

Supplementary Information

Manganese/cobalt-catalyzed oxidative C(sp³)-H / C(sp³)-H coupling: a route to α -tertiary β -arylethylamines

Meiling Tan, Kaizhi Li, Jiangliang Yin and Jingsong You*

Key Laboratory of Green Chemistry and Technology of Ministry of Education,

College of Chemistry, Sichuan University, 29 Wangjiang Road,

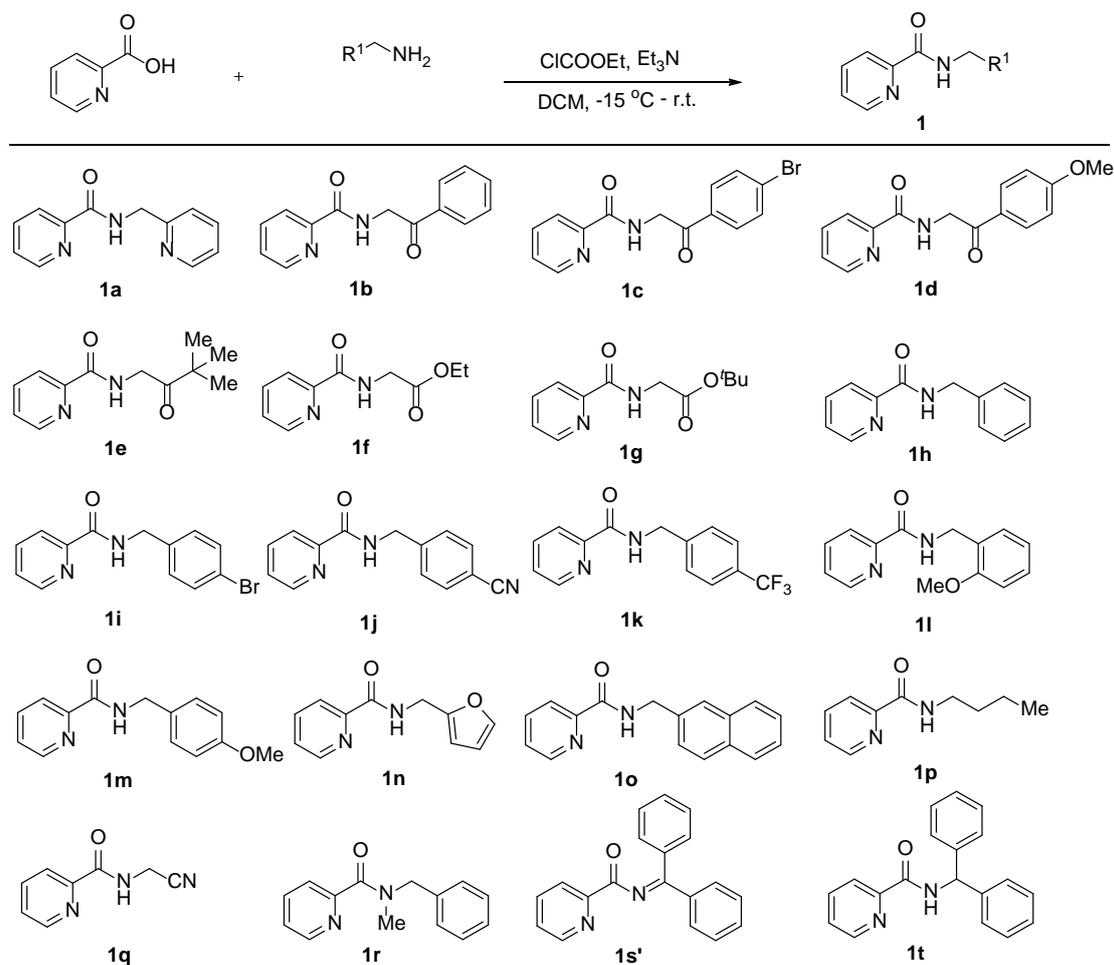
Chengdu 610064, P.R. China

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I. General remarks

All NMR spectra were obtained on a Varian Inova 400 MHz or a Bruker AV II-400 MHz spectrometer. The ^1H NMR (400 MHz) chemical shifts were measured relative to CDCl_3 or $\text{DMSO}-d_6$ which acted as the internal reference (CDCl_3 : $\delta = 7.26$ ppm; $\text{DMSO}-d_6$: $\delta = 2.50$ ppm; TMS: $\delta = 0.00$ ppm;). The ^{13}C NMR (100 MHz) chemical shifts were obtained by using CDCl_3 or $\text{DMSO}-d_6$ as the internal standard (CDCl_3 : $\delta = 77.16$ ppm; $\text{DMSO}-d_6$: $\delta = 39.52$ ppm). High-resolution mass spectra (HRMS) were gained with a Waters-Q-TOF-Premier (ESI). Melting points were determined by XRC-1 and are uncorrected. The solvent (toluene) was dried by Innovative Technology PS-MD-5 Solvent Purification System.



II. Synthesis of N-(pyridin-2-ylmethyl)picolinamides

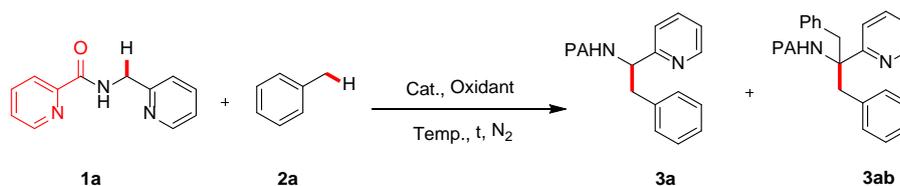
General procedure: Carboxylic acid (3.5 mmol, 0.43 g) was dissolved in dry dichloromethane (10.0 mL) in 50.0 mL round-bottom flask, and then triethylamine (7.0 mmol, 0.97 mL) was added under an N_2 atmosphere at -15°C . After ethyl chloroformate (3.5 mmol, 0.33 mL) was added to the solution, the mixture was stirred at the same temperature for half an hour, and then a solution of amine (2.0 mmol) in DCM (2.0 mL) was added dropwise at -15°C . The suspension was stirred at the same temperature for an hour, and then the mixture was warmed to room temperature and stirred for overnight.

Water (10.0 mL) was added to the suspension and the organic phase was separated. The aqueous phase was extracted with dichloromethane (2 × 10.0 mL), and the combined organic phases were dried over by anhydrous MgSO₄ and concentrated. The residue was purified by column chromatography on silica gel employing hexane/ethyl acetate as the eluent to get the desired *N*-(pyridin-2-ylmethyl)picolinamides.

III. Optimization of oxidative coupling reaction

A magnetic stirrer and amine derivative **1a** (0.25 mmol), toluene **2a** (1.0 mL) were added into an oven-dried Schlenk tube with catalyst under an N₂ atmosphere. The reaction mixture was stirred for several minutes at room temperature, and then DTBP (184.2 μL, 1.0 mmol) was added. The tube was sealed with a teflon-coated cap, and then the solution was stirred at 140 °C for 24 h. The solution was cooled to ambient temperature when the reaction was finished. Then the mixture was diluted with 10.0 mL of CH₂Cl₂, filtered by celite, and washed with 20.0 mL of CH₂Cl₂. The combined organic phases were concentrated and the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate =2/1, v/v) to get **3a**. The reaction condition was optimized as showed in Table S1. 1.0 mL of toluene was more suitable than 0.5 mL and 2.0 mL.

Table S1. Optimization of the oxidative coupling of *N*-(pyridin-2-ylmethyl)picolinamide with toluene^a



Entry	Cat. (mol %)	Oxidant(equiv)	Temp (°C)	T (h)	Yield ^b
1	Cu(OAc) ₂ ·H ₂ O (20.0)	DTBP(4.0)	140	24	ND
2	FeCl ₃ ·6H ₂ O (20.0)	DTBP(4.0)	140	24	ND
3	Ni(acac) ₂ (20.0)	DTBP(4.0)	140	24	40 ^c
4	Co(OAc) ₂ ·4H ₂ O (20.0)	DTBP(4.0)	140	24	20 ^c
5	MnCl ₂ ·4H ₂ O (20.0)	DTBP(4.0)	140	24	56
6	Mn(acac) ₂ ·2H ₂ O (20.0)	DTBP(4.0)	140	24	19
7	Mn(acac) ₃ (20.0)	DTBP(4.0)	140	24	20
8	Mn(OAc) ₂ ·4H ₂ O (20.0)	DTBP(4.0)	140	24	40
9 ^d	MnCl ₂ ·4H ₂ O (20.0)	DTBP(4.0)	140	24	50
10	none	DTBP(4.0)	140	24	ND
11	MnCl ₂ ·4H ₂ O (10.0)	DTBP(4.0)	140	24	45
12	MnCl ₂ ·4H ₂ O (20.0)	DTBP(4.0)	140	24	56
13	MnCl ₂ ·4H ₂ O (20.0)	TBHP (4.0)	140	24	ND
14	MnCl ₂ ·4H ₂ O (20.0)	TBPB (4.0)	140	24	ND
15	MnCl ₂ ·4H ₂ O (20.0)	K ₂ S ₂ O ₈ (4.0)	140	24	ND
16	MnCl ₂ ·4H ₂ O (20.0)	H ₂ O ₂ (4.0)	140	24	ND

17	MnCl ₂ ·4H ₂ O (20.0)	DCP (4.0)	140	24	42
18	MnCl ₂ ·4H ₂ O (20.0)	none	140	24	ND
19 ^e	MnCl ₂ ·4H ₂ O (20.0)	DTBP(4.0)	140	24	17
20	MnCl ₂ ·4H ₂ O (20.0)	DTBP(4.0)	140	24	56
21	MnCl ₂ ·4H ₂ O (20.0)	DTBP(3.0)	140	24	45
22	MnCl ₂ ·4H ₂ O (20.0)	DTBP(5.0)	140	24	44
23	MnCl ₂ ·4H ₂ O (20.0)	DTBP(4.0)	130	24	53
24	MnCl ₂ ·4H ₂ O (20.0)	DTBP(4.0)	150	24	57
25	Mn(OAc) ₂ ·4H ₂ O (20.0)	DTBP(4.0)	150	24	53
26	Mn(OAc)₂·4H₂O (20.0)	DTBP(4.0)	150	18	62
27	Mn(OAc) ₂ ·4H ₂ O (20.0)	DTBP(4.0)	150	12	43

^aReaction condition: **1a** (0.25 mmol), **2a** (1.0 mL), catalyst, and oxidant under an N₂ atmosphere for 24 hours.

^bIsolated yield. ^c**3ab** was obtained. ^dH₂O (20.0 equiv) was used as the additive. ^eUnder air. ^fDTBP = Di-tert-butyl peroxide, TBHP = tert-butyl hydroperoxide, TBPB = tert-butyl peroxybenzoate, and DCP = dicumyl peroxide. PAHN = picolinamido group.

IV. General procedure for the oxidative coupling reactions of amines with toluene derivatives

General procedure A: A magnetic stirrer and amine derivative **1a** (0.25 mmol), toluene derivative **2** (1.0 mL) were added into an oven-dried Schlenk tube under an N₂ atmosphere. The reaction mixture was stirred for several minutes at room temperature, and then DTBP (184.2 μL, 1.0 mmol) was added. The tube was sealed with a teflon-coated cap, and then the solution was stirred at 150 °C for 18 h. The solution was cooled to ambient temperature when the reaction was finished. Then the mixture was diluted with 10.0 mL of CH₂Cl₂, filtered by celite, and washed with 20.0 mL of CH₂Cl₂. The combined organic phases were concentrated and the residue was purified by column chromatography on silica gel to get the desired product.

General procedure B: A magnetic stirrer and amine derivative **1** (0.25 mmol), **2** (10.0 equiv) were added into an oven-dried Schlenk tube under an N₂ atmosphere, and benzene (0.5 mL) was used as the solvent. The reaction mixture was stirred for several minutes at room temperature, and then DTBP (184.2 μL, 1.0 mmol) was added. The tube was sealed with a teflon-coated cap, and then the solution was stirred at 150 °C for 18 h. The solution was cooled to ambient temperature when the reaction was finished. Then the mixture was diluted with 10.0 mL of CH₂Cl₂, filtered by celite, and washed with 20.0 mL of CH₂Cl₂. The combined organic phases were concentrated and the residue was purified by column chromatography on silica gel to get the desired product.

V. General procedure for removal of coordinating group and preparation of 3-(pyridin-2-yl)isoquinoline

(1) Removal of coordinating group

A magnetic stirrer and product **3a** (75.8 mg, 0.25 mmol), ethanol (2.0 mL) were added into an oven-dried Schlenk tube, and then BF₃·Et₂O (315.4 μL, 2.5 mmol) was added drop by

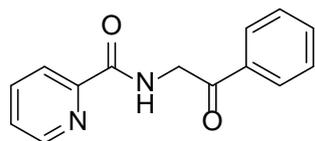
drop under an N₂ atmosphere. The tube was sealed with a teflon-coated cap, and the reaction mixture was stirred for several minutes at room temperature. The solution was stirred at 140 °C for 32 h. The solution was cooled to ambient temperature when the reaction was finished. Saturated Na₂CO₃ aqueous solution was dropped slowly. Subsequently, the mixture was washed by ethyl acetate (3 × 10.0 mL), and then the organic phases were combined and anhydrous Na₂SO₄ was used for desiccation. Thereafter, the solution was filtered by celite, and the residue was obtained after the solvent was removed by rotary evaporateion. The residue was dissolve in DCM (3.0 mL), and Et₃N (70.0 μL, 0.5 mmol) and Boc₂O (109.1 mg, 0.5 mmol) was next add to the reaction mixture. The reaction was stirred under room temperature overnight. The solvent was removed after the reaction was finished, and the residue was purified by column chromatography on silica gel to get the desired product **5a**.

(2) Preparation of 3-(pyridin-2-yl)isoquinoline

A magnetic stirrer and product **3a** (75.8 mg, 0.25 mmol,), ethanol (2.0 mL) were added into an oven-dried Schlenk tube, and then BF₃·Et₂O (315.4 μL, 2.5 mmol) was added drop by drop under an N₂ atmosphere. The tube was sealed with a teflon-coated cap, and the reaction mixture was stirred for several minutes at room temperature. Next, the solution was stirred at 140 °C for 32 h. The solution was cooled to ambient temperature when the reaction was finished, and then saturated Na₂CO₃ aqueous solution was dropped slowly. Subsequently, the mixture was washed by ethyl acetate (3 × 10.0 mL), and then the organic phases were combined and anhydrous Na₂SO₄ was used for desiccation. Thereafter, the solution was filtered by celite, and the residue was gotten after the solvent was removed by rotary evaporateion.

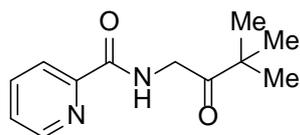
Concentrated HCl (0.75 mL) was added to the mixture of the residue in CHCl₃ (1.0 mL) and HCHO (0.45 mL), and the mixture was stirred under an N₂ atmosphere and 80~90 °C for 10 hours .The solution was cooled to ambient temperature when the reaction was finished. Saturated Na₂CO₃ aqueous solution was dropped slowly. Subsequently, the mixture was washed by ethyl acetate (3 × 10.0 mL), and then the organic phases were combined and anhydrous Na₂SO₄ was used for desiccation. Thereafter, the solution was filtered by celite, and the residue was gotten after the solvent was removed by rotary evaporateion. The residue was add to DMF (2.0 mL), and then KMnO₄ (0.25 mmol) was added for several times. The reaction was next stirred under room temperature. The solvent was removed after the reaction was finished, and the residue was purified by column chromatography on silica gel to get the desired product **5b**.

VI. Experimental data of the described compounds



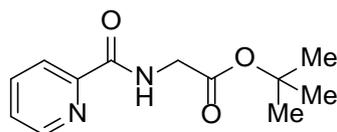
N-(2-Oxo-2-phenylethyl)picolinamide (**1b**)

¹H NMR (400 MHz, CDCl₃): δ = 8.96 (s, 1H), 8.62 (s, 1H), 8.19 (d, *J* = 7.6 Hz, 1H), 8.03 (d, *J* = 7.6 Hz, 2H), 7.85 (t, *J* = 7.6 Hz, 1H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.51 (t, *J* = 7.2 Hz, 2H), 7.44 (s, 1H), 4.97 (s, 2H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 193.93, 164.72, 149.58, 148.52, 137.34, 134.67, 134.13, 129.01, 128.06, 126.46, 122.30, 46.49 ppm.



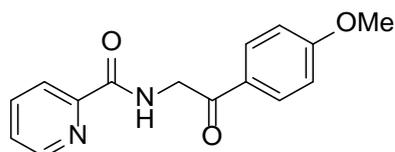
N-(3,3-Dimethyl-2-oxobutyl)picolinamide (1e)

$^1\text{H NMR}$ (400 MHz, CDCl_3): δ = 8.69 (s, 1H), 8.58 (s, 1H), 8.15 (d, J = 7.6 Hz, 1H), 7.82 (t, J = 7.6 Hz, 1H), 7.42 (s, 1H), 4.47 (s, 2H), 1.23 (s, 9H) ppm. $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ = 210.28, 164.66, 149.61, 148.48, 137.31, 126.39, 122.20, 44.77, 43.31, 26.50 ppm.



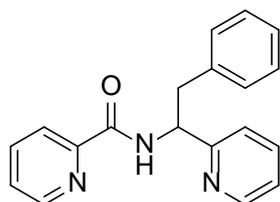
tert-Butyl picolinoylglycinate (1g)

$^1\text{H NMR}$ (400 MHz, CDCl_3): δ = 8.57 (d, J = 4.8 Hz, 1H), 8.46 (s, 1H), 8.17 (d, J = 8.0 Hz, 1H), 7.83 (t, J = 7.6 Hz, 1H), 7.44-7.40 (m, 1H), 4.15 (d, J = 5.6 Hz, 2H), 1.49 (s, 9H) ppm. $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ = 169.02, 164.60, 149.60, 148.41, 137.37, 126.43, 122.35, 82.41, 42.16, 28.21 ppm.



N-(2-(4-Methoxyphenyl)-2-oxoethyl)picolinamide (1m)

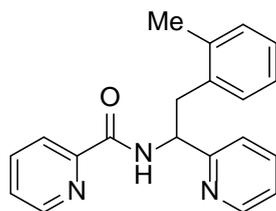
$^1\text{H NMR}$ (400 MHz, CDCl_3): δ = 8.97 (s, 1H), 8.63 (s, 1H), 8.20 (d, J = 8.0 Hz, 1H), 8.02 (d, J = 8.4 Hz, 2H), 7.85 (t, J = 7.4 Hz, 1H), 7.44 (s, 1H), 6.98 (d, J = 8.4 Hz, 2H), 4.92 (s, 2H), 3.88 (s, 3H) ppm. $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ = 192.35, 164.73, 164.28, 149.70, 148.55, 137.34, 130.41, 127.75, 126.43, 122.28, 114.21, 55.69, 46.11 ppm.



N-(2-Phenyl-1-(pyridin-2-yl)ethyl)picolinamide (3a)

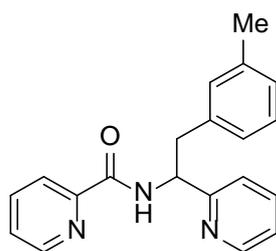
Following the general procedure A. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3a** as yellow oil (46.9 mg, 62% yield). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ = 9.11 (d, J = 7.6 Hz, 1H), 8.61 (dd, J = 23.6, 3.6 Hz, 2H), 8.17 (d, J = 8.0 Hz, 1H), 7.80 (t, J = 7.6 Hz, 1H), 7.48 (t, J = 7.6 Hz, 1H), 7.40 – 7.38 (m, 1H), 7.17 - 7.15 (m, 4H), 7.03 (d, J = 6.8 Hz, 2H), 6.92 (d, J = 7.6 Hz, 1H), 5.49-5.44 (m, 1H), 3.41-3.36 (m, 1H), 3.24-3.18 (m, 1H) ppm. $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ = 163.78, 159.18, 150.05, 149.59, 148.36, 137.52, 137.26, 136.25, 129.59, 128.28, 126.49, 126.16, 122.66, 122.49, 122.24, 55.93, 42.50 ppm. HRMS (ESI⁺): calcd for $\text{C}_{19}\text{H}_{18}\text{N}_3\text{O}$ [M+H]⁺

304.1444, found 304.1441.



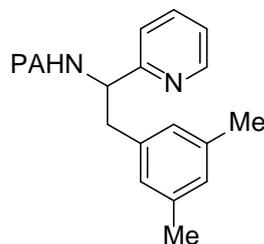
N-(1-(Pyridin-2-yl)-2-(*o*-tolyl)ethyl)picolinamide (3b)

Following the standard procedure A. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3b** as yellow oil (53.9 mg, 68% yield). ^1H NMR (400 MHz, CDCl_3): δ = 9.24 (d, J = 7.6 Hz, 1H), 8.64 (dd, J = 23.6, 4.4 Hz, 2H), 8.18 (d, J = 8.0 Hz, 1H), 7.82 (t, J = 7.6 Hz, 1H), 7.48 – 7.38 (m, 2H), 7.19 – 7.13 (m, 1H), 7.11 – 7.03 (m, 2H), 6.98 (t, J = 8.0 Hz, 1H), 6.89 (d, J = 7.6 Hz, 1H), 6.74 (d, J = 8.0 Hz, 1H), 5.38-5.44 (m, 1H), 3.46-3.41 (m, 1H), 3.17-3.11 (m, 1H), 2.23 (s, 3H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 163.86, 159.10, 150.18, 149.71, 148.43, 137.32, 137.00, 136.17, 135.85, 130.54, 130.31, 126.69, 126.19, 125.76, 122.90, 122.62, 122.28, 55.35, 40.18, 19.35. ppm. HRMS (ESI $^+$): calcd for $\text{C}_{20}\text{H}_{20}\text{N}_3\text{O}$ $[\text{M}+\text{H}]^+$ 318.1601, found 318.1606.



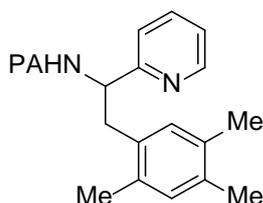
N-(1-(Pyridin-2-yl)-2-(*m*-tolyl)ethyl)picolinamide (3c)

Following the standard procedure A. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3c** as yellow oil (40.2 mg, 51% yield). ^1H NMR (400 MHz, CDCl_3): δ = 9.09 (d, J = 7.6 Hz, 1H), 8.63 (dd, J = 22.2, 3.8 Hz, 2H), 8.18 (d, J = 7.6 Hz, 1H), 7.82 (t, J = 7.6 Hz, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.43 – 7.38 (m, 1H), 7.19 – 7.13 (m, 1H), 7.06 (t, J = 7.6 Hz, 1H), 6.96 (d, J = 7.2 Hz, 1H), 6.94 – 6.88 (m, 2H), 6.80 (d, J = 7.6 Hz, 1H), 5.47-5.41 (m, 1H), 3.35-3.34 (m, 1H), 3.19-3.13 (m, 1H), 2.23 (s, 3H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 163.85, 159.38, 150.17, 149.62, 148.40, 137.88, 137.45, 137.31, 136.24, 130.50, 128.18, 127.27, 126.65, 126.19, 122.76, 122.50, 122.31, 56.07, 42.51, 21.41 ppm. HRMS (ESI $^+$): calcd for $\text{C}_{20}\text{H}_{20}\text{N}_3\text{O}$ $[\text{M}+\text{H}]^+$ 318.1601, found 318.1597.



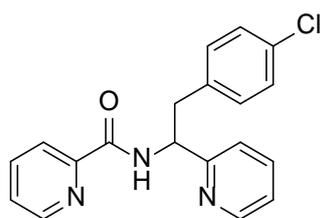
***N*-2-(3,5-Dimethylphenyl)-1-(pyridin-2-yl)ethylpicolinamide (3d)**

Following the general procedure A. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3d** as yellow oil (42.6 mg, 51% yield). ¹H NMR (400 MHz, CDCl₃): δ = 9.08 (d, *J* = 7.6 Hz, 1H), 8.63 (dd, *J* = 22.6, 3.8 Hz, 2H), 8.18 (d, *J* = 7.6 Hz, 1H), 7.83 (t, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.44 – 7.39 (m, 1H), 7.19 – 7.13 (m, 1H), 6.92 (d, *J* = 7.6 Hz, 1H), 6.79 (s, 1H), 6.65 (s, 2H), 5.44–5.38 (m, 1H), 3.32–3.30 (m, Hz, 1H), 3.14–3.08 (m, 1H), 2.19 (s, 6H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 163.86, 159.51, 150.22, 149.60, 148.40, 137.72, 137.32, 136.17, 128.16, 127.54, 126.19, 122.79, 122.47, 122.32, 56.14, 42.47, 21.29 ppm. HRMS (ESI⁺): calcd for C₂₁H₂₁N₃NaO [M+Na]⁺ 354.1577, found 354.1580.



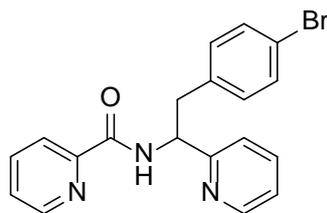
***N*-1-(Pyridin-2-yl)-2-(2,4,5-trimethylphenyl)ethylpicolinamide (3e)**

Following the general procedure B. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3e** as yellow oil (45.9 mg, 54% yield). ¹H NMR (400 MHz, CDCl₃): δ = 9.24 (d, *J* = 7.6 Hz, 1H), 8.64 (dd, *J* = 20.6, 3.8 Hz, 2H), 8.19 (d, *J* = 8.0 Hz, 1H), 7.83 (t, *J* = 7.6 Hz, 1H), 7.48–7.40 (m, 2H), 7.19 – 7.14 (m, 1H), 6.83 (s, 1H), 6.77 (d, *J* = 7.6 Hz, 1H), 6.72 (s, 1H), 5.40–5.35 (m, 1H), 3.37–3.32 (m, 1H), 3.10–3.05 (m, 1H), 2.15 (s, 3H), 2.07 (d, *J* = 5.2 Hz, 6H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 163.83, 159.29, 150.23, 149.61, 148.40, 137.29, 136.08, 134.59, 134.05, 133.67, 132.92, 131.91, 131.61, 126.15, 122.91, 122.51, 122.25, 55.66, 39.62, 19.32, 19.09, 18.65 ppm. HRMS (ESI⁺): calcd for C₂₂H₂₄N₃O [M+H]⁺ 346.1914, found 346.1914.



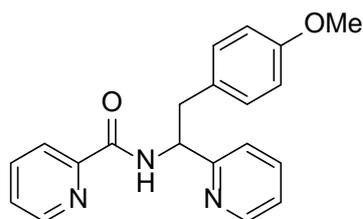
***N*-2-(4-Chlorophenyl)-1-(pyridin-2-yl)ethylpicolinamide (3f)**

Following the general procedure A. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3f** as yellow oil (40.4 mg, 48% yield). ¹H NMR (400 MHz, CDCl₃): δ = 9.10 (d, *J* = 6.4 Hz, 1H), 8.62 (d, *J* = 20.4 Hz, 2H), 8.17 (d, *J* = 7.6 Hz, 1H), 7.85–7.82 (m, 1H), 7.52–7.52 (m, 1H), 7.42 (s, 1H), 7.20 – 7.11 (m, 3H), 6.94 (d, *J* = 7.6 Hz, 3H), 5.48–5.48 (m, 1H), 3.35–3.33 (m, 1H), 3.25 – 3.12 (m, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 163.85, 158.77, 149.93, 149.71, 148.43, 137.36, 136.46, 136.02, 132.36, 130.96, 128.45, 126.30, 122.71, 122.30, 55.69, 41.77 ppm. HRMS (ESI⁺): calcd for C₁₉H₁₇ClN₃O [M+H]⁺ 338.1055, found 338.1063.



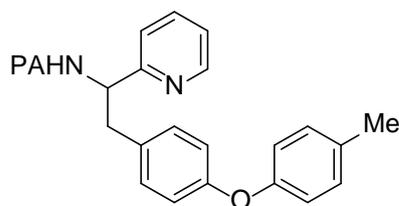
N-(2-(4-Bromophenyl)-1-(pyridin-2-yl)ethyl)picolinamide (3g)

Following the general procedure B. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3g** as yellow oil (30.9 mg, 32% yield). ^1H NMR (400 MHz, CDCl_3): δ = 9.09 (d, J = 7.6 Hz, 1H), 8.62 (d, J = 18.8, 2.8 Hz, 2H), 8.17 (d, J = 7.6 Hz, 1H), 7.83 (t, J = 7.6 Hz, 1H), 7.53 (t, J = 7.4 Hz, 1H), 7.44 – 7.39 (m, 1H), 7.29 (d, J = 7.6 Hz, 2H), 7.20 – 7.16 (m, 1H), 6.95 (d, J = 7.6 Hz, 1H), 6.90 (d, J = 7.6 Hz, 2H), 5.46-5.41 (m, 1H), 3.35-3.30 (m, 1H), 3.21-3.16 (m, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 163.89, 158.83, 149.99, 149.75, 148.46, 137.39, 136.58, 136.50, 131.44, 131.38, 126.32, 122.75, 122.72, 122.35, 120.54, 55.67, 41.85 ppm. HRMS (ESI $^+$): calcd for $\text{C}_{19}\text{H}_{17}^{79}\text{BrN}_3\text{O}$ $[\text{M}+\text{H}]^+$ 382.0550, found 382.0541; calcd for $\text{C}_{19}\text{H}_{17}^{81}\text{BrN}_3\text{O}$ $[\text{M}+\text{H}]^+$ 384.0529, found 384.0536.



N-(2-(4-Methoxyphenyl)-1-(pyridin-2-yl)ethyl)picolinamide (3h)

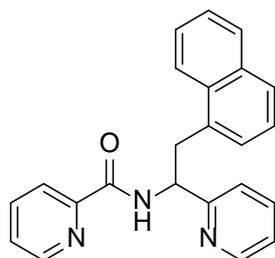
Following the general procedure A. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3h** as yellow oil (35.8 mg, 43% yield). ^1H NMR (400 MHz, CDCl_3): δ = 9.11 (d, J = 6.4 Hz, 1H), 8.62 (d, J = 20.4 Hz, 2H), 8.17 (d, J = 7.6 Hz, 1H), 7.83-7.81 (m, 1H), 7.51-7.49 (m, 1H), 7.40 (s, 1H), 7.15 (s, 1H), 6.93 (d, J = 6.8 Hz, 3H), 6.71 (d, J = 8.0 Hz, 2H), 5.42-5.40 (m, 1H), 3.73 (s, 3H), 3.36-3.30 (m, 1H), 3.19 – 3.10 (m, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 163.80, 159.27, 158.21, 150.06, 149.59, 148.40, 137.29, 136.27, 130.58, 129.51, 126.19, 122.74, 122.48, 122.25, 113.69, 56.04, 55.23, 41.62 ppm. HRMS (ESI $^+$): calcd for $\text{C}_{20}\text{H}_{20}\text{N}_3\text{O}_2$ $[\text{M}+\text{H}]^+$ 334.1550, found 334.1550.



N-(1-(Pyridin-2-yl)-2-(4-(p-tolyloxy)phenyl)ethyl)picolinamide (3i)

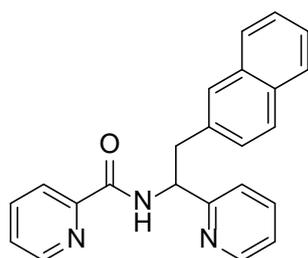
Following the general procedure B. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3i** as yellow oil (47.3 mg, 46% yield). ^1H

NMR (400 MHz, CDCl₃): δ = 9.11 (d, J = 8.4 Hz, 1H), 8.62 (dd, J = 21.6, 3.6 Hz, 2H), 8.18 (d, J = 7.6 Hz, 1H), 7.82 (t, J = 7.6 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.43 – 7.38 (m, 1H), 7.19 – 7.14 (m, 1H), 7.10 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 7.6 Hz, 3H), 6.85 (d, J = 7.6 Hz, 2H), 6.80 (d, J = 7.6 Hz, 2H), 5.47-5.42 (m, 1H), 3.36-3.34 (m, 1H), 3.22-3.17 (m, 1H), 2.31 (s, 3H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 163.83, 159.21, 156.33, 154.99, 150.07, 149.65, 148.41, 137.31, 136.31, 132.77, 132.08, 130.81, 130.25, 126.21, 122.74, 122.55, 122.28, 118.94, 118.38, 55.99, 41.74, 20.79 ppm. HRMS (ESI⁺): calcd for C₂₆H₂₄N₃O₂ [M+H]⁺ 410.1863, found 410.1863.



***N*-(2-(Naphthalen-1-yl)-1-(pyridin-2-yl)ethyl)picolinamide (3j)**

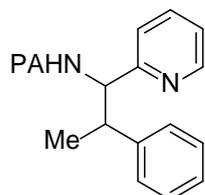
Following the general procedure B. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3j** as yellow oil (41.4 mg, 47% yield). ¹H NMR (400 MHz, CDCl₃): δ = 9.38 (d, J = 6.8 Hz, 1H), 8.66 (d, J = 29.6 Hz, 2H), 7.58 (t, J = 7.6 Hz, 1H), 8.47 (d, J = 8.4 Hz, 1H), 8.24 (d, J = 8.0 Hz, 1H), 7.87-7.82 (m, 2H), 7.68 (d, J = 8.0 Hz, 1H), 7.48 (t, J = 7.2 Hz, 1H), 7.45 – 7.41 (m, 1H), 7.30 (t, J = 7.6 Hz, 1H), 7.19 (t, J = 7.6 Hz, 1H), 7.15 – 7.11 (m, 1H), 6.88 (d, J = 6.8 Hz, 1H), 6.44 (d, J = 7.6 Hz, 1H), 5.64-5.59 (m, 1H), 4.07 (d, J = 13.2 Hz, 1H), 3.46 – 3.37 (m, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 164.16, 158.74, 150.21, 149.71, 148.48, 137.37, 135.95, 133.88, 133.76, 132.41, 128.67, 128.02, 127.43, 126.45, 126.25, 125.74, 125.19, 124.38, 123.08, 122.62, 122.27, 55.51, 40.32 ppm. HRMS (ESI⁺): calcd for C₂₃H₂₀N₃O [M+H]⁺ 354.1601, found 354.1607.



***N*-(2-(Naphthalen-2-yl)-1-(pyridin-2-yl)ethyl)picolinamide (3k)**

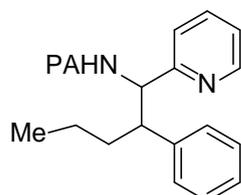
Following the general procedure B. Purification via column chromatography on silica gel (petroleum ether / ethyl acetate = 2/1, v/v) afforded **3k** as yellow oil (39.6 mg, 45% yield). ¹H NMR (400 MHz, CDCl₃): δ = 9.18 (d, J = 7.6 Hz, 1H), 8.63 (dd, J = 31.8, 3.4 Hz, 2H), 8.18 (d, J = 7.6 Hz, 1H), 7.82 (t, J = 7.6 Hz, 1H), 7.78 – 7.74 (m, 1H), 7.68 (d, J = 8.0 Hz, 2H), 7.50 (s, 1H), 7.45 – 7.38 (m, 4H), 7.19-7.14 (m, 2H), 6.89 (d, J = 7.6 Hz, 1H), 5.60-5.54 (m, 1H), 3.59-3.55 (m, 1H), 3.40-3.34 (m, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 163.91, 159.15, 150.11, 149.70, 148.42, 137.33, 136.34, 135.16, 133.54, 132.34,

128.25, 128.02, 127.90, 127.69, 126.23, 125.93, 125.49, 122.78, 122.59, 122.32, 56.00, 42.72 ppm. HRMS (ESI⁺): calcd for C₂₃H₂₀N₃O [M+H]⁺ 354.1601, found 354.1601.



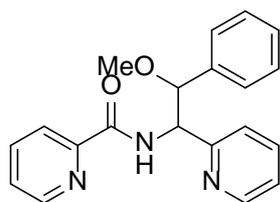
N-(2-Phenyl-1-(pyridin-2-yl)propyl)picolinamide (31)

Following the general procedure A. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **31** as yellow oil (53.1 mg, 67% yield). **31** was obtained as a mixture of two diastereomers, dr (anti/syn) \approx 1:1. ¹H NMR (400 MHz, CDCl₃): δ = 9.11(d, *J* = 9.2 Hz, 1H), 9.02 (d, *J* = 8.0 Hz, 1H), 8.66 – 8.59 (m, 2H), 8.57-8.55 (m, 2H), 8.19 (d, *J* = 8.0 Hz, 1H), 8.10 (d, *J* = 7.6 Hz, 1H), 7.83 (t, *J* = 7.6 Hz, 1H), 7.77 (t, *J* = 7.6 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.44 – 7.39 (m, 1H), 7.39 – 7.34 (m, 1H), 7.25 (d, *J* = 5.2 Hz, 2H), 7.21 – 7.08 (m, 8H), 7.04-7.03 (m, 3H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.73 (d, *J* = 7.6 Hz, 1H), 5.45 (t, *J* = 7.8 Hz, 1H), 5.38 (t, *J* = 9.2 Hz, 1H), 3.69-3.62 (m, 1H), 3.42-3.35 (m, 1H), 1.48 (d, *J* = 6.8 Hz, 3H), 1.22 (d, *J* = 7.0 Hz, 3H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 164.09, 163.80, 159.35, 158.86, 150.12, 150.04, 149.44, 148.41, 148.36, 143.35, 142.70, 137.32, 137.22, 136.12, 135.85, 128.35, 128.26, 128.15, 128.00, 126.71, 126.51, 126.20, 126.09, 123.24, 123.18, 122.45, 122.24, 122.21, 60.00, 59.48, 46.46, 44.47, 18.35, 17.27 ppm. HRMS (ESI⁺): calcd for C₂₀H₂₀N₃O [M+H]⁺ 318.1601, found 318.1604.



N-(2-Phenyl-1-(pyridin-2-yl)pentyl)picolinamide(3m)

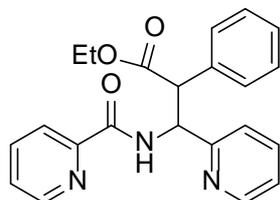
Following the general procedure A. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3m** as yellow oil (56.1 mg, 65% yield). **3m** was obtained as a mixture of two diastereomers, dr (anti/syn) \approx 1:1. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 9.05 (d, *J* = 9.2 Hz, 1H), 8.80 (d, *J* = 9.2 Hz, 1H), 8.69 (s, 1H), 8.60 (s, 1H), 8.55 (s, 1H), 8.48 (s, 1H), 8.08 (d, *J* = 7.6 Hz, 1H), 8.01 (t, *J* = 7.2 Hz, 1H), 7.92 (s, 2H), 7.74 (t, *J* = 7.4 Hz, 1H), 7.63-7.61 (m, 1H), 7.57 – 7.48 (m, 2H), 7.39 (d, *J* = 7.2 Hz, 1H), 7.29-7.27 (m, 1H), 7.20 (d, *J* = 6.8 Hz, 2H), 7.15-7.12 (m, 6H), 7.08 (d, *J* = 6.4 Hz, 1H), 7.01 - 6.95 (m, 3H), 5.45-5.41 (m, 1H), 5.38-5.33 (m, 1H), 3.33-3.32 (m, 1H), 3.22-3.17 (m, 1H), 1.82 (d, *J* = 10.0 Hz, 1H), 1.76-1.72 (m, 1H), 1.58-1.57 (m, 1H), 1.36-1.35 (m, 1H), 1.05 – 0.96 (m, 4H), 0.74 (t, *J* = 6.8 Hz, 3H), 0.68 (t, *J* = 6.8 Hz, 3H) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 162.89, 162.43, 159.67, 158.97, 149.40, 149.24, 149.01, 148.91, 148.64, 148.51, 141.11, 140.99, 138.05, 137.90, 136.58, 136.09, 128.35, 128.02, 128.00, 126.80, 126.66, 126.41, 126.27, 122.77, 122.63, 122.55, 122.31, 121.95, 121.74, 58.37, 57.92, 50.95, 49.98, 33.91, 33.71, 20.08, 19.96, 13.86, 13.78 ppm. HRMS (ESI⁺): calcd for C₂₂H₂₃N₃NaO [M+Na]⁺ 368.1733, found 368.1732.



N-(2-Methoxy-2-phenyl-1-(pyridin-2-yl)ethyl)picolinamide (3n)

Following the general procedure B. Purification via column chromatography on silica gel (petroleum ether / ethyl acetate = 2/1, v/v) afforded **3n** as yellow oil (43.3 mg, 52% yield). **3n** was obtained as a mixture of two diastereomers, dr (anti/syn) = 1:1. ¹H NMR (400 MHz,

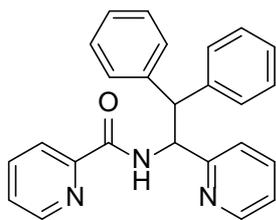
DMSO-*d*₆): δ = 9.09 (d, *J* = 8.8 Hz, 1H), 8.96 (d, *J* = 9.2 Hz, 1H), 8.73 (s, 1H), 8.64 (s, 1H), 8.56 (s, 1H), 8.52 (s, 1H), 8.00 (s, 2H), 7.97-7.93 (m, 2H), 7.71 (t, *J* = 7.2 Hz, 2H), 7.66-7.64 (m, 1H), 7.60-7.58 (m, 1H), 7.26-7.22 (m, 12H), 7.16-7.14 (m, 2H), 5.48-5.44 (m, 1H), 5.35 – 5.30 (m, 1H), 4.90 (s, 1H), 4.76 (d, *J* = 6.4 Hz, 1H), 3.14 (s, 3H), 3.07 (s, 3H) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 163.01, 162.41, 157.82, 157.71, 149.15, 148.88, 148.74, 148.58, 138.34, 138.08, 138.01, 137.96, 136.53, 136.33, 128.09, 127.99, 127.88, 127.75, 127.41, 126.91, 126.79, 123.16, 122.73, 122.59, 122.23, 121.84, 121.81, 84.78, 84.15, 58.87, 57.83, 56.94, 56.62 ppm. HRMS (ESI⁺): calcd for C₂₀H₂₀N₃O₂ [M+H]⁺ 334.1550, found 334.1550.



Ethyl 2-phenyl-3-(picolinamido)-3-(pyridin-2-yl)propanoate (3o)

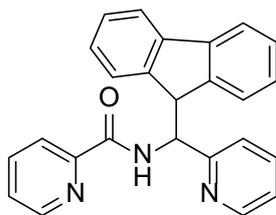
Following the general procedure A. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **3o** as yellow oil (70.3 mg, 75% yield). **3o** was obtained as a mixture of two diastereomers, dr (anti/syn) = 1:1. ¹H NMR (400 MHz,

CDCl₃): δ = 9.50 (d, *J* = 9.6 Hz, 1H), 8.64-8.60 (m, 3H), 8.55 (d, *J* = 4.8 Hz, 1H), 8.46 (d, *J* = 4.8 Hz, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.80 (t, *J* = 8.0 Hz, 1H), 7.72 (t, *J* = 7.2 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.51 – 7.43 (m, 4H), 7.43-7.40 (m, 1H), 7.34 – 7.30 (m, 3H), 7.29 – 7.26 (m, 1H), 7.25-7.24 (m, 1H), 7.22-7.17 (m, 6H), 7.11-7.08 (m, 1H), 6.05 (t, *J* = 10.2 Hz, 1H), 5.84-5.80 (m, 1H), 4.63 (d, *J* = 6.8 Hz, 1H), 4.48 (d, *J* = 10.2 Hz, 1H), 4.19-4.06 (m, 2H), 4.03-3.92 (m, 2H), 1.15 (t, *J* = 7.2 Hz, 3H), 1.04 (t, *J* = 7.2 Hz, 3H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 172.54, 171.70, 164.12, 163.54, 159.01, 158.76, 149.84, 149.59, 149.56, 149.28, 148.51, 148.18, 137.27, 137.19, 136.73, 136.54, 135.79, 135.53, 129.07, 128.78, 128.62, 128.60, 127.83, 127.66, 126.28, 126.16, 123.87, 122.89, 122.69, 122.52, 122.49, 122.31, 61.17, 60.97, 57.07, 56.47, 55.63, 55.27, 14.14, 14.03 ppm. HRMS (ESI⁺): calcd for C₂₂H₂₂N₃O₃ [M+H]⁺ 376.1656, found 376.1663.



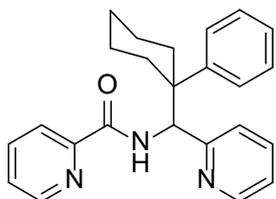
N-(2,2-Diphenyl-1-(pyridin-2-yl)ethyl)picolinamide (3p)

Following the general procedure B. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3p** as a white solid (58.7 mg, 62% yield), melting point: 140~142 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 8.86 (d, *J* = 9.2 Hz, 1H), 8.52 (d, *J* = 27.2 Hz, 2H), 7.93-7.91 (m, 2H), 7.53-7.51 (m, 4H), 7.29-7.21 (m, 5H), 7.11-7.09 (m, 4H), 7.02-6.98 (m, 1H), 6.12 (t, *J* = 10.4 Hz, 1H), 4.81 (d, *J* = 11.2 Hz, 1H) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 162.45, 159.70, 149.12, 148.46, 142.19, 141.91, 137.93, 136.25, 128.32, 128.29, 128.21, 128.17, 126.72, 126.39, 126.20, 123.33, 122.43, 121.82, 56.42, 56.22 ppm. HRMS (ESI⁺): calcd for C₂₅H₂₂N₃O [M+H]⁺ 380.1757, found 380.1763.



N-((9H-Fluoren-9-yl)(pyridin-2-yl)methyl)picolinamide (3q)

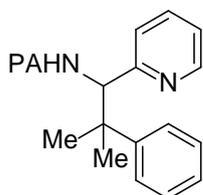
Following the general procedure B. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3q** as yellow oil (53.6 mg, 57% yield). ¹H NMR (400 MHz, DMSO-*d*₆): δ = 9.08 (d, *J* = 8.8 Hz, 1H), 8.60 (d, *J* = 27.6 Hz, 2H), 8.03-7.96 (m, 2H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.75 (d, *J* = 7.2 Hz, 1H), 7.66 (t, *J* = 7.2 Hz, 1H), 7.61-7.59 (m, 1H), 7.39 (t, *J* = 7.2 Hz, 1H), 7.28-7.25 (m, 4H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.13 (d, *J* = 7.6 Hz, 1H), 5.86-5.84 (m, 1H), 4.93 (d, *J* = 2.0 Hz, 1H) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 162.97, 157.57, 149.10, 148.71, 143.36, 142.81, 141.35, 140.71, 138.04, 136.57, 127.81, 127.42, 126.92, 126.74, 125.24, 125.06, 122.86, 121.90, 120.19, 119.83, 55.83, 51.04 ppm. HRMS (ESI⁺): calcd for C₂₅H₂₀N₃O [M+H]⁺ 378.1601, found 378.1608.



N-((1-Phenylcyclohexyl)(pyridin-2-yl)methyl)picolinamide (3r)

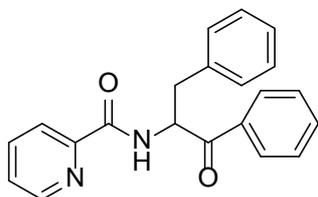
Following the general procedure A. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3r** as yellow oil (53.8 mg, 58% yield). ¹H NMR (400 MHz, DMSO-*d*₆): δ = 9.05 (d, *J* = 10.0 Hz, 1H), 8.68 (s, 1H), 8.43 (s, 1H), 8.05 (d, *J* = 7.6 Hz, 1H), 7.99 (t, *J* = 7.4 Hz, 1H), 7.62-7.60 (m, 1H), 7.50 (t, *J* = 7.4 Hz, 1H),

7.25-7.17 (m, 4H), 7.00 (d, $J = 7.2$ Hz, 2H), 6.64 (d, $J = 7.6$ Hz, 1H), 5.23 (d, $J = 9.6$ Hz, 1H), 2.27 (t, $J = 13.8$ Hz, 2H), 1.73 (t, $J = 12.6$ Hz, 1H), 1.60 (t, $J = 11.8$ Hz, 1H), 1.51-1.40 (m, 4H), 1.12-1.02 (m, 2H) ppm. ^{13}C NMR (100 MHz, DMSO- d_6): $\delta = 162.69, 156.97, 149.34, 148.68, 148.16, 140.63, 138.03, 135.39, 127.96, 127.93, 126.78, 126.06, 123.60, 122.36, 121.91, 61.88, 47.44, 33.06, 31.09, 25.81, 21.64, 21.50$ ppm. HRMS (ESI $^+$): calcd for $\text{C}_{24}\text{H}_{26}\text{N}_3\text{O}$ [M+H] $^+$ 372.2070, found 372.2072.



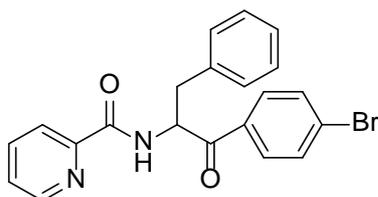
N-(2-Methyl-2-phenyl-1-(pyridin-2-yl)propyl)picolinamide (3s)

Following the general procedure A. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3s** as yellow oil (73.6 mg, 77% yield). ^1H NMR (400 MHz, DMSO- d_6): $\delta = 9.17$ (d, $J = 9.6$ Hz, 1H), 8.70 (s, 1H), 8.53 (s, 1H), 8.05 – 7.95 (m, 2H), 7.62 (s, 1H), 7.51 (t, $J = 7.4$ Hz, 1H), 7.28 – 7.15 (m, 6H), 6.73 (d, $J = 7.6$ Hz, 1H), 5.47 (d, $J = 10.0$ Hz, 1H), 1.39 (s, 3H), 1.27 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO- d_6): $\delta = 162.68, 157.43, 149.29, 148.69, 148.37, 145.83, 138.06, 135.60, 127.88, 126.82, 126.49, 126.19, 123.64, 122.47, 121.88, 60.87, 43.21, 26.07, 23.76$ ppm. HRMS (ESI $^+$): calcd for $\text{C}_{21}\text{H}_{22}\text{N}_3\text{O}$ [M+H] $^+$ 332.1757, found 332.1765.



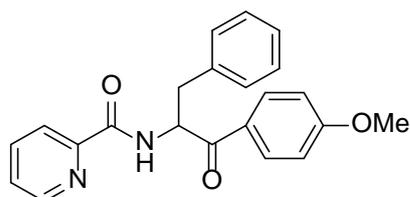
N-(1-Oxo-1,3-diphenylpropan-2-yl)picolinamide (4a)

Following the general procedure. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **4a** as yellow oil (65.3 mg, 80% yield). ^1H NMR (400 MHz, CDCl_3): $\delta = 8.82$ (d, $J = 7.6$ Hz, 1H), 8.57 (s, 1H), 8.16 (d, $J = 8.0$ Hz, 1H), 8.01 (d, $J = 7.6$ Hz, 2H), 7.82 (t, $J = 7.6$ Hz, 1H), 7.58 (t, $J = 7.2$ Hz, 1H), 7.47 (t, $J = 7.4$ Hz, 2H), 7.43-7.41 (m, 1H), 7.19-7.16 (m, 3H), 7.08 (d, $J = 6.4$ Hz, 2H), 6.06-6.01 (m, 1H), 3.41-3.36 (m, 1H), 3.19-3.14 (m, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 197.97, 163.97, 149.57, 148.48, 137.30, 136.07, 135.16, 133.82, 129.56, 128.94, 128.86, 128.49, 127.00, 126.41, 122.31, 54.86, 39.10$ ppm. HRMS (ESI $^+$): calcd for $\text{C}_{21}\text{H}_{19}\text{N}_2\text{O}_2$ [M+H] $^+$ 331.1441, found 331.1443.



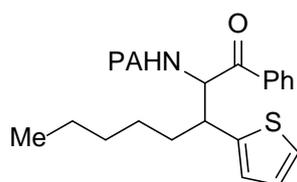
N-(1-(4-Bromophenyl)-1-oxo-3-phenylpropan-2-yl)picolinamide (4b)

Following the general procedure. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **4b** as yellow oil (47.7 mg, 77% yield). ¹H NMR (400 MHz, CDCl₃): δ = 8.78 (d, *J* = 4.4 Hz, 1H), 8.56 (s, 1H), 8.15 (d, *J* = 6.0 Hz, 1H), 7.85-7.83 (m, 3H), 7.59 (d, *J* = 6.4 Hz, 2H), 7.42 (s, 1H), 7.18 (s, 3H), 7.09 (s, 2H), 5.95-5.94 (m, 1H), 3.34 (d, *J* = 6.4 Hz, 1H), 3.16 (d, *J* = 8.4 Hz, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 197.21, 163.96, 149.40, 148.47, 137.35, 135.91, 133.99, 132.23, 130.30, 129.50, 129.09, 128.57, 127.10, 126.50, 122.34, 54.77, 39.02 ppm. HRMS (ESI⁺): calcd for C₂₁H₁₇⁷⁹BrN₂NaO₂ [M+Na]⁺ 431.0366, found 431.0365; calcd for C₂₁H₁₇⁸¹BrN₂NaO₂ [M+Na]⁺ 433.0345, found 433.0337.



N-(1-(4-Methoxyphenyl)-1-oxo-3-phenylpropan-2-yl)picolinamide (**4c**)

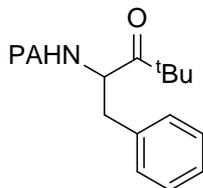
Following the general procedure. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **4c** as yellow oil (66.0 mg, 73% yield). ¹H NMR (400 MHz, CDCl₃): δ = 8.83 (d, *J* = 8.0 Hz, 1H), 8.57 (s, 1H), 8.15 (d, *J* = 7.6 Hz, 1H), 7.99 (d, *J* = 8.0 Hz, 2H), 7.82 (t, *J* = 7.6 Hz, 1H), 7.42-7.39 (m, 1H), 7.19-7.17 (m, 3H), 7.09 (d, *J* = 6.4 Hz, 2H), 6.93 (d, *J* = 8.4 Hz, 2H), 6.00-5.95 (m, 1H), 3.87 (s, 3H), 3.39-3.34 (m, 1H), 3.18-3.13 (m, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 196.26, 164.13, 163.92, 149.67, 148.48, 137.28, 136.31, 131.25, 129.59, 128.46, 128.05, 126.93, 126.37, 122.29, 114.15, 55.65, 54.45, 39.42 ppm. HRMS (ESI⁺): calcd for C₂₂H₂₁N₂O₃ [M+H]⁺ 361.1547, found 361.1547.



N-(1-Oxo-1-phenyl-3-(thiophen-2-yl)octan-2-yl)picolinamide (**4d**)

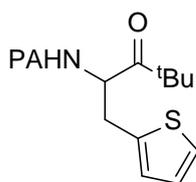
Following the general procedure. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1, v/v) afforded **4d** as yellow oil (51.7 mg, 51% yield). **4d** was obtained as a mixture of two diastereomers, dr (anti/syn) = 1:1. ¹H NMR (400 MHz, CDCl₃): δ = 8.88 (d, *J* = 9.2 Hz, 1H), 8.79 (d, *J* = 10.0 Hz, 1H), 8.61 (d, *J* = 4.4 Hz, 2H), 8.17 (d, *J* = 8.0 Hz, 2H), 8.00 (d, *J* = 8.0 Hz, 2H), 7.93 (d, *J* = 8.0 Hz, 2H), 7.87 – 7.80 (m, 2H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 3H), 7.46-7.38 (m, 4H), 7.16 (d, *J* = 5.2 Hz, 1H), 7.04 (d, *J* = 4.8 Hz, 1H), 6.91 – 6.86 (m, 1H), 6.80-6.77 (m, 2H), 6.62 (d, *J* = 3.2 Hz, 1H), 6.10-6.06 (m, 1H), 6.01 – 5.97 (m, 1H), 3.68-3.64 (m, 1H), 3.59 – 3.53 (m, 1H), 1.79 – 1.68 (m, 4H), 1.29 – 1.12 (m, 12H), 0.85 – 0.76 (m, 6H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 199.19, 197.65, 164.47, 164.23, 149.58, 149.43, 148.58, 148.46, 143.69, 142.18, 137.43, 137.28, 135.96, 135.60, 133.74, 133.58, 129.04, 128.81, 128.74, 128.68, 126.67, 126.63, 126.55, 126.40, 126.00, 125.76, 124.38, 124.19, 122.55, 122.42, 57.81, 57.70, 44.72,

44.37, 34.36, 32.37, 31.68, 31.62, 27.31, 26.95, 22.58, 22.54, 14.15, 14.10 ppm. HRMS (ESI⁺): calcd for C₂₄H₂₇N₂O₂S [M+H]⁺ 407.1788, found 407.1797.



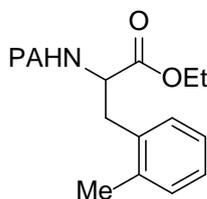
N-(4,4-Dimethyl-3-oxo-1-phenylpentan-2-yl)picolinamide (4e)

Following the general procedure. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **4e** as yellow oil (68.7 mg, 88% yield). ¹H NMR (400 MHz, DMSO-*d*₆): δ = 8.68-8.64 (m, 2H), 7.95 (s, 2H), 7.59 (s, 1H), 7.25 (s, 4H), 7.17 (s, 1H), 5.35-5.32 (m, 1H), 3.09 (d, *J* = 13.2 Hz, 1H), 2.97 – 2.89 (m, 1H), 1.11 (s, 9H) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 213.34, 162.74, 149.03, 148.56, 137.94, 137.28, 129.27, 128.26, 126.84, 126.55, 121.96, 53.06, 43.56, 37.05, 25.85 ppm. HRMS (ESI⁺): calcd for C₁₉H₂₂N₂NaO₂ [M+Na]⁺ 333.1573, found 333.1578.



N-(4,4-Dimethyl-3-oxo-1-(thiophen-2-yl)pentan-2-yl)picolinamide (4f)

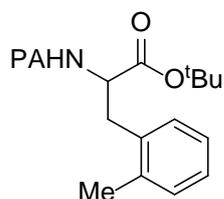
Following the general procedure. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1, v/v) afforded **4f** as yellow oil (46.6 mg, 59% yield). ¹H NMR (400 MHz, CDCl₃): δ = 8.56 (d, *J* = 2.8 Hz, 1H), 8.46 (d, *J* = 9.6 Hz, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.82 (t, *J* = 8.0 Hz, 1H), 7.44-7.40 (m, 1H), 7.12 (d, *J* = 5.2 Hz, 1H), 6.89-6.87 (m, 1H), 6.84-6.83 (m, 1H), 5.56-5.50 (m, 1H), 3.42-3.37 (m, 1H), 3.18-3.13 (m, 1H), 1.11 (s, 9H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 213.60, 163.38, 149.37, 148.38, 138.36, 137.40, 127.05, 126.84, 126.51, 124.74, 122.43, 59.96, 52.72, 44.38, 33.18, 25.76 ppm. HRMS (ESI⁺): calcd for C₁₇H₂₁N₂O₂S [M+H]⁺ 317.1318, found 317.1321.



Ethyl 2-(picolinamido)-3-*o*-tolylpropanoate (4g)

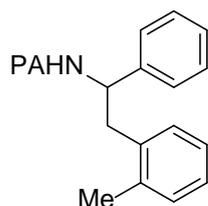
Following the general procedure. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1, v/v) afforded **4g** as yellow oil (41.4 mg, 52% yield). ¹H NMR (400 MHz, CDCl₃): δ = 8.61 – 8.43 (m, 2H), 8.13 (d, *J* = 7.6 Hz, 1H), 7.82 (t, *J* = 7.2 Hz, 1H), 7.43-7.41 (m, 1H), 7.15-7.12 (m, 4H), 5.04-4.98 (m, 1H), 4.20 – 4.09 (m, 2H), 3.22 (t, *J* = 6.8 Hz, 2H), 2.39 (s, 3H), 1.17 (t, *J* = 6.8 Hz, 3H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 171.96, 164.11, 149.45, 148.39, 137.38, 136.86, 134.66, 130.63, 130.04, 127.23,

126.45, 126.06, 122.37, 61.52, 52.89, 36.41, 19.56, 14.14 ppm. HRMS (ESI⁺): calcd for C₁₈H₂₀N₂NaO₃ [M+Na]⁺ 335.1366, found 335.1372.



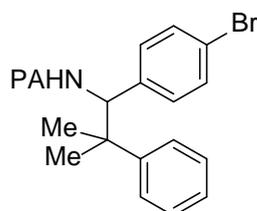
tert-Butyl 2-(picolinamido)-3-(o-tolyl)propanoate (4h)

Following the general procedure. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1, v/v) afforded **4h** as light yellow oil (45.0 mg, 53% yield). ¹H NMR (400 MHz, CDCl₃): δ = 8.58 – 8.50 (m, 2H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.81 (t, *J* = 7.6 Hz, 1H), 7.42-7.39 (m, 1H), 7.19 – 7.16 (m, 1H), 7.15 – 7.11 (m, 2H), 7.10-7.08 (m, 1H), 4.97-4.91 (m, 1H), 3.18 (d, *J* = 7.6 Hz, 2H), 2.41 (s, 3H), 1.36 (s, 9H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 171.02, 163.96, 149.54, 148.35, 137.31, 136.87, 134.93, 130.48, 130.26, 127.07, 126.34, 125.90, 122.26, 82.19, 53.17, 36.69, 27.94, 19.63 ppm. HRMS (ESI⁺): calcd for C₂₀H₂₄N₂NaO₃ [M+Na]⁺ 363.1679, found 363.1685.



N-(1-Phenyl-2-(o-tolyl)ethyl)picolinamide (4i)

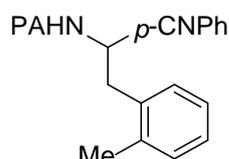
Following the general procedure. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1, v/v) afforded **4i** as yellow oil (40.2 mg, 51% yield). ¹H NMR (400 MHz, CDCl₃): δ = 8.57-8.55 (m, 2H), 8.14 (d, *J* = 8.0 Hz, 1H), 7.81 (t, *J* = 7.6 Hz, 1H), 7.43 – 7.39 (m, 1H), 7.31-7.26 (m, 5H), 7.13-7.09 (m, 2H), 7.03 (s, 2H), 5.43-5.37 (m, 1H), 3.32-3.28 (m, 1H), 3.21-3.16 (m, 1H), 2.30 (s, 3H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 163.65, 149.91, 148.17, 141.93, 137.43, 136.82, 135.88, 130.40, 130.23, 128.68, 127.53, 126.76, 126.72, 126.28, 125.85, 122.34, 54.26, 40.69, 19.58 ppm. HRMS (ESI⁺): calcd for C₂₁H₂₁N₂O [M+H]⁺ 317.1648, found 317.1653.



N-(1-(4-Bromophenyl)-2-methyl-2-phenylpropyl)picolinamide (4j)

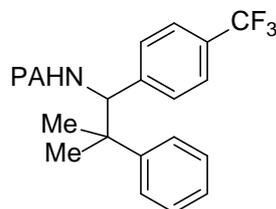
Following the general procedure. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1, v/v) afforded **4j** as light yellow oil (57.1 mg, 56% yield). ¹H NMR (400 MHz, DMSO-*d*₆): δ = 8.68 (d, *J* = 9.6 Hz, 1H), 8.64 (d, *J* = 4.8 Hz, 1H),

7.97 – 7.90 (m, 2H), 7.60-7.57 (m, 1H), 7.40 (d, $J = 8.4$ Hz, 2H), 7.33-7.27 (m, 4H), 7.20 (t, $J = 6.8$ Hz, 1H), 7.01 (d, $J = 8.4$ Hz, 2H), 5.31 (d, $J = 9.6$ Hz, 1H), 1.33 (s, 3H), 1.31 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO- d_6): $\delta = 162.77, 149.22, 148.59, 145.18, 139.14, 138.02, 130.45, 130.29, 128.03, 126.81, 126.57, 126.41, 121.80, 120.21, 60.71, 41.59, 25.98, 24.41$ ppm. HRMS (ESI $^+$): calcd for $\text{C}_{22}\text{H}_{22}^{79}\text{BrN}_2\text{O}$ $[\text{M}+\text{H}]^+$ 409.0910, found 409.0901; calcd for $\text{C}_{22}\text{H}_{22}^{81}\text{BrN}_2\text{O}$ $[\text{M}+\text{H}]^+$ 411.0890, found 411.0881.



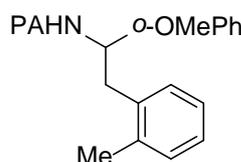
***N*-(1-(4-Cyanophenyl)-2-(*o*-tolyl)ethyl)picolinamide (4k)**

Following the general procedure. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1, v/v) afforded **4k** as yellow oil (38.0 mg, 48% yield). ^1H NMR (400 MHz, CDCl_3): $\delta = 8.62\text{--}8.53$ (m, 2H), 8.11 (d, $J = 7.6$ Hz, 1H), 7.83 (t, $J = 7.2$ Hz, 1H), 7.58 (d, $J = 7.6$ Hz, 2H), 7.45-7.43 (m, 1H), 7.37 (d, $J = 7.2$ Hz, 2H), 7.13 (s, 2H), 7.07-7.05 (m, 1H), 6.97 (d, $J = 6.8$ Hz, 1H), 5.41-5.36 (m, 1H), 3.27-3.24 (m, 1H), 3.16-3.13 (m, 1H), 2.26 (s, 3H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 163.94, 149.43, 148.29, 147.57, 137.61, 136.65, 134.80, 132.48, 130.71, 130.13, 127.50, 127.23, 126.62, 126.15, 122.41, 118.88, 111.35, 54.13, 40.31, 19.55$ ppm. HRMS (ESI $^+$): calcd for $\text{C}_{22}\text{H}_{20}\text{N}_3\text{O}$ $[\text{M}+\text{H}]^+$ 342.1601, found 342.1607.



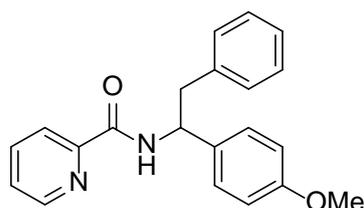
***N*-(2-Methyl-2-phenyl-1-(4-(trifluoromethyl)phenyl)propyl)picolinamide (4l)**

Following the general procedure. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1, v/v) afforded **4l** as colourless oil (55.7 mg, 56% yield). ^1H NMR (400 MHz, CDCl_3): $\delta = 8.77$ (d, $J = 9.6$ Hz, 1H), 8.57 (d, $J = 4.8$ Hz, 1H), 8.11 (d, $J = 8.0$ Hz, 1H), 7.81 (t, $J = 7.2$ Hz, 1H), 7.45 – 7.38 (m, 3H), 7.36 – 7.30 (m, 2H), 7.28-7.27 (m, 3H), 7.01 (d, $J = 8.4$ Hz, 2H), 5.37 (d, $J = 9.6$ Hz, 1H), 1.48 (s, 3H), 1.44 (s, 3H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 163.72, 149.64, 148.32, 144.29, 143.62, 137.49, 129.35$ (q, $J = 32.3$ Hz), 128.79, 128.31, 127.18, 126.88, 126.42, 124.48 (q, $J = 3.8$ Hz), 124.25 (q, $J = 270.4$ Hz), 122.39, 61.87, 42.28, 26.10, 25.95 ppm. HRMS (ESI $^+$): calcd for $\text{C}_{23}\text{H}_{22}\text{F}_3\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ 399.1679, found 399.1681.



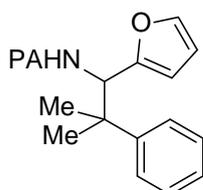
***N*-(1-(2-Methoxyphenyl)-2-(*o*-tolyl)ethyl)picolinamide (4m)**

Following the general procedure. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1, v/v) afforded **4m** as yellow oil (43.6 mg, 50% yield). ^1H NMR (400 MHz, CDCl_3): δ = 9.09 (d, J = 8.8 Hz, 1H), 8.57 (s, 1H), 8.14 (d, J = 7.6 Hz, 1H), 7.80 (t, J = 7.6 Hz, 1H), 7.42 – 7.36 (m, 1H), 7.22 (t, J = 7.8 Hz, 1H), 7.07-6.99 (m, 5H), 6.91 (d, J = 8.0 Hz, 1H), 6.82 (t, J = 7.4 Hz, 1H), 5.62-5.56 (m, 1H), 3.94 (s, 3H), 3.31 – 3.18 (m, 2H), 2.32 (s, 3H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 163.41, 157.37, 150.39, 148.23, 137.30, 136.91, 136.67, 130.41, 130.19, 129.29, 128.78, 128.57, 126.45, 126.04, 125.63, 122.39, 120.75, 111.06, 55.59, 52.06, 39.24, 19.39 ppm. HRMS (ESI⁺): calcd for $\text{C}_{22}\text{H}_{23}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 347.1754, found 347.1751.



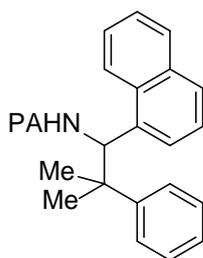
***N*-(1-(4-Methoxyphenyl)-2-phenylethyl)picolinamide (4n)**

Following the general procedure. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1, v/v) afforded **4n** as yellow oil (40.8 mg, 49% yield). ^1H NMR (400 MHz, $\text{DMSO-}d_6$): δ = 9.15 (d, J = 8.8 Hz, 1H), 8.65 (s, 1H), 7.93 (s, 2H), 7.57 (s, 1H), 7.40 (d, J = 8.0 Hz, 2H), 7.27 – 7.18 (m, 4H), 7.14-7.12 (m, 1H), 6.87 (d, J = 8.0 Hz, 2H), 5.27-5.25 (m, 1H), 3.71 (s, 3H), 3.35 – 3.26 (m, 1H), 3.09 (d, J = 9.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$): δ = 163.03, 158.19, 149.91, 148.41, 138.94, 137.82, 135.18, 129.16, 128.08, 128.06, 126.54, 126.10, 121.97, 113.60, 55.04, 53.97, 41.42 ppm. HRMS (ESI⁺): calcd for $\text{C}_{21}\text{H}_{20}\text{N}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$ 355.1417, found 355.1423.



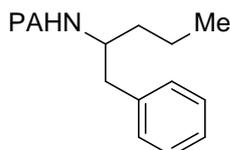
***N*-(1-(Furan-2-yl)-2-methyl-2-phenylpropyl)picolinamide (4o)**

Following the general procedure. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1, v/v) afforded **4o** as yellow oil (40.7 mg, 51% yield). ^1H NMR (400 MHz, CDCl_3): δ = 8.61 (d, J = 9.2 Hz, 1H), 8.56 (s, 1H), 8.15 (d, J = 7.6 Hz, 1H), 7.81 (t, J = 6.8 Hz, 1H), 7.41 (s, 1H), 7.32-7.29 (m, 4H), 7.23-7.21 (m, 2H), 6.18 (s, 1H), 5.80 (s, 1H), 5.53 (d, J = 10.0 Hz, 1H), 1.49 (s, 3H), 1.47 (s, 3H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 163.63, 152.74, 149.79, 148.30, 145.53, 141.37, 137.38, 128.06, 126.78, 126.43, 126.30, 122.53, 110.03, 107.66, 56.23, 43.24, 26.15, 25.04 ppm. HRMS (ESI⁺): calcd for $\text{C}_{20}\text{H}_{21}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 321.1598, found 321.1598.



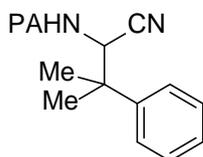
N-(2-Methyl-1-(naphthalen-1-yl)-2-phenylpropyl)picolinamide (4p)

Following the general procedure. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1, v/v) afforded **4p** as yellow oil (51.3 mg, 54% yield). ^1H NMR (400 MHz, CDCl_3): δ = 8.85 (d, J = 10.0 Hz, 1H), 8.58 – 8.56 (m, 1H), 8.43 (d, J = 8.6 Hz, 1H), 8.14 – 8.10 (m, 1H), 7.82 (d, J = 8.4 Hz, 1H), 7.80 – 7.75 (m, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.57-7.53 (m, 1H), 7.48-7.44 (m, 1H), 7.40-7.37 (m, 1H), 7.34-7.33 (m, 4H), 7.30 – 7.27 (m, 1H), 7.24 (d, J = 8.0 Hz, 1H), 6.71 (d, J = 7.6 Hz, 1H), 6.41 (d, J = 9.6 Hz, 1H), 1.62 (s, 3H), 1.42 (s, 3H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 163.51, 150.03, 148.28, 144.49, 137.36, 136.53, 133.50, 132.52, 128.78, 128.04, 127.89, 127.75, 126.69, 126.19, 126.17, 125.74, 125.44, 124.54, 123.94, 122.43, 55.23, 43.54, 27.93, 26.09 ppm. HRMS (ESI⁺): calcd for $\text{C}_{26}\text{H}_{25}\text{N}_2\text{O}$ [M+H]⁺ 381.1961, found 381.1968.



N-(1-Phenylpentan-2-yl)picolinamide (4q)

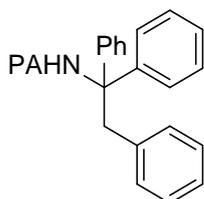
Following the general procedure. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1, v/v) afforded **4q** as yellow oil (26.8 mg, 40% yield). ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ = 8.62 (s, 1H), 8.49 (d, J = 9.2 Hz, 1H), 7.96 (s, 2H), 7.57 (s, 1H), 7.24-7.20 (m, 4H), 7.14-7.13 (m, 1H), 4.22-4.21 (m, 1H), 2.94 – 2.86 (m, 1H), 2.83-2.78 (m, 1H), 1.64 – 1.44 (m, 2H), 1.39 – 1.19 (m, 2H), 0.84 (t, J = 7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ = 163.24, 149.99, 148.29, 139.17, 137.75, 129.06, 128.09, 126.37, 125.93, 121.85, 50.00, 40.45, 36.19, 18.95, 13.82 ppm. HRMS (ESI⁺): calcd for $\text{C}_{17}\text{H}_{20}\text{N}_2\text{NaO}$ [M+Na]⁺ 291.1468, found 291.1466.



N-(1-Cyano-2-methyl-2-phenylpropyl)picolinamide (4r)

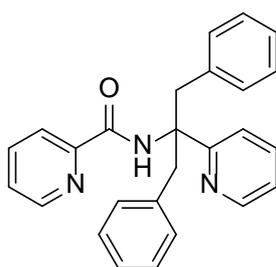
Following the general procedure. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 7/1, v/v) afforded **4r** as yellow oil (37.6 mg, 54% yield). ^1H NMR (400 MHz, CDCl_3): δ = 8.53 (d, J = 4.8 Hz, 1H), 8.31 (d, J = 10.0 Hz, 1H), 8.15 (d, J = 7.6 Hz, 1H), 7.86 (t, J = 7.6 Hz, 1H), 7.53 – 7.49 (m, 2H), 7.46-7.44 (m, 1H), 7.43 – 7.38 (m, 2H), 7.34 – 7.29 (m, 1H), 5.33 (d, J = 10.0 Hz, 1H), 1.62 (s, 3H), 1.57 (s, 3H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 163.91, 148.48, 148.45, 142.34, 137.65, 128.89, 127.70,

127.03, 126.55, 122.82, 117.59, 59.03, 57.42, 50.74, 41.91, 25.45, 24.96 ppm. HRMS (ESI⁺): calcd for C₁₇H₁₈N₃O [M+H]⁺ 280.1444, found 280.1444.



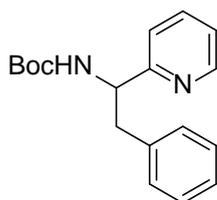
***N*-(2-phenyl-1,1-diphenylethyl)picolinamide (4s)**

Following the general procedure. Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1, v/v) afforded **4s** as yellow oil (23.6 mg, 25% yield). ¹H NMR (400 MHz, CDCl₃): δ = 9.20 (s, 1H), 8.53 (d, *J* = 4.8 Hz, 1H), 8.16 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.85 – 7.81 (m, 1H), 7.44 – 7.41 (m, 1H), 7.31 – 7.27 (m, 8H), 7.26 – 7.24 (m, 1H), 7.11 (dd, *J* = 10.3, 4.3 Hz, 2H), 7.02 (t, *J* = 7.4 Hz, 2H), 6.67 – 6.64 (m, 2H), 4.09 (s, 2H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 163.50, 150.46, 148.09, 145.31, 137.43, 136.68, 131.09, 128.13, 127.49, 127.18, 127.03, 126.32, 126.25, 121.97, 64.98, 43.39 ppm. HRMS (ESI⁺): calcd for C₂₆H₂₂N₂NaO [M+Na]⁺ 401.1624, found 401.1621.



***N*-(1,3-Diphenyl-2-(pyridin-2-yl)propan-2-yl)picolinamide (3ab)**

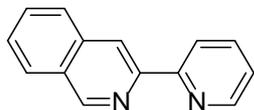
Melting point: 132~134 °C. ¹H NMR (400 MHz, CDCl₃): δ = 9.93 (s, 1H), 8.52 (s, 1H), 8.45 (s, 1H), 8.31 (d, *J* = 7.6 Hz, 1H), 7.87 (t, *J* = 7.6 Hz, 1H), 7.73 (t, *J* = 7.6 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.39-7.37 (m, 1H), 7.16-7.14 (m, 1H), 7.02 – 6.94 (m, 6H), 6.77 (d, *J* = 6.4 Hz, 4H), 4.32 (d, *J* = 13.6 Hz, 2H), 3.50 (d, *J* = 13.6 Hz, 2H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 164.34, 159.81, 151.17, 148.51, 148.05, 137.19, 136.88, 136.10, 130.25, 127.77, 126.30, 125.90, 121.86, 121.83, 121.67, 64.90, 43.84 ppm. HRMS (ESI⁺): calcd for C₂₆H₂₄N₃O [M+H]⁺ 394.1914, found 394.1912.



***tert*-Butyl (2-phenyl-1-(pyridin-2-yl)ethyl)carbamate (5a)**

Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **5a** as a white solid (63.5 mg, 85% yield), melting point: 78~80 °C. ¹H NMR (400 MHz, CDCl₃): δ = 8.55 (s, 1H), 7.50-7.46 (m, 1H), 7.17-7.15 (m, 4H), 6.99-6.96 (m,

2H), 6.85 (d, $J = 6.8$ Hz, 1H), 5.81-5.79 (m, 1H), 4.97-4.95 (m, 1H), 3.21 (d, $J = 8.0$ Hz, 1H), 3.06 (d, $J = 8.0$ Hz, 1H), 1.42 (s, 9H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 159.54, 155.34, 149.30, 137.57, 136.20, 129.61, 128.24, 126.42, 122.50, 122.37, 79.39, 56.90, 42.96, 28.50$ ppm. HRMS (ESI⁺): calcd for $\text{C}_{18}\text{H}_{22}\text{N}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$ 321.1573, found 321.1575.



3-(Pyridin-2-yl)isoquinoline (**5b**)

Purification via column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1, v/v) afforded **5b** as yellow oil (21.6 mg, 42% yield). ^1H NMR (400 MHz, CDCl_3): $\delta = 9.33$ (s, 1H), 8.79 (s, 1H), 8.73 (s, 1H), 8.52 (d, $J = 7.6$ Hz, 1H), 8.01 (d, $J = 8.0$ Hz, 1H), 7.97 (d, $J = 8.0$ Hz, 1H), 7.86 (t, $J = 7.4$ Hz, 1H), 7.71 (t, $J = 7.0$ Hz, 1H), 7.62 (t, $J = 6.8$ Hz, 1H), 7.31 (s, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 156.59, 152.24, 149.97, 149.49, 137.18, 136.75, 130.71, 128.86, 127.83, 127.77, 127.67, 123.47, 121.40, 117.81$ ppm. HRMS (ESI⁺): calcd for $\text{C}_{14}\text{H}_{11}\text{N}_2$ $[\text{M}+\text{H}]^+$ 207.0917, found 207.0912.

VII. Copies of ^1H NMR and ^{13}C NMR spectra

