

extract was washed with saturated brine, and dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure. The obtained solid was triturated with hexane/ethyl acetate, and washed with hexane/ethyl acetate to
5 give the title compound (13.8 g).

MS (API-): $[M-H]^-$ 250.2.

[0370]

D) tert-butyl (1-(4-(difluoromethoxy)phenyl)propyl)carbamate

Under chlorodifluoromethane atmosphere, to a solution of
10 tert-butyl (1-(4-hydroxyphenyl)propyl)carbamate (833 mg) and benzyltriethylammonium chloride (226 mg) in tetrahydrofuran (20 mL) was slowly added 8 M aqueous sodium hydroxide solution under ice-cooling. The reaction mixture was stirred at room temperature for 2 hr, water was added thereto, and the mixture
15 was extracted with ethyl acetate. The extract was washed with saturated brine, and dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/ethyl acetate) to give the title compound (832 mg).

20 ^1H NMR (300 MHz, DMSO- d_6) δ 0.81 (3H, t, $J = 7.3$ Hz), 1.35 (9H, s), 1.49-1.71 (2H, m), 4.26-4.45 (1H, m), 6.90-7.47 (6H, m).

[0371]

E) tert-butyl 1-(4-(difluoromethoxy)phenyl)propan-1-amine hydrochloride

25 To a solution of tert-butyl (1-(4-(difluoromethoxy)phenyl)propyl)carbamate (830 mg) in ethyl acetate (5 mL) was added 4 M hydrogen chloride/ethyl acetate (10 mL) solution. The reaction mixture was stirred at room temperature for 3 hr, and the solvent was evaporated under
30 reduced pressure to give the title compound (643 mg).

^1H NMR (300 MHz, DMSO- d_6) δ 0.75 (3H, t, $J = 7.3$ Hz), 1.67-2.10 (2H, m), 4.06-4.24 (1H, m), 6.99-7.62 (5H, m), 8.51 (3H, brs).

[0372]

F) N-(1-(4-(difluoromethoxy)phenyl)propyl)-2-oxo-2,3-dihydropyrido[2,3-b]pyrazine-4(1H)-carboxamide
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