Supporting Information

Reversible Competitive α-Ketoheterocycle Inhibitors of Fatty Acid Amide Hydrolase Containing Additional Conformational Contraints in the Acyl Side Chain: Orally Active, Long Acting Analgesics

Cyrine Ezzili,[†] Mauro Mileni,[‡] Nicholas McGlinchey,[§] Jonathan Z. Long,[∥] Steven G. Kinsey,[x] Dustin G. Hochstatter,[†] Raymond C. Stevens,[‡,#] Aron H. Lichtman,[x] Benjamin F. Cravatt,[∥,#] Edward J. Bilsky,[§] and Dale L. Boger*[,†,#]

Departments of Chemistry,[†] Molecular Biology,[‡] Chemical Physiology,[∥] and The Skaggs Institute for Chemical Biology,[#] The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, California 92037 and Department of Pharmacology,[§] College of Osteopathic Medicine, University of New England, Biddeford, ME 04005 and Department of Pharmacology and Toxicolgy,[x] Virginia Commonwealth University, Richmond, VA 23298

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General Procedure A. The methyl ester (1 equiv) was dissolved in THF and cooled to 0 °C. $LiAlH_4$ (2 equiv) was added portionwise to the cooled solution due to the evolution of H_2 gas. The mixture was allowed to slowly warm to room temperature and after 2 h the reaction was quenched with the addition of 5% HOAc in EtOH (1 mL). The solution was diluted with EtOAc, washed with H_2O, saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation yielded the crude alcohol that was purified by flash chromatography (SiO_2).

General Procedure B. The alcohol (1 equiv) was dissolved in CH_2Cl_2 (0.03 M) and Dess–Martin periodinane (1.5 equiv) was added. The mixture was stirred at room temperature for 2 h before the reaction mixture was reduced to half volume and then was directly loaded onto silica gel and purified by flash chromatography (SiO_2) yielding the desired aldehyde.

General Procedure C. The stannane intermediate (1 equiv), $(Ph_3P)_4Pd$ (0.1 equiv), and aryl halide (2 equiv) were dissolved in anhydrous 1,4-dioxane (8 mL / 0.150 mmol of stannane) and the mixture was warmed to reflux for 16 h under Ar. The mixture was diluted with EtOAc, washed with saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude coupling product that was purified by flash chromatography (SiO_2).

General Procedure D. The TBS ether (1 equiv) was dissolved in THF (3 mL / 0.163 mmol of TBS ether), treated with Bu_4NF (1 M in THF, 1.2 equiv) and stirred at room temperature for 2 h under Ar. The reaction mixture was diluted with EtOAc, washed with saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude alcohol that was filtered through a short silica gel pad.

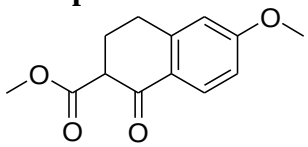
General Procedure E. The alcohol (1 equiv) was dissolved in CH_2Cl_2 (3 mL / 0.068 mmol of alcohol) and Dess–Martin periodinane (1.2 equiv) was added. The mixture was stirred at room temperature for 2 h before silica gel was added and the reaction mixture was evaporated in vacuo to afford the crude ketone absorbed on silica gel. This mixture was subsequently purified by flash chromatography (SiO_2) yielding the pure α-ketoheterocycle.

General Procedure F. The ester (1 equiv) was dissolved in a mixture of 3:2 THF/H_2O and LiOH (1 equiv) was added. The reaction mixture was stirred for 2 h at room temperature before the mixture was made acidic with the addition of aqueous 1 N HCl. The solution was diluted with EtOAc and the organic layer was separated

from the aqueous layer. The aqueous layer was extracted with EtOAc. The combined organic extracts were washed with saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude acid that was purified by chromatography (SiO_2).

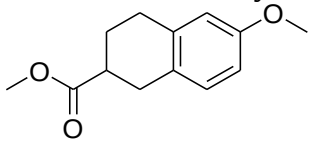
General Procedure G. The ester (0.01 mmol) was dissolved in 1,2-dichloroethane and after addition of trimethyltin hydroxide[1] (3 equiv), the mixture was warmed to 70°C for 16 h. The mixture was concentrated in vacuo and diluted with EtOAc and the organic layer was washed with aqueous 0.01 N $KHSO_4$, saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude acid that was purified by flash chromatography (SiO_2).

Methyl 1,2,3,4-Tetrahydro-6-methoxy-1-oxonaphthalene-2-carboxylate (S1)



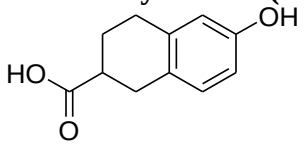
A solution of NaH (4.70 g, 323.5 mmol) in anhydrous THF (50 mL) was treated with dimethylcarbonate (19 mL, 215.6 mmol). The reaction mixture was cooled to 0° C under Ar and a solution of 6-methoxy-3,4-dihydronaphthalen-1(2*H*)-one (10 g, 56.75 mmol) in THF (10 mL) was added dropwise. The reaction mixture was warmed at reflux for 12 h then quenched with the addition of HOAc (until pH = 7) and diluted with EtOAc. The organic layer was washed with H_2O, saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude product that was purified by flash chromatography (SiO_2, 30% EtOAc–hexanes) to provide the title compound (11.70 g, 88%) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.98 (d, 1H, *J* = 9.0 Hz), 6.81 (dd, 1H, *J* = 2.5, 9.0 Hz), 6.66 (d, 1H, *J* = 2.5 Hz), 3.83 (s, 3H), 3.74 (s, 3H), 3.56–3.53 (m, 1H), 3.03–2.89 (m, 2H), 2.47–2.43 (m, 1H), 2.33–2.30 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 191.6, 170.7, 163.8, 146.1, 130.1, 125.1, 113.4, 112.4, 55.3, 54.0, 52.1, 27.9, 26.3.

Methyl 1,2,3,4-Tetrahydro-6-methoxynaphthalene-2-carboxylate (S2)



A sample of methyl 1,2,3,4-tetrahydro-6-methoxy-1-oxonaphthalene-2-carboxylate (**S1**, 11.70 g, 49.9 mmol) was dissolved in HOAc (60 mL), containing perchloric acid (0.5 mL) and 10% Pd/C (2 g, 4.99 mmol). The mixture was flushed with H_2 and kept under an atmosphere of H_2 for 16 h. Upon completion, the reaction mixture was filtered through a pad of Celite and washed with EtOAc. The organic layer was washed with H_2O then saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude product that was purified by flash chromatography (SiO_2, 10% EtOAc–hexanes) to provide the title compound (6.41 g, 58%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.01 (d, 1H, *J* = 8.4 Hz), 6.69 (dd, 1H, *J* = 2.4, 8.4 Hz), 6.62 (d, 1H, *J* = 2.4 Hz), 3.77 (s, 3H), 3.72 (s, 3H), 2.97–2.92 (m, 2H), 2.89–2.82 (m, 2H), 2.73–2.70 (m, 1H), 2.20–2.17 (m, 1H), 1.87–1.82 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 175.9, 157.7, 136.7, 129.8, 126.9, 113.3, 112.1, 55.2, 51.7, 40.1, 30.8, 28.8, 25.8.

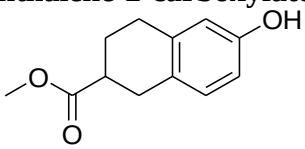
1,2,3,4-Tetrahydro-6-hydroxynaphthalene-2-carboxylic Acid (S3)



A sample of methyl 1,2,3,4-tetrahydro-6-methoxynaphthalene-2-carboxylate (**S2**, 6.41 g, 29.1 mmol) was dissolved in HOAc (50 mL) and 10% aqueous HBr (50 mL). The mixture was warmed to reflux under Ar for 2 h then cooled to room temperature and diluted with EtOAc. The organic layer was washed with H_2O then saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude product that was purified by flash chromatography (SiO_2, 50% EtOAc–hexanes) to provide the title compound (6.6 g, 98%) as a white solid: ^{1}H NMR ($CDCl_3$ + 0.1% DMSO-d_6, 400 MHz) δ 7.99 (brs, 1H), 6.89 (d, 1H, *J* = 8.4 Hz), 6.61 (dd, 1H, *J* = 2.4, 8.4 Hz), 6.55 (d, 1H, *J* = 2.4 Hz), 2.95–2.62 (m, 5H), 2.18–2.14 (m, 1H), 1.84–1.78 (m, 1H); ^{13}C

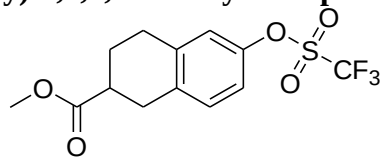
NMR ($CDCl_3$ + 0.1% DMSO-d_6, 100 MHz) δ 179.0, 154.5, 136.7, 129.8, 125.9, 114.9, 113.3, 39.9, 30.7, 28.5, 25.6.

Methyl 1,2,3,4-Tetrahydro-6-hydroxynaphthalene-2-carboxylate (S4)



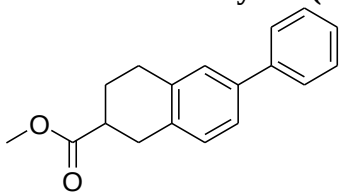
A sample of 1,2,3,4-tetrahydro-6-hydroxynaphthalene-2-carboxylic acid (**S3**, 6.6 g, 34.3 mmol) was dissolved in MeOH (30 mL) and concentrated H_2SO_4 (3 mL). The mixture was warmed to reflux under Ar for 1 h then cooled to room temperature and diluted with EtOAc. The organic layer was washed with H_2O then saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude product that was purified by flash chromatography (SiO_2, 50% EtOAc–hexanes) to provide the title compound (4.75 g, 67%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.93 (d, 1H, *J* = 8.4 Hz), 6.64 (dd, 1H, *J* = 2.4, 8.4 Hz), 6.58 (d, 1H, *J* = 2.4 Hz), 6.22 (s, 1H), 3.75 (s, 3H), 2.97–2.87 (m, 2H), 2.79–2.70 (m, 3H), 2.19–2.16 (m, 1H), 1.86–1.80 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 176.6, 153.7, 136.7, 129.9, 126.4, 114.9, 113.2, 51.9, 40.1, 30.8, 28.4, 25.6.

Methyl 6-(Trifluoromethanesulfonyloxy)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (S5)



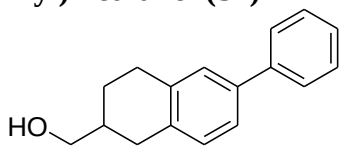
A sample of methyl 1,2,3,4-tetrahydro-6-hydroxynaphthalene-2-carboxylate (**S4**, 1 g, 4.84 mmol) was dissolved in anhydrous pyridine (20 mL), cooled to 0°C and triflic anydride (1.2 mL, 7.27 mmol) was added. The reaction mixture was warmed to room temperature and stirred under Ar for 2 h. The mixture was diluted with CH_2Cl_2, washed with H_2O, saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude product that was not further purified to provide the title compound (1.74 g, 98%) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.11 (d, 1H, *J* = 8.5 Hz), 6.99–6.96 (m, 2H), 3.68 (s, 3H), 2.98–2.94 (m, 2H), 2.85–2.79 (m, 2H), 2.74–2.68 (m, 1H), 2.19–2.15 (m, 1H), 1.86–1.80 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 174.9, 147.4, 138.1, 135.3, 130.5, 120.9, 118.5 (q, CF_3, *J* = 320 Hz), 118.4, 51.5, 39.3, 39.1, 30.8, 28.2, 25.0.

Methyl 6-Phenyl-1,2,3,4-tetrahydronaphthalene-2-carboxylate (S6)



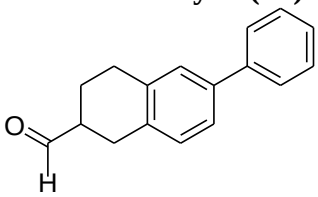
A mixture of methyl 6-(trifluoromethanesulfonyloxy)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**S5**, 1.74 g, 5.14 mmol), $(PPh_3)_4Pd$ (178 mg, 0.15 mmol), and phenylboronic acid (760 mg, 6.17 mmol) and 2 M aqueous Na_2CO_3 (5 mL) were dissolved in anhydrous THF (30 mL) and the mixture was warmed at reflux for 16 h under Ar. The mixture was diluted with EtOAc, washed with saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded crude product that was purified by column chromatography (SiO_2, 10% EtOAc–hexanes) to give the title compound (1.09 g, 79%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.66 (d, 2H, *J* = 8.5 Hz), 7.50 (t, 2H, *J* = 7.8 Hz), 7.45–7.39 (m, 3H), 7.25 (d, 1H, *J* = 7.8 Hz), 3.82 (s, 3H), 3.16–3.13 (m, 2H), 3.04–2.93 (m, 2H), 2.87–2.82 (m, 1H), 2.34–2.30 (m, 1H), 2.02–1.97 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 175.8, 141.0, 138.9, 136.0, 134.0, 129.4, 128.6 (2C), 127.4, 127.0, 126.9 (2C), 124.6, 51.8, 39.9, 31.3, 28.6, 25.9.

(6-Phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methanol (S7)



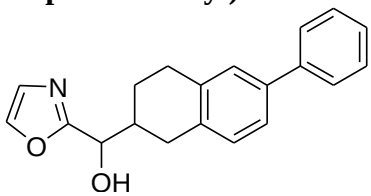
The title compound was prepared from methyl 6-phenyl-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**S6**, 1.09 g, 4.09 mmol) following general procedure A. Flash chromatography (SiO_2, 50% EtOAc–hexanes) afforded the title compound (910 mg, 93%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.69 (d, 2H, *J* = 8.5 Hz), 7.52 (t, 2H, *J* = 7.8 Hz), 7.46–7.41 (m, 3H), 7.25 (d, 1H, *J* = 7.8 Hz), 3.72 (d, 2H, *J* = 6.5 Hz), 3.05–2.96 (m, 3H), 2.73 (s, 1H), 2.66–2.61 (m, 1H), 2.15–2.07 (m, 2H), 1.59–1.55 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 141.0, 138.4, 136.9, 135.0, 129.5 (2C), 128.5, 127.3, 126.7 (3C), 124.3, 67.3, 36.9, 32.0, 28.7, 25.8.

6-Phenyl-1,2,3,4-tetrahydronaphthalene-2-carboxaldehyde (S8)



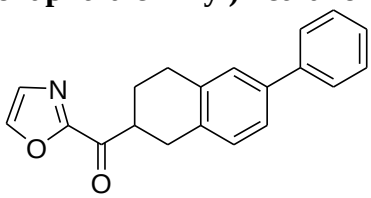
The title compound was prepared from (6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methanol (**S7**, 910 mg, 3.81 mmol) following general procedure B. Flash chromatography (SiO_2, 20% EtOAc–hexanes) afforded the title compound (720 mg, 79%) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.79 (s, 1H), 7.63 (d, 2H, *J* = 8.5 Hz), 7.48 (t, 2H, *J* = 7.8 Hz), 7.42–7.36 (m, 3H), 7.23 (d, 1H, *J* = 7.8 Hz), 3.02 (d, 2H, *J* = 6.5 Hz), 2.98–2.88 (m, 2H), 2.72–2.66 (m, 1H), 2.26–2.21 (m, 1H), 1.86–1.78 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 203.2, 140.6, 138.7, 136.0, 133.2, 129.4, 128.5, 128.4 (2C), 127.1, 126.8, 126.7, 126.6 (2C), 124.4, 46.5, 27.9, 27.8, 22.6, 13.9.

Oxazol-2-yl(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methanol (S9)



Oxazole (0.2 mL, 3.04 mmol) in anhydrous THF (30 mL) was treated with BH_3•THF (1 M, 3.32 mL, 3.32 mmol) and the solution was stirred at room temperature for 1 h before being cooled to –78 °C and treated with 2.16 M *n*-BuLi (1.8 mL, 3.95 mmol) dropwise. The reaction mixture was stirred at –78 °C for 40 min before a solution of 6-phenyl-1,2,3,4-tetrahydronaphthalene-2-carboxaldehyde (**S8**, 720 mg, 3.04 mmol) in THF (20 mL) was added. The reaction mixture was stirred at –78 °C for 2 h before being warmed to room temperature. A 5% HOAc–EtOH solution (50 mL) was added and this mixture was stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the residue was dissolved in EtOAc, and washed with H_2O, saturated aqueous $NaHCO_3$ and saturated aqueous NaCl before the organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 40% EtOAc–hexanes) afforded the title compound (510 mg, 55%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.65 (d, 1H, *J* = 2.0 Hz), 7.58 (d, 2H, *J* = 8.5 Hz), 7.43 (t, 2H, *J* = 7.8 Hz), 7.37–7.33 (m, 3H), 7.18 (d, 1H, *J* = 7.8 Hz), 7.11–7.10 (m, 1H), 4.80 (q, 1H, *J* = 6.5 Hz), 4.42 (s, 1H, OH), 3.00–2.83 (m, 3H), 2.69–2.68 (m, 1H), 2.45–2.40 (m, 1H), 2.23–2.19 (m, 0.5H), 1.86–1.83 (m, 0.5H), 1.68–1.56 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 165.4, 165.3, 141.0, 138.8, 138.6, 136.7, 136.5, 134.7, 134.5, 129.6, 129.5, 128.5 (2C), 127.35, 127.31, 126.8 (2C), 126.5, 124.47, 124.43, 71.2, 71.0, 39.7, 39.6, 31.1, 30.7, 28.9, 28.8, 25.3, 24.6.

Oxazol-2-yl(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methanone (3)



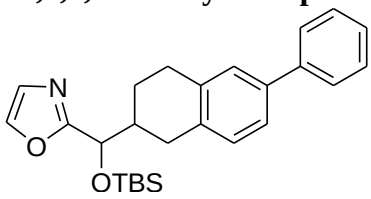
The title compound was prepared from oxazol-2-yl(6-phenyl-1,2,3,4-tetrahydronapthalen-2-yl)methanol (**S9**, 50 mg, 0.163 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (44.8 mg, 90%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.86 (s, 1H), 7.58 (d, 2H, *J* = 8.5 Hz), 7.43 (t, 2H, *J* = 7.8 Hz), 7.38–7.33 (m, 4H), 7.20 (d, 1H, *J* = 7.8 Hz), 3.92–3.87 (m, 1H), 3.19–3.01 (m, 4H), 2.36–2.33 (m, 1H), 1.99–1.93 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 190.4, 157.5, 141.6, 141.0,

139.0, 135.9, 133.9, 129.4, 129.0, 128.6 (2C), 127.4, 127.0, 126.9 (2C), 124.7, 43.5, 30.7, 28.8, 25.9; HRMS-ESI-TOF *m/z* 304.1322 ($[M + H]^+$, $C_{20}H_{17}NO_2$ requires 304.1332). The enantiomers were separated using a semipreparative chiral phase HPLC column (ChiralPAK AD, 10 μm, 2 × 25 cm, 1% *i*-PrOH–hexanes, 7 mL/min, α = 1.18).

(*S*)-**3**: $[\alpha]^{23}_D$ –16 (*c* 0.1, THF).

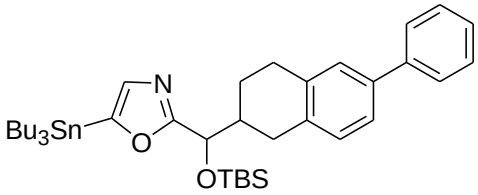
(*R*)-**3**: $[\alpha]^{23}_D$ +15 (*c* 0.1, THF).

2-((*tert*-Butyldimethylsilyloxy)(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole (S10)



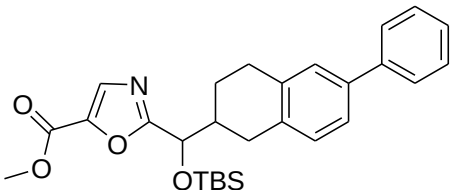
A solution of oxazol-2-yl(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methanol (**S9**, 400 mg, 1.3 mmol), TBSCl (470 mg, 3.12 mmol) and imidazole (445 mg, 6.54 mmol) in DMF (20 mL) was stirred at room temperature for 16 h before it was diluted with EtOAc, washed with H_2O, and saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 10% EtOAc–hexanes) yielded the title compound (420 mg, 77%) as a thick colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.68 (s, 1H), 7.62–7.60 (d, 2H, *J* = 8.5 Hz), 7.45 (t, 2H, *J* = 7.8 Hz), 7.40–7.34 (m, 3H), 7.22 (d, 1H, *J* = 7.8 Hz), 7.16–7.12 (m, 1H), 4.85 (d, 0.5H, *J* = 7.0 Hz), 4.80 (d, 0.5H, *J* = 7.0 Hz), 3.08–2.82 (m, 1H), 2.69–2.57 (m, 2H), 2.46–2.24 (m, 2H), 1.82–1.79 (m, 1H), 1.63–1.55 (m, 1H), 0.98 (s, 9H), 0.16 (s, 1.5H), 0.15 (s, 1.5H), –0.01 (s, 1.5H), –0.02 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 164.5, 164.4, 141.1, 138.6, 138.56, 138.50, 138.4, 136.8, 136.6, 135.0, 134.6, 129.7, 129.5, 128.5 (2C), 127.3, 127.2, 126.87, 126.83 (2C), 126.7, 124.4, 72.35, 72.31, 40.4, 40.3, 31.0, 30.9, 28.98, 28.91, 25.6 (3C), 25.4, 25.1, 18.1, –5.31, –5.39.

2-((*tert*-Butyldimethylsilyloxy)(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)-5-(tributylstannyl)oxazole (S11)



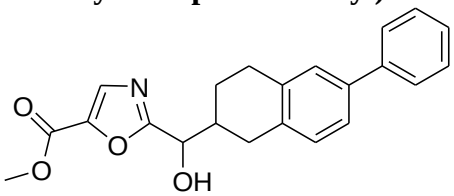
A solution of 2-((*tert*-butyldimethylsilyloxy)(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole (**S10**, 219 mg, 0.52 mmol) in THF (10 mL) was cooled to –78 °C before it was treated with 2.16 M *n*-BuLi (0.26 mL, 0.57 mmol) dropwise. The reaction mixture was stirred at –78 °C for 2 h, and treated with a solution of Bu_3SnCl (0.28 mL, 1.04 mmol) and stirred for 5 min. The solution was warmed to room temperature and diluted with EtOAc, and washed with saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 0–5% EtOAc–hexanes) yielded the title compound (350 mg, 65%) as a thick colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.58–7.56 (d, 2H, *J* = 8.5 Hz), 7.41 (t, 2H, *J* = 7.8 Hz), 7.35–7.30 (m, 3H), 7.18–7.13 (m, 2H), 4.83 (d, 0.5H, *J* = 7.0 Hz), 4.77 (d, 0.5H, *J* = 7.0 Hz), 3.00–2.81 (m, 4H), 2.39–2.20 (m, 4H), 1.59–1.12 (m, 25H), 0.94 (s, 9H), 0.05 (s, 1.5H), 0.04 (s, 1.5H), –0.12 (s, 1.5H), –0.13 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 168.6, 168.4, 154.9, 154.8, 141.28, 141.27, 138.66, 138.60, 137.3, 137.2, 137.05, 137.02, 136.8, 135.3, 135.0, 129.7, 129.63, 128.60 (2C), 127.4, 127.3, 126.96, 126.91 (2C), 126.8, 124.44, 124.41, 72.5, 40.7, 31.2, 29.36, 29.30, 29.23 (3C), 29.1, 28.9, 27.8, 27.6, 27.4 (3C), 27.2, 27.1, 26.8, 25.7, 18.2, 17.4, 13.7 (3C), 13.6, 13.5, 10.2, 9.78, 9.73, 8.7 (3C), 7.75, 7.71, –5.29, –5.30, –5.34, –5.36.

Methyl 2-((*tert*-Butyldimethylsilyloxy)(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole-5-carboxylate (S12)



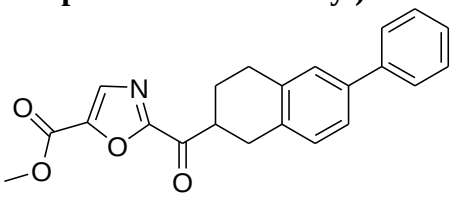
A solution of 2-((*tert*-butyldimethylsilyloxy)(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole (**S11**, 28.7 mg, 0.068 mmol) in THF (0.5 mL) was cooled to –78 °C before it was treated with 2.16 M *n*-BuLi (0.034 mL, 0.075 mmol) dropwise. The reaction mixture was stirred at –78 °C for 2 h, treated with a solution of Mander's reagent (MeO_2CCN, 0.027 mL, 0.34 mmol) in THF (0.5 mL), and stirred for 5 min. The solution was warmed to room temperature and diluted with EtOAc, and washed with saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 10% EtOAc–hexanes) yielded the title compound (28.5 mg, 87%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.75 (d, 1H, *J* = 4.8 Hz), 7.57–7.55 (m, 2H), 7.41 (t, 2H *J* = 7.8 Hz), 7.34–7.30 (m, 2H), 7.16 (d, 1H, *J* = 8.4 Hz), 7.08 (d, 1H, *J* = 8.4 Hz), 4.83 (d, 0.5H, *J* = 6.0 Hz), 4.76 (d, 0.5H, *J* = 6.0 Hz), 3.93 (s, 3H), 2.94–2.80 (m, 3H), 2.64–2.60 (m, 2H), 2.43–2.40 (m, 1H), 2.23–2.20 (m, 0.5H), 1.84–1.79 (m, 0.5H), 0.92 (s, 9H), 0.10 (s, 1.5H), 0.08 (s, 1.5H), –0.05 (s, 1.5H), –0.04 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 167.8, 167.6, 158.08, 158.06, 142.26, 142.20, 141.14, 141.11, 138.8, 138.7, 136.8, 136.5, 134.8, 134.4, 134.06, 134.03, 129.7, 129.5, 128.6 (2C), 127.4, 127.3, 126.9 (2C), 126.8, 124.54, 124.51, 72.4, 72.3, 52.2, 40.4, 40.3, 31.1, 30.4, 28.97, 28.95, 25.6 (3C), 24.8, 18.2, –5.14, –5.27, –5.29.

Methyl 2-(Hydroxy(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole-5-carboxylate (S13)



The title compound was prepared from methyl 2-((*tert*-butyldimethylsilyloxy)(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole-5-carboxylate (**S12**, 9.4 mg, 0.019 mmol) following general procedure D. Flash chromatography (SiO_2, 50–100% EtOAc–hexanes) yielded the title compound (7.8 mg, 98%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.76 (s, 1H), 7.56 (d, 2H, *J* = 4.8 Hz), 7.41 (t, 2H, *J* = 7.8 Hz), 7.34–7.31 (m, 3H), 7.15 (d, 0.5H, *J* = 7.8 Hz), 7.10 (d, 0.5H, *J* = 7.8 Hz), 4.86 (s, 0.5H), 4.83 (s, 0.5H), 3.93 (s, 3H), 2.96–2.74 (m, 3H), 2.45–2.41 (m, 1H), 2.11–2.09 (m, 0.5H), 1.93–1.90 (m, 0.5H), 1.68–1.58 (m, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 167.76, 167.71, 157.96, 157.95, 142.75, 142.73, 141.0, 138.8, 136.5, 136.4, 134.4, 134.3, 133.79, 133.77, 129.7, 129.5, 128.6 (2C), 127.4, 126.99 (2C), 126.96, 124.63, 124.61, 124.5, 71.6, 71.4, 52.3, 39.9, 39.8, 31.1, 30.8, 28.95, 28.91, 25.4, 24.2.

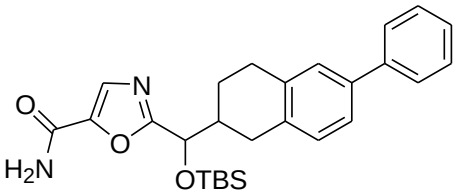
Methyl 2-(6-Phenyl-1,2,3,4-tetrahydronaphthalene-2-carbonyl)oxazole-5-carboxylate (4)



The title compound was prepared from methyl 2-(hydroxy(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole-5-carboxylate (**S13**, 7.8 mg, 0.021 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (5 mg, 65%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.92 (s, 1H), 7.58 (d, 2H, *J* = 4.8 Hz), 7.42 (t, 2H, *J* = 7.8 Hz), 7.37–7.33 (m, 2H), 7.19 (d, 1H, *J* = 7.8 Hz), 3.98 (s, 3H), 3.90–3.87 (m, 1H), 3.15–3.02 (m, 2H), 2.35–2.32 (m, 2H), 1.96–1.94 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 190.2, 157.8, 157.4, 143.9, 141.0, 139.1, 135.8, 134.6, 133.6, 129.5, 128.8, 128.7, 127.4, 127.08, 127.04, 124.8, 52.7, 43.8, 30.68, 30.60, 28.7, 25.7; HRMS-ESI-TOF *m/z* 362.1385 ([M +

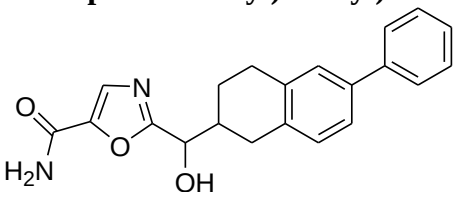
H]$^+$, $C_{22}H_{19}NO_4$ requires 362.1387). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 1% EtOH–hexanes, 7 mL/min, α = 1.55).
(*S*)-**4**: $[\alpha]^{23}_D$ –20 (*c* 0.1, THF).
(*R*)-**4**: $[\alpha]^{23}_D$ +22 (*c* 0.1, THF).

2-((*tert*-Butyldimethylsilyloxy)(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole-5-carboxamide (S14)



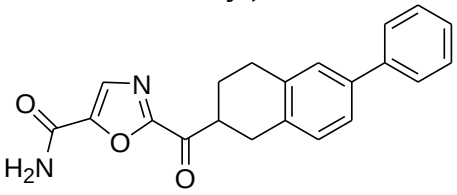
A solution of methyl 2-((*tert*-butyldimethylsilyloxy)(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole-5-carboxylate (**S12**, 16.4 mg, 0.034 mmol) was dissolved in a saturated solution of NH_3–CH_3OH (3 mL) and the mixture was stirred for 2 h at room temperature. Evaporation in vacuo yielded the crude carboxamide that was purified by flash chromatography (SiO_2, 50% EtOAc–hexanes) to provide the title compound (17 mg, 98%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.74 (d, 1H, *J* = 4.8 Hz), 7.57–7.55 (m, 4H), 7.41 (t, 2H, *J* = 7.8 Hz), 7.35–7.31 (m, 2H), 7.16 (d, 0.5H, *J* = 7.8 Hz), 7.09 (d, 0.5H, *J* = 7.8 Hz), 6.18 (brs, 1H, NH), 5.99 (brs, 1H, NH), 4.80 (d, 0.5H, *J* = 6.0 Hz), 4.75 (d, 0.5H, *J* = 6.0 Hz), 2.93–2.80 (m, 2H), 2.62–2.60 (m, 1H), 2.38–2.34 (m, 1H), 1.81–1.79 (m, 1H), 1.62–1.55 (m, 1H), 0.87 (s, 9H), 0.12 (s, 1.5H), 0.11 (s, 1.5H), –0.05 (s, 1.5H), –0.04 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.9, 165.8, 158.5, 158.4, 144.6, 144.5, 141.07, 141.03, 138.9, 138.8, 136.6, 136.4, 134.6, 134.2, 131.66, 131.64, 129.7, 129.6, 128.6 (3C), 127.4, 127.3, 127.1, 127.0 (2C), 126.98, 126.95, 72.5, 72.4, 40.55, 40.53, 31.1, 30.7, 28.9, 28.8, 25.6 (3C), 25.5, 25.0, 18.1, –5.15, –5.20, –5.22.

2-(Hydroxy(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole-5-carboxamide (S15)



The title compound was prepared from 2-((*tert*-butyldimethylsilyloxy)(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole-5-carboxamide (**S14**, 13.9 mg, 0.03 mmol) following general procedure D. Flash chromatography (SiO_2, 5% MeOH–CH_2Cl_2) yielded the title compound (10.4 mg, 98%) as a white solid: ^{1}H NMR ($CDCl_3$ + 0.1% TFA, 600 MHz) δ 7.96 (s, 1H), 7.55 (d, 2H, *J* = 7.8 Hz), 7.42 (t, 2H, *J* = 7.8 Hz), 7.38–7.32 (m, 3H), 7.17 (d, 0.5H, *J* = 7.8 Hz), 7.10 (d, 0.5H, *J* = 7.8 Hz), 5.03 (t, 1H, *J* = 6.0 Hz), 3.02–2.85 (m, 3H), 2.66–2.64 (m, 1H), 2.47–2.45 (m, 1H), 2.21–2.17 (m, 1H), 1.83–1.80 (m, 1H), 1.63–1.60 (m, 1H), 1.31–1.27 (m, 2H); ^{13}C NMR ($CDCl_3$ + 0.1% TFA, 150 MHz) δ 165.9, 165.8, 144.33, 144.30, 140.8, 140.7, 139.47, 139.41, 136.1, 135.8, 133.2, 132.8, 130.5, 129.7, 129.4, 128.7 (3C), 127.5, 127.4, 127.23, 127.21, 126.96, 129.90 (2C), 124.99, 124.91, 71.6, 71.2, 39.7, 31.0, 30.5, 29.7, 28.4, 28.3, 25.3, 24.5.

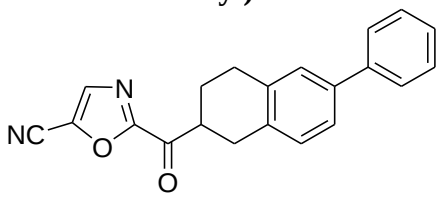
2-(6-Phenyl-1,2,3,4-tetrahydronaphthalene-2-carbonyl)oxazole-5-carboxamide (S16)



The title compound was prepared from 2-(hydroxy(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole-5-carboxamide (**S15**, 10.4 mg, 0.029 mmol) following general procedure E. Flash chromatography (SiO_2, 50% EtOAc–hexanes) yielded the title compound (5.9 mg, 58%) as a white solid: ^{1}H NMR ($CDCl_3$ + 0.1% TFA, 600 MHz) δ 8.06 (s, 1H), 7.57 (d, 2H, *J* = 7.8 Hz), 7.43 (t, 2H, *J* = 7.8 Hz), 7.40–7.34 (m, 4H), 3.92–3.90 (m, 1H), 3.17–3.14 (m, 2H), 3.06–3.03 (m, 2H), 2.37–2.33 (m, 1H), 1.99–1.96 (m, 1H); ^{13}C NMR ($CDCl_3$ + 0.1% TFA,

150 MHz) δ 191.8, 169.7, 150.6, 140.8, 139.4, 135.5, 133.9, 133.0, 129.4, 128.7 (2C), 127.5, 127.2, 126.9 (2C), 125.0, 44.0, 30.5, 29.7, 28.5, 25.9.

2-(6-Phenyl-1,2,3,4-tetrahydronaphthalene-2-carbonyl)oxazole-5-carbonitrile (5)

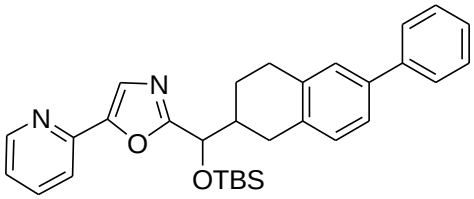


A solution of 2-(6-phenyl-1,2,3,4-tetrahydronaphthalene-2-carbonyl)oxazole-5-carboxamide (**S16**, 5.9 mg, 0.017 mmol) was dissolved in 1,4-dioxane (1 mL) and pyridine (0.0034 mL, 0.042 mmol) and trifluoroacetic anhydride (0.003 mL, 0.022 mmol) were added. The reaction mixture stirred for 2 h at room temperature. The mixture was diluted with CH_2Cl_2 and the combined organic layers were washed with saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude nitrile that was purified by flash chromatography (SiO_2, 10% EtOAc–hexanes) to afford the title compound (4 mg, 71%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.89 (s, 1H), 7.58 (d, 2H, *J* = 7.8 Hz), 7.43 (t, 2H, *J* = 7.8 Hz), 7.39–7.32 (m, 3H), 7.20 (d, 1H, *J* = 7.8 Hz), 3.87–3.82 (m, 1H), 3.15–3.12 (m, 2H), 3.03–3.02 (m, 2H), 2.35–2.33 (m, 1H), 1.99–1.93 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 189.3, 158.2, 140.9, 139.3, 138.1, 135.6, 133.3, 129.4, 128.7 (2C), 127.5, 127.1, 126.9, 126.6, 124.9, 108.1, 44.2, 30.5, 29.6, 28.6, 25.7; HRMS-ESI-TOF *m/z* 329.1288 ($[M + H]^+$, $C_{21}H_{16}N_2O_2$ requires 329.1284). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 1% EtOH–hexanes, 7 mL/min, α = 1.16).

(*S*)-**5**: $[\alpha]^{23}_D$ –14 (*c* 0.1, THF).

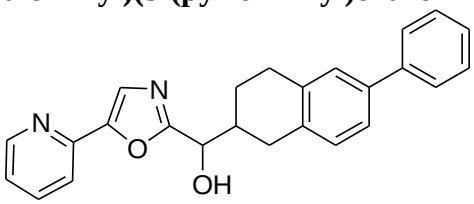
(*R*)-**5**: $[\alpha]^{23}_D$ +15 (*c* 0.1, THF).

2-((*tert*-Butyldimethylsilyloxy)(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)-5-(pyridin-2-yl)oxazole (S17)



The title compound was prepared from 2-((*tert*-butyldimethylsilyloxy)(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)-5-(tributylstannyl)oxazole (**S11**, 64.9 mg, 0.15 mmol) and 2-bromopyridine following general procedure C. Flash chromatography (SiO_2, 10% EtOAc–hexanes) yielded the title compound (28 mg, 36%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.64 (d, 1H, *J* = 4.8 Hz), 7.77 (qd, 1H, *J* = 1.8, 7.8 Hz), 7.70–7.66 (m, 2H), 7.55 (t, 2H, *J* = 7.8 Hz), 7.42 (t, 2H, *J* = 7.8 Hz), 7.34–7.31 (m, 3H), 7.24–7.21 (m, 1H), 7.18 (d, 0.5H, *J* = 8.4 Hz), 7.08 (d, 0.5H, *J* = 7.0 Hz), 4.83 (d, 0.5H, *J* = 7.0 Hz), 4.77 (d, 0.5H, *J* = 7.0 Hz), 3.02–2.81 (m, 2H), 2.66–2.63 (m, 1H), 2.45–2.42 (m, 1H), 2.39–2.34 (m, 1H), 1.86–1.83 (m, 1H), 1.67–1.57 (m, 1H), 0.94 (s, 4.5H), 0.98 (s, 4.5H), 0.13 (s, 1.5H), 0.11 (s, 1.5H), –0.04 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 164.9, 164.7, 150.89, 150.80, 149.9, 147.4, 147.3, 141.18, 141.15, 138.7, 138.6, 136.9, 136.6, 135.0, 134.7, 129.7 (3C), 129.6, 128.6, 127.4, 127.3, 126.95, 126.92, 126.91 (2C), 125.19, 125.14, 124.4, 122.87, 122.84, 119.1, 119.0, 72.57, 72.53, 40.55, 40.50, 31.2, 30.9, 29.6, 29.06, 29.01, 25.7 (3C), 25.6, 25.1, 18.2, 13.5, –5.07, –5.22, –5.24.

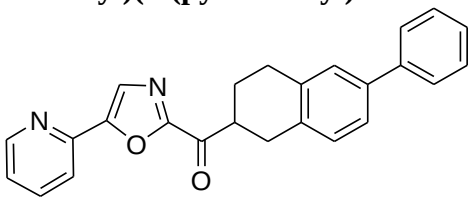
(6-Phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)(5-(pyridin-2-yl)oxazol-2-yl)methanol (S18)



The title compound was prepared from 2-((*tert*-butyldimethylsilyloxy)(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)-5-(pyridin-2-yl)oxazole (**S17**, 28 mg, 0.05 mmol) following general procedure D. Flash chromatography (SiO_2, 50–100% EtOAc–hexanes) yielded the title compound (19.3 mg, 90%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.64 (d, 1H, *J* = 4.8 Hz), 7.78 (td, 2H, *J* = 1.2, 7.2 Hz), 7.70 (s, 1H), 7.55 (d, 2H,

J = 7.8 Hz), 7.40 (t, 2H, *J* = 7.2 Hz), 7.33–7.23 (m, 4H), 7.16 (d, 0.5H, *J* = 8.4 Hz), 7.09 (d, 0.5H, *J* = 7.0 Hz), 4.88 (d, 0.5H, *J* = 7.0 Hz), 4.85 (d, 0.5H, *J* = 7.0 Hz), 2.98–2.87 (m, 2H), 2.77 (d, 1H, *J* = 7.8 Hz), 2.49–2.47 (m, 1H), 2.23–2.20 (m, 1H), 1.97–1.94 (m, 2H), 1.72–1.66 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 149.6, 146.8, 141.11, 141.10, 138.79, 138.77, 137.1, 136.7, 136.5, 134.7, 134.5, 129.7, 129.6, 128.6 (2C), 127.43, 127.40, 126.9 (3C), 125.1, 124.56, 124.53, 123.0, 119.4, 71.5, 71.3, 39.88, 39.85, 31.3, 30.4, 29.0, 28.7, 25.5, 24.5.

(6-Phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)(5-(pyridin-2-yl)oxazol-2-yl)methanone (6)

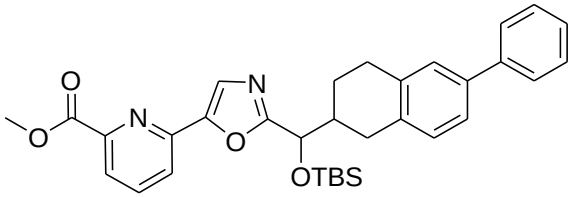


The title compound was prepared from (6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)(5-(pyridin-2-yl)oxazol-2-yl)methanol (**S18**, 19.3 mg, 0.05 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (16.3 mg, 85%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.68 (d, 1H, *J* = 4.8 Hz), 7.94 (s, 1H), 7.90 (d, 1H, *J* = 7.2 Hz), 7.83 (td, 1H, *J* = 1.2, 7.2 Hz), 7.59 (d, 2H, *J* = 7.8 Hz), 7.44–7.31 (m, 6H), 7.22 (d, 1H, *J* = 7.8 Hz), 3.97–3.94 (m, 1H), 3.19–3.15 (m, 2H), 3.07–3.02 (m, 2H), 2.39–2.36 (m, 1H), 2.00–1.96 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 190.5, 156.8, 153.3, 150.0, 146.1, 141.0, 139.0, 137.2, 136.0, 134.0, 129.5, 128.6 (2C), 127.4, 127.08, 127.03, 126.9 (2C), 124.7, 124.1, 120.4, 43.3, 30.8, 28.8, 26.0; HRMS-ESI-TOF *m/z* 381.1600 ($[M + H]^+$, $C_{25}H_{20}N_2O_2$ requires 381.1597). The enantiomers were separated using a semipreparative chiral phase HPLC column (ChiralPAK AD, 10 μm, 2 × 25 cm, 10% *i*-PrOH–hexanes, 7 mL/min, α = 1.13).

(*S*)-**6**: $[\alpha]^{23}_D$ –18 (*c* 0.1, THF).

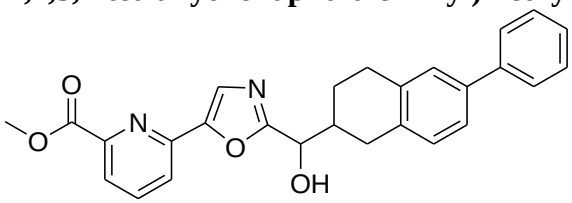
(*R*)-**6**: $[\alpha]^{23}_D$ +20 (*c* 0.1, THF).

Methyl 6-(2-((*tert*-Butyldimethylsilyloxy)(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazol-5-yl)picolinate (S19)



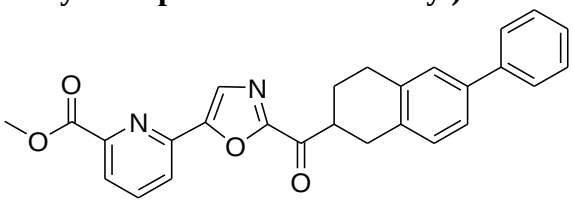
The title compound was prepared from 2-((*tert*-butyldimethylsilyloxy)(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)-5-(tributylstannyl)oxazole (**S11**, 220 mg, 0.52 mmol) and methyl 6-bromopicolinate following general procedure C. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (232 mg, 80%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.34 (d, 1H, *J* = 4.8 Hz), 8.24 (d, 1H, *J* = 4.8 Hz), 8.02–8.00 (m, 1H), 7.91–7.87 (m, 1H), 7.84–7.81 (m, 1H), 7.64–7.61 (m, 1H), 7.55–7.52 (m, 2H), 7.39–7.31 (m, 2H), 7.36–7.31 (m, 1H), 7.18 (d, 0.5H, *J* = 8.4 Hz), 7.08 (d, 0.5H, *J* = 7.0 Hz), 4.85 (d, 0.5H, *J* = 7.0 Hz), 4.78 (d, 0.5H, *J* = 7.0 Hz), 3.99 (s, 1.5H), 3.96 (s, 1.5H), 2.97–2.84 (m, 1H), 2.63–2.60 (m, 1H), 2.44–2.42 (m, 1H), 1.63–1.59 (m, 1H), 1.35–1.30 (m, 3H), 0.92 (s, 9H), 0.12 (s, 1.5H), 0.11 (s, 1.5H), –0.03 (s, 1.5H), –0.04 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 165.1, 165.0, 164.9, 164.1, 149.99, 149.90, 148.5, 148.1, 147.46, 147.43, 141.8, 140.9, 139.0, 138.5, 138.4, 137.8, 136.6, 136.4, 134.8, 134.4, 131.6, 129.6 (3C), 129.4, 128.4, 127.2, 127.1 (2C), 126.7, 126.28, 126.23, 124.3, 123.8, 123.7, 72.4, 72.3, 52.9, 52.7, 40.3, 31.1, 30.7, 28.86, 28.81, 27.9, 26.5, 25.57 (3C), 25.50, 24.9, 18.0, 17.2, 13.4, –5.23, –5.37.

Methyl 6-(2-(Hydroxy(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazol-5-yl)picolinate (S20)



The title compound was prepared from methyl 6-(2-((*tert*-butyldimethylsilyloxy)(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazol-5-yl)picolinate (**S19**, 232 mg, 0.41 mmol) following general procedure D. Flash chromatography (SiO_2, 50–100% EtOAc–hexanes) yielded the title compound (175 mg, 94%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.98 (d, 1H, *J* = 4.8 Hz), 7.84–7.75 (m, 3H), 7.53 (d, 2H, *J* = 4.8 Hz), 7.38 (t, 2H, *J* = 7.5 Hz), 7.30–7.27 (m, 3H), 7.11 (d, 0.5H, *J* = 8.4 Hz), 7.04 (d, 0.5H, *J* = 7.0 Hz), 4.88 (d, 0.5H, *J* = 7.0 Hz), 4.84 (d, 0.5H, *J* = 7.0 Hz), 3.98 (s, 3H), 3.01–2.84 (m, 3H), 2.73–2.68 (m, 2H), 2.50–2.47 (m, 1H), 2.28–2.25 (m, 0.5H), 1.91–1.88 (m, 0.5H), 1.70–1.58 (m, 1H), 1.39–1.32 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 165.8, 165.7, 165.0, 150.1, 147.9, 147.1, 140.9, 138.5, 138.4, 137.8, 136.6, 136.4, 134.6, 134.4, 129.5, 129.4, 128.4 (2C), 127.2, 127.1, 126.76 (2C), 126.72, 125.9, 124.34, 124.30, 123.8, 122.1, 71.2, 71.0, 64.1, 60.2, 52.7, 51.8, 39.6, 39.5, 31.2, 30.5, 30.4, 28.7, 25.4, 24.6, 20.8, 20.0, 18.9, 14.0, 13.5, 13.4.

Methyl 6-(2-(6-Phenyl-1,2,3,4-tetrahydronaphthalene-2-carbonyl)oxazol-5-yl)picolinate (7)

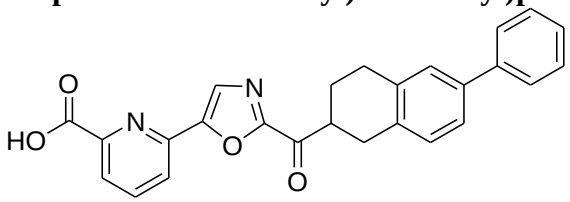


The title compound was prepared from methyl 6-(2-(hydroxy(6-phenyl-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazol-5-yl)picolinate (**S20**, 170 mg, 0.38 mmol) following general procedure E. Flash chromatography (SiO_2, 30% EtOAc–hexanes) yielded the title compound (130 mg, 77%) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.10 (dd, 1H, *J* = 1.0, 8.0 Hz), 8.05 (s, 1H), 8.01 (dd, 1H, *J* = 1.0, 8.0 Hz), 7.94 (t, 1H, *J* = 7.5 Hz), 7.58 (d, 2H, *J* = 8.5 Hz), 7.41 (t, 2H, *J* = 8.4 Hz), 7.36–7.29 (m, 3H), 7.18 (d, 1H, *J* = 8.0 Hz), 4.02 (s, 3H), 3.97–3.91 (m, 1H), 3.17–3.00 (m, 4H), 2.37–2.34 (m, 1H), 1.98–1.93 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 190.3, 164.9, 156.8, 152.3, 148.3, 146.3, 140.8, 138.8, 138.1, 135.8, 133.8, 129.3, 128.5 (2C), 127.8, 127.2, 126.9, 126.8 (2C), 125.0, 124.5, 123.1, 52.8, 43.3, 30.6, 28.7, 25.9; HRMS-ESI-TOF *m/z* 439.1658 ($[M + H]^+$, $C_{27}H_{22}N_2O_4$ requires 439.1652). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 40% EtOH–hexanes, 7 mL/min, α = 1.12).

(*S*)-**7**: $[\alpha]^{23}_D$ +7 (*c* 0.1, THF).

(*R*)-**7**: $[\alpha]^{23}_D$ –7 (*c* 0.1, THF).

6-(2-(6-Phenyl-1,2,3,4-tetrahydronaphthalene-2-carbonyl)oxazol-5-yl)picolinic acid (8)

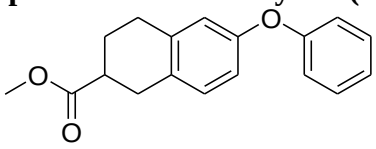


The title compound was prepared from methyl 6-(2-(6-phenyl-1,2,3,4-tetrahydronaphthalene-2-carbonyl)oxazol-5-yl)picolinate (**7**, 6.6 mg, 0.015 mmol) following general procedure F. Each pure enantiomer of the methyl ester were converted to their corresponding carboxylic acid using general procedure G. Flash chromatography (SiO_2, 0–5% HOAc–EtOAc) yielded the title compound (5 mg, 90%) as a white solid: ^{1}H NMR ($CDCl_3$ + 0.1% TFA, 600 MHz) δ 8.32 (d, 1H, *J* = 6.0 Hz), 8.20–8.15 (m, 2H), 8.12 (s, 1H), 7.60 (d, 2H, *J* = 8.0 Hz), 7.44 (t, 2H, *J* = 8.0 Hz), 7.41–7.35 (m, 3H), 7.22 (d, 1H, *J* = 7.8 Hz), 3.90–3.89 (m, 1H), 3.20–3.06 (m, 4H), 2.40–2.37 (m, 1H), 2.01–1.99 (m, 1H); ^{13}C NMR ($CDCl_3$ + 0.1% TFA, 150 MHz) δ 190.7, 166.2, 156.8, 151.5, 145.9, 145.1, 140.9, 140.2, 139.3, 135.6, 133.1, 129.4, 128.7 (2C), 127.7, 127.5, 127.1, 127.0 (2C), 125.3, 125.0, 124.9, 43.8, 30.5, 28.6, 26.1; HRMS-ESI-TOF *m/z* 425.1492 ($[M + H]^+$, $C_{26}H_{20}N_2O_4$ requires 425.1496).

(*S*)-**8**: $[\alpha]^{23}_D$ +4.2 (*c* 0.1, THF).

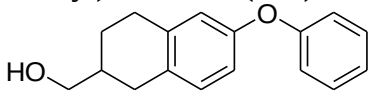
(*R*)-**8**: $[\alpha]^{23}_D$ –3.5 (*c* 0.4, THF).

Methyl 6-Phenoxy-1,2,3,4-tetrahydronaphthalene-2-carboxylate (S21)



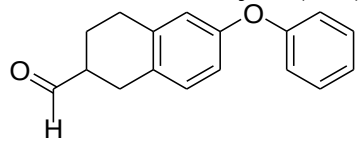
A sample of methyl 1,2,3,4-tetrahydro-6-hydroxynaphthalene-2-carboxylate (**S4**, 1 g, 4.84 mmol), phenylboronic acid (1.20 g, 9.69 mmol), $Cu(OAc)_2$ (879 mg, 4.84 mmol), and 4Å MS (1 g) were placed in anhydrous CH_2Cl_2 (60 mL). The reaction mixture was stirred at room temperature for 15 min before Et_3N (1.4 mL, 9.69 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 17 h under Ar. The mixture was diluted with EtOAc, washed with saturated aqueous NH_4Cl, saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude product that was purified by flash chromatography (SiO_2, 10% EtOAc–hexanes) to provide the title compound (800 mg, 59%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.32 (t, 2H, *J* = 7.2 Hz), 7.09–7.05 (m, 2H), 6.99 (d, 2H, *J* = 8.4 Hz), 6.80 (dd, 1H, *J* = 2.4, 8.4 Hz), 6.74–6.70 (m, 1H), 3.73 (s, 3H), 3.02–2.94 (m, 2H), 2.83–2.80 (m, 2H), 2.77–2.72 (m, 1H), 2.21–2.18 (m, 1H), 1.89–1.83 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 175.7, 157.5, 155.0, 137.2, 130.1, 129.7, 129.6 (2C), 122.8, 118.8, 118.5 (2C), 116.8, 51.7, 39.9, 31.0, 28.6, 25.6.

(6-Phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methanol (S22)



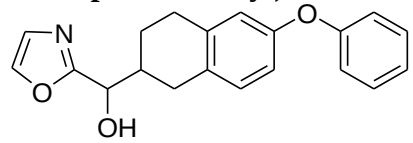
The title compound was prepared from methyl 6-phenoxy-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**S21**, 800 mg, 2.83 mmol) following general procedure A. Flash chromatography (SiO_2, 50% EtOAc–hexanes) afforded the title compound (743 mg, 98%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33 (t, 2H, *J* = 7.2 Hz), 7.11–7.01 (m, 4H), 6.82–6.79 (m, 2H), 3.65 (d, 2H, *J* = 6.4 Hz), 2.92–2.80 (m, 2H), 2.52–2.45 (m, 2H), 2.30 (s, 1H), 2.08–1.99 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.5, 154.6, 138.1, 130.8, 130.2, 129.5 (2C), 122.6, 118.8, 118.3 (2C), 116.6, 67.3, 37.0, 31.6, 28.7, 25.6.

6-Phenoxy-1,2,3,4-tetrahydronaphthalene-2-carboxaldehyde (S23)



The title compound was prepared from (6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methanol (**S22**, 200 mg, 0.78 mmol) following general procedure B. Flash chromatography (SiO_2, 20% EtOAc–hexanes) afforded the title compound (196 mg, 98%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.79 (s, 1H), 7.36 (t, 2H, *J* = 7.2 Hz), 7.13–7.09 (m, 2H), 7.03 (d, 2H, *J* = 8.0 Hz), 6.85–6.74 (m, 2H), 2.99–2.95 (m, 2H), 2.87–2.78 (m, 2H), 2.73–2.66 (m, 1H), 2.24–2.17 (m, 1H), 1.85–1.78 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 203.4, 157.2, 154.9, 137.3, 130.2, 129.5 (2C), 129.0, 122.7, 118.7, 118.3 (2C), 116.8, 46.6, 28.0, 27.6, 22.5.

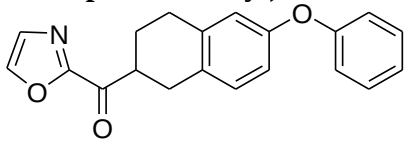
Oxazol-2-yl(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methanol (S24)



Oxazole (0.226 mL, 3.44 mmol) in anhydrous THF (20 mL) was treated with BH_3•THF (1 M, 3.74 mL, 3.74 mmol) and the solution was stirred at room temperature for 1 h before being cooled to –78 °C and treated with 2.16 M *n*-BuLi (2 mL, 4.47 mmol) dropwise. The reaction mixture was stirred at –78 °C for 40 min before a solution of 6-phenoxy-1,2,3,4-tetrahydronaphthalene-2-carboxaldehyde (**S23**, 870 mg, 3.44 mmol) in THF (20 mL) was added. The reaction mixture was stirred at –78 °C for 2 h before being warmed to room temperature. A 5% HOAc–EtOH solution (50 mL) was added and this mixture was stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the residue was dissolved in EtOAc, washed with H_2O, saturated aqueous $NaHCO_3$ and saturated aqueous NaCl before the organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 40% EtOAc–hexanes) afforded the title compound (740 mg, 67%) as colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.65 (s, 1H), 7.32–7.31 (m, 2H),

7.10–6.98 (m, 5H), 6.78–6.75 (m, 2H), 4.78–4.74 (m, 1H), 2.88–2.78 (m, 4H), 2.61–2.59 (m, 0.5H), 2.34 (m, 0.5H), 2.14–2.12 (m, 0.5H), 1.80–1.77 (m, 0.5H), 1.62–1.51 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.3, 157.5, 154.8, 138.9, 137.9, 137.7, 130.5, 130.3, 130.2, 130.1, 129.5 (2C), 126.5, 122.8, 122.7, 118.86 (2C), 118.82, 118.49, 118.42, 116.78, 116.73, 71.2, 71.0, 39.8, 39.7, 30.8, 30.2, 29.6, 28.9, 28.8, 25.1, 24.4.

Oxazol-2-yl(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methanone (9)

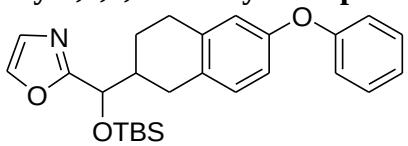


The title compound was prepared from oxazol-2-yl(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methanol (**S24**, 58.5 mg, 0.182 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (21.4 mg, 37%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.85 (s, 1H), 7.36 (s, 1H), 7.32 (t, 2H, *J* = 7.8 Hz), 7.09–7.06 (m, 2H), 7.00 (d, 2H, *J* = 9.0 Hz), 6.81–6.78 (m, 2H), 3.87–3.84 (m, 1H), 3.05 (d, 2H, *J* = 8.4 Hz), 2.94–2.88 (m, 2H), 2.30–2.26 (m, 1H), 1.93–1.86 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 190.4, 157.5, 157.4, 155.0, 141.6, 137.2, 130.1, 129.7, 129.6 (2C), 129.0, 122.8, 118.8, 118.5 (2C), 116.9, 43.5, 30.4, 28.7, 25.6; HRMS-ESI-TOF *m/z* 320.1281 ($[M + H]^+$, $C_{20}H_{17}NO_3$ requires 320.1281). The enantiomers were separated using a semipreparative chiral phase HPLC column (ChiralPAK AD, 10 μm, 2 × 25 cm, 1% *i*-PrOH–hexanes gradient, 7 mL/min, α = 1.19).

(*S*)-**9**: $[\alpha]^{23}_D$ –38 (*c* 0.1, THF).

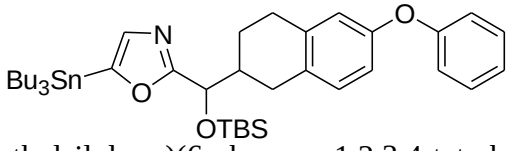
(*R*)-**9**: $[\alpha]^{23}_D$ +42 (*c* 0.1, THF).

2-((*tert*-Butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole (S25)



A solution of oxazol-2-yl(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methanol (**S24**, 400 mg, 1.24 mmol), TBSCl (450 mg, 2.98 mmol) and imidazole (421 mg, 6.2 mmol) in DMF (20 mL) was stirred at room temperature for 16 h before it was diluted with EtOAc, washed with H_2O, and saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 10% EtOAc–hexanes) yielded the title compound (459 mg, 85%) as a thick colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.65 (s, 1H), 7.31 (t, 2H, *J* = 8.5 Hz), 7.12 (d, 1H, *J* = 8.0 Hz), 7.01–6.97 (m, 4H), 6.81–6.75 (m, 2H), 4.80 (d, 0.5H, *J* = 7.0 Hz), 4.74 (d, 0.5H, *J* = 7.0 Hz), 2.99–2.73 (m, 3H), 2.55–2.51 (m, 1H), 2.39–2.25 (m, 1H), 1.74–1.71 (m, 1H), 1.53–1.49 (m, 1H), 0.96 (s, 4.5H), 0.93 (s, 4.5H), –0.03 (s, 1.5H), –0.04 (s, 1.5H), –0.05 (s, 1.5H), –0.06 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 164.4, 164.3, 157.6, 157.5, 154.7, 154.6, 138.47, 138.41, 138.0, 137.7, 130.7, 130.4, 130.3, 130.1 (2C), 129.4, 126.7, 122.6, 122.5, 118.8, 118.3, 118.2, 116.7, 116.6, 72.2, 72.1, 40.3, 30.67, 30.62, 28.8, 28.7, 25.6 (3C), 25.1, 24.8, 18.0, –5.3, –5.41, –5.44, –5.6.

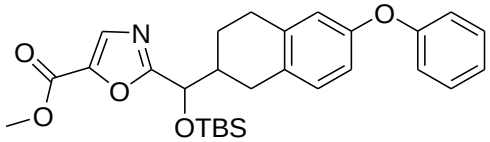
2-((*tert*-Butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)-5-(tributylstannyl)oxazole (S26)



A solution of 2-((*tert*-butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole (**S25**, 459.3 mg, 1.05 mmol) in THF (15 mL) was cooled to –78 °C before it was treated with 2.16 M *n*-BuLi (0.6 mL, 1.15 mmol) dropwise. The reaction mixture was stirred at –78 °C for 2 h, and treated with a solution of Bu_3SnCl (0.6 mL, 2.1 mmol) and stirred for 5 min. The solution was warmed to room temperature, diluted with EtOAc, and washed with saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 10% EtOAc–hexanes) yielded the title compound (500 mg, 78%) as a thick colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.30 (t, 2H, *J* = 7.5 Hz), 7.12 (d, 1H, *J* = 6.0 Hz), 7.06 (t, 2H, *J* = 7.0 Hz), 6.97 (m, 2H), 6.77 (dd, 2H, *J* = 2.5, 8.5 Hz), 4.80 (d, 0.5H, *J* = 7.0 Hz), 4.75 (d, 0.5H, *J* = 7.0 Hz), 2.96–2.92 (m, 2H), 2.82–2.70 (m, 2H), 2.52–2.22 (m, 2H), 1.58–1.46 (m, 8H),

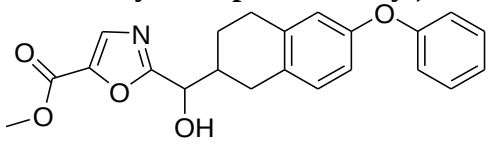
1.36–1.30 (m, 7H), 1.15–1.11 (m, 5H), 0.94–0.90 (m, 18H), 0.08 (s, 1.5H), 0.06 (s, 1.5H), –0.11 (s, 1.5H), –0.12 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 168.5, 168.4, 157.8, 154.9, 154.8, 154.7, 154.6, 138.2, 138.0, 137.1, 131.2, 130.8, 130.4, 130.2, 129.5 (2C), 122.67, 122.64, 118.9, 118.4, 118.3, 116.8, 116.6, 72.5, 72.3, 40.69, 40.64, 30.85, 30.81, 29.3, 29.2 (3C), 29.1, 29.0, 28.98, 28.90, 28.8, 28.5, 27.6, 27.4, 27.3, 27.2 (3C), 27.1, 27.0, 26.8, 25.7, 25.2, 25.0, 18.1, 13.69, 13.60 (3C), 11.6, 10.7, 10.2 (3C), 9.98, –5.3, –5.4, –5.61, –5.62.

Methyl 2-((*tert*-Butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole-5-carboxylate (S27)



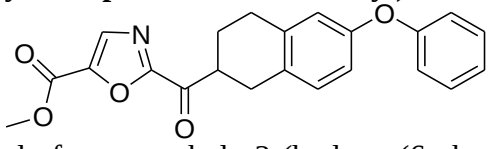
A solution of 2-((*tert*-butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole (**S25**, 148 mg, 0.33 mmol) in THF (2 mL) was cooled to –78 °C before it was treated with 2.16 M *n*-BuLi (0.18 mL, 0.37 mmol) dropwise. The reaction mixture was stirred at –78 °C for 2 h, and treated with a solution of Mander's reagent (MeO_2CCN, 0.165 mL, 1.65 mmol) in THF (2 mL) and stirred for 5 min. The solution was warmed to room temperature and diluted with EtOAc and washed with saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 10% EtOAc–hexanes) yielded the title compound (174 mg, 98%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.74 (d, 1H, *J* = 4.0 Hz), 7.30 (t, 2H, *J* = 8.5 Hz), 7.07–7.04 (m, 2H), 6.98–6.96 (m, 2H), 6.79–6.73 (m, 2H), 4.81 (d, 0.5H, *J* = 7.0 Hz), 4.75 (d, 0.5H, *J* = 7.0 Hz), 3.92 (s, 3H), 2.87–2.73 (m, 3H), 2.57–2.54 (m, 1H), 2.39–2.16 (m, 1H), 1.77–1.74 (m, 1H), 1.57–1.50 (m, 1H), 0.97 (s, 9H), –0.03 (s, 1.5H), –0.04 (s, 1.5H), –0.05 (s, 1.5H), –0.06 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 167.7, 167.5, 157.9, 157.6, 157.5, 154.7, 142.2, 142.1, 137.9, 137.6, 133.9, 130.6, 130.4, 130.2, 129.5 (2C), 122.74, 122.70, 118.8, 118.4, 118.3 (2C), 116.8, 116.7, 99.5, 72.3, 72.2, 52.1, 40.3, 30.7, 30.1, 28.88, 28.80, 25.6 (3C), 25.3, 24.5, 18.1, –5.1, –5.31, –5.34.

Methyl 2-(Hydroxy(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole-5-carboxylate (S28)



The title compound was prepared from methyl 2-((*tert*-butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole-5-carboxylate (**S27**, 75 mg, 0.15 mmol) following general procedure D. Flash chromatography (SiO_2, 50% EtOAc–hexanes) yielded the title compound (41.8 mg, 73%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.74 (s, 1H), 7.31 (t, 2H, *J* = 8.5 Hz), 7.08–7.01 (m, 2H), 6.98–6.96 (m, 2H), 6.78–6.73 (m, 2H), 4.84 (t, 0.5H, *J* = 7.0 Hz), 4.80 (t, 0.5H, *J* = 7.0 Hz), 3.92 (s, 3H), 3.18–3.15 (m, 1H), 2.82–2.77 (m, 3H), 2.66–2.65 (m, 1H), 2.41–2.37 (m, 1H), 2.08–2.04 (m, 0.5H), 1.86–1.83 (m, 0.5H), 1.80–1.72 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 157.9, 157.5, 154.9, 137.7, 137.6, 133.7, 133.6, 130.3, 130.2, 130.1, 130.0, 129.6 (2C), 122.8, 118.86, 118.85, 118.4 (2C), 116.87, 116.83, 71.4, 71.3, 52.3, 39.9, 39.8, 30.8, 29.7, 28.87, 28.84, 25.2, 24.0.

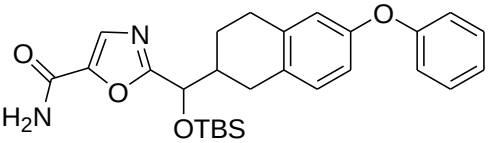
Methyl 2-(6-Phenoxy-1,2,3,4-tetrahydronaphthalene-2-carbonyl)oxazole-5-carboxylate (10)



The title compound was prepared from methyl 2-(hydroxy(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole-5-carboxylate (**S28**, 41.8 mg, 0.11 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (27.5 mg, 66%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.91 (s, 1H), 7.32 (t, 2H, *J* = 7.2 Hz), 7.08 (t, 2H, *J* = 7.2 Hz), 7.00 (d, 2H, *J* = 7.5 Hz), 6.81–6.77 (m, 2H), 3.97 (s, 3H), 3.85–3.82 (m, 1H), 3.07 (d, 2H, *J* = 8.0 Hz), 2.93–2.89 (m, 2H), 2.29–2.26 (m, 1H), 1.91–1.88 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 190.2, 157.8, 157.49, 157.45, 155.2, 143.9, 137.0, 134.6, 130.1, 129.6 (2C), 129.3, 122.9, 118.8, 118.5 (2C), 117.0, 52.7, 43.8, 30.3, 28.7, 25.4; HRMS-ESI-TOF *m/z* 378.1335 ($[M + H]^+$, $C_{22}H_{19}NO_5$ requires 378.1336). The enantiomers were separated using a

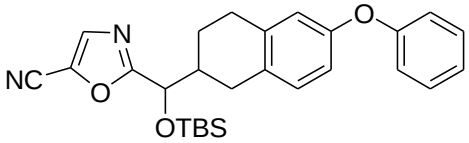
semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 1% EtOH–hexanes, 7 mL/min, α = 1.14).
(*S*)-**10**: $[\alpha]^{23}_{D}$ –14 (*c* 0.1, THF).
(*R*)-**10**: $[\alpha]^{23}_{D}$ +16 (*c* 0.1, THF).

2-((*tert*-Butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole-5-carboxamide (S29)



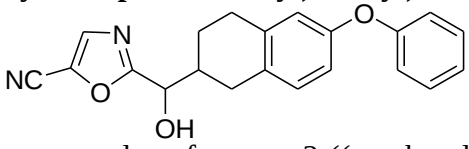
A solution of methyl 2-((*tert*-butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)-oxazole-5-carboxylate (**S27**, 100 mg, 0.20 mmol) was dissolved in a saturated solution of NH_3–CH_3OH (5 mL) and the mixture was stirred for 2 h at room temperature. Evaporation in vacuo yielded the crude carboxamide that was purified by flash chromatography (SiO_2, 50% EtOAc–hexanes) to provide the title compound (98.2 mg, 98%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.74 (d, 1H, *J* = 6.6 Hz), 7.30 (t, 2H, *J* = 8.5 Hz), 7.07–7.03 (m, 2H), 6.98–6.96 (m, 2H), 6.79–6.73 (m, 2H), 6.45 (brs, 1H, NH), 6.24 (brs, 1H, NH), 4.79 (d, 0.5H, *J* = 7.0 Hz), 4.72 (d, 0.5H, *J* = 7.0 Hz), 2.87–2.70 (m, 3H), 2.54–2.50 (m, 1H), 2.34–2.04 (m, 1H), 1.75–1.72 (m, 1H), 1.54–1.49 (m, 1H), 0.97 (s, 9H), –0.03 (s, 1.5H), –0.04 (s, 1.5H), –0.05 (s, 1.5H), –0.06 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 166.5, 165.7, 158.78, 158.74, 157.58, 157.51, 154.9, 154.8, 144.6, 144.5, 137.8, 137.6, 131.53, 131.51, 130.4, 130.3, 130.2, 130.0, 129.5 (2C), 122.8, 122.7, 118.8, 118.4, 118.3 (2C), 116.8, 116.7, 72.4, 72.3, 40.53, 40.50, 30.8, 30.3, 28.8, 28.7, 25.6 (3C), 25.2, 24.7, 18.1, –5.2, –5.24, –5.27.

2-((*tert*-Butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole-5-carbonitrile (S30)



A solution of 2-((*tert*-butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole-5-carboxamide (**S29**, 98.2 mg, 0.20 mmol) was dissolved in 1,4-dioxane (6 mL) and pyridine (0.042 mL, 0.51 mmol) and trifluoroacetic anhydride (0.036 mL, 0.26 mmol) were added. The reaction mixture stirred for 2 h at room temperature. The mixture was diluted with CH_2Cl_2 and the organic layer was washed with saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude nitrile that was purified by flash chromatography (SiO_2, 10% EtOAc–hexanes) to afford the title compound (81.2 mg, 88%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.71 (d, 1H, *J* = 6.6 Hz), 7.32 (t, 2H, *J* = 8.5 Hz), 7.09–7.05 (m, 2H), 6.99–6.97 (d, 2H, *J* = 7.8 Hz), 6.80–6.75 (m, 2H), 4.84 (d, 0.5H, *J* = 7.0 Hz), 4.77 (d, 0.5H, *J* = 7.0 Hz), 2.85–2.72 (m, 3H), 2.56–2.53 (m, 1H), 2.35–2.31 (m, 1H), 2.14–2.12 (m, 0.5H), 1.77–1.74 (m, 0.5H), 1.55–1.48 (m, 1H), 0.91 (s, 9H), 0.11 (s, 1.5H), 0.09 (s, 1.5H), –0.04 (s, 1.5H), –0.05 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 168.6, 157.57, 157.52, 154.99, 154.91, 137.8, 137.5, 130.4, 130.2, 129.8, 129.5 (2C), 124.5, 124.4, 122.9, 122.8, 118.6, 118.47, 118.41 (2C), 116.9, 116.8, 109.04, 109.00, 72.2, 72.1, 40.4, 30.6, 30.0, 28.8, 28.7, 25.5 (3C), 25.2, 24.5, 18.1, –5.23, –5.29, –5.31.

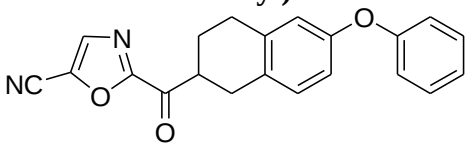
2-(Hydroxy(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole-5-carbonitrile (S31)



The title compound was prepared from 2-((*tert*-butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole-5-carbonitrile (**S30**, 81.2 mg, 0.17 mmol) following general procedure D. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (29.3 mg, 48%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.72 (s, 1H), 7.31 (t, 2H, *J* = 8.5 Hz), 7.08 (t, 1H, *J* = 8.5 Hz), 7.04 (d, 1H, *J* = 8.5 Hz), 7.00–6.97 (m, 2H), 6.79–6.75 (m, 2H), 4.84 (d, 0.5H, *J* = 7.0 Hz), 4.80 (d, 0.5H, *J* = 7.0 Hz), 2.84–2.76 (m, 3H), 2.66–2.63 (m, 1H), 2.38–2.36 (m, 1H), 2.07–2.04 (m, 1H), 1.85–1.82 (m, 1H), 1.63–1.55 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 168.5, 157.4, 155.0, 137.6, 137.44, 137.41, 137.40, 130.3, 130.2,

129.7, 129.6 (2C), 124.9, 122.9, 118.85, 118.83, 118.5, 116.94, 116.90, 108.7, 71.4, 71.3, 39.87, 39.80, 30.7, 29.8, 28.7, 25.1, 24.0.

2-(6-Phenoxy-1,2,3,4-tetrahydronaphthalene-2-carbonyl)oxazole-5-carbonitrile (11)

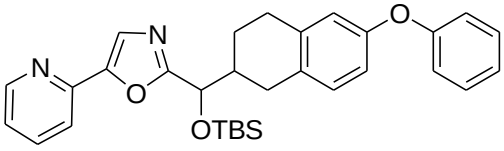


The title compound was prepared from 2-(hydroxy(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole-5-carbonitrile (**S31**, 29.3 mg, 0.08 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (28.4 mg, 98%) as a yellow solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.88 (s, 1H), 7.33 (t, 2H, *J* = 7.2 Hz), 7.10 (t, 2H, *J* = 7.2 Hz), 7.00 (d, 2H, *J* = 7.5 Hz), 6.82–6.78 (m, 2H), 3.82–3.80 (m, 1H), 3.07 (d, 2H, *J* = 8.0 Hz), 2.93–2.90 (m, 2H), 2.30–2.27 (m, 1H), 1.93–1.89 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 189.2, 158.1, 157.3, 155.3, 138.0, 136.9, 130.1, 129.6 (2C), 129.0, 126.5, 123.0, 118.8, 118.5 (2C), 117.0, 108.1, 44.1, 30.2, 28.6, 25.4; HRMS-ESI-TOF *m/z* 345.1240 ([M + H]$^+$, $C_{21}H_{16}N_2O_3$ requires 345.1234). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 1% EtOH–hexanes, 7 mL/min, α = 1.12).

(*S*)-**11**: $[\alpha]^{23}_D$ –19 (*c* 0.1, THF).

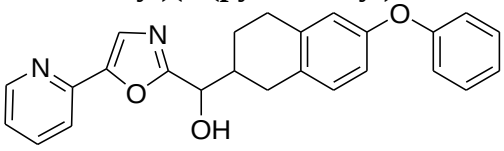
(*R*)-**11**: $[\alpha]^{23}_D$ +20 (*c* 0.1, THF).

2-((*tert*-Butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)-5-(pyridin-2-yl)oxazole (S32)



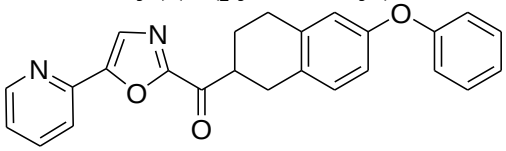
The title compound was prepared from 2-((*tert*-butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)-5-(tributylstannyl)oxazole (**S26**, 5 g, 6.89 mmol) and 2-bromopyridine following general procedure C. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (1.49 g, 42%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.64 (d, 1H, *J* = 4.5 Hz), 7.78–7.76 (m, 1H), 7.71–7.67 (m, 2H), 7.30 (t, 2H, *J* = 7.5 Hz), 7.24–7.22 (m, 1.5H), 7.07–7.04 (m, 1.5H), 6.98–6.95 (m, 2H), 6.78–7.72 (m, 2H), 4.81 (d, 0.5H, *J* = 7.0 Hz), 4.75 (d, 0.5H, *J* = 7.0 Hz), 2.96–2.73 (m, 2H), 2.58–2.55 (m, 1H), 2.39–2.34 (m, 1H), 2.26–2.20 (m, 1H), 1.81–1.77 (m, 1H), 1.58–1.53 (m, 1H), 0.90 (s, 9H), 0.11 (s, 1.5H), 0.09 (s, 1.5H), –0.05 (s, 1.5H), –0.04 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 157.7, 157.6, 154.8, 154.7, 149.6, 138.1, 137.9, 137.18, 137.14, 132.1, 130.8, 130.5, 130.4 (2C), 130.3, 129.5, 128.5 (2C), 125.5, 125.4, 122.8, 122.78, 122.73, 119.1, 118.9, 118.4, 118.3, 116.8, 116.7, 72.5, 72.4, 40.5, 30.9, 30.5, 29.0, 28.9, 25.7 (3C), 25.3, 24.9, 18.2, –5.0, –5.23, –5.26.

(6-Phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)(5-(pyridin-2-yl)oxazol-2-yl)methanol (S33)



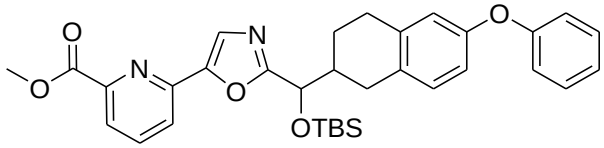
The title compound was prepared from 2-((*tert*-butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)-5-(pyridin-2-yl)oxazole (**S32**, 1.49 g, 2.90 mmol) following general procedure D. Flash chromatography (SiO_2, 50–100% EtOAc–hexanes) yielded the title compound (740 mg, 64%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.63 (d, 1H, *J* = 4.2 Hz), 7.78 (t, 1H, *J* = 7.8 Hz), 7.71–7.65 (m, 2H), 7.30 (t, 2H, *J* = 7.2 Hz), 7.27–7.25 (m, 2H), 7.07–6.96 (m, 3H), 6.77–6.73 (m, 2H), 4.87 (d, 0.5H, *J* = 7.0 Hz), 4.82 (d, 0.5H, *J* = 7.0 Hz), 2.86–2.68 (m, 4H), 2.45–2.42 (m, 1H), 2.17–2.15 (m, 1H), 1.92–1.89 (m, 1H), 1.66–1.61 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 157.6, 154.8, 149.5, 146.7, 137.9, 137.7, 137.3, 130.5, 130.4, 130.3, 130.2, 129.6 (2C), 125.37, 125.34, 123.1, 122.8, 119.4, 118.9, 118.8, 118.4 (2C), 116.85, 116.81, 71.5, 71.3, 39.9, 39.8, 30.9, 30.0, 29.6, 28.98, 28.94, 25.3, 24.3.

(6-Phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)(5-(pyridin-2-yl)oxazol-2-yl)methanone (12)



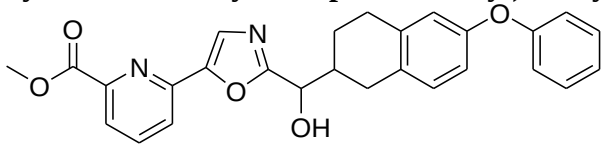
The title compound was prepared from (6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)(5-(pyridin-2-yl)oxazol-2-yl)methanol (**S33**, 740 mg, 1.85 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (650 mg, 88%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.68 (d, 1H, *J* = 4.2 Hz), 7.93 (s, 1H), 7.90–7.83 (m, 2H), 7.34–7.31 (m, 3H), 7.19–7.14 (m, 4H), 6.88–6.78 (m, 2H), 3.92–3.90 (m, 1H), 3.10–2.90 (m, 4H), 2.32–2.30 (m, 1H), 1.95–1.93 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 190.5, 157.5, 156.8, 155.1, 153.3, 150.0, 146.1, 137.2, 137.0, 130.2, 129.7, 129.6 (2C), 127.0, 124.2, 122.9, 120.4, 118.9, 118.5 (2C), 116.9, 43.5, 30.6, 28.8, 25.7; HRMS-ESI-TOF *m/z* 397.1551 ($[M + H]^+$, $C_{25}H_{20}N_2O_3$ requires 397.1547). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 10% EtOH–hexanes, 7 mL/min, α = 1.35).
(*S*)-**12**: $[\alpha]^{23}_D$ –2.0 (*c* 0.1, THF).
(*R*)-**12**: $[\alpha]^{23}_D$ +1.8 (*c* 0.1, THF).

Methyl 6-(2-((*tert*-Butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazol-5-yl)picolinate (S34)



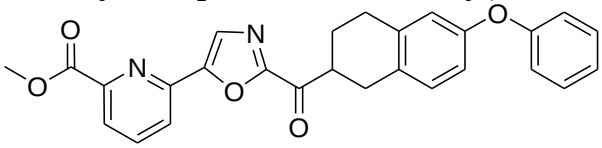
The title compound was prepared from 2-((*tert*-butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)-5-(tributylstannyl)oxazole (**S26**, 5 g, 6.89 mmol) and methyl 6-bromopicolinate following general procedure C. Flash chromatography (SiO_2, 30% EtOAc–hexanes) yielded the title compound (2.88 g, 73%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.01 (dd, 1H, *J* = 4.5, 7.0 Hz), 7.99–7.97 (m, 1H), 7.89–7.85 (m, 1H), 7.80–7.78 (m, 1H), 7.65–7.59 (m, 1H), 7.25–7.22 (m, 2H), 7.01–6.97 (m, 1H), 6.92–6.90 (m, 2H), 6.73–6.66 (m, 2H), 4.80 (d, 0.5H, *J* = 7.0 Hz), 4.77 (d, 0.5H, *J* = 7.0 Hz), 3.96 (s, 1.5H), 3.93 (s, 1.5H), 2.91–2.87 (m, 1H), 2.78–2.76 (m, 3H), 2.73–2.71 (m, 1H), 2.38–2.33 (m, 0.5H), 2.23–2.20 (m, 0.5H), 1.62–1.52 (m, 1H), 0.90 (s, 9H), 0.11 (s, 1.5H), 0.09 (s, 1.5H), –0.05 (s, 1.5H), –0.04 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 165.0, 164.9, 164.8, 164.0, 157.47, 157.40, 154.6, 154.5, 149.9, 149.8, 148.4, 148.0, 147.38, 147.35, 141.8, 138.9, 137.8, 137.6, 131.8, 131.7, 131.5, 130.5, 130.2, 130.1, 130.0, 129.3 (2C), 128.3, 128.23, 126.20, 126.1, 123.8, 123.7, 122.56, 122.52, 121.8 (2C), 118.7, 118.2, 118.1, 72.3, 72.1, 52.8, 52.6, 40.2, 30.7, 30.3, 28.7, 28.6, 27.6, 26.5, 25.5 (3C), 25.1, 24.6, 17.9, 17.3, 13.3, –5.2, –5.40, –5.44.

Methyl 6-(2-(Hydroxy(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazol-5-yl)picolinate (S35)



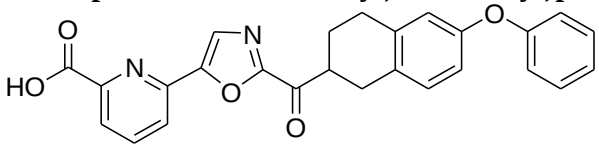
The title compound was prepared from methyl 6-(2-((*tert*-butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazol-5-yl)picolinate (**S34**, 2.88 g, 5.04 mmol) following general procedure D. Flash chromatography (SiO_2, 50–100% EtOAc–hexanes) yielded the title compound (2 g, 86%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.20 (dd, 1H, *J* = 1.2, 7.6 Hz), 8.05 (t, 1H, *J* = 8.0 Hz), 7.98–7.96 (m, 2H), 7.48 (t, 2H, *J* = 7.2 Hz), 7.25–7.12 (m, 4H), 6.95–6.90 (m, 2H), 5.06 (d, 0.5H, *J* = 6.8 Hz), 5.01 (d, 0.5H, *J* = 6.8 Hz), 4.18 (s, 3H), 3.08–2.95 (m, 3H), 2.84–2.81 (m, 1H), 2.65–2.61 (m, 1H), 2.38–2.03 (m, 1H), 1.81–1.45 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.8, 165.7, 165.1, 157.4, 154.77, 154.74, 150.1, 148.0, 147.1, 137.8, 137.6, 130.4, 130.3, 130.2, 130.1, 129.49 (2C), 129.47, 125.9, 123.9, 122.6, 122.2, 118.79, 117.74, 118.33, 118.30, 116.7, 116.6, 71.2, 71.0, 64.2, 52.8, 39.69, 39.65, 30.9, 30.1, 28.8, 25.2, 24.4, 18.9, 17.4, 13.4.

Methyl 6-(2-(6-Phenoxy-1,2,3,4-tetrahydronaphthalene-2-carbonyl)oxazol-5-yl)picolinate (13)



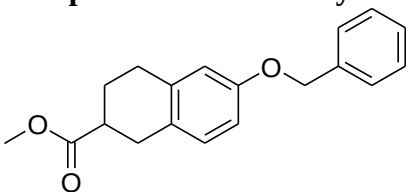
The title compound was prepared from methyl 6-(2-(hydroxy(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazol-5-yl)picolinate (**S35**, 2 g, 4.38 mmol) following general procedure E. Flash chromatography (SiO_2, 30% EtOAc–hexanes) yielded the title compound (1.67 g, 70%) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.09 (dd, 1H, *J* = 1.0, 8.0 Hz), 8.03 (s, 1H), 8.01 (dd, 1H, *J* = 1.5, 8.0 Hz), 7.95 (t, 1H, *J* = 7.5 Hz), 7.29 (t, 2H, *J* = 7.5 Hz), 7.06 (t, 2H, *J* = 7.5 Hz), 6.98–6.96 (m, 2H), 6.79–6.77 (m, 2H), 4.01 (s, 3H), 3.91–3.86 (m, 1H), 3.08 (d, 2H, *J* = 8.0 Hz), 2.93–2.87 (m, 2H), 2.31–2.27 (m, 1H), 1.94–1.89 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 190.3, 164.9, 157.4, 156.8, 154.9, 152.3, 148.4, 146.3, 138.1, 137.1, 130.0, 129.6 (2C), 129.5, 127.8, 125.0, 123.1, 122.7, 118.8, 118.4 (2C), 116.8, 52.9, 43.4, 30.4, 28.6, 25.6; HRMS-ESI-TOF *m/z* 455.1617 ($[M + H]^+$, $C_{27}H_{22}N_2O_5$ requires 455.1601). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 40% EtOH–hexanes, 7 mL/min, α = 1.19).
(*S*)-**13**: $[\alpha]^{23}_D$ –0.7 (*c* 0.8, THF).
(*R*)-**13**: $[\alpha]^{23}_D$ +0.5 (*c* 0.8, THF).

6-(2-(6-Phenoxy-1,2,3,4-tetrahydronaphthalene-2-carbonyl)oxazol-5-yl)picolinic acid (14)



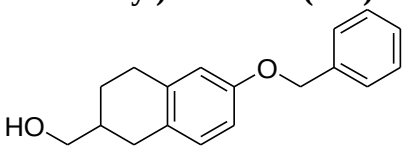
The title compound was prepared from methyl 6-(2-(6-phenoxy-1,2,3,4-tetrahydronaphthalene-2-carbonyl)-oxazol-5-yl)picolinate (**13**, 5 mg, 0.010 mmol) following general procedure F. Each pure enantiomer of the methyl esters were converted to their corresponding carboxylic acid using general procedure G. Flash chromatography (SiO_2, 5% HOAc–EtOAc) yielded the title compound (3 mg, 70%) as a yellow solid: ^{1}H NMR ($CDCl_3$ + 0.1% TFA, 600 MHz) δ 8.34 (d, 1H, *J* = 6.0 Hz), 8.22–8.19 (m, 2H), 7.98 (s, 1H), 7.36 (t, 2H, *J* = 8.0 Hz), 7.13–7.10 (m, 2H), 7.03 (d, 2H, *J* = 7.8 Hz), 6.85–6.78 (m, 2H), 3.85–3.84 (m, 1H), 3.13–3.09 (m, 2H), 2.96–2.90 (m, 2H), 2.34–2.31 (m, 1H), 1.97–1.94 (m, 1H); ^{13}C NMR ($CDCl_3$ + 0.1% TFA, 150 MHz) δ 191.0, 157.2, 156.8, 155.3, 151.2, 145.0, 140.5, 136.8, 130.2, 129.7 (2C), 128.9, 127.9, 125.8, 125.2, 123.2, 118.9 (2C), 118.6, 117.1, 43.9, 30.2, 28.5, 25.7; HRMS-ESI-TOF *m/z* 441.1451 ($[M + H]^+$, $C_{26}H_{20}N_2O_5$ requires 441.1445).
(*S*)-**14**: $[\alpha]^{23}_D$ –4.5 (*c* 0.7, THF).
(*R*)-**14**: $[\alpha]^{23}_D$ +5.4 (*c* 0.6, THF).

Methyl 6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (S36)



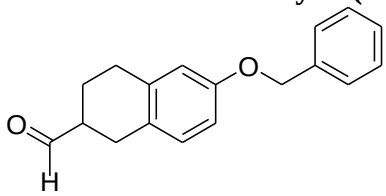
A sample of methyl 1,2,3,4-tetrahydro-6-hydroxynaphthalene-2-carboxylate (**S4**, 4.0 g, 19.39 mmol), benzyl alcohol (2.2 mL, 21.3 mmol) and triphenylphosphine (6.60 g, 25.2 mmol) were dissolved in anhydrous THF (100 mL). The reaction mixture was cooled to 0°C before diethyl azodicarboxylate (4 mL, 25.2 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 17 h under Ar. The mixture was diluted with EtOAc, washed with saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude product that was purified by flash chromatography (SiO_2, 10% EtOAc–hexanes) to provide the title compound (4.3 g, 75%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.49 (d, 2H, *J* = 7.0 Hz), 7.44 (t, 2H, *J* = 7.5 Hz), 7.38 (t, 1H, *J* = 7.5 Hz), 7.07 (d, 1H, *J* = 8.5 Hz), 6.84 (dd, 1H, *J* = 2.5, 8.5 Hz), 6.78 (d, 1H, *J* = 2.5 Hz), 5.07 (s, 2H), 3.78 (s, 3H), 3.03–3.00 (m, 2H), 2.90–2.86 (m, 2H), 2.79–2.75 (m, 1H), 2.27–2.23 (m, 1H), 1.94–1.90 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.5, 156.7, 137.0, 136.5, 129.6 (2C), 128.2, 127.5, 127.1 (2C), 127.0, 114.2, 112.7, 69.6, 51.4, 39.8, 30.7, 28.5, 25.5.

(6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)methanol (S37)



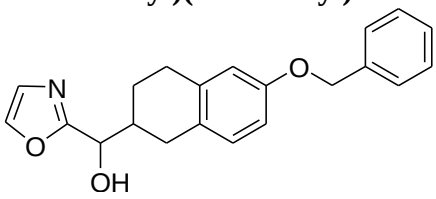
The title compound was prepared from methyl 6-(benzyloxy)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**S36**, 4.30 g, 14.5 mmol) following general procedure A. Flash chromatography (SiO_2, 50% EtOAc–hexanes) afforded the title compound (4.10 g, 98%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.53 (d, 2H, *J* = 6.8 Hz), 7.48 (t, 2H, *J* = 6.8 Hz), 7.41 (t, 1H, *J* = 7.2 Hz), 7.09 (d, 1H, *J* = 8.4 Hz), 6.89–6.83 (m, 2H), 5.10 (s, 2H), 3.67 (d, 2H, *J* = 5.2 Hz), 2.94–2.85 (m, 4H), 2.54–2.47 (m, 1H), 2.09–1.98 (m, 2H), 1.54–1.49 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.5, 137.6, 137.0, 129.8, 128.3, 128.2 (2C), 128.1, 127.6, 114.3, 114.2, 112.6, 112.4, 69.7, 67.3, 37.0, 31.4, 28.8, 25.6.

6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalene-2-carboxaldehyde (S38)



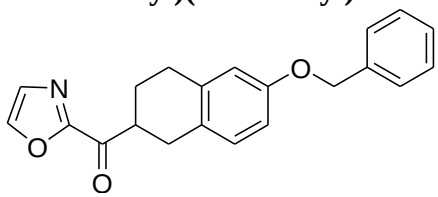
The title compound was prepared from (6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)methanol (**S37**, 4.10 g, 15.27 mmol) following general procedure B. Flash chromatography (SiO_2, 10% EtOAc–hexanes) afforded the title compound (3.13 g, 77%) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.79 (s, 1H), 7.46 (d, 2H, *J* = 7.0 Hz), 7.42 (t, 2H, *J* = 7.0 Hz), 7.35 (t, 1H, *J* = 7.5 Hz), 7.09 (d, 1H, *J* = 8.0 Hz), 6.82 (dd, 1H, *J* = 2.5, 8.5 Hz), 6.76 (d, 1H, *J* = 2.5 Hz), 5.06 (s, 2H), 2.98–2.81 (m, 4H), 2.69–2.67 (m, 1H), 2.22–2.19 (m, 1H), 1.84–1.78 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 203.7, 156.9, 137.0, 136.9, 129.9 (2C), 128.4, 127.7, 127.2, 126.5, 114.4, 113.0, 69.8, 46.9, 28.2, 27.6, 22.7.

(6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(oxazol-2-yl)methanol (S39)



Oxazole (0.815 mL, 12.4 mmol) in anhydrous THF (100 mL) was treated with BH_3•THF (1 M, 13.5 mL, 13.5 mmol) and the solution was stirred at room temperature for 1 h before being cooled to –78 °C and treated with 1.7 M *n*-BuLi (10 mL, 16.2 mmol) dropwise. The reaction mixture was stirred at –78 °C for 40 min before a solution of 6-(benzyloxy)-1,2,3,4-tetrahydronaphthalene-2-carboxaldehyde (**S38**, 3.13 g, 12.4 mmol) in THF (40 mL) was added. The reaction mixture was stirred at –78 °C for 2 h before being warmed to room temperature. A 5% HOAc–EtOH solution (100 mL) was added and this mixture was stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the residue was dissolved in EtOAc, and washed with H_2O, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl before the organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. Flash chromatography (SiO_2, 50% EtOAc–hexanes) afforded the title compound (3.5 g, 84%) as white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.64 (s, 1H), 7.43 (d, 2H, *J* = 7.5 Hz), 7.38 (t, 2H, *J* = 7.0 Hz), 7.31 (t, 1H, *J* = 7.5 Hz), 7.10 (s, 1H), 7.00 (d, 0.5H, *J* = 8.5 Hz), 6.93 (d, 0.5H, *J* = 8.5 Hz), 6.77–6.71 (m, 2H), 5.02 (s, 2H), 4.76–4.72 (m, 1H), 3.66 (s, 1H), 2.84–2.69 (m, 2H), 2.56 (d, 1H, *J* = 8.0 Hz), 2.36–2.31 (m, 1H), 2.13–2.10 (m, 1H), 1.81–1.78 (m, 1H), 1.60–1.52 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 165.2, 156.8, 138.9, 137.5, 137.3, 137.2, 130.0, 129.9, 128.4 (2C), 127.9, 127.7 (2C), 127.3, 126.6, 114.4, 112.86, 112.84, 71.3, 71.2, 69.9, 40.0, 39.9, 30.6, 30.0, 29.0, 25.2, 24.5.

(6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(oxazol-2-yl)methanone (15)

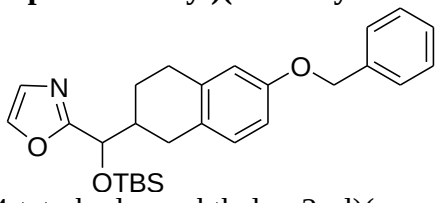


The title compound was prepared from (6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(oxazol-2-yl)methanol (**S39**, 40 mg, 0.119 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (35 mg, 88%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.84 (s, 1H), 7.43 (d, 2H, *J* = 7.2 Hz), 7.39 (t, 2H, *J* = 7.8 Hz), 7.37 (s, 1H), 7.30 (t, 1H, *J* = 7.2 Hz), 7.02 (d, 1H, *J* = 8.4 Hz), 6.77 (dd, 1H, *J* = 2.4, 8.4 Hz), 6.748–6.744 (m, 1H), 5.04 (s, 2H), 3.85–3.80 (m, 1H), 3.03 (d, 2H, *J* = 8.4 Hz), 2.95–2.90 (m, 2H), 2.28–2.25 (m, 1H), 1.91–1.87 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 190.6, 157.5, 157.0, 141.6, 137.1, 136.7, 129.9, 129.0, 128.5 (2C), 127.8, 127.4 (2C), 127.1, 114.4, 113.0, 70.0, 43.7, 30.3, 29.0, 25.7; HRMS-ESI-TOF *m/z* 334.1442 ($[M + H]^+$, $C_{21}H_{19}NO_3$ requires 334.1438). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 1% EtOH–hexanes, 7 mL/min, α = 1.12).

(*S*)-**15**: $[\alpha]^{23}_D$ –19 (*c* 0.2, THF).

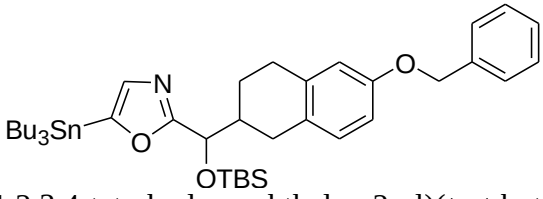
(*R*)-**15**: $[\alpha]^{23}_D$ +20 (*c* 0.2, THF).

2-((6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(*tert*-butyldimethylsilyloxy)methyl)oxazole (S40)



A solution of (6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(oxazol-2-yl)methanol (**S39**, 3.34 g, 9.95 mmol), TBSCl (3.6 g, 23.89 mmol) and imidazole (3.30 g, 49.75 mmol) in DMF (60 mL) was stirred at room temperature for 16 h before it was diluted with EtOAc, washed with H_2O, and saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 5% EtOAc–hexanes) yielded the title compound (5.10 g, 98%) as a thick colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.65 (s, 1H), 7.43 (d, 2H, *J* = 6.0 Hz), 7.38 (t, 2H, *J* = 7.2 Hz), 7.31 (t, 1H, *J* = 7.2 Hz), 7.10 (d, 1H, *J* = 6.0 Hz), 7.01 (d, 0.5H, *J* = 8.4 Hz), 6.92 (d, 0.5H, *J* = 8.4 Hz), 6.77–6.70 (m, 2H), 5.02 (s, 2H), 4.76 (d, 0.5H, *J* = 7.2 Hz), 4.68 (d, 0.5H, *J* = 7.2 Hz), 2.91–2.65 (m, 1.5H), 2.50–2.40 (m, 1H), 2.31–2.22 (m, 1.5H), 1.69–1.68 (m, 1H), 1.49–1.43 (m, 2H), 0.89 (s, 9H), 0.09 (s, 1.5H), 0.07 (s, 1.5H), –0.09 (s, 1.5H), –0.10 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 164.6, 164.5, 156.77, 156.74, 138.5, 138.4, 137.6, 137.4, 137.2, 130.1, 129.9, 128.4 (2C), 128.2, 127.9, 127.7, 127.3, 126.7, 114.4, 114.3, 112.8, 112.7, 72.4, 72.3, 69.9, 40.6, 40.5, 30.5, 29.1, 29.0, 25.6 (3C), 25.3, 25.0, 18.1, –5.2, –5.31, –5.34, –5.37.

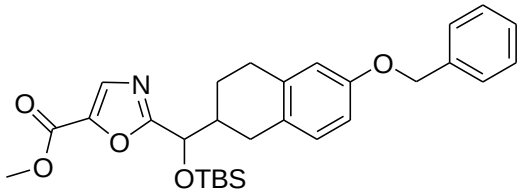
2-((6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(*tert*-butyldimethylsilyloxy)methyl)-5-(tributylstannyl)oxazole (S41)



A solution of 2-((6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(*tert*-butyldimethylsilyloxy)methyl)oxazole (**S40**, 500 mg, 1.1 mmol) in THF (20 mL) was cooled to –78 °C before it was treated with 2.16 M *n*-BuLi (0.60 mL, 1.2 mmol) dropwise. The reaction mixture was stirred at –78 °C for 2 h, and treated with a solution of Bu_3SnCl (0.60 mL, 2.2 mmol) and stirred for 5 min. The solution was warmed to room temperature and diluted with EtOAc, and washed with saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 0–5% EtOAc–hexanes) yielded the title compound (499 mg, 62%) as a thick colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.43 (d, 2H, *J* = 7.5 Hz),

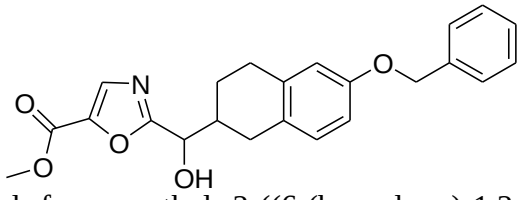
7.38 (t, 2H, *J* = 7.5 Hz), 7.32 (t, 1H, *J* = 7.0 Hz), 7.15 (s, 0.5H), 7.14 (s, 0.5H), 7.02 (d, 0.5H, *J* = 8.5 Hz), 6.92 (d, 0.5H, *J* = 8.5 Hz), 6.79–6.70 (m, 2H), 5.02 (s, 2H), 4.80 (d, 0.5H, *J* = 7.5 Hz), 4.75 (d, 0.5H, *J* = 7.5 Hz), 2.95–2.67 (m, 3H), 2.51–2.24 (m, 2H), 1.62–1.57 (m, 8H), 1.39–1.33 (m, 6H), 1.17–1.31 (m, 6H), 0.94–0.90 (m, 18H), 0.09 (s, 1.5H), 0.08 (s, 1.5H), –0.09 (s, 1.5H), –0.10 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 168.5, 168.4, 156.6, 154.8, 154.7, 137.7, 137.4, 137.2, 137.1, 130.1, 129.9, 128.49, 128.42 (2C), 128.1, 127.7, 127.3 (2C), 114.37, 114.31, 112.7, 112.6, 72.5, 72.4, 69.9, 40.7, 40.6, 30.6, 30.5, 29.2, 29.1, 28.9 (3C), 28.8, 28.7, 27.3, 27.2 (3C), 27.0, 26.8, 25.6 (3C), 25.3, 25.1, 18.1, 13.6 (3C), 13.5, 11.6, 11.5 (3C), 10.1, 8.76, 8.70, –5.33, –5.36, –5.37, –5.40.

Methyl 2-((6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(*tert*-butyldimethylsilyloxy)methyl)oxazole-5-carboxylate (S42)



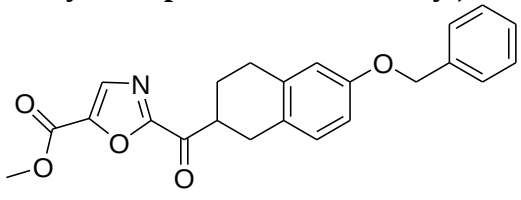
A solution of 2-((6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(*tert*-butyldimethylsilyloxy)methyl)oxazole (**S40**, 200 mg, 0.44 mmol) in THF (4 mL) was cooled to –78 °C before it was treated with 2.16 M *n*-BuLi (0.30 mL, 0.53 mmol) dropwise. The reaction mixture was stirred at –78 °C for 2 h, and treated with a solution of Mander's reagent (MeO_2CCN, 0.175 mL, 2.2 mmol) in THF (2 mL) and stirred for 5 min. The solution was warmed to room temperature and diluted with EtOAc and washed with saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 10% EtOAc–hexanes) yielded the title compound (134 mg, 59%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.75–7.73 (m, 1H), 7.42 (d, 2H, *J* = 7.8 Hz), 7.37 (t, 2H, *J* = 7.8 Hz), 7.31 (t, 1H, *J* = 7.2 Hz), 6.99 (d, 1H, *J* = 8.4 Hz), 6.91 (d, 1H, *J* = 8.4 Hz), 6.76–6.69 (m, 1H), 5.02 (s, 2H), 4.79 (d, 0.5H, *J* = 6.6 Hz), 4.73 (d, 0.5H, *J* = 7.8 Hz), 3.92 (s, 3H), 2.83–2.79 (m, 2H), 2.50–2.48 (m, 1H), 2.35–2.33 (m, 1H), 2.22–2.20 (m, 1H), 1.75–1.73 (m, 1H), 1.52–1.47 (m, 1H), 0.90 (s, 9H), 0.09 (s, 1.5H), 0.07 (s, 1.5H), –0.05 (s, 1.5H), –0.06 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 167.8, 167.6, 158.0, 156.82, 156.80, 156.7, 142.2, 142.1, 137.5, 137.2, 134.0, 133.9, 130.1, 129.9, 128.4 (2C), 127.9, 127.7, 127.3 (2C), 114.4, 114.3, 112.8, 112.7, 72.45, 72.41, 72.3, 69.9, 52.1, 40.6, 39.0, 30.6, 30.0, 29.3, 26.0 (3C), 24.7, 18.1, 13.7, –5.1, –5.30, –5.33.

Methyl 2-((6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(hydroxy)methyl)oxazole-5-carboxylate (S43)



The title compound was prepared from methyl 2-((6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(*tert*-butyldimethylsilyloxy)methyl)oxazole-5-carboxylate (**S42**, 70 mg, 0.13 mmol) following general procedure D. Flash chromatography (SiO_2, 50% EtOAc–hexanes) yielded the title compound (33.5 mg, 62%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.75 (s, 1H), 7.42 (d, 2H, *J* = 7.8 Hz), 7.37 (t, 2H, *J* = 7.8 Hz), 7.31 (t, 1H, *J* = 7.2 Hz), 6.98 (d, 0.5H, *J* = 8.4 Hz), 6.92 (d, 0.5H, *J* = 8.4 Hz), 6.75–6.70 (m, 2H), 5.02 (s, 2H), 4.82 (d, 0.5H, *J* = 6.6 Hz), 4.77 (d, 0.5H, *J* = 7.8 Hz), 3.92 (s, 3H), 2.84–2.74 (m, 3H), 2.38–2.35 (m, 2H), 2.22–2.20 (m, 1H), 1.85–1.83 (m, 1H), 1.61–1.47 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 157.9, 156.8, 137.3, 137.1, 133.7, 130.1, 129.9, 128.5 (2C), 127.8, 127.5, 127.4 (2C), 127.3, 114.4, 112.94, 112.91, 71.5, 71.4, 69.9, 52.3, 40.08, 40.01, 30.6, 29.6, 29.0, 25.3, 24.2.

Methyl 2-(6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalene-2-carbonyl)oxazole-5-carboxylate (16)

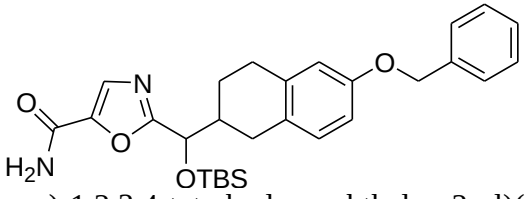


The title compound was prepared from methyl 2-((6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(hydroxy)methyl)oxazole-5-carboxylate (**S43**, 33.5 mg, 0.07 mmol) following general procedure E. Flash chromatography (SiO_2, 30% EtOAc–hexanes) yielded the title compound (21.3 mg, 70%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.91 (s, 1H), 7.42 (d, 2H, *J* = 7.8 Hz), 7.38 (t, 2H, *J* = 7.8 Hz), 7.32 (t, 1H, *J* = 7.2 Hz), 7.02 (d, 1H, *J* = 8.4 Hz), 6.79–6.74 (m, 2H), 5.04 (s, 2H), 3.97 (s, 3H), 3.82–3.80 (m, 1H), 3.03–2.90 (m, 4H), 2.28–2.25 (m, 1H), 1.90–1.87 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 190.3, 157.8, 157.4, 157.0, 143.8, 137.1, 136.6, 134.6, 129.8, 128.5 (2C), 127.8, 127.4, 126.8, 114.4, 113.1, 69.9, 52.7, 44.0, 30.2, 28.8, 25.5; HRMS-ESI-TOF *m/z* 392.1494 ($[M + H]^+$, $C_{23}H_{21}NO_5$ requires 392.1492). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 3% EtOH–hexanes, 7 mL/min, α = 1.20).

(*S*)-**16**: $[\alpha]^{23}_D$ –15 (*c* 0.1, THF).

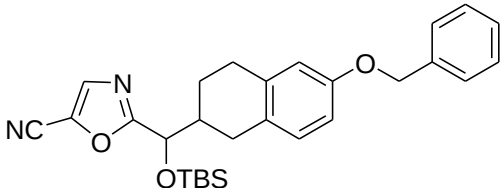
(*R*)-**16**: $[\alpha]^{23}_D$ +17 (*c* 0.1, THF).

2-((6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(*tert*-butyldimethylsilyloxy)methyl)oxazole-5-carboxamide (S44)



A solution of methyl 2-((6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(*tert*-butyldimethylsilyloxy)methyl)-oxazole-5-carboxylate (**S42**, 75 mg, 0.14 mmol) was dissolved in a saturated solution of NH_3–CH_3OH (4 mL) and the mixture was stirred for 2 h at room temperature. Evaporation in vacuo yielded the crude carboxamide that was purified by flash chromatography (SiO_2, 50% EtOAc–hexanes) to provide the title compound (49.7 mg, 68%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.71 (d, 1H, *J* = 5.4 Hz), 7.42 (d, 2H, *J* = 7.8 Hz), 7.37 (t, 2H, *J* = 7.8 Hz), 7.30 (t, 1H, *J* = 7.2 Hz), 6.99 (d, 0.5H, *J* = 8.4 Hz), 6.91 (d, 0.5H, *J* = 8.4 Hz), 6.77–6.70 (m, 2H), 6.18–6.17 (m, 2H), 5.02 (s, 2H), 4.77 (d, 0.5H, *J* = 6.6 Hz), 4.70 (d, 0.5H, *J* = 7.8 Hz), 2.85–2.76 (m, 2 H), 2.68–2.66 (m, 1H), 2.49–2.45 (m, 1H), 2.31–2.05 (m, 2H), 1.51–1.48 (m, 1H), 0.89 (s, 9H), 0.10 (s, 1.5H), 0.08 (s, 1.5H), –0.06 (s, 1.5H), –0.07 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.9, 165.8, 158.6, 158.5, 156.89, 156.85, 144.6, 144.5, 137.4, 137.1, 131.58, 131.56, 130.1, 129.9, 128.5 (2C), 127.8, 127.7, 127.4, 127.3 (2C), 114.4, 114.3, 112.9, 112.8, 72.5, 72.4, 69.9, 40.6, 30.6, 30.2, 29.0, 28.9, 25.6 (3C), 25.3, 24.9, 18.1, –5.18, –5.19, –5.22, –5.25.

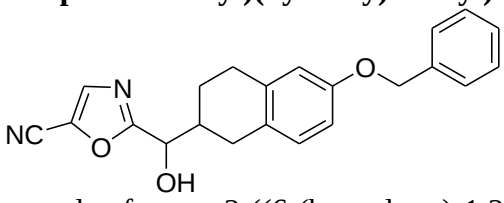
2-((6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(*tert*-butyldimethylsilyloxy)methyl)oxazole-5-carbonitrile (S45)



A solution of 2-((6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(*tert*-butyldimethylsilyloxy)methyl)oxazole-5-carboxamide (**S44**, 49.7 mg, 0.10 mmol) was dissolved in 1,4-dioxane (5 mL) and pyridine (0.020 mL, 0.25 mmol) and trifluoroacetic anhydride (0.018 mL, 0.13 mmol) were added. The reaction mixture was stirred for 2 h at room temperature. The mixture was diluted with CH_2Cl_2 and the organic layer was washed with saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude nitrile that was purified by flash chromatography (SiO_2, 10% EtOAc–hexanes) to afford the title compound (33.2 mg, 69%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.70 (d, 1H, *J* = 5.4 Hz), 7.42 (d, 2H, *J* = 7.8 Hz), 7.37 (t, 2H, *J* = 7.8 Hz), 7.31 (t, 1H, *J* = 7.2 Hz), 7.00 (d, 0.5H, *J* = 8.4 Hz), 6.92 (d, 0.5H, *J* = 8.4 Hz), 6.77–6.70 (m, 2H), 5.02 (s, 2H), 4.80 (d, 0.5H, *J* = 6.6 Hz), 4.74 (d, 0.5H, *J* = 7.8 Hz), 2.83–2.76 (m, 2H), 2.69–2.66 (m, 1H), 2.50–2.47 (m, 1H), 2.31–2.28 (m, 1H), 2.13–2.11 (m, 0.5H), 1.74–1.72 (m, 0.5H), 1.58–1.48 (m, 1H), 0.88 (s, 9H), 0.10 (s, 1.5H), 0.08 (s, 1.5H), –0.06 (s, 1.5H), –0.07 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 168.7, 168.5, 156.9, 156.8, 137.5, 137.3, 137.1, 137.0, 130.1, 129.9, 128.5 (2C), 127.8, 127.6, 127.4 (2C), 127.2, 124.49, 124.46, 114.4, 114.3,

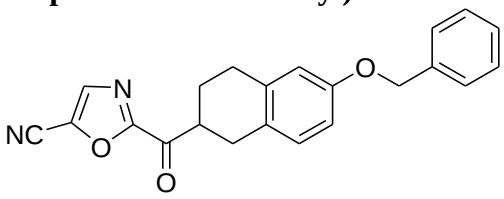
112.9, 112.8, 109.09, 109.06, 72.3, 72.2, 69.9, 40.6, 30.5, 29.9, 28.99, 28.94, 25.5 (3C), 25.3, 24.6, 18.1, –5.22, –5.27, –5.29.

2-((6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(hydroxy)methyl)oxazole-5-carbonitrile (S46)



The title compound was prepared from 2-((6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(*tert*-butyldimethylsilyloxy)methyl)oxazole-5-carbonitrile (**S45**, 33.2 mg, 0.06 mmol) following general procedure D. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (8 mg, 32%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.72 (d, 1H, *J* = 5.4 Hz), 7.41 (d, 2H, *J* = 7.8 Hz), 7.37 (t, 2H, *J* = 7.8 Hz), 7.31 (t, 1H, *J* = 7.2 Hz), 6.98 (d, 0.5H, *J* = 8.4 Hz), 6.94 (d, 0.5H, *J* = 8.4 Hz), 6.77–6.71 (m, 2H), 5.02 (s, 2H), 4.82–4.79 (m, 1H), 2.85–2.60 (m, 4H), 2.36–2.33 (m, 2H), 2.06–2.04 (m, 1H), 1.84–1.80 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 168.5, 157.0, 137.45, 137.43, 137.17, 137.15, 137.0, 130.1, 129.9, 128.5 (2C), 127.8, 127.4 (2C), 127.1, 127.0, 125.0, 114.47, 114.45, 113.06, 113.02, 108.8, 71.5, 71.4, 70.0, 40.0, 39.9, 30.5, 29.6, 28.8, 25.2, 24.2.

2-(6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalene-2-carbonyl)oxazole-5-carbonitrile (17)

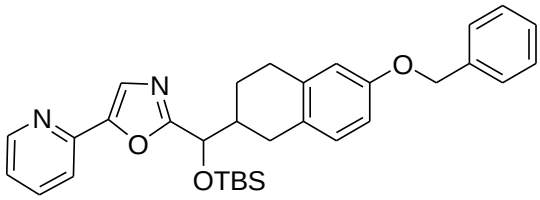


The title compound was prepared from 2-((6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(hydroxy)methyl)-oxazole-5-carbonitrile (**S46**, 8 mg, 0.02 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (7.2 mg, 95%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.88 (s, 1H), 7.42 (d, 2H, *J* = 6.6 Hz), 7.38 (t, 2H, *J* = 7.2 Hz), 7.32 (t, 1H, *J* = 7.2 Hz), 7.02 (d, 1H, *J* = 8.4 Hz), 6.78 (dd, 1H, *J* = 2.4, 8.4 Hz), 6.74 (s, 1H), 5.04 (s, 2H), 3.79–3.77 (m, 1H), 3.02 (d, 2H, *J* = 7.2 Hz), 2.95–2.91 (m, 2H), 2.28–2.26 (m, 1H), 1.91–1.87 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 189.4, 158.2, 157.1, 138.0, 137.0, 136.4, 129.8, 128.5 (2C), 127.9, 127.4 (2C), 126.57, 126.50, 114.5, 113.2, 108.1, 70.0, 44.3, 30.1, 28.8, 25.5; HRMS-ESI-TOF *m/z* 381.1220 ($[M + Na]^+$, $C_{22}H_{18}N_2O_3$ requires 381.1210). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 10% EtOH–hexanes, 7 mL/min, α = 1.24).

(*S*)-**17**: $[\alpha]^{23}_D$ –19 (*c* 0.1, THF).

(*R*)-**17**: $[\alpha]^{23}_D$ +21 (*c* 0.1, THF).

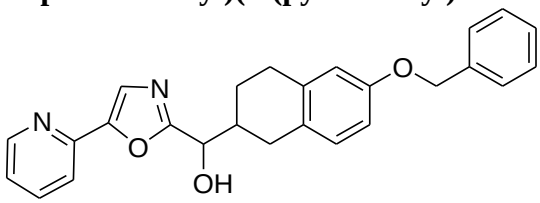
2-((6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(*tert*-butyldimethylsilyloxy)methyl)-5-(pyridin-2-yl)oxazole (S47)



The title compound was prepared from 2-((6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(*tert*-butyldimethylsilyloxy)methyl)-5-(tributylstannyl)oxazole (**S41**, 250 mg, 0.33 mmol) and 2-bromopyridine following general procedure C. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (129 mg, 74%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.64 (d, 1H, *J* = 7.5 Hz), 7.77–7.66 (m, 2H), 7.43–7.41 (m, 2H), 7.39 (t, 2H, *J* = 7.5 Hz), 7.36 (t, 1H, *J* = 7.0 Hz), 7.23–7.20 (m, 1H), 7.03 (d, 0.5H, *J* = 8.4 Hz), 6.95 (d, 0.5H, *J* = 8.4 Hz), 6.76–6.63 (m, 2H), 5.028 (s, 1H), 5.023 (s, 1H), 4.81 (d, 0.5H, *J* = 6.6 Hz), 4.76 (d, 0.5H, *J* = 7.8 Hz), 2.91–2.65 (m, 3H), 2.58–2.52 (m, 1H), 2.44–2.39 (m, 1H), 2.36–2.26 (m, 0.5H), 1.80–1.79 (m, 0.5H), 1.68–1.63 (m, 2H), 1.67–1.63 (m, 2H), 1.58–1.55 (m, 2H), 0.93 (s, 3H), 0.91 (s, 3H), 0.13 (s,

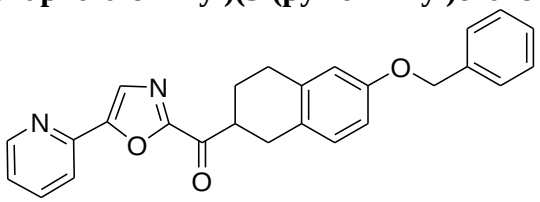
1.5H), 0.11 (s, 1.5H), –0.02 (s, 1.5H), –0.03 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 164.81, 164.71, 156.7, 150.8, 150.7, 149.8, 147.35, 147.32, 137.5, 137.3, 137.2, 136.8, 130.1, 129.9, 128.4 (2C), 128.1, 127.8, 127.7, 127.3, 125.1, 125.0, 122.7, 118.9, 114.4, 114.3, 112.8, 112.7, 72.5, 72.4, 69.9, 40.6, 30.7, 30.4, 29.1, 29.0, 27.7, 26.7, 25.6 (3C), 25.4, 24.9, 18.1, 17.4, 13.5, –5.1, –5.28, –5.31.

(6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(5-(pyridin-2-yl)oxazol-2-yl)methanol (S48)



The title compound was prepared from 2-((6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(*tert*-butyldimethylsilyloxy)methyl)-5-(pyridin-2-yl)oxazole (**S47**, 128.6 mg, 0.24 mmol) following general procedure D. Flash chromatography (SiO_2, 50–100% EtOAc–hexanes) yielded the title compound (96.2 mg, 95%) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.61 (d, 1H, *J* = 7.5 Hz), 7.74–7.61 (m, 3H), 7.42–7.41 (m, 2H), 7.38 (t, 2H, *J* = 7.5 Hz), 7.30 (t, 1H, *J* = 7.0 Hz), 7.22–7.20 (m, 2H), 6.98 (d, 0.5H, *J* = 8.4 Hz), 6.91 (d, 0.5H, *J* = 8.4 Hz), 6.76–6.63 (m, 2H), 5.01 (s, 2H), 4.83 (d, 0.5H, *J* = 6.6 Hz), 4.79 (d, 0.5H, *J* = 7.8 Hz), 4.08 (s, 0.5H), 3.98 (s, 1H), 2.91–2.74 (m, 3H), 2.45–2.39 (m, 1H), 2.22–2.18 (m, 0.5H), 1.89–1.86 (m, 0.5H), 1.67–1.55 (m, 1H), 1.45–1.40 (m, 0.5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 165.4, 156.8, 151.0, 149.8, 146.9, 137.5, 137.3, 137.2, 136.8, 130.1, 129.9, 128.4 (2C), 127.9, 127.7, 127.3 (2C), 124.8, 122.9, 119.3, 114.4, 114.3, 112.85, 112.82, 71.4, 71.3, 69.9, 39.9, 30.8, 30.5, 29.8, 25.4, 24.5; HRMS-ESI-TOF *m/z* 413.1856 ([M + H]$^+$, $C_{26}H_{24}N_2O_3$ requires 413.1860).

(6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(5-(pyridin-2-yl)oxazol-2-yl)methanone (18)

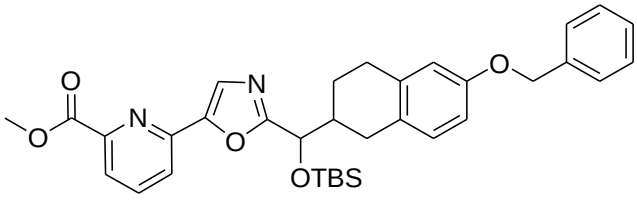


The title compound was prepared from (6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(5-(pyridin-2-yl)oxazol-2-yl)methanol (**S48**, 96.2 mg, 0.23 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (72 mg, 76%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.68 (d, 1H, *J* = 7.5 Hz), 7.91 (s, 1H), 7.88 (d, 1H, *J* = 7.5 Hz), 7.80 (td, 1H, *J* = 2.5, 7.5 Hz), 7.43 (d, 2H, *J* = 7.5 Hz), 7.38 (t, 2H, *J* = 7.5 Hz), 7.31 (t, 2H, *J* = 7.0 Hz), 7.03 (d, 1H, *J* = 8.4 Hz), 6.78 (d, 1H, *J* = 8.4 Hz), 6.76–6.74 (m, 1H), 5.04 (s, 2H), 3.91–3.86 (m, 1H), 3.06–2.89 (m, 4H), 2.32–2.28 (m, 1H), 1.95–1.86 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 190.6, 156.9, 156.8, 153.3, 150.0, 146.2, 137.17, 137.12, 136.7, 129.8, 128.5 (2C), 127.8, 127.4 (2C), 127.1, 126.9, 124.1, 120.4, 114.4, 113.0, 69.9, 43.6, 30.4, 29.0, 25.8; HRMS-ESI-TOF *m/z* 411.1700 ([M + H]$^+$, $C_{26}H_{22}N_2O_3$ requires 411.1703). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 5% EtOH–hexanes, 7 mL/min, α = 1.26).

(*S*)-**18**: $[\alpha]^{23}_D$ –3.2 (*c* 0.3, THF).

(*R*)-**18**: $[\alpha]^{23}_D$ +5.5 (*c* 0.2, THF).

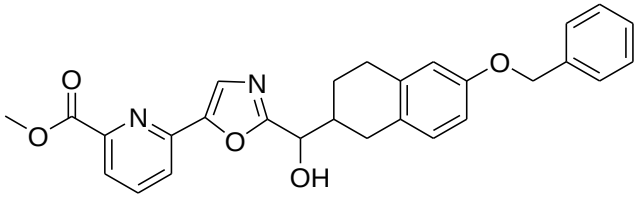
Methyl 6-(2-((6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(*tert*-butyldimethylsilyloxy)methyl)oxazol-5-yl)picolinate (S49)



The title compound was prepared from 2-((6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(*tert*-butyldimethylsilyloxy)methyl)-5-(tributylstannyl)oxazole (**S41**, 250 mg, 0.33 mmol) and methyl 6-bromopicolinate following general procedure C. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded

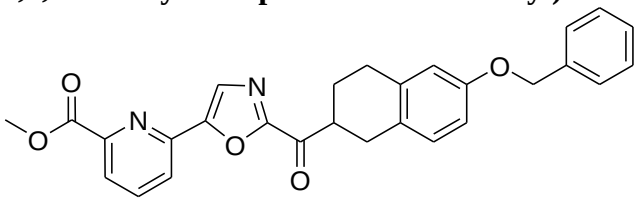
the title compound (160 mg, 67%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.04 (d, 1H, *J* = 7.5 Hz), 7.90 (q, 1H, *J* = 7.8 Hz), 7.84–7.81 (m, 2H), 7.42–7.40 (m, 2H), 7.37 (t, 2H, *J* = 7.5 Hz), 7.30 (t, 1H, *J* = 7.0 Hz), 7.00 (d, 0.5H, *J* = 8.4 Hz), 6.90 (d, 0.5H, *J* = 8.4 Hz), 6.76–6.69 (m, 1H), 5.018 (s, 1H), 5.013 (s, 1H), 4.80 (d, 0.5H, *J* = 6.6 Hz), 4.75 (d, 0.5H, *J* = 7.8 Hz), 4.02 (s, 3H), 2.91–2.70 (m, 2H), 2.54–2.49 (m, 1H), 2.39–2.34 (m, 1H), 2.27–2.24 (m, 1H), 1.66–1.62 (m, 1H), 1.54–1.52 (m, 1H), 1.38–1.28 (m, 1H), 0.90 (s, 4.5H), 0.88 (s, 4.5H), 0.11 (s, 1.5H), 0.09 (s, 1.5H), –0.05 (s, 1.5H), –0.06 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.3, 165.2, 165.0, 156.79, 156.76, 150.0, 149.9, 148.2, 147.6, 147.5, 137.9, 137.5, 137.3, 137.2, 137.1, 130.1, 129.9, 128.4 (2C), 128.1, 127.7, 127.36, 127.34, 126.38, 126.32, 123.9, 123.8, 122.05, 122.02, 114.4, 114.3, 112.8, 112.7, 72.5, 72.4, 69.9, 52.9, 40.6, 30.7, 30.3, 29.1, 29.0, 27.7, 26.7, 25.6 (3C), 25.4, 25.0, 18.1, 17.4, 13.5, –5.14, –5.15, –5.25, –5.28.

Methyl 6-(2-((6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(hydroxy)methyl)oxazol-5-yl)picolinate (S50)



The title compound was prepared from methyl 6-(2-((6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(*tert*-butyldimethylsilyloxy)methyl)oxazol-5-yl)picolinate (**S49**, 160 mg, 0.28 mmol) following general procedure D. Flash chromatography (SiO_2, 50–100% EtOAc–hexanes) yielded the title compound (96.6 mg, 75%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.03 (d, 1H, *J* = 7.2 Hz), 7.88 (t, 1H, *J* = 7.8 Hz), 7.78–7.76 (m, 3H), 7.41–7.35 (m, 2H), 7.36 (t, 1H, *J* = 7.2 Hz), 7.30 (t, 1H, *J* = 7.0 Hz), 6.98 (d, 0.5H, *J* = 8.4 Hz), 6.90 (d, 0.5H, *J* = 8.4 Hz), 6.74–6.69 (m, 2H), 5.00 (s, 2H), 4.85 (d, 0.5H, *J* = 6.6 Hz), 4.79 (d, 0.5H, *J* = 7.8 Hz), 4.01 (s, 3H), 3.74 (s, 1H), 2.86–2.73 (m, 4H), 2.42–2.39 (m, 1H), 1.87–1.85 (m, 1H), 1.64–1.57 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.2, 156.8, 150.3, 148.1, 147.2, 137.9, 137.4, 137.2, 137.1, 130.0, 129.9, 128.4 (2C), 127.8, 127.7 (2C), 127.6, 127.3, 126.0, 124.0, 122.2, 114.39, 114.36, 112.84, 112.80, 71.4, 71.3, 69.9, 52.9, 39.95, 39.91, 30.7, 29.9, 29.06, 29.04, 25.3, 24.5; HRMS-ESI-TOF *m/z* 471.1922 ($[M + H]^+$, $C_{28}H_{26}N_2O_5$ requires 471.1914).

Methyl 6-(2-(6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalene-2-carbonyl)oxazol-5-yl)picolinate (19)

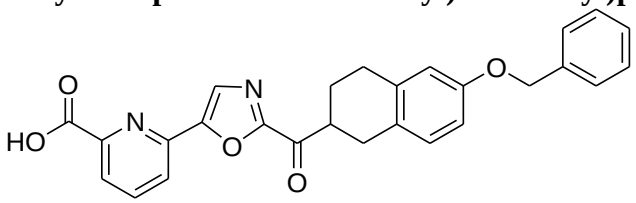


The title compound was prepared from methyl 6-(2-((6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(hydroxy)methyl)oxazol-5-yl)picolinate (**S50**, 96.6 mg, 0.21 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (26.5 mg, 48%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.11 (dd, 1H, *J* = 1.2, 9.0 Hz), 8.04 (s, 1H), 8.03 (dd, 1H, *J* = 1.2, 9.0 Hz), 7.97 (t, 1H, *J* = 7.8 Hz), 7.43 (d, 2H, *J* = 7.8 Hz), 7.38 (t, 2H, *J* = 7.8 Hz), 7.30 (t, 1H, *J* = 7.0 Hz), 7.03 (d, 1H, *J* = 8.4 Hz), 6.79 (dd, 1H, *J* = 2.4, 8.4 Hz), 6.75–6.72 (m, 1H), 5.07 (s, 2H), 4.03 (s, 3H), 3.91–3.86 (m, 1H), 3.08–2.88 (m, 4H), 2.32–2.28 (m, 1H), 1.95–1.88 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 190.6, 165.0, 157.0, 156.9, 152.4, 148.4, 146.5, 138.2, 137.1, 136.7, 129.8, 128.4 (2C), 127.9, 127.8 (2C), 127.3, 127.0, 125.1, 123.2, 114.4, 113.0, 69.9, 53.0, 43.6, 30.4, 28.9, 25.8; HRMS-ESI-TOF *m/z* 469.1760 ($[M + H]^+$, $C_{28}H_{24}N_2O_5$ requires 469.1758). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 40% EtOH–hexanes, 7 mL/min, α = 1.22).

(*S*)-**19**: $[\alpha]^{23}_D$ –0.9 (*c* 1.2, THF).

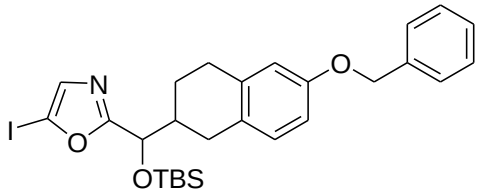
(*R*)-**19**: $[\alpha]^{23}_D$ +0.9 (*c* 1.2, THF).

6-(2-(6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalene-2-carbonyl)oxazol-5-yl)picolinic acid (20)



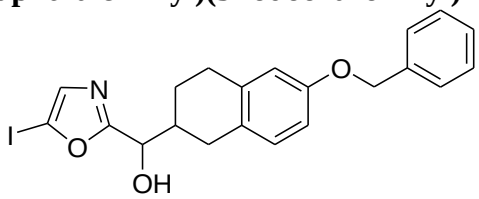
The title compound was prepared from methyl 6-(2-(6-(benzyloxy)-1,2,3,4-tetrahydronaphthalene-2-carbonyl)oxazol-5-yl)picolinate (**19**, 5 mg, 0.010 mmol) following general procedure G. Each pure enantiomer of the methyl esters were converted to their corresponding carboxylic acid using general procedure G. Flash chromatography (SiO_2, 5% MeOH–CH_2Cl_2) yielded the title compound (4 mg, 75%) as a white solid: ^{1}H NMR ($CDCl_3$ + 0.1% TFA, 600 MHz) δ 10.05 (s, 1H), 8.32 (q, 1H, *J* = 3.0 Hz), 8.16 (d, 3H, *J* = 4.2 Hz), 7.42 (d, 2H, *J* = 9.0 Hz), 7.39 (t, 2H, *J* = 7.8 Hz), 7.33 (t, 1H, *J* = 7.8 Hz), 7.06 (d, 1H, *J* = 8.4 Hz), 6.82 (dd, 1H, *J* = 2.4, 8.4 Hz), 6.78–6.75 (m, 1H), 5.08 (s, 2H), 3.85–3.80 (m, 1H), 3.09–2.92 (m, 4H), 2.33–2.30 (m, 1H), 1.97–1.91 (m, 1H); ^{13}C NMR ($CDCl_3$ + 0.1% TFA, 150 MHz) δ 190.7, 166.0, 156.87, 156.80, 151.5, 146.0, 145.1, 140.1, 136.71, 136.54, 129.9, 128.6 (2C), 128.0, 127.7, 127.6 (2C), 126.8, 125.2, 124.9, 114.8, 113.3, 70.5, 44.0, 30.2, 28.7, 25.9; HRMS-ESI-TOF *m/z* 455.1604 ([M + H]$^+$, $C_{27}H_{22}N_2O_5$ requires 455.1601).
(*S*)-**20**: $[\alpha]^{23}_D$ +4.2 (*c* 0.5, THF).
(*R*)-**20**: $[\alpha]^{23}_D$ –4.8 (*c* 0.5, THF).

2-((6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(*tert*-butyldimethylsilyloxy)methyl)-5-iodooxazole (S51)



A solution of 2-((6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(*tert*-butyldimethylsilyloxy)methyl)oxazole (**S40**, 100 mg, 0.22 mmol) in THF (4 mL) was cooled to –78 °C before it was treated with 2.16 M *n*-BuLi (0.10 mL, 0.24 mmol) dropwise. The reaction mixture was stirred at –78 °C for 2 h, and treated with a solution of iodine (72 mg, 0.28 mmol) in THF (2 mL) and stirred for 5 min. The solution was warmed to room temperature and diluted with EtOAc, and washed with saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 5% EtOAc–hexanes) yielded the title compound (94.9 mg, 83%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.43 (d, 2H, *J* = 7.2 Hz), 7.39 (t, 2H, *J* = 7.8 Hz), 7.30 (t, 1H, *J* = 7.2 Hz), 7.12 (d, 1H, *J* = 4.2 Hz), 7.02 (d, 0.5H, *J* = 8.4 Hz), 6.95 (d, 0.5H, *J* = 8.4 Hz), 6.78–6.71 (m, 2H), 5.04 (s, 2H), 4.73 (d, 0.5H, *J* = 6.6 Hz), 4.66 (d, 0.5H, *J* = 7.8 Hz), 2.91–2.78 (m, 2H), 2.70–2.66 (m, 1H), 2.50–2.48 (m, 1H), 2.34–2.29 (m, 1H), 2.22–2.20 (m, 0.5H), 1.75–1.73 (m, 0.5H), 1.52–1.47 (m, 1H), 0.91 (s, 9H), 0.09 (s, 1.5H), 0.05 (s, 1.5H), –0.05 (s, 1.5H), –0.06 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 169.3, 169.2, 156.79, 156.75, 137.5, 137.3, 137.23, 137.21, 135.3, 135.2, 130.1, 129.9, 128.4 (2C), 128.0, 127.77 (2C), 127.73, 127.37, 127.36, 114.4, 114.3, 112.8, 112.7, 86.6, 86.4, 72.4, 72.3, 69.9, 40.4, 30.5, 30.3, 29.1, 28.9, 25.6 (3C), 25.3, 24.9, 18.4, –5.1, –5.2, –5.3.

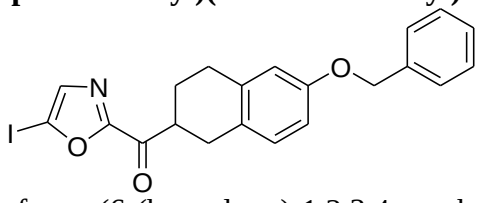
(6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(5-iodooxazol-2-yl)methanol (S52)



The title compound was prepared from 2-((6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(*tert*-butyldimethylsilyloxy)methyl)-5-iodooxazole (**S51**, 94.9 mg, 0.16 mmol) following general procedure D. Flash chromatography (SiO_2, 50% EtOAc–hexanes) yielded the title compound (70 mg, 92%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.42 (d, 2H, *J* = 7.2 Hz), 7.37 (t, 2H, *J* = 7.8 Hz), 7.31 (t, 1H, *J* = 7.2 Hz), 7.25 (s, 1H), 7.12 (s, 1H), 6.98 (d, 0.5H, *J* = 8.4 Hz), 6.94 (d, 0.5H, *J* = 8.4 Hz), 6.76–6.70 (m, 2H), 5.02 (s, 2H), 4.76

(t, 0.5H, J = 6.6 Hz), 4.71 (t, 0.5H, J = 7.8 Hz), 2.84–2.70 (m, 2H), 2.33–2.30 (m, 1H), 2.17–2.04 (m, 1H), 1.84–1.82 (m, 1H), 1.62–1.53 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 156.8, 137.4, 137.28, 137.21, 135.32, 135.30, 130.1, 130.0, 128.5 (2C), 127.8, 127.7, 127.6, 127.4 (2C), 114.4, 112.92, 112.90, 71.4, 71.3, 69.9, 39.9, 39.8, 30.6, 29.7, 29.0, 25.2, 24.3; HRMS-ESI-TOF *m/z* 462.0565 ($[M + H]^+$, $C_{21}H_{20}INO_3$ requires 462.0561).

(6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(5-iodooxazol-2-yl)methanone (21)



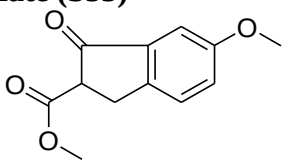
The title compound was prepared from (6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)(5-iodooxazol-2-yl)methanol (**S52**, 62 mg, 0.13 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (51.9 mg, 84%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.42 (d, 2H, J = 7.2 Hz), 7.39 (t, 2H, J = 7.8 Hz), 7.31 (t, 2H, J = 7.2 Hz), 7.02 (d, 1H, J = 8.4 Hz), 6.79–6.74 (m, 2H), 5.04 (s, 2H), 3.79–3.75 (m, 1H), 3.01–2.90 (m, 3H), 2.25–2.22 (m, 1H), 1.90–1.87 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 189.2, 162.0, 157.0, 137.4, 137.1, 136.6, 129.8, 128.5 (2C), 127.8, 127.4, 127.0 (2C), 114.4, 113.0, 93.9, 69.9, 43.3, 30.4, 28.9, 25.7; HRMS-ESI-TOF *m/z* 460.0403 ($[M + H]^+$, $C_{21}H_{18}INO_3$ requires 460.0404). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 1% EtOH–hexanes, 7 mL/min, α = 1.13).

(*S*)-**21**: $[\alpha]^{23}_D$ –6.7 (*c* 2.9, THF).

(*R*)-**21**: $[\alpha]^{23}_D$ +5.8 (*c* 2.0, THF).

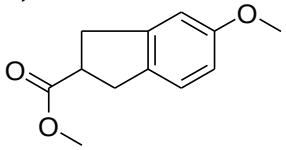
The structure and absolute stereochemistry of (*S*)-**21** (CCDC 790167) was confirmed with a single-crystal X-ray structure determination conducted on a colorless needle grown from MeOH.

Methyl 6-Methoxy-1-oxo-indan-2-carboxylate (S53)



A solution of NaH (5.40 g, 122 mmol) in anhydrous THF (20 mL) was treated with dimethylcarbonate (6.6 mL, 81.3 mmol). The reaction mixture was cooled to 0 °C and a solution of 6-methoxyindanone (3.46 g, 21.33 mmol) in THF (10 mL) was added dropwise. The reaction mixture was warmed at reflux for 12 h before being quenched with the addition of HOAc (until pH = 7) and diluted with EtOAc. The organic layer was washed with H_2O, saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude product that was purified by flash chromatography (SiO_2, 20–30% EtOAc–hexanes) to provide the title compound (3.14 g, 67%) as a purple solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.27 (d, 1H, J = 8.5 Hz), 7.09 (dd, 1H, J = 2.0, 8.5 Hz), 7.05 (d, 1H, J = 2.5 Hz), 3.70 (s, 3H), 3.67 (s, 3H), 3.65–3.63 (m, 1H), 3.36–3.16 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 199.0, 169.2, 159.3, 146.1, 136.0, 126.8, 124.4, 105.3, 55.2, 53.5, 52.3, 29.3.

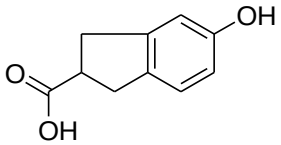
Methyl 5-Methoxyindan-2-carboxylate (S54)



A sample of methyl 6-methoxy-1-oxo-indan-2-carboxylate (**S53**, 3.05 g, 13.87 mmol) was dissolved in acetic acid (60 mL), containing perchloric acid (0.5 mL) and 10% Pd/C (300 mg, 1.38 mmol). The mixture was flushed with H_2 and kept under an atmosphere of H_2 for 16 h. Upon completion, the reaction mixture was filtered through a pad of Celite and washed with EtOAc. The organic layer was washed with H_2O, saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude product that was purified by flash chromatography (SiO_2, 10% EtOAc–hexanes) to provide the title compound (921 mg, 32%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.10 (d, 1H, J = 8.5 Hz), 6.76 (s, 1H), 6.71 (dd, 1H, J = 2.5, 8.0 Hz), 3.78 (s,

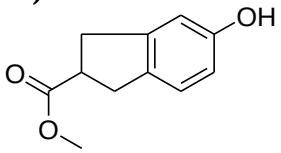
3H), 3.72 (s, 3H), 3.38–3.31 (m, 1H), 3.27–3.12 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.6, 158.9, 143.0, 133.3, 124.7, 112.5, 109.6, 55.3, 51.8, 43.8, 36.2, 35.3.

5-Hydroxyindane-2-carboxylic Acid (S55)



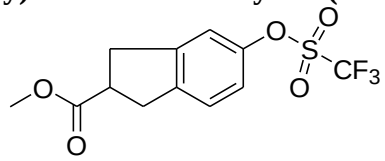
A sample of methyl 5-methoxy-indan-2-carboxylate (**S54**, 667 mg, 3.03 mmol) was dissolved in acetic acid (5 mL) and aqueous 10% HBr (5 mL). The mixture was warmed at reflux under Ar for 2 h then cooled to room temperature and diluted with EtOAc. The organic layer was washed with H_2O, saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude product that was purified by flash chromatography (SiO_2, 50% EtOAc–hexanes) to provide the title compound (520 mg, 89%) as a white solid: ^{1}H NMR (acetone-d_6, 600 MHz) δ 10.73 (brs, 1H), 8.04 (brs, 1H), 7.00 (d, 1H, J = 8.5 Hz), 6.69 (s, 1H), 6.62 (dd, 1H, J = 2.5, 8.0 Hz), 3.33–3.29 (m, 1H), 3.16–3.08 (m, 4H); ^{13}C NMR (acetone-d_6, 150 MHz) δ 177.5, 158.3, 145.0, 134.0, 126.5, 115.4, 112.9, 45.2, 37.8, 36.9.

Methyl 5-Hydroxyindane-2-carboxylate (S56)



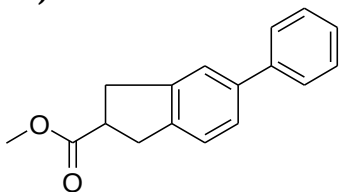
A sample of 5-hydroxyindane-2-carboxylic acid (**S55**, 270 mg, 1.51 mmol) was dissolved in MeOH (15 mL) and concentrated H_2SO_4 (3 mL). The mixture was warmed at reflux under Ar for 1 h then cooled to room temperature and diluted with EtOAc. The organic layer was washed with H_2O, saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude product that was purified by flash chromatography (SiO_2, 50% EtOAc–hexanes) to provide the title compound (120 mg, 41%) as a white solid: ^{1}H NMR (acetone-d_6, 500 MHz) δ 8.04 (s, 1H), 6.99 (d, 1H, J = 8.5 Hz), 6.69 (s, 1H), 6.62 (dd, 1H, J = 2.5, 8.0 Hz), 3.65 (s, 3H), 3.32–3.29 (m, 1H), 3.11–3.05 (m, 4H); ^{13}C NMR (acetone-d_6, 125 MHz) δ 176.9, 158.2, 144.8, 133.8, 126.4, 115.4, 112.9, 52.9, 45.3, 37.7, 36.8.

Methyl 5-(Trifluoromethanesulfonyloxy)indane-2-carboxylate (S57)



A sample of methyl 5-hydroxyindane-2-carboxylate (**S56**, 800 mg, 4.16 mmol) was dissolved in pyridine (15 mL) and the reaction mixture was cooled to 0 °C and triflic anhydride (1.1 mL, 6.24 mmol) was added slowly. The reaction mixture was warmed to room temperature and stirred for 3 h. The reaction mixture was diluted with CH_2Cl_2 and washed with saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the title compound (1.34 g, 98%) as a white solid: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.19 (d, 1H, J = 8.5 Hz), 7.07 (s, 1H), 7.00 (dd, 1H, J = 2.0, 8.0 Hz), 3.67 (s, 3H), 3.83–3.31 (m, 1H), 3.27–3.13 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 174.6, 148.4, 144.1, 141.9, 125.3, 119.3, 118.5 (q, CF_3, J = 320 Hz), 117.1, 51.6, 43.3, 35.8, 35.3.

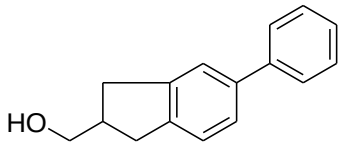
Methyl 5-Phenylindane-2-carboxylate (S58)



A sample of methyl 5-(trifluoromethylsulfonyloxyindane-2-carboxylate (**S57**, 1.34 g, 4.13 mmol), $(Ph_3P)_4Pd$ (144 mg, 0.123 mmol), phenylboronic acid (604 mg, 4.95 mmol), and 2 M aqueous Na_2CO_3 (5 mL) were dissolved in anhydrous THF (20 mL) and the mixture was warmed at reflux for 16 h under Ar. The mixture was diluted with EtOAc, washed with saturated aqueous NH_4Cl, saturated aqueous NaCl, and dried over Na_2SO_4.

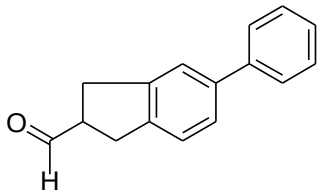
Evaporation in vacuo yielded the crude coupling product. Flash chromatography (SiO_2, 10% EtOAc–hexanes) yielded the title compound (963 mg, 92%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.68 (d, 2H, *J* = 8.5 Hz), 7.54–7.51 (m, 4H), 7.44 (d, 1H, *J* = 8.0 Hz), 7.36 (d, 1H, *J* = 8.0 Hz), 3.83 (s, 3H), 3.49–3.40 (m, 3H), 3.37–3.15 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.3, 142.0, 141.1, 140.4, 139.7, 128.5, 128.4, 126.8 (2C), 126.7, 125.5, 124.3, 122.8, 51.5, 43.3, 35.9, 35.6.

(5-Phenylindan-2-yl)methanol (S59)



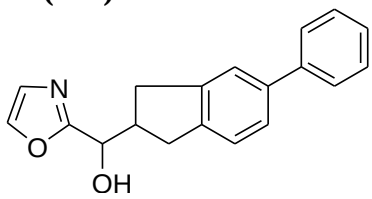
The title compound was prepared from methyl 5-phenylindane-2-carboxylate (**S58**, 963 mg, 3.81 mmol) following general procedure A. Flash chromatography (SiO_2, 50–100% EtOAc–hexanes) afforded the title compound (710 mg, 83%) as a white solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.72 (dd, 2H, *J* = 1.6, 8.4 Hz), 7.57–7.43 (m, 5H), 7.38 (d, 1H, *J* = 8.0 Hz), 3.77 (d, 2H, *J* = 6.4 Hz), 3.27–3.19 (m, 3H), 2.95–2.85 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.2, 141.7, 141.3, 139.3, 128.4 (2C), 126.8 (2C), 126.7, 125.2, 124.6, 123.1, 66.0, 41.4, 35.5, 35.2.

5-Phenylindane-2-carboxaldehyde (S60)



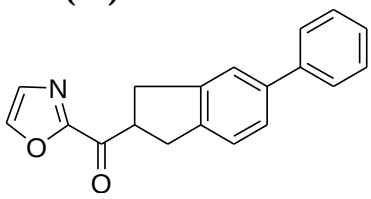
The title compound was prepared from (5-phenylindan-2-yl)methanol (**S59**, 710 mg, 3.16 mmol) following general procedure B. Flash chromatography (SiO_2, 10% EtOAc–hexanes) afforded the title compound (404 mg, 57%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 9.82 (s, 1H), 7.63 (d, 2H, *J* = 8.4 Hz), 7.51–7.47 (m, 4H), 7.40 (t, 1H, *J* = 7.2 Hz), 7.34 (d, 1H, *J* = 7.8 Hz), 3.41–3.32 (m, 3H), 3.27–3.22 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 202.5, 141.6, 141.0, 140.1, 139.9, 128.5 (2C), 126.94 (2C), 126.90, 125.7, 124.6, 123.1, 50.5, 32.6, 32.3.

Oxazol-2-yl(5-phenylindan-2-yl)methanol (S61)



Oxazole (0.120 mL, 1.81 mmol) in anhydrous THF (7 mL) was treated with BH_3•THF (1 M, 1.9 mL, 1.97 mmol) and the solution was stirred at room temperature for 1 h before being cooled to –78 °C and treated with 2.41 M *n*-BuLi (0.80 mL, 1.97 mmol) dropwise. The reaction mixture was stirred at –78 °C for 40 min before a solution of 5-phenylindane-2-carboxaldehyde (**S60**, 404 mg, 1.81 mmol) in THF (2 mL) was added. The reaction mixture was stirred at –78 °C for 2 h before being warmed to room temperature. A 5% HOAc–EtOH solution (50 mL) was added and this mixture was stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the residue was dissolved in EtOAc, washed with H_2O, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl before the organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 40% EtOAc–hexanes) afforded the title compound (310 mg, 58%) as colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.63–7.60 (m, 3H), 7.49–7.36 (m, 5H), 7.34–7.28 (m, 1H), 7.10 (s, 1H), 5.08 (s, 1H), 4.88 (d, 1H, *J* = 5.6 Hz), 3.26–3.18 (m, 4H), 3.07–2.85 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.6, 142.9, 142.8, 141.4, 141.36, 141.32, 139.6, 139.5, 138.7, 128.5 (2C), 126.9 (2C), 126.8, 126.3, 125.4, 125.3, 124.6, 124.5, 123.1, 123.0, 70.08, 70.04, 44.2, 35.2, 35.0, 34.8, 34.7.

Oxazol-2-yl(5-phenylindan-2-yl)methanone (22)

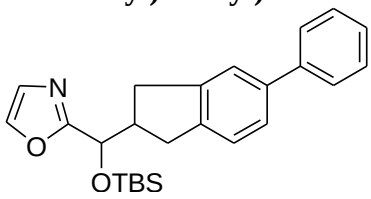


The title compound was prepared from oxazol-2-yl(5-phenylindan-2-yl)methanol (**S61**, 20 mg, 0.068 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (18 mg, 91%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.86 (s, 1H), 7.56 (d, 2H, *J* = 7.8 Hz), 7.45–7.41 (m, 4H), 7.39 (s, 1H), 7.34 (t, 1H, *J* = 7.2 Hz), 7.29 (d, 1H, *J* = 7.8 Hz), 4.48–4.42 (m, 1H), 3.47–3.40 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 188.9, 157.7, 141.9, 141.6, 141.3, 140.3, 140.1, 129.1, 128.6 (2C), 127.1 (2C), 127.0, 125.9, 124.6, 123.1, 47.4, 35.5, 35.3; HRMS-ESI-TOF *m/z* 290.1179 ($[M + H]^+$, $C_{19}H_{15}NO_2$ requires 290.1175). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 0.5% EtOH–hexanes, 7 mL/min, α = 1.63).

(*R*)-**22**: $[\alpha]^{23}_D$ –36 (*c* 0.1, THF).

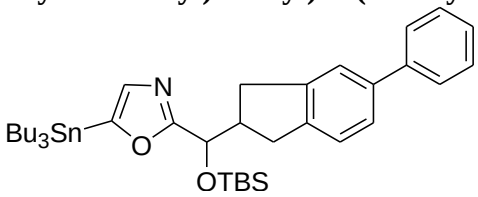
(*S*)-**22**: $[\alpha]^{23}_D$ +38 (*c* 0.1, THF).

2-((*tert*-Butyldimethylsilyloxy)(5-phenylindan-2-yl)methyl)oxazole (S62)



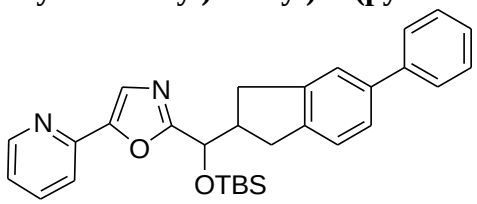
A solution of oxazol-2-yl(5-phenylindan-2-yl)methanol (**S61**, 150 mg, 0.51 mmol), TBSCl (186 mg, 1.23 mmol) and imidazole (174 mg, 2.55 mmol) in DMF (2 mL) was stirred at room temperature for 16 h before it was diluted with EtOAc, washed with H_2O, and saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 10% EtOAc–hexanes) yielded the title compound (200 mg, 97%) as a thick colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.67 (s, 1H), 7.64–7.60 (m, 2H), 7.50–7.32 (m, 6H), 7.15 (s, 1H), 4.89 (d, 1H, *J* = 6.8 Hz), 3.26–3.13 (m, 3H), 2.99–2.82 (m, 2H), 0.95 (s, 9H), 0.16 (s, 3H), –0.02 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.2, 142.9, 141.7, 141.5, 136.9, 139.5, 138.4, 128.5 (2C), 126.9, 126.8, 125.4, 125.3, 124.6, 124.5, 123.17, 123.13, 71.3, 45.3, 35.5, 35.2, 34.9, 34.6, 25.6 (3C), 18.0, –5.2, –5.3.

2-((*tert*-Butyldimethylsilyloxy)(5-phenylindan-2-yl)methyl)-5-(tributylstannyl)oxazole (S63)



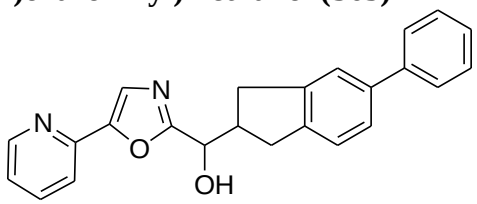
A solution of 2-((*tert*-butyldimethylsilyloxy)(5-phenylindan-2-yl)methyl)oxazole (**S62**, 100 mg, 0.24 mmol) in THF (3 mL) was cooled to –78 °C before it was treated with 2.16 M *n*-BuLi (0.150 mL, 0.27 mmol) dropwise. The reaction mixture was stirred at –78 °C for 2 h, and treated with a solution of Bu_3SnCl (0.140 mL, 0.48 mmol) and stirred for 5 min. The solution was warmed to room temperature and diluted with EtOAc and washed with saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 0–5% EtOAc–hexanes) yielded the title compound (300 mg, 65%) as a thick colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.58–7.54 (m, 2H), 7.43–7.27 (m, 7H), 7.12 (d, 1H, *J* = 0.8 Hz), 4.87 (d, 1H, *J* = 6.8 Hz), 3.14–3.08 (m, 3H), 2.89–2.78 (m, 2H), 1.70–1.56 (m, 10H), 1.42–1.25 (m, 13H), 0.96–0.88 (m, 12H), 0.85 (s, 9H), 0.07 (s, 3H), –0.11 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.5, 154.8, 143.4, 143.1, 141.9, 141.7, 141.5, 139.5, 139.4, 137.1, 128.5 (2C), 126.9 (2C), 126.7, 125.3, 125.2, 124.56, 124.52, 123.1, 123.0, 71.4, 45.9, 35.5, 35.2, 35.0, 34.6, 28.8, 27.8 (3C), 27.7, 27.6, 27.3 (3C), 27.0, 26.7, 26.4, 25.5, 19.1 (3C), 19.0, 18.0, 17.4, 15.8, 15.7, 13.56 (3C), 13.50, 10.1, –5.3, –5.4.

2-((*tert*-Butyldimethylsilyloxy)(5-phenylindan-2-yl)methyl)-5-(pyridin-2-yl)oxazole (S64)



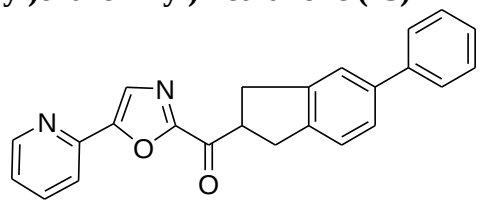
The title compound was prepared from 2-((*tert*-butyldimethylsilyloxy)(5-phenylindan-2-yl)methyl)-5-(tributylstannyl)oxazole (**S63**, 167 mg, 0.24 mmol) and 2-bromopyridine following general procedure C. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (26.1 mg, 22%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.64–8.62 (m, 1H), 7.79–7.73 (m, 1H), 7.68–7.65 (m, 2H), 7.56–7.51 (m, 2H), 7.44–7.25 (m, 7H), 4.87–4.86 (m, 1H), 3.19–3.13 (m, 3H), 2.96–2.85 (m, 2H), 0.96 (m, 9H), 0.10 (s, 3H), –0.05 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 150.8, 149.8, 147.3, 141.7, 141.5, 136.8, 128.6 (2C), 127.0, 126.8 (2C), 125.5, 125.4, 125.1, 124.6, 123.2, 122.8, 119.0, 71.57, 71.54, 45.39, 45.36, 35.5, 35.1, 35.0, 34.8, 27.8, 26.8, 25.6 (3C), 18.1, 17.5, 13.5, –5.0, –5.2.

(5-Phenylindan-2-yl)(5-(pyridin-2-yl)oxazol-2-yl)methanol (S65)



The title compound was prepared from 2-((*tert*-butyldimethylsilyloxy)(5-phenylindan-2-yl)methyl)-5-(pyridin-2-yl)oxazole (**S64**, 26.1 mg, 0.054 mmol) following general procedure D. Flash chromatography (SiO_2, 50–100% EtOAc–hexanes) yielded the title compound (20.9 mg, 98%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.62 (d, 1H, *J* = 4.8 Hz), 7.75–7.72 (m, 1H), 7.64–7.61 (m, 2H), 7.53–7.51 (m, 2H), 7.42–7.23 (m, 7H), 4.92 (d, 1H, *J* = 6.6 Hz), 3.22–3.16 (m, 3H), 3.08–2.95 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.3, 151.0, 149.8, 146.9, 142.9, 142.8, 141.47, 141.45, 141.3, 139.77, 139.72, 136.9, 128.6 (2C), 127.0 (2C), 126.8, 125.59, 125.53, 124.9, 124.7, 124.6, 123.3, 123.2, 123.0, 119.3, 70.48, 70.45, 44.3, 35.2, 35.0, 34.8, 34.7.

(5-Phenylindan-2-yl)-(5-(pyridin-2-yl)oxazol-2-yl)methanone (23)

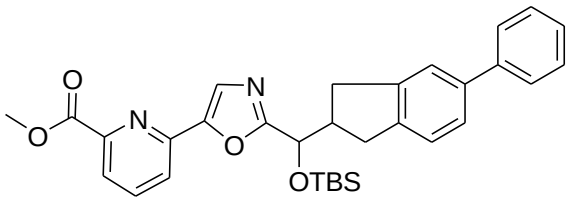


The title compound was prepared from (5-phenylindan-2-yl)(5-(pyridin-2-yl)oxazol-2-yl)methanol (**S65**, 20.9 mg, 0.056 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (18 mg, 87%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.68 (d, 1H, *J* = 4.2 Hz), 7.94 (s, 1H), 7.87 (d, 1H, *J* = 7.8 Hz), 7.82 (t, 1H, *J* = 7.8 Hz), 7.57 (d, 2H, *J* = 7.8 Hz), 7.46–7.41 (m, 4H), 7.34–7.29 (m, 3H), 4.50 (q, 1H, *J* = 7.8 Hz), 3.48–3.43 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 188.9, 157.1, 153.4, 150.1, 146.2, 141.9, 141.3, 140.4, 140.1, 137.1, 128.6 (2C), 127.1 (3C), 127.0, 125.9, 124.6, 124.1, 123.1, 120.4, 47.4, 35.7, 35.4; HRMS-ESI-TOF *m/z* 367.1444 ($[M + H]^+$, $C_{24}H_{18}N_2O_2$ requires 367.1441). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 10% EtOH–hexanes, 7 mL/min, α = 2.08).

(*R*)-**23**: $[\alpha]^{23}_D$ –58 (*c* 0.2, THF).

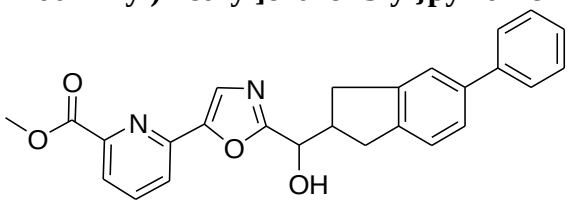
(*S*)-**23**: $[\alpha]^{23}_D$ +60 (*c* 0.3, THF).

Methyl 6-{2-[(*tert*-Butyldimethylsilyloxy)-(5-phenylindan-2-yl)methyl]oxazol-5-yl}-pyridine-2-carboxylate (S66)



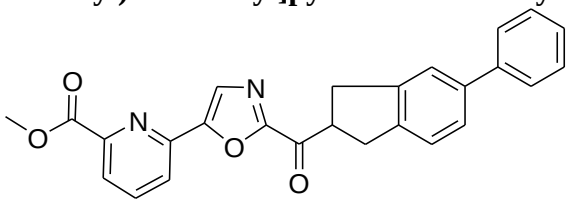
The title compound was prepared from 2-((*tert*-butyldimethylsilyloxy)(5-phenylindan-2-yl)methyl)-5-(tributylstannyl)oxazole (**S63**, 222 mg, 0.44 mmol) and methyl 6-bromopicolinate following general procedure C. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (216 mg, 90%) as a yellow solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.08–8.01 (m, 2H), 7.92–7.80 (m, 3H), 7.69–7.64 (m, 2H), 7.43–7.19 (m, 5H), 4.87–4.86 (m, 1H), 3.98 (s, 3H), 3.19–3.09 (m, 3H), 2.97–2.85 (m, 2H), 0.87 (m, 9H), 0.09 (s, 3H), –0.06 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.2, 165.1, 164.3, 149.9, 148.5, 148.1, 147.5, 143.1, 142.9, 141.9, 141.5, 141.4, 141.3, 139.5, 139.1, 137.98, 137.96, 131.7, 128.55, 128.53, 126.99, 126.95, 126.8, 126.7, 126.35, 126.31, 125.4, 125.3, 124.64, 124.62, 123.9, 123.8, 123.18, 123.15, 121.9, 71.48, 71.44, 53.0, 52.8, 45.28, 45.23, 35.4, 35.0, 34.9, 34.7, 27.7, 26.7, 25.5 (3C), 18.0, 17.4, 13.5, –5.1, –5.2.

Methyl 6-{2-[Hydroxy-(5-phenylindan-2-yl)methyl]oxazol-5-yl}pyridine-2-carboxylate (S67)



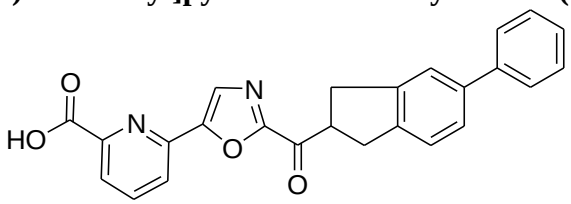
The title compound was prepared from methyl 6-{2-[(*tert*-butyldimethylsilyloxy)-(5-phenylindan-2-yl)-methyl]-oxazol-5-yl}-pyridine-2-carboxylic (**S66**, 216 mg, 0.39 mmol) and methyl 6-bromopicolinate following general procedure C. Flash chromatography (SiO_2, 50–100% EtOAc–hexanes) yielded the title compound (108 mg, 64%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.00 (d, 1H, *J* = 7.8Hz), 7.85–7.82 (td, 1H, J = 2.4, 7.8 Hz), 7.76–7.75 (m, 2H), 7.52–7.50 (m, 2H), 7.40–7.18 (m, 6H), 4.92 (d, 1H, *J* = 6.0 Hz), 4.66 (s, 1H, OH), 3.99 (s, 3H), 3.22–3.15 (m, 3H), 3.05–3.01 (m, 1H), 2.94–2.90 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 171.3, 165.9, 165.1, 150.0, 147.9, 147.0, 142.9, 142.7, 141.4, 141.27, 141.23, 139.59, 139.53, 137.9, 128.5 (2C), 126.9 (2C), 126.8, 125.9, 126.8, 125.9, 125.48, 125.40, 127.7, 124.6, 124.0, 123.2, 123.1, 122.3, 70.3, 70.2, 44.1, 35.1, 35.0, 34.8, 34.7.

Methyl 6-[2-(5-Phenylindane-2-carbonyl)oxazol-5-yl]pyridine-2-carboxylate (24)



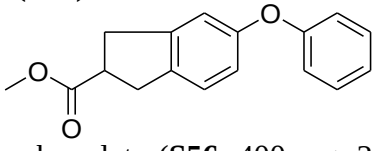
The title compound was prepared from methyl 6-{2-[hydroxy-(5-phenylindan-2-yl)methyl]oxazol-5-yl}-pyridine-2-carboxylic (**S67**, 107.6 mg, 0.25 mmol) following general procedure E. Flash chromatography (SiO_2, 30% EtOAc–hexanes) yielded the title compound (76.6 mg, 72%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.13 (d, 1H, *J* = 7.8 Hz), 8.08 (s, 1H), 8.03 (d, 1H, *J* = 7.8 Hz), 7.97 (t, 1H, *J* = 7.8 Hz), 7.57 (d, 2H, *J* = 7.8 Hz), 7.45–7.41 (m, 4H), 7.34–7.29 (m, 2H), 4.50 (q, 1H, *J* = 7.8 Hz), 4.04 (s, 3H), 3.47–3.43 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 188.8, 165.0, 157.1, 152.3, 148.3, 146.4, 141.8, 141.2, 140.3, 140.0, 138.2, 128.6 (2C), 128.0, 127.0 (2C), 126.9, 125.8, 125.1, 124.6, 123.3, 123.1, 53.0, 47.3, 35.5, 35.3; HRMS-ESI-TOF *m/z* 425.1500 ($[M + H]^+$, $C_{26}H_{20}N_2O_4$ requires 425.1496). The enantiomers could not be separated using chiral phase HPLC.

6-[2-(5-Phenylindane-2-carbonyl)oxazol-5-yl]pyridine-2-carboxylic Acid (25)



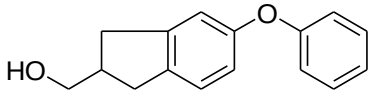
The title compound was prepared from methyl 6-[2-(5-phenylindane-2-carbonyl)oxazol-5-yl]pyridine-2-carboxylate (**24**, 5 mg, 0.011 mmol) following general procedure G. Flash chromatography (SiO_2, 5% HOAc–EtOAc) yielded the title compound (3.9 mg, 86%) as a yellow solid: ^{1}H NMR (THF-d_8, 600 MHz) δ 8.13–8.08 (m, 4H), 7.58 (dd, 2H, *J* = 1.2, 8.4 Hz), 7.48 (s, 1H), 7.42–7.36 (m, 3H), 7.28–7.26 (m, 2H), 4.51–4.45 (m, 1H), 3.42–3.38 (m, 4H); ^{13}C NMR (THF-d_8, 150 MHz) δ 188.9, 165.6, 158.8, 153.7, 150.1, 147.2, 143.3, 142.5, 141.8, 141.0, 139.7, 129.5 (2C), 128.8, 127.8 (2C), 126.6, 125.5, 125.4, 123.8, 123.7, 48.6, 36.5, 36.2; HRMS-ESI-TOF *m/z* 411.1342 ($[M + H]^+$, $C_{25}H_{18}N_2O_4$ requires 411.1339).

Methyl 5-Phenoxyindane-2-carboxylate (S68)



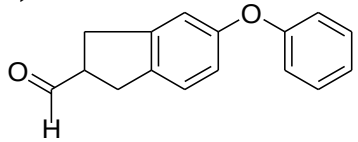
A sample of methyl 5-hydroxyindane-2-carboxylate (**S56**, 400 mg, 2.08 mmol), phenylboronic acid (507 mg, 4.16 mmol), $Cu(OAc)_2$ (377 mg, 2.08 mmol), and 4Å MS (400 mg) were placed in anhydrous CH_2Cl_2 (30 mL). The reaction mixture was stirred at room temperature for 15 min before Et_3N (0.584 mL, 4.16 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 17 h under Ar. The mixture was diluted with EtOAc, washed with saturated aqueous NH_4Cl, saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude product that was purified by flash chromatography (SiO_2, 10% EtOAc–hexanes) to provide the title compound (263 mg, 47%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.31 (t, 2H, *J* = 7.8 Hz), 7.15 (d, 1H, *J* = 7.2 Hz), 7.07 (t, 1H, *J* = 7.2 Hz), 6.98 (d, 2H, *J* = 8.4 Hz), 6.82 (dd, 2H, *J* = 2.4, 8.4 Hz), 3.73 (s, 3H), 3.40–3.34 (m, 1H), 3.25–3.14 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 175.5, 157.7, 156.1, 143.4, 136.4, 129.6 (2C), 125.1, 122.8, 118.5 (2C), 117.7, 115.1, 51.9, 43.8, 36.2, 35.5.

(5-Phenoxyindan-2-yl)methanol (S69)



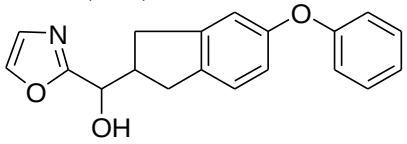
The title compound was prepared from methyl 5-phenoxyindane-2-carboxylate (**S68**, 242 mg, 0.90 mmol) following general procedure A. Flash chromatography (SiO_2, 30% EtOAc–hexanes) afforded the title compound (214 mg, 97%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.34 (t, 2H, *J* = 7.8 Hz), 7.17 (d, 1H, *J* = 7.2 Hz), 7.10 (t, 1H, *J* = 7.2 Hz), 7.04 (d, 2H, *J* = 8.4 Hz), 6.91 (s, 1H), 6.85 (dd, 1H, *J* = 2.4, 8.4 Hz), 3.67 (d, 2H, *J* = 6.5 Hz), 3.07–3.03 (m, 2H), 2.77–2.72 (m, 3H), 2.58 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 157.7, 155.6, 144.4, 137.5, 129.4 (2C), 125.2, 122.6, 118.2 (2C), 117.2, 115.4, 66.1, 41.7, 35.7, 34.8.

5-Phenoxyindane-2-carboxaldehyde (S70)



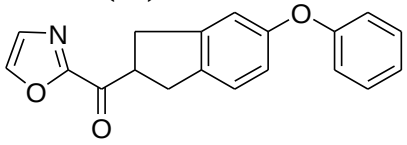
The title compound was prepared from (5-phenoxyindan-2-yl)methanol (**S69**, 214 mg, 0.89 mmol) following general procedure B. Flash chromatography (SiO_2, 30% EtOAc–hexanes) afforded the title compound (163 mg, 76%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.77 (s, 1H), 7.34 (t, 2H, *J* = 7.8 Hz), 7.18 (d, 1H, *J* = 7.2 Hz), 7.09 (t, 1H, *J* = 7.2 Hz), 7.00 (d, 2H, *J* = 8.4 Hz), 6.90 (s, 1H), 6.86 (dd, 1H, *J* = 2.4, 8.4 Hz), 3.32–3.26 (m, 3H), 3.19–3.12 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 202.3, 157.5, 156.2, 142.9, 135.7, 129.5 (2C), 125.3, 122.8, 118.4 (2C), 117.7, 115.2, 50.8, 32.8, 32.0.

Oxazol-2-yl(5-phenoxyindan-2-yl)methanol (S71)



Oxazole (0.027 mL, 0.41 mmol) in anhydrous THF (5 mL) was treated with BH_3•THF (1 M, 0.50 mL, 0.44 mmol) and the solution was stirred at room temperature for 1 h before being cooled to –78 °C and treated with 1.7 M *t*-BuLi (0.40 mL, 0.53 mmol) dropwise. The reaction mixture was stirred at –78 °C for 40 min before a solution of 5-phenoxyindane-2-carboxaldehyde (**S70**, 98 mg, 0.41 mmol) in THF (2 mL) was added. The reaction mixture was stirred at –78 °C for 2 h before being warmed to room temperature. A 5% HOAc–EtOH solution (50 mL) was added and this mixture was stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the residue was dissolved in EtOAc, washed with H_2O, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl before the organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 50% EtOAc–hexanes) afforded the title compound (60.4 mg, 47%) as colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.61 (d, 1H, *J* = 2.5 Hz), 7.32 (t, 2H, *J* = 7.8 Hz), 7.14–7.04 (m, 3H), 6.98–6.96 (m, 2H), 6.85–6.75 (m, 2H), 4.80 (d, 1H, *J* = 7.0 Hz), 3.48 (brs, 1H, OH), 3.12–3.02 (m, 3H), 2.95–2.75 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 157.7, 155.8, 144.1, 144.0, 138.9, 137.2, 137.1, 129.5 (2C), 126.6, 125.2, 125.1, 122.7, 118.3, 117.5, 117.4, 115.4, 115.3, 70.1, 44.6, 35.1, 34.3.

Oxazol-2-yl(5-phenoxyindan-2-yl)methanone (26)

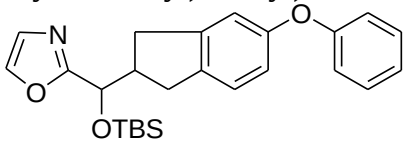


The title compound was prepared from oxazol-2-yl(5-phenoxyindan-2-yl)methanol (**S71**, 5 mg, 0.016 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (4.7 mg, 96%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.85 (s, 1H), 7.37 (s, 1H), 7.32 (t, 2H, *J* = 7.0 Hz), 7.16 (d, 1H, *J* = 7.2 Hz), 7.07 (t, 1H, *J* = 7.1 Hz), 6.98 (d, 2H, *J* = 7.0 Hz), 6.87–6.83 (m, 2H), 4.45–4.39 (m, 1H), 3.38–3.28 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 188.7, 157.77, 157.71, 156.2, 143.1, 141.6, 136.0, 129.6 (2C), 129.1, 125.2, 122.8, 118.5 (2C), 117.8, 115.2, 47.7, 35.5, 35.0; HRMS-ESI-TOF *m/z* 306.1120 ([M + H]$^+$, $C_{19}H_{15}NO_3$ requires 306.1125). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 1% EtOH–hexanes, 7 mL/min, α = 1.1).

(*R*)-**26**: $[\alpha]^{23}_D$ –12 (*c* 0.1, THF).

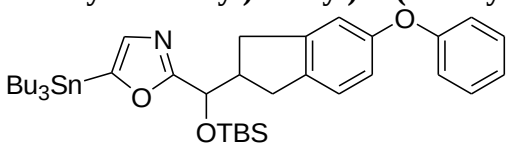
(*S*)-**26**: $[\alpha]^{23}_D$ +13 (*c* 0.1, THF).

2-((*tert*-Butyldimethylsilyloxy)(5-phenoxyindan-2-yl)methyl)oxazole (S72)



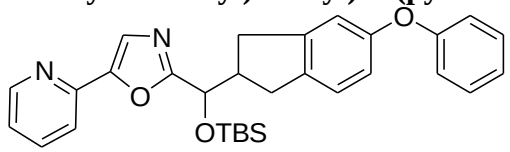
A solution of oxazol-2-yl(5-phenoxyindan-2-yl)methanol (**S71**, 60.4 mg, 0.19 mmol), TBSCl (72 mg, 0.47 mmol) and imidazole (54 mg, 0.78 mmol) in DMF (4 mL) was stirred at room temperature for 16 h before it was diluted with EtOAc, washed with H_2O, and saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 10% EtOAc–hexanes) yielded the title compound (38.2 mg, 47%) as a thick colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.62 (d, 1H, *J* = 2.5 Hz), 7.30 (t, 2H, *J* = 7.8 Hz), 7.14–7.04 (m, 2H), 6.98–6.96 (m, 2H), 6.85–6.78 (m, 2H), 4.80 (d, 1H, *J* = 7.0 Hz), 4.79–4.77 (m, 1H), 3.09–2.98 (m, 3H), 2.82–2.74 (m, 2H), 0.90 (s, 4.5H), 0.85 (s, 4.5H), 0.07 (s, 1.5H), 0.05 (s, 1.5H), –0.112 (s, 1.5H), –0.116 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 157.9, 157.8, 155.8, 155.7, 144.4, 144.2, 138.5, 137.5, 137.3, 129.5 (2C), 126.8, 125.1, 122.6, 118.4, 118.3, 117.4, 115.4, 115.3, 71.4, 45.6, 35.7, 35.1, 34.8, 34.3, 25.6 (3C), 18.1, –5.2, –5.3.

2-((*tert*-Butyldimethylsilyloxy)(5-phenoxyindan-2-yl)methyl)-5-(tributylstannyl)oxazole (S73)



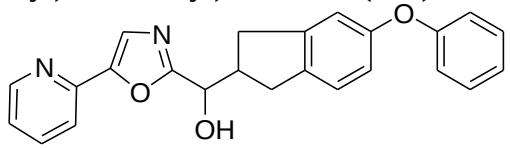
A solution of 2-((*tert*-butyldimethylsilyloxy)(5-phenoxyindan-2-yl)methyl)oxazole (**S72**, 38.2 mg, 0.09 mmol) in THF (3 mL) was cooled to –78 °C before it was treated with 2.35 M *n*-BuLi (0.045 mL, 0.09 mmol) dropwise. The reaction mixture was stirred at –78 °C for 2 h, and treated with a solution of Bu_3SnCl (0.05 mL, 0.18 mmol) and stirred for 5 min. The solution was warmed to room temperature and diluted with EtOAc, and washed with saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 0–5% EtOAc–hexanes) yielded the title compound (21.8 mg, 34%) as a thick colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.42 (t, 2H, *J* = 7.8 Hz), 7.39–7.30 (m, 3H), 7.09–7.00 (m, 2H), 6.84–6.73 (m, 2H), 5.02 (d, 2H, *J* = 7.0 Hz), 4.80 (d, 1H, *J* = 7.2 Hz), 3.06–2.95 (m, 3H), 2.75–2.64 (m, 2H), 1.57–1.53 (m, 6H), 1.35–1.30 (m, 7H), 1.13–1.08 (m, 6H), 0.89 (t, 6H, *J* = 7.0 Hz), 0.84 (s, 9H), 0.03 (s, 3H), 0.05 (s, 1.5H), –0.15 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 168.6, 157.86, 157.80, 154.9, 144.3, 144.0, 137.33, 137.32, 137.1, 135.1, 134.8, 128.5 (2C), 127.7, 127.3 (2C), 124.88, 124.85, 113.03, 113.02, 110.9, 71.55, 71.51, 70.1, 45.84, 45.81, 35.9, 35.2, 34.8, 34.1, 28.8 (3C), 27.2 (3C), 25.6 (3C), 18.1 (3C), 13.6, 10.1 (3C), –5.2, –5.3.

2-((*tert*-Butyldimethylsilyloxy)(5-phenoxyindan-2-yl)methyl)-5-(pyridin-2-yl)oxazole (S74)



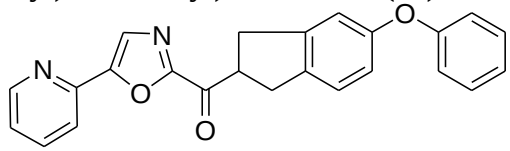
The title compound was prepared from 2-((*tert*-butyldimethylsilyloxy)(5-phenoxyindan-2-yl)methyl)-5-(tributylstannyl)oxazole (**S73**, 740 mg, 1.04 mmol) and 2-bromopyridine following general procedure C. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (153 mg, 30%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.62 (d, 1H, *J* = 4.5 Hz), 7.76 (t, 1H, *J* = 7.8 Hz), 7.66–7.64 (m, 2H), 7.31–7.21 (m, 4H), 7.15–7.03 (m, 2H), 6.97–6.95 (m, 1H), 6.90–6.82 (m, 1H), 4.84 (dd, 1H, *J* = 2.5, 7.5 Hz), 3.17–3.04 (m, 2H), 2.91–2.79 (m, 4H), 0.89 (s, 9H), 0.10 (s, 1.5H), 0.09 (s, 1.5H), –0.04 (s, 1.5H), –0.05 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 164.7, 157.8, 155.7, 150.8, 149.8, 147.3, 144.3, 137.3, 136.8, 129.5 (2C), 125.18, 125.13, 122.8, 122.69, 122.65, 119.0 (2C), 118.38, 118.30, 117.4, 117.3, 115.4, 115.3, 71.4, 45.5, 35.5, 35.1, 34.7, 34.3, 26.7, 25.6 (3C), 18.1, 13.5, –5.0, –5.2.

(5-Phenoxyindan-2-yl)(5-(pyridin-2-yl)oxazol-2-yl)methanol (S75)



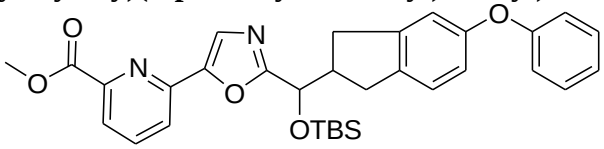
The title compound was prepared from 2-((*tert*-butyldimethylsilyloxy)(5-phenoxyindan-2-yl)methyl)-5-(pyridin-2-yl)oxazole (**S74**, 153 mg, 0.30 mmol) following general procedure D. Flash chromatography (SiO_2, 50% EtOAc–hexanes) yielded the title compound (109 mg, 95%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.58 (d, 1H, *J* = 4.5 Hz), 7.79 (t, 1H, *J* = 7.8 Hz), 7.29–7.26 (m, 2H), 7.21–7.18 (m, 4H), 7.12–7.02 (m, 2H), 6.95–6.91 (m, 2H), 6.88–6.82 (m, 1H), 4.90 (dd, 1H, *J* = 2.5, 7.5 Hz), 4.64 (brs, 1H, OH), 3.21–3.09 (m, 3H), 2.98–2.83 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 165.5, 157.7, 155.8, 155.7, 150.8, 149.7, 146.8, 144.1, 143.9, 137.2, 137.0, 136.8, 129.5 (2C), 125.2, 125.1, 124.8, 122.9, 122.6, 119.2, 118.2 (2C), 117.45, 117.40, 115.4, 115.3, 70.2, 44.55, 44.52, 35.2, 34.4.

(5-Phenoxyindan-2-yl)(5-(pyridin-2-yl)oxazol-2-yl)methanone (27)



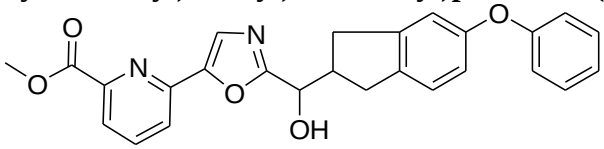
The title compound was prepared from (5-phenoxyindan-2-yl)(5-(pyridin-2-yl)oxazol-2-yl)methanol (**S75**, 109.3 mg, 0.28 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (77 mg, 72%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.67 (d, 1H, *J* = 4.5 Hz), 7.92 (s, 1H), 7.86 (d, 1H, *J* = 7.8 Hz), 7.80 (t, 1H, *J* = 7.8 Hz), 7.33–7.30 (m, 3H), 7.16 (d, 1H, *J* = 8.4 Hz), 7.07 (t, 1H, *J* = 7.2 Hz), 6.98 (d, 2H, *J* = 7.8 Hz), 6.87–6.83 (m, 2H), 4.50–4.45 (m, 1H), 3.41–3.30 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 188.7, 157.5, 156.9, 156.1, 153.3, 150.0, 146.0, 143.0, 137.1, 136.0, 129.5 (2C), 126.9, 125.1, 124.1, 122.8, 120.3, 118.3 (2C), 117.7, 115.1, 47.5, 35.5, 35.0; HRMS-ESI-TOF *m/z* 383.1395 ($[M + H]^+$, $C_{24}H_{18}N_2O_3$ requires 383.1390). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 10% EtOH–hexanes, 7 mL/min, α = 1.21).
(*R*)-**27**: $[\alpha]^{23}_D$ +78 (*c* 0.1, THF).
(*S*)-**27**: $[\alpha]^{23}_D$ –68 (*c* 0.1, THF).

Methyl 6-(2-((*tert*-Butyldimethylsilyloxy)(5-phenoxyindan-2-yl)methyl)oxazol-5-yl)picolinate (S76)



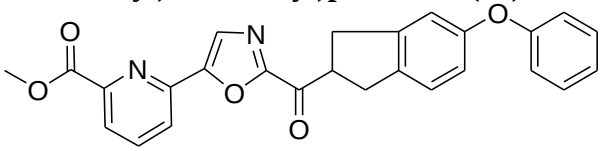
The title compound was prepared from 2-((*tert*-butyldimethylsilyloxy)(5-phenoxyindan-2-yl)methyl)-5-(tributylstannyl)oxazole (**S73**, 21.8 mg, 0.03 mmol) and methyl 6-bromopicolinate following general procedure C. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (12.8 mg, 76%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.03 (d, 1H, *J* = 4.5 Hz), 7.92 (t, 1H, *J* = 7.8 Hz), 7.82–7.79 (m, 2H), 7.42–7.35 (m, 4H), 7.32–7.30 (m, 1H), 7.09 (d, 0.5H, *J* = 6.5 Hz), 7.02 (d, 0.5H, *J* = 6.5 Hz), 6.84–6.72 (m, 2H), 5.02 (d, 1H, *J* = 5.5 Hz), 4.81 (d, 1H, *J* = 5.5 Hz), 4.02 (s, 3H), 3.17–2.97 (m, 2H), 2.86–2.70 (m, 2H), 0.87 (s, 9H), 0.08 (s, 3H), –0.07 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.39, 165.31, 165.2, 157.9, 157.8, 149.9, 148.2, 147.6, 143.9, 143.7, 138.0, 137.27, 137.25, 134.7, 134.5, 132.1, 132.0, 128.5 (2C), 128.4, 127.8 (2C), 127.3, 126.4, 124.9, 123.9, 122.0, 113.2, 113.1, 110.99, 110.96, 71.57, 71.55, 70.1, 52.9, 45.64, 45.62, 35.7, 35.2, 34.7, 34.1, 29.6, 25.6 (3C), 18.1, –5.0, –5.2.

Methyl 6-(2-(Hydroxy(5-phenoxyindan-2-yl)methyl)oxazol-5-yl)picolinate (S77)



The title compound was prepared from methyl 6-(2-((*tert*-butyldimethylsilyloxy)(5-phenoxyindan-2-yl)methyl)oxazol-5-yl)picolinate (**S76**, 12.8 mg, 0.02 mmol) following general procedure D. Flash chromatography (SiO_2, 50% EtOAc–hexanes) yielded the title compound (7.4 mg, 76%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.05 (d, 1H, *J* = 4.5 Hz), 7.91 (t, 1H, *J* = 7.8 Hz), 7.79–7.77 (m, 2H), 7.41–7.40 (m, 2H), 7.38–7.35 (m, 2H), 7.32–7.30 (m, 1H), 7.08 (d, 0.5H, *J* = 6.5 Hz), 7.05 (d, 0.5H, *J* = 6.5 Hz), 6.84–6.73 (m, 2H), 5.00 (s, 1H), 4.88 (d, 1H, *J* = 5.5 Hz), 4.02 (s, 3H), 3.16–2.94 (m, 5H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.6, 165.3, 158.0, 157.9, 150.3, 148.2, 147.3, 143.6, 143.5, 137.9, 137.2, 134.4, 134.3, 128.5 (2C), 127.8, 127.3 (2C), 126.2, 125.0, 124.9, 124.1, 122.3, 113.38, 113.31, 111.0, 110.9, 70.6, 70.1, 53.0, 44.6, 35.4, 35.1, 34.3, 34.0.

Methyl 6-(2-(5-Phenoxyindane-2-carbonyl)oxazol-5-yl)picolinate (28)



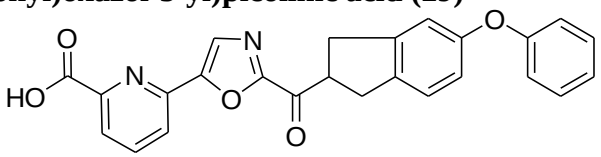
The title compound was prepared from methyl 6-(2-(hydroxy(5-phenoxyindan-2-yl)methyl)oxazol-5-yl)picolinate (**S77**, 119 mg, 0.26 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (80 mg, 69%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.11 (d, 1H, *J* = 4.5 Hz), 8.06 (s, 1H), 8.04 (d, 2H, *J* = 7.8 Hz), 7.97 (t, 1H, *J* = 4.5 Hz), 7.32 (t, 1H, *J* = 7.8 Hz), 7.17 (d, 1H, *J* = 7.8 Hz), 7.07 (t, 1H, *J* = 4.5 Hz), 6.98 (d, 2H, *J* = 4.5 Hz), 6.88–6.84 (m, 2H), 4.51–4.45 (m, 1H), 3.04 (s, 3H), 3.41–3.31 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz) 188.8, 165.0, 157.6, 157.2, 156.3, 152.4,

148.5, 146.5, 143.0, 138.3, 136.0, 129.6 (2C), 128.0, 125.2, 125.1, 123.3, 122.9, 118.5 (2C), 117.8, 115.2, 53.0, 47.7, 35.6, 35.1; HRMS-ESI-TOF *m/z* 441.1440 ($[M + H]^+$, $C_{26}H_{20}N_2O_5$ requires 441.1445). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 40% EtOH–hexanes, 7 mL/min, α = 1.17).

(*R*)-**28**: $[\alpha]^{23}_D$ +28 (*c* 0.1, THF).

(*S*)-**28**: $[\alpha]^{23}_D$ –30 (*c* 0.1, THF).

6-(2-(5-Phenoxyindane-2-carbonyl)oxazol-5-yl)picolinic acid (29)

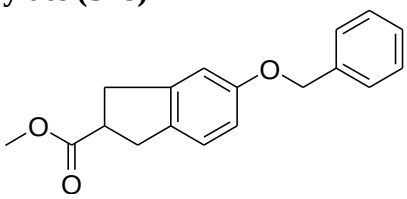


The title compound was prepared from methyl 6-(2-(5-(benzyloxy)indane-2-carbonyl)oxazol-5-yl)picolinate (**28**, 5 mg, 0.011 mmol) following general procedure G. Each pure enantiomer of the methyl esters were converted to their corresponding carboxylic acid using general procedure G. Flash chromatography (SiO_2, 5% HOAc–EtOAc) yielded the title compound (4 mg, 85%) as a white solid: ^{1}H NMR ($CDCl_3$ + 0.1% TFA, 600 MHz) δ 8.28 (d, 1H, *J* = 4.2 Hz), 8.10 (d, 2H, *J* = 7.8 Hz), 8.07 (s, 1H), 7.32 (t, 2H, *J* = 7.8 Hz), 7.18 (d, 1H, *J* = 7.8 Hz), 7.08 (t, 1H, *J* = 4.5 Hz), 7.00 (d, 2H, *J* = 4.5 Hz), 6.88–6.85 (m, 2H), 4.48–4.43 (m, 1H), 3.42–3.36 (m, 4H); ^{13}C NMR ($CDCl_3$ + 0.1% TFA, 150 MHz) 188.9, 164.9, 157.5, 157.2, 156.4, 151.4, 146.3, 145.1, 142.7, 139.9, 135.6, 129.7 (2C), 127.9, 125.2, 124.8, 124.6, 123.0, 118.5 (2C), 117.9, 117.3, 115.1, 47.7, 35.5, 35.0; HRMS-ESI-TOF *m/z* 449.1106 ($[M + Na]^+$, $C_{25}H_{18}N_2O_5$ requires 449.1108).

(*R*)-**29**: $[\alpha]^{23}_D$ +24 (*c* 0.1, THF).

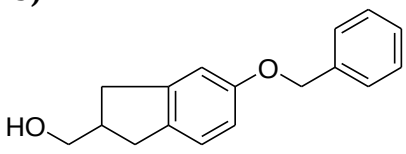
(*S*)-**29**: $[\alpha]^{23}_D$ –22 (*c* 0.1, THF).

Methyl 5-(Benzyloxy)indane-2-carboxylate (S78)



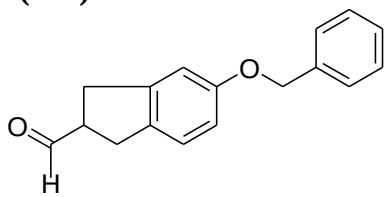
A sample of methyl 5-hydroxyindane-2-carboxylate (**S56**, 120 mg, 0.62 mmol), benzyl alcohol (0.084 mL, 0.81 mmol) and triphenylphosphine (212 mg, 0.81 mmol) were dissolved in anhydrous THF (10 mL). The reaction mixture was cooled to 0°C before diethyl azodicarboxylate (0.128 mL, 0.81 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 17 h under Ar. The mixture was diluted with EtOAc, washed with saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude product that was purified by flash chromatography (SiO_2, 5% EtOAc–hexanes) to provide the title compound (82.9 mg, 47%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.45 (d, 2H, *J* = 7.2 Hz), 7.40 (t, 2H, *J* = 7.2 Hz), 7.34 (t, 1H, *J* = 7.2 Hz), 7.12 (d, 1H, *J* = 8.4 Hz), 6.87 (s, 1H), 6.83 (dd, 1H, *J* = 2.4, 8.4 Hz), 5.05 (s, 2H), 3.74 (s, 3H), 3.38–3.34 (m, 1H), 3.28–3.15 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 175.5, 158.0, 143.0, 137.1, 133.6, 128.4 (2C), 127.7, 127.3 (2C), 124.7, 113.4, 110.7, 70.1, 51.8, 43.8, 36.2, 35.3.

(5-(Benzyloxy)indan-2-yl)methanol (S79)



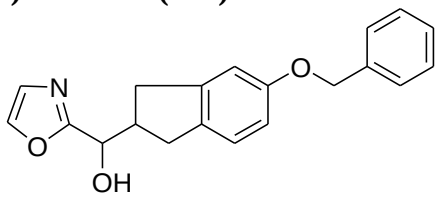
The title compound was prepared from methyl 5-(benzyloxy)indane-2-carboxylate (**S78**, 82.9 mg, 0.29 mmol) following general procedure A. Flash chromatography (SiO_2, 50% EtOAc–hexanes) afforded the title compound (82 mg, 98%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.45 (d, 2H, *J* = 7.2 Hz), 7.40 (t, 2H, *J* = 7.2 Hz), 7.34 (t, 1H, *J* = 7.2 Hz), 7.11 (d, 1H, *J* = 8.4 Hz), 6.87 (s, 1H), 6.83 (dd, 1H, *J* = 2.4, 8.4 Hz), 5.05 (s, 2H), 3.66 (d, 2H, *J* = 6.4 Hz), 3.06–2.99 (m, 2H), 2.76–2.65 (m, 3H), 1.87 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.8, 144.1, 137.2, 134.8, 128.4 (2C), 127.7, 127.3 (2C), 125.0, 113.0, 111.0, 70.1, 66.4, 41.8, 35.9, 34.7.

5-(Benzyloxy)indane-2-carboxaldehyde (S80)



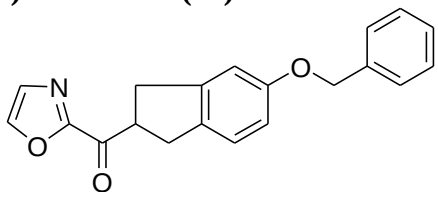
The title compound was prepared from (5-(benzyloxy)indan-2-yl)methanol (**S79**, 82 mg, 0.32 mmol) following general procedure B. Flash chromatography (SiO_2, 10% EtOAc–hexanes) afforded the title compound (50 mg, 62%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 9.76 (s, 1H), 7.43 (d, 2H, *J* = 7.2 Hz), 7.39 (t, 2H, *J* = 7.2 Hz), 7.33 (t, 1H, *J* = 7.2 Hz), 7.12 (d, 1H, *J* = 8.4 Hz), 6.87 (s, 1H), 6.82 (dd, 1H, *J* = 2.4, 8.4 Hz), 5.04 (s, 2H), 3.29–3.20 (m, 3H), 3.16–3.11 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 202.7, 158.2, 142.6, 137.0, 133.2, 128.5 (2C), 127.8, 127.3 (2C), 125.0, 113.7, 110.9, 70.1, 51.0, 33.0, 32.1.

(5-(Benzyloxy)indan-2-yl)(oxazol-2-yl)methanol (S81)



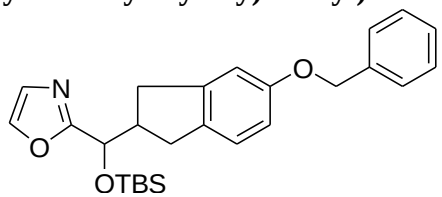
Oxazole (0.052 mL, 0.79 mmol) in anhydrous THF (10 mL) was treated with BH_3•THF (1 M, 0.086 mL, 0.86 mmol) and the solution was stirred at room temperature for 1 h before being cooled to –78 °C and treated with 1.5 M *t*-BuLi (0.100 mL, 1.27 mmol) dropwise. The reaction mixture was stirred at –78 °C for 40 min before a solution of 5-(benzyloxy)indane-2-carboxaldehyde (**S80**, 249 mg, 0.79 mmol) in THF (4 mL) was added. The reaction mixture was stirred at –78 °C for 2 h before being warmed to room temperature. A 5% HOAc–EtOH solution (50 mL) was added and this mixture was stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the residue was dissolved in EtOAc, washed with H_2O, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl before the organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 50% EtOAc–hexanes) afforded the title compound (160 mg, 63%) as colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.62 (s, 1H), 7.43–7.40 (m, 2H), 7.39–7.36 (m, 2H), 7.32–7.30 (m, 1H), 7.09–7.07 (m, 2H), 7.04 (d, 1H, *J* = 7.8 Hz), 6.79–6.74 (m, 2H), 5.03 (d, 2H, *J* = 5.4 Hz), 4.79–4.77 (m, 1H), 3.07–2.88 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.2, 157.97, 157.92, 143.7, 143.6, 138.9, 137.2, 134.5, 134.4, 128.5 (2C), 127.8, 127.3 (2C), 126.7, 124.99, 124.90, 113.29, 113.27, 110.98, 110.92, 70.4, 70.1, 53.4, 44.76, 44.74, 35.3, 35.2, 34.2, 34.1; HRMS-ESI-TOF *m/z* 322.1437 ($[M + H]^+$, $C_{20}H_{19}NO_3$ requires 322.1438).

(5-(Benzyloxy)indan-2-yl)(oxazol-2-yl)methanone (30)



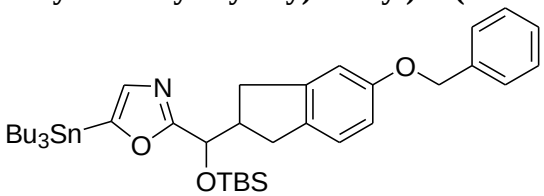
The title compound was prepared from (5-(benzyloxy)indan-2-yl)(oxazol-2-yl)methanol (**S81**, 10 mg, 0.031 mmol) following general procedure E. Flash chromatography (SiO_2, 5–20% EtOAc–hexanes) yielded the title compound (8 mg, 75%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.43 (s, 1H), 7.42 (d, 2H, *J* = 6.6 Hz), 7.39 (m, 3H), 7.32 (t, 1H, *J* = 7.2 Hz), 7.11 (d, 1H, *J* = 7.8 Hz), 6.85 (d, 1H, *J* = 7.8 Hz), 6.80 (d, 1H, *J* = 2.4 Hz), 5.04 (s, 2H), 4.41–4.38 (m, 1H), 3.39–3.26 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 188.9, 158.2, 157.8, 142.7, 141.6, 137.1, 133.3, 129.1, 128.5 (2C), 127.8, 127.4 (2C), 124.9, 113.7, 110.8, 70.2, 47.7, 35.6, 34.9; HRMS-ESI-TOF *m/z* 320.1277 ($[M + H]^+$, $C_{20}H_{17}NO_3$ requires 320.1281). The enantiomers could not be separated using chiral phase HPLC.

2-((5-(Benzyloxy)indan-2-yl)(*tert*-butyldimethylsilyloxy)methyl)oxazole (S82)



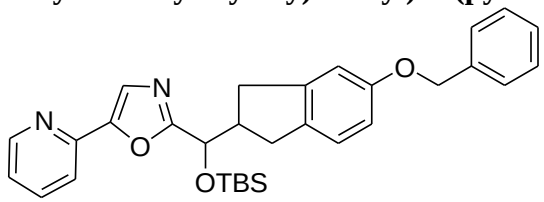
A solution of (5-(benzyloxy)indan-2-yl)(oxazol-2-yl)methanone (**S81**, 130 mg, 0.40 mmol), TBSCl (147 mg, 0.97 mmol) and imidazole (137 mg, 2 mmol) in DMF (10 mL) was stirred at room temperature for 16 h before it was diluted with EtOAc, washed with H_2O, and saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 10% EtOAc–hexanes) yielded the title compound (155 mg, 89%) as a thick colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.64 (s, 1H), 7.46–7.33 (m, 5H), 7.13–7.10 (m, 1H), 7.04 (d, 1H, *J* = 7.8 Hz), 6.88 (d, 1H, *J* = 2.4 Hz), 6.81–6.77 (m, 2H), 5.05 (d, 2H, *J* = 7.2 Hz), 4.80 (d, 1H, *J* = 5.4 Hz), 3.12–2.97 (m, 3H), 2.84–2.64 (m, 2H), 0.92 (s, 9H), 0.01 (s, 3H), –0.07 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 164.6, 157.8, 157.7, 143.9, 143.7, 138.49, 138.41, 137.2, 134.7, 134.5, 128.4 (2C), 127.7, 127.3 (2C), 126.7, 124.8, 113.0, 110.9, 110.8, 99.8, 71.4, 71.2, 70.0, 69.9, 45.5, 35.8, 35.1, 34.7, 34.0, 25.5 (3C), 18.0, –5.2.

2-((5-(Benzyloxy)indan-2-yl)(*tert*-butyldimethylsilyloxy)methyl)-5-(tributylstannyl)oxazole (S83)



A solution of 2-((5-(benzyloxy)indan-2-yl)(*tert*-butyldimethylsilyloxy)methyl)oxazole (**S82**, 155 mg, 0.35 mmol) in THF (10 mL) was cooled to –78 °C before it was treated with 2.29 M *n*-BuLi (0.20 mL, 0.39 mmol) dropwise. The reaction mixture was stirred at –78 °C for 2 h, treated with a solution of Bu_3SnCl (0.20 mL, 0.7 mmol), and stirred for 5 min. The solution was warmed to room temperature and diluted with EtOAc and washed with saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 0–5% EtOAc–hexanes) yielded the title compound (181 mg, 72%) as a thick colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.45–7.43 (m, 2H), 7.40–7.37 (m, 2H), 7.34–7.31 (m, 1H), 7.14 (s, 1H), 7.11 (d, 0.5H, *J* = 7.8 Hz), 7.04 (d, 0.5H, *J* = 7.8 Hz), 6.87 (d, 0.5H, *J* = 2.4 Hz), 6.80–6.76 (m, 1.5H), 5.04 (d, 2H, *J* = 7.2 Hz), 4.84 (d, 1H, *J* = 5.4 Hz), 3.12–2.99 (m, 3H), 2.78–2.69 (m, 2H), 1.62–1.57 (m, 6H), 1.40–1.35 (m, 6H), 1.17–1.14 (m, 6H), 0.95–0.92 (m, 9H), 0.89 (s, 9H), 0.08 (s, 3H), –0.10 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 168.6, 157.8, 157.7, 154.8, 144.2, 143.9, 137.34, 137.30, 137.1, 135.0, 134.8, 128.4 (2C), 127.6, 127.2, 124.8 (2C), 124.7, 112.9, 110.9, 71.5, 71.4, 70.1, 45.7, 35.8, 35.2, 34.8, 34.1, 28.8 (3C), 27.2 (3C), 25.6 (3C), 18.0, 13.5 (3C), 10.1 (3C), –5.27, –5.37.

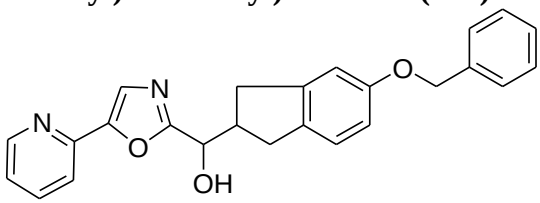
2-((5-(Benzyloxy)indan-2-yl)(*tert*-butyldimethylsilyloxy)methyl)-5-(pyridin-2-yl)oxazole (S84)



The title compound was prepared from 2-((5-(benzyloxy)indan-2-yl)(*tert*-butyldimethylsilyloxy)methyl)-5-(tributylstannyl)oxazole (**S83**, 167 mg, 0.22 mmol) and 2-bromopyridine following general procedure C. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (66.8 mg, 59%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.63 (d, 1H, *J* = 7.2 Hz), 7.76 (t, 1H, *J* = 7.8 Hz), 7.67–7.65 (m, 2H), 7.43–7.35 (m, 4H), 7.33–7.30 (m, 1H), 7.25–7.21 (m, 1H), 7.23–7.21 (m, 1H), 7.08 (d, 0.5H, *J* = 7.8 Hz), 7.04 (d, 0.5H, *J* = 7.8 Hz), 6.84 (d, 1H, *J* = 2.4 Hz), 6.78–6.73 (m, 1H), 5.02 (d, 2H, *J* = 7.2 Hz), 4.82 (d, 1H, *J* = 5.4 Hz), 3.14–2.99 (m, 3H), 2.85–2.72 (m, 2H), 0.89 (s, 9H), 0.09 (s, 3H), –0.05 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 164.93, 164.90, 157.9, 157.8, 150.7, 149.8, 147.3, 144.0, 143.8, 137.2, 136.8, 134.7, 134.6, 128.4 (2C), 127.7,

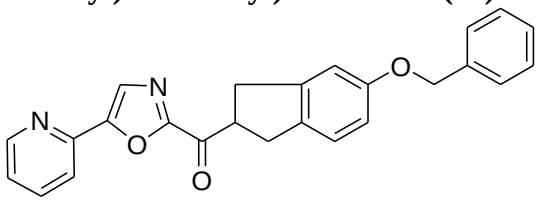
127.3 (2C), 125.1, 124.9, 122.8, 119.0, 113.18, 113.14, 110.98, 110.95, 71.5, 70.1, 45.6, 35.7, 35.2, 34.7, 34.2, 25.6 (3C), 18.1, –5.03, –5.22.

(5-(Benzyloxy)indan-2-yl)(5-(pyridin-2-yl)oxazol-2-yl)methanol (S85)



The title compound was prepared from 2-((5-(benzyloxy)indan-2-yl)(*tert*-butyldimethylsilyloxy)methyl)-5-(pyridin-2-yl)oxazole (**S84**, 66.8 mg, 0.13 mmol) following general procedure D. Flash chromatography (SiO_2, 50–100% EtOAc–hexanes) yielded the title compound (56.8 mg, 98%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.60 (d, 1H, *J* = 7.2 Hz), 7.72 (t, 1H, *J* = 7.8 Hz), 7.61–7.62 (m, 2H), 7.42–7.35 (m, 4H), 7.32–7.30 (m, 1H), 7.22–7.20 (m, 1H), 7.23–7.21 (m, 1H), 7.07 (d, 0.5H, *J* = 7.8 Hz), 7.03 (d, 0.5H, *J* = 7.8 Hz), 6.83 (d, 1H, *J* = 2.4 Hz), 6.78–6.73 (m, 1H), 4.99 (d, 2H, *J* = 7.2 Hz), 4.86 (d, 1H, *J* = 5.4 Hz), 3.18–3.05 (m, 3H), 2.96–2.90 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.5, 157.88, 157.83, 150.8, 149.7, 146.8, 143.7, 143.6, 137.1, 136.9, 134.5, 134.3, 128.4 (2C), 127.7, 127.3 (2C), 124.9, 124.88, 124.85, 122.9, 119.3, 113.2, 113.1, 110.9, 110.8, 70.3, 70.0, 44.57, 44.55, 35.4, 34.3.

(5-(Benzyloxy)indan-2-yl)(5-(pyridin-2-yl)oxazol-2-yl)methanone (31)

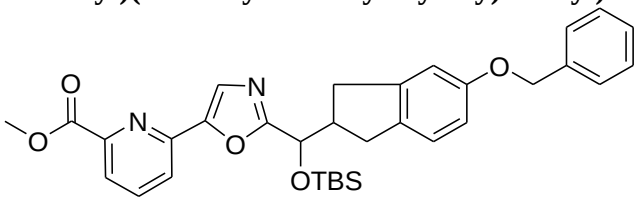


The title compound was prepared from (5-(benzyloxy)indan-2-yl)(5-(pyridin-2-yl)oxazol-2-yl)methanol (**S85**, 56.8 mg, 0.14 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (26.5 mg, 48%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.67 (d, 1H, *J* = 7.2 Hz), 7.92 (s, 1H), 7.87 (d, 1H, *J* = 7.8 Hz), 7.81 (t, 1H, *J* = 7.8 Hz), 7.43 (d, 2H, *J* = 7.8 Hz), 7.38 (t, 1H, *J* = 7.8 Hz), 7.32 (t, 2H, *J* = 7.8 Hz), 7.11 (d, 1H, *J* = 7.8 Hz), 7.03 (d, 1H, *J* = 7.8 Hz), 6.82 (d, 1H, *J* = 2.4 Hz), 6.81 (d, 1H, *J* = 7.8 Hz), 5.04 (d, 2H, *J* = 7.2 Hz), 4.48–4.42 (m, 1H), 3.39–3.28 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 188.9, 158.2, 157.0, 153.3, 150.0, 146.2, 142.7, 137.13, 137.10, 133.4, 128.5 (2C), 127.8, 127.3 (2C), 126.9, 124.8, 124.1, 120.4, 113.6, 110.7, 70.1, 47.7, 35.7, 35.0; HRMS-ESI-TOF *m/z* 397.1550 ($[M + H]^+$, $C_{25}H_{20}N_2O_3$ requires 397.1547). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 1% EtOH–hexanes, 7 mL/min, α = 1.12).

(*S*)-**31**: $[\alpha]^{23}_D$ –22 (*c* 0.1, THF).

(*R*)-**31**: $[\alpha]^{23}_D$ +24 (*c* 0.1, THF).

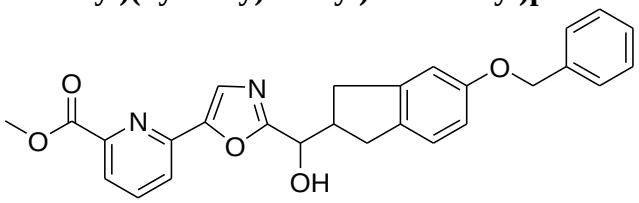
Methyl 6-(2-((5-(Benzyloxy)indan-2-yl)(*tert*-butyldimethylsilyloxy)methyl)oxazol-5-yl)picolinate (S86)



The title compound was prepared from 2-((5-(benzyloxy)indan-2-yl)(*tert*-butyldimethylsilyloxy)methyl)-5-(tributylstannyl)oxazole (**S83**, 60 mg, 0.082 mmol) and methyl 6-chloropicolinate following general procedure C. Flash chromatography (SiO_2, 30% EtOAc–hexanes) yielded the title compound (31.8 mg, 67%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.04 (d, 1H, *J* = 7.2 Hz), 7.90 (t, 1H, *J* = 7.8 Hz), 7.82 (m, 2H), 7.42–7.30 (m, 4H), 7.08 (d, 0.5H, *J* = 7.8 Hz), 7.03 (d, 0.5H, *J* = 7.8 Hz), 6.84 (d, 1H, *J* = 2.4 Hz), 6.78–6.73 (m, 1H), 5.02 (d, 2H, *J* = 7.2 Hz), 4.82 (d, 1H, *J* = 5.4 Hz), 4.01 (s, 3H), 3.10–2.98 (m, 3H), 2.86–2.70 (m, 2H), 0.87 (s, 9H), 0.08 (s, 3H), –0.07 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.3, 165.29, 165.27, 157.9, 157.8, 149.9, 148.2, 147.6, 143.9, 143.7, 138.0, 137.26, 137.24, 134.6, 134.5, 128.4 (2C), 127.7, 127.3 (2C), 126.4, 124.9,

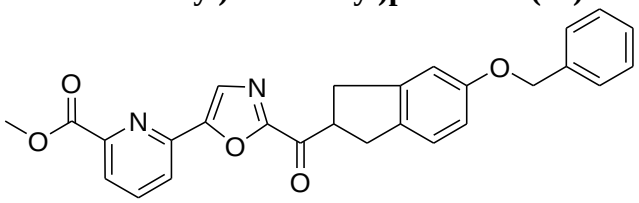
123.9, 122.0, 113.2, 113.1, 110.98, 110.95, 71.56, 71.54, 70.1, 52.9, 45.62, 45.60, 35.7, 35.2, 34.7, 34.1, 25.6 (3C), 18.1, 13.5, –5.05, –5.21.

Methyl 6-(2-((5-(Benzyloxy)indan-2-yl)(hydroxy)methyl)oxazol-5-yl)picolinate (S87)



The title compound was prepared from methyl 6-(2-((5-(benzyloxy)indan-2-yl)(*tert*-butyldimethylsilyloxy)methyl)oxazol-5-yl)picolinate (**S86**, 31.8 mg, 0.055 mmol) following general procedure D. Flash chromatography (SiO_2, 60% EtOAc–hexanes) yielded the title compound (21.7 mg, 86%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.04 (d, 1H, *J* = 7.2 Hz), 7.89 (t, 1H, *J* = 7.8 Hz), 7.77 (m, 2H), 7.41–7.30 (m, 4H), 7.08 (d, 1H, *J* = 7.8 Hz), 7.04 (d, 0.5H, *J* = 7.8 Hz), 6.84 (d, 0.5H, *J* = 2.4 Hz), 6.76–6.72 (m, 2H), 5.00 (d, 2H, *J* = 7.2 Hz), 4.88 (d, 1H, *J* = 5.4 Hz), 4.01 (s, 3H), 3.16–2.93 (m, 3H), 2.89–2.70 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.2, 157.98, 157.94, 148.2, 147.3, 143.7, 143.5, 137.9, 137.2, 134.4, 134.3, 128.5 (2C), 127.8, 127.3 (2C), 126.1, 125.0, 124.9, 124.0, 122.3, 113.3, 113.2, 110.98, 110.91, 70.5, 70.1, 52.9, 44.6, 35.4, 35.2, 34.3, 34.1.

Methyl 6-(2-(5-(Benzyloxy)indane-2-carbonyl)oxazol-5-yl)picolinate (32)

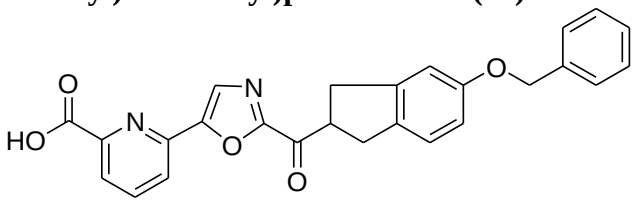


The title compound was prepared from methyl 6-(2-((5-(benzyloxy)indan-2-yl)(hydroxy)methyl)oxazol-5-yl)picolinate (**S87**, 21.7 mg, 0.047 mmol) following general procedure E. Flash chromatography (SiO_2, 30% EtOAc–hexanes) yielded the title compound (16.2 mg, 75%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.12 (d, 1H, *J* = 7.2 Hz), 8.05 (s, 1H), 8.04 (d, 1H, *J* = 7.8 Hz), 7.97 (t, 1H, *J* = 7.8 Hz), 7.43 (d, 2H, *J* = 7.2 Hz), 7.38 (t, 2H, *J* = 7.8 Hz), 7.30 (t, 1H, *J* = 7.8 Hz), 7.11 (d, 1H, *J* = 7.8 Hz), 6.86 (d, 1H, *J* = 2.4 Hz), 6.81 (dd, 1H, *J* = 2.4, 7.8 Hz), 5.04 (s, 2H), 4.48–4.38 (m, 1H), 4.04 (s, 3H), 3.41–3.30 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 188.9, 165.0, 158.2, 157.3, 152.4, 148.5, 146.5, 142.7, 138.2, 137.1, 133.3, 128.5 (2C), 128.0, 127.8 (2C), 127.4, 125.1, 124.9, 123.3, 113.7, 110.8, 70.2, 53.0, 47.7, 35.7, 35.0; HRMS-ESI-TOF *m/z* 455.1602 ($[M + H]^+$, $C_{27}H_{22}N_2O_5$ requires 455.1601). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 20% EtOH–hexanes, 7 mL/min, α = 1.09).

(*S*)-**32**: $[\alpha]^{23}_D$ +84 (*c* 0.1, THF).

(*R*)-**32**: $[\alpha]^{23}_D$ –88 (*c* 0.1, THF).

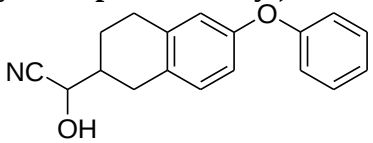
6-(2-(5-(Benzyloxy)indane-2-carbonyl)oxazol-5-yl)picolinic acid (33)



The title compound was prepared from methyl 6-(2-(5-(benzyloxy)indane-2-carbonyl)oxazol-5-yl)picolinate (**32**, 1.88 mg, 0.004 mmol) following general procedure G. Each pure enantiomer of the methyl esters were converted to their corresponding carboxylic acid using general procedure G. Flash chromatography (SiO_2, 5% HOAc–EtOAc) yielded the title compound (1.3 mg, 73%) as a white solid: ^{1}H NMR ($CDCl_3$ + 0.1% TFA, 600 MHz) δ 8.31 (d, 1H, *J* = 7.2 Hz), 8.17 (m, 3H), 7.43 (d, 2H, *J* = 7.2 Hz), 7.38 (t, 2H, *J* = 7.8 Hz), 7.33 (t, 1H, *J* = 7.8 Hz), 7.14 (d, 1H, *J* = 7.8 Hz), 6.88 (d, 1H, *J* = 2.4 Hz), 6.84 (dd, 1H, *J* = 2.4, 7.8 Hz), 5.08 (s, 2H), 4.41–4.38 (m, 1H), 3.43–3.31 (m, 4H); ^{13}C NMR ($CDCl_3$ + 0.1% TFA, 150 MHz) δ 200.1, 189.1, 158.0, 157.1, 145.1, 142.2, 140.3, 136.6, 133.2, 128.6 (2C), 128.1, 127.8 (2C), 127.6, 125.4, 125.1, 125.0, 114.3, 111.2, 70.8, 53.4, 47.7, 35.5, 34.9, 14.2; HRMS-ESI-TOF *m/z* 441.1445 ($[M + H]^+$, $C_{26}H_{20}N_2O_5$ requires 441.1445).

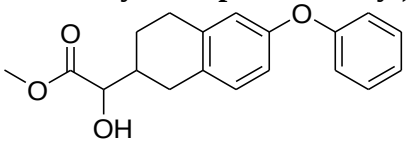
(*S*)-**33**: $[\alpha]^{23}_{D}$ –80 (*c* 0.1, THF).
(*R*)-**33**: $[\alpha]^{23}_{D}$ +72 (*c* 0.1, THF).

2-Hydroxy-2-(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)acetonitrile (S88)



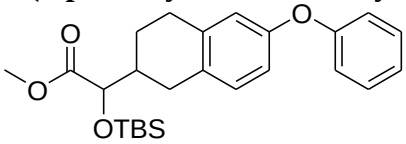
A solution of 6-phenoxy-1,2,3,4-tetrahydronaphthalene-2-carboxaldehyde (**S23**, 470 mg, 1.86 mmol) and KCN (912 mg, 18.6 mmol) in a mixture of THF/H_2O (10/10 mL) was stirred at room temperature for 16 h before it was diluted with EtOAc, washed with H_2O, and saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (410 mg, 79%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.34 (t, 2H, *J* = 7.2 Hz), 7.11–7.06 (m, 2H), 7.02 (d, 2H, *J* = 8.0 Hz), 6.82–6.77 (m, 2H), 4.45–4.43 (m, 1H), 3.96 (s, 1H), 3.03–2.96 (m, 1H), 2.85–2.81 (m, 2H), 2.74–2.68 (m, 1H), 2.24–2.19 (m, 2H), 1.67–1.62 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 157.3, 155.1, 137.3, 130.3, 130.2, 129.6 (2C), 129.25, 129.21, 122.9, 119.2, 118.7, 118.5 (2C), 116.9, 67.9, 65.2, 65.1, 39.2, 39.1, 30.3, 30.2, 28.3, 25.4, 24.4, 24.3.

Methyl 2-Hydroxy-2-(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)acetate (S89)



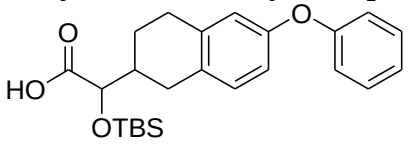
A sample of 2-hydroxy-2-(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)acetonitrile (**S88**, 310 mg, 1.10 mmol) was dissolved in a solution of 4 N HCl/EtOAc (4 mL) and MeOH (4 mL) and the mixture was warmed at reflux for 16 h under Ar. The mixture was diluted with EtOAc, and washed with saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 30% EtOAc–hexanes) yielded the title compound (263 mg, 73%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.32 (t, 2H, *J* = 7.2 Hz), 7.10–7.02 (m, 2.5H), 6.99 (d, 2H, *J* = 8.0 Hz), 6.81–6.73 (m, 2.5H), 4.26 (t, 1H, *J* = 7.2 Hz), 4.22 (t, 0.5H, *J* = 7.2 Hz), 3.83 (s, 3H), 2.83–2.67 (m, 5H), 2.53–2.49 (m, 0.5H), 2.22–2.17 (m, 1.5H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 175.09, 175.05, 157.6, 154.8, 137.73, 173.70, 130.8, 130.5, 130.39, 130.36, 130.2, 129.66, 129.61 (2C), 129.1, 123.0, 122.8, 118.9, 118.86, 118.82, 118.6, 118.4 (2C), 117.0, 116.81, 116.80, 73.9, 73.8, 65.4, 65.3, 52.64, 52.62, 39.4, 39.2, 38.8, 38.5, 31.1, 30.3, 30.2, 29.6, 29.4, 29.2, 28.45, 28.43, 25.6, 24.49, 24.42, 23.3.

Methyl 2-(*tert*-Butyldimethylsilyloxy)-2-(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)acetate (S90)



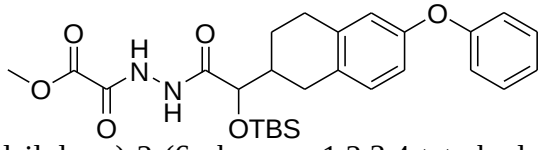
A solution of methyl 2-hydroxy-2-(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)acetate (**S89**, 410 mg, 1.31 mmol), TBSCl (474 mg, 3.15 mmol) and imidazole (450 mg, 6.55 mmol) in DMF (5 mL) was stirred at room temperature for 16 h before it was diluted with EtOAc, washed with H_2O, and saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 5% EtOAc–hexanes) yielded the title compound (380 mg, 67%) as a thick colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.32 (t, 2H, *J* = 7.2 Hz), 7.08–7.03 (m, 2H), 6.99–6.97 (m, 2H), 6.78–6.73 (m, 2H), 4.23 (d, 0.5H, *J* = 7.2 Hz), 4.16 (d, 0.5H, *J* = 7.2 Hz), 3.76 (s, 1.5H), 3.75 (s, 1.5H), 2.82–2.74 (m, 2.5H), 2.68–2.64 (m, 2H), 2.22–2.14 (m, 1H), 1.93–1.90 (m, 1H), 1.83–1.80 (m, 0.5H), 0.91 (s, 9H), 0.08 (s, 3H), 0.05 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 173.67, 173.62, 157.6, 157.5, 154.7, 154.6, 138.0, 137.6, 131.0, 130.8, 130.4, 130.2, 129.5 (2C), 122.78, 122.74, 118.9, 118.8, 118.4 (2C), 118.3, 116.7, 116.6, 75.8, 75.4, 51.7, 39.1, 39.0, 31.2, 29.3, 29.1, 28.9, 26.1, 25.7 (3C), 23.9, 18.3, –4.9, –5.0, –5.32, –5.39.

2-(*tert*-Butyldimethylsilyloxy)-2-(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)acetic acid (S91)



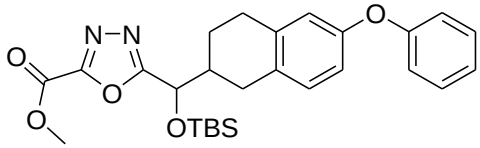
A sample of methyl 2-(*tert*-butyldimethylsilyloxy)-2-(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)acetate (**S90**, 380 mg, 0.89 mmol) was dissolved in a mixture of 3:2:1 THF/H_2O/MeOH (4:2:2 mL) and LiOH (75 mg, 1.78 mmol) was added. The reaction mixture was stirred for 16 h at room temperature before the mixture was diluted with EtOAc, washed with aqueous 0.01 N $KHSO_4$, saturated aqueous NaCl, and dried over Na_2SO_4. Evaporation in vacuo yielded the crude acid that was purified by chromatography (SiO_2, 10% EtOAc–hexanes) yielding the title compound (258 mg, 70%) as a thick colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.31 (t, 2H, *J* = 7.2 Hz), 7.08–7.02 (m, 2H), 6.99–6.97 (m, 2H), 6.78–6.73 (m, 2H), 4.29 (d, 0.5H, *J* = 7.2 Hz), 4.25 (d, 0.5H, *J* = 7.2 Hz), 2.86–2.76 (m, 3H), 2.69–2.64 (m, 1H), 2.23–2.19 (m, 1H), 1.91–1.90 (m, 0.5H), 1.65–1.60 (m, 1.5H), 0.95 (s, 9H), 0.16 (s, 3H), 0.14 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 177.5, 177.4, 157.59, 157.53, 155.0, 154.8, 137.6, 137.4, 130.48, 130.43, 130.3, 130.2, 129.6 (2C), 122.88, 122.84, 118.8, 118.5, 118.4 (2C), 116.8, 116.7, 75.8, 75.4, 39.3, 39.2, 31.1, 29.6, 29.3, 29.2, 28.9, 25.7 (3C), 25.6, 23.9, 18.1, –4.9, –5.16, –5.19.

Methyl {*N*'-[2-(*tert*-Butyldimethylsilyloxy)-2-(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)-acetyl]-hydrazino}-2-oxo-acetate (S92)



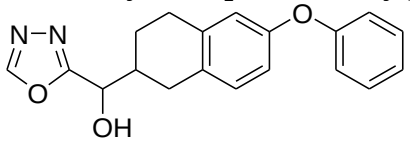
A sample of 2-(*tert*-butyldimethylsilyloxy)-2-(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)acetic acid (**S91**, 60 mg, 0.14 mmol) and methyl oxalylhydrazide (18 mg, 0.14 mmol) were dissolved in CH_2Cl_2 (2 mL). EDCI (27 mg, 0.14 mmol) was added as a solid. The reaction mixture was stirred at room temperature for 16 h. The solvent was evaporated in vacuo and the residue was dissolved in EtOAc, washed with 1 N aqueous HCl, 5% aqueous $NaHCO_3$, saturated aqueous NaCl, and dried over Na_2SO_4. The solvent was removed under reduced pressure and flash chromatography (SiO_2, 5% MeOH–EtOAc) afforded the title compound (72.7 mg, 98%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 9.11 (brs, 1H, NH), 9.02 (brs, 1H, NH), 7.31 (t, 2H, *J* = 7.2 Hz), 7.06–7.01 (m, 2H), 6.97–6.95 (m, 2H), 6.76–6.73 (m, 2H), 4.30 (d, 0.5H, *J* = 7.2 Hz), 4.26 (d, 0.5H, *J* = 7.2 Hz), 3.93 (s, 1.5H), 3.88 (s, 1.5H), 2.82–2.66 (m, 3H), 2.69–2.64 (m, 1H), 2.23–2.19 (m, 1H), 1.91–1.90 (m, 2H), 1.65–1.60 (m, 2H), 0.95 (s, 9H), 0.16 (s, 3H), 0.14 (s, 3H).

Methyl 5-((*tert*-Butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)-1,3,4-oxadiazole-2-carboxylate (S93)



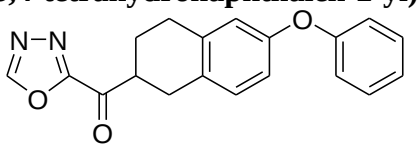
A sample of {*N*'-[2-(*tert*-butyldimethylsilyloxy)-2-(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)-acetyl]-hydrazino}-2-oxo-acetate (**S92**, 72.7 mg, 0.14 mmol) was dissolved in CH_2Cl_2 (3 mL). TsCl (82 mg, 0.42 mmol) and Et_3N (0.060 mL, 0.42 mmol) were added. The reaction mixture was stirred at room temperature for 16 h. The solvent was evaporated in vacuo and the residue was dissolved in EtOAc, washed with saturated aqueous NaCl, and dried over Na_2SO_4. The solvent was removed under reduced pressure. Purification by flash chromatography (SiO_2, 20% EtOAc–hexanes) afforded the title compound (17.9 mg, 26%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.69 (d, 2H, *J* = 8.4 Hz), 7.31 (t, 2H, *J* = 7.2 Hz), 7.08–7.03 (m, 1H), 6.98–6.95 (m, 2H), 6.78–6.72 (m, 2H), 4.99 (d, 0.5H, *J* = 7.2 Hz), 4.93 (d, 0.5H, *J* = 7.2 Hz), 4.06 (s, 1.5H), 4.05 (s, 1.5H), 2.85–2.74 (m, 2.5H), 2.69–2.64 (m, 1H), 2.23–2.19 (m, 1H), 1.91–1.90 (m, 1H), 1.65–1.60 (m, 1.5H), 0.95 (s, 9H), 0.16 (s, 3H), 0.14 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 169.1, 169.0, 157.57, 157.51, 156.8, 156.7, 155.0, 154.9, 154.6, 154.5, 146.7, 142.8, 141.6, 137.7, 137.4, 137.3, 130.4, 130.2, 130.1, 130.0, 129.68, 129.65 (2C), 129.5, 127.03, 127.0, 126.9 (2C), 122.88, 122.84, 118.8, 118.5, 118.4, 116.9, 116.8, 70.4, 70.2, 52.8, 41.9, 40.1, 40.0, 30.7, 30.1, 29.6, 28.8, 25.5 (3C), 25.2, 24.5, 21.8, 21.4, 18.1, 14.1, –5.15, –5.17, –5.23, –5.26.

(1,3,4-Oxadiazol-2-yl)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methanol (S94)



The title compound was prepared from methyl 5-((*tert*-butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)-1,3,4-oxadiazole-2-carboxylate (**S93**, 17.9 mg, 0.036 mmol) following general procedure D. Flash chromatography (SiO_2, 50–100% EtOAc–hexanes) yielded the title compound (15.9 mg, 98%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.44 (d, 1H, *J* = 1.8 Hz), 7.69 (d, 1H, *J* = 8.4 Hz), 7.32–7.27 (m, 2H), 7.08–7.04 (m, 2H), 6.98–6.96 (m, 2H), 6.79–6.72 (m, 2H), 4.99 (t, 0.5H, *J* = 6.0 Hz), 4.95 (t, 0.5H, *J* = 6.0 Hz), 2.98–2.62 (m, 2H), 2.41–2.38 (m, 1H), 2.17–2.15 (m, 1H), 1.84–1.81 (m, 1H), 1.65–1.55 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 157.49, 157.47, 155.0, 153.2, 142.8, 137.7, 137.5, 130.4, 130.2, 129.8, 129.66, 129.63 (2C), 129.5, 127.0, 122.9, 118.85, 118.82, 118.59 (2C), 118.53, 116.9, 116.8, 69.5, 69.4, 41.9, 39.35, 39.30, 31.9, 30.7, 30.1, 29.69, 29.64, 29.3, 28.7, 28.6, 25.1, 24.2, 22.6, 21.4, 14.1.

(1,3,4-Oxadiazol-2-yl)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methanone (34)

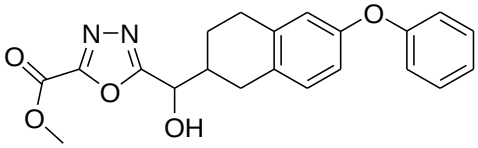


The title compound was prepared from (1,3,4-oxadiazol-2-yl)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methanol (**S94**, 15.9 mg, 0.049 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (5 mg, 32%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.59 (s, 1H), 7.33 (t, 2H, *J* = 7.2 Hz), 7.09 (t, 2H, *J* = 6.6 Hz), 7.00 (d, 2H, *J* = 9.0 Hz), 6.82–6.78 (m, 2H), 3.91–3.87 (m, 1H), 3.12–3.09 (m, 2H), 2.96–2.90 (m, 2H), 2.37–2.34 (m, 1H), 1.97–1.91 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 189.2, 160.2, 157.4, 155.3, 154.2, 136.9, 130.1, 129.6 (2C), 128.9, 123.0, 118.8, 118.6 (2C), 117.0, 44.8, 30.1, 28.6, 25.4; HRMS-ESI-TOF *m/z* 321.1233 ($[M + H]^+$, $C_{19}H_{16}N_2O_3$ requires 321.1234). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 40% EtOH–hexanes, 7 mL/min, α = 1.23).

(*S*)-**34**: $[\alpha]^{23}_D$ –16 (*c* 0.1, THF).

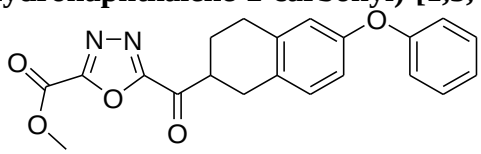
(*R*)-**34**: $[\alpha]^{23}_D$ +20 (*c* 0.1, THF).

Methyl 5-[Hydroxy-(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl]-[1,3,4]oxadiazole-2-carboxylate (S95)



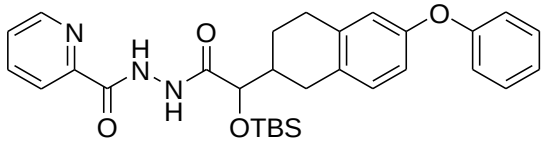
A sample of methyl 5-((*tert*-butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)-1,3,4-oxadiazole-2-carboxylate (**S93**, 62.5 mg, 0.12 mmol) was dissolved in THF (2 mL), and TASF[2] (35 mg, 0.12 mmol) was added as a solid. The reaction mixture was stirred at room temperature for 1 h under Ar. The reaction mixture was diluted with EtOAc, washed with saturated aqueous NaCl, and dried over Na_2SO_4. Flash chromatography (SiO_2, 50% EtOAc–hexanes) yielded the title compound (18.9 mg, 41%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.31 (t, 2H, *J* = 7.8 Hz), 7.08–7.03 (m, 2H), 6.98 (d, 2H, *J* = 7.8 Hz), 6.79 (m, 2H), 5.01 (t, 0.5H, *J* = 7.0 Hz), 4.97 (t, 0.5H, *J* = 7.0 Hz), 4.06 (s, 3H), 2.88–2.77 (m, 3H), 2.45–2.41 (m, 1H), 2.17–2.04 (m, 1H), 1.87–1.58 (m, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 157.4, 155.1, 154.5, 137.6, 137.4, 130.4, 130.2, 129.6 (2C), 129.4, 122.9, 118.85, 118.82 (2C), 118.5, 116.97, 116.93, 69.8, 69.6, 53.9, 39.38, 39.33, 30.7, 29.9, 28.6, 28.5, 25.1, 24.1.

Methyl 5-(6-Phenoxy-1,2,3,4-tetrahydronaphthalene-2-carbonyl)-[1,3,4]oxadiazole-2-carboxylate (35)



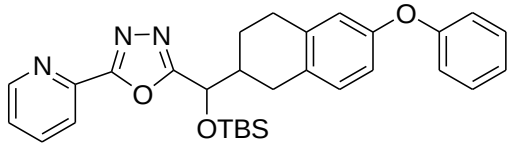
The title compound was prepared from methyl 5-[hydroxy-(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl]-[1,3,4]oxadiazole-2-carboxylate (**S95**, 18.9 mg, 0.049 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (14 mg, 75%) as a yellow solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.33 (t, 2H, *J* = 7.8 Hz), 7.09 (t, 2H, *J* = 7.8 Hz), 7.00 (d, 2H, *J* = 8.4 Hz), 6.82–6.77 (m, 2H), 4.10 (s, 3H), 3.90–3.86 (m, 1H), 3.12–3.10 (m, 2H), 2.95–2.90 (m, 2H), 2.36–2.33 (m, 1H), 1.98–1.90 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 188.8, 160.6, 157.4, 157.1, 155.3, 153.9, 136.8, 130.1, 129.6 (2C), 128.7, 123.0, 118.8, 118.6 (2C), 117.1, 54.2, 44.9, 30.0, 28.5, 25.3; HRMS-ESI-TOF *m/z* 379.1292 ($[M + H]^+$, $C_{21}H_{18}N_2O_5$ requires 379.1288). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 40% EtOH–hexanes, 7 mL/min, α = 1.05).
(*S*)-**35**: $[\alpha]^{23}_D$ –46 (*c* 0.1, THF).
(*R*)-**35**: $[\alpha]^{23}_D$ +36 (*c* 0.1, THF).

N'-(2-(*tert*-Butyldimethylsilyloxy)-2-(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)acetyl)picolinohydrazide (S96)



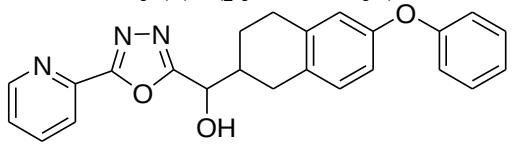
A sample of 2-(*tert*-butyldimethylsilyloxy)-2-(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)acetic acid (**S91**, 62 mg, 0.15 mmol) and pyridine-2-carboxylic acid hydrazide (21 mg, 0.15 mmol) were dissolved in CH_2Cl_2 (2 mL). EDCI (29 mg, 0.15 mmol) was added as a solid. The reaction mixture was stirred at room temperature for 16 h. The solvent was evaporated in vacuo and the residue was dissolved in EtOAc, washed with 1 N aqueous HCl, 5% aqueous $NaHCO_3$, saturated aqueous NaCl, and dried over Na_2SO_4. The solvent was removed under reduced pressure and flash chromatography (SiO_2, 10% MeOH–CH_2Cl_2) afforded the title compound (85.6 mg, 98%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 9.10 (s, 1H), 9.07 (s, 1H), 8.58–8.53 (m, 1H), 8.29–8.13 (m, 1H), 7.87–7.83 (m, 1H), 7.47–7.40 (m, 1H), 7.30–7.27 (m, 3H), 7.06–6.80 (m, 4H), 6.75–7.67 (m, 3H), 4.35 (d, 0.5H, *J* = 7.2 Hz), 4.31 (d, 0.5H, *J* = 7.2 Hz), 1.67–1.63 (m, 3H), 1.24–1.14 (m, 2H), 0.95 (s, 9H), 0.16 (s, 3H), 0.14 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 168.8, 168.7, 160.3, 160.2, 157.58, 157.54, 154.7, 154.6, 148.4, 148.2, 147.97, 147.96, 137.7, 137.5, 137.4, 137.2, 130.84, 130.82, 130.4, 130.1, 129.5 (2C), 126.8, 126.4, 126.3, 122.7, 122.6, 122.3, 122.1, 118.8, 118.4, 118.38, 118.35, 118.30, 116.7, 116.6, 76.4, 76.3, 39.6, 39.3, 31.3, 29.6, 29.4, 29.3, 28.5, 26.0, 25.7 (3C), 25.49, 25.47, 23.5, 18.2, 17.9, 14.6, –4.95, –4.99, –5.08.

2-((*tert*-Butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)-5-(pyridin-2-yl)-1,3,4-oxadiazole (S97)



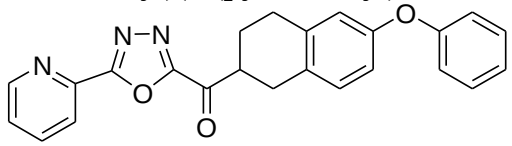
A sample of *N*'-(2-(*tert*-butyldimethylsilyloxy)-2-(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)acetyl)picolinohydrazide (**S96**, 85.6 mg, 0.16 mmol) was dissolved in CH_2Cl_2 (3 mL). TsCl (92 mg, 0.48 mmol) and Et_3N (0.068 mL, 0.48 mmol) were added. The reaction mixture was stirred at room temperature for 16 h. The solvent was evaporated in vacuo and the residue was dissolved in EtOAc, washed with saturated aqueous NaCl, and dried over Na_2SO_4. The solvent was removed under reduced pressure. Purification by flash chromatography (SiO_2, 20% EtOAc–hexanes) afforded the title compound (53 mg, 64%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.80 (s, 1H), 8.23 (d, 1H, *J* = 8.4 Hz), 7.88 (t, 1H, *J* = 8.4 Hz), 7.46 (t, 1H, *J* = 7.2 Hz), 7.30 (t, 2H, *J* = 7.2 Hz), 7.05 (t, 2H, *J* = 7.2 Hz), 6.97–6.94 (m, 2H), 6.78–6.72 (m, 2H), 5.00 (d, 1H, *J* = 7.2 Hz), 4.94 (d, 1H, *J* = 7.2 Hz), 2.95–2.76 (m, 2H), 2.60–2.44 (m, 2H), 1.82–1.80 (m, 1H), 1.62–1.53 (m, 1H), 0.91 (s, 9H), 0.14 (s, 1.5H), 0.11 (s, 1.5H), –0.01 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 167.7, 167.6, 164.2, 164.1, 157.6, 157.5, 154.88, 154.81, 143.43, 143.40, 137.9, 137.6, 137.1, 130.4, 130.3, 130.2, 129.9, 129.5 (2C), 125.86, 125.84, 123.0, 122.78, 122.74, 118.8, 118.4, 118.3, 116.8, 116.7, 70.5, 70.4, 39.99, 39.96, 30.8, 30.3, 29.6, 28.8, 28.6, 25.6 (3C), 25.3, 24.7, 18.14, 18.12, –5.06, –5.25, –5.28.

(6-Phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanol (S98)



The title compound was prepared from 2-((*tert*-butyldimethylsilyloxy)(6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)-5-(pyridin-2-yl)-1,3,4-oxadiazole (**S97**, 53 mg, 0.10 mmol) following general procedure D. Flash chromatography (SiO_2, 50–100% EtOAc–hexanes) yielded the title compound (48 mg, 98%) as a yellow solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.75 (d, 1H, *J* = 8.4 Hz), 8.23 (d, 1H, *J* = 8.4 Hz), 7.87 (t, 1H, *J* = 8.4 Hz), 7.46 (t, 1H, *J* = 7.2 Hz), 7.29 (t, 2H, *J* = 7.2 Hz), 7.05 (t, 2H, *J* = 7.2 Hz), 6.97–6.95 (m, 2H), 6.76–6.72 (m, 2H), 5.00 (t, 0.5H, *J* = 8.0 Hz), 5.01 (t, 0.5H, *J* = 8.0 Hz), 4.20–4.17 (m, 1H), 2.99–2.76 (m, 1H), 2.53–2.49 (m, 1H), 2.27–2.24 (m, 1H), 2.06–1.90 (m, 2H), 1.68–1.54 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 168.1, 168.0, 164.1, 157.5, 154.8, 150.1, 143.1, 137.8, 137.6, 137.3, 130.3, 130.2, 130.1, 129.9, 129.5 (2C), 126.0, 123.2, 122.7, 118.86, 118.81, 118.4 (2C), 116.85, 116.81, 69.7, 69.5, 39.38, 39.26, 30.9, 30.1, 28.75, 28.72, 25.6, 25.3, 24.3, 17.9.

(6-Phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanone (36)

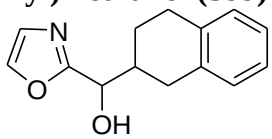


The title compound was prepared from (6-phenoxy-1,2,3,4-tetrahydronaphthalen-2-yl)(5-(pyridin-2-yl)-1,3,4-oxadiazol-2-yl)methanol (**S98**, 48 mg, 0.12 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (15 mg, 31%) as a yellow solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.85 (s, 1H), 8.30 (d, 1H, *J* = 7.2 Hz), 7.93 (t, 1H, *J* = 6.6 Hz), 7.54 (t, 1H, *J* = 6.6 Hz), 7.33 (t, 2H, *J* = 9.0 Hz), 7.09–6.99 (m, 4H), 6.82–6.78 (m, 2H), 3.96–3.91 (m, 1H), 3.14–2.88 (m, 4H), 2.38–2.35 (m, 1H), 1.99–1.94 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 189.2, 165.1, 160.7, 157.4, 155.2, 150.7, 142.5, 137.3, 137.0, 130.1, 129.6 (2C), 129.1, 126.7, 124.0, 122.9, 118.8, 118.5 (2C), 117.0, 44.5, 30.2, 28.6, 25.5; HRMS-ESI-TOF *m/z* 398.1502 ($[M + H]^+$, $C_{24}H_{19}N_3O_3$ requires 398.1499). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 40% EtOH–hexanes, 7 mL/min, α = 1.08).

(*S*)-**36**: $[\alpha]^{23}_D$ –14 (*c* 0.1, THF).

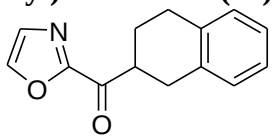
(*R*)-**36**: $[\alpha]^{23}_D$ +18 (*c* 0.1, THF).

Oxazol-2-yl-1,2,3,4-tetrahydronaphthalen-2-yl)methanol (S99)



Oxazole (0.205 mL, 3.12 mmol) in anhydrous THF (10 mL) was treated with BH_3•THF (1 M, 3.4 mL, 3.40 mmol) and the solution was stirred at room temperature for 1 h before being cooled to –78 °C and treated with 2.41 M *n*-BuLi (1.7 mL, 4.05 mmol) dropwise. The reaction mixture was stirred at –78 °C for 40 min before a solution of commercially available 1,2,3,4-tetrahydronaphthalene-2-carboxaldehyde (500 mg, 3.12 mmol) in THF (3 mL) was added. The reaction mixture was stirred at –78 °C for 2 h before being warmed to room temperature. A 5% HOAc–EtOH solution (50 mL) was added and this mixture was stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the residue was dissolved in EtOAc, and washed with H_2O, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 40% EtOAc–hexanes) afforded the title compound (264 mg, 37%) as a white solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.62 (s, 1H), 7.12–7.00 (m, 5H), 5.22 (brs, 1H), 4.78 (d, 0.5H, *J* = 5.6 Hz), 4.75 (d, 0.5H, *J* = 5.6 Hz), 3.49–2.63 (m, 2H), 2.63–2.60 (m, 1H), 2.42–2.36 (m, 2H), 2.22–2.19 (m, 1H), 1.79–1.76 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.4, 138.6, 136.2, 136.0, 135.4, 135.2, 129.0, 128.9, 128.57, 128.51, 126.2, 125.45 (2C), 125.40, 70.9, 70.7, 39.46, 39.41, 31.3, 31.0, 28.6, 28.5, 25.1, 24.6.

Oxazol-2-yl(1,2,3,4-tetrahydronaphthalen-2-yl)methanone (37)

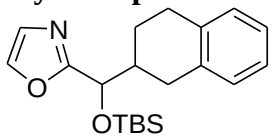


The title compound was prepared from oxazol-2-yl-1,2,3,4-tetrahydronaphthalen-2-yl)methanol (**S99**, 45 mg, 0.196 mmol) following general procedure E. Flash chromatography (SiO_2, 30% EtOAc–hexanes) yielded the title compound (37.8 mg, 84%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.85 (s, 1H), 7.36 (s, 1H), 7.12–7.10 (m, 4H), 3.88–3.83 (m, 1H), 3.14–3.06 (m, 2H), 2.98–2.92 (m, 2H), 2.32–2.28 (m, 1H), 1.94–1.86 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 190.5, 157.5, 141.6, 135.6, 134.7, 129.05, 129.02, 128.7, 125.9, 125.8, 43.4, 30.9, 28.6, 25.8; HRMS-ESI-TOF *m/z* 228.1016 ($[M + H]^+$, $C_{14}H_{13}NO_2$ requires 228.1019). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 0.5 % EtOH–hexanes, 7 mL/min, α = 1.21).

(*S*)-**37**: $[\alpha]^{23}_D$ –46 (*c* 0.1, THF).

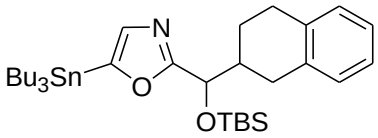
(*R*)-**37**: $[\alpha]^{23}_D$ +50 (*c 0*.1, THF).

2-((*tert*-Butyldimethylsilyloxy)-(1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole (S100)



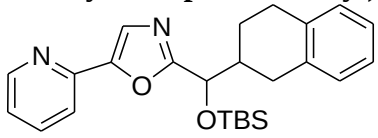
A solution of oxazol-2-yl-(1,2,3,4-tetrahydronaphthalen-2-yl)methanol (**S99**, 215 mg, 0.93 mmol), TBSCl (339 mg, 2.24 mmol) and imidazole (316 mg, 4.65 mmol) in DMF (3 mL) was stirred at room temperature for 16 h before it was diluted with EtOAc, washed with H_2O, and saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 10% EtOAc–hexanes) yielded the title compound (184 mg, 57%) as a thick colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.66 (s, 1H), 7.13–7.02 (m, 5H), 4.78 (d, 0.5H, *J* = 5.6 Hz), 4.74 (d, 0.5H, *J* = 5.6 Hz), 2.90–2.76 (m, 3H), 2.59–2.53 (m, 2H), 2.37–2.26 (m, 1H), 1.76–1.73 (m, 1H), 0.96 (s, 9H), 0.12 (s, 1.5H), 0.10 (s, 1.5H), –0.05 (s, 1.5H), –0.07 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 164.5, 164.4, 138.46, 138.40, 136.4, 136.2, 135.7, 135.4, 129.2, 129.0, 128.67, 128.61, 126.7, 125.54, 125.50, 72.37, 72.30, 40.3, 31.29, 31.25, 28.8, 28.7, 25.6 (3C), 25.3, 25.0, 18.1, –5.35, –5.39, –5.4.

2-((*tert*-Butyldimethylsilyloxy)-(1,2,3,4-tetrahydronaphthalen-2-yl)methyl)-5-(tributylstannyl)oxazole (S101)



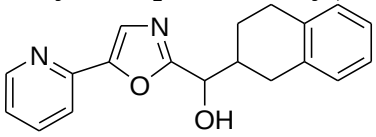
A solution of 2-((*tert*-butyldimethylsilyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)oxazole (**S100**, 184 mg, 0.53 mmol) in THF (5 mL) was cooled to –78 °C before it was treated with 2.41 M *n*-BuLi (0.25 mL, 0.58 mmol) dropwise. The reaction mixture was stirred at –78 °C for 2 h, treated with a solution of Bu_3SnCl (0.30 mL, 1.06 mmol) and stirred for 5 min. The solution was warmed to room temperature and diluted with EtOAc and washed with saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 10% EtOAc–hexanes) yielded the title compound (332 mg, 65%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.13 (s, 1H), 7.09–7.00 (m, 3H), 6.99–6.80 (m, 1H), 4.78 (d, 0.5H, *J* = 5.6 Hz), 4.74 (d, 0.5H, *J* = 5.6 Hz), 2.85–2.75 (m, 3H), 2.56–2.48 (m, 1H), 2.36–2.24 (m, 2H), 1.69–1.56 (m, 27H), 1.36–1.33 (s, 9H), 0.09 (s, 1.5H), 0.05 (s, 1.5H), –0.12 (s, 1.5H), –0.13 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 168.5, 154.6, 137.0, 136.3, 136.0, 135.7, 129.2, 129.0, 128.6, 128.5, 125.4, 125.3, 72.4, 40.5, 31.3, 28.88, 28.81 (3C), 27.7, 27.0, 26.7, 25.6 (3C), 25.4 (3C), 18.0, 17.4, 13.55 (3C), 13.53, 13.52, 10.1 (3C), –5.38, –5.40, –5.42, –5.44.

2-((*tert*-Butyldimethylsilyloxy)-(1,2,3,4-tetrahydronaphthalen-2-yl)methyl)-5-(pyridin-2-yl)oxazole (S102)



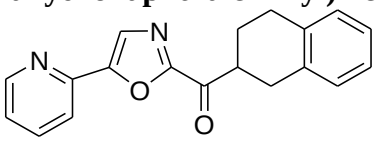
The title compound was prepared from 2-((*tert*-butyldimethylsilyloxy)-(1,2,3,4-tetrahydronaphthalen-2-yl)methyl)-5-(tributylstannyl)oxazole (**S101**, 332 mg, 0.52 mmol) and 2-bromopyridine following general procedure C. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (128 mg, 59%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.63 (d, 1H, *J* = 4.2 Hz), 7.77–7.66 (m, 2H), 7.23–7.21 (m, 1H), 7.09–7.00 (m, 3H), 4.82 (d, 0.5H, *J* = 5.6 Hz), 4.76 (d, 0.5H, *J* = 5.6 Hz), 2.88–2.79 (m, 3H), 2.67–2.57 (m, 1H), 2.42–2.27 (m, 2H), 1.83–1.81 (m, 3H), 0.98 (s, 9H), 0.11 (s, 1.5H), 0.05 (s, 1.5H), –0.12 (s, 1.5H), –0.13 (s, 1.5H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 164.8, 164.6, 150.8, 150.7, 149.8, 147.34, 147.30, 136.8, 136.4, 136.2, 135.7, 135.4, 129.2, 129.1, 128.7, 128.6, 125.58, 125.53, 125.51, 125.1, 125.0, 122.77, 122.75, 119.0, 118.9, 72.5, 72.4, 40.38, 40.35, 31.4, 31.1, 28.8, 28.7, 26.7, 25.6 (3C), 25.5, 25.0, 18.3, 13.5, –5.14, –5.28, –5.32.

(5-(Pyridin-2-yl)oxazol-2-yl)(-1,2,3,4-tetrahydronaphthalen-2-yl)methanol (S103)



The title compound was prepared from 2-((*tert*-butyldimethylsilyloxy)-1,2,3,4-tetrahydronaphthalen-2-yl)methyl)-5-(pyridin-2-yl)oxazole (**S102**, 128 mg, 0.30 mmol) following general procedure D. Flash chromatography (SiO_2, 50–100% EtOAc–hexanes) yielded the title compound (84.4 mg, 92%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.62 (d, 1H, *J* = 4.2 Hz), 7.74 (t, 1H, *J* = 7.0 Hz), 7.65 (s, 1H), 7.62 (d, 1H, *J* = 7.5 Hz), 7.23–7.21 (m, 1H), 7.09–7.01 (m, 3H), 4.86 (d, 0.5H, *J* = 5.6 Hz), 4.82 (d, 0.5H, *J* = 5.6 Hz), 3.64 (s, 0.5H), 3.61 (s, 0.5H), 2.92–2.81 (m, 2H), 2.72–2.70 (m, 2H), 2.46–2.44 (m, 1H), 2.21–2.18 (m, 0.5H), 1.92–1.90 (m, 0.5H), 1.67–1.60 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.3, 165.2, 151.1, 149.8, 147.03, 147.01, 136.9, 136.3, 136.2, 135.5, 135.3, 129.3, 129.1, 128.76, 128.73, 125.7, 125.68, 125.66, 125.62, 124.93, 124.91, 123.0, 119.3, 71.5, 71.3, 39.79, 39.75, 31.5, 30.7, 28.84, 28.81, 25.5, 24.5.

(5-(Pyridin-2-yl)oxazol-2-yl)(1,2,3,4-tetrahydronaphthalen-2-yl)methanone (38)

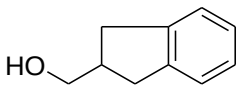


The title compound was prepared from (5-(pyridin-2-yl)oxazol-2-yl)(1,2,3,4-tetrahydronaphthalen-2-yl)methanol (**S103**, 84.4 mg, 0.27 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (78.6 mg, 96%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.67 (d, 1H, *J* = 4.2 Hz), 7.91 (s, 1H), 7.87 (d, 1H, *J* = 7.0 Hz), 7.81 (t, 1H, *J* = 7.0 Hz), 7.32–7.30 (m, 1H), 7.13–7.10 (m, 4H), 3.93–3.88 (m, 1H), 3.17–3.07 (m, 2H), 3.02–2.92 (m, 2H), 2.34–2.30 (m, 1H), 1.99–1.93 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 190.4, 156.8, 153.3, 150.0, 146.2, 137.0, 135.5, 134.7, 129.0, 128.7, 126.9, 125.8, 125.7, 124.0, 120.3, 43.3, 31.0, 28.6, 25.9; HRMS-ESI-TOF *m/z* 305.1289 ($[M + H]^+$, $C_{19}H_{16}N_2O_2$ requires 305.1284). The enantiomers were separated using a semipreparative chiral phase HPLC column (Daicel ChiraCel OD, 10 μm, 2 × 25 cm, 0.5 % EtOH–hexanes, 7 mL/min, α = 1.15).

(*S*)-**38**: $[\alpha]^{23}_D$ –18 (*c* 0.1, THF).

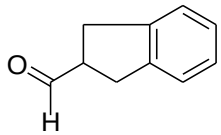
(*R*)-**38**: $[\alpha]^{23}_D$ +24 (*c* 0.1, THF).

(Indan-2-yl)methanol (S104)



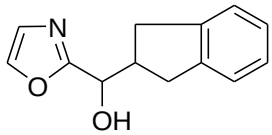
A solution of indane-2-carboxylic acid (800 mg, 4.93 mmol) was dissolved in anhydrous THF (20 mL) and cooled to 0 °C and $LiAlH_4$ (187 mg, 4.93 mmol) was added portion wise. The reaction mixture was stirred for 1 h at 0 °C. The solution was warmed to room temperature and diluted with EtOAc and washed with saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (481 mg, 66%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.29–7.26 (m, 2H), 7.23–7.19 (m, 2H), 3.69 (d, 2H, *J* = 6.4 Hz), 3.16–3.09 (m, 2H), 2.83–2.67 (m, 3H), 2.67 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 142.5 (2C), 126.1 (2C), 124.5 (2C), 66.2, 41.2, 35.6 (2C).

Indane-2-carboxaldehyde (S105)



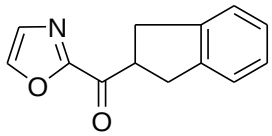
The title compound was prepared from (indan-2-yl)methanol (**S104**, 300 mg, 2.02 mmol) following general procedure B. Following fast filtration through Florisil, the solvent was removed under reduced pressure to afford the title compound (300 mg, 88%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.78 (s, 1H), 7.26–7.18 (m, 4H), 3.33–3.18 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 202.4, 140.7 (2C), 126.3 (2C), 124.2 (2C), 50.2, 32.5 (2C).

(Indan-2-yl)(oxazol-2-yl)methanol (S106)



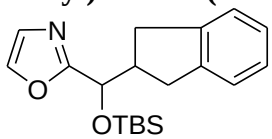
Oxazole (0.135 mL, 2.05 mmol) in anhydrous THF (7 mL) was treated with BH_3•THF (1 M, 2.3 mL, 2.23 mmol) and the solution was stirred at room temperature for 1 h before being cooled to –78 °C and treated with 2.41 M *n*-BuLi (1.1 mL, 2.66 mmol) dropwise. The reaction mixture was stirred at –78 °C for 40 min before a solution of indane-2-carboxaldehyde (**S105**, 300 mg, 2.05 mmol) in THF (2 mL) was added. The reaction mixture was stirred at –78 °C for 2 h before being warmed to room temperature. A 5% HOAc–EtOH solution (50 mL) was added and the mixture was stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the residue was dissolved in EtOAc, washed with H_2O, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 20% EtOAc–hexanes) afforded the title compound (161 mg, 35%) as white solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.59 (s, 1H), 7.26–7.12 (m, 3H), 7.05 (s, 1H), 4.78 (d, 1H, J = 6.8 Hz), 4.51 (s, 1H), 3.14–3.04 (m, 3H), 2.96–2.75 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.6, 142.2, 142.1, 138.7, 126.4, 126.28, 126.22, 124.4, 124.3, 70.1, 44.0, 35.2, 35.0.

(Indan-2-yl)(oxazol-2-yl)methanone (39)



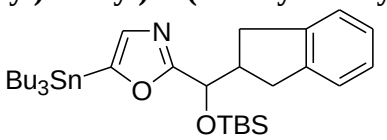
The title compound was prepared from (indan-2-yl)(oxazol-2-yl)methanol (**S106**, 20 mg, 0.092 mmol) following general procedure E. Flash chromatography (SiO_2, 20% EtOAc–hexanes) yielded the title compound (15.2 mg, 77%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.85 (s, 1H), 7.37 (s, 1H), 7.23–7.21 (m, 2H), 7.19–7.16 (m, 2H), 4.42–4.37 (m, 1H), 3.41–3.30 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 188.9, 157.8, 141.6, 141.1, 129.1 (2C), 126.7 (2C), 124.3 (2C), 47.3, 35.5 (2C); HRMS-ESI-TOF *m/z* 214.0862 ($[M + H]^+$, $C_{13}H_{11}NO_2$ requires 214.0863).

2-((*tert*-Butyldimethylsilyloxy)(indan-2-yl)methyl)oxazole (S107)



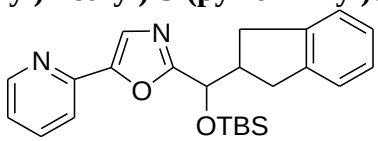
A solution of (indan-2-yl)(oxazol-2-yl)methanol (**S105**, 100 mg, 0.46 mmol), TBSCl (168 mg, 1.11 mmol) and imidazole (156 mg, 2.3 mmol) in DMF (1 mL) was stirred at room temperature for 16 h before it was diluted with EtOAc, and washed with H_2O, and saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 10% EtOAc–hexanes) yielded the title compound (43.2 mg, 28%) as a thick colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.63 (s, 1H), 7.20–7.19 (m, 1H), 7.13–7.11 (m, 3H), 7.08 (s, 1H), 4.78 (d, 1H, J = 6.8 Hz), 3.12–3.01 (m, 3H), 2.84–2.70 (m, 2H), 0.86 (s, 9H), 0.06 (s, 3H), –0.11 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 164.7, 142.5, 142.3, 138.5, 126.8, 126.2, 126.1, 124.44, 124.40, 71.4, 45.1, 35.6, 34.9, 25.6 (3C), 18.1, –5.2, –5.3.

2-((*tert*-Butyldimethylsilyloxy)(indan-2-yl)methyl)-5-(tributylstannyl)oxazole (S108)



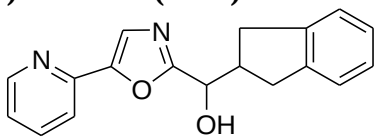
A solution of 2-((*tert*-butyldimethylsilyloxy)(indan-2-yl)methyl)oxazole (**S107**, 43.2 mg, 0.13 mmol) in THF (1 mL) was cooled to –78 °C before it was treated with 2.16 M *n*-BuLi (0.10 mL, 0.14 mmol) dropwise. The reaction mixture was stirred at –78 °C for 2 h, and treated with a solution of Bu_3SnCl (0.07 mL, 0.26 mmol) and stirred for 5 min. The solution was warmed to room temperature and diluted with EtOAc and washed with saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash chromatography (SiO_2, 0–10% EtOAc–hexanes) yielded the title compound (80.5 mg, 65%) as a thick colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.19–7.09 (m, 5H), 4.81 (d, 1H, *J* = 6.8 Hz), 3.10–3.01 (m, 3H), 2.82–2.69 (m, 2H), 1.66–1.62 (m, 6H), 1.38–1.27 (m, 6H), 1.12–1.09 (m, 6H), 0.94–0.85 (m, 9H), 0.80 (s, 9H), 0.03 (s, 3H), –0.14 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 168.6, 154.9, 142.5, 137.2, 126.1 (2C), 126.0, 124.4 (2C), 124.3, 99.5, 71.5, 45.3, 35.6, 35.0, 28.8, 27.8, 27.0, 26.8, 25.6 (3C), 17.5, 13.6, 13.5, 10.2, –5.2, –5.3.

2-((*tert*-Butyldimethylsilyloxy)(indan-2-yl)methyl)-5-(pyridin-2-yl)oxazole (S109)



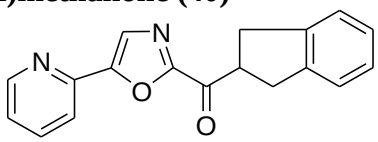
The title compound was prepared from 2-((*tert*-butyldimethylsilyloxy)(indan-2-yl)methyl)-5-(tributylstannyl)-oxazole (**S108**, 80 mg, 0.12 mmol) and 2-bromopyridine following general procedure C. Flash chromatography (SiO_2, 30% EtOAc–hexanes) yielded the title compound (28.7 mg, 59%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.63 (d, 1H, *J* = 4.8 Hz), 7.76 (t, 1H, *J* = 7.8 Hz), 7.67–7.64 (m, 2H), 7.24–7.10 (m, 5H), 4.82 (d, 1H, *J* = 6.8 Hz), 3.14–3.07 (m, 3H), 2.91–2.78 (m, 2H), 0.88 (s, 9H), 0.09 (s, 3H), –0.06 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 164.9, 150.8, 149.8, 147.3, 142.5, 142.3, 136.8, 126.2, 126.1, 125.1, 124.46, 124.44, 122.8, 119.0, 71.5, 45.1, 35.5, 35.0, 25.6 (3C), 18.1, –5.0, –5.2.

(Indan-2-yl)(5-(pyridin-2-yl)oxazol-2-yl)methanol (S110)



The title compound was prepared from 2-((*tert*-butyldimethylsilyloxy)(indan-2-yl)methyl)-5-(pyridin-2-yl)oxazole (**S109**, 28.7 mg, 0.07 mmol) following general procedure D. Flash chromatography (SiO_2, 50–100% EtOAc–hexanes) yielded the title compound (20.9 mg, 98%) as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.63 (d, 1H, *J* = 4.8 Hz), 7.74 (t, 1H, *J* = 7.8 Hz), 7.62–7.60 (m, 2H), 7.24–7.10 (m, 5H), 4.88 (d, 1H, *J* = 6.8 Hz), 3.91 (s, 1H), 3.16–3.11 (m, 3H), 3.03–2.88 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.4, 151.0, 149.8, 146.9, 142.2, 142.1, 136.9, 126.35, 126.30, 124.9, 124.5, 124.4, 123.0, 119.3, 70.4, 44.1, 35.2, 35.1.

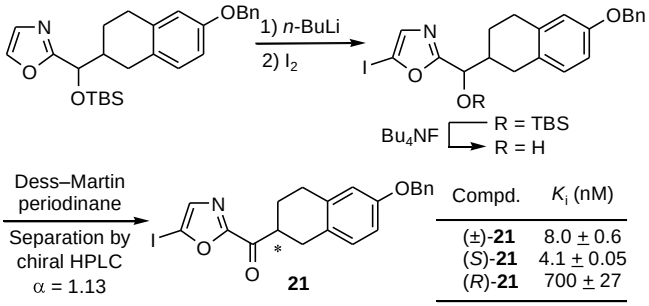
(Indan-2-yl)(5-(pyridin-2-yl)oxazol-2-yl)methanone (40)



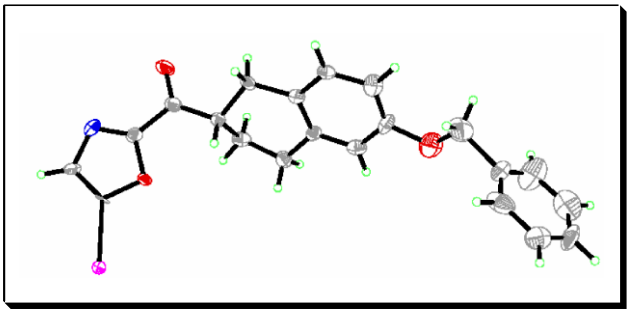
The title compound was prepared from (indan-2-yl)(5-(pyridin-2-yl)oxazol-2-yl)methanol (**S110**, 20.9 mg, 0.071 mmol) following general procedure E. Flash chromatography (SiO_2, 30% EtOAc–hexanes) yielded the title compound (15.5 mg, 75%) as a white solid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.67 (d, 1H, *J* = 4.8 Hz), 7.93 (s, 1H), 7.88 (d, 1H, *J* = 7.8 Hz), 7.82 (t, 1H, *J* = 7.8 Hz), 7.33–7.31 (m, 1H), 7.24–7.16 (m, 4H), 4.48–4.42 (m, 1H), 3.44–3.37 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 189.0, 157.1, 153.3, 150.1, 146.2, 141.2, 137.1, 126.9, 126.7 (2C), 124.4 (2C), 124.1, 120.4, 47.3, 35.7 (2C); HRMS-ESI-TOF *m/z* 291.1129 ($[M + H]^+$, $C_{18}H_{14}N_2O_2$ requires 291.1128).

(1) Nicolaou, K. C.; Estrada, A. A.; Zak, M.; Lee, S. H.; Safina, B. S. A Mild and Selective Method for the Hydrolysis of Esters with Trimethyltin hydroxide. *Angew. Chem. Int. Ed.* **2005**, *44*, 1378–1382.
(2) Scheidt, K. A.; Chen, H.; Follows, B. C.; Chemler, S. R.; Coffey, D. S.; Roush, W. R. Tris(dimethylamino)sulfonium Difluorotrimethylsilicate, a Mild Reagent for the Removal of Silicon Protecting Group. *J. Org. Chem.* **1998**, *63*, 6436–6437.

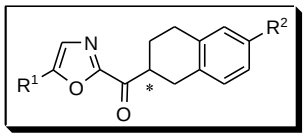
Scheme 3

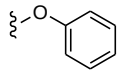
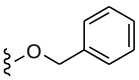


Compd.	K_i (nM)
(±)-**21**	8.0 ± 0.6
(*S*)-**21**	4.1 ± 0.05
(*R*)-**21**	700 ± 27



X-Ray crystal structure of the most potent (*S*)-enantiomer



R^2 = 
R^2 = 
R^2 = 

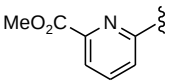
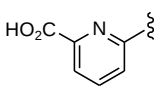
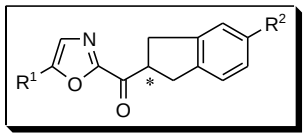
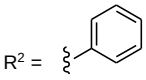
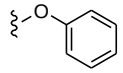
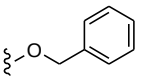
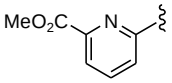
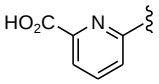
R^1	(*S*)	(*R*)		(*S*)	(*R*)		(*S*)	(*R*)	
–H	57 ± 8	460 ± 0.23	(**3**)	2.2 ± 0.07	410 ± 1.8	(**9**)	6.1 ± 0.6	87 ± 8	(**15**)
$-CO_2Me$	55 ± 1	1400 ± 10	(**4**)	5.4 ± 0.02	59 ± 0.3	(**10**)	2.9 ± 0.003	53 ± 1	(**16**)
–CN	3.4 ± 0.01	62 ± 0.01	(**5**)	1.3 ± 0	54 ± 0.01	(**11**)	3.2 ± 0.02	120 ± 2	(**17**)
	7.2 ± 0.1	240 ± 0.02	(**6**)	4.4 ± 0.05	290 ± 7	(**12**)	3.2 ± 0.01	300 ± 16	(**18**)
	27 ± 0.01	700 ± 0.6	(**7**)	2.2 ± 0.02	870 ± 1	(**13**)	18 ± 0.1	4500 ± 500	(**19**)
	39 ± 3	500 ± 7	(**8**)	25 ± 0.02	220 ± 8	(**14**)	34 ± 2	740 ± 20	(**20**)

Figure 4. FAAH inhibitors with 1,2,3,4-tetrahydronaphthalene C2 acyl side chain, K_i (nM).

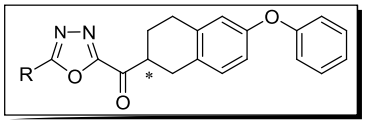
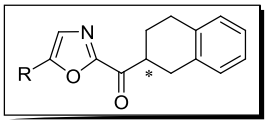
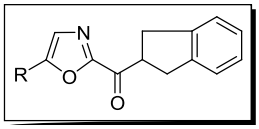


R^2 = 
R^2 = 
R^2 = 

R^1	(*S*)	(*R*)		(*S*)	(*R*)		(*S*)	(*R*)	
–H	27 ± 0.03	140 ± 1	(**22**)	10 ± 0.09	200 ± 4	(**26**)	24[a] ± 1		(**30**)
	1.9 ± 0.06	600 ± 2	(**23**)	2.1 ± 0.1	42 ± 0.1	(**27**)	1.4 ± 0.001	110 ± 1	(**31**)
	6.2[a] ± 0.12		(**24**)	98 ± 3.6	790 ± 34	(**28**)	5.8 ± 0.11	130 ± 16	(**32**)
	57[a] ± 1.2		(**25**)	71 ± 4.5	550 ± 44	(**29**)	51 ± 0.31	660 ± 35	(**33**)

[a]Racemate. Enantiomers not separable.

Figure 5. FAAH inhibitors with indane C2 acyl side chain, K_i (nM).

R	(*S*)	(*R*)		(*S*)	(*R*)		meso	
–H	0.5 ± 0.1	1.4 ± 0.03	(**34**)	5100 ± 1	12000 ± 20	(**37**)	7100 ± 10	(**39**)
–CO_2Me	1.5 ± 0.1	1.6 ± 0.1	(**35**)		-		-	
	1.0 ± 0.2	6.3 ± 1.1	(**36**)	430 ± 5	3200 ± 30	(**38**)	1100 ± 10	(**40**)

Figure 6. Additional FAAH inhibitors, K_i (nM).

Compound	rFAAH	hFAAH
12	4.4 ± 0.05	5.8 ± 0.17
14	25 ± 0.02	110 ± 2.2

Figure 7. Inhibition of human versus rat fatty acid amide hydrolase (hFAAH vs rFAAH), K_i (nM).

Table S1: Data processing and refinement statistics for FAAH-**12**.

Data collection	
Space group	$P3_221$
Cell dimensions	
a, *b*, *c* (Å)	103.30, 103.30, 253.36
α, β, γ (°)	90, 90, 120
Resolution (Å)	30-1.90 (1.96–1.90)
R_{merge} (%)	9.4 (62.0)
$I / \sigma I$	12.9 (2.6)
Completeness (%)	95.6(87.4)
Redundancy	6.2 (5.7)
Refinement	
Resolution (Å)	1.90(1.92–1.90)
No. reflections	118622
R_{work} / R_{free} (%)	15.4(21.6)/18.5(25.0)
No. atoms	9527
Protein	8481
Ligand/ion	61
Water	985
B-factors	25.65
Protein	24.4
Ligand/ion	19.5
Water	36.5
R.m.s. deviations	
Bond lengths (Å)	0.013
Bond angles (°)	1.644

Table S2. Inhibitor Purity Analysis[a]

Compd	Purity	Compd	Purity	Compd	Purity
(*S*)-**3**	98	(*S*)-**16**	98	**30**	98
(*R*)-**3**	98	(*R*)-**16**	98	(*S*)-**31**	95
(*S*)-**4**	98	(*S*)-**17**	95	(*R*)-**31**	95
(*R*)-**4**	98	(*R*)-**17**	95	(*S*)-**32**	98
(*S*)-**5**	98	(*S*)-**18**	98	(*R*)-**32**	98
(*R*)-**5**	98	(*R*)-**18**	98	(*S*)-**33**	98
(*S*)-**6**	98	(*S*)-**19**	98	(*R*)-**33**	98
(*R*)-**6**	98	(*R*)-**19**	98	(*S*)-**34**	98
(*S*)-**7**	>99	(*S*)-**20**	98	(*R*)-**34**	95
(*R*)-**7**	>99	(*R*)-**20**	95	(*S*)-**35**	95
(*S*)-**8**	98	(*S*)-**21**	98	(*R*)-**35**	95
(*R*)-**8**	98	(*R*)-**21**	98	(*S*)-**36**	98
(*S*)-**9**	98	(*S*)-**22**	98	(*R*)-**36**	98
(*R*)-**9**	98	(*R*)-**22**	98	(*S*)-**37**	98
(*S*)-**10**	99	(*S*)-**23**	95	(*R*)-**37**	98
(*R*)-**10**	99	(*R*)-**23**	95	(*S*)-**38**	95
(*S*)-**11**	98	**24**	98	(*R*)-**38**	95
(*R*)-**11**	98	**25**	98	**39**	99
(*S*)-**12**	98	(*S*)-**26**	95	**40**	98
(*R*)-**12**	98	(*R*)-**26**	95		
(*S*)-**13**	98	(*S*)-**27**	95		
(*R*)-**13**	98	(*R*)-**27**	95		
(*S*)-**14**	98	(*S*)-**28**	98		
(*R*)-**14**	98	(*R*)-**28**	98		
(*S*)-**15**	98	(*S*)-**29**	98		
(*R*)-**15**	98	(*R*)-**29**	98		

[a] Purity of each compound was determined on an Agilent 1100 LC/MS instrument on a ZORBAX® SB-C18, 3.5 mm, 4.6×50, a flow rate of 0.75 mL/min, detection at 220 and 254 nm, with a 10–98% acetonitrile/water/0.1% formic acid gradient and a 50–98% acetonitrile/water/0.1% formic acid gradient.