Diastereoselective Synthesis of N-tert-Butanesulfinylamines through Addition of p-Nitrobenzyl Chloride to N-tert-Butanesulfinimines using TDAE Strategy

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General experimental details

Melting points were determined on a Büchi melting point B-540 apparatus and are uncorrected. Element analyses were performed on a Thermo Finnigan EA1112 at the spectropole of the Aix-Marseille University. Both $^1$H and $^{13}$C NMR spectra were determined on a Bruker AC 200 spectrometer. The $^1$H and the $^{13}$C chemical shifts are reported from CDCl$_3$ peaks: $^1$H (7.26 ppm) and $^{13}$C (76.9 ppm). Multiplicities are represented by the following notations: s, singlet; d, doublet; t, triplet; q, quartet; m, a more complex multiplet or overlapping multiplets. The following adsorbents were used for column chromatography: silica gel 60 (Merck, particle size 0.063-0.200 mm, 70-230 mesh ASTM). TLC was performed on 5 cm x 10 cm aluminium plates coated with silica gel 60 F$_{254}$ (Merck) in an appropriate solvent.

General experimental procedure

To a stirred solution of $N$-sulfinimine (0.24 mmol) in DMF (1 mL) at -20 °C was added TDAE (0.2 mmol) followed by dropwise addition of a solution of $p$-nitrobenzyl chloride in DMF (1 mL). The solution was vigorously stirred at -20 °C for 1 h and then maintained at room temperature for 2 h. Water (5 mL) was added and the aqueous solution was extracted with CH$_2$Cl$_2$ (3 x 15 mL). The combined organic layer was washed with H$_2$O (20 mL) and dried over MgSO$_4$. Evaporation of the solvent furnished the crude product. Purification by silica gel chromatography (EtOAc/petroleum ether: from 6/4 to 8/2 depending on the polarity of substrates) allowed pure amine products as a mixture of diastereoisomers.

Product characterization data

(R)-N-(2-(4-nitrophenyl)-1-phenyl)ethyl)-2-methylpropane-2-sulfinamide (3a)

Major diastereoisomer ($R$, $R$); yellow solid; mp 118–120 °C; $^1$H NMR (200 MHz, CDCl$_3$) $\delta$ 8.03 (d, $J$ = 8.6 Hz, 2H), 7.30–7.10 (m, 7H), 4.67–4.58 (m, 1H), 3.59 (d, $J$ = 2.8 Hz, 1H), 3.47 (dd, $J$ = 13.2, 5.9 Hz, 1H), 3.08 (dd, $J$ = 13.2, 8.3 Hz, 1H), 1.20 (s, 9H); $^{13}$C NMR (50 MHz, CDCl$_3$) $\delta$ 146.8, 145.4, 140.8, 130.6, 128.9, 128.5, 127.3, 123.5, 60.2, 56.2, 43.2, 22.7; HRMS (ESI): $m/z$ [M + Na]$^+$ calcd for [C$_{18}$H$_{22}$N$_2$O$_3$SNa]$^+$: 369.12433; found: 369.12458.
(R)-N-(1-(3-nitrophenyl)-2-(4-nitrophenyl)ethyl)-2-methylpropane-2-sulfinamide (3c)

![Chemical structure of 3c]

Major diastereoisomer (R, R); yellow solid; mp 182–186 °C; \(^1\)H NMR (200 MHz, CDCl\(_3\)) \(\delta\) 8.20–8.12 (m, 4H), 7.53–7.45 (m, 2H), 7.22 (d, \(J\) = 8.6 Hz, 2H), 4.80–4.70 (m, 1H), 3.75 (d, \(J\) = 5.0 Hz, 1H), 3.50 (dd, \(J\) = 13.5, 6.9 Hz, 1H), 3.15 (dd, \(J\) = 13.5, 7.6 Hz, 1H), 1.17 (s, 9H); \(^13\)C NMR (50 MHz, CDCl\(_3\)) \(\delta\) 148.6, 147.1, 144.5, 143.3, 133.8, 130.6, 130.0, 123.8, 123.5, 122.0, 60.3, 56.6, 43.1, 22.6; HRMS (ESI): m/z [M + Na]\(^+\) calcd for [C\(_{18}\)H\(_{21}\)N\(_3\)O\(_5\)SNa]\(^+\): 414.10941; found: 414.10958.

(R)-N-(1-(2-nitrophenyl)-2-(4-nitrophenyl)ethyl)-2-methylpropane-2-sulfinamide (3d)

![Chemical structure of 3d]

Major diastereoisomer (R, R); yellow solid; mp 151–155 °C; \(^1\)H NMR (200 MHz, CDCl\(_3\)) \(\delta\) 8.15 (d, \(J\) = 8.6 Hz, 2H), 7.94 (d, \(J\) = 8.0 Hz, 1H), 7.66–7.43 (m, 3H), 7.39 (d, \(J\) = 8.6 Hz, 2H), 5.27–5.16 (m, 1H), 4.06 (d, \(J\) = 8.3 Hz, 1H), 3.37 (dd, \(J\) = 13.7, 5.3 Hz, 1H), 3.20 (dd, \(J\) = 13.7, 8.8 Hz, 1H), 1.03 (s, 9H); \(^13\)C NMR (50 MHz, CDCl\(_3\)) \(\delta\) 148.6, 147.1, 145.2, 136.7, 133.7, 130.6, 129.7, 129.2, 125.5, 123.8, 58.3, 56.9, 43.1, 22.4; HRMS (ESI): m/z [M + Na]\(^+\) calcd for [C\(_{18}\)H\(_{21}\)N\(_3\)O\(_5\)SNa]\(^+\): 414.10941; found: 414.10949.

(R)-N-(1-(4-bromophenyl)-2-(4-nitrophenyl)ethyl)-2-methylpropane-2-sulfinamide (3e)

![Chemical structure of 3e]
Major diastereoisomer ($R, R$); yellow solid; mp 53–57 °C; $^1$H NMR (200 MHz, CDCl3) δ 8.06 (d, $J = 8.7$ Hz, 2H), 7.42 (d, $J = 8.4$ Hz, 2H), 7.15 (d, $J = 8.7$ Hz, 2H), 7.07 (d, $J = 8.4$ Hz, 2H), 4.63–4.54 (m, 1H), 3.61 (d, $J = 3.8$ Hz, 1H), 3.45 (dd, $J = 13.4$, 6.2 Hz, 1H), 3.05 (dd, $J = 13.4$, 8.1 Hz, 1H), 1.18 (s, 9H); $^{13}$C NMR (50 MHz, CDCl3) δ 147.0, 144.9, 139.8, 132.1, 130.6, 128.8, 123.7, 122.5, 59.8, 56.3, 43.0, 22.7; HRMS (ESI): $m/z$ [M + Na]$^+$ calcd for [C$_{18}$H$_{21}$BrN$_2$O$_3$SNa]$^+$: 447.03485; found: 447.03446.

($R$)-N-(1-(3-bromophenyl)-2-(4-nitrophenyl)ethyl)-2-methylpropane-2-sulfinamide (3f)

Major diastereoisomer ($R, R$); yellow solid; mp 55–58 °C; $^1$H NMR (200 MHz, CDCl3) δ 8.07 (d, $J = 8.7$ Hz, 2H), 7.44–7.38 (m, 2H), 7.19–7.05 (m, 4H), 4.64–4.54 (m, 1H), 3.59 (br s, 1H), 3.44 (dd, $J = 13.4$, 6.3 Hz, 1H), 3.07 (dd, $J = 13.4$, 8.0 Hz, 1H), 1.18 (s, 9H); $^{13}$C NMR (50 MHz, CDCl3) δ 146.9, 145.0, 143.2, 131.6, 130.6, 130.5, 130.2, 126.2, 123.6, 123.0, 60.0, 56.4, 43.0, 22.7; HRMS (ESI): $m/z$ [M + Na]$^+$ calcd for [C$_{18}$H$_{21}$BrN$_2$O$_3$SNa]$^+$: 447.03485; found: 447.03516.

($R$)-N-(1-(2-bromophenyl)-2-(4-nitrophenyl)ethyl)-2-methylpropane-2-sulfinamide (3g)

Major diastereoisomer ($R, R$); yellow solid; mp 68–70 °C; $^1$H NMR (200 MHz, CDCl3) δ 8.09 (d, $J = 8.6$ Hz, 2H), 7.53 (d, $J = 7.7$ Hz, 1H), 7.36–7.10 (m, 5H), 5.12–5.02 (m, 1H), 3.85 (d, $J = 6.3$ Hz, 1H), 3.25 (d, $J = 6.9$ Hz, 2H), 1.10 (s, 9H); $^{13}$C NMR (50 MHz, CDCl3) δ 146.9, 145.2, 140.1, 134.0, 130.7, 129.6, 128.7, 128.0, 123.5, 123.3, 59.8, 56.6, 42.4, 22.5; HRMS (ESI): $m/z$ [M + Na]$^+$ calcd for [C$_{18}$H$_{21}$BrN$_2$O$_3$SNa]$^+$: 447.03485; found: 447.03473.
(R)-N-(1-(4-methoxyphenyl)-2-(4-nitrophenyl)ethyl)-2-methylpropane-2-sulfinamide (3h)

Major diastereoisomer (R, R); yellow solid; mp 48–51 °C; ¹H NMR (200 MHz, CDCl₃) δ 8.04 (d, J = 8.6 Hz, 2H), 7.12 (d, J = 8.6 Hz, 2H), 7.10 (d, J = 8.6 Hz, 2H), 6.80 (d, J = 8.6 Hz, 2H), 4.62–4.53 (m, 1H), 3.77 (s, 3H), 3.53–3.41 (m, 2H), 3.05 (dd, J = 13.2, 8.5 Hz, 1H), 1.20 (s, 9H); ¹³C NMR (50 MHz, CDCl₃) δ 159.6, 146.8, 145.6, 132.8, 130.7, 128.5, 123.5, 114.2, 59.6, 56.1, 55.4, 43.1, 22.7; HRMS (ESI): m/z [M + Na]⁺ calcd for [C₁₉H₂₄N₂O₄SNa]⁺: 399.13490; found: 399.13487.

(R)-N-(1-(3-methoxyphenyl)-2-(4-nitrophenyl)ethyl)-2-methylpropane-2-sulfinamide (3i)

Major diastereoisomer (R, R); yellow solid; mp 55–58 °C; ¹H NMR (200 MHz, CDCl₃) δ 8.05 (d, J = 8.6 Hz, 2H), 7.25–7.12 (m, 3H), 6.82–6.74 (m, 3H), 4.66–4.56 (m, 1H), 3.75 (s, 3H), 3.56 (br s, 1H), 3.29 (dd, J = 13.3, 5.9 Hz, 1H), 3.08 (dd, J = 13.3, 8.2 Hz, 1H), 1.20 (s, 9H); ¹³C NMR (50 MHz, CDCl₃) δ 159.9, 146.9, 145.4, 142.4, 130.6, 130.0, 123.5, 119.6, 113.4, 113.3, 60.1, 56.2, 55.4, 43.1, 22.7; HRMS (ESI): m/z [M + Na]⁺ calcd for [C₁₉H₂₄N₂O₄SNa]⁺: 399.13490; found: 399.13517.
(R)-N-(1-(2-methoxyphenyl)-2-(4-nitrophenyl)ethyl)-2-methylpropane-2-sulfinamide (3j)

Major diastereoisomer (R, R); yellow solid; mp 45–48 °C; $^1$H NMR (200 MHz, CDCl₃) $\delta$
8.05 (d, $J = 8.6$ Hz, 2H), 7.26–7.09 (m, 4H), 6.91–6.83 (m, 2H), 4.86–4.75 (m, 1H), 4.13 (d, $J = 7.7$ Hz, 1H), 3.79 (s, 3H), 3.29 (dd, $J = 13.4$, 6.7 Hz, 1H), 3.15 (dd, $J = 13.4$, 6.9 Hz, 1H), 1.10 (s, 9H); $^{13}$C NMR (50 MHz, CDCl₃) $\delta$ 156.7, 146.7, 146.5, 130.6, 129.5, 129.2, 128.0, 123.3, 121.0, 111.1, 58.1, 56.2, 55.4, 42.7, 22.6; HRMS (ESI): $m/z$ [M + Na]$^+$ calcd for [C₁₉H₂₄N₂O₄SNa]$^+$: 399.13490; found: 399.13519.