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Supporting Online Material for

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Discovery of an α-Amino C-H Arylation Reaction Using the Strategy of Accelerated Serendipity.

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Supporting Online Material

General Information. Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego (*44*). All solvents were purified according to the method of Grubbs (*45*). 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 (*46*). 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. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 500 (500 and 125 MHz) instrument, and are internally referenced to residual protio solvent signals (note: $CDCl_3$ referenced at δ 7.27 and 77.0 ppm respectively). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz) and assignment. Data for ^{13}C 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 Paragon 1000 spectrometer and are reported in terms of frequency of absorption (cm^{-1}). High resolution mass spectra were obtained at Princeton University mass spectrometry facilities. Gas chromatography-mass spectrometry (GC-MS) was performed on an Agilent 6890 GC-5975C MSD equipt with a Gerstel AOC-5000 autosampler and using a HP-5MS column (30 meters, 0.25mm, 0.25 μm film) at 1.0 mL/min. Melting points (m.p.) were recorded using Reichert hot stage apparatus and reported uncorrected. 1,4-dicyanobenzene (Aldrich) was crushed with a mortar and pestle before use. Other cyano aromatics were used from commercial suppliers or prepared using standard literature procedures;

colored impurities were removed by passing a solution (Et_2O) of the cyano aromatic through a plug of charcoal. For optimal results sodium acetate is crushed using a mortar and pestle then dried under vacuum at 100 ºC (12h) before use.

Description of the Accelerated Serendipity Discovery Process.

1) Reaction Matrices

Reaction matrices were constructed by considering all possible pair-wise combinations of substrate pools as of a given size (typically 19). A 19-substrate matrix is shown below in Figure S1 that leads to a total of 171 reactions. Substrates in isolation (i.e. 19 self-paired) were also included in the screen to identify homo-dimerization products. (Note that these self-paired reactions were not included in the statistical information in references (*12*) and (*15*) and in the main text.)

Substrate Number

Substrate Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
1	1																		
2	2	3																	
3	4	5	6																
4	7	8	9	10															
5	11	12	13	14	15														
6	16	17	18	19	20	21													
7	22	23	24	25	26	27	28												
8	29	30	31	32	33	34	35	36											
9	37	38	39	40	41	42	43	44	45										
10	46	47	48	49	50	51	52	53	54	55									
11	56	57	58	59	60	61	62	63	64	65	66								
12	67	68	69	70	71	72	73	74	75	76	77	78							
13	79	80	81	82	83	84	85	86	87	88	89	90	91						
14	92	93	94	95	96	97	98	99	100	101	102	103	104	105					
15	106	107	108	109	110	111	112	113	114	115	116	117	118	119	120				
16	121	122	123	124	125	126	127	128	129	130	131	132	133	134	135	136			
17	137	138	139	140	141	142	143	144	145	146	147	148	149	150	151	152	153		
18	154	155	156	157	158	159	160	161	162	163	164	165	166	167	168	169	170	171	
19	172	173	174	175	176	177	178	179	180	181	182	183	184	185	186	187	188	189	190

Figure S1. Reaction Matrix for 19 Substrates.

2) Substrate Pools

A typical substrate pool of 19 reactants is shown in Figure S2. Substrate pools were periodically altered to introduce new members and to remove problematic substrates that continually participated in existing chemical reactions for example. The complete list of substrates examined in this study is shown in Figure S3.

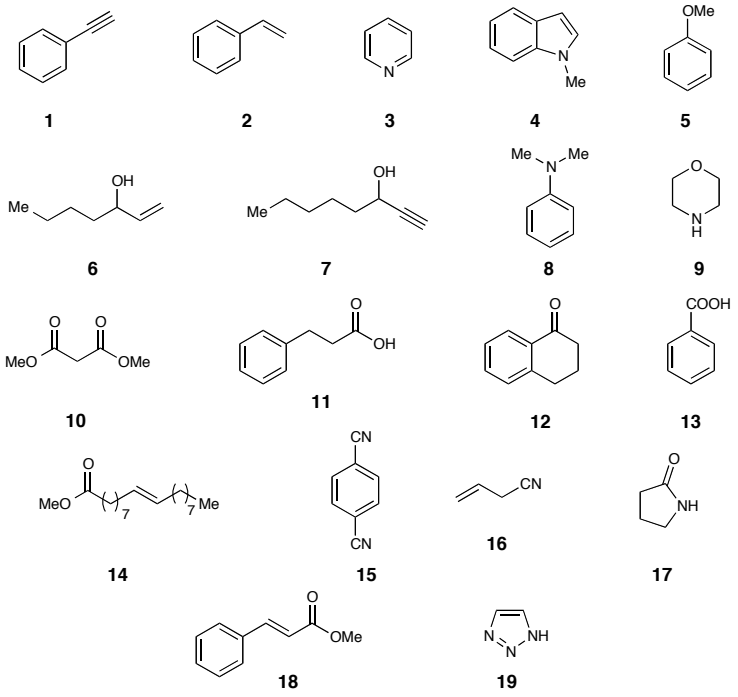


Figure S2. Typical Substrate Pool of 19-members.

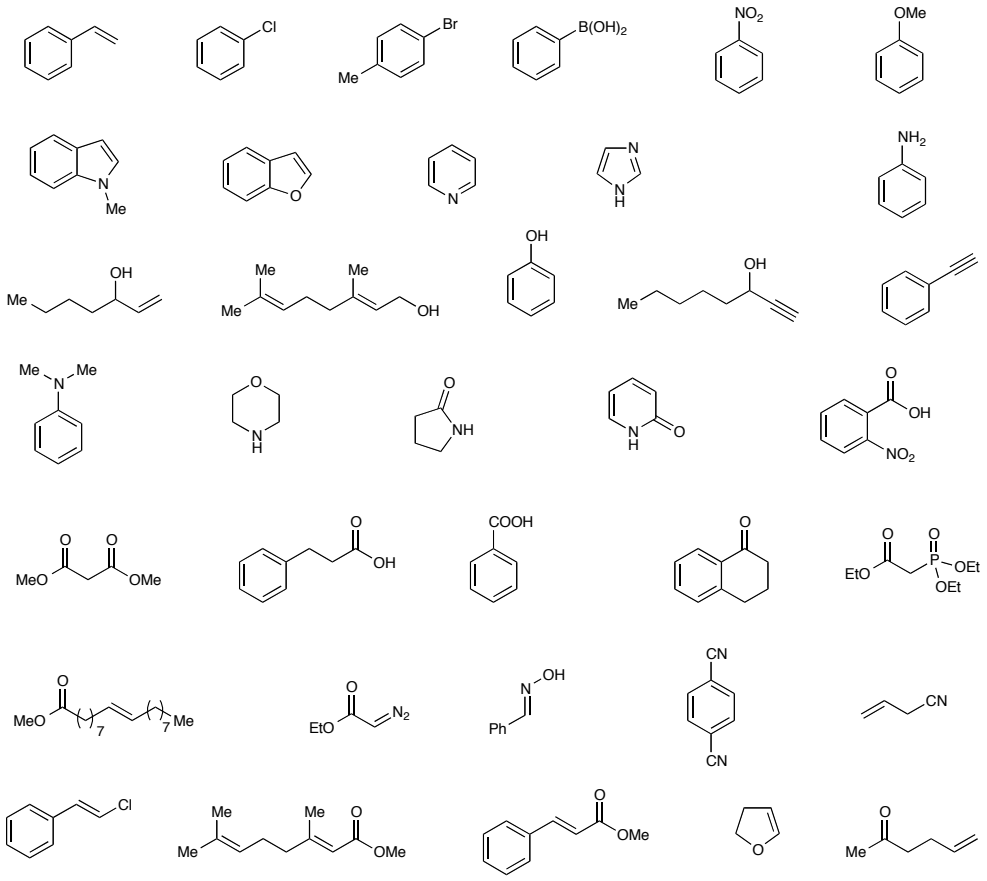


Figure S3. Complete list of substrates examined in this study.

2) Reaction Setup

Substrate combinations were arranged into 96-well plates using a Chemspeed Accelerator robotic platform. Figure S3 shows the translation of the reaction matrix into a 96-well plate format for a 19-member substrate pool. This was followed by the addition of a catalyst system (catalyst, ligand, base, additives solvents etc.). The assembly process was repeated with the catalyst system being the most common variable.

	1	2	3	4	5	6	7	8	9	10	11	12
A	1	2	3	4	5	6	7	8	9	10	11	12
B	13	14	15	16	17	18	19	20	21	22	23	24
C	25	26	27	28	29	30	31	32	33	34	35	36
D	37	38	39	40	41	42	43	44	45	46	47	48
E	49	50	51	52	53	54	55	56	57	58	59	60
F	61	62	63	64	65	66	67	68	69	70	71	72
G	73	74	75	76	77	78	79	80	81	82	83	84
H	85	86	87	88	89	90	91	92	93	94	95	96

	1	2	3	4	5	6	7	8	9	10	11	12
A	97	98	99	100	101	102	103	104	105	106	107	108
B	109	110	111	112	113	114	115	116	117	118	119	120
C	121	122	123	124	125	126	127	128	129	130	131	132
D	133	134	135	136	137	138	139	140	141	142	143	144
E	145	146	147	148	149	150	151	152	153	154	155	156
F	157	158	159	160	161	162	163	164	165	166	167	168
G	169	170	171	172	173	174	175	176	177	178	179	180
H	181	182	183	184	185	186	187	188	189	190		

Figure S4. Assembly of a 19-substrate matrix into 96-well plates.

Reactions were typically run on a 0.1 mmol scale and in a total volume of 500 μL of reaction components and solvent. Substrates, reagents, additives and catalysts etc. were added using the following methods:

- Stock Solutions. The desired reaction component was added to an 8 mL or 40 mL vial and solvent was then added under an inert atmosphere to reach the required concentration. Stock solutions were degassed (argon bubbling, 10 minutes) prior to each use. The liquid handling capabilities of the Chemspeed robotic system were used to add solutions to the required positions of the 96-well plate.
- Solid Dispensing. The solid dispensing function of the Chemspeed robot can be used to add solid material to the 96-well plate. In certain circumstances, solid components were added by hand.
- Slurry Technique. Substances not amenable to solid dispensing or which have limited solubility in organic solvents were added as a slurry to the 96-well plate form using eppenendorf pipettes. The solvent (e.g. CH_2Cl_2 or THF) was then removed using a Genevac centrifuge evaporation system.

All reaction components were typically brought into the Chemspeed Accelerator enclosure which was then flushed with N_2 for 30 minutes. After the assembly of the reaction matrix, the 96-well plates were sealed (Teflon mat and screw-down lid) to avoid air contamination. The plates were then vortexed at 800 rpm on the robot deck or removed from the robot enclosure and placed on a conventional stirrer hot plate for a given time period. To effect stirring on a stirrer hot plate Teflon coated magnetic stir bars were added to the wells prior to stock solutions and heating could be achieved by placing a glass vial containing silicone oil adjacent to the 96-well plate on the hot plate surface into which a temperature probe could be inserted. In the case of photoredox reaction assemblies, modified 96-well plates (Chemglass) containing a polycarbonate transparent bottom were employed. 26 W fluorescent lamps were positioned below the vortex section of the robot deck approximately 5 cm from the bottom of the modified plates.

Note that the above setup can be recreated using stock-solutions dispensed using eppendorf pipettes. The matrix system described above can also be employed, or for convenience, the substrates can be arranged into a row / column format (i.e. 12 substrates in columns 1 to 12 and 8 substrates in rows 1-8) on the 96-well plate and multi-channel eppendorf pipettes can quickly

assemble the screen. This assembly method reduces the number of substrate combinations leading to fewer reactions per screen.

3) Reaction Analysis

After the desired reaction time, the 96-well plates were removed from the robot enclosure and were diluted with 400 μL of EtOAc. The vials were allowed to settle before an aliquot was taken from each vial (multichannel eppendorf pipette) and transferred to the identical position of a vacant 96-well analysis plate. A further 800 μL of EtOAc was added to each vial of the new 96-well plate, the vials were covered with a rubber septa mat and taken for GC-MS analysis. AOC-5000 auto-sampling equipment was used to directly sample from the analysis plate.

GC-MS assays were performed on multiple instruments using a ramped profile with a starting point at 120-160 ºC and rising to 260 ºC (4-8 minutes). Example: 160 ºC (1 min), then 20 ºC/min (1 min) and then 40 ºC/min (2 min).

After collection of all of the data for each reaction matrix, the GC-MS traces were examined individually for peaks of significant intensity ahead of the predetermined positions of the starting materials in the run. Reactions that contained large numbers of peaks in these regions indicate the appearance of complicated mixtures and were therefore ignored. The associated mass spectrum from promising peaks is then examined for higher molecular weight compounds than that of the starting materials from which an initial estimate of product structure made from loss of simple fragments (halides, H_2 etc.). NIST mass spectral database software was also used to match new products to library members or provide a structural estimate based on closely related library compounds. Reactions that have likely formed uninteresting products based on mass-spectral and NIST analysis were disregarded at this point. By examining the GC-MS traces of reactions using these criteria, the preliminary analysis of the screens can be quickly completed to produce a narrowed list of promising hits.

Hits at this stage were taken from the corresponding position on the 96-well plate and subjected to a standard aqueous work-up. The screening scale typically provides sufficient material to obtain a ^{1}H NMR spectrum of the crude reaction and also allow for isolation of new products via column chromatography of preparative TLC. New products can be fully characterized to confirm product structure. If the new product was deemed sufficiently important then the reaction was

repeated on larger scale (0.5 mmol) to obtain accurate yield/conversion. Reactions that produced promising hits but did not provide sufficient material form the 96-well plate were also repeated on a 0.5 mmol scale.

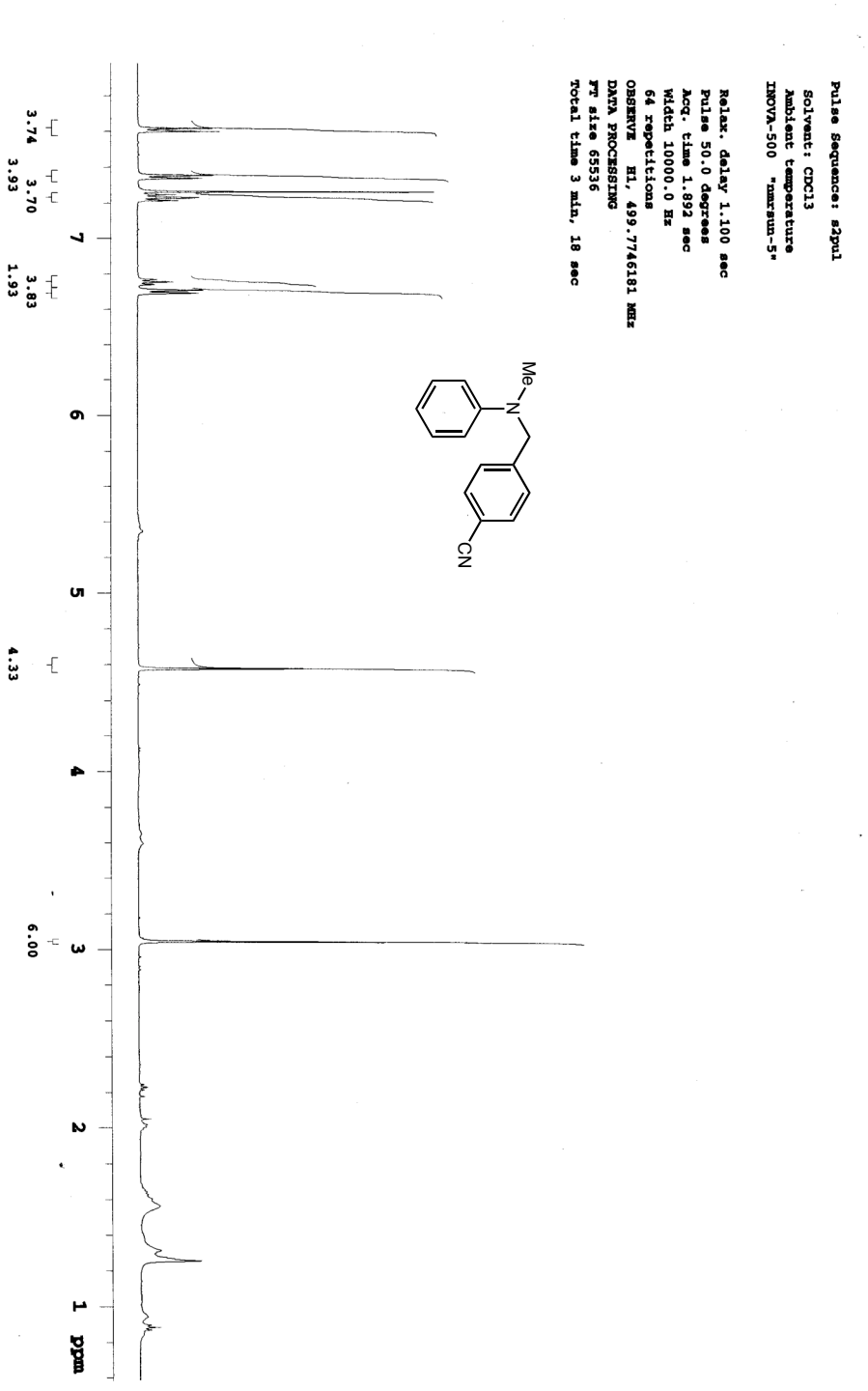
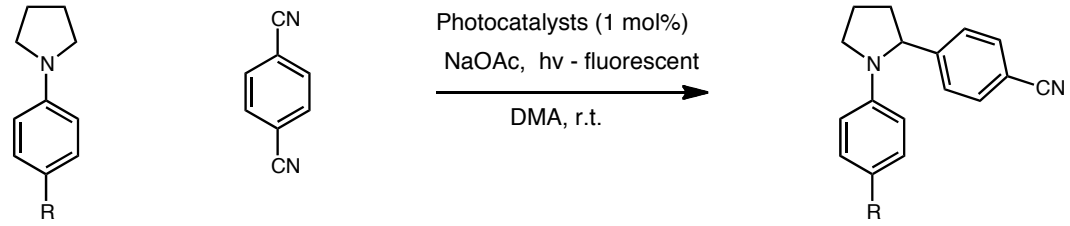


Figure S5. ^{1}H NMR of Isolated Product (**2**) of 'Initial Hit' from Reaction Well

Optimization Studies



Equiv. Arene	Equiv. Amine	Product %* (R = H)
3	1	9
2	1	38
1.5	1	50
1	1	47
1	1.5	68
1	2	73
1	**3**	**82**

Using $Ir(ppy)_2(dtbby)PF_6$ (1 mol%), 2 equiv. NaOAc, 0.25 M DMA at 23 ºC

Base	Product %* (R = H)
NaOAc	**82**
LiOAc	82
NaOTFA	30
LiOTFA	24
NaOTFA	66
KOTFA	29
NaOBz	7
NaOPiv	72

Using $Ir(ppy)_2(dtbby)PF_6$ (1 mol%), 2 equiv. base, 0.25 M, 3:1 (amine/1,4-DCB), DMA at 23 ºC,

Equiv. Amine	Product %* (R = OMe)
0.5	66
1.0	43
1.25	62
1.50	71
1.75	78
2.0	82
2.5	84
3.0	**89**

Using $Ir(ppy)_3$ (1 mol%), 2 equiv. NaOAc, 0.25 M DMA at 23 ºC

Photocat.	Product %* (R = H)
$Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$	1
$Ir(FMppy)_2(dtbbpy)PF_6$	25
$Ir(ppy)_2(dtbbpy)PF_6$	79
$Ir(ppy)_3$	**95**
$Ir(ppy)_2(4\text{-}MeObpy)PF_6$	49
$Ir(ppy)_2(bath)PF_6$	0
$Ir(ppy)_2(phen)PF_6$	0
$Ru(dpp)2PF_6$	0

Using photocatalyst (1 mol%), 2 equiv. NaOAc, 3:1 (amine/1,4-DCB), 0.25 M DMA at 23 ºC

* % Yields calculated by GC with methyl benzoate as an internal standard.

Figure S6. Effect of stoichiometry, base and photocatalyst on the α-amine C–H arylation reaction.

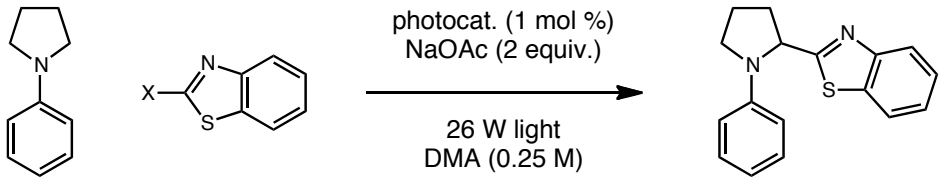


Table 1: Photocatalyst is $Ir(ppy)_3$.

	time	α-Ar*	2-X-benzothiazole*	benzothiazole*
X = CN	39 h	5%	70%	4%
X = Cl	24 h	56%	28%	17%
X = Br	39 h	32%	11%	26%
X = I	13 h	4%	36%	30%

*^{1}H NMR yields.

Table 2: Photocatalyst is $Ir(ppy)_2(dtbbpy)PF_6$.

	time	α-Ar*	2-X-benzothiazole*	benzothiazole*
X = CN	39 h	3%	75%	1%
X = Cl	24 h	79%†	---	10%
X = Br	39 h	36%	12%	26%
X = I	13 h	4%	40%	49%

*^{1}H NMR yields. †Isolated yield.

Figure S7. Study of benzothiazole leaving groups.

Examples of Discoveries from the Accelerated Serendipty Process

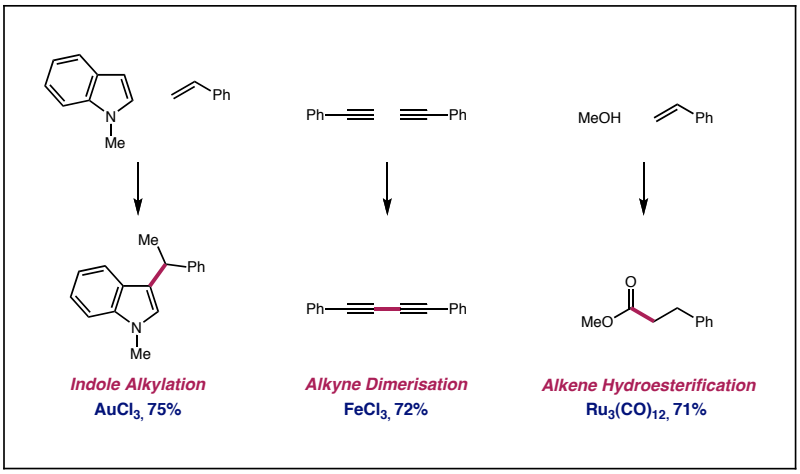
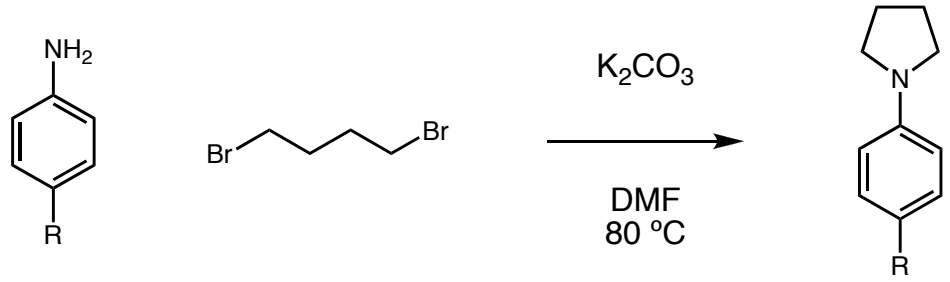


Figure S8. Examples of discoveries based on transition metal catalysis.

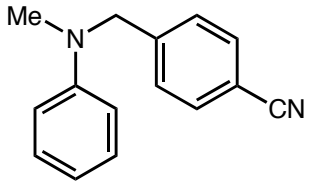


General Procedure for *N*-Aryl Pyrrolidine Synthesis: To a suspension of K_2CO_3 (15.2 g, 110 mmol, 1.1 equiv.) in DMF (100 mL, 1.0 M) was added the appropriate aniline (100 mmol, 1.0 equiv.). The reaction was degassed (10 min) and backfilled with argon. 1,4-Dibromobutane (13.0 mL, 110 mmol, 1.1 equiv.) was added, and the reaction was heated to 80 ºC for 10 h. The reaction was let cool and diluted with EtOAc (200 mL) and H_2O (200 mL). The layers were separated, and the organic layer was extracted with 1 N HCl (3 x 50 mL). The acid layers were combined and adjusted to pH 8 with 1 N 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.

General Procedure for the α-Arylation of Amines: An oven-dried 8 mL vial equipped with a Teflon septum and magnetic stir bar was charged with the photocatalyst (5.0-10.0 μmol, 0.005-0.01 equiv., either tris[2-phenylpyridinato-C^2,*N*]iridium(III) or bis[2-phenylpyridinato-C^2,*N*]-

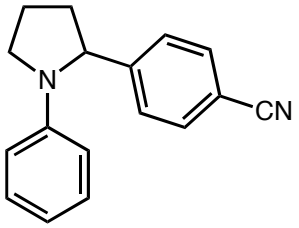
[4,4'-di-*tert*-butyl-2,2'-bipyridyl]iridium(III) hexafluorophosphate), the corresponding amine (1.25-1.5 mmol, 2.5-3.0 equiv, if solid), the corresponding aromatic nitrile or chloride (*S4*) (0.5 mmol, 1.0 equiv) and sodium acetate (*S5*) (1.0 mmol, 2.0 equiv). The vial was purged with a stream of argon and 2.0 mL of DMA (previously degassed via argon bubbling) was added via syringe followed by the corresponding amine (1.25-1.5 mmol, 2.5-3.0 equiv, if liquid). The reaction mixture was then degassed via three cycles of vacuum evacuation (5 min)/argon backfill. After the reaction was thoroughly degassed, the vial was sealed with parafilm and placed approximately 2 cm from a 26 W fluorescent lamp. After the indicated time period, the reaction was diluted with ethyl acetate and added to a separatory funnel containing 25 mL of a saturated aqueous solution of Na_2CO_3. The layers were separated and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude product by flash chromatography on silica gel using the indicated solvent system afforded the desired α-arylated amine product.

Caution! NaCN produced is toxic and could lead to the release on HCN gas. Reactions should be conducted in a well-ventilated fume cupboard and aqueous cyanide-containing waste should be kept basic and disposed of in accord with institutional guidelines.

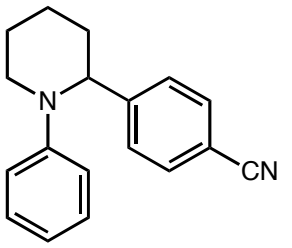


4-((methyl(phenyl)amino)methyl)benzonitrile (2). Prepared according to the general procedure using 3.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (5.0 mmol, 0.005 equiv), 128.1 mg of 1,4-dicyanobenzene (1.0 mmol, 1.0 equiv), 164.1 mg of sodium acetate (2.0 mmol, 2.0 equiv), 380.3 mL of *N, N*-dimethylaniline (3.0 mmol, 3.0 equiv) and 4.0 mL of DMA. After 22 h, the reaction mixture 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 (189 mg, 0.85 mmol, 85%). IR (film) 2896, 2227, 1597, 1504, 1447, 1426, 1307, 1347 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.59 (2H, d, *J* = 8.2 Hz, Ar<u>H</u>), 7.32 (2H, d, *J* = 8.1 Hz, Ar<u>H</u>), 7.21 (2H, dd, *J* = 8.6, 7.4 Hz, Ar<u>H</u>), 6.73 (1H, d, *J* = 7.3 Hz, Ar<u>H</u>), 6.67 (2H, d, *J* = 8.2 Hz, Ar<u>H</u>), 4.56 (2H, s, NC<u>H</u>$_2$(Ph-4-CN)), 3.02 (3H, s, NC<u>H</u>$_3$); ^{13}C NMR (125 MHz,

$CDCl_3$) δ 149.3, 145.2, 132.7, 129.5, 127.5, 119.2, 117.4, 112.5, 110.9, 56.8, 39.1; HRMS (ESI) exact mass calculated for [M+1] ($C_{15}H_{15}N_2$) requires *m/z* 223.1230, found *m/z* 223.1229.

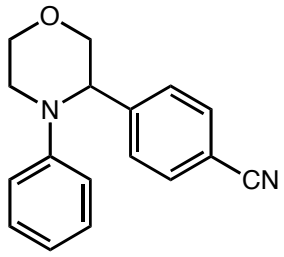


4-(1-Phenylpyrrolidin-2-yl)benzonitrile (entry 1, Table 1). Prepared according to the general procedure using 3.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (5.0 mmol, 0.005 equiv), 128.1 mg of 1,4-dicyanobenzene (1.0 mmol, 1.0 equiv), 164.1 mg of sodium acetate (2.0 mmol, 2.0 equiv), 433.6 μL of *N*-phenylpyrrolidine (3.0 mmol, 3.0 equiv) and 4.0 mL of DMA. After 12 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 2% ethyl acetate in hexanes to 10% ethyl acetate in hexanes) to afford the title compound as a colorless oil (237 mg, 0.96 mmol, 96%). IR (film) 2970, 2871, 2226, 1596, 1503, 1361, 1342, 1299, 1182, 1160 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.58 (2H, d, *J* = 8.3 Hz, Ar<u>H</u>), 7.53 (2H, d, *J* = 8.3 Hz, Ar<u>H</u>), 7.14 (2H, dd, *J* = 8.7, 7.3 Hz, Ar<u>H</u>), 6.66 (1H, m, Ar<u>H</u>), 6.45-6.41 (2H, m, Ar<u>H</u>), 4.73 (1H, dd, *J* = 8.5, 2.2 Hz, C<u>H</u>(Ph-4-CN)), 3.75-3.69 (1H, m, $CH_A\underline{H}_BN$), 3.45-3.38 (1H, m, $CH_A\underline{H}_BN$), 2.48-2.38 (1H, m, $C\underline{H}_ACH_BCH$(Ph-4-CN)) 2.06-1.86 (3H, m, $CH_AC\underline{H}_BCH$(Ph-4-CN) and $C\underline{H}_2CH_2N$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.6, 146.8, 132.7, 129.3, 126.9, 119.2, 116.7, 112.6, 110.7, 62.9, 49.4, 36.0, 23.3; HRMS (ESI) exact mass calculated for [M+1] ($C_{17}H_{17}N_2$) requires *m/z* 249.1392, found *m/z* 249.1387.



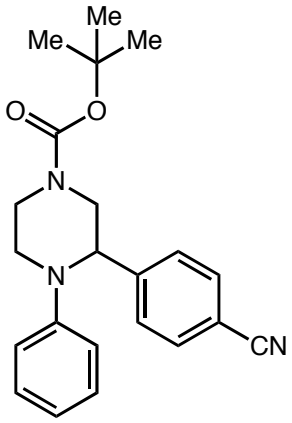
4-(1-Phenylpiperidin-2-yl)benzonitrile (entry 2, Table 1). Prepared according to the general procedure using 3.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (5.0 μmol, 0.005 equiv), 128.1 mg of 1,4-dicyanobenzene (1.0 mmol, 1.0 equiv), 164.1 mg of sodium acetate (2.0 mmol,

2.0 equiv), 483.7 μL of *N*-phenylpiperidine (3.0 mmol, 3.0 equiv) and 4.0 mL of DMA. After 12 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 2% ethyl acetate in hexanes to 5% ethyl acetate in hexanes) to afford the title compound as a yellow oil (256 mg, 0.98 mmol, 98%). IR (film) 2935, 2226, 1596, 1501, 1449, 1354, 1258, 1240, 1212, 1124 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.47 (2H, d, *J* = 8.3 Hz, Ar<u>H</u>), 7.36 (2H, d, *J* = 8.2 Hz, Ar<u>H</u>), 7.11 (2H, dd, *J* = 8.6, 7.3 Hz, Ar<u>H</u>), 6.85 (2H, dd, *J* = 8.6, 0.9 Hz, Ar<u>H</u>), 6.79 (1H, t, *J* = 7.3 Hz, Ar<u>H</u>), 4.37 (1H, dd, *J* = 8.0, 4.0 Hz, C<u>H</u>(Ph-4-CN)), 3.39 (1H, ddd, *J* = 12.4, 5.3, 4.9 Hz, C<u>H</u>$_A$H$_B$N), 3.11 (1H, ddd, *J* = 12.6, 7.6, 4.6 Hz, CH$_A$<u>H</u>$_B$N), 1.98-1.92 (1H, m, C<u>H</u>$_A$CH$_B$CH(Ph-4-CN)), 1.86-1.65 (4H, m, C<u>H</u>$_2$CH$_2$N, C<u>H</u>$_A$CH$_B$CH$_2$CH$_2$N and CH$_A$C<u>H</u>$_B$CH(Ph-4-CN)), 1.59-1.48 (1H, m, CH$_A$C<u>H</u>$_B$CH$_2$CH$_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.8, 150.2, 132.4, 129.1, 128.1, 121.2, 120.4, 119.2, 110.2, 62.0, 52.9, 34.6, 25.9, 22.8; HRMS (ESI) exact mass calculated for [M+1] ($C_{18}H_{19}N_2$) requires *m/z* 263.1543, found *m/z* 263.1544.

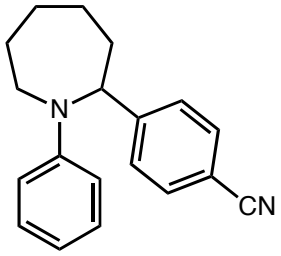


4-(4-Phenylmorpholin-3-yl)benzonitrile (entry 3, Table 1). Prepared according to the general procedure using 3.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (5.0 μmol, 0.005 equiv), 128.1 mg of 1,4-dicyanobenzene (1.0 mmol, 1.0 equiv), 164.1 mg of of sodium acetate (2.0 mmol, 2.0 equiv), 489.7 μL of *N*-phenylmorpholine (3.0 mmol, 3.0 equiv) and 4.0 mL of DMA. After 12 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 10% ethyl acetate in hexanes to 30% ethyl acetate in hexanes) to afford the title compound as an amorphous white solid (254 mg, 0.96 mmol, 96%). IR (film) 2852, 2227, 1598, 1493, 1216 cm^{-1}; m.p. 58-59 ºC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.48 (2H, d, *J* = 8.3 Hz, Ar<u>H</u>), 7.41 (2H, d, *J* = 8.3 Hz, Ar<u>H</u>), 7.14 (2H, dd, *J* = 7.9, 7.1 Hz, Ar<u>H</u>), 6.90-6.85 (3H, m, Ar<u>H</u>), 4.40 (1H, dd, *J* = 8.0, 3.5 Hz, C<u>H</u>(Ph-4-CN)), 3.43-3.37 (1H, m, C<u>H</u>$_A$H$_B$N), 3.15-3.06 (1H, m, CH$_A$<u>H</u>$_B$N), 3.99-3.91 (3H, m, C<u>H</u>$_A$CH$_B$CH(Ph-4-CN) and C<u>H</u>$_2$CH$_2$N), 3.59 (1H, dd, *J* = 11.5, 8.1 Hz CH$_A$C<u>H</u>$_B$CH(Ph-4-CN));

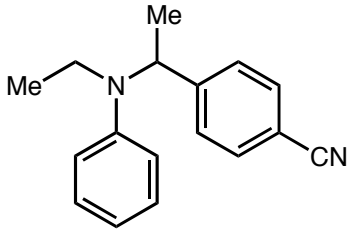
^{13}C NMR (125 MHz, $CDCl_3$) δ 150.5, 145.1, 132.4, 129.2, 128.8, 122.6, 121.4, 118.9, 111.2, 72.9, 67.8, 61.6, 52.9; HRMS (ESI) exact mass calculated for [M+1] ($C_{17}H_{17}N_2O$) requires *m/z* 265.1335, found *m/z* 265.1335.



***tert*-Butyl 3-(4-cyanophenyl)-4-phenylpiperazine-1-carboxylate (entry 4, Table 1).** Prepared according to the general procedure using 3.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (5.0 μmol, 0.005 equiv), 128.1 mg of 1,4-dicyanobenzene (1.0 mmol, 1.0 equiv), 164.1 mg of of sodium acetate (2.0 mmol, 2.0 equiv), 787.1 mg of *tert*-butyl 4-phenylpiperazine-1-carboxylate (3.0 mmol, 3.0 equiv) and 4.0 mL of DMA. After 12 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 2% ethyl acetate in hexanes to 10% ethyl acetate in hexanes) to afford the title compound as an off-white powder (345 mg, 0.95 mmol, 95%). IR (film) 2972, 2227, 1693, 1599, 1496, 1453, 1419, 1365, 1231, 1167 cm^{-1}; m.p. 119-121 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (2H, d, *J* = 8.2 Hz, Ar<u>H</u>), 7.42 (2H, d, *J* = 8.2 Hz, Ar<u>H</u>), 7.14 (2H, dd, *J* = 8.4, 7.6 Hz, Ar<u>H</u>), 6.86-6.75 (3H, m, Ar<u>H</u>), 4.48 (1H, dd, *J* = 6.8, 3.7 Hz, C<u>H</u>(Ph-4-CN)), 4.05-3.67 (2H, br m, C<u>H</u>$_A$H$_B$N and C<u>H</u>$_A$CH$_B$CH(Ph-4-CN)), 3.65-3.10 (4H, br m, C<u>H</u>$_2$CH$_2$N, CH$_A$<u>H</u>$_B$N and CH$_A$C<u>H</u>$_B$CH(Ph-4-CN)), 1.39 (9H, s, C(C<u>H</u>$_3$)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) (mixture of rotamers) δ 154.7, 150.2, 146.6, 132.7, 132.5, 129.9, 129.4, 128.3, 121.4, 119.0, 112.6, 80.4, 61.5, 49.8, 49.5, 49.0, 48.2, 44.4, 43.4, 28.5; HRMS (ESI) exact mass calculated for [M+1] ($C_{22}H_{26}N_3O_2$) requires *m/z* 364.2020, found *m/z* 364.2020.

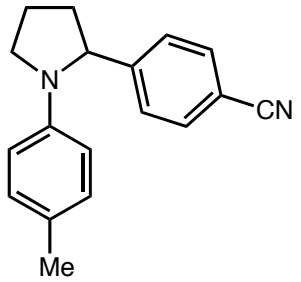


4-(1-Phenylazepan-2-yl)benzonitrile (entry 5, Table 1). Prepared according to the general procedure using 3.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (5.0 μmol, 0.005 equiv), 128.1 mg of 1,4-dicyanobenzene (1.0 mmol, 1.0 equiv), 164.1 mg of sodium acetate (2.0 mmol, 2.0 equiv), 526.0 mg of *N*-phenylazepane (3.0 mmol, 3.0 equiv) and 4.0 mL of DMA. After 12 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 2% ethyl acetate in hexanes to 4% ethyl acetate in hexanes) to afford the title compound as a yellow amorphous solid (251 mg, 0.91 mmol, 91%). IR (film) 2953, 2226, 1595, 1501, 1410, 1383, 1343, 1267, 1241, 1203, 1162 cm^{-1}; m.p. 103-104 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (2H, d, *J* = 8.3 Hz, Ar<u>H</u>), 7.29 (2H, d, *J* = 8.1 Hz, Ar<u>H</u>), 7.14 (2H, dd, *J* = 8.8, 7.3 Hz, Ar<u>H</u>), 6.64 (1H, t, *J* = 7.2 Hz, Ar<u>H</u>), 6.54 (2H, d, *J* = 8.3 Hz Ar<u>H</u>), 4.61 (1H, dd, *J* = 11.9, 5.8 Hz, C<u>H</u>(Ph-4-CN)), 3.88-3.81 (1H, m, C<u>H$_A$</u>H$_B$N), 3.46 (1H, ddd, *J* = 15.5, 11.0, 1.3 Hz, CH$_A$<u>H$_B$</u>N), 2.47-2.38 (1H, m, C<u>H$_A$</u>CH$_B$CH(Ph-4-CN)), 2.00-1.63 (5H, m, CH$_A$C<u>H$_B$</u>CH(Ph-4-CN), C<u>H$_2$</u>CH$_2$(Ph-4-CN) and C<u>H$_2$</u>CH$_2$N), 1.52-1.28 (2H, m, C<u>H$_2$</u>CH$_2$CH$_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.3, 148.7, 132.9, 129.5, 126.8, 119.2, 116.3, 111.6, 110.6, 63.2, 45.5, 38.4, 29.8, 28.5, 26.8; HRMS (ESI) exact mass calculated for [M+1] ($C_{19}H_{21}N_2$) requires *m/z* 277.1699, found *m/z* 263.1700.

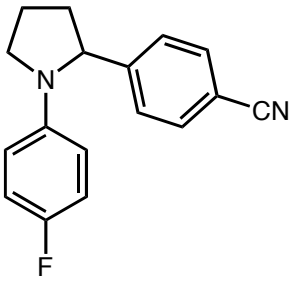


4-(1-(Ethyl(phenyl)amino)ethyl)benzonitrile (entry 6, Table 1). Prepared according to the general procedure using 3.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (5.0 μmol, 0.005 equiv), 128.1 mg of 1,4-dicyanobenzene (1.0 mmol, 1.0 equiv), 164.1 mg of sodium acetate (2.0 mmol, 2.0 equiv), 479.9 μL of *N*,*N*-diethylaniline (3.0 mmol, 3.0 equiv) and 4.0 mL of DMA.

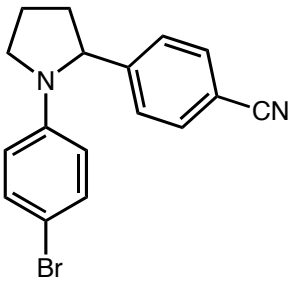
After 12 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 2% ethyl acetate in hexanes to 4% ethyl acetate in hexanes) to afford the title compound as an amorphous white solid (235 mg, 0.94 mmol, 94%). IR (film) 2975, 2934, 2227, 1596, 1500, 1377, 1268, 1208, 1121 cm^{-1}; m.p. 58-59 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (2H, d, *J* = 8.3 Hz, Ar<u>H</u>), 7.46 (2H, d, *J* = 8.1 Hz, Ar<u>H</u>), 7.30-7.21 (2H, m, Ar<u>H</u>), 6.84-6.71 (3H, m, Ar<u>H</u>), 5.06 (1H, q, *J* = 6.9 Hz, C<u>H</u>(Ph-4-CN)), 3.26 (2H, t, *J* = 7.0 Hz, $CH_3C\underline{H}_2N$), 1.63 (3H, d, *J* = 6.9 Hz, CH(Ph-4-CN)C<u>H</u>$_3$), 1.15 (3H, t, C<u>H</u>$_3$$CH_2N$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.5, 148.2, 132.5, 129.4, 127.9, 119.2, 117.7, 114.6, 110.8, 57.4, 41.1, 18.1, 14.4; HRMS (ESI) exact mass calculated for [M+1] ($C_{17}H_{19}N_2$) requires *m/z* 251.1543, found *m/z* 251.1542.



4-(1-*p*-Tolylpyrrolidin-2-yl)benzonitrile (entry 7, Table 1). Prepared according to the general procedure using 3.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (5.0 μmol, 0.005 equiv), 128.1 mg of 1,4-dicyanobenzene (1.0 mmol, 1.0 equiv), 164.1 mg of sodium acetate (2.0 mmol, 2.0 equiv), 483.7 mg of *N*-*p*-tolylpyrrolidine (3.0 mmol, 3.0 equiv) and 4.0 mL of DMA. After 12 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 2% ethyl acetate in hexanes to 4% ethyl acetate in hexanes) to afford the title compound as an orange solid (245 mg, 0.93 mmol, 93%). IR (film) 2970, 2869, 2226, 1618, 1606, 1518, 1411, 1359, 1341, 1180, 1162 cm^{-1}; m.p. 84 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (2H, d, *J* = 8.2 Hz, Ar<u>H</u>), 7.33 (2H, d, *J* = 8.2 Hz, Ar<u>H</u>), 6.95 (2H, d, *J* = 8.4 Hz, Ar<u>H</u>), 6.34 (2H, d, *J* = 8.5 Hz, Ar<u>H</u>), 4.68 (1H, dd, *J* = 8.5, 2.1 Hz, C<u>H</u>(Ph-4-CN)), 3.75-3.68 (1H, m, C<u>H</u>$_A$$H_B$N), 3.42-3.34 (1H, m, CH_A<u>H</u>$_B$N), 2.47-2.36 (1H, m, C<u>H</u>$_A$$CH_B$CH(Ph-4-CN)), 2.20 (3H, s, NPhC<u>H</u>$_3$), 2.04-1.84 (3H, m, CH_AC<u>H</u>$_B$CH(Ph-4-CN) and C<u>H</u>$_2$$CH_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.0, 144.8, 132.6, 129.9, 127.0, 125.7, 119.3, 112.6, 110.6, 63.0, 49.6, 36.1, 23.4, 20.4; HRMS (ESI) exact mass calculated for [M+1] ($C_{18}H_{19}N_2$) requires *m/z* 263.1543, found *m/z* 263.1543.

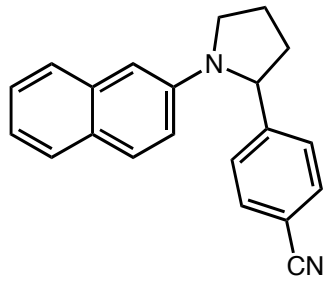


4-(1-(4-Fluorophenyl)pyrrolidin-2-yl)benzonitrile (entry 8, Table 1). Prepared according to the general procedure using 3.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (5.0 μmol, 0.005 equiv), 128.1 mg of 1,4-dicyanobenzene (1.0 mmol, 1.0 equiv), 164.1 mg of sodium acetate (2.0 mmol, 2.0 equiv), 510.6 mg of *N*-(4-fluorophenyl)pyrrolidine (3.0 mmol, 3.0 equiv) and 4.0 mL of DMA. After 12 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 2% ethyl acetate in hexanes to 5% ethyl acetate in hexanes) to afford the title compound as a yellow oil (241 mg, 0.91 mmol, 91%). IR (film) 2970, 2227, 1606, 1508, 1412, 1363, 1223, 1160 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.58 (2H, d, *J* = 8.3 Hz, Ar<u>H</u>), 7.32 (2H, d, *J* = 8.3 Hz, Ar<u>H</u>), 6.89-6.80 (2H, m, Ar<u>H</u>), 6.37-6.28 (2H, m, Ar<u>H</u>), 4.65 (1H, dd, *J* = 8.5, 2.3 Hz, C<u>H</u>(Ph-4-CN)), 3.73-3.66 (1H, m, C<u>H</u>$_A$H$_B$N), 3.40-3.33 (1H, m, CH$_A$<u>H</u>$_B$N), 2.50-2.38 (1H, m, C<u>H</u>$_A$CH$_B$CH(Ph-4-CN)), 2.10-1.84 (3H, m, CH$_A$C<u>H</u>$_B$CH(Ph-4-CN) and C<u>H</u>$_2$CH$_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.4 (d, J^1 = 232.5 Hz), 150.5, 143.5, 132.7, 126.9, 119.2, 115.7 (d, J^2 = 22.5 Hz), 113.0 (d, J^3 = 7.5 Hz), 110.8, 63.3, 49.9, 36.2, 23.5; HRMS (ESI) exact mass calculated for [M+1] ($C_{17}H_{16}FN_2$) requires *m/z* 267.1292, found *m/z* 267.1293.



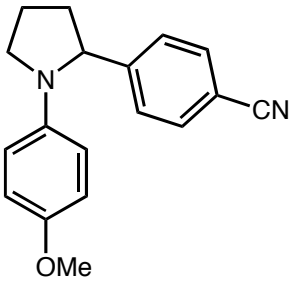
4-(1-(4-Bromophenyl)pyrrolidin-2-yl)benzonitrile (entry 9, Table 1). Prepared according to the general procedure using 3.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (5.0 μmol, 0.005 equiv), 128.1 mg of 1,4-dicyanobenzene (1.0 mmol, 1.0 equiv), 164.1 mg of sodium acetate (2.0

mmol, 2.0 equiv), 678.3 mg of *N*-(4-bromophenyl)pyrrolidine (3.0 mmol, 3.0 equiv) and 4.0 mL of DMA. After 12 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 5% ethyl acetate in hexanes to 10% ethyl acetate in hexanes) to afford the title compound as a tan solid (276 mg, 0.84 mmol, 84%). IR (film) 2970, 2840, 2226, 1592, 1492, 1413, 1361, 1182, 1161 cm^{-1}; m.p. 143-144 ºC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.58 (2H, d, *J* = 8.3 Hz, Ar<u>H</u>), 7.28 (2H, d, *J* = 8.1 Hz, Ar<u>H</u>), 7.27 (2H, d, *J* = 9.0 Hz, Ar<u>H</u>), 7.19 (2H, d, *J* = 9.0 Hz, Ar<u>H</u>) 4.68 (1H, dd, *J* = 8.5, 2.2 Hz, C<u>H</u>(Ph-4-CN)), 3.70-3.64 (1H, m, C<u>H</u>$_A$H$_B$N), 3.40-3.34 (1H, m, CH$_A$<u>H</u>$_B$N), 2.48-2.38 (1H, m, C<u>H</u>$_A$CH$_B$CH(Ph-4-CN)), 2.06-1.86 (3H, m, CH$_A$C<u>H</u>$_B$CH(Ph-4-CN) and C<u>H</u>$_2$CH$_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.9, 145.7, 132.7, 132.0, 126.9, 119.0, 114.2, 111.0, 108.6, 63.0, 49.5, 36.1, 23.0; HRMS (ESI) exact mass calculated for [M+1] ($C_{17}H_{16}BrN_2$) requires *m/z* 327.0491, found *m/z* 327.0492.

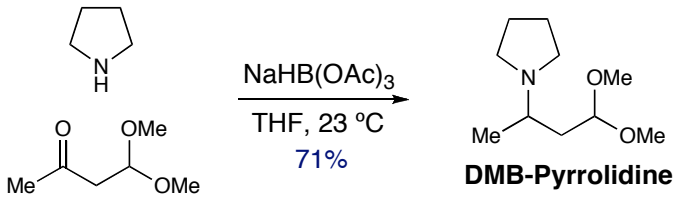


4-(1-(Naphthalen-2-yl)pyrrolidin-2-yl)benzonitrile (entry 10, Table 1). Prepared according to the general procedure using 2.8 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (4.2 μmol, 0.01 equiv), 53.8 mg of 1,4-dicyanobenzene (0.42 mmol, 1.0 equiv), 68.9 mg of sodium acetate (0.84 mmol, 2.0 equiv), 248.6 mg of *N*-(naphthalen-2-yl)pyrrolidine (1.26 mmol, 3.0 equiv) and 1.68 mL of DMA. After 12 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 5% ethyl acetate in hexanes to 10% ethyl acetate in hexanes) to afford the title compound as clear oil (101 mg, 0.34 mmol, 81%). IR (film) 2969, 2226, 1626, 1600, 1508, 1474, 1390, 1370, 1236 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.67-7.49 (5H, m, Ar<u>H</u>), 7.38-7.27 (3H, m, Ar<u>H</u>), 7.14 (1H, ddd, *J* = 8.1, 6.8, 1.2 Hz, Ar<u>H</u>), 6.77 (1H, dd, *J* = 8.9, 2.5 Hz, Ar<u>H</u>), 6.66 (1H, d, *J* = 2.3 Hz, Ar<u>H</u>), 4.89 (1H, dd, *J* = 8.3, 1.9 Hz, C<u>H</u>(Ph-4-CN)), 3.86-3.80 (1H, m, C<u>H</u>$_A$H$_B$N), 3.58-3.50 (1H, m, CH$_A$<u>H</u>$_B$N), 2.53-2.42 (1H, m, C<u>H</u>$_A$CH$_B$CH(Ph-4-CN)), 2.12-1.87 (3H, m, CH$_A$C<u>H</u>$_B$CH(Ph-4-CN) and C<u>H</u>$_2$CH$_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.5, 14.7, 135.1, 132.7, 129.1, 127.8, 127.0,

126.8, 126.6, 126.1, 122.1, 119.2, 116.0, 110.8, 106.1, 62.9, 49.6, 36.1, 23.3; HRMS (ESI) exact mass calculated for [M+1] ($C_{21}H_{19}N_2$) requires *m/z* 299.1543, found *m/z* 299.1543.

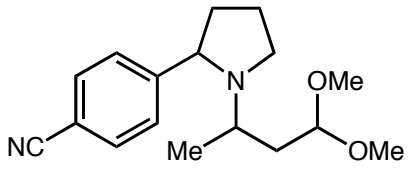


4-(1-(4-Methoxyphenyl)pyrrolidin-2-yl)benzonitrile (entry 11, Table 1). Prepared according to the general procedure using 3.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (5.0 μmol, 0.01 equiv), 64.1 mg of 1,4-dicyanobenzene (0.5 mmol, 1.0 equiv), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv), 265.8 mg of *N-(p*-methoxyphenyl)pyrrolidine (1.5 mmol, 3.0 equiv) and 2.0 mL of DMA. After 12 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 2% ethyl acetate in hexanes to 10% ethyl acetate in hexanes) to afford the title compound as a tan solid (122 mg, 0.44 mmol, 88%). IR (film) 2947, 2830, 2226, 1606, 1504, 1463, 1361, 1260, 1236, 1178 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.57 (2H, d, *J* = 8.2 Hz, Ar<u>H</u>), 7.34 (2H, d, *J* = 8.2 Hz, Ar<u>H</u>), 6.74 (2H, d, *J* = 9.0 Hz, Ar<u>H</u>), 6.36 (2H, d, *J* = 9.0 Hz, Ar<u>H</u>), 4.63 (1H, dd, *J* = 8.6, 2.5 Hz, C<u>H</u>(Ph-4-CN)), 3.73-3.63 (4H, m, C<u>H</u>$_A$H$_B$N and OC<u>H</u>$_3$), 3.39-3.31 (1H, m, CH$_A$<u>H</u>$_B$N), 2.47-2.36 (1H, m, C<u>H</u>$_A$CH$_B$CH(Ph-4-CN)), 2.02-1.91 (2H, m, C<u>H</u>$_2$CH$_2$N), 1.91-1.83 (1H, m, CH$_A$C<u>H</u>$_B$CH(Ph-4-CN)); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.4, 151.1, 141.7, 132.6, 130.9, 119.3, 115.0, 113.2, 110.6, 63.4, 56.0, 50.0, 36.2, 23.5; HRMS (ESI) exact mass calculated for [M+1] ($C_{18}H_{19}N_2O$) requires *m/z* 279.1492, found *m/z* 279.1491.



Formation of 1-(4,4-dimethoxybutan-2-yl)pyrrolidine (DMB-pyrrolidine). Pyrrolidine (375.6 mL, 4.5 mmol) was added to a solution of 4,4-dimethoxy-2-butanone ((90% technical grade (Sigma Aldrich) previously purified by flash chromatography eluting with 30% ethyl acetate in

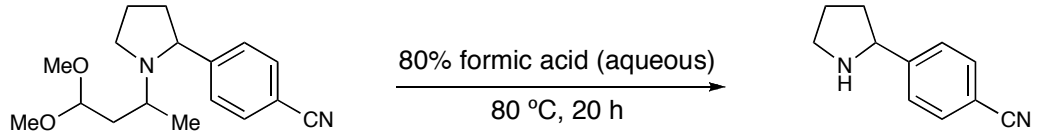
hexanes) 398.1 mL, 3.0 mmol) in 15 mL of tetrahydrofuran at 0 ºC. After stirring for 5 minutes sodium triacetoxy borohydride (890.2 mg, 4.2 mmol) was added, the ice bath was removed and the reaction was stirred at room temperature for 10 hours. The reaction was quenched with 10% aqueous NaOH solution and stirred at room temperature for 30 minutes. The layers were separated and the aqueous layer was extracted with EtOAc (5 x 20 mL). The combined organic extracts were the washed with brine, dried (Na_2SO_4) and concentrated *in vacuo* to give an oil. The residue was then purified by flash chromatography (basic alumina, elution: 5% ethyl acetate in hexane then 100% ethyl acetate directly into a round bottom flask) to afford the title compound as a clear liquid (400 mg, 2.14 mmol, 71%). IR (film) 2965, 2829, 1463, 1384, 1218 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.48 (1H, dd, *J* = 7.1, 4.5 Hz, C<u>H</u>$(OCH_3)_2$), 3.31 (3H, s, CH$(OC\underline{H}_3)_A(OCH_3)_B$), 3.29 (3H, s, CH$(OCH_3)_A(OC\underline{H}_3)_B$), 2.61-2.39 (5H, m, $(C\underline{H}_2)_2N$ and $CH_3C\underline{H}N$), 2.04-1.95 (1H, m, $C\underline{H}_ACH_BCH(OCH_3)_2$), 1.78-1.71 (4H, m, $(C\underline{H}_2CH_2)_2N$), 1.56-1.48 (1H, m, $CH_AC\underline{H}_BCH(OCH_3)_2$), 1.10 (3H, d, *J* = 6.4 Hz, $C\underline{H}_3CHN$) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 102.9, 55.1, 53.3, 52.3, 50.8, 38.0, 23.6, 18.0; HRMS (ESI) exact mass calculated for [M+1] ($C_{10}H_{22}NO_2$) requires *m/z* 186.1645, found *m/z* 186.1643.



(1.17:1 mixture of diastereomers)

4-(1-(4,4-dimethoxybutan-2-yl)pyrrolidin-2-yl)benzonitrile (entry 12, Table 1). Prepared according to the general procedure using 1.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) 2.5 μmol, 0.01 equiv), 32.0 mg of 1,4-dicyanobenzene (0.25 mmol, 1.0 equiv), 41.0 mg of sodium acetate (0.5 mmol, 2.0 equiv), 140.5 mg of 1-(4,4-dimethoxybutan-2-yl)pyrrolidine (0.75 mmol, 3.0 equiv) and 1 mL of DMA. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (neutral alumina eluting with 5% ethyl acetate in hexanes) to afford the title compound as a clear oil (56 mg, 0.19 mmol, 78%). *Major Diastereomer*: IR (film) 2961, 2829, 2227, 1607, 1501, 1449, 1383 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.56 (2H, d, *J* = 8.2 Hz, Ar<u>H</u>), 7.45 (2H, d, *J* = 8.2 Hz, Ar<u>H</u>), 4.28 (1H, dd, *J* = 6.9, 4.8 Hz, C<u>H</u>$(OCH_3)_2$), 3.80 (1H, dd, *J* = 7.8, 6.6 Hz, C<u>H</u>(Ph-4-CN)), 3.25 (3H, s, CH$(OC\underline{H}_3)_A(OCH_3)_B$), 3.14-3.08 (4H, m, CH$(OCH_3)_A(OC\underline{H}_3)_B$ and $C\underline{H}_AH_BN$), 2.74-2.65 (1H, m,

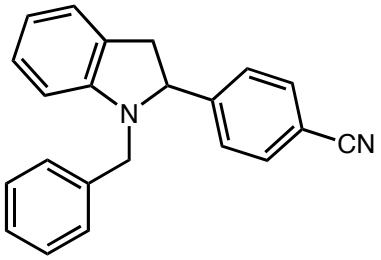
$CH_3C\underline{H}N$), 2.61 (1H, app q, J = 8.5 Hz, $CH_A\underline{H}_BN$), 2.18-2.07 (1H, m, $C\underline{H}_ACH_BCH$(Ph-4-CN)), 1.89-1.68 (3H, m, $C\underline{H}_2CH_2N$ and $C\underline{H}_ACH_BCH(OCH_3)_2$), 1.61-1.36 (2H, m, $CH_AC\underline{H}_BCH$(Ph-4-CN) and $CH_AC\underline{H}_BCH(OCH_3)_2$), 1.04 (3H, d, J = 6.7 Hz, $C\underline{H}_3CHN$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.5, 132.3, 128.1, 119.5, 110.4, 103.2, 63.6, 53.3, 52.4, 50.1, 47.7, 36.1, 33.9, 23.6, 19.3; HRMS (ESI) exact mass calculated for [M+1] ($C_{17}H_{25}N_2O_2$) requires *m/z* 289.1911, found *m/z* 289.1911. *Minor Diastereomer*: IR (film) 2962, 2827, 2232, 1607, 1504, 1372, 1278 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (2H, d, J = 8.2 Hz, Ar$\underline{H}$), 7.43 (2H, d, J = 8.2 Hz, Ar$\underline{H}$), 4.55 (1H, dd, J = 7.7, 3.7 Hz, $C\underline{H}(OCH_3)_2$), 3.71 (1H, app t, J = 7.7 Hz, $C\underline{H}$(Ph-4-CN)), 3.22 (3H, s, $CH(OC\underline{H}_3)_A(OCH_3)_B$), 3.18 (3H, s, $CH(OCH_3)_A(OC\underline{H}_3)_B$), 2.96 (1H, td, J = 8.2, 3.6 Hz, $C\underline{H}_AH_BN$), 2.72-2.58 (2H, m, $CH_A\underline{H}_BN$ and $CH_3C\underline{H}N$), 2.16-2.06 (1H, m, $C\underline{H}_ACH_BCH$(Ph-4-CN)), 1.92-1.80 (1H, m, $C\underline{H}_ACH_BCH_2N$), 1.79-1.65 (2H, m, $CH_AC\underline{H}_BCH_2N$ and $C\underline{H}_ACH_BCH(OCH_3)_2$), 1.63-1.49 (2H, m, $CH_AC\underline{H}_BCH$(Ph-4-CN) and $CH_AC\underline{H}_BCH(OCH_3)_2$), 0.87 (3H, d, J = 6.5 Hz, $C\underline{H}_3CHN$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.3, 132.2, 128.4, 119.5, 110.5, 102.2, 64.5, 53.6, 51.6, 48.3, 44.2, 39.0, 35.9, 23.5, 11.6; HRMS (ESI) exact mass calculated for [M+1] ($C_{17}H_{25}N_2O_2$) requires *m/z* 289.1911, found *m/z* 289.1915.



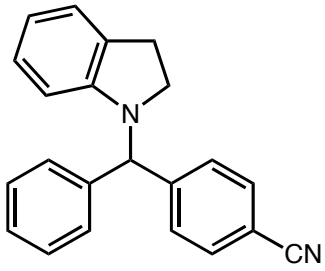
(1.17:1 mixture of diastereomers)

Procedure procedure: 4-(Pyrrolidin-2-yl)benzonitrile. An 8mL vial was charged with 4-(1-(4,4-dimethoxybutan-2-yl)pyrrolidin-2-yl)benzonitrile (0.25 mmol, 72.1 mg) and 4mL of a 4:1 mixture of 98% formic acid and water. The vial was flushed with argon and then heated at 80 ºC for 20 hours. The reaction was then concentrated *in vacuo* using a rotary evaporator and azeotroped five times with a 1:1 mixture of chloroform / benzene whilst maintaining the temperature of the water bath at 30 ºC. The residue was concentrated further under high vacuum before dichloromethane and 100 μL of triethylamine were added and then purified by flash chromatography (silica gel neutralized with dichloromethane previously shaken with aqueous ammonium hydroxide followed by dichoromethane, gradient elution: dichloromethane, 30% ethyl acetate in dichloromethane then 2% methanol in dicholormethane) to afford the title compound as an yellow oil (34 mg, 0.20 mmol, 79%). IR (film) 2964, 2872, 2227, 1607, 1502, 1413, 1219 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (2H, d, J = 8.3 Hz, Ar$\underline{H}$), 7.46 (2H, d, J = 8.2 Hz, Ar$\underline{H}$),

4.18 (1H, app t, J = 7.7 Hz, C<u>H</u>(Ar)), 3.16 (1H, ddd, J = 10.0, 7.5, 5.4 Hz, C<u>H</u>$_A$H$_B$N), 3.04 (1H, ddd, J = 10.0, 8.1, 6.9 Hz, C<u>H</u>$_A$H$_B$N), 2.25-2.16 (1H, m, C<u>H</u>$_A$CH$_B$CH(Ar)), 1.95-1.78 (2H, m, C<u>H</u>$_2$CH$_2$N), 1.67-1.53 (1H, m, CH$_A$C<u>H</u>$_B$CH(Ar)); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.2, 132.4, 127.4, 119.4, 110.5, 62.1, 47.3, 34.9, 25.8; HRMS (ESI) exact mass calculated for [M+1] ($C_{17}H_{13}N_2$) requires m/z 173.1073, found m/z 173.1072.



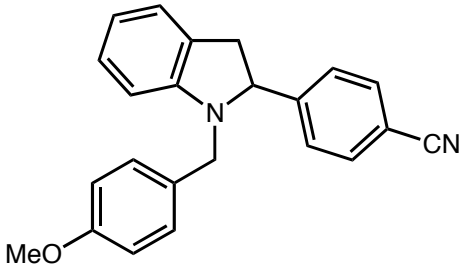
Ring Isomer



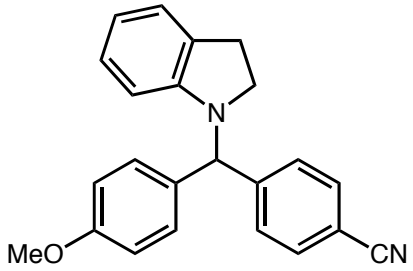
Benzyl Isomer

4-(1-benzylindolin-2-yl)benzonitrile and 4-(indolin-1-yl(phenyl)methyl)benzonitrile (entry 13, Table 1). Prepared according to the general procedure using 35.7 mg of tris[2-phenylpyridinato-C^2,N]iridium(III) (8.7 μmol, 0.01 equiv), 111.5 mg of 1,4-dicyanobenzene (0.87 mmol, 1.0 equiv), 142.7 mg of sodium acetate (1.74 mmol, 2.0 equiv), 457.0 mg of *N*-benzylindoline (2.18 mmol, 2.5 equiv) and 3.48 mL of DMA. After 12 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 2% ethyl acetate in hexanes to 6% ethyl acetate in hexanes) to afford the title compounds as an inseparable mixture (6.7:1 *ring isomer*/*benzyl isomer*, colorless oil). A minor impurity was removed from the mixture after submission to Lotus Separations® resulting in 242 mg, 0.78 mmol, 90% combined yield. *Ring isomer*; IR (film) 3053, 3029, 2847, 2227, 1605, 1482, 1464, 1453, 1417, 1387, 1349, 1231, 1139 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (2H, d, J = 8.0 Hz, Ar<u>H</u>), 7.49 (2H, d, J = 8.0 Hz, Ar<u>H</u>), 7.28-7.14 (5H, m, Ar<u>H</u>), 7.09-7.02 (2H, m, Ar<u>H</u>), 6.71, (1H, dd, J = 7.5, 7.3 Hz, Ar<u>H</u>), 6.46 (1H, d, J = 8.0 Hz, Ar<u>H</u>), 4.65 (1H, app t, J = 9.6 Hz, C<u>H</u>(Ph-4-CN)), 4.34 (1H, d, J = 15.8 Hz, C<u>H</u>$_A$CH$_B$N), 3.96 (1H, d, J = 15.8 Hz, CH$_A$C<u>H</u>$_B$N), 3.41 (1H, dd, J = 15.7, 9.3 Hz, C<u>H</u>$_A$CH$_B$CH(Ph-4-CN)), 2.92 (1H, dd, J = 15.6, 10.2 Hz, CH$_A$C<u>H</u>$_B$CH(Ph-4-CN)); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.1, 148.5, 137.7, 132.6, 128.6, 128.2, 128.0, 127.8, 127.7, 127.3, 124.4, 118.9, 118.6, 111.5, 107.9, 68.8, 51.4, 39.5; HRMS (ESI) exact mass calculated for [M+1] ($C_{22}H_{19}N_2$) requires m/z 311.1543,

found *m/z* 311.1544. *Benzyl isomer*; IR (film) 3027, 2922, 2846, 2227, 1603, 1484, 1453, 1409, 1389, 1334, 1304, 1259, 1242 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ, 7.59 (2H, d, *J* = 8.3 Hz, Ar<u>H</u>), 7.48 (2H, d, *J* = 8.2 Hz, Ar<u>H</u>), 7.31-7.20 (5H, m, Ar<u>H</u>), 7.07 (1H, d, *J* = 7.2 Hz, Ar<u>H</u>), 6.91 (1H, app t, *J* = 7.6 Hz, Ar<u>H</u>), 6.66 (1H, dd, *J* = 7.5, 6.7 Hz, Ar<u>H</u>), 6.09 (1H, d, *J* = 7.9 Hz, Ar<u>H</u>), 5.51 (1H, s, NC<u>H</u>), 3.21-3.14 (1H, m, C<u>H</u>$_A$CH$_B$N), 3.12-3.05 (1H, m, C<u>H</u>$_A$CH$_B$CH$_2$N), 2.99-2.86 (2H, m, CH$_A$C<u>H</u>$_B$N and CH$_A$C<u>H</u>$_B$CH$_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.6, 147.4, 139.8, 132.6, 130.7, 129.0 (2C), 128.9, 128.1, 127.3, 124.7, 119.1, 118.4, 111.2, 108.4, 66.9, 51.9, 28.5; HRMS (ESI) exact mass calculated for [M+1] ($C_{22}H_{19}N_2$) requires *m/z* 311.1543, found *m/z* 311.1544.



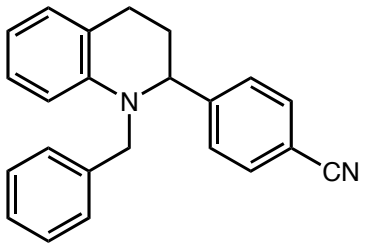
Ring Isomer



Benzyl Isomer

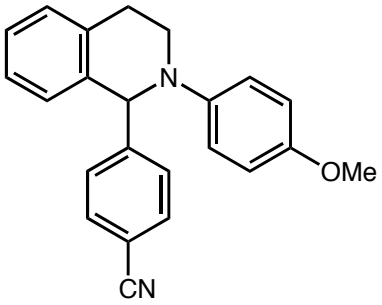
4-(1-(4-methoxybenzyl)indolin-2-yl)benzonitrile and 4-(indolin-1-yl(4-methoxyphenyl)methyl)benzonitrile (entry 14, Table 1). Prepared according to the general procedure using 3.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (5.0 μmol, 0.01 equiv), 64.1 mg of 1,4-dicyanobenzene (0.5 mmol, 1.0 equiv), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv), 299.1 mg of *N*-(*p*-methoxybenzyl)indoline (1.25 mmol, 2.5 equiv) and 2.0 mL of DMA. After 12 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 5% ethyl acetate in hexanes to 20% ethyl acetate in hexanes) to afford the title compounds as an inseparable mixture (4.4:1, colorless oil, 162 mg, 0.48 mmol, 95% combined yield). IR (film) 3028, 2932, 2835, 2226, 1605, 1509, 1481, 1462, 1440, 1348, 1301, 1245, 1175, 1032 cm^{-1}; *Ring isomer*; ^1H NMR (500 MHz, $CDCl_3$) δ 7.61 (2H, d, *J* = 8.1 Hz, Ar<u>H</u>), 7.49 (2H, d, *J* = 8.1 Hz, Ar<u>H</u>), 7.10-7.01 (4H, m, Ar<u>H</u>), 6.77 (2H, d, *J* = 8.6 Hz, Ar<u>H</u>), 6.70, (1H, dd, *J* = 8.1, 7.4 Hz, Ar<u>H</u>), 6.50 (1H, d, *J* = 7.9 Hz, Ar<u>H</u>), 4.61 (1H, app t, *J* = 9.7 Hz, C<u>H</u>(Ph-4-CN)), 4.31 (1H, d, *J* = 15.4 Hz, C<u>H</u>$_A$CH$_B$N), 3.88 (1H, d, *J* = 15.5 Hz, CH$_A$C<u>H</u>$_B$N), 3.76 (3H, s, OC<u>H</u>$_3$), 3.39 (1H, dd, *J* = 15.7, 9.3 Hz, C<u>H</u>$_A$CH$_B$CH(Ph-4-CN)), 2.89 (1H, dd, *J* = 15.5, 9.9 Hz, CH$_A$C<u>H</u>$_B$CH(Ph-4-CN)); *Benzyl isomer*;

^{1}H NMR (500 MHz, $CDCl_3$) δ, 7.49 (2H, d, *J* = 8.1 Hz, Ar<u>H</u>), 7.14 (2H, d, *J* = 8.4 Hz, Ar<u>H</u>), 7.05 (1H, d, *J* = 7.2 Hz, Ar<u>H</u>), 6.91 (1H, app t, *J* = 7.7 Hz, Ar<u>H</u>), 6.83 (2H, d, *J* = 8.5 Hz, Ar<u>H</u>), 6.65 (1H, dd, *J* = 7.5, 6.9 Hz, Ar<u>H</u>), 6.08 (1H, d, *J* = 8.1 Hz, Ar<u>H</u>), 5.45 (1H, s, NC<u>H</u>), 3.77 (3H, s, OC<u>H</u>$_3$), 3.22-3.14 (1H, m, C<u>H</u>$_A$CH$_B$N), 3.11-3.02 (1H, m, C<u>H</u>$_A$CH$_B$CH$_2$N), 3.00-2.87 (2H, m, CH$_A$C<u>H</u>$_B$N and CH$_A$C<u>H</u>$_B$CH$_2$N); *Both isomers;* ^{13}C NMR (125 MHz, $CDCl_3$) δ159.3, 158.9, 152.2, 151.6, 148.7, 147.9, 132.7, 132.6, 132.0, 130.7, 130.2, 129.6, 129.1, 128.8, 128.3, 128.1, 127.9, 127.3, 124.7, 124.5, 119.1, 119.0, 118.6, 118.4, 114.2, 114.0, 111.5, 111.0, 108.4, 107.9, 68.5, 66.4, 55.5 (2C), 51.9, 50.7, 39.6, 28.5; HRMS (ESI) exact mass calculated for [M+1] ($C_{23}H_{21}N_2O$) requires *m/z* 341.1654, found *m/z* 341.1650.

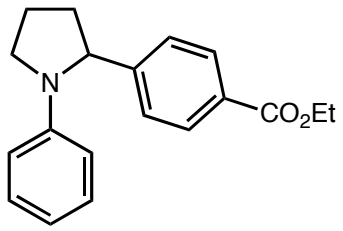


4-(1-benzyl-1,2,3,4-tetrahydroquinolin-2-yl)benzonitrile (entry 15, Table 1). Prepared according to the general procedure using 1.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (2.5 μmol, 0.01 equiv), 32.0 mg of 1,4-dicyanobenzene (0.25 mmol, 1.0 equiv), 41.0 mg of sodium acetate (0.5 mmol, 2.0 equiv), 139.5 mg of *N*-benzyl-1,2,3,4-tetrahydroquinoline (0.625 mmol, 3.0 equiv) and 1.0 mL of DMA. After 14 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 2% ethyl acetate in hexanes to 4% ethyl acetate in hexanes) to afford the title compound as an amorphous white solid (71 mg, 0.22 mmol, 88%). IR (film) 3027, 2924, 2227, 1602, 1575, 1496, 1464, 1451, 1343, 1217 cm^{-1}; m.p. 121-123 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (2H, d, *J* = 8.3 Hz, Ar<u>H</u>), 7.33-7.14 (7H, m, Ar<u>H</u>), 7.07-6.97 (2H, m, Ar<u>H</u>), 6.64 (1H, dd, *J* = 8.0, 7.1 Hz, Ar<u>H</u>), 6.59 (1H, d, *J* = 8.2 Hz, Ar<u>H</u>), 4.77-4.68 (2H, m, C<u>H</u>(Ph-4-CN) and C<u>H</u>$_A$CH$_B$N), 4.13 (1H, d, *J* = 17.4 Hz, CH$_A$<u>H</u>$_B$N), 2.63 (1H, ddd, *J* = 15.9, 3.8, 3.7 Hz, C<u>H</u>$_A$H$_B$CH$_2$CH(Ph-4-CN)), 2.50 (1H, ddd, *J* = 16.1, 12.6, 4.2 Hz, CH$_A$<u>H</u>$_B$CH$_2$CH(Ph-4-CN)), 2.37-2.25 (1H, m, C<u>H</u>$_A$CH$_B$CH(Ph-4-CN)), 2.10-2.01 (1H, m, CH$_A$C<u>H</u>$_B$CH(Ph-4-CN)); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.0, 144.8, 138.1, 132.6, 129.2, 129.0, 127.9, 127.7, 127.2, 126.5, 121.9, 119.0, 116.5, 111.1, 110.8, 61.3, 53.1, 29.2, 23.5; HRMS (ESI) exact mass calculated for [M+1]

($C_{23}H_{21}N_2$) requires *m/z* 325.1699, found *m/z* 325.1701.

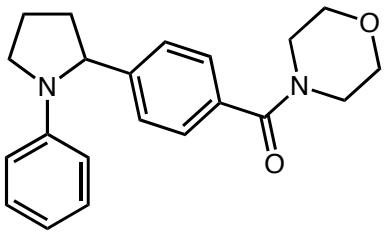


4-(2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)benzonitrile (entry 16, Table 1). Prepared according to the general procedure using 1.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (2.5 μmol, 0.01 equiv), 32.0 mg of 1,4-dicyanobenzene (0.25 mmol, 1.0 equiv), 41.0 mg of sodium acetate (0.5 mmol, 2.0 equiv), 149.6 mg of *N*-(*p*-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (0.625 mmol, 3.0 equiv) and 1.0 mL of DMA. After 12 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel flushed with NEt_3 eluting with hexane, then gradient elution: 2% ethyl acetate in hexanes to 5% ethyl acetate in hexanes) to afford the title compound as a colorless oil (69 mg, 0.2 mmol, 81%). IR (film) 2906, 2832, 2227, 1603, 1509, 1243, 1037 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.48 (2H, d, *J* = 8.3 Hz, Ar<u>H</u>), 7.30-7.13 (5H, m, Ar<u>H</u>), 7.10-7.04 (1H, m, Ar<u>H</u>), 6.77 (4H, s, Ar<u>H</u>), 5.62 (1H, s, C<u>H</u>N), 3.73 (3H, s, OC<u>H</u>$_3$), 3.54-3.45 (1H, m, C<u>H</u>$_A$H$_B$N), 3.42-3.33 (1H, m, CH$_A$<u>H</u>$_B$N), 2.99-2.88 (2H, m, C<u>H</u>$_2$CH$_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.6, 149.0, 144.1, 136.5, 135.7, 132.1, 129.0, 128.9, 128.2, 126.5, 121.3, 119.2, 118.5, 114.7, 110.9, 64.6, 55.8, 45.3, 28.5; HRMS (ESI) exact mass calculated for [M+1] ($C_{21}H_{22}N_2O$) requires *m/z* 341.1648, found *m/z* 341.1648.



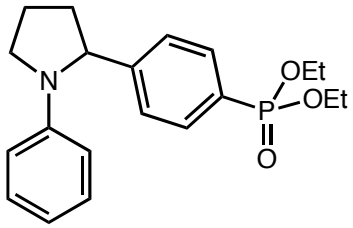
Ethyl 4-(1-phenylpyrrolidin-2-yl)benzoate (entry 1, Table 2). Prepared according to the general procedure using 3.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (5.0 μmol, 0.01 equiv), 87.6 mg of ethyl-4-cyanobenzoate (0.5 mmol, 1.0 equiv), 82.0 mg of sodium acetate (1.0

mmol, 2.0 equiv), 216.9 μL of *N*-phenylpyrrolidine (1.5 mmol, 3.0 equiv) and 2.0 mL of DMA. After 16 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 2% ethyl acetate in hexanes to 5% ethyl acetate in hexanes) to afford the title compound as a colorless oil (118 mg, 0.4 mmol, 80%). IR (film) 2974, 1715, 1598, 1505, 1414, 1364, 1173, 1101 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.95 (2H, d, *J* = 8.2 Hz, Ar<u>H</u>), 7.28 (2H, d, *J* = 8.3 Hz, Ar<u>H</u>), 7.12 (2H, dd, *J* = 8.3, 7.5 Hz, Ar<u>H</u>), 6.66 (1H, t, *J* = 7.3 Hz, Ar<u>H</u>), 6.44 (2H, d, *J* = 8.1 Hz, Ar<u>H</u>), 4.73 (1H, dd, *J* = 8.4, 1.8 Hz, C<u>H</u>(Ph-4-CO_2Et)), 4.33 (2H, q, *J* = 7.1 Hz, C<u>H_2</u>CH_3), 3.75-3.68 (1H, m, C<u>H_A</u><u>H_B</u>N), 3.44-3.36 (1H, m, CH_A<u>H_B</u>N), 2.45-2.35 (1H, m, C<u>H_A</u>CH_BCH(Ph-4-CO_2Et)), 2.02-1.95 (2H, m, C<u>H_2</u>CH_2N), 1.94-1.87 (1H, m, CH_AC<u>H_B</u>CH(Ph-4-CO_2Et)), 1.35 (3H, d, *J* = 7.1 Hz, CH_2C<u>H_3</u>); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.8, 150.3, 147.1, 130.1, 129.3, 126.1 (2C), 116.3, 112.6, 63.0, 61.1, 49.3, 36.1, 23.4, 14.6; HRMS (ESI) exact mass calculated for [M+1] ($C_{19}H_{22}NO_2$) requires *m/z* 296.1645, found *m/z* 296.1645.

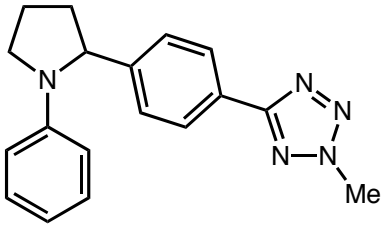


Morpholino(4-(1-phenylpyrrolidin-2-yl)phenyl)methanone (entry 2, Table 2). Prepared according to the general procedure using 3.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (5.0 μmol, 0.01 equiv), 108.1 mg of 4-(morpholine-4-carbonyl)benzonitrile (0.5 mmol, 1.0 equiv), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv), 216.9 μL of *N*-phenylpyrrolidine (1.5 mmol, 3.0 equiv) and 2.0 mL of DMA. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 20% ethyl acetate in hexanes to 40% ethyl acetate in hexanes) to afford the title compound as a colorless oil (107 mg, 0.32 mmol, 64%). IR (film) 2967, 2854, 1625, 1597, 1504, 1455, 1427, 1361, 1276, 1257, 1112 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.32 (2H, d, *J* = 8.2 Hz, Ar<u>H</u>), 7.25 (2H, d, *J* = 8.3 Hz, Ar<u>H</u>), 7.13 (2H, dd, *J* = 8.6, 7.3 Hz, Ar<u>H</u>), 6.63 (1H, t, *J* = 7.3 Hz, Ar<u>H</u>), 6.45 (2H, d, *J* = 8.4 Hz, Ar<u>H</u>), 4.71 (1H, dd, *J* = 8.2, 1.6 Hz, C<u>H</u>(Ph-4-CON(CH_2CH_2)$_2$O)), 3.86-3.32 (10H, m, C<u>H_2</u>N and CON(C<u>H_2</u>C<u>H_2</u>)$_2$O)), 2.44-2.31 (1H, m, C<u>H_A</u>CH_BCH(Ph-4-CON(CH_2CH_2)$_2$O)), 2.02-1.95 (3H, m, C<u>H_2</u>CH_2N and CH_AC<u>H_B</u>CH(Ph-4-CON(CH_2CH_2)$_2$O); ^{13}C

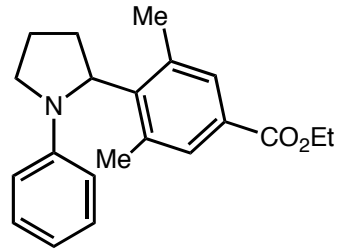
NMR (125 MHz, $CDCl_3$) δ 170.7, 147.1 (2C), 133.8, 129.3, 127.7, 126.3, 116.2, 112.6, 67.1, 66.8, 62.9, 49.3, 36.1, 23.3; HRMS (ESI) exact mass calculated for [M+1] ($C_{21}H_{25}N_2O$) requires *m/z* 337.1911, found *m/z* 337.1912.



Diethyl 4-(1-phenylpyrrolidin-2-yl)phenylphosphonate (entry 3, Table 2). Prepared according to the general procedure using 3.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (5.0 μmol, 0.01 equiv), 119.6 mg of diethyl 4-cyanophenylphosphonate (0.5 mmol, 1.0 equiv), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv), 216.9 μL of *N*-phenylpyrrolidine (1.5 mmol, 3.0 equiv) and 2.0 mL of DMA. After 12 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 5% ethyl acetate in hexanes to 8% ethyl acetate in hexanes) to afford the title compound as a colorless oil (134 mg, 0.37 mmol, 74%). IR (film) 2977, 1596, 1505, 1362, 1243, 1160, 1127 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.71 (2H, dd, *J* = 13.0, 8.1 Hz, Ar$\underline{H}$), 7.31 (2H, dd, *J* = 8.1, 3.9 Hz, Ar$\underline{H}$), 7.13 (2H, dd, *J* = 8.4, 7.5 Hz, Ar$\underline{H}$), 6.64 (1H, t, *J* = 7.3 Hz, Ar$\underline{H}$), 6.44 (2H, d, *J* = 8.0 Hz, Ar$\underline{H}$), 4.72 (1H, dd, *J* = 8.1, 3.9 Hz, C$\underline{H}$(Ph-4-P(O)(OCH_2CH_3)$_2$), 4.17-3.98 (4H, m, ($OC\underline{H}_2CH_3$)$_2$), 3.74-3.67 (1H, m, C$\underline{H}_A$$H_B$N), 3.43-3.35 (1H, m, $CH_A\underline{H}_B$N), 2.44-2.34 (1H, m, C$\underline{H}_A$$CH_B$CH(Ph-4-P(O)($OCH_2CH_3$)$_2$)), 2.05-1.85 (3H, m, C$\underline{H}_2CH_2$N and $CH_AC\underline{H}_B$CH(Ph-4-P(O)(OCH_2CH_3)$_2$)), 1.30 (2 x 3H, t, *J* = 7.1 Hz, ($OCH_2C\underline{H}_3$)$_A$ and ($OCH_2C\underline{H}_3$)$_B$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.9 (d, J^4 = 3.2 Hz), 147.1, 132.3, (d, J^3 = 10.5 Hz), 129.3, 126.6 (d, J^1 = 189.8 Hz), 126.3 (d, J^2 = 15.4 Hz), 116.3, 112.6, 63.0, 62.3, (2C, d, *J* = 5.4 Hz), 49.3, 36.1, 23.3, 16.6 (d, *J* = 6.6 Hz); HRMS (ESI) exact mass calculated for [M+1] ($C_{10}H_{27}NO_3P$) requires *m/z* 360.1723, found *m/z* 360.1724.

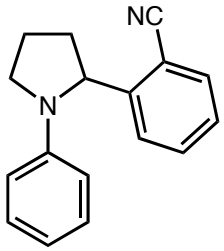


2-Methyl-5-(4-(1-phenylpyrrolidin-2-yl)phenyl)-2*H*-tetrazole (entry 4, Table 2). Prepared according to the general procedure using 1.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (2.6 μmol, 0.005 equiv), 92.6 mg of 4-(2-methyl-2*H*-tetrazol-5-yl)benzonitrile (0.5 mmol, 1.0 equiv), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv), 216.9 μL of *N*-phenylpyrrolidine (1.5 mmol, 3.0 equiv) and 2.0 mL of DMA. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, dry load: 20% ethyl acetate in hexanes) to afford the title compound as a yellow oil (67 mg, 0.22 mmol, 44%). IR (film) 2967, 1597, 1504, 1463, 1425, 1365, 1188, 1160 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.04 (2H, d, *J* = 8.3 Hz, Ar<u>H</u>), 7.35 (2H, d, *J* = 8.3 Hz, Ar<u>H</u>), 7.13 (2H, dd, *J* = 8.6, 7.4 Hz, Ar<u>H</u>), 6.63 (1H, t, *J* = 7.3 Hz, Ar<u>H</u>), 6.49 (2H, d, *J* = 7.9 Hz, Ar<u>H</u>), 4.75 (1H, dd, *J* = 8.3, 1.7 Hz, C<u>H</u>(Ar)), 4.36 (3H, s, C<u>H</u>$_3$), 3.79-3.67 (1H, m, C<u>H</u>$_A$H$_B$N), 3.47-3.34 (1H, m, CH$_A$<u>H</u>$_B$N), 2.48-2.32 (1H, m, C<u>H</u>$_A$CH$_B$CH(Ar)), 2.12-1.89 (3H, m, CH$_A$C<u>H</u>$_B$CH(Ar) and C<u>H</u>$_2$CH$_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.4, 147.5, 147.2, 129.3, 127.2, 126.7, 126.0, 116.2, 112.6, 63.0, 49.4, 39.7, 36.3, 23.6; HRMS (ESI) exact mass calculated for [M+1] ($C_{16}H_{20}N_5$) requires *m/z* 306.1713, found *m/z* 306.1712.



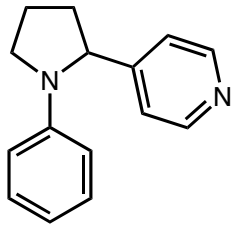
Ethyl 3,5-dimethyl-4-(1-phenylpyrrolidin-2-yl)benzoate (entry 5, Table 2). Prepared according to the general procedure using 3.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (5.0 μmol, 0.01 equiv), 101.6 mg of ethyl 4-cyano-3,5-dimethylbenzoate (0.5 mmol, 1.0 equiv), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv), 216.9 μL of *N*-phenylpyrrolidine (1.5 mmol, 3.0 equiv) and 2.0 mL of DMA. After 14 h, the reaction mixture was subjected to the workup

protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 2% ethyl acetate in hexanes to 4% ethyl acetate in hexanes) to afford the title compound as a white powder (87 mg, 0.27 mmol, 54%). IR (film) 2968, 1714, 1597, 1505, 1356, 1301, 1215, 1150, 1031 cm^{-1}; m.p. 144-145 ºC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.70 (1H, br s, Ar$\underline{H}$), 7.52 (1H, br s, Ar$\underline{H}$), 7.05 (2H, dd, *J* = 8.7, 7.3 Hz, Ar$\underline{H}$), 6.58 (1H, t, *J* = 7.2 Hz, Ar$\underline{H}$), 6.27 (2H, d, *J* = 8.5 Hz, Ar$\underline{H}$), 5.02 (1H, app t, *J* = 7.7 Hz, C$\underline{H}$(Ar)), 4.32 (2H, q, *J* = 7.1 Hz, C$\underline{H}_2$CH$_3$), 3.64-3.57 (1H, m, C$\underline{H}_A$H$_B$N), 3.52-3.43 (1H, m, CH$_A\underline{H}_B$N), 2.63-2.36 (4H, m, C$\underline{H}_A$CH$_B$CH(Ar) and Ar(C$\underline{H}_3$)$_A$), 2.25-2.07 (4H, m, C$\underline{H}_A$H$_B$CH$_2$N and Ar(C$\underline{H}_3$)$_B$), 2.06-1.87 (2H, m, CH$_A$C$\underline{H}_B$CH(Ar) and CH$_A\underline{H}_B$CH$_2$N), 1.35 (3H, d, *J* = 7.1 Hz, CH$_2$C$\underline{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 147.0, 145.0, 135.7 (br), 132.0 (br), 129.9 (br), 129.2, 128.3, 116.1, 111.8, 61.0, 60.0, 49.6, 33.2, 25.2, 21.2 (br), 20.9 (br), 14.6; HRMS (ESI) exact mass calculated for [M+1] ($C_{21}H_{26}NO_2$) requires *m/z* 324.1958, found *m/z* 324.1959.

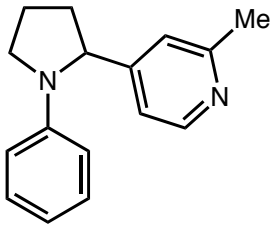


2-(1-Phenylpyrrolidin-2-yl)benzonitrile (entry 6, Table 2). Prepared according to the general procedure using 16.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (25.0 μmol, 0.05 equiv), 64.1 mg of 1,2-dicyanobenzene (0.5 mmol, 1.0 equiv), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv), 216.9 μL of *N*-phenylpyrrolidine (1.5 mmol, 3.0 equiv) and 2.0 mL of DMA. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 2% ethyl acetate in hexanes to 4% ethyl acetate in hexanes) to afford the title compound as a white solid (87 mg, 0.35 mmol, 70%). IR (film) 2970, 2221, 1596, 1503, 1480, 1446, 1364, 1341, 1260, 1208, 1186, 1160 cm^{-1}; m.p. 91-92 ºC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.68 (1H, d, *J* = 7.6 Hz, Ar$\underline{H}$), 7.45 (1H, app t, *J* = 7.7 Hz, Ar$\underline{H}$), 7.34-7.26 (2H, m, Ar$\underline{H}$), 7.14 (2H, dd, *J* = 8.6, 7.4 Hz, Ar$\underline{H}$), 6.66 (1H, t, *J* = 7.3 Hz, Ar$\underline{H}$), 6.42 (2H, d, *J* = 8.6 Hz Ar$\underline{H}$), 5.03 (1H, dd, *J* = 8.9, 2.0 Hz, C$\underline{H}$(Ph-2-CN)), 3.80-3.73 (1H, m, C$\underline{H}_A$H$_B$N), 3.48-3.38 (1H, m, CH$_A\underline{H}_B$N), 2.62-2.49 (1H, m, C$\underline{H}_A$CH$_B$CH(Ph-2-CN)), 2.09-1.94 (3H, m, CH$_A$C$\underline{H}_B$CH(Ph-2-CN) and C$\underline{H}_2$CH$_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.1, 146.6,

133.8, 133.2, 129.3, 127.5, 127.0, 117.9, 116.7, 112.7, 110.2, 61.7, 49.5, 25.5, 23.4; HRMS (ESI) exact mass calculated for [M+1] ($C_{17}H_{17}N_2$) requires *m/z* 243.1386, found *m/z* 243.1387.

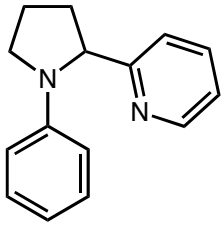


4-(1-Phenylpyrrolidin-2-yl)pyridine (entry 7, Table 2). Prepared according to the general procedure using 3.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (5.0 μmol, 0.01 equiv), 52.1 mg of 4-cyanopyridine (0.5 mmol, 1.0 equiv), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv), 180.7 μL of *N*-phenylpyrrolidine (1.5 mmol, 3.0 equiv) and 2.0 mL of DMA. After 12 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 10% ethyl acetate in hexanes to 50% ethyl acetate in hexanes) to afford the title compound as a yellow oil (81 mg, 0.36 mmol, 72%). IR (film) 2969, 1595, 1504, 1411, 1365, 1343,1187, 1161 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.55 (2H, d, *J* = 5.5 Hz, Ar<u>H</u>), 7.22-7.13 (4H, m, Ar<u>H</u>), 6.71 (1H, t, *J* = 7.3 Hz, Ar<u>H</u>), 6.48 (2H, d, *J* = 8.3 Hz Ar<u>H</u>), 4.71 (1H, dd, *J* = 8.9, 2.2 Hz, C<u>H</u>(Ar)), 3.79-3.69 (1H, m, C<u>H</u>$_A$H$_B$N), 3.49-3.37 (1H, m, CH$_A$<u>H</u>$_B$N), 2.51-2.39 (1H, m, C<u>H</u>$_A$CH$_B$CH(Ar)), 2.08-1.91 (3H, m, CH$_A$C<u>H</u>$_B$CH(Ar) and C<u>H</u>$_2$CH$_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.1, 150.2, 146.9, 129.4, 121.5, 116.6, 112.6, 62.3, 49.3, 35.7, 23.3; HRMS (ESI) exact mass calculated for [M+1] ($C_{15}H_{17}N_2$) requires *m/z* 225.1386, found *m/z* 225.1387.

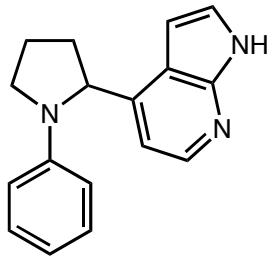


2-Methyl-4-(1-phenylpyrrolidin-2-yl)pyridine (entry 8, Table 2). Prepared according to the general procedure using 1.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (2.5 μmol, 0.01 equiv), 29.5 mg of 2-methyl-4-cyanopyridine (0.25 mmol, 1.0 equiv), 41.0 mg of sodium acetate (0.5 mmol, 2.0 equiv), 108.5 μL of *N*-phenylpyrrolidine (0.75 mmol, 3.0 equiv) and 1.0 mL of

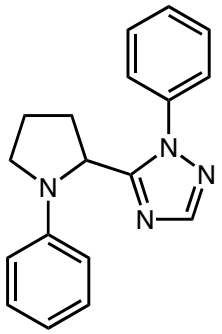
DMA. After 16 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 10% ethyl acetate in hexanes to 30% ethyl acetate in hexanes) to afford the title compound as a yellow oil (52 mg, 0.22 mmol, 87%). IR (film) 2969, 1596, 1561, 1503, 1481, 1399, 1358, 1343, 1158, 1186 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.38 (1H, d, *J* = 5.1 Hz, Ar<u>H</u>), 7.15 (2H, dd, *J* = 8.2, 7.5 Hz, Ar<u>H</u>), 7.01 (1H, s, Ar<u>H</u>), 6.95 (1H, d, *J* = 5.1 Hz, Ar<u>H</u>), 6.66 (1H, t, *J* = 7.3 Hz, Ar<u>H</u>), 6.44 (2H, d, *J* = 8.6 Hz, Ar<u>H</u>), 4.61 (1H, dd, *J* = 8.7, 1.6 Hz, C<u>H</u>(Ar)), 3.73-3.66 (1H, m, C<u>H</u>$_A$H$_B$N), 3.43-3.34 (1H, m, CH$_A$<u>H</u>$_B$N), 2.51 (3H, s, C<u>H</u>$_3$), 2.44-2.33 (1H, m, C<u>H</u>$_A$CH$_B$CH(Ar)), 2.04-1.84 (3H, m, CH$_A$C<u>H</u>$_B$CH(Ar) and C<u>H</u>$_2$CH$_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.8, 154.5, 149.5, 147.0, 129.3, 120.8, 118.7, 116.5, 112.5, 62.4, 49.3, 35.7, 24.7, 23.4; HRMS (ESI) exact mass calculated for [M+1] ($C_{16}H_{18}N_2$) requires *m/z* 239.1543, found *m/z* 239.1543.



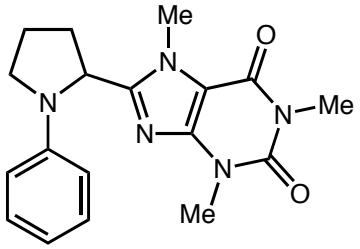
2-(1-phenylpyrrolidin-2-yl)pyridine (entry 9, Table 2). Prepared according to the general procedure using 3.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (5.0 μmol, 0.01 equiv), 52.1 mg of 4-cyanopyridine (0.5 mmol, 1.0 equiv), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv), 180.7 μL of *N*-phenylpyrrolidine (1.5 mmol, 3.0 equiv) and 2.0 mL of DMA. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 5% ethyl acetate in hexanes to 20% ethyl acetate in hexanes) to afford the title compound as a yellow solid (29 mg, 0.13 mmol, 26%). IR (film) 2972, 1598, 1505, 1481, 1433, 1362, 1186 cm^{-1}; m.p. 90-91 ºC; ^1H NMR (500 MHz, $CDCl_3$) δ 8.59 (1H, m, Ar<u>H</u>), 7.53 (1H, ddd, *J* = 9.3, 7.7, 1.7 Hz, Ar<u>H</u>), 7.17-7.09 (4H, m, Ar<u>H</u>), 6.64 (1H, t, *J* = 7.3 Hz Ar<u>H</u>), 6.47 (2H, d, *J* = 7.9 Hz, Ar<u>H</u>), 4.80 (1H, dd, *J* = 8.7, 2.0 Hz, C<u>H</u>(Ar)), 3.75-3.68 (1H, m, C<u>H</u>$_A$H$_B$N), 3.50-3.38 (1H, m, CH$_A$<u>H</u>$_B$N), 2.49-2.38 (1H, m, C<u>H</u>$_A$CH$_B$CH(Ar)), 2.15-2.07 (1H, m, CH$_A$C<u>H</u>$_B$CH(Ar)), 2.08-1.91 (2H, m, C<u>H</u>$_2$CH$_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.1, 149.8, 147.2 136.9, 129.3, 122.0, 120.4, 116.3, 112.5, 65.0, 49.4, 34.5, 23.4; HRMS (ESI) exact mass calculated for [M+1] ($C_{15}H_{17}N_2$) requires *m/z* 225.1386, found *m/z* 225.1384.



4-(1-Phenylpyrrolidin-2-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (entry 10, Table 2). Prepared according to the general procedure using 3.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (5.0 μmol, 0.01 equiv), 52.1 mg of 7-azaindole-4-carbonitrile (0.5 mmol, 1.0 equiv), 82.0 mg of sodium acetate (1.0 mmol, 2.0 equiv), 216.9 μL of *N*-phenylpyrrolidine (1.5 mmol, 3.0 equiv) and 2.0 mL of DMA. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel, gradient elution: 30% ethyl acetate in hexanes to 40% ethyl acetate in hexanes) to afford the title compound as a white solid (80 mg, 0.30 mmol, 61%). IR (film) 2871, 1598, 1504, 1404, 1345, 1188, 1154 cm^{-1}; m.p. 212-215 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.86 (1H, br m, N<u>H</u>), 8.15 (1H, d, *J* = 4.9 Hz, Ar<u>H</u>), 7.31 (1H, m, Ar<u>H</u>), 7.08 (2H, dd, *J* = 8.4, 7.2 Hz, Ar<u>H</u>), 6.87 (1H, d, *J* = 4.9 Hz, Ar<u>H</u>), 6.60 (1H, t, *J* = 7.1 Hz, Ar<u>H</u>), 6.54 (1H, m, Ar<u>H</u>), 6.44 (2H, d, *J* = 8.4 Hz, Ar<u>H</u>), 5.05 (1H, dd, *J* = 8.8, 1.6 Hz, C<u>H</u>(Ar)), 3.77-3.70 (1H, m, C<u>H</u>$_A$H$_B$N), 3.46-3.39 (1H, m, CH$_A$<u>H</u>$_B$N), 2.51-2.38 (1H, m, C<u>H</u>$_A$CH$_B$CH(Ar)), 2.11-1.94 (3H, m, CH$_A$C<u>H</u>$_B$CH(Ar) and C<u>H</u>$_2$CH$_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.0, 147.2, 146.2, 143.5, 129.3, 124.6, 117.7, 116.3, 113.2, 112.5, 99.0, 60.9, 49.2, 34.6, 24.0; HRMS (ESI) exact mass calculated for [M+1] ($C_{17}H_{18}N_3$) requires *m/z* 264.1495, found *m/z* 264.1495.

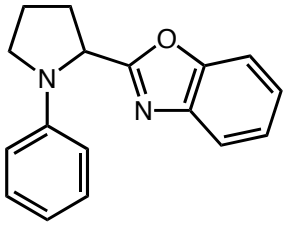


1-Phenyl-5-(1-phenylpyrrolidin-2-yl)-1*H*-1,2,4-triazole (entry 11, Table 2). Prepared according to the general procedure using 1.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (2.5 μmol. 0.01 equiv.), 42.5 mg of 1-phenyl-1*H*-1,2,4-triazole-5-carbonitrile (0.25 mmol, 1.0 equiv.), 41.5 mg of sodium acetate (0.50 mmol, 2.0 equiv.), 108.5 μL of *N*-phenylpyrrolidine (0.75 mmol, 3.0 equiv.) and 1.0 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, 25% ethyl acetate in hexanes) to afford the title compound as a colorless oil (35.5 mg, 0.12 mmol, 49%). IR (film) 3061, 2967, 2852, 1597, 1504, 1364, 1192, 748, 692 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) d 7.95 (1H, s, C=NC<u>H</u>N=N), 7.55-7.46 (3H, m, $N_{triazole}$-$C_6\underline{H}_5$), 7.38-7.31 (2H, m, $N_{triazole}$-$C_6\underline{H}_5$), 7.10 (2H, dd, *J* = 8.7, 7.3 Hz, $N_{pyrrolidine}$-$C_6\underline{H}_5$), 6.65 (1H, t, *J* = 7.3 Hz, $N_{pyrrolidine}$-$C_6\underline{H}_5$), 6.29 (2H, d, *J* = 7.8 Hz, $N_{pyrrolidine}$-$C_6\underline{H}_5$), 4.98 (1H, dd, *J* = 8.3, 3.2 Hz, NC<u>H</u>Ar), 3.41 (1H, td, *J* = 8.3, 8.2, 3.9 Hz, NC<u>H</u>$_A$H$_B$), 3.30 (1H, dd, *J* = 16.1, 7.6 Hz, NCH$_A$<u>H</u>$_B$), 2.48-2.35 (1H, m, NCHArC<u>H</u>$_A$H$_B$), 2.30-2.18 (1H, m, NCHArCH$_A$<u>H</u>$_B$), 2.17-2.11 (1H, m, NCH$_2$C<u>H</u>$_A$H$_B$), 2.08-2.00 (1H, m, NCH$_2$CH$_A$<u>H</u>$_B$); ^{13}C NMR (500 MHz, $CDCl_3$) d 158.1, 151.6, 146.3, 137.5, 129.6, 129.5, 129.3, 125.8, 116.9, 112.3, 55.2, 48.7, 33.4, 23.9; HRMS (ESI) exact mass calculated for [M+1] ($C_{18}H_{19}N_4$) requires *m/z* 291.1604, found 291.1607.

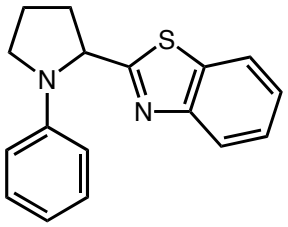


8-(1-Phenylpyrrolidin-2-yl)caffeine (entry 12, Table 2). Prepared according to the general procedure using 2.3 mg of $Ir(ppy)_2(dtbbpy)PF_6$ (2.5 μmol. 0.01 equiv.), 57.2 mg of 8-chlorocaffeine (0.25 mmol, 1.0 equiv.), 41.5 mg of sodium acetate (0.50 mmol, 2.0 equiv.), 108.5 μL of *N*-phenylpyrrolidine (0.75 mmol, 3.0 equiv.) and 1.0 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, 50% ethyl acetate in hexanes) to afford the title compound as a colorless oil (55.7 mg, 0.16 mmol, 66%). IR (film) 2949, 2851, 1701, 1857, 1599, 1505, 1438, 747 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) d 7.18 (2H, dd, *J* = 8.5, 7.4 Hz, $NC_6\underline{H}_5$), 6.72 (1H, t, *J* = 7.3 Hz, $NC_6\underline{H}_5$), 6.49 (2H, d, *J* = 8.0 Hz, $NC_6\underline{H}_5$), 4.98 (1H, dd, *J* = 8.2, 5.2 Hz, NC<u>H</u>Ar), 3.90

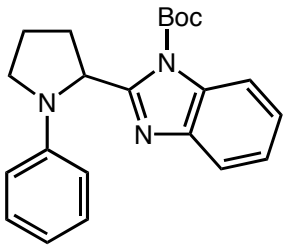
(3H, s, NC$\underline{H}_3$), 3.74-3.67 (1H, m, NC$\underline{H}_A$H$_B$), 3.57 (3H, s, NC$\underline{H}_3$), 3.52-3.45 (1H, m, NCH$_A\underline{H}_B$), 3.37 (3H, s, NC$\underline{H}_3$), 2.58-2.47 (1H, m, NCHArC$\underline{H}_A$H$_B$), 2.28-2.19 (1H, m, NCHArCH$_A\underline{H}_B$), 2.16-2.06 (2H, m, NCH$_2$C$\underline{H}_2$); ^{13}C NMR (500 MHz, $CDCl_3$) d 155.5, 154.8, 151.8, 148.0, 146.5, 129.5, 117.5, 112.4, 108.0, 57.7, 49.4, 33.3, 32.2, 30.0, 28.0, 24.4; HRMS (ESI) exact mass calculated for [M+1] ($C_{18}H_{22}N_5O_2$) requires *m/z* 340.1768, found 340.1765.



2-(1-Phenylpyrrolidin-2-yl)benzoxazole (entry 13, Table 2). Prepared according to the general procedure using 2.3 mg of Ir(ppy)$_2$(dtbbpy)PF$_6$ (2.5 μmmol. 0.01 equiv.), 28.5 mL of 2-chlorobenzoxazole (0.25 mmol, 1.0 equiv.), 41.5 mg of sodium acetate (0.50 mmol, 2.0 equiv.), 108.5 μL of *N*-phenylpyrrolidine (0.75 mmol, 3.0 equiv.) and 1.0 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, 2% ethyl acetate in hexanes) to afford the title compound as a colorless oil (60.1 mg, 0.23 mmol, 91%). IR (film) 3058, 2973, 2846, 1598, 1504, 1454, 1358, 1344, 1240, 744, 691 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 7.74-7.67 (1H, m, Ar$\underline{H}$), 7.51-7.44 (1H, m, Ar$\underline{H}$), 7.34-7.28 (2H, m, Ar$\underline{H}$), 7.22-7.17 (2H, dd, *J* = 7.3, 8.8 Hz, Ar$\underline{H}$), 6.73-6.68 (3H, m, Ar$\underline{H}$), 5.04 (1H, dd, *J* = 7.9, 2.0 Hz, NC$\underline{H}$Ar), 3.82-3.75 (1H, m, NC$\underline{H}_A$H$_B$), 3.44 (1H, dd, *J* = 15.6, 8.6 Hz, NCH$_A\underline{H}_B$), 2.50-2.38 (2H, m, NCHArC$\underline{H}_2$), 2.37-2.28 (1H, m, NCH$_2$C$\underline{H}_A$H$_B$), 2.23-2.13 (1H, m, NCH$_2$CH$_A\underline{H}_B$); ^{13}C NMR (500 MHz, $CDCl_3$) d 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+1] ($C_{17}H_{17}N_2O$) requires *m/z* 265.1335, found 265.1334.

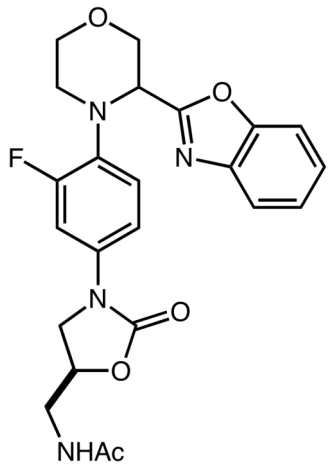


2-(1-Phenylpyrrolidin-2-yl)benzothiazole (entry 14, Table 2). Prepared according to the general procedure using 2.3 mg of $Ir(ppy)_2(dtbbpy)PF_6$ (2.5 μmol. 0.01 equiv.), 32.5 mL of 2-chlorobenzothiazole (0.25 mmol, 1.0 equiv.), 41.5 mg of sodium acetate (0.50 mmol, 2.0 equiv.), 108.5 μL of *N*-phenylpyrrolidine (0.75 mmol, 3.0 equiv.) and 1.0 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, 5% ethyl acetate in hexanes) to afford the title compound as a colorless oil (55.1 mg, 0.20 mmol, 79%). IR (film) 3061, 2971, 2942, 2841, 1597, 1502, 1357, 1313, 1336, 748, 730, 691 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) d 8.00 (1H, d, *J* = 8.1 Hz, Ar<u>H</u>), 7.78 (1H, d, *J* = 7.9 Hz, Ar<u>H</u>), 7.48 (1H, t, *J* = 7.7 Hz, Ar<u>H</u>), 7.34 (1H, t, *J* = 7.6 Hz, Ar<u>H</u>), 7.20 (2H, t, *J* = 7.7 Hz, Ar<u>H</u>), 6.75 (1H, t, *J* = 7.2 Hz, Ar<u>H</u>), 6.66 (2H, d, *J* = 8.3 Hz, Ar<u>H</u>), 5.12 (1H, d, *J* = 8.7 Hz, NC<u>H</u>Ar), 3.81 (1H, t, *J* = 8.0 Hz, $NC\underline{H}_AH_B$), 3.37 (1H, m, $NCH_A\underline{H}_B$), 2.56-2.46 (1H, m, $NCHArC\underline{H}_AH_B$), 2.32 (1H, m, $NCH_A\underline{H}_B$), 2.27-2.16 (1H, m, $NCH_2C\underline{H}_AH_B$), 2.11 (1H, m, $NCH_2CH_A\underline{H}_B$); ^{13}C NMR (500 MHz, $CDCl_3$) d 179.8, 154.3, 147.1, 135.2, 129.3, 126.0, 124.8, 122.8, 122.0, 117.7, 113.0, 62.4, 49.4, 34.7, 23.8; HRMS (ESI) exact mass calculated for [M+1] ($C_{17}H_{17}N_2S$) requires *m/z* 281.1107, found 281.1107.



2-(1-Phenylpyrrolidin-2-yl)-1-(*tert*-butoxycarbonyl)-benzimidazole (entry 15, Table 2). Prepared according to the general procedure using 2.3 mg of $Ir(ppy)_2(dtbbpy)PF_6$ (2.5 μmol. 0.01 equiv.), 63.2 mg of 2-chloro-1-(*tert*-butoxycarbonyl)-benzimidazole (0.25 mmol, 1.0 equiv.), 41.5 mg of sodium acetate (0.50 mmol, 2.0 equiv.), 108.5 μL of *N*-phenylpyrrolidine (0.75 mmol, 3.0 equiv.) and 1.0 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% ethyl acetate in hexanes) to afford the title compound as a colorless oil (83.8 mg, 0.23 mmol, 92%). IR (film) 2978, 1741, 1599, 1505, 1452, 1344, 1318, 1148, 1116, 906, 727 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) d 7.96 (1H, d, *J* = 8.0 Hz, Ar<u>H</u>), 7.69 (1H, d, *J* = 7.6 Hz, Ar<u>H</u>), 7.34-7.27 (2H, m, Ar<u>H</u>), 7.15 (2H, t, *J* = 7.6 Hz, Ar<u>H</u>), 6.65 (1H, t, *J* = 7.2 Hz, Ar<u>H</u>), 6.50 (2H, d, *J* = 8.1 Hz, Ar<u>H</u>), 5.57

(1H, d, *J* = 8.5 Hz, NC<u>H</u>Ar), 3.87 (1H, t, J = 8.3 Hz, NC<u>H</u>$_A$H$_B$), 3.46 (1H, dd, *J* = 16.4, 8.6 Hz, NCH$_A$<u>H</u>$_B$), 2.46 (1H, m, NCHArC<u>H</u>$_A$H$_B$), 2.29-2.16 (1H, m, NCHArCH$_A$<u>H</u>$_B$), 2.16-2.01 (2H, m, NCH$_2$C<u>H</u>$_2$), 1.75 (9H, s, NCO$_2$C(C<u>H</u>$_3$)$_3$); ^{13}C NMR (500 MHz, $CDCl_3$) d 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+1] ($C_{22}H_{26}N_3O_2$) requires *m/z* 364.2020, found 364.2021.



***N*-(((5*S*)-3-(4-(3-(benzoxazol-2-yl)morpholino)-3-fluorophenyl)-2-oxooxazolidin-5-yl)methyl)ethanamide (entry 15, Table 2).** Prepared according to the general procedure using 4.6 mg of Ir(ppy)$_2$(dtbbpy)PF_6 (5.0 μmol. 0.01 equiv.), 57.1 μL of 2-chlorobenzoxazole (0.50 mmol, 1.0 equiv.), 83.1 mg of sodium acetate (1.0 mmol, 2.0 equiv.), 506.0 mg of Zyvox (linezolid) (1.50 mmol, 3.0 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, 100% ethyl acetate) to afford the title compound as a colorless oil (132.9 mg, 0.29 mmol, 58%, 1:1 d.r.). IR (film) 3305, 2924, 2859, 1748, 1659, 1516, 1454, 1222, 1119, 748, 732 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 7.64 (1H, m, Ar<u>H</u>), 7.43 (2H, m, Ar<u>H</u>), 7.27 (2H, m, Ar<u>H</u>), 7.08 (1H, t, *J* = 9.0 Hz, Ar<u>H</u>), 6.98 (1H, d, *J* = 8.2 Hz, Ar<u>H</u>), 6.23 (1H, br, N<u>H</u>Ac), 4.89 (1H, s, NC<u>H</u>Ar), 4.72 (1H, m, NCO$_2$C<u>H</u>CH$_2$), 4.31 (1H, dd, *J* = 11.4, 3.1 Hz, NCHArC<u>H</u>$_2$O), 4.19 (1H, dd, *J* = 11.4, 3.3 Hz, NCHArC<u>H</u>$_2$O), 4.06 (1H, m, NCH$_2$C<u>H</u>$_2$O), 3.93 (2H, m, NCH$_2$C<u>H</u>$_2$O and NC<u>H</u>$_2$CH$_2$O), 3.85 (1H, m, NC<u>H</u>$_2$CH$_2$O), 3.66 (2H, m, C<u>H</u>$_2$NHAc), 3.55 (1H, m, NCO$_2$CHC<u>H</u>$_2$), 3.05 (1H, m, NCO$_2$CHC<u>H</u>$_2$), 1.98 (3H, s, NHCOCH$_3$); ^{13}C NMR (500 MHz, $CDCl_3$) d 171.2, 163.8, 157.0, 155.0, 154.3, 150.5, 140.9, 134.3 (d, *J* = 9.0 Hz), 133.8 (d, *J* = 10.6 Hz), 125.1,

124.4, 121.8, 120.3, 113.8, 110.8, 107.4 (d, J = 3.3 Hz), 107.2 (d, J = 3.2 Hz), 72.0, 69.4, 67.4, 56.1, 47.5, 47.4, 42.0, 23.2; HRMS (ESI) exact mass calculated for [M+1] ($C_{23}H_{24}FN_4O_5$) requires m/z 455.1725, found 455.1727.

Emission Quenching experiments

Emission intensities were recorded using a Perkin Elmer LS50 luminescence spectrometer. All $Ir(ppy)_3$ solutions were exited at 385 nm and the emission intensity at 518 nm was observed. In a typical experiment, a 0.0001 M solution of $Ir(ppy)_3$ in DMA was added to the appropriate amount of quencher in a screw-top 1.0 cm quartz curvette. After degassing the sample with a stream of argon for 15 minutes the emission of the sample was collected.

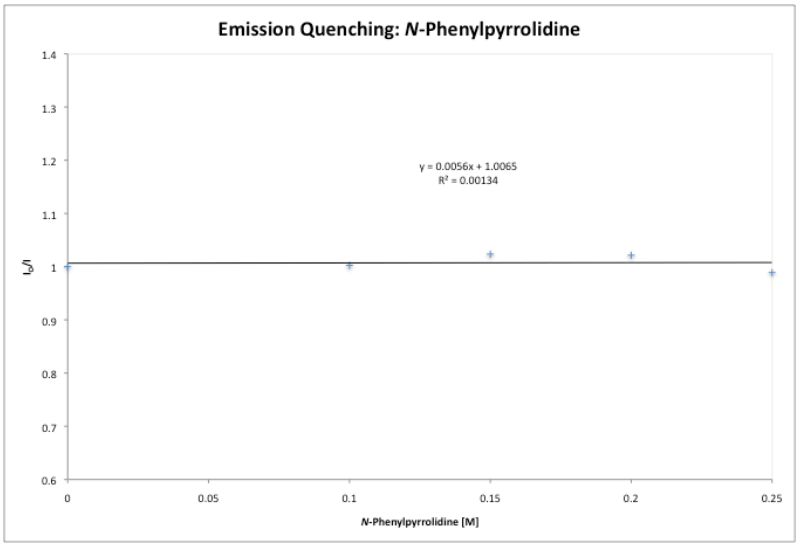


Figure S9. $Ir(ppy)_3$ Emission Quenching by *N*-Phenylpyrrolidine.

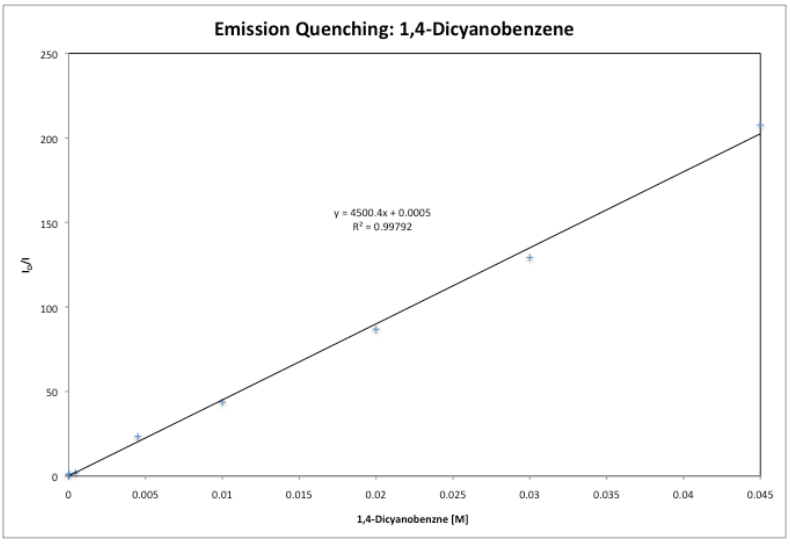


Figure S10. $Ir(ppy)_3$ Emission Quenching by 1,4-Dicyanobenzene.

Sodium acetate was insoluble in DMA even at low concentrates and was therefore omitted from the emission quenching experiments.

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