Asymmetric Organocatalytic [3+2]-Annulation Strategy for the Synthesis of N-Fused Heteroaromatic Compounds

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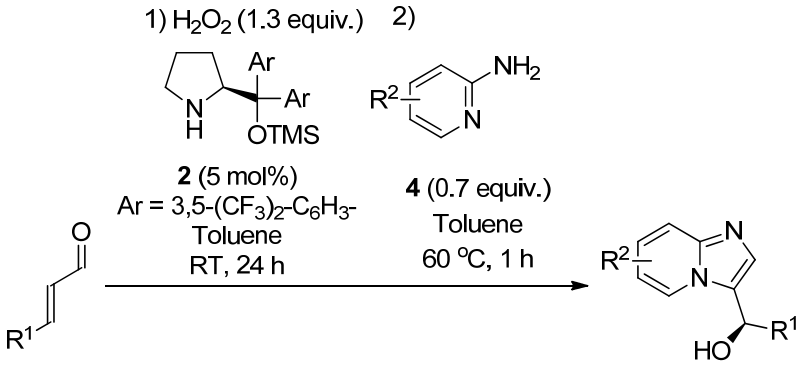
Supporting Information

1. General Methods.

NMR spectra were acquired on a Varian AS 400 spectrometer, running at 400 MHz for ^{1}H and 100 MHz for ^{13}C, respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CDCl_3$: 7.26 ppm for ^{1}H NMR, 77.0 ppm for ^{13}C NMR. DMSO-d6: 2.50 ppm for ^{1}H NMR, 39.4 ppm for ^{13}C NMR. CD_3OD: 3.31 ppm for ^{1}H NMR, 49.5 ppm for ^{13}C NMR). The following abbreviations are used to indicate the multiplicity in NMR spectra: s - singlet; d - doublet; t - triplet; q - quartet; quint. - quintet; dd – double doublet; ddd - double double doublet; td - triple doublet; dt - double triplet; m - multiplet; bs - broad signal. ^{13}C NMR spectra were acquired on a broad band decoupled mode. Mass spectra were recorded on a micromass LCT spectrometer using electrospray (ES^+) ionization techniques. Melting points were determined in open capillaries and are uncorrected. Analytical thin layer chromatography (TLC) was performed using pre-coated aluminum-backed plates (Merck Kieselgel 60 F254) and visualized by ultraviolet irradiation or $KMnO_4$ dip. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. The enantiomeric excess (*ee*) of the products was determined by chiral stationary phase HPLC (Daicel Chiralpak AS/AD and Daicel Chiralcel OD/OJ/OB columns) or by GC using a chiral Chrompack CP Chiralsil-Dex Cβ column. Unless otherwise noted, analytical grade solvents and commercially available reagents were used without further purification. For flash chromatography (FC) silica gel (Silica gel 60, 230-400 mesh, Fluka) was used. Aldehyde **1h**,**i**, TsNHOTs and *tert*-butyl (6-aminopyridin-2-yl)carbamate **4b** were synthesized according to literature.[1]

[1] Aldehyde **1h** was synthesized from crotonaldehyde and 4-phenyl-1-butene by cross-methatesis using the 2nd generation Grubbs-Hoveyda catalyst, see: (*a*) A. Michrowska and B. List, *Nature Chemistry,* 2009, **1**, 225. Aldehyde **1i** was synthesized by PCC oxidation of the commercially available (*Z*)-4-(benzyloxy)but-2-en-1-ol, see: (*b*) M. Avi, R. Gaisberger, S. Feichtenhofer and H. Griengl, *Tetrahedron,* 2009, **65**, 5418. For the synthesis of TsNHOTs, see: (*c*) Ł. Albrecht, H. Jiang, G. Dickmeiss, B. Gschwend, S. G. Hansen and K. A. Jørgensen, *J. Am. Chem. Soc.,* 2010, **132**, 9188. For the synthesis of **4b**, see: (*d*) S. T. Caldwell, G. Cooke, S. G. Hewage, S. Mabruk, G. Rabani, V. Rotello, B. O. Smith, C. Subramani and P. Woisel, *Chem. Commun.,* 2008, 4126.

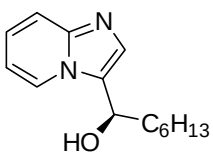
2. Enantioselective synthesis of 3-hydroxyalkyl imidazo[1,2-*a*]pyridines 5



1 **5**

General procedure: A glass vial equipped with a magnetic stirring bar was charged with the aldehyde **1** (0.2 mmol, 1 equiv.), the aminocatalyst **2** (0.01 mmol, 0.05 equiv.) and toluene (0.4 mL). After short stirring at RT, H_2O_2 (35 wt% in water, 0.26 mmol, 1.3 equiv.) was added. The stirring was maintained at ambient temperature for 24 h to achieve full conversion of the aldehyde **1**. Upon completion of the reaction, the corresponding 2-aminopyridine **4** (0.14 mmol, 0.7 equiv.) was added. The resulting mixture was heated at 60 ˚C for 1 h and then directly subjected to FC on silica gel to afford the target imidazo[1,2-*a*]pyridine **5**.

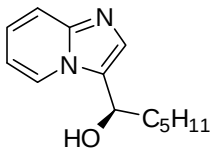
Representative procedure for up-scale reaction: A 50 mL round-bottom flask equipped with a magnetic stirring bar was charged with the aldehyde **1a** (10 mmol, 1 equiv.), the aminocatalyst **2** (0.5 mmol, 0.05 equiv.) and toluene (20 mL). After short stirring at RT, H_2O_2 (35 wt% in water, 13 mmol, 1.3 equiv.) was added. The stirring was maintained at ambient temperature for 24 h to achieve full conversion of the aldehyde **1**. Upon completion of the reaction, the corresponding 2-aminopyridine **4g** (9 mmol, 0.9 equiv.) was added. The resulting mixture was heated at 60 ˚C for 1 h and then directly subjected to FC on silica gel. The off-white solid obtained was suspended in Et_2O and filtered to afford the target imidazo[1,2-*a*]pyridine **5o** in 48% yield as a white solid (98% *ee*).



5a (*R*)-1-(Imidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol (Entry 1, Table 2)

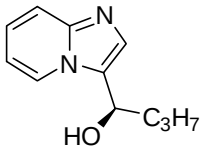
Following modified general procedure (using 0.8 equiv. of 2-aminopyridine **4a** in the annulation step) **5a** was isolated by FC (gradient: EtOAc/pentane 4:1 to pure EtOAc) in 58% yield as a white solid. Mp: 79-81 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 6.9 Hz, 1H), 7.48 (d, *J* = 8.9 Hz, 1H), 7.22-7.11 (m, 2H), 6.77 (t, *J* = 6.7 Hz, 1H), 4.89 (t, *J* = 6.9 Hz, 1H), 3.46 (bs, 1H), 2.04-1.95 (m, 2H), 1.62-1.49 (m, 1H), 1.45-1.22 (m, 7H), 0.88 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.6, 129.7, 126.8, 125.3, 124.3, 117.1, 111.8, 65.1, 34.9, 31.7,

29.0, 26.0, 22.5, 14.0. HR-MS: calculated for $(M+H)^+$: 233.1654; measured: 233.1654. The *ee* was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 90:10+0.09% DEA, 1 mL min^{-1}); τ_{major} = 13.3 min, τ_{minor} = 14.9 min (94% *ee*). $[\alpha]_D^{rt}$: -73.1 (c = 1.01, $CHCl_3$).



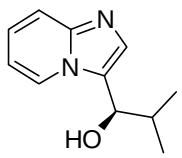
5b (*R*)-1-(Imidazo[1,2-*a*]pyridin-3-yl)hexan-1-ol (Entry 2, Table 2)

Following the general procedure **5b** was isolated by FC (gradient: EtOAc/pentane 4:1 to pure EtOAc) in 52% yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (td, *J* = 6.9, 1.1 Hz, 1H), 7.46 (d, *J* = 9.1 Hz, 1H), 7.18-7.11 (m, 2H), 6.77 (dt, *J* = 6.8, 1.1 Hz, 1H), 4.89 (t, *J* = 6.9 Hz, 1H), 3.67 (bs, 1H), 2.04-1.94 (m, 2H), 1.61-1.24 (m, 6H), 0.89 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.9, 130.1, 126.5, 125.2, 124.3, 117.4, 111.9, 65.4, 34.9, 31.5, 25.7, 22.5, 13.9. HR-MS: calculated for $(M+H)^+$: 219.1497; measured: 219.1492. The *ee* was determined by HPLC using a Chiralpak AS column (hexane/*i*PrOH 95:5+0.095% DEA, 1 mL min^{-1}); τ_{major} = 28.3 min, τ_{minor} = 22.5 min (95% *ee*). $[\alpha]_D^{rt}$: -81.9 (c = 0.98, $CHCl_3$).



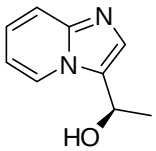
5c (*R*)-1-(Imidazo[1,2-*a*]pyridin-3-yl)butan-1-ol (Entry 3, Table 2)

Following the general procedure **5c** was isolated by FC (gradient: EtOAc/pentane 4:1 to pure EtOAc) in 54% yield as a pale yellow solid. Mp: 64-67 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (td, *J* = 6.9, 1.1 Hz, 1H), 7.39 (td, *J* = 9.1, 1.1 Hz, 1H), 7.11 (s, 1H), 7.07 (ddd, *J* = 9.1, 6.7, 1.3 Hz, 1H), 6.70 (dt, *J* = 6.8 Hz, 1H), 4.85 (t, *J* = 6.8 Hz, 1H), 3.18 (bs, 1H), 1.99-1.85 (m, 2H), 1.59-1.45 (m, 1H), 1.43-1.29 (m, 1H), 0.91 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0, 130.1, 126.6, 125.3, 124.4, 117.4, 112.0, 65.1, 37.0, 19.2, 13.8. HR-MS: calculated for $(M+Na)^+$: 213.1004; measured: 213.1001. The *ee* was determined by HPLC using a Chiralcel OB column (hexane/*i*PrOH 90:10+0.09% DEA, 0.5 mL min^{-1}); τ_{major} = 16.5 min, τ_{minor} = 19.1 min (92% *ee*). $[\alpha]_D^{rt}$: -79.5 (c = 1.01, $CHCl_3$).



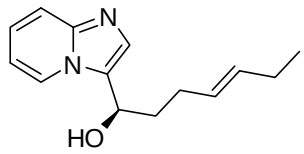
5d (*R*)-1-(Imidazo[1,2-*a*]pyridin-3-yl)-2-methylpropan-1-ol (Entry 4, Table 2)

Following the general procedure **5d** was isolated by FC (gradient: EtOAc/pentane 4:1 to pure EtOAc) in 54% yield as a yellow gel. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (td, *J* = 7.0, 1.2 Hz, 1H), 7.48 (td, *J* = 9.1, 1.1 Hz, 1H), 7.29 (s, 1H), 7.09 (ddd, *J* = 9.1, 6.7, 1.3 Hz, 1H), 6.72 (dt, *J* = 6.8, 1.2 Hz, 1H), 4.58 (d, *J* = 8.0 Hz, 1H), 2.70 (bs, 1H), 2.33-2.21 (m, 1H), 1.12 (d, *J* = 6.6 Hz, 3H), 0.83 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.9, 131.1, 125.6, 125.3, 124.2, 117.5, 111.9, 71.6, 32.2, 19.8, 18.8. HR-MS: calculated for $(M+Na)^+$: 213.1004; measured: 213.1006. The *ee* was determined by HPLC using a Chiralcel OJ column (hexane/*i*PrOH 90:10+0.09% DEA, 1 mL min^{-1}); τ_{major} = 11.1 min, τ_{minor} = 9.6 min (98% *ee*). $[\alpha]_D^{rt}$: -59.3 (c = 0.99, $CHCl_3$).



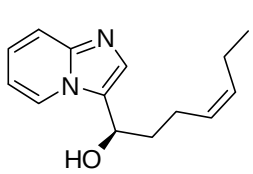
5e (*R*)-1-(Imidazo[1,2-*a*]pyridin-3-yl)ethanol (Entry 5, Table 2)

Following the modified general procedure (using 10 mol% of catalyst **2**) **5e** was isolated by FC (EtOAc) in 31% yield as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (td, *J* = 6.9, 1.0 Hz, 1H), 7.48 (td, *J* = 9.0, 1.0 Hz, 1H), 7.23 (s, 1H), 7.15 (ddd, *J* = 9.1, 6.7, 1.2 Hz, 1H), 6.79 (dt, *J* = 6.8 Hz, 1H), 5.12 (q, *J* = 6.6 Hz, 1H), 3.21 (bs, 1H), 1.72 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.1, 129.8, 127.3, 125.2, 124.5, 117.5, 112.1, 61.3, 21.4. HR-MS: calculated for $(M+Na)^+$: 185.0691; measured: 185.0692. The *ee* was determined by HPLC using a Chiralcel OB column (hexane/*i*PrOH 90:10+0.09% DEA, 0.5 mL min^{-1}); τ_{major} = 56.4 min, τ_{minor} = 38.2 min (91% *ee*). $[\alpha]_D^{rt}$: +65.6 (c = 0.49, CH_3OH).



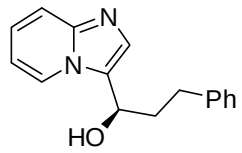
5f (*R*,*E*)-1-(Imidazo[1,2-*a*]pyridin-3-yl)hept-4-en-1-ol (Entry 6, Table 2)

Following the general procedure **5f** was isolated by FC (gradient: EtOAc/pentane 4:1 to pure EtOAc) in 52% yield as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 6.9 Hz, 1H), 7.46 (d, *J* = 9.1 Hz, 1H), 7.17 (s, 1H), 7.13 (ddd, *J* = 9.1, 6.7, 1.2 Hz, 1H), 6.77 (dt, *J* = 6.8 Hz, 1H), 5.58-5.33 (m, 2H), 4.92 (t, *J* = 7.3 Hz, 1H), 3.66 (bs, 1H), 2.30-2.10 (m, 2H), 2.11-1.94 (m, 4H), 0.96 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0, 133.3, 130.2, 130.2, 127.8, 126.4, 125.3, 124.4, 117.4, 112.0, 64.8, 34.7, 25.5, 13.8. HR-MS: calculated for $(M+H)^+$: 231.1497; measured: 231.1495. The *ee* was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 90:10+0.09% DEA, 1 mL min^{-1}); τ_{major} = 11.7 min, τ_{minor} = 13.1 min (90% *ee*). $[\alpha]_D^{rt}$: -57.6 (c = 0.99, $CHCl_3$).



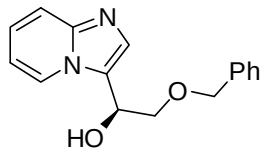
5g (*R*,*Z*)-1-(Imidazo[1,2-*a*]pyridin-3-yl)hept-4-en-1-ol (Entry 7, Table 2)

Following the modified general procedure (using 0.6 equiv. of 2-aminopyridine **4a** in the annulation step) **5g** was isolated by FC (gradient: EtOAc/pentane 4:1 to pure EtOAc) in 37% yield as a white solid. Mp: 61-63 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (td, *J* = 6.9, 1.1 Hz, 1H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.28 (s, 1H), 7.22-7.13 (m, 1H), 6.81 (t, *J* = 6.4 Hz, 1H), 5.50-5.32 (m, 2H), 4.95 (t, *J* = 6.6 Hz, 1H), 2.86 (bs, 1H), 2.37-2.16 (m, 2H), 2.16-1.96 (m, 4H), 0.94 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.1, 133.1, 130.3, 127.5, 125.2 (2C), 124.6, 117.6, 112.1, 65.1, 34.8, 23.7, 20.6, 14.3. HR-MS: calculated for $(M+Na)^+$: 253.1317; measured: 253.1315. The *ee* was determined by HPLC using a Chiralpak AS column (hexane/*i*PrOH 95:5+0.095% DEA, 1 mL min^{-1}); τ_{major} = 30.5 min, τ_{minor} = 35.8 min (94% *ee*). $[\alpha]_D^{rt}$: -64.7 (c = 1.00, $CHCl_3$).



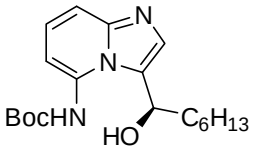
5h (*R*)-1-(Imidazo[1,2-*a*]pyridin-3-yl)-3-phenylpropan-1-ol (Entry 8, Table 2)

Following the general procedure **5h** was isolated by FC (gradient: EtOAc/pentane 4:1 to pure EtOAc) in 52% yield as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 6.9 Hz, 1H), 7.63-7.41 (m, 1H), 7.36-7.26 (m, 3H), 7.24-7.07 (m, 4H), 6.82-6.70 (m, 1H), 4.90 (t, *J* = 7.6 Hz, 1H), 3.38 (bs, 1H) 2.91 (ddd, *J* = 14.5, 8.6, 6.2 Hz, 1H), 2.85-2.73 (m, 1H), 2.41-2.23 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0, 141.2, 130.1, 128.5 (5C), 126.0, 125.2, 124.6, 117.4, 112.1, 64.5, 36.5, 32.1. HR-MS: calculated for $(M+Na)^+$: 275.1160; measured: 275.1160. The *ee* was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 90:10+0.09% DEA, 1 mL min^{-1}); τ_{major} = 17.9 min, τ_{minor} = 20.7 min (94% *ee*). $[\alpha]_D^{rt}$: -39.2 (c = 0.99, $CHCl_3$).



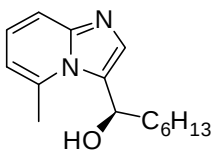
5i (*S*)-2-(Benzyloxy)-1-(imidazo[1,2-*a*]pyridin-3-yl)ethanol (Entry 9, Table 2)

Following the general procedure **5i** was isolated by FC (gradient: EtOAc/pentane 4:1 to pure EtOAc) in 41% yield as an orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (td, *J* = 6.9, 1.2 Hz, 1H), 7.53 (td, *J* = 9.1, 1.1 Hz, 1H), 7.41-7.28 (m, 6H), 7.15 (ddd, *J* = 9.1, 6.7, 1.3 Hz, 1H), 6.77 (dt, *J* = 6.8, 1.2 Hz, 1H), 5.20 (ddd, *J* = 6.8, 4.1, 0.5 Hz, 1H), 4.69-4.61 (m, 2H), 4.01-3.89 (m, 2H), 3.69 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.3, 137.7, 131.4, 128.7 (2C), 128.2, 128.1 (2C), 125.3, 124.7, 123.3, 117.9, 112.3, 73.9, 72.2, 64.9. HR-MS: calculated for $(M+Na)^+$: 291.1109; measured: 291.1117. The *ee* was determined by HPLC using a Chiralcel OJ column (hexane/*i*PrOH 90:10+0.09% DEA, 1 mL min^{-1}); τ_{major} = 50.5 min, τ_{minor} = 35.5 min (92% *ee*). $[\alpha]_D^{rt}$: -58.2 (c = 0.88, $CHCl_3$).



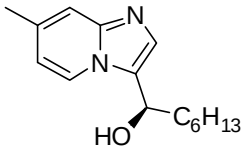
5j (*R*)-*tert*-Butyl 3-(1-hydroxyheptyl)imidazo[1,2-*a*]pyridin-5-ylcarbamate (Entry 1, Table 4)

Following the general procedure **5j** was isolated by FC (gradient: EtOAc/pentane 3:2 to EtOAc/pentane 9:1) in 40% yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.67 (s, 1H), 7.22-7.08 (m, 3H), 6.67 (s, 1H), 4.91 (dd, *J* = 8.0, 6.3 Hz, 1H), 1.97-1.69 (m, 3H), 1.55 (s, 9H), 1.39-1.21 (m, 8H), 0.87 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.6, 148.3, 134.3, 131.0, 126.5 (2C), 111.2, 103.2, 81.1, 65.8, 36.2, 31.7, 28.9, 28.2 (3C), 26.1, 22.5, 14.0. HR-MS: calculated for $(M+Na)^+$: 370.2107; measured: 370.2100. The *ee* was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 90:10+0.09% DEA, 1 mL min^{-1}); τ_{major} = 10.3 min, τ_{minor} = 11.8 min (90% *ee*). $[\alpha]_D^{rt}$: -47.0 (c = 1.00, $CHCl_3$).



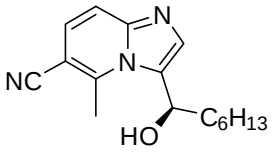
5k (*R*)-1-(5-Methylimidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol (Entry 3, Table 4)

Following the general procedure **5k** was isolated by FC (gradient: EtOAc/pentane 4:1 to pure EtOAc) in 60% yield as a orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.34 (d, *J* = 9.0 Hz, 1H), 7.00 (dd, *J* = 8.9, 6.7 Hz, 1H), 6.48 (d, *J* = 6.8 Hz, 1H), 5.11 (dd, *J* = 7.9, 5.7 Hz, 1H), 2.95 (s, 3H), 2.21-1.98 (m, 2H), 1.70-1.57 (m, 1H), 1.54-1.37 (m, 3H), 1.36-1.28 (m, 5H), 0.90 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 136.9, 132.0, 128.9, 124.8, 115.5, 113.6, 65.7, 36.7, 31.8, 29.2, 26.6, 22.6, 20.0, 14.0. HR-MS: calculated for $(M+Na)^+$: 269.1630; measured: 269.1631. The *ee* was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 90:10+0.09% DEA, 1 mL min^{-1}); τ_{major} = 10.7 min, τ_{minor} = 15.7 min (90% *ee*). $[\alpha]_D^{rt}$: -97.5 (c = 1.01, $CHCl_3$).



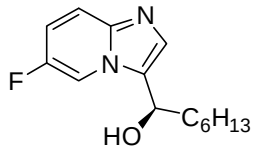
5l (*R*)-1-(7-Methylimidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol (Entry 5, Table 4)

Following the modified general procedure (using 0.6 equiv. of 2-aminopyridine **4d** in the annulation step) **5l** was isolated by FC (gradient: EtOAc/pentane 4:1 to pure EtOAc) in 45% yield as a white solid. Mp: 101-102 °C.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 7.0 Hz, 1H), 7.16 (s, 1H), 7.04 (s, 1H), 6.59 (dd, *J* = 7.0, 1.6 Hz, 1H), 4.83 (t, *J* = 6.9 Hz, 1H), 2.34 (s, 3H), 2.04-1.88 (m, 2H), 1.42-1.20 (m, 9H), 0.87 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.4, 135.3, 129.8, 126.1, 124.5, 115.8, 114.6, 65.4, 35.0, 31.7, 29.1, 26.0, 22.6, 21.2, 14.1. HR-MS: calculated for $(M+Na)^+$: 269.1630; measured: 269.1636. The *ee* was determined by HPLC using a Chiralpak AS column (hexane/*i*PrOH 90:10+0.09% DEA, 1 mL min^{-1}); τ_{major} = 12.4 min, τ_{minor} = 19.8 min (94% *ee*). $[\alpha]_D^{rt}$: -55.6 (c = 1.00, $CHCl_3$).



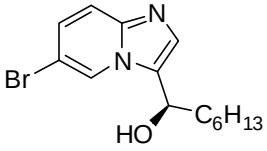
5m (*R*)-3-(1-Hydroxyheptyl)-5-methylimidazo[1,2-*a*]pyridine-6-carbonitrile (Entry 7, Table 4)

Following the modified general procedure (using 0.6 equiv. of 2-aminopyridine **4e** in the annulation step) **5m** was isolated by FC (gradient: EtOAc/pentane 3:2 to EtOAc/pentane 9:1) in 36% yield as a pale yellow foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.41 (d, *J* = 9.3 Hz, 1H), 7.21 (d, *J* = 9.3 Hz, 1H), 5.14-5.06 (m, 1H), 3.28 (s, 3H), 2.84 (bs, 1H), 2.21-2.00 (m, 2H), 1.70-1.27 (m, 8H), 0.90 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.0, 144.9, 134.1, 130.6, 125.1, 117.2, 116.5, 99.5, 65.5, 36.4, 31.7, 29.1, 26.4, 22.5, 18.5, 14.0. HR-MS: calculated for $(M+Na)^+$: 294.1582; measured: 294.1573. The *ee* was determined by HPLC using two combined Chiralpak AS columns (hexane/*i*PrOH 95:5+0.095% DEA, 0.5 mL min^{-1}); τ_{major} = 68.2 min, τ_{minor} = 60.0 min (91% *ee*). $[\alpha]_D^{rt}$: -124.4 (c = 0.48, $CHCl_3$).



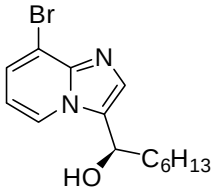
5n (*R*)-1-(6-Fluoroimidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol (Entry 9, Table 4)

Following the modified general procedure (using 0.9 equiv. of 2-aminopyridine **4f** in the annulation step) **5n** was isolated by FC (gradient: EtOAc/pentane 2:1 to EtOAc/pentane 3:1) in 47% yield as a white solid. Mp: 118-120 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (dd, *J* = 4.3, 2.4 Hz, 1H), 7.44 (dd, *J* = 9.8, 5.1 Hz, 1H), 7.29 (s, 1H), 7.07 (ddd, *J* = 10.0, 7.8, 2.4 Hz, 1H), 4.88 (t, *J* = 6.9 Hz, 1H), 3.27 (bs, 1H), 2.06-1.95 (m, 2H), 1.63-1.48 (m, 1H), 1.47-1.20 (m, 7H), 0.88 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.9 (d, *J* = 236.3 Hz), 143.6, 131.4, 127.9, 117.8 (d, *J* = 9.0 Hz), 116.5 (d, *J* = 25.2 Hz), 112.1 (d, *J* = 41.1 Hz), 65.5, 34.8, 31.7, 29.0, 25.9, 22.6, 14.0. HR-MS: calculated for $(M+H)^+$: 251.1559; measured: 251.1561. The *ee* was determined by HPLC using a Chiralpak AS column (hexane/*i*PrOH 95:5+0.095% DEA, 1 mL min^{-1}); τ_{major} = 17.8 min, τ_{minor} = 14.7 min (91% *ee*). $[\alpha]_D^{rt}$: -66.7 (c = 0.35, CH_3OH).



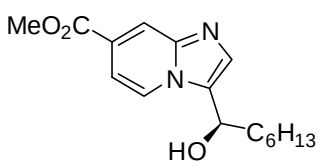
5o (*R*)-1-(6-Bromoimidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol (Entry 11, Table 4)

Following the modified general procedure (using 0.9 equiv. of 2-aminopyridine **4g** in the annulation step) **5o** was isolated by FC (gradient: EtOAc/pentane 4:1 to pure EtOAc) in 44% yield as a white solid. Mp: 148-150 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (dd, *J* = 1.9, 0.8 Hz, 1H), 7.44 (dd, *J* = 9.5, 0.6 Hz, 1H), 7.37 (s, 1H), 7.24 (dd, *J* = 9.5, 1.9 Hz, 1H), 4.93 (t, *J* = 6.9 Hz, 1H), 2.52 (bs, 1H), 2.03 (dd, *J* = 14.4, 7.4 Hz, 2H), 1.63-1.27 (m, 8H), 0.89 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5, 131.1, 127.9, 126.8, 125.4, 118.1, 106.9, 65.5, 34.9, 31.7, 29.0, 25.9, 22.5, 14.0. HR-MS: calculated for $(M+Na)^+$: 333.0578; measured: 333.0583. The *ee* was determined by HPLC using a Chiralpak AS column (hexane/*i*PrOH 90:10+0.09% DEA, 1 mL min^{-1}); τ_{major} = 10.8 min, τ_{minor} = 8.0 min (96% *ee*). $[\alpha]_D^{rt}$: -72.8 (c = 0.48, $CHCl_3$).



5p (*R*)-1-(8-Bromoimidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol (Entry 14, Table 4)

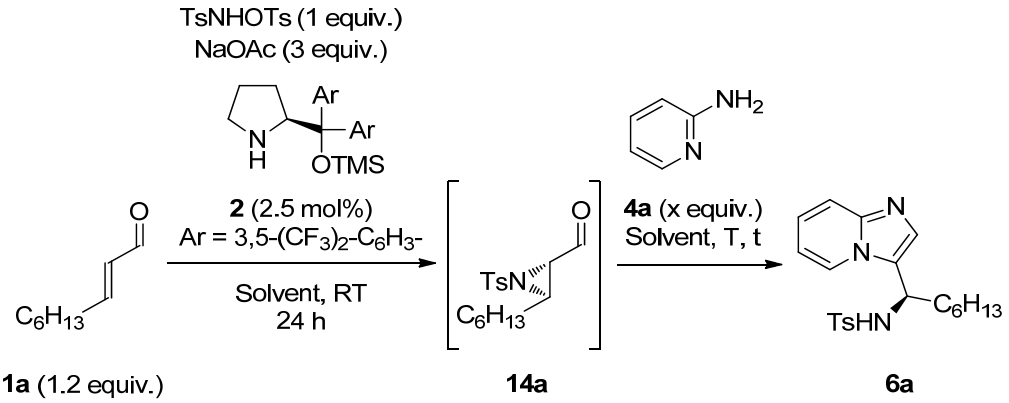
Following the general procedure **5p** was isolated by FC (gradient: EtOAc/pentane 1:1) in 44% yield as a white solid. Mp: 93-94 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 6.8 Hz, 1H), 7.40 (d, *J* = 7.2 Hz, 1H), 7.17 (s, 1H), 6.66 (t, *J* = 7.1 Hz, 1H), 4.87 (t, *J* = 6.8 Hz, 1H), 3.34 (bs, 1H), 2.23-1.82 (m, 2H), 1.47-1.19 (m, 8H), 0.87 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 130.6, 128.5, 127.0, 124.8, 112.1, 111.3, 65.6, 34.9, 31.7, 29.0, 25.9, 22.5, 14.0. HR-MS: calculated for $(M+Na)^+$: 333.0578; measured: 333.0575. The *ee* was determined by HPLC using a Chiralpak AS column (hexane/*i*PrOH 90:10+0.09% DEA, 1 mL min^{-1}); τ_{minor} = 7.1 min, τ_{major} = 9.2 min (92% *ee*). $[\alpha]_D^{rt}$: -48.5 (c = 1.00, $CHCl_3$).



5q (*R*)-Methyl 3-(1-hydroxyheptyl)imidazo[1,2-*a*]pyridine-7-carboxylate (Entry 16, Table 4)

Following the modified general procedure (using 0.8 equiv. of 2-aminopyridine **4i** in the annulation step performed for 90 minutes) **5q** was isolated by FC (gradient: EtOAc/pentane 2:1 to EtOAc/pentane 3:1) in 52% yield as white solid. Mp: 166-168 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.57 (dd, *J* = 7.2 Hz, 1H), 8.23 (dd, *J* = 1.6 Hz, 1H), 7.68 (s, 1H), 7.48 (dd, *J* = 7.2 Hz, 1H), 5.05 (t, *J* = 6.9 Hz, 1H), 3.96 (s, 3H), 2.10-1.97 (m, 2H), 1.65-1.51 (m, 1H), 1.46-1.26 (m, 7H), 0.90 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ 166.9, 146.0, 133.3, 130.7, 127.9, 126.7, 120.1, 112.4, 65.9, 53.1, 36.1, 33.0, 30.3, 27.1, 23.7, 14.4. HR-MS: calculated for $(M+Na)^+$: 313.1528; measured: 313.1532. The *ee* was determined by HPLC using a Chiralpak AS column (hexane/*i*PrOH 90:10+0.09% DEA, 1 mL min^{-1}); τ_{major} = 18.1 min, τ_{minor} = 12.3 min (94% *ee*). $[\alpha]_D^{rt}$: -69.0 (c = 0.16, CH_3OH).

3. Optimization of the enantioselective synthesis of 3-aminoalkyl imidazo[1,2-*a*]pyridines 6 using *trans*-2-nonenal 1a and 2-aminopyridine 4a as model substrates[a]

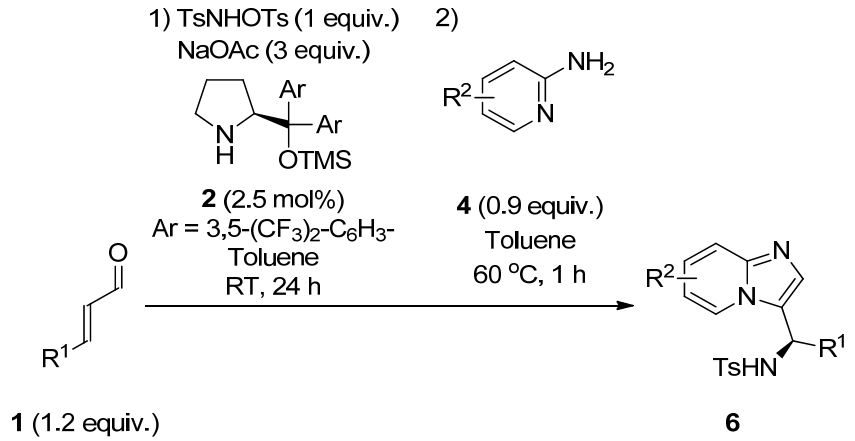


1a (1.2 equiv.) **14a** **6a**

Entry	Solvent	**4a** [equiv.]	T [°C][b]	t [h][c]	Conv. [%][d]	Yield [%][e]	*ee* [%][f]
1	DCM	1	RT	20	80	nd	nd
2	Toluene	0.8	60	1	>95	62	96
3	Toluene	0.9	60	1	>95	68	97
4	Toluene	1	60	1	90	75[g]	95

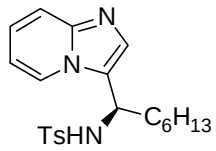
[a] Reactions performed on 0.1 mmol scale in 0.5 mL of the solvent (for details see General procedure below). [b] Reaction temperature for the 2nd step. [c] Reaction time for the 2nd step. [d] Conversion of 2-aminopyridine **4a** in the 2nd step as determined by ^{1}H NMR spectroscopy. [e] Overall yield of isolated product **6a** is given. [f] Determined by chiral stationary phase HPLC. [g] 95% purity - 5% of unreacted 2-aminopyridine **4a** present.

4. Enantioselective synthesis of 3-aminoalkyl imidazo[1,2-*a*]pyridines 6



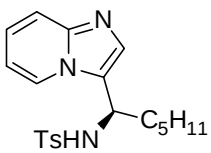
1 (1.2 equiv.) **6**

General procedure: A glass vial equipped with a magnetic stirring bar was charged with the aldehyde **1** (0.12 mmol, 1.2 equiv), the catalyst **2** (0.0025 mmol, 0.025 equiv) and toluene (0.5 mL). After short stirring at RT, TsNHOTs (0.1 mmol, 1 equiv) was added followed by NaOAc (0.3 mmol, 3 equiv.). The stirring was maintained at ambient temperature for 24 h to achieve full conversion of the nucleophile. Upon completion of the reaction, the corresponding 2-aminopyridine **4** (0.09 mmol, 0.9 equiv.) was added. The resulting mixture was heated at 60 ˚C for 1 h and then directly subjected to FC on silica gel to afford the target imidazo[1,2-*a*]pyridine **6**.



6a (*R*)-*N*-(1-(Imidazo[1,2-*a*]pyridin-3-yl)heptyl)-4-methylbenzenesulfonamide (Entry 1, Table 3)

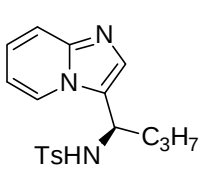
Following the general procedure **6a** was isolated by FC (gradient: EtOAc/pentane 4:1) in 68% yield as a white solid. Mp: 135-137 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 6.9 Hz, 1H), 7.58 (d, *J* = 8.3 Hz, 2H), 7.49 (d, *J* = 9.1 Hz, 1H), 7.35 (s, 1H), 7.18-7.05 (m, 3H), 6.70 (t, *J* = 6.4 Hz, 1H), 6.30 (bs, 1H), 4.76 (dd, *J* = 13.6, 7.5 Hz, 1H), 2.32 (s, 3H), 2.00-1.87 (m, 1H), 1.83-1.71 (m, 1H), 1.42-0.98 (m, 8H), 0.81 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 143.1, 137.9, 131.8, 129.4, 129.3, 126.6 (2C), 124.2 (2C), 122.5, 117.5, 112.4, 49.2, 33.5, 31.4, 28.7, 26.2, 22.4, 21.4, 13.9. HR-MS: calculated for $(M+Na)^+$: 408.1722; measured: 408.1725. The *ee* was determined by HPLC using a Chiralcel AD column (hexane/*i*PrOH 80:20+0.08% DEA, 1 mL min^{-1}); τ_{major} = 13.1 min, τ_{minor} = 32.3 min (97% *ee*). $[\alpha]_D^{rt}$: -13.0 (c = 0.99, $CHCl_3$).



6b (*R*)-*N*-(1-(Imidazo[1,2-*a*]pyridin-3-yl)hexyl)-4-methylbenzenesulfonamide (Entry 2, Table 3)

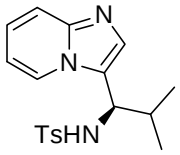
Following the general procedure **6b** was isolated by FC (gradient: EtOAc/pentane 4:1 to pure EtOAc) in 58% yield as a white solid. Mp: 139-142 °C. ^{1}H NMR (400

MHz, $CDCl_3$) δ 8.13 (dt, *J* = 6.9, 0.9 Hz, 1H), 7.58 (d, *J* = 8.3 Hz, 2H), 7.49 (td, *J* = 9.1, 1.1 Hz, 1H), 7.36 (s, 1H), 7.13-7.07 (m, 3H), 6.70 (dt, *J* = 6.8, 1.1 Hz, 1H), 6.05 (bs, 1H), 4.80-4.72 (m, 1H), 2.33 (s, 3H), 1.98-1.72 (m, 2H), 1.30-1.12 (m, 6H), 0.79 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 143.2, 137.7, 131.7, 129.3 (2C), 126.6 (2C), 124.5, 124.2, 122.4, 117.5, 112.4, 49.2, 33.4, 31.2, 25.9, 22.2, 21.3, 13.8. HR-MS: calculated for $(M+Na)^+$: 394.1565; measured: 394.1557. The *ee* was determined by HPLC using a Chiralcel AD column (hexane/*i*PrOH 80:20+0.08% DEA, 1 mL min^{-1}); τ_{major} = 12.6 min, τ_{minor} = 33.9 min (92% *ee*). $[\alpha]_D^{rt}$: -21.6 (c = 1.02, $CHCl_3$).



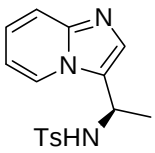
6c (*R*)-*N*-(1-(Imidazo[1,2-*a*]pyridin-3-yl)butyl)-4-methylbenzenesulfonamide (Entry 3, Table 4)

Following the general procedure **6c** was isolated by FC (EtOAc) in 64% yield as a white solid. Mp: 165-167 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (td, *J* = 6.9, 1.1 Hz, 1H), 7.56 (d, *J* = 8.3 Hz, 2H), 7.48 (td, *J* = 9.1, 1.1 Hz, 1H), 7.37 (s, 1H), 7.12-7.06 (m, 3H), 6.70 (dt, *J* = 6.8, 1.2 Hz, 1H), 5.90 (d, *J* = 7.1 Hz, 1H), 4.79 (td, *J* = 8.9, 6.6 Hz, 1H), 2.32 (s, 3H), 2.03-1.88 (m, 1H), 1.82-1.71 (m, 1H), 1.36-1.23 (m, 2H), 0.82 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.9, 143.2, 137.7, 132.0, 129.3 (2C), 126.6 (2C), 124.4, 124.1, 122.4, 117.6, 112.3, 48.9, 35.6, 21.4, 19.5, 13.5. HR-MS: calculated for $(M+Na)^+$: 366.1252; measured: 366.1252. The *ee* was determined by HPLC using a Chiralcel AD column (hexane/*i*PrOH 80:20+0.08% DEA, 1 mL min^{-1}); τ_{major} = 15.9 min, τ_{minor} = 39.7 min (96% *ee*). $[\alpha]_D^{rt}$: -24.5 (c = 1.00, $CHCl_3$).



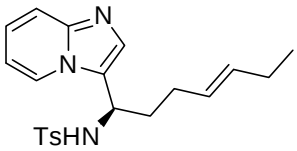
6d (*R*)-*N*-(1-(Imidazo[1,2-*a*]pyridin-3-yl)-2-methylpropyl)-4-methylbenzenesulfonamide (Entry 4, Table 3)

Following the general procedure **6d** was isolated by FC (gradient: EtOAc/pentane 4:1 to pure EtOAc) in 62% yield as a white solid. Mp: 222-225 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.0 Hz, 1H), 7.45 (d, *J* = 9.1 Hz, 1H), 7.37 (d, *J* = 7.2 Hz, 2H), 7.34 (s, 1H), 7.11-7.02 (m, 1H), 6.87 (d, *J* = 8.0 Hz, 2H), 6.66 (t, *J* = 6.8 Hz, 1H), 5.82 (bs, 1H), 4.50 (t, *J* = 7.74 Hz, 1H), 2.29-2.16 (m, 4H), 1.09 (d, *J* = 6.6 Hz, 3H), 0.83 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.6, 143.1, 137.0, 132.8, 129.1 (2C), 126.4 (2C), 123.9, 123.8, 122.7, 117.9, 112.4, 55.5, 32.4, 21.5, 19.8, 19.6. HR-MS: calculated for $(M+Na)^+$: 366.1252; measured: 366.1257. The *ee* was determined by HPLC using a Chiralcel AD column (hexane/*i*PrOH 70:30+0.07% DEA, 1 mL min^{-1}); τ_{major} = 8.5 min, τ_{minor} = 10.0 min (96% *ee*). $[\alpha]_D^{rt}$: -50.7 (c = 0.20, $CHCl_3$).



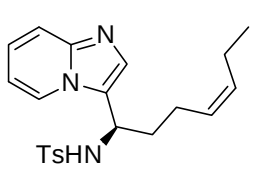
6e (*R*)-*N*-(1-(Imidazo[1,2-*a*]pyridin-3-yl)ethyl)-4-methylbenzenesulfonamide (Entry 5, Table 3)

Following the general procedure **6e** was isolated by FC (EtOAc) in 53% yield as a white solid. Mp: 222-224 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.30-8.27 (m, 1H), 8.07 (d, *J* = 7.8 Hz, 1H), 7.62 (d, *J* = 8.2 Hz, 2H), 7.53-7.49 (m, 1H), 7.45 (s, 1H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.23 (ddd, *J* = 9.1, 6.7, 1.2 Hz, 1H), 6.89 (dt, *J* = 6.8, 1.2 Hz, 1H), 4.86 (quint., *J* = 6.8 Hz, 1H), 2.34 (s, 3H), 1.32 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d6) δ 145.6, 143.2, 139.2, 131.9, 130.1 (2C), 126.9 (2C), 125.2, 125.2, 124.8, 117.7, 112.5, 44.5, 21.6, 19.5. HR-MS: calculated for $(M+Na)^+$: 338.0939; measured: 338.0932. The *ee* was determined by HPLC using a Chiralcel AD column (hexane/*i*PrOH 70:30+0.07% DEA, 1 mL min^{-1}); τ_{major} = 10.7 min, τ_{minor} = 32.2 min (96% *ee*). $[\alpha]_D^{rt}$: -10.8 (c = 0.10, CH_3OH).



6f (*R*,*E*)-*N*-(1-(Imidazo[1,2-*a*]pyridin-3-yl)hept-4-en-1-yl)-4-methylbenzenesulfonamide (Entry 6, Table 3)

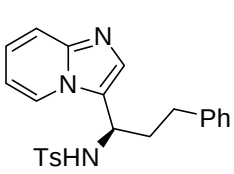
Following the general procedure **6f** was isolated by FC (gradient: EtOAc/pentane 4:1) in 60% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 6.8 Hz, 1H), 7.64-7.47 (m, 3H), 7.42 (s, 1H), 7.17-7.08 (m, 3H), 6.73 (t, *J* = 6.8 Hz, 1H), 5.47 (bs, 1H), 5.37-5.12 (m, 2H), 4.79 (dd, *J* = 13.9, 6.6 Hz, 1H), 2.35 (s, 3H), 2.12-1.75 (m, 6H), 0.93 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.7, 143.3, 137.6, 134.0, 131.7, 129.3 (2C), 126.7, 126.6 (2C), 124.7, 124.2, 122.3, 117.5, 112.5, 48.4, 33.2, 29.1, 25.5, 21.4, 13.7. HR-MS: calculated for $(M+Na)^+$: 406.1565; measured: 406.1559. The *ee* was determined by HPLC using a Chiralcel AD column (hexane/*i*PrOH 70:30+0.07% DEA, 1 mL min^{-1}); τ_{major} = 13.0 min, τ_{minor} = 35.0 min (94% *ee*). $[\alpha]_D^{rt}$: -10.3 (c = 1.00, $CHCl_3$).



6g (*R*,*Z*)-*N*-(1-(Imidazo[1,2-*a*]pyridin-3-yl)hept-4-en-1-yl)-4-methylbenzenesulfonamide (Entry 7, Table 3)

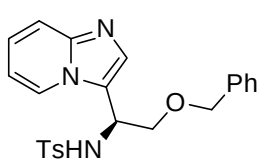
Following the general procedure **6g** was isolated by FC (gradient: EtOAc/pentane 4:1 to pure EtOAc) in 60% yield as a off-white solid. Mp: 121-123 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (td, *J* = 6.9, 1.1 Hz, 1H), 7.53 (d, *J* = 8.2 Hz, 2H), 7.45-7.42 (m, 1H), 7.31 (s, 1H), 7.07-7.01 (m, 3H), 6.64 (t, *J* = 6.8 Hz, 1H), 6.32-6.09 (m, 1H), 5.36-5.25 (m, 1H), 5.14-5.04 (m, 1H), 4.76-4.68 (m, 1H), 2.27 (s, 3H), 2.03-1.87 (m, 3H), 1.79-1.57 (m, 3H), 0.71 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.9, 143.2, 137.8, 133.5, 131.8, 129.4 (2C), 126.6 (2C), 126.5, 124.5, 124.1, 122.2, 117.6, 112.4, 48.4, 33.4, 23.9, 21.4, 20.4, 14.1. HR-MS: calculated for $(M+Na)^+$: 406.1565; measured: 406.1569. The *ee* was determined by HPLC using a Chiralcel AD column

(hexane/*i*PrOH 80:20+0.08% DEA, 1 mL min^{-1}); τ_{major} = 13.6 min, τ_{minor} = 30.5 min (95% *ee*). $[\alpha]_D^{rt}$: +12.4 (c = 1.01, $CHCl_3$).



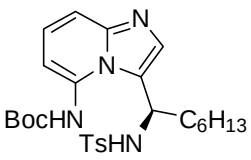
6h (*R*)-*N*-(1-(Imidazo[1,2-*a*]pyridin-3-yl)-3-phenylpropyl)-4-methylbenzenesulfonamide (Entry 8, Table 3)

Following the general procedure **6h** was isolated by FC (gradient: EtOAc/pentane 4:1) in 60% yield as a white solid. Mp: 190-191 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 6.9 Hz, 1H), 7.62-7.44 (m, 4H), 7.25-7.17 (m, 3H), 7.21-7.10 (m, 3H), 6.98-6.90 (m, 2H), 6.73 (t, *J* = 6.8 Hz, 1H), 5.46 (bs, 1H), 4.72 (dd, *J* = 14.1, 6.8 Hz, 1H), 2.71-2.60 (m, 1H), 2.59-2.49 (m, 1H), 2.36 (s, 3H), 2.34-2.22 (m, 1H), 2.15-2.02 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.5, 143.4, 140.1, 137.6, 131.1, 129.5 (2C), 128.5 (2C), 128.3 (2C), 126.7 (2C), 126.3, 125.2, 124.3, 122.3, 117.3, 112.9, 48.2, 35.0, 32.5, 21.4. HR-MS: calculated for $(M+Na)^+$: 428.1409; measured: 428.1404. The *ee* was determined by HPLC using a Chiralcel AD column (hexane/*i*PrOH 70:30+0.07% DEA, 1 mL min^{-1}); τ_{major} = 12.3 min, τ_{minor} = 28.1 min (96% *ee*). $[\alpha]_D^{rt}$: -9.4 (c = 1.00, $CHCl_3$).



6i (*S*)-*N*-(2-(Benzyloxy)-1-(imidazo[1,2-*a*]pyridin-3-yl)ethyl)-4-methylbenzenesulfonamide (Entry 9, Table 3)

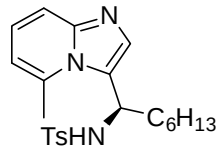
Following the general procedure **6i** was isolated by FC (gradient: EtOAc/pentane 4:1 to pure EtOAc) in 61% yield as a beige solid. Mp: 189-190 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 6.9 Hz, 1H), 7.60 (d, *J* = 8.2 Hz, 2H), 7.49 (d, *J* = 9.1 Hz, 1H), 7.45 (s, 1H), 7.35-7.28 (m, 3H), 7.24-7.20 (m, 2H), 7.15-7.08 (m, 3H), 6.70 (t, *J* = 6.8 Hz, 1H), 5.96 (d, *J* = 6.8 Hz, 1H), 4.98-4.92 (m, 1H), 4.42-4.34 (m, 2H), 3.77 (dd, *J* = 9.6, 4.3 Hz, 1H), 3.54 (dd, *J* = 9.5, 4.3 Hz, 1H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 143.3, 137.5, 136.9, 133.0, 129.4 (2C), 128.5 (2C), 128.0, 127.8 (2C), 126.7 (2C), 124.4 (2C), 120.4, 117.5, 112.3, 73.5, 69.7, 48.9, 21.4. HR-MS: calculated for $(M+Na)^+$: 444.1358; measured: 444.1356. The *ee* was determined by HPLC using a Chiralcel AD column (hexane/*i*PrOH 70:30+0.07% DEA, 1 mL min^{-1}); τ_{major} = 13.5 min, τ_{minor} = 27.6 min (95% *ee*). $[\alpha]_D^{rt}$: -28.7 (c = 0.34, $CHCl_3$).



6j (*R*)-*tert*-Butyl (3-(1-(4-methylphenylsulfonamido)heptyl)imidazo[1,2-*a*]pyridin-5-yl)carbamate (Entry 2, Table 4)

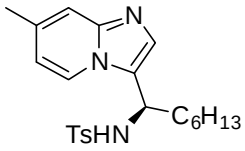
Following the general procedure **6j** was isolated by FC (gradient: EtOAc/pentane 1:1 to EtOAc/pentane 9:1) in 68% yield as a pale yellow foam. ^{1}H NMR (400 MHz, DMSO-d6) δ 9.52 (bs, 1H), 8.13 (d, *J* = 9.2 Hz, 1H), 7.48 (d, *J* = 7.9 Hz, 2H), 7.30 (d, *J* = 8.9 Hz, 1H), 7.24 (s, 1H), 7.14-7.08 (m, 1H), 7.01 (d, *J* = 8.0 Hz, 2H), 6.62 (d, *J* = 6.8 Hz, 1H), 5.03-4.93 (m, 1H), 2.20 (s, 3H), 1.82-1.70 (m, 1H), 1.48 (s, 9H), 1.32-1.11 (m, 9H), 0.84 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d6) δ 154.2, 149.9, 146.4, 141.6, 138.4, 131.9, 128.7 (2C), 127.3, 126.0 (2C),

123.5, 115.5, 111.8, 80.1, 59.6, 50.2, 37.3, 31.3, 27.9 (3C), 25.6, 21.9, 20.7, 13.8. HR-MS: calculated for $(M+Na)^+$: 523.2355; measured: 523.2366. The *ee* was determined by HPLC using a Chiralcel AD column (hexane/*i*PrOH 70:30+0.07% DEA, 1 mL min^{-1}); τ_{major} = 7.5 min, τ_{minor} = 9.6 min (91% *ee*). $[\alpha]_D^{rt}$: -2.6 (c = 1.00, $CHCl_3$).



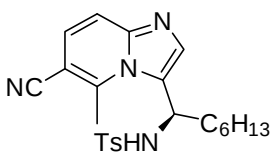
6k (*R*)-4-Methyl-*N*-(1-(5-methylimidazo[1,2-*a*]pyridin-3-yl)heptyl)benzenesulfonamide (Entry 4, Table 4)

Following the general procedure **6k** was isolated by FC (gradient: EtOAc/pentane 4:1) in 83% yield as a white solid. Mp: 183-185 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 1H), 7.46-7.36 (m, 3H), 7.01-6.94 (m, 1H), 6.95-6.90 (m, 2H), 6.59 (bs, 1H), 6.43 (d, *J* = 6.8 Hz, 1H), 5.20 (q, *J* = 7.6 Hz, 1H), 2.79 (s, 3H), 2.22 (s, 3H), 2.02-1.80 (m, 2H), 1.45-0.99 (m, 8H), 0.80 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.9, 142.8, 137.9, 135.8, 133.0, 129.1 (3C), 126.2 (2C), 124.3, 115.9, 114.2, 50.6, 37.4, 31.5, 28.7, 26.4, 22.5, 21.3, 21.1, 14.0. HR-MS: calculated for $(M+Na)^+$: 422.1878; measured: 422.1870. The *ee* was determined by HPLC using a Chiralcel AD column (hexane/*i*PrOH 70:30+0.07% DEA, 1 mL min^{-1}); τ_{major} = 14.7 min, τ_{minor} = 17.5 min (97% *ee*). $[\alpha]_D^{rt}$: -113.1 (c = 1.00, $CHCl_3$).



6l (*R*)-4-Methyl-*N*-(1-(7-methylimidazo[1,2-*a*]pyridin-3-yl)heptyl)benzenesulfonamide (Entry 6, Table 4)

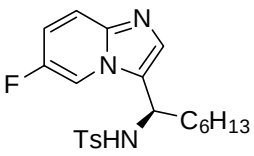
Following the general procedure **6l** was isolated by FC (gradient: EtOAc/pentane 4:1) in 63% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.0 Hz, 1H), 7.63 (d, *J* = 8.3 Hz, 2H), 7.31-7.23 (m, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 6.56 (d, *J* = 5.8 Hz, 1H), 5.85 (bs, 1H), 4.85-4.60 (m, 1H), 2.36 (s, 3H), 2.35 (s, 3H), 2.05-1.82 (m, 1H), 1.81-1.64 (m, 1H), 1.35-0.98 (m, 8H), 0.82 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0, 143.1, 138.1, 135.7, 131.0, 129.3 (2C), 126.6 (2C), 123.5, 121.9, 115.7, 115.0, 49.2, 33.4, 31.4, 28.7, 26.2, 22.4, 21.4, 21.1, 14.0. HR-MS: calculated for $(M+Na)^+$: 422.1878; measured: 422.1883. The *ee* was determined by HPLC using a Chiralcel AD column (hexane/*i*PrOH 70:30+0.07% DEA, 1 mL min^{-1}); τ_{major} = 7.4 min, τ_{minor} = 11.8 min (96% *ee*). $[\alpha]_D^{rt}$: -8.2 (c = 1.00, $CHCl_3$).



6m (*R*)-*N*-(1-(6-Cyano-5-methylimidazo[1,2-*a*]pyridin-3-yl)heptyl)-4-methylbenzenesulfonamide (Entry 8, Table 4)

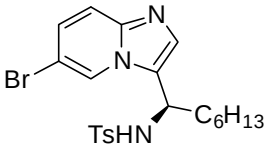
Following the general procedure **6m** was isolated by FC (gradient: EtOAc/pentane 2:3 to EtOAc/pentane 7:3) in 51% yield as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (s, 1H), 7.44-7.37 (m, 3H), 7.14 (d, *J* = 9.3 Hz, 1H), 7.01 (d, *J* = 8.0 Hz, 2H), 5.79 (d, *J* = 6.5 Hz, 1H), 5.14 (q, *J* = 7.4 Hz, 1H), 3.05 (s, 3H), 2.28 (s, 3H), 2.03-1.87 (m, 2H), 1.34-

1.12 (m, 8H), 0.84 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 143.3, 137.4, 135.9, 135.8, 129.2 (2C), 128.6, 126.2 (2C), 124.3, 116.9, 116.9, 99.9, 50.5, 37.1, 31.4, 28.6, 26.3, 22.4, 21.3, 19.5, 13.9. HR-MS: calculated for $(M+Na)^+$: 447.1831; measured: 447.1830. The *ee* was determined by HPLC using a Chiralcel AD column (hexane/*i*PrOH 70:30+0.07% DEA, 1 mL min^{-1}); τ_{major} = 14.4 min, τ_{minor} = 12.6 min (98% *ee*). $[\alpha]_D^{rt}$: -144.8 (c = 0.98, $CHCl_3$).



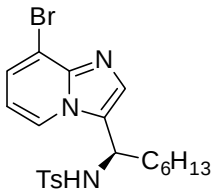
6n ((*R*)-*N*-(1-(6-Fluoroimidazo[1,2-*a*]pyridin-3-yl)heptyl)-4-methylbenzenesulfonamide (Entry 10, Table 4)

Following the general procedure **6n** was isolated by FC (EtOAc/pentane 3:1) in 64% yield as a pale-yellow solid. Mp: 115-117 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (ddd, *J* = 4.3, 2.3, 0.6 Hz, 1H), 7.58 (d, *J* = 8.3 Hz, 2H), 7.47 (ddd, *J* = 9.7, 5.2, 0.6 Hz, 1H), 7.40 (s, 1H), 7.12 (d, *J* = 7.9 Hz, 2H), 7.01 (ddd, *J* = 10.0, 7.8, 2.4 Hz, 1H), 6.05 (d, *J* = 6.6 Hz, 1H), 4.73-4.63 (m, 1H), 2.34 (s, 3H), 2.02-1.87 (m, 1H), 1.87-1.75 (m, 1H), 1.27-1.06 (m, 8H), 0.82 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ 154.6 (d, *J* = 235.6 Hz), 144.4, 144.3, 139.4, 133.6, 130.2 (2C), 127.4 (2C), 126.9 (d, *J* = 2.1 Hz), 118.3 (d, *J* = 9.3 Hz), 118.0 (d, *J* = 26.1 Hz), 112.8 (d, *J* = 42.4 Hz), 50.1, 34.4, 32.7, 29.8, 27.4, 23.6, 21.4, 14.4. HR-MS: calculated for $(M+Na)^+$: 426.1627; measured: 426.1627. The *ee* was determined by HPLC using a Chiralcel AD column (hexane/*i*PrOH 70:30+0.07% DEA, 1 mL min^{-1}); τ_{major} = 7.4 min, τ_{minor} = 12.2 min (94% *ee*). $[\alpha]_D^{rt}$: -11.0 (c = 1.02, $CHCl_3$).



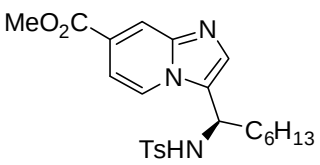
6o (*R*)-*N*-(1-(6-Bromoimidazo[1,2-*a*]pyridin-3-yl)heptyl)-4-methylbenzenesulfonamide (Entry 13, Table 4)

Following the general procedure **6o** was isolated by FC (gradient: EtOAc/pentane 3:2 to EtOAc/pentane 4:1) in 50% yield as a white solid. Mp: 179-184 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.50 (d, *J* = 8.3 Hz, 2H), 7.41 (s, 1H), 7.36 (dd, *J* = 9.5, 0.8 Hz, 1H), 7.13 (dd, *J* = 9.5, 1.8 Hz, 1H), 7.08 (d, *J* = 7.9 Hz, 2H), 5.78-5.72 (m, 1H), 4.74-4.66 (m, 1H), 2.31 (s, 3H), 1.99-1.81 (m, 2H), 1.28-1.08 (m, 8H), 0.83 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5, 143.5, 137.3, 133.3, 129.5 (2C), 127.8, 126.7 (2C), 124.6, 123.0, 118.4, 107.4, 49.4, 33.7, 31.6, 28.9, 26.4, 22.6, 21.4, 14.4. HR-MS: calculated for $(M+Na)^+$: 486.0827; measured: 486.0831. The *ee* was determined by HPLC using a Chiralcel AD column (hexane/*i*PrOH 70:30+0.07% DEA, 1 mL min^{-1}); τ_{major} = 8.8 min, τ_{minor} = 17.0 min (92% *ee*). $[\alpha]_D^{rt}$: -12.7 (c = 1.02, $CHCl_3$).



6p (*R*)-*N*-(1-(8-Bromoimidazo[1,2-*a*]pyridin-3-yl)heptyl)-4-methylbenzenesulfonamide (Entry 15, Table 4)

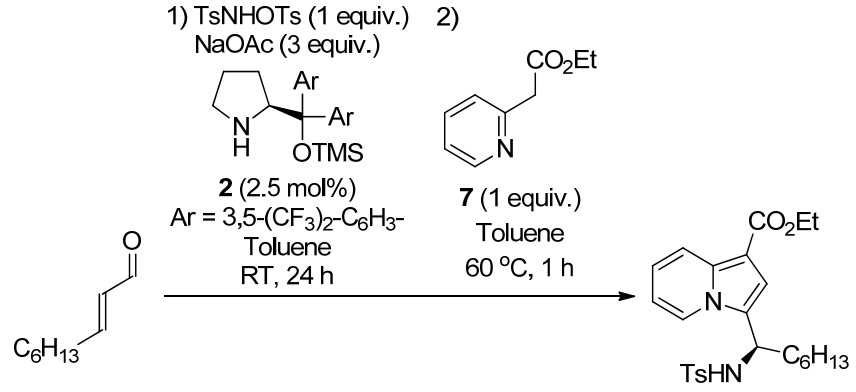
Following the modified general procedure (using 0.6 equiv. of 2-aminopyridine **4h** in the annulation step) **6p** was isolated by FC (gradient: EtOAc/pentane 1:1) in 56% yield as a white solid. Mp: 125-126 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.6 Hz, 1H), 7.48 (s, 2H), 7.46 (s, 1H), 7.39 (dd, *J* = 7.3, 0.8 Hz, 1H), 7.05 (d, *J* = 7.9 Hz, 2H), 6.61 (t, *J* = 7.1 Hz, 1H), 5.25 (d, *J* = 6.3 Hz, 1H), 4.73 (q, *J* = 6.7 Hz, 1H), 2.32 (s, 3H), 2.03-1.86 (m, 1H), 1.86-1.71 (m, 1H), 1.34-1.00 (m, 8H), 0.82 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 143.5, 136.9, 132.9, 129.2 (2C), 126.8, 126.5 (2C), 124.1, 123.7, 112.5, 111.7, 49.5, 33.2, 31.4, 28.6, 26.2, 22.4, 21.4, 14.0. HR-MS: calculated for $(M+Na)^+$: 486.0827; measured: 486.0832. The *ee* was determined by HPLC using a Chiralcel AD column (hexane/*i*PrOH 70:30+0.07% DEA, 1 mL min^{-1}); τ_{major} = 10.5 min, τ_{minor} = 28.2 min (97% *ee*). $[\alpha]_D^{rt}$: -9.7 (c = 1.00, $CHCl_3$).



6q (*R*)-Methyl 3-(1-(4-methylphenylsulfonamido)heptyl)imidazo[1,2-*a*]pyridine-7-carboxylate (Entry 17, Table 4)

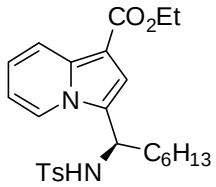
Following the modified general procedure (using 0.8 equiv. of 2-aminopyridine **4i** in the annulation step) **6q** was isolated by FC (gradient: EtOAc/pentane 1:1 to EtOAc/pentane 2:1) in 63% yield as a white solid. Mp: 152-154 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.28 (dd, *J* = 7.2, 0.9 Hz, 1H), 8.05 (dd, *J* = 1.7, 0.9 Hz, 1H), 7.58 (s, 1H), 7.38 (d, *J* = 8.3 Hz, 2H), 7.32 (dd, *J* = 7.2, 1.7 Hz, 1H), 6.98 (d, *J* = 7.9 Hz, 2H), 4.78 (t, *J* = 7.6 Hz, 1H), 3.96 (s, 3H), 2.21 (s, 3H), 1.96-1.88 (m, 2H), 1.44-1.13 (m, 8H), 0.85 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ 166.8, 145.6, 144.2, 139.3, 134.9, 130.2 (2C), 127.6, 127.6, 127.4 (2C), 125.7, 120.0, 112.6, 53.2, 50.0, 34.6, 32.7, 29.8, 27.3, 23.6, 21.3, 14.4. HR-MS: calculated for $(M+Na)^+$: 466.1776; measured: 466.1776. The *ee* was determined by HPLC using a Chiralcel AD column (hexane/*i*PrOH 70:30+0.07% DEA, 1 mL min^{-1}); τ_{major} = 7.9 min, τ_{minor} = 10.8 min (95% *ee*). $[\alpha]_D^{rt}$: -23.9 (c = 1.01, CH_3OH).

5. Enantioselective synthesis of (*R*)-ethyl 3-(1-(4-methylphenylsulfonamido)heptyl)indolizine-1-carboxylate 8b



1a (1.2 equiv.) **8b**

Procedure: A glass vial equipped with a magnetic stirring bar was charged with the aldehyde **1a** (0.12 mmol, 1.2 equiv), the catalyst **2** (0.0025 mmol, 0.025 equiv) and toluene (0.5 mL). After short stirring at RT, TsNHOTs (0.1 mmol, 1 equiv) was added followed by NaOAc (0.3 mmol, 3 equiv.). The stirring was maintained at ambient temperature for 24 h to achieve full conversion of the nucleophile. Upon completion of the reaction, the corresponding ethyl pirydylacetate **7** (0.1 mmol, 1 equiv.) was added. The resulting mixture was heated at 60 ˚C for 1 h and then directly subjected to FC on silica gel (gradient: EtOAc/pentane 1:5 to EtOAc/pentane 1:4) to afford the target indolizine **8b** in 63% yield as a yellow oil.

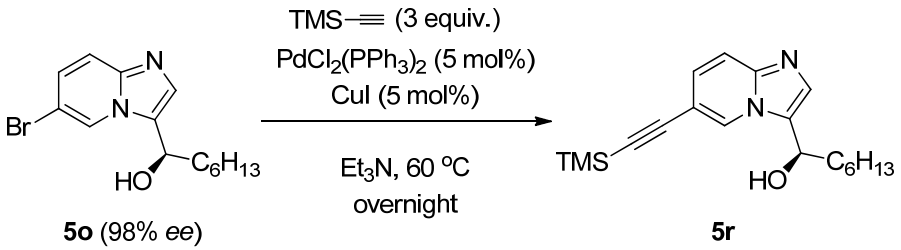


8b (*R*)-Ethyl 3-(1-(4-methylphenylsulfonamido)heptyl)indolizine-1-carboxylate (Scheme 2)

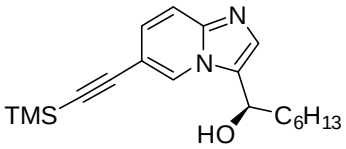
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10-8.05 (m, 2H), 7.52 (d, *J* = 8.3 Hz, 2H), 7.07 (d, *J* = 7.8 Hz, 2H), 7.06 (s, 1H), 7.02 (ddd, *J* = 9.2, 6.6, 0.6 Hz, 1H), 6.66 (dt, *J* = 6.9, 1.2 Hz, 1H), 4.96 (d, *J* = 7.7 Hz, 1H), 4.75-4.68 (m, 1H), 4.40-4.28 (m, 2H), 2.32 (s, 3H), 2.01-1.87 (m, 1H), 1.84-1.71 (m, 1H), 1.40 (t, *J* = 7.1 Hz, 3H), 1.31-1.06 (m, 8H), 0.83 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 143.2, 137.5, 136.2, 129.2 (2C), 126.6 (2C), 123.7, 122.9, 122.2, 119.7, 115.2, 112.6, 103.2, 59.5, 50.2, 33.9, 31.4, 28.7, 26.2, 22.4, 21.4, 14.6, 14.0. HR-MS: calculated for $(M+Na)^+$: 479.1980; measured: 479.1985. The *ee* was determined by HPLC using a Chiralcel OD column (hexane/*i*PrOH 90:10, 1 mL min^{-1}); τ_{major} = 14.2 min, τ_{minor} = 21.0 min (97% *ee*). $[\alpha]_D^{rt}$: -25.3 (c = 1.00, $CHCl_3$).

6. Transformations

6.1. Synthesis of (*R*)-1-(6-((trimethylsilyl)ethynyl)imidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol 5r



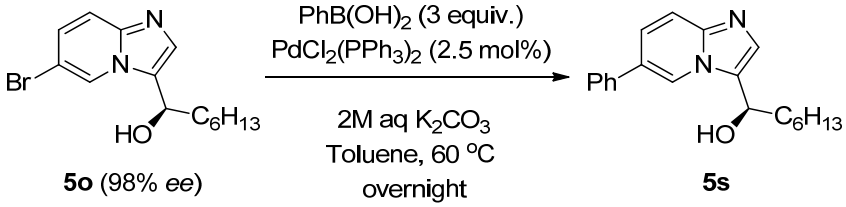
Procedure: A glass vial equipped with a magnetic stirring bar under Ar-atmosphere was charged with **5o** (0.1 mmol, 1 equiv.), $PdCl_2(PPh_3)_2$ (0.05 mmol, 0.05 equiv.), CuI (0.05 mmol, 0.05 equiv.), Et_3N (0.5 mL, degassed) and ethynyltrimethylsilane (0.30 mmol, 3 equiv.) and the resulting mixture was vigorously stirred at 60 °C overnight.[2] When the reaction was estimated to be complete by ^{1}H NMR spectroscopy the reaction mixture was directly subjected to FC on silica gel (1% Et_3N in EtOAc/pentane 1:1) to afford **5r** in 95% yield as a white solid. Mp: 127-129 °C.



5r (*R*)-1-(6-((Trimethylsilyl)ethynyl)imidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol (Scheme 3, left side)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52-8.51 (m, 1H), 7.37 (d, *J* = 9.3 Hz, 1H), 7.18-7.14 (m, 1H), 7.17 (s, 1H), 4.87 (t, *J* = 6.8 Hz, 1H), 3.55 (bs, 1H), 2.07-1.89 (m, 2H), 1.66-1.48 (m, 1H), 1.47-1.21 (m, 7H), 0.88 (t, *J* = 6.8 Hz, 3H), 0.26 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 131.0, 129.0, 127.5, 127.0, 116.9, 108.9, 101.1, 95.9, 65.4, 34.9, 31.7, 29.0, 26.0, 22.6, 14.0, -0.1 (3C). HR-MS: calculated for $(M+Na)^+$: 351.1869; measured: 351.1866. The *ee* was determined by HPLC using a Chiralpak AS column (hexane/*i*PrOH 90:10+0.09% DEA, 1 mL min^{-1}); τ_{major} = 6.4 min, τ_{minor} = 5.1 min (98% *ee*). $[\alpha]_D^{rt}$: -81.5 (c = 1.00, $CHCl_3$).

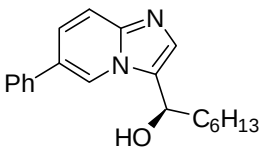
6.2. Synthesis of (*R*)-1-(6-phenylimidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol 5s



Procedure: A glass vial equipped with a magnetic stirring bar was charged with **5o** (0.1 mmol, 1 equiv.), $PhB(OH)_2$ (0.3 mmol, 3 equiv.) and $PdCl_2(PPh_3)_2$ (0.025 mmol, 0.025 equiv.). The flask was placed under vacuum and purged with argon, after which toluene (0.35 mL, degassed) and 2 M aq. K_2CO_3 (0.10 mL, degassed) were added and the resulting mixture was vigorously stirred at 60 °C

[2] For the original procedure, see: Q. Zhang and J. M. Takacs, *Org. Lett.,* 2008, **10**, 545.

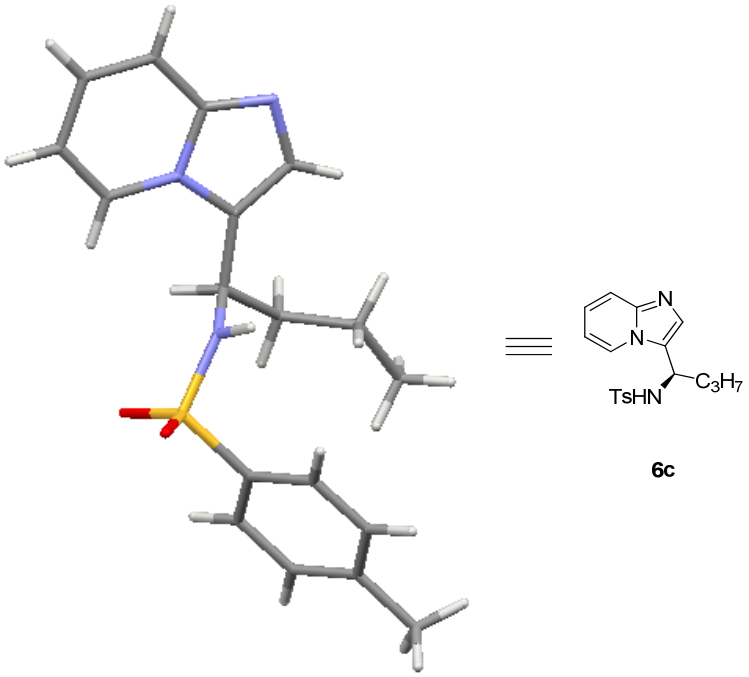
overnight. When the reaction was estimated to be complete by ^{1}H NMR spectroscopy the reaction mixture was diluted with EtOAc (25 mL), successively washed with 2M aq. Na_2CO_3 solution (3x10 mL) and brine (1x10mL), and then dried ($MgSO_4$). After filtration and concentration of the solvents the product **5s** was isolated by FC on silica gel (1% Et_3N in EtOAc) in 96% yield as a white solid. Mp: 140-143 °C.



5s (*R*)-1-(6-Phenylimidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol (Scheme 3, right side)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52-8.49 (m, 1H), 7.56-7.32 (m, 7H), 7.24 (s, 1H), 4.94 (t, *J* = 6.9 Hz, 1H), 3.80 (bs, 1H), 2.10-1.99 (m, 2H), 1.66-1.52 (m, 1H), 1.50-1.24 (m, 7H), 0.88 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.3, 137.3, 130.7, 129.0 (2C), 127.8, 127.0, 127.0 (2C), 126.4, 125.1, 122.5, 117.2, 65.4, 35.0, 31.7, 29.1, 26.0, 22.6, 14.0. HR-MS: calculated for $(M+H)^+$: 309.1967; measured: 309.1968. The *ee* was determined by HPLC using a Chiralcel OJ column (hexane/*i*PrOH 90:10+0.09% DEA, 1 mL min^{-1}); τ_{major} = 36.1 min, τ_{minor} = 20.2 min (96% *ee*). $[\alpha]_D^{rt}$: -81.9 (c = 0.54, $CHCl_3$).

7. X-Ray structure of (*R*)-*N*-(1-(imidazo[1,2-*a*]pyridin-3-yl)butyl)-4-methylbenzenesulfonamide 6c



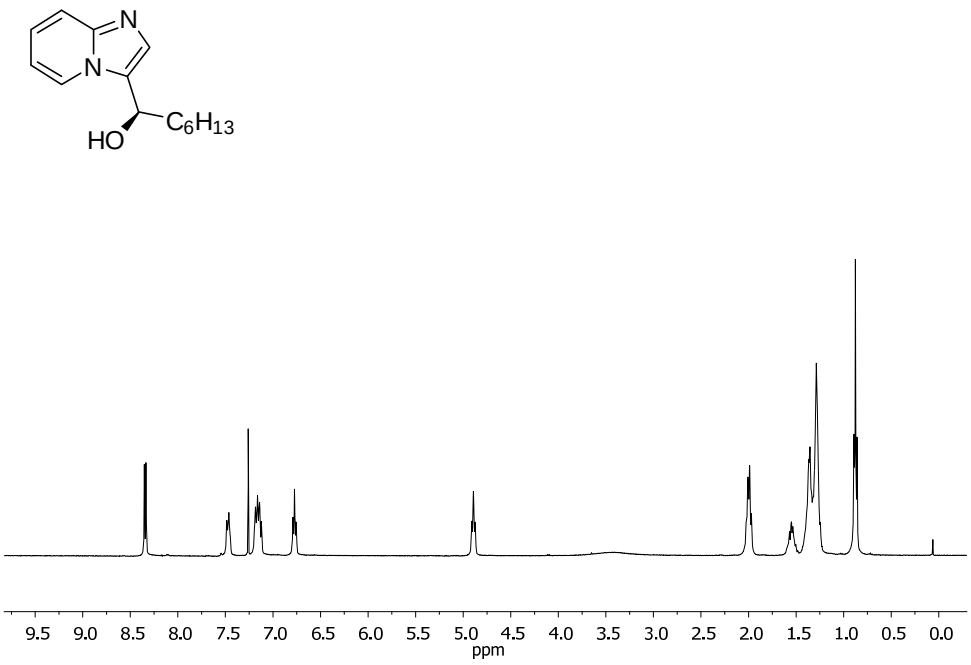
6c

Crystal data for [**6c**]: C18 H21 N3 O2 S, M = 343.44, monoclinic, space group P 1 21 1 (no. 6), a = 7.7381(4) Å, b = 7.317(4) Å, c = 14.5532(8) Å, β = 91.323(2)°, V = 823.78(8) Å^3, T = 100 K, Z = 2, d_c = 1.385 g cm^{-3}, μ(Mo Kα, λ = 0.71073 Å) = 0.213 mm^{-1}, 35228 reflections collected, 4451 unique [R_{int} = 0.0229], which were used in all calculations. Refinement on F^2, final R(F) = 0.0243, R_w(F2) = 0.0656. CCDC number 812281.

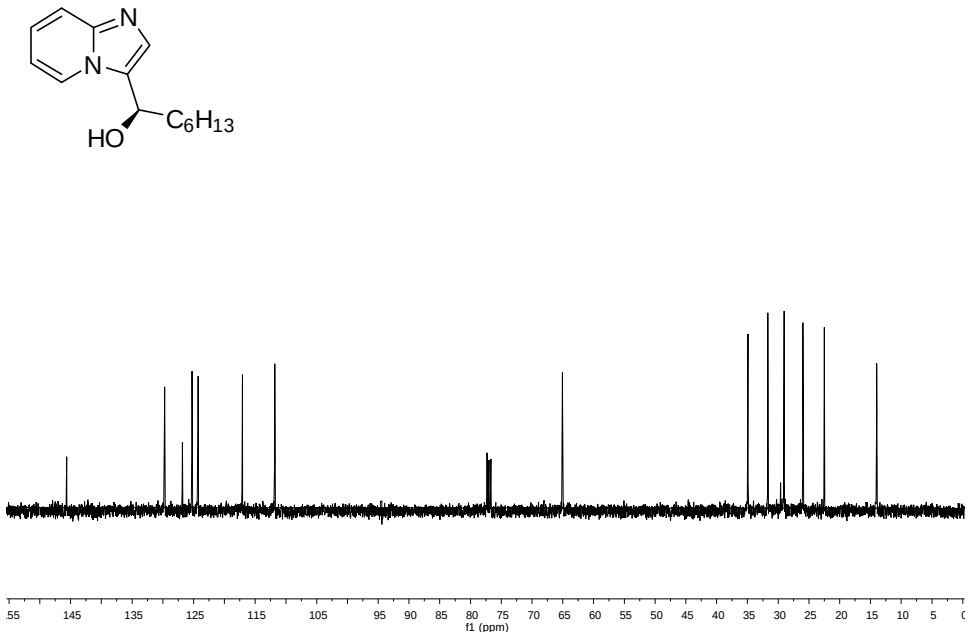
8. NMR data

5a (*R*)-1-(Imidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol

^{1}H NMR

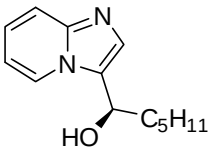


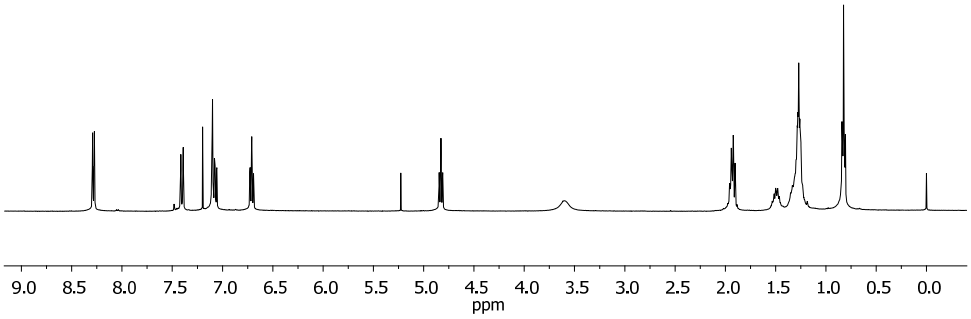
^{13}C NMR



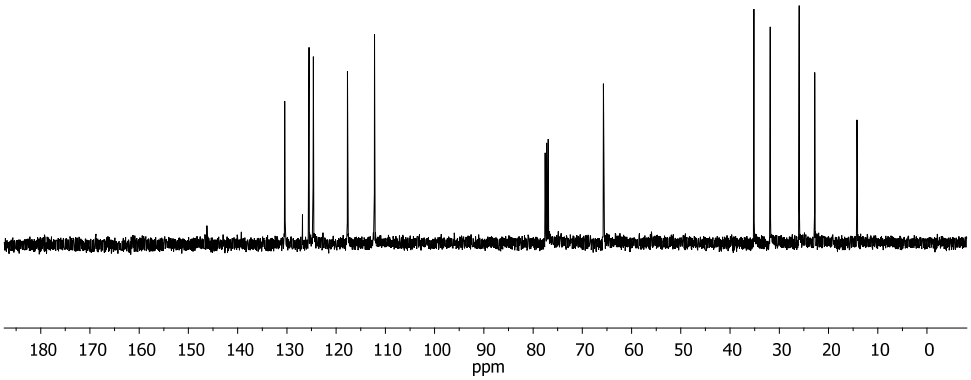
5b (*R*)-1-(Imidazo[1,2-*a*]pyridin-3-yl)hexan-1-ol (Entry 2, Table 2)

^{1}H NMR



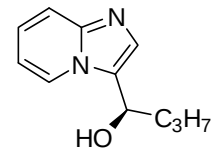


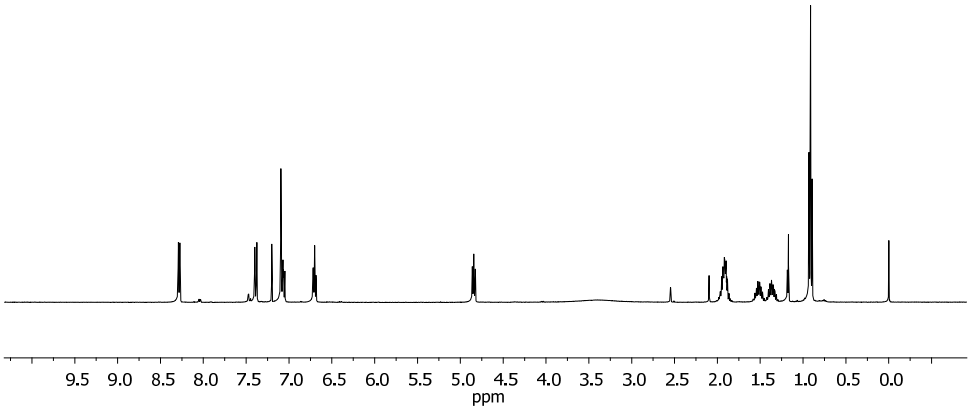
^{13}C NMR



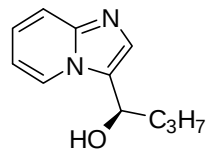
5c (*R*)-1-(Imidazo[1,2-*a*]pyridin-3-yl)butan-1-ol (Entry 3, Table 2)

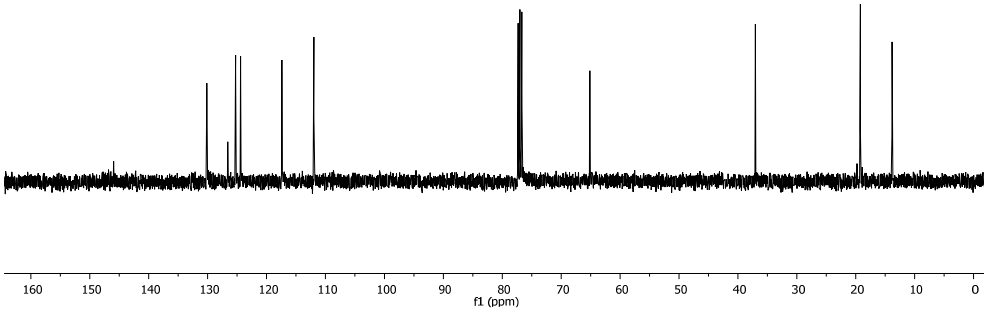
^{1}H NMR





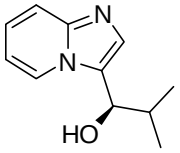
^{13}C NMR

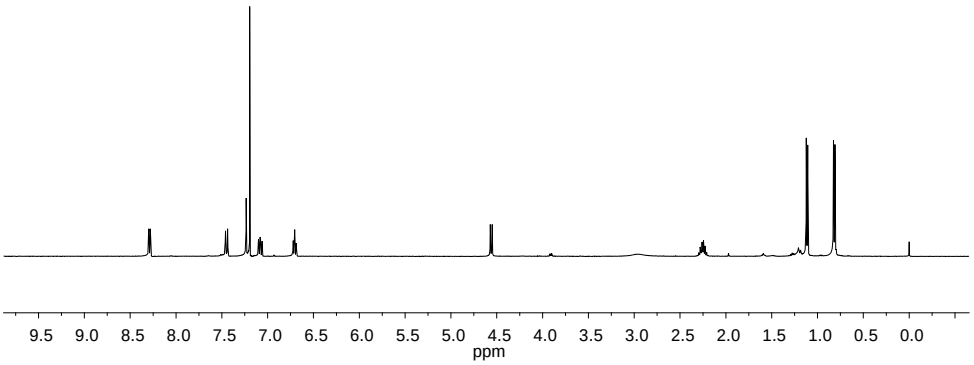




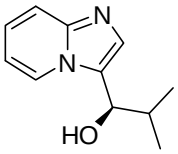
5d (*R*)-1-(Imidazo[1,2-*a*]pyridin-3-yl)-2-methylpropan-1-ol (Entry 4, Table 2)

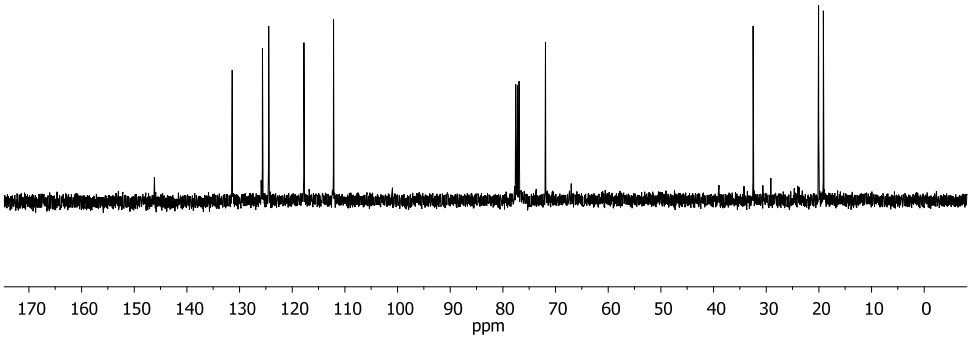
^{1}H NMR





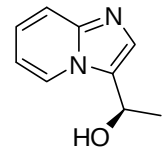
^{13}C NMR

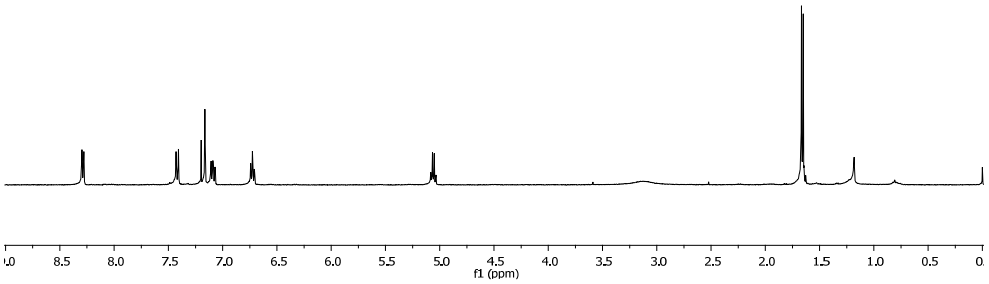




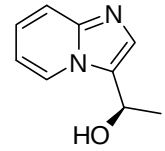
5e (*R*)-1-(Imidazo[1,2-*a*]pyridin-3-yl)ethanol (Entry 5, Table 2)

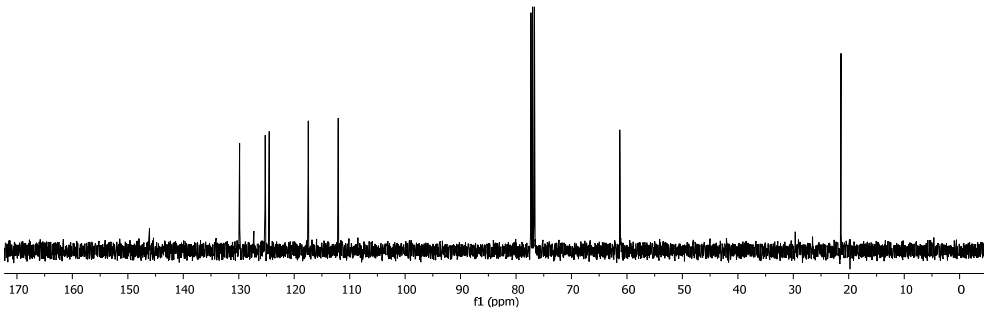
^{1}H NMR





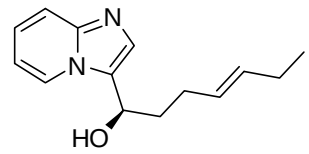
^{13}C NMR

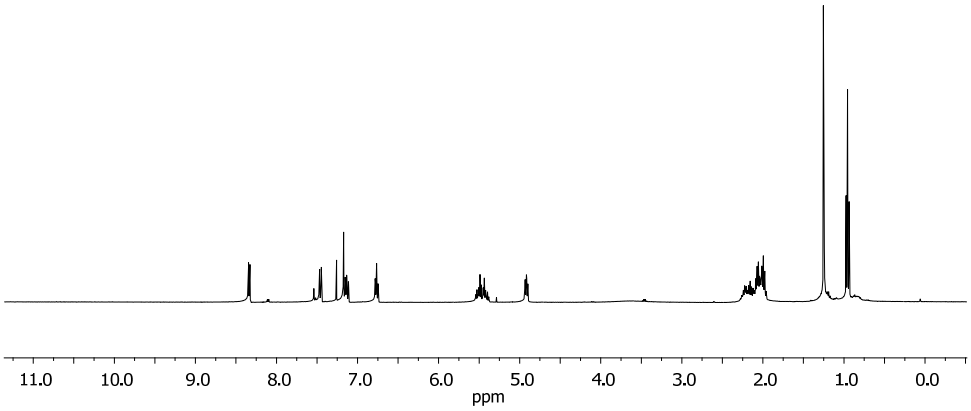




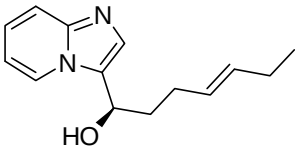
5f (*R*,*E*)-1-(Imidazo[1,2-*a*]pyridin-3-yl)hept-4-en-1-ol (Entry 6, Table 2)

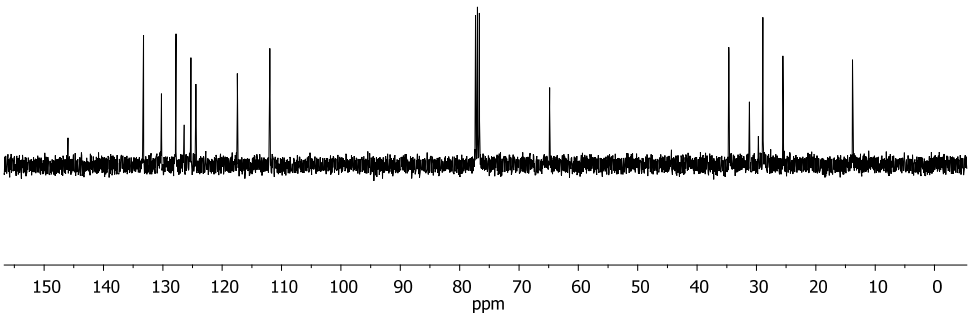
^{1}H NMR





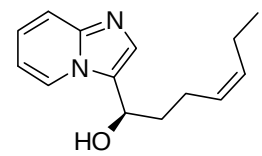
^{13}C NMR

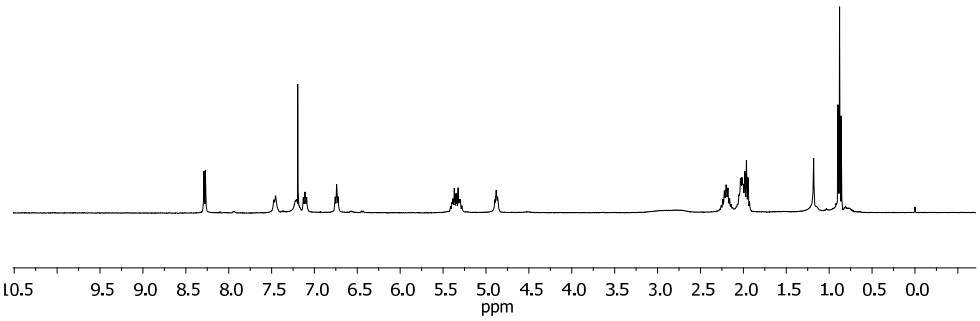




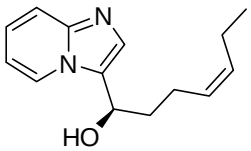
5g (*R*,*Z*)-1-(Imidazo[1,2-*a*]pyridin-3-yl)hept-4-en-1-ol (Entry 7, Table 2)

^{1}H NMR



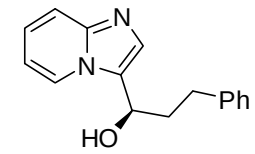


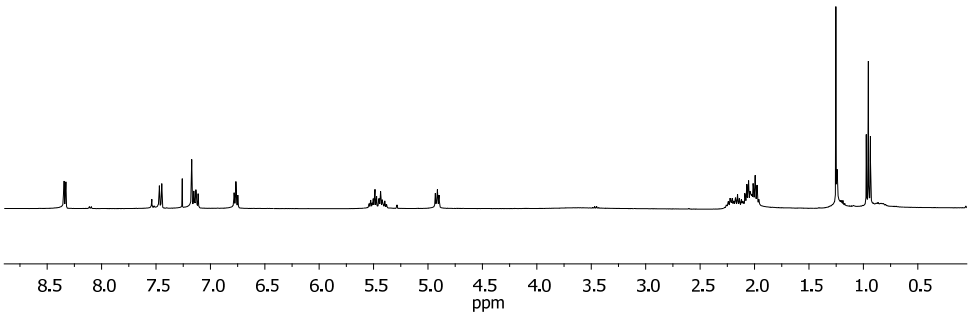
^{13}C NMR



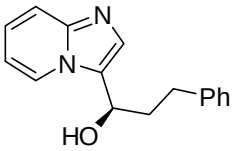
5h (*R*)-1-(Imidazo[1,2-*a*]pyridin-3-yl)-3-phenylpropan-1-ol (Entry 8, Table 2)

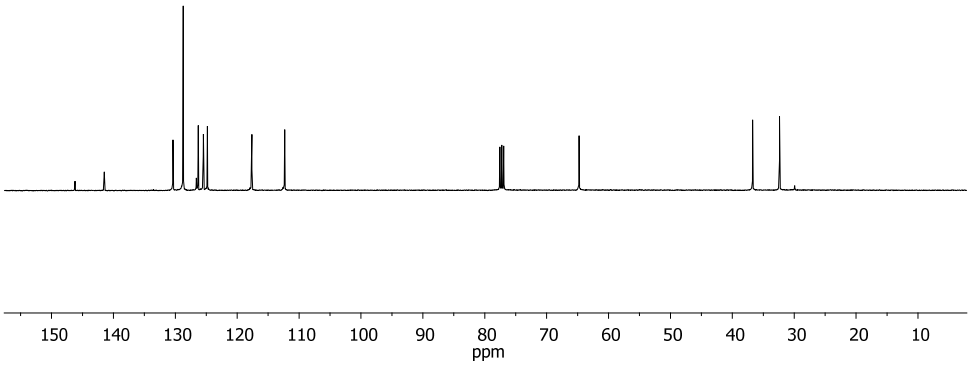
^{1}H NMR





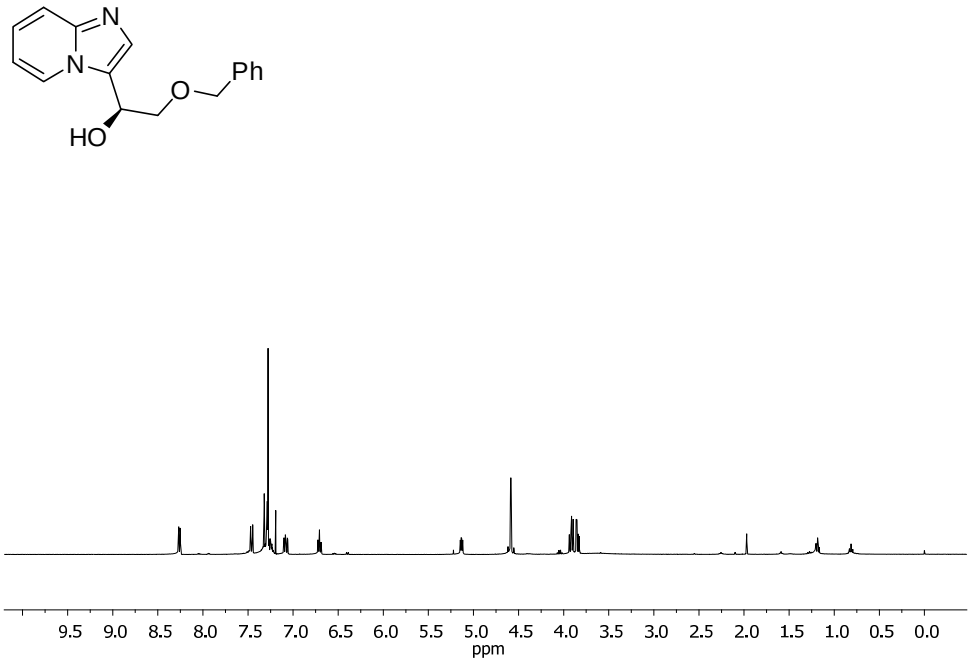
^{13}C NMR



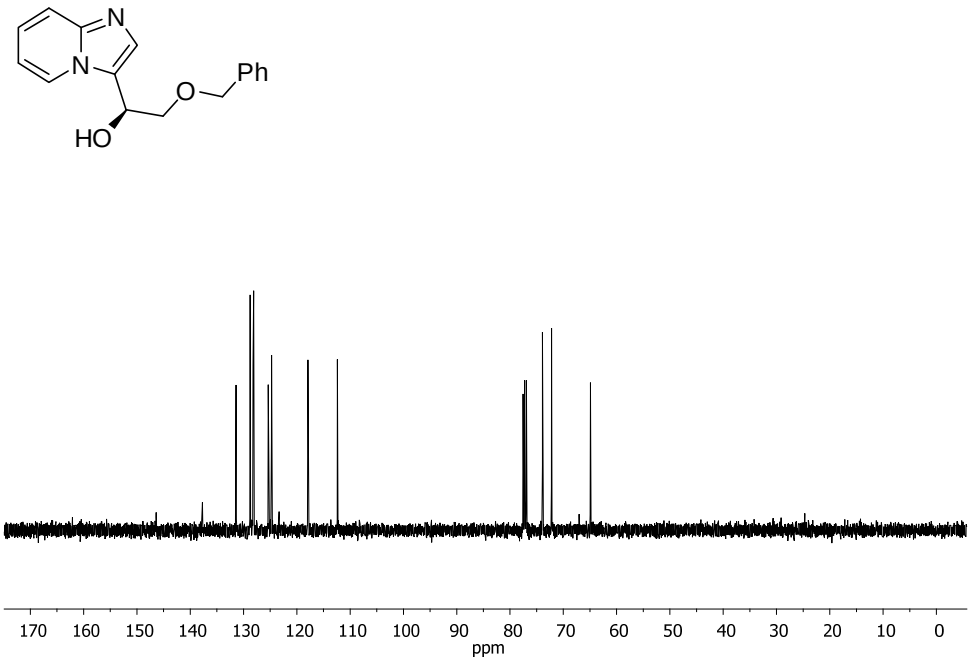


5i (*S*)-2-(Benzyloxy)-1-(imidazo[1,2-*a*]pyridin-3-yl)ethanol (Entry 9, Table 2)

^{1}H NMR

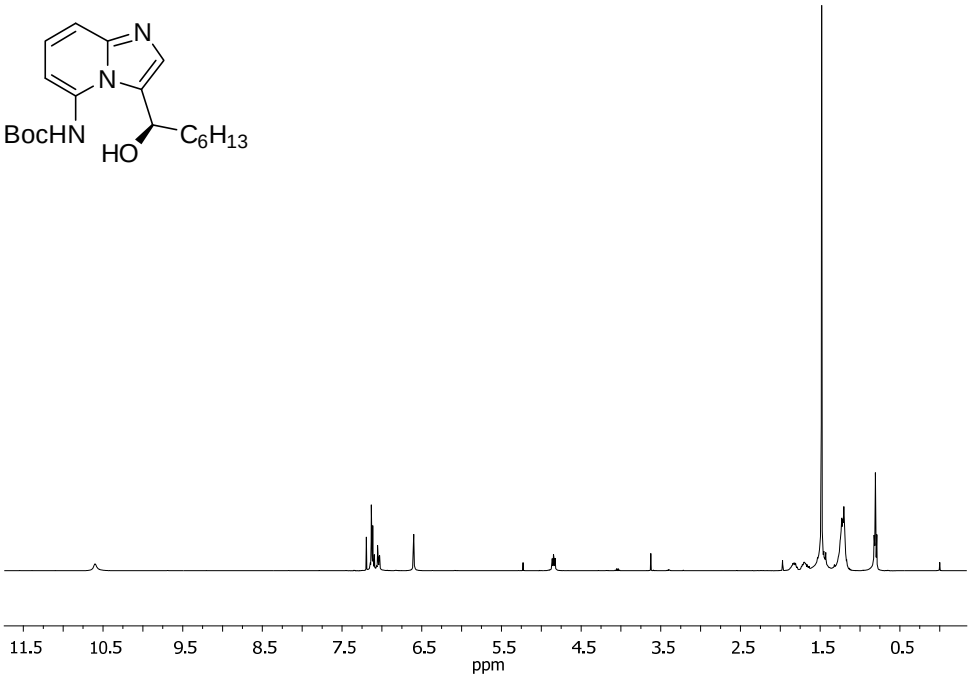


^{13}C NMR

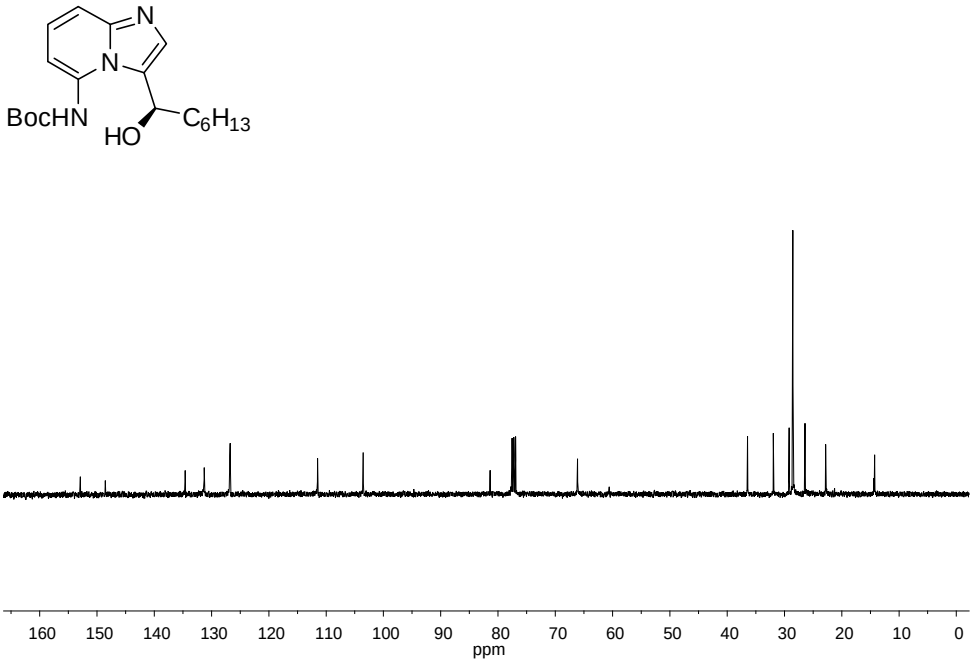


5j (*R*)-*tert*-Butyl 3-(1-hydroxyheptyl)imidazo[1,2-*a*]pyridin-5-ylcarbamate (Entry 1, Table 4)

^{1}H NMR

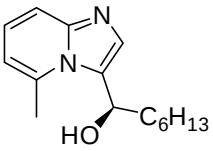


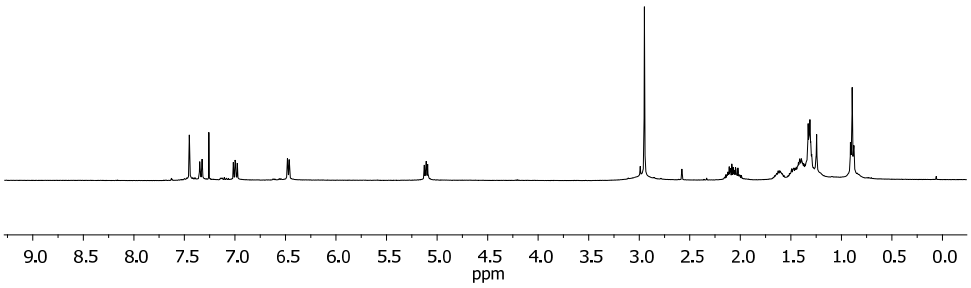
^{13}C NMR



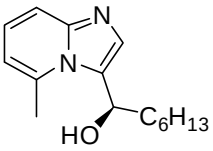
5k (*R*)-1-(5-Methylimidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol (Entry 3, Table 4)

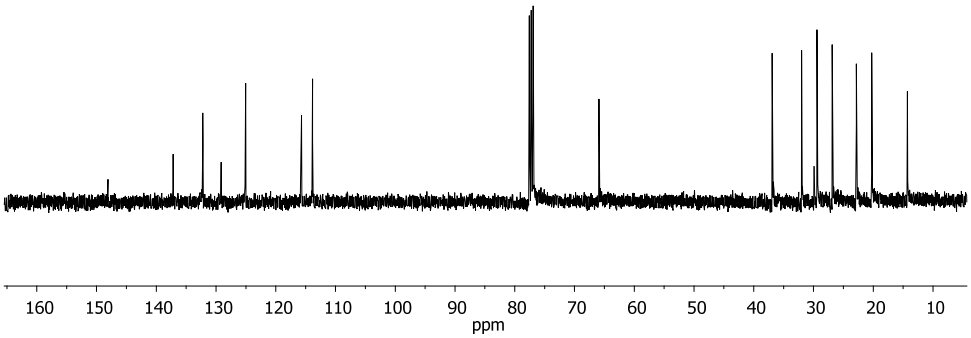
^{1}H NMR





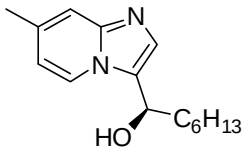
^{13}C NMR

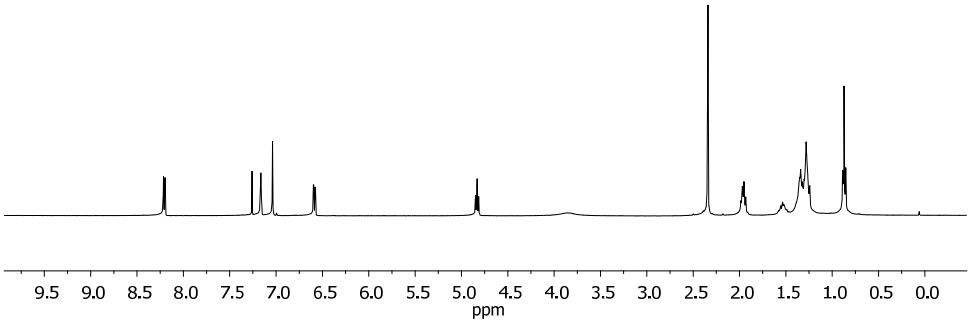




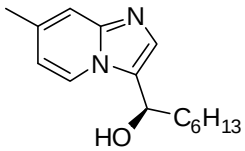
5l (*R*)-1-(7-Methylimidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol (Entry 5, Table 4)

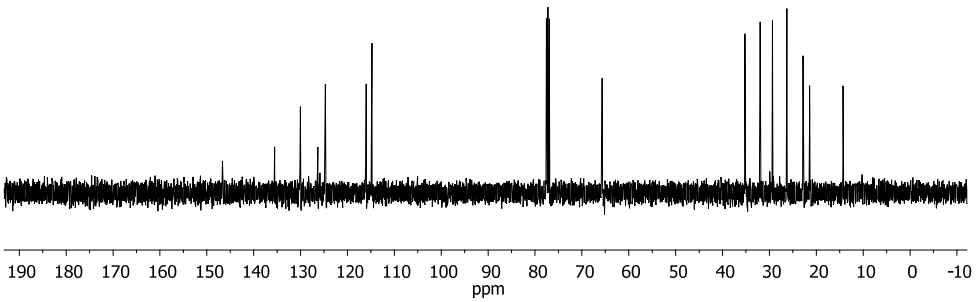
^{1}H NMR





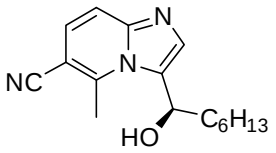
^{13}C NMR

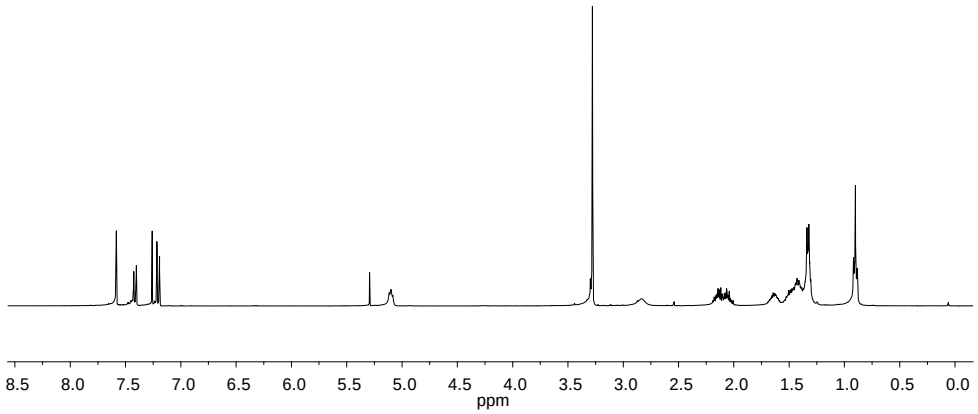




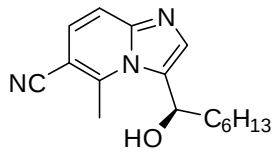
5m (*R*)-3-(1-Hydroxyheptyl)-5-methylimidazo[1,2-*a*]pyridine-6-carbonitrile (Entry 7, Table 4)

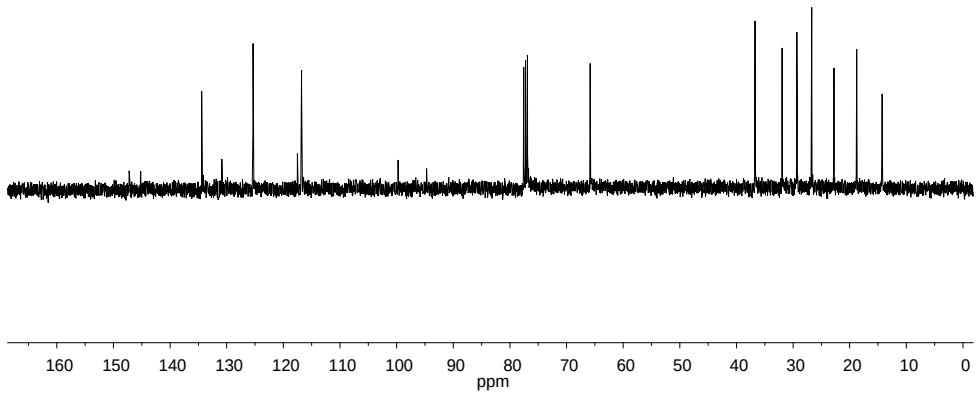
^{1}H NMR





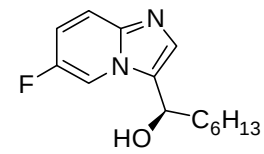
^{13}C NMR

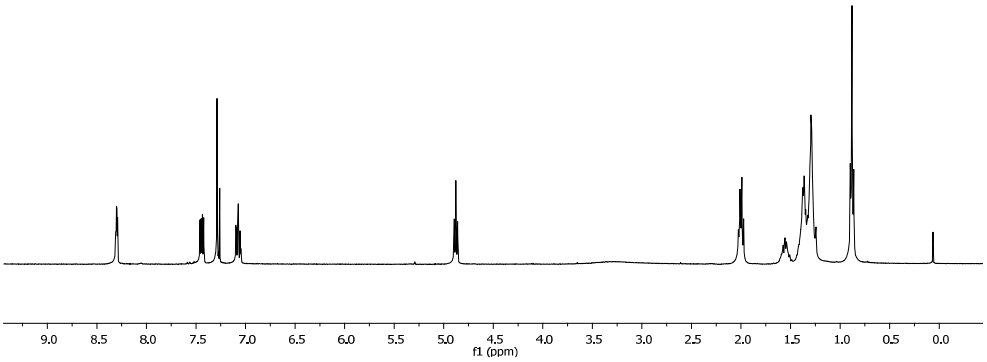




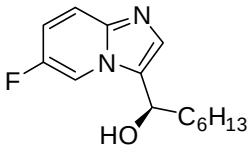
5n (*R*)-1-(6-Fluoroimidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol (Entry 9, Table 4)

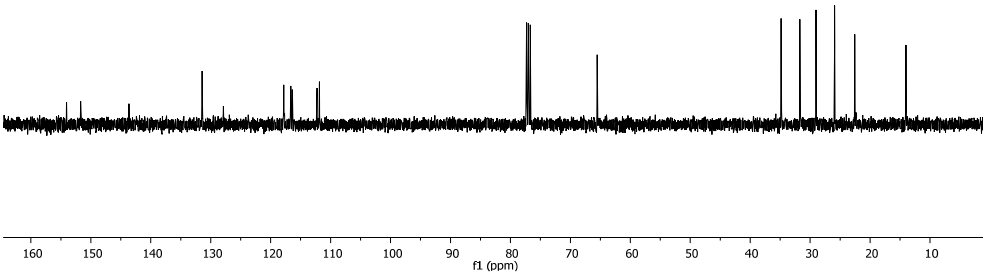
^{1}H NMR





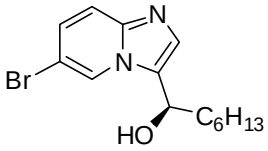
^{13}C NMR

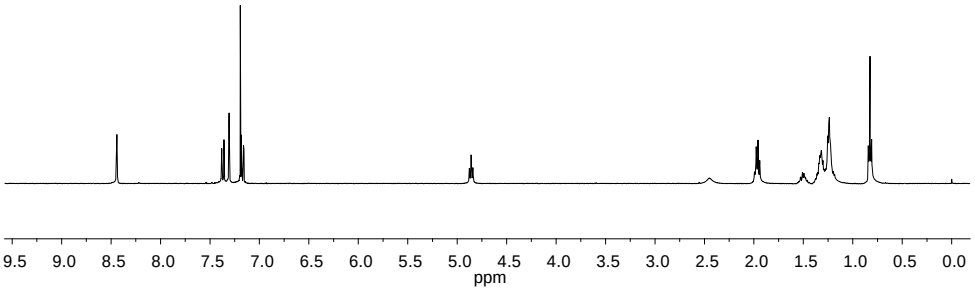




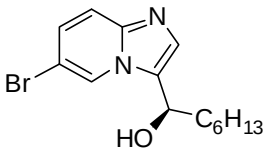
5o (*R*)-1-(6-Bromoimidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol (Entry 11, Table 4)

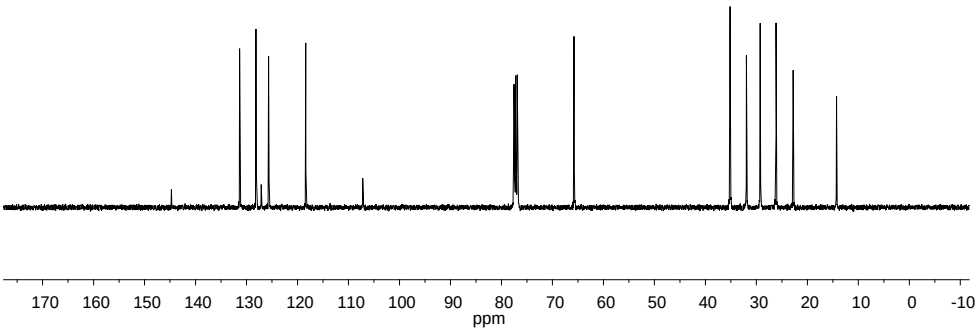
^{1}H NMR





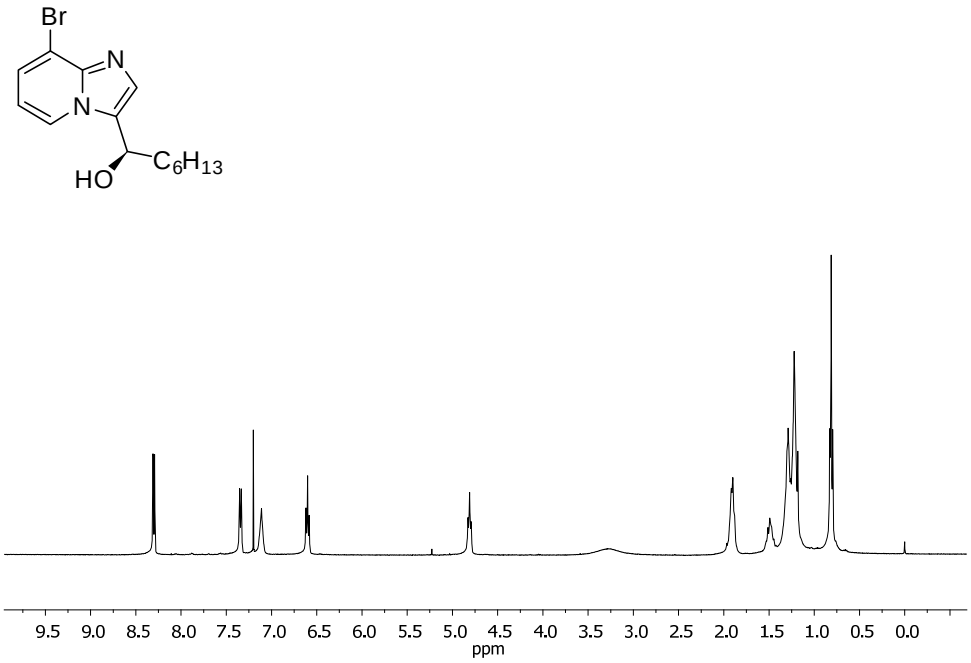
^{13}C NMR



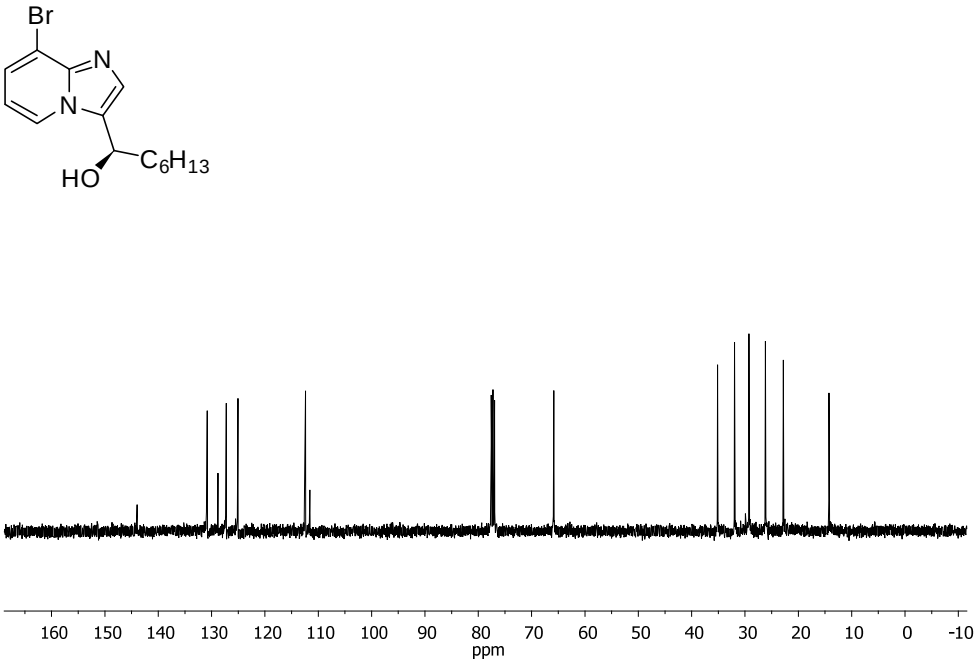


5p (*R*)-1-(8-Bromoimidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol (Entry 14, Table 4)

^{1}H NMR

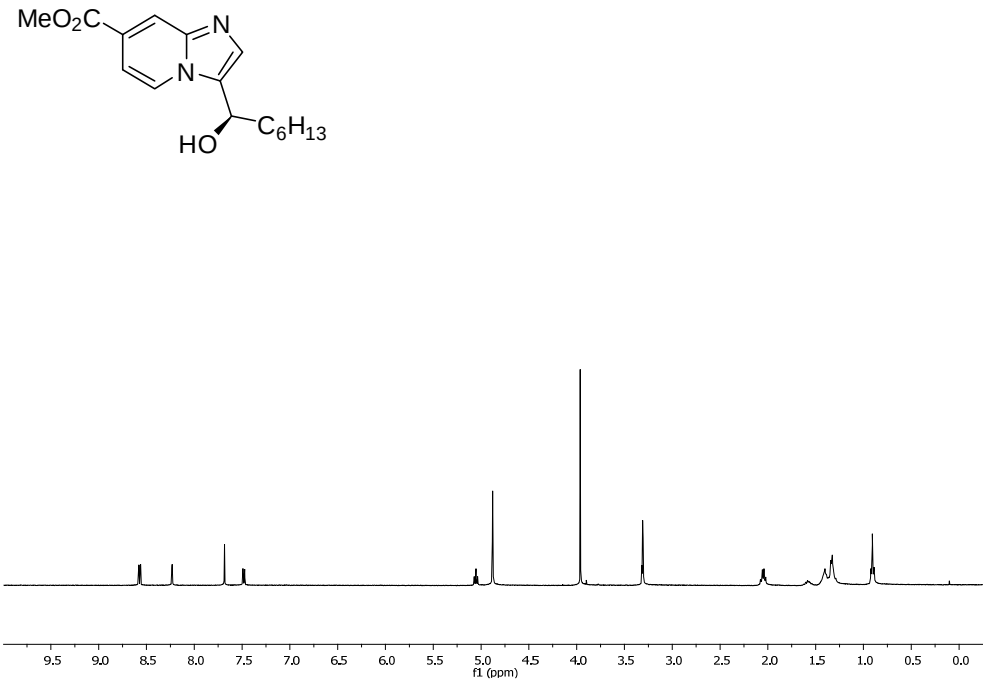


^{13}C NMR

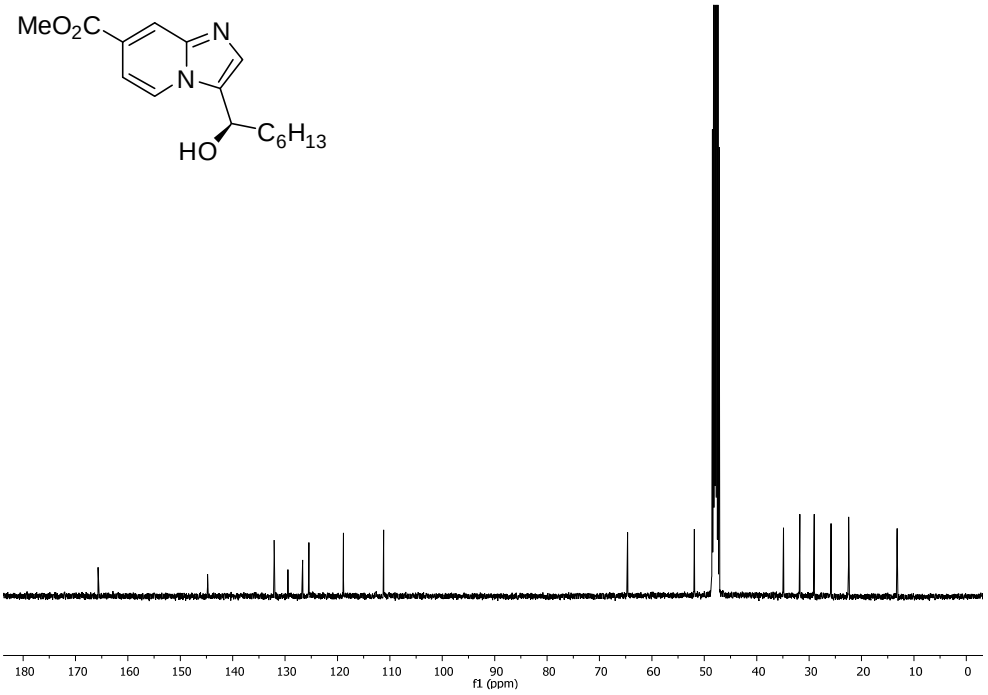


5q (*R*)-Methyl 3-(1-hydroxyheptyl)imidazo[1,2-*a*]pyridine-7-carboxylate (Entry 16, Table 4)

^{1}H NMR

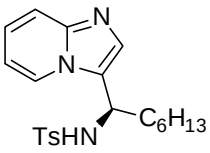


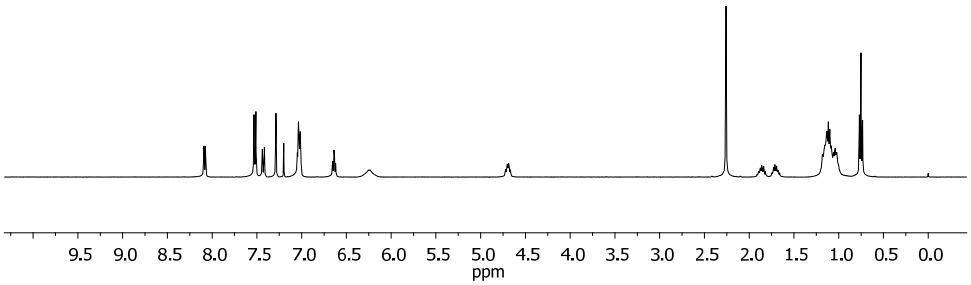
^{13}C NMR



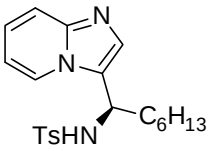
6a (*R*)-*N*-(1-(Imidazo[1,2-*a*]pyridin-3-yl)heptyl)-4-methylbenzenesulfonamide (Entry 1, Table 3)

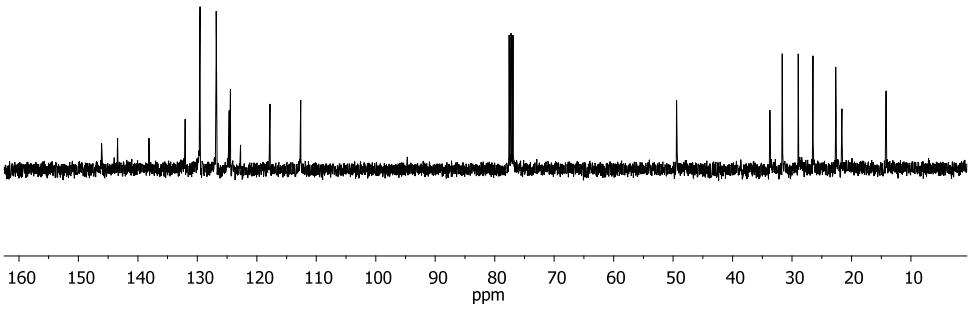
^{1}H NMR





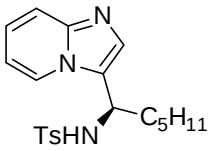
^{13}C NMR

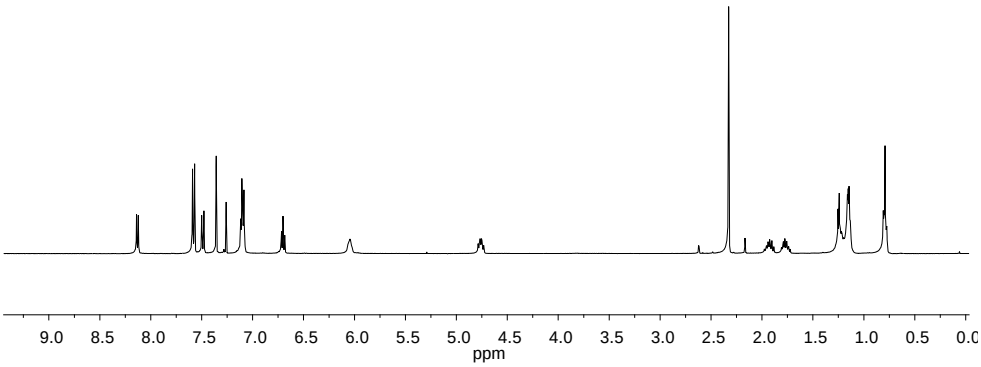




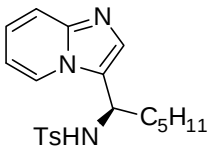
6b (*R*)-*N*-(1-(Imidazo[1,2-*a*]pyridin-3-yl)hexyl)-4-methylbenzenesulfonamide (Entry 2, Table 3)

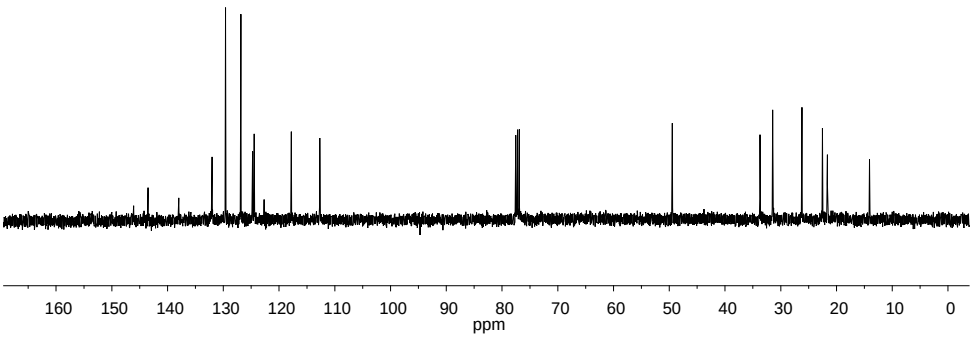
^{1}H NMR





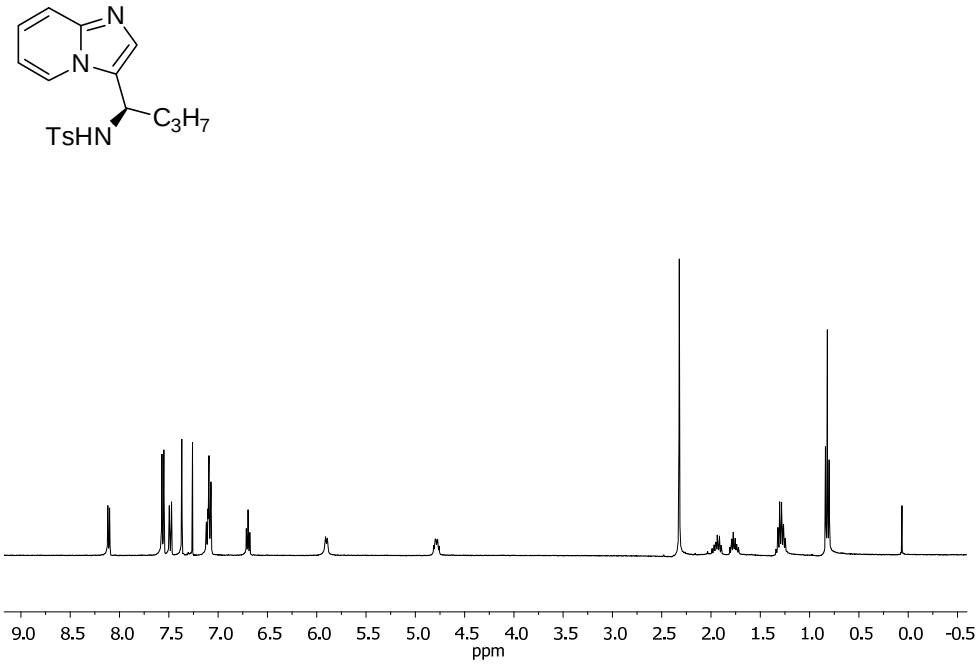
^{13}C NMR



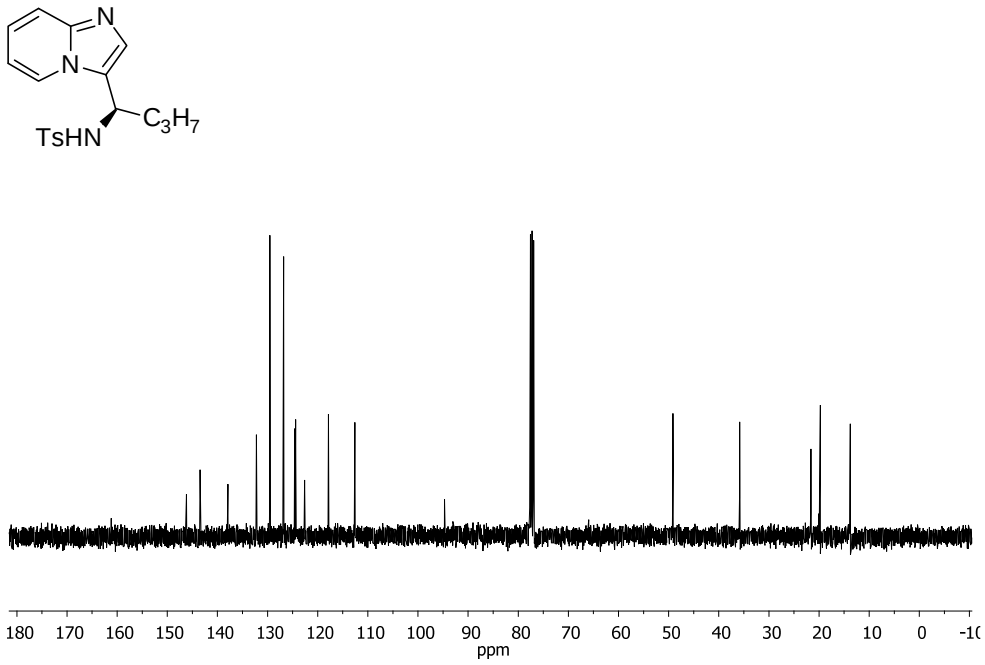


6c (*R*)-*N*-(1-(Imidazo[1,2-*a*]pyridin-3-yl)butyl)-4-methylbenzenesulfonamide (Entry 3, Table 4)

^{1}H NMR

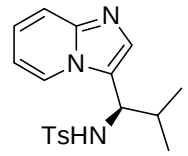


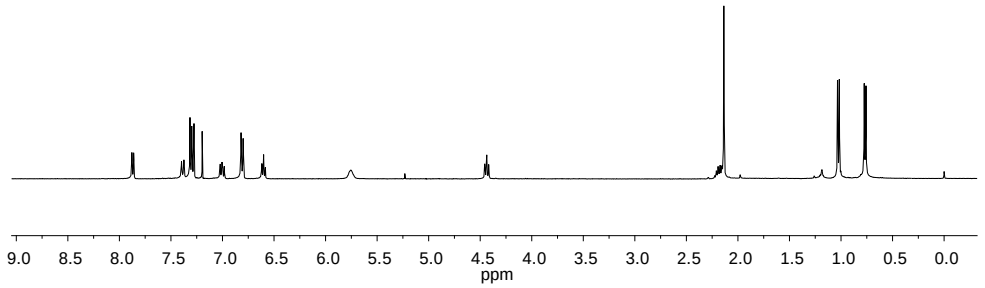
^{13}C NMR



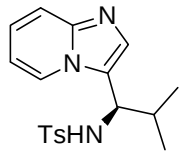
6d (*R*)-*N*-(1-(Imidazo[1,2-*a*]pyridin-3-yl)-2-methylpropyl)-4-methylbenzenesulfonamide (Entry 4, Table 3)

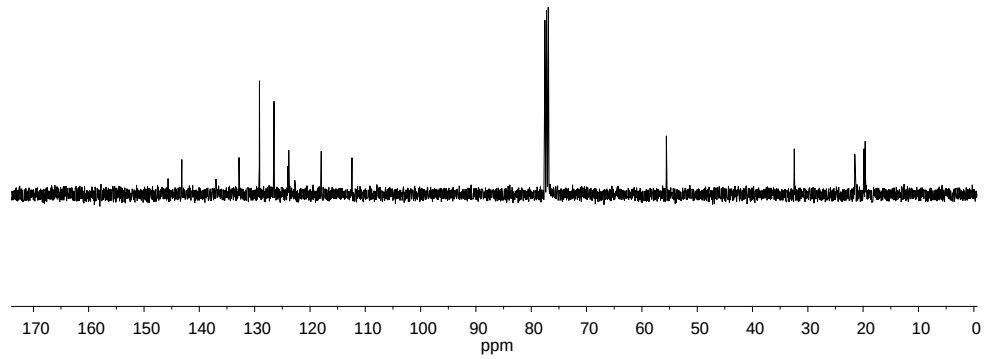
^{1}H NMR





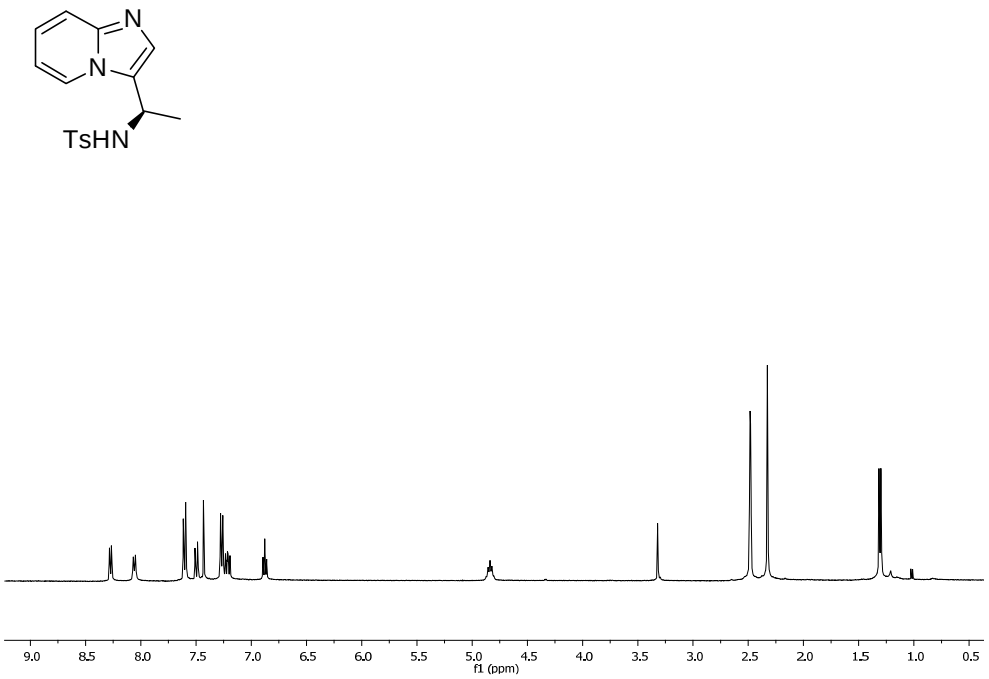
^{13}C NMR



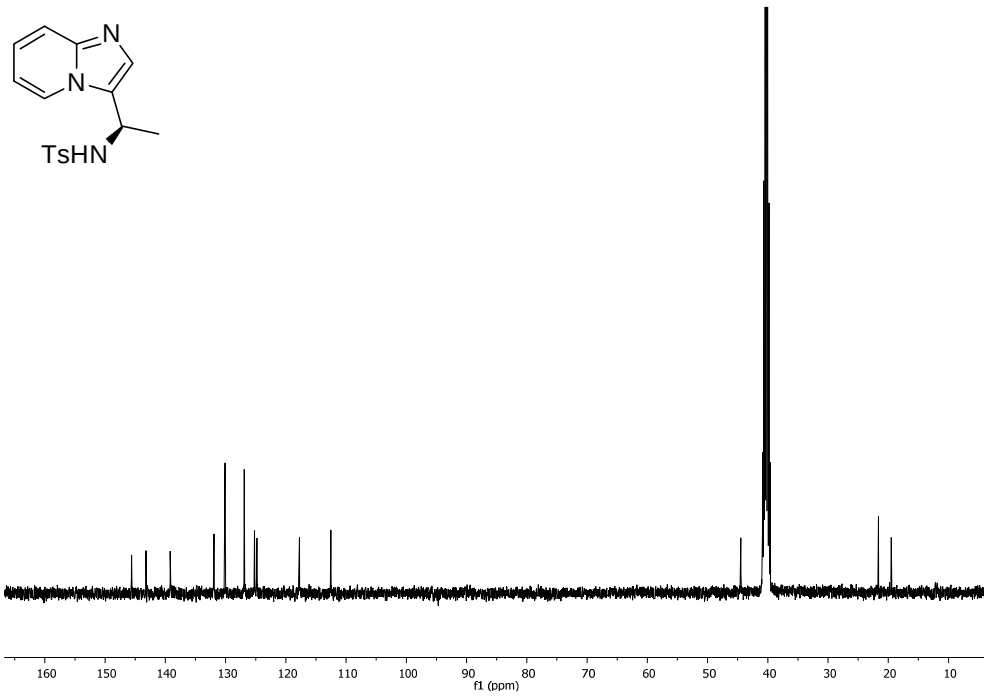


6e (*R*)-*N*-(1-(Imidazo[1,2-*a*]pyridin-3-yl)ethyl)-4-methylbenzenesulfonamide (Entry 5, Table 3)

^{1}H NMR

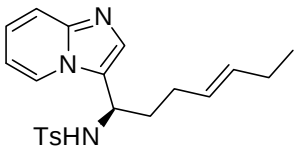


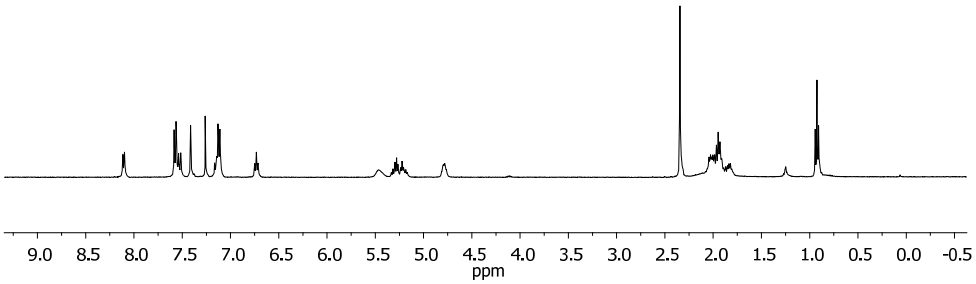
^{13}C NMR



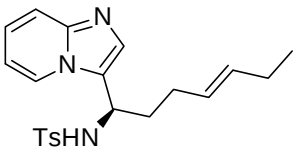
6f (*R*,*E*)-*N*-(1-(Imidazo[1,2-*a*]pyridin-3-yl)hept-4-en-1-yl)-4-methylbenzenesulfonamide (Entry 6, Table 3)

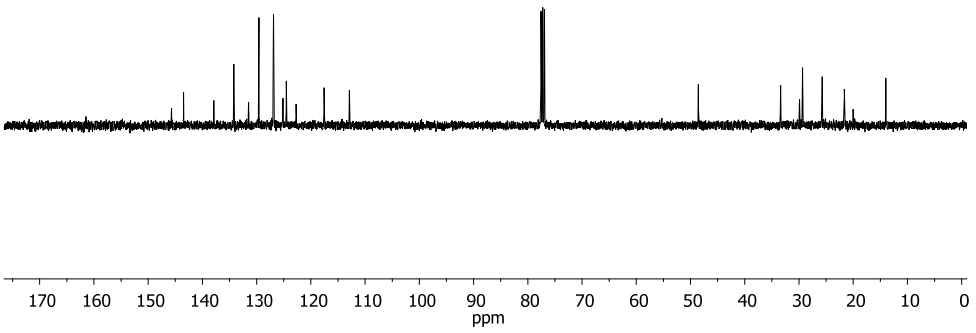
^{1}H NMR





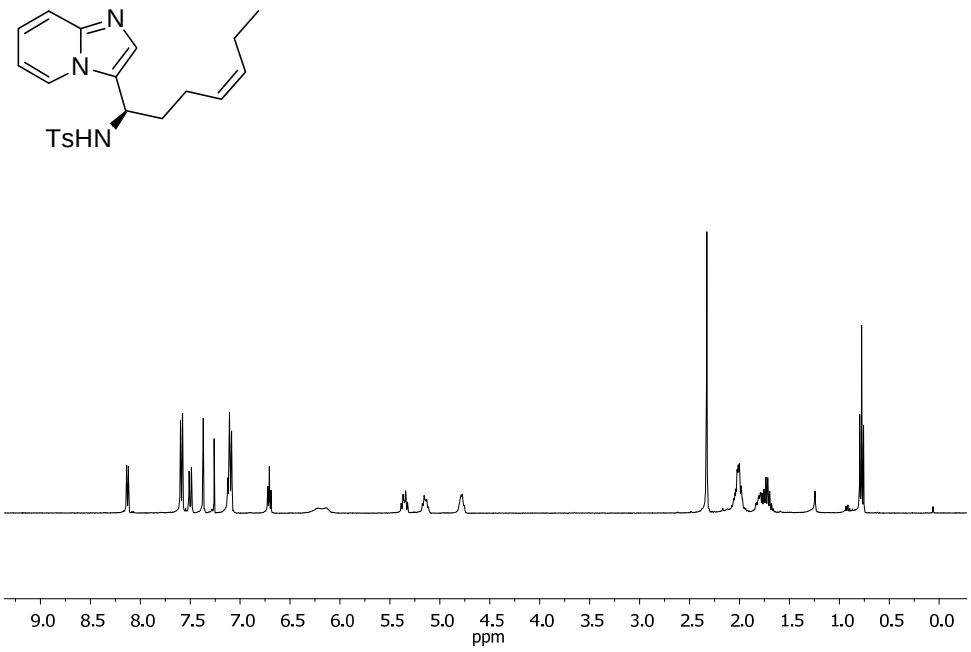
^{13}C NMR



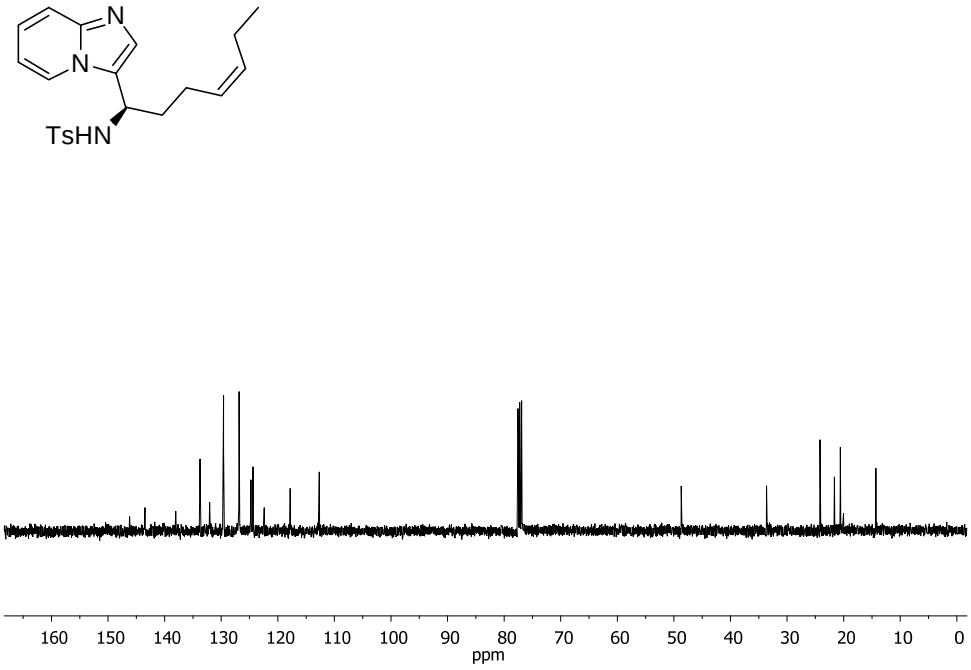


6g (*R*,*Z*)-*N*-(1-(Imidazo[1,2-*a*]pyridin-3-yl)hept-4-en-1-yl)-4-methylbenzenesulfonamide (Entry 7, Table 3)

^{1}H NMR

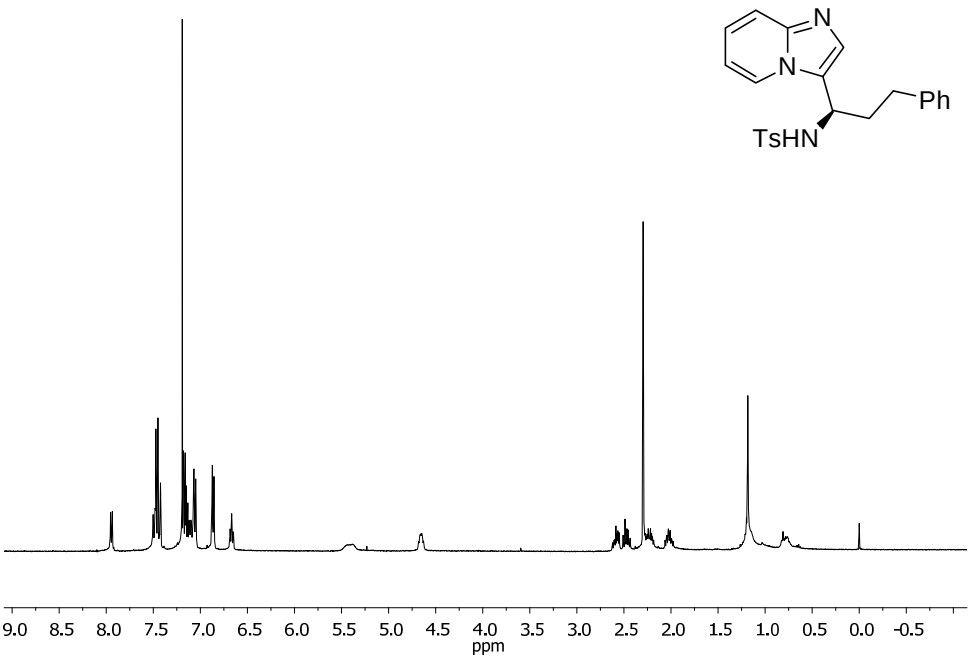


^{13}C NMR

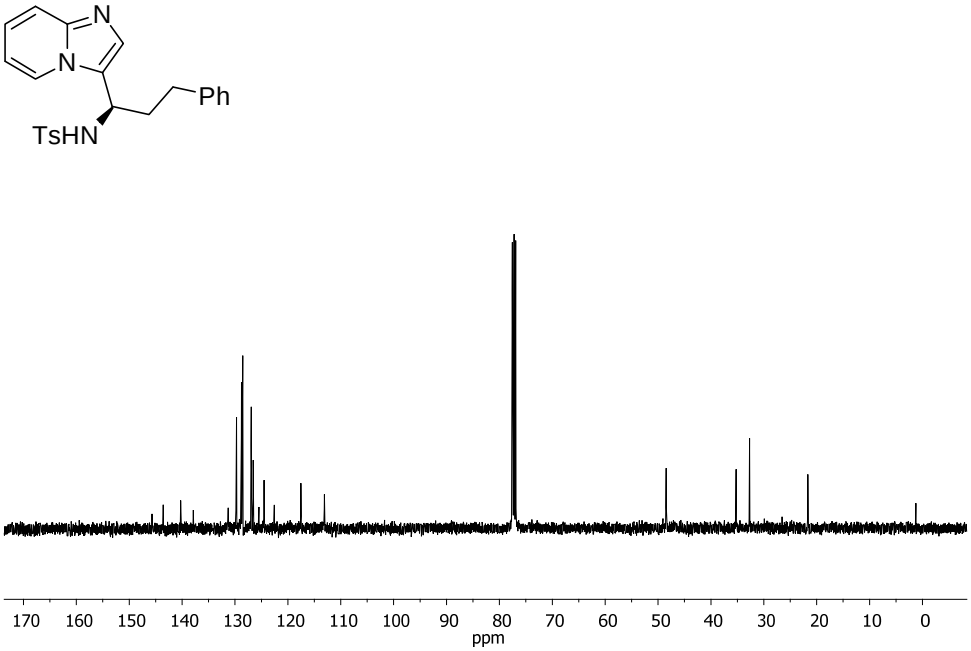


6h (*R*)-*N*-(1-(Imidazo[1,2-*a*]pyridin-3-yl)-3-phenylpropyl)-4-methylbenzenesulfonamide (Entry 8, Table 3)

^{1}H NMR

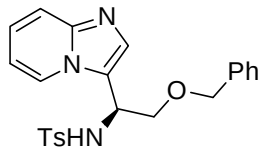


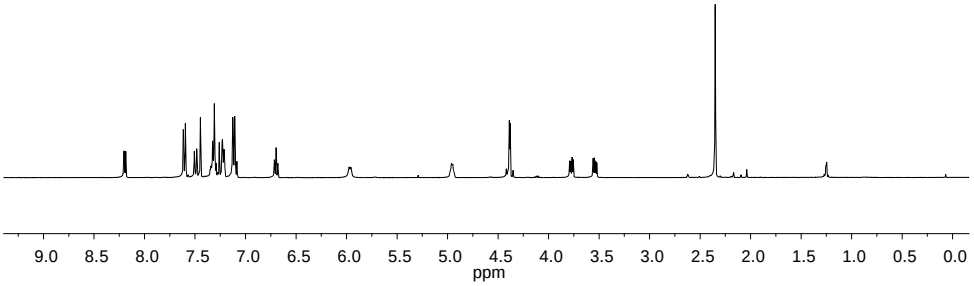
^{13}C NMR



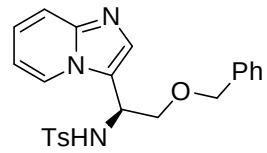
6i (*S*)-*N*-(2-(Benzyloxy)-1-(imidazo[1,2-*a*]pyridin-3-yl)ethyl)-4-methylbenzenesulfonamide (Entry 9, Table 3)

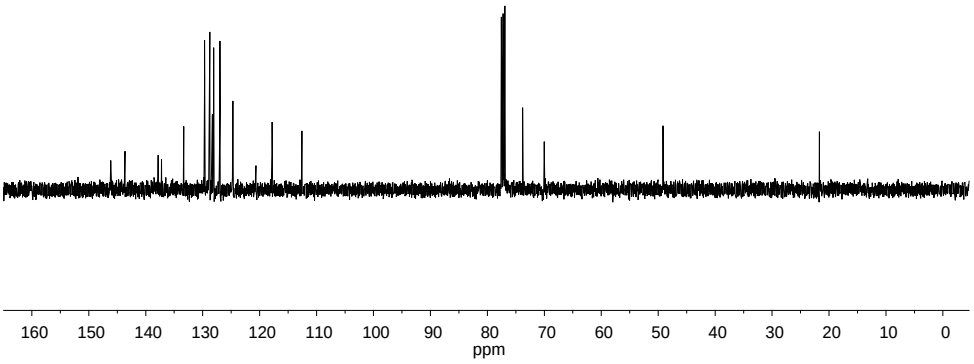
^{1}H NMR





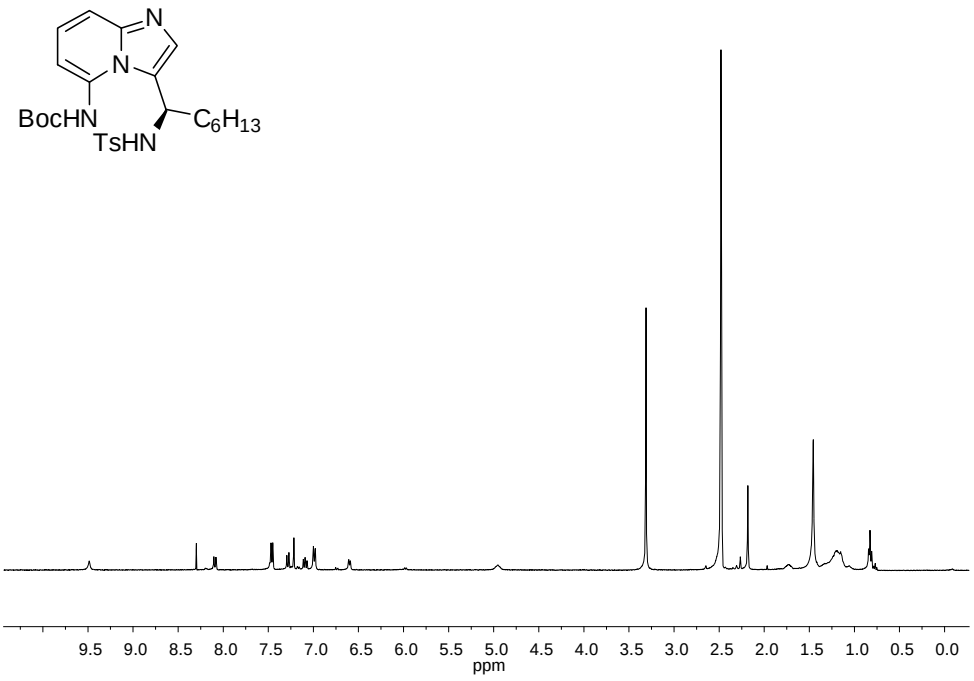
^{13}C NMR



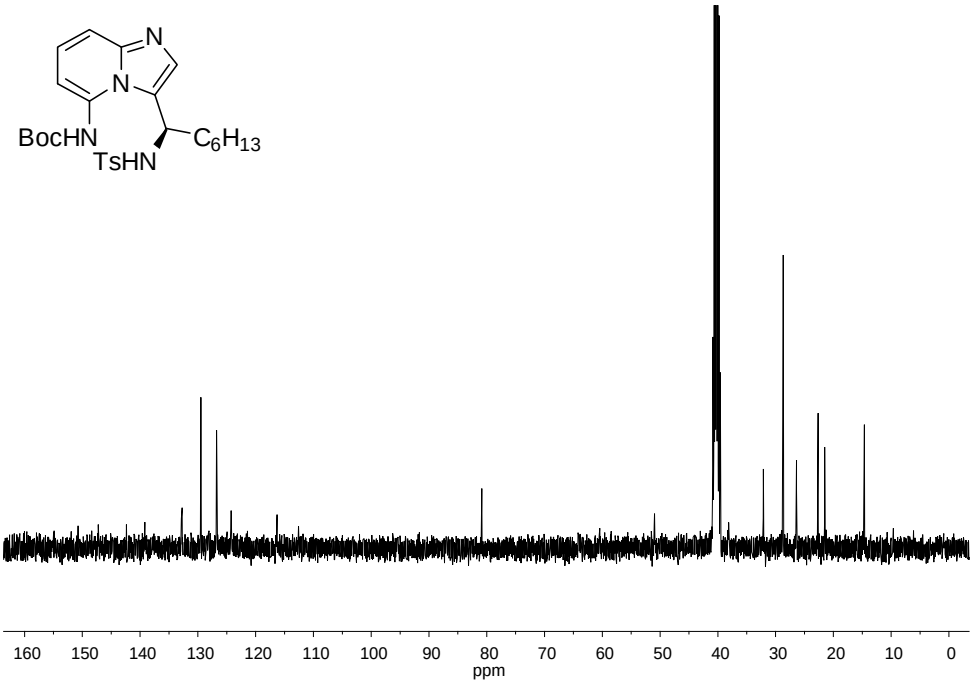


6j (*R*)-*tert*-Butyl (3-(1-(4-methylphenylsulfonamido)heptyl)imidazo[1,2-*a*]pyridin-5-yl)carbamate (Entry 2, Table 4)

^{1}H NMR

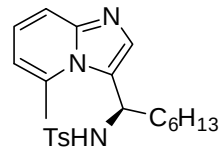


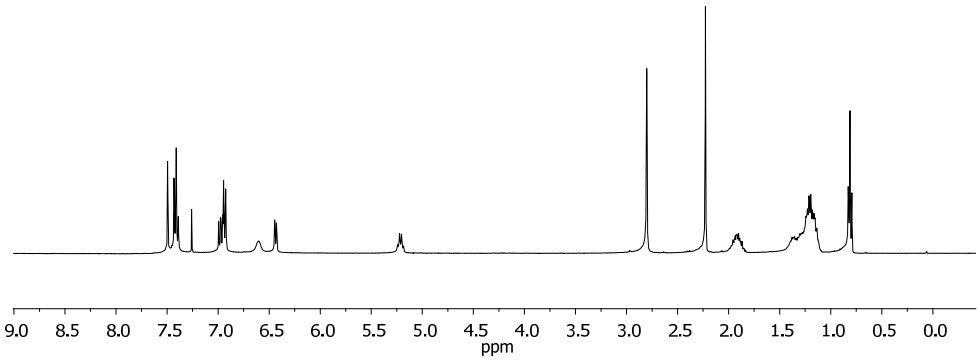
^{13}C NMR



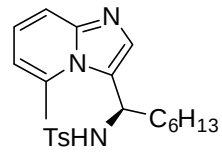
6k (*R*)-4-Methyl-*N*-(1-(5-methylimidazo[1,2-*a*]pyridin-3-yl)heptyl)benzenesulfonamide (Entry 4, Table 4)

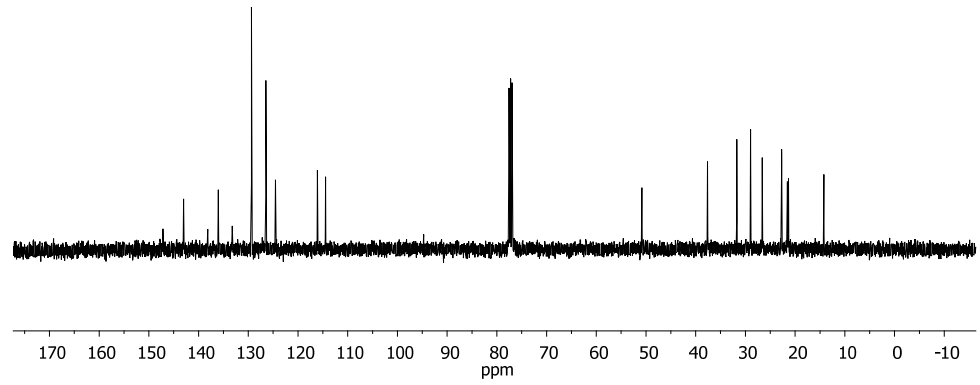
^{1}H NMR





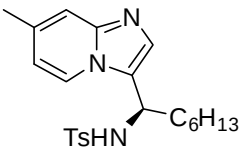
^{13}C NMR

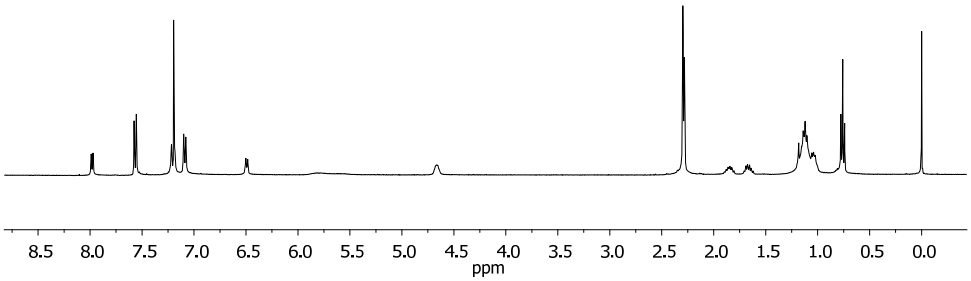




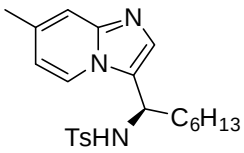
6l (*R*)-4-Methyl-*N*-(1-(7-methylimidazo[1,2-*a*]pyridin-3-yl)heptyl)benzenesulfonamide (Entry 6, Table 4)

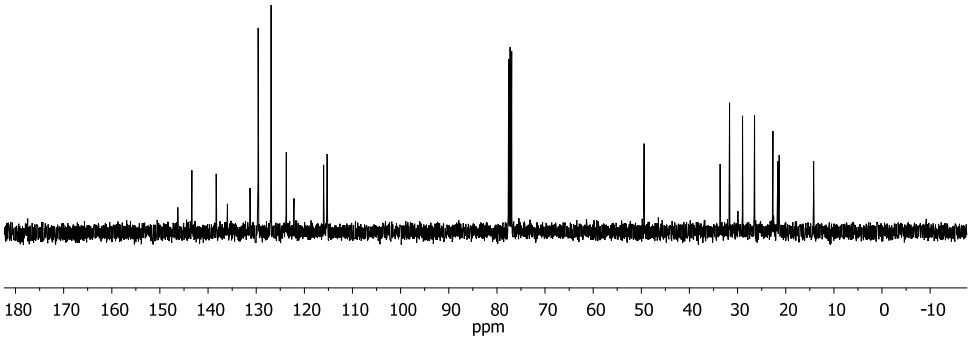
^{1}H NMR





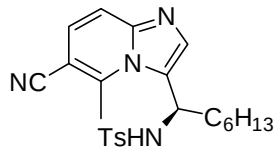
^{13}C NMR

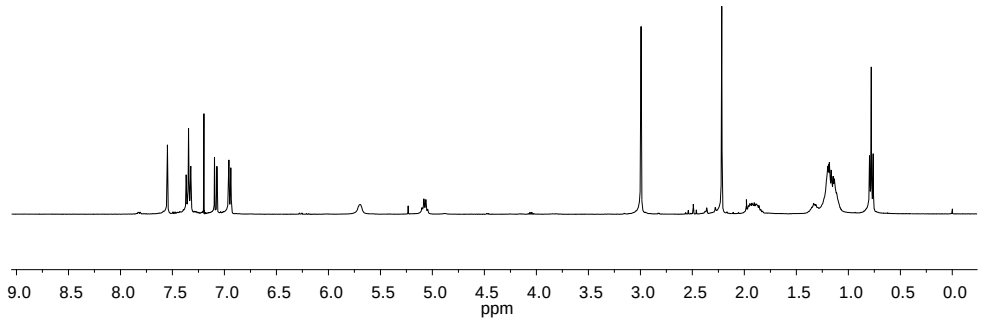




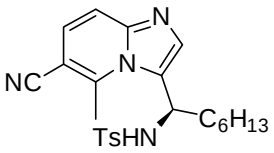
6m (*R*)-*N*-(1-(6-Cyano-5-methylimidazo[1,2-*a*]pyridin-3-yl)heptyl)-4-methylbenzenesulfonamide (Entry 8, Table 4)

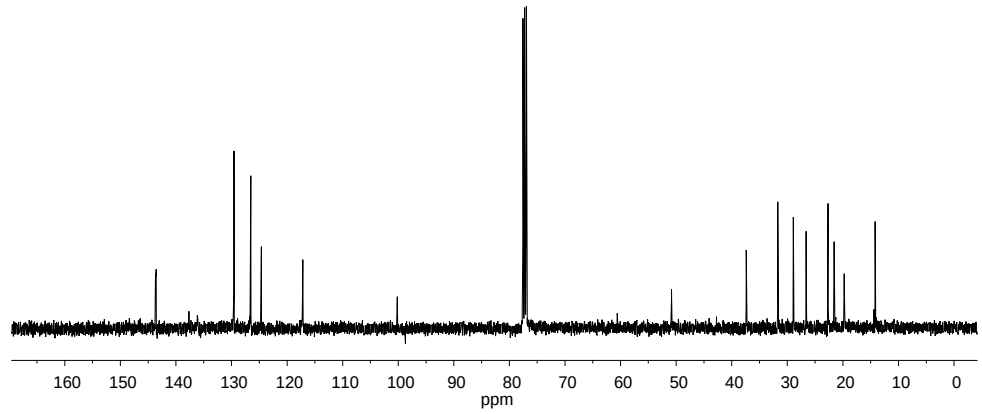
^{1}H NMR





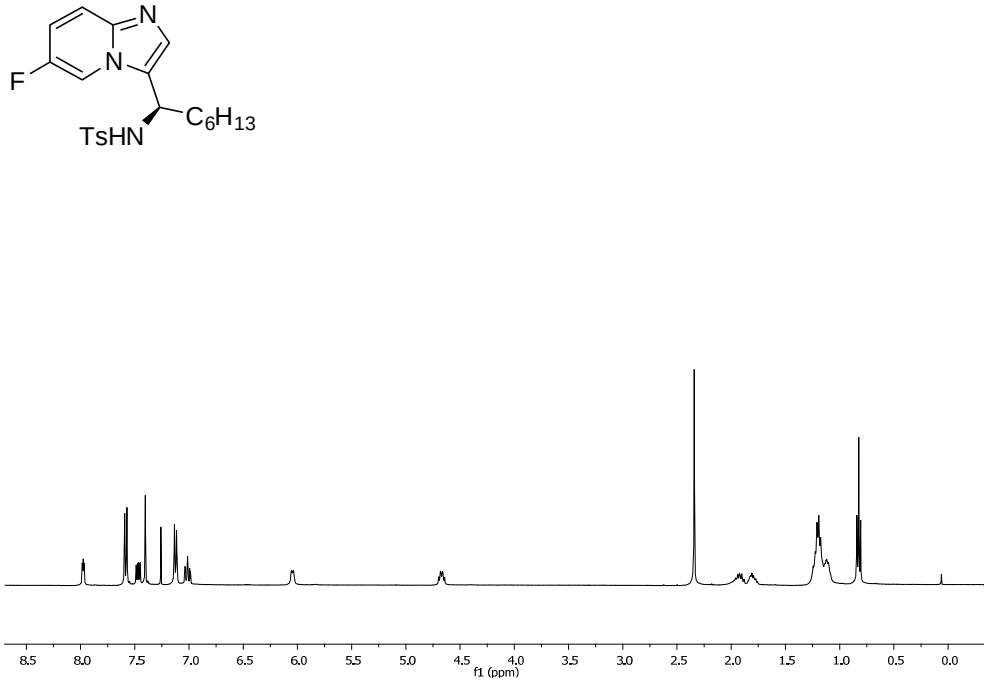
^{13}C NMR



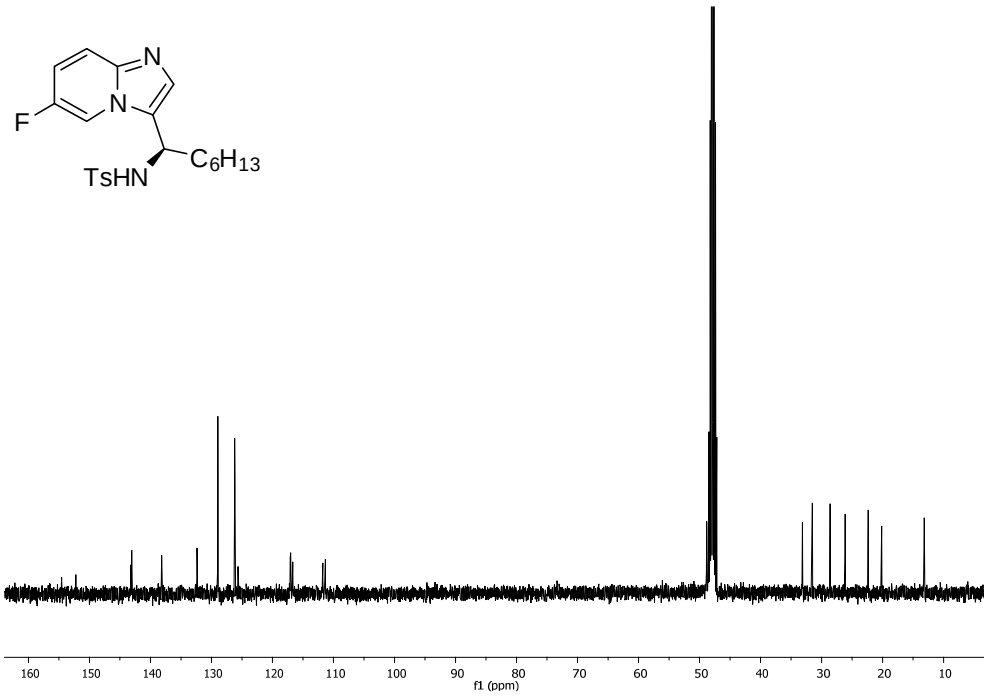


6n ((*R*)-*N*-(1-(6-Fluoroimidazo[1,2-*a*]pyridin-3-yl)heptyl)-4-methylbenzenesulfonamide (Entry 10, Table 4)

^{1}H NMR

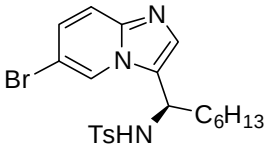


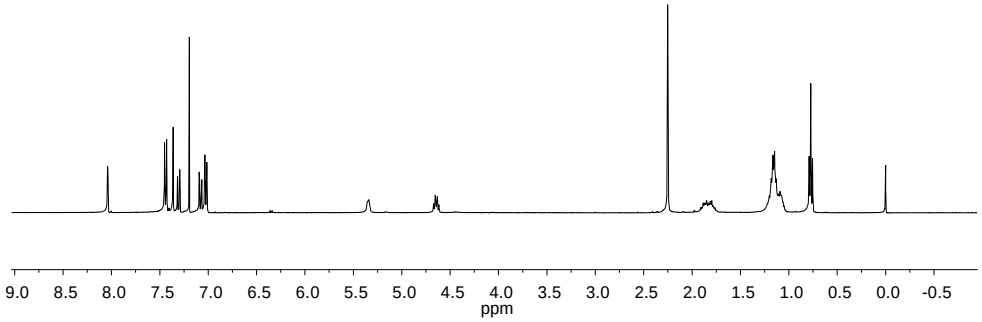
^{13}C NMR



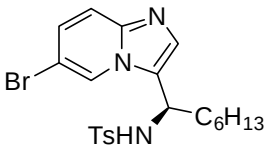
6o (*R*)-*N*-(1-(6-Bromoimidazo[1,2-*a*]pyridin-3-yl)heptyl)-4-methylbenzenesulfonamide (Entry 13, Table 4)

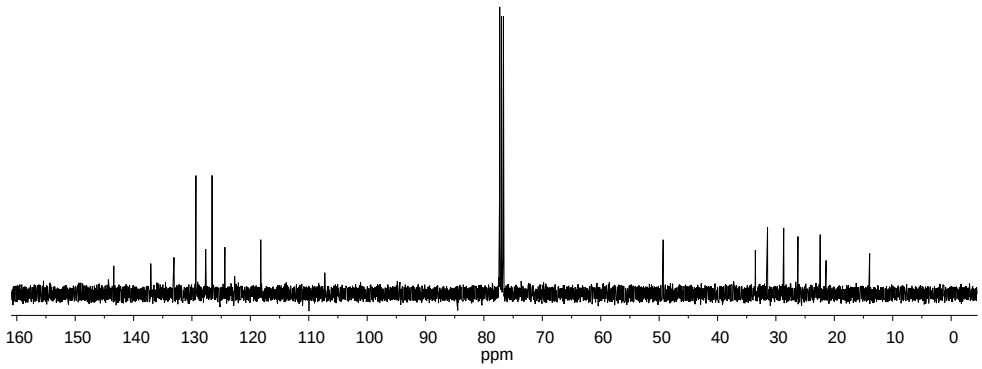
^{1}H NMR





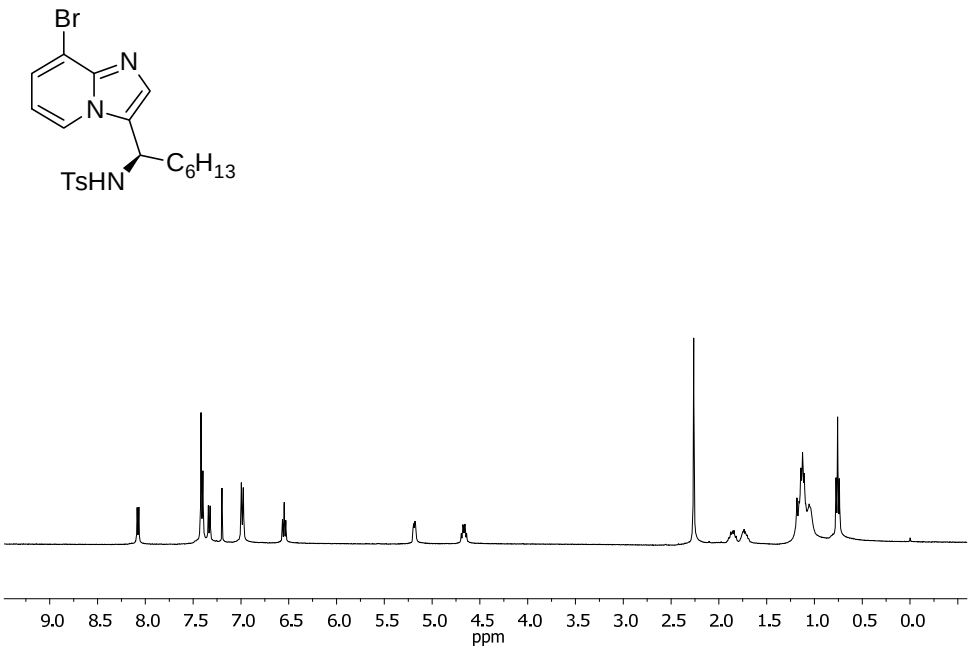
^{13}C NMR



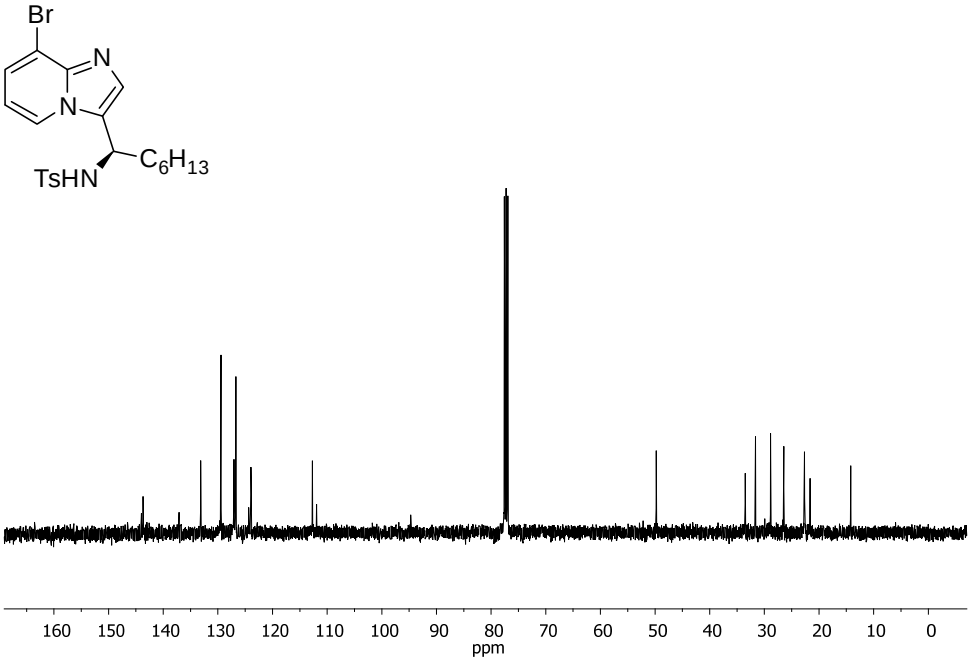


6p (*R*)-*N*-(1-(8-Bromoimidazo[1,2-*a*]pyridin-3-yl)heptyl)-4-methylbenzenesulfonamide (Entry 15, Table 4)

^{1}H NMR

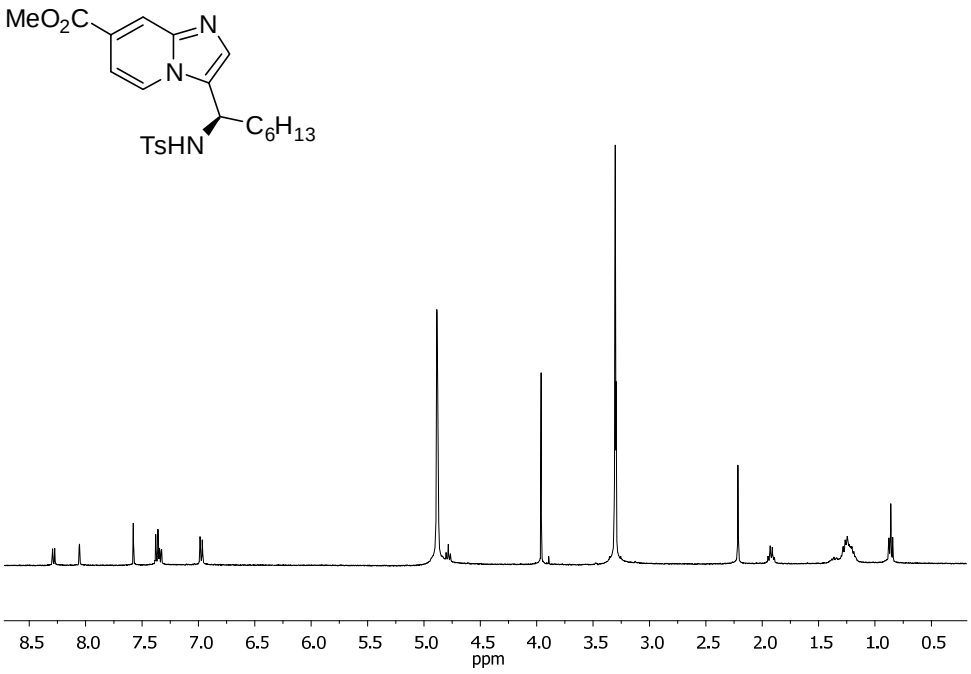


^{13}C NMR

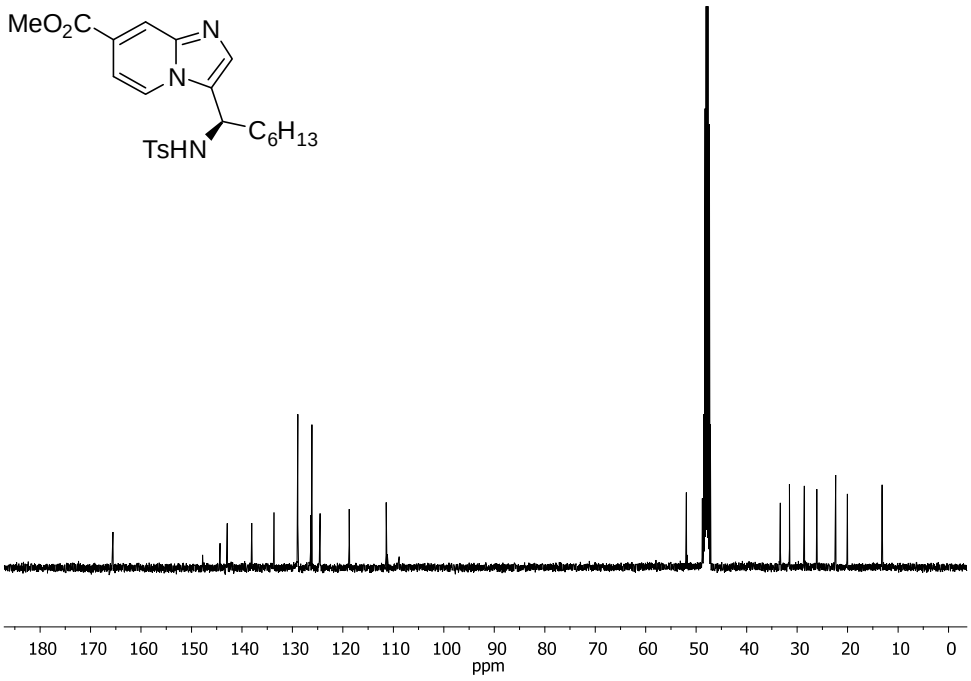


6q (*R*)-Methyl 3-(1-(4-methylphenylsulfonamido)heptyl)imidazo[1,2-*a*]pyridine-7-carboxylate (Entry 17, Table 4)

^{1}H NMR

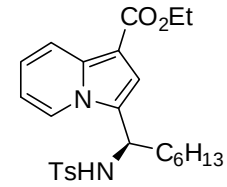


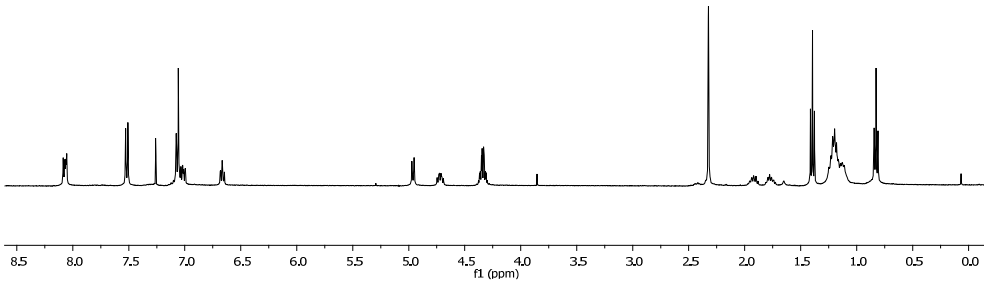
^{13}C NMR



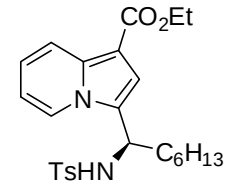
8b (*R*)-Ethyl 3-(1-(4-methylphenylsulfonamido)heptyl)indolizine-1-carboxylate (Scheme 2)

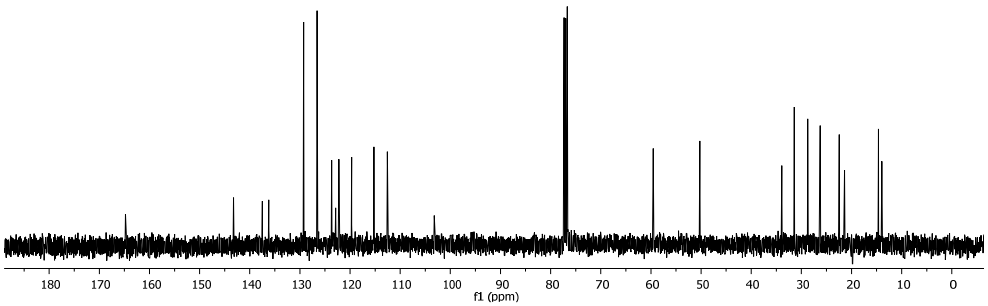
^{1}H NMR





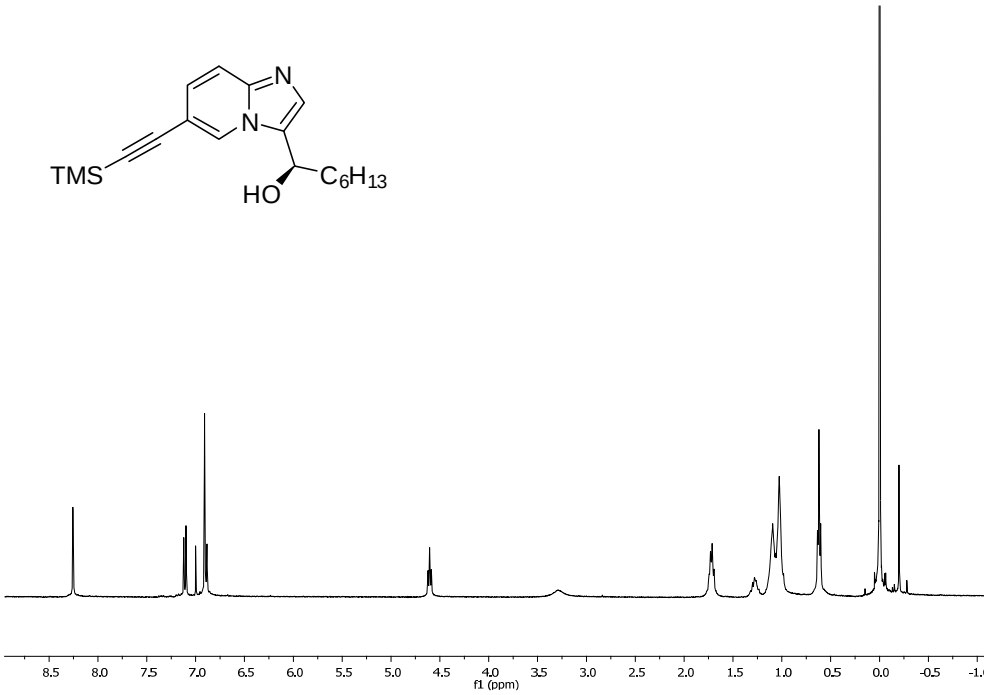
^{13}C NMR



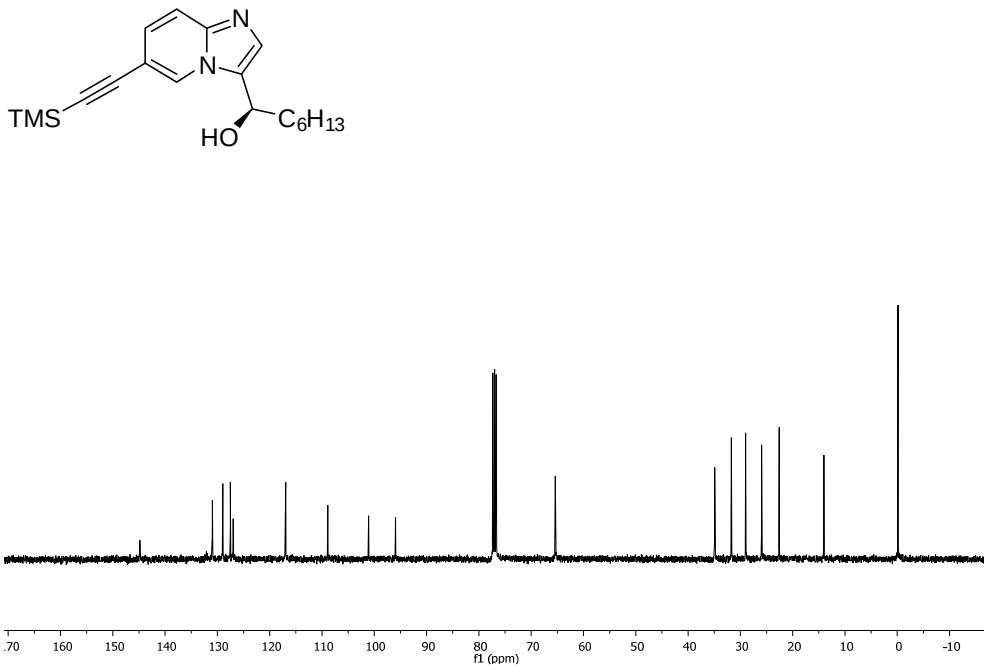


5r (*R*)-1-(6-((Trimethylsilyl)ethynyl)imidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol (Scheme 3, left side)

^{1}H NMR

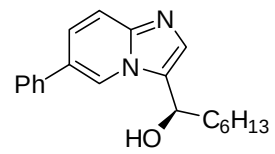


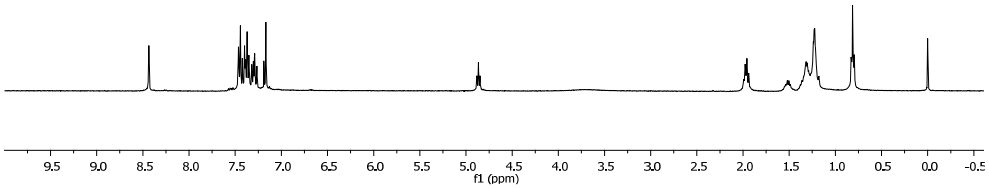
^{13}C NMR



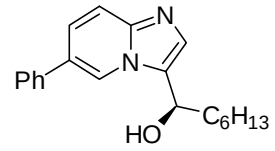
5s (*R*)-1-(6-Phenylimidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol (Scheme 3, right side)

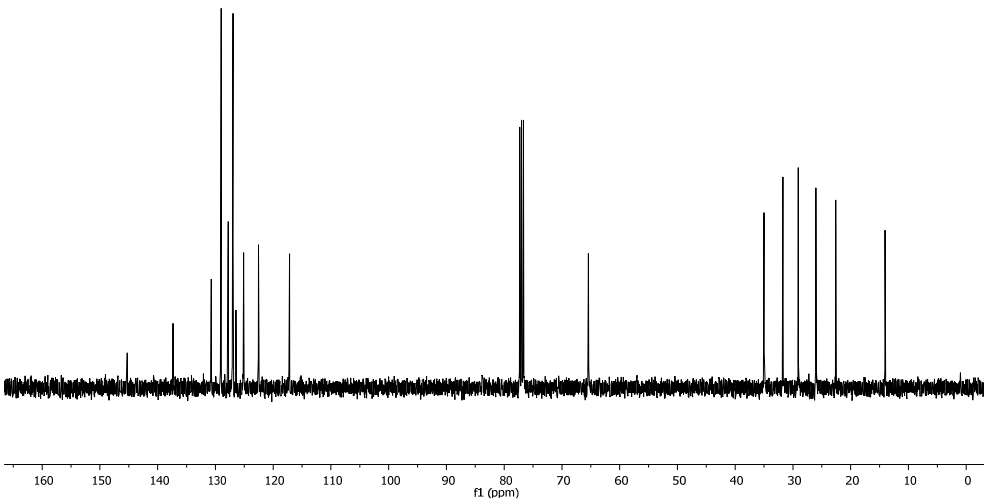
^{1}H NMR





^{13}C NMR

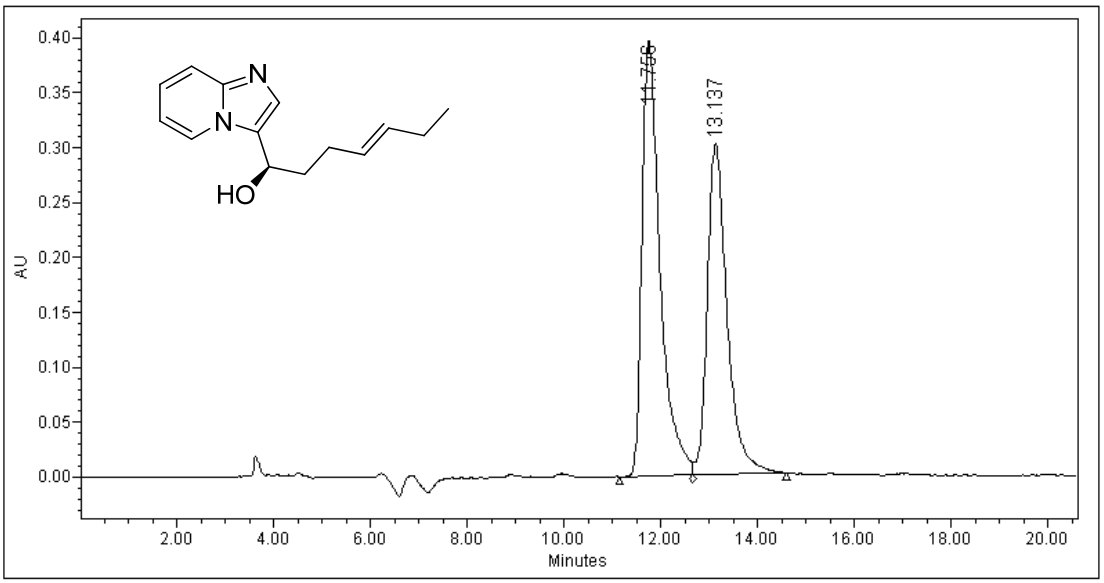




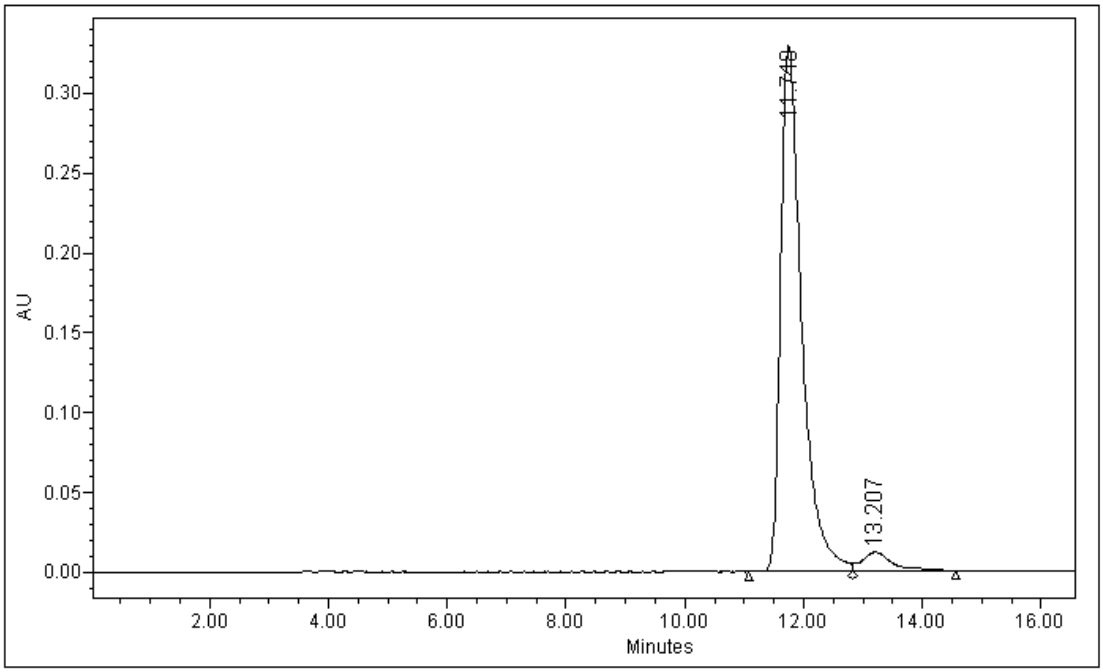
9. Representative examples of HPLC chromatograms of products 5, 6 and 8

5f (*R*,*E*)-1-(Imidazo[1,2-*a*]pyridin-3-yl)hept-4-en-1-ol (Entry 6, Table 2)

Racemic sample



Enatiomerically enriched sample

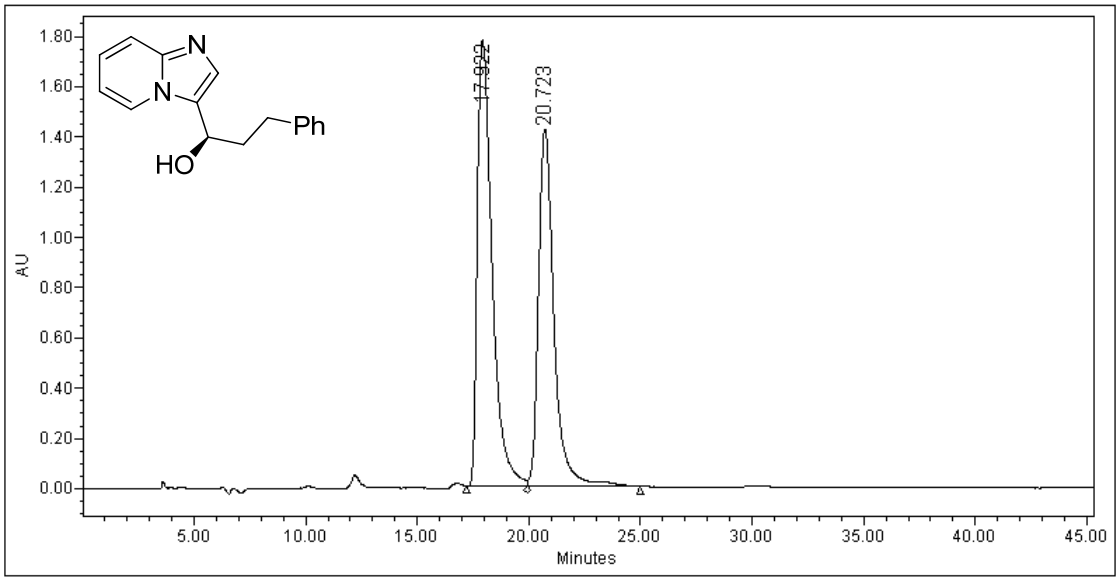


Processed Channel: PDA 280.9 nm

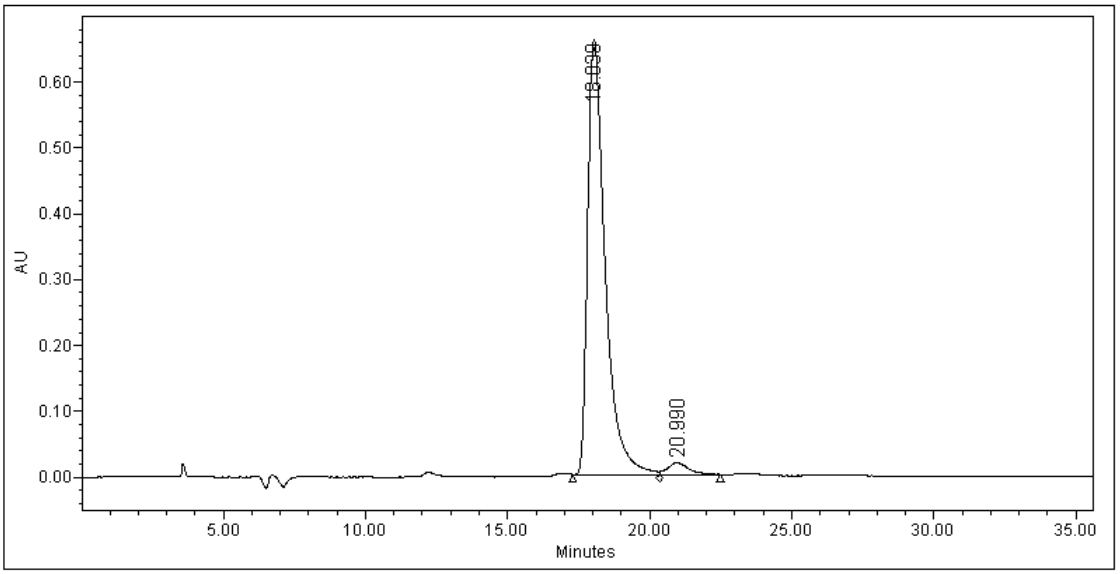
*	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 280.9 nm	11.748	8115781	95.05	329436
2	PDA 280.9 nm	13.207	422434	4.95	11819

5h (*R*)-1-(Imidazo[1,2-*a*]pyridin-3-yl)-3-phenylpropan-1-ol (Entry 8, Table 2)

Racemic sample



Enantiomerically enriched sample

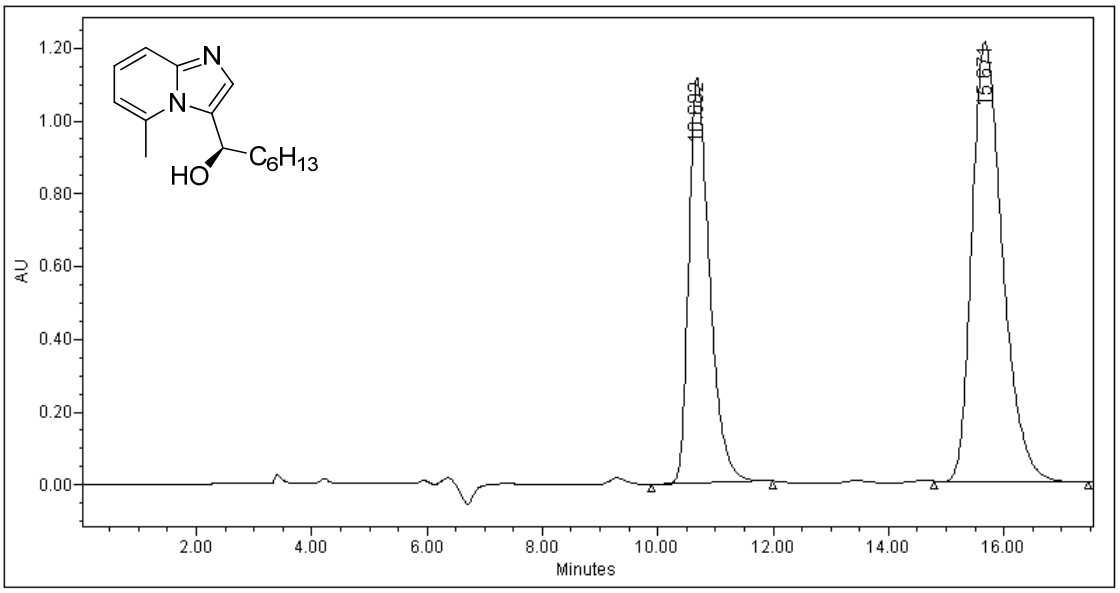


Processed Channel: PDA 235.9 nm

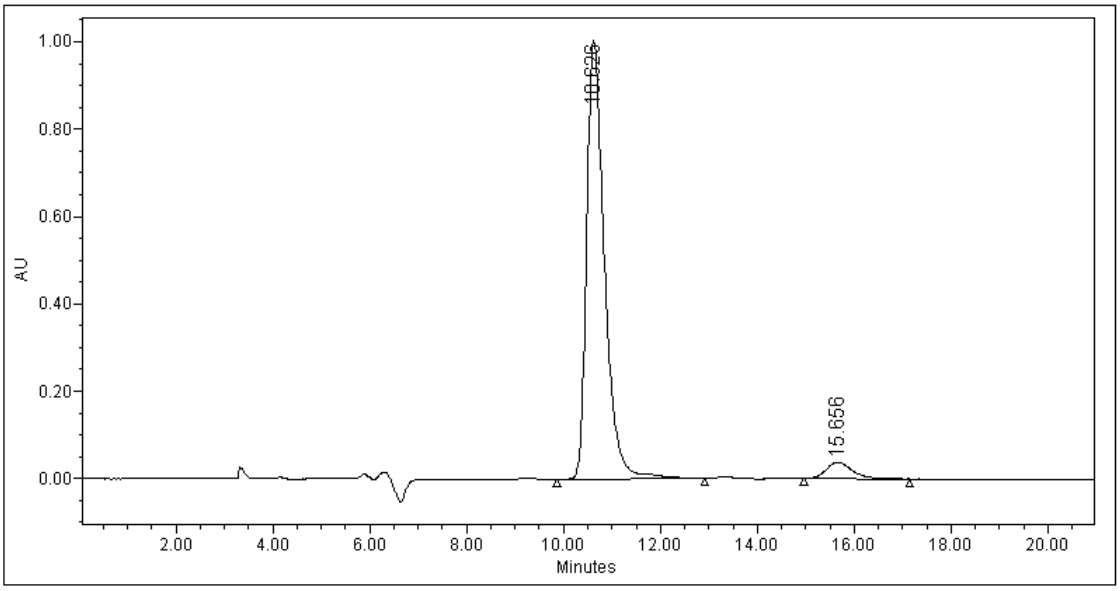
*	Processed Channel	Retention Time (min)	Area	% Area
1	PDA 235.9 nm	18.039	28247214	96.88
2	PDA 235.9 nm	20.990	910607	3.12

5k (*R*)-1-(5-Methylimidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol (Entry 3, Table 4)

Racemic sample



Enantiomerically enriched sample

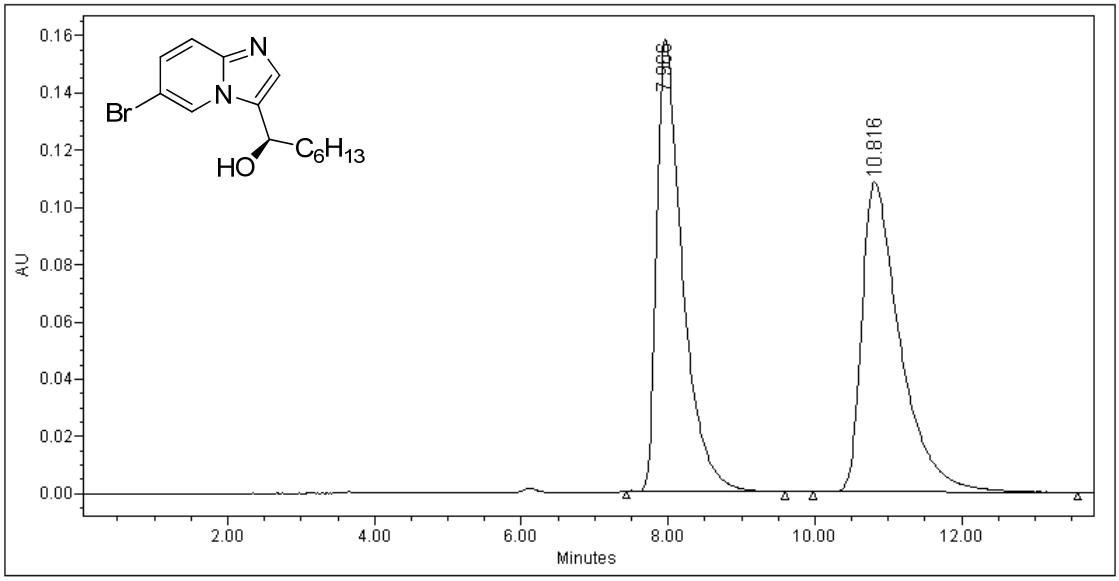


Processed Channel: PDA 234.5 nm

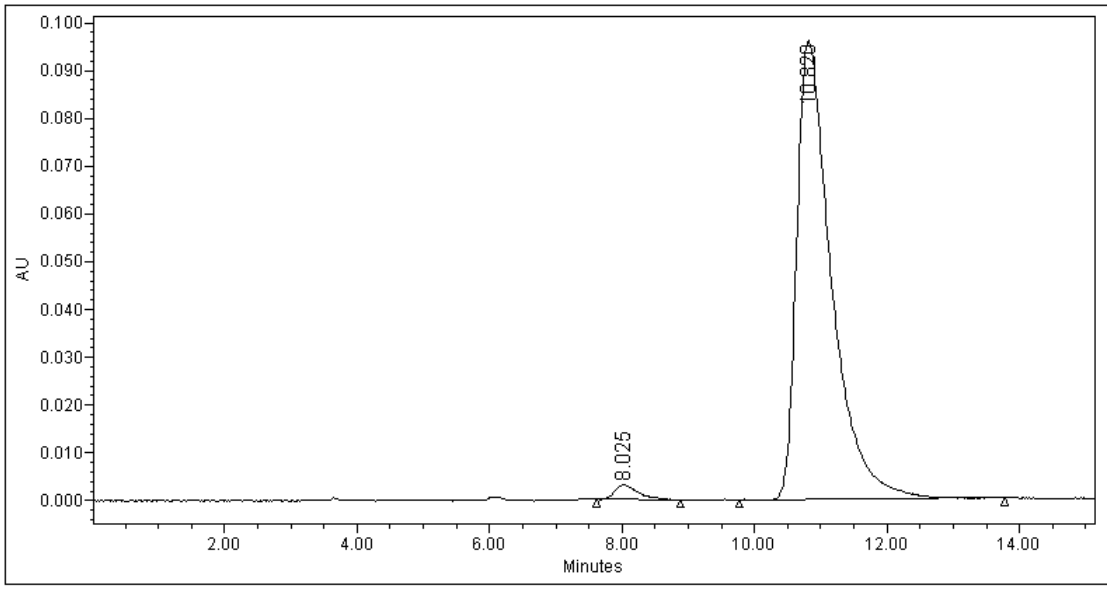
	Processed Channel	Retention Time (min)	Area	% Area
1	PDA 234.5 nm	10.626	25652234	94.97
2	PDA 234.5 nm	15.656	1358227	5.03

5o (*R*)-1-(6-Bromoimidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol (Entry 11, Table 4)

Racemic sample



Enantiomerically enriched sample

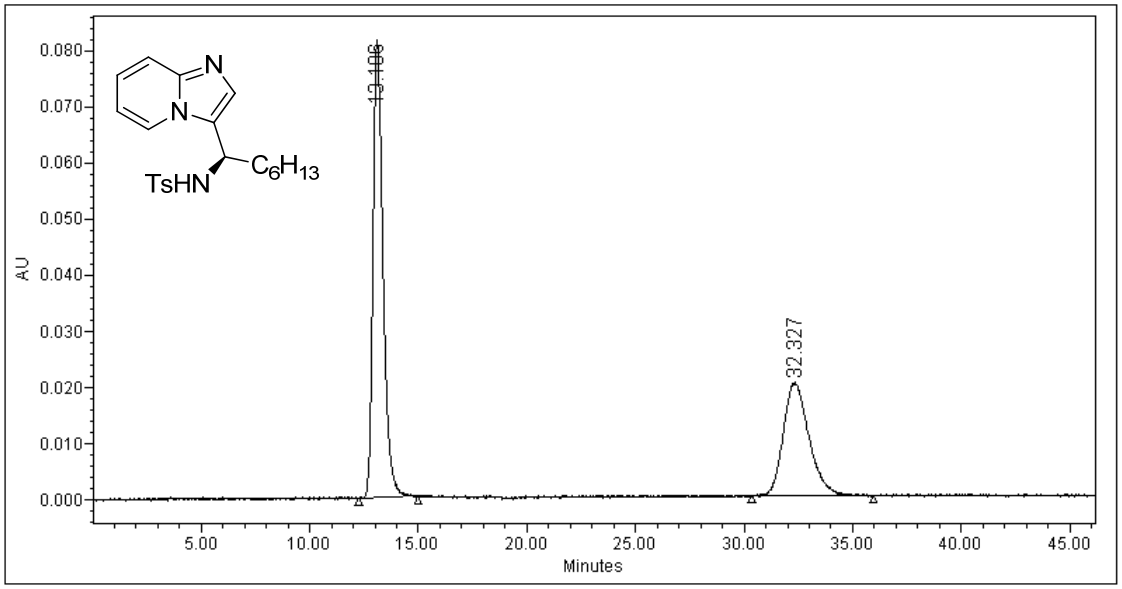


Processed Channel: PDA 290.6 nm

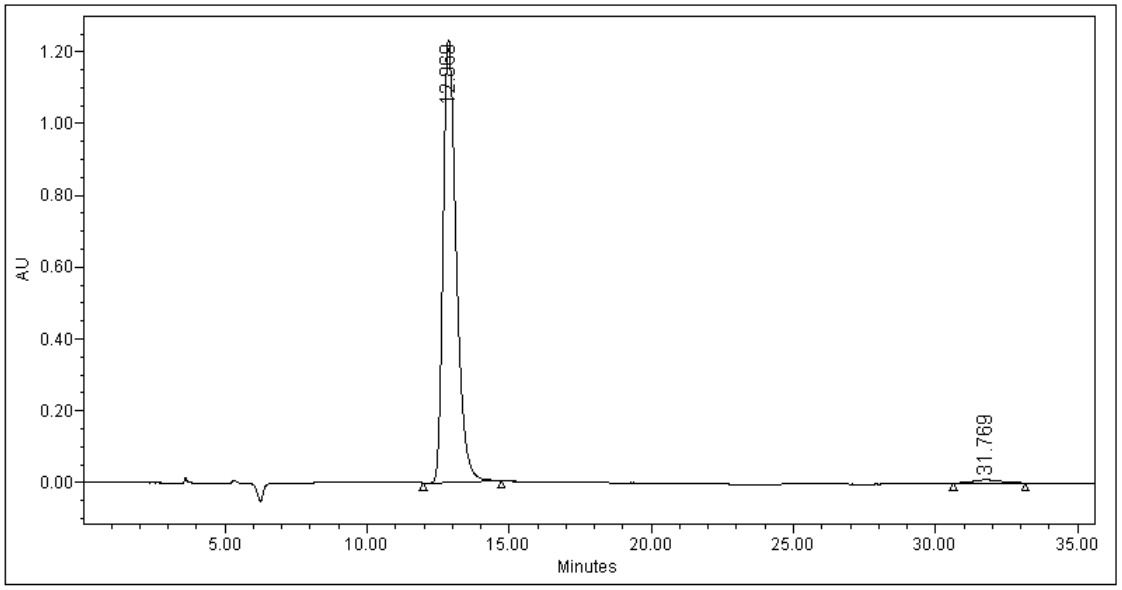
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 290.6 nm	8.025	72616	2.04	2964
2	PDA 290.6 nm	10.820	3482787	97.96	96011

6a (*R*)-*N*-(1-(Imidazo[1,2-*a*]pyridin-3-yl)heptyl)-4-methylbenzenesulfonamide (Entry 1, Table 3)

Racemic sample



Enantiomerically enriched sample

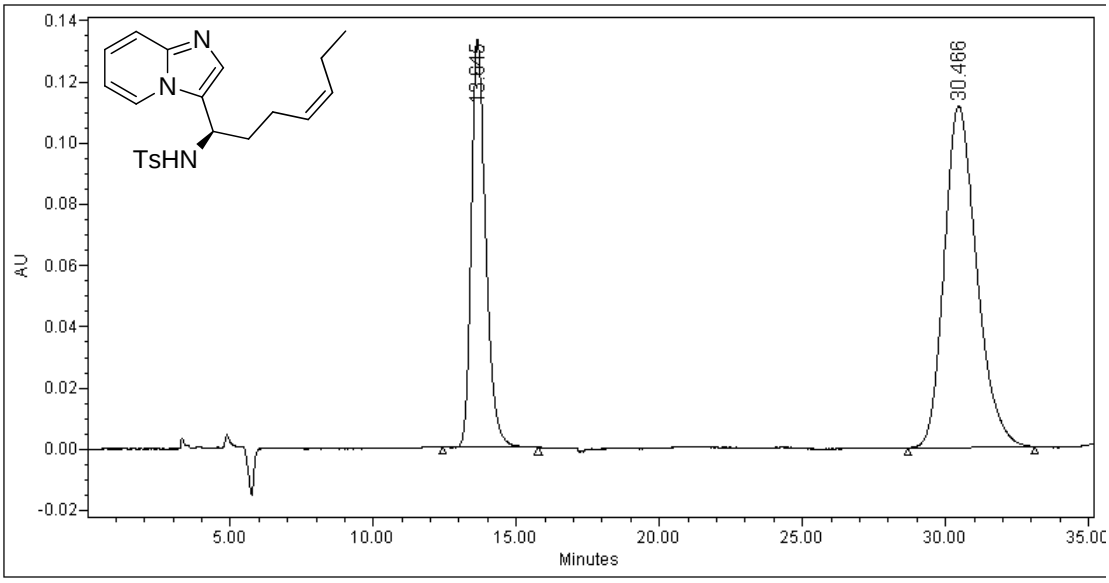


Processed Channel: PDA 227.0 nm

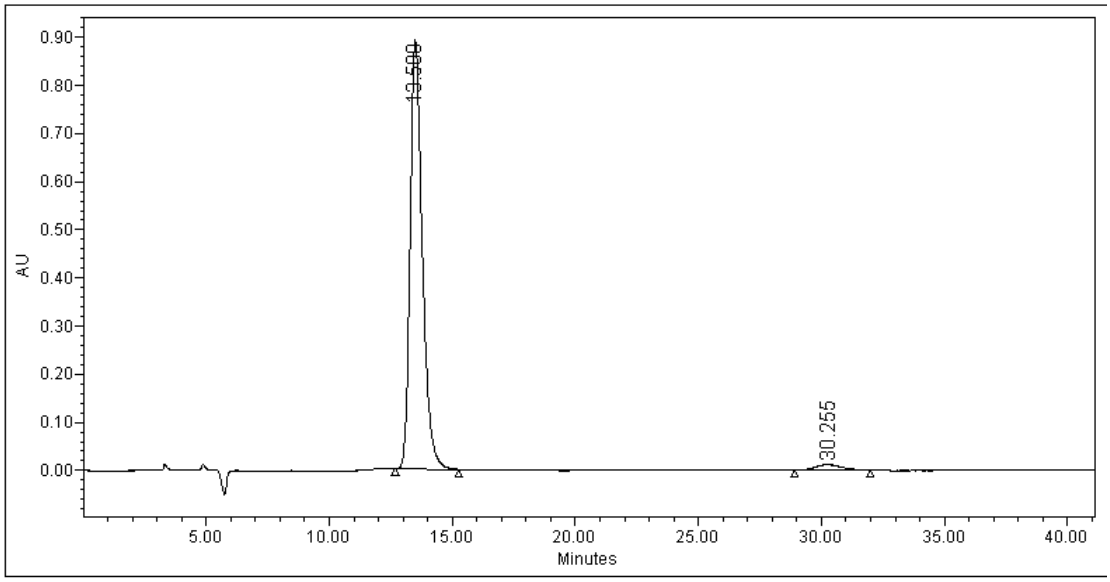
	Processed Channel	Retention Time (min)	Area	% Area
1	PDA 227.0 nm	12.869	39078077	98.43
2	PDA 227.0 nm	31.769	625200	1.57

6g (*R*,*Z*)-*N*-(1-(Imidazo[1,2-*a*]pyridin-3-yl)hept-4-en-1-yl)-4-methylbenzenesulfonamide (Entry 7, Table 3)

Racemic sample



Enantiomerically enriched sample



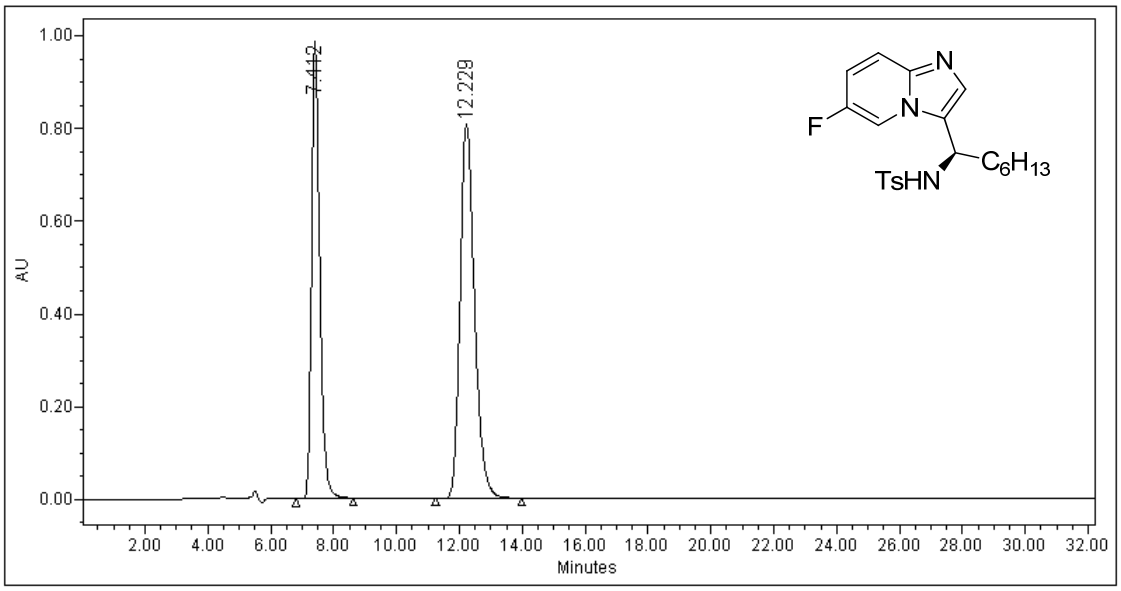
Processed Channel: PDA 227.6 nm

*	Processed Channel	Retention Time (min)	Area	% Area
1	PDA 227.6 nm	13.500	30794893	97.43
2	PDA 227.6 nm	30.255	813879	2.57

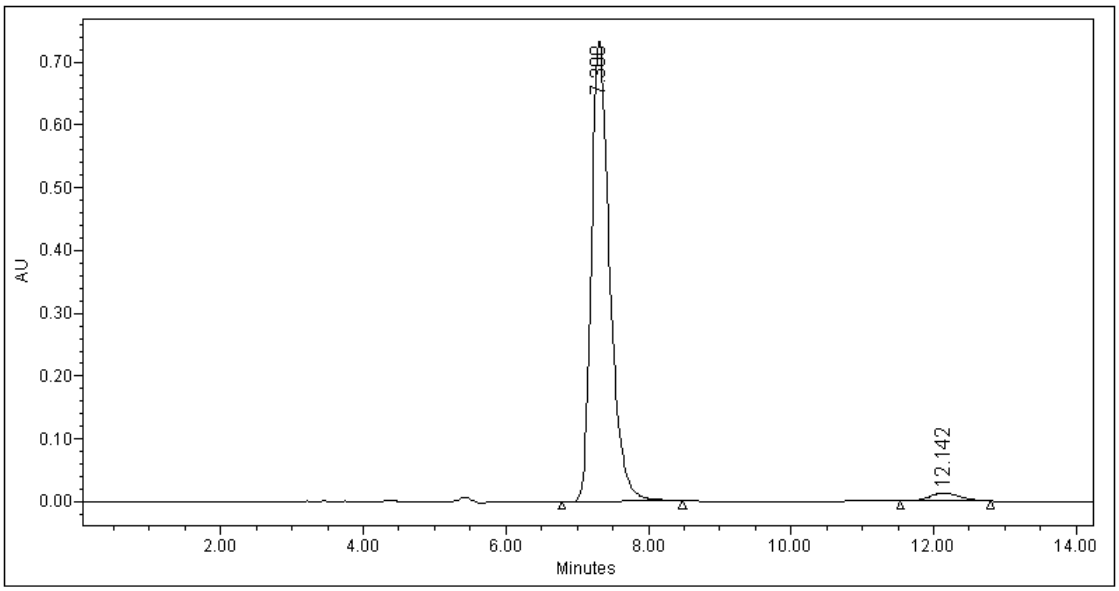
6n ((*R*)-*N*-(1-(6-Fluoroimidazo[1,2-*a*]pyridin-3-yl)heptyl)-4-methylbenzenesulfonamide

(Entry 10, Table 4)

Racemic sample



Enantiomerically enriched sample

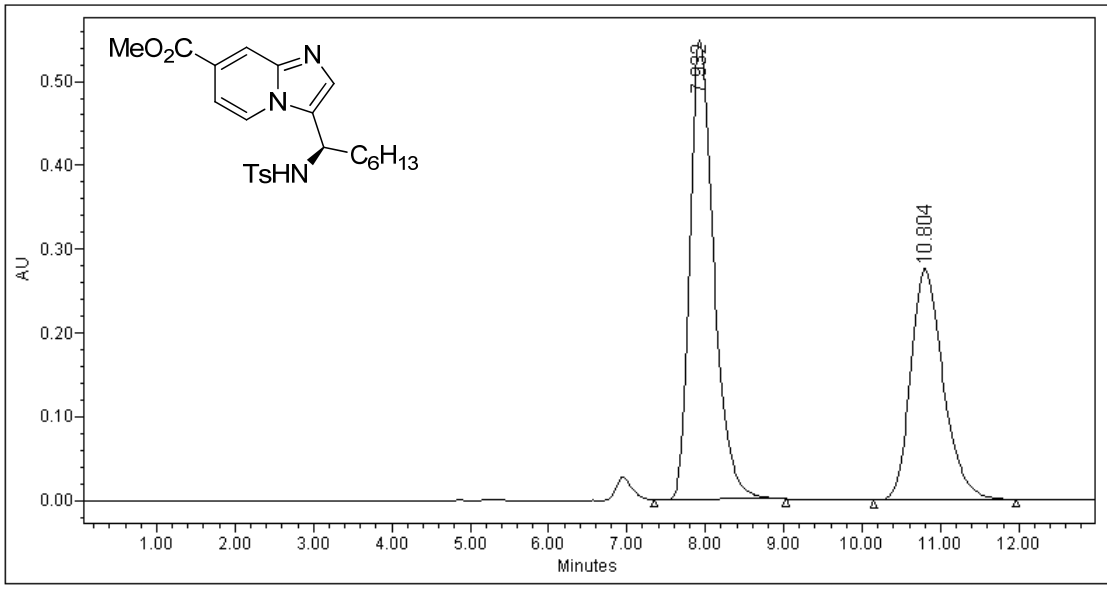


Processed Channel: PDA 242.3 nm

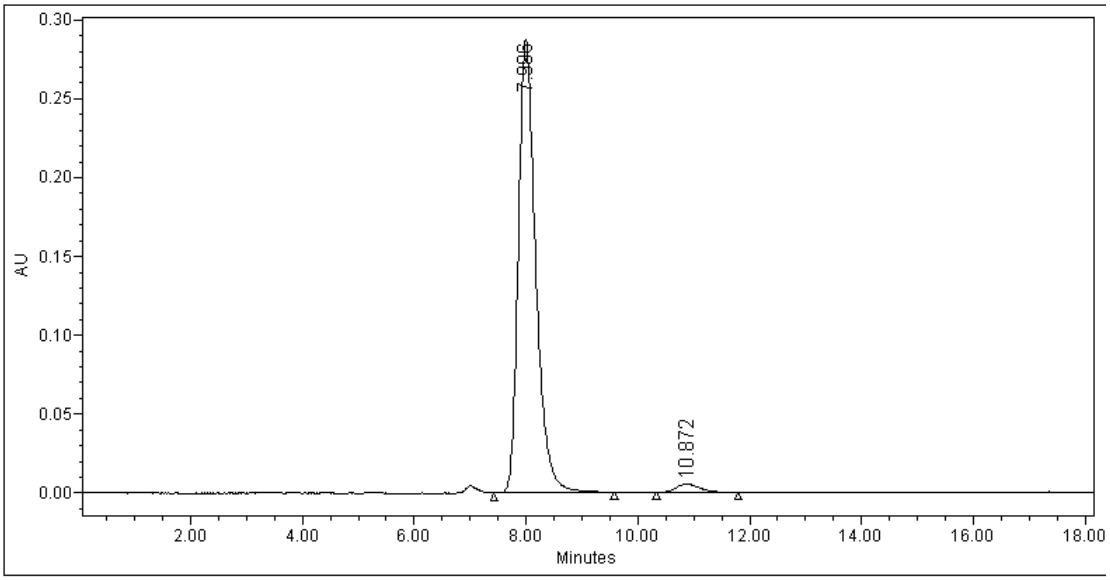
*	Processed Channel	Retention Time (min)	Area	% Area
1	PDA 242.3 nm	7.308	13164800	97.16
2	PDA 242.3 nm	12.142	384337	2.84

6q (*R*)-Methyl 3-(1-(4-methylphenylsulfonamido)heptyl)imidazo[1,2-*a*]pyridine-7-carboxylate (Entry 17, Table 4)

Racemic sample



Enantiomerically enriched sample

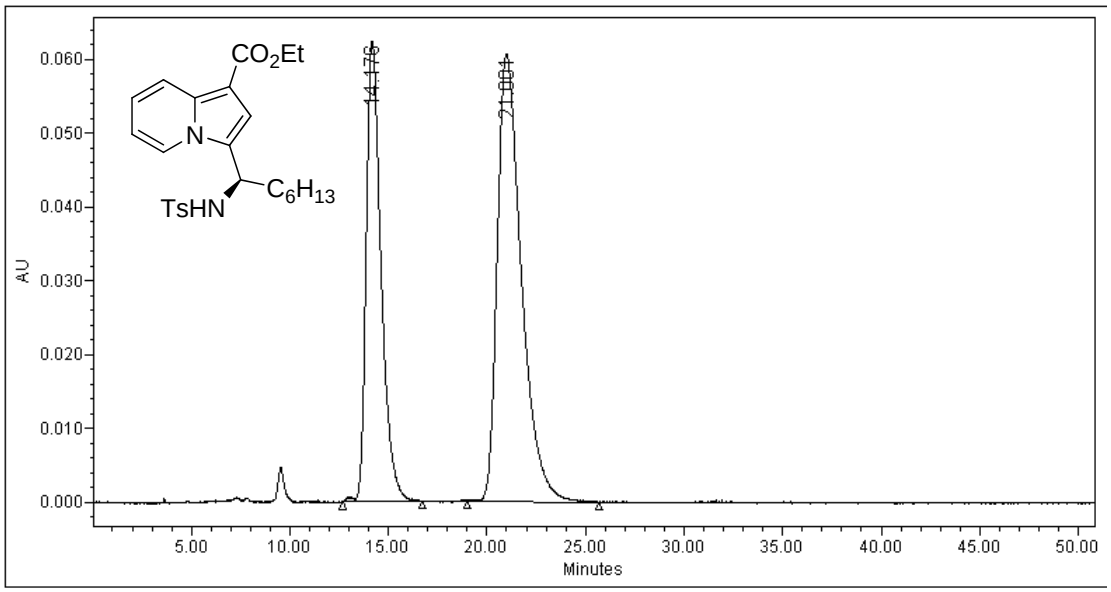


Processed Channel: PDA 254.0 nm

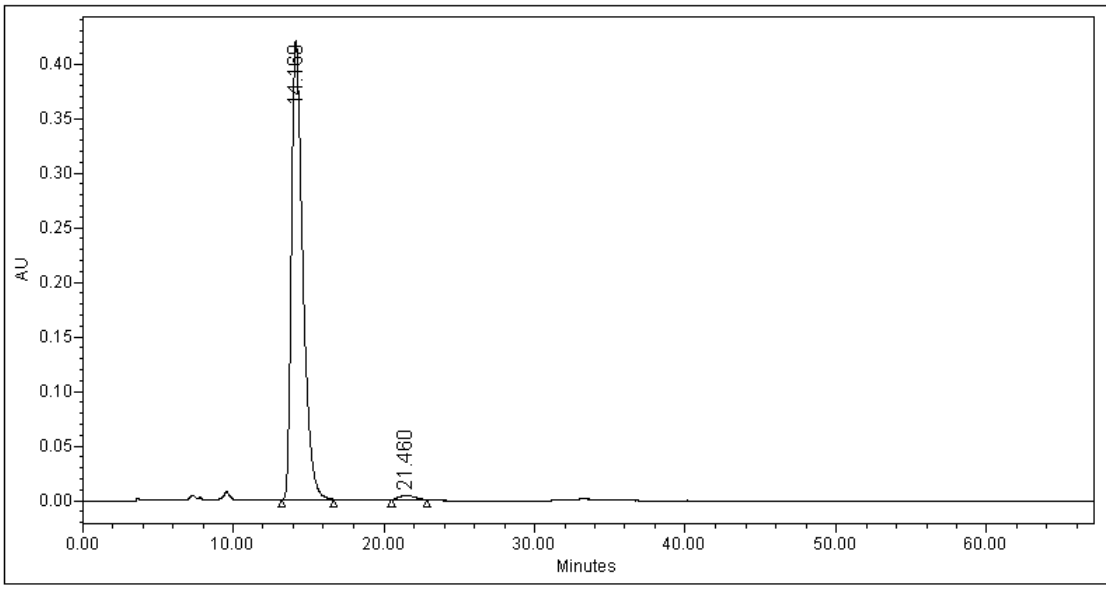
*	Processed Channel	Retention Time (min)	Area	% Area
1	PDA 254.0 nm	7.996	6184363	97.50
2	PDA 254.0 nm	10.872	158640	2.50

8b (*R*)-Ethyl 3-(1-(4-methylphenylsulfonamido)heptyl)indolizine-1-carboxylate (Scheme 2)

Racemic sample



Enantiomerically enriched sample

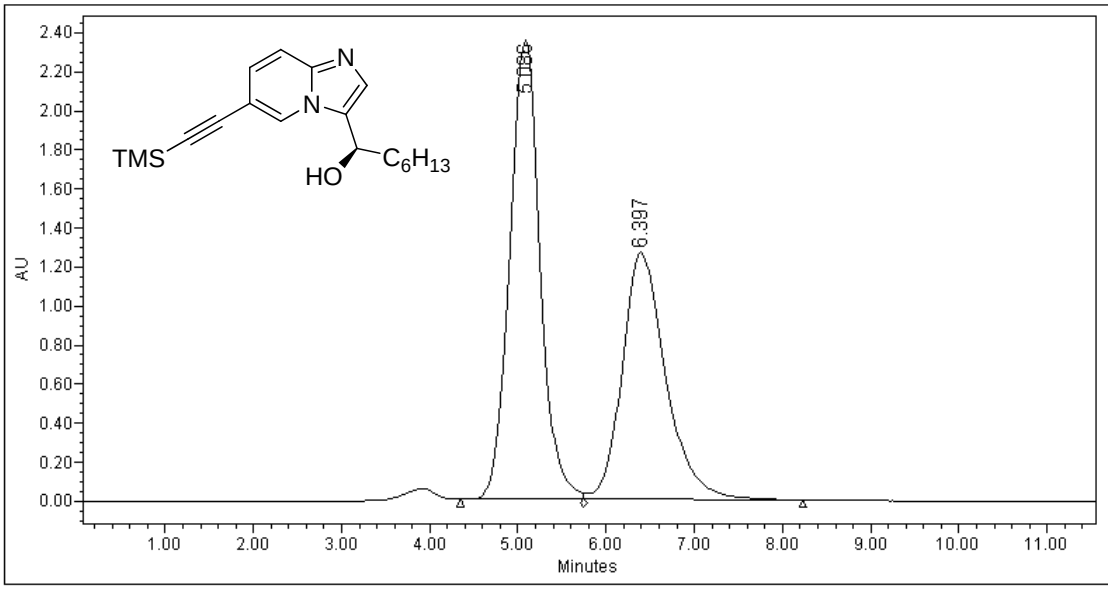


Processed Channel: PDA 231.1 nm

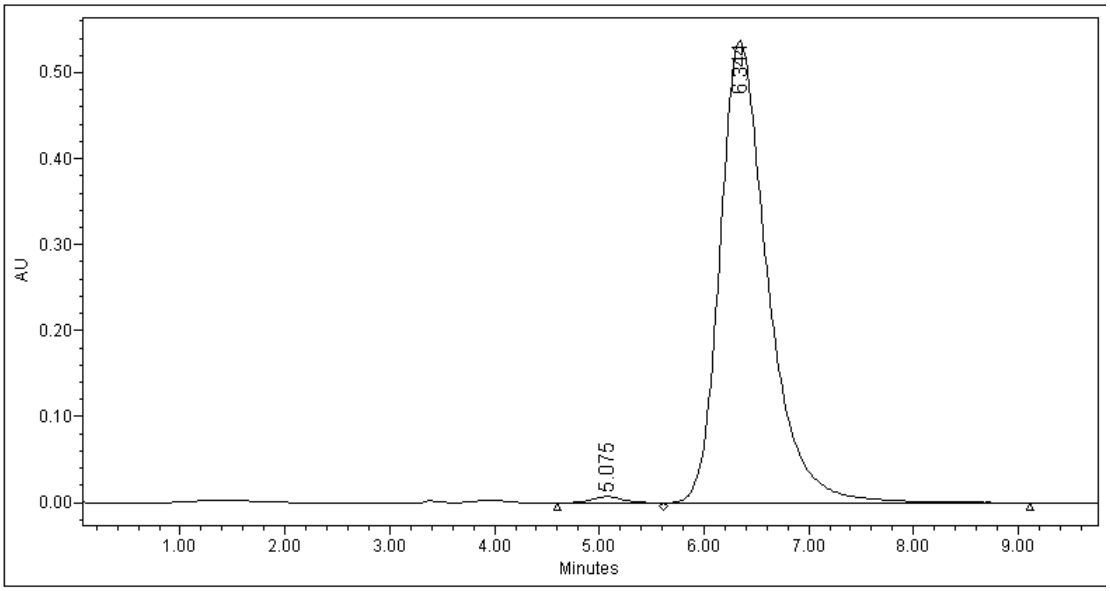
	Processed Channel	Retention Time (min)	Area	% Area
1	PDA 231.1 nm	14.169	22028488	98.67
2	PDA 231.1 nm	21.460	297352	1.33

5r (*R*)-1-(6-((Trimethylsilyl)ethynyl)imidazo[1,2-*a*]pyridin-3-yl)heptan-1-ol (Scheme 3, left side)

Racemic sample



Enantiomerically enriched sample



Processed Channel: PDA 254.0 nm

*	Processed Channel	Retention Time (min)	Area	% Area
1	PDA 254.0 nm	5.075	149601	0.87
2	PDA 254.0 nm	6.344	16970947	99.13