Supporting Information
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Enantioselective Fluorination of Spirocyclic β-Prolinals Scaffolds Using Enamine Catalysis

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Supporting Information

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**General Methods**

The LCMS data were acquired on a Waters Acquity UPLC-MS instrument with a Waters Acquity system including column manager, binary solvent manager, sample organizer, PDA detector (operating at 254 nm), ELS detector, and TQ-MS equipped with APPI-source operating in positive ion mode. The LC conditions were: Acquity UPLC BEH C18 1.7 μm; 2.1 × 50 mm operating at 60 °C with 1.2 mL/min binary gradient consisting of H2O+0.05% trifluoroacetic acid (TFA) (A) and MeCN+5% H2O+0.05% TFA (B). Gradient: 0.00 min: 10% B; 1.00 min: 100% B; 1.01 min: 10% B; 1.15 min: 10% B. Retention times must be compared to a total run time of 1.15 min. HRMS data were acquired on a Bruker Daltonic MicroTOF using internal calibration and ESI in positive mode. NMR data were collected with a Bruker 600-Avance-III spectrometer equipped with a 5 mm TCI cryoprobe operating at 600 and 151 MHz for 1H and 13C, respectively. 19F NMR spectra were recorded on a Bruker 500-Avance spectrometer equipped with a 5 mm QNP probe operating at 470.6 Hz using CFCl3 as reference. The solvents used for NMR were CDC13, with reference signals for CHCl3 (δ = 7.26 ppm, 1H) and (δ = 77.16 ppm, 13C), and DMSO-d6 with the reference signals for residual DMSO (δ = 2.50 ppm, 1H) and (δ = 39.51 ppm, 13C) using TMS as internal reference. The chemical shifts are provided in ppm and broad proton signals are labeled (br). N-Fluorobenzenesulfonimide (NFSI), (R)-2-(bis(3,5-bis(trifluoromethyl)phenyl)((trimethylsilyl)oxy)methyl)pyrrolidine (R)-7, (R)-5-benzyl-2,2,3-trimethylimidazolidin-4-one 2,2-dichloroacetate and NaBH4 were purchased from Sigma-Aldrich. Each of the aldehydes 1a-h were also fluorinated using a 1:1 mixture of (S)- and (R)-9 in order to get a racemic mixture of 2a-h for the determination of ee’s using chiral supercritical fluid chromatography (SFC). The optical rotation is reported in degrees at a given concentration (c) in g/100 mL.

**General Procedure for the Enantioselective Fluorination of Aldehydes (A)**

To a solution of 1a-h in MTBE (0.5M) was added catalyst (R)-9 (10 mol %) and the mixture was stirred for 5 min at rt after which N-fluorobenzenesulfonimide (NFSI) (1.2 equiv) was added and the resulting mixture was stirred at 40 °C for 18 h. Subsequently, the reaction mixture was diluted with MTBE and passed through a filter directly onto SiO2 for flash chromatographic purification to yield 2a-h.

**General Procedure for the Reduction of Purified Aldehydes to the Corresponding Alcohols (B)**

To a solution of the purified aldehyde in MeOH (0.1M) was added NaBH4 (3 equiv) and the reaction mixture was stirred for 30 min at rt. Subsequently, H2O was added and the aqueous phase was extracted twice with EtOAc after which the combined organic phases were washed with brine, dried over MgSO4, filtered and concentrated in vacuo to provide the corresponding alcohol.

**General Procedure for the Reduction of Purified Aldehydes to the Corresponding p-Nitrobenzoates (C)**

The purified fluorinated aldehyde was reduced to the corresponding alcohol using the general procedure. The alcohol was then placed in a 4 mL vial and dissolved in THF (0.3M), after which 4-dimethylaminopyridine (0.2 equiv) and p-nitrobenzoyl chloride (2 equiv) were added and the resulting mixture stirred at 40 ° overnight. Subsequently, NaOH (1M) was added followed by EtOAc, a separation of phases and extraction of the aqueous phase twice with EtOAc. The combined organic phases were washed with brine, dried over MgSO4, filtered, concentrated in vacuo and purified using silica gel chromatography to provide the corresponding p-nitrobenzyolated product.
Preparation of the Fluorinated Products

**Benzy1 (5)-8-fluoro-8-formyl-2-oxa-6-azaspiro[3.4]octane-6-carboxylate (2a):** The enantioselective fluorination provided 2a (76 mg, 0.259 mmol, 71% yield, 79% ee) as a colorless oil. 1H NMR (400 MHz, CDCl3) δ 10.01 – 10.07 (m, 1H), 7.39 – 7.30 (m, 5H), 5.14 – 5.12 (m, 2H), 4.88 – 4.39 (m, 4H), 4.06 – 3.50 (m, 4H). (conformers and hydrate formation). 13C NMR (151 MHz, CDCl3) δ 197.10 – 196.44 (m, 154.4, 154.2, 80.1, 140.4, 132.8, 128.7, 128.6, 128.3, 128.1, 127.3, 76.4 – 75.9 (m), 73.56 – 72.73 (m), 53.3, 52.5, 51.74 – 50.87 (m), 28.4, 28.3. 19F NMR (471 MHz, CDCl3) δ -169.64, -170.53 (m), 10.09 – 10.03 (m, 1H), 7.50 – 7.30 (m, 5H), 5.75 – 4.59 (m, 6H), 3.79 – 3.38 (m, 2H). (conformers). 13C NMR (151 MHz, CDCl3) δ 197.16 – 196.2 (m), 154.0, 140.4, 132.8, 128.7, 128.6, 128.3, 128.1, 127.3, 76.4 – 75.9 (m), 74.9 – 74.3 (m), 67.9, 67.1, 45.1, 44.5, 44.5, 34.5 – 33.6 (m), 28.6, 28.5. (conformers). 19F NMR (471 MHz, CDCl3) δ -171.97, -172.35. (conformers). HR MS-ESI: m/z for C13H12FNO3 [MH]+ calcd. 294.1136; found 294.1137. [α]D = +9.9° (c = 0.27, CHCl3, 79% ee).

**Benzyl (R)-8-fluoro-8-formyl-2-oxa-6-azaspiro[3.4]octane-6-carboxylate (2b):** The enantioselective fluorination provided 2b (97 mg, 0.363 mmol, 77% yield, 77% ee) as a colorless oil. 1H NMR (400 MHz, CDCl3) δ 7.74 – 7.52 (m, 5H), 5.75 – 4.59 (m, 6H), 3.79 – 3.38 (m, 2H), 2.92 – 2.70 (m, 2H). 13C NMR (151 MHz, CDCl3) δ 196.6 – 196.2 (m), 154.0, 140.4, 132.8, 128.7, 128.6, 128.3, 128.1, 127.3, 76.4 – 75.9 (m), 74.9 – 74.3 (m), 67.9, 67.1, 45.1, 44.5, 29.7 – 28.9 (m). (conformers and hydrate formation). 19F NMR (471 MHz, CDCl3) δ -171.97, -172.35. (conformers). HR MS-ESI: m/z for C13H12FNO3 [MH]+-tBu calced. 204.0677; found 204.0676. [α]D = +11.3° (c = 0.69, CHCl3, 77% ee).

** tert-Butyl 3-fluoro-3-formylpyrrolidine-1-carboxylate (2d):** The enantioselective fluorination provided 2d (60 mg, 0.276 mmol, 68% yield, 26% ee) as a yellow oil. 1H NMR (400 MHz, CDCl3) δ 9.89 – 9.86 (m, 1H), 3.81 – 3.41 (m, 4H), 2.34 – 2.06 (m, 2H), 1.49 – 1.43 (m, 9H). (conformers). 13C NMR (151 MHz, CDCl3) δ 198.6 – 198.0 (m), 154.8, 154.5, 105.3 – 103.8 (m), 80.5 – 79.7 (m), 54.0 – 53.3 (m). 19F NMR (471 MHz, CDCl3) δ -165.21, -165.80. (conformers). HR MS-ESI: m/z for C13H12FNO3 [MH]+-tBu calced. 162.0561; found 162.0561. [α]D = -10.7° (c = 0.2, CHCl3, 26% ee).

** tert-Butyl (S)-3-fluoro-3-formyl-4,4-dimethylpyrrolidine-1-carboxylate (2e):** The enantioselective fluorination provided 2e (40 mg, 0.163 mmol, 66% yield, 97% ee) as a yellow oil. 1H NMR (400 MHz, CDCl3) δ 9.81 – 9.77 (m, 1H), 4.01 – 3.87 (m, 1H), 3.67 – 3.52 (m, 1H), 3.43 – 3.28 (m, 2H), 1.47 – 1.46 (m, 3H), 1.08 – 1.05 (m, 3H). 13C NMR (151 MHz, CDCl3) δ 197.9 – 197.3 (m), 154.5, 154.2, 80.1, 62.6, 62.5, 58.7, 58.1, 58.0, 57.5, 53.8 – 52.6 (m), 52.1 – 51.1 (m), 28.5, 28.4, 22.9 – 22.8 (m), 19.4 – 19.2 (m). (conformers). 19F NMR (471 MHz, CDCl3) δ -169.64, -170.53. (conformers). HR MS-ESI: m/z for C13H12FNO3 [MH]+-tBu calced. 190.0874; found 190.0867. [α]D = +1.3° (c = 1.27, CHCl3, 97% ee).

6-Benzyl 2-((tert-buty1) (S)-8-fluoro-8-formyl-2,6-diaza-8simo[3.4]octane-2,6-dicarboxylate (2f): The enantioselective fluorination provided 2f (85 mg, 0.212 mmol, 68% yield, 78% ee) as a colorless oil. 1H NMR (600 MHz, CDCl3) δ 9.98 – 9.93 (m, 1H), 7.40 – 7.29 (m, 5H), 5.15 – 5.10 (m, 2H), 4.00 – 3.55 (m, 8H), 1.44 – 1.39 (m, 9H). (conformers and hydrate formation). Due to hydrate formation, 2f was additionally characterized after reduction to the corresponding alcohol 2fr using the general procedure. 1H NMR (600 MHz, CDCl3) δ 7.40 – 7.30 (m, 5H), 5.16 – 5.09 (m, 2H), 4.21 – 3.93 (m, 4H), 3.90 – 3.66 (m, 5H), 3.62 – 3.51 (m, 1H), 2.79 – 2.56 (br, 1H), 1.46 – 1.39 (m, 9H). (conformers). 13C NMR (151 MHz, CDCl3) δ 154.0, 154.7, 154.5, 136.3, 128.6, 128.6, 128.2, 128.2, 128.1, 128.0, 103.0 – 100.8 (m), 80.3, 67.3, 67.3, 62.4, 62.2, 55.2, 52.7, 52.5, 52.4, 44.5 – 43.2 (m), 28.3. (conformers). 19F NMR (471 MHz, CDCl3) δ -168.32, -168.40. (conformers). HR MS-ESI: m/z for C13H12F3NO3 [MH]+ calcd. 395.1977; found 395.1975. [α]D = +1.5° (c = 0.73, CHCl3, 78% ee).
**tert-Butyl (S)-4-fluoro-4-formyl-8-oxa-2-azaspiro[4.5]decane-2-carboxylate (2g):** The enantioselective fluorination provided 2g (41 mg, 0.143 mmol, 57% yield, 93% ee) as a yellow oil. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 9.83 – 9.79 (m, 1H), 3.95 – 3.77 (m, 4H), 3.69 – 3.45 (m, 2H), 3.40 – 3.30 (m, 2H), 1.84 – 1.54 (m, 3H), 1.48 – 1.44 (m, 9H), 1.35 – 1.27 (m, 1H). (conformers). \(^1^3\)C NMR (151 MHz, CDCl\(_3\)) \(\delta\) 198.01 – 197.41 (m), 154.2, 80.5, 65.0, 65.0, 63.7, 52.2, 51.8, 51.3 – 50.5 (m), 33.1, 29.9 – 29.5 (m), 29.3 – 29.1 (m), 28.5, 28.4. (conformers). \(^1^9\)F NMR (471 MHz, CDCl\(_3\)) \(\delta\) -173.48, -174.40. (conformers). HR MS and optical rotation data was acquired for the corresponding alcohol 2gr: HR MS-ESI: \(m/z\) for C\(_{16}\)H\(_{17}\)FNO\(_4\) [MH+-tBu] calcd. 234.1136; found 234.1140. \([\alpha]_D^{22} = +5.2^o\ (c = 0.1, \text{CHCl}_3, 93\% \text{ ee}).

**Di-tert-butyl (S)-4-fluoro-4-formyl-2,8-diazaspiro[4.5]decane-2,8-dicarboxylate (2h):** The enantioselective fluorination provided 2h (52 mg, 0.135 mmol, 67% yield, 87% ee) as a yellow oil. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 9.81 – 9.77 (m, 1H), 4.10 – 3.54 (m, 5H), 3.39 – 3.30 (m, 1H), 2.93 – 2.82 (m, 1H), 2.71 – 2.52 (m, 1H), 1.94 – 1.85 (m, 1H), 1.66 – 1.59 (m, 1H), 1.50 – 1.43 (m, 20H). (conformers). \(^1^3\)C NMR (151 MHz, CDCl\(_3\)) \(\delta\) 198.2 – 197.2 (m), 154.5, 154.4, 154.3, 154.2, 106.5 – 103.7 (m), 80.4, 80.4, 80.0, 80.0, 53.4, 51.6, 51.3, 51.1, 51.1, 50.9, 48.7 – 47.5 (m), 41.8 – 38.8 (m), 29.1, 28.9, 28.6, 28.4, 28.4. (conformers and overlapping signals). HR MS data was acquired for the corresponding alcohol 2hr: HR MS-ESI: \(m/z\) for C\(_{16}\)H\(_{18}\)FN\(_2\)O\(_5\) [MH+-2 x tBu] calcd. 277.1194; found 277.1197. \(^1^9\)F NMR (471 MHz, CDCl\(_3\)) \(\delta\) -172.5 (broad signal). \([\alpha]_D^{22} = +4.2^o\ (c = 0.85, \text{EtOAc}, 87\% \text{ ee}).\)
Synthesis of Starting Materials

General Procedure for the Oxidation of Alcohols to Aldehydes

To a solution of alcohol in CH₂Cl₂ (0.17M) was added Dess-Martin Periodinane (1.5 equiv) at rt. To the stirred suspension was added tert-butyl dicarbonate (1.352 g, 6.20 mmol) and the mixture was stirred for 14 h and subsequently concentrated in vacuo to provide the crude product that was purified by silica gel chromatography to provide 1d (226 mg, 1.134 mmol, 37% yield) as a colorless oil. ¹H NMR (600 MHz, CDCl₃) δ 9.70 – 9.69 (m, 1H), 3.76 – 3.64 (m, 1H), 3.58 – 3.46 (m, 1H), 3.44 – 3.29 (m, 2H), 3.07 – 2.99 (m, 1H), 2.26 – 2.05 (m, 2H), 1.46 (s, 9H). (conformers). ¹³C NMR (151 MHz, CDCl₃) δ 200.8, 200.6, 154.3, 79.7, 50.5, 49.6, 45.0, 41.3, 40.4, 28.5, 25.8, 25.3. (conformers). HR MS-ESI: m/z for C₁₆H₁₅NO₃ [MH⁺-tBu] calcd. 262.1; found 262.1.

Substrate 1e

Ethyl 1-benzyl-4,4-dimethylpyrrolidine-3-carboxylate (S1e): To a stirred solution of ethyl 3-methylbut-2-enolate (2.465 g, 19.23 mmol) in toluene (33 mL) was added N-benzyl-1-methoxy-N-((trimethylsilyl)methyl)methanamine (6.02 g, 6.49 mL, 23.08 mmol, 91%) at 0 °C under inert atmosphere. After 20 min, a solution of TFA (0.219 g, 0.148 mL, 1.923 mmol) in CH₂Cl₂ (2 mL) was added slowly at 0 °C. The mixture was stirred at 0 °C for 45 min followed by the addition of water (3 mL), NaOH (5 mL, 5M) then water (9 mL). The white suspension was heavily stirred for 12 h followed by filtration directly into a separation funnel. The white precipitate was washed with EtOAc (2 x 25 mL) and the combined organic extracts were washed with brine, dried over Na₂SO₄, filtered and concentrated in vacuo to provide S1e (1.72 g, 6.58 mmol, 34% yield) as a colorless oil. ¹H NMR (600 MHz, CDCl₃) δ 7.35 - 7.29 (m, 4H), 7.25 - 7.21 (m, 1H), 4.20 - 4.14 (m, 1H), 4.14 - 4.08 (m, 1H), 3.65 (d, J = 13.1 Hz, 1H), 3.58 (d, J = 13.1 Hz, 1H), 2.93 - 2.87 (m, 2H), 2.70 (t, J = 8.2 Hz, 1H), 2.54 (d, J = 8.8 Hz, 1H), 2.28 (d, J = 8.8 Hz, 1H), 1.27 (t, J = 7.1 Hz, 3H), 1.24 (s, 3H), 0.99 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 173.6, 139.6, 128.7, 128.4, 128.7, 128.0, 68.3, 60.4, 56.0, 53.6, 41.7, 29.8, 24.3, 14.6. LC MS: RTₑ₆ₛ₃ (0.45 min) m/z = 262.1.

(1-Benzyl-4,4-dimethylpyrrolidin-3-yl)methanol (S2e): To a solution of ethyl S1e (1.72 g, 6.58 mmol) in THF (22 mL, 6.58 mmol, 0.3M) was slowly added LiAlH₄ (7.24 mL, 7.24 mmol, 1M) in THF at 0 °C. The mixture was stirred at 0 °C for 45 min followed by the addition of water (3 mL), NaOH (5 mL, 5M) then water (9 mL). The white suspension was heavily stirred for 12 h followed by filtration directly into a separation funnel. The white precipitate was washed with EtOAc (2 x 25 mL) followed by a separation of the phases. The aqueous phase was washed with EtOAc (2 x 30 mL) and the combined organic extracts were washed with brine, dried over Na₂SO₄, filtered and concentrated in vacuo to provide a colorless oil that was passed through a plug of SiO₂ using EtOAc (60 mL). The filtrate was concentrated in vacuo to provide S2e (1.319 g, 6.01 mmol, 91% yield) as a colorless oil. ¹H NMR (600 MHz, CDCl₃) δ 7.33 - 7.27 (m, 4H), 7.26 - 7.23 (m, 1H), 3.71 (dd, J = 10.4, 4.3 Hz, 1H), 3.67 (dd, J = 10.4, 4.7 Hz, 1H), 3.62 (d, J = 12.9 Hz, 1H), 3.57 (d, J = 12.9 Hz, 1H), 2.80 (dd, J = 9.2, 6.6 Hz, 1H), 2.72 (dd, J = 9.2, 3.8 Hz, 1H), 2.60 (d, J = 9.2 Hz, 1H), 2.23 (d, J = 9.2 Hz, 1H), 1.83 - 1.79 (m, 1H), 1.13 (s, 3H), 1.10 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 138.98, 128.76, 128.52, 127.20, 68.49, 64.24, 60.50, 58.31, 49.69, 39.29, 31.21, 24.15. LC MS: RTₑ₆ₛ₃ (0.32 min) m/z = 220.1.
**tert-Butyl 4-(hydroxymethyl)-3,3-dimethylpyrrolidine-1-carboxylate (S3e):** To a solution of S2e (1.319 g, 6.01 mmol) in EtOH (8 mL) was added Pd(OH)$_2$/C (0.220 g, 1.568 mmol) 20% wt. The mixture was stirred under H$_2$ (7 bar, 50 °C) for 12 h and subsequently passed through a plug of Celite using THF (2 x 30 mL). To the filtrate was then added di-tert-butyl dicarbonate (1.563 g, 7.16 mmol) and the mixture was stirred 7 h at rt. The mixture was subsequently concentrated in vacuo to provide an oil that was purified using silica gel chromatography to provide S3e (1.03 g, 4.49 mmol, 75% yield) as a colorless oil. 1H NMR (600 MHz, CDCl$_3$) δ 3.81 - 3.71 (m, 1H), 3.67 - 3.59 (m, 1H), 3.59 - 3.51 (m, 1H), 3.24 - 3.12 (m, 2H), 3.10 - 2.94 (m, 1H), 2.07 - 1.97 (m, 1H), 1.68 - 1.54 (m, 1H), 1.46 - 1.43 (m, 9H), 1.12 - 1.10 (m, 3H), 0.95 - 0.92 (m, 3H) (rotamers). 13C NMR (151 MHz, CDCl$_3$) δ 155.0, 154.9, 79.4, 62.3, 60.4, 59.8, 50.1, 49.3, 49.2, 48.7, 28.7, 26.6, 26.4, 21.3, 21.3. (rotamers). HR MS-ESI: m/z for C$_{12}$H$_{23}$NNaO$_3$ [MNa+] calcd. 252.1570; found 252.1574.

**tert-Butyl 4-formyl-3,3-dimethylpyrrolidine-1-carboxylate (1e):** Synthesized from S3e using the general procedure for oxidation of alcohols to aldehydes, yielding 1e (0.795 g, 3.50 mmol, 78% yield) as a yellow oil. 1H NMR (600 MHz, CDCl$_3$) δ 9.75 - 9.71 (m, 1H), 3.78 - 3.67 (m, 1H), 3.61 - 3.47 (m, 1H), 3.31 - 3.18 (m, 1H), 3.17 - 3.11 (m, 1H), 2.73 - 2.60 (m, 1H), 1.45 (s, 9H), 1.31 - 1.23 (m, 3H), 1.09 - 1.04 (m, 3H) (rotamers). 13C NMR (151 MHz, CDCl$_3$) δ 201.6, 201.4, 79.8, 59.9, 59.6, 59.5, 58.7, 44.7, 42.1, 41.0, 28.7, 26.7, 26.5, 22.3. (rotamers). HR MS-ESI: m/z for C$_{12}$H$_{22}$NO$_3$ [MH+] calcd. 228.1594; found 228.1589.

**Determination of The Absolute Configuration of The Products**

The absolute configuration of the fluorinated products 2a-h were assigned analogously to the configuration determined by both X-Ray crystallography of 10 and vibrational circular dichroism (VCD) analysis of (S)-2er and (R)-2er, the corresponding alcohols of (S)-2e and (R)-2e.

**tert-Butyl (S)-3-fluoro-3-(hydroxymethyl)-4,4-dimethylpyrrolidine-1-carboxylate ((S)-2er):** Compound 1e was fluorinated using the general procedure A to yield 2e that was subsequently reduced using the general procedure B to the alcohol (S)-2er. 1H NMR (600 MHz, CDCl$_3$) δ 3.93 – 3.85 (m, 1H), 3.82 – 3.64 (m, 2H), 3.63 – 3.54 (m, 1H), 3.35 – 3.22 (m, 2H), 1.88 (s, 1H), 1.46 (s, 9H), 1.15 – 1.12 (m, 3H), 1.05 – 1.02 (m, 3H) (conformers). 13C NMR (151 MHz, CDCl$_3$) δ 154.7, 154.4, 106.0 – 103.9 (m), 79.7, 79.7, 62.7 – 62.3 (m), 58.7, 58.0, 53.6 – 52.8 (m), 43.56 – 42.35 (m), 28.5, 24.0 – 23.8 (m), 19.0 – 18.9 (m) (conformers). 19F NMR (471 MHz, CDCl$_3$) δ -167.5, -167.6. HR MS-ESI: m/z for C$_8$H$_{15}$FNO$_3$ [MH⁻-tBu] calcd. 192.1059; found 192.1037. [α]$_D^{22}$ = -4.0° (c = 0.25, CHCl$_3$, 97% ee).

Compound 1e was also fluorinated using the other enantiomer of the catalyst ((S)-9) and after reduction using the general procedure B provided the alcohol (R)-2er. [α]$_D^{22}$ = +6.4° (c = 0.40, CHCl$_3$). The spectral data are in good accordance with (S)-2er.
Vibrational Circular Dichroism (VCD) Analysis of (S)-2er and (R)-2er

The VCD spectra were recorded using CDCl₃ as a solvent. Baseline corrections were introduced using the spectrum of a virtual racemate as both enantiomers of 2er were available. The absolute configuration of (S)-2er was confirmed with a 99% confidence level. Below are shown the experimental IR and VCD spectra that were used for comparison with the virtual spectra generated for the lowest energy conformations of (S)-2er obtained using SCRF-B3LYP/6-31G(d).

Experimental IR and VCD spectra for (S)-2er

![Experimental IR and VCD spectra for (S)-2er](image)

Calculated IR and VCD spectra for the (S)-2er.

![Calculated IR and VCD spectra for the (S)-2er](image)

X-Ray Crystallography of Compound 10

The X-Ray crystallography data for of 10 was collected at 298 K confirming the absolute configuration as (S). The Flack parameter is -0.001(4). Analysis of the structure using Bayesian probability statistics yields probability values of P3(ok), P3(twin) and P3(wrong) of 1.000, 0.000 and 0.000, respectively. The calculation was based on 4686 Bijvoet pairs with 77% coverage. The Hooft parameter is 0.001(3).
**Determination of Enantiomeric Excess for the Fluorinated Products**

In order to determine the enantiomeric excess of the fluorinated products, the aldehydes 2a-h were reduced to the corresponding alcohols (2a-h)r and if sufficiently UV active they were analyzed on this stage. Otherwise, they were converted to a p-nitrobenzoyl derivative (2a-h)-deriv prior to chiral SFC analysis.

**Compound 2a**

The ee of 2ar was determined using chiral SFC on a ChiralPak IA column with the modifier containing 0.1% diethylamine in 20% EtOH.

**Racemic sample of 2ar:**

![Racemic sample of 2ar](image)

| Peak RetTime Type Width Area Height Area |
|---|---|---|---|---|
| 1 | 2.616 Min 0.0531 682.92464 214.30372 49.3949 |
| 2 | 2.676 Min 0.0584 699.60248 199.12924 50.4031 |

**Enantioenriched sample of 2ar:**

![Enantioenriched sample of 2ar](image)

| Peak RetTime Type Width Area Height Area |
|---|---|---|---|---|
| 1 | 2.616 Min 0.0499 77.90323 25.93818 10.3037 |
| 2 | 2.676 Min 0.0668 674.91043 192.40682 89.6963 |

**Compound 2b**

The ee of 2b-deriv was determined using chiral SFC on a ChiralPak OJ column with the modifier containing 0.1% diethylamine in 10% EtOH.

**Racemic sample of 2b-deriv:**

![Racemic sample of 2b-deriv](image)

| Peak RetTime Type Width Area Height Area |
|---|---|---|---|---|
| 1 | 1.466 Min 0.0398 210.01160 58.82514 50.4036 |
| 2 | 1.759 Min 0.0442 209.78525 73.75036 49.9564 |
Enantioenriched sample of 2b-deriv:

![Enantioenriched sample of 2b-deriv](image)

**Compound 2c**

The ee of 2cr was determined using chiral SFC on a ChiralPak OJ column with the modifier containing 0.1% diethylamine in 10% EtOH.

Racemic sample of 2cr:

![Racemic sample of 2cr](image)

Enantioenriched sample of 2cr:

![Enantioenriched sample of 2cr](image)
Compound 2d

The ee of 2d-deriv was determined using chiral SFC on a ChiralPak IA column with the modifier containing 0.1% diethylamine in 10% i-PrOH.

Racemic sample of 2d-deriv:

Enantioenriched sample of 2d-deriv:

Compound 2e

The ee of 2e-deriv was determined using chiral SFC on a ChiralPak OJ column with the modifier containing 0.1% diethylamine in 10% i-PrOH.

Racemic sample of 2e-deriv:

Enantioenriched sample of 2e-deriv using catalyst (R)-7:
Enantioenriched sample of 2e-deriv using catalyst (R)-9:

Compound 2f

The ee of 2fr was determined using chiral SFC on a ChiralPak AS-H column with the modifier containing 0.1% diethylamine in 8% EtOH.

Racemic sample of 2fr:

Enantioenriched sample of 2fr:
<table>
<thead>
<tr>
<th>#</th>
<th>RetTime</th>
<th>Type</th>
<th>Width [min]</th>
<th>Area [RAU]</th>
<th>Height [RAU]</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.979</td>
<td>MM</td>
<td>0.160</td>
<td>32.78545</td>
<td>4.67451</td>
<td>88.754</td>
</tr>
<tr>
<td>2</td>
<td>3.213</td>
<td>MM</td>
<td>0.143</td>
<td>4.15325</td>
<td>6.05634e-1</td>
<td>11.246</td>
</tr>
</tbody>
</table>
**Compound 2g**

The ee of 2g-deriv was determined using chiral SFC on a ChiralPak IA column with the modifier containing 0.1% diethylamine in 10% i-PrOH.

Racemic sample of 2g-deriv:

![Racemic sample of 2g-deriv](image)

<table>
<thead>
<tr>
<th>Peak RetTime</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.035 min</td>
<td>0.1001</td>
<td>14.3658</td>
<td>2.3567</td>
</tr>
<tr>
<td>2</td>
<td>4.419 min</td>
<td>0.1139</td>
<td>61.8502</td>
<td>96.675</td>
</tr>
</tbody>
</table>

Enantioenriched sample of 2g-deriv:

![Enantioenriched sample of 2g-deriv](image)

<table>
<thead>
<tr>
<th>Peak RetTime</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.035 min</td>
<td>0.1001</td>
<td>14.3658</td>
<td>2.3567</td>
</tr>
<tr>
<td>2</td>
<td>4.419 min</td>
<td>0.1139</td>
<td>61.8502</td>
<td>96.675</td>
</tr>
</tbody>
</table>

**Compound 2h**

The ee of 2h-deriv was determined using chiral SFC on a Lux Cellulose 1 column with the modifier containing 0.1% diethylamine in 10% i-PrOH.

Racemic sample of 2h-deriv:

![Racemic sample of 2h-deriv](image)

<table>
<thead>
<tr>
<th>Peak RetTime</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.725 min</td>
<td>0.0790</td>
<td>171.0598</td>
<td>50.1400</td>
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<tr>
<td>2</td>
<td>3.235 min</td>
<td>0.1021</td>
<td>1705.1474</td>
<td>49.8600</td>
</tr>
</tbody>
</table>

Enantioenriched sample of 2h-deriv:

![Enantioenriched sample of 2h-deriv](image)
<table>
<thead>
<tr>
<th>Peak RetTime Type</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[min]</td>
<td>[µm]</td>
<td>[µm²]</td>
<td>[µm²]</td>
</tr>
<tr>
<td>1</td>
<td>2.757</td>
<td>0.0859</td>
<td>126.8761</td>
<td>24.60558</td>
</tr>
<tr>
<td>2</td>
<td>3.294</td>
<td>0.1108</td>
<td>186.12305</td>
<td>250.55978</td>
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</tbody>
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