Mild and Metal-Free Regioselective 1,2-Addition of Carbon Nucleophiles to α,β- Unsaturated Imines

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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 250 spectrometer. The $^1$H and the $^{13}$C chemical shifts are reported from CDCl$_3$ peaks: $^1$H (7.26 ppm) and $^{13}$C (77.16 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 $p$-nitrobenzyl chloride 1 or 2,3-bis(bromomethyl)quinoxaline 4 (0.2 mmol) and N-tosylimine 2 (0.24 mmol) in DMF (1 mL) at -20 °C was added TDAE (0.2 mmol). 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 (petroleum ether/EtOAc: from 8/2 to 7/3 depending on the polarity of substrates) allowed pure amine products 3 or 5.

Product characterization data

(E)-4-methyl-N-(1-(4-nitrophenyl)-4-phenylbut-3-en-2-yl)benzenesulfonamide (3a)

![Chemical Structure](image)

81% yield; yellow solid; mp 189–191 °C; $^1$H NMR (250 MHz, CDCl$_3$) δ 8.04 (d, $J = 8.5$ Hz, 2H), 7.60 (d, $J = 8.1$ Hz, 2H), 7.26-7.12 (m, 9H), 6.24 (d, $J = 15.9$ Hz, 1H), 5.85 (dd, $J = 15.9$, 7.0 Hz, 1H), 4.75 (d, $J = 7.9$ Hz, 1H), 4.29-4.18 (m, 1H), 3.03-2.98 (m, 2H), 2.31 (s, 3H); $^{13}$C NMR (63 MHz, CDCl$_3$) δ 147.0, 144.4, 143.8, 137.6, 135.8, 132.5, 130.5, 129.7, 128.7, 128.3, 127.4, 127.2, 126.6, 123.8, 56.9, 42.3, 21.5; HRMS (ESI): m/z [M + NH$_4$]$^+$ calcd for [C$_{23}$H$_{26}$N$_3$O$_4$S]: 440.1639; found: 440.1640.
(E)-N-(1,4-bis(4-nitrophenyl)but-3-en-2-yl)-4-methylbenzenesulfonamide (3b)

\[ \text{Ts}\text{N}H \text{C} \text{C} \text{C} \text{O}_2\text{N} \]

61% yield; yellow solid; mp 181–183 °C; \(^1H\) NMR (250 MHz, CDCl\(_3\)) \(\delta\) 8.12 (d, \(J = 8.5\) Hz, 2H), 8.00 (d, \(J = 8.3\) Hz, 2H), 7.56 (d, \(J = 8.0\) Hz, 2H), 7.30-7.19 (m, 4H), 7.12 (d, \(J = 7.9\) Hz, 2H), 6.41 (d, \(J = 15.8\) Hz, 1H), 6.12 (dd, \(J = 15.8, 6.6\) Hz, 1H), 5.14 (d, \(J = 7.7\) Hz, 1H), 4.29-4.24 (m, 1H), 3.02-2.88 (m, 2H), 2.32 (s, 3H); \(^13\)C NMR (63 MHz, CDCl\(_3\)) \(\delta\) 147.4, 147.1, 144.0, 143.9, 142.3, 137.4, 132.7, 130.3, 130.2, 129.7, 127.2, 127.1, 124.1, 123.9, 56.8, 41.8, 21.5; HRMS (ESI): \(m/z\) [M + NH\(_4\)]\(^+\) calcd for [C\(_{23}\)H\(_{25}\)N\(_4\)O\(_6\)S]\(^+\): 485.1489; found: 485.1489.

(E)-N-(4-(4-chlorophenyl)-1-(4-nitrophenyl)but-3-en-2-yl)-4-methylbenzenesulfonamide (3c)

\[ \text{Ts}\text{N}H \text{C} \text{C} \text{C} \text{Cl} \]

68% yield; yellow solid; mp 156–159 °C; \(^1H\) NMR (250 MHz, CDCl\(_3\)) \(\delta\) 7.99 (d, \(J = 8.6\) Hz, 2H), 7.57 (d, \(J = 8.2\) Hz, 2H), 7.26-7.20 (m, 4H), 7.10 (d, 8.0 Hz, 2H), 7.03 (d, 8.5 Hz, 2H), 6.21 (d, \(J = 15.9\) Hz, 1H), 5.84 (dd, \(J = 15.9, 7.0\) Hz, 1H), 5.20 (d, \(J = 8.1\) Hz, 1H), 4.27-4.17 (m, 1H), 2.98-2.93 (m, 2H), 2.30 (s, 3H); \(^13\)C NMR (63 MHz, CDCl\(_3\)) \(\delta\) 147.0, 144.4, 143.8, 137.5, 134.4, 133.9, 131.1, 130.4, 129.7, 128.8, 128.3, 127.8, 127.1, 123.7, 57.0, 42.0, 21.5; HRMS (ESI): \(m/z\) [M + NH\(_4\)]\(^+\) calcd for [C\(_{23}\)H\(_{25}\)N\(_3\)O\(_4\)SCl]\(^+\): 474.1249; found: 474.1247.

(E)-N-(4-(4-methoxyphenyl)-1-(4-nitrophenyl)but-3-en-2-yl)-4-methylbenzenesulfonamide (3d)

\[ \text{Ts}\text{N}H \text{C} \text{C} \text{C} \text{O}_2\text{MeO} \]

72% yield; yellow solid; mp 167–169 °C; \(^1H\) NMR (250 MHz, CDCl\(_3\)) \(\delta\) 8.03 (d, \(J = 8.5\) Hz, 2H), 7.60 (d, \(J = 8.0\) Hz, 2H), 7.26-7.23 (m, 2H), 7.13 (d, \(J = 7.9\) Hz, 2H), 7.06 (d, \(J = 8.3\) Hz,
2H), 6.79 (d, J = 8.6 Hz, 2H), 6.17 (d, J = 15.8 Hz, 1H), 5.71 (dd, J = 15.8, 7.1 Hz, 1H), 4.88 (d, J = 8.0 Hz, 1H), 4.22-4.17 (m, 1H), 3.80 (s, 3H), 3.01-2.96 (m, 2H), 2.32 (s, 3H); 13C NMR (63 MHz, CDCl3) δ 159.7, 146.9, 144.7, 143.7, 137.7, 132.0, 130.5, 129.7, 128.6, 127.8, 127.2, 125.2, 123.7, 114.1, 57.1, 55.4, 42.3, 21.5; HRMS (ESI): m/z [M + NH4]+ calcd for [C24H28N3O5S]+: 470.1744; found: 470.1747.

(E)-N-(4-(furan-2-yl)-1-(4-nitrophenyl)but-3-en-2-yl)-4-methylbenzenesulfonamide (3e)

51% yield; yellow solid; mp 171–173 °C; 1H NMR (250 MHz, CDCl3) δ 8.01 (d, J = 8.7 Hz, 2H), 7.57 (d, J = 8.3 Hz, 2H), 7.29-7.20 (m, 3H), 7.13 (d, J = 8.4 Hz, 2H), 6.34-6.32 (m, 2H), 6.15-6.08 (m, 2H), 5.86 (dd, J = 15.8, 6.7 Hz, 1H), 4.86 (d, J = 8.2 Hz, 1H), 4.21-4.15 (m, 1H), 2.99-2.92 (m, 2H), 2.34 (s, 3H); 13C NMR (63 MHz, CDCl3) δ 151.5, 147.0, 144.4, 143.8, 142.5, 137.5, 130.5, 129.7, 127.1, 126.0, 123.7, 120.6, 111.5, 109.2, 56.7, 42.1, 21.5; HRMS (ESI): m/z [M + NH4]+ calcd for [C21H24N3O5S]+: 430.1431; found: 430.1432.

4-methyl-N-(1-(4-nitrophenyl)-4,4-diphenylbut-3-en-2-yl)benzenesulfonamide (3f)

69% yield; white solid; mp 175–178 °C; 1H NMR (250 MHz, CDCl3) δ 7.84 (d, J = 8.3 Hz, 2H), 7.41 (d, J = 7.8 Hz, 2H), 7.22-7.12 (m, 6H), 7.02 (d, J = 8.0 Hz, 2H), 6.95-6.90 (m, 4H), 6.68 (d, J = 7.8 Hz, 2H), 5.69 (d, J = 9.5 Hz, 1H), 5.26 (d, J = 6.8 Hz, 1H), 4.06-3.94 (m, 1H), 2.86-2.83 (m, 2H), 2.28 (s, 3H); 13C NMR (63 MHz, CDCl3) δ 146.8, 144.6, 144.1, 143.6, 140.8, 138.5, 137.3, 130.4, 129.6, 129.2, 128.4, 128.3, 128.0, 127.7, 127.3, 127.2, 126.8, 123.5, 54.4, 42.6, 21.6; HRMS (ESI): m/z [M + NH4]+ calcd for [C29H30N3O4S]+: 516.1952; found: 516.1954.
(E)-3-styryl-2-tosyl-1,2,3,4-tetrahydropyrido[3,4-b]quinoxaline (5a)

61% yield; yellow solid; mp 72–75 °C; \(^1\)H NMR (250 MHz, CDCl\(_3\)) \(\delta\) \(^1\)H NMR (250 MHz, CDCl\(_3\)) \(\delta\) 8.02-7.95 (m, 2H), 7.79 (d, \(J = 8.2\) Hz, 2H), 7.75-7.71 (m, 2H), 7.22-7.16 (m, 5H), 7.05-7.01 (m, 2H), 6.38 (d, \(J = 16.1\) Hz, 1H), 5.86 (dd, \(J = 16.1, 5.5\) Hz, 1H), 5.32 (br-s, 1H), 5.12 (d, \(J = 17.6\) Hz, 1H), 4.50 (d, \(J = 17.6\) Hz, 1H), 3.55 (dd, \(J = 17.3, 5.9\) Hz, 1H), 3.38 (dd, \(J = 17.3, 2.0\) Hz, 1H), 2.34 (s, 3H); 13C NMR (63 MHz, CDCl\(_3\)) \(\delta\) 149.4, 148.0, 144.1, 141.9, 141.4, 136.3, 135.7, 134.2, 130.1, 130.0, 128.8, 128.7, 128.6, 128.3, 127.7, 126.6, 124.6, 53.4, 46.4, 36.9, 21.6 (one carbon missing due to overlap); HRMS (ESI): m/z [M + H]\(^+\) calcd for \([\text{C}_{26}\text{H}_{24}\text{N}_{3}\text{O}_{2}\text{S}]^+\): 442.1584; found: 442.1584.

(E)-3-(4-chlorostyryl)-2-tosyl-1,2,3,4-tetrahydropyrido[3,4-b]quinoxaline (5c)

59% yield; yellow solid; mp 76–79 °C; \(^1\)H NMR (250 MHz, CDCl\(_3\)) \(\delta\) 8.01-7.95 (m, 2H), 7.79-7.71 (m, 4H), 7.23 (d, \(J = 8.0\) Hz, 2H), 7.15 (d, \(J = 8.5\) Hz, 2H), 6.97 (d, \(J = 8.5\) Hz, 2H), 6.36 (d, \(J = 16.1\) Hz, 1H), 5.86 (dd, \(J = 16.1, 5.6\) Hz, 1H), 5.30 (br-s, 1H), 5.10 (d, \(J = 17.6\) Hz, 1H), 4.50 (d, \(J = 17.6\) Hz, 1H), 3.53 (dd, \(J = 17.3, 6.0\) Hz, 1H), 3.34 (dd, \(J = 17.3, 2.2\) Hz, 1H), 2.34 (s, 3H); 13C NMR (63 MHz, CDCl\(_3\)) \(\delta\) 149.2, 147.9, 144.1, 141.9, 141.4, 136.2, 135.7, 134.0, 132.9, 130.1, 130.0, 129.97, 128.8, 128.7, 128.6, 127.7, 126.6, 124.6, 53.4, 46.4, 36.9, 21.6 (one carbon missing due to overlap); HRMS (ESI): m/z [M + H]\(^+\) calcd for \([\text{C}_{26}\text{H}_{23}\text{N}_{3}\text{O}_{2}\text{SCl}]^+\): 476.1194; found: 476.1187.

(E)-3-(4-methoxystyryl)-2-tosyl-1,2,3,4-tetrahydropyrido[3,4-b]quinoxaline (5d)
45% yield; yellow solid; mp 127–130 °C; $^1$H NMR (250 MHz, CDCl$_3$) $\delta$ 8.01-7.95 (m, 2H), 7.80-7.70 (m, 4H), 7.31-7.20 (m, 2H), 6.97 (d, $J = 8.7$ Hz, 2H), 6.71 (d, $J = 8.8$ Hz, 2H), 6.32 (dd, $J = 16.1$, 1.1 Hz, 1H), 5.72 (dd, $J = 16.0$, 5.6 Hz, 1H), 5.29 (br-s, 1H), 5.10 (d, $J = 17.6$ Hz, 1H), 4.49 (d, $J = 17.6$ Hz, 1H), 3.73 (s, 3H), 3.53 (dd, $J = 17.3$, 5.9 Hz, 1H), 3.36 (dd, $J = 17.3$, 2.1 Hz, 1H), 2.34 (s, 3H); $^{13}$C NMR (63 MHz, CDCl$_3$) $\delta$ 159.7, 149.5, 148.1, 144.0, 141.3, 136.3, 133.6, 130.0, 129.9, 128.7, 128.6, 128.4, 127.8, 127.6, 126.6, 122.2, 114.0, 55.4, 53.5, 46.4, 36.9, 21.6; HRMS (ESI): $m/z$ [M + H]$^+$ calcd for [C$_{27}$H$_{26}$N$_3$O$_3$S]$^+$: 472.1689; found: 472.1684.

(E)-3-(2-(furan-2-yl)vinyl)-2-tosyl-1,2,3,4-tetrahydropyrido[3,4-b]quinoxaline (5e)

59% yield; brown solid; mp 69–72 °C; $^1$H NMR (250 MHz, CDCl$_3$) $\delta$ 7.99-7.95 (m, 2H), 7.78-7.70 (m, 4H), 7.26-7.19 (m, 2H), 6.08 (d, $J = 3.3$ Hz, 1H), 5.85 (dd, $J = 16.0$, 5.5 Hz, 1H), 5.29 (br-s, 1H), 5.08 (d, $J = 17.7$ Hz, 1H), 4.52 (d, $J = 17.7$ Hz, 1H), 3.49 (dd, $J = 17.2$, 5.9 Hz, 1H), 3.30 (d, $J = 17.1$ Hz, 1H), 2.33 (s, 3H); $^{13}$C NMR (63 MHz, CDCl$_3$) $\delta$ 151.4, 149.3, 148.1, 144.1, 142.5, 141.8, 141.4, 136.3, 130.1, 130.0, 129.8, 128.8, 128.6, 127.6, 123.3, 122.3, 111.5, 109.4, 53.2, 46.3, 36.8, 21.6; HRMS (ESI): $m/z$ [M + H]$^+$ calcd for [C$_{24}$H$_{22}$N$_3$O$_3$S]$^+$: 432.1376; found: 432.1378.

3-(2,2-diphenylvinyl)-2-tosyl-1,2,3,4-tetrahydropyrido[3,4-b]quinoxaline (5f)

44% yield; yellow solid; mp 82–85 °C; $^1$H NMR (250 MHz, CDCl$_3$) $\delta$ 8.02-7.96 (m, 2H), 7.75-7.71 (m, 2H), 7.64-7.60 (m, 2H), 7.52-7.44 (m, 3H), 7.26-7.10 (m, 7H), 6.70 (d, $J = 8.0$ Hz, 2H), 5.63 (dd, $J = 9.8$, 1.2 Hz 1H), 5.23 (d, $J = 15.6$ Hz, 1H), 5.19 (d, $J = 17.6$ Hz, 1H), 4.63 (d, $J = 17.6$ Hz, 1H), 3.64 (dd, $J = 16.9$, 5.7 Hz, 1H), 3.26 (d, $J = 16.9$ Hz, 1H), 2.34 (s, 3H); $^{13}$C NMR (63 MHz, CDCl$_3$) $\delta$ 149.4, 148.0, 145.7, 143.9, 142.0, 141.6, 141.5, 138.5, 135.3, 130.1, 130.0, 129.8, 129.6, 128.84, 128.75, 128.7, 128.3, 128.1, 128.0, 127.9, 127.7, 122.2, 51.5, 46.7, 40.1, 21.6; HRMS (ESI): $m/z$ [M + H]$^+$ calcd for [C$_{32}$H$_{28}$N$_3$O$_2$S]$^+$: 518.1897; found: 518.1898.