Supporting Information

Continuous Flow Synthesis of 2*H*-Azirines and their Diastereoselective Transformation to Aziridines

Marcus Baumann[a] and Ian R. Baxendale[a]

[a]*Department of Chemistry, University of Durham, South Road, DH13LE Durham, United Kingdom*

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1. Materials and methods:

Unless otherwise stated, all solvents, substrates and reagents were used as purchased without further purification.

^{1}H-NMR spectra were recorded on either 400 MHz, 600 MHz or 700 MHz instruments and are reported relative to residual solvent: $CHCl_3$ (δ 7.26 ppm). ^{13}C-NMR spectra were recorded on the same instruments and are reported relative to $CHCl_3$ (δ 77.16 ppm). Data for ^{1}H-NMR are reported as follows: chemical shift (δ/ ppm) (integration, multiplicity, coupling constant (Hz)). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br. s = broad singlet, app = apparent. Data for ^{13}C-NMR are reported in terms of chemical shift (δ/ ppm) and multiplicity (C, CH, CH_2 or CH_3). Data for ^{19}F-NMR were recorded on the above instruments at a frequency of 376 MHz using $CFCl_3$ as external standard. DEPT-135, COSY, HSQC, HMBC and NOESY/HOESY experiments were used in the structural assignment. IR spectra were recorded neat (ATR sampling) with the intensities of the characteristic signals being reported as weak (w, <20% of tallest signal), medium (m, 21-70% of tallest signal) or strong (s, >71% of tallest signal). Low and high resolution mass spectrometry was performed using the indicated techniques on instruments equipped with Acquity UPLC and a lock-mass electrospray ion source. For accurate mass measurements the deviation from the calculated formula is reported in mDa. Melting points were recorded on an automated melting point system with a heating rate of 1 °C/min and are uncorrected.

2. Preparation and characterisation of oxime starting materials

General Procedure:

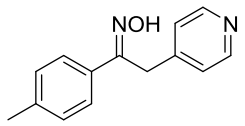
Freshly distilled diisopropylamine (X g; 10 mmol) was dissolved in dry THF (1 M). After cooling this solution to -78 °C a solution of *n*BuLi (X mL; 2.5 M) in hexanes was slowly added. After 15 minutes 4-methylpyridine (X g; 10 mmol) was added dropwise resulting in a colour change to amber. After further 30 minutes the desired arylnitrile (10 mmol, 2 M THF) was added dropwise. The resulting dark red solution was stirred at -78 °C for 1 h prior to warming up to ambient temperature. After 4 h the reaction mixture was carefully quenched with saturated aqueous ammonium chloride (X mL) and extracted (3 × DCM/water). The combined organic layers were dried over sodium sulfate, filtered and evaporated under reduced pressure yielding a yellow oil. Column chromatography was used to remove residual starting material (eluent 20-25% EtOAc/hexanes).

To the intermediate ketone product (X mmol) dissolved in MeOH (1 M) was added hydroxylamine hydrochloride (X g, X mmol, 1.5 equiv.) and NaOMe (X g, X mmol, 1.5 equiv.). This suspension is stirred at room temperature for 8 h until complete conversion of the substrate into the desired oxime is achieved (monitored by tlc and/or ^{1}H-NMR). Aqueous extraction (3 × DCM/water) followed by drying the combined organic layers over sodium sulfate, filtration and evaporation to yield the oxime products as solids or oils that solidify upon storage.

2-(Pyridin-4-yl)-1-(*p*-tolyl)ethanone oxime 4a:

Yield: 2.0 mg (8.7 mmol, 88%). Appearance: orange solid.

Comment [I1]: Mg?

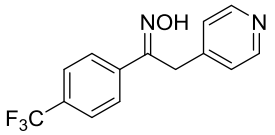


Chemical Formula: $C_{14}H_{14}N_2O$
Exact Mass: 226.1106

^{1}H-NMR (CDCl$_3$, 400 MHz): δ/ppm 10.87 (1H, br s), 8.52 (2H, d, *J* = 8.0 Hz), 7.53 (2H, d, *J* = 8.0 Hz), 7.27 (2H, d, *J* = 8.0 Hz), 7.16 (2H, d, *J* = 8.0 Hz), 4.24 (2H, s), 2.35 (3H, s). **^{13}C-NMR (CDCl$_3$, 101 MHz):** δ/ppm 154.7 (C), 149.2 (2CH), 147.4 (C), 139.4 (C), 132.7 (C), 129.3 (2CH), 126.1 (2CH), 124.3 (2CH), 31.4 (CH_2), 21.3 (CH_3). **IR (neat):** ν/cm^{-1} 2500-3200 (broad), 1603 (s), 1424 (m), 1317 (m), 952 (s), 802 (s), 757 (s), 588 (m), 528 (s), 481 (s). **LC-MS (ESI-TOF):** 227.1 (M+H). **HR-MS (ESI-TOF):** calculated for $C_{14}H_{15}N_2O$ 227.1184, found: 227.1181 (Δ 0.3 mDa). **Melting range:** 138.0-140.7 °C (MeOH).

2-(Pyridin-4-yl)-1-(4-(trifluoromethyl)phenyl)ethanone oxime 4b:

Yield: 2.2 g (8.0 mmol, 80%). Appearance: yellow solid.

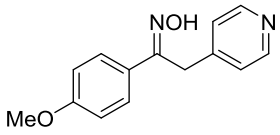


Chemical Formula: $C_{14}H_{11}F_3N_2O$
Exact Mass: 280.0823

^{1}H-NMR (CDCl$_3$, 400 MHz): δ/ppm 12.27 (1H, br s), 8.54 (2H, d, *J* = 8.0 Hz), 7.74 (2H, d, *J* = 8.0 Hz), 7.60 (2H, d, *J* = 8.0 Hz), 7.27 (2H, d, *J* = 8.0 Hz), 4.27 (2H, s). **^{13}C-NMR (CDCl$_3$, 101 MHz):** δ/ppm 153.3 (C), 149.3 (2CH), 147.0 (C), 139.1 (C), 130.9 (C, q, *J* = 32 Hz), 126.4 (2CH), 125.5

(2CH, q, *J* = 4 Hz), 123.9 (CF_3, q, *J* = 273 Hz), 124.2 (2CH), 31.4 (CH_2). **^{19}F-NMR ($CDCl_3$, 376 MHz):** δ/ppm -62.8 (s). **IR (neat):** ν/cm^{-1} 2500-3200 (broad), 1605 (m), 1407 (w), 1321 (s), 1164 (m), 1110 (s), 1056 (s), 973 (s), 835 (s), 597 (m), 468 (m). **LC-MS (ESI-TOF):** 281.0 (M+H). **HR-MS (ESI-TOF):** calculated for $C_{14}H_{12}N_2OF_3$ 281.0902, found: 281.0901 (Δ 0.1 mDa). **Melting range:** 134.1-136.1 °C (MeOH).

1-(4-Methoxyphenyl)-2-pyridin-4-yl)ethanone oxime 4c:



Chemical Formula: $C_{14}H_{14}N_2O_2$
Exact Mass: 242.1055

Yield: 1.98 g (8.2 mmol, 82%). Appearance: yellow waxy solid.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ/ppm 10.90 (1H, br s), 8.51 (2H, d, *J* = 8.0 Hz), 7.57 (2H, d, *J* = 7.2 Hz), 7.24 (2H, d, *J* = 8.0 Hz), 6.87 (2H, d, *J* = 7.2 Hz), 4.22 (2H, s), 3.81 (3H, s). **^{13}C-NMR ($CDCl_3$, 101 MHz):** δ/ppm 160.5 (C), 154.5 (C), 149.5 (2CH), 146.9 (C), 128.0 (C), 127.6 (2CH), 124.1 (2CH), 114.0 (2CH), 55.3 (CH_3), 31.5 (CH_2). **IR (neat):** ν/cm^{-1} 2500-3200 (broad), 1602 (s), 1576 (s), 1417 (s), 1291 (m), 1216 (m), 980 (s), 863 (m), 780 (s), 755 (s), 651 (s), 497 (m). **LC-MS (ESI-TOF):** 243.1 (M+H). **HR-MS (ESI-TOF):** calculated for $C_{14}H_{15}N_2O_2$ 243.1130, found: 243.1131 (Δ 0.1 mDa).

3. Flow synthesis of 2*H*-azirines and aziridines

Typical flow procedure for the synthesis of 2*H*-azirines (**5a-c**):

Using a Vapourtec E-Series flow system two streams containing the oxime substrate (**4**, 0.1 M in MeCN, 1.0 equiv.; stream A) and triethylamine (1.2 equiv.; 0.3 mL/min; stream A) and mesyl chloride (0.12 M MeCN, 1.2 equiv.; 0.3 mL/min; stream B) were mixed at a T-piece prior to entering a tubular flow coil (10 mL volume, 40 °C) in which the mesylation occurs. The exiting flow stream was directed into an Omnifit glass column (10 mm i.d., 150 mm length) filled with silica supported pyridine (2.5 g, 1.39 mmol/g loading) and silica gel (1 g) which is maintained at ambient temperature. After exiting this column the crude reaction mixture passes a backpressure regulator (100 psi) before being collected. Final purification can be achieved via silica column chromatography (20-50% EtOAc/ hexanes) yielding the desired 2*H*-aziridines typically in high yield as yellow oils.

Comment [I2]: In the main text of the paper and scheme this says rt not 40 oC

Typical flow procedure for the telescoped synthesis of CN-aziridines (**6a-c**):

Upon exiting the glass column filled with silica-supported pyridine and silica gel the flow stream was mixed at a T-piece with a stream containing NaCN (0.1 M in H_2O, 2 equiv.). The combined flow stream then enters a tubular flow coil (10 mL volume, 25 °C, 5 min residence time) followed by a 100 psi backpressure regulator and product was collected. Purification was achieved by column chromatography (20-50% EtOac/hexanes).

Typical flow procedure for the telescoped synthesis of CF_3-aziridines (**10a-c**):

Upon exiting the glass column filled with silica-supported pyridine and silica gel the flow stream was mixed at a T-piece with a stream containing $TMSCF_3$ (0.2 M THF, 2 equiv.). The combined stream then enters a fluoride monolith maintained at 50 °C followed by a tubular flow coil (10 mL volume, 50 °C, 5 min residence time). After passing a 100 psi backpressure regulator the product was collected and isolated in pure form after column chromatography (20-50% EtOAc/hexanes).

Typical flow procedure for the telescoped synthesis of 2*H*-aziridines (**11a-c**):

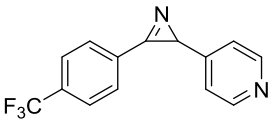
Upon exiting the glass column filled with silica-supported pyridine and silica gel the flow stream passes a 100 psi backpressure regulator and was collected into a stirred flask containing $NaBH_4$ (2 equiv.) suspended in THF (10 mL). The reduction process was continued for 30 minutes after the collection was complete followed by acidification and work-up of the crude reaction mixture. The aziridine product was isolated in pure form after column chromatography (20-80% EtOac/hexanes).

Comment [I3]: With what?

4. Characterisation of 2*H*-azirines and aziridines

4-(3-(4-(Trifluoromethyl)phenyl)-2*H*-azirin-2-yl)pyridine 5a:

Yield: 201 mg (0.77 mmol, 77%). Appearance: yellow oil.

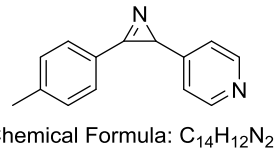


Chemical Formula: $C_{14}H_9F_3N_2$
Exact Mass: 262.0718

^{1}H-NMR ($CDCl_3$, 400 MHz): δ/ppm 8.47 (2H, d, *J* = 8.0 Hz), 7.97 (2H, d, *J* = 8.0 Hz), 7.79 (2H, d, *J* = 8.0 Hz), 7.02 (2H, d, *J* = 8.0 Hz), 3.29 (1H, s). **^{13}C-NMR ($CDCl_3$, 101 MHz):** δ/ppm 161.9 (C), 149.5 (2CH), 149.4 (C), 135.1 (C, q, *J* = 23 Hz), 130.3 (2CH), 126.4 (2CH, q, *J* = 4 Hz), 126.3 (C), 123.3 (CF_3, q, *J* = 271 Hz), 120.9 (2CH), 33.6 (CH). **^{19}F-NMR ($CDCl_3$, 376 MHz):** δ/ppm -63.3 (s). **IR (neat):** ν/cm^{-1} 1602 (w), 1413 (w), 1322 (s), 1168 (m), 1126 (s), 1065 (s), 1017 (m), 851 (m). **LC-MS (ESI-TOF):** 263.1 (M+H). **HR-MS (ESI-TOF):** calculated for $C_{14}H_{10}N_2F_3$ 263.0796, found: 263.0792 (Δ 0.4 mDa).

4-(3-(*p*-Tolyl)-2*H*-azirin-2-yl)pyridine 5b:

Yield: 173 mg (0.83 mmol, 83%). Appearance: yellow oil.

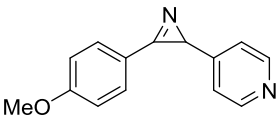


Chemical Formula: $C_{14}H_{12}N_2$
Exact Mass: 208.1000

^{1}H-NMR ($CDCl_3$, 400 MHz): δ/ppm 8.43 (2H, d, *J* = 8.0 Hz), 7.72 (2H, d, *J* = 8.0 Hz), 7.32 (2H, d, *J* = 8.0 Hz), 7.02 (2H, d, *J* = 8.0 Hz), 3.16 (1H, s), 2.40 (3H, s). **^{13}C-NMR ($CDCl_3$, 101 MHz):** δ/ppm 161.3 (C), 150.5 (C), 149.4 (2CH), 144.8 (C), 130.2 (2CH), 130.1 (2CH), 121.0 (2CH), 120.0 (C), 32.8 (CH), 21.9 (CH_3). **IR (neat):** ν/cm^{-1} 2922 (w), 1748 (m), 1604 (s), 1506 (m), 1415 (m), 1178 (m), 1040 (m), 820 (s), 759 (m), 579 (m), 523 (s). **LC-MS (ESI-TOF):** 209.1 (M+H). **HR-MS (ESI-TOF):** calculated for $C_{14}H_{13}N_2$ 209.1079, found: 209.1068 (Δ 1.1 mDa).

4-(3-(4-Methoxyphenyl)-2*H*-azirin-2-yl)pyridine 5c:

Yield: 195 mg (0.87 mmol, 87%). Appearance: yellow oil.

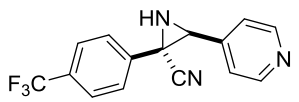


Chemical Formula: $C_{14}H_{12}N_2O$
Exact Mass: 224.0950

^{1}H-NMR ($CDCl_3$, 400 MHz): δ/ppm 8.48 (2H, d, *J* = 8.0 Hz), 7.82 (2H, d, *J* = 8.0 Hz), 7.05-7.13 (4H, m), 3.89 (3H, s), 3.19 (1H, s). **^{13}C-NMR ($CDCl_3$, 101 MHz):** δ/ppm 163.9 (C), 160.4 (C), 150.7 (C), 149.4 (2CH), 132.2 (2CH), 121.0 (2CH), 115.1 (C), 115.0 (2CH), 55.7 (CH_3), 32.8 (CH) **IR (neat):** ν/cm^{-1} 2839 (w), 1748 (m), 1598 (s), 1485 (m), 1414 (m), 1287 (s), 1247 (m), 1216 (m), 1036 (m), 991 (m), 787 (s), 684 (s), 581 (s). **LC-MS (ESI-TOF):** 225.5 (M+H). **HR-MS (ESI-TOF):** calculated for $C_{14}H_{13}N_2O$ 225.1028, found: 225.1027 (Δ 0.1 mDa).

***Rac*-(2*R*,3*S*)-3-(Pyridin-4-yl)-2-(4-(trifluoromethyl)phenyl)aziridine-2-carbonitrile 6a:**

Yield: 231 mg (0.8 mmol, 80%). Appearance: red solid.

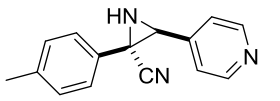


Chemical Formula: $C_{15}H_{10}F_3N_3$
Exact Mass: 289.0827

^{1}H-NMR ($CDCl_3$, 400 MHz): δ/ppm 8.40 (2H, d, *J* = 8.0 Hz), 7.47 (4H, m), 7.08 (2H, d, *J* = 8.0 Hz), 4.20 (1H, d, *J* = 9.8 Hz), 2.85 (1H, d, *J* = 9.8 Hz). **^{13}C-NMR ($CDCl_3$, 101 MHz):** δ/ppm 149.6 (2CH), 141.2 (C), 134.0 (C), 131.3 (C, q, *J* = 33 Hz), 128.4 (2CH), 125.5 (2CH, q, *J* = 4 Hz), 123.6 (CF_3, q, *J* = 272 Hz), 122.6 (2CH), 119.9 (CN), 46.7 (CH), 35.3 (C). **^{19}F-NMR ($CDCl_3$, 376 MHz):** δ/ppm -63.9 (s). **IR (neat):** ν/cm^{-1} 3079 (broad), 2237 (w), 1603 (m), 1412 (m), 1322 (s), 1165 (s), 1122 (s), 1108 (s), 1067 (s), 1017 (m), 831 (m), 696 (m), 619 (m). **LC-MS (ESI-TOF):** 290.1 (M+H). **HR-MS (ESI-TOF):** calculated for $C_{15}H_{11}N_3F_3$ 290.0905, found: 290.0909 (Δ 0.3 mDa). **Melting range:** decomposition ~110 °C ($CHCl_3$).

***Rac*-(2*R*,3*S*)-3-(Pyridin-4-yl)-2-(*p*-tolyl)aziridine-2-carbonitrile 6b:**

Yield: 167 mg (0.71 mmol, 71%). Appearance: red solid.

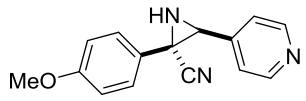


Chemical Formula: $C_{15}H_{13}N_3$
Exact Mass: 235.1109

^{1}H-NMR ($CDCl_3$, 400 MHz): δ/ppm 8.38 (2H, d, *J* = 8.0 Hz), 7.19 (2H, d, *J* = 8.0 Hz), 7.07 (2H, d, *J* = 8.0 Hz), 7.00 (2H, d, *J* = 8.0 Hz), 4.10 (1H, d, *J* = 9.8 Hz), 2.61 (1H, d, *J* = 9.8 Hz), 2.23 (3H, s). **^{13}C-NMR ($CDCl_3$, 101 MHz):** δ/ppm 149.2 (2CH), 142.2 (C), 139.1 (C), 129.2 (2CH), 127.9 (2CH), 126.7 (C), 122.8 (2CH), 120.8 (C), 46.2 (CH), 35.6 (C), 21.1 (CH_3). **IR (neat):** ν/cm^{-1} 3119 (broad), 2235 (m), 1603 (s), 1513 (m), 1405 (s), 1185 (m), 999 (s), 975 (m), 811 (s), 785 (s), 738 (m), 623 (s), 583 (s), 497 (s), 450 (s). **LC-MS (ESI-TOF):** 236.1 (M+H). **HR-MS (ESI-TOF):** calculated for $C_{15}H_{14}N_3$ 236.1188, found: 236.1184 (Δ 0.4 mDa). **Melting range:** decomposition ~100 °C (DCM).

***Rac*-(2*R*,3*S*)-2-(4-Methoxyphenyl)-3-(pyridin-4-yl)aziridine-2-carbonitrile 6c:**

Yield: 183 mg (0.73 mmol, 73%). Appearance: orange solid.

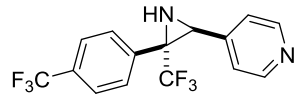


Chemical Formula: $C_{15}H_{13}N_3O$
Exact Mass: 251.1059

^{1}H-NMR ($CDCl_3$, 400 MHz): δ/ppm 8.38 (2H, d, *J* = 7.8 Hz), 7.23 (2H, d, *J* = 7.6 Hz), 7.05 (2H, d, *J* = 7.8 Hz), 6.72 (2H, d, *J* = 7.6 Hz), 4.09 (1H, d, *J* = 9.5 Hz), 3.72 (3H, s), 2.53 (1H, d, *J* = 7.3 Hz). **^{13}C-NMR ($CDCl_3$, 101 MHz):** δ/ppm 160.0 (C), 149.4 (2CH), 142.0 (C), 129.4 (2CH), 122.7 (2CH), 121.6 (C), 120.8 (C), 114.0 (2CH), 55.2 (CH_3), 46.2 (CH), 35.3 (C). **IR (neat):** ν/cm^{-1} 3000-3200 (broad), 2836 (w), 2234 (w), 1675 (w), 1600 (s), 1512 (s), 1419 (m), 1302 (m), 1249 (s), 1172 (s), 1027 (s), 829 (s), 734 (s), 608 (m), 582 (m). **LC-MS (ESI-TOF):** 252.3.1 (M+H). **HR-MS (ESI-TOF):** calculated for $C_{15}H_{14}N_3O$ 252.1137, found: 252.1146 (Δ 0.9 mDa).

***Rac*-(2*S*,3*R*)-3-(Trifluoromethyl)-3-(4-(trifluoromethyl)phenyl)aziridin-2-yl)pyridine 10a:**

Yield: 242 mg (0.73 mmol, 73%). Appearance: yellow solid.

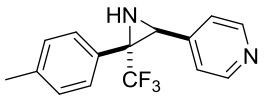


Chemical Formula: $C_{15}H_{10}F_6N_2$
Exact Mass: 332.0748

^{1}H-NMR ($CDCl_3$, 400 MHz): δ/ppm 8.36 (2H, d, *J* = 8.0 Hz), 7.48 (2H, d, *J* = 8.0 Hz), 7.42 (2H, d, *J* = 8.0 Hz), 6.98 (2H, d, *J* = 8.0 Hz), 3.86 (1H, d, *J* = 9.7 Hz), 2.31 (1H, d, *J* = 9.7 Hz). **^{19}F-NMR ($CDCl_3$, 376 MHz):** δ/ppm -63.9 (s), -72.2 (s). **^{13}C-NMR ($CDCl_3$, 101 MHz):** δ/ppm 149.3 (2CH), 143.1 (C), 133.2 (C), 131.2 (C, q, *J* = 33 Hz), 130.7 (2CH), 125.2 (2CH, m), 124.1 (CF_3, q, *J* = 278 Hz), 123.6 (CF_3, q, *J* = 273 Hz), 122.3 (2CH), 48.6 (C, q, *J* = 34 Hz), 40.0 (CH). **IR (neat):** ν/cm^{-1} 3300 (broad), 1603 (w), 1412 (w), 1325 (s), 1165 (s), 1128 (s), 1067 (s), 1018 (m), 907 (m), 835 (m), 611 (w). **LC-MS (ESI-TOF):** 333.1 (M+H). **HR-MS (ESI-TOF):** calculated for $C_{15}H_{11}N_2F_6$ 333.0826, found: 333.0831 (Δ 0.5 mDa). **Melting range:** decomposition ~120 °C ($CHCl_3$).

***Rac*-(2*S*,3*R*)-3-(p-Tolyl)-3-(trifluoromethyl)aziridin-2-yl)pyridine 10b:**

Yield: 195 mg (0.7 mmol, 70%). Appearance: pale yellow solid.

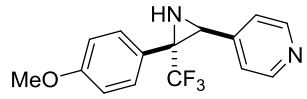


Chemical Formula: $C_{15}H_{13}F_3N_2$
Exact Mass: 278.1031

^{1}H-NMR ($CDCl_3$, 600 MHz): δ/ppm 8.38 (2H, m), 7.10-7.18 (2H, m), 6.95-7.05 (4H, m), 3.76 (1H, d, *J* = 8.8 Hz), 2.26 (3H, s), 2.20 (1H, d, *J* = 8.8 Hz). **^{13}C-NMR ($CDCl_3$, 151 MHz):** δ/ppm 149.0 (2CH), 144.0 (C), 138.8 (C), 130.1 (2CH), 128.9 (2CH), 125.9 (C), 124.4 (CF_3, q, *J* = 277 Hz), 122.6 (2CH), 48.7 (C, q, *J* = 34 Hz), 39.7 (CH), 21.7 (CH_3). **^{19}F-NMR ($CDCl_3$, 376 MHz):** δ/ppm -72.7 (s). **IR (neat):** ν/cm^{-1} 3157 (m), 2929 (w), 1604 (w), 1409 (w), 1268 (m), 1162 (s), 905 (m), 810 (s), 727 (s), 650 (s), 630 (s), 621 (s), 513 (s). **LC-MS (ESI-TOF):** 278.9 (M+H). **HR-MS (ESI-TOF):** calculated for $C_{15}H_{15}N_2F_3$ 279.1109, found: 279.1111 (Δ 0.2 mDa).

***Rac*-(2*S*,3*R*)-3-(3-Methoxyphenyl)-3-(trifluoromethyl)aziridin-2-yl)pyridine 10c:**

Yield: 237 mg (0.81 mmol, 81%). Appearance: yellow solid.

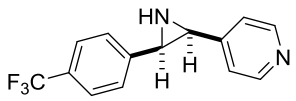


Chemical Formula: $C_{15}H_{13}F_3N_2O$
Exact Mass: 294.0980

^{1}H-NMR ($CDCl_3$, 400 MHz): δ/ppm 8.38 (2H, br s), 7.17 (2H, d, *J* = 7.8 Hz), 7.03 (2H, br s), 6.73 (2H, d, *J* = 7.8 Hz), 3.78 (1H, d, *J* = 9.5 Hz), 3.74 (3H, s), 2.22 (1H, d, *J* = 9.5 Hz). **^{13}C-NMR ($CDCl_3$, 101 MHz):** δ/ppm 159.9 (C), 148.2 (2CH), 145.1 (C), 131.5 (2CH), 124.5 (CF_3, q, *J* = 276 Hz), 122.9 (2CH), 120.8 (C), 113.7 (2CH), 55.2 (CH_3), 48.7 (C, q, *J* = 34 Hz), 39.8 (CH). **^{19}F-NMR ($CDCl_3$, 376 MHz):** δ/ppm -72.9 (s). **IR (neat):** ν/cm^{-1} 3000-3200 (broad), 2839 (w), 1612 (m), 1517 (s), 1294 (m), 1250 (s), 1140 (s), 1028 (m), 905 (m), 828 (s), 734 (m), 582 (m), 530 (m). **LC-MS (ESI-TOF):** 294.9 (M+H). **HR-MS (ESI-TOF):** calculated for $C_{15}H_{14}N_2OF_3$ 295.1058, found: 295.1072 (Δ 1.4 mDa).

***Rac*-4-((2*S*,3*R*)-3-(4-(Trifluoromethyl)phenyl)aziridin-2-yl)pyridine 11a:**

Yield: 235 mg (0.89 mmol, 89%). Appearance: yellow oil.

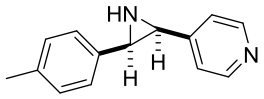


Chemical Formula: $C_{14}H_{11}F_3N_2$
Exact Mass: 264.0874

^{1}H-NMR ($CDCl_3$, 400 MHz): δ/ppm 8.34 (2H, d, *J* = 8.0 Hz), 7.40 (2H, d, *J* = 8.0 Hz), 7.30 (2H, d, *J* = 8.0 Hz), 7.09 (2H, d, *J* = 8.0 Hz), 3.71 (1H, m), 3.60 (1H, m), 1.76 (1H, br s). **^{13}C-NMR ($CDCl_3$, 101 MHz):** δ/ppm 149.1 (2CH), 145.4 (C), 139.7 (C), 129.2 (C, q, *J* = 32 Hz), 128.2 (2CH), 124.8 (2CH, q, *J* = 4 Hz), 124.1 (CF_3, q, *J* = 271 Hz), 122.9 (2CH), 39.8 (CH), 38.9 (CH). **^{19}F-NMR ($CDCl_3$, 376 MHz):** δ/ppm -62.5 (s). **IR (neat):** ν/cm^{-1} 3217 (broad), 1603 (w), 1407 (w), 1322 (s), 1161 (s), 1117 (s), 1104 (s), 1064 (s), 1017 (s), 863 (m), 826 (m), 597 (m). **LC-MS (ESI-TOF):** 265.1 (M+H). **HR-MS (ESI-TOF):** calculated for $C_{14}H_{12}N_2F_3$ 265.0953, found: 265.0947 (Δ 0.6 mDa).

***Rac*-4-((2*S*,3*R*)-3-(*p*-Tolyl)aziridin-2-yl)pyridine 11b:**

Yield: 193 mg (0.92 mmol, 92%). Appearance: yellow oil.

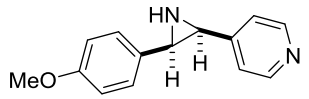


Chemical Formula: $C_{14}H_{14}N_2$
Exact Mass: 210.1157

^{1}H-NMR ($CDCl_3$, 400 MHz): δ/ppm 8.32 (2H, d, *J* = 8.0 Hz), 7.11 (2H, d, *J* = 8.0 Hz), 7.06 (2H, d, *J* = 8.0 Hz), 6.96 (2H, d, *J* = 8.0 Hz), 3.67 (1H, d, *J* = 6.6 Hz), 3.51 (1H, d, *J* = 6.6 Hz), 2.22 (3H, s). **^{13}C-NMR ($CDCl_3$, 101 MHz):** δ/ppm 148.6 (2CH), 146.7 (C), 136.6 (C), 132.2 (C), 128.6 (2CH), 127.7 (2CH), 123.1 (2CH), 40.3 (CH), 38.6 (CH), 21.1 (CH_3). **IR (neat):** ν/cm^{-1} 3210 (broad), 1602 (s), 1491 (m), 1411 (m), 1253 (m), 1175 (m), 1041 (s), 839 (m), 777 (m), 726 (s), 695 (s), 528 (m). **LC-MS (ESI-TOF):** 211.1 (M+H). **HR-MS (ESI-TOF):** calculated for $C_{14}H_{15}N_2$ 211.1235., found: 211.1231 (Δ 0.4 mDa).

***Rac*-4-((2*S*,3*R*)-3-(4-Methoxyphenyl)aziridin-2-yl)pyridine 11c:**

Yield: 203 mg (0.9 mmol, 90%). Appearance: yellow oil.



Chemical Formula: $C_{14}H_{14}N_2O$
Exact Mass: 226.1106

^{1}H-NMR ($CDCl_3$, 400 MHz): δ/ppm 8.34 (2H, d, *J* = 7.6 Hz), 7.06-7.14 (4H, m), 6.69 (2H, d, *J* = 8.0 Hz), 3.71 (3H, s), 3.65 (1H, d, *J* = 6.6 Hz), 3.49 (1H, d, *J* = 6.6 Hz). **^{13}C-NMR ($CDCl_3$, 101 MHz):** δ/ppm 158.6 (C), 148.9 (2CH), 146.3 (C), 129.0 (2CH), 127.5 (C), 123.0 (2CH), 113.3 (2CH), 55.1 (CH_3), 39.9 (CH), 38.6 (CH). **IR (neat):** ν/cm^{-1} 3211 (broad), 2833 (w), 1601 (s), 1582 (s), 1490 (m), 1409 (m), 1253 (m), 1173 (m), 1042 (s), 838 (m), 777 (s), 695 (s). **LC-MS (ESI-TOF):** 227.1 (M+H). **HR-MS (ESI-TOF):** calculated for $C_{14}H_{15}N_2O$ 227.1184, found: 227.1194 (Δ 1.0 mDa).

5. X-Ray Data for 6a, 9 and 10a

X-ray data for 6a (=15srv267)

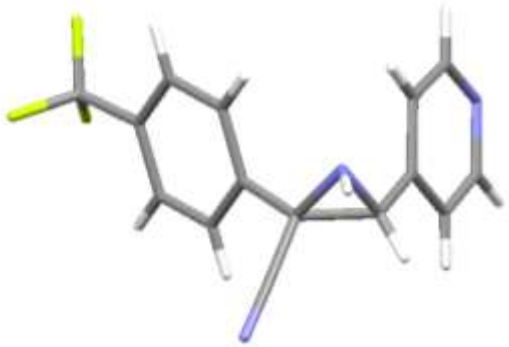


Table 1 Crystal data and structure refinement for 15srv267.

Identification code	15srv267
Empirical formula	$C_{15}H_{10}F_3N_3$
Formula weight	289.26
Temperature/K	120
Crystal system	triclinic
Space group	P-1
a/Å	7.4334(7)
b/Å	7.9720(8)
c/Å	11.9616(12)
α/°	82.649(4)
β/°	86.200(4)
γ/°	69.197(3)
Volume/Å^3	657.01(11)
Z	2
ρ_{calc}g/cm^3	1.462
μ/mm^{-1}	0.119
F(000)	296.0
Crystal size/mm^3	0.412 × 0.343 × 0.078
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.502 to 60.452
Index ranges	-10 ≤ h ≤ 10, -11 ≤ k ≤ 11, -16 ≤ l ≤ 16
Reflections collected	13656
Independent reflections	3923 [R_{int} = 0.0300, R_{sigma} = 0.0309]
Data/restraints/parameters	3923/0/198
Goodness-of-fit on F^2	1.042
Final R indexes [I>=2σ (I)]	R_1 = 0.0406, wR_2 = 0.1064
Final R indexes [all data]	R_1 = 0.0504, wR_2 = 0.1131
Largest diff. peak/hole / e Å^{-3}	0.39/-0.30

Table 2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for 15srv267. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
F(1)	3781.3(12)	6587.1(12)	-1376.7(7)	37.1(2)
F(2)	1431.9(13)	8955.0(11)	-981.2(8)	42.2(2)
F(3)	1606.2(11)	6364(1)	-153.3(7)	31.82(19)
N(1)	9436.4(15)	1654.1(13)	3672.8(9)	23.9(2)
N(2)	8810.9(13)	8346.8(12)	2935.6(8)	18.90(19)
N(3)	4567.2(16)	11697.2(14)	3812.5(10)	28.3(2)
C(2)	8302.1(18)	2517.0(16)	4490.1(10)	24.5(2)
C(3)	7823.4(16)	4346.0(15)	4572.3(10)	21.2(2)
C(4)	8555.5(15)	5360.2(14)	3758.0(9)	16.9(2)
C(5)	9739.8(16)	4481.3(15)	2909.7(10)	20.4(2)
C(6)	10132.0(16)	2644.2(15)	2903.2(10)	22.1(2)
C(7)	8083.5(15)	7319.6(14)	3836.5(9)	17.7(2)
C(8)	6725.9(15)	8730.4(14)	3003.6(9)	17.6(2)
C(9)	5525.8(16)	10385.6(15)	3469.4(10)	20.6(2)
C(10)	2684.8(18)	7367.8(16)	-530.2(10)	24.1(2)
C(11)	3813.2(16)	7617.2(14)	386.8(9)	19.6(2)
C(12)	5676.0(16)	7602.5(15)	185.1(9)	20.3(2)
C(13)	6662.6(15)	7922.1(15)	1038.7(9)	19.4(2)
C(14)	5766.3(15)	8277.1(14)	2082.2(9)	17.5(2)
C(15)	3896.6(16)	8271.3(16)	2275.7(10)	21.8(2)
C(16)	2916.7(16)	7940.2(16)	1434.2(10)	22.7(2)

Table 3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for 15srv267. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
F(1)	40.7(5)	48.7(5)	28.2(4)	-12.7(4)	-0.7(3)	-20.6(4)
F(2)	51.5(5)	20.7(4)	53.3(5)	3.6(3)	-34.5(4)	-8.3(4)
F(3)	35.1(4)	29.5(4)	38.6(4)	-5.1(3)	-4.6(3)	-19.7(3)
N(1)	30.4(5)	15.7(4)	27.0(5)	-2.1(4)	-8.5(4)	-8.6(4)
N(2)	16.7(4)	14.5(4)	26.3(5)	-3.7(3)	-0.4(3)	-6.0(3)
N(3)	26.0(5)	22.5(5)	33.6(6)	-7.3(4)	0.3(4)	-3.7(4)
C(2)	33.7(6)	20.5(5)	23.0(5)	1.0(4)	-5.4(4)	-14.2(5)
C(3)	24.2(5)	20.5(5)	20.4(5)	-2.8(4)	-2.6(4)	-9.2(4)
C(4)	15.7(4)	14.1(4)	21.1(5)	-2.4(4)	-5.2(4)	-4.5(4)
C(5)	20.1(5)	15.6(5)	25.3(5)	-2.6(4)	-0.4(4)	-6.1(4)
C(6)	22.1(5)	16.6(5)	27.1(5)	-5.5(4)	-3.9(4)	-4.6(4)
C(7)	17.3(5)	14.1(4)	21.4(5)	-3.4(4)	-1.8(4)	-4.4(4)
C(8)	16.3(4)	14.0(4)	21.3(5)	-2.7(4)	0.1(4)	-3.9(4)
C(9)	19.0(5)	18.1(5)	23.7(5)	-2.3(4)	-1.4(4)	-5.1(4)
C(10)	26.9(6)	18.5(5)	27.4(6)	-0.6(4)	-6.2(4)	-8.5(4)

C(11)	21.1(5)	14.0(5)	23.1(5)	-0.2(4)	-4.6(4)	-5.3(4)
C(12)	22.3(5)	17.9(5)	20.1(5)	-2.2(4)	0.6(4)	-6.2(4)
C(13)	17.0(5)	17.5(5)	23.5(5)	-2.4(4)	1.1(4)	-6.2(4)
C(14)	17.4(5)	12.6(4)	21.2(5)	-1.1(4)	-1.7(4)	-3.6(4)
C(15)	19.3(5)	24.2(5)	21.2(5)	-3.6(4)	1.6(4)	-6.9(4)
C(16)	16.9(5)	23.8(5)	27.5(6)	-1.6(4)	-1.0(4)	-7.6(4)

Table 4 Bond Lengths for 15srv267.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
F(1)	C(10)	1.3298(15)	C(5)	C(6)	1.3889(15)
F(2)	C(10)	1.3469(14)	C(7)	C(8)	1.5219(15)
F(3)	C(10)	1.3424(14)	C(8)	C(9)	1.4606(15)
N(1)	C(2)	1.3381(16)	C(8)	C(14)	1.4978(15)
N(1)	C(6)	1.3337(16)	C(10)	C(11)	1.4976(16)
N(2)	C(7)	1.4614(14)	C(11)	C(12)	1.3858(15)
N(2)	C(8)	1.4681(13)	C(11)	C(16)	1.3892(16)
N(3)	C(9)	1.1452(15)	C(12)	C(13)	1.3943(16)
C(2)	C(3)	1.3878(16)	C(13)	C(14)	1.3885(15)
C(3)	C(4)	1.3926(15)	C(14)	C(15)	1.3953(15)
C(4)	C(5)	1.3859(15)	C(15)	C(16)	1.3840(16)
C(4)	C(7)	1.4886(14)			

Table 5 Bond Angles for 15srv267.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C(6)	N(1)	C(2)	116.65(10)	N(3)	C(9)	C(8)	178.53(13)
C(7)	N(2)	C(8)	62.60(7)	F(1)	C(10)	F(2)	106.74(10)
N(1)	C(2)	C(3)	123.99(11)	F(1)	C(10)	F(3)	106.95(9)
C(2)	C(3)	C(4)	118.56(11)	F(1)	C(10)	C(11)	113.33(10)
C(3)	C(4)	C(7)	119.56(10)	F(2)	C(10)	C(11)	111.64(9)
C(5)	C(4)	C(3)	118.04(10)	F(3)	C(10)	F(2)	105.25(10)
C(5)	C(4)	C(7)	122.39(10)	F(3)	C(10)	C(11)	112.40(10)
C(4)	C(5)	C(6)	118.92(10)	C(12)	C(11)	C(10)	120.98(10)
N(1)	C(6)	C(5)	123.84(11)	C(12)	C(11)	C(16)	120.70(10)
N(2)	C(7)	C(4)	117.64(9)	C(16)	C(11)	C(10)	118.27(10)
N(2)	C(7)	C(8)	58.92(7)	C(11)	C(12)	C(13)	119.82(10)
C(4)	C(7)	C(8)	120.47(9)	C(14)	C(13)	C(12)	119.88(10)
N(2)	C(8)	C(7)	58.48(7)	C(13)	C(14)	C(8)	121.83(9)
N(2)	C(8)	C(14)	119.69(9)	C(13)	C(14)	C(15)	119.62(10)
C(9)	C(8)	N(2)	117.24(9)	C(15)	C(14)	C(8)	118.52(10)
C(9)	C(8)	C(7)	114.83(9)	C(16)	C(15)	C(14)	120.71(10)
C(9)	C(8)	C(14)	112.79(9)	C(15)	C(16)	C(11)	119.24(10)

C(14)	C(8)	C(7)	123.68(9)

Table 6 Hydrogen Bonds for 15srv267.

D	H	A	d(D-H)/Å	d(H-A)/Å	d(D-A)/Å	D-H-A/°
N(2)	H(2)	N(1)[1]	0.946(18)	2.138(18)	3.0766(13)	171.1(15)

[1]+X,1+Y,+Z

Table 7 Torsion Angles for 15srv267.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
F(1)	C(10)	C(11)	C(12)	20.25(15)	C(5)	C(4)	C(7)	N(2)	4.04(15)
F(1)	C(10)	C(11)	C(16)	−162.42(10)	C(5)	C(4)	C(7)	C(8)	72.44(14)
F(2)	C(10)	C(11)	C(12)	−100.33(13)	C(6)	N(1)	C(2)	C(3)	0.14(17)
F(2)	C(10)	C(11)	C(16)	77.01(14)	C(7)	N(2)	C(8)	C(9)	103.79(11)
F(3)	C(10)	C(11)	C(12)	141.66(11)	C(7)	N(2)	C(8)	C(14)	−113.53(10)
F(3)	C(10)	C(11)	C(16)	−41.01(14)	C(7)	C(4)	C(5)	C(6)	179.15(10)
N(1)	C(2)	C(3)	C(4)	0.17(17)	C(7)	C(8)	C(14)	C(13)	−86.09(13)
N(2)	C(7)	C(8)	C(9)	−107.94(10)	C(7)	C(8)	C(14)	C(15)	95.96(13)
N(2)	C(7)	C(8)	C(14)	106.83(11)	C(8)	N(2)	C(7)	C(4)	110.65(10)
N(2)	C(8)	C(14)	C(13)	−16.16(15)	C(8)	C(14)	C(15)	C(16)	177.10(10)
N(2)	C(8)	C(14)	C(15)	165.89(9)	C(9)	C(8)	C(14)	C(13)	128.06(11)
C(2)	N(1)	C(6)	C(5)	−0.15(17)	C(9)	C(8)	C(14)	C(15)	−49.89(13)
C(2)	C(3)	C(4)	C(5)	−0.45(15)	C(10)	C(11)	C(12)	C(13)	177.00(10)
C(2)	C(3)	C(4)	C(7)	−179.20(10)	C(10)	C(11)	C(16)	C(15)	−176.55(10)
C(3)	C(4)	C(5)	C(6)	0.44(15)	C(11)	C(12)	C(13)	C(14)	−0.85(16)
C(3)	C(4)	C(7)	N(2)	−177.27(9)	C(12)	C(11)	C(16)	C(15)	0.79(17)
C(3)	C(4)	C(7)	C(8)	−108.87(12)	C(12)	C(13)	C(14)	C(8)	−176.51(10)
C(4)	C(5)	C(6)	N(1)	−0.14(17)	C(12)	C(13)	C(14)	C(15)	1.42(16)
C(4)	C(7)	C(8)	N(2)	−105.89(11)	C(13)	C(14)	C(15)	C(16)	−0.89(17)
C(4)	C(7)	C(8)	C(9)	146.17(10)	C(14)	C(15)	C(16)	C(11)	−0.21(17)
C(4)	C(7)	C(8)	C(14)	0.94(15)	C(16)	C(11)	C(12)	C(13)	−0.27(16)

Table 8 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 15srv267.

Atom	*x*	*y*	*z*	U(eq)

H(2)	9110(20)	9270(20)	3212(14)	35(4)
H(2A)	7794	1836	5048	29
H(3)	7014	4894	5171	25
H(5)	10275	5125	2342	24
H(6)	10943	2059	2316	27
H(7)	7965(19)	7647(18)	4595(12)	16(3)
H(12)	6279	7375	-533	24
H(13)	7946	7897	907	23
H(15)	3290	8497	2993	26
H(16)	1645	7934	1571	27

Experimental

Single crystals of $C_{15}H_{10}F_3N_3$ **[15srv267]** were **[]**. A suitable crystal was selected and **[]** on a **D8V_Mo** diffractometer. The crystal was kept at 120 K during data collection. Using Olex2 [1], the structure was solved with the ShelXS [2] structure solution program using Direct Methods and refined with the ShelXL [3] refinement package using Least Squares minimisation.

1. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.
2. Sheldrick, G.M. (2008). Acta Cryst. A64, 112-122.
3. Sheldrick, G.M. (2015). Acta Cryst. C71, 3-8.

Crystal structure determination of [15srv267]

Crystal Data for $C_{15}H_{10}F_3N_3$ (M =289.26 g/mol): triclinic, space group P-1 (no. 2), a = 7.4334(7) Å, b = 7.9720(8) Å, c = 11.9616(12) Å, α = 82.649(4)°, β = 86.200(4)°, γ = 69.197(3)°, V = 657.01(11) Å^3, Z = 2, T = 120 K, μ(MoKα) = 0.119 mm^{-1}, *Dcalc* = 1.462 g/cm^3, 13656 reflections measured (5.502° ≤ 2Θ ≤ 60.452°), 3923 unique (R_{int} = 0.0300, R_{sigma} = 0.0309) which were used in all calculations. The final R_1 was 0.0406 (I > 2σ(I)) and wR_2 was 0.1131 (all data).

Refinement model description

Number of restraints - 0, number of constraints - unknown.

Details:

```
1. Fixed Uiso
 At 1.2 times of:
  All C(H) groups
2.a Aromatic/amide H refined with riding coordinates:
 C2(H2A), C3(H3), C5(H5), C6(H6), C12(H12), C13(H13), C15(H15), C16(H16)
```

X-ray data for 9 (=15srv254)

X-ray data for 10a (=15srv252)