Asymmetric synthesis of 2-arylpyrrolidines starting from $\gamma$-chloro $N$-(tert-butanesulfinyl)ketimines

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Received (in XXX, XXX) Xth XXXXXXXXX 200X, Accepted Xth XXXXXXXXX 200X
First published on the web Xth XXXXXXXXX 200X
DOI: 10.1039/b000000x

Experimental data

General Experimental Methods

$^1$H NMR (300 MHz) and $^{13}$C NMR (75 MHz) spectra were recorded with a JEOL EX 300 Eclipse NMR spectrometer. Peak assignments were obtained with the aid of DEPT, 2D-COSY and 2D-HSQC spectra. The compounds were diluted in deuterated solvents and the used solvent is indicated for each compound. Low resolution mass spectra were recorded with an Agilent 1100 Series VS (ES = 4000 V) mass spectrometer. IR spectra were recorded on a Perkin-Elmer Spectrum BX FT-IR spectrophotometer. All compounds were analysed in neat form with an ATR (Attenuated Total Reflectance) accessory. Melting points of crystalline compounds were measured with a Büchi 540 apparatus. The elemental analysis was performed with a Perkin-Elmer 2400 Elemental Analyzer. The purification of reaction mixtures by column chromatography was performed in a glass column with silica gel (Acros, particle size, 0.035-0.070 mm, pore diameter ca. 6 nm). TLC was performed on glass plates coated with silica gel 60 with F254 indicator (Merck, 0.25 mm), using UV and KMnO$_4$ as a visualizing agent.

All common reagents and solvents were obtained from commercial suppliers and used without further purification. Dichloromethane was distilled over calcium hydride, while diethyl ether and
toluene was dried over sodium benzophenone ketyl. Other solvents were used as received from the supplier.

NMR data are reported as follows: chemical shift, integration, multiplicity (s: singlet, d: doublet, t: triplet, q: quadruplet, br: broad, m: multiplet), coupling constants ($J$ in Hz), allocation of the peaks.

**Typical procedure for the synthesis of (R,S)-N-[1-aryl-4-chlorobutylidene]-tert-butanesulfinamides 1**

As a representative example, the synthesis of (R,S)-N-[4-chloro-1-phenylbutylidene]-tert-butanesulfinamide 1a is described here. Titanium(IV) ethoxide (12.49 g, 54.8 mol) and (R,S)-tert-butanesulfinamide (3.32 g, 27.4 mmol) were added to a solution of 4-chlorobutyrophenone (5 g, 27.4 mmol) in tetrahydrofuran (30 mL). The reaction was stirred for 48 hours at reflux temperature. After cooling, brine was added, and the resulting mixture was subsequently filtered over Celite®. The solution was extracted with EtOAc (3 x 25 mL), and the combined organic layers were dried (MgSO$_4$), filtered and evaporated under reduced pressure to afford (R,S)-1a (6.73 g) in 86% yield. The crude compound was purified by column chromatography (petroleum ether/EtOAc 17/3) to yield (R,S)-N-[4-chloro-1-phenylbutylidene]-tert-butanesulfinamide (R,S)-1a in 75% yield (5.87 g) as a brown oil. **Chromatography:** petroleum ether/EtOAc 17/3 $R_f$ = 0.10;

**Elemental analysis (%)**: Found: C, 58.50; H, 7.21; N, 4.98. C$_{14}$H$_{20}$ClNOS requires C, 58.83; H, 7.05; N, 4.90; **IR**: $\nu_{\text{max}}$/cm$^{-1}$ 2956, 1570, 1360, 1077; $\delta$$_{t}$ (300 MHz, CDCl$_3$, Me$_4$Si) 1.33 (9H, s, tBu), 2.03-2.27 (2H, m, CH$_2$CH$_2$Cl), 3.23-3.36 and 3.40-3.52 (2H, m, CH$_2$-C=N), 3.64 (2H, t, $J$ = 6.3 Hz, CH$_2$Cl), 7.40-7.51 and 7.87-7.89 (5H, m, C$_6$H$_5$); $\delta$$_{c}$ (75 MHz, CDCl$_3$, Me$_4$Si) 22.70 (CH$_3$, tBu), 30.03 (CH$_2$-C=N), 31.62 (CH$_2$-CH$_2$Cl), 44.64 (CH$_2$Cl), 57.85 (C$_q$, tBu), 127.40 (CH,
((S,S)-N-[4-Chloro-1-phenylbutylidene]-tert-butanesulfinamide 1a (63%)

\[\alpha_D = +11.9 \quad (c 0.64, \text{CH}_2\text{Cl}_2)\].

((R,S)-N-[4-Chloro-1-(4-methylphenyl)butylidene]-tert-butanesulfinamide 1b (68%)

Brown oil; Chromatography: petroleum ether/EtOAc 17/3 \(R_f = 0.19\); Elemental analysis (%): Found: C, 59.94; H, 7.48; N, 4.73. C_{15}H_{22}ClNOS requires C, 60.08; H, 7.40; N, 4.67; IR: \(\nu_{\text{max}}/\text{cm}^{-1} 2958, 1590, 1455, 1360, 1077\); \(\delta_H (300 \text{ MHz, CDCl}_3, \text{Me}_4\text{Si}) 1.32 (9H, s, tBu), 2.06-2.27 (2H, m, CH_2CH_2Cl), 2.41 (3H, s, CH_3-Ar), 3.21-3.34 and 3.38-3.49 (2H, m, CH_2-C=N), 3.63-3.67 (2H, m, CH_2Cl), 7.24 (2H, d, \(J = 7.4 \text{ Hz, CH, Ar}\)), 7.79 (2H, d, \(J = 7.4 \text{ Hz, CH, Ar}\)); \(\delta_C (75 \text{ MHz, CDCl}_3, \text{Me}_4\text{Si}) 21.39 (\text{CH}_3, \text{CH}_3-\text{Ar}), 22.61 (\text{CH}_3, tBu), 29.89 (\text{CH}_2-\text{C}=\text{N}), 31.67 (\text{CH}_2-\text{CH}_2\text{Cl}), 44.57 (\text{CH}_2\text{Cl}), 57.58 (\text{C}_q, tBu), 127.38 (\text{CH}, \text{Ar}), 129.35 (\text{CH}, \text{Ar}), 134.66 (\text{C}_q-\text{C}=\text{N, Ar}), 142.27 (\text{C}_q-\text{CH}_3, \text{Ar}), 177.84 (\text{C}=\text{N}); m/z (ESI) 300.3/302.3 ([M+H]^+, 100%); \(\alpha_D = +26.9 \quad (c 1.07, \text{CH}_2\text{Cl}_2)\].

((S,S)-N-[4-Chloro-1-(4-methylphenyl)butylidene]-tert-butanesulfinamide 1b (66%)

\[\alpha_D = -10.0 \quad (c 1.00, \text{CH}_2\text{Cl}_2)\].

((R,S)-N-[4-Chloro-1-(4-chlorophenyl)butylidene]-tert-butanesulfinamide 1c (62%)

Orange oil; Chromatography: petroleum ether/EtOAc 17/3 \(R_f = 0.16\); Elemental analysis (%): Found: C, 52.44; H, 6.02; N, 4.29. C_{14}H_{10}Cl_2NOS requires C, 52.50; H, 5.98; N, 4.37; IR: \(\nu_{\text{max}}/\text{cm}^{-1} 2959, 1585, 1456, 1360, 1077\); \(\delta_H (300 \text{ MHz, CDCl}_3, \text{Me}_4\text{Si}) 1.33 (9H, s, tBu), 2.03-2.27 (2H, m, CH_2CH_2Cl), 3.22-3.34 and 3.38-3.50 (2H, m, CH_2-\text{C}=\text{N}), 3.63-3.67 (2H, m,
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CH₂Cl), 7.39-7.44 and 7.81-7.84 (4H, m, C₆H₄); δ̇ (75 MHz, CDCl₃, Me₄Si) 22.70 (CH₃, tBu), 29.80 (CH₂-C=N), 31.56 (CH₂-CH₂Cl), 44.57 (CH₂Cl), 57.97 (Cq, tBu), 128.73 (CH, Ar), 128.91 (CH, Ar), 135.79 (Cq, Ar), 137.95 (Cq, Ar), 176.67 (C=N); m/z (ESI) 320.2/322.3/324.2 ([M+H]⁺, 100%); [α]D = +43.4 (c 1.10, CH₂Cl₂).

(S₅)-N-[4-Chloro-1-(4-chlorophenyl)butylidene]- tert-butanesulfinamide 1c (73%)

[α]D = -51.9 (c 0.99, CH₂Cl₂)

(R₅)-N-[4-Chloro-1-(4-methoxyphenyl)butylidene]- tert-butanesulfinamide 1d (63%)

Orange oil; Chromatography: hexane/EtOAc 17/3 Rf = 0.08; Elemental analysis (%): Found: C, 57.21; H, 7.13; N, 4.17. C₁₅H₂₂ClNO₂S requires C, 57.04; H, 7.02; N, 4.43; IR: νmax/cm⁻¹ 2958, 1586, 1456, 1360, 1253, 1063; δ̇ (300 MHz, CDCl₃, Me₄Si) 1.32 (9H, s, tBu), 2.05-2.29 (2H, m, CH₂CH₂Cl), 3.21-3.30 and 3.38-3.47 (2H, m, CH₂-C=N), 3.63-3.68 (2H, m, CH₂Cl), 3.86 (3H, s, OMe), 6.91-6.96 and 7.87-7.90 (4H, m, C₆H₄); δ̇ (75 MHz, CDCl₃, Me₄Si) 22.61 (CH₃, tBu), 29.91 (CH₂-C=N), 31.76 (CH₂-CH₂Cl), 44.77 (CH₂Cl), 55.39 (OMe), 57.44 (Cq, tBu), 113.95 (CH, Ar), 129.43 (CH, Ar), 129.89 (Cq-C=N, Ar), 162.59 (Cq-OMe, Ar), 177.51 (C=O); m/z (ESI) 316.3/318.3 ([M+H]⁺, 100%); [α]D = +46.2 (c 0.95, CH₂Cl₂).

(S₅)-N-[4-Chloro-1-(4-methoxyphenyl)butylidene]- tert-butanesulfinamide 1d (68%)

[α]D = -54.6 (c 1.02, CH₂Cl₂).

Typical procedure for the synthesis of N-[1-aryl-4-chlorobutyl]- tert-butanesulfinamides (R₅,R₅)-2a-d and (R₅,S₅)-2a-d

As a representative example, the synthesis of N-[4-chloro-1-phenylbutyl]- tert-butanesulfinamides (R₅,R₅)-2a and (R₅,S₅)-2a is described here. (R₅)-N-[4-chloro-1-phenylbutylidene]- tert-
butanesulfinamide 1a (1.45 g, 5.08 mmol) was dissolved in tetrahydrofuran (10 mL) and cooled to -78 °C. To the stirred solution was then added MeOH (0.33 g, 10.16 mmol) and NaBH₄ (0.38 g, 10.16 mmol). The reaction was stirred for one hour at -78 °C before quenching with NaHCO₃ (15 mL) and EtOAc (15 mL). The reaction mixture was filtered and the filtrate was extracted three times with EtOAc (20 mL). The combined organic layers were dried (MgSO₄), filtered and concentrated to furnish a mixture of N-[4-chloro-1-phenylbutyl]-tert-butanesulfinamides (Rₛ,Rₛ)-2a and (Rₛ,Sₛ)-2a in a diastereomeric ratio of 74:26. The two diastereomers were separated via column chromatography (petroleum ether/EtOAc 3/2 + 2% Et₃N) in 53% yield for (Rₛ,Rₛ)-2a (0.77 g) and 26% yield for (Rₛ,Sₛ)-2a (0.38 g). (Rₛ,Rₛ)-2a: White crystals; Chromatography: petroleum ether/EtOAc 3/2 + 2% Et₃N Rᵣ = 0.16; Melting point: 59.2 °C - 60.2 °C; Elemental analysis (%): Found: C, 58.12; H, 7.87; N, 4.63. C₁₄H₂₂ClNOS requires C, 58.42; H, 7.70; N, 4.87; IR: νmax/cm⁻¹ 3214, 2957, 1454, 1363, 1054; δH (300 MHz, CDCl₃, Me₄Si) 1.24 (9H, s, tBu), 1.52-1.82 (2H, m, CH₂CH₂Cl), 1.85-1.97 and 2.11-2.23 (2H, m, CHCH₂), 3.40 (1H, d, J = 3.3 Hz, NH), 3.48 (2H, t, J = 6.3 Hz, CH₂Cl), 4.38 (1H, d x d x d, J = 8.5 Hz, J = 5.2 Hz, J = 3.3 Hz, CHNH), 7.28-7.39 (5H, m, C₆H₅); δC (75 MHz, CDCl₃, Me₄Si) 22.58 (CH₃, tBu), 28.73 (CH₂-CH₂Cl), 33.88 (CH₂-CH₂-CH₂-CH₂Cl), 44.63 (CH₂Cl), 55.70 (C₉, tBu), 58.35 (CH-NH), 127.02 (CH, Ar), 127.93 (CH, Ar), 128.73 (CH, Ar), 141.93 (C₉, Ar); m/z (ESI) 288.3/290.3 ([M+H]⁺, 100%); [α]D = -56.3 (c 0.54, CH₂Cl₂).
(Rₛ,Sₛ)-2a: Pale yellow (off-white) crystals; Chromatography: petroleum ether/EtOAc 3/1 + 2% Et₃N Rᵣ = 0.05; Melting point: 81.5 °C - 82.5 °C; Elemental analysis (%): Found: C, 58.20; H, 8.04; N, 4.56. C₁₄H₂₂ClNOS requires C, 58.42; H, 7.70; N, 4.87; IR: νmax/cm⁻¹ 3197, 2924, 1451, 1366, 1028; δH (300 MHz, CDCl₃, Me₄Si) 1.18 (9H, s, tBu), 1.55-2.04 (4H, m, CHCH₂CH₂CH₂Cl), 3.44 (1H, dbr, J = 2.8 Hz, NH), 3.49 (2H, t x d, J = 6.6 Hz, J = 1.7 Hz,
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CH$_2$Cl), 4.39 (1H, d x d x d, $J = 8.3$ Hz, $J = 6.1$ Hz, $J = 3.3$ Hz, CH$_2$NH), 7.26-7.37 (5H, m, C$_6$H$_5$); $\delta$ (75 MHz, CDCl$_3$, Me$_4$Si) 22.52 (CH$_3$, tBu), 28.95 (CH$_2$-CH$_2$Cl), 35.86 (CH$_2$-CH), 44.55 (CH$_2$Cl), 55.56 (C$_q$, tBu), 58.77 (CH-NH), 127.55 (CH, Ar), 127.84 (CH, Ar), 128.60 (CH, Ar), 141.35 (C$_q$, Ar); m/z (ESI) 288.3/290.3 ([M+H]$^+$, 100%); $[\alpha]_D = -98.9$ (c 0.69, CH$_2$Cl$_2$).

(R$_S$,R)-N-[4-Chloro-1-(4-methylphenyl)butyl]-tert-butanesulfinamide 2b (41%)

Orange oil; Chromatography: petroleum ether/EtOAc 17/3 + 2% Et$_3$N $R_f = 0.07$; Elemental analysis (%): Found: C, 59.61; H, 8.14; N, 4.56. C$_{15}$H$_{24}$ClNOS requires C, 59.68; H, 8.01; N, 4.64; IR: $\nu_{\max}$/cm$^{-1}$ 3218, 2955, 1455, 1362, 1054; $\delta$ (300 MHz, CDCl$_3$, Me$_4$Si) 1.23 (9H, s, tBu), 1.52-1.67 and 1.68-1.79 (2H, m, CH$_2$-CH$_2$Cl), 1.81-1.94 and 2.10-2.21 (2H, m, CHCH$_2$), 2.34 (3H, s, CH$_3$-Ar), 3.36 (1H, sbr, NH), 3.48 (2H, t, $J = 6.6$ Hz, CH$_2$Cl), 4.34 (1H, d x d, $J = 8.3$ Hz, $J = 5.5$ Hz, CH$_2$NH), 7.14-7.22 (4H, m, C$_6$H$_4$); $\delta$ (75 MHz, CDCl$_3$, Me$_4$Si) 21.12 (CH$_3$, CH$_3$-Ar), 22.63 (CH$_3$, tBu), 28.84 (CH$_2$-CH$_2$Cl), 33.76 (CH$_2$-CH), 44.71 (CH$_2$Cl), 55.70 (C$_q$, tBu), 58.17 (CH-NH), 127.02 (CH, Ar), 129.52 (CH, Ar), 137.81 (C$_q$, Ar), 138.88 (C$_q$, Ar); m/z (ESI) 302.3/304.3 ([M+H]$^+$, 100%); $[\alpha]_D = -51.0$ (c 1.11, CH$_2$Cl$_2$).

(R$_S$,S)-N-[4-Chloro-1-(4-methylphenyl)butyl]-tert-butanesulfinamide 2b (11%)

Pale yellow crystals (off-white); Elemental analysis (%): Found: C, 59.58; H, 8.12; N, 4.50. C$_{15}$H$_{24}$ClNOS requires C, 59.68; H, 8.01; N, 4.64; Chromatography: petroleum ether/EtOAc 17/3 + 2% Et$_3$N $R_f = 0.02$; Melting point: 59.9 °C - 60.9 °C; IR: $\nu_{\max}$/cm$^{-1}$ 3140, 2922, 1458, 1024; $\delta$ (300 MHz, CDCl$_3$, Me$_4$Si) 1.18 (9H, s, tBu), 1.55-2.04 (4H, m, CHCH$_3$CH$_2$CH$_2$Cl), 2.35 (3H, s, CH$_3$-Ar), 3.39 (1H, dbr, $J = 2.2$ Hz, NH), 3.50 (2H, d x d x d, $J = 6.9$ Hz, $J = 5.8$ Hz, $J = 1.1$ Hz, CH$_2$Cl), 4.35 (1H, d x d x d, $J = 8.3$ Hz, $J = 6.1$ Hz, $J = 2.2$ Hz, CH$_2$NH), 7.13-7.20 (4H, m, C$_6$H$_4$); $\delta$ (75 MHz, CDCl$_3$, Me$_4$Si) 21.13 (CH$_3$, CH$_3$-Ar), 22.51 (CH$_3$, tBu), 28.95
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$$\text{CH}_2\text{-CH}_2\text{Cl}, 35.85 \text{ (CH}_2\text{-CH), 44.57 \text{ (CH}_2\text{Cl), 55.45 \text{ (C}_q\text{-tBu), 58.43 \text{ (CH-NH), 127.44 \text{ (CH, Ar), 129.26 \text{ (CH, Ar), 137.43 \text{ (C}_q\text{-Ar), 138.22 \text{ (C}_q\text{-Ar); m/z (ESI) 302.3/304.3 ([M+H]^+, 100%); [\alpha]_D = -91.6 (c 1.01, CH}_2\text{Cl}_2).}$$

$$(R_S,R)-N-[4\text{-Chloro-1-(4-chlorophenyl)butyl}-\text{tert-}\text{butanesulfinamide 2c (48%)}}$$

Orange oil; Chromatography: petroleum ether/EtOAc 1/1 + 2% Et$_3$N $R_f = 0.27$; Elemental analysis (%): Found: C, 51.88; H, 6.69; N, 4.53. C$_{14}$H$_{21}$Cl$_2$NOS requires C, 52.17; H, 6.57; N, 4.35; IR: $\nu_\text{max/cm}^{-1}$ 3214, 2957, 1491, 1363, 1053; $\delta_\text{H} \text{(300 MHz, CDCl}_3\text{, Me}_4\text{Si)}$ 1.23 (9H, s, tBu), 1.52-1.66 and 1.68-1.95 (3H, m, CHCH$_2$CH$_2$Cl), 2.09-2.21 (1H, m, CHCH(H)), 3.36 (1H, d, $J = 3.9$ Hz, NH), 3.49 (2H, t, $J = 6.3$ Hz, CH$_2$Cl), 4.35 (1H, d x d x d, $J = 8.5$ Hz, $J = 5.2$ Hz, $J = 3.9$ Hz, CHNH), 7.25-7.28 and 7.32-7.36 (4H, m, C$_6$H$_4$); $\delta_\text{C} \text{(75 MHz, CDCl}_3\text{, Me}_4\text{Si)}$ 22.60 (CH$_3$, tBu), 28.73 (CH$_2$-CH$_2$Cl), 33.83 (CH$_2$-CH$_2$), 44.57 (CH$_2$Cl), 55.91 (C$_q$, tBu), 58.02 (CH-NH), 128.50 (CH, Ar), 129.03 (CH, Ar), 133.81 (C$_q$, Ar), 140.44 (C$_q$, Ar); m/z (ESI) 322.2/324.2/326.2 ([M+H]$^+$, 100%), 218.2/220.2/222.2 ([M+H-tBuS(O)]$^+$, 50%); $[\alpha]_D = -36.0 (c 1.08, CH$_2$Cl$_2$).

$$(R_S,S)-N-[4\text{-Chloro-1-(4-chlorophenyl)butyl}-\text{tert-}\text{butanesulfinamide 2c (17%)}}$$

Yellow crystals; Chromatography: petroleum ether/EtOAc 7/3 + 2% Et$_3$N $R_f = 0.09$; Melting point: 91.5 °C - 92.5 °C; Elemental analysis (%): Found: C, 52.03; H, 6.66; N, 4.29. C$_{14}$H$_{21}$Cl$_2$NOS requires C, 52.17; H, 6.57; N, 4.35; IR: $\nu_\text{max/cm}^{-1}$ 3205, 2956, 1490, 1364, 1051; $\delta_\text{H} \text{(300 MHz, CDCl}_3\text{, Me}_4\text{Si)}$ 1.18 (9H, s, tBu), 1.51-2.04 (4H, m, CHCH$_3$CH$_2$CH$_2$Cl), 3.43 (1H, dbr, $J = 2.2$ Hz, NH), 3.50 (2H, t, $J = 6.3$ Hz, CH$_2$Cl), 4.38 (1H, d x d x d, $J = 8.0$ Hz, $J = 5.8$ Hz, $J = 2.2$ Hz, CHNH), 7.22-7.34 (4H, m, C$_6$H$_4$); $\delta_\text{C} \text{(75 MHz, CDCl}_3\text{, Me}_4\text{Si)}$ 22.51 (CH$_3$, tBu), 28.83 (CH$_2$-CH$_2$Cl), 35.76 (CH$_2$-CH$_2$Cl), 44.43 (CH$_2$Cl), 55.62 (C$_q$, tBu), 58.00 (CH-NH),
Electronic Supplementary Information

128.85 (CH, Ar), 128.97 (CH, Ar), 133.61 (C\(_q\), Ar), 139.89 (C\(_q\), Ar); \(m/z\) (ESI) 322.0/324.0/326.0 ([M+H]\(^+\), 100%); \([\alpha]_D = -75.3\) (c 0.97, CH\(_2\)Cl\(_2\)).

\((R_S,R)-N-[4-Chloro-1-(4-methoxyphenyl)butyl]-tert-butanesulfimamide 2d\) (39%)

Viscous colorless oil; Chromatography: petroleum ether/EtOAc 1/1 + 2% Et\(_3\)N \(R_f = 0.17\);
Elemental analysis (%): Found: C, 56.61; H, 7.74; N, 4.53. C\(_{15}\)H\(_{24}\)ClNO\(_2\)S requires C, 56.68; H, 7.61; N, 4.41; IR: \(\nu_{\text{max}}/\text{cm}^{-1}\) 3218, 2955, 1513, 1362, 1052; \(\delta_{H}(300 \text{ MHz, CDCl}_3, \text{Me}_4\text{Si})\) 1.23 (9H, s, tBu), 1.51-1.93 (3H, m, CHCH(H)CH\(_2\)CH\(_2\)Cl ), 2.10-2.21 (1H, m, CHCH(H)), 3.33 (1H, d, \(J = 3.3\) Hz, NH), 3.48 (2H, t, \(J = 6.6\) Hz, CH\(_2\)Cl), 3.81 (3H, s, OMe), 4.33 (1H, d x d x d, \(J = 8.3\) Hz, \(J = 5.0\) Hz, \(J = 3.3\) Hz, CHNH), 6.87-6.91 and 7.22-7.26 (4H, m, C\(_6\)H\(_4\)); \(\delta_{C}(75 \text{ MHz, CDCl}_3, \text{Me}_4\text{Si})\) 22.64 (CH\(_3\), tBu), 28.89 (C\(_H\)\(_2\)-CH\(_2\)Cl), 33.77 (C\(_H\)\(_2\)-CH), 44.74 (CH\(_2\)Cl), 55.29 (MeO), 55.68 (C\(_q\), tBu), 57.88 (CH-NH), 114.19 (CH, Ar), 128.28 (CH, Ar), 133.89 (C\(_q\)-CHN, Ar), 159.38 (C\(_q\)-OMe, Ar); \(m/z\) (ESI) 318.3/320.2 ([M+H]\(^+\), 100%); \([\alpha]_D = -38.6\) (c 1.03, CH\(_2\)Cl\(_2\)).

\((R_S,S)-N-[4-Chloro-1-(4-methoxyphenyl)butyl]-tert-butanesulfimamide 2d\) (14%)

Yellow crystals; Chromatography: petroleum ether/EtOAc 7/3 + 2% Et\(_3\)N \(R_f = 0.06\); Melting point: 77.3 °C - 78.3 °C; Elemental analysis (%): Found: C, 56.58; H, 7.44; N, 4.61. C\(_{15}\)H\(_{24}\)ClNO\(_2\)S requires C, 56.68; H, 7.61; N, 4.41; IR: \(\nu_{\text{max}}/\text{cm}^{-1}\) 3210, 2955, 1512, 1363, 1244, 1050; \(\delta_{H}(300 \text{ MHz, CDCl}_3, \text{Me}_4\text{Si})\) 1.18 (9H, s, tBu), 1.54-2.01 (4H, m, CHCH\(_2\)CH\(_2\)CH\(_2\)Cl), 3.37 (1H, d\(_{br}\), \(J = 2.2\) Hz, NH), 3.49 (2H, d x d x d, \(J = 6.3\) Hz, \(J = 5.8\) Hz, \(J = 1.1\) Hz, CH\(_2\)Cl), 3.81 (3H, s, OMe), 4.34 (1H, d x d x d, \(J = 8.5\) Hz, \(J = 5.8\) Hz, \(J = 2.2\) Hz, CHNH), 6.85-6.90 and 7.19-7.23 (4H, m, C\(_6\)H\(_4\)); \(\delta_{C}(75 \text{ MHz, CDCl}_3, \text{Me}_4\text{Si})\) 22.52 (CH\(_3\), tBu), 28.98 (CH\(_2\)-CH\(_2\)Cl), 35.83 (CH\(_2\)-CH\(_2\)Cl), 44.58 (CH\(_2\)Cl), 55.19 (OMe), 55.42 (C\(_q\), tBu), 58.06 (CH-NH), 113.93 (CH,
Electronic Supplementary Information

Ar), 128.71 (CH, Ar), 133.11 (Cq-CHN, Ar), 159.15 (Cq-OMe, Ar); m/z (ESI) 318.3/320.2 ([M+H]+, 100%); \([\alpha]_D = -89.2\ (c\ 0.39,\ CH_2Cl_2)\).

Typical procedure for the synthesis of 2-aryl-1-(tert-butanesulfinyl)pyrrolidines (R,S,R)-3a-d

As a representative example, the synthesis of (R,S,R)-1-tert-butylsulfinyl-2-phenylpyrrolidine 3a is described here. To a solution of (R,S,R)-N-[4-chloro-1-phenylbutyl]-tert-butanesulfinamide 2a (0.35 g, 1.22 mmol) in a 1:1 mixture of H2O/THF (10 mL) was added KOH (0.20 g, 3.65 mmol) and the reaction mixture was stirred for 24 hours at reflux temperature. After cooling to room temperature, a saturated solution of NaHCO3 (10 mL) was added and the mixture was extracted with EtOAc (3 x 10 mL). The combined organic fractions were dried (MgSO4), filtered and the solvent was removed under reduced pressure to afford (R,S,R)-1-tert-butylsulfinyl-2-phenylpyrrolidine 3a, which was purified by recrystallisation from diethyl ether in 94% yield (0.29 g, 1.14 mmol), \([\alpha]_D = +124.0\ (c\ 0.84,\ CH_2Cl_2)\). All 1H-NMR data were in good agreement with reported data for (R,S,R)-1-tert-butylsulfinyl-2-phenylpyrrolidine 3a, \([\alpha]_D = +108.8\ (c\ 1.00,\ CHCl_3), 1\ [\alpha]_D = +141.2\ (c\ 1.10,\ CHCl_3). 2

(R,S,R)-1-tert-Butylsulfinyl-2-phenylpyrrolidine 3a (94%)

Pale yellow crystals; Melting point: 89.9 °C - 90.9 °C; Elemental analysis (%): Found: C, 66.68; H, 8.43; N, 5.77. C14H21NOS requires C, 66.89; H, 8.42; N, 5.57; IR: \(\nu_{\max}/cm^{-1}\) 2924, 1448, 1057; \(\delta_1\) (300 MHz, CDCl3, Me4Si) 1.05 (9H, s, tBu), 1.71-1.94 (3H, m, CHCH(H)CH3), 2.10-2.23 (1H, m, CHCH(H)), 3.46-3.71 (2H, m, CH2N), 5.08 (1H, d x d, \(J = 7.7\ Hz,\ J = 2.8\ Hz,\ CHN)), 7.18-7.34 (5H, m, C6H5); \(\delta_2\) (75 MHz, CDCl3, Me4Si) 23.10 (CH3, tBu), 24.18 (CH2-

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CH$_2$N), 36.66 (CH$_2$-CH), 54.98 (CH$_2$N), 57.47 (CHN), 57.47 (C$_q$, tBu), 126.51 (CH, Ar), 126.56 (CH, Ar), 128.36 (CH, Ar), 144.65 (C$_q$, Ar); $m/z$ (ESI) 252.2 ([M+H]$^+$, 100%); [α]$_D$ = +124.0 (c 0.84, CH$_2$Cl$_2$).

**($R$$_S$),$($R$$_R$)-1-tert-Butylsulfinyl-2-(4-methylphenyl)pyrrolidine 3b (85%)**

Yellow crystals; **Melting point:** 116.2 °C - 117.2 °C; **Elemental analysis (%)**: Found: C, 67.79; H, 8.85; N, 5.31. C$_{15}$H$_{23}$NOS requires C, 67.88; H, 8.73; N, 5.28; **IR**: $\nu$ (max)/cm$^{-1}$ 2949, 1454, 1362, 1057; $\delta$$_H$ (300 MHz, CDCl$_3$, Me$_4$Si) 1.06 (9H, s, tBu), 1.69-1.92 (3H, m, CHCH$_2$(H)CH$_2$), 2.07-2.19 (1H, m, CHCH$_2$(H)), 2.33 (3H, s, CH$_3$-Ar), 3.45-3.70 (2H, m, CH$_2$N), 5.04 (1H, d x d, $J$ = 8.3 Hz, $J$ = 2.2 Hz, CHN), 7.07-7.19 (4H, m, C$_6$H$_4$); $\delta$$_C$ (75 MHz, CDCl$_3$, Me$_4$Si) 21.05 (CH$_3$, CH$_3$-Ar), 23.16 (CH$_3$, tBu), 24.12 (CH$_2$-CH$_2$N), 36.69 (CH$_2$-CH), 54.68 (CH$_2$N), 57.45 (CHN), 126.45 (CH, Ar), 129.05 (CH, Ar), 136.12 (C$_q$, Ar), 141.60 (C$_q$, Ar); $m/z$ (ESI) 266.2 ([M+H]$^+$, 100%); [α]$_D$ = +145.4 (c 0.99, CH$_2$Cl$_2$).

**($R$$_S$),$($R$$_R$)-1-tert-Butylsulfinyl-2-(4-chlorophenyl)pyrrolidine 3c (91%)**

White crystals; **Melting point:** 108.8 °C - 109.8 °C; **Elemental analysis (%)**: Found: C, 58.61; H, 7.32; N, 4.97. C$_{14}$H$_{20}$ClNOS requires C, 58.83; H, 7.05; N, 4.90; **IR**: $\nu$ (max)/cm$^{-1}$ 2962, 1489, 1364, 1057; $\delta$$_H$ (300 MHz, CDCl$_3$, Me$_4$Si) 1.05 (9H, s, tBu), 1.67-1.99 (3H, m, CHCH$_2$(H)CH$_2$), 2.10-2.21 (1H, m, CHCH$_2$(H)), 3.51-3.68 (2H, m, CH$_2$N), 5.04 (1H, d x d, $J$ = 7.7 Hz, $J$ = 2.2 Hz, CHN), 7.17-7.30 (4H, m, C$_6$H$_4$); $\delta$$_C$ (75 MHz, CDCl$_3$, Me$_4$Si) 23.07 (CH$_3$, tBu), 24.17 (CH$_2$-CH$_2$N), 36.57 (CH$_2$-CH), 54.93 (CH$_2$N), 57.50 (CH$_2$N), 57.50 (C$_q$, tBu), 127.92 (CH, Ar), 128.56 (CH, Ar), 132.30 (C$_q$, Ar), 143.26 (C$_q$, Ar); $m/z$ (ESI) 286.2/288.3 ([M+H]$^+$, 100%); [α]$_D$ = +161.3 (c 0.73, CH$_2$Cl$_2$).
(R,S,R)-1-tert-Butylsulfinyl-2-(4-methoxyphenyl)pyrrolidine 3d (87%) All $^1$H-NMR data were in good agreement with reported data for (R,S,R)-1-tert-butylsulfinyl-2-phenylpyrrolidine 3a, $[\alpha]_D = +139.98$ (c 1.13, MeOH).²

Yellow crystals; **Melting point:** 89.6 °C - 90.6 °C; **Elemental analysis (%)**: Found: C, 64.15; H, 8.23; N, 4.71. C$_{16}$H$_{23}$NO$_2$S requires C, 64.02; H, 8.24; N, 4.98; **IR**: $\nu\nu\nu_{\text{max}}$/cm$^{-1}$ 2862, 1607, 1509, 1357, 1054; $\delta\delta\delta_{\text{H}}$ (300 MHz, CDCl$_3$, Me$_4$Si) 1.06 (9H, s, tBu), 1.68-1.94 (3H, m, CHCH$_2$(H)CH$_2$), 2.07-2.18 (1H, m, CHCH$_2$(H)), 3.47-3.56 and 3.63-3.70 (2H, m, CH$_2$N), 3.80 (3H, s, OMe), 5.00 (1H, d x d, $J = 8.0$ Hz, $J = 2.5$ Hz, CHN), 6.83-6.87 and 7.14-7.18 (4H, m, C$_6$H$_4$); $\delta_{\text{C}}$ (75 MHz, CDCl$_3$, Me$_4$Si) 23.16 (CH$_3$, tBu), 24.14 (CH$_2$-CH$_2$N), 36.66 (CH$_2$-CH), 54.34 (CH$_2$N), 55.21 (MeO), 57.35 (CHN), 57.44 (C$_q$, tBu), 113.70 (CH, Ar), 127.40 (CH, Ar), 136.66 (C$_q$-CHN, Ar), 158.25 (C$_q$-OMe, Ar); $m/z$ (ESI) 282.3 ([M+H]$^+$, 100%), 176.2 ((M+H$^+$)-tBuS(O), 10%); $[\alpha]_D = +148.0$ (c 1.02, CH$_2$Cl$_2$).

**Typical procedure for the synthesis of 2-aryl-1-(tert-butanesulfinyl)pyrrolidines (R,S)-3a-d and (S,S,R)-3a-d**

As a representative example, the synthesis of (S,S,R)-1-(tert-butanesulfinyl)-2-phenylpyrrolidine 3a is described here. To a solution of (S)-N-[4-chloro-1-phenylbutyliedene]-tert-butanesulfinamide 1a (1.53 g, 5.36 mmol) in tetrahydrofuran (20 mL) at -78 °C was added LiBEt$_3$H (5.90 mL, 1 M solution in THF, 5.90 mmol). The reaction was stirred at -78 °C for one hour, subsequently allowed to warm up to room temperature and stirred for 20 hours. The reaction was quenched by adding a saturated solution of NaHCO$_3$ (15 mL) and filtered. The mixture was extracted with EtOAc (3 x 20 mL) and the combined organic fractions were dried (MgSO$_4$), filtered and the solvent was removed under reduced pressure to afford (S,S,R)-1-(tert-
butanesulfinyl)-2-phenylpyrrolidine 3a (1.31 g) in 97% yield. Purification by means of column chromatography (petroleum ether/EtOAc 4/1) yielded (S,S,R)-3a (1.10 g) in 82% as a yellow viscous oil. [α]D = +122.2 (c 1.02, CH2Cl2). All spectroscopic data were in good agreement with reported data for (S,S,R)-3a, [α]D = +93.6 (c 0.99, CHCl3).1

(RS,S)-1-tert-Butylsulfinyl-2-phenylpyrrolidine 3a (91%)

Yellow viscous oil; Chromatography: petroleum ether/EtOAc 3/1 + 2% Et3N Rf = 0.10; Elemental analysis (%): Found: C, 66.74; H, 8.53; N, 5.51. C14H21NOS requires C, 66.89; H, 8.42; N, 5.57; IR: νmax/cm⁻¹ 3464, 2961, 1454, 1362, 1059; δH (300 MHz, CDCl3, Me4Si) 1.09 (9H, s, tBu), 1.72-2.01 (3H, m, CHCH(H)CH2), 2.18-2.29 (1H, m, CHCH(H)), 2.93-3.01 (1H, m, CH(H)N), 3.86-3.93 (1H, m, CH(H)N), 4.63 (1H, d x d, J = 7.7 Hz, J = 7.2 Hz, CHN), 7.19-7.35 (5H, m, C6H5); δC (75 MHz, CDCl3, Me4Si) 23.74 (CH3, tBu), 26.31 (C6H4-CH2N), 35.93 (C6H4-CH), 42.03 (CH2N), 57.06 (Cq, tBu), 69.26 (CHN), 127.15 (CH, Ar), 128.22 (CH, Ar), 143.17 (Cq, Ar); m/z (ESI) 252.2 ([M+H]+, 100%); [α]D = -135.4 (c 0.60, CH2Cl2).

(RS,S)-1-tert-Butylsulfinyl-2-(4-methylphenyl)pyrrolidine 3b (87%)

White crystals; Chromatography: petroleum ether/EtOAc 3/1 + 2% Et3N, Rf = 0.14; Melting point: 68.1 °C - 69.1 °C; Elemental analysis (%): Found: C, 67.73; H, 8.82; N, 5.33. C15H23NOS requires C, 67.88; H, 8.73; N, 5.28; IR: νmax/cm⁻¹ 2968, 1455, 1364, 1056; δH (300 MHz, CDCl3, Me4Si) 1.10 (9H, s, tBu), 1.17-2.03 (3H, m, CHCH(H)CH2), 2.17-2.25 (1H, m, CHCH(H)), 2.33 (3H, s, Me), 2.97 (1H, d x d x d, J = 10.5 Hz, J = 8.3 Hz, J = 6.6 Hz, CH(H)N), 3.88 (1H, d x d x d, J = 10.5 Hz, J = 8.3 Hz, J = 3.9 Hz, CH(H)N), 4.60 (1H, d x d, J = 7.7 Hz, J = 6.6 Hz, CHN), 7.12 and 7.18 (2 x 2H, 2 x d, J = 8.3 Hz, C6H4); δC (75 MHz, CDCl3, Me4Si) 21.07 (CH3, CH3-Ar), 23.82 (CH3, tBu), 26.31 (CH2-CH2N), 36.02 (CH2-CH), 42.00 (CH2N),
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57.09 (C₉, tBu), 69.00 (CHN), 127.12 (CH, Ar), 128.95 (CH, Ar), 136.74 (C₉, Ar), 140.13 (C₉, Ar); m/z (ESI) 266.2 ([M+H]+, 100%), 160.5 (M-(tBuS(O))+H+, 60%); [α]D = -129.0 (c 0.48, CH₂Cl₂).

(S₅,R)-1-tert-Butylsulfinyl-2-(4-methylphenyl)pyrrolidine 3b (86%)

[α]D = +141.4 (c 1.01, CH₂Cl₂).

(R₅,S)-1-tert-Butylsulfinyl-2-(4-chlorophenyl)pyrrolidine 3c (92%)

Yellow crystals; Chromatography: petroleum ether/EtOAc 7/3 + 2% Et₃N Rf = 0.12; Melting point: 74.3 °C - 75.3 °C; Elemental analysis (%): Found: C, 59.02; H, 6.84; N, 5.03. C₁₄H₂₀ClNOS requires C, 58.83; H, 7.05; N, 4.90; IR: νmax/cm⁻¹ 2923, 1490, 1361, 1060; δH (300 MHz, CDCl₃, Me₄Si) 1.10 (9H, s, tBu), 1.71-2.05 (3H, m, CHCH(H)CH₂), 2.20-2.29 (1H, m, CHCH(H)), 2.97 (1H, d x d x d, J = 10.2 Hz, J = 8.3 Hz, J = 6.6 Hz, CH(CH)(N)), 3.89 (1H, d x d x d, J = 10.5 Hz, J = 8.3 Hz, J = 4.4 Hz, CH(CH)(N)), 4.60 (1H, d x d, J = 8.3 Hz, J = 6.6 Hz, CHN), 7.21-7.31 (4H, m, C₆H₄); δC (75 MHz, CDCl₃, Me₄Si) 23.82 (CH₃, tBu), 26.34 (C(H₂-C)), 36.02 (C-H₂), 42.11 (C(CH₂)), 57.22 (C₉, tBu), 68.63 (CHN), 128.48 (CH, Ar), 128.62 (CH, Ar), 132.89 (C₉, Ar), 141.83 (C₉, Ar); m/z (ESI) 286.2/288.3 ([M+H]+, 100%); [α]D = -134.3 (c 1.05, CH₂Cl₂).

(S₅,R)-1-tert-Butylsulfinyl-2-(4-chlorophenyl)pyrrolidine 3c (91%)

[α]D = +110.6 (c 1.00, CH₂Cl₂).

(R₅,S)-1-tert-Butylsulfinyl-2-(4-methoxyphenyl)pyrrolidine 3d (85%)

Yellow crystals; Chromatography: petroleum ether/EtOAc 7/3 + 2% Et₃N Rf = 0.12; Melting point: 61.2 °C - 62.2 °C; Elemental analysis (%): Found: C, 64.09; H, 8.32; N, 4.69.
C\textsubscript{15}H\textsubscript{23}NO\textsubscript{2}S requires C, 64.02; H, 8.24; N, 4.98; IR: \( \nu /\text{cm}^{-1} \) 2963, 1509, 1364, 1244, 1053; \( \delta /\text{H} (300 \text{ MHz, CDCl}_3, \text{Me}_4\text{Si}) \) 1.09 (9H, s, tBu), 1.17-2.05 and 2.17-2.27 (4H, m, CHCH\textsubscript{2}CH\textsubscript{2}), 2.96 (1H, d x d x d, \( J = 9.9 \) Hz, \( J = 8.3 \) Hz, CH(H)N), 3.80 (3H, s, OMe), 3.87 (1H, d x d x d, \( J = 10.5 \) Hz, \( J = 8.3 \) Hz, CH(H)N), 4.58 (1H, d x d, \( J = 8.3 \) Hz, \( J = 6.6 \) Hz, CHN), 6.83-6.88 and 7.19-7.29 (2 x 2H, 2 x m, C\textsubscript{6}H\textsubscript{4}); \( \delta /\text{C} (75 \text{ MHz, CDCl}_3, \text{Me}_4\text{Si}) \) 23.83 (CH\textsubscript{3}, tBu), 26.32 (CH\textsubscript{2}-CH\textsubscript{2}N), 35.93 (CH\textsubscript{2}-CH), 41.93 (CH\textsubscript{2}N), 55.21 (OMe), 57.09 (C\textsubscript{q}, tBu), 68.65 (CHN), 113.63 (CH, Ar), 128.40 (CH, Ar), 135.11 (C\textsubscript{q}-CHN, Ar), 158.79 (C\textsubscript{q}-OMe, Ar); \( m/z \) (ESI) 282.3 ([M+H]\textsuperscript{+}, 65%), 176.2 ([M-tBuS(O)+H]\textsuperscript{+}, 100%); \([\alpha]_D = -123.9 \) (c 1.05, CH\textsubscript{2}Cl\textsubscript{2}).

\((S,S,R)-1\text{-tert-Butylsulfinyl-2-(4-methoxyphenyl)pyrrolidine 3d (85\%)}\)

\([\alpha]_D = +131.2 \) (c 1.01, CH\textsubscript{2}Cl\textsubscript{2}).

**Typical procedure for the synthesis of 2-arylpyrrolidine hydrochlorides (S)-4a-d and (R)-4a-d**

As a representative example, the synthesis of \((S)-2-(4\text{-methoxyphenyl})\text{pyrrolidine hydrochloride 4d}\) is described here. To a solution of \((R,S)-1\text{-}\text{(tert-butanesulfinyl)-2-(4\text{-methoxyphenyl)pyrrolidine 3d (0.17 g, 0.60 mmol)}\) in dioxane (10 mL) was added dropwise a freshly prepared saturated solution of dioxane/HCl (1.5 mL, ~4 M solution, 6.05 mmol) under stirring. The mixture was allowed to stir for one hour at room temperature and then concentrated in vacuo. \((S)-2-(4\text{-Methoxyphenyl)pyrrolidine hydrochloride 4d}\) was obtained after precipitation in diethyl ether in 91% yield as white crystals. **Melting point:** 158.5 °C - 159.5 °C; **Elemental analysis (%)**: Found: C, 61.54; H, 7.89; N, 6.26. C\textsubscript{11}H\textsubscript{16}ClNO requires: C, 61.82; H, 7.55; N, 6.55; IR: \( \nu /\text{cm}^{-1} \) 2851, 1514, 1250; \( \delta /\text{H (300 MHz, D}_2\text{O)} \) 2.07-2.29 and 2.35-2.48 (4H, m, CHCH\textsubscript{2}CH\textsubscript{2}), 3.35-3.49 (2H, m, CH\textsubscript{2}N), 3.82 (3H, s, OMe), 4.61 (1H, d x d, \( J = 9.4 \) Hz, \( J = 7.2 \) Hz, \( J = 6.6 \) Hz, CHN).
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Hz, CHN), 7.00-7.06 and 7.39-7.44 (2 x 2H, 2 x m, C₆H₄); δ (75 MHz, D₂O, MeCN) 24.10 (CH₂-CH₂N), 30.57 (CH₂-CH), 45.76 (CH₂N), 56.02 (OMe), 63.46 (CHN), 115.20 (CH, Ar), 127.36 (Cq, Ar), 129.75 (CH, Ar), 160.21 (Cq, Ar); m/z (ESI) 178.2 ([M-HCl]+H⁺, 100%); [α]D = +9.8 (c 1.05, EtOH).

(R)-2-(4-Methoxyphenyl)pyrrolidine hydrochloride 4d (99%)

[α]D = -12.4 (c 1.01, MeOH). All spectroscopic data were in good agreement with reported data for (R)-2-(4-methoxyphenyl)pyrrolidine hydrochloride 4d, [α]D = -14.3 (c 0.98, MeOH).³

(S)-2-Phenylpyrrolidine hydrochloride 4a (84%)

[α]D = +12.8 (c 1.00, MeOH).

(R)-2-Phenylpyrrolidine hydrochloride 4a (88%)

[α]D = -9.3 (c 1.01, MeOH). All spectroscopic data were in good agreement with reported data for (R)-4a, [α]D = -9.1 (c 1.00, MeOH).¹

(S)-2-(4-Methylphenyl)pyrrolidine hydrochloride 4b (81%)

Viscous orange oil; Elemental analysis (%): Found: C, 66.63; H, 8.21; N, 7.15. C₁₁H₁₆ClN requires: C, 66.83; H, 8.16; N, 7.08; IR: ν max/cm⁻¹ 3396, 2918, 1454, 1022; δ (300 MHz, D₂O)

2.10-2.28 and 2.38-2.47 (4H, m, CHCH₂CH₂H), 2.34 (3H, s, Me), 3.41-3.47 (2H, m, CH₂N), 4.62 (1H, d x d, J = 9.4 Hz, J = 7.2 Hz, CHN), 7.30-7.38 (2 x 2H, 2 x m, C₆H₄); δ (75 MHz, D₂O, MeCN) 20.83 (CH₃, CH₃-Ar), 24.08 (CH₂-CH₂N), 30.68 (CH₂-CH), 45.87 (CH₂N), 63.67


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(CHN), 128.07 (CH, Ar), 130.39 (CH, Ar), 132.00 (C_q, Ar), 140.59 (C_q, Ar); \[m/z\ (ESI)\ 162.2 ([M-HCl+H]^+, 100%); [\alpha]_D = +12.9 (c 0.65, MeOH).

\((R)-2-(4-Methylphenyl)pyrrolidine hydrochloride 4b (99%)\)

\[[\alpha]_D = +12.9 (c 0.65, MeOH).\]

\((S)-2-(4-Chlorophenyl)pyrrolidine hydrochloride 4c (87%)\)

Viscous orange oil; **Elemental analysis (%)**: Found: C, 54.93; H, 6.17; N, 6.33. \(C_{10}H_{13}Cl_2N\) requires: C, 55.06; H, 6.01; N, 6.42; **IR**: \(\nu\nu\nu \text{cm}^{-1}\ 2910, 1496, 1014; \delta\delta\delta (300 MHz, D_2O)\ 2.12-2.32 and 2.43-2.54 (4H, m, CHCH₂CH₂), 3.42-3.51 (2H, m, CH₂N), 4.68 (1H, d x d, \(J = 8.8\ Hz, J = 7.2\ Hz, \text{CHN}), 7.43-7.53 (2 x 2H, 2 x m, C₆H₄); \delta\delta (75 MHz, D₂O, MeCN)\ 24.07 (CH₂-CH₂N), 30.65 (CH₂-CH), 46.01 (CH₂N), 63.15 (CHN), 129.71 (CH, Ar), 129.83 (CH, Ar), 133.69 (C_q, Ar), 135.39 (C_q, Ar); \[m/z\ (ESI)\ 182.3/184.2 ([M-HCl+H]^+, 100%); [\alpha]_D = +7.7 (c 0.98, MeOH).\]

\((R)-2-(4-Chlorophenyl)pyrrolidine hydrochloride 4c (99%)\)

\[[\alpha]_D = +7.7 (c 0.98, MeOH).\]

**Typical procedure for the synthesis of 2-arylpyrrolidines (S)-5a-d and (R)-5a-d**

As a representative example, the synthesis of (S)-2-(4-methoxyphenyl)pyrrolidine 5d is described here. To a suspension of (S)-2-(4-methoxyphenyl)pyrrolidine hydrochloride 4d (0.050 g, 0.23 mmol) in diethyl ether (5 mL) was added a saturated solution of sodium bicarbonate (5 mL) and the resulting mixture was stirred for ten minutes at room temperature. Subsequently the mixture
was extracted three times with diethyl ether (3 x 5 mL) and the combined organic fractions were dried (MgSO₄), filtered and the solvent was removed under reduced pressure to afford \((S)-2-(4\text{-methoxyphenyl)}\)pyrrolidine 5d (0.04 g, 0.23 mmol) as a yellow liquid in quantitative yield without further purification. All spectroscopic data were in good agreement with reported data for racemic 2-(4-methoxyphenyl)pyrrolidine 5d,\(^{3b}\) \((S)-5d: [\alpha]_D = -25.6 (c 0.89, \text{MeOH}).

\((R)-2-(4\text{-Methoxyphenyl})\)pyrrolidine 5d (99%)  

\([\alpha]_D = +23.4 (c 0.75, \text{MeOH}).\)

\((R)-2\text{-Phenylpyrrolidine} 5a \text{ (99%)}\)

\([\alpha]_D = +29.7 (c 0.32, \text{MeOH}).\) All spectroscopic data were in good agreement with reported data for \((R)-5a, [\alpha]_D = +24.3 (c 0.30, \text{MeOH})\) for an enantiomeric excess of 75%,\(^4\) and \([\alpha]_D = +64.2 (c 1.02, \text{CH}_2\text{Cl}_2).\)^\(^2\)

\((S)-2\text{-Phenylpyrrolidine} 5a \text{ (99%)}\)

\([\alpha]_D = -27.9 (c 0.38, \text{MeOH}).\) All spectroscopic data were in good agreement with reported data for \((S)-5a, [\alpha]_D = -22 (c 0.30, \text{MeOH}),\)^\(^4,5\) and \([\alpha]_D = -64.4 (c 1.02, \text{CH}_2\text{Cl}_2).\)^\(^2\)

\((S)-2-(4\text{-Methylphenyl})\)pyrrolidine 5b (99%)\(^6\)

\([\alpha]_D = -37.1 (c 0.38, \text{MeOH}).\)

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(R)-2-(4-Methylphenyl)pyrrolidine 5b (99%)

$[\alpha]_D = +35.3$ (c 0.20, MeOH).

(R)-2-(4-Chlorophenyl)pyrrolidine 5c (99%)

$[\alpha]_D = +53.2$ (c 0.99, MeOH). All spectroscopic data were in good agreement with reported data for racemic 2-(4-chlorophenyl)pyrrolidine 5c.\(^7\)

(S)-2-(4-Chlorophenyl)pyrrolidine 5c (99%)

$[\alpha]_D = -48.2$ (c 0.24, MeOH).

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Unblank_time = 2[us]
Filename = 271(b)_(c)_PROTON−6.jdf
Author = delta3
Experiment = single_pulse.exp
Sample_id = KL/271(b)_(c)
Solvent = CHLOROFORM-D
Creation_time = 30−APR−2009 15:30:32
Revision_time = 30−APR−2009 15:59:51
Current_Time = 13−OCT−2009 07:33:52
Data_format = 1D COMPLEX
Dim_size = 8192
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = Eclipse+ 300
Spectrometer = DELTA_NMR
Field_strength = 7.0586013[T] (300[MHz
X_acq_duration = 1.8169856[s]
X_domain = 1H
X_freq = 300.52965592[MHz]
X_offset = 5[ppm]
X_points = 8192
X_prescans = 0
X_resolution = 0.111036209[Hz]
X_sweep = 4.50856628[kHz]
Clipped = FALSE
Mod_return = 1
Scans = 16
Total_scans = 16
X_90_width = 15.4[us]
X_acq_time = 1.8169856[s]
X_angle = 90[deg]
X_pulse = 15.4[us]
Initial_wait = 1[s]
Phase_preset = 3[us]
Recvr_gain = 22
Relaxation_delay = 5[s]
Temp_get = 21.4[dc]
Unblank_time = 2[us]
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