Switchable Photocatalysis for the Chemodivergent Benzylation of 4-Cyanopyridines

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A. General Information

The NMR spectra were recorded at 300 MHz, 400 MHz and 500 MHz for $^1$H and 75, 100 or 125 MHz for $^{13}$C. The chemical shift (δ) for $^1$H and $^{13}$C are given in ppm relative to residual signals of the solvents (CHCl$_3$ @ 7.26 ppm $^1$H NMR and 77.16 ppm $^{13}$C NMR, and tetramethylsilane @ 0 ppm). Coupling constants are given in hertz (Hz). The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; q, quartet; m, multiplet; bs, broad signal; app, apparent.

High resolution mass spectra (HRMS) were obtained from the ICIQ HRMS unit on MicroTOF Focus and Maxis Impact (Bruker Daltonics) with electrospray ionization (ESI).

UV-vis measurements were carried out on a Shimadzu UV-2401PC spectrophotometer equipped with photomultiplier detector, double beam optics and D$_2$ and W light sources or an Agilent Cary60 spectrophotometer. Emission spectra of light sources were recorded on Ocean Optics USB4000 fiber optic spectrometer.

Yields refer to isolated materials of >95% purity, as determined by $^1$H NMR.

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General Procedures. All reactions were set up under an argon atmosphere (unless indicated otherwise) in oven-dried glassware. Synthesis grade solvents were used as purchased, anhydrous solvents were taken from a commercial SPS solvent dispenser. Chromatographic purification of products was accomplished using flash chromatography (FC) on silica gel (35-70 mesh). For thin layer chromatography (TLC) analysis throughout this work, Merck pre-coated TLC plates (silica gel 60 GF$_{254}$, 0.25 mm) were employed, using UV light as the visualizing agent and an acidic mixture of vanillin or basic aqueous potassium permanganate (KMnO$_4$) stain solutions, and heat as developing agents. Organic solutions were concentrated under reduced pressure on a Büchi rotatory evaporator.

Materials. Most of the starting materials used in this study are commercial and were purchased at the highest purity available from Sigma-Aldrich, Fluka, Alfa Aesar, Fluorochem, and used as received, without further purifications.
**B. Substrate Synthesis**

![Radical precursors]

![4-Cyanopyridines]

**Figure S1**: Starting materials synthesized according to literature precedents and corresponding references.

*N-(tert-butyl)-N-fluoro-2,2-dimethyl-4-phenylbutanamide (1l)*: To a round-bottom flask with a stirrer bar was added 2,2-dimethyl-4-phenylbutanoic acid (5 mmol, 961 mg, 1.0 equiv.) and CH₂Cl₂ (17 mL, 0.3 M). N,N-Dimethylformamide (DMF; 0.05 equiv.) was added at room temperature. Oxalyl chloride (1.5 equiv.) was added dropwise. The reaction was stirred at room temperature until effervescence subsided (45 min). The volatile components were then removed by rotary evaporation. The crude reaction product was dissolved in CH₂Cl₂ (0.3 M) and stirred. *tert*-Butylamine (1.5 equiv.) and triethylamine (2.0 equiv.) were added sequentially at room temperature, and the reaction was stirred for 3 hours. The reaction was quenched with aqueous HCl (1 M) and diluted with CH₂Cl₂ (0.1 M) and water (0.1 M) before being transferred to a separatory funnel. The organic layer was removed, and the aqueous layer was then extracted with CH₂Cl₂ (3 x 0.1 M). The combined organic layers were washed with saturated aqueous NaHCO₃ and then brine. The organic layer was dried with MgSO₄, filtered, and concentrated by rotary evaporation. The crude amide was used for the next step without further purification. To the crude residue was added anhydrous THF (0.13 M), and the solution stirred at 0 °C for 15 min. *n*-Butyllithium (1.1 equiv, 2.5 M in hexanes) was added dropwise. The reaction was maintained at 0 °C for 1.5 h, then *N*-fluorodibenzenesulfonylimide (1.5 equiv, 0.6 M in THF) was added dropwise as solution in THF (0.6 M). The reaction was left overnight in the ice bath and allowed to warm to room temperature. After 12 h, the reaction was quenched with aqueous HCl (1 M) and transferred to a separatory funnel. The crude mixture was diluted with CHCl₃ (0.1 M) and water (0.1 M). The organic layer was removed, and the aqueous layer was extracted with CHCl₃ (3 x 0.1 M). The combined organic layers were washed with saturated aqueous NaHCO₃ and then brine, dried over MgSO₄, filtered, and concentrated by rotary evaporation. The crude residue was purified by flash column chromatography (SiO₂: hexanes/EtOAc 95:5) to give the product as a yellowish oil (633 mg, 60% yield).

*¹H NMR (400 MHz, CDCl₃) 6 7.32 – 7.28 (m, 2H), 7.22 – 7.18 (m, 3H), 2.63 – 2.59 (m, 2H), 1.94 – 1.89 (m, 2H), 1.49 (d, J = 2.1 Hz, 9H), 1.30 (d, J = 2.2 Hz, 6H).
C. Experimental Procedures

C.1 Experimental set-up

- **Set-up 1:** 3D printed reactor with blue LED strip

For reactions performed using a blue LED strip as the light source, a 3D-printed photoreactor was used, consisting of a 9 cm diameter crystallizing dish with a 3D printed support of 6 positions, and a hole of 22 mm in the middle to allow ventilation (Figure S2, left). A commercial 1-meter LED strip was wrapped around the crystallizing dish, while a fan was used to cool down the reactor (the reaction temperature was measured to be 35–40 °C). Each of the positions could be used to fit a standard 16 mm diameter vial with a Teflon screw cap. Experiments at 465 nm were conducted using a 1 m strip, 14.4 W “LEDXON MODULAR 9009083 LED, SINGLE 5050” purchased from Farnell, catalog number 9009083. The emission spectrum of these LEDs is shown in Figure S2, right panel.
Figure S2: Blue LED photoreactor used for reactions where temperature control was not needed (left). Emission spectrum of the 465 nm LED strip used in this reactor (right).

- **Set-up 2**: HP single LED

Figure S3: Detailed set-up and illumination system. The light source for illuminating the reaction vessel consisted in a 460 nm high-power single LED (LZ1-00DB00) purchased from OSA OPTO.

C.2 General Procedure (A): Ipso Substitution

Reactions performed using **Set-up 1** in Figure S2. In an oven dried vial with a Teflon septum screw cap, 2-alkyl N-fluorobenzamide 2 (0.1 mmol, 1 equiv.) was added and dissolved in 1,2-DCE (2 mL, synthesis grade solvent). Cyano-pyridine 1 (0.3 mmol, 3 equiv.), 4DPAIPN (photocatalyst A, 0.8 mg, 0.01 mmol, 0.01 equiv.), and DIPEA (52 µL, 0.3 mmol, 3 equiv.) were then added. The resulting yellow mixture was degassed with argon sparging for 60 seconds. The vial was irradiated under stirring for 16 hours, unless otherwise specified. Volatiles were evaporated and the residue purified by column chromatography on silica gel to afford the corresponding product in the stated yield with >95% purity according to 1H-NMR analysis. The exact conditions for chromatography are reported for each compound.
C.3 Characterization of ipso substitution products

\[ \text{N-}(\text{tert-butyl})-2-(\text{pyridin-4-ylmethyl})\text{benzamide (3a):} \] Synthesized according to General Procedure A using \( \text{N-}(\text{tert-butyl})-\text{N-fluoro-2-methylbenzamide 2a} \) (21.0 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile 1a (31.2 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 1:1) to afford 3a (16 mg, 60% yield) as an off-white solid.

\[^{1}\text{H NMR (500 MHz, CDCl}_3\text{)}\delta 8.50 – 8.39 (m, 2H), 7.35 (td, J = 7.5, 1.1 Hz, 2H), 7.29 – 7.26 (m, 1H), 7.22 – 7.18 (m, 1H), 7.11 – 7.07 (m, 2H), 5.47 (s, 1H), 4.20 (s, 2H), 1.32 (s, 9H).\]

\[^{13}\text{C}\left[^{1}\text{H}\right]\text{NMR (126 MHz, CDCl}_3\text{)}\delta 169.2, 150.2, 149.8, 137.9, 137.0, 131.4, 130.1, 127.3, 127.0, 124.4, 52.0, 38.3, 28.7.\]

HRMS: (ESI\(^+\)) calculated for \( \text{C}_{17}\text{H}_{21}\text{N}_2\text{O} \) (M+H\(^+\)): 269.1648, found 269.1642.

\[ \text{N-}(\text{tert-butyl})-2-(1-(\text{pyridin-4-yl})\text{ethyl})\text{benzamide (3b):} \] Synthesized according to General Procedure A using \( \text{N-}(\text{tert-butyl})-2\text{-ethyl-N-fluorobenzamide 2b} \) (22.5 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile 1a (31.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc from 7:3 to 1:1) to afford 3b (21 mg, 74% yield) as an off-white solid.

\[^{1}\text{H NMR (500 MHz, CDCl}_3\text{)}\delta 8.49 – 8.44 (m, 2H), 7.37 (td, J = 7.6, 1.5 Hz, 1H), 7.31 (dt, J = 7.6, 1.0 Hz, 1H), 7.29 – 7.20 (m, 2H), 7.14 – 7.12 (m, 2H), 5.41 (brs, 1H), 4.78 (q, J = 7.2 Hz, 1H), 1.63 (d, J = 7.2 Hz, 3H), 1.4 (s, 9H).\]

\[^{13}\text{C}\left[^{1}\text{H}\right]\text{NMR (126 MHz, CDCl}_3\text{)}\delta 169.6, 155.3, 150.0, 142.2, 137.9, 130.0, 128.0, 127.0, 126.7, 123.3, 52.0, 39.6, 28.8, 21.5.\]

HRMS: (ESI\(^+\)) calculated for \( \text{C}_{18}\text{H}_{23}\text{N}_2\text{O} \) (M+H\(^+\)): 283.1805, found 283.1794.

\[ \text{N-}(\text{tert-butyl})-\text{N-fluoro-3-methoxy-2-(pyridin-4-ylmethyl)benzamide (3c):} \] Synthesized according to General Procedure A using \( \text{N-}(\text{tert-butyl})-\text{N-fluoro-3-methoxy-2-methylbenzamide 2c} \) (22.0 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile 1a (31.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc from 8:2 to 1:1) to afford 3c (15 mg, 47% yield) as an off-white solid.

\[^{1}\text{H NMR (300 MHz, CDCl}_3\text{)}\delta 8.42 (d, J = 4.9 Hz, 2H), 7.31 – 7.22 (m, 1H), 7.12 (d, J = 5.3 Hz, 2H), 6.98 (dd, J = 7.6, 1.2 Hz, 1H), 6.93 (dd, J = 8.3, 1.1 Hz, 1H), 5.41 (s, 1H), 4.17 (s, 2H), 3.78 (s, 3H), 1.32 (s, 9H).\]

\[^{13}\text{C}\left[^{1}\text{H}\right]\text{NMR (75 MHz, CDCl}_3\text{)}\delta 169.2, 158.1, 150.6, 149.5, 139.7, 128.29, 125.1, 124.2, 119.2, 112.0, 55.8, 52.0, 31.7, 29.0.\]

HRMS: (ESI\(^+\)) calculated for \( \text{C}_{18}\text{H}_{22}\text{FNO}_2 \) (M+H\(^+\)): 299.1754, found 299.1746.

\[ \text{N-}(\text{tert-butyl})-3\text{-methyl-2-(pyridin-4-ylmethyl)benzamide (3d):} \] Synthesized according to General Procedure A using \( \text{N-}(\text{tert-butyl})-\text{N-fluoro-2-3-dimethylbenzamide 2d} \) (20.0 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile 1a (31.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc from 8:2 to 1:1) to afford 3d (16.5 mg, 59% yield) as an off-white solid.
**N-(tert-buty)-4-methoxy-2-(pyridin-4-ylmethyl)benzamide (3e):**

Synthesized according to General Procedure A using N-(tert-buty)-N-fluoro-4-methoxy-2-methylbenzamide \( \text{2f} \) (22.0 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile \( \text{1a} \) (31.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc from 8:2 to 1:1) to afford \( \text{3e} \) (17 mg, 57% yield) as an off-yellow solid.

**1H NMR** (400 MHz, CDCl\(_3\)) \( \delta 8.47 \) (s, 2H), 7.29 – 7.21 (m, 3H), 7.06 (d, \( J = 5.3 \) Hz, 2H), 5.47 (s, 1H), 4.21 (s, 2H), 2.20 (s, 3H), 1.32 (s, 9H).

**13C \( ^{1} \)H NMR** (75 MHz, CDCl\(_3\)) \( \delta 169.2, 158.1, 150.6, 149.5, 139.7, 128.9, 125.1, 124.2, 119.2, 112.0, 55.8, 52.0, 31.7, 29.0.

**HRMS:** (ESI\(^{+}\)) calculated for \( \text{C}_{18}\text{H}_{23}\text{N}_{2}\text{O} \) (M+H\(^{+}\)): 283.1805, found 283.1805.

**N-(tert-buty)-4-fluoro-2-(pyridin-4-ylmethyl)benzamide (3f):**

Synthesized according to General Procedure A using \( \text{N-(tert-buty)-N,4-difluoro-2-methylbenzamide 2f} \) (22.0 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile \( \text{1a} \) (31.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 7:3) to afford \( \text{3f} \) (17 mg, 59% yield) as an off-white solid.

**1H NMR** (400 MHz, CDCl\(_3\)) \( \delta 8.54 – 8.43 \) (m, 2H), 7.36 (dd, \( J = 8.4, 5.7 \) Hz, 1H), 7.10 (ddd, \( J = 4.5, 1.6, 0.8 \) Hz, 2H), 6.95 (td, \( J = 8.3, 2.6 \) Hz, 1H), 6.90 (dd, \( J = 9.5, 2.6 \) Hz, 1H), 5.44 (s, 1H), 4.19 (s, 2H), 1.33 (s, 9H).

**13C \( ^{1} \)H NMR** (101 MHz, CDCl\(_3\)) \( \delta 168.2, 163.2 \) (d, \( J = 250.3 \) Hz), 149.8, 149.2, 140.0 (d, \( J = 7.6 \) Hz), 133.93 (d, \( J = 3.3 \) Hz), 129.1 (d, \( J = 8.7 \) Hz), 124.2, 118.1 (d, \( J = 21.8 \) Hz), 113.7 (d, \( J = 21.4 \) Hz), 51.9, 38.1, 28.6. **19F NMR** (376 MHz, CDCl\(_3\)) \( \delta -110.3. \)

**HRMS:** (ESI\(^{+}\)) calculated for \( \text{C}_{17}\text{H}_{21}\text{F}_{2}\text{N}_{2}\text{O} \) (M+H\(^{+}\)): 287.1554, found 287.1548.

**N-(tert-buty)-4-chloro-2-(pyridin-4-ylmethyl)benzamide (3g):**

Synthesized according to General Procedure A using \( \text{N-(tert-buty)-4-chloro-N,fluoro-2-methylbenzamide 2g} \) (24.0 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile \( \text{1a} \) (31.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 8:2 to 1:1) to afford \( \text{3g} \) (14.5 mg, 48% yield) as an off-white solid.

**1H NMR** (400 MHz, CDCl\(_3\)) \( \delta 8.54 – 8.42 \) (m, 2H), 7.31 (d, \( J = 8.1 \) Hz, 1H), 7.26 – 7.23 (m, 1H), 7.19 (d, \( J = 2.1 \) Hz, 1H), 7.13 (d, \( J = 5.4 \) Hz, 2H), 5.48 (br s, 1H), 4.18 (s, 2H), 1.31 (s, 9H).

**13C \( ^{1} \)H NMR** (101 MHz, CDCl\(_3\)) \( \delta 168.2, 149.9, 149.4, 139.1, 136.2, 136.0, 131.3, 128.7, 127.3, 124.6, 52.1, 38.2, 28.8.

**HRMS:** (ESI\(^{+}\)) calculated for \( \text{C}_{17}\text{H}_{20}\text{ClN}_{2}\text{O} \) (M+H\(^{+}\)): 303.1259, found 303.1254.
**N-(tert-butyl)-N-fluoro-5-methoxy-2-(pyridin-4-ylmethyl)benzamide** (3h): Synthesized according to General Procedure A using **N-(tert-butyl)-N-fluoro-5-methoxy-2-methylbenzamide** 2h (24.0 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile 1a (31.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc from 8:2 to 1:1) to afford 3h (17 mg, 54% yield) as an white solid.

1H NMR (500 MHz, CDCl3) δ 8.50 – 8.36 (m, 2H), 7.11 (d, J = 7.8 Hz, 1H), 7.08 (d, J = 6.0, 2H), 6.91 – 6.87 (m, 2H), 5.42 (s, 1H), 4.11 (s, 2H), 3.82 (s, 3H), 1.30 (s, 9H).

13C{1H} NMR (126 MHz, CDCl3) δ 168.9, 158.4, 150.7, 150.0, 137.8, 136.8, 133.8, 131.3, 130.7, 128.0, 124.4, 51.9, 38.0, 29.0, 21.0.

HRMS: (ESI+) calculated for C19H19FNO2 (M+H+): 299.1754, found 299.1747.

**N-(tert-butyl)-5-methyl-2-(pyridin-4-ylmethyl)benzamide** (3i): Synthesized according to General Procedure A using 5-bromo-N-(tert-butyl)-N-fluoro-2,5-dimethylbenzamide 2i (22.5 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile 1a (31.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 7:3) to afford 3i (16 mg, 53% yield) as an off-white solid.

1H NMR (400 MHz, CDCl3) δ 8.45 (s, 2H), 7.19 – 7.14 (m, 2H), 7.09 (q, J = 4.9, 3.8 Hz, 3H), 5.42 (s, 1H), 4.15 (s, 2H), 2.34 (s, 3H), 1.32 (s, 9H).

13C{1H} NMR (101 MHz, CDCl3) δ 169.4, 150.5, 149.8, 137.8, 136.8, 133.8, 131.3, 130.7, 128.0, 124.4, 51.9, 38.0, 29.0, 21.0.

HRMS: (ESI+) calculated for C19H19N2O (M+H+): 283.1805, found 283.1796.

**5-Bromo-N-(tert-butyl)-2-(pyridin-4-ylmethyl)benzamide** (3j): Synthesized according to General Procedure A using 5-bromo-N-(tert-butyl)-N-fluoro-2,5-dimethylbenzamide 2j (29.0 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile 1a (31.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 7:3) to afford 3j (20 mg, 58% yield) as an off-white solid.

1H NMR (400 MHz, CDCl3) δ 8.51 (d, J = 5.1 Hz, 2H), 7.54 – 7.49 (m, 2H), 7.29 (d, J = 5.1 Hz, 2H), 7.12 – 7.08 (m, 1H), 5.54 (s, 1H), 4.21 (s, 2H), 1.33 (s, 9H).

13C{1H} NMR (101 MHz, CDCl3) δ 167.5, 151.9, 150.7, 149.4, 139.6, 135.9, 133.1, 133.0, 130.3, 124.5, 120.8, 52.2, 37.9, 28.7.

HRMS: (ESI+) calculated for C17H19BrNO (M+H+): 347.0754, found 347.0748.

**N-(tert-butyl)-3-(pyridin-4-ylmethyl)thiophene-2-carboxamide** (3k): Synthesized according to General Procedure A using N-(tert-butyl)-N-fluoro-3-methylthiophene-2-carboxamide 2k (21.5 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile 1a (31.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 7:3) to afford 3k (12.6 mg, 46% yield) as a yellow oil.

1H NMR (400 MHz, CDCl3) δ 8.57 (d, J = 5.9 Hz, 2H), 7.74 (d, J = 5.9 Hz, 2H), 7.34 (d, J = 5.1 Hz, 1H), 6.92 (d, J = 5.1 Hz, 1H), 5.67 (s, 1H), 4.58 (s, 2H), 1.41 (s, 9H).

13C{1H} NMR (101 MHz, CDCl3) δ 161.7, 142.6, 140.3, 133.0, 131.0, 127.9, 126.7, 52.5, 35.2, 29.0.

HRMS: (ESI+) calculated for C15H19NO2S (M+H+): 275.1213, found 275.1212.
**N-(tert-butyl)-2,2-dimethyl-4-phenyl-4-(pyridin-4-yl)butanamide (3l):** Synthesized according to General Procedure A using \(N\)-(tert-butyl)-2,2-dimethyl-4-phenylbutanamide 2l (25.0 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile 1a (31.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 1:1) to afford 3l (26 mg, 80% yield) as an white solid.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.48 (d, \(J = 5.7\) Hz, 2H), 7.34 – 7.25 (m, 3H), 7.24 – 7.18 (m, 3H), 5.33 (s, 1H), 4.00 (t, \(J = 6.6\) Hz, 1H), 2.44 (dd, \(J = 14.2, 6.2\) Hz, 1H), 2.34 (dd, \(J = 14.2, 7.1\) Hz, 1H), 1.31 (s, 9H), 1.08 (s, 3H), 1.02 (s, 3H).

\(^13\)C\[^1\]H NMR (126 MHz, CDCl\(_3\)) \(\delta\) 176.1, 154.8, 150.0, 144.0, 128.9, 128.1, 126.9, 123.3, 51.1, 48.32, 46.1, 43.2, 28.8, 27.2, 26.3.

HRMS: (ESI\(^+\)) calculated for \(C_{21}H_{35}N_3O\) (M+H\(^+\)): 325.2274, found 325.2276.

**N-(tert-butyl)-2-(1-(2-methylpyridin-4-yl)ethyl)benzamide (3m):** Synthesized according to General Procedure A using \(N\)-(tert-butyl)-2-ethyl-N-fluorobenzamide 2b (22.5 mg, 0.1 mmol, 1 equiv.) and 2-methylisonicotinonitrile 1b (50.5 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc from 7:3 to 1:1) to afford 3m (23 mg, 78% yield) as a white solid.

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 8.34 (d, \(J = 5.5\) Hz, 1H), 7.42 – 7.33 (m, 1H), 7.33 – 7.26 (m, 2H), 7.26 – 7.18 (m, 1H), 7.01 (d, \(J = 1.7\) Hz, 1H), 6.91 (dd, \(J = 5.2, 1.7\) Hz, 1H), 5.39 (s, 1H), 4.73 (q, 
\(J = 7.2\) Hz, 1H), 2.49 (s, 3H), 1.60 (d, \(J = 7.2\) Hz, 3H), 1.35 (s, 9H).

\(^13\)C\[^1\]H NMR (75 MHz, CDCl\(_3\)) \(\delta\) 169.6, 158.4, 155.5, 149.2, 142.3, 137.9, 130.0, 127.9, 127.0, 126.6, 122.9, 120.3, 51.9, 39.6, 28.8, 24.6, 21.5.

HRMS: (ESI\(^+\)) calculated for \(C_{16}H_{13}N_3O\) (M+H\(^+\)): 297.1961, found 297.1961.

**N-(tert-butyl)-2-(1-(2-ethylpyridin-4-yl)ethyl)benzamide (3n):** Synthesized according to General Procedure A using \(N\)-(tert-butyl)-2-ethyl-N-fluorobenzamide 2b (22.5 mg, 0.1 mmol, 1 equiv.) and 2-ethylisonicotinonitrile 1c (39.5 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc from 6:1 to 3:2) to afford 3n (23 mg, 76% yield) as a yellow solid.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.38 (d, \(J = 5.2\) Hz, 1H), 7.37 (td, \(J = 7.5, 1.6\) Hz, 1H), 7.32 – 7.27 (m, 2H), 7.26 – 7.21 (m, 1H), 7.04 (s, 1H), 6.94 (dd, \(J = 5.4, 1.7\) Hz, 1H), 5.40 (s, 1H), 4.76 (q, 
\(J = 7.2\) Hz, 1H), 2.78 (q, \(J = 7.6\) Hz, 2H), 1.61 (d, \(J = 7.2\) Hz, 3H), 1.34 (s, 9H), 1.27 (t, \(J = 7.6\) Hz, 3H).

\(^13\)C\[^1\]H NMR (101 MHz, CDCl\(_3\)) \(\delta\) 169.6, 163.3, 156.3, 148.7, 142.1, 137.9, 130.0, 128.0, 127.0, 126.7, 121.9, 120.7, 51.9, 39.8, 31.2, 28.8, 21.6, 14.0.

HRMS: (ESI\(^+\)) calculated for \(C_{20}H_{17}N_3O\) (M+H\(^+\)): 311.2118, found 311,2114.

**N-(tert-butyl)-N-fluoro-2-(1-(2-isopropylpyridin-4-yl)ethyl)benzamide (3o):** Synthesized according to General Procedure A using \(N\)-(tert-butyl)-2-ethyl-N-fluorobenzamide 2b (22.5 mg, 0.1 mmol, 1 equiv.) and 2-isopropylisonicotinonitrile 1d (44.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 8:2) to afford 3o (22 mg, 64% yield) as a whit gum.

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.41 (d, \(J = 5.2\) Hz, 1H), 7.39 (td, \(J = 7.5, 1.5\) Hz, 1H), 7.34 (dd, \(J = 7.6, 1.6\) Hz, 1H), 7.31 – 7.29 (m, 1H), 7.26 (td, \(J = 7.4, 1.3\) Hz, 1H), 7.08 – 7.00
(m, 1H), 6.92 (dd, J = 5.1, 1.8 Hz, 1H), 5.39 (s, 1H), 4.77 (q, J = 7.2 Hz, 1H), 3.02 (hept, J = 6.9 Hz, 1H), 1.64 (d, J = 7.2 Hz, 3H), 1.35 (s, 9H), 1.29 (d, 6H).

$^{1}$H NMR (126 MHz, CDCl$_3$) δ 169.7, 167.4, 155.8, 149.1, 142.1, 138.0, 130.0, 128.0, 127.0, 126.63 120.6, 120.3, 51.9, 39.8, 36.4, 28.8, 22.8, 22.7, 21.7.

HRMS: (ESI$^+$) calculated for C$_{31}$H$_{30}$N$_{2}$O (M+H$^+$): 325.2274, found 325.2277.

N-(tert-butyl)-2-(1-(2-(p-tolyl)pyridin-4-yl)ethyl)benzamidemotions according to General Procedure A using N-(tert-butyl)-2-ethyl-N-fluorobenzamide 2b (22.5 mg, 0.1 mmol, 1 equiv.) and 2-(p-tolyl)isonicotinonitrile 1e (58.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 8:2) to afford 3p (17 mg, 46% yield) as a white solid.

$^1$H NMR (300 MHz, CDCl$_3$) δ 8.53 (d, J = 5.1, 1H), 7.89 – 7.77 (m, 2H), 7.58 – 7.53 (m, 1H), 7.43 – 7.28 (m, 3H), 7.26 – 7.20 (m, 3H), 7.03 (dd, J = 5.1, 1.7 Hz, 1H), 5.40 (s, 1H), 4.85 (q, J = 7.2 Hz, 1H), 2.39 (s, 3H), 1.67 (d, J = 7.2 Hz, 3H), 1.32 (s, 9H).

$^{13}$C$^{1}$H NMR (75 MHz, CDCl$_3$) δ 169.7, 157.7, 156.0, 149.7, 142.1, 139.0, 138.0, 136.9, 130.0, 129.5, 128.0, 127.0, 126.7, 121.5, 120.0, 52.0, 39.9, 28.8, 21.6, 21.4.

HRMS: (ESI$^+$) calculated for C$_{25}$H$_{29}$N$_{2}$O (M+H$^+$): 373.2274, found 373.2273.

N-(tert-butyl)-2-(1-(2-(4-methoxyphenyl)pyridin-4-yl)ethyl)benzamide (3q): Synthesized according to General Procedure A using N-(tert-butyl)-2-ethyl-N-fluorobenzamide 2b (22.5 mg, 0.1 mmol, 1 equiv.) and 2-(4-methoxyphenyl)isonicotinonitrile 1f (59.5 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc from 86:14 to 1:1) to afford 3q (18 mg, 46% yield) as a white solid.

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.51 (d, J = 5.2 Hz, 1H), 7.92 – 7.86 (m, 2H), 7.53 (s, 1H), 7.37 (td, J = 7.1, 1.4 Hz, 1H), 7.34 – 7.29 (m, 2H), 7.23 (td, J = 7.5, 1.4 Hz, 1H), 7.01 (d, J = 5.1, 1.6 Hz, 1H), 6.99 – 6.94 (m, 2H), 5.41 (br s, 1H), 4.85 (q, J = 7.2 Hz, 1H), 3.85 (s, 3H), 1.67 (d, J = 7.2 Hz, 3H), 1.33 (s, 10H).

$^{13}$C$^{1}$H NMR (101 MHz, CDCl$_3$) δ 169.7, 160.6, 157.2, 156.3, 149.4, 142.1, 138.0, 130.1, 128.4, 128.0, 127.1, 126.7, 121.1, 119.7, 114.2, 55.5, 52.0, 39.9, 28.8, 21.6.

HRMS: (ESI$^+$) calculated for C$_{25}$H$_{30}$N$_{2}$O (M+H$^+$): 389.2224, found 389.2212.

N-(tert-butyl)-2-(1-(2-(4-fluorophenyl)pyridin-4-yl)ethyl)benzamide (3r): Synthesized according to General Procedure A using N-(tert-butyl)-2-ethyl-N-fluorobenzamide 2b (22.5 mg, 0.1 mmol, 1 equiv.) and 2-(4-fluorophenyl)isonicotinonitrile 1g (59.5 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc from 86:14 to 1:1) to afford 3r (24 mg, 64% yield) as a white solid.

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.53 (d, J = 5.2 Hz, 1H), 7.96 – 7.86 (m, 2H), 7.55 – 7.53 (m, 1H), 7.41 – 7.35 (m, 1H), 7.35 – 7.29 (m, 2H), 7.24 (m, 1H), 7.18 – 7.10 (m, 2H), 7.09 – 7.02 (m, 1H), 5.42 (s, 1H), 4.87 (q, J = 7.2 Hz, 1H), 1.67 (d, J = 7.2 Hz, 3H), 1.34 (s, 9H).

$^{13}$C$^{1}$H NMR (101 MHz, CDCl$_3$) δ 169.5, 163.5 (d, J = 248.3 Hz, C), 156.5, 156.1, 149.6, 142.1, 137.8, 135.7 (d, J = 3.1 Hz), 130.0, 128.8 (d, J = 8.4 Hz), 127.8, 126.9, 126.6, 121.5, 119.9, 115.6 (d, J = 21.6 Hz), 51.8, 39.7, 28.7, 21.4.
**19F NMR** (376 MHz, CDCl₃) δ -113.4.

**HRMS**: (ESI⁺) calculated for C₄₉H₂₆FN₂O (M+H⁺): 377.2024, found 377.2022.

**2-(1-(2-(1H-pyrazol-1-yl)pyridin-4-yl)-ethyl)-N-(tert-butyl)benzamide (3s):** Synthesized according to General Procedure A using N-(tert-butyl)-2-ethyl-N-fluorobenzamide 2b (22.5 mg, 0.1 mmol, 1 equiv.) and 2-(1H-pyrazol-1-yl)isonicotinonitrile 1k (51.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc from 86:14 to 1:1) to afford 3s (18 mg, 53% yield) as an off-white solid.

**1H NMR** (400 MHz, CDCl₃) δ 8.53 (d, J = 2.6 Hz, 1H), 8.26 (d, J = 5.2 Hz, 1H), 7.86 (s, 1H), 7.70 (s, 1H), 7.36 (td, J = 7.5, 1.6 Hz, 1H), 7.30 (td, J = 8.0, 1.4 Hz, 2H), 7.23 (td, J = 7.3, 1.4 Hz, 1H), 7.09 (dd, J = 5.3, 1.6 Hz, 1H), 6.44 (t, J = 2.2 Hz, 1H), 5.54 (s, 1H), 4.84 (q, J = 7.2 Hz, 1H), 1.69 (d, J = 7.2 Hz, 3H), 1.38 (s, 9H).  **13C [1H] NMR** (101 MHz, CDCl₃) δ 169.7, 158.4, 142.1, 137.8, 130.2, 128.1, 126.7, 52.0, 40.0, 28.8, 21.3.

**HRMS**: (ESI⁺) calculated for C₂₁H₁₉N₃O (M+H⁺): 349.2017, found 349.2016.

**N-(tert-butyl)-2-(1-(2-(3-(trifluoromethyl)phenoxy)pyridin-4-yl)ethyl)benzamide (3t):** Synthesized according to General Procedure A using N-(tert-butyl)-2-ethyl-N-fluorobenzamide 2b (22.5 mg, 0.1 mmol, 1 equiv.) and 2-(3-(trifluoromethyl)phenoxy)isonicotinonitrile 1l (79.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc from 86:14 to 1:1) to afford 3t (18.5 mg, 42% yield) as an off-white solid.

**1H NMR** (400 MHz, CDCl₃) δ 8.04 (d, J = 5.3 Hz, 1H), 7.49 (t, J = 7.9 Hz, 1H), 7.45 – 7.35 (m, 3H), 7.31 (ddd, J = 11.0, 7.8, 1.4 Hz, 3H), 7.25 (td, J = 7.4, 1.3 Hz, 2H), 6.92 (dd, J = 5.4, 1.5 Hz, 1H), 6.85 (s, 1H), 5.48 (s, 1H), 4.81 (q, J = 7.2 Hz, 1H), 1.65 (d, J = 7.2 Hz, 3H), 1.39 (s, 9H).

**13C [1H] NMR** (126 MHz, cryoprobe, CDCl₃) δ 169.6, 163.3, 160.0, 154.4, 147.2, 141.9, 137.8, 132.1 (q, J = 32.7 Hz), 130.2, 130.2, 128.0, 127.0, 126.8, 124.6, 123.1 (q, J = 274 Hz), 121.3 (q, J = 3.8 Hz), 119.4, 118.2 (q, J = 3.8 Hz), 111.0, 52.0, 39.7, 28.9, 21.4.

**19F NMR** (376 MHz, CDCl₃) δ -62.76.

**HRMS**: (ESI⁺) calculated for C₄₉H₂₆FN₂O (M+H⁺): 443.1941, found 443.1953.

**N-(tert-butyl)-2-(1-(3-chloropyridin-4-yl)ethyl)benzamide (3u):** Synthesized according to General Procedure A using N-(tert-butyl)-2-ethyl-N-fluorobenzamide 2b (22.5 mg, 0.1 mmol, 1 equiv.) and 3-chloroisocianonitrile 1h (41.5 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 84:16) to afford 3u (18 mg, 57% yield) as a white solid.

**1H NMR** (300 MHz, CDCl₃) δ 8.49 (s, 1H), 8.41 (d, J = 5.0 Hz, 1H), 7.40 – 7.30 (m, 2H), 7.25 – 7.23 (m, 1H), 7.17 – 7.08 (m, 2H), 5.44 (s, 1H), 5.03 (q, J = 7.0 Hz, 1H), 1.64 (d, J = 7.1 Hz, 3H), 1.36 (s, 9H).

**13C [1H] NMR** (75 MHz, CDCl₃) δ 169.4, 152.5, 149.7, 148.0, 140.9, 138.1, 132.4, 130.0, 128.0, 127.1, 127.0, 123.2, 52.0, 38.0, 29.0, 20.6.

**HRMS**: (ESI⁺) calculated for C₁₉H₁₂ClN₂O (M+H⁺): 317.1415, found 317.1415.
**N-(tert-butyl)-2-(1-(3-phenylpyridin-4-yl)ethyl)benzamide (3v):** Synthesized according to General Procedure A using **N-(tert-butyl)-2-ethyl-N-fluorobenzamide 2b** (22.5 mg, 0.1 mmol, 1 equiv.) and 3-phenylisonicotinonitrile 1i (54.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 84:16) to afford **3v** (16.5 mg, 46% yield) as an off-white solid.

**1H NMR** (400 MHz, CDCl₃) δ 8.52 (d, J = 5.1 Hz, 1H), 8.31 (s, 1H), 7.35 – 7.27 (m, 4H), 7.22 – 7.20 (m, 2H), 7.17 (d, J = 5.2 Hz, 1H), 7.15 – 7.12 (m, 2H), 7.06 (d, J = 7.8 Hz, 1H), 4.99 (s, 1H), 4.74 (q, J = 7.1 Hz, 1H), 1.50 (d, J = 7.1 Hz, 3H), 1.25 (s, 9H).

**HRMS:** (ESI⁺) calculated for C₂₄H₂₁N₃O (M+H⁺): 359.2118, found 359.2124.

**N-(tert-butyl)-2-(1-(6,7-dihydro-5H-cyclopenta[b]pyridin-4-yl)ethyl)-N-fluorobenzamide (3w):** Synthesized according to General Procedure A using **N-(tert-butyl)-2-ethyl-N-fluorobenzamide 2b** (22.5 mg, 0.1 mmol, 1 equiv.) and 6,7-dihydro-5H-cyclopenta[b]pyridine-4-carbonitrile 1j (59.5 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc from 86:14 to 1:1) to afford **3w** (12.5 mg, 36% yield) as a white wax.

**1H NMR** (300 MHz, CDCl₃) δ 8.28 (d, J = 5.3 Hz, 1H), 7.38 – 7.29 (m, 2H), 7.27 – 7.14 (m, 2H), 6.80 (d, J = 5.3 Hz, 1H), 5.38 (s, 1H), 4.84 (q, J = 7.1 Hz, 1H), 3.01 – 2.64 (m, 4H), 2.13 – 1.98 (m, 2H), 1.59 (d, J = 7.1 Hz, 3H), 1.33 (s, 9H).

**HRMS:** (ESI⁺) calculated for C₂₁H₂₀N₃O (M+H⁺):323.2118, found 323.2114.

**N-(tert-butyl)-2-(1-(perfluoropyridin-4-yl)ethyl)benzamide (3x):** Synthesized according to General Procedure A using **N-(tert-butyl)-2-ethyl-N-fluorobenzamide 2b** (22.5 mg, 0.1 mmol, 1 equiv.) and 2,3,5,6-tetrafluorisonicotinonitrile 1m (53.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/CH₂Cl₂/EtOAc 80:16:4) to afford **3x** (14 mg, 40% yield) as a yellow solid.

**1H NMR** (300 MHz, CDCl₃) δ 7.56 – 7.38 (m, 2H), 7.36 – 7.27 (m, 2H), 5.56 (s, 1H), 5.24 (t, J = 7.3 Hz, 1H), 1.78 (d, J = 7.3 Hz, 3H), 1.39 (s, 9H).

**13C [1H] NMR** (101 MHz, CDCl₃) δ 169.1, 153.0, 150.5, 148.7, 142.8, 138.2, 137.8, 129.9, 129.5, 128.5, 128.4, 127.6, 127.2, 126.5, 52.1, 33.0, 28.7, 21.1.

**HRMS:** (ESI⁺) calculated for C₁₅H₁₈F₃N₃O (M+Na⁺): 377.1242, found 377.1247.

**N-(tert-butyl)-2-(1-(isoquinolin-1-yl)ethyl)benzamide (3y):** Synthesized according to General Procedure A using **N-(tert-butyl)-2-ethyl-N-fluorobenzamide 2b** (22.5 mg, 0.1 mmol, 1 equiv.) and isoquinoline-1-carbonitrile 1n (46.5 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/CH₂Cl₂/EtOAc 50:48:2) to afford **3y** (25 mg, 79% yield) as a yellowish solid.

**1H NMR** (300 MHz, CDCl₃) δ 7.27 (m, 4H), 7.22 (d, J = 7.8 Hz, 1H), 3.01 (t, J = 5.2 Hz, 1H), 4.99 (s, 1H), 4.74 (q, J = 7.1 Hz, 1H), 1.50 (d, J = 7.1 Hz, 3H), 1.25 (s, 9H).

**HRMS:** (ESI⁺) calculated for C₂₄H₂₁N₃O (M+Na⁺): 359.2118, found 359.2124.
\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\): 8.53 (d, \(J = 5.7\) Hz, 1H), 8.44 (d, \(J = 8.6\), 1H), 7.83 − 7.72 (m, 1H), 7.64 − 7.56 (m, 1H), 7.54 (dt, \(J = 7.3, 1.5\) Hz, 2H), 7.37 − 7.30 (m, 1H), 7.21 − 7.09 (m, 3H), 5.78 (q, \(J = 6.9\) Hz, 1H), 5.74 (s, 1H), 1.79 (d, \(J = 7.0\) Hz, 1H), 1.79 (d, \(J = 7.0\) Hz, 3H), 1.42 (s, 9H).

\(^1\)C\(^{1}\)H NMR (126 MHz, CDCl\(_3\)) \(\delta\): 170.3, 163.6, 143.7, 141.6, 136.9, 136.5, 129.9, 129.8, 128.4, 127.5, 127.3, 127.2, 126.7, 126.2, 126.1, 119.8, 52.0, 38.8, 28.9, 21.8.

HRMS: (ESI\(^+\)) calculated for C\(_{22}\)H\(_{25}\)N\(_2\)O (M+H\(^+\)): 333.1961, found 333.1951.

C.4 General procedure (B): Minisci reaction

![Minisci reaction scheme]

Reactions performed using set-up 1 in Figure S2. In an oven dried vial with a Teflon septum screw cap, 2-alkyl N-fluorobenzamide \(2\) (0.1 mmol, 1 equiv.) was added and dissolved in 1,2-DCE (2 mL, synthesis grade solvent). Cyanopyridine \(1\) (0.3 mmol, 3 equiv.), 4DPAIPN catalyst \(\mathbf{A}\) (0.8 mg, 0.01 mmol, 0.01 equiv.), and PPh\(_3\) (79 mg, 0.3 mmol, 3 equiv.) were added. Finally, water is added (9 \(\mu\)L, 0.5 mmol, 5 equiv.). The resulting yellow mixture was irradiated under stirring for 12 hours. The mixture was transferred to an extraction funnel, saturated aqueous NaHCO\(_3\) was added and the organic layer was extracted with EtOAc. The organic layer was washed with brine twice. The combined organic layers were dried over anhydrous MgSO\(_4\), filtered, and concentrated to dryness. The residue purified by column chromatography on silica gel to afford the corresponding product in the stated yield with >95% purity according to \(^1\)H-NMR analysis. The exact conditions for chromatography are reported for each compound.

C.5 Characterization of Minisci products

**N-(tert-butyl)-2-((4-cyanopyridin-2-yl)methyl)benzamide (4a):** Synthesized according to General Procedure B using \(N\)-(tert-butyl)-N-fluoro-2-methylbenzamide \(2a\) (21.0 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile \(1a\) (31.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/CH\(_2\)Cl\(_2\)/acetone 50:48:2) to afford \(4a\) (15 mg, 51% yield) as a white solid.

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\): 8.66 (dd, \(J = 5.0, 0.9\) Hz, 1H), 7.58 (brs, 1H), 7.56 − 7.51 (dd, \(J = 7.3, 1.6\) Hz, 1H), 7.39 (dd, \(J = 5.0, 1.5\) Hz, 1H), 7.36 − 7.28 (m, 2H), 7.21 − 7.17 (m, 2H), 4.38 (s, 2H), 1.44 (s, 9H).

\(^1\)C\(^{1}\)H NMR (126 MHz, CDCl\(_3\)) \(\delta\): 169.0, 162.8, 150.1, 138.3, 135.3, 131.0, 130.1, 128.3, 127.4, 125.2, 123.1, 121.4, 116.6, 52.0, 41.3, 28.9.

HRMS: (ESI\(^+\)) calculated for C\(_{18}\)H\(_{19}\)N\(_3\)NaO (M+Na\(^+\)): 316.1420, found 316.1420.

**N-(tert-butyl)-2-(1-(4-cyanopyridin-2-yl)ethyl)benzamide (4b):** Synthesized according to General Procedure B using \(N\)-(tert-butyl)-2-ethyl-N-fluorobenzamide \(2b\) (22.5 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile \(1a\) (31.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/CH\(_2\)Cl\(_2\)/acetone 50:48:2) to afford \(4b\) (19.0 mg, 62% yield) as a white solid.
N-(tert-butyl)-2-((4-cyanopyridin-2-yl)methyl)-3-methoxybenzamide (4c): Synthesized according to General Procedure B using N-(tert-butyl)-N-fluoro-3-methoxy-2-methylbenzamide 2c (24.0 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile 1a (31.0 mg, 0.3 mmol, 1 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 93:7 to 85:15) to afford 4c (22 mg, 68% yield) as a white solid.

\( ^1\text{H} \text{NMR} \) (400 MHz, CDCl\(_3\)) \( \delta \) 8.56 (dd, \( J = 5.0, 0.9 \) Hz, 1H), 8.30 (s, 1H), 7.62 (t, \( J = 1.2 \) Hz, 1H), 7.35 (dd, \( J = 5.1, 1.5 \) Hz, 1H), 7.27 (t, \( J = 7.9 \) Hz, 1H), 7.19 (dd, \( J = 7.7, 1.2 \) Hz, 1H), 6.82 (dd, \( J = 8.1, 1.2 \) Hz, 1H), 4.25 (s, 2H), 3.73 (s, 3H), 1.42 (s, 9H).

\( ^{13}\text{C} \)\(^{1}\text{H} \text{NMR} \) (101 MHz, CDCl\(_3\)) \( \delta \) 169.8, 162.1, 149.8, 137.9, 133.0, 131.9, 127.6, 125.6, 125.5, 123.0, 121.4, 116.6, 51.9, 38.9, 28.9, 28.9, 20.3.

HRMS: (ESI\(^{+}\)) calculated for C\(_{19}\)H\(_{22}\)N\(_3\)NaO\(_2\) (M+Na\(^{+}\)): 346.1526, found 346.1533.

N-(tert-butyl)-2-((4-cyanopyridin-2-yl)methyl)-3-methylbenzamide (4d): Synthesized according to General Procedure B using N-(tert-butyl)-N-fluoro-2,3-dimethylbenzamide 2d (22.5 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile 1a (31.0 mg, 0.3 mmol, 1 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 93:7 to 85:15) to afford 4d (13 mg, 42% yield) as a white solid.

\( ^1\text{H} \text{NMR} \) (400 MHz, CDCl\(_3\)) \( \delta \) 8.64 (d, \( J = 4.9 \) Hz, 1H), 7.49 (s, 1H), 7.36 (dt, \( J = 5.5, 1.6 \) Hz, 2H), 7.25 – 7.15 (m, 2H), 6.99 (s, 1H), 4.34 (s, 2H), 2.14 (s, 3H), 1.37 (s, 9H).

\( ^{13}\text{C} \)\(^{1}\text{H} \text{NMR} \) (101 MHz, CDCl\(_3\)) \( \delta \) 169.8, 162.1, 149.8, 139.8, 137.9, 133.0, 131.9, 127.6, 125.6, 125.5, 123.0, 121.4, 116.6, 51.9, 38.9, 28.9, 28.9, 20.3.

HRMS: (ESI\(^{+}\)) calculated for C\(_{19}\)H\(_{22}\)N\(_3\)O (M+H\(^{+}\)): 308.1757, found 308.1749.

N-(tert-butyl)-2-((4-cyanopyridin-2-yl)methyl)-4-methoxybenzamide (4e): Synthesized according to General Procedure B using N-(tert-butyl)-N-fluoro-4-methoxy-2-methylbenzamide 2e (24.0 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile 1a (31.0 mg, 0.3 mmol, 1 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 93:7 to 75:25) to afford 4e (15.5 mg, 48% yield) as a white solid.

\( ^1\text{H} \text{NMR} \) (400 MHz, CDCl\(_3\)) \( \delta \) 8.64 (d, \( J = 5.0 \) Hz, 1H), 7.58 (s, 1H), 7.47 (d, \( J = 8.5 \) Hz, 1H), 7.37 (dd, \( J = 5.1, 1.5 \) Hz, 1H), 7.05 (s, 1H), 6.79 (dd, \( J = 8.6, 2.6 \) Hz, 1H), 6.70 (d, \( J = 2.6 \) Hz, 1H), 4.36 (s, 2H), 3.77 (s, 3H), 1.40 (s, 9H).

\( ^{13}\text{C} \)\(^{1}\text{H} \text{NMR} \) (101 MHz, CDCl\(_3\)) \( \delta \) 168.8, 162.7, 160.7, 149.8, 137.4, 130.8, 130.0, 125.5, 123.2, 121.6, 116.6, 116.4, 112.4, 55.5, 51.9, 41.4, 29.0.

HRMS: (ESI\(^{+}\)) calculated for C\(_{19}\)H\(_{22}\)N\(_3\)O\(_2\) (M+H\(^{+}\)): 324.1707, found 324.1712.
**N-(tert-butyl)-2-((4-cyanopyridin-2-yl)methyl)-4-fluorobenzamide (4f):**
Synthesized according to General Procedure B using using N-(tert-butyl)-N,4-
difluoro-2-methylbenzamide 2f (22.5 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile 1a (31.0 mg, 0.3 mmol, 3.0 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 93:7 to 87:13) to afford 4f (12 mg, 39% yield) as a white solid.

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.65 (d, J = 5.0 Hz, 1H), 7.59 (s, 1H), 7.51 (dd, J = 8.6, 5.8 Hz, 1H), 7.39 (dt, J = 5.4, 2.6 Hz, 1H), 7.23 (s, 1H), 6.96 (td, J = 8.3, 2.6 Hz, 1H), 6.87 (dd, J = 9.5, 2.6 Hz, 1H), 4.34 (s, 2H), 1.41 (s, 9H).

$^{13}$C[1H] NMR (101 MHz, CDCl$_3$) δ 168.0, 163.1 (d, J = 255.5 Hz), 150.0, 137.9, 137.9 (d, J = 7.7 Hz), 134.4 (d, J = 3.3 Hz), 130.4 (d, J = 8.7 Hz), 125.2, 123.3, 121.5, 117.3 (d, J = 22.1 Hz), 116.3, 114.3 (d, J = 21.1 Hz), 52.0, 41.0, 28.8.

$^{19}$F NMR (376 MHz, CDCl$_3$) δ -110.25.

HRMS: (ESI$^+$) calculated for C$_{18}$H$_{16}$FN$_3$O (M+H$^+$): 312.1507, found 312.1512.

**N-(tert-butyl)-4-chloro-2-((4-cyanopyridin-2-yl)methyl)benzamide (4g):**
Synthesized according to General Procedure B using N-(tert-butyl)-4-chloro-N-
fluoro-2-methylbenzamide 2g (24.5 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile 1a (31.0 mg, 0.3 mmol, 3.0 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 93:7 to 85:15) to afford 4g (13 mg, 40% yield) as a white solid.

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.64 (d, J = 5.1 Hz, 1H), 7.59 (s, 1H), 7.46 (d, J = 8.3 Hz, 1H), 7.40 (dd, J = 5.0, 1.5 Hz, 1H), 7.36 (s, 1H), 7.25 (m, 2H), 7.16 (d, J = 2.1 Hz, 1H), 4.31 (s, 2H), 1.40 (s, 9H).

$^{13}$C[1H] NMR (101 MHz, CDCl$_3$) δ 168.0, 161.9, 150.1, 137.1, 136.8, 135.8, 130.7, 129.9, 127.6, 125.7, 123.6, 121.7, 116.4, 52.2, 41.0, 28.9.

HRMS: (ESI$^+$) calculated for C$_{18}$H$_{16}$ClN$_3$O (M+H$^+$): 328.1211, found 328.1208.

**N-(tert-butyl)-2-((4-cyanopyridin-2-yl)methyl)-5-methoxybenzamide (4h):**
Synthesized according to General Procedure B using using N-(tert-butyl)-N-fluoro-5-methoxy-2-methylbenzamide 2h (24.0 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile 1a (31.0 mg, 0.3 mmol, 3.0 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 93:7 to 85:15) to afford 4h (16.5 mg, 51% yield) as a white solid.

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.63 (d, J = 5.0 Hz, 1H), 7.56 (s, 1H), 7.42 (s, 1H), 7.37 (dd, J = 5.1, 1.5 Hz, 1H), 7.07 (d, J = 8.5 Hz, 1H), 7.04 (d, J = 2.8 Hz, 1H), 6.86 (dd, J = 8.5, 2.8 Hz, 1H), 4.28 (s, 2H), 3.81 (s, 3H), 1.41 (s, 9H).

$^{13}$C[1H] NMR (101 MHz, CDCl$_3$) δ 168.7, 163.0, 158.6, 149.7, 139.4, 132.0, 127.0, 125.3, 123.2, 121.7, 116.5, 116.4, 113.1, 55.6, 52.0, 40.4, 28.9.

HRMS: (ESI$^+$) calculated for C$_{19}$H$_{21}$N$_3$NaO$_2$ (M+Na$^+$): 346.1526, found 346.1522.

**N-(tert-butyl)-2-((4-cyanopyridin-2-yl)methyl)-5-methylbenzamide (4i):**
Synthesized according to General Procedure B using using N-(tert-butyl)-N-fluoro-2,5-dimethylbenzamide 2i (22.5 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile 1a (31.0 mg, 0.3 mmol, 3.0 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 93:7 to 85:15) to afford 4i (15 mg, 50% yield) as an off-white solid.
5-bromo-N-(tert-butyl)-2-((4-cyanopyridin-2-yl)methyl)benzamide (4j): Synthesized according to General Procedure B using 5-bromo-N-(tert-butyl)-N-flouro-2-methylbenzamide 2j (29.0 mg, 0.1 mmol, 1 equiv.) and isonicotonitrile 1a (31.0 mg, 0.3 mmol, 3.0 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/AcOEt 93:7 to 85:15) and (toluene/EtOAc 9:4 for further purification from dibenzyolated side-product) to afford 4j (17 mg, 46% yield) as a white solid.

1H NMR (400 MHz, CDCl3) δ 8.63 (d, J = 5.0 Hz, 1H), 7.64 (d, J = 2.2 Hz, 1H), 7.58 (s, 1H), 7.43 (dd, J = 8.2, 2.2 Hz, 1H), 7.40 (dd, J = 5.1, 1.5 Hz, 1H), 7.23 (br s, 1H), 7.06 (d, J = 8.2 Hz, 1H), 4.30 (s, 2H), 1.41 (s, 9H).

13C [1H] NMR (101 MHz, CDCl3) δ 165.4, 163.7, 162.6, 149.6, 149.2, 140.2, 134.1, 133.1, 132.6, 131.3, 125.5, 123.5, 121.8, 121.2, 116.3, 52.3, 40.7, 28.9.

HRMS: (ESI+) calculated for C19H18N3O (M+H+): 320.1757, found 320.1759.

N-(tert-butyl)-3-((4-cyanopyridin-2-yl)methyl)thiophene-2-carboxamide (4k): Synthesized according to General Procedure B using using N-(tert-butyl)-N-flouro-3-methylthiophene-2-carboxamide 2k (21.5 mg, 0.1 mmol, 1 equiv.) and isonicotonitrile 1a (31.0 mg, 0.3 mmol, 3.0 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 93:7 to 85:15) to afford 4k (13 mg, 45% yield) as a yellowish wax.

1H NMR (400 MHz, CDCl3) δ 8.66 (d, J = 5.1 Hz, 1H), 8.08 (s, 1H), 7.63 (s, 1H), 7.42 (dd, J = 5.1, 1.5 Hz, 1H), 7.28 (d, J = 5.1 Hz, 1H), 6.89 (d, J = 5.1 Hz, 1H), 4.40 (s, 2H), 1.48 (s, 9H).

13C [1H] NMR (101 MHz, CDCl3) δ 162.1, 161.5, 149.3, 137.3, 137.1, 129.9, 127.5, 125.4, 123.7, 122.3, 116.3, 52.3, 37.3, 29.1.

HRMS: (ESI+) calculated for C16H16N3O (M+H+): 372.0706, found 372.0704.

N-(tert-butyl)-2-(1-(4-cyano-6-methylpyridin-2-yl)ethyl)benzamide (4m): Synthesized according to General Procedure B using using N-(tert-butyl)-2-ethyl-N-fluorobenamide 2b (22.5 mg, 0.1 mmol, 1 equiv.) and 2-methylisonicotinonitrile 1b (35.5 mg, 0.3 mmol, 3.0 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc form 95:5 to 80:20) to afford 4m (18 mg, 56% yield) as a white solid.

1H NMR (500 MHz, CDCl3) δ 7.49 – 7.45 (m, 1H), 7.40 (brs, 1H), 7.32 (td, J = 7.6, 1.5 Hz, 1H), 7.24 (td, J = 7.5, 1.3 Hz, 1H), 7.21 (brs, 1H), 7.18 (dd, J = 7.8, 1.3 Hz, 1H), 7.08 (s, 1H), 4.86 (q, J = 7.1 Hz, 1H), 2.56 (s, 3H), 1.71 (d, J = 7.1 Hz, 3H), 1.49 (s, 9H).

13C [1H] NMR (126 MHz, CDCl3) δ 169.4, 166.0, 159.4, 141.3, 138.0, 130.0, 128.0, 127.6, 126.7, 122.6, 121.3, 119.7, 117.1, 52.1, 42.0, 29.0, 24.6, 20.1.

HRMS: (ESI+) calculated for C20H24N3O (M+H+): 322.1914, found 322.1915.
**N-(tert-butyl)-2-(1-(4-cyano-6-ethylypyridin-2-yl)ethyl)benzamide (4n):** Synthesized according to General Procedure B using N-(tert-butyl)-2-ethyl-N-fluorobenzamide 2a (22.5 mg, 0.1 mmol, 1 equiv.) and 2-ethylyisonicotinonitrile 1e (40.0 mg, 0.3 mmol, 3.0 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 95:5 to 80:20) to afford 4n (20 mg, 60% yield) as a yellow oil.

_1H NMR (400 MHz, CDCl₃) δ 7.44 – 7.38 (m, 1H), 7.39 (d, J = 0.7 Hz, 1H), 7.33 – 7.27 (m, 1H), 7.24 – 7.18 (m, 3H), 6.70 (s, 1H), 4.85 (q, J = 7.1 Hz, 1H), 2.82 (q, J = 7.6 Hz, 2H), 1.69 (d, J = 7.1 Hz, 3H), 1.45 (s, 9H), 1.25 (t, J = 7.6 Hz, 3H).

_13C{[1]H} NMR (101 MHz, CDCl₃) δ 169.5, 165.8, 164.3, 141.5, 137.9, 129.9, 127.8, 127.6, 126.7, 121.3, 120.4, 117.2, 52.1, 42.0, 31.2, 29.0, 20.4, 13.5.

HRMS: (ESI⁺) calculated for C₂₁H₂₆N₃O (M+H⁺): 336.2070, found 336.2062.

**N-(tert-butyl)-2-(1-(4-cyano-6-isopropylpyridin-2-yl)ethyl)-N-fluorobenzamide (4o):** Synthesized according to General Procedure B using N-(tert-butyl)-2-ethyl-N-fluorobenzamide 2a (22.5 mg, 0.1 mmol, 1 equiv.) and 2-isopropylisonicotinonitrile 1d (44.0 mg, 0.3 mmol, 3.0 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 8:2) to afford 4o (16 mg, 44% yield) as a yellowish wax.

_1H NMR (300 MHz, CDCl₃) δ 7.42 – 7.35 (m, 1H), 7.30 (dd, J = 4.1, 1.3 Hz, 3H), 7.25 – 7.15 (m, 2H), 6.25 (s, 1H), 4.84 (q, J = 7.1 Hz, 1H), 3.05 (p, J = 6.9 Hz, 1H), 1.45 (s, 9H), 1.26 (d, J = 2.0 Hz, 6H).

_13C{[1]H} NMR (75 MHz, CDCl₃) δ 169.5, 168.1, 165.4, 141.8, 137.6, 130.0, 128.0, 127.1, 126.5, 121.3, 119.5, 117.2, 52.0, 42.0, 36.2, 29.0, 22.3, 22.2, 20.6.

HRMS: (ESI⁺) calculated for C₂₂H₂₅N₃O (M+H⁺): 350.2227, found 350.2226.

**N-(tert-butyl)-2-(1-(4-cyano-6-(p-tolyl)pyridin-2-yl)ethyl)benzamide (4p):** Synthesized according to General Procedure B using N-(tert-butyl)-2-ethyl-N-fluorobenzamide 2a (22.5 mg, 0.1 mmol, 1 equiv.) and 3-chloroisonicotinonitrile 1e (41.5 mg, 0.3 mmol, 3.0 equiv.) and 10 mol% of the photocatalyst. The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 86:14) to afford 4p (13 mg, 34% yield) as an yellowish solid.

_1H NMR (400 MHz, CDCl₃) δ 7.80 (d, J = 8.2 Hz, 2H), 7.71 (d, J = 1.2 Hz, 1H), 7.46 – 7.40 (m, 2H), 7.33 (d, J = 4.0 Hz, 2H), 7.28 (d, J = 8.1 Hz, 2H), 7.25 – 7.21 (m, 1H), 6.53 (s, 1H), 4.93 (q, J = 7.1 Hz, 1H), 2.41 (s, 3H), 1.77 (d, J = 7.1 Hz, 3H), 1.36 (s, 9H).

_13C{[1]H} NMR (101 MHz, CDCl₃) δ 169.6, 166.0, 157.8, 142.0, 140.5, 137.5, 135.0, 130.0, 129.8, 128.1, 127.4, 127.1, 126.7, 121.6, 121.5, 119.3, 117.2, 52.0, 42.1, 29.0, 21.5, 20.4.

HRMS: (ESI⁺) calculated for C₂₆H₂₇N₃NaO (M+Na⁺): 420.2046, found 420.2047.

**N-(tert-butyl)-2-(1-(4-cyano-6-(4-methoxyphenyl)pyridin-2-yl)ethyl)benzamide (4q):** Synthesized according to General Procedure B using N-(tert-butyl)-2-ethyl-N-fluorobenzamide 2a (22.5 mg, 0.1 mmol, 1 equiv.) and 2-(4-methoxyphenyl)isonicotinonitrile 1f (63.0 mg, 0.3 mmol, 3.0 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 93:7 to 85:15) to afford 4q (17 mg, 41% yield) as an yellowish solid.
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.89 – 7.83 (m, 2H), 7.67 (d, $J = 1.2$ Hz, 1H), 7.43 (dt, $J = 7.6$, 1.1 Hz, 1H), 7.41 – 7.39 (m, 1H), 7.34 – 7.30 (m, 2H), 7.23 (ddd, $J = 7.6$, 5.3, 3.4 Hz, 1H), 7.02 – 6.96 (m, 2H), 6.58 (s, 1H), 4.92 (q, $J = 7.1$ Hz, 1H), 3.87 (s, 3H), 1.77 (d, $J = 7.1$ Hz, 3H), 1.36 (s, 9H).

$^{13}$C [$^1$H] NMR (101 MHz, CDCl$_3$) $\delta$ 169.6, 165.9, 161.5, 157.5, 141.9, 137.9, 130.2, 130.0, 128.6, 128.0, 127.4, 126.7, 121.6, 120.9, 118.9, 117.3, 114.5, 55.6, 52.0, 42.1, 28.9, 20.4.

HRMS: (ESI$^+$) calculated for C$_{26}$H$_{33}$N$_3$O (M+H$^+$): 414.2176, found 414.2185.

$N$-(tert-butyl)-2-(1-(4-cyano-6-(4-phenylpyridin-2-yl)ethyl)benzamide (4r): Synthesized according to General Procedure B using using N-(tert-butyl)-2-ethyl-N-fluorobenzamide 2a (22.5 mg, 0.1 mmol, 1 equiv.) and 2-(4-fluorophenyl)isonicotinonitrile 1g (59.5 mg, 0.3 mmol, 3.0 equiv.) The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 93:7 to 85:15) to afford 4r (15 mg, 38% yield) as a yellowish solid.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.96 – 7.91 (m, 2H), 7.69 (d, $J = 1.2$ Hz, 1H), 7.46 (d, $J = 1.2$ Hz, 1H), 7.40 (dt, $J = 7.5$, 1.0 Hz, 1H), 7.36 – 7.33 (m, 2H), 7.25 – 7.21 (m, 1H), 7.20 – 7.14 (m, 2H), 6.29 (s, 1H), 4.95 (q, $J = 7.1$ Hz, 1H), 1.77 (d, $J = 7.1$ Hz, 3H), 1.39 (s, 9H).

$^{13}$C [$^1$H] NMR (101 MHz, CDCl$_3$) $\delta$ 169.6, 166.2, 164.2 (d, $^1$J = 250.7 Hz), 156.7, 141.8, 137.8, 133.8 (d, $^2$J = 3.1 Hz), 130.1, 129.1 (d, $^3$J = 8.5 Hz), 128.1, 127.3, 126.8, 122.2, 121.8, 119.2, 117.1, 116.2 (d, $^4$J = 21.8 Hz), 52.1, 42.2, 28.9, 20.5.

HRMS: (ESI$^+$) calculated for C$_{23}$H$_{24}$FNO (M+H$^+$): 402.1976, found 402.1967.

$N$-(tert-butyl)-2-(1-(3-chloro-4-cyanopyridin-2-yl)ethyl)benzamide (4s): Synthesized according to General Procedure B using using N-(tert-butyl)-2-ethyl-N-fluorobenzamide 2a (22.5 mg, 0.1 mmol, 1 equiv.) and 2-(p-tolyl)isonicotinonitrile 1h (58.5 mg, 0.3 mmol, 3.0 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/acetone 92:8) to afford 4s (19 mg, 56% yield) as a white solid.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.65 (d, $J = 4.9$ Hz, 1H), 7.41 (d, $J = 4.9$ Hz, 1H), 7.34 (dd, $J = 7.5$, 1.5 Hz, 1H), 7.30 (td, $J = 7.6$, 1.5 Hz, 1H), 7.22 (td, $J = 7.5$, 1.3 Hz, 1H), 7.19 (dd, $J = 7.8$, 1.3 Hz, 1H), 5.66 (s, 1H), 5.51 (q, $J = 6.9$ Hz, 1H), 1.71 (d, $J = 6.9$ Hz, 4H), 1.45 (s, 9H).

$^{13}$C [$^1$H] NMR (126 MHz, CDCl$_3$) $\delta$ 169.5, 163.7, 147.3, 141.3, 137.5, 132.5, 130.1, 128.4, 126.8, 126.7, 124.4, 121.7, 114.4, 52.0, 40.0, 29.0, 21.0.

HRMS: (ESI$^+$) calculated for C$_{19}$H$_{19}$ClN$_3$NaO (M+Na$^+$): 364.1187, found 364.1188.

$N$-(tert-butyl)-2-(1-(4-cyano-5-phenylpyridin-2-yl)ethyl)benzamide (4t): Synthesized according to General Procedure B using using N-(tert-butyl)-2-ethyl-N-fluorobenzamide 2a (22.5 mg, 0.1 mmol, 1 equiv.) and 3-phenylisonicotinonitrile 1i (54.0 mg, 0.3 mmol, 3.0 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/acetone 92:8) to afford 4t (21 mg, 55% yield) as a white solid.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.69 (s, 1H), 7.68 (s, 1H), 7.54 – 7.43 (m, 7H), 7.35 (ddd, $J = 8.5$, 7.2, 1.5 Hz, 1H), 7.29 – 7.26 (m, 1H), 7.24 (dd, $J = 7.4$, 1.4 Hz, 1H), 6.98 (s, 1H), 4.94 (q, $J = 7.2$ Hz, 1H), 1.76 (d, $J = 7.1$ Hz, 3H), 1.47 (s, 9H).
$^{13}$C $^{[1]H}$ NMR (101 MHz, CDCl$_3$) δ 169.4, 164.6, 150.0, 141.3, 138.0, 136.4, 134.5, 130.1, 129.5, 129.3, 128.9, 127.9, 127.8, 126.9, 124.1, 119.6, 116.7, 52.1, 41.7, 29.0, 20.1.

HRMS: (ESI$^+$) calculated for C$_{25}$H$_{28}$N$_2$O (M+H$^+$): 384.2070, found 384.2054.

$N$-(tert-butyl)-2-(1-(4-cyano-6,7-dihydro-5H-cyclopenta[b]pyridin-2-yl)ethyl)benzamide (4u): Synthesized according to General Procedure B using using $N$-(tert-butyl)-2-ethyl-N-fluorobenzamide 2a (22.5 mg, 0.1 mmol, 1 equiv.) and 6,7-dihydro-5H-cyclopenta[b]pyridine-4-carbonitrile 1j (43.5 mg, 0.3 mmol, 3.0 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 93:7 to 87:13) to afford 4u (13 mg, 38% yield) as a yellow oil.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.51 (s, 1H), 7.48 – 7.45 (m, 1H), 7.32 (d, $J = 0.8$ Hz, 1H), 7.29 (td, $J = 7.6$, 1.7 Hz, 1H), 7.21 (td, $J = 7.5$, 1.4 Hz, 1H), 7.14 (dd, $J = 7.8$, 1.3 Hz, 1H), 4.83 (q, $J = 7.2$ Hz, 1H), 3.07 (t, $J = 7.5$ Hz, 2H), 3.01 (t, $J = 7.8$ Hz, 2H), 2.23 – 2.11 (m, 2H), 1.68 (d, $J = 7.2$ Hz, 3H), 1.47 (s, 9H).

$^{13}$C $^1$H NMR (101 MHz, CDCl$_3$) δ 169.4, 167.0, 164.2, 141.3, 138.1, 137.9, 129.9, 128.2, 127.4, 126.8, 119.3, 116.2, 52.1, 41.5, 34.3, 30.0, 29.0, 22.7, 20.2.

HRMS: (ESI$^+$) calculated for C$_{22}$H$_{25}$N$_2$O (M+H$^+$): 348.2070, found 348.2073.

$N$-(tert-butyl)-2-(1-(4-(trifluoromethyl)pyridin-2-yl)ethyl)benzamide (4v): Synthesized according to General Procedure B using using $N$-(tert-butyl)-2-ethyl-N-fluorobenzamide 2a (22.5 mg, 0.1 mmol, 1 equiv.) and 4-(trifluoromethyl)pyridine 1o (44.0 mg, 0.3 mmol, 3.0 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 93:7 to 85:15) to afford 4v (16 mg, 46% yield) as an off-yellow solid.

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.65 (d, $J = 5.1$ Hz, 1H), 7.59 (s, 1H), 7.45 (dd, $J = 7.7$, 1.5 Hz, 1H), 7.35 (d, $J = 5.2$ Hz, 1H), 7.32 (br s, 1H), 7.30 (td, $J = 7.6$, 1.6 Hz, 1H), 7.23 (dd, $J = 7.5$, 1.4 Hz, 1H), 7.19 (dd, $J = 8.0$, 1.2 Hz, 1H), 4.94 (q, $J = 7.2$ Hz, 1H), 1.74 (d, $J = 7.1$ Hz, 3H), 1.44 (s, 9H).

$^{13}$C $^1$H NMR (126 MHz, cryoprobe, CDCl$_3$) δ 169.4, 166.5, 149.8, 141.3, 139.1 (q, $J = 33.4$ Hz) 138.2, 129.9, 128.0, 127.6, 126.8, 122.8 (q, $J = 272.2$ Hz), 117.3 (q, $J = 3.3$ Hz), 116.9 (q, $J = 3.9$ Hz), 52.0, 42.0, 28.9, 20.1.

$^{19}$F NMR (376 MHz, CDCl$_3$) δ -64.8.

HRMS: (ESI$^+$) calculated for C$_{10}$H$_{12}$F$_3$N$_2$O (M+H$^+$): 351.1679, found 351.1672.

Ethyl-2-(1-(2-(tert-butylcarbamoyl)phenyl)ethyl)isonicotinate (5w): Synthesized according to General Procedure B using using $N$-(tert-butyl)-2-ethyl-N-fluorobenzamide 2a (22.5 mg, 0.1 mmol, 1 equiv.) and ethyl isonicotinate 1p (45.5 mg, 0.3 mmol, 3.0 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 93:7 to 85:15) to afford 4w (18.5 mg, 52% yield) as off-yellow solid.

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.59 (d, $J = 5.0$ Hz, 1H), 7.97 (s, 1H), 7.81 (s, 1H), 7.70 (d, $J = 5.1$ Hz, 1H), 7.47 (dd, $J = 7.5$, 1.6 Hz, 1H), 7.27 (td, $J = 7.5$, 1.6 Hz, 2H), 7.20 (td, $J = 7.5$, 1.4 Hz, 1H), 7.16 (dd, $J = 7.7$, 1.4 Hz, 1H).

$^{13}$C $^1$H NMR (101 MHz, CDCl$_3$) δ 169.5, 166.0; 165.2, 149.2, 141.4, 138.3, 129.8, 128.2, 127.5, 126.7, 121.0, 120.1, 62.1, 52.0, 41.8, 28.9, 19.9, 14.4.

HRMS: (ESI$^+$) calculated for C$_{21}$H$_{27}$N$_2$O$_3$ (M+H$^+$): 355.2016, found 355.2008.
N-(tert-buty1)-2-(1-(4-(tert-buty1amino)-3,3-dimethyl-4-oxo-1-phenylbuty1)pyridin-2-yl)ethyl)benzamide (4): Synthesized according to General Procedure B using N-(tert-buty1)-N-fluro-2,2-dimethyl-4-phenylbutanamide 2e (26.5 mg, 0.1 mmol, 1 equiv.) and N-(tert-buty1)-2-(1-(4-cyanopyridin-2-yl)ethyl)benzamide 4b (92.0 mg, 0.3 mmol, 3.0 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 8:2) to afford 5 (42 mg, 80% yield) as a white solid.

1H NMR (500 MHz, CDCl3) δ 8.53 (d, J = 5.3 Hz, 1H), 8.24 (t, J = 5.3 Hz, 1H), 7.49 (ddd, J = 7.5, 5.8, 1.6 Hz, 1H), 7.31 – 7.24 (m, 5H), 7.23 – 7.13 (m, 3H), 7.09 – 6.99 (m, 2H), 5.32 (s, 1H), 4.73 (q, J = 7.2 Hz, 1H), 3.99 (td, J = 6.6, 3.1 Hz, 1H), 2.47 – 2.25 (m, 2H), 1.66 (d, J = 7.2 Hz, 3H), 1.41 (d, J = 5.4 Hz, 9H), 1.27 (d, J = 3.6 Hz, 9H), 1.06 (brs, 3H), 1.00 (d, J = 12.7 Hz, 3H).

13C{1H} NMR (126 MHz, CDCl3) δ 176.0, 176.0, 169.4, 169.3, 164.7, 164.6, 159.8, 148.5, 148.4, 143.8, 143.8, 141.7, 138.3, 138.3, 132.9, 128.8, 128.3, 128.3, 128.0, 127.9, 127.2, 127.1, 126.8, 126.3, 121.0, 120.7, 119.6, 119.2, 51.7, 51.6, 51.0, 51.0, 48.5, 48.5, 46.0, 45.9, 43.1, 41.5, 41.5, 28.7, 28.7, 27.1, 27.1, 26.2, 26.0.

HRMS: (ESI+) calculated for C34H26N6O2 (M+H+): 528.3585, found 528.3569.

4-benzy1pyridine (7): Synthesized according to General Procedure A using 1-benzy1-2,4,6-triphenylpyridin-1-ium tetrafluoroborate 6 (48.5 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile 1a (31.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 8:2) to afford 7 (7.5 mg, 44% yield) as an off-white solid, with characterization data in accordance with the literature.12
\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 8.52 – 8.44\) (m, 2H), 7.36 – 7.28 (m, 2H), 7.25 (d, \(J = 2.3\) Hz, 1H), 7.21 – 7.15 (m, 2H), 7.13 – 7.06 (m, 2H), 3.97 (s, 2H).

\(^{13}\)C\(^{\text{\(^1\)H}}\) NMR (75 MHz, CDCl\(_3\)) \(\delta 150.2, 150.0, 139.0, 129.2, 128.9, 126.8, 124.3, 41.4\).

2-benzylisonicotinonitrile (8): Synthesized according to General Procedure B using 1-benzyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate 6 (48.5 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile 1a (31.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/EtOAc 8:2) to afford 8 (11 mg, 57% yield) as an off-yellow solid with characterization data in accordance with the literature.\(^{13}\)

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 8.70\) (dd, \(J = 5.0, 0.9\) Hz, 1H), 7.35 – 7.20 (m, 7H), 4.19 (s, 2H).

\(^{13}\)C\(^{\text{\(^1\)H}}\) NMR (101 MHz, CDCl\(_3\)) \(\delta 163.0, 150.5, 138.0, 129.3, 129.1, 127.2, 124.8, 122.8, 121.0, 116.7, 44.7.

D. Unsuccessful substrates

| Cyanoarenes | Cyanoheteroarenes |
|-------------|-------------------|
| ![Structure](image1.png) | ![Structure](image2.png) |
| ipso-substitution reaction: 20% yield | n.d. |
| Minisci-type reaction: n.d. | n.d. |
| ![Structure](image3.png) | ![Structure](image4.png) |
| ipso-substitution reaction: n.d. | n.d. |
| ![Structure](image5.png) | ![Structure](image6.png) |
| ipso-substitution reaction: n.d. | Minisci-type reaction: 18% yield |

| N-Fluoramides |
|---------------|
| ![Structure](image7.png) | ![Structure](image8.png) |
| ipso-substitution reaction: n.d. | Minisci-type reaction: n.d. |
| ![Structure](image9.png) | ![Structure](image10.png) |
| ipso-substitution reaction: 20% | Minisci-type reaction: 17% yield |
| ![Structure](image11.png) | ![Structure](image12.png) |
| ipso-substitution reaction: 10% | Minisci-type reaction: n.d. |

Figure S4. Moderately successful and unsuccessful substrates. *n.d.*: not detected; yield determined by NMR analysis.
E. Optimization and Mechanistic Studies

E.1 Optimization studies: *Ipso substitution*

All reactions performed under inert atmosphere using the illumination set-up 1 in Figure S2. Yield determined by $^1$H NMR analysis of the crude mixture using trimethoxybenzene as the internal standard.

**Table S1.** Screening of the Photocatalysts

| entry | Photocatalyst (mol %) | yield (%) |
|-------|-----------------------|-----------|
| 1     | 4-DPAIPN (Cat. A, 3%) | 75        |
| 2     | fac-Ir(ppy)$_3$ (1%)  | 59        |
| 3     | Ir(ppy)$_2$(dtbpy)PF$_6$ (1%) | 25 |
| 4     | 5CzBN (3%)            | 25        |
| 5     | 4CzIPN (3%)           | 20        |
| 6     | 3DPA2FPN (3%)         | 6         |

**Table S2.** Further optimization.

| entry | deviation     | yield (%) |
|-------|---------------|-----------|
| 1     | none          | 25        |
| 2     | Ir(ppy)$_3$   | 59        |
| 3     | DABCO as quencher | 0     |
| 4     | 2a (3 equiv.) | 65        |
| 5     | 4-DPAIPN (1%) | 75        |
| 6     | 15 ºC         | 0         |
| 7     | 60 ºC         | 31        |
| 8     | Reaction under air | 0     |
| 9     | No light, no photocatalyst | 0     |
E.2 Optimization studies: Minisci reaction.

All reactions performed under inert atmosphere using the illumination set-up 1 in Figure S2. Yield determined by $^1$H NMR analysis of the crude mixture using 1,3,5-trimethoxybenzene as the internal standard.

Table S3. Optimization studies of the Minisci pathway.

| entry | deviation | yield (%) |
|-------|-----------|-----------|
| 1     | none      | 60 (51)   |
| 2     | 4-DPAIPN (3%) | 61        |
| 3     | Hantzsch ester as quencher | 45        |
| 4     | terpinene as quencher | 10        |
| 5     | tris(4-fluorophenyl)phosphane as quencher | 63        |
| 6     | TFA (10 mol%) | 61        |
| 7     | under air | 60        |
| 8     | 5 equiv. 1a | 70        |
| 9     | PPh$_3$ (1.2 equiv.) | 50        |
| 10    | No light, no photocatalyst | 0        |
| 11    | PPh$_3$ (10 mol%) | 0        |
| 12    | No PPh$_3$, TFA (2 equiv.), Ir(ppy)$_3$ | 0        |
| 13    | No PPh$_3$, TFA (1 equiv.) | 0        |

F. pH measurements

We measured the pH of the reaction mixture upon complete conversion of the both DIPEA- and PPh$_3$-enabled processes. Upon reaction completion, 4 mL of H$_2$O was added. The aqueous phase of the biphasic mixture was transferred to a clean vial. The pH was measured using a Mettler Toledo FG2-Kit FiveGo™ Portable pH Meter (Figure S5). A sample for crude pH measurement was taken using standard pH universal indicator paper.

Ipso-substitution process of 1a and 2a to afford 3a enabled by DIPEA conditions as in entry 1 of Figure 2b in the main manuscript

\[ \text{pH} = 9.8 \]

Minisci reaction of 1a and 2a to afford 3a enabled by PPh$_3$ - water conditions as in entry 7 of Figure 2b in the main manuscript

\[ \text{pH} = 3.1 \]

These measurements indicate that the C2-selective reaction operates under a typical Minisci mechanistic regime, whereby protonation of the N-heterocycle leads to radical addition at the C2 position. In contrast, the basicity of the aqueous solution derived from the reaction with DIPEA indicates that any protons generated during the process are quenched by the excess of DIPEA. This implies that protonation of the pyridine substrate is not feasible, and therefore a Minisci pathway is unavailable.
G. Alternative mechanistic scenarios

G.1 Proposed mechanism for the ipso substitution

Experimental evidence prompted us to propose the mechanism depicted in Figure S6, since product 3a is not formed when using quenchers other than tertiary amines (see Figure 2b in the manuscript). The mechanism would start with the reductive quenching of the photoredox catalyst A (4-DPAIPN) by DIPEA (see section J.1 for Stern-Volmer quenching studies). The SET event would generate a highly reducing catalyst PC⁻¹ (E¹/² (PC/PC⁻) = -1.65 vs SCE)¹¹ capable of activating 4-cyanopyridine 1a (E⁰⁺⁺ (1a/1a⁻⁺⁺) = -1.60 V vs SCE)¹⁴ by SET reduction, leading to the radical anion I. The catalyst reductive quenching would also generate the radical cation of DIPEA, which is known to undergo rapid deprotonation to deliver an α-amino radical b. The latter intermediate b has recently been reported to be a good SET reductant.¹⁵ In the context of this so-called reductant upconversion process,¹⁶ the α-amino radical b (E⁰⁺⁺(Bu₃N⁺/Bu₃N) = -1.2 V vs SCE)¹⁵ could perform a thermodynamically favorable SET reduction of the N-F bond within N-(tern-butyl)-N-fluoro-2-methylbenzamide 2a (E⁰⁺⁺(2a/2a⁻⁺⁺) = -0.84 V vs SCE).¹⁷ Alternatively, reduction of the N-F bond of 2a could be achieved via an atom transfer mechanism (XAT), again from α-amino radical b. This event would afford an N-centered amidyl radical, which upon 1,5-HAT would lead to the benzylic radical III. Radical-radical coupling between III and I, followed by decyanation, would deliver the desired product 3.

![Figure S6. Plausible mechanism for the ipso substitution pattern.](image)
G.2 Probing α-amino radicals as SET reductants for N-F bond activation

The main feature of the mechanism proposed in Figure S6 is that the photocatalyst would reduce the cyanopyridine 1, while the transiently generated α-amino radical b would activate the N-F fluoramde 2. To gain evidence that the intermediate α-amino radical may perform the N-F bond reduction, we performed the mechanistic experiment detailed in Figure S7. This method, which is based on a protocol recently reported by Ritter and coworkers,\textsuperscript{15} generates the α-amino radical in situ using a stoichiometric oxidant.

Sodium persulfate is known to oxidize tertiary amines, delivering α-amino radicals. Treatment of the N-fluoroamide 2b with Na\textsubscript{2}S\textsubscript{2}O\textsubscript{8} in the presence of DIPEA resulted in 20% of the corresponding hydrodefluorinated product 2b'. This result suggests that SET reduction of 2b by the α-amino radical b is feasible.

In addition, also the quantum yield measurement of the ipso-substitution (see section H.1 for details), which was found to be as low as 0.01, hints to a close catalytic cycle being operational, which is congruent with the mechanistic scenario depicted in Figure S6.

G.3 Minisci-type reaction, plausible mechanism

A plausible mechanism for the Minisci-type reaction is depicted in Figure S8. Reductive quenching of the excited-state photocatalyst A by triphenylphosphone (see section J.2 for Stern-Volmer quenching studies) generates the reducing photocatalyst PC\textsuperscript{cat} (E\textsc{ox} (PC/PC\textsuperscript{cat}) = -1.65 vs SCE)\textsuperscript{11} and the phosphorus-based radical cation d. Upon nucleophilic attack by water into d, followed by deprotonation, the phosphoranyl radical f is formed. Based on previously reported redox potentials of similar phosphoranyl radicals (e.g., E\textsubscript{ox} (Ph\textsubscript{3}POMe\textsuperscript{+}/Ph\textsubscript{3}POMe\textsuperscript{−}) = -1.63 vs SCE), intermediate f would be capable to trigger SET reduction of N-fluoroamide 2a delivering the benzylic radical III, after 1.5-HAT. Alternatively, reduction of the N-F bond of 2a could be achieved via an atom transfer mechanism (XAT), again from phosphoranyl radical f.\textsuperscript{18} The increased acidic conditions facilitate the Minisci-type addition of III into cyano-pyridine 1a, delivering V. Upon deprotonation and oxidation of intermediate V by another molecule of 2a (or by traces of oxygen, since the reaction is performed under air), the desired product 5a would be formed. The oxidation of V by 2a would result in a radical chain process, which could be probed by quantum yield measurement. However, our efforts along this line met with failure, because of the heterogeneity of the reaction mixture which prevented a precise quantum yield determination (see section H2 for details).
**G.4 Minisci reaction: probing the phosphoranyl radical as SET reductant for N-F activation**

The main feature of the mechanism proposed in Figure S8 is that, upon reductive quenching of the photocatalyst by PPh₃, the resulting phosphoranyl radical f would activate the N-F fluoramide 2. Recent studies reported that phosphoranyl radicals can serve as strong SET reducing agents (e.g., $E_{\text{ox}}(\text{Ph}_3\text{POMe}^+/	ext{Ph}_3\text{POMe}^-) = -1.63$ vs SCE). We surmised that, since SET reduction of 2b by a phosphoranyl radical is thermodynamically feasible, stoichiometric generation of such a radical should give the hydrodefluorinated amide 2b'. We therefore treated 2b with an excess of triphenylphosphine and persulfate as the stoichiometric oxidant in the presence of water. As shown in Figure 9, this control experiment afforded the reduced product 2b' in 40% yield.

![Figure S8](image1)

**Figure S8.** Plausible mechanism for the C2-selective Minisci-type reaction.

![Figure S9](image2)

**Figure S9.** Benzyl radical generation upon SET from f.

**G.5 Oxygen isotope experiment**

Following the general procedure B, the standard Minisci reaction was performed using H₂¹⁸O in place of H₂O. The formation of labelled triphenylphosphine oxide was detected by HR-MS (Figure S10).

![Figure S10](image3)
H. Quantum yield determination

H.1 Ipso-substitution

A ferrioxalate actinometer solution was prepared by following the Hammond variation of the Hatchard and Parker procedure outlined in the Handbook of Photochemistry. The ferrioxalate actinometer solution measures the decomposition of ferric ions to ferrous ions, which are complexed by 1,10-phenanthroline and monitored by UV/Vis absorbance at 510 nm. The moles of iron-phenanthroline complex formed are related to moles of photons absorbed. The following solutions were prepared and stored in a dark laboratory (red light):

1. Potassium ferrioxalate solution: 294.8 mg of potassium ferrioxalate (commercially available from Alfa Aesar) and 139 μL of sulfuric acid (96%) were added to a 50 mL volumetric flask, and filled to the mark with water (HPLC grade).

2. Phenanthroline solution: 0.2% by weight of 1,10-phenanthroline in water (100 mg in 50 mL volumetric flask).

3. Buffer solution: 2.47 g of NaOAc and 0.5 mL of sulfuric acid (96%) were added to a 50 mL volumetric flask and filled to the mark with water (HPLC grade).

The actinometry measurements were done as follows:

1. 1 mL of the actinometer solution was added to a Schlenk tube (diameter = 12 mm). The Schlenk tube was placed in a single HP LED 1.5 cm (set-up 2, Figure S3) away from the light source (760uA). The solution was irradiated at 460 nm. This procedure was repeated 4 times, quenching the solutions after different time intervals: 5 sec, 10 sec, 20 sec, and 40 sec.

2. Then 1 mL of the model reaction following general procedure A with 1b (0.10 mmol) and 2b as substrates was placed in a Schlenk tube, degassed via argon bubbling, placed in the irradiation set up and irradiated for 15 minutes. This procedure was performed a total of four times with different irradiation times (15 min, 30 min, 45 min, and 60 min).

3. After irradiation, the actinometer solutions were removed and placed in a 10 mL volumetric flask containing 0.5 mL of 1,10-phenanthroline solution and 2 mL of buffer solution. These flasks were filled to the mark with water (HPLC grade).

4. The UV-Vis spectra of the complexed actinometer samples were recorded for each time interval. The absorbance of the complexed actinometer solution was monitored at 510 nm.

The moles of Fe$^{2+}$ formed for each sample is determined using Beers’ Law (Eq. 1):
Mols of Fe(II) = \( V_1 \times V_3 \times \Delta A(510 \text{ nm})/10^3 \times l \times \varepsilon(510 \text{ nm}) \) (Eq. 1)

where \( V_1 \) is the irradiated volume (1 mL), \( V_2 \) is the aliquot of the irradiated solution taken for the determination of the ferrous ions (1 mL), \( V_3 \) is the final volume after complexation with phenanthroline (10 mL), \( l \) is the optical path-length of the irradiation cell (1 cm), \( \Delta A(510 \text{ nm}) \) is the optical difference in absorbance between the irradiated solution and the one stored in the dark, \( \varepsilon(510 \text{ nm}) \) is the extinction coefficient the complex Fe(phen)_3^{2+} at 510 nm (11100 L mol\(^{-1}\) cm\(^{-1}\)).

The moles of Fe\(^{2+} \) formed (\( x \)) are plotted as a function of time (\( t \)). The slope of this line was correlated to the moles of incident photons by unit of time (\( q_0 \text{ n.p} \)) by the use of the following Equation 2:

\[ \Phi(\lambda) = \frac{dx}{dt} qn.p \left[ 1 - 10^{-A(\lambda)} \right] \] (Eq. 2)

where \( \frac{dx}{dt} \) is the rate of change of a measurable quantity (spectral or any other property), the quantum yield (\( \Phi \)) for Fe\(^{2+} \) at 458 nm is 1.1,\(^{21} \) [1 - 10\(^{-A(\lambda)} \)] is the ratio of absorbed photons by the solution, and \( A(\lambda) \) is the absorbance of the actinometer at the wavelength used to carry out the experiments (460 nm). The absorbance at 460 nm \( A(460) \) was measured using a Shimadzu 2401PC UV-Vis spectrophotometer in a 10 mm path quartz cuvette, obtaining an absorbance of 0.182. \( q_0 \text{ n.p} \), which is the photon flux, was determined to be 4,14*10\(^{-10}\).

**Figure S11.** Plot of mols of Fe\(^{2+} \) formed vs irradiation time. Slope of the line correlates to the moles of incident photons by unit of time.

The moles of product 3m formed for the model reaction were determined by GC measurement (FID detector) using 1,3,5-trimethoxybenzene as internal standard. The moles of product per unit of time are related to the number of photons absorbed.

The photons absorbed are correlated to the number of incident photons by the use of Equation 1. According to this, if we plot the moles of product (3m) versus the moles of incident photons (\( q_0 \text{ n.p} \cdot dt \)), the slope is equal to: \( \Phi \cdot (1 - 10^{-A(460 \text{ nm})}) \), where \( \Phi \) is the quantum yield to be determined and \( A(460 \text{ nm}) \) is the absorption of the reaction under study. \( A(460 \text{ nm}) \) was measured using a Shimadzu 2401PC UV-Vis spectrophotometer in 10 mm path quartz. An absorbance of 1.52 was determined for the model reaction mixture (1:4 dilution). The quantum yield (\( \Phi \)) of the photochemical transformation was measured to be 0.01.
Figure S12. Plot of mols of incident photons vs mols of product formed. Slope of the line correlates to quantum yield of the photochemical transformation.

H.2 Minisci reaction

While the reaction mixture for the ipso substitution remains homogenous during irradiation, the Minisci reaction mixture becomes heterogenous and blurry upon irradiation. Light scattering prevented a precise quantum yield determination. In addition, the induction time observed in the kinetic studies reported in section I below further complicated our efforts to precisely measure the quantum yield of the C2-selective process.

Figure S13. Reaction mixture before and after 20 mins under irradiation.

I. Kinetic profile analyses

The kinetic profile of both the ipso-substitution and the Minisci reaction have been followed for 75 minutes. The two reactions have been conducted under inert conditions using the illumination set-up 2 in Figure S3. Product yield was determined by GC-FID analysis upon calibration with trimethoxybenzene as the internal standard. The three processes in Figure S14 has been analyzed: a) the DIPEA-enabled ipso-substitution; b) the PPh₃-enabled Minisci reaction; c) and the same PPh₃-enabled Minisci reaction adding TFA.
As shown in Figure S15, the PPh₃-enabled Minisci reaction (reaction b, red line) exhibits an induction period with low product 4m formation. After about 45 minutes, the reaction rate rapidly increases, reaching 62% yield after 75 minutes. The induction time is not observed when the Minisci reaction is performed in the presence of a catalytic amount of trifluoroacetic acid (TFA, reaction c, blue line). In contrast, the ipso-substitution reaction exhibits a slow but steady kinetic rate profile, delivering 5% of product after 75 minutes (reaction a, grey line).
J. Stern Volmer quenching studies

J.1 Stern-Volmer quenching studies with DIPEA

Stern-Volmer fluorescence quenching experiments were conducted with a Fluorolog Horiba Jobin Yvon spectrophotometer equipped with a photomultiplier detector, a double monochromator, and a 350W xenon light source. 2.5 mL of 1,2-DCE, thoroughly degassed by freeze pump thaw, were placed in a 10 x 10 mm light path quartz fluorescence cuvette equipped with Silicone/PTFE 3.2 mm septum under an argon atmosphere. Then, 10 μL of a 1·10^{-3} M solution of photocatalyst in 1,2-DCE was added to give a final concentration of 4-DPAIPN of 4·10^{-6} M.

A 0.43M solution of DIPEA and 15 μL of this stock solution were added to the solution of photocatalyst. Between each addition the fluorescence spectra was measured. The emission intensity was recorded at 527 nm. After each addition, an absorption spectrum and an emission spectrum of the solution were recorded. The excitation wavelength was fixed at 390 nm (incident light slit regulated to 2 mm); the emission light was acquired from 410 nm to 650 nm (emission light slit regulated to 2 mm).

![Figure S16](image-url) Quenching of the photocatalyst emission (4·10^{-6} M in 1,2-DCE) in the presence of increasing amounts of DIPEA.

The Stern-Volmer plot, reported in Figure S17, shows a linear correlation between the amounts of DIPEA and the ratio I_0/I. On the basis of the following Equation (Eq. 1), it is possible to calculate the Stern-Volmer constant K_{SV}.^{22}

\[
\frac{I_0}{I} = 1 + K_{SV}Q
\]  

(Eq. 1)

We calculated a Stern-Volmer quenching constant of 5.9 M^{-1}. 
Figure S17. Stern-Volmer quenching plot using DIPEA as a quencher.

J.2 Stern-Volmer quenching studies with PPh₃

A 2M solution of PPh₃ was added via Hamilton syringe in portions 5 µL, 10 µL, 20 µL, 40 µL and between each addition the fluorescence spectra was measured. The emission intensity was recorded at 527 nm. After each addition, an absorption spectrum and an emission spectrum of the solution were recorded. The excitation wavelength was fixed at 390 nm (incident light slit regulated to 2 mm); the emission light was acquired from 410 nm to 650 nm (emission light slit regulated to 2 mm).

Figure S18. Quenching of the photocatalyst emission (4·10⁻⁶ M in 1,2-DCE) in the presence of increasing amounts of PPh₃.

The Stern-Volmer plot, reported in Figure S19, shows a linear correlation between the amounts of PPh₃ and the ratio I₀/I. On the basis of the following Equation (Eq. 1), it is possible to calculate the Stern-Volmer constant Kₜₐₚₚ₄."²²

\[
\frac{I_0}{I} = 1 + K_{SV}[Q] \quad \text{(Eq. 1)}
\]

We calculated a Stern-Volmer quenching constant of 45.3 M⁻¹.

S33
J.3 Stern-Volmer quenching studies with 2a model

A 0.43 M solution of N-fluorobenzamide 2a and 15 μL of this stock solution were added to the solution of photocatalyst. Between each addition the fluorescence spectra was measured. The emission intensity was recorded at 527 nm. After each addition, an absorption spectrum and an emission spectrum of the solution were recorded. The excitation wavelength was fixed at 390 nm (incident light slit regulated to 2 mm); the emission light was acquired from 410 nm to 650 nm (emission light slit regulated to 2 mm).

The Stern-Volmer plot, reported in Figure S21, shows a linear correlation between the amounts of NF and the ratio I₀/I. On the basis of the following Equation (Eq. 1), it is possible to calculate the Stern-Volmer constant $K_{SV}$.\textsuperscript{22}

\[
\frac{I_0}{I} = 1 + K_{SV}*[Q] \quad (\text{Eq. 1})
\]

We calculated a Stern-Volmer quenching constant of 18.8 M$^{-1}$. 

---

**Figure S19.** Stern-Volmer quenching plot using PPh$_3$ as a quencher.

**Figure S20.** Quenching of the photocatalyst emission (4·10$^{-6}$ M in 1,2-DCE) in the presence of increasing amounts of N-fluorobenzamide 2a.
Figure S21. Stern-Volmer quenching plot using N-fluorobenzamide 2a as a quencher.

J.4 Stern-Volmer quenching studies with 4-cyanopyridine 1a
A 1.22 M solution of 4-cyanopyridine 1a and 10 μL of this stock solution were added to the solution of photocatalyst. Between each addition the fluorescence spectra was measured. The emission intensity was recorded at 527 nm. After each addition, an absorption spectrum and an emission spectrum of the solution were recorded. The excitation wavelength was fixed at 390 nm (incident light slit regulated to 2 mm); the emission light was acquired from 410 nm to 650 nm (emission light slit regulated to 2 mm).

Figure S22. Quenching of the photocatalyst emission (4·10⁻⁶ M in 1,2-DCE) in the presence of increasing amounts of 4-cyanopyridine 1a.

The Stern-Volmer plot, reported in Figure S23, shows a linear correlation between the amounts of NF and the ratio I₀/I. On the basis of the following Equation (eq. 1), it is possible to calculate the Stern-Volmer constant K_{SV}.²²

\[ \frac{I_0}{I} = 1 + K_{SV}*[Q] \]  
(eq. 1)

We calculated a Stern-Volmer quenching constant of 4.4 M⁻¹.
Figure S23. Stern-Volmer quenching plot using 4-cyanopyridine 1a as a quencher.
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J. NMR spectra and UPC$^2$ trace

$^1$H NMR (500 MHz, CDCl$_3$)

13C NMR (126 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
$^1$H NMR (300 MHz, CDCl$_3$)

$^{13}$C NMR (75 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^{19}$F NMR (376 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
$^1$H NMR (300 MHz, CDCl₃)

$^{13}$C NMR (75 MHz, CDCl₃)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
$^1$H NMR (300 MHz, CDCl$_3$)

$^{13}$C NMR (75 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^{19}$F NMR (376 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, cryoprobe, CDCl$_3$)
$^{19}\text{F NMR (376 MHz, CDCl}_3)$
$^1$H NMR (300 MHz, CDCl$_3$)

$^{13}$C NMR (75 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (300 MHz, CDCl$_3$)

$^{13}$C NMR (75 MHz, CDCl$_3$)
$^1$H NMR (300 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^{19}$F NMR (376 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
\[ ^1H \text{NMR} \ (500 \text{ MHz, CDCl}_3) \]

\[ ^13C \text{NMR} \ (126 \text{ MHz, CDCl}_3) \]
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (75 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^{1}H$ NMR (400 MHz, CDCl$_3$)

$^{13}C$ NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^{1}H$ NMR (400 MHz, CDCl$_3$)

$^{13}C$ NMR (101 MHz, CDCl$_3$)
\(^1\)H NMR (400 MHz, CDCl\(_3\))

\[^{13}\]C NMR (101 MHz, CDCl\(_3\)) of 5k
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (300 MHz, CDCl$_3$)

$^{13}$C NMR (75 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1\text{H NMR} \ (400 \text{ MHz, CDCl}_3)$

$^{13}\text{C NMR} \ (101 \text{ MHz, CDCl}_3)$
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^{19}$F NMR (376 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
$^1\text{H NMR (400 MHz, CDCl}_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, cryoprobe CDCl$_3$)
$^{19}$F NMR (376 MHz, CDCl3)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
UPC² trace for compound 4x
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)