Claims

1. A manufacturing method for 4-methoxypyrrole derivatives, comprising:

1) a step of preparing a compound represented by the following Chemical Formula 4 by reacting a compound represented by the following Chemical Formula 2 with a compound represented by the following Chemical Formula 3;

2) a step of preparing a compound represented by the following Chemical Formula 5 by reacting a compound represented by the following Chemical Formula 4 with sodium borohydride;

3) a step of preparing a compound represented by the following Chemical Formula 6 by reacting a compound represented by the following Chemical Formula 5 with an oxidant; and

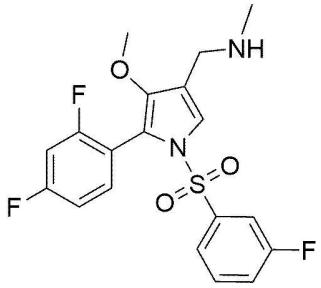
4) a step of reacting a compound represented by the following Chemical Formula 6 with methylamine to produce an intermediate, and converting the intermediate to a compound represented by the following Chemical Formula 1 by adding a reductant; and

wherein the step 1 is performed in the presence of a N,N-diisopropylethylamine and 4-(dimethylamino)-pyridine;

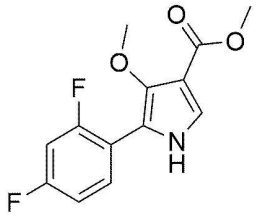
wherein the step 2 is performed in the presence of zinc chloride and dimethylaniline; and

wherein the oxidation of the step 3 is performed in the presence of a mixture of the (diacetoxyiodo)benzene and the (2,2,6,6-tetramethylpiperidin-1-yl)oxyl:

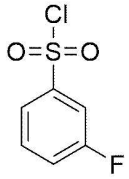
[Chemical Formula 1]



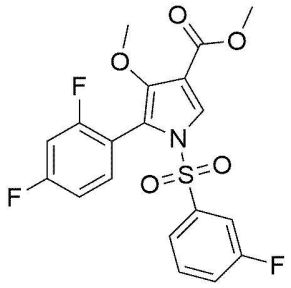
[Chemical Formula 2]



[Chemical Formula 3]



[Chemical Formula 4]



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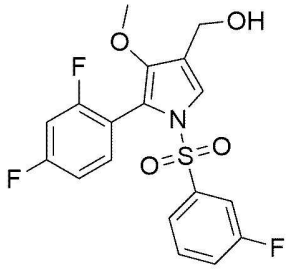
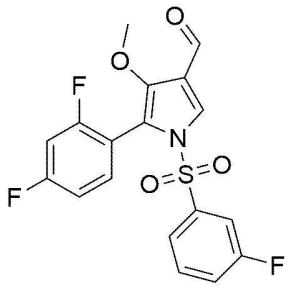


[Chemical Formula 6]



~~2. The manufacturing method of claim 1,~~

~~wherein the step 1 is performed in the presence of a base and 4-(dimethylamino)-pyridine.~~

~~3. The manufacturing method of claim 2,~~

~~wherein the base of the step 1 is N,N-diisopropylethylamine, triethylamine, diisopropylamine, diisopropylethylamine, potassium carbonate, potassium hydrogen carbonate, sodium carbonate, sodium hydrogen carbonate, sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium methylate, potassium butyrate, cesium carbonate, or a mixture of two or more thereof.~~

2~~4~~. The manufacturing method of claim 1,

wherein a molar ratio of the compound represented by the Chemical Formula 2 and the compound represented by the Chemical Formula 3 is 10:1 to 1:10 in the step 1.

3~~5~~. The manufacturing method of claim 1,

wherein a reaction solvent of the step 1 is acetonitrile, tetrahydrofuran, methylene chloride, methanol, ethanol, propanol, iso-propanol, butanol, tert-butanol, or a mixture of two or more thereof.

4~~6~~. The manufacturing method of claim 1,

wherein a reaction temperature in the step 1 is 10 to 35 ℃.

~~7. The manufacturing method of claim 1,~~

~~wherein the step 2 is performed in the presence of zinc chloride and dimethylaniline.~~

5~~8~~. The manufacturing method of claim 1~~7~~,

wherein the zinc chloride and the dimethylaniline are mixed to satisfy a molar ratio of the compound represented by the Chemical Formula 4 and the zinc chloride of 10:1 to 1:10, and a molar ratio of the compound represented by the Chemical Formula 4 and the dimethylaniline of 10:1 to 1:10 at the same time, and then used in the reaction of step 2.

6~~9~~. The manufacturing method of claim 1,

wherein a reaction solvent of the step 2 is dimethylacetamide, tetrahydrofuran, dimethyl sulfoxide, toluene, methanol, ethanol, dichloromethane, or a mixture of two or more thereof.

7~~10~~. The manufacturing method of claim 1,

wherein a reaction temperature in the step 2 is -15 to 80 ℃.

~~11. The manufacturing method of claim 1,~~

~~wherein the oxidation of the step 3 is performed in the presence of~~

~~1) an oxidant selected from (diacetoxyiodo)benzene, iodine, iodobenzene dichloride, iodosylbenzene, and trichloroisocyanuric acid;~~

~~2) a catalyst selected from (2,2,6,6-tetramethylpiperidin-1-yl)oxyl, 4-acetamido-2,2,6,6-tetramethylpiperidine 1-oxyl, 4-hydroxy-2,2,6,6-tetramethylpiperidine 1-oxyl, 4-methacryloyloxy-2,2,6,6-tetramethylpiperidine-1-oxyl, 4-oxo-2,2,6,6-tetramethyl-1-piperidinyloxy, 4-amino-2,2,6,6-~~

~~tetramethylpiperidin-1-oxyl, 4-carboxy-2,2,6,6-tetramethylpiperidine 1-oxyl, 4-hydroxy-2,2,6,6-tetramethylpiperidine 1-oxyl benzoate, 4-(2-iodoacetamido)-2,2,6,6-tetramethyl-1-piperidinyloxy, 4-maleimido-2,2,6,6-tetramethyl-1-piperidinyloxy, 4-isothiocyanato-2,2,6,6-tetramethylpiperidine 1-oxyl, 4-methoxy-2,2,6,6-tetramethyl-1-piperidinyloxy, and 4-phosphonooxy-2,2,6,6-tetramethyl-1-piperidinyloxy; or~~

~~a mixture of one oxidant selected from 1) and one catalyst selected from 2).~~

8~~12~~. The manufacturing method of claim 1~~1~~,

~~wherein the oxidation of the step 3 is performed in the presence of a mixture of the (diacetoxyiodo)benzene and the (2,2,6,6-tetramethylpiperidin-1-yl)oxyl, and~~

the (diacetoxyiodo)benzene and the (2,2,6,6-tetramethylpiperidin-1-yl)oxyl are mixed to satisfy a molar ratio of the compound represented by the Chemical Formula 5 and the (diacetoxyiodo)benzene of 10:1 to 1:10, and a molar ratio of the compound represented by the Chemical Formula 5 and the (2,2,6,6-tetramethylpiperidin-1-yl)oxyl of 10:1 to 1:10 at the same time.

9~~13~~. The manufacturing method of claim 1,

wherein a reaction solvent of the step 3 is dichloromethane, dichloroethane, acetonitrile, ethyl acetate, methanol, toluene, dimethylformamide, dimethyl sulfoxide, tetrahydrofuran, or a mixture of two or more thereof.

10~~14~~. The manufacturing method of claim 1,

wherein a reaction temperature in the step 3 is 10 to 40 ℃.

11~~15~~. The manufacturing method of claim 1,

wherein a reaction solvent of the step 4 is methanol, ethanol, isopropanol, dichloromethane, dichloroethane, tetrahydrofuran, ethyl acetate, dimethyl ether, acetonitrile, or a mixture of two or more thereof.

1216. The manufacturing method of claim 1,

wherein the reaction of the compound represented by the Chemical Formula 6 and the methylamine is performed at a reaction temperature of 10 to 30 ℃ in the step 4.

1317. The manufacturing method of claim 1,

wherein the reductant of the step 4 is sodium borohydride, sodium cyanoborohydride, sodium triacetoxyborohydride, or a mixture of two or more thereof.

1418. The manufacturing method of claim 1,

wherein the reaction of the reductant and the intermediate is performed at a reaction temperature of -5 to 10 ℃ in the step 4.

1519. The manufacturing method of claim 1,

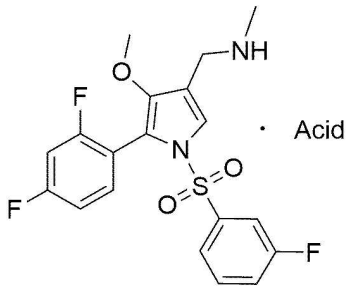
wherein a molar ratio of the compound represented by the Chemical Formula 6 and the methylamine is 10:1 to 1:10, and a molar ratio of the compound represented by the Chemical Formula 6 and the reductant is 10:1 to 1:10 in the step 4.

1620. The manufacturing method of claim 1,

further comprising

a step preparing an acidic salt represented by the following Chemical Formula 1-1 by adding an acid to the compound represented by the Chemical Formula 1, after the step 4:

[Chemical Formula 1-1]



1721. The manufacturing method of claim 1620,

wherein the step after step 45 comprises a step of crystallizing the acidic salt represented by the Chemical Formula 1-1 by supplying an organic solvent to the compound represented by the Chemical Formula 1 and then supplying an acid or a mixed solution thereof with an organic solvent.

1822. The manufacturing method of claim 1721,

wherein the crystallization temperature is -15 to 20 ℃.