carboxylate, yield 97.1%; ESI-MS(m/z): 573.3 $[M+H]^+$.

step b): Preparation of (*R*)-4-((1-(3-(difluoromethyl)-2-fluorophenyl)ethyl)amino)-6-(1-methylcyclopropyl)-1-(piperazin-1-yl)pyrido[3,4-*d*]pyridazin-7(6*H*)-one

Tert-butyl (*R*)-4-(4-((1-(3-(difluoromethyl)-2-fluorophenyl)ethyl)amino)-6-(1-methylcyclopropyl)-7-oxo-6,7-dihydropyrido[3,4-*d*]pyridazin-1-yl)piperazine-1-carboxylate (230 mg, 0.402 mmol), 1,4-dioxane (2 mL) and a solution of hydrogen chloride in 1,4-dioxane (8 mL, 4 N) were added to a reaction flask. The mixture was stirred to react at room temperature for 1 h. After the reaction was completed, the mixture was concentrated under reduced pressure. The residue was purified by Prep-HPLC (separation method 3) to obtain (*R*)-4-((1-(3-(difluoromethyl)-2-fluorophenyl)ethyl)amino) -6-(1-methylcyclopropyl)-1-(piperazin-1-yl)pyrido[3,4-*d*]pyridazin-7(6*H*)-one, yield 22.0%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.22 (s, 1H), 7.62 (t, J = 7.2 Hz, 1H), 7.55 (d, J = 6.8 Hz, 1H), 7.48 (t, J = 6.8 Hz, 1H), 7.38-7.11 (m, 2H), 6.41 (s, 1H), 5.61-5.51 (m, 1H), 2.95-2.86 (m, 4H), 2.86-2.80 (m, 4H), 1.58-1.49 (m, 6H), 1.20-1.04 (m, 4H); ESI-MS(m/z): 473.0 $[M+H]^+$.

Example 79

Preparation of (*R*)-1-(4-acetylpiperazin-1-yl)-4-((1-(3-(difluoromethyl)-2-fluorophenyl)ethyl)amino)-6-(1-methylcyclopropyl)pyrido[3,4-*d*]pyridazin-7(6*H*)-one