Electronic Supplementary Material (ESI) for Chemical Science.

Supporting Information

Switchable Photocatalysis for the Chemodivergent Benzylation of 4-Cyanopyridines

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[#] Deceased, March 16, 2020

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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.

The authors are indebted to the team of the Research Support Area at ICIQ, particularly to the NMR and the High-Resolution Mass Spectrometry Units. Grace Fox is thanked for proofreading the manuscript.

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

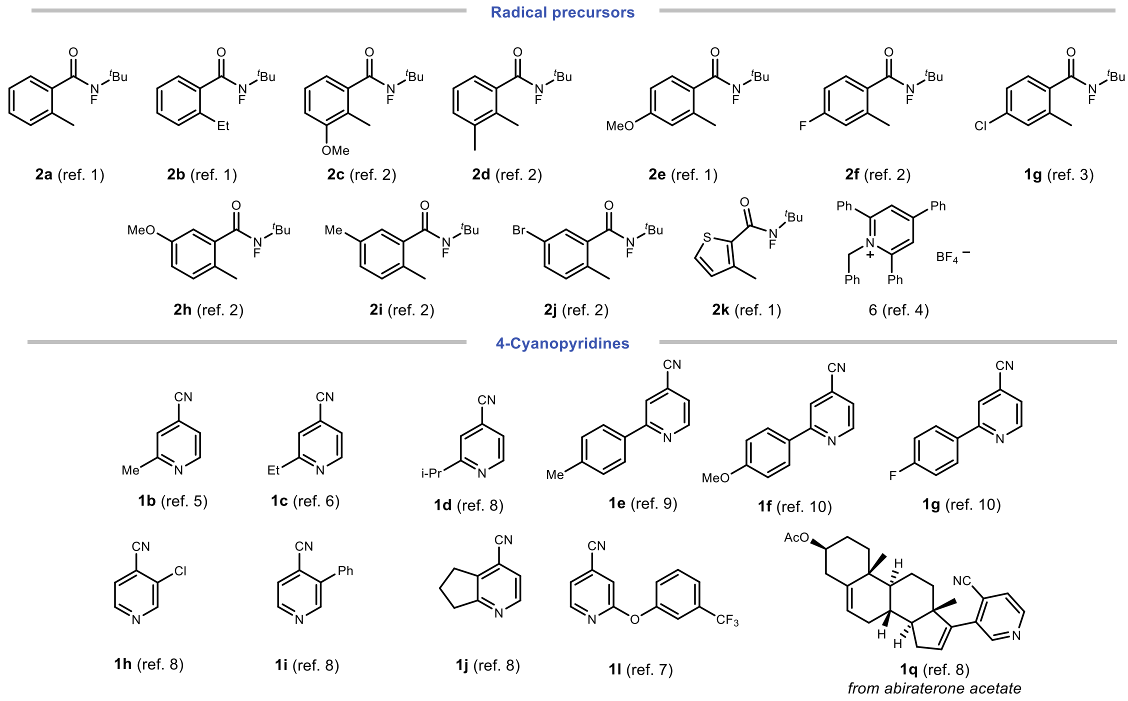
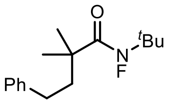


Figure S1: Starting materials synthesized according to literature precedents and corresponding references.

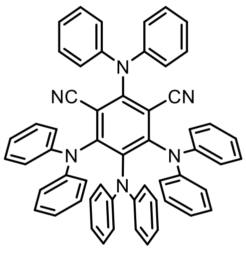


1l

***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 CH_2Cl_2 (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 CH_2Cl_2 (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 CH_2Cl_2 (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 CH_2Cl_2 (3 x 0.1 M). The combined organic layers were washed with saturated aqueous $NaHCO_3$ 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 ºC for 1.5 h, then *N*-fluorodibenzenesulfonimide (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 $CHCl_3$ (0.1 M) and water (0.1 M). The organic layer was removed, and the aqueous layer was extracted with $CHCl_3$ (3 x 0.1 M). The combined organic layers were washed with saturated aqueous $NaHCO_3$ and then brine, dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. The crude residue was purified by flash column chromatography (SiO_2: hexanes/EtOAc 95:5) to give the product as a yellowish oil (633 mg, 60% yield).

^{1}H NMR (400 MHz, CDCl3) δ 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).

^{13}C{^{1}H} NMR (101 MHz, CDCl3) δ 181.8 (d, J = 3.3 Hz), 142.5, 128.4, 128.3, 125.8, 64.4 (d, J = 10.2 Hz), 45.1 (d, J = 3.2 Hz), 41.6 (d, J = 7.8 Hz), 31.5, 27.2 (d, J = 6.6 Hz), 25.2 (d, J = 5.4 Hz).
^{19}F NMR (376 MHz, CDCl3) δ -78.8 (s).



4DPAIPN

4DPAIPN (photocatalyst **A**)**:** Following a modified procedure of a reported protocol,[11] sodium hydride (60% suspension in mineral oil, 1.92 g, 48 mmol, 12 equiv.) was added slowly to a stirred solution of diphenylamine (4.06 g, 24.0 mmol, 6 equiv.) in anhydrous DMF (40 mL). The resulting suspension was heated to 60 °C under argon for 1.5–2 h. Then, 2,4,5,6-tetrafluoroisophthalonitrile (0.80 g, 4.0 mmol, 1.0 equiv.) was added and the resulting reaction mixture was stirred at 50 °C for 4 h, and then at room temperature overnight. Water (10 mL) was added and the mixture was diluted with 160 mL H_2O, extracted with CH_2Cl_2 (3 x 80 mL) and dried over Na_2SO_4. The solution was concentrated *in vacuo* and the residue was suspensended in hexane/EtOAc (2:1, 150 mL). The precipitate was filtered and washed with THF (30 mL) to remove excess diphenylamine, affording the title compound as a yellow-orange crystalline solid (1.42 g, 1.78 mmol, 45% yield) with characterization data in accordance with the literature.[4]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.22 (m, 4H), 7.12 – 7.05 (m, 12H), 7.07 – 6.98 (m, 2H), 6.96 – 6.84 (m, 8H), 6.73 – 6.63 (m, 10H), 6.56 (d, J = 7.4 Hz, 4H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.2, 151.7, 145.5, 144.6, 143.1, 140.3, 129.4, 128.6, 127.5, 124.2, 123.9, 122.9, 122.6, 122.6, 121.1, 113.1, 113.0.

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 ºC). 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.

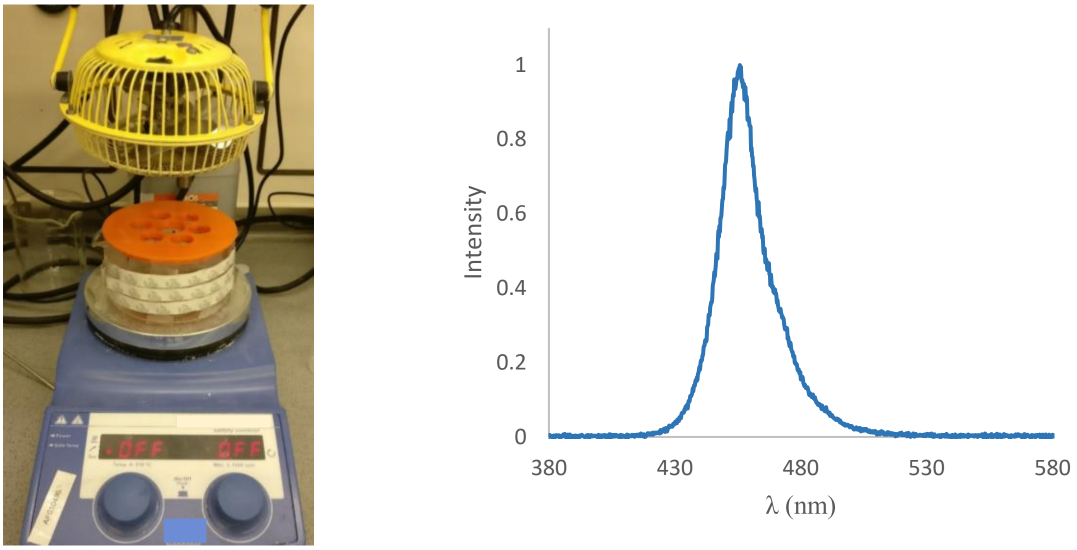


Figure S2: Blue LED photoreactor used for reactions where temperature control was not needed (*left*). Emission spectrum of the 465 nm LED strip used in this reactor (*right*).

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

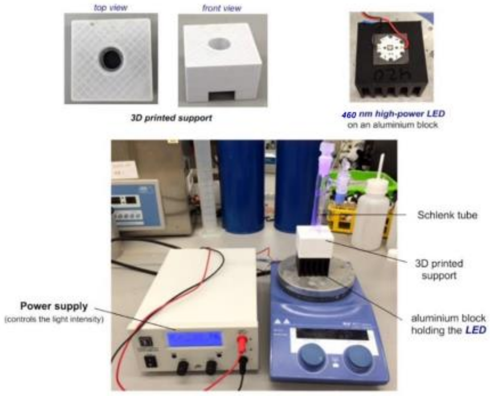
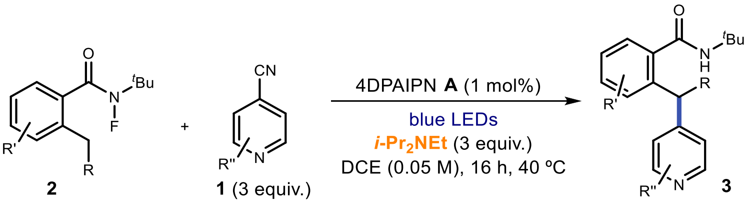


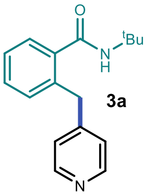
Figure S3: Detailed set-up and illumination system. The light source for illuminating the reaction vessel consisted in a 460 nm high-power single LED (LZ1-00DB00) purchased from OSA OPTO.

C.2 General procedure (A): Ipso subtitution



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 ^{1}H-NMR analysis. The exact conditions for chromatography are reported for each compound.

C.3 Characterization of ipso substitution products



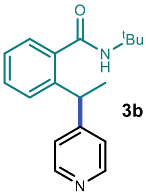
3a

***N*-(*tert*-butyl)-2-(pyridin-4-ylmethyl)benzamide (3a):** Synthesized according to General Procedure A using *N*-(*tert*-butyl)-*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}H NMR (500 MHz, $CDCl_3$) δ 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}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 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 $C_{17}H_{21}N_2O$ (M+H$^+$): 269.1648, found 269.1642.



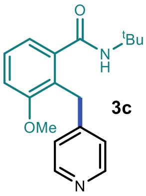
3b

***N*-(*tert*-butyl)-2-(1-(pyridin-4-yl)ethyl)benzamide (3b):** Synthesized according to General Procedure A 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/EtOAc from 7:3 to 1:1) to afford **3b** (21 mg, 74% yield) as an off-white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 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}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 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 $C_{18}H_{23}N_2O$ (M+H$^+$): 283.1805, found 283.1794.



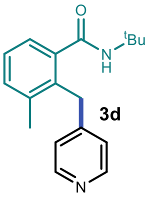
3c

***N*-(*tert*-butyl)-*N*-fluoro-3-methoxy-2-(pyridin-4-ylmethyl)benzamide (3c):** Synthesized according to General Procedure A using *N*-(*tert*-butyl)-*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}H NMR (300 MHz, $CDCl_3$) δ 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}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 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 $C_{18}H_{23}N_2O_2$ (M+H$^+$): 299.1754, found 299.1746.



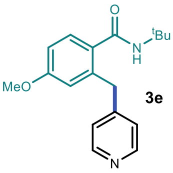
3d

***N*-(*tert*-butyl)-3-methyl-2-(pyridin-4-ylmethyl)benzamide (3d):** Synthesized according to General Procedure A using *N*-(*tert*-butyl)-*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.

^{1}H NMR (400 MHz, $CDCl_3$) δ 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).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 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 $C_{18}H_{23}N_2O$ ($M+H^+$): 283.1805, found 283.1805.



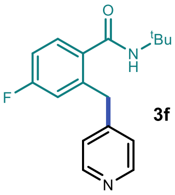
3e

N-($tert$-butyl)-4-methoxy-2-(pyridin-4-ylmethyl)benzamide (3e): Synthesized according to General Procedure A using *N*-(*tert*-butyl)-*N*-fluoro-4-methoxy-2-methylbenzamide **2e** (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 **3e** (17 mg, 57% yield) as an off-yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 – 8.48 (m, 2H), 7.45 (d, J = 5.5 Hz, 2H), 7.37 (d, J = 8.5 Hz, 1H), 6.81 (dd, J = 8.5, 2.6 Hz, 1H), 6.74 (d, J = 2.6 Hz, 1H), 5.52 (s, 1H), 4.33 (s, 2H), 3.82 (s, 3H), 1.33 (s, 9H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.2, 162.5, 161.4, 140.0, 137.2, 129.4, 129.3, 127.3, 118.1, 112.6, 77.5, 77.2, 76.8, 55.7, 52.0, 40.1, 28.9.

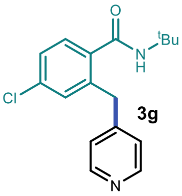
HRMS: (ESI^+) calculated for $C_{18}H_{23}N_2O_2$ ($M+H^+$): 299.1754, found 299.1750.



3f

N-($tert$-butyl)-4-fluoro-2-(pyridin-4-ylmethyl)benzamide (3f): Synthesized according to General Procedure A using *N*-(*tert*-butyl)-*N*,4-difluoro-2-methylbenzamide **2f** (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 7:3) to afford **3f** (17 mg, 59% yield) as an off-white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 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).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 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, ^{2}J = 21.8 Hz), 113.7 (d, J = 21.4 Hz), 51.9, 38.1, 28.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.3.
HRMS: (ESI^+) calculated for $C_{17}H_{20}FN_2O$ ($M+H^+$): 287.1554, found 287.1548.



3g

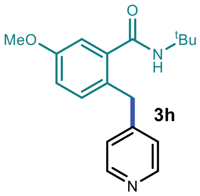
N-($tert$-butyl)-4-chloro-2-(pyridin-4-ylmethyl)benzamide (3g): Synthesized according to General Procedure A *N*-(*tert*-butyl)-4-chloro-*N*-fluoro-2-methylbenzamide **2g** (24.0 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile **1a** (31.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash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

^{1}H NMR (400 MHz, $CDCl_3$) δ 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).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 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 $C_{17}H_{20}ClN_2O$ ($M+H^+$): 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.

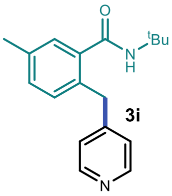


3h

^{1}H NMR (500 MHz, $CDCl_3$) 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).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 168.9, 158.4, 150.7, 150.0, 139.0, 132.5, 128.57, 124.3, 115.1, 113.3, 55.6, 52.0, 37.6, 28.7.

HRMS: (ESI$^+$) calculated for $C_{18}H_{23}N_2O_2$ (M+H$^+$): 299.1754, found 299.1747.



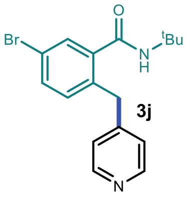
3i

N-(*tert*-butyl)-5-methyl-2-(pyridin-4-ylmethyl)benzamide (3h): Synthesized according to General Procedure A 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 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.

^{1}H NMR (400 MHz, $CDCl_3$) 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).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) 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 $C_{18}H_{23}N_2O$ (M+H$^+$): 283.1805, found 283.1796.



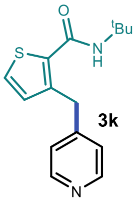
3j

5-Bromo-*N*-(*tert*-butyl)-2-(pyridin-4-ylmethyl)benzamide (3i): Synthesized according to General Procedure A using 5-bromo-*N*-(*tert*-butyl)-*N*-fluoro-2-methylbenzamide **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.

^{1}H NMR (400 MHz, $CDCl_3$) 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).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 167.5, 150.2, 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 $C_{17}H_{20}BrN_2O$ (M+H$^+$): 347.0754, found 347.0748.



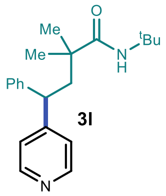
3k

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.

^{1}H NMR (400 MHz, $CDCl_3$) 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).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) 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 $C_{15}H_{19}N_2OS$ (M+H$^+$): 275.1213, found 275.1212.



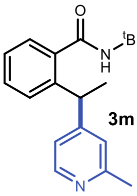
3l

***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, $CDCl_3$) δ 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, $CDCl_3$) δ 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 $C_{21}H_{29}N_2O$ (M+H$^+$): 325.2274, found 325.2276.



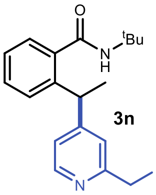
3m

***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, $CDCl_3$) δ 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, $CDCl_3$) δ 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 $C_{19}H_{25}N_2O$ (M+H$^+$): 297.1961, found 297.1961.



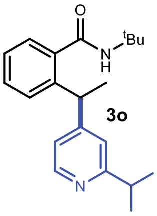
3n

***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, $CDCl_3$) δ 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, $CDCl_3$) δ 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 $C_{20}H_{27}N_2O$ (M+H$^+$): 311.2118, found 311,2114.



3o

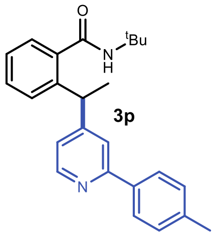
***N*-(*tert*-butyl)-*N*-fluoro-2-(1-(2-isopropylpyridin-4-yl)ethyl)benzamide (3o):** Synthesized according to General Procedure A using *N*-(*tert*-butyl)-2-ethyl-*N*-fluorobenzamide **2b** (22.5 mg, 0.1 mmol, 1 equiv.) and 2-isopropylisonicotinonitrile **1d** (44.0 mg, 0.3 mmol, 3 equiv.). The crude 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, $CDCl_3$) δ 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).

^{13}C{^{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 $C_{21}H_{29}N_2O$ (M+H$^+$): 325.2274, found 325.2277.

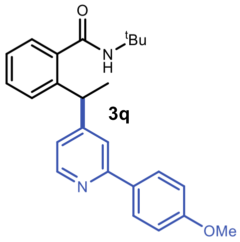


***N*-(*tert*-butyl)-2-(1-(2-(p-tolyl)pyridin-4-yl)ethyl)benzamide (3p):** Synthesized according to General Procedure A using *N*-(*tert*-butyl)-2-ethyl-*N*-fluorobenzamide **2b** (22.5 mg, 0.1 mmol, 1 equiv.) and 2-(p-tolyl)isonicotinonitrile **1e** (58.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was 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, 127.0, 126.7, 121.5, 120.0, 52.0, 39.9, 28.8, 21.6, 21.4.

HRMS: (ESI$^+$) calculated for $C_{25}H_{29}N_2O$ (M+H$^+$): 373.2274, found 373.2273.

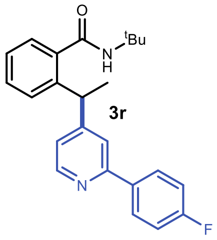


***N*-(*tert*-butyl)-2-(1-(2-(4-methoxyphenyl)pyridin-4-yl)ethyl)benzamide (3q):** Synthesized according to General Procedure A using *N*-(*tert*-butyl)-2-ethyl-*N*-fluorobenzamide **2b** (22.5 mg, 0.1 mmol, 1 equiv.) and 2-(4-methoxyphenyl)isonicotinonitrile **1f** (59.5 mg, 0.3 mmol, 3 equiv.). The 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 (dd, *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 $C_{25}H_{29}N_2O_2$ (M+H$^+$): 389.2224, found 389.2212.



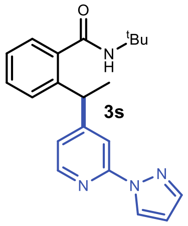
***N*-(*tert*-butyl)-2-(1-(2-(4-fluorophenyl)pyridin-4-yl)ethyl)benzamide (3r):** Synthesized according to General Procedure A using *N*-(*tert*-butyl)-2-ethyl-*N*-fluorobenzamide **2b** (22.5 mg, 0.1 mmol, 1 equiv.) and 2-(4-fluorophenyl)isonicotinonitrile **1g** (59.5 mg, 0.3 mmol, 1.5 equiv.). The 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.

^{19}F NMR (376 MHz, CDCl$_3$) δ -113.4.

HRMS: (ESI$^+$) calculated for $C_{24}H_{26}FN_2O$ (M+H$^+$): 377.2024, found 377.2022.

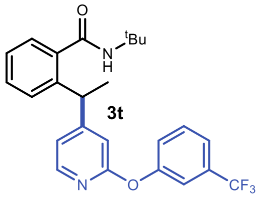


2-(1-(2-(1*H*-pyrazol-1-yl)pyridin-4-yl)ethyl)-*N*-(*tert*-butyl)benzamide (3s): Synthesized according to General Procedure A using *N*-(*tert*-butyl)-2-ethyl-*N*-fluorobenzamide **2b** (22.5 mg, 0.1 mmol, 1 equiv.) and 2-(1*H*-pyrazol-1-yl)isonicotinonitrile **1k** (51.0 mg, 0.3 mmol, 3 equiv.). The 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 a off-white solid.

^{1}H NMR (400 MHz, CDCl$_3$) 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).

^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ 169.7, 158.4, 142.1, 137.8, 130.2, 128.1, 127.0, 126.7, 52.0, 40.0, 28.8, 21.3.

HRMS: (ESI$^+$) calculated for $C_{21}H_{25}N_4O$ (M+H+): 349.2023, found 349.2017.



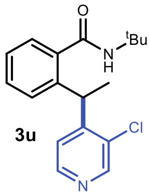
***N*-(*tert*-butyl)-2-(1-(2-(3-(trifluoromethyl)phenoxy)pyridin-4-yl)ethyl)benzamide (3t):** Synthesized according to General Procedure A using *N*-(*tert*-butyl)-2-ethyl-N-fluorobenzamide **2b** (22.5 mg, 0.1 mmol, 1 equiv.) and 2-(3-(trifluoromethyl)phenoxy)isonicotinonitrile **1l** (79.0 mg, 0.3 mmol, 3.0 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 a off-white solid.

^{1}H NMR (400 MHz, CDCl$_3$) 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).

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

^{19}F NMR (376 MHz, CDCl$_3$) δ -62.76.

HRMS: (ESI$^+$) calculated for $C_{25}H_{26}N_2O_2$ (M+H$^+$):443.1941, found 443.1953.

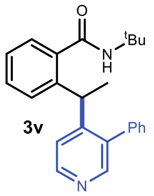


***N*-(*tert*-butyl)-2-(1-(3-chloropyridin-4-yl)ethyl)benzamide (3u:** Synthesized according to General Procedure A using *N*-(*tert*-butyl)-2-ethyl-*N*-fluorobenzamide **2b** (22.5 mg, 0.1 mmol, 1 equiv.) and 3-chloroisonicotinonitrile **1h** (41.5 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified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

^{1}H NMR (300 MHz, CDCl$_3$) 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).

^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$) 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 $C_{18}H_{22}ClN_2O$ (M+H$^+$): 317.1415, found 317.1415.



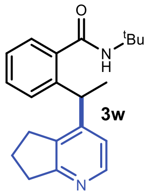
3v

***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 a off-white solid.

^{1}<u>H NMR</u> (400 MHz, $CDCl_3$) 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).

^{13}<u>C{^{1}H} NMR</u> (101 MHz, $CDCl_3$) δ 169.4, 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, 122.2, 51.6, 38.1, 28.7, 21.1.

<u>HRMS</u>: (ESI$^+$) calculated for $C_{24}H_{27}N_2O$ (M+H$^+$): 359.2118, found 359.2124.



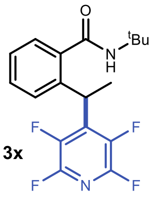
3w

***N*-(*tert*-butyl)-2-(1-(6,7-dihydro-5*H*-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-5*H*-cyclopenta[*b*]pyridine-4-carbonitrile **1j** (59.5 mg, 0.3 mmol, 3.0 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.

^{1}<u>H NMR</u> (300 MHz, $CDCl_3$) 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).

^{13}<u>C{^{1}H} NMR</u> (75 MHz, $CDCl_3$) δ 169.6, 165.5, 147.9, 142.0, 138.0, 130.0, 129.2, 127.9, 127.2, 127.0, 126.5, 119.1, 51.8, 37.7, 34.4, 29.3, 28.7, 22.5, 20.7.

<u>HRMS</u>: (ESI$^+$) calculated for $C_{21}H_{27}N_2O$ (M+H$^+$):323.2118, found 323.2114.



3x

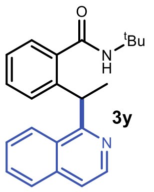
***N*-(*tert*-butyl)-2-(1-(perfluoropyridin-4-yl)ethyl)benzamide (3x):** Synthesized according to General Procedure A using *N*-(*tert*-butyl)-2-ethyl-*N*-fluorobenzamide **2b** (22.5 mg, 0.1 mmol, 1 equiv.) and 2,3,5,6-tetrafluoroisonicotinonitrile **1m** (53.0 mg, 0.3 mmol, 3 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/CH_2Cl_2/EtOAc 80:16:4) to afford **3x** (14 mg, 40% yield) as a yellow solid.

^{1}<u>H NMR </u>(300 MHz, $CDCl_3$) 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).

^{13}<u>C{^{1}H} NMR</u> (101 MHz, $CDCl_3$) δ 169.1, 139.3, 137.3, 130.4, 128.1, 127.4, 127.1, 52.1, 33.0, 28.8, 19.5.

^{19}<u>F NMR</u> (376 MHz, $CDCl_3$) δ -91.3 – -92.5 (m, 2F), -142.1 – -143.50 (m, 2F).

<u>HRMS</u>: (ESI$^+$) calculated for $C_{18}H_{18}F_4N_2NaO$ (M+Na$^+$): 377.1247, found 377.1242.



3y

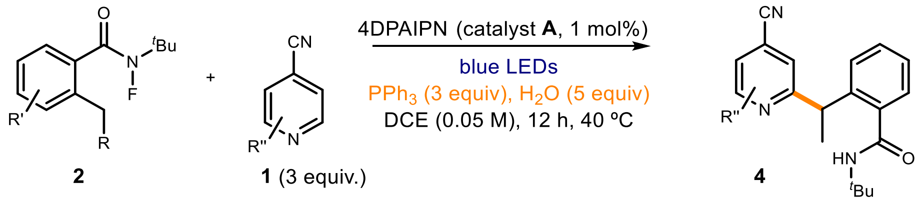
***N*-(*tert*-butyl)-2-(1-(isoquinolin-1-yl)ethyl)benzamide (3y):** Synthesized according to General Procedure A using *N*-(*tert*-butyl)-2-ethyl-*N*-fluorobenzamide **2b** (22.5 mg, 0.1 mmol, 1 equiv.) and isoquinoline-1-carbonitrile **1n** (46.5 mg, 0.3 mmol, 3.0 equiv.). The crude mixture was purified by flash column chromatography on silica gel (hexanes/CH_2Cl_2/EtOAc 50:48:2) to afford **3y** (25 mg, 79% yield) as a yellowish solid.

^{1}H NMR (500 MHz, CDCl$_3$) δ 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, 3H), 1.42 (s, 9H).

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

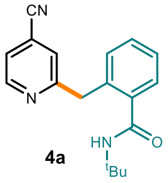
HRMS: (ESI$^+$) calculated for $C_{22}H_{25}N_2O$ (M+H$^+$): 333.1961, found 333.1951.

C.4 General procedure (B): Minisci reaction



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 **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 uL, 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



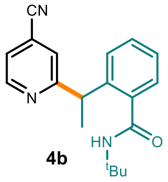
4a

***N*-(*tert*-butyl)-2-((4-cyanopyridin-2-yl)methyl)benzamide (4a):** Synthesized according to General Procedure B using 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, 3.0 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, CDC13) δ 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).

^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$) δ 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 $C_{18}H_{19}N_3NaO$ (M+Na$^+$): 316.1420, found 316.1420.



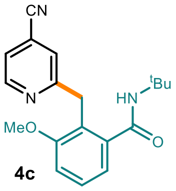
4b

***N*-(*tert*-butyl)-2-(1-(4-cyanopyridin-2-yl)ethyl)benzamide (4b):** Synthesized according to General Procedure B using 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, 3.0 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.

<u>^{1}H NMR</u> (500 MHz, CDCl$_3$) δ 8.65 (dd, J = 5.0, 0.9 Hz, 1H), 7.60 – 7.58 (m, 1H), 7.42 (dd, J = 7.6, 1.5 Hz, 1H), 7.36 – 7.29 (m, 2H), 7.25 – 7.20 (m, 2H), 6.85 (s, 1H), 4.91 (q, J = 7.2 Hz, 1H), 1.72 (d, J = 7.2 Hz, 3H), 1.45 (s, 9H).

<u>^{13}C{^{1}H} NMR</u> (75 MHz, CDCl$_3$) δ 169.4, 166.6, 150.0, 141.3, 138.0, 130.1, 128.0, 127.0, 123.5, 123.0, 121.19, 117.0, 52.0, 42.0, 29.0, 20.1.

<u>HRMS</u>: (ESI$^+$) calculated for $C_{19}H_{21}N_3NaO$ (M+Na$^+$): 330.1577, found 330.1573.



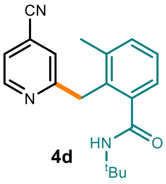
4c

***N*-(*tert*-butyl)-2-((4-cyanopyridin-2-yl)methyl)-3-methoxybenzamide (4c):** Synthesized according to General Procedure B using 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, 3.0 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 off-white solid.

<u>^{1}H NMR</u> (400 MHz, CDCl$_3$) δ 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).

<u>^{13}C{^{1}H} NMR</u> (101 MHz, CDCl$_3$) δ 168.7, 162.5, 157.4, 149.1, 140.4, 128.6, 126.2, 123.3, 123.0, 121.1, 120.7, 116.7, 111.3, 55.7, 52.0, 35.8, 28.9.

<u>HRMS</u>: (ESI$^+$) calculated for $C_{19}H_{21}N_3NaO_2$ (M+Na$^+$): 346.1526, found 346.1533.



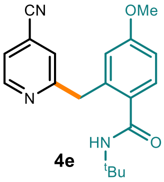
4d

***N*-(*tert*-butyl)-2-((4-cyanopyridin-2-yl)methyl)-3-methylbenzamide (4d):** Synthesized according to General Procedure B using 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, 3.0 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.

<u>^{1}H NMR</u> (400 MHz, CDCl$_3$) δ 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).

<u>^{13}C{^{1}H} NMR</u> (101 MHz, CDCl$_3$) δ 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.

<u>HRMS</u>: (ESI$^+$) calculated for $C_{19}H_{22}N_3O$ (M+H$^+$): 308.1757, found 308.1749.



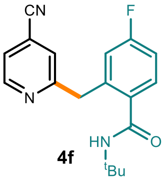
4e

***N*-(*tert*-butyl)-2-((4-cyanopyridin-2-yl)methyl)-4-methoxybenzamide (4e):** Synthesized according to General Procedure B using 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, 3.0 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 off-white solid.

<u>^{1}H NMR</u> (400 MHz, CDCl$_3$) δ 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).

<u>^{13}C{^{1}H} NMR</u> (101 MHz, CDCl$_3$) δ 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.

<u>HRMS</u>: (ESI$^+$) calculated for $C_{19}H_{22}N_3O_2$ (M+H$^+$): 324.1707, found 324.1712.



4f

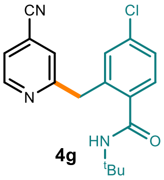
***N*-(*tert*-butyl)-2-((4-cyanopyridin-2-yl)methyl)-4-fluorobenzamide (4f):** Synthesized according to General Procedure B using using *N*-(*tert*-butyl)-*N*,4-difluoro-2-methylbenzamide **2f** (22.5 mg, 0.1 mmol, 1 equiv.) and isonicotinonitrile **1a** (31.0 mg, 0.3 mmol, 3.0 equiv.). The crude mixture 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{^{1}H} 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 $\mathrm{C_{18}H_{19}FN_3O}$ (M+H$^+$): 312.1507, found 312.1512.



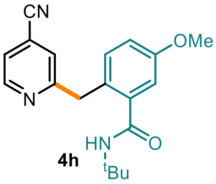
4g

***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{^{1}H} 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 $\mathrm{C_{18}H_{19}ClN_3O}$ (M+H$^+$): 328.1211, found 328.1208.

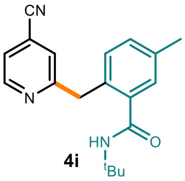


4h

***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{^{1}H} 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 $\mathrm{C_{19}H_{21}N_3NaO_2}$ (M+Na$^+$): 346.1526, found 346.1522.



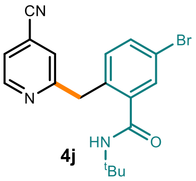
4i

***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 a off-white solid.

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.63 (d, J = 5.1 Hz, 1H), 7.55 (s, 1H), 7.36 (dd, J = 5.0, 1.5 Hz, 1H), 7.32 (d, J = 1.9 Hz, 1H), 7.19 (s, 1H), 7.13 (ddd, J = 7.8, 2.0, 0.8 Hz, 1H), 7.06 (d, J = 7.8 Hz, 1H), 4.31 (s, 2H), 2.33 (s, 3H), 1.41 (s, 9H).

^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ 169.1, 163.0, 149.6, 138.2, 137.3, 132.1, 130.9, 130.9, 128.8, 125.4, 123.2, 121.7, 116.5, 52.0, 40.8, 28.9, 21.1.

HRMS: (ESI$^+$) calculated for $C_{19}H_{22}N_3O$ (M+H$^+$): 308.1757, found 308.1759.



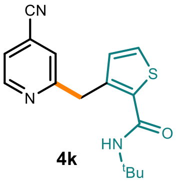
4j

5-bromo-*N*-(*tert*-butyl)-2-((4-cyanopyridin-2-yl)methyl)benzamide (4j): Synthesized according to General Procedure B using using 5-bromo-*N*-(*tert*-butyl)-*N*-fluoro-2-methylbenzamide **2j** (29.0 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/AcOEt 93:7 to 85:15) and (toluene/EtOAc 9:4 for further purification from dibenzylated side-product) to afford **4j** (17 mg, 46% yield) as a white solid.

^{1}H NMR (400 MHz, CDCl$_3$) 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).

^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ 167.4, 162.0, 149.9, 140.0, 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 $C_{18}H_{19}BrN_3O$ (M+H$^+$): 372.0706, found 372.0704.



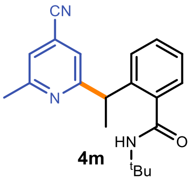
4k

***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*-fluoro-3-methylthiophene-2-carboxamide **2k** (21.5 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 gel (hexanes/EtOAc 93:7 to 85:15) to afford **4k** (13 mg, 45% yield) as a yellowish wax.

^{1}H NMR (400 MHz, CDCl$_3$) 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).

^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) 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 $C_{16}H_{18}N_3OS$ (M+H$^+$): 300.1165, found 300.1152.



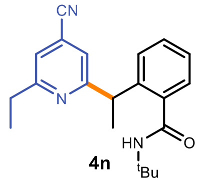
4m

***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*-fluorobenzamide **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.

^{1}H NMR (500 MHz, CDCl$_z$) 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).

^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$) 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$C_{20}H_{24}N_3O$ (M+H$^+$): 322.1914, found 322.1915.



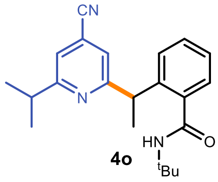
4n

***N*-(*tert*-butyl)-2-(1-(4-cyano-6-ethylpyridin-2-yl)ethyl)benzamide (4n):** 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-ethylisonicotinonitrile **1c** (40.0 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 **4n** (20 mg, 60% yield) as a yellow oil.

^{1}<u>H NMR</u> (400 MHz, CDCl$_3$) δ 7.44 – 7.38 (m, 1H), 7.35 (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).

^{13}<u>C{^{1}H} NMR</u> (101 MHz, CDCl$_3$) 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.

<u>HRMS</u>: (ESI$^+$) calculated for$C_{21}H_{26}N_3O$ (M+H$^+$): 336.2070, found 336.2062.



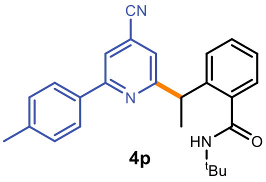
4o

***N*-(*tert*-butyl)-2-(1-(4-cyano-6-isopropylpyridin-2-yl)ethyl)-*N*-fluorobenzamide (4o):** 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-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.

^{1}<u>H NMR</u> (300 MHz, CDCl$_3$) 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).

^{13}<u>C{^{1}H} NMR</u> (75 MHz, CDCl$_3$) δ 169.5, 168.1, 165.4, 141.8, 137.6, 130.0, 128.0, 127.1, 126.5, 1., 120.8, 119.5, 117.2, 52.0, 42.0, 36.2, 29.0, 22.3, 22.2, 20.6.

<u>HRMS</u>: (ESI$^+$) calculated for $C_{22}H_{28}N_3O$ (M+H$^+$): 350.2227, found 350.2226.



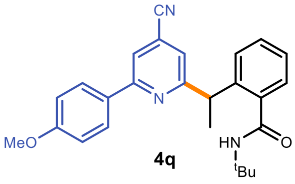
4p

***N*-(*tert*-butyl)-2-(1-(4-cyano-6-(p-tolyl)pyridin-2-yl)ethyl)benzamide (4e):** 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-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 **4e** (13 mg, 34% yield) as an yellowish solid.

^{1}<u>H NMR</u> (400 MHz, CDCl$_3$) 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).

^{13}<u>C{^{1}H} NMR</u> (101 MHz, CDCl$_3$) δ 169.6, 166.0, 157.8, 142.0, 140.5, 137.8, 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.

<u>HRMS</u>: (ESI$^+$) calculated for $C_{26}H_{27}N_3NaO$ (M+Na$^+$): 420.2046, found 420.2047.



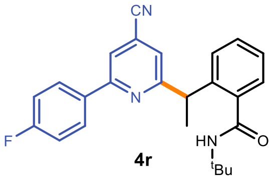
4q

***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.

<u>^{1}H NMR</u> (400 MHz, CDCl$_3$) δ 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).

<u>^{13}C{^{1}H} NMR</u> (101 MHz, CDCl$_3$) δ 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.

<u>HRMS</u>: (ESI$^+$) calculated for $C_{26}H_{28}N_3O$ (M+H$^+$): 414.2176, found 414.2185.



4r

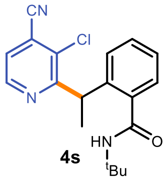
***N*-(*tert*-butyl)-2-(1-(4-cyano-6-(4-fluorophenyl)pyridin-2-yl)ethyl)benzamide (4r):** Synthesized according to General Procedure B using using *N*-(*tert*-butyl)-2-ethyl-*N*-fluorobenzamide **2a** (22.5 mg, 0.1 mmol, 1 equiv.) and 2-(4-fluorophenyl)isonicotinonitrile **1g** (59.5 mg, 0.3 mmol, 3.0 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 an yellowish solid.

<u>^{1}H NMR</u> (400 MHz, CDCl$_3$) δ 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).

<u>^{13}C{^{1}H} NMR</u> (101 MHz, CDCl$_3$) δ 169.6, 166.2, 164.2 (d, ^{1}J = 250.7 Hz), 156.7, 141.8, 137.8, 133.8 (d, ^{4}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, ^{2}J = 21.8 Hz), 52.1, 42.2, 28.9, 20.5.

<u>^{19}F NMR</u> (376 MHz, CDCl$_3$) δ -111.00.

<u>HRMS</u>: (ESI$^+$) calculated for $C_{25}H_{25}FN_3O$ (M+H$^+$): 402.1976, found 402.1967.



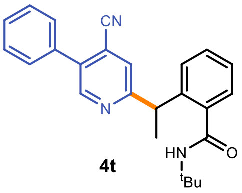
4s

***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.

<u>^{1}H NMR</u> (500 MHz, CDCl$_3$) δ 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), 5.31 (q, J = 6.9 Hz, 1H), 1.71 (d, J = 6.9 Hz, 4H), 1.45 (s, 9H).

<u>^{13}C{^{1}H} NMR</u> (126 MHz, CDCl$_3$) δ 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.

<u>HRMS</u>: (ESI$^+$) calculated for $C_{19}H_{20}ClN_3NaO$ (M+Na$^+$): 364.1187, found 364.1188.



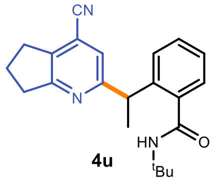
4t

***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.

<u>^{1}H NMR</u> (400 MHz, CDCl$_3$) δ 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).

<u>^{13}C{^{1}H} NMR</u> (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.

<u>HRMS</u>: (ESI^+) calculated for $C_{25}H_{26}N_3O$ ($M+H^+$): 384.2070, found 384.2054.



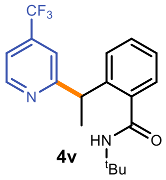
4u

***N*-(*tert*-butyl)-2-(1-(4-cyano-6,7-dihydro-5*H*-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-5*H*-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.

<u>^{1}H NMR</u> (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).

<u>^{13}C{^{1}H} NMR</u> (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.

<u>HRMS</u>: (ESI^+) calculated for $C_{22}H_{26}N_3O$ ($M+H^+$): 348.2070, found 348.2073.



4v

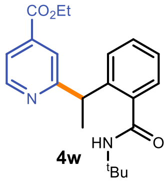
***N*-(*tert*-butyl)-2-(1-(4-(trifluoromethyl)pyridin-2-yl)ethyl)benzamide (4v):** Synthesized according to General Procedure B using using *N*-(*tert*-butyl)-2-ethyl-*N*-fluorobenzamide **2a** (22.5 mg, 0.1 mmol, 1 equiv.) and 4-(trifluoromethyl)pyridine **1o** (44.0 mg, 0.3 mmol, 3.0 equiv.). The crude 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.

<u>^{1}H NMR</u> (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).

<u>^{13}C{^{1}H} NMR</u> (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.

<u>^{19}F NMR</u> (376 MHz, $CDCl_3$) δ -64.8.

<u>HRMS</u>: (ESI^+) calculated for $C_{19}H_{22}F_3N_2O$ ($M+H^+$): 351.1679, found 351.1672.



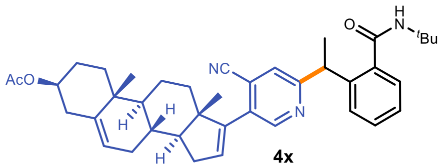
4w

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.

<u>^{1}H NMR</u> (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).

<u>^{13}C{^{1}H} NMR</u> (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.

<u>HRMS</u>: (ESI^+) calculated for $C_{21}H_{27}N_2O_3$ ($M+H^+$): 355.2016, found 355.2008.



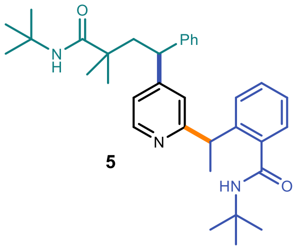
4x

(3*S*,8*R*,9*S*,10*R*,13*S*,14*S*)-17-(6-((*S*)-1-(2-(*tert*-butylcarbamoyl)phenyl)ethyl)-4-cyanopyridin-3-yl)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15-dodecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl acetate (4x): 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*S*,8*R*,9*S*,10*R*,13*S*,14*S*)-17-(4-cyanopyridin-3-yl)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15-dodecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl acetate **1q** (125 mg, 0.3 mmol, 3.0 equiv.). The crude mixture was purified by flash column chromatography on silica gel (toluene/EtOAc 97:3) to afford **4x** (17 mg, 28% yield) as a white solid. The diastereomeric ratio was determined to be 1:1 by UPC^2 analysis on a Daicel Chiralpak ID-3 column (eluent: 100% CO$_2$ for 1 min, gradient 100% - 90% CO$_2$ in isopropanol for 5 min, 90% CO$_2$ in isopropanol for 2 min, gradient 90% - 100% CO$_2$ in isopropanol for 1 min; flow rate 2.0 mL/min, λ = 300 nm, τ_1 = 7.12 min, τ_2 = 7.57 min.

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.54 (s, 1H), 7.59 (s, 1H), 7.45 – 7.41 (m, 1H), 7.34 (ddd, *J* = 8.6, 7.0, 1.5 Hz, 1H), 7.26 – 7.21 (m, 1H), 6.97 (s, 1H), 6.91 (s, 1H), 6.15 (ddd, *J* = 5.0, 3.3, 1.7 Hz, 1H), 5.41 (d, *J* = 5.1 Hz, 1H), 4.88 (q, *J* = 7.1 Hz, 1H), 4.61 (tt, *J* = 10.7, 5.2 Hz, 1H), 2.42 – 2.30 (m, 3H), 2.20 – 2.12 (m, 1H), 2.12 – 2.05 (m, 1H), 2.03 (s, 3H), 1.90 – 1.81 (m, 2H), 1.78 – 1.50 (m, 8H), 1.73 (d, *J* = 7.2 Hz, 3H), 1.45 (s, 9H), 1.19 – 1.11 (m, *J* = 13.9, 13.1, 4.2 Hz, 2H), 1.06 (s, 3H), 1.00 (d, *J* = 1.5 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ 170.7, 169.4, 163.3, 147.9, 147.9, 147.7, 140.9, 140.1, 138.0, 138.0, 135.7, 135.6, 133.3, 130.1, 127.9, 127.8, 127.1, 124.7, 122.3, 121.4, 116.9, 73.9, 57.2, 52.1, 50.3, 49.4, 41.5, 38.2, 37.1, 36.9, 35.2, 32.7, 31.6, 30.7, 29.0, 27.9, 21.6, 20.8, 20.1, 19.4, 16.8, 16.7.

HRMS: (ESI$^+$) calculated for C$_{40}$H$_{50}$N$_3$O$_3$ (M+H$^+$): 620.3847, found 620.3840.



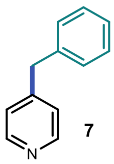
5

***N*-(*tert*-butyl)-2-(1-(4-(4-(*tert*-butylamino)-3,3-dimethyl-4-oxo-1-phenylbutyl)pyridin-2-yl)ethyl)benzamide (4y):** Synthesized according to General Procedure B using using *N*-(*tert*-butyl)-*N*-fluoro-2,2-dimethyl-4-phenylbutanamide **2e** (26.5 mg, 0.1 mmol, 1 equiv.) and *N*-(*tert*-butyl)-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.

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.53 (d, J = 53.5 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).

^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$) δ 176.0, 176.0, 169.4, 169.3, 164.7, 164.6, 156.0, 155.8, 148.5, 148.5, 143.8, 143.8, 141.7, 138.3, 138.3, 129.4, 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 C$_{34}$H$_{46}$N$_3$O$_2$ (M+H$^+$): 528.3585, found 528.3569.

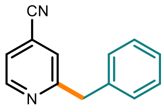


7

4-benzylpyridine (7): Synthesized according to General Procedure A 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 **7** (7.5 mg, 44% yield) as an off-white solid, with characterization data in accordance with the literature.[12]

<u>^{1}H NMR</u> (300 MHz, $CDCl_3$) δ 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).

<u>^{13}C{^{1}H} NMR</u> (75 MHz, $CDCl_3$) δ 150.2, 150.0, 139.0, 129.2, 128.9, 126.8, 124.3, 41.4.



8

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]

<u>^{1}H NMR</u> (400 MHz, $CDCl_3$) δ 8.70 (dd, J = 5.0, 0.9 Hz, 1H), 7.35 – 7.20 (m, 7H), 4.19 (s, 2H).

<u>^{13}C{^{1}H} NMR</u> (101 MHz, $CDCl_3$) δ 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

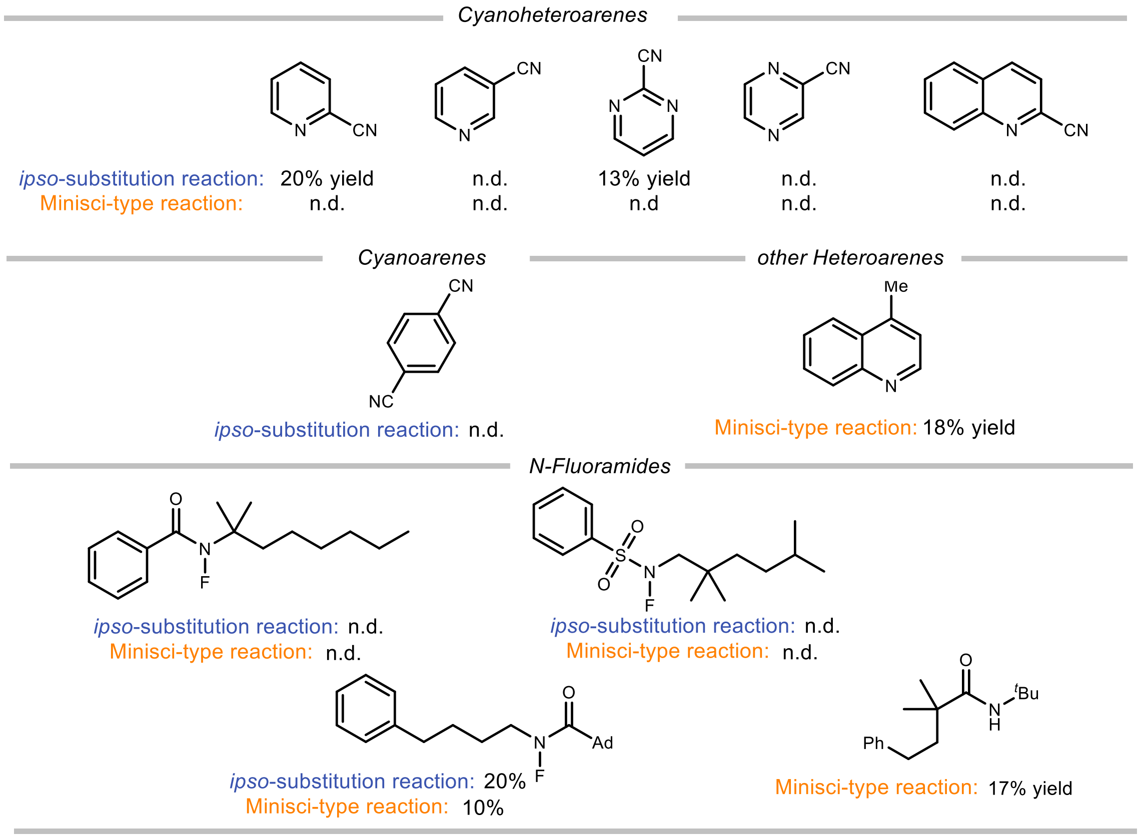


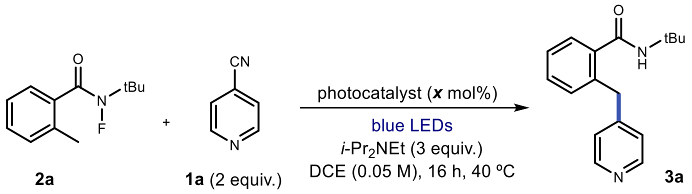
Figure S4. Moderately successful and unsuccessful substrates. *n.d.*: not detected; yield determined by NMR analysis.

E. Optimization and Mechanistic Studies

E.1 Optimization studies: Ipso substitution

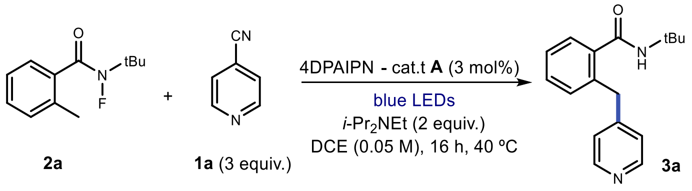
All reactions performed under inert atmosphere using the illumination set-up 1 in Figure S2. Yield determined by ^{1}H NMR analysis of the crude mixture using trimethoxybenzene as the internal standard.

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.

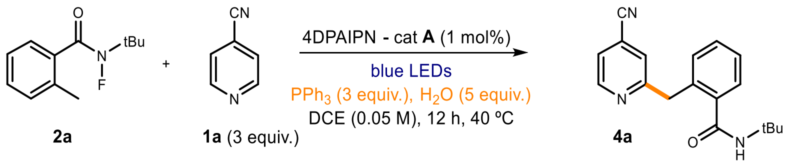


entry	deviation	yield (%)
1	none	25
2	Ir(ppy)$_3$	59
3	DABCO as quencher	0
4	**2a** (3 equiv.)	65
5	4-DPAIPN (1%)	75
6	15 ºC	0
7	60 ºC	31
8	Reaction under air	0
9	No light, no photocatalyst	0

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_2O 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
pH = 9.8

*Minisci reaction of **1a** and **2a** to afford **3a** enabled by PPh3 - water*
conditions as in entry 7 of Figure 2b in the main manuscript
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.

Figure S5. pH measurements.

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^{n-1} ($E^{1/2}$ (**PC**/**PC**$^{-}$) = -1.65 vs SCE)[11] capable of activating 4-cyanopyridine **1a** (E^{ox} (**1a**/**1a**$^{\cdot-}$) = -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** (E^{ox}($Bu_3N^{\cdot+}$/Bu_3N) = -1.2 V vs SCE)[15] could perform a thermodynamically favorable SET reduction of the N-F bond within *N*-(*tert*-butyl)-*N*-fluoro-2-methylbenzamide **2a** (E^{ox}(**2a**/**2a**$^{\cdot-}$) = -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 upon1,5-HAT would lead to the benzylic radical **III**. Radical-radical coupling between **III** and **I**, followed by decyanation, would deliver the desired product **3**.

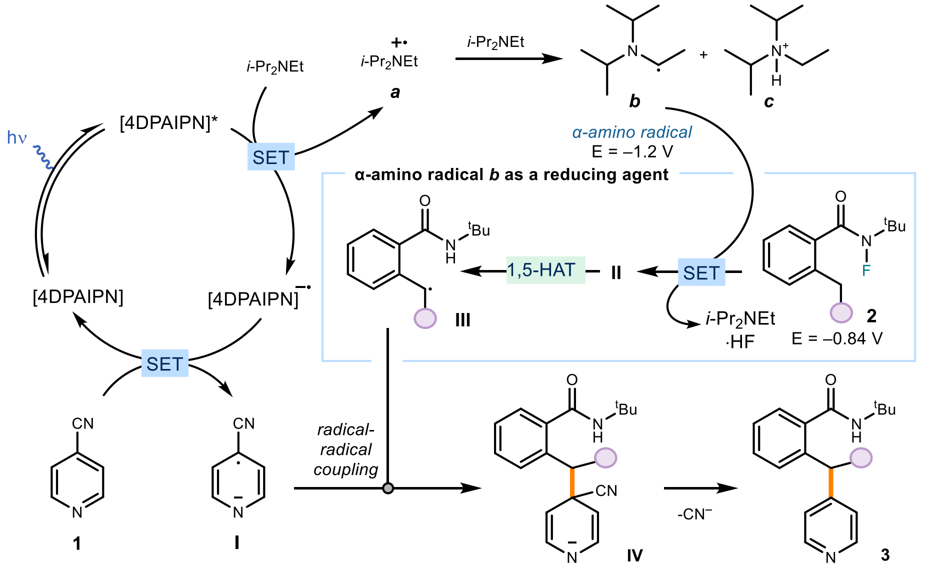


Figure S6. Plausible mechanism for the *ipso* substitution pattern.

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 fluoramide **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,[15] generates the α-amino radical in situ using a stoichiometric oxidant.

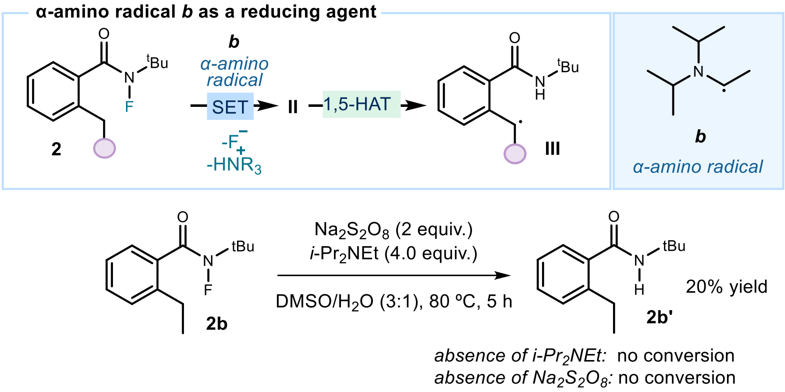


Figure S7. Benzyl radical generation driven by the α-amino radical **b**.

Sodium persulfate is known to oxidize tertiary amines, delivering α-amino radicals. Treatment of the *N*-fluoroamide **2b** with $Na_2S_2O_8$ 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 triphenylphopshine (see section J.2 for Stern-Volmer quenching studies) generates the reducing photocatalyst PC^{n-1} ($E^{1/2}$ (**PC**/**PC**$^{-}$) = -1.65 vs SCE)[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 phopshoranyl radicals (e.g., E_{ox} (Ph_3POMe^+/$Ph_3POMe^{\cdot}$) = -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**.[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 heterogenicity of the reaction mixture which prevented a precise quantum yield determination (see section H2 for details).

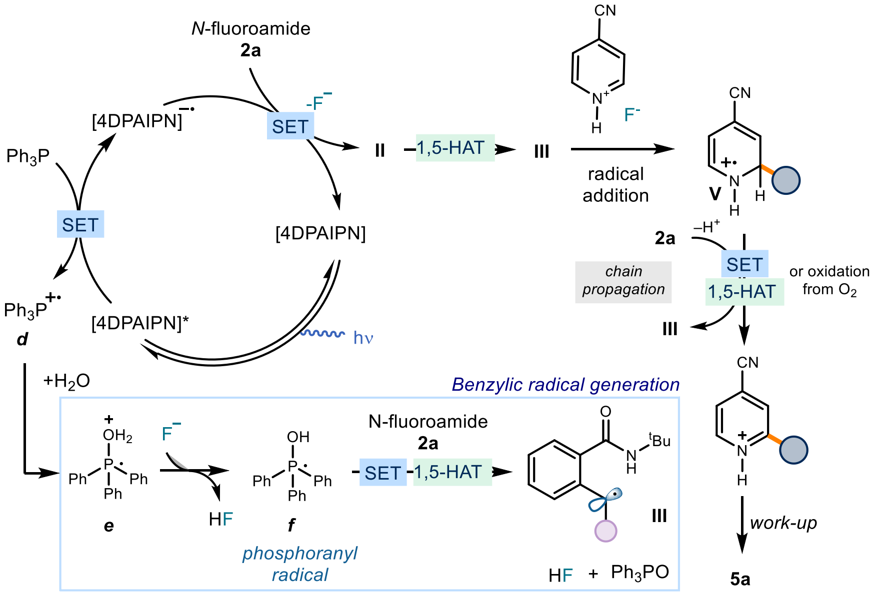


Figure S8. Plausible mechanism for the C2-selective Minisci-type reaction.

G.4 Minisci reaction: probing the phopshoranyl 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 PPh_3, the resulting phopshoranyl radical **f** would activate the N-F fluoramide **2**. Recent studies reported that phopshoranyl radicals can serve as strong SET reducing agents (e.g., E_{ox} ($Ph_3POMe^+/Ph_3POMe^{\cdot}$) = -1.63 vs SCE).[18] We surmised that, since SET reduction of **2b** by a phosporanyl radical is thermodyanamically 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.

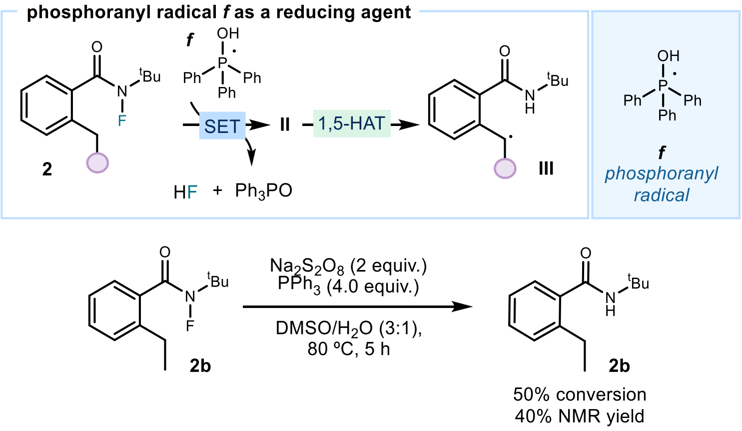


Figure S9. Benzyl radical generation upon SET from **f**.

G.5 Oxygen isotope experiment

Following the general procedure B, the standard Minisci reaction was performed using $H_2{}^{18}O$ in place of H_2O. The formation of labelled triphenylphosphine oxide was detected by HR-MS (Figure S10).[19]

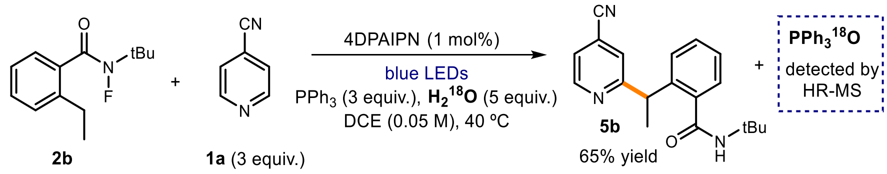
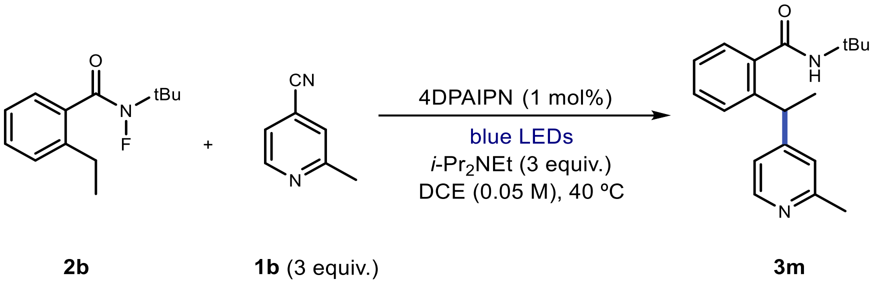


Figure S10. Detection of ^{18}O-labelled triphenylphosphine oxide.

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.[20] 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) :

$$\text{Mols of Fe(II)} = V_1 \times V_3 \times \Delta A(510\text{ nm})/10^3 \times V_2 \times l \times \varepsilon(510\ nm) \text{ (Eq. 1)}$$

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), ΔA(510 nm) is the optical difference in absorbance between the irradiated solution and the one stored in the dark, ε(510 nm) is the extinction coefficient the complex $Fe(phen)_3^{2+}$ at 510 nm (11100 L mol^{-1} cm^{1}). The moles of Fe2+ 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 (q0 n,p) by the use of the following Equation 2:

$$\Phi(\lambda) = dx/dt\ qn,p\ 0\ [1-10-A(\lambda)\ ] \text{ (Eq. 2)}$$

where dx/dt is the rate of change of a measurable quantity (spectral or any other property), the quantum yield (Φ) for Fe^{2+} at 458 nm is 1.1,[21] $[1\text{-}10^{-A(\lambda)}]$ is the ratio of absorbed photons by the solution, and A(λ) 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. $q^0_{n,p}$, which is the photon flux, was determined to be $4{,}14{*}10^{-08}$.

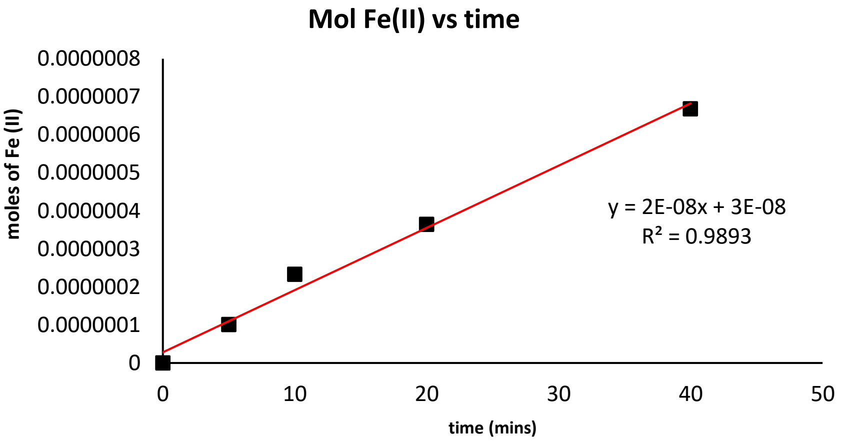


Figure S11. Plot of mols of Fe^{2+} formed vs irradiation time. Slope of the line correlates to the moles of incident photons by unit of time.

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 (q0 n,p·dt), the slope is equal to: $\Phi\cdot(1\text{-}10^{-A(460\text{ nm})})$, where Φ is the quantum yield to be determined and A(460 nm) is the absorption of the reaction under study. A(460 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 (Φ) of the photochemical transformation was measured to be 0.01.

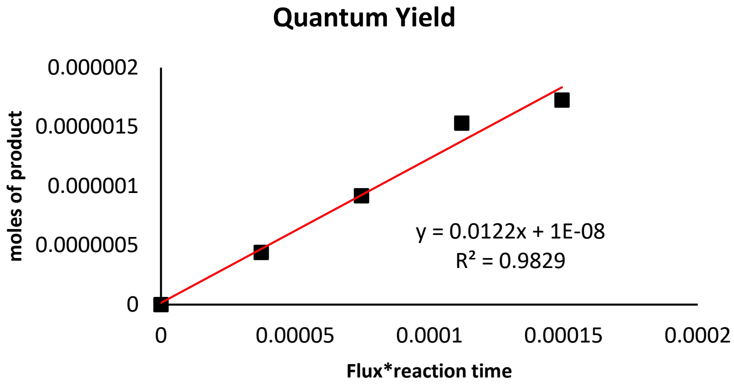
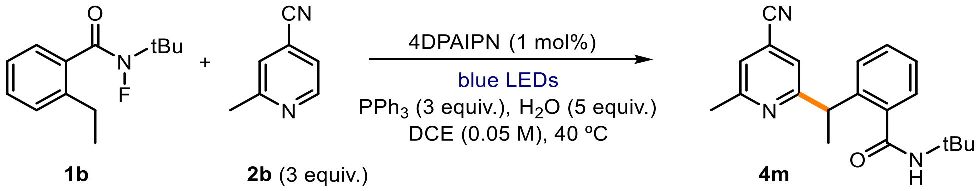


Figure S12. Plot of mols of incident photons vs mols of product formed. Slope of the line correlates to quantum yield of the photochemical transformation.

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-selectvie process.

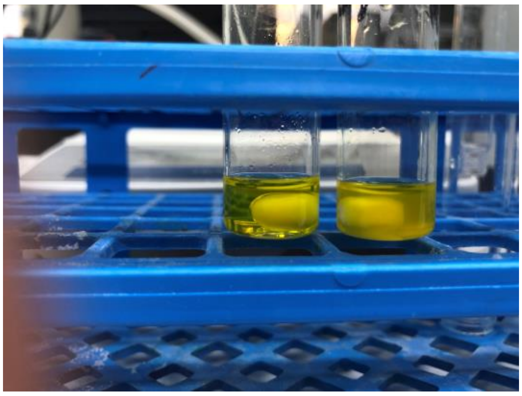


Figure S13. Reaction mixture before and after 20 mins under irradiation.

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 PPh_3-enabled Minisci reaction; c) and the same PPh_3-enabled Minisci reaction adding TFA.

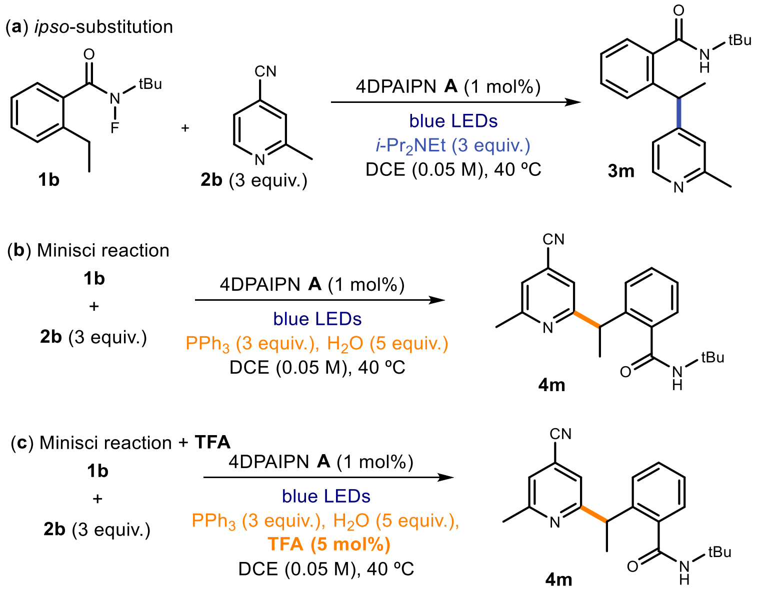


Figure S14. The three processes analysed in our kinetic investigations.

As shown in Figure **S15**, the PPh_3-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).

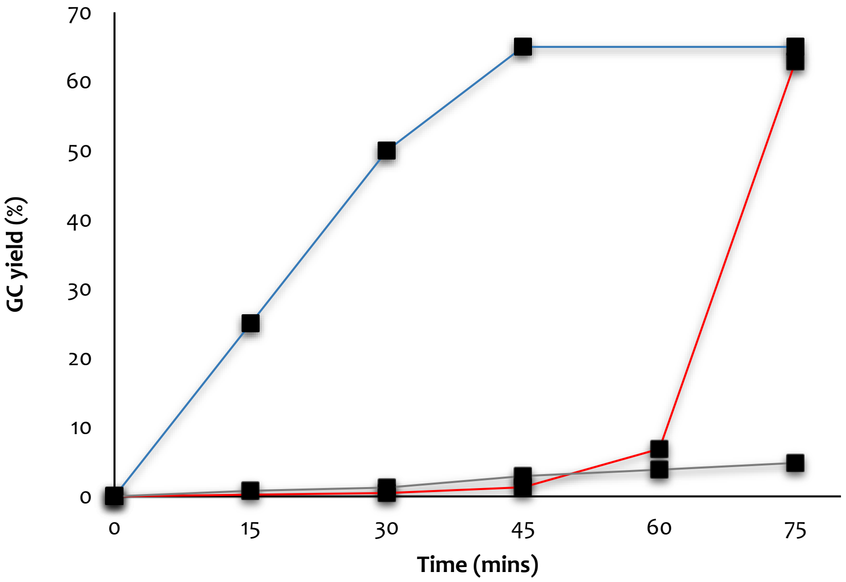


Figure S15. *Ipso*-substitution: grey profile; *Minisci reaction*: red profile; Minisci reaction with 5 mol% of TFA: blue profile.

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 spectrofluorimeter 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 x10 mm light path quartz fluorescence cuvette equipped with Silicone/PTFE 3.2 mm septum under an argon atmosphere. Then, 10 μL of a $1 \cdot 10^{-3}$ M solution of photocatalyst in 1,2-DCE was added to give a final concentration of 4-DPAIPN of $4 \cdot 10^{-6}$ 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).

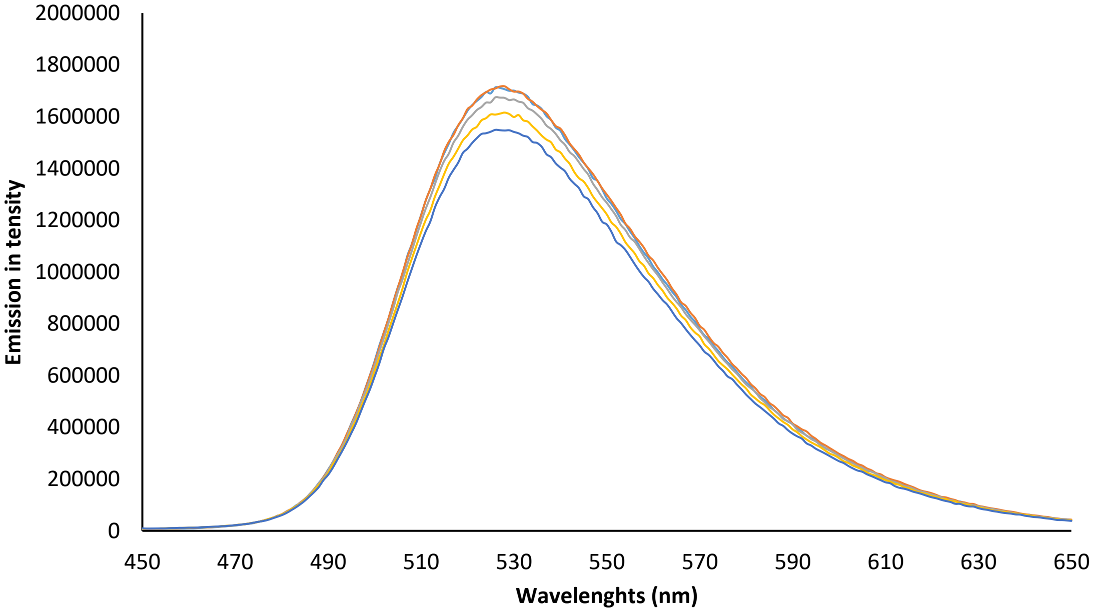


Figure S16. Quenching of the photocatalyst emission ($4 \cdot 10^{-6}$ M in 1,2-DCE) in the presence of increasing amounts of DIPEA.

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]

$$I_0/I = 1 + K_{SV} * [Q] \qquad \text{(Eq. 1)}$$

We calculated a Stern-Volmer quenching constant of 5.9 M^{-1} .

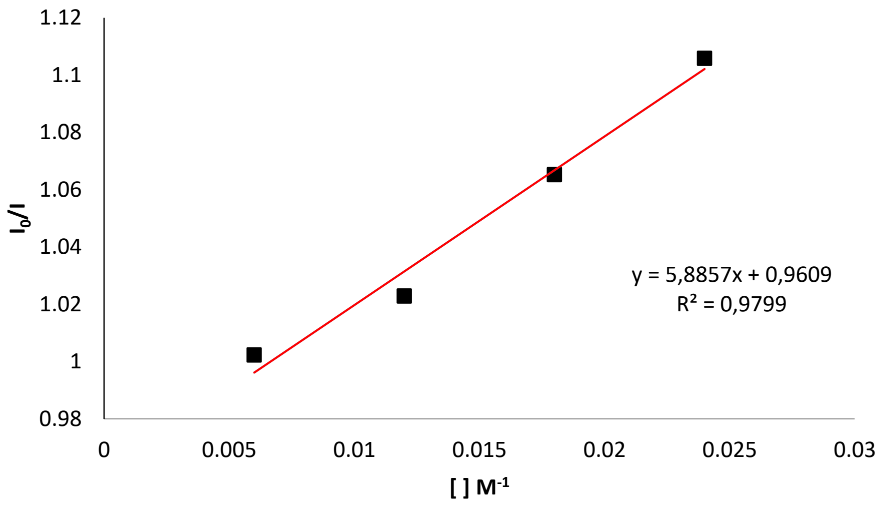


Figure S17. Stern-Volmer quenching plot using DIPEA as a quencher.

J.2 Stern-Volmer quenching studies with PPh_3

A 2M solution of PPh_3 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).

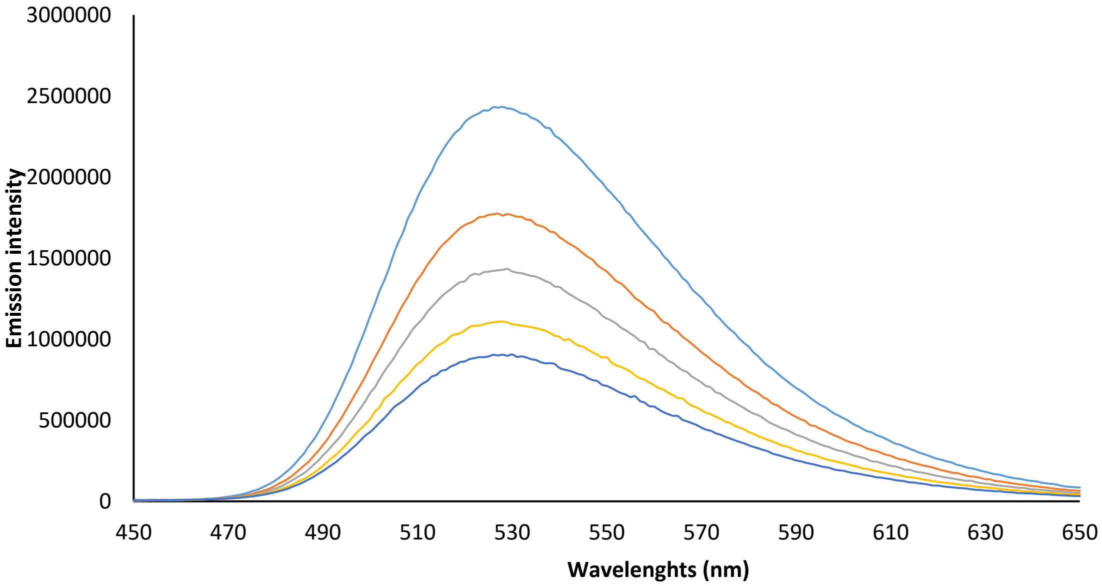


Figure S18. Quenching of the photocatalyst emission ($4\cdot10^{-6}$ M in 1,2-DCE) in the presence of increasing amounts of PPh_3.

The Stern-Volmer plot, reported in Figure **S19**, shows a linear correlation between the amounts of PPh_3 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]

$$I_0/I = 1 + K_{SV}*[Q] \qquad \text{(Eq. 1)}$$

We calculated a Stern-Volmer quenching constant of 45.3 M^{-1} .

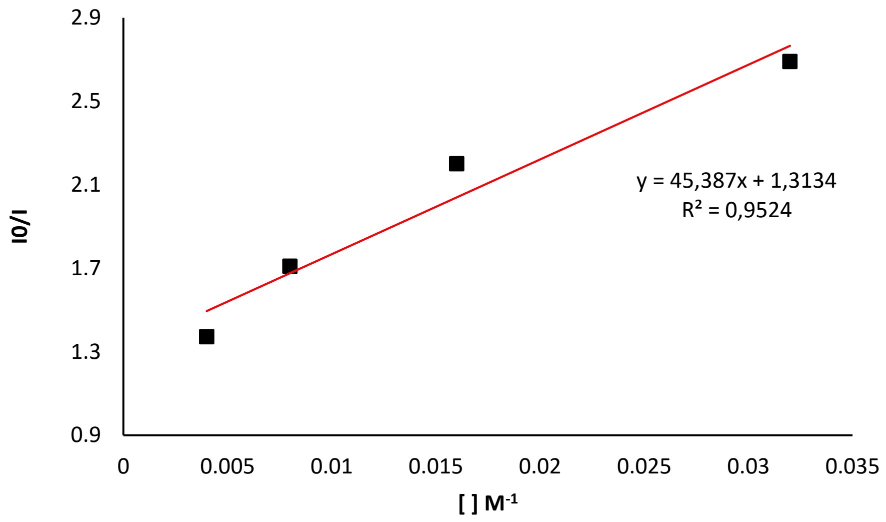


Figure S19. Stern-Volmer quenching plot using PPh_3 as a quencher.

*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).

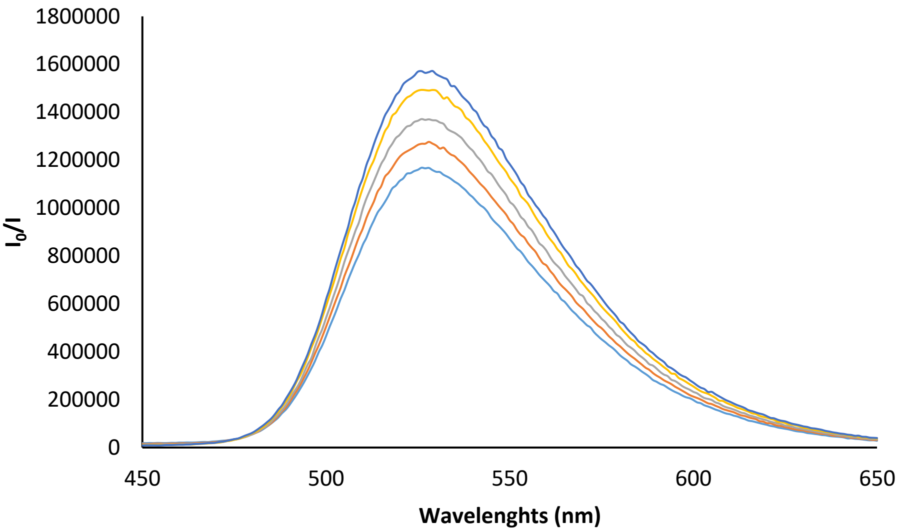


Figure S20. Quenching of the photocatalyst emission ($4{\cdot}10^{-6}$ M in 1,2-DCE) in the presence of increasing amounts of N-fluorobenzamide **2a**.

The Stern-Volmer plot, reported in Figure S21, shows a linear correlation between the amounts of NF 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]

$$I_0/I = 1 + K_{SV}*[Q] \qquad \text{(Eq. 1)}$$

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

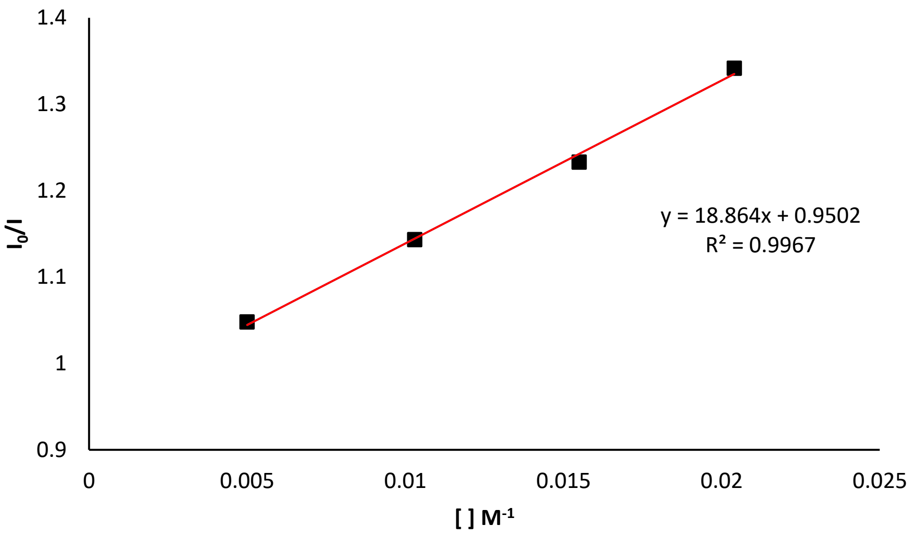


Figure S21. Stern-Volmer quenching plot using N-fluorobenzamide **2a** as a quencher.

*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).

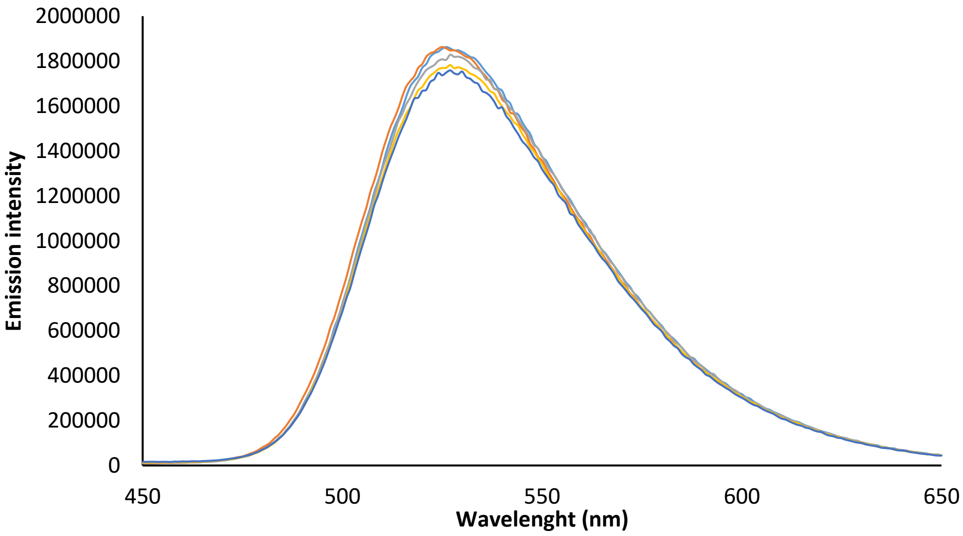


Figure S22. Quenching of the photocatalyst emission ($4{\cdot}10^{-6}$ M in 1,2-DCE) in the presence of increasing amounts of 4-cyanopyridine **1a**.

The Stern-Volmer plot, reported in Figure S23, shows a linear correlation between the amounts of NF and the ratio I_0/I. On the basis of the following Equation (eq. 1), it is possible to calculate the Stern-Volmer constant K_{SV}.[22]

$$I_0/I = 1 + K_{SV}*[Q] \qquad \text{(eq. 1)}$$

We calculated a Stern-Volmer quenching constant of 4.4 M^{-1} .

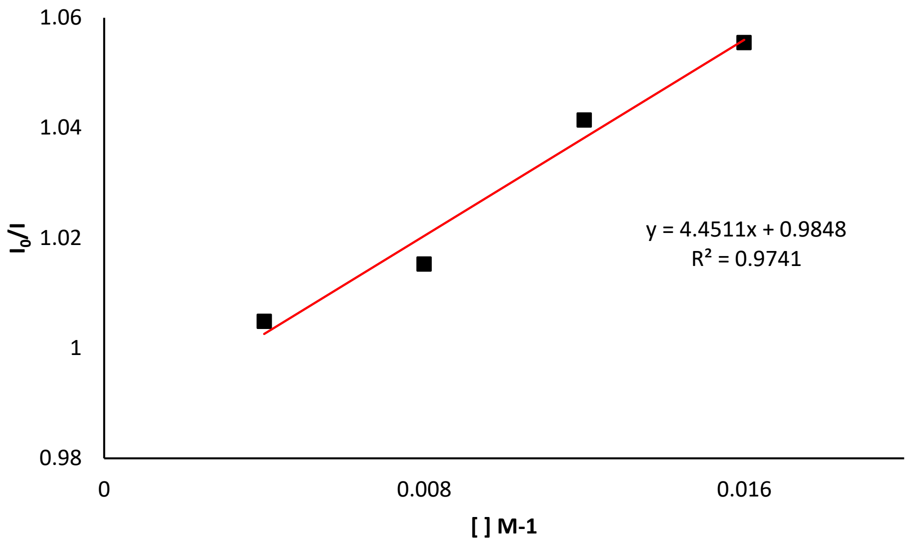


Figure S23. Stern-Volmer quenching plot using 4-cyanopyridine **1a** as a quencher.

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J. NMR spectra and UPC^2 trace

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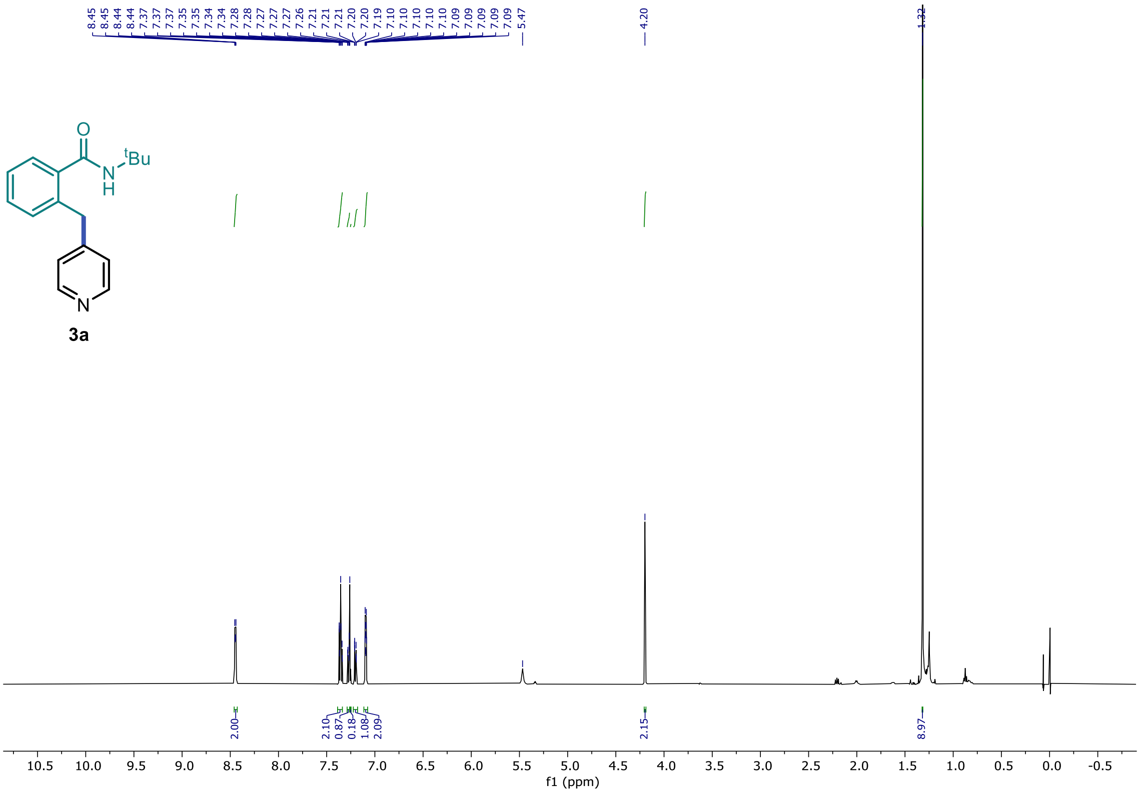

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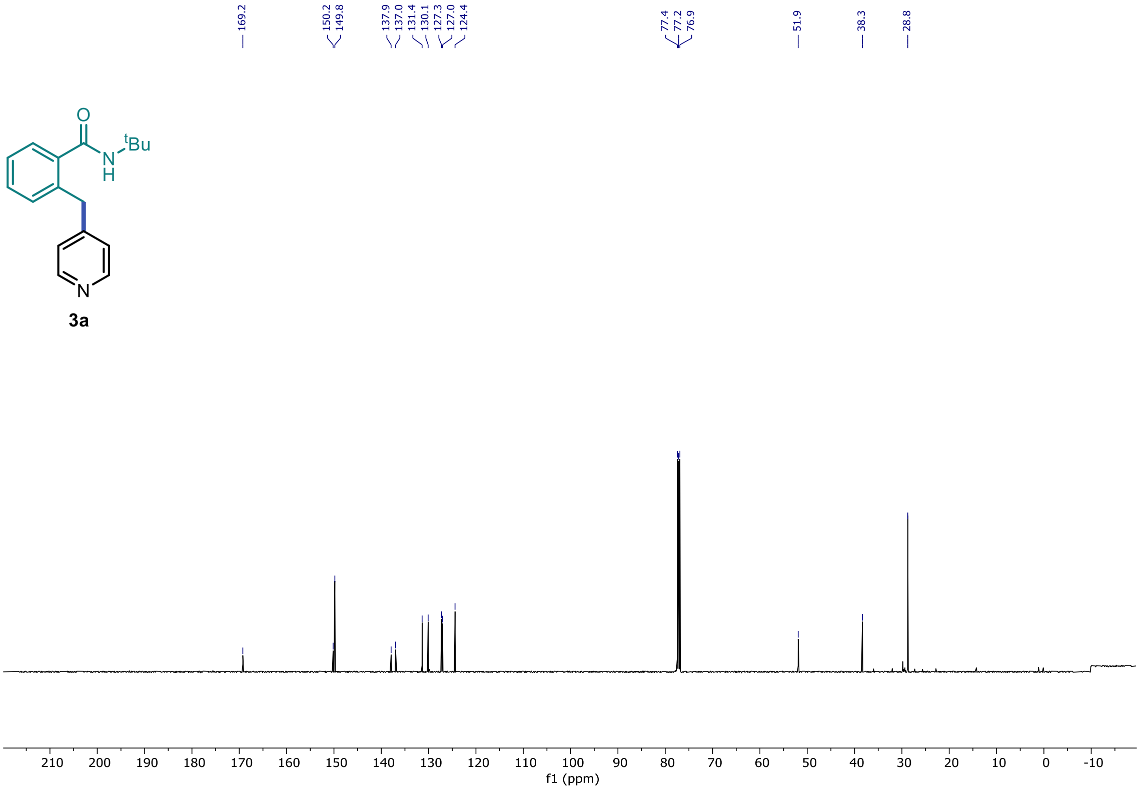

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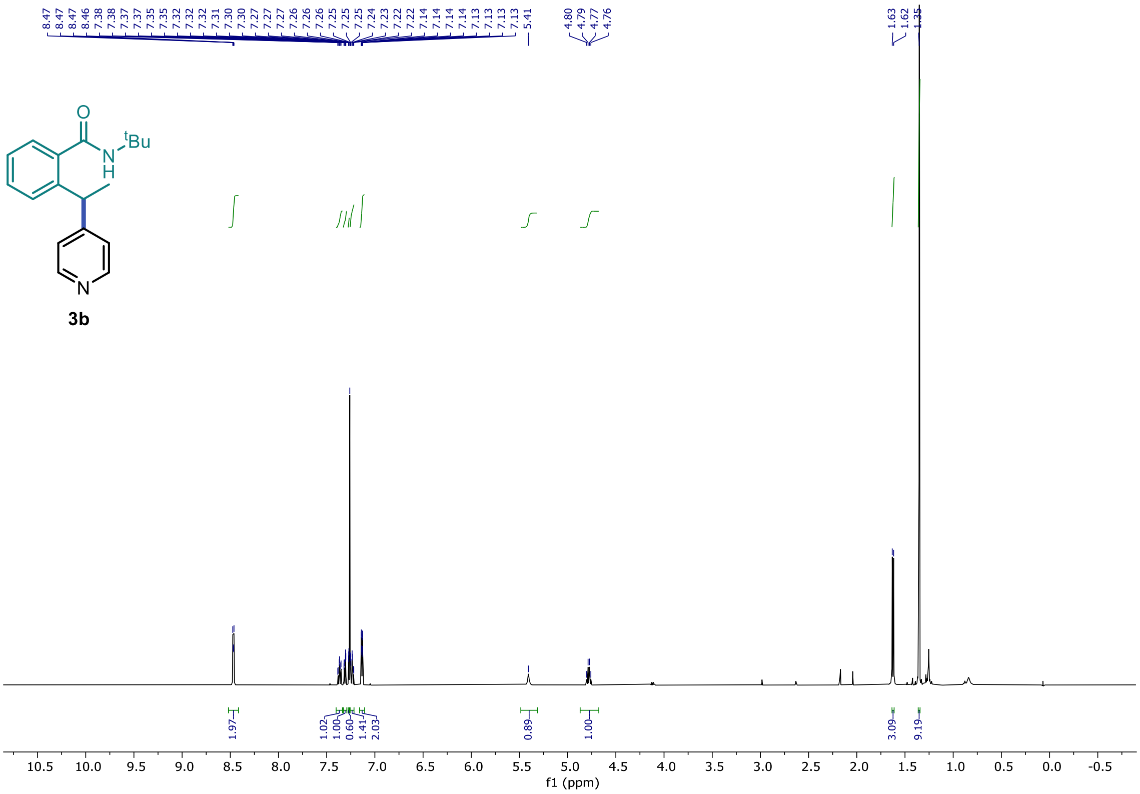

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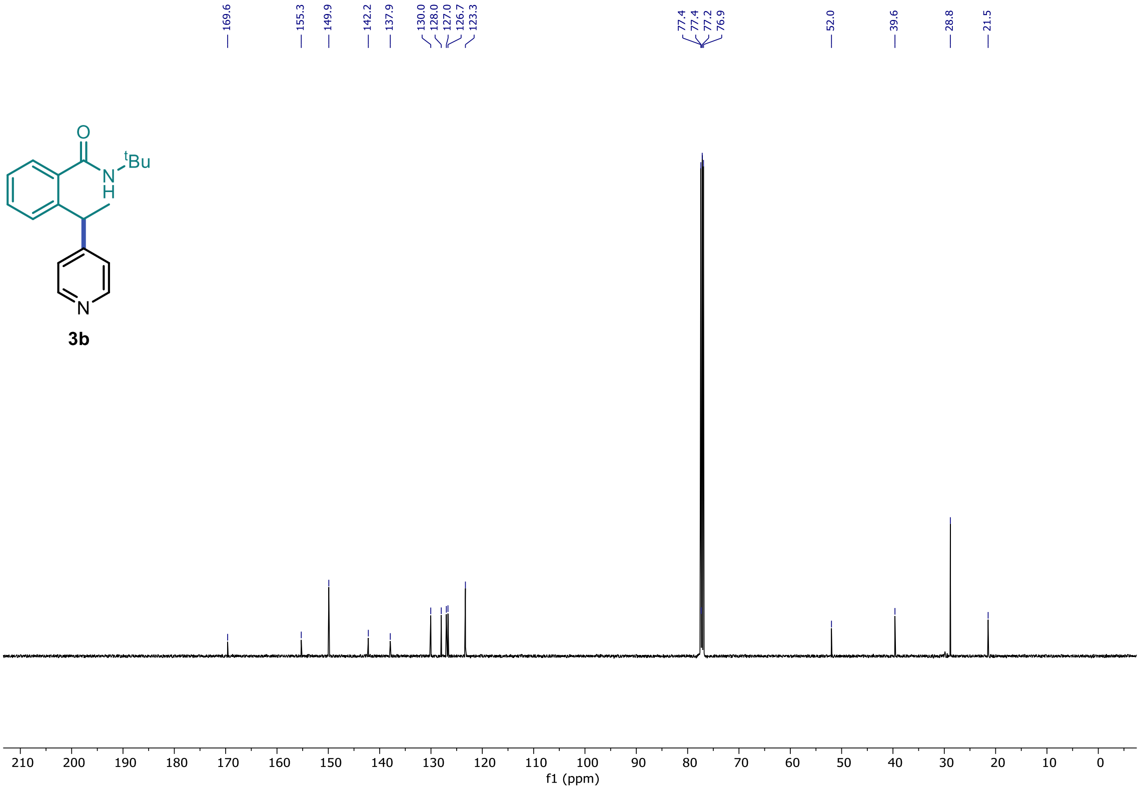

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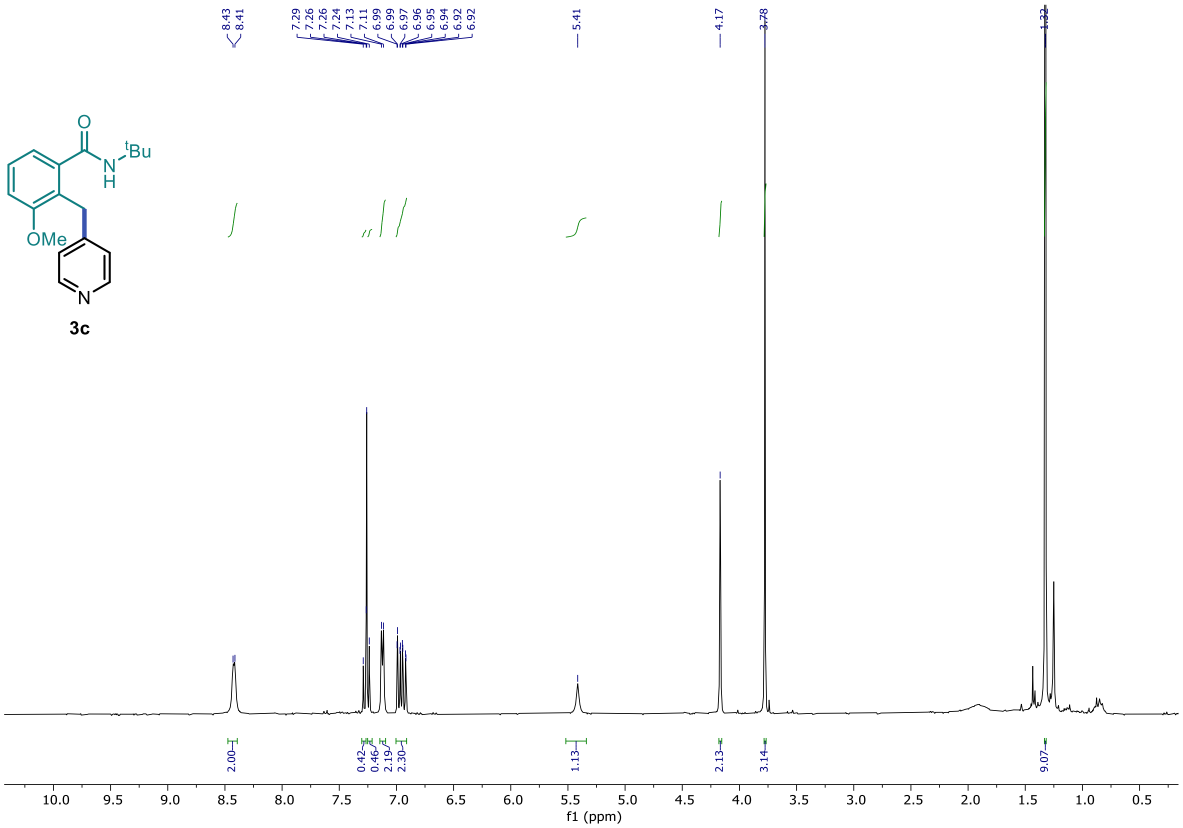

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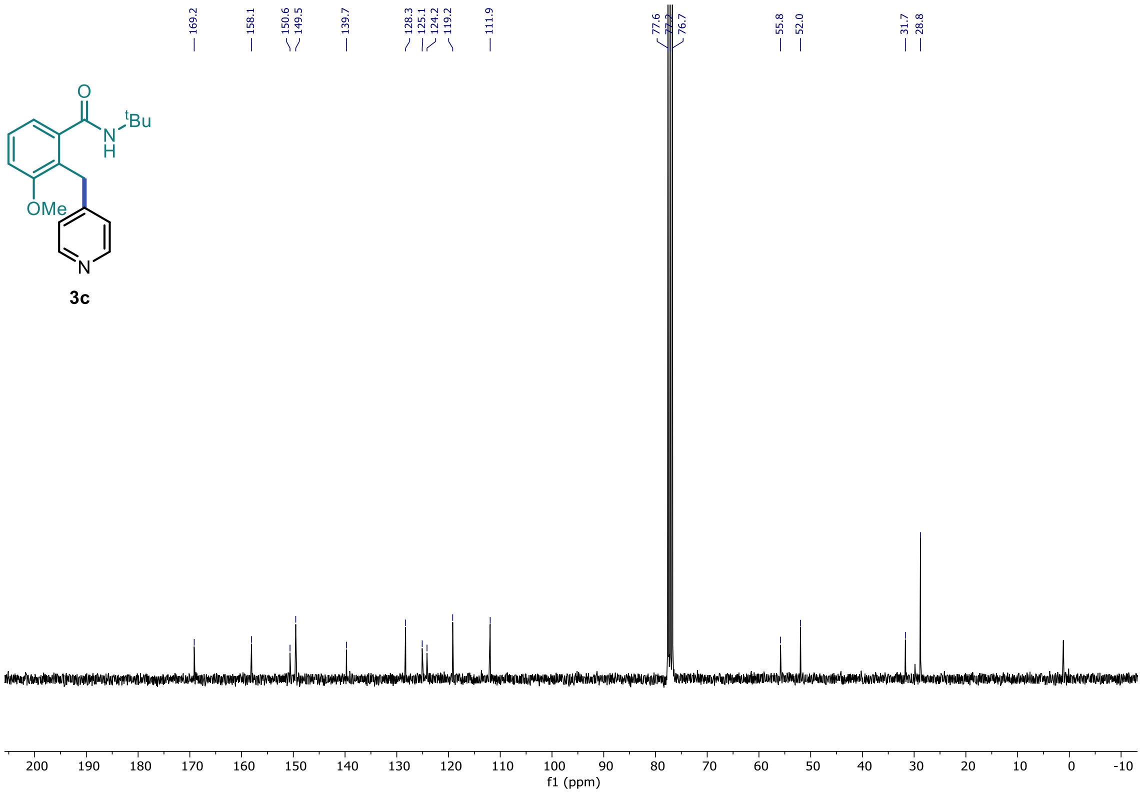

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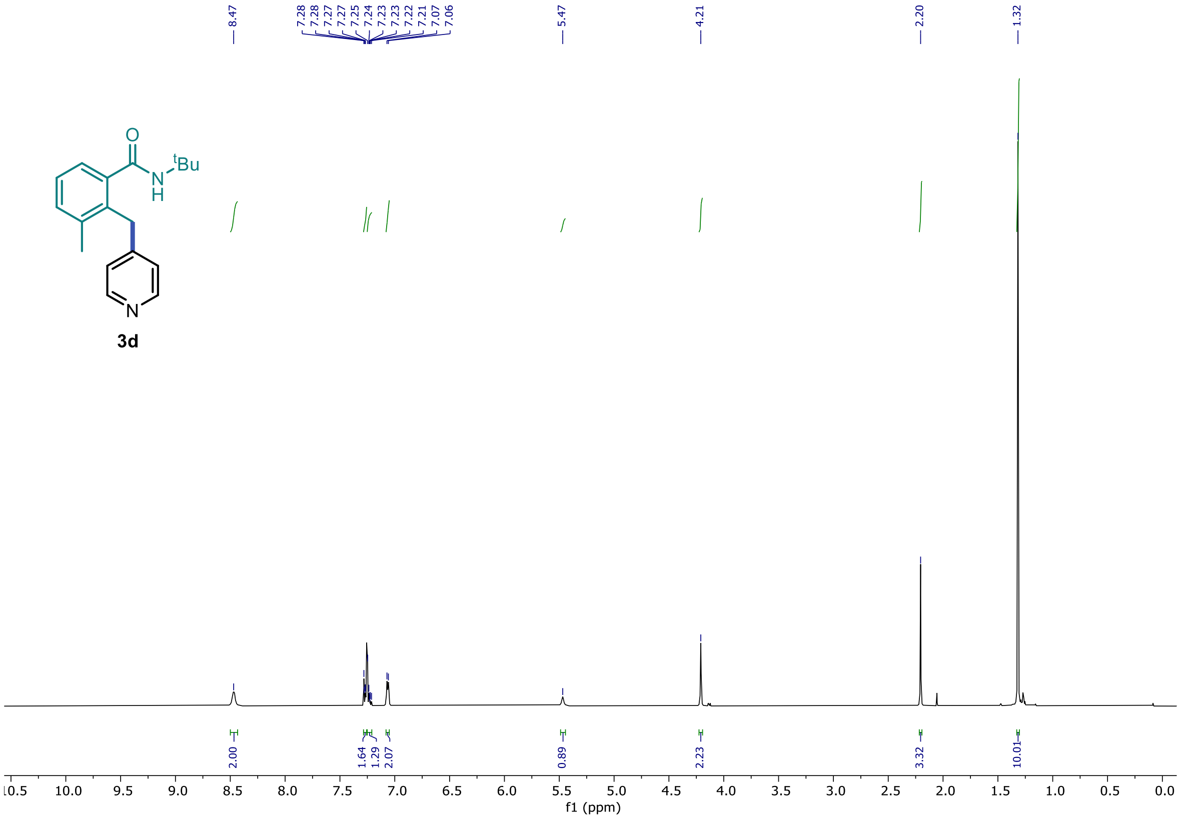

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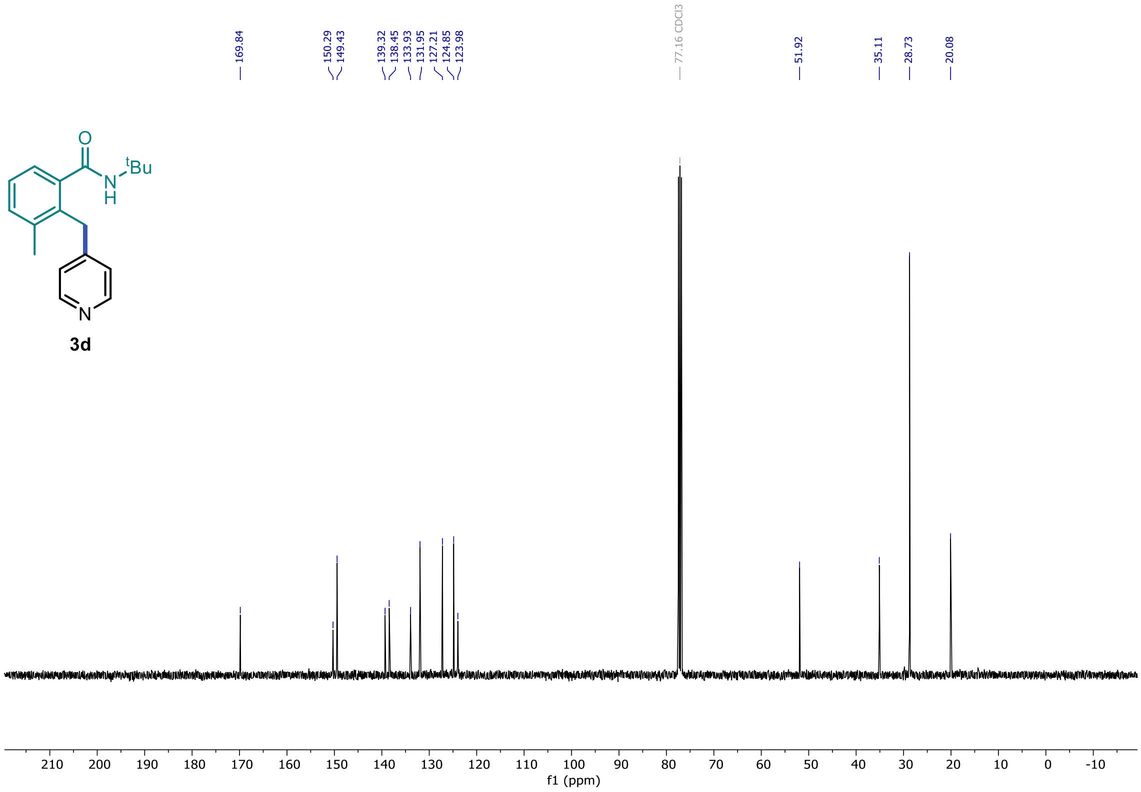

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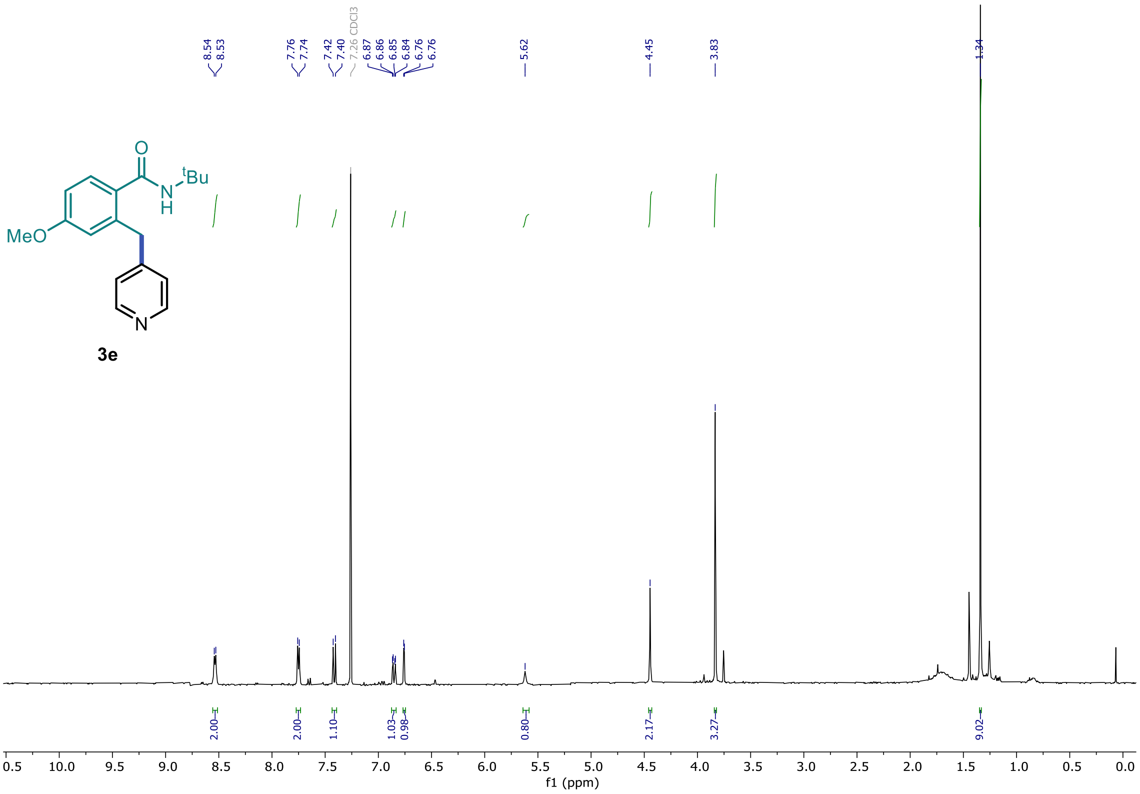

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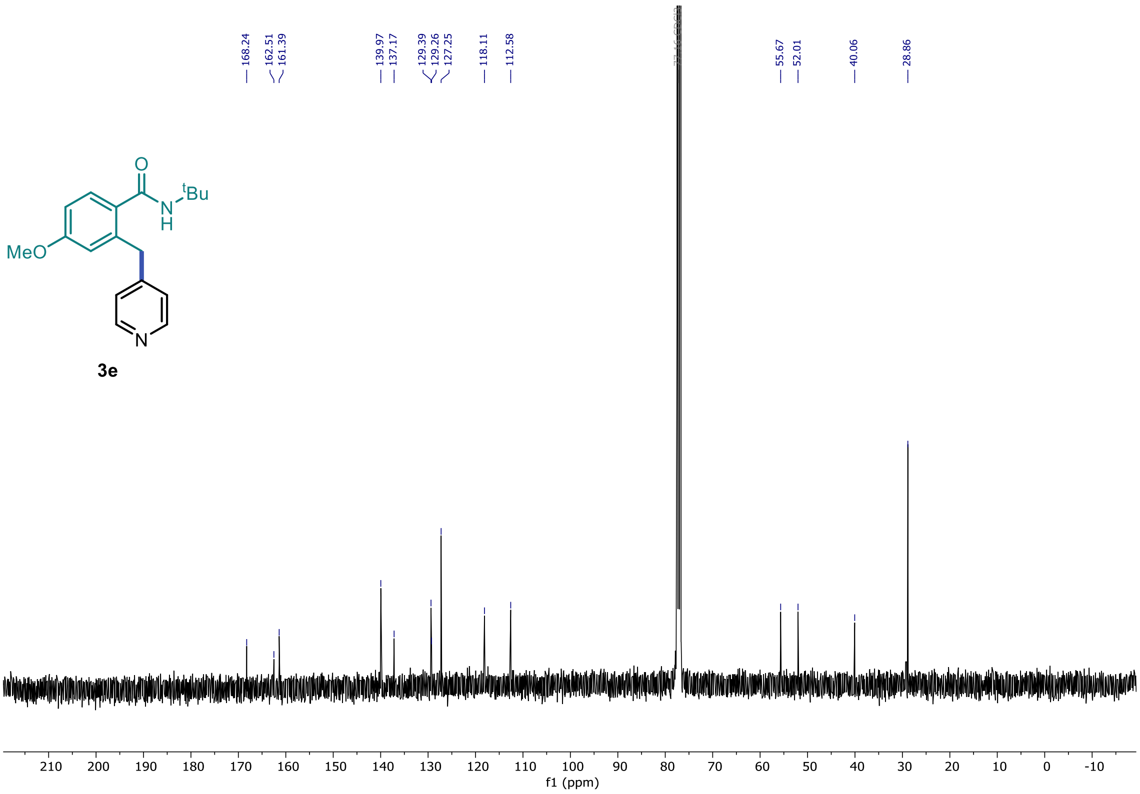

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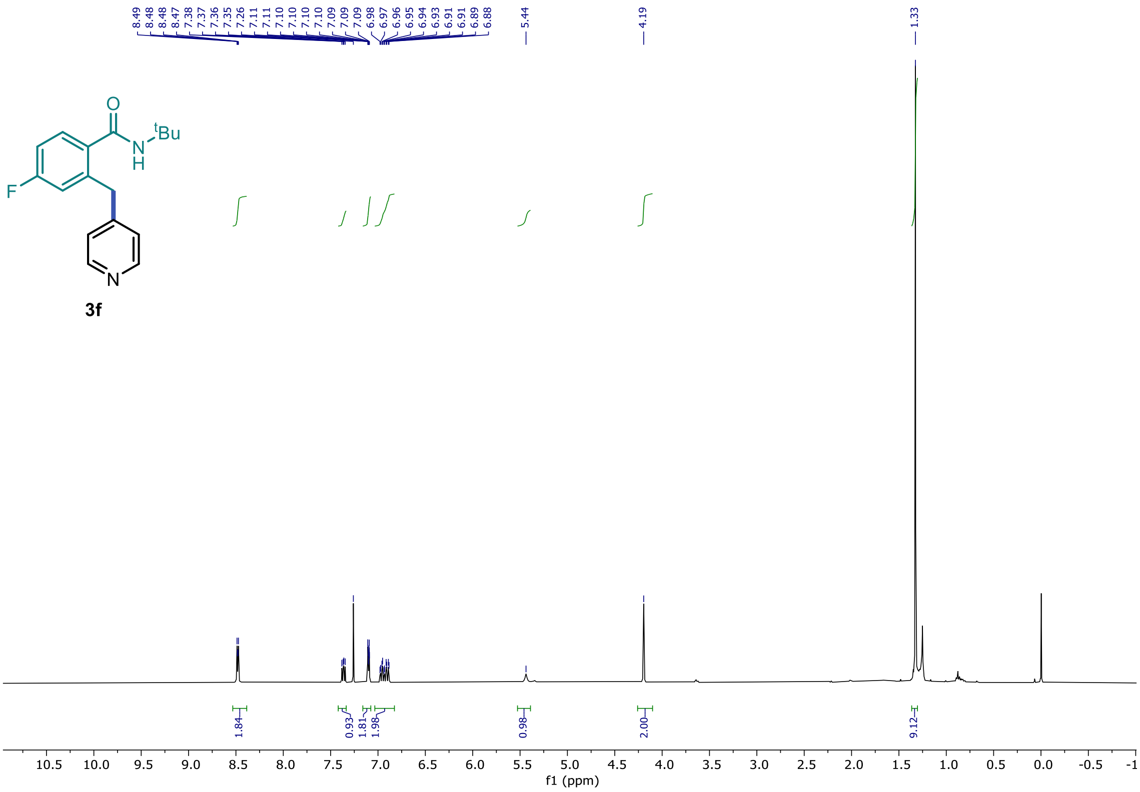

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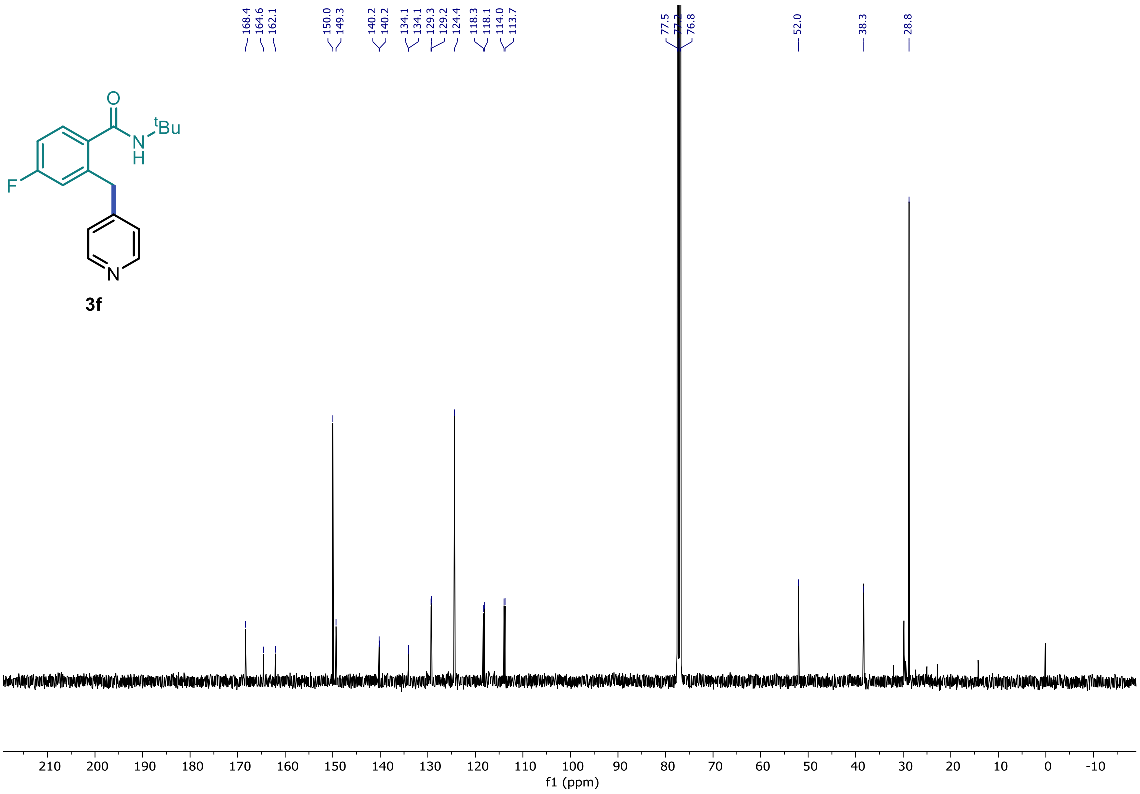

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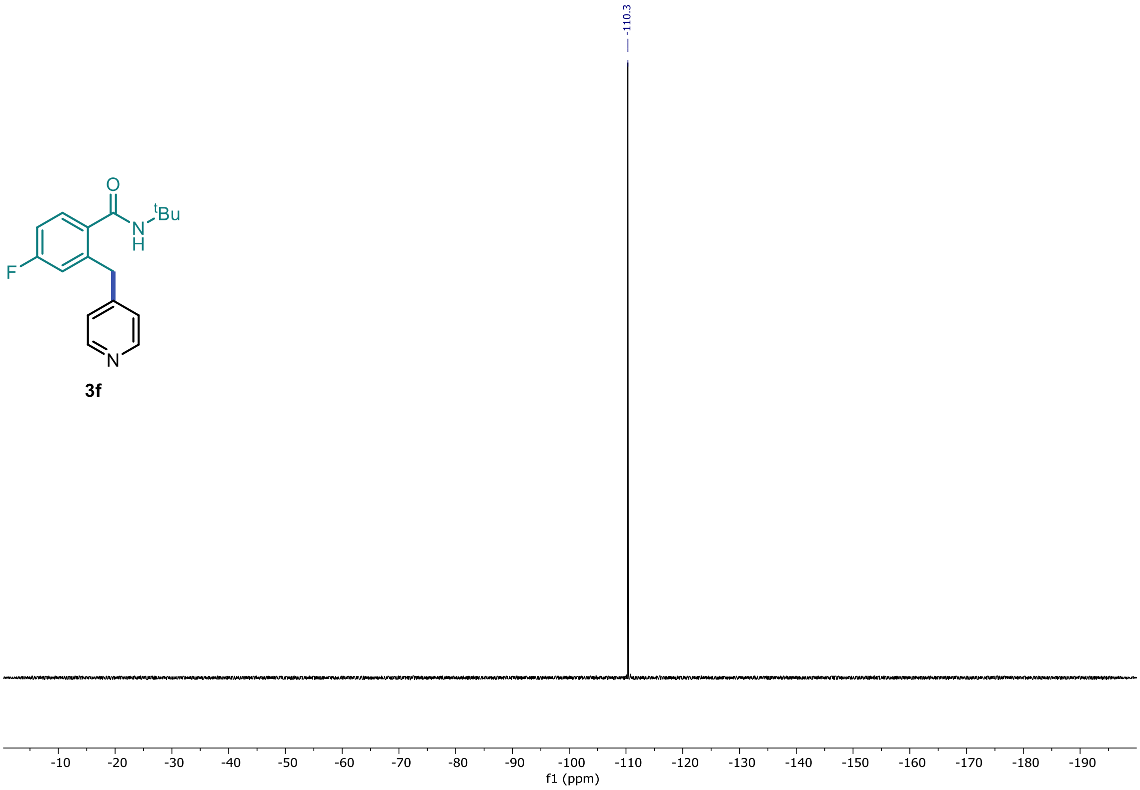

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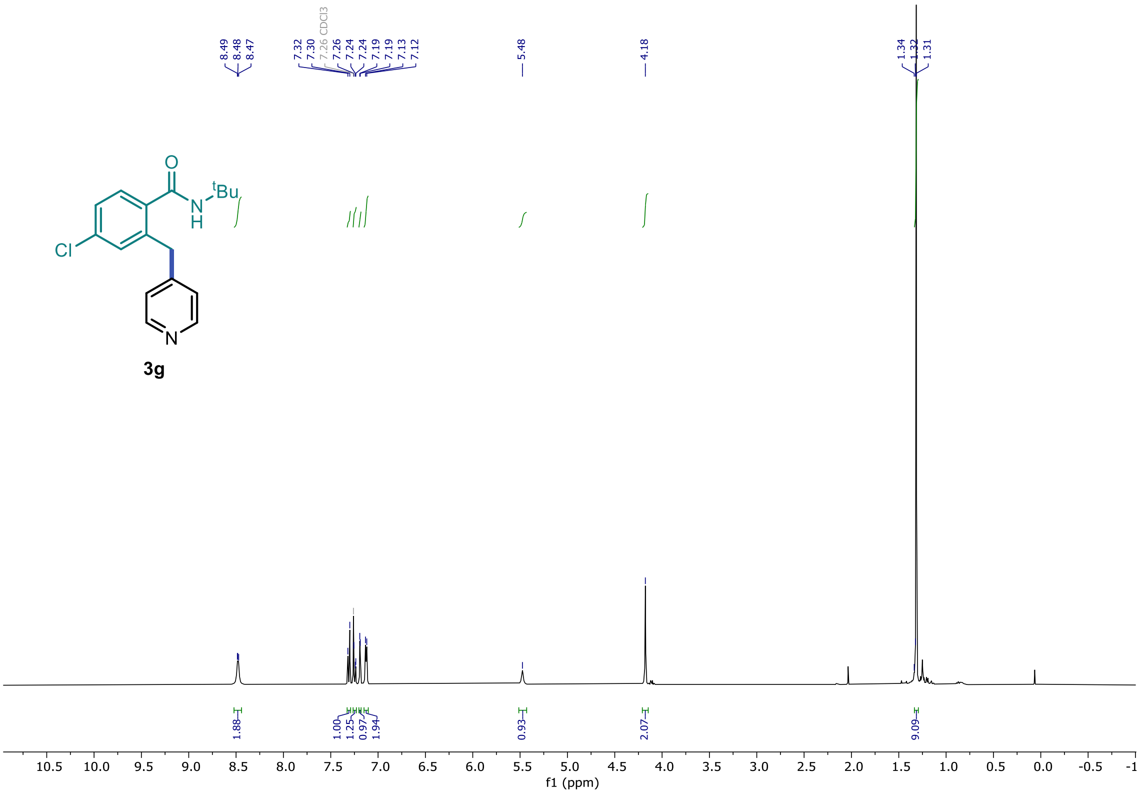

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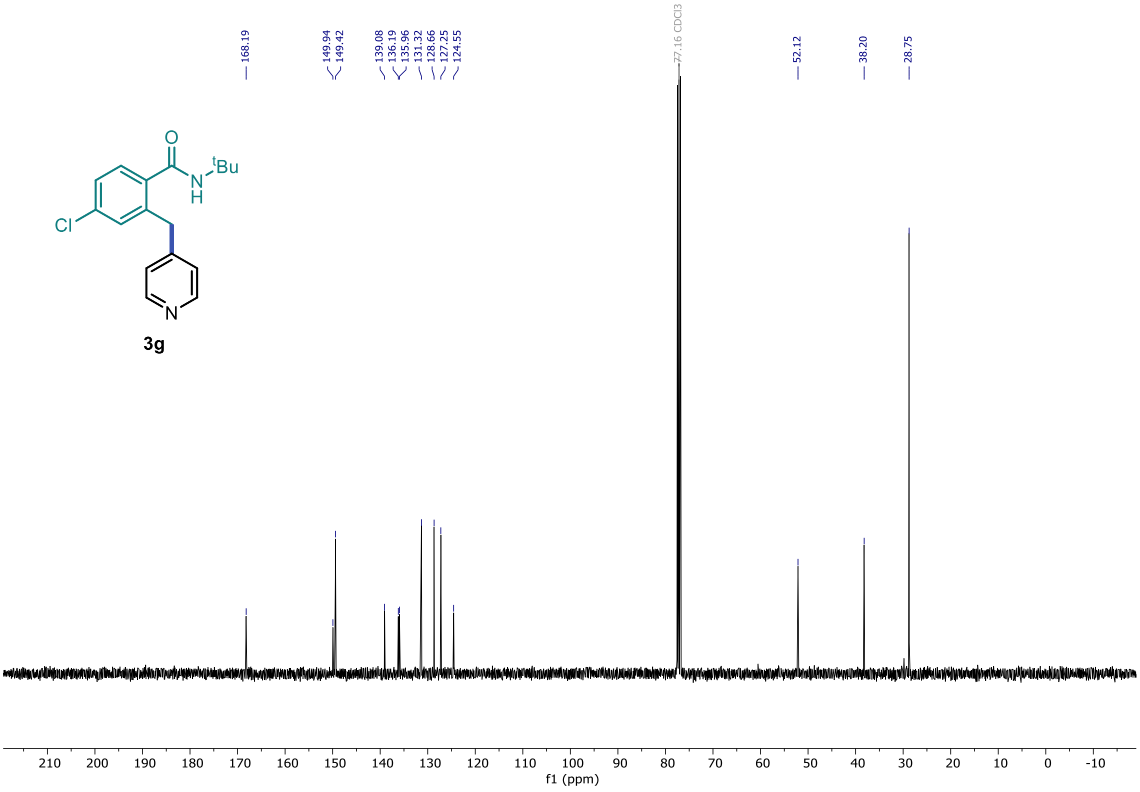

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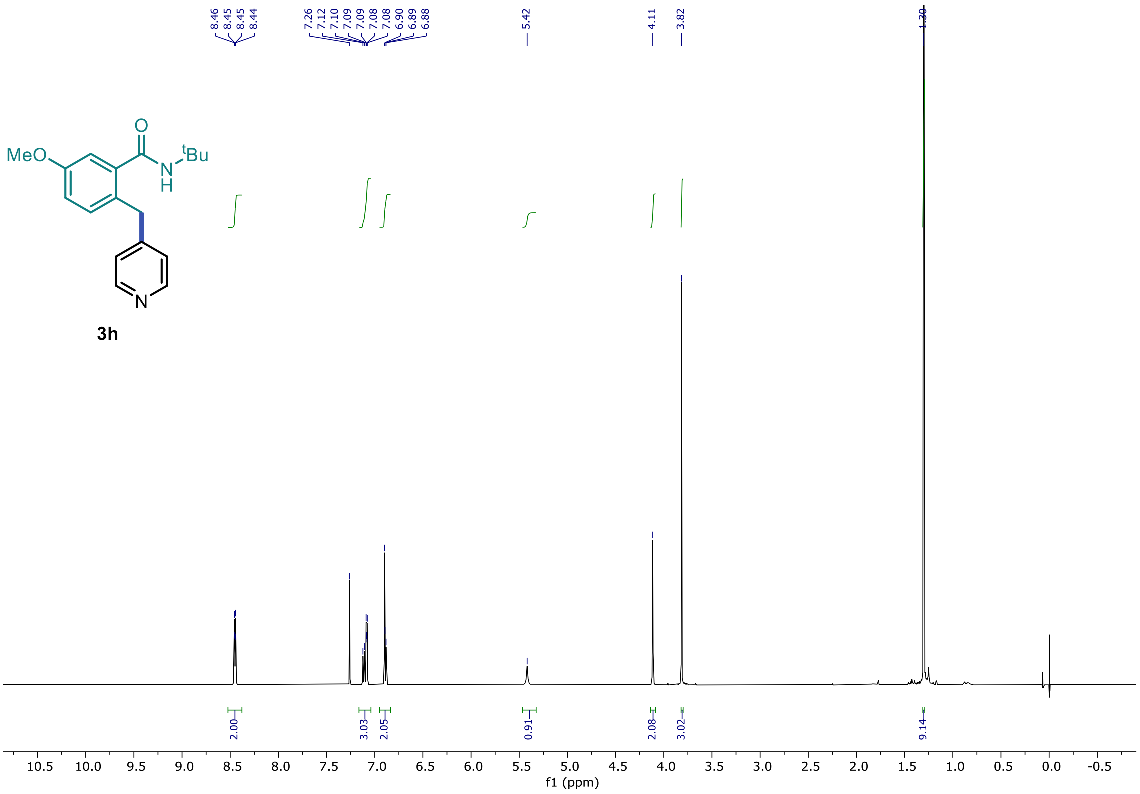

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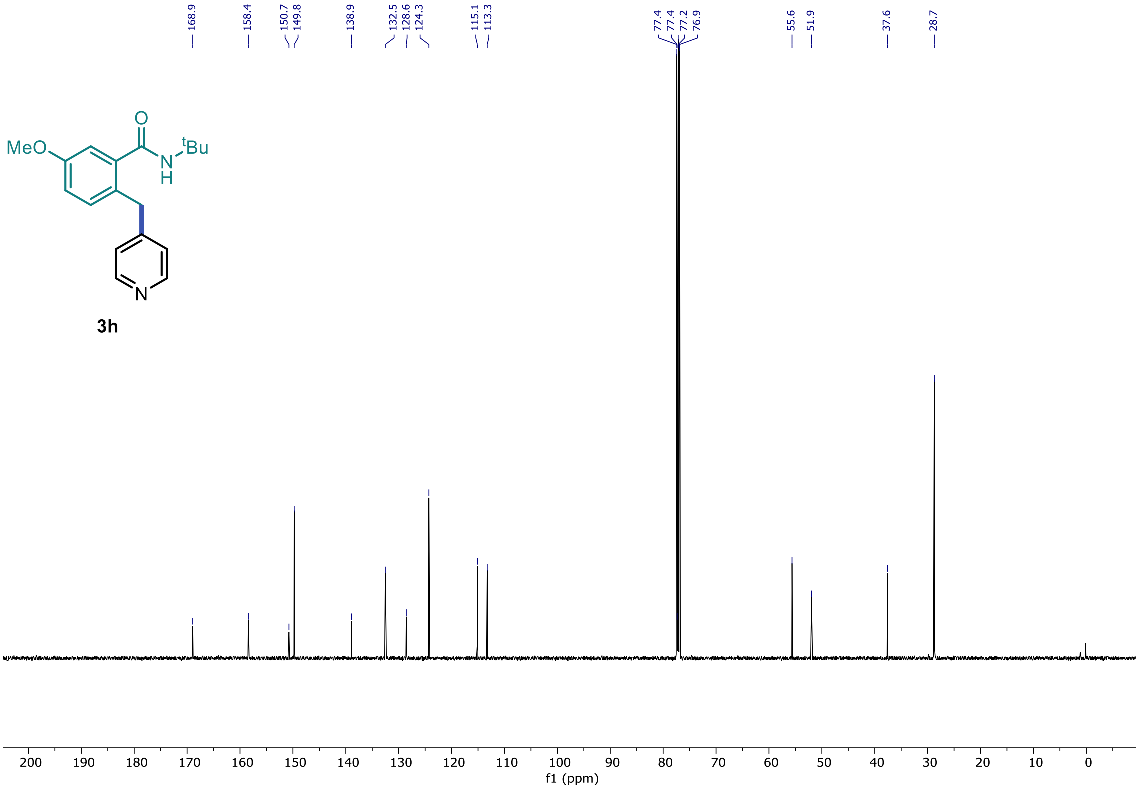

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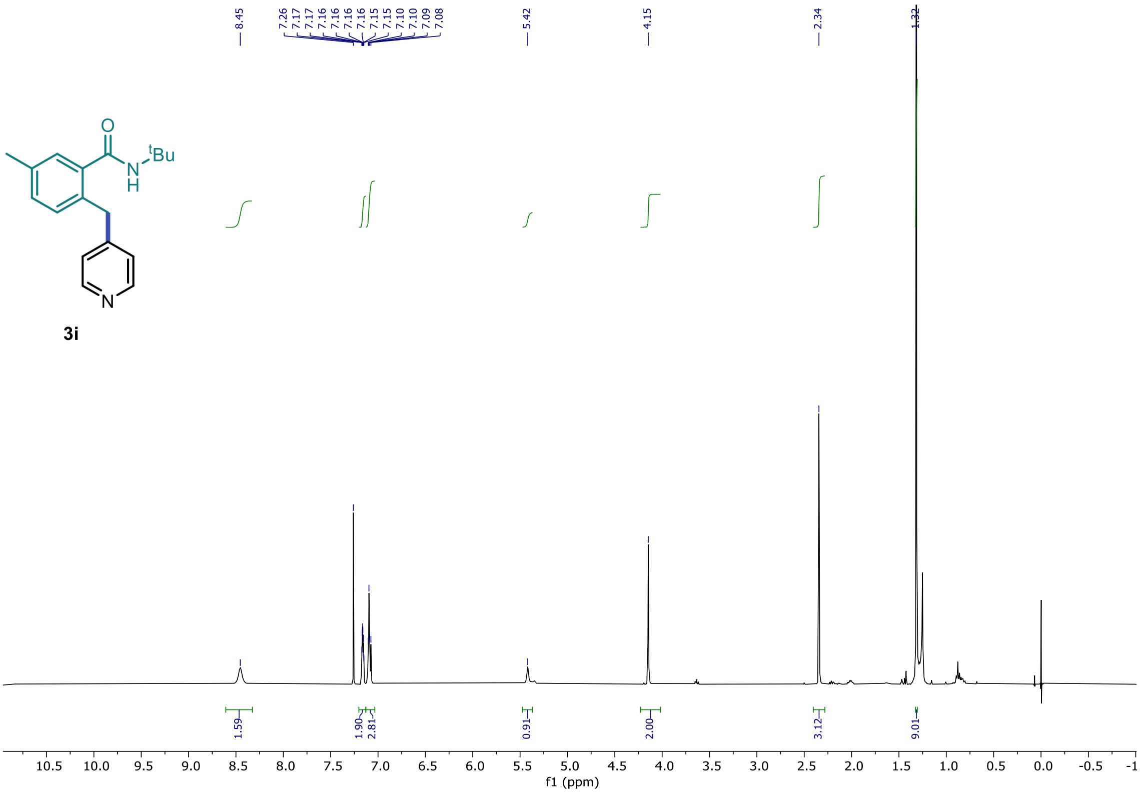

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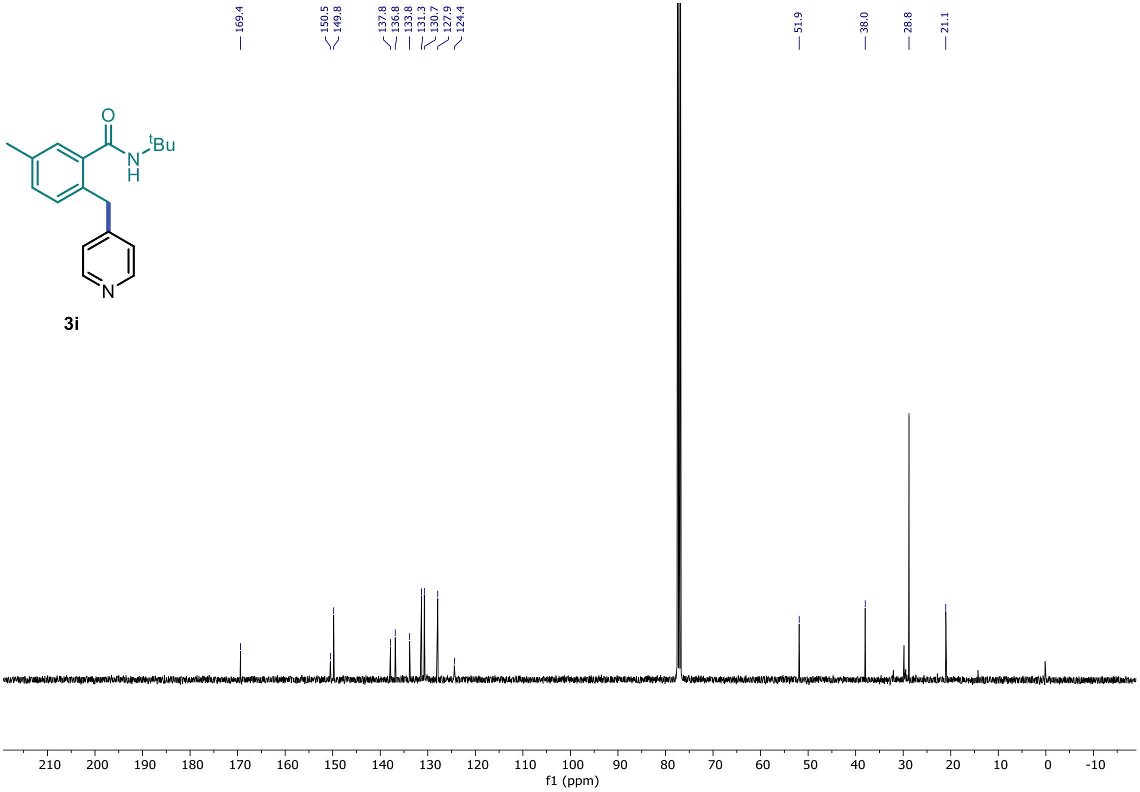

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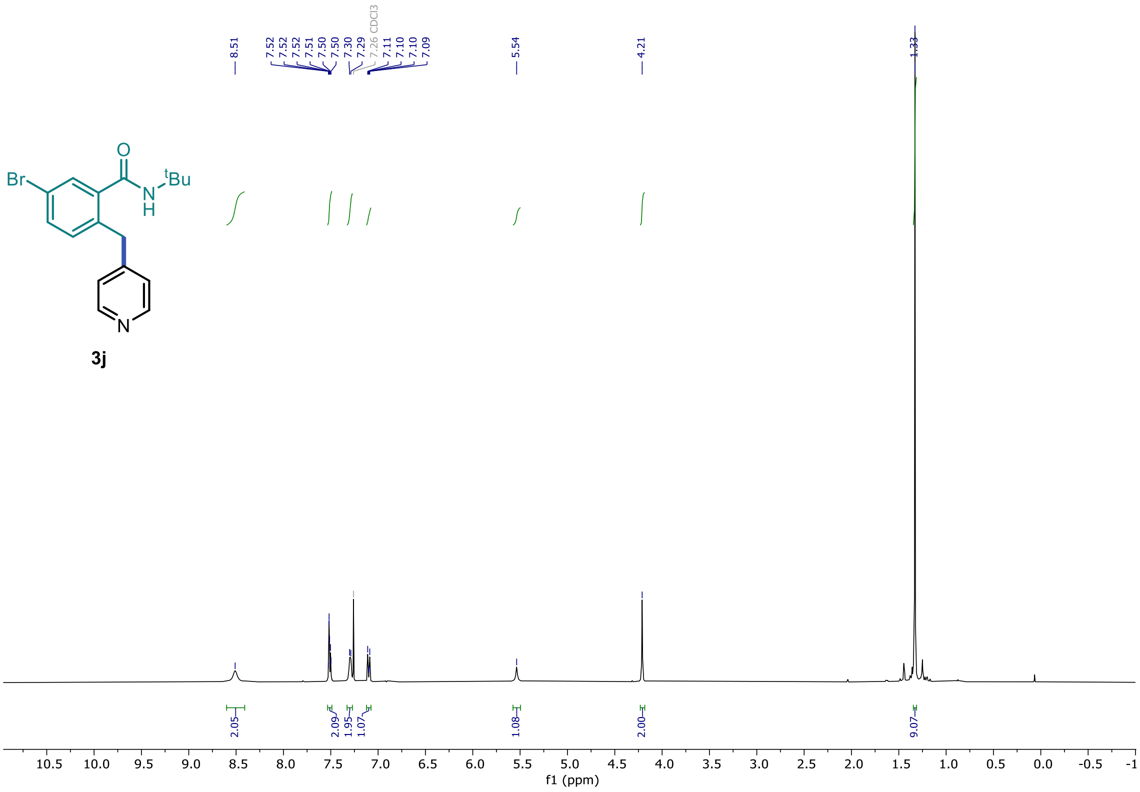

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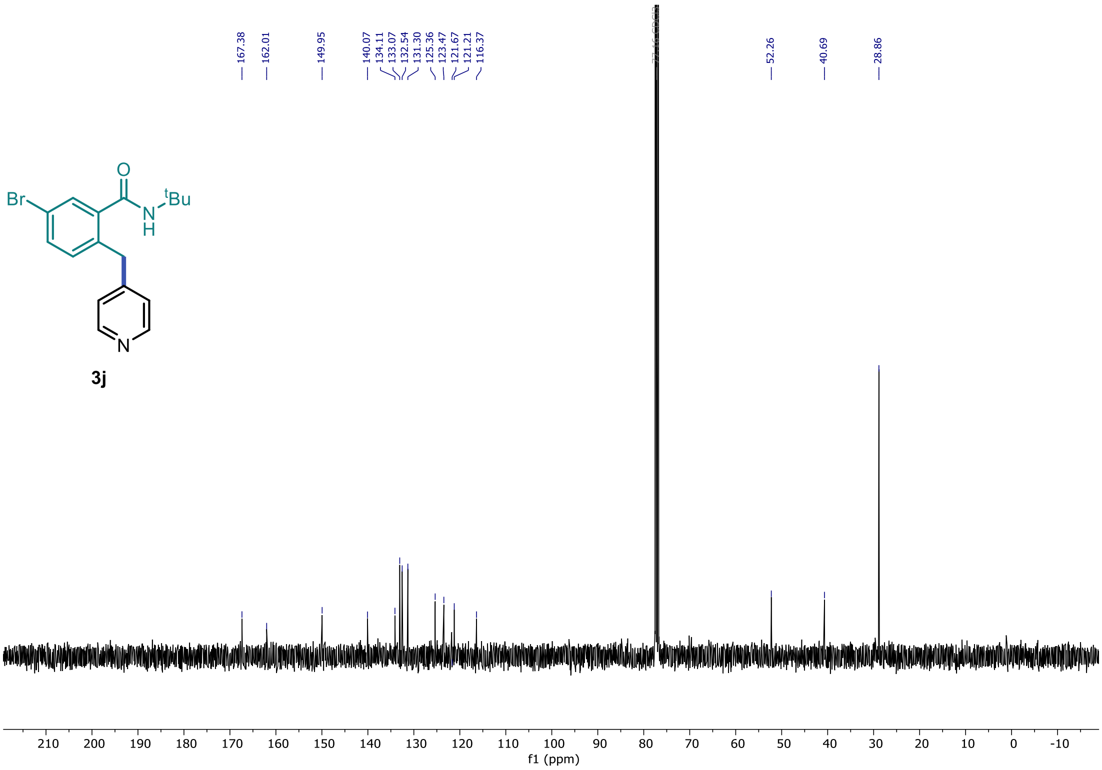

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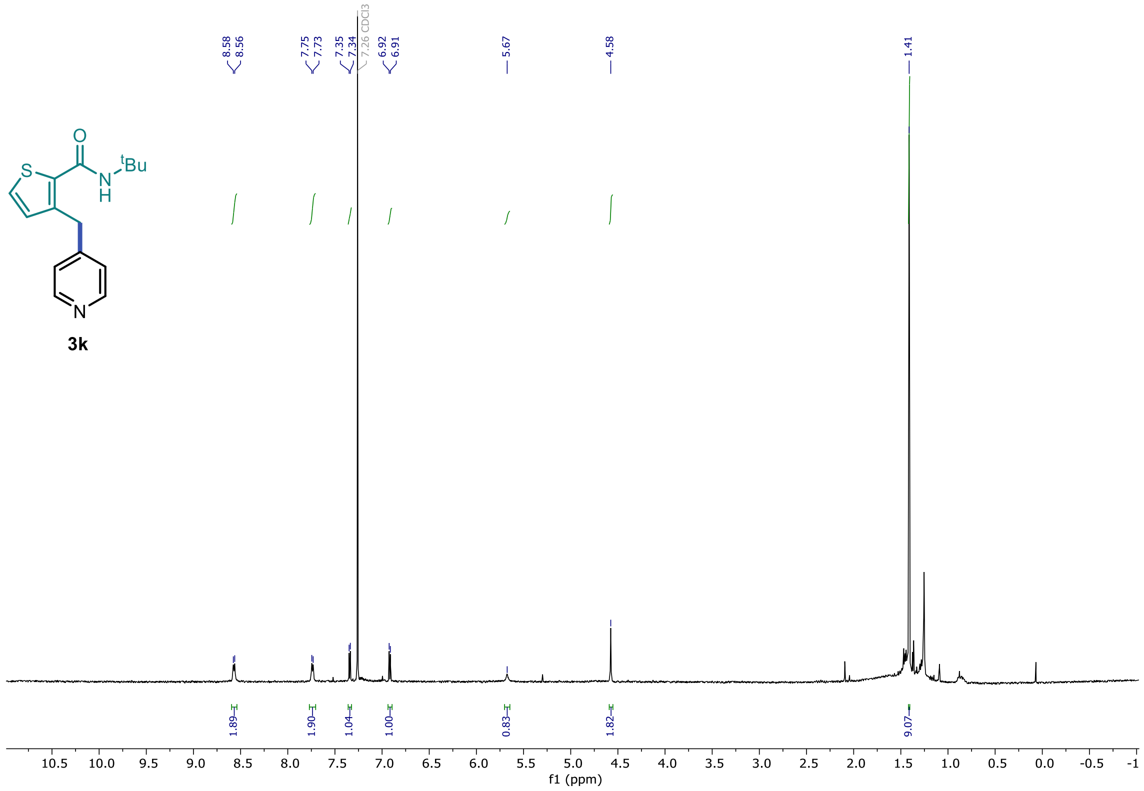

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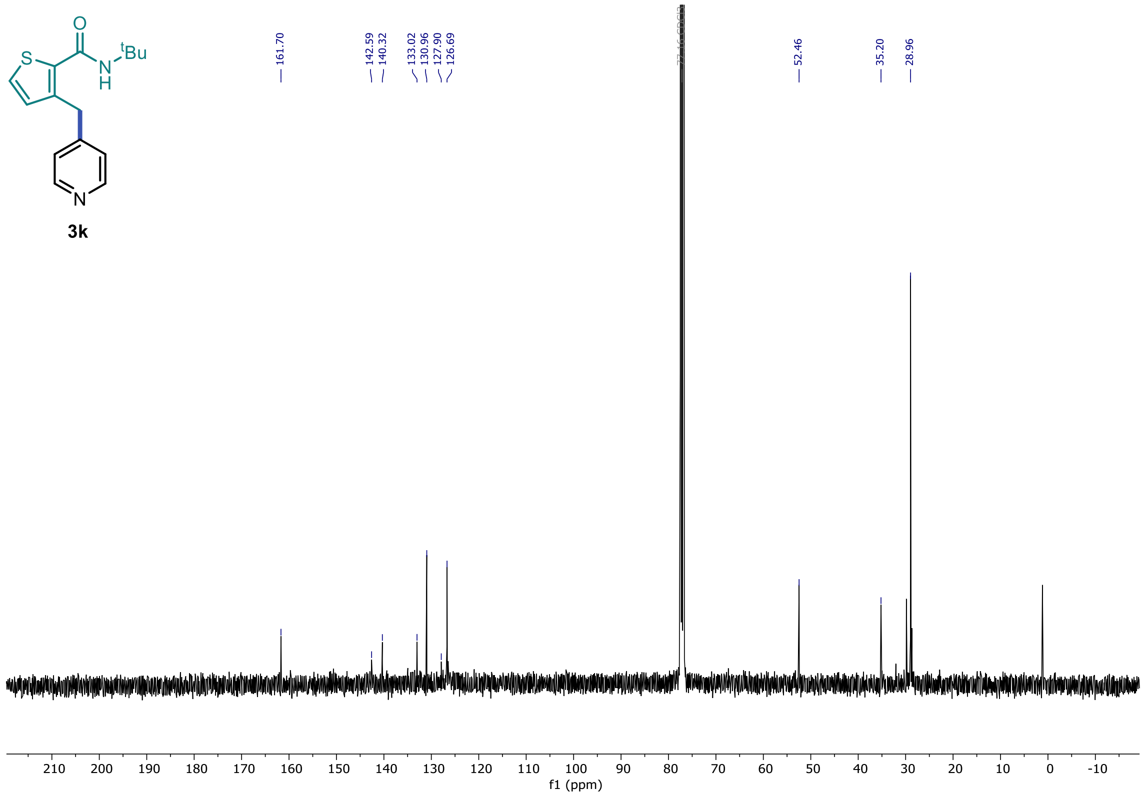

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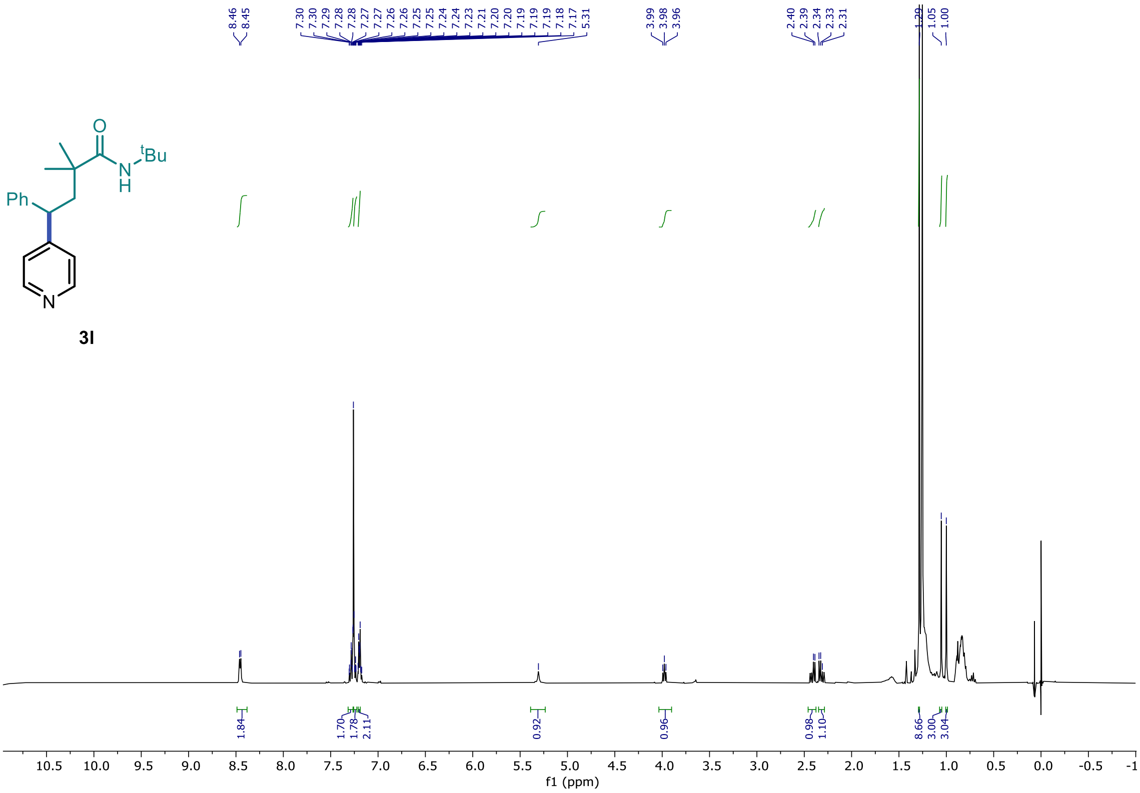

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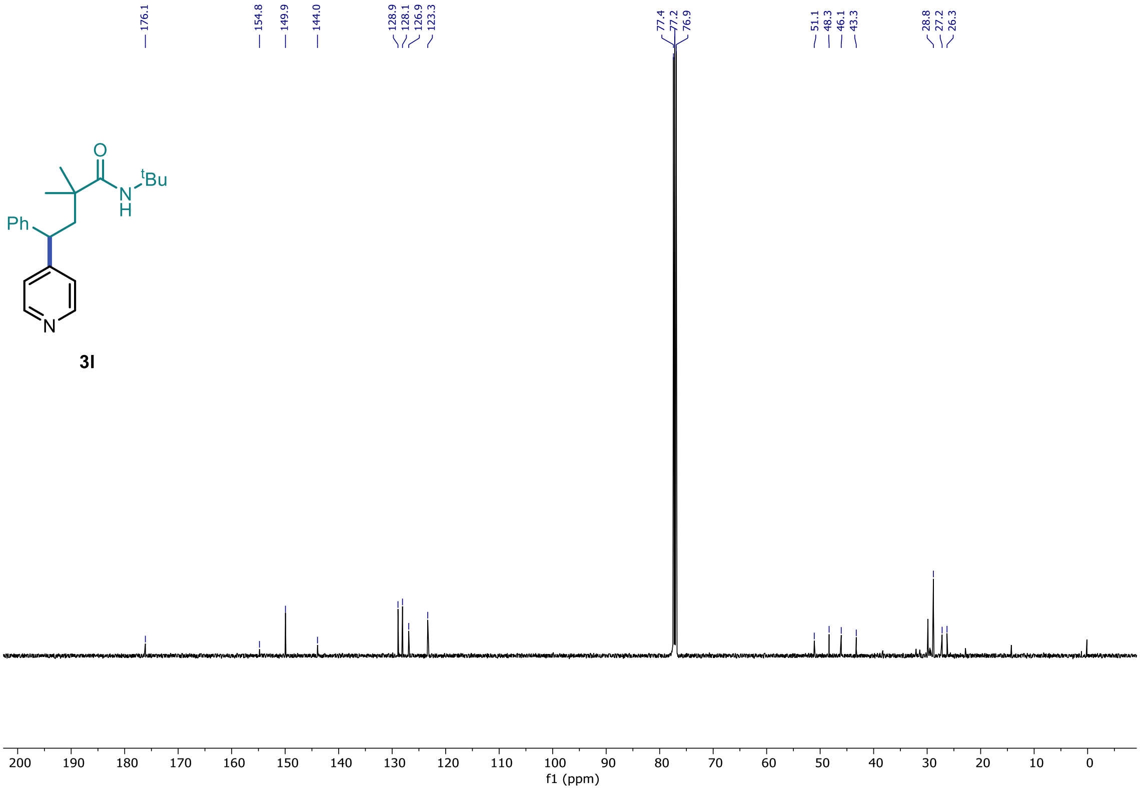

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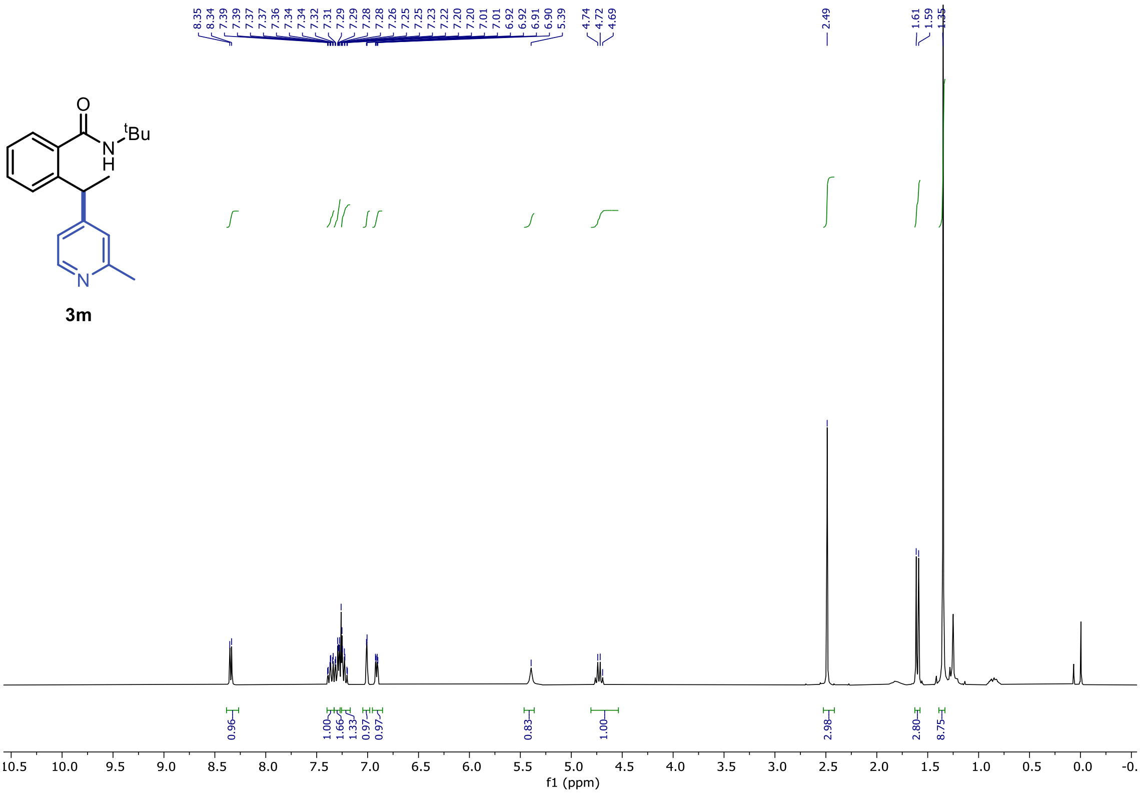

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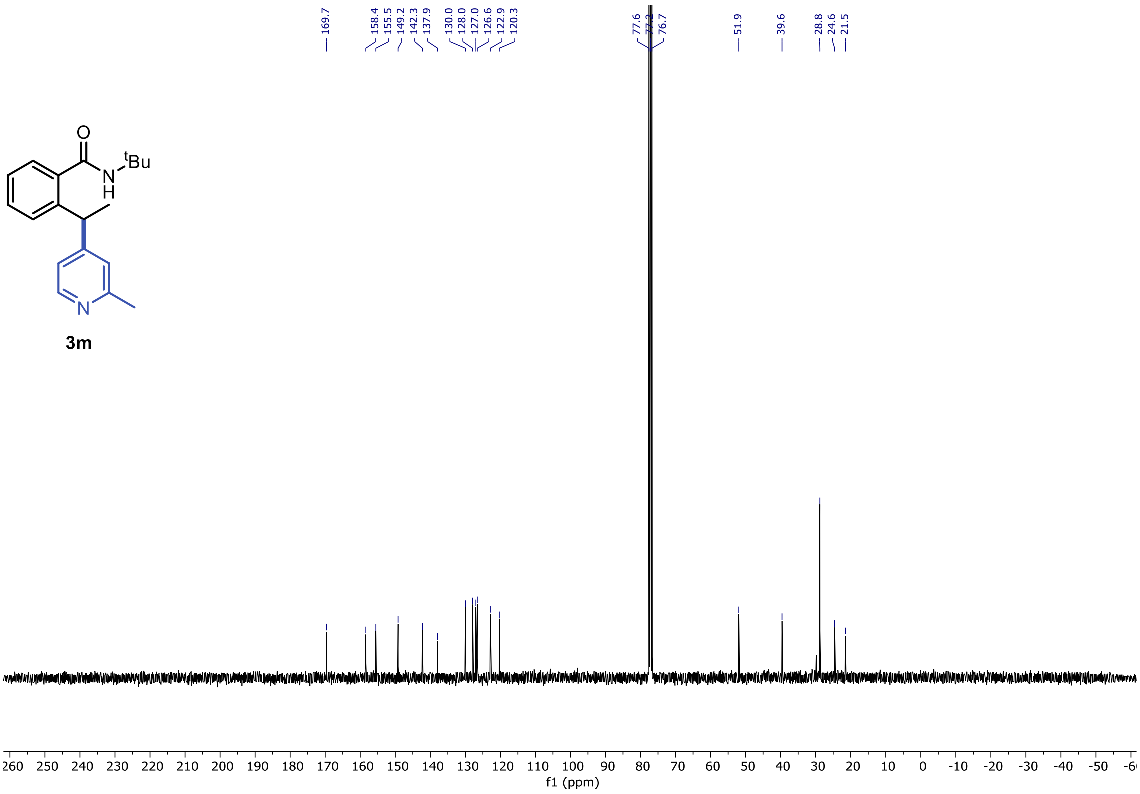

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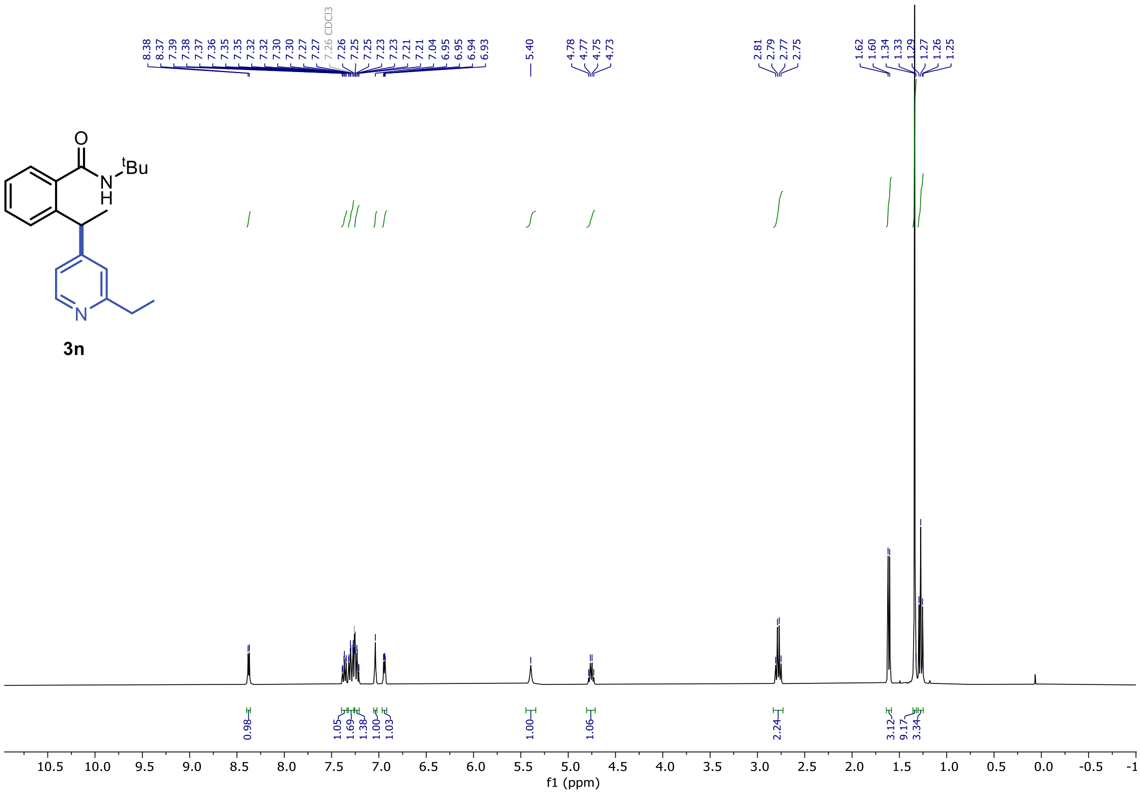

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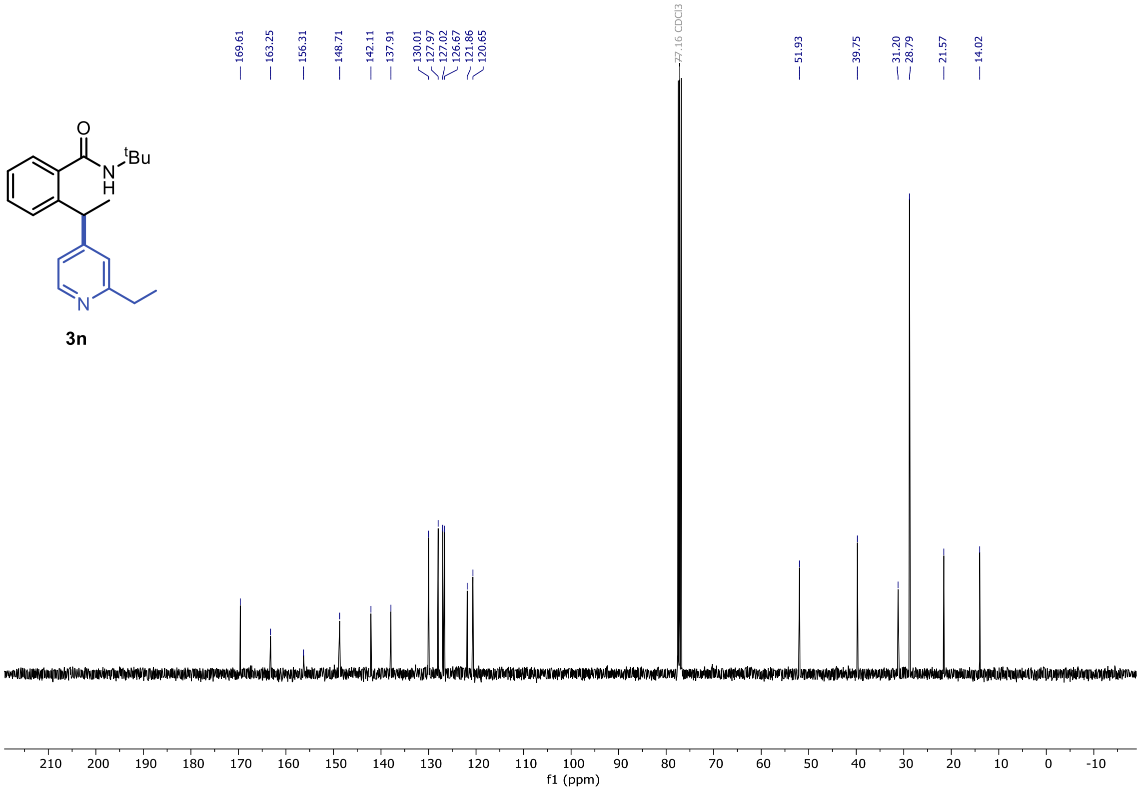

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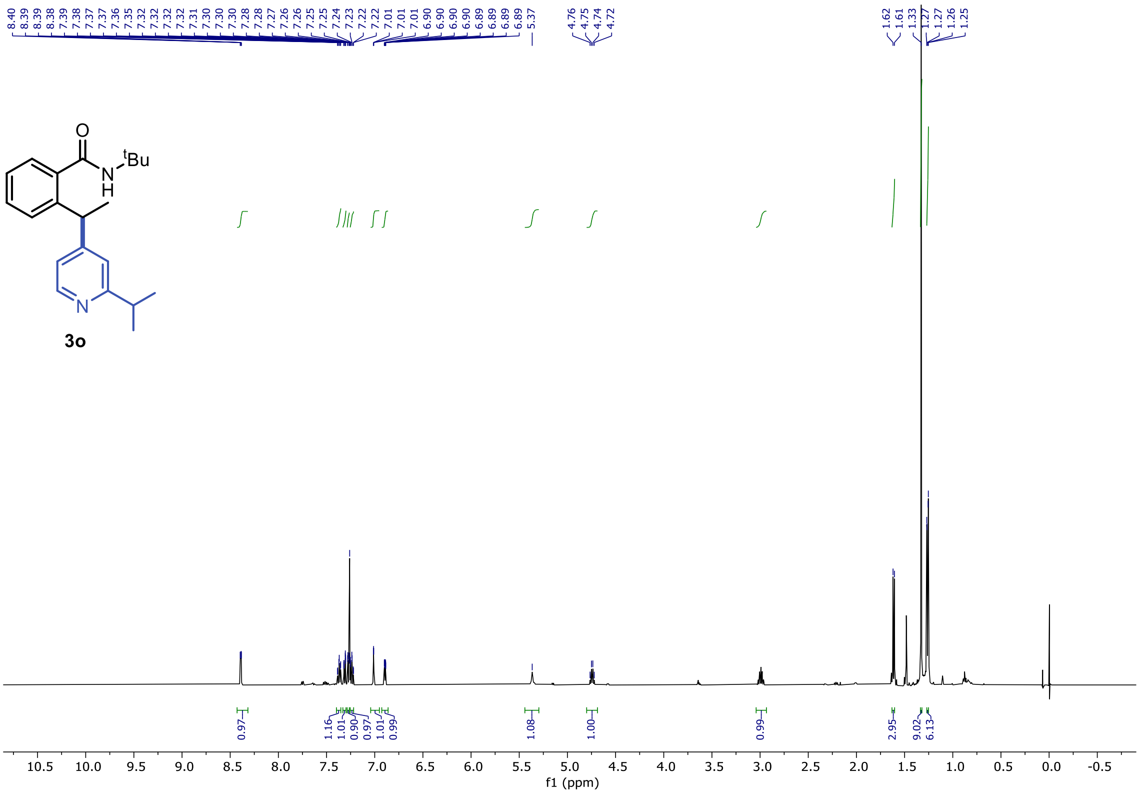

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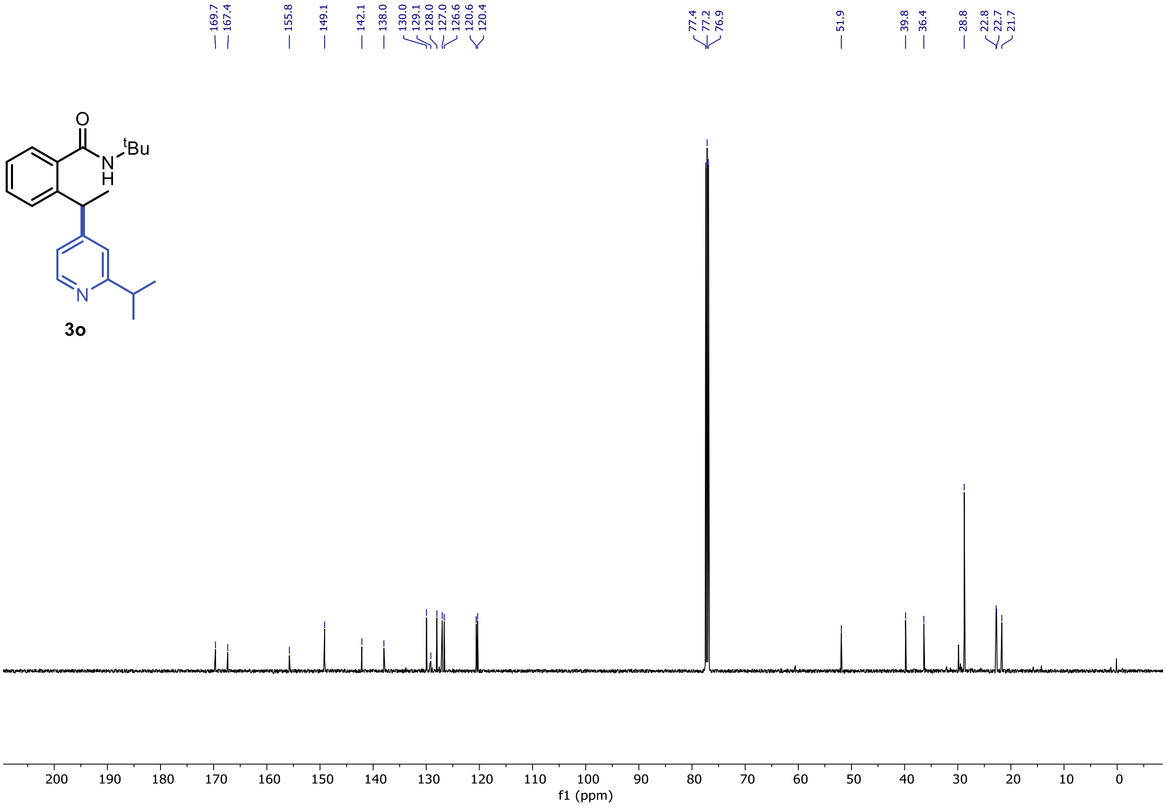

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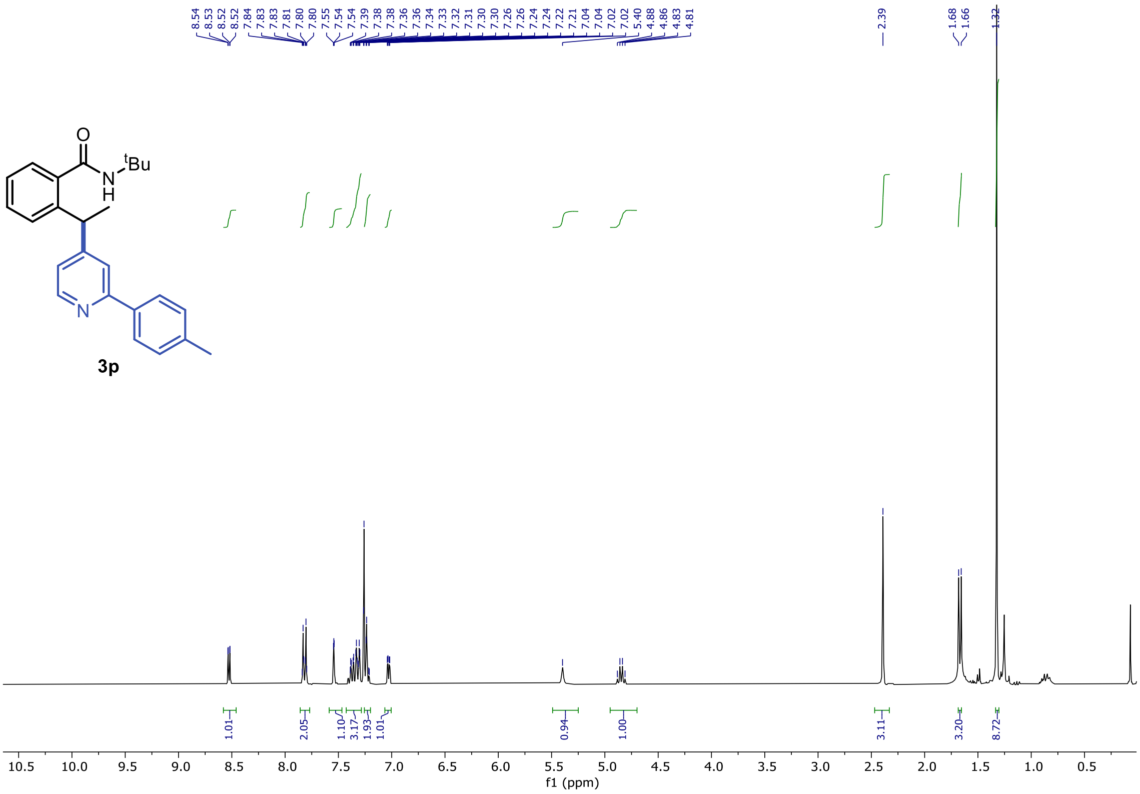

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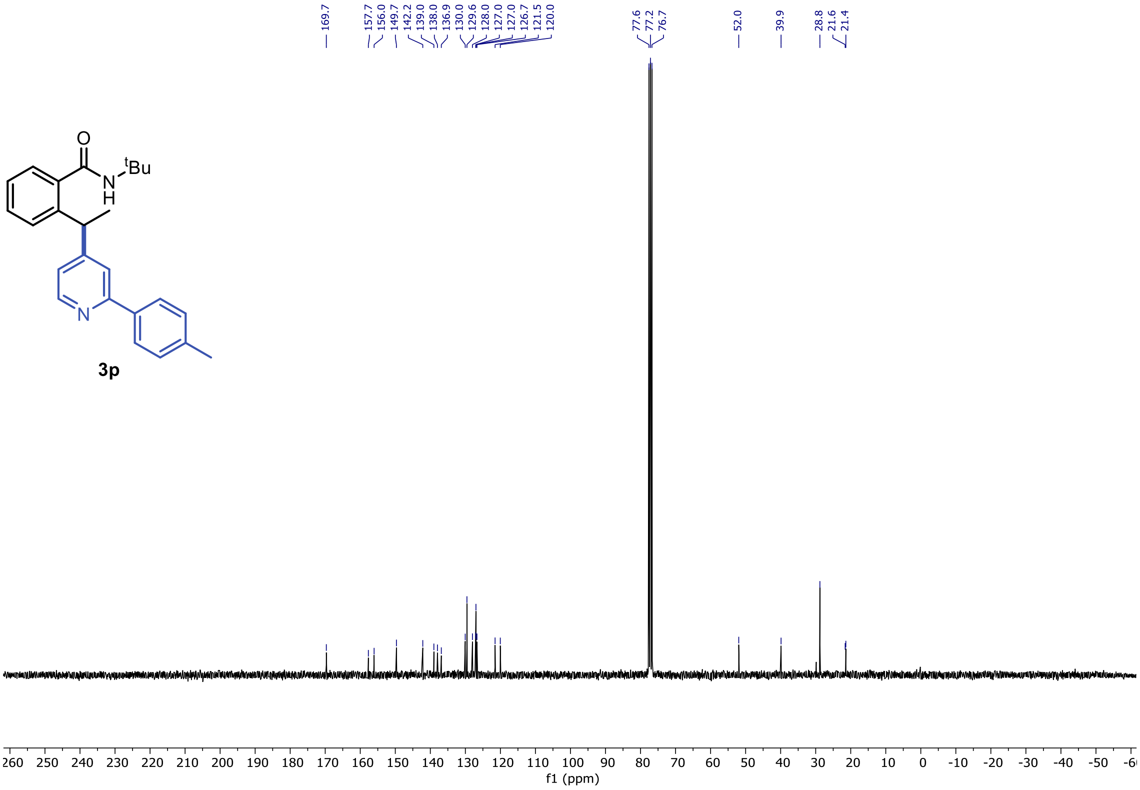

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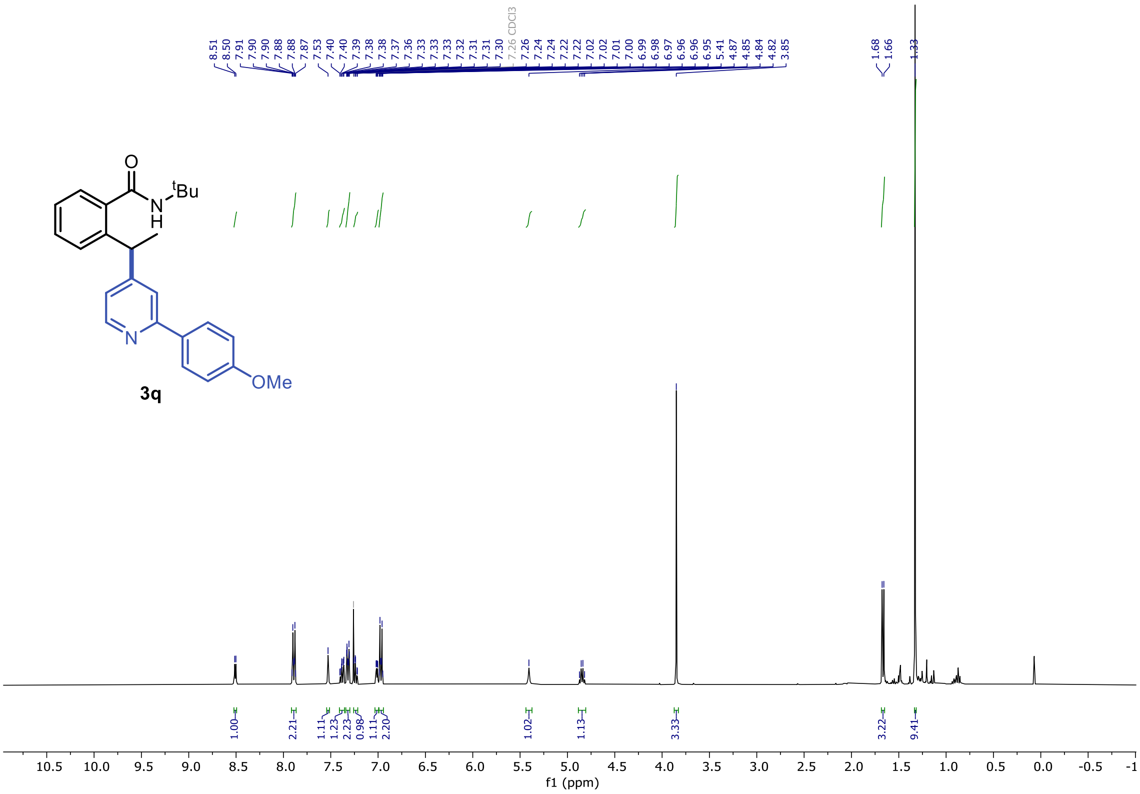

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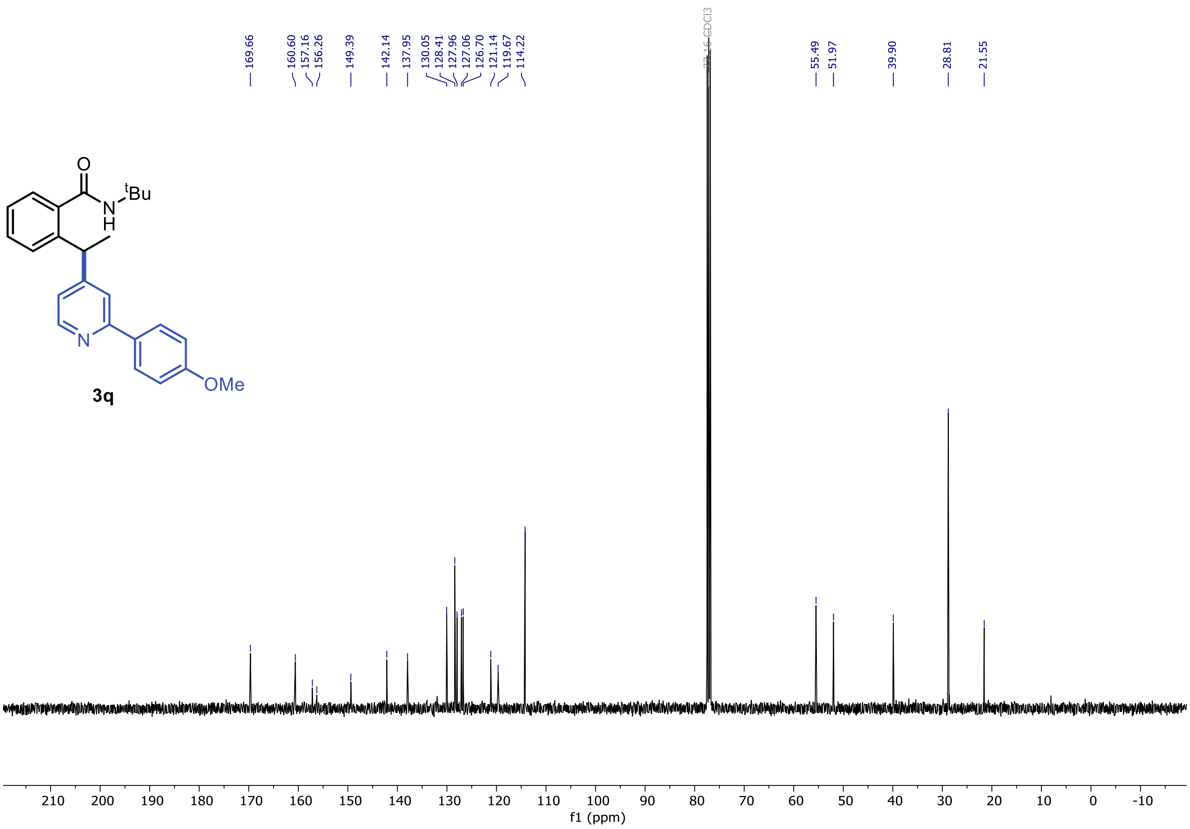
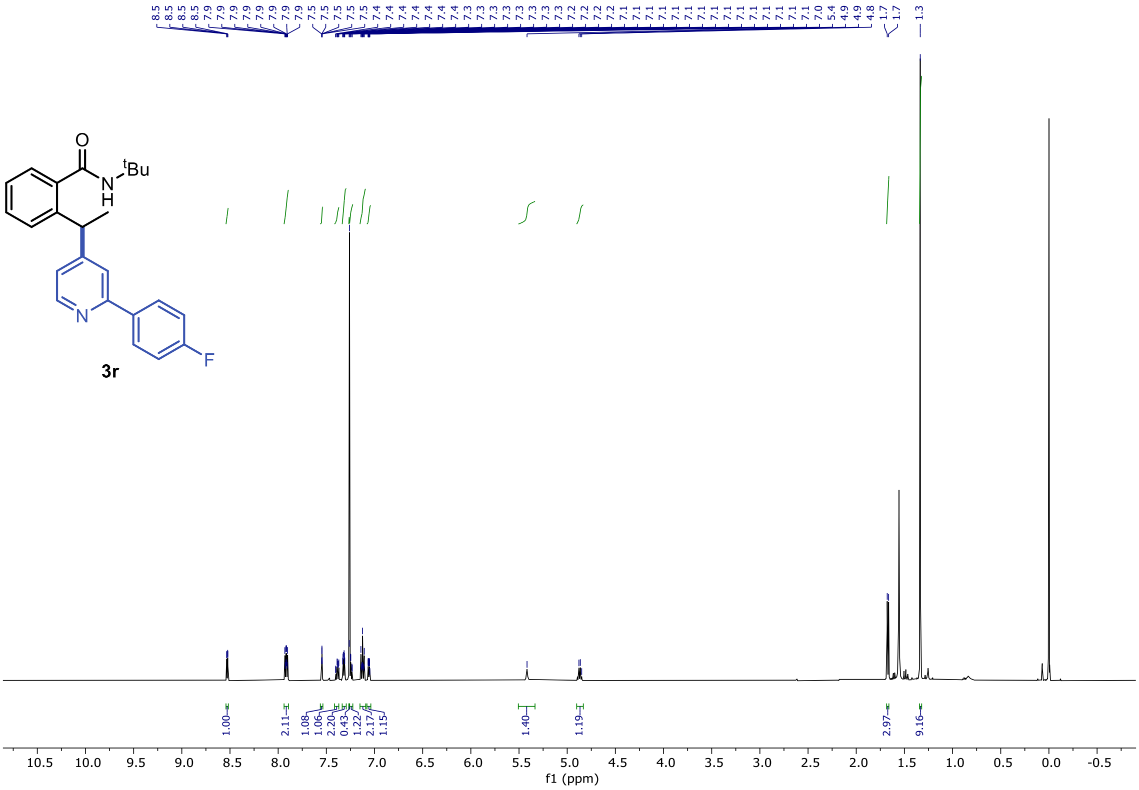


^{1}H NMR (500 MHz, CDCl$_3$)



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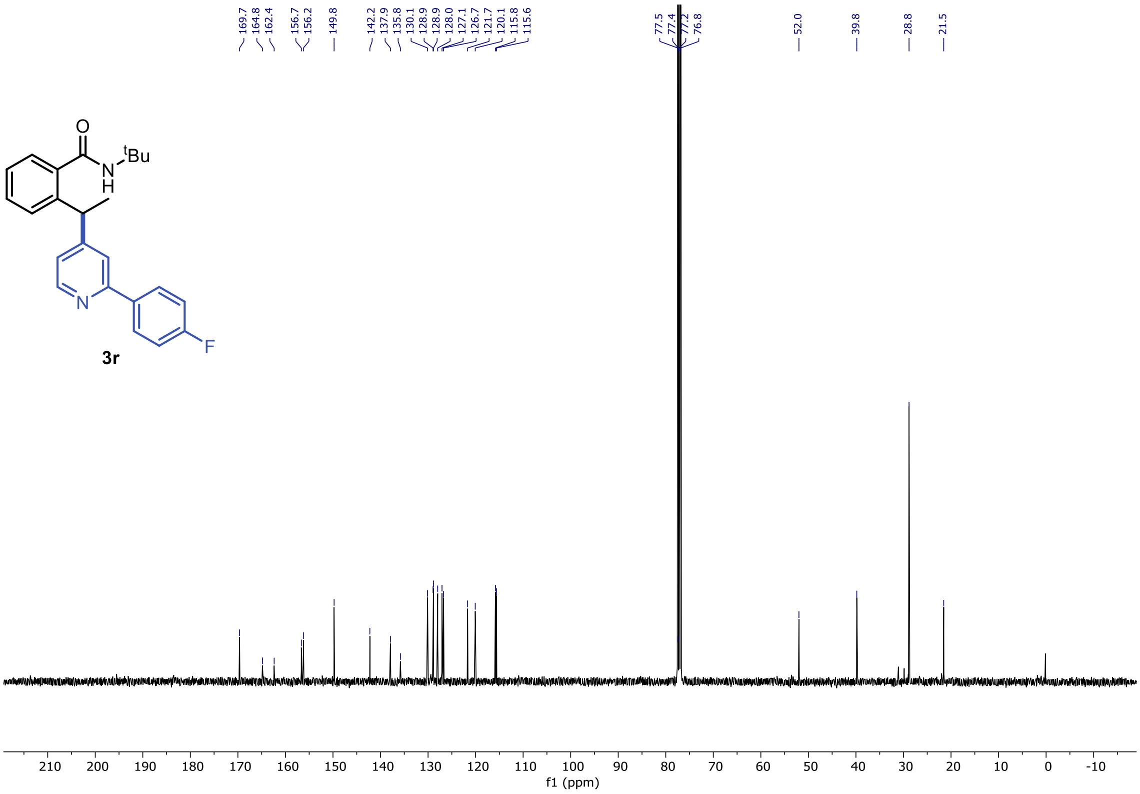
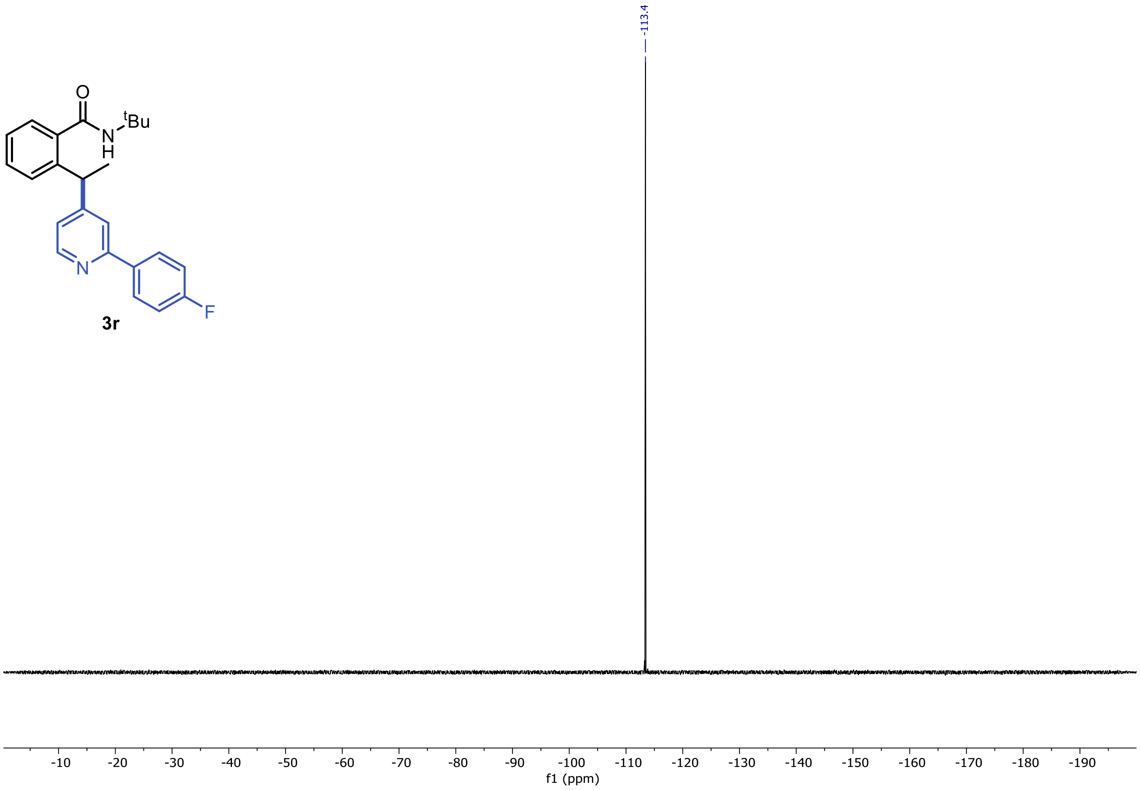
^{13}C NMR (101 MHz, CDCl$_3$)



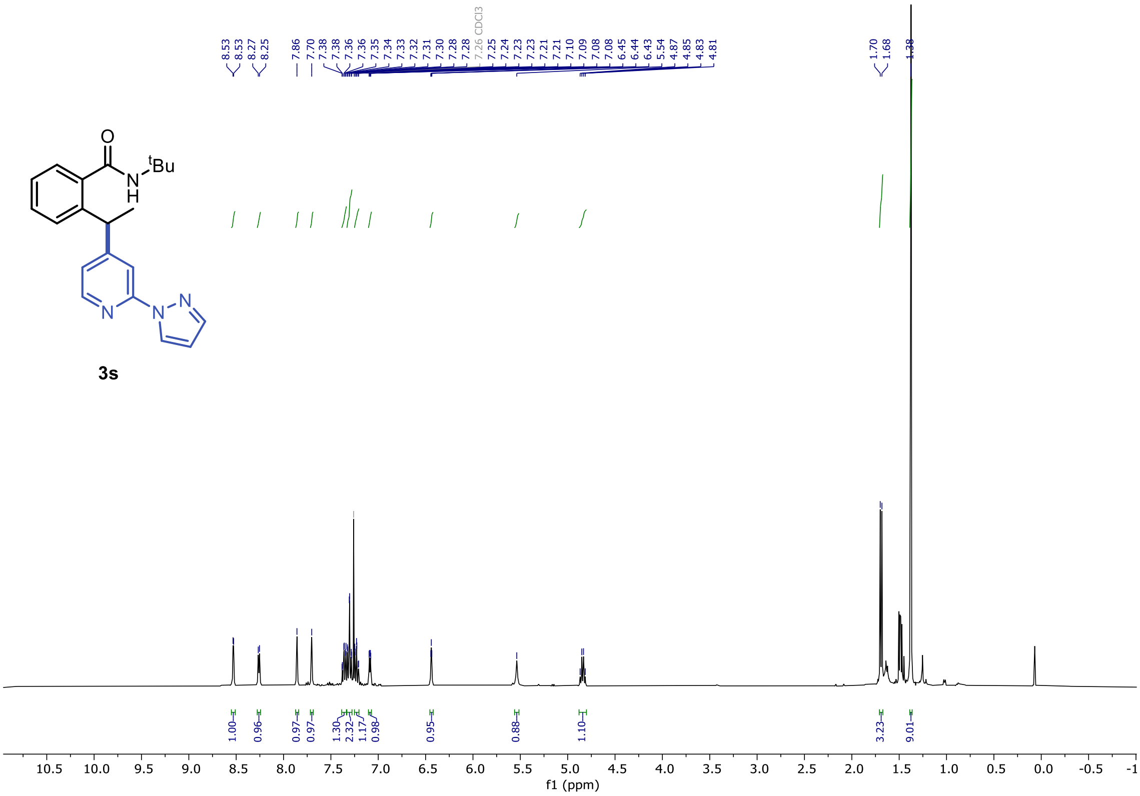
3r

$\underline{^{19}\text{F NMR}}$ (376 MHz, $CDCl_3$)

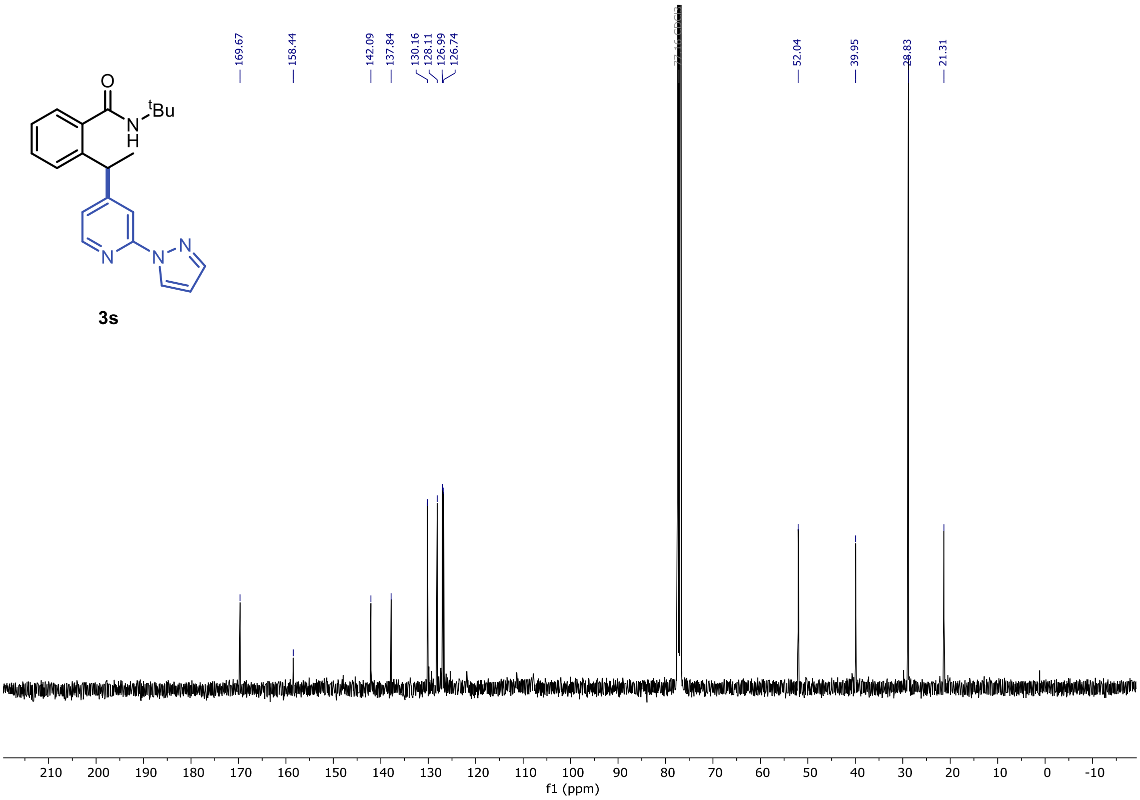
3r



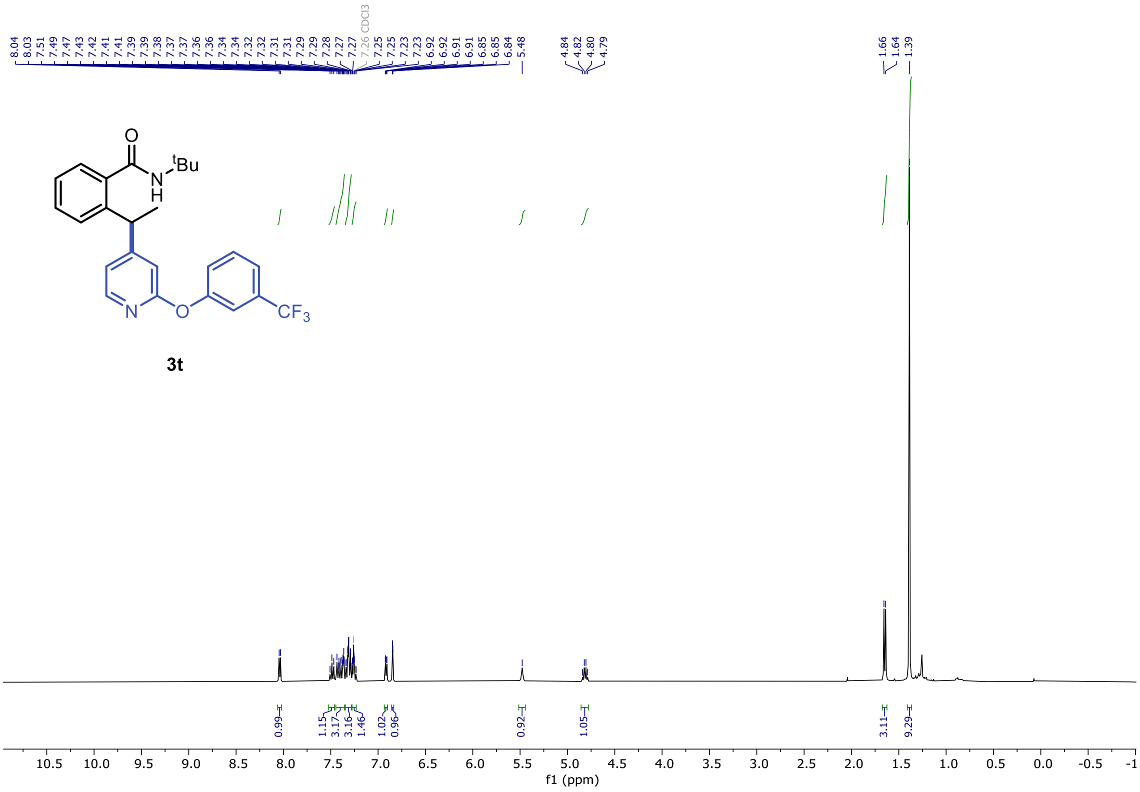
^{1}H NMR (400 MHz, $CDCl_3$)



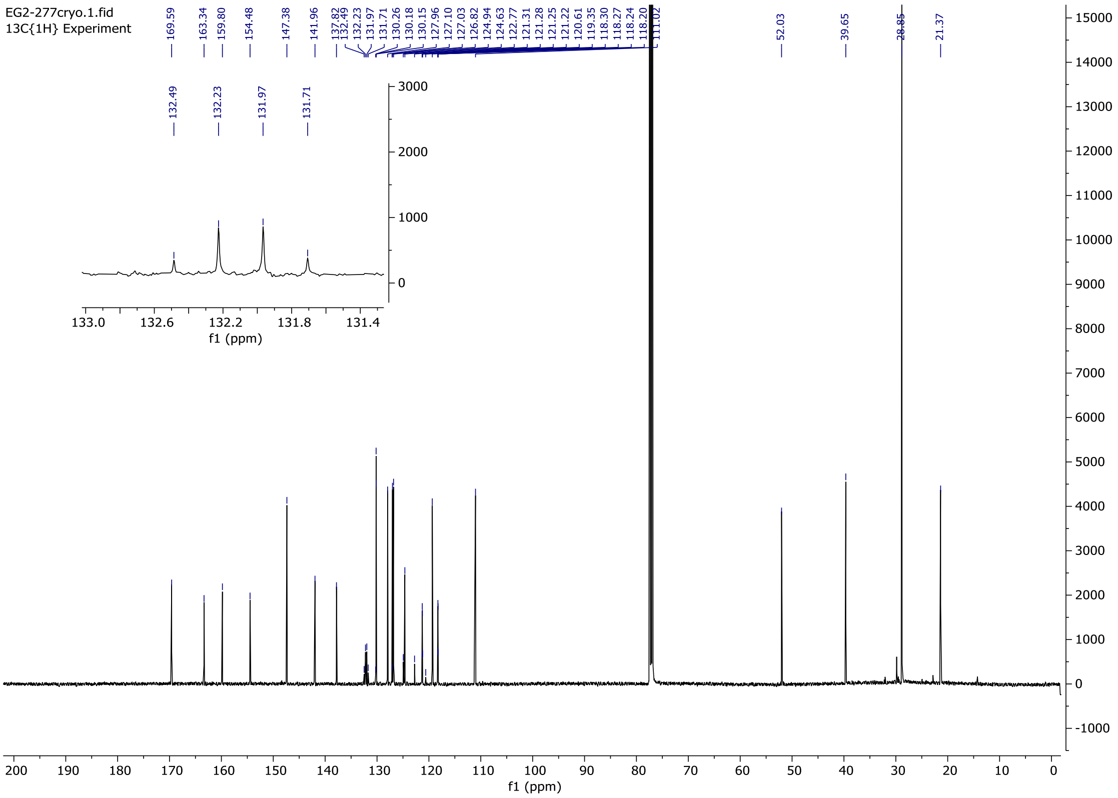
^{13}C NMR (101 MHz, $CDCl_3$)



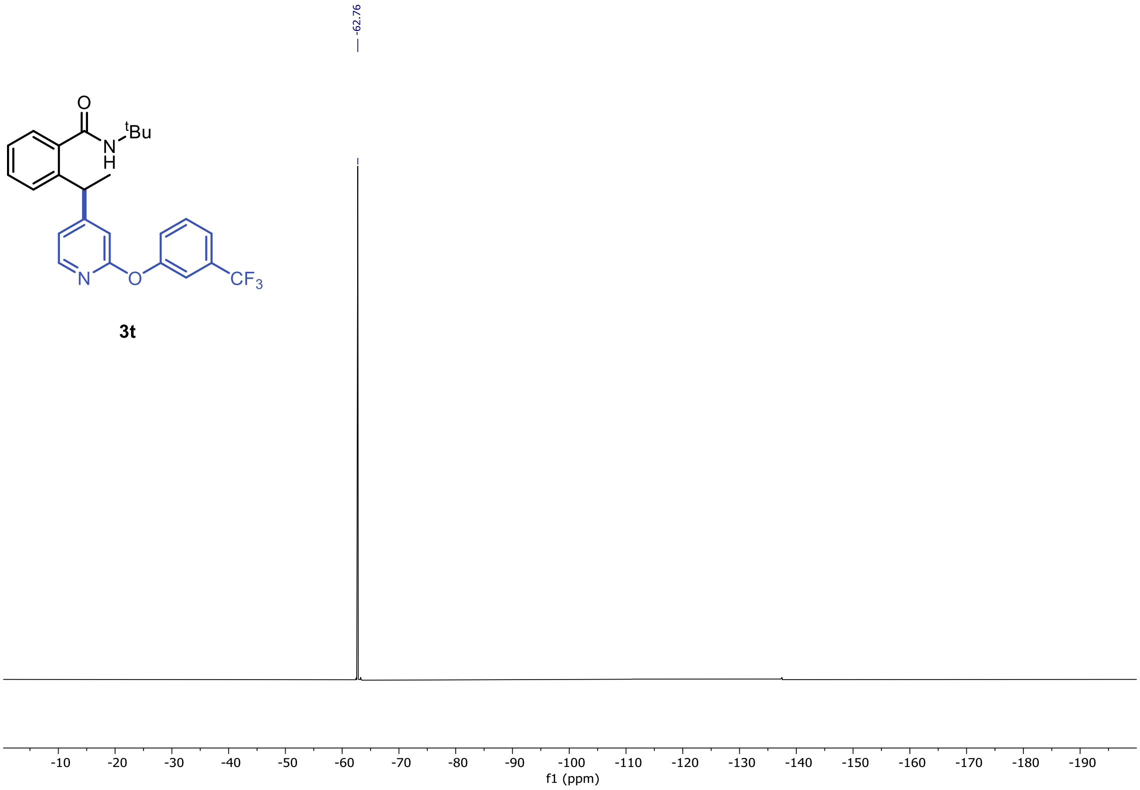
^{1}H NMR (400 MHz, $CDCl_3$)



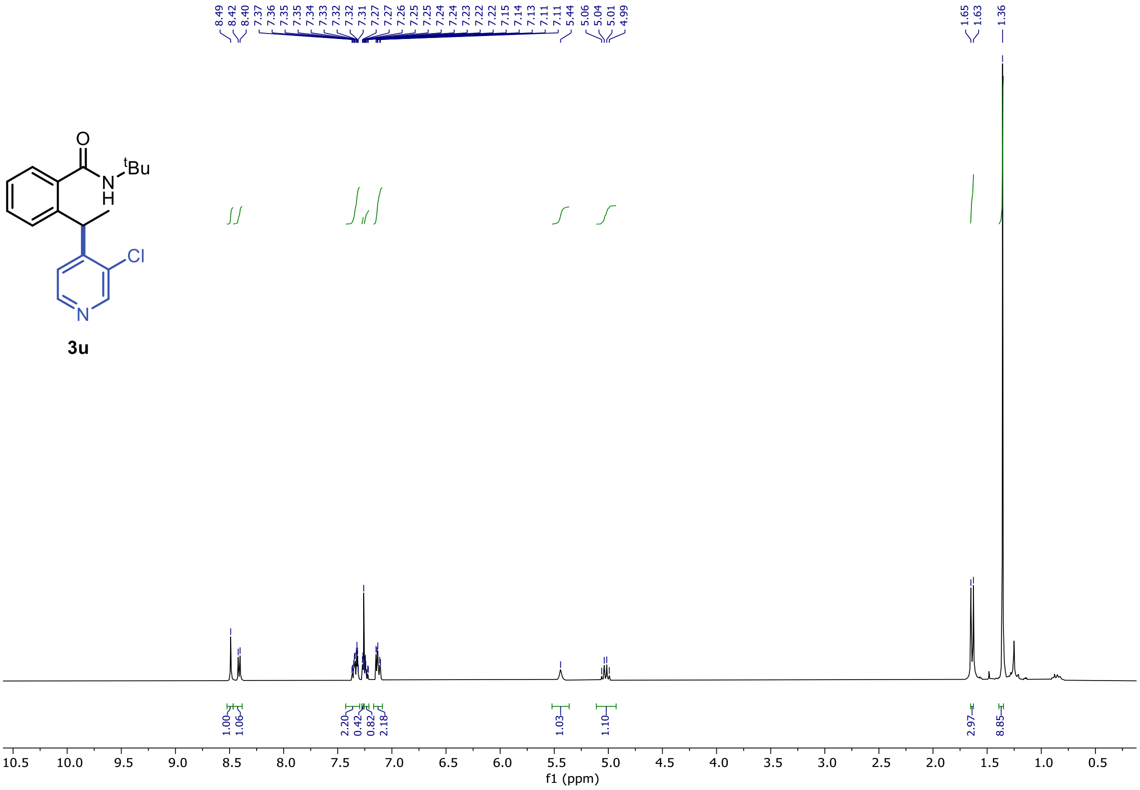
^{13}C NMR (126 MHz, cryoprobe, $CDCl_3$)



^{19}F NMR (376 MHz, CDCl$_3$)

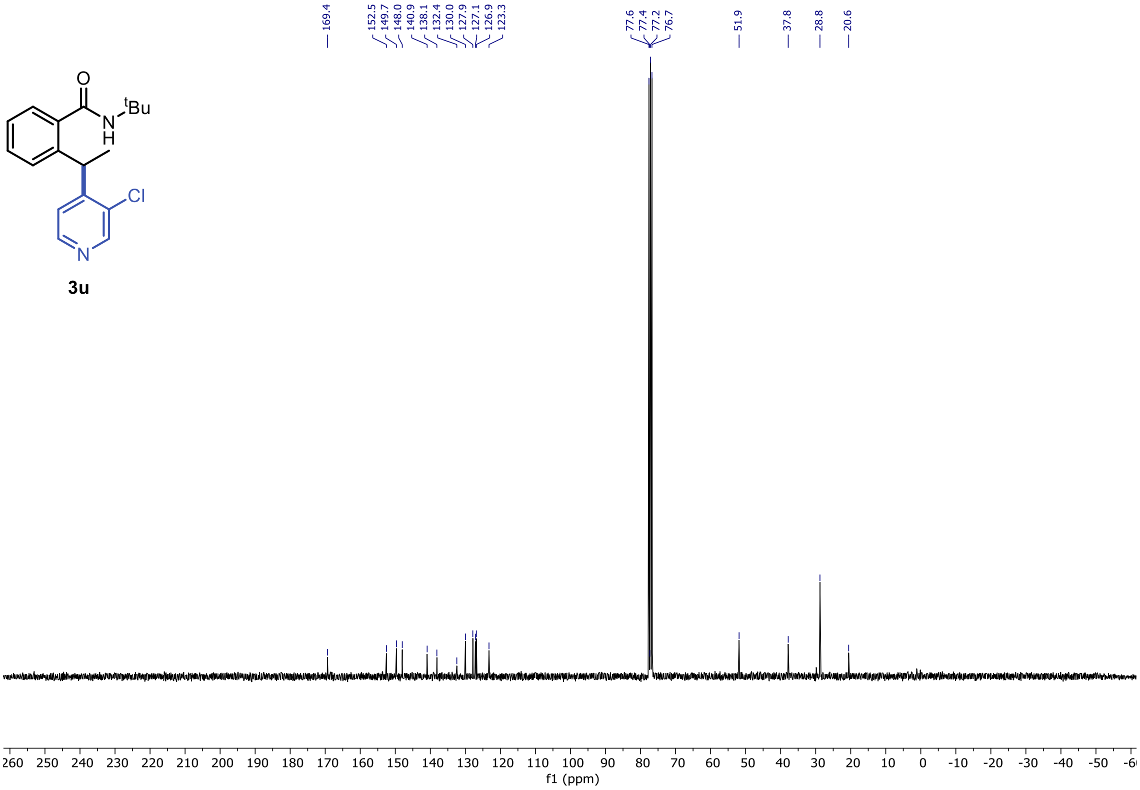


^{1}H NMR (300 MHz, CDCl$_3$)



3u

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



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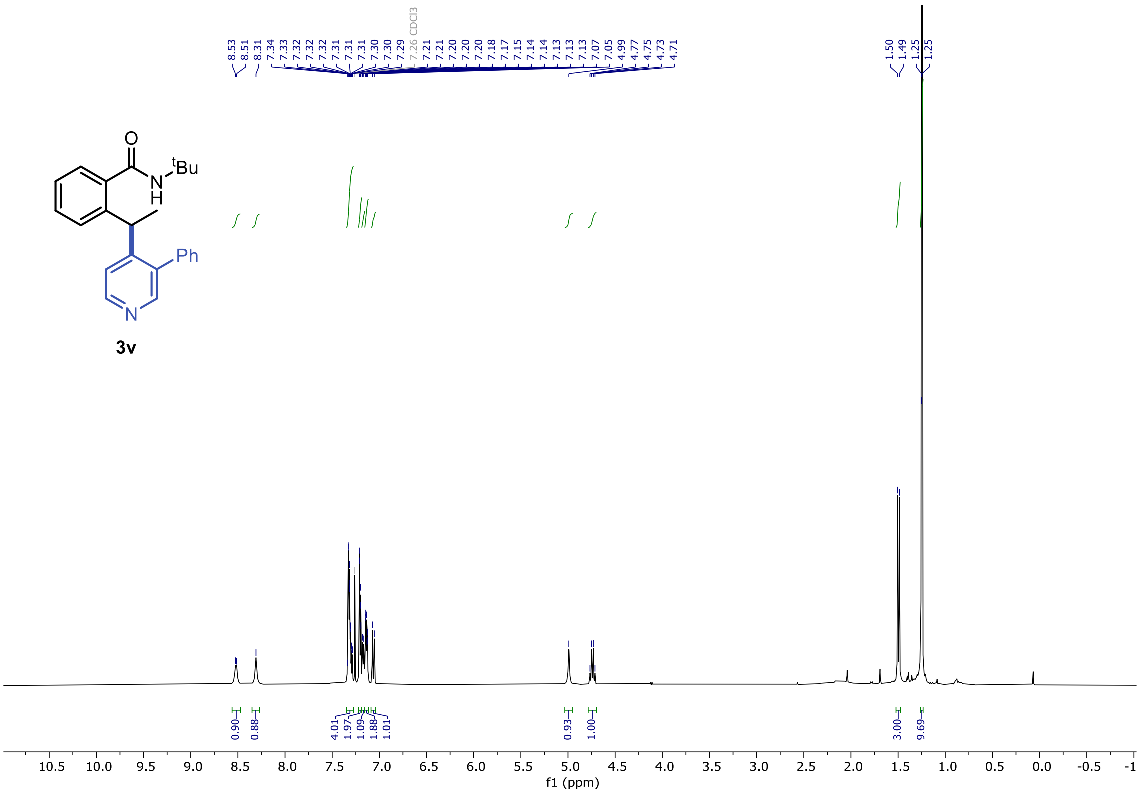
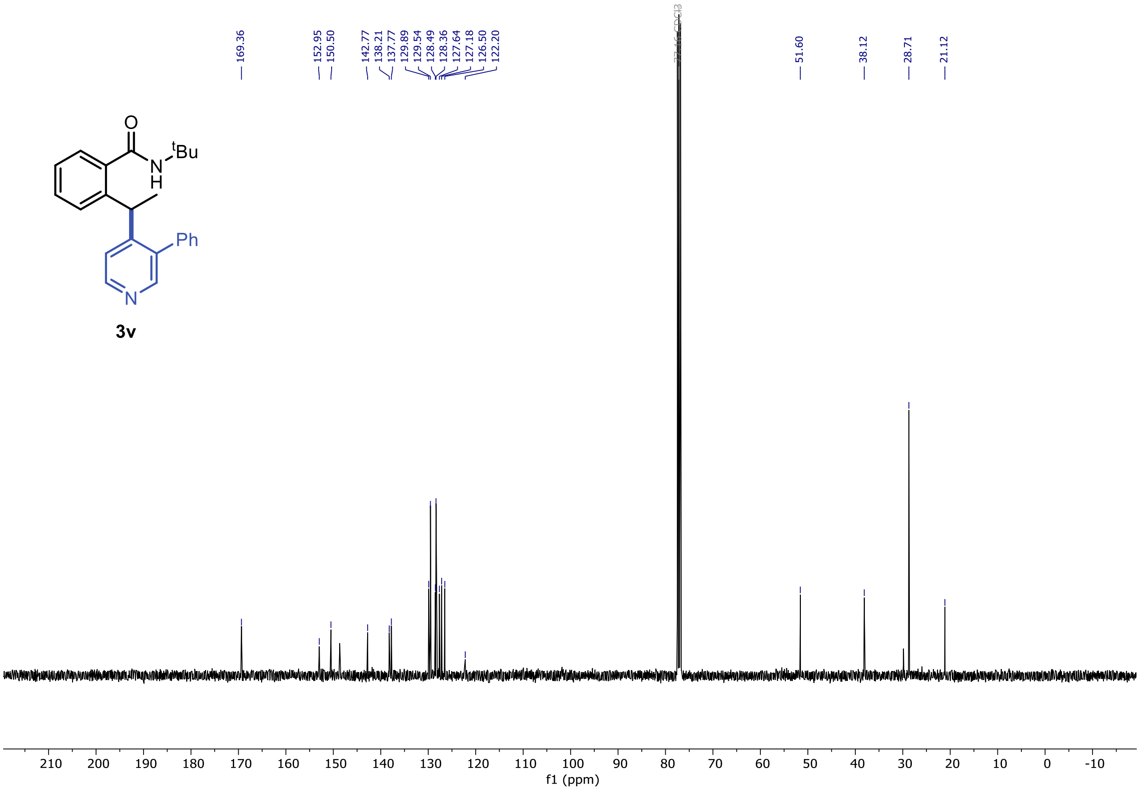
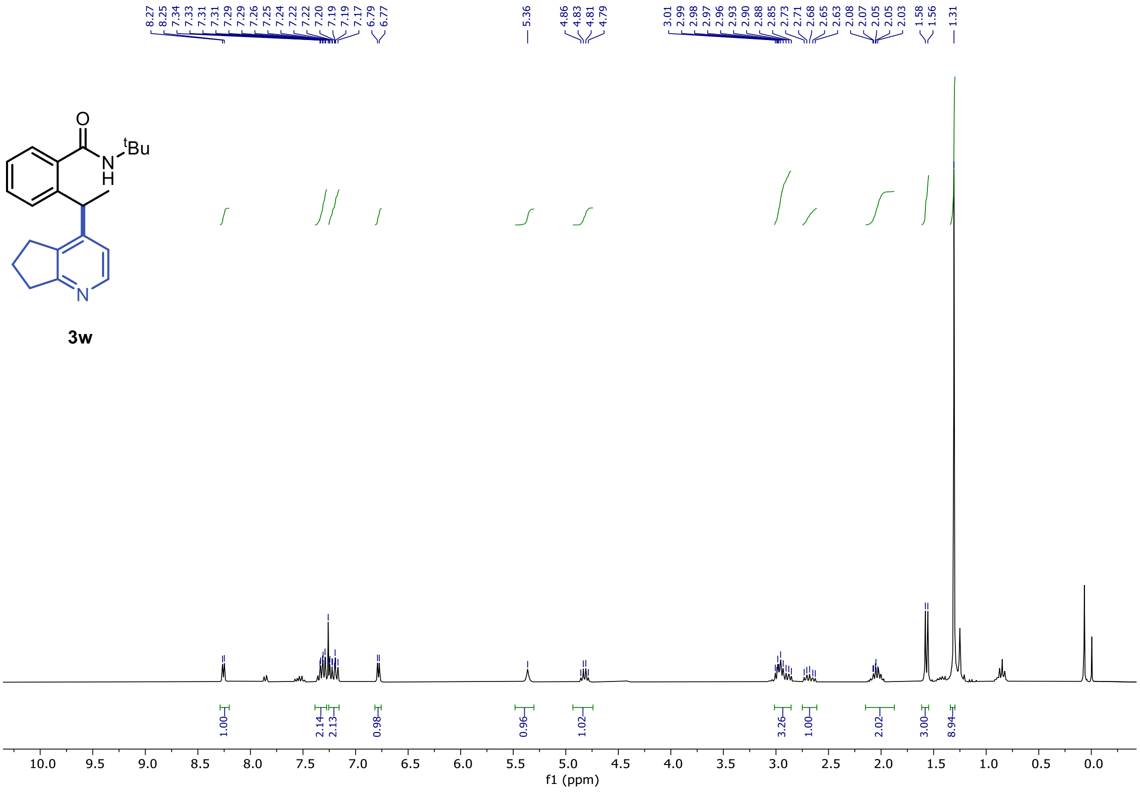
^{1}H NMR (400 MHz, CDCl$_3$)


3v

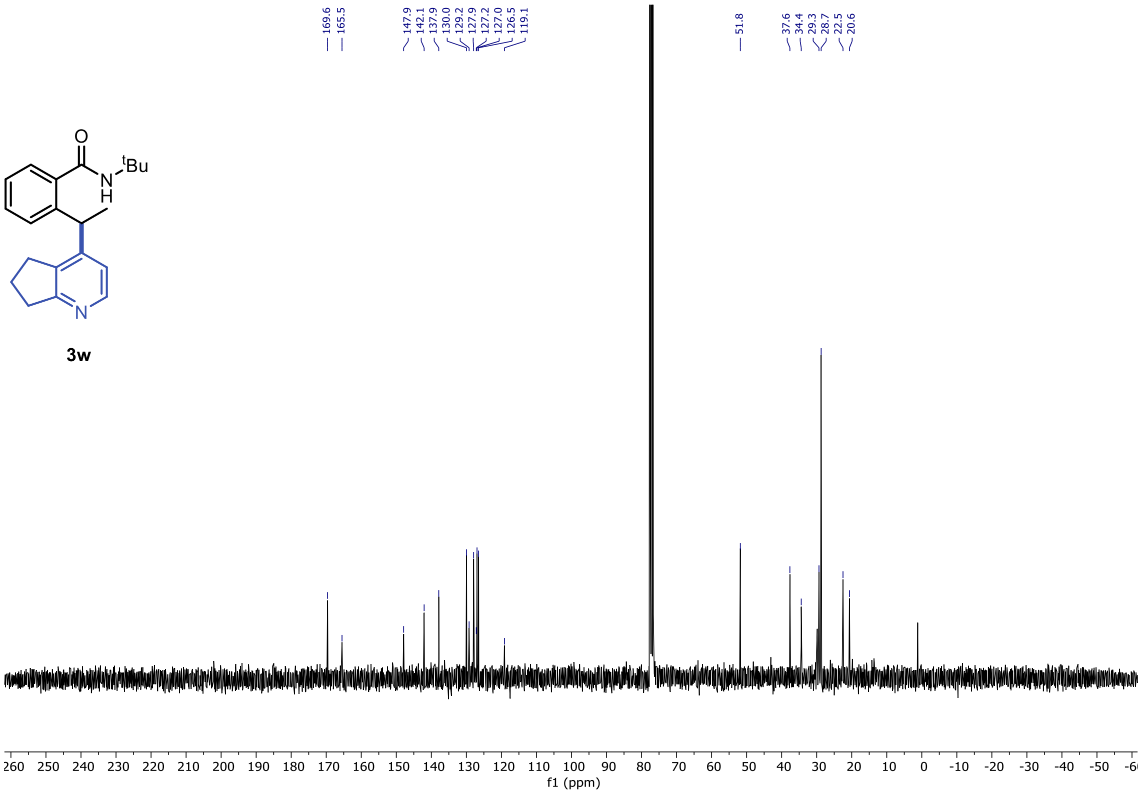
^{13}C NMR (101 MHz, CDCl$_3$)


3v

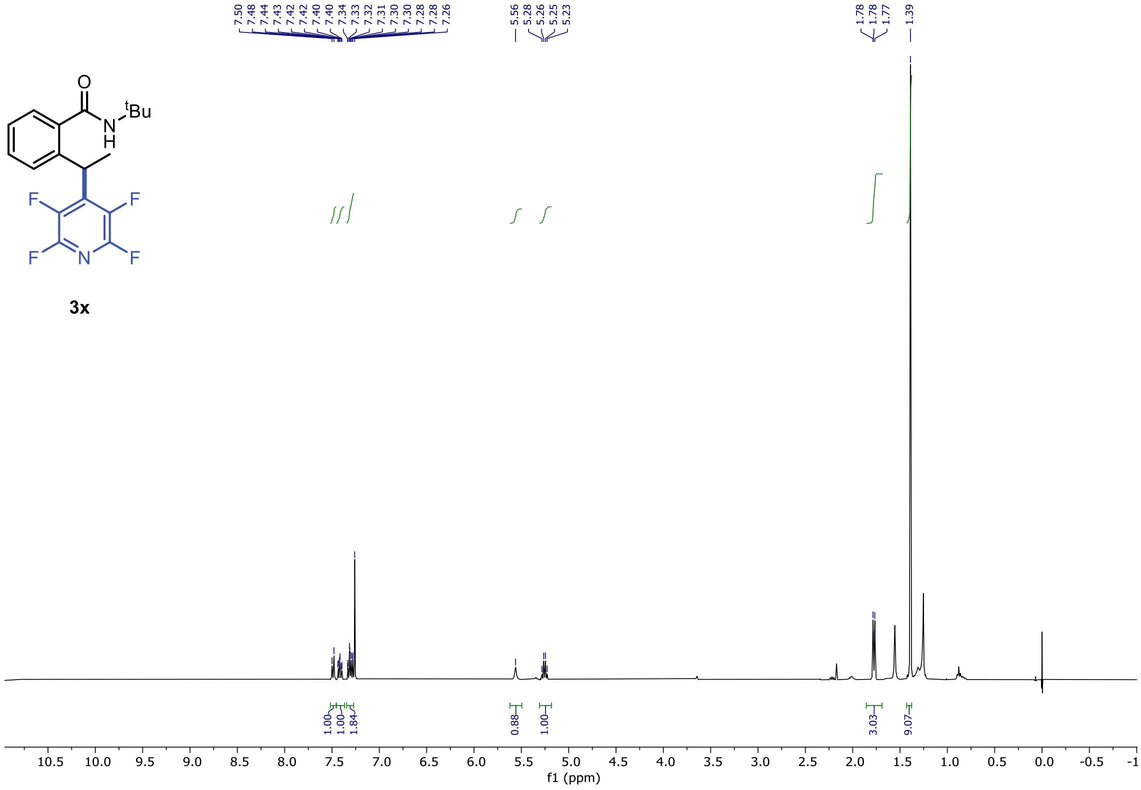
^{1}H NMR (300 MHz, CDCl$_3$)



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

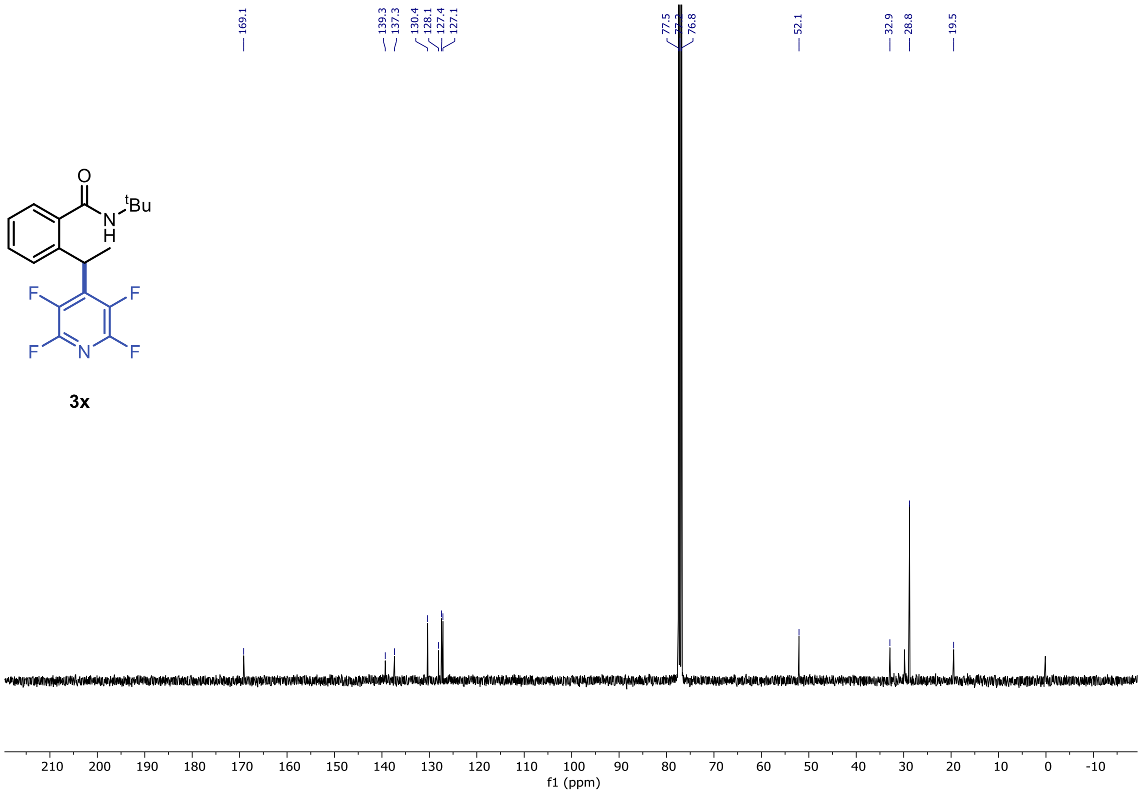


^{1}H NMR (300 MHz, $CDCl_3$)



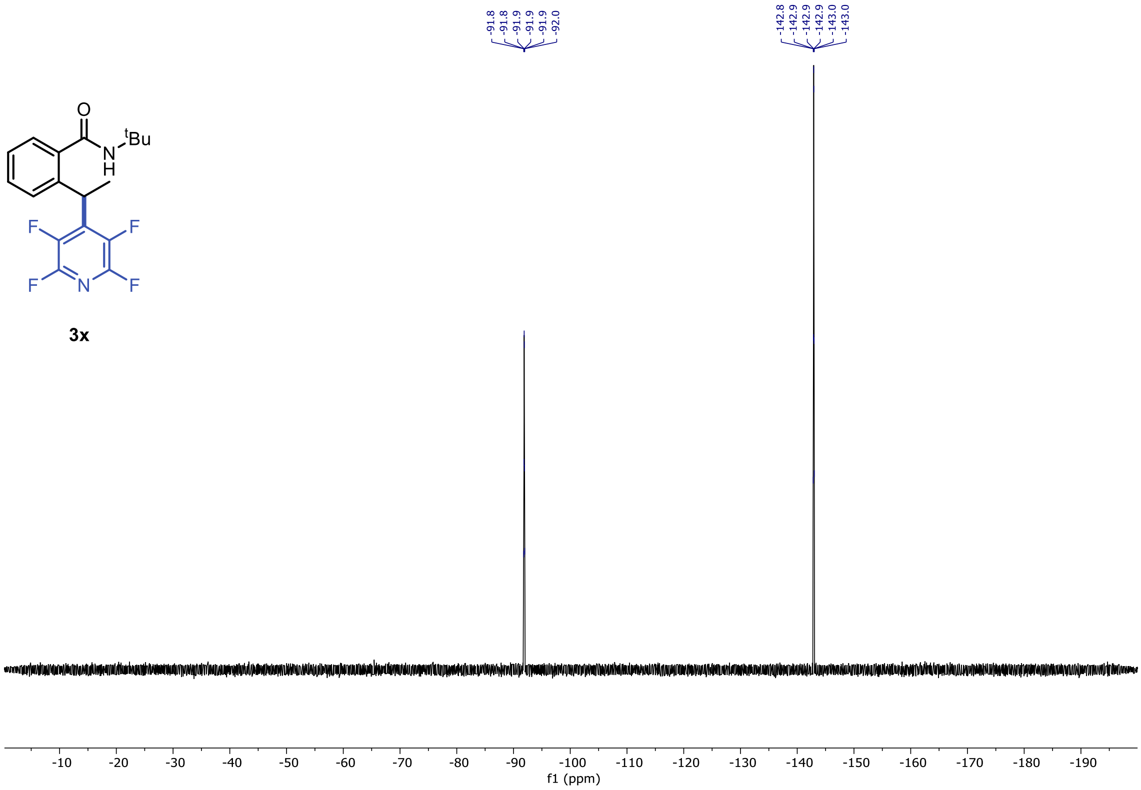
3x

^{13}C NMR (101 MHz, $CDCl_3$)



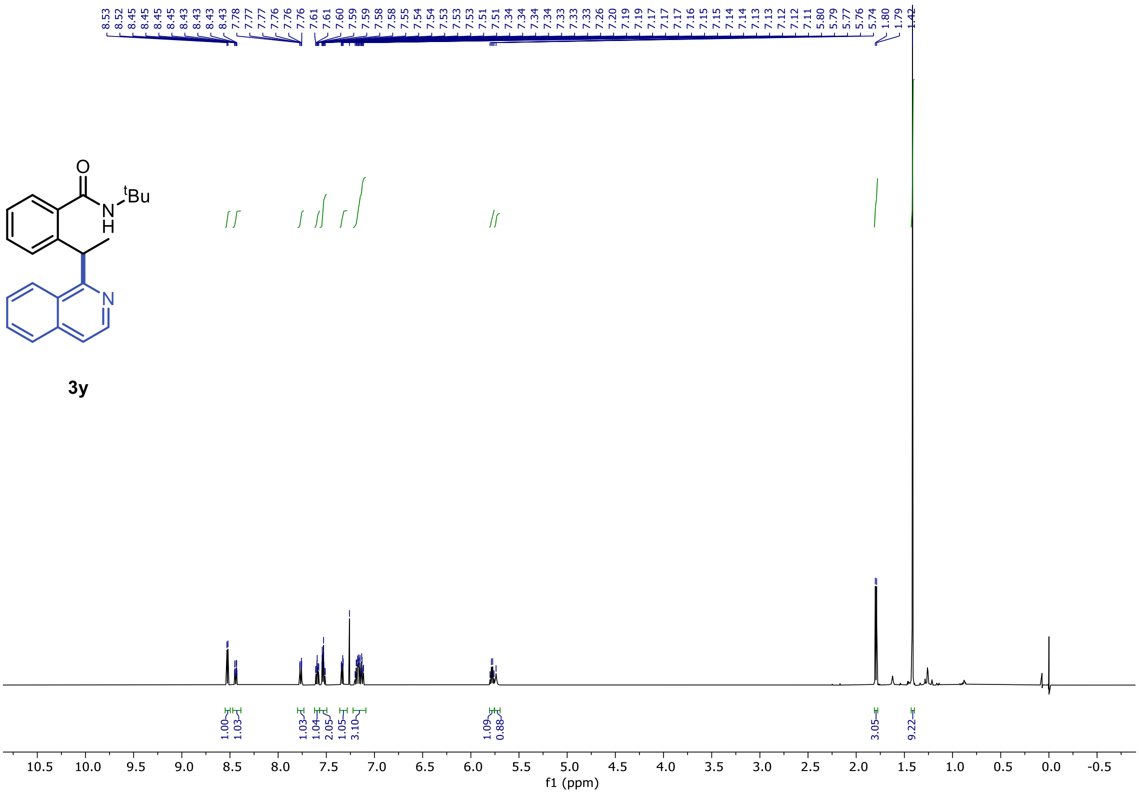
3x

^{19}F NMR (376 MHz, $CDCl_3$)



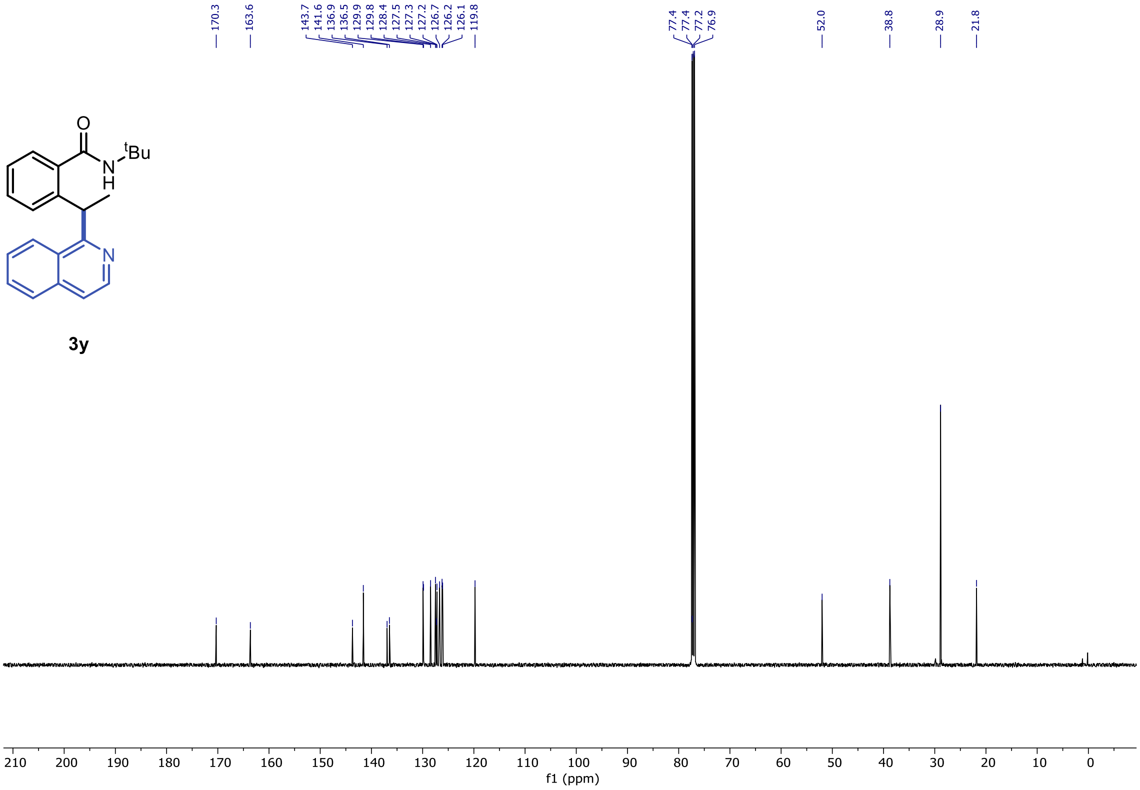
3x

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



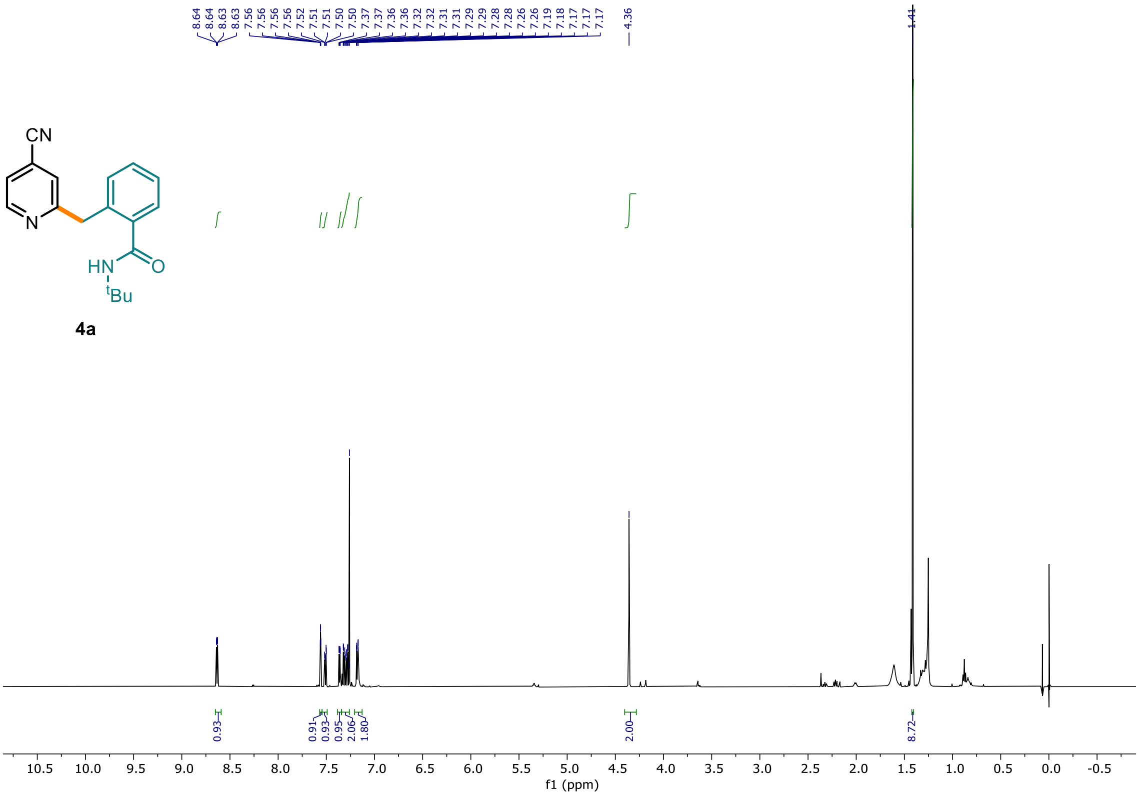
3y

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



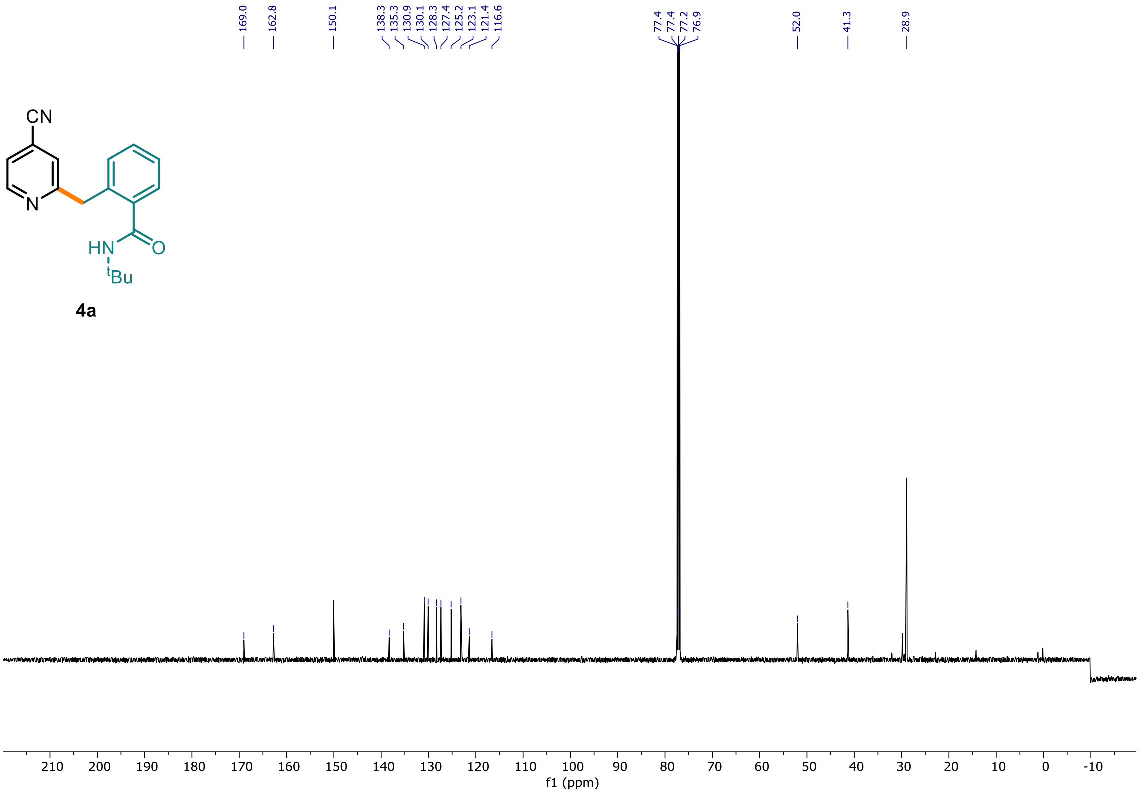
3y

^{1}H NMR (500 MHz, CDCl3)



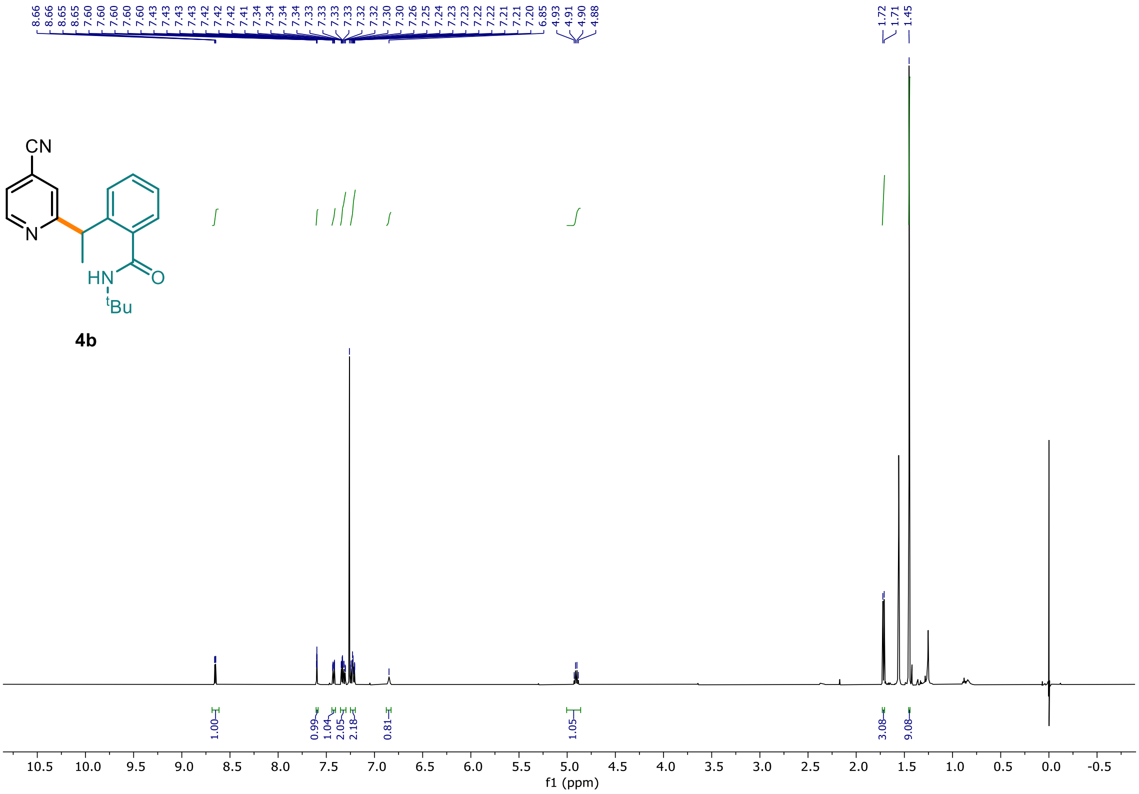
4a

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

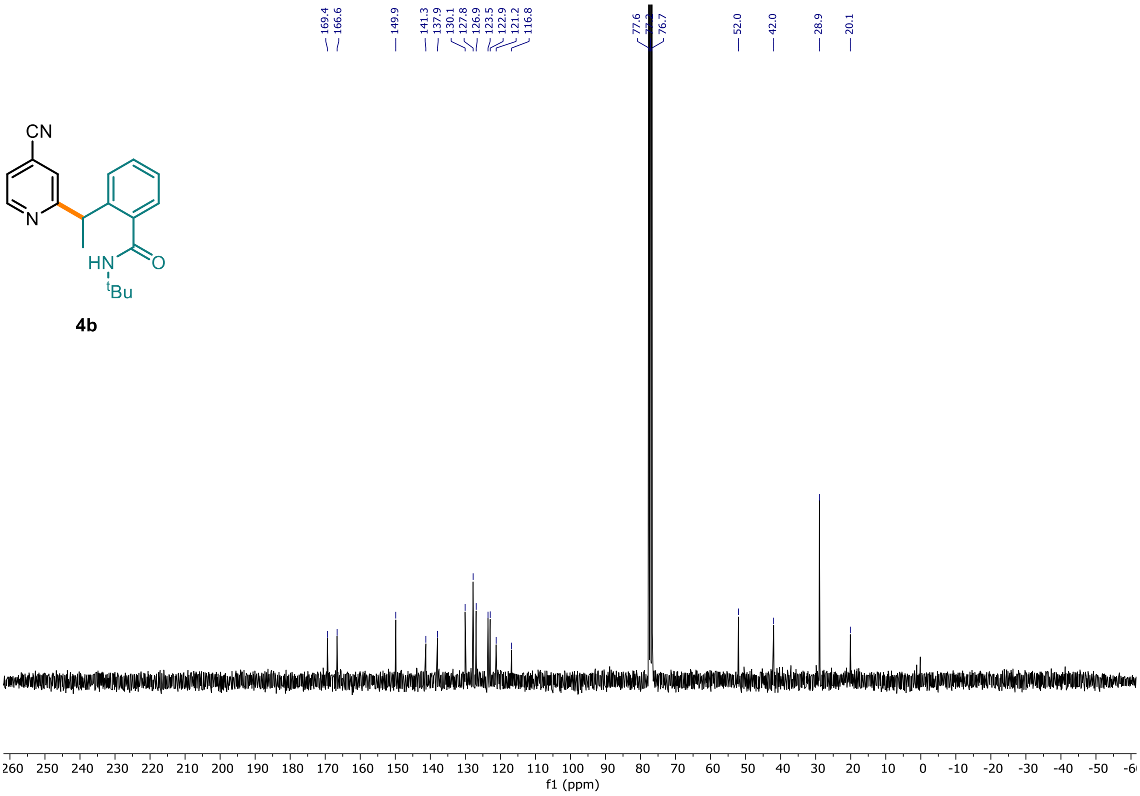


4a

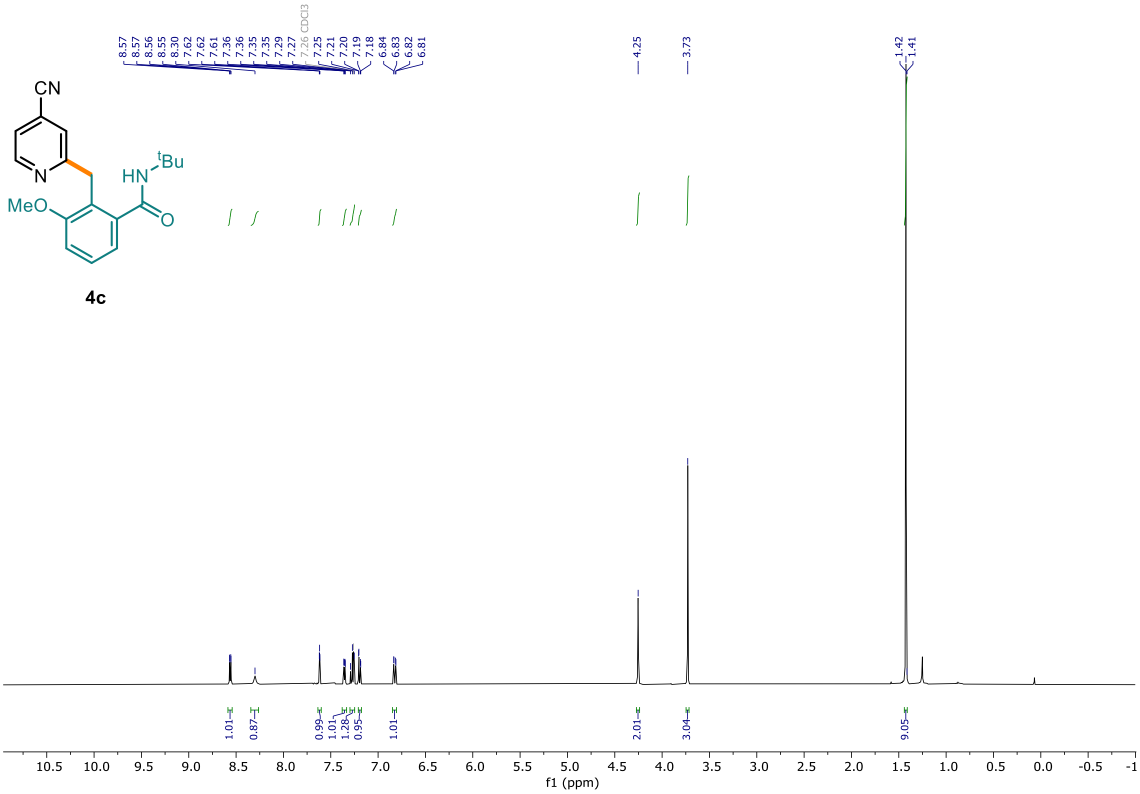
^{1}H NMR (500 MHz, CDCl$_3$)


4b

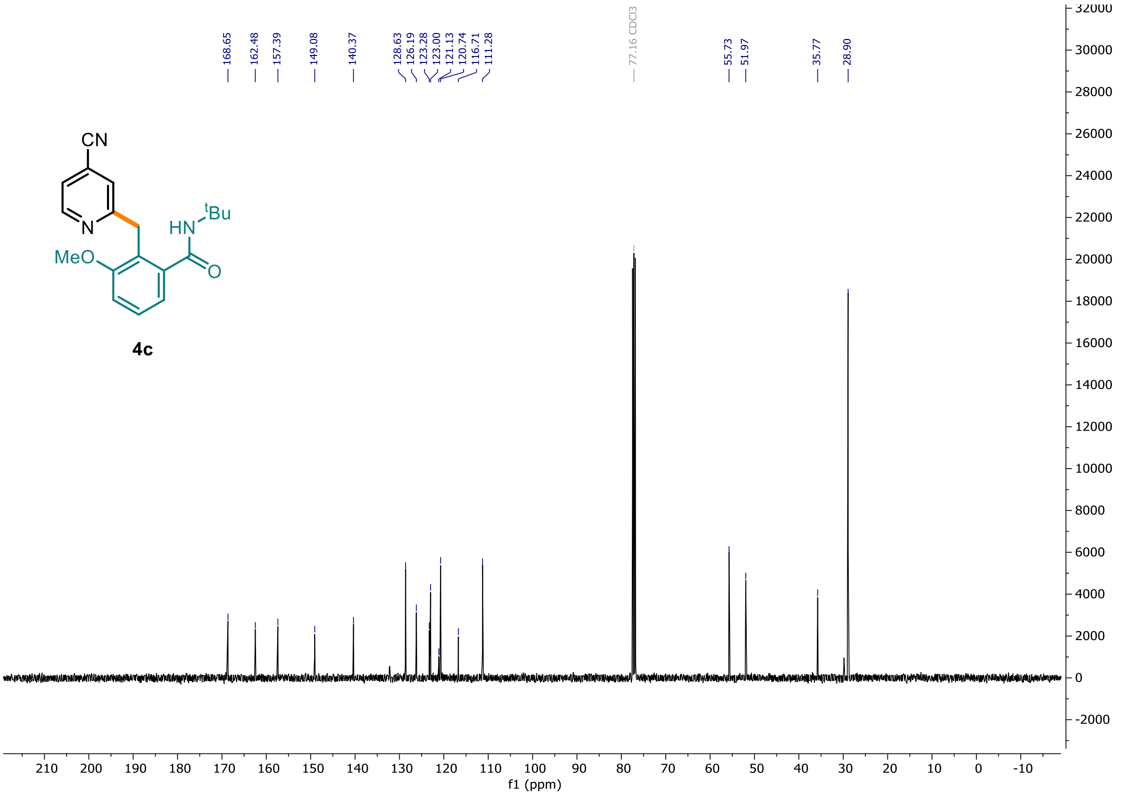
^{13}C NMR (75 MHz, CDCl$_3$)


4b

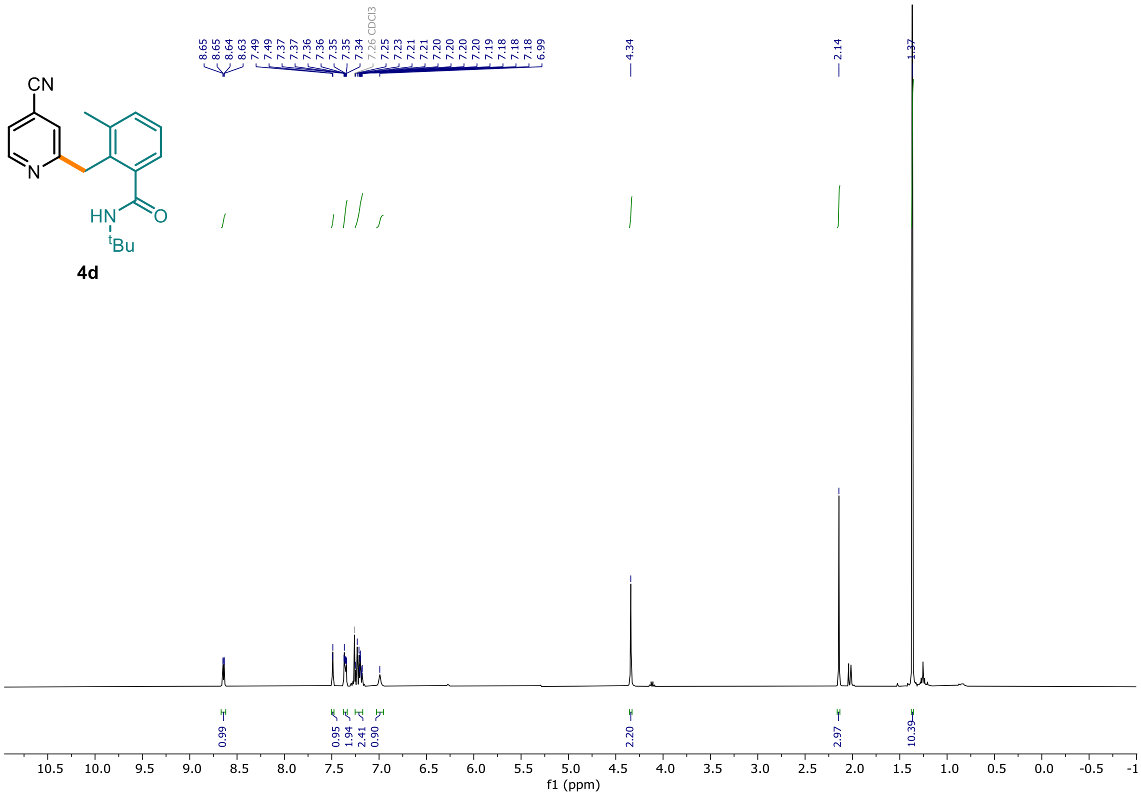
^{1}H NMR (400 MHz, CDCl$_3$)



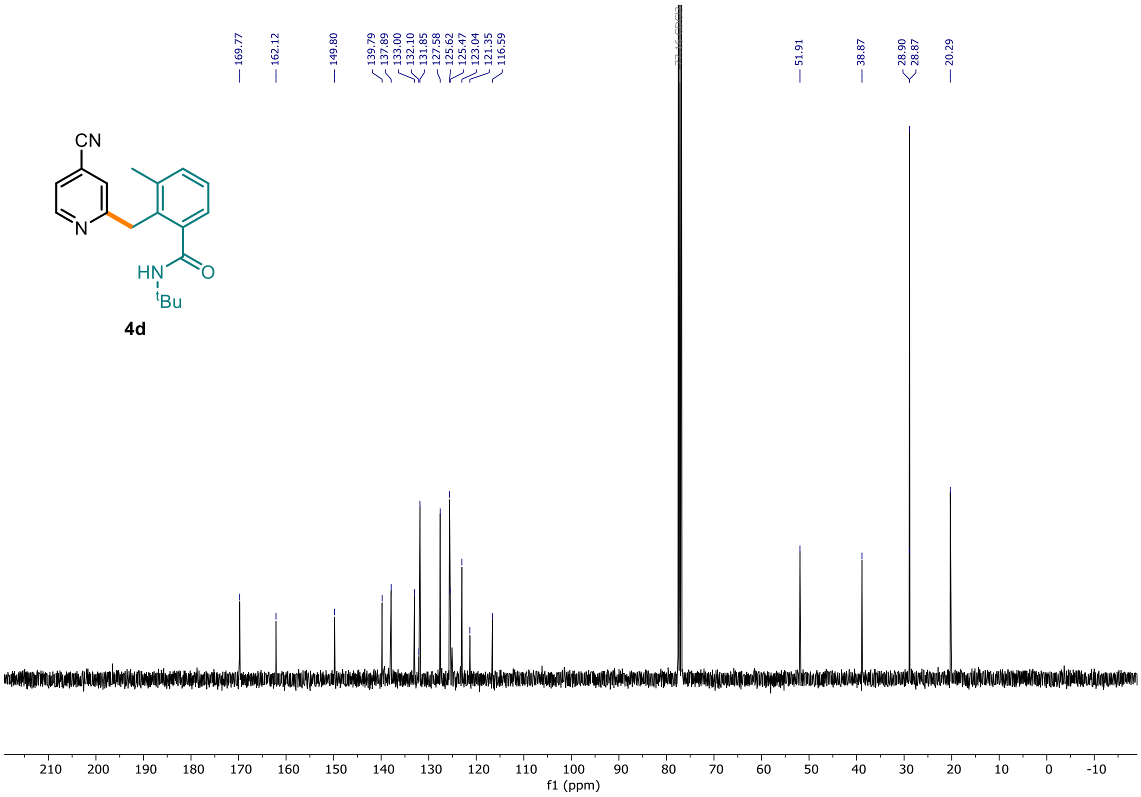
^{13}C NMR (101 MHz, CDCl$_3$)



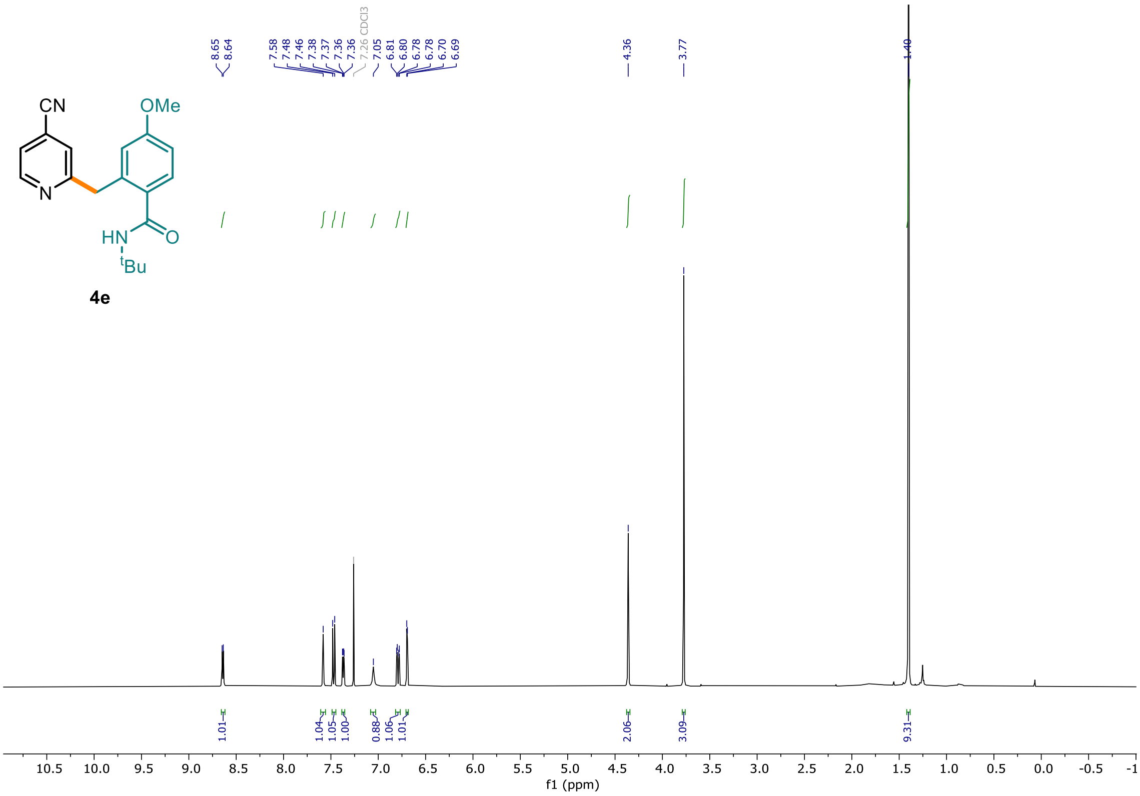
^{1}H NMR (400 MHz, CDCl$_3$)



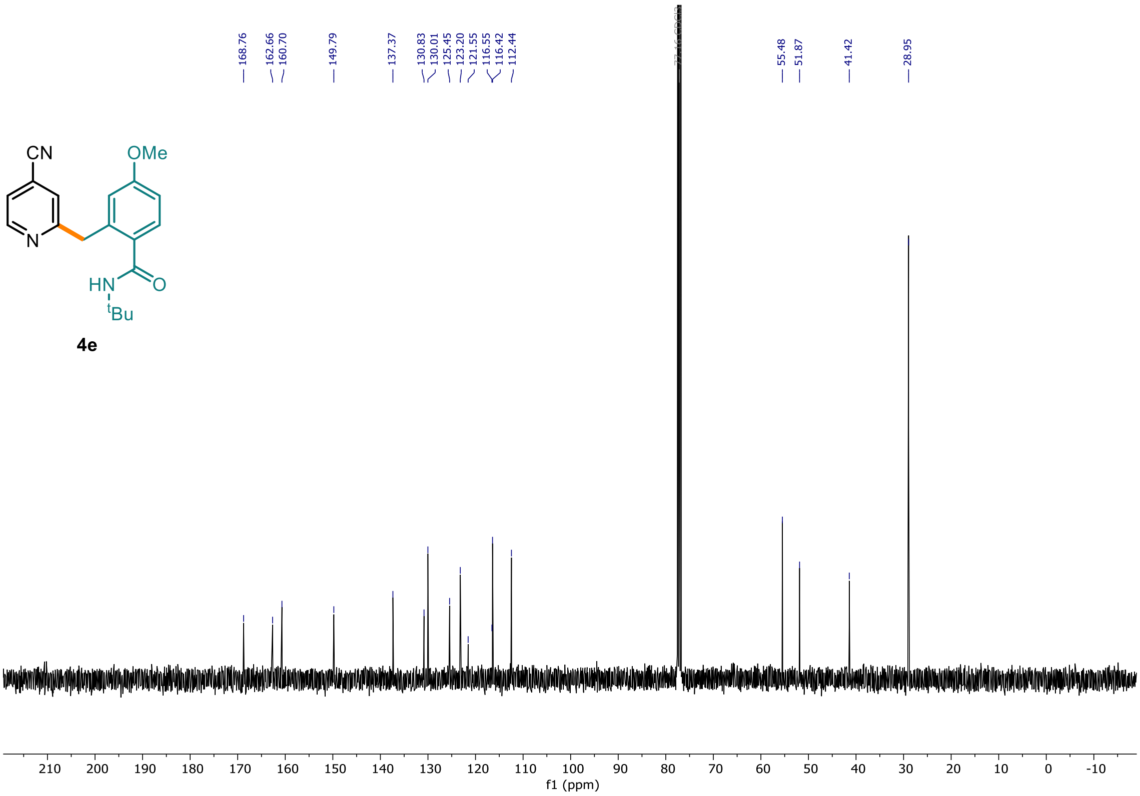
^{13}C NMR (101 MHz, CDCl$_3$)



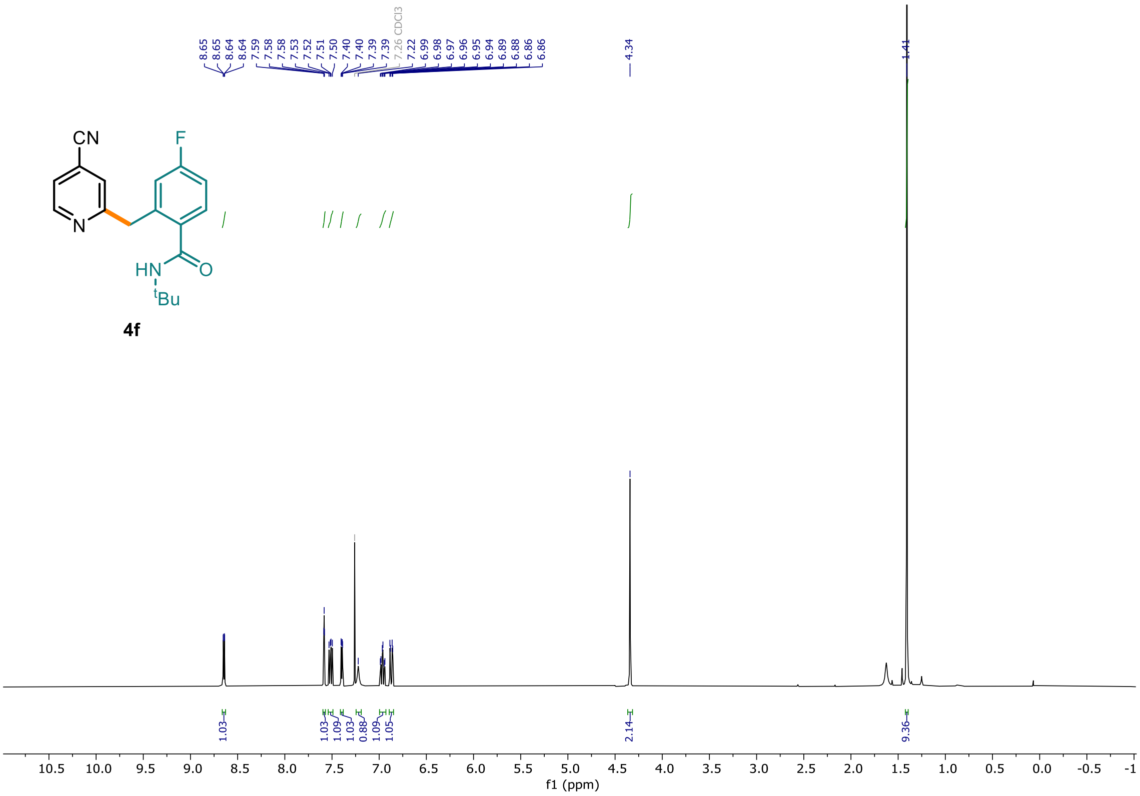
<u>^{1}H NMR</u> (400 MHz, $CDCl_3$)


4e

<u>^{13}C NMR</u> (101 MHz, $CDCl_3$)

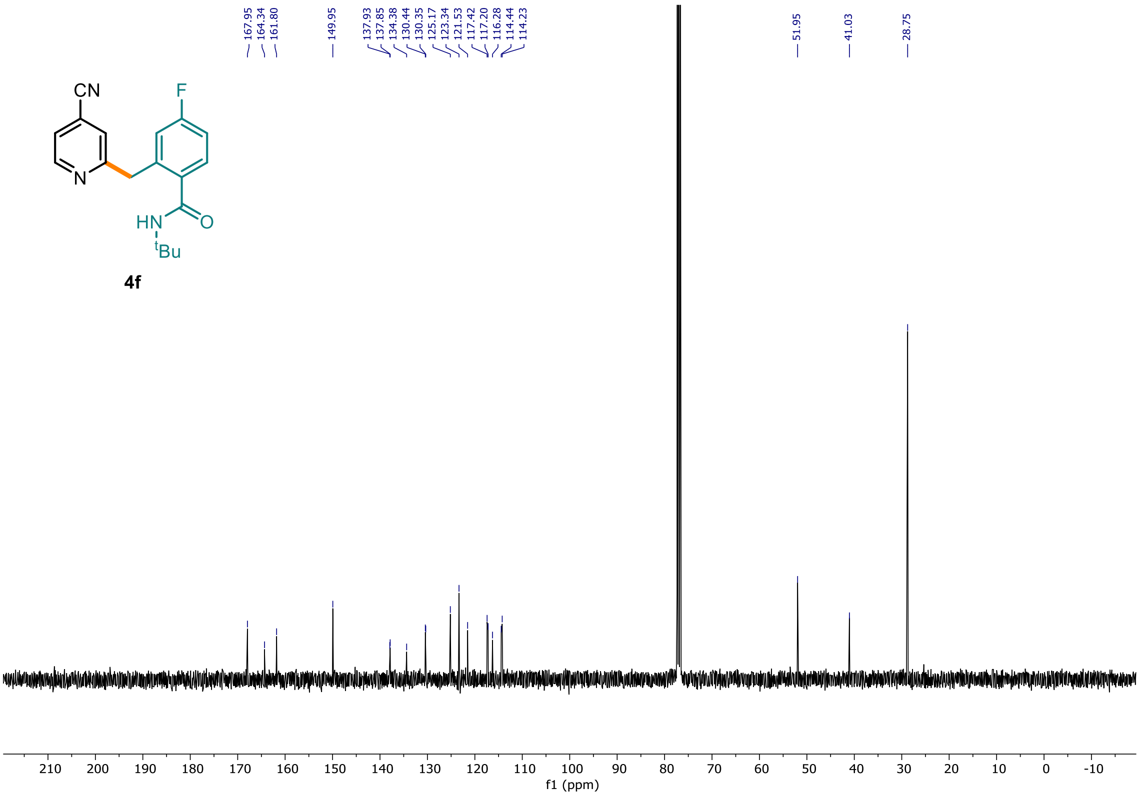

4e

^{1}H NMR (400 MHz, $CDCl_3$)

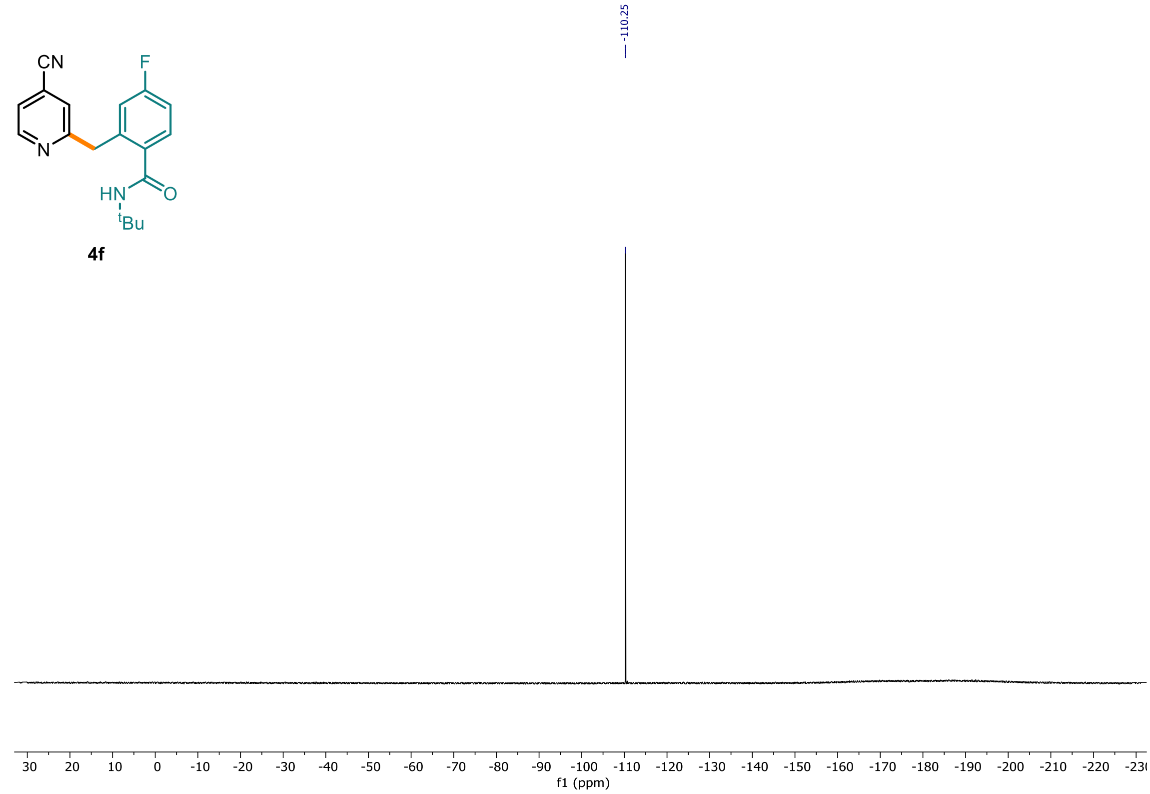


4f

^{13}C NMR (101 MHz, $CDCl_3$)



4f


CN
F
N
HN
O
tBu
-110.25
30
20
10
0
-10
-20
-30
-40
-50
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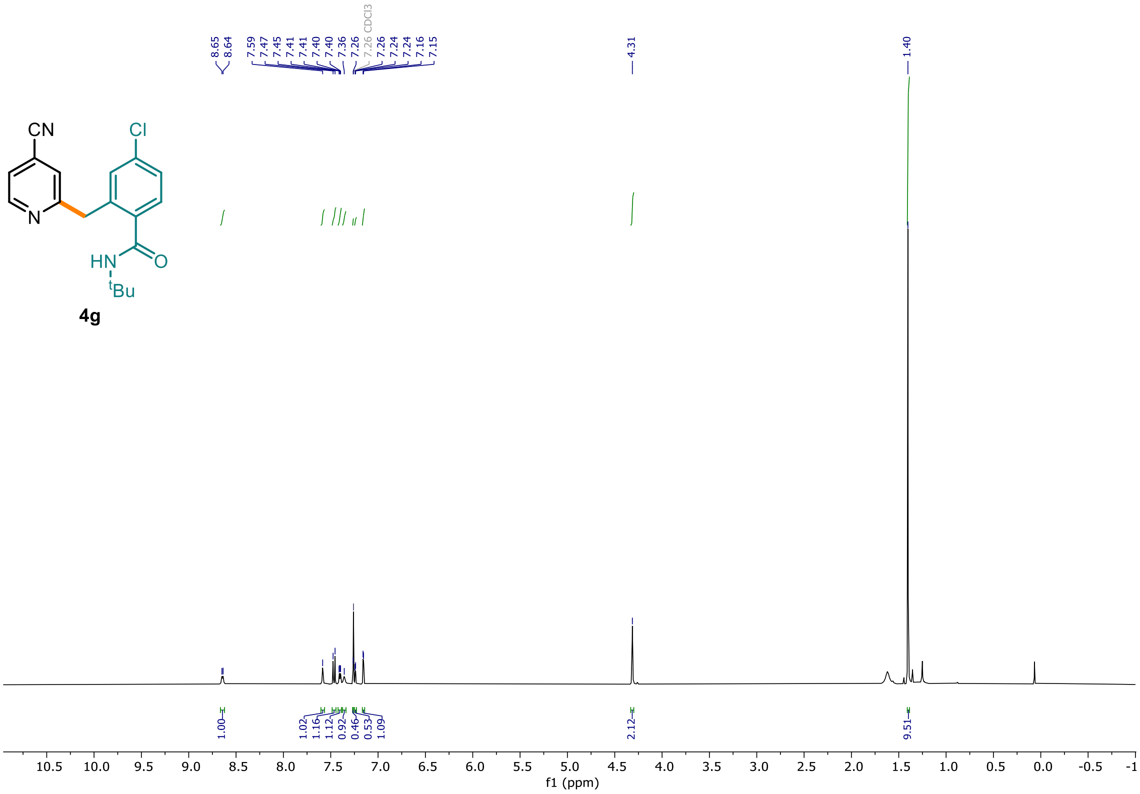
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
f1 (ppm)

4f

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



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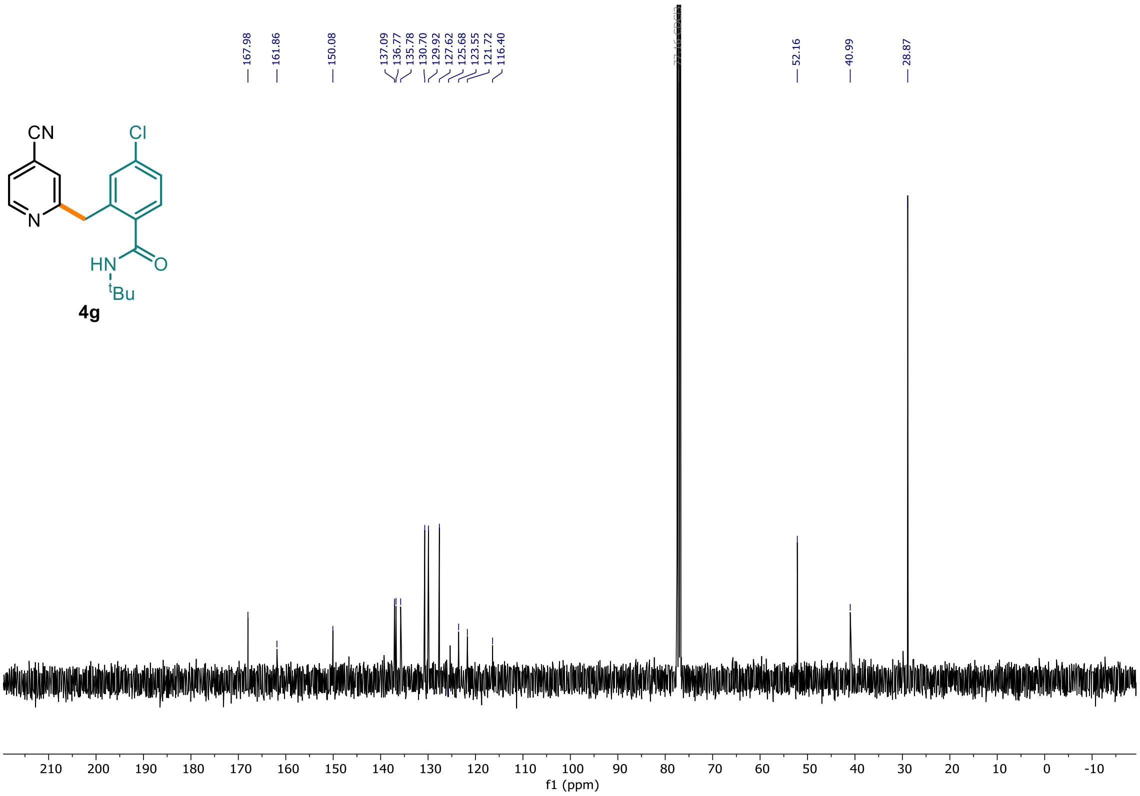

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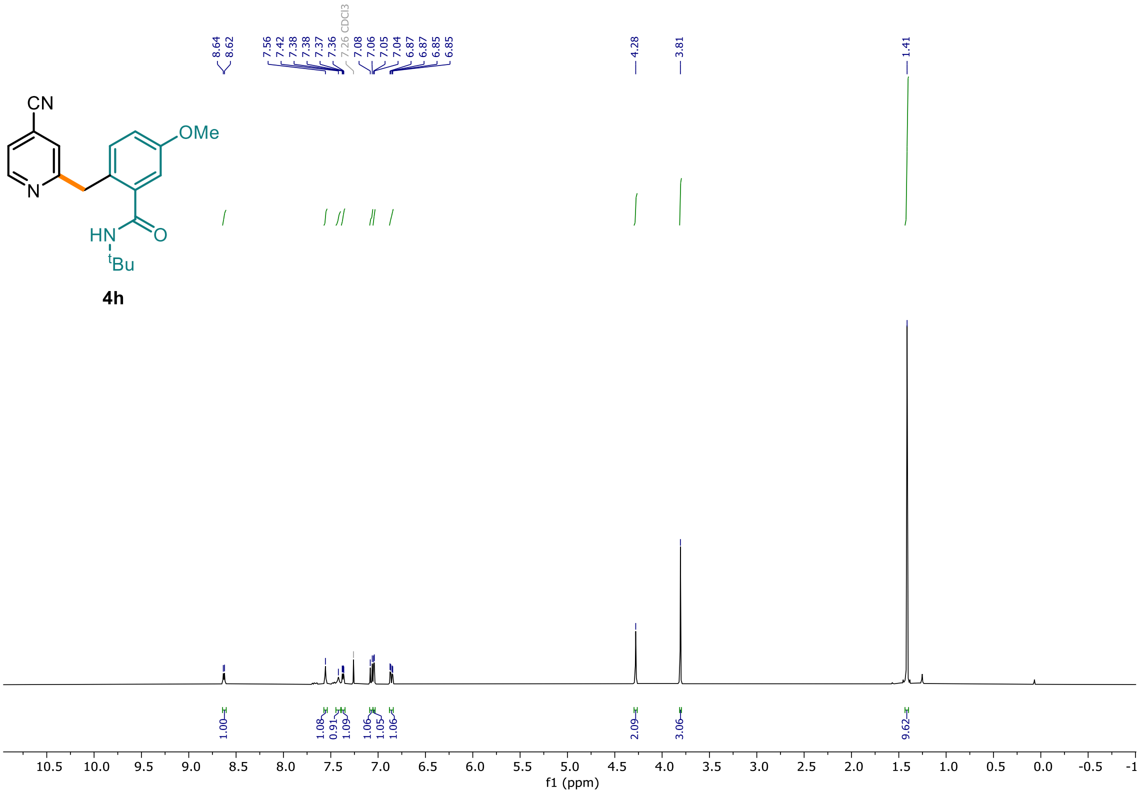
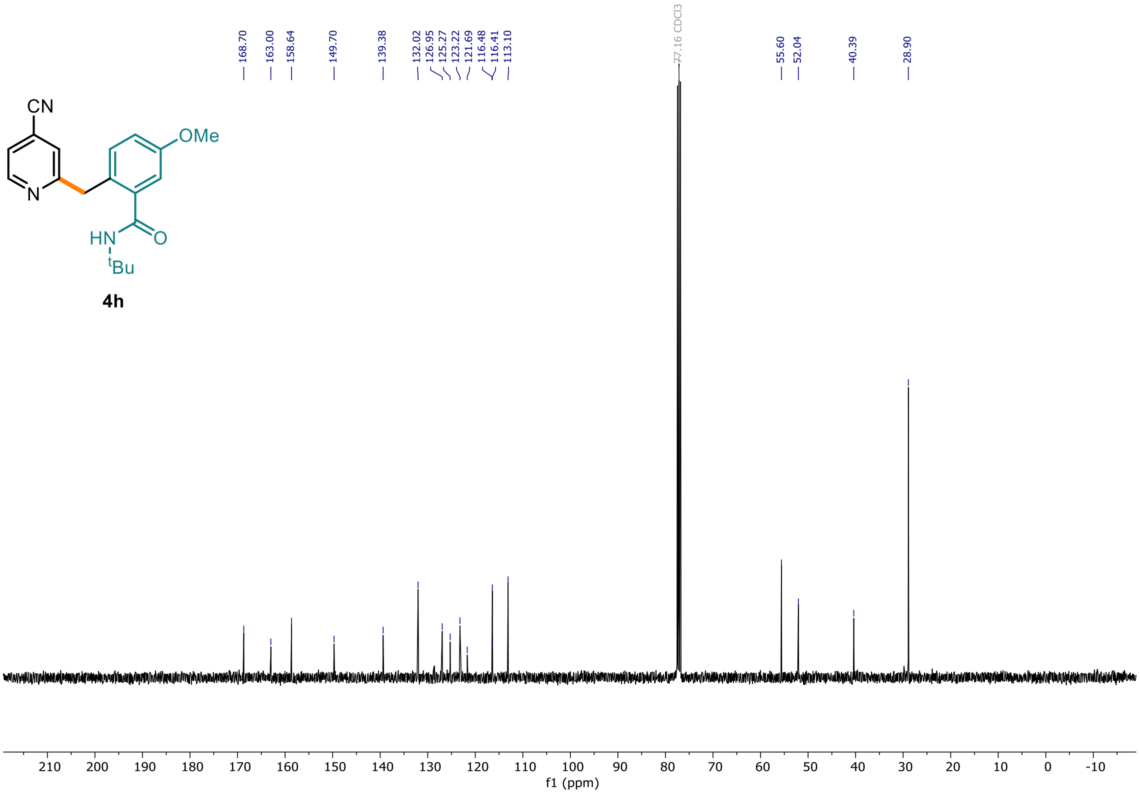
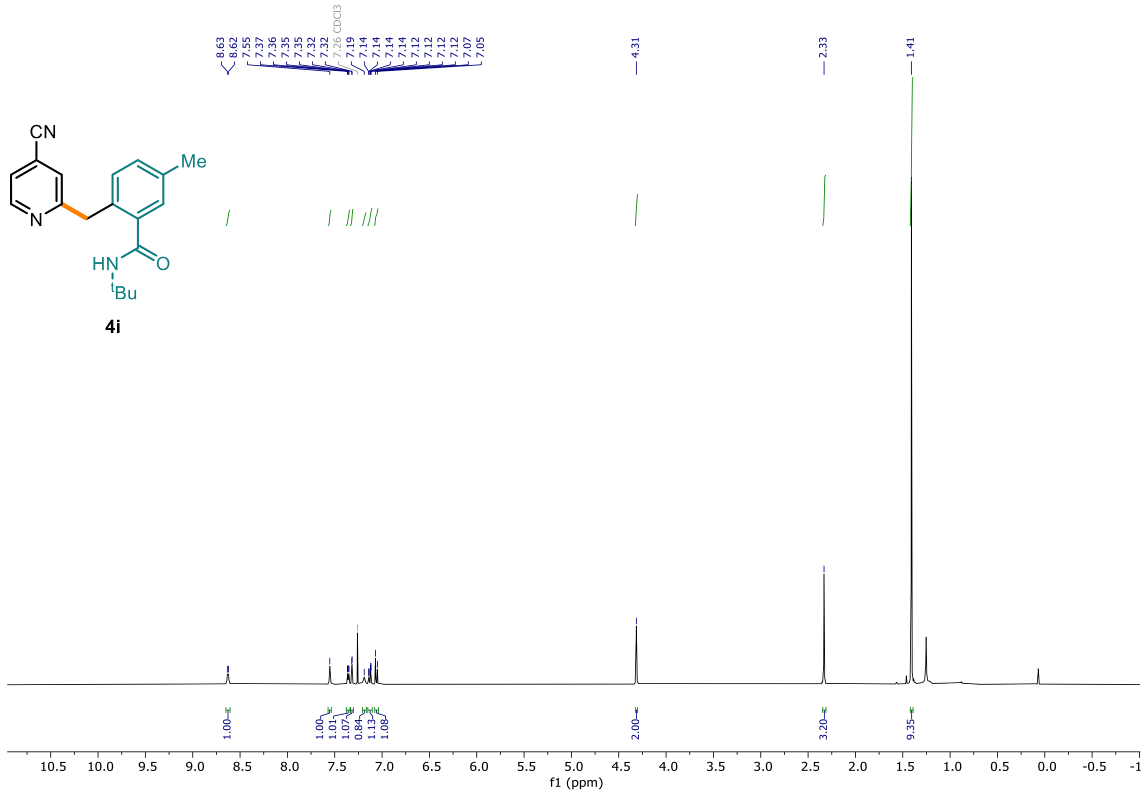


^{13}C NMR (101 MHz, CDCl$_3$)

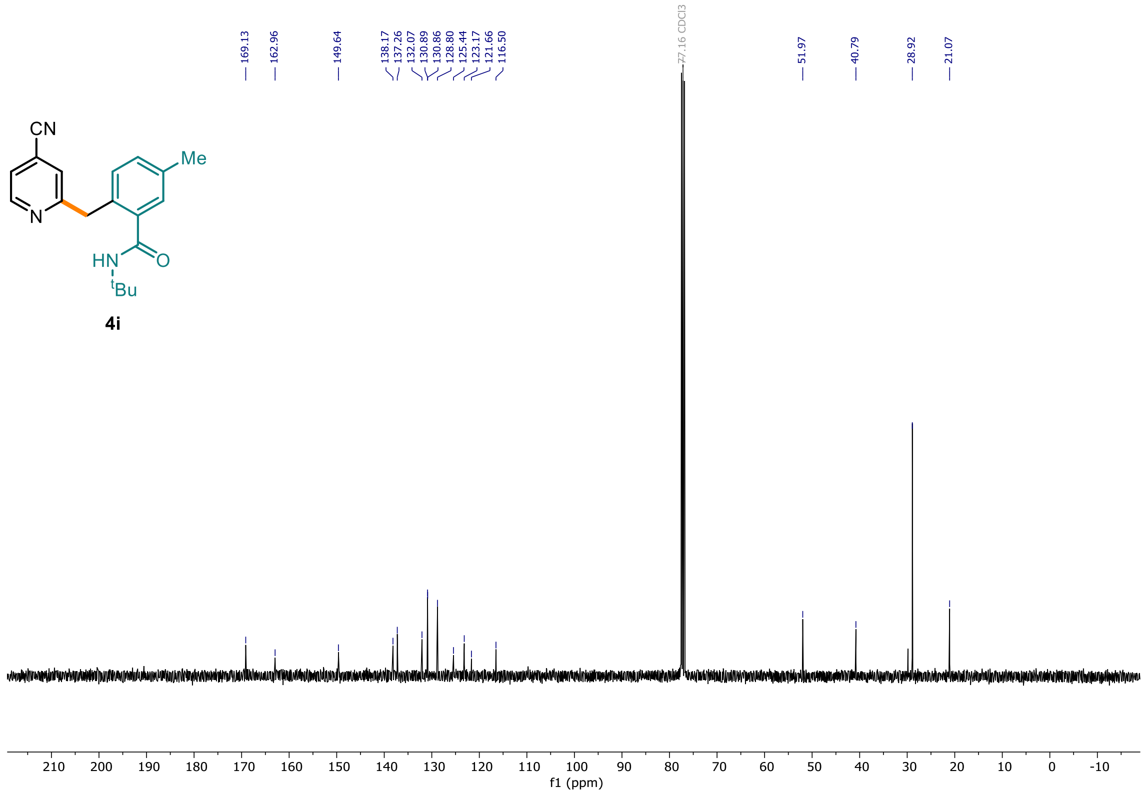


^{1}H NMR (400 MHz, CDCl$_3$)



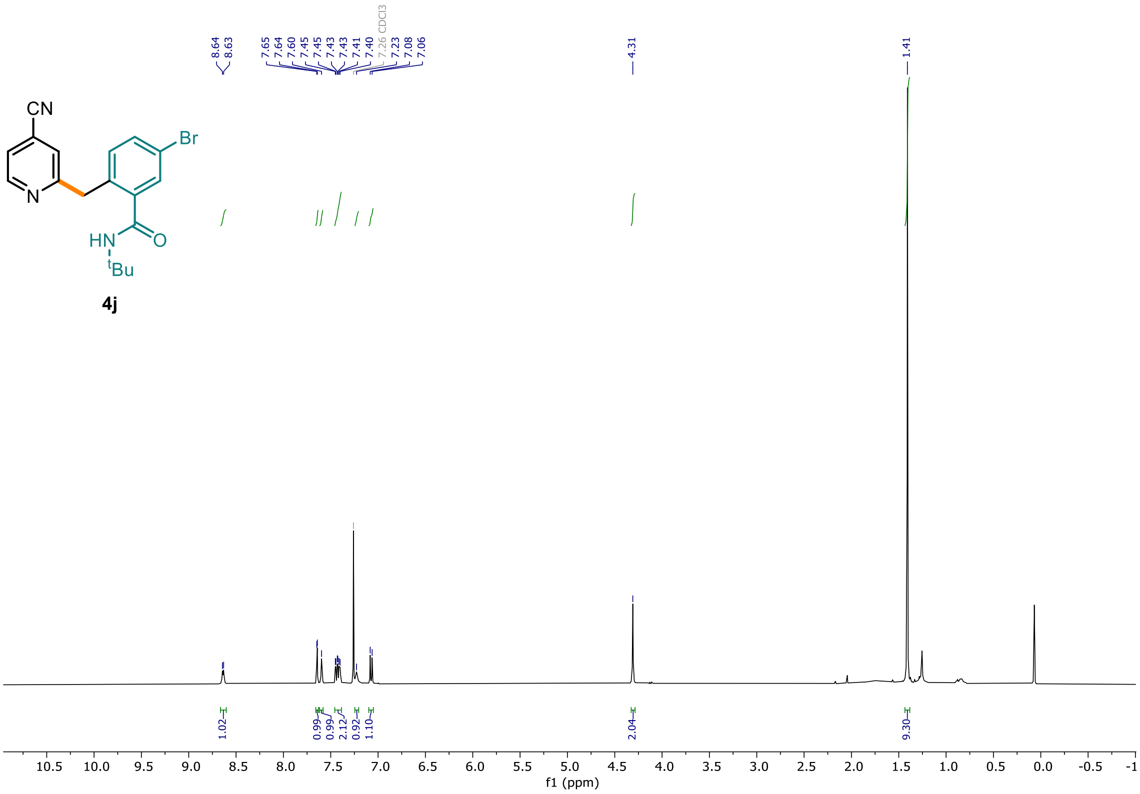
4i

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

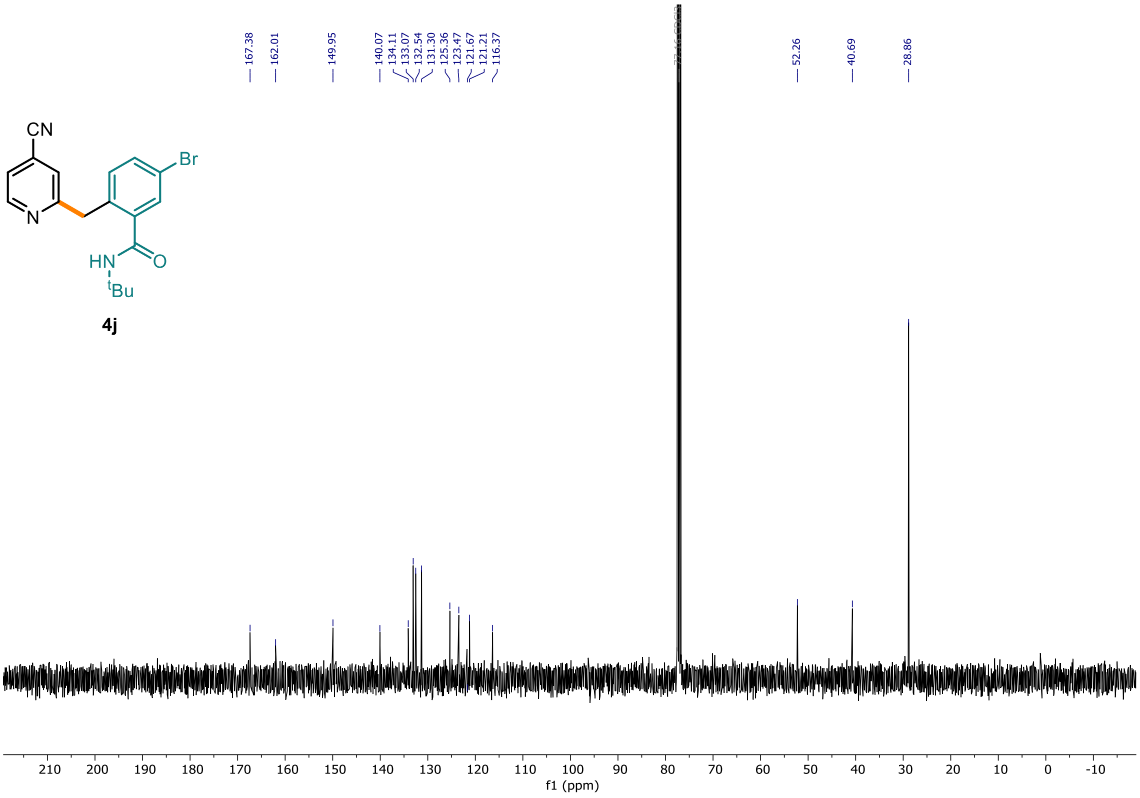


4i

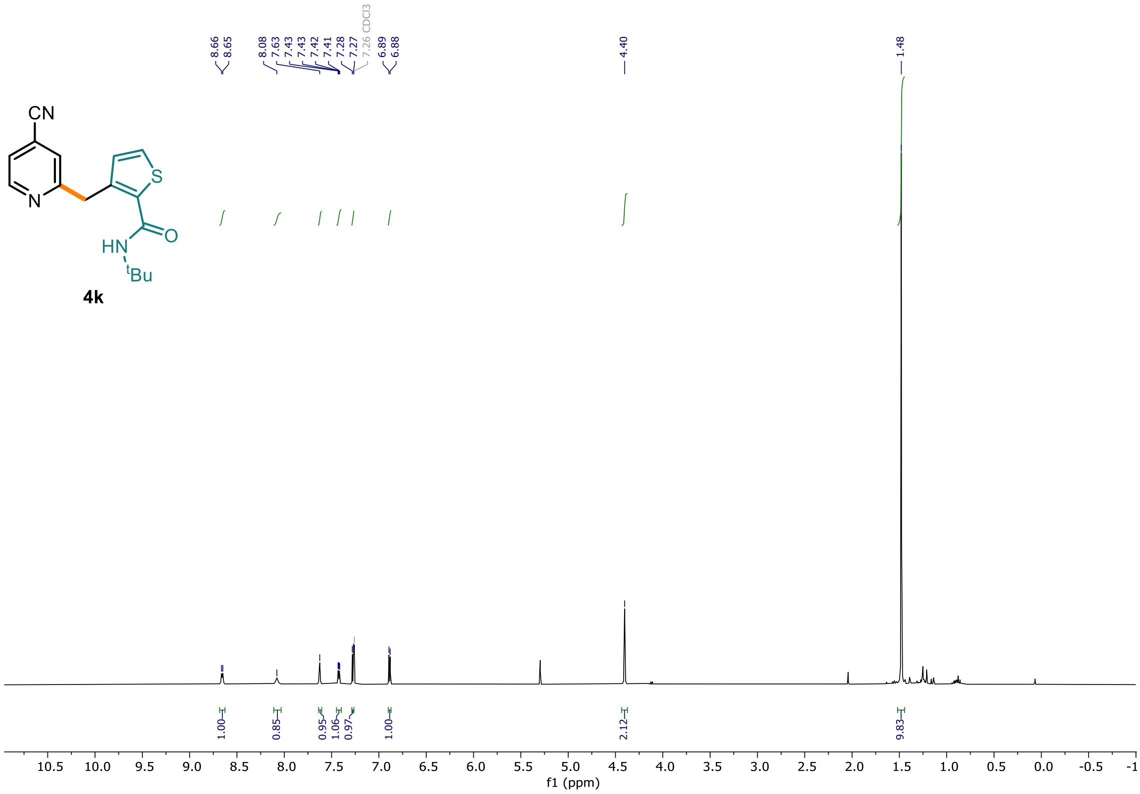
^{1}H NMR (400 MHz, CDCl$_3$)



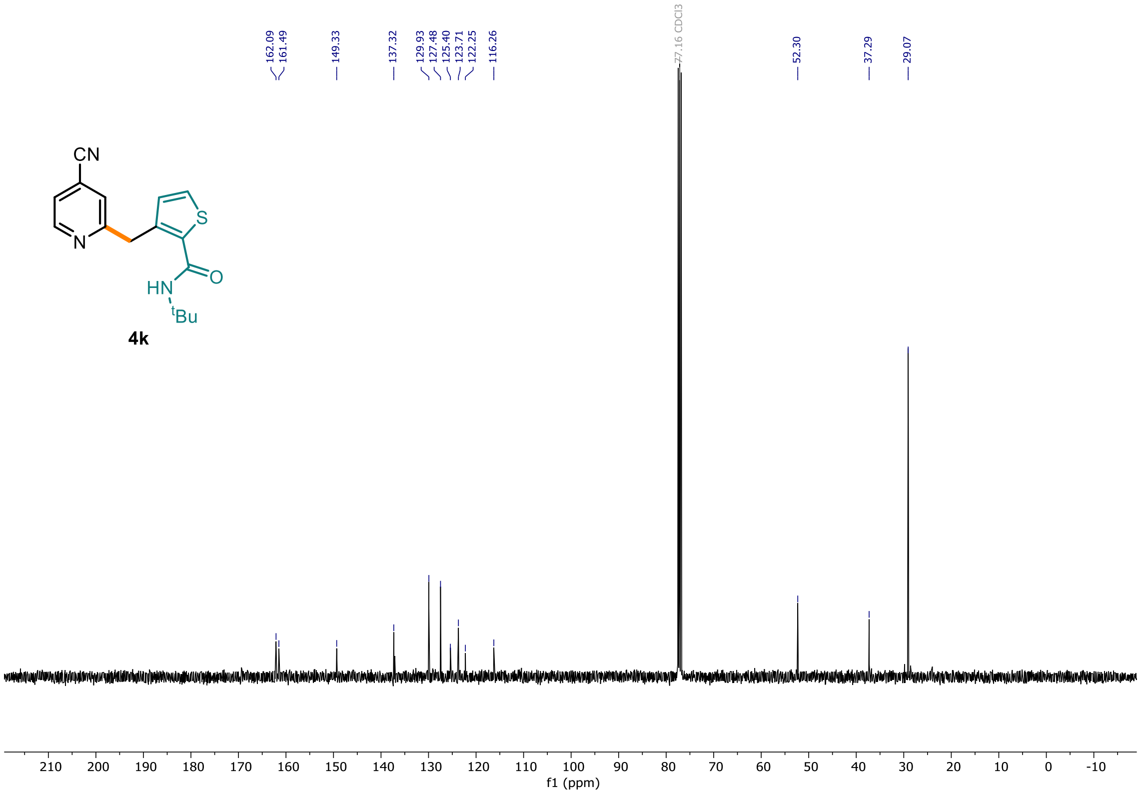
^{13}C NMR (101 MHz, CDCl$_3$)



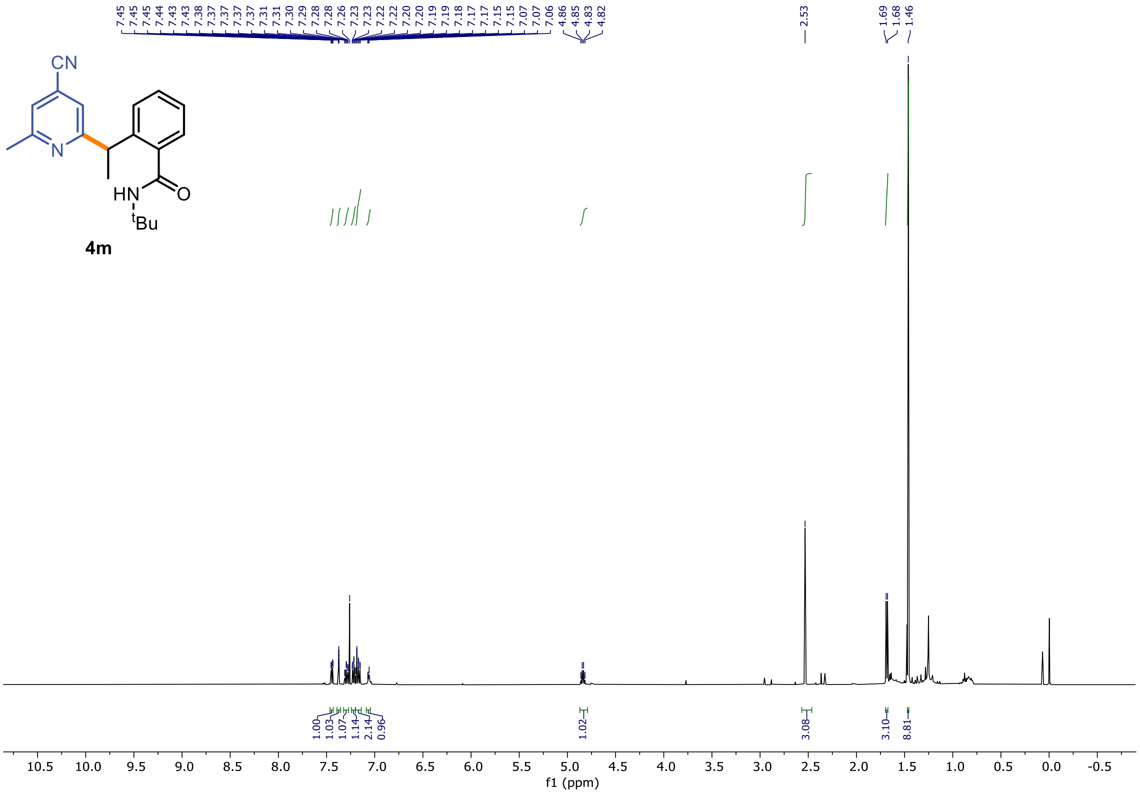
^{1}H NMR (400 MHz, CDCl$_3$)



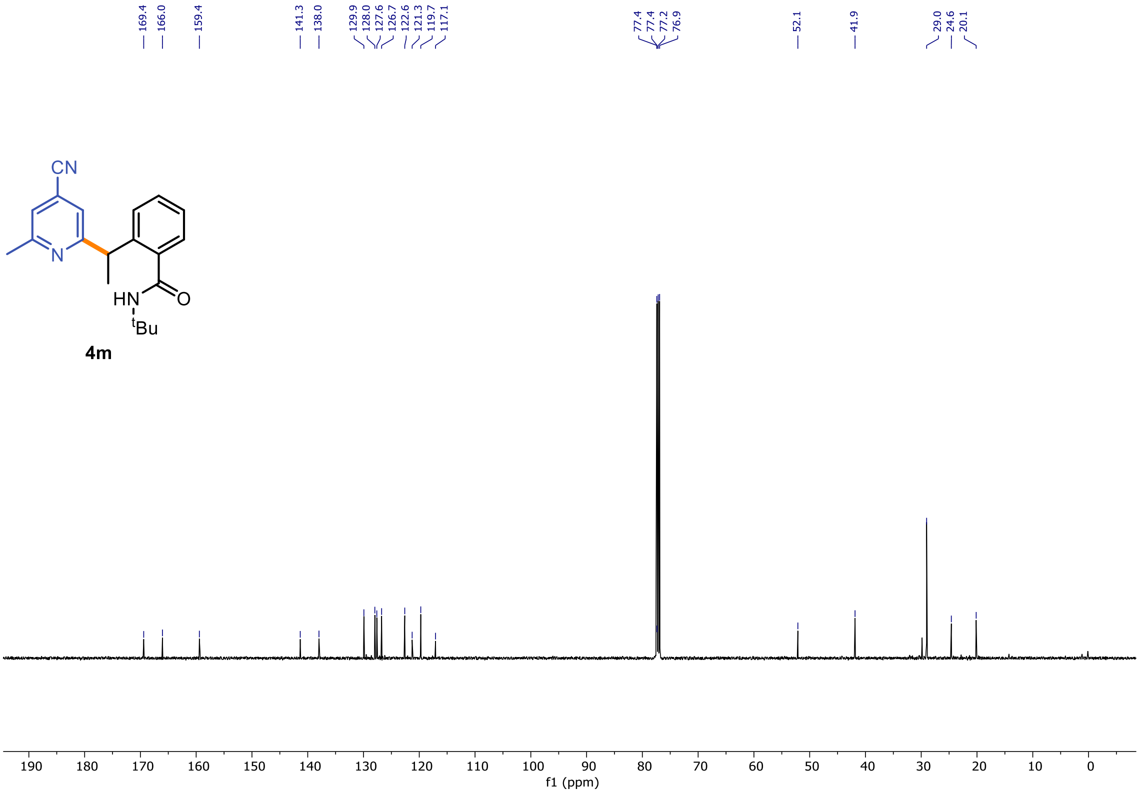
^{13}C NMR (101 MHz, CDCl$_3$) of **5k**



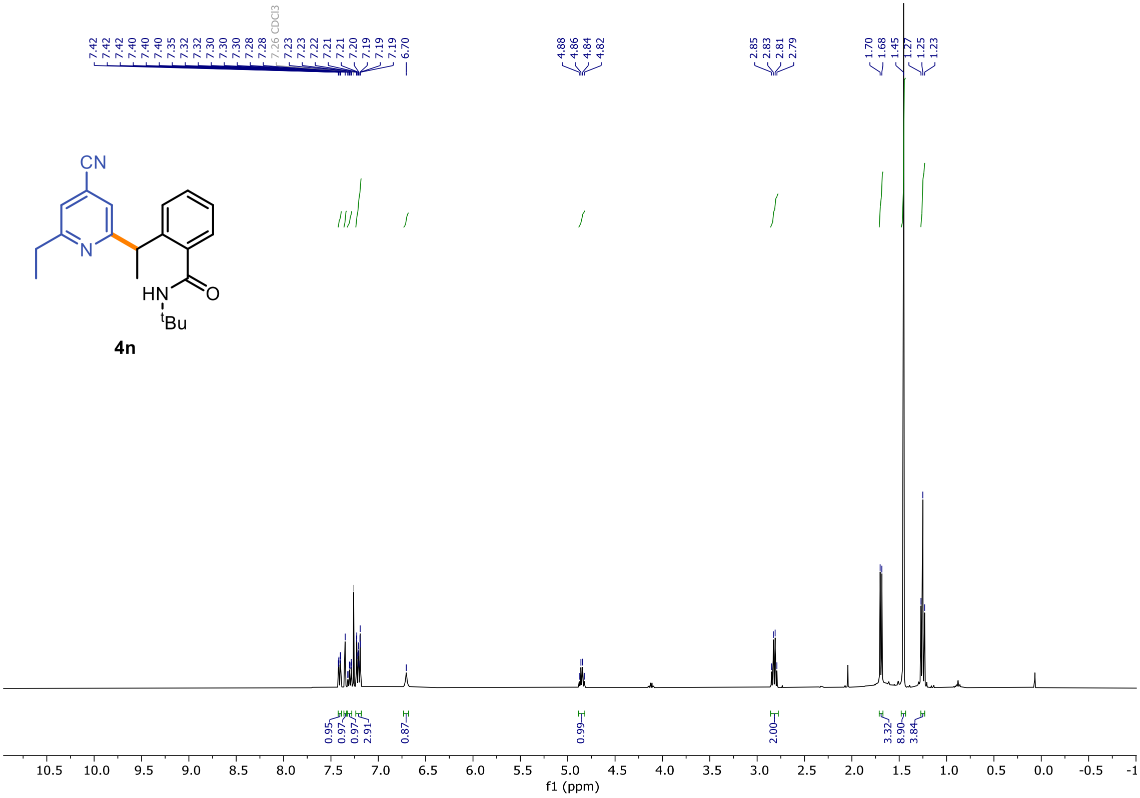
^{1}H NMR (500 MHz, CDCl$_3$)



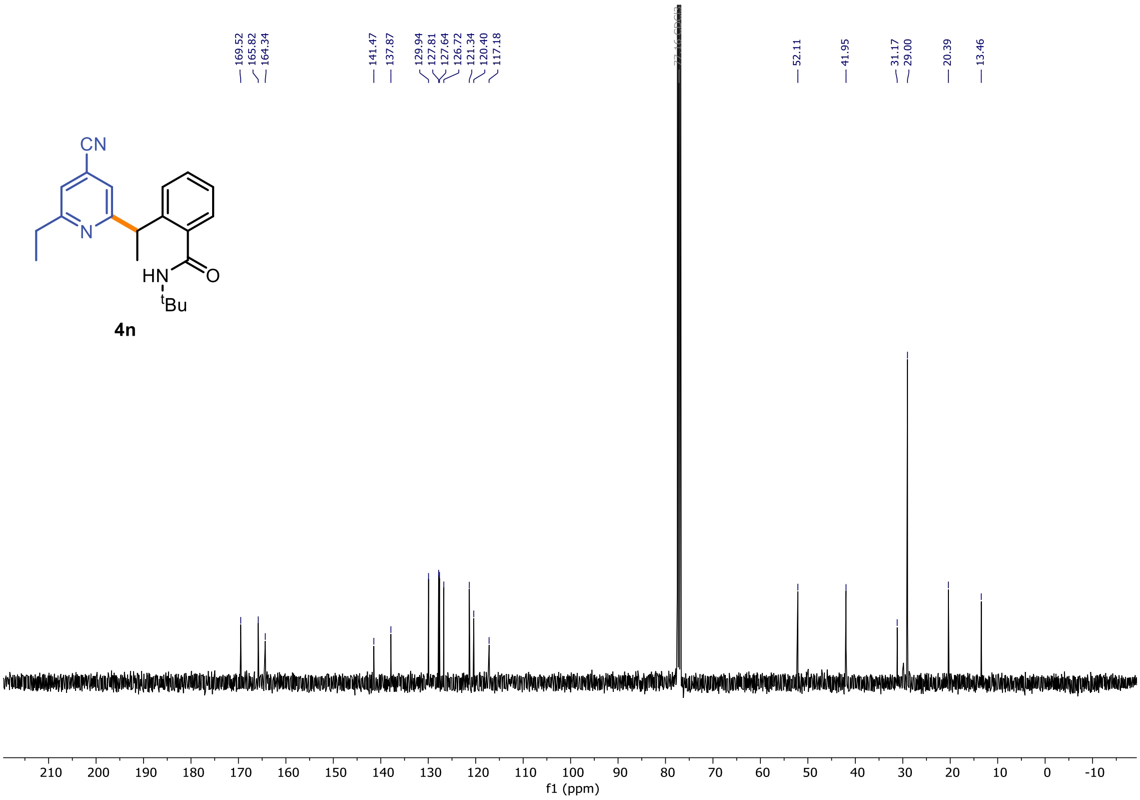
^{13}C NMR (126 MHz, CDCl$_3$)



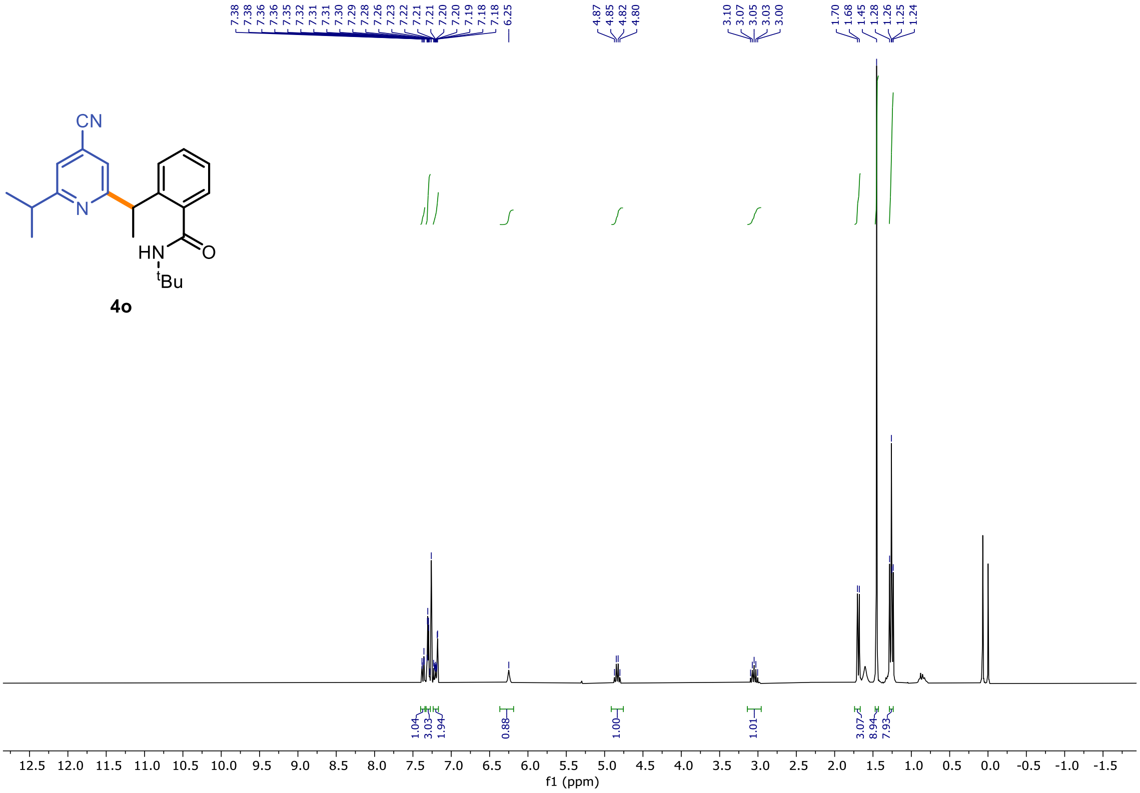
^1H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

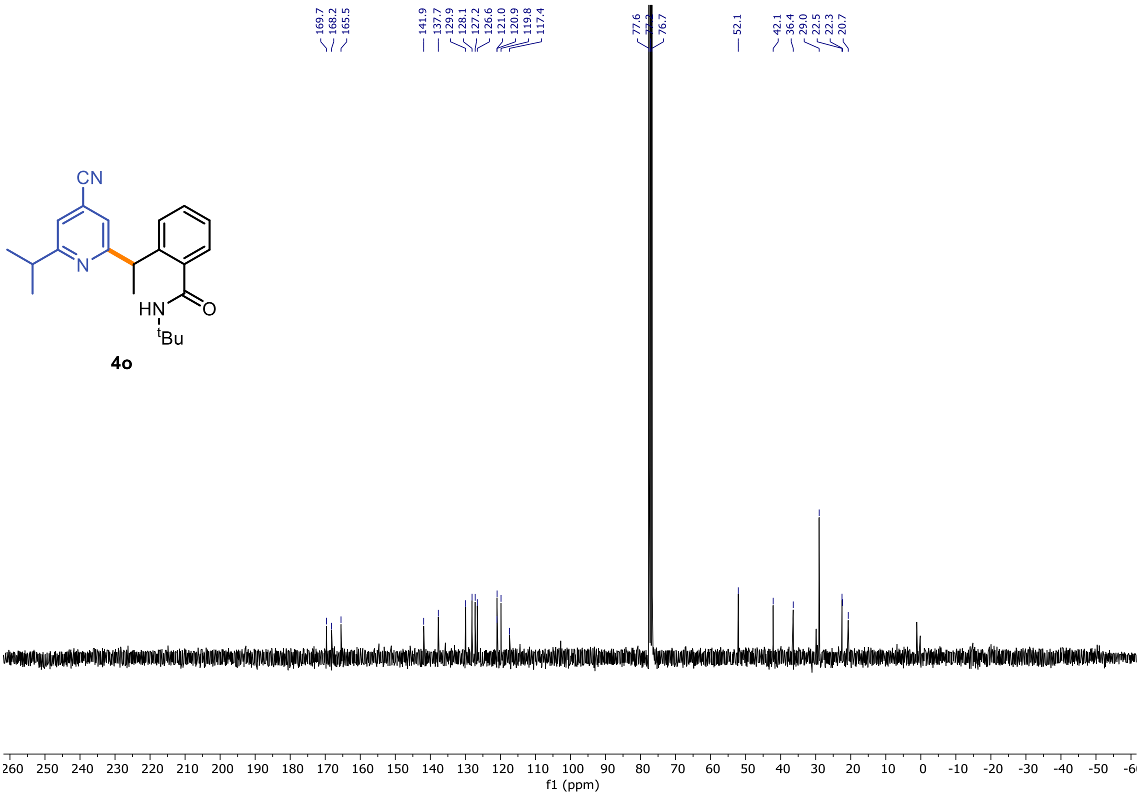


^{1}H NMR (300 MHz, CDCl$_3$)



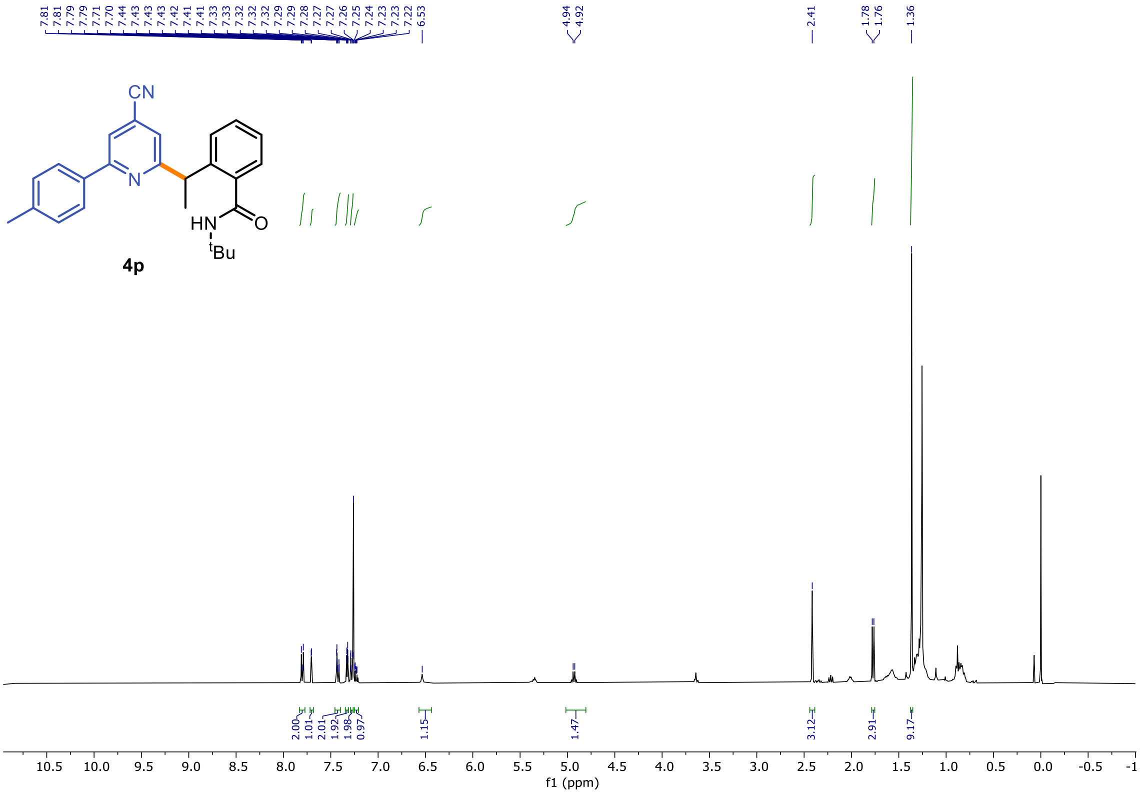
4o

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

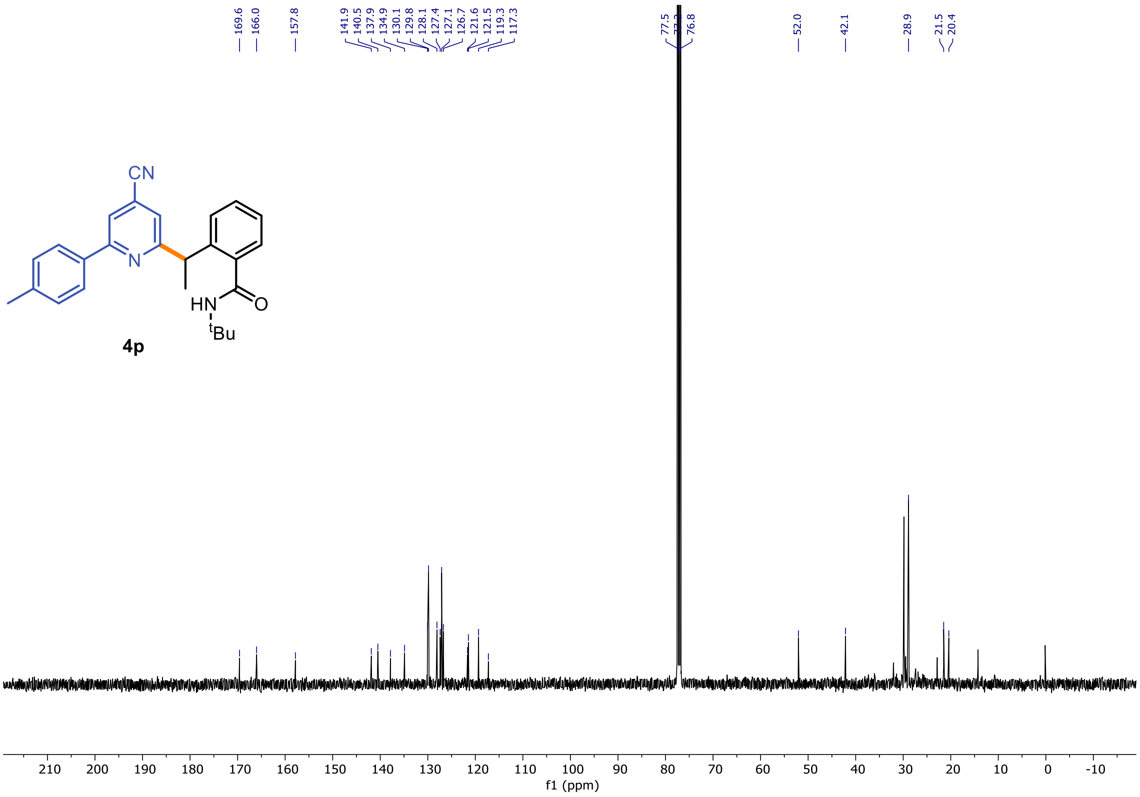


4o

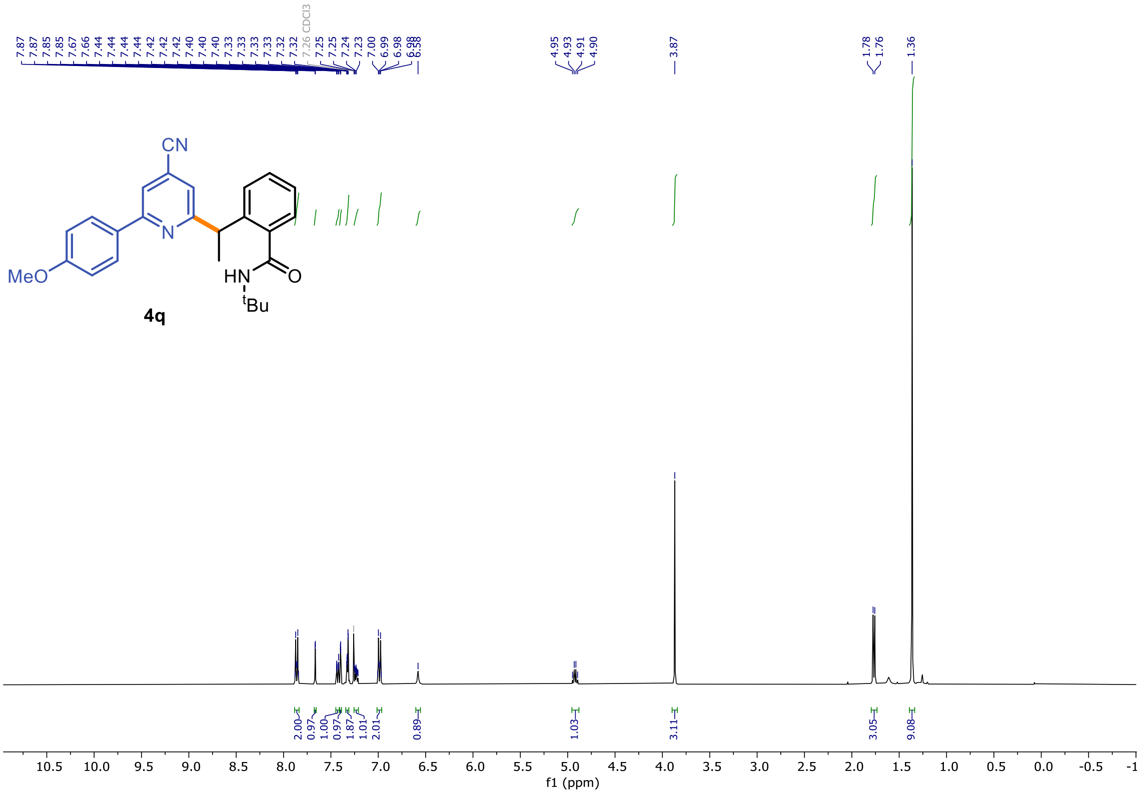
^{1}H NMR (400 MHz, CDCl$_3$)



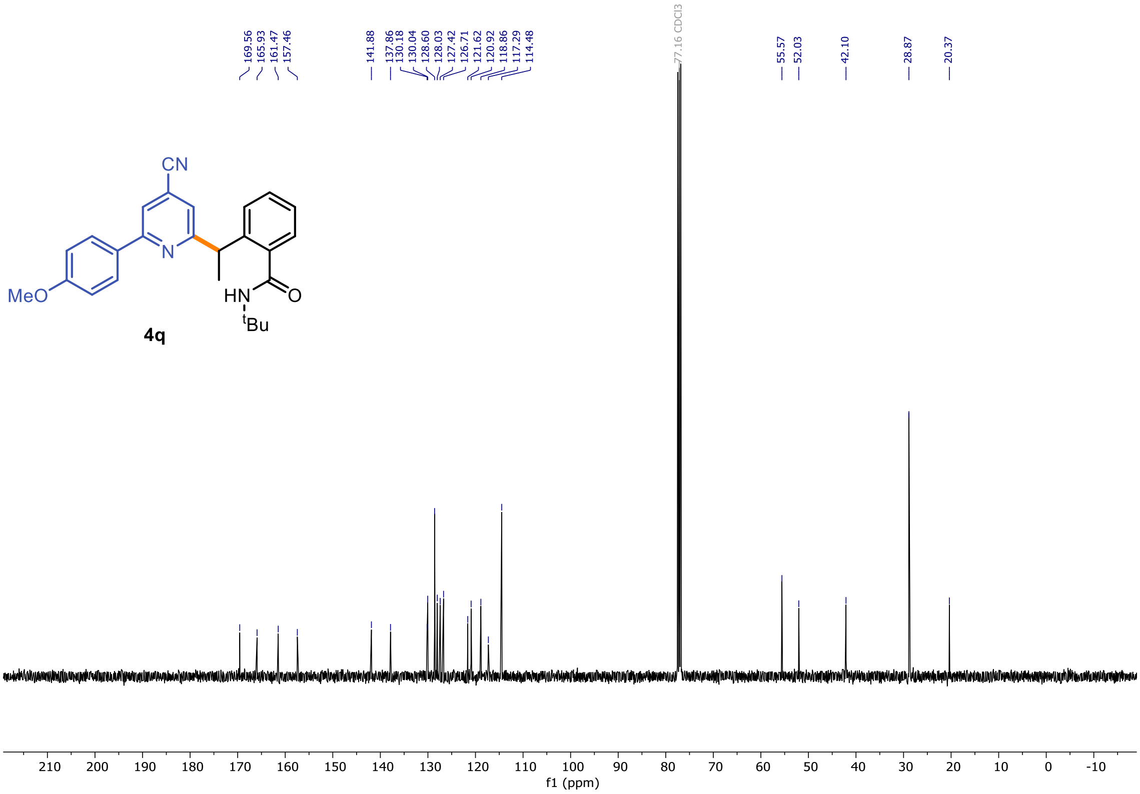
^{13}C NMR (101 MHz, CDCl$_3$)



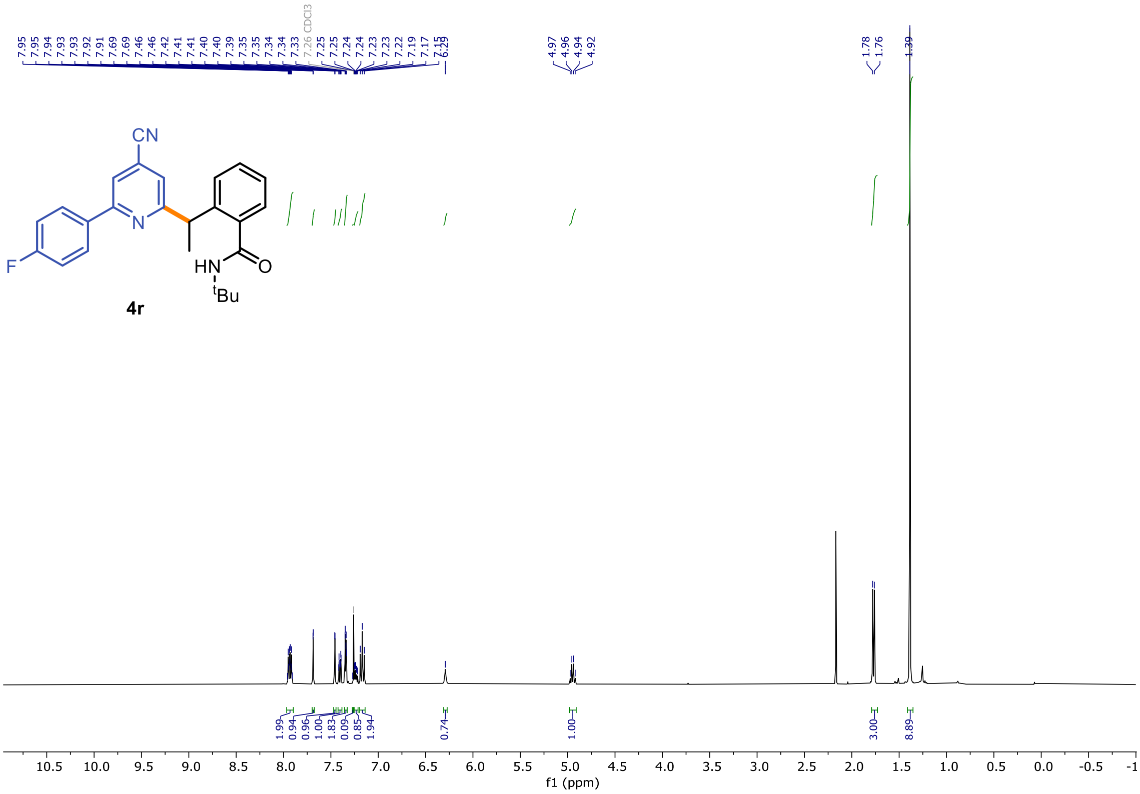
^{1}H NMR (400 MHz, CDCl$_3$)



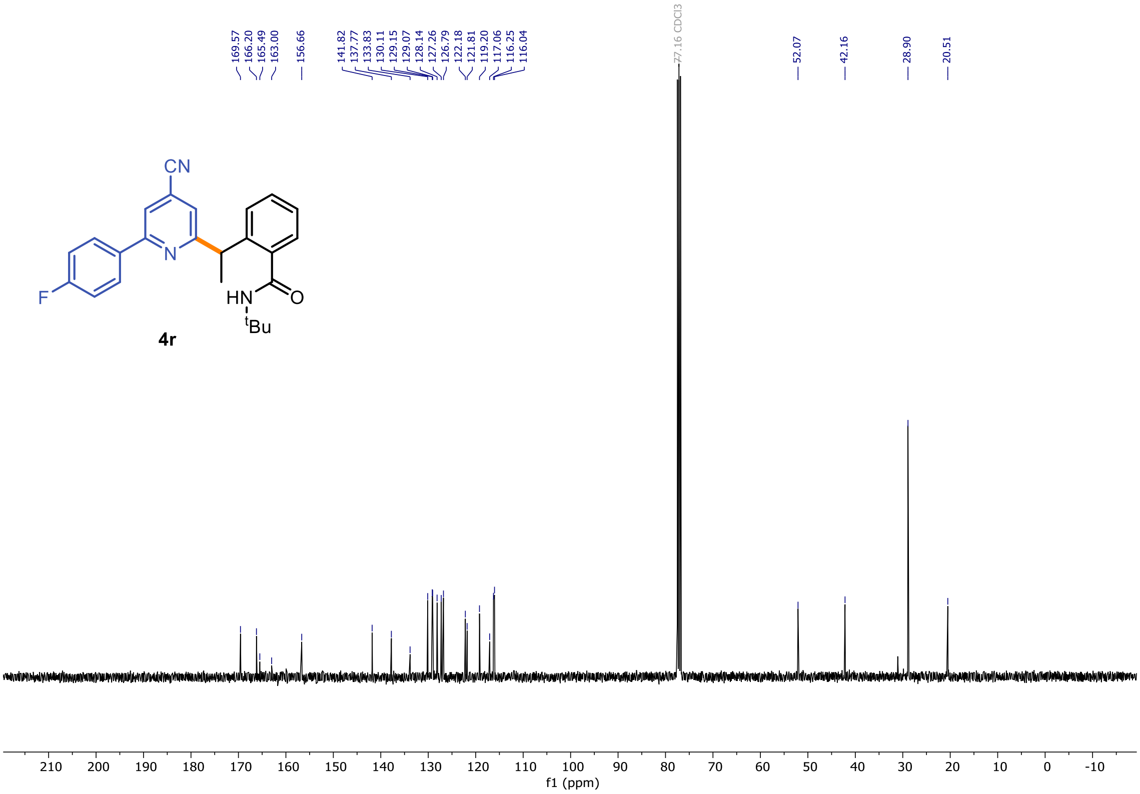
^{13}C NMR (101 MHz, CDCl$_3$)



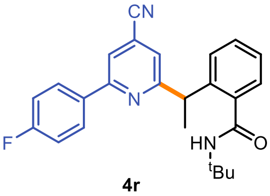
^{1}H NMR (400 MHz, CDCl$_3$)



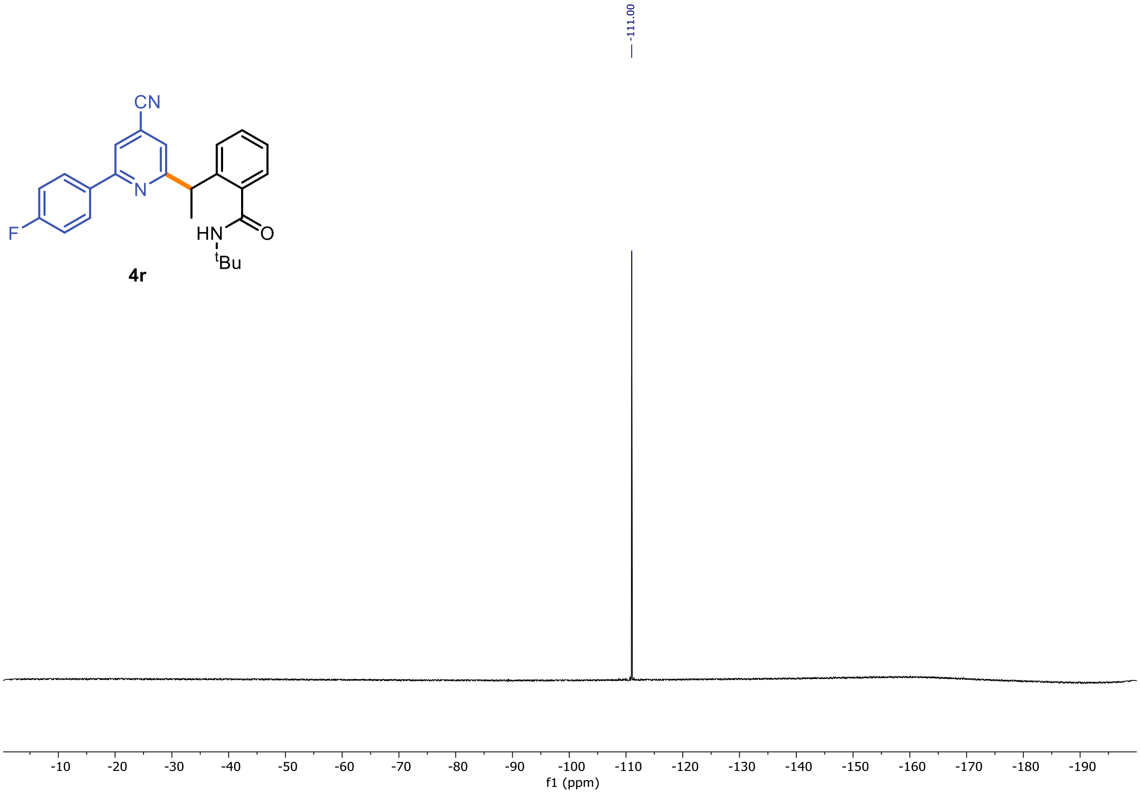
^{13}C NMR (101 MHz, CDCl$_3$)



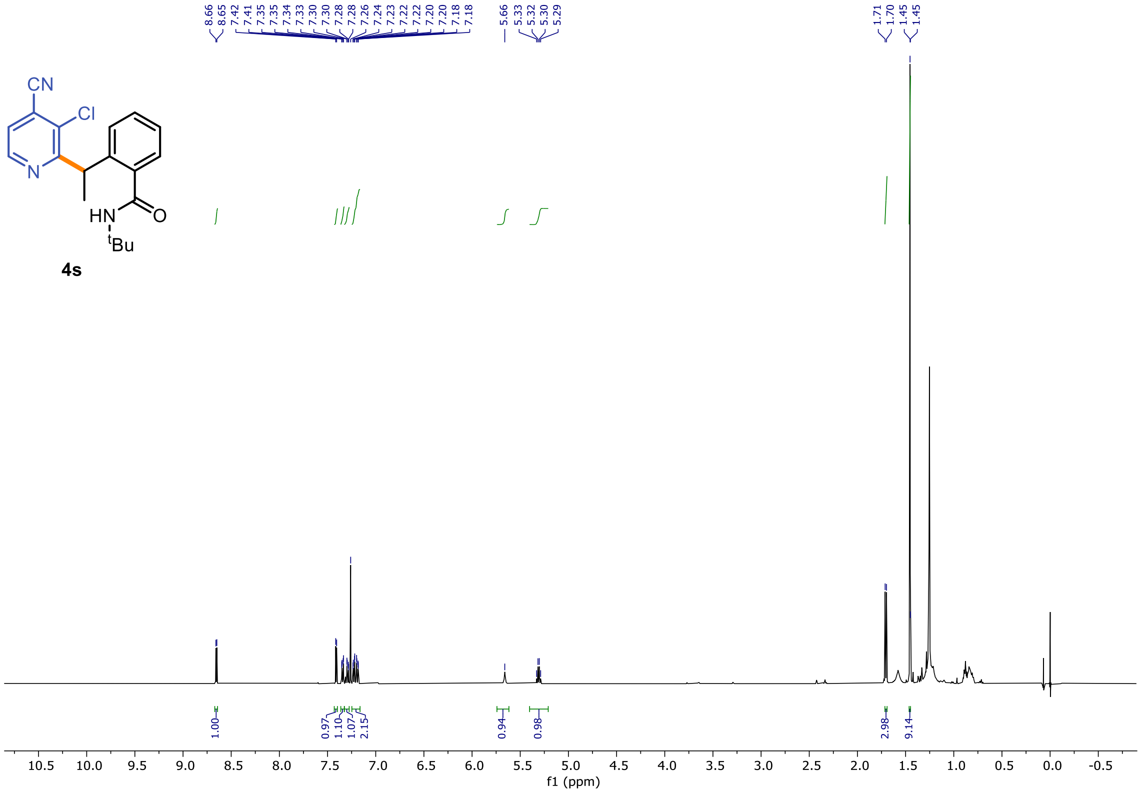
^{19}F NMR (376 MHz, CDCl$_3$)



4r

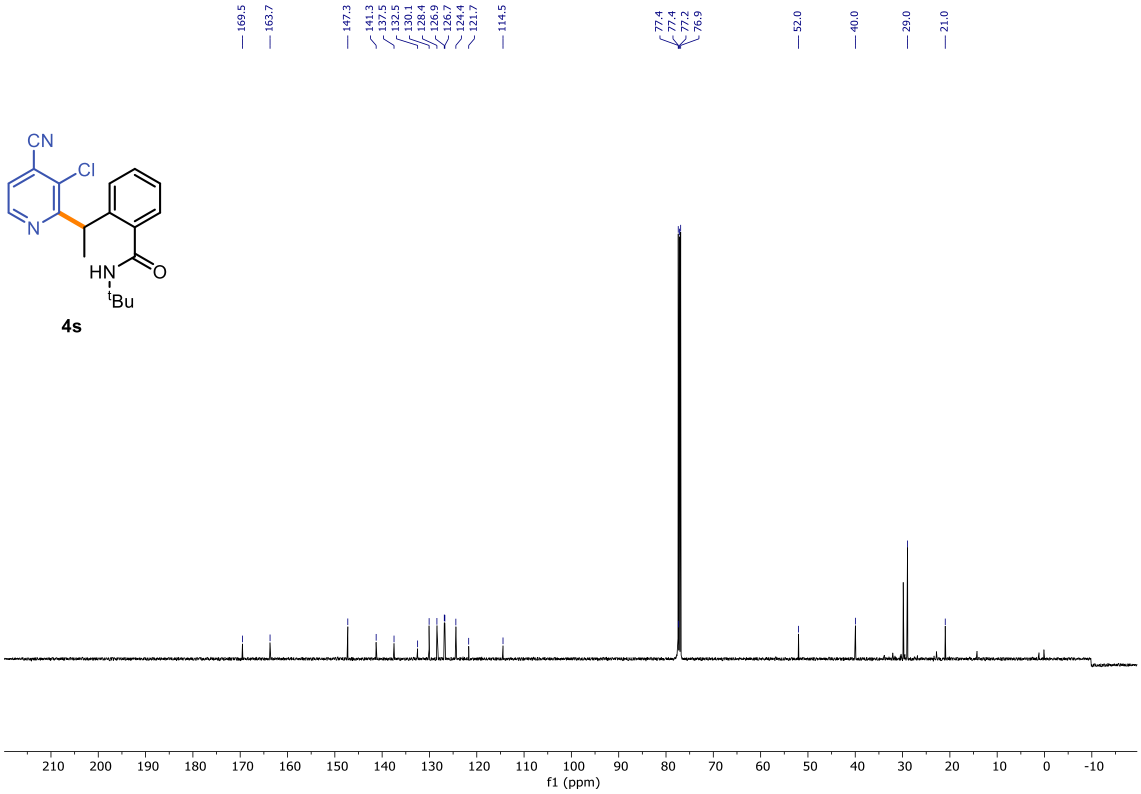


^{1}H NMR (500 MHz, CDCl$_3$)



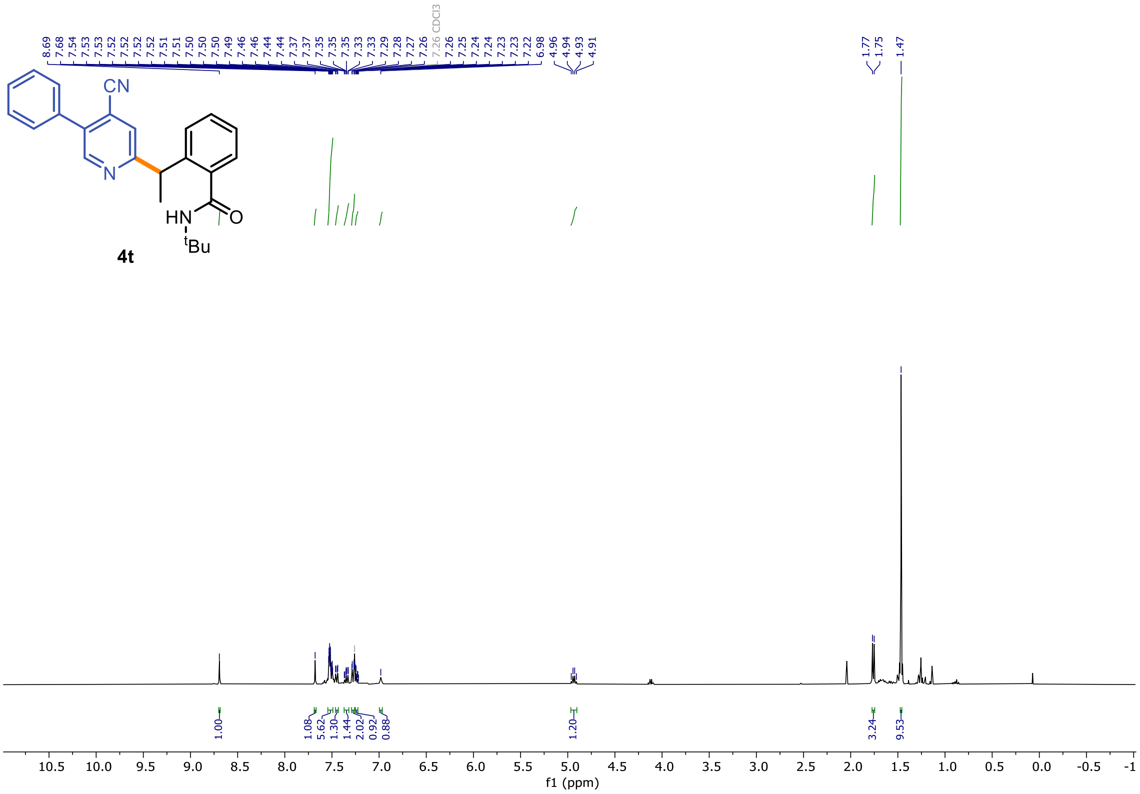
4s

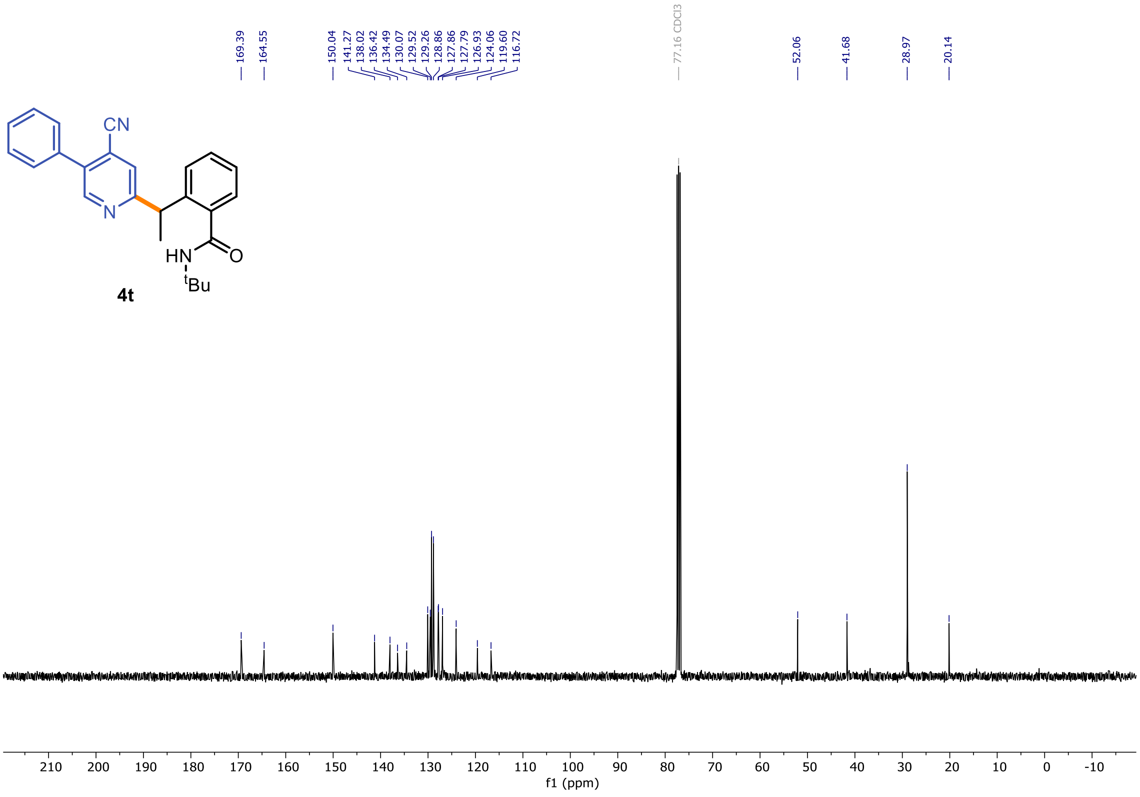
^{13}C NMR (126 MHz, CDCl$_3$)



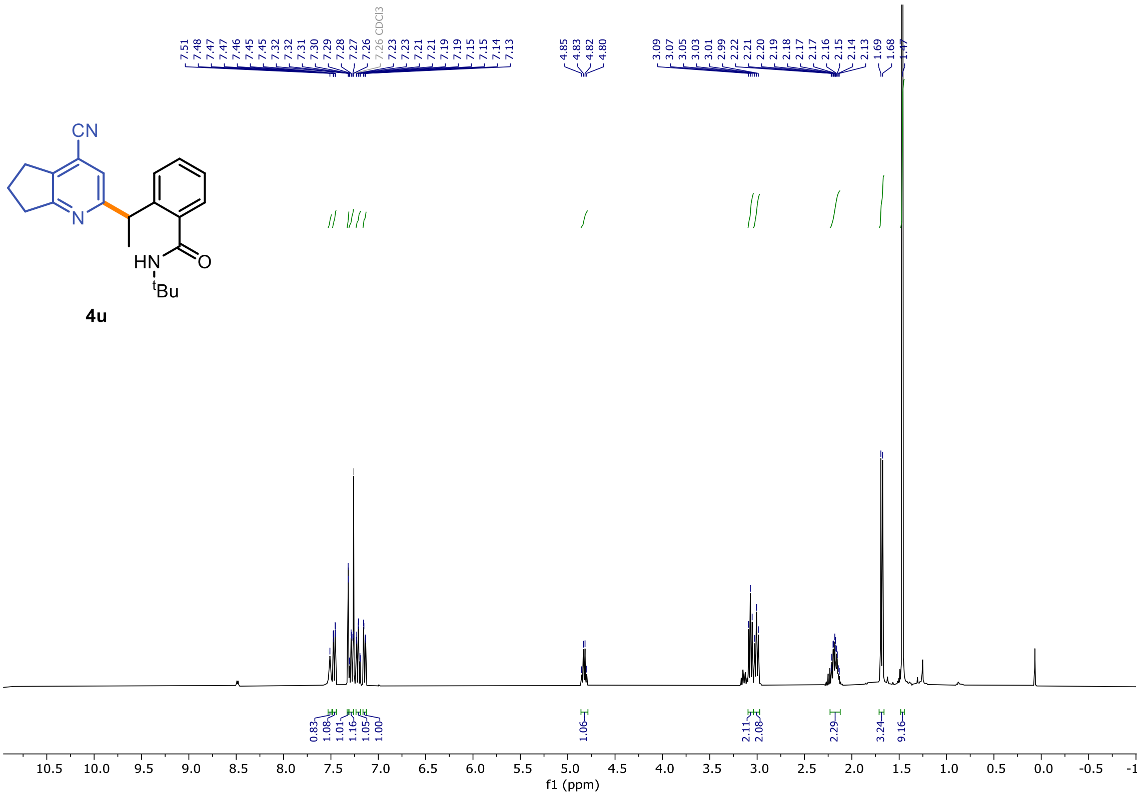
4s

^{1}H NMR (400 MHz, $CDCl_3$)



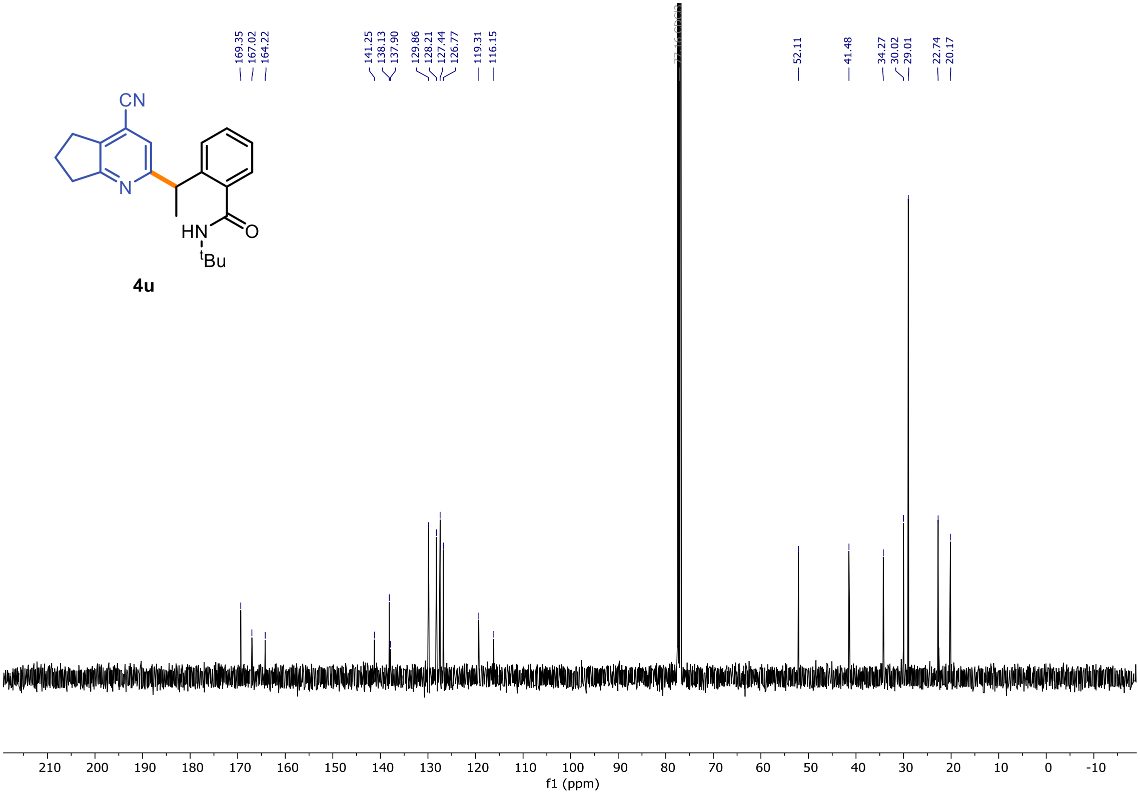


^{1}H NMR (400 MHz, CDCl$_3$)



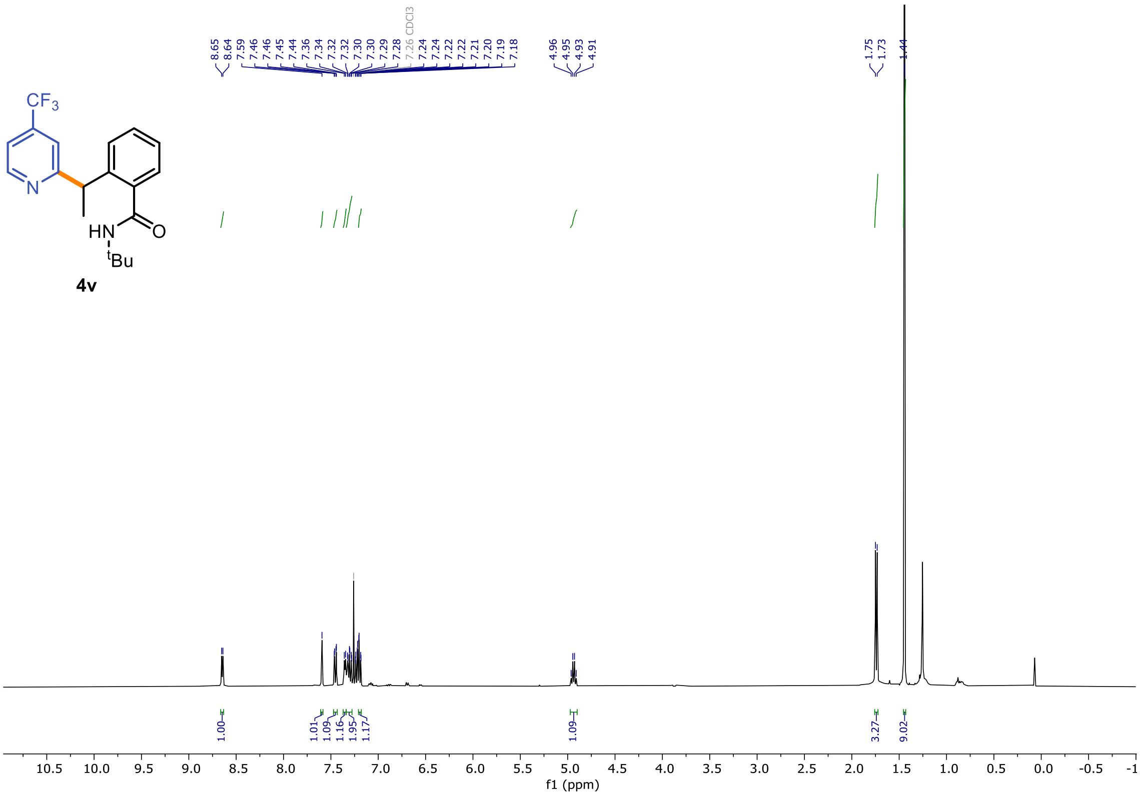
4u

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

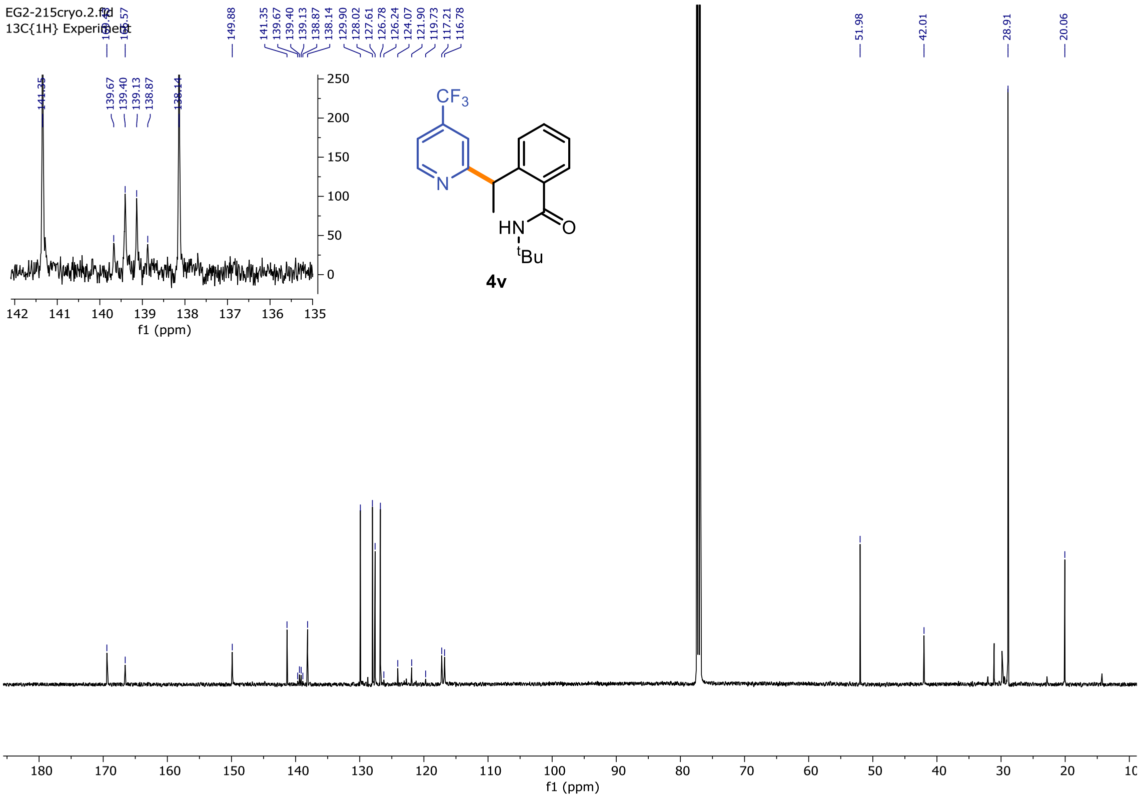


4u

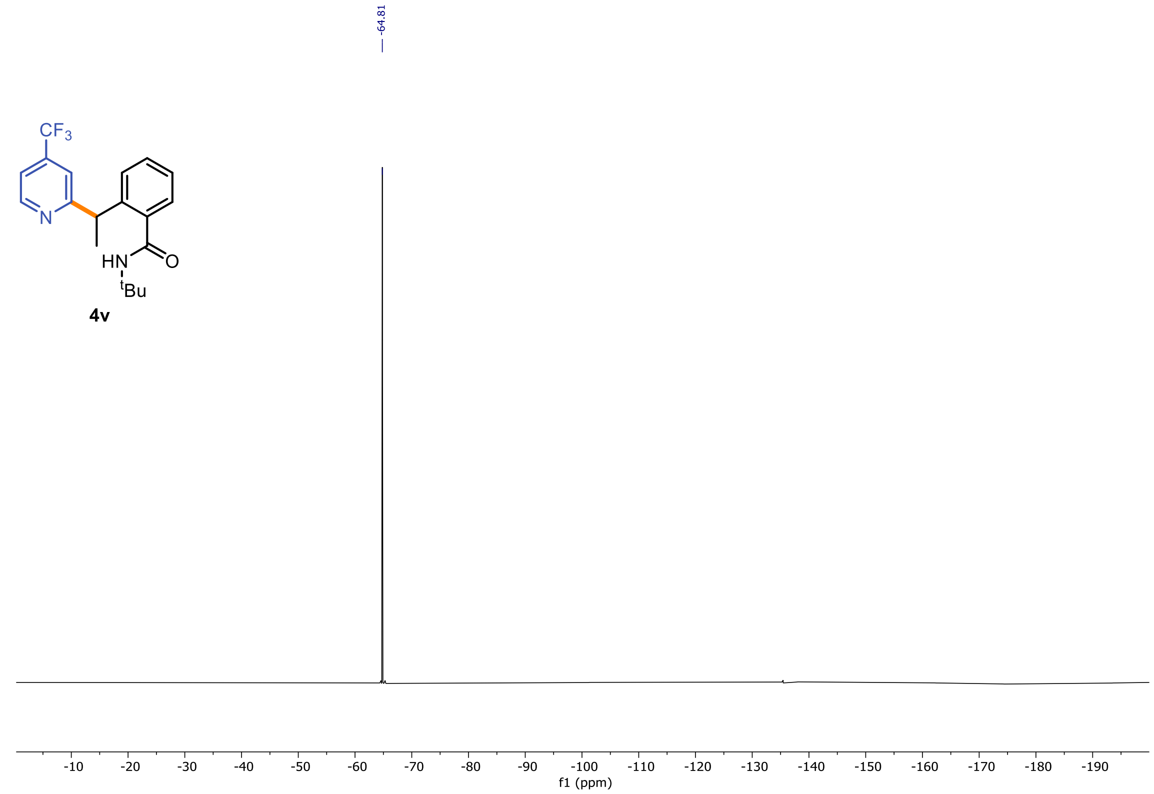
^{1}H NMR (400 MHz, CDCl$_3$)



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

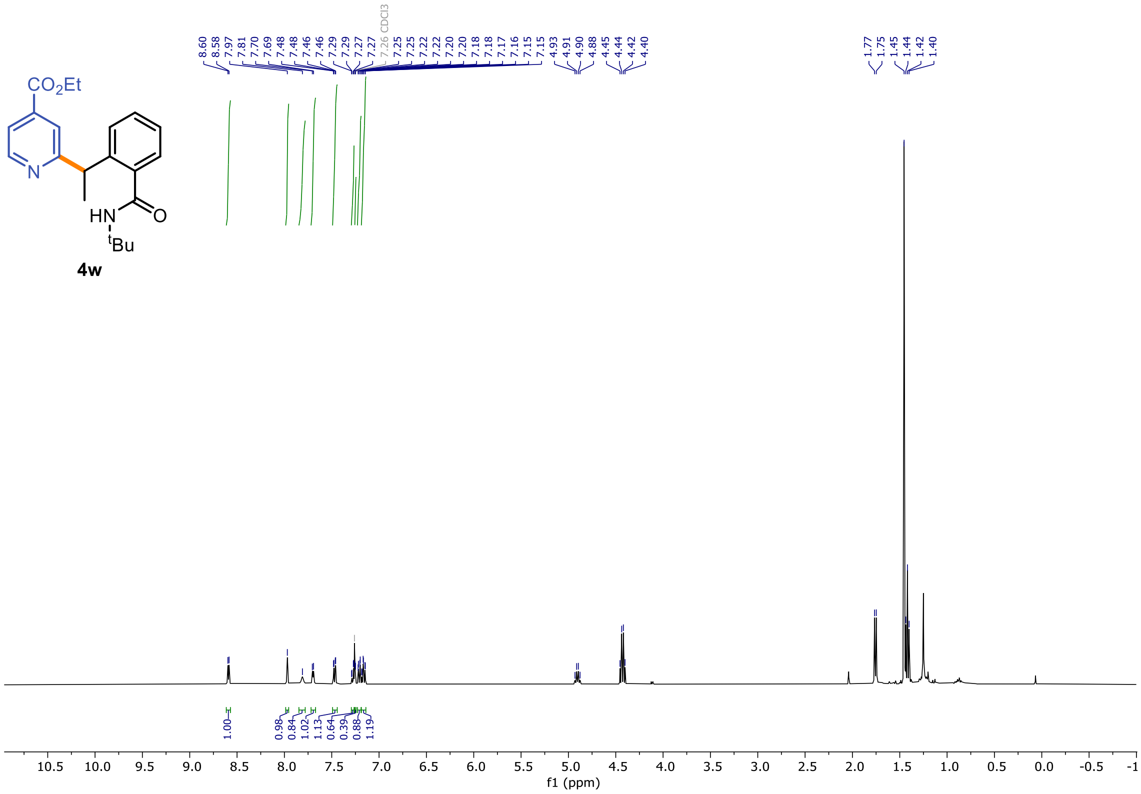


<u>^{19}F NMR</u> (376 MHz, CDCl3)

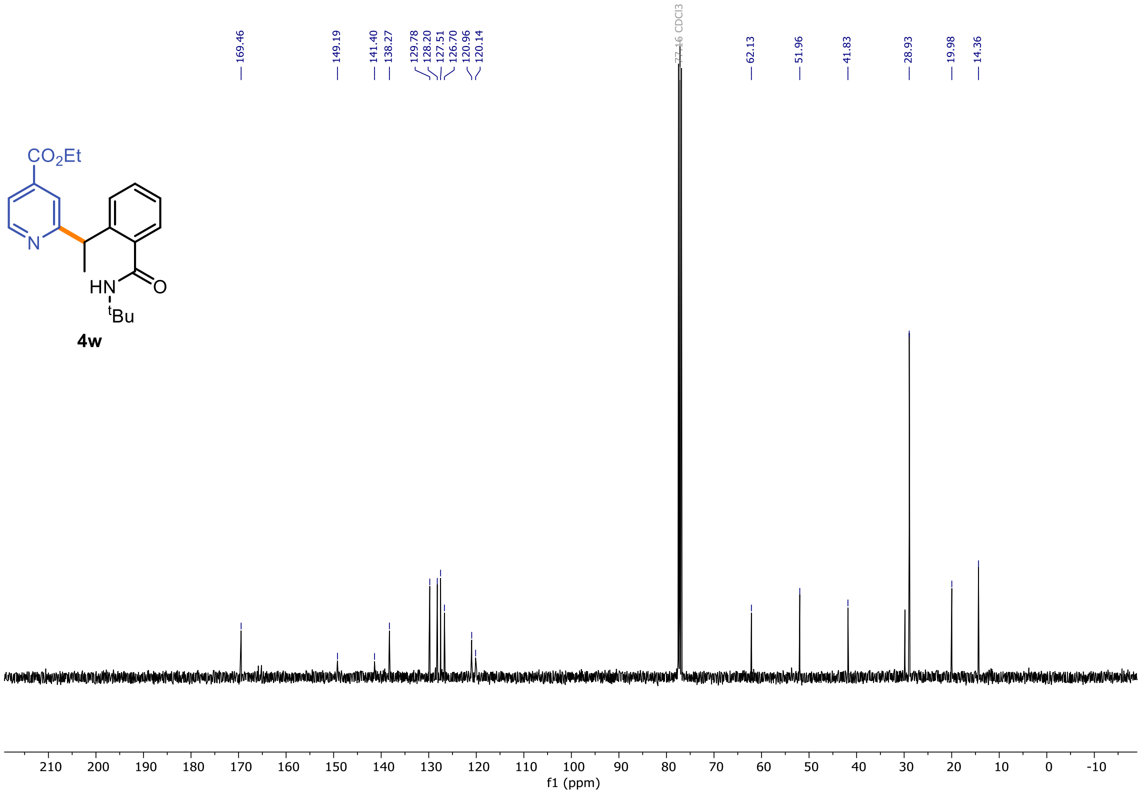


4v

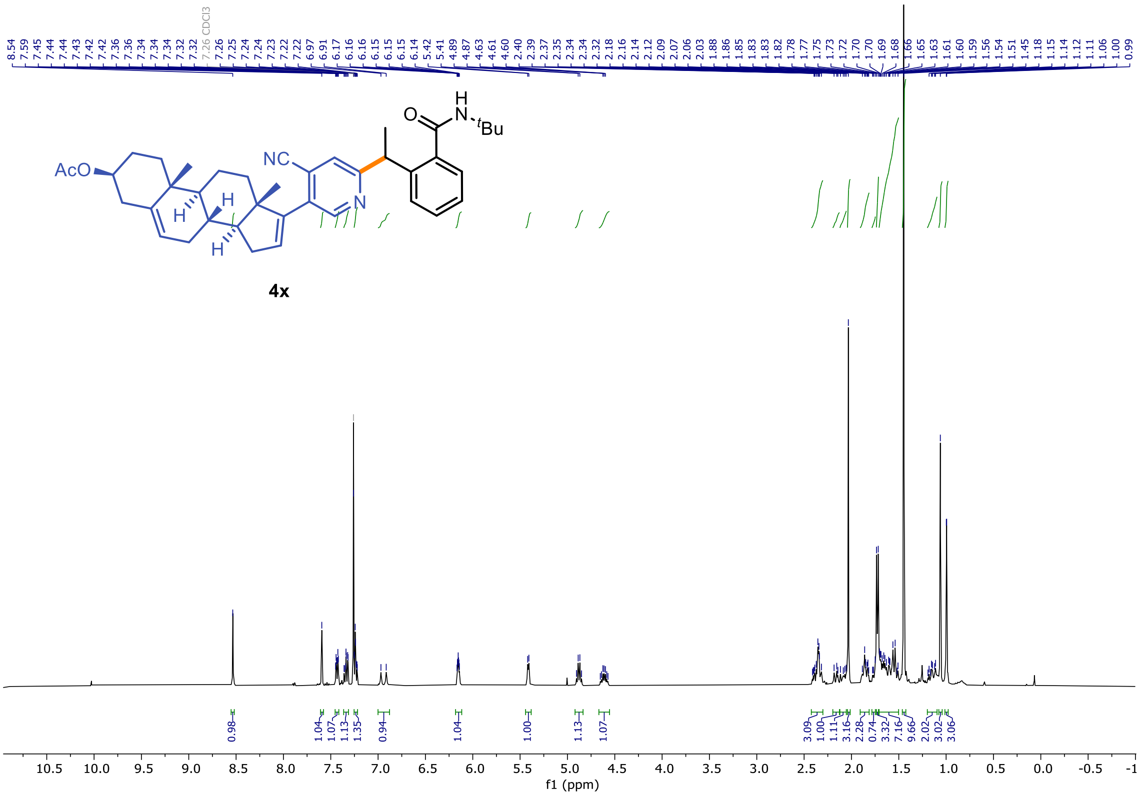
^{1}H NMR (400 MHz, $CDCl_3$)



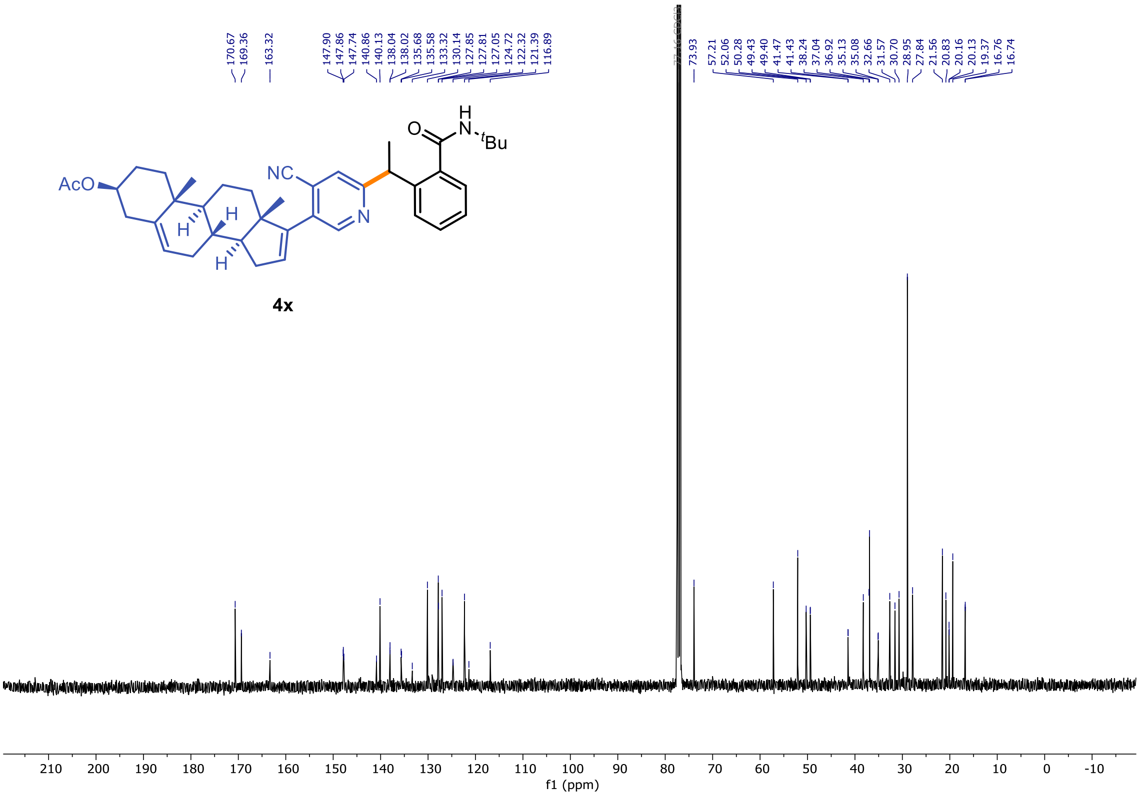
^{13}C NMR (101 MHz, $CDCl_3$)



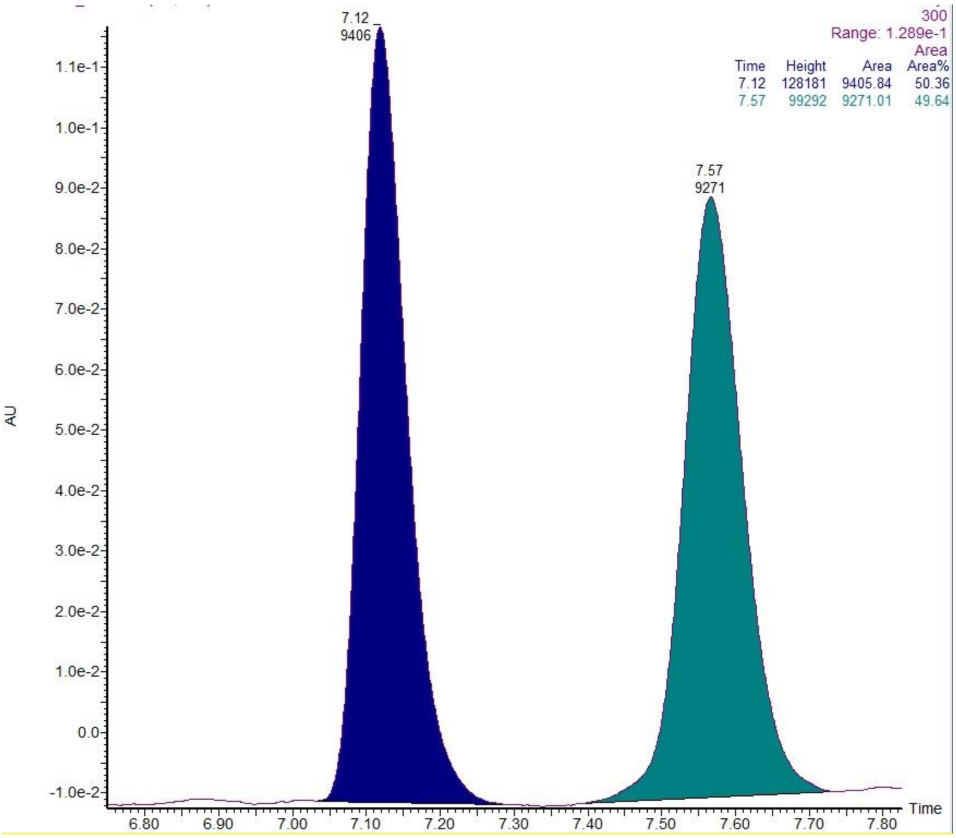
^{1}H NMR (400 MHz, CDCl$_3$)


4x

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

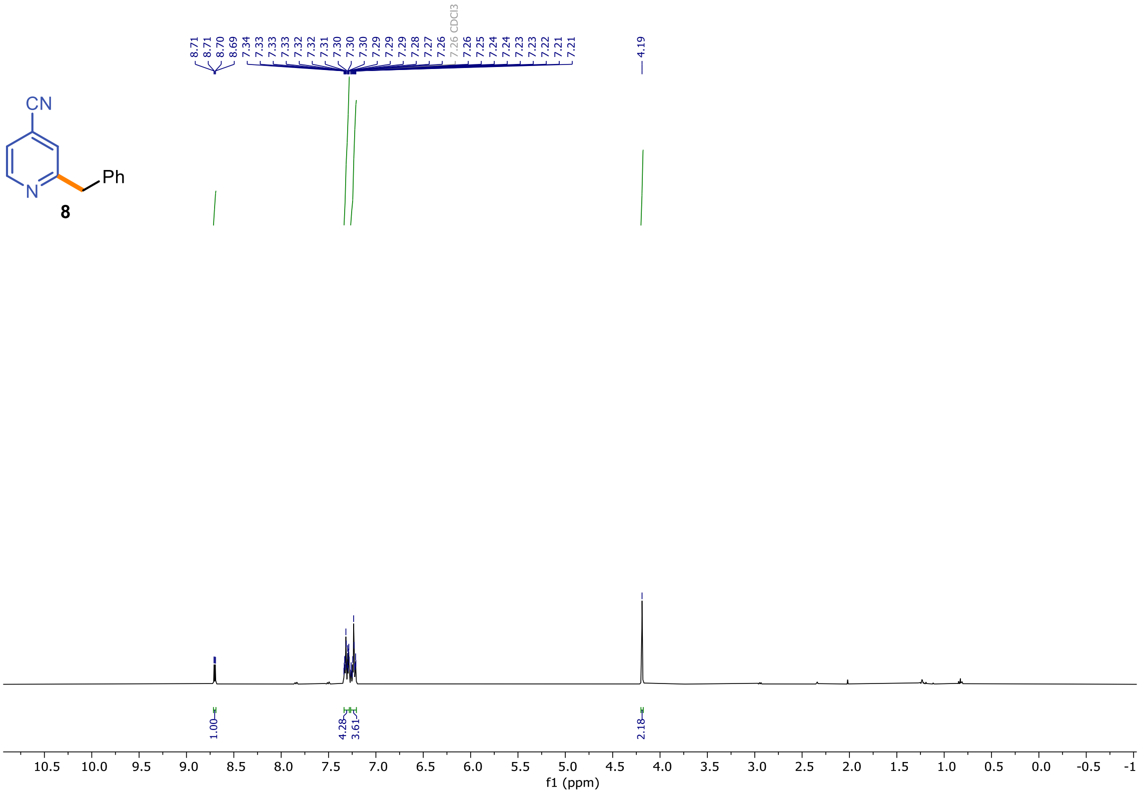

4x

UPC^2 trace for compound **4x**



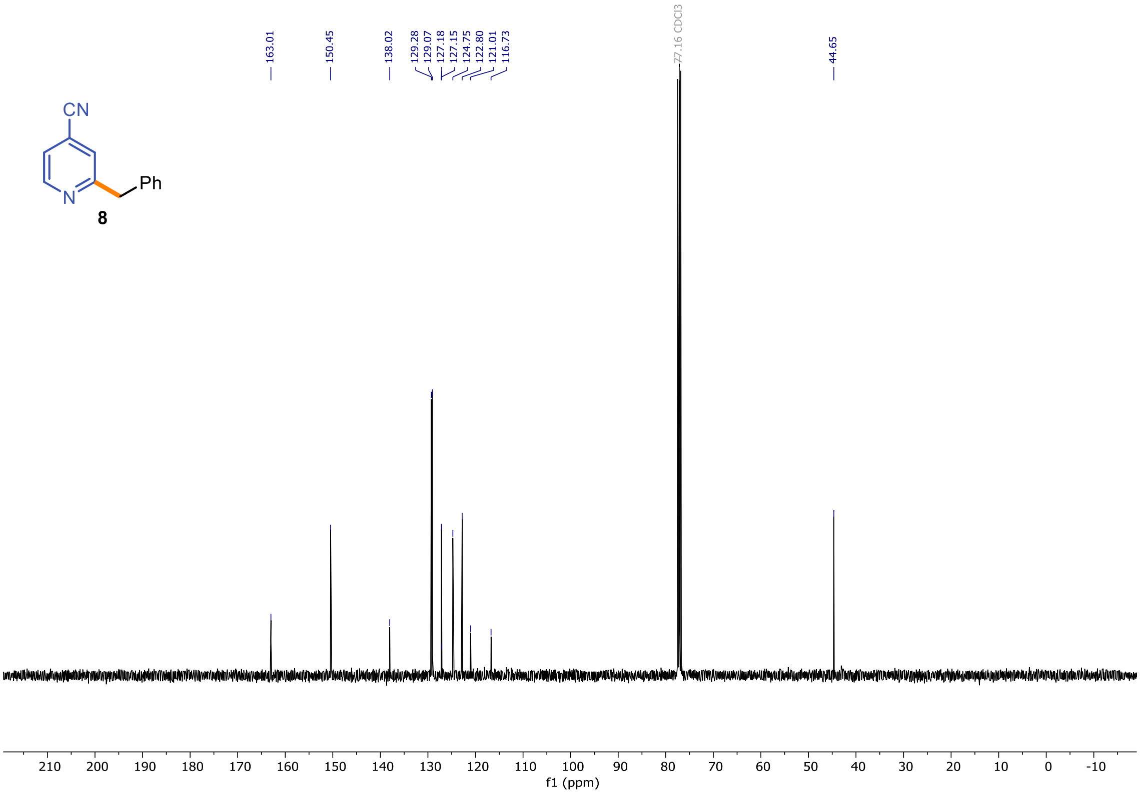
^{1}H NMR (400 MHz, CDCl$_3$)

8

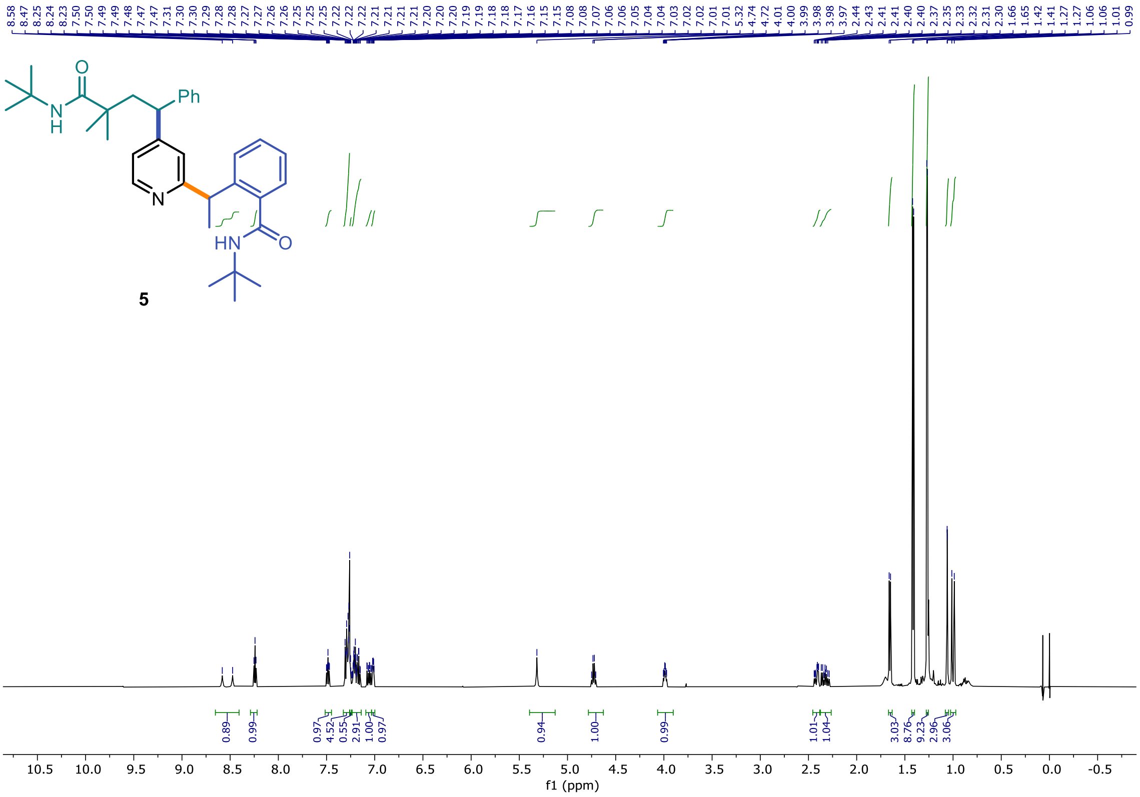


^{13}C NMR (101 MHz, CDCl$_3$)

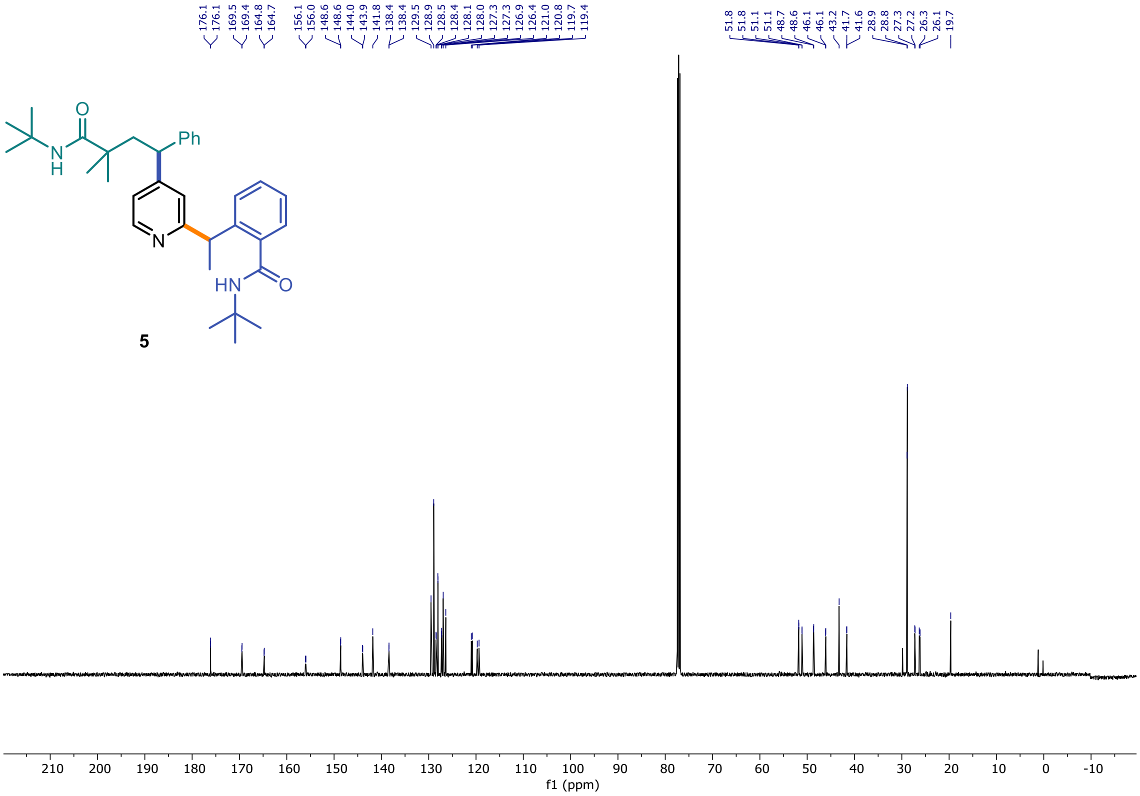
8



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


5

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