

Amine α -Heteroarylation via Photoredox Catalysis: A Homolytic Aromatic
Substitution Pathway

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Supplementary Information

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1. General Information

Commercial reagents were purified prior to use following the guidelines of Armarego and Chai.¹ All solvents were purified according to the method of Grubbs.² Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator using an acetone-dry ice bath for volatile compounds. Chromatographic purification of products was accomplished by flash chromatography on Silicycle F60 silica gel according to the method of Still.³ Thin-layer chromatography (TLC) was performed on Silicycle 250 µm silica gel plates. Visualization of the developed chromatogram was performed by fluorescence quenching, *p*-anisaldehyde or ceric ammonium molybdate stain. ¹H and ¹³C

¹ W. L. F. Armarego, C. L. L. Chai, *Purification of Laboratory Chemicals*, 5th ed., Butterworth-Heinemann, **2003**.

² A. B. Pangborn, M. A. Giardello, R. H. Grubbs, R. K. Rosen, F. J. Timmers, *Organometallics* **1996**, *15*, 1518 – 1520.

³ W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem.* **1978**, *43*, 2923 – 2925.

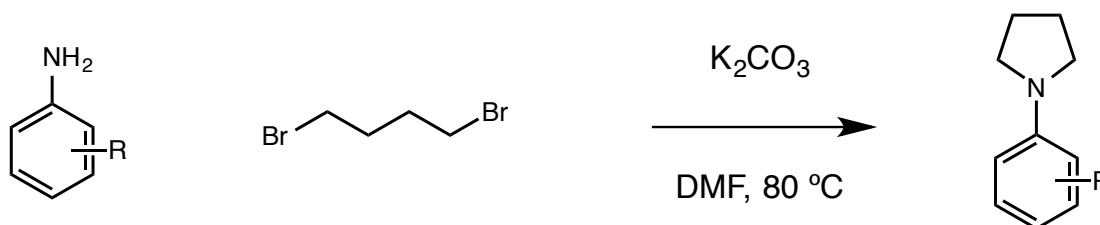
NMR spectra were recorded on a Bruker 500 (500 and 125 MHz) instrument, and are internally referenced to residual protio solvent signals (note: CDCl₃ referenced at δ 7.26 and 77.16 ppm respectively). Data for ¹H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, dd = doublet of doublets, ddd = doublet of doublet of doublets, td = triplet of doublets), coupling constant (Hz), integration, and assignment. Data for ¹³C NMR are reported in terms of chemical shift and no special nomenclature is used for equivalent carbons. IR spectra were recorded on a Perkin Elmer Spectrum 100 spectrometer and are reported in terms of frequency of absorption (cm⁻¹). High resolution mass spectra were obtained at Princeton University mass spectrometry facilities.

General Procedure for the Photoredox α -Heteroarylation of Amines: An oven-dried 8 mL vial equipped with a Teflon septum and magnetic stir bar was charged with the photocatalyst (2.3 mg, 2.5 μ mol, 0.005 equiv., bis[2-phenylpyridinato-C²,N]-[4,4'-di-*tert*-butyl-2,2'-bipyridyl]iridium(III) hexafluorophosphate or Ir(ppy)₂(dtbbpy)PF₆), the corresponding amine (0.5 – 0.75 mmol, 1.0 – 1.5 equiv.), the corresponding chloroheterocycle (0.5 – 1.5 mmol, 1.0 – 3.0 equiv) and sodium acetate (82 mg, 1.0 mmol, 2.0 equiv). *N,N*-Dimethylacetamide (DMA, 2.0 mL, previously distilled over CaH₂ and degassed via argon bubbling) was added followed by deionized water (0 – 25.0 mmol, 0 – 50 equiv.) The reaction mixture was then degassed via three cycles of freeze-pump-thaw, backfilling with argon after each cycle. After the reaction was degassed, the vial was sealed with parafilm and placed approximately 2 cm from a 26 W fluorescent lamp. For reactions performed at room temperature, a fan was employed to blow air over the reaction set-up and maintain the reaction temperature at 23 °C. For reactions performed at 0 °C, the reaction vials were placed in a cryocool acetone bath and irradiated with a lamp encased in a Pyrex glass tube. After the indicated time period, the reaction was quenched with brine and extracted with EtOAc (3x). The organic extracts were dried (MgSO₄) and concentrated *in vacuo*. Purification of the crude product by

flash chromatography on silica gel using the indicated solvent system afforded the desired α -heteroarylated amine product.

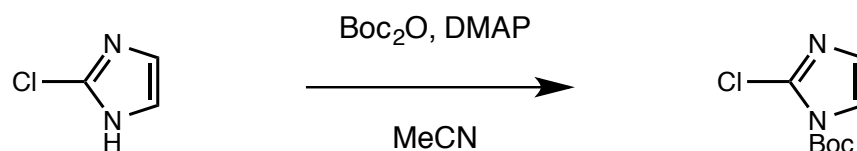
The photocatalyst $\text{Ir}(\text{ppy})_2(\text{dtbbpy})\text{PF}_6$ was prepared as described by Bernhard.⁴ The various chloroheterocycles were purchased from commercial suppliers and purified (by recrystallization or flash chromatography) or prepared following literature procedures. While a variety of fluorescent lights may be used to promote the photoredox reaction, the specific lamps employed in this work are the Double-Brite Pro Grade 26-Watt fluorescent work light (model # CE-926PDQ) (used for room temperature experiments) and the GE spiral 26-Watt CFL (model # FLE26HT3/2/D) (used for 0 °C experiments).

2. Substrate Preparation

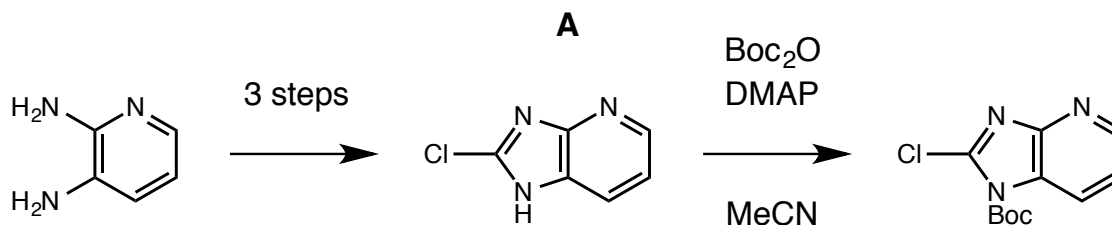


General Procedure for *N*-Aryl Pyrrolidine Synthesis: To a suspension of K_2CO_3 (15.2 g, 110 mmol, 1.1 equiv.) in DMF (100 mL, 1.0 M) was added the appropriate aniline (100 mmol, 1.0 equiv.). The reaction was degassed (10 min) and backfilled with argon. 1,4-Dibromobutane (13.0 mL, 110 mmol, 1.1 equiv.) was added, and the reaction was heated to $80\text{ }^\circ\text{C}$ for 10 h. The reaction was cooled to room temperature and diluted with EtOAc (200 mL) and H_2O (200 mL). The layers were separated, and the organic layer was extracted with 1 N aq. HCl (3 x 50 mL). The aqueous layers were combined and adjusted to pH 8 with 1 N aq. NaOH and then extracted with EtOAc (3 x 100 mL). The organic layers were washed with brine (50 mL), dried over MgSO_4 , filtered, concentrated, and purified by flash chromatography.

⁴ J. D. Slinker, A. A. Gorodetsky, M. S. Lowry, J. Wang, S. Parker, R. Rohl, S. Bernhard, G. G. Malliaras, *J. Am. Chem. Soc.* **2004**, *126*, 2763 – 2767.



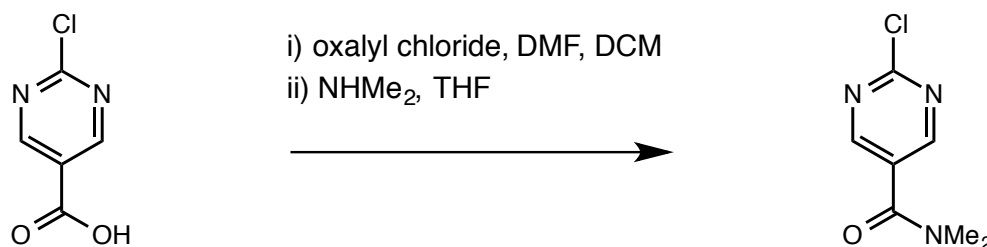
***tert*-Butyl 2-chloroimidazole-1-carboxylate.** To a solution of 2-chloroimidazole (320 mg, 3.12 mmol, 1.0 equiv.) in MeCN (15 mL, 0.2 M) at room temperature were added di-*tert*-butyl dicarbonate (817 mg, 3.75 mmol, 1.2 equiv.) and DMAP (38 mg, 0.31 mmol, 0.1 equiv.). After 1 hour, the reaction was diluted with EtOAc (50 mL) and H₂O (50 mL). The organic layer was separated, washed with brine (20 mL), dried over MgSO₄, filtered, and concentrated. Purification by flash chromatography (silica gel, 10% ethyl acetate in hexanes) afforded the title compound as a clear, colorless liquid (587 mg, 2.90 mmol, 93%). IR (film) 2983, 2938, 1762, 1453, 1360, 1332, 1285, 1125, 1094, 843 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.38 (d, *J* = 1.8 Hz, 1H, ArH), 6.88 (d, *J* = 1.8 Hz, 1H, ArH), 1.62 (s, 9H, *t*-Bu); ¹³C NMR (125 MHz, CDCl₃) δ 146.2, 132.5, 128.1, 120.4, 86.6, 27.8; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₈H₁₂ClN₂O₂) requires *m/z* 203.0582, found 203.0580.



***tert*-Butyl 2-chloroimidazo[4,5-*b*]pyridine-1-carboxylate.** 2-Chloroimidazo[4,5-*b*]pyridine (**A**) was prepared in three steps from 2,3-diaminopyridine following a known procedure.⁵ A solution of 2-chloroimidazo[4,5-*b*]pyridine (**A**, 1.12 g, 7.29 mmol, 1.0 equiv.) in MeCN (40 mL, 0.2 M) was then cooled to 0 °C and treated with di-*tert*-butyl

⁵ T. Taniguchi, M. Yoshikawa, K. Miura, T. Hasui, E. Honda, K. Imamura, M. Kamata, H. Kamisaki, J. F. Quinn, J. Raker, F. Camara, Y. Wang, Fused Heterocyclic Compounds as Phosphodiesterases (PDES) Inhibitors, WO 2011/163355 A1, December 29, 2011.

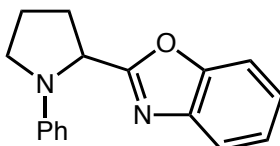
dicarbonate (2.07 g, 9.48 mmol, 1.3 equiv.) and DMAP (89 mg, 0.73 mmol, 0.1 equiv.). After 30 minutes, the reaction was diluted with EtOAc (50 mL) and H₂O (50 mL). The organic layer was separated, washed with brine (20 mL), dried over MgSO₄, filtered, and concentrated. Purification by flash chromatography (silica gel, 30% ethyl acetate in hexanes) afforded the title compound as a white solid (367 mg, 1.45 mmol, 20%). IR (film) 2978, 1766, 1485, 1401, 1314, 1279, 1151 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 8.58 (dd, *J* = 4.9, 1.6 Hz, 1H, ArH), 8.21 (dd, *J* = 8.2, 1.6 Hz, 1H, ArH), 7.31 (dd, *J* = 8.2, 4.9 Hz, 1H, ArH), 1.72 (s, 9H, *t*-Bu); ¹³C NMR (125 MHz, CDCl₃) δ 153.4, 147.0, 146.7, 143.2, 126.8, 123.2, 120.4, 87.8, 28.1; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₁H₁₃ClN₃O₂) requires *m/z* 254.0691, found 254.0693.



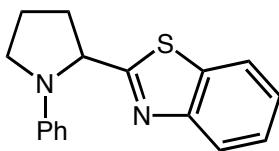
2-Chloro-*N,N*-dimethylpyrimidine-5-carboxamide. To a solution of 2-chloropyrimidine-5-carboxylic acid (400 mg, 2.52 mmol, 1.0 equiv.) in DCM (12 mL, 0.2 M) cooled to 0 °C were added oxalyl chloride (440 μL, 5.05 mmol, 2.0 equiv.) and DMF (1 drop). The reaction was warmed to room temperature and stirred for 1 h. The solution was then added dropwise to a solution of dimethylamine (20.2 mmol, 8 equiv.) in THF (36 mL) cooled to -10 °C. The reaction was warmed to room temperature and after 1 h was diluted with EtOAc (50 mL) and H₂O (50 mL). The organic layer was separated, washed with brine (20 mL), dried over MgSO₄, filtered, and concentrated. Purification by flash chromatography (silica gel, 50% ethyl acetate in hexanes) afforded the title compound as a white solid (239 mg, 1.29 mmol, 51%). IR (film) 3041, 2937, 1638, 1577, 1389, 1158 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 8.72 (s, 2H, ArH), 3.13 (s, 3H, NCH₃), 3.06 (s, 3H, NCH₃); ¹³C NMR (125 MHz, CDCl₃) δ 165.4; 162.1; 158.3;

128.7, 39.6, 35.8; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_7H_9ClN_3O$) requires m/z 186.0429, found 186.0429.

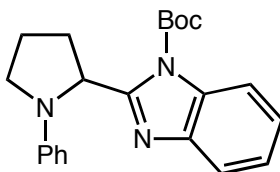
3. Experimental Data for Arylated Products



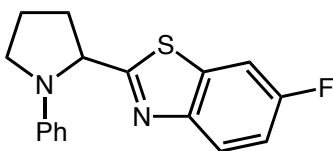
2-(1-Phenylpyrrolidin-2-yl)benzoxazole (Table 2, Entry 1). Prepared according to the general procedure at r.t. using 2.3 mg of $Ir(ppy)_2(dtbbpy)PF_6$ (2.5 μ mol, 0.005 equiv.), 57.1 μ L of 2-chlorobenzoxazole (0.50 mmol, 1.0 equiv.), 108.5 μ L of *N*-phenylpyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 90 μ L water (5.0 mmol, 10 equiv.), and 2.0 mL of DMA. After 2 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 5% ethyl acetate in hexanes) to afford the title compound as a white solid (122.2 mg, 0.462 mmol, 92%). IR (film) 3058, 2973, 2846, 1598, 1504, 1454, 1358, 1344, 1240, 744, 691 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 7.74 – 7.67 (m, 1H, benzoxazole ArH), 7.51 – 7.44 (m, 1H, benzoxazole ArH), 7.34 – 7.28 (m, 2H, benzoxazole ArH), 7.19 (dd, $J = 8.0$ Hz, 2H, phenyl *m*-ArH), 6.73 – 6.68 (m, 3H, phenyl *o,p*-ArH), 5.04 (dd, $J = 7.9, 2.0$ Hz, 1H, NCHAr), 3.82 – 3.75 (m, 1H, NCH_AH_B), 3.44 (dd, $J = 15.6, 8.6$ Hz, 1H, NCH_AH_B), 2.50 – 2.38 (m, 2H, NCH(Ar)CH₂), 2.37 – 2.28 (m, 1H, NCH₂CH_AH_B), 2.23 – 2.13 (m, 1H, NCH₂CH_AH_B); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.1, 150.9, 146.9, 141.1, 129.3, 125.0, 124.4, 120.1, 117.0, 112.4, 110.9, 57.2, 48.8, 32.5, 24.2; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{17}H_{17}N_2O$) requires m/z 265.1335, found 265.1334.



2-(1-Phenylpyrrolidin-2-yl)benzothiazole (Table 2, Entry 2). Prepared according to the general procedure at r.t. using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 65.1 μL of 2-chlorobenzothiazole (0.50 mmol, 1.0 equiv.), 108.5 μL of *N*-phenylpyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 90 μL water (5.0 mmol, 10 equiv.), and 2.0 mL of DMA. After 24 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 1% ethyl acetate in toluene) to afford the title compound as a white solid (121.9 mg, 0.435 mmol, 87%). IR (film) 3061, 2971, 2942, 2841, 1597, 1502, 1357, 1313, 1336, 748, 730, 691 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 8.00 (d, *J* = 8.1 Hz, 1H, benzothiazole ArH), 7.78 (d, *J* = 7.9 Hz, 1H, benzothiazole ArH), 7.48 (dd, *J* = 7.7 Hz, 1H, benzothiazole ArH), 7.34 (dd, *J* = 7.6 Hz, 1H, benzothiazole ArH), 7.20 (dd, *J* = 7.7 Hz, 2H, phenyl *m*-ArH), 6.75 (t, *J* = 7.2 Hz, 1H, phenyl *p*-ArH), 6.66 (d, *J* = 8.3 Hz, 2H, phenyl *o*-ArH), 5.12 (d, *J* = 8.7 Hz, 1H, NCHAr), 3.81 (dd, *J* = 8.0 Hz, 1H, NCH_AH_B), 3.37 (m, 1H, NCH_AH_B), 2.56 – 2.46 (m, 1H, NCH(Ar)CH_AH_B), 2.32 (m, 1H, NCH(Ar)CH_AH_B), 2.27 – 2.16 (m, 1H, NCH₂CH_AH_B), 2.11 (m, 1H, NCH₂CH_AH_B); ¹³C NMR (125 MHz, CDCl₃) δ 179.8, 154.3, 147.1, 135.2, 129.3, 126.0, 124.8, 122.8, 121.9, 117.7, 113.0, 62.4, 49.4, 34.7, 23.8; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₇H₁₇N₂S) requires *m/z* 281.1107, found 281.1107.

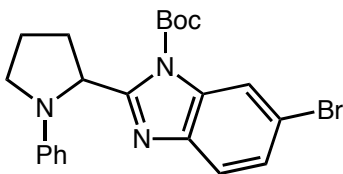


***tert*-Butyl 2-(1-phenylpyrrolidin-2-yl)-benzimidazole-1-carboxylate (Table 2, Entry 3).** Prepared according to the general procedure at r.t. using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 126.3 mg of *tert*-butyl 2-chlorobenzimidazole-1-carboxylate (0.50 mmol, 1.0 equiv.), 108.5 μL of *N*-phenylpyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 90 μL water (5.0 mmol, 10 equiv.), and 2.0 mL of DMA. After 4 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 10% ethyl acetate in hexanes) to afford the title compound as a clear, colorless oil (161.3 mg, 0.444 mmol, 89%). IR (film) 2978, 1741, 1599, 1505, 1452, 1344, 1318, 1148, 1116, 906, 727 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.96 (d, *J* = 8.0 Hz, 1H, benzimidazole ArH), 7.69 (d, *J* = 7.6 Hz, 1H, benzimidazole ArH), 7.34 – 7.27 (m, 2H, benzimidazole ArH), 7.15 (dd, *J* = 7.6 Hz, 2H, phenyl *m*-ArH), 6.65 (t, *J* = 7.2 Hz, 1H, phenyl *p*-ArH), 6.50 (d, *J* = 8.1 Hz, 2H, phenyl *o*-ArH), 5.57 (d, *J* = 8.5 Hz, 1H, NCHAr), 3.87 (dd, *J* = 8.3 Hz, 1H, NCH_AH_B), 3.46 (dd, *J* = 16.4, 8.6 Hz, 1H, NCH_AH_B), 2.46 (m, 1H, NCH(Ar)CH_AH_B), 2.29 – 2.16 (m, 1H, NCH(Ar)CH_AH_B), 2.16 – 2.01 (m, 2H, NCH₂CH₂), 1.75 (s, 9H, *t*-Bu); ¹³C NMR (125 MHz, CDCl₃) δ 157.5, 149.1, 147.0, 142.4, 133.6, 129.1, 124.5, 124.2, 120.5, 116.3, 115.0, 112.4, 86.0, 58.8, 48.8, 33.3, 28.3, 23.3; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₂₂H₂₆N₃O₂) requires *m/z* 364.2020, found 364.2021.



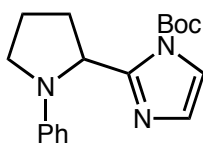
6-Fluoro-2-(1-phenylpyrrolidin-2-yl)benzothiazole (Table 2, Entry 4). Prepared according to the general procedure at r.t. using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 93.8 mg of 2-chloro-6-fluorobenzothiazole (0.50 mmol, 1.0 equiv.), 108.5 μL of *N*-phenylpyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 90 μL water (5.0 mmol, 10 equiv.), and 2.0 mL of DMA. After 24 h,

the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 20% CH₂Cl₂ in hexanes to neat CH₂Cl₂) to afford the title compound as a clear, pale yellow oil (134.5 mg, 0.451 mmol, 90%). IR (film) 3064, 2972, 2839, 1597, 1502, 1454, 1357, 1336, 1314, 1247, 1187, 810, 747, 692 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.93 (dd, *J* = 8.9, 4.8 Hz, 1H, benzothiazole ArH), 7.45 (dd, *J* = 8.1, 2.6 Hz, 1H, benzothiazole ArH), 7.24 – 7.17 (m, 3H, benzothiazole ArH and phenyl *m*-ArH), 6.76 (t, *J* = 7.3 Hz, 1H, phenyl *p*-ArH), 6.66 (d, *J* = 8.4 Hz, 2H, phenyl *o*-ArH), 5.09 (dd, *J* = 8.8, 1.6 Hz, 1H, NCHAr), 3.84 – 3.76 (m, 1H, NCH_ACH_B), 3.37 (td, *J* = 9.4, 6.5 Hz, 1H, NCH_ACH_B), 2.57 – 2.44 (m, 1H, NCH(Ar)CH_AH_B), 2.31 (m, 1H, NCH(Ar)CH_AH_B), 2.27 – 2.07 (m, 2H, NCH₂CH₂); ¹³C NMR (125 MHz, CDCl₃) δ 179.6 (d, *J* = 3.2 Hz), 160.3 (d, *J* = 243.1 Hz), 150.9 (d, *J* = 1.5 Hz), 147.0, 136.1 (d, *J* = 11.0 Hz), 129.4, 123.6 (d, *J* = 9.3 Hz), 117.8, 114.6 (d, *J* = 24.5 Hz), 113.0, 108.1 (d, *J* = 26.3 Hz), 62.3, 49.4, 34.7, 23.8; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₇H₁₆FN₂S) requires *m/z* 299.1013, found 299.1014.



***tert*-Butyl 5-bromo-2-(1-phenylpyrrolidin-2-yl)-benzimidazole-1-carboxylate (Table 2, Entry 5).** Prepared according to the general procedure at r.t. using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 165.8 mg of *tert*-butyl 5-bromo-2-chlorobenzimidazole-1-carboxylate (0.50 mmol, 1.0 equiv., a 1:1 mixture of regioisomers with respect to the Boc group), 108.5 μL of *N*-phenylpyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 90 μL water (5.0 mmol, 10 equiv.), and 2.0 mL of DMA. After 4 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 10% EtOAc in hexanes) to afford the title compound as a clear, colorless oil (206.7 mg, 0.467 mmol, 93%). The product is a 1:1 mixture of regioisomers with respect to the Boc group.

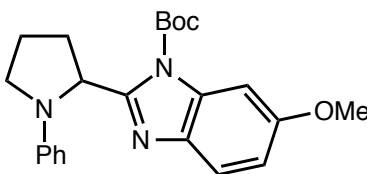
IR (film) 2977, 1744, 1598, 1505, 1340, 1149, 1124, 910, 731 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.16 (d, $J = 1.7$ Hz, 1H regioisomer A, benzimidazole ArH), 7.82 (m, 1H regioisomer A and 1H regioisomer B, benzimidazole ArH), 7.52 (d, $J = 8.5$ Hz, 1H regioisomer B, benzimidazole ArH), 7.40 (m, 1H regioisomer A and 1H regioisomer B, benzimidazole ArH), 7.15 (dd, $J = 7.9$ Hz, 2H, phenyl *m*-ArH), 6.66 (t, $J = 7.3$ Hz, 1H, phenyl *p*-ArH), 6.48 (d, $J = 8.2$ Hz, 2H, phenyl *o*-ArH), 5.53 (dd, $J = 8.7$ Hz, 1H, NCHAr), 3.84 (dd, $J = 8.2$ Hz, 1H, NCH_ACH_B), 3.46 (dd, $J = 16.3, 8.6$ Hz, 1H, NCH_ACH_B), 2.52 – 2.40 (m, 1H, NCH(Ar)CH_ACH_B), 2.28 – 2.02 (m, 3H, NCH(Ar)CH_ACH_B and NCH₂CH₂), 1.75 (s, 9H, *t*-Bu); ^{13}C NMR (125 MHz, CDCl_3) δ 158.7, 158.0, 148.7, 148.7, 146.8, 143.6, 141.3, 134.6, 132.7, 129.2, 127.5, 127.5, 123.4, 121.6, 118.3, 117.9, 117.2, 116.4, 116.4, 116.2, 112.3, 86.7, 86.5, 58.7, 48.7, 33.3, 28.3, 28.2, 23.2; HRMS (ESI) exact mass calculated for $[\text{M}+\text{H}]^+$ ($\text{C}_{22}\text{H}_{25}\text{BrN}_3\text{O}_2$) requires m/z 442.1125, found 442.1130.



***tert*-Butyl 2-(1-phenylpyrrolidin-2-yl)imidazole-1-carboxylate (Table 2, Entry 6).**

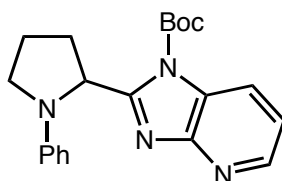
Prepared according to the general procedure at r.t. using 2.3 mg of $\text{Ir}(\text{ppy})_2(\text{dtbbpy})\text{PF}_6$ (2.5 μmol , 0.005 equiv.), 304.0 mg of *tert*-butyl 2-chloroimidazole-1-carboxylate (1.5 mmol, 3.0 equiv.), 72.3 μL of *N*-phenylpyrrolidine (0.5 mmol, 1.0 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 270 μL water (15.0 mmol, 30 equiv.), and 2.0 mL of DMA. After 48 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 20% ethyl acetate in hexanes) to afford the title compound as a clear, colorless oil (128.5 mg, 0.410 mmol, 82%). IR (film) 2978, 2871, 1747, 1598, 1506, 1368, 1305, 1157, 1132, 1098, 745 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.36 (d, $J = 1.6$ Hz, 1H, imidazole ArH), 7.15 (dd, $J = 8.6, 7.4$ Hz, 2H, phenyl *m*-ArH), 6.85 (d, $J = 1.6$ Hz, 1H, imidazole ArH), 6.63 (t, $J = 7.3$ Hz, 1H, phenyl *p*-ArH), 6.44 (d, $J = 7.9$ Hz, 2H, phenyl *o*-ArH), 5.40 (d, $J = 7.8$ Hz, 1H,

NCH_AAr), 3.76 (dd, $J = 8.5, 7.3$ Hz, 1H, NCH_ACH_B), 3.40 (td, $J = 9.0, 7.0$ Hz, 1H, NCH_ACH_B), 2.35 (m, 1H, NCH(Ar)CH_ACH_B), 2.23 – 2.09 (m, 1H, NCH(Ar)CH_ACH_B), 2.07 – 1.96 (m, 2H, NCH₂CH₂), 1.66 (s, 9H, *t*-Bu); ¹³C NMR (125 MHz, CDCl₃) δ 152.2, 148.0, 146.7, 129.1, 127.9, 118.9, 116.0, 112.0, 85.8, 57.6, 48.4, 33.1, 28.1, 23.1; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₈H₂₄N₃O₂) requires m/z 314.1863, found 314.1862.

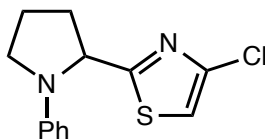


***Tert*-butyl 5-methoxy-2-(1-phenylpyrrolidin-2-yl)-benzimidazole-1-carboxylate (Table 2, Entry 7).** Prepared according to the general procedure at r.t. using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 141.4 mg of *tert*-butyl 2-chloro-5-methoxybenzimidazole-1-carboxylate (0.50 mmol, 1.0 equiv., a 1:1 mixture of regioisomers with respect to the Boc group), 108.5 μL of *N*-phenylpyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 90 μL water (5.0 mmol, 10 equiv.), and 2.0 mL of DMA. After 5 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 10% to 20% ethyl acetate in hexanes) to afford the title compound as a clear, colorless oil (178.5 mg, 0.454 mmol, 91%). The product is a 1:1 mixture of regioisomers with respect to the Boc group. IR (film) 2977, 1740, 1598, 1506, 1484, 1351, 1146, 1121, 729 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.81 (d, $J = 9.0$ Hz, 1H regioisomer A, benzimidazole ArH), 7.58 – 7.50 (m, 1H regioisomer A and 1H regioisomer B, benzimidazole ArH), 7.22 – 7.09 (m, 1H regioisomer B, benzimidazole ArH, and 2H both regioisomers, phenyl *m*-ArH), 6.90 (m, 1H regioisomer A and 1H regioisomer B, benzimidazole ArH), 6.64 (t, $J = 7.3$ Hz, 1H, phenyl *p*-ArH), 6.50 (d, $J = 8.6$ Hz, 2H, phenyl *o*-ArH), 5.53 (dd, $J = 8.6$ Hz, 1H, NCHAr), 3.90 – 3.77 (m, 4H, OCH₃ and NCH_ACH_B), 3.45 (m, 1H, NCH_ACH_B), 2.55 – 2.35 (m, 1H, NCH(Ar)CH_ACH_B), 2.33 –

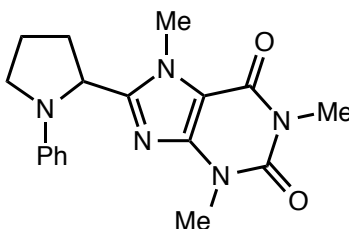
1.99 (m, 3H, NCH(Ar)CH_ACH_B and NCH₂CH₂), 1.75 (9H, *t*-Bu); ¹³C NMR (125 MHz, CDCl₃) δ 158.0, 157.6, 157.1, 156.1, 149.1, 149.0, 146.9, 146.9, 143.2, 136.5, 134.4, 129.1, 127.7, 120.7, 116.2, 115.4, 113.6, 112.6, 112.3, 112.3, 102.9, 99.4, 85.9, 85.8, 58.8, 58.7, 55.9, 55.8, 48.7, 33.3, 33.3, 28.3, 23.2; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₂₃H₂₈N₃O₃) requires *m/z* 394.2125, found 394.2121.



***Tert*-butyl 2-(1-phenylpyrrolidin-2-yl)imidazo[4,5-*b*]pyridine-1-carboxylate (Table 2, Entry 8).** Prepared according to the general procedure at 0 °C using 1.1 mg of Ir(ppy)₂(dtbbpy)PF₆ (1.25 μmol, 0.005 equiv.), 63.4 mg of *tert*-butyl 2-chloroimidazo[4,5-*b*]pyridine-1-carboxylate (0.25 mmol, 1.0 equiv.), 54.2 μL of *N*-phenylpyrrolidine (0.375 mmol, 1.5 equiv.), 41.0 mg of sodium acetate (0.5 mmol, 2.0 equiv.), 45 μL water (2.5 mmol, 10 equiv.), and 1.0 mL of DMA. After 12 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 40% ethyl acetate in hexanes) to afford the title compound as a clear, colorless oil (85.5 mg, 0.235 mmol, 94%). IR (film) 2978, 1745, 1598, 1505, 1407, 1326, 1295, 1140, 1122, 1080, 909, 726, 689 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 8.48 (dd, *J* = 4.8, 1.4 Hz, 1H, pyridine ArH), 8.20 (dd, *J* = 8.2, 1.5 Hz, 1H, pyridine ArH), 7.23 (dd, *J* = 8.2, 4.8 Hz, 1H, pyridine ArH), 7.12 (dd, *J* = 8.5, 7.4 Hz, 2H, phenyl *m*-ArH), 6.61 (t, *J* = 7.3 Hz, 1H, phenyl *p*-ArH), 6.47 (d, *J* = 8.0 Hz, 2H, phenyl *o*-ArH), 5.68 (d, *J* = 8.2 Hz, 1H, NCHAr), 3.91 – 3.83 (m, 1H, NCH_ACH_B), 3.51 (dd, *J* = 16.2, 8.6 Hz, 1H, NCH_ACH_B), 2.53 – 2.41 (m, 1H, NCH(Ar)CH_ACH_B), 2.37 – 2.23 (m, 1H, NCH(Ar)CH_ACH_B), 2.17 – 2.02 (m, 2H, NCH₂CH₂), 1.76 (s, 9H, *t*-Bu); ¹³C NMR (125 MHz, CDCl₃) δ 160.5, 155.0, 148.5, 146.5, 146.3, 129.1, 126.2, 123.1, 119.6, 116.1, 112.1, 86.8, 57.8, 48.1, 32.9, 28.2, 22.8; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₂₁H₂₅N₄O₂) requires *m/z* 365.1972, found 365.1973.

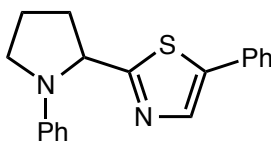


4-Chloro-2-(1-phenylpyrrolidin-2-yl)thiazole (Table 2, Entry 9). Prepared according to the general procedure at r.t. using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 115.5 mg of 2,4-dichlorothiazole (0.75 mmol, 1.5 equiv.), 72.3 μL of *N*-phenylpyrrolidine (0.5 mmol, 1.0 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 90 μL water (5.0 mmol, 10 equiv.), and 2.0 mL of DMA. After 18 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 1% to 5% ethyl acetate in hexanes) to afford the title compound as a clear, colorless oil (102.5 mg, 0.387 mmol, 77%). IR (film) 3114, 2973, 2843, 1598, 1503, 1482, 1358, 1335, 1310, 1257, 1244, 1088, 748, 692 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.22 (dd, *J* = 8.7, 7.4 Hz, 2H, phenyl *m*-ArH), 6.95 (s, 1H, thiazole ArH), 6.77 (t, *J* = 7.3 Hz, 1H, phenyl *p*-ArH), 6.61 (d, *J* = 7.8 Hz, 2H, phenyl *o*-ArH), 4.99 (dd, *J* = 8.7, 1.4 Hz, 1H, NCHAr), 3.80 – 3.67 (m, 1H, NCH_AH_B), 3.30 (dd, *J* = 16.9, 8.8 Hz, 1H, NCH_AH_B), 2.47 – 2.31 (m, 1H, NCH(Ar)CH_AH_B), 2.26 – 2.19 (m, 1H, NCH(Ar)CH_AH_B), 2.16 – 2.02 (m, 2H, NCH₂CH₂); ¹³C NMR (125 MHz, CDCl₃) δ 178.0, 147.0, 138.7, 129.3, 117.9, 113.5, 113.0, 62.1, 49.3, 34.5, 23.5; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₃H₁₄ClN₂S) requires *m/z* 265.0561, found 265.0555.



8-(1-Phenylpyrrolidin-2-yl)caffeine (Table 2, Entry 10). Prepared according to the general procedure at r.t. using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.),

114.3 mg of 8-chlorocaffeine (0.50 mmol, 1.0 equiv.), 108.5 μ L of *N*-phenylpyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 360 μ L water (20.0 mmol, 40 equiv.), and 2.0 mL of DMA. After 70 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 50% ethyl acetate in hexanes) to afford the title compound as a clear, colorless oil (136.7 mg, 0.405 mmol, 81%). IR (film) 2949, 2851, 1701, 1657, 1599, 1505, 1438, 747 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.18 (dd, $J = 8.5, 7.4$ Hz, 2H, phenyl *m*-ArH), 6.72 (dd, $J = 7.3$ Hz, 1H, phenyl *p*-ArH), 6.49 (d, $J = 8.0$ Hz, 2H, phenyl *o*-ArH), 4.98 (dd, $J = 8.2, 5.2$ Hz, 1H, NCHAr), 3.90 (s, 3H, NCH₃), 3.74 – 3.67 (m, 1H, NCH_AH_B), 3.57 (s, 3H, NCH₃), 3.52 – 3.45 (m, 1H, NCH_AH_B), 3.37 (s, 3H, NCH₃), 2.58 – 2.47 (m, 1H, NCH(Ar)CH_AH_B), 2.28 – 2.19 (m, 1H, NCH(Ar)CH_AH_B), 2.16 – 2.06 (m, 2H, NCH₂CH₂); ^{13}C NMR (125 MHz, CDCl_3) δ 155.5, 154.8, 151.8, 148.0, 146.5, 129.5, 117.5, 112.4, 107.9, 57.7, 49.4, 33.3, 32.2, 30.0, 28.0, 24.4; HRMS (ESI) exact mass calculated for $[\text{M}+\text{H}]^+$ ($\text{C}_{18}\text{H}_{22}\text{N}_5\text{O}_2$) requires m/z 340.1768, found 340.1765.

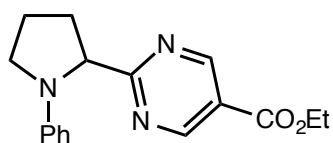


5-Phenyl-2-(1-phenylpyrrolidin-2-yl)thiazole (Table 2, Entry 11). Prepared according to the general procedure at r.t. using 2.3 mg of $\text{Ir}(\text{ppy})_2(\text{dtbbpy})\text{PF}_6$ (2.5 μ mol, 0.005 equiv.), 146.8 mg of 2-chloro-5-phenylthiazole (0.75 mmol, 1.5 equiv.), 72.3 μ L of *N*-phenylpyrrolidine (0.5 mmol, 1.0 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), and 2.0 mL of DMA. After 27 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 10% ethyl acetate in hexanes) to afford the title compound as a clear, colorless oil (125.9 mg, 0.411 mmol, 82%). IR (film) 3060, 3026, 2971, 2945, 2841, 1597, 1503, 1357, 1338, 1158, 1135, 748, 690 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.93 (s, 1H, thiazole ArH), 7.49 (d, $J = 7.8$ Hz, 2H, ArH), 7.35 (dd, $J = 7.6$ Hz, 2H, ArH), 7.30 – 7.20 (m, 3H, ArH), 6.76 (t, $J = 7.3$ Hz, 1H, *N*-phenyl *p*-ArH), 6.67 (d, $J = 8.1$ Hz, 2H, *N*-

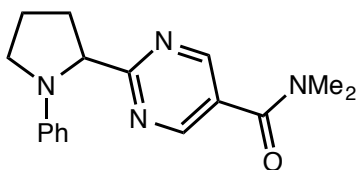
phenyl *o*-ArH), 5.02 (d, $J = 8.6$ Hz, 1H, NCHAr), 3.77 (dd, $J = 7.9$ Hz, 1H, NCH_AH_B), 3.33 (td, $J = 9.5, 6.5$ Hz, 1H, NCH_AH_B), 2.49 – 2.37 (m, 1H, NCH(Ar)CH_AH_B), 2.31 – 2.04 (m, 3H, NCH(Ar)CH_AH_B and NCH₂CH₂); ¹³C NMR (125 MHz, CDCl₃) δ 177.2, 147.1, 139.1, 138.6, 131.7, 129.3, 129.1, 128.1, 126.6, 117.5, 112.9, 62.1, 49.2, 34.6, 23.6; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₉H₁₉N₂S) requires m/z 307.1263, found 307.1262.



2-Phenyl-5-(1-phenylpyrrolidin-2-yl)-1,3,4-thiadiazole (Table 2, Entry 12). Prepared according to the general procedure at r.t. using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 147.5 mg of 2-chloro-5-phenyl-1,3,4-thiadiazole (0.75 mmol, 1.5 equiv.), 72.3 μL of *N*-phenylpyrrolidine (0.5 mmol, 1.0 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 90 μL water (5.0 mmol, 10 equiv.), and 2.0 mL of DMA. After 24 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 15% ethyl acetate in hexanes) to afford the title compound as a clear, pale green oil (100.3 mg, 0.326 mmol, 65%). IR (film) 3062, 2972, 2846, 1598, 1503, 1457, 1357, 1337, 1158, 907, 748, 728, 688 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.89 (dd, $J = 7.8, 1.8$ Hz, 2H, ArH), 7.48 – 7.40 (m, 3H, ArH), 7.23 (dd, $J = 8.7, 7.4$ Hz, 2H, *N*-phenyl *m*-ArH), 6.77 (t, $J = 7.3$ Hz, 1H, *N*-phenyl *p*-ArH), 6.68 (d, $J = 7.9$ Hz, 2H, *N*-phenyl *o*-ArH), 5.21 (dd, $J = 8.7, 1.9$ Hz, 1H, NCHAr), 3.76 (ddd, $J = 9.3, 5.4, 2.7$ Hz, 1H, NCH_AH_B), 3.35 (td, $J = 9.1, 7.2$ Hz, 1H, NCH_AH_B), 2.57 – 2.47 (m, 1H, NCH(Ar)CH_AH_B), 2.37 – 2.27 (m, 1H, NCH(Ar)CH_AH_B), 2.25 – 2.11 (m, 2H, NCH₂CH₂); ¹³C NMR (125 MHz, CDCl₃) δ 177.9, 169.0, 146.7, 131.1, 130.3, 129.5, 129.2, 127.9, 117.9, 112.9, 59.4, 49.2, 34.7, 23.9; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₈H₁₈N₃S) requires m/z 308.1216, found 308.1219.

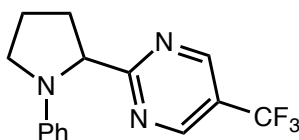
**Ethyl 2-(1-phenylpyrrolidin-2-yl)pyrimidine-5-carboxylate (Table 3, Entry 1).**

Prepared according to the general procedure at 0 °C using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 93.3 mg of ethyl 2-chloropyrimidine-5-carboxylate (0.50 mmol, 1.0 equiv.), 108.5 μL of *N*-phenylpyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 225 μL water (12.5 mmol, 25 equiv.), and 2.0 mL of DMA. After 10 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 10% ethyl acetate in hexanes) to afford the title compound as a pale yellow solid (114.4 mg, 0.385 mmol, 77%). IR (film) 3041, 2976, 2871, 1722, 1585, 1504, 1365, 1288, 1124, 1036, 746, 691 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 9.21 (s, 2H, pyrimidine ArH), 7.12 (dd, *J* = 8.6, 7.4 Hz, 2H, phenyl *m*-ArH), 6.63 (t, *J* = 7.3 Hz, 1H, phenyl *p*-ArH), 6.52 (d, *J* = 7.9 Hz, 2H, phenyl *o*-ArH), 5.00 (dd, *J* = 8.5, 2.9 Hz, 1H, NCHAr), 4.41 (q, *J* = 7.1 Hz, 2H, CO₂CH₂CH₃), 3.82 (td, *J* = 8.4, 3.4 Hz, 1H, NCH_AH_B), 3.50 (dd, *J* = 15.6, 8.2 Hz, 1H, NCH_AH_B), 2.56 – 2.46 (m, 1H, NCH(Ar)CH_AH_B), 2.38 – 2.26 (m, 1H, NCH(Ar)CH_AH_B), 2.17 – 2.03 (m, 2H, NCH₂CH₂), 1.39 (t, *J* = 7.1 Hz, 3H, CO₂CH₂CH₃); ¹³C NMR (125 MHz, CDCl₃) δ 176.8, 163.9, 158.7, 147.0, 129.2, 122.3, 116.4, 112.4, 65.1, 61.9, 49.4, 33.8, 23.9, 14.4; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₇H₂₀N₃O₂) requires *m/z* 298.1550, found 298.1557.



***N,N*-Dimethyl-2-(1-phenylpyrrolidin-2-yl)pyrimidine-5-carboxamide (Table 3, Entry 2).** Prepared according to the general procedure at 0 °C using 2.3 mg of

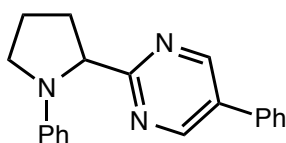
$\text{Ir}(\text{ppy})_2(\text{dtbbpy})\text{PF}_6$ (2.5 μmol , 0.005 equiv.), 92.8 mg of 2-chloro-*N,N*-dimethylpyrimidine-5-carboxamide (0.50 mmol, 1.0 equiv.), 108.5 μL of *N*-phenylpyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 225 μL water (12.5 mmol, 25 equiv.), and 2.0 mL of DMA. After 18 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 50% ethyl acetate in hexanes) to afford the title compound as a white solid (107.7 mg, 0.363 mmol, 73%). IR (film) 3028, 2926, 2874, 1634, 1597, 1582, 1505, 1429, 1397, 1366, 1097, 747, 693 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.78 (s, 2H, pyrimidine ArH), 7.13 (dd, $J = 8.5, 7.5$ Hz, 2H, phenyl *m*-ArH), 6.63 (t, $J = 7.3$ Hz, 1H, phenyl *p*-ArH), 6.53 (d, $J = 8.0$ Hz, 2H, phenyl *o*-ArH), 4.96 (dd, $J = 8.5, 2.6$ Hz, 1H, NCHAr), 3.81 (td, $J = 8.4, 3.1$ Hz, 1H, NCH_AH_B), 3.48 (dd, $J = 15.6, 8.3$ Hz, 1H, NCH_AH_B), 3.13 (s, 3H, NCH₃), 3.04 (s, 3H, NCH₃), 2.55 – 2.42 (m, 1H, NCH(Ar)CH_AH_B), 2.38 – 2.24 (m, 1H, NCH(Ar)CH_AH_B), 2.18 – 2.01 (m, 2H, NCH₂CH₂); ^{13}C NMR (125 MHz, CDCl_3) δ 174.2, 166.7, 156.2, 147.1, 129.2, 127.8, 116.3, 112.4, 65.0, 49.4, 39.7, 35.7, 33.8, 23.9; HRMS (ESI) exact mass calculated for $[\text{M}+\text{H}]^+$ ($\text{C}_{17}\text{H}_{21}\text{N}_4\text{O}$) requires m/z 297.1710, found 297.1706.



2-(1-Phenylpyrrolidin-2-yl)-5-(trifluoromethyl)pyrimidine (Table 3, Entry 3).

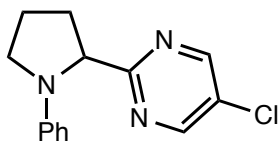
Prepared according to the general procedure at 0 °C using 2.3 mg of $\text{Ir}(\text{ppy})_2(\text{dtbbpy})\text{PF}_6$ (2.5 μmol , 0.005 equiv.), 136.9 mg of 2-chloro-5-(trifluoromethyl)pyrimidine (0.75 mmol, 1.5 equiv.), 72.3 μL of *N*-phenylpyrrolidine (0.5 mmol, 1.0 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 45 μL water (2.5 mmol, 5 equiv.), and 2.0 mL of DMA. After 6 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 2% to 5% ethyl acetate in hexanes) to afford the title compound as a clear, pale yellow oil (123.7 mg, 0.422 mmol, 84%). IR (film) 2971, 2851, 1596, 1505, 1325, 1182, 1132, 1096, 1020,

746, 692 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.93 (s, 2H, pyrimidine ArH), 7.15 (dd, $J = 7.6$ Hz, 2H, phenyl *m*-ArH), 6.65 (t, $J = 7.2$ Hz, 1H, phenyl *p*-ArH), 6.52 (d, $J = 8.2$ Hz, 2H, phenyl *o*-ArH), 5.03 (d, $J = 8.2$ Hz, 1H, NCHAr), 3.81 (td, $J = 8.5, 2.8$ Hz, 1H, NCH_AH_B), 3.51 (dd, $J = 15.7, 8.1$ Hz, 1H, NCH_AH_B), 2.57 – 2.47 (m, 1H, NCH(Ar)CH_AH_B), 2.39 – 2.25 (m, 1H, NCH(Ar)CH_AH_B), 2.16 – 2.05 (m, 2H, NCH₂CH₂); ^{13}C NMR (125 MHz, CDCl_3) δ 176.9, 154.8 (q, $J = 3.5$ Hz), 146.9, 129.3, 122.9 (m), 116.5, 112.3, 64.9, 49.3, 33.7, 23.8; HRMS (ESI) exact mass calculated for $[\text{M}+\text{H}]^+$ ($\text{C}_{15}\text{H}_{15}\text{F}_3\text{N}_3$) requires m/z 294.1213, found 294.1216.

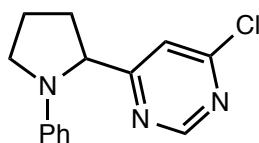


5-Phenyl-2-(1-phenylpyrrolidin-2-yl)pyrimidine (Table 3, Entry 4). Prepared according to the general procedure at 10 °C using 2.3 mg of $\text{Ir}(\text{ppy})_2(\text{dtbbpy})\text{PF}_6$ (2.5 μmol , 0.005 equiv.), 95.3 mg of 2-chloro-5-phenylpyrimidine (0.50 mmol, 1.0 equiv.), 108.5 μL of *N*-phenylpyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 225 μL water (12.5 mmol, 25 equiv.), and 2.0 mL of DMA. After 46 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 10% ethyl acetate in hexanes) to afford the title compound as a white solid (109.9 mg, 0.365 mmol, 73%). IR (film) 3027, 2967, 2849, 1596, 1504, 1432, 1364, 1188, 993, 746, 692 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.90 (s, 2H, pyrimidine ArH), 7.55 (d, $J = 7.6$ Hz, 2H, ArH), 7.50 (dd, $J = 7.5$ Hz, 2H, ArH), 7.44 (t, $J = 7.2$ Hz, 1H, ArH), 7.15 (dd, $J = 7.7$ Hz, 2H, *N*-phenyl *m*-ArH), 6.64 (t, $J = 7.3$ Hz, 1H, *N*-phenyl *p*-ArH), 6.59 (d, $J = 8.1$ Hz, 2H, *N*-phenyl *o*-ArH), 4.99 (dd, $J = 8.4, 2.4$ Hz, 1H, NCHAr), 3.85 (td, $J = 8.3, 3.1$ Hz, 1H, NCH_AH_B), 3.51 (dd, $J = 16.0, 8.0$ Hz, 1H, NCH_AH_B), 2.57 – 2.45 (m, 1H, NCH(Ar)CH_AH_B), 2.44 – 2.31 (m, 1H, NCH(Ar)CH_AH_B), 2.20 – 2.14 (m, 1H, NCH₂CH_AH_B), 2.14 – 2.04 (m, 1H, NCH₂CH_AH_B); ^{13}C NMR (125 MHz, CDCl_3) δ 171.9, 155.6, 147.3, 134.5, 132.0, 129.5,

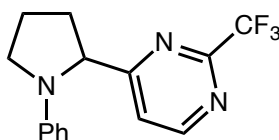
129.2, 128.9, 127.0, 116.2, 112.4, 65.0, 49.5, 33.9, 24.0; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{20}H_{20}N_3$) requires m/z 302.1652, found 302.1653.



5-Chloro-2-(1-phenylpyrrolidin-2-yl)pyrimidine (Table 3, Entry 5). Prepared according to the general procedure at 0 °C using 2.3 mg of $Ir(ppy)_2(dtbbpy)PF_6$ (2.5 μ mol, 0.005 equiv.), 223.5 mg of 2,5-dichloropyrimidine (1.5 mmol, 3.0 equiv.), 72.3 μ L of *N*-phenylpyrrolidine (0.5 mmol, 1.0 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 360 μ L water (20.0 mmol, 40 equiv.), and 2.0 mL of DMA. After 40 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 5% ethyl acetate in hexanes) to afford the title compound as a clear, colorless oil (96.3 mg, 0.371 mmol, 74%). IR (film) 3032, 2969, 2870, 2846, 1597, 1541, 1504, 1421, 1365, 1344, 1189, 1131, 746, 692 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 8.63 (s, 2H, pyrimidine ArH), 7.14 (dd, $J = 7.9$ Hz, 2H, phenyl *m*-ArH), 6.64 (t, $J = 7.3$ Hz, 1H, phenyl *p*-ArH), 6.53 (d, $J = 8.1$ Hz, 2H, phenyl *o*-ArH), 4.93 (dd, $J = 8.4, 2.6$ Hz, 1H, NCHAr), 3.79 (td, $J = 8.5, 3.3$ Hz, 1H, NCH_AH_B), 3.48 (dd, $J = 15.7, 8.2$ Hz, 1H, NCH_AH_B), 2.53 – 2.43 (m, 1H, NCH(Ar)CH_AH_B), 2.37 – 2.23 (m, 1H, NCH(Ar)CH_AH_B), 2.13 – 2.00 (m, 2H, NCH₂CH₂); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.2, 156.0, 147.0, 129.5, 129.2, 116.3, 112.3, 64.4, 49.3, 33.8, 23.8; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{14}H_{15}ClN_3$) requires m/z 260.0949, found 260.0953.

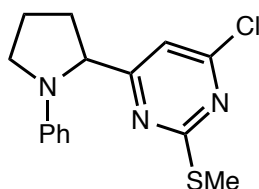


4-Chloro-6-(1-phenylpyrrolidin-2-yl)pyrimidine (Table 3, Entry 6). Prepared according to the general procedure at 0 °C using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 74.5 mg of 4,6-dichloropyrimidine (0.50 mmol, 1.0 equiv.), 108.5 μL of *N*-phenylpyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 225 μL water (12.5 mmol, 25 equiv.), and 2.0 mL of DMA. After 23 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 10% ethyl acetate in hexanes) to afford the title compound as a colorless oil (110.6 mg, 0.426 mmol, 85%). IR (film) 3045, 2972, 2846, 1597, 1560, 1528, 1502, 1361, 1340, 1311, 747, 692 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 8.97 (s, 1H, pyrimidine ArH), 7.24 (s, 1H, pyrimidine ArH), 7.21 (dd, *J* = 8.4, 7.5 Hz, 2H, phenyl *m*-ArH), 6.75 (t, *J* = 7.3 Hz, 1H, phenyl *p*-ArH), 6.48 (d, *J* = 8.1 Hz, 2H, phenyl *o*-ArH), 4.73 (dd, *J* = 9.1, 1.8 Hz, 1H, NCHAr), 3.76 (dd, *J* = 8.3 Hz, 1H, NCH_AH_B), 3.42 (td, *J* = 9.4, 6.6 Hz, 1H, NCH_AH_B), 2.53 – 2.43 (m, 1H, NCH(Ar)CH_AH_B), 2.15 – 2.02 (m, 2H, NCH(Ar)CH_AH_B and NCH₂CH_AH_B), 2.00 – 1.89 (m, 1H, NCH₂CH_AH_B); ¹³C NMR (125 MHz, CDCl₃) δ 175.3, 162.3, 159.0, 146.7, 129.5, 118.4, 117.3, 112.6, 64.3, 49.5, 34.0, 23.4; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₄H₁₅ClN₃) requires *m/z* 260.0949, found 260.0949.



4-(1-Phenylpyrrolidin-2-yl)-2-(trifluoromethyl)pyrimidine (Table 3, Entry 7). Prepared according to the general procedure at 0 °C using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 91.3 mg of 4-chloro-2-(trifluoromethyl)pyrimidine (0.50 mmol, 1.0 equiv.), 108.5 μL of *N*-phenylpyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 225 μL water (12.5 mmol, 25 equiv.), and 2.0 mL of DMA. After 24 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 10% ethyl acetate in hexanes) to afford the title compound as a pale yellow oil (106.3 mg, 0.362 mmol, 72%).

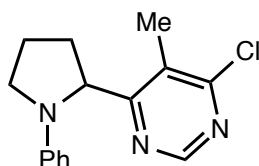
IR (film) 2976, 2877, 2850, 1600, 1582, 1505, 1361, 1330, 1200, 1138, 994, 748, 692 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.73 (d, $J = 5.1$ Hz, 1H, pyrimidine ArH), 7.37 (d, $J = 5.1$ Hz, 1H, pyrimidine ArH), 7.21 (dd, $J = 8.3, 7.6$ Hz, 2H, phenyl *m*-ArH), 6.74 (t, $J = 7.3$ Hz, 1H, phenyl *p*-ArH), 6.47 (d, $J = 8.2$ Hz, 2H, phenyl *o*-ArH), 4.84 (dd, $J = 9.0, 1.7$ Hz, 1H, NCHAr), 3.77 (dd, $J = 8.5$ Hz, 1H, NCH_AH_B), 3.46 (td, $J = 9.4, 6.7$ Hz, 1H, NCH_AH_B), 2.58 – 2.48 (m, 1H, NCH(Ar)CH_AH_B), 2.22 – 2.14 (m, 1H, NCH(Ar)CH_AH_B), 2.13 – 2.03 (m, 1H, NCH₂CH_AH_B), 1.97 – 1.85 (m, 1H, NCH₂CH_AH_B); ^{13}C NMR (125 MHz, CDCl_3) δ 175.1, 158.4, 156.9 (q, $J = 36.5$ Hz), 146.6, 129.5, 119.9, 119.7 (q, $J = 275.7$ Hz), 117.3, 112.6, 64.1, 49.5, 34.2, 23.4; HRMS (ESI) exact mass calculated for $[\text{M}+\text{H}]^+$ ($\text{C}_{15}\text{H}_{15}\text{F}_3\text{N}_3$) requires m/z 294.1213, found 294.1219.



4-Chloro-2-(methylthio)-6-(1-phenylpyrrolidin-2-yl)pyrimidine (Table 3, Entry 8).

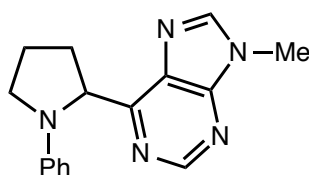
Prepared according to the general procedure at 0 °C using 2.3 mg of $\text{Ir}(\text{ppy})_2(\text{dtbbpy})\text{PF}_6$ (2.5 μmol , 0.005 equiv.), 97.5 mg of 4,6-dichloro-2-(methylthio)pyrimidine (0.50 mmol, 1.0 equiv.), 108.5 μL of *N*-phenylpyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 225 μL water (12.5 mmol, 25 equiv.), and 2.0 mL of DMA. After 14 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 2% ethyl acetate in hexanes) to afford the title compound as a clear, colorless oil (140.9 mg, 0.461 mmol, 92%). IR (film) 2972, 2927, 2841, 1598, 1528, 1502, 1359, 1286, 1246, 1185, 852, 812, 747, 691 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.21 (dd, $J = 7.9$ Hz, 2H, phenyl *m*-ArH), 6.86 (s, 1H, pyrimidine ArH), 6.74 (t, $J = 7.3$ Hz, 1H, phenyl *p*-ArH), 6.48 (d, $J = 8.2$ Hz, 2H, phenyl *o*-ArH), 4.64 (d, $J = 8.9$ Hz, 1H, NCHAr), 3.72 (dd, $J = 8.1$ Hz, 1H, NCH_AH_B), 3.40 (td, $J = 9.4, 6.8$ Hz, 1H, NCH_AH_B), 2.60 (s, 3H, SCH₃), 2.47 – 2.37 (m, 1H, NCH(Ar)CH_AH_B), 2.16 – 2.09 (m, 1H, NCH(Ar)CH_AH_B), 2.08 – 2.01 (m, 1H,

NCH₂CH_AH_B), 1.99 – 1.88 (m, 1H, NCH₂CH_AH_B); ¹³C NMR (125 MHz, CDCl₃) δ 175.3, 173.6, 162.0, 146.8, 129.4, 117.1, 113.0, 112.6, 64.2, 49.4, 33.9, 23.5, 14.5; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₅H₁₇ClN₃S) requires *m/z* 306.0826, found 306.0827.

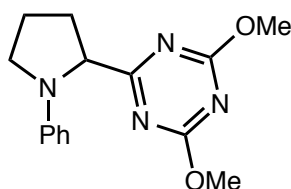


4-Chloro-5-methyl-6-(1-phenylpyrrolidin-2-yl)pyrimidine (Table 3, Entry 9).

Prepared according to the general procedure at 0 °C using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 122.3 mg of 4,6-dichloro-5-methylpyrimidine (0.75 mmol, 1.5 equiv.), 72.3 μL of *N*-phenylpyrrolidine (0.5 mmol, 1.0 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 225 μL water (12.5 mmol, 25 equiv.), and 2.0 mL of DMA. After 33 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 5% ethyl acetate in toluene) to afford the title compound as a white solid (88.1 mg, 0.322 mmol, 64%). IR (film) 3039, 2967, 2850, 1597, 1554, 1528, 1504, 1359, 746, 690 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 8.71 (s, 1H, pyrimidine ArH), 7.13 (dd, *J* = 8.6, 7.4 Hz, 2H, phenyl *m*-ArH), 6.65 (t, *J* = 7.3 Hz, 1H, phenyl *p*-ArH), 6.35 (d, *J* = 7.9 Hz, 2H, phenyl *o*-ArH), 4.98 (dd, *J* = 8.5, 3.5 Hz, 1H, NCHAr), 3.79 (td, *J* = 8.4, 3.9 Hz, 1H, NCH_AH_B), 3.51 (dd, *J* = 16.1, 7.7 Hz, 1H, NCH_AH_B), 2.54 – 2.44 (m, 4H, ArCH₃ and NCH(Ar)CH_AH_B), 2.25 – 2.14 (m, 1H, NCH(Ar)CH_AH_B), 2.12 – 2.02 (m, 1H, NCH₂CH_AH_B), 1.95 – 1.87 (m, 1H, NCH₂CH_AH_B); ¹³C NMR (125 MHz, CDCl₃) δ 171.8, 162.0, 156.0, 146.5, 129.3, 126.8, 116.5, 112.1, 61.6, 49.3, 33.0, 23.7, 14.2; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₅H₁₇ClN₃) requires *m/z* 274.1106, found 274.1105.

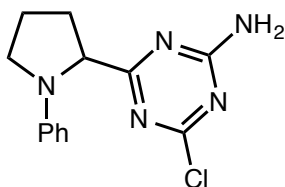


9-Methyl-6-(1-phenylpyrrolidin-2-yl)-purine (Table 3, Entry 10). Prepared according to the general procedure at 0 °C using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 84.3 mg of 6-chloro-9-methylpurine (0.50 mmol, 1.0 equiv.), 108.5 μL of *N*-phenylpyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 225 μL water (12.5 mmol, 25 equiv.), and 2.0 mL of DMA. After 16 h, the reaction was subjected to the workup protocol outlined in the general procedure. As the remaining 6-chloro-9-methylpurine was difficult to separate from the desired product, this reagent was consumed by treating the crude mixture with ethanol (5 mL), morpholine (0.5 mL), and *N,N*-diisopropylethylamine (100 μL) and heating to reflux (110 °C) for 4 h. The reaction mixture was concentrated and purified by flash chromatography (silica gel, 60% ethyl acetate in hexanes) to afford the title compound as a clear, colorless oil (102.0 mg, 0.365 mmol, 73%). IR (film) 3061, 2950, 2852, 1585, 1505, 1367, 1326, 1223, 748, 732, 694 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 8.90 (s, 1H, purine ArH), 8.01 (s, 1H, purine ArH), 7.06 (dd, *J* = 8.2, 7.7 Hz, 2H, phenyl *m*-ArH), 6.56 (t, *J* = 7.3 Hz, 1H, phenyl *p*-ArH), 6.53 (d, *J* = 8.0 Hz, 2H, phenyl *o*-ArH), 5.44 (dd, *J* = 8.5, 3.0 Hz, 1H, NCHAr), 3.93 (td, *J* = 8.2, 3.5 Hz, 1H, NCH_AH_B), 3.87 (s, 3H, NCH₃), 3.53 (dd, *J* = 15.6, 8.0 Hz, 1H, NCH_AH_B), 2.62 – 2.52 (m, 1H, NCH(Ar)CH_AH_B), 2.46 – 2.35 (m, 1H, NCH(Ar)CH_AH_B), 2.18 – 2.05 (m, 2H, NCH₂CH₂); ¹³C NMR (125 MHz, CDCl₃) δ 164.1, 152.7, 151.8, 147.0, 144.7, 131.3, 129.0, 115.8, 112.1, 60.2, 49.2, 33.9, 29.8, 24.3; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₆H₁₈N₅) requires *m/z* 280.1557, found 280.1559.



2,4-Dimethoxy-6-(1-phenylpyrrolidin-2-yl)-1,3,5-triazine (Table 3, Entry 11). Prepared according to the general procedure at 0 °C using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆

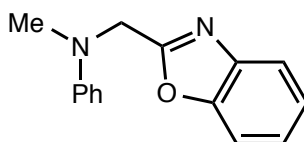
(2.5 μmol , 0.005 equiv.), 87.8 mg of 2-chloro-4,6-dimethoxy-1,3,5-triazine (0.50 mmol, 1.0 equiv.), 108.5 μL of *N*-phenylpyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 450 μL water (25 mmol, 50 equiv.), and 2.0 mL of DMA. After 21 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 20% ethyl acetate in hexanes) to afford the title compound as a clear, colorless oil (126.2 mg, 0.441 mmol, 88%). IR (film) 2951, 2872, 1599, 1545, 1498, 1459, 1348, 1312, 1197, 1109, 830, 746, 692 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.15 (dd, $J = 8.0, 7.5$ Hz, 2H, phenyl *m*-ArH), 6.64 (t, $J = 7.0$ Hz, 1H, phenyl *p*-ArH), 6.56 (d, $J = 8.5$ Hz, 2H, phenyl *o*-ArH), 4.71 (dd, $J = 8.3, 2.1$ Hz, 1H, NCHAr), 3.99 (s, 6H, OCH₃), 3.71 (td, $J = 8.3, 3.1$ Hz, 1H, NCH_AH_B), 3.47 (dd, $J = 15.4, 8.1$ Hz, 1H, NCH_AH_B), 2.46 – 2.27 (m, 2H, NCH(Ar)CH₂), 2.13 – 2.02 (m, 2H, NCH₂CH₂); ^{13}C NMR (125 MHz, CDCl_3) δ 185.7, 172.8, 146.9, 129.2, 116.2, 112.2, 63.9, 55.3, 48.9, 32.9, 23.9; HRMS (ESI) exact mass calculated for $[\text{M}+\text{H}]^+$ ($\text{C}_{15}\text{H}_{19}\text{N}_4\text{O}_2$) requires m/z 287.1503, found 287.1501.



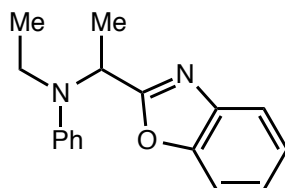
2-Amino-4-chloro-6-(1-phenylpyrrolidin-2-yl)-1,3,5-triazine (Table 3, Entry 12).

Prepared according to the general procedure at 0 $^{\circ}\text{C}$ using 2.3 mg of $\text{Ir}(\text{ppy})_2(\text{dtbbpy})\text{PF}_6$ (2.5 μmol , 0.005 equiv.), 82.5 mg of 2-amino-4,6-dichloro-1,3,5-triazine (0.50 mmol, 1.0 equiv.), 108.5 μL of *N*-phenylpyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 225 μL water (12.5 mmol, 25 equiv.), and 2.0 mL of DMA. After 12 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 30% ethyl acetate in hexanes) to afford the title compound as a pale yellow oil (115.9 mg, 0.420 mmol, 84%). IR (film) 3317, 3192, 2971, 2846, 1635, 1598, 1550, 1499, 1362, 1332, 1254, 1189, 906, 726, 690 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.19 (dd, $J = 7.9$ Hz, 2H, phenyl *m*-ArH),

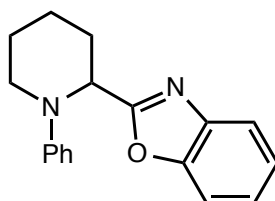
6.75 – 6.40 (br, 1H, NH₂), 6.70 (t, $J = 7.3$ Hz, 1H, phenyl *p*-ArH), 6.48 (d, $J = 8.2$ Hz, 2H, phenyl *o*-ArH), 5.78 (br, 1H, NH₂), 4.56 (d, $J = 8.9$ Hz, 1H, NCHAr), 3.65 (m, 1H, NCH_AH_B), 3.38 (dd, $J = 15.9, 8.2$ Hz, 1H, NCH_AH_B), 2.47 – 2.36 (m, 1H, NCH(Ar)CH_AH_B), 2.24 – 2.12 (m, 1H, NCH(Ar)CH_AH_B), 2.12 – 1.98 (m, 2H, NCH₂CH₂); ¹³C NMR (125 MHz, CDCl₃) δ 183.8, 171.0, 167.3, 146.8, 129.5, 116.9, 112.2, 64.3, 49.3, 33.3, 23.7; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₃H₁₅ClN₅) requires m/z 276.1010, found 276.1014.



***N*-(Benzoxazol-2-ylmethyl)-*N*-methylaniline (Table 4, Entry 1).** Prepared according to the general procedure at r.t. using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 57.1 μL of 2-chlorobenzoxazole (0.50 mmol, 1.0 equiv.), 95.1 μL of *N,N*-dimethylaniline (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 90 μL water (5.0 mmol, 10 equiv.), and 2.0 mL of DMA. After 17 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 5% to 10% ethyl acetate in hexanes) to afford the title compound as a pale yellow oil (99.4 mg, 0.417 mmol, 83%). IR (film) 3060, 2900, 2820, 1599, 1505, 1454, 1240, 831, 745, 691 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.74 – 7.68 (m, 1H, benzoxazole ArH), 7.52 – 7.45 (m, 1H, benzoxazole ArH), 7.33 – 7.29 (m, 2H, benzoxazole ArH), 7.26 (dd, $J = 8.0$ Hz, 2H, phenyl *m*-ArH), 6.90 (d, $J = 8.2$ Hz, 2H, phenyl *o*-ArH), 6.78 (t, $J = 7.3$ Hz, 1H, phenyl *p*-ArH), 4.75 (s, 2H, NCH₂Ar), 3.19 (s, 3H, NCH₃); ¹³C NMR (125 MHz, CDCl₃) δ 164.0, 151.0, 148.8, 141.0, 129.4, 125.1, 124.5, 120.2, 117.9, 113.0, 110.8, 50.6, 39.4; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₅H₁₅N₂O) requires m/z 239.1179, found 239.1178.

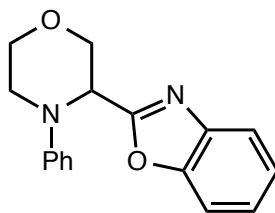


***N*-(1-(Benzoxazol-2-yl)ethyl)-*N*-ethylaniline (Table 4, Entry 2).** Prepared according to the general procedure at r.t. using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 57.1 μL of 2-chlorobenzoxazole (0.50 mmol, 1.0 equiv.), 119.3 μL of *N,N*-diethylaniline (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 45 μL water (2.5 mmol, 5 equiv.), and 2.0 mL of DMA. After 18 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 2% to 5% ethyl acetate in hexanes) to afford the title compound as a clear, colorless oil (95.7 mg, 0.359 mmol, 72%). IR (film) 3060, 2979, 2934, 1597, 1562, 1454, 1268, 1241, 744, 692 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.77 – 7.70 (m, 1H, benzoxazole ArH), 7.52 – 7.46 (m, 1H, benzoxazole ArH), 7.37 – 7.30 (m, 2H, benzoxazole ArH), 7.27 (dd, *J* = 8.8, 7.3 Hz, 2H, phenyl *m*-ArH), 6.92 (d, *J* = 8.1 Hz, 2H, phenyl *o*-ArH), 6.79 (t, *J* = 7.3 Hz, 1H, phenyl *p*-ArH), 5.26 (q, *J* = 7.0 Hz, 1H, NCHAr), 3.46 – 3.33 (m, 2H, NCH₂CH₃), 1.78 (d, *J* = 7.0 Hz, 3H, NCH(Ar)CH₃), 1.11 (dd, *J* = 7.1 Hz, 3H, NCH₂CH₃); ¹³C NMR (125 MHz, CDCl₃) δ 167.1, 150.9, 147.8, 141.0, 129.4, 125.2, 124.4, 120.2, 117.9, 114.3, 110.9, 52.8, 41.0, 16.6, 14.3; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₇H₁₉N₂O) requires *m/z* 267.1492, found 267.1487.



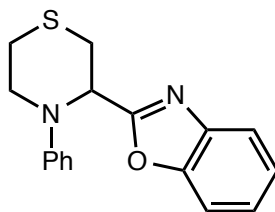
2-(1-Phenylpiperidin-2-yl)benzoxazole (Table 4, Entry 3). Prepared according to the general procedure at 0 °C using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.),

57.1 μL of 2-chlorobenzoxazole (0.50 mmol, 1.0 equiv.), 122.9 μL of *N*-phenylpiperidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 90 μL water (5.0 mmol, 10 equiv.), and 2.0 mL of DMA. After 72 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 5% ethyl acetate in hexanes) to afford the title compound as a white solid (110.3 mg, 0.396 mmol, 79%). IR (film) 3060, 2937, 2855, 1597, 1501, 1454, 1241, 1135, 1023, 922, 746, 690 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.70 – 7.63 (m, 1H, benzoxazole ArH), 7.48 – 7.41 (m, 1H, benzoxazole ArH), 7.31 – 7.24 (m, 2H, benzoxazole ArH), 7.21 (dd, $J = 8.8, 7.3$ Hz, 2H, phenyl *m*-ArH), 7.01 (d, $J = 8.1$ Hz, 2H, phenyl *o*-ArH), 6.80 (t, $J = 7.3$ Hz, 1H, phenyl *p*-ArH), 5.20 (dd, $J = 4.4$ Hz, 1H, NCHAr), 3.63 – 3.45 (m, 2H, NCH₂), 2.38 – 2.28 (m, 1H, NCH(Ar)CH_AH_B), 2.18 – 2.10 (m, 1H, NCH(Ar)CH_AH_B), 1.90 – 1.83 (m, 1H, NCH₂CH_AH_B), 1.81 – 1.66 (m, 3H, NCH₂CH_AH_B and NCH₂CH₂CH₂); ^{13}C NMR (125 MHz, CDCl_3) δ 166.9, 150.6, 150.6, 141.1, 129.3, 124.8, 124.2, 120.1, 119.7, 116.6, 110.7, 55.0, 46.6, 29.7, 25.5, 20.6; HRMS (ESI) exact mass calculated for $[\text{M}+\text{H}]^+$ ($\text{C}_{18}\text{H}_{19}\text{N}_2\text{O}$) requires m/z 279.1492, found 279.1492.



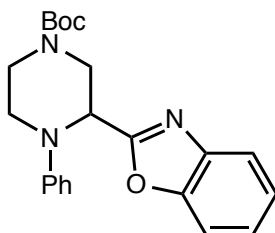
2-(4-Phenylmorpholin-3-yl)benzoxazole (Table 4, Entry 4). Prepared according to the general procedure at r.t. using 2.3 mg of $\text{Ir}(\text{ppy})_2(\text{dtbbpy})\text{PF}_6$ (2.5 μmol , 0.005 equiv.), 57.1 μL of 2-chlorobenzoxazole (0.50 mmol, 1.0 equiv.), 122.4 mg of *N*-phenylmorpholine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 90 μL water (5.0 mmol, 10 equiv.), and 2.0 mL of DMA. After 20 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 10% ethyl acetate in hexanes) to afford the title

compound as a white solid (115.3 mg, 0.411 mmol, 82%). IR (film) 3063, 2970, 2919, 2859, 1598, 1502, 1454, 1260, 1240, 1226, 1122, 1059, 934, 747, 689 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.72 – 7.62 (m, 1H, benzoxazole ArH), 7.49 – 7.41 (m, 1H, benzoxazole ArH), 7.32 – 7.20 (m, 4H, benzoxazole ArH and phenyl *m*-ArH), 6.97 (d, $J = 8.1$ Hz, 2H, phenyl *o*-ArH), 6.85 (t, $J = 7.3$ Hz, 1H, phenyl *p*-ArH), 5.05 (dd, $J = 2.8$ Hz, 1H, NCHAr), 4.43 (dd, $J = 11.4, 2.3$ Hz, 1H, NCH(Ar)CH_AH_BO), 4.19 – 4.08 (m, 2H, NCH(Ar)CH_AH_BO and NCH₂CH_AH_BO), 3.92 – 3.78 (m, 2H, NCH₂CH_AH_BO and NCH_AH_B), 3.49 – 3.42 (m, 1H, NCH_AH_B); ^{13}C NMR (125 MHz, CDCl_3) δ 164.7, 150.7, 149.4, 141.0, 129.4, 125.0, 124.4, 120.3, 120.3, 115.5, 110.8, 69.7, 67.3, 54.2, 45.1; HRMS (ESI) exact mass calculated for $[\text{M}+\text{H}]^+$ ($\text{C}_{17}\text{H}_{17}\text{N}_2\text{O}_2$) requires m/z 281.1285, found 281.1287.



2-(4-Phenylthiomorpholin-3-yl)benzoxazole (Table 4, Entry 5). Prepared according to the general procedure at r.t. using 2.3 mg of $\text{Ir}(\text{ppy})_2(\text{dtbbpy})\text{PF}_6$ (2.5 μmol , 0.005 equiv.), 57.1 μL of 2-chlorobenzoxazole (0.50 mmol, 1.0 equiv.), 134.5 mg of *N*-phenylthiomorpholine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 135 μL water (7.5 mmol, 15 equiv.), and 2.0 mL of DMA. After 5 days, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 5% to 10% ethyl acetate in hexanes) to afford the title compound as a white solid (92.1 mg, 0.311 mmol, 62%). IR (film) 3058, 2913, 1596, 1500, 1454, 1240, 1142, 977, 745, 693 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.74 – 7.67 (m, 1H, benzoxazole ArH), 7.52 – 7.45 (m, 1H, benzoxazole ArH), 7.34 – 7.28 (m, 2H, benzoxazole ArH), 7.25 (dd, $J = 7.9$ Hz, 2H, phenyl *m*-ArH), 7.01 (d, $J = 8.1$ Hz, 2H, phenyl *o*-ArH), 6.87 (t, $J = 7.3$ Hz, 1H, phenyl *p*-ArH), 5.37 (dd, $J = 3.9$ Hz,

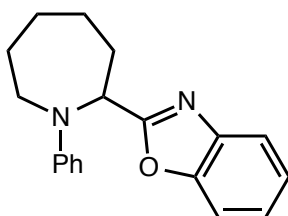
1H, NCH_AAr), 3.96 (ddd, *J* = 13.5, 11.0, 2.6 Hz, 1H, NCH_AH_B), 3.87 (ddd, *J* = 13.4, 3.7 Hz, 1H, NCH_AH_B), 3.40 – 3.28 (m, 2H, NCH(Ar)CH₂S), 3.00 (ddd, *J* = 13.9, 10.9, 3.3 Hz, 1H, NCH₂CH_AH_BS), 2.71 – 2.60 (m, 1H, NCH₂CH_AH_BS); ¹³C NMR (125 MHz, CDCl₃) δ 164.9, 150.8, 150.7, 141.2, 129.4, 125.0, 124.4, 120.7, 120.3, 117.8, 110.8, 56.2, 47.5, 30.8, 27.4; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₇H₁₇N₂OS) requires *m/z* 297.1056, found 297.1053.



***Tert*-butyl 3-(benzoxazol-2-yl)-4-phenylpiperazine-1-carboxylate (Table 4, Entry 6).**

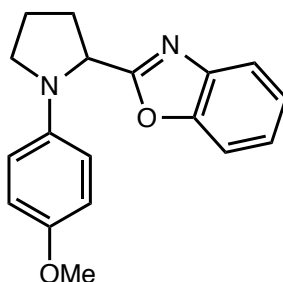
Prepared according to the general procedure at r.t. using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 57.1 μL of 2-chlorobenzoxazole (0.50 mmol, 1.0 equiv.), 196.8 mg of *tert*-butyl 4-phenylpiperazine-1-carboxylate (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 90 μL water (5.0 mmol, 10 equiv.), and 2.0 mL of DMA. After 18 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 10% to 20% ethyl acetate in hexanes) to afford the title compound as a white solid (159.3 mg, 0.420 mmol, 84%). **Reaction performed on 4.0 mmol scale:** Reaction performed according to the general procedure at r.t. using 37 mg of Ir(ppy)₂(dtbbpy)PF₆ (0.040 mmol, 0.01 equiv.), 457 μL of 2-chlorobenzoxazole (4.0 mmol, 1.0 equiv.), 3.15 g of *tert*-butyl 4-phenylpiperazine-1-carboxylate (12.0 mmol, 3.0 equiv.), 656 mg of sodium acetate (8.0 mmol, 2.0 equiv.), and 16 mL of DMA. After 48 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 10% to 20% ethyl acetate in hexanes) to afford the title compound as a white solid (1.22 g, 3.21 mmol, 80%, average of three experiments). IR (film) 2976, 2930, 1690, 1599, 1454, 1421, 1241, 1159, 1126, 910, 746, 729, 689 cm⁻¹; ¹H NMR (500 MHz,

CDCl₃) δ 7.69 – 7.58 (m, 1H, benzoxazole ArH), 7.47 – 7.55 (m, 1H, benzoxazole ArH), 7.33 – 7.18 (m, 4H, benzoxazole ArH and phenyl *m*-ArH), 6.98 (d, $J = 8.2$ Hz, 2H, phenyl *o*-ArH), 6.84 (t, $J = 7.3$ Hz, 1H, phenyl *p*-ArH), 5.10 (s, 1H, NCHAr), 4.51 (d, $J = 13.5$ Hz, 1H, NCH(Ar)CH_AH_BNBoc), 4.36 – 3.18 (m, 5H, NCH(Ar)CH_AH_BNBoc and NCH₂CH₂NBoc), 1.47 – 1.06 (br, 9H, *t*-Bu); ¹³C NMR (125 MHz, CDCl₃) δ 164.6, 154.1, 150.6, 149.4, 140.9, 129.3, 124.9, 124.3, 120.2 (2), 115.9, 110.6, 79.9, 54.1, 47.6, 44.4, 43.0, 28.0; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₂₂H₂₆N₃O₃) requires m/z 380.1969, found 380.1961.

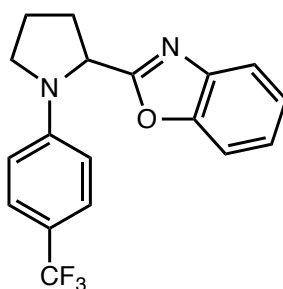


2-(1-Phenylazepan-2-yl)benzoxazole (Table 4, Entry 7). Prepared according to the general procedure at r.t. using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μ mol, 0.005 equiv.), 57.1 μ L of 2-chlorobenzoxazole (0.50 mmol, 1.0 equiv.), 131.5 mg of *N*-phenylazepane (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 90 μ L water (5.0 mmol, 10 equiv.), and 2.0 mL of DMA. After 20 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 5% ethyl acetate in hexanes) to afford the title compound as a clear, colorless oil (136.7 mg, 0.468 mmol, 94%). IR (film) 3059, 2927, 2852, 1595, 1504, 1454, 1385, 1241, 1165, 825, 742, 691 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.75 – 7.67 (m, 1H, benzoxazole ArH), 7.51 – 7.45 (m, 1H, benzoxazole ArH), 7.34 – 7.28 (m, 2H, benzoxazole ArH), 7.22 (dd, $J = 8.3, 7.7$ Hz, 2H, phenyl *m*-ArH), 6.86 (d, $J = 8.4$ Hz, 2H, phenyl *o*-ArH), 6.70 (t, $J = 7.2$ Hz, 1H, phenyl *p*-ArH), 4.95 (dd, $J = 11.7, 6.2$ Hz, 1H, NCHAr), 3.82 – 3.67 (m, 2H, NCH₂), 2.55 (ddd, $J = 14.6, 8.0, 6.6$ Hz, 1H, NCH(Ar)CH_AH_B), 2.22 – 2.11 (m, 1H, NCH(Ar)CH_AH_B), 2.05 – 1.90 (m, 2H, NCH₂CH₂), 1.89 – 1.72 (m, 2H, NCH(Ar)CH₂CH₂), 1.57 – 1.37 (m, 2H, NCH₂CH₂CH₂);

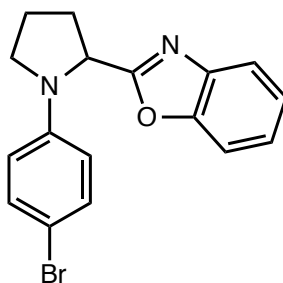
^{13}C NMR (125 MHz, CDCl_3) δ 168.1, 150.7, 148.6, 141.0, 129.5, 124.9, 124.4, 120.1, 116.6, 111.5, 110.8, 56.7, 45.5, 34.4, 29.9, 28.2, 25.8; HRMS (ESI) exact mass calculated for $[\text{M}+\text{H}]^+$ ($\text{C}_{19}\text{H}_{21}\text{N}_2\text{O}$) requires m/z 293.1648, found 293.1647.



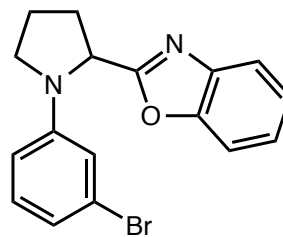
2-(1-(4-Methoxyphenyl)pyrrolidin-2-yl)benzoxazole (Table 4, Entry 8). Prepared according to the general procedure at r.t. using 2.3 mg of $\text{Ir}(\text{ppy})_2(\text{dtbbpy})\text{PF}_6$ (2.5 μmol , 0.005 equiv.), 57.1 μL of 2-chlorobenzoxazole (0.50 mmol, 1.0 equiv.), 132.9 mg of *N*-(4-methoxyphenyl)pyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 45 μL water (2.5 mmol, 5 equiv.), and 2.0 mL of DMA. After 3 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 10% ethyl acetate in hexanes) to afford the title compound as a white solid (135.0 mg, 0.459 mmol, 92%). IR (film) 2950, 2831, 1511, 1454, 1238, 1181, 1144, 1038, 813, 748 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.74 – 7.67 (m, 1H, benzoxazole ArH), 7.52 – 7.44 (m, 1H, benzoxazole ArH), 7.34 – 7.27 (m, 2H, benzoxazole ArH), 6.80 (d, $J = 8.4$ Hz, 2H, phenyl ArH), 6.67 (d, $J = 8.4$ Hz, 2H, phenyl ArH), 4.98 – 4.94 (m, 1H, NCHAr), 3.76 (td, $J = 8.1, 2.6$ Hz, 1H, NCH_AH_B), 3.71 (s, 3H, OCH₃), 3.38 (ddd, $J = 8.4, 6.9$ Hz, 1H, NCH_AH_B), 2.49 – 2.35 (m, 2H, NCH(Ar)CH₂), 2.35 – 2.26 (m, 1H, NCH₂CH_AH_B), 2.21 – 2.11 (m, 1H, NCH₂CH_AH_B); ^{13}C NMR (125 MHz, CDCl_3) δ 168.4, 151.7, 150.9, 141.7, 141.1, 124.9, 124.4, 120.1, 115.0, 113.3, 110.9, 57.7, 55.9, 49.4, 32.5, 24.4; HRMS (ESI) exact mass calculated for $[\text{M}+\text{H}]^+$ ($\text{C}_{18}\text{H}_{19}\text{N}_2\text{O}_2$) requires m/z 295.1441, found 295.1436.

**2-(1-(4-(Trifluoromethyl)phenyl)pyrrolidin-2-yl)benzoxazole (Table 4, Entry 9).**

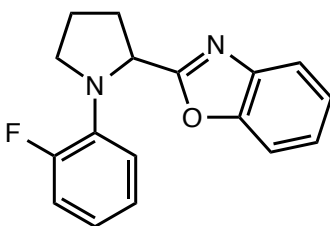
Prepared according to the general procedure at r.t. using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 57.1 μL of 2-chlorobenzoxazole (0.50 mmol, 1.0 equiv.), 161.4 mg of *N*-(4-(trifluoromethyl)phenyl)pyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 90 μL water (5.0 mmol, 10 equiv.), and 2.0 mL of DMA. After 18 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 10% ethyl acetate in hexanes) to afford the title compound as a white solid (131.6 mg, 0.396 mmol, 79%). IR (film) 2977, 2955, 2862, 1614, 1530, 1454, 1319, 1241, 1197, 1150, 1102, 1068, 816, 748 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.76 – 7.68 (m, 1H, benzoxazole ArH), 7.54 – 7.46 (m, 1H, benzoxazole ArH), 7.42 (d, *J* = 8.7 Hz, 2H, phenyl ArH), 7.37 – 7.29 (m, 2H, benzoxazole ArH), 6.72 (d, *J* = 8.7 Hz, 2H, phenyl ArH), 5.12 – 5.06 (m, 1H, NCHAr), 3.83 – 3.77 (m, 1H, NCH_AH_B), 3.48 (dd, *J* = 15.8, 8.3 Hz, 1H, NCH_AH_B), 2.57 – 2.31 (m, 3H, NCH(Ar)CH₂ and NCH₂CH_AH_B), 2.25 – 2.13 (m, 1H, NCH₂CH_AH_B); ¹³C NMR (125 MHz, CDCl₃) δ 167.0, 150.9, 148.9, 140.9, 126.6 (q, *J* = 3.7 Hz), 125.2, 125.1 (q, *J* = 270.4 Hz), 124.6, 120.2, 118.5 (q, *J* = 32.6 Hz), 111.8, 110.9, 56.9, 48.6, 32.3, 24.0; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₈H₁₆F₃N₂O) requires *m/z* 333.1209, found 333.1204.



2-(1-(4-Bromophenyl)pyrrolidin-2-yl)benzoxazole (Table 4, Entry 10). Prepared according to the general procedure at r.t. using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 57.1 μL of 2-chlorobenzoxazole (0.50 mmol, 1.0 equiv.), 169.6 mg of *N*-(4-bromophenyl)pyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 45 μL water (2.5 mmol, 5 equiv.), and 2.0 mL of DMA. After 2 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 5% to 10% ethyl acetate in hexanes) to afford the title compound as a white solid (150.7 mg, 0.439 mmol, 88%). IR (film) 3044, 2974, 2849, 1592, 1493, 1454, 1360, 1241, 1144, 805, 748 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.75 – 7.66 (m, 1H, benzoxazole ArH), 7.48 – 7.43 (m, 1H, benzoxazole ArH), 7.35 – 7.28 (m, 2H, benzoxazole ArH), 7.25 (d, *J* = 8.9 Hz, 2H, phenyl ArH), 6.56 (d, *J* = 8.9 Hz, 2H, phenyl ArH), 5.01 – 4.96 (m, 1H, NCHAr), 3.77 – 3.68 (m, 1H, NCH_AH_B), 3.40 (dd, *J* = 15.6, 8.5 Hz, 1H, NCH_AH_B), 2.55 – 2.27 (m, 3H, NCH(Ar)CH₂ and NCH₂CH_AH_B), 2.20 – 2.11 (m, 1H, NCH₂CH_AH_B); ¹³C NMR (125 MHz, CDCl₃) δ 167.4, 150.9, 145.7, 141.0, 131.9, 125.1, 124.5, 120.2, 114.0, 100.9, 109.0, 57.1, 48.8, 32.4, 24.2; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₇H₁₆BrN₂O) requires *m/z* 343.0441, found 343.0450.

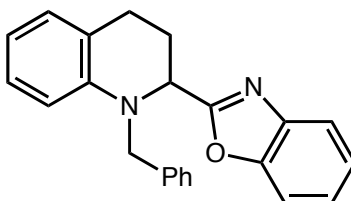


2-(1-(3-Bromophenyl)pyrrolidin-2-yl)benzoxazole (Table 4, Entry 11). Prepared according to the general procedure at r.t. using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 57.1 μL of 2-chlorobenzoxazole (0.50 mmol, 1.0 equiv.), 169.6 mg of *N*-(3-bromophenyl)pyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 90 μL water (5.0 mmol, 10 equiv.), and 2.0 mL of DMA. After 16 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 5% to 10% ethyl acetate in hexanes) to afford the title compound as a clear, colorless oil (147.3 mg, 0.429 mmol, 86%). IR (film) 3066, 2974, 2952, 2851, 1590, 1556, 1486, 1453, 1359, 1240, 1144, 985, 818, 748 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.74 – 7.67 (m, 1H, benzoxazole ArH), 7.52 – 7.44 (m, 1H, benzoxazole ArH), 7.36 – 7.28 (m, 2H, benzoxazole ArH), 7.01 (dd, *J* = 8.1 Hz, 1H, phenyl ArH), 6.86 – 6.77 (m, 2H, phenyl ArH), 6.59 (dd, *J* = 8.3, 2.2 Hz, 1H, phenyl ArH), 5.03 – 4.99 (m, 1H, NCHAr), 3.77 – 3.70 (m, 1H, NCH_AH_B), 3.41 (dd, *J* = 8.6 Hz, 1H, NCH_AH_B), 2.50 – 2.28 (m, 3H, NCH(Ar)CH₂ and NCH₂CH_AH_B), 2.23 – 2.12 (m, 1H, NCH₂CH_AH_B); ¹³C NMR (125 MHz, CDCl₃) δ 167.3, 150.9, 147.9, 141.0, 130.5, 125.1, 124.5, 123.5, 120.2, 119.8, 115.2, 111.1, 110.9, 57.0, 48.7, 32.4, 24.0; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₇H₁₆BrN₂O) requires *m/z* 343.0441, found 343.0437.



2-(1-(2-Fluorophenyl)pyrrolidin-2-yl)benzoxazole (Table 4, Entry 12). Prepared according to the general procedure at r.t. using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 57.1 μL of 2-chlorobenzoxazole (0.50 mmol, 1.0 equiv.), 123.9 mg of *N*-(2-fluorophenyl)pyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 45 μL water (2.5 mmol, 5 equiv.), and 2.0 mL of DMA. After 11 h,

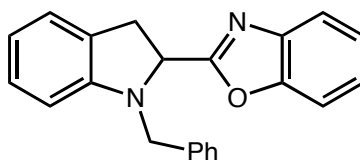
the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 5% to 10% ethyl acetate in hexanes) to afford the title compound as a clear, colorless oil (131.1 mg, 0.464 mmol, 93%). IR (film) 3066, 2973, 2875, 1613, 1503, 1454, 1343, 1241, 1206, 1142, 740 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.71 – 7.65 (m, 1H, benzoxazole ArH), 7.51 – 7.44 (m, 1H, benzoxazole ArH), 7.32 – 7.26 (m, 2H, benzoxazole ArH), 6.98 – 6.88 (m, 2H, phenyl ArH), 6.81 (dd, $J = 8.4$ Hz, 1H, phenyl ArH), 6.71 – 6.62 (m, 1H, phenyl ArH), 5.30 – 5.24 (m, 1H, NCHAr), 3.96 – 3.89 (m, 1H, NCH_AH_B), 3.56 – 3.48 (m, 1H, NCH_AH_B), 2.52 – 2.40 (m, 1H, NCH(Ar)CH_AH_B), 2.33 – 2.18 (m, 2H, NCH(Ar)CH_AH_B and NCH₂CH_AH_B), 2.15 – 2.02 (m, 1H, NCH₂CH_AH_B); ^{13}C NMR (125 MHz, CDCl_3) δ 168.1, 152.2 (d, $J = 241.2$ Hz), 150.8, 141.2, 135.6 (d, $J = 9.0$ Hz), 124.8, 124.6 (d, $J = 3.1$ Hz), 124.3, 120.1, 118.7 (d, $J = 7.4$ Hz), 116.4 (d, $J = 21.4$ Hz), 116.2 (d, $J = 4.5$ Hz), 110.8, 58.2 (d, $J = 5.3$ Hz), 50.7 (d, $J = 4.5$ Hz), 32.5, 23.8 (d, $J = 1.6$ Hz); HRMS (ESI) exact mass calculated for $[\text{M}+\text{H}]^+$ ($\text{C}_{17}\text{H}_{16}\text{FN}_2\text{O}$) requires m/z 283.1241, found 283.1240.



2-(1-Benzyl-1,2,3,4-tetrahydroquinolin-2-yl)benzoxazole (Table 4, Entry 13).

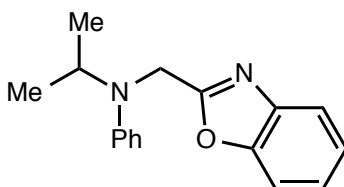
Prepared according to the general procedure at 0 °C using 2.3 mg of $\text{Ir}(\text{ppy})_2(\text{dtbbpy})\text{PF}_6$ (2.5 μmol , 0.005 equiv.), 57.1 μL of 2-chlorobenzoxazole (0.50 mmol, 1.0 equiv.), 167.5 mg of *N*-benzyl-1,2,3,4-tetrahydroquinoline (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 90 μL water (5.0 mmol, 10 equiv.), and 2.0 mL of DMA. After 72 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 5% ethyl acetate in hexanes) to afford the title compound as a clear, colorless oil (113.5 mg, 0.333 mmol, 67%). The product was obtained as a single regioisomer. IR (film) 3062, 3027, 2931, 2857, 1602, 1494, 1452, 1240, 826, 739 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.77 – 7.69 (m, 1H,

benzoxazole ArH), 7.53 – 7.46 (m, 1H, benzoxazole ArH), 7.35 – 7.20 (m, 7H, ArH), 7.06 (m, 2H, ArH), 6.74 – 6.63 (m, 2H, ArH), 4.98 (dd, $J = 3.5$ Hz, 1H, NCHAr), 4.90 (d, $J = 17.3$ Hz, 1H, NCH_AH_BPh), 4.51 (d, $J = 17.3$ Hz, 1H, NCH_AH_BPh), 3.00 – 2.89 (m, 1H, NCH(Ar)CH_AH_B), 2.85 – 2.75 (m, 1H, NCH(Ar)CH_AH_B), 2.63 – 2.52 (m, 1H, NCH(Ar)CH₂CH_AH_B), 2.41 (m, 1H, NCH(Ar)CH₂CH_AH_B); ¹³C NMR (125 MHz, CDCl₃) δ 167.1, 151.0, 143.9, 141.1, 138.1, 129.0, 128.8, 127.6, 127.1, 126.5, 125.0, 124.4, 121.9, 120.2, 117.0, 111.7, 110.9, 56.5, 54.0, 26.2, 24.7; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₂₃H₂₁N₂O) requires m/z 341.1648, found 341.1647.

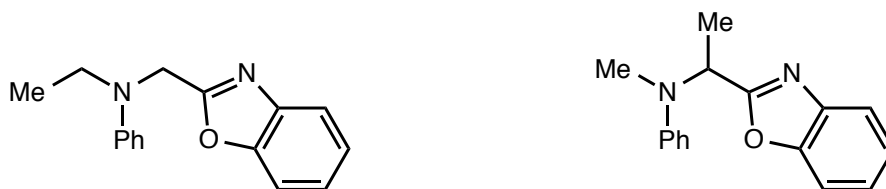


2-(1-Benzylindolin-2-yl)benzoxazole (Table 4, Entry 14). Prepared according to the general procedure at r.t. using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 57.1 μL of 2-chlorobenzoxazole (0.50 mmol, 1.0 equiv.), 157.0 mg of *N*-benzylindoline (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 90 μL water (5.0 mmol, 10 equiv.), and 2.0 mL of DMA. After 72 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 5% to 10% ethyl acetate in hexanes) to afford the title compound as a clear, colorless oil (101.3 mg, 0.310 mmol, 62%). The product was obtained as a single regioisomer. IR (film) 3056, 3029, 2916, 2851, 1606, 1483, 1453, 1239, 1142, 815, 743, 699 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.73 – 7.67 (m, 1H, benzoxazole ArH), 7.53 – 7.47 (m, 1H, benzoxazole ArH), 7.37 – 7.31 (m, 2H, benzoxazole ArH), 7.29 (d, $J = 7.5$ Hz, 2H, ArH), 7.22 (dd, $J = 7.5$ Hz, 2H, ArH), 7.18 – 7.07 (m, 3H, ArH), 6.76 (dd, $J = 7.4$ Hz, 1H, ArH), 6.54 (d, $J = 7.9$ Hz, 1H, ArH), 5.00 (dd, $J = 9.5$ Hz, 1H, NCHAr), 4.53 (d, $J = 15.6$ Hz, 1H, NCH_AH_BPh), 4.30 (d, $J = 15.6$ Hz, 1H, NCH_AH_BPh), 3.59 – 3.45 (m, 2H, NCH(Ar)CH₂); ¹³C NMR (125 MHz, CDCl₃) δ 165.8, 151.2, 151.0, 140.9, 137.5, 128.5, 128.0, 127.9, 127.2, 127.2, 125.3, 124.5, 120.2, 118.7, 110.9, 107.9, 62.0, 51.9,

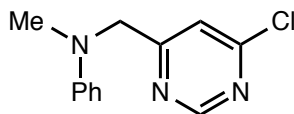
34.8; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{22}H_{19}N_2O$) requires m/z 327.1492, found 327.1487.



***N*-(Benzoxazol-2-ylmethyl)-*N*-isopropylaniline (Table 4, Entry 15).** Prepared according to the general procedure at r.t. using 2.3 mg of $Ir(ppy)_2(dtbbpy)PF_6$ (2.5 μ mol, 0.005 equiv.), 57.1 μ L of 2-chlorobenzoxazole (0.50 mmol, 1.0 equiv.), 112 mg of *N*-isopropyl-*N*-methylpyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 90 μ L water (5.0 mmol, 10 equiv.), and 2.0 mL of DMA. After 22 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 5% EtOAc in hexanes) to afford the title compound as a clear, colorless oil (99.3 mg, 0.373 mmol, 75%). IR (film) 3060, 2971, 2930, 1598, 1503, 1454, 1240, 831, 743, 692 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 7.75–7.68 (m, 1H, benzoxazole ArH), 7.53–7.46 (m, 1H, benzoxazole ArH), 7.35–7.28 (m, 2H, benzoxazole ArH), 7.28–7.19 (m, 2H, phenyl *m*-ArH), 6.92 (d, $J = 8.1$ Hz, 2H, phenyl *o*-ArH), 6.76 (t, $J = 7.3$ Hz, 1H, phenyl *p*-ArH), 4.65 (s, 2H, NCH_2Ar), 4.28 (hept, $J = 6.5$ Hz, 1H, $NCH(CH_3)_2$), 1.31 (d, $J = 6.7$ Hz, 6H, $NCH(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.7, 151.0, 148.7, 141.3, 129.4, 124.9, 124.4, 120.1, 117.8, 113.7, 110.8, 48.8, 43.0, 20.1; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{17}H_{19}N_2O$) requires m/z 267.1492, found 267.1490.

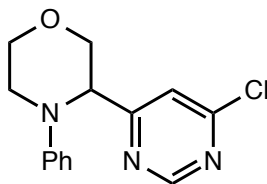


***N*-(Benzoxazol-2-ylmethyl)-*N*-ethylaniline and *N*-(1-(benzoxazol-2-yl)ethyl)-*N*-methylaniline (Table 4, Entry 16).** Prepared according to the general procedure at r.t. using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μmol, 0.005 equiv.), 57.1 μL of 2-chlorobenzoxazole (0.50 mmol, 1.0 equiv.), 101 mg of *N*-ethyl-*N*-methylpyrrolidine (0.75 mmol, 1.5 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 90 μL water (5.0 mmol, 10 equiv.), and 2.0 mL of DMA. After 22 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 5% EtOAc in hexanes) to afford the title compounds as a 9:1 mixture of regioisomers and as a clear, colorless oil (106.5 mg, 0.422 mmol, 84%). ***N*-(Benzoxazol-2-ylmethyl)-*N*-ethylaniline (major regioisomer):** ¹H NMR (500 MHz, CDCl₃) δ 7.74–7.68 (m, 1H, benzoxazole ArH), 7.53–7.46 (m, 1H, benzoxazole ArH), 7.36–7.29 (m, 2H, benzoxazole ArH), 7.24 (dd, *J* = 9.0, 7.3 Hz, 2H, phenyl *m*-ArH), 6.88 (d, *J* = 7.8 Hz, 2H, phenyl *o*-ArH), 6.75 (t, *J* = 7.2 Hz, 1H, phenyl *p*-ArH), 4.73 (s, 2H, NCH₂Ar), 3.63 (q, *J* = 7.1 Hz, 2H, NCH₂CH₃), 1.27 (t, *J* = 7.1 Hz, 3H, NCH₂CH₃); ¹³C NMR (125 MHz, CDCl₃) δ 164.4, 151.0, 147.8, 141.1, 129.5, 125.1, 124.5, 120.1, 117.4, 112.9, 110.8, 48.2, 45.9, 12.3. ***N*-(1-(benzoxazol-2-yl)ethyl)-*N*-methylaniline (minor regioisomer):** ¹H NMR (500 MHz, CDCl₃, characteristic signals) δ 6.96 (d, *J* = 7.8 Hz, 2H, phenyl *o*-ArH), 6.82 (t, *J* = 7.3 Hz, 1H, phenyl *p*-ArH), 5.33 (q, *J* = 7.0 Hz, 1H, NCHAr), 2.87 (s, 3H, NCH₃), 1.75 (d, *J* = 7.0 Hz, 3H, NCH(Ar)CH₃); ¹³C NMR (125 MHz, CDCl₃) δ 166.8, 151.0, 149.5, 141.0, 129.4, 125.2, 124.4, 120.2, 118.2, 114.1, 110.9, 53.3, 32.7, 15.6. **For the mixture of regioisomers:** IR (film) 3059, 2972, 2928, 1598, 1504, 1454, 1239, 742, 691 cm⁻¹; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₆H₁₇N₂O) requires *m/z* 253.1335, found 253.1332.



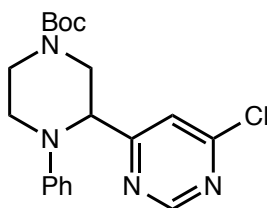
***N*-(6-Chloropyrimidin-4-ylmethyl)-*N*-methylaniline (Table 4, Entry 17).** Prepared according to the general procedure at 0 °C using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5

μmol , 0.005 equiv.), 111.7 mg of 4,6-dichloropyrimidine (0.75 mmol, 1.5 equiv.), 63.4 μL of *N,N*-dimethylaniline (0.5 mmol, 1.0 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 360 μL water (20.0 mmol, 40 equiv.), and 2.0 mL of DMA. After 72 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 10% ethyl acetate in hexanes) to afford the title compound as a clear, colorless oil (77.6 mg, 0.332 mmol, 66%). IR (film) 3055, 2900, 2820, 1600, 1563, 1531, 1505, 1349, 1314, 748, 736, 692 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.98 (s, 1H, pyrimidine ArH), 7.32 – 7.23 (m, 3H, pyrimidine ArH and phenyl *m*-ArH), 6.82 (t, $J = 7.3$ Hz, 1H, phenyl *p*-ArH), 6.69 (d, $J = 8.1$ Hz, 2H, phenyl *o*-ArH), 4.62 (s, 2H, NCH₂), 3.15 (s, 3H, NCH₃); ^{13}C NMR (125 MHz, CDCl_3) δ 171.1, 162.4, 159.0, 148.7, 129.6, 118.8, 117.8, 112.3, 58.5, 39.5; HRMS (ESI) exact mass calculated for $[\text{M}+\text{H}]^+$ ($\text{C}_{12}\text{H}_{13}\text{ClN}_3$) requires m/z 234.0793, found 234.0795.



3-(6-Chloropyrimidin-4-yl)-4-phenylmorpholine (Table 4, Entry 18). Prepared according to the general procedure at 0 °C using 2.3 mg of $\text{Ir}(\text{ppy})_2(\text{dtbbpy})\text{PF}_6$ (2.5 μmol , 0.005 equiv.), 111.7 mg of 4,6-dichloropyrimidine (0.75 mmol, 1.5 equiv.), 81.6 mg of *N*-phenylmorpholine (0.5 mmol, 1.0 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 180 μL water (10.0 mmol, 20 equiv.), and 2.0 mL of DMA. After 48 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 10% to 20% ethyl acetate in hexanes) to afford the title compound as a white solid (30.4 mg, 0.110 mmol, 22%). IR (film) 3058, 2964, 2921, 2855, 1598, 1561, 1530, 1500, 1313, 1262, 1121, 932, 753, 741, 691 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.92 (d, $J = 0.8$ Hz, 1H, pyrimidine ArH), 7.26 – 7.19 (m, 3H, pyrimidine ArH and phenyl *m*-ArH), 6.94 – 6.83 (m, 3H, phenyl *o,p*-ArH), 4.67 (dd, $J = 4.4$ Hz, 1H, NCHAr), 4.13 – 4.04 (m, 2H, NCH(Ar)CH₂O), 4.01 (ddd, $J = 11.2, 5.9,$

3.5 Hz, 1H, NCH₂CH_AH_BO), 3.90 (ddd, $J = 11.5, 3.7$ Hz, 1H, NCH₂CH_AH_BO), 3.52 (ddd, $J = 12.3, 7.2, 3.5$ Hz, 1H, NCH_AH_B), 3.36 (ddd, $J = 12.5, 5.9, 3.5$ Hz, 1H, NCH_AH_B); ¹³C NMR (125 MHz, CDCl₃) δ 170.7, 161.7, 158.9, 149.3, 129.6, 121.1, 120.5, 117.2, 70.7, 67.3, 60.4, 48.1; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₄H₁₅ClN₃O) requires m/z 276.0898, found 276.0896.



tert-Butyl 3-(6-chloropyrimidin-4-yl)-4-phenylpiperazine-1-carboxylate (Table 4, Entry 19). Prepared according to the general procedure at 0 °C using 2.3 mg of Ir(ppy)₂(dtbbpy)PF₆ (2.5 μ mol, 0.005 equiv.), 111.7 mg of 4,6-dichloropyrimidine (0.75 mmol, 1.5 equiv.), 131.2 mg of *tert*-butyl 4-phenylpiperazine-1-carboxylate (0.5 mmol, 1.0 equiv.), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 180 μ L water (10.0 mmol, 20 equiv.), and 2.0 mL of DMA. After 48 h, the reaction was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, 10% ethyl acetate in hexanes) to afford the title compound as a clear, colorless oil (65.9 mg, 0.176 mmol, 35%). IR (film) 2976, 2930, 1691, 1561, 1531, 1503, 1413, 1365, 1311, 1248, 1227, 1161, 1122, 914, 751, 731, 691 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 8.95 (s, 1H, pyrimidine ArH), 7.34 (s, 1H, pyrimidine ArH), 7.23 (dd, $J = 8.5, 7.5$ Hz, 2H, phenyl *m*-ArH), 6.87 (t, $J = 7.3$ Hz, 1H, phenyl *p*-ArH), 6.78 (d, $J = 7.9$ Hz, 2H, phenyl *o*-ArH), 4.68 (dd, $J = 4.3$ Hz, 1H, NCHAr), 4.3 – 3.3 (br, 6H, piperazine methylenes), 1.36 (br, 9H, *t*-Bu); ¹³C NMR (125 MHz, CDCl₃) δ 172.1, 162.1, 158.9, 154.5, 149.3, 129.6, 120.4, 120.1, 115.9, 80.4, 61.7, 47.2, 45.8, 43.0, 28.4; HRMS (ESI) exact mass calculated for [M+H]⁺ (C₁₉H₂₄ClN₄O₂) requires m/z 375.1582, found 375.1582.

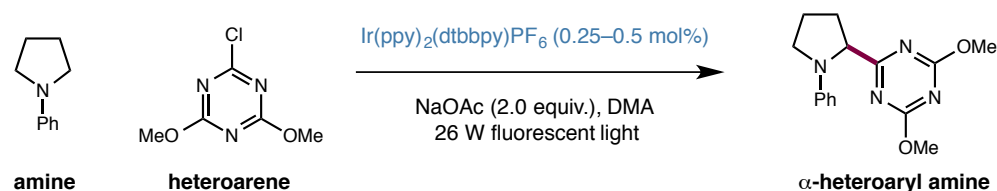
4. Selected Optimization Studies

Table S1 Optimization of photoredox α -heteroarylation with 4,6-dichloropyrimidine

amine + heteroarene $\xrightarrow[\text{NaOAc (2.0 equiv.), DMA, 26 W fluorescent light}]{\text{photocatalyst}}$ α -heteroaryl amine

entry	amine (equiv.)	water (equiv.)	temperature (°C)	photocatalyst (mol%)	yield (%) ^a
1	3	0	23	Ir(ppy) ₃ (1 mol%)	29%
2	3	0	23	Ir(Fppy) ₃ (1 mol%)	8%
3	3	0	23	Ru(bpy) ₃ Cl ₂ (1 mol%)	0%
4	3	0	23	Ir(ppy) ₂ (dtbbpy)PF ₆ (0.5 mol%)	51%
5	3	10	23	Ir(ppy) ₂ (dtbbpy)PF ₆ (0.5 mol%)	71%
6	3	20	23	Ir(ppy) ₂ (dtbbpy)PF ₆ (0.5 mol%)	79%
7	1.5	20	23	Ir(ppy) ₂ (dtbbpy)PF ₆ (0.5 mol%)	78%
8	1.5	20	0	Ir(ppy) ₂ (dtbbpy)PF ₆ (0.5 mol%)	77%
9 ^b	1.5	25	0	Ir(ppy) ₂ (dtbbpy)PF ₆ (0.5 mol%)	85%

^aYield determined by ¹H NMR analysis of crude reaction mixture with 1,3-benzodioxole as an internal standard. Entries 1–3 performed for 31 h, entries 4–9 performed for 22–24 h. ^bIsolated yield.

Table S2 Effects of water and temperature on the coupling of a chlorotriazine.

entry	amine (equiv.)	water (equiv.)	temperature (°C)	yield (%) ^a
1 ^b	3	0	23	18%
2 ^b	3	0	10	29%
3 ^b	3	0	0	40%
4	3	1	0	46%
5	3	3	0	53%
6	3	5	0	62%
7	3	10	0	72%
8	3	20	0	75%
9	3	30	0	82%
10	3	40	0	84%
11 ^c	3	50	0	86%
12 ^c	1.5	50	0	88%

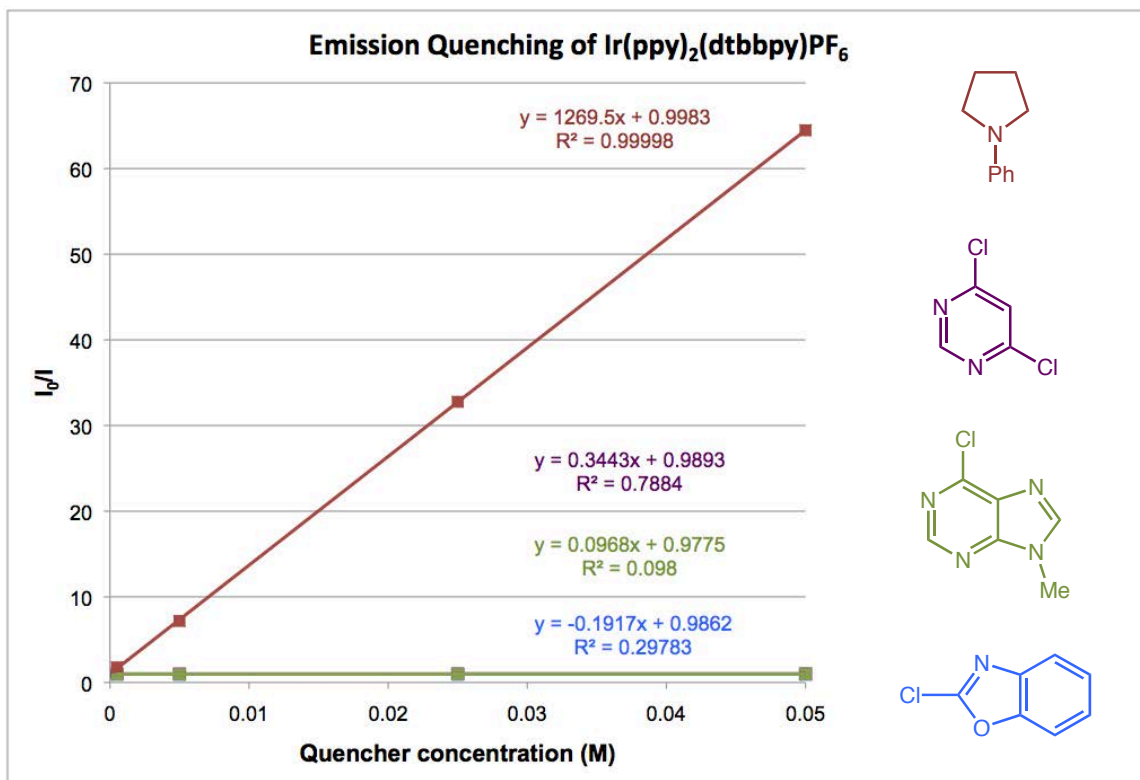
^aYield determined by ¹H NMR analysis of crude reaction mixture with 1,3-benzodioxole as an internal standard. Entries 1–3 performed for 28 h, entries 4–12 performed for 20–21 h.

^bEmployed is NaCO₂Et (2 equiv). instead of NaOAc. ^cIsolated yield.

While the effect of water is modest in the case of 2-chlorobenzothiazole (Table 1), water exerts a remarkable impact on the couplings of pyrimidine and triazine substrates (Tables S1 and S2). While the origin of this effect is not entirely clear, we speculate that water may aid in solvating polar, charged species such as the amine radical cation, perhaps through dipole-dipole interactions. Water may thus accelerate electron-transfer events that form charged species, or it might aid in the dissociation of electron-transfer complexes and thereby limit unproductive back-electron transfer. Alternatively, the effect of water may be related to solvation of the sodium acetate base.

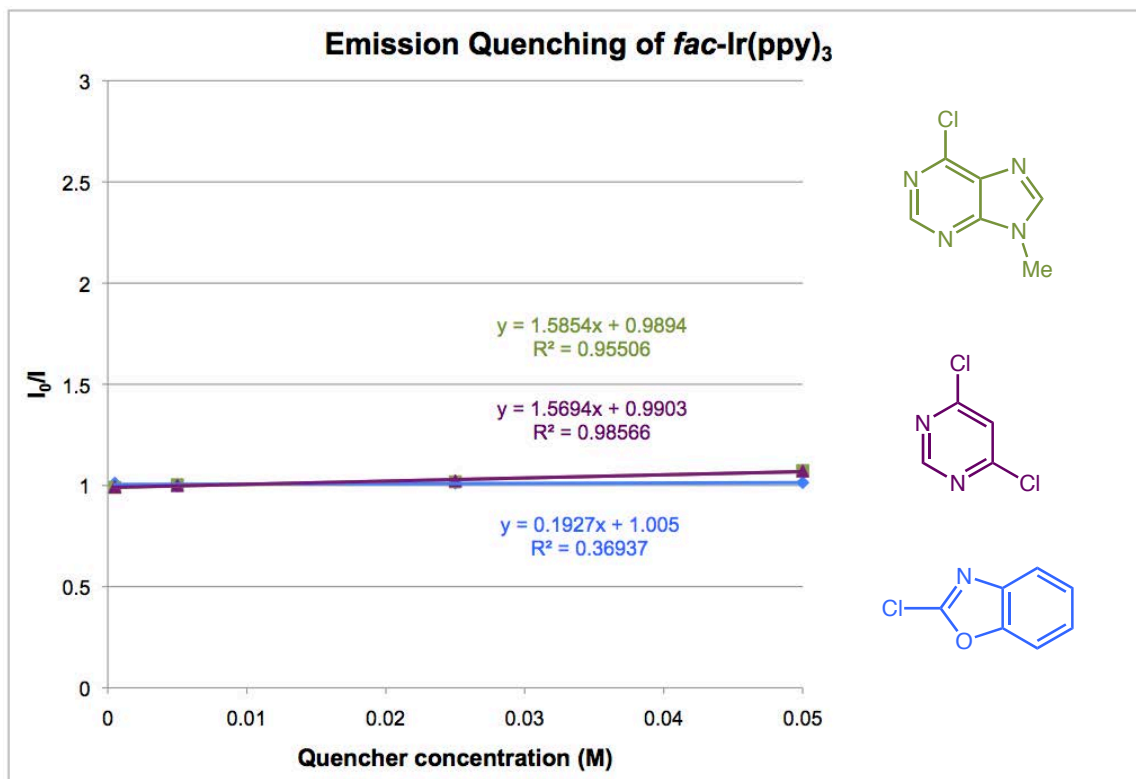
5. Stern–Volmer Fluorescence Quenching Studies

Fluorescence quenching studies were performed using an Agilent Cary Eclipse Fluorescence Spectrophotometer. In each experiment, the photocatalyst and varying concentrations of quencher were combined in DMA in screw-top 1.0 cm quartz cuvettes and degassed by sparging with argon for ten minutes. For the emission quenching of $\text{Ir}(\text{ppy})_2(\text{dtbbpy})\text{PF}_6$, the photocatalyst concentration was 5.0×10^{-4} M, the solution was irradiated at 460 nm, and the emission intensity was observed at 580 nm. For the emission quenching of *fac*- $\text{Ir}(\text{ppy})_3$, the photocatalyst concentration was 3.5×10^{-6} M, the solution was irradiated at 350 nm, and the emission intensity was observed at 520 nm. Plots were constructed according to the Stern–Volmer equation $I_0/I = 1 + k_q\tau_0[\text{Q}]$.⁶



(Plots for the three chloroheteroarenes are overlapping.)

⁶ N. J. Turro, *Modern Molecular Photochemistry*, Benjamin/Cummings: Menlo Park, CA, 1978.

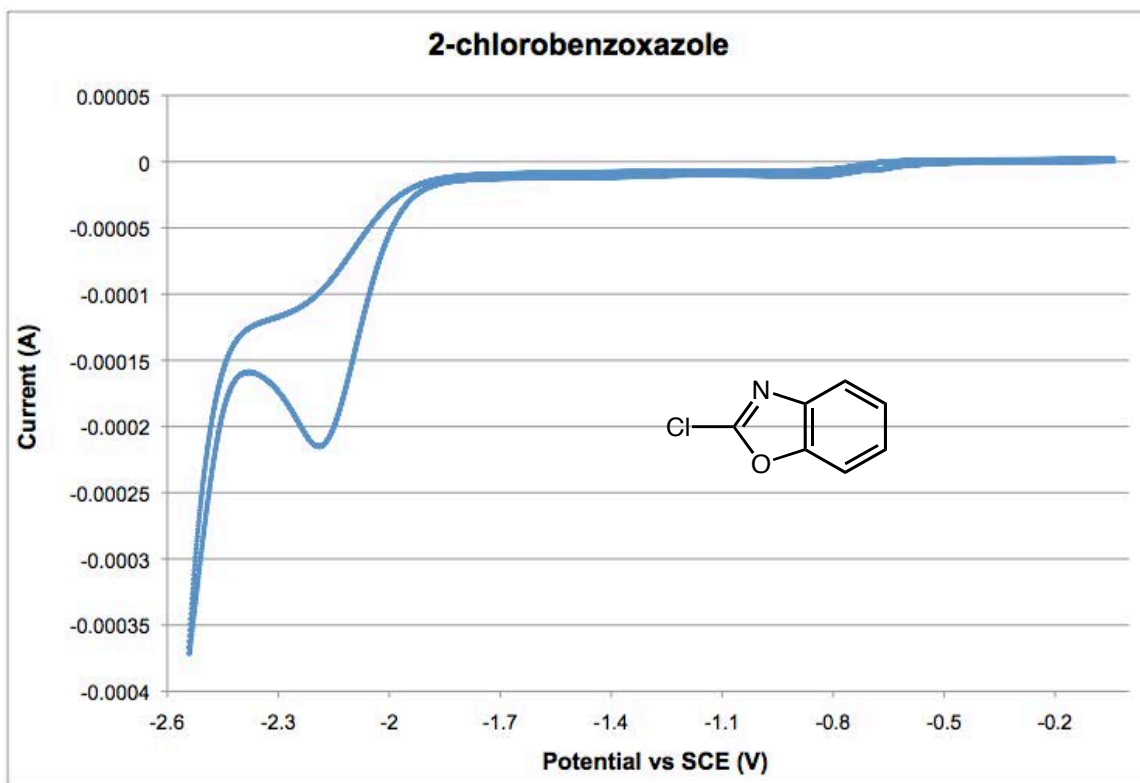


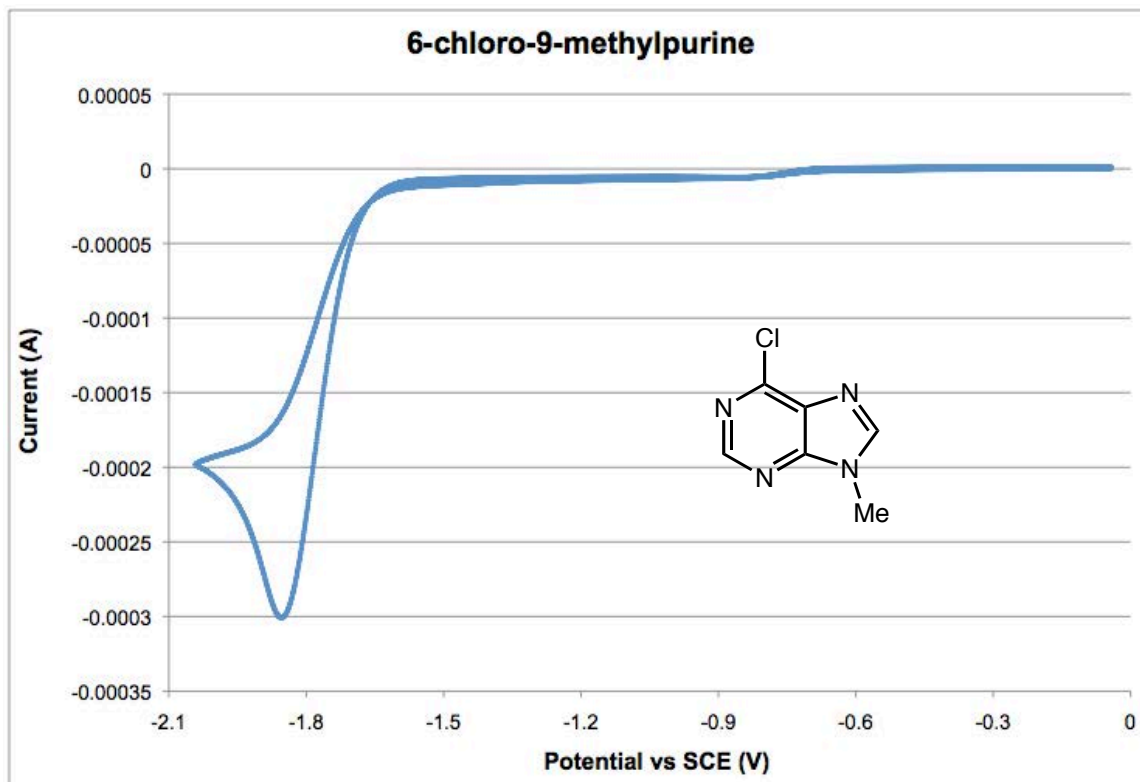
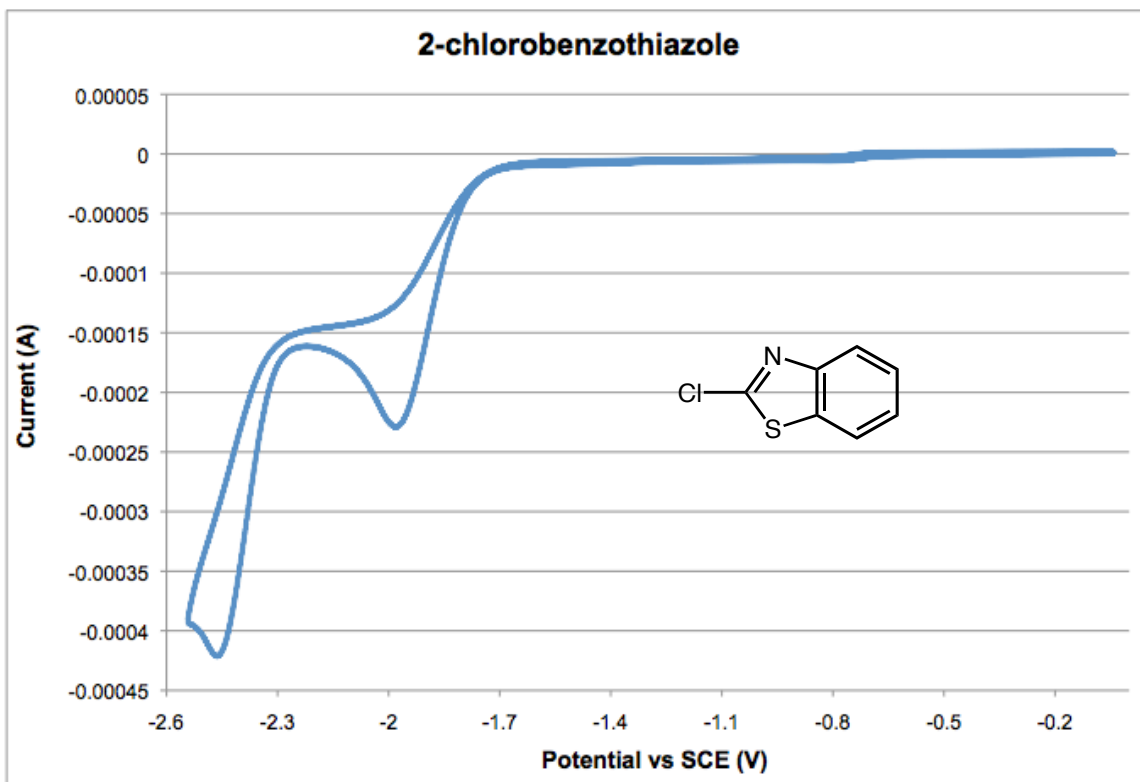
6. Cyclic Voltammetry Measurements

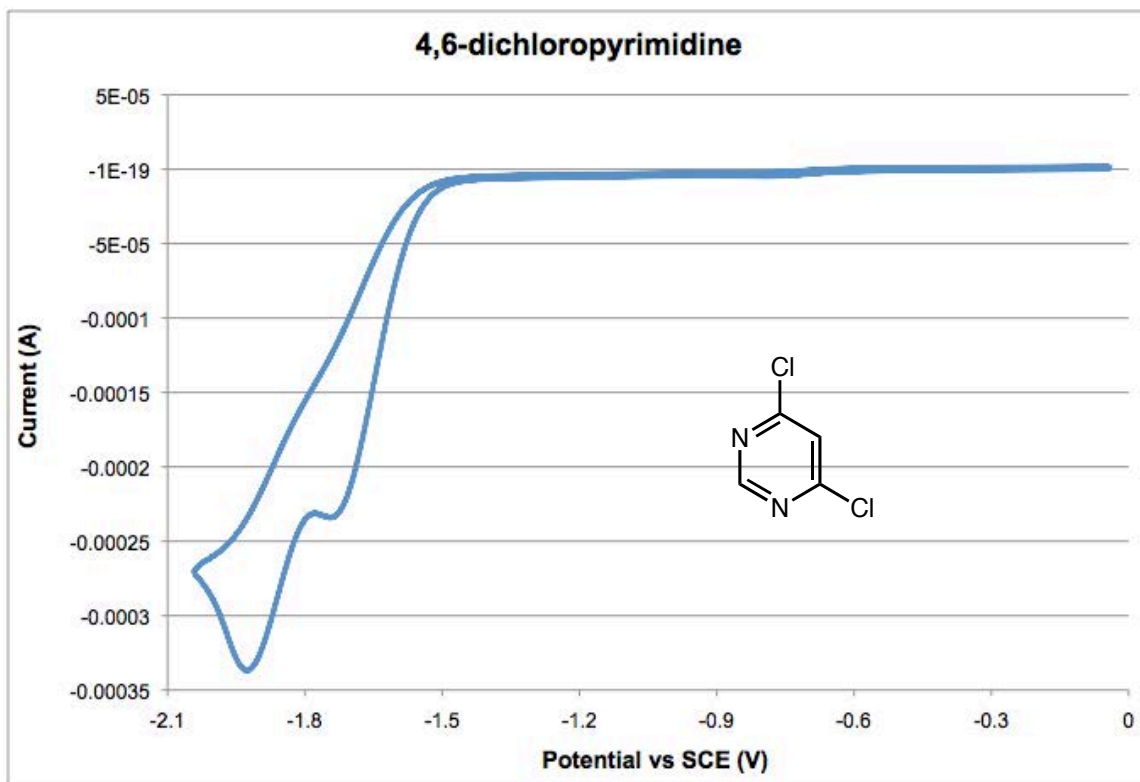
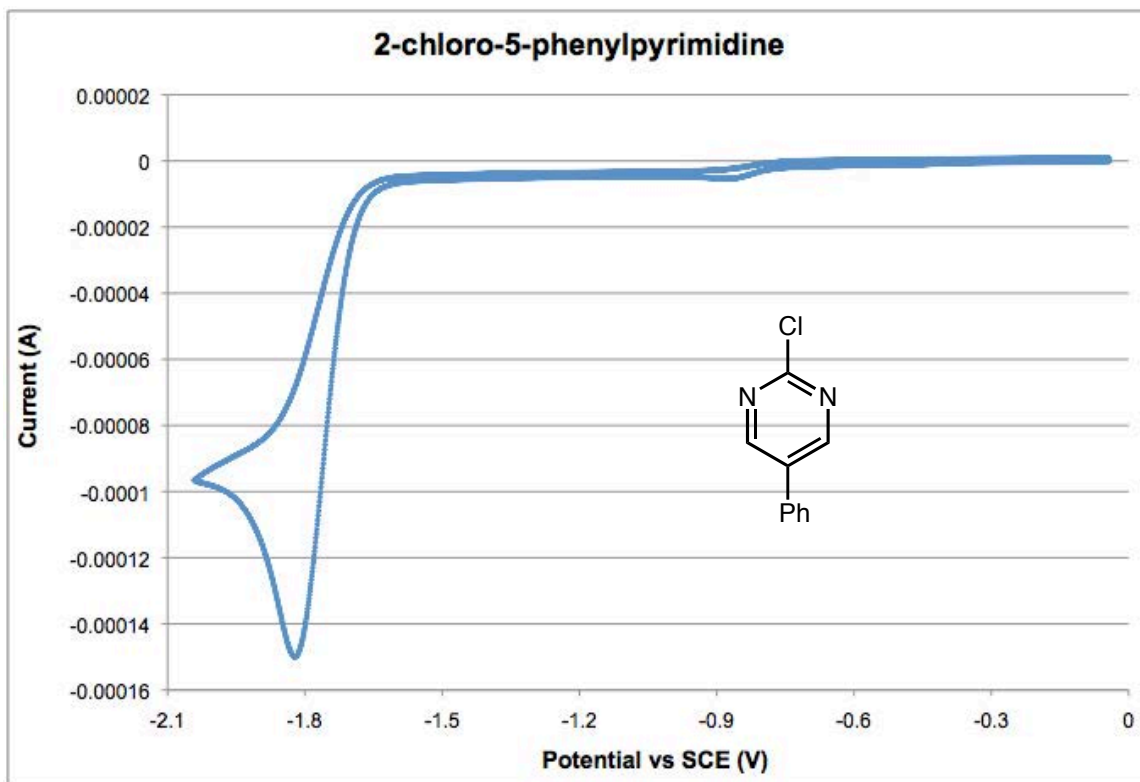
Cyclic voltammetry was performed using a CHI 1140A potentiostat, a glassy carbon working electrode, a platinum mesh counter electrode, and a Ag/AgCl reference electrode. Samples were prepared with a substrate concentration of 0.01 M in a 0.1 M tetrabutylammonium tetrafluoroborate in acetonitrile electrolyte solution. Data was collected with a sweep rate of 20 mV/s, and all chloroheterocycles displayed an irreversible reduction wave. Reduction potentials were converted to reference the saturated calomel electrode (SCE) by subtracting 42 mV from the measured values.

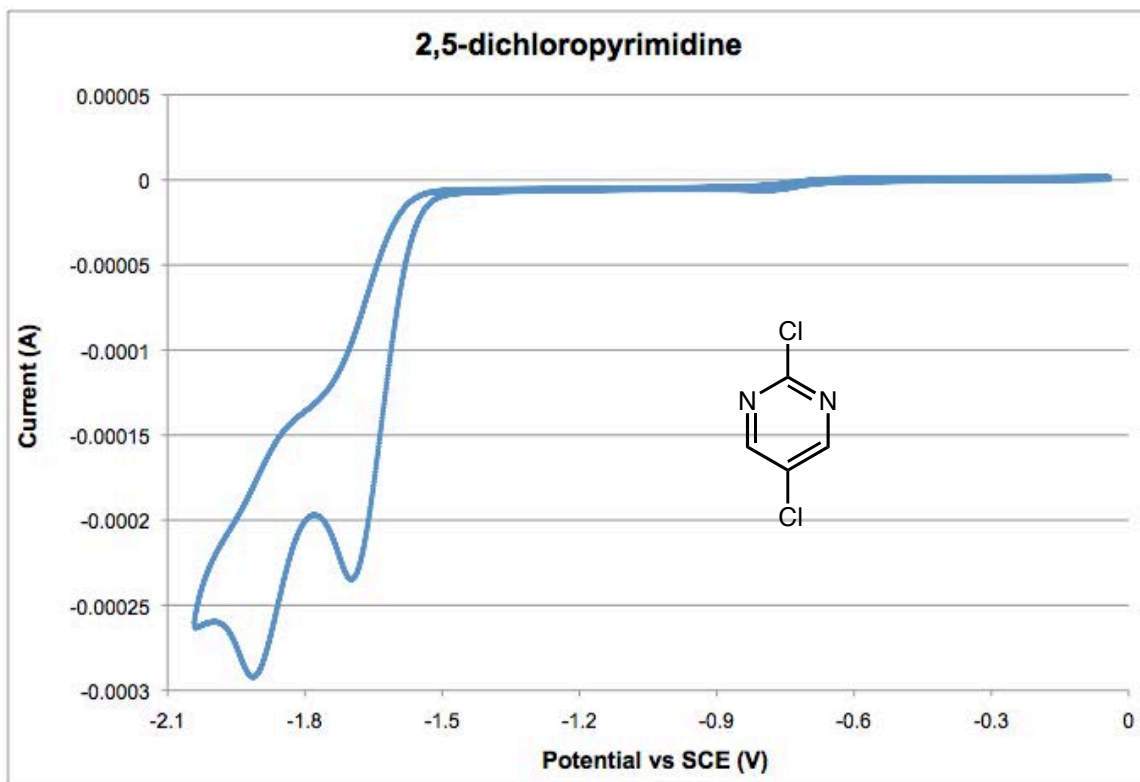
Chloroheterocycle	Peak reduction potential vs SCE (V)
2-chlorobenzoxazole	-2.19
2-chlorobenzothiazole	-1.98
6-chloro-9-methylpurine	-1.86
2-chloro-5-phenylpyrimidine	-1.82
4,6-dichloropyrimidine	-1.75
2,5-dichloropyrimidine	-1.70

Table S3: Measured reduction potentials for several chloroheterocycles.









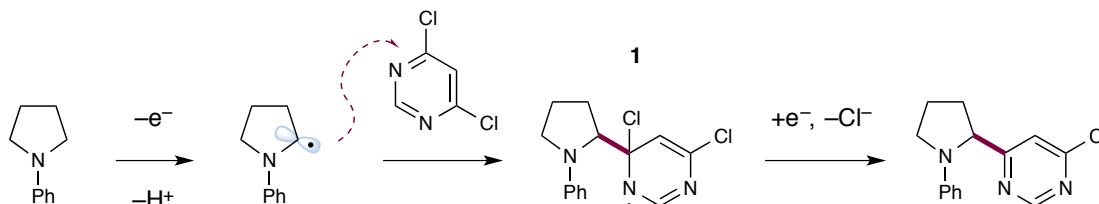
7. Discussion of Mechanism and Selectivity

As discussed in the manuscript, we favor a homolytic aromatic substitution pathway for the mechanism of amine α -arylation with chloroheterocycles (Eq. 1). In this mechanism, addition of a nucleophilic α -amino radical to a neutral arene electrophile generates a radical σ -complex **1**; single-electron reduction of this intermediate and loss of chloride provides the product. In contrast, we have recently reported an amine α -arylation with cyanoarenes that we postulate proceeds via a radical–radical coupling mechanism (Eq. 2).⁷ In this reaction, single-electron reduction of an electron-deficient aryl nitrile such as 1,4-dicyanobenzene provides the long-lived radical anion **2**. Radical–radical coupling between this species and an α -amino radical provides a dienyl anion, which may expel cyanide to furnish the α -aryl amine **3**. Our studies suggest that single-electron reduction of the chloroheteroarene substrates (to give radical anions analogous to

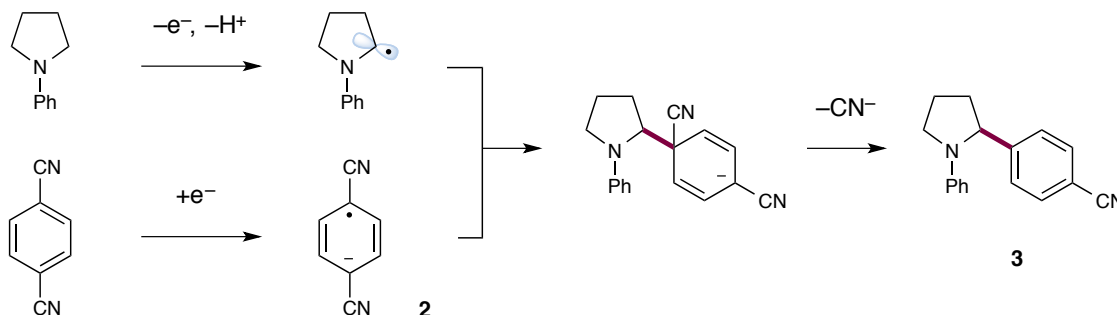
⁷ A. McNally, C. K. Prier and D. W. C. MacMillan, *Science*, 2011, **334**, 1114.

2) is not feasible under the photoredox conditions. Thus, we postulate that divergent mechanistic pathways are operative for the α -arylation reactions employing cyanoarenes (radical–radical coupling) and chloroheteroarenes (homolytic aromatic substitution).

Eq. 1: Homolytic aromatic substitution pathway for photoredox amine α -heteroarylation



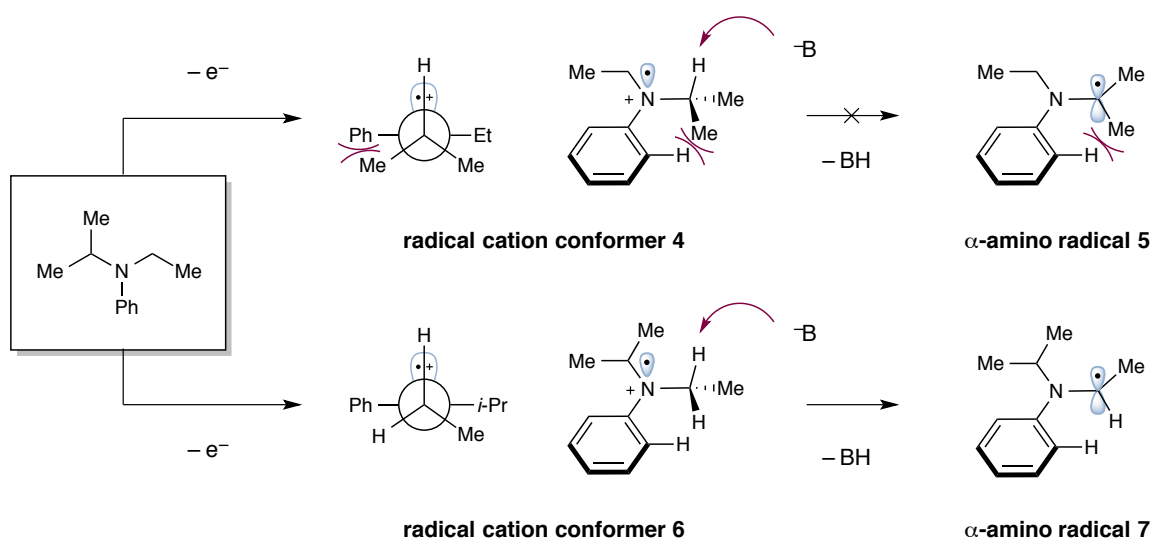
Eq. 2: Amine α -arylation with cyanoarenes proceeds via radical–radical coupling



Regioselectivity. In Table 4, two dialkylanilines (entries 15 and 16) are shown that react with high regioselectivity in favor of arylation at an *N*-methyl substituent over a methine or methylene α -substituent. We propose that this regioselectivity arises from stereoelectronic effects in the transition state for radical cation deprotonation. Specifically, α -deprotonation requires the C–H bond being broken to align with the half-vacant orbital on nitrogen;⁸ Scheme S1 illustrates how this effect contributes to selectivity in the reaction of *N*-ethyl-*N*-isopropylaniline (Table 4, entry 15). In the case of deprotonation on the isopropyl substituent, formation of the required orientation of the C–H bond incurs steric interactions between the *N*-phenyl group (presumably oriented in the plane of the α -amino radical) and a methyl of the isopropyl group (conformer 4).

⁸ F. D. Lewis, *Acc. Chem. Res.*, 1986, **19**, 401.

Deprotonation at this position would additionally build up significant A^{1,2} strain⁹ in the resulting α -amino radical **5**. On the other hand, deprotonation on the *N*-ethyl group may proceed via conformer **6**, in which one C–H bond is aligned with the nitrogen SOMO and another is oriented toward the *N*-phenyl group. Deprotonation then proceeds to give α -amino radical **7**, in which A^{1,2} strain is minimized. Similar considerations in the transition state for deprotonation may be used to rationalize the selectivity observed in the case of *N*-ethyl-*N*-methylaniline (Table 4, entry 16).



Scheme S1. Regioselectivity of α -arylation is determined in the α -deprotonation step

⁹ P. Renaud, L. Giraud, *Synthesis* **1996**, 913 – 926.

8. ^1H and ^{13}C NMR Spectra