

Metallaphotoredox-Catalyzed sp^3-sp^3 Cross-Coupling of Carboxylic Acids with Alkyl Halides

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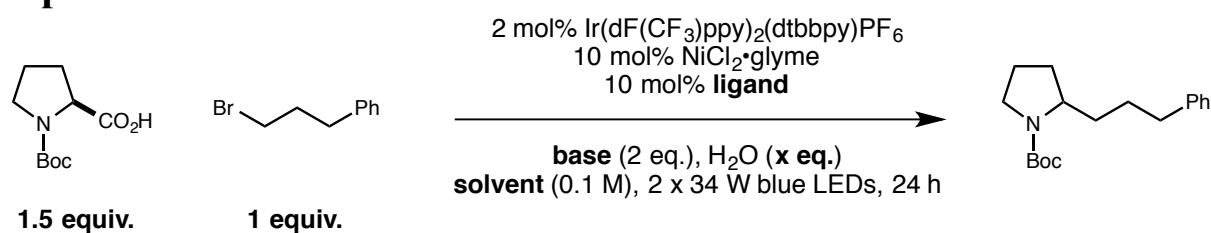
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General Information

All solvents were purified according to the method of Grubbs.¹ The photocatalyst Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**), Ir[dF(Me)ppy]₂(dtbbpy)PF₆ (**II**) and Ir[dF(F)ppy]₂(dtbbpy)PF₆ (**III**) were prepared using literature procedures.² All of the alkyl halides and carboxylic acids, with the exception of 9-bromononanal, which was synthesized according to a literature procedure³, were used as received. 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 staining with KMnO₄, ninhydrin, CAM, or PMA. ¹H NMR spectra were recorded on a Bruker UltraShield Plus Avance III 500 MHz unless otherwise noted and are internally referenced to residual protio CDCl₃ signals (7.26 ppm), CD₃CN (1.94 ppm) or CD₃OD (3.31 ppm). Data for ¹H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = quintet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets...etc, br = broad), coupling constant (Hz) and integration. ¹³C 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 CDCl₃ (77.16 ppm) or CD₃CN (1.32 ppm). 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.

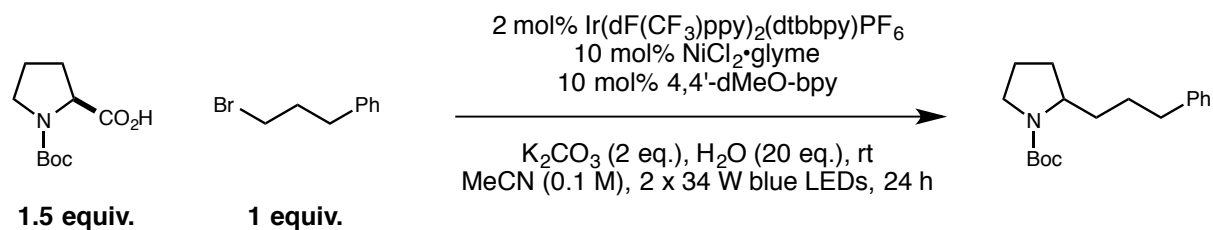
Optimization Table



Solvent	Base	Ligand	H ₂ O	Product	PhProp-Br	Ester
DMF	Cs ₂ CO ₃	dtbbpy	none	0%	0%	100%
DME	Cs ₂ CO ₃	dtbbpy	none	9%	68%	27%
dioxane	Cs ₂ CO ₃	dtbbpy	none	10%	81%	13%
EtOAc	Cs ₂ CO ₃	dtbbpy	none	9%	80%	11%
Acetone	Cs ₂ CO ₃	dtbbpy	none	11%	22%	69%
MeCN	Cs ₂ CO ₃	dtbbpy	none	49%	0%	38%
MeCN	K ₂ CO ₃	dtbbpy	none	68%	0%	11%
MeCN	K ₂ CO ₃	dMeO-bpy	none	74%	0%	14%
MeCN	K ₂ CO ₃	dMeO-bpy	10 eq.	91%	0%	2%
MeCN	K ₂ CO ₃	dMeO-bpy	20 eq.	92%	0%	2%
MeCN (48 h)	K ₂ CO ₃	dMeO-bpy	20 eq.	96%	0%	2%

Figure S1. Optimization of the reaction conditions for the decarboxylative cross-coupling of carboxylic acids and alkyl halides. Yields determined by GC analysis using hexadecane as an internal standard. Reactions were performed on a 0.100 mmol scale.

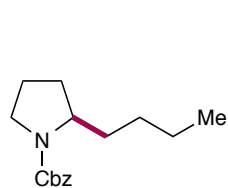
Control Reactions



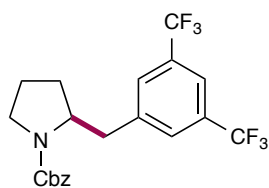
Control	Product
No nickel	0%
No ligand	0%
No photocat.	0%
No light	0%
No base	0%
No degas	26%

Figure S2. Control reactions for the decarboxylative cross-coupling of carboxylic acids and alkyl halides. Yields determined by GC analysis using hexadecane as an internal standard. Reactions were performed on a 0.100 mmol scale.

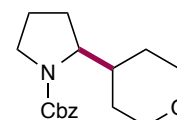
Additional Examples



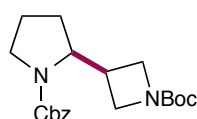
(±)-**46** 76% yield



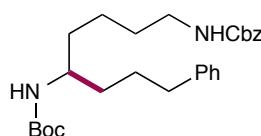
(±)-**47** 59% yield



(±)-**48** 83% yield



(±)-**49** 50% yield



(±)-**50** 65% yield

Figure S3. Additional examples of decarboxylative cross-coupling of carboxylic acids with alkyl halides. Isolated yields are reported. Reactions for **45** - **47** were performed following general procedure A, **48** was synthesized following general procedure B.

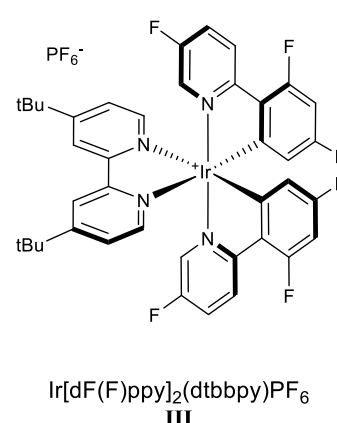
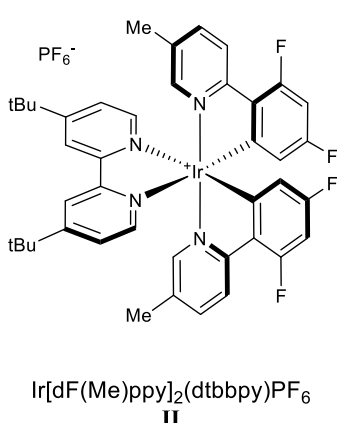
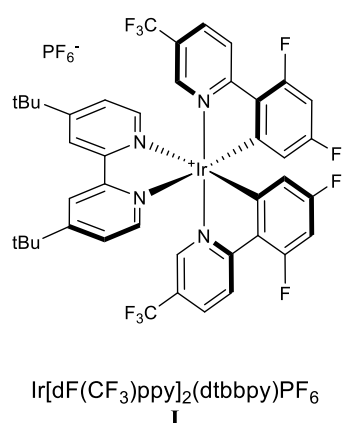


Figure S4. Used Ir-Photocatalysts.

Experimental Data

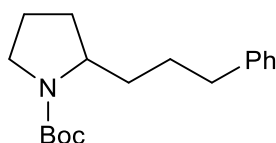
General Procedure A for Decarboxylative Alkylation (Alkyl Halide Scope):

An oven dried* 8 mL vial equipped with a Teflon septum and magnetic stir bar was charged with Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (10.0 μmol, 0.02 equiv), NiCl₂•glyme (0.05 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (0.05 mmol, 0.1 equiv), Boc-Pro-OH (0.75 mmol, 1.5 equiv), K₂CO₃ (1.00 mmol, 2.0 equiv), and 5 mL of MeCN. The reaction mixture was degassed by bubbling nitrogen stream for 15 min at 0 °C. Water (10.0 mmol, 20 equiv) and the appropriate alkyl halide (0.50 mmol, 1.0 equiv) were then added. The reaction mixture was then stirred and irradiated with two 34 W blue LEDs (vials approximately 6 cm away from the light source) with a fan placed above for cooling. After 48 h, the reaction mixture was diluted with EtOAc, filtered, and concentrated in vacuo. Purification of the crude product by flash chromatography on silica gel using the indicated solvent system afforded the desired product.

General Procedure B for Decarboxylative Alkylation (Acyclic Amino Acids):

An oven dried* 40 mL vial equipped with a Teflon septum and magnetic cross stir bar was charged with Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (10.0 μmol, 0.02 equiv), NiCl₂•glyme (0.05 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (0.05 mmol, 0.1 equiv), the appropriate acid (0.75 mmol, 1.5 equiv), Cs₂CO₃ (1.00 mmol, 2.0 equiv), and 10 mL of MeCN. The reaction mixture was degassed by bubbling nitrogen stream for 15 min at 0 °C. Water (10 mmol, 20 equiv) and 1-bromo-3-phenylpropane (0.50 mmol, 1.0 equiv) were then added. The reaction mixture was then stirred and irradiated with two 34 W blue LEDs (vials approximately 6 cm away from the light source) with a fan placed above for cooling. After 24 h, the reaction mixture was diluted with EtOAc, filtered, and concentrated in vacuo. Purification of the crude product by preparative SFC afforded the desired product.

* Although water is an essential additive for this reaction, the vials were stored in the oven to eliminate unwanted variations of the reaction conditions and assure reproducibility throughout the entire process.

***tert*-Butyl 2-(3-phenylpropyl)pyrrolidine-1-carboxylate (12)**

According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.6 mg, 10.3 μmol, 0.02 equiv), NiCl₂•glyme (11.3 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (11.2 mg, 0.05 mmol, 0.1 equiv), 1-bromo-3-phenylpropane (80 μL, 0.52 mmol, 1.0 equiv), Boc-Pro-OH (167 mg, 0.77 mmol, 1.5 equiv), K₂CO₃ (143 mg, 1.03 mmol, 2 equiv), water (186 μL, 10.3 mmol, 20 equiv), and 5 mL of MeCN were used. The product was isolated by flash chromatography (0 to 2% EtOAc/hexanes) as a colorless oil (127 mg, 85%).

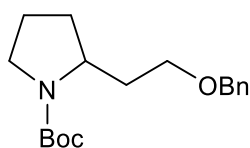
¹H-NMR (500 MHz, CDCl₃) rotameric mixture: δ 7.31 – 7.23 (m, 2H), 7.21 – 7.14 (m, 3H), 3.81 and 3.70 (2 br s, 1H, rotamer), 3.38 and 3.29 (2 br s, 2H, rotamer), 2.61 (br s, 2H), 1.98 – 1.53 (m, 7H), 1.51 – 1.28 (m, 10H).

¹³C-NMR (126 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ 154.8, (142.8), 142.5, 128.5, 128.4, 125.8, 79.0, 57.3, (46.6), 46.2, 36.1, 34.5 (34.1), 30.8 (30.0), 28.7, 28.2, (23.9), 23.2.

IR (film): ν_{max} 2971, 2930, 1691, 1497, 1478, 1454, 1393, 1364, 1249, 1170, 1103, 914, 877, 772, 748, 699.

HRMS (ESI-TOF): m/z calcd. for C₁₈H₂₇NNaO₂ ([M+Na]⁺) 312.19340, found 312.19361.

Data are consistent with those reported in the literature.⁵

***tert*-Butyl 2-(2-(benzyloxy)ethyl)pyrrolidine-1-carboxylate (13)**

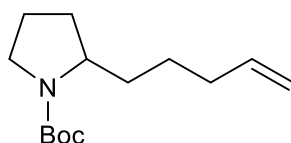
According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.2 mg, 10.0 μmol 0.02 equiv), NiCl₂•glyme (11.0 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (10.8 mg, 0.05 mmol, 0.1 equiv), benzyl 2-bromoethyl ether (79 μL, 0.5 mmol, 1.0 equiv), Boc-Pro-OH (161 mg, 0.75 mmol, 1.5 equiv), K₂CO₃ (138 mg, 1.00 mmol, 2.0 equiv), water (180 μL, 10 mmol, 20 equiv), and 5 mL of MeCN were used. The product was isolated by flash chromatography (5 to 20% EtOAc/hexanes) as a colorless oil (99 mg, 65%).

¹H-NMR (500 MHz, CDCl₃) rotameric mixture: δ 7.37 – 7.30 (m, 4H), 7.30 – 7.25 (m, 1H), 4.52 (d, *J* = 11.9 Hz, 1H), 4.47 (d, *J* = 11.9 Hz, 1H), 3.89 and 3.84 (2 br s, 1H, rotamer), 3.52 (br s, 2H), 3.38 and 3.30 (2 br s, 1H, rotamer), 2.10 and 2.05 (2 br s, 1H, rotamer), 1.98 – 1.72 (m, 4H), 1.68 – 1.57 (m, 1H), 1.45 (s, 9H).

¹³C-NMR (126 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ 154.7, 138.7, 131.0, 128.5, 127.6, 79.3 (79.0), 73.0, (68.5) 68.3, (55.5) 55.3, (46.5) 46.1, 34.9 (34.4), 31.3 (30.7), 28.7, (23.9) 23.2.

IR (film): ν_{max} 2969, 2871, 1689, 1478, 1454, 1390, 1364, 1251, 1166, 1100, 1028, 911, 865, 772, 732, 697.

HRMS (ESI-TOF): *m/z* calcd. for C₁₈H₂₈NO₃ ([M+H]⁺) 306.20637, found 306.20664.

***tert*-Butyl 2-(pent-4-en-1-yl)pyrrolidine-1-carboxylate (14)**

According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (12.3 mg, 11.0 μmol 0.02 equiv), NiCl₂•glyme (12.1 mg, 0.06 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (11.9 mg, 0.06 mmol, 0.1 equiv), 5-bromopentene (65 μL, 0.55 mmol, 1.0 equiv), Boc-Pro-OH (177 mg, 0.82 mmol, 1.5 equiv), K₂CO₃ (152 mg, 1.1 mmol, 2.0 equiv), water (198 μL, 11 mmol, 20 equiv), and 5.5 mL of MeCN were used. The product was isolated by flash chromatography (5 to 7.5% EtOAc/hexanes) as a colorless oil (110 mg, 84%).

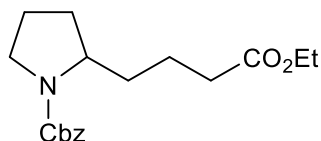
¹H-NMR (500 MHz, CDCl₃): δ 5.80 (ddt, *J* = 17.0, 10.2, 6.6 Hz, 1H), 5.00 (dq, *J* = 17.1, 1.7 Hz, 1H), 4.94 (dd, *J* = 10.2, 1.1 Hz, 1H), 3.78 – 3.69 (m, 1H), 3.40 – 3.26 (m, 2H), 2.13 – 1.99 (m, 2H), 1.96 – 1.68 (m, 4H), 1.67 – 1.60 (m, 1H), 1.46 (s, 9H), 1.41 – 1.25 (m, 3H).

¹³C-NMR (126 MHz, CDCl₃): δ 154.8, 139.0, 114.6, 79.0, 57.4, 46.4, 34.1, 33.9, 30.5, 28.7, 25.8, 23.6.

IR (film): ν_{max} 2972, 2931, 2874, 1692, 1641, 1479, 1455, 1392, 1365, 1251, 1172, 1107, 992, 911, 878, 772.

HRMS (ESI-TOF): *m/z* calcd. for C₁₄H₂₅NNaO₂ ([M+Na]⁺) 262.17775, found 262.17793.

Data are consistent with those reported in the literature.⁶

Benzyl 2-(4-ethoxy-4-oxobutyl)pyrrolidine-1-carboxylate (15)

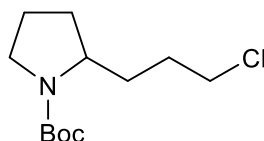
According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.0 mg, 9.8 μmol 0.02 equiv), NiCl₂•glyme (10.8 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (10.6 mg, 0.05 mmol, 0.1 equiv), ethyl 4-bromobutyrate (70 μL, 0.49 mmol, 1.0 equiv), Cbz-Pro-OH (183 mg, 0.73 mmol, 1.5 equiv), K₂CO₃ (135 mg, 0.98 mmol, 2.0 equiv), water (176 μL, 9.7 mmol, 20 equiv), and 4.9 mL of MeCN were used. The product was isolated by flash chromatography (15% Et₂O/pentane) as a colorless oil (100 mg, 64%).

¹H-NMR (500 MHz, CDCl₃) rotameric mixture: δ 7.46 – 7.30 (m, 5H), 5.24 – 5.05 (m 2H, rotamer), 4.23 – 4.05 (m, 2H, rotamer), 3.84 (m, 1H, rotamer), 3.55 – 3.31 (m, 2H), 2.29 (m, 2H, rotamer), 1.99 – 1.77 (m, 4H), 1.73 – 1.60 (m, 3H), 1.40 – 1.31 (m, 1H), 1.28 – 1.21 (m, 3H).

¹³C-NMR (126 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ 173.8 (173.6), (155.2) 155.0, 137.2 (137.1), 128.6, 128.0, 127.9, 66.8 (66.6), 60.4, 57.8 (57.1), (46.7) 46.4, 34.3 (close rotamers), 33.5, (30.7) 30.0, 24.0 (23.2), 21.8, 14.4

IR (film): ν_{max} 2957, 1732, 1698, 1498, 1452, 1410, 1357, 1336, 1251, 1181, 1100, 1030, 917, 868, 769, 746, 698.

HRMS (ESI-TOF): m/z calcd. for C₁₈H₂₅NNaO₄ ([M+Na]⁺) 319.17836, found 319.17772.

***tert*-Butyl 2-(3-chloropropyl)pyrrolidine-1-carboxylate (16)**

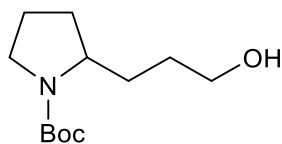
According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.3 mg, 10.1 μmol 0.02 equiv), NiCl₂•glyme (11.1 mg, 0.051 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (10.9 mg, 0.05 mmol, 0.1 equiv), 1-bromo-3-chloropropane (50 μL, 0.51 mmol, 1.0 equiv), Boc-Pro-OH (163 mg, 0.76 mmol, 1.5 equiv), K₂CO₃ (140 mg, 1.0 mmol, 2.0 equiv), water (182 μL, 10.1 mmol, 20 equiv), and 5.1 mL of MeCN were used. The product was isolated by flash chromatography (7% EtOAc/hexanes) as a colorless oil (123 mg, 96%).

¹H-NMR (500 MHz, CDCl₃): δ 3.79 – 3.71 (m, 1H), 3.58 – 3.46 (m, 2H), 3.40 – 3.31 (m, 1H), 3.31 – 3.23 (m, 1H), 1.97 – 1.85 (m, 1H), 1.88 – 1.69 (m, 5H), 1.66 – 1.56 (m, 1H), 1.44 (s, 10H).

¹³C-NMR (126 MHz, CDCl₃): δ 154.8, 79.3, 56.8, 46.4, 45.2, 32.1, 30.6, 29.8, 28.7, 23.5.

IR (film): ν_{max} 2696, 2874, 1869, 1478, 1454, 1391, 1364, 1251, 1168, 1116, 1100, 913, 875, 772, 725.

HRMS (ESI-TOF): m/z calcd. for C₁₂H₂₂ClNNaO₂ ([M+Na]⁺) 270.12313, found 270.12348.

***tert*-Butyl 2-(3-hydroxypropyl)pyrrolidine-1-carboxylate (17)**

According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.2 mg, 10.0 μmol 0.02 equiv), NiCl₂•glyme (11.0 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (10.8 mg, 0.05 mmol, 0.1 equiv), 3-bromopropan-1-ol (45 μL, 0.5 mmol, 1.0 equiv), Boc-Pro-OH (161 mg, 0.75 mmol, 1.5 equiv), K₂CO₃ (138 mg, 1.00 mmol, 2.0 equiv), water (180 μL, 10 mmol, 20 equiv), and 5 mL of MeCN were used. The product was isolated by flash chromatography (17 to 25% EtOAc/hexanes) as a yellow oil (99 mg, 86%).

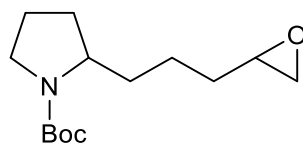
¹H-NMR (500 MHz, CDCl₃): δ 3.87 – 3.78 (m, 1H), 3.73 – 3.63 (m, 2H), 3.40 – 3.26 (m, 2H), 1.99 – 1.73 (m, 4H), 1.67 – 1.48 (m, 3H), 1.46 (s, 9H), 1.45 – 1.32 (m, 1H).

¹³C-NMR (126 MHz, CDCl₃): δ 155.0, 79.3, 62.8, 56.9, 46.4, 31.0, 30.6, 29.3, 28.7, 23.6.

IR (film): ν_{max} 3428, 2971, 2872, 1780, 1692, 1672, 1478, 1457, 1397, 1366, 1251, 1169, 1109, 1059, 920, 862, 772.

HRMS (ESI-TOF): m/z calcd. for C₁₂H₂₃NNaO₃ ([M+Na]⁺) 252.15701, found 252.15713.

Data are consistent with those reported in the literature.⁷

***tert*-Butyl 2-(3-(oxiran-2-yl)propyl)pyrrolidine-1-carboxylate (18)**

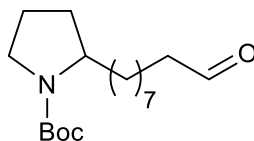
According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.2 mg, 10.0 μmol 0.02 equiv), NiCl₂•glyme (11.0 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (10.8 mg, 0.05 mmol, 0.1 equiv), 2-(3-bromopropyl)oxirane (83.0 mg, 0.5 mmol, 1.0 equiv), Boc-Pro-OH (161 mg, 0.75 mmol, 1.5 equiv), K₂CO₃ (138 mg, 1.00 mmol, 2.0 equiv), water (180 μL, 10 mmol, 20 equiv), and 5 mL of MeCN were used. The product was isolated by flash chromatography (10 to 15% EtOAc/hexanes) as a colorless oil and as a 1 : 1 mixture of diastereomers (106 mg, 83%).

¹H-NMR (500 MHz, CDCl₃) rotameric mixture: δ 3.78 and 3.71 (2 br s, 1H, rotamer), 3.40 and 3.30 (2 br s, 2H, rotamer), 2.98 – 2.85 (m, 1H), 2.75 (t, *J* = 4.5 Hz, 1H), 2.52 – 2.41 (m, 1H), 1.97 – 1.69 (m, 4H), 1.69 – 1.61 (m, 1H), 1.60 – 1.54 (m, 1H), 1.53 – 1.31 (m, 14H).

¹³C-NMR (126 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ 154.8, 79.1 (79.0), (57.4) 57.2, (52.5) 52.3, 47.2, (46.6) 46.2, (34.7) 34.6, 34.2 (33.9), (32.8) 32.7, 32.6 (32.5), 30.8 (30.0), 28.7 (28.6), (23.9) 23.2, (22.9) 22.8.

IR (film): ν_{max} 2971, 2931, 2871, 1689, 1479, 1455, 1391, 1365, 1253, 1168, 1107, 913, 849, 772.

HRMS (ESI-TOF): *m/z* calcd. for C₁₄H₂₅NNaO₃ ([M+Na]⁺) 278.17266, found 278.17287.

***tert*-Butyl 2-(9-oxononyl)pyrrolidine-1-carboxylate (19)**

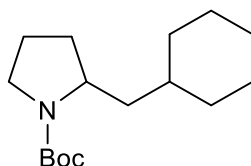
According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**1**) (11.2 mg, 10.0 μmol 0.02 equiv), NiCl₂•glyme (11.0 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (10.8 mg, 0.05 mmol, 0.1 equiv), 9-bromononanal (111 mg, 0.5 mmol, 1.0 equiv), Boc-Pro-OH (161 mg, 0.75 mmol, 1.5 equiv), K₂CO₃ (138 mg, 1.00 mmol, 2.0 equiv), water (180 μL, 10 mmol, 20 equiv), and 5 mL of MeCN were used. The product was isolated by flash chromatography (7.5% EtOAc/hexanes) as a colorless oil (97 mg, 62%).

¹H-NMR (500 MHz, CDCl₃): δ 9.76 (t, *J* = 1.9 Hz, 1H), 3.75 – 3.67 (m, 1H), 3.39 – 3.26 (m, 2H), 2.42 (td, *J* = 7.4, 1.9 Hz, 2H), 1.94 – 1.67 (m, 3H), 1.67 – 1.57 (m, 4H), 1.46 (s, 9H), 1.35 – 1.20 (m, 10H).

¹³C-NMR (126 MHz, CDCl₃): δ 203.1, 154.8, 79.0, 57.4, 46.4, 44.1, 34.5, 30.4, 29.7, 29.6, 29.4, 29.3, 28.7, 26.5, 23.6, 22.2.

IR (film): ν_{max} 2928, 2856, 1726, 1691, 1456, 1393, 1365, 1253, 1171, 1106, 913, 772.

HRMS (ESI-TOF): *m/z* calcd. for C₁₈H₃₃NNaO₃ ([M+Na]⁺) 334.23527, found 334.23557.

***tert*-Butyl 2-(cyclohexylmethyl)pyrrolidine-1-carboxylate (20)**

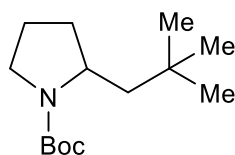
According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.2 mg, 10.0 μmol 0.02 equiv), NiCl₂•glyme (11.0 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (10.8 mg, 0.05 mmol, 0.1 equiv), (bromomethyl)cyclohexane (69 μL, 0.5 mmol, 1.0 equiv), Boc-Pro-OH (161 mg, 0.75 mmol, 1.5 equiv), K₂CO₃ (138 mg, 1.00 mmol, 2.0 equiv), water (180 μL, 10 mmol, 20 equiv), and 5 mL of MeCN were used. The product was isolated by flash chromatography (5 to 7.5% EtOAc/hexanes) as a colorless oil (100 mg, 75%).

¹H-NMR (500 MHz, CDCl₃): δ 3.87 – 3.80 (m, 1H), 3.38 – 3.25 (m, 2H), 1.94 – 1.73 (m, 4H), 1.72 – 1.53 (m, 6H), 1.46 (s, 9H), 1.29 – 1.07 (m, 5H), 1.00 – 0.86 (m, 2H).

¹³C-NMR (126 MHz, CDCl₃): δ 154.7, 79.0, 55.2, 46.1, 42.3, 35.5, 34.6, 32.8, 30.7, 28.7, 26.7, 26.6, 26.4, 23.3.

IR (film): ν_{max} 2971, 2922, 1851, 1692, 1478, 1449, 1391, 1364, 1254, 1171, 1105, 914, 878, 772.

HRMS (ESI-TOF): m/z calcd. for C₁₆H₂₉NNaO₂ ([M+Na]⁺) 290.20905, found 290.20948.

***tert*-Butyl 2-neopentylpyrrolidine-1-carboxylate (21)**

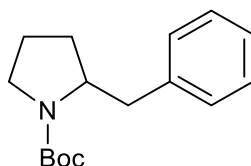
According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**1**) (11.2 mg, 10.0 μmol 0.02 equiv), NiCl₂•glyme (11.0 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (10.8 mg, 0.05 mmol, 0.1 equiv), 1-bromo-2,2-dimethylpropane (63 μL, 0.5 mmol, 1.0 equiv), Boc-Pro-OH (161 mg, 0.75 mmol, 1.5 equiv), K₂CO₃ (138 mg, 1.00 mmol, 2.0 equiv), water (180 μL, 10 mmol, 20 equiv), and 5 mL of MeCN were used. The product was isolated by flash chromatography (4% EtOAc/hexanes) as a pale yellow oil (63 mg, 52%).

¹H-NMR (500 MHz, CDCl₃): δ 3.87 – 3.78 (m, 1H), 3.36 – 3.23 (m, 2H), 2.00 – 1.73 (m, 3H), 1.72 – 1.65 (m, 1H), 1.65 – 1.57 (m, 1H), 1.46 (s, 9H), 1.21 (dd, *J* = 13.5, 10.2 Hz, 1H), 0.94 (s, 9H).

¹³C-NMR (126 MHz, CDCl₃): δ 154.5, 79.2, 54.6, 48.6, 45.9, 32.9, 30.4, 30.4, 28.9, 23.4.

IR (film): ν_{max} 2956, 2871, 1691, 1455, 1477, 1389, 1364, 1345, 1308, 1294, 1248, 1169, 1114, 1096, 1063, 994, 967, 923, 878, 771.

HRMS (ESI-TOF): *m/z* calcd. for C₁₄H₂₇NNaO₂ ([M+Na]⁺) 264.19340, found 264.19302.

***tert*-Butyl 2-benzylpyrrolidine-1-carboxylate (22)**

According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.2 mg, 10.0 μmol, 0.02 equiv), NiCl₂•glyme (11.0 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (10.8 mg, 0.05 mmol, 0.1 equiv), benzyl chloride (58 μL, 0.5 mmol, 1.0 equiv), Boc-Pro-OH (161 mg, 0.75 mmol, 1.5 equiv), K₂CO₃ (138 mg, 1.00 mmol, 2.0 equiv), water (180 μL, 10 mmol, 20 equiv), and 5 mL of MeCN were used. The product was isolated by flash chromatography (5 to 7.5% EtOAc/hexanes) as a colorless oil (109 mg, 84%).

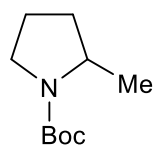
¹H-NMR (500 MHz, CDCl₃): δ 7.21 (t, *J* = 7.4 Hz, 2H), 7.16 – 7.10 (m, 3H), 3.91 (br s, 1H), 3.26 (br s, 2H), 3.03 (d, *J* = 12.9 Hz, 1H), 2.47 (dd, *J* = 13.0, 9.5 Hz, 1H), 1.75 – 1.59 (m, 4H), 1.44 (s, 9H).

¹³C-NMR (126 MHz, CDCl₃): δ 154.7, 139.4, 129.6, 128.5, 126.3, 79.3, 58.9, 46.6, 40.4, 29.5, 28.8, 23.1.

IR (film): ν_{max} 3027, 2973, 1876, 1690, 1604, 1497, 1479, 1454, 1292, 1365, 1343, 1276, 1256, 1170, 1115, 1096, 1030, 967, 902, 867, 765, 748, 701.

HRMS (ESI-TOF): *m/z* calcd. for C₁₆H₂₃NNaO₂ ([M+Na]⁺) 284.16210, found 284.16220.

Data are consistent with those reported in the literature.⁸

***tert*-Butyl 2-methylpyrrolidine-1-carboxylate (23)**

According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (13.5 mg, 12.0 μmol 0.02 equiv), NiCl₂•glyme (13.2 mg, 0.06 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (13 mg, 0.06 mmol, 0.1 equiv), bromomethane (3.6 M in MeCN, 166 μL, 0.6 mmol, 1.0 equiv), Boc-Pro-OH (129.0 mg, 0.6 mmol, 1.0 equiv), K₂CO₃ (166 mg, 1.2 mmol, 2.0 equiv), water (216 μL, 12 mmol, 20 equiv), and 6 mL of MeCN were used. However, to limit esterification, the reaction was run for 24 hours at 7 °C in an isopropanol bath maintained via a portable cryo-cool. The product was isolated by flash chromatography (10% Et₂O/pentane) as a colorless oil (69 mg, 62%).

Procedure for Flow reaction:

Using Vapourtec E-series equipped with a 10 ml UV-150 Photochemical reactor (420 nm), a solution of Boc-Pro-OH (107.6 mg, 0.5 mmol, 1.0 equiv.), Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.3 mg, 0.01 μmol 0.02 equiv), NiCl₂•glyme (2.14 mg, 0.01 mmol, 0.02 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (2.71 mg, 0.01 mmol, 0.02 equiv), 1,1,3,3-tetramethylguanidine (63.0 μl, 0.50 mmol, 1.0 equiv.) and water (45.0 μl, 2.50 mmol, 5.0 equiv.) in MeCN (1 ml) and a separate solution of bromomethane (0.79 M in MeCN, 1.0 ml, 0.79 mmol, 1.58 equiv.) were pumped through the system, mixing just before entering the photoreactor with a flow rate of 0.333 ml/ min each. The yield was determined by GC vs MeOBz as internal standard (55%). Under these conditions, one could produce 22 grams (120 mmol) in 24 hours.

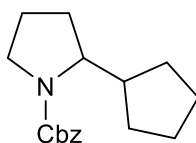
¹H-NMR (500 MHz, CDCl₃): δ 3.90 – 3.81 (m, 1H), 3.39 – 3.28 (m, 2H), 1.97 (ddt, *J* = 12.0, 9.5, 7.4 Hz, 1H), 1.92 – 1.72 (m, 2H), 1.58 – 1.48 (m, 1H), 1.45 (s, 9H), 1.14 (d, *J* = 6.3 Hz, 3H).

¹³C-NMR (126 MHz, CDCl₃): δ 154.7, 78.9, 52.9, 46.4, 33.1, 28.7, 23.4, 20.7.

IR (film): ν_{max} 2969, 2875, 1693, 1479, 1456, 1391, 1366, 1287, 1250, 1172, 1138, 1110, 1084, 1029, 1003, 972, 902, 856, 773.

HRMS (ESI-TOF): *m/z* calcd. for C₁₀H₁₉NNaO₂ ([M+Na]⁺) 208.13080, found 208.13105.

Data are consistent with those reported in the literature.⁹

Benzyl 2-cyclopentylpyrrolidine-1-carboxylate (24)

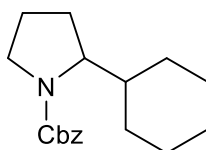
According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (9.9 mg, 8.8 μmol 0.02 equiv), NiCl₂•glyme (9.7 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (9.6 mg, 0.04 mmol, 0.1 equiv), bromocyclopentane (48 μL, 0.44 mmol, 1.0 equiv), Cbz-Pro-OH (165 mg, 0.66 mmol, 1.5 equiv), K₂CO₃ (122 mg, 0.88 mmol, 2.0 equiv), water (159 μL, 8.80 mmol, 20 equiv), and 4.4 mL of MeCN were used. The product was isolated by flash chromatography (5% EtOAc/hexanes) as a colorless oil (88 mg, 72%).

¹H-NMR (500 MHz, CDCl₃) rotameric mixture: δ 7.40 – 7.27 (m, 5H), 5.18 – 5.07 (m, 2H), 3.95 and 3.89 (2 br s, 1H, rotamer), 3.61 – 3.55 (m, 1H), 3.54 – 3.46 (m, 1H), 3.39 – 3.29 (m, 1H), 2.19 – 1.99 (m, 1H), 1.95 – 1.78 (m, 3H), 1.78 – 1.35 (m, 8H), 1.34 – 1.10 (m, 1H).

¹³C-NMR (126 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ 155.6, 137.4 (137.1), 128.5, 128.1, 127.9 (127.9), (66.9) 66.6, 61.5 (60.9), (46.7) 46.5, 44.2, 30.1 (28.9), (29.3) 28.5, 25.4 (25.2), 24.0, (23.1).

IR (film): ν_{max} 3033, 2950, 2869, 1696, 1587, 1498, 1451, 1406, 1355, 1330, 1284, 1205, 1185, 1151, 1098, 1029, 981, 915, 867, 768, 749, 697.

HRMS (ESI-TOF): m/z calcd. for C₁₇H₂₃NNaO₂ ([M+Na]⁺) 296.16210, found 296.16183.

Benzyl 2-cyclohexylpyrrolidine-1-carboxylate (25)

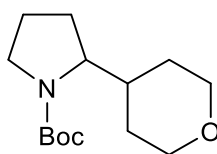
According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (10.9 mg, 9.7 μmol 0.02 equiv), NiCl₂•glyme (10.7 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (10.5 mg, 0.05 mmol, 0.1 equiv), bromocyclohexane (60 μL, 0.49 mmol, 1.0 equiv), Cbz-Pro-OH (182 mg, 0.73 mmol, 1.5 equiv), K₂CO₃ (135 mg, 0.97 mmol, 2.0 equiv), water (176 μL, 9.70 mmol, 20 equiv), and 4.9 mL of MeCN were used. The product was isolated by flash chromatography (3 to 30% EtOAc/hexanes) as a colorless oil (80 mg, 57%).

¹H-NMR (500 MHz, CDCl₃): δ 7.41 – 7.27 (m, 5H), 5.26 – 5.03 (m, 2H), 3.82 – 3.70 (m, 1H), 3.64 – 3.45 (m, 1H), 3.34 – 3.24 (m, 1H), 1.90 – 1.49 (m, 10H), 1.30 – 0.83 (m, 5H).

¹³C-NMR (126 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ (155.6) 155.4, 137.4 (137.2), 128.5, 127.9, 127.9, (66.7) 66.6, 62.7 (62.0), (47.2) 46.9, (41.4) 40.7, 30.2, 27.9, 27.4, 26.7 - 26.3 (m), 24.5 (23.8).

IR (film): ν_{max} 2925, 2852, 1699, 1498, 1449, 1408, 1354, 1332, 1182, 1101, 1028, 976, 920, 880, 768, 750, 697.

HRMS (ESI-TOF): m/z calcd. for C₁₈H₂₅NNaO₂ ([M+Na]⁺) 310.17775, found 310.17726.

***tert*-Butyl 2-(tetrahydro-2H-pyran-4-yl)pyrrolidine-1-carboxylate (26)**

According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.2 mg, 10.0 μmol 0.02 equiv), NiCl₂•glyme (11.0 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (10.8 mg, 0.05 mmol, 0.1 equiv), 4-bromotetrahydro-2H-pyran (57 μL, 0.5 mmol, 1.0 equiv), Boc-Pro-OH (161 mg, 0.75 mmol, 1.5 equiv), K₂CO₃ (138 mg, 1.00 mmol, 2.0 equiv), water (180 μL, 10 mmol, 20 equiv), and 5 mL of MeCN were used. The product was isolated by flash chromatography (10 to 15% EtOAc/hexanes) as a pale yellow oil (116 mg, 91%).

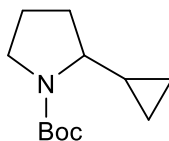
¹H-NMR (500 MHz, CDCl₃): δ 4.02 – 3.96 (m, 2H), 3.72 (br s, 1H), 3.52 - 3.41 (m, 1H), 3.33 (tdd, *J* = 11.6, 3.7, 2.3 Hz, 2H), 3.26 – 3.17 (m, 1H), 1.92 (br s, 1H), 1.87 – 1.72 (m, 4H), 1.53 – 1.28 (m, 13H).

¹³C-NMR (126 MHz, CDCl₃): δ 155.3, 79.3, 68.4, 68.2, 61.3, 46.9, 38.7, 30.2, 28.7, 28.3, 27.1, 24.1.

IR (film): *v*_{max} 2957, 2843, 1691, 1479, 1455, 1391, 1365, 1240, 1169, 1142, 1104, 1014, 985, 958, 923, 876, 772.

HRMS (ESI-TOF): *m/z* calcd. for C₁₄H₂₅NNaO₃ ([M+Na]⁺) 278.17266, found 278.17250.

Data are consistent with those reported in the literature.⁵

***tert*-Butyl 2-cyclopropylpyrrolidine-1-carboxylate (27)**

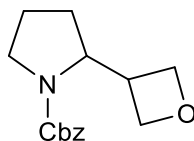
According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.2 mg, 10.0 μmol 0.02 equiv), NiCl₂•glyme (11.0 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (10.8 mg, 0.05 mmol, 0.1 equiv), bromocyclopropane (40 μL, 0.5 mmol, 1.0 equiv), Boc-Pro-OH (161 mg, 0.75 mmol, 1.5 equiv), K₂CO₃ (138 mg, 1.00 mmol, 2.0 equiv), water (180 μL, 10 mmol, 20 equiv), and 5 mL of MeCN were used. The product was isolated by flash chromatography (5% EtOAc/hexanes) as a colorless oil (53 mg, 50%).

¹H-NMR (500 MHz, CDCl₃): δ 3.41 – 3.31 (m, 3H), 1.99 – 1.69 (m, 4H), 1.46 (s, 9H), 0.85 (qt, *J* = 8.1, 5.0 Hz, 1H), 0.56 – 0.43 (m, 2H), 0.39 – 0.31 (m, 1H), 0.11 (ddt, *J* = 9.5, 5.8, 4.7 Hz, 1H).

¹³C-NMR (126 MHz, CDCl₃): δ 155.2, 79.1, 60.9, 46.7, 31.5, 28.7, 23.5, 16.0, 4.5, 1.8.

IR (film): ν_{max} 3084, 2973, 2879, 1690, 1478, 1453, 1384, 1365, 1272, 1251, 1168, 1105, 1058, 1044, 1017, 985, 946, 928, 908, 867, 819, 771.

HRMS (ESI-TOF): *m/z* calcd. for C₁₂H₂₁NNaO₂ ([M+Na]⁺) 234.14645, found 234.14643.

Benzyl 2-(oxetan-3-yl)pyrrolidine-1-carboxylate (28)

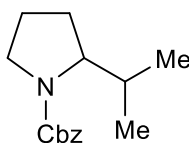
According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (10 mg, 8.9 μmol 0.02 equiv), NiCl₂•glyme (9.8 mg, 0.045 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (9.60 mg, 0.05 mmol, 0.1 equiv), 3-bromooxetane (37 μL, 0.45 mmol, 1.0 equiv), Cbz-Pro-OH (167 mg, 0.67 mmol, 1.5 equiv), K₂CO₃ (123 mg, 0.89 mmol, 2.0 equiv), water (161 μL, 8.90 mmol, 20 equiv), and 4.5 mL of MeCN were used. The product was isolated by flash chromatography (25% EtOAc/hexanes) as a colorless oil (92 mg, 79%).

¹H-NMR (500 MHz, CDCl₃) rotameric mixture: δ 7.39 – 7.29 (m, 5H), 5.17 – 5.03 (m, 2H), 4.87 and 4.72 (2 t, *J* = 6.5 Hz, 1H, rotamer), 4.68 – 4.37 (m, 3H), 4.25 – 4.12 (m, 1H), 3.62 – 3.47 (m, 1H), 3.37 (dt, *J* = 11.3, 6.6 Hz, 1H), 3.30 – 3.11 (m, 1H), 2.01 (dq, *J* = 12.5, 7.7 Hz, 1H), 1.84 (p, *J* = 6.9 Hz, 2H), 1.57 (br s, 1H).

¹³C-NMR (126 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ 155.6 (155.3), 136.9 (136.4), 128.6 (128.6), 128.4, (128.0) 127.9, 76.6 (76.5), 73.8, (67.3) 66.8, 59.8 (59.2), (47.4) 47.1, 40.2, (29.2) 28.5, 23.9 (23.1).

IR (film): ν_{\max} 3563, 2961, 2877, 1696, 1498, 1451, 1409, 1356, 1334, 1274, 1244, 1207, 1186, 1102, 1029, 974, 919, 869, 7770, 753, 699.

HRMS (ESI-TOF): *m/z* calcd. for C₁₅H₂₀NO₃ ([M+H]⁺) 262.14377, found 262.14361.

Benzyl 2-isopropylpyrrolidine-1-carboxylate (29)

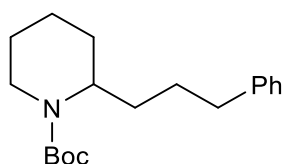
According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (10.0 mg, 9.0 μmol 0.02 equiv), NiCl₂•glyme (9.80 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (9.70 mg, 0.05 mmol, 0.1 equiv), 2-bromopropane (42 μL, 0.45 mmol, 1.0 equiv), Cbz-Pro-OH (167 mg, 0.67 mmol, 1.5 equiv), K₂CO₃ (124 mg, 0.90 mmol, 2.0 equiv), water (161 μL, 9.00 mmol, 20 equiv), and 4.5 mL of MeCN were used. The product was isolated by flash chromatography (5% EtOAc/hexanes) as a colorless oil (76 mg, 69%).

¹H-NMR (500 MHz, CDCl₃) rotameric mixture: δ 7.42 – 7.27 (m, 5H), 5.19 – 5.06 (m, 2H), 3.84 – 3.72 (m, 1H), 3.68 – 3.59 and 3.59 – 3.51 (2 m, 1H, rotamer), 3.35 – 3.26 (m, 1H), 2.29 – 2.20 and 2.15 – 2.04 (2 m, 1H, rotamer), 1.91 – 1.68 (m, 4H), 0.97 – 0.74 (m, 6H).

¹³C-NMR (126 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ (155.7) 155.4, 137.4 (137.2), 128.5, 127.8, 127.9, (66.8) 66.6, 63.1 (62.5), (47.4) 47.1, (30.8) 30.0, (26.6) 25.7, 24.5 (23.8), 19.6, (17.0) 16.8.

IR (film): ν_{max} 3034, 2960, 2874, 1698, 1498, 1455, 1408, 1345, 1332, 1244, 1205, 1184, 1099, 1029, 981, 916, 869, 769, 744, 697.

HRMS (ESI-TOF): m/z calcd. for C₁₅H₂₁NNaO₂ ([M+Na]⁺) 270.14645, found 270.14630.

***tert*-Butyl 2-(3-phenylpropyl)piperidine-1-carboxylate (30)**

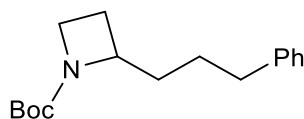
An oven dried 40 mL vial equipped with a Teflon septum and cross-shape magnetic stir bar was charged with Ir[dF(Me)ppy]₂(dtbbpy)PF₆ (**II**) (10.1 mg, 10.0 μmol, 0.02 equiv), NiCl₂•glyme (11.0 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (13.4 mg, 0.05 mmol, 0.1 equiv), Boc-Pip-OH (115 mg, 0.50 mmol, 1.0 equiv), Cs₂CO₃ (326 mg, 1.00 mmol, 2.0 equiv), and 10 mL MeCN. The reaction mixture was degassed by bubbling nitrogen stream for 15 min at 0 °C. Water (360 μL, 20.0 mmol, 40 equiv) and 1-bromo-3-phenylpropane (152 μL, 1.00 mmol, 2.0 equiv) were then added. The reaction mixture was then stirred and irradiated with two 34 W blue LEDs (vials approximately 6 cm away from the light source) with a fan placed above for cooling. After 24 h, the reaction mixture was diluted with EtOAc, filtered, and concentrated in vacuo. The product was isolated by flash chromatography (2 to 20% EtOAc/hexanes) as a colorless oil (92 mg, 61%).

¹H-NMR (500 MHz, CD₃CN): δ 7.31 – 7.23 (m, 2H), 7.23 – 7.13 (m, 3H), 4.20 (br s, 1H), 3.92 – 3.77 (m, 1H), 2.75 – 2.53 (m, 3H), 1.73 (dtd, *J* = 13.3, 9.3, 5.0 Hz, 1H), 1.59 – 1.41 (m, 8H), 1.39 (s, 9H), 1.35 – 1.24 (m, 1H).

¹³C-NMR (126 MHz, CD₃CN): δ 155.7, 143.8, 129.3, 129.2, 126.6, 79.4, 51.1 (br & weak), 39.4 (br & weak), 36.1, 29.8, 29.3, 29.1, 28.6, 26.5, 19.7.

IR (film): *v*_{max} 2974, 2933, 2859, 1686, 1474, 1453, 1415, 1364, 1269, 1254, 1156, 1076, 1045, 870, 767, 748, 699.

HRMS (ESI-TOF): *m/z* calcd. for C₁₉H₂₉NNaO₂ ([M+Na]⁺) 326.20905, found 326.20920.

tert-Butyl 2-(3-phenylpropyl)azetidine-1-carboxylate (31)

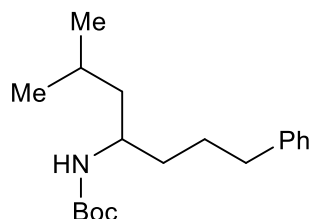
An oven dried 40 mL vial equipped with a Teflon septum and cross-shape magnetic stir bar was charged with Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.2 mg, 10.0 μmol, 0.02 equiv), NiCl₂•glyme (11.0 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (10.8 mg, 0.05 mmol, 0.1 equiv), Boc-Azetidine-2-Carboxylic Acid (151 mg, 0.75 mmol, 1.5 equiv), K₂CO₃ (276 mg, 2.00 mmol, 4.0 equiv), 5 mL MeCN, and 5 mL EtOAc. The reaction mixture was degassed by bubbling nitrogen stream for 15 min at 0 °C. Water (180 μL, 10.0 mmol, 20 equiv) and 1-bromo-3-phenylpropane (76 μL, 0.50 mmol, 1.0 equiv) were then added. The reaction mixture was then stirred and irradiated with two 34 W blue LEDs (vials approximately 6 cm away from the light source) with a fan placed above for cooling. After 24 h, the reaction mixture was diluted with EtOAc, filtered, and concentrated in vacuo. The product was isolated by flash chromatography (5 to 7.5% EtOAc/hexanes) as a colorless oil (97 mg, 70%).

¹H-NMR (500 MHz, CDCl₃): δ 7.32 – 7.24 (m, 2H), 7.23 – 7.13 (m, 3H), 4.23 – 4.17 (m, 1H), 3.86 – 3.71 (m, 2H), 2.70 – 2.57 (m, 2H), 2.23 (dtd, *J* = 11.3, 8.8, 5.4 Hz, 1H), 1.95 – 1.87 (m, 1H), 1.80 (ddt, *J* = 11.3, 9.2, 6.5 Hz, 1H), 1.70 – 1.57 (m, 3H), 1.41 (s, 9H).

¹³C-NMR (126 MHz, CDCl₃): δ 156.8, 142.5, 128.5, 128.4, 125.9, 79.2, 62.1, 46.5, 36.0, 35.1, 28.6, 26.5, 22.0.

IR (film): *v*_{max} 2974, 2932, 1698, 1454, 1390, 1365, 1254, 1182, 1136, 1099, 749, 699.

HRMS (ESI-TOF): *m/z* calcd. for C₁₇H₂₅NNaO₂ ([M+Na]⁺) 298.17775, found 298.17812.

***tert*-Butyl (6-methyl-1-phenylheptan-4-yl)carbamate (32)**

According to the general procedure B, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.2 mg, 10.0 μmol 0.02 equiv), NiCl₂•glyme (11.0 mg, 0.050 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (10.8 mg, 0.05 mmol, 0.1 equiv), 1-bromo-3-phenylpropane (76 μL, 0.50 mmol, 1.0 equiv), Boc-Leu-OH (173 mg, 0.75 mmol, 1.5 equiv), Cs₂CO₃ (326 mg, 1.00 mmol, 2.0 equiv), water (180 μL, 9.7 mmol, 20 equiv), and 10 mL of MeCN were used. The product was isolated by flash chromatography (5% EtOAc/hexanes) as a colorless oil (110 mg, 72%).

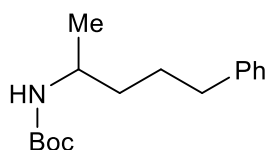
¹H-NMR (500 MHz, CDCl₃) rotameric mixture: δ 7.31 – 7.24 (m, 3H), 7.21 – 7.14 (m, 3H), 4.17 and 3.89 (br d and br s, *J* = 9.5 Hz, 1H, rotamers), 3.67 and 3.54 (br d and br s, *J* = 7.7 Hz, 1H, rotamers), 2.69 – 2.54 (m, 2H), 1.71 – 1.59 (m, 3H), 1.51 – 1.40 (m, 1H), 1.44 (s, 9H), 1.39 - 1.29 (m, 1H), 1.25 – 1.16 (m, 2H), 0.89 (t, *J* = 6.6 Hz, 6H).

¹³C-NMR (126 MHz, CDCl₃):δ 155.8, 142.6, 128.6, 128.4, 125.8, 79.0, 48.7, 45.2, 36.0, 35.9, 28.6, 27.8, 25.0, 23.3, 22.4.

IR (film): ν_{max} 3346, 2943, 2868, 1690, 1604, 1492, 1454, 1389, 1365, 1247, 1167, 1109, 1086, 1046, 1030, 1006, 946, 874, 777, 746, 698.

HRMS (ESI-TOF): *m/z* calcd. for C₁₉H₃₁NNaO₂ ([M+Na]⁺) 328.22470, found 328.22444.

Data are consistent with those reported in the literature.¹⁰

***tert*-Butyl (5-phenylpentan-2-yl)carbamate (33)**

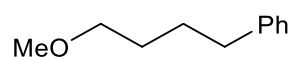
According to the general procedure B, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.2 mg, 10.0 μmol 0.02 equiv), NiCl₂•glyme (11.0 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (10.8 mg, 0.05 mmol, 0.1 equiv), 1-bromo-3-phenylpropane (76 μL, 0.50 mmol, 1.0 equiv), Boc-Ala-OH (142 mg, 0.75 mmol, 1.5 equiv), Cs₂CO₃ (326 mg, 1.0 mmol, 2.0 equiv), water (180 μL, 9.7 mmol, 20 equiv), and 10 mL of MeCN were used. The product was isolated by flash chromatography (5% EtOAc/hexanes) as a colorless oil (94 mg, 71%).

¹H-NMR (500 MHz, CDCl₃): δ 7.31 – 7.24 (m, 2H), 7.21 – 7.14 (m, 3H), 4.30 (br s, 1H), 3.68 (br s, 1H), 2.67 – 2.56 (m, 2H), 1.70 – 1.61 (m, 2H), 1.44 (s, 11H), 1.10 (d, *J* = 6.6 Hz, 3H).

¹³C-NMR (126 MHz, CDCl₃): δ 155.4, 142.3, 128.4, 128.3, 125.7, 79.0, 46.3, 36.9, 35.7, 28.5, 27.9, 21.3.

IR (film): ν_{max} 3343, 2972, 2932, 2861, 1691, 1604, 1498, 1453, 1390, 1365, 1246, 1167, 1105, 1077, 1031, 989, 858, 779, 746, 698.

HRMS (ESI-TOF): *m/z* calcd. for C₁₆H₂₅NNaO₂ ([M+Na]⁺) 286.17775, found 286.17799.

(4-Methoxybutyl)benzene (34)

An oven dried 40 mL vial equipped with a Teflon septum and cross-shape magnetic stir bar was charged with Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.6 mg, 10.3 μmol, 0.02 equiv), NiCl₂•glyme (11.3 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-tert-butyl-2,2'-bipyridyl (13.9 mg, 0.05 mmol, 0.1 equiv), 2-methoxyacetic acid (79 μL, 1.03 mmol, 2 equiv), Cs₂CO₃ (504 mg, 1.55 mmol, 3.0 equiv), and 20 mL MeCN. The reaction mixture was degassed by bubbling nitrogen stream for 15 min at 0 °C. Water (112 μL, 6.20 mmol, 12 equiv) and 1-bromo-3-phenylpropane (80 μL, 0.52 mmol, 1.0 equiv) were then added. The reaction mixture was then stirred and irradiated with two 34 W blue LEDs (vials approximately 6 cm away from the light source) with a fan placed above for cooling. After 24 h, the reaction mixture was diluted with EtOAc, filtered, and concentrated in vacuo. The product was isolated by flash chromatography (2% Et₂O/pentane) as a colorless oil (52 mg, 61%).

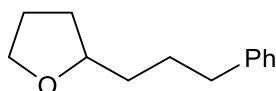
¹H-NMR (500 MHz, CDCl₃): δ 7.31 – 7.24 (m, 2H), 7.22 – 7.14 (m, 3H), 3.39 (t, *J* = 6.3 Hz, 2H), 3.33 (s, 3H), 2.64 (t, *J* = 7.5 Hz, 2H), 1.76 – 1.53 (m, 4H).

¹³C-NMR (126 MHz, CDCl₃): δ 142.6, 128.5, 128.4, 125.8, 72.8, 58.7, 35.9, 29.4, 28.1.

IR (film): ν_{max} 3063, 3027, 2929, 2859, 2827, 1604, 1496, 1453, 1387, 1174, 1117, 1030, 946, 910, 745.

HRMS (EI-TOF): *m/z* calcd. for C₁₁H₁₆O ([M]⁺) 164.1196, found 164.1193.

Data are consistent with those reported in the literature.¹¹

2-(3-Phenylpropyl)tetrahydrofuran (35)

An oven dried 40 mL vial equipped with a Teflon septum and cross-shape magnetic stir bar was charged with Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.6 mg, 10.3 μmol, 0.02 equiv), NiCl₂•glyme (11.3 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (13.9 mg, 0.05 mmol, 0.1 equiv), tetrahydro-2-furoic acid (124 mg, 1.03 mmol, 2.0 equiv), Cs₂CO₃ (420 mg, 1.29 mmol, 2.5 equiv), 7 mL of EtOAc and 3 mL of MeCN. The reaction mixture was degassed by bubbling nitrogen stream for 15 min at 0 °C. Water (56 μL, 3.10 mmol, 6.0 equiv) and 1-bromo-3-phenylpropane (80 μL, 0.52 mmol, 1.0 equiv) were then added. The reaction mixture was then stirred and irradiated with two 34 W blue LEDs (vials approximately 6 cm away from the light source) with a fan placed above for cooling. After 24 h, the reaction mixture was diluted with EtOAc, filtered, and concentrated in vacuo. The product was isolated by flash chromatography (0 to 5% Et₂O/pentane) as a colorless oil (73 mg, 74%).

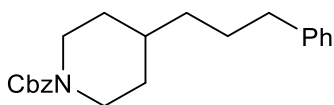
¹H-NMR (500 MHz, CDCl₃): δ 7.29 – 7.24 (m, 2H), 7.21 – 7.15 (m, 3H), 3.88 – 3.77 (m, 2H), 3.71 (td, *J* = 7.9, 6.3 Hz, 1H), 2.70 – 2.59 (m, 2H), 2.00 – 1.92 (m, 1H), 1.91 – 1.71 (m, 3H), 1.71 – 1.57 (m, 2H), 1.56 – 1.36 (m, 2H).

¹³C-NMR (126 MHz, CDCl₃): δ 142.6, 128.5, 128.4, 125.8, 79.3, 67.8, 36.1, 35.4, 31.5, 28.3, 25.8.

IR (film): ν_{max} 3026, 2933, 2858, 1603, 1496, 1454, 1067, 1029, 919, 747

HRMS (EI-TOF): *m/z* calcd. for C₁₃H₁₈O ([M]⁺) 190.1352, found 190.1354.

Data are consistent with those reported in the literature.¹²

Benzyl 4-(3-phenylpropyl)piperidine-1-carboxylate (36)

An oven dried 40 mL vial equipped with a Teflon septum and cross-shape magnetic stir bar was charged with Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.6 mg, 10.3 μmol, 0.02 equiv), NiCl₂•glyme (11.3 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (13.9 mg, 0.05 mmol, 0.1 equiv), Cbz-Inp-OH (272 mg, 1.03 mmol, 2.0 equiv), Cs₂CO₃ (420 mg, 1.29 mmol, 2.5 equiv), and 10 mL of MeCN. The reaction mixture was degassed by bubbling nitrogen stream for 15 min at 0 °C. Water (56 μL, 3.10 mmol, 6.0 equiv) and 1-bromo-3-phenylpropane (80 μL, 0.52 mmol, 1.0 equiv) were then added. The reaction mixture was then stirred (300 rpm) and irradiated with two 34 W blue LEDs (vials approximately 6 cm away from the light source) with a fan placed above for cooling. After 26 h, the reaction mixture was diluted with EtOAc, filtered, and concentrated in vacuo. The product was isolated by flash chromatography (0 to 1% EtOAc/toluene) as a colorless oil (107 mg, 62%).

¹H-NMR (500 MHz, CDCl₃): rotameric mixture δ 7.40 – 7.35 (m, 4H), 7.35 – 7.27 (m, 3H), 7.23 – 7.16 (m, 3H), 5.14 (s, 2H), 4.17 (br s, 2H), 2.76 (br s, 2H), 2.61 (t, *J* = 7.7 Hz, 2H), 1.76 – 1.59 (m, 4H), 1.49 – 1.37 (m, 1H), 1.34 – 1.26 (m, 2H), 1.11 (br s, 2H).

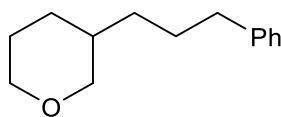
¹³C-NMR (126 MHz, CDCl₃): rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ 155.4, 142.6, 137.1, 128.5, 128.4, 128.4, 128.0, 127.9, 125.8, 67.0, 44.4, 36.2*, 35.9, (32.2) 32.1, 28.6.

IR (film): ν_{max} 3027, 2928, 2853, 1697, 1497, 1429, 1363, 1277, 1232, 1163, 1120, 1082, 1020, 965, 748, 698.

HRMS (ESI-TOF): *m/z* calcd. for C₂₂H₂₇NNaO₂ ([M+Na]⁺) 360.19340, found 360.19353.

Data are consistent with those reported in the literature.¹³

* This peak corresponds to two coincident ¹³C signals

3-(3-Phenylpropyl)tetrahydro-2H-pyran (37)

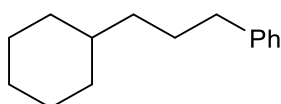
An oven dried 40 mL vial equipped with a Teflon septum and cross-shape magnetic stir bar was charged with Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.6 mg, 10.3 μmol, 0.02 equiv), NiCl₂•glyme (11.3 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (13.9 mg, 0.05 mmol, 0.1 equiv), tetrahydro-2*H*-pyran-3-carboxylic acid (134 mg, 1.03 mmol, 2.0 equiv), Cs₂CO₃ (504 mg, 1.29 mmol, 3.0 equiv) and 10 mL of MeCN. The reaction mixture was degassed by bubbling nitrogen stream for 15 min at 0 °C. Water (56 μL, 3.10 mmol, 6.0 equiv) and 1-bromo-3-phenylpropane (80 μL, 0.52 mmol, 1.0 equiv) were then added. The reaction mixture was then stirred and irradiated with two 34 W blue LEDs (vials approximately 6 cm away from the light source) in a water bath with a fan placed above for cooling. After 24 h, the reaction mixture was diluted with EtOAc, filtered, and concentrated in vacuo. The product was isolated by flash chromatography (2 to 5% EtOAc/hexanes) as a light yellow oil (70 mg, 66%).

¹H-NMR (500 MHz, CDCl₃): δ 7.31 – 7.26 (m, 2H), 7.21 – 7.14 (m, 3H), 3.91 – 3.82 (m, 2H), 3.33 (ddd, *J* = 11.0, 9.5, 4.0 Hz, 1H), 3.03 (dd, *J* = 11.2, 10.1 Hz, 1H), 2.59 (t, *J* = 7.7 Hz, 2H), 1.91 – 1.82 (m, 1H), 1.70 – 1.53 (m, 5H), 1.30 – 1.04 (m, 3H).

¹³C-NMR (126 MHz, CDCl₃): δ 142.6, 128.5, 128.4, 125.8, 73.6, 68.6, 36.2, 36.0, 32.2, 30.1, 28.6, 26.0.

IR (film): ν_{max} 3026, 2929, 2846, 1603, 1496, 1453, 1278, 1186, 1093, 1035, 944, 907, 873, 856, 747.

HRMS (EI-TOF): *m/z* calcd. for C₁₄H₂₀O ([M]⁺) 204.1509, found 204.1512

(3-Cyclohexylpropyl)benzene (38)

An oven dried 40 mL vial equipped with a Teflon septum and cross-shape magnetic stir bar was charged with Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.6 mg, 10.3 μmol, 0.02 equiv), NiCl₂•glyme (11.3 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (13.9 mg, 0.05 mmol, 0.1 equiv), cyclohexanecarboxylic acid (132 mg, 1.03 mmol, 2.0 equiv), Cs₂CO₃ (504 mg, 1.29 mmol, 3.0 equiv), 14 mL of EtOAc and 6 mL of MeCN. The reaction mixture was degassed by bubbling nitrogen stream for 15 min at 0 °C. Water (140 μL, 7.70 mmol, 15 equiv) and 1-bromo-3-phenylpropane (80 μL, 0.52 mmol, 1.0 equiv) were then added. The reaction mixture was then stirred and irradiated with two 34 W blue LEDs (vials approximately 6 cm away from the light source) in a water bath with a fan placed above for cooling. After 24 h, an additional portion of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.6 mg, 10.3 μmol, 0.02 equiv) was added in a minimal amount of MeCN. After a further 24 h of irradiation, the reaction mixture was diluted with EtOAc, filtered, and concentrated in vacuo. The product was isolated by flash chromatography (pentane) as a colorless oil (54 mg, 52%).

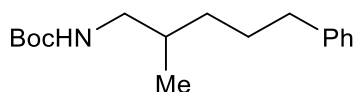
¹H-NMR (500 MHz, CDCl₃): δ 7.30 – 7.24 (m, 2H), 7.21 – 7.14 (m, 3H), 2.58 (t, *J* = 7.6 Hz, 2H), 1.75 – 1.56 (m, 7H), 1.29 – 1.07 (m, 6H), 0.93 – 0.79 (m, 2H).

¹³C-NMR (126 MHz, CDCl₃): δ 143.1, 128.5, 128.3, 125.7, 37.7, 37.3, 36.4, 33.5, 29.0, 26.9, 26.6.

IR (film): ν_{max} 3027, 2921, 2850, 1496, 1449, 745, 697.

HRMS (EI-TOF): *m/z* calcd. for C₁₅H₂₂ ([M]⁺) 202.1716, found 202.1719

Data are consistent with those reported in the literature.¹³

***tert*-Butyl (2-methyl-5-phenylpentyl)carbamate (39)**

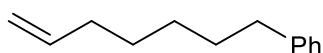
An oven dried 8 mL vial equipped with a Teflon septum and magnetic stir bar was charged with Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.6 mg, 10.3 μmol, 0.02 equiv), NiCl₂•glyme (11.3 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (13.9 mg, 0.05 mmol, 0.1 equiv), 3-((*tert*-butoxycarbonyl)amino)-2-methylpropanoic acid (210 mg, 1.03 mmol, 2.0 equiv), Cs₂CO₃ (504 mg, 1.29 mmol, 3.0 equiv), 3.5 mL of EtOAc and 1.5 mL of MeCN. The reaction mixture was degassed by bubbling nitrogen stream for 15 min at 0 °C. Water (28 μL, 1.55 mmol, 3.0 equiv) and 1-bromo-3-phenylpropane (80 μL, 0.52 mmol, 1.0 equiv) were then added. The reaction mixture was then stirred and irradiated with two 34 W blue LEDs (vials approximately 6 cm away from the light source) in a water bath with a fan placed above for cooling. After 24 h, the reaction mixture was diluted with EtOAc, filtered, and concentrated in vacuo. The product was isolated by flash chromatography (0 to 0.5% EtOAc/toluene) as a colorless oil (83 mg, 58%).

¹H-NMR (500 MHz, CDCl₃): δ 7.30 – 7.24 (m, 2H), 7.21 – 7.13 (m, 3H), 4.52 (br s, NH), 3.12 – 2.97 (m, 1H), 2.96 – 2.81 (m, 1H), 2.65 – 2.53 (m, 2H), 1.74 – 1.54 (m, 3H), 1.44 (s, 9H), 1.42 – 1.34 (m, 1H), 1.20 – 1.10 (m, 1H), 0.88 (d, *J* = 6.7 Hz, 3H).

¹³C-NMR (126 MHz, CDCl₃): δ 156.2, 142.6, 128.5, 128.4, 125.8, 79.1, 46.7, 36.2, 33.9, 33.7, 28.9, 28.5, 17.6.

IR (film): ν_{max} 3353, 2930, 1695, 1512, 1454, 1391, 1365, 1248, 1170, 996, 748, 699.

HRMS (ESI-TOF): *m/z* calcd. for C₁₇H₂₇NNaO₂ ([M+Na]⁺) 300.19340, found 300.19326

Hept-6-en-1-ylbenzene (40)

An oven dried 40 mL vial equipped with a Teflon septum and cross-shape magnetic stir bar was charged with Ir[dF(F)ppy]₂(dtbbpy)PF₆ (**III**) (11.7 mg, 11.0 μmol, 0.02 equiv), NiCl₂•glyme (12.6 mg, 0.06 mmol, 0.1 equiv), 4,4'-di-methyl-2,2'-bipyridyl (10.6 mg, 0.06 mmol, 0.1 equiv), cyclopropylacetic acid (107 μL, 115 mg, 1.15 mmol, 2.0 equiv), Cs₂CO₃ (560 mg, 1.72 mmol, 3.0 equiv), 11 mL of EtOAc and 11 mL of MeCN. The reaction mixture was degassed by bubbling nitrogen stream for 15 min at 0 °C. Water (155 μL, 8.60 mmol, 15 equiv) and 1-bromo-3-phenylpropane (87 μL, 0.57 mmol, 1.0 equiv) were then added. The reaction mixture was then stirred and irradiated with two 34 W blue LEDs (vials approximately 6 cm away from the light source) in a water bath with a fan placed above for cooling. After 24 h, an additional portion of Ir[dF(F)ppy]₂(dtbbpy)PF₆ (**III**) (11.7 mg, 11.0 μmol, 0.02 equiv) was added in a minimal amount of MeCN. After a further 24 h of irradiation, the reaction mixture was diluted with EtOAc, filtered, and concentrated in vacuo. The product was isolated by flash chromatography (pentane) as a colorless oil (43 mg, 43%).

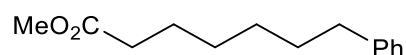
¹H-NMR (500 MHz, CDCl₃): δ 7.31 – 7.23 (m, 2H), 7.21 – 7.13 (m, 3H), 5.81 (ddt, *J* = 16.9, 10.3, 6.7 Hz, 1H), 5.05 – 4.83 (m, 2H), 2.61 (t, *J* = 7.9 Hz, 2H), 2.05 (q, *J* = 7.1 Hz, 2H), 1.63 (p, *J* = 7.5 Hz, 2H), 1.46 – 1.31 (m, 4H).

¹³C-NMR (126 MHz, CDCl₃): δ 143.0, 139.2, 128.5, 128.4, 125.7, 114.4, 36.1, 33.9, 31.5, 29.0, 28.9.

IR (film): ν_{max} 3064, 3028, 2928, 2855, 1641, 1605, 1496, 1454, 1030, 993, 909, 745.

HRMS (EI-TOF): *m/z* calcd. for C₁₃H₁₈ ([M]⁺) 174.1403, found 174.1402

Data are consistent with those reported in the literature.¹⁵

Methyl 7-phenylheptanoate (41)

An oven dried 40 mL vial equipped with a Teflon septum and cross-shape magnetic stir bar was charged with Ir[dF(F)ppy]₂(dtbbpy)PF₆ (**III**) (11.7 mg, 11.0 μmol, 0.02 equiv), NiCl₂•glyme (12.6 mg, 0.06 mmol, 0.1 equiv), 4,4'-di-methyl-2,2'-bipyridyl (10.6 mg, 0.06 mmol, 0.1 equiv), mono-Methyl glutarate (143 μL, 167 mg, 1.15 mmol, 2.0 equiv), Cs₂CO₃ (560 mg, 1.72 mmol, 3.0 equiv), and 23 mL of MeCN. The reaction mixture was degassed by bubbling nitrogen stream for 15 min at 0 °C. Water (155 μL, 8.60 mmol, 15 equiv) and 1-bromo-3-phenylpropane (87 μL, 0.57 mmol, 1.0 equiv) were then added. The reaction mixture was then stirred and irradiated with two 34 W blue LEDs (vials approximately 6 cm away from the light source) in a water bath with a fan placed above for cooling. After 24 h, the reaction mixture was diluted with EtOAc, filtered, and concentrated in vacuo. The product was isolated by flash chromatography (2% Et₂O/pentane) as a colorless oil (50 mg, 40%).

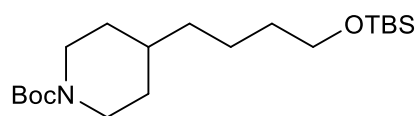
¹H-NMR (500 MHz, CDCl₃): δ 7.31 – 7.23 (m, 2H), 7.21 – 7.13 (m, 3H), 3.66 (s, 3H), 2.60 (t, *J* = 7.7 Hz, 2H), 2.30 (t, *J* = 7.5 Hz, 2H), 1.68 – 1.57 (m, 4H), 1.40 – 1.28 (m, 4H).

¹³C-NMR (126 MHz, CDCl₃): δ 174.4, 142.8, 128.5, 128.4, 125.7, 51.6, 36.0, 34.2, 31.4, 29.1, 29.0, 25.0.

IR (film): ν_{max} 3027, 2930, 2857, 1738, 1604, 1496, 1454, 1436, 1361, 1251, 1197, 1171, 1093, 1015, 879, 747, 699.

HRMS (ESI-TOF): *m/z* calcd. for C₁₄H₂₁O₂ ([M+H]⁺) 221.15361, found 221.15362

Data are consistent with those reported in the literature.¹⁴

***tert*-Butyl 4-(4-((*tert*-butyldimethylsilyloxy)butyl)piperidine-1-carboxylate**

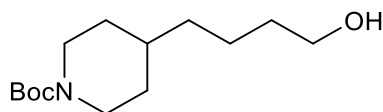
According to the procedure as for **36**, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.2 mg, 10.0 μmol, 0.02 equiv), NiCl₂•glyme (11.0 mg, 0.050 mmol, 0.1 equiv), 4,4'-di-*tert*butyl-2,2'-bipyridyl (10.8 mg, 0.05 mmol, 0.1 equiv), (4-bromobutoxy)(*tert*-butyl)dimethylsilane (100 mg, 0.5 mmol, 1.0 equiv), 1-(*tert*-butoxycarbonyl)piperidine-4-carboxylic acid (229 mg, 1.00 mmol, 2.0 equiv), Cs₂CO₃ (407 mg, 1.25 mmol, 2.5 equiv), water (54 μL, 3.00 mmol, 6.0 equiv), and 10 mL of MeCN were used. The product was isolated by flash chromatography (3% EtOAc/hexanes) as a colorless oil (118 mg, 64%).

¹H-NMR (500 MHz, CDCl₃): δ 4.06 (br s, 2H), 3.60 (t, *J* = 6.5 Hz, 2H), 2.66 (br s, 2H), 1.64 (br d, *J* = 13.2 Hz, 2H), 1.54 – 1.41 (m, 11H), 1.40 – 1.29 (m, 3H), 1.27 – 1.20 (m, 2H), 1.13 – 1.00 (m, 2H), 0.89 (s, 9H), 0.04 (s, 6H).

¹³C-NMR (126 MHz, CDCl₃): δ 155.1, 79.3, 63.3, 44.5, 43.8, 36.5, 36.1, 33.1, 32.3, 28.6, 26.1, 23.0, 18.5, -5.1.

IR (film): ν_{max} 2929, 2856, 1695, 1472, 1420, 1390, 1365, 1277, 1243, 1166, 1096, 1045, 1006, 960, 937, 834, 773, 661.

HRMS (ESI-TOF): *m/z* calcd. for C₂₀H₄₁NNaO₃Si ([M+Na]⁺) 394.27479, found 394.27435.

***tert*-Butyl 4-(4-hydroxybutyl)piperidine-1-carboxylate (44)**

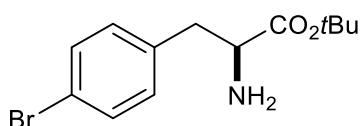
tert-Butyl 4-(4-((*tert*-butyldimethylsilyl)oxy)butyl)piperidine-1-carboxylate (380 mg, 1.02 mmol) was dissolved in dry THF (5 ml) and cooled to 0 °C. TBAF (1 M in THF, 1.50 ml, 1.50 mmol, 1.5 equiv) was slowly added and the mixture was allowed to stir over night at room temperature, quenched by the addition of aq. NH₄Cl (sat, 10 ml) and the aqueous phase was extracted with DCM (3x). The combined organic phases were dried over Na₂SO₄ and the solvent removed. The product was isolated by flash chromatography (33% EtOAc/hexanes) as yellow oil (246 mg, 93%).

¹H-NMR (500 MHz, CDCl₃): δ 4.06 (br s, 2H), 3.64 (t, *J* = 6.6 Hz, 2H), 2.66 (br s, 2H), 1.64 (d, *J* = 13.1 Hz, 2H), 1.60 – 1.51 (m, 2H), 1.45 (s, 9H), 1.42 – 1.33 (m, 3H), 1.31 – 1.20 (m, 3H), 1.07 (qd, *J* = 12.4, 4.3 Hz, 2H).

¹³C-NMR (126 MHz, CDCl₃): δ 155.1, 79.3, 63.1, 44.2 (br & weak), 36.4, 36.1, 33.1, 32.3 (br), 28.6, 23.0.

IR (film): ν_{\max} 3425, 1927, 2854, 1692, 1669, 1422, 1366, 1277, 1240, 1159, 1067, 1035, 977, 962, 943, 865, 822, 769.

HRMS (ESI-TOF): *m/z* calcd. for C₁₄H₂₇NNaO₃ ([M+Na]⁺) 280.18831, found 280.18863.

***tert*-Butyl (*S*)-2-amino-3-(4-bromophenyl)propanoate**

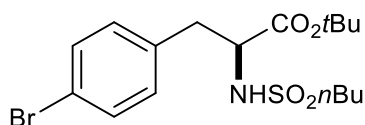
(*S*)-2-amino-3-(4-bromophenyl)propanoic acid (2.00 g, 8.19 mmol) was suspended in *t*BuOAc (22 ml), cooled to 0 °C and HClO₄ (70%, 1.10 ml, 13.1 mmol, 1.5 equiv) was added slowly under N₂ and the resulting clear solution was stirred over night at room temperature. The solution was washed with water and aq. HCl (1 M), the combined aqueous phases were basified with aq. K₂CO₃ (10%) to pH 9 and extracted with DCM (4x). The organic phases were washed with brine, dried over Na₂SO₄ and the solvent removed. The product was isolated as colorless oil and used for the next step without further purification (1.62 g, 66%).

¹H-NMR (500 MHz, CDCl₃): δ 7.42 (d, *J* = 8.3 Hz, 2H), 7.10 (d, *J* = 8.3 Hz, 2H), 3.57 (t, *J* = 6.7 Hz, 1H), 2.98 (dd, *J* = 13.6, 5.7 Hz, 1H), 2.79 (dd, *J* = 13.6, 7.7 Hz, 1H), 1.43 (s, 9H).

¹³C-NMR (126 MHz, CDCl₃): δ 174.3, 136.8, 131.6, 131.3, 120.7, 81.5, 56.3, 40.7, 28.2.

IR (film): ν_{max} 3382, 2977, 2932, 1725, 1592, 1488, 1456, 1393, 1367, 1283, 1248, 1149, 1072, 1012, 843, 800, 747, 712.

HRMS (ESI-TOF): *m/z* calcd. for C₁₃H₁₉BrNO₂ ([M+H]⁺) 300.05937, found 300.05946.

***tert*-Butyl (*S*)-3-(4-bromophenyl)-2-(butylsulfonamido)propanoate**

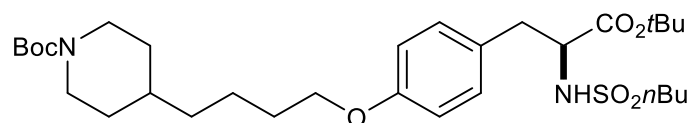
tert-Butyl (*S*)-2-amino-3-(4-bromophenyl)propanoate (1.00 g, 3.33 mmol) was dissolved in DCM (17 ml) and cooled to 0 °C. Triethylamine (0.93 ml, 6.66 mmol, 2.0 equiv) was added followed by dropwise addition of butane-1-sulfonyl chloride (0.65 ml, 5.00 mmol, 1.5 equiv). The clear solution was stirred 2 h at room temperature and after completion (TLC) quenched by the addition of aq. HCl (1 M). The phases were separated, the organic phase washed with aq. NaHCO₃ (sat.) and brine, dried over Na₂SO₄ and evaporated to dryness. The product was isolated by flash chromatography (20% EtOAc/hexanes) as yellow oil (1.20 g, 86%).

¹H-NMR (500 MHz, CDCl₃): δ 7.44 (d, *J* = 8.3 Hz, 2H), 7.10 (d, *J* = 8.4 Hz, 2H), 4.74 (d, *J* = 9.2 Hz, 1H), 4.20 (ddd, *J* = 9.2, 7.0, 5.8 Hz, 1H), 3.05 (dd, *J* = 13.9, 5.8 Hz, 1H), 2.95 (dd, *J* = 13.9, 7.0 Hz, 1H), 2.77 (t, *J* = 8.1 Hz, 2H), 1.72 – 1.58 (m, 2H), 1.44 (s, 9H), 1.33 (h, *J* = 7.5 Hz, 2H), 0.89 (t, *J* = 7.4 Hz, 3H).

¹³C-NMR (126 MHz, CDCl₃): δ 170.5, 134.9, 131.8, 131.5, 121.4, 83.4, 57.4, 53.6, 39.4, 28.1, 25.5, 21.6, 13.7.

IR (film): ν_{max} 3274, 2964, 2934, 2875, 1729, 1489, 1456, 1407, 1394, 1368, 1327, 1277, 1258, 1143, 1112, 1072, 1012, 956, 937, 840, 812, 766, 748, 712.

HRMS (ESI-TOF): *m/z* calcd. for C₁₇H₂₆BrNNaO₄ ([M+Na]⁺) 442.06581, found 442.06602.

***tert*-butyl (S)-4-(4-(4-(3-(*tert*-butoxy)-2-(butylsulfonamido)-3-oxopropyl)phenoxy)butyl)piperidine-1-carboxylate**

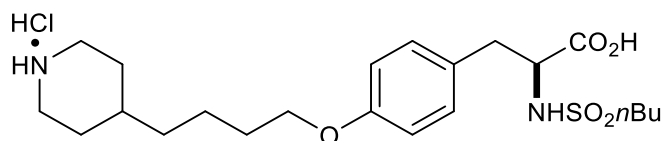
tert-Butyl (*S*)-3-(4-bromophenyl)-2-(butylsulfonamido)propanoate (168 mg, 0.40 mmol) was weighed into an 8 ml oven dried vial and evacuated for 30 min. K_2CO_3 (55.0 mg, 0.40 mmol, 1.0 equiv) was added, followed by a solution of $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (**I**) (4.50 mg, 4.00 μ mol 0.01 equiv), $NiCl_2 \cdot glyme$ (8.79 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*butyl-2,2'-bipyridyl (10.7 mg, 0.04 mmol, 0.1 equiv) and Quinuclidine (4.45 mg, 0.04 mmol, 0.1 equiv) in acetonitrile (1.5 ml). *Tert*-Butyl 4-(4-hydroxybutyl)piperidine-1-carboxylate **43** (154 mg, 0.60 mmol, 1.5 equiv) was added in acetonitrile (0.5 ml) and the mixture was evacuated and cooled to -78 °C. After evacuating for 5 min the vial was backfilled with nitrogen and warmed to room temperature. This process was repeated three times, then the vial was sealed with parafilm, placed 1 cm away from 3 blue LED strips, and irradiated under fan cooling. After 48 h, EtOAc (10 ml) and water (10 ml) was added, the phases separated and the aqueous phase extracted with EtOAc (5x). The combined organic phases were washed with brine, dried over Na_2SO_4 and evaporated to dryness. The product was isolated by flash chromatography (10% EtOAc/hexanes) as colorless oil (146 mg, 60%). In addition non reacted aryl bromide was reisolated (57 mg, 34%).

1H -NMR (500 MHz, $CDCl_3$): δ 7.11 (d, $J = 8.5$ Hz, 2H), 6.82 (d, $J = 8.5$ Hz, 2H), 4.68 (d, $J = 9.3$ Hz, 1H), 4.18 (ddd, $J = 9.1, 6.9, 5.7$ Hz, 1H), 4.07 (br s, 2H), 3.92 (t, $J = 6.4$ Hz, 2H), 3.03 (dd, $J = 13.9, 5.6$ Hz, 1H), 2.93 (dd, $J = 13.9, 7.0$ Hz, 1H), 2.78 – 2.71 (m, 2H), 2.67 (br s, 2H), 1.76 (p, $J = 6.7$ Hz, 2H), 1.69 – 1.59 (m, 4H), 1.53 – 1.37 (m, 20H), 1.30 (p, $J = 7.3$ Hz, 5H), 1.08 (qd, $J = 12.4, 4.3$ Hz, 2H), 0.87 (t, $J = 7.3$ Hz, 3H).

^{13}C -NMR (126 MHz, $CDCl_3$): δ 170.9, 158.5, 155.1, 130.8, 127.6, 114.7, 83.0, 79.3, 68.0, 57.8, 53.6, 39.0, 36.4, 36.1, 32.3, 29.6, 28.6, 28.1, 25.5, 23.3, 21.6, 13.6.

IR (film): ν_{max} 3270, 2932, 2866, 1732, 1690, 1613, 1513, 1424, 1393, 1366, 1328, 1300, 1277, 1245, 1145, 1116, 1032, 962, 914, 841, 769, 730.

HRMS (ESI-TOF): m/z calcd. for $C_{31}H_{52}N_2NaO_7S$ ($[M+Na]^+$) 619.33874, found 619.33839.

(S)-2-(butylsulfonamido)-3-(4-(4-(piperidin-4-yl)butoxy)phenyl) propanoic acid hydrochloride (Tirofiban, 45)

tert-butyl (S)-4-(4-(4-(3-(*tert*-butoxy)-2-(butylsulfonamido)-3-oxopropyl)phenoxy)butyl) piperidine-1-carboxylate (50.0 mg, 0.08 mmol) was dissolved in DCM (0.5 ml) and cooled to 0 °C. Under vigorous stirring, HCl (4 M in Dioxane, 0.84 ml, 3.35 mmol, 40 equiv) was added and the mixture stirred over night at room temperature. The solution was sparged with nitrogen to remove excess HCl and evaporated to dryness. The resulting gum was layered with Et₂O, and the precipitate was dried on high vacuum and washed thoroughly with Et₂O. The product was isolated by decantation as colorless solid (39.0 mg 98%).

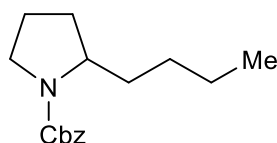
¹H-NMR (500 MHz, CD₃OD): 7.19 (d, *J* = 8.2 Hz, 2H), 6.85 (d, *J* = 8.2 Hz, 2H), 4.09 (dd, *J* = 9.7, 4.7 Hz, 1H), 3.97 (t, *J* = 6.2 Hz, 2H), 3.36 (d, *J* = 12.9 Hz, 2H), 3.11 (dd, *J* = 13.9, 4.7 Hz, 1H), 2.95 (td, *J* = 13.0, 3.0 Hz, 2H), 2.78 (dd, *J* = 13.8, 9.7 Hz, 1H), 2.66 (ddd, *J* = 9.0, 6.2, 2.0 Hz, 2H), 1.96 (d, *J* = 12.5 Hz, 2H), 1.78 (p, *J* = 6.6 Hz, 2H), 1.68 – 1.58 (m, 1H), 1.53 (dtd, *J* = 18.6, 11.4, 9.0, 5.4 Hz, 3H), 1.42 – 1.29 (m, 5H), 1.28 – 1.20 (m, 2H), 0.85 (t, *J* = 7.3 Hz, 3H).

¹³C-NMR (126 MHz, CD₃OD): δ 175.2, 159.5, 131.7, 130.5, 115.4, 68.7, 59.5, 54.1, 45.4, 39.1, 36.8, 34.8, 30.4, 30.1, 26.5, 24.0, 22.5, 13.9.

IR (film): ν_{\max} 2934, 2871, 1730, 1612, 1512, 1455, 1379, 1299, 1243, 1177, 1140, 1115, 1077, 1040, 958, 836, 731.

HRMS (ESI-TOF): *m/z* calcd. for C₂₂H₃₇N₂O₅S ([M+H]⁺) 441.24177, found 441.24123.

Data are consistent with those reported in the literature.¹⁶

Benzyl 2-butylpyrrolidine-1-carboxylate (46)

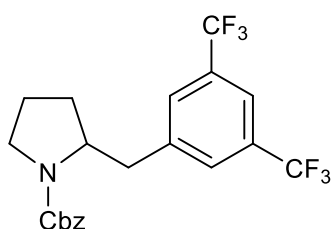
According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (10.5 mg, 9.3 μmol 0.02 equiv), NiCl₂•glyme (10.2 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (10.1 mg, 0.05 mmol, 0.1 equiv), bromobutane (50 μL, 0.47 mmol, 1.0 equiv), Cbz-Pro-OH (174 mg, 0.70 mmol, 1.5 equiv), K₂CO₃ (129 mg, 0.93 mmol, 2.0 equiv), water (168 μL, 9.3 mmol, 20 equiv), and 4.7 mL of MeCN were used. The product was isolated by flash chromatography (5% EtOAc/hexanes) as a colorless oil (93 mg, 76%).

¹H-NMR (500 MHz, CDCl₃) rotameric mixture: δ 7.45 – 7.27 (m, 5H), 5.22 – 5.07 (m, 2H), 3.88 – 3.79 (m, 1H), 3.54 – 3.32 (m, 2H), 1.98 – 1.75 (m, 4H), 1.72 – 1.63 (m, 1H), 1.40 – 1.11 (m, 5H), 0.89 and 0.84 (2 t, *J* = 7.0 Hz, 3H, rotamer).

¹³C-NMR (126 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ (155.2) 155.0, 137.3 (137.2), 128.5, 127.9, (66.7) 66.5, 58.2 (57.5), (46.7) 46.4, (34.4) 33.7, 30.7 (29.9), 28.6 (28.5), 23.9 (23.2), 22.9 (22.7), 14.3 (14.2).

IR (film): ν_{\max} 3033, 2955, 2930, 2872, 1698, 1498, 1453, 1409, 1356, 1335, 1249, 1213, 1186, 1099, 1029, 983, 914, 866, 769, 739, 697.

HRMS (ESI-TOF): *m/z* calcd. for C₁₆H₂₃NNaO₂ ([M+Na]⁺) 284.16210, found 284.16200.

Benzyl 2-(3,5-bis(trifluoromethyl)benzyl)pyrrolidine-1-carboxylate (47)

According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (7.90 mg, 7.00 μmol 0.02 equiv), NiCl₂•glyme (7.70 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (7.60 mg, 0.04 mmol, 0.1 equiv), 1-(chloromethyl)-3,5-bis(trifluoromethyl)benzene (92 mg, 0.35 mmol, 1.0 equiv), Cbz-Pro-OH (131 mg, 0.53 mmol, 1.5 equiv), K₂CO₃ (97.0 mg, 0.70 mmol, 2.0 equiv), water (126 μL, 7.00 mmol, 20 equiv), and 3.5 mL of MeCN were used. The product was isolated by flash chromatography (5% EtOAc/hexanes) as a colorless oil (89 mg, 59%).

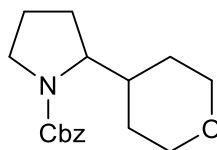
¹H-NMR (500 MHz, CDCl₃) rotameric mixture: δ 7.76–7.65 (m, 2H), 7.50 (s, 1H), 7.42–7.30 (m, 5H), 5.21–5.11 (m, 2H), 4.11 and 4.04 (2 br s, 1H, rotamer), 3.54–3.11 (m, 3H), 2.77 and 2.65 (2 dd, *J* = 13.1, 9.4 Hz, 1H), 1.96–1.56 (m, 4H).

¹³C-NMR (126 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ 155.1 (154.9), 141.5, 137.0 (136.5), (131.8 (q, *J* = 33.5 Hz)) 131.7 (q, *J* = 32.7 Hz), 129.7–128.0 (m), 123.5 (q, *J* = 272.8 Hz) (123.4 (q, *J* = 273.1 Hz)), 120.6, (67.4) 66.9, 58.9 (58.7), (47.0) 46.8, (40.8) 39.4, (30.1) 29.2, 23.7 (22.9).

¹⁹F-NMR (282 MHz, CDCl₃): δ –62.8.

IR (film): *v*_{max} 3037, 2962, 2882, 1698, 1622, 1499, 1454, 1311, 1379, 1357, 1338, 1277, 1170, 1127, 1089, 1030, 977, 934, 897, 844, 770, 735, 707, 698, 683.

HRMS (ESI-TOF): *m/z* calcd. for C₂₁H₂₀F₆NO₂ ([M+H]⁺) 432.13927, found 432.14008.

Benzyl 2-(tetrahydro-2H-pyran-4-yl)pyrrolidine-1-carboxylate (48)

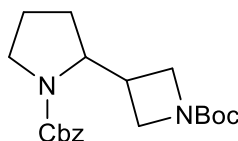
According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (9.30 mg, 8.30 μmol 0.02 equiv), NiCl₂•glyme (9.10 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (9.00 mg, 0.041 mmol, 0.1 equiv), 4-bromotetrahydro-2H-pyran (47 μL, 0.42 mmol, 1.0 equiv), Cbz-Pro-OH (155 mg, 0.62 mmol, 1.5 equiv), K₂CO₃ (115 mg, 0.83 mmol, 2.0 equiv), water (150 μL, 8.30 mmol, 20 equiv), and 4.2 mL of MeCN were used. The product was isolated by flash chromatography (15% EtOAc/hexanes) as a colorless oil (100 mg, 83%).

¹H-NMR (500 MHz, CDCl₃): δ 7.41 – 7.28 (m, 5H), 5.24 – 5.05 (m, 2H), 4.03 – 3.89 (m, 2H), 3.88 – 3.73 (m, 1H), 3.66 – 3.47 (m, 1H), 3.42 – 3.17 (m, 3H), 2.16 – 2.02 (m, 1H), 1.92 – 1.73 (m, 4H), 1.55 – 1.23 (m, 4H).

¹³C-NMR (126 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ (155.6) 155.5, 137.2 (137.0), 128.6, 128.2 (128.1), (128.0) 127.9, (68.3) 68.1, (67.0) 66.7, 61.9 (61.4), (47.1) 47.0, (38.9) 38.1, (30.1) 30.1, (28.2) 27.8, (27.4) 26.5, 24.5 (23.6).

IR (film): ν_{max} 2949, 2843, 1698, 1498, 1455, 1409, 1354, 1332, 1269, 1238, 1184, 1139, 1100, 1014, 985, 920, 832, 770, 750, 698.

HRMS (ESI-TOF): m/z calcd. for C₁₇H₂₄NO₃ ([M+H]⁺) 290.17507, found 290.17507.

Benzyl 2-(1-(*tert*-butoxycarbonyl)azetidin-3-yl)pyrrolidine-1-carboxylate (49)

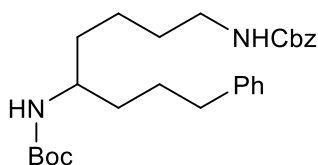
According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**1**) (8.20 mg, 7.30 μmol 0.02 equiv), NiCl₂•glyme (8.10 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (7.90 mg, 0.04 mmol, 0.1 equiv), 3-bromo-Boc-azetidine (87.0 mg, 0.37 mmol, 1.0 equiv), Cbz-Pro-OH (137 mg, 0.55 mmol, 1.5 equiv), K₂CO₃ (101 mg, 0.73 mmol, 2.0 equiv), water (132 μL, 7.30 mmol, 20 equiv), and 3.7 mL of MeCN were used. The product was isolated by preparative SFC as a colorless oil (65 mg, 50%).

¹H-NMR (500 MHz, CDCl₃): δ 7.42 – 7.29 (m, 5H), 5.19 – 5.03 (m, 2H), 4.17 – 3.73 (m, 4H), 3.69 – 3.47 (m, 2H), 3.41 – 3.30 (m, 1H), 2.87 – 2.65 (m, 1H), 2.06 – 1.93 (m, 1H), 1.92 – 1.79 (m, 2H), 1.70 – 1.59 (m, 1H), 1.42 (s, 9H).

¹³C-NMR (126 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ 156.4, 155.6 (155.3), 136.9 (136.5), 128.5, (128.3) 128.0, 127.9, 79.3, (67.2) 66.8, 60 (59.3), 54.0, 50.6, (47.3) 47.1, 33.0, (28.8) 28.0, 28.5, 23.8 (23.1)

IR (film): ν_{max} 2971, 2884, 1693, 1479, 1453, 1404, 1360, 1250, 1128, 1099, 1025, 972, 918, 863, 770, 753, 698.

HRMS (ESI-TOF): m/z calcd. for C₂₀H₂₈NS₂NaO₄ ([M+Na]⁺) 383.19413, found 383.19438.

Benzyl *tert*-butyl (8-phenyloctane-1,5-diyl)dicarbamate (50)

According to the general procedure B, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (**I**) (11.2 mg, 10.0 μmol 0.02 equiv), NiCl₂•glyme (11.0 mg, 0.05 mmol, 0.1 equiv), 4,4'-di-methoxy-2,2'-bipyridyl (10.8 mg, 0.05 mmol, 0.1 equiv), 1-bromo-3-phenylpropane (76 μL, 0.50 mmol, 1.0 equiv), Boc-Lys(Cbz)-OH (285 mg, 0.75 mmol, 1.5 equiv), Cs₂CO₃ (326 mg, 1.0 mmol, 2.0 equiv), water (180 μL, 9.70 mmol, 20 equiv), and 10 mL of MeCN were used. The product was isolated by flash chromatography (20% EtOAc/hexanes) as a colorless solid (144 mg, 65%).

¹H-NMR (500 MHz, CDCl₃) rotameric mixture: δ 7.37 – 7.34 (m, 3H), 7.34 – 7.30 (m, 1H), 7.31 – 7.24 (m, 3H), 7.20 – 7.15 (m, 3H), 5.18 – 5.05 (m, 2H), 4.81 and 4.72 (2 br s, 1H, rotamers), 4.24 and 4.17 (d and br s, *J* = 9.3 Hz, 1H, rotamers), 3.57 and 3.43 (2 br s, 1H), 3.18 (q, *J* = 6.7 Hz, 2H), 2.69 – 2.54 (m, 2H), 1.73 – 1.57 (m, 3H), 1.57 – 1.24 (m, 16H).

¹³C-NMR (126 MHz, CDCl₃): δ 156.6, 156.0, 142.4, 136.8, 128.6, 128.6, 128.4, 128.3, 128.2, 125.9, 79.2, 77.2, 66.7, 50.3, 41.0, 35.8, 35.4, 35.4, 29.8, 28.6, 27.9, 23.0.

IR (film): ν_{max} 3366, 2980, 2940, 2856, 1697, 1684, 1521, 1455, 1390, 1363, 1310, 1293, 1277, 1262, 1235, 1171, 1145, 1091, 1060, 1047, 1030, 1003, 901, 862, 777, 747, 730, 695.

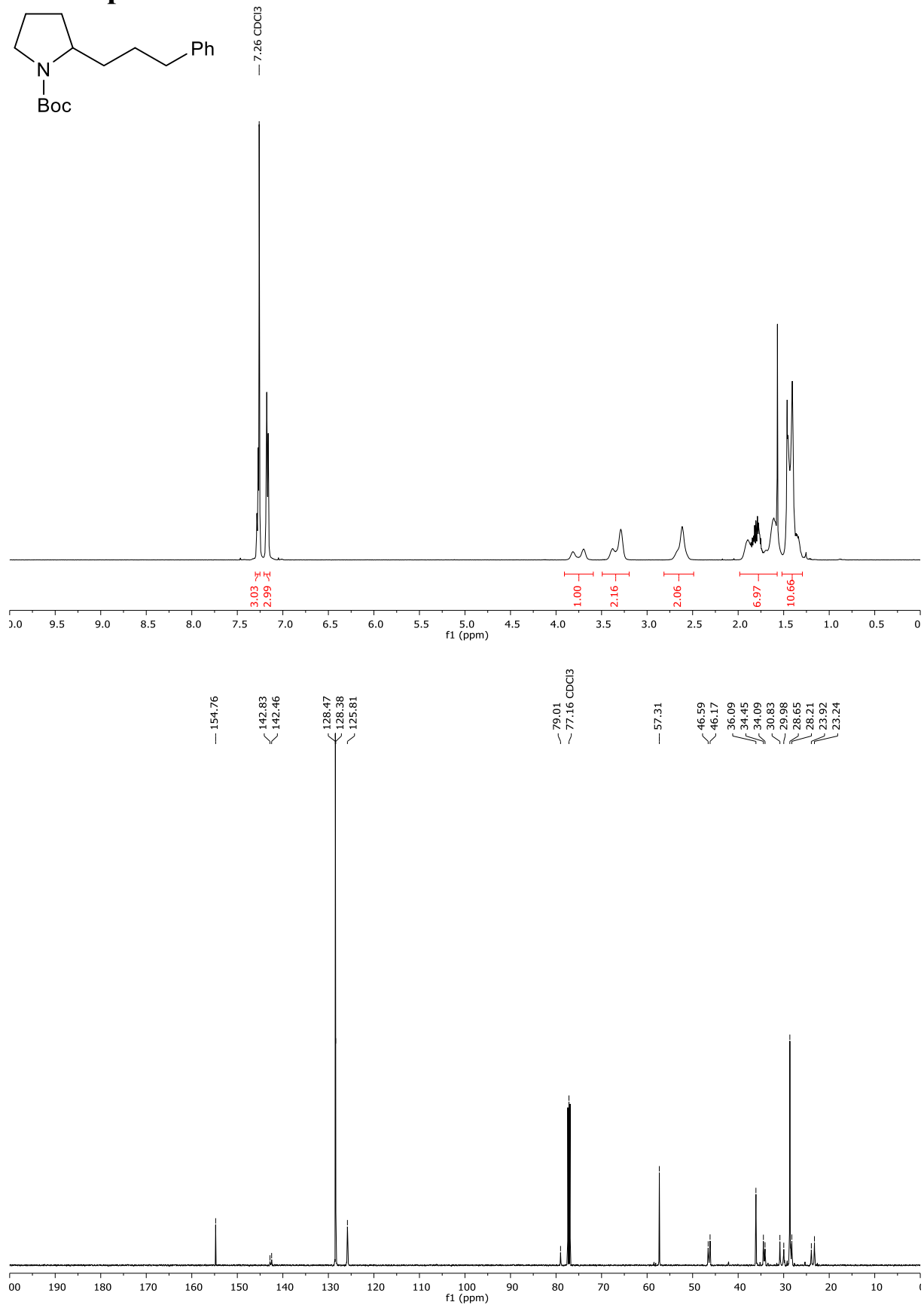
HRMS (ESI-TOF): *m/z* calcd. for C₁₈H₂₅NNaO₄ ([M+Na]⁺) 477.27238, found 477.27190.

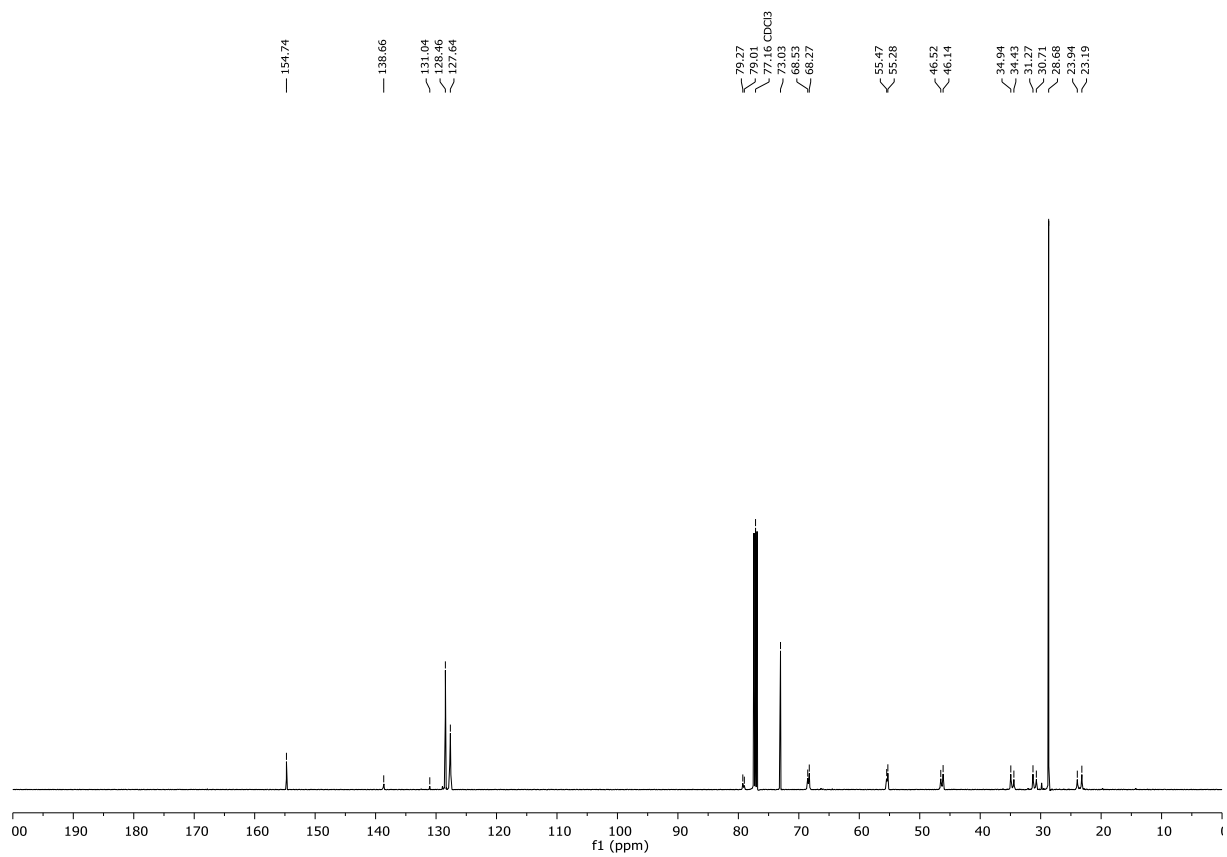
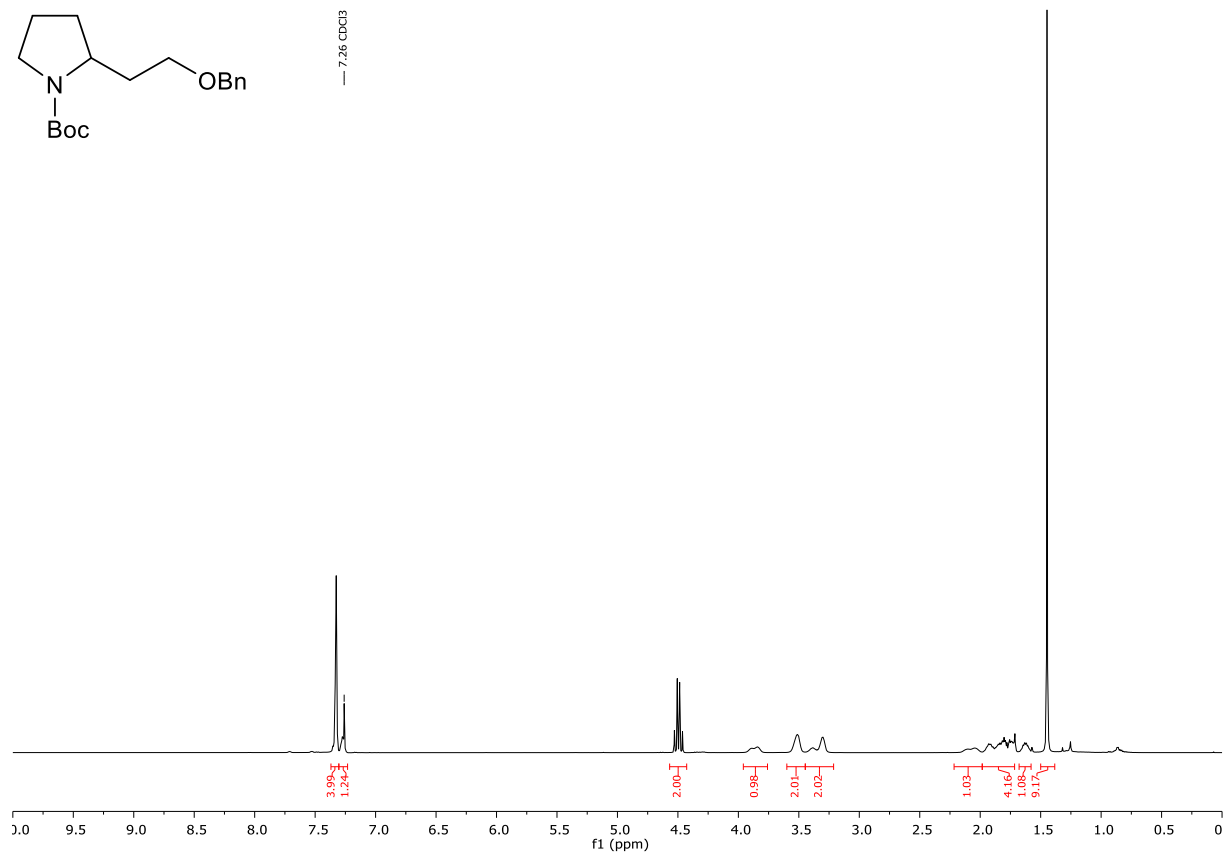
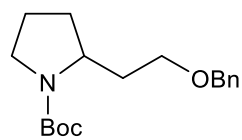
Bibliography

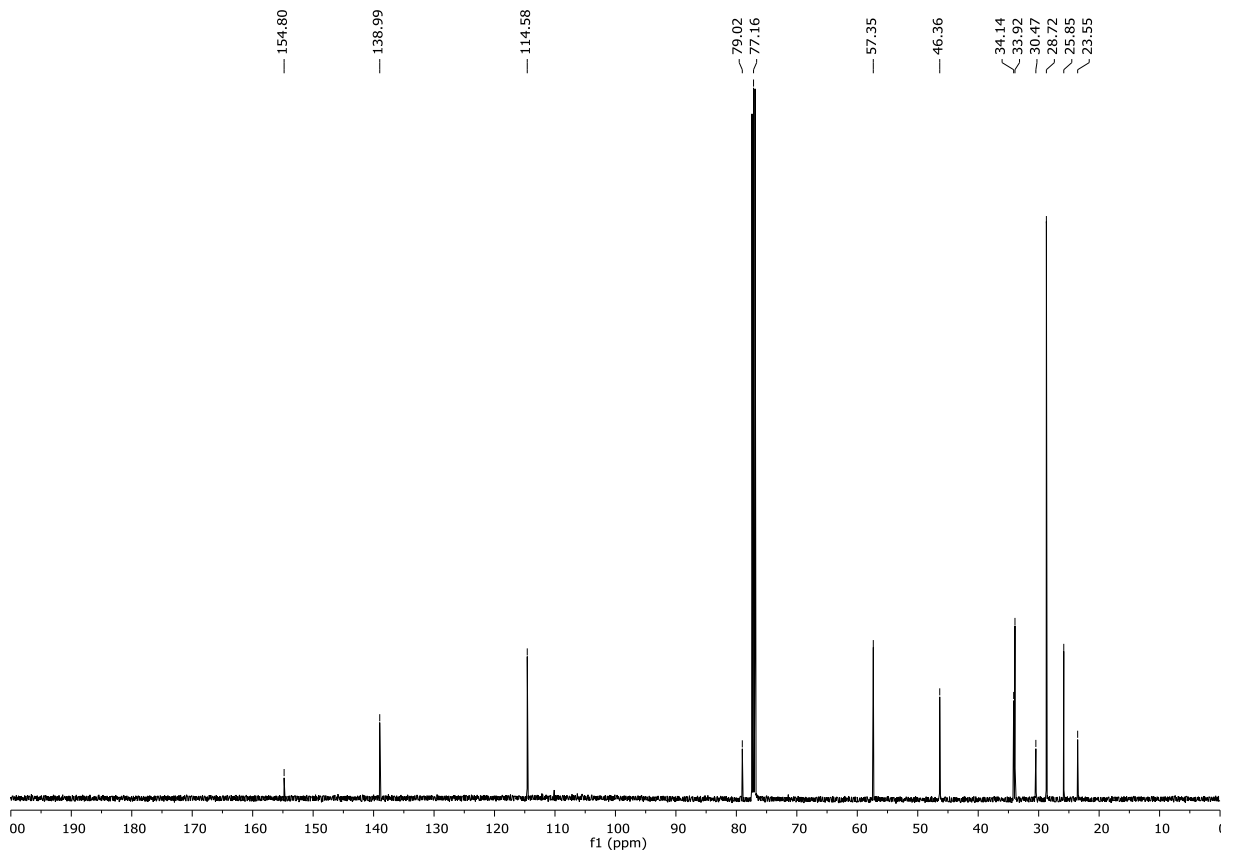
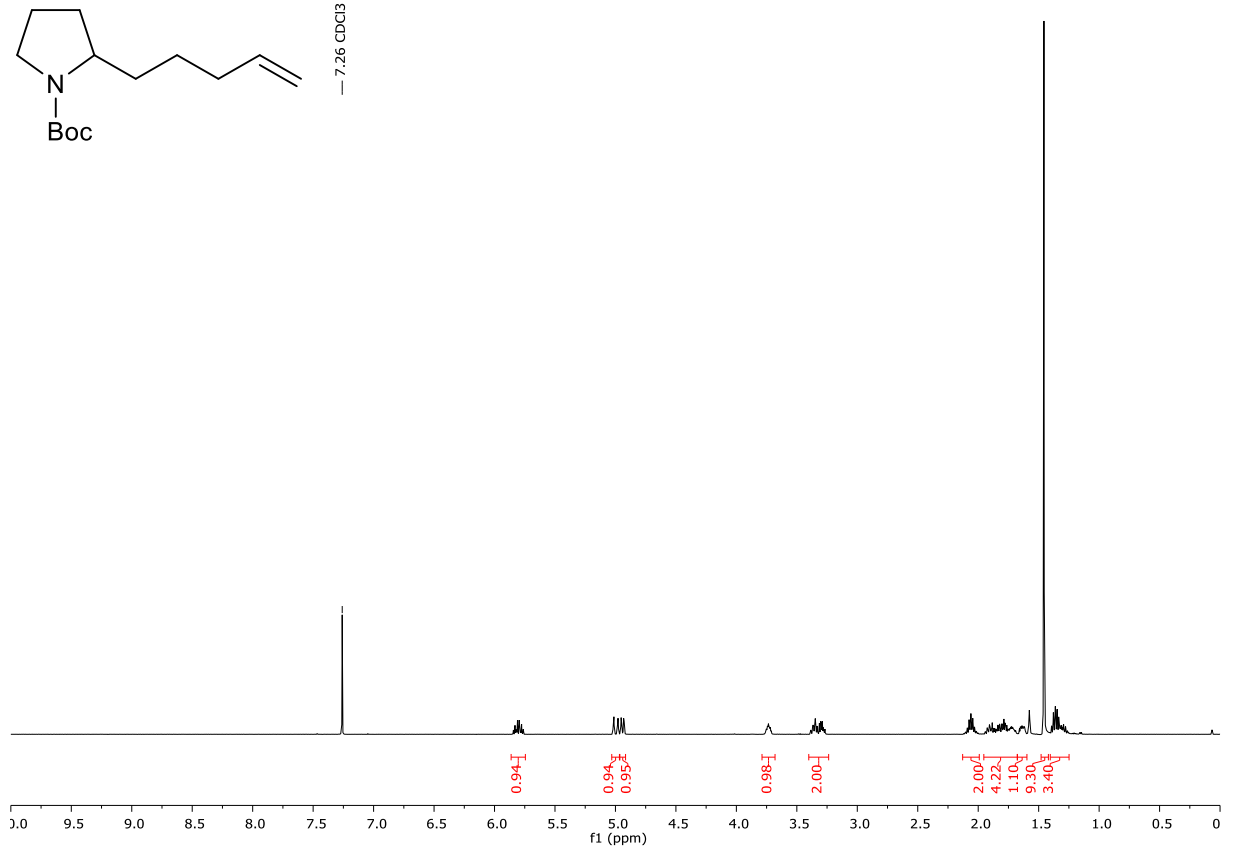
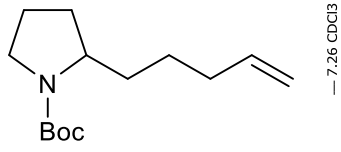
1. Pangborn, A. B., Giardello, M. A., Grubbs, R. H., Rosen, R. K. & Timmers, F. J. Safe and convenient procedure for solvent purification. *Organometallics* **15**, 1518–1520 (1996).
2. a) Lowry, M. S., Hudson, W. R., Pascal, R. A. Jr. & Bernhard, S. Accelerated luminophore discovery through combinatorial synthesis *J. Am. Chem. Soc.* **126**, 14129–14135 (2004); b) Ladouceur, S., Fortin, D. & Zsyman-Colman, E. enhanced luminescent iridium(III) complexes bearing aryltriazole cyclometallated ligands. *Inorg. Chem.* **50**, 11514–11526 (2011).
3. Liang, Y. & Fu, G. C. Nickel-catalyzed alkyl–alkyl cross-couplings of fluorinated secondary electrophiles: A general approach to the synthesis of compounds having a perfluoroalkyl substituent. *Angew. Chem. Int. Ed.* **54**, 9047–9051 (2015).
4. Still, W. C.; Kahn, M. & Mitra, A. J. Rapid chromatographic technique for preparative separations with moderate resolution *J. Org. Chem.* **43**, 2923–2925 (1978).
5. Cordier, C. J., Lundgren, R. J. & Fu, G. C. Enantioconvergent cross-couplings of racemic alkylmetal reagents with unactivated secondary alkyl electrophiles: catalytic asymmetric Negishi α -alkylations of *N*-Boc-pyrrolidine. *J. Am. Chem. Soc.* **135**, 10946–10949 (2013).
6. In, J., Lee, S., Kwon, Y. & Kim, S. Divergent total synthesis of the tricyclic marine alkaloids Lepadiformine, Fascicularin, and isomers of polycitorols by reagent-controlled diastereoselective reductive amination. *Chem. Eur. J.* **20**, 17433–17442 (2014).
7. Limpachayaporn, P., Schafers, M., Schober, O., Kopka, K. & Haufe, G. Synthesis of new fluorinated, 2-substituted 5-pyrrolidinylsulfonyl isatin derivatives as caspase-3 and caspase-7 inhibitors: Nonradioactive counterparts of putative PET-compatible apoptosis imaging agents. *Bioorg. Med. Chem.* **21**, 2025–2036 (2013).
8. Hsu, S.-F., Ko, C.-W. & Wu, Y.-T. Cobalt-catalyzed carbon-carbon bond formation: synthesis and applications of enantiopure pyrrolidine derivatives. *Adv. Synth. Catal.* **353**, 1756–1762 (2011).
9. Barker, G.; O'Brien, P. & Campos, K.R. Diamine-free lithiation–trapping of *N*-Boc heterocycles using *s*-BuLi in THF. *Organic Letters* **12**, 4176–4179 (2010).
10. Moutevelis-Minakakis, P., Sinanoglou, C., Loukas, V. & Kokotos, G. Synthesis of non-natural amino acids based on the ruthenium-catalysed oxidation of a phenyl group to carboxylic acid. *Synthesis* **6**, 933–938 (2005).
11. Yato, Michihisa, Y.; Homma, K. & Ishida, A. Reduction of carboxylic esters to ethers with triethyl silane in the combined use of titanium tetrachloride and trimethylsilyl trifluoromethanesulfonate. *Tetrahedron* **57**, 5353–5359 (2001).
12. Kang, S.H.; Lee, S.B. & Park, C.M. Catalytic enantioselective iodocyclization of γ -hydroxy-cis-alkenes *J. Am. Chem. Soc.* **125**, 15748–15749 (2003).
13. Lu, Z. & Fu, G. C. Alkyl–alkyl Suzuki cross-coupling of unactivated secondary alkyl chlorides. *Angew. Chem. Int. Ed.* **49**, 6676–6678 (2010).

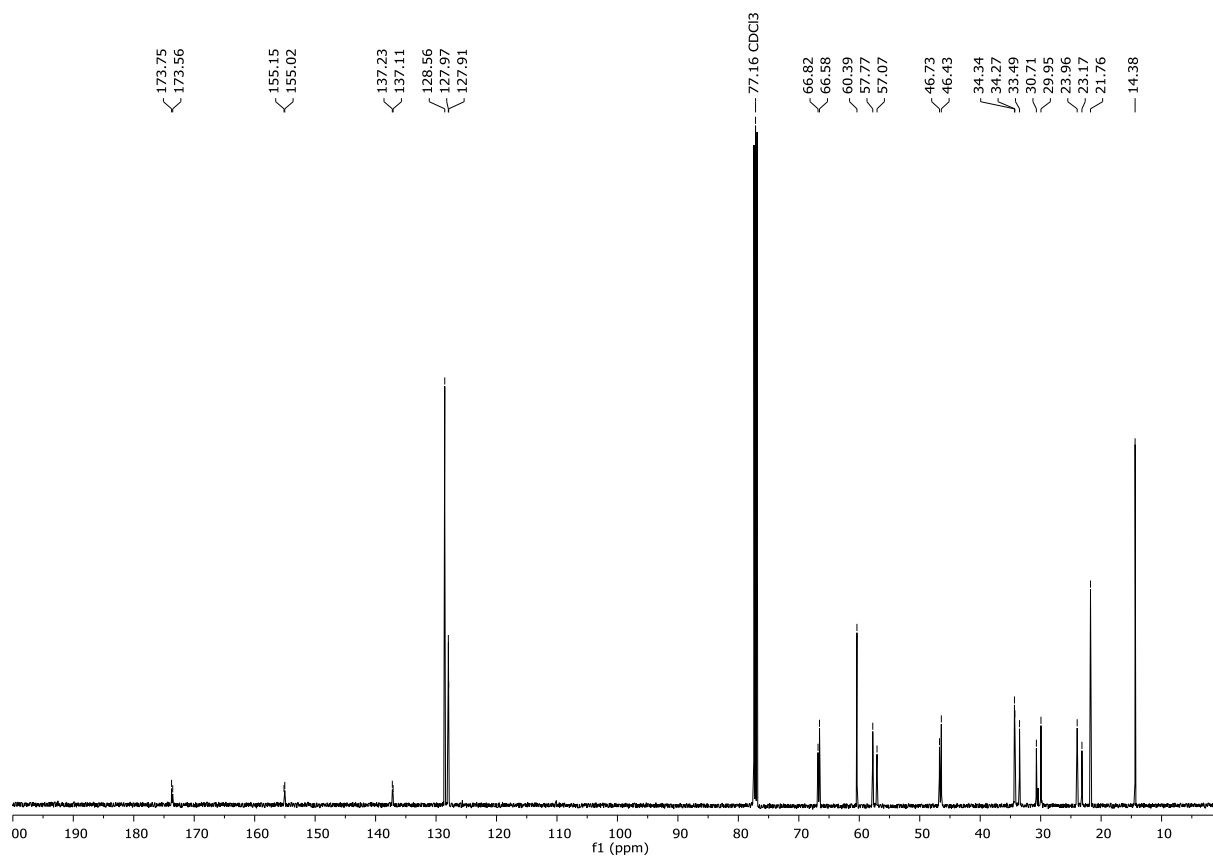
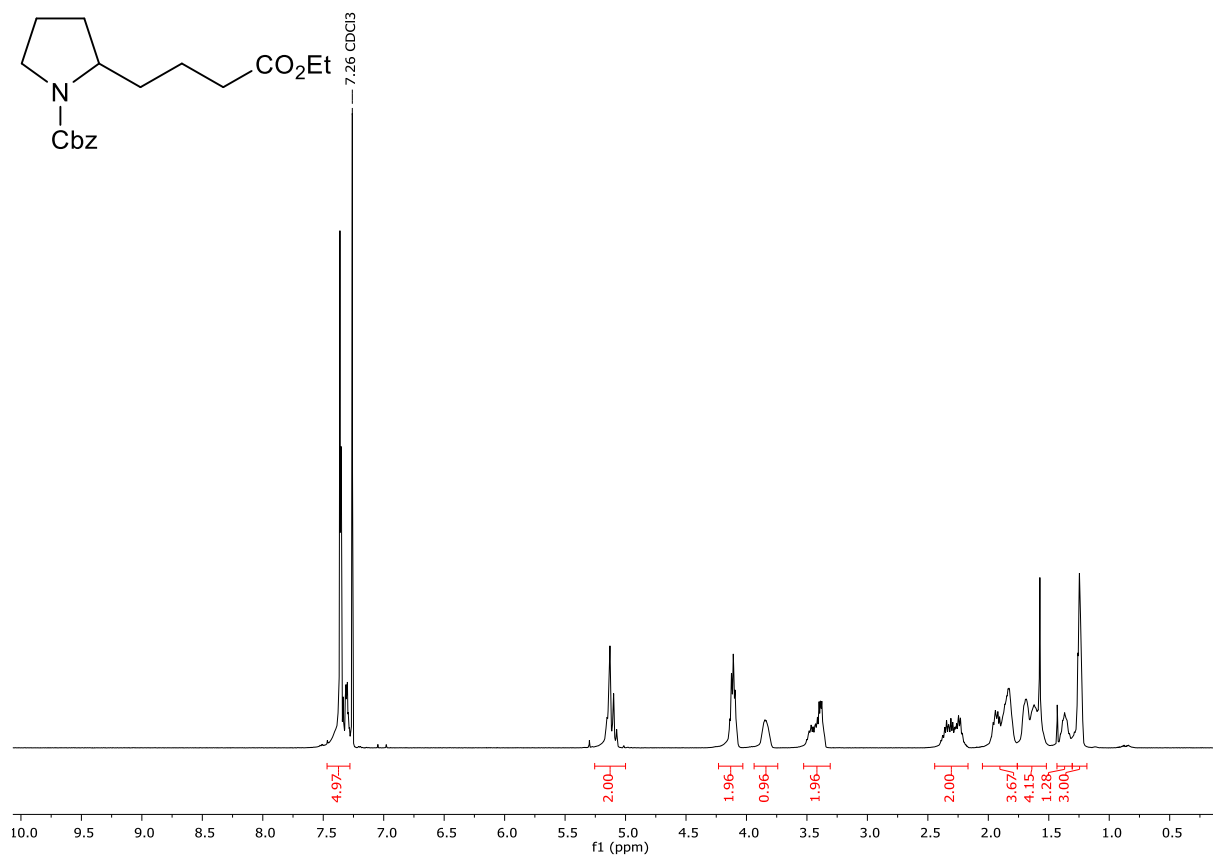
14. Guisán-Ceinos, M., Soler-Yanes, R., Collado-Sanz, D., Phapale, V. B., Buñuel, E. & Cárdenas, D. J. Ni-catalyzed cascade cyclization–Kumada alkyl–alkyl cross-coupling. *Chem. Eur. J.* **19**, 8405–8410 (2013).
15. Wang, G.; Jiang, J.; Bu, X.; Dai, J.; Xu, J.; Fu, Y. & Xu, H. Copper-catalyzed cross-coupling reaction of allyl boron ester with 1°/2°/3°-halogenated alkanes. *Organic Letters* **17**, 3682–3685 (2015).
16. Chung, J. Y. L. , Zhao, D. , Hughes, D. L. & Grabowski, E. J. J. A practical synthesis of fibrinogen receptor antagonist MK-383. selective functionalization of (S)-tyrosine *Tetrahedron* **49**, 5767–5776 (1993).

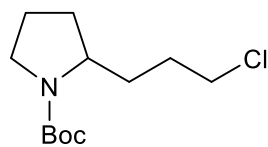
NMR spectra











— 7.26 CDCl₃

