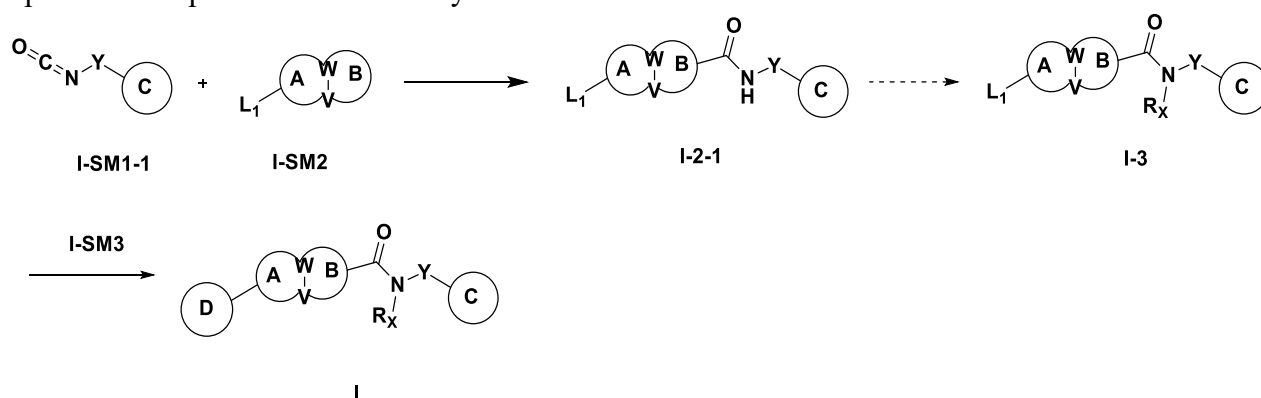


T384	
T385	
T386	
T387	
T388	
<u>T388'</u>	
T389	
T390	
T391	

wherein, A, B, C, D, W, V, Y and R_x are defined as in the formula (I) above; R_x' is selected from R_x and a group which may be converted to R_x by derivatization step (c2); L_1 is selected from halogen, and the halogen may be selected from F, Cl, Br and I; the compound I-SM3 is borate containing a ring D group.

5

Specific examples of scheme 1 may include scheme 1-1:



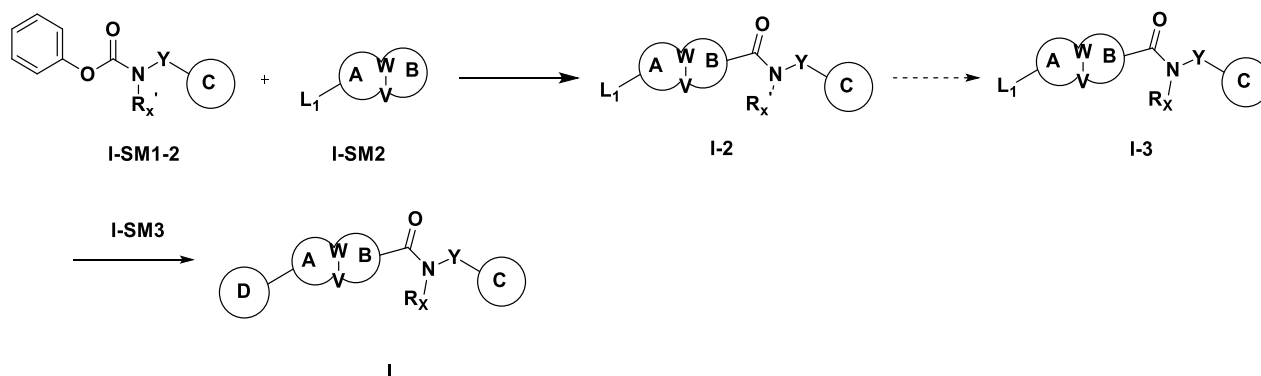
a1') reacting a compound I-SM1-1 with a compound I-SM2 under an alkaline condition to obtain a compound I-2-1;

a2) optionally, further subjecting the compound I-2-1 to derivatization treatment of R_x' on amide nitrogen to obtain a compound I-3; and

a3') subjecting the compound I-2-1 or I-3 and a compound I-SM3 to Suzuki coupling reaction to obtain a compound I;

wherein, A, B, C, D, W, V, Y and R_x are defined as in the formula (I) above; R_x is not H; L_1 is selected from halogen, and the halogen may be selected from F, Cl, Br and I; the compound I-SM3 is borate containing a ring D group;

or scheme 1-2:



20

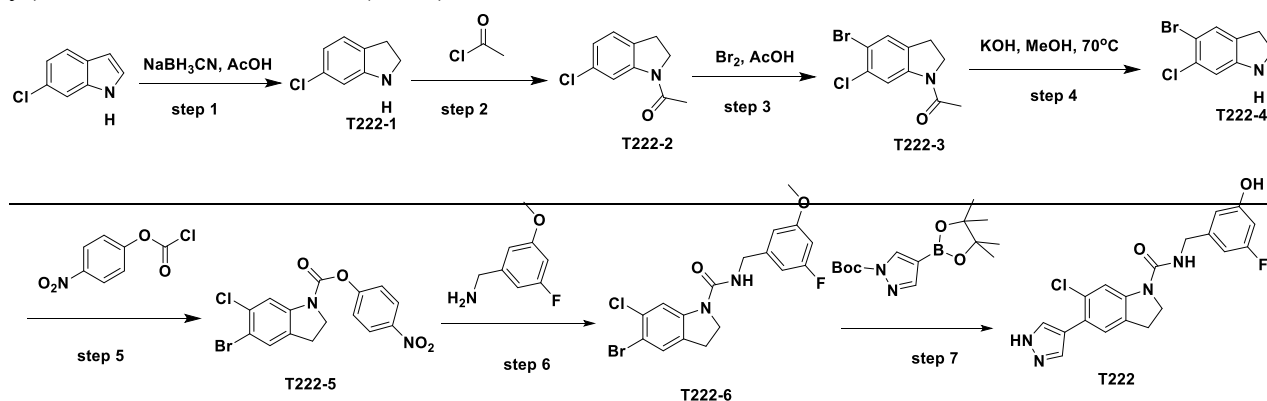
carboxamide (T221-3)

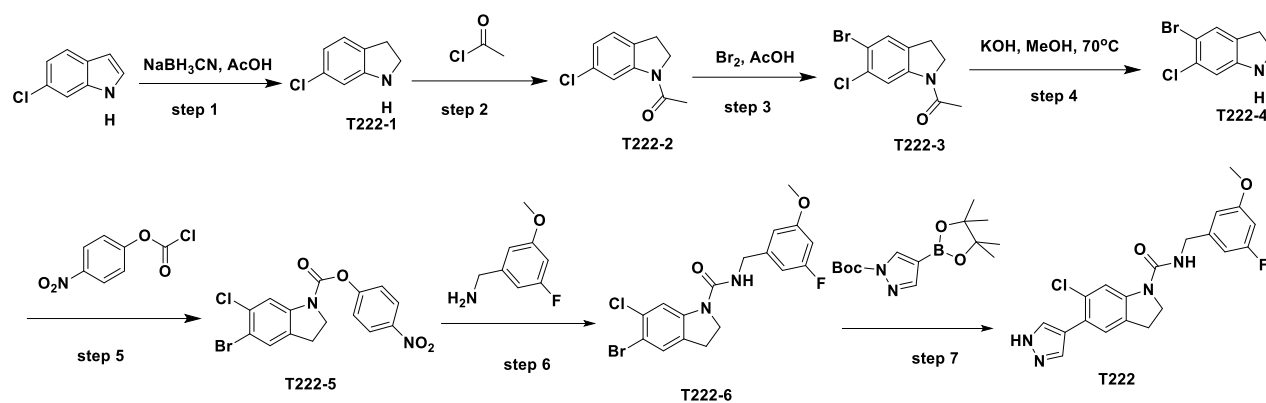
(3-fluoro-5-methoxyphenyl)methylamine (1333 mg) was added directly to the reaction solution obtained in the previous step, and the mixture was stirred overnight under reflux. The reaction solution was concentrated by rotary evaporation, and the residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 2:1) to give a pale yellow oily liquid (700 mg, 85% purity, 68% yield). LC-MS [M+H]⁺: 412.6.

7 Preparation of compound 7-chloro-*N*-(3-fluoro-5-methoxybenzyl)-5-(1*H*-pyrazol-4-yl)indoline-1-carboxamide (T221)

Compound T221-3 (500 mg), 1-Boc-pyrazole-4-boronic acid pinacol ester (714 mg), potassium carbonate (500 mg) and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (89 mg) were dissolved in anhydrous dioxane (15 mL) and water (3 mL) under nitrogen atmosphere, and the mixture was reacted at 90 °C for 12 h. The reaction solution was cooled to room temperature, diluted with water (20 mL) and extracted with ethyl acetate (15 mL × 2). The organic phases were combined, washed with saturated brine (15 mL), dried over anhydrous sodium sulfate, filtered and concentrated, and the resulting crude product was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 0–100%) and then purified by preparative chromatography to give a white solid (40 mg, 8.7% yield). LC-MS [M+H]⁺: 400.9. ¹H NMR (400 MHz, DMSO) δ 12.91(brs, 1H), 8.05 (brs, 2H), 7.66 (t, J = 6.0 Hz, 1H), 7.46 (s, 1H), 7.44 (s, 1H), 6.78 – 6.67 (m, 3H), 4.30 (d, J = 5.8 Hz, 2H), 4.03 (t, J = 7.9 Hz, 2H), 3.77 (s, 3H), 3.09 (t, J = 7.9 Hz, 2H).

Example 16: Preparation of 7-chloro-*N*-(3-fluoro-5-methoxybenzyl)-5-(1*H*-pyrazol-4-yl)indoline-1-carboxamide (T222)





1. Preparation of compound 6-chloroindoline (T222-1)

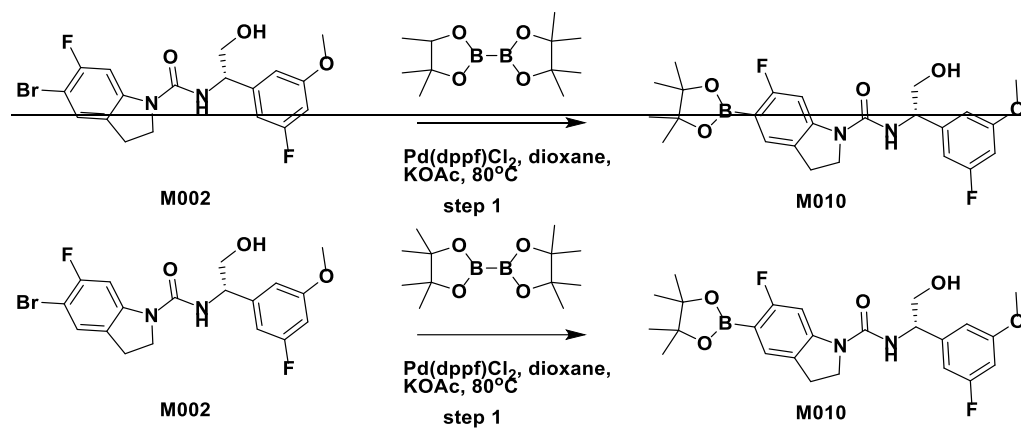
6-chloroindole (2.0 g) was dissolved in acetic acid (20 mL), and in an ice water bath, sodium cyanoborocyanide (1.0 g) was slowly added at 0 °C. After the addition was completed, the mixture was warmed to room temperature and stirred for 12 h. After the reaction was completed, the reaction solution was placed in an ice bath, the pH was adjusted to be alkaline with NaOH solution (1 N), and dichloromethane was added for extraction. The organic phase was dried over anhydrous sodium sulfate and concentrated by rotary evaporation to give a crude product in the form of a white solid (2.2 g). LC-MS $[M+H]^+$: 153.9.

2 Preparation of compound 1-(6-chloroindoline-1-yl)ethan-1-one (T222-2)

Compound T222-1 (2.2 g) and pyridine (1.3 g) were dissolved in tetrahydrofuran (50 mL), and in an ice water bath, acetyl chloride (1.1 g) was slowly added dropwise at 0 °C. The mixture was warmed to room temperature and stirred overnight. Water (50 mL) was added to quench the reaction, and ethyl acetate (60 mL $\times$ 3) was added for extraction. The organic phases were combined, washed with saturated brine (40 mL $\times$ 2), dried over anhydrous sodium sulfate, filtered and concentrated by rotary evaporation. The resulting crude product was purified by silica gel column chromatography (petroleum ether:ethyl acetate = 10:1) to give a white solid (2.5 g, 97% two-step yield). LC-MS $[M+H]^+$: 239.8.

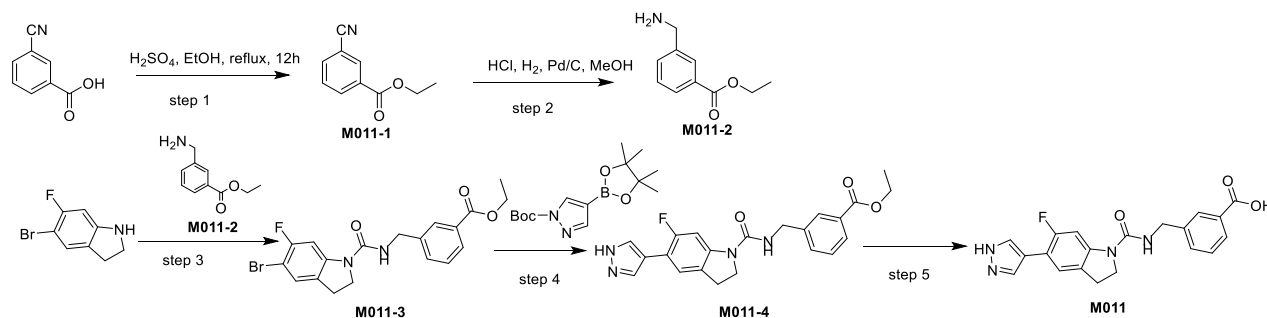
3 Preparation of compound 1-(5-bromo-6-chloroindoline-1-yl)ethan-1-one (T222-3)

Compound T222-2 (2.3 g) was dissolved in acetic acid (30 mL), and in an ice water bath, bromine (2.1 g) was slowly added dropwise. The mixture was warmed to room temperature and reacted for 4 h. Solid was precipitated out during the reaction, and after the reaction was completed, the mixture was filtered under vacuum. The filter cake was washed once with ethyl



A solution of compound M002 (200 mg), 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (238 mg) and potassium acetate (138 mg) were dissolved in dioxane (4 mL) under nitrogen atmosphere, and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (34 mg) was added. The mixture was reacted at 80 °C for 6 h. The reaction solution was concentrated under reduced pressure to give the compound (crude product), MS (M+H)⁺ = 475.3.

10 Example 32: Preparation of Intermediate 11, Compound 3-((6-fluoro-5-(1*H*-pyrazol-4-yl)indoline-1-carboxamido<oxalylamino>)methyl)benzoic acid (M011)



(1) Preparation of compound ethyl 3-cyanobenzoate (M011-1)

3-cyanobenzoic acid (3.0 g) was dissolved in ethanol (30 mL), and concentrated sulfuric acid (3 mL) was added. The mixture was stirred under reflux for 12 h. The reaction solution was concentrated under reduced pressure, diluted with water (50 mL) and extracted with ethyl acetate (30 mL × 2). The organic phases were combined, washed with saturated brine (30 mL), dried over anhydrous sodium sulfate, filtered and concentrated, and the residue was purified by silica gel column chromatography (PE/EA = 10/1) to give a yellow oily liquid (2.0 g, 57% yield). LC-MS [M+H]⁺: 176.0.

(2) Preparation of compound ethyl 3-(aminomethyl)benzoate (M011-2)

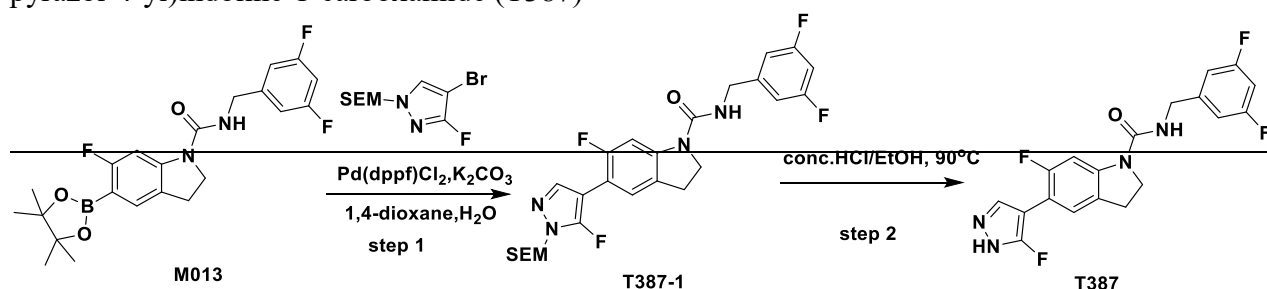
1,4-dioxane (3 mL) and water (0.5 mL) under nitrogen atmosphere, and compound T380-3 (500 mg), potassium carbonate (296 mg) and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (78 mg) were added. The mixture was reacted at 80 °C for 3 h. The reaction solution was cooled to room temperature, water (30 mL) was added, and then ethyl acetate (30 mL × 3) was added for extraction. The organic phases were combined, washed with saturated brine (30 mL × 2), dried over anhydrous sodium sulfate, filtered and concentrated by rotary evaporation, and the resulting crude product was purified by silica gel column chromatography (eluent: petroleum ether:ethyl acetate = 2:1) to give compound T380-4 (200 mg, 33.00% yield). MS $[M+H]^+ = 555.3$.

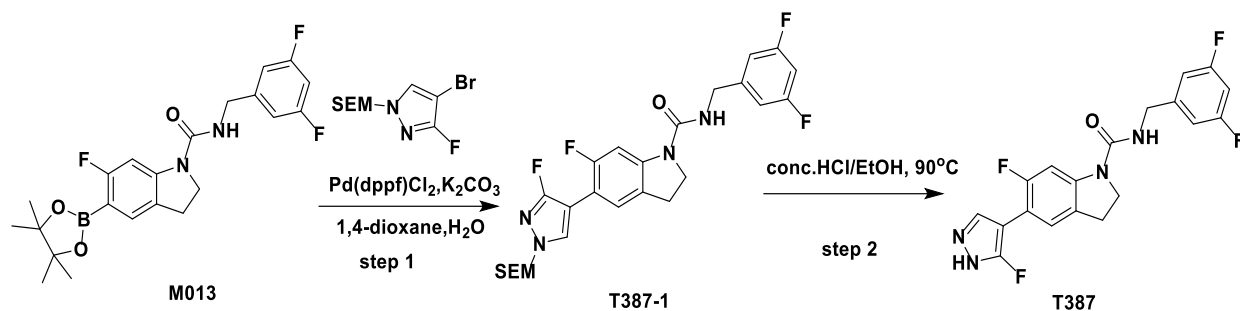
5 Preparation of compound *N*-(3-(cyclopropylmethoxy)benzyl)-6-fluoro-5-(3-fluoro-1*H*-pyrazol-4-yl)indoline-1-carboxamide (T380)

Compound T380-4 (210 mg) was dissolved in dichloromethane (5 mL), and trifluoroacetic acid (2 mL) was added. The mixture was reacted at room temperature for 5 h. After the reaction was completed, the reaction solution was directly concentrated by rotary evaporation, and the resulting crude product was purified by high pressure liquid phase chromatography to give compound T380 in the form of a white solid (14.4 mg, 8.92% yield). MS $[M+H]^+ = 425.1$.

^1H NMR (400 MHz, DMSO) δ 12.61 (s, 1H), 7.90 (s, 1H), 7.65 (d, $J = 12.9$ Hz, 1H), 7.37 (t, $J = 5.9$ Hz, 1H), 7.31 (d, $J = 7.7$ Hz, 1H), 7.21 (t, $J = 8.1$ Hz, 1H), 6.91 – 6.84 (m, 2H), 6.78 (dd, $J = 8.2, 1.5$ Hz, 1H), 4.30 (d, $J = 5.8$ Hz, 2H), 4.01 (t, $J = 8.7$ Hz, 2H), 3.79 (d, $J = 7.0$ Hz, 2H), 3.15 (t, $J = 8.6$ Hz, 2H), 1.25 – 1.18 (m, 1H), 0.60 – 0.51 (m, 2H), 0.36 – 0.27 (m, 2H).

Example 51: Preparation of Compound *N*-(3,5-difluorobenzyl)-6-fluoro-5-(5-fluoro-1*H*-pyrazol-4-yl)indoline-1-carboxamide (T387)





1 Preparation of compound *N*-(3,5-difluorobenzyl)-6-fluoro-5-((~~53~~-5-fluoro-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-pyrazol-4-yl)indoline-1-carboxamide (T387-1)

5 4-bromo-3-fluoro-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-pyrazole (172 mg) was dissolved in 1,4-dioxane (3 mL) and water (0.5 mL) under nitrogen atmosphere, and compound M013 (250 mg), potassium carbonate (240 mg) and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (42 mg) were added. The mixture was reacted at 80 °C for 3 h. The reaction solution was cooled to room temperature, water (30 mL)

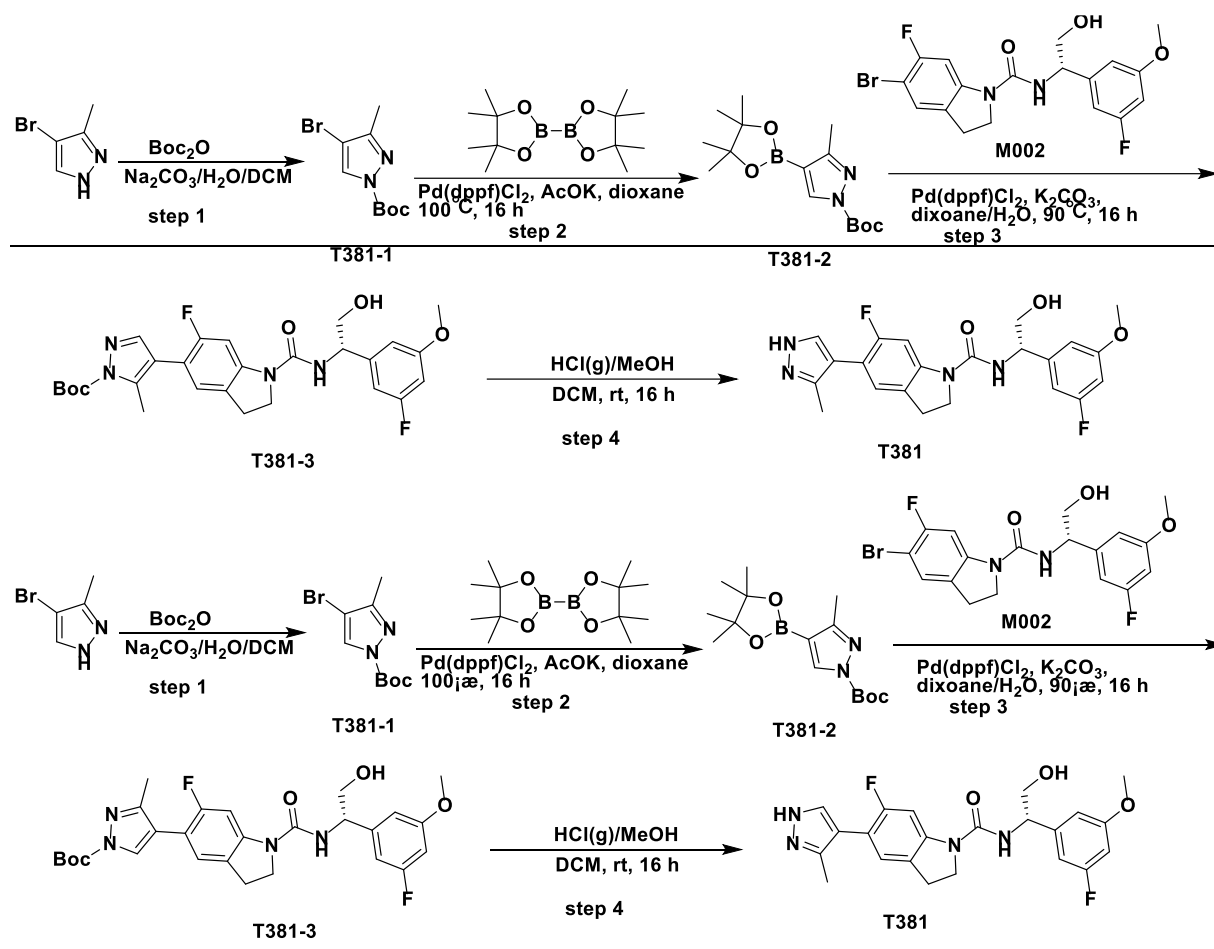
10 was added, and then ethyl acetate (30 mL × 3) was added for extraction. The organic phases were combined, washed with saturated brine (30 mL × 2), dried over anhydrous sodium sulfate, filtered and concentrated by rotary evaporation, and the resulting crude product was purified by silica gel column chromatography (eluent: petroleum ether:ethyl acetate = 2:1) to give compound T387-1 in the form of a yellow oil (100 mg, 32.40% yield). MS $[M+Na]^+ = 543.0$.

15 2 Preparation of compound *N*-(3,5-difluorobenzyl)-6-fluoro-5-(5-fluoro-1*H*-pyrazol-4-yl)indoline-1-carboxamide (T387)

Compound T387-1 (100 mg) was dissolved in ethanol (5 mL), and concentrated hydrochloric acid (1 mL) was added. The mixture was reacted at 90 °C for 1 h. After the reaction was completed, the reaction solution was directly concentrated by rotary evaporation, and the

20 resulting crude product was dissolved in dichloromethane, basified with triethylamine and purified by preparative plate (petroleum ether:ethyl acetate = 1:1) to give compound T387 in the form of a white solid (21.76 mg, 29.05% yield). MS $[M+H]^+ = 493.4$.

^1H NMR (400 MHz, DMSO) δ 12.61 (s, 1H), 7.90 (d, $J = 1.6$ Hz, 1H), 7.65 (d, $J = 12.8$ Hz, 1H), 7.46 (t, $J = 5.9$ Hz, 1H), 7.32 (d, $J = 7.7$ Hz, 1H), 7.13 – 7.02 (m, 3H), 4.35 (d, $J = 5.8$ Hz, 2H), 4.04 (t, $J = 8.7$ Hz, 2H), 3.16 (t, $J = 8.6$ Hz, 2H).

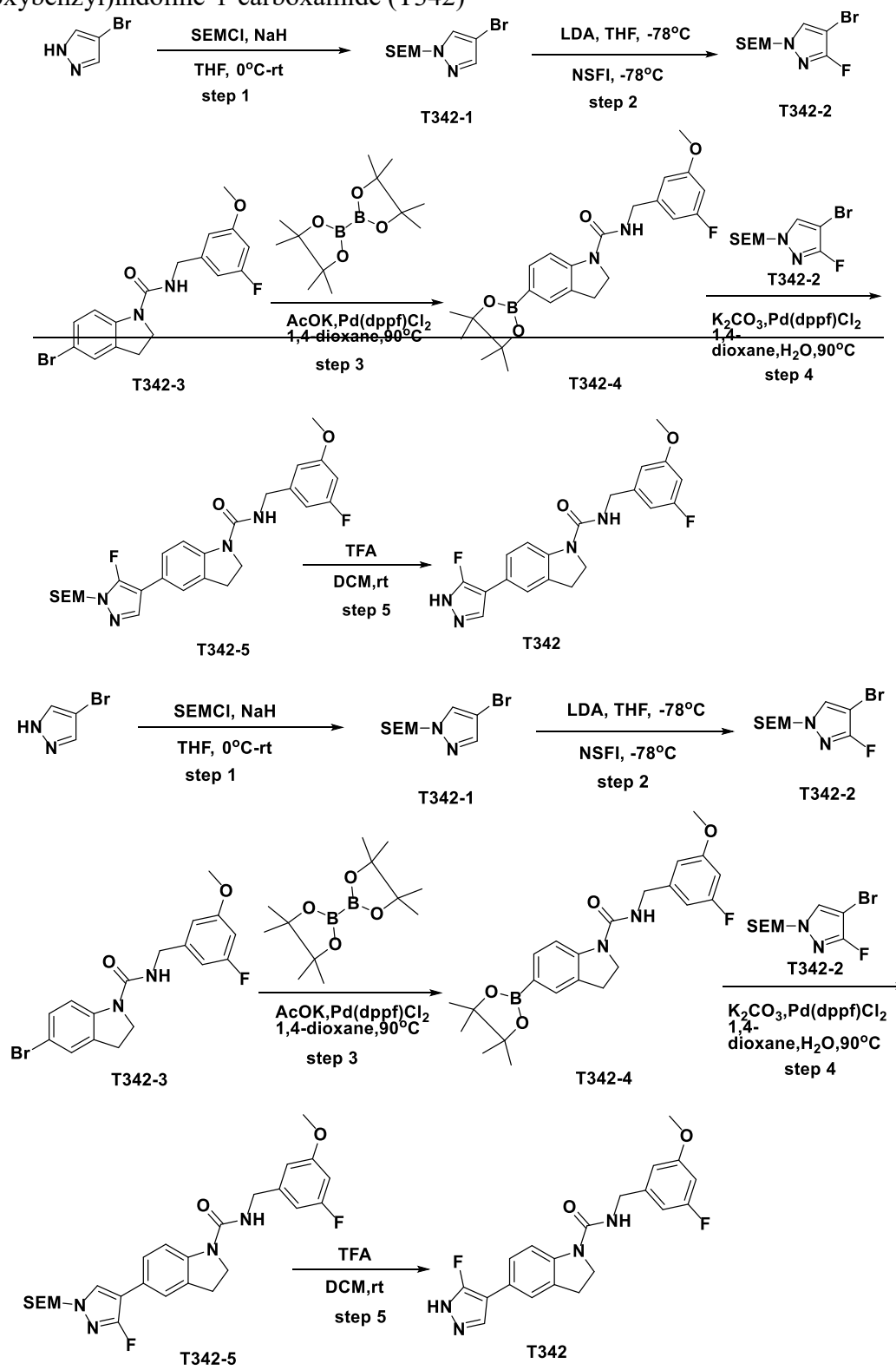


1 Preparation of compound *tert*-butyl 4-bromo-3-methyl-1*H*-pyrazole-1-carboxylate (T381-1)
 4-bromo-3-methylpyrazole (3.00 g) was dissolved in dichloromethane (30 mL), and sodium
 5 carbonate (10.32 g) and 4-dimethylaminopyridine (2.93 g) were added, and then di-*tert*-butyl
 dicarbonate (4.87 g) was added at room temperature. The mixture was reacted at room
 temperature for 16 h. Dichloromethane (50 mL) was added, and the mixture was washed with
 water (50 mL) and saturated brine (30 mL), dried over anhydrous sodium sulfate, filtered and
 concentrated to give a crude product in the form of a colorless oil (6 g). MS $[M+Na]^+ =$
 10 282.9/285.0.

2 Preparation of compound *tert*-butyl 3-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazole-1-carboxylate (T381-2)

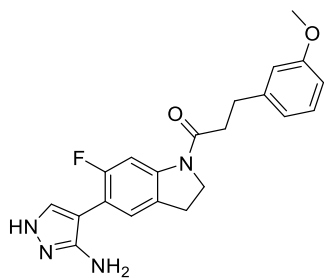
Compound T381-1 (6.00 g), potassium acetate (2.69 g), bis(pinacolato)diboron (5.58 g) and
 [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (1.07 g) were added in a 250 mL
 15 single-necked flask, followed by addition of 1,4-dioxane (60 mL). The mixture was heated to
 100 °C and reacted for 16 h under nitrogen atmosphere. The reaction solution was filtered and
 concentrated, and the resulting crude product was separated by silica gel column

Example 73: Preparation of Compound 5-(5-fluoro-1*H*-pyrazol-4-yl)-*N*-(3-fluoro-5-methoxybenzyl)indoline-1-carboxamide (T342)

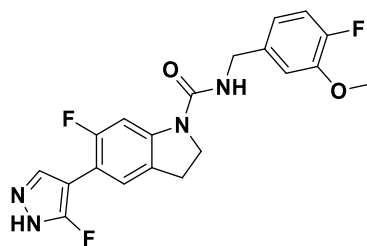


5 1 Preparation of compound 4-bromo-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-pyrazole (T342-1)

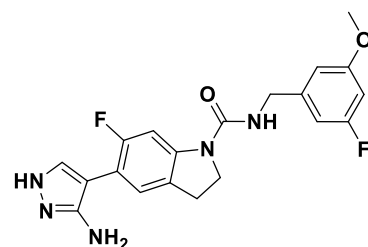
4-bromo-1*H*-pyrazole (10.0 g) was dissolved in anhydrous tetrahydrofuran (100 mL) under



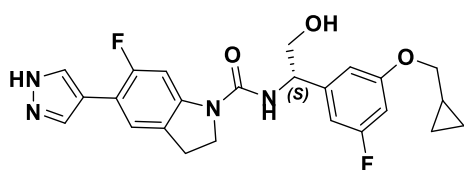
T383



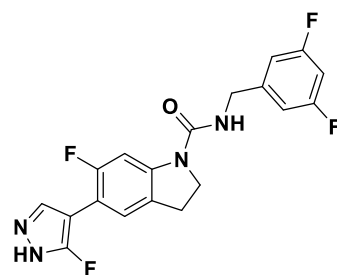
T384



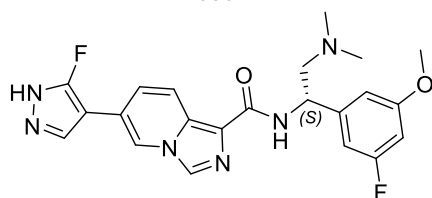
T385



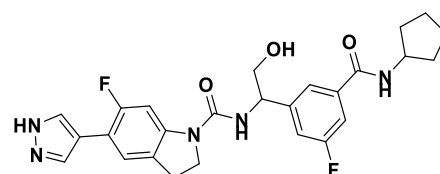
T386



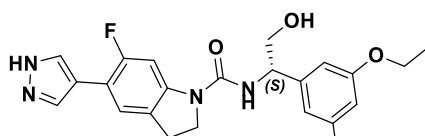
T387



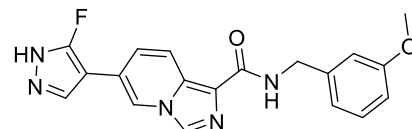
T388



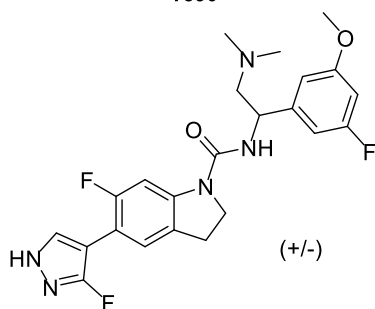
T389



T390

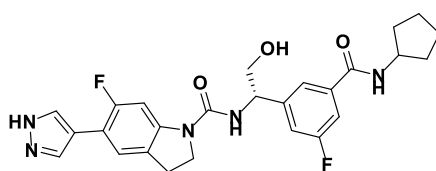


T391

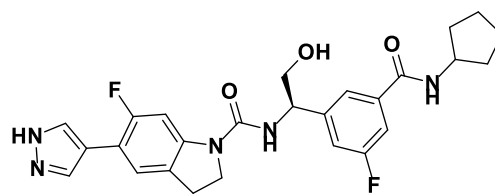


T388'

5



T389-S



T389-R

7. A method for preparing the compound of formula (I) or the racemate, the stereoisomer, the