

Design, Synthesis and Structure-activity Relationship of New Pyrimidinamine Derivatives Containing an Aryloxy Pyridine Moiety

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Supporting Information

Index of Contents:

S2 – S4: ^1H NMR for intermediates M-1, 3-7, 11-20

S5 – S13: ^1H NMR, elemental analyses, HRMS for intermediates compounds 1-8, 10-25

6-(4-chlorophenoxy)nicotinonitrile (M-1)

^1H NMR (300 MHz, CDCl_3) δ 8.45 (d, $J=2.1\text{Hz}$, 1H, pyridine 6-H), 7.93 (dd, $J=8.7, 2.1\text{Hz}$, 1H, pyridine 4-H), 7.40 (dd, $J=6.6, 2.1\text{Hz}$, 2H, 4-Cl-Ph-3,5-2H), 7.10 (dd, $J=6.9, 2.1\text{Hz}$, 2H, 4-Cl-Ph-2,6-2H), 7.04 (d, $J=8.7\text{Hz}$, 1H, pyridine 3-H).

methyl 6-(4-chlorophenoxy)nicotinate (M-3)

^1H NMR (300MHz, CDCl_3) δ 3.92(s, 3H, OCH_3), 6.96(d, $J=8.4\text{Hz}$, 1H, pyridine 3-H), 7.11(d, $J=6.6\text{Hz}$, 2H, Ph-2,6-2H), 7.37(d, $J=6.6\text{Hz}$, 2H, Ph-3,5-2H), 8.30 (dd, $J=8.4, 2.1\text{Hz}$, 1H, pyridine 4-H), 8.80(s, 1H, pyrimidine 2-H).

(6-(4-chlorophenoxy)pyridin-3-yl)methanol (M-4)

^1H NMR (300MHz, CDCl_3) δ 3.20(bs, 1H, OH), 4.56(s, 2H, CH_2), 6.87(d, $J=8.4\text{Hz}$, 1H, pyridine 3-H), 7.04(d, $J=6.6\text{Hz}$, 2H, Ph-2,6-2H), 7.33(d, $J=6.6\text{Hz}$, 2H, Ph-3,5-2H), 7.69 (dd, $J=8.4, 2.1\text{Hz}$, 1H, pyridine 4-H), 8.06(s, 1H, pyrimidine 2-H).

5-(chloromethyl)-2-(4-chlorophenoxy)pyridine (M-5)

^1H NMR (300MHz, CDCl_3) δ 4.55(s, 2H, CH_2), 6.94(d, $J=8.7\text{Hz}$, 1H, pyridine 3-H), 7.09(d, $J=6.6\text{Hz}$, 2H, Ph-2,6-2H), 7.36(d, $J=6.6\text{Hz}$, 2H, Ph-3,5-2H), 7.75 (dd, $J=8.7, 2.4\text{Hz}$, 1H, pyridine 4-H), 8.15(s, 1H, pyrimidine 2-H).

2-(6-(4-chlorophenoxy)pyridin-3-yl)acetonitrile (M-6)

^1H NMR (300MHz, CDCl_3) δ 3.70(s, 2H, CH_2), 6.97(d, $J=8.7\text{Hz}$, 1H, pyridine 3-H), 7.08(d, $J=6.6\text{Hz}$, 2H, Ph-2,6-2H), 7.37(d, $J=6.6\text{Hz}$, 2H, Ph-3,5-2H), 7.71 (dd, $J=8.7, 2.7\text{Hz}$, 1H, pyridine 4-H), 8.10(s, 1H, pyrimidine 2-H).

2-(6-(4-chlorophenoxy)pyridin-3-yl)ethanamine (M-7)

^1H NMR (300MHz, CDCl_3) δ 1.46(bs, 2H, NH_2), 2.70(t, $J=6.9\text{Hz}$, 2H, $\text{CH}_2\text{CH}_2\text{NH}_2$), 2.94(t, $J=6.9\text{Hz}$, 2H, $\text{CH}_2\text{CH}_2\text{NH}_2$), 6.87(d, $J=8.4\text{Hz}$, 1H, pyridine 3-H), 7.07(d, $J=6.6\text{Hz}$, 2H, Ph-2,6-2H), 7.34(d, $J=6.6\text{Hz}$, 2H,

Ph-3,5-2H), 7.55 (dd, $J=8.4,2.4\text{Hz}$, 1H, pyridine 4-H), 8.02(s, 1H, pyrimidine 2-H).

methyl 2-(4-chlorophenoxy)nicotinate (M-11)

white solid in 79% yield, m.p. 125.8°C . ^1H NMR (300MHz, CDCl_3) δ 3.95(s, 3H, CH_3), 7.05-7.11(m, 3H, pyridine 5-H, Ph-2,6-2H), 7.37(d, $J=8.7\text{Hz}$, 2H, Ph-3,5-2H), 8.26-8.29(m, 2H, pyridine 4-H, pyridine 6-H).

(2-(4-chlorophenoxy)pyridin-3-yl)methanol (M-12)

brown solid in 90% yield, m.p. 95.1°C . ^1H NMR (300MHz, CDCl_3) δ 2.21(bs, 1H, OH), 4.83(s, 2H, CH_2), 7.01-7.10(m, 3H, pyridine 5-H, Ph-2,6-2H), 7.37(d, $J=8.7\text{Hz}$, 2H, Ph-3,5-2H), 7.79(d, $J=6.6\text{Hz}$, 1H, pyridine 6-H), 8.07(d, $J=4.8\text{Hz}$, 1H, pyridine 4-H).

3-(chloromethyl)-2-(4-chlorophenoxy)pyridine (M-13)

pale yellow solid in 89% yield, m.p. 51.1°C . ^1H NMR (300MHz, CDCl_3) δ 4.74(s, 2H, CH_2), 7.01-7.06(m, 1H, pyridine 5-H), 7.10(d, $J=8.7\text{Hz}$, 2H, Ph-2,6-2H), 7.37(d, $J=8.7\text{Hz}$, 2H, Ph-3,5-2H), 7.80(d, $J=7.5\text{Hz}$, 1H, pyridine 6-H), 8.10(d, $J=4.8\text{Hz}$, 1H, pyridine 4-H).

2-(2-(4-chlorophenoxy)pyridin-3-yl)acetonitrile (M-14)

white solid in 96% yield, ^1H NMR (300MHz, CDCl_3) δ 3.86(s, 2H, CH_2), 7.05-7.11(m, 3H, pyridine 5-H, Ph-2,6-2H), 7.38(d, $J=8.7\text{Hz}$, 2H, Ph-3,5-2H), 7.82(d, $J=7.2\text{Hz}$, 1H, pyridine 6-H), 8.11(d, $J=4.8\text{Hz}$, 1H, pyridine 4-H).

2-(2-(4-chlorophenoxy)pyridin-3-yl)ethanamine (M-15)

pale green oil in 95% yield.

ethyl 2-(4-chlorophenoxy)isonicotinate (M-16)

pale brown solid in 80% yield, m.p. 65.1°C . ^1H NMR (300MHz, CDCl_3) δ 1.41(t, $J=7.5\text{Hz}$, 3H, CH_2CH_3), 4.43(q, 2H, CH_2CH_3), 7.08(d, $J=6.6\text{Hz}$, 2H, Ph-2,6-2H), 7.37(d, $J=6.6\text{Hz}$, 2H, Ph-3,5-2H), 7.50(s, 1H, pyridine 3-H), 7.55(dd, $J=5.1,1.5\text{Hz}$, 1H, pyridine 5-H), 8.29(d, $J=5.1\text{Hz}$, 1H, pyridine 6-H).

(2-(4-chlorophenoxy)pyridin-4-yl)methanol (M-17)

yellow oil in 89% yield. ^1H NMR (300MHz, CDCl_3) δ 3.95(bs, 1H, OH), 4.70(s, 2H, CH_2), 6.91(s, 1H, pyridine 3-H), 6.98(d, $J=5.1\text{Hz}$, 1H, pyridine 5-H), 7.06(d, $J=5.4\text{Hz}$, 2H, Ph-2,6-2H), 7.35(d, $J=5.4\text{Hz}$, 2H, Ph-3,5-2H), 8.11(d, $J=4.5\text{Hz}$, 1H, pyridine 6-H).

4-(chloromethyl)-2-(4-chlorophenoxy)pyridine (M-18)

white solid in 90% yield, m.p. 79.0°C. ^1H NMR (300MHz, CDCl_3) δ 4.59(s, 2H, CH_2), 6.95(s, 1H, pyridine 3-H), 7.17(d, $J=5.4\text{Hz}$, 2H, Ph-2,6-2H), 7.33(d, $J=5.1\text{Hz}$, 1H, pyridine 5-H), 7.46(d, $J=5.4\text{Hz}$, 2H, Ph-3,5-2H), 8.40(d, $J=4.8\text{Hz}$, 1H, pyridine 6-H).

2-(2-(4-chlorophenoxy)pyridin-4-yl)acetonitrile (M-19)

white solid in 83% yield, ^1H NMR (300MHz, CDCl_3) δ 3.77(s, 2H, CH_2), 6.94(s, 1H, pyridine 3-H), 6.99 (d, $J=5.1\text{Hz}$, 1H, pyridine 5-H), 7.08(d, $J=6.6\text{Hz}$, 2H, Ph-2,6-2H), 7.37(d, $J=6.6\text{Hz}$, 2H, Ph-3,5-2H), 8.17(d, $J=5.1\text{Hz}$, 1H, pyridine 6-H).

2-(2-(4-chlorophenoxy)pyridin-4-yl)ethanamine (M-20)

brown oil in 95% yield.

5-chloro-6-methyl-*N*-((6-phenoxy pyridin-3-yl)methyl)pyrimidin-4-amine (1)

white solid. m.p. 110°C. ¹H NMR (300 MHz, CDCl₃) δ 2.47(s, 3H, CH₃), 4.67(d, *J*=6.0 Hz, 2H, CH₂), 5.68(bs, 1H, NH), 6.89(d, *J*=8.7Hz, 1H, pyridine 3-H), 7.17-7.22(m, 1H, Ph-5-H), 7.12(d, *J*=8.4Hz, 2H, Ph-2,6-2H), 7.38(d, *J*=8.4Hz, 2H, Ph-3,5-2H), 7.70 (dd, *J*=8.4,2.1Hz, 1H, pyridine 4-H), 8.18(s, 1H, pyridine 6-H), 8.40(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for C₁₇H₁₅ClN₄O: C, 62.48; H, 4.63; N, 17.15. Found: C, 62.53; H, 4.60; N, 17.09. HRMS *m/z* 326.0941 [M + H]⁺ (calcd [M + H]⁺ 326.0934).

5-chloro-6-ethyl-*N*-((6-phenoxy pyridin-3-yl)methyl)pyrimidin-4-amine (2)

yellow solid. m.p. 99 °C. ¹H NMR (300 MHz, CDCl₃) δ 1.27(t, *J*=7.5Hz, 3H, CH₂CH₃), 2.80(q, 2H, CH₂CH₃), 4.68(d, *J*=5.7 Hz, 2H, CH₂), 5.64(bs, 1H, NH), 6.91(d, *J*=8.4Hz, 1H, pyridine 3-H), 7.18-7.23(m, 1H, Ph-5-H), 7.12(d, *J*=8.4Hz, 2H, Ph-2,6-2H), 7.39(d, *J*=8.4Hz, 2H, Ph-3,5-2H), 7.70 (dd, *J*=8.4,2.1Hz, 1H, pyridine 4-H), 8.18(s, 1H, pyridine 6-H), 8.40(s, 1H, Pyrimidine 2-H). Anal. Calcd (%) for C₁₈H₁₇ClN₄O: C, 63.44; H, 5.03; N, 16.44. Found: C, 63.40; H, 5.10; N, 16.39. HRMS *m/z* 341.1088 [M + H]⁺ (calcd [M + H]⁺ 341.1091).

5-chloro-6-methyl-*N*-(2-(6-phenoxy pyridin-3-yl)ethyl)pyrimidin-4-amine (3)

colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 2.50(s, 3H, CH₃), 2.88(t, *J*=6.9Hz, 2H, CH₂CH₂NH), 3.74(q, 2H, CH₂CH₂NH), 5.42(bs, 1H, NH), 6.87(d, *J*=8.7Hz, 1H, pyridine 3-H), 7.09-7.22(m, 3H, Ph-2,6-2H, Ph-4-H), 7.36-7.43(m, 2H, Ph-3,5-2H), 7.56(dd, *J*=8.4,2.7Hz, 1H, pyridine 4-H), 8.05(s, 1H, pyridine 6-H), 8.38(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for C₁₈H₁₇ClN₄O: C, 63.44; H, 5.03; N, 16.44. Found: C, 63.40; H, 4.99; N, 16.51. HRMS *m/z* 340.1086 [M + H]⁺ (calcd [M + H]⁺ 340.1091).

5-chloro-6-ethyl-*N*-(2-(6-phenoxy pyridin-3-yl)ethyl)pyrimidin-4-amine (4)

colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 1.26(t, *J*=7.5Hz, 3H, CH₂CH₃), 2.81(q, 2H, CH₂CH₃), 2.90(t, 2H, CH₂CH₂NH), 3.75(q, 2H, CH₂CH₂NH), 5.42(bs, 1H, NH), 6.87(d, *J*=8.1Hz, 1H, pyridine 3-H), 7.11-7.22(m, 3H, Ph-2,6-2H, Ph-4-H), 7.36-7.42(m, 2H, Ph-3,5-2H), 7.56(dd, *J*=8.4,2.4Hz, 1H, pyridine 4-H), 8.05(s, 1H, pyridine 6-H), 8.43(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for C₁₉H₁₉ClN₄O: C, 64.31; H, 5.40; N, 15.79. Found: C, 64.26; H, 5.40; N, 15.86. HRMS *m/z* 354.1252 [M + H]⁺ (calcd [M + H]⁺ 354.1247).

5-chloro-*N*-(2-(6-(2-chlorophenoxy)pyridin-3-yl)ethyl)-6-methylpyrimidin-

4-amine (5)

colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 2.45(s, 3H, CH_3), 2.89(t, $J=6.9\text{Hz}$, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 3.74(q, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 5.42(bs, 1H, NH), 6.94(d, $J=8.4\text{Hz}$, 1H, pyridine 3-H), 7.18-7.29(m, 3H, Ph-4,5,6-3H), 7.47(d, $J=7.2\text{Hz}$, 1H, Ph-3-H), 7.58(dd, $J=8.4, 2.4\text{Hz}$, 1H, pyridine 4-H), 7.99(s, 1H, pyridine 6-H), 8.38(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $\text{C}_{18}\text{H}_{16}\text{Cl}_2\text{N}_4\text{O}$: C, 57.61; H, 4.30; N, 14.93. Found: C, 57.55; H, 4.36; N, 14.88. HRMS m/z 374.0708 $[\text{M} + \text{H}]^+$ (calcd $[\text{M} + \text{H}]^+$ 374.0701).

5-chloro-*N*-(2-(6-(2-chlorophenoxy)pyridin-3-yl)ethyl)-6-ethylpyrimidin-4-amine (6)

colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 1.26(t, $J=7.5\text{Hz}$, 3H, CH_2CH_3), 2.78(q, 2H, CH_2CH_3), 2.90(t, $J=6.9\text{Hz}$, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 3.74(q, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 5.42(bs, 1H, NH), 6.94(d, $J=8.4\text{Hz}$, 1H, pyridine 3-H), 7.18-7.29(m, 3H, Ph-4,5,6-3H), 7.47(d, $J=6.9\text{Hz}$, 1H, Ph-3-H), 7.59(dd, $J=8.4, 2.7\text{Hz}$, 1H, pyridine 4-H), 8.00(s, 1H, pyridine 6-H), 8.43(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $\text{C}_{19}\text{H}_{18}\text{Cl}_2\text{N}_4\text{O}$: C, 58.62; H, 4.66; N, 14.39. Found: C, 58.68; H, 4.70; N, 14.33. HRMS m/z 388.0860 $[\text{M} + \text{H}]^+$ (calcd $[\text{M} + \text{H}]^+$ 388.0858).

5-chloro-*N*-(2-(6-(3-chlorophenoxy)pyridin-3-yl)ethyl)-6-methylpyrimidin-4-amine (7)

colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 2.46(s, 3H, CH_3), 2.91(t, $J=6.9\text{Hz}$, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 3.75(q, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 5.47(bs, 1H, NH), 6.90(d, $J=8.4\text{Hz}$, 1H, pyridine 3-H), 7.02(d, $J=9.0\text{Hz}$, 1H, Ph-6-H), 7.13-7.18(m, 2H, Ph-2,5-2H), 7.29(d, $J=8.1\text{Hz}$, 1H, Ph-4-H), 7.59(dd, $J=8.4, 2.1\text{Hz}$, 1H, pyridine 4-H), 8.05(s, 1H, pyridine 6-H), 8.39(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $\text{C}_{18}\text{H}_{16}\text{Cl}_2\text{N}_4\text{O}$: C, 57.61; H, 4.30; N, 14.93. Found: C, 57.70; H, 4.32; N, 14.87. HRMS m/z 374.0697 $[\text{M} + \text{H}]^+$ (calcd $[\text{M} + \text{H}]^+$ 374.0701).

5-chloro-*N*-(2-(6-(3-chlorophenoxy)pyridin-3-yl)ethyl)-6-ethylpyrimidin-4-amine (8)

colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 1.24(t, $J=7.5\text{Hz}$, 3H, CH_2CH_3), 2.79(q, 2H, CH_2CH_3), 2.92(t, $J=6.9\text{Hz}$, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 3.75(q, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 5.47(bs, 1H, NH), 6.90(d, $J=8.1\text{Hz}$, 1H, pyridine 3-H), 7.03(d, $J=9.0\text{Hz}$, 1H, Ph-6-H), 7.13-7.19(m, 2H, Ph-2,5-2H), 7.30(d, $J=8.1\text{Hz}$, 1H, Ph-4-H), 7.60(dd, $J=8.4, 2.7\text{Hz}$, 1H, pyridine 4-H), 8.06(s, 1H, pyridine 6-H), 8.44(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $\text{C}_{19}\text{H}_{18}\text{Cl}_2\text{N}_4\text{O}$: C, 58.62; H, 4.66; N, 14.39. Found: C, 58.69; H, 4.61; N, 14.44. HRMS m/z 388.0861 $[\text{M} +$

$\text{H}]^+$ (calcd $[\text{M} + \text{H}]^+$ 388.0858).

5-chloro-*N*-(2-(6-(4-chlorophenoxy)pyridin-3-yl)ethyl)-6-ethylpyrimidin-4-amine (10)

colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 1.26(t, $J=7.5\text{Hz}$, 3H, CH_2CH_3), 2.79(q, 2H, CH_2CH_3), 2.91(t, $J=6.9\text{Hz}$, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 3.75(q, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 5.43(bs, 1H, NH), 6.89(d, $J=8.1\text{Hz}$, 1H, pyridine 3-H), 7.07(d, $J=8.7\text{Hz}$, 2H, Ph-2,6-2H), 7.35(d, $J=8.7\text{Hz}$, 2H, Ph-3,5-2H), 7.59 (dd, $J=8.4, 2.7\text{Hz}$, 1H, pyridine 4-H), 8.03(s, 1H, pyridine 6-H), 8.43(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $\text{C}_{19}\text{H}_{18}\text{Cl}_2\text{N}_4\text{O}$: C, 58.62; H, 4.66; N, 14.39. Found: C, 58.58; H, 4.62; N, 14.45. HRMS m/z 388.0864 $[\text{M} + \text{H}]^+$ (calcd $[\text{M} + \text{H}]^+$ 388.0858).

5-chloro-6-methyl-*N*-(2-(6-(*p*-tolylloxy)pyridin-3-yl)ethyl)pyrimidin-4-amine (11)

colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 2.35(s, 3H, Ph- CH_3), 2.46(s, 3H, CH_3), 2.88(t, $J=6.9\text{Hz}$, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 3.73(q, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 5.42(bs, 1H, NH), 6.84(d, $J=8.4\text{Hz}$, 1H, pyridine 3-H), 7.01(d, $J=8.4\text{Hz}$, 2H, Ph-2,6-2H), 7.19(d, $J=8.4\text{Hz}$, 2H, Ph-3,5-2H), 7.53 (dd, $J=8.4, 2.7\text{Hz}$, 1H, pyridine 4-H), 8.03(s, 1H, pyridine 6-H), 8.38(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $\text{C}_{19}\text{H}_{19}\text{ClN}_4\text{O}$: C, 64.31; H, 5.40; N, 15.79. Found: C, 64.38; H, 5.44; N, 15.70. HRMS m/z 354.1241 $[\text{M} + \text{H}]^+$ (calcd $[\text{M} + \text{H}]^+$ 354.1247).

5-chloro-6-ethyl-*N*-(2-(6-(*p*-tolylloxy)pyridin-3-yl)ethyl)pyrimidin-4-amine (12)

colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 1.26(t, $J=7.5\text{Hz}$, 3H, CH_2CH_3), 2.35(s, 3H, Ph- CH_3), 2.78(q, 2H, CH_2CH_3), 2.89(t, $J=6.9\text{Hz}$, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 3.73(q, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 5.46(bs, 1H, NH), 6.84(d, $J=8.4\text{Hz}$, 1H, pyridine 3-H), 7.01(d, $J=8.1\text{Hz}$, 2H, Ph-2,6-2H), 7.19(d, $J=8.1\text{Hz}$, 2H, Ph-3,5-2H), 7.54 (dd, $J=8.4, 2.4\text{Hz}$, 1H, pyridine 4-H), 8.03(s, 1H, pyridine 6-H), 8.43(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $\text{C}_{20}\text{H}_{21}\text{ClN}_4\text{O}$: C, 65.12; H, 5.74; N, 15.19. Found: C, 65.10; H, 5.69; N, 15.23. HRMS m/z 368.1410 $[\text{M} + \text{H}]^+$ (calcd $[\text{M} + \text{H}]^+$ 368.1404).

5-chloro-*N*-(2-(6-(4-methoxyphenoxy)pyridin-3-yl)ethyl)-6-methylpyrimidin-4-amine (13)

colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 2.46(s, 3H, CH_3), 2.89(t, $J=6.9\text{Hz}$, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 3.73(q, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 3.82(s, 3H, OCH_3), 5.42(bs, 1H, NH), 6.83(d, $J=8.4\text{Hz}$, 1H, pyridine 3-H), 6.92(d, $J=6.6\text{Hz}$, 2H, Ph-2,6-2H),

7.06(d, $J=6.6\text{Hz}$, 2H, Ph-3,5-2H), 7.53 (dd, $J=8.7,2.4\text{Hz}$, 1H, pyridine 4-H), 8.03(s, 1H, pyridine 6-H), 8.38(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $\text{C}_{19}\text{H}_{19}\text{ClN}_4\text{O}_2$: C, 61.54; H, 5.16; N, 15.11. Found: C, 61.61; H, 5.09; N, 15.09. HRMS m/z 370.1194 $[\text{M} + \text{H}]^+$ (calcd $[\text{M} + \text{H}]^+$ 370.1197).

5-chloro-6-ethyl-*N*-(2-(6-(4-methoxyphenoxy)pyridin-3-yl)ethyl)pyrimidin-4-amine (14)

colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 1.26(t, $J=7.5\text{Hz}$, 3H, CH_2CH_3), 2.79(q, 2H, CH_2CH_3), 2.89(t, $J=6.9\text{Hz}$, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 3.73(q, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 3.82(s, 3H, OCH_3), 5.42(bs, 1H, NH), 6.83(d, $J=8.4\text{Hz}$, 1H, pyridine 3-H), 6.92(d, $J=6.6\text{Hz}$, 2H, Ph-2,6-2H), 7.06(d, $J=6.6\text{Hz}$, 2H, Ph-3,5-2H), 7.54 (dd, $J=8.4,2.4\text{Hz}$, 1H, pyridine 4-H), 8.03(s, 1H, pyridine 6-H), 8.43(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $\text{C}_{20}\text{H}_{21}\text{ClN}_4\text{O}_2$: C, 62.42; H, 5.50; N, 14.56. Found: C, 62.36; H, 5.49; N, 14.65. HRMS m/z 384.1349 $[\text{M} + \text{H}]^+$ (calcd $[\text{M} + \text{H}]^+$ 384.1353).

5-chloro-6-methyl-*N*-(2-(6-(4-(trifluoromethyl)phenoxy)pyridin-3-yl)ethyl)pyrimidin-4-amine (15)

colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 2.46(s, 3H, CH_3), 2.92(t, $J=6.9\text{Hz}$, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 3.76(q, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 5.43(bs, 1H, NH), 6.95(d, $J=8.4\text{Hz}$, 1H, pyridine 3-H), 7.07(d, $J=8.4\text{Hz}$, 2H, Ph-2,6-2H), 7.61-7.66(m, 3H, Ph-3,5-2H, pyridine 4-H), 8.06(s, 1H, pyridine 6-H), 8.39(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $\text{C}_{19}\text{H}_{16}\text{ClF}_3\text{N}_4\text{O}$: C, 55.82; H, 3.95; N, 13.71. Found: C, 55.77; H, 3.89; N, 13.81. HRMS m/z 408.0962 $[\text{M} + \text{H}]^+$ (calcd $[\text{M} + \text{H}]^+$ 408.0965).

5-chloro-6-ethyl-*N*-(2-(6-(4-(trifluoromethyl)phenoxy)pyridin-3-yl)ethyl)pyrimidin-4-amine (16)

colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 1.26(t, $J=7.5\text{Hz}$, 3H, CH_2CH_3), 2.79(q, 2H, CH_2CH_3), 2.93(t, $J=6.9\text{Hz}$, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 3.76(q, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 5.42(bs, 1H, NH), 6.95(d, $J=8.4\text{Hz}$, 1H, pyridine 3-H), 7.22(d, $J=8.4\text{Hz}$, 2H, Ph-2,6-2H), 7.61-7.66(m, 3H, Ph-3,5-2H, pyridine 4-H), 8.06(s, 1H, pyridine 6-H), 8.44(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $\text{C}_{20}\text{H}_{18}\text{ClF}_3\text{N}_4\text{O}$: C, 56.81; H, 4.29; N, 13.25. Found: C, 56.72; H, 4.35; N, 13.29. HRMS m/z 422.1127 $[\text{M} + \text{H}]^+$ (calcd $[\text{M} + \text{H}]^+$ 422.1121).

5-chloro-*N*-(2-(6-(4-chloro-2-methylphenoxy)pyridin-3-yl)ethyl)-6-methylpyrimidin-4-amine (17)

colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 2.15(s, 3H, Ph- CH_3), 2.46(s, 3H,

pyrimidine CH₃), 2.89(t, *J*=6.9Hz, 2H, CH₂CH₂NH), 3.73(q, 2H, CH₂CH₂NH), 5.42(bs, 1H, NH), 6.86(d, *J*=8.4Hz, 1H, pyridine 3-H), 6.97(d, *J*=8.4Hz, 1H, Ph-6-H), 7.19 (dd, *J*=8.7,2.7Hz, 1H, Ph-5-H), 7.25 (s, 1H, Ph-3-H), 7.56 (dd, *J*=8.4,2.7Hz, 1H, pyridine 4-H), 7.99(s, 1H, pyridine 6-H), 8.38(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for C₁₉H₁₈Cl₂N₄O: C, 58.62; H, 4.66; N, 14.39. Found: C, 58.68; H, 4.70; N, 14.31. HRMS *m/z* 388.0563 [M + H]⁺ (calcd [M + H]⁺ 388.0858).

5-chloro-*N*-(2-(6-(4-chloro-2-methylphenoxy)pyridin-3-yl)ethyl)-6-ethylpyrimidin-4-amine (18)

colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 1.26(t, *J*=7.5Hz, 3H, CH₂CH₃), 2.14(s, 3H, Ph-CH₃), 2.78(q, 2H, CH₂CH₃), 2.89(t, *J*=6.9Hz, 2H, CH₂CH₂NH), 3.74(q, 2H, CH₂CH₂NH), 5.42(bs, 1H, NH), 6.86(d, *J*=8.4Hz, 1H, pyridine 3-H), 6.97(d, *J*=8.4Hz, 1H, Ph-6-H), 7.19 (dd, *J*=8.4,2.7Hz, 1H, Ph-5-H), 7.25 (s, 1H, Ph-3-H), 7.57 (dd, *J*=8.4,2.7Hz, 1H, pyridine 4-H), 8.00(s, 1H, pyridine 6-H), 8.43(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for C₂₀H₂₀Cl₂N₄O: C, 59.56; H, 5.00; N, 13.89. Found: C, 59.60; H, 5.01; N, 13.82. HRMS *m/z* 402.1009 [M + H]⁺ (calcd [M + H]⁺ 402.1014).

5-chloro-*N*-(2-(6-(2,4-dichlorophenoxy)pyridin-3-yl)ethyl)-6-methylpyrimidin-4-amine (19)

colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 2.46(s, 3H, CH₃), 2.90(t, *J*=6.9Hz, 2H, CH₂CH₂NH), 3.74(q, 2H, CH₂CH₂NH), 5.42(bs, 1H, NH), 6.97(d, *J*=8.4Hz, 1H, pyridine 3-H), 7.14(d, *J*=8.4Hz, 1H, Ph-6-H), 7.28(dd, *J*=8.7,2.7Hz, 1H, Ph-5-H), 7.48(s, 1H, Ph-3-H), 7.60(dd, *J*=8.4,2.1Hz, 1H, pyridine 4-H), 7.97(s, 1H, pyridine 6-H), 8.38(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for C₁₈H₁₅Cl₃N₄O: C, 52.77; H, 3.69; N, 13.68. Found: C, 52.79; H, 3.64; N, 13.70. HRMS *m/z* 408.0316 [M + H]⁺ (calcd [M + H]⁺ 408.0311).

5-chloro-*N*-(2-(6-(2,4-dichlorophenoxy)pyridin-3-yl)ethyl)-6-ethylpyrimidin-4-amine (20)

colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 1.26(t, *J*=7.5Hz, 3H, CH₂CH₃), 2.79 (q, 2H, CH₂CH₃), 2.90(t, *J*=6.9Hz, 2H, CH₂CH₂NH), 3.74(q, 2H, CH₂CH₂NH), 5.30(bs, 1H, NH), 6.97(d, *J*=8.4Hz, 1H, pyridine 3-H), 7.14(d, *J*=9.0Hz, 1H, Ph-6-H), 7.29(dd, *J*=8.4,2.4Hz, 1H, Ph-5-H), 7.48(s, 1H, Ph-3-H), 7.61(dd, *J*=8.4,2.4Hz, 1H, pyridine 4-H), 7.97(s, 1H, pyridine 6-H), 8.43(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for C₁₉H₁₇Cl₃N₄O: C, 53.86; H, 4.04; N, 13.22. Found: C, 53.93; H, 4.01; N, 13.17. HRMS *m/z* 422.0464 [M + H]⁺ (calcd [M + H]⁺ 422.0468).

5-chloro-*N*-(2-(6-(2,5-dichlorophenoxy)pyridin-3-yl)ethyl)-6-methylpyrimidin-4-amine (21)

colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 2.46(s, 3H, CH_3), 2.91(t, $J=6.9\text{Hz}$, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 3.75(q, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 5.42(bs, 1H, NH), 6.98(d, $J=8.4\text{Hz}$, 1H, pyridine 3-H), 7.16(dd, $J=8.4, 2.4\text{Hz}$, 1H, Ph-4-H), 7.22(s, 1H, Ph-6-H), 7.39(d, $J=8.4\text{Hz}$, 1H, Ph-3-H), 7.61(dd, $J=8.4, 2.4\text{Hz}$, 1H, pyridine 4-H), 7.99(s, 1H, pyridine 6-H), 8.39(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $\text{C}_{18}\text{H}_{15}\text{Cl}_3\text{N}_4\text{O}$: C, 52.77; H, 3.69; N, 13.68. Found: C, 52.81; H, 3.72; N, 13.62. HRMS m/z 408.0308 $[\text{M} + \text{H}]^+$ (calcd $[\text{M} + \text{H}]^+$ 408.0311).

5-chloro-*N*-(2-(6-(2,5-dichlorophenoxy)pyridin-3-yl)ethyl)-6-ethylpyrimidin-4-amine (22)

colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 1.26(t, $J=7.5\text{Hz}$, 3H, CH_2CH_3), 2.81(q, 2H, CH_2CH_3), 2.91(t, $J=6.9\text{Hz}$, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 3.75(q, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 5.42(bs, 1H, NH), 6.98(d, $J=8.4\text{Hz}$, 1H, pyridine 3-H), 7.17(dd, $J=8.4, 2.4\text{Hz}$, 1H, Ph-4-H), 7.22(s, 1H, Ph-6-H), 7.39(d, $J=8.4\text{Hz}$, 1H, Ph-3-H), 7.61(dd, $J=8.4, 2.4\text{Hz}$, 1H, pyridine 4-H), 7.99(s, 1H, pyridine 6-H), 8.44(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $\text{C}_{19}\text{H}_{17}\text{Cl}_3\text{N}_4\text{O}$: C, 53.86; H, 4.04; N, 13.22. Found: C, 53.80; H, 4.09; N, 13.25. HRMS m/z 423.0470 $[\text{M} + \text{H}]^+$ (calcd $[\text{M} + \text{H}]^+$ 423.0468).

5-chloro-*N*-(2-(6-(2-chloro-4-(trifluoromethyl)phenoxy)pyridin-3-yl)ethyl)-6-methylpyrimidin-4-amine (23)

colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 2.46(s, 3H, CH_3), 2.92(t, $J=6.9\text{Hz}$, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 3.75(q, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 5.44(bs, 1H, NH), 7.02(d, $J=8.4\text{Hz}$, 1H, pyridine 3-H), 7.30(d, $J=8.4\text{Hz}$, 1H, Ph-6-H), 7.57(d, $J=8.4\text{Hz}$, 1H, Ph-5-H), 7.64(dd, $J=8.4, 2.4\text{Hz}$, 1H, pyridine 4-H), 7.73(s, 1H, Ph-3-H), 7.98(s, 1H, pyridine 6-H), 8.34(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $\text{C}_{19}\text{H}_{15}\text{Cl}_2\text{F}_3\text{N}_4\text{O}$: C, 51.49; H, 3.41; N, 12.64. Found: C, 51.44; H, 3.37; N, 12.70. HRMS m/z 442.0579 $[\text{M} + \text{H}]^+$ (calcd $[\text{M} + \text{H}]^+$ 442.0575).

5-chloro-*N*-(2-(6-(2-chloro-4-(trifluoromethyl)phenoxy)pyridin-3-yl)ethyl)-6-ethylpyrimidin-4-amine (24)

colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 1.26(t, $J=7.5\text{Hz}$, 3H, CH_2CH_3), 2.79(q, 2H, CH_2CH_3), 2.92(t, $J=6.9\text{Hz}$, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 3.75(q, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 5.45(bs, 1H, NH), 7.01(d, $J=7.8\text{Hz}$, 1H, pyridine 3-H), 7.30(d, $J=8.4\text{Hz}$, 1H, Ph-6-H), 7.56(d, $J=7.8\text{Hz}$, 1H, Ph-5-H), 7.64(dd, $J=8.4, 2.7\text{Hz}$, 1H, pyridine 4-H), 7.75(s, 1H, Ph-3-H), 7.75(s, 1H, pyridine 6-H), 8.43(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $\text{C}_{20}\text{H}_{17}\text{Cl}_2\text{F}_3\text{N}_4\text{O}$: C, 52.53; H, 3.75; N, 12.25. Found:

C, 52.50; H, 3.81; N, 12.22. HRMS m/z 456.0737 $[M + H]^+$ (calcd $[M + H]^+$ 456.0732).

5-chloro-*N*-((6-(4-chlorophenoxy)pyridin-3-yl)methyl)-6-methylpyrimidin-4-amine (25)

yellow solid. m.p. 108°C. ^1H NMR (300 MHz, CDCl_3) δ 2.48(s, 3H, CH_3), 4.68(d, $J=5.7\text{Hz}$, 2H, CH_2), 5.69(bs, 1H, NH), 6.91(d, $J=8.4\text{Hz}$, 1H, pyridine 3-H), 7.07(d, $J=6.6\text{Hz}$, 2H, Ph-2,6-2H), 7.34(d, $J=6.6\text{Hz}$, 2H, Ph-3,5-2H), 7.72 (dd, $J=8.4, 2.7\text{Hz}$, 1H, pyridine 4-H), 8.16(s, 1H, pyridine 6-H), 8.40(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $\text{C}_{17}\text{H}_{14}\text{Cl}_2\text{N}_4\text{O}$: C, 56.53; H, 3.91; N, 15.51. Found: C, 56.59; H, 3.94; N, 15.45. HRMS m/z 360.0540 $[M + H]^+$ (calcd $[M + H]^+$ 360.0545).

5-chloro-4-((6-(4-chlorophenoxy)pyridin-3-yl)methoxy)-6-ethylpyrimidine (28)

colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 1.23(t, $J=7.5\text{Hz}$, 3H, CH_2CH_3), 2.76 (q, 2H, CH_2CH_3), 5.07 (s, 2H, CH_2), 6.93 (d, $J=8.4\text{Hz}$, 1H, pyridine 3-H), 7.06(d, $J=6.6\text{Hz}$, 2H, Ph-2,6-2H), 7.36(d, $J=6.6\text{Hz}$, 2H, Ph-3,5-2H), 7.82 (dd, $J=8.7, 2.1\text{Hz}$, 1H, pyridine 6-H), 8.08(s, 1H, pyrimidine 2-H), 8.17(d, $J=2.7\text{Hz}$, 1H, pyridine 4-H). Anal. Calcd (%) for $\text{C}_{18}\text{H}_{15}\text{Cl}_2\text{N}_3\text{O}_2$: C, 57.46; H, 4.02; N, 11.17. Found: C, 57.49; H, 3.98; N, 11.20. HRMS m/z 376.0544 $[M + H]^+$ (calcd $[M + H]^+$ 376.0541).

***N*-(1-(6-(4-(*tert*-butyl)phenoxy)pyridin-3-yl)ethyl)-5-chloro-6-ethylpyrimidin-4-amine (29)**

colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 1.25 (t, $J=7.5\text{Hz}$, 3H, CH_2CH_3), 1.62(d, $J=6.9\text{Hz}$, 3H, CHCH_3), 2.79(q, 2H, CH_2CH_3), 5.35(q, 1H, CHCH_3), 5.52(bs, 1H, NH), 6.88(d, $J=8.7\text{Hz}$, 1H, pyridine 3-H), 7.12(d, $J=7.8\text{Hz}$, 2H, Ph-2,6-2H), 7.38(d, $J=7.8\text{Hz}$, 2H, Ph-3,5-2H), 7.69 (dd, $J=8.4, 2.7\text{Hz}$, 1H, pyridine 4-H), 8.21(s, 1H, pyridine 6-H), 8.39(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $\text{C}_{23}\text{H}_{27}\text{ClN}_4\text{O}$: C, 67.22; H, 6.62; N, 13.63. Found: C, 67.20; H, 6.56; N, 13.71. HRMS m/z 411.1869 $[M + H]^+$ (calcd $[M + H]^+$ 411.1873).

5-chloro-6-methyl-*N*-(2-(2-phenoxy)pyridin-3-yl)ethyl)pyrimidin-4-amine (32)

colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 2.41 (s, 3H, CH_3), 3.08 (t, $J=6.9\text{Hz}$, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 3.85 (q, 2H, $\text{CH}_2\text{CH}_2\text{NH}$), 5.62 (bs, 1H, NH), 6.94-6.98 (m, 1H, pyridine 5-H), 7.12(d, $J=8.4\text{Hz}$, 2H, Ph-2,6-2H), 7.16-7.21(m, 1H, Ph-5-H), 7.38(d, $J=8.1\text{Hz}$, 2H, Ph-3,5-2H), 7.57 (dd, $J=7.2, 1.8\text{Hz}$, 1H, pyridine 6-H),

8.04(dd, $J=4.8, 1.8$ Hz, 1H, pyridine 4-H), 8.41(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $C_{18}H_{17}ClN_4O$: C, 63.44; H, 5.03; N, 16.44. Found: C, 63.49; H, 5.00; N, 16.41. HRMS m/z 340.1086 $[M + H]^+$ (calcd $[M + H]^+$ 340.1091).

5-chloro-6-ethyl-N-(2-(2-phenoxy)pyridin-3-yl)ethyl)pyrimidin-4-amine (33)

colorless oil. 1H NMR (300 MHz, $CDCl_3$) δ 1.25(t, $J=7.5$ Hz, 3H, CH_2CH_3), 2.77 (q, 2H, CH_2CH_3), 3.09 (t, $J=6.9$ Hz, 2H, CH_2CH_2NH), 3.86 (q, 2H, CH_2CH_2NH), 5.61 (bs, 1H, NH), 6.94-6.98 (m, 1H, pyridine 5-H), 7.13(d, $J=8.4$ Hz, 2H, Ph-2,6-2H), 7.17-7.22(m, 1H, Ph-5-H), 7.39(d, $J=8.1$ Hz, 2H, Ph-3,5-2H), 7.56 (dd, $J=7.2, 1.8$ Hz, 1H, pyridine 6-H), 8.05(dd, $J=4.8, 1.8$ Hz, 1H, pyridine 4-H), 8.42(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $C_{19}H_{19}ClN_4O$: C, 64.31; H, 5.40; N, 15.79. Found: C, 64.28; H, 5.39; N, 15.85. HRMS m/z 355.1250 $[M + H]^+$ (calcd $[M + H]^+$ 355.1247).

5-chloro-N-(2-(2-(4-chlorophenoxy)pyridin-3-yl)ethyl)-6-methylpyrimidin-4-amine (34)

colorless oil. 1H NMR (300 MHz, $CDCl_3$) δ 2.44 (s, 3H, CH_3), 3.07 (t, $J=6.9$ Hz, 2H, CH_2CH_2NH), 3.85 (q, 2H, CH_2CH_2NH), 5.59 (bs, 1H, NH), 6.95-6.99 (m, 1H, pyridine 5-H), 7.08(d, $J=6.6$ Hz, 2H, Ph-2,6-2H), 7.36(d, $J=6.6$ Hz, 2H, Ph-3,5-2H), 7.56 (dd, $J=7.2, 1.8$ Hz, 1H, pyridine 6-H), 8.04(dd, $J=4.8, 1.8$ Hz, 1H, pyridine 4-H), 8.36(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $C_{18}H_{16}Cl_2N_4O$: C, 57.61; H, 4.30; N, 14.93. Found: C, 57.66; H, 4.28; N, 14.89. HRMS m/z 374.0707 $[M + H]^+$ (calcd $[M + H]^+$ 374.0701).

5-Chloro-N-(2-(2-(4-chlorophenoxy)pyridin-3-yl)ethyl)-6-ethylpyrimidin-4-amine (35)

white solid in 72% yield, m.p. 127.2°C. 1H NMR (300 MHz, $CDCl_3$) δ 1.25(t, $J=7.5$ Hz, 3H, CH_2CH_3), 2.77 (q, 2H, CH_2CH_3), 3.08 (t, $J=6.9$ Hz, 2H, CH_2CH_2NH), 3.85 (q, 2H, CH_2CH_2NH), 5.59 (bs, 1H, NH), 6.95-6.99 (m, 1H, pyridine 5-H), 7.08(d, $J=6.6$ Hz, 2H, Ph-2,6-2H), 7.35(d, $J=6.6$ Hz, 2H, Ph-3,5-2H), 7.57 (dd, $J=7.2, 1.8$ Hz, 1H, pyridine 6-H), 8.03(dd, $J=4.8, 1.8$ Hz, 1H, pyridine 4-H), 8.41(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $C_{19}H_{19}ClN_4O$: C, 64.31; H, 5.40; N, 15.79. Found: C, 64.33; H, 5.46; N, 15.72. HRMS m/z 388.0853 $[M + H]^+$ (calcd $[M + H]^+$ 388.0858).

5-chloro-N-(2-(2-(4-chlorophenoxy)pyridin-4-yl)ethyl)-6-methylpyrimidin-4-amine (36)

yellow oil. 1H NMR (300 MHz, $CDCl_3$) δ 2.17 (s, 3H, CH_3), 2.98 (t, $J=6.9$ Hz, 2H, CH_2CH_2NH), 3.87 (q, 2H, CH_2CH_2NH), 6.56 (bs, 1H, NH), 6.90 (d, $J=8.4$ Hz,

1H, pyridine 6-H), 7.06(d, $J=6.9\text{Hz}$, 2H, Ph-2,6-2H), 7.35(d, $J=6.9\text{Hz}$, 2H, Ph-3,5-2H), 7.63 (dd, $J=8.4,2.1\text{Hz}$, 1H, pyridine 5-H), 8.07(s, 1H, pyridine 3-H), 8.47(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $\text{C}_{18}\text{H}_{16}\text{Cl}_2\text{N}_4\text{O}$: C, 57.61; H, 4.30; N, 14.93. Found: C, 57.58; H, 4.36; N, 14.90. HRMS m/z 375.0706 $[\text{M} + \text{H}]^+$ (calcd $[\text{M} + \text{H}]^+$ 375.0701).

5-chloro-*N*-(2-(2-(4-chlorophenoxy)pyridin-4-yl)ethyl)-6-ethylpyrimidin-4-amine (37)

yellow oil. 71% yield. ^1H NMR (300MHz, CDCl_3) δ 1.27(s, 3H, CH_2CH_3), 2.81 (q, 2H, CH_2CH_3), 2.96 (t, $J=6.9\text{Hz}$, 2H, $\text{CH}_2\text{CH}_2\text{NH}_2$), 3.80 (q, 2H, $\text{CH}_2\text{CH}_2\text{NH}_2$), 5.42 (bs, 1H, NH), 6.79(s 1H, pyridine 3-H), 6.89 (d, $J=5.7\text{Hz}$, 1H, pyridine 5-H), 7.07(d, $J=6.9\text{Hz}$, 2H, Ph-2,6-2H), 7.35(d, $J=6.6\text{Hz}$, 2H, Ph-3,5-2H), 8.11 (d, $J=5.1\text{Hz}$, 1H, Pyridine 6-H), 8.45(s, 1H, pyrimidine 2-H). Anal. Calcd (%) for $\text{C}_{19}\text{H}_{18}\text{Cl}_2\text{N}_4\text{O}$: C, 58.62; H, 4.66; N, 14.39. Found: C, 58.70; H, 4.62; N, 14.33. HRMS m/z 388.0862 $[\text{M} + \text{H}]^+$ (calcd $[\text{M} + \text{H}]^+$ 388.0858).