Direct Aldehyde C–H Arylation and Alkylation via the Combination of Nickel, HAT and Photoredox Catalysis

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Supporting Information

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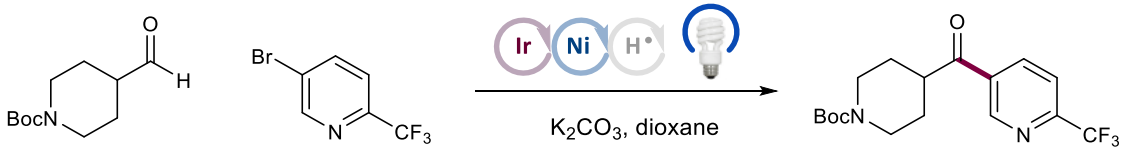
1) General Information

Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.[1] $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ was prepared using literature procedures.[2] All solvents were purified according to the method of Grubbs.[3] Additionally, aldehydes (if liquid) were distilled prior to use; aldehydes (if solid) were purified by column chromatography prior to use. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator using a water bath. Chromatographic purification of products was accomplished using forced-flow chromatography on silica gel (Fluka, 230–400 mesh) according to the method of Still.[4] Thin-layer chromatography (TLC) was performed on Silicycle 0.25 mm silica gel F-254 plates. Visualization of the developed chromatogram was performed by fluorescence quenching or $KMnO_4$ stain. ^1H NMR spectra were recorded on a Bruker UltraShield Plus Avance III 500 MHz and are internally referenced to residual protic $CDCl_3$ (δ 7.26 ppm). Data for ^1H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, br = broad), coupling constant (Hz), and integration. ^{13}C NMR spectra were recorded on a Bruker UltraShield Plus Avance III 500 MHz (125 MHz) and data are reported in terms of chemical shift relative to $CDCl_3$ (77.16 ppm). ^{19}F NMR spectra were recorded on a Bruker NanoBay 300 MHz (282 MHz). IR spectra were recorded on a Perkin Elmer Spectrum 100 FTIR spectrometer and are reported in wavenumbers (cm-1). High Resolution Mass Spectra were obtained from the Princeton University Mass Spectral Facility.

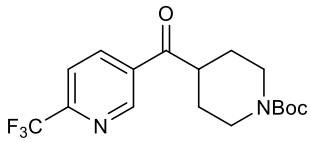
2) Procedure for Optimization Studies

To an 8 mL vial equipped with a stir bar was added photocatalyst $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (1.2 mg, 1.1 μmol, 0.01 equiv.), 5-bromo-2-(trifluoromethyl)pyridine (24.1 mg, 0.11 mmol, 1.0 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (45.5 mg, 0.21 mmol, 2.0 equiv.), quinuclidine (1.2 mg, 11 μmol, 0.10 equiv.), and anhydrous potassium carbonate (22 mg, 0.16 mmol, 1.5 equiv.). The vial was sealed and placed under nitrogen before 1 mL of solvent was added. To a separate vial was added $NiBr_2$•glyme (3.3 mg, 11 μmmol, 0.10 equiv.) and 4,4'-di-*tert*-butyl-2,2'-bipyridine (2.9 mg, 11 μmmol, 0.10 equiv). The precatalyst vial was sealed, purged with nitrogen, dissolved in 2 ml of solvent and then sonicated until it became homogeneous. Subsequently, the precatalyst solution was syringed into the reaction vessel and the solution was degassed by sparging with nitrogen for 15 minutes before sealing with parafilm. The reaction was stirred and irradiated using 34 W blue LED lamps (Kessil KSH150B Blue LED Grow Light; 6 cm away, with cooling fan to keep the reaction at room temperature) for 20 hours. The reaction was quenched by exposure to air. 1,3-Benzodioxole (internal standard, 11 μL, 0.11 mmol, 1.0 equiv.) was added then the reaction mixture was analyzed by ^1H NMR.

3) General Procedure for Aldehyde C–H Functionalization



To an 40 mL vial equipped with a stir bar was added photocatalyst $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), 5-bromo-2-(trifluoromethyl)pyridine (90 mg, 0.40 mmol, 1.0 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), and anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.). The vial was sealed and placed under nitrogen before 1,4-dioxane (6 mL) was added. To a separate vial was added $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.) and 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.). The precatalyst vial was sealed, purged with nitrogen, dissolved in 1,4-dioxane (6 mL) and then sonicated until it became homogeneous. Subsequently, the precatalyst solution was syringed into the reaction vessel and the solution was degassed by sparging with nitrogen for 15 minutes before sealing with parafilm. The reaction was stirred and irradiated using 34 W blue LED lamps (Kessil KSH150B Blue LED Grow Light; 6 cm away, with cooling fan to keep the reaction at room temperature) for 20 hours. The reaction mixture was removed from the light, cooled to ambient temperature, diluted with water and EtOAc, and the aqueous layer was extracted with three portions of EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography on silica gel to afford the desired ketone product.



***tert*-Butyl 4-(6-(trifluoromethyl)nicotinoyl)piperidine-1-carboxylate**

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg,

0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 5-bromo-2-(trifluoromethyl)pyridine (90 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (20-25% EtOAc/hexanes), followed by preparative TLC (12% acetone/hexanes) provided the title compound (125 mg, 87% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.22 (brs, 1H), 8.38 (d, J = 7.1 Hz, 1H), 7.82 (d, J = 8.1 Hz, 1H), 4.17 (brs, 2H), 3.37 (tt, J = 10.9, 3.0 Hz, 1H), 2.92 (brs, 2H), 1.88-1.83 (m, 2H), 1.74-1.68 (m, 2H), 1.46 (s, 9H).

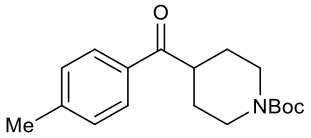
^{13}C NMR (125 MHz, $CDCl_3$) δ 199.84, 154.75, 151.38 (q, $J_{C,F}$ = 35.5 Hz), 149.75, 137.59, 133.27, 121.13 (q, $J_{C,F}$ = 274.5 Hz), 120.88 (q, $J_{C,F}$ = 2.9 Hz), 80.04, 44.50, 44.07 (br), 28.56, 28.10 (br).

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.29.

IR (film) ν_{max} 2976, 2933, 2860, 1685, 1422, 1330, 1143, 1084, 970, 861, 771 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{17}H_{21}F_3N_2NaO_3$ ($[M+Na]^+$) 381.1397, found 381.1398.

4) Aryl Halide Scope



***tert*-Butyl 4-(4-methylbenzoyl)piperidine-1-carboxylate (15)**

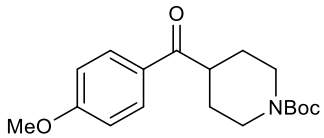
Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 4-bromotoluene (68 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (10-15% EtOAc/hexanes) provided the title compound (100 mg, 82% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.2 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 4.16 (brs, 2H), 3.38 (tt, *J* = 11.1, 3.7 Hz, 1H), 2.89 (brs, 2H), 2.41 (s, 3H), 1.92-1.76 (m, 2H), 1.73-1.64 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 201.85, 154.86, 144.08, 133.44, 129.57, 128.52, 79.74, 43.51, 28.59, 21.78.

IR (film) ν_{max} 2975, 2928, 2858, 1681, 1419, 1365, 1166, 1122, 969, 770 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{18}H_{25}NNaO_3$ ($[M+Na]^+$) 326.1727, found 326.1730.



***tert*-Butyl 4-(4-methoxybenzoyl)piperidine-1-carboxylate (16)**

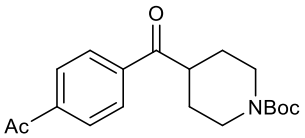
Prepared following the general procedure outlined above using

$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 4-bromoanisole (50 μL, 75 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (30-40% EtOAc/hexanes), followed by preparative TLC (20% acetone/hexanes) provided the title compound (104 mg, 81% yield) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.9 Hz, 2H), 6.95 (d, *J* = 8.9 Hz, 2H), 4.16 (brs, 2H), 3.87 (s, 3H), 3.36 (tt, *J* = 11.1, 3.7 Hz, 1H), 2.88 (brs, 2H), 1.86-1.77 (m, 2H), 1.76-1.66 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 200.74, 163.63, 154.88, 130.68, 128.88, 114.02, 79.75, 55.64, 43.30, 28.59.

Spectroscopic data matches with previously reported data.[5]



***tert*-Butyl 4-(4-acetylbenzoyl)piperidine-1-carboxylate (17)**

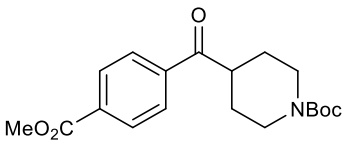
Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 1-acetyl-4-bromobenzene (80 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (20-25% EtOAc/hexanes) provided the title compound (122 mg, 92% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.6 Hz, 2H), 8.00 (d, *J* = 8.6 Hz, 2H), 4.16 (brs, 2H), 3.40 (tt, *J* = 11.1, 3.7 Hz, 1H), 2.91 (brs, 2H), 2.65 (s, 3H), 1.89-1.82 (m, 2H), 1.76-1.65 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 201.71, 197.53, 154.80, 140.27, 139.24, 128.78, 128.59, 79.86, 44.04, 28.57, 28.38 (br), 27.05.

IR (film) ν_{max} 2975, 2931, 2858, 1681, 1422, 1365, 1266, 1167, 971 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{19}H_{25}NNaO_4$ ($[M+Na]^+$) 354.1676, found 354.1677.



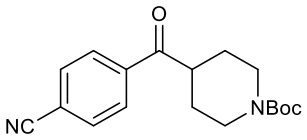
***tert*-Butyl 4-(4-(methoxycarbonyl)benzoyl)piperidine-1-carboxylate (18)**

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), methyl 4-bromobenzoate (86 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (25-30% EtOAc/hexanes), followed by preparative TLC (12% acetone/hexanes) provided the title compound (126 mg, 91% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.4 Hz, 2H), 7.97 (d, *J* = 8.4 Hz, 2H), 4.16 (brs, 2H), 3.95 (s, 3H), 3.40 (tt, *J* = 11.1, 3.6 Hz, 1H), 2.90 (brs, 2H), 1.89-1.81 (m, 2H), 1.73-1.66 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 201.75, 166.28, 154.80, 139.30, 134.02, 130.11, 128.29, 79.84, 52.65, 44.01, 28.57, 28.39 (br).

Spectroscopic data matches with previously reported data.[5]



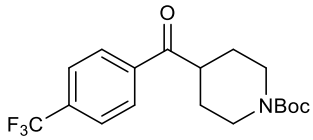
***tert*-Butyl 4-(4-cyanobenzoyl)piperidine-1-carboxylate (19)**

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 4-bromobenzonitrile (73 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (20-25% EtOAc/hexanes) provided the title compound (113 mg, 90% yield) as a pale yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.3 Hz, 2H), 7.78 (d, *J* = 8.3 Hz, 2H), 4.16 (brs, 2H), 3.37 (tt, *J* = 11.1, 3.5 Hz, 1H), 2.89 (brs, 2H), 1.86-1.80 (m, 2H), 1.72-1.63 (m, 2H), 1.45 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 200.82, 154.73, 138.99, 132.77, 128.80, 117.98, 116.50, 79.92, 43.96, 28.53, 28.29 (br).

Spectroscopic data matches with previously reported data.[5]



***tert*-Butyl 4-(4-(trifluoromethyl)benzoyl)piperidine-1-carboxylate (20)**

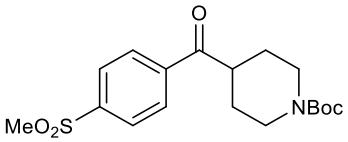
Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.),

quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 1-bromo-4-(trifluoromethyl)benzene (56 μL, 90 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (15-20% EtOAc/hexanes) provided the title compound (126 mg, 88% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.2 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 2H), 4.16 (brs, 2H), 3.39 (tt, *J* = 11.1, 3.6 Hz, 1H), 2.91 (t, *J* = 11.9 Hz, 2H), 1.86-1.82 (m, 2H), 1.73-1.66 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 201.24, 154.78, 138.71, 134.53 (q, $J_{C,F}$ = 33.0 Hz), 128.71, 125.96 (q, $J_{C,F}$ = 4.1 Hz), 123.66 (q, $J_{C,F}$ = 272.5 Hz), 79.88, 43.97, 28.55, 28.34.

Spectroscopic data matches with previously reported data.[5]



***tert*-Butyl 4-(4-(methylsulfonyl)benzoyl)piperidine-1-carboxylate (21)**

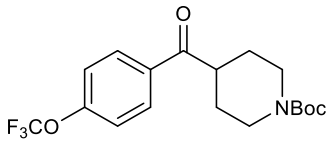
Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 1-bromo-4-(methylsulfonyl)benzene (94 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (100-120% EtOAc/hexanes) provided the title compound (135 mg, 92% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.4 Hz, 2H), 8.04 (d, *J* = 8.2 Hz, 2H), 4.15 (brs, 2H), 3.39 (tt, *J* = 11.1, 3.6 Hz, 1H), 3.08 (s, 3H), 2.90 (brs, 2H), 1.88-1.80 (m, 2H), 1.71-1.64 (m, 2H), 1.45 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 200.98, 154.73, 144.25, 140.07, 129.21, 128.05, 79.91, 44.42, 44.11, 28.53, 28.24 (br).

IR (film) ν_{max} 2975, 2930, 2860, 2251, 1681, 1422, 1315, 1151, 960, 769, 729 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{18}H_{25}NNaO_5S$ ($[M+Na]^+$) 390.1346, found 390.1346.



***tert*-Butyl 4-(4-(trifluoromethoxy)benzoyl)piperidine-1-carboxylate (22)**

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 1-bromo-4-(trifluoromethoxy)benzene (59 μL, 96 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (15-20% EtOAc/hexanes) provided the title compound (122 mg, 82% yield) as a white solid.

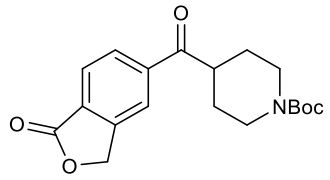
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 8.8 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 4.16 (brs, 2H), 3.36 (tt, J = 11.1, 3.7 Hz, 1H), 2.89 (t, J = 12.1 Hz, 2H), 1.86-1.80 (m, 2H), 1.76-1.62 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 200.62, 154.80, 152.73 (q, $J_{C,F}$ = 1.9 Hz), 134.16, 130.41, 120.68 (d, $J_{C,F}$ = 1.1 Hz), 120.40 (q, $J_{C,F}$ = 258.9 Hz), 79.84, 43.71, 28.56, 28.47 (br).

^{19}F NMR (282 MHz, $CDCl_3$) δ -57.62.

IR (film) ν_{max} 2976, 2860, 1683, 1419, 1254, 1207, 1161, 970, 858 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{18}H_{22}F_3NNaO_4$ ([M+Na]$^+$) 396.1393, found 396.1396.



***tert*-Butyl 4-(1-oxo-1,3-dihydroisobenzofuran-5-carbonyl)piperidine-1-carboxylate (23)**

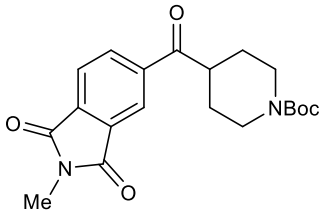
Prepared following the general procedure outlined above using Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 5-bromophthalide (85 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (100-120% EtOAc/hexanes) provided the title compound (128 mg, 93% yield) as a pale yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.0 Hz, 1H), 8.04 (s, 1H), 8.01 (d, *J* = 7.9 Hz, 1H), 5.39 (s, 2H), 4.16 (brs, 2H), 3.41 (tt, *J* = 11.1, 3.7 Hz, 1H), 2.91 (brs, 2H), 1.88-1.82 (m, 2H), 1.74-1.65 (m, 2H), 1.45 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 201.31, 170.01, 154.74, 147.01, 140.76, 129.41, 129.05, 126.35, 122.20, 79.94, 69.83, 44.32, 28.54, 28.34 (br).

IR (film) ν_{max} 2973, 2860, 1765, 1682, 1422, 1317, 1153, 1006, 730 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{19}H_{23}NNaO_5$ ([M+Na]$^+$) 368.1468, found 368.1469.



***tert*-Butyl 4-(2-methyl-1,3-dioxoisoindoline-5-carbonyl)piperidine-1-carboxylate (24)**

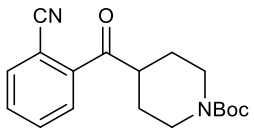
Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 4-bromo-*N*-methylphthalimide (96 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (50-60% EtOAc/hexanes) provided the title compound (120 mg, 81% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (s, 1H), 8.28 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.95 (d, *J* = 7.7 Hz, 1H), 4.17 (brs, 2H), 3.42 (tt, *J* = 11.2, 3.7 Hz, 1H), 3.21 (s, 3H), 2.92 (brs, 2H), 1.86-1.82 (m, 2H), 1.75-1.66 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 200.46, 167.65, 167.48, 154.77, 140.78, 135.54, 134.22, 132.92, 123.89, 122.70, 80.01, 44.14, 28.56, 28.29 (br), 24.41.

IR (film) ν_{max} 2971, 2947, 2861, 1775, 1713, 1683, 1421, 1377, 1166, 1147, 1009, 719 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{20}H_{24}N_2NaO_5$ ($[M+Na]^+$) 395.1577, found 395.1578.



***tert*-Butyl 4-(2-cyanobenzoyl)piperidine-1-carboxylate (25)**

Prepared following the general procedure outlined above using

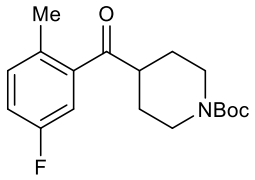
$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 2-bromobenzonitrile (73 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (50-60% EtOAc/hexanes) provided the title compound (111 mg, 88% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88-7.80 (m, 2H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.65 (t, *J* = 7.6 Hz, 1H), 4.14 (brs, 2H), 3.40 (tt, *J* = 10.9, 3.6 Hz, 1H), 2.90 (brs, 2H), 1.91-1.84 (m, 2H), 1.74-1.66 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 201.24, 154.77, 140.02, 135.27, 132.80, 132.27, 129.02, 117.97, 111.32, 79.91, 45.31, 28.57, 28.10 (br).

IR (film) ν_{max} 2975, 2930, 2858, 2226, 1683, 1421, 1366, 1164, 969, 762 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{18}H_{22}N_2NaO_3$ ($[M+Na]^+$) 337.1523, found 337.1520.



***tert*-Butyl 4-(5-fluoro-2-methylbenzoyl)piperidine-1-carboxylate (26)**

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 2-bromo-4-fluoro-1-methylbenzene (50 μL, 76 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (10-15% EtOAc/hexanes)

provided the title compound (115 mg, 90% yield) as a pale yellow oil.

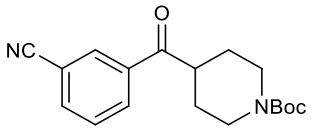
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (dd, *J* = 8.4, 5.5 Hz, 1H), 7.17 (dd, *J* = 9.0, 2.6 Hz, 1H), 7.05 (td, *J* = 8.3, 2.7 Hz, 1H), 4.12 (brs, 2H), 3.10 (tt, *J* = 11.2, 3.7 Hz, 1H), 2.83 (brs, 2H), 2.35 (s, 3H), 1.83-1.77 (m, 2H), 1.74-1.56 (m, 2H), 1.45 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 205.53 (d, $J_{C,F}$ = 2.4 Hz), 160.69 (d, $J_{C,F}$ = 245.7 Hz), 154.76, 139.35 (d, $J_{C,F}$ = 5.6 Hz), 133.34 (d, $J_{C,F}$ = 7.5 Hz), 133.11 (d, $J_{C,F}$ = 3.8 Hz), 117.77 (d, $J_{C,F}$ = 20.8 Hz), 114.13 (d, $J_{C,F}$ = 22.4 Hz), 79.80, 46.82, 28.56, 27.81, 19.98.

^{19}F NMR (282 MHz, $CDCl_3$) δ -116.79.

IR (film) ν_{max} 2975, 2931, 2859, 1684, 1420, 1365, 1275, 1229, 1159, 1120, 974, 918, 799 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{18}H_{24}FNNaO_3$ ($[M+Na]^+$) 344.1632, found 344.1634.



***tert*-Butyl 4-(3-cyanobenzoyl)piperidine-1-carboxylate (27)**

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 3-bromobenzonitrile (73 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (30-40% EtOAc/hexanes) provided the title compound (116 mg, 92% yield) as a pale yellow solid.

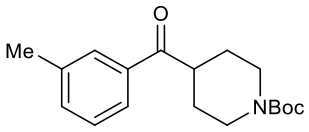
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (s, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 7.7 Hz,

1H), 7.62 (t, *J* = 7.8 Hz, 1H), 4.16 (brs, 2H), 3.36 (tt, *J* = 11.1, 3.6 Hz, 1H), 2.90 (t, *J* = 12.0 Hz, 2H), 1.85-1.80 (m, 2H), 1.74-1.61 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 200.05, 154.73, 136.70, 136.11, 132.35, 132.05, 129.98, 118.00, 113.46, 79.91, 43.77, 28.54, 28.29 (br).

IR (film) ν_{max} 2976, 2931, 2859, 2232, 1681, 1421, 1365, 1156, 1122, 975, 731 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{18}H_{22}N_2NaO_3$ ($[M+Na]^+$) 337.1523, found 337.1520.



***tert*-Butyl 4-(3-methylbenzoyl)piperidine-1-carboxylate (28)**

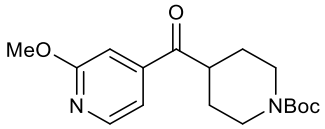
Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 1-bromo-3-methylbenzene (48 μL, 68 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (15-20% EtOAc/hexanes) provided the title compound (102 mg, 85% yield) as a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74-7.70 (m, 2H), 7.39-7.32 (m, 2H), 4.16 (brs, 2H), 3.39 (tt, *J* = 11.1, 3.7 Hz, 1H), 2.89 (brs, 2H), 2.41 (s, 3H), 1.87-1.79 (m, 2H), 1.74-1.62 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 202.46, 154.83, 138.72, 136.04, 133.99, 128.87, 128.71, 125.54, 79.72, 43.63, 28.57, 21.53.

IR (film) ν_{max} 2972, 2929, 2859, 1680, 1420, 1365, 1228, 1158, 974, 772 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{18}H_{25}NNaO_3$ ([M+Na]$^+$) 326.1727, found 326.1724.



***tert*-Butyl 4-(2-methoxyisonicotinoyl)piperidine-1-carboxylate (29)**

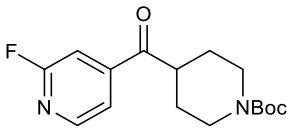
Prepared following the general procedure outlined above using Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 4-bromo-2-methoxypyridine (75 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (25-35% EtOAc/hexanes) provided the title compound (115 mg, 90% yield) as a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, *J* = 5.3 Hz, 1H), 7.26 (d, *J* = 5.2 Hz, 1H), 7.13 (s, 1H), 4.14 (brs, 2H), 3.98 (s, 3H), 3.27 (tt, *J* = 11.1, 3.6 Hz, 1H), 2.88 (brs, 2H), 1.88-1.80 (m, 2H), 1.69-1.62 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 201.52, 165.27, 154.77, 148.34, 145.16, 114.34, 109.76, 79.90, 54.08, 44.22, 28.56, 28.15 (br).

IR (film) ν_{max} 2939, 2859, 1688, 1556, 1388, 1317, 1232, 1162, 974 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{17}H_{24}N_2O_4$ ([M+H]$^+$) 321.1809, found 321.1810.



***tert*-Butyl 4-(2-fluoroisonicotinoyl)piperidine-1-carboxylate (30)**

Prepared following the general procedure outlined above using

$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 4-bromo-2-fluoropyridine (41 μL, 70 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (30-35% EtOAc/hexanes) provided the title compound (105 mg, 85% yield) as a colorless oil.

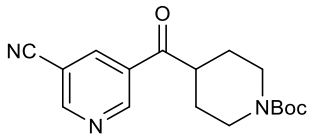
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (d, J = 5.1 Hz, 1H), 7.59 (d, J = 5.1 Hz, 1H), 7.33 (s, 1H), 4.15 (brs, 2H), 3.29 (tt, J = 11.1, 3.7 Hz, 1H), 2.90 (t, J = 11.8 Hz, 2H), 1.88-1.81 (m, 2H), 1.76-1.58 (m, 2H), 1.45 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 200.00 (d, $J_{C,F}$ = 3.1 Hz), 164.71 (d, $J_{C,F}$ = 241.3 Hz), 154.70, 149.29 (d, $J_{C,F}$ = 14.5 Hz), 147.64 (d, $J_{C,F}$ = 6.8 Hz), 119.31 (d, $J_{C,F}$ = 4.9 Hz), 108.25 (d, $J_{C,F}$ = 38.4 Hz), 79.99, 44.37, 28.53, 28.02 (br).

^{19}F NMR (282 MHz, $CDCl_3$) δ -65.44.

IR (film) ν_{max} 2975, 2932, 2861, 1686, 1563, 1405, 1393, 1231, 1158, 1122, 1008, 908, 801 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{21}FN_2NaO_3$ ($[M+Na]^+$) 331.1428, found 331.1427.



***tert*-Butyl 4-(5-cyanonicotinoyl)piperidine-1-carboxylate (31)**

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg,

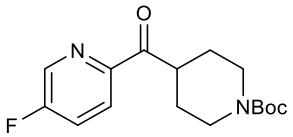
0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 5-bromonicotinonitrile (73 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (60-70% EtOAc/hexanes) provided the title compound (98 mg, 78% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.31 (s, 1H), 9.04 (s, 1H), 8.47 (t, *J* = 1.9 Hz, 1H), 4.18 (brs, 2H), 3.34 (tt, *J* = 11.1, 3.6 Hz, 1H), 2.92 (brs, 2H), 1.88-1.82 (m, 2H), 1.80-1.61 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 198.80, 155.45, 154.68, 152.35, 139.20, 130.88, 115.76, 110.89, 80.06, 44.34, 28.54, 28.06 (br).

IR (film) ν_{max} 2974, 2860, 2237, 1684, 1423, 1366, 1157, 1007, 732 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{17}H_{21}N_3NaO_3$ ($[M+Na]^+$) 338.1475, found 338.1477.



***tert*-Butyl 4-(5-fluoropicolinoyl)piperidine-1-carboxylate (32)**

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 2-bromo-5-fluoropyridine (70 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (20-25% EtOAc/hexanes) provided the title compound (62 mg, 50% yield) as a pale yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.50 (d, *J* = 2.8 Hz, 1H), 8.10 (dd, *J* = 8.7, 4.4 Hz, 1H), 7.56-7.48 (m, 1H), 4.17 (brs, 2H), 3.96 (tt, *J* = 11.5, 3.6 Hz, 1H), 2.90 (brs, 2H), 1.96-

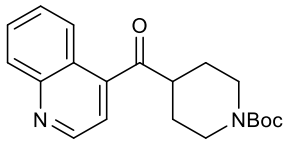
1.78 (m, 2H), 1.67-1.58 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 201.70, 161.58 (d, $J_{C,F}$ = 263.8 Hz), 154.88, 149.13 (d, $J_{C,F}$ = 4.3 Hz), 137.43 (d, $J_{C,F}$ = 24.5 Hz), 124.73 (d, $J_{C,F}$ = 5.9 Hz), 123.83 (d, $J_{C,F}$ = 18.6 Hz), 79.66, 42.36, 28.60, 28.05 (br).

^{19}F NMR (282 MHz, $CDCl_3$) δ -119.63.

IR (film) ν_{max} 2975, 2930, 2858, 1689, 1580, 1421, 1319, 1210, 1167, 970, 857 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{21}FN_2NaO_3$ ($[M+Na]^+$) 331.1428, found 331.1431.



***tert*-Butyl 4-(quinoline-4-carbonyl)piperidine-1-carboxylate (33)**

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 4-bromoquinoline (83 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (100-120% EtOAc/hexanes) provided the title compound (118 mg, 87% yield) as a white solid.

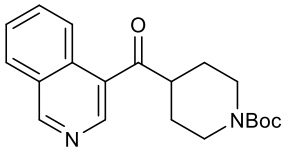
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.00 (d, J = 4.3 Hz, 1H), 8.17 (d, J = 8.4 Hz, 1H), 8.02 (d, J = 8.4 Hz, 1H), 7.77 (ddd, J = 8.3, 7.0, 1.3 Hz, 1H), 7.61 (ddd, J = 8.2, 7.0, 1.1 Hz, 1H), 7.45 (d, J = 4.4 Hz, 1H), 4.13 (brs, 2H), 3.24 (tt, J = 11.1, 3.7 Hz, 1H), 2.85 (brs, 2H), 1.97-1.80 (m, 2H), 1.74-1.66 (m, 2H), 1.45 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 205.80, 154.71, 149.71, 149.01, 144.13, 130.26, 130.17,

128.30, 125.13, 124.26, 118.04, 79.93, 47.96, 28.55, 27.59.

IR (film) ν_{max} 2975, 2930, 2858, 1687, 1422, 1164, 1128, 953, 773, 731 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{20}H_{25}N_2O_3$ ($[M+H]^+$) 341.1860, found 341.1861.



***tert*-Butyl 4-(isoquinoline-4-carbonyl)piperidine-1-carboxylate (34)**

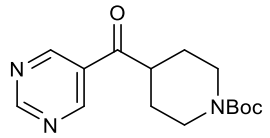
Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 4-bromoisoquinoline (83 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (100-120% EtOAc/hexanes) provided the title compound (115 mg, 85% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.35 (s, 1H), 8.89 (s, 1H), 8.46 (d, *J* = 8.6 Hz, 1H), 8.05 (d, *J* = 8.2 Hz, 1H), 7.76 (dt, *J* = 62.5, 7.5 Hz, 2H), 4.15 (brs, 2H), 3.40 (tt, *J* = 10.9, 3.2 Hz, 1H), 2.91 (brs, 2H), 1.93-1.88 (m, 2H), 1.80-1.69 (m, 2H), 1.47 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 204.75, 156.21, 154.80, 143.21, 133.31, 132.68, 128.87, 128.59, 128.41, 128.25, 125.01, 79.86, 47.36, 28.59, 28.19.

IR (film) ν_{max} 2971, 2945, 2858, 1739, 1684, 1423, 1366, 1230, 1169, 956, 757 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{20}H_{25}N_2O_3$ ($[M+H]^+$) 341.1860, found 341.1862.



***tert*-Butyl 4-(pyrimidine-5-carbonyl)piperidine-1-carboxylate (35)**

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 5-bromopyrimidine (64 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (150-170% EtOAc/hexanes) provided the title compound (92 mg, 79% yield) as a pale yellow solid.

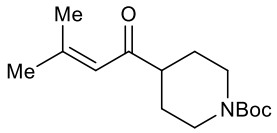
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.37 (s, 1H), 9.21 (s, 2H), 4.17 (brs, 2H), 3.31 (tt, *J* = 11.1, 3.7 Hz, 1H), 2.91 (brs, 2H), 1.90-1.82 (m, 2H), 1.76-1.66 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 199.41, 161.50, 156.87, 154.70, 128.55, 80.03, 44.40, 28.54, 27.97 (br).

IR (film) ν_{max} 2971, 2931, 2860, 1739, 1682, 1574, 1419, 1366, 1224, 1164, 1128, 969, 717 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{15}H_{21}N_3NaO_3$ ($[M+Na]^+$) 314.1475, found 314.1474.

5) Vinyl and Alkyl Halide Scope



***tert*-Butyl 4-(3-methylbut-2-enoyl)piperidine-1-carboxylate (36)**

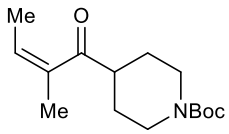
Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (111 mg, 0.80 mmol, 2.0 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), 1-bromo-2-methyl-1-propene (54 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (10-15% EtOAc/hexanes) provided the title compound (77 mg, 72% yield) as a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.17-6.06 (m, 1H), 4.09 (brs, 2H), 2.77 (brs, 2H), 2.43 (tt, *J* = 11.3, 3.7 Hz, 1H), 2.14 (d, *J* = 1.2 Hz, 3H), 1.90 (d, *J* = 1.2 Hz, 3H), 1.80-1.74 (m, 2H), 1.57-1.47 (m, 2H), 1.44 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 202.15, 156.93, 154.86, 122.43, 79.62, 49.40, 28.57, 27.98, 27.73, 21.02.

IR (film) ν_{max} 2976, 2934, 2857, 1687, 1620, 1420, 1168, 1135, 1016, 925, 767 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{15}H_{25}NNaO_3$ ($[M+Na]^+$) 290.1727, found 290.1727.



***tert*-Butyl (*Z*)-4-(2-methylbut-2-enoyl)piperidine-1-carboxylate (37)**

Prepared following the general procedure outlined above using

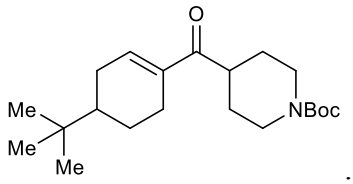
$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (111 mg, 0.80 mmol, 2.0 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (171 mg, 0.80 mmol, 2.0 equiv.), (*Z*)-2-bromo-2-butene (54 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (10-15% EtOAc/hexanes) provided the title compound (79 mg, 74% yield) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.77- 6.73 (m, 1H), 4.12 (brs, 2H), 3.17-3.11 (m, 1H), 2.78 (brs, 2H), 1.88 (dd, *J* = 6.9, 1.1 Hz, 3H), 1.79-1.76 (m, 3H), 1.67-1.58 (m, 4H), 1.45 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 203.60, 154.86, 137.28, 137.07, 79.67, 42.23, 29.85, 28.59, 15.00, 11.47.

IR (film) ν_{max} 2927, 2857, 1692, 1664, 1422, 1169, 1127, 1019, 769 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{15}H_{25}NNaO_3$ ($[M+Na]^+$) 290.1727, found 290.1725



***tert*-Butyl 4-(4-(*tert*-butyl)cyclohex-1-ene-1-carbonyl)piperidine-1-carboxylate (38)**

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (111 mg, 0.80 mmol, 2.0 equiv.), *N*-Boc-4-piperidinecarboxaldehyde (256 mg, 1.20 mmol, 3.0 equiv.), 1-bromo-4-(*tert*-butyl)cyclohex-1-ene[6] (87 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (10-15% EtOAc/hexanes)

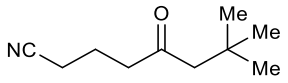
provided the title compound (78 mg, 56% yield) as a pale yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.91 (d, *J* = 5.4 Hz, 1H), 4.13 (brs, 2H), 3.17-3.04 (m, 1H), 2.77 (brs, 2H), 2.58-2.46 (m, 1H), 2.30 (dt, *J* = 18.7, 5.1 Hz, 1H), 2.08-1.95 (m, 2H), 1.93-1.90 (m, 1H), 1.68-1.55 (m, 4H), 1.44 (s, 9H), 1.33-1.20 (m, 2H), 1.11-1.03 (m, 1H), 0.88 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 203.04, 154.84, 140.26, 138.01, 79.63, 43.52, 42.21, 32.27, 28.57, 28.03, 27.23, 24.93, 23.54.

IR (film) ν_{max} 2951, 2866, 1691, 1662, 1421, 1365, 1161, 1016, 972, 869 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{21}H_{35}NNaO_3$ ($[M+Na]^+$) 372.2509, found 372.2506.



7,7-Dimethyl-5-oxooctanenitrile (39)

To an 40 mL vial equipped with a stir bar was added photocatalyst $Ir[dF(Me)ppy]_2(dtbbpy)PF_6$ (9.1 mg, 9.0 μmol, 0.02 equiv.), quinuclidine (5.0 mg, 45 μmol, 0.10 equiv.), and anhydrous sodium carbonate (143 mg, 1.35 mmol, 3.0 equiv.). The vial was sealed and placed under nitrogen before acetone (5 mL) was added. To a separate vial was added $NiBr_2$•glyme (13.8 mg, 45 μmol, 0.10 equiv.) and 4,4'-di-*tert*-butyl-2,2'-bipyridine (12.0 mg, 45 μmol, 0.10 equiv.). The precatalyst vial was sealed, purged with nitrogen, dissolved in acetone (5 mL) and then sonicated until it became homogeneous. Subsequently, the precatalyst solution was syringed into the reaction vessel and the solution was degassed by sparging with nitrogen for 15 minutes. 4-Bromobutanenitrile (45 μL, 67 mg, 0.45 mmol, 1.0 equiv.) and 3,3-dimethylbutanal (170 μL, 135 mg, 1.35 mmol, 3.0 equiv.) were then added. The reaction vial was then sealed with parafilm, placed 6 cm away from one blue LED, and irradiated (heated to approximately 55 °C by the blue LED without fan cooling). After 20 h, the reaction mixture was purified directly by flash column chromatography (20-25% EtOAc/hexanes)

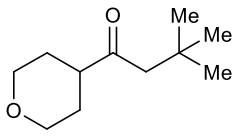
to give the title compound (41 mg, 55% yield) as a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.59 (t, *J* = 6.8 Hz, 2H), 2.42 (t, *J* = 7.0 Hz, 2H), 2.32 (s, 2H), 1.89 (p, *J* = 6.9 Hz, 2H), 1.01 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 209.09, 119.47, 55.17, 42.74, 31.27, 29.86, 19.37, 16.58.

IR (film) ν_{max} 2954, 2870, 2247, 1710, 1365, 1097, 751 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{10}H_{18}NO$ ($[M+H]^+$) 168.1383, found 168.1383.



3,3-Dimethyl-1-(tetrahydro-2*H*-pyran-4-yl)butan-1-one (40)

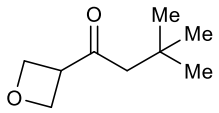
To an 40 mL vial equipped with a stir bar was added photocatalyst $Ir[dF(Me)ppy]_2(dtbbpy)PF_6$ (9.1 mg, 9.0 μmol, 0.02 equiv.), quinuclidine (5.0 mg, 45 μmol, 0.10 equiv.), and anhydrous sodium carbonate (143 mg, 1.35 mmol, 3.0 equiv.). The vial was sealed and placed under nitrogen before acetone (5 mL) was added. To a separate vial was added $NiBr_2$•glyme (13.8 mg, 45 μmol, 0.10 equiv.) and 4,4'-di-*tert*-butyl-2,2'-bipyridine (12.0 mg, 45 μmol, 0.10 equiv.). The precatalyst vial was sealed, purged with nitrogen, dissolved in acetone (5 mL) and then sonicated until it became homogeneous. Subsequently, the precatalyst solution was syringed into the reaction vessel and the solution was degassed by sparging with nitrogen for 15 minutes. 4-Bromotetrahydropyran (50 μL, 74 mg, 0.45 mmol, 1.0 equiv.) and 3,3-dimethylbutanal (170 μL, 135 mg, 1.35 mmol, 3.0 equiv.) were then added. The reaction vial was then sealed with parafilm, placed 6 cm away from one blue LED, and irradiated (heated to approximately 55 °C by the blue LED without fan cooling). After 20 h, the reaction mixture was purified directly by flash column chromatography (15-20% EtOAc/hexanes) to give the title compound (47 mg, 56% yield) as a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.01-3.98 (m, 2H), 3.40 (td, *J* = 11.4, 2.9 Hz, 2H), 2.53-2.47 (m, 1H), 2.33 (s, 2H), 1.72-1.61 (m, 4H), 1.01 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 211.99, 67.44, 52.57, 49.17, 31.18, 29.87, 28.12.

IR (film) ν_{max} 2952, 2847, 1707, 1365, 1240, 1112, 1090, 1022 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{11}H_{21}O_2$ ($[M+H]^+$) 185.1536, found 185.1537.



3,3-Dimethyl-1-(oxetan-3-yl)butan-1-one (41)

To an 40 mL vial equipped with a stir bar was added photocatalyst $Ir[dF(Me)ppy]_2(dtbbpy)PF_6$ (9.1 mg, 9.0 μmol, 0.02 equiv.), quinuclidine (5.0 mg, 45 μmol, 0.10 equiv.), and anhydrous sodium carbonate (143 mg, 1.35 mmol, 3.0 equiv.). The vial was sealed and placed under nitrogen before acetone (5 mL) was added. To a separate vial was added $NiBr_2$•glyme (13.8 mg, 45 μmol, 0.10 equiv.) and 4,4'-di-*tert*-butyl-2,2'-bipyridine (12.0 mg, 45 μmol, 0.10 equiv.). The precatalyst vial was sealed, purged with nitrogen, dissolved in acetone (5 mL) and then sonicated until it became homogeneous. Subsequently, the precatalyst solution was syringed into the reaction vessel and the solution was degassed by sparging with nitrogen for 15 minutes. 3-Bromooxetane (37 μL, 62 mg, 0.45 mmol, 1.0 equiv.) and 3,3-dimethylbutanal (170 μL, 135 mg, 1.35 mmol, 3.0 equiv.) were then added. The reaction vial was then sealed with parafilm, placed 6 cm away from one blue LED, and irradiated (heated to approximately 55 °C by the blue LED without fan cooling). After 20 h, the reaction mixture was purified directly by flash column chromatography (20-25% EtOAc/hexanes) to give the title compound (39 mg, 56% yield) as a colorless oil.

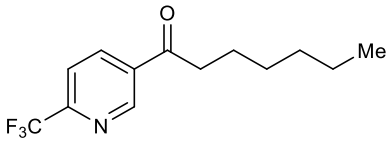
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.79-4.74 (m, 4H), 3.89 (tt, *J* = 8.5, 6.9 Hz, 1H), 2.27 (s, 2H), 1.01 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 207.75, 72.54, 53.42, 46.53, 31.16, 29.82.

IR (film) ν_{max} 2954, 2877, 1712, 1365, 1109, 984, 924 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_9H_{17}O_2$ ($[M+H]^+$) 157.1223, found 157.1224.

6) Aldehyde Scope



1-(6-(Trifluoromethyl)pyridin-3-yl)heptan-1-one (42)

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), heptanal (112 μL, 91 mg, 0.80 mmol, 2.0 equiv.), 5-bromo-2-(trifluoromethyl)pyridine (90 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (2-5% EtOAc/hexanes) provided the title compound (95 mg, 92% yield) as a colorless solid.

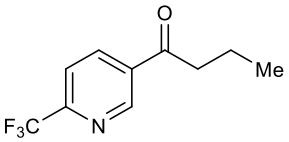
1H NMR (500 MHz, $CDCl_3$) δ 9.23 (brs, 1H), 8.40 (d, J = 8.1 Hz, 1H), 7.80 (d, J = 8.2 Hz, 1H), 3.01 (t, J = 7.3 Hz, 2H), 1.76 (p, J = 7.4 Hz, 2H), 1.42-1.30 (m, 6H), 0.89 (t, J = 7.0 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 198.19, 151.18 (q, $J_{C,F}$ = 35.1 Hz), 149.77, 137.16, 134.29 (q, $J_{C,F}$ = 0.9 Hz), 121.22 (q, $J_{C,F}$ = 274.6 Hz), 120.67 (q, $J_{C,F}$ = 2.9 Hz), 39.41, 31.72, 28.99, 23.94, 22.62, 14.15.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.26.

IR (film) ν_{max} 2959, 2927, 2852, 1739, 1677, 1334, 1181, 1128, 1087, 984, 861, 764, 724 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{13}H_{17}F_3NO$ ($[M+H]^+$) 260.1257, found 260.1258.



1-(6-(Trifluoromethyl)pyridin-3-yl)butan-1-one (43)

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), butyraldehyde (71 μL, 58 mg, 0.80 mmol, 2.0 equiv.), 5-bromo-2-(trifluoromethyl)pyridine (90 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (5-8% EtOAc/hexanes) provided the title compound (78 mg, 90% yield) as a white solid.

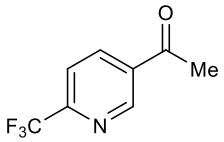
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.24 (brs, 1H), 8.40 (dd, J = 8.1, 1.7 Hz, 1H), 7.80 (d, J = 8.1 Hz, 1H), 3.00 (t, J = 7.2 Hz, 2H), 1.84-1.77 (m, 2H), 1.03 (t, J = 7.4 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 198.02, 151.20 (q, $J_{C,F}$ = 35.2 Hz), 149.76, 137.14, 134.40 (q, $J_{C,F}$ = 0.9 Hz), 121.22 (q, $J_{C,F}$ = 274.5 Hz), 120.68 (q, $J_{C,F}$ = 2.9 Hz), 41.25, 17.40, 13.85.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.25.

IR (film) ν_{max} 2969, 2880, 1696, 1332, 1180, 1141, 1084, 996, 847 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{10}H_{11}F_3NO$ ($[M+H]^+$) 218.0787, found 218.0787.



1-(6-(Trifluoromethyl)pyridin-3-yl)ethan-1-one (44)

Prepared following the general procedure outlined above using

$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), acetaldehyde (67 μL, 53 mg, 1.20 mmol, 3.0 equiv.), 5-bromo-2-(trifluoromethyl)pyridine (90 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (10-15% EtOAc/hexanes) provided the title compound (53 mg, 70% yield) as a white solid.

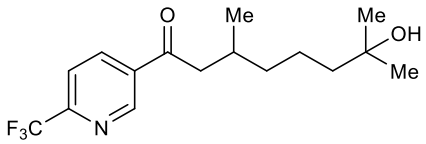
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.24 (brs, 1H), 8.41 (dd, J = 8.1, 1.5 Hz, 1H), 7.82 (d, J = 8.6 Hz, 1H), 2.70 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 195.58, 151.41 (q, $J_{C,F}$ = 35.3 Hz), 150.08, 137.32, 134.27 (q, $J_{C,F}$ = 0.9 Hz), 121.18 (q, $J_{C,F}$ = 274.7 Hz), 120.70 (q, $J_{C,F}$ = 2.9 Hz), 27.15.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.27.

IR (film) ν_{max} 3051, 2926, 2854, 1689, 1595, 1386, 1332, 1272, 1182, 1129, 1098, 1019, 862, 729 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_8H_7F_3NO$ ($[M+H]^+$) 190.0474, found 190.0476.



7-Hydroxy-3,7-dimethyl-1-(6-(trifluoromethyl)pyridin-3-yl)octan-1-one (45)

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), 7-hydroxycitronellal (149 μL, 137 mg, 0.80 mmol, 2.0 equiv.), 5-bromo-2-(trifluoromethyl)pyridine (90 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12

mL). Purification by flash chromatography (20-25% EtOAc/hexanes) provided the title compound (110 mg, 87% yield) as a pale yellow oil.

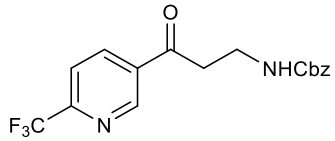
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.23 (brs, 1H), 8.39 (d, *J* = 8.1 Hz, 1H), 7.80 (d, *J* = 8.2 Hz, 1H), 3.00 (dd, *J* = 16.3, 5.7 Hz, 1H), 2.82 (dd, *J* = 16.3, 7.8 Hz, 1H), 2.25-2.16 (m, 1H), 1.46-1.36 (m, 5H), 1.31-1.25 (m, 1H), 1.21 (s, 6H), 0.99 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 197.99, 151.20 (q, $J_{C,F}$ = 35.2 Hz), 149.80, 137.21, 134.55, 121.21 (q, $J_{C,F}$ = 274.6 Hz), 120.69 (q, $J_{C,F}$ = 2.9 Hz), 71.06, 46.69, 43.95, 37.54, 29.67, 29.56, 29.41, 21.84.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.23.

IR (film) ν_{max} 3417, 2967, 2937, 1692, 1465, 1384, 1331, 1180, 1141, 1083, 845 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{22}F_3NNaO_2$ ($[M+Na]^+$) 340.1495, found 340.1492.



Benzyl (3-oxo-3-(6-(trifluoromethyl)pyridin-3-yl)propyl)carbamate (46)

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), 3-[(benzyloxycarbonyl)amino]propionaldehyde (166 mg, 0.80 mmol, 2.0 equiv.), 5-bromo-2-(trifluoromethyl)pyridine (90 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (60-70% EtOAc/hexanes) provided the title compound (100 mg, 71% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.22 (brs, 1H), 8.38 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.1

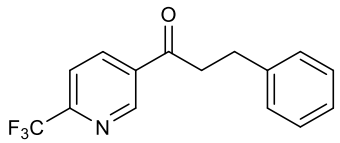
Hz, 1H), 7.38-7.28 (m, 5H), 5.39 (brs, 1H), 5.08 (s, 2H), 3.65 (q, J = 5.5 Hz, 2H), 3.28 (t, J = 5.3 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 197.02, 156.49, 151.56 (q, $J_{C,F}$ = 35.3 Hz), 149.73, 137.13, 136.41, 133.73, 128.65, 128.31, 128.22, 121.10 (q, $J_{C,F}$ = 274.8 Hz), 120.70 (q, $J_{C,F}$ = 3.0 Hz), 66.92, 39.36, 35.68.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.28.

IR (film) ν_{max} 3341, 2931, 1695, 1521, 1332, 1251, 1141, 1086, 850, 740, 698 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{17}H_{16}F_3N_2O_3$ ($[M+H]^+$) 353.1108, found 353.1110.



3-Phenyl-1-(6-(trifluoromethyl)pyridin-3-yl)propan-1-one (47)

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), 3-phenylpropanal (105 μL, 107 mg, 0.80 mmol, 2.0 equiv.), 5-bromo-2-(trifluoromethyl)pyridine (90 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (3-5% EtOAc/hexanes) provided the title compound (90 mg, 81% yield) as a colorless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.22 (brs, 1H), 8.38 (d, J = 8.1 Hz, 1H), 7.79 (d, J = 8.2 Hz, 1H), 7.33-7.30 (m, 2H), 7.26-7.21 (m, 3H), 3.35 (t, J = 7.5 Hz, 2H), 3.11 (t, J = 7.5 Hz, 2H).

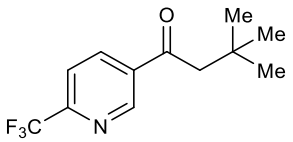
^{13}C NMR (125 MHz, $CDCl_3$) δ 197.05, 151.33 (q, $J_{C,F}$ = 35.2 Hz), 149.73, 140.49,

137.16, 134.12, 128.83, 128.54, 126.62, 121.17 (q, $J_{C,F}$ = 274.7 Hz), 120.68 (q, $J_{C,F}$ = 2.9 Hz), 41.21, 29.81.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.25.

IR (film) ν_{max} 3030, 2931, 1695, 1386, 1330, 1177, 1138, 1084, 980, 853, 749, 700 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{15}H_{13}F_3NO$ ($[M+H]^+$) 280.0944, found 280.0942.



3,3-Dimethyl-1-(6-(trifluoromethyl)pyridin-3-yl)butan-1-one (48)

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), 3,3-dimethylbutanal (100 μL, 80 mg, 0.80 mmol, 2.0 equiv.), 5-bromo-2-(trifluoromethyl)pyridine (90 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (2-4% EtOAc/hexanes) provided the title compound (89 mg, 91% yield) as a pale yellow solid.

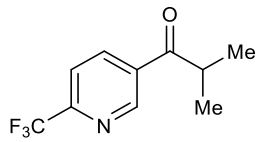
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.22 (brs, 1H), 8.38 (d, J = 8.1 Hz, 1H), 7.79 (d, J = 8.2 Hz, 1H), 2.90 (s, 2H), 1.08 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 198.03, 151.03 (q, $J_{C,F}$ = 35.2 Hz), 149.90, 137.22, 135.60, 121.23 (q, $J_{C,F}$ = 274.6 Hz), 120.61 (q, $J_{C,F}$ = 2.9 Hz), 50.93, 31.82, 30.11.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.22.

IR (film) ν_{max} 2962, 2871, 1739, 1695, 1331, 1177, 1140, 1085, 1011, 909, 734 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_{15}F_3NO$ ($[M+H]^+$) 246.1100, found 246.1100.



2-Methyl-1-(6-(trifluoromethyl)pyridin-3-yl)propan-1-one (49)

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), isobutyraldehyde (73 μL, 58 mg, 0.80 mmol, 2.0 equiv.), 5-bromo-2-(trifluoromethyl)pyridine (90 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (2-4% EtOAc/hexanes) provided the title compound (79 mg, 91% yield) as a pale yellow oil.

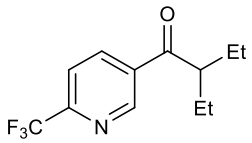
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.23 (brs, 1H), 8.40 (dd, J = 8.1, 2.0 Hz, 1H), 7.81 (d, J = 8.2 Hz, 1H), 3.52 (hept, J = 6.8 Hz, 1H), 1.26 (d, J = 6.8 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 202.10, 151.11 (q, $J_{C,F}$ = 35.2 Hz), 149.92, 137.57, 133.57 (q, $J_{C,F}$ = 1.0 Hz), 121.22 (q, $J_{C,F}$ = 274.6 Hz), 120.75 (q, $J_{C,F}$ = 2.9 Hz), 36.60, 18.79.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.27.

IR (film) ν_{max} 2978, 2940, 1694, 1331, 1179, 1143, 1086, 981, 859, 735 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{10}H_{11}F_3NO$ ($[M+H]^+$) 218.0787, found 218.0785.



2-Ethyl-1-(6-(trifluoromethyl)pyridin-3-yl)butan-1-one (50)

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), 2-ethylbutanal (98 μL, 80 mg, 0.80 mmol, 2.0 equiv.), 5-bromo-2-(trifluoromethyl)pyridine (90 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (2-4% EtOAc/hexanes) provided the title compound (89 mg, 91% yield) as a pale yellow oil.

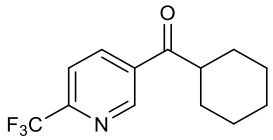
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.24 (brs, 1H), 8.40 (d, J = 8.1 Hz, 1H), 7.81 (d, J = 8.2 Hz, 1H), 3.27 (ddd, J = 13.0, 7.5, 5.6 Hz, 1H), 1.82 (dq, J = 14.8, 7.4 Hz, 2H), 1.61 (ddd, J = 13.7, 7.4, 5.7 Hz, 2H), 0.90 (t, J = 7.4 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 202.24, 151.11 (q, $J_{C,F}$ = 35.1 Hz), 149.80, 137.36, 134.86, 121.24 (q, $J_{C,F}$ = 274.7 Hz), 120.74 (q, $J_{C,F}$ = 2.9 Hz), 50.37, 24.58, 11.90.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.25.

IR (film) ν_{max} 2968, 2934, 2879, 1689, 1461, 1332, 1179, 1144, 1085, 987, 853 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_{15}F_3NO$ ($[M+H]^+$) 246.1100, found 246.1101.



Cyclohexyl(6-(trifluoromethyl)pyridin-3-yl)methanone (51)

Prepared following the general procedure outlined above using

$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), cyclohexanecarboxaldehyde (97 μL, 90 mg, 0.80 mmol, 2.0 equiv.), 5-bromo-2-(trifluoromethyl)pyridine (90 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (2-3% EtOAc/hexanes) provided the title compound (93 mg, 90% yield) as a pale yellow solid.

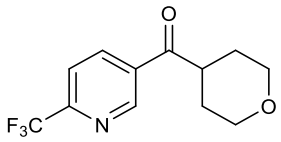
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.21 (brs, 1H), 8.37 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 3.22 (tt, *J* = 11.4, 3.2 Hz, 1H), 1.92-1.85 (m, 4H), 1.78-1.74 (m, 1H), 1.54-1.36 (m, 4H), 1.32-1.19 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 201.51, 151.02 (q, $J_{C,F}$ = 35.2 Hz), 149.87, 137.49, 133.69, 121.23 (q, $J_{C,F}$ = 274.5 Hz), 120.71 (q, $J_{C,F}$ = 2.9 Hz), 46.61, 29.12, 25.89, 25.73.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.25.

IR (film) ν_{max} 2946, 2930, 2857, 1678, 1333, 1253, 1181, 1132, 1087, 977, 866, 764, 710 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{13}H_{15}F_3NO$ ($[M+H]^+$) 258.1100, found 258.1103.



(Tetrahydro-2H-pyran-4-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (52)

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), tetrahydropyran-4-carboxaldehyde (83 μL, 91 mg, 0.80 mmol,

2.0 equiv.), 5-bromo-2-(trifluoromethyl)pyridine (90 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (30-40% EtOAc/hexanes) provided the title compound (91 mg, 88% yield) as a white solid.

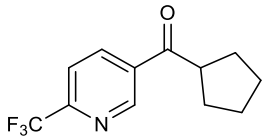
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.22 (brs, 1H), 8.39 (d, J = 8.0 Hz, 1H), 7.82 (d, J = 8.1 Hz, 1H), 4.07 (d, J = 11.5 Hz, 2H), 3.57 (t, J = 11.4 Hz, 2H), 3.50-3.44 (m, 1H), 1.93-1.80 (m, 4H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 199.56, 151.35 (q, $J_{C,F}$ = 35.2 Hz), 149.76, 137.62, 133.24, 121.14 (q, $J_{C,F}$ = 274.5 Hz), 120.88 (q, $J_{C,F}$ = 2.9 Hz), 67.13, 43.58, 28.70.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.28.

IR (film) ν_{max} 2957, 2850, 1690, 1331, 1135, 1085, 984, 833, 710 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_{13}F_3NO_2$ ($[M+H]^+$) 260.0893, found 260.0891.



Cyclopentyl(6-(trifluoromethyl)pyridin-3-yl)methanone (53)

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), cyclopentanecarboxaldehyde (85 μL, 78 mg, 0.80 mmol, 2.0 equiv.), 5-bromo-2-(trifluoromethyl)pyridine (90 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (3-5% EtOAc/hexanes) provided the title compound (82 mg, 85% yield) as a pale yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.25 (brs, 1H), 8.41 (d, J = 9.8 Hz, 1H), 7.80 (d, J = 8.5

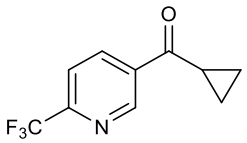
Hz, 1H), 3.69 (tt, J = 8.6, 7.0 Hz, 1H), 2.01-1.89 (m, 4H), 1.76-1.67 (m, 4H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 200.39, 151.00 (q, $J_{C,F}$ = 35.1 Hz), 150.14, 137.61, 134.16, 121.24 (q, $J_{C,F}$ = 274.6 Hz), 120.65 (q, $J_{C,F}$ = 2.9 Hz), 47.24, 29.67, 26.41.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.24.

IR (film) ν_{max} 2968, 2873, 1683, 1337, 1251, 1178, 1130, 1089, 866 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_{13}F_3NO$ ($[M+H]^+$) 244.0944, found 244.0943.



Cyclopropyl(6-(trifluoromethyl)pyridin-3-yl)methanone (54)

Prepared following the general procedure outlined above using Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), cyclopropanecarboxaldehyde (60 μL, 56 mg, 0.80 mmol, 2.0 equiv.), 5-bromo-2-(trifluoromethyl)pyridine (90 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (8-10% EtOAc/hexanes) provided the title compound (70 mg, 81% yield) as a pale yellow solid.

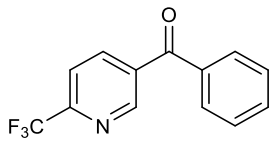
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.31 (brs, 1H), 8.42 (d, J = 9.4 Hz, 1H), 7.81 (d, J = 8.1 Hz, 1H), 2.66 (tt, J = 7.9, 4.5 Hz, 1H), 1.36-1.33 (m, 2H), 1.20-1.17 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 198.49, 151.03 (q, $J_{C,F}$ = 35.1 Hz), 149.68, 137.07, 135.23, 121.26 (q, $J_{C,F}$ = 274.6 Hz), 120.58 (q, $J_{C,F}$ = 2.9 Hz), 18.20, 12.97.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.20.

IR (film) ν_{max} 3069, 3021, 1677, 1330, 1177, 1127, 1084, 1026, 998, 855, 721 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{10}H_9F_3NO$ ($[M+H]^+$) 216.0631, found 216.0632.



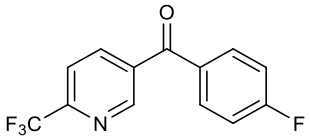
Phenyl(6-(trifluoromethyl)pyridin-3-yl)methanone (55)

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), benzaldehyde (407 μL, 424 mg, 4.00 mmol, 10.0 equiv.), 5-bromo-2-(trifluoromethyl)pyridine (90 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). The reaction was stirred and irradiated using 34 W blue LED lamps (6 cm away, without cooling fan to heat the reaction vial to approximately 55 °C by the blue LED). Purification by flash chromatography (3-5% EtOAc/hexanes) provided the title compound (73 mg, 73% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.07 (brs, 1H), 8.28 (dd, J = 8.1, 1.6 Hz, 1H), 7.85-7.82 (m, 3H), 7.70-7.66 (m, 1H), 7.55 (t, J = 7.8 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 193.66, 150.89, 150.68 (q, $J_{C,F}$ = 35.1), 138.81, 136.13, 135.74, 133.95, 130.23, 129.00, 121.26 (q, $J_{C,F}$ = 274.7 Hz), 120.40 (q, $J_{C,F}$ = 2.9 Hz).

Spectroscopic data matches with previously reported data.[7]



(4-Fluorophenyl)(6-(trifluoromethyl)pyridin-3-yl)methanone (56)

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), 4-fluorobenzaldehyde (429 μL, 496 mg, 4.00 mmol, 10.0 equiv.), 5-bromo-2-(trifluoromethyl)pyridine (90 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (3-5% EtOAc/hexanes) provided the title compound (75 mg, 70% yield) as a white solid.

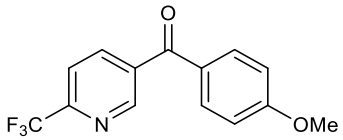
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.04 (brs, 1H), 8.25 (dd, J = 8.1, 1.5 Hz, 1H), 7.88-7.84 (m, 3H), 7.22 (t, J = 8.5 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 192.11, 166.26 (d, $J_{C,F}$ = 257.0 Hz), 150.78 (q, $J_{C,F}$ = 35.1), 150.64, 138.68, 135.66, 132.94 (d, $J_{C,F}$ = 9.6 Hz), 132.47 (d, $J_{C,F}$ = 3.2 Hz), 121.21 (q, $J_{C,F}$ = 274.7 Hz), 120.48 (q, $J_{C,F}$ = 2.9 Hz), 116.33 (d, $J_{C,F}$ = 22.1 Hz).

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.20, -103.11.

IR (film) ν_{max} 3110, 3076, 1739, 1652, 1595, 1506, 1331, 1140, 1129, 933, 856, 747, 691 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{13}H_8F_4NO$ ($[M+H]^+$) 270.0537, found 270.0536.



(4-Methoxyphenyl)(6-(trifluoromethyl)pyridin-3-yl)methanone (57)

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg,

0.60 mmol, 1.5 equiv.), 4-methoxybenzaldehyde (291 μL, 327 mg, 2.40 mmol, 6.0 equiv.), 5-bromo-2-(trifluoromethyl)pyridine (90 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (5-8% EtOAc/hexanes) provided the title compound (81 mg, 72% yield) as a white solid.

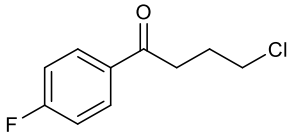
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.03 (brs, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.9 Hz, 3H), 7.01 (d, *J* = 8.9 Hz, 2H), 3.91 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 192.16, 164.38, 150.51, 150.29 (q, $J_{C,F}$ = 35.2), 138.52, 136.52, 132.79, 128.89, 121.32 (q, $J_{C,F}$ = 274.8), 120.36 (q, *J* = 2.9 Hz), 114.29, 55.80.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.12.

IR (film) ν_{max} 3022, 2946, 1738, 1637, 1599, 1271, 1128, 1085, 1017, 845 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{14}H_{11}F_3NO_2$ ($[M+H]^+$) 282.0736, found 282.0739.



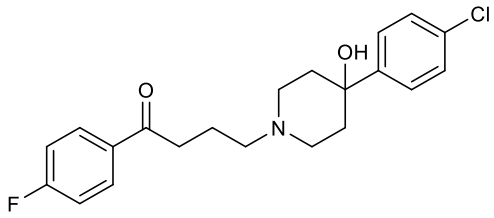
4-Chloro-1-(4-fluorophenyl)butan-1-one (60)

Prepared following the general procedure outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiBr_2$•glyme (12.4 mg, 40 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (10.8 mg, 40 μmol, 0.10 equiv.), quinuclidine (4.5 mg, 40 μmol, 0.10 equiv.), anhydrous potassium carbonate (83 mg, 0.60 mmol, 1.5 equiv.), 4-chlorobutanal[8] (85 mg, 0.80 mmol, 2.0 equiv.), 1-bromo-4-fluorobenzene (44 μL, 70 mg, 0.40 mmol, 1.0 equiv.), and 1,4-dioxane (12 mL). Purification by flash chromatography (3-5% EtOAc/hexanes) provided the title compound (62 mg, 77% yield) as a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02-7.99 (m, 2H), 7.16-7.12 (m, 2H), 3.68 (t, J = 6.2 Hz, 2H), 3.16 (t, J = 7.0 Hz, 2H), 2.25-2.20 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.47, 165.93 (d, $J_{C,F}$ = 254.9 Hz), 133.29 (d, $J_{C,F}$ = 3.4 Hz), 130.78 (d, $J_{C,F}$ = 9.7 Hz), 115.88 (d, $J_{C,F}$ = 22.0 Hz), 44.77, 35.31, 26.80.

Spectroscopic data matches with previously reported data.[9]



Haloperidol

To an 8 mL vial equipped with a stir bar was added 4-chloro-1-(4-fluorophenyl)butan-1-one (54 mg, 0.27 mmol, 1.0 equiv.), 4-(4-chlorophenyl)-4-hydroxypiperidine (114 mg, 0.54 mmol, 2.0 equiv.), and anhydrous potassium iodide (1.3 mg, 8.0 μmol,, 0.03 equiv.). The vial was sealed after 2 mL of anhydrous toluene was added. The mixture was stirred at 130 ^{o}C for 45 h. After cooling to room temperature, the reaction mixture was diluted with aq. $NaHCO_3$ and EtOAc, and the aqueous layer was extracted with three portions of EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography (5-8% MeOH/CH_2Cl_2 with 1% Et_3N) provided the title compound (80 mg, 79% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02-7.99 (m, 2H), 7.38 (d, J = 8.6 Hz, 2H), 7.29 (d, J = 8.6 Hz, 2H), 7.15-7.11 (m, 2H), 2.99 (t, J = 7.0 Hz, 2H), 2.82 (d, J = 10.7 Hz, 2H), 2.53-2.46 (m, 4H), 2.07-1.97 (m, 4H), 1.69 (d, J = 12.3 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 198.38, 165.76 (d, $J_{C,F}$ = 254.5 Hz), 146.85, 133.69 (d, $J_{C,F}$ = 3.3 Hz), 132.89, 130.80 (d, $J_{C,F}$ = 9.4 Hz), 128.50, 126.20, 115.75 (d, $J_{C,F}$ = 21.9 Hz), 71.07, 57.87, 49.40, 38.25, 36.32, 21.73.

^{19}F NMR (282 MHz, $CDCl_3$) δ -105.55.

IR (film) ν_{max} 3122, 2954, 2823, 1682, 1597, 1362, 1221, 1157, 998, 828, 740 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{21}H_{24}ClFNO_2$ ($[M+H]^+$) 376.1474, found 376.1475.

7) References

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