Catalytic Enantioselective Synthesis of 3-substituted Benzosultams via Corey-Bakshi-Shibata Reduction of Cyclic N-Sulfonylimines

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Supporting Information

General remarks

All reactions were performed in oven-dried glassware under a slight pressure of argon. Starting materials and reagents were purchased from commercial suppliers and used without further purification unless otherwise stated. Cyclic N-sulfonylimines 1a-d were prepared according to the procedure of Boen and coworkers.1 The synthesis of cyclic N-sulfonylimine 1e is described below. All solvents were dried by conventional methods. Preparative column chromatography: Silica gel 60 M, 0.04-0.063 / 230-400 mesh, Macherey-Nagel. Analytical TLC: Pre-coated TLC plates SIL G-25 UV254, Macherey-Nagel. Visualization of the developed TLC plates was performed with ultraviolet irradiation (254 nm) and by staining with a solution of potassium permanganate or ninhydrin. 1H- and 13C- NMR spectra were recorded at ambient temperature on Varian Mercury 300 or Varian Inova 400 intruments with tetramethylsilane as internal standard. Chemical shifts for 1H-NMR and 13C-NMR are reported in parts per million (ppm), with coupling constants reported in Hertz (Hz). The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, dd = doublet of doublet, t = triplet, dt = doublet of triplet, q = quartet, m = multiplet. Mass spectra were acquired on a Finnigan SSQ7000 (EI 70 eV) spectrometer. IR spectra were obtained on a PerkinElmer Spectrum 100 FT-IR Spectrometer and the following abbreviations are used: vw = very weak, w = weak, m = medium, s = strong and vs = very strong. Microanalyses were performed with an Elementar varioEL or Elementar varioEL cube. Analytical HPLC was carried out on a Hewlett-Packard 1100 Series instrument using chiral stationary phases. Optical rotation values were measured on a Perkin-Elmer 241 polarimeter.

General procedure of the CBS-reduction of cyclic N-sulfonylimines

In a dry, argon-flushed Schlenk tube (R)-(+)2-methyl-CBS-oxazaborolidine (3a) (50 µL, 0.05 mmol, 1m solution in toluene) and catecholborane (85 µL, 96 mg, 0.8 mmol) were dissolved in dry toluene (10 mL). The solution was cooled to 0 °C and cyclic N-sulfonylimine 2 (0.5 mmol) was added in one portion. Stirring was continued at 0 °C until full conversion was reached. The reaction was subsequently quenched with 3 mL of an 1:2 mixture of ethanolamine and water. After stirring for 15 min at room temperature the phases were separated and the aqueous phase was extracted with diethyl ether (3 x 10 mL). The combined organic layers were dried over magnesium sulphate, filtered and concentrated under reduced pressure. Column chromatography over silica gel (diethyl ether/hexane) afforded the pure product. Racemic samples were prepared by reduction with sodium borohydride in methanol at room temperature.

Analytical data

(S)-3-Methyl-2,3-dihydrobenzo[d]isothiazole-1,1-dioxide (2a), known compound, was isolated as a colourless solid (68 mg, 74% yield, mp 87 °C). \([\alpha]_D^{25} = -28.7 \ (c = 1.01, \text{CHCl}_3, 94\% \text{ ee})\).

\(^1\text{H-NMR}\) (300 MHz, CDCl\(_3\)): \(\delta = 1.61\) (d, 3H, \(J = 6.9 \text{ Hz}, \text{CH}_3\)), 4.74 - 4.83 (m, 1H, CH), 4.98 (broad s, 1H, NH), 7.39 (d, 1H, \(J = 7.7 \text{ Hz}, \text{CH}_\text{ar}\)), 7.52 (t, 1H, \(J = 7.7 \text{ Hz}, \text{CH}_\text{ar}\)), 7.63 (dt, 1H, \(J = 1.2/7.7 \text{ Hz}, \text{CH}_\text{ar}\)), 7.76 (d, 1H, \(J = 7.7 \text{ Hz}, \text{CH}_\text{ar}\)) ppm. \(^{13}\text{C-NMR}\) (75 MHz, CDCl\(_3\)): \(\delta = 21.4\) (CH\(_3\)), 53.4 (CH), 121.2 (CH\(_\text{ar}\)), 123.9 (CH\(_\text{ar}\)), 129.2 (CH\(_\text{ar}\)), 133.2 (CH\(_\text{ar}\)), 135.5 (C\(_\text{ar}\)), 141.7 (C\(_\text{ar}\)) ppm. \textbf{MS} (EI, 70 eV): \(m/z\) (+) = 183 (5[M\(^+\]), 168 (100), 150 (17), 77 (17). \textbf{HPLC} (n-heptane/ethanol, 9:1, 1.0 mL/min, Daicel Chiralpak AS column): \(t_R = 25.7\) min (major), \(t_R = 33.6\) min (minor).

(S)-3-Ethyl-2,3-dihydrobenzo[d]isothiazole-1,1-dioxide (2b) was isolated as a colourless oil (85 mg, 86% yield). \([\alpha]_D^{25} = -50.1\) (c = 1.06, CHCl\(_3\), 81% ee).

\(^1\text{H-NMR}\) (400 MHz, CDCl\(_3\)): \(\delta = 1.03\) (t, 1H, \(J = 7.4 \text{ Hz}, \text{CH}_2\text{CH}_3\)), 1.75 - 1.88 (m, 1H, CH\(_2\text{CH}_3\)), 1.99 - 2.10 (m, 1H, CH\(_2\text{CH}_3\)), 4.65 - 4.71 (m, 1H, CH), 4.93 (broad s, 1H, NH), 7.39 (dd, 1H, \(J = 0.8/7.7 \text{ Hz}, \text{CH}_\text{ar}\)), 7.52 (t, 1H, \(J = 7.7 \text{ Hz}, \text{CH}_\text{ar}\)), 7.63 (dt, 1H, \(J = 1.1/7.7 \text{ Hz}, \text{CH}_\text{ar}\)), 7.77 (d, 1H, \(J = 7.7 \text{ Hz}, \text{CH}_\text{ar}\)) ppm. \(^{13}\text{C-NMR}\) (100 MHz, CDCl\(_3\)): \(\delta = 10.0\) (CH\(_2\text{CH}_3\)), 28.8 (CH\(_2\text{CH}_3\)), 59.1 (CH), 121.3 (CH\(_\text{ar}\)), 124.1 (CH\(_\text{ar}\)), 129.2 (CH\(_\text{ar}\)).

(S)-3-Butyl-2,3-dihydrobenzo[d]isothiazole-1,1-dioxide (2c), known compound,\(^3\) was isolated as a colourless oil (103 mg, 91% yield). \([\alpha]_D^{25} = -46.4 (c = 1.04, \text{CHCl}_3, 84\% \text{ ee})\). \(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta = 0.92\) (t, 1H, \(J = 7.1\) Hz, \(CH_3\)), 1.30 - 1.52 (m, 4H, \(CH_2\)), 1.71 - 1.82 (m, 1H, \(CH_2\)), 1.94 - 2.04 (m, 1H, \(CH_2\)), 4.66 - 4.73 (m, 1H, \(CH\)), 4.88 (broad d, 1H, \(J = 4.4\) Hz, \(NH\)), 7.39 (dd, 1H, \(J = 0.6/7.7\) Hz, \(CH_2\)), 7.52 (t, 1H, \(J = 7.7\) Hz, \(CH_3\)), 7.62 (dt, 1H, \(J = 1.1/7.7\) Hz, \(CH_2\)), 7.77 (d, 1H, \(J = 7.7\) Hz, \(CH_2\)) ppm. \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)): \(\delta = 13.9\) (CH\(_3\)), 22.3 (CH\(_2\)), 27.8 (CH\(_2\)), 35.4 (CH\(_2\)), 57.8 (CH), 121.2 (CH\(_{ar}\)), 123.9 (CH\(_{ar}\)), 129.0 (CH\(_{ar}\)), 132.9 (CH\(_{ar}\)), 135.4 (C\(_{ar}\)), 140.4 (C\(_{ar}\)) ppm. MS (EI, 70 eV): \(m/z\) (+) = 226 (2) [M\(^+\) + H], 168 (100), 150 (17), 77 (25), 51 (13). HPLC (n-heptane/i-propanol, 7:3, 1.0 mL/min, Daicel Chiralpak OD column): \(t_R = 6.4\) min (major), \(t_R = 9.6\) min (minor).

(S)-3-Phenyl-2,3-dihydrobenzo[d]isothiazole-1,1-dioxide (2d), known compound,\(^4\) was isolated as a colourless solid (117 mg, 95% yield, mp 124 °C). \([\alpha]_D^{25} = +69.0\) (c = 1.01, CHCl\(_3\), 69% ee). \(^1\)H-NMR (400 MHz, CDCl\(_3\)): \(\delta = 5.06\) (broad d, 1H, \(J = 3.6\) Hz, \(NH\)), 5.71 (d, 1H, \(J = 3.9\) Hz, \(CH\)), 7.11 - 7.16 (m, 1H, CH\(_2\)), 7.33 - 7.41 (m, 5H, CH\(_{ar}\)), 7.51 - 7.58 (m, 2H, CH\(_{ar}\)), 7.79 - 7.85 (m, 1H, CH\(_{ar}\)) ppm. \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)): \(\delta = 61.3\) (CH), 121.0 (CH\(_{ar}\)), 125.2 (CH\(_{ar}\)), 127.4 (2C, CH\(_{ar}\)), 128.9 (CH\(_{ar}\)), 129.1 (2C, CH\(_{ar}\)), 129.3 (CH\(_{ar}\)), 133.1 (CH\(_{ar}\)), 134.6 (C\(_{ar}\)), 138.5 (C\(_{ar}\)), 139.6 (C\(_{ar}\)) ppm. MS (EI, 70 eV): \(m/z\) (+) = 246 (19), 245 (100) [M\(^+\)], 244 (44), 181 (18), 180 (38), 168 (44), 152 (14), 150 (16), 104 (99), 103 (23), 78 (25), 77 (37), 76 (11), 51 (14). HPLC (n-heptane/i-propanol, 8:2, 1.0 mL/min, Daicel Chiralpak AD column): \(t_R = 11.3\) min (minor), \(t_R = 12.7\) min (major).


(S)-6-Bromo-3-methyl-2,3-dihydrobenzo[d]isothiazole-1,1-dioxide (2e) was isolated as a colourless oil (121 mg, 92% yield). $[\alpha]_D^{25} = -35.0$ (c = 1.00, CHCl$_3$, 74% ee). $^1$H-NMR (300 MHz, CDCl$_3$): $\delta$ = 1.60 (d, 1H, $J = 6.7$ Hz, CH$_3$), 4.68 - 4.78 (m, 1H, CH), 5.01 (broad d, 1H, $J = 3.7$ Hz, NH), 7.27 (d, 1H, $J = 8.4$ Hz, CH$_{ar}$), 7.73 (dd, 1H, $J = 1.7/8.2$ Hz, CH$_{ar}$), 7.87 (d, 1H, $J = 1.7$ Hz, CH$_{ar}$) ppm. $^{13}$C-NMR (75 MHz, CDCl$_3$): $\delta$ = 21.2 (CH$_3$), 53.2 (CH), 122.8 (C$_{ar}$), 124.2 (C$_{ar}$), 125.5 (C$_{ar}$), 136.3 (C$_{ar}$), 137.4 (C$_{ar}$), 140.7 (C$_{ar}$) ppm. MS (EI, 70 eV): $m/z$ (+) = 263 (14) [M$^+$, $^{81}$Br], 261 (15) [M$^+$, $^{79}$Br], 248 (100), 246 (96), 230 (17), 228 (16), 182 (10), 103 (26), 102 (10), 76 (19), 75 (27), 74 (13), 51 (10), 50 (14). IR (film): $\nu$ (cm$^{-1}$) = 3256 (m), 3085 (vw), 2980 (w), 1592 (vw), 1465 (m), 1396 (m), 1288 (vs), 1200 (w), 1160 (vs), 1080 (s), 1020 (m), 891 (m), 830 (m), 803 (vw), 723 (w). EA (CHN): calculated for C$_8$H$_8$BrNO$_2$S, C = 36.66%, H = 3.08%, N = 5.34%; found C = 36.58%, H = 3.33%, N = 5.39%. HPLC (n-heptane/ethanol, 90:10, 0.5 mL/min, Daicel Chiralpak OD column): $t_R$ = 21.5 min (major), $t_R$ = 25.8 min (minor).

6-Bromo-3-methylbenzo[d]isothiazole-1,1-dioxide (1e) was prepared by slow addition of methylmagnesium bromide (5 mL, 10.5 mmol, 2.1M solution in diethyl ether) to a solution of 6-bromobenzo[d]isothiazol-3(2H)-one,1,1-dioxide (1.31 g, 5.0 mmol) in dry THF (20 mL) at 0 °C. After stirring the reaction mixture overnight at room temperature the solvent was removed under reduced pressure. The residue was suspended in water (25 mL), acidified to pH = 1 with concentrated hydrochloric acid and stirred for 10 min. The precipitated product was collected by filtration, washed with water and dried under high vacuum. Recrystallization from acetone furnished the pure product as a colourless solid (463 mg, 36% yield, mp 239 °C). $^1$H-NMR (300 MHz, CDCl$_3$): $\delta$ = 2.71 (s, 3H, CH$_3$), 7.96 (d, 1H, $J = 8.2$ Hz, CH$_{ar}$), 8.13 (dd, 1H, $J = 1.7/8.2$ Hz, CH$_{ar}$), 8.56 (d, 1H, $J = 1.7$ Hz, CH$_{ar}$) ppm. $^{13}$C-NMR (75 MHz, CDCl$_3$): $\delta$ = 18.2 (CH$_3$), 126.0 (C$_{ar}$), 128.1 (C$_{ar}$), 129.3 (C$_{ar}$), 131.1 (C$_{ar}$), 138.2 (C$_{ar}$), 140.8 (C$_{ar}$), 175.5 (C) ppm. MS (EI, 70 eV): $m/z$ (+) = 361 (64) [M$^+$, $^{81}$Br], 259 (61) [M$^+$, $^{79}$Br], 213 (25), 211 (24), 198 (10), 197 (21), 195 (23), 156 (37), 155 (12), 154 (36), 116 (31), 100 (11), 89 (19), 76 (10), 75 (100), 74 (52), 69 (11), 63 (17), 57 (21), 50 (20). IR (film): $\nu$ (cm$^{-1}$) = 3086 (vw), 1608 (w), 1580 (w), 1549 (m), 1403 (m), 1380 (m), 1322 (vs), 1271 (s), 1165 (vs), 1171 (m), 1031 (vw), 879 (vw), 808 (vs), 705 (vw). EA (CHN): calculated for C$_8$H$_8$BrNO$_2$S, C = 36.94%; H = 2.33%, N = 5.38%; found C = 37.45%, H = 2.22%, N = 5.41%. 