Supporting Information for

Amine Directed Pd(II)-Catalyzed C-H bond Functionalization under Ambient Conditions
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Table of Contents:

General Experimental .............................................................- 2 -
Synthesis of Palladacycle 1a.Pd and Stoichiometric studies............................- 3 -
General Procedures ................................................................- - 5 -
C-H Carbonylation Products .....................................................- 7 -
C-H Arylation Products .............................................................- 15 -
Iterative C-H Functionalization ................................................--- - 16 -
C-H Amination Products .............................................................- 18 -
PMP group deprotection .............................................................- 20 -
Synthesis of Starting Materials ......................................................- 21 -
References ..............................................................................- 32 -
NMR Spectra ...........................................................................- 33 -
General Experimental

$^1$H NMR spectra were recorded on a Bruker DPX 400 spectrometer operating at 400 MHz or on a Bruker DPX-500 operating at 500 MHz in deuterochloroform (CDCl$_3$) unless otherwise stated. $^{13}$C NMR spectra were recorded on a Bruker DPX 400 spectrometer operating at 100 MHz. Chemical shifts ($\delta$) are quoted relative to residual solvent (CHCl$_3$, $\delta = 7.26$ ppm for $^1$H and $\delta = 77.0$ for $^{13}$C in CDCl$_3$) and coupling constants ($J$) are corrected and quoted to the nearest 0.1 Hz. The following abbreviations are used to indicate the multiplicity of the signals: s = singlet; d = doublet; t = triplet; q = quartet; qn = quintet; m = multiplet; b = broad; app = apparent; and associated combinations, e.g. dd = doublet of doublets. The temperature of the acquisition of the NMR spectra was 298 ± 3K. DEPT135 and 2-dimensional experiments (COSY, HMBC and HMQC) were used to support assignments where appropriate but are not included. High resolution mass spectra (HRMS) were measured on a Micromass Q-TOF spectrometer using EI (electron impact) or ESI (electrospray ionisation) techniques at the Department of Chemistry, University of Cambridge or at the EPSRC Mass Spectrometry Service at the University of Swansea. Infared (IR) spectra were recorded on a Perkin Elmer 1FT-IR Spectrometer fitted with an ATR sampling accessory as neat films, either through direct application or deposited in CHCl$_3$. Optical rotations were measured in CHCl$_3$ on a Perkin Elmer 343 Polarimeter; $[\alpha]D$ values are reported in 10-1 degrees cm$^2$ g$^{-1}$ at 589 nm. Chiral HPLC analysis was performed on HP Agilent 1100 apparatus. Melting points (m.p.) were recorded using a Reichert hot stage apparatus and are reported uncorrected. All anhydrous solvents were dried by standard techniques and freshly distilled before use. Diethyl ether and tetrahydrofuran were distilled from lithium aluminium hydride; acetonitrile, dichloromethane and toluene from calcium hydride; and triethylamine from potassium hydroxide. N, N-dimethylformamide, Acetic acid, 1,2-Dichoroethane, 2-propanol and dimethyl sulfoxide were purchased in anhydrous form. All flash chromatography were carried out using dry packed Merck 9385 Kieselgel 60 silica gel. Reactions monitored by thin layer chromatography (TLC) were carried out on Kieselgel 60 PF254 (Merck) 0.2 mm plates.

All reagents were purified by standard procedures or used as obtained from commercial sources. Reactions were carried out using oven dried glassware and under an atmosphere of nitrogen unless otherwise stated.
Synthesis of Palladacycle 1a.Pd and Stoichiometric studies

**Palladacycle Synthesis**

![Chemical structure of 1a.Pd]

Amine 1a (200mg, 0.71 mmol, 1 eq) and palladium acetate (160mg, 0.71 mmol, 1 eq) were stirred in toluene (20 mL) at room temperature for 16 hours. The solvent was then removed in *vacuo*, to the resulting slurry was added 40-60°C petroleum ether (7 mL) and a solid crashed out. The solid was filtered off and washed with 40-60°C petroleum ether (3x5 mL) and dried under vacuum overnight to afford palladacycle **1a.Pd** as a beige solid (268mg, 0.60 mmol, 85% yield); IR ν max (film) / cm⁻¹: 3154, 2931, 1547, 1509, 1426, 1031, 837, 743. ¹H NMR (400MHz, (CD)₂SO) δH: 9.75 (1H, d, J = 7.2 Hz, NH) 7.47 (1H, d, J = 7.6 Hz), 7.08-6.97 (3H, m), 6.78 (2H, d, J = 8.8 Hz), 6.64 (2H, d, J = 9.2 Hz), 3.69 (3H, s), 3.40-3.30 (1H, m), 3.00 (1H, d, J = 13.2 Hz), 2.71 (1H, d, J = 3.6 Hz), 2.29-2.19 (1H, m), 1.92 (3H, q, J = 10.8 Hz), 1.82 (3H, s), 1.64-1.44 (3H, m). ¹³C NMR (100MHz, (CD)₂SO) δC: 178.6, 156.8, 146.0, 142.0, 141.5, 134.3, 126.9, 125.8, 125.4, 124.1, 114.7, 61.9, 55.6, 54.4, 31.3, 27.1, 26.1, 25.2, 19.1; Elem. Analysis C = 57.30, H = 5.85, N = 3.02, requires C = 56.57, H = 5.65, N = 3.14.

**Stoichiometric Carbonylation**

![Chemical structure of 2a]

Palladacycle **1a.Pd** (25mg, 0.056 mmol) was added in a microwave vial followed by chloroform (2 mL). The solution was bubbled for 5 mn with carbon monoxide then stirred for 3h under an atmosphere of carbon monoxide delivered form a toy balloon. The black precipitate was then filtered off on Celite and the solvent was removed in *vacuo* to afford carbonylated compound **2a** (15mg, 0.049 mmol, 88% yield). See catalytic procedure for full characterization.
Stoichiometric Arylation

Palladacycle 1a.Pd (25mg, 0.056 mmol, 1 eq) was added in a microwave vial followed by phenylboronic acid (7.6 mg, 0.062 mmol, 1.1 eq) mL) and benzoquinone (6.1mg, 0.056 mmol, 1 eq). A 1:1 mixture of dichloromethane and methanol (1 mL) was added and the solution was stirred at room temperature for 20 hours. The solid precipitates were filtered off on celite and the solvent was removed in vacuo. Purification by flash column chromatography (99/1 40-60°C Petroleum Ether/EtOAc) afforded amine 3a (17 mg, 0.048 mmol, 86% yield). See catalytic procedure for full characterization.

Stoichiometric Amination

Palladacycle 1a.Pd (25mg, 0.056 mmol, 1 eq) was added in a microwave vial followed by cesium carbonate (37 mg, 0.11 mmol, 2 eq) mL) and toluene (2 mL). The solution was heated at 110°C for 18 hours. The solid precipitates were filtered off on celite and the solvent was removed in vacuo to get indoline 4a (14 mg, 0.0504 mmol, 90% yield). See catalytic procedure for full characterization.
General Procedures

**General Procedure A for C-H bond carbonylation**

Palladium acetate (4.5 mg, 0.02 mmol, 10 mol%), Benzoquinone (43.6 mg, 0.40 mmol, 2 eq) and sodium acetate (98 mg, 1.20 mmol, 6 eq) were added in a dry flask which was then sealed with a teflon septa. A solution of the appropriate amine (0.1 M, 0.20 mmol, 1 eq) in acetic acid (2 mL) was added via syringe. The solution was then stirred until the base dissolved (usually 5 minutes). The flask was then fitted with one balloon containing CO and one balloon containing O₂ and the solution was stirred at the appropriate temperature for the appropriate time. The completion of the reaction was checked by TLC, the solution was then filtered through Celite eluting with ethyl acetate. The organic phase was washed with a saturated aqueous solution of sodium bicarbonate (×3), dried over magnesium sulfate and concentrated in vacuo. The crude product was purified by flash column chromatography.

**General Procedure B for C-H bond carbonylation**

Palladium acetate (4.5 mg, 0.02 mmol, 10 mol%), Benzoquinone (43.6 mg, 0.40 mmol, 2 eq) and sodium acetate (98 mg, 1.20 mmol, 6 eq) were added in a dry flask which was then sealed with a teflon septa. A solution of the appropriate amine (0.1 M, 0.20 mmol, 1 eq) in acetic acid (2 mL) was added via syringe followed by t-BuOOAc (105 mg, 50% solution, 0.40 mmol, 2 eq). The solution was then stirred until the base dissolved (usually 5 minutes). The flask was then fitted with one balloon containing CO and one balloon containing O₂ and the solution was stirred at the appropriate temperature for the appropriate time. The completion of the reaction was checked by TLC, the solution was then filtered through Celite eluting with ethyl acetate. The organic phase was washed with a saturated aqueous solution of sodium bicarbonate (×3), dried over magnesium sulfate and concentrated in vacuo. The crude product was purified by flash column chromatography.
**General Procedure for C-H bond Arylation.**

\[ \text{R}_1 \text{R}_2 \text{NH} \xrightarrow{\text{20 mol\% Pd(OAc)}_2, \text{2 eq Benzoquinone, 2 eq ArB(OH)_2, 1.5 eq t-BuOOAc}} \text{DCM/PrOH} \rightarrow \text{R}_1 \text{R}_2 \text{NH} \]

Palladium acetate (9 mg, 0.040 mmol, 20 mol%), benzoquinone (43.2 mg, 0.40 mmol, 2eq) and the appropriate boronic acid (0.40 mmol, 2 eq) were added in a dry flask. Dry dichloromethane (1.5 mL) was added followed by a solution of the appropriate amine (0.20 mmol, 1 eq) in isopropanol (0.3 mL). t-BuOOAc (50% solution, 78 mg, 0.30 mmol, 1.5 eq) was then added via syringe and the solution was stirred at room temperature for the appropriate time. The reaction was monitored by TLC until completion, solvent was removed under vacuum and the crude product was purified by flash column chromatography.

**General Procedure for C-H bond Amination**

\[ \text{R}_1 \text{R}_2 \text{NH} \xrightarrow{\text{10 mol\% Pd(OAc)}_2, \text{2 eq NaHCO}_3, \text{1 eq Pivalic acid, 4 eq Cu(OAc)}_2} \text{DCE, 110°C} \rightarrow \text{R}_1 \text{R}_2 \text{N} \]

In a dry flask were added the appropriate amine (0.20 mmol, 1 eq), palladium acetate (4.5 mg, 0.20 mmol, 10 mol%), sodium bicarbonate (42 mg, 0.40 mmol, 2 eq), pivalic acid (20.4 mg, 0.20 mmol, 1 eq) and copper acetate (144 mg, 0.80 mmol, 4 eq). The tube was then sealed and purged with argon. 1,2-dichloroethane (4 mL) was added and the solution was bubbled for 5 minutes with argon then heated at 110°C for the required amount of time. The completion of the reaction was checked by TLC, the solution was filtered on silica eluting with ethyl acetate and the organic phase was evaporated under vacuum. The residue was purified by flash column chromatography.
C-H Carbonylation Products

(±)-cis-5-(4-methoxyphenyl)-1,3,4,4a,5,10b-hexahydrophenanthridin-6(2H)-one

Prepared according to general procedure B for C-H bond carbonylation. (±)-4-methoxy-N-(cis-2-phenylcyclohexyl)aniline 1a (56 mg, 0.20 mmol) was reacted at room temperature for 36 hours. The crude product was purified by flash column chromatography (95/5 to 70/30 40-60°C Petroleum Ether/EtOAc) to afford compound 2a as a brown solid (52 mg, 85% yield); Rf 0.21 (80/20 40-60°C Petroleum Ether/EtOAc); IR ν max (film) / cm⁻¹: 2926, 2850, 1625, 1595, 1509, 1458, 1246, 826, 756; ¹H NMR (400MHz, CDCl₃) δ: 8.16 (1H, dd, J = 7.6 Hz and J = 1.3 Hz), 7.52 (1H, td, J = 7.6 Hz and J = 1.2 Hz), 7.35 (2H, q, J = 7.6 Hz), 7.27-7.23 (2H, m), 6.97-6.94 (2H, m), 3.87 (1H, qu, J = 4.8 Hz), 3.81 (3H, s), 3.56 (1H, d, J = 4.4 Hz), 2.41 (1H, d, J = 10.8 Hz), 1.82-1.71 (2H, m), 1.60-1.44 (4H, m), 1.28-1.20 (1H, m); ¹³C NMR (100MHz, CDCl₃) δ: 164.1, 158.3, 134.5, 132.2, 129.5, 129.0, 128.8, 126.7, 125.3, 116.1, 114.4, 61.4, 55.5, 38.0, 27.3, 27.1, 23.8, 21.0; m/z HRMS (ESI) found [M+H]⁺ 308.1647, C₂₀H₂₂NO₂ requires 308.1645.

(±)-cis-8-methoxy-5-(4-methoxyphenyl)-1,3,4,4a,5,10b-hexahydrophenanthridin-6(2H)-one

Prepared according to general procedure A for C-H bond carbonylation. (±)-4-methoxy-N-(cis-2-(4-methoxyphenyl)cyclohexyl)aniline 1f (62 mg, 0.20 mmol) was reacted at room temperature for 16 hours. The crude product was purified by flash column chromatography (95/5 to 70/30 40-60°C Petroleum Ether/EtOAc) to afford compound 2f as a grey solid (59 mg, 87% yield); TLC Rf 0.22 (80/20 Petroleum Ether/EtOAc); IR ν max (film) / cm⁻¹: 2926, 2845, 1641, 1600, 1507, 1456, 1241, 1021, 804, 735; ¹H NMR (500MHz, CDCl₃) δ: 7.70 (1H, d, J = 2.5 Hz), 7.25-7.23 (3H, m), 7.08 (1H, dd, J = 8.5 Hz and J = 3.0 Hz), 6.95 (2H, d, J = 8.5 Hz), 3.86 (3H, s), 3.83 (4H, bs), 3.52 (1H, bs), 2.40 (1H, d, J = 11.5 Hz), 1.80-1.70 (2H, m), 1.60-1.44 (4H, m), 1.26-1.18 (1H, m); ¹³C NMR (100MHz, CDCl₃) δ: 164.1, 158.4, 158.3, 134.5, 131.8, 130.6, 128.8, 126.6, 119.5, 114.3, 112.3,
61.6, 55.5, 55.4, 37.2, 27.2, 27.1, 23.9, 20.8; m/z HRMS (ESI) found [M+H]\(^+\) 338.1748, C\(_{21}\)H\(_{24}\)NO\(_3\) requires 338.1751.

\((\pm)-\text{cis-8-bromo-5-(4-methoxyphenyl)-1,3,4,4a,5,10b-hexahydrophenanthridin-6(2H)-one}\)

Prepared according to general procedure B for C-H bond carbonylation. \((\pm)-N-(\text{cis-2-(4-bromophenyl)cyclohexyl)-4-methoxyaniline \(1g\)}} (72 mg, 0.20 mmol) was reacted at 50°C for 36 hours. The crude product was purified by flash column chromatography (95/5 to 70/30 40-60°C Petroleum Ether/EtOAc) to afford compound 2g as a red sticky oil (40 mg, 52% yield); TLC Rf 0.18 (80/20 Petroleum Ether/EtOAc); IR ν max (film) / cm\(^{-1}\): 3064, 2928, 2850, 1650, 1588, 1504, 1441, 1238, 1030, 807, 708; \(^1\)H NMR (400MHz, CDCl\(_3\)) δ\(_H\): 8.29 (1H, d, \(J = 2.0\) Hz), 7.64 (1H, d, \(J = 7.6\) Hz), 7.26-7.23 (3H, m), 6.95 (2H, d, \(J = 7.2\) Hz), 3.86-3.83 (4H, m), 3.52 (1H, bs), 2.41 (1H, bd, \(J = 11.6\) Hz), 1.82-1.72 (2H, m), 1.61-1.29 (4H, m), 1.26-1.19 (1H, m); \(^13\)C NMR (100MHz, CDCl\(_3\)) δ\(_C\): 162.8, 158.5, 138.5, 135.0, 134.1, 131.9, 131.4, 128.7, 127.3, 120.7, 114.5, 61.4, 55.5, 37.7, 27.2, 26.9, 23.8, 20.7; m/z HRMS (ESI) found [M+H]\(^+\) 386.0742, C\(_{20}\)H\(_{21}\)NO\(_3\)Br requires 386.0750.

\((\pm)-\text{cis-9-methoxy-5-(4-methoxyphenyl)-1,3,4,4a,5,10b-hexahydrophenanthridin-6(2H)-one}\)

Prepared according to general procedure B for C-H bond carbonylation. \((\pm)-\text{4-methoxy-N-(cis-2-(3-methoxyphenyl)cyclohexyl)aniline \(1h\)}} (62 mg, 0.20 mmol) was reacted at 50°C for 36 hours. The crude product was purified by flash column chromatography (95/5 to 70/30 40-60°C Petroleum Ether/EtOAc) to afford compound 2h as a brown solid (44 mg, 65% yield); TLC Rf 0.28 (80/20 Petroleum Ether/EtOAc); IR ν max (film) / cm\(^{-1}\): 2916, 2878, 1640, 1520, 1222, 1019, 822, 720; \(^1\)H NMR (400MHz, CDCl\(_3\)) δ\(_H\): 8.11 (1H, d, \(J = 8.8\) Hz), 7.24 (2H, d, \(J = 8.8\) Hz), 6.94 (2H, d, \(J = 9.2\) Hz), 6.86 (1H, dd, \(J = 8.8\) Hz and \(J = 2.4\) Hz), 6.82 (1H, d, \(J = 1.6\) Hz), 3.88 (3H, s), 3.85 (1H, d, \(J = 4.8\) Hz), 3.83 (3H, s), 3.51 (1H, d, \(J = 4\) Hz), 2.37 (1H, dd, \(J = 14\) Hz and \(J = 4\) Hz), 1.79-1.21 (7H, m); \(^13\)C NMR (100MHz, CDCl\(_3\)) δ\(_C\): 164.1, 162.9, 158.2, 141.9, 134.6, 131.2, 128.9, 122.4, 114.3,
111.3, 111.2, 61.4, 55.5, 55.4, 38.3, 27.3, 27.2, 23.8, 21.1; m/z HRMS (ESI) found [M+H]$^+$ 338.1748, C$_{21}$H$_{24}$NO$_3$ requires 338.1751.

(±)-cis-5-(4-methoxyphenyl)-9-methyl-1,3,4,4a,5,10b-hexahydropyridin-6(2H)-one

Prepared according to general procedure A for C-H bond carbonylation. (±)-4-methoxy-N-(cis-2-methyl-2-phenylcyclohexyl)aniline 1i (59 mg, 0.20 mmol) was reacted at room temperature for 36 hours. The crude product was purified by flash column chromatography (95/5 to 70/30 40-60°C Petroleum Ether/EtOAc) to afford compound 2i as a slightly red solid (61 mg, 96% yield). TLC Rf 0.23 (80/20 Petroleum Ether/EtOAc); IR ν max (film) / cm$^{-1}$: 2926, 2858, 1645, 1607, 1509, 1432, 1250, 1026, 830, 728; $^1$H NMR (400MHz, CDCl$_3$) δ$_H$: 8.04 (1H, d, J = 8.0 Hz), 7.24 (2H, d, J = 9.2 Hz), 7.16 (1H, d, J = 8.0 Hz), 7.13 (1H, s), 6.94 (2H, d, J = 8.8 Hz), 3.88-3.81 (1H, m), 3.87 (3H, s), 3.50 (1H, d, J = 3.6 Hz), 2.43 (3H, s), 2.41 (1H, bs), 1.80-1.20 (7H, m); $^{13}$C NMR (100MHz, CDCl$_3$) δ$_C$: 164.3, 158.3, 142.6, 139.8, 134.6, 129.1, 128.9, 127.5, 127.0, 125.9, 114.3, 61.2, 55.5, 38.1, 27.3, 27.1, 23.8, 21.9, 21.1; m/z HRMS (ESI) found [M+H]$^+$ 322.1799, C$_{21}$H$_{24}$NO$_2$ requires 322.1802.

(±)-cis-9-chloro-5-(4-methoxyphenyl)-1,3,4,4a,5,10b-hexahydropyridin-6(2H)-one

Prepared according to general procedure B for C-H bond carbonylation. (±)-N-(cis-2-(3-chlorophenyl)cyclohexyl)-4-methoxyaniline 1j (63 mg, 0.20 mmol) was reacted at 50°C for 36 hours. The crude product was purified by flash column chromatography (95/5 to 70/30 40-60°C Petroleum Ether/EtOAc) to afford compound 2j as a brown solid (47 mg, 69% yield); TLC Rf 0.22 (80/20 Petroleum Ether/EtOAc); IR ν max (film) / cm$^{-1}$: 3060, 3024, 2929, 2854, 1648, 1590, 1507, 1470, 1321, 1036, 815, 702; $^1$H NMR (400MHz, CDCl$_3$) δ$_H$: 8.10 (1H, d, J = 8.4 Hz), 7.32-7.26 (2H, m), 7.24 (2H, d, J = 9.2 Hz), 6.95 (2H, d, J = 9.2 Hz), 3.88-3.84 (1H, m), 3.83 (3H, s), 3.55 (1H, d, J = 4.0 Hz), 2.38 (1H, bd, J = 13.6 Hz), 1.84-1.72 (2H, m), 1.63-1.45 (4H, m), 1.26-1.19 (1H, m); $^{13}$C NMR (100MHz, CDCl$_3$) δ$_C$: 163.3, 158.4, 141.6, 138.5, 134.2, 130.7, 128.7, 128.1, 127.0, 125.6, 114.4,
61.4, 55.5, 38.0, 27.3, 26.9, 23.7, 20.8; m/z HRMS (ESI) found [M+H]+ 342.1256, C_{20}H_{21}NO_2Cl requires 342.1255.

(±)-cis-5-(4-methoxyphenyl)-1,3,4,4a,5,12b-hexahydrobenzo[j]phenanthridin-6(2H)-one

Prepared according to general procedure A for C-H bond carbonylation. (±)-4-methoxy-N-(cis-2-(naphthalen-2-yl)cyclohexyl)aniline 1k (66 mg, 0.20 mmol) was reacted at room temperature for 36 hours. The crude product was purified by flash column chromatography (95/5 to 70/30 40-60°C Petroleum Ether/EtOAc) to afford compound 2k as a grey solid (60 mg, 84% yield). TLC Rf 0.32 (70/30 Petroleum Ether/EtOAc); IR ν max (film) / cm\(^{-1}\): 3062, 2999, 2926, 2851, 1648, 1625, 1601, 1507, 1427, 1230, 1025, 876; \(^1\)H NMR (500MHz, CDCl\(_3\)) \(\delta\)H: 8.73 (1H, s), 7.97 (1H, d, \(J = 8.0\) Hz), 7.86 (1H, d, \(J = 8.0\) Hz), 7.74 (1H, s), 7.47 (1H, t, \(J = 1.6\) Hz), 7.36 (2H, d, \(J = 8.8\) Hz), 6.98 (2H, d, \(J = 9.0\) Hz), 3.90-3.86 (1H, m), 3.85 (3H, s), 3.77 (1H, bs), 2.66 (1H, d, \(J = 13.0\) Hz), 1.90-1.81 (2H, m), 1.49-1.43 (3H, m), 1.46 (1H, q, \(J = 11.0\) Hz), 1.29-1.22 (1H, m); \(^{13}\)C NMR (100MHz, CDCl\(_3\)) \(\delta\)C: 164.1, 158.4, 135.6, 135.2, 134.8, 131.8, 130.2, 129.3, 128.7, 127.8, 127.6, 127.3, 126.0, 124.2, 114.4, 62.3, 55.5, 38.1, 27.7, 27.0, 24.4, 20.3; m/z HRMS (ESI) found [M+H]\(^+\) 358.1798, C_{24}H_{24}NO_2 requires 358.1802.

(±)-cis-5-(4-methoxyphenyl)-10b-methyl-1,3,4,4a,5,10b-hexahydrophenanthridin-6(2H)-one

Prepared according to general procedure B for C-H bond carbonylation. (±)-4-methoxy-N-(cis-2-methyl-2-phenylcyclohexyl)aniline 1l (59 mg, 0.20 mmol) was reacted at 50°C for 36 hours. The crude product was purified by flash column chromatography (95/5 to 70/30 40-60°C Petroleum Ether/EtOAc) to afford compound 2l as a green oil (32 mg, 50% yield). TLC Rf 0.32 (70/30 Petroleum Ether/EtOAc); IR ν max (film) / cm\(^{-1}\): 3063, 2932, 2856, 1653, 1602, 1507, 1248, 1036, 830, 761; \(^1\)H NMR (400MHz, CDCl\(_3\)) \(\delta\)H: 8.19 (1H, dd, \(J = 7.6\) Hz and \(J = 1.2\) Hz), 7.35 (1H, dd, \(J = 7.6\) Hz and \(J = 1.6\) Hz), 7.35 (1H, t, \(J = 7.6\) Hz and \(J = 1.2\) Hz), 7.32 (1H, d, \(J = 7.6\) Hz), 6.96 (2H, d, \(J = 8.8\) Hz), 3.83 (3H, s), 3.42 (1H, dd, \(J = 11.6\) Hz and \(J = 4.0\) Hz), 2.53 (1H, dd, \(J = 8.8\) Hz), 2.18 (1H, d, \(J = 11.6\) Hz)
14.0 Hz and $J = 2.4$ Hz), 1.97 (1H, dd, $J = 12.8$ Hz and $J = 2.8$ Hz), 1.66-1.45 (3H, m), 1.49 (3H, s), 1.44-1.14 (3H, m); $^{13}$C NMR (100MHz, CDCl$_3$) $\delta_{C}$: 163.1, 158.3, 143.7, 135.2, 132.4, 129.2, 128.4, 126.5, 124.2, 114.4, 69.1, 55.5, 39.1, 35.0, 31.4, 28.7, 25.2, 21.6; m/z HRMS (ESI) found [M+H]$^+$ 322.1799, C$_{21}$H$_{24}$NO$_2$ requires 322.1802.

(±)-cis-5-(4-methoxyphenyl)-3,4,4a,5-tetrahydro-1$H$-pyrano[4,3-c]isoquinolin-6(10b$H$)-one

Prepared according to general procedure B for C-H bond carbonylation. (±)-cis-N-(4-methoxyphenyl)-4-phenyltetrahydro-2$H$-pyran-3-amine 1m (57 mg, 0.20 mmol) was reacted at room temperature for 16 hours. The crude product was purified by flash column chromatography (95/5 to 70/30 40-60°C Petroleum Ether/EtOAc) to afford compound 2m as a grey solid (34 mg, 55% yield); TLC Rf 0.28 (80/20 Petroleum Ether/EtOAc); IR ν max (film) / cm$^{-1}$: 3068, 2960, 2847, 1648, 1509, 1459, 1243, 1029, 732; $^1$H NMR (400MHz, CDCl$_3$) $\delta_{H}$: 8.17 (1H, dd, $J = 8.0$ Hz and $J = 1.6$ Hz), 7.55 (1H, td, $J = 7.6$ Hz and $J = 1.6$ Hz), 7.24-7.39 (2H, m), 7.24 (2H, d, $J = 8.8$ Hz), 6.97 (2H, d, $J = 8.8$ Hz), 4.40 (1H, dd, $J = 8.4$ Hz and $J = 5.2$ Hz), 4.17 (1H, q, $J = 4.0$ Hz), 3.83 (3H, s), 3.81-3.74 (2H, m), 3.50-3.44 (2H, m), 1.87-1.74 (2H, m); $^{13}$C NMR (100MHz, CDCl$_3$) $\delta_{C}$: 164.5, 158.5, 137.0, 133.6, 132.5, 129.2, 129.1, 128.8, 127.4, 126.0, 114.6, 67.2, 65.3, 57.3, 55.5, 38.9, 28.0; m/z HRMS (ESI) found [M+H]$^+$ 310.1436, C$_{19}$H$_{20}$NO$_3$ requires 310.1438.

(±)-cis-8-methoxy-5-(4-methoxyphenyl)-1,3,4,4a,5,10b-hexahydrophenanthridin-6(2$H$)-one

Prepared according to general procedure B for C-H bond carbonylation. (±)-cis-N-(4-methoxyphenyl)-4-phenyl-1-tosylpiperidin-3-amine 1n (87 mg, 0.20 mmol) was reacted at 50°C for 16 hours. The crude product was purified by flash column chromatography (100/0 to 99.5/0.5 CH$_2$Cl$_2$/MeOH) to afford compound 2n as a white foam (50 mg, 54% yield); TLC Rf 0.37 (98/2 CH$_2$Cl$_2$/MeOH); IR ν max (film) / cm$^{-1}$: 2930, 2849, 1651, 1601, 1510, 1460, 1244, 1162, 910, 812, 725; $^1$H NMR (400MHz, CDCl$_3$) $\delta_{H}$: 8.12 (1H, dd, $J = 8.0$ Hz and $J = 1.2$ Hz), 7.62 (2H, d, $J = 8.4$ Hz), 7.58 (1H, dd,
$J = 7.6\text{ Hz and } J = 1.6\text{ Hz}$, 7.52 (1H, d, $J = 7.6\text{ Hz}$), 7.42 (1H, td, $J = 8.0\text{ Hz and } J = 1.2\text{ Hz}$), 7.33 (2H, d, $J = 8.0\text{ Hz}$), 7.06 (2H, d, $J = 8.0\text{ Hz}$), 6.90 (2H, d, $J = 8.6\text{ Hz}$), 3.93 (1H, dd, $J = 12.0\text{ Hz and } J = 4.8\text{ Hz}$), 3.81 (4H, bs), 3.57-3.54 (1H, m), 3.14 (1H, bs), 3.02 (1H, dd, $J = 12.0\text{ Hz and } J = 1.2\text{ Hz}$), 2.67 (1H, bs), 2.45 (3H, s), 1.90-1.85 (2H, m); $^{13}$C NMR (100MHz, CDCl$_3$) $\delta_C$: 164.4, 158.6, 144.0, 136.7, 133.2, 132.9, 132.3, 129.8, 129.0, 128.8, 128.7, 127.7, 126.5, 114.6, 110.0, 57.3, 55.5, 46.3, 43.6, 38.1, 26.5, 21.5; m/z HRMS (ESI) found [M+H]$^+$ 463.1681, $C_{26}$H$_{27}$N$_2$O$_4$S requires 463.1686.

(±)-cis-5-(4-methoxyphenyl)-2-(triisopropylsilyl)-5a,6,7,8,9,9a-hexahydro-2H-pyrrolo[3,4-c]quinolin-4(5H)-one

Prepared according to general procedure A for C-H bond carbonylation. (±)-4-methoxy-$N$-(cis-2-(1-(triisopropylsilyl)-1H-pyrrol-3-yl)cyclohexyl)aniline 1o (85 mg, 0.20 mmol) was reacted at room temperature for 14 hours. The crude product was purified by flash column chromatography (95/5 to 70/30 40-60°C Petroleum Ether/EtOAc) to afford compound 2o as an orange oil (68 mg, 75% yield). TLC Rf 0.25 (80/20 Petroleum Ether/EtOAc); IR $\nu$ max (film) / cm$^{-1}$: 2936, 2860, 1645, 1506, 1461, 1248, 1092, 878, 692; $^1$H NMR (400MHz, CDCl$_3$) $\delta_H$: 7.47 (1H, d, $J = 2.0\text{ Hz}$), 7.25 (2H, d, $J = 9.2\text{ Hz}$), 6.92 (2H, d, $J = 9.2\text{ Hz}$), 6.48 (1H, t, $J = 2.0\text{ Hz}$), 3.82 (3H, s), 3.69-3.61 (2H, m), 2.25 (1H, d, $J = 13.6\text{ Hz}$), 1.85-1.54 (5H, m), 1.51-1.42 (5H, m), 1.11 (18H, d, $J = 7.6\text{ Hz}$), $^{13}$C NMR (100MHz, CDCl$_3$) $\delta_C$: 163.4, 158.0, 135.4, 128.9, 127.6, 125.0 119.6, 118.8, 114.2, 65.3, 55.4, 33.8, 27.6, 27.0, 25.1, 20.4, 17.8, 11.6; m/z HRMS (ESI) found [M+H]$^+$ 453.2930, $C_{27}$H$_{41}$N$_2$O$_2$Si requires 453.2932.

(S)-methyl 2-(4-methoxyphenyl)-1-oxo-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole-3-carboxylate

Prepared according to general procedure A for C-H bond carbonylation. (S)-methyl 3-(1H-indol-3-yl)-2-((4-methoxyphenyl)amino)propanoate 1p (65 mg, 0.20 mmol) was reacted at room temperature for 13 hours. The crude product was purified by flash column chromatography (100/0 to 99.5/0.5C CH$_2$Cl$_2$/MeOH) to afford compound 2p as a brown solid (63 mg, 90% yield); TLC Rf 0.25 (98/2 CH$_2$Cl$_2$/MeOH); IR $\nu$ max (film) / cm$^{-1}$: 3417, 2946, 1742, 1651, 1608, 1507, 1405, 1206, 1011, 826.


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\begin{align*}
&\text{\textsuperscript{1}H NMR (500MHz, CDCl}_{3}\text{) }\delta_H: 9.25 (1H, bs), 7.60 (1H, d, J = 8.0 Hz), 7.42-7.37 (3H, m), 7.32 (1H, t, J = 8.0 Hz), 7.17 (1H, t, J = 6.0 Hz), 6.95 (2H, d, J = 9.0 Hz), 4.75 (1H, t, J = 4.0 Hz), 3.84 (3H, s), 3.65 (3H, s), 3.62 (2H, d, J = 4.0 Hz); \text{\textsuperscript{13}C NMR (100MHz, CDCl}_{3}\text{) }\delta_C: 172.0, 160.5, 158.4, 137.5, 134.4, 128.3, 127.1, 125.2, 120.5, 120.3, 115.7, 114.4, 112.5, 60.4, 55.5, 52.9, 25.1; m/z HRMS (ESI) found [M+H]+ 351.1336, C\textsubscript{20}H\textsubscript{19}N\textsubscript{2}O\textsubscript{4} requires 351.1339; [\alpha]D\textsubscript{25} = -13.2° (C = 0.4 in CHCl\textsubscript{3}) for 97% ee; HPLC: DAICEL OD Chiralpak, 80:20 Hexane / isopropanol, flow 1 ml / min; retention time : major enantiomer 31.48 min, minor enantiomer 21.49 min.
\end{align*}
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(±)-2-(4-methoxy-2-methylphenyl)-3-methylisoindolin-1-one

Prepared according to general procedure B for C-H bond carbonylation. (±)-4-methoxy-2-methyl-N-(3-methyl-1-phenylbutan-2-yl)aniline 1q (57 mg, 0.20 mmol) was reacted at 50°C for 36 hours. The crude product was purified by flash column chromatography (95/5 to 70/30 40-60°C Petroleum Ether/EtOAc) to afford compound 2q as a green oil (40 mg, 65% yield, atropisomers mixture); TLC Rf 0.18 (80/20 Petroleum Ether/EtOAc); IR ν max (film) / cm\textsuperscript{-1}: 2963, 2834, 1651, 1604, 1501, 1463, 1222, 1060, 734; \textsuperscript{1}H NMR (400MHz, CDCl\textsubscript{3}); 8.09-8.06 (1H, m), 7.44 (1H, td, J = 7.2 Hz and J = 1.2 Hz), 7.33 (1H, td, J = 7.6 Hz and J = 0.8 Hz), 7.20 (1H, d, J = 7.2 Hz), 7.14 (0.7H, d, J = 8.4 Hz), 7.11 (0.3H, d, J = 8.4 Hz), 6.86 (0.7H, d, J = 2.8 Hz), 6.80-6.77 (1.3H, m), 3.98-3.94 (0.3H, m), 3.81 (3H, s), 3.45-3.35 (0.7H, m), 3.46 (0.7H, dd, J = 12.4 Hz and J = 7.6 Hz), 3.38 (0.3H, dd, J = 16.0 Hz and J = 6.8 Hz), 3.09-3.03 (1H, m), 2.28 (2H, s), 2.27 (1H, s), 2.19-2.11 (0.7H, m), 1.99-1.91 (0.3H, m), 0.92 (2H, d, J = 7.2 Hz), 0.88 (1H, d, J = 7.2 Hz), 0.66 (3H, d, J = 7.2 Hz); \textsuperscript{13}C NMR (400MHz, CDCl\textsubscript{3}) δC: 164.5, 163.6, 158.7, 158.3, 149.5, 138.4, 137.8, 137.7, 136.2, 134.5, 133.7, 132.1, 132.0, 130.7, 129.7, 128.2, 128.1, 126.9, 126.8, 126.6, 122.4, 116.5, 116.1, 115.9, 115.6, 112.5, 111.6, 65.1, 63.0, 55.4, 30.8, 30.7, 28.3, 27.5, 20.2, 20.0, 19.2, 18.3, 17.6; m/z HRMS (ESI) found [M+H]\textsuperscript{+} 310.1816, C\textsubscript{20}H\textsubscript{24}NO\textsubscript{2} requires 310.1807.

(±)-2-(4-methoxy-2-methylphenyl)-3-methylisoindolin-1-one

![Image](attachment:image.png)

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\begin{align*}
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Prepared according to general procedure B for C-H bond carbonylation. (±)-4-methoxy-2-methyl-N-(1-phenylethyl)aniline 1r (48 mg, 0.20 mmol) was reacted at 50°C for 36 hours. The crude product was purified by flash column chromatography (95/5 to 70/30 40-60°C Petroleum Ether/EtOAc) to afford compound 2r as a green oil (44 mg, 83% yield, atropisomers mixture); TLC Rf 0.18 (80/20 Petroleum Ether/EtOAc); IR ν max (film) / cm⁻¹: 3053, 2972, 2931, 2839, 1686, 1606, 1502, 1377, 1233, 757, 693; ¹H NMR (500MHz, CDCl₃) δH: 7.93 (1H, d, J = 7.5 Hz), 7.59 (1H, t, J = 6.5 Hz), 7.51 (1H, d, J = 7.5 Hz), 7.47 (1H, t, J = 6.0 Hz), 7.09 (1H, bs), 6.87 (1H, s), 6.81 (1H, d, J = 8.5 Hz), 4.87 (1H, bd), 3.83 (3H, s), 2.21 (3H, bd), 1.40 (3H, bd); ¹³C NMR (100MHz, CDCl₃) δC: 158.8, 147.2, 131.7, 131.2, 128.3, 127.7, 124.1, 122.0, 116.5, 116.0, 112.3, 112.0, 59.8, 58.0, 55.4, 19.2, 18.8, 18.1, 18.0; m/z HRMS (ESI) found [M+H]+ 268.1333, C₁₇H₁₇NO₂ requires 268.1332.

5-isopropylphenanthridin-6(5H)-one

Prepared according to general procedure B for C-H bond carbonylation. N-isopropyl-[1,1'-biphenyl]-2amine 1s (42 mg, 0.20 mmol) was reacted at room temperature for 36 hours. The crude product was purified by flash column chromatography (95/5 to 70/30 40-60°C Petroleum Ether/EtOAc) to afford compound 2s as a colorless oil (29 mg, 61% yield); TLC Rf 0.69 (90/10 Petroleum Ether/EtOAc); IR ν max (film) / cm⁻¹: 2967, 2926, 1638, 1605, 1582, 1438, 1307, 1170, 741, 660; ¹H NMR (400MHz, CDCl₃) δH: 8.52 (1H, dd, J = 8.0 Hz and J = 0.8 Hz), 8.29 (1H, dd, J = 8.0 Hz and J = 1.2 Hz), 8.25 (1H, d, J = 8.0 Hz), 7.74 (1H, td, J = 7.2 Hz and J = 1.6 Hz) 7.62 (1H, d, J = 7.2 Hz), 7.57 (1H, td, J = 8.0 Hz and J = 1.2 Hz), 7.50 (1H, td, J = 7.2 Hz and J = 1.6 Hz), 7.29 (1H, td, J = 7.2 Hz and J = 0.8 Hz), 5.51 (1H, bs), 1.72 (6H, d, J = 7.2 Hz); ¹³C NMR (100MHz, CDCl₃) δC: 162.0, 137.3, 133.6, 132.3, 128.9, 128.7, 127.9, 126.4, 123.7, 122.1, 121.4, 120.1, 115.9, 47.6, 19.9; m/z HRMS (ESI) found [M+H]+ 238.1224, C₁₆H₁₆NO requires 238.1226.

Unreactive Substrates

Under our optimised set of carboxylative conditions, substrates 1u and 1v were unreactive and no product formation was observed.
C-H Arylation Products

(±)-4-methoxy-N-(cis-2-(4-methyl-[1,1'-biphenyl]-2-yl)cyclohexyl)aniline

Prepared according to the general procedure for C-H bond arylation. (±)-4-methoxy-N-(cis-2-(m-tolyl)cyclohexyl)aniline 1a (59 mg, 0.20 mmol) was reacted with benzenboronic acid (49 mg, 0.40 mmol). The solution was stirred at room temperature for 24 hours. The crude product was purified by flash column chromatography (100/0 to 99/1 40-60°C Petroleum Ether/EtOAc) to afford compound 3a as a yellow oil (63 mg, 85%); TLC Rf 0.77 (90/10 Petroleum Ether/EtOAc); IR ν max (film) / cm⁻¹: 2916, 2868, 1507, 1441, 1233, 1031, 814, 703; ¹H NMR (400MHz, CDCl₃) δH: 7.43-7.33 (3H, m), 7.28-7.25 (2H, m), 7.21 (1H, s), 7.05-6.99 (2H, m), 6.64 (2H, d, J = 8.8 Hz), 6.30 (2H, bs), 3.70 (3H, s), 3.32 (1H, bs), 3.17 (1H, bs), 2.32 (3H, s), 2.04-1.69 (4H, m), 1.52-1.14 (4H, m). ¹³C NMR (100MHz, CDCl₃) δC: 142.1, 140.9, 139.1, 136.7, 130.1, 129.4, 128.2, 128.0, 126.7, 126.5, 115.2, 114.6, 55.8, 53.4, 42.4, 30.4, 26.1, 26.0, 21.4, 20.1; m/z HRMS (ESI) found [M+H]⁺ 372.2313, C₂₆H₃₀NO requires 372.2322.

(±)-N-(cis-2-(4-chloro-[1,1'-biphenyl]-2-yl)cyclohexyl)-4-methoxyaniline

Prepared according to the general procedure for C-H bond arylation. (±)-4-methoxy-N-(cis-2-(3-chlorophenyl)cyclohexyl)aniline 1j (63 mg, 0.20 mmol) was reacted with benzenboronic acid (49 mg, 0.40 mmol). The solution was stirred at room temperature for 24 hours. The crude product was purified by flash column chromatography (100/0 to 99/1 40-60°C Petroleum Ether/EtOAc) to afford compound 3b as an orange oil (40 mg, 51% yield); TLC Rf 0.81 (90/10 Petroleum Ether/EtOAc); IR ν max (film) / cm⁻¹: 2936, 2850, 1509, 1426, 1244, 1026, 829, 710; ¹H NMR (400MHz, CDCl₃) δH: 7.44-7.36 (4H, m), 7.26-7.24 (2H, m), 7.15 (1H, dd, J = 8.4Hz and J = 2.4 Hz), 7.06 (1H, d, J = 8.0 Hz), 6.65 (2H, d, J = 8.8 Hz), 6.28 (2H, d, J = 8.0 Hz), 3.70 (3H, s), 3.44 (1H, bs), 3.34 (1H, bs), 3.12 (1H, d, J = 12.4 Hz), 1.95-1.67 (4H, m), 1.47-1.09 (4H, m); ¹³C NMR (100MHz, CDCl₃) δC: 151.8,
143.4, 142.2, 141.0, 140.2, 133.1, 131.2, 129.1, 128.2, 127.8, 127.1, 125.8, 115.1, 114.7, 55.8, 53.1, 42.6, 30.4, 26.0, 25.9, 20.0; m/z HRMS (ESI) found [M+H]⁺ 392.1773, C₃₃H₃₇NOCl requires 392.1776.

(±)-N-(cis-2-(3’,4-dimethyl-[1,1'-biphenyl]-2-yl)cyclohexyl)-4-methoxyaniline

Prepared according to the general procedure for C-H bond arylation. (±)-4-methoxy-N-(cis-2-(m-tolyl)cyclohexyl)aniline ii (59 mg, 0.20 mmol) was reacted with m-tolylboronic acid (55 mg, 0.40 mmol). The solution was stirred at room temperature for 24 hours. The crude product was purified by flash column chromatography (100/0 to 99/1 40-60°C Petroleum Ether/EtOAc) to afford compound 3c as a yellow oil (56 mg, 73% yield); TLC RF 0.78 (90/10 Petroleum Ether/EtOAc); IR ν max (film) / cm⁻¹: 2916, 2855, 1504, 1458, 1228, 1031, 786, 703; ¹H NMR (400MHz, CDCl₃) δH: 7.28 (1H, t, J = 7.6 Hz), 7.18-7.15 (2H, m), 7.08-7.06 (2H, m), 7.03-7.00 (2H, m), 6.63 (2H, d, J = 8.8 Hz), 6.27 (2H, d, J = 8.8 Hz), 3.70 (3H, s), 3.35 (1H, bs), 3.34 (1H, s), 3.16 (1H, d, J = 12.0 Hz), 2.40 (3H, s), 2.30 (3H, s), 1.95 (1H, qd, J = 12.8 Hz and J = 3.6 Hz), 1.85-1.74 (2H, m), 1.69 (1H, dd, J = 12.8 Hz and J = 2.4 Hz), 1.51-1.41 (2H, m), 1.37-1.27 (1H, m), 1.22-1.13 (1H, m); ¹³C NMR (100MHz, CD₃OD) δC: 142.6, 137.8, 136.6, 130.1, 129.8, 128.9, 127.9, 127.4, 126.4, 126.3, 115.0, 113.5, 60.7, 55.3, 46.0, 26.4, 26.1, 20.6, 20.4, 20.1; m/z HRMS (ESI) found [M+H]⁺ 386.2483, C₂₇H₂₇NO requires 386.2478.

Iterative C-H Functionalization

(±)-cis-5-(4-methoxyphenyl)-7-methyl-10-phenyl-1,3,4,4a,5,10b-hexahydrophenanthridin-6(2H)-one
Arylation:
Pd(OAc)$_2$ (9 mg, 0.04 mmol, 20 mol%), Benzoquinone (43.2 mg, 0.40 mmol, 2 eq) and phenylboronic acid (48.8 mg, 0.40 mmol, 2 eq) were added to a flask. Then a solution of (±)-4-methoxy-N-(cis-2-(m-tolyl)cyclohexyl)aniline 1i (59 mg, 0.20 mmol, 1 eq) in CH$_2$Cl$_2$/$i$-PrOH (1.5 mL/0.3 mL) was added to the flask and t-BuOOAc (50% solution, 78 mg, 0.30 mmol, 1.5 eq) was added via syringe. The solution was stirred at room temperature for 36 hours until all starting material was consumed. The solution was filtered through a plug of Silica Gel eluting with 10mL of a 9/1 mixture of 40-60°C Petroleum Ether/EtOAc. The organic layer was washed with brine, dried over magnesium sulfate then reduced in vacuo to obtain crude arylated amine 3a. The crude product was used without further purification.

Carbonylation:
Pd(OAc)$_2$ (4.5 mg, 0.02 mmol, 10 mol%), Benzoquinone (43.2 mg, 0.40 mmol, 2 eq) and NaOAc (98 mg, 1.20 mmol, 6 eq) were added to a flask which was then fitted with a Teflon septa. A solution of crude amine 3a in acetic acid (2 mL) was added via the septa into the flask followed by t-BuOOAc (50% solution, 105 mg, 0.40 mmol, 2 eq). The solution was stirred for 5 minutes at room temperature until the base was fully dissolved, then the flask was fitted with one balloon containing CO and one balloon containing O$_2$. The solution was then heated at 80°C for 36 hours. After complete consumption of starting material, the organic phase was filtered through Celite and the Celite pad washed with EtOAc (3×5mL). The organic phase was then washed with saturated aqueous solution of sodium bicarbonate (3×10mL), dried over magnesium sulfate and evaporated in vacuo. The crude product was purified by flash chromatography (95/5 to 70/30 40-60°C Petroleum Ether/EtOAc) to afford compound 3d as a brown solid (50mg, 63% yield over 2 steps); TLC Rf 0.25 (80/20 Petroleum Ether/EtOAc); IR ν max (film) / cm$^{-1}$: 3017, 2925, 2850, 1653, 1605, 1509, 1442, 1248, 1018, 831, 692; $^1$H NMR (400MHz, CDCl$_3$) δ$_H$ 7.46-7.37 (4H, m), 7.31 (2H, dd, $J = 8.0$ Hz and $J = 1.6$ Hz), 7.25-7.18 (3H, m), 6.95 (2H, d, $J = 7.6$ Hz), 4.23 (1H, d, $J = 3.2$ Hz), 3.82 (3H, s), 2.95 (1H, dt, $J = 12.0$ Hz and $J = 3.2$ Hz), 2.70 (3H, s), 1.82-1.53 (4H, m), 1.39-1.00 (4H, m). $^{13}$C NMR (100MHz, CDCl$_3$) δ$_C$ 166.9, 158.1, 141.9, 141.0, 140.6, 137.9, 132.7, 132.1, 130.6, 129.3, 128.2, 127.2, 126.7, 113.9, 55.4, 54.3, 38.6, 28.6, 28.5, 25.1, 23.3, 19.5; m/z HRMS (ESI) found [M+H]$^+$ 398.2109, C$_{23}$H$_{29}$NO$_2$ requires 398.2115.
C-H Amination Products

(±)-cis-9-(4-methoxyphenyl)-2,3,4,4a,9,9a-hexahydro-1H-carbazole

Prepared according to the general procedure for C-H bond amination. (±)-4-methoxy-N-(cis-2-phenylcyclohexyl)aniline 1a (56 mg, 0.20 mmol) was reacted at 110°C for 18 hours. The crude product was purified by flash column chromatography (100/0 to 98/20 40-60°C Petroleum Ether/EtOAc) to afford indoline 4a as a pale yellow oil (49 mg, 0.173 mmol, 86% yield) along with indole (5 mg, 0.018 mmol, 10% yield); Rf 0.37 (3:7 Toluene:40-60°C petroleum ether); IR ν max (film) / cm⁻¹: 2921, 2835, 1603, 1504, 1451, 1279, 1239, 1026, 832, 735; ¹H NMR (400MHz, CDCl₃) δ: 7.18 (2H, d, J = 8.8 Hz), 7.12 (1H, d, J = 7.2 Hz), 7.00 (1H, td, J = 7.6 Hz and J = 1.2 Hz), 6.93 (2H, d, J = 8.8 Hz), 6.72 (1H, td, J = 7.2 Hz and J = 0.8 Hz), 6.51 (1H, d, J = 8.0 Hz), 3.92 (q, J = 4.4 Hz), 3.83 (3H, s), 3.12 (1H, q, J = 6.8 Hz), 1.85-1.75 (2H, m), 1.62-1.51 (4H, m), 1.43-1.30 (2H, m); ¹³C NMR (100MHz, CD₃CN) δ: 157.5, 151.3, 137.3, 135.8, 127.6, 126.7, 123.9, 119.1, 115.3, 109.0, 65.7, 55.8, 41.0, 29.4, 26.0, 23.7, 21.4; m/z HRMS (ESI) found [M+H]+ 280.1705, C₁₉H₂₂NO requires 280.1701.

(±)-cis-7-methoxy-9-(4-methoxyphenyl)-2,3,4,4a,9,9a-hexahydro-1H-carbazole

Prepared according to the general procedure for C-H bond amination. (±)-4-methoxy-N-(cis-2-(4-methoxyphenyl)cyclohexyl)aniline 1f (62 mg, 0.20 mmol) was reacted at 110°C for 18 hours. The crude product was purified by flash column chromatography (100/0 to 98/20 40-60°C Petroleum Ether/EtOAc) to afford indoline 4b as a pale yellow oil (38 mg, 0.122 mmol, 61% yield) along with indole (12 mg, 0.039 mmol, 20% yield); Rf 0.82 (0.5:9.5 EtOAc:40-60°C petroleum ether); IR ν max (film) / cm⁻¹ 2921, 2835, 1613, 1507, 1451, 1362, 1282, 1241, 1153, 1031. ¹H NMR (400MHz, CD₃CN): δ 7.18 (2H, d, J = 9.2 Hz), 7.00 (1H, d, J = 8.0 Hz), 6.97 (2H, d, J = 8.8 Hz), 6.23 (1H, dd, J
= 8.0 Hz and \( J = 2.0 \) Hz), 6.01 (1H, d, \( J = 2.4 \) Hz), 3.93 (1H, q, \( J = 4.4 \) Hz), 3.80 (3H, s), 3.64 (3H, s), 3.05 (1H, q, \( J = 6.4 \) Hz), 1.81-7.5 (1H, m), 1.70-1.65 (1H, m), 1.60-1.32 (6H, m). \(^{13}\)C NMR (100MHz, CD\(_3\)CN) \( \delta \): 159.4, 156.7, 151.5, 136.0, 127.3, 125.7, 123.1, 114.3, 102.5, 95.3, 65.3, 54.8, 54.5, 39.3, 28.6, 25.1, 22.6, 20.4; m/z HRMS (ESI) found [M+H]\(^+\) 310.1815, C\(_{20}\)H\(_{24}\)NO\(_2\) requires 310.1807.

\((\pm)-\text{cis-9-}(3-(\text{trifluoromethyl})\text{phenyl})-2,3,4,4a,9,9a\text{-hexahydro-1H-carbazole}\)

Prepared according to the general procedure for C-H bond amination. \((\pm)-\text{N-(cis-2-phenylcyclohexyl)-3-(trifluoromethyl)aniline 1t (64 mg, 0.20 mmol) was reacted at 110°C for 24 hours. The crude product was purified by flash column chromatography (100/0 to 98/2 40-60°C Petroleum Ether/EtOAc) to afford indoline 4c as a pale yellow oil (40 mg, 0.12 mmol, 60% yield); Rf 0.37 (3:7 Toluene:40-60°C petroleum ether); IR \( \nu \) max (film) / cm\(^{-1}\): 2921, 2855, 1592, 1499, 1471, 1458, 1378, 1319, 1264, 1163, 1120, 1067. \(^1\)H NMR (400MHz, CD\(_3\)CN) \( \delta \): 7.54-7.48 (3H, m), 7.29 (1H, d, \( J = 7.2 \) Hz), 7.20 (1H, d, \( J = 7.6 \) Hz), 7.07 (1H, tt, \( J = 8.0 \) Hz and \( J = 0.8 \) Hz), 6.93 (1H, d, \( J = 8.0 \) Hz), 6.83 (1H, td, \( J = 7.6 \) Hz and \( J = 0.8 \) Hz), 4.22 (1H, q, \( J = 7.2 \) Hz), 3.35 (1H, q, \( J = 7.2 \) Hz), 1.90-1.83 (3H, m), 1.56-1.33 (5H, m). \(^{13}\)C NMR (100MHz, CD\(_3\)CN) \( \delta \): 147.5, 144.9, 136.0, 131.0, 127.7, 124.1, 124.0, 120.8, 118.7, 118.6, 116.7, 116.6, 110.2, 64.8, 41.0, 27.2, 26.6, 22.7, 22.1; m/z HRMS (ESI) found [M+H]\(^+\) 318.1471, C\(_{19}\)H\(_{19}\)NF\(_3\) requires 318.1470.
PMP group deprotection

Carbonylated product $2i$ (26mg, 0.081 mmol, 1 eq) was dissolved in acetonitrile (5 mL) and cooled to -5°C using NaCl/ice bath. Ceric Ammonium Nitrate (CAN) (178mg, 0.324 mmol, 4 eq) in water (5 mL) was then added dropwise to the solution. After addition, the resulting yellow solution was stirred at -5°C for 30 minutes until complete consumption of the starting material was observed by TLC. A saturated aqueous solution of sodium bicarbonate (8 mL) was added to quench any excess of CAN, the reaction mixture was then extracted with ethyl acetate (3×15 mL). The organic phase was washed with a saturated aqueous solution of sodium sulfite (10 mL) then brine (10 mL), dried over magnesium sulfate and reduced in vacuo. The crude product was purified by preparative TLC (2/1 40-60°C Petroleum Ether/EtOAc) to give deprotected amide $5i$ as a white solid (13 mg, 0.060 mmol, 75% yield); Rf 0.17 (2/1 40-60°C Petroleum Ether/EtOAc); IR ν max (film) / cm$^{-1}$: 2931, 2855, 1663, 1443; $^1$H NMR (400MHz, CDCl$_3$) δ$_H$: 7.96 (1H, d, $J = 7.6$ Hz), 7.14 (1H, d, $J = 7.6$ Hz), 7.00 (1H, s), 5.47 (1H, bs), 3.90 (1H, d, $J = 4.0$ Hz), 2.74 (1H, t, $J = 5.2$ Hz), 2.38 (3H, s), 1.80-1.55 (7H, m), 1.42-1.33 (1H, m); $^{13}$C NMR (100MHz, CDCl$_3$) δ$_C$: 166.7, 144.0, 142.9, 128.2, 127.8, 127.3, 124.9, 50.0, 40.2, 30.3, 29.1, 24.6, 21.6, 19.8; m/z HRMS (ESI) found [M+H]$^+$ 216.1382, C$_{14}$H$_{18}$NO requires 216.1383.
Synthesis of Starting Materials

(±)-4-methoxy-N-(cis-2-phenylcyclohexyl)aniline

2-phenylcyclohexanone (1.0 g, 5.75 mmol, 1 eq), *para*-methoxyaniline (707 mg, 5.75 mmol, 1 eq) and acetic acid (345 µL, 5.75 mmol, 1 eq) were stirred in of 1.2-dichloroethane (30 mL) at room temperature for 1 hour. Then sodium triacetoxyborohydride (1.83 g, 8.63 mmol, 1.5 eq) was added to the solution and the suspension was allowed to stir at room temperature for 18 hours. A saturated aqueous solution of sodium bicarbonate (40 mL) was then added to the solution to quench any excess of sodium triacetoxyborohydride. The organic phase was separated then dried over magnesium sulfate and concentrated in vacuo. The crude product was purified by flash chromatography (95/5 40-60°C Petroleum Ether/EtOAc) to afford amine 1a as a white solid (1.2 g, 4.27 mmol, 74% yield): Rf 0.80 (1:9 EtOAc:40-60°C petroleum ether); IR ν max (film) / cm⁻¹ 3356, 2926, 2850, 1509, 1464, 1446, 1297, 1233; ¹H NMR (400MHz, CDCl₃): δH: 7.20-7.16 (4H, m), 7.10-7.06 (1H, m), 6.57 (2H, d, J = 10.0 Hz), 6.28 (2H, d, J = 9.2 Hz), 3.63 (1H, bs), 3.61 (3H, s), 3.29 (1H, bs), 2.89 (1H, d, J = 11.6 Hz), 2.01-1.96 (1H, m), 1.87-1.81 (2H, m), 1.77-1.73 (1H, m), 1.55-1.43 (3H, m), 1.39-1.34 (1H, m). ¹³C NMR (100MHz, CDCl₃) δc: 152.2, 144.4, 142.6, 128.7, 128.0, 126.6, 115.4, 115.1, 56.2, 55.2, 46.8, 30.7, 26.4, 26.2, 20.8; m/z HRMS (ESI) found [M+H]^+ 282.1850, C₁₉H₂₄NO requires 282.1852; m.p. 54-56°C.

General procedure for preparation of 4-methoxy-N-*cis*-(2-phenylcyclohexyl)aniline derivatives

Step 1:

In a dry flask, Arylhalide (2 eq) was diluted in THF (0.7M) and the solution cooled to -78°C under a nitrogen atmosphere. n-BuLi (1.6 M in hexanes, 2.02 eq) was added dropwise with a syringe to the
solution which was stirred for 1 hour at -78°C. Cyclohexene oxide (1 eq) was then added dropwise with a syringe, followed quickly by dropwise addition of trifluoroborane etherate (1.5 eq). The resulting solution was stirred for 2 hours at -78°C then quenched by addition of a saturated aqueous solution of sodium bicarbonate (15 mL) and allowed to warm to room temperature. The aqueous phase was extracted with EtOAc (3×20 mL), the organic phase was washed with a cold aqueous solution of 10% sodium hydroxide (3×10 mL), dried over magnesium sulfate and concentrated in vacuo to give the crude product which was purified by flash chromatography (90/10 40-60°C Petroleum Ether/EtOAc) to afford the corresponding alcohol.

**Step 2:**

In a dry flask oxalyl chloride (1.1 eq) was diluted in dry dichloromethane (0.35 M) and the resulting solution was cooled to -78°C. A solution of dimethylsulfoxide (2 eq) in dichloromethane (3M) was added dropwise and the solution stirred for 5 minutes after complete addition. A solution of the alcohol (1 eq) in dichloromethane (0.6M) was then added dropwise and the resulting solution was stirred for 15 minutes at -78°C. Triethylamine (1 mL / mmol of alcohol) was then added and the solution allowed to warm to room temperature. 40 mL of water were then added to the slurry and the aqueous phase was extracted once with dichloromethane (15 mL), the combined organic phases were washed with 50 mL of a 1% aqueous solution of hydrochloric acid, then with a saturated aqueous solution of sodium bicarbonate (3×15mL) then dried over magnesium sulfate and concentrated in vacuo. The crude product was purified by flash chromatography (90/10 40-60°C Petroleum Ether/EtOAc) to afford the desired ketone.

**Step 3:**

The ketone (1 eq) was dissolved in 1,2-dichloroethane (0.2M) and paramethoxyaniline (1.1 eq) was added followed by acetic acid (1 eq). The solution was stirred at room temperature for 1 hour, then sodium triacetoxyborohydride (1.5-2eq) was added and the resulting suspension was stirred at room temperature for 36 hours. Completion of the reaction was checked by TLC and a saturated aqueous solution of sodium bicarbonate (20 mL) was added to the solution to quench any excess of sodium triacetoxyborohydride. The organic phase was separated then dried over magnesium sulfate and concentrated in vacuo. The crude product was purified by flash chromatography (90/10 40-60°C Petroleum Ether/EtOAc) to afford the corresponding amine.
(±)-4-methoxy-\(N\)-(cis-2-(4-methoxyphenyl)cyclohexyl)aniline

Prepared according to the general procedure from 4-bromoanisole (1.91 g, 10.2 mmol) and cyclohexene oxide (500 mg, 5.1 mmol) to give amine 1f as a beige solid (315 mg, 33% yield over 3 steps); Rf 0.82 (1:9 EtOAc:40-60°C petroleum ether). IR ν max (film) / cm\(^{-1}\): 3367, 2926, 2855, 1608, 1577, 1507, 1458, 1360, 1289, 1233. \(^1\)H NMR (400MHz, CDCl\(_3\)) δ\(_H\): 7.12 (2H, d, \(J = 6.2\) Hz), 6.74 (2H, dd, \(J = 5.2\) Hz and \(J = 3.2\) Hz), 6.58 (2H, d, \(J = 8.8\) Hz), 6.34 (2H, d, \(J = 6.8\) Hz), 3.68 (3H, s), 3.62 (4H, bs), 2.86 (1H, bs), 2.01-1.97 (1H, m), 1.89-1.71 (3H, m), 1.56-1.33 (4H, m); \(^{13}\)C NMR (100MHz, CDCl\(_3\)) δ\(_c\): 158.4, 152.2, 136.4, 128.9, 115.6, 115.5, 115.1, 114.1, 56.2, 55.6, 45.8, 30.4, 26.5, 26.3, 20.8; m/z HRMS (ESI) found [M+H]\(^+\) 312.1957, C\(_{20}\)H\(_{26}\)NO\(_2\) requires 312.1958; m.p. 70-72°C.

(±)-\(N\)-(cis-2-(4-bromophenyl)cyclohexyl)-4-methoxyaniline

Prepared according to the general procedure in 3 steps from 1,4-dibromobenzene (4.77 g, 20.4 mmol) and cyclohexene oxide (1.0 g, 10.2 mmol) to give amine 1g as a white solid (1.0 g, 33% yield over 3 steps); Rf 0.82 (1:9 EtOAc:40-60°C petroleum ether); IR ν max (film) / cm\(^{-1}\): 3367, 2916, 2887, 1504, 1436, 1223, 1039, 809, 751; \(^1\)H NMR (400MHz, CDCl\(_3\)) δ\(_H\): 7.38 (2H, d, \(J = 8.4\) Hz), 7.16 (2H, d, \(J = 8.0\) Hz), 6.67 (2H, d, \(J = 9.2\) Hz), 6.36 (2H, d, \(J = 8.0\) Hz), 3.71 (4H, bs), 3.37 (1H, bs), 2.92 (1H, d, \(J = 11.6\) Hz), 2.07-2.04 (1H, m), 1.93-1.78 (3H, m), 1.59-1.44 (4H, m); \(^{13}\)C NMR (100MHz, CDCl\(_3\)) δ\(_c\): 151.9, 143.1, 141.9, 131.2, 129.4, 120.0, 115.0, 114.7, 55.8, 54.6, 45.9, 30.2, 25.8, 20.2; m/z HRMS (ESI) found [M+H]\(^+\) 360.0954, C\(_{19}\)H\(_{23}\)NOBr requires 360.0958.
Prepared according to the general procedure from 3-bromoanisole (1.91 g, 10.2 mmol) and cyclohexene oxide (500 mg, 5.1 mmol) to give amine 1h as a brown oil (278 mg, 42% yield over 3 steps); Rf 0.82 (1:9 EtOAc:40-60°C petroleum ether); Rf 0.78 (1:9 EtOAc:40-60°C petroleum ether).

IR ν max (film) / cm⁻¹: 3397, 2926, 2845, 1598, 1577, 1512, 1453, 1284, 1231, 1165, 1034.¹H NMR (400MHz, CDCl₃) δ H: 7.21 (1H, t, J = 8.0 Hz), 6.90 (1H, d, J = 7.6 Hz), 6.86 (1H, s), 6.74 (1H, dd, J = 8.0 Hz and J = 2.4 Hz), 6.69 (2H, bs), 6.44 (2H, bs), 3.77 (3H, s), 3.72 (4H, bs), 3.00 (1H, bs), 2.11 (1H, bs), 1.98-1.86 (3H, m), 1.70-1.45 (4H, m); ¹³C NMR (100MHz, CDCl₃) δ c: 160.0, 146.0, 129.6, 124.9, 115.4, 114.7, 56.2, 46.5, 30.6, 26.4, 26.2, 21.9, 20.8; m/z HRMS (ESI) found [M+H]⁺ 312.1963, C₂₀H₂₆NO₂ requires 312.1964.

Prepared according to the general procedure from 3-bromotoluene (3.47 g, 20.38 mmol, 2 eq) and cyclohexene oxide (1.0 g, 10.19 mmol, 1 eq) to afford 1.19 g of amine 1i as an orange oil (4.03 mmol, 40% yield over 3 steps); Rf 0.70 (1:9 EtOAc:40-60°C petroleum ether). IR ν max (film) / cm⁻¹: 3387, 2926, 2855, 1605, 1509, 1453, 1443, 1284, 1231; ¹H NMR (400MHz, CDCl₃) δ H: 7.08 (1H, t, J = 8.0 Hz), 7.05 (2H, bs), 6.90 (1H, d, J = 7.6 Hz), 6.58 (2H, d, J = 6.8 Hz), 6.30 (2H, d, J = 8.4 Hz), 3.61 (4H, bs), 2.87 (1H, d, J = 11.6 Hz), 3.29 (1H, bs), 2.22 (3H, s), 2.06-1.97 (1H, m), 1.90-1.72 (3H, m), 1.55-1.35 (4H, m). ¹³C NMR (100MHz, CDCl₃) δ c: 152.1, 144.3, 142.7, 138.2, 128.9, 128.5, 127.4, 124.9, 115.4, 114.7, 56.2, 55.0, 46.5, 30.6, 26.4, 26.2, 21.9, 20.8; m/z HRMS (ESI) found [M+H]⁺ 296.2010, C₂₀H₂₆NO requires 296.2009.
(±)-4-methoxy-N-(cis-2-(3-chlorophenyl)cyclohexyl)aniline

Prepared according to the general procedure from 1-bromo-3-chlorobenzene (4.3 g, 20.4 mmol) and cyclohexene oxide (1.0 g, 20.4 mmol) to give amine 1j as a brown oil (1.08 g, 35% over 3 steps); Rf 0.74 (1:9 EtOAc:40-60°C petroleum ether). IR ν max (film) / cm⁻¹: 2921, 2855, 1592, 1570, 1504, 1284, 1228, 1175, 1135, 1036, 907. ¹H NMR (400MHz, CDCl₃) δH: 7.18 (1H, bs), 7.12-7.04 (3H, m), 6.58 (2H, d, J = 9.2 Hz), 6.30 (2H, d, J = 8.4 Hz), 3.64 (1H, bs), 3.61 (3H, s), 2.86 (1H, td, J = 11.6 Hz and J = 3.2 Hz), 2.00-1.94 (1H, m), 1.87-1.70 (3H, m), 1.53-1.31 (4H, m). ¹³C NMR (100MHz, CDCl₃) δc: 152.4, 146.6, 142.1, 134.5, 129.8, 128.4, 126.8, 126.3, 115.7, 115.1, 56.2, 55.2, 46.6, 30.6, 26.2, 26.1, 20.6; m/z HRMS (ESI) found [M+H]^+ 316.1465, C₁₉H₂₃NOCl requires 316.1463.

(±)-4-methoxy-N-(cis-2-(naphthalen-2-yl)cyclohexyl)aniline

Prepared according to the general procedure in 3 steps from 2-bromonapthalene (4.2 g, 20.4 mmol) and cyclohexene oxide (1.0 g, 10.2 mmol) to give amine 1k as a white solid (1.1 g, 33% yield over 3 steps); Rf 0.82 (1:9 EtOAc:40-60°C petroleum ether); IR ν max (film) / cm⁻¹: 2921, 2837, 1507, 1443, 1236, 1034, 819, 753; ¹H NMR (400MHz, CDCl₃) δH: 7.79-7.75 (2H, m), 7.73 (1H, d, J = 8.4 Hz), 7.70 (1H, s), 7.45-7.38 (3H, m), 6.61 (2H, d, J = 9.2 Hz), 6.37 (2H, d, J = 9.2 Hz), 3.84 (1H, d, J = 1.6 Hz), 3.65 (3H, s), 3.40 (1H, bs), 3.14 (1H, td, J = 12.0 Hz and J = 3.6 Hz), 2.15-1.94 (4H, m), 1.67-1.50 (4H, m); ¹³C NMR (100MHz, CDCl₃) δc: 151.8, 142.0, 141.5, 133.4, 132.2, 127.8, 127.7, 127.5, 126.5, 125.8, 125.7, 125.3, 115.1, 114.7, 55.7, 54.5, 46.4, 30.2, 26.0, 25.8, 20.4; m/z HRMS (ESI) found [M+H]^+ 332.2009, C₂₃H₂₆NO requires 332.2008.
(±)-4-methoxy-N-(cis-2-(1-(triisopropylsilyl)-1H-pyrrol-3-yl)cyclohexyl)aniline

3-iodo-1-(triisopropylsilyl)-1H-pyrrole was prepared following a reported procedure.\(^2\)

Prepared according to the general procedure in 3 steps from 3-iodo-1-(triisopropylsilyl)-1H-pyrrole (3.0 g, 8.67 mmol) and cyclohexene oxide (690 mg, 7 mmol) to give amine 1o as an orange oil (337 mg, 21% yield over 3 steps); IR ν max (film) / cm\(^{-1}\): 2931, 2860, 1507, 1464, 1239, 1102, 882, 816, 692, 657; \(^1\)H NMR (400MHz, CD\(_3\)OD) δH: 6.71 (1H, t, J = 2.4 Hz), 6.66 (2H, d, J = 8.8 Hz), 6.57 (1H, s), 6.46 (2H, d, J = 8.8 Hz), 6.18 (1H, q, J = 1.2 Hz), 3.68 (3H, s), 3.35 (1H, qn, J=3.2Hz), 3.07 (1H, dd, J = 10.4 Hz and J = 6.0 Hz), 1.84-1.39 (8H, m), 1.41 (3H, qn, J = 7.6 Hz), 1.06 (18H, dd, J = 7.6 Hz and J = 2.4 Hz); \(^13\)C NMR (100MHz, CD\(_3\)OD) δC: 153.8, 135.1, 128.5, 125.2, 122.9, 116.9, 115.9, 112.0, 56.8, 56.3, 40.0, 31.0, 30.0, 25.7, 23.4, 18.4, 13.0; m/z HRMS (ESI) found [M+H]\(^+\) 427.3138, C\(_{26}\)H\(_{43}\)N\(_2\)OSi requires 427.3139.

(±)-4-methoxy-N-(cis-2-methyl-2-phenylcyclohexyl)aniline

Commercially available 2-phenylcyclohexanone (1.0 g, 5.75 mmol, 1 eq) was dissolved in \(t\)-butanol (10 mL) and potassium \(t\)-butoxide (672 mg, 6.00 mmol, 1.05 eq) was added and the resulting solution was stirred at room temperature for 45 minutes. Iodomethane (700 µL, 11.5 mmol, 2 eq) was then added and the reaction was further stirred at room temperature for 2.5 hours. Water (5 mL) was added and the mixture was extracted with EtOAc (3×15mL), the organic phase was washed with brine, dried over magnesium sulfate and concentrated in \textit{vacuo}. The crude product was purified by flash column chromatography (90/10 40-60°C Petroleum Ether/EtOAc) to afford 2-methyl-2-phenylcyclohexanone as a colourless oil (880 mg, 82% yield); \(^1\)H NMR (400MHz, CDCl\(_3\)) δH: 7.35 (2H, t, J = 7.2 Hz), 7.23 (1H, tt, J = 7.6 Hz and J = 1.2 Hz), 7.19 (2H, dd, J = 8.4 Hz and J = 1.2 Hz), 2.71-2.67 (1H, m), 2.42-2.29 (2H, m), 1.98-1.93 (1H, m), 1.77-1.69 (4H, m), 1.27 (3H, s); \(^13\)C NMR (100MHz, CDCl\(_3\)) δC: 214.4, 143.7, 129.4, 126.9, 126.5, 54.8, 40.3, 38.6, 28.9, 22.3. Analytical data in Agreement with reported synthesis.\(^2\)
2-methyl-2-phenylcyclohexanone (650 mg, 3.46 mmol, 1 eq) was dissolved in dry 1,2-dichloroethane (20 mL) and acetic acid (200 µL, 3.46 mmol, 1 eq) was added followed by paramethoxyaniline (510 mg, 4.15 mmol, 1.20 eq). The solution was stirred at room temperature for 1 hour, then sodium triacetoxyborohydride (1.4 g, 6.92 mmol, 2 eq) was added and the suspension was stirred at room temperature for 36 hours. Sodium borohydride (260 mg, 6.92 mmol, 2 eq) was then added carefully to reduce any unreacted ketone which was found to co-run with the desired product. After 10 minutes stirring, a saturated aqueous solution of sodium bicarbonate (15 mL) was added to quench any excess of sodium borohydride, the organic phase was separated, dried over magnesium sulfate and concentrated in vacuo. The crude product was purified by flash column chromatography (90/10 40-60°C Petroleum Ether/EtOAc) to afford amine 1l as a colourless oil (358 mg, 34% yield); Rf 0.80 (1:9 EtOAc:40-60°C petroleum ether); IR ν max (film) /cm⁻¹ 3356, 2926, 2850, 1509, 1464, 1446, 1297, 1233; ¹H NMR (400MHz, CDCl₃): δH: 7.38 (2H, dd, J = 8.4 Hz, J = 1.2 Hz), 7.29 (2H, td, J = 7.6 Hz and J = 1.2 Hz), 7.17 (1H, t, J = 7.6 Hz), 6.70 (2H, d, J = 8.4 Hz), 6.44 (2H, bs), 3.72 (3H, s), 3.62 (1H, bs), 2.10 (1H, bs), 1.89-1.49 (7H, m), 1.40 (3H, s). ¹³C NMR (100MHz, CDCl₃) δc: 152.0, 148.2, 128.4, 126.0, 125.8, 114.7, 58.5, 55.7, 41.4, 31.7, 28.0, 25.4, 21.6, 20.6; m/z HRMS (ESI) found [M+H]+ 296.2010, C₂₀H₂₆NO requires 296.2009.

(±)-cis-N-(4-methoxyphenyl)-4-phenyltetrahydro-2H-pyran-3-amine

![](image)

3-phenyldihydro-2H-pyran-4(3H)-one was prepared following a reported procedure.³

3-phenyldihydro-2H-pyran-4(3H)-one (116 mg, 0.66 mmol, 1 eq) was dissolved in 1,2-dichloroethane (7 mL) and acetic acid (40 µL, 0.66 mmol, 1 eq) was added followed by paramethoxyaniline (122 mg, 0.98 mmol, 1.5 eq). The solution was stirred at room temperature for 1 hour then sodium triacetoxyborohydride (280 mg, 1.22 mmol, 2 eq) was added and the resulting suspension was stirred at room temperature for 16 hours. Excess triacetoxyborohydride was quenched by the careful addition of a saturated aqueous solution of sodium bicarbonate (5 mL), the organic phase was separated, dried over magnesium sulfate and concentrated in vacuo. The crude product was purified by flash column chromatography (80/20 40-60°C Petroleum Ether/EtOAc) to afford amine 1m as a yellow solid (150 mg, 81% yield); Rf 0.72 (1:9 EtOAc:40-60°C petroleum ether), IR ν max (film) /cm⁻¹: 3356, 3026, 2961, 2844, 1508, 1461, 1236, 1093, 1038, 909, 809, 700; ¹H NMR (400MHz, CDCl₃): δH 7.44 (2H, d, J = 8.0 Hz), 7.32-7.24 (3H, m), 6.77 (2H, dd, J = 8.8 Hz and J = 1.6 Hz), 6.53 (2H, d, J = 8.8 Hz),
4.26 (1H, dd, J = 11.6 Hz and J = 3.2 Hz), 4.13 (1H, dt, J = 7.6 Hz and J = 3.6 Hz), 3.91 (1H, dd, J = 12.0 Hz and J = 3.2 Hz), 3.81 (1H, m), 3.76 (3H, s), 3.68 (1H, q, J = 6.8 Hz), 3.22 (1H, d, J = 3.6 Hz), 1.79-1.74 (2H, m); 13C NMR (100MHz, CDCl3) δc: 152.3, 140.3, 139.6, 129.9, 128.1, 126.8, 115.4, 115.0, 70.4, 67.0, 55.7, 52.5, 43.4, 28.8; m/z HRMS (ESI) found [M+H]+ 284.1645, C18H22NO2 requires 284.1641.

(+)- cis-N-(4-methoxyphenyl)-4-phenyl-1-tosylpiperidin-3-amine

4-phenylpiperidin-3-one hydrochloride was prepared following a reported procedure.4

4-phenylpiperidin-3-one hydrochloride (200 mg, 1.14 mmol, 1 eq) was dissolved in dichloromethane (10 mL) then cooled to 0°C. Triethylamine (400 µL, 2.86 mmol, 2.5 eq) was added followed by dropwise addition of a solution of tosyl chloride (260 mg, 1.37 mmol, 1.2 eq) in dichloromethane (2 mL). After 30 minutes stirring at 0°C, the solution was allowed to warm to room temperature and stirred for a further hour. The solution was quenched with a saturated solution of aqueous sodium bicarbonate (5 mL), the organic phase was separated, dried over magnesium sulfate then concentrated in vacuo. The crude product was purified by flash chromatography (99/1 DCM/MeOH) to afford 4-phenyl-1-tosylpiperidin-3-one as a white solid (270 mg, 72% yield); Rf 0.23 (99/1 DCM/MeOH); IR ν max (film) / cm⁻¹: 1719, 1337, 1158, 993, 940, 741, 695, 660; 1H NMR (400MHz, CDCl3) δH: 7.68 (2H, d, J = 8.4 Hz), 7.37-7.28 (5H, m), 7.19 (2H, d, J = 7.8 Hz), 3.93-3.83 (3H, m), 3.24-3.13 (2H, m), 2.75-2.68 (1H, m), 2.60 (1H, dt, J = 14.8 Hz and J = 4.4 Hz), 2.45 (3H, s); 13C NMR (100MHz, CDCl3) δc: 205.0, 144.2, 134.8, 133.2, 129.9, 128.7, 128.6, 127.8, 127.6, 55.6, 51.6, 46.5, 40.0, 21.5; m/z HRMS (ESI) found [M+H]+ 330.1160, C18H20NO3S requires 330.1158.

4-phenyl-1-tosylpiperidin-3-one (100 mg, 0.31 mmol, 1 eq) was dissolved in 1,2-dichloroethane (3.5 mL) and acetic acid (19 µL, 0.32 mmol, 1 eq) was added followed by para-methoxyaniline (40 mg, 0.32 mmol, 1.01 eq). The solution was stirred at room temperature for 1 hour then sodium triacetoxyborohydride (132 mg, 0.62 mmol, 2 eq) was added and the resulting suspension was stirred at room temperature for 16 hours. Excess triacetoxyborohydride was quenched by the careful addition of a saturated aqueous solution of sodium bicarbonate (5 mL), the organic phase was separated, dried over magnesium sulfate and concentrated in vacuo. The crude product was purified by flash chromatography (99/1 DCM/MeOH) to afford amine 1n as a yellow solid (101 mg, 75% yield); Rf
0.26 (99/1 DCM/MeOH); IR ν max (film) / cm⁻¹: 2932, 2853, 1507, 1464, 1335, 1233, 1160, 1089, 1034, 809, 698; ¹H NMR (400MHz, CDCl₃) δH: 7.65 (2H, d, J = 8.0 Hz), 7.35-7.21 (7H, m), 3.88-3.79 (1H, m), 3.66 (3H, s), 3.59 (1H, q, J = 5.6 Hz), 3.53 (1H, qn, J = 4.0 Hz), 3.47-3.42 (1H, m), 3.27 (1H, dd, J = 10.0 Hz and J = 4.0 Hz), 2.95-2.89 (1H, m), 2.42 (3H, s), 1.91-1.83 (2H, m); ¹³C NMR (100MHz, CDCl₃) δc: 152.5, 143.7, 140.3, 138.7, 132.7, 129.7, 129.0, 128.4, 127.8, 127.2, 115.4, 114.8, 55.7, 52.6, 47.8, 44.2, 42.4, 27.8, 21.5; m/z HRMS (ESI) found [M+H⁺] + 437.1888, C₂₅H₂₉N₂O₃S requires 437.1893.

(S)-methyl 3-(1H-indol-3-yl)-2-((4-methoxyphenyl)amino)propanoate

L-Tryptophan methyl ester hydrochloride (500 mg, 1.96 mmol, 1 eq) was stirred in acetonitrile (10mL) with 1.3g of basic Amberlyst 21 for 45 minutes. The resin was then removed by filtration and the solvent evaporated to give L-Tryptophan methyl ester as the free amine.

Copper acetate (37 mg, 0.196 mmol, 0.10 mol%), (4-methoxyphenyl)boronic acid (357 mg, 2.35 mmol, 1.2 eq) and 4Å molecular sieves (100 mg) were dissolved in dichloromethane (15 mL). The flask was placed under an atmosphere of oxygen and heated to 40°C for 20 minutes. L-Tryptophan methyl ester (427 mg, 1.96 mmol, 1 eq) in solution in acetonitrile (1.8 mL) was then added to the preheated solution. The reaction mixture was stirred at 40°C for 18 hours. Molecular sieves were filtered off and the solvent removed under vacuum. The crude product was purified by flash column chromatography (99.5/0.5 DCM/MeOH) to afford amine 1p as an orange solid (249 mg, 40%); Rf 0.21 (99/1 DCM/MeOH); IR ν max (film) / cm⁻¹: 3179, 2921, 1729, 1507, 1347, 1208, 1026, 811, 735; ¹H NMR (400MHz, CDCl₃) δH: 8.10 (1H, bs), 7.59 (1H, d, J = 8.0 Hz), 7.34 (1H, d, J = 8.0 Hz), 7.20 (1H, td, J = 6.8 Hz and J = 1.2 Hz), 7.13 (1H, td, J = 7.2 Hz and J = 1.2 Hz), 7.03 (1H, d, J = 2.4 Hz), 6.76 (2H, d, J = 8.8 Hz), 6.57 (2H, d, J = 8.8 Hz), 4.36 (1H, t, J = 6.0 Hz), 4.00 (1H, bs), 3.74 (3H, s), 3.63 (3H, s); ¹³C NMR (100MHz, CDCl₃) δc: 174.4, 152.7, 140.7, 136.1, 127.5, 122.9, 122.1, 119.6, 118.6, 115.1, 114.9, 111.2, 110.5, 58.2, 55.7, 52.0, 28.6; m/z HRMS (ESI) found [M+H⁺] + 325.1551, C₁₉H₂₁NO₃ requires 325.1547.
(±)-4-methoxy-2-methyl-N-(3-methyl-1-phenylbutan-2-yl)aniline

3-methyl-1-phenylbutan-2-one (400 mg, 2.47 mmol, 1 eq), 4-methoxy-2methylaniline (406 mg, 2.96 mmol, 1.2 eq) and acetic acid (170 µL, 2.96 mmol, 1.2 eq) were stirred in 1,2-dichloroethane (15 mL) at room temperature for 1 hour. Then sodium triacetoxyborohydride (785 mg, 3.71 mmol, 1.5 eq) was added to the solution and the suspension was allowed to stir at room temperature for 3 days. A saturated aqueous solution of sodium bicarbonate (20 mL) was then added to the solution to quench any excess of sodium triacetoxyborohydride. The organic phase was separated then dried over magnesium sulfate and concentrated in vacuo. The crude product was dissolved in methanol (10 mL) and cooled down to 0°C, then sodium hydride (200 mg, excess) was added carefully to reduce any unreacted ketone which was found to co-run with the desired product. Excess sodium borohydride was quenched by the careful addition of a saturated aqueous solution of sodium bicarbonate (10 mL) and the aqueous phase was extracted with dichloromethane (3×15mL), the combined organic phase were dried over magnesium sulfate and concentrated under vacuum. The crude product was purified by flash column chromatography (90/10 40-60°C Petroleum Ether/EtOAc) to afford amine 1q as a yellow oil (310 mg, 44%). Rf 0.73 (1:9 EtOAc:40-60°C petroleum ether); IR ν max (film) / cm⁻¹: 2956, 2870, 1507, 1221, 1041, 794, 698; ¹H NMR (400MHz, CDCl₃) δH: 7.34-7.27 (2H, m), 7.21-7.16 (3H, m), 6.69-6.65 (2H, m), 6.53 (1H, d, J = 9.6 Hz), 3.73 (3H, s), 3.46 (1H, q, J = 6.4 Hz), 3.14 (1H, bs), 2.79 (2H, AB system, dd, J = 16.8 Hz and J = 5.6 Hz), 2.06 (3H, s), 1.92 (1H, s, J = 6.8 Hz), 1.00 (6H, dd, J = 14.8 Hz and J = 7.2 Hz); ¹³C NMR (100MHz, CDCl₃) δc: 151.5, 139.9, 129.8, 129.6, 129.0, 128.7, 126.5, 117.5, 112.2, 111.6, 60.4, 56.2, 37.3, 30.0, 19.4, 18.3, 18.2; m/z HRMS (ESI) found [M+H]+ 284.2010, C₁₉H₂₆NO requires 284.2009.

(±)-4-methoxy-2-methyl-N-(1-phenylethyl)aniline

Acetophenone (240 mg, 2.0 mmol, 1 eq), 4-methoxy-2methylaniline (275 mg, 2.0 mmol, 1eq), acetic acid (120 µL, 2.0 mmol, 1 eq) and molecular sieves (100 mg) were stirred in toluene (3 mL) at 100°C for 15 hours. The solution was cooled down to room temperature and molecular sieves were filtered
off and the solvent removed under vacuum. The residue was dissolved in methanol (10 mL), cooled to 0°C and sodium borohydride (500 mg, excess) was added carefully. The reaction mixture was stirred at 0°C for 1 hour, then a saturated aqueous solution of sodium bicarbonate (10 mL) was added and the aqueous layer was extracted with dichloromethane (3×10 mL), the organic phase was dried over magnesium sulfate and concentrated under vacuum. The crude product was purified by flash column chromatography (90/10 40-60°C Petroleum Ether/EtOAc) to afford amine 1r as a yellow solid (301 mg, 64%). Rf 0.61 (1:9 EtOAc:40-60°C petroleum ether); IR ν max (film) / cm⁻¹: 2928, 1509, 1450, 1230, 1051, 799, 701 ¹H NMR (400MHz, CDCl₃) δ H: 7.37-7.29 (4H, m), 7.21 (1H, tt, J = 7.2 Hz and J = 1.6 Hz), 6.69 (1H, d, J = 2.8 Hz), 6.52 (1H, dd, J = 8.8 Hz and J = 3.2 Hz), 6.30 (1H, d, J = 8.4 Hz), 4.46 (1H, q, J = 6.4 Hz), 3.69 (3H, s), 3.60 (1H, bs), 2.22 (3H, s), 1.54 (3H, d, J = 8.4 Hz), 13C NMR (100MHz, CDCl₃) δ c: 151.4, 145.5, 139.4, 128.6, 125.8, 123.4, 116.8, 112.2, 111.4, 55.7, 53.9, 25.3, 17.8; m/z HRMS (ESI) found [M+H]+ 241.1459, C₁₆H₁₉NO requires 241.1461.

N-isopropyl-[1,1′-biphenyl]-2-amine

[1,1′-biphenyl]-2-amine (1.0 g, 5.91 mmol, 1 eq) was dissolved in 1,2-dichloroethane (25 mL) and acetic acid (355 µL, 5.91 mmol, 1 eq) was added followed by acetone (900 µL, 11.83 mmol, 2 eq). The solution was stirred at room temperature for 1 hour then sodium triacetoxyborohydride (1.88 g, 8.86 mmol, 1.5 eq) was added and the resulting suspension was stirred at room temperature for 16 hours. Excess triacetoxyborohydride was quenched by careful addition of a saturated aqueous solution of sodium bicarbonate (10 mL), the organic phase was separated, dried over magnesium sulfate and concentrated in vacuo. The crude product was purified by flash column chromatography (80/20 40-60°C Petroleum Ether/EtOAc) to afford amine 1s as an orange oil (888 mg, 71% yield); Rf (1:9 EtOAc:40-60°C petroleum ether); IR ν max (film) / cm⁻¹: 3063, 2967, 1577, 1507, 1433, 1314, 1175, 703; ¹H NMR (400MHz, CDCl₃) δ H: 7.47-7.41 (4H, m), 7.36 (1H, tt, J = 6.8 Hz and J = 1.6 Hz), 7.24 (1H, dd, J = 6.4 Hz and J = 1.6 Hz), 7.08 (1H, dd, J = 7.2 Hz and J = 1.6 Hz), 6.74 (2H, t, J = 7.2 Hz), 3.75 (1H, bs), 3.66 (1H, sept, J = 6.4 Hz), 1.15 (6H, d, J = 6.0 Hz); ¹³C NMR (100MHz, CDCl₃) δ c: 144.1, 139.6, 130.4, 129.3, 128.8, 128.6, 127.8, 127.1, 116.6, 111.1, 44.4, 22.8; m/z HRMS (ESI) found [M+H]+ 212.1434, C₁₅H₁₈N requires 212.1434.
(±)-N-(cis-2-phenylcyclohexyl)-3-(trifluoromethyl)aniline

2-phenylcyclohexanone (1.0 g, 5.75 mmol, 1 eq), 3-(trifluoromethyl)aniline (925 mg, 5.75 mmol, 1 eq) and acetic acid (345 µL, 5.75 mmol, 1 eq) were stirred in 1.2-dichloroethane (25 mL) at room temperature for 1 hour. Then sodium triacetoxyborohydride (1.83 g, 8.63 mmol, 1.5 eq) was added to the solution and the suspension was allowed to stir at room temperature for 2 days. A saturated aqueous solution of sodium bicarbonate (40mL) was then added to the solution to quench any excess of sodium triacetoxyborohydride. The organic phase was separated then dried over magnesium sulfate and concentrated in vacuo. The crude product was purified by flash column chromatography (95/5 40-60°C Petroleum Ether/EtOAc) to afford amine 1t as a yellow oil (720 mg, 2.26 mmol, 40% yield); Rf 0.64 (1:9 EtOAc:40-60°C petroleum ether). IR ν max (film) / cm⁻¹: 3427, 2931, 2850, 1608, 1517, 1484, 1436, 1337, 1279. 1H NMR (400MHz, CDCl₃) δH: 7.18-7.16 (4H, m), 7.12-7.09 (1H, m), 7.01 (1H, t, J = 9.6 Hz), 6.70 (1H, d, J = 7.6 Hz), 6.46 (1H, s), 6.43 (1H, d, J = 8.8 Hz), 3.77 (1H, dd, J = 6.0 Hz and J = 3.2 Hz), 2.94 (1H, td, J = 10.8 Hz and J = 4.4 Hz), 2.02-1.98 (1H, m), 1.88-1.79 (3H, m), 1.65-1.39 (4H, m). 13C NMR (100MHz, CDCl₃) δC: 148.2, 143.8, 129.7, 128.8, 127.9, 126.9, 116.6, 113.6, 109.8, 54.1, 46.6, 30.7, 26.2, 26.0, 20.8, 14.6; m/z HRMS (ESI) found [M+H]+ 320.1622, C₁₉H₂₁NF₃ requires 320.1621.

References
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