A [3+3] Annulation Approach to Tetrahydropyridines

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General Considerations

All reactions were conducted in oven or flame-dried glassware under an inert atmosphere of dry nitrogen. Flash chromatography was performed on silica gel (Davisil). Thin layer chromatography (TLC) was performed on aluminium backed plates pre-coated with silica (0.2 mm, Merck DC-alufolien Kieselgel 60 F₂₅₄) which were developed using standard visualizing agents: Ultra Violet light or potassium permanganate

¹H NMR spectra were recorded on a Bruker AC-250 (250 MHz) or AMX-400 (400 MHz) supported by an Aspect 3000 data system, unless otherwise stated. Chemical shifts are reported in ppm with the solvent resonance as the internal standard (CHCl₃: δ 7.27 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, br=broad, m=multiplet) and coupling constants (*J*) in Hz.

¹³C NMR spectra were recorded on a Bruker AC-250 (62.9 MHz) or AMX-400 (100.6 MHz) with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard (CDCl₃: δ 77.0 ppm).

Infrared (FTIR) spectra were recorded on a Perkin Elmer Paragon 100 FTIR spectrophotometer, ν_{max} in cm⁻¹. Bands are characterized as broad (br), strong (s), medium (m) and weak (w). Samples were recorded as thin films using sodium chloride plates, as a DCM solution.

Low resolution mass spectra were recorded on Micromass Autospec, operating in E.I., C.I. or FAB mode; or a Perkin-Elmer Turbomass Benchtop GC-MS operating in either E.I. or C.I mode. High-resolution mass spectra (HRMS) recorded for accurate mass analysis, were performed on either a MicroMass LCT operating in Electrospray mode (TOF ES⁺) or a MicroMass Prospec operating in either FAB (FAB⁺), EI (EI⁺) or CI (CI⁺) mode.

Elemental microanalysis performed using a Perkin-Elmer 2400 CHNS / O Series II Elemental Analyser.

Melting points were performed on recrystallised solids, were recorded on a Gallenkamp melting point apparatus and are uncorrected.

All solvents and reagents were purified using standard laboratory techniques according to methods published in "Purification of Laboratory Chemicals" by Perrin, Armarego, and Perrin (Pergamon Press, 1966). Aziridines were prepared by methods previously reported.¹

Purification of solvents and reagents

Solvents and reagents were used either as received from commercial suppliers or, when necessary, purified in accordance with standard procedures as outlined below.

Dichloromethane was freshly distilled from calcium hydride immediately prior to use.

Diethyl ether (anhydrous grade) was distilled from sodium metal / benzophenone ketyl immediately prior to use.

Petroleum ether refers to 40-60 °C petroleum distillates, which was distilled prior to use.

Tetrahydrofuran (anhydrous grade) was distilled from sodium metal / benzophenone ketyl immediately prior to use.

Triethylamine was distilled from potassium hydroxide and stored over 4 Å molecular sieves.

Methanol was distilled from magnesium and iodine immediately prior to use.

Acetone was distilled from Drierite.

¹ (a) Goodenough, K. M., Raubo, P., Harrity, J. P. A., *Org. Lett.* **2005**, 7, 14, 2993. (b) Jeong, J. U., Tao, B., Sagesser, I., Henniges, H., and Sharpless, B., *J. Am. Chem. Soc.*, **1998**, 120, 6844. (c) Berry, M. B., Craig, D., *Synlett*, **1992**, 41

Preparation of the Büchi Grignard Reagent:

To a 50 mL two-necked flask fitted with a reflux condenser was added magnesium turnings (484 mg, 17.25 mmol, 1.7 eq) and THF (10 mL), then 2-(2-bromo-ethyl)-[1,3]dioxolane (1.2 mL, 10.2 mmol, 1 eq) was added. The solution was allowed to cool to room temperature and the concentration of the Büchi Grignard solution assessed by titration.² An aliquot was removed and placed into a separate flask.

Synthesis of (R)-N-(1-Benzyl-4-[1,3]dioxolan-2-yl-butyl)-4-methylbenzenesulfonamide **9**

A solution of CuBr.DMS (93 mg, 0.45 mmol, 0.4 eq) in DMS (1 mL) was added to the Büchi Grignard solution (1.8 mL, 0.4 M, 0.72 mmol, 2 eq) at -78 °C and stirred for 1 hour. Then a solution of **8** (103 mg, 0.36 mmol, 1 eq) in THF (1 mL) was added at -78 °C and stirred for 10 minutes. The solution was left stirring and allowed to warm to room temperature overnight. The reaction was quenched with water and the organic layer was separated. The aqueous layer was re-extracted with ethyl acetate (2 portions), the organic layers were combined and washed with brine. The solution was dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 5:1 petroleum ether/ethyl acetate) to give **9** as a white solid, 138 mg (98%).

Mp 115-116 °C

$[\alpha]_D^{25}$ -13 (*c* 1.0 g/mL, CH₂Cl₂).

² Titration carried out with 31 mg (DL)-menthol, 5mg 1,10-phenanthroline and 1.5 mL THF creating a 2 mmol solution. The Grignard solution was added to the solution until a red-purple colour persisted. The molarity was calculated by dividing 0.2 by the amount in mL used to achieve the colour change. See Lin, H., Paquette, L. A., *Synth. Commun.*, **1994**, 24, 17, 2503

^1H NMR (250 MHz, CDCl_3): δ 1.13-1.51 (6H, m), 2.33 (3H, s), 2.59 (2H, d, $J=6.5$ Hz), 3.25-3.45 (1H, m), 3.67-3.89 (4H, m), 4.51 (1H, d, $J=8.0$ Hz), 4.64 (1H, t, $J=4.5$ Hz), 6.87-6.98 (2H, m), 7.06-7.21 (5H, m), 7.57 (2H, d, $J=8.0$ Hz).

^{13}C NMR (62.9 MHz, CDCl_3): δ 19.8, 21.5, 33.3, 34.1, 41.2, 54.9, 64.8, 104.2, 126.5, 127.0, 128.5, 129.5, 129.6, 137.2, 137.8, 143.1.

FTIR (thin film): 3279 (br), 2950 (s), 2877 (s), 1599 (m), 1495 (m), 1454 (s), 1417 (s), 1327 (s), 1158 (s), 1091 (s), 1030 (s), 946 (m) cm^{-1} .

HRMS (TOF ES) calcd. for $\text{C}_{21}\text{H}_{27}\text{NO}_4\text{SNa}$ (MNa^+): 412.1559. Found: 412.1553.

Anal. Calcd. For: $\text{C}_{21}\text{H}_{27}\text{NO}_4\text{S}$: C, 64.75; H, 6.99; N, 3.60; S, 8.23; Found: C, 64.48; H, 7.25; N, 3.56; S, 8.35.

Synthesis of (R)-2-Benzyl-1-(toluene-4-sulfonyl)-1,2,3,4-tetrahydropyridine 11

An aqueous solution of hydrogen chloride (1M, 2 mL, 2.0 mmol, 7.5 eq) was added to a solution of **9** (104 mg, 0.267 mmol, 1 eq) in acetone (2 mL) and stirred overnight at room temperature. Reaction was quenched with a saturated solution of K_2CO_3 and the product was extracted with ethyl acetate, dried over MgSO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/ethyl acetate) to give **11** as a colourless solid, 77 mg (88%).

Mp 106-108 $^\circ\text{C}$.

$[\alpha]_D^{25} +290$ (c 1.0 g/mL, CH_2Cl_2).

^1H NMR (250 MHz, CDCl_3): δ 0.72-0.90 (1H, m), 1.28-1.42 (1H, m), 1.74 (1H, dt, $J=18.5, 5.5$ Hz), 1.92-2.12 (1H, m), 2.33 (3H, s), 2.66 (1H, dd, $J=13.5, 10.5$ Hz), 2.92 (1H, dd, $J=13.5, 5.0$ Hz), 3.98-4.10 (1H, m), 4.94-5.05 (1H, m), 6.62 (1H, d, $J=8.0$ Hz), 7.09-7.29 (7H, m), 7.60 (2H, d, $J=8.0$ Hz).

^{13}C NMR (62.9 MHz, CDCl_3): δ 17.1, 20.9, 21.5, 38.1, 54.3, 108.2, 123.6, 126.5, 126.9, 128.5, 129.4, 129.7, 136.3, 138.0, 143.4.

FTIR (thin film): 3086 (m), 3063 (m), 3028 (s), 2927 (s), 2857 (s), 1917 (w), 1807 (w), 1737 (m), 1646 (s), 1597 (s), 1495 (s), 1455 (s), 1401 (s), 1344 (s), 1305 (s), 1261 (s), 1167 (s), 1098 (s), 1049 (s), 1018 (s), 954 (s), 930 (s).

HRMS (TOF ES) calcd. for $C_{19}H_{23}NO_2S$ (MH^+): 328.1371. Found: 328.1386.

Anal. Calcd. For: $C_{19}H_{22}NO_2S$: C, 69.69; H, 6.46; N, 4.28; S, 9.79; Found: C, 69.53; H, 6.53; N, 4.26; S, 9.84.

Synthesis of (S)-N-(4-[1,3]dioxolan-2-yl-1-methyl-butyl)-4-methyl-benzenesulfonamide **13**

A solution of CuBr.DMS (135 mg, 0.66 mmol, 0.4 eq) in DMS (2 mL) was added to the Büchi Grignard solution (7 mL, 0.47 M, 3.29 mmol, 2 eq) at $-78\text{ }^{\circ}\text{C}$ and stirred for 1 hour. Then a solution of **12** (347 mg, 1.65 mmol, 1 eq) in THF (3 mL) was added at $-78\text{ }^{\circ}\text{C}$ and stirred for 10 minutes. The solution was left stirring and allowed to warm to room temperature overnight. The reaction was quenched with water and the organic layer was separated. The aqueous layer was re-extracted with ethyl acetate (2 portions), the organic layers were combined and washed with brine. The solution was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 5:1 petroleum ether/ethyl acetate) to give **13** as a white solid, 360 mg (70%).

Mp $89\text{--}93\text{ }^{\circ}\text{C}$

$[\alpha]_D^{25} -27$ (c 0.009 g/mL, CH_2Cl_2).

1H NMR (250 MHz, $CDCl_3$): δ 1.03 (3H, d, $J=6.5$ Hz), 1.21–1.71 (6H, m), 2.42 (3H, s), 3.21–3.39 (1H, m), 3.78–3.97 (4H, m), 4.33 (1H, d, $J=8.0$ Hz), 4.75 (1H, t, $J=4.5$ Hz), 7.26–7.32 (2H, m), 7.72–7.78 (2H, m).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ 20.0, 21.5, 21.6, 33.3, 37.2, 49.9, 64.8, 104.2, 127.0, 129.6, 138.2, 143.1.

FTIR (thin film): 3272 (br), 2950 (m), 1323 (m), 1160 (s), 1092 (m), 1030 (w) cm^{-1} .
 m/z (TOF ES): 252, 320, 336 (MNa^+). HRMS (TOF ES) calcd. for $\text{C}_{15}\text{H}_{23}\text{NO}_4\text{SNa}$ (MNa^+): 336.1245. Found: 336.1259.

Synthesis of (S)-2-methyl-1-(toluene-4-sulfonyl)-1,2,3,4-tetrahydropyridine 14

An aqueous solution of hydrogen chloride (1M, 1.4 mL, 1.40 mmol, 7.7 eq) was added to a solution of **13** (56 mg, 0.18 mmol, 1 eq) in acetone (3.6 mL) and stirred overnight at room temperature. Reaction was quenched with a saturated solution of K_2CO_3 and the product was extracted with ethyl acetate, dried over MgSO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/ethyl acetate) to give **14** as a yellow oil, 38 mg (84%).

Rotation $[\alpha]_{\text{D}}^{25} +511$ (c 0.009 g/mL, CH_2Cl_2).

^1H NMR (250 MHz, CDCl_3): δ 0.99-1.12 (1H, m), 1.17 (3H, d, $J=6.5$ Hz), 1.38-1.49 (1H, m), 1.56-1.89 (1H, m), 1.75-2.08 (1H, m), 2.41 (3H, s), 4.02-4.15 (1H, m), 4.94-5.02 (1H, m), 6.58-6.65 (1H, m), 7.29 (2H, d, $J=8.0$ Hz), 7.68 (2H, d, $J=8.0$ Hz).

^{13}C NMR (62.9 MHz, CDCl_3): δ 16.9, 18.2, 21.5, 25.2, 48.5, 107.7, 123.2, 126.8, 129.6, 136.4, 143.3.

FTIR (thin film): 3063 (w), 2977 (m), 2929 (m), 2848 (w), 1645 (m), 1362 (s), 1340 (s), 1262 (m), 1170 (s), 1136 (m), 1103 (s) cm^{-1} .

m/z (TOF ES): 252 (MH^+), 274 (MNa^+). HRMS (TOF ES) calcd. for $\text{C}_{13}\text{H}_{18}\text{NO}_2\text{S}$ (MH^+): 252.1058. Found: 252.1048.

**Synthesis of N-(4-[1,3]dioxolan-2-yl-1-isopropyl-butyl)-4-methyl-
benzenesulfonamide 16**

A solution of CuBr.DMS (137 mg, 0.67 mmol, 0.4 eq) in DMS (2 mL) was added to the Büchi Grignard solution (8 mL, 0.4 M, 3.33 mmol, 2 eq) at -78 °C and stirred for 1 hour. Then a solution of **15** (396 mg, 1.67 mmol, 1 eq) in THF (2 mL) was added at -78 °C and stirred for 10 minutes. The solution was left stirring and allowed to warm to room temperature overnight. The reaction was quenched with water and the organic layer was separated. The aqueous layer was re-extracted with ethyl acetate (2 portions), the organic layers were combined and washed with brine. The solution was dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 5:1 petroleum ether/ethyl acetate) to give **16** as a white solid, 469 mg (82%).

mp 117-120 °C

¹H NMR (250 MHz, CDCl₃): δ 0.78 (6H, d, *J*=6.5 Hz), 1.04-1.80 (7H, m), 2.41 (3H, s), 3.01-3.13 (1H, m), 3.75-3.96 (4H, m), 4.30 (1H, d, *J*=9.0 Hz), 4.69 (1H, t, *J*=4.5 Hz), 7.29 (2H, d, *J*=8.5 Hz), 7.75 (2H, d, *J*=8.5 Hz).

¹³C NMR (62.9 MHz, CDCl₃): δ 17.5, 18.3, 20.1, 21.5, 31.0, 31.4, 33.4, 59.1, 64.8, 104.2, 127.0, 129.5, 138.6, 142.9.

FTIR (thin film): 3281 (w), 2958 (m), 2875 (m), 1323 (s), 1160 (s), 1093 (s), 1029 (s) cm⁻¹.

m/z (TOF ES): 280, 364 (MNa⁺). HRMS (TOF ES) calcd. for C₁₇H₂₇NO₄SN_a (MNa⁺): 364.1559. Found: 364.1553.

Synthesis of 2-isopropyl-1-(toluene-4-sulfonyl)-1,2,3,4-tetrahydropyridine **17**

An aqueous solution of hydrogen chloride (1 M, 4 mL, 4.0 mmol, 7.1 eq) was added to a solution of **16** (190 mg, 0.56 mmol, 1 eq) in acetone (4 ml) and stirred overnight at room temperature. Reaction was quenched with a saturated solution of K_2CO_3 and the product was extracted with ethyl acetate, dried over MgSO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/ethyl acetate) to give **17** as a white solid, 154 mg (98%).

Mp 84-88 °C

^1H NMR (250 MHz, CDCl_3): δ 0.61-0.78 (1H, m), 0.90 (3H, d, $J=6.5$ Hz), 1.11 (3H, d, $J=6.5$ Hz), 1.55-1.97 (4H, m), 2.42 (3H, s), 3.52 (1H, dt, $J_1=10.0$ Hz, $J_2=2.5$ Hz), 5.05-5.13 (1H, m), 6.54-6.61 (1H, m), 7.31 (2H, d, $J=8.0$ Hz), 7.68 (2H, d, $J=8.0$ Hz).

^{13}C NMR (62.9 MHz, CDCl_3): 17.6, 19.0, 20.6, 20.8, 21.5, 27.5, 59.13, 111.4, 123.9, 127.0, 129.6, 136.0, 143.2.

FTIR (thin film): 2961 (m), 1644 (w), 1354 (w), 1340 (s), 1171 (s), 1092 (m) cm^{-1} .

m/z (ES): 280 (MH^+). HRMS (ES) calcd. for $\text{C}_{15}\text{H}_{22}\text{O}_2\text{S}$ (MH^+): 280.1371. Found: 280.1364.

Synthesis of (S)-2-trimethylsilanyl-ethanesulfonic acid (4-[1,3]dioxolan-2-yl)-1-methyl-butyl)-amide **19**

A solution of CuBr.DMS (37 mg, 0.18 mmol, 0.5 eq) in DMS (2 mL) was added to the Büchi Grignard solution (2.8 mL, 0.34 M, 0.91 mmol, 2.5 eq) at -78 °C and stirred

for an hour. Then a solution of **18** (79 mg, 0.36 mmol, 1 eq) in THF (1 mL) was added at -78 °C and stirred for 10 minutes. The solution was left stirring and allowed to warm to room temperature overnight. The reaction was quenched with water and the organic layer was separated. The aqueous layer was re-extracted with ethyl acetate (2 portions), the organic layers were combined and washed with brine. The solution was dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 5:1 petroleum ether/ethyl acetate) to give **19** as a white solid, 102 mg (88%).

Mp 76-78 °C.

$[\alpha]_D^{25} +40$ (*c* 1.0 g/mL, CH₂Cl₂).

¹H NMR (250 MHz, CDCl₃): δ -0.30-0.04 (9H, m), 0.93-1.03 (2H, m), 1.19 (3H, d, *J*=6.5 Hz), 1.35-1.69 (6H, m), 2.82-2.92 (2H, m), 3.34-3.47 (1H, m), 3.75-3.95 (4H, m), 4.79 (1H, d, *J*=4.5 Hz).

¹³C NMR (62.9 MHz, CDCl₃): δ -2.0, 10.7, 20.3, 22.5, 33.4, 37.7, 50.0, 50.2, 64.8, 104.2.

FTIR (thin film): 3544 (w,br), 3278 (br), 2953 (s), 2895 (m), 1316 (s), 1250 (s), 1134 (s), 1027 (m) cm⁻¹.

m/z (TOF ES): 346 (MNa⁺), 363 (MK⁺). HRMS (TOF ES) calcd. for C₁₃H₂₉NO₄SiSNa (MNa⁺): 346.1484. Found: 346.1497.

Synthesis of (S)-2-methyl-1-(2-trimethylsilanyl-ethanesulfonyl)-1,2,3,4-tetrahydropyridine **20**

An aqueous solution of hydrogen chloride (1 M, 1.1 mL, 1.1 mmol, 8.3 eq) was added to a solution of **19** (42 mg, 0.13 mmol, 1 eq) in acetone (1.3 mL) and stirred at room temperature for 5 hours. Reaction was quenched with a saturated solution of K₂CO₃ and the product was extracted with ethyl acetate, dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by column chromatography (using a

continuous gradient from petroleum ether and ending with 19:1 petroleum ether/ethyl acetate) to give **20** as a colourless oil, 20 mg (62%).

$[\alpha]_D^{25} +271$ (*c* 0.009 g/mL, CH₂Cl₂).

¹H NMR (250 MHz, CDCl₃): δ -0.10-0.10 (9H, m), 0.90-1.03 (2H, m), 1.20 (3H, d, *J*=6.5 Hz), 1.62-1.77 (2H, m), 1.89-2.17 (2H, m), 2.81-2.95 (2H, m), 4.09-4.21 (1H, m), 4.83-4.91 (1H, m), 6.39-6.46 (1H, m).

¹³C NMR (62.9 MHz, CDCl₃): δ -2.0, 10.4, 16.9, 18.4, 26.8, 48.8, 48.9, 105.2, 125.9.

FTIR (thin film): 3508 (br), 2952 (s), 1648 (m), 1337 (s), 1251 (s), 1156 (s), 1100 (m), 1000 (s) cm⁻¹.

m/z (TOF ES): 262 (MH⁺). HRMS (TOF ES) calcd. for C₁₁H₂₄NO₂SiS (MH⁺): 262.1297. Found: 262.1305.

Synthesis of N-[2-(2-[1,3]dioxolan-2-yl-ethyl)-cyclohexyl]-4-methyl-benzenesulfonamide **22**

A solution of CuBr.DMS (70 mg, 0.34 mmol, 0.4 eq) in DMS (1 mL) was added to the Büchi Grignard solution (4 mL, 0.43 M, 1.70 mmol, 2 eq) at -78 °C and stirred for an hour. Then a solution of **21** (215 mg, 0.85 mmol, 1 eq) in THF (1 mL) was added at -78 °C and stirred for 10 minutes. The solution was left stirring and allowed to warm to room temperature overnight. The reaction was quenched with water and the organic layer was separated. The aqueous layer was re-extracted with ethyl acetate (2 portions), the organic layers were combined and washed with brine. The solution was dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 5:1 petroleum ether/ethyl acetate) to give **22** as a white solid, 234 mg (78%).

Mp 170-174 °C

^1H NMR (250 MHz, CDCl_3): δ 0.81-1.28 (6H, m), 1.34-1.88 (7H, m), 2.40 (3H, s), 2.73-2.91 (1H, m), 3.74-3.99 (4H, m), 4.50 (1H, d, $J=8.5$ Hz), 4.68 (1H, t, $J=4.5$ Hz), 7.29 (2H, d, $J=8.0$ Hz), 7.76 (2H, d, $J=8.0$ Hz).

^{13}C NMR (62.9 MHz, CDCl_3): δ 21.5, 25.0 (x2), 26.4, 30.7, 30.8, 34.6, 42.7, 57.3, 64.8, 104.7, 127.0, 129.6, 138.6, 143.0.

FTIR (thin film): 3268 (br), 2929 (m), 2857 (m), 1325 (m), 1160 (s), 1092 (m), 1072 (w) cm^{-1} .

m/z (ES): 292, 376 (MNa^+), 392 (MK^+), 729 (2MNa^+). HRMS (ES) calcd. for $\text{C}_{18}\text{H}_{27}\text{O}_4\text{SNa}$ (MNa^+): 376.1559. Found: 376.1543.

Synthesis of 1-(toluene-4-sulfonyl)-1,4,4a,5,6,7,8,8a-octahydroquinoline **23**

A hydrogen chloride solution in ether (1M, 1.2 mL, 1.23 mol, 5 eq) was added to a solution of **22** (87.2 mg, 0.25 mmol, 1 eq) in ether (2.5 mL) and acetone (1 mL). Then THF (2 mL) was added and stirred at room temperature for 4 hours. Reaction mixture was poured into a saturated solution of K_2CO_3 (10 mL) and the product was extracted with ethyl acetate, dried over MgSO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/ethyl acetate) to give **23** as a white solid, 45 mg (63%).

Mp 71-73 °C

^1H NMR (250 MHz, CDCl_3): δ 0.84-1.03 (1H, m), 1.14-1.65 (6H, m), 1.68-1.87 (3H, m), 2.42 (3H, s), 2.63-2.76 (2H, m), 5.00-5.10 (1H, m), 6.67-6.74 (1H, m), 7.31 (2H, d, $J=8.5$ Hz), 7.66 (2H, d, $J=8.5$ Hz).

^{13}C NMR (62.9 MHz, CDCl_3): δ 21.6, 25.3 (x2), 28.6, 32.7, 33.3, 39.3, 61.6, 109.1, 127.1, 127.4, 129.5, 135.7, 143.4.

FTIR (thin film): 2927 (m), 2855 (m), 1658 (w), 1346 (m), 1241 (w), 1170 (s), 1092 (m) cm^{-1} .

m/z (TOF ES): 292 (MH^+), 314 (MNa^+). HRMS (TOF ES) calcd. for $\text{C}_{16}\text{H}_{22}\text{NO}_2\text{S}$ (MH^+): 292.1371. Found: 292.1359.

Synthesis of N-[1-(3-[1,3]dioxolan-2-yl-propyl)-cyclohexyl]-4-methyl-benzenesulfonamide **25**

A solution of CuBr.DMS (35 mg, 0.17 mmol, 0.4 eq) in DMS (0.5 mL) was added to the Buchi Grignard solution (2 mL, 0.43 M, 0.85 mmol, 2 eq) at $-78\text{ }^{\circ}\text{C}$ and stirred for an hour. Then a solution of **24** (113 mg, 0.43 mmol, 1 eq) in THF (0.5 mL) was added at $-78\text{ }^{\circ}\text{C}$ and stirred for 10 minutes. The solution was left stirring and allowed to warm to room temperature overnight. The reaction was quenched with water and the organic layer was separated. The aqueous layer was re-extracted with ethyl acetate (2 portions), the organic layers were combined and washed with brine. The solution was dried over MgSO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 5:1 petroleum ether/ethyl acetate) to give **25** as a white solid, 141 mg (90%).

Mp 109-111 $^{\circ}\text{C}$

^1H NMR (250 MHz, CDCl_3): δ 1.16-1.79 (16H, m), 2.40 (3H, s), 3.78-3.96 (4H, m), 4.38 (1H, s), 4.68 (1H, t, $J=5.0\text{ Hz}$), 7.28 (2H, d, $J=8.5\text{ Hz}$), 7.78 (2H, d, $J=8.5\text{ Hz}$).

^{13}C NMR (100.6 MHz, CDCl_3): δ 17.5, 21.4, 21.5, 25.3, 33.7, 35.9, 38.3, 59.7, 64.7, 104.4, 126.9, 129.4, 140.6, 142.7.

FTIR (thin film): 3280 (br), 2935 (m), 2864 (m), 1329 (m), 1152 (s), 1094 (m) cm^{-1} .

m/z (TOF ES): 306, 390 (MNa^+), 406. HRMS (TOF ES) calcd. for $\text{C}_{19}\text{H}_{29}\text{NO}_4\text{SNa}$ (MNa^+): 390.1715. Found: 390.1700.

Synthesis of 1-(toluene-4-sulfonyl)-1-aza-spiro[5.5]undec-2-ene **26**

A hydrogen chloride solution in ether (1M, 0.3 mL, 0.27 mol, 2.1 eq) was added to a solution of **25** (50 mg, 0.14 mmol, 1 eq) in acetone (1.4 mL). The mixture was stirred at room temperature overnight. Reaction was quenched with a saturated solution of K_2CO_3 and the product was extracted with ethyl acetate, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/ethyl acetate) to give **26** as a white solid, 23 mg (54%).

Mp 119-122 °C.

1H NMR (250 MHz, $CDCl_3$): δ 1.34-1.42 (4H, m), 1.50-1.66 (4H, m), 1.74 (2H, t, $J=6.5$ Hz), 1.93-2.02 (2H, m), 2.04-2.18 (2H, m), 2.41 (3H, s), 4.96 (1H, dt, $J=4.0$ Hz, 8.5 Hz), 6.97 (1H, dt, $J=2.0$ Hz, 8.5 Hz), 7.23-7.29 (2H, m), 7.69 (2H, d, $J=8.5$ Hz).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ 18.6, 21.5, 22.4, 25.2, 28.1, 32.9, 62.3, 105.1, 126.4 (x2), 129.5, 140.9, 142.8.

FTIR (thin film): 2928 (m), 2864 (w), 1656 (m), 1332 (s), 1252 (m), 1161 (s), 1103 (s) cm^{-1} .

m/z (TOF ES): 306 (MH^+), 328 (MNa^+). HRMS (TOF ES) calcd. for $C_{17}H_{24}NO_2S$ (MH^+): 306.1528. Found: 306.1521.

Synthesis of N-[4-tert-butyl-1-(3-[1,3]dioxolan-2-yl-propyl)-cyclohexyl]-4-methyl-benzenesulfonamide **28**

A solution of copper-bromide DMS (45 mg, 0.22 mmol, 0.4 eq) in DMS (1 mL) was added to the Buchi Grignard solution (4 mL, 0.28 M, 1.12 mmol, 2 eq) at -78 °C and stirred for an hour. Then a solution of **27** (180 mg, 0.56 mmol, 1 eq) in THF (2 mL) was added at -78 °C and stirred for 10 minutes. The solution was left stirring and allowed to warm up to room temperature over night. The reaction was quenched with water and the organic layer was separated. Then extracted with ethyl acetate (2 portions), the organic layers were combined and washed with brine. The solution was dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 3:1 petroleum ether/ethyl acetate) to give **28** as a white solid, 189 mg (79%).

Mp 133-134 °C

¹H NMR (250 MHz, CDCl₃): δ 0.80-1.10 (2H, m), 0.78 (9H, s), 1.18-1.65 (11H, m), 1.75-1.86 (2H, m), 2.41 (3H, s), 3.79-3.99 (4H, m), 4.47 (1H, s), 4.74 (1H, t, *J*=4.5 Hz), 7.28 (2H, d, *J*=8.5 Hz), 7.77 (2H, d, *J*=8.5 Hz).

¹³C NMR (62.9 MHz, CDCl₃): δ 17.3, 21.5, 23.0, 27.5, 32.2, 33.3, 33.7, 36.2, 47.0, 59.9, 64.8, 104.5, 126.9, 129.4, 141.0, 142.7.

FTIR (thin film): 3273 (br), 2948 (s), 2868 (m), 1331 (m), 1156 (s), 1094 (m), 1032 (w) cm⁻¹.

m/z (TOF ES): 446 (MNa⁺). HRMS (TOF ES) calcd. for C₂₃H₃₇NO₄SN⁺ (MNa⁺): 446.2341. Found: 446.2357.

Synthesis of 9-tert-butyl-1-(toluene-4-sulfonyl)-1-aza-spiro[5.5]undec-2-ene **29**

An aqueous solution of hydrogen chloride (1M, 1.7 mL, 1.7 mol, 7.1 eq) was added to a solution of **28** (100 mg, 0.24 mmol, 1 eq) in acetone (2.4 mL). The mixture was stirred at room temperature overnight. Reaction was quenched with a saturated solution of K₂CO₃ (30 mL) and the product was extracted with ethyl acetate, dried

over MgSO_4 , filtered and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/ethyl acetate) to give **29** as a white solid, 69 mg (83%).

Mp 139-142 °C

^1H NMR (250 MHz, CDCl_3): δ 0.74 (9H, s), 0.89-1.09 (3H, m), 1.44-1.65 (6H, m), 1.86-1.95 (2H, m), 1.99-2.15 (2H, m), 2.34 (3H, s), 4.83-4.91 (1H, m), 6.86-6.92 (1H, m), 7.20 (2H., d, $J=8.0$ Hz), 7.62 (2H., d, $J=8.0$ Hz).

^{13}C NMR (62.9 MHz, CDCl_3): δ 18.6, 21.5, 23.1, 27.5, 28.1, 32.2, 33.0, 46.9, 62.1, 105.0, 126.5 (x2), 129.5, 140.9, 142.8

FTIR (thin film): 2943 (s), 1657 (m), 1325 (m), 1255 (m), 1162 (s), 1098 (s) cm^{-1} .

m/z (TOF ES): 384 (MNa^+). HRMS (TOF ES) calc. for $\text{C}_{21}\text{H}_{31}\text{NO}_2\text{SNa}$ (MNa^+): 384.1973. Found: 384.1965.

Synthesis of (S)-2-allyl-6-benzyl-1-(toluene-4-sulfonyl)-piperidine **30**

To a solution of **11** (105 mg, 0.322 mmol, 1 eq) in DCM (4 mL) at -20 °C was added allyltrimethylsilane (307 μL , 1.95 mmol, 6 eq) and trifluoroacetic acid (99 μL , 1.29 mmol, 4 eq). The reaction mixture was stirred at -20 °C for 2 h and was then allowed to warm to room temperature overnight. The reaction was quenched with NaHCO_3 and extracted using DCM (3 portions). The combined organic layers were washed with water and brine, dried over MgSO_4 , filtered and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/ethyl acetate) to give **30** as a colourless solid, 101 mg (85%).

Mp 106-108 °C.

$[\alpha]_D^{25} +50$ (c 1.0 g/mL, CH_2Cl_2).

^1H NMR (250 MHz, C_6D_6): δ 0.68-1.45 (6H, m), 1.88 (3H, s), 2.19-2.35 (1H, m), 2.61 (1H, dt, $J=13.5$, 6.0 Hz), 2.78 (1H, dd, $J=12.5$, 12.0 Hz), 3.23 (1H, dd, $J=13.0$, 3.0 Hz), 3.95-4.20 (1H, m), 4.24-4.36 (1H, m), 5.00-5.11 (2H, m), 5.77-5.95 (1H, m), 6.74 (2H, d, $J=8.0$ Hz), 7.02-7.29 (5H, m), 7.71 (2H, d, $J=8.0$ Hz).

^{13}C NMR (62.9 MHz, CDCl_3): δ 13.3, 21.5, 24.8, 26.3, 40.1, 41.8, 52.0, 54.5, 117.4, 126.4, 126.7, 128.5, 129.4, 129.6, 134.8, 135.8, 139.5, 142.8.

FTIR (thin film): 3063 (m), 3027 (m), 2940 (s), 2859 (s), 1951 (w), 1917 (w), 1303 (s), 1287 (m), 1220 (m), 1161 (s), 1102 (s), 1046 (m) cm^{-1} .

HRMS (TOF ES) calcd. for $\text{C}_{22}\text{H}_{28}\text{NO}_4\text{S}$ (MH^+): 370.1841. Found: 370.1849.

Synthesis of acetic acid 2-acetoxy-6-benzyl-1-(toluene-4-sulfonyl)-piperidin-3-yl ester **31**

To a solution of **11** (200 mg, 0.61 mmol, eq) in acetone (5.5 mL) was added NMO (215 mg, 1.83 mmol, 3 eq) and water (0.6 mL), followed by osmium tetroxide (2 crystals) and the reaction mixture was stirred at room temperature for 13 hours. The reaction was quenched with sodium metabisulfite with ice cooling, water was added the product was extracted with diethyl ether (3 portions). The combined organic layers were washed with brine and dried over MgSO_4 , filtered and concentrated under reduced pressure.

To a solution of crude diol in DCM (5 mL) at room temperature was added acetic anhydride (288 μL , 3.05 mmol, 5 eq), Et_3N (425 μL , 3.05 mmol, 5 eq), followed by DMAP (8 mg, 0.06 mmol, 0.1 eq). After 1 h the reaction mixture was diluted with water and extracted with DCM (3 portions). The combined organic layers were dried over MgSO_4 , filtered and concentrated under reduced pressure. The residue purified by column chromatography (using a continuous gradient from petroleum ether and ending with 2:1 petroleum ether/diethyl ether) to give a mixture of diastereoisomers of **31** as a white solid 245 mg (90%).

^1H NMR (250 MHz, CDCl_3) for Major Diastereoisomer: δ 0.90-0.80 (1H, m), 1.56-1.35 (1H, m), 1.61-1.76 (2H, m), 1.99 (3H, s), 2.07 (3H, s), 2.40 (3H, s), 2.92-3.12 (2H, m), 4.07-4.17 (1H, m), 4.74 (1H, dt, $J=12.0$ Hz, 4.0 Hz), 6.86 (1H, d, $J=4.0$ Hz), 7.15-7.34 (7H, m), 7.76 (2H, d, $J=8.0$ Hz).

^{13}C NMR (62.9 MHz, CDCl_3) for Major Diastereoisomer: δ 18.9, 20.8, 21.1, 21.6, 24.2, 39.6, 54.1, 69.7, 75.9, 126.6, 127.2, 128.7, 129.5, 129.9, 137.5, 138.9, 144.0, 169.1, 169.9.

FTIR (thin film): 3480 (br), 3062 (w), 3027 (w), 2955 (m), 2867 (w), 1748 (s), 1599 (w), 1346 (m), 1242 (m), 1163 (s), 1097 (m) cm^{-1} .

m/z (TOF ES): 326, 386, 426, 468 (MNa^+). HRMS (TOF ES) calc. for $\text{C}_{23}\text{H}_{27}\text{NO}_6\text{SNa}$ (MNa^+): 468.1457. Found: 468.1440.

Synthesis of 2-benzyl-5-bromo-1-(toluene-4-sulfonyl)-1,2,3,4-tetrahydropyridine

To a stirred solution of **11** (100 mg, 0.31 mmol, 1 eq) in DCM (2.7 mL) at $-78\text{ }^\circ\text{C}$ was added bromine (40 μL , 0.78 mmol 2.5 eq) in DCM (1 mL) dropwise until an orange colour persisted. Hünig's base (59 μL , 0.34 mmol, 1.1 eq) was added and the reaction was left to warm to room temperature, then stirred for a further hour. Aqueous $\text{Na}_2\text{S}_2\text{O}_3$ solution was added to the reaction mixture and the product was extracted with DCM (3 portions). The combined organic layers were washed with brine and dried over MgSO_4 , filtered and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 5:1 petroleum ether/ethyl acetate) to give **32** as a pale yellow solid, 83 mg (66%).

Mp $127\text{--}129\text{ }^\circ\text{C}$

^1H NMR (250 MHz, CDCl_3): δ 0.95-1.13 (1H, m), 1.43-1.59 (1H, m), 2.11-2.25 (1H, m), 2.44-2.57 (4H, m), 2.65-2.77 (1H, dd, $J=10.0$ Hz, 13.0 Hz), 2.93-3.05 (1H, dd,

$J=5.0$ Hz, 13.0 Hz), 4.05 - 4.18 (1H, m), 7.04 (1H, s), 7.17 - 7.36 (7H, m), 7.69 (2H, d, $J=8.0$ Hz).

^{13}C NMR (62.9 MHz, CDCl_3): δ 21.6, 22.8, 27.2, 38.1, 53.4, 104.3, 123.8, 126.8, 127.0, 128.7, 129.3, 129.9, 135.7, 137.4, 143.9

FTIR (thin film): 3061 (w), 3027 (w), 2930 (w), 2877 (w), 1645 (w), 1598 (w), 1362 (m), 1342 (m), 1248 (m), 1167 (s), 1096 (m), 1049 (m) cm^{-1} .

m/z (TOF ES): 408 (MH^+), 430 (MNa^+). HRMS (TOF ES) calc. for $\text{C}_{19}\text{H}_{20}\text{NO}_2\text{SBr}$ (MH^+): 406.0476. Found: 406.0493.

Synthesis of (R)-2-allyl-6-methyl-1-(toluene-4-sulfonyl)-piperidine **33**

To a solution of **ent-15** (586 mg, 2.33 mmol, 1 eq) in DCM (44 mL) at -20 °C was added allyltrimethylsilane (2.2 mL, 13.99 mmol, 6 eq) and TFA (719 μL , 9.33 mmol, 4 eq). The reaction mixture was stirred at -20 °C for 2 h and was then allowed to warm to room temperature overnight. The reaction was quenched with NaHCO_3 and extracted using DCM (3 portions). The combined organic layers were washed with water and brine, dried over MgSO_4 , filtered and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/ethyl acetate) to give **33** as a white solid, 571 mg (83%).

Mp 66 - 70 °C

$[\alpha]_D^{25} +32$ (c 0.010 g/mL, CH_2Cl_2).

^1H NMR (250 MHz, CDCl_3): δ 1.11-1.45 (7H, m), 1.51-1.77 (2H, m), 2.31-2.57 (5H, m), 3.96-4.22 (2H, m), 4.99-5.13 (2H, m), 5.69-5.88 (1H, m), 7.27 (2H, d, $J=8.0$ Hz), 7.71 (2H, d, $J=8.0$ Hz).

^{13}C NMR (62.9 MHz, CDCl_3): δ 13.4, 21.5, 21.9, 26.2, 29.4, 40.1, 47.9, 52.1, 117.2, 126.7, 129.5, 136.0, 138.9, 142.6.

FTIR (thin film): 2939 (m), 2361 (m), 1332 (m), 1221 (w), 1165 (s), 1105 (m) cm^{-1} .

m/z (TOF ES): 294 (MH^+). HRMS (TOF ES) calc. for $\text{C}_{16}\text{H}_{24}\text{NO}_2\text{S}$ (MH^+): 294.1528. Found: 294.1535.

Synthesis of 2-methyl-6-propyl-1-(toluene-4-sulfonyl)-piperidine **34³**

To a solution of **33** (67 mg, 0.17 mmol) in methanol (2.3 mL) was added palladium on 10% carbon (16 mg) and the mixture was stirred under an atmosphere of Hydrogen for 2 h. The reaction mixture was filtered over hyflo supercel and washed with methanol. The solvent from the filtrate was removed under reduced pressure. The residue was then filtered again over hyflo supercel and washed with DCM. The solvent was removed from the filtrate under reduced pressure and gave **34** as a clear oil, 50 mg (100%)

$[\alpha]_{\text{D}}^{25} +20$ (c 0.010 g/mL, CH_2Cl_2).

^1H NMR (250 MHz, CDCl_3): δ 0.94 (3H, t, $J=7.0$ Hz), 1.16-1.81 (13H, m), 2.42 (3H, s), 3.94-4.19 (2H, m), 7.29 (2H, d, $J=8.0$ Hz), 7.73 (2H, d, $J=8.0$ Hz).

^{13}C NMR (62.9 MHz, CDCl_3): δ 13.7, 14.0, 20.5, 21.5, 21.8, 27.3, 29.3, 37.8, 48.0, 52.5, 126.7, 129.5, 139.0, 124.5.

FTIR (thin film): 2938 (m), 2872 (m), 1598 (w), 1331 (m), 1286 (m), 1167 (s), 1099 (s) cm^{-1} .

m/z (TOF ES): 296 (MH^+), 318 (MNa^+). HRMS (TOF ES) calc. for $\text{C}_{16}\text{H}_{26}\text{NO}_2\text{S}$: 296.1684. Found: 296.1683.

³ Lu, Z., Zhou, W., *J. Chem. Soc. Perkin. Trans. 1*, **1993**, 593

(R)-N-(1-Benzyl-4-[1,3]dioxolan-2-yl-butyl)-4-methyl-benzenesulfonamide 9

(R)-2-Benzyl-1-(toluene-4-sulfonyl)- 1,2,3,4-tetrahydropyridine 11

(S)-N-(4-[1,3]dioxolan-2-yl-1-methyl-butyl)-4-methyl-benzenesulfonamide 13

(S)-2-methyl-1-(toluene-4-sulfonyl)-1,2,3,4-tetrahydropyridine 14

N-(4-[1,3]dioxolan-2-yl-1-isopropyl-butyl)-4-methyl-benzenesulfonamide 16

2-isopropyl-1-(toluene-4-sulfonyl)-1,2,3,4-tetrahydropyridine 17

CC[C@H](N)CCCC1OCCO1

3.65 (m, 4H)
 3.50 (m, 4H)
 3.25 (m, 4H)
 2.85 (m, 4H)
 2.35 (m, 4H)
 1.85 (m, 4H)
 1.25 (d, 3H)

(S)-2-methyl-1-(2-trimethylsilanyl-ethanesulfonyl)-1,2,3,4-tetrahydropyridine 20

N-[2-(2-[1,3]dioxolan-2-yl-ethyl)-cyclohexyl]-4-methyl-benzenesulfonamide 22

1-(toluene-4-sulfonyl)-1,4,4a,5,6,7,8,8a-octahydroquinoline 23

N-[1-(3-[1,3]dioxolan-2-yl-propyl)-cyclohexyl] -4-methyl-benzenesulfonamide 25

**N-[4-tert-butyl-1-(3-[1,3]dioxolan-2-yl-propyl)-cyclohexyl]-4-methyl-
benzenesulfonamide 28**

9-tert-butyl-1-(toluene-4-sulfonyl)-1-aza-spiro[5.5]undec-2-ene 29

(S)-2-allyl-6-benzyl-1-(toluene-4-sulfonyl)-piperidine 30

acetic acid 2-acetoxy-6-benzyl-1-(toluene-4-sulfonyl)-piperidin-3-yl ester 31

2-benzyl-5-bromo-1-(toluene-4-sulfonyl)-1,2,3,4-tetrahydropyridine 32

(R)-2-allyl-6-methyl-1-(toluene-4-sulfonyl)-piperidine 33

2-methyl-6-propyl-1-(toluene-4-sulfonyl)-piperidine 34

Chromatographs:

(R)-2-Benzyl-1-(toluene-4-sulfonyl)-1,2,3,4-tetrahydropyridine 11

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	9.147	76.152	2.782	0.3	0.3	0.41
2	10.557	26190.228	1064.874	99.7	99.7	0.38
	Total	26266.380	1067.656	100.0	100.0	

2-Benzyl-1-(toluene-4-sulfonyl)-1,2,3,4-tetrahydropyridine 11

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	9.013	5605.194	270.743	50.0	52.9	0.33
2	10.470	5596.156	241.169	50.0	47.1	0.36
	Total	11201.349	511.912	100.0	100.0	

(S)-2-allyl-6-benzyl-1-(toluene-4-sulfonyl)-piperidine 30

Table 1. Crystal data and structure refinement for rowan1m.

Identification code	rowan1m	
Empirical formula	C ₂₂ H ₂₇ N O ₂ S	
Formula weight	369.51	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2 ₁ 2 ₁ 2 ₁	
Unit cell dimensions	a = 8.084(3) Å	α = 90°.
	b = 15.313(6) Å	β = 90°.
	c = 16.268(6) Å	γ = 90°.
Volume	2013.7(14) Å ³	
Z	4	
Density (calculated)	1.219 Mg/m ³	
Absorption coefficient	0.176 mm ⁻¹	
F(000)	792	
Crystal size	0.41 x 0.32 x 0.28 mm ³	
Theta range for data collection	1.83 to 27.57°.	
Index ranges	-10 ≤ h ≤ 10, -19 ≤ k ≤ 19, -20 ≤ l ≤ 20	

Reflections collected	23080
Independent reflections	4566 [R(int) = 0.0716]
Completeness to theta = 27.57°	99.1 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9524 and 0.9313
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	4566 / 0 / 236
Goodness-of-fit on F ²	1.019
Final R indices [I>2sigma(I)]	R1 = 0.0476, wR2 = 0.0886
R indices (all data)	R1 = 0.0842, wR2 = 0.1006
Absolute structure parameter	-0.03(9)
Largest diff. peak and hole	0.543 and -0.354 e.Å ⁻³

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for rowan1m. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	1195(1)	9591(1)	3682(1)	30(1)
N(1)	1153(3)	9610(2)	4673(1)	30(1)
O(1)	1545(2)	8712(1)	3433(1)	40(1)
O(2)	-286(2)	10014(1)	3398(1)	36(1)
C(1)	347(3)	10356(2)	5099(2)	29(1)
C(2)	1542(4)	10806(2)	5684(2)	42(1)
C(3)	2469(4)	10170(2)	6230(2)	50(1)
C(4)	3403(3)	9518(2)	5701(2)	48(1)
C(5)	2251(3)	9007(2)	5142(2)	37(1)
C(6)	2880(3)	10241(2)	3361(2)	26(1)
C(7)	2633(3)	11124(2)	3194(2)	34(1)
C(8)	3959(4)	11627(2)	2948(2)	41(1)
C(9)	5537(4)	11279(2)	2855(2)	38(1)
C(10)	5749(3)	10399(2)	3032(2)	37(1)
C(11)	4440(3)	9876(2)	3284(2)	32(1)
C(12)	-1287(4)	10080(2)	5515(2)	34(1)
C(13)	-2466(3)	10825(2)	5655(2)	29(1)
C(14)	-2976(3)	11064(2)	6441(2)	34(1)
C(15)	-4140(3)	11720(2)	6559(2)	37(1)
C(16)	-4780(3)	12159(2)	5890(2)	36(1)

C(17)	-4279(3)	11935(2)	5109(2)	36(1)
C(18)	-3136(3)	11281(2)	4994(2)	32(1)
C(19)	1207(4)	8314(2)	5591(2)	39(1)
C(20)	2237(4)	7585(2)	5936(2)	57(1)
C(21)	2066(5)	6803(2)	5807(3)	67(1)
C(22)	6966(4)	11836(2)	2564(2)	61(1)

Table 3. Bond lengths [$\text{\AA}$] and angles [$^\circ$] for rowan1m.

S(1)-O(1)	1.433(2)
S(1)-O(2)	1.4375(19)
S(1)-N(1)	1.613(2)
S(1)-C(6)	1.766(3)
N(1)-C(1)	1.487(3)
N(1)-C(5)	1.490(3)
C(1)-C(2)	1.521(4)
C(1)-C(12)	1.543(4)
C(1)-H(1)	0.9800
C(2)-C(3)	1.516(4)
C(2)-H(2A)	0.9700
C(2)-H(2B)	0.9700
C(3)-C(4)	1.520(5)
C(3)-H(3A)	0.9700
C(3)-H(3B)	0.9700
C(4)-C(5)	1.518(4)
C(4)-H(4A)	0.9700
C(4)-H(4B)	0.9700
C(5)-C(19)	1.541(4)
C(5)-H(5)	0.9800
C(6)-C(11)	1.385(3)
C(6)-C(7)	1.394(4)
C(7)-C(8)	1.380(4)
C(7)-H(7)	0.9300
C(8)-C(9)	1.391(4)
C(8)-H(8)	0.9300
C(9)-C(10)	1.390(4)
C(9)-C(22)	1.511(4)

C(10)-C(11)	1.388(4)
C(10)-H(10)	0.9300
C(11)-H(11)	0.9300
C(12)-C(13)	1.504(4)
C(12)-H(12A)	0.9700
C(12)-H(12B)	0.9700
C(13)-C(14)	1.393(4)
C(13)-C(18)	1.391(4)
C(14)-C(15)	1.390(4)
C(14)-H(14)	0.9300
C(15)-C(16)	1.380(4)
C(15)-H(15)	0.9300
C(16)-C(17)	1.376(4)
C(16)-H(16)	0.9300
C(17)-C(18)	1.376(4)
C(17)-H(17)	0.9300
C(18)-H(18)	0.9300
C(19)-C(20)	1.501(4)
C(19)-H(19A)	0.9700
C(19)-H(19B)	0.9700
C(20)-C(21)	1.224(4)
C(20)-H(20)	0.9300
C(21)-H(21A)	0.9300
C(21)-H(21B)	0.9300
C(22)-H(22A)	0.9600
C(22)-H(22B)	0.9600
C(22)-H(22C)	0.9600

O(1)-S(1)-O(2)	119.85(12)
O(1)-S(1)-N(1)	107.66(12)
O(2)-S(1)-N(1)	107.20(12)
O(1)-S(1)-C(6)	107.06(12)
O(2)-S(1)-C(6)	107.01(12)
N(1)-S(1)-C(6)	107.52(12)
C(1)-N(1)-C(5)	119.9(2)
C(1)-N(1)-S(1)	119.32(18)
C(5)-N(1)-S(1)	119.19(18)
N(1)-C(1)-C(2)	111.2(2)

N(1)-C(1)-C(12)	111.7(2)
C(2)-C(1)-C(12)	113.2(2)
N(1)-C(1)-H(1)	106.8
C(2)-C(1)-H(1)	106.8
C(12)-C(1)-H(1)	106.8
C(3)-C(2)-C(1)	112.8(3)
C(3)-C(2)-H(2A)	109.0
C(1)-C(2)-H(2A)	109.0
C(3)-C(2)-H(2B)	109.0
C(1)-C(2)-H(2B)	109.0
H(2A)-C(2)-H(2B)	107.8
C(2)-C(3)-C(4)	109.7(3)
C(2)-C(3)-H(3A)	109.7
C(4)-C(3)-H(3A)	109.7
C(2)-C(3)-H(3B)	109.7
C(4)-C(3)-H(3B)	109.7
H(3A)-C(3)-H(3B)	108.2
C(3)-C(4)-C(5)	111.9(2)
C(3)-C(4)-H(4A)	109.2
C(5)-C(4)-H(4A)	109.2
C(3)-C(4)-H(4B)	109.2
C(5)-C(4)-H(4B)	109.2
H(4A)-C(4)-H(4B)	107.9
N(1)-C(5)-C(4)	110.7(2)
N(1)-C(5)-C(19)	110.1(2)
C(4)-C(5)-C(19)	114.0(3)
N(1)-C(5)-H(5)	107.3
C(4)-C(5)-H(5)	107.3
C(19)-C(5)-H(5)	107.3
C(11)-C(6)-C(7)	120.3(3)
C(11)-C(6)-S(1)	120.1(2)
C(7)-C(6)-S(1)	119.6(2)
C(8)-C(7)-C(6)	119.2(3)
C(8)-C(7)-H(7)	120.4
C(6)-C(7)-H(7)	120.4
C(7)-C(8)-C(9)	122.0(3)
C(7)-C(8)-H(8)	119.0
C(9)-C(8)-H(8)	119.0

C(10)-C(9)-C(8)	117.5(3)
C(10)-C(9)-C(22)	121.2(3)
C(8)-C(9)-C(22)	121.3(3)
C(11)-C(10)-C(9)	121.8(3)
C(11)-C(10)-H(10)	119.1
C(9)-C(10)-H(10)	119.1
C(6)-C(11)-C(10)	119.2(3)
C(6)-C(11)-H(11)	120.4
C(10)-C(11)-H(11)	120.4
C(13)-C(12)-C(1)	113.6(2)
C(13)-C(12)-H(12A)	108.8
C(1)-C(12)-H(12A)	108.8
C(13)-C(12)-H(12B)	108.8
C(1)-C(12)-H(12B)	108.8
H(12A)-C(12)-H(12B)	107.7
C(14)-C(13)-C(18)	117.6(2)
C(14)-C(13)-C(12)	121.6(2)
C(18)-C(13)-C(12)	120.7(2)
C(13)-C(14)-C(15)	121.0(3)
C(13)-C(14)-H(14)	119.5
C(15)-C(14)-H(14)	119.5
C(16)-C(15)-C(14)	119.9(3)
C(16)-C(15)-H(15)	120.1
C(14)-C(15)-H(15)	120.1
C(15)-C(16)-C(17)	119.7(3)
C(15)-C(16)-H(16)	120.1
C(17)-C(16)-H(16)	120.1
C(18)-C(17)-C(16)	120.3(3)
C(18)-C(17)-H(17)	119.8
C(16)-C(17)-H(17)	119.8
C(17)-C(18)-C(13)	121.4(3)
C(17)-C(18)-H(18)	119.3
C(13)-C(18)-H(18)	119.3
C(20)-C(19)-C(5)	112.7(3)
C(20)-C(19)-H(19A)	109.0
C(5)-C(19)-H(19A)	109.1
C(20)-C(19)-H(19B)	109.1
C(5)-C(19)-H(19B)	109.1

H(19A)-C(19)-H(19B)	107.8
C(21)-C(20)-C(19)	126.9(4)
C(21)-C(20)-H(20)	116.5
C(19)-C(20)-H(20)	116.5
C(20)-C(21)-H(21A)	120.0
C(20)-C(21)-H(21B)	120.0
H(21A)-C(21)-H(21B)	120.0
C(9)-C(22)-H(22A)	109.5
C(9)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
C(9)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for rowan1m. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	29(1)	35(1)	25(1)	-1(1)	1(1)	0(1)
N(1)	31(1)	34(1)	25(1)	2(1)	3(1)	5(1)
O(1)	49(1)	32(1)	40(1)	-10(1)	4(1)	-2(1)
O(2)	28(1)	49(1)	33(1)	5(1)	-4(1)	0(1)
C(1)	33(1)	29(2)	25(1)	0(1)	5(1)	-4(1)
C(2)	42(2)	48(2)	36(2)	-1(1)	4(1)	-17(2)
C(3)	47(2)	69(2)	34(2)	2(2)	-7(2)	-23(2)
C(4)	31(2)	69(2)	42(2)	21(2)	-4(1)	-5(2)
C(5)	26(2)	49(2)	36(2)	11(1)	8(1)	8(1)
C(6)	30(1)	33(2)	16(1)	-2(1)	1(1)	2(1)
C(7)	32(2)	36(2)	32(2)	1(1)	3(1)	5(1)
C(8)	50(2)	39(2)	32(2)	3(1)	-1(2)	-5(2)
C(9)	35(2)	58(2)	21(2)	-4(2)	-2(1)	-13(2)
C(10)	28(2)	61(2)	22(1)	-11(2)	-1(1)	0(2)
C(11)	31(1)	39(2)	25(2)	-5(1)	1(1)	3(1)
C(12)	34(2)	28(2)	42(2)	-1(1)	11(1)	-2(1)
C(13)	28(1)	30(2)	29(2)	-2(1)	3(1)	-6(1)

C(14)	39(2)	37(2)	27(2)	5(1)	4(1)	3(1)
C(15)	39(2)	39(2)	33(2)	-5(1)	7(1)	4(1)
C(16)	35(2)	25(2)	48(2)	-3(1)	1(1)	2(1)
C(17)	32(2)	39(2)	38(2)	3(1)	-10(1)	-5(1)
C(18)	34(2)	37(2)	24(1)	-4(1)	-1(1)	-8(1)
C(19)	33(2)	40(2)	45(2)	11(1)	10(2)	9(1)
C(20)	41(2)	55(2)	74(3)	15(2)	12(2)	8(2)
C(21)	50(2)	44(2)	107(3)	8(2)	22(2)	9(2)
C(22)	49(2)	88(3)	46(2)	5(2)	1(2)	-29(2)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for rowan1m.

	x	y	z	U(eq)
H(1)	59	10783	4675	35
H(2A)	2333	11142	5367	50
H(2B)	929	11211	6028	50
H(3A)	1695	9864	6582	60
H(3B)	3241	10486	6576	60
H(4A)	3996	9114	6053	57
H(4B)	4210	9826	5368	57
H(5)	2942	8700	4740	44
H(7)	1587	11371	3248	40
H(8)	3792	12217	2841	49
H(10)	6796	10153	2982	45
H(11)	4609	9288	3399	38
H(12A)	-1826	9644	5175	41
H(12B)	-1035	9811	6040	41
H(14)	-2530	10779	6895	41
H(15)	-4487	11863	7087	44
H(16)	-5547	12605	5966	43
H(17)	-4714	12228	4657	44
H(18)	-2806	11139	4463	38
H(19A)	603	8592	6035	47
H(19B)	404	8072	5210	47

H(20)	3095	7745	6286	68
H(21A)	1226	6608	5462	80
H(21B)	2777	6404	6054	80
H(22A)	6766	12023	2010	91
H(22B)	7969	11501	2584	91
H(22C)	7071	12337	2914	91

Crystal data for $C_{22}H_{27}NO_2S$; $M = 369.51$. Crystallises from hexane as colourless blocks; crystal dimensions $0.41 \times 0.32 \times 0.28 \text{ mm}^3$. Orthorhombic, $a = 8.084(3)$ $b = 15.313(6)$ $c = 16.268(6)$ Å, $U = 2013.7(14)$ Å³, $Z = 4$, $D_c = 1.219 \text{ Mg/m}^3$, space group $P2_12_12_1$ (D_2^4 , No.19), Mo- K_α radiation ($\bar{\lambda} = 0.71073$ Å), $\mu(\text{Mo-}K_\alpha) = 0.176 \text{ mm}^{-1}$, $F(000) = 792$.

Data collected were measured on a Bruker Smart CCD area detector with Oxford Cryosystems low temperature system. Cell parameters were refined from the setting angles of 898 reflections (θ range $1.83 < 27.57^\circ$).

Reflections were measured from a hemisphere of data collected of frames each covering 0.3 degrees in omega. Of the 23080 reflections measured, all of which were corrected for Lorentz and polarisation effects and for absorption by semi empirical methods based on symmetry-equivalent and repeated reflections (minimum and maximum transmission coefficients 0.9313 and 0.9542), 3242 independent reflections exceeded the significance level $|F|/\sigma(|F|) > 4.0$. The structure was solved by direct methods and refined by full matrix least squares methods on F^2 . Hydrogen atoms were placed geometrically and refined with a riding model (including torsional freedom for methyl groups) and with U_{iso} constrained to be 1.2 (1.5 for methyl groups) times U_{eq} of the carrier atom. Refinement converged at a final $R = 0.0476$ ($wR_2 = 0.1006$, for all 4566 data, 236 parameters, mean and maximum δ/σ 0.000, 0.000) with allowance for the thermal anisotropy of all non-hydrogen atoms. Minimum and maximum final electron density -0.354 and 0.543 e.Å^{-3} . A weighting scheme $w = 1/[\sigma^2(F_o^2) + (0.0265 * P)^2 + 1.0450 * P]$ where $P = (F_o^2 + 2 * F_c^2)/3$ was used in the latter stages of refinement. Complex scattering factors were taken from the program package SHELXTL^Y as implemented on the Viglen Pentium computer.

Reference Y SHELXTL version, An integrated system for solving and refining crystal structures from diffraction data (Revision 5.1), Bruker AXS LTD

Supplementary material

anisotropic thermal vibrational parameters with e.s.d.s

hydrogen atom position parameters

observed structure amplitudes and calculated structure factors.