Supporting Information

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Alkylation of N-(2-pyridyl)sulfonyl aryl aldimines with organozinc halides: conciliation of reactivity and chemoselectivity

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EXPERIMENTAL SECTION

General methods.

Melting points were taken in open-end capillary tubes. NMR spectra were recorded [300 MHz ($^1$H), 75 MHz ($^{13}$C)] at room temperature in CDCl$_3$ calibrated at 7.26 ppm ($^1$H) or 77.0 ppm ($^{13}$C). Mass spectra (MS) were determined at an ionizing voltage of 70 eV. All the reactions were carried out in anhydrous solvents and under nitrogen atmosphere. CH$_2$Cl$_2$ was dried and stored over microwave-activated 4Å molecular sieves. Flash column chromatography was performed using silica gel (230-400 mesh). Alkylzinc bromides were purchased to Aldrich or prepared following the literature procedure.

Synthesis of 2-pyridylsulfonyl imines

The starting sulfonylimines were prepared in good yields by direct condensation between the corresponding aldehyde and 2-pyridylsulfonamide following the procedure described by Davis (see Scheme below).

1f, R= Ph, 80%
4f, R= 4-MeOC$_6$H$_4$, 68%
5f, R= 4-FC$_6$H$_4$, 78%
6f, R= 2-BrC$_6$H$_4$, 72%
7f, R= 3-MeC$_6$H$_4$, 82%
8f, R= 2-Naph, 78%
9f, R= 2-Furyl, 83%
10f, R= 2-Thienyl, 71%
11f, R= N-Bn-2-pyrrol, 79%
12f, R= 4-AcC$_6$H$_4$, 67%

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1 S. Hou, Org. Lett. 2003, 5, 423
Representative procedure for the synthesis of (E)-phenyl-N-(2-
pyridylsulfonyl)methanimine (1f)  

A mixture of benzaldehyde (712 µL, 7.0 mmol), N-2-pyridylsulfonamide (1.10 g, 7.0 mmol), Amberlyst-15 (100 mg) and 4Å molecular sieves in dry toluene (10 mL) was heated to reflux in a sealed tube overnight. The mixture was cooled to room temperature before it was filtered through celite. The filtrate was concentrated and the resulting yellow solid was triturated with diethyl ether to afford pure imine 1f as a white solid; yield: 1.30 g (80%); m.p.: 118-120 °C. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 9.28 (s, 1H), 8.75 (ddd, $J$ = 0.8, 1.6 and 4.7 Hz, 1H), 8.26 (m, 1H), 8.11-7.90 (m, 3H), 7.66 (m, 1H), 7.58-7.48 (m, 3H). $^{13}$C NMR (75 MHz, CDCl$_3$): 174.3, 155.9, 150.4, 138.1, 135.4, 132.4, 131.7, 129.2, 127.2, 123.4.

Representative procedure for the addition of alkylzinc bromides to imines:

Synthesis of 1-phenyl-N-(2-pyridylsulfonyl)heptan-1-amine (2f).  

To a solution of Cu(OTf)$_2$ (3.6 mg, 5.0 mol%) and 1f (49.2 mg, 0.2 mmol.) in CH$_2$Cl$_2$ (2 mL, 0.1 M) under nitrogen atmosphere, was added commercially available 0.5 M solution of hexylzinc bromide solution in THF (800 µL, 0.4 mmol.). The mixture was stirred 10 min at rt before it was quenched with water (2 mL) and extracted with CH$_2$Cl$_2$ (3x 2 mL). The combined organic phase was dried (Na$_2$SO$_4$) and evaporated. The residue was purified by flash chromatography using Et$_3$N neutralized silica gel (n-Hexane-EtOAc 2:1) to afford pure amine 2f as a white solid; yield: 123.6 mg (93%); m.p.: 58-60 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.54 (d, $J$ = 4.4 Hz, 1H), 7.61-7.50 (m, 2H), 7.23 (m, 1H), 7.05-6.90 (m, 5H), 5.81 (d, $J$ = 7.7 Hz, 1H), 4.32 (q, $J$ = 7.6 Hz, 1H), 1.76 (m, 1H), 1.61

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5 When hexylzinc bromide is prepared according to the literature procedure (ref. 1), a 1 M solution of this reagent in DMA (400 µL, 0.4 mmol) is added to the reaction mixture containing Cu(OTf)$_2$ and 1f in CH$_2$Cl$_2$. 
(m, 1H), 1.30-0.98 (m, 8H), 0.75 (t, J= 6.7 Hz, 3H). $^{13}$C NMR (75 MHz, CDCl$_3$): 157.8, 149.7, 140.6, 137.4, 128.2, 127.2, 126.7, 126.0, 122.0, 58.9, 37.3, 31.6, 28.8, 25.9, 22.5, 14.0. MS (FAB+) m/z 333.2 (M+H', 100), FAB+ HRMS for C$_{18}$H$_{25}$O$_2$N$_2$S (M+H'): Calcd: 333.1636. Found: 333.1650. Anal. Calcd for C$_{18}$H$_{24}$O$_2$N$_2$S: C 65.03, H 7.28, N 8.43, S 9.65; found: C 64.67, H 7.13, N 8.31, S 9.55.

2-Ethyl-1-phenyl-N-(2-pyridylsulfonyl)butan-1-amine (3f). yield 92%, yellow solid; m.p.: 70-71 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.36 (d, J= 4.4 Hz, 1H), 7.60-7.47 (m, 2H), 7.17 (m, 1H), 6.98-6.82 (m, 5H), 5.53 (d, J= 9.1 Hz, 1H), 4.30 (dd, J= 7.6 and 9.0 Hz, 1H), 1.62-1.30 (m, 3H), 0.79 (t, J= 7.3 Hz, 3H). $^{13}$C NMR (75 MHz, CDCl$_3$): 157.6, 149.6, 139.8, 137.3, 128.0, 127.1, 126.8, 125.9, 122.0, 60.5, 46.6, 21.5, 20.8, 10.7, 10.5. Anal. Calcd for C$_{17}$H$_{22}$O$_2$N$_2$S: C 65.03, H 7.28, N 8.43, S 9.64; found: C 64.51, H 7.03, N 8.88, S 9.93.

2-Cyclohexyl-1-phenyl-N-(2-pyridylsulfonyl)ethanamine (13f). yield 88%, white solid; m.p.: 122-124 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.41 (d, J= 4.4 Hz, 1H), 7.60-7.50 (m, 2H), 7.21 (m, 1H), 7.10-6.90 (m, 5H), 5.43 (d, J= 8.1 Hz, 1H), 4.42 (q, J= 8.1 Hz, 1H), 1.70-1.41 (m, 7H), 1.22-1.01 (m, 4H) 0.91-0.72 (m, 2H). $^{13}$C NMR (75 MHz, CDCl$_3$): 157.8, 149.7, 141.0, 137.4, 128.2, 127.2, 126.6, 126.0, 122.0, 56.3, 45.3, 33.8, 33.2, 32.8, 26.4, 26.0, 25.9. Anal. Calcd for C$_{19}$H$_{24}$O$_2$N$_2$S: C 66.25, H 7.02, N 8.13, S 9.29; found: C 65.91, H 7.07, N 8.10, S 9.00.

1-Cyclohexyl-1-phenyl-N-(2-pyridylsulfonyl)methanamine (14f). yield 81%, white solid; m.p.: 150-151 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.34 (d, J= 4.4 Hz, 1H), 7.58-7.48 (m, 2H), 7.17 (m, 1H), 6.98-6.92 (m, 3H), 6.84-6.80 (m, 2H), 5.40 (d, J= 8.9 Hz, 1H), 4.06 (t, J= 8.7 Hz, 1H), 1.99 (m, 1H), 1.70 (m, 1H), 1.60-1.46 (m, 3H) 1.24-0.72 (m,
$^{13}$C NMR (75 MHz, CDCl$_3$): 157.7, 149.6, 139.5, 137.3, 128.0, 127.1, 127.0, 125.9, 122.0, 63.9, 43.5, 29.8, 29.6, 26.2, 25.9. Anal. Calcd for C$_{18}$H$_{22}$O$_2$N$_2$S: C 65.42, H 6.71, N 8.48, S 9.70; found: C 64.97, H 6.76, N 8.38, S 9.32. MS (FAB+) m/z 331.1 (M+H', 64.5), FAB+ HRMS for C$_{18}$H$_{22}$O$_2$N$_2$S (M+H'): Calcd: 331.1480. Found: 331.1488.

1-Phenyl-N-(2-pyridylsulfonyl)pent-4-en-1-amine (15f). yield 90%, white solid; m.p.: 75-76 ºC; $^1$H NMR (300 MHz, CDCl$_3$): δ 8.41 (d, J= 4.4 Hz, 1H), 7.62-7.53 (m, 2H), 7.23 (m, 1H), 7.02-6.97 (m, 3H), 6.95-6.90 (m, 2H), 5.72-5.58 (m, 2H), 4.90 (m, 1H), 4.86 (m. 1H), 4.35 (q, J= 7.4 Hz, 1H), 2.00-1.60 (m, 4H). $^{13}$C NMR (75 MHz, CDCl$_3$): 157.7, 149.7, 140.2, 137.5, 137.1, 128.3, 127.3, 126.7, 126.1, 122.0, 115.6, 58.3, 41.2, 48.6. MS (FAB+) m/z 303.1 (M+H', 100), FAB+ HRMS for C$_{16}$H$_{19}$O$_2$N$_2$S (M+H'): Calcd: 303.1167. Found: 303.1178. Anal. Calcd for C$_{16}$H$_{18}$O$_2$N$_2$S: C 63.55, H 6.00, N 9.26, S 10.60; found: C 63.07, H 6.02, N 9.17, S 10.36.

4-Phenoxy-1-phenyl-N-(2-pyridylsulfonyl)butan-1-amine (16f). yield 84%, white solid; m.p.: 58-60 ºC; $^1$H NMR (300 MHz, CDCl$_3$): δ 8.38 (d, J= 4.4 Hz, 1H), 7.62-7.50 (m, 2H), 7.25-7.10 (m, 4H), 7.02-6.93 (m, 4H), 6.88-6.80 (m, 2H), 6.78-6.72 (m, 1H), 5.85 (d, J= 8.2 Hz, 1H), 4.40 (q, J= 7.3 Hz, 1H), 4.05 (t, J= 6.0 Hz, 1H), 3.81 (t, J= 6.0 Hz, 1H), 2.02-1.50 (m, 4H). $^{13}$C NMR (75 MHz, CDCl$_3$): 158.8, 157.7, 149.7, 140.3, 137.5, 129.5, 129.4, 128.3, 127.4, 126.7, 126.1, 122.0, 120.8, 120.7, 114.5, 114.4, 67.0, 65.6, 60.4, 58.6. MS (FAB+) m/z 383.1 (M+H', 100), FAB+ HRMS for C$_{21}$H$_{23}$O$_3$N$_2$S (M+H'): Calcd: 383.1429. Found: 383.1432.

3-(1,3-Dioxolan-2-yl)-1-phenyl-N-(2-pyridylsulfonyl)propan-1-amine (17f). yield 92%, white solid; m.p.: 112-113 ºC; $^1$H NMR (300 MHz, CDCl$_3$): δ 8.87 (d, J= 4.4 Hz, 1H), 7.63-7.48 (m, 2H), 7.37 (m, 1H), 7.04 (s, 5H), 6.71 (d, J= 7.1 Hz, 1H), 4.83 (t, J= 4.3 Hz, 1H), 4.47 (q, J= 7.5 Hz, 1H), 4.00-3.61 (m, 4H), 2.00-1.55 (m, 4H).
$^{13}$C NMR (75 MHz, CDCl$_3$): 149.9, 140.2, 138.4, 128.3, 127.3, 126.7, 126.5, 122.6, 103.6, 64.9, 58.8, 31.4, 30.0. MS (FAB+) m/z 349.1 (M+H', 20), FAB+ HRMS for C$_{17}$H$_{21}$O$_2$N$_2$S (M+H'): Calcd: 349.1222. Found: 349.1237.

5-Chloro-1-phenyl-N-(2-pyridylsulfonyl)pentan-1-amine (18f). yield 95%, white solid; m.p.: 79-80 ºC; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.42 (d, $J$ = 4.4 Hz, 1H), 7.65-7.55 (m, 2H), 7.23 (m, 1H), 7.03-6.90 (m, 5H), 5.77 (d, $J$ = 8.2 Hz, 1H), 4.33 (q, $J$ = 7.6 Hz, 1H), 3.37 (t, $J$ = 6.6 Hz, 2H), 1.83 (m, 1H), 1.72-1.59 (m, 3H), 1.40 (m, 1H), 1.23 (m 1H). $^{13}$C NMR (75 MHz, CDCl$_3$): 157.7, 149.7, 140.2, 137.5, 128.4, 127.4, 126.7, 126.1, 122.0, 58.7, 44.6, 36.5, 32.0. MS (FAB+) m/z 339.1 (M+H', 100), FAB+ HRMS for C$_{16}$H$_{19}$O$_2$N$_2$SCl (M+H'): Calcd: 339.0934. Found: 339.0942, Anal. Calcd for C$_{16}$H$_{19}$O$_2$N$_2$SCl: C 56.71, H 5.65, N 8.27, S 9.46; found: C 56.27, H 5.64, N 8.19, S 9.30.

Ethyl 5-phenyl-5-N-(2-pyridylsulfonylamino)pentanoate (19f). yield 88%, white solid; m.p.: 71-72 ºC; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.50 (d, $J$ = 4.4 Hz, 1H), 7.73-7.62 (m, 2H), 7.32 (m, 1H), 7.12-7.00 (m, 5H), 5.81 (d, $J$ = 8.1 Hz, 1H), 4.45 (q, $J$ = 7.3 Hz, 1H), 4.11 (q, $J$ = 7.1 Hz, 2H), 2.26 (t, $J$ = 7.2 Hz, 2H), 1.92 (m, 1H), 1.85-1.65 (m, 2H), 1.54 (m, 1H), 1.25 (t, $J$ = 7.1 Hz, 3H) . $^{13}$C NMR (75 MHz, CDCl$_3$): 173.1, 157.8, 149.7, 140.2, 137.5, 128.3, 127.4, 126.1, 122.0, 60.3, 58.6, 36.5, 33.6, 21.4, 14.2. MS (FAB+) m/z 363.1 (M+H', 90), FAB+ HRMS for C$_{18}$H$_{23}$O$_2$N$_2$S (M+H'): Calcd: 363.1378. Found: 363.1396, Anal. Calcd for C$_{18}$H$_{23}$O$_2$N$_2$S: C 59.65, H 6.12, N 7.73, S 8.85; found: C 59.30, H 6.14, N 7.70, S 8.61.

5-Phenyl-5-N-(2-pyridylsulfonylamino)pentanenitrile (20f).

yield 90%, yellow oil; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.39 (d, $J$ = 4.4 Hz, 1H), 7.68-7.57 (m, 2H), 7.24 (ddd, $J$ = 1.4, 4.7 and 7.2 Hz, 1H), 7.06-7.00 (m, 3H), 6.95-6.90 (m, 2H), 5.68 (d, $J$ = 8.5 Hz, 1H), 4.36 (q, $J$ = 7.9 Hz, 1H), 2.37-2.28 (t, $J$ = 7.0 Hz, 2H), 2.00-1.45 (m, 4H). $^{13}$C NMR (75 MHz, CDCl$_3$): 157.5, 149.7, 139.6, 137.6,
128.5, 127.7, 126.5, 126.3, 122.0, 119.2, 58.1, 35.9, 22.1, 16.7. MS (FAB+): m/z 316.1 (M+H', 10), FAB+ HRMS for C_{16}H_{18}O_{2}N_{3}S (M+H'): Calcd: 316.1119. Found: 316.1109.

3-[2-Phenyl-N-(2-pyridylsulfonylamino)ethyl]benzonitrile (21f). yield 90%, white solid; m.p.: 85-86 °C; ^1H NMR (300 MHz, CDCl$_3$): δ 8.34 (d, $J$ = 4.4 Hz, 1H), 7.61-7.57 (m, 2H), 7.34 (m, 1H), 7.25-7.10 (m, 4H), 7.05-6.98 (m, 3H), 6.94-6.90 (m, 2H), 6.20 (d, $J$ = 7.9 Hz, 1H), 4.63 (q, $J$ = 7.4 Hz, 1H), 3.16 (dd, $J$ = 7.1 and 13.8 Hz, 1H), 2.98 (dd, $J$ = 7.6 and 13.8 Hz, 1H). ^13C NMR (75 MHz, CDCl$_3$): 157.5, 149.7, 139.2, 138.4, 137.7, 134.1, 132.9, 129.1, 128.4, 127.8, 126.8, 126.3, 121.9, 118.7, 112.3, 59.8, 43.1.

3-(1H-Indol-3-yl)-1-phenyl-N-(2-pyridylsulfanyl)propan-1-amine (22f). yield 82%, yellow solid; m.p.: 107-109 °C; ^1H NMR (300 MHz, CDCl$_3$): δ 7.99 (d, $J$ = 4.4 Hz, 1H), 7.30-6.90 (m, 12H), 6.76 (d, $J$ = 8.3 Hz, 1H), 6.58 (s, 1H), 4.05 (q, $J$ = 7.4 Hz, 1H), 2.45-2.35 (m, 2H), 1.09 (t, $J$ = 7.4 Hz, 2H). ^13C NMR (75 MHz, CDCl$_3$): 156.1, 149.0, 136.7, 128.9, 128.5, 126.5, 125.8, 122.0, 121.1 119.4, 118.7, 110.1, 67.2, 18.0, 13.9. MS (FAB+) m/z 392.1 (M+H', 8.4), FAB+ HRMS for C_{22}H_{22}O_{2}N_{3} (M+H'): Calcd: 392.1433. Found: 392.1380.

1-(4-Methoxyphenyl)-N-(2-pyridylsulfonyl)heptan-1-amine (23f). yield 80%, yellow solid; m.p.: 58-60 °C; ^1H NMR (300 MHz, CDCl$_3$): δ 8.45 (d, $J$ = 4.4 Hz, 1H), 7.63-7.56 (m, 2H), 7.25 (m, 1H), 6.84 (d, $J$ = 8.6 Hz, 2H), 6.52 (d, $J$ = 8.6 Hz, 2H), 5.33 (d, $J$ = 7.7 Hz, 1H), 4.26 (q, $J$ = 7.6 Hz, 1H), 3.64 (s, 3H), 1.75 (m, 1H), 1.60 (m, 1H), 1.24-1.02 (m, 8H), 0.76 (t, $J$ = 6.7 Hz, 3H). ^13C NMR (75 MHz, CDCl$_3$): 158.6, 157.9, 148.7, 137.4, 132.7, 132.0, 127.9, 126.0, 122.6, 114.3, 113.6, 58.3, 55.4, 37.3, 31.6, 28.8, 25.9, 22.5, 14.0. MS (FAB+) m/z 363.2 (M+H', 15), FAB+ HRMS for C_{19}H_{27}O_{2}N_{2}S (M+H'): Calcd: 363.1742. Found: 363.1744.
1-(4-Methoxyphenyl)-N-(2-pyridylsulfonyl)pent-4-en-1-amine (24f). Yield 83%, yellow solid; m.p.: 73-75 °C; $^1$H NMR (300 MHz, CDCl$_3$): δ 8.43 (d, $J$ = 4.4 Hz, 1H), 7.62-7.57 (m, 2H), 7.24 (m, 1H), 6.85 (d, $J$ = 8.7 Hz, 2H), 6.53 (d, $J$ = 8.7 Hz, 2H), 5.65 (m, 1H), 4.90 (m, 1H), 4.85 (m, 1H), 4.30 (q, $J$ = 7.4 Hz, 1H), 3.65 (s, 3H), 1.96-1.83 (m, 3H), 1.71 (m, 1H). $^{13}$C NMR (75 MHz, CDCl$_3$): 158.7, 157.9, 149.7, 137.4, 137.2, 128.0, 126.0, 122.1, 115.6, 113.6, 57.8, 55.2, 36.2, 30.0. MS (FAB+) m/z 333.1 (M+H$^+$, 20), FAB+ HRMS for C$_{17}$H$_{21}$O$_3$N$_2$S (M+H$^+$): Calcd: 333.1272. Found: 333.1276.

5-Chloro-1-(4-fluorophenyl)-N-(2-pyridylsulfonyl)pentan-1-amine (25f). Yield 88%, white solid; m.p.: 87-89 °C; $^1$H NMR (300 MHz, CDCl$_3$): δ 8.44 (d, $J$ = 4.4 Hz, 1H), 7.65-7.60 (m, 2H), 7.27 (m, 1H), 6.93 (m, 2H), 6.70 (m, 2H), 5.61 (d, $J$ = 8.0 Hz, 1H), 4.32 (q, $J$ = 7.6 Hz, 1H), 3.37 (t, $J$ = 6.6 Hz, 2H), 1.80 (m, 1H), 1.71-1.58 (m, 3H), 1.39 (m, 1H), 1.21 (m 1H). $^{13}$C NMR (75 MHz, CDCl$_3$): 157.8, 149.8, 137.6, 136.2, 128.4, 128.3, 126.2, 122.0, 115.3, 115.0, 58.0, 44.5, 36.4, 31.9, 23.4. MS (FAB+) m/z 357.1 (M+H$^+$, 70), FAB+ HRMS for C$_{16}$H$_{19}$O$_2$N$_2$SFCl (M+H$^+$): Calcd: 357.0839. Found: 357.0836.

3-(1,3-Dioxolan-2-yl)-1-(4-fluorophenyl)-N-(2-pyridylsulfonyl)propan-1-amine (26f). Yield 85%, colorless oil; $^1$H NMR (300 MHz, CDCl$_3$): δ 8.46 (d, $J$ = 4.4 Hz, 1H), 7.63-7.59 (m, 2H), 7.27 (m, 1H), 6.95 (m, 2H), 6.69 (m, 2H), 5.76 (d, $J$ = 7.4 Hz, 1H), 4.77 (t, $J$ = 4.3 Hz, 1H), 4.39 (q, $J$ = 7.4 Hz, 1H), 3.90-3.70 (m, 4H), 1.95-1.44 (m, 4H). $^{13}$C NMR (75 MHz, CDCl$_3$): 157.7, 149.8, 137.5, 136.3, 136.2, 128.4, 128.3, 126.2, 122.1, 115.2, 114.9, 103.5, 65.0, 64.9, 57.8, 31.0, 29.8. MS (FAB+) m/z 367.1 (M+H$^+$, 25), FAB+ HRMS for C$_{17}$H$_{20}$O$_2$NSF (M+H$^+$): Calcd: 367.1127. Found: 367.1132

Ethyl 5-(2-bromophenyl)-5-N-(2-pyridylsulfonlamino)pentanoate (27f). Yield 87%, white solid; m.p.: 100-102 °C; $^1$H NMR (300 MHz, CDCl$_3$): δ 8.43 (d, $J$ =
4.4 Hz, 1H), 7.73 (m, 1H), 7.61 (dt, J = 1.7 and 7.7 Hz, 1H), 7.29-7.20 (m, 2H), 7.11 (dd, J = 1.7 and 7.8 Hz, 1H), 7.01 (dt, J = 1.1 and 7.4 Hz, 1H), 6.87 (dt, J = 1.7 and 7.9 Hz, 1H), 5.94 (d, J = 8.2 Hz, 1H), 4.79 (q, J = 7.9 Hz, 1H), 4.03 (q, J = 7.2 Hz, 2H), 2.23 (t, J = 6.3 Hz, 2H), 1.81-1.60 (m, 3H), 1.51 (m, 1H), 1.16 (t, J = 7.1 Hz, 3H).

\(^{13}\text{C} \text{NMR} \ (75 \text{ MHz}, \text{CDCl}_3): 173.1, 157.2, 149.8, 149.6, 137.5, 132.7, 128.7, 128.3, 127.6, 126.3, 122.5, 122.2, 60.4, 57.2, 36.5, 33.4, 21.1, 14.2. \text{MS (FAB+)} m/z 443.1 (M+H\(^ +\), 100), \text{FAB+ HRMS for C}_{18}\text{H}_{22}\text{O}_{4}\text{N}_{2}\text{SBr (M+H\(^ +\))}: \text{Calcd: 441.0483. Found: 441.0492.}

Ethyl \text{-N-(2-pyridylsulfonylamino)-5-(3-tolyl)pentanoate (28f).} \text{ yield 84%, white solid; m.p.: 70-71 °C; } ^1\text{H NMR (300 MHz, CDCl}_3): \delta

8.41 (d, J = 4.4 Hz, 1H), 7.63-7.54 (m, 2H), 7.22 (m, 1H), 6.90 (m, 1H), 6.81 (m, 1H), 6.73 (m, 1H), 6.68 (m, 1H), 6.49 (d, J = 8.1 Hz, 1H), 4.29 (q, J = 7.2 Hz, 1H), 4.02 (q, J = 7.2 Hz, 2H), 2.19 (t, J = 7.2 Hz, 2H), 2.09 (s, 3H), 1.85-1.55 (m, 3H), 1.45 (m, 1H), 1.16 (t, J = 7.1 Hz, 3H). \(^{13}\text{C} \text{NMR (75 MHz, CDCl}_3): 173.1, 149.8, 149.6, 137.9, 137.3, 128.3, 128.2, 127.3, 126.0, 123.8, 122.0, 60.4, 56.4, 36.5, 33.6, 21.2, 14.2. \text{MS (FAB+)} m/z 377.2 (M+H\(^ +\), 65), \text{FAB+ HRMS for C}_{19}\text{H}_{25}\text{O}_{4}\text{N}_{2} \text{S (M+H\(^ +\))}: \text{Calcd: 377.1535. Found: 377.1553.}

1-(Naphthalen-2-yl)-\text{-N-(2-pyridylsulfonyl)heptan-1-amine (29f).} \text{ yield 91%, yellow solid; m.p.: 71-73 °C; } ^1\text{H NMR (300 MHz, CDCl}_3): \delta

8.29 (d, J = 4.4 Hz, 1H), 7.65-7.55 (m, 2H), 7.48-7.41 (m, 2H), 7.38-7.32 (m, 3H), 7.06 (dd, J = 1.7 and 8.5 Hz, 1H), 7.23 (m, 1H), 6.93 (ddd, J = 1.0, 4.7 and 7.6 Hz, 1H), 5.85 (m, 1H), 4.49 (q, J = 7.6 Hz, 1H), 1.85 (m, 1H), 1.74 (m, 1H), 1.29-1.00 (m, 8H), 0.75 (t, J = 6.7 Hz, 3H). \(^{13}\text{C} \text{NMR (75 MHz, CDCl}_3): 157.7, 149.5, 137.7, 137.1, 132.8, 132.5, 128.1, 127.1, 127.4, 126.2, 126.0, 125.9, 125.7, 124.3, 122.0, 59.1, 37.0, 31.5, 28.8, 25.9, 22.5, 14.0. \text{MS (FAB+)} m/z 383.2 (M+H\(^ +\), 25), \text{FAB+ HRMS for C}_{23}\text{H}_{27}\text{O}_{2}\text{N}_{2}\text{S (M+H\(^ +\))}: \text{Calcd: 383.1793. Found: 383.1802.}
5-Chloro-1-(naphthalen-2-yl)-N-(2-pyridylsulfonyl)pentan-1-amine (30f).

yield 89%, yellow oil; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta 8.29 (d, J= 4.4 \text{ Hz}, 1H), 7.65-7.46 \text{ (m, 4H)}, 7.4-7.29 \text{ (m, 4H)}, 7.06 \text{ (dd, } J= 1.8 \text{ and } 8.5 \text{ Hz, 1H}), 6.97 \text{ (ddd, } J= 1.1, 4.7 \text{ and } 7.7 \text{ Hz, 1H}), 5.45 \text{ (m, 1H)}, 4.50 \text{ (q, } J= 7.5 \text{ Hz, 1H}), 3.37 \text{ (t, } J= 6.7 \text{ Hz, } 2H), 1.62-1.20 \text{ (m, 4H)}, 1.45 \text{ (m, 1H)}, 1.26 \text{ (m, 1H)}. \({}^{13}\)C NMR (75 MHz, CDCl\(_3\)): 157.6, 149.5, 137.2, 137.1, 132.8, 132.6, 128.3, 127.7, 127.4, 126.2, 126.0, 125.8, 122.0, 58.9, 44.6, 36.2, 32.0, 23.4. MS (FAB+) m/z 389.1 (M+H\(^+\), 15), FAB+ HRMS for C\(_{20}\)H\(_{22}\)O\(_2\)N\(_2\)SCl (M+H\(^+\)): Calcd: 389.1090. Found: 389.1093.

1-(Furan-2-yl)-N-(2-pyridylsulfonyl)heptan-1-amine (31f).

yield 92%, white solid; m.p.: 58-60 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta 8.46 (d, J= 4.4 \text{ Hz, 1H}), 7.82-7.70 \text{ (m, 2H)}, 7.32 \text{ (ddd, } J= 1.4, 4.7 \text{ and } 7.2 \text{ Hz, 1H}), 6.96 \text{ (dd, } J= 0.7 \text{ and } 1.7 \text{ Hz, 1H}), 5.78 \text{ (d, } J= 3.2 \text{ Hz, 1H}), 5.45 \text{ (d, } J= 9.2 \text{ Hz, 1H}), 4.40 \text{ (q, } J= 7.5 \text{ Hz, 1H}), 1.80-1.65 \text{ (m, 2H)}, 1.30-1.05 \text{ (m, 8H)}, 0.78 \text{ (t, } J= 7.0 \text{ Hz, } 3H). \({}^{13}\)C NMR (75 MHz, CDCl\(_3\)): 157.6, 152.8, 149.7, 141.8, 137.8, 126.2, 122.0, 109.8, 106.9, 127.4, 126.2, 126.0, 125.9, 125.7, 124.3, 122.0, 52.1, 34.6, 31.5, 28.6, 25.6, 22.5, 14.0. MS (FAB+) m/z 323.2 (M+H\(^+\), 27), FAB+ HRMS for C\(_{16}\)H\(_{23}\)O\(_3\)N\(_2\)S (M+H\(^+\)): Calcd: 323.1429. Found: 323.1441.

5-Chloro-1-(furan-2-yl)-N-(2-pyridylsulfonyl)pentan-1-amine (32f).

yield 90%, yellow oil; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta 8.47 (d, J= 4.4 \text{ Hz, 1H}), 7.83-7.70 \text{ (m, 2H)}, 7.31 \text{ (ddd, } J= 1.4, 4.7 \text{ and } 7.2 \text{ Hz, 1H}), 7.01 \text{ (dd, } J= 0.8 \text{ and } 1.7 \text{ Hz, 1H}), 5.97 \text{ (dd, } J= 1.8 \text{ and } 3.3 \text{ Hz, 1H}), 5.79 \text{ (d, } J= 3.2 \text{ Hz, 1H}), 5.25 \text{ (d, } J= 8.9 \text{ Hz, 1H}), 4.43 \text{ (q, } J= 7.5 \text{ Hz, 1H}), 3.41 \text{ (t, } J= 6.7 \text{ Hz, } 2H), 1.82-1.20 \text{ (m, 6H)}. \({}^{13}\)C NMR (75 MHz, CDCl\(_3\)): 157.6, 152.4, 149.9, 141.9, 137.7, 126.3, 121.8, 110.0, 107.0, 51.9, 44.6, 33.9, 31.9, 23.1. MS (FAB+) m/z 329.0 (M+H\(^+\), 20), FAB+ HRMS for C\(_{14}\)H\(_{18}\)O\(_2\)N\(_2\)SCl (M+H\(^+\)): Calcd: 329.0726. Found: 329.0712.
5-N-(2-Pyridylsulfonylamino)-5-(thiophen-2-yl)pentanenitrile (33f). Yield 80%, colorless oil; \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): \(\delta\) 8.47 (d, \(J = 4.4\) Hz, 1H), 7.82-7.75 (m, 2H), 7.34 (ddd, \(J = 1.4, 4.7\) and 7.2 Hz, 1H), 6.99 (dd, \(J = 1.4\) and 4.9 Hz, 1H), 6.68-6.62 (m, 2H), 5.66 (d, \(J = 8.5\) Hz, 1H), 4.69 (q, \(J = 7.9\) Hz, 1H), 2.31 (t, \(J = 7.0\) Hz, 2H), 2.00-1.55 (m, 4H). \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}): 157.4, 149.7, 138.1, 126.7, 125.3, 125.0, 122.1, 119.2, 53.4, 36.6, 22.1, 16.7. MS (FAB+) m/z 322.0 (M+H\textsuperscript{+}, 37), FAB+ HRMS for C\textsubscript{14}H\textsubscript{16}O\textsubscript{2}N\textsubscript{3}S\textsubscript{2}(M+H\textsuperscript{+}): Calcd: 322.0684. Found: 322.0688.

1-(1-Benzyl-1H-pyrrol-2-yl)-2-cyclohexyl-N-(2-pyridylsulfonyl)ethanamine (34f). Yield 68%, white solid; m.p.: 110-112 °C; \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): \(\delta\) 8.53 (d, \(J = 4.4\) Hz, 1H), 7.73-7.68 (m, 2H), 7.33 (m, 1H), 7.25-7.10 (m, 3H), 6.92-6.87 (m, 2H), 6.45 (dd, \(J = 1.8\) and 2.5 Hz, 1H), 5.90-5.85 (m, 2H), 5.21 (d, \(J = 16.3\) Hz, 1H), 5.05 (d, \(J = 8.4\) Hz, 1H), 4.88 (d, \(J = 16.3\) Hz, 1H), 4.42 (q, \(J = 8.1\) Hz, 1H), 1.50-1.13 (m, 6H), 1.05-1.65 (m, 5H) 0.51-0.32 (m, 2H). \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}): 158.3, 149.9, 138.4, 137.7, 131.6, 128.7, 127.5, 126.4, 126.2, 122.4, 121.5, 107.3, 50.4, 48.0, 43.5, 34.0, 32.9, 32.5, 26.3, 25.9. MS (FAB+) m/z 424.2 (M+H\textsuperscript{+}, 5), FAB+ HRMS for C\textsubscript{24}H\textsubscript{30}O\textsubscript{2}N\textsubscript{3}S(M+H\textsuperscript{+}): Calcd: 424.2059. Found: 424.2050.

1-[[4-[5-Chloro-1-N-(2-pyridylsulfonylamino)pentyl]phenyl]ethanone (35f). Yield 77%, yellow oil; \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): \(\delta\) 8.45 (d, \(J = 4.4\) Hz, 1H), 7.75-7.55 (m, 4H), 7.27 (m, 1H), 7.11 (d, \(J = 8.3\) Hz, 2H), 6.00 (d, \(J = 7.9\) Hz, 1H), 4.43 (q, \(J = 7.6\) Hz, 1H), 3.36 (t, \(J = 6.5\) Hz, 2H), 2.47 (s, 3H), 1.93-1.60 (m, 4H), 1.52-1.20 (m, 2H). \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}): 197.5, 157.7, 149.7, 145.9, 137.7, 136.2, 128.4, 127.1, 126.9, 126.3, 122.0, 58.3, 44.5, 36.3, 31.8, 23.3. MS (FAB+) m/z 381.1 (M+H\textsuperscript{+}, 65), FAB+ HRMS for C\textsubscript{16}H\textsubscript{22}O\textsubscript{2}NSCl (M+H\textsuperscript{+}): Calcd: 381.0961. Found: 381.0953.
Ethyl 5-(4-acetylphenyl)-5-(2-pyridylsulfonylamino)pentanoate (36f). yield 83%, yellow oil; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.43 (d, $J$ = 4.4 Hz, 1H), 7.75-7.55 (m, 4H), 7.25 (m, 1H), 7.12 (d, $J$ = 8.3 Hz, 2H), 6.16 (d, $J$ = 7.7 Hz, 1H), 4.44 (q, $J$ = 7.5 Hz, 1H), 4.01 (q, $J$ = 7.1 Hz, 2H), 2.46 (s, 3H), 2.16 (t, $J$ = 7.2 Hz, 2H), 1.90-1.55 (m, 3H), 1.42 (m, 1H), 1.14 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (75 MHz, CDCl$_3$): 197.5, 173.0, 157.7, 149.7, 145.9, 137.6, 128.9, 128.4, 126.9, 126.3, 122.0, 60.4, 58.2, 36.3, 33.4, 26.6, 21.3, 14.2. MS (FAB+) m/z 405.2 (M+H$^+$, 100), FAB+ HRMS for C$_{20}$H$_{25}$O$_5$N$_2$S (M+H$^+$): Calcd: 405.1484. Found: 405.1484.

1-[[4-[2-Ethyl-1-N-(2-pyridylsulfonylamino)butyl]phenyl]ethanone (37f). yield 85%, yellow solid; m.p.: 87-88 ºC; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.28 (d, $J$ = 4.4 Hz, 1H), 7.52-7.40 (m, 4H), 7.09 (m, 1H), 6.92 (d, $J$ = 8.2 Hz, 2H), 5.42 (d, $J$ = 8.8 Hz, 1H), 4.29 (dd, $J$ = 7.4 and 8.5 Hz, 1H), 2.34 (s, 3H), 1.42-1.15 (m, 3H), 1.15-0.95 (m, 3H), 0.65 (t, $J$ = 7.3 Hz, 3H), 0.58 (t, $J$ = 7.3 Hz, 3H). $^{13}$C NMR (75 MHz, CDCl$_3$): 197.5, 157.6, 149.7, 145.7, 137.4, 135.8, 128.0, 127.3, 126.2, 122.0, 60.0, 46.9, 30.9, 26.6, 21.6, 20.8, 10.8, 10.6. MS (FAB+) m/z 361.1.0 (M+H$^+$, 100), FAB+ HRMS for C$_{19}$H$_{25}$O$_3$N$_2$S (M+H$^+$): Calcd: 361.1586. Found: 361.1591.

(Z)-1,3-Diphenyl-N-(2-pyridylsulfonyl)non-1-en-1-amine (39). yield 97%, white solid; m.p.: 68-70 ºC; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.56 (d, $J$ = 4.4 Hz, 1H), 7.59-7.50 (m, 2H), 7.30-7.05 (m, 11H), 6.91 (s, 1H), 5.66 (d, $J$ = 9.7 Hz, 1H), 3.52 (m, 1H), 1.60-1.35 (m, 2H), 1.30-1.09 (m, 8H), 0.77 (t, $J$ = 6.7 Hz, 3H). $^{13}$C NMR (75 MHz, CDCl$_3$): 157.3, 150.0, 143.7, 137.7, 137.4, 133.6, 130.8, 128.7, 128.1, 127.9, 127.4, 127.1, 126.7, 126.5, 122.8, 63.1, 43.5, 37.6, 31.7, 29.3, 27.4, 22.6, 14.1. MS (FAB+) m/z 435.2 (M+H$^+$, 80), FAB+ HRMS for C$_{26}$H$_{31}$O$_3$N$_2$S (M+H$^+$): Calcd: 435.2106. Found: 435.2100.
(Z)-8-Chloro-1,3-diphenyl-N-(2-pyridylsulfonyl)-1-octen-1-amine (40). yield 94%, white gummy solid; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 8.56 (d, \(J = 4.4\) Hz, 1H), 7.62-7.50 (m, 2H), 7.28 (m, 1H), 7.24-7.15 (m, 4H), 7.12-7.02 (m, 6H), 6.93 (m, 1H), 5.68 (d, \(J = 9.3\) Hz, 1H), 3.58 (q, \(J = 7.1\), 1H), 3.38 (t, \(J = 6.7\) Hz, 2H), 1.70-1.40 (m, 4H), 1.32-0.90 (m, 2H). \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): 157.3, 150.0, 143.3, 137.7, 137.5, 133.9, 130.6, 128.9, 128.8, 128.1, 127.4, 127.2, 126.8, 126.7, 122.7, 44.8, 43.3, 36.5, 32.4, 24.6.

Ethyl (Z)-5,7-diphenyl-7-N-(2-pyridylsulfonyl)hept-6-enoate (41). yield 88%, white oil; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 8.69 (d, \(J = 4.4\) Hz, 1H), 7.75-7.60 (m, 2H), 7.41 (m, 1H), 7.35-7.15 (m, 10H), 7.04 (s, 1H), 5.79 (d, \(J = 9.5\) Hz, 1H), 4.16 (q, \(J = 7.1\) Hz, 2H), 3.71 (q, \(J = 7.2\) Hz, 1H), 2.29 (t, \(J = 7.2\) Hz, 2H), 1.80-1.40 (m, 4H), 1.29 (t, \(J = 7.1\) Hz, 3H). \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): 173.5, 157.3, 150.0, 143.2, 137.6, 137.5, 134.0, 130.4, 128.8, 128.1, 127.9, 127.4, 127.1, 126.7, 126.6, 122.7, 60.3, 43.1, 36.5, 34.0, 22.7, 14.3.

Representative procedure for the deprotection of \(N\)-(2-pyridyl) sulfonyl amines: Synthesis of 3-(1,3-dioxolan-2-yl)-1-phenylpropan-1-amine (43).

To a suspension of magnesium turnings (303 mg, 12.4 mmol) in dry MeOH (10 mL) cooled to 0ºC, was added a solution of sulfonamide 17f in dry MeOH (2 mL). The resulting mixture was stirred at room temperature for 3 h. Then it was filtered over Celite and the filtrated was washed with NaHCO\(_3\). The organic phase was dried (Na\(_2\)SO\(_4\)) and concentrated to afford the pure amine 43 as a brown oil, yield: 239 mg (92%); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.18-7.12 (m, 4H), 7.08 (m, 1H), 4.68 (t, \(J = 4.6\) Hz, 1H), 3.80-3.61 (m, 5H), 1.91 (bs, 2H), 1.70-1.35 (m, 4H). \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): 145.8, 128.5, 127.1, 126.4, 104.3, 64.9, 56.1, 33.4, 30.1. MS (FAB+) m/z 208.1 (M+H\(^+\), 90), FAB+ HRMS for C\(_{12}\)H\(_{18}\)NO\(_2\) (M+H\(^+\)): Calcd: 208.1337. Found: 208.1348.
5-Chloro-1-phenylpentan-1-amine (44). yield 90%, brown oil; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.32-7.10 (m, 5H), 3.83 (t, $J$= 7.1 Hz, 1H), 3.42 (t, $J$= 6.7 Hz, 2H), 2.80 (bs, 2H), 1.70-1.65 (m, 4H), 1.50-1.15 (m, 2H). $^{13}$C NMR (75 MHz, CDCl$_3$): 145.4, 128.6, 127.2, 126.4, 56.1, 44.8, 38.3, 32.4, 23.9. MS (FAB+) m/z 162.1 (M-Cl$^+$, 100) 198.1 (M+H$^+$, 10), FAB+ HRMS for C$_{11}$H$_{17}$NCl (M+H$^+$): Calcd: 198.1049. Found: 198.1043.

2-Phenylpiperidine$^6$ (45). yield 78%, yellow oil; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.50-7.02 (m, 5H), 3.70 (dd, $J$= 2.6 and 11.2 Hz, 1H), 3.20 (m, 1H), 2.90 (m, 1H), 2.00-1.51 (m, 6H). $^{13}$C NMR (75 MHz, CDCl$_3$): 145.8, 128.8, 127.7, 127.0, 62.8, 48.2, 35.4, 26.3, 25.8.

6-Phenylpiperidin-2-one$^7$ (46). yield 94%, brown solid; m.p.: 115-116; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.40-7.12 (m,5H), 5.90 (bs, 1H), 4.47 (dd, $J$= 4.6 and 8.8 Hz, 1H), 2.45-2.31 (m, 2H), 2.04 (m, 1H), 1.90-1.51 (m, 3H). $^{13}$C NMR (75 MHz, CDCl$_3$): 172.5, 142.7, 128.7, 126.1, 57.5, 32.1, 31.3, 19.5.

6-(4-Acetylphenyl)piperidin-2-one (47). yield 90%, brown oil; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.60 (d, $J$= 8.2 Hz, 2H), 7.08 (d, $J$= 8.2 Hz, 2H), 5.96 (bs, 1H), 4.45 (dd, $J$= 4.9 and 9.1 Hz, 1H), 2.44 (s, 3H), 2.42-2.34 (m, 2H), 2.01 (m, 1H), 1.90-1.50 (m, 3H). $^{13}$C NMR (75 MHz, CDCl$_3$): 197.5, 172.3, 142.7, 134.0, 128.1, 126.7, 57.1, 32.1, 31.3, 29.3, 19.4.

NMR SPECTRA

1f
Suitable crystals of complex 42 for X-ray diffraction analysis were grown by slow diffusion of a mixture of diethyl ether/n-hexane into a solution of 42 in CH₂Cl₂ at 4 °C.