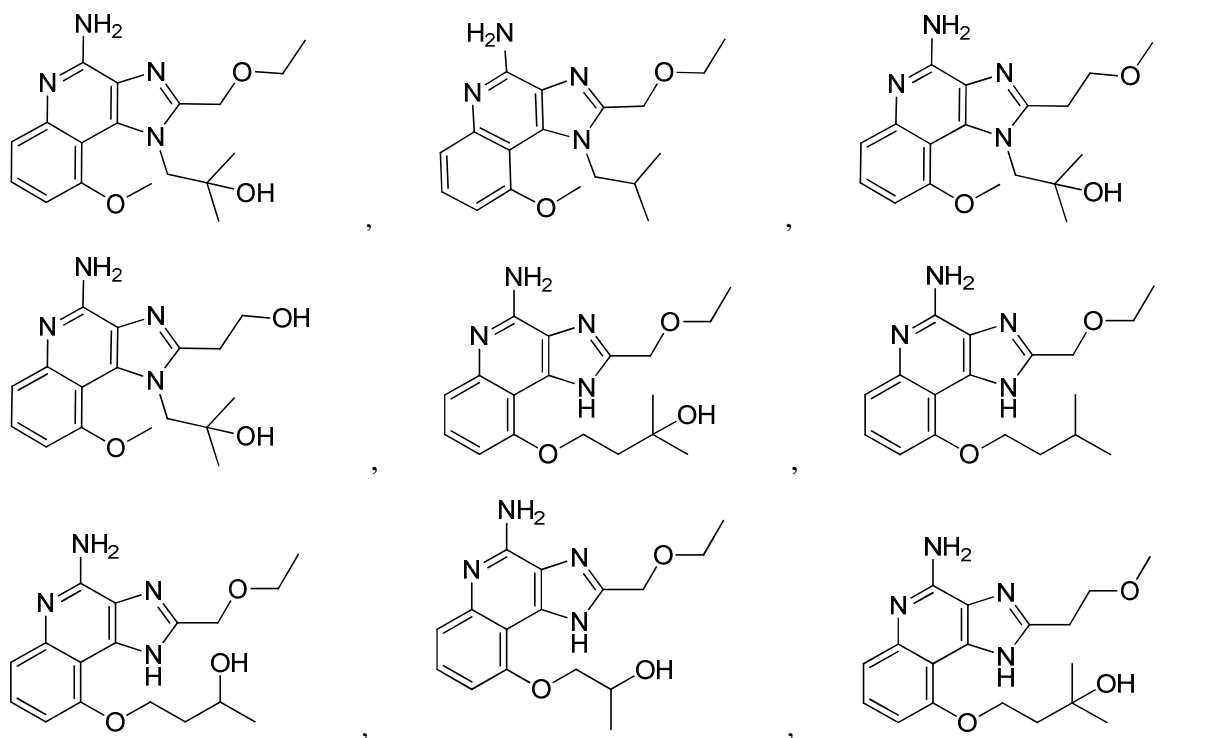
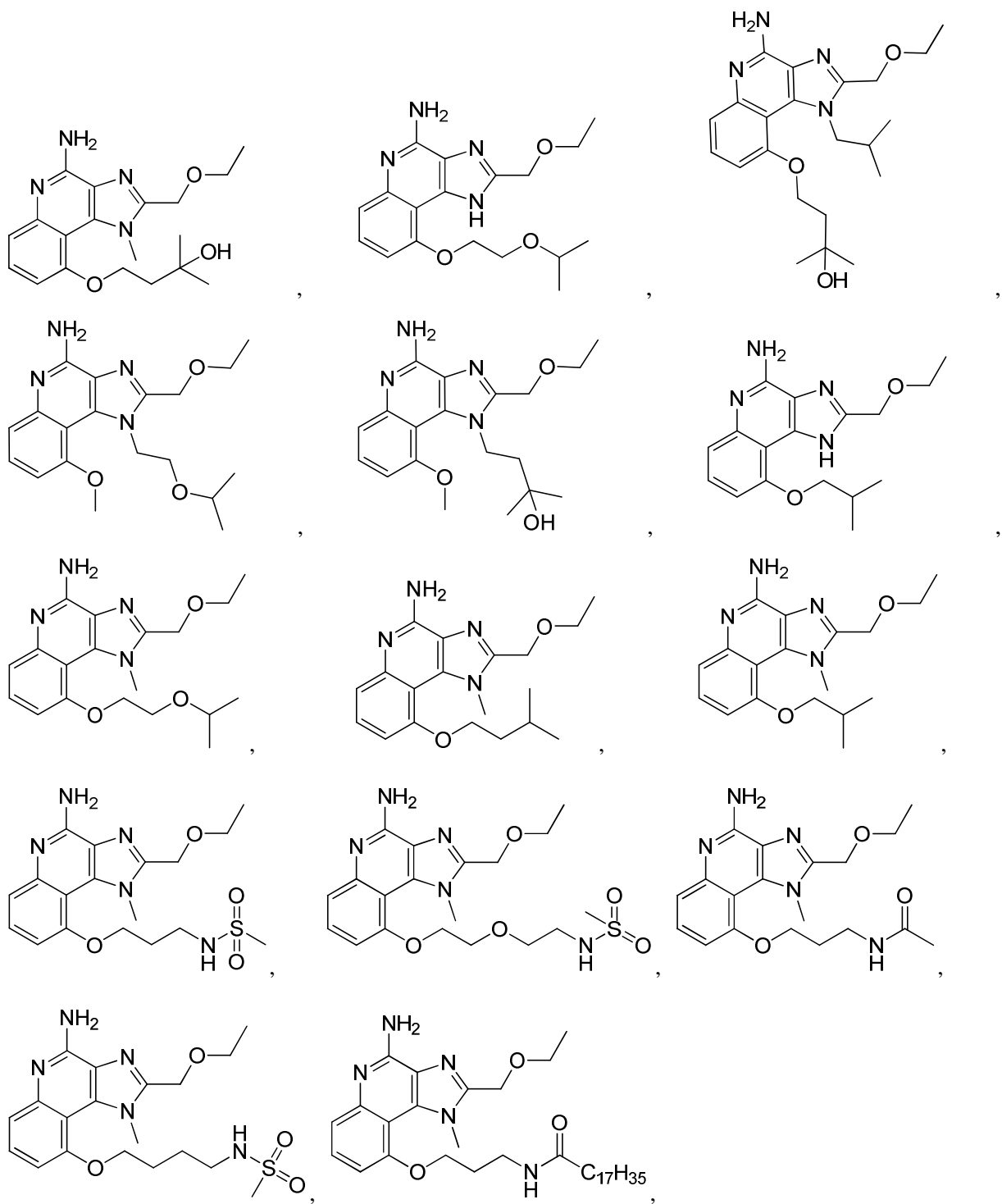


NR^a, -CO-, -SO-, or -SO₂-; Z is a bond, O, NHSO₂, or NHCO; m is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and n is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, or 23.

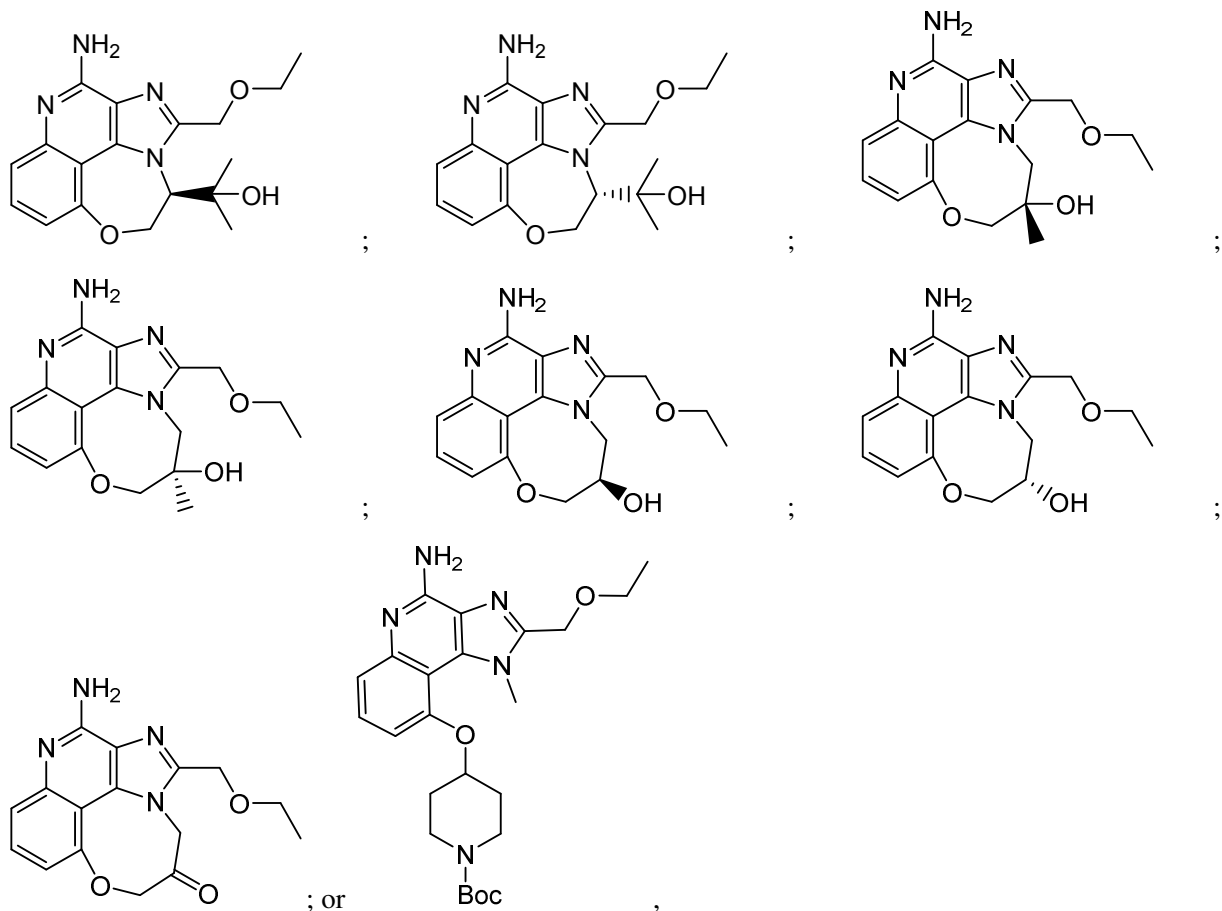
[0007] Some embodiments include a pharmaceutical dosage form comprising a subject compound. A subject compound or a subject composition may be used for activating TLR7/8. In addition to its use as a stand-alone immunotherapeutic agent, such as an antiviral and anticancer agent, a subject compound or composition may be used as adjuvants in cancer vaccine or adoptive T cell transfer protocols.

[0007a] In another aspect, there is provided a compound which is









a salt of any of these compounds, or an ester of any of these compounds having an -OH group.

[0007b] In yet another aspect, there is provided a compound which is optionally substituted 9-methoxy-1*H*-imidazo[4,5-*c*]quinolin-4-amine.

[0007c] In a further aspect, there is provided a compound which is optionally substituted 9-methoxy-2*H*-pyrazolo[3,4-*c*]quinolin-4-amine.

[0008] Some embodiments include a method of treating a disease or disorder associated with a TLR7/8 agonist comprising administering an effective amount of a subject compound to a mammal in need thereof.

[0009] Some embodiments include use of a subject compound in the manufacture of a medicament for the treatment of a disease or disorder associated with a TLR7/8 agonist.

[0009a] In one aspect, there is provided a dosage form to be administered to a mammal, comprising a compound as described herein.

DETAILED DESCRIPTION OF THE INVENTION

[0010] Unless otherwise indicated, when a compound or chemical structural feature, such as alkyl, alkenyl, alkynyl, aryl, heteroaryl, etc., is referred to as being “optionally substituted,” it includes a feature that has no substituents (i.e. unsubstituted), or a feature that is “substituted,” meaning that the feature has one or more substituents. The term “substituent” has the broadest meaning known to one of ordinary skill in the art, and includes a moiety that occupies a position normally occupied by one or more hydrogen atoms attached to a parent compound or structural feature. In some embodiments, a substituent may be an ordinary organic moiety known in the art, which may have a molecular weight (e.g. the sum of the atomic masses of the atoms of the substituent) of 15-50 g/mol, 15-100 g/mol, 15-150 g/mol, 15-200 g/mol, 15-300 g/mol, or 15-500 g/mol. In some embodiments, a substituent comprises, or consists of: 0-30, 0-20, 0-10, or 0-5 carbon atoms; and 0-30, 0-20, 0-10, or 0-5 heteroatoms, wherein each heteroatom may independently be: N, O, S, Si, F, Cl, Br, or I; provided that the substituent includes one C, N, O, S, Si, F, Cl, Br, or I atom. Examples of substituents include, but are not limited to, alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, hydroxy, alkoxy, aryloxy, acyl, acyloxy, alkylcarboxylate, thiol, alkylthio, cyano, halo, thiocarbonyl, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, C-amido, N-amido, S-sulfonamido, N-sulfonamido, isocyanato, thiocyanato, isothiocyanato, nitro, silyl, sulfenyl, sulfinyl, sulfonyl, haloalkyl, haloalkoxyl, trihalomethanesulfonyl, trihalomethanesulfonamido, amino, etc.

[0011] For convenience, the term “molecular weight” is used with respect to a moiety or part of a molecule to indicate the sum of the atomic masses of the atoms in the moiety or part of a molecule, even though it may not be a complete molecule.

NHSO₂, or NHCO, m is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, and n is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, or 23.

[0075] Embodiment 29. The compound of embodiment 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27 or 28, wherein R⁷ is R^a, F, Cl, -CO₂R^a, -CONR^aR^b, CN, -OR^a, -NR^aR^b, -OCOR^a, or -SO₂R^a, wherein R^a and R^b are independently H or C₁₋₆ alkyl.

[0076] Embodiment 30. The compound of embodiment 29, wherein R⁷ is H.

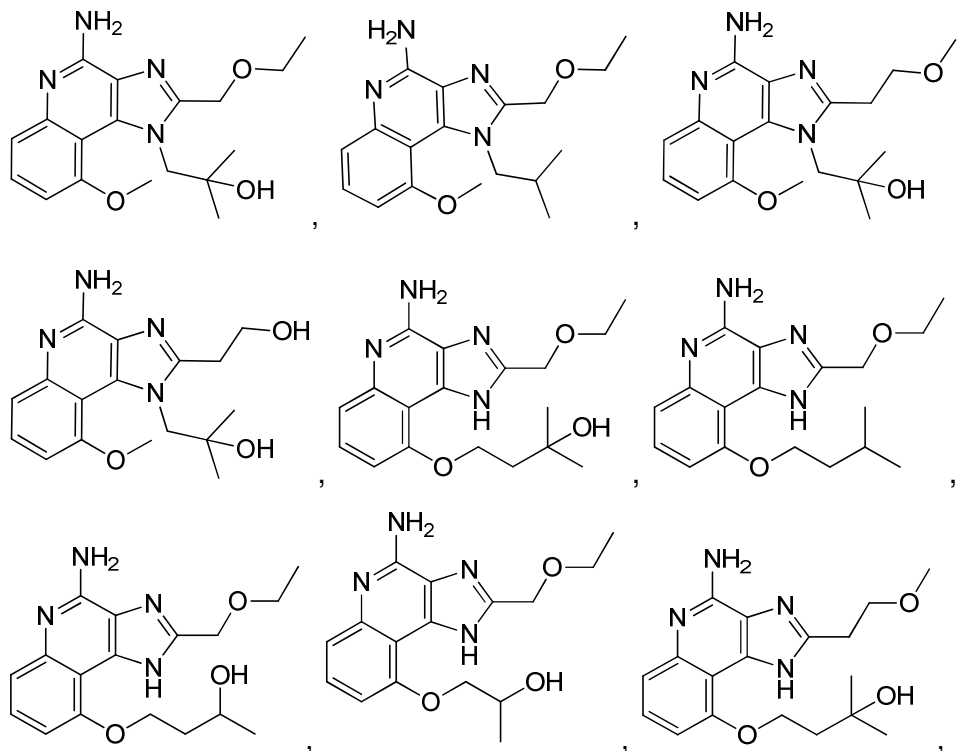
[0077] Embodiment 31. The compound of embodiment 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, or 28, wherein R⁷ is -(C_mH_{2m}O₀₋₁)-Z-(C_nH_{2n+1}), wherein Z is a bond, O, NHSO₂, or NHCO, m is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, and n is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, or 23.

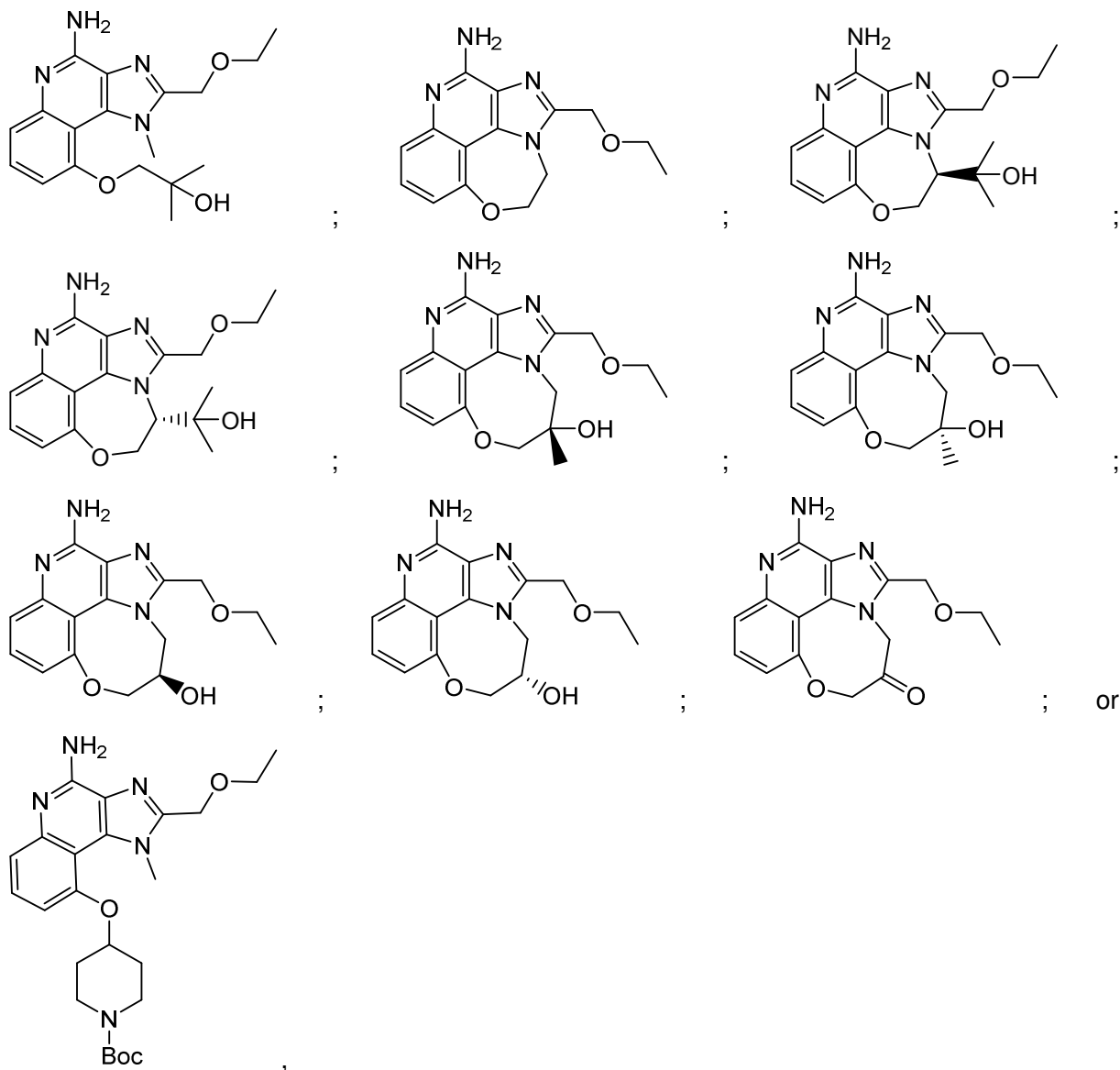
[0078] Embodiment 32. The compound of embodiment 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31, R⁸ is H, OH, or CH₃.

[0079] Embodiment 33. The compound of embodiment 32, wherein R⁸ is OH.

[0080] Embodiment 34. The compound of embodiment 32, wherein R⁸ is H.

[0081] Embodiment 35. A compound, which is:





a salt of any of these compounds, or an ester of any of these compounds having an -OH group.

[0082] Embodiment 36. A compound which is optionally substituted 9-methoxy-1*H*-imidazo[4,5-*c*]quinolin-4-amine.

[0083] Embodiment 37. A compound which is optionally substituted 9-methoxy-2*H*-pyrazolo[3,4-*c*]quinolin-4-amine.

[0084] Embodiment 38. The compound of embodiment 36, which is optionally substituted 1-(4-amino-2-(ethoxymethyl)-9-methoxy-1*H*-imidazo[4,5-*c*]quinolin-1-yl)-2-methylpropan-2-ol or a salt thereof; optionally substituted 2-(ethoxymethyl)-1-isobutyl-9-methoxy-1*H*-imidazo[4,5-*c*]quinolin-4-amine or a

c]quinolin-4-amine or a salt thereof; optionally substituted 2-(ethoxymethyl)-1-methyl-9-(piperidin-4-yloxy)-1H-imidazo[4,5-c]quinolin-4-amine or a salt thereof; optionally substituted N-(3-((4-amino-2-(ethoxymethyl)-1-methyl-1H-imidazo[4,5-c]quinolin-9-yl)oxy)propyl)palmitamide or a salt thereof; optionally substituted N-(4-((4-amino-2-(ethoxymethyl)-1-methyl-1H-imidazo[4,5-c]quinolin-9-yl)oxy)butyl)palmitamide or a salt thereof; optionally substituted 9-(3-aminopropoxy)-2-(ethoxymethyl)-1-methyl-1H-imidazo[4,5-c]quinolin-4-amine or a salt thereof; optionally substituted 2-(ethoxymethyl)-9-isopropoxy-1-methyl-1H-imidazo[4,5-c]quinolin-4-amine or a salt thereof; optionally substituted 1-((4-amino-2-(ethoxymethyl)-1-methyl-1H-imidazo[4,5-c]quinolin-9-yl)oxy)-2-methylpropan-2-ol or a salt thereof; optionally substituted 2-(ethoxymethyl)-3,4-dihydro-5-oxa-1,2a,9-triazanaphtho[2,1,8-cde]azulen-10-amine or a salt thereof; optionally substituted (R)-2-(10-amino-2-(ethoxymethyl)-3,4-dihydro-5-oxa-1,2a,9-triazanaphtho[2,1,8-cde]azulen-3-yl)propan-2-ol or a salt thereof; optionally substituted (S)-2-(10-amino-2-(ethoxymethyl)-3,4-dihydro-5-oxa-1,2a,9-triazanaphtho[2,1,8-cde]azulen-3-yl)propan-2-ol or a salt thereof; optionally substituted (S)-2-amino-12-(ethoxymethyl)-6-methyl-6,7-dihydro-5H-3,4-(azenometheno)[1,5]oxazocino[4,3,2-de]quinolin-6-ol or a salt thereof; optionally substituted (R)-2-amino-12-(ethoxymethyl)-6-methyl-6,7-dihydro-5H-3,4-(azenometheno)[1,5]oxazocino[4,3,2-de]quinolin-6-ol or a salt thereof; optionally substituted (R)-2-amino-12-(ethoxymethyl)-6,7-dihydro-5H-3,4-(azenometheno)[1,5]oxazocino[4,3,2-de]quinolin-6-ol or a salt thereof; optionally substituted (S)-2-amino-12-(ethoxymethyl)-6,7-dihydro-5H-3,4-(azenometheno)[1,5]oxazocino[4,3,2-de]quinolin-6-ol or a salt thereof; optionally substituted 2-amino-12-(ethoxymethyl)-5H-3,4-(azenometheno)[1,5]oxazocino[4,3,2-de]quinolin-6(7H)-one or a salt thereof; or optionally substituted tert-butyl 4-((4-amino-2-(ethoxymethyl)-1-methyl-1H-imidazo[4,5-c]quinolin-9-yl)oxy)piperidine-1-carboxylate or a salt thereof.

[0085] Embodiment 39. The compound of embodiment 37 which is optionally substituted 4-amino-2*H*-pyrazolo[3,4-c]quinolin-9-ol or a salt thereof; optionally substituted 4-amino-2-isopentyl-2*H*-pyrazolo[3,4-c]quinolin-9-ol or a salt thereof; optionally substituted 2-isopentyl-9-(isopentyloxy)-2*H*-pyrazolo[3,4-c]quinolin-4-amine or a salt thereof; or optionally substituted 2-butyl-9-(isopentyloxy)-2*H*-pyrazolo[3,4-c]quinolin-4-amine or a salt thereof.

[0086] Embodiment 40. A method of treating viral infection, cancer, or an allergic disease, comprising administering a compound according to embodiment 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, or 39, to a mammal in need thereof.

[0087] Embodiment 41. Use of a compound of embodiment 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, or 39, in the manufacture of a medicament for the treatment of viral infection, cancer, or an allergic disease.

[0088] Embodiment 42. The method of embodiment 40 or use of embodiment 41, wherein the viral infection comprises HCV infection.

[0089] Embodiment 43. A dosage form suitable for administration to a mammal, comprising a compound of embodiment 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, or 39.

Examples

[0090] In the synthetic schemes described below, unless otherwise indicated all temperatures are set forth in degrees Celsius and all parts and percentages are by weight. Reagents and solvents were purchased from commercial suppliers such as Aldrich Chemical Company and were used without further purification unless otherwise indicated. Tetrahydrofuran (THF) and N,N-dimethylformamide (DMF) were purchased from commercial sources in Sure Seal bottles and used as received.

[0091] The reactions set forth below were done generally under a positive pressure of argon or nitrogen at an ambient temperature (unless otherwise stated) in anhydrous solvents. Glassware was oven dried and/or heat dried. The reactions were assayed by TLC and/or analyzed by LC-MS and terminated as judged by the consumption of starting material. Analytical thin layer chromatography (TLC) was performed on glass plates pre-coated with silica gel 60 F254 0.25 mm plates (EM Science), and visualized with UV light (254 nm) and/ or heating with commercial ethanolic phosphomolybdic acid. Preparative thin layer chromatography (TLC) was performed on glass-plates pre-coated with silica gel 60 F254 0.5 mm plates (20 x 20 cm, from commercial sources) and visualized with UV light (254 nm).

[0092] Work-ups were typically done by doubling the reaction volume with the reaction solvent or extraction solvent and then washing with the indicated aqueous solutions using 25% by volume of the extraction volume unless otherwise indicated. Product solutions were dried over anhydrous Na₂SO₄ and/or Mg₂SO₄ prior to filtration and evaporation of the solvents under reduced pressure on a rotary evaporator and noted as solvents removed in *vacuo*. Column chromatography was completed under positive pressure using 230-400 mesh silica gel.

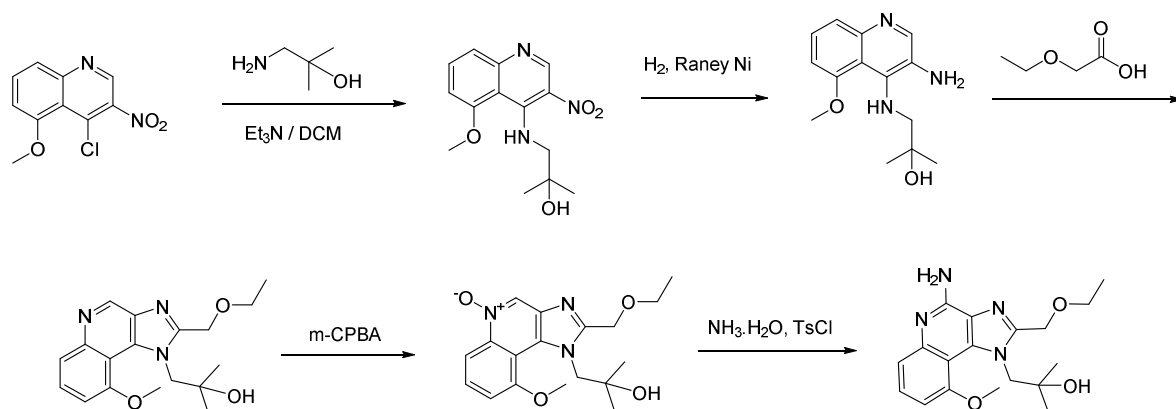
[0093] ¹H-NMR spectra and ¹³C-NMR were recorded on a Varian Mercury-VX400 instrument operating at 400 MHz. NMR spectra were obtained as CDCl₃ solutions (reported in ppm), using chloroform as the reference standard (7.27 ppm for the proton and 77.00 ppm for carbon), CD₃OD (3.4 and 4.8 ppm for the

protons and 49.3 ppm for carbon), DMSO- d_6 (2.49 ppm for proton), or internally tetramethylsilane (0.00 ppm) when appropriate. Other NMR solvents were used as needed.

Example 1

[0094] Synthesis of 1-[4-Amino-2-(ethoxymethyl)-9-methoxy-imidazo[4,5-*c*]quinolin-1-yl]-2-methyl-propan-2-ol

Scheme 1



[0095] Step 1: Synthesis of 1-[(5-Methoxy-3-nitro-4-quinolyl)amino]-2-methyl-propan-2-ol

[0096] To a solution of 1-amino-2-methyl-propan-2-ol (747.10 mg, 8.38 mmol, 2.0 eq.) and Et_3N (2.12 g, 20.95 mmol, 2.90 mL, 5.0 eq.) in DCM (50.00 mL) was added 4-chloro-5-methoxy-3-nitro-quinoline (1.00 g, 4.19 mmol, 1.0 eq.). The resulting mixture was stirred at 25 °C for 0.5 h. The reaction mixture was washed with water (30 mL) and brine (30 mL) via extraction. The organic phase was dried over anhydrous Na_2SO_4 , filtered, and concentrated in *vacuo*. The residue was purified with column chromatography (DCM to DCM/MeOH = 20/1). The desired product of 1-[(5-methoxy-3-nitro-4-quinolyl)amino]-2-methyl-propan-2-ol (1.00 g, 3.43 mmol, 81.86% yield) was obtained as a yellow solid. ^1H NMR (400 MHz, CDCl_3) δ ppm: 9.51 (s, 1H), 9.03 (s, 1H), 7.63 (t, J = 8.0 Hz, 1H), 7.58 (d, J = 8.4 Hz, 1H), 6.94 (d, J = 7.2 Hz, 1H), 4.10 (s, 3H), 2.95 (d, J = 4.8 Hz, 2H), 1.29 (s, 6H); ES-LCMS m/z 292.3 $[\text{M}+\text{H}]^+$.

[0097] Step 2: Synthesis of 1-[(3-Amino-5-methoxy-4-quinolyl)amino]-2-methyl-propan-2-ol

[0098] To a solution of 1-[(5-methoxy-3-nitro-4-quinolyl)amino]-2-methyl-propan-2-ol (1.00 g, 3.43 mmol, 1.0 eq.) in MeOH (100.00 mL) was added Raney-Ni (626.42 mg, 7.31 mmol, 2.1 eq.) under N_2 . The suspension was degassed under vacuum and purged with H_2 several times. The resulting mixture was stirred under H_2 (15 psi) at 25 °C for 3 h. The reaction mixture was filtered. The filtrate was concentrated in *vacuo*. The desired product of 1-[(3-amino-5-methoxy-4-quinolyl)amino]-2-methyl-propan-2-ol (870.00

mg, 3.33 mmol, 97.08% yield) was obtained as a yellow solid. ¹H NMR (400 MHz, CD₃OD) δ ppm: 8.26 (s, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.31 (t, *J* = 8.0 Hz, 1H), 6.88 (d, *J* = 7.6 Hz, 1H), 4.02 (s, 3H), 3.22 (s, 2H), 1.29 (s, 6H); ES-LCMS *m/z* 262.3 [M+H]⁺.

[0099] *Step 3: Synthesis of 1-[2-(Ethoxymethyl)-9-methoxy-imidazo[4,5-c]quinolin-1-yl]-2-methyl-propan-2-ol*

[0100] A solution of 1-[(3-amino-5-methoxy-4-quinolyl)amino]-2-methyl-propan-2-ol (400.00 mg, 1.53 mmol, 1.0 eq.) and 4Å MS (200 mg) in 2-ethoxyacetic acid (3.30 g, 31.7 mmol, 3 mL, 20.7 eq.) was stirred at 120 °C for 4 h under microwave. The reaction mixture was then filtered. The filtrate was dissolved in DCM (80 mL) and adjusted to pH = 8 with 2 M NaOH. The organic layer was separated and dried over anhydrous Na₂SO₄, filtered and concentrated in *vacuo*. The mixture was purified with column chromatography (DCM to DCM/MeOH = 10/1). The desired product of 1-[2-(ethoxymethyl)-9-methoxy-imidazo[4,5-c]quinolin-1-yl]-2-methyl-propan-2-ol (230.00 mg, 698.26 μmol, 45.62% yield) was obtained as a yellow solid. ¹H NMR (400 MHz, CD₃OD) δ ppm: 9.09 (s, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.67 (t, *J* = 8.2 Hz, 1H), 7.25 (d, *J* = 7.2 Hz, 1H), 5.68 (s, 1H), 5.39 (s, 1H), 4.63 (m, 2H), 4.14 (s, 3H), 3.62 (m, 2H), 1.32-1.26 (m, 3H), 1.25-1.23 (m, 3H), 0.76 (m, 3H); ES-LCMS *m/z*: 330.3 [M+H]⁺.

[0101] *Step 4: Synthesis of 1-[2-(Ethoxymethyl)-9-methoxy-5-oxido-imidazo[4,5-c]quinolin-5-ium-1-yl]-2-methyl-propan-2-ol*

[0102] To a solution of 1-[2-(ethoxymethyl)-9-methoxy-imidazo[4,5-c]quinolin-1-yl]-2-methyl-propan-2-ol (230.00 mg, 698.26 μmol, 1.0 eq.) in DCM (30.00 mL) was added *m*-CPBA (212.64 mg, 1.05 mmol, 85% purity, 1.5 eq.). The resulting mixture was stirred at 25 °C for 1 h. The reaction mixture was then adjusted to pH = 8 with aqueous K₂CO₃ and partitioned between DCM (50 mL) and water (20 mL). The organic layer was separated, washed with brine (20 mL), dried over Na₂SO₄, and filtered. After filtration, the filtrate was concentrated in *vacuo*. The residue was purified with prep-TLC (DCM/MeOH = 8/1, R_f = 0.3). The desired product of 1-[2-(ethoxymethyl)-9-methoxy-5-oxido-imidazo[4,5-c]quinolin-5-ium-1-yl]-2-methyl-propan-2-ol (150.00 mg, 434.29 μmol, 62.20% yield) was obtained as a yellow solid. ¹H NMR (400 MHz, CD₃OD) δ ppm: 9.10 (s, 1H), 8.52 (d, *J* = 8.8 Hz, 1H), 7.85 (t, *J* = 8.6 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 5.54 (s, 1H), 5.31 (s, 1H), 4.58 (s, 2H), 4.19 (s, 3H), 3.62 (m, 2H), 1.28-1.23 (m, 6H), 0.84 (m, 3H); ES-LCMS *m/z*: 346.3 [M+H]⁺.

[0103] *Step 5: Synthesis of 1-[4-Amino-2-(ethoxymethyl)-9-methoxy-imidazo[4,5-c]quinolin-1-yl]-2-methyl-propan-2-ol*

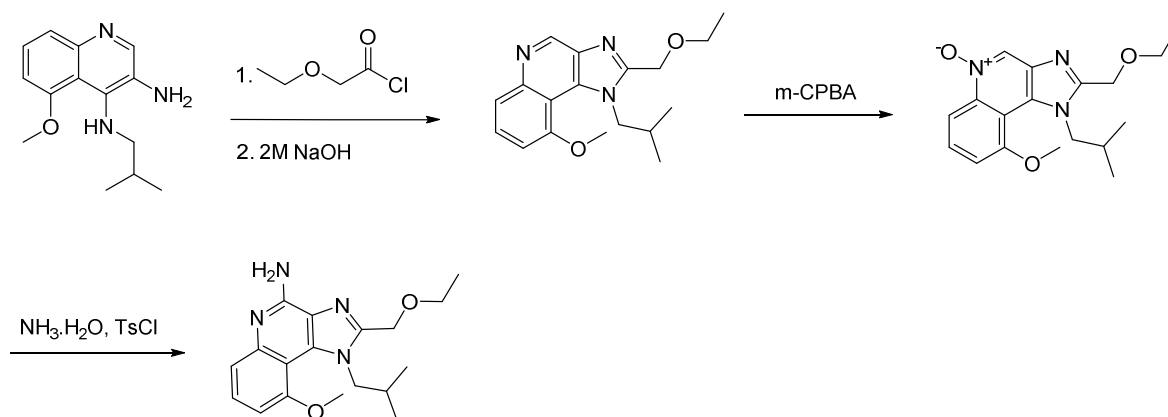
[0104] To a solution of 1-[2-(ethoxymethyl)-9-methoxy-5-oxido-imidazo[4,5-c]quinolin-5-ium-1-yl]-2-methyl-propan-2-ol (150.00 mg, 434.29 μmol, 1.0 eq.) and NH₃·H₂O (543.64 mg, 4.34 mmol, 597.41 μL,

28% purity, 10.0 eq.) in CHCl_3 (20.00 mL) was added TsCl (99.36 mg, 521.15 μmol , 1.2 eq.). The resulting mixture was stirred at 20 °C for 0.5 h. The solvent was removed in *vacuo*. The residue was purified with prep-HPLC (MeCN/ H_2O as eluents, acidic condition). After lyophilization, the desired product of 1-[4-amino-2-(ethoxymethyl)-9-methoxy-imidazo[4,5-*c*]quinolin-1-yl]-2-methyl-propan-2-ol (50.00 mg, 131.28 μmol , 30.23% yield, 100% purity, as HCl salt) was obtained as a white solid. ^1H NMR (400 MHz, CD_3OD) δ ppm: 7.63 (t, J = 8.2 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 7.13 (d, J = 8.0 Hz, 1H), 5.50 (s, 1H), 5.21 (s, 1H), 4.76 (s, 1H), 4.55 (s, 1H), 4.09 (s, 3H), 3.59 (m, 2H), 1.23-1.20 (m, 6H), 0.82 (m, 3H); ES-LCMS m/z : 345.3 $[\text{M}+\text{H}]^+$

Example 2

[0105] Synthesis of 2-(Ethoxymethyl)-1-isobutyl-9-methoxy-imidazo[4,5-*c*]quinolin-4-amine

Scheme 2



[0106] Step 1: Synthesis of 2-(Ethoxymethyl)-1-isobutyl-9-methoxy-imidazo[4,5-*c*]quinoline

[0107] To a solution of N^4 -isobutyl-5-methoxy-quinoline-3,4-diamine (100.00 mg, 407.63 μmol , 1.0 eq.) and pyridine (322.44 mg, 4.08 mmol, 329.02 μL , 10.0 eq.) in DCM (4.00 mL) was added 2-ethoxyacetyl chloride (99.91 mg, 815.26 μmol , 2.0 eq.). The resulting mixture was stirred at 25 °C for 1 h. The solvent was removed in *vacuo*. The residue was dissolved in NaOH (2 M, 4.95 mL, 24.3 eq.) and stirred at 100 °C for 5 h. The mixture was dissolved in water (10 mL) and extracted with DCM (50 mL x 2). The combined organic phase was washed with brine (20 mL), dried over anhydrous Na_2SO_4 , filtered and concentrated in *vacuo*. The residue was purified with prep-TLC (DCM/MeOH = 15/1). The desired product of 2-(ethoxymethyl)-1-isobutyl-9-methoxy-imidazo[4,5-*c*]quinoline (80.00 mg, 255.27 μmol , 62.62% yield) was obtained as a brown solid. ^1H NMR (400 MHz, CDCl_3) δ ppm: 9.27 (s, 1H), 7.70 (d, J = 8.4 Hz, 1H), 7.60 (t, J = 8.2 Hz, 1H), 7.04 (d, J = 8.0 Hz, 1H), 4.89 (s, 2H), 4.62 (br, s, 2H), 4.08 (s,

3H), 3.65-3.59 (m, 2H), 2.11-2.02 (m, 1H), 1.26 (t, $J = 7.0$ Hz, 3H), 0.75-0.72 (m, 6H); ES-LCMS m/z : 314.3 $[M+H]^+$.

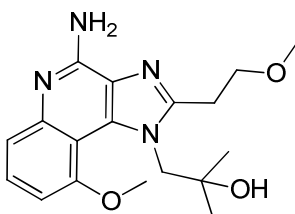
[0108] Step 2: 2-(Ethoxymethyl)-1-isobutyl-9-methoxy-5-oxido-imidazo[4,5-*c*]quinolin-5-ium

[0109] To a solution of 2-(ethoxymethyl)-1-isobutyl-9-methoxy-imidazo[4,5-*c*]quinoline (50.00 mg, 159.55 μmol , 1.0 eq.) in DCM (5.00 mL) was added *m*-CPBA (48.59 mg, 239.33 μmol , 85% purity, 1.5 eq.). The resulting mixture was stirred at 25 °C for 0.5 h. DCM (40 mL) and water (10 mL) were added, and pH was adjusted to 8 by addition of aqueous NaOH. The organic layer was then separated, washed with brine (10 mL), dried over Na_2SO_4 and filtered. The filtrate was concentrated in *vacuo*. The desired product of 2-(ethoxymethyl)-1-isobutyl-9-methoxy-5-oxido-imidazo[4,5-*c*]quinolin-5-ium (50.00 mg, 151.80 μmol , 95.14% yield) was obtained as a yellow solid. ^1H NMR (400 MHz, CDCl_3) δ ppm: 9.05 (s, 1H), 8.71 (d, $J = 8.8$ Hz, 1H), 7.70 (t, $J = 8.2$ Hz, 1H), 7.17 (d, $J = 7.2$ Hz, 1H), 4.56 (s, 2H), 4.44 (br, s, 2H), 4.11 (s, 3H), 3.65-3.59 (m, 2H), 2.06-1.99 (m, 1H), 1.27 (t, $J = 7.0$ Hz, 3H), 0.76-0.72 (m, 6H); ES-LCMS m/z : 330.2 $[M+H]^+$.

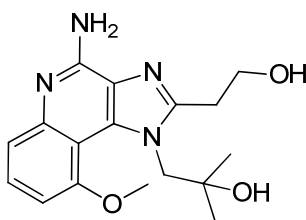
[0110] Step 3: 2-(Ethoxymethyl)-1-isobutyl-9-methoxy-imidazo[4,5-*c*]quinolin-4-amine

[0111] To a solution of 2-(ethoxymethyl)-1-isobutyl-9-methoxy-5-oxido-imidazo[4,5-*c*]quinolin-5-ium (50.00 mg, 151.80 μmol , 1.0 eq.) and $\text{NH}_3\cdot\text{H}_2\text{O}$ (190.27 mg, 1.52 mmol, 209.09 μL , 28% purity, 10.0 eq.) in CHCl_3 (10.00 mL) was added TsCl (34.73 mg, 182.16 μmol , 1.2 eq.). The resulting mixture was stirred at 25 °C for 0.5 h. The solvent was removed in *vacuo*. The residue was purified with prep-HPLC (MeCN/ H_2O as eluents, acidic condition). After lyophilization, the desired product of 2-(ethoxymethyl)-1-isobutyl-9-methoxy-imidazo[4,5-*c*]quinolin-4-amine (30.00 mg, 78.31 μmol , 51.59% yield, 95.24% purity, as HCl salt) was obtained as a white solid. ^1H NMR (400 MHz, CD_3OD) δ ppm: 7.69 (t, $J = 8.2$ Hz, 1H), 7.36 (d, $J = 8.0$ Hz, 1H), 7.18 (d, $J = 8.4$ Hz, 1H), 4.87 (s, 2H), 4.62 (br, s, 2H), 4.13 (s, 3H), 3.69-3.64 (m, 2H), 2.05-1.95 (m, 1H), 1.27 (t, $J = 7.0$ Hz, 3H), 0.80-0.75 (m, 6H); ES-LCMS m/z : 329.4 $[M+H]^+$.

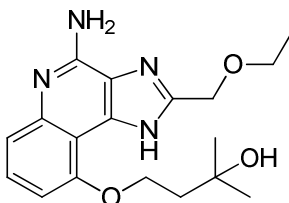
[0112] The following compounds were prepared using the same method as that in Example 1 or 2 using corresponding reagents.



[0113] 1-[4-Amino-9-methoxy-2-(2-methoxyethyl)imidazo[4,5-*c*]quinolin-1-yl]-2-methyl-propan-2-ol was obtained as a white solid in 9.18% yield as a HCl salt with 98.5% purity. ¹H NMR (400 MHz, CD₃OD) δ ppm: 7.67 (t, *J* = 8.4 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 1H), 5.60 (m, 1H), 4.48 (m, 1H), 4.14 (s, 3H), 3.97 (m, 2H), 3.47-3.44 (m, 2H), 3.42 (s, 3H), 1.26 (s, 3H), 0.89 (s, 3H); ES-LCMS *m/z*: 345.3 [M+H]⁺.



[0114] 1-[4-Amino-2-(2-hydroxyethyl)-9-methoxy-imidazo[4,5-*c*]quinolin-1-yl]-2-methyl-propan-2-ol was obtained as a white solid in 3.47% yield as a HCl salt with 100% purity. ¹H NMR (400 MHz, CD₃OD) δ ppm: 7.61 (t, *J* = 8.4 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.12 (d, *J* = 7.6 Hz, 1H), 5.54 (m, 1H), 4.41 (m, 1H), 4.08 (s, 3H), 4.07-4.05 (m, 2H), 3.27 (m, 2H), 1.20 (s, 3H), 0.85 (s, 3H); ES-LCMS *m/z*: 331.2 [M+H]⁺.

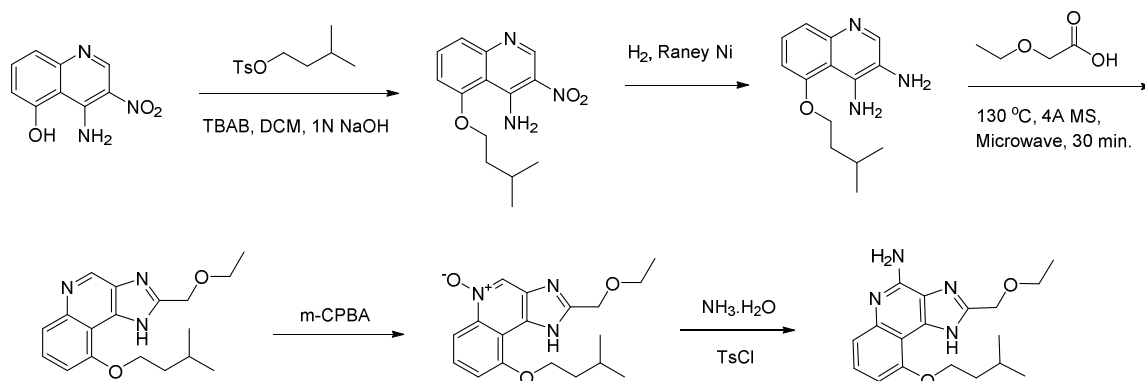


[0115] 4-[[4-Amino-2-(ethoxymethyl)-1*H*-imidazo[4,5-*c*]quinolin-9-yl]oxy]-2-methyl-butan-2-ol was obtained as a white solid in 40.57% yield as a HCl salt. ¹H NMR (400 MHz, CD₃OD) δ ppm: 7.68 (t, *J* = 8.4 Hz, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 4.84 (s, 2H), 4.50 (t, *J* = 6.0 Hz, 2H), 3.76-3.70 (m, 2H), 2.19 (t, *J* = 5.8 Hz, 2H), 1.43 (s, 6H), 1.31 (t, *J* = 7.0 Hz, 3H); ES-LCMS *m/z*: 345.3 [M+H]⁺.

Example 3

[0116] Synthesis of 2-(Ethoxymethyl)-9-isopentyloxy-1*H*-imidazo[4,5-*c*]quinolin-4-amine

Scheme 3



[0117] Step 1: Synthesis of 5-Isopentyloxy-3-nitro-quinolin-4-amine

[0118] To a solution of 4-amino-3-nitro-quinolin-5-ol (300.00 mg, 1.46 mmol, 1.0 eq.), TBAB (470.66 mg, 1.46 mmol, 1.0 eq.) and KI (242.36 mg, 1.46 mmol, 1.0 eq.) in NaOH (1 M, 4.38 mL, 3.0 eq.) was added a solution of isopentyl 4-methylbenzenesulfonate (1.06 g, 4.38 mmol, 3.0 eq.) in DCM (4.00 mL). The resulting mixture was stirred at 20 °C for 40 h. The reaction mixture was diluted with H₂O (10 mL) and extracted with DCM (30 mL x 2). The combined organic layers were washed with brine (10 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure to give a residue. The residue was purified with column chromatography (PE to PE/EA = 1/2). The desired product of 5-isopentyloxy-3-nitro-quinolin-4-amine (140.00 mg, 508.54 μmol, 34.83% yield) was obtained as a yellow solid. ¹H NMR (400 MHz, CDCl₃) δ ppm: 9.33 (s, 1H), 9.25 (s, 1H), 9.10 (s, 1H), 7.66 (t, *J* = 8.2 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 6.94 (d, *J* = 7.6 Hz, 1H), 4.28 (t, *J* = 6.2 Hz, 2H), 1.88 (m, 3H), 1.05 (d, *J* = 6.0 Hz, 6H); ES-LCMS *m/z*: 276.3 [M+H]⁺.

[0119] Step 2: Synthesis of 5-Isopentyloxyquinoline-3,4-diamine

[0120] To a solution of 5-isopentyloxy-3-nitro-quinolin-4-amine (140.00 mg, 508.54 μmol, 1.0 eq.) in MeOH (50.00 mL) was added Raney-Ni (100.00 mg, 1.17 mmol, 2.3 eq.) under N₂. The suspension was degassed under vacuum and purged with H₂ three times. The resulting mixture was stirred under H₂ (15 psi) at 20 °C for 2 h. The reaction mixture was filtered. The filtrate was concentrated in *vacuo*. The desired product of 5-isopentyloxyquinoline-3,4-diamine (120.00 mg, 489.16 μmol, 96.19% yield) was obtained as a green solid. ¹H NMR (400 MHz, CD₃OD) δ ppm: 8.01 (s, 1H), 7.53 (t, *J* = 8.2 Hz, 1H), 7.27 (d, *J* = 8.8 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 4.30 (t, *J* = 6.2 Hz, 2H), 1.89-1.87 (m, 3H), 1.04 (d, *J* = 6.4 Hz, 6H); ES-LCMS *m/z*: 246.3 [M+H]⁺.

[0121] Step 3: Synthesis of 2-(Ethoxymethyl)-9-isopentyloxy-1H-imidazo[4,5-c]quinoline

[0122] 5-Isopentyloxyquinoline-3,4-diamine (110.00 mg, 448.39 μmol, 1.0 eq.), 2-ethoxyacetic acid (1.21 g, 11.62 mmol, 1.10 mL, 25.9 eq.) and 4 Å MS (150.00 mg) were placed into a microwave tube.

The sealed tube was heated at 130 °C for 1 h under microwave. The solid was filtered off. The filtrate was diluted with DCM (50 mL) and water (20 mL). The mixture was adjusted to pH = 7 with aqueous NaOH (1 M). The layers were separated. The organic phase was washed with brine (20 mL), dried over anhydrous Na₂SO₄, filtered and concentrated in *vacuo*. The residue was purified with prep-TLC (DCM/MeOH = 20/1). The desired product of 2-(ethoxymethyl)-9-isopentyloxy-1*H*-imidazo[4,5-*c*]quinoline (130.00 mg, 414.82 μmol, 92.51% yield) was obtained as a yellow solid. ¹H NMR (400 MHz, CD₃OD) δ ppm: 9.10 (s, 1H), 7.73 (d, *J* = 8.8 Hz, 1H), 7.66 (t, *J* = 8.4 Hz, 1H), 7.20 (d, *J* = 7.6 Hz, 1H), 4.80 (s, 2H), 4.48 (t, *J* = 6.6 Hz, 2H), 3.73-3.68 (m, 2H), 1.95-1.88 (m, 3H), 1.29 (t, *J* = 7.0 Hz, 3H), 1.05 (d, *J* = 6.0 Hz, 6H); ES-LCMS *m/z*: 314.3 [M+H]⁺.

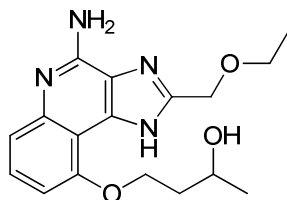
[0123] *Step 4: Synthesis of 2-(Ethoxymethyl)-9-isopentyloxy-5-oxido-1H-imidazo[4,5-c]quinolin-5-ium*

[0124] To a solution of 2-(ethoxymethyl)-9-isopentyloxy-1*H*-imidazo[4,5-*c*]quinoline (130.00 mg, 414.82 μmol, 1.0 eq.) in DCM (30.00 mL) was added *m*-CPBA (126.33 mg, 622.23 μmol, 85% purity, 1.5 eq.). The resulting mixture was stirred at 20 °C for 0.5 h. The reaction mixture was diluted with DCM (20 mL) and washed with saturated K₂CO₃ (10 mL) via extraction. The combined organic layers were washed with brine (15 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The desired product of 2-(ethoxymethyl)-9-isopentyloxy-5-oxido-1*H*-imidazo[4,5-*c*]quinolin-5-ium (130.00 mg, 394.67 μmol, 95.14% yield) was obtained as a brown solid. ¹H NMR (400 MHz, CD₃OD) δ ppm: 9.11 (s, 1H), 8.31 (d, *J* = 8.4 Hz, 1H), 7.82 (t, *J* = 8.8 Hz, 1H), 7.41-7.38 (m, 1H), 4.88 (s, 2H), 4.54 (t, *J* = 6.6 Hz, 2H), 3.73-3.67 (m, 2H), 1.94-1.86 (m, 3H), 1.29 (t, *J* = 7.0 Hz, 3H), 1.04 (d, *J* = 6.0 Hz, 6H); ES-LCMS *m/z*: 330.3 [M+H]⁺.

[0125] *Step 5: Synthesis of 2-(Ethoxymethyl)-9-isopentyloxy-1H-imidazo[4,5-c]quinolin-4-amine*

[0126] To a solution of 2-(ethoxymethyl)-9-isopentyloxy-5-oxido-1*H*-imidazo[4,5-*c*]-quinolin-5-ium (130.00 mg, 394.67 μmol, 1.0 eq.) and NH₃·H₂O (494.04 mg, 3.95 mmol, 542.90 μL, 28% purity, 10.0 eq.) in CHCl₃ (6.00 mL) was added TsCl (112.87 mg, 592.00 μmol, 1.5 eq.). The resulting mixture was stirred at 25 °C for 0.5 h. The solvent was then removed in *vacuo*. The residue was purified with prep-HPLC (MeCN/H₂O as eluents, acidic condition). After lyophilization, the desired product of 2-(ethoxymethyl)-9-isopentyloxy-1*H*-imidazo[4,5-*c*]quinolin-4-amine (75.00 mg, 196.61 μmol, 49.82% yield, 95.65% purity, as HCl salt) was obtained as a white solid. ¹H NMR (400 MHz, CD₃OD) δ ppm: 7.68 (t, *J* = 8.2 Hz, 1H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.17 (d, *J* = 8.4 Hz, 1H), 4.86 (s, 2H), 4.51 (t, *J* = 6.8 Hz, 2H), 3.75-3.70 (m, 2H), 1.94-1.86 (m, 3H), 1.31 (t, *J* = 7.0 Hz, 3H), 1.05 (d, *J* = 6.4 Hz, 6H); ES-LCMS *m/z*: 329.3 [M+H]⁺.

[0127] The following compound was prepared using the same method as that described in Example 3 using corresponding reagents.

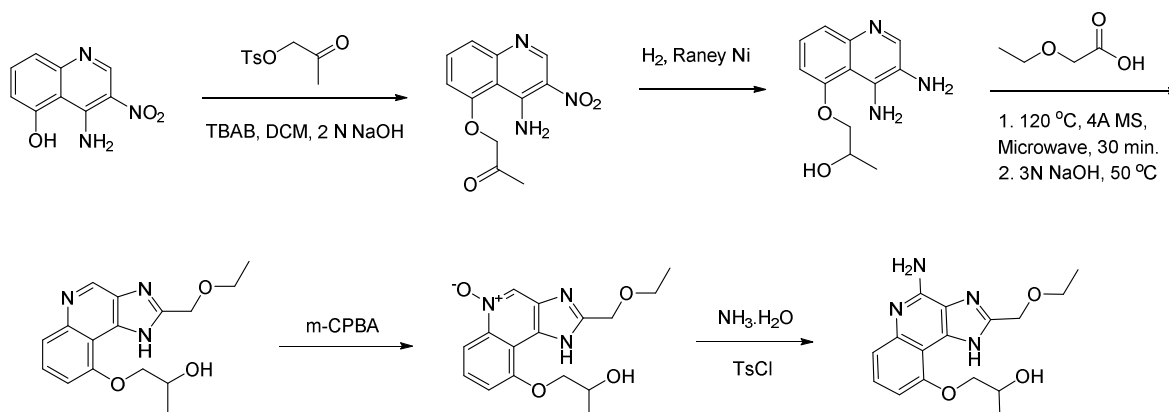


[0128] 4-[[4-Amino-2-(ethoxymethyl)-1H-imidazo[4,5-c]quinolin-9-yl]oxy]butan-2-ol HCl salt was obtained in 20.06% yield with 100% purity as a white solid. ^1H NMR (400MHz, CD_3OD) δ ppm: 7.65 (t, $J = 8.4$ Hz, 1H), 7.31 (d, $J = 8.0$ Hz, 1H), 7.13 (d, $J = 8.4$ Hz, 1H), 4.79 (s, 2H), 4.54-4.53 (m, 1H), 4.42-4.40 (m, 1H), 4.25-4.16 (m, 1H), 3.72-3.66 (m, 2H), 2.15-2.09 (m, 2H), 1.35 (d, $J = 6.4$ Hz, 3H), 1.27 (t, $J = 7.0$ Hz, 3H); ES-LCMS m/z : 330.9 $[\text{M}+\text{H}]^+$.

Example 4

[0129] Synthesis of 1-((4-amino-2-(ethoxymethyl)-1H-imidazo[4,5-c]quinolin-9-yl)oxy)propan-2-ol

Scheme 4



[0130] Step 1: Synthesis of 1-[(4-Amino-3-nitro-5-quinolyl)oxy]propan-2-one

[0131] To a solution of 4-amino-3-nitro-quinolin-5-ol (1.00 g, 4.87 mmol, 1.0 eq.), TBAB (1.57 g, 4.87 mmol, 1.0 eq.), KI (809.09 mg, 4.87 mmol, 1.0 eq.) in NaOH (2 M, 7.31 mL, 3.0 eq.) was added acetyl 4-methylbenzenesulfonate (3.33 g, 14.61 mmol, 3.0 eq.) in DCM (8.00 mL) at 25 °C. The mixture was stirred at 25 °C for 48 h. The reaction mixture was diluted with H_2O (20 mL) and extracted with DCM (50 mL x 2). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4 , filtered and concentrated under reduced pressure to give a residue. The residue was purified with column chromatography (DCM to DCM/MeOH = 20/1). The desired product of 1-[(4-amino-3-nitro-5-

quinolyl)oxy]propan-2-one (220.00 mg, 842.17 μmol , 17.29% yield) was obtained as a yellow solid. ^1H NMR (400 MHz, CDCl_3) δ ppm: 9.84 (br s, 1H), 9.41 (br s, 1H), 9.35 (s, 1H), 7.66-7.60 (m, 2H), 6.80-6.77 (m, 1H), 4.92 (s, 2H), 2.37 (s, 3H); ES-LCMS m/z : 262.2 $[\text{M}+\text{H}]^+$.

[0132] *Step 2: Synthesis of 1-[(3,4-Diamino-5-quinolyl)oxy]propan-2-ol*

[0133] To a solution of 1-[(4-amino-3-nitro-5-quinolyl)oxy]propan-2-one (220.00 mg, 842.17 μmol , 1.0 eq.) in MeOH (100.00 mL) was added Raney-Ni (100.29 mg, 1.17 mmol, 1.39 eq.) under N_2 . The suspension was degassed under vacuum and purged with H_2 several times. The mixture was stirred under H_2 (15 psi) at 25 $^\circ\text{C}$ for 1 h. The solid was filtered off. The filtrate was concentrated in *vacuo*. The desired product of 1-[(3,4-diamino-5-quinolyl)oxy]propan-2-ol (160.00 mg, 685.90 μmol , 81.44% yield) was obtained as a green solid. ^1H NMR (400 MHz, CD_3OD) δ ppm: 7.95 (s, 1H), 7.64-7.60 (m, 1H), 7.28-7.26 (m, 1H), 7.02-6.90 (m, 1H), 4.32-4.29 (m, 2H), 4.07-4.04 (m, 1H), 1.33 (d, $J = 6.4$ Hz, 3H); ES-LCMS m/z : 234.1 $[\text{M}+\text{H}]^+$.

[0134] *Step 3: Synthesis of 1-[[2-(Ethoxymethyl)-1H-imidazo[4,5-c]quinolin-9-yl]oxy]propan-2-ol*

[0135] 1-[(3,4-Diamino-5-quinolyl)oxy]propan-2-ol (150.00 mg, 643.03 μmol , 1.0 eq.), 2-ethoxyacetic acid (1.10 g, 10.57 mmol, 1.00 mL, 16.4 eq.) and 4 $\text{\AA}$ MS (50.00 mg) were placed into a microwave tube. The sealed tube was heated at 120 $^\circ\text{C}$ for 0.5 h under microwave. An aqueous solution of 3 M NaOH (10 mL) and THF (3 mL) were added into the reaction mixture. The resulting mixture was stirred at 50 $^\circ\text{C}$ for 2 h. The mixture was extracted with ethyl acetate (50 mL x 3). The combined organic layers were washed with saturated brine (10 mL), dried over anhydrous Na_2SO_4 , filtered and concentrated under reduced pressure to give a residue. The residue was purified with prep-TLC (DCM/MeOH = 15/1). The desired product of 1-[[2-(ethoxymethyl)-1H-imidazo[4,5-c]quinolin-9-yl]oxy]propan-2-ol (23.00 mg, 76.33 μmol , 11.87% yield) was obtained as a yellow solid. ^1H NMR (400 MHz, CDCl_3) δ ppm: 11.52 (s, 1H), 9.20 (s, 1H), 7.81 (d, $J = 8.4$ Hz, 1H), 7.50 (t, $J = 8.0$ Hz, 1H), 6.97 (d, $J = 7.6$ Hz, 1H), 4.83 (s, 2H), 4.42 (m, 1H), 4.32-4.28 (m, 1H), 4.02 (t, $J = 8.2$ Hz, 1H), 3.64-3.61 (m, 2H), 1.40 (m, 3H), 1.25 (m, 3H); ES-LCMS m/z : 302.2 $[\text{M}+\text{H}]^+$.

[0136] *Step 4: Synthesis of 1-[[2-(Ethoxymethyl)-5-oxido-1H-imidazo[4,5-c]quinolin-5-ium-9-yl]oxy]propan-2-ol*

[0137] To a mixture of 1-[[2-(ethoxymethyl)-1H-imidazo[4,5-c]quinolin-9-yl]oxy]propan-2-ol (23.00 mg, 76.33 μmol , 1.0 eq.) in DCM (8.00 mL) was added *m*-CPBA (30.99 mg, 152.65 μmol , 85% purity, 2.0 eq.) in one portion at 25 $^\circ\text{C}$. The mixture was stirred at 25 $^\circ\text{C}$ for 1 h. The solvent was removed in *vacuo*. The crude product was used for the next step without further purification. The crude product of 1-[[2-(ethoxymethyl)-5-oxido-1H-imidazo[4,5-c]quinolin-5-ium-9-yl]oxy]propan-2-ol (20.00 mg, 63.02

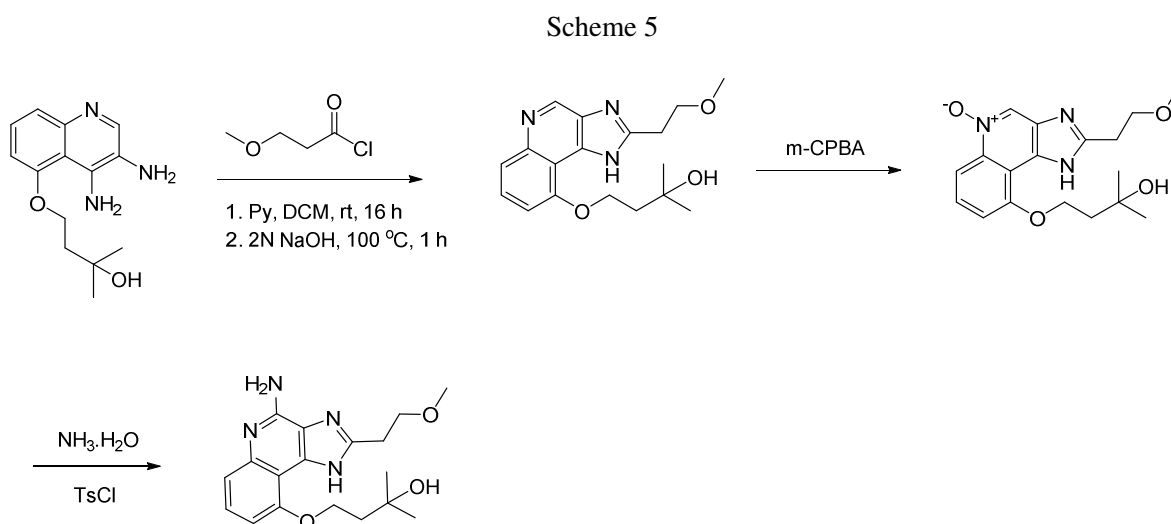
μmol , 82.57% yield) was obtained as a brown solid. ^1H NMR (400 MHz, CDCl_3) δ ppm: 9.17 (s, 1H), 8.39 (d, $J = 8.8$ Hz, 1H), 7.47-7.45 (m, 1H), 7.05-7.01 (m, 1H), 4.86 (s, 2H), 4.48 (m, 1H), 4.37 (m, 1H), 4.06 (d, $J = 8.4$ Hz, 1H), 3.74-3.71 (m, 2H), 1.47 (br d, $J = 6.4$ Hz, 3H), 1.35 (t, $J = 7.2$ Hz, 3H); ES-LCMS m/z : = 318.2 $[\text{M}+\text{H}]^+$.

[0138] Step 5: Synthesis of 1-[[4-Amino-2-(ethoxymethyl)-1H-imidazo[4,5-c]quinolin-9-yl]oxy]-propan-2-ol

[0139] To a mixture of 1-[[2-(ethoxymethyl)-5-oxido-1H-imidazo[4,5-c]quinolin-5-ium-9-yl]oxy]propan-2-ol (20.00 mg, 63.02 μmol , 1.0 eq.) and $\text{NH}_3\cdot\text{H}_2\text{O}$ (78.89 mg, 630.24 μmol , 86.69 μL , 28% purity, 10.0 eq.) in CHCl_3 (6.00 mL) was added TsCl (24.03 mg, 126.05 μmol , 2.0 eq.) at 25 °C. The mixture was stirred at 25 °C for 3 h. The reaction mixture was concentrated under reduced pressure to remove the solvent. The residue was purified with preparative HPLC (MeCN/ H_2O as eluents, acidic condition). After lyophilization, the desired product of 1-[[4-amino-2-(ethoxymethyl)-1H-imidazo[4,5-c]quinolin-9-yl]oxy]propan-2-ol (4.68 mg, 13.26 μmol , 21.04% yield, as HCl salt) was obtained as a white solid. ^1H NMR (400 MHz, CD_3OD) δ ppm: 7.66 (t, $J = 8.4$ Hz, 1H), 7.35 (d, $J = 8.4$ Hz, 1H), 7.20 (d, $J = 8.4$ Hz, 1H), 4.83 (s, 2H), 4.42-4.39 (m, 1H), 4.36 (m, 1H), 4.18-4.16 (m, 1H), 3.71-3.68 (m, 2H), 1.36 (d, $J = 6.4$ Hz, 3H), 1.29 (t, $J = 7.2$ Hz, 3H); ES-LCMS m/z : 317.2 $[\text{M}+\text{H}]^+$.

Example 5

[0140] Synthesis of 4-[[4-Amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-9-yl]oxy]-2-methylbutan-2-ol



[0141] Step 1: Synthesis of 4-[[2-(2-Methoxyethyl)-1H-imidazo[4,5-c]quinolin-9-yl]oxy]-2-methylbutan-2-ol

[0142] To a solution of 4-[(3,4-diamino-5-quinolyl)oxy]-2-methyl-butan-2-ol (179.17 mg, 329.10 μ mol, 1.0 eq.) and pyridine (260.32 mg, 3.29 mmol, 265.63 μ L, 10.0 eq.) in DCM (2.00 mL) was added 3-methoxypropanoyl chloride (80.66 mg, 658.20 μ mol, 2.0 eq.). The resulting mixture was stirred at 25 °C for 16 h. The solvent was removed in *vacuo*. The residue was dissolved in NaOH (2 M, 4.00 mL, 24.3 eq.) and stirred at 100 °C for 1 h. The mixture was diluted with water (10 mL) and extracted with DCM (50 mL x 2). The combined organic phase was washed with brine (30 mL), dried over Na₂SO₄, filtered and concentrated in *vacuo*. The residue was purified with prep-TLC (DCM/MeOH = 15/1). The desired product of 4-[[2-(2-methoxyethyl)-1*H*-imidazo[4,5-*c*]quinolin-9-yl]oxy]-2-methyl-butan-2-ol (90.00 mg, 273.23 μ mol, 83.02% yield) was obtained as a brown solid. ¹H NMR (400 MHz, CD₃OD) δ ppm: 9.08 (s, 1H), 7.73 (d, *J* = 8.4 Hz, 1H), 7.65 (t, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 7.2 Hz, 1H), 4.51 (t, *J* = 6.0 Hz, 2H), 3.93 (t, *J* = 6.4 Hz, 2H), 3.42 (s, 3H), 3.33-3.28 (m, 2H), 2.23 (t, *J* = 6.0 Hz, 2H), 1.44 (s, 6H); ES-LCMS *m/z*: 330.3 [M+H]⁺.

[0143] *Step 2: Synthesis of 4-[[2-(2-Methoxyethyl)-5-oxido-1*H*-imidazo[4,5-*c*]quinolin-5-ium-9-yl]oxy]-2-methyl-butan-2-ol*

[0144] To a solution of 4-[[2-(2-methoxyethyl)-1*H*-imidazo[4,5-*c*]quinolin-9-yl]oxy]-2-methyl-butan-2-ol (90.00 mg, 273.23 μ mol, 1.0 eq.) in DCM (10.00 mL) was added *m*-CPBA (83.21 mg, 409.85 μ mol, 85% purity, 1.5 eq.). The resulting mixture was stirred at 25 °C for 0.5 h. The solvent was removed in *vacuo*. The residue was purified with prep-TLC (DCM/MeOH = 15/1). The desired product of 4-[[2-(2-methoxyethyl)-5-oxido-1*H*-imidazo[4,5-*c*]quinolin-5-ium-9-yl]oxy]-2-methyl-butan-2-ol (60.00 mg, 173.72 μ mol, 63.58% yield) was obtained as a yellow solid. ¹H NMR (400 MHz, CDCl₃) δ ppm: 8.97 (s, 1H), 8.36 (d, *J* = 8.8 Hz, 1H), 7.54 (t, *J* = 8.4 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 4.38 (t, *J* = 5.6 Hz, 2H), 3.81 (t, *J* = 6.2 Hz, 2H), 3.40 (s, 3H), 3.17 (t, *J* = 6.0 Hz, 2H), 2.24 (t, *J* = 5.6 Hz, 2H), 1.48 (s, 6H); ES-LCMS *m/z*: 345.9 [M+H]⁺.

[0145] *Step 3: Synthesis of 4-[[4-Amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-*c*]quinolin-9-yl]oxy]-2-methyl-butan-2-ol*

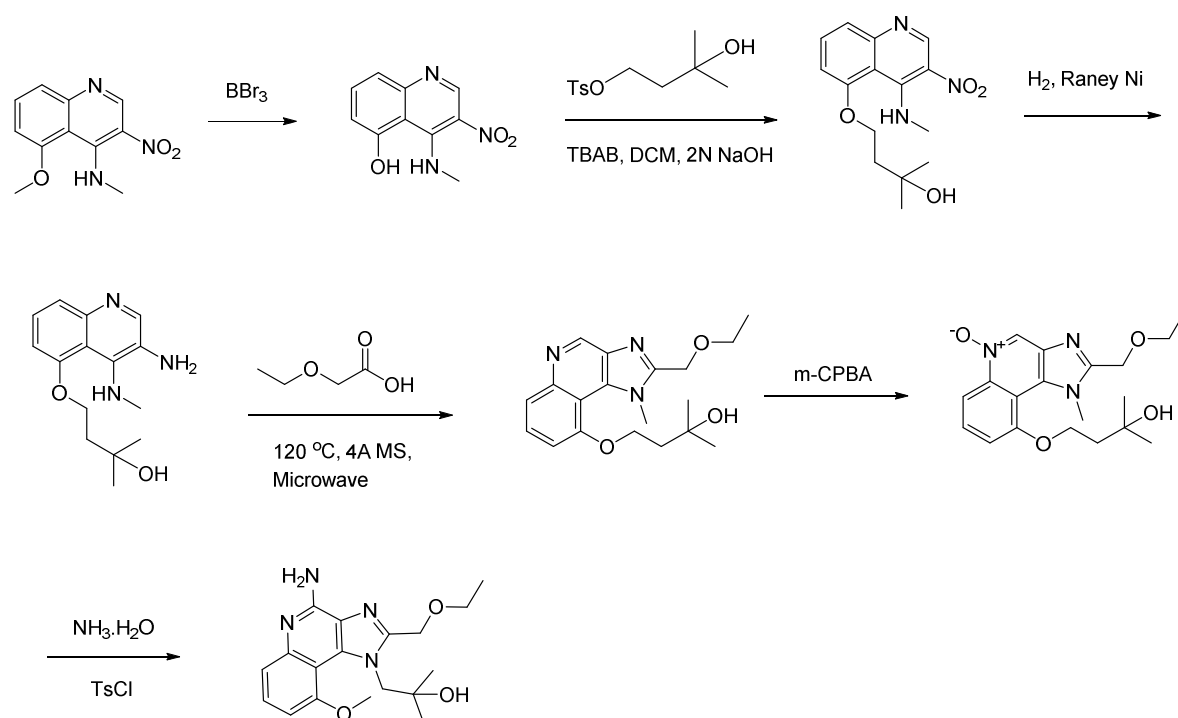
[0146] To a solution of 4-[[2-(2-methoxyethyl)-5-oxido-1*H*-imidazo[4,5-*c*]quinolin-5-ium-9-yl]oxy]-2-methyl-butan-2-ol (60.00 mg, 173.72 μ mol, 1.0 eq.) and NH₃·H₂O (217.81 mg, 1.74 mmol, 239.35 μ L, 28% purity, 10.0 eq.) in CHCl₃ (6.00 mL) was added TsCl (66.24 mg, 347.44 μ mol, 2.0 eq.). The resulting mixture was stirred at 25 °C for 0.5 h. The solvent was removed in *vacuo*. The residue was purified with prep-HPLC (MeCN/H₂O as eluents, acidic condition). After lyophilization, the desired product of 4-[[4-amino-2-(2-methoxyethyl)-1*H*-imidazo[4,5-*c*]quinolin-9-yl]oxy]-2-methyl-butan-2-ol (24.95 mg, 63.20 μ mol, 36.38% yield, 96.48% purity, as HCl salt) was obtained as a white solid. ¹H NMR (400 MHz, CD₃OD) δ ppm: 7.66 (t, *J* = 8.2 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.13 (d, *J* = 8.0 Hz,

1H), 4.49 (t, $J = 6.0$ Hz, 2H), 3.93 (t, $J = 6.6$ Hz, 2H), 3.42 (s, 3H), 3.26 (t, $J = 6.2$ Hz, 2H), 2.19 (t, $J = 5.8$ Hz, 2H), 1.43 (s, 6H); ES-LCMS m/z : 345.3 $[M+H]^+$.

Example 6

[0147] Synthesis of 4-[4-Amino-2-(ethoxymethyl)-1-methyl-imidazo[4,5-*c*]quinolin-9-yl]oxy-2-methylbutan-2-ol

Scheme 6



[0148] Step 1: Synthesis of 4-(methylamino)-3-nitro-quinolin-5-ol

[0149] To a solution of 5-methoxy-*N*-methyl-3-nitro-quinolin-4-amine (300.00 mg, 1.29 mmol, 1.0 eq.) in DCM (15.00 mL) was added BBr_3 (1.62 g, 6.45 mmol, 621.48 μL , 5.0 eq.) dropwise at -78°C . The resulting mixture was stirred at 60°C for 2 h. The mixture was added to MeOH (100 mL) dropwise at -30°C . The solvent was removed in *vacuo*. The desired product of 4-(methylamino)-3-nitro-quinolin-5-ol (300.00 mg, crude) was obtained as a brown solid. ^1H NMR (400 MHz, CD_3OD) δ ppm: 9.22 (s, 1H), 7.79 (m, 1H), 7.33 (m, 1H), 7.15-7.13 (m, 1H), 3.08 (s, 3H); ES-LCMS m/z : 220.2 $[M+H]^+$.

[0150] Step 2: Synthesis of 2-methyl-4-[[4-(methylamino)-3-nitro-5-quinolyl]oxy]butan-2-ol

[0151] To a solution of 4-(methylamino)-3-nitro-quinolin-5-ol (250.00 mg, 1.14 mmol, 1.0 eq.), TBAB (367.67 mg, 1.14 mmol, 1.0 eq.) and KI (189.32 mg, 1.14 mmol, 1.0 eq.) in NaOH (2 M, 1.71 mL, 3.0 eq.) was added a solution of (3-hydroxy-3-methyl-butyl)4- methylbenzenesulfonate (883.49 mg, 3.42

mmol, 3.0 eq.) in DCM (3.00 mL). The resulting mixture was stirred at 25 °C for 64 h. The reaction mixture was diluted with H₂O (10 mL) and extracted with DCM (30 mL x 2). The combined organic layers were washed with brine (10 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure to give a residue. The residue was purified with column chromatography (DCM to DCM/MeOH = 20/1). The desired product of 2-methyl-4-[[4-(methylamino)-3-nitro-5-quinolyl]oxy]butan-2-ol (100.00 mg, 327.51 μmol, 28.73% yield) was obtained as a yellow solid. ¹H NMR (400 MHz, CDCl₃) δ ppm: 9.36 (s, 1H), 9.02 (s, 1H), 7.61-7.55 (m, 2H), 6.91 (d, *J* = 6.8 Hz, 1H), 4.36 (t, *J* = 5.8 Hz, 2H), 2.84 (d, *J* = 5.2 Hz, 3H), 2.13 (t, *J* = 5.8 Hz, 2H), 1.41 (s, 6H); ES-LCMS *m/z*: 306.0 [M+H]⁺.

[0152] *Step 3: Synthesis of 4-[[3-Amino-4-(methylamino)-5-quinolyl]oxy]-2-methyl-butan-2-ol*

[0153] To a solution of 2-methyl-4-[[4-(methylamino)-3-nitro-5-quinolyl]oxy]butan-2-ol (100.00 mg, 327.51 μmol, 1.0 eq.) in MeOH (50.00 mL) was added Raney-Ni (100.00 mg, 1.17 mmol, 3.6 eq.) under N₂. The suspension was degassed under vacuum and purged with H₂ several times. The mixture was stirred under H₂ (15 psi) at 25 °C for 1 h. The mixture was filtered. The filtrate was concentrated in *vacuo*. The desired product of 4-[[3-amino-4-(methylamino)-5-quinolyl]oxy]-2-methyl-butan-2-ol (80.00 mg, 290.54 μmol, 88.71% yield) was obtained as a green solid. ¹H NMR (400 MHz, CD₃OD) δ ppm: 8.07 (s, 1H), 7.44 (t, *J* = 8.0 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 4.35 (t, *J* = 6.4 Hz, 2H), 3.19 (d, *J* = 10.4 Hz, 3H), 2.10 (d, *J* = 6.4 Hz, 2H), 1.33 (s, 6H); ES-LCMS *m/z*: 276.3 [M+H]⁺.

[0154] *Step 4: Synthesis of 4-[2-(ethoxymethyl)-1-methyl-imidazo[4,5-*c*]quinolin-9-yl]oxy-2-methyl-butan-2-ol*

[0155] 4-[[3-Amino-4-(methylamino)-5-quinolyl]oxy]-2-methyl-butan-2-ol (70.00 mg, 254.22 μmol, 1.0 eq.), 2-ethoxyacetic acid (1.65 g, 15.85 mmol, 1.50 mL, 62.4 eq.) and 4Å MS (100.00 mg) were placed into a microwave tube. The sealed tube was heated at 120 °C for 30 minutes under microwave. The mixture was filtered. The filtrate was diluted with DCM (50 mL) and water (10 mL) and was adjusted to pH = 7 by aqueous NaOH (2 M). The organic layer was separated and washed with brine (10 mL), dried with anhydrous Na₂SO₄, filtered and concentrated in *vacuo*. The crude product was purified with prep-TLC (DCM/MeOH = 15/1). The desired product of 4-[2-(ethoxymethyl)-1-methyl-imidazo [4,5-*c*]quinolin-9-yl]oxy-2-methyl-butan-2-ol (20.00 mg, 58.24 μmol, 22.91% yield) was obtained as a yellow solid. ¹H NMR (400 MHz, CDCl₃) δ ppm: 9.25 (s, 1H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.59 (t, *J* = 8.2 Hz, 1H), 7.10 (d, *J* = 7.2 Hz, 1H), 4.89 (s, 2H), 4.48 (t, *J* = 7.6 Hz, 2H), 4.32 (s, 3H), 3.66-3.61 (m, 2H), 2.20 (t, *J* = 7.6 Hz, 2H), 1.38 (s, 6H), 1.26 (m, 3H); ES-LCMS *m/z*: 344.3 [M+H]⁺.

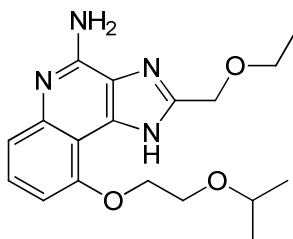
[0156] *Step 5: Synthesis of 4-[2-(Ethoxymethyl)-1-methyl-5-oxido-imidazo[4,5-c]quinolin-5-ium-9-yl]oxy-2-methyl-butan-2-ol*

[0157] To a solution of 4-[2-(ethoxymethyl)-1-methyl-imidazo[4,5-c]quinolin-9-yl]-oxy- 2-methyl-butan-2-ol (20.00 mg, 58.24 μmol , 1.0 eq.) in DCM (5.00 mL) was added *m*-CPBA (23.65 mg, 116.48 μmol , 85% purity, 2.0 eq.). The resulting mixture was stirred at 25 °C for 0.5 h. The solvent was removed in *vacuo*. The residue was purified with prep-TLC (DCM/MeOH = 10/1). The desired product of 4-[2-(ethoxymethyl)-1-methyl-5-oxido-imidazo[4,5-c]quinolin-5-ium-9-yl]oxy-2-methyl-butan-2-ol (20.00 mg, crude) was obtained as a white solid. ^1H NMR (400 MHz, CDCl_3) δ ppm: 9.28 (s, 1H), 8.70 (d, J = 8.8 Hz, 1H), 7.71 (t, J = 8.2 Hz, 1H), 7.22 (d, J = 8.0 Hz, 1H), 4.86 (s, 2H), 4.52-4.48 (m, 2H), 4.28 (s, 3H), 3.67-3.61 (m, 2H), 2.23-2.16 (m, 2H), 1.35 (s, 6H), 1.29-1.27 (m, 3H); ES-LCMS m/z : 360.3 $[\text{M}+\text{H}]^+$.

[0158] *Step 6: Synthesis of 4-[4-Amino-2-(ethoxymethyl)-1-methyl-imidazo[4,5-c]quinolin-9-yl]oxy-2-methyl-butan-2-ol*

[0159] To a solution of 4-[2-(ethoxymethyl)-1-methyl-5-oxido-imidazo[4,5-c]quinolin-5-ium-9-yl]oxy-2-methyl-butan-2-ol (20.00 mg, 55.65 μmol , 1.0 eq.) and $\text{NH}_3\cdot\text{H}_2\text{O}$ (69.66 mg, 556.45 μmol , 76.54 μL , 28% purity, 10.0 eq.) in CHCl_3 (2.00 mL) was added TsCl (15.91 mg, 83.47 μmol , 1.5 eq.). The resulting mixture was stirred at 25 °C for 0.5 h. The solvent was removed in *vacuo*. The residue was purified with prep-HPLC (MeCN/ H_2O as eluents, acidic condition). After lyophilization, the desired product of 4-[4-amino-2-(ethoxymethyl)-1-methyl-imidazo[4,5-c]quinolin-9-yl]oxy-2-methyl-butan-2-ol (6.00 mg, 15.19 μmol , 27.30% yield, as a HCl salt) was obtained as a white solid: ^1H NMR (400MHz, CD_3OD) δ ppm: 7.65 (t, J = 8.2 Hz, 1H), 7.31 (d, J = 8.4 Hz, 1H), 7.18 (d, J = 8.0 Hz, 1H), 4.85 (s, 2H), 4.48 (t, J = 7.8 Hz, 2H), 4.26 (s, 3H), 3.68-3.63 (m, 2H), 2.16 (t, J = 7.8 Hz, 2H), 1.31 (s, 6H), 1.26 (t, J = 6.8 Hz, 3H); ES-LCMS m/z : 359.3 $[\text{M}+\text{H}]^+$.

[0160] The following compound was prepared in a similar way as that described in Examples 5 and 6 using corresponding reagents.

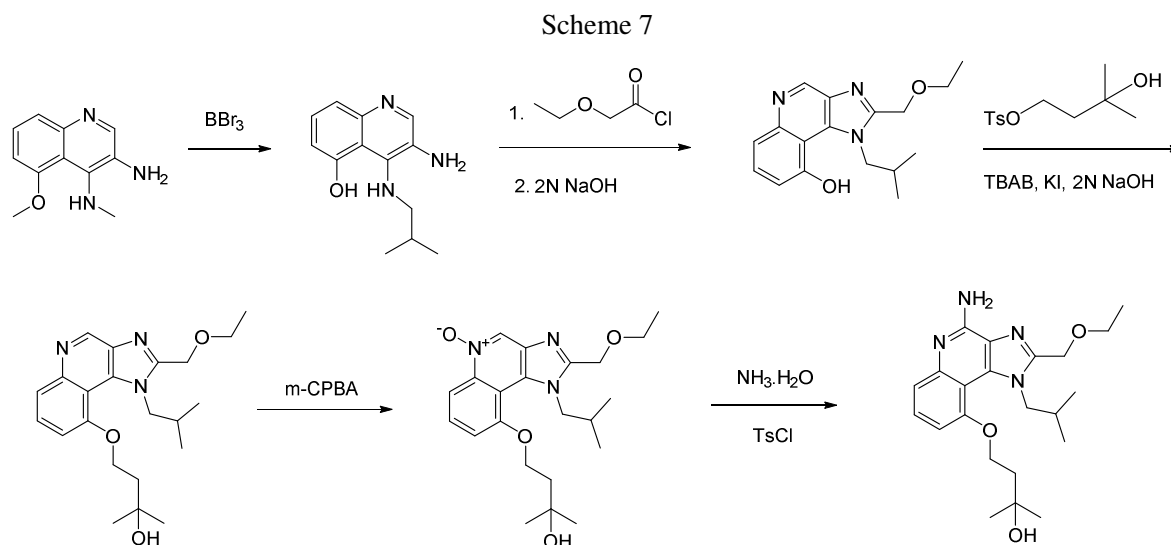


[0161] 2-(Ethoxymethyl)-9-(2-isopropoxyethoxy)-1H-imidazo[4,5-c]quinolin-4-amine was obtained in 40.79% yield with 100% purity as a HCl salt as a white solid. ^1H NMR (400 MHz, CD_3OD) δ ppm: 7.63

(t, $J = 8.2$ Hz, 1H), 7.30 (d, $J = 8.4$ Hz, 1H), 7.18 (d, $J = 8.0$ Hz, 1H), 4.79 (s, 2H), 4.54-4.51 (m, 2H), 3.94-3.91 (m, 2H), 3.75-3.69 (m, 1H), 3.66-3.64 (m, 2H), 1.24 (t, $J = 7.0$ Hz, 3H), 1.15 (d, $J = 6.0$ Hz, 6H); ES-LCMS m/z : 345.3 [M+H].

Example 7

[0162] Synthesis of 4-[4-Amino-2-(ethoxymethyl)-1-isobutyl-imidazo[4,5-*c*]quinolin-9-yl]oxy-2-methyl-butan-2-ol



[0163] Step 1: Synthesis of 3-Amino-4-(isobutylamino)quinolin-5-ol

[0164] To a solution of *N*⁴-isobutyl-5-methoxy-quinoline-3,4-diamine (450.00 mg, 1.83 mmol, 1.0 eq.) in DCM (30.00 mL) was added BBr₃ (2.30 g, 9.17 mmol, 883.73 μ L, 5.0 eq.) dropwise at -78 °C. The resulting mixture was stirred at 60 °C for 2 h. The mixture was added to MeOH (100 mL) dropwise at -30 °C. The solvent was removed in *vacuo*. The desired product of 3-amino-4-(isobutylamino) quinolin-5-ol (500.00 mg, 1.64 mmol, 89.81% yield, as 2HCl salt) was obtained as a brown solid. ¹H NMR (400 MHz, CD₃OD) δ ppm: 8.19 (s, 1H), 7.65 (t, $J = 8.2$ Hz, 1H), 7.24 (d, $J = 8.4$ Hz, 1H), 6.97 (d, $J = 7.2$ Hz, 1H), 3.80 (d, $J = 6.4$ Hz, 2H), 2.07-2.02 (m, 1H), 1.10 (d, $J = 6.4$ Hz, 6H); ES-LCMS m/z : 232.3 [M+H]⁺.

[0165] Step 2: Synthesis of 2-(Ethoxymethyl)-1-isobutyl-imidazo[4,5-*c*]quinolin-9-ol

[0166] To a solution of 3-amino-4-(isobutylamino)quinolin-5-ol (450.00 mg, 1.48 mmol, 1.0 eq., as 2HCl salt) in Pyridine (4.90 g, 61.95 mmol, 5.0 mL, 41.9 eq.) was added 2-ethoxyacetyl chloride (271.92 mg, 2.22 mmol, 1.5 eq.). The resulting mixture was stirred at 25 °C for 1 h. The solvent was removed in *vacuo*. The residue was dissolved in NaOH (2 M, 7.40 mmol, 3.0 mL, 5.0 eq.) and stirred at 100 °C for 2 h. The mixture was partitioned between DCM (40 mL) and water (10 mL). The organic layer was separated,

washed with brine (10 mL), dried over Na₂SO₄, filtered and concentrated in *vacuo*. The residue was purified with column chromatography (DCM to DCM/MeOH = 10/1). The desired product of 2-(ethoxymethyl)-1-isobutyl-imidazo[4,5-*c*]quinolin-9-ol (100.00 mg, 334.03 μmol, 22.58% yield) was obtained as a red solid. ¹H NMR (400 MHz, CD₃OD) δ ppm: 9.06 (s, 1H), 7.69-7.67 (m, 1H), 7.56 (t, *J* = 8.0 Hz, 1H), 7.11-7.08 (m, 1H), 4.89 (s, 2H), 4.65-4.63 (m, 2H), 3.68-3.62 (m, 2H), 2.24-2.16 (m, 1H), 1.26 (t, *J* = 7.0 Hz, 3H), 0.79-0.76 (m, 6H); ES-LCMS *m/z*: 300.3 [M+H]⁺.

[0167] *Step 3: Synthesis of 4-[2-(Ethoxymethyl)-1-isobutyl-imidazo[4,5-*c*]quinolin-9-yl]oxy-2-methyl-butan-2-ol*

[0168] To a solution of 2-(ethoxymethyl)-1-isobutyl-imidazo[4,5-*c*]quinolin-9-ol (60.00 mg, 200.42 μmol, 1.0 eq.), TBAB (64.61 mg, 200.42 μmol, 1.0 eq.) and KI (33.27 mg, 200.42 μmol, 1.0 eq.) in NaOH (2 M, 300.63 μL, 3.0 eq.) was added a solution of (3-hydroxy-3-methyl-butyl)4-methylbenzenesulfonate (155.32 mg, 601.26 μmol, 3.0 eq.) in DCM (3.00 mL). The resulting mixture was stirred at 25 °C for 64 h. The reaction mixture was diluted with H₂O (20 mL) and extracted with DCM (50 mL x 2). The combined organic layers were washed with brine (20 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure to give a residue. The residue was purified with column chromatography (DCM to DCM/MeOH = 10/1). The desired product of 4-[2-(ethoxymethyl)-1-isobutyl-imidazo[4,5-*c*]quinolin-9-yl]oxy-2-methyl-butan-2-ol (60.00 mg, 155.64 μmol, 77.66% yield) was obtained as a red solid. ¹H NMR (400 MHz, CDCl₃) δ ppm: 9.26 (s, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.59 (t, *J* = 8.2 Hz, 1H), 7.09 (d, *J* = 7.2 Hz, 1H), 4.88 (s, 2H), 4.68 (br, s, 2H), 4.48 (t, *J* = 7.4 Hz, 2H), 3.65-3.59 (m, 2H), 2.19 (t, *J* = 7.6 Hz, 2H), 2.06-2.02 (m, 1H), 1.34 (s, 6H), 1.28-1.24 (m, 3H), 0.66 (d, *J* = 6.0 Hz, 6H); ES-LCMS *m/z*: 386.4 [M+H]⁺.

[0169] *Step 4: Synthesis of 4-[2-(Ethoxymethyl)-1-isobutyl-5-oxido-imidazo[4,5-*c*]quinolin-5-ium-9-yl]oxy-2-methyl-butan-2-ol*

[0170] To a solution of 4-[2-(ethoxymethyl)-1-isobutyl-imidazo[4,5-*c*]quinolin-9-yl]oxy-2-methyl-butan-2-ol (60.00 mg, 155.64 μmol, 1.0 eq.) in DCM (10.00 mL) was added *m*-CPBA (47.40 mg, 233.46 μmol, 85% purity, 1.5 eq.). The resulting mixture was stirred at 25 °C for 0.5 h. The solvent was removed in *vacuo*. The residue was purified with prep-TLC (DCM/MeOH = 10/1). The desired product of 4-[2-(ethoxymethyl)-1-isobutyl-5-oxido-imidazo[4,5-*c*]quinolin-5-ium-9-yl]oxy-2-methyl-butan-2-ol (50.00 mg, 124.53 μmol, 80.01% yield) was obtained as a yellow solid. ¹H NMR (400 MHz, CDCl₃) δ ppm: 9.07 (s, 1H), 8.68 (d, *J* = 8.0 Hz, 1H), 7.68 (t, *J* = 8.4 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 4.84 (s, 2H), 4.61 (br, s, 2H), 4.51 (t, *J* = 7.8 Hz, 2H), 3.65-3.59 (m, 2H), 2.19 (t, *J* = 7.6 Hz, 2H), 1.99-1.94 (m, 1H), 1.35 (s, 6H), 1.29-1.27 (m, 3H), 0.67 (d, *J* = 6.0 Hz, 6H); ES-LCMS *m/z*: 402.4 [M+H]⁺.

[0171] *Step 5: Synthesis of 4-[4-Amino-2-(ethoxymethyl)-1-isobutyl-imidazo[4,5-c]quinolin-9-yl]oxy-2-methyl-butan-2-ol*

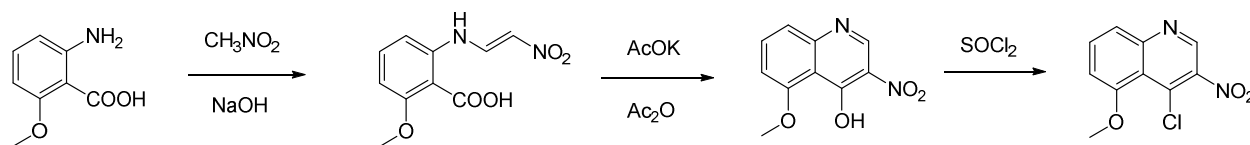
[0172] To a solution of 4-[2-(ethoxymethyl)-1-isobutyl-5-oxido-imidazo[4,5-c]quinolin-5-ium-9-yl]oxy-2-methyl-butan-2-ol (50.00 mg, 124.53 μ mol, 1.0 eq.) and $\text{NH}_3 \cdot \text{H}_2\text{O}$ (155.89 mg, 1.25 mmol, 171.31 μ L, 28% purity, 10.0 eq.) in CHCl_3 (5.00 mL) was added TsCl (28.49 mg, 149.44 μ mol, 1.2 eq.). The resulting mixture was stirred at 25 °C for 0.5 h. The solvent was removed in *vacuo*. The residue was purified with prep-HPLC (MeCN/ H_2O as eluents, acidic condition). After lyophilization, the desired product of 4-[4-amino-2-(ethoxymethyl)-1-isobutyl-imidazo[4,5-c]quinolin-9-yl]oxy-2-methyl-butan-2-ol (26.50 mg, 60.38 μ mol, 48.48% yield, 99.56% purity, as a HCl salt) was obtained as a white solid. ^1H NMR (400 MHz, CD_3OD) δ ppm: 7.69 (t, J = 8.2 Hz, 1H), 7.34 (t, J = 8.0 Hz, 1H), 7.22 (d, J = 8.4 Hz, 1H), 4.87 (s, 2H), 4.71 (br, s, 2H), 4.53 (t, J = 7.6 Hz, 1H), 3.69-3.63 (m, 2H), 2.18 (t, J = 7.6 Hz, 2H), 2.02-1.97 (m, 1H), 1.29 (s, 6H), 1.26 (t, J = 7.0 Hz, 3H), 0.74 (d, J = 4.2 Hz, 6H); ES-LCMS m/z : 401.4 $[\text{M}+\text{H}]^+$.

Example 8

[0173] Preparation of Intermediates

[0174] Intermediate 1: 4-Chloro-5-methoxy-3-nitro-quinoline

Scheme 8



[0175] *Step 1: Synthesis of 2-methoxy-6-[[*(E)*-2-nitrovinyl]amino]benzoic acid*

[0176] To a solution of NaOH (40.20 g, 1.01 mol, 3.4 eq.) in water (100 mL) was added CH_3NO_2 (23.73 g, 388.84 mmol, 21.00 mL, 1.3 eq.) at 0 °C. The mixture was warmed to 40 °C and additional amount of CH_3NO_2 (23.73 g, 388.84 mmol, 21.00 mL, 1.3 eq.) was added slowly at 40 °C. This temperature was maintained until all solids dissolved and a clear red solution was obtained. The solution was cooled to 30 °C, poured into 300 g of chipped ice, and acidified with concentrated HCl (100 mL). The mixture was immediately added to a solution of 2-amino-6-methoxy-benzoic acid (50.00 g, 299.11 mmol, 1.0 eq.) and conc. HCl (35 mL) in water (1400 mL). The solution was allowed to stir at 20 °C for 16 h. The mixture was filtered. The cake was washed with water (300 mL x 3), and dried in *vacuo*. The desired product of 2-methoxy-6-[[*(E)*-2-nitrovinyl] amino]benzoic acid (67.00 g, 281.28 mmol, 94.04% yield) was obtained as a yellow solid. ^1H NMR (400 MHz, CD_3OD) δ ppm: 7.70 (d, J = 6.0 Hz, 1H), 7.51 (t, J = 8.4 Hz, 1H),

7.11 (d, $J = 8.4$ Hz, 1H), 6.93 (d, $J = 8.4$ Hz, 1H), 6.68 (d, $J = 6.0$ Hz, 1H), 3.89 (d, $J = 4.4$ Hz, 3H); ES-LCMS m/z : 261.1 [M+Na]⁺.

[0177] *Step 2: Synthesis of 5-methoxy-3-nitro-quinolin-4-ol*

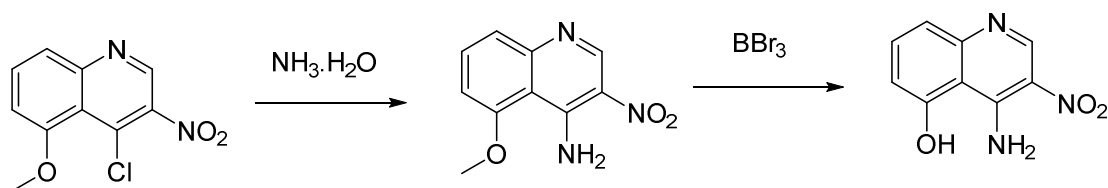
[0178] A solution of 2-methoxy-6-[[*(E)*-2-nitrovinyl]amino]benzoic acid (56.00 g, 235.10 mmol, 1.0 eq.) in Ac₂O (300.00 mL) was heated at 105 °C for 0.5 h, and a clear solution was obtained. AcOK (27.69 g, 282.12 mmol, 1.2 eq.) was added. The resulting mixture was stirred at 105 °C for 2 h. The mixture was filtered. The cake was washed with acetic acid (30 mL x 2) and water (100 mL x 3). The cake was dried on oil pump. The desired product of 5-methoxy-3-nitro-quinolin-4-ol (19.00 g, 86.29 mmol, 36.70% yield) was obtained as an off-white solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ ppm: 12.59 (s, 1H), 8.96 (s, 1H), 7.62 (t, $J = 8.2$ Hz, 1H), 7.16 (d, $J = 8.0$ Hz, 1H), 6.95 (d, $J = 8.0$ Hz, 1H), 3.83 (s, 3H); ES-LCMS m/z : 221.2 [M+H]⁺.

[0179] *Step 3: Synthesis of 4-chloro-5-methoxy-3-nitro-quinoline*

[0180] To a suspension of 5-methoxy-3-nitro-quinolin-4-ol (2.00 g, 9.08 mmol, 1.0 eq.) in SOCl₂ (8.20 g, 68.92 mmol, 5.00 mL, 7.6 eq.) was added DMF (66.39 mg, 908.35 μ mol, 69.89 μ L, 0.1 eq.). The resulting mixture was stirred at 80 °C for 4 h. The solvent was removed in *vacuo*. The desired product of 4-chloro-5-methoxy-3-nitro-quinoline (2.10 g, 8.80 mmol, 96.92% yield) was obtained as a brown solid. ¹H NMR (400 MHz, CDCl₃) δ ppm: 9.12 (s, 1H), 8.08 (t, $J = 8.8$ Hz, 1H), 7.96-7.92 (m, 1H), 7.20 (d, $J = 8.4$ Hz, 1H), 4.08 (s, 3H); ES-LCMS m/z : 239.2 [M+H]⁺.

[0181] Intermediate 2: 4-Amino-3-nitro-quinolin-5-ol

Scheme 9



[0182] *Step 1: Synthesis of 5-methoxy-3-nitro-quinolin-4-amine*

[0183] A solution of 4-chloro-5-methoxy-3-nitro-quinoline (5.28 g, 22.13 mmol, 1.0 eq.) in THF (50 mL) was added to NH₃.H₂O (91.00 g, 726.96 mmol, 100.00 mL, 28% purity, 32.9 eq.) in THF (100 mL) dropwise at 0 °C. The mixture was stirred at 25 °C for 2 h. The reaction mixture was filtered. The residue was washed with H₂O (50 mL x 3) and dried in *vacuo*. The desired product of 5-methoxy-3-nitro-quinolin-4-amine (4.83 g, 22.03 mmol, 99.55% yield) was obtained as a yellow solid. ¹H NMR (400

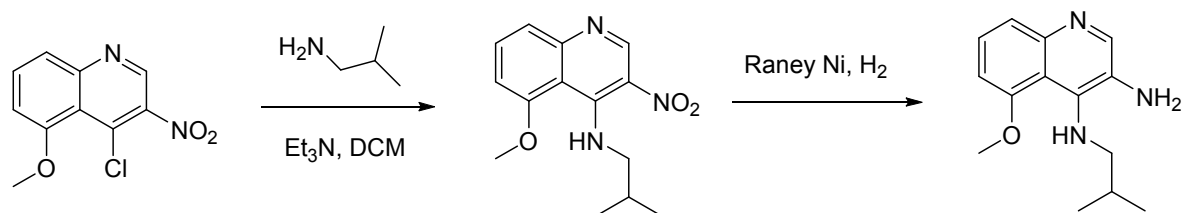
MHz, CD₃OD) δ ppm: 9.17 (s, 1H), 7.75 (t, J = 8.4 Hz, 1H), 7.46 (d, J = 8.4 Hz, 1H), 7.15 (d, J = 8.0 Hz, 1H), 4.13 (s, 3H); ES-LCMS m/z : 220.2 [M+H]⁺.

[0184] Step 2: Synthesis of 4-amino-3-nitro-quinolin-5-ol

[0185] To a solution of 5-methoxy-3-nitro-quinolin-4-amine (2.00 g, 9.12 mmol, 1.0 eq.) in DCM (100.00 mL) was added BBr₃ (22.86 g, 91.20 mmol, 8.79 mL, 10.0 eq.) dropwise at -78 °C. The reaction mixture was stirred at 60 °C for 16 h. The reaction mixture was added to MeOH (200 mL) at -30 °C, and then concentrated under reduced pressure to give a residue. The residue was suspended in DCM and filtered. The cake was dried in *vacuo*. The desired product of 4-amino-3-nitro-quinolin-5-ol (2.53 g, crude) was obtained as a green solid. ¹H NMR (400 MHz, CD₃OD) δ ppm: 9.41 (s, 1H), 7.83 (t, J = 8.4 Hz, 1H), 7.33 (d, J = 8.4 Hz, 1H), 7.13 (d, J = 8.4 Hz, 1H); ES-LCMS m/z : 206.2 [M+H]⁺.

[0186] Intermediate 3: *N*⁴-Isobutyl-5-methoxy-quinoline-3,4-diamine

Scheme 10



[0187] Step 1: Synthesis of *N*-isobutyl-5-methoxy-3-nitro-quinolin-4-amine

[0188] To a solution of 2-methylpropan-1-amine (612.91 mg, 8.38 mmol, 828.26 μ L, 2.0 eq.) and Et₃N (2.12 g, 20.95 mmol, 2.90 mL, 5.0 eq.) in DCM (50.00 mL) was added 4-chloro-5-methoxy-3-nitro-quinoline (1.00 g, 4.19 mmol, 1.0 eq.). The resulting mixture was stirred at 25 °C for 0.5 h. The reaction mixture was washed with water (30 mL) and brine (30 mL) via extraction. The organic phase was dried over anhydrous Na₂SO₄, filtered and concentrated in *vacuo*. The residue was purified with column chromatography (PE to PE/EtOAc = 1/1). The desired product of *N*-isobutyl-5-methoxy-3-nitro-quinolin-4-amine (1.00 g, 3.63 mmol, 86.69% yield) was obtained as a yellow solid. ¹H NMR (400 MHz, CD₃OD) δ ppm: 8.85 (s, 1H), 7.70 (t, J = 8.2 Hz, 1H), 7.47 (d, J = 7.6 Hz, 1H), 7.16 (d, J = 8.0 Hz, 1H), 4.14 (s, 3H), 2.85 (d, J = 6.4 Hz, 2H), 2.04-1.94 (m, 1H), 1.00 (d, J = 6.8 Hz, 6H); ES-LCMS m/z : 276.2 [M+H]⁺.

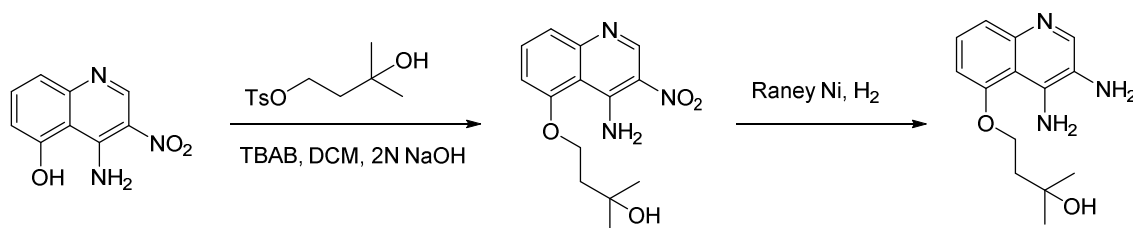
[0189] Step 2: Synthesis of *N*⁴-isobutyl-5-methoxy-quinoline-3,4-diamine

[0190] To a solution of *N*-isobutyl-5-methoxy-3-nitro-quinolin-4-amine (300.00 mg, 1.09 mmol, 1.0 eq.) in MeOH (50.00 mL) was added Raney-Ni (100.00 mg, 1.17 mmol, 1.1 eq.) under N₂. The suspension was degassed under vacuum and purged with H₂ several times. The mixture was stirred under H₂ (15 psi)

at 25 °C for 1 h. The reaction mixture was filtered. The filtrate was concentrated in *vacuo*. The desired product of *N*⁴-isobutyl-5-methoxy-quinoline-3,4-diamine (250.00 mg, 1.02 mmol, 93.49% yield) was obtained as a yellow solid. ¹H NMR (400 MHz, CD₃OD) δ ppm: 8.28 (s, 1H), 7.42-7.40 (m, 1H), 7.33 (t, *J* = 8.2 Hz, 1H), 6.91 (d, *J* = 7.6 Hz, 1H), 4.03 (s, 3H), 3.08 (d, *J* = 6.8 Hz, 2H), 1.90-1.80 (m, 1H), 1.02 (d, *J* = 6.8 Hz, 6H); ES-LCMS *m/z*: 246.3 [M+H]⁺.

[0191] Intermediate 4: 4-[(3,4-Diamino-5-quinolyl)oxy]-2-methyl-butan-2-ol

Scheme 11



[0192] Step 1: Synthesis of 4-[(4-amino-3-nitro-5-quinolyl)oxy]-2-methyl-butan-2-ol

[0193] To a solution of 4-amino-3-nitro-quinolin-5-ol (1.50 g, 7.31 mmol, 1.0 eq.), TBAB (2.36 g, 7.31 mmol, 1.0 eq.) and KI (405.04 mg, 2.44 mmol, 1.0 eq.) in NaOH (2 M, 3.66 mL, 3.0 eq.) was added a solution of (3-hydroxy-3-methyl-butyl)4-methylbenzenesulfonate (5.67 g, 21.93 mmol, 3.0 eq.) in DCM (15.00 mL). The resulting mixture was stirred at 25 °C for 64 h. The reaction mixture was diluted with H₂O (10 mL) and extracted with DCM (50 mL x 2). The combined organic layers were washed with brine (10 mL), dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure to give a residue. The residue was purified with column chromatography (SiO₂, DCM/MeOH = 100/1 to 20/1). The desired product of 4-[(4-amino-3-nitro-5-quinolyl)oxy]-2-methyl-butan-2-ol (646.00 mg, 2.22 mmol, 30.34% yield) was obtained as a yellow solid. ¹H NMR (400 MHz, CDCl₃) δ ppm: 9.59 (br s, 1H), 9.29 (s, 1H), 9.22 (br s, 1H), 7.63 (t, *J* = 8.2 Hz, 1H), 7.54 (dd, *J* = 8.4, 0.8 Hz, 1H), 6.92 (d, *J* = 7.6 Hz, 1H), 4.38 (t, *J* = 6.2 Hz, 2H), 2.14 (t, *J* = 6.2 Hz, 2H), 1.41 (s, 6H); ES-LCMS *m/z*: 292.3 [M+H]⁺.

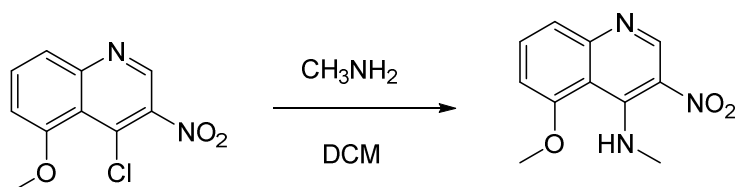
[0194] Step 2: Synthesis of 4-[(3,4-diamino-5-quinolyl)oxy]-2-methyl-butan-2-ol

[0195] To a solution of 4-[(4-amino-3-nitro-5-quinolyl)oxy]-2-methyl-butan-2-ol (640.00 mg, 2.20 mmol, 1.0 eq.) in MeOH (150.00 mL) was added Raney-Ni (200.00 mg, 2.33 mmol, 1.1 eq.) under N₂. The suspension was degassed under vacuum and purged with H₂ several times. The mixture was stirred under H₂ (15 psi) at 25 °C for 1 h. The reaction mixture was filtered. The filtrate was concentrated under reduced pressure to give a residue. The product was directly used in the next step without further purification. The desired crude product of 4-[(3,4-diamino-5-quinolyl)oxy]-2-methyl-butan-2-ol (570.00 mg, 2.18 mmol, 99.15% yield) was obtained as a black brown solid. ¹H NMR (400 MHz, CDCl₃) δ ppm:

8.24 (s, 1H), 7.47 (d, $J = 8.4$ Hz, 1H), 7.30 (t, $J = 8.0$ Hz, 1H), 6.68 (d, $J = 7.6$ Hz, 1H), 5.89 (br s, 2H), 4.28 (t, $J = 6.4$ Hz, 2H), 2.11 (t, $J = 6.4$ Hz, 2H), 1.36 (s, 6H); ES-LCMS m/z : 262.2 [M+H].

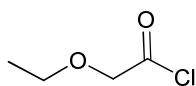
[0196] Intermediate 5: 5-Methoxy-*N*-methyl-3-nitro-quinolin-4-amine

Scheme 12



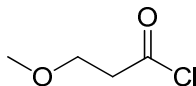
[0197] A solution of 4-chloro-5-methoxy-3-nitro-quinoline (1.00 g, 4.19 mmol, 1.0 eq.) in DCM (30.00 mL) was added to MeNH₂ (2 M in THF, 40.00 mL, 19.1 eq.). The mixture was stirred at 25 °C for 2 h. The mixture was concentrated to give a residue. The residue was purified with column chromatography (SiO₂, DCM/MeOH = 50/1 to 20/1). The desired product of 5-methoxy-*N*-methyl-3-nitro-quinolin-4-amine (400.00 mg, 1.72 mmol, 40.93% yield) was obtained as a yellow solid. ¹H NMR (400 MHz, CDCl₃) δ ppm: 9.03 (s, 1H), 8.79 (s, 1H), 7.62-7.60 (m, 2H), 6.94-6.92 (m, 1H), 4.09 (s, 3H), 2.94 (d, $J = 5.6$ Hz, 3H); ES-LCMS m/z : 234.0 [M+H]⁺.

[0198] Intermediate 6: 2-Ethoxyacetyl chloride



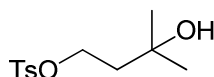
[0199] To a solution of 2-ethoxyacetic acid (1.00 g, 9.61 mmol, 909.09 μ L, 1.0 eq.) and catalytic amount of DMF (10.00 mg, 136.82 μ mol, 10.53 μ L, 0.01 eq.) in DCM (30.00 mL) was added oxalyl chloride (1.83 g, 14.41 mmol, 1.26 mL, 1.5 eq.) at 0 °C. The resulting mixture was stirred at 25 °C for 2 h. The reaction mixture was concentrated under reduced pressure to remove the solvent. 2-Ethoxyacetyl chloride (900.00 mg, 7.34 mmol, 76.42% yield) was obtained as yellow oil.

[0200] Intermediate 7: 3-Methoxypropanoyl chloride



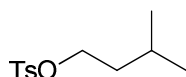
[0201] 3-Methoxypropanoyl chloride was prepared in the same way as intermediate 6 using the corresponding starting material of 3-methoxypropanoic acid in 84.9% yield as yellow oil.

[0202] Intermediate 8: (3-Hydroxy-3-methyl-butyl) 4-methylbenzenesulfonate



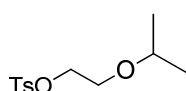
[0203] To a solution of 3-methylbutane-1,3-diol (10.00 g, 96.02 mmol, 10.20 mL, 1.0 eq.), Et₃N (14.57 g, 144.03 mmol, 19.96 mL, 1.5 eq.) and DMAP (14.08 g, 115.22 mmol, 1.2 eq.) in DCM (200.00 mL) was added a solution of TsCl (17.39 g, 91.22 mmol, 0.95 eq) in DCM (100 mL) dropwise at 0 °C. The resulting mixture was stirred at 0 °C for 1 h. The mixture was adjusted to pH = 6 with citric acid. The organic layer was separated and washed with brine (100 mL), dried over anhydrous Na₂SO₄, filtered and concentrated in *vacuo*. (3-Hydroxy-3-methyl-butyl)4-methylbenzenesulfonate (19.80 g, 76.65 mmol, 79.83% yield) was obtained as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ ppm: 7.80-7.78 (m, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 4.22-4.19 (m, 2H), 2.45 (s, 3H), 1.87-1.84 (m, 2H), 1.21 (d, *J* = 1.2 Hz, 6H); ES-LCMS *m/z*: 276.2 [M+H₂O]⁺.

[0204] Intermediate 9: Isopentyl 4-methylbenzenesulfonate



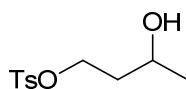
[0205] Isopentyl 4-methylbenzenesulfonate was prepared in a similar way as intermediate 8 using the corresponding starting material of 3-methylbutan-1-ol and purified with silica gel chromatography (PE/EA = 20/1 to 10/1) to give 72.76% isolated yield as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm: 7.81-7.79 (m, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 4.06 (t, *J* = 6.6 Hz, 2H), 2.46 (s, 3H), 1.70-1.67 (m, 1H), 1.57-1.51 (m, 2H), 0.88-0.84 (m, 6H); ES-LCMS *m/z*: 264.9 [M+Na]⁺.

[0206] Intermediate 10: 2-Isopropoxyethyl 4-methylbenzenesulfonate



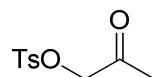
[0207] 2-Isopropoxyethyl 4-methylbenzenesulfonate was prepared in a similar way as intermediate 8 using the corresponding starting material of 2-isopropoxyethanol in 81.44% yield as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ ppm: 7.80 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 4.14-4.11 (m, 2H), 3.60-3.58 (m, 2H), 3.55-3.54 (m, 1H), 2.44 (s, 3H), 1.08 (d, *J* = 6.0 Hz, 6H); ES-LCMS *m/z*: 259.3 [M+H]⁺.

[0208] Intermediate 11: 3-Hydroxybutyl 4-methylbenzenesulfonate



[0209] 3-Hydroxybutyl 4-methylbenzenesulfonate was prepared in a similar way as intermediate 8 using the corresponding starting material of butane-1,3-diol in 59.04% yield as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ ppm: 7.83-7.79 (m, 2H), 7.37-7.34 (m, 2H), 4.26-4.22 (m, 1H), 4.15-4.12 (m, 1H), 3.98-3.93 (m, 1H), 2.46 (s, 3H), 1.85-1.81 (m, 1H), 1.74-1.68 (m, 1H), 1.20 (m, 3H); ES-LCMS *m/z*: 245.2 [M+H]⁺.

[0210] Intermediate 12: Acetonyl 4-methylbenzenesulfonate:



[0211] Acetonyl 4-methylbenzenesulfonate was prepared in a similar way as intermediate 8 using the corresponding starting material of 1-hydroxypropan-2-one in 25.31% yield as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ ppm: 7.82 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 4.48 (s, 2H), 2.46 (s, 3H), 2.22 (s, 3H); ES-LCMS *m/z*: 229.2 [M+H]⁺.

[0212] Other 2-aminoquinoline derivatives were prepared in a similar way as that described in Examples 1-7, and they are listed in Table 1. These compounds were prepared in HCl salt forms, and/or in the forms of neutral amine. A person skilled in the art can clearly understand and know that the other analogs could be prepared by the same or similar methods as described in Examples 1-7. These examples are not in any way to limit the analogs that can be made by applying the same or similar methods presented herein.

Table 1: Continued					
Cmpd No.	Structure	Cmpd No.	Structure	Cmpd No.	Structure
37		38		39	
40		41		42	
43		44		45	
46		47			

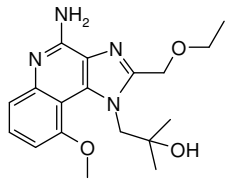
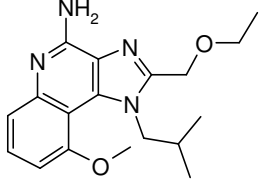
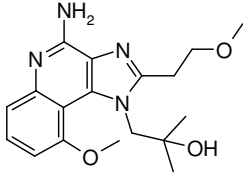
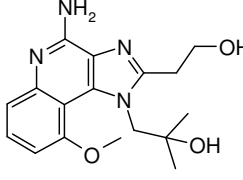
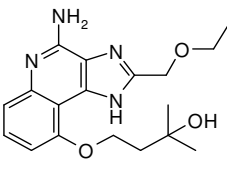
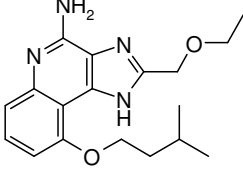
[0213] The compound functionality was tested for some of the compounds prepared by stimulation and determination of cytokine production in PBMCs.

[0214] Human PBMCs were prepared from buffy coat obtained from healthy volunteer donor by Ficoll centrifugation and were adjusted to the final cell concentration to 1×10^6 cells/mL.

[0215] For evaluation of compound activities, 1×10^5 PBMCs were plated in a 96-well plate in 100 μ L of RPMI 1640 complete medium (cat no. 31800-022, GIBCO by Life Technologies, Grand Island, NY, USA) supplemented with 10% fetal bovine serum, the tested compound was first dissolved in DMSO and further diluted in PBS and RPMI 1640 medium to the final concentration of 20 μ M (corresponding to 6.28 μ g/mL), then 3-fold serially dilution was made in a 96-well round-bottom plate. 100 μ L diluted compound was added to the same volume of 1×10^5 PBMCs plate and cultured for 20-22 hours at 37°C in a humidified atmosphere of 5% CO₂. The supernatant was collected for human IFN- α , IL12(p70) and IL-6 analysis by ELISA assay according to the manufacturer's instructions (Mabtech AB, Sweden). Resiquimod was used as a positive control.

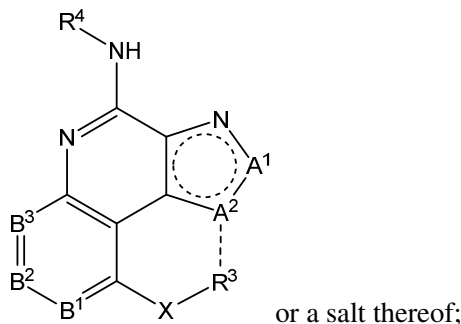
[0216] Table 2 below lists the testing results on the evaluation of cytokine production for most of the compounds prepared.

Table 2*

Compound No.	Structure	M.W.	Production of IFN α on PBMC*	Production of IL-6 on PBMC*
1		344.41	+	+
2		328.41	+	+
3		344.41	-	-
4		330.38	-	-
5		344.41	+	+
6		328.41	N/A	+

WHAT IS CLAIMED IS:

1. A compound represented by a formula:



wherein a dashed line represents the presence or absence of a bond;

A¹ is CR¹, NR^{1A}, or N;

A² is CR², NR^{2A}, O, or S;

B¹ is CR⁵ or N;

B² is CR⁶ or N;

B³ is CR⁷ or N;

R¹ and R² are independently F, Cl, Br, I, NO₂, CN, R^a, -OR^a, -NR^aR^b, -NHCOR^a, -NHSO₂R^a, -OCOR^a, or -SO₂R^a;

X is a bond, O, NR^a, -CO-, -SO-, or -SO₂-, -CONR^a, hydrocarbonyl, and R³ is H or C₁₋₃₀ organyl; or X-R³ is F or Cl;

R^{1A}, R^{2A}, R⁴, R^a, and R^b are independently H or C₁₋₃₀ organyl;

R⁵, R⁶, and R⁷ are independently F, Cl, Br, I, NO₂, CN, R^a, -OR^a, -NR^aR^b, -NHCOR^a, -NHSO₂R^a, -OCOR^a, -SO₂R^a, -SO₂NHR^a, or -X¹-(C_mH_{2m}O₀₋₁)-Z-(C_nH_{2n+1}), -(C_mH_{2m}O₀₋₁)-Z-(C_nH_{2n+1}), wherein R⁵ and R⁶ or R⁶ and R⁷ can be optionally linked to form a ring;

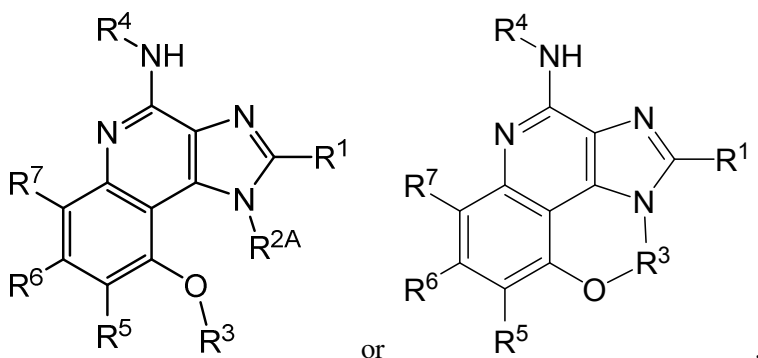
wherein X¹ is a bond, O, NR^a, -CO-, -SO-, or -SO₂-;

Z is a bond, O, NHSO₂, or NHCO;

m is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

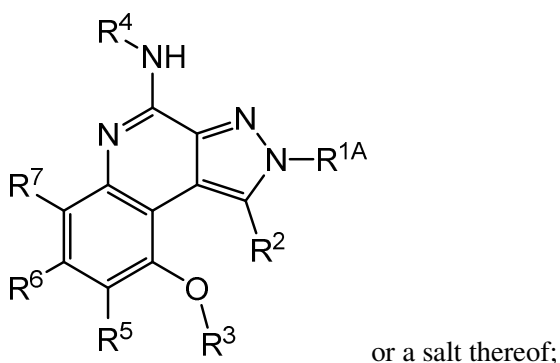
n is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, or 23.

2. The compound of claim b further represented by a formula:



or a salt thereof, wherein R^3 is C_{1-30} organyl.

3. The compound of claim 1, further represented by a formula:



wherein R^4 is H, C_{1-30} non-aromatic organyl, or C_{1-30} aromatic organyl containing an aromatic group that is not directly attached to the N atom.

4. The compound of claim 1, 2 or 3, wherein R^1 or R^{1A} is C_{1-12} optionally substituted alkyl.
5. The compound of claim 4, wherein R^1 or R^{1A} is $-C_rH_{2r+1}O$, or an ester thereof, wherein r is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.
6. The compound of claim 5, wherein R^1 or R^{1A} is $-C_3H_7O$.
7. The compound of claim 6, wherein R^1 or R^{1A} is $-CH_2OCH_2CH_3$.
8. The compound of any one claims 1 to 7, wherein R^2 or R^{2A} is H or C_{1-12} optionally substituted alkyl.
9. The compound of claim 8, wherein R^2 or R^{2A} is C_{1-6} alkyl, or $-C_yH_{2y+1}O$ or an ester thereof, wherein y is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.
10. The compound of claim 9, wherein R^2 or R^{2A} is CH_3 .
11. The compound of claim 8, wherein R^2 or R^{2A} is H.

12. The compound of claim 8, wherein R^2 or R^{2A} is C_4H_9 .
13. The compound of any one of claims 1 to 12, wherein R^3 is C_{1-30} optionally substituted alkyl.
14. The compound of claim 13, wherein R^3 is C_{1-10} alkyl, or $-C_wH_{2w+1}O$ or an ester thereof, wherein w is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.
15. The compound of any one of claims 1 to 13, wherein R^3 is $-(C_tH_{2t}O_{0-1})-Ht$, wherein t is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, and Ht is optionally substituted C_{3-6} heterocyclyl.
16. The compound of any one of claims 1 to 13, wherein R^3 is $-(C_uH_{2u}O_{0-1})-Z-(C_vH_{2v+1})$, wherein Z is a bond, O, $NHSO_2$, or $NHCO$, u is 0, 1, 2, 3, 4, 5, or 6, and v is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, or 23.
17. The compound of any one of claims 1 to 13, wherein R^3 is $-(C_uH_{2u}O_{0-1})-NR^aR^b$, and u is 1, 2, 3, 4, 5, or 6, wherein R^a and R^b are independently H or C_{1-6} alkyl.
18. The compound of claim 14, wherein R^3 is $C_5H_{11}O$.
19. The compound of claim 18, wherein R^3 is $-CH_2-CH_2-CH(CH_3)_2OH$.
20. The compound of claim 17, wherein R^3 is $-CH_2-CH_2-CH_2-NH_2$.
21. The compound of any one of claims 1 to 20, wherein R^4 is H or C_{1-6} alkyl.
22. The compound of claim 21, wherein R^4 is H.
23. The compound of any one of claims 1 to 22, wherein R^5 is R^a , F, Cl, $-CO_2R^a$, $-CONR^aR^b$, CN, $-OR^a$, $-NR^aR^b$, $-OCOR^a$, or $-SO_2R^a$, $-SO_2NHR^a$, wherein R^a and R^b are independently H or C_{1-6} alkyl.
24. The compound of claim 23, wherein R^5 is H.
25. The compound of any one of claims 1 to 20, wherein R^5 is $-(C_mH_{2m}O_{0-1})-Z-(C_nH_{2n+1})$, wherein Z is a bond, O, $NHSO_2$, or $NHCO$, m is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, and n is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 or 25.
26. The compound of any one of claims 1 to 25, wherein R^6 is R^a , F, Cl, $-CO_2R^a$, $-CONR^aR^b$, CN, $-OR^a$, $-NR^aR^b$, $-OCOR^a$, or $-SO_2R^a$, $-SO_2NHR^a$, wherein R^a and R^b are independently H or C_{1-6} alkyl.
27. The compound of claim 26, wherein R^6 is H.
28. The compound of any one of claims 1 to 25, wherein R^6 is $-(C_mH_{2m}O_{0-1})-Z-(C_nH_{2n+1})$, wherein Z is a bond, O, $NHSO_2$, or $NHCO$, m is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, and n is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, or 23.

29. The compound of any one of claims **1** to **28**, wherein R^7 is R^a , F, Cl, $-\text{CO}_2R^a$, $-\text{CONR}^aR^b$, CN, $-\text{OR}^a$, $-\text{NR}^aR^b$, $-\text{OCOR}^a$, or $-\text{SO}_2R^a$, $-\text{SO}_2\text{NHR}^a$, wherein R^a and R^b are independently H or C_{1-6} alkyl.

30. The compound of claim **29**, wherein R^7 is H.

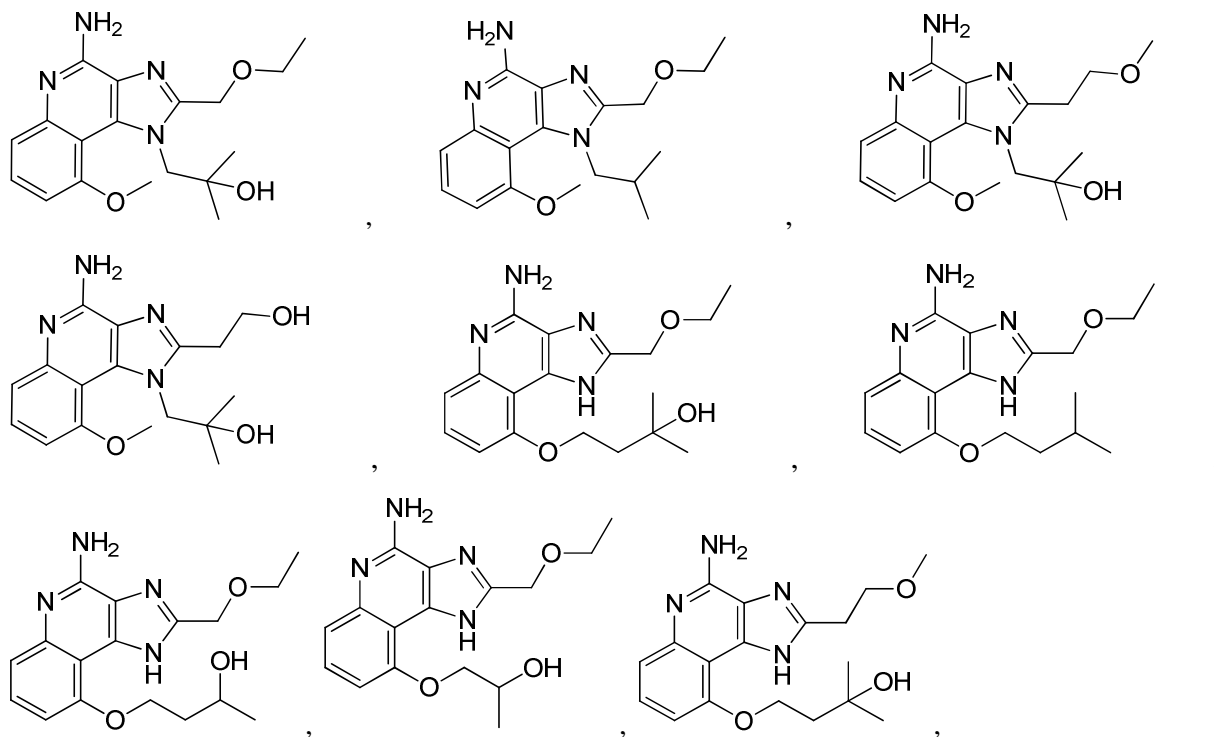
31. The compound of any one of claims **1** to **28**, wherein R^7 is $-(\text{C}_m\text{H}_{2m}\text{O}_{0-1})-\text{Z}-(\text{C}_n\text{H}_{2n+1})$, wherein Z is a bond, O, NHSO_2 , or NHCO , m is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, and n is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, or 23.

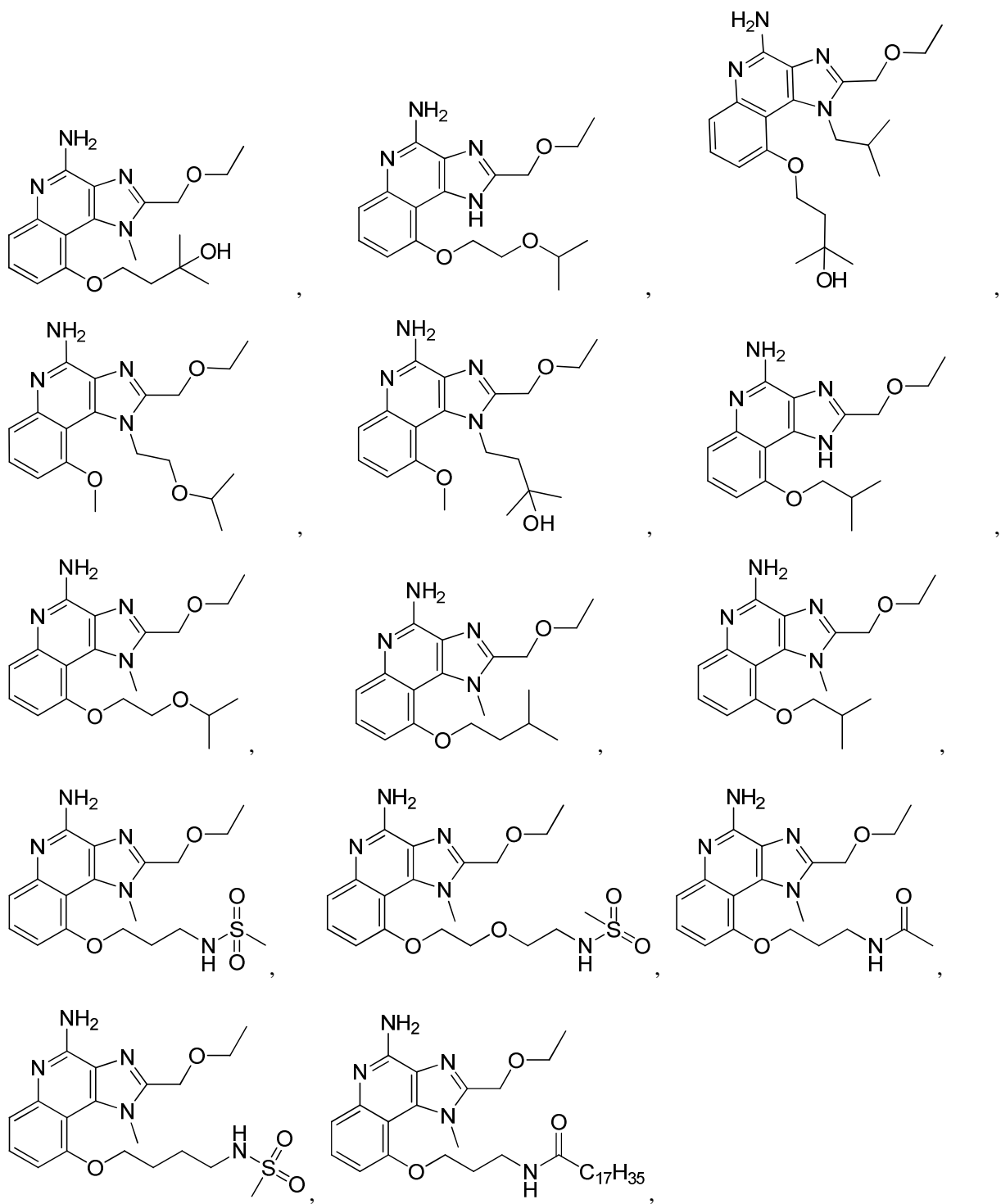
32. The compound of any one of claims **1** to **31**, R^8 is H, OH, or CH_3 .

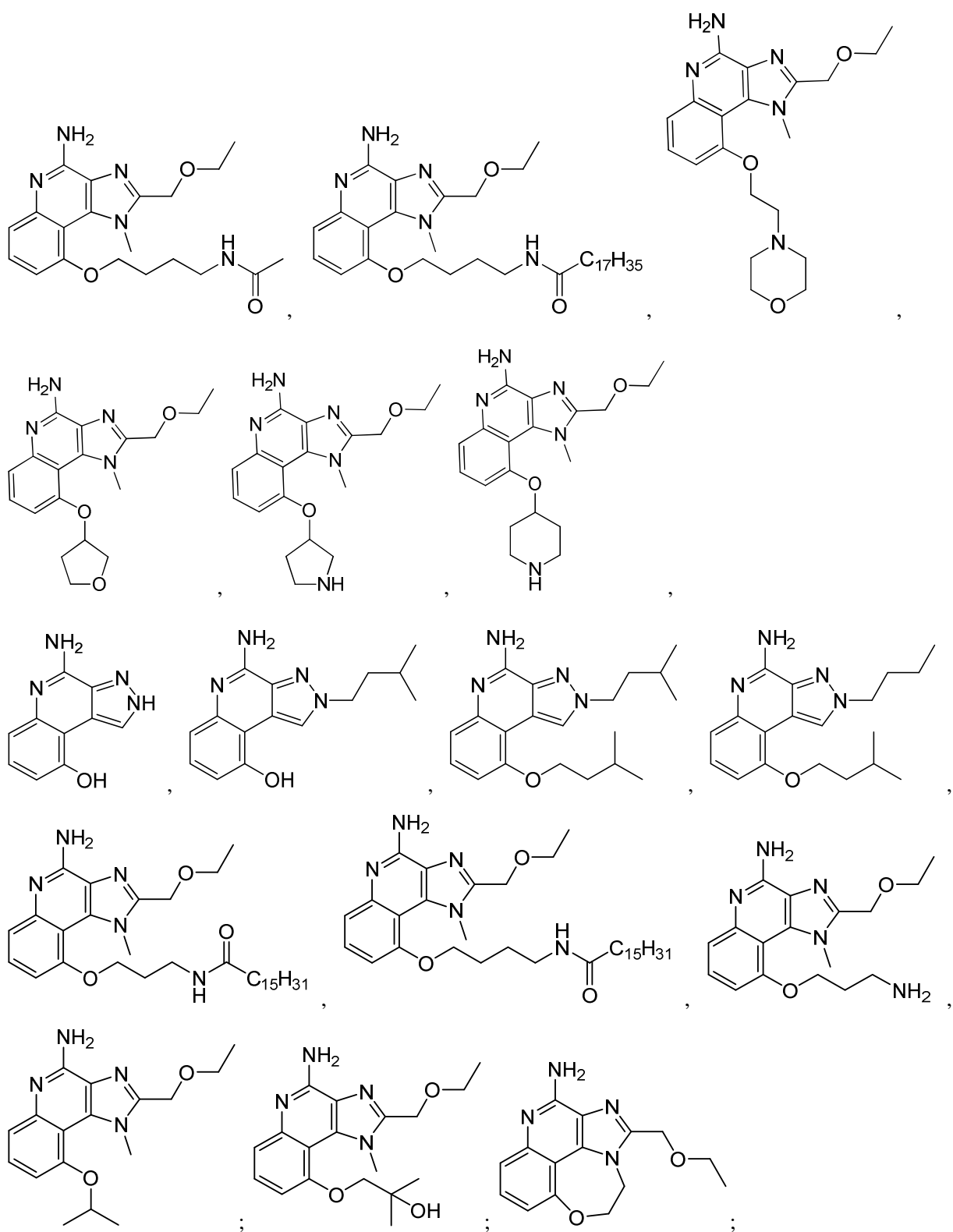
33. The compound of claim **32**, wherein R^8 is OH.

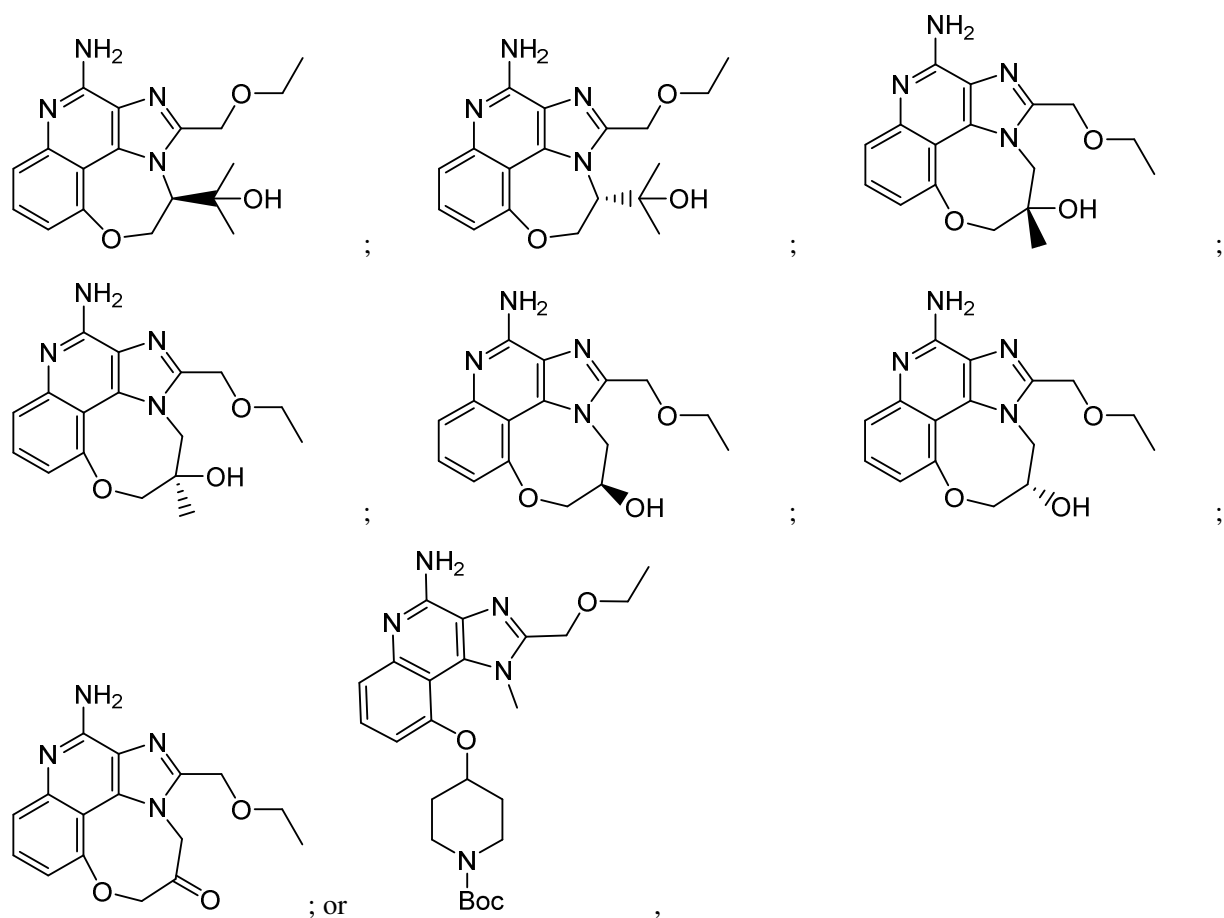
34. The compound of claim **32**, wherein R^8 is H.

35. A compound, which is:









a salt of any of these compounds, or an ester of any of these compounds having an -OH group.

- 36.** A compound which is optionally substituted 9-methoxy-1*H*-imidazo[4,5-*c*]quinolin-4-amine.
- 37.** A compound which is optionally substituted 9-methoxy-2*H*-pyrazolo[3,4-*c*]quinolin-4-amine.
- 38.** The compound of claim **36**, which is optionally substituted 1-(4-amino-2-(ethoxymethyl)-9-methoxy-1*H*-imidazo[4,5-*c*]quinolin-1-yl)-2-methylpropan-2-ol or a salt thereof; optionally substituted 2-(ethoxymethyl)-1-isobutyl-9-methoxy-1*H*-imidazo[4,5-*c*]quinolin-4-amine or a salt thereof; optionally substituted 1-(4-amino-9-methoxy-2-(2-methoxyethyl)-1*H*-imidazo[4,5-*c*]quinolin-1-yl)-2-methylpropan-2-ol or a salt thereof; optionally substituted 1-(4-amino-2-(2-hydroxyethyl)-9-methoxy-1*H*-imidazo[4,5-*c*]quinolin-1-yl)-2-methylpropan-2-ol or a salt thereof; optionally substituted 4-((4-amino-2-(ethoxymethyl)-1*H*-imidazo[4,5-*c*]quinolin-9-yl)oxy)-2-methylbutan-2-ol or a salt thereof; optionally substituted 2-(ethoxymethyl)-9-(isopentyloxy)-1*H*-imidazo[4,5-*c*]quinolin-4-amine or a salt thereof; optionally substituted 4-((4-amino-2-(ethoxymethyl)-1*H*-imidazo[4,5-*c*]quinolin-9-yl)oxy)butan-2-ol or a salt thereof; optionally substituted 1-((4-amino-2-(ethoxymethyl)-1*H*-imidazo[4,5-*c*]quinolin-9-yl)oxy)propan-2-ol or a salt thereof; optionally substituted 4-((4-amino-2-(2-methoxyethyl)-1*H*-

imidazo[4,5-c]quinolin-9-yl)oxy)-2-methylbutan-2-ol or a salt thereof; optionally substituted 4-((4-amino-2-(ethoxymethyl)-1-methyl-1*H*-imidazo[4,5-c]quinolin-9-yl)oxy)-2-methylbutan-2-ol or a salt thereof; optionally substituted 2-(ethoxymethyl)-9-(2-isopropoxyethoxy)-1*H*-imidazo[4,5-c]quinolin-4-amine or a salt thereof; optionally substituted 4-((4-amino-2-(ethoxymethyl)-1-isobutyl-1*H*-imidazo[4,5-c]quinolin-9-yl)oxy)-2-methylbutan-2-ol or a salt thereof; optionally substituted 2-(ethoxymethyl)-1-(2-isopropoxyethyl)-9-methoxy-1*H*-imidazo[4,5-c]quinolin-4-amine or a salt thereof; optionally substituted 4-(4-amino-2-(ethoxymethyl)-9-methoxy-1*H*-imidazo[4,5-c]quinolin-1-yl)-2-methylbutan-2-ol or a salt thereof; optionally substituted 2-(ethoxymethyl)-9-isobutoxy-1*H*-imidazo[4,5-c]quinolin-4-amine or a salt thereof; optionally substituted 2-(ethoxymethyl)-9-(2-isopropoxyethoxy)-1-methyl-1*H*-imidazo[4,5-c]quinolin-4-amine or a salt thereof; optionally substituted 2-(ethoxymethyl)-9-(isopentyloxy)-1-methyl-1*H*-imidazo[4,5-c]quinolin-4-amine or a salt thereof; optionally substituted 2-(ethoxymethyl)-9-isobutoxy-1-methyl-1*H*-imidazo[4,5-c]quinolin-4-amine or a salt thereof; optionally substituted N-(3-((4-amino-2-(ethoxymethyl)-1-methyl-1*H*-imidazo[4,5-c]quinolin-9-yl)oxy)propyl)methanesulfonamide or a salt thereof; optionally substituted N-(2-(2-((4-amino-2-(ethoxymethyl)-1-methyl-1*H*-imidazo[4,5-c]quinolin-9-yl)oxy)ethoxy)ethyl)-methanesulfonamide or a salt thereof; optionally substituted N-(3-((4-amino-2-(ethoxymethyl)-1-methyl-1*H*-imidazo[4,5-c]quinolin-9-yl)oxy)propyl)acetamide or a salt thereof; optionally substituted N-(4-((4-amino-2-(ethoxymethyl)-1-methyl-1*H*-imidazo[4,5-c]quinolin-9-yl)oxy)butyl)methanesulfonamide or a salt thereof; optionally substituted N-(3-((4-amino-2-(ethoxymethyl)-1-methyl-1*H*-imidazo[4,5-c]quinolin-9-yl)oxy)propyl)stearamide or a salt thereof; optionally substituted N-(4-((4-amino-2-(ethoxymethyl)-1-methyl-1*H*-imidazo[4,5-c]quinolin-9-yl)oxy)butyl)acetamide or a salt thereof; optionally substituted N-(4-((4-amino-2-(ethoxymethyl)-1-methyl-1*H*-imidazo[4,5-c]quinolin-9-yl)oxy)butyl)-stearamide or a salt thereof; optionally substituted 2-(ethoxymethyl)-1-methyl-9-(2-morpholinoethoxy)-1*H*-imidazo[4,5-c]quinolin-4-amine or a salt thereof; optionally substituted 2-(ethoxymethyl)-1-methyl-9-((tetrahydrofuran-3-yl)oxy)-1*H*-imidazo[4,5-c]quinolin-4-amine or a salt thereof; optionally substituted 2-(ethoxymethyl)-1-methyl-9-(pyrrolidin-3-yl)oxy)-1*H*-imidazo[4,5-c]quinolin-4-amine or a salt thereof; optionally substituted 2-(ethoxymethyl)-1-methyl-9-(piperidin-4-yl)oxy)-1*H*-imidazo[4,5-c]quinolin-4-amine or a salt thereof; optionally substituted N-(3-((4-amino-2-(ethoxymethyl)-1-methyl-1*H*-imidazo[4,5-c]quinolin-9-yl)oxy)propyl)palmitamide or a salt thereof; optionally substituted N-(4-((4-amino-2-(ethoxymethyl)-1-methyl-1*H*-imidazo[4,5-c]quinolin-9-yl)oxy)butyl)palmitamide or a salt thereof; optionally substituted 9-(3-aminopropoxy)-2-(ethoxymethyl)-1-methyl-1*H*-imidazo[4,5-c]quinolin-4-amine or a salt thereof; optionally substituted 2-(ethoxymethyl)-9-isopropoxy-1-methyl-1*H*-imidazo[4,5-c]quinolin-4-amine or a salt thereof; optionally substituted 1-((4-amino-2-(ethoxymethyl)-1-methyl-1*H*-imidazo[4,5-c]quinolin-9-yl)oxy)-2-methylpropan-2-ol or a salt thereof; optionally substituted 2-(ethoxymethyl)-3,4-dihydro-5-oxa-1,2a,9-

triazanaphtho[2,1,8-cde]azulen-10-amine or a salt thereof; optionally substituted (R)-2-(10-amino-2-(ethoxymethyl)-3,4-dihydro-5-oxa-1,2a,9-triazanaphtho[2,1,8-cde]azulen-3-yl)propan-2-ol or a salt thereof; optionally substituted (S)-2-(10-amino-2-(ethoxymethyl)-3,4-dihydro-5-oxa-1,2a,9-triazanaphtho[2,1,8-cde]azulen-3-yl)propan-2-ol or a salt thereof; optionally substituted (S)-2-amino-12-(ethoxymethyl)-6-methyl-6,7-dihydro-5H-3,4-(azenometheno)[1,5]oxazocino[4,3,2-de]quinolin-6-ol or a salt thereof; optionally substituted (R)-2-amino-12-(ethoxymethyl)-6-methyl-6,7-dihydro-5H-3,4-(azenometheno)[1,5]oxazocino[4,3,2-de]quinolin-6-ol or a salt thereof; optionally substituted (R)-2-amino-12-(ethoxymethyl)-6,7-dihydro-5H-3,4-(azenometheno)[1,5]oxazocino[4,3,2-de]quinolin-6-ol or a salt thereof; optionally substituted (S)-2-amino-12-(ethoxymethyl)-6,7-dihydro-5H-3,4-(azenometheno)[1,5]oxazocino-[4,3,2-de]quinolin-6-ol or a salt thereof; optionally substituted 2-amino-12-(ethoxymethyl)-5H-3,4-(azenometheno)[1,5]oxazocino[4,3,2-de]quinolin-6(7H)-one or a salt thereof; or optionally substituted tert-butyl 4-((4-amino-2-(ethoxymethyl)-1-methyl-1H-imidazo[4,5-c]quinolin-9-yl)oxy)piperidine-1-carboxylate or a salt thereof.

39. The compound of claim **37** which is optionally substituted 4-amino-2*H*-pyrazolo[3,4-c]quinolin-9-ol or a salt thereof; optionally substituted 4-amino-2-isopentyl-2*H*-pyrazolo[3,4-c]quinolin-9-ol or a salt thereof; optionally substituted 2-isopentyl-9-(isopentyloxy)-2*H*-pyrazolo[3,4-c]quinolin-4-amine or a salt thereof; or optionally substituted 2-butyl-9-(isopentyloxy)-2*H*-pyrazolo[3,4-c]quinolin-4-amine or a salt thereof.

40. Use of a compound of any one of claims **1** to **39**, in the manufacture of a medicament for the treatment of viral infection, cancer, or an allergic disease.

41. The use of claim **41**, wherein the viral infection comprises HCV infection.

42. A dosage form suitable to be administered to a mammal, comprising a compound of any one of claims **1** to **39**.