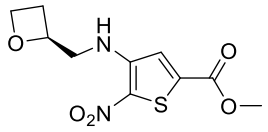
liquid; after the dropwise addition, the reaction was continued for 30 minutes in the ice-salt bath. The reaction liquid was slowly poured into an ice-water solution, and a large amount of white solids precipitated out. The filter cake was collected by filtration, washed with water (10 mL × 2), and dried to obtain 1b (2.6 g, yield 99.3%).

[0244] LCMS m/z = 265.9 $[M+1]^+$.

[0245] ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 3.96 (s, 3H).

Step 2: methyl (S)-5-nitro-4-((oxetan-2-ylmethyl)amino)thiophene-2-carboxylate (1c)



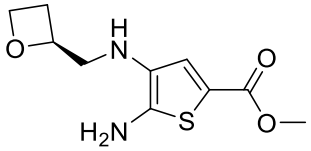
1c

[0246] At room temperature, 1b (1.3 g, 5.0 mmol) was dissolved in acetonitrile (30 mL), then 1c-1 (436.0 mg, 5.0 mmol) and potassium carbonate (2.1 g, 15.0 mmol) were added ~~(100 mL)~~ successively, heated to 60°C, and continued to react for 18 h. The reaction liquid was cooled to room temperature, filtered, and the filtrate was collected and concentrated. The obtained crude product was separated and purified by silica gel column chromatography (petroleum ether/ethyl acetate (v/v) = 2:1), and concentrated to obtain 1c (854.0 mg, yield 62.7%).

[0247] LCMS m/z = 273.1 $[M+1]^+$.

[0248] ^1H NMR (400 MHz, $CDCl_3$) δ 8.12 – 8.03 (m, 1H), 7.35 (s, 1H), 5.10 – 5.00 (m, 1H), 4.74 – 4.66 (m, 1H), 4.58 – 4.50 (m, 1H), 3.92 (s, 3H), 3.71 – 3.57 (m, 2H), 2.80 – 2.68 (m, 1H), 2.60 – 2.48 (m, 1H).

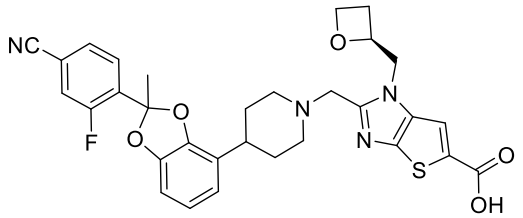
Step 3: methyl (S)-5-amino-4-((oxetan-2-ylmethyl)amino)thiophene-2-carboxylate (1d)



1d

[0249] At room temperature, 1c (854.0 mg, 3.1 mmol) was dissolved in methanol (30 mL), then palladium on carbon (170.0 mg, 1.6 mmol) was added, and the reaction was continued for 18 h under hydrogen atmosphere. The reaction liquid was filtered to remove palladium on carbon, the filtrate was collected and concentrated to obtain a crude product, and the obtained crude product was separated and purified by silica gel column

Step 4: 2-((4-(2-(4-cyano-2-fluorophenyl)-2-methylbenzo[d][1,3]dioxol-4-yl)piperidin-1-yl)methyl)-1-(((S)-oxetan-2-yl)methyl)-1H-thieno[2,3-d]imidazole-5-carboxylic acid (Compound 5)

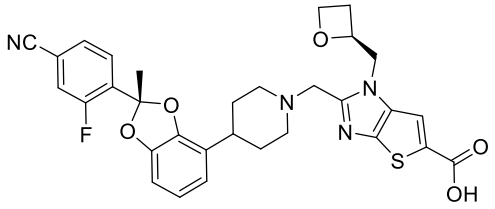


Compound 5

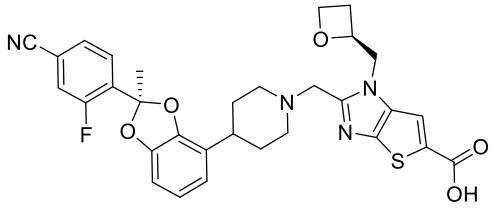
[0310] 5j (100mg, ~~0.~~0.17 mmol) and lithium hydroxide monohydrate (115 mg, 2.73 mmol) were added to a mixed solvent of acetonitrile (4 mL) and water (1 mL), and stirred at 50°C for 8 hours. The reaction liquid was cooled to room temperature, adjusted with 1N hydrochloric acid to pH=6, and extracted with ethyl acetate. The organic phase was dried with anhydrous sodium sulfate, filtered and spin-dried. The residue was separated and purified by silica gel column chromatography to obtain (2-((4-(2-(4-cyano-2-fluorophenyl)-2-methylbenzo[d][1,3]dioxol-4-yl)piperidine-1-yl)methyl)-1-((S)-oxoalkane-2-yl)methyl)-1H-thieno[2,3-d]imidazole-5-carboxylic acid (compound 5) (50 mg, 48% yield).

[0311] LCMS m/z = 589.2 $[M+1]^+$.

[0312] ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.94 (br, 1H), 7.97 (d, 1H), 7.81 (s, 1H), 7.77 – 7.69 (m, 2H), 6.85– 6.70 (m, 3H), 5.14 – 5.05 (m, 1H), 4.69 – 4.61 (m, 1H), 4.57 – 4.44 (m, 2H), 4.40 – 4.32(m, 1H), 3.82 (d, 1H), 3.72 (d, 1H), 2.98 (d, 1H), 2.88 (d, 1H), 2.73– 2.60 (m, 2H), 2.45– 2.36 (m, 1H), 2.24 – 2.10 (m, 2H), 2.05 (s, 3H), 1.79 – 1.63 (m, 4H).



Compound 5-a



Compound 5-b

[0313] 2g compound 5 was prepared by SFC and dried to obtain **compound 5-1** (600 mg, yield 30%) as a white solid with a retention time of 6.441 minutes. **compound 5-2** (500 mg, yield 25%) as a white solid with a retention time of 7.104 minutes.