃H₁₇BrO, expected (M+NH₄)⁺ m/z 310.0802, 312.0781; observed (M+NH₄)⁺ m/z 310.0805, 312.0784. [α]²⁰ Retrofit -33.7 (c = 1.00, acetone).

**β-Bromo Spiroketone (C₆⁻)**

According to the General Procedure: chiral, racemic allylic cyclopropanol (rac-A₆) (43 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₆)-H₈-TRIP (L₈) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T₃) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na₂PO₄ (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/Et₂O 95:5). White crystalline solid. Isolated yield 43% (25 mg, 0.09 mmol). Rₚ (silica gel, n-Hex/Et₂O 9:1) 0.52. > 20:1 d.r. (¹H NMR). 96.5:3.5 e.r. Chiral HPLC. Chiralpak IC. n-Hex/i-PrOH 99:5:0.5. 1.0 mL/min. tᵣ 18.6 (major), 23.8 (minor). **¹H NMR** (500 MHz, C₆D₆): δ 6.93 (1H, t, J 7.7, C₆H), 6.86 (1H, d, J 7.9, C₆H), 6.80 (1H, d, J 7.8, C₆H), 4.42 (1H, dd, J 13.4, J 3.4, α-bromo CH), 3.10 (1H, ddd, J 18.7, J 11.2, J 6.0, diastereotopic CH₂), 3.02 (1H, td, J 13.1, J 5.4, diastereotopic CH₂), 2.64-2.75 (2H, m, CH₂ + benzylic CH), 2.37 (1H, ddd, J 12.5, J 11.3, J 7.7, CH₂), 2.01-2.06 (2H, m, CH₂), 1.90 (3H, s, CH₃), 0.74 (3H, d, J 7.1, CH₃) ppm. **¹³C NMR** (125 MHz, C₆D₆): δ 205.3 (ketone Cq), 139.2 (Cq), 136.7 (Cq), 133.8 (Cq), 129.9 (CH), 127.0 (CH), 124.7 (CH), 73.8 (α-carbonyl Cq), 51.4 (α-bromo CH), 44.7 (benzylic CH), 39.3 (CH₂), 32.2 (CH₂), 25.0 (CH₂), 20.7 (CH₃), 19.1 (CH₃) ppm. **ESI-HRMS (positif)** M = C₁₃H₁₇BrO, expected (M+NH₄)⁺ m/z 310.0802, 312.0781; observed (M+NH₄)⁺ m/z 310.0805, 312.0784. [α]²⁰ Retrofit -12.0 (c = 1.00, acetone).
**β-Bromo Spiroketone (C₇)**

![diastereomer 1](image)

Chemical Formula: C_{14}H_{14}BrFO

Molecular Weight: 297.16

According to the General Procedure: chiral, racemic allylic cyclopropanol (rac-A₇) (44 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₆)-H₂-TRIP (L₅) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T₃) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na₃PO₄ (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/Et₂O 95:5). White crystalline solid. Isolated yield 45% (27 mg, 0.09 mmol). R₉ (silica gel, n-Hex/Et₂O 9:1) 0.75. > 20:1 d.r. (¹H NMR). 94.5:5.5 e.r. Chiral HPLC. Chiralpak IC. n-Hex/i-PrOH 99:1. 1.0 mL/min. tᵣ 12.0 (minor), 14.0 (major). ¹H NMR (500 MHz, C₅D₅): δ 6.64-6.72 (2H, m, C₆⁻H), 6.57 (1H, d, J 8.5, C₆⁻H), 4.28 (1H, dd, J 12.9, J 3.2, α-bromo CH), 3.10 (1H, dd, J 18.8, J 11.1, J 6.0, diastereotopic CH₂), 2.96 (1H, dd, J 13.2, J 5.9, CH₂), 2.86 (1H, broad quint., J 6.1, benzylic CH), 2.58 (1H, dd, J 18.6, J 10.7, J 7.7, CH₂), 2.15 (1H, dd, J 12.6, J 11.1, J 7.7, CH₂), 2.05 (1H, dt, J 12.9, J 3.1, CH₂), 1.88 (1H, dd, J 12.6, J 10.8, J 6.0, CH₂), 0.92 (3H, d, J 6.8, CH₃) ppm. ¹³C NMR (125 MHz, C₅D₅): δ 205.1 (ketone Cq), 161.6 (d, J₉⁻F 244, ipso(F)-Cq), 135.3 (d, J₉⁻F 4.5, meta(F)-Cq), 128.0 (d, J₉⁻F 25.0, ortho(F)-Cq), 125.9 (para(F)-CH), 122.4 (d, J₉⁻F 3.2, meta(F)-CH), 114.0 (d, J₉⁻F 22.4, ortho(F)-CH), 72.8 (d, J₉⁻F 1.8, α-carbonyl Cq), 44.0 (α-bromo CH), 40.6 (CH₃), 30.5 (CH₃), 29.9 (d, J₉⁻F 2.3, benzylic CH), 26.9 (CH₂), 21.3 (d, J₉⁻F 1.7, CH₃) ppm. ESI-HRMS (positif) M = C₁₄H₁₄BrFO, expected (M+NH₄)⁺ m/z 314.0551, 316.0530; observed (M+NH₄)⁺ m/z 314.0555, 316.0533. [α]ᵢ²b -16.9 (c = 1.00, acetone).

**β-Bromo Spiroketone (C₇)**

![diastereomer 2](image)

Chemical Formula: C_{14}H_{14}BrFO

Molecular Weight: 297.16

According to the General Procedure: chiral, racemic allylic cyclopropanol (rac-A₇) (44 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₆)-H₂-TRIP (L₅) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T₃) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na₃PO₄ (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/Et₂O 95:5). Colorless oil. Isolated yield 41% (24 mg, 0.08 mmol). R₉ (silica gel, n-Hex/Et₂O 9:1) 0.55. > 20:1 d.r. (¹H NMR). 96.4:4 e.r. Chiral HPLC. Chiralcel OJ-H. n-Hex/i-PrOH 99:1. 1.0 mL/min. tᵣ 14.3 (major), 19.1 (minor). ¹H NMR (500 MHz, C₅D₅): δ 6.72 (1H, td, J 8.0, J 6.0, C₆⁻H), 6.66 (1H, td, J 9.6, J 2.2, C₆⁻H), 6.56 (1H, d, J 7.8, C₆⁻H), 4.18 (1H, dd, J 13.1, J 3.4, α-bromo CH₂), 2.96-3.07 (2H, m, CH₂ + benzylic CH₂), 2.89 (1H, td, J 13.1, J 5.8, diastereotopic CH₂), 2.64 (1H, dd, J 18.4, J 10.7, J 7.6, CH₂), 2.26 (1H, dd, J 12.5, J 11.2, J 7.6, CH₂), 1.85-1.93 (2H, m, CH₂), 0.90 (3H, d, J 7.2, CH₃) ppm. ¹³C NMR (125 MHz, C₅D₅): δ 204.5 (ketone Cq), 161.5 (d, J₉⁻F 245, ipso(F)-Cq), 136.1 (d, J₉⁻F 4.5, meta(F)-Cq), 128.4 (d, J₉⁻F 24.8, ortho(F)-Cq), 128.1 (para(F)-CH), 122.1 (d, J₉⁻F 3.2, meta(F)-CH), 114.1 (d, J₉⁻F 22.2, ortho(F)-CH), 73.0 (d, J₉⁻F 1.6, α-carbonyl Cq), 50.3 (α-bromo CH), 44.7 (CH₂), 38.1 (CH₂), 29.1 (d, J₉⁻F 2.5, benzylic CH₂), 24.8 (CH₂), 21.1 (d, J₉⁻F 1.9, CH₃) ppm. ESI-HRMS (positif) M = C₁₄H₁₄BrFO, expected (M+NH₄)⁺ m/z 314.0551, 316.0530; observed (M+NH₄)⁺ m/z 314.0552, 316.0532. [α]ᵢ²b -12.0 (c = 1.00, acetone).
β-Bromo Spiroketone (C₈⁻)

According to the General Procedure: chiral, racemic allylic cyclopropanol (rac-As) (47 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₃)-H₂-TRIP (La) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T₃) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na₂PO₄ (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/Et₂O 95:5). White crystalline solid. Isolated yield 43% (26 mg, 0.08 mmol). Rf (silica gel, n-Hex/Et₂O 9:1) 0.60. > 20:1 d.r. (¹H NMR). 95:5 e.r. Chiral HPLC. Chiralcel OJ-H. n-Hex/i-PrOH 98:2. 1.0 mL/min. tR 13.1 (major), 15.7 (minor). ¹H NMR (500 MHz, CDCl₃): δ 7.02-7.06 (1H, m, C²H), 6.63-6.67 (2H, m, C²H), 4.25 (1H, dd, J = 13.4, J = 3.4, β-bromo CH), 3.03-3.10 (2H, m, CH₂ + benzylic CH), 2.87 (1H, td, J = 13.2, J = 5.5, diastereotopic CH₂), 2.63 (1H, dd, J = 18.5, J = 10.7, J = 7.6, CH₂), 2.24-2.30 (1H, m, CH₂), 1.94-1.97 (1H, m, CH₂), 1.83-1.89 (1H, m, CH₂), 0.91 (3H, d, J = 7.1, CH₃) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 204.4 (ketone Cq), 138.5 (Cq), 136.1 (Cq), 135.2 (Cq), 129.0 (CH), 128.0 (CH), 125.4 (CH), 73.3 (α-carbonyl Cq), 50.3 (α-bromo CH), 44.9 (CH₂), 38.6 (CH₂), 33.0 (benzylic CH), 24.8 (CH₂), 20.2 (CH₃) ppm. ESI-HRMS (positif) M = C₁₄H₁₄BrClO, expected (M+NH₄)⁺ m/z 330.0255, 332.0235; observed (M+NH₄)⁺ m/z 330.0256, 332.0237. [α]²⁰D -32.6 (c = 1.00, acetone).

β-Bromo Spiroketone (C₈⁺)

According to the General Procedure: chiral, racemic allylic cyclopropanol (rac-As) (47 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R₃)-H₂-TRIP (La) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T₃) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na₂PO₄ (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/Et₂O 95:5). White crystalline solid. Isolated yield 42% (26 mg, 0.08 mmol). Rf (silica gel, n-Hex/Et₂O 9:1) 0.46. > 20:1 d.r. (¹H NMR). 96:5:3.5 e.r. Chiral HPLC. Chiralcel OD-H. n-Hex/i-PrOH 98:2. 1.0 mL/min. tR 7.9 (minor), 11.5 (major). ¹H NMR (500 MHz, CDCl₃): δ 7.02-7.06 (1H, m, C²H), 6.63-6.67 (2H, m, C²H), 4.25 (1H, dd, J = 13.4, J = 3.4, α-bromo CH), 3.03-3.10 (2H, m, CH₂ + benzylic CH), 2.87 (1H, td, J = 13.2, J = 5.5, diastereotopic CH₂), 2.63 (1H, dd, J = 18.5, J = 10.7, J = 7.6, CH₂), 2.24-2.30 (1H, m, CH₂), 1.94-1.97 (1H, m, CH₂), 1.83-1.89 (1H, m, CH₂), 0.91 (3H, d, J = 7.1, CH₃) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 204.4 (ketone Cq), 138.5 (Cq), 136.1 (Cq), 135.2 (Cq), 129.0 (CH), 128.0 (CH), 125.4 (CH), 73.3 (α-carbonyl Cq), 50.3 (α-bromo CH), 44.9 (CH₂), 38.6 (CH₂), 33.0 (benzylic CH), 24.8 (CH₂), 20.2 (CH₃) ppm. ESI-HRMS (positif) M = C₁₄H₁₄BrClO, expected (M+NH₄)⁺ m/z 330.0255, 332.0235; observed (M+NH₄)⁺ m/z 330.0256, 332.0237. [α]²⁰D -22.2 (c = 1.00, acetone).

β-Bromo Spiroketone (C₈⁻)
**β-Bromo Spiroketone (C₅)**

According to the General Procedure: allylic cyclobutanol (A₅) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (Rₛ)-Hₛ-TRIP (L₅) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T₅) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na₃PO₄ (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/Et₂O 95:5). White crystalline solid. Isolated yield 88% (54 mg, 0.18 mmol). R₇ (silica gel, n-Hex/Et₂O 9:1) 0.50. > 20:1 d.r. (¹H NMR).

94.5:5.5 e.r. Chiral HPLC. Chiralpak IA. n-Hex/i-PrOH 99:1. 1.0 mL/min. tₗ 8.4 (minor), 10.9 (major). ¹H NMR (500 MHz, C₅D₅): δ 7.09 (1H, dd, J₁ 8.0, J₂ 1.4, C₅H), 7.01 (1H, td, J₁ 7.1, J₂ 1.3, C₅H), 6.93 (1H, td, J₁ 7.8, J₂ 1.5, C₅H), 6.83 (1H, dd, J₁ 8.0, J₂ 1.1, C₅H), 4.32 (1H, dd, J₁ 13.5, J₂ 3.7, α-bromo CH₃), 3.38 (1H, t, J 13.5, diastereotopic CH₃), 2.43-2.50 (2H, m, CH₂), 2.16-2.22 (1H, m, CH₂), 2.07-2.14 (1H, m, CH₂), 1.99 (1H, dd, J₁ 13.1, J₂ 3.7, CH₂), 1.85-1.93 (1H, m, CH₂), 1.58-1.68 (1H, m, CH₂), 1.20 (3H, s, diastereotopic CH₃), 0.96 (3H, s, diastereotopic CH₃) ppm. ¹³C NMR (125 MHz, C₅D₅): δ 215.0 (ketone Cₗ), 145.3 (Cₗ), 138.4 (Cₗ), 127.24 (CH), 127.16 (CH), 127.5 (CH), 127.0 (CH), 125.2 (CH), 56.9 (α-carbonyl Cₗ), 56.0 (α-bromo CH), 45.2 (CH₂), 39.3 (CH₃), 39.0 (CH₃), 37.0 (benzylic Cₗ), 32.4 (CH₃), 31.2 (CH₃), 20.5 (CH₃) ppm. ESI-HRMS (positif) M = C₁₅H₁₉BrO₂, expected (M+NH₄)⁺ m/z 324.0958, 326.0938; observed (M+NH₄)⁺ m/z 324.0962, 326.0942. |α|²⁰ⁿ - 24.6 (c = 1.00, acetone).

**β-Bromo Spiroketone (C₁₀⁵)**

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A₁₀) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (Rₛ)-Hₛ-TRIP (L₅) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T₅) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na₃PO₄ (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/Et₂O 95:5). Pale-yellow oil. Isolated yield 42% (26 mg, 0.08 mmol). R₇ (silica gel, n-Hex/Et₂O 9:1) 0.70. > 20:1 d.r. (¹H NMR). 94.5:5.5 e.r. Chiral HPLC. Chiralcel OD-H. n-Hex/i-PrOH 99:1. 1.0 mL/min. tₗ 7.4 (minor), 10.5 (major). ¹H NMR (500 MHz, C₅D₅): δ 7.01 (1H, dd, J₁ 6.9, J₂ 1.3, C₅H), 6.89-6.94 (2H, m, C₅H), 6.66 (1H, dd, J₁ 7.7, J₂ 1.2, C₅H), 4.87 (1H, dd, J₁ 10.5, J₂ 3.1, α-bromo CH), 2.54-2.59 (1H, m, benzylic CH), 2.35-2.43 (2H, m, CH₂), 2.18-2.26 (2H, m, CH₂), 2.04 (1H, dd, J₁ 11.8, J₃ 8.8, J₄ 4.9, diastereotopic CH₃), 1.92 (1H, dd, J₁ 12.9, J₃ 7.8, J₄ 4.8, diastereotopic CH₃), 1.45-1.67 (4H, m, CH₂), 0.74 (3H, t, J 7.4, CH₃) ppm. ¹³C NMR (125 MHz, C₅D₅): δ 216.8 (ketone Cₗ), 139.1 (Cₗ), 138.9 (Cₗ), 129.5 (CH), 127.1 (CH), 126.8 (CH), 126.5 (CH), 58.4 (α-carbonyl Cₗ), 40.9 (α-bromo CH), 39.6 (CH₃), 38.7 (CH₂), 36.5 (benzylic CH), 36.1 (CH₂), 30.3 (CH₃), 18.8 (CH₃), 12.0 (CH₃) ppm. ESI-HRMS (positif) M = C₁₅H₁₉BrO₂, expected (M+NH₄)⁺ m/z 324.0958, 326.0938; observed (M+NH₄)⁺ m/z 324.0962, 326.0940. |α|²⁰ⁿ - 39.5 (c = 1.00, acetone).
**β-Bromo Spiroketone (C_{10}^R)**

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A_{10}) (46 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_{chiral})-H_{3}-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_{2}PO_{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_{2}O 95:5). Colorless oil. Isolated yield 43% (26 mg, 0.09 mmol). R_{f} (silica gel, n-Hex/Et_{2}O 9:1) 0.50. > 20:1 d.r. (^1H 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). ^1H NMR (500 MHz, C_{6}D_{6}): δ 6.94-7.01 (2H, m, C''''H), 6.80-6.86 (2H, m, C''''H), 4.29 (1H, dd, J_{1} 12.7, J_{2} 3.5, α-bromo CH), 3.30 (1H, td, J_{1} 13.0, J_{2} 5.8, diastereotopic CH_{2}), 2.30-2.54 (3H, m, CH_{2} + benzylic CH), 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} 7.4, CH_{3}) ppm. ^13C NMR (125 MHz, C_{6}D_{6}): δ 214.9 (ketone C=q), 140.7 (C=q), 139.1 (C=q), 129.9 (CH), 127.3 (CH), 127.0 (CH), 126.8 (CH), 55.8 (α-carbonyl C=q), 55.7 (α-bromo CH), 41.7 (benzylic CH), 39.5 (CH_{2}), 38.7 (CH_{2}), 33.8 (CH_{2}), 20.8 (CH_{2}), 20.2 (CH_{2}), 12.5 (CH_{3}) ppm. ESI-HRMS (positive) M = C_{10}H_{19}BrO, expected (M+NH_{4})^{+} m/z 324.0958, 326.0938; observed (M+NH_{4})^{+} m/z 324.0959, 326.0939. [α]^{19}D -15.3 (c = 1.00, acetone).

**β-Bromo Spiroketone (C_{11}^S)**

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A_{11}) (51 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R_{chiral})-H_{3}-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_{2}PO_{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_{2}O 95:5). Pale-yellow oil. Isolated yield 44% (30 mg, 0.09 mmol). R_{f} (silica gel, n-Hex/Et_{2}O 9:1) 0.81. > 20:1 d.r. (^1H 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). ^1H NMR (500 MHz, C_{6}D_{6}): δ 7.14 (1H, d, J_{8} 8.0, C''''H), 7.04 (1H, t, J_{7} 8.3, C''''H), 6.96 (1H, t, J_{7} 7.8, C''''H), 6.85 (1H, d, J_{7} 9.1, C''''H), 3.95 (1H, dd, J_{1} 13.1, J_{2} 3.8, α-bromo CH), 3.15 (1H, q, J 13.0, benzylic CH), 2.59-2.65 (1H, m, diastereotropic 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, CH_{3}) ppm. ^13C NMR (125 MHz, C_{6}D_{6}): δ 215.3 (ketone C=q), 140.0 (C=q), 139.8 (C=q), 127.7 (CH), 127.1 (CH), 127.0 (CH), 126.6 (CH), 59.3 (α-bromo CH), 55.7 (α-carbonyl C=q), 39.3 (CH_{2}), 39.14 (CH_{2}), 39.08 (benzylic CH), 36.2 (CH_{2}), 35.7 (CH_{2}), 28.3 (CH_{2}), 23.4 (CH_{2}), 20.5 (CH_{2}), 14.2 (CH_{3}) ppm. ESI-HRMS (positive) M = C_{11}H_{20}BrO, expected (M+NH_{4})^{+} m/z 352.1271, 354.1251; observed (M+NH_{4})^{+} m/z 352.1274, 354.1254. [α]^{19}D -30.1 (c = 1.00, acetone).
According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A11) (51 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R)-H8-TRIP (L9) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T3) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na2PO4 (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/Et2O 95:5). Colorless oil. Isolated yield 40% (26 mg, 0.08 mmol). Rf (silica gel, n-Hex/Et2O 9:1) 0.63. > 20:1 d.r. (1H NMR). 96:4 e.r. Chiral HPLC. Chiralpak IC. n-Hex/i-PrOH 99.5:0.5. 0.8 mL/min. tR 16.8 (minor), 21.2 (major).1H NMR (500 MHz, CD3): δ 6.95-7.02 (2H, m, CαH), 6.89 (1H, dd, J1 7.3, J2 1.7, CαβH), 6.83 (1H, dd, J1 7.7, J2 1.4, CαβH), 4.36 (1H, dd, J1 12.8, J2 3.5, α-bromo CH), 3.36 (1H, id, J1 13.1, J2 5.8, diastereotopic CH2), 2.62-2.67 (1H, m, benzylic CH), 2.33-2.48 (2H, m, CH2), 2.16-2.23 (2H, m, CH2), 2.10 (1H, ddd, J1 15.2, J2 6.4, J3 2.3, CαβH), 1.85-1.94 (1H, m, CH2), 1.58-1.68 (1H, m, CH2), 1.24-1.36 (3H, m, CH3), 1.03-1.17 (4H, m, CH2), 0.80 (3H, t, J 6.9, CH2) ppm. 13C NMR (125 MHz, CD3): δ 215.0 (ketone Cq), 140.9 (Cq), 139.1 (Cq), 129.9 (CH), 127.3 (CH), 126.9 (CH), 126.8 (CH), 55.86 (α-bromo CH), 55.76 (α-carbonyl Cq), 40.1 (benzylic CH), 39.5 (CH3), 38.7 (CH3), 38.0 (CH2), 34.4 (CH2), 30.3 (CH2), 23.0 (CH2), 20.3 (CH2), 14.2 (CH3) ppm. ESI-HRMS (positif) M = C11H23BrO, expected (M+NH4)+ m/z 352.1271, 354.1251; observed (M+NH4)+ m/z 352.1273, 354.1253. [α]20D -17.4 (c = 1.00, acetone).

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A12) (49 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (R)-H8-TRIP (L9) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T3) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na2PO4 (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/Et2O 95:5). Pale-yellow oil. Isolated yield 45% (29 mg, 0.09 mmol). Rf (silica gel, n-Hex/Et2O 9:1) 0.79. > 20:1 d.r. (1H NMR). 94:6 e.r. Chiral HPLC. Chiralpak IC. n-Hex/i-PrOH 99:1. 1.0 mL/min. tR 7.9 (minor), 9.3 (major).1H NMR (500 MHz, CD3): δ 6.97-7.01 (2H, m, CαH), 6.91-6.94 (1H, m, CαβH), 6.81-6.84 (1H, m, CαβH), 4.36 (1H, dd, J1 11.8, J2 3.6, α-bromo CH), 3.05 (1H, ddd, J1 14.7, J2 11.8, J3 6.2, diastereotopic CH2), 2.53 (1H, dq, J1 6.8, J2 5.2, benzylic CH), 2.40 (1H, ddd, J1 18.2, J2 9.8, J3 7.4, CH2), 2.22-2.28 (2H, m, CH2), 2.12-2.18 (1H, m, CH2), 2.03-2.10 (1H, m, CH2), 1.78-1.86 (1H, m, CH2), 1.68 (1H, oct., J 6.8, isopropyl CH), 1.53-1.62 (1H, m, CH2), 0.75 (3H, d, J 6.8, isopropyl CH3), 0.60 (3H, d, J 6.8, isopropyl CH3) ppm. 13C NMR (125 MHz, CD3): δ 214.6 (ketone Cq), 139.5 (Cq), 139.3 (Cq), 130.0 (CH), 127.6 (CH), 126.9 (CH), 126.4 (CH), 56.1 (α-carbonyl Cq), 55.7 (α-bromo CH), 45.2 (benzylic CH), 39.9 (CH3), 38.5 (CH3), 33.3 (isopropyl CH), 32.1 (CH), 21.6 (isopropyl CH3), 19.9 (CH3), 19.5 (isopropyl CH3) ppm. ESI-HRMS (positif) M = C12H25BrO, expected (M+NH4)+ m/z 338.1115, 340.1094; observed (M+NH4)+ m/z 338.1118, 340.1097. [α]20D -28.3 (c = 1.00, acetone).
β-Bromo Spiroketone (C₁₂⁺)

According to the General Procedure: chiral, racemic allylic cyclobutanol (rac-A₁₂) (49 mg, 0.20 mmol, 1.0 equiv.), chiral phosphoric acid (Rᵥ)-H₅-TRIP (L₉) (15 mg, 0.02 mmol, 10 mol%), brominating reagent (T₃) (260 mg, 0.26 mmol, 1.3 equiv.), and dried Na₂PO₄ (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/Et₂O 95:5). Colorless oil. Isolated yield 44% (28 mg, 0.09 mmol). Rᵥ (silica gel, n-Hex/Et₂O 9:1) 0.58. > 20:1 d.r. (¹H NMR). 97:3 e.r. Chiral HPLC. Chiralcel OJ-H. n-Hex/i-PrOH 99.5:0.5. 0.8 mL/min. f₁₅ 15.6 (major), 20.0 (minor). ¹H NMR (500 MHz, C₅D₅): δ 6.96–7.02 (2H, m, CαH), 6.93 (1H, dd, J₁ 6.9, J₂ 1.9, CαH), 6.82 (1H, dd, J₁ 7.4, J₂ 1.6, CαH), 4.42 (1H, dd, J₁ 11.1, J₂ 3.4, α-bromo CH), 3.05 (1H, ddd, J₁ 13.9, J₂ 11.1, J₂ 6.1, diastereotopic CH₂), 2.50 (1H, broad q, J 6.1, benzylic CH), 2.43 (1H, ddd, J₁ 17.9, J₂ 8.5, J₃ 7.8, CH₂), 2.29 (1H, dt, J₁ 13.9, J₂ 3.8, CH₂), 2.08–2.15 (2H, m, CH₂), 2.01 (1H, ddd, J₁ 18.1, J₂ 8.0, J₃ 7.6, CH₂), 1.70–1.80 (2H, m, CH₂ + isopropyl CH₃), 1.51–1.58 (1H, m, CH₂), 0.75 (3H, d, J 6.8, isopropyl CH₃), 0.61 (3H, d, J 6.8, isopropyl CH₃) ppm. ¹³C NMR (125 MHz, C₅D₅): δ 215.4 (ketone Cq), 139.2 (Cq), 138.8 (Cq), 129.9 (CH), 127.8 (CH), 126.8 (CH), 126.4 (CH), 56.1 (α-carbonyl Cq), 45.9 (α-bromo CH), 40.8 (benzylic CH), 37.6 (CH₂), 34.9 (CH₂), 34.1 (CH₂), 32.9 (isopropyl CH), 30.5 (CH₂), 21.5 (isopropyl CH₃), 19.5 (CH₂), 19.4 (isopropyl CH₃) ppm. ESI-HRMS (positif) M = C₁₇H₂₁BrO₄, expected (M+NH₄)⁺ m/z 338.1115, 340.1094; observed (M+NH₄)⁺ 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 \( \beta \)-fluoro spiroketones \( B_2^R \), \( B_1^S \) and \( B_4^S \). Thermal ellipsoids are set at 50% probability level.

Figure 3. X-ray crystal structures of \( \beta \)-bromo spiroketone \( C_2^S \). Thermal ellipsoids are set at 50% probability level.

Synthetic Derivatizations

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

Figure 4. Synthetic manipulations of the product optically active \( \beta \)-halo spiroketones.

Baeyer-Villiger Oxidation
**Spiro γ-Lactone (D<sup>R</sup>)**

To a solution of β-fluoro spiroketone B<sub>3R</sub> (> 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<sub>2</sub>S<sub>2</sub>O<sub>3</sub> followed by saturated aqueous NaHCO<sub>3</sub>. The mixture was extracted with diethyl ether. The combined organic layers were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo. The crude residue was purified by flash chromatography on silica gel (n-hexane/Et<sub>2</sub>O 9:1 → 3:2). Colorless oil. Isolated yield 89% (18 mg, 0.07 mmol). R<sub>f</sub> (silica gel, n-Hex/Et<sub>2</sub>O 1:1) 0.17. > 20:1 d.r. (1H NMR). 95.5:4.5 e.r. Chiral HPLC. Chiralpak IC. Hex/PrOH 90:10; 1.0 mL/min. f<sub>R</sub> 18.9 (major), 24.2 (minor).<sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>): δ 6.69-6.75 (3H, m, Cα'H), 4.00 (1H, ddd, J<sub>1</sub>H-F 48.7, J<sub>2</sub> 8.7, J<sub>3</sub> 3.1, α-fluoro CH<sub>2</sub>), 2.86 (1H, sext., J 7.0, benzylic CH<sub>2</sub>), 2.07-2.19 (2H, m, diastereotopic β-fluoro CH<sub>2</sub>), 1.75-1.83 (1H, m, CH<sub>2</sub>), 1.44-1.65 (3H, m, CH<sub>2</sub>), 1.31 (3H, dt, J<sub>1</sub> 7.0, J<sub>2</sub> 1.3, CH<sub>3</sub>) ppm. <sup>19</sup>F NMR (376 MHz, C<sub>6</sub>D<sub>6</sub>): δ -113.0 (1F, s, Cα'F), -188.3 (1F, s, C<sup>sp</sup>-F) ppm. <sup>13</sup>C NMR (125 MHz, C<sub>6</sub>D<sub>6</sub>): δ 174.9 (γ-lactone Cq), 161.3 (d, J<sup>C-F</sup> 245, ipso(F)-Cq), 137.8 (dd, J<sub>1</sub> 4.3, J<sub>2</sub> 3.4, meta(F)-Cq), 129.0 (d, J<sup>C-F</sup> 15.3, ortho(F)-Cq), 121.9 (d, J<sup>C-F</sup> 3.1, meta(F)-CH), 115.7 (d, J<sup>C-F</sup> 22.6, ortho(F)-CH), 91.9 (d, J<sup>C-F</sup> 183, CH-F), 83.2 (dd, J<sub>1</sub> 17.0, J<sub>2</sub> 2.9, Cq-O), 31.5 (d, J<sup>C-F</sup> 3.4, CH<sub>2</sub>), 31.2 (d, J<sup>C-F</sup> 18.6, benzylic CH), 28.5 (d, J<sup>C-F</sup> 1.3, CH<sub>2</sub>), 27.0 (d, J<sup>C-F</sup> 6.7, CH<sub>2</sub>), 22.8 (dd, J<sub>1</sub> 5.4, J<sub>2</sub> 2.3, CH<sub>3</sub>) ppm. ESI-HRMS (positive) M = C14H14F2O2, expected (M+H)<sup>+</sup> m/z 253.1035, observed (M+H)<sup>+</sup> m/z 253.1035. [α]<sup>198</sup>D +75.9 (c = 1.00, CH<sub>2</sub>Cl<sub>2</sub>).

**Diastereoselective Reduction**

![Red-Al Toluene, -78 °C → HO](image)

**Spirocyclic Fluoro-Alcohol (E<sub>2</sub> R)**

To a cooled (−78 °C, dry ice/acetone bath) solution of β-fluoro spiroketone B<sub>3R</sub> (> 20:1 d.r., 95.5:4.5 e.r.) (20 mg, 0.08 mmol, 1.0 equiv.) in anhydrous toluene (2.5 mL) was added Red-Al<sup>TM</sup> (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<sub>4</sub>Cl 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<sub>2</sub>SO<sub>4</sub>, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane → n-hexane/Et<sub>2</sub>O 4:1). Colorless crystalline solid.
Isolated yield 94% (19 mg, 0.075 mmol). Rf (silica gel, n-Hex/Et2O 4:1) 0.49. > 20:1 d.r. (1H NMR).

**Chemical Formula:**

**Molecular Weight:** 329.66

**Spirocyclic Fluoro-Alcohol (E5 R)**

![spirocyclic fluoro-alcohol](image)

To a cooled (-78 °C, dry ice/acetone bath) solution of β-fluoro spiroketone B5 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™ (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 NH4Cl 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 Na2SO4, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane → n-hexane/Et2O 4:1). Colorless crystalline solid. Isolated yield 92% (17 mg, 0.06 mmol). Rf (silica gel, n-Hex/Et2O 4:1) 0.39. > 20:1 d.r. (1H NMR).

**Spirocyclic Bromo-Alcohol (F4 S)**

![spirocyclic bromo-alcohol](image)

To a cooled (-78 °C, dry ice/acetone bath) solution of β-bromo spiroketone C4 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™ (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 NH4Cl 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$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (n-hexane → n-hexane/Et$_2$O 4:1). Colorless oil. Isolated yield 87% (23 mg, 0.07 mmol). $R_f$ (silica gel, n-Hex/Et$_2$O 4:1) 0.43. > 20:1 d.r. ($^1$H NMR). 95.5:4.5 e.r. Chiral HPLC. Chiralpak IC. $^6$Hex/PrOH 95:5; 1.0 mL/min. $t_R$ 12.2 (major), 15.4 (minor). $^1$H NMR (500 MHz, C$_6$D$_6$): $\delta$ 7.14 (1H, dd, $J_1$ 7.8, $J_2$ 1.2, C$q$H), 6.67 (1H, td, $J_1$ 7.9, $J_2$ 0.3, C$q$H), 6.56 (1H, dd, $J_1$ 8.0, $J_2$ 1.0, C$q$H), 4.26-4.29 (2H, m, $\alpha$-bromo C$_H$-Br + C$_H$-O), 3.20-3.27 (1H, m, benzylic C$_H$), 2.29 (1H, d, $J_1$ 7.2, C$_H$), 1.57-1.62 (1H, m, C$_H$), 1.22-1.27 (2H, m, C$_H$) ppm. $^{13}$C NMR (125 MHz, C$_6$D$_6$): $\delta$ 142.5 (C$q$), 137.8 (C$q$), 135.3 (C$q$), 128.9 (CH), 126.7 (CH), 124.9 (CH), 80.1 (CH-O), 57.4 (C$_H$-Br), 57.1 (C$_q$-carbonyl C$q$), 39.1 (CH$_2$), 37.1 (CH$_2$), 35.4 (CH$_2$), 30.6 (benzylic CH), 23.9 (CH$_3$), 22.9 (CH$_3$) 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$_2$Cl$_2$).

References and Notes


NMR Spectra

Fluorinated Compounds

Substrate rac-A$_1$
$^1$H NMR 400 MHz, C$_6$D$_6$

$^{13}$C NMR 125 MHz, C$_6$D$_6$

β-Fluoro Spiroketone B$_1^R$
\H NMR 400 MHz, \C\textsubscript{6}D\textsubscript{6}

diastereomer 1

\C\textsubscript{13} NMR 100 MHz, \C\textsubscript{6}D\textsubscript{6}

diastereomer 1
$^{19}$F NMR 375 MHz, C$_6$D$_6$

Diastereomer 1
β-Fluoro Spiroketone B$_1^S$

$^1$H NMR 400 MHz, C$_6$D$_6$

$^{13}$C NMR 100 MHz, C$_6$D$_6$
$^{19}$F NMR 375 MHz, C$_6$D$_6$

Me diastereomer 2
Substrate \textit{rac-A}_2

\( ^1 \text{H NMR 400 MHz, C}_6 \text{D}_6 \)

\( ^{13} \text{C NMR 100 MHz, C}_6 \text{D}_6 \)
β-Fluoro Spirokctone B₂R

$^1$H NMR 500 MHz, C₆D₆

$^{13}$C NMR 125 MHz, C₆D₆
β-Fluoro Spiroketone B$_2^S$

$^1$H NMR 400 MHz, C$_6$D$_6$

$^{13}$C NMR 100 MHz, C$_6$D$_6$
$^{19}$F NMR 375 MHz, C$_6$D$_6$

diastereomer 2
Substrate \textit{rac-}A_3

\textsuperscript{1}H NMR 500 MHz, C\textsubscript{6}D\textsubscript{6}

\textsuperscript{13}C NMR 125 MHz, C\textsubscript{6}D\textsubscript{6}
β-Fluoro Spiroketone B₃⁺

$^1$H NMR 500 MHz, C₆D₆

$^{13}$C NMR 125 MHz, C₆D₆
\[ ^{19}\text{F NMR 375 MHz, C}_6\text{D}_6 \]

diastereomer 1
β-Fluoro Spiroketone B₃^S

$^{1}H$ NMR 500 MHz, C₆D₆

$^{13}C$ NMR 125 MHz, C₆D₆
$^{19}$F NMR 375 MHz, C$_6$D$_6$

diastereomer 2
Substrate rac-A_4

$^{1}H$ NMR 400 MHz, C$_6$D$_6$
$^{19}$F NMR 375 MHz, C$_6$D$_6$
β-Fluoro Spiroketone B₄⁺

¹H NMR 500 MHz, C₆D₆

¹³C NMR 125 MHz, C₆D₆

diastereomer 1
$^{19}\text{F NMR}$ 375 MHz, C$_6$D$_6$

Me diastereomer 1
β-Fluoro Spiroketone B₄⁺

¹H NMR 500 MHz, C₆D₆

¹³C NMR 125 MHz, C₆D₆

Me

diastereomer 2
Substrate rac-As

$^1$H NMR 500 MHz, C$_6$D$_6$

$^{13}$C NMR 125 MHz, C$_6$D$_6$
β-Fluoro Spiroketone B5^R

\(^1\)H NMR 500 MHz, C\(_6\)D\(_6\)

\(^{13}\)C NMR 125 MHz, C\(_6\)D\(_6\)
$^{19}$F NMR 375 MHz, C$_6$D$_6$

diastereomer 1
β-Fluoro Spiroketone B$_5^S$

$^1$H NMR 500 MHz, C$_6$D$_6$

$^13$C NMR 125 MHz, C$_6$D$_6$
$^{19}$F NMR 375 MHz, $C_6D_6$

diastereomer 2
$^1$H-$^1$H NOESY 500 MHz, C$_6$D$_6$

diastereomer 2

$^1$H-$^1$F HOESY 300 MHz, C$_6$D$_6$

diastereomer 2
Substrate rac-A₆

¹H NMR 400 MHz, C₆D₆

¹³C NMR 100 MHz, C₆D₆
β-Fluoro Spiroketone $\text{B}_6^R$

$^1\text{H NMR} 500\text{ MHz, C}_6\text{D}_6$

$^{13}\text{C NMR} 125\text{ MHz, C}_6\text{D}_6$
$^{19}$F NMR 375 MHz, C$_6$D$_6$

Md diastereomer 1
β-Fluoro Spiroketone B$_6^S$

$^1$H NMR 500 MHz, C$_6$D$_6$

$^{13}$C NMR 125 MHz, C$_6$D$_6$
$^{19}\text{F NMR } 375 \text{ MHz, C}_6\text{D}_6$

Diastereomer 2
Substrate \textit{rac-A}_7

$^1$H NMR 500 MHz, C$_6$D$_6$

$^{13}$C NMR 125 MHz, C$_6$D$_6$
β-Fluoro Spiroketone B$_7^R$

$^1$H NMR 500 MHz, C$_6$D$_6$

$^{13}$C NMR 125 MHz, C$_6$D$_6$
$^{19}$F NMR 375 MHz, C$_6$D$_6$

diastereomer 1
β-Fluoro Spiroketone B₁⁻

¹H NMR 500 MHz, C₆D₆

¹³C NMR 125 MHz, C₆D₆
\[19\text{F} \text{NMR 375 MHz, } \text{C}_6\text{D}_6\]

\text{diastereomer 2}

\[\text{H-19F HOESY 300 MHz, } \text{C}_6\text{D}_6\]

\text{diastereomer 2}
Substrate rac-\(\text{A}_8\)

\(^1\text{H NMR 500 MHz, C}_6\text{D}_6\)

\(^{13}\text{C NMR 125 MHz, C}_6\text{D}_6\)
$^{19}$F NMR 375 MHz, $C_6D_6$

![NMR Spectrum Image](image_url)
β-Fluoro Spiroketone B₈ᴿ

¹H NMR 500 MHz, C₆D₆

¹³C NMR 125 MHz, C₆D₆
β-Fluoro Spiroketone B$_8^S$

$^1$H NMR 500 MHz, C$_6$D$_6$

$^13$C NMR 125 MHz, C$_4$D$_6$
$^{19}$F NMR 375 MHz, C$_6$D$_6$
Substrate \textit{rac-}A_9

$^1$H NMR 500 MHz, C$_6$D$_6$

$^{13}$C NMR 125 MHz, C$_6$D$_6$
β-Fluoro Spiroketone B$_2^R$

$^1$H NMR 500 MHz, C$_6$D$_6$

$^{13}$C NMR 125 MHz, C$_6$D$_6$
$^{19}$F NMR 375 MHz, C$_6$D$_6$

[Diagram of a chemical structure with labels: F, C, O, Cl, Me, diastereomer 1]
β-Fluoro Spiroketone B₃<sup>S</sup>

<sup>1</sup>H NMR 500 MHz, C₆D₆

<sup>1</sup>C NMR 125 MHz, C₆D₆
$^{19}$F NMR 375 MHz, C$_6$D$_6$

diastereomer 2
Substrate A₁₀

$^1$H NMR 500 MHz, C₆D₆

$^{13}$C NMR 125 MHz, C₆D₆
Substrate $\text{rac-A}_{11}$

$^1\text{H NMR 400 MHz, C}_6\text{D}_6$

$^{13}\text{C NMR 100 MHz, C}_6\text{D}_6$
β-Fluoro Spiroketone B$_{11}^R$

$^1$H NMR 500 MHz, C$_6$D$_6$

$^{13}$C NMR 125 MHz, C$_6$D$_6$
$^{19}$F NMR 375 MHz, $C_6D_6$

diastereomer 1
β-Fluoro Spiroketone B_{11}^S

$^1$H NMR 500 MHz, C$_6$D$_6$

$^{13}$C NMR 125 MHz, C$_6$D$_6$
$^{19}$F NMR 375 MHz, C$_6$D$_6$

diastereomer 2
Substrate $\text{rac-}A_{12}$

$^1\text{H NMR}$ 500 MHz, $\text{C}_6\text{D}_6$

$^{13}\text{C NMR}$ 125 MHz, $\text{C}_6\text{D}_6$
β-Fluoro Spiroketone B₁₂<sup>R</sup>

<sup>1</sup>H NMR 500 MHz, C₆D₆

<sup>1</sup>C NMR 125 MHz, C₆D₆
\[^{19}F\] NMR 375 MHz, C\textsubscript{6}D\textsubscript{6}

diastereomer 1
β-Fluoro Spiroketone B_{12}^S

$^1$H NMR 500 MHz, C₆D₆

$^{13}$C NMR 125 MHz, C₆D₆
Substrate rac-$A_{13}$

$^1$H NMR 500 MHz, C$_6$D$_6$

$^{13}$C NMR 125 MHz, C$_6$D$_6$
β-Fluoro Spiroketone B$_{13}^R$

$^1$H NMR 500 MHz, C$_6$D$_6$

$^{13}$C NMR 125 MHz, C$_6$D$_6$
$^{19}$F NMR 375 MHz, C$_6$D$_6$

β-Fluoro Spiroketone B$_{13}^S$
$^{19}\text{F NMR 375 MHz, C}_6\text{D}_6$

$^{1}\text{H-}^{19}\text{F HOESY 300 MHz, C}_6\text{D}_6$
γ-Lactone $D_8^R$

$^1$H NMR 500 MHz, $C_6D_6$

$^{13}$C NMR 125 MHz, $C_6D_6$
$^{19}\text{F NMR} 375 \text{ MHz, C}_6\text{D}_6$
Fluoro Alcohol $E_2^R$

$^1\text{H NMR} 500 \text{ MHz, } C_6\text{D}_6$

$^{13}\text{C NMR} 125 \text{ MHz, } C_6\text{D}_6$
Fluoro Alcohol E₅⁺

¹H NMR 500 MHz, C₆D₆

¹³C NMR 125 MHz, C₆D₆

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Brominated Compounds

β-Bromo Spiroketone C₁⁻R

¹H NMR 500 MHz, C₆D₆

¹³C NMR 125 MHz, C₆D₆
β-Bromo Spiroketone $C_1^S$

$^1$H NMR 500 MHz, C$_6$D$_6$

$^{13}$C NMR 125 MHz, C$_6$D$_6$
β-Bromo Spiroketone C$_2^R$

$^1$H NMR 400 MHz, C$_6$D$_6$

$^{13}$C NMR 100 MHz, C$_6$D$_6$
β-Bromo Spiroketone C$_2^S$

$^1$H NMR 500 MHz, C$_6$D$_6$

$^{13}$C NMR 125 MHz, C$_6$D$_6$
β-Bromo Spiroketone C₃

¹H NMR 500 MHz, C₆D₆

¹³C NMR 125 MHz, C₆D₆
\textbf{\textsuperscript{19}F NMR 375 MHz, C\textsubscript{6}D\textsubscript{6}}

\[\text{diastereomer 1}\]
β-Bromo Spiroketone C₃⁺

¹H NMR 500 MHz, C₆D₆

¹³C NMR 125 MHz, C₆D₆
$^{19}$F NMR 375 MHz, C$_6$D$_6$

diastereomer 2
$\beta$-Bromo Spiroketone $C_4^R$

$^1\text{H} \text{NMR} 500 \text{ MHz, C}_6\text{D}_6$

$\text{C}^1\text{C NMR} 125 \text{ MHz, C}_6\text{D}_6$
β-Bromo Spiroketone C₄S

\(^1\)H NMR 500 MHz, C₆D₆

\(^{13}\)C NMR 125 MHz, C₆D₆
β-Bromo Spiroketone C₅⁺

¹H NMR 500 MHz, C₆D₆

¹³C NMR 125 MHz, C₆D₆
β-Bromo Spiroketone $C_5^S$

$^1H$ NMR 400 MHz, C$_6$D$_6$

$^{13}C$ NMR 100 MHz, C$_6$D$_6$
β-Bromo Spiroketone C₆ᵣ

¹H NMR 500 MHz, C₆D₆

¹³C NMR 125 MHz, C₆D₆

diastereomer 1
$^1$H-$^1$H NOESY 500 MHz, C$_6$D$_6$

diastereomer 1
β-Bromo Spiroketone $C_6^S$

$^1$H NMR 500 MHz, C$_6$D$_6$

$^{13}$C NMR 125 MHz, C$_6$D$_6$
β-Bromo Spiroketone $C_7^R$

$^1$H NMR 500 MHz, C$_6$D$_6$

$^{13}$C NMR 125 MHz, C$_6$D$_6$
$^{19}\text{F NMR 375 MHz, C}_6\text{D}_6$

![Diagram](image-url)
β-Bromo Spiroketone C₇⁻

\(^1\)H NMR 500 MHz, C₆D₆

\(^{13}\)C NMR 125 MHz, C₆D₆
$^{19}$F NMR 375 MHz, C$_6$D$_6$

diastereomer 2
β-Bromo Spiroketone $C^R_8$

$^1$H NMR 500 MHz, C$_6$D$_6$

$^{13}$C NMR 125 MHz, C$_6$D$_6$
β-Bromo Spiroketone C₉

¹H NMR 500 MHz, C₆D₆

¹³C NMR 125 MHz, C₆D₆
β-Bromo Spiroketone C<sub>10</sub><sup>R</sup>

$^1$H NMR 500 MHz, C<sub>6</sub>D<sub>6</sub>

$^{13}$C NMR 125 MHz, C<sub>6</sub>D<sub>6</sub>
β-Bromo Spiroketone $C_{10}^S$

$^1$H NMR 500 MHz, $C_6D_6$

$^{13}$C NMR 125 MHz, $C_6D_6$
β-Benzyl Spiroketone C_{11}^R

$^1$H NMR 500 MHz, C_{6}D_{6}

$^{13}$C NMR 125 MHz, C_{6}D_{6}
β-Bromo Spiroketone C<sub>11</sub><sup>S</sup>

<sup>1</sup>H NMR 500 MHz, C<sub>6</sub>D<sub>6</sub>

<sup>13</sup>C NMR 125 MHz, C<sub>6</sub>D<sub>6</sub>
β-Bromo Spiroketone C₁₂ᵣ

¹H NMR 500 MHz, C₆D₆

¹³C NMR 125 MHz, C₆D₆
β-Bromo Spiroketone C$_{12}^S$

$^1$H NMR 500 MHz, C$_6$D$_6$

$^{13}$C NMR 125 MHz, C$_6$D$_6$
Bromo Alcohol $F_4^S$

$^1H$ NMR 500 MHz, $C_6D_6$

$^{13}C$ NMR 125 MHz, $C_6D_6$
HPLC Traces

Fluorinated Compounds
$$\beta$$-Fluoro Spiroketone $B_1^R$

\[
\begin{array}{c}
\text{Peak} & \text{Retention Time} & \text{Width} & \text{Area} & \text{Height} & \text{Area} \\
1 & 22.482 \text{ min} & 0.4974 & 9035.70996 & 273.54646 & 49.8604 \\
2 & 30.903 \text{ min} & 0.6961 & 9086.30371 & 194.83844 & 50.1396 \\
\end{array}
\]

$$\beta$$-Fluoro Spiroketone $B_1^S$

\[
\begin{array}{c}
\text{Peak} & \text{Retention Time} & \text{Width} & \text{Area} & \text{Height} & \text{Area} \\
1 & 17.328 \text{ min} & 0.4601 & 1039.8044 & 336.85147 & 50.7118 \\
2 & 23.550 \text{ min} & 0.7282 & 10106.1404 & 207.49112 & 49.2882 \\
\end{array}
\]
**β-Fluoro Spiroketone $B_3^R$**

![Diagram of β-Fluoro Spiroketone $B_3^R$](image)

**β-Fluoro Spiroketone $B_3^S$**

![Diagram of β-Fluoro Spiroketone $B_3^S$](image)
**β-Fluoro Spiroketone $B_4^R$**

![Diagram of $\beta$-Fluoro Spiroketone $B_4^R$]

<table>
<thead>
<tr>
<th>Peak RetTime</th>
<th>Type</th>
<th>Width [min]</th>
<th>Area [mAU*s]</th>
<th>Height [mAU]</th>
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<tbody>
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<td>0.4177</td>
<td>1674.75720</td>
<td>60.73676</td>
<td>43.1122</td>
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**β-Fluoro Spiroketone $B_4^S$**

![Diagram of $\beta$-Fluoro Spiroketone $B_4^S$]

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β-Fluoro Spiroketoacetone $B_5^R$

[Chemical Structure Image]

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β-Fluoro Spiroketoacetone $B_5^S$

[Chemical Structure Image]

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β-Fluoro Spiroketone $B^R_o$

β-Fluoro Spiroketone $B^S_o$
β-Fluoro Spiroketone $B_7^R$

β-Fluoro Spiroketone $B_7^S$
### β-Fluoro Spiroketone B₈⁺

![Chemical Structure](image)

<table>
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### β-Fluoro Spiroketone B₈⁻

![Chemical Structure](image)

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**β-Fluoro Spiroketone \( B_9^R \)**

![Diagram of β-Fluoro Spiroketone \( B_9^R \)]

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**β-Fluoro Spiroketone \( B_9^S \)**

![Diagram of β-Fluoro Spiroketone \( B_9^S \)]

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<td>7562.55127</td>
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<tr>
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β-Fluoro Spiroketone B_{10}
\( \beta\)-Fluoro Spiroketone \( B_{11}^R \)

\[
\begin{align*}
&\text{El} \\
&\text{B}_{11}^R
\end{align*}
\]

\( \beta\)-Fluoro Spiroketone \( B_{11}^S \)

\[
\begin{align*}
&\text{El} \\
&\text{B}_{11}^S
\end{align*}
\]
\[ \beta\text{-Fluoro Spiroketone } B_{13}^R \]

\[ \beta\text{-Fluoro Spiroketone } B_{13}^S \]
Brominated Compounds

β-Bromo Spiroketone $C_1^R$

β-Bromo Spiroketone $C_1^S$
β-Bromo Spiroketone $C_2^R$

$\begin{align*}
\text{Me} & \quad \text{O} \\
\text{Me} & \quad \text{Br}
\end{align*}$

<table>
<thead>
<tr>
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</table>

β-Bromo Spiroketone $C_2^S$

$\begin{align*}
\text{Me} & \quad \text{O} \\
\text{Me} & \quad \text{Br}
\end{align*}$

<table>
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<tr>
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<tbody>
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β-Bromo Spiroketone $C_3^R$

β-Bromo Spiroketone $C_3^S$
β-Bromo Spiroketone $C_4^R$

β-Bromo Spiroketone $C_4^S$
**β-Bromo Spiroketone C₅⁵**

![Chemical Structure Image]

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**β-Bromo Spiroketone C₅⁸**

![Chemical Structure Image]

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**β-Bromo Spiroketone C₆⁵**

![Structure Image]

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**β-Bromo Spiroketone C₆⁶**

![Structure Image]

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**β-Bromo Spiroketone C\textsubscript{7}^R**

![β-Bromo Spiroketone C\textsubscript{7}^R](image)

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<td>0.5199</td>
<td>2.1943e+04</td>
<td>677.49371</td>
<td>51.2558</td>
</tr>
</tbody>
</table>

**β-Bromo Spiroketone C\textsubscript{7}^S**

![β-Bromo Spiroketone C\textsubscript{7}^S](image)

<table>
<thead>
<tr>
<th>Peak RetTime Type</th>
<th>Width [min]</th>
<th>Area [mAU*sec]</th>
<th>Height [mAU]</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 11.866 VB</td>
<td>0.2836</td>
<td>1.1292e+04</td>
<td>636.69049</td>
<td>49.6135</td>
</tr>
<tr>
<td>2 11.859 BB</td>
<td>0.2700</td>
<td>1.0808e+04</td>
<td>582.64884</td>
<td>51.3865</td>
</tr>
<tr>
<td>1 11.859 BB</td>
<td>0.2700</td>
<td>1.0808e+04</td>
<td>582.64884</td>
<td>48.32244</td>
</tr>
<tr>
<td>2 14.017 BB</td>
<td>0.3668</td>
<td>1.4984e+04</td>
<td>622.60999</td>
<td>94.5563</td>
</tr>
</tbody>
</table>
\[ \beta\text{-Bromo Spiroketone } C_8^R \]

\[ \beta\text{-Bromo Spiroketone } C_8^S \]
**β-Bromo Spiroketone C₉**

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>Peak RetTime Type</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area %</th>
<th>Peak RetTime Type</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.279 VB</td>
<td>0.2527</td>
<td>4796.5966</td>
<td>204.54424</td>
<td>50.3438</td>
<td>1</td>
<td>8.400 BV</td>
<td>0.2478</td>
<td>253.25462</td>
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<tr>
<td>2</td>
<td>10.711 VB</td>
<td>0.3070</td>
<td>4731.08301</td>
<td>230.90935</td>
<td>49.6562</td>
<td>2</td>
<td>10.530 VB</td>
<td>0.3134</td>
<td>4349.50732</td>
</tr>
</tbody>
</table>
β-Bromo Spiroketone $C_{10}^R$

β-Bromo Spiroketone $C_{10}^S$

189
β-Bromo Spiroketone C_{11}^R

β-Bromo Spiroketone C_{11}^S
β-Bromo Spiroketone $C_{12}^R$

β-Bromo Spiroketone $C_{12}^S$
Spiro γ-Lactone ($D_e^R$)

Peaks RetTime Type Width Area Height Area %
--- | [min] | [min] | [mAU$^a$] | [nAU] | | | | | | 1 | 18.720 | BB | 0.6128 | 2.14635e4 | 578.60938 | 49.8481 | | | | | | 2 | 23.686 | BB | 0.5859 | 2.15943e4 | 540.79346 | 50.1519 | | | | | | 1 | 18.822 | BB | 0.4809 | 1.19352e4 | 389.85699 | 95.2437 | | | | | | 2 | 24.228 | BB | 0.4766 | 596.02618 | 17.10369 | 4.7563
Spirocyclic Bromo-Alcohol ($F_4^S$)

Spirocyclic Fluoro-Alcohol ($E_2^R$)
Spirocyclic Fluoro-Alcohol ($E_5^R$)