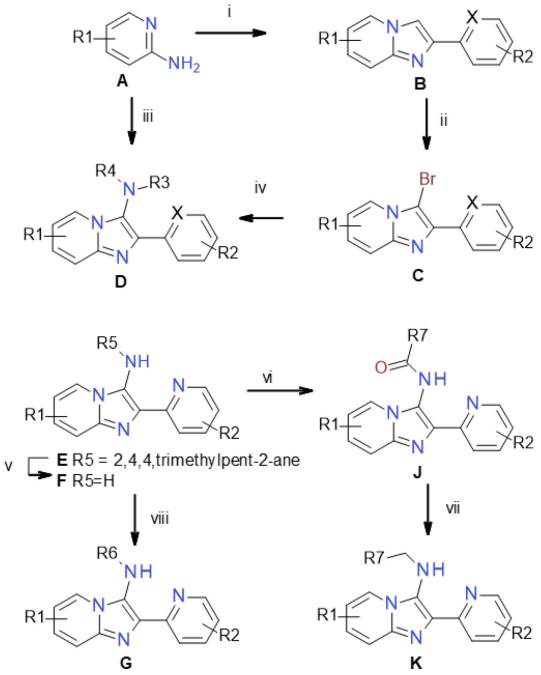
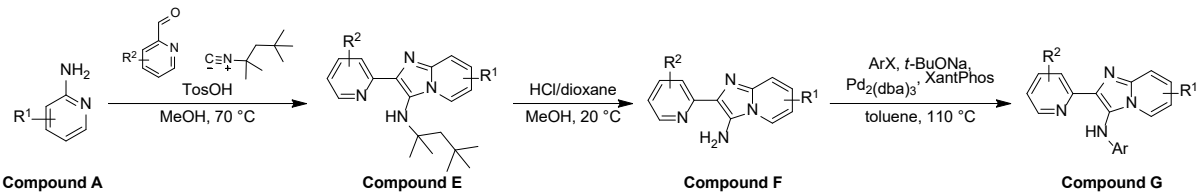
Synthesis



General Procedures



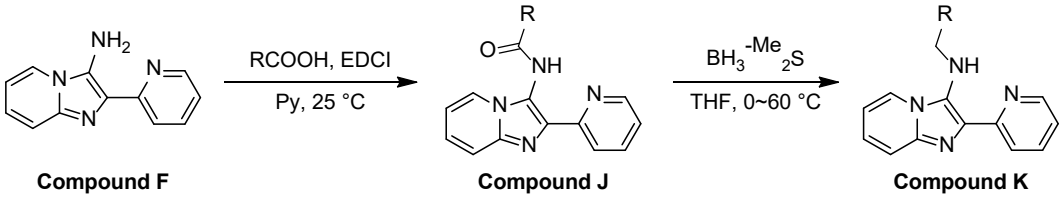
Method A: Preparation for compound E. To a mixture of substituted pyridin-2-amine (1 eq) and substituted pyridine-2-carbaldehyde (1 eq) in MeOH, TosOH (0.2 eq) and 2-isocyano-2,4,4-trimethyl-pentane (1 eq) were added. The mixture was stirred at 70 °C for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic phase were dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give a residue. The residue was purified by silica gel chromatography to give the product.

Method B: Preparation for compound F. HCl/dioxane was added to a solution of the corresponding 2-(pyridin-2-yl)-N-(2,4,4-trimethylpentan-2-yl)imidazo[1,2-a]pyridin-3-amine (1 eq) in MeOH. The mixture was stirred at 20 °C for 12 h. The reaction mixture was concentrated under reduced pressure to give a residue. The residue was diluted with water

and adjusted to pH 8 with saturated sodium bicarbonate solution, then extracted with dichloromethane. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure to give the product.

Method C: Preparation for compound G. To a mixture of the corresponding 2-(pyridin-2-yl)imidazo[1,2-a]pyridin-3-amine (1 eq) and Aryl halide 1-bromo-3-fluoro-benzene (1.2 eq) in toluene were added xantphos (0.2 eq), $Pd_2(dba)_3$ (0.1 eq) and *t*-BuONa (2 eq). The mixture was stirred at 110 °C for 12 h under N_2. The reaction mixture was concentrated under reduced pressure to give a residue. The residue was purified by prep-HPLC to give the product.

General procedure 2

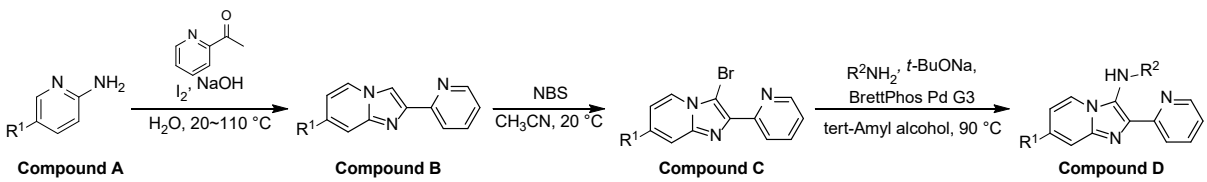


Compound F **Compound J** **Compound K**

Method D: Preparation for compound J. To a solution of 2-(2-pyridyl)imidazo[1,2-*a*]pyridin-3-amine (1 eq) in Py were added the corresponding acid (1.3 eq) and EDCI (3 eq). The mixture was stirred at 25 °C for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic phase was washed with brine, dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give the product.

Method E: Preparation for compound K. BH_3-Me_2S (10 M, 10 eq) at 0 °C was added to a solution of the corresponding amide (1 eq) in THF. The mixture was stirred at 25 °C for 1 hr and then stirred at 60 °C for 6 hr. LCMS showed the reaction was complete. The reaction mixture was quenched by addition of MeOH and water and extracted with ethyl acetate. The combined organic phase was washed with brine, dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give a residue which was purified by prep-HPLC to give the product.

General procedure 3



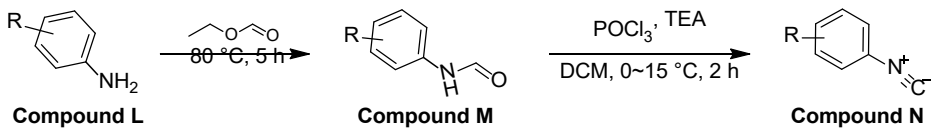
Compound A **Compound B** **Compound C** **Compound D**

Method F: Preparation for compound B. I_2 (1.2 eq) was added to a mixture of 1-(2-pyridyl)ethanone (1 eq) and the substituted pyridin-2-amine (2.3 eq) .The mixture was stirred at 110 °C for 4 h and then stirred at 70 °C for 12 h. H_2O and NaOH (10 eq) were added and the mixture was stirred at 100 °C for 1 h. The reaction mixture was diluted with dichloromethane and adjusted to pH 8 with 6 M HCl solution. The mixture was extracted with dichloromethane. The combined organic phase was washed with water, dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give the product.

Method G: Preparation for compound C. NBS (1.2 eq) was added to a solution of the corresponding 2-(2-pyridyl)imidazo[1,2-*a*]pyridine (1 eq) in CH_3CN. The mixture was stirred at 30 °C for 5 h. The reaction mixture was diluted with water and extracted with dichloromethane. The combined organic phase was washed with brine, dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give a residue. The residue was purified by silica gel chromatography to give the product.

Method H: Preparation for compound D. To a mixture of the corresponding 3-bromo-2-(2-pyridyl)imidazo[1,2-*a*]pyridine (1 eq) and amine (1.5 eq) in tert-Amyl alcohol were added methanesulfonato(2-dicyclohexylphosphino-3,6-dimethoxy-2,4,6-tri-*i*-propyl-1,1-biphenyl)-(2-amino-1,1-biphenyl-2-yl)palladium(II) (0.1 eq) and *t*-BuONa (2.7 eq). The mixture was stirred at 90 °C for 12 h under N_2. The reaction mixture was filtered and concentrated under reduced pressure to give a residue which was purified by prep-HPLC to give the product.

General procedure 4



Compound L **Compound M** **Compound N**

Method I: Preparation for compound M. A mixture of substituted aniline (1 eq) and ethyl formate (1.5 eq) was stirred at 80 °C for 5 h. The reaction mixture was concentrated under reduced pressure to give a residue. The residue was purified by silica gel chromatography to obtain the product.

Method J: Preparation for compound N. To a mixture of the substituted aryl formamide (1 eq) and TEA (5 eq) in anhydrous dichloromethane, $POCl_3$ (1.2 eq) was added dropwise under N_2 at 0 °C. The mixture was stirred at 0 °C for 0.5 h and stirred at 15 °C for 1.5 h. The mixture

was quenched with saturated $NaHCO_3$ solution at 0 °C. The aqueous phase was extracted with ethyl acetate. The combined organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure to give the product.

Synthesis of intermediates

2-(Pyridin-2-yl)imidazo[1,2-*a*]pyridine (B1). The title compound was synthesized according to method F to give 2-(pyridin-2-yl)imidazo[1,2-*a*]pyridine (4.5 g, crude) as a brown solid.

3-Bromo-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridine (C1). The title compound was synthesized according to method G from **B1** to give 3-bromo-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridine (1.2 g) as a brown solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.80-8.79 (m, 1H), 8.61 (d, *J* = 6.8 Hz, 1H), 8.36 (d, *J* = 7.6 Hz, 1H), 8.18 (m, 1H), 7.82 (d, *J* = 9.2 Hz, 1H), 7.69-7.62 (m, 2H), 7.35-7.32 (m, 1H).

7-Methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridine (B2). The title compound was synthesized according to method F to give 7-methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridine (9.81 g, crude) as a brown solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.58-8.56 (m, 1H), 8.43 (d, *J* = 7.6 Hz, 1H), 8.29 (s, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.30-7.28 (m, 1H), 6.99-6.98 (m, 1H), 6.66-6.63 (m, 1H), 5.82 (s, 1H), 3.84 (s, 3H). MS (ESI): m/z 226 $[M+1]^+$.

3-Bromo-7-methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridine (C2). The title compound was synthesized according to method G to give 3-bromo-7-methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridine (4.55 g, 100% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.67-8.66 (m, 1H), 8.28 (d, *J* = 7.6 Hz, 1H), 8.12 (d, *J* = 7.6 Hz, 1H), 7.92-7.88 (m, 1H), 7.38-7.35 (m, 1H), 7.10-7.09 (m, 1H), 6.83-6.80 (m, 1H), 3.88 (s, 3H). MS (ESI): m/z 306 $[M+1]^+$.

2-(Pyridin-2-yl)-N-(2,4,4-trimethylpentan-2-yl)imidazo[1,2-a]pyridin-3-amine (E1) The title compound was synthesized according to method A using pyridin-2-amine (1.90 g, 20.18 mmol), pyridine-2-carbaldehyde (2.16 g, 20.18 mmol), TosOH (695.05 mg, 4.04 mmol) and 2-isocyano-2,4,4-trimethyl-pentane (2.81 g, 20.18 mmol, 3.52 mL) in MeOH (50 mL) to yield 2-(pyridin-2-yl)-*N*-(2,4,4-trimethylpentan-2-yl)imidazo[1,2-*a*]pyridin-3-amine (6.2 g, 19.23

mmol, 95.28% yield) as yellow oil. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.60 (d, *J* = 4.0 Hz, 1H), 8.36 (d, *J* = 6.8 Hz, 1H), 8.07 (d, *J* = 7.6 Hz, 1H), 7.91-7.88 (m, 1H), 7.50-7.48 (m, 1H), 7.32-7.30 (m, 1H), 7.20 (m, 1H), 6.90-6.88 (m, 1H), 5.43 (s, 1H), 1.67 (s, 2H), 1.10 (s, 9H), 1.00 (s, 6H). MS (ESI): m/z 323 $[M+1]^+$.

2-(Pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (F1) The title compound was synthesized according to method B using 2-(pyridin-2-yl)-*N*-(2,4,4-trimethylpentan-2-yl)imidazo[1,2-*a*]pyridin-3-amine (6.2 g, 19.23 mmol) and HCl/dioxane (4 M, 60 mL) in MeOH (50 mL) to yield 2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (3.9 g, 18.55 mmol, 96.48% yield) as a yellow solid. MS (ESI): m/z 211 $[M+1]^+$.

7-Methoxy-2-(pyridin-2-yl)-*N*-(2,4,4-trimethylpentan-2-yl)imidazo[1,2-*a*]pyridin-3-amine E2 The title compound was synthesized according to method A to give 7-methoxy-2-(pyridin-2-yl)-*N*-(2,4,4-trimethylpentan-2-yl)imidazo[1,2-*a*]pyridin-3-amine (7.2 g, 20.43 mmol, 84.53% yield) as yellow oil. MS (ESI): m/z 353 $[M+1]^+$.

7-Methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine F2a The title compound was synthesized according to method B from E2 to give 7-methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine **F2** (5.6 g, 20.24 mmol, 99.07% yield, HCl salt) as a yellow solid. MS (ESI): m/z 241 $[M+1]^+$.

7-Methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine To a solution of 7-methoxy-2-(2-pyridyl)imidazo[1,2-*a*]pyridin-3-amine HCl salt (**F2b**, 3 g, 10.84 mmol, HCl salt) in MeOH (30 mL) was added Amberlyst(R)A-26(OH) (2 g). The mixture was stirred at 25 °C for 0.5 hr. The reaction mixture was filtered and concentrated under reduced pressure to give 7-methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (2.5 g, 10.41 mmol, 95.98% yield) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.57-8.56 (m, 1H), 8.18 (d, *J* = 7.6 Hz, 1H), 7.92 (d, *J* = 8.4 Hz, 1H), 7.85-7.81 (m, 1H), 7.16 (t, *J* = 6.0 Hz, 1H), 6.84 (m, 1H), 6.75-6.73 (m, 1H), 6.43 (s, 2H), 3.86 (s, 3H).

7-Methyl-2-(pyridin-2-yl)-*N*-(2,4,4-trimethylpentan-2-yl)imidazo[1,2-*a*]pyridin-3-amine (E3) The title compound was synthesized according to method A to give 7-methyl-2-(pyridin-2-yl)-*N*-(2,4,4-trimethylpentan-2-yl)imidazo[1,2-*a*]pyridin-3-amine (1.55 g, crude) as brown yellow oil. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.58-8.57 (m, 1H), 8.24 (d, *J* = 7.2 Hz, 1H), 8.04 (d, *J*

= 8.0 Hz, 1H), 7.88-7.86 (m, 1H), 7.29-7.25 (m, 2H), 6.73-6.71 (m, 1H), 5.38 (s, 1H), 2.34 (s, 3H), 1.65 (s, 2H), 1.08 (s, 9H), 0.98 (s, 6H).

7-Methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (F3). The title compound was synthesized according to method B to give 7-methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (860 mg, 3.83 mmol, 83.25% yield) as a yellow solid. MS (ESI): m/z 225 $[M+1]^+$.

6-Methyl-2-(pyridin-2-yl)-*N*-(2,4,4-trimethylpentan-2-yl)imidazo[1,2-*a*]pyridin-3-amine (E4). The title compound was synthesized according to method A to give 6-methyl-2-(2-pyridyl)-*N*-(1,1,3,3-tetramethylbutyl)imidazo[1,2-*a*]pyridin-3-amine (1.50 g, 4.46 mmol, 96.49% yield) as a yellow solid. MS (ESI): m/z 337 $[M+1]^+$.

6-Methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (F4) . The title compound was synthesized according to method B to give 6-methyl-2-(2-pyridyl)imidazo[1,2-*a*]pyridin-3-amine (850 mg, 3.79 mmol, 85.02% yield) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.55-8.49 (m, 1H), 7.97-7.94 (m, 2H), 7.81-7.77 (m, 1H), 7.31 (d, *J* = 9.2 Hz, 1H), 7.15-7.12 (m, 1H), 6.90 (d, *J* = 9.2 Hz, 1H), 6.34 (s, 2H), 2.27 (s, 3H). MS (ESI): m/z 225 $[M+1]^+$.

6-Chloro-2-(pyridin-2-yl)-*N*-(2,4,4-trimethylpentan-2-yl)imidazo[1,2-*a*]pyridin-3-amine (E5). The title compound was synthesized according to method A to give 6-chloro-2-(pyridin-2-yl)-*N*-(2,4,4-trimethylpentan-2-yl)imidazo[1,2-*a*]pyridin-3-amine (1.20 g, 3.36 mmol, 86.44% yield) as a yellow solid. MS (ESI): m/z 357 $[M+1]^+$.

6-Chloro-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (F5). The title compound was synthesized according to method B to give 6-chloro-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (700 mg, 2.86 mmol, 92.82% yield) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.57-8.56 (m, 1H), 8.40 (s, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.84-7.82 (m, 1H), 7.45 (d, *J* = 9.6 Hz, 1H), 7.19-7.16 (m, 1H), 7.04-7.02 (m, 1H), 6.54 (s, 2H). MS (ESI): m/z 245 $[M+1]^+$.

***N*-(4-fluorophenyl)formamide (M1).** The title compound was synthesized according to method I to give *N*-(4-fluorophenyl)formamide (8.3 g) as a white solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 10.23 (s, 1H), 8.25 (s, 1H), 7.62-7.59 (m, 2H), 7.18-7.13 (m, 2H).

1-Fluoro-4-isocyanobenzene (N1). The title compound was synthesized according to method J to give 1-fluoro-4-isocyano-benzene (1.18 g, crude) as a black-brown solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 7.69-7.66 (m, 2H), 7.39-7.35 (m, 2H).

***N*-cyclopentylformamide (M2).** Ethyl formate (9.92 g, 133.89 mmol, 10.77 mL) was added to a solution of cyclopentanamine (9.5 g, 111.57 mmol, 11.01 mL) in EtOH (100 mL), the mixture was stirred at 90 °C for 9 h. The reaction mixture was concentrated under reduced pressure and ethyl acetate (50 mL) was added. The mixture was washed with 10% citric acid solution (50 mL), water (50 mL) and brine (50 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated under reduced pressure to give a residue. The residue was purified by silica gel chromatography (SiO_2, Dichloromethane/Methanol = 1/0 to 20/1) to give *N*-cyclopentylformamide (8.0g, 49.49 mmol, 44.36% yield, 70% purity) as light brown oil. ^{1}H NMR (400MHz, $CDCl_3$) δ 8.09 (s, 1H), 4.31-4.23 (m, 1H), 2.00-1.97 (m, 2H), 1.68-1.42 (m, 7H).

Isocyanocyclopentane (N2) To a mixture of *N*-cyclopentylformamide (5 g, 44.19 mmol) and NMM (10.28 g, 101.63 mmol, 11.17 mL) in anhydrous dichloromethane (30 mL), a solution of triphosgene (4.59 g, 15.47 mmol) in anhydrous dichloromethane (10 mL) was added dropwise under N_2 at -45 °C over 30 min. The mixture was stirred at 15 °C for 1 h. TLC showed the reaction was complete. The mixture was quenched with 2 M sodium carbonate solution at 0 °C. The organic layer was collected and dried over Na_2SO_4, filtered and concentrated under reduced pressure to give isocyanocyclopentane (11.0 g, crude) as red brown oil.

***N*-(3-fluorophenyl)formamide (M3).** The title compound was synthesized according to method I to give *N*-(3-fluorophenyl)formamide (1.34 g, 9.63 mmol, 21.40% yield) as a red solid. MS (ESI): m/z 140 $[M+1]^+$.

1-Fluoro-3-isocyanobenzene (N3) . The title compound was synthesized according to method J to give 1-fluoro-3-isocyanobenzene (1.1 g, 9.08 mmol, 97.20% yield) as black-brown oil.

Synthesis of Final Compounds

***N*-(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)-6-methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (6)** The title compound was synthesized from **F4** according to method C to give **6** *N*-

(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)-6-methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (128.0 mg, 342.86 µMol, 46.13% yield, 96% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.82-8.81 (m, 1H), 8.57 (s, 1H), 8.31 (s, 1H), 8.04-7.97 (m, 2H), 7.87 (s, 2H), 7.58-7.56 (m, 1H), 6.70 (d, *J* = 8.4 Hz, 1H), 6.34-6.33 (m, 1H), 6.28-6.25 (m, 1H), 4.18-4.14 (m, 4H), 2.43 (s, 3H). MS (ESI): m/z 359 $[M+1]^+$.

6-Chloro-*N*-(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (7). The title compound was synthesized from **F5** according to method C to give **7** 6-chloro-*N*-(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (130.0 mg, 326.02 µMol, 27.35% yield, 95% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.81-8.80 (m, 1H), 8.66-8.63 (m, 2H), 8.14-8.12 (m, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.93 (s, 2H), 7.64-7.61 (m, 1H), 6.70 (d, *J* = 8.4 Hz, 1H), 6.34-6.33 (m, 1H), 6.28-6.25 (m, 1H), 4.17-4.13 (m, 4H). MS (ESI): m/z 379 $[M+1]^+$.

2,2,2-Trifluoro-*N*-(2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-yl)acetamide J1. To a solution of 2-(2-pyridyl)imidazo[1,2-*a*]pyridin-3-amine (**F1**, 500 mg, 2.03 mmol, HCl salt) in DMF (10 mL), DIPEA (654.87 mg, 5.07 mmol, 882.58 µL) and (2,2,2-trifluoroacetyl)2,2,2-trifluoroacetate (425.69 mg, 2.03 mmol, 281.91 µL) were added drop-wise at 0 °C. The mixture was stirred at 20 °C for 1 h. LCMS showed the reaction was complete. The reaction mixture was diluted with water (10 mL) and extracted with ethyl acetate (20 mL*2). The combined organic phase was washed with brine (20 mL), dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give 2,2,2-trifluoro-*N*-(2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-yl)acetamide (120 mg, 391.85 µMol, 19.33% yield) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.60-8.59 (m, 1H), 8.26 (d, *J* = 6.8 Hz, 1H), 8.16 (d, *J* = 7.6 Hz, 1H), 7.93-7.92 (m, 1H), 7.70 (d, *J* = 8.8 Hz, 1H), 7.44-7.36 (m, 1H), 7.35-7.33 (m, 1H), 7.08 (t, *J* = 6.8 Hz, 1H). MS (ESI): m/z 307 $[M+1]^+$. **2-(Pyridin-2-yl)-*N*-(2,2,2-trifluoroethyl)imidazo[1,2-*a*]pyridin-3-amine (9)** To a solution of 2,2,2-trifluoro-*N*-[2-(2-pyridyl)imidazo[1,2-*a*]pyridin-3-yl]acetamide (**J1,** 30 mg, 97.96 µMol) in THF (5 mL), BH_3-Me_2S (10 M, 97.96 µL) was added at 25°C. The mixture was stirred at 60 °C for 12 h. LCMS showed the reaction completed. The reaction mixture was quenched by addition MeOH (2 mL) and water (2 mL) and extracted with ethyl acetate (5 mL*2). The combined organic phase was dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give a residue. The residue was purified by prep-HPLC (column: Phenomenex Synergi C18 150*25*10µm;mobile phase: [water (0.225%FA)-

ACN]; B%: 5%-35%,10min) to give **9** 2-(pyridin-2-yl)-*N*-(2,2,2-trifluoroethyl)imidazo[1,2-*a*]pyridin-3-amine (9.0 mg, 25.27 μMol, 25.80% yield, 95% purity, formic acid) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.65-8.64 (m, 1H), 8.50 (s, 1H), 8.25 (d, *J* = 6.8 Hz, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.92-7.90 (m, 1H), 7.55 (d, *J* = 9.2 Hz, 1H), 7.33-7.24 (m, 2H), 6.98-6.97 (m, 1H), 6.34-6.30 (m, 1H), 4.06-3.97 (m, 2H). MS (ESI): m/z 293 $[M+1]^+$.

2-(Dimethylamino)-*N*-(2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-yl)acetamide. The title compound was synthesized according to method D using 2-(2-pyridyl)imidazo[1,2-*a*]pyridin-3-amine (**F1**, 200 mg, 951.32 μMol), 2-(dimethylamino)acetic acid (127.53 mg, 1.24 mmol) and EDCI (547.11 mg, 2.85 mmol) in Py (2 mL) to give 2-(dimethylamino)-*N*-[2-(2-pyridyl)imidazo[1,2-*a*]pyridin-3-yl]acetamide (160 mg, crude) as a yellow solid. MS (ESI): m/z 296 $[M+1]^+$. ***N*^{1},*N*^{1}-dimethyl-*N*^{2}-(2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-yl)ethane-1,2-diamine (10).** The title compound was synthesized according to method E using 2-(dimethylamino)-*N*-[2-(2-pyridyl)imidazo[1,2-*a*]pyridin-3-yl]acetamide (**J2**, 150 mg, 507.89 μMol) and BH_3-Me_2S (10 M, 507.89 μL) in THF (20 mL) to give *N*^{1},*N*^{1}-dimethyl-*N*^{2}-(2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-yl)ethane-1,2-diamine (57.3 mg, 92% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.59-8.57 (m, 1H), 8.25-8.24 (m, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.87 (m, 1H), 7.50 (d, *J* = 9.2 Hz, 1H), 7.28-7.26 (m, 1H), 7.18 (m, 1H), 6.90-6.89 (m, 1H), 6.42 (s, 1H), 3.16-3.13 (m, 2H), 2.53 (m, 2H), 2.24 (s, 6H). MS (ESI): m/z 282 $[M+1]^+$.

2-Methyl-1-((2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-yl)amino)propan-2-ol (11). 2,2-dimethyloxirane (514.47 mg, 7.13 mmol, 633.58 μL) was added to a solution of 2-(2-pyridyl)imidazo[1,2-*a*]pyridin-3-amine (from **F1** 150 mg, 713.49 μMol) in EtOH (5 mL). The mixture was stirred at 90 °C for 12 h. The reaction mixture was concentrated under reduced pressure to give a residue. The residue was purified by prep-HPLC (column: Phenomenex Gemini 150*25mm*10um;mobile phase: [water (0.05% ammonia hydroxide v/v)-ACN];B%: 18%-48%,12min) to give **11** 2-methyl-1-((2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-yl)amino)propan-2-ol (15.0 mg, 52.60 μMol, 7.37% yield, 99% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.56-8.55 (m, 1H), 8.18 (d, *J* = 6.4 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.88-7.86 (m, 1H), 7.49-7.47 (m, 1H), 7.26-7.13 (m, 2H), 6.87 (t, *J* = 6.4 Hz, 1H), 6.58-6.56 (m, 1H), 4.68 (s, 1H), 2.99 (d, *J* = 6.8 Hz, 1H), 1.20 (s, 6H). MS (ESI): m/z 283 $[M+1]^+$.

N-(cyclopropylmethyl)-2-(pyridin-2-yl)imidazo[1,2-a]pyridin-3-amine (12). $Ti(i\text{-}PrO)_4$ (675.95 mg, 2.38 mmol) was added in one portion to a mixture of 2-(2-pyridyl)imidazo[1,2-a]pyridin-3-amine (200 mg, 951.32 μMol) and cyclopropanecarbaldehyde (80.01 mg, 1.14 mmol) in dioxane (2 mL). The mixture was stirred at 60 °C for 16 h. Then $NaBH_3CN$ (179.35 mg, 2.85 mmol) was added and the mixture was stirred for another 2 hours. Water (50 mL) and EtOAc (20 mL) were added and the mixture was stirred for 1 h and filtered. The filter cake was added to NaHCO3 (20 mL) and EtOAc (50 mL) and stirred for 1 h. The mixture was filtered and the two part filtrates were combined. The two phases were separated and the water phase was extracted with EtOAc (20 mL x 2). The combined organic phases were washed with brine (30 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure to give a residue. The residue was purified by prep-HPLC (column: Gemini 150*25 5u; mobile phase: [water (0.05% ammonia hydroxide v/v)-ACN];B%: 35%-65%,12min) to give N-(cyclopropylmethyl)-2-(2-pyridyl)imidazo[1,2-a]pyridin-3-amine (46.6 mg, 174.54 μMol, 18.35% yield, 99% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.60 (d, *J* = 4.0 Hz, 1H), 8.21 (dd, *J* = 1.2, 8.0 Hz, 1H), 8.06 (dd, *J* = 1.2, 7.2 Hz, 1H), 7.86 (t, *J* = 2.0 Hz, 1H), 7.49 (d, *J* = 9.2 Hz, 1H), 7.27-7.26 (m, 1H), 7.17-7.16 (m, 1H), 6.88 (t, *J* = 5.6 Hz, 1H), 6.40 (t, *J* = 7.2 Hz, 1H), 2.97 (t, *J* = 7.2 Hz, 2H), 1.00-0.96 (m, 1H), 0.38-0.36 (m, 2H), 0.14-0.11 (m, 2H). MS (ESI): m/z 265 $[M+1]^+$.

***N*-(oxetan-2-ylmethyl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (13).** The title compound was synthesized from **C1** according to method H to give **13** *N*-(oxetan-2-ylmethyl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (13 mg, 44.06 μMol, 12.08% yield, 95% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.79 (s, 1H), 8.53 (s, 1H), 8.45-8.33 (m, 2H), 7.85 (t, *J* = 6.0 Hz, 1H), 7.42 (d, *J* = 9.6 Hz, 1H), 7.19-7.15 (m, 1H), 6.89-6.86 (m, 1H), 4.58-4.28 (m, 2H), 3.60 (s, 2H), 3.51 (s, 1H), 3.01 (s, 1H), 2.11 (s, 1H). MS (ESI): m/z 281 $[M+1]^+$.

2-(Pyridin-2-yl)-*N*-(tetrahydrofuran-3-yl)imidazo[1,2-*a*]pyridin-3-amine (14). The title compound was synthesized from **C1** according to method H to give **14** 2-(pyridin-2-yl)-*N*-(tetrahydrofuran-3-yl)imidazo[1,2-*a*]pyridin-3-amine (16.4 mg, 57.33 μMol, 15.72% yield, 98% purity) as yellow oil. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.58 (d, *J* = 4.0 Hz, 1H), 8.27 (d, *J* = 6.8 Hz, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.88-7.87 (m, 1H), 7.52 (d, *J* = 9.2 Hz, 1H), 7.29-7.27 (m, 1H), 7.22-7.20 (m, 1H), 6.92-6.90 (m, 1H), 6.31 (d, *J* = 10.4 Hz, 1H), 4.16-4.13 (m, 1H), 3.89-

3.87 (m, 1H), 3.73-3.66 (m, 3H), 1.95-1.90 (m, 1H), 1.75-1.72 (m, 1H). MS (ESI): m/z 281 $[M+1]^+$.

***Tert*-butyl 3-((2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-yl)amino)pyrrolidine-1-carboxylate** The title compound was synthesized from **C1** according to method H to give *tert*-butyl 3-((2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-yl)amino)pyrrolidine-1-carboxylate (20.0 mg, 52.71 µMol, 16.05% yield) as a yellow solid. MS (ESI): m/z 380 $[M+1]^+$. **2-(Pyridin-2-yl)-*N*-(pyrrolidin-3-yl)imidazo[1,2-*a*]pyridin-3-amine (15)** HCl/MeOH (4 M, 5 mL) was added to a solution of *tert*-butyl 3-[[2-(2-pyridyl)imidazo[1,2-*a*]pyridin-3-yl]amino]pyrrolidine-1-carboxylate (20.0 mg, 52.71 µMol) in MeOH (1 mL). The mixture was stirred at 20 °C for 1 h. TLC showed the reaction was complete. The reaction mixture was concentrated under reduced pressure to give **15** 2-(pyridin-2-yl)-*N*-(pyrrolidin-3-yl)imidazo[1,2-*a*]pyridin-3-amine (12.93 mg, 40.12 µMol, 76.13% yield, 98% purity, HCl salt) as yellow oil. ^{1}H NMR (400MHz, DMSO-d_6) δ 9.76-9.51 (m, 2H), 9.04 (d, *J* = 6.8 Hz, 1H), 8.82 (d, *J* = 4.4 Hz, 1H), 8.40-8.38 (m, 1H), 8.11 (m, 1H), 7.95-7.92 (m, 2H), 7.58-7.51 (m, 2H), 4.11-4.09 (m, 1H), 3.88-3.68 (m, 1H), 3.50-3.38 (m, 2H), 3.31-3.28 (m, 1H), 2.02-2.01 (m, 1H), 1.92 (s, 1H). MS (ESI): m/z 280 $[M+1]^+$.

4-(2-(Pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-yl)morpholine (16). The title compound was synthesized from **C1** according to method H to give **16** 4-(2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-yl)morpholine (12.0 mg, 42.38 µMol, 7.74% yield, 99% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.73 (d, *J* = 4.0 Hz, 1H), 8.43 (d, *J* = 6.8 Hz, 1H), 8.16 (d, *J* = 7.6 Hz, 1H), 7.89-7.88 (m, 1H), 7.55 (d, *J* = 8.8 Hz, 1H), 7.35-7.30 (m, 2H), 7.00-6.98 (m, 1H), 3.81 (s, 4H), 3.35 (s, 4H). MS (ESI): m/z 281 $[M+1]^+$.

***N*-(4-fluorophenyl)-6-methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (19).** The title compound was synthesized from **F4** according to method C to give **19** *N*-(4-fluorophenyl)-6-methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (32.0 mg, 99.51 µMol, 22.32% yield, 99% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.54-8.53 (m, 1H), 8.23 (s, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.85-7.84 (m, 1H), 7.67 (s, 1H), 7.56 (d, *J* = 9.6 Hz, 1H), 7.26-7.25 (m, 1H), 7.19-7.17 (m, 1H), 6.99-6.94 (m, 2H), 6.51-6.48 (m, 2H), 2.27 (s, 3H). MS (ESI): m/z 319 $[M+1]^+$.

***N*-(4-fluorophenyl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine.** The title compound was synthesized from **N1** according to method A to give *N*-(4-fluorophenyl)-2-(pyridin-2-

yl)imidazo[1,2-*a*]pyridin-3-amine (340 mg, crude) as a yellow solid. MS (ESI): m/z 305 $[M+1]^+$.

***N*-(4-fluorophenyl)-*N*-methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (20).** Iodomethane (83.95 mg, 591.48 μMol, 36.82 μL) was added to a mixture of *N*-(4-fluorophenyl)-2-(2-pyridyl)imidazo[1,2-*a*]pyridin-3-amine (150 mg, 492.90 μMol) and Cs_2CO_3 (192.72 mg, 591.48 μMol) in DMF (10 mL). The mixture was stirred at 15 °C for 1 h. LCMS showed the reaction was complete. The reaction mixture was diluted with water (20 mL) and extracted with dichloromethane (20 mL*2). The combined organic phase was washed with brine (20 mL*2), dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give a residue. The residue was purified by prep-HPLC (column: Phenomenex Synergi C18 150*30mm*4um;mobile phase: [water(0.225%FA)-ACN];B%: 13%-43%,10.5min) to give **20** *N*-(4-fluorophenyl)-*N*-methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (40.8 mg, 126.88 μMol, 25.74% yield, 99% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.48 (d, *J* = 4.0 Hz, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.99 (d, *J* = 6.8 Hz, 1H), 7.83 (m, 1H), 7.67 (d, *J* = 9.2 Hz, 1H), 7.37-7.36 (m, 1H), 7.24 (m, 1H), 6.98-6.94 (m, 3H), 6.46-6.42 (m, 2H), 3.37 (s, 3H). MS (ESI): m/z 319 $[M+1]^+$.

***N*-(3-fluorophenyl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (21)** title compound was synthesized according to method C using **F1** 2-(2-pyridyl)imidazo[1,2-*a*]pyridin-3-amine (120 mg, 570.79 μMol), 1-bromo-3-fluoro-benzene (119.87 mg, 684.95 μMol, 76.35 μL), xantphos (66.05 mg, 114.16 μMol), $Pd_2(dba)_3$ (52.27 mg, 57.08 μMol) and t-BuONa (109.71 mg, 1.14 mmol) in toluene (10 mL) to yield **21** *N*-(3-fluorophenyl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (72.3 mg, 235.20 μMol, 41.21% yield, 99% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.57-8.56 (m, 2H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.91-7.89 (m, 1H), 7.86-7.85 (m, 1H), 7.66 (d, *J* = 8.8 Hz, 1H), 7.34-7.27 (m, 2H), 7.13-7.11 (m, 1H), 6.97-6.96 (m, 1H), 6.51-6.50 (m, 1H), 6.31-6.27 (m, 2H). MS (ESI): m/z 305 $[M+1]^+$.

***N*-(2-fluorophenyl)-7-methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (22).** The title compound was synthesized from **F2b** according to method C to give **22** *N*-(2-fluorophenyl)-7-methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (80.16 mg, 234.96 μMol, 32.51% yield, 98% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.51-8.50 (m, 1H), 8.07-8.03 (m, 2H), 7.84-7.82 (m, 2H), 7.24-7.23 (m, 2H), 7.04 (m, 1H), 6.86 (m, 1H), 6.68-6.66 (m, 2H), 6.16-6.12 (m, 1H), 3.88 (s, 3H). MS (ESI): m/z 335 $[M+1]^+$.

***N*-(3,5-difluorophenyl)-7-methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (23)** The title compound was synthesized from **F2b** according to method C to give **23** *N*-(3,5-difluorophenyl)-7-methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (130.5 mg, 314.49 µMol, 43.51% yield, 96% purity, formic acid) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.70 (s, 1H), 8.54-8.53 (m, 1H), 8.17 (s, 1H), 8.08 (d, *J* = 7.6 Hz, 1H), 7.87-7.83 (m, 2H), 7.27-7.25 (m, 1H), 7.05-7.04 (m, 1H), 6.70-6.67 (m, 1H), 6.45 (m, 1H), 6.14-6.11 (m, 2H), 3.88 (s, 3H). MS (ESI): m/z 353 $[M+1]^+$.

***N*-(2,5-dichlorophenyl)-7-methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (24).** The title compound was synthesized from **F2b** according to method C to give **24** *N*-(2,5-dichlorophenyl)-7-methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (155.5 mg, 353.35 µMol, 98% purity, formic acid) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.48-8.47 (m, 1H), 8.18 (s, 1H), 8.14 (s, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.88-7.84 (m, 2H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.26 (m, 1H), 7.07-7.06 (m, 1H), 6.82-6.79 (m, 1H), 6.71-6.69 (m, 1H), 6.06-6.05 (m, 1H), 3.89 (s, 3H). MS (ESI): m/z 385 $[M+1]^+$.

***N*-(5-fluoropyridin-2-yl)-7-methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (25).** The title compound was synthesized from **F2b** according to method C to give **25** *N*-(5-fluoropyridin-2-yl)-7-methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (156.6 mg, 398.32 µMol, 55.11% yield, 97% purity, formic acid) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.90 (s, 1H), 8.54-8.53 (m, 1H), 8.15 (s, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.93-7.92 (m, 1H), 7.84-7.83 (m, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.54 (m, 1H), 7.25-7.24 (m, 1H), 7.00-6.99 (m, 1H), 6.88-6.87 (m, 1H), 6.62-6.60 (m, 1H), 3.87 (s, 3H). MS (ESI): m/z 336 $[M+1]^+$.

7-Methyl-*N*,2-di(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (26). The title compound was synthesized from **F3** according to method C to give **26** 7-methyl-*N*,2-di(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (25.9 mg, 81.65 µMol, 26.16% yield, 95% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.76-8.74 (m, 1H), 8.47 (d, *J* = 6.8 Hz, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 8.03-8.02 (m, 2H), 7.98-7.97 (m, 1H), 7.78 (s, 1H), 7.54 (m, 1H), 7.38-7.36 (m, 1H), 7.36-7.30 (m, 1H), 7.00-6.99 (m, 1H), 2.58 (s, 3H). MS (ESI): m/z 302 $[M+1]^+$.

2-(Pyridin-2-yl)-N-(4-(trifluoromethoxy)phenyl)imidazo[1,2-a]pyridin-3-amine (27). The title compound was synthesized according to method C to give **27** 2-(pyridin-2-yl)-N-(4-

(trifluoromethoxy)phenyl)imidazo[1,2-a]pyridin-3-amine (89 mg, 235.52 µMol, 41.26% yield, 98% purity) as a white solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.55 (d, *J* = 4.0 Hz, 1H), 8.52 (s, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.93-7.86 (m, 2H), 7.66 (d, *J* = 9.2 Hz, 1H), 7.34-7.32 (m, 1H), 7.29-7.27 (m, 1H), 7.12 (d, *J* = 8.4 Hz, 2H), 6.97-6.96 (m, 1H), 6.56 (d, *J* = 8.8 Hz, 2H). MS (ESI): m/z 371 $[M+1]^+$.

4-((2-(Pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-yl)amino)benzonitrile (28) The title compound was synthesized from **F1** according to method C to give **28** 4-((2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-yl)amino)benzonitrile (94.0 mg, 298.90 µMol, 52.37% yield, 99% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 9.06 (s, 1H), 8.52 (d, *J* = 4.0 Hz, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.95 (d, *J* = 6.8 Hz, 1H), 7.86-7.85 (m, 1H), 7.68 (d, *J* = 9.2 Hz, 1H), 7.53-7.51 (m, 2H), 7.36 (m, 1H), 7.26 (m, 1H), 6.99-6.97 (m, 1H), 6.58 (d, *J* = 8.4 Hz, 2H). MS (ESI): m/z 312 $[M+1]^+$.

***N*-(4-methoxyphenyl)-6-methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (29).** The title compound was synthesized from **F4** according to method C to give **29** *N*-(4-methoxyphenyl)-6-methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (24.5 mg, 64.44 µMol, 18.06% yield, 99% purity, formic acid) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.56-8.55 (m, 1H), 8.30 (s, 1H), 8.07 (d, *J* = 7.6 Hz, 2H), 7.86-7.83 (m, 1H), 7.59-7.54 (m, 2H), 7.27-7.24 (m, 1H), 7.17-7.15 (m, 1H), 6.78-6.74 (m, 2H), 6.49 (d, *J* = 8.8 Hz, 2H), 3.64 (s, 3H), 2.26 (s, 3H). MS (ESI): m/z 331 $[M+1]^+$.

***N*-(3-methoxyphenyl)-6-methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (30).** The title compound was synthesized from **F4** according to method C to give **30** *N*-(3-methoxyphenyl)-6-methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (42.6 mg, 112.04 µMol, 31.41% yield, 99% purity, formic acid) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.57-8.56 (m, 1H), 8.27-8.26 (m, 2H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.85-7.84 (m, 1H), 7.67 (s, 1H), 7.57 (d, *J* = 9.2 Hz, 1H), 7.26 (m, 1H), 7.20-7.18 (m, 1H), 7.04-7.00 (m, 1H), 6.34-6.32 (m, 1H), 6.12-6.11 (m, 1H), 6.04-6.02 (m, 1H), 3.63 (s, 3H), 2.28 (s, 3H). MS (ESI): m/z 331 $[M+1]^+$.

***N*-(2-methoxyphenyl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (31)** The title compound was synthesized from **F1** according to method C to give **31** *N*-(2-methoxyphenyl)-

2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (83.1 mg, 260.05 µMol, 45.56% yield, 99% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.56 (d, *J* = 4.8 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 8.00 (s, 1H), 7.86 (m, 1H), 7.78-7.77 (m, 1H), 7.65 (d, *J* = 9.2 Hz, 1H), 7.31-7.26 (m, 2H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.94 (m, 1H), 6.78 (m, 1H), 6.66 (m, 1H), 5.89-5.87 (m, 1H), 3.96 (s, 3H). MS (ESI): m/z 317 $[M+1]^+$.

***N*-cyclopentyl-2-(5-methoxypyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (32).** The title compound was synthesized from **N2** according to method A to give *N*-cyclopentyl-2-(5-methoxy-2-pyridyl)imidazo[1,2-*a*]pyridin-3-amine (44.1 mg, 138.72 µMol, 16.50% yield, 97% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.31 (m, 1H), 8.20-8.16 (m, 1H), 8.03 (d, *J* = 8.8 Hz, 1H), 7.52-7.46 (m, 2H), 7.17-7.13 (m, 1H), 6.88-6.85 (m, 1H), 5.98 (d, *J* = 10.0 Hz, 1H), 3.87-3.83 (m, 4H), 1.68-1.67 (m, 4H), 1.53-1.46 (m, 4H). MS (ESI): m/z 309 $[M+1]^+$.

***N*-cyclopentyl-2-(4-methoxypyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (33).** The title compound was synthesized from **N2** according to method A to give **33** *N*-cyclopentyl-2-(4-methoxy-2-pyridyl)imidazo[1,2-*a*]pyridin-3-amine (83.1 mg, 269.48 µMol, 32.05% yield, 100% purity) as a light yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.39 (d, *J* = 6.0 Hz, 1H), 8.21 (d, *J* = 6.8 Hz, 1H), 7.60 (m, 1H), 7.50 (d, *J* = 9.2 Hz, 1H), 7.17 (m, 1H), 6.89-6.82 (m, 2H), 6.40 (d, *J* = 10.4 Hz, 1H), 3.95-3.91(m, 4H), 1.73-1.68 (m, 4H), 1.51-1.46 (m, 4H). MS (ESI): m/z 309 $[M+1]^+$.

***N*-cyclopentyl-2-(pyridin-3-yl)imidazo[1,2-*a*]pyridin-3-amine (34).** The title compound was synthesized from **N2** according to method A to give **34** *N*-cyclopentyl-2-(3-pyridyl)imidazo[1,2-*a*]pyridin-3-amine (48.7 mg, 166.21 µMol, 17.57% yield, 95% purity) as a white solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 9.37 (s, 1H), 8.50-8.47 (m, 2H), 8.32 (d, *J* = 6.8 Hz, 1H), 7.51 (d, *J* = 9.2 Hz, 1H), 7.47-7.44 (m, 1H), 7.24-7.20 (m, 1H), 6.94-6.91 (m, 1H), 4.89 (d, *J* = 4.8 Hz, 1H), 3.56-3.51 (m, 1H), 1.72-1.58 (m, 4H), 1.45-1.43 (m, 4H). MS (ESI): m/z 279 $[M+1]^+$.

***N*-cyclopentyl-2-(2-methylpyridin-4-yl)imidazo[1,2-*a*]pyridin-3-amine (35).** The title compound was synthesized from **N2** according to method A to give **35** *N*-cyclopentyl-2-(2-methyl-4-pyridyl)imidazo[1,2-*a*]pyridin-3-amine (21.15 mg, 61.87 µMol, 5.82% yield, 99% purity, formic acid) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.46 (d, *J* = 4.8 Hz, 1H), 8.32 (d, *J* = 6.8 Hz, 1H), 8.16 (s, 1H), 8.02 (s, 1H), 7.94 (d, *J* = 4.8 Hz, 1H), 7.50 (d, *J* = 9.2 Hz,

1H), 7.25-7.21 (m, 1H), 6.95-6.91 (m, 1H), 4.94 (d, *J* = 5.2 Hz, 1H), 3.55-3.53 (m, 1H), 2.50 (s, 3H), 1.72-1.63 (m, 4H), 1.62-1.47 (m, 4H). MS (ESI): m/z 293 $[M+1]^+$.

***N*-cyclopentyl-2-(4-(dimethylamino)phenyl)-7-methylimidazo[1,2-*a*]pyridin-3-amine (37).** The title compound was synthesized from **N2** according to method A to give **37** *N*-cyclopentyl-2-(4-(dimethylamino)phenyl)-7-methylimidazo[1,2-*a*]pyridin-3-amine (179.9 mg, 527.13 µMol, 25.08% yield, 98% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.13 (d, *J* = 6.8 Hz, 1H), 8.02 (d, *J* = 9.2 Hz, 2H), 7.18 (s, 1H), 6.76 (d, *J* = 8.8 Hz, 2H), 6.70-6.67 (m, 1H), 4.53 (d, *J* = 4.4 Hz, 1H), 3.56-3.50 (m, 1H), 2.93 (s, 6H), 2.33 (s, 3H), 1.73-1.57 (m, 2H), 1.56-1.45 (m, 6H). MS (ESI): m/z 335 $[M+1]^+$.

***N*-cyclopentyl-2-(2-fluorophenyl)imidazo[1,2-*a*]pyridin-3-amine (40).** The title compound was synthesized from **N2** according to method A to give **40** *N*-cyclopentyl-2-(2-fluorophenyl)imidazo[1,2-*a*]pyridin-3-amine (82.86 mg, 274.93 µMol, 25.88% yield, 98% purity) as a yellow oil. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.27 (d, *J* = 6.4 Hz, 1H), 7.77 (m, 1H), 7.50-7.48 (m, 1H), 7.41-7.32 (m, 1H), 7.30-7.27 (m, 2H), 7.22-7.20 (m, 1H), 6.93-6.90 (m, 1H), 4.33 (d, *J* = 2.4 Hz, 1H), 3.42-3.35 (m, 1H), 1.55-1.54 (m, 2H), 1.47-1.46 (m, 2H), 1.36-1.35 (m, 2H), 1.29-1.27 (m, 2H). MS (ESI): m/z 296 $[M+1]^+$.

***N*-cyclopentyl-2-(2-fluoro-4-methoxyphenyl)imidazo[1,2-*a*]pyridin-3-amine (41).** The title compound was synthesized from **N2** according to method A to give **41** *N*-cyclopentyl-2-(2-fluoro-4-methoxy-phenyl)imidazo[1,2-*a*]pyridin-3-amine (71.73 mg, 191.20 µMol, 18.04% yield, 99% purity, formic acid) as a yellow oil. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.25 (d, *J* = 7.2 Hz, 1H), 8.14 (s, 1H), 7.68 (t, *J* = 8.8 Hz, 1H), 7.46 (d, *J* = 9.2 Hz, 1H), 7.20-7.18 (m, 1H), 6.94-6.87 (m, 3H), 4.26 (s, 1H), 3.82 (s, 3H), 3.36 (s, 1H), 1.58-1.57 (m, 2H), 1.48-1.45 (m, 2H), 1.40-1.38 (m, 2H), 1.31-1.28 (m, 2H). MS (ESI): m/z 326$[M+1]^+$.

***N*-cyclopentyl-2-(thiazol-2-yl)imidazo[1,2-*a*]pyridin-3-amine (42).** The title compound was synthesized from **N2** according to method A to give **42** *N*-cyclopentyl-2-thiazol-2-yl-imidazo[1,2-*a*]pyridin-3-amine (25.3 mg, 85.41 µMol, 9.03% yield, 96% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.27 (d, *J* = 6.8 Hz, 1H), 7.90 (d, *J* = 3.2 Hz, 1H), 7.66 (d, *J* = 3.2 Hz, 1H), 7.50 (d, *J* = 9.2 Hz, 1H), 7.23-7.19 (m, 1H), 6.93-6.91 (m, 1H), 5.39 (d, *J* = 9.2 Hz, 1H), 4.06-4.02 (m, 1H), 1.71-1.70 (m, 4H), 1.53-1.47 (m, 4H). MS (ESI): m/z 285 $[M+1]^+$.

***N*-cyclopentyl-2-(1-methyl-1*H*-imidazol-2-yl)imidazo[1,2-*a*]pyridin-3-amine (43).** The title compound was synthesized from **N2** according to method A to give **43** *N*-cyclopentyl-2-(1-methyl-1*H*-imidazol-2-yl)imidazo[1,2-*a*]pyridin-3-amine (62.2 mg, 214.44 µMol, 22.67% yield, 97% purity) as an off-white solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.67 (t, *J* = 6.4 Hz, 1H), 7.94 (s, 1H), 7.87 (s, 1H), 7.73 (d, *J* = 9.2 Hz, 1H), 7.61-7.56 (m, 1H), 7.25-7.21 (m, 1H), 4.02 (s, 3H), 3.47-3.42 (m, 1H), 1.61-1.50 (m, 4H), 1.48-1.40 (m, 4H). MS (ESI): m/z 282 $[M+1]^+$.

***N*-(4-fluorophenyl)-2-(5-methoxypyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (47)** The title compound was synthesized from **N1** according to method A to give **47** *N*-(4-fluorophenyl)-2-(5-methoxy-2-pyridyl)imidazo[1,2-*a*]pyridin-3-amine (129.9 mg, 384.63 µMol, 44.37% yield, 99% purity) as a white solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.27 (d, *J* = 2.8 Hz, 1H), 8.17 (s, 1H), 8.05 (d, *J* = 8.8 Hz, 1H), 7.84 (d, *J* = 6.8 Hz, 1H), 7.61 (d, *J* = 9.2 Hz, 1H), 7.48-7.47 (m, 1H), 7.29 (m, 1H), 6.98-6.92 (m, 3H), 6.50-6.46 (m, 2H), 3.84 (s, 3H). MS (ESI): m/z 335 $[M+1]^+$.

***N*-(4-fluorophenyl)-2-(4-methoxypyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (48).** The title compound was synthesized from **N1** according to method A to give **48** *N*-(4-fluorophenyl)-2-(4-methoxy-2-pyridyl)imidazo[1,2-*a*]pyridin-3-amine (78.0 mg, 196.86 µMol, 22.71% yield, 96% purity, formic acid) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.40-8.36 (m, 2H), 8.14 (s, 1H), 7.84 (d, *J* = 6.8 Hz, 1H), 7.68-7.66 (m, 2H), 7.35-7.33 (m, 1H), 7.01-6.96 (m, 3H), 6.89-6.87 (m, 1H), 6.54-6.51 (m, 2H), 3.89 (s, 3H). MS (ESI): m/z 335 $[M+1]^+$.

2-(5-Chloropyridin-2-yl)-*N*-(4-fluorophenyl)imidazo[1,2-*a*]pyridin-3-amine (49). The title compound was synthesized from **N1** according to method A to give **49** 2-(5-chloro-2-pyridyl)-*N*-(4-fluorophenyl)imidazo[1,2-*a*]pyridin-3-amine (27.4 mg, 80.07 µMol, 9.24% yield, 99% purity) as a white solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.58 (d, *J* = 2.4 Hz, 1H), 8.26 (s, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 8.00-7.97 (m, 1H), 7.88 (d, *J* = 7.2 Hz, 1H), 7.66-7.64 (m, 1H), 7.34 (m, 1H), 7.00-6.95 (m, 3H), 6.52-6.49 (m, 2H). MS (ESI): m/z 339 $[M+1]^+$.

***N*-(4-fluorophenyl)-2-(1-methyl-1*H*-imidazol-2-yl)imidazo[1,2-*a*]pyridin-3-amine (50).** The title compound was synthesized from **N1** according to method A to give **50** *N*-(4-fluorophenyl)-2-(1-methylimidazol-2-yl)imidazo[1,2-*a*]pyridin-3-amine (20.5 mg, 56.28 µMol, 6.49% yield, 97% purity, formic acid) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.17-8.16 (m, 2H), 7.82 (d, *J* = 6.8 Hz, 1H), 7.66-7.64 (m, 1H), 7.34-7.32 (m, 1H), 7.22 (s, 1H), 6.98-6.94 (m, 4H), 6.50-6.46 (m, 2H), 4.03 (s, 3H). MS (ESI): m/z 308 $[M+1]^+$.

***N*-(3-fluorophenyl)-7-methoxy-2-(1-methyl-1*H*-imidazol-4-yl)imidazo[1,2-*a*]pyridin-3-amine (51).** The title compound was synthesized according to method A to give **51** *N*-(3-fluorophenyl)-7-methoxy-2-(1-methyl-1*H*-imidazol-4-yl)imidazo[1,2-*a*]pyridin-3-amine (32.87 mg, 96.46 μMol, 3.99% yield, 99% purity) as yellow oil. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.43 (s, 1H), 8.00 (d, *J* = 6.8 Hz, 1H), 7.90 (s, 1H), 7.43 (s, 1H), 7.17-7.13 (m, 1H), 7.01 (m, 1H), 6.89-6.87 (m, 1H), 6.55-6.54 (m, 1H), 6.43-6.37 (m, 2H), 3.93 (s, 3H), 3.70 (s, 3H). MS (ESI): m/z 338 $[M+1]^+$.

***N*-(3-fluorophenyl)-7-methoxy-2-(thiazol-4-yl)imidazo[1,2-*a*]pyridin-3-amine (52).** The title compound was synthesized according to method A to give **52** *N*-(3-fluorophenyl)-7-methoxy-2-(thiazol-4-yl)imidazo[1,2-*a*]pyridin-3-amine (53.01 mg, 135.82 μMol, 33.72% yield, 99% purity, formic acid) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 9.27-8.96 (m, 1H), 8.33 (s, 1H), 7.90 (s, 2H), 7.12-7.00 (m, 2H), 6.66-6.65 (m, 1H), 6.47 (t, *J* = 8.4 Hz, 1H), 6.26-6.22 (m, 2H), 3.86 (s, 3H). MS (ESI): m/z 341 $[M+1]^+$.

***N*-(3-fluorophenyl)-7-methoxy-2-(1-methyl-1*H*-pyrazol-3-yl)imidazo[1,2-*a*]pyridin-3-amine (53).** The title compound was synthesized according to method A to give *N*-(3-fluorophenyl)-7-methoxy-2-(1-methyl-1*H*-pyrazol-3-yl)imidazo[1,2-*a*]pyridin-3-amine (68.34 mg, 198.53 μMol, 8.22% yield, 98% purity) as a white solid. ^{1}H NMR (400MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.90 (d, *J* = 7.2 Hz, 1H), 7.39-7.38 (m, 1H), 7.26-7.21 (m, 1H), 7.13-7.12 (m, 1H), 6.70-6.68 (m, 1H), 6.62-6.61 (m, 2H), 6.46 (m, 1H), 6.36-6.33 (m, 1H), 3.89 (s, 3H), 3.83 (s, 3H). MS (ESI): m/z 338 $[M+1]^+$.

6-Bromo-*N*-(4-fluorophenyl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine. The title compound was synthesized according to method A to give 6-bromo-*N*-(4-fluorophenyl)-2-(2-pyridyl)imidazo[1,2-*a*]pyridin-3-amine (400 mg) as a yellow solid. MS (ESI): m/z 383 $[M+1]^+$.

3-((4-Fluorophenyl)amino)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridine-6-carbonitrile (54). To a solution of 6-bromo-*N*-(4-fluorophenyl)-2-(2-pyridyl)imidazo[1,2-*a*]pyridin-3-amine (300 mg, 782.85 μMol) in DMA (5 mL), $Pd_2(dba)_3$ (71.69 mg, 78.28 μMol), DPPF (43.40 mg, 78.28 μMol), Zn (10.24 mg, 156.57 μMol) and dicyanozinc (91.93 mg, 782.85 μMol, 49.69 μL) were added. The mixture was stirred at 120 °C for 4 h. LCMS showed the reaction was complete. The reaction mixture was diluted with water (20 mL) and extracted with ethyl acetate (20 mL*2). The combined organic phase was washed with brine (20 mL*2), dried with anhydrous Na_2SO_4,

filtered and concentrated under reduced pressure to give a residue. The residue was purified by prep-HPLC(column: Phenomenex Synergi C18 150*30mm*4um;mobile phase:[water(0.225%FA)-ACN];B%: 30%-60%,10.5min) to give **54** 3-(4-fluoroanilino)-2-(2-pyridyl)imidazo[1,2-*a*]pyridine-6-carbonitrile (6.3 mg, 98% purity, formic acid) as a white solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.71 (s, 1H), 8.57 (d, *J* = 4.8 Hz, 1H), 8.46 (s, 1H), 8.36 (s, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.88-7.87 (m, 1H), 7.80 (d, *J* = 9.2 Hz, 1H), 7.56-7.54 (m, 1H), 7.32-7.31 (m, 1H), 6.97 (t, *J* = 8.8 Hz, 2H), 6.58-6.55 (m, 2H). MS (ESI): m/z 330 $[M+1]^+$.

***N*-(4-fluorophenyl)-2-(pyridin-2-yl)-6-(trifluoromethyl)imidazo[1,2-*a*]pyridin-3-amine (55).** The title compound was synthesized according to method A to give **55** *N*-(4-fluorophenyl)-2-(2-pyridyl)-6-(trifluoromethyl)imidazo[1,2-*a*]pyridin-3-amine (38.3 mg, 101.84 μMol, 11.75% yield, 99% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 9.10 (s, 1H), 8.80 (s, 1H), 8.75 (d, *J* = 4.4 Hz, 1H), 8.17-8.16 (m, 1H), 8.07-8.00 (m, 2H), 7.92-7.90 (m, 1H), 7.61 (m, 1H), 7.00 (t, *J* = 8.8 Hz, 2H), 6.77-6.74 (m, 2H). MS (ESI): m/z 373 $[M+1]^+$.

***N*-(4-fluorophenyl)-6-methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (56).** The title compound was synthesized according to method A to give **56** *N*-(4-fluorophenyl)-6-methoxy-2-(2-pyridyl)imidazo[1,2-*a*]pyridin-3-amine (74.5 mg, 220.59 μMol, 25.44% yield, 99% purity) as a white solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.54 (d, *J* = 4.0 Hz, 1H), 8.30 (s, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.84 (m, 1H), 7.60 (d, *J* = 9.6 Hz, 1H), 7.31 (s, 1H), 7.30-7.25 (m, 1H), 7.13-7.11 (m, 1H), 7.01-6.96 (m, 1H), 6.56-6.52 (m, 2H), 3.70 (s, 3H). MS (ESI): m/z 335 $[M+1]^+$.

6-Chloro-*N*-(4-fluorophenyl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (57). The title compound was synthesized from **F5** according to method C to give **57** 6-chloro-*N*-(4-fluorophenyl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (32.0 mg, 93.52 μMol, 22.88% yield, 99% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.56 (d, *J* = 4.4 Hz, 1H), 8.34 (s, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 7.99 (s, 1H), 7.87 (m, 1H), 7.72 (d, *J* = 9.6 Hz, 1H), 7.38-7.35 (m, 1H), 7.28 (m, 1H), 7.01-6.96 (m, 2H), 6.57-6.53 (m, 2H). MS (ESI): m/z 339 $[M+1]^+$.

7-Bromo-*N*-(4-fluorophenyl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine. The title compound was synthesized according to method A was followed to give 7-bromo-*N*-(4-fluorophenyl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (400 mg, 1.04 mmol, 60.20% yield) as a yellow solid. MS (ESI): m/z 383 $[M+1]^+$. **3-((4-Fluorophenyl)amino)-2-(pyridin-2-**

yl)imidazo[1,2-*a*]pyridine-7-carbonitrile (58). The title compound was synthesized according to method of preparation of **54** to give **58** 3-(4-fluoroanilino)-2-(2-pyridyl)imidazo[1,2-*a*]pyridine-7-carbonitrile (17.0 mg, 96% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.66 (s, 2H), 8.46 (s, 1H), 8.19-8.17 (m, 1H), 8.04-8.02 (m, 2H), 7.47 (s, 1H), 7.28-7.26 (m, 1H), 7.01 (t, *J* = 8.8 Hz, 2H), 6.64-6.61 (m, 2H). MS (ESI): m/z 330 $[M+1]^+$.

***N*-(4-fluorophenyl)-2-(pyridin-2-yl)-7-(trifluoromethyl)imidazo[1,2-*a*]pyridin-3-amine (59).** The title compound was synthesized according to method A to give **59** *N*-(4-fluorophenyl)-2-(2-pyridyl)-7-(trifluoromethyl)imidazo[1,2-*a*]pyridin-3-amine (76.0 mg, 200.04 µMol, 23.07 % yield, 98% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.93 (s, 1H), 8.74 (d, *J* = 4.8 Hz, 1H), 8.28-8.15 (m, 4H), 7.60 (m, 1H), 7.39-7.37 (m, 1H), 7.05-7.00 (m, 2H), 6.72-6.68 (m, 2H). MS (ESI): m/z 373 $[M+1]^+$.

***N*-(4-fluorophenyl)-7-methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (60).** The title compound was synthesized according to method A to give **60** *N*-(4-fluorophenyl)-7-methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (62.5 mg, 159.38 µMol, 18.38% yield, 97% purity, formic acid) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.54 (d, *J* = 4.0 Hz, 1H), 8.17 (d, *J* = 8.0 Hz, 2H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.83 (m, 1H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.23 (m, 1H), 7.02-6.94 (m, 3H), 6.66-6.64 (m, 1H), 6.53-6.50 (m, 2H), 3.87 (s, 3H). MS (ESI): m/z 335 $[M+1]^+$.

***N*-(4-fluorophenyl)-7-methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (61).** The title compound was synthesized from **F3** according to method C to give **61** *N*-(4-fluorophenyl)-7-methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (298.1 mg, 801.76 µMol, 44.95% yield, 98% purity, formic acid) as a brown solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.55-8.54 (m, 1H), 8.24 (s, 1H), 8.18 (s, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.84-7.83 (m, 1H), 7.74-7.72 (m, 1H), 7.40 (s, 1H), 7.25 (m, 1H), 6.99-6.94 (m, 2H), 6.79-6.77 (m, 1H), 6.52-6.49 (m, 2H), 2.38 (s, 3H). MS (ESI): m/z 319 $[M+1]^+$.

5-(Methoxymethyl)pyridin-2-amine. NaH (96.66 mg, 2.42 mmol, 60% purity) at 0 °C was added to a solution of (6-amino-3-pyridyl)methanol (200 mg, 1.61 mmol) in THF (5 mL). The reaction mixture was stirred at 0 °C for 1 h. Then MeI (343.01 mg, 2.42 mmol, 150.44 µL) was added and the mixture was stirred at 25 °C for 2 hr. The reaction mixture was diluted with water (10 mL) and extracted with ethyl acetate (10 mL*3). The combined organic phase was

dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give a residue. The residue was purified by prep-TLC (SiO_2, Petroleum ether/Ethyl acetate = 1/2) to give 5-(methoxymethyl)pyridin-2-amine (60 mg, 434.26 µMol, 26.95% yield) as yellow oil. ^{1}H NMR (400MHz, DMSO-d_6) δ 7.84-7.83 (m, 1H), 7.38-7.31 (m, 1H), 6.43-6.39 (m, 1H), 5.93 (s, 2H), 4.21-4.19 (m, 2H), 3.20 (s, 3H).***N*-(3-fluorophenyl)-6-(methoxymethyl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (62).** The title compound was synthesized from **N3** according to method A to give **62** *N*-(3-fluorophenyl)-6-(methoxymethyl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (25.38 mg, 71.40 µMol, 16.44% yield, 98% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.55-8.52 (m, 2H), 8.10-8.08 (m, 1H), 7.88-7.85 (m, 2H), 7.64 (d, *J* = 9.2 Hz, 1H), 7.29-7.25 (m, 2H), 7.12-7.10 (m, 1H), 6.50 (m, 1H), 6.31-6.27 (m, 2H), 4.43 (s, 2H), 3.26 (s, 3H). MS (ESI): m/z 349 $[M+1]^+$.

6-Amino-*N*,*N*-dimethylnicotinamide.To a mixture of 6-aminopyridine-3-carboxylic acid (300 mg, 2.17 mmol) and *N*-methylmethanamine (117.50 mg, 1.44 mmol, 132.03 µL, HCl salt) in dichloromethane (5 mL), TEA (439.56 mg, 4.34 mmol, 604.62 µL) and EDCI (499.64 mg, 2.61 mmol) were added. The mixture was stirred at 20 °C for 12 h. LCMS showed the reaction was complete. The reaction mixture was concentrated under reduced pressure to give a residue. The residue was purified by silica gel chromatography (SiO_2, Dichloromethane/Methanol = 10/1) to give 6-amino-*N*,*N*-dimethylnicotinamide (180 mg, 1.09 mmol, 50.17% yield, 100% purity) as a white solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.02 (m, 1H), 7.47-7.44 (m, 1H), 6.43-6.41 (m, 1H), 6.34 (s, 2H), 2.95 (s, 6H). MS (ESI): m/z 166 $[M+1]^+$. **5-((Dimethylamino)methyl)pyridin-2-amine.** $AlCl_3$ (37.51 mg, 281.27 µMol, 15.37 µL) at 5 °C was added to a solution of $LiAlH_4$ (213.51 mg, 5.63 mmol) in THF (10 mL) . The mixture was stirred at 5 °C for 0.5 h. Then 6-amino-*N*,*N*-dimethyl-pyridine-3-carboxamide (55 mg, 319.63 µMol) and 6-amino-*N*,*N*-dimethyl-pyridine-3-carboxamide (180 mg, 1.09 mmol) were added and the mixture was stirred at 20 °C for 1 h. $Na_2SO_4.10\ H_2O$ was added to the reaction mixture at 0 °C. The mixture was filtered and washed with MeOH (10 mL). The filtrate was concentrated under reduced pressure to give 5-((dimethylamino)methyl)pyridin-2-amine (190 mg, crude) as yellow oil. ^{1}H NMR (400MHz, DMSO-d_6) δ 7.74 (s, 1H), 7.25 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1H), 6.40 (d, *J* = 8.8 Hz, 1H), 5.79 (s, 2H), 3.16 (s, 2H), 2.09-2.07 (m, 6H). **6-((Dimethylamino)methyl)-*N*-(3-fluorophenyl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (63).** The title compound was synthesized according to method A to give **63** 6-

((dimethylamino)methyl)-*N*-(3-fluorophenyl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (9.0 mg, 99% purity) as a white solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.55-8.54 (m, 2H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.85 (m, 1H), 7.75 (s, 1H), 7.61 (d, *J* = 9.2 Hz, 1H), 7.30-7.27 (m, 2H), 7.13-7.11 (m, 1H), 6.51-6.50 (m, 1H), 6.30-6.27 (m, 2H), 3.39 (s, 2H), 2.13 (s, 6H). MS (ESI): m/z 362 $[M+1]^+$.

***N*-(3-fluorophenyl)-7-(methoxymethyl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (64).** The title compound was synthesized according to method A to give *N*-(3-fluorophenyl)-7-(methoxymethyl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (24.28 mg, 68.30 μMol, 15.73% yield, 98% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.55-8.53 (m, 2H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.87-7.83 (m, 2H), 7.53 (s, 1H), 7.25 (m, 1H), 7.12-7.10 (m, 1H), 6.89-6.87 (m, 1H), 6.49 (m, 1H), 6.30-6.25 (m, 2H), 4.48 (s, 2H), 3.34 (s, 3H). MS (ESI): m/z 349 $[M+1]^+$.

7-((Dimethylamino)methyl)-*N*-(3-fluorophenyl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (65). The title compound was synthesized according to method A to give **65** 7-((dimethylamino)methyl)-*N*-(3-fluorophenyl)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (6.87 mg, 99% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.56-8.55 (m, 1H), 8.55-8.52 (m, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.86-7.84 (m, 2H), 7.49 (s, 1H), 7.26 (m, 1H), 7.13-7.11 (m, 1H), 6.94-6.92 (m, 1H), 6.51 (m, 1H), 6.32-6.28 (m, 2H), 3.46 (s, 2H), 2.20 (s, 6H). MS (ESI): m/z 362 $[M+1]^+$.

***N*-(3-Fluorophenyl)-7-methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine.** The title compound was synthesized according to method A to give *N*-(3-fluorophenyl)-7-methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (180 mg, 538.36 μMol, 44.56% yield) as a yellow solid. MS (ESI): m/z 335 $[M+1]^+$. **3-((3-Fluorophenyl)amino)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-7-ol (66).** BBr_3 (292.22 mg, 583.23 μMol, 112.39 μL, 50% purity) was added dropwise at 0 °C to a solution of *N*-(3-fluorophenyl)-7-methoxy-2-(2-pyridyl)imidazo[1,2-*a*]pyridin-3-amine (130 mg, 388.82 μMol) in dichloromethane (3 mL). The mixture was stirred at 0 °C for 0.5 h and stirred at 25 °C for 11.5 h. The reaction mixture was added saturated aqueous sodium bicarbonate solution until no gas was produced. The mixture was filtered and the filter cake was dried under reduced pressure to give a residue. The residue was purified by prep-HPLC (column: Phenomenex Synergi C18 150*30mm*4um;mobile phase:

[water(0.225%FA)-ACN];B%: 10%-40%,10.5min) to give **66** 3-((3-fluorophenyl)amino)-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-7-ol (60.77 mg, 184.03 μMol, 47.33% yield, 97% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.54-8.53 (m, 1H), 8.39 (s, 1H), 8.24 (s, 1H), 8.03 (d, *J* = 7.6 Hz, 1H), 7.84-7.82 (m, 1H), 7.74-7.72 (m, 1H), 7.23 (m, 1H), 7.13-7.11 (m, 1H), 6.75 (s, 1H), 6.61-6.59 (m, 1H), 6.59-6.49 (m, 1H), 6.31-6.27 (m, 2H). MS (ESI): m/z 321 $[M+1]^+$.

***N*-(3-fluorophenyl)-7-methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (67).** The title compound was synthesized from **F3** according to method C to give **67** *N*-(3-fluorophenyl)-7-methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (21.3 mg, 66.24 μMol, 21.22% yield, 99% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 9.26 (s, 1H), 8.83-8.82 (m, 1H), 8.37 (d, *J* = 7.2 Hz, 1H), 8.03-8.00 (m, 2H), 7.75 (s, 1H), 7.56-7.55 (m, 1H), 7.38-7.36 (m, 1H), 7.24-7.23 (m, 1H), 6.69-6.65 (m, 3H), 2.58 (s, 3H). MS (ESI): m/z 319 $[M+1]^+$.

***N*-cyclopentyl-7-methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (68).** The title compound was synthesized from **N2** according to method A to give **68** *N*-cyclopentyl-7-methyl-2-(2-pyridyl)imidazo[1,2-*a*]pyridin-3-amine (30.5 mg, 100.14 μMol, 19.06% yield, 96% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.55-8.54 (m, 1H), 8.11 (d, *J* = 6.8 Hz, 1H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.86-7.82 (m, 1H), 7.25-7.22 (m, 2H), 6.73-6.70 (m, 1H), 6.21 (d, *J* = 10.4 Hz, 1H), 3.92-3.87 (m, 1H), 2.34 (s, 3H), 1.69-1.67 (m, 4H), 1.51-1.46 (m, 4H). MS (ESI): m/z 293 $[M+1]^+$.

***N*-benzyl-6-methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (69).** To a mixture of 6-methyl-2-(2-pyridyl)imidazo[1,2-*a*]pyridin-3-amine (**F4,** 50 mg, 222.95 μMol) and benzaldehyde (28.39 mg, 267.55 μMol, 27.04 μL) in dioxane (3 mL), AcOH (53.55 mg, 891.82 μMol, 51.00 μL) and Ti(i-PrO)$_4$ (158.41 mg, 557.39 μMol, 164.50 μL) were added. The mixture was stirred at 35 °C for 16 h. Then $NaBH_3CN$ (42.03 mg, 668.86 μMol) was added and the mixture was stirred at 35 °C for 2 h. The reaction mixture was diluted with water (20 mL) and extracted with dichloromethane (20 mL*2). The combined organic phase were dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give a residue. The residue was purified by prep-HPLC (column: Phenomenex Synergi C18 150*30mm*4um; mobile phase: [water(0.225%FA)-ACN];B%: 10%-40%,10.5min) to give **69** *N*-benzyl-6-methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-amine (20.3 mg, 95% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.64 (d, *J* = 4.4 Hz, 1H), 8.26 (s, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.92-7.89

(m, 1H), 7.54 (m, 1H), 7.36-7.31 (m, 4H), 7.24-7.19 (m, 3H), 6.54 (s, 1H), 4.32 (s, 2H), 2.36 (s, 3H). MS (ESI): m/z 315 $[M+1]^+$.

4-(7-Methoxy-2-(pyridin-2-yl)imidazo[1,2-*a*]pyridin-3-yl)morpholine (71) The title compound was synthesized from **C2** according to method H to give **71** 4-(7-methoxy-2-(pyridin-2-yl)imidazo [1,2-a]pyridin-3-yl)morpholine (9.29 mg, 29.34 µMol, 5.95% yield, 98% purity) as a yellow solid. ^{1}H NMR (400MHz, DMSO-d_6) δ 8.70-8.69 (m, 1H), 8.26-8.24 (m, 1H), 8.09 (d, *J* = 7.6 Hz, 1H), 7.87-7.83 (m, 1H), 7.30-7.27 (m, 1H), 6.91-6.90 (m, 1H), 6.68-6.66 (m, 1H), 3.85-3.84 (m, 3H), 3.77 (s, 4H), 2.52-2.49 (m, 4H). MS (ESI): m/z 311 $[M+1]^+$.