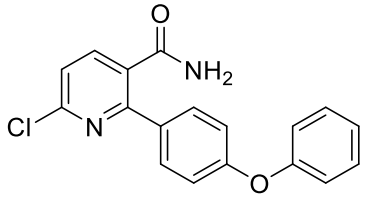
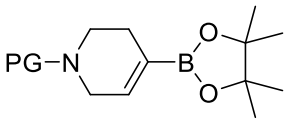
**CLAIMS**

1. A method for preparing 6-(1-acryloylpiperidin-4-yl)-2-(4-phenoxyphenyl)nicotinamide (Compound I), comprising:

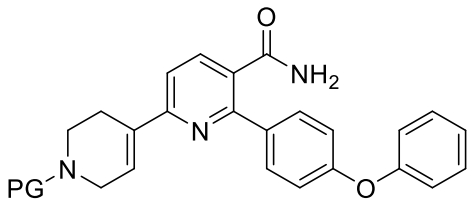
(a) heating a mixture of INA, SMC, and a first palladium-containing catalyst at 60-140 ºC to obtain INB,




INA



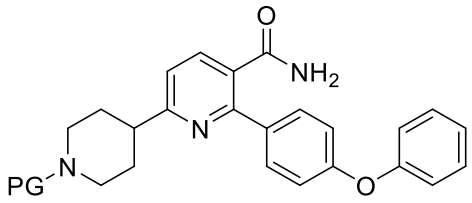

SMC




INB

wherein PG is a protecting group of tert-butyloxycarbonyl;

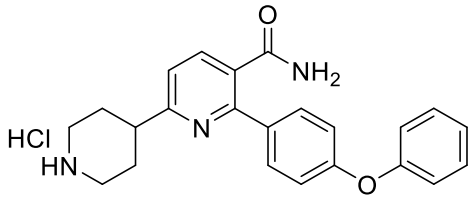
(b) hydrogenating INB under $H_2$ in the presence of a second palladium-containing catalyst to obtain a first solution comprising crude INC;




INC

(c) adding activated carbon to purify the crude INC, and then concentrating and dissolving the purified INC in ethyl acetate and ethanol to obtain a second solution comprising the purified INC;

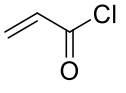
(d) adding HCl gas into the second solution to deprotect INC and obtain IND-HCl salt in a solid form;

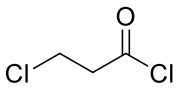


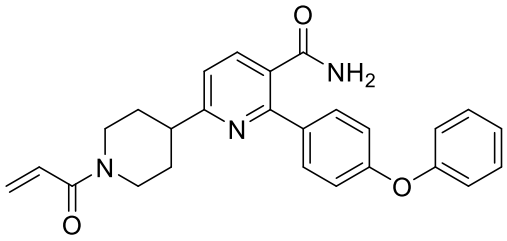

IND-HCl salt

(e) adding THF, $H_2O$ and $NaHCO_3$ to dissolve and neutralize the IND-HCl salt;

(f) reacting the IND-HCl salt with acryloyl chloride or 3-chloropropanoyl chloride under a basic condition to obtain 6-(1-acryloylpiperidin-4-yl)-2-(4-phenoxyphenyl)nicotinamide



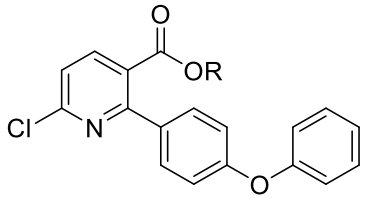



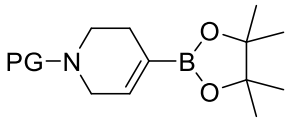

acryloyl chloride 3-chloropropanoyl chloride Compound I .

2. A method for preparing 6-(1-acryloylpiperidin-4-yl)-2-(4-phenoxyphenyl)nicotinamide (Compound I), comprising:

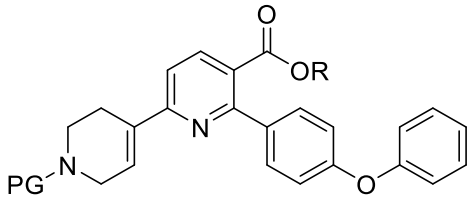
(a) heating a mixture of INA', SMC, and a first palladium-containing catalyst at 60-140 ºC to obtain INB',




INA'



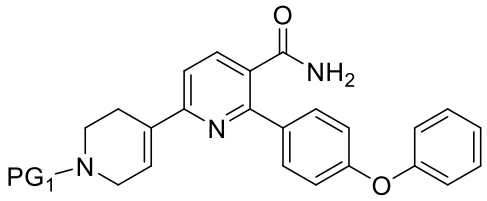

SMC



INB’

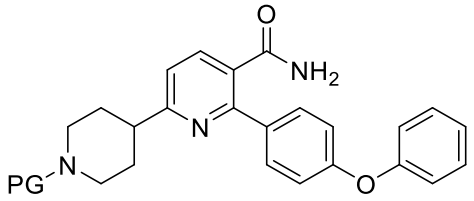
wherein R is H or $C_{1-4}$ alkyl,
PG is a protecting group of tert-butyloxycarbonyl;

(b) amidating INB’ by first treating with oxalyl chloride and then ammonia when R is H, or by reacting with ammonia when R is $C_{1-4}$ alkyl, to obtain INB;



INB

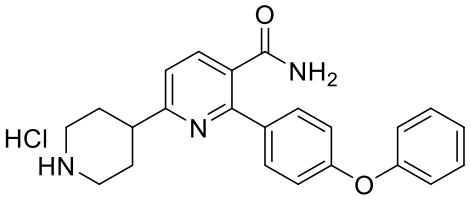
(c) hydrogenating INB under $H_2$ in the presence of a second palladium-containing catalyst to obtain a first solution comprising crude INC;



INC

(d) adding activated carbon to purify the crude INC, and then concentrating and dissolving the purified INC in ethyl acetate and ethanol to obtain a second solution comprising the purified INC;

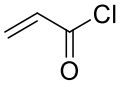
(e) adding HCl gas into the second solution to deprotect INC and obtain IND-HCl salt in a solid form;

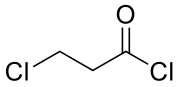


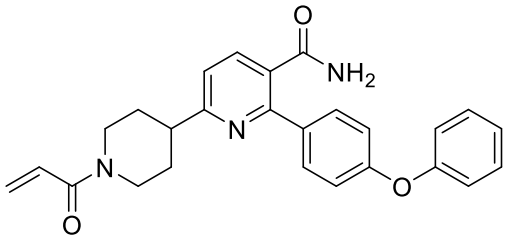

IND-HCl salt

(f) adding THF, $H_2O$ and $NaHCO_3$ to dissolve and neutralize the IND-HCl salt;

(g) reacting the IND-HCl salt with acryloyl chloride or 3-chloropropanoyl chloride under a basic condition to obtain 6-(1-acryloylpiperidin-4-yl)-2-(4-phenoxyphenyl)nicotinamide

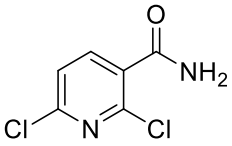


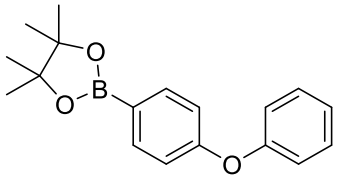



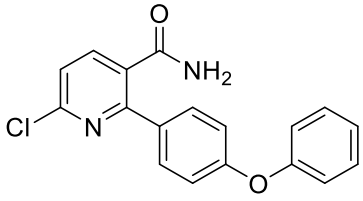




acryloyl chloride 3-chloropropanoyl chloride Compound I .

3. The method according to Claim 1, further comprising a step of heating a mixture of 2,6-dichloronicotinamide (SMA), SMB, and a palladium-containing catalyst in a basic solvent or solvent mixture at 60-140 ºC for 8-12 hours to prepare INA.



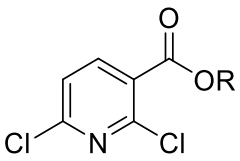



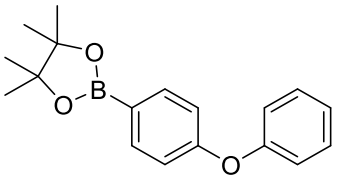

SMA SMB INA .

4. The method according to Claim 3, further comprising a step of reacting 2,6-dichloronicotinic acid with oxalyl chloride $(COCl)_2$, followed by reacting with an aqueous ammonia in an organic solvent, to obtain SMA.

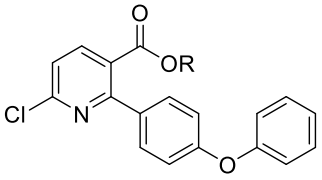
5. The method according to Claim 2, further comprising a step of heating a mixture of 2,6-dichloronicotinic acid/ester **(**SMA'), SMB, and a palladium-containing catalyst in a basic solvent or solvent mixture at 60-140 ºC for 8-12 hours to prepare INA'




SMA'




SMB




INA' .