Asymmetric Aza-Friedel-Crafts Reaction of 2-Naphthol with Ts-imines Catalyzed by a Dinuclear Zinc Catalyst

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1. General Information

All reactions were carried out under nitrogen atmosphere. Aldehydes were purchased from Aldrich and used directly. Triethylamine was distilled over KOH pellets and stored in a septum-sealed flask. Solvents were dried under refluxing for at least 12 h over P2O5 (dichloromethane) or sodium / benzophenone (toluene and THF), and were freshly distilled prior to use. 1H NMR spectra were recorded on a Bruker AM-400 Varian (400 MHz) spectrometer using TMS as an internal standard. 13C-NMR spectra were recorded on a Bruker AM-400 Varian (100 MHz) or Mercury-300 (75 MHz) spectrometer. Melting points were determined on an XT-4 melting point apparatus and were uncorrected. HRMS data were performed on Bruker Apex II mass instrument (ESI). MS were measured on a VG-7070E spectrometer (EI at 70 eV). Enantiomeric excess values were determined by HPLC using a chiral column (Chiralcel OD-H, OJ-H or AD-H) on Waters 600 Delta or Agilent 1100 and eluting with i-PrOH and n-hexane. Optical rotation was measured on a Jasco DIP-100 polarimeter in 5 cm cells at the indicated temperature.

Diethylzinc (1.0 M solution in toluene) was prepared following the literature method.1 (S)-(−)-Betti base [(S)-5a] was prepared according to the literature.2–3

2. Synthesis of Chiral Ligands

The bis-ProPhenol ligands were prepared as previously reported procedure.4–5

Ligand 1. Yield 44%; white solid; [α]D20  = +129° (c = 1.0, CHCl3); mp 84–85 °C. 1H NMR (300 MHz, CDCl3): δ 7.35–7.30 (m, 4H), 7.25–7.23 (m, 12H), 7.21–7.08 (m, 6H), 6.73 (s, 2H), 4.24 (d, J = 12.6 Hz, 2H), 3.32 (s, 1H), 3.20 (dd, J = 4.2, 12.6 Hz, 4H), 2.88–2.81 (m, 6H), 2.66 (t, J = 12.0 Hz, 4H), 2.41 (dd, J = 7.8, 18.0 Hz, 2H), 2.20 (s, 3H), 2.03–1.96 (m, 2H), 1.83–1.73 (m, 6H). 13C NMR (100 MHz, CDCl3): δ 138.0, 137.3, 131.4, 130.7, 129.3, 128.1, 127.9, 126.0, 125.6, 69.3, 60.4, 55.0, 43.2, 41.0, 27.9, 25.0, 20.5.

3. Preparation of Ts-imines

3.1 Preparation of aryl aldimine6

Titanium tetrachloride (1.05 mL, 9.5 mmol) in dry dichloromethane (10 mL) was added dropwisely to a stirred ice-cooled solution of the aldehyde (17 mmol), sulphonamide (17 mmol) and anhydrous triethylamine (5.76 mL, 57 mmol) in dry dichloromethane (46 mL). After the addition was complete, the mixture was stirred at 0 °C for 1 h and at room temperature for 1 h. The titanium dioxide was removed by suction filtration through Celite and washed with dichloromethane (40 mL). Rotary evaporation of the filtrate gave a solid mixture of the imine and triethylamine hydrochloride which was broken up and stirred at room temperature for 30 min in dry toluene. The residual
triethylamine hydrochloride was removed by suction filtration and the residue extracted a second time. Concentration of the toluene extracts gave the crude \(N\)-sulphonylimine, which was recrystallized from petroleum ether and ethyl acetate.

### 3.2 Preparation of \((E)\)-\(N\)-butylidene 4-methylbenzenesulphonamide

A mixture of TsNH\(_2\) (1.71 g, 10.0 mmol), TolSO\(_2\)Na (1.78 g, 10.0 mmol), and sulfamic acid (1.94 g, 20.0 mmol) was dissolved in water–methanol (1:1, 30 mL) by stirring. \(n\)-Butyraldehyde (0.72 g, 0.9 mL, 10.0 mmol) was added in one portion. The reaction mixture was stirred for 12 h at room temperature. The white solid product was collected by filtration, washed with water (2 \(\times\) 10 mL) and hexane (10 mL), and then dissolved in CH\(_2\)Cl\(_2\) (50 mL). Saturated aqueous NaHCO\(_3\) solution (50 mL) was added and the biphasic liquid was stirred for 2 h at room temperature. The organic phase was separated and the aqueous phase was extracted with CH\(_2\)Cl\(_2\) (3\(\times\)10 mL). The combined organic phase was dried (MgSO\(_4\)) and the solvent was vacuum evaporated. The residue obtained was pure \((E)\)-\(N\)-butylidene 4-methylbenzenesulphonamide.

### 4. Typical Procedure for aza-Friedel-Crafts Reaction of 2-Naphthol with PG-imine

Under a nitrogen atmosphere, to a room temperature solution of ligand 2 (192 mg, 0.3 mmol) in toluene (4 mL) in Schlenk tube was added dropwisely a solution of diethylzinc (0.68 mL, 0.6 mmol) and continued to stir for 1 h to give a solution of complex 2 (0.75 M in toluene). 2-Naphthol (43 mg, 0.3 mmol) and Ts-imine or \(N\)-Boc imine (0.9 mmol) were added and the reaction was stirred for 48 h at 30°C. After the reaction was completed, the mixture was quenched with saturated ammonium chloride solution (5 mL) and ethyl acetate (5 mL). The organic layer was separated and the aqueous phase was extracted with ethyl acetate (3\(\times\)5 mL). The combined organic layers were dried over sodium sulfate. The solvent was removed under reduced pressure using a rotary evaporator. The residue obtained was purified by column chromatography using DCM : petroether : EtOAc = 10 : 10 : 1 to give the desired product.

\(N\)-((2-Hydroxynaphthalen-1-yl)(phenyl)methyl)-4-methylbenzenesulfonamide (4a). Yield 90%; light yellow solid; \([\alpha]_D^{20} = -55^\circ\) (c = 1.0, CHCl\(_3\)); mp 142–144 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 7.72 (d, \(J = 7.2\) Hz, 1H), 7.70 (d, \(J = 4.4\) Hz, 1H), 7.65–7.50 (m, 1H), 7.40–7.37 (m, 1H), 7.33–7.30 (m, 5H), 7.25–7.20 (m, 3H), 6.87–6.83 (m, 1H), 6.64 (d, \(J = 8.0\) Hz, 3H), 6.48 (s, 1H), 6.39 (d, \(J = 8.4\) Hz, 1H), 2.09 (s, 3H). \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\): 151.1, 142.8, 139.9, 135.9, 132.3, 129.6, 128.8, 128.7, 128.3, 127.2, 127.1, 126.7, 126.5, 123.3, 121.8, 118.1, 117.3, 54.4, 21.1. HRMS (ESI) exact mass cacld for (C\(_{24}\)H\(_{21}\)NO\(_3\)S\(\text{+Na}\)) requires 426.1140, found 426.1134. Enantiomeric excess: 96%, determined by HPLC (Chiralcel OD-H, \(n\)-hexane/i-PrOH = 95:5, flow rate: 1.0 mL/min): minor isomer: \(t_R\) = 20.36 min; major isomer: \(t_R\) = 25.71 min.
N-((2-Fluorophenyl)(2-hydroxynaphthalen-1-yl)methyl)-4-methylbenzenesulfonamide (4b).

Yield 92%; light yellow solid; [α]D20 = −88° (c = 1.0, CHCl3); mp 132–134 °C. 1H NMR (400 MHz, CDCl3) δ: 7.84 (d, J = 8.8 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.48–7.42 (m, 5H), 7.30–7.25 (m, 1H), 7.19–7.14 (m, 1H), 6.97–9.92 (m, 2H), 6.85 (d, J = 8.8 Hz, 1H), 6.77 (d, J = 8.0 Hz, 2H), 6.66 (s, 1H), 2.15 (s, 3H).

13C NMR (100 MHz, CDCl3) δ: 159.9 (d, J = 247 Hz), 151.7, 143.1, 135.8, 131.7, 129.8, 129.4 (d, J = 9 Hz), 128.9 (d, J = 7 Hz), 128.4, 126.9 (d, J = 11 Hz), 126.8, 126.7, 126.4, 124.1, 124.0, 123.3, 121.8 (d, J = 3 Hz), 118.3, 115.9, 115.3 (d, J = 22 Hz), 49.7 (d, J = 3 Hz), 21.2.

HRMS (ESI) exact mass calcld for (C24H20FNO3S+Na) requires 444.1046, found 444.1040. Enantiomeric excess: 82%, determined by HPLC (Chiralcel OD-H, n-hexane/i-PrOH = 98:2, flow rate: 1.0 mL/min): minor isomer: tR = 63.76 min; major isomer: tR = 73.34 min.

N-((4-Fluorophenyl)(2-hydroxynaphthalen-1-yl)methyl)-4-methylbenzenesulfonamide (4c).

Yield 88%; light yellow solid; [α]D20 = −60° (c = 1.0, CHCl3); mp 130–131 °C. 1H NMR (400 MHz, CDCl3) δ: 7.70 (d, J = 8.8 Hz, 1H), 7.65 (d, J = 7.6 Hz, 1H), 7.52 (d, J = 8.8 Hz, 1H), 7.43–7.39 (m, 1H), 7.32–7.24 (m, 4H), 6.92–6.87 (m, 3H), 6.82 (d, J = 8.8 Hz, 3H), 6.65 (d, J = 8.0 Hz, 1H), 6.37–6.31 (m, 1H), 2.09 (s, 3H).

13C NMR (100 MHz, CDCl3) δ: 162.0 (d, J = 245 Hz), 150.8, 142.9, 136.2, 135.7 (d, J = 3 Hz), 132.2, 129.8, 129.0, 128.7, 128.5 (d, J = 7 Hz), 127.3, 126.6, 123.6, 121.8, 118.0, 117.5, 115.3, 115.1, 53.8, 21.2. HRMS (ESI) exact mass calcld for (C24H20FNO3S+Na) requires 444.1046, found 444.1040. Enantiomeric excess: 93%, determined by HPLC (Chiralcel OD-H, n-hexane/i-PrOH = 95:5, flow rate: 1.0 mL/min): major isomer: tR = 15.89 min; minor isomer: tR = 19.91 min.

N-((2-Hydroxynaphthalen-1-yl)(o-tolyl)methyl)-4-methylbenzenesulfonamide (4d).

Yield 83%; light yellow solid; [α]D20 = −195° (c = 1.0, CHCl3); mp 152–154 °C. 1H NMR (400 MHz, CDCl3) δ: 7.69 (d, J = 8.0 Hz, 1H), 7.61 (d, J = 8.8 Hz, 1H), 7.56 (d, J = 8.8 Hz, 1H), 7.41–7.28 (m, 4H), 7.32–7.24 (m, 4H), 6.92–6.87 (m, 3H), 6.82 (d, J = 8.8 Hz, 3H), 6.65 (d, J = 8.0 Hz, 1H), 6.37–6.31 (m, 1H), 2.09 (s, 3H). 13C NMR (100 MHz, DMSO-d6) δ: 153.3, 142.1, 138.8, 138.2, 136.7, 132.6, 130.9, 129.6, 128.7, 128.7, 127.5, 126.5, 126.4, 125.7, 122.6, 118.4, 116.1, 52.5, 21.3, 19.7. HRMS (ESI) exact mass calcld for (C25H23NO3S+Na) requires 440.1296, found 440.1291. Enantiomeric excess: 83%, determined by HPLC (Chiralcel OD-H, n-hexane/i-PrOH = 95:5, flow rate: 1.0 mL/min): minor isomer: tR = 13.80 min; major isomer: tR = 23.40 min.

N-((2-Hydroxynaphthalen-1-yl)(p-tolyl)methyl)-4-methylbenzenesulfonamide (4e).

Yield 87%; light yellow solid; [α]D20 = −71° (c = 1.0, CHCl3); mp 131–132 °C. 1H NMR (400 MHz, CDCl3)
\[ \delta: 7.72 \text{ (d, } J = 8.4 \text{ Hz, 1H)}, 7.64 \text{ (d, } J = 7.6 \text{ Hz, 1H)}, 7.49 \text{ (d, } J = 8.8 \text{ Hz, 1H)}, 7.40-7.39 \text{ (m, 1H)}, 7.33-7.28 \text{ (m, 2H)}, 7.18 \text{ (d, } J = 8.0 \text{ Hz, 2H)}, 7.03 \text{ (d, } J = 8.8 \text{ Hz, 1H)}, 6.82 \text{ (d, } J = 8.8 \text{ Hz, 1H)}, 6.66-6.58 \text{ (m, 3H)}, 6.51 \text{ (s, 1H)}, 6.36 \text{ (d, } J = 8.8 \text{ Hz, 1H)}, 2.27 \text{ (s, 3H)}, 2.09 \text{ (s, 3H)} \]

\[ ^{13}C \text{ NMR (100 MHz, CDCl}_3): \delta: 151.1, 142.7, 136.9, 136.1, 132.3, 129.5, 128.9, 128.7, 128.3, 127.0, 126.7, 126.6, 123.2, 121.9, 118.2, 117.4, 54.3, 21.1, 21.0 \]

HRMS (ESI) exact mass cacld for (C\(_{25}\)H\(_{23}\)NO\(_3\)S+Na) requires 440.1296, found 440.1291. Enantiomeric excess: 90%, determined by HPLC (Chiralcel AD-H, \(n\)-hexane/\(i\)-PrOH = 80:20, flow rate: 1.0 mL/min): major isomer: \(t_R = 10.93\) min; minor isomer: \(t_R = 14.48\) min.

\(N\)-((2-Chlorophenyl)(2-hydroxynaphthalen-1-yl)methyl)-4-methylbenzenesulfonamide (4f).

Yield 92%; white solid; \([\alpha]_{D}^{20} = -193^\circ \text{ (c = 1.0, CHCl}_3); \text{ mp 146–148 °C.} \)

\(^1H \text{ NMR (400 MHz, CDCl}_3\) \(\delta: 7.71-7.67 \text{ (m, 2H)}, 7.59 \text{ (d, } J = 9.2 \text{ Hz, 1H)}, 7.47 \text{ (d, } J = 8.4 \text{ Hz, 2H)}, 7.42-7.28 \text{ (m, 4H)}, 7.20-7.18 \text{ (m, 1H)}, 7.16-7.05 \text{ (m, 1H)}, 6.95 \text{ (d, } J = 8.0 \text{ Hz, 2H)}, 6.89 \text{ (d, } J = 8.8 \text{ Hz, 1H)}, 6.71 \text{ (s, 1H)}, 5.90 \text{ (s, 1H)}, 2.28 \text{ (s, 3H)} \)

\[^{13}C \text{ NMR (100 MHz, DMSO-\_d}_6\) \(\delta: 153.8, 142.4, 139.0, 138.6, 132.5, 132.4, 131.4, 129.5, 129.1, 128.8, 128.5, 126.8, 126.5, 122.8, 122.6, 118.7, 116.1, 52.3, 21.3 \)

HRMS (ESI) exact mass cacld for (C\(_{24}\)H\(_{20}\)ClNO\(_3\)S+Na) requires 460.0750, found 460.0745. Enantiomeric excess: 80%, determined by HPLC (Chiralcel OD-H, \(n\)-hexane/\(i\)-PrOH = 95:5, flow rate: 1.0 mL/min): minor isomer: \(t_R = 22.26\) min; major isomer: \(t_R = 36.40\) min.

\(N\)-((3-Chlorophenyl)(2-hydroxynaphthalen-1-yl)methyl)-4-methylbenzenesulfonamide (4g).

Yield 90%; light yellow solid; \([\alpha]_{D}^{20} = -30^\circ \text{ (c = 1.0, CHCl}_3); \text{ mp 58–60 °C.} \)

\(^1H \text{ NMR (400 MHz, CDCl}_3\) \(\delta: 7.72 \text{ (d, } J = 8.4 \text{ Hz, 2H)}, 7.67 \text{ (d, } J = 8.0 \text{ Hz, 1H)}, 7.55 \text{ (d, } J = 8.8 \text{ Hz, 1H)}, 7.45-7.29 \text{ (m, 4H)}, 7.17-7.15 \text{ (m, 3H)}, 6.81 \text{ (d, } J = 8.8 \text{ Hz, 1H)}, 6.66 \text{ (d, } J = 8.0 \text{ Hz, 2H)}, 6.55 \text{ (s, 1H)}, 6.37 \text{ (s, 1H)}, 5.96 \text{ (s, 1H)}, 2.11 \text{ (s, 3H)} \)

\[^{13}C \text{ NMR (75 MHz, CDCl}_3\) \(\delta: 150.8, 142.9, 142.3, 135.9, 134.2, 132.1, 129.9, 129.5, 128.8, 128.7, 128.4, 127.4, 127.3, 126.8, 126.5, 125.0, 123.4, 121.6, 117.9, 116.9, 53.8, 21.1 \)

HRMS (ESI) exact mass cacld for (C\(_{24}\)H\(_{20}\)ClNO\(_3\)S+Na) requires 460.0750, found 460.0745. Enantiomeric excess: 74%, determined by HPLC (Chiralcel OJ-H, \(n\)-hexane/\(i\)-PrOH = 80:20, flow rate: 1.0 mL/min): major isomer: \(t_R = 15.93\) min; minor isomer: \(t_R = 24.03\) min.

\(N\)-((4-Chlorophenyl)(2-hydroxynaphthalen-1-yl)methyl)-4-methylbenzenesulfonamide (4h).

Yield 89%; white solid; \([\alpha]_{D}^{20} = -47^\circ \text{ (c = 1.0, CHCl}_3); \text{ mp 140–142 °C.} \)

\(^1H \text{ NMR (400 MHz, CDCl}_3\) \(\delta: 7.71 \text{ (d, } J = 8.4 \text{ Hz, 1H)}, 7.67 \text{ (d, } J = 7.6 \text{ Hz, 1H)}, 7.55 \text{ (d, } J = 8.8 \text{ Hz, 1H)}, 7.44-7.40 \text{ (m, 1H)}, 7.34-7.30 \text{ (m, 3H)}, 7.24-7.17 \text{ (m, 3H)}, 6.80 \text{ (d, } J = 8.8 \text{ Hz, 1H)}, 6.60 \text{ (d, } J = 8.0 \text{ Hz, 2H)}, 6.53 \text{ (s, 1H)}, 6.37 \text{ (s, 1H)}, 5.96 \text{ (s, 1H)}, 2.11 \text{ (s, 3H)} \)

\[^{13}C \text{ NMR (75 MHz, CDCl}_3\) \(\delta: 150.8, 142.9, 138.6, 136.1, 133.1, 132.1, 129.9, 128.9, 128.7, 128.4, 128.1, 127.4, 126.5, 123.5, 121.7, 117.9, 117.3, 53.7, 21.2 \)

HRMS (ESI) exact mass cacld for (C\(_{24}\)H\(_{20}\)ClNO\(_3\)S+Na) requires 460.0750, found 460.0745.
Enantiomeric excess: 98%, determined by HPLC (Chiralcel OD-H, n-hexane/i-PrOH = 95:5, flow rate: 1.0 mL/min): major isomer: $t_R = 16.26$ min; minor isomer: $t_R = 20.49$ min.

$N$-((2-Hydroxynaphthalen-1-yl)(2-methoxyphenyl)methyl)-4-methylbenzenesulfonamide (4i). Yield 91%; light yellow solid; [$\alpha$]$^\circ_{D} = -186^\circ$ (c = 1.0, CHCl$_3$); mp 87–89 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.68 (d, $J$ = 7.6 Hz, 1H), 7.61 (d, $J$ = 8.4 Hz, 1H), 7.55 (d, $J$ = 8.8 Hz, 1H), 7.41–7.30 (m, 4H), 7.19–7.17 (m, 1H), 7.09 (d, $J$ = 3.3 Hz, 1H), 7.00–6.97 (m, 1H), 6.79 (d, $J$ = 8.0 Hz, 1H), 6.71 (d, $J$ = 8.8 Hz, 1H), 6.60 (s, 1H), 5.79 (s, 1H), 2.60 (s, 3H), 2.23 (s, 3H). $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$: 156.3, 153.2, 142.2, 138.5, 132.5, 129.4, 129.4, 129.3, 129.0, 128.5, 128.5, 126.7, 126.2, 123.4, 122.6, 120.1, 118.8, 118.2, 111.1, 55.6, 49.2, 21.3. HRMS (ESI) exact mass calcd for (C$_{25}$H$_{23}$NO$_4$S$+Na$) requires 456.1245, found 456.1336. Enantiomeric excess: 89%, determined by HPLC (Chiralcel OD-H, n-hexane/i-PrOH = 95:5, flow rate: 1.0 mL/min): minor isomer: $t_R = 30.68$ min; major isomer: $t_R = 42.92$ min.

$N$-((2-Hydroxynaphthalen-1-yl)(4-methoxyphenyl)methyl)-4-methylbenzenesulfonamide (4j). Yield 82%; light yellow solid; [$\alpha$]$^\circ_{D} = -69^\circ$ (c = 1.0, CHCl$_3$); mp 65–67 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.72 (d, $J$ = 8.8 Hz, 1H), 7.66 (d, $J$ = 8.0 Hz, 1H), 7.54 (d, $J$ = 8.8 Hz, 1H), 7.42–7.38 (m, 1H), 7.34–7.29 (m, 3H), 7.21 (d, $J$ = 8.8 Hz, 2H), 6.81–6.76 (m, 1H), 6.70 (d, $J$ = 8.0 Hz, 2H), 6.37 (d, $J$ = 8.8 Hz, 2H), 6.32 (d, $J$ = 8.8 Hz, 2H), 6.09 (s, 1H), 3.74 (s, 3H), 2.13 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 158.9, 151.1, 142.8, 136.2, 132.3, 131.9, 129.6, 129.0, 128.7, 128.4, 128.1, 127.1, 126.7, 123.4, 121.9, 118.2, 117.5, 113.8, 55.2, 54.3, 21.2. HRMS (ESI) exact mass calcd for (C$_{25}$H$_{23}$NO$_4$S$+Na$) requires 456.1245, found 456.1240. Enantiomeric excess: 90%, determined by HPLC (Chiralcel AD-H, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min): major isomer: $t_R = 11.75$ min; minor isomer: $t_R = 22.28$ min.

$N$-((4-Bromophenyl)(2-hydroxynaphthalen-1-yl)methyl)-4-methylbenzenesulfonamide (4k). Yield 95%; light yellow solid; [$\alpha$]$^\circ_{D} = -33^\circ$ (c = 1.0, CHCl$_3$); mp 139–140 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.71–7.65 (m, 2H), 7.52 (d, $J$ = 9.2 Hz, 1H), 7.42 (d, $J$ = 7.2 Hz, 1H), 7.32–7.26 (m, 5H), 7.16 (d, $J$ = 8.4 Hz, 2H), 6.81 (d, $J$ = 8.8 Hz, 1H), 6.65 (d, $J$ = 8.0 Hz, 2H), 6.33 (s, 1H), 2.10 (s, 3H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$: 150.9, 142.9, 139.2, 136.0, 132.1, 131.3, 129.8, 128.8, 128.7, 128.5, 128.4, 127.3, 126.5, 123.5, 121.6, 121.2, 117.9, 117.1, 53.8, 21.2. HRMS (ESI) exact mass calcd for (C$_{24}$H$_{20}$BrNO$_3$S$+Na$) requires 504.0245, found 504.0239. Enantiomeric excess: 92%, determined by HPLC (Chiralcel OD-H, n-hexane/i-PrOH = 95:5, flow rate: 1.0 mL/min): major isomer: $t_R = 16.50$ min; minor isomer: $t_R = 21.51$ min.

$N$-(1-(2-Hydroxynaphthalen-1-yl)butyl)-4-methylbenzenesulfonamide (4l). Yield 74%; light
yellow solid; \([\alpha]_{D}^{20} = -111^\circ (c = 1.0, \text{CHCl}_3)\); mp 143–144 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 7.77 (d, \(J = 8.4\) Hz, 1H), 7.59 (d, \(J = 8.0\) Hz, 1H), 7.44–7.39 (m, 2H), 7.30–7.25 (m, 4H), 6.77 (d, \(J = 8.4\) Hz, 1H), 6.58 (d, \(J = 7.6\) Hz, 2H), 6.46 (s, 1H), 5.13 (d, \(J = 7.6\) Hz, 1H), 2.04 (s, 3H), 1.88–1.66 (m, 2H), 1.53 (t, \(J = 6.4\) Hz, 1H), 1.32–1.27 (m, 1H), 0.92 (t, \(J = 6.4\) Hz, 3H). \(^13\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\): 150.9, 142.6, 136.1, 132.0, 128.7, 128.5, 128.25, 126.6, 126.4, 123.0, 121.6, 118.2, 118.0, 52.1, 37.0, 21.1, 19.6, 13.7. EI–MS (\(m/z\)): 361 (4) \([\text{M}^+]\), 326 (14) \([\text{M-C}_7\text{H}_4\text{NO}_3\text{S}]\), 226 (12) \([\text{M-C}_{11}\text{H}_4\text{NO}_2\text{S}]\), 198 (65) \([\text{M-C}_7\text{H}_7\text{O}]\), 155 (56) \([\text{M-C}_{11}\text{H}_7\text{O}]\), 91 (100) \([\text{M-C}_5\text{H}_3\text{}]\). Enantiomeric excess: 91%, determined by HPLC (Chiralcel OD-H, \(n\)-hexane/i-PrOH = 95:5, flow rate: 1.0 mL/min): major isomer: \(t_R = 9.93\) min; minor isomer: \(t_R = 12.15\) min.

**tert-Butyl (2-hydroxynaphthalen-1-yl)(phenyl)methylcarbamate (4m).** Yield 88%; white solid; \([\alpha]_{D}^{20} = +26^\circ (c = 1.0, \text{CHCl}_3)\); mp 140–142 °C. \(^1\)H NMR (400 MHz, DMSO-\(d_6\)) \(\delta\): 10.14 (s, 1H), 7.95 (d, \(J = 7.2\) Hz, 1H), 7.82 (d, \(J = 8.0\) Hz, 1H), 7.78 (d, \(J = 8.8\) Hz, 1H), 7.44–7.14 (m, 9H), 6.81 (d, \(J = 8.4\) Hz, 1H), 1.34 (s, 9 H). \(^13\)C NMR (100 MHz, DMSO-\(d_6\)) \(\delta\): 155.3, 152.8, 142.7, 132.1, 129.2, 128.6, 128.3, 128.2, 128.1, 126.7, 126.3, 125.9, 122.6, 119.1, 118.5, 78.4, 49.8, 28.2. EI–MS (\(m/z\)): 349 (2), 293 (4), 249 (5), 231 (100), 202 (14). Enantiomeric excess: 91%, determined by HPLC (Chiralcel OD-H, \(n\)-hexane/i-PrOH = 95:5, flow rate: 1.0 mL/min): major isomer: \(t_R = 10.62\) min; minor isomer: \(t_R = 8.77\) min.

5. **Synthesis of compound (S)-4a**

![](image)

To a stirred solution of (S)-5a (25 mg, 0.1 mmol) in a mixture of water (1 mL) and dioxane (2 mL) was added NaHCO\(_3\) (84 mg, 0.1 mmol). After the reaction mixture was stirred for 30 min, TsCl (23 mg, 0.1 mmol) was added at 0°C. The reaction mixture was stirred at 0°C and monitored by TLC until TsCl was disappeared. The solvent was removed under reduced pressure using a rotary evaporator. The residue was purified by column chromatography to give (S)-4a (29 mg, 72%), \([\alpha]_{D}^{20} = +54^\circ (c = 1.0, \text{CHCl}_3)\).

6. **References**


7. NMR Spectra of Compounds 4a–l

$^1$H NMR of Compound 4a
$^{13}$C NMR of Compound 4a
$^1$H NMR of Compound 4c
$^{13}$C NMR of Compound 4c
$^1$H NMR of Compound 4d
\textsuperscript{13}C NMR of Compound 4d
$^1$H NMR of Compound 4e
$^{13}$C NMR of Compound 4e

![NMR Spectrum of Compound 4e]
$^1$H NMR of Compound 4f
$^1$H NMR of Compound 4g
$^{13}$C NMR of Compound 4g
$^1$H NMR of Compound 4h
$^{13}\text{C}$ NMR of Compound 4h
$^1$H NMR of Compound 4i
$^{13}$C NMR of Compound 4i

![Graph of the spectrum showing various chemical shifts and peaks for Compound 4i.]
$^1$H NMR of Compound 4j
$^{13}$C NMR of Compound 4j
$^1$H NMR of Compound 4k
$^{13}$C NMR of Compound 4k
$^{13}$C NMR of Compound 4l
8. HPLC Spectra of Compounds 4a–m

HPLC of Compound 4a

處理通道: W2996 PDA 254.0 nm at 1.2

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處理通道: PDA 270.0 纳米

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HPLC of Compound 4b

HPLC of Compound 4c

-34-
HPLC of Compound 4d

处理通道: PDA 231.6 纳米

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HPLC of Compound 4e

处理通道: PDA 226.5 纳米

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HPLC of Compound 4f

处理通道：PDA 223.7 纳米

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处理通道：PDA 228.5 纳米

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HPLC of Compound 4g

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处理通道：PDA 229.9 纳米

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HPLC of Compound 4h

处理通道: PDA 269.7 纳米

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HPLC of Compound 4k

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HPLC of Compound 4l

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HPLC of Compound 4m