**3-(4-Chlorophenyl)-5-((3,4-difluorobenzyl)oxy)-[1,2,4]triazolo[4,3-a]pyrazine, OSM-S-259**



Representative Example: http://malaria.ourexperiment.org/uri/68a

Prepared according to General Procedure **D** from: **OSM-S-220** (154 mg, 0.58 mmol, 1.0 equiv.), **OSM-S-XXX** (80 μL, 100 mg, 0.69 mmol, 1.2 equiv.), KOH (110 mg, 2.00 mmol, 3.4 equiv.) and 18-crown-6 (18 mg, 0.07 mmol, 0.12 equiv.); 40 ˚C, 1.25 h; purified by automated flash chromatography over silica (Biotage Isolera, 30–100% EtOAc in hexanes) to give the title compound as fluffy white needles (86 mg, 38%); **m.p.** 181–182 °C; **IR** νmax (film)/cm-1 3070, 1612, 1509, 1303; **1H NMR** (500 MHz; DMSO-d*6*) δ: 9.11 (1H, s), 7.67 (1H, s), 7.66–7.64 (2H, m), 7.36–7.33 (2H, m), 7.13–7.05 (3H, m), 5.29 (2H, s); **13C NMR** (126 MHz; DMSO-d*6*) δ: 147.4, 145.4, 143.8, 135.4, 134.6, 132.4, 127.4, 126.7, 131.7 (2C), 125.4 (2C), 117.4, 117.3, 109.2, 70.9; **m/z** (APCI+) 373 [M+H]+; **HRMS** (APCI+) found 373.06609 [M+H]+, C18H12ClF2N4O requires 373.06622.

Part 1 of this procedure was adapted from a procedure developed by Ms Katrina Badiola.78 To a dry flask was added 3,4-difluorobenzaldehyde (0.4 mL, 520 mg, 3.7 mmol, 1.0 equiv.) and tetrahydrofuran (10 mL). The mixture was cooled in an ice bath (0 °C) under argon. Sodium borohydride (500 mg, 13.0 mmol, 3.5 equiv.) was added carefully in portions. The reaction mixture was stirred for 15 min on ice before warming to room temperature and stirring for a further 25 min. The solution was adjusted to pH 7 with hydrochloric acid (1 M) and extracted with dichloromethane (3 × 15 mL). The combined organic fractions were dried (MgSO4) and concentrated under reduced pressure and dried *in vacuo* to give the crude material ((3,4-difluorophenyl)methanol) as a pale yellow oil (620 mg, 116%). The identity of the crude material was verified by 1H NMR (CDCl3) and carried through to the next step without purification.

*ClC(C=C1)=CC=C1C2=NN=C3C=NC=C(OCC4=CC=C(F)C(F)=C4)N32*

*InChI=1S/C18H11ClF2N4O/c19-13-4-2-12(3-5-13)18-24-23-16-8-22-9-17(25(16)18)26-10-11-1-6-14(20)15(21)7-11/h1-9H,10H2*