--- Electronic Supplementary Information---

Substrate-controlled divergent remote C-H and N-H polyfluoroarylation of 2-aminopyrimidines with polyfluoroarenes via Pd(II)/Pd(0) catalysis

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1. General information

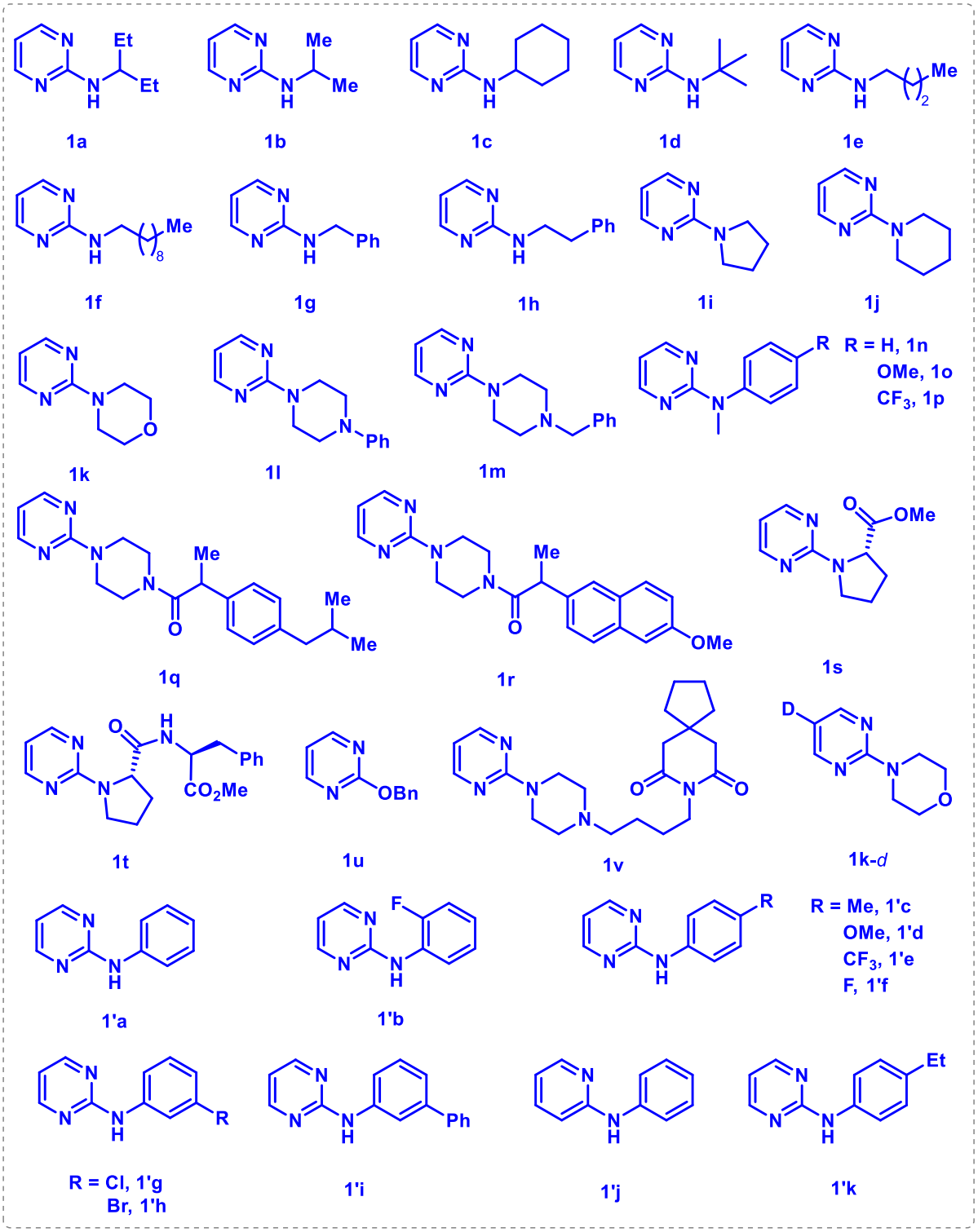
Reaction temperatures are reported as the temperature of the bath surrounding the vessel unless otherwise stated. Non-halogenated solvents were dried over calcium hydride. All the solvents were degassed with argon and stored over activated molecular sieves (4 Å).

Analytical: ^{1}H, ^{13}C ^{1}, ^{19}F ^{1} NMR spectra were collected using Bruker (^{1}H: 500 MHz, ^{13}C ^{1}: 126 MHz, ^{19}F {^{1}H}: 470 MHz) and JEOL (^{1}H: 400 MHz, 13C {^{1}H}: 100 MHz, ^{19}F {^{1}H}: 376 MHz) and were referenced to the resonances of the solvent used. Coupling constants (*J*) are reported in Hertz (Hz). Coupling patterns are indicated as: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublet), dt (doublet of triplet), ddd (doublet of doublets of doublets), m (multiplet), or br (broad). Mass spectra were recorded on Bruker micrOTOF-Q II spectrometer. For thin-layer chromatography (TLC) analysis Merck pre-coated TLC plates (silica gel 60 F254 0.25 mm) were used. Visualization was accomplished by UV light (254 nm), KMnO4, and ceric ammonium molybdate strain.

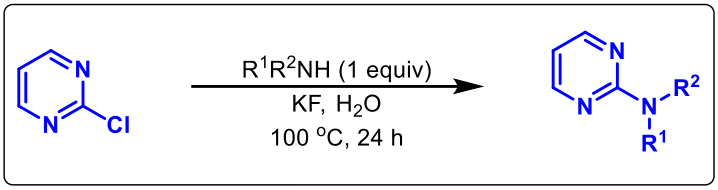
Chemicals: Commercially available chemicals were purchased from Sigma–Aldrich, Combi-Blocks, TCI Chemicals, BLD Pharma, Alfa–Aesar, and Avra Synthesis and used without further purification. 2-Aminoazines, polyfluoroarenes,[2] **1'l**,[3] and **5b**[3] were prepared by following the literature procedures.

2. Preparation of starting materials and their characterization

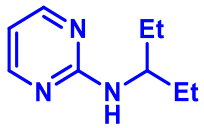
Table S1. Preparation of 2-aminopyrimidines



General procedure for preparation of substrates 1a-1l

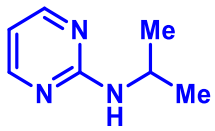


2-Aminopyrimidines **1a-1l** were prepared according to the literature procedure.[4] To a 15 mL sealed tube was added 2-chloropyrimidine (4 mmol), amine (4 mmol), and potassium fluoride (8 mmol) in water (2.5 mL), and the resulting mixture was heated to 100 °C for 17 h on an oil bath. Once cooled, the mixture was quenched with aqueous potassium carbonate solution (40 mL) and extracted into ethyl acetate (2 x 30 mL). The organic extracts were then combined and washed with brine before being dried over sodium sulfate, and the solvent evaporated under reduced pressure. The purification was carried out by column chromatography over silica gel. Yields are not optimized.



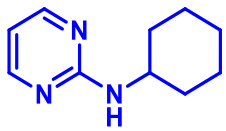
1a

N-(pentan-3-yl)pyrimidin-2-amine (1a):[5] Yield: 85% (3.4 mmol, 561 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.22 (d, *J* = 4.6 Hz, 2H), 6.45 (t, *J* = 4.8 Hz, 1H), 5.30 (d, *J* = 7.2 Hz, 1H), 3.88 (dd, *J* = 7.3, 1.7 Hz, 1H), 1.67 – 1.57 (m, 2H), 1.53 – 1.43 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.1, 110.0, 53.4, 27.2, 10.2.



1b

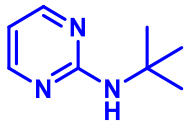
N-isopropylpyrimidin-2-amine (1b):[5] Yield: 84% (3.36 mmol, 460 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 4.7 Hz, 4H), 6.48 (d, *J* = 4.8 Hz, 2H), 4.12 (d, *J* = 7.4 Hz, 2H), 1.23 (d, *J* = 6.5 Hz, 13H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.0, 158.2, 110.3, 42.9, 23.0.



1c

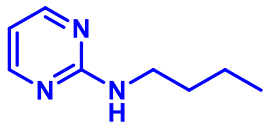
N-cyclohexylpyrimidin-2-amine (1c):[5] Yield: 77% (3.1 mmol, 545 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.22 (d, *J* = 4.7 Hz, 2H), 6.44 (t, *J* = 4.8 Hz, 1H), 5.27 (d, *J* = 4.3 Hz, 1H), 3.79 (ddd, *J* = 10.4, 9.3, 4.3 Hz, 1H), 2.06 – 1.98 (m, 2H), 1.76 – 1.68 (m, 2H), 1.65 – 1.57 (m, 1H), 1.39 (dd, *J* = 20.8, 7.7 Hz,

2H), 1.21 (dd, *J* = 16.9, 8.0 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.0, 158.1, 110.2, 49.7, 33.4, 25.9, 25.0.



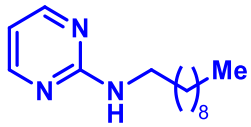
1d

N-(tert-butyl)pyrimidin-2-amine (1d):[5-6] Yield: 86% (3.44 mmol, 519 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.23 (d, *J* = 4.7 Hz, 2H), 6.46 (t, *J* = 4.8 Hz, 1H), 5.12 (s, 1H), 1.44 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.3, 157.7, 110.2, 50.9, 29.0.



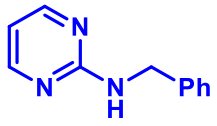
1e

N-butylpyrimidin-2-amine (1e):[5, 7] Yield: 76% (3.05 mmol, 459 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 4.7 Hz, 2H), 6.48 (t, *J* = 4.8 Hz, 1H), 5.30 (s, 1H), 3.38 (td, *J* = 7.2, 5.9 Hz, 2H), 1.63 – 1.53 (m, 2H), 1.40 (dd, *J* = 15.2, 7.4 Hz, 2H), 0.93 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.6, 158.1, 110.35, 41.3, 31.8, 20.2, 13.9.



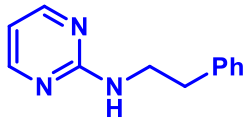
1f

N-decylpyrimidin-2-amine (1f):[8] Yield: 73% (2.9 mmol, 686 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.27 (d, *J* = 4.7 Hz, 2H), 6.51 (t, *J* = 4.8 Hz, 1H), 5.24 (s, 1H), 3.39 (td, *J* = 7.1, 5.9 Hz, 2H), 1.60 (dt, *J* = 14.8, 7.3 Hz, 2H), 1.27 (d, *J* = 13.1 Hz, 14H), 0.88 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.6, 158.1, 110.4, 41.6, 32.0, 29.8 – 29.7 (m), 29.5, 29.5, 27.1, 22.8, 15.0.



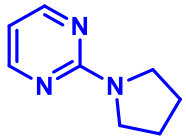
1g

N-benzylpyrimidin-2-amine (1g):[9] Yield: 59% (2.4 mmol, 436 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.20 (s, 2H), 7.34 (q, *J* = 8.0 Hz, 4H), 7.30 – 7.25 (m, 1H), 6.51 (t, *J* = 4.8 Hz, 1H), 5.97 (s, 1H), 4.64 (d, *J* = 5.9 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.4, 158.2, 128.7, 127.7, 127.4, 110.9, 45.6.



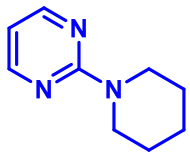
1h

N-phenethylpyrimidin-2-amine (1h):[10] Yield: 78% **(**3.1 mmol, 620 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 4.7 Hz, 4H), 7.33 – 7.27 (m, 5H), 7.23 (d, *J* = 7.5 Hz, 7H), 6.52 (t, *J* = 4.8 Hz, 2H), 5.18 (s, 2H), 3.77 – 3.63 (m, 5H), 2.92 (t, *J* = 7.0 Hz, 5H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.2, 139.3, 129.0, 128.7, 126.5, 110.7, 42.7, 35.8.



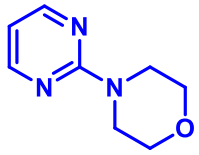
1i

2-(pyrrolidin-1-yl)pyrimidine (1i):[11] Yield: 72% (2.9 mmol, 429 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 4.7 Hz, 2H), 6.41 (t, *J* = 4.7 Hz, 1H), 3.56 – 3.51 (m, 4H), 1.96 (dd, *J* = 6.5, 3.3 Hz, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.3, 157.8, 108.9, 46.7, 25.7.



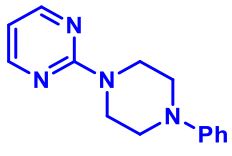
1j

2-(piperidin-1-yl)pyrimidine (1j):[11] Yield: 85% (3.4 mmol, 554 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 4.7 Hz, 2H), 6.40 (t, *J* = 4.7 Hz, 1H), 3.78 – 3.74 (m, 4H), 1.69 – 1.63 (m, 2H), 1.62 – 1.56 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.7, 157.8, 109.1, 44.8, 25.8, 25.0.



1k

4-(pyrimidin-2-yl)morpholine (1k):[11] Yield: 84% (3.4 mmol, 554 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.29 (d, *J* = 4.7 Hz), 6.49 (t, *J* = 4.7 Hz), 3.75 (tt, *J* = 6.9, 2.8 Hz). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.9, 157.8, 110.4, 66.9, 44.3.

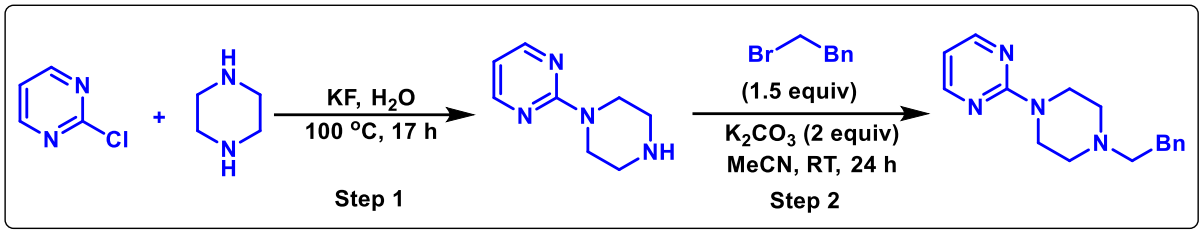


1l

2-(4-phenylpiperazin-1-yl)pyrimidine (1l):[4] Yield: 79% (3.2 mmol, 758 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.34 (d, *J* = 4.7 Hz), 7.29 (t, *J* = 7.8 Hz), 6.98 (d, *J* = 8.4 Hz), 6.89 (t, *J* = 7.3 Hz), 6.51 (t, *J* =

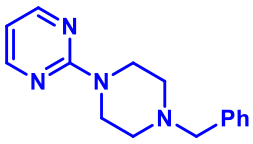
4.7 Hz), 4.01 – 3.98 (m), 3.27 – 3.24 (m). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.8, 157.9, 151.5, 129.3, 120.2, 116.6, 110.2, 49.4, 43.8.

General procedure for preparation of substrates 1m



Step 1: To a 15 mL sealed tube was added 2-chloropyrimidine (4 mmol), piperazine (4 mmol), and potassium fluoride (8 mmol) in solvent (2.5 mL), and the resulting mixture was heated to 100 °C for 17 h on an oil bath. Once cooled, the mixture was quenched with aqueous potassium carbonate solution (40 mL) and extracted into ethyl acetate (2 x 30 mL). The organic extracts were then combined and washed with brine before being dried over anhydrous sodium sulfate, and the solvent evaporated under reduced pressure. The 2-(piperazin-1-yl)pyrimidine was purified by column chromatography over silica gel using a mixture of MeOH/DCM as eluent.

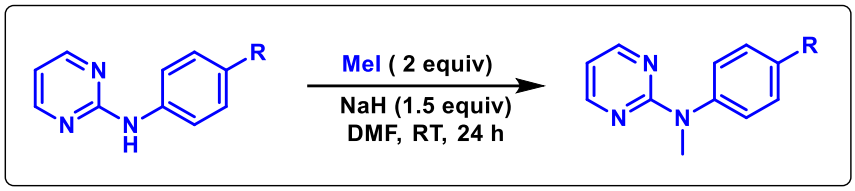
Step 2: To a solution of 2-(piperazin-1-yl)pyrimidine (3 mmol) in MeCN (6 mL) was added K_2CO_3 (6 mmol), followed by dropwise addition of benzyl bromide (4.5 mmol). The reaction mixture was stirred for 24 hours at 70 °C. The reaction mixture was cooled to room temperature and diluted with water and EtOAc. The organic layer was washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The product was purified by silica gel column chromatography using a mixture of EtOAc/n-hexane as eluent.



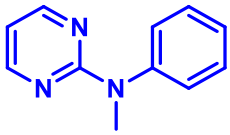
1m

2-(4-benzylpiperazin-1-yl)pyrimidine (1m): Yield: 52% (1.56, 396 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 4.8 Hz, 2H), 7.37 – 7.31 (m, 4H), 7.28 (dd, *J* = 5.7, 2.7 Hz, 1H), 6.46 (t, *J* = 4.8 Hz, 1H), 3.85 – 3.81 (m, 4H), 3.56 (s, 2H), 2.53 – 2.49 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.8, 157.8, 138.0, 129.4, 128.4, 127.3, 109.9, 63.3, 53.1, 43.8. **HRMS** calcd. for $C_{15}H_{19}N_4$ $[M+H]^+$: 255.1604 Found: 255.1601.

General procedure for preparation of substrates 1n-1p

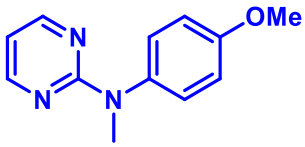


To a solution of *N*-arylpyrimidin-2-amine derivative (3 mmol) in dry DMF (6 mL) was added NaH (4.5 mmol), followed by dropwise addition of iodomethane (6 mmol). The reaction mixture was stirred for 24 hours at room temperature. Upon completion, the reaction mixture was diluted with water and EtOAc. The organic layer was washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The mixture was purified by silica gel column chromatography using a mixture of EtOAc/n-hexane as eluent to afford the desired product *N*-methyl-*N*-arylpyrimidin-2-amine derivatives.



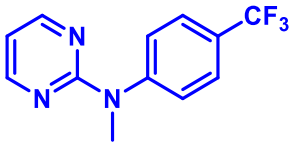
1n

N-methyl-N-phenylpyrimidin-2-amine (1n):[12] Yield: 84% (2.52 mmol, 466 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.34 (d, *J* = 4.6 Hz, 2H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.32 (d, *J* = 7.6 Hz, 2H), 7.24 (t, *J* = 7.4 Hz, 1H), 6.57 (t, *J* = 4.4 Hz, 1H), 3.53 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 1578, 145.7, 129.3, 126.7, 126.0, 110.9, 38.8.



1o

N-(4-methoxyphenyl)-N-methylpyrimidin-2-amine (1o):[13] Yield: 90% (2.7 mmol, 580 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 4.8 Hz, 2H), 7.24 – 7.19 (m, 2H), 6.97 – 6.92 (m, 2H), 6.53 (t, *J* = 4.7 Hz, 1H), 3.81 (s, 3H), 3.48 (s, 3H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.3, 157.8, 138.5, 128.0, 114.7, 110.4, 55.5, 39.0.

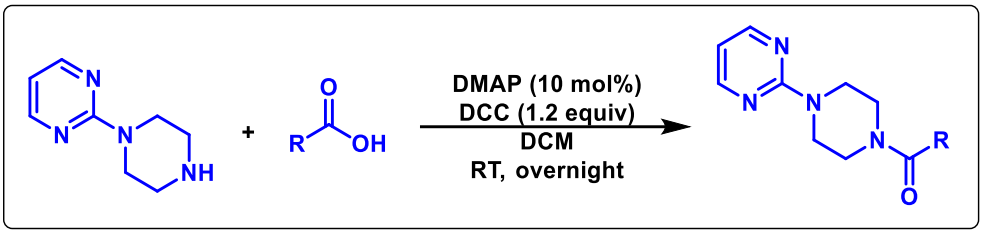


1p

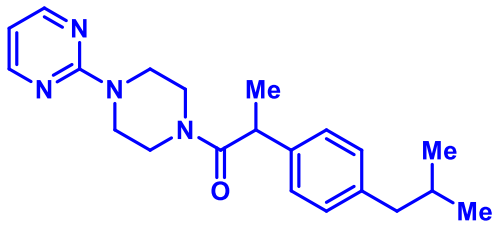
N-methyl-N-(4-(trifluoromethyl)phenyl)pyrimidin-2-amine (1p):[14] Yield: 75% (2.25 mmol, 570 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.38 (d, *J* = 3.8 Hz, 2H), 7.64 (d, *J* = 7.6 Hz, 2H), 7.48 (d, *J* = 7.8 Hz, 2H), 6.65 (d, *J* = 3.4 Hz, 1H), 3.58 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.6, 157.8, 148.6,

127.1 (q, $^{2}J_{C\text{-}F}$ = 32.8 Hz), 126.2 (q, $^{1}J_{C\text{-}F}$ = 2.5 Hz), 126.1, 124.3 (q, $^{3}J_{C\text{-}F}$ = 272.2 Hz), 111.9, 38.3. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -62.25.

General procedure for preparation of substrates 1q and **1r**

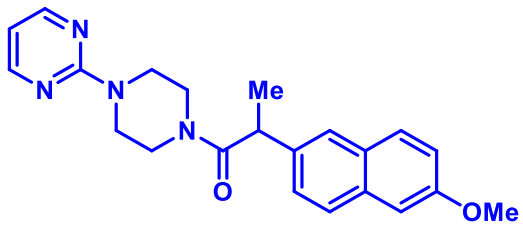


The piperazine derivatives **1q** and **1r** were prepared according to the literature procedure.[15] To a stirred solution of 2-(piperazin-1-yl)pyrimidine (3 mmol) and the carboxylic acid (3 mmol) in DCM (9 mL) was added DCC (3.6 mmol) and DMAP (10 mol%). The solution was stirred for 24 h at room temperature, during which a white precipitate was formed. The solids were filtered, and the filtrate was washed with saturated $NaHCO_3$ solution (2 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude mixture was purified by silica gel column chromatography using a mixture of EtOAc/n-hexane as eluent.



1q

2-(4-isobutylphenyl)-1-(4-(pyrimidin-2-yl)piperazin-1-yl)propan-1-one (1q): Yield: 82% (2.5 mmol, 865 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 4.7 Hz, 2H), 7.15 (d, *J* = 8.2 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 6.48 (t, *J* = 4.8 Hz, 1H), 3.99 – 3.85 (m, 3H), 3.81 – 3.75 (m, 1H), 3.58 – 3.47 (m, 2H), 3.46 – 3.37 (m, 2H), 3.10 – 3.03 (m, 1H), 2.42 (d, *J* = 7.2 Hz, 2H), 1.87 – 1.77 (m, 1H), 1.46 (d, *J* = 6.8 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.6, 161.5, 157.8, 140.4, 129.8, 127.0, 110.4, 45.4, 45.1, 43.5 (d, *J* = 6.3 Hz), 43.3, 42.0, 30.3, 22.5, 20.8. **HRMS** calcd. for $C_{21}H_{29}N_4O$ $[M+H]^+$: 353.2336 Found: 353.2343.

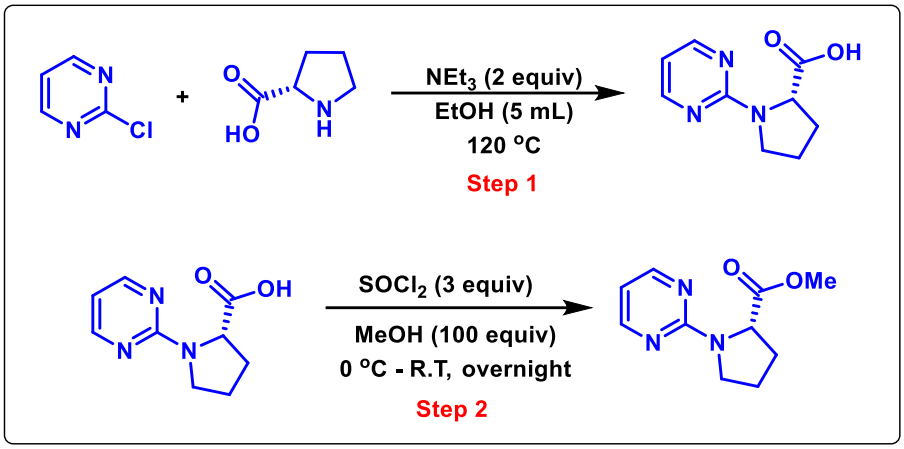


1r

2-(6-methoxynaphthalen-2-yl)-1-(4-(pyrimidin-2-yl)piperazin-1-yl)propan-1-one (1r): Yield: 69% (2.1 mmol, 778 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 4.8 Hz, 2H), 7.69 (dd, *J* = 11.5, 8.8

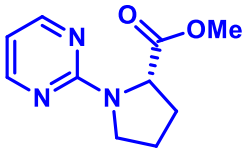
Hz, 2H), 7.62 (s, 1H), 7.37 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.16 – 7.08 (m, 2H), 6.46 (t, *J* = 4.6 Hz, 1H), 4.04 (q, *J* = 6.7 Hz, 1H), 3.99 – 3.92 (m, 2H), 3.90 (s, 3H), 3.75 (dt, *J* = 13.0, 4.5 Hz, 1H), 3.55 (d, *J* = 10.4 Hz, 2H), 3.47 (t, *J* = 4.6 Hz, 2H), 3.09 – 3.00 (m, 1H), 1.54 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.8, 129.2, 127.8, 126.1, 125.6, 110.4, 105.7, 55.4, 45.4, 43.6, 42.0, 20.9. **HRMS** calcd. for $C_{22}H_{25}N_4O_2$ $[M+H]^+$: 377.1972 Found: 377.1973.

Procedure for preparation of substrates 1s



Step 1: To a solution of 2-chloropyrimidine (4 mmol) in ethanol (5 mL) was added triethylamine (2 equiv) followed by the addition of L-proline (1.3 equiv). The reaction mixture was stirred at 120 °C overnight. Upon completion, the reaction mixture was quenched with water, diluted with EtOAc, and acidified to pH < 4 with 3 M HCl (aq.). Then, the aqueous layer was extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude carboxylic acid was used without further purification.

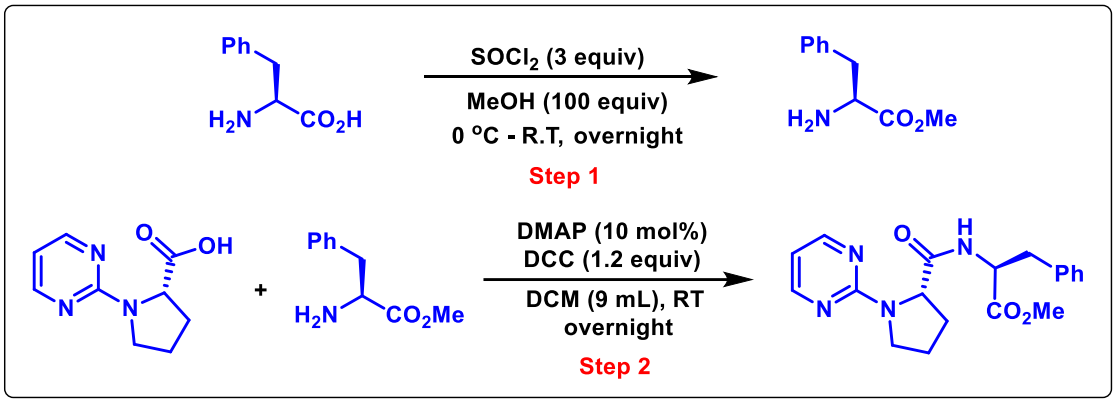
Step 2: pyrimidin-2-ylproline (2 mmol, 1.00 equiv) was dissolved in methanol (100 equiv), and the mixture was cooled with an ice bath to 0°C. Subsequently, thionyl chloride (3.00 equiv) was added dropwise, and the solution was stirred at room temperature overnight. The solution was neutralized with saturated $NaHCO_3$-solution, and then K_2CO_3 was added till a pH value of eight was acquired. Precipitating salts were dissolved by the addition of water. Afterward, the organic phase was extracted with DCM (7 × 150 mL), and the combined organic layers were dried over sodium sulfate, filtered, and concentrated *in vacuo*. The ester product was purified by silica gel column chromatography using a mixture of EtOAc/n-hexane as eluent to give **1s** in 58% yield.



1s

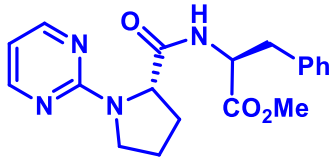
methyl pyrimidin-2-ylprolinate (1s):[16] Yield: 58% (1.2 mmol, 240 mg).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.29 (s, 2H), 6.50 (t, *J* = 4.8 Hz, 1H), 4.57 (dd, *J* = 8.6, 3.3 Hz, 1H), 3.84 – 3.76 (m, 1H), 3.71 (s, 3H), 3.69 – 3.64 (m, 1H), 2.39 – 2.27 (m, 1H), 2.19 – 1.92 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.3, 160.1, 157.8, 110.2, 59.6, 52.2, 47.1, 30.6, 24.2.

Procedure for preparation of substrates 1t



Step 1: L-phenylalanine (5 mmol, 1.00 equiv) was dissolved in methanol (100 equiv), and the mixture was cooled with an ice bath to 0°C. Subsequently, thionyl chloride (3.00 equiv) was added dropwise, and the solution was stirred at room temperature overnight. The solution was neutralized with saturated $NaHCO_3$-solution, and then K_2CO_3 was added till a pH value of eight was acquired. Precipitating salts were dissolved by the addition of water. Afterward, the organic phase was extracted with DCM (7 × 150 mL), the combined organic layers were dried over sodium sulfate, filtered, and concentrated under a vacuum. The ester product was purified by silica gel column chromatography using a mixture of EtOAc/n-hexane as eluent.

Step 2: To a stirred solution of methyl L-phenylalaninate (3 mmol) and the pyrimidin-2-ylproline (3 mmol) in DCM (9 mL) was added DCC (3.6 mmol) and DMAP (10 mol%). The solution was stirred for 24 h at room temperature, during which a white precipitate was formed. The solids were filtered, and the filtrate was washed with saturated $NaHCO_3$ solution (2 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude mixture was purified by silica gel column chromatography using a mixture of EtOAc/n-hexane as eluent to give **1t** in 68% yield.

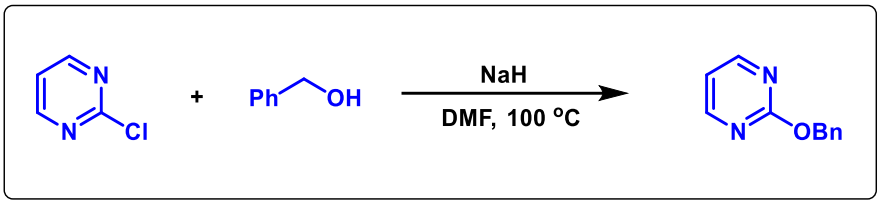


1t

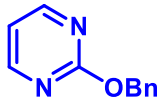
methyl pyrimidin-2-ylprolylphenylalaninate (1t): Yield: 68% (2.04 mmol, 722 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 4.6 Hz, 2H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.14 – 7.09 (m, 3H), 6.94 (dd, *J* = 6.4, 3.1 Hz, 2H), 6.51 (t, *J* = 4.8 Hz, 1H), 4.89 – 4.84 (m, 1H), 4.60 – 4.53 (m, 1H), 3.67 (s, 3H), 3.63

– 3.57 (m, 1H), 3.56 – 3.47 (m, 1H), 3.13 (dd, *J* = 13.9, 5.5 Hz, 1H), 2.96 (dd, *J* = 13.9, 6.4 Hz, 1H), 2.37 – 2.30 (m, 1H), 1.98 – 1.91 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.2, 172.0, 160.7, 157.7, 136.0, 129.2, 128.3, 126.9, 110.6, 60.8, 53.1, 52.3, 47.7, 37.9, 29.0, 24.4. **HRMS** calcd. for $C_{19}H_{23}N_4O_3$ $[M+H]^+$: 355.1765 Found: 355.1768.

Procedure for preparation of substrate 1u



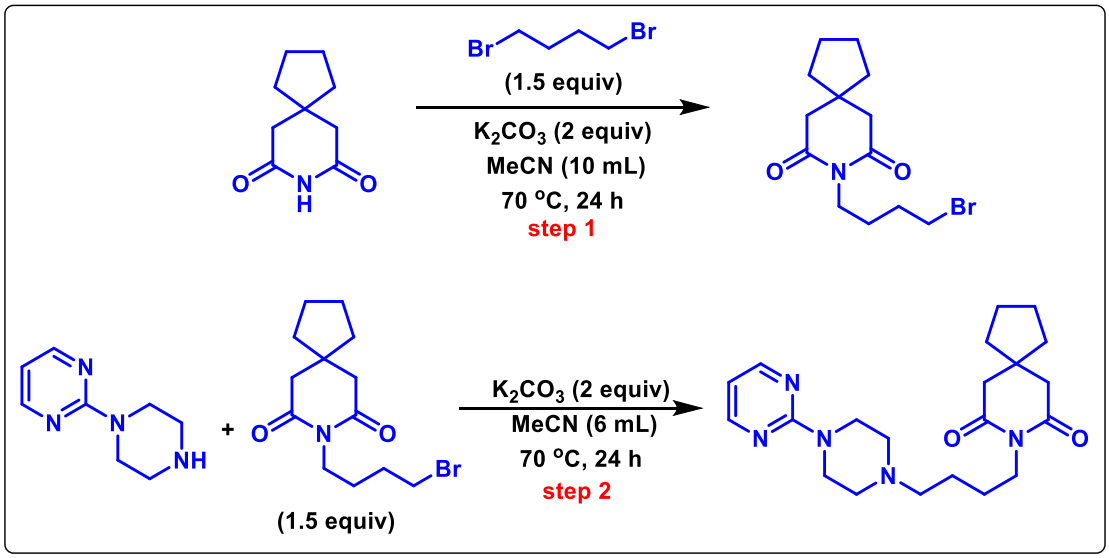
To a solution of benzylalcohol (1.5 equiv.) in DMF was added NaH (1.5 equiv.) slowly, and the reaction mixture was stirred for 1 hour at room temperature. A solution of 2-chloropyrimidine (3 mmol) was added slowly, and then the reaction mixture was stirred overnight at 100 °C. After cooling down, the resulting suspension was quenched with saturated NH_4Cl, diluted with EtOAc, and washed with water and brine. The solvents were removed, and the resulting mixture was purified by silica gel-packed flash chromatography.



1u

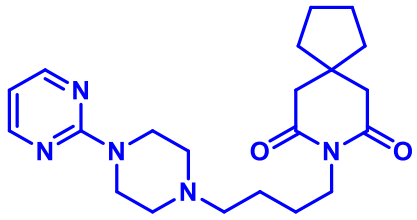
2-(benzyloxy)pyrimidine (1u):[11] Yield: 82% (2.46 mmol, 457 mg).**^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.51 (d, *J* = 4.8 Hz, 2H), 7.48 (d, *J* = 7.3 Hz, 2H), 7.36 (dd, *J* = 10.1, 4.7 Hz, 2H), 7.32 – 7.28 (m, 1H), 6.92 (t, *J* = 4.8 Hz, 1H), 5.45 (s, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.2, 159.4, 136.6, 128.5, 128.0, 115.2, 69.1.

Procedure for preparation of substrate 1v



Step 1: To a solution of amide (4 mmol) in MeCN (10 mL) was added K_2CO_3 (8 mmol), followed by dropwise addition of 1,4-dibromobutane (6 mmol). The reaction mixture was stirred for 24 hours at 70 °C. The reaction mixture was cooled to room temperature and diluted with water and EtOAc. The organic layer was washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The product was purified by silica gel column chromatography using a mixture of EtOAc/n-hexane as eluent.

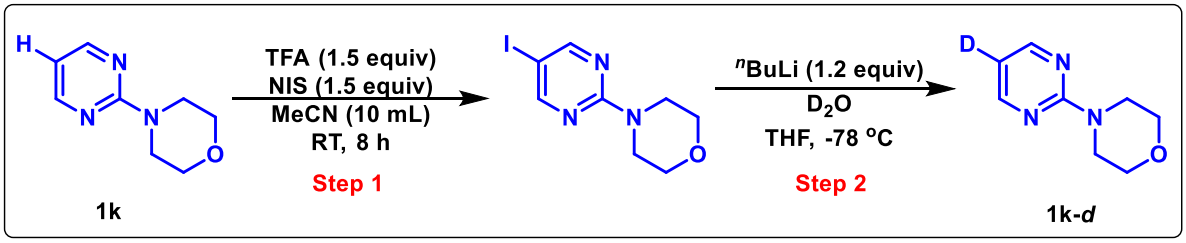
Step 2: To a solution of 2-(piperazin-1-yl)pyrimidine (2 mmol) in MeCN (6 mL) was added K_2CO_3 (4 mmol), followed by dropwise addition of alkyl bromide (3 mmol). The reaction mixture was stirred for 24 hours at 70 °C. The reaction mixture was cooled to room temperature and diluted with water and EtOAc. The organic layer was washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The product was purified by silica gel column chromatography using a mixture of EtOAc/n-hexane as eluent.



1v

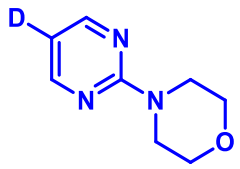
8-(4-(4-(pyrimidin-2-yl)piperazin-1-yl)butyl)-8-azaspiro[4.5]decane-7,9-dione (1v): Yield: 72% (1.44 mmol, 555 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 4.8 Hz, 2H), 6.45 (t, *J* = 4.7 Hz, 1H), 3.82 – 3.75 (m, 6H), 2.57 (s, 4H), 2.51 – 2.44 (m, 4H), 2.38 (t, *J* = 6.9 Hz, 2H), 1.73 – 1.66 (m, 4H), 1.53 – 1.46 (m, 8H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.3, 161.8, 157.8, 109.9, 58.4, 53.2, 45.0, 43.7, 39.6, 39.4, 37.7, 26.1, 24.3.

Procedure for preparation of substrates 1k-*d*



Step 1: To a solution of **1k** (3 mmol) in 10 mL of acetonitrile was added NIS (4.5 mmol) and TFA (1.5 equiv), and the resulting solution was stirred at room temperature for 8 h. The reaction mixture was diluted with 30 mL of CH_2Cl_2, washed with 10% sodium thiosulfate solution (30 mL) and 5% $NaHCO_3$ (2 × 20 mL), dried over MgSO4, filtered, and concentrated *in vacuo* to give a residue which was purified by silica gel column chromatography using a mixture of EtOAc/n-hexane as eluent.

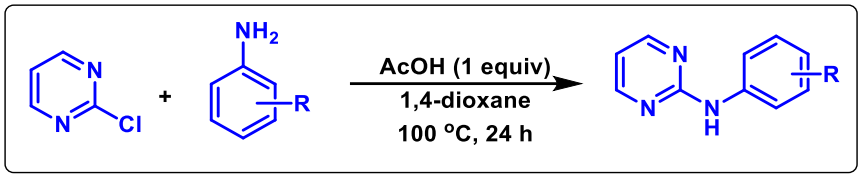
Step 2: To an oven-dried, two neck round bottom flask was added 4-(5-iodopyrimidin-2-yl)morpholine (1.5 mmol) and THF (15 mL) under nitrogen condition, the solution was cooled to -78 °C, and *n*-BuLi (1.5 mL, 2.5 M in THF) was added slowly. After stirring for one hour, D_2O (1 mL) was added to the reaction mixture. After stirring for two hours, the reaction mixture was allowed to warm to room temperature. The mixture was diluted with ethyl acetate, washed with water, dried over Na_2SO_4, and concentrated. The product was purified with silica gel chromatography using a mixture of EtOAc/n-hexane as eluent to give **1k**-*d* as a yellow oil (130 mg, 88%).



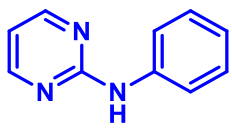
1k-*d*

4-(pyrimidin-2-yl-5-d)morpholine (**1k**-*d*)**: ^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.31 (s, 2H), 6.51 (t, *J* = 4.9 Hz, 0.09H), 3.81 – 3.78 (m, 4H), 3.77 – 3.74 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.9, 157.8, 110.4, 67.0, 44.3.

General procedure for preparation of substrates 1'a-1'h and 1'k

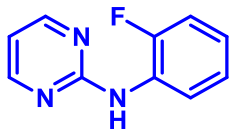


N-arylpyrimidin-2-amine derivatives were prepared according to the literature procedure.[17] To an oven-dried flask charged with aniline (7.5 mmol), 2-chloropyrimidine (5.0 mmol), and acetic acid (5 mL) in 1,4-dioxane (14 mL) were added. The reaction mixture was stirred at 110 °C for 24 h and monitored by TLC. Upon completion, the reaction mixture was extracted with EtOAc (3 × 20 mL) and washed with brine. The organic layer was dried over sodium sulfate and concentrated *in vacuo*. The residue was purified by silica gel column chromatography using a mixture of EtOAc/n-hexane as eluent.



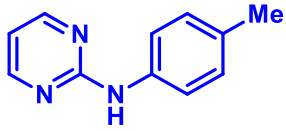
1'a

N-phenylpyrimidin-2-amine (1'a):[18] Yield: 76% (3.8 mmol, 650 mg) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.43 (d, *J* = 4.8 Hz, 2H), 7.71 (br s, 1H), 7.65 – 7.61 (m, 2H), 7.41 – 7.31 (m, 2H), 7.06 (t, *J* = 7.4 Hz, 1H), 6.72 (t, *J* = 4.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.4, 158.1, 139.5, 129.1, 122.9, 119.7, 112.6.



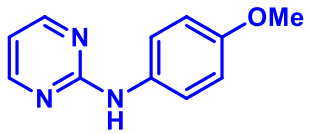
1'b

N-(2-fluorophenyl)pyrimidin-2-amine (1'b):[19] Yield: 70% (3.5 mmol, 661 mg) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.47 – 8.40 (m, 3H), 7.52 (br s, 1H), 7.19 – 7.08 (m, 2H), 7.01 – 6.95 (m, 1H), 6.76 (t, *J* = 4.8 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.1, 158.1, 152.8 (d, *J* = 243.0 Hz), 128.1 (d, *J* = 9.6 Hz), 124.4 (d, *J* = 3.7 Hz), 122.6 (d, *J* = 7.5 Hz), 121.1, 114.9 (d, *J* = 19.4 Hz), 113.2. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -131.04 (s).



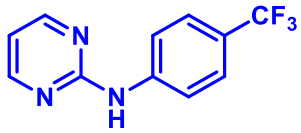
1'c

N-(p-tolyl)pyrimidin-2-amine (1'c):[18] Yield: 74% (3.7 mmol, 684 mg) **^{1}H NMR** (400 MHz $CDCl_3$) δ 8.40 (d, *J* = 4.8 Hz, 2H), 7.78 (s, 1H), 7.48 (d, *J* = 8.3 Hz, 2H), 7.15 (d, *J* = 8.3 Hz, 2H), 6.67 (t, *J* = 4.8 Hz, 1H), 2.33 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.6, 158.1, 136.9, 132.6, 129.6, 120.3, 112.3, 20.9.



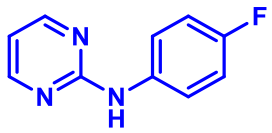
1'd

N-(4-methoxyphenyl)pyrimidin-2-amine (1'd):[18] Yield: 79% (3.95 mmol, 794 mg) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 4.8 Hz, 2H), 7.51 – 7.44 (m, 2H), 7.36 (br s, 1H), 6.93 – 6.88 (m, 2H), 6.68 – 6.64 (m, 1H), 3.80 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.8, 158.2, 156.0, 132.4, 122.4, 114.4, 112.2, 55.7.



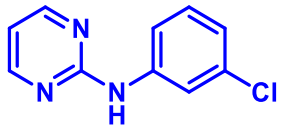
1'e

N-(4-(trifluoromethyl)phenyl)pyrimidin-2-amine (1'e):[20] Yield: 74% (3.7 mmol, 884 mg) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.48 (d, *J* = 4.8 Hz, 2H), 8.06 (br s, 1H), 7.77 (d, *J* = 8.5 Hz, 2H), 7.58 (d, *J* = 8.5 Hz, 2H), 6.81 (t, *J* = 4.8 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 159.9, 158.2, 142.8, 126.3 (q, $^{1}J_F$ = 3.7 Hz), 124.5 (q, $^{3}J_F$ = 272.2 Hz), 124.2 (q, $^{2}J_F$ = 32.8 Hz), 118.7, 113.5.



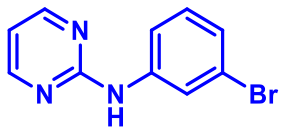
1'f

N-(4-fluorophenyl)pyrimidin-2-amine (1'f):[20] Yield: 82% (4.1 mmol, 775 mg) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 4.8 Hz, 2H), 7.59 – 7.51 (m, 2H), 7.36 (br s, 1H), 7.08 – 7.00 (m, 2H), 6.74 – 6.70 (m, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.3, 158.9 (d, *J* = 241.9 Hz), 158.2, 135.4 (d, *J* = 2.6 Hz), 121.7 (d, *J* = 7.6 Hz), 115.7 (d, *J* = 22.5 Hz), 112.7.



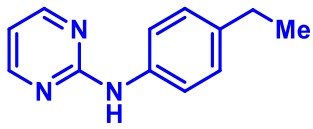
1'g

N-(3-chlorophenyl)pyrimidin-2-amine (1'g):[18] Yield: 80% (4.0 mmol, 820 mg) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.49 (d, *J* = 4.7 Hz, 2H), 7.92 – 7.87 (m, 1H), 7.55 (br s, 1H), 7.43 (d, *J* = 8.2 Hz, 1H), 7.31 – 7.27 (m, 1H), 7.05 (dd, *J* = 7.9, 0.8 Hz, 1H), 6.81 (t, *J* = 4.8 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 159.9, 158.1, 140.8, 134.8, 130.0, 122.7, 119.3, 117.4, 113.2.



1'h

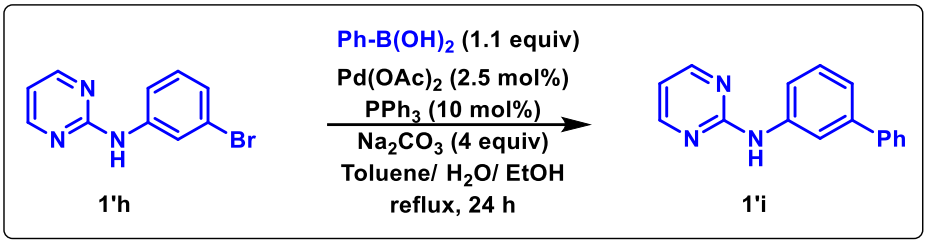
N-(3-bromophenyl)pyrimidin-2-amine (1'h):[21] Yield: 55% (2.2 mmol, 545 mg) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.45 (d, *J* = 4.8 Hz, 2H), 7.99 (t, *J* = 1.8 Hz, 1H), 7.64 (s, 1H), 7.46 (dt, *J* = 7.4, 2.0 Hz, 1H), 7.21 – 7.15 (m, 2H), 6.77 (t, *J* = 4.8 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.0, 158.1, 141.0, 130.3, 125.5, 122.8, 122.2, 117.9, 113.2.



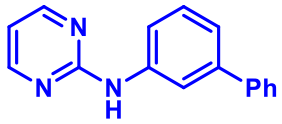
1'k

N-(4-ethylphenyl)pyrimidin-2-amine (1'k):[22] Yield: 59% (2.95 mmol, 587 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.40 (d, *J* = 4.8 Hz, 2H), 7.95 (br s, 1H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 6.67 (t, *J* = 4.8 Hz, 1H), 2.64 (q, *J* = 7.6 Hz, 2H), 1.24 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.6, 158.1, 139.1, 137.1, 128.4, 120.4, 112.2, 28.4, 15.8.

Procedure for preparation of substrate 1'i



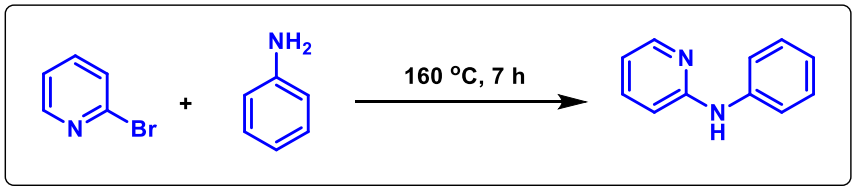
1'i was prepared by the following procedure. An oven-dried two-neck round bottom flask equipped with a reflux condenser and a stir bar. **1'h** (3 mmol), phenylboronic acid (1.1 equiv), $Pd(OAc)_2$ (2.5 mol%), PPh_3 (10 mol%), Na_2CO_3 (4 equiv) and Toluene/H_2O/EtOH (25 mL, 5/1/1) were taken under N_2. The reaction mixture was stirred at reflux overnight. To quench 1M NaOH was added. The reaction mixture was extracted with DCM (3× 20 mL), dried over Na_2SO_4, and concentrated in vacuo. The crude residue was purified by silica-gel column chromatography using a mixture of EtOAc/n-hexane as an eluent to give the title product **1'i** as a white solid.



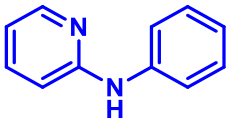
1'i

N-([1,1'-biphenyl]-3-yl)pyrimidin-2-amine (1'i): Yield: 72% (2.16 mmol, 533 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.44 (d, *J* = 4.8 Hz, 2H), 7.86 (t, *J* = 1.9 Hz, 1H), 7.74 (br s, 1H), 7.66 – 7.61 (m, 3H), 7.47 – 7.40 (m, 3H), 7.38 – 7.34 (m, 1H), 7.31 – 7.29 (m, 1H), 6.74 (t, *J* = 4.8 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.1, 158.1, 142.3, 141.3, 139.8, 129.4, 128.9, 127.5, 127.4, 122.0, 118.8, 118.7, 112.6. **HRMS** calcd. for $C_{16}H_{14}N_3$ $[M+H]^+$: 248.1182 Found: 248.1181.

Procedure for preparation of substrate 1'j



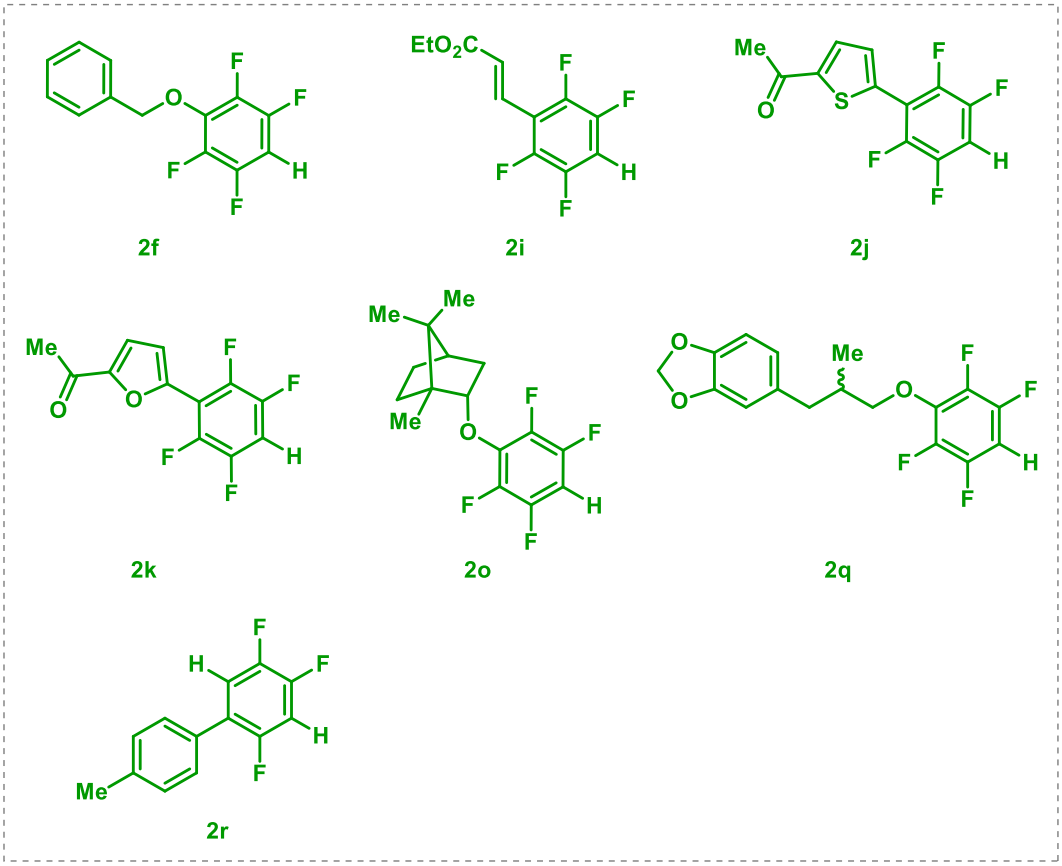
To an oven-dried flask containing 2-bromopyridine (5.0 mmol), aniline (5.0 mmol) was added. The reaction mixture was stirred at 160 °C for 7 h and monitored by TLC. Upon completion, saturated $NaHCO_3$ was added, and the reaction mixture was extracted with ethyl acetate (3×30 mL). The combined organic phase was washed with brine and dried over Na_2SO_4. After that, the solid was filtered off through a thin pad of celite, and the filtrate was evaporated in a vacuum to give the crude product which was purified by column chromatography on silica gel to give **1'j** as a white solid. 52% yield



1'j

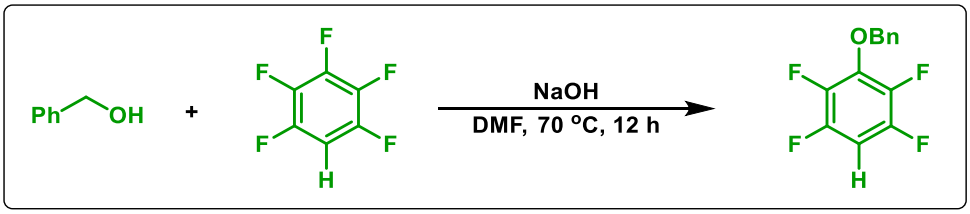
N-phenylpyridin-2-amine (1'j):[18] Yield: 52% (2.6 mmol, 442 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.21 (ddd, *J* = 5.0, 1.9, 0.9 Hz, 1H), 7.52 – 7.46 (m, 1H), 7.34 (dd, *J* = 4.1, 3.6 Hz, 4H), 7.09 – 7.02 (m, 1H), 6.89 (d, *J* = 8.4 Hz, 1H), 6.82 (br s, 1H), 6.76 – 6.71 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.2, 148.6, 140.6, 137.8, 129.4, 122.9, 120.5, 115.1, 108.3.

Table S2. Preparation of polyfluoroarene substrates

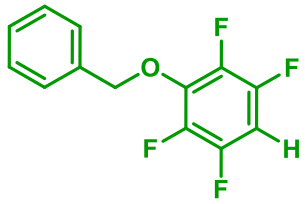


Polyfluoroarenes **2f**, **2i-2k**, **2o**, **2q** and **2r** were prepared by following the reported literature procedures, and the rest of the polyfluoroarenes were previously synthesized[2] and characterized by our group or commercially available.

Procedure for preparation of substrates 2f, 2o and 2q

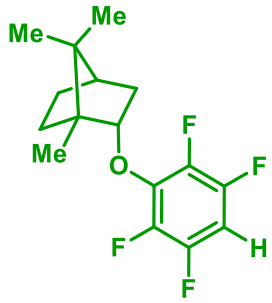


Polyfluoroarene **2f**, **2o**, and **2q** were prepared by following the literature procedures.[23] To an oven-dried round bottom flask were added benzyl alcohol (5 mmol), pentafluorobenzene (6 mmol), and sodium hydroxide (1.5 equiv) in anhydrous DMF (5 mL). The reaction was capped and stirred at 70 °C for 12 h. The reaction mixture was cooled to room temperature, quenched with water (30 mL), and extracted with EtOAc (3 x 50 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude mixture was purified by silica gel column chromatography using a mixture of EtOAc/n-hexane as eluent.



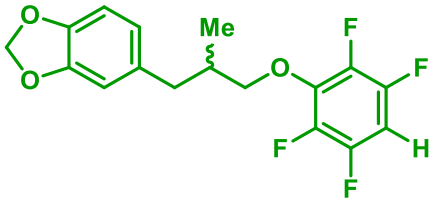
2f

3-(benzyloxy)-1,2,4,5-tetrafluorobenzene (2f):[23] Yield: 64% (3.2 mmol, 819 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 6.6 Hz, 2H), 7.38 (td, *J* = 8.4, 4.5 Hz, 3H), 6.76 (tt, *J* = 10.0, 7.0 Hz, 1H), 5.26 (s, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 147.8 – 147.5 (m), 145.3 – 145.0 (m), 142.8 – 142.6 (m), 140.4 – 140.1 (m), 137.8 – 137.5 (m), 135.7, 129.0, 128.8, 128.5, 99.9 (t, *J* = 23.1 Hz), 76.5 (t, *J* = 3.6 Hz).



2o

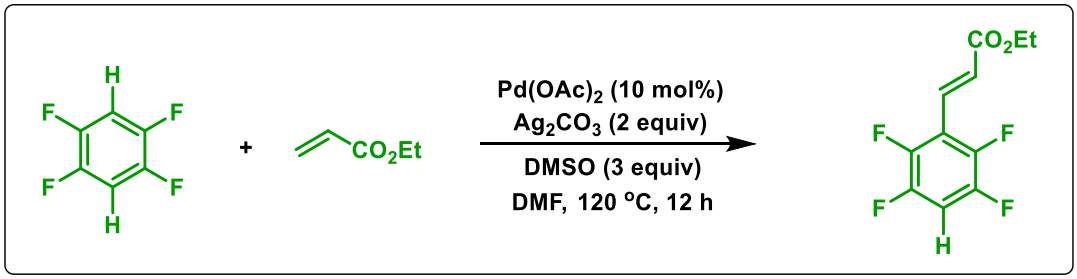
(1S,2S,4R)-1,7,7-trimethyl-2-(2,3,5,6-tetrafluorophenoxy)bicyclo[2.2.1]heptane (2o): Yield: 43% (1.7 mmol, 519 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.73 (tt, *J* = 9.9, 7.0 Hz, 6H), 4.50 (dd, *J* = 9.7, 1.5 Hz, 6H), 2.26 (dq, *J* = 7.8, 5.3 Hz, 13H), 1.79 (ddd, *J* = 10.0, 8.9, 5.1 Hz, 7H), 1.41 – 1.24 (m, 22H), 0.95 (s, 18H), 0.90 (s, 18H), 0.87 (s, 18H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 147.5 (dt, *J* = 12.6, 6.2 Hz), 145.5 (td, *J* = 12.7, 4.1 Hz), 142.6 – 142.2 (m), 140.7 – 140.2 (m), 139.0 (tq, *J* = 10.6, 3.5 Hz), 99.2, 99.0, 98.8, 91.5 (d, *J* = 2.5 Hz), 50.4, 48.2, 45.1, 36.4, 28.2, 26.3, 19.9, 19.0, 13.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -145.55 (ddd, *J* = 10.5, 8.9, 4.5 Hz), -155.27 (dd, *J* = 23.3, 9.4 Hz). **HRMS** calcd. for $C_{16}H_{17}F_4O$ $[M\text{-}H]^-$: 301.1221 Found: 301.1224.



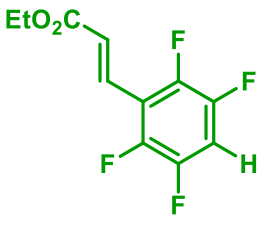
2q

5-(2-methyl-3-(2,3,5,6-tetrafluorophenoxy)propyl)benzo[d][1,3]dioxole (2q): Yield; 37% (1.5 mmol, 506 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.80 – 6.71 (m, 1H), 6.68 (d, *J* = 1.4 Hz, 1H), 6.63 (dd, *J* = 7.9, 1.5 Hz, 1H), 5.93 (s, 2H), 4.04 (p, *J* = 9.2 Hz, 2H), 2.82 (dd, *J* = 13.6, 6.4 Hz, 1H), 2.47 (dd, *J* = 13.6, 7.9 Hz, 1H), 2.23 – 2.08 (m, 1H), 1.04 (d, *J* = 6.8 Hz, 3H).. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 147.8 – 147.3 (m), 146.1, 145.5 (td, *J* = 12.8, 4.1 Hz), 142.5 – 142.1 (m), 140.4 – 140.1 (m), 138.7 (tt, *J* = 11.9, 3.6 Hz), 133.8, 122.2, 109.6, 108.2, 100.9, 99.6, 99.4, 99.2, 79.2, 39.1, 36.3, 16.4. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -139.27 – -140.77 (m), -156.85 (dt, *J* = 17.3, 9.8 Hz). **HRMS** calcd. for $C_{17}H_{15}F_4O_3$ $[M+H]^+$: 343.0952 Found: 303.0953.

Procedure for preparation of substrate 2i



To an oven-dried 25 mL sealed tube were added $Pd(OAc)_2$ (10 mol%) and Ag_2CO_3 (2.0 equiv) under N_2, followed by DMF (2.4 mL) and DMSO (3 equiv) with stirring. Next, 1,2,4,5-tetrafluorobenzene (0.6 mmol, 1.0 equiv) and ethyl acrylate (1.0 equiv) were added subsequently. The sealed tube was screw-capped and kept in a preheated oil bath at 120 °C. A total of three batches of this reaction were kept. After stirring for 12 h, the reaction mixture was cooled to room temperature and diluted with ethyl acetate, washed with 1 N HCl and brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified with silica gel chromatography to provide the product.

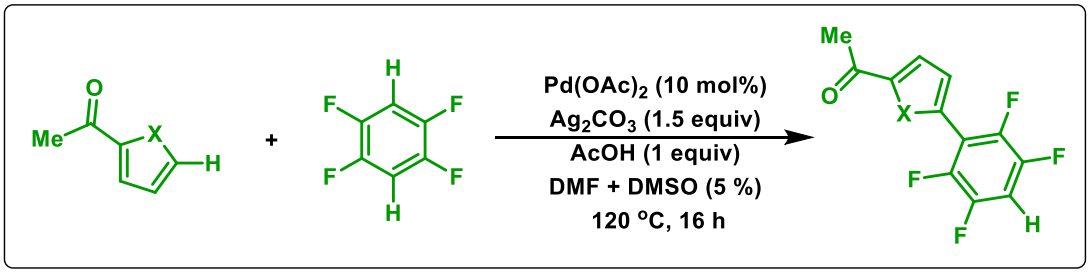


2i

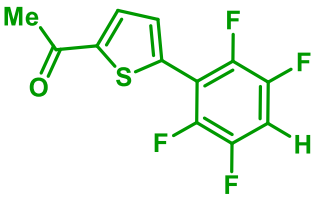
ethyl (E)-3-(2,3,5,6-tetrafluorophenyl)acrylate (2i):[24] Combined yield: 24% (0.43 mmol, 107 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 16.5 Hz, 1H), 7.09 (dq, *J* = 9.4, 7.5 Hz, 1H), 6.78 (d, *J* =

16.5 Hz, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.3, 147.5 – 147.2 (m), 146.6 – 146.4 (m), 145.1 – 144.8 (m), 144.2 – 143.9 (m), 143.2 – 142.9 (m) 129.2, 126.9 (t, *J* = 8.7 Hz), 106.9 (t, *J* = 22.7 Hz), 61.2, 14.4.

General procedure for preparation of substrates 2j and **2k**

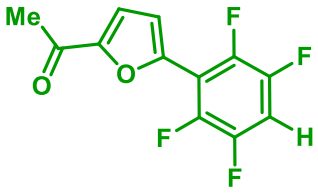


Polyfluoroarenes **2j** and **2k** were prepared according to the literature procedure.[25] To an oven-dried 25 mL sealed tube, were added $Pd(OAc)_2$ (10 mol%) and Ag_2CO_3 (1.5 equiv) under N_2, followed by solvent (2 mL) and additive with stirring. 1,2,4,5-tetrafluorobenzene (2.0 equiv) and heteroarene (thiophene or furan) (0.6 mmol, 1 equiv) were then added subsequently. The sealed tube was screw-capped and heated to 120 °C (oil bath). Two batches of this reaction were kept with 0.6 mmol each. After stirring for 16 h, the reaction mixture was cooled to room temperature, and the reaction mixture was diluted with ethyl acetate, washed with 1 N HCl and brine, dried over Na_2SO_4, filtered, and concentrated. The crude residue was purified with silica gel chromatography using a mixture of EtOAc/n-hexane as eluent to provide the pure product.



2j

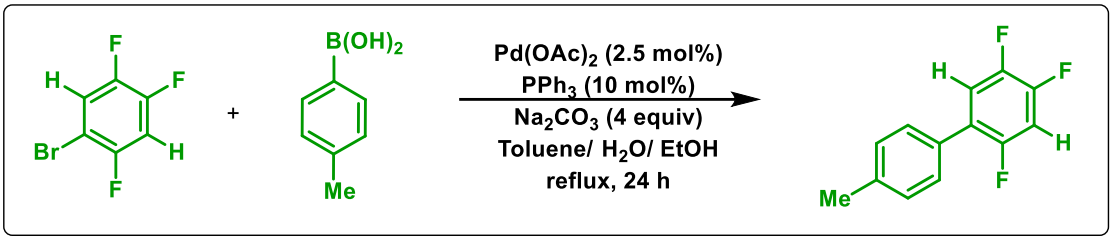
1-(5-(2,3,5,6-tetrafluorophenyl)thiophen-2-yl)ethan-1-one (2j): Combined yield: 71% (1.2 mmol, 233 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 3.7 Hz, 1H), 7.59 – 7.55 (m, 1H), 7.09 (tt, *J* = 9.3, 7.3 Hz, 1H), 2.60 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 190.7, 147.5 (ddd, *J* = 14.7, 10.6, 4.2 Hz), 146.0 (t, *J* = 3.5 Hz), 145.5 (ddd, *J* = 14.8, 10.6, 4.2 Hz), 144.8 (dt, *J* = 15.0, 4.3 Hz), 142.8 (dt, *J* = 14.8, 4.3 Hz), 135.7 – 135.1 (m), 132.0, 131.1 (t, *J* = 5.8 Hz), 114.3 (t, *J* = 14.6 Hz), 105.9, 105.7, 105.5, 27.0. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -137.95 – -138.13 (m), -139.12 – -139.29 (m). **HRMS** calcd. for $C_{12}H_7F_4OS$ $[M+H]^+$: 275.0148 Found: 275.0145.



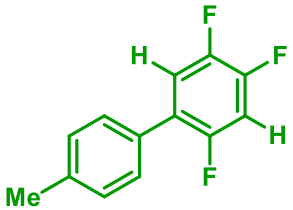
2k

1-(5-(2,3,5,6-tetrafluorophenyl)furan-2-yl)ethan-1-one (2k): Combined yield: 82% (1.2 mmol, 254 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 3.8 Hz, 1H), 7.11 (tt, *J* = 9.3, 7.3 Hz, 1H), 7.03 (dt, *J* = 3.7, 1.8 Hz, 1H), 2.56 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 190.7, 147.5 (ddd, *J* = 14.7, 10.6, 4.2 Hz), 146.0 (t, *J* = 3.5 Hz), 145.5 (ddd, *J* = 14.8, 10.6, 4.2 Hz), 144.8 (dt, *J* = 15.0, 4.3 Hz), 142.8 (dt, *J* = 14.8, 4.3 Hz), 135.7 – 135.1 (m), 132.0, 131.1 (t, *J* = 5.8 Hz), 114.3 (t, *J* = 14.6 Hz), 105.9, 105.7, 105.5, 27.0. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -137.97 – -138.29 (m), -139.97 – -140.43 (m). **HRMS** calcd. for $C_{12}H_7F_4O_2$ $[M+H]^+$: 259.0377 Found: 259.0379.

Procedure for preparation of substrates 2r



2r was prepared by the following procedure. An oven-dried two-neck round bottom flask equipped with a reflux condenser and a stir bar. 1-bromo-2,4,5-trifluorobenzene (3 mmol), 4-methylphenyllboronic acid (1.1 equiv), $Pd(OAc)_2$ (2.5 mol%), PPh_3 (10 mol%), Na_2CO_3 (4 equiv) and Toluene/H_2O/EtOH (25 mL, 5/1/1) were taken under N_2. The reaction mixture was stirred at reflux overnight. To quench 1M NaOH was added. The reaction mixture was extracted with DCM (3× 20 mL), dried over Na_2SO_4, and concentrated in vacuo. The crude residue was purified by silica-gel column chromatography using a mixture of EtOAc/n-hexane as an eluent to give the title product **2r** as colorless oil.



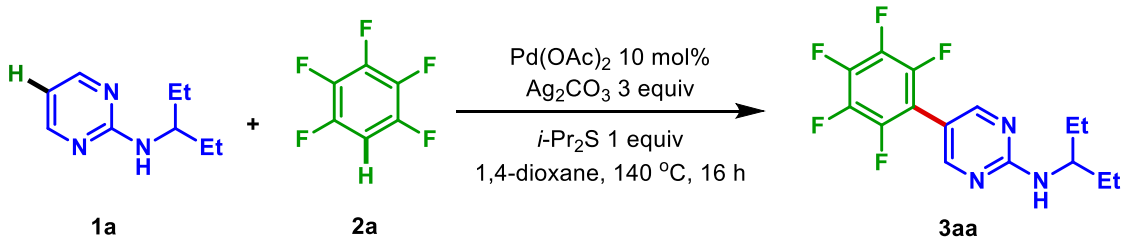
2r

2,4,5-trifluoro-4'-methyl-1,1'-biphenyl (2r):[26] Combined yield: 83% (2.48 mmol, 552 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 – 7.37 (m, 2H), 7.30 – 7.20 (m, 3H), 7.01 (td, *J* = 10.0, 6.7 Hz, 1H), 2.41 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 155.8 (dd, *J* = 9.2, 2.5 Hz), 153.8 (dd, *J* = 9.1, 2.1 Hz), 150.2 (dd, *J* = 14.3, 12.3 Hz), 148.3 – 148.0 (m), 146.1 (dd, *J* = 12.6, 3.6 Hz), 138.3, 131.2, 129.5, 128.8 (d, *J* =

2.9 Hz), 125.7 – 125.5 (m), 118.2 (dd, *J* = 19.5, 5.0 Hz), 106.2 (dd, *J* = 29.1, 20.7 Hz), 21.3. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -119.23 – -119.48 (m), -135.48 (ddd, *J* = 7.6, 4.2, 1.9 Hz), -142.74 – -143.05 (m).

3. Optimization studies for C5-H and N-H polyfluoroarylation of 2-aminopyrimidines

Table S3. Optimization of the reaction conditions for C5-H polyfluoroarylation[a]

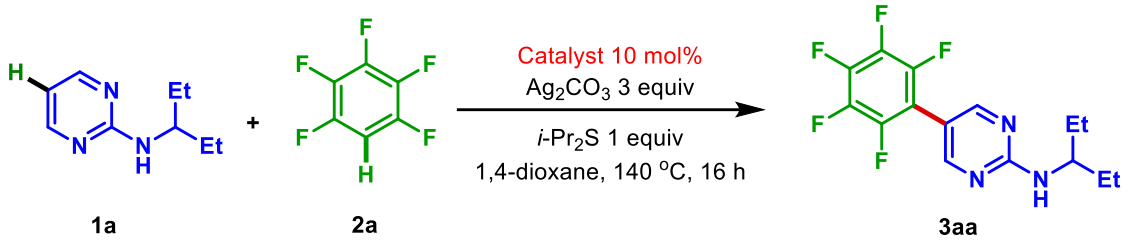


1a **2a** **3aa**

Entry	Deviation from above	Yield (%)[b]
1	**none**	**94**
2	AgOAc instead of Ag_2CO_3	61
3	$AgNO_3$ instead of Ag_2CO_3	55
4	Ag_2O instead of Ag_2CO_3	26
5	1 equiv Ag_2CO_3 + O_2 (1 atm) instead of 3 equiv Ag_2CO_3	38
6	1,4-Benzoquinone instead Ag_2CO_3	n.d.
7	DMSO instead of *i*-Pr_2S	38
8	PhSMe instead of *i*-Pr_2S	64
9	20 mol% pyridine instead of *i*-Pr_2S	15
10	DMF instead of 1,4-dioxane	12
11	DCE instead of 1,4-dioxane	8
12	MeCN instead of 1,4-dioxane	trace
13	DMSO instead of 1,4-dioxane	36
14	120 °C instead of 140 °C	58
15	24 h instead of 16 h	92

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), $Pd(OAc)_2$ (10 mol%), Ag_2CO_3 (3 equiv), *i*-Pr_2S (1 equiv), 1,4-dioxane (0.5 mL), 140 °C, 16 h. [b]Isolated yield. n.d. = not detected.

Table S4. Screening of metal salts[a]

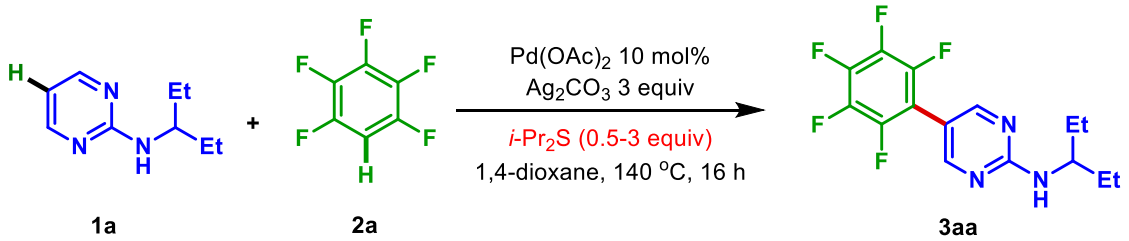


1a 2a 3aa

Entry	Catalyst	Yield (%)[b]
1	$Co(OAc)_2$	n.d.
2	$Ni(OAc)_2.4H_2O$	n.d.
3	$PdCl_2$	10
4	**$Pd(OAc)_2$**	**94**

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), catalyst (10 mol%), Ag_2CO_3 (3 equiv), *i*-Pr_2S (1 equiv), 1,4-dioxane (0.5 mL), 140 °C, 16 h. [b]Isolated yield.

Table S5. Optimization of equivalency of *i*-Pr_2S[a]

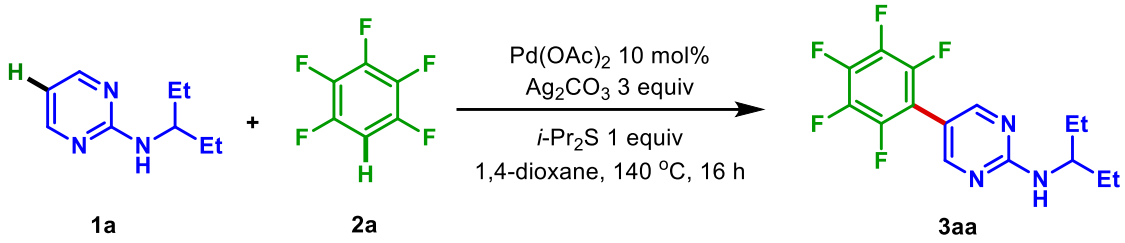


1a 2a 3aa

Entry	Equivalency of *i*-Pr_2S	Yield (%)[b]
1	0.5	68
2	**1**	**94**
3	3	95

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), $Pd(OAc)_2$ (10 mol%), Ag_2CO_3 (3 equiv), *i*-Pr_2S (0.5-3 equiv), 1,4-dioxane (0.5 mL), 140 °C, 16 h. [b]Isolated yield.

Table S6: Control experiments[a]

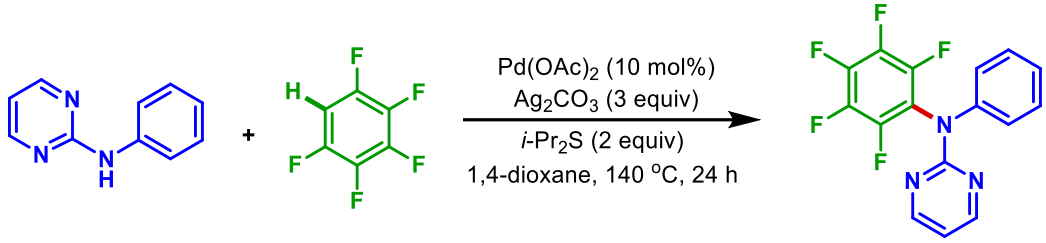


1a 2a 3aa

Entry	Deviation from above	Yield (%)[b]
1	Without Ag_2CO_3	10
2	Without *i*-Pr_2S	35
3	Without $Pd(OAc)_2$	n.d.

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), $Pd(OAc)_2$ (10 mol%), Ag_2CO_3 (3 equiv), *i*-Pr_2S (1 equiv), 1,4-dioxane (0.5 mL), 140 °C, 16 h. [b]Isolated yield. n.d. = not detected.

Table S7. Optimization of the reaction conditions for N-H polyfluoroarylation[a]

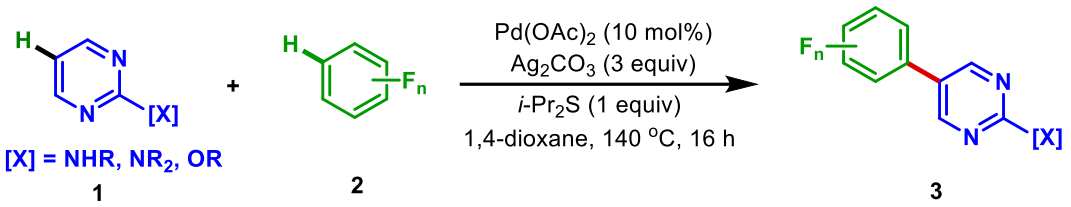


1'a 2a 4aa

Entry	Deviation from above	Yield (%)[b]
1	**none**	**56**
2	AgOAc instead of Ag_2CO_3	37
3	2 equiv of Ag_2CO_3 instead of 3 equiv	41
4	130 °C instead of 140 °C	36
5	PhSMe instead of *i*-Pr_2S	32
6	1 equiv of *i*-Pr_2S instead of 3 equiv	35
7	36 h instead of 24 h	53
8	Without *i*-Pr_2S	12
9	Without Ag_2CO_3	n.d.
10	Without $Pd(OAc)_2$	n.d.

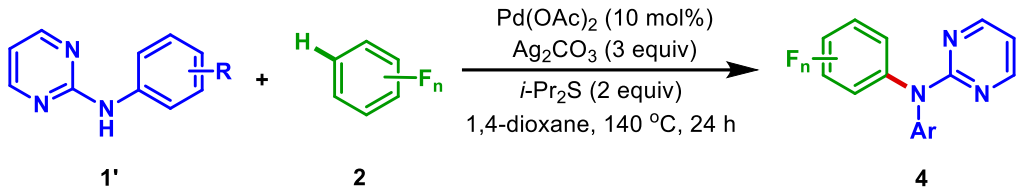
[a]Reaction conditions: **1'a** (0.1 mmol), **2a** (0.2 mmol), $Pd(OAc)_2$ (10 mol%), Ag_2CO_3 (3 equiv), *i*-Pr_2S (2 equiv), 1,4-dioxane (0.5 mL), 140 °C, 24 h. [b]Isolated yield. n.d. = not detected.

4. General procedure for Pd-catalyzed C-5 polyfluoroarylation of 2-aminopyrimidines



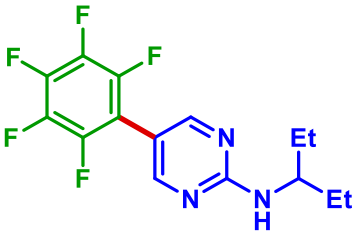
An oven-dried screw cap reaction tube was charged with a magnetic stir-bar, 2-aminopyrimidine substrate **1** (0.1 mmol, 1.0 equiv), $Pd(OAc)_2$ (10 mol%, 0.01 mmol, 2.3 mg) and Ag_2CO_3 (0.3 mmol, 3 equiv, 82 mg) were taken in air. Subsequently, 1,4-dioxane (0.5 mL), polyfluororarene **2** (0.4 mmol, 2 equiv), and isopropyl sulfide (0.1 mmol, 1 equiv, 14 μL) were added. The reaction tube was capped tightly and placed in a preheated oil bath at 140 °C. The reaction mixture was stirred vigorously for 16 h. After that, the resulting mixture was diluted with EtOAc, filtered through a plug of Celite, and concentrated under reduced pressure. The purification was carried out by column chromatography over silica gel using a mixture of EtOAc/n-hexane as eluent to afford the C-H polyfluoroarylated products **3**.

5. General procedure for Pd-catalyzed N-H polyfluoroarylation of *N*-phenylpyrimidin-2-amines



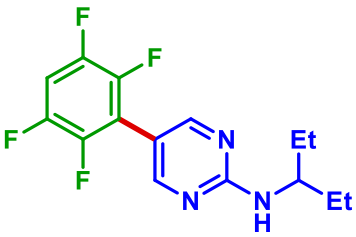
An oven-dried screw cap reaction tube was charged with a magnetic stir-bar, *N*-arylpyrimidin-2-amine substrate **1'** (0.1 mmol, 1.0 equiv), $Pd(OAc)_2$ (10 mol%, 0.01 mmol, 2.3 mg) and Ag_2CO_3 (0.3 mmol, 3 equiv, 82 mg) were taken in air. Subsequently, 1,4-dioxane (0.5 mL), polyfluororarene **2** (0.5 mmol, 2 equiv), and isopropyl sulfide (0.2 mmol, 2 equiv, 29 μL) were added. The reaction tube was capped tightly and placed in a preheated oil bath at 140 °C. The reaction mixture was stirred vigorously for 24 h. After that, the resulting mixture was diluted with EtOAc, filtered through a plug of Celite, and concentrated under reduced pressure. The purification was carried out by column chromatography over silica gel using a mixture of EtOAc/n-hexane as eluent to afford the C-H polyfluoroarylated products **4**.

6. Characterisation of product 3 and 4



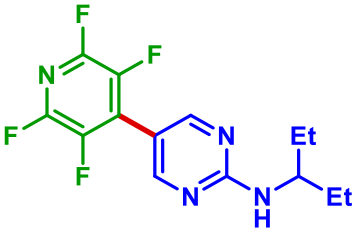
3aa

N-(pentan-3-yl)-5-(perfluorophenyl)pyrimidin-2-amine (3aa): Yield: 94% (0.094 mmol, 31 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.33 (s, 2H), 5.53 (s, 1H), 1.47 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.8, 158.2, 145.4 – 145.0 (m), 143.4 – 143.2 (m), 141.7 – 141.1 (m), 139.6 – 138.9 (m), 137.4 – 136.8 (m), 111.1 (td, *J* = 16.9, 4.0 Hz), 109.6, 51.5, 28.9. **^{19}F** (376 MHz, $CDCl_3$) δ -143.47 (d, *J* = 22.8 Hz), -155.34 (td, *J* = 20.7, 5.2 Hz), -161.62 (dd, *J* = 28.6, 15.3 Hz). **HRMS** calcd. for $C_{15}H_{15}F_5N_3$ $[M+H]^+$: 332.1181. Found: 332.1142.



3ab

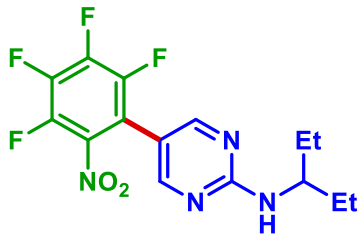
N-(pentan-3-yl)-5-(2,3,5,6-tetrafluorophenyl)pyrimidin-2-amine (3ab): Yield: 81% (0.081 mmol, 25.5 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.38 (s, 2H), 7.03 (tt, *J* = 9.6, 7.4 Hz, 1H), 5.61 (s, 1H), 3.96 (dqd, *J* = 8.9, 7.3, 5.6 Hz, 1H), 1.72 – 1.61 (m, 2H), 1.57 – 1.46 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.3, 158.7, 147.5 (ddd, *J* = 14.7, 10.9, 4.0 Hz), 145.5 (ddd, *J* = 14.9, 10.7, 4.0 Hz), 145.0 – 144.4 (m), 143.0 – 142.4 (m), 116.5 (t, *J* = 16.4 Hz), 110.6, 104.9 (d, *J* = 22.7 Hz), 104.6, 104.4 – 104.1 (m), 53.8, 27.2, 10.2. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -138.60 (dd, *J* = 22.7, 12.9 Hz), -144.09 (dd, *J* = 22.8, 12.9 Hz). **HRMS** calcd. for $C_{15}H_{16}F_4N_3$ $[M+H]^+$: 314.1275 Found: 314.1280.



3ac

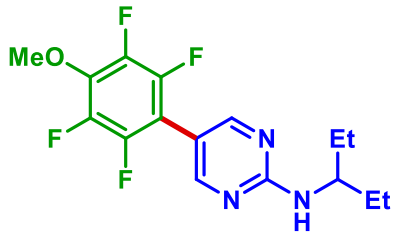
N-(pentan-3-yl)-5-(perfluoropyridin-4-yl)pyrimidin-2-amine (3ac): Yield: 72% (0.072 mmol, 22.5 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.50 (d, *J* = 37.5 Hz, 2H), 5.56 (d, *J* = 8.7 Hz, 1H), 4.04 – 3.94 (m, 1H), 1.73 – 1.63 (m, 2H), 1.53 (dp, *J* = 14.7, 7.4 Hz, 2H), 0.96 (t, *J* = 7.4 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.4, 159.0, 158.5, 145.4 – 145.2 (m), 143.6 – 143.2 (m), 140.2 – 139.7 (m), 138.3 – 137.7

(m), 128.7 – 128.5 (m), 109.9 – 109.4 (m), 54.1, 27.3, 10.2. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -90.30 – -90.66 (m), -145.43 – -145.60 (m). **HRMS** calcd. for $C_{14}H_{15}F_4N_4$ $[M+H]^+$: 315.1227 Found: 315.1227.



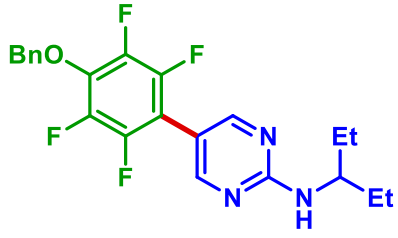
3ad

N-(pentan-3-yl)-5-(2,3,4,5-tetrafluoro-6-nitrophenyl)pyrimidin-2-amine (3ad): Yield: 58% (0.058 mmol, 21 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.20 (s, 2H), 5.36 (d, *J* = 8.8 Hz, 1H), 3.93 (dqd, *J* = 8.7, 7.1, 5.7 Hz, 1H), 1.65 (ddd, *J* = 9.1, 7.5, 3.8 Hz, 2H), 1.53 (td, *J* = 14.4, 7.3 Hz, 2H), 0.95 (t, *J* = 7.4 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.6, 157.9, 146.2 – 145.9 (m), 144.2 – 143.3 (m), 142.5 – 142.1 (m), 142.0 – 141.0 (m), 140.2 (ddd, *J* = 8.1, 4.7, 2.8 Hz), 139.5 – 138.9 (m), 116.1 (dd, *J* = 18.5, 4.2 Hz), 109.5 (s), 54.0, 27.1, 10.2. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -136.82 (ddd, *J* = 23.2, 11.0, 4.1 Hz), -146.34 (ddd, *J* = 21.9, 10.8, 5.6 Hz), -148.58 (ddd, *J* = 22.9, 20.5, 5.7 Hz), -151.27 (td, *J* = 20.9, 4.0 Hz). **HRMS** calcd. for $C_{15}H_{15}F_4N_4O_2$ $[M+H]^+$: 359.1126 Found: 359.1139.



3ae

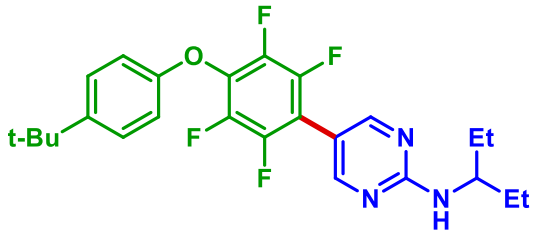
N-(pentan-3-yl)-5-(2,3,5,6-tetrafluoro-4-methoxyphenyl)pyrimidin-2-amine (3ae): Yield: 80% (0.08 mmol, 27.5 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.34 (s, 2H), 5.49 (d, *J* = 8.9 Hz, 1H), 4.10 (s, 3H), 3.99 – 3.91 (m, 1H), 1.70 – 1.61 (m, 2H), 1.56 – 1.47 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.1, 158.6, 145.6 – 145.2 (m), 143.6 – 143.2 (m), 142.4 (dt, *J* = 15.8, 4.2 Hz), 140.4 (dt, *J* = 15.8, 4.4 Hz), 137.7 – 137.5 (m), 110.4, 109.1 (t, *J* = 17.1 Hz), 62.3, 53.8, 27.2, 10.2. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -145.30 (d, *J* = 21.2 Hz), -157.67 (d, *J* = 20.6 Hz). **HRMS** calcd. for $C_{16}H_{18}F_4N_3O$ $[M+H]^+$: 344.1381 Found: 344.1379.



3af

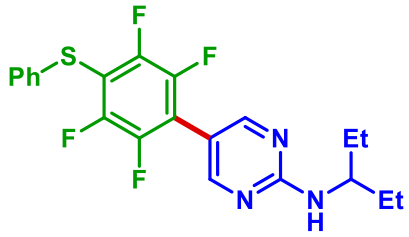
5-(4-(benzyloxy)-2,3,5,6-tetrafluorophenyl)-N-(pentan-3-yl)pyrimidin-2-amine (3af): Yield: 57% (0.057 mmol, 24 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.34 (s, 2H), 7.46 (dd, *J* = 7.7, 1.4 Hz, 2H), 7.42

– 7.33 (m, 3H), 5.29 (s, 2H), 5.26 (d, *J* = 9.1 Hz, 1H), 3.95 (dqd, *J* = 8.9, 7.2, 5.6 Hz, 1H), 1.72 – 1.60 (m, 2H), 1.58 – 1.46 (m, 2H), 0.95 (t, *J* = 7.5 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.1, 158.6, 145.4 – 145.2 (m), 143.7 – 143.1 (m), 142.9 (dt, *J* = 15.7, 4.3 Hz), 140.9 (dt, *J* = 15.7, 4.4 Hz), 136.4 – 135.9 (m), 110.5, 109.6 (t, *J* = 17.1 Hz), 76.6 (t, *J* = 3.5 Hz), 53.8, 27.2, 10.2.**^{19}F NMR** (376 MHz, $CDCl_3$) δ -145.10 (dd, *J* = 23.4, 9.7 Hz), -155.72 (dd, *J* = 23.0, 9.3 Hz). **HRMS** calcd. for $C_{22}H_{22}F_4N_3O$ $[M+H]^+$: 420.1694 Found: 420.1684.



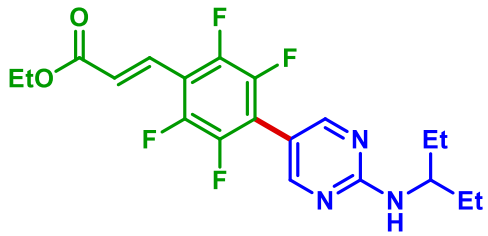
3ag

5-(4-(4-(tert-butyl)phenoxy)-2,3,5,6-tetrafluorophenyl)-N-(pentan-3-yl)pyrimidin-2-amine (3ag): Yield: 76% (0.076 mmol, 35 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.40 (br s, 2H), 7.37 – 7.33 (m, 2H), 6.97 – 6.92 (m, 2H), 5.38 (br s, 1H), 4.03 – 3.92 (m, 1H), 1.73 – 1.63 (m, 2H), 1.55 (td, *J* = 14.4, 7.3 Hz, 2H), 1.31 (s, 9H), 0.97 (t, *J* = 7.5 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.1, 158.7, 155.2, 146.9, 145.6 – 145.3 (m), 143.7 – 143.0 (m), 141.2 (dt, *J* = 16.0, 3.9 Hz), 133.1 (tt, *J* = 14.5, 4.0 Hz), 126.8, 115.2, 111.6 (t, *J* = 17.0 Hz), 110.2, 53.8, 34.5, 31.57, 27.2, 10.2. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -144.09 (dd, *J* = 23.5, 10.0 Hz), -153.81 (dd, *J* = 23.1, 9.8 Hz). **HRMS** calcd. for $C_{25}H_{28}F_4N_3O$ $[M+H]^+$: 462.2163 Found: 462.2161.



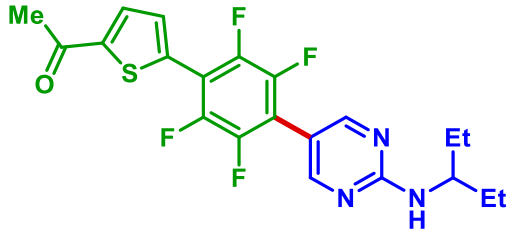
3ah

N-(pentan-3-yl)-5-(2,3,5,6-tetrafluoro-4-(phenylthio)phenyl)pyrimidin-2-amine (3ah): Yield: 56% (0.056 mmol, 23.5 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.41 (br s, 2H), 7.45 – 7.37 (m, 2H), 7.35 – 7.26 (m, 3H), 5.53 (d, *J* = 8.6 Hz, 1H), 4.02 – 3.93 (m), 1.72 – 1.62 (m, 2H), 1.59 – 1.47 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.0, 158.6, 148.5 (dt, *J* = 14.6, 3.3 Hz), 146.6 (dt, *J* = 14.6, 3.6 Hz), 145.2 – 144.6 (m), 143.3 – 142.8 (m), 133.2, 130.8, 129.5, 128.0, 116.7 (t, *J* = 16.5 Hz), 112.9, 112.8, 112.6, 110.4, 53.9, 27.2, 10.2.**^{19}F NMR** (471 MHz, $CDCl_3$) δ -108.59 (t, *J* = 5.6 Hz), -111.54 (d, *J* = 5.8 Hz). **HRMS** calcd. for $C_{21}H_{20}F_4N_3S$ $[M+H]^+$: 422.1309 Found: 422.1302.



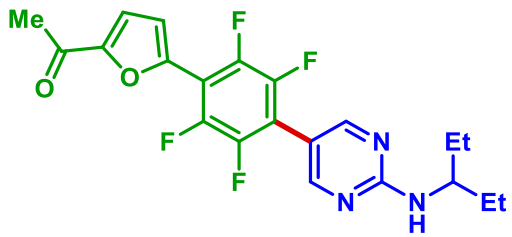
3ai

ethyl (E)-3-(2,3,5,6-tetrafluoro-4-(2-(pentan-3-ylamino)pyrimidin-5-yl)phenyl)acrylate (3ai): Yield: 65% (0.065 mmol, 27 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.45 (s, 2H), 7.72 (d, *J* = 16.5 Hz, 1H), 6.79 (d, *J* = 16.4 Hz, 1H), 5.45 (d, *J* = 8.4 Hz, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 4.02 – 3.92 (m, 1H), 1.71 – 1.62 (m, 2H), 1.58 – 1.48 (m, 2H), 1.35 (t, *J* = 7.2 Hz, 3H), 0.95 (t, *J* = 7.5 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.3, 162.1, 159.0 – 158.4 (m), 146.8 (ddd, *J* = 14.6, 6.6, 3.3 Hz), 145.2 – 144.6 (m), 143.1 – 142.6 (m), 129.1, 126.5 (t, *J* = 8.6 Hz), 116.7 (t, *J* = 16.4 Hz), 113.2 (t, *J* = 13.4 Hz), 110.5 (d, *J* = 4.0 Hz), 61.2, 53.9, 27.2, 14.4, 10.2. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -140.01 (td, *J* = 14.0, 2.8 Hz), -144.27 (dd, *J* = 22.9, 13.4 Hz). **HRMS** calcd. for $C_{20}H_{22}F_4N_3O_2$ $[M+H]^+$: 412.1643 Found: 412.1631.



3aj

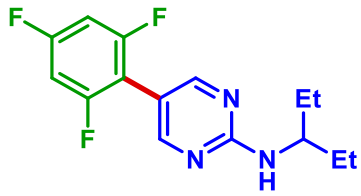
1-(5-(2,3,5,6-tetrafluoro-4-(2-(pentan-3-ylamino)pyrimidin-5-yl)phenyl)thiophen-2-yl)ethan-1-one (3aj): Yield: 64% (0.064 mmol, 28 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.43 (s, 2H), 7.73 (d, *J* = 3.8 Hz, 1H), 7.61 (d, *J* = 4.1 Hz, 1H), 5.57 (d, *J* = 9.0 Hz, 1H), 3.97 (dtd, *J* = 9.0, 7.3, 1.7 Hz, 1H), 2.60 (s, 3H), 1.73 – 1.61 (m, 2H), 1.52 (dt, *J* = 21.4, 7.4 Hz, 2H), 0.95 (t, *J* = 7.4 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 190.7, 162.2, 158.7, 145.8 (t, *J* = 3.5 Hz), 145.6 – 145.1 (m), 143.4 – 143.2 (m), 135.9 – 135.3 (m), 132.1, 131.0 (t, *J* = 6.1 Hz), 115.4 (t, *J* = 16.6 Hz), 112.2 (t, *J* = 14.7 Hz), 110.3, 53.8, 27.2, 27.0, 10.2. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -138.99 (td, *J* = 13.6, 3.1 Hz), -143.08 – -144.43 (m). **HRMS** calcd. for $C_{21}H_{19}F_4N_3OS$ $[M+H]^+$: 438.1258 Found: 438.1260.



3ak

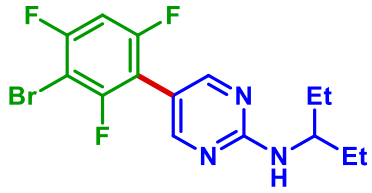
1-(5-(2,3,5,6-tetrafluoro-4-(2-(pentan-3-ylamino)pyrimidin-5-yl)phenyl)furan-2-yl)ethan-1-one (3ak): Yield: 44% (0.044 mmol, 18.5 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.45 (s, 2H), 7.32 (d, *J* = 3.7

Hz, 1H), 7.06 (dt, *J* = 3.6, 1.7 Hz, 1H), 5.37 (d, *J* = 9.1 Hz, 1H), 3.98 (ddq, *J* = 11.1, 7.3, 5.6 Hz, 1H), 2.57 (s, 3H), 1.73 – 1.63 (m, 2H), 1.59 – 1.48 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 187.2, 162.0, 159.3 – 157.9 (m), 153.3, 145.8 – 144.7 (m), 143.5 – 142.9 (m), 117.5, 115.9 (t, *J* = 6.5 Hz), 110.3, 108.7 (t, *J* = 13.7 Hz), 54.0, 27.2, 26.3, 10.2. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -140.04 (ddd, *J* = 23.6, 13.4, 2.4 Hz), -143.57 – -143.91 (m). **HRMS** calcd. for $C_{21}H_{20}F_4N_3O_2$ $[M+H]^+$: 422.1486 Found: 422.1445.



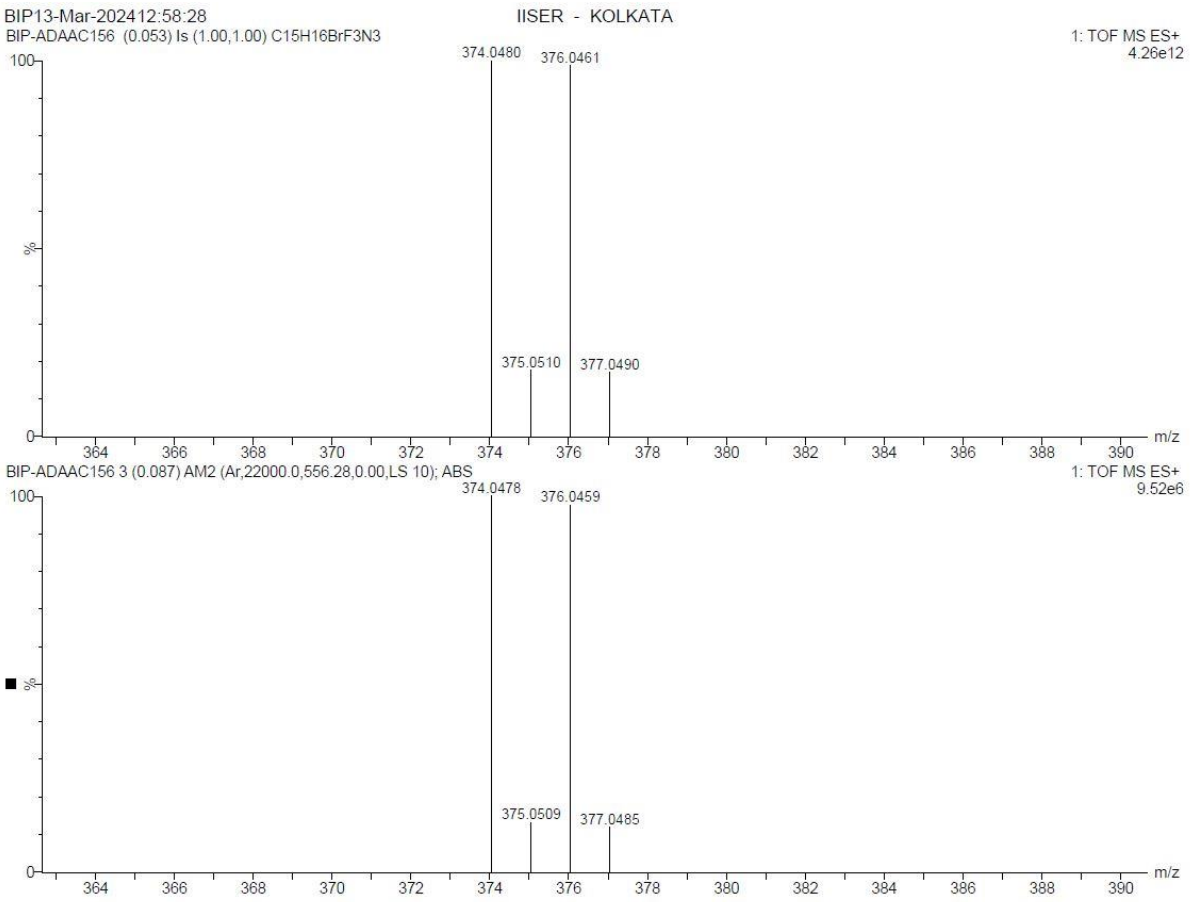
3al

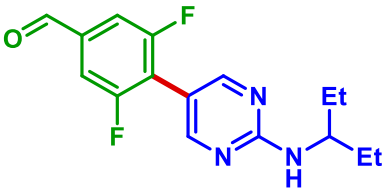
N-(pentan-3-yl)-5-(2,4,6-trifluorophenyl)pyrimidin-2-amine (3al): Yield: 68% (0.068 mmol, 20 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.33 (s, 2H), 6.83 – 6.65 (m, 2H), 5.38 (d, *J* = 8.8 Hz, 1H), 3.94 (dqd, *J* = 14.3, 7.2, 5.7 Hz, 1H), 1.71 – 1.59 (m, 2H), 1.50 (dt, *J* = 21.4, 7.4 Hz, 2H), 0.94 (t, *J* = 7.4 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.8 (t, *J* = 15.6 Hz), 162.0, 161.4 (dd, *J* = 14.7, 9.8 Hz), 160.9 (t, *J* = 15.7 Hz), 159.4 (dd, *J* = 14.8, 9.8 Hz), 158.7, 111.2, 109.8 (td, *J* = 19.2, 4.8 Hz), 101.3 – 100.4 (m), 53.7, 27.2, 10.2. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -108.59 (t, *J* = 5.6 Hz), -111.54 (d, *J* = 5.8 Hz). **HRMS** calcd. for $C_{15}H_{17}F_3N_3$ $[M+2H]^+$: 296.1369 Found: 296.1369.



3am

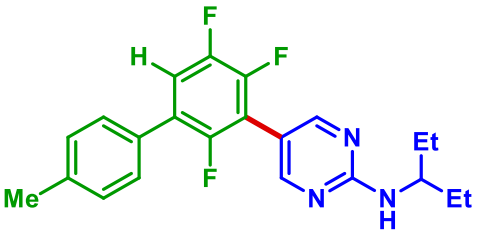
5-(3-bromo-2,4,6-trifluorophenyl)-N-(pentan-3-yl)pyrimidin-2-amine (3am): Yield: 70% (0.07 mmol, 26 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.32 (s, 2H), 6.95 – 6.82 (m, 1H), 5.26 (d, *J* = 8.8 Hz, 1H), 4.00 – 3.91 (m, 1H), 1.70 – 1.62 (m, 2H), 1.53 (td, *J* = 14.4, 7.3 Hz, 2H), 0.95 (t, *J* = 7.4 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.1, 160.3 – 159.9 (m), 159.9 – 159.5 (m), 158.7, 158.5 – 158.0 (m), 157.8 (dd, *J* = 15.2, 6.5 Hz), 156.4 (dd, *J* = 9.4, 6.2 Hz), 111.4 – 110.6 (m), 101.4 (td, *J* = 27.5, 3.7 Hz), 94.7 – 94.3 (m), 53.8, 27.2, 10.2. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -103.46 (s), -105.12 (s), -112.66 (s). **HRMS** calcd. for $C_{15}H_{16}{}^{79}BrF_3N_3$ $[M+H]^+$: 374.0480; Found: 374.0478. $C_{15}H_{16}{}^{81}BrF_3N_3$ $[M+H]^+$: 376.0461; Found: 374.0459.





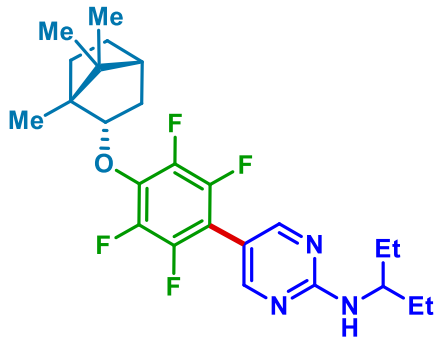
3an

3,5-difluoro-4-(2-(pentan-3-ylamino)pyrimidin-5-yl)benzaldehyde (3an): Yield: 36% (0.036 mmol, 11 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.94 (t, *J* = 1.7 Hz, 1H), 8.45 (s, 2H), 7.58 – 7.45 (m, 2H), 5.32 (d, *J* = 8.9 Hz, 1H), 4.02 – 3.39 (m, 1H), 1.73 – 1.62 (m, 2H), 1.54 (td, *J* = 14.4, 7.3 Hz, 2H), 0.96 (t, *J* = 7.4 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 189.1, 161.9, 161.4 (d, *J* = 7.2 Hz), 159.4 (d, *J* = 6.9 Hz), 159.2 – 158.4 (m), 136.7 (t, *J* = 7.8 Hz), 119.5 (t, *J* = 18.6 Hz), 112.8 (dd, *J* = 20.6, 7.0 Hz), 111.1 (s), 53.9, 27.3, 10.2. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.80 (dq, *J* = 7.9, 1.6 Hz). **HRMS** calcd. for $C_{16}H_{17}F_2N_3O$ $[M+H]^+$: 306.1412 Found: 306.1418.



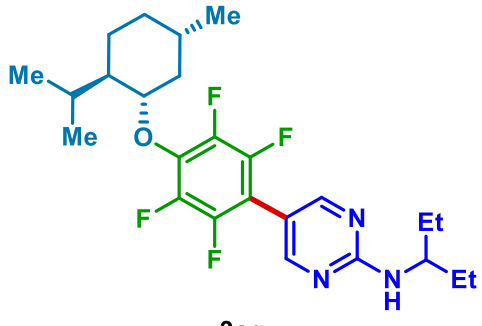
3ao

N-(pentan-3-yl)-5-(2,4,5-trifluoro-4'-methyl-[1,1'-biphenyl]-3-yl)pyrimidin-2-amine (3ao): Yield: 47% (0.047 mmol, 18 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.43 (s, 2H), 7.43 – 7.36 (m, 2H), 7.31 – 7.18 (m, 3H), 5.66 (s, 1H), 4.05 – 3.93 (m, 1H), 2.41 (s, 3H), 1.74 – 1.62 (m, 2H), 1.61– 1.50 (m, 2H), 0.97 (t, *J* = 7.4 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.1, 153.2 (dd, *J* = 4.1, 2.5 Hz), 150.8 (dd, *J* = 4.0, 2.6 Hz), 148.7 – 148.5 (m), 148.1 – 147.8 (m), 146.2 (dd, *J* = 13.3, 3.5 Hz), 145.5 (dd, *J* = 14.6, 6.8 Hz), 138.5, 131.2, 129.6, 128.9 (d, *J* = 3.0 Hz), 125.9 (ddd, *J* = 17.2, 6.2, 4.4 Hz), 116.8 (dd, *J* = 19.2, 4.7 Hz), 114.9 (dd, *J* = 21.7, 14.9 Hz), 111.6, 54.0, 27.2, 21.4, 10.2. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -123.77 – -123.92 (m), -139.57 (dt, *J* = 7.6, 2.9 Hz), -141.23 – -141.34 (m). **HRMS** calcd. for $C_{22}H_{23}F_3N_3$ $[M+H]^+$: 386.1839 Found: 386.1828.



3ap

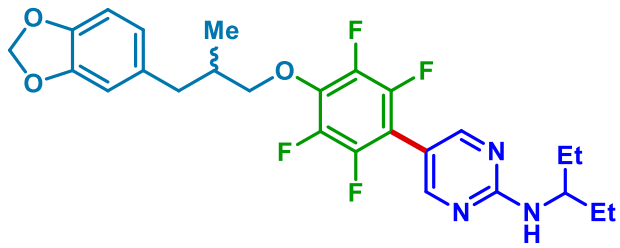
N-(pentan-3-yl)-5-(2,3,5,6-tetrafluoro-4-(((1S,2S,4R)-1,7,7-trimethylbicyclo[2.2.1]heptan-2 yl)oxy)phenyl)pyrimidin-2-amine (3ap): Yield: 64% (0.064 mmol, 30 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.35 (s, 2H), 5.38 (d, *J* = 9.0 Hz, 1H), 4.59 – 4.47 (m, 1H), 3.95 (ddt, *J* = 14.5, 9.0, 3.6 Hz, 1H), 2.36 – 2.20 (m, 2H), 1.88 – 1.43 (m, 6H), 1.43 – 1.28 (m, 3H), 0.99 – 0.85 (m, 14H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.0, 158.6, 145.6 – 145.2 (m), 143.7 – 143.1 (m), 142.7 (dt, *J* = 15.4, 4.2 Hz), 140.8 (dt, *J* = 15.5, 4.3 Hz), 137.5 (tt, *J* = 11.6, 2.9 Hz), 110.6, 108.6 (t, *J* = 17.1 Hz), 91.6 (t, *J* = 2.1 Hz), 53.8, 50.4, 48.3, 45.1, 36.5, 28.2, 27.2, 26.3, 19.9, 19.0, 13.6, 10.2. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -145.68 (dd, *J* = 23.7, 11.6 Hz), -156.32 (dd, *J* = 23.3, 11.6 Hz). **HRMS** calcd. for $C_{25}H_{32}F_4N_3O$ $[M+H]^+$: 466.2476 Found: 466.2490.



3aq

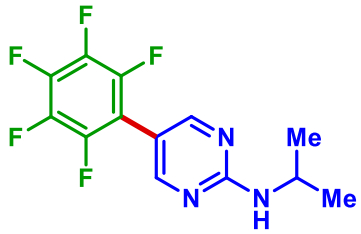
N-(pentan-3-yl)-5-(2,3,5,6-tetrafluoro-4-(((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)oxy)phenyl)pyrimidin-2-amine (3aq): Yield: 75% (0.075 mmol, 35 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.36 (s, 2H), 5.33 (d, *J* = 9.0 Hz, 1H), 4.17 (td, *J* = 10.6, 4.3 Hz, 1H), 4.03 – 3.90

(m, 1H), 2.40 (dtd, *J* = 13.6, 6.8, 2.3 Hz, 1H), 1.95 (d, *J* = 12.2 Hz, 1H), 1.76 – 1.61 (m, 4H), 1.53 (dt, *J* = 21.2, 7.2 Hz, 3H), 1.45 – 1.34 (m, 1H), 1.12 (ddd, *J* = 20.8, 18.2, 10.8 Hz, 2H), 1.01 – 0.85 (m, 17H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.8, 158.7, 145.3 (dd, *J* = 14.3, 9.5 Hz), 143.5 – 143.0 (m), 141.3 (dt, *J* = 22.5, 7.6 Hz), 136.0 – 135.6 (m), 110.7, 108.9, 84.5, 53.8, 48.6, 40.7, 34.3, 31.6, 27.2, 25.9 (d, *J* = 9.5 Hz), 23.3, 22.2, 21.1, 16.2, 10.2. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -145.56 (dd, *J* = 23.2, 9.4 Hz), -155.31 (dd, *J* = 23.3, 9.5 Hz). **HRMS** calcd. for $C_{25}H_{33}F_4N_3O$ $[M+H]^+$: 467.2560 Found: 467.2558.



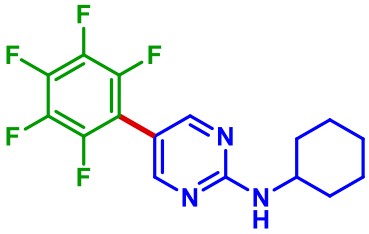
3ar

5-(4-(3-(benzo[d][1,3]dioxol-5-yl)-2-methylpropoxy)-2,3,5,6-tetrafluorophenyl)-N-(pentan-3-yl)pyrimidin-2-amine (3ar): Yield: 52 % (0.052 mmol, 26 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.35 (br s, 2H), 6.74 (d, *J* = 7.9 Hz, 1H), 6.69 (d, *J* = 1.4 Hz, 1H), 6.64 (dd, *J* = 7.9, 1.6 Hz, 1H), 5.93 (s, 2H), 5.32 (d, *J* = 9.1 Hz, 1H), 4.12 – 4.02 (m, 2H), 4.00 – 3.91 (m, 1H), 2.83 (dd, *J* = 13.6, 6.4 Hz, 1H), 2.48 (dd, *J* = 13.6, 7.8 Hz, 1H), 2.17 (dq, *J* = 13.2, 6.4 Hz, 1H), 1.72 – 1.61 (m, 2H), 1.58 – 1.47 (m, 2H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.96 (t, *J* = 7.5 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.0, 158.7, 147.7, 146.0, 145.6 – 145.1 (m), 143.6 – 143.3 (m), 142.9 – 142.4 (m), 140.7 (dt, *J* = 8.4, 4.7 Hz), 137.4 – 137.0 (m), 133.8, 122.2, 110.6, 109.6, 109.1 (t, *J* = 17.2 Hz), 108.3, 101.0, 79.3, 53.8, 39.0, 36.3, 27.2, 16.5, 10.2. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -145.18 – 145.26 (m), -156.63 (dd, *J* = 22.9, 9.3 Hz). **HRMS** calcd. for $C_{26}H_{28}F_4N_3O_3$ $[M+H]^+$: 506.2061 Found: 506.2056.



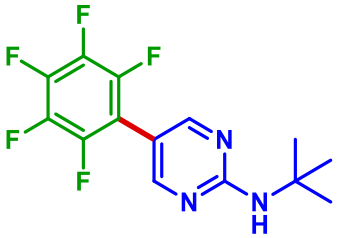
3ba

N-isopropyl-5-(perfluorophenyl)pyrimidin-2-amine (3ba): Yield: 76% (0.076 mmol, 23 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.35 (s, 2H), 5.90 (s, 1H), 4.24 – 4.16 (m, 1H), 1.27 (d, *J* = 6.5 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.9, 158.6, 145.4 – 144.8 (m), 143.4 – 143.2 (m), 141.8 – 141.1 (m), 139.7 – 138.9 (m), 137.4 – 136.9 (m), 110.8 (td, *J* = 16.9, 3.7 Hz), 109.5, 43.3, 22.8. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -143.40 (dd, *J* = 22.9, 8.2 Hz), -154.93 (t, *J* = 20.9 Hz), -161.46 (td, *J* = 22.6, 8.2 Hz). **HRMS** calcd. for $C_{13}H_{11}F_5N_3$ $[M+H]^+$: 304.0868. Found: 304.0882.



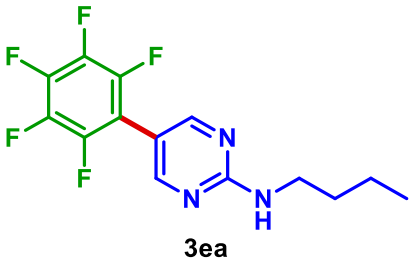
3ca

N-cyclohexyl-5-(perfluorophenyl)pyrimidin-2-amine (3ca): Yield: 72% (0.072 mmol, 25 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.34 (s, 2H), 5.63 (d, *J* = 8.0 Hz, 1H), 3.86 (tdd, *J* = 10.6, 7.4, 4.0 Hz, 1H), 2.11 – 2.01 (m, 2H), 1.82 – 1.71 (m, 2H), 1.69 – 1.60 (m, 1H), 1.48 – 1.36 (m, 2H), 1.29 – 1.19 (m, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.4, 158.7, 145.5 – 145.0 (m), 143.4 – 143.2 (m), 141.6 – 141.3 (m), 139.8 – 138.8 (m), 137.3 – 136.9 (m), 111.0 (td, *J* = 17.1, 3.9 Hz), 109.6, 50.0, 33.2, 25.8, 25.0. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -143.37 (d, *J* = 20.5 Hz), -155.03 (t, *J* = 18.1 Hz), -161.50 (t, *J* = 20.9 Hz). **HRMS** calcd. for $C_{16}H_{15}F_5N_3$ $[M+H]^+$: 344.1181. Found: 344.1183.



3da

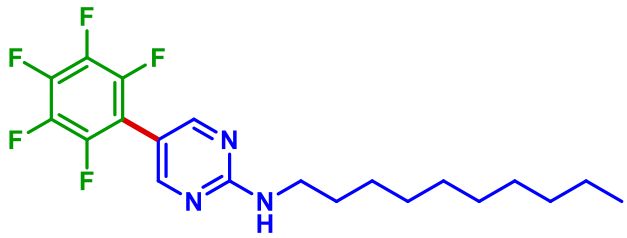
N-(tert-butyl)-5-(perfluorophenyl)pyrimidin-2-amine (3da): Yield: 82% (0.082 mmol, 26 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.33 (s, 2H), 5.53 (s, 1H), 1.47 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.8, 158.2, 145.4 – 145.0 (m), 143.4 – 143.2 (m), 141.7 – 141.1 (m), 139.6 – 138.9 (m), 137.4 – 136.8 (m), 111.1 (td, *J* = 16.9, 4.0 Hz), 109.6, 51.5, 28.9. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -143.40 (d, *J* = 19.4 Hz), -155.20 (t, *J* = 21.9 Hz), -161.60 (t, *J* = 27.0 Hz). **HRMS** calcd. for $C_{14}H_{13}F_5N_3$ $[M+H]^+$: 318.1024. Found: 318.1024.



3ea

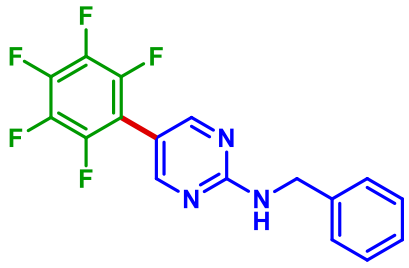
N-butyl-5-(perfluorophenyl)pyrimidin-2-amine (3ea): Yield: 79% (0.079 mmol, 25 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.35 (s, 2H), 5.58 (d, *J* = 9.3 Hz, 1H), 3.47 (dd, *J* = 13.2, 6.8 Hz, 2H), 1.63 (dt, *J* = 14.8, 7.3 Hz, 2H), 1.43 (dq, *J* = 14.7, 7.4 Hz, 2H), 0.96 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.1, 158.7, 145.4 – 145.2 (m), 143.5 – 142.8 (m), 141.6 – 141.4 (m), 139.6 – 138.7 (m), 137.3 – 137.0 (m), 111.2 – 110.6 (m), 109.8, 41.5, 31.7, 20.2, 13.9. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -

143.22 – -143.44 (m), -155.09 (t, *J* = 20.6 Hz), -161.55 (dd, *J* = 23.8, 16.8 Hz). **HRMS** calcd. for $C_{14}H_{13}F_5N_3$ $[M+H]^+$: 318.1024. Found: 318.1022.



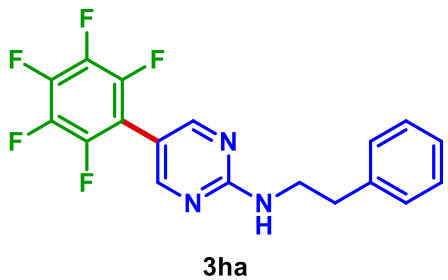
3fa

N-decyl-5-(perfluorophenyl)pyrimidin-2-amine (3fa): Yield: 71% (0.071 mmol, 28.5 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.35 (s, 2H), 5.73 (s, 1H), 3.45 (dd, *J* = 13.1, 7.0 Hz, 2H), 1.68 – 1.59 (m, 2H), 1.25 (br s, 14H), 0.87 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.1, 158.7, 145.4 – 145.2 (m), 143.4 – 143.2 (m), 141.7 – 141.2 (m), 139.7 – 138.9 (m), 137.6 – 136.9 (m), 111.0 (td, *J* = 17.1, 3.9 Hz), 109.7 (s), 41.8 (s), 32.0 (s), 29.9 – 29.6 (m), 29.5, 27.1, 22.8, 14.2. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -143.35 – -143.47 (m), -155.16 (t, *J* = 21.6 Hz), -161.11 – -162.18 (m). **HRMS** calcd. for $C_{20}H_{25}F_5N_3$ $[M+H]^+$: 402.1963. Found: 402.1951.



3ga

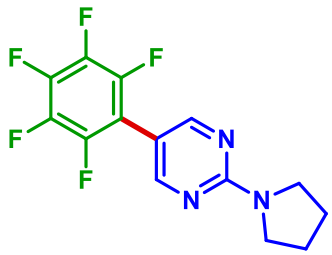
N-benzyl-5-(perfluorophenyl)pyrimidin-2-amine (3ga): Yield: 65% (0.065 mmol, 22.5 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.31 (s, 2H), 7.39 – 7.33 (m, 4H), 7.29 (d, *J* = 6.8 Hz, 1H), 6.17 (s, 1H), 4.70 (d, *J* = 5.8 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.91, 158.7, 145.4 – 145.2 (m), 143.4 – 143.2 (m), 141.7 – 141.5 (m), 139.7 – 139.0 (m), 138.6, 137.3 – 137.0 (m), 128.9, 127.8, 127.6, 111.0 – 110.7 (m), 110.4, 45.8; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -143.1 (dd, *J* = 23.7, 8.8 Hz), -154.6 – -154.7 (m), -161.2 – -161.4 (m); **HRMS** calcd. for $C_{17}H_{11}F_5N_3$ $[M+H]^+$: 352.0868. Found: 352.0873.



3ha

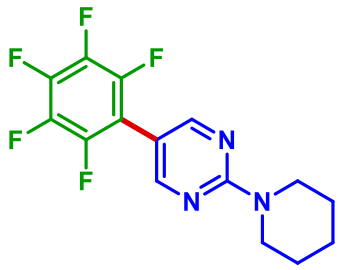
5-(perfluorophenyl)-N-phenethylpyridin-2-amine (3ha): Yield: 43% (0.043 mmol, 15.5 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.36 (s, 2H), 7.36 – 7.29 (m, 2H), 7.26 – 7.22 (m, 3H), 5.50 (s, 1H), 3.76 (dd, *J* = 13.2, 6.8 Hz, 2H), 2.96 (t, *J* = 7.0 Hz, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.0, 158.7, 145.4

– 145.2 (m), 143.4 – 143.2 (m), 141.7 – 141.4 (m), 139.7 – 139.0 (m), 137.3 – 137.0 (m), 129.0, 128.8, 126.7, 110.9 (td, *J* = 17.2, 4.4 Hz), 110.2, 42.9, 35.8. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -143.31 (d, *J* = 20.5 Hz), -154.92 (t, *J* = 22.0 Hz), -161.48 (t, *J* = 20.1 Hz). **HRMS** calcd. for $C_{18}H_{13}F_5N_3$ $[M+H]^+$: 366.1024. Found: 366.1034.



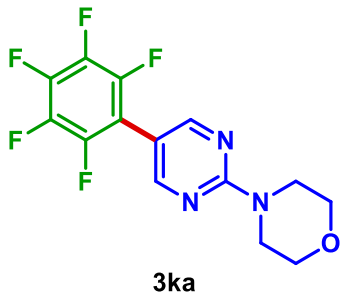
3ia

5-(perfluorophenyl)-2-(pyrrolidin-1-yl)pyrimidine (3ia): Yield: 61% (0.061 mmol, 19.5 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.38 (s, 2H), 3.62 (t, *J* = 6.7 Hz, 4H), 2.06 – 1.99 (m, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 159.7, 158.3 (t, *J* = 2.5 Hz), 145.4 – 145.2 (m), 143.4 – 143.2 (m), 141.5 – 141.2 (m), 139.5 – 139.0 (m), 137.3 – 137.0 (m), 111.5 – 111.4 (m), 110.5 (s), 108.3 (d, *J* = 1.4 Hz), 47.0, 25.6; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -143.4 (dd, *J* = 23.6, 8.8 Hz), -155.4 – -155.7 (m), -161.6 – -161.7 (m). **HRMS** calcd. for $C_{14}H_{11}F_5N_3$ $[M+H]^+$: 316.0868. Found: 316.0867.



3ja

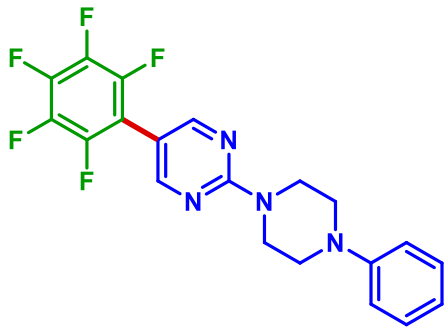
5-(perfluorophenyl)-2-(piperidin-1-yl)pyrimidine (3ja): Yield: 58%. (0.058 mmol, 19 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.35 (s, 2H), 3.86 – 3.82 (m, 4H), 1.73 – 1.67 (m, 2H), 1.66 – 1.60 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.95 (s), 158.30 (s), 145.51 (s), 143.02 (s), 141.84 – 141.06 (m), 139.15 (dt, *J* = 17.9, 13.3 Hz), 136.86 (t, *J* = 13.4 Hz), 108.22 (s), 45.00 (s), 25.91 (s), 24.90 (s). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -143.43 (dd, *J* = 23.1, 8.2 Hz), -155.61 (t, *J* = 21.0 Hz), -161.59 – -161.81 (m). **HRMS** calcd. for $C_{15}H_{13}F_5N_3$ $[M+H]^+$: 330.1024 Found: 330.1041.



3ka

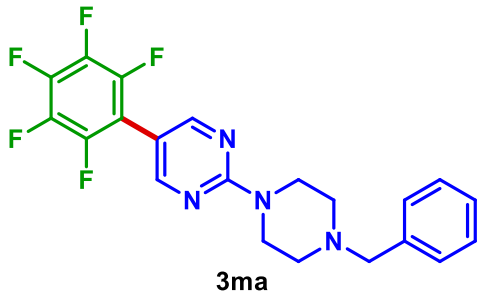
4-(5-(perfluorophenyl)pyrimidin-2-yl)morpholine (3ka): Yield: 65%. (0.065 mmol, 21.5 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.37 (s, 2H), 3.89 – 3.82 (m, 4H), 3.78 – 3.72 (m, 4H). **^{13}C NMR** (126

MHz, $CDCl_3$) δ 161.1, 158.3 (t, *J* = 2.5 Hz), 145.3 – 145.1 (m), 143.4 – 143.2 (m), 141.6 – 141.3 (m), 139.8 – 138.9 (m), 137.3 – 136.8 (m), 110.9 (td, *J* = 17.1, 3.9 Hz), 109.5, 66.8, 44.3. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -143.14 – -143.44 (m), -154.94 (t, *J* = 21.0 Hz), -161.44 (td, *J* = 22.6, 8.3 Hz). **HRMS** calcd. for $C_{14}H_{11}F_5N_3O$ $[M+H]^+$: 332.0817 Found: 332.0810.



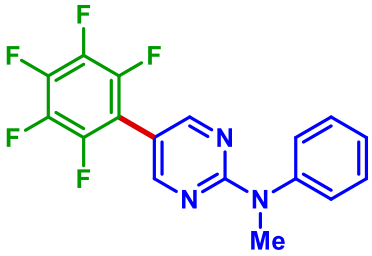
3la

5-(perfluorophenyl)-2-(4-phenylpiperazin-1-yl)pyrimidine (3la): Yield: 48% (0.048 mmol, 19.5 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.42 (t, *J* = 1.3 Hz, 2H), 7.33 – 7.27 (m, 2H), 6.99 (d, *J* = 8.1 Hz, 2H), 6.91 (t, *J* = 7.3 Hz, 1H), 4.10 – 4.06 (m, 4H), 3.32 – 3.26 (m, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.1, 158.4, 151.3, 145.5 – 145.0 (m), 143.4 – 143.3 (m), 141.7 – 141.3 (m), 139.2 (tdd, *J* = 27.5, 18.0, 12.0 Hz), 137.8 – 136.7 (m), 129.4, 120.5, 116.7, 110.9 (td, *J* = 17.4, 4.1 Hz), 109.4, 49.5, 43.9. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -143.27 (dd, *J* = 23.8, 8.8 Hz), -154.96 (t, *J* = 22.56 Hz), -161.21 – -161.57 (m). **HRMS** calcd. for $C_{20}H_{16}F_5N_4$ $[M+H]^+$: 407.1290 Found: 407.1281.



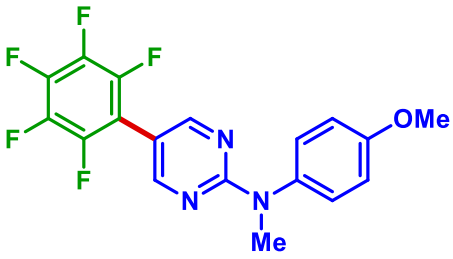
3ma

2-(4-benzylpiperazin-1-yl)-5-(perfluorophenyl)pyrimidine (3ma): Yield: 42% (0.042 mmol, 17.5 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.38 (s, 2H), 7.39 – 7.30 (m, 4H), 7.30 – 7.25 (m, 1H), 3.95 – 3.90 (m, 4H), 3.57 (s, 2H), 2.56 – 2.52 (m, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.0, 158.3, 145.4 – 145.2 (m), 143.4 – 143.2 (m), 141.7 – 141.2 (m), 139.6 – 138.9 (m), 137.9, 137.4 – 136.9 (m), 129.3, 128.5, 127.4, 111.1 (td, *J* = 17.2, 3.9 Hz), 108.9, 63.2, 53.0, 43.9. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -143.42 (dd, *J* = 23.2, 8.1 Hz), -155.26 (t, *J* = 21.0 Hz), -161.57 (td, *J* = 22.8, 8.2 Hz). **HRMS** calcd. for $C_{21}H_{18}F_5N_4$ $[M+H]^+$: 421.1446 Found: 421.1432.



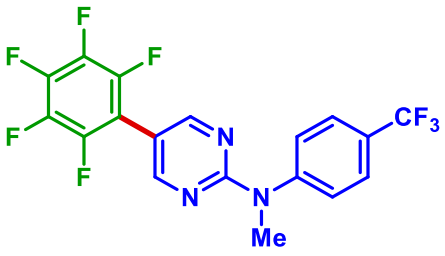
3na

N-methyl-5-(perfluorophenyl)-N-phenylpyrimidin-2-amine (3na): Yield: 45% (0.045 mmol, 16 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 1.0 Hz, 2H), 7.45 (dt, *J* = 9.2, 4.6 Hz, 2H), 7.38 – 7.34 (m, 2H), 7.32 – 7.27 (m, 1H), 3.60 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.5, 158.3 (t, *J* = 2.5 Hz), 145.6 – 144.9 (m), 143.3 (ddt, *J* = 10.9, 7.2, 3.8 Hz), 141.6 (tt, *J* = 13.0, 4.7 Hz), 140.0 – 138.9 (m), 137.4 – 136.7 (m), 129.5, 126.7 (d, *J* = 14.5 Hz), 110.9 (td, *J* = 17.2, 4.0 Hz), 110.2 (d, *J* = 1.3 Hz), 39.1. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -143.22 (dd, *J* = 23.5, 8.6 Hz), -154.79 (t, *J* = 21.2 Hz), -161.31 (ddd, *J* = 23.3, 21.1, 8.4 Hz). **HRMS** calcd. for $C_{17}H_{11}F_5N_3$ $[M+H]^+$: 352.0868 Found: 352.0857.



3oa

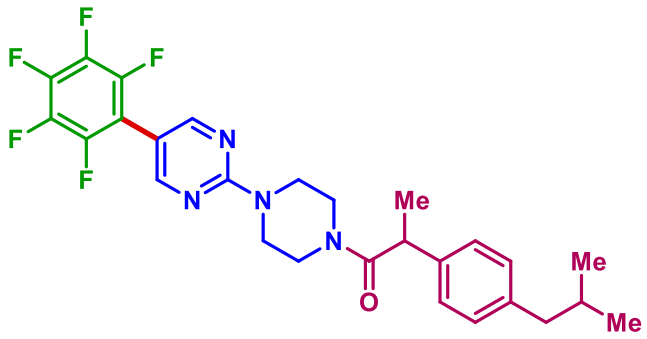
N-(4-methoxyphenyl)-N-methyl-5-(perfluorophenyl)pyrimidin-2-amine (3oa): Yield: 52% (0.052 mmol, 20 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.42 (s, 2H), 7.25 (dd, *J* = 7.2, 5.1 Hz, 2H), 6.99 – 6.96 (m, 2H), 3.84 (s, 3H), 3.55 (s, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.8, 158.3, 158.1, 145.4 – 145.2 (m), 143.4 – 143.2 (m), 141.6 – 141.4 (m), 139.6 – 139.0 (m), 137.8, 137.3 – 137.0 (m), 128.0, 114.9, 111.0 (td, *J* = 17.0, 3.9 Hz), 109.9, 55.6, 39.3. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -143.26 (dd, *J* = 23.6, 8.6 Hz), -154.94 (t, *J* = 22.56 Hz), -161.30 – -161.45 (m). **HRMS** calcd. for $C_{18}H_{13}F_5N_3O$ $[M+H]^+$: 382.0973 Found: 382.0954.



3pa

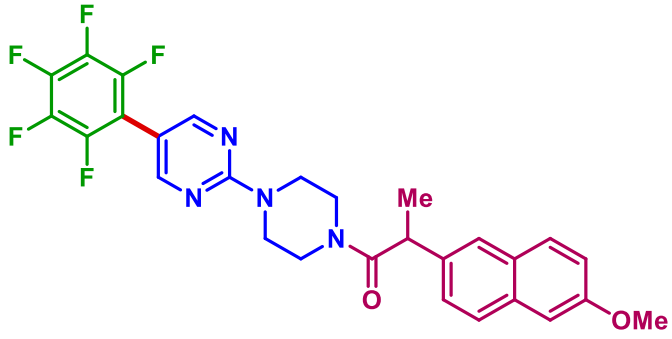
N-methyl-5-(perfluorophenyl)-N-(4-(trifluoromethyl)phenyl)pyrimidin-2-amine (3pa): Yield: 60% (0.06 mmol, 25 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.47 (s, 2H), 7.69 (d, *J* = 8.1 Hz, 2H), 7.51 (d, *J* = 8.1 Hz, 2H), 3.64 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.1, 158.3 (t, *J* = 2.5 Hz), 147.9, 145.4 – 145.2 (m), 143.4 – 143.2 (m), 142.0 – 141.5 (m), 140.0 – 139.4 (m), 139.4 – 138.7 (m), 137.5

– 137.0 (m), 128.02 (q, $^{2}J_{F}$ = 32.8 Hz), 126.5, 126.45 (q, $^{1}J_{F}$ = 3.6 Hz), 124.2 (q, $^{3}J_{F}$ = 272.16 Hz) 111.3, 110.5 (td, *J* = 17.0, 3.9 Hz), 38.7. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -62.40 (s), -143.28 (dd, *J* = 24.8, 10.4 Hz), -154.28 (t, *J* = 22.0 Hz), -161.16 (dd, *J* = 33.1, 23.2 Hz). **HRMS** calcd. for $C_{18}H_{10}F_8N_3$ $[M+H]^+$: 420.0741 Found:420.0726.



3qa

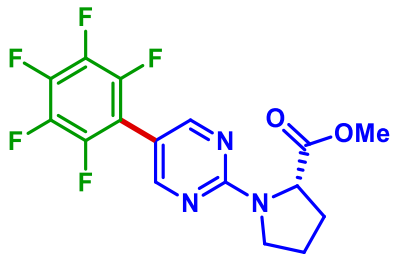
2-(4-isobutylphenyl)-1-(4-(5-(perfluorophenyl)pyrimidin-2-yl)piperazin-1-yl)propan-1-one (3qa): Yield: 87% (0.087 mmol, 45 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.35 (s, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 4.11 – 4.03 (m, 1H), 4.00 – 3.96 (m, 1H), 3.88 (q, *J* = 6.8 Hz, 2H), 3.65 – 3.39 (m, 4H), 3.16 – 3.05 (m, 1H), 2.43 (d, *J* = 7.2 Hz, 2H), 1.83 (dt, *J* = 13.5, 6.7 Hz, 1H), 1.46 (d, *J* = 6.8 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.7, 160.9, 158.3, 145.5 – 145.0 (m), 143.4 – 143.2 (m), 141.8 – 141.3 (m), 140.5, 139.7 – 138.9 (m), 137.4 – 136.8 (m), 129.9, 127.0, 110.8 (td, *J* = 16.8, 3.6 Hz), 109.6, 45.4, 45.1, 43.6 (d, *J* = 15.0 Hz), 43.3, 44.0, 30.3, 22.5, 20.8. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -143.30 (dd, *J* = 23.8, 8.8 Hz), -154.73 (t, *J* = 22.56), -161.10 – -161.47 (m). **HRMS** calcd. for $C_{27}H_{28}F_5N_4O$ $[M+H]^+$: 519.2178 Found:519.2175.



3ra

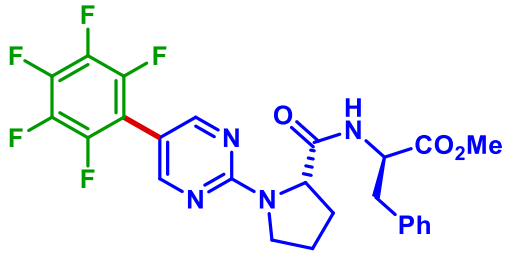
2-(6-methoxynaphthalen-2-yl)-1-(4-(5-(perfluorophenyl)pyrimidin-2-yl)piperazin-1-yl)propan-1-one (3ra): Yield: 86% (0.086 mmol, 46.6 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.32 (s, 2H), 7.70 (dd, *J* = 16.1, 8.7 Hz, 2H), 7.63 (s, 1H), 7.37 (d, *J* = 8.4 Hz, 1H), 7.17 – 7.08 (m, 2H), 4.07 – 3.96 (m, 3H), 3.90 (s, 3H), 3.84 (d, *J* = 13.3 Hz, 1H), 3.64 – 3.48 (m, 4H), 3.15 – 3.06 (m, 1H), 1.55 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.6, 160.8, 158.3, 157.9, 145.3 – 145.2 (m), 143.5 – 142.8 (m), 141.7 – 141.3 (m), 139.8 – 138.8 (m), 137.4 – 136.9 (m), 133.7, 129.3 (d, *J* = 3.4 Hz), 127.9, 126.0, 125.7, 119.3, 110.7 (td, *J* = 17.1, 3.8 Hz), 109.6, 105.8, 55.5, 45.4, 43.6 (t, *J* = 7.5 Hz), 42.0, 20.8. **^{19}F**

NMR (376 MHz, $CDCl_3$) δ -143.33 (dd, *J* = 23.8, 8.8 Hz), -154.61 – -155.04 (m), -161.32 (qd, *J* = 21.3, 8.4 Hz). **HRMS** calcd. for $C_{28}H_{24}F_5N_4O_2$ $[M+H]^+$: 543.1814 Found:543.1808.



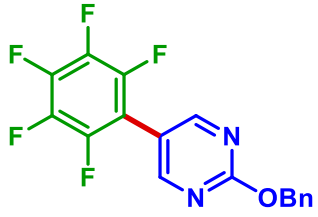
3sa

methyl (5-(perfluorophenyl)pyrimidin-2-yl)prolinate (3sa): Yield: 78% (0.078 mmol, 29 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 28.0 Hz, 2H), 4.63 (dd, *J* = 8.6, 3.3 Hz, 1H), 3.89 – 3.82 (m, 1H), 3.77 – 3.69 (m, 4H), 2.41 – 2.30 (m, 1H), 2.19 – 2.01 (m, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.8, 159.5, 158.4, 158.2, 145.3 – 145.1 (m), 143.4 – 143.2 (m), 141.6 – 141.3 (m), 139.7 – 138.9 (m), 137.3 – 137.0 (m), 111.0 (td, *J* = 16.9, 3.7 Hz), 109.7, 59.8, 52.4, 47.4, 30.6, 24.1. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -143.30 (dd, *J* = 23.4, 8.6 Hz), -154.92 – -155.15 (m), -161.34 – -161.61 (m). **HRMS** calcd. for $C_{16}H_{13}F_5N_3O_2$ $[M+H]^+$: 374.0922 Found:374.0892.



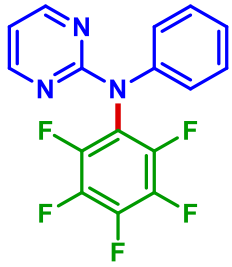
3ta

methyl (5-(perfluorophenyl)pyrimidin-2-yl)prolylphenylalaninate (3ta): Yield: 48% (0.048 mmol, 25 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.32 (s, 2H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.12 – 7.03 (m, 3H), 6.95 (dd, *J* = 7.5, 1.5 Hz, 2H), 4.88 (dt, *J* = 7.7, 5.8 Hz, 1H), 4.65 – 4.59 (m, 1H), 3.71 – 3.58 (m, 5H), 3.16 (dd, *J* = 13.9, 5.6 Hz, 1H), 2.99 (dd, *J* = 13.9, 6.0 Hz, 1H), 2.37 (ddd, *J* = 11.8, 7.3, 4.4 Hz, 1H), 2.07 – 1.98 (m, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.9, 171.5, 160.0, 158.2, 145.3 – 145.2 (m), 143.54 – 143.11 (m), 142.16 – 141.32 (m), 139.7 – 139.0 (m), 137.4 – 136.8 (m), 135.9, 129.2, 128.3, 127.0, 110.7 (td, *J* = 17.2, 3.7 Hz), 110.0, 60.9, 53.2, 52.4, 48.1, 37.8, 29.1, 24.4. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -143.31 (dd, *J* = 23.8, 8.9 Hz), -154.56 (t, *J* = 18.8 Hz), -161.01 – -161.40 (m). **HRMS** calcd. for $C_{25}H_{22}F_5N_4O_3$ $[M+H]^+$: 521.1607 Found: 521.1595.



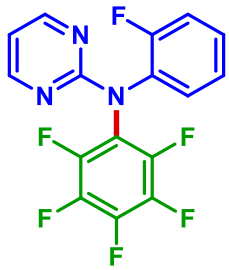
3ua

2-(benzyloxy)-5-(perfluorophenyl)pyrimidine (3ua): Yield: 42% (0.042 mmol, 15.7 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.63 (s, 2H), 7.51 (d, *J* = 7.3 Hz, 2H), 7.39 (t, *J* = 7.3 Hz, 2H), 7.34 (t, *J* = 7.3 Hz, 1H), 5.53 (s, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.2, 160.0 (d, *J* = 2.4 Hz), 145.4 – 145.2 (m), 143.5 – 143.2 (m), 142.4 – 142.1 (m), 140.4 – 140.1 (m), 139.4 – 139.0 (m), 137.4 – 137.1 (m), 136.1, 128.7, 128.4, 128.3, 115.4, 109.7 (td, *J* = 17.2, 4.3 Hz), 69.8. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -142.77 (dd, *J* = 22.5, 8.2 Hz), -152.79 (t, *J* = 21.0 Hz), -160.63 (td, *J* = 22.1, 7.8 Hz). **HRMS** calcd. for $C_{17}H_9F_5N_2O$ $[M+Na]^+$: 375.0527 Found: 375.0544.



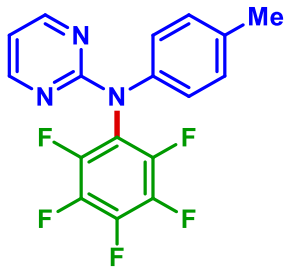
4aa

N-(perfluorophenyl)-N-phenylpyrimidin-2-amine (**4aa**): Yield: 56% (0.056 mmol, 19 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.39 (d, *J* = 4.8 Hz, 2H), 7.45 – 7.37 (m, 4H), 7.31 (dt, *J* = 8.4, 1.3 Hz, 1H), 6.81 (t, *J* = 4.8 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.0, 158.4, 146.3 – 146.2 (m), 144.3 – 144.2 (m), 142.2 – 141.9 (m), 141.7, 140.2 – 139.8 (m), 139.5 – 139.2 (m), 137.5 – 137.2 (m), 129.7, 127.5, 127.3, 119.3 – 119.0 (m), 113.9. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -144.40 – -144.59 (m), -155.65 (t, *J* = 21.5 Hz), -161.93 – -162.18 (m). **HRMS** calcd. for $C_{16}H_9F_5N_3$ $[M+H]^+$: 338.0711 Found: 338.0715.



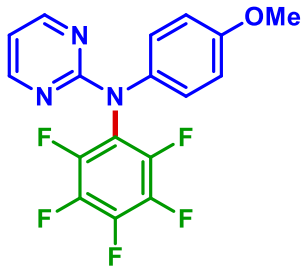
4ba

N-(2-fluorophenyl)-N-(perfluorophenyl)pyrimidin-2-amine (**4ba**)**:** Yield: 50% (0.050 mmol, 17.75 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.40 (d, *J* = 4.8 Hz, 2H), 7.39 – 7.31 (m, 2H), 7.22 – 7.16 (m, 2H), 6.84 (t, *J* = 4.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.3, 159.9, 158.5, 157.4, 146.5 – 146.3 (qd, *J* = 6.8, 2.7 Hz), 144.0 – 143.8 (m), 142.4 – 141.9 (m), 139.7 – 139.3 (m), 137.1 – 136.8 (m), 129.6, 129.5 (d, *J* = 8.1 Hz), 129.0 (d, *J* = 12.0 Hz), 125.0 (d, *J* = 3.8 Hz), 118.4 – 118.1 (m), 117.2, 117.0, 114.3. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.45 – -117.89 (m), -143.89 (dd, *J* = 16.3, 8.3 Hz), -155.79 (t, *J* = 21.5 Hz), -162.10 – -162.43 (m). **HRMS** calcd. for $C_{16}H_8F_6N_3$ $[M+H]^+$: 356.0617 Found: 356.0612.



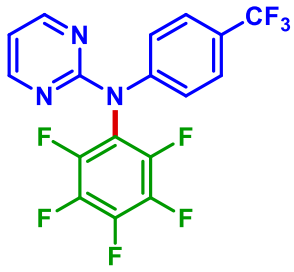
4ca

N-(perfluorophenyl)-N-(p-tolyl)pyrimidin-2-amine (**4ca**): Yield: 35% (0.035 mmol, 12.3 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.38 (d, *J* = 4.8 Hz, 2H), 7.28 (d, *J* = 8.3 Hz, 2H), 7.23 (d, *J* = 8.2 Hz, 2H), 6.78 (t, *J* = 4.8 Hz, 1H), 2.37 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.5, 158.4, 146.4 – 146.0 (m), 144.4 – 144.0 (m), 142.1 – 141.6 (m), 140.1 – 139.6 (m), 139.5 – 138.7 (m), 137.6 – 137.0 (m), 130.3, 127.3, 119.4 (td, *J* = 14.3, 4.3 Hz), 113.7, 21.3. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -144.64 (d, *J* = 20.2 Hz), -156.14 – -156.32 (m), -161.88 – -162.94 (m). **HRMS** calcd. for $C_{17}H_{11}F_5N_3$ $[M+H]^+$: 352.0868 Found: 352.0856.



4da

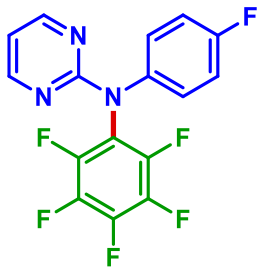
N-(4-methoxyphenyl)-N-(perfluorophenyl)pyrimidin-2-amine (4da): Yield: 36% (0.036 mmol, 13.2 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 4.8 Hz, 2H), 7.36 – 7.31 (m, 2H), 6.97 – 6.91 (m, 2H), 6.78 (t, *J* = 4.8 Hz, 1H), 3.82 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.3, 158.7, 158.2, 146.3 – 146.0 (m), 143.8 – 143.5 (m), 142.1 – 141.8 (m), 139.6 – 139.2 (m), 137.0 – 136.7 (m), 134.3, 128.9, 119.4 – 119.1 (m), 114.8, 113.4, 55.4. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -144.80 (dd, *J* = 22.4, 5.7 Hz), -156.11 (t, *J* = 21.5 Hz), -162.25 (td, *J* = 21.8, 5.0 Hz). **HRMS** calcd. for $C_{17}H_{11}F_5N_3O$ $[M+H]^+$: 368.0817 Found: 368.0832.



4ea

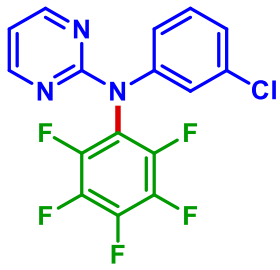
N-(perfluorophenyl)-N-(4-(trifluoromethyl)phenyl)pyrimidin-2-amine (4ea): Yield: 54% (0.054 mmol, 21.9 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.42 (d, *J* = 4.8 Hz, 2H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.48

(d, J = 8.4 Hz, 2H), 6.88 (t, J = 4.8 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.7, 158.5, 146.4 – 146.2 (m), 144.9, 144.4 – 144.2 (m), 142.4 – 142.2 (m), 140.4 – 140.1 (m), 139.5 – 139.2 (m), 137.5 – 137.2 (m), 128.8 (q, ^2J_F = 32.8 Hz), 128.1, 126.7 – 126.6 (m), 124.0 (q, ^3J_F = 272.2 Hz),118.9 – 118.4 (m), 114.7. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -62.51 (s), -144.61 (d, J = 18.8 Hz), -154.00 – -155.85 (m), -161.70 (t, J = 20.5 Hz). **HRMS** calcd. for $C_{17}H_8F_8N_3$ $[M+H]^+$: 406.0585 Found: 406.0576.



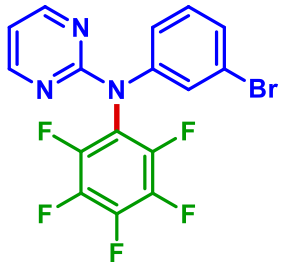
4fa

N-(4-fluorophenyl)-N-(perfluorophenyl)pyrimidin-2-amine (4fa): Yield: 53% (0.053 mmol, 18.8 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.39 (d, J = 4.8 Hz, 1H), 7.41 – 7.35 (m, 2H), 7.16 – 7.07 (m, 2H), 6.81 (t, J = 4.8 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.5, 161.3, 160.5, 158.4, 146.3 – 146.1 (m), 144.3 – 144.1 (m), 142.2 – 141.9 (m), 140.2 – 139.9 (m), 139.6 – 139.0 (m), 137.7 (d, J = 3.0 Hz), 137.4 – 137.2 (m), 129.4 (d, J = 8.8 Hz), 119.1 (td, J = 14.4, 4.3 Hz), 116.7, 116.5, 113.9. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -113.82 (s), -144.76 (d, J = 24.1 Hz), -155.56 (t, J = 22.6 Hz), -162.04 (t, J = 20.1 Hz). **HRMS** calcd. for $C_{16}H_8F_6N_3$ $[M+H]^+$: 356.0617 Found: 356.0628.



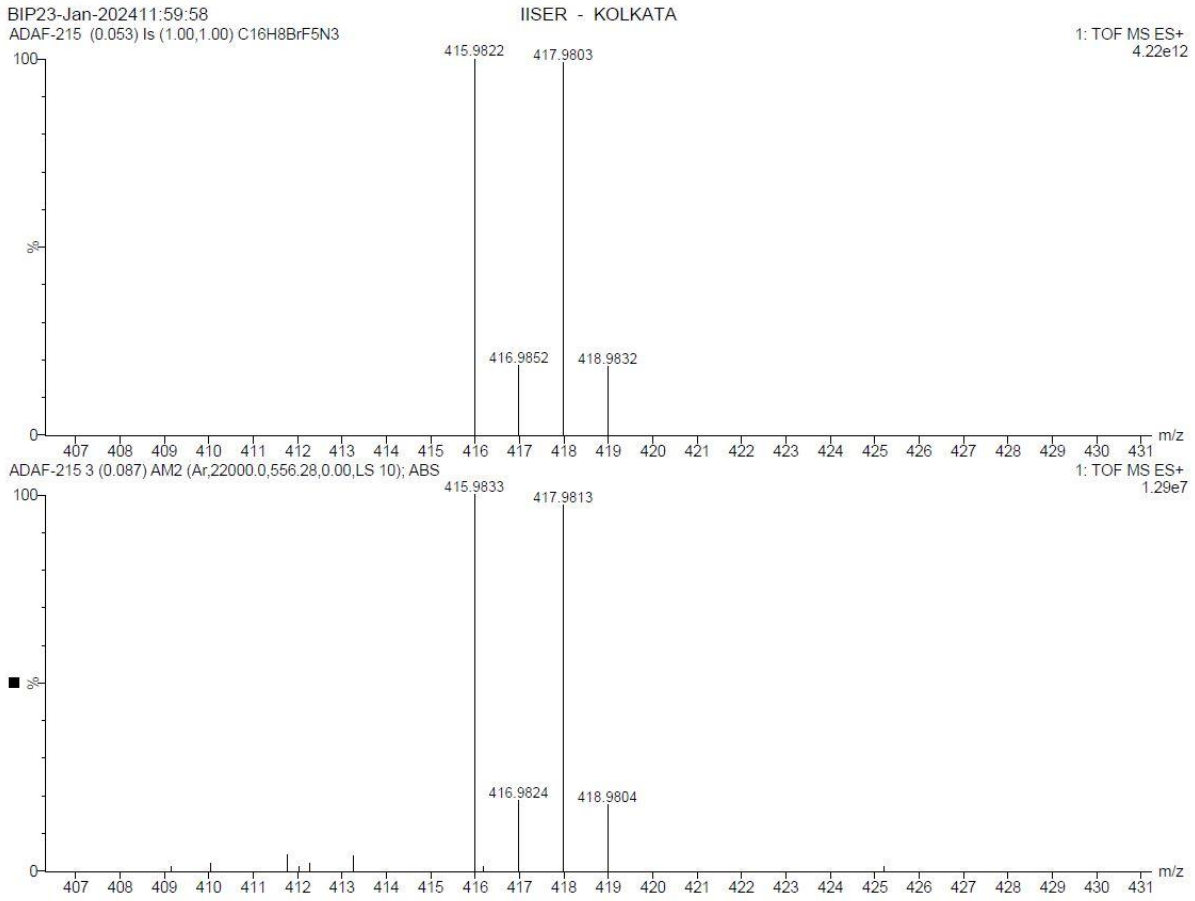
4ga

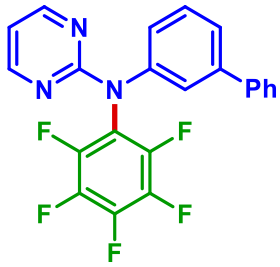
N-(3-chlorophenyl)-N-(perfluorophenyl)pyrimidin-2-amine (4ga): Yield: 48% (0.048 mmol, 17.8 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.40 (d, J = 4.8 Hz, 2H), 7.39 – 7.32 (m, 2H), 7.30 – 7.26 (m, 2H), 6.84 (t, J = 4.8 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.9, 158.4, 146.3 – 146.1 (m), 144.3 – 144.1 (m), 142.9, 142.3 – 142.0 (m), 140.3 – 140.0 (m), 139.5 – 139.2 (m), 137.5 – 137.2 (m), 133.0, 130.4, 127.5, 127.4, 125.3, 118.8 (td, J = 14.3, 4.4 Hz), 114.4. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -143.42 – -145.60 (m), -155.03 (t, J = 21.5 Hz), -160.83 – -162.85 (m). **HRMS** calcd. for $C_{16}H_8ClF_5N_3$ $[M+H]^+$: 372.0321 Found: 372.0322.



4ha

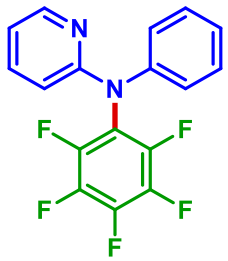
N-(3-bromophenyl)-N-(perfluorophenyl)pyrimidin-2-amine (4ha): Yield: 38% (0.038 mmol, 15.7 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.40 (d, *J* = 4.8 Hz, 2H), 7.52 (t, *J* = 1.8 Hz, 1H), 7.44 – 7.42 (m, 1H), 7.35 – 7.31 (m, 1H), 7.28 (t, *J* = 7.9 Hz, 1H), 6.84 (t, *J* = 4.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.8, 158.4, 146.6 – 146.3 (m), 144.1 – 143.8 (m), 143.0, 142.6 – 142.3 (m), 140.0 – 139.4 (m), 137.3 – 136.9 (m), 130.7, 130.4, 130.2, 125.9, 122.8, 118.8 – 118.5 (m), 114.4. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -144.54 (d, *J* = 18.8 Hz), -155.14 (t, *J* = 21.7 Hz), -161.83 (t, *J* = 20.6 Hz). **HRMS** calcd. for $C_{16}H_8{}^{79}BrF_5N_3$ $[M+H]^+$: 415.9822 Found: 415.9833, $C_{16}H_8{}^{81}$BrF5N3 $[M+H]^+$: 417.9803 Found: 417.9813.





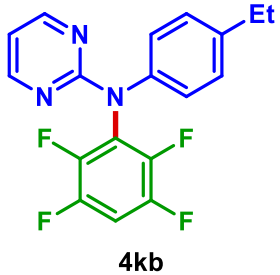
4ia

N-([1,1'-biphenyl]-3-yl)-N-(perfluorophenyl)pyrimidin-2-amine (4ia): Yield: 54% (0.054 mmol, 22.3 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.41 (d, *J* = 4.8 Hz), 7.61 – 7.53 (m), 7.50 (t, *J* = 7.7 Hz), 7.47 – 7.42 (m), 7.36 (ddd, *J* = 6.3, 5.6, 4.3 Hz), 6.82 (t, *J* = 4.8 Hz). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.2, 158.4, 146.4 – 146.2 (m), 144.4 – 144.2 (m), 143.0, 142.2 – 141.9 (m), 140.5, 140.2 – 139.9 (m), 139.5 – 139.2 (m), 137.5 – 137.2 (m), 123.0, 129.0, 127.8, 127.4, 126.3, 126.1, 119.2 (td, *J* = 14.6, 4.4 Hz), 113.9. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -144.49 (d, *J* = 20.2 Hz), -155.75 (t, *J* = 21.1 Hz), -162.09 (dd, *J* = 31.1, 13.9 Hz). **HRMS** calcd. for $C_{22}H_{13}F_5N_3$ $[M+H]^+$: 414.1024 Found: 414.1026.



4ja

N-(perfluorophenyl)-N-phenylpyridin-2-amine (4ja): Yield: 52% (0.052 mmol, 17.5 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.17 – 8.15 (m, 1H), 7.51 – 7.47 (m, 1H), 7.43 – 7.39 (m, 2H), 7.33 – 7.26 (m, 3H), 6.82 (ddd, *J* = 7.2, 5.0, 0.9 Hz, 1H), 6.72 (dt, *J* = 8.5, 0.8 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 157.3, 148.4, 146.5 – 146.3 (m), 144.5 – 144.3 (m), 143.0, 141.6 – 141.3 (m), 139.5 – 139.2 (m), 137.9, 137.5 – 137.2 (m), 130.1, 126.9, 126.5, 120.2 – 119.8 (m), 116.6, 110.0. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -144.81 (d, *J* = 19.3 Hz), -157.39 (t, *J* = 20.5 Hz), -162.64 (t, *J* = 20.8 Hz). **HRMS** calcd. for $C_{17}H_{10}F_5N_2$ $[M+H]^+$: 337.0759 Found: 337.0763.



4kb

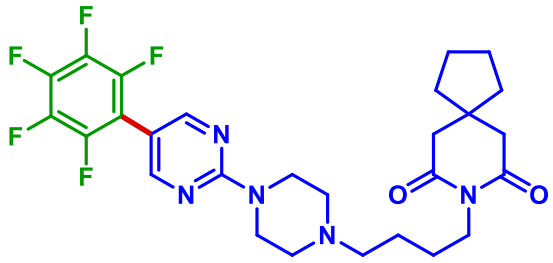
N-(4-ethylphenyl)-N-(2,3,5,6-tetrafluorophenyl)pyrimidin-2-amine (4kb): Yield: 44% (0.044 mmol, 15.3 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.39 (d, *J* = 4.8 Hz, 2H), 7.31 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 8.5 Hz, 2H), 7.04 (tt, *J* = 9.8, 7.2 Hz, 1H), 6.77 (t, *J* = 4.8 Hz, 1H), 2.67 (q, *J* = 7.6 Hz, 2H),

1.28 – 1.24 (m, 3H). **^{13}C NMR** (101 MHz,) δ 161.5, 158.3, 147.8 – 147.5 (m), 145.9 – 145.7 (ddd, *J* = 10.5, 4.2, 2.7 Hz), 145.4 – 145.1 (m), 143.4 – 143.2 (m), 139.4, 129.0, 127.3, 124.5 – 124.2 (tt, *J* = 13.8, 2.9 Hz), 113.6, 105.0, 104.8, 104.5, 28.6, 15.3. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -139.10 (dd, *J* = 21.9, 10.9 Hz), -144.95 (dd, *J* = 21.9, 11.0 Hz). **HRMS** calcd. for $C_{18}H_{14}F_4N_3$ $[M+H]^+$: 348.1118 Found: 348.1114.

7. Synthetic applications

7.1 Late-stage functionalization of Buspirone

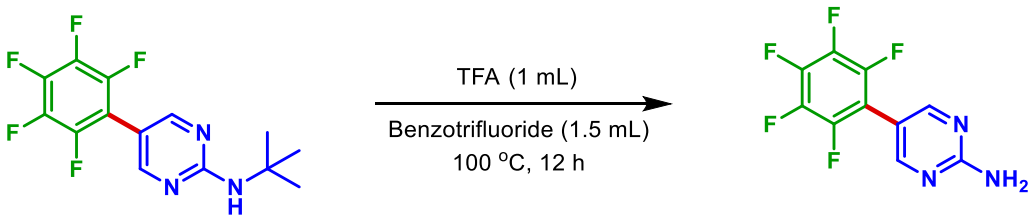
The reaction was performed according to the standard procedure.



3va

8-(4-(4-(5-(perfluorophenyl)pyrimidin-2-yl)piperazin-1-yl)butyl)-8-azaspiro[4.5]decane-7,9-dione (3va): Yield: 55% (0.2 mmol, 61 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 3.93 (s, 2H), 3.79 (t, *J* = 6.8 Hz, 1H), 2.59 – 2.54 (m, 8H), 2.44 (br s, 2H), 1.73 – 1.69 (m, 4H), 1.56 (s, 4H), 1.50 (t, *J* = 7.0 Hz, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.4, 160.9, 158.4, 145.5 – 145.1 (m), 143.5 – 143.1 (m), 141.6 – 141.3 (m), 139.6 – 138.9 (m), 137.4 – 136.8 (m), 111.0 (t, *J* = 18.5 Hz), 109.2, 58.2, 53.0, 45.1, 43.5, 39.6, 39.3, 37.7, 26.0, 24.3. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -142.11 – -146.57 (m), -153.98 – -157.43 (m), -161.39 – -161.77 (m). **HRMS** calcd. for $C_{27}H_{31}F_5N_5O_2$ $[M+H]^+$: 552.2392 Found: 552.2395.

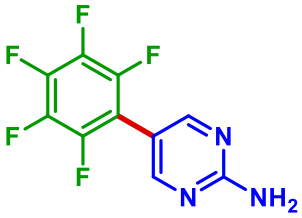
7.2 Deprotection of tert-butyl group



3da, 0.2 mmol

3da', 62%

An oven-dried 10 mL round bottom flask was charged with a magnetic stir-bar, **3da** (0.2 mmol) and benzotrifluoride (1.5 mL) were taken under a nitrogen atmosphere. Subsequently, TFA (1.0 mL) was added. The round bottom flask was placed in a preheated oil bath at 100 °C and refluxed for 12 h. The reaction mixture was allowed to cool at room temperature, basified with saturated Na_2CO_3 to pH 9, and extracted with DCM. The organic layer was dried with sodium sulfate, filtered, and concentrated under reduced pressure. The purification was carried out by column chromatography over silica gel (hexane/EtOAc) to give **3da'** in 62% yield.



3da'

5-(perfluorophenyl)pyrimidin-2-amine (3da', FAP):[27] **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.48 (d, *J* = 1.1 Hz, 2H), 6.26 (s, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 163.4, 158.7, 145.0 – 144.9 (m), 142.7 – 142.4 (m), 140.9 – 140.7 (m), 138.7 – 138.3 (m), 136.2 – 135.9 (m), 111.10 (td, *J* = 17.6, 3.7 Hz), 108.6. **^{19}F NMR** (376 MHz, DMSO-d_6) δ -143.47 (dd, *J* = 24.4, 7.3 Hz), -156.36 (t, *J* = 22.3 Hz), -162.48 – -162.72 (m).

8. Crystal Data

8.1 Product 3aa and 4ca

Compounds **3aa** and **4ca** were dissolved in a minimum volume of methanol and kept in room temperature for slow evaporation (5 days). Needle-shaped colorless crystals were formed, which were subjected to X-ray diffraction.

Intensity data were collected on an XtaLAB Synergy, Dualflex, HyPix3000 diffractometer. The crystal was kept at 100.00 K during the data collection. The software Olex2 was used for space group, structure determination, and refinements. The least-squares refinement techniques on F2 were performed until the model converged. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were fixed at calculated positions, and their positions were refined by a riding model.

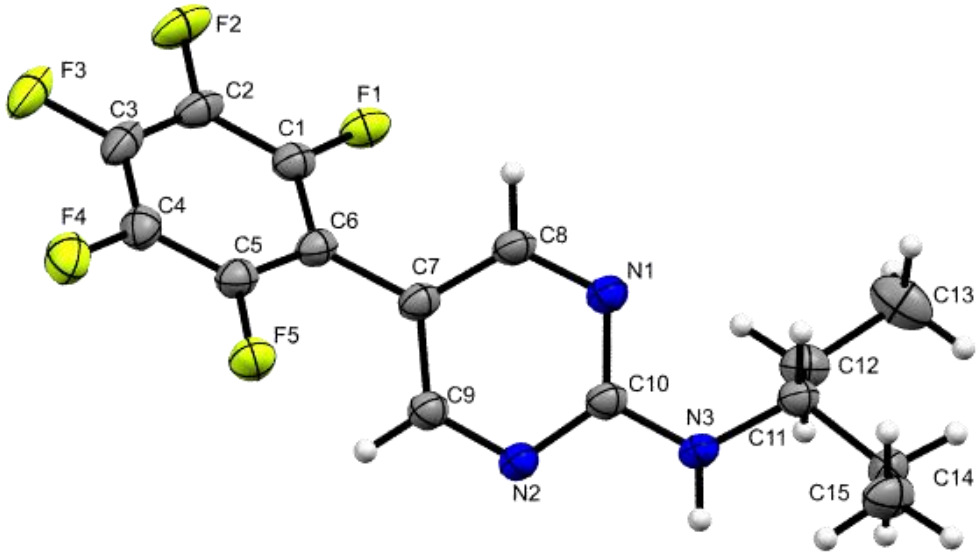


Fig S1: Molecular structure of final product **3aa** (ORTEP view)

Table S8: Crystal data and structure refinement for 3aa (CCDC 2327240).

Identification code	ADA_AB_272_auto_1
Empirical formula	$C_{15}H_{14}F_5N_3$
Formula weight	331.29
Temperature/K	100.4(9)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	12.4951(3)
b/Å	7.6806(2)
c/Å	16.1712(5)
α/°	90
β/°	108.511(3)
γ/°	90
Volume/Å^3	1471.65(7)
Z	4
ρ_{calc}g/cm^3	1.495
μ/mm^{-1}	1.187
F(000)	680.0
Crystal size/mm^3	0.2 × 0.07 × 0.01
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.462 to 136.144
Index ranges	$-14 \leq h \leq 15$, $-9 \leq k \leq 9$, $-19 \leq l \leq 17$
Reflections collected	16716
Independent reflections	2682 [R_{int} = 0.0663, R_{sigma} = 0.0353]
Data/restraints/parameters	2682/0/210
Goodness-of-fit on F^2	1.054
Final R indexes [I>=2σ (I)]	R_1 = 0.0446, wR_2 = 0.1260
Final R indexes [all data]	R_1 = 0.0504, wR_2 = 0.1326
Largest diff. peak/hole / e Å^{-3}	0.32/-0.23

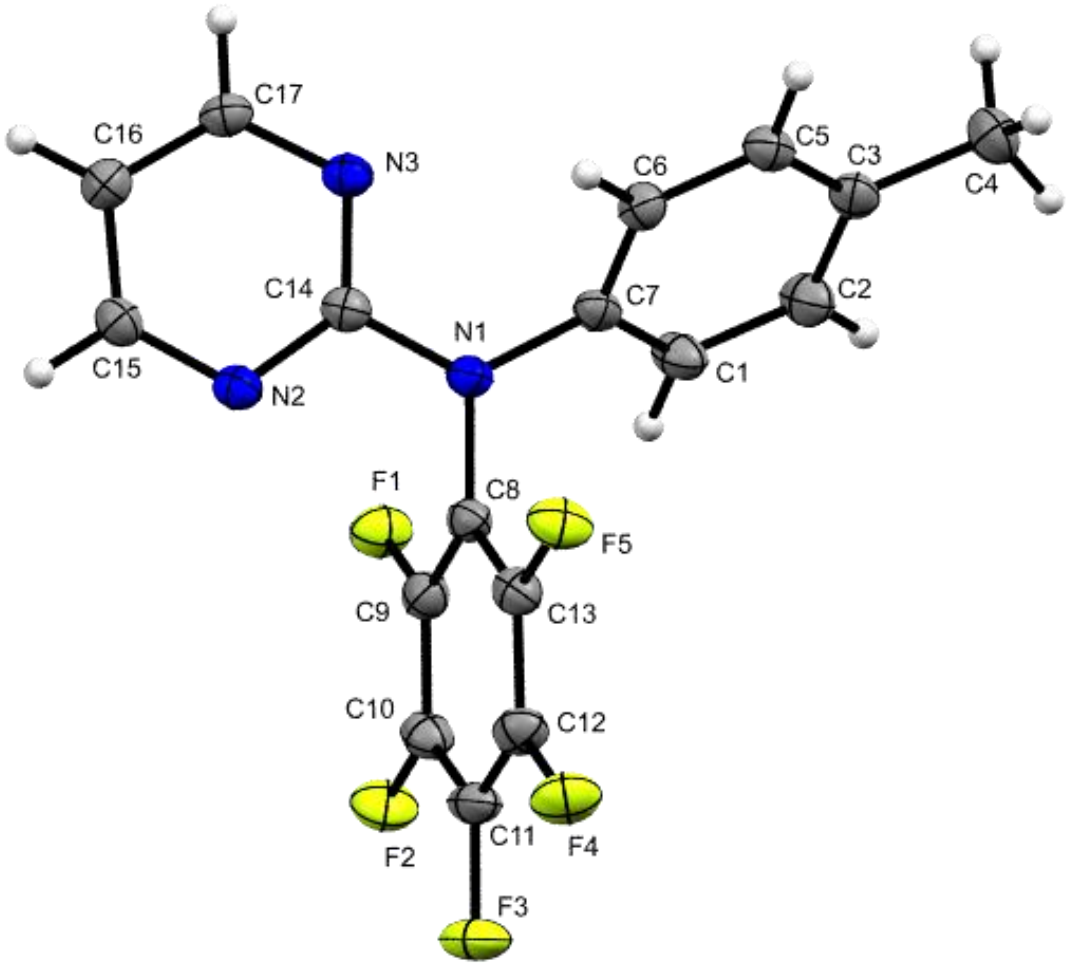


Fig S2: Molecular structure of final product **4ca** (ORTEP view)

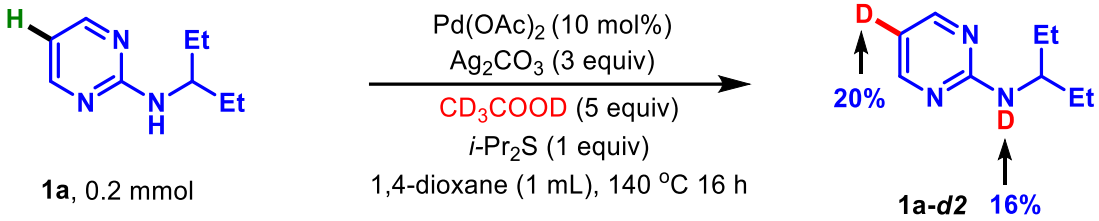
Table S9: Crystal data and structure refinement for 4ca (CCDC 2311113).

Identification code	ADAAF115_auto
Empirical formula	$C_{17}H_{10}F_5N_3$
Formula weight	351.28
Temperature/K	99.99(11)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	14.4065(2)
b/Å	6.17670(10)
c/Å	17.7705(3)
α/°	90
β/°	109.917(2)
γ/°	90

Volume/Å^3	1486.72(4)
Z	4
ρ_{calc}g/cm^3	1.569
μ/mm^{-1}	1.223
F(000)	712.0
Crystal size/mm^3	0.3 × 0.04 × 0.01
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	6.526 to 136.282
Index ranges	-17 ≤ h ≤ 17, -7 ≤ k ≤ 7, -21 ≤ l ≤ 21
Reflections collected	19619
Independent reflections	2708 [R_{int} = 0.0362, R_{sigma} = 0.0190]
Data/restraints/parameters	2708/0/227
Goodness-of-fit on F^2	1.045
Final R indexes [I>=2σ (I)]	R_1 = 0.0330, wR_2 = 0.0888
Final R indexes [all data]	R_1 = 0.0355, wR_2 = 0.0912
Largest diff. peak/hole / e Å^{-3}	0.25/-0.23

9. Mechanistic investigations

9.1 H/D exchange experiment with 2-aminopyrimidine 1a using CD_3COOD



An oven-dried screw cap reaction tube was charged with a magnetic stir-bar, 2-aminopyrimidine **1a** (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (10 mol%, 0.02 mmol, 4.6 mg) and Ag_2CO_3 (0.6 mmol, 3 equiv, 165 mg) were taken in air. Subsequently, 1,4-dioxane (1.0 mL), isopropyl sulfide (0.1 mmol, 1 equiv, 15 µL), and CD_3COOD (5 equiv) were added. The reaction tube was capped tightly and placed in a preheated oil bath at 140 °C for 12 hours. Upon completion, the resulting mixture was diluted with EtOAc, filtered through a plug of Celite, and concentrated under reduced pressure. The starting material was recovered by column chromatography over silica gel using a mixture of EtOAc/n-hexane as eluent to afford **1a**-*d2*. The amount of D-exchange was measured using ^1H NMR. The D-exchange was found to be 20% at the C5-position, and 15% D-exchange was found at NH proton of pyrimidine.

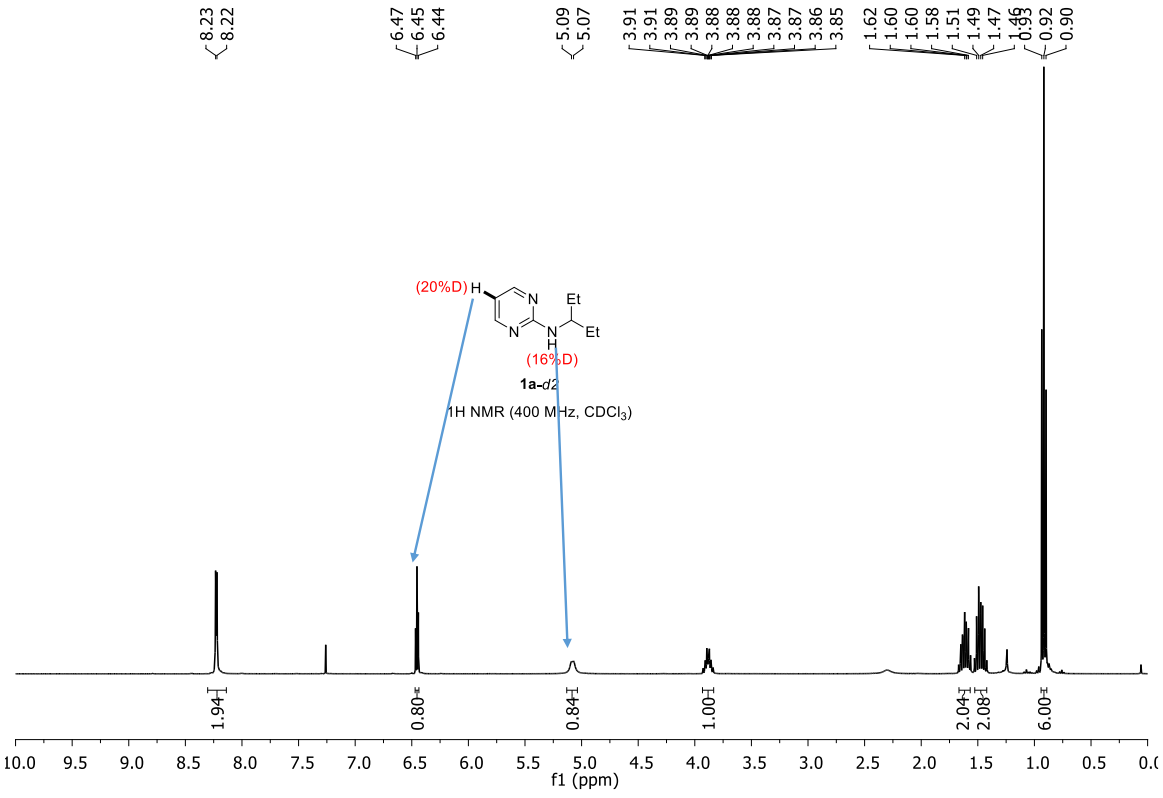
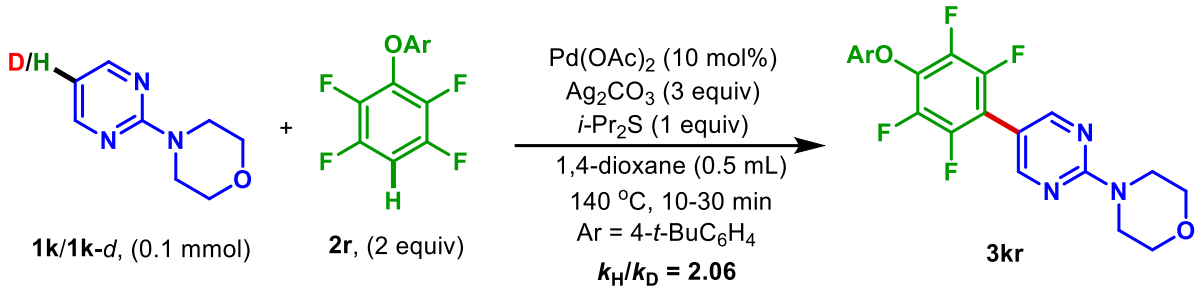


Figure S3: ^1H spectrum of **1a**-*d2* (400 MHz, $CDCl_3$)

9.2 Kinetic isotope effect Experiments



Two oven-dried 15 mL sealed tubes were added $Pd(OAc)_2$ (10 mol%) and Ag_2CO_3 (0.3 mmol). In one tube, **1k** (0.1 mmol), **2r** (2 equiv), isopropyl sulfide (0.1 mmol, 1 equiv), and 1,4-dioxane (0.5 mL) were added subsequently. In the other tube, **1k**-*d* (0.1 mmol), **2r** (2 equiv), isopropyl sulfide (0.1 mmol, 1 equiv) and 1,4-dioxane (0.5 mL) were added. Then, the reaction tubes were capped tightly and stirred at 140 °C. After a respective time, the reactions were stopped and charged with 1,3,5-trimethoxybenzene (0.1 mmol) as an internal standard. Then, the resulting mixture was diluted with EtOAc, filtered through a plug of celite, and concentrated under reduced pressure. The ^{1}H NMR of the crude samples was recorded to measure the NMR yields. This experiment was performed for three different time intervals. The yield (%) vs time (min) plot was found to be a linear plot, and from the slope of such plots, the KIE value k_H/k_D = 2.06 was determined.

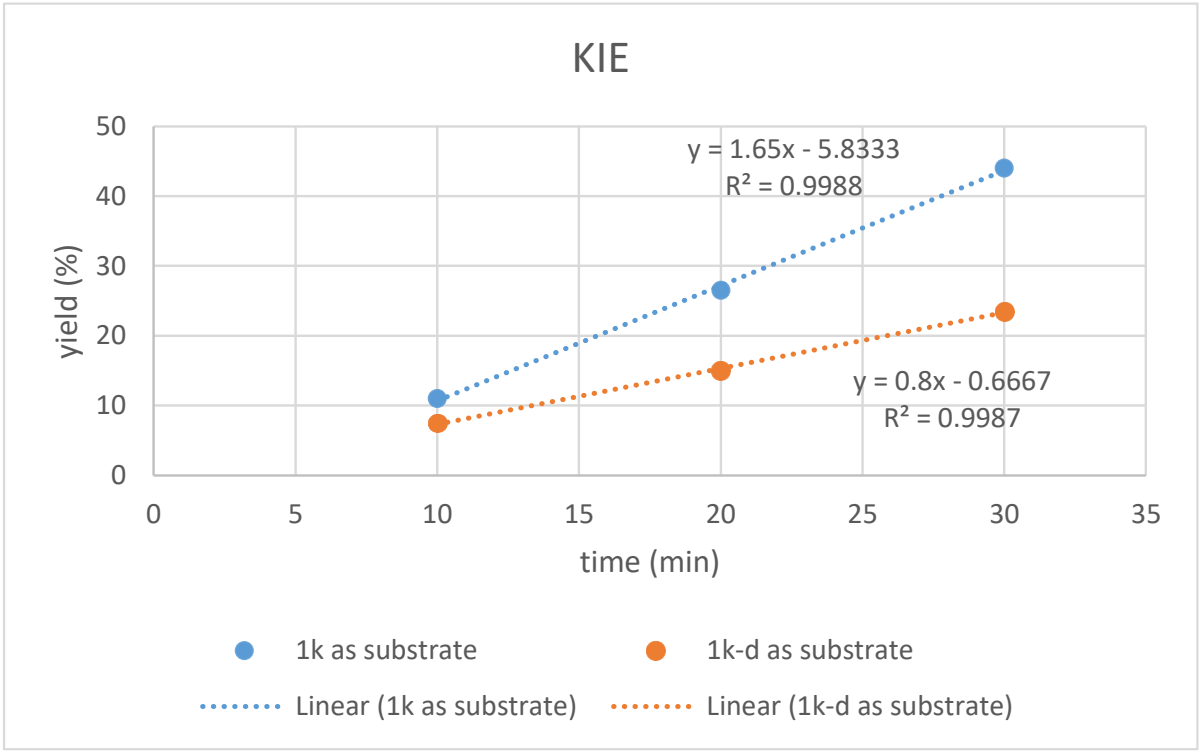
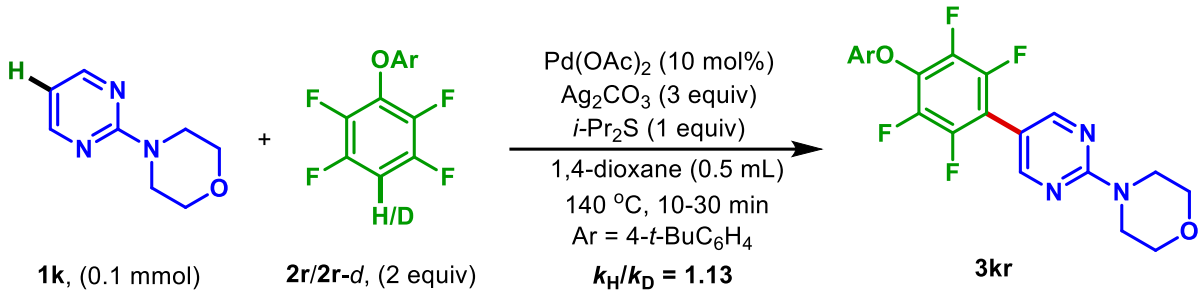


Figure S3: Measurement of KIE for substrate **1k** and **1k**-*d*



Two oven-dried 15 mL sealed tubes were added $Pd(OAc)_2$ (10 mol%) and Ag_2CO_3 (0.3 mmol). In one tube, **1k** (0.1 mmol), **2r** (2 equiv), isopropyl sulfide (0.1 mmol, 1 equiv), and 1,4-dioxane (0.5 mL) were added subsequently. In the other tube, **1k** (0.1 mmol), **2r**-*d* (2 equiv), isopropyl sulfide (0.1 mmol, 1 equiv) and 1,4-dioxane (0.5 mL) were added. Then, the reaction tubes were capped tightly and stirred at 140 °C. After a respective time, the reactions were stopped and charged with 1,3,5-trimethoxybenzene (0.1 mmol) as an internal standard. Then, the resulting mixture was diluted with EtOAc, filtered through a plug of celite, and concentrated under reduced pressure. The ^{1}H NMR of the crude samples was recorded to measure the NMR yields. This experiment was performed for three different time intervals. The yield (%) vs time (min) plot was found to be a linear plot, and from the slope of such plots, the KIE value k_H/k_D = 1.13 was determined.

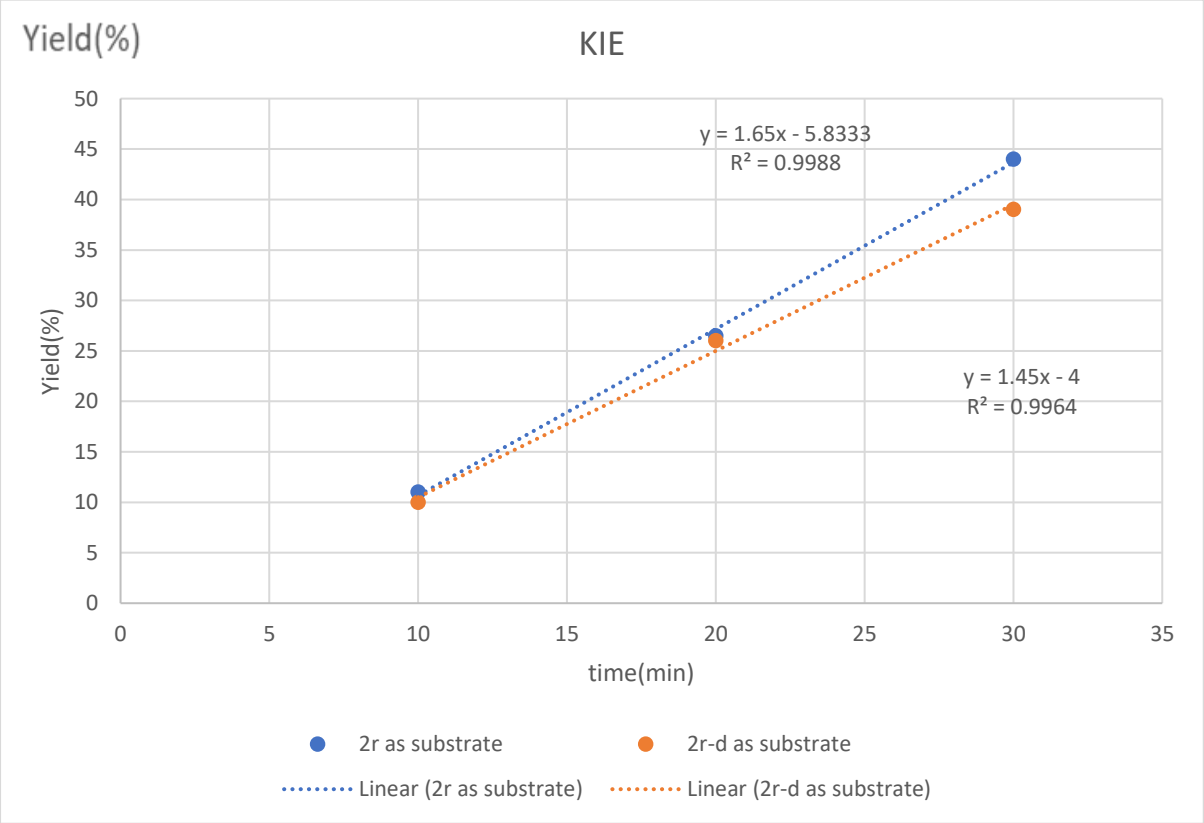
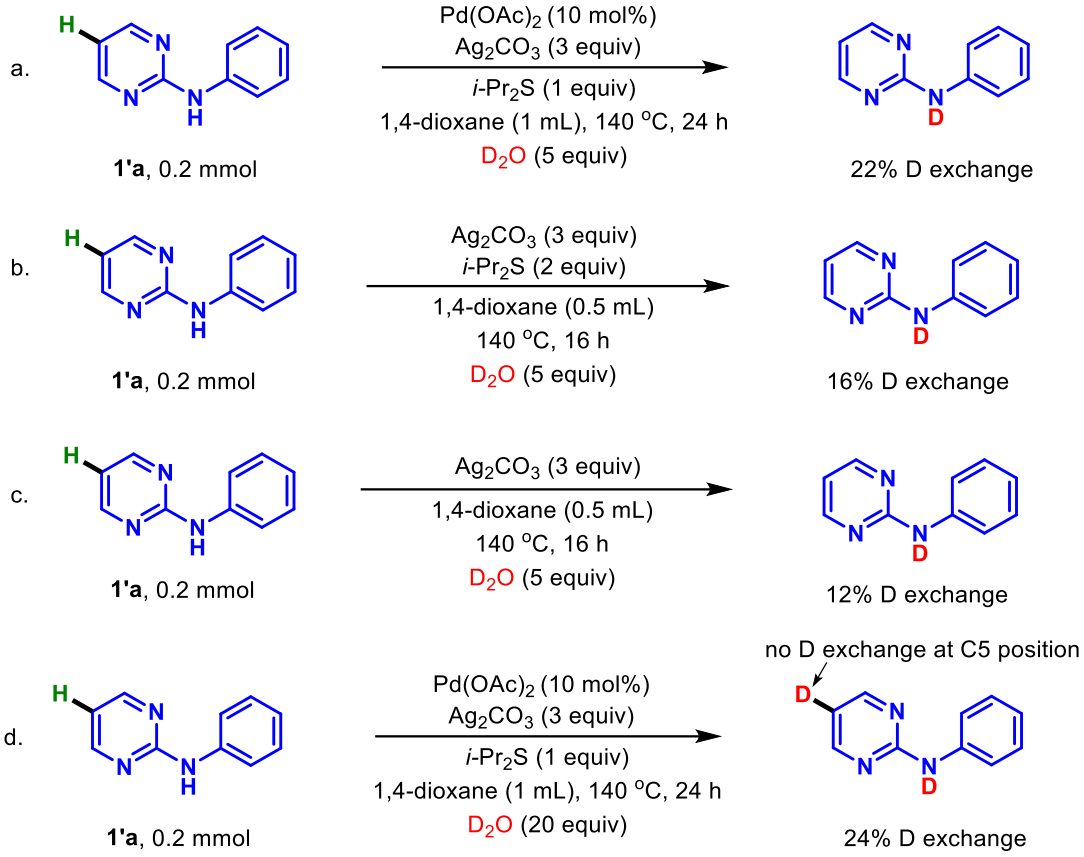


Figure S4: Measurement of KIE for substrate **2r** and **2r**-*d*

9.3 H/D exchange experiments with N-phenylpyrimidin-2-amine 1'a using D_2O



An oven-dried screw cap reaction tube was charged with a magnetic stir-bar, N-phenylpyrimidin-2-amine **1'a** (0.2 mmol, 1.0 equiv) and other reagents were taken in air. Subsequently, 1,4-dioxane (1.0 mL) and D_2O (5 equiv) were added. The reaction tube was capped tightly and placed on a preheated oil bath at 140 °C for 24 hours. Upon completion, the resulting mixture was diluted with EtOAc, filtered through a plug of Celite, and concentrated under reduced pressure. The starting material was recovered by column chromatography over silica gel using a mixture of EtOAc/n-hexane as eluent to afford **1'a**-*d*. The amount of D-exchange was measured using ^1H NMR. The D-exchange was found to be 22%, 16%, 12% and 24 % at the NH position under four different conditions, and no D-exchange was found at the C5-position of pyrimidine or at the ortho position of aniline.

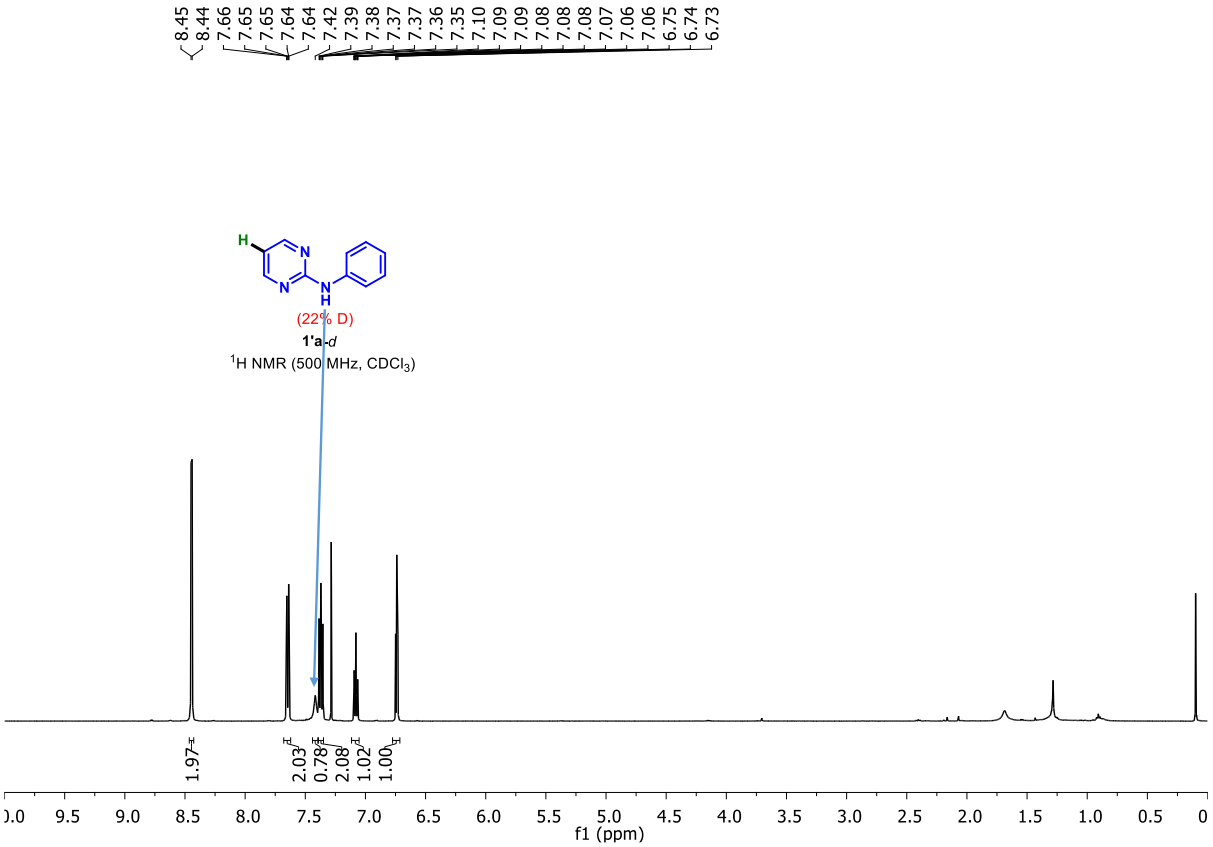


Figure S5: ^{1}H spectrum of **1'a**-*d2* (500 MHz, $CDCl_3$) for equation 9.3a

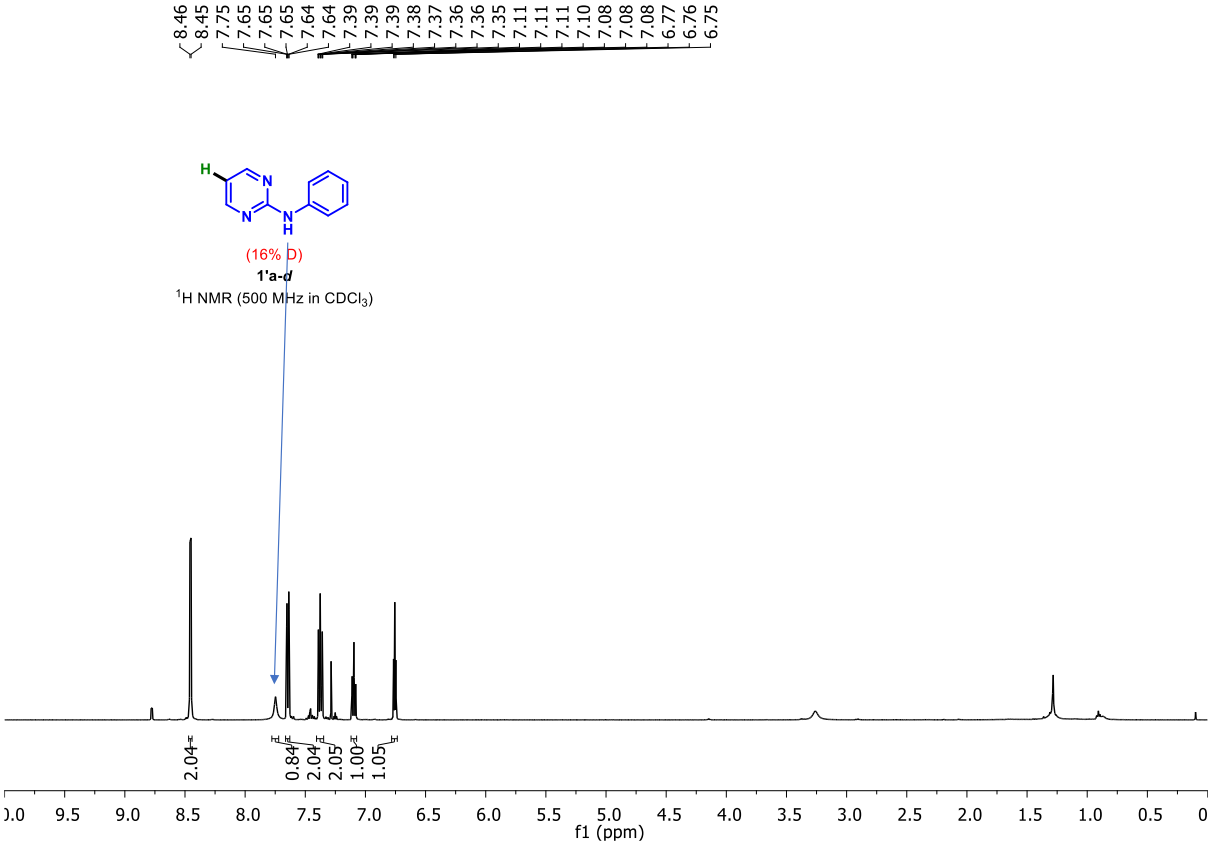


Figure S6: ^{1}H spectrum of **1'a**-*d2* (500 MHz, $CDCl_3$) for equation 9.3b

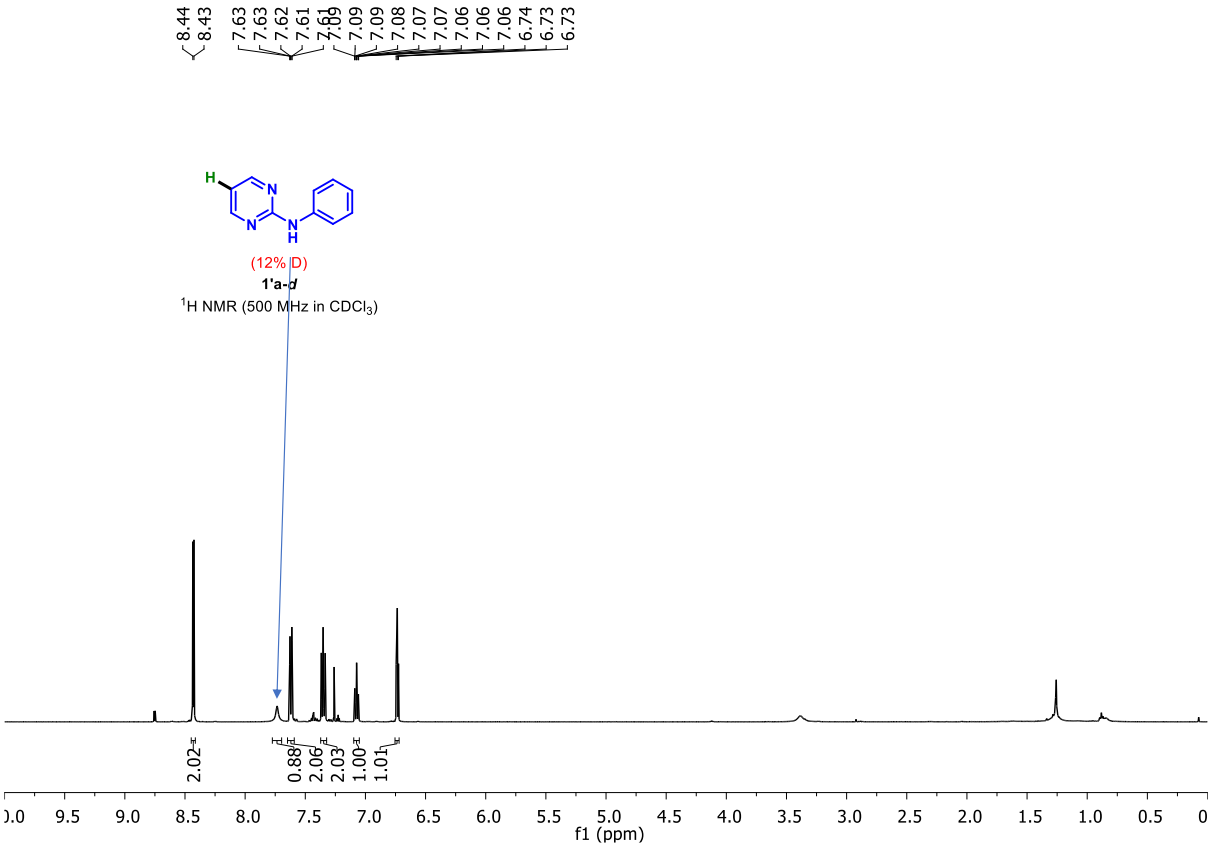


Figure S7: ^{1}H spectrum of **1'a**-*d2* (500 MHz, $CDCl_3$) for equation 9.3c

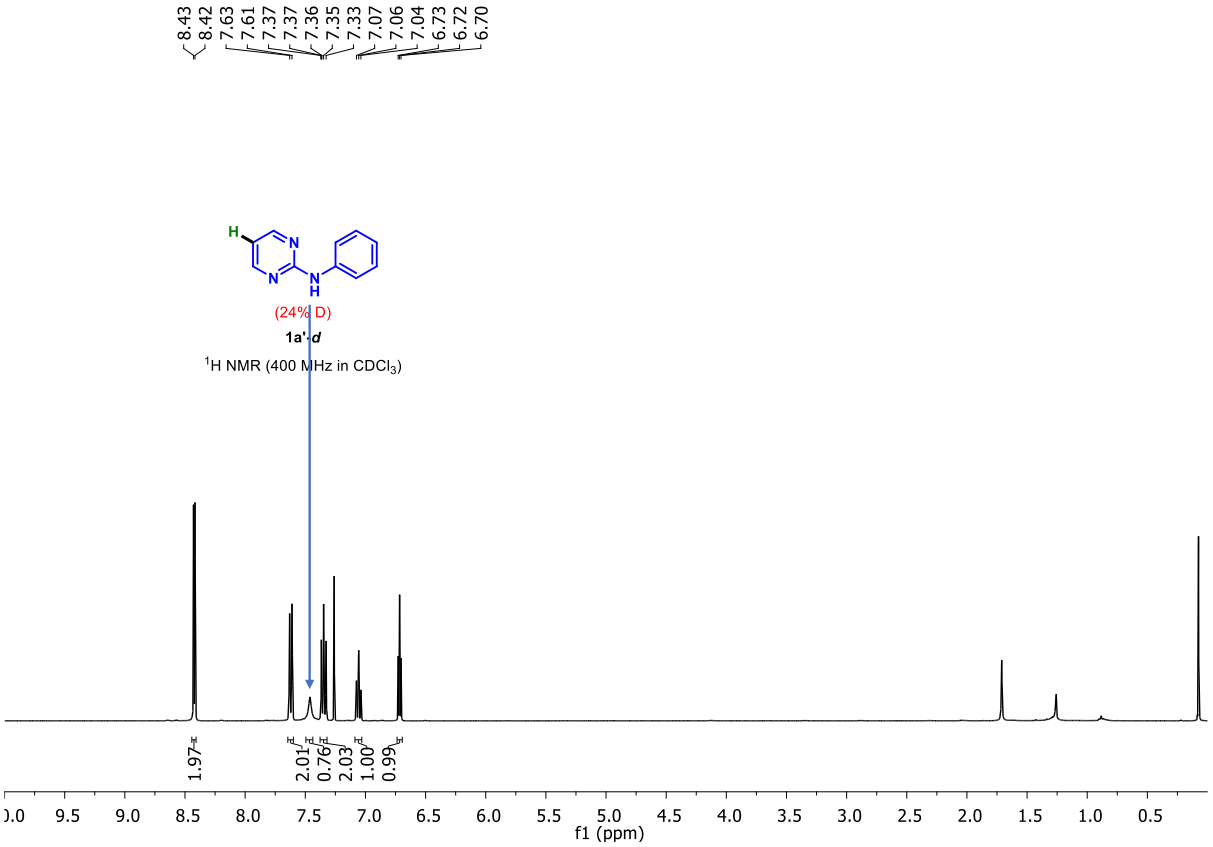
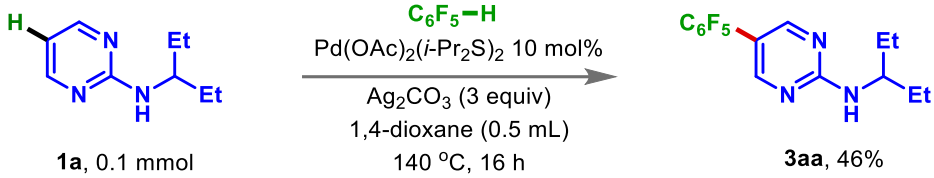


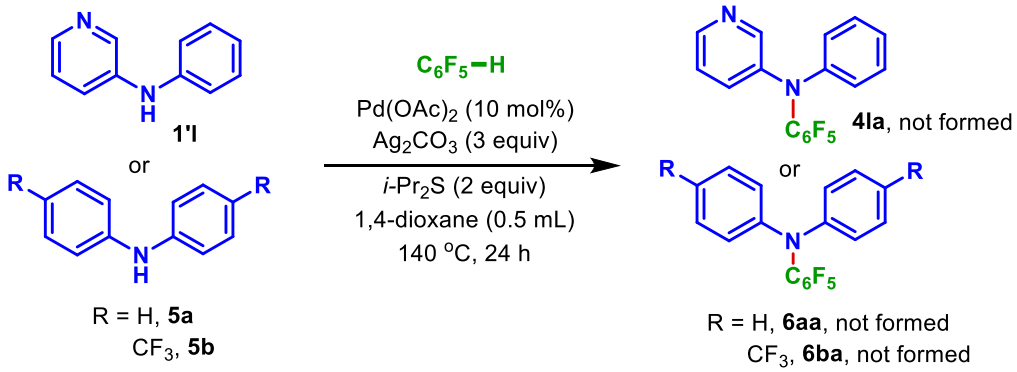
Figure S8: ^{1}H spectrum of **1'a**-*d2* (400 MHz, $CDCl_3$) for equation 9.3d

9.4 Control experiment with $Pd(OAc)_2(i\text{-}Pr_2S)_2$



An oven-dried screw cap reaction tube was charged with a magnetic stir-bar, N-phenylpyrimidin-2-amine **1a** (0.1 mmol, 1.0 equiv), $Pd(OAc)_2(i\text{-}Pr_2S)_2$ (10 mol%, 0.01 mmol, 4.6 mg) and Ag_2CO_3 (0.3 mmol, 3 equiv, 82 mg) were taken in air. Subsequently, pentafluorobenzene (0.2 mmol, 2.0 equiv) and 1,4-dioxane (0.5 mL) were added. The reaction tube was capped tightly and placed in a preheated oil bath at 140 °C for 16 hours. Upon completion, the resulting mixture was diluted with EtOAc, filtered through a plug of Celite, and concentrated under reduced pressure. Product **3aa** was isolated in 46% yield by column chromatography over silica gel using a mixture of EtOAc/n-hexane as eluent. It suggested that the $(i\text{-}Pr_2S)_2Pd(OAc)_2$ could likely be involved in the catalytic cycle.

9.5 Control experiment with 1'l, 5a and 5b



Three oven-dried 15 mL sealed tubes were added **1'l**, **5a**, and **5b** separately. Following this, $Pd(OAc)_2$ (10 mol%), Ag_2CO_3 (0.3 mmol, 3 equiv), isopropyl sulfide (0.1 mmol, 1 equiv), pentafluorobenzene (0.2 mmol, 2 equiv) and 1,4-dioxane (0.5 mL) were added subsequently to each tube. Then, the reaction tubes were capped tightly and stirred at 140 °C for 24 hours. After a respective time, the reactions were stopped, and the resulting mixture was diluted with EtOAc. The TLC and GC analysis showed that **4la**, **6aa**, and **6ba** were not formed. Filtered through a plug of celite and concentrated under reduced pressure. These experiments suggested that (1) N-chelation is crucial, for which the position of the nitrogen atom is vital, and (2) the N-H polyfluoroarylation is not guided by electronics.

9.6 Equilibrium study with 1a and $Pd(OAc)_2$

An equilibrium study was performed by conducting a stoichiometric reaction of N-(pentan-3-yl)pyrimidin-2-amine **1a** (1 equiv) in the presence of $Pd(OAc)_2$ (1 equiv) at room temperature in DMSO-d_6 in an NMR tube. We have found that the pyrimidyl C4-, and C6-protons degeneracy was broken as 1 equivalent of $Pd(OAc)_2$ was mixed with **1a**. It might due to the

coordination of the palladium center to one of the nitrogen atoms and formation of a species **1a.Pd**.

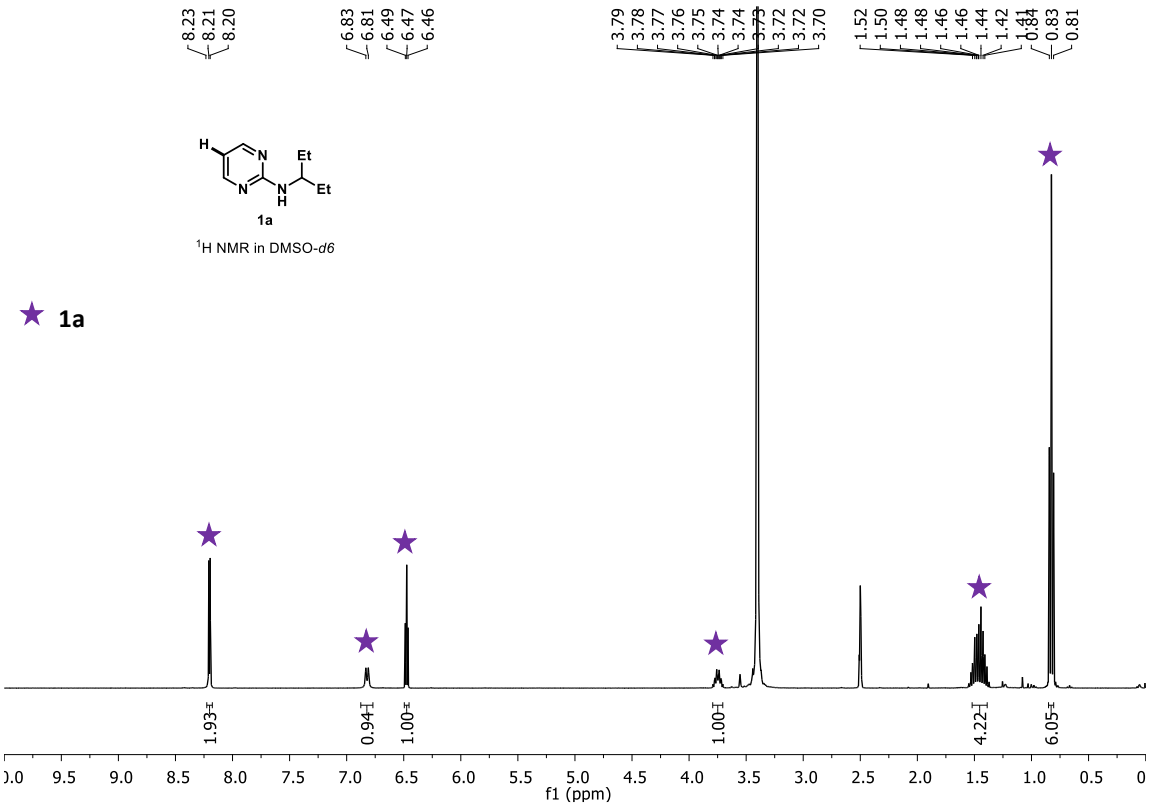


Figure S9: ^{1}H spectrum of **1a** (400 MHz, DMSO-d6)

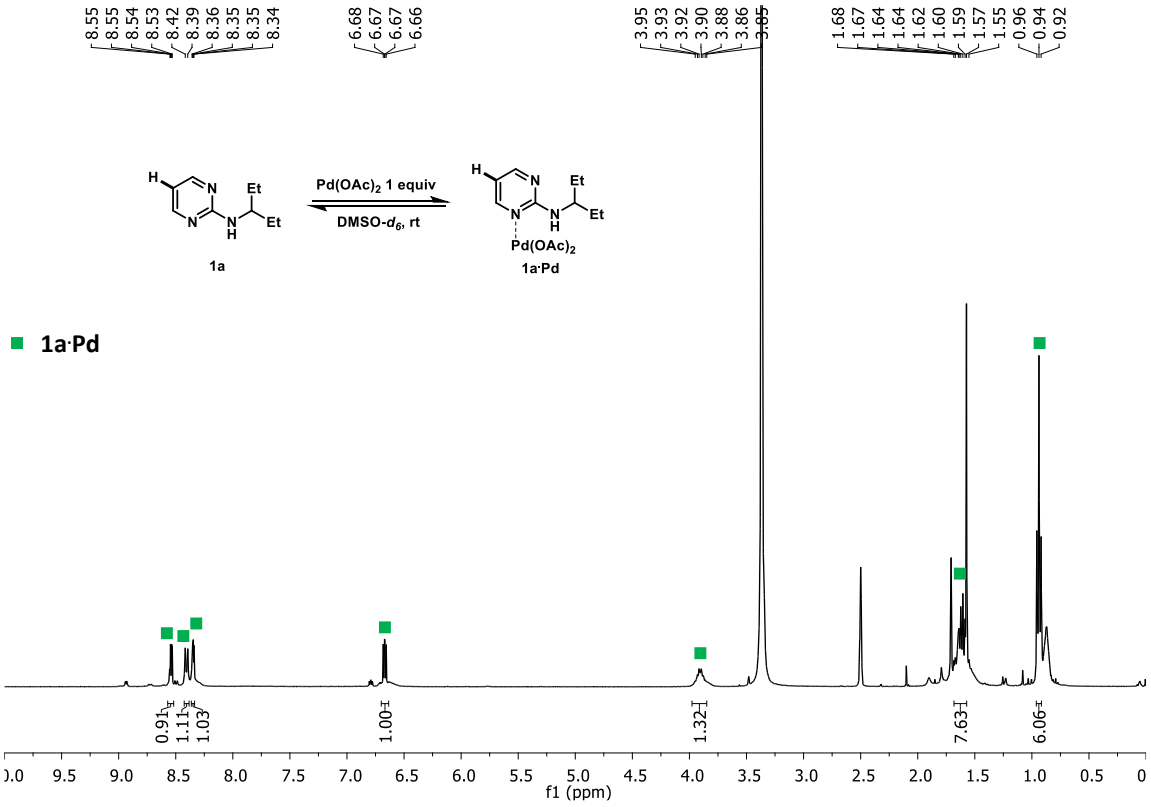


Figure S10: ^{1}H spectrum of **1a + Pd(OAc)$_2$** (400 MHz, DMSO-d6

10. Proposed mechanism

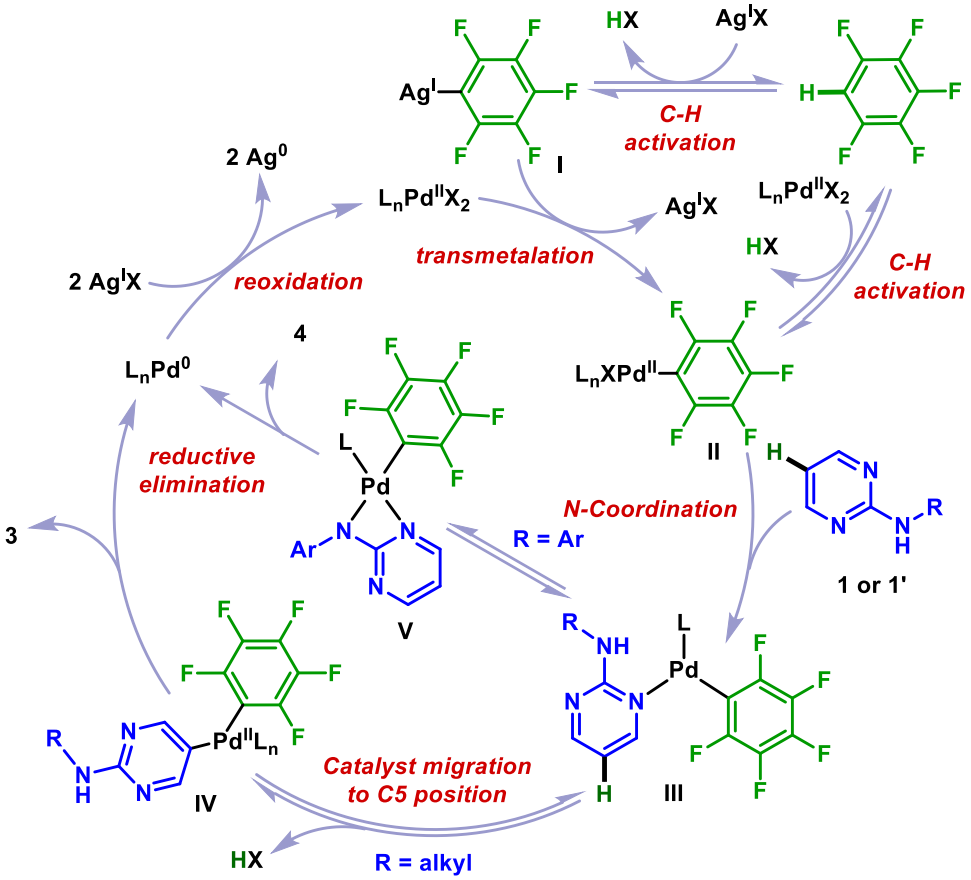


Figure S11: Proposed mechanism for C5- and N-polyfluoroarylation of 2-aminopyrimidines

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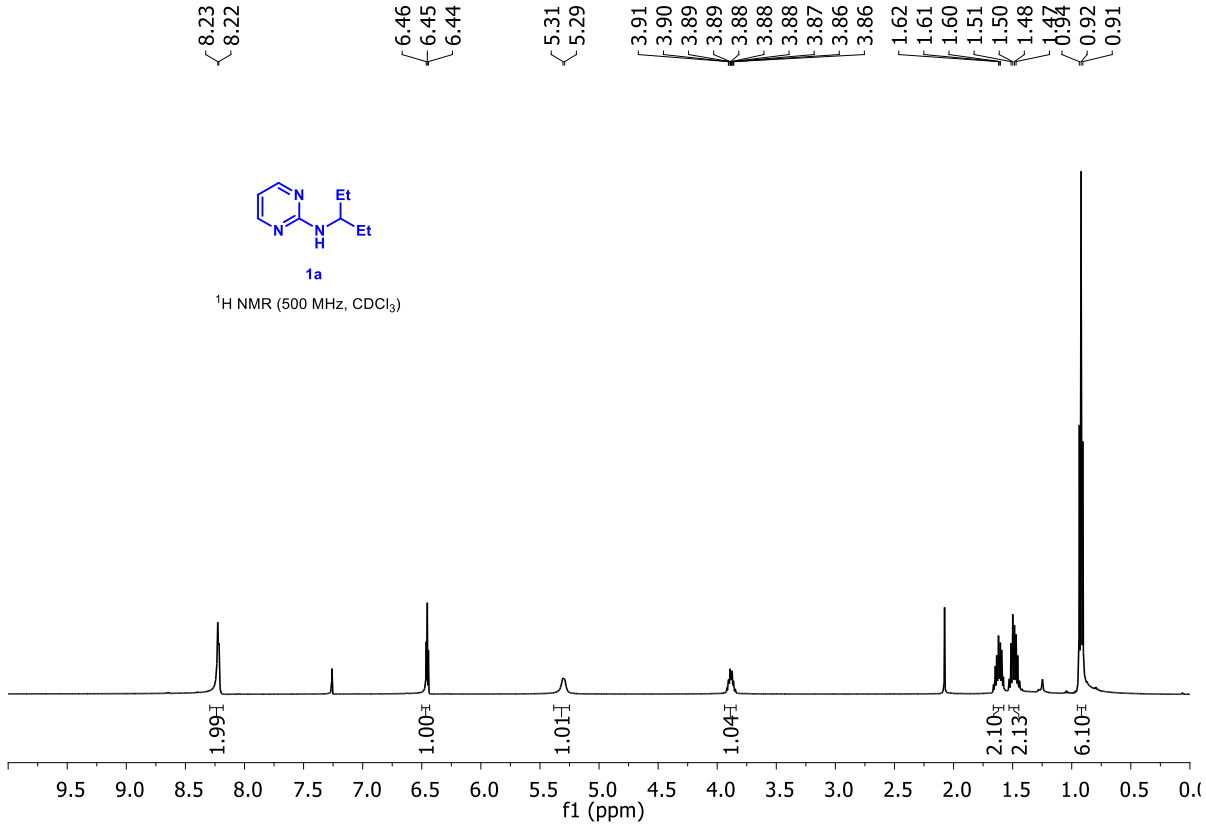
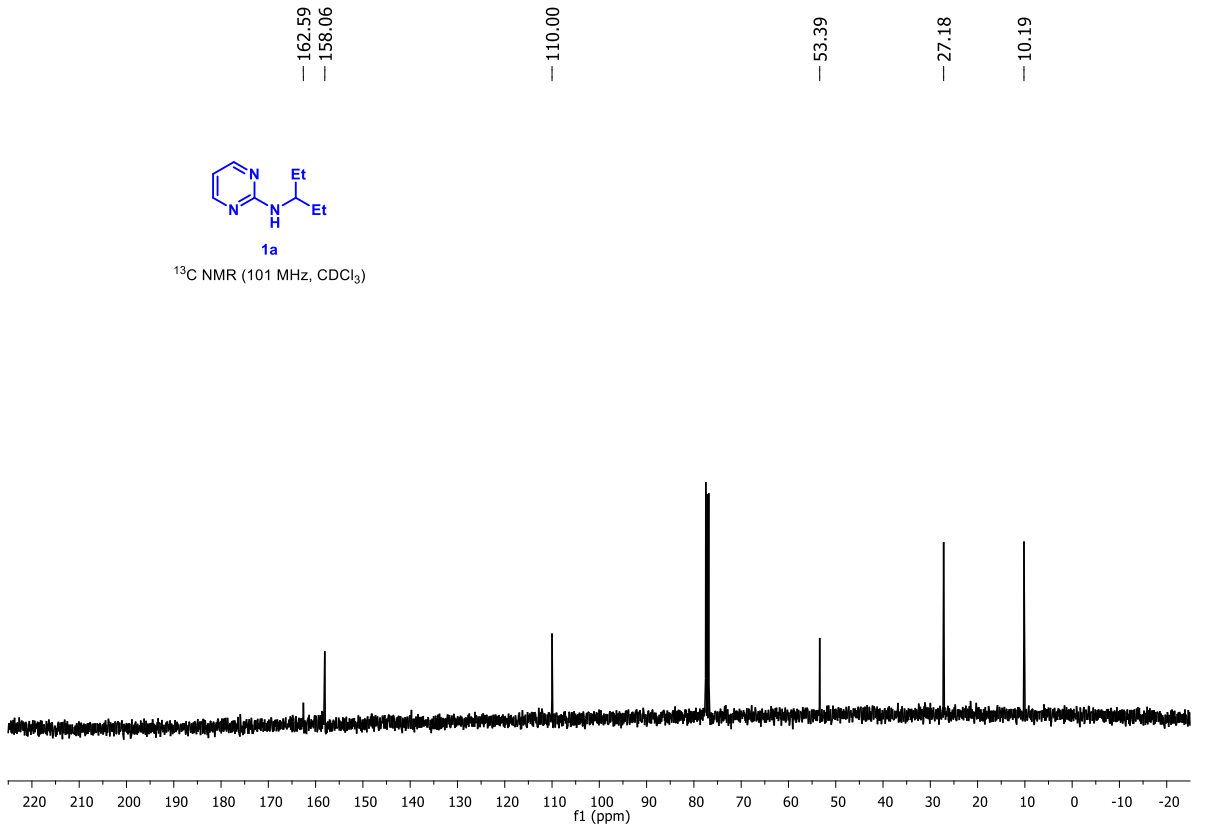
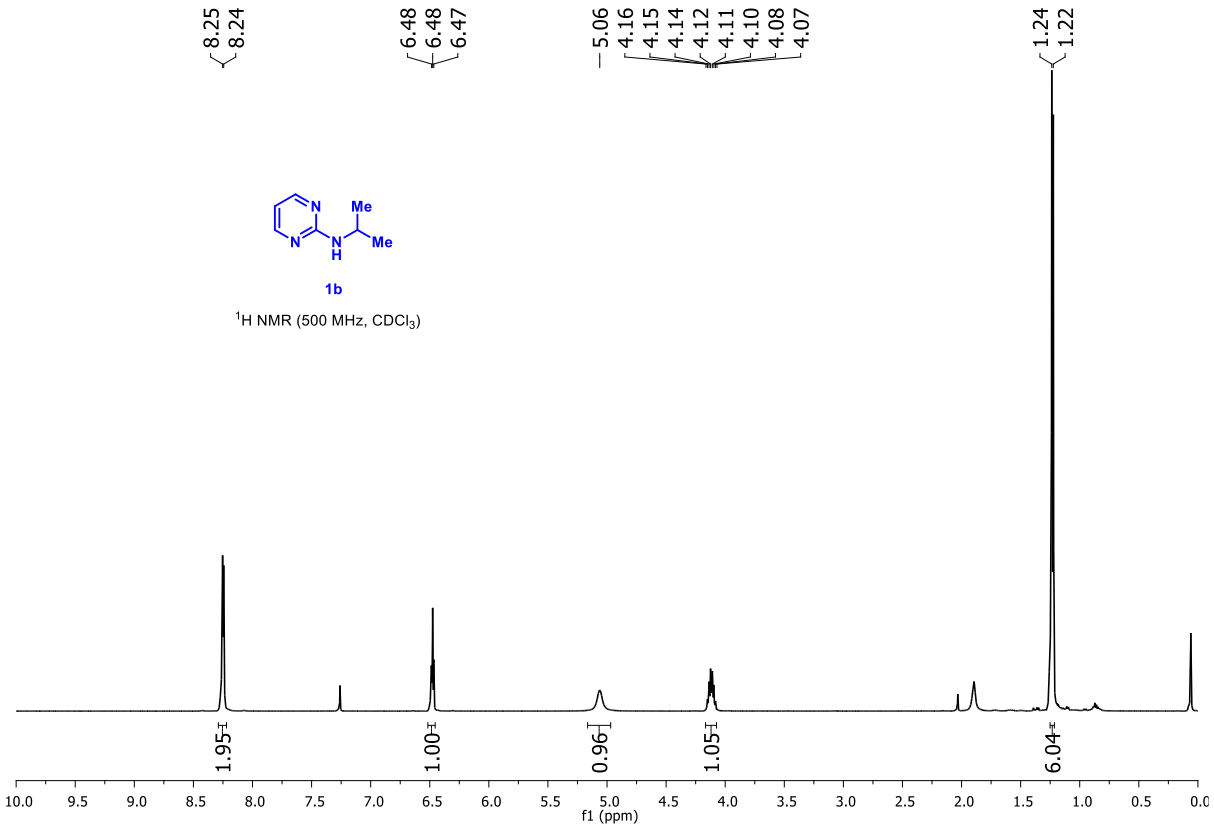
12. Copies of NMR spectra



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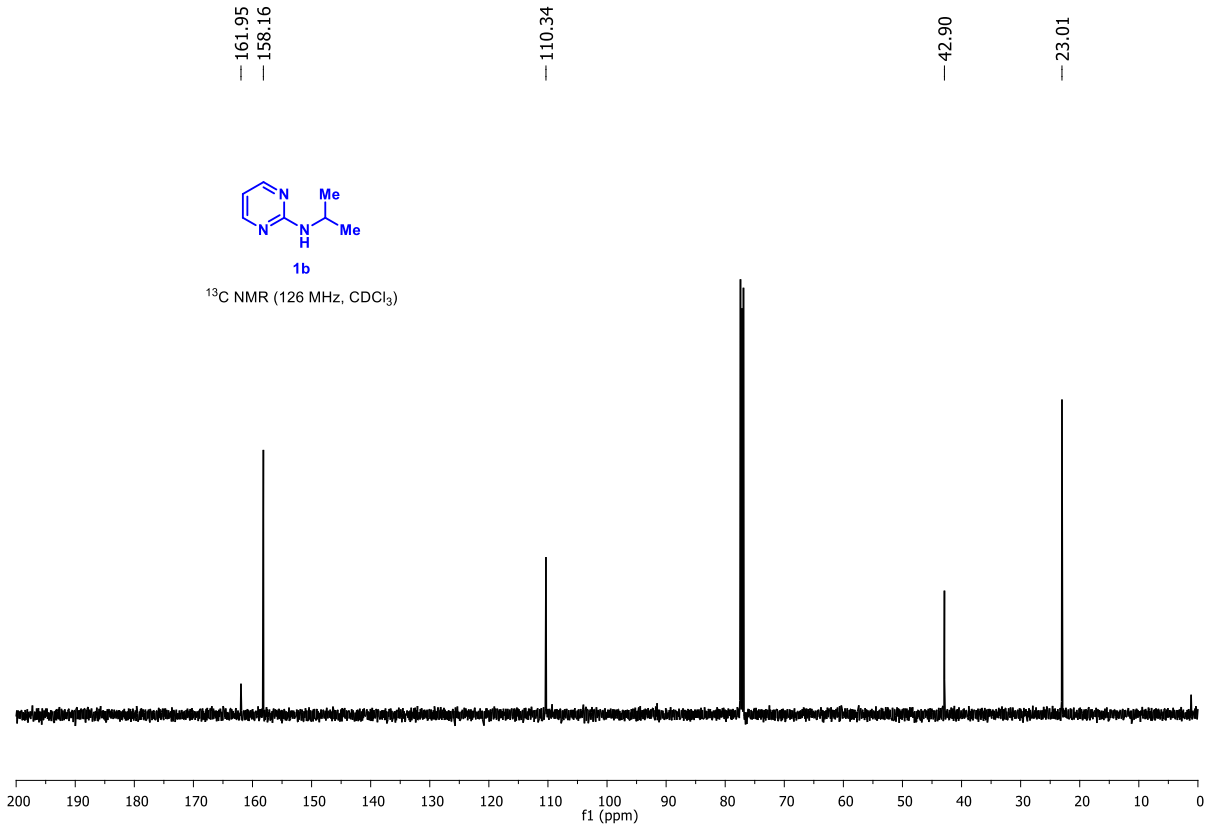
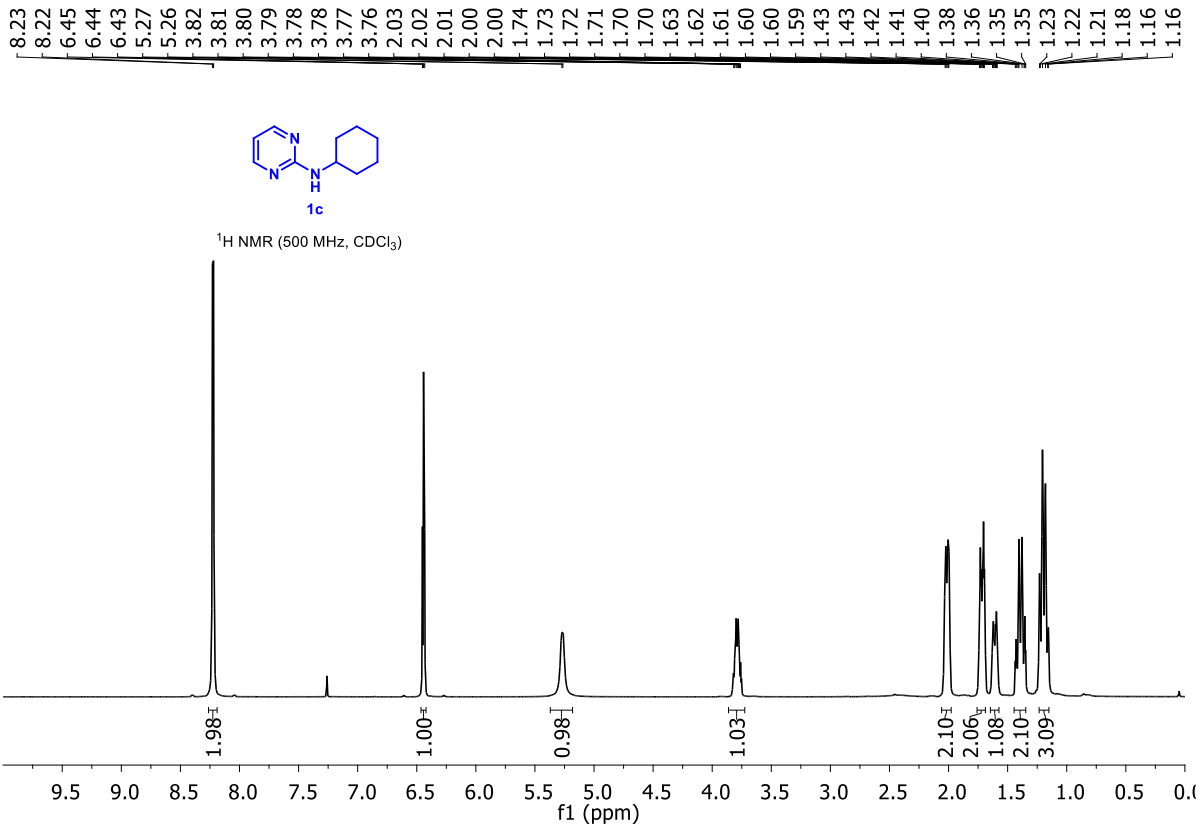
8.24
6.48
6.48
6.47
5.06
4.16
4.15
4.14
4.12
4.11
4.10
4.08
4.07
1.24
1.22
Me
N
N
H
Me
1b
1H NMR (500 MHz, CDCl3)
1.95
1.00
0.96
1.05
6.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


161.95
158.16
110.34
42.90
23.01
Me
N
N
H
Me
1b
13C NMR (126 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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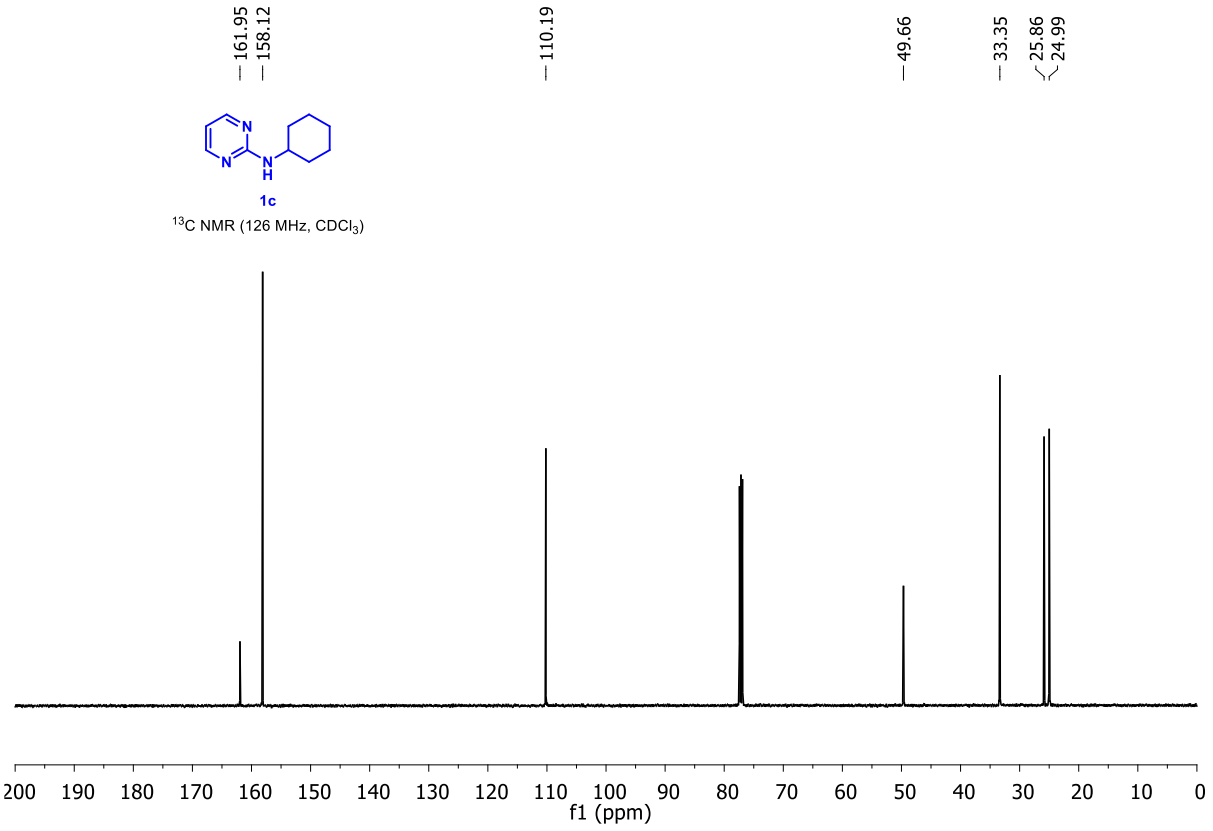
1c
1H NMR (500 MHz, CDCl3)
1.98 1.00 0.98 1.03 2.10 2.06 1.08 2.10 3.09
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


161.95 158.12 110.19 49.66 33.35 25.86 24.99
1c
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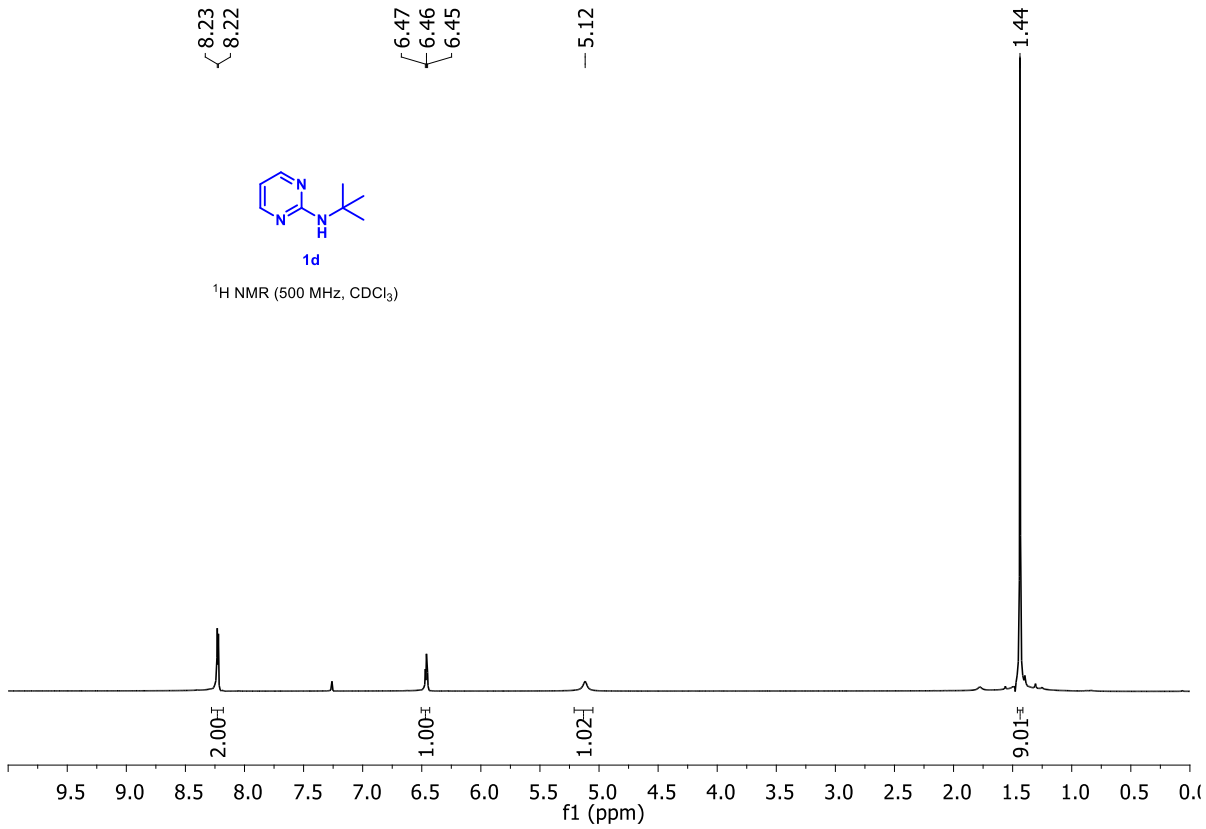
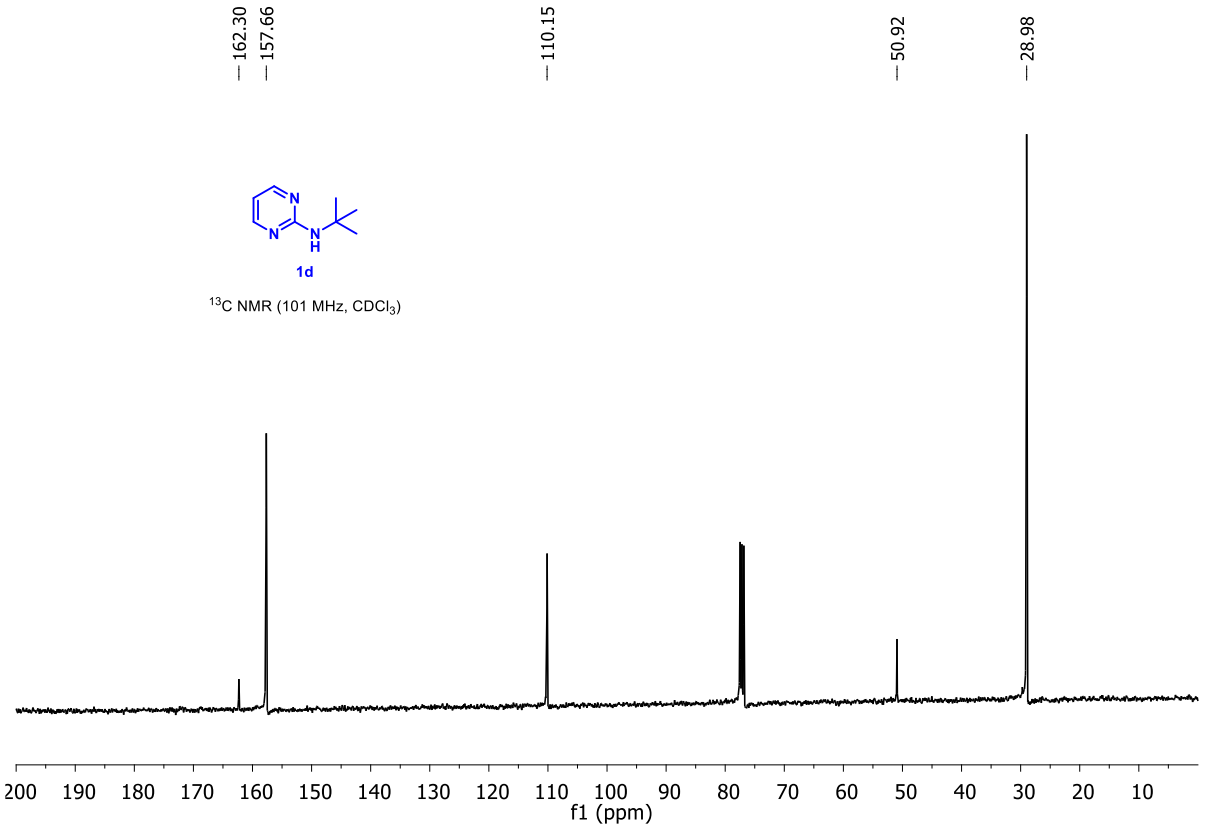
f1 (ppm)


8.23
8.22
6.47
6.46
6.45
5.12
1.44
1d
^{1}H NMR (500 MHz, $CDCl_3$)
2.00
1.00
1.02
9.01
f1 (ppm)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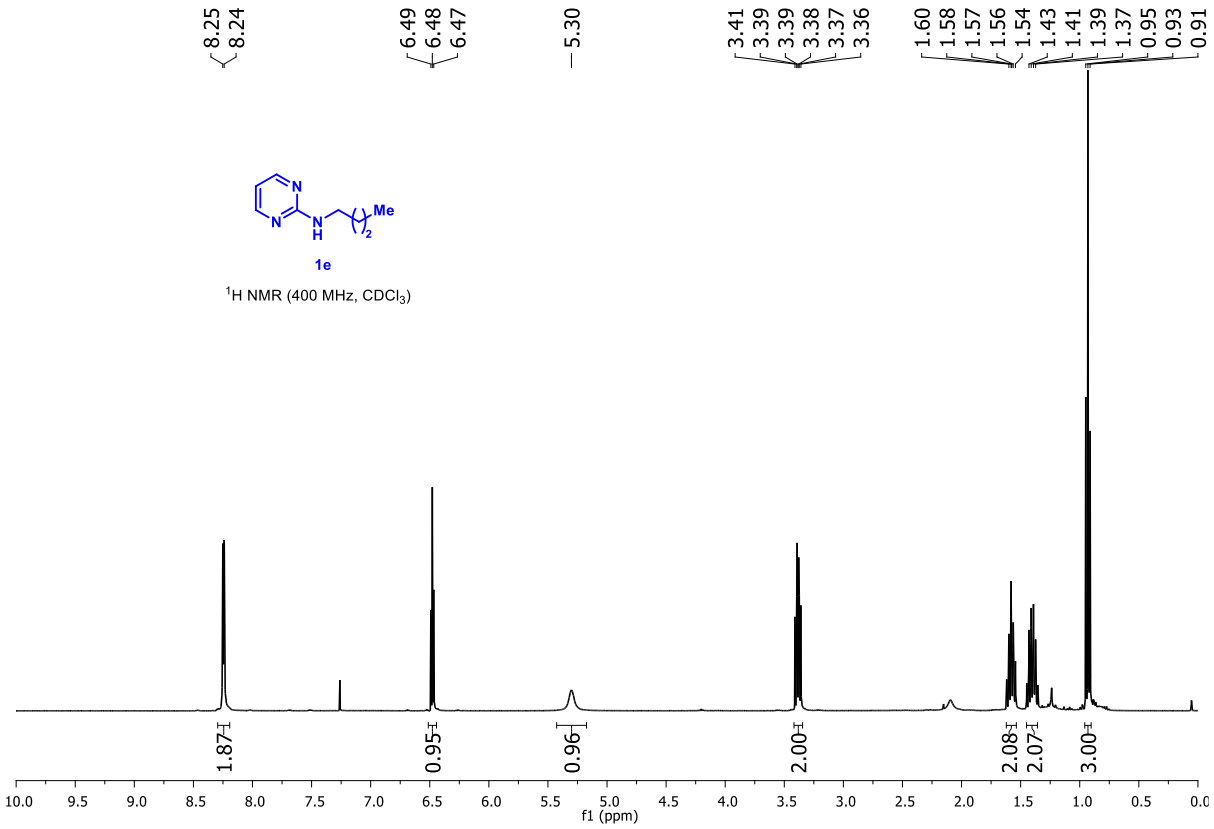
157.66
110.15
50.92
28.98
1d
^{13}C NMR (101 MHz, $CDCl_3$)
f1 (ppm)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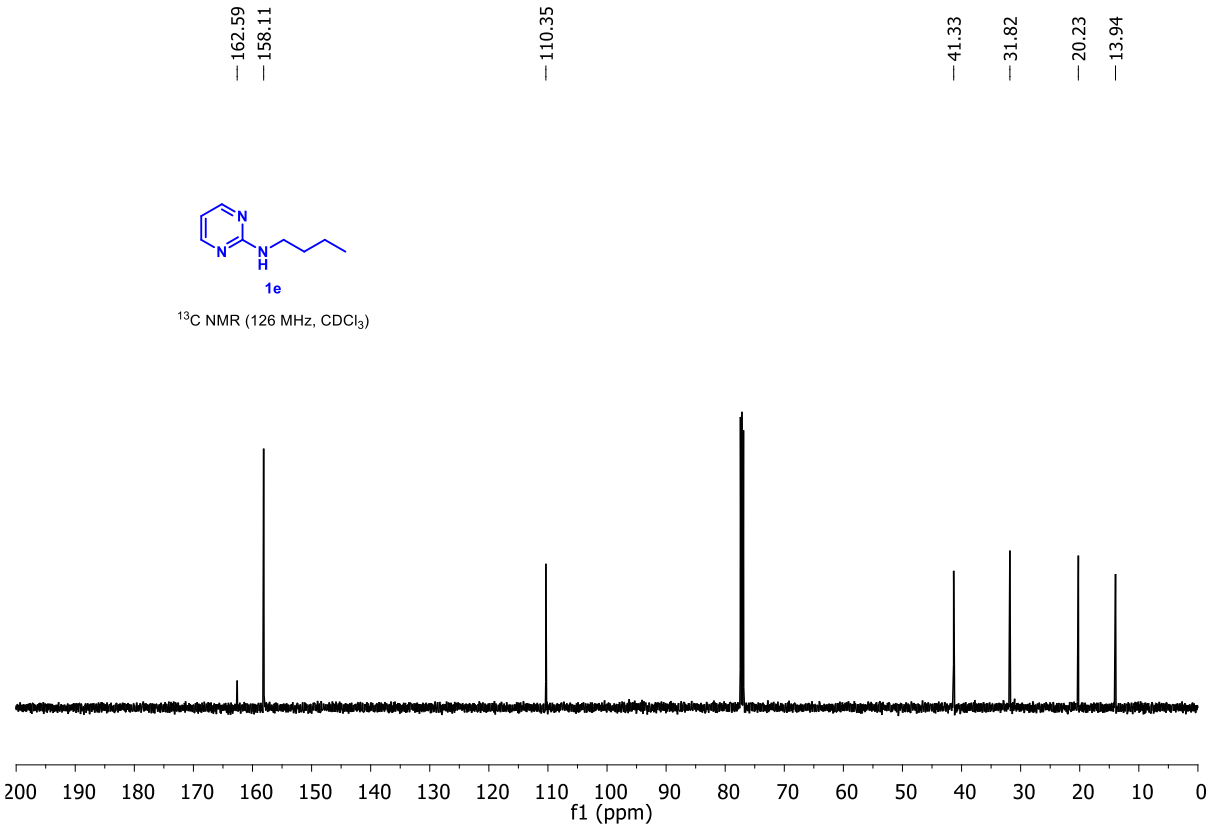
8.24
6.49
6.48
6.47
5.30
3.41
3.39
3.39
3.38
3.37
3.36
1.60
1.58
1.57
1.56
1.54
1.43
1.41
1.39
1.37
0.95
0.93
0.91
Me
1e
1H NMR (400 MHz, CDCl3)
1.87
0.95
0.96
2.00
2.08
2.07
3.00
f1 (ppm)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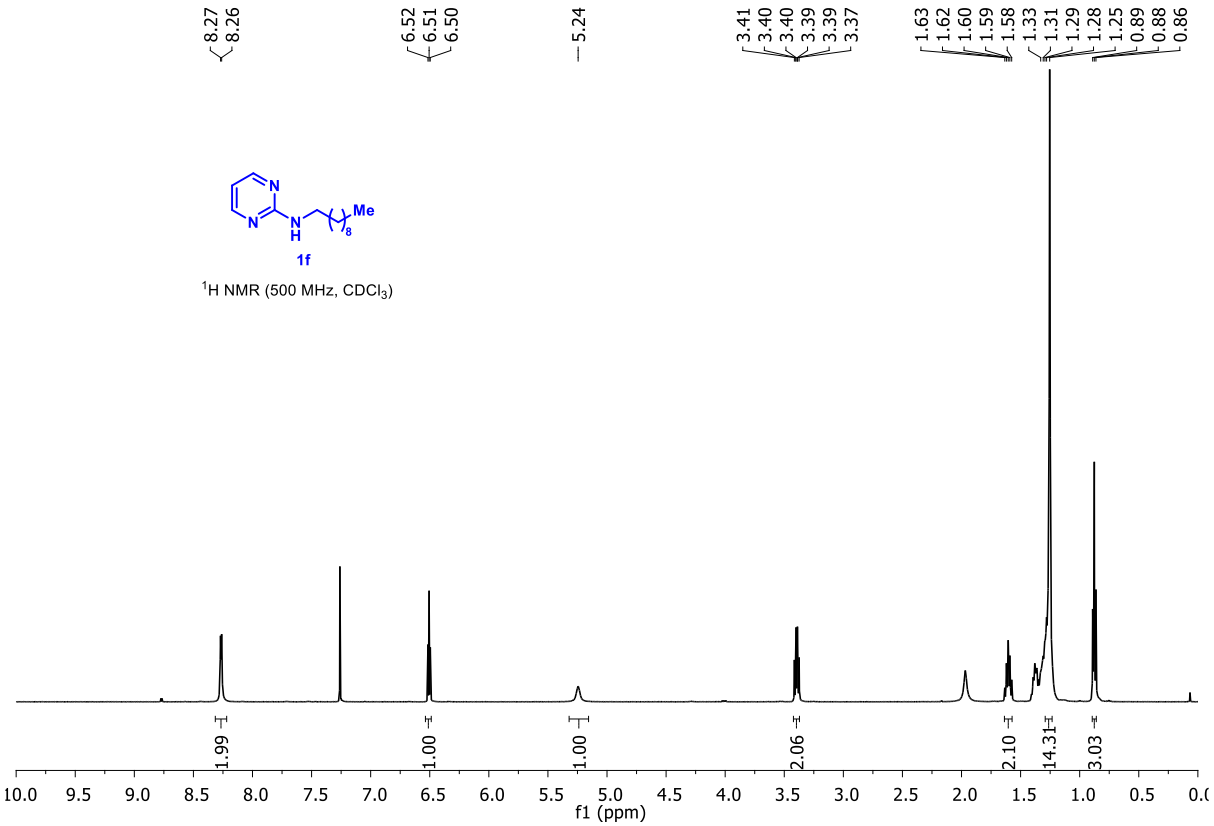
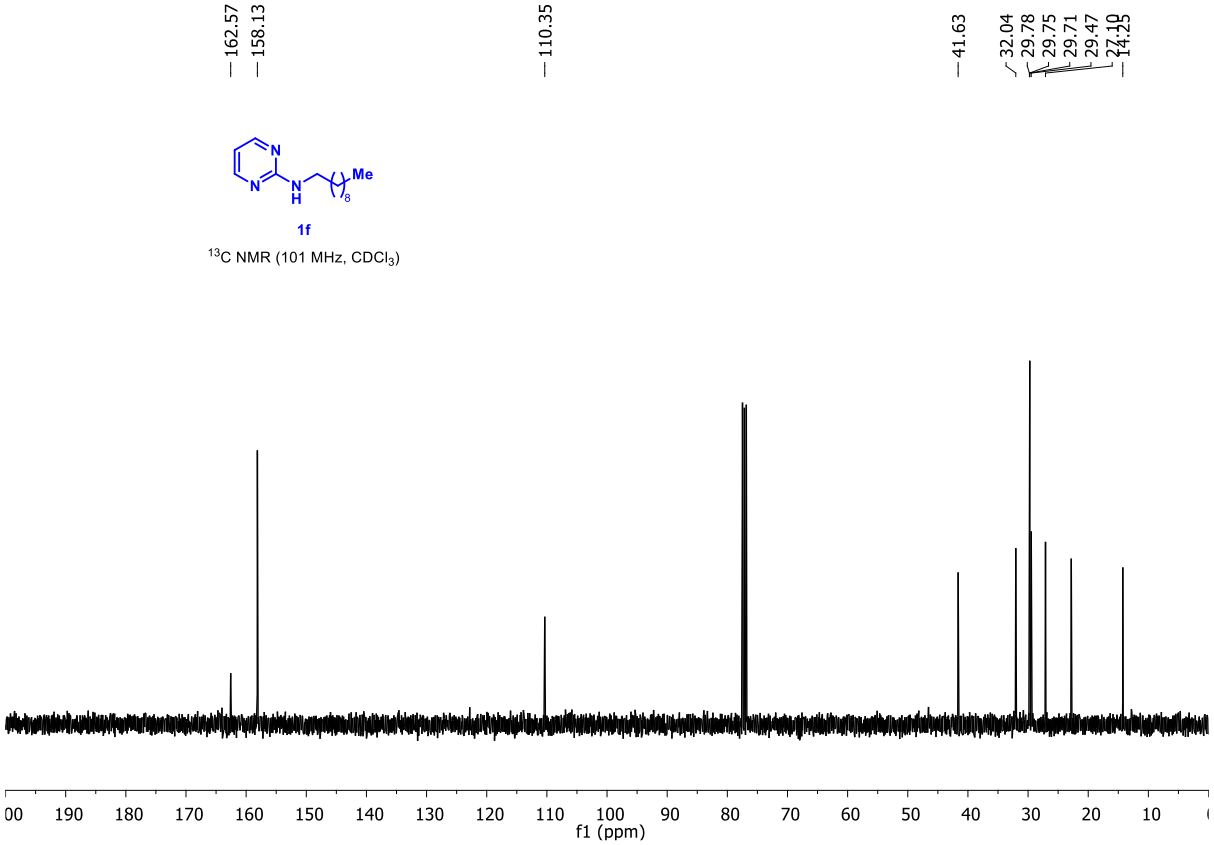
31.82
20.23
13.94
1e
13C NMR (126 MHz, CDCl3)
f1 (ppm)



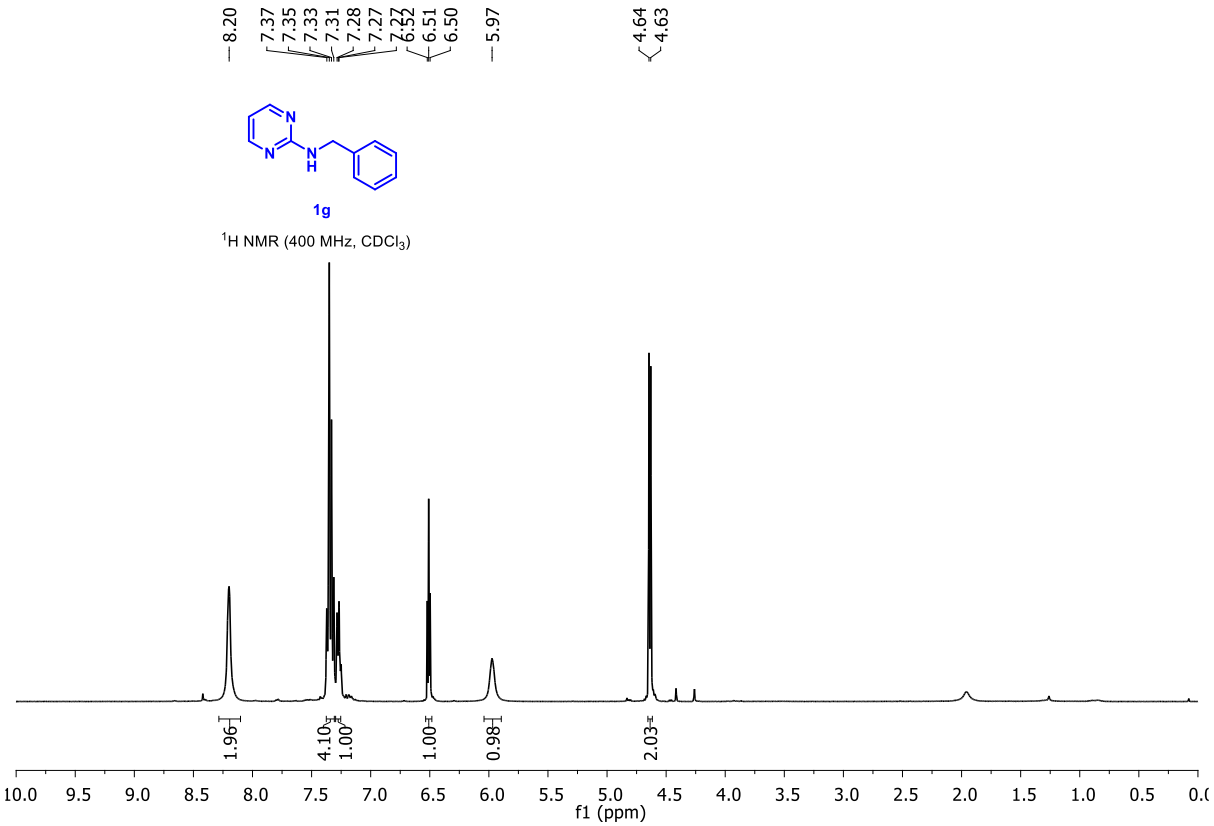
1f

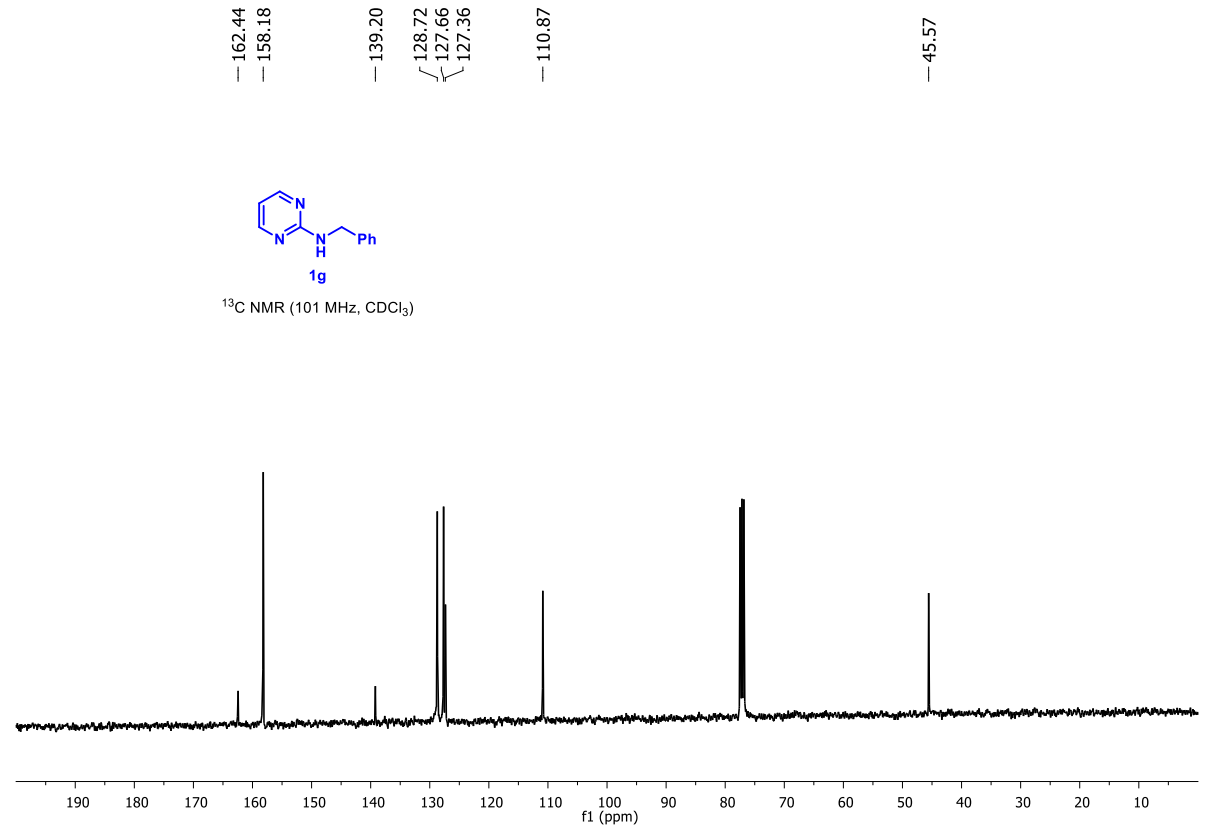
^{1}H NMR (500 MHz, $CDCl_3$)

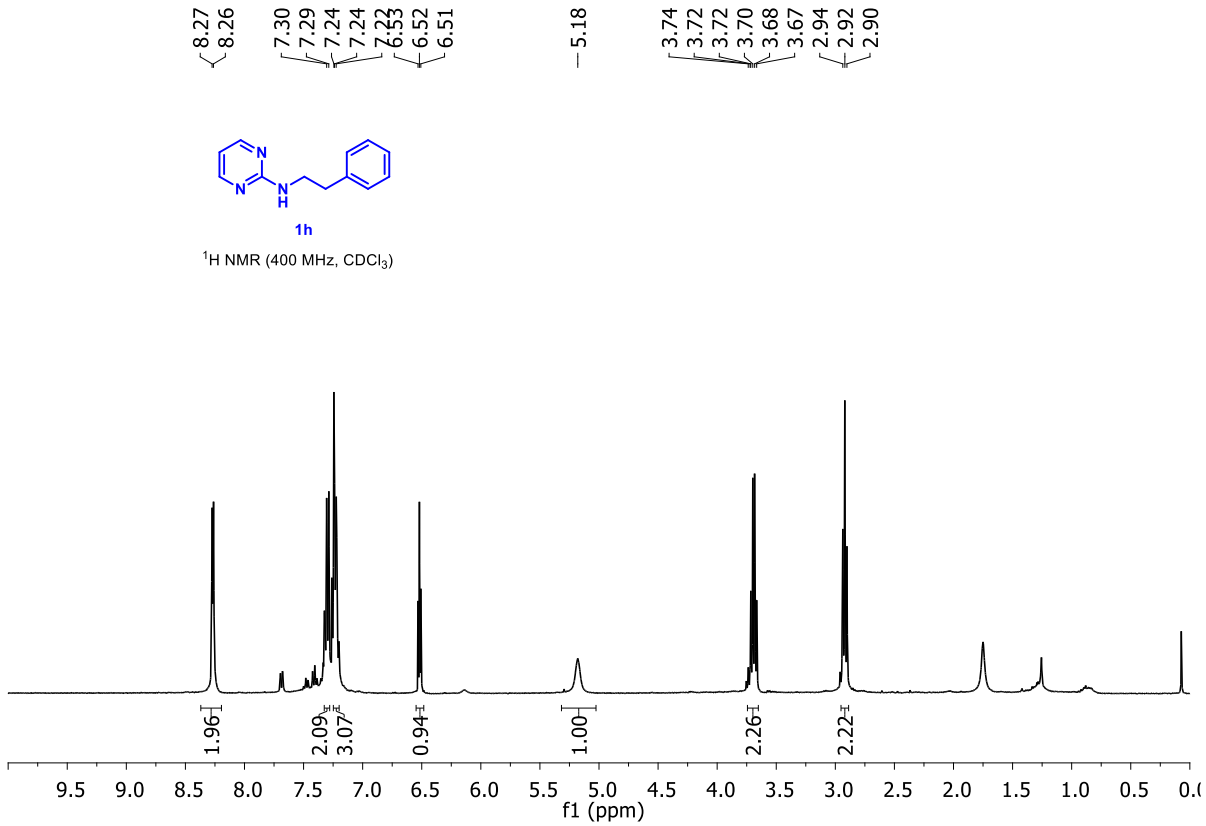


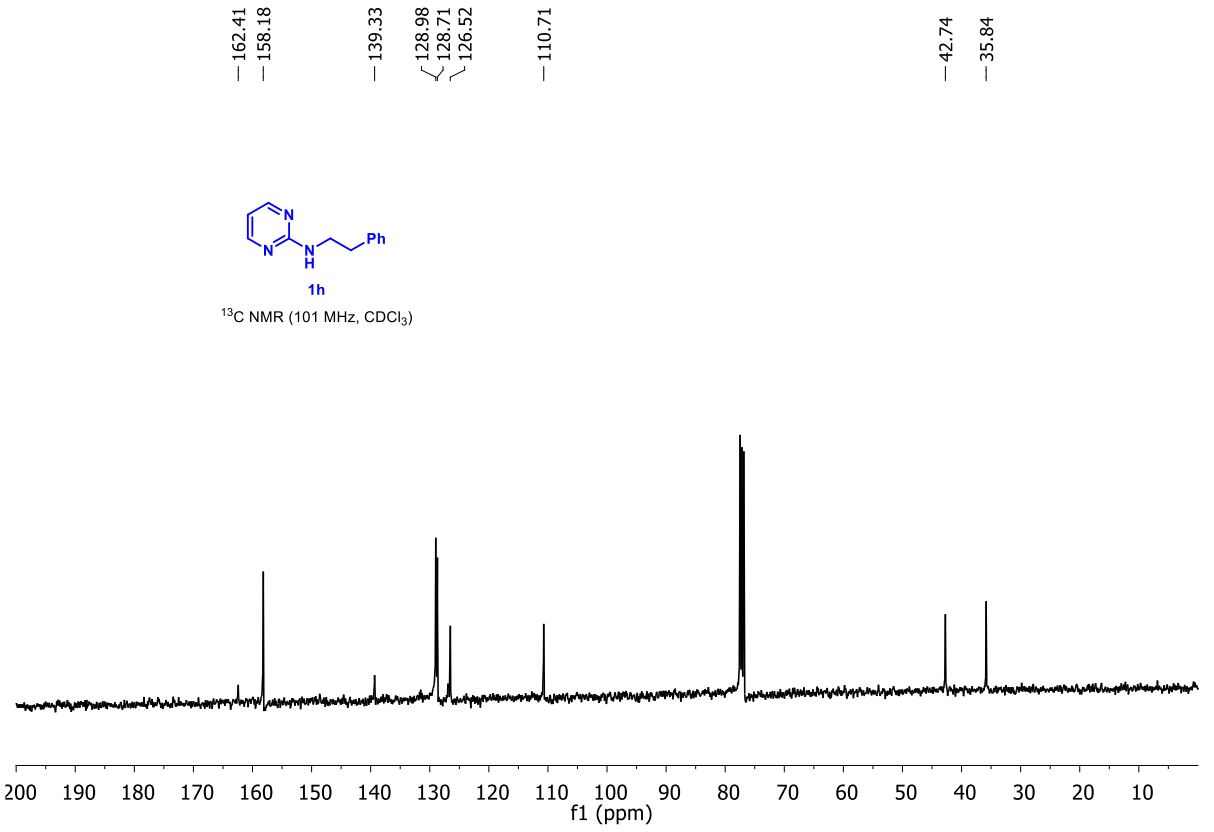
1f

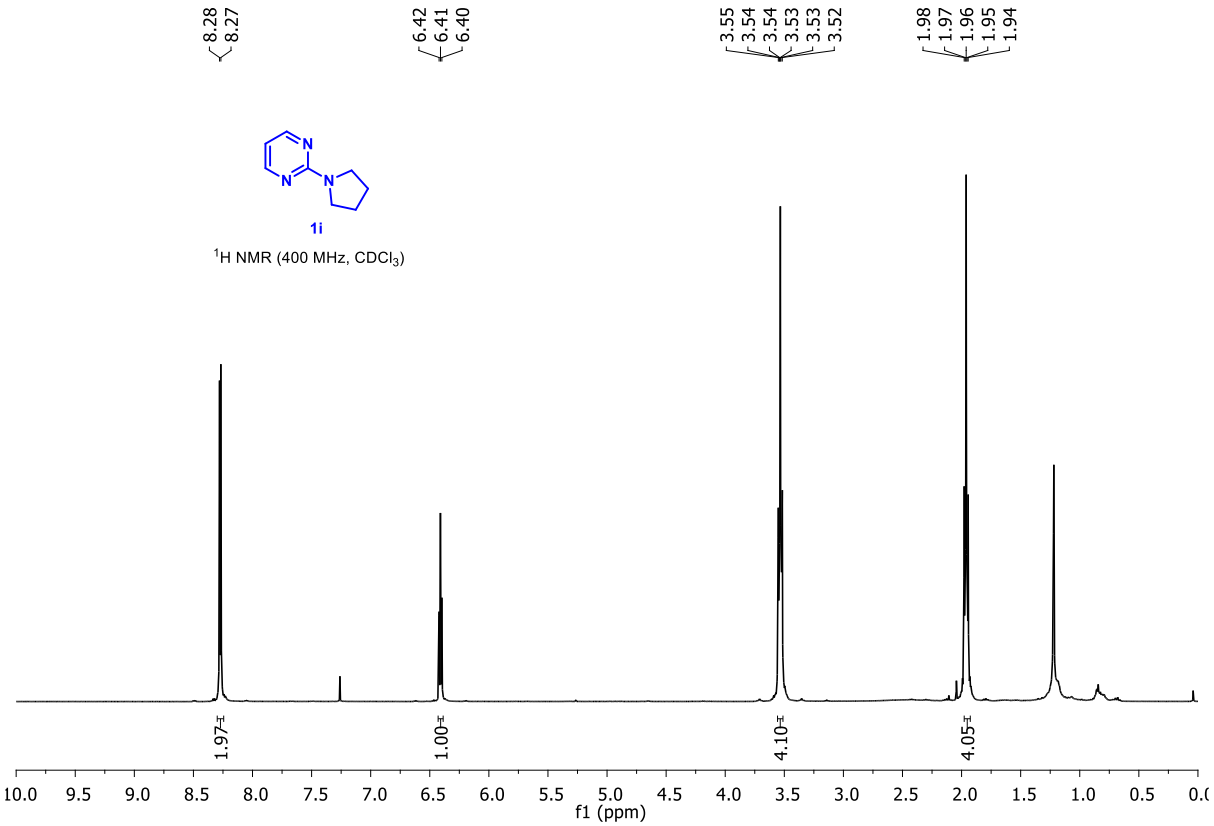
^{13}C NMR (101 MHz, $CDCl_3$)

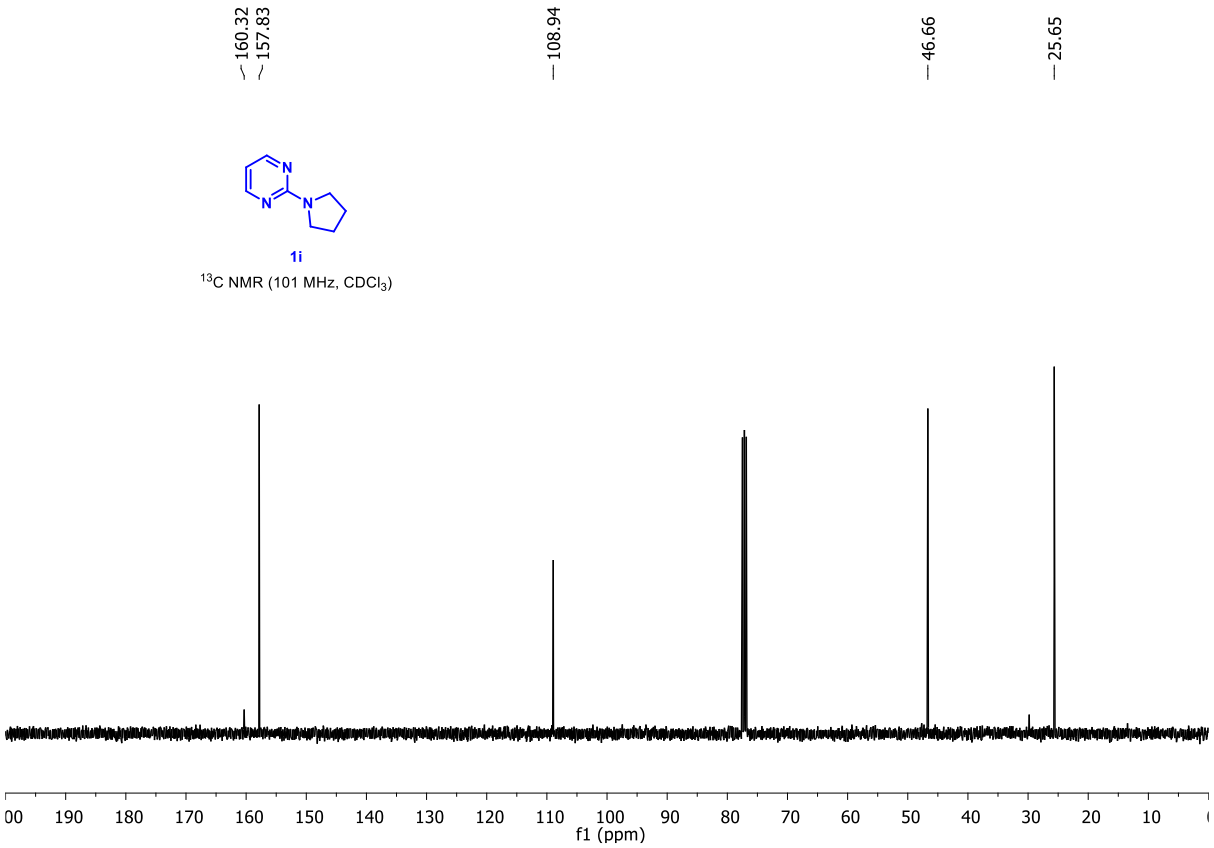

8.20
7.37
7.35
7.33
7.31
7.28
7.27
7.22
6.52
6.51
6.50
5.97
4.64
4.63
1g
1H NMR (400 MHz, CDCl3)
1.96
4.10
1.00
1.00
0.98
2.03
f1 (ppm)

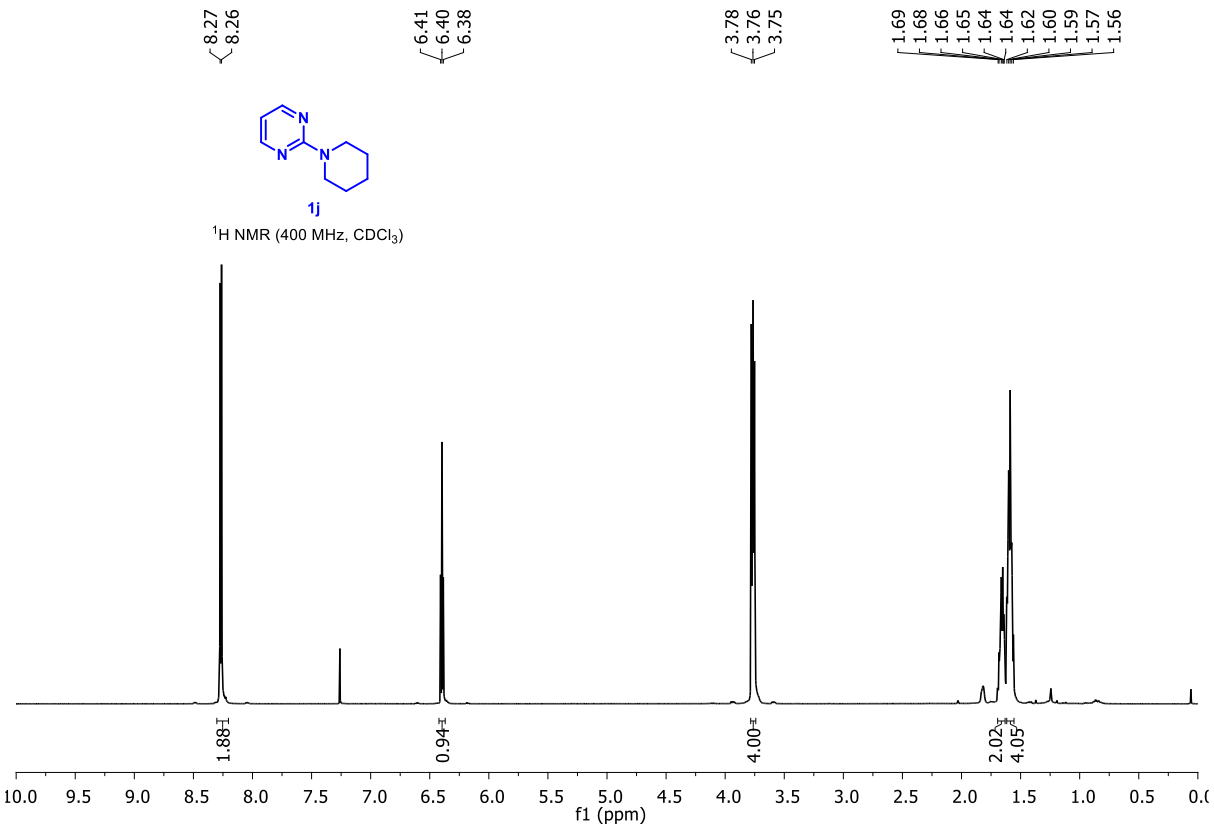

162.44
158.18
139.20
128.72
127.66
127.36
110.87
45.57
1g
13C NMR (101 MHz, CDCl3)
f1 (ppm)

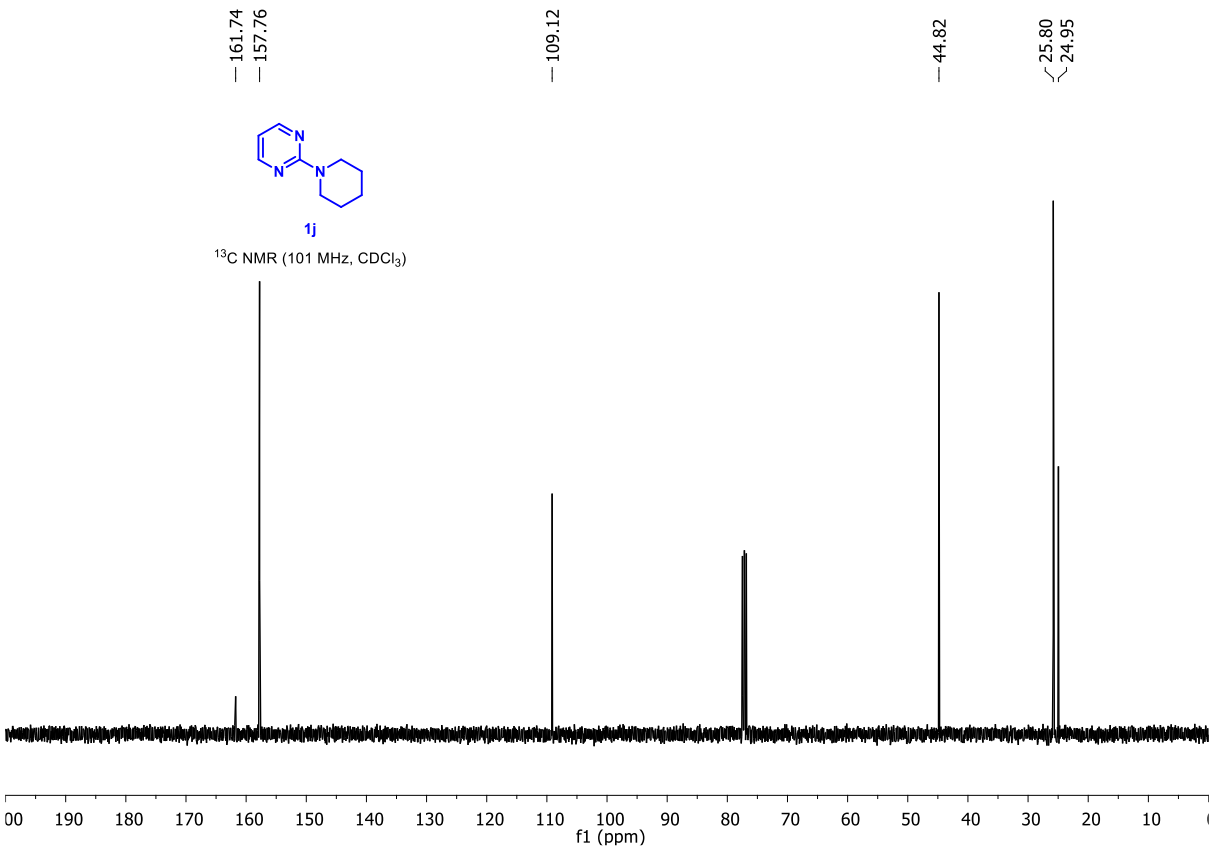

8.27
8.26
7.30
7.29
7.24
7.24
6.53
6.52
6.51
5.18
3.74
3.72
3.72
3.70
3.68
3.67
2.94
2.92
2.90
1h
1H NMR (400 MHz, CDCl3)
1.96
2.09
3.07
0.94
1.00
2.26
2.22
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

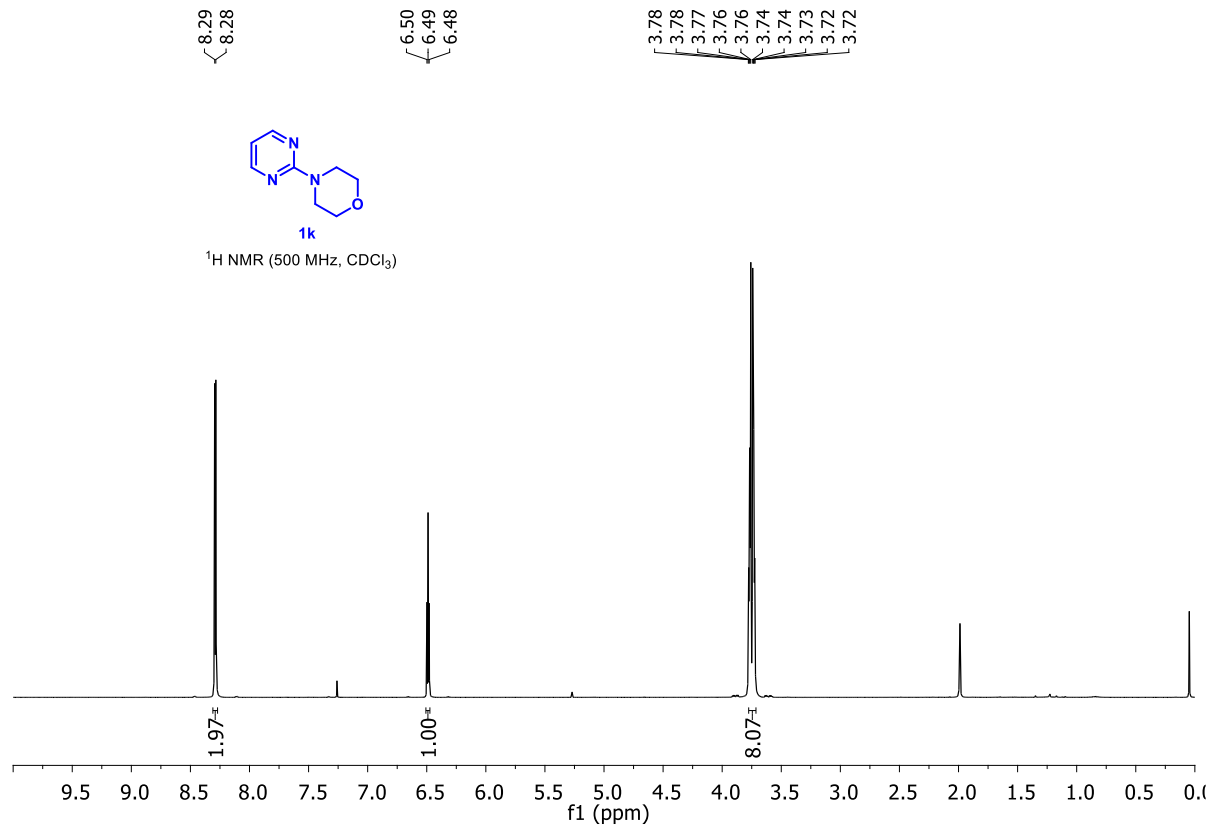

162.41
158.18
139.33
128.98
128.71
126.52
110.71
42.74
35.84
Ph
1h
13C NMR (101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

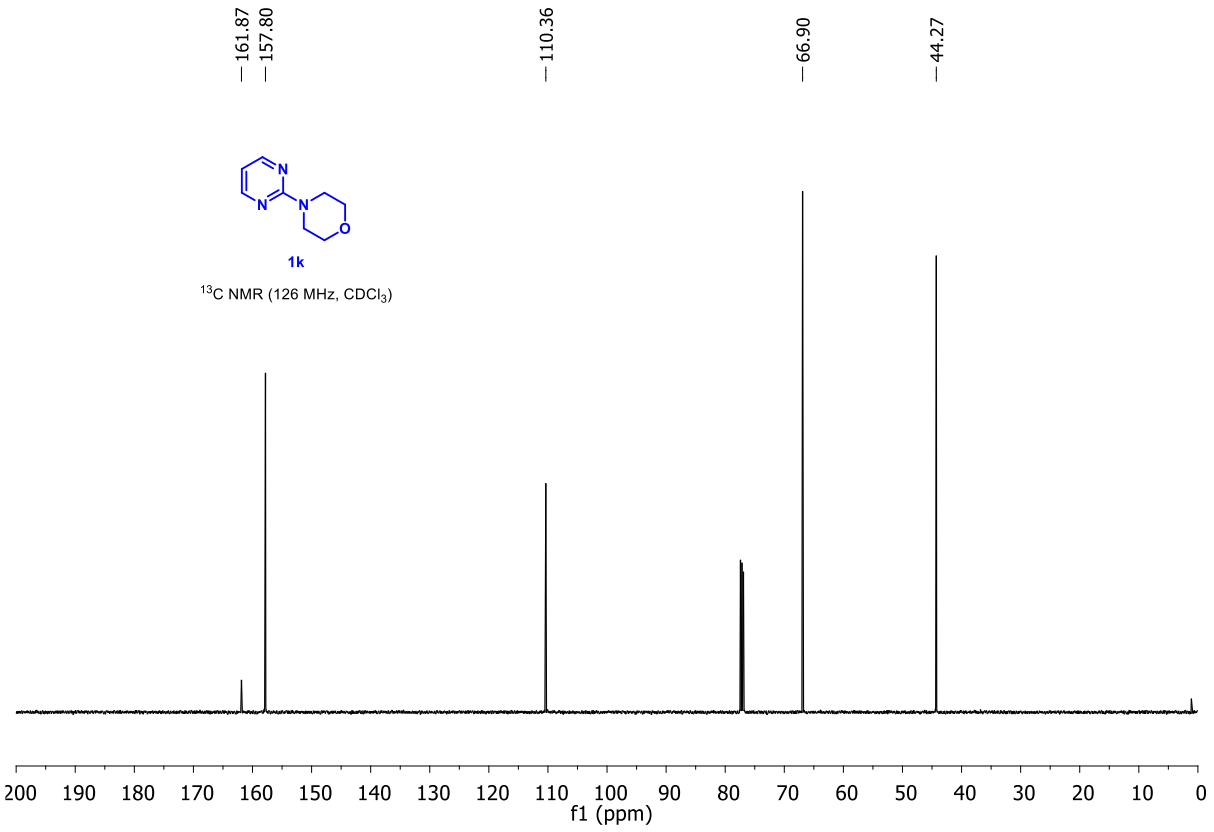

8.28
8.27
6.42
6.41
6.40
3.55
3.54
3.54
3.53
3.53
3.52
1.98
1.97
1.96
1.95
1.94
1i
1H NMR (400 MHz, CDCl3)
1.97
1.00
4.10
4.05
f1 (ppm)

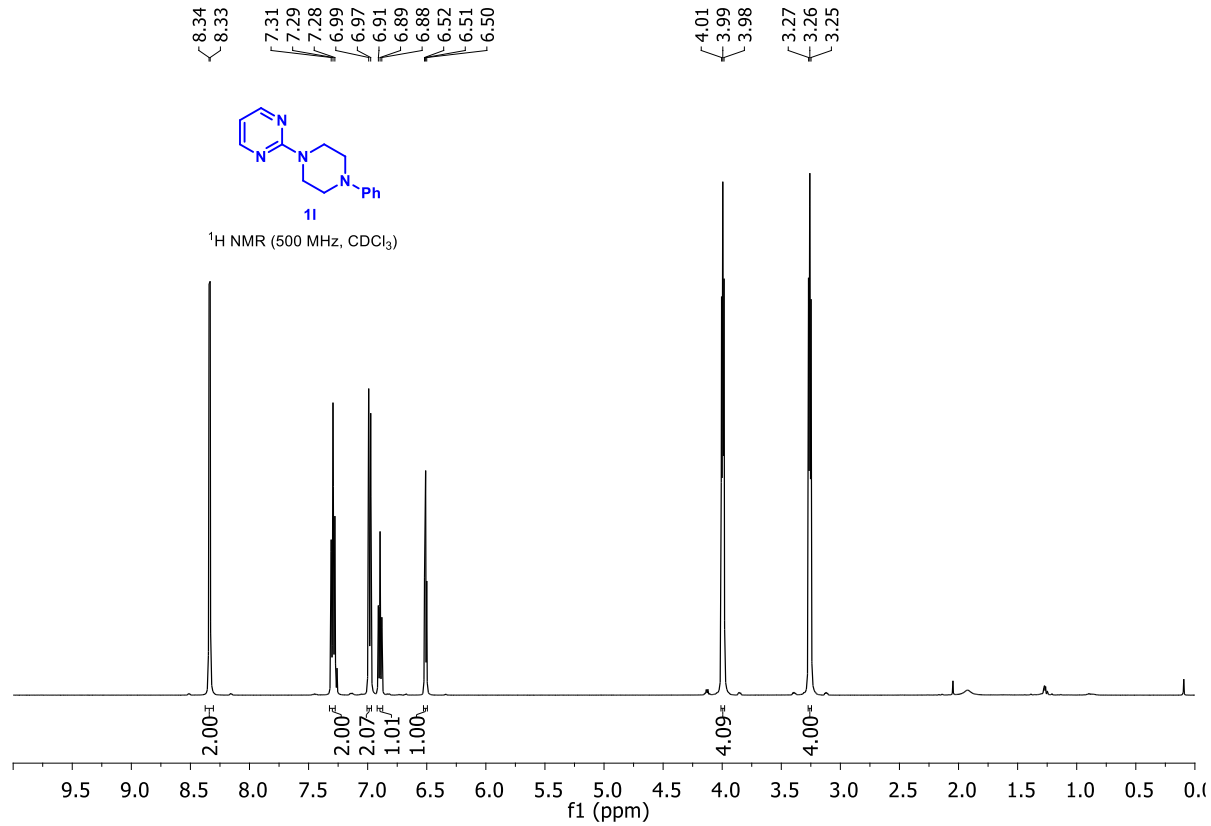

160.32
157.83
108.94
46.66
25.65
1i
13C NMR (101 MHz, CDCl3)
f1 (ppm)

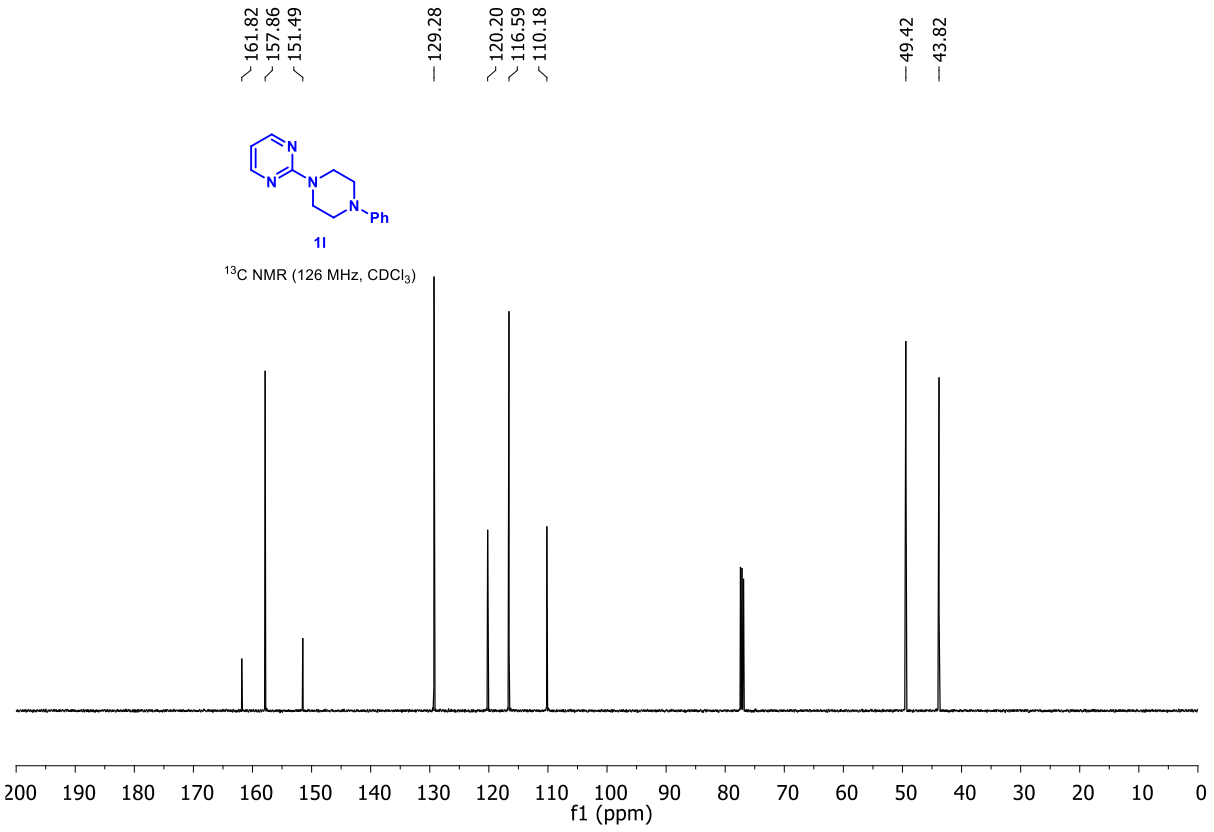

8.27
8.26
6.41
6.40
6.38
3.78
3.76
3.75
1.69
1.68
1.66
1.65
1.64
1.64
1.62
1.60
1.59
1.57
1.56
1j
1H NMR (400 MHz, CDCl3)
1.88
0.94
4.00
2.02
4.05
f1 (ppm)

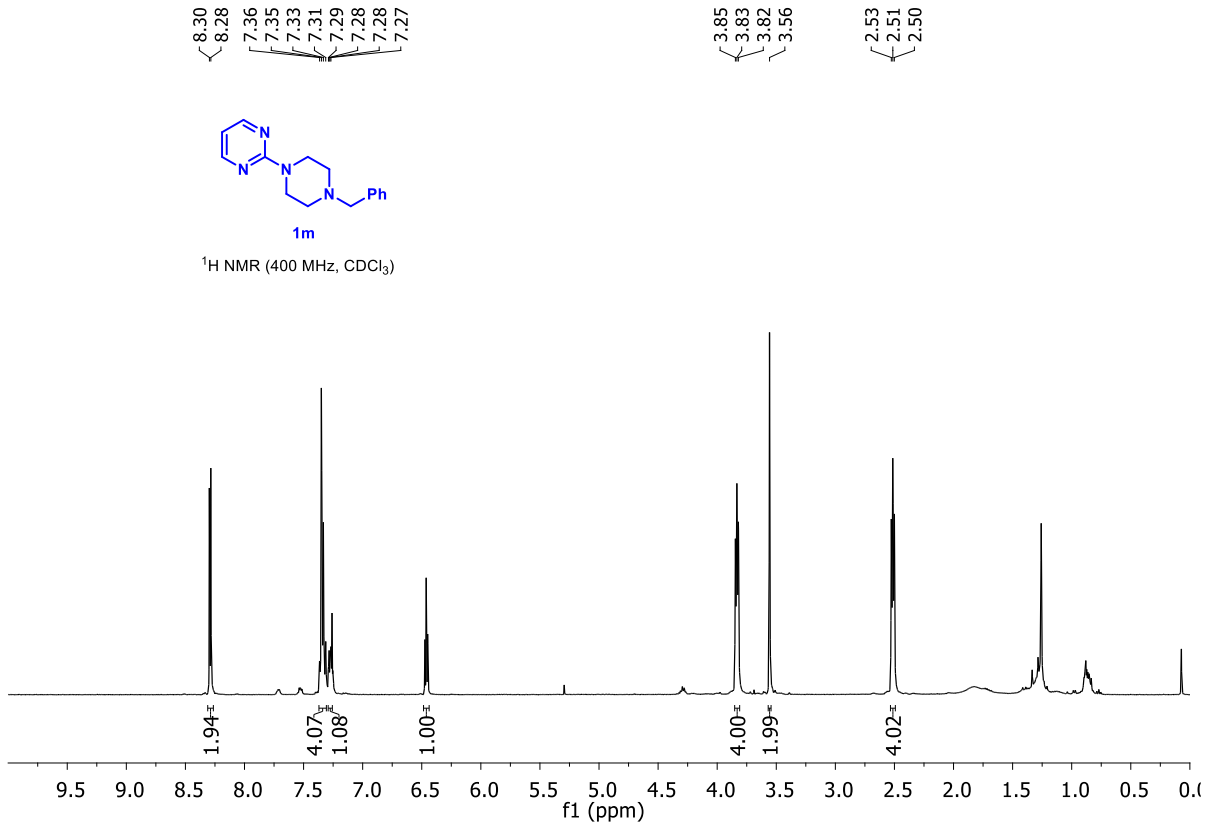

161.74
157.76
109.12
44.82
25.80
24.95
1j
13C NMR (101 MHz, CDCl3)
f1 (ppm)

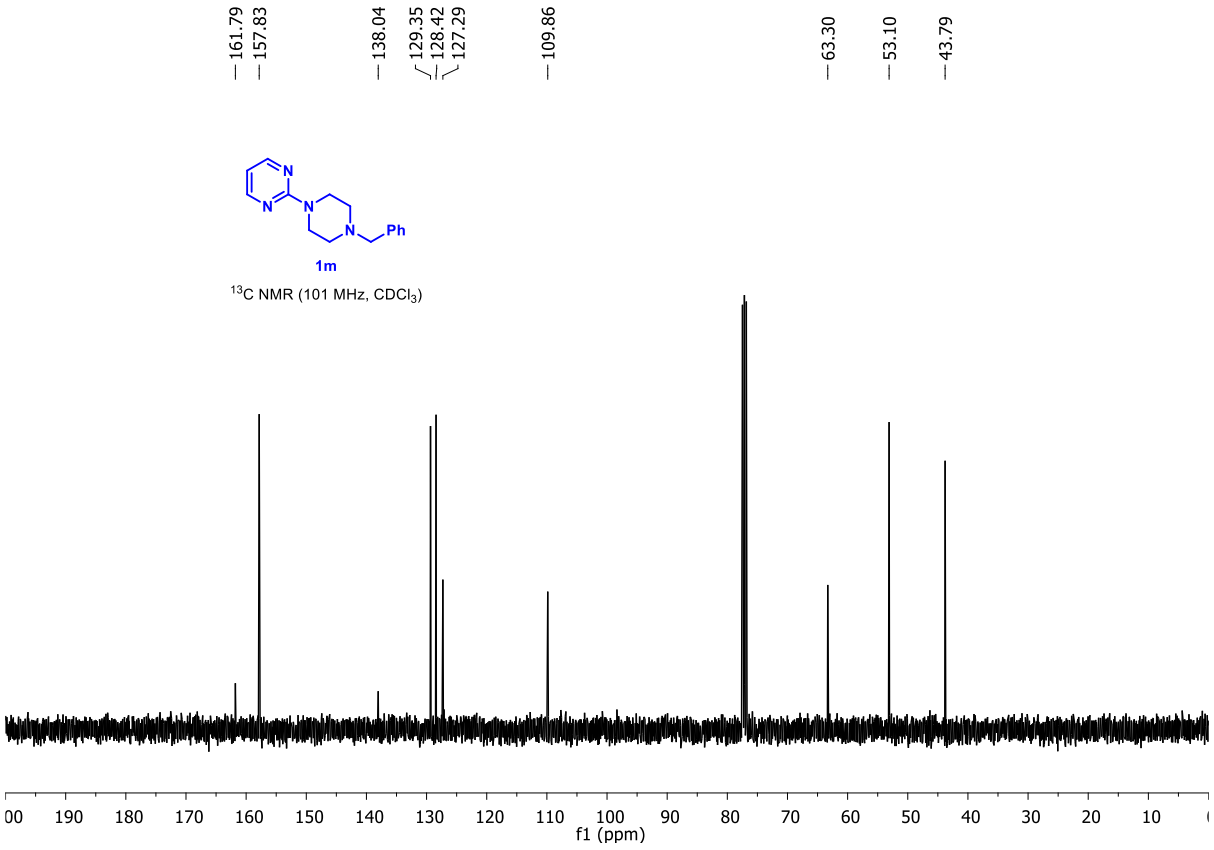

8.29
8.28
6.50
6.49
6.48
3.78
3.78
3.77
3.76
3.76
3.74
3.74
3.73
3.72
3.72
1k
1H NMR (500 MHz, CDCl3)
1.97
1.00
8.07
f1 (ppm)

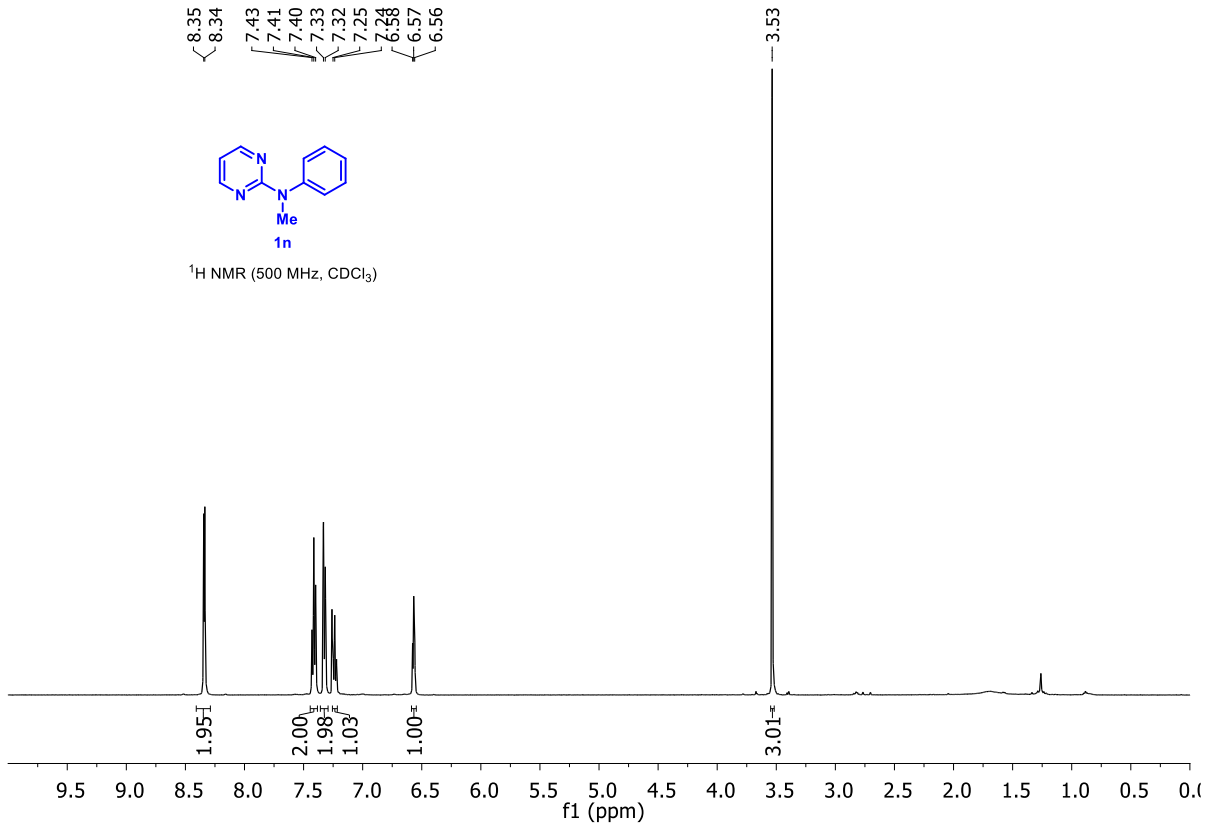

161.87
157.80
110.36
66.90
44.27
1k
13C NMR (126 MHz, CDCl3)
f1 (ppm)

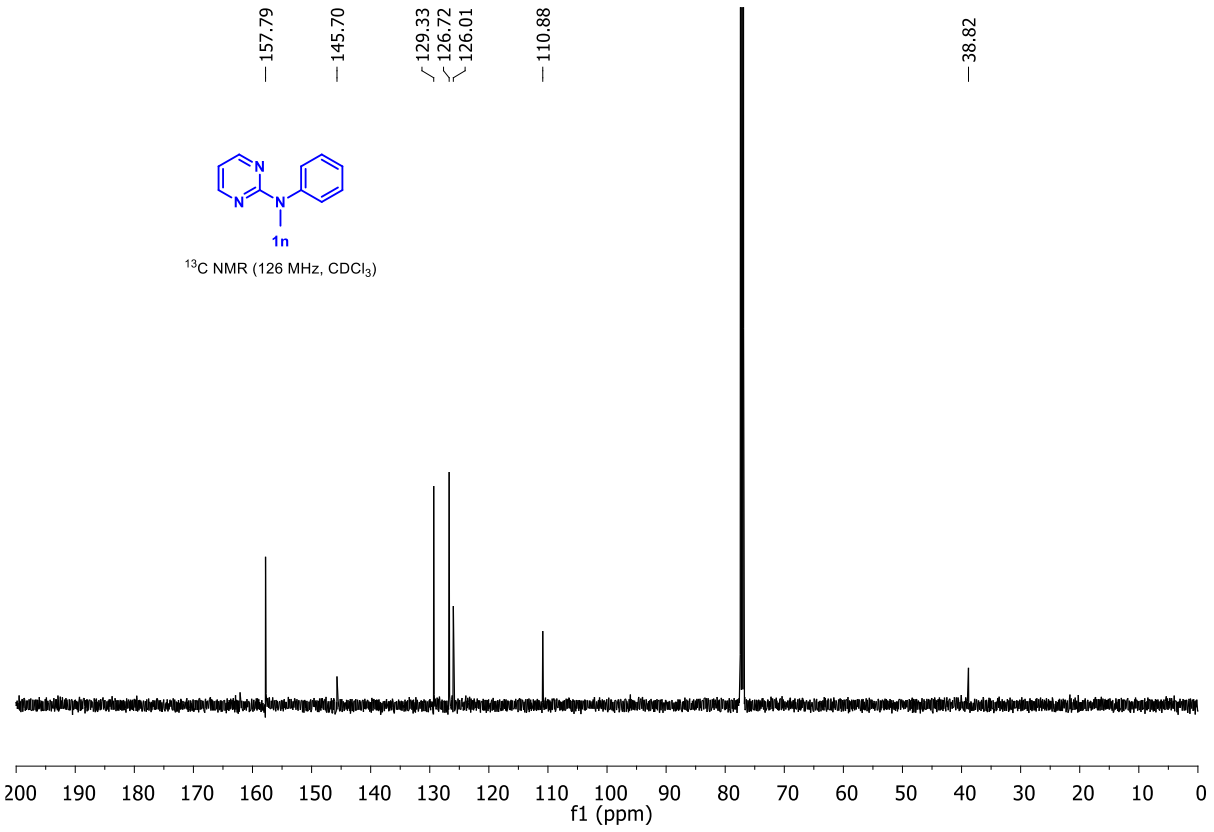

8.34
8.33
7.31
7.29
7.28
6.99
6.97
6.91
6.89
6.88
6.52
6.51
6.50
4.01
3.99
3.98
3.27
3.26
3.25
N
N
N
N
Ph
1l
1H NMR (500 MHz, CDCl3)
2.00
2.00
2.07
1.01
1.00
4.09
4.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

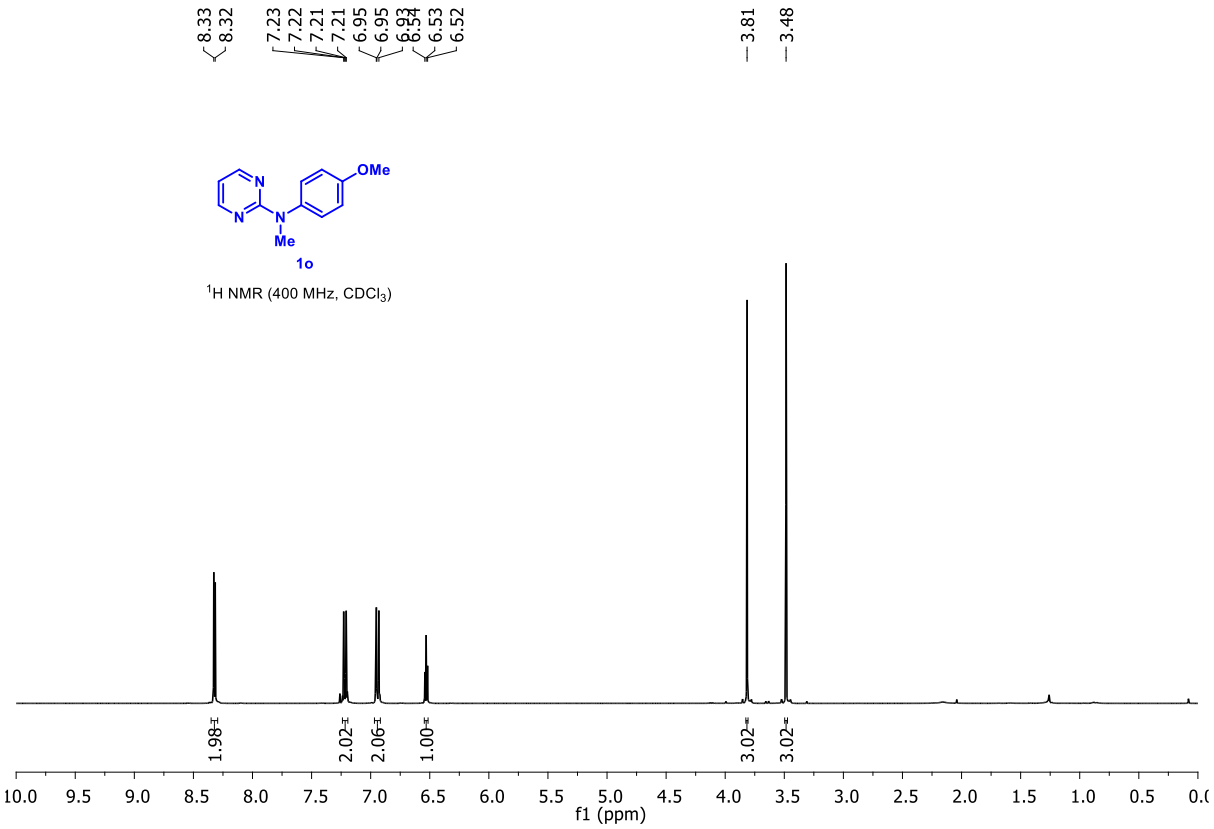

161.82
157.86
151.49
129.28
120.20
116.59
110.18
49.42
43.82
N
N
N
N
Ph
1l
13C NMR (126 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

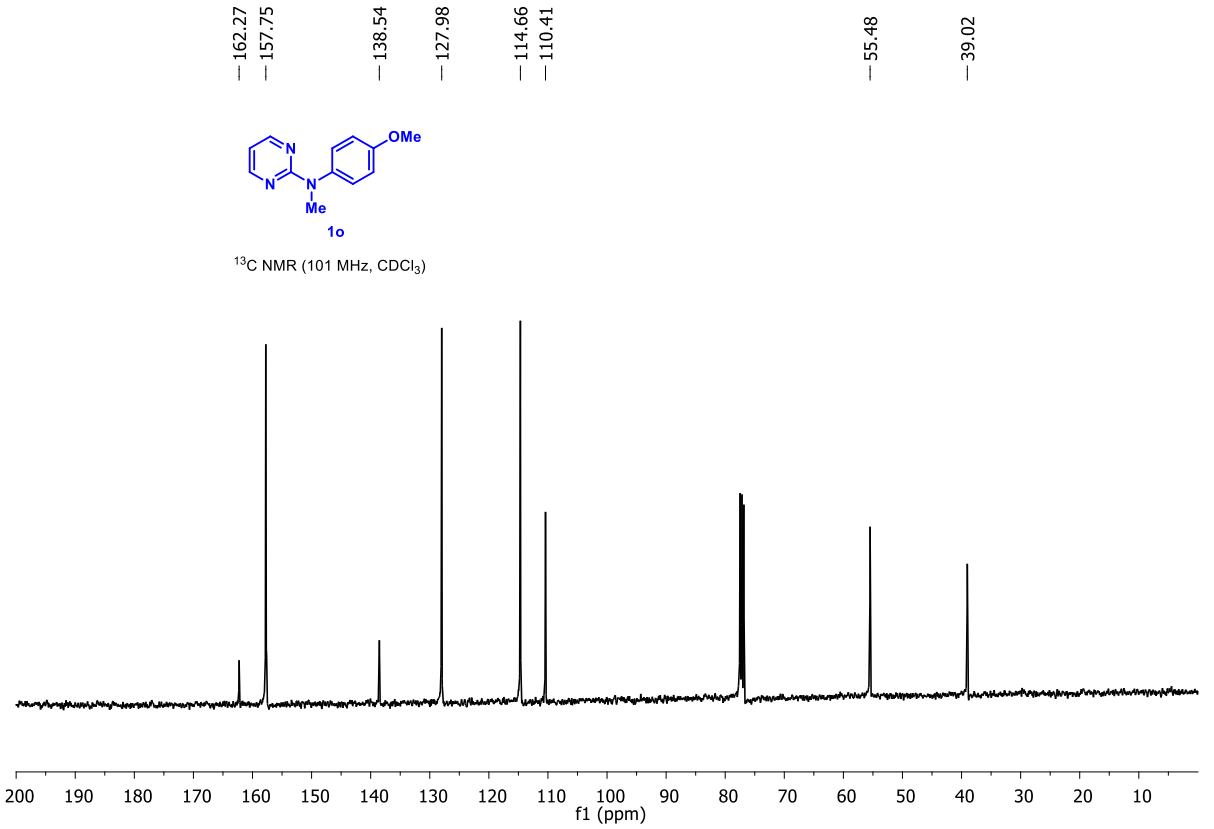

8.30
8.28
7.36
7.35
7.33
7.31
7.29
7.28
7.28
7.27
3.85
3.83
3.82
3.56
2.53
2.51
2.50
N
N
N
N
Ph
1m
1H NMR (400 MHz, CDCl3)
1.94
4.07
1.08
1.00
4.00
1.99
4.02
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

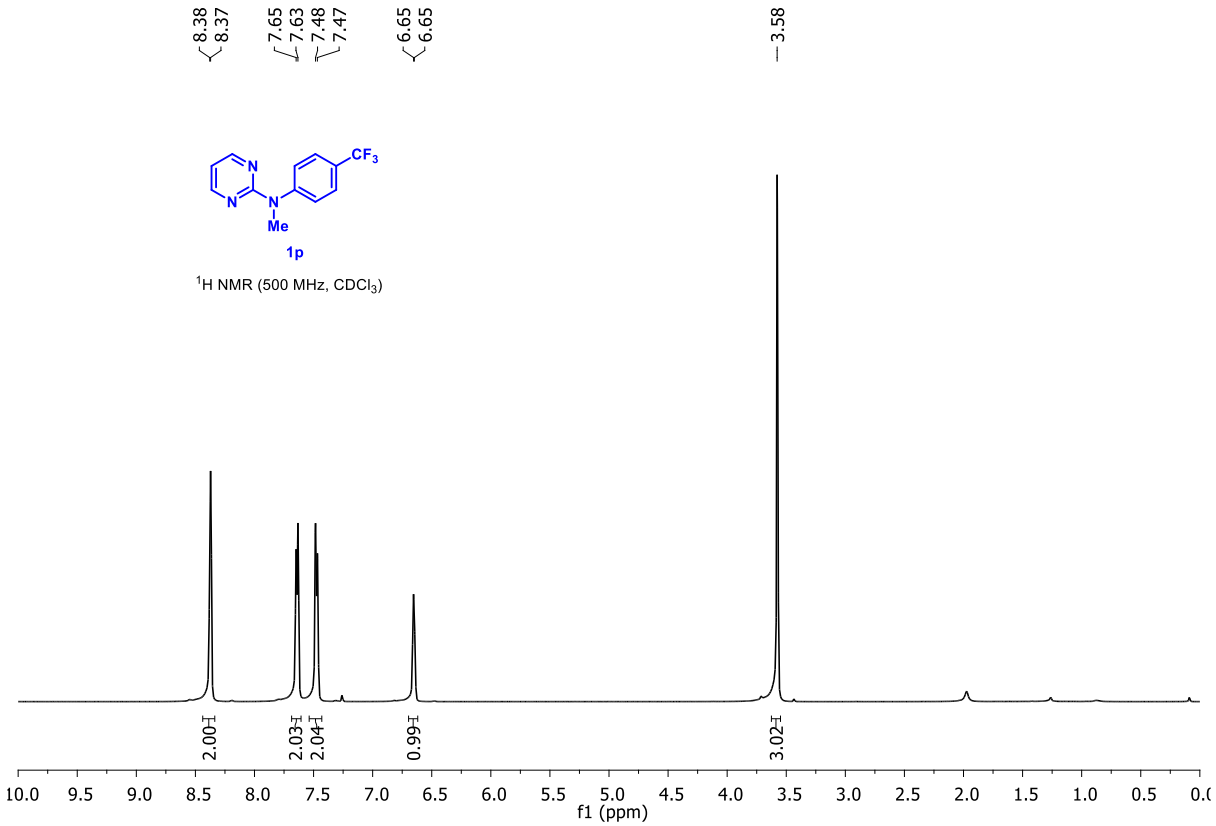

161.79
157.83
138.04
129.35
128.42
127.29
109.86
63.30
53.10
43.79
N
N
N
N
Ph
1m
13C NMR (101 MHz, CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

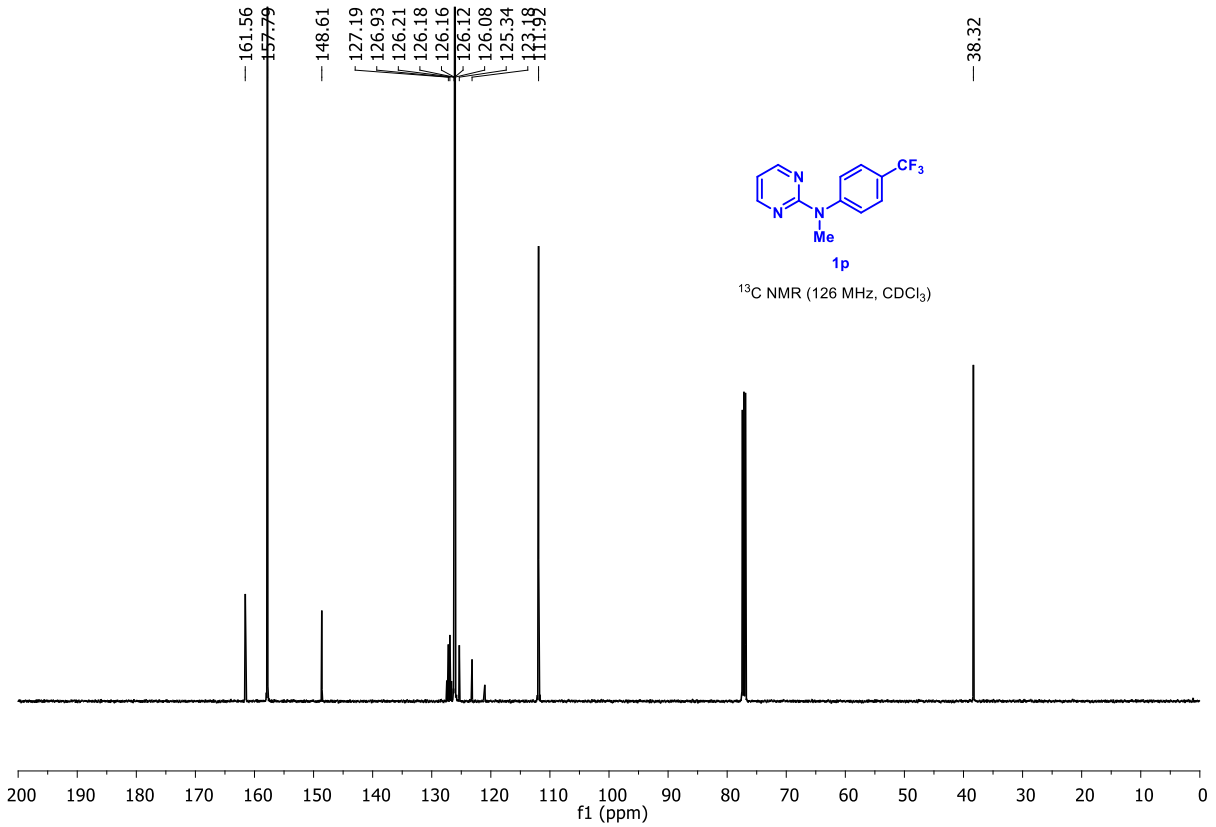

8.35
8.34
7.43
7.41
7.40
7.33
7.32
7.25
7.24
6.58
6.57
6.56
3.53
N
N
N
Me
1n
1H NMR (500 MHz, CDCl3)
1.95
2.00
1.98
1.03
1.00
3.01
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

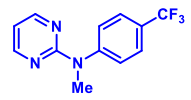

157.79
145.70
129.33
126.72
126.01
110.88
38.82
N
N
N
1n
13C NMR (126 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.33
8.32
7.23
7.22
7.21
7.21
6.95
6.95
6.53
6.52
3.81
3.48
OMe
N
N
N
Me
1o
1H NMR (400 MHz, CDCl3)
1.98
2.02
2.06
1.00
3.02
3.02
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


162.27
157.75
138.54
127.98
114.66
110.41
55.48
39.02
OMe
N
N
N
Me
1o
13C NMR (101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

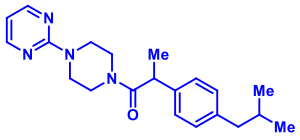

8.38
8.37
7.65
7.63
7.48
7.47
6.65
6.65
3.58
CF3
N
N
N
Me
1p
1H NMR (500 MHz, CDCl3)
2.00
2.03
2.04
0.99
3.02
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


161.56
157.79
148.61
127.19
126.93
126.21
126.18
126.16
126.12
126.08
125.34
123.18
111.92
38.32
CF3
N
N
N
Me
1p
13C NMR (126 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



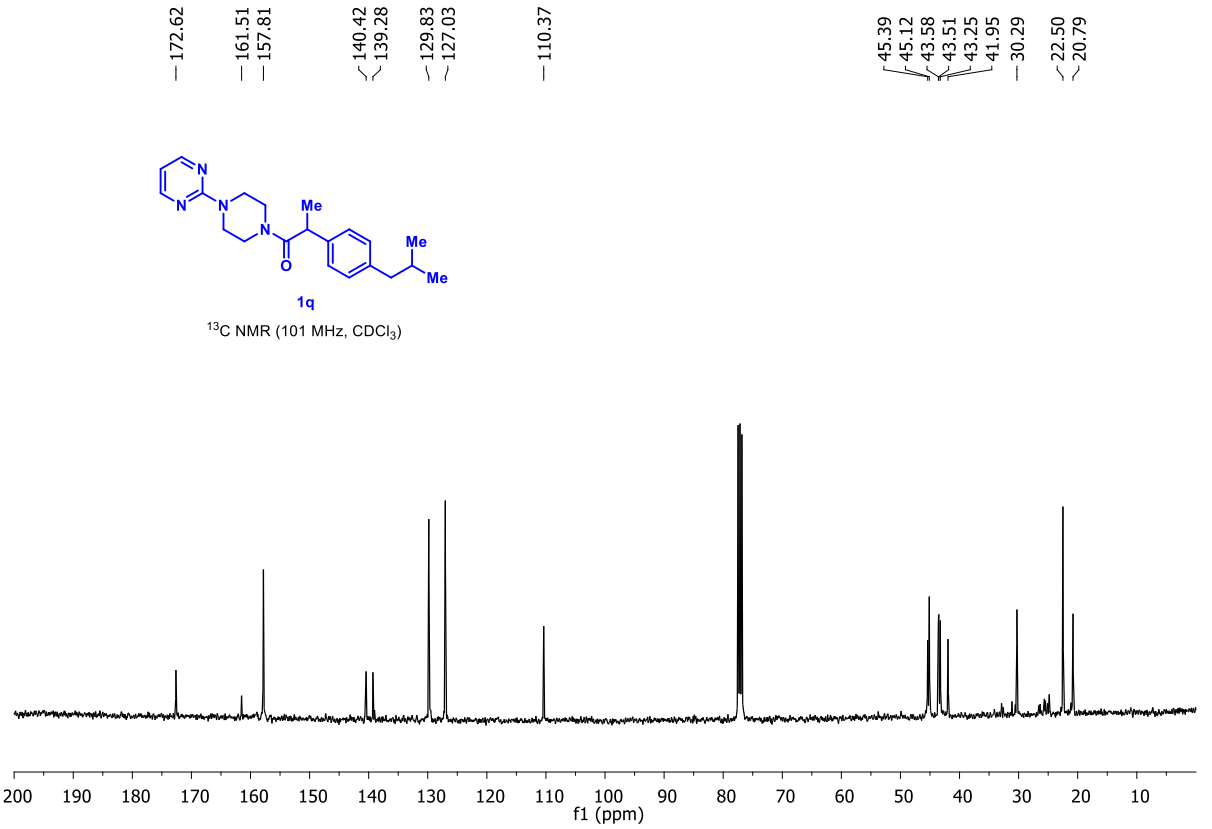
1p

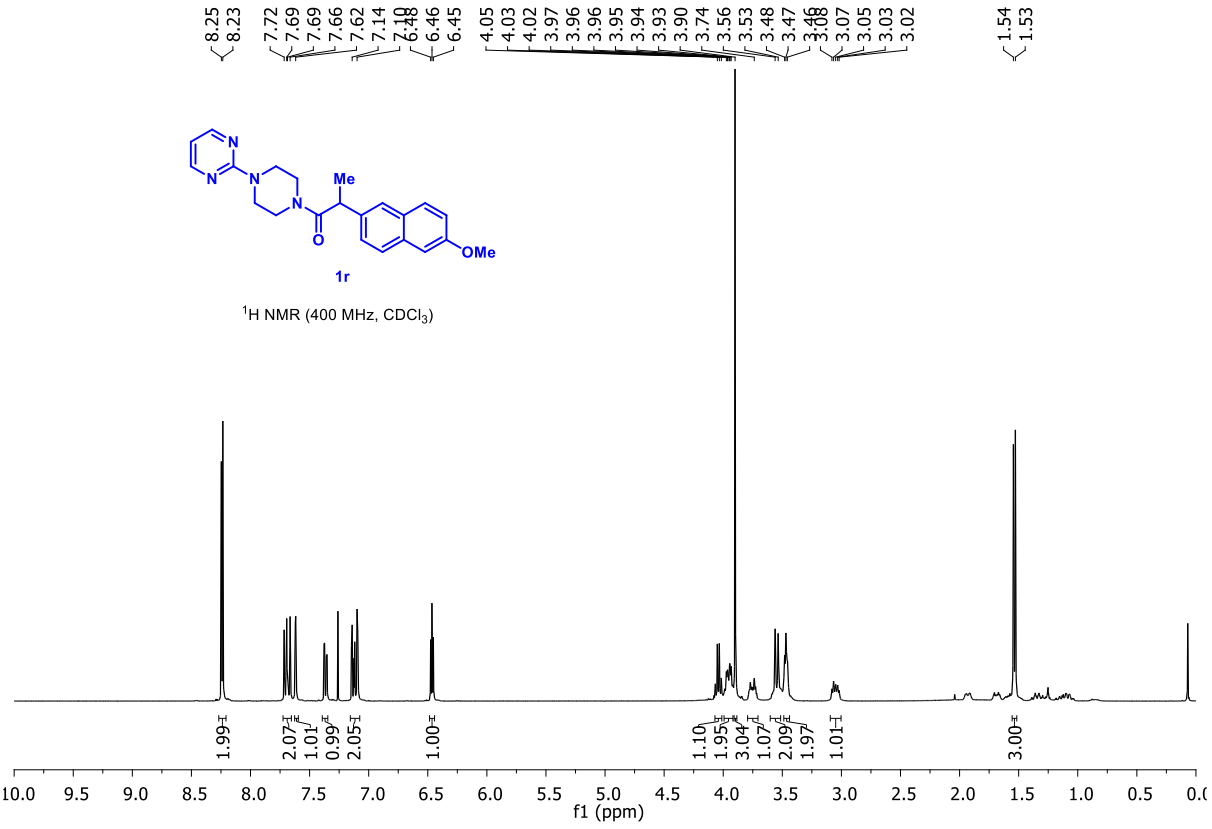
^{19}F NMR (471 MHz, $CDCl_3$)

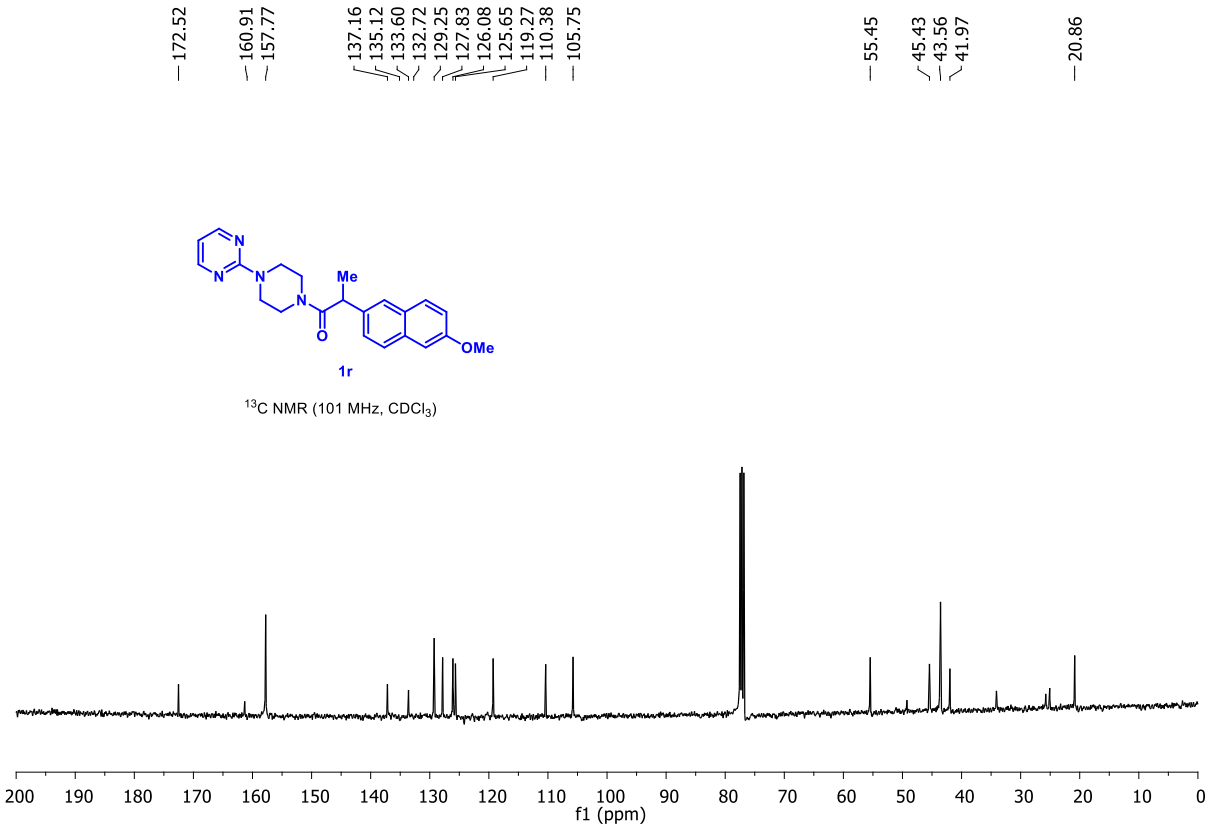


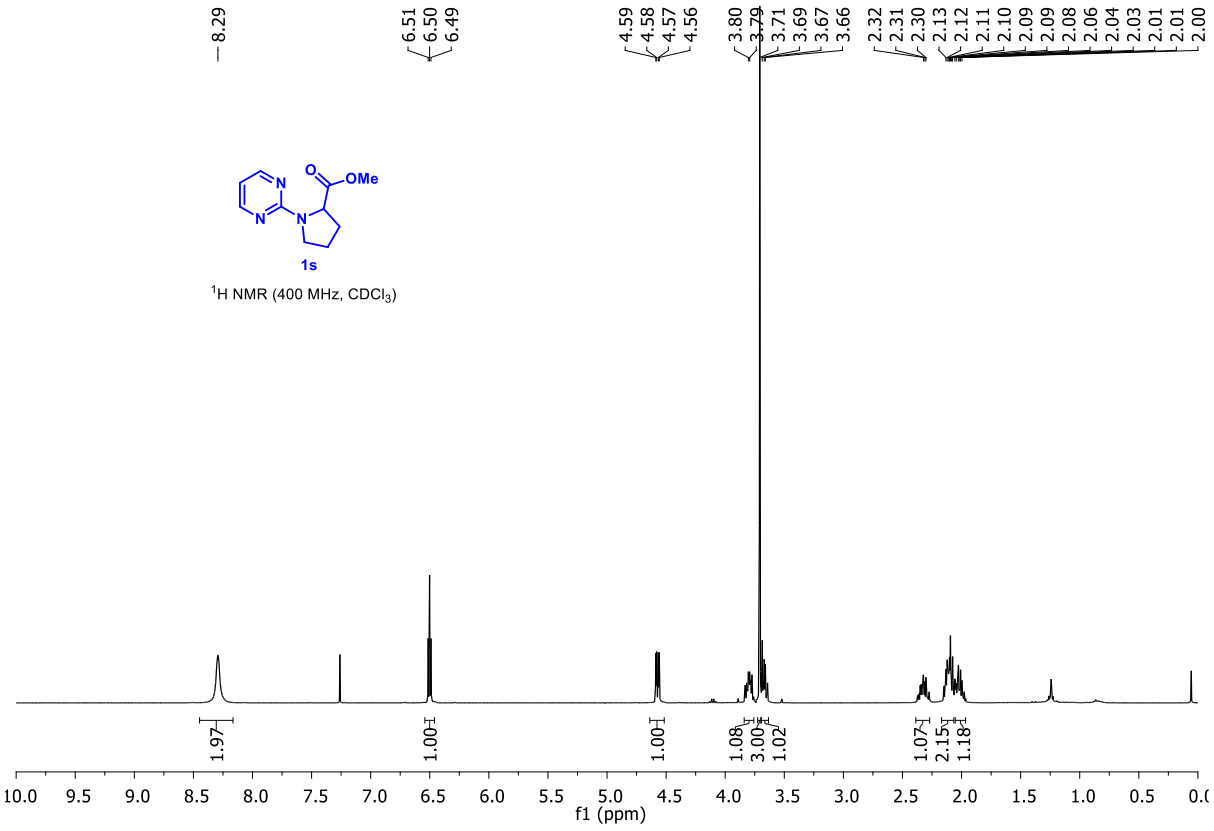
1q

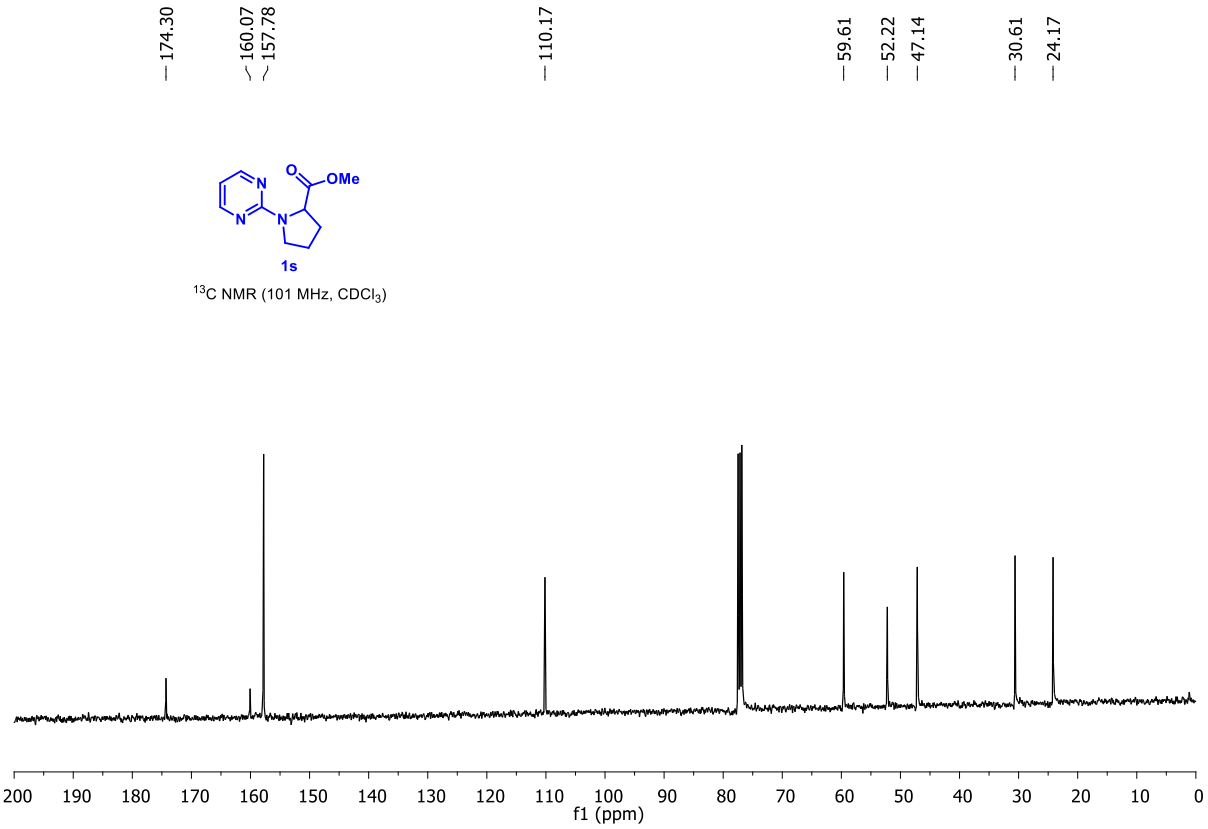
^{1}H NMR (400 MHz, $CDCl_3$)

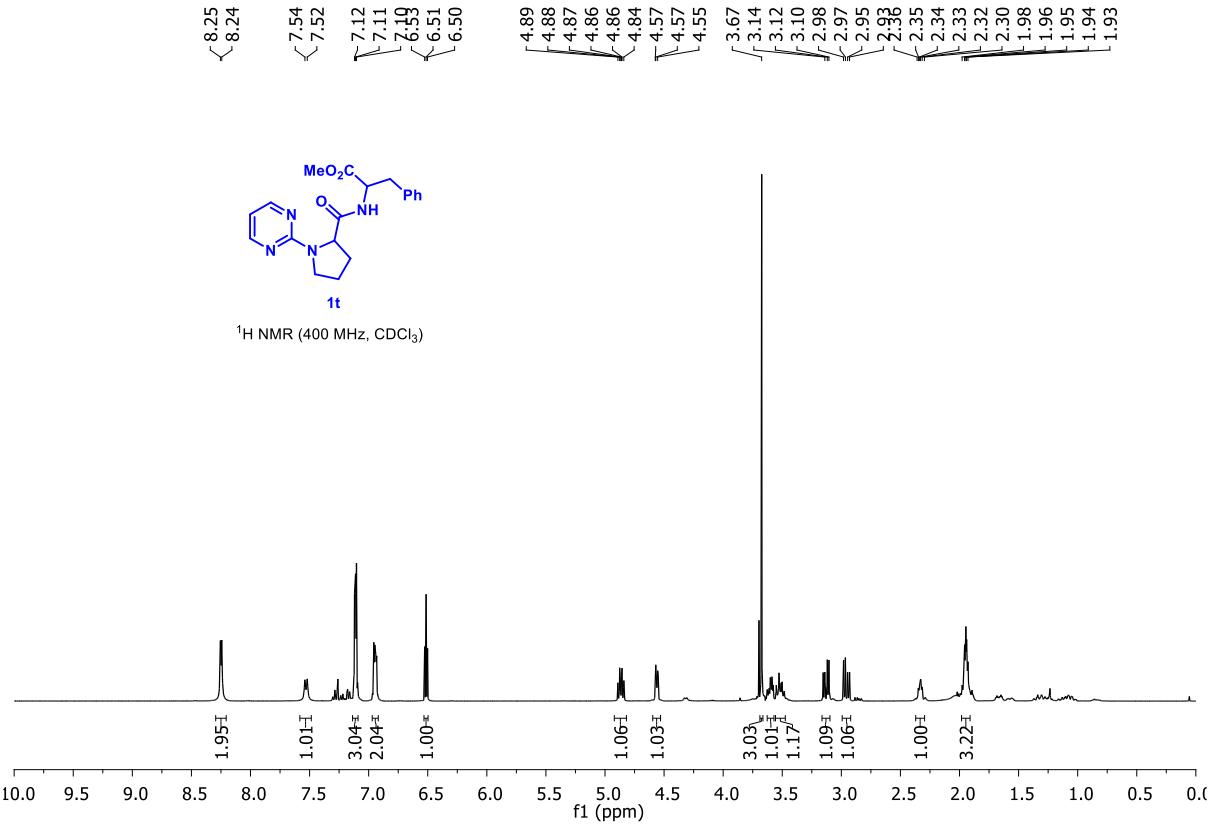

172.62
161.51
157.81
140.42
139.28
129.83
127.03
110.37
45.39
45.12
43.58
43.51
43.25
41.95
30.29
22.50
20.79
Me
Me
Me
1q
13C NMR (101 MHz, CDCl3)
f1 (ppm)

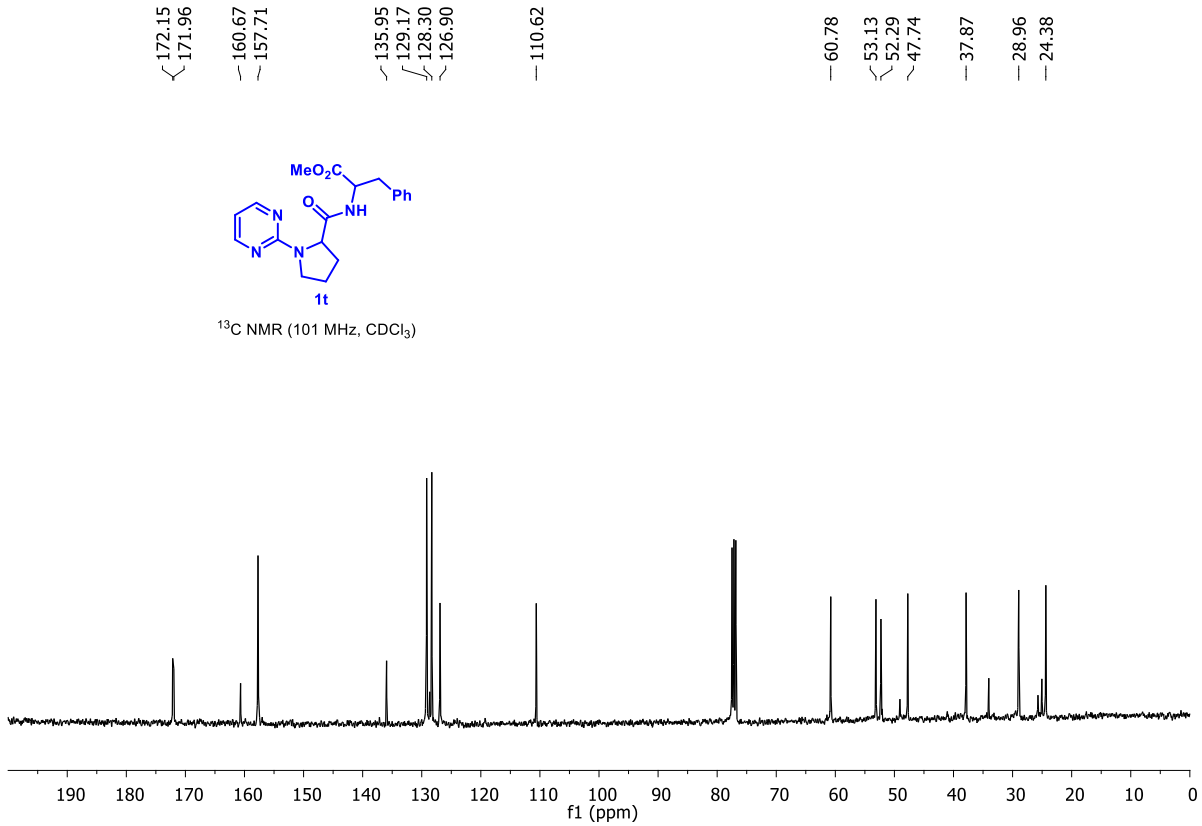

8.25
8.23
7.72
7.69
7.69
7.66
7.62
7.14
7.10
6.48
6.46
6.45
4.05
4.03
4.02
3.97
3.96
3.96
3.95
3.94
3.93
3.90
3.74
3.56
3.53
3.48
3.47
3.46
3.08
3.07
3.05
3.03
3.02
1.54
1.53
Me
OMe
1r
1H NMR (400 MHz, CDCl3)
1.99
2.07
1.01
0.99
2.05
1.00
1.10
1.95
3.04
1.07
2.09
1.97
1.01
3.00
f1 (ppm)

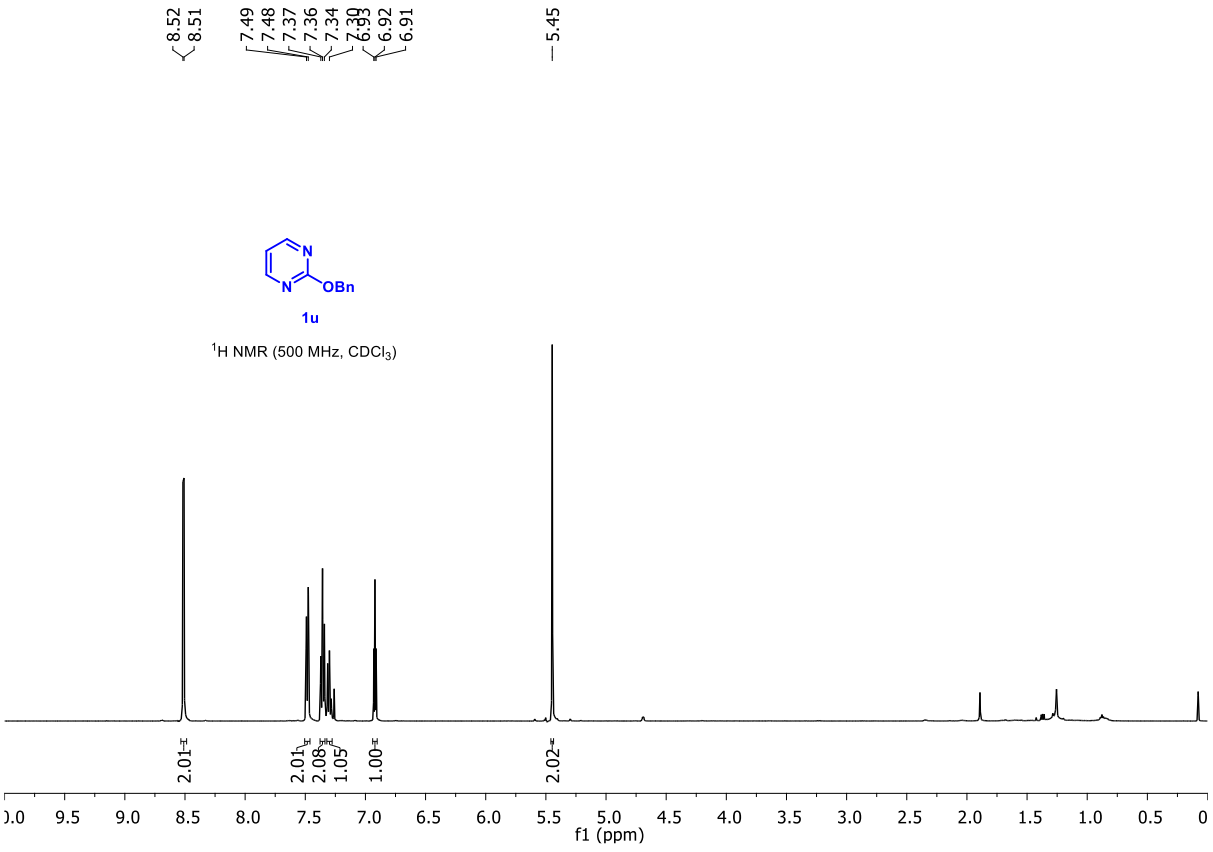

172.52
160.91
157.77
137.16
135.12
133.60
132.72
129.25
127.83
126.08
125.65
119.27
110.38
105.75
55.45
45.43
43.56
41.97
20.86
Me
OMe
1r
13C NMR (101 MHz, CDCl3)
f1 (ppm)

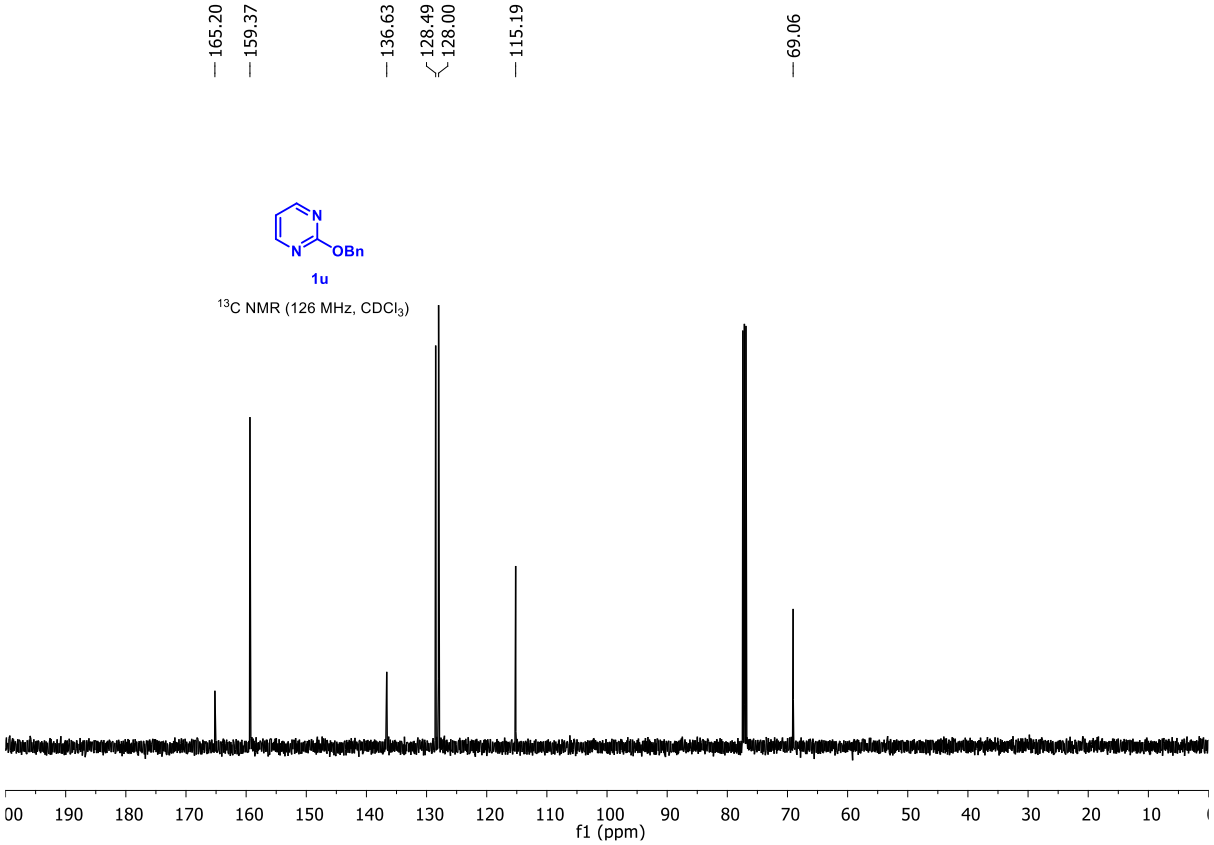

8.29
6.51
6.50
6.49
4.59
4.58
4.57
4.56
3.80
3.79
3.71
3.69
3.67
3.66
2.32
2.31
2.30
2.13
2.12
2.11
2.10
2.09
2.09
2.08
2.06
2.04
2.03
2.01
2.01
2.00
O
OMe
1s
1H NMR (400 MHz, CDCl3)
1.97
1.00
1.00
1.08
3.00
1.02
1.07
2.15
1.18
f1 (ppm)

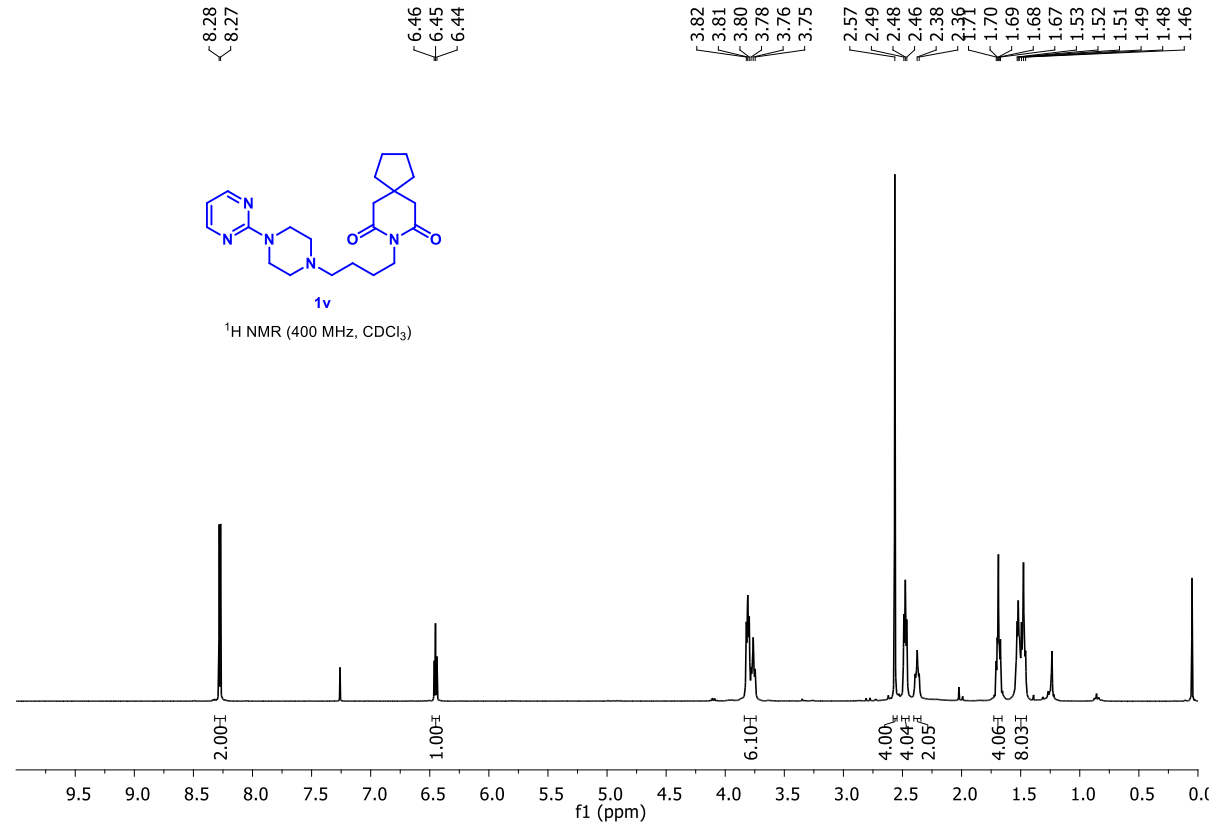

174.30
160.07
157.78
110.17
59.61
52.22
47.14
30.61
24.17
OMe
1s
13C NMR (101 MHz, CDCl3)
f1 (ppm)

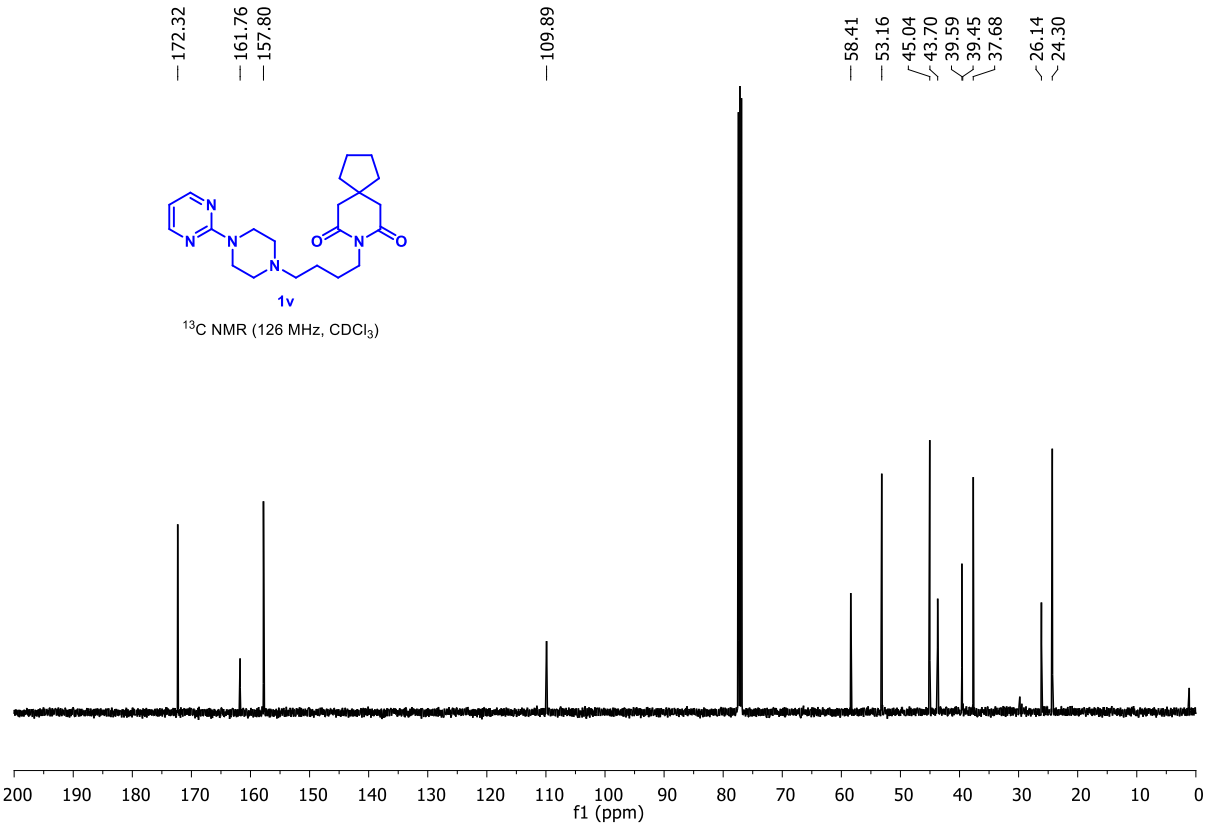

8.25
8.24
7.54
7.52
7.12
7.11
6.53
6.51
6.50
4.89
4.88
4.87
4.86
4.86
4.84
4.57
4.57
4.55
3.67
3.14
3.12
3.10
2.98
2.97
2.95
2.35
2.34
2.33
2.32
2.30
1.98
1.96
1.95
1.94
1.93
MeO2C
Ph
NH
1t
1H NMR (400 MHz, CDCl3)
1.95
1.01
3.04
2.04
1.00
1.06
1.03
3.03
1.01
1.17
1.09
1.06
1.00
3.22
f1 (ppm)


172.15
171.96
160.67
157.71
135.95
129.17
128.30
126.90
110.62
60.78
53.13
52.29
47.74
37.87
28.96
24.38
MeO2C
Ph
O
NH
N
N
N
1t
13C NMR (101 MHz, CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.52
8.51
7.49
7.48
7.37
7.36
7.34
7.30
6.93
6.92
6.91
5.45
N
N
OBn
1u
1H NMR (500 MHz, CDCl3)
2.01
2.01
2.08
1.05
1.00
2.02
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

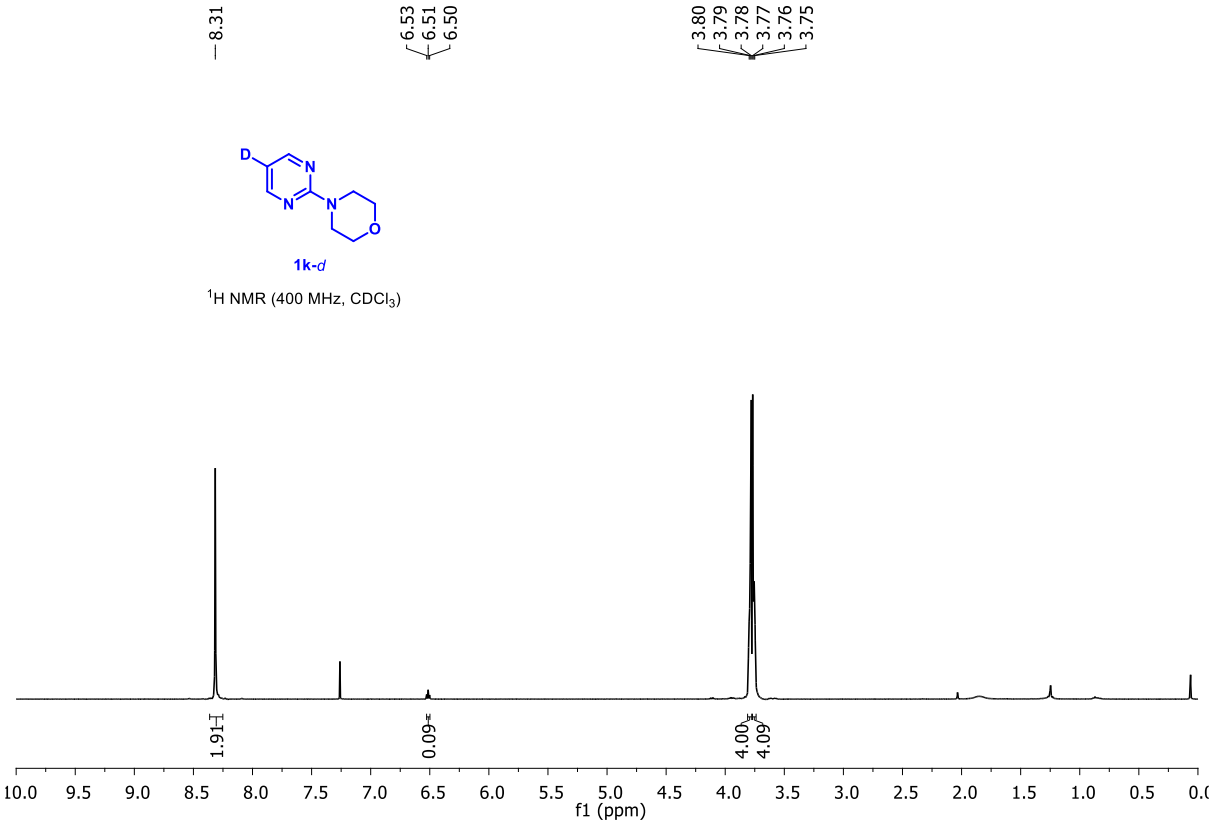

165.20
159.37
136.63
128.49
128.00
115.19
69.06
OBn
1u
13C NMR (126 MHz, CDCl3)
f1 (ppm)


8.28
8.27
6.46
6.45
6.44
3.82
3.81
3.80
3.78
3.76
3.75
2.57
2.49
2.48
2.46
2.38
2.36
1.71
1.70
1.69
1.68
1.67
1.53
1.52
1.51
1.49
1.48
1.46
1v
1H NMR (400 MHz, CDCl3)
2.00
1.00
6.10
4.00
4.04
2.05
4.06
8.03
f1 (ppm)



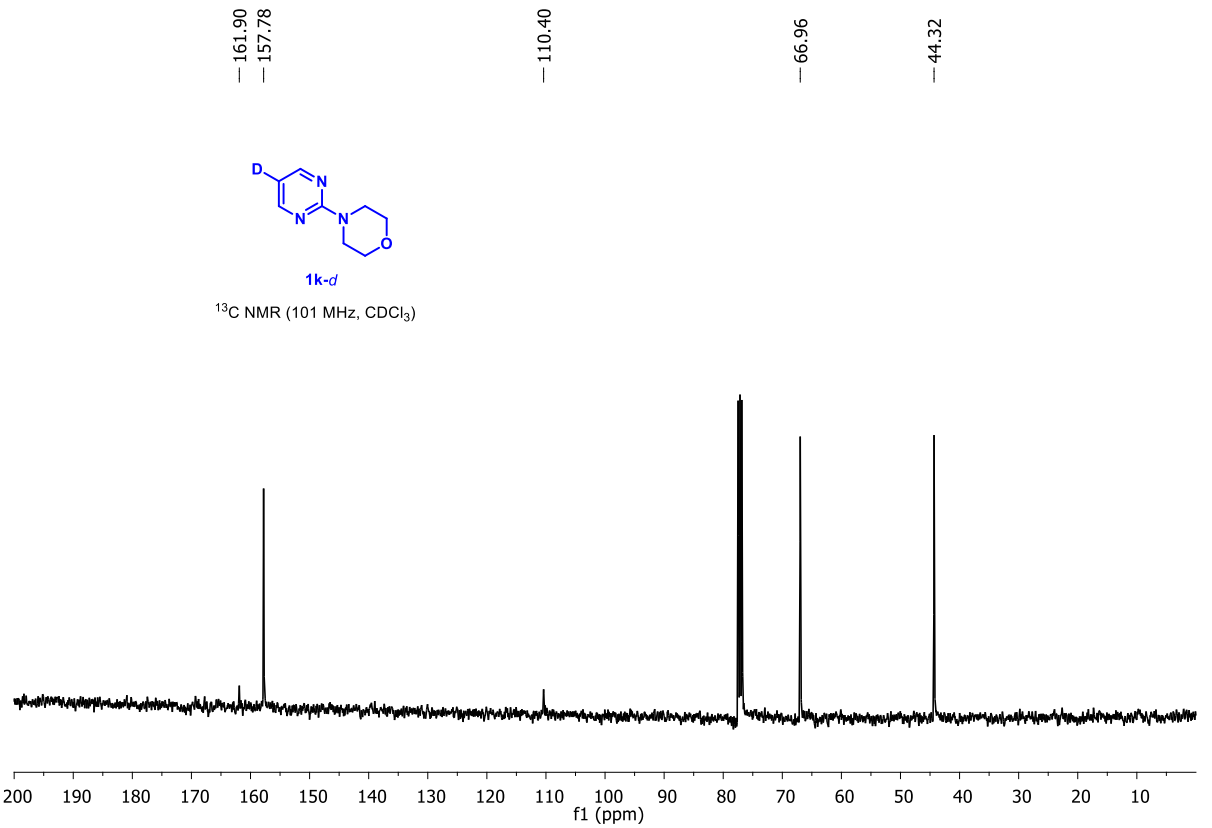
1v

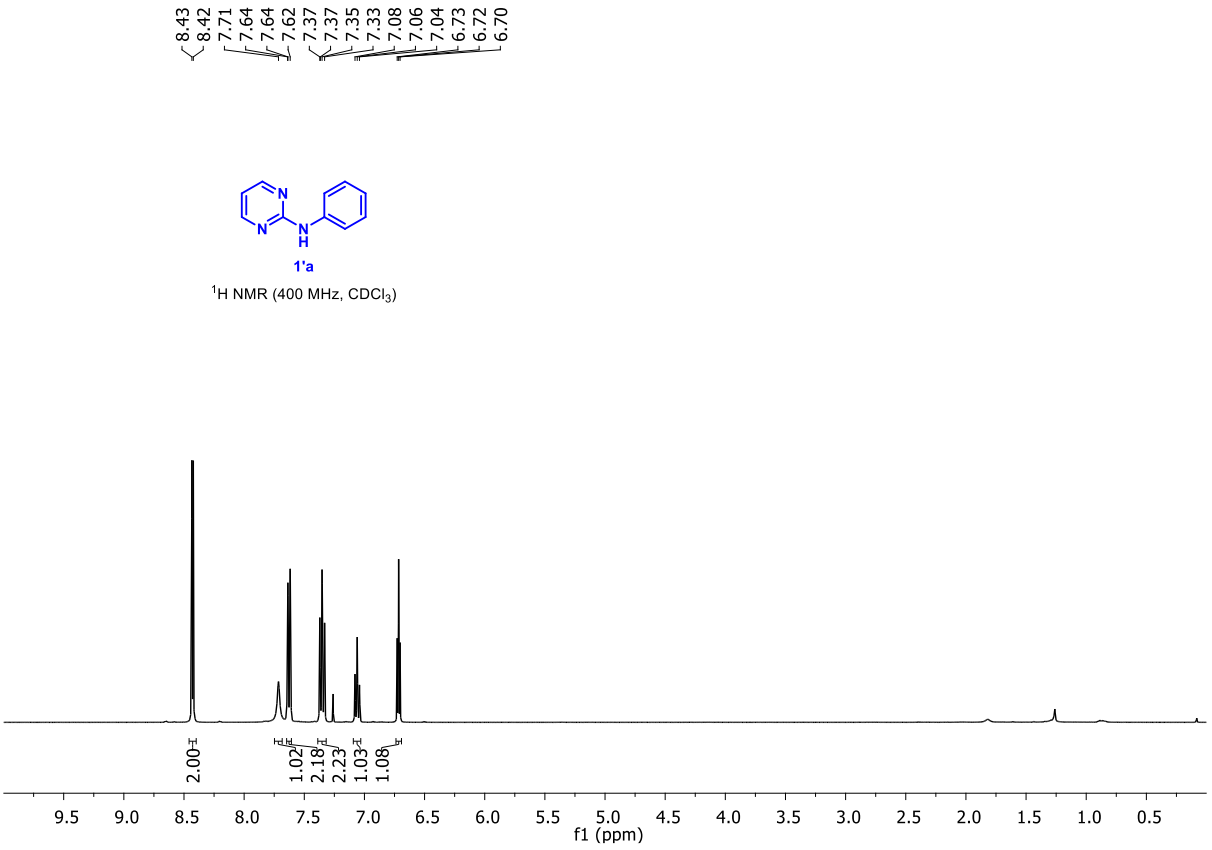
^{13}C NMR (126 MHz, $CDCl_3$)

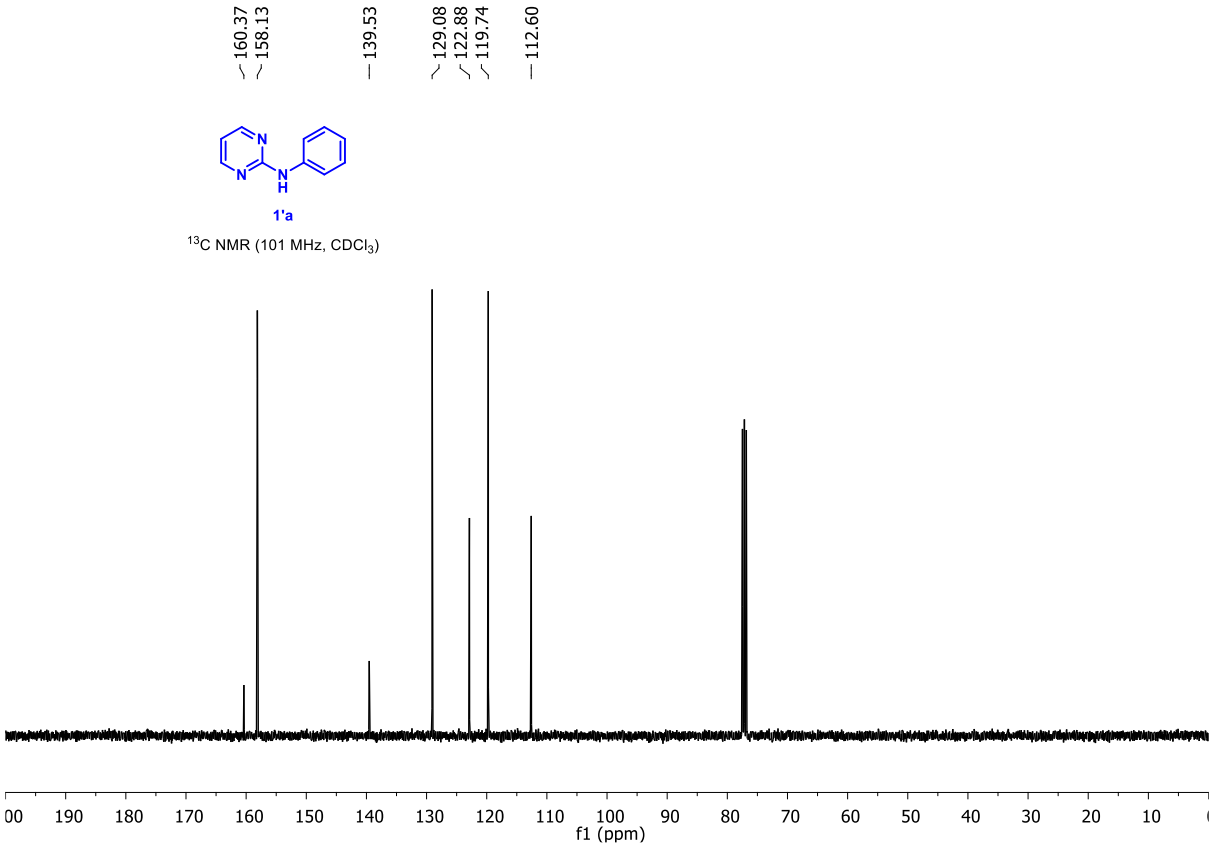


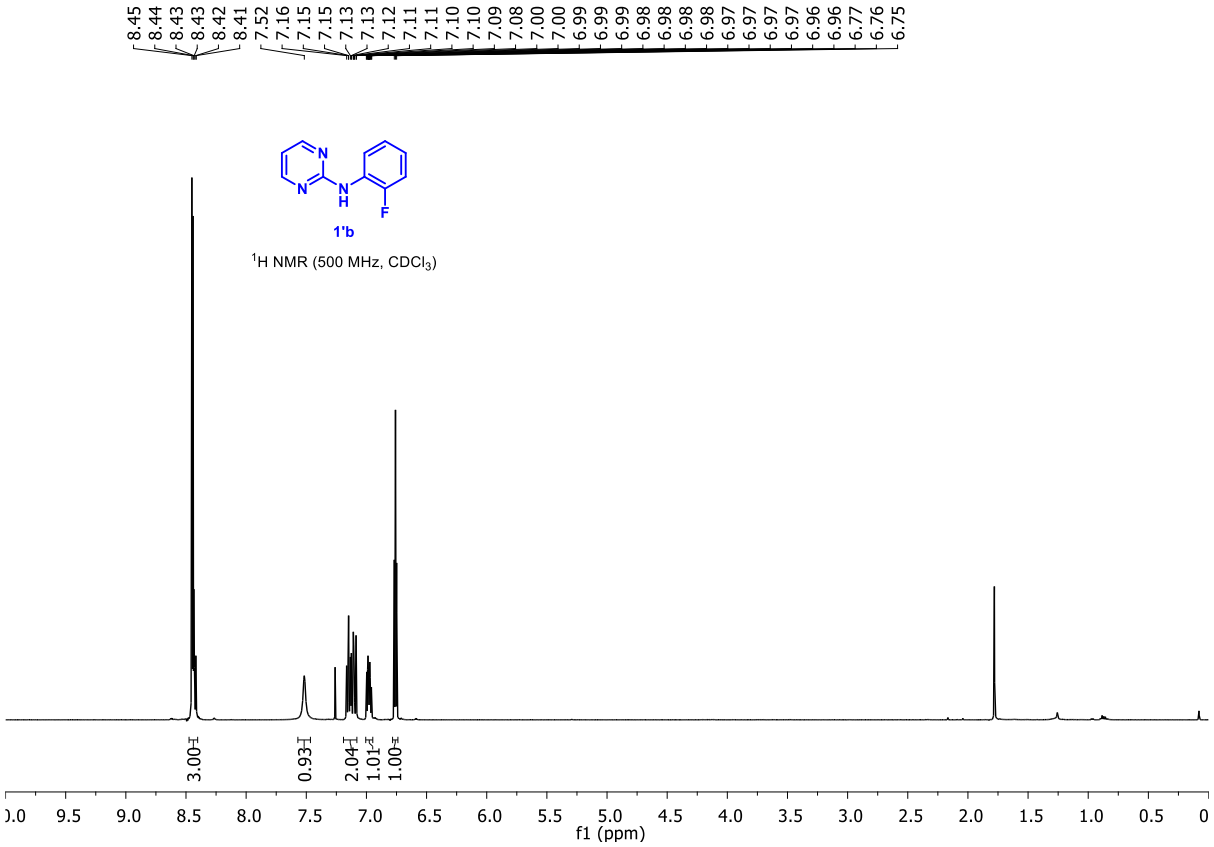
1k-*d*

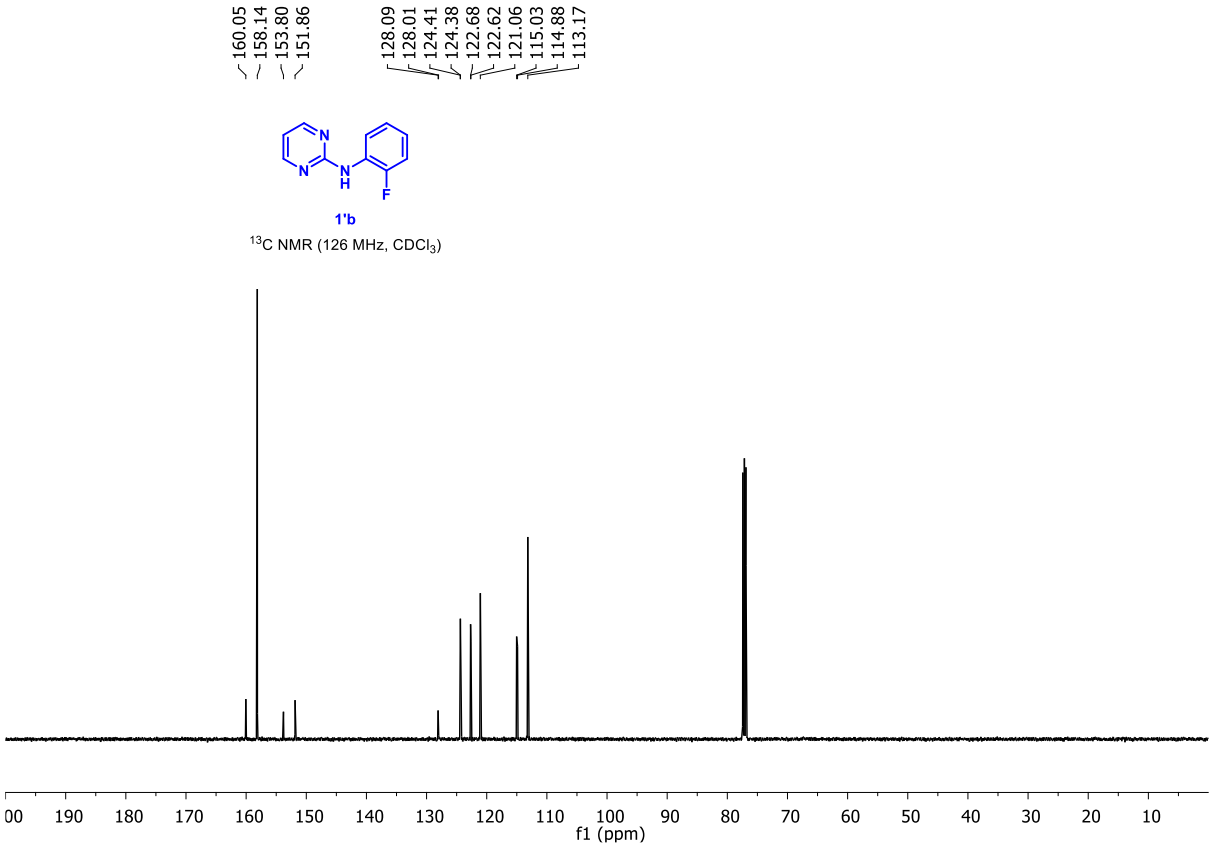
^{1}H NMR (400 MHz, $CDCl_3$)

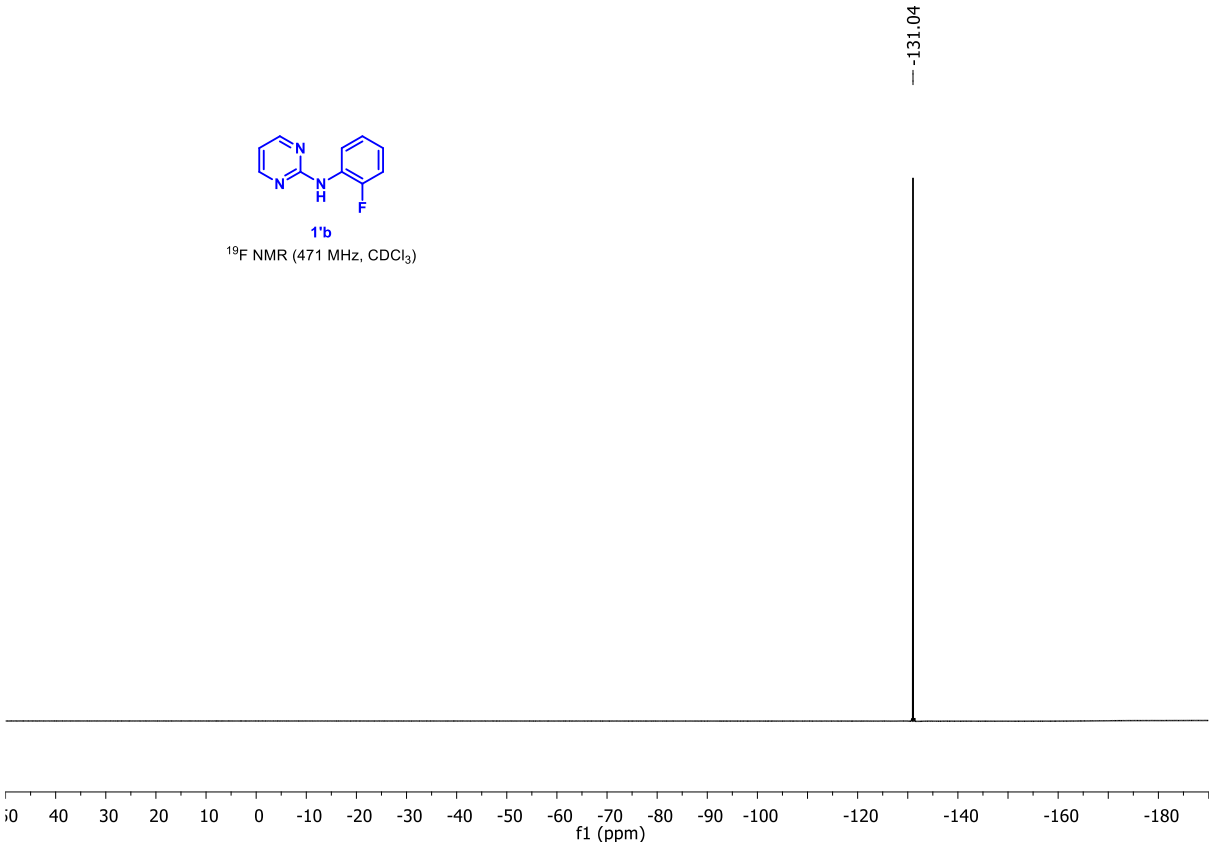

161.90
157.78
110.40
66.96
44.32
D
N
N
N
O
1k-d
13C NMR (101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

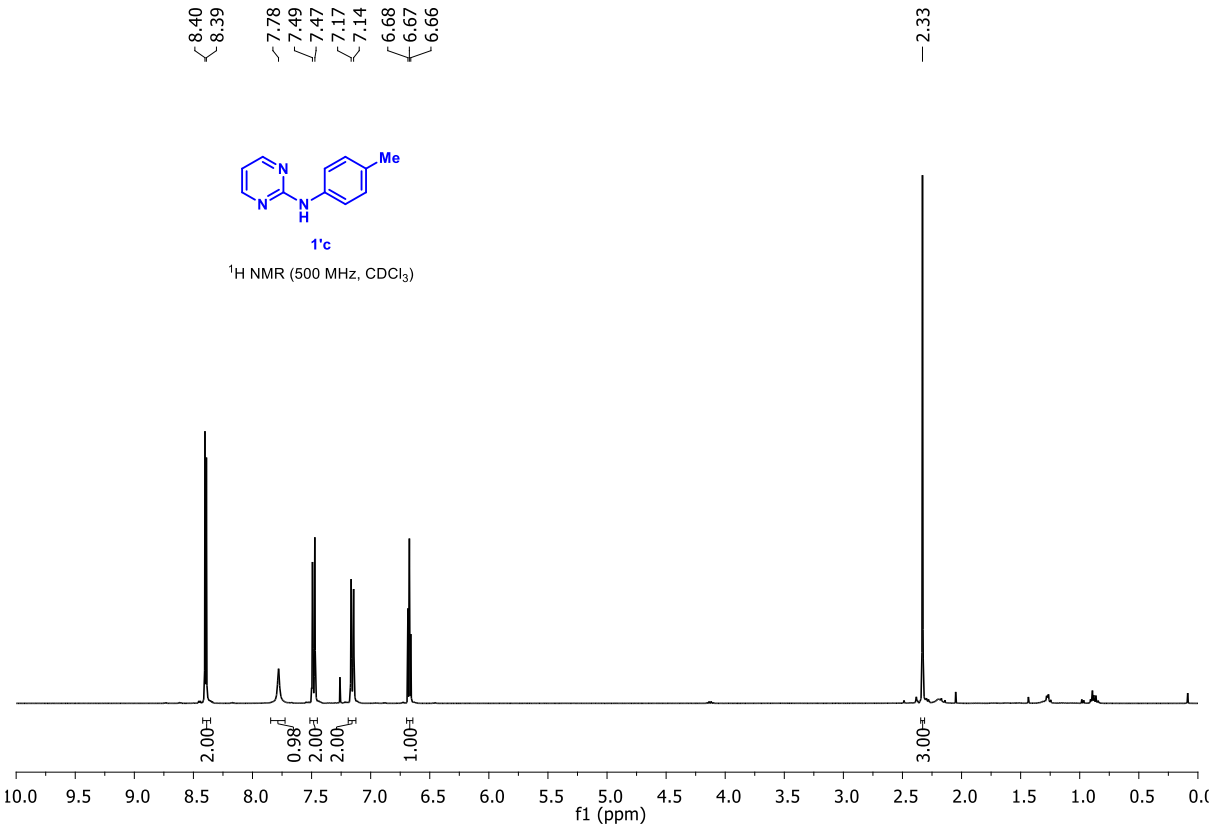

8.43
8.42
7.71
7.64
7.64
7.62
7.37
7.37
7.35
7.33
7.08
7.06
7.04
6.73
6.72
6.70
N
N
H
1'a
1H NMR (400 MHz, CDCl3)
2.00
1.02
2.18
2.23
1.03
1.08
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

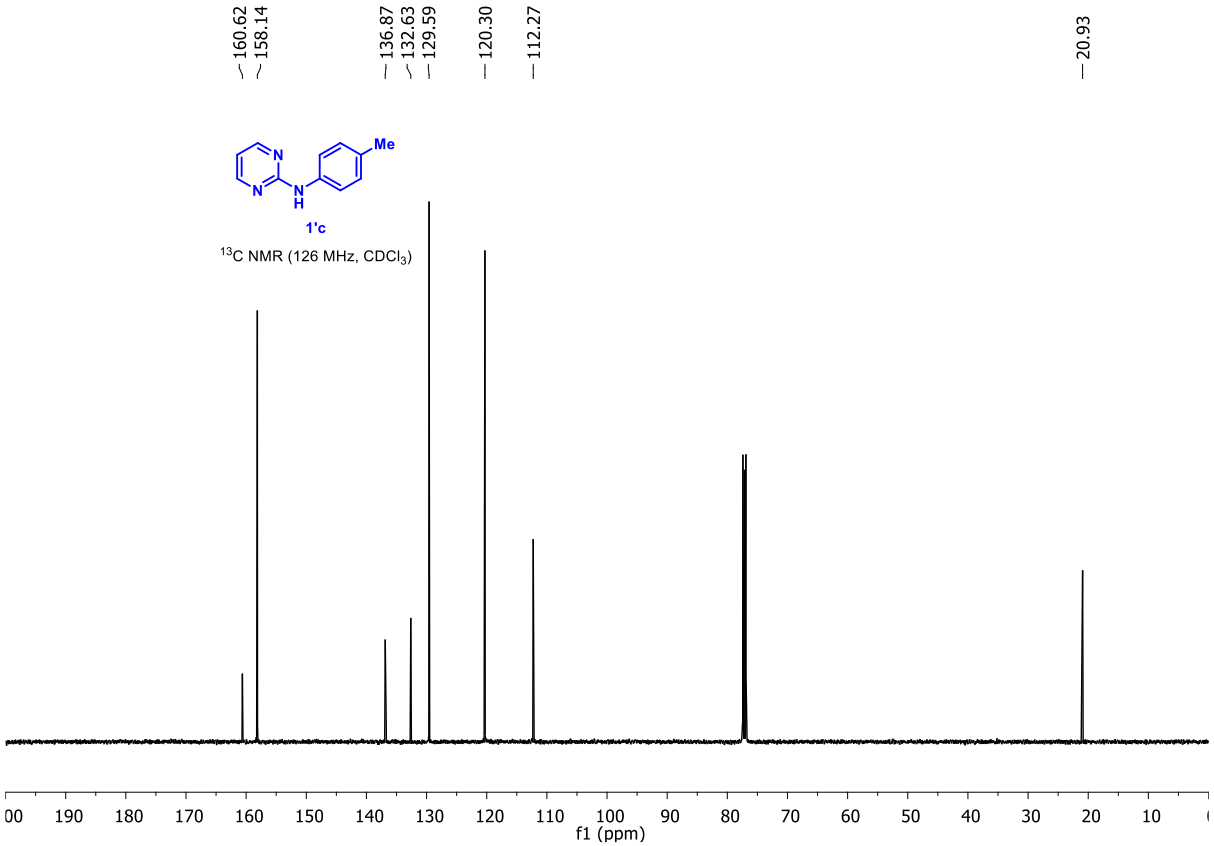

160.37
158.13
139.53
129.08
122.88
119.74
112.60
1'a
13C NMR (101 MHz, CDCl3)
f1 (ppm)

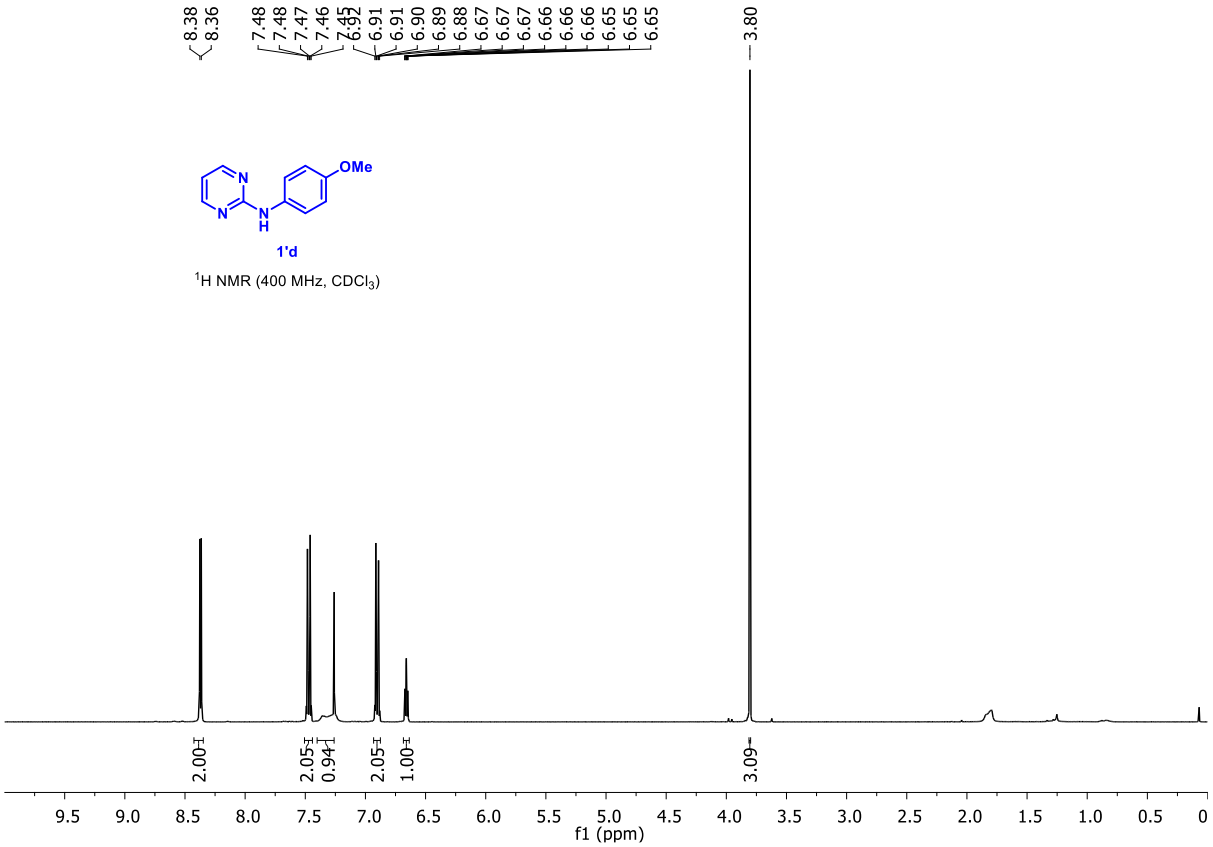

8.45
8.44
8.43
8.43
8.42
8.41
7.52
7.16
7.15
7.15
7.13
7.13
7.12
7.11
7.11
7.10
7.10
7.09
7.08
7.00
7.00
6.99
6.99
6.99
6.98
6.98
6.98
6.98
6.97
6.97
6.97
6.97
6.96
6.96
6.77
6.76
6.75
1'b
1H NMR (500 MHz, CDCl3)
3.00
0.93
2.04
1.01
1.00
f1 (ppm)


160.05
158.14
153.80
151.86
128.09
128.01
124.41
124.38
122.68
122.62
121.06
115.03
114.88
113.17
N
N
H
F
1'b
^{13}C NMR (126 MHz, CDCl$_3$)
f1 (ppm)

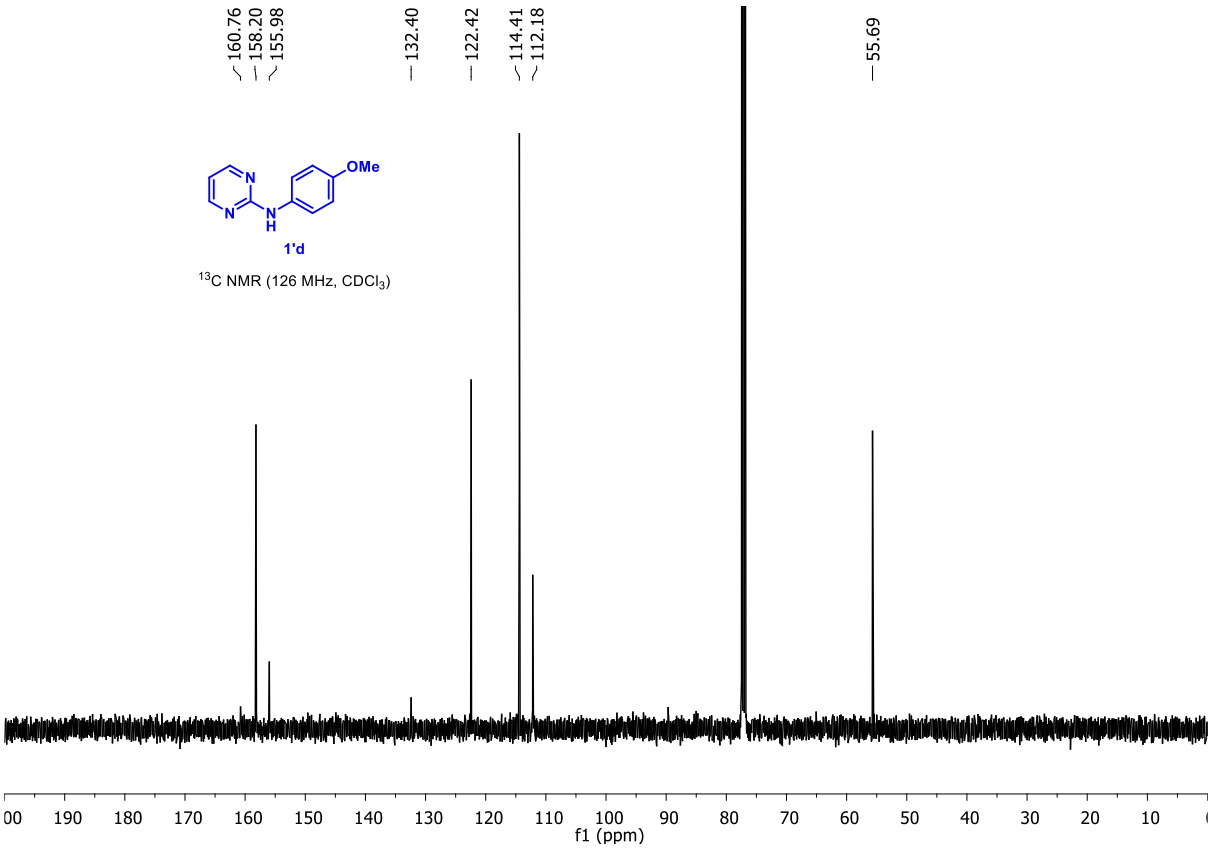

-131.04
N
N
H
F
1'b
^{19}F NMR (471 MHz, CDCl$_3$)
f1 (ppm)


8.40
8.39
7.78
7.49
7.47
7.17
7.14
6.68
6.67
6.66
2.33
Me
N
N
H
1'c
^{1}H NMR (500 MHz, CDCl$_3$)
2.00
0.98
2.00
2.00
1.00
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

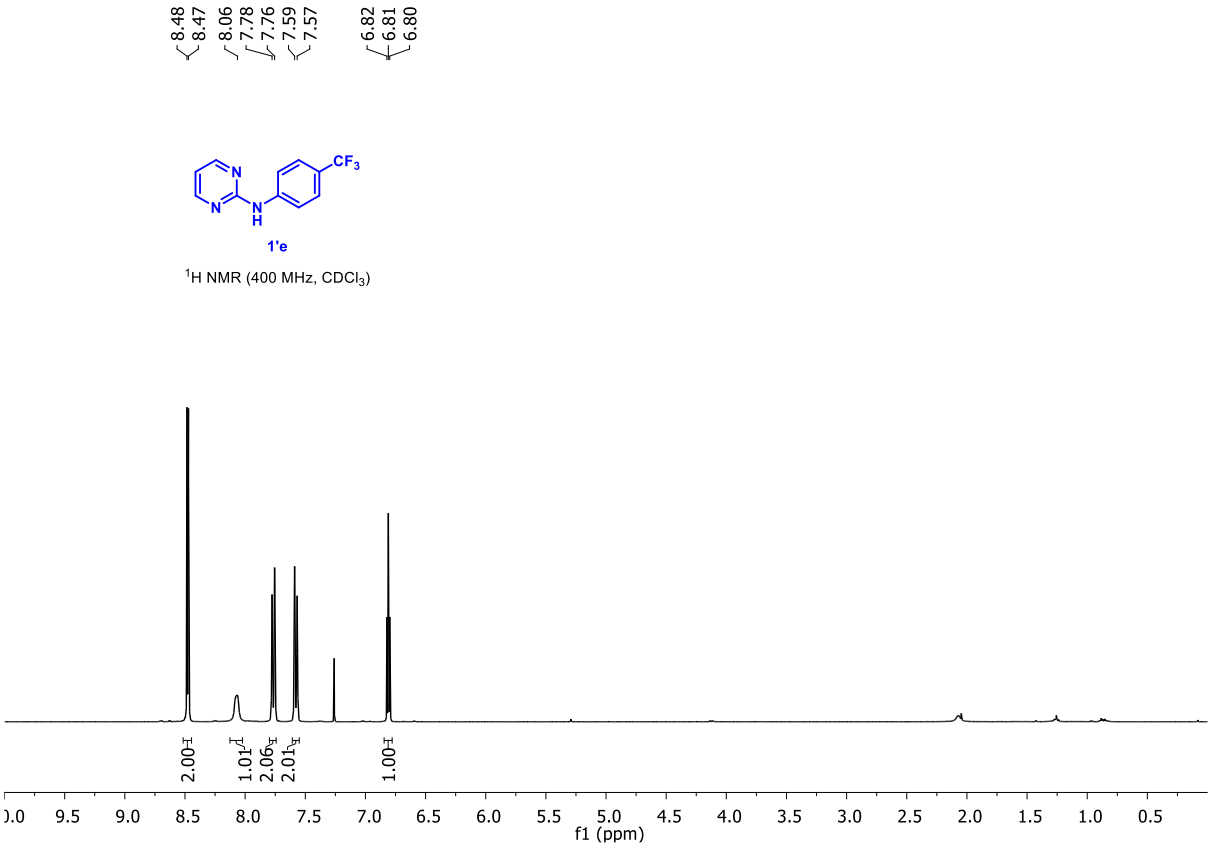

160.62
158.14
136.87
132.63
129.59
120.30
112.27
20.93
Me
N
N
H
1'c
^{13}C NMR (126 MHz, CDCl$_3$)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

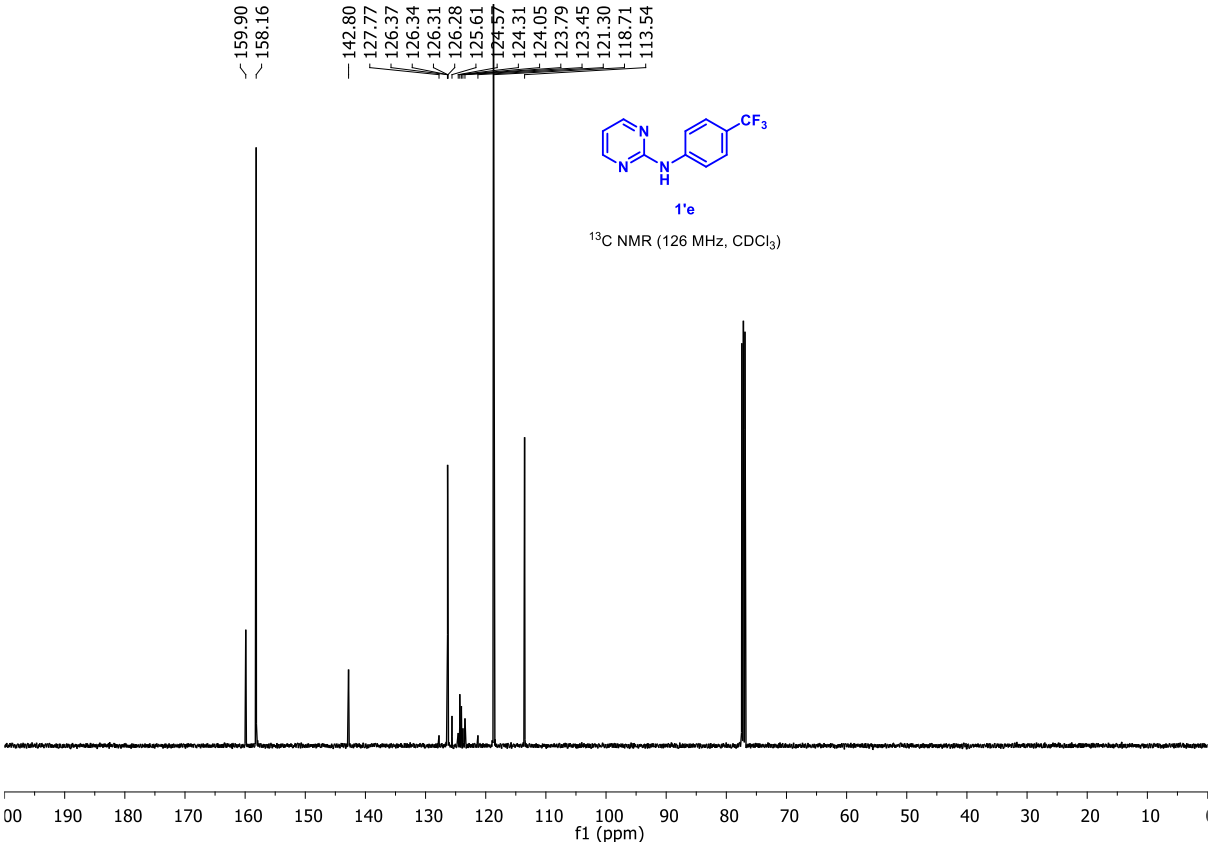


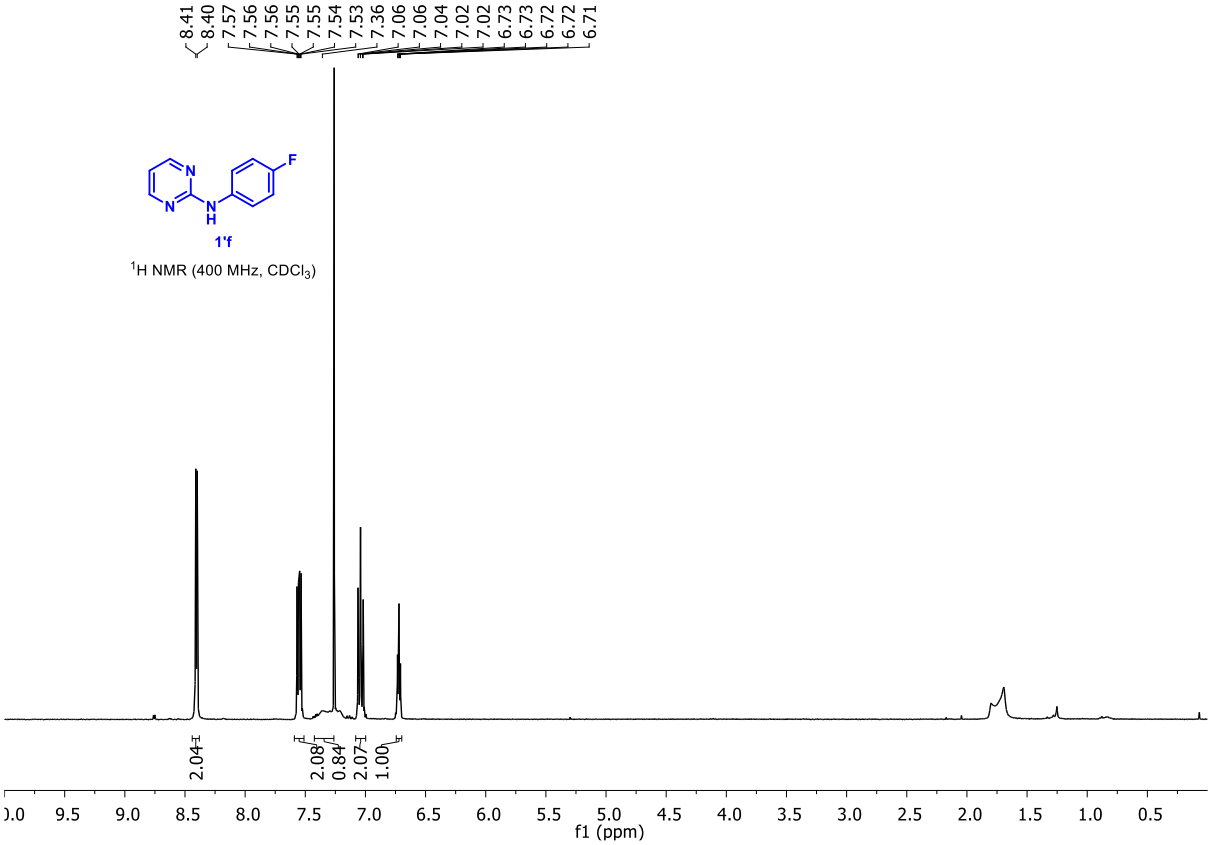
^{1}H NMR (400 MHz, $CDCl_3$)

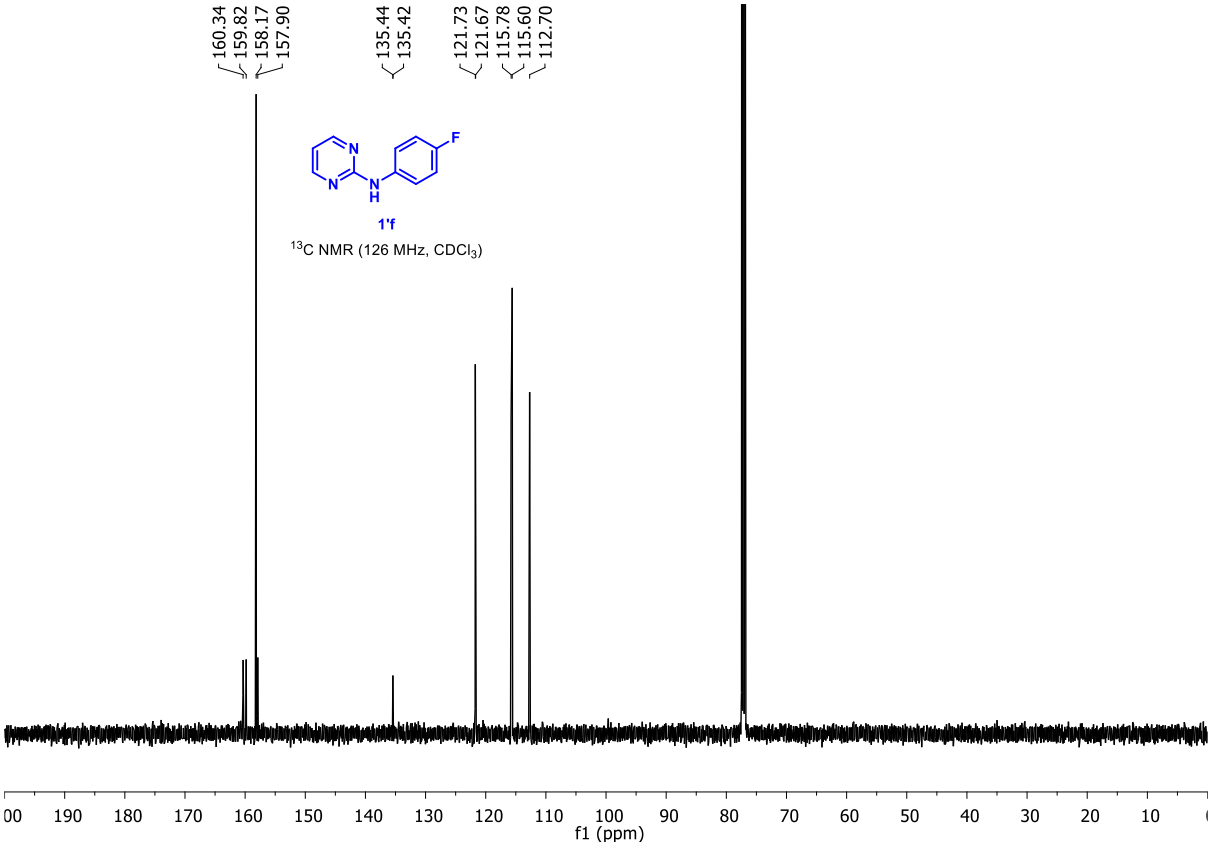


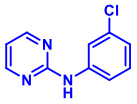
^{13}C NMR (126 MHz, $CDCl_3$)


8.48
8.47
8.06
7.78
7.76
7.59
7.57
6.82
6.81
6.80
CF3
N
N
H
1'e
1H NMR (400 MHz, CDCl3)
2.00
1.01
2.06
2.01
1.00
f1 (ppm)


159.90
158.16
142.80
127.77
126.37
126.34
126.31
126.28
125.61
124.57
124.31
124.05
123.79
123.45
121.30
118.71
113.54
CF3
N
N
H
1'e
13C NMR (126 MHz, CDCl3)
f1 (ppm)

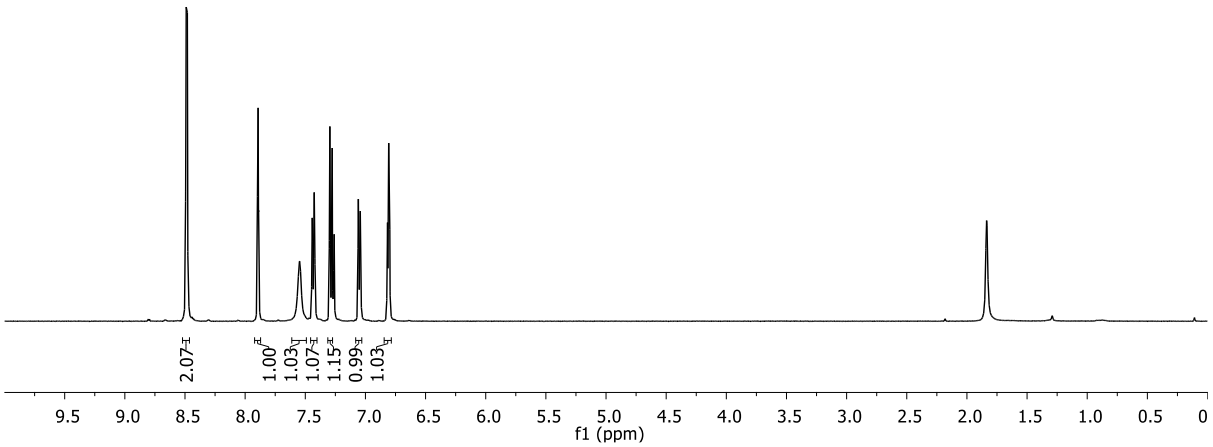

8.41
8.40
7.57
7.56
7.56
7.55
7.55
7.54
7.53
7.36
7.06
7.06
7.04
7.02
7.02
6.73
6.73
6.72
6.72
6.71
F
N
N
H
1'f
^{1}H NMR (400 MHz, CDCl$_3$)
2.04
2.08
0.84
2.07
1.00
f1 (ppm)

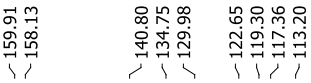

160.34
159.82
158.17
157.90
135.44
135.42
121.73
121.67
115.78
115.60
112.70
F
N
N
H
1'f
^{13}C NMR (126 MHz, CDCl$_3$)
f1 (ppm)

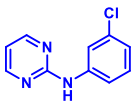


1'g

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

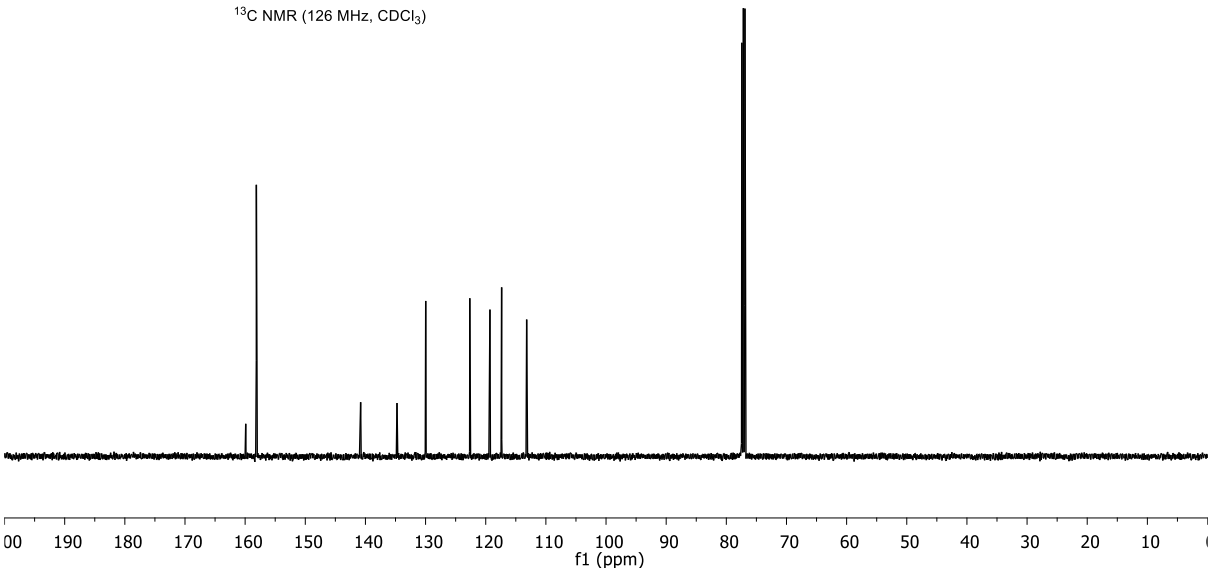


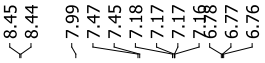


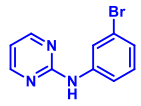


1'g

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

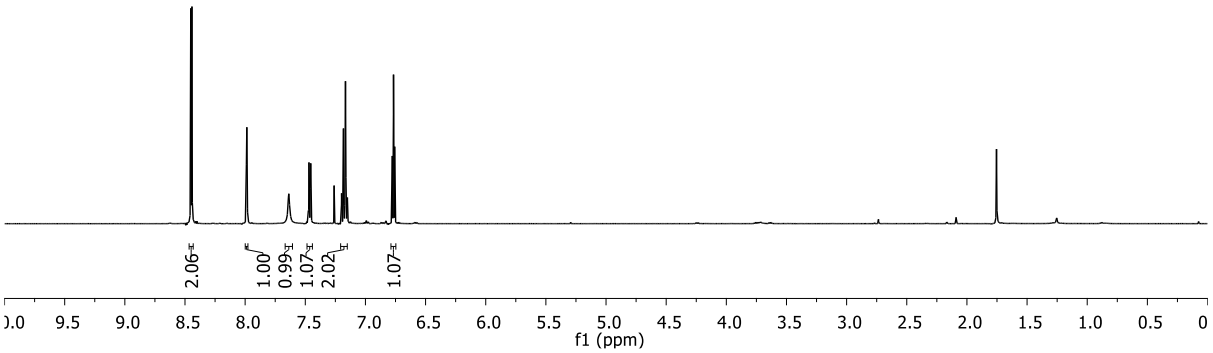


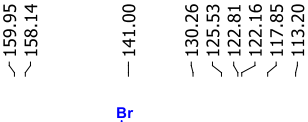


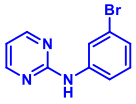


1'h

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

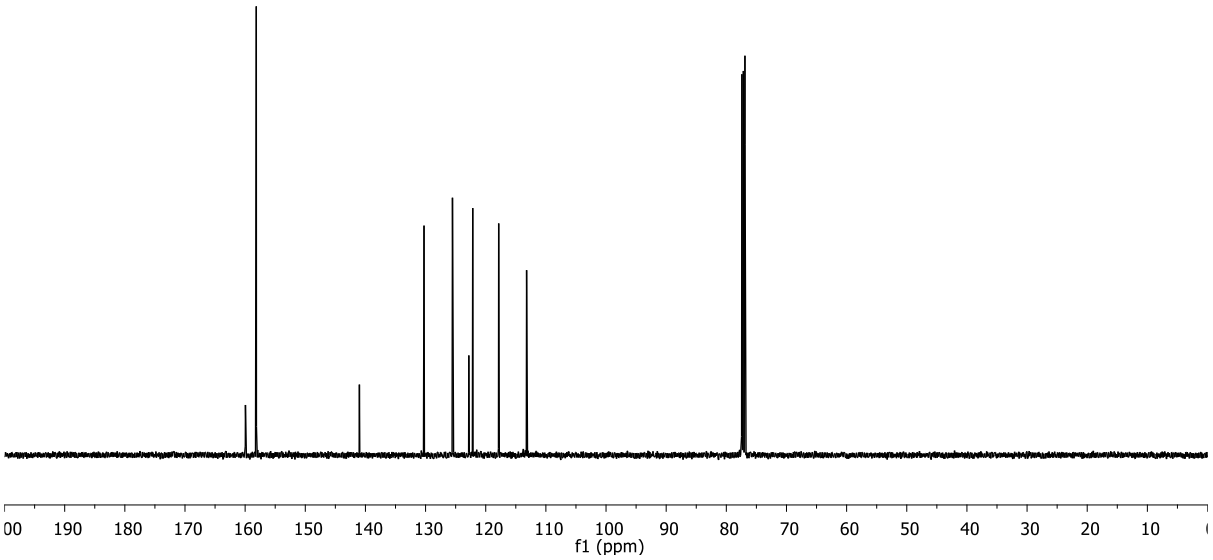


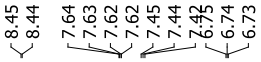


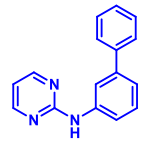


1'h

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

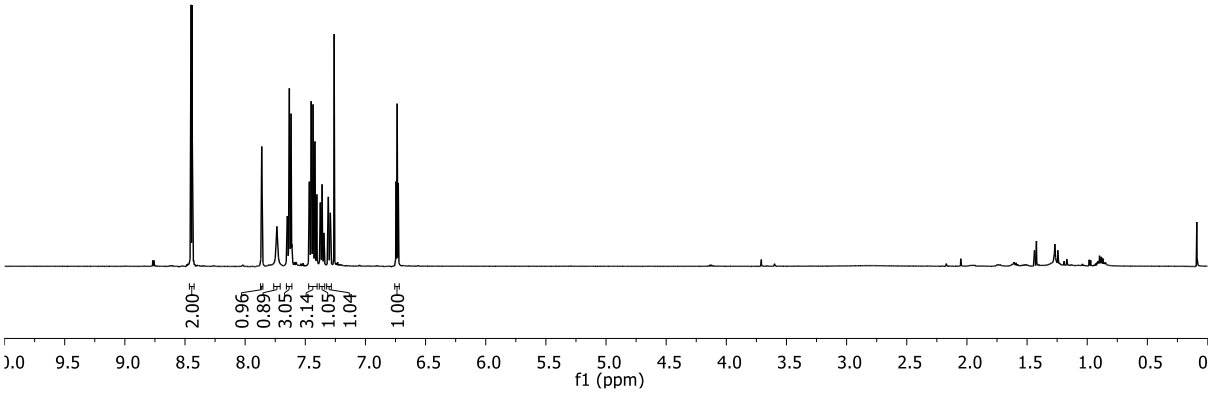


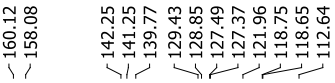


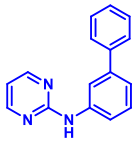


1'i

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

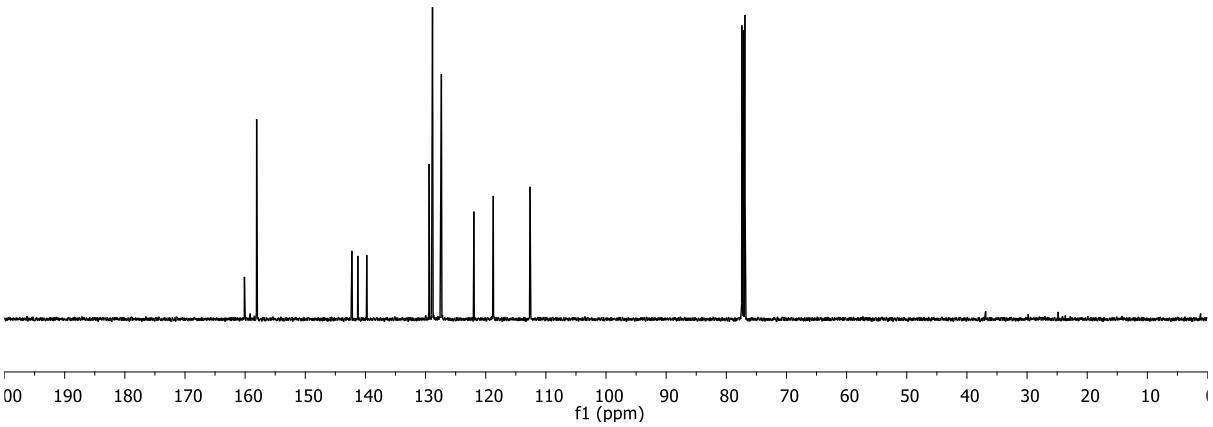


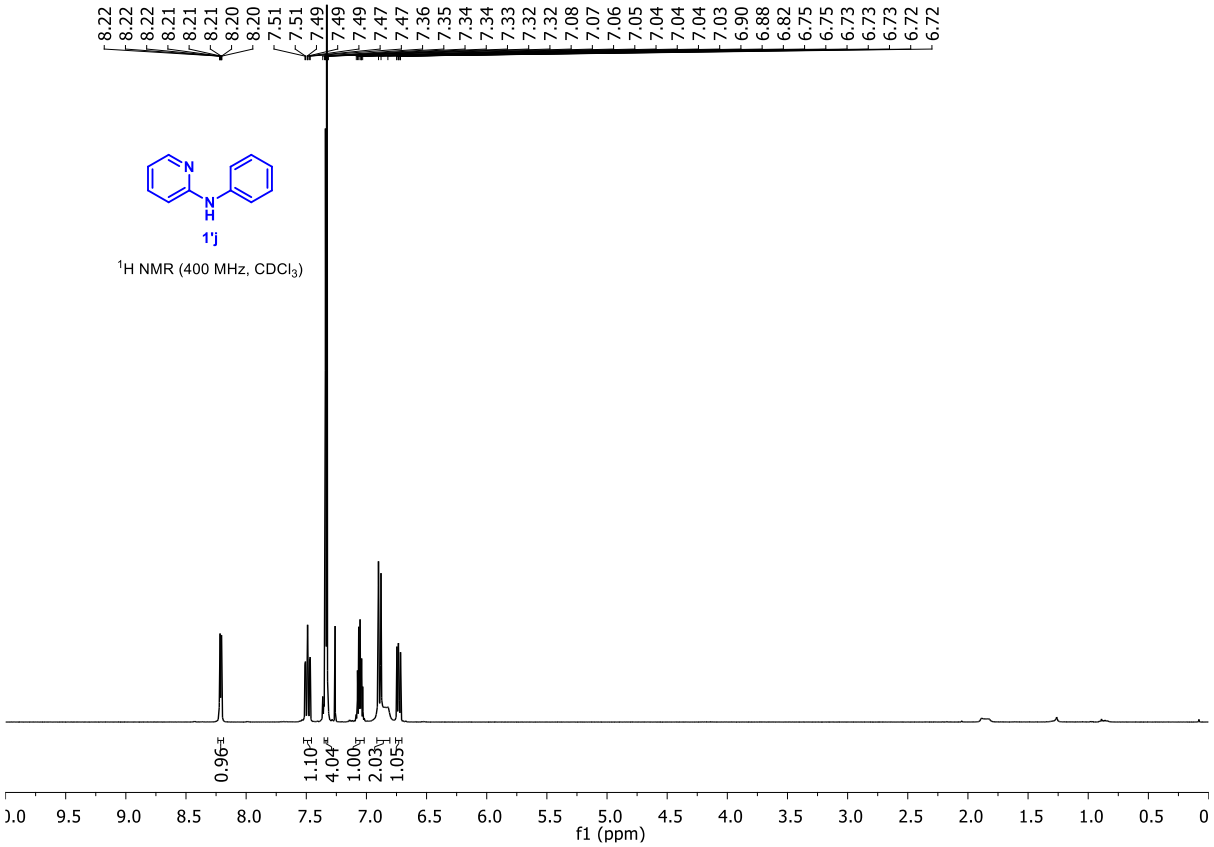


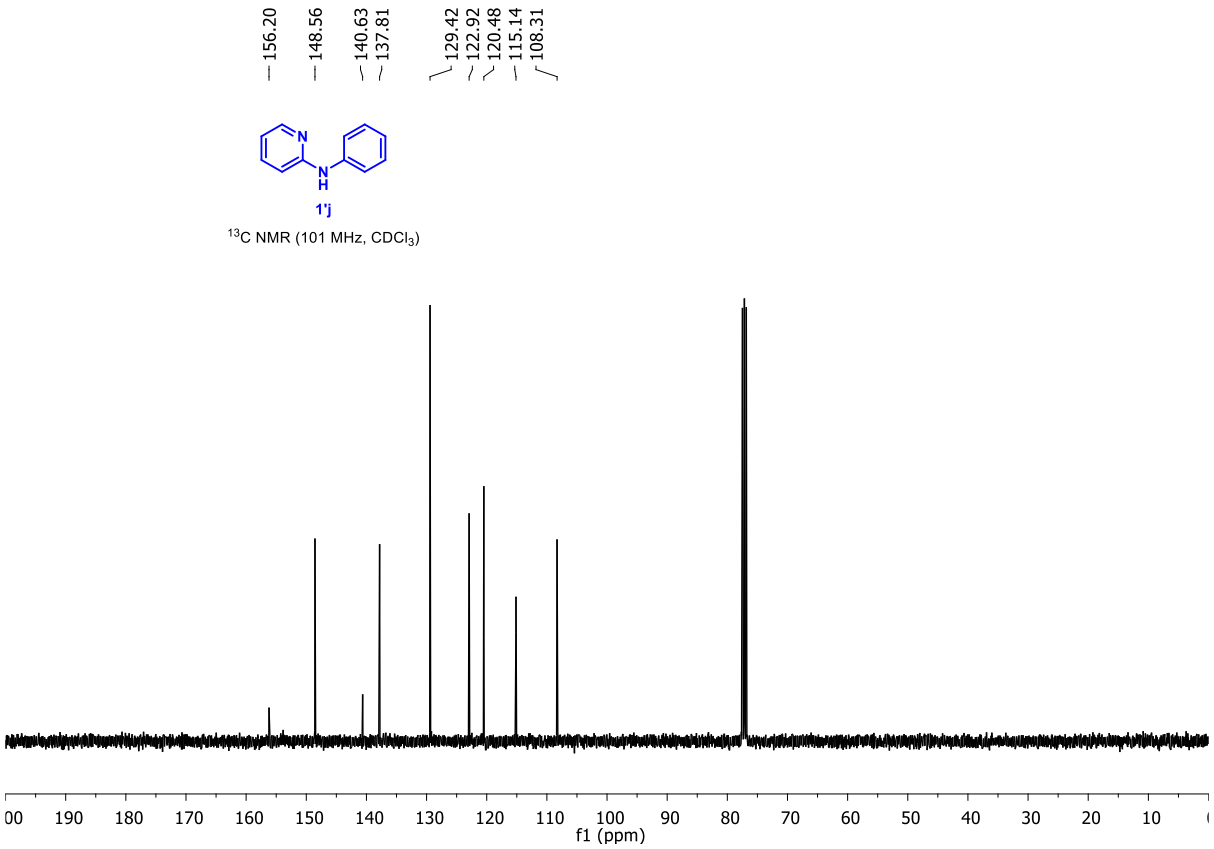


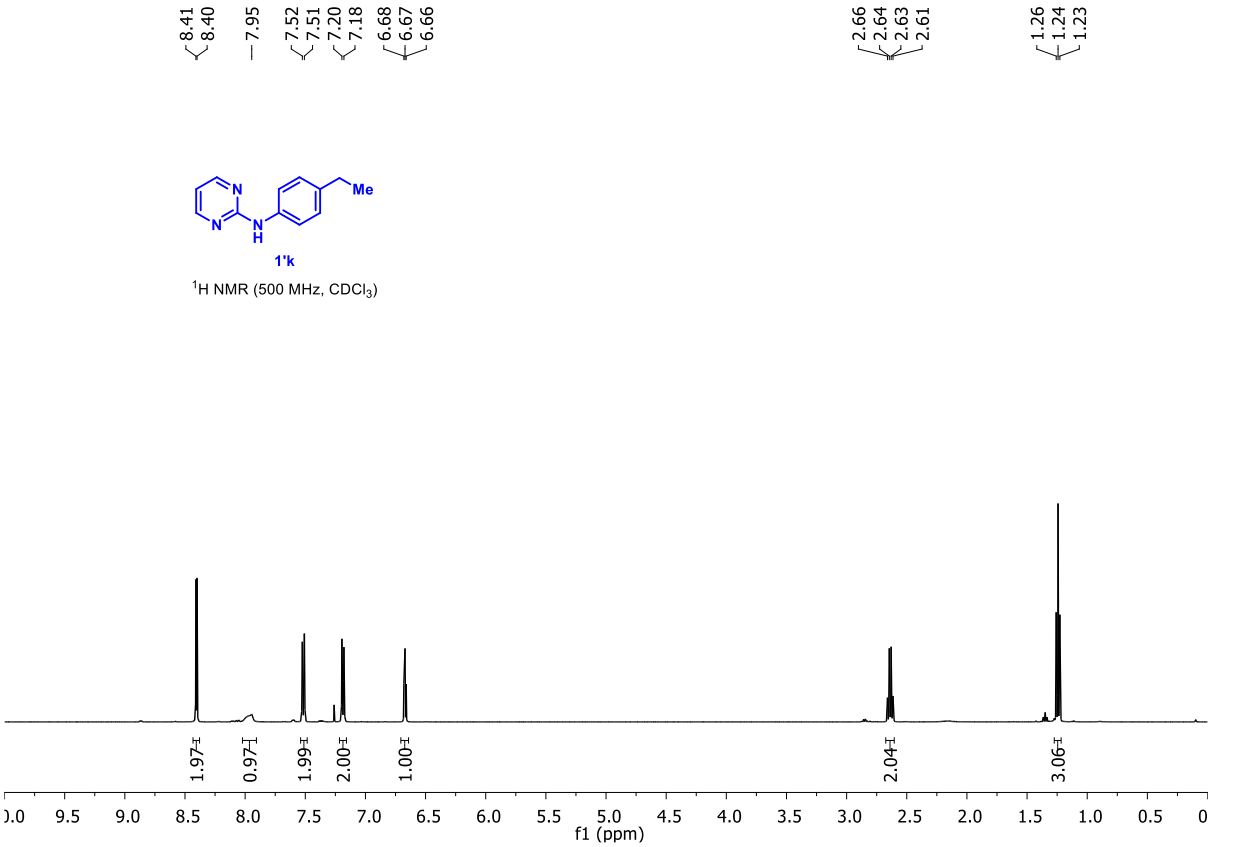
1'i

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



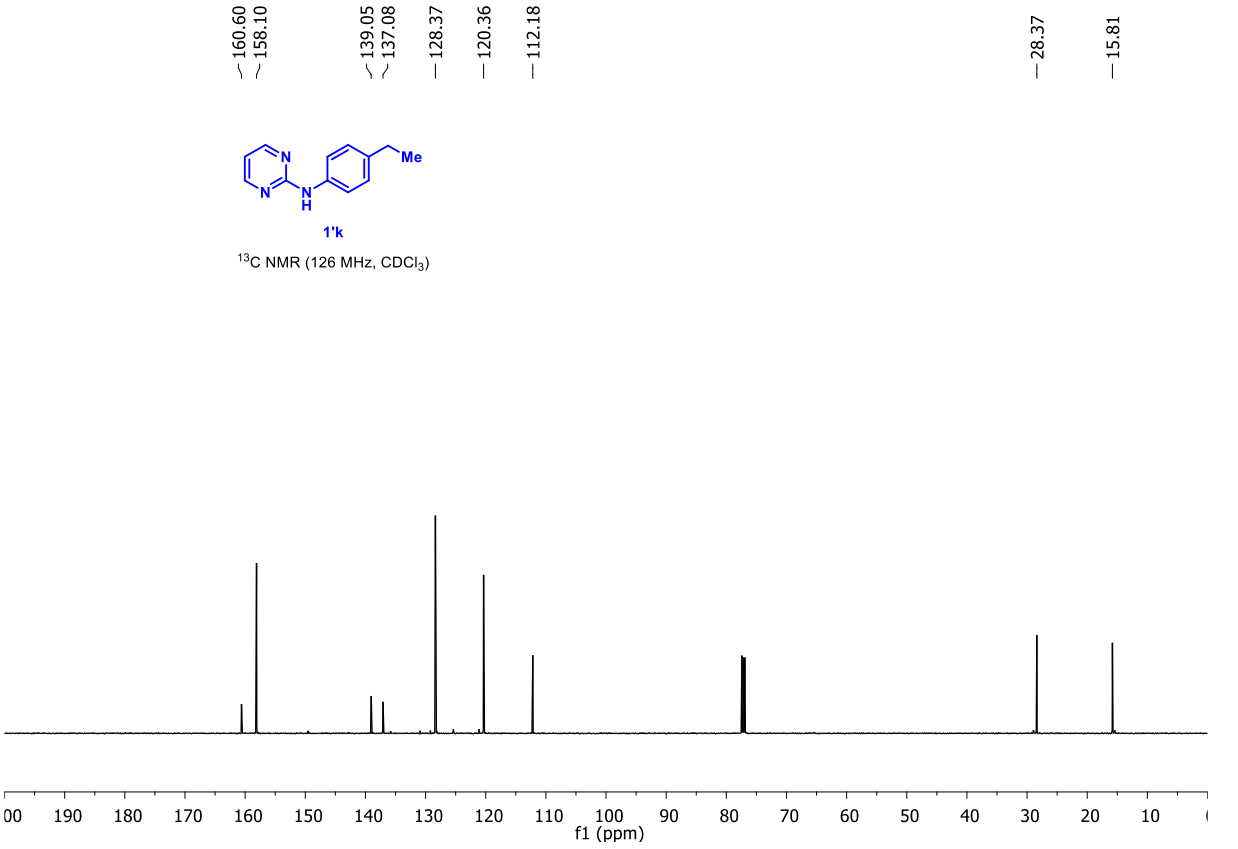

8.22
8.22
8.22
8.21
8.21
8.21
8.20
8.20
7.51
7.51
7.49
7.49
7.49
7.47
7.47
7.36
7.35
7.34
7.34
7.33
7.32
7.32
7.08
7.07
7.06
7.05
7.04
7.04
7.04
7.03
6.90
6.88
6.82
6.75
6.75
6.73
6.73
6.73
6.72
6.72
N
H
1'j
^{1}H NMR (400 MHz, CDCl$_3$)
0.96
1.10
4.04
1.00
2.03
1.05
f1 (ppm)


156.20
148.56
140.63
137.81
129.42
122.92
120.48
115.14
108.31
N
H
1'j
^{13}C NMR (101 MHz, CDCl$_3$)
f1 (ppm)



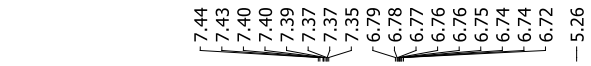
1'k

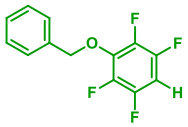
^{1}H NMR (500 MHz, $CDCl_3$)



1'k

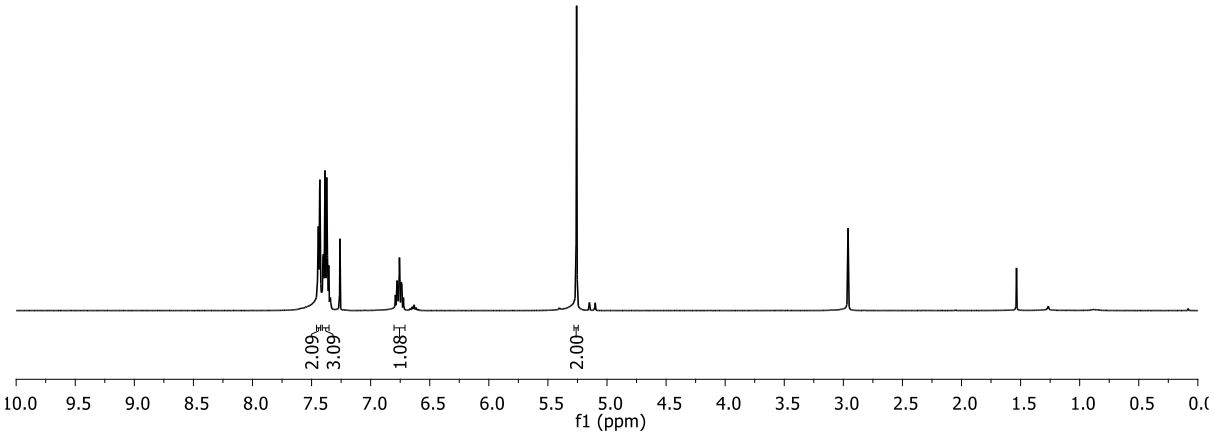
^{13}C NMR (126 MHz, $CDCl_3$)

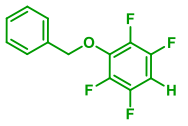




2f

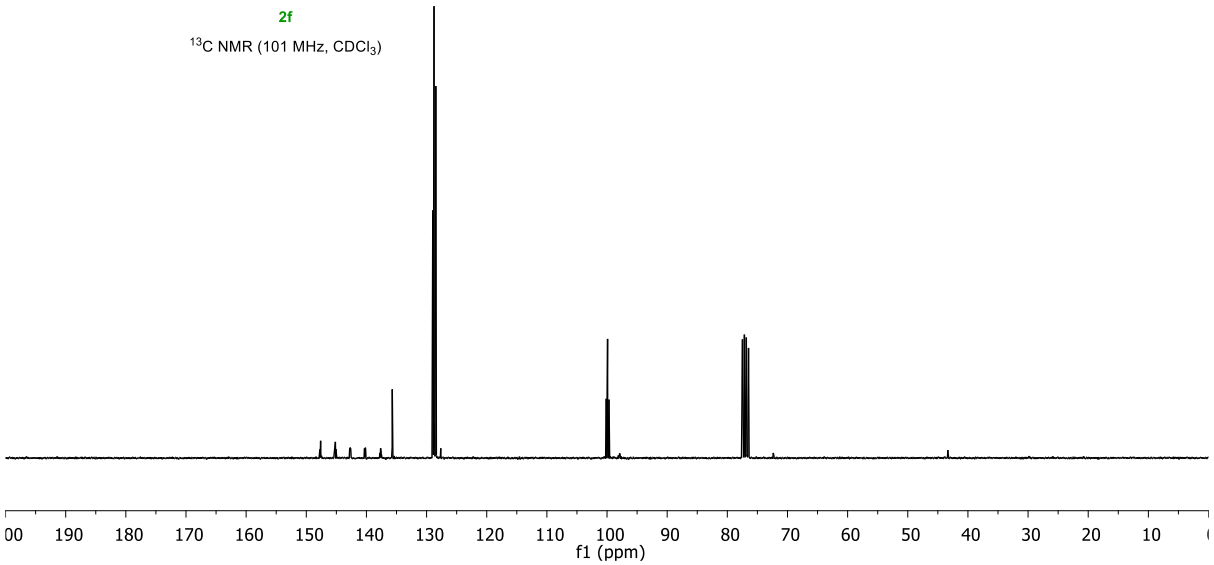
^{1}H NMR (500 MHz, $CDCl_3$)

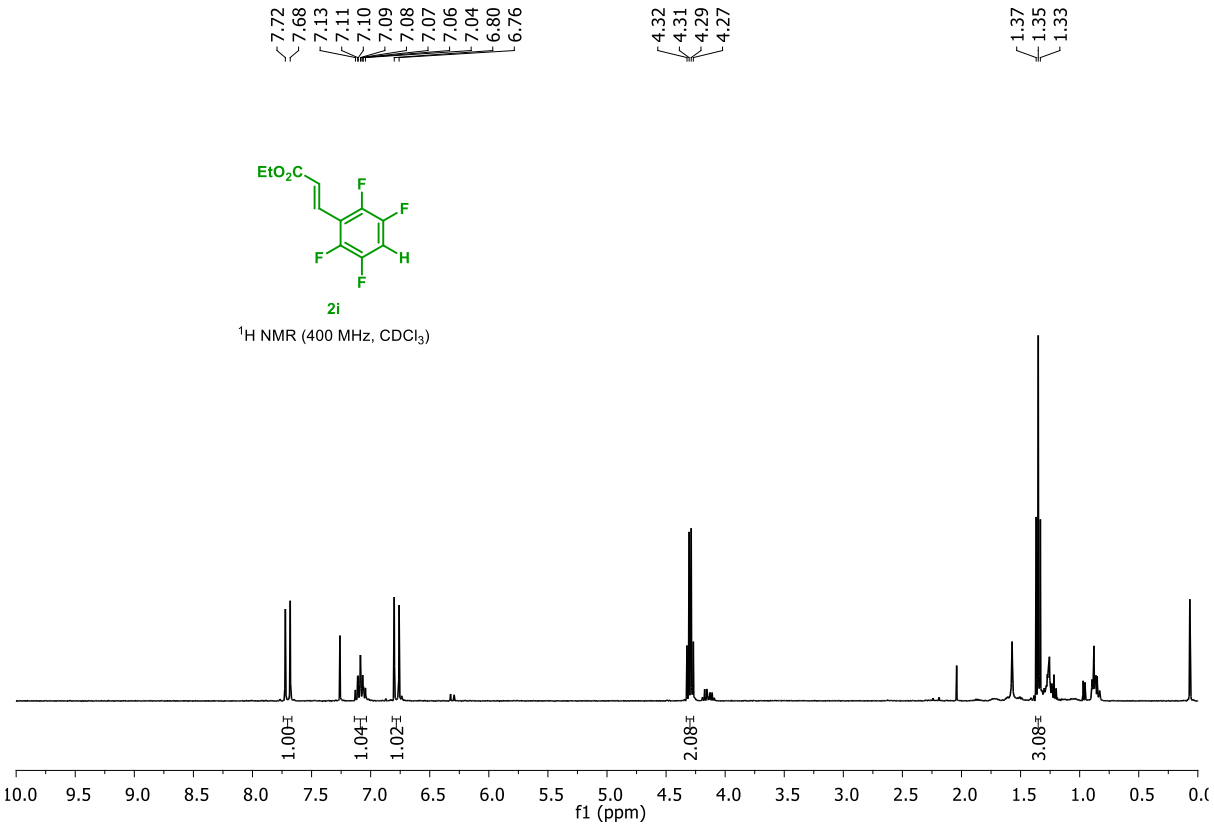


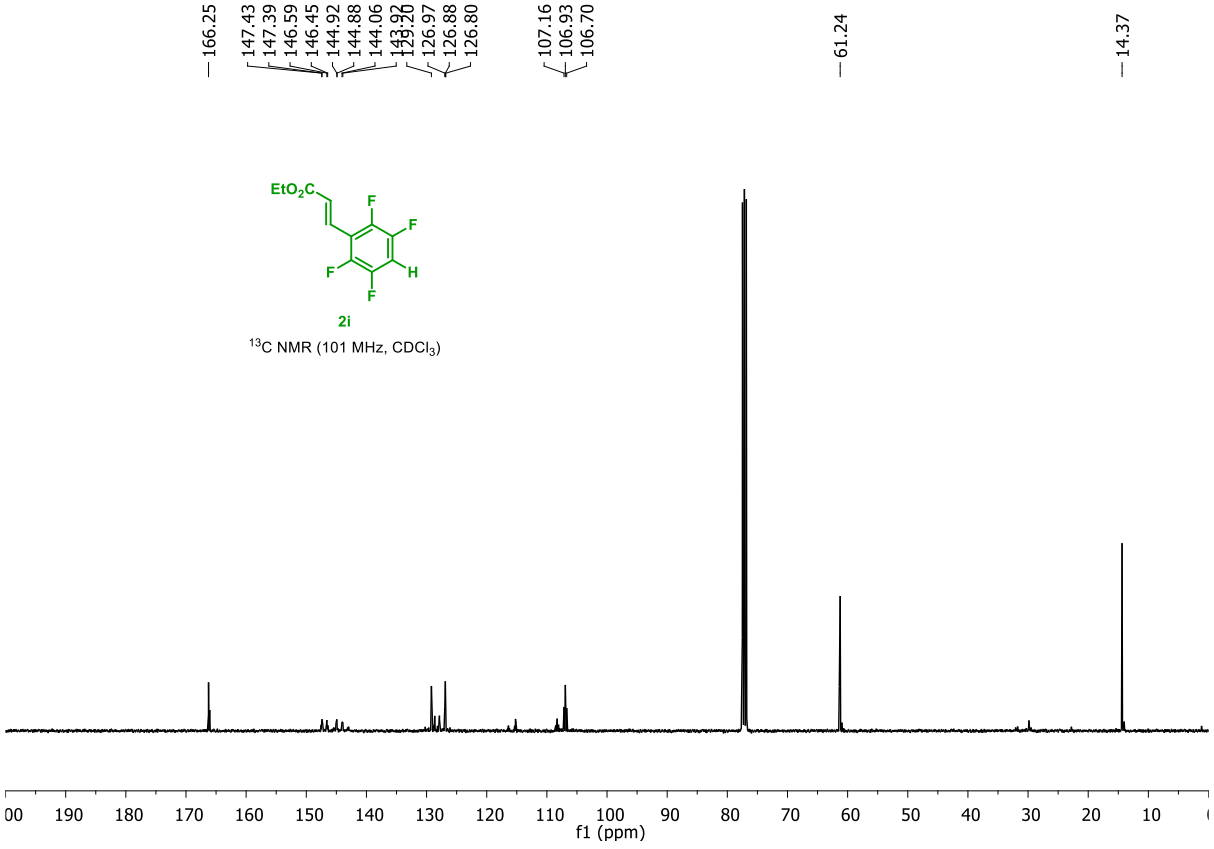


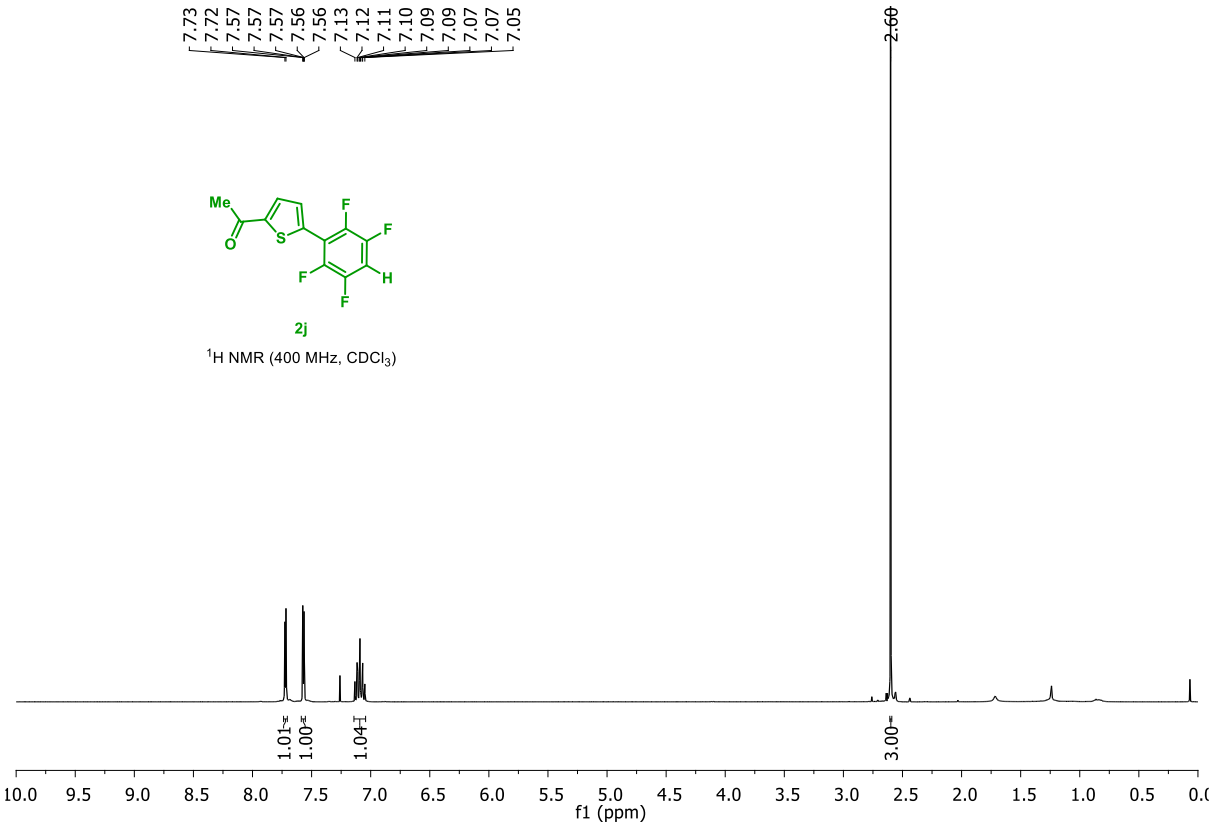
2f

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



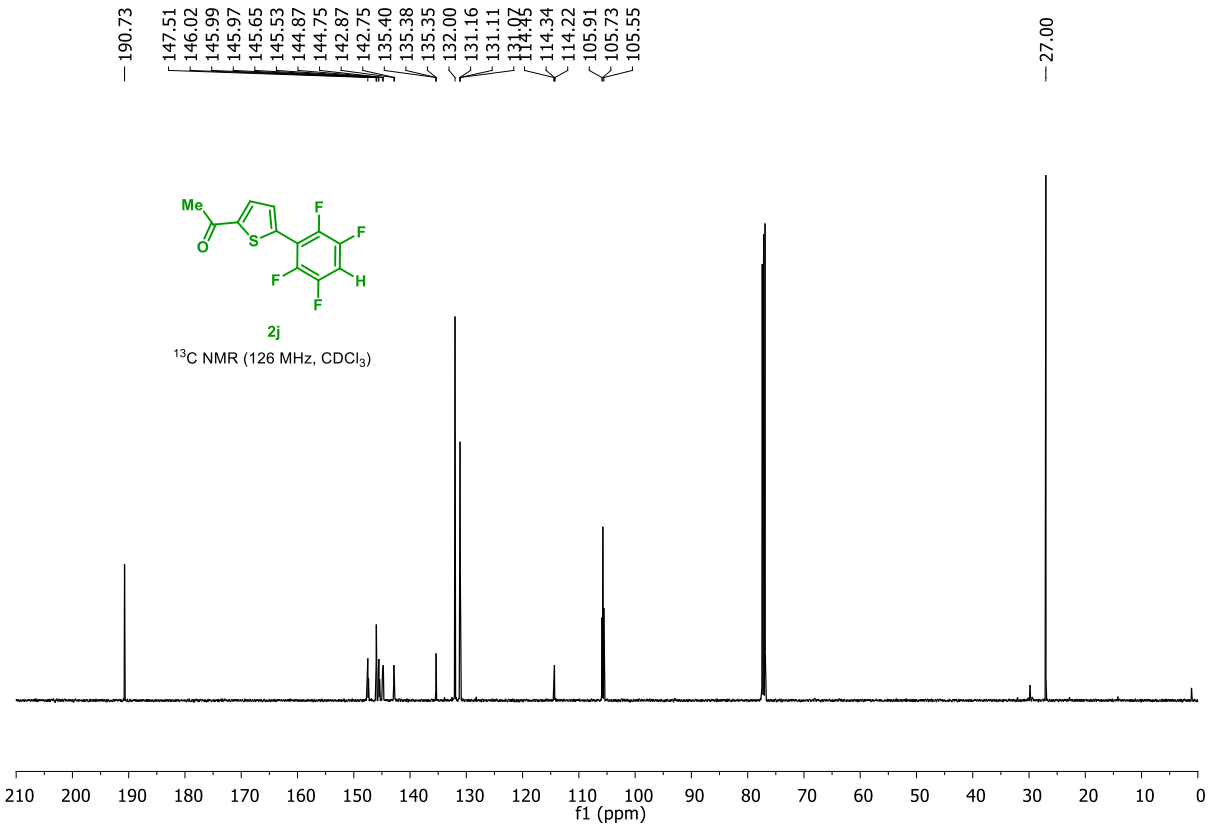

7.72
7.68
7.13
7.11
7.10
7.09
7.08
7.07
7.06
7.04
6.80
6.76
4.32
4.31
4.29
4.27
1.37
1.35
1.33
EtO2C
F
F
F
H
F
2i
1H NMR (400 MHz, CDCl3)
1.00
1.04
1.02
2.08
3.08
f1 (ppm)


166.25
147.43
147.39
146.59
146.45
144.92
144.88
144.06
126.97
126.88
126.80
107.16
106.93
106.70
61.24
14.37
EtO2C
F
F
F
H
F
2i
13C NMR (101 MHz, CDCl3)
f1 (ppm)



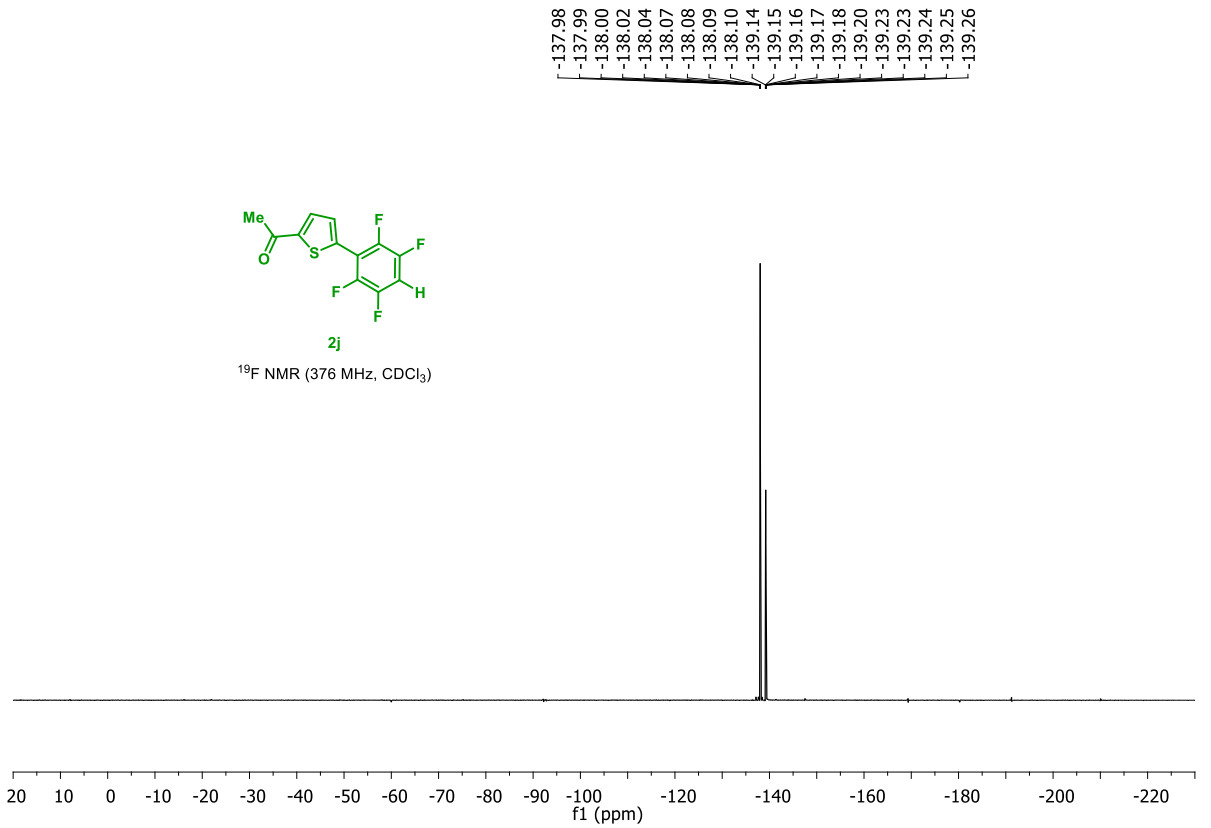
2j

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



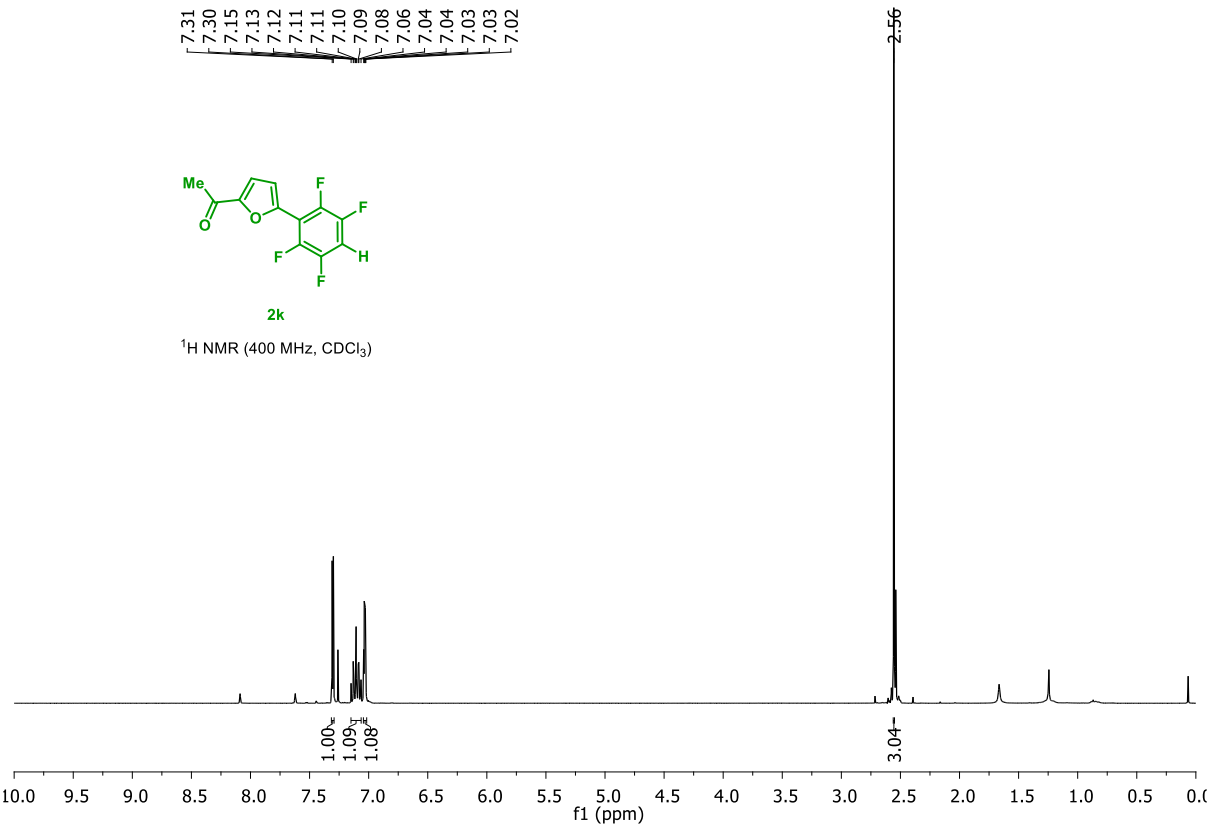
2j

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



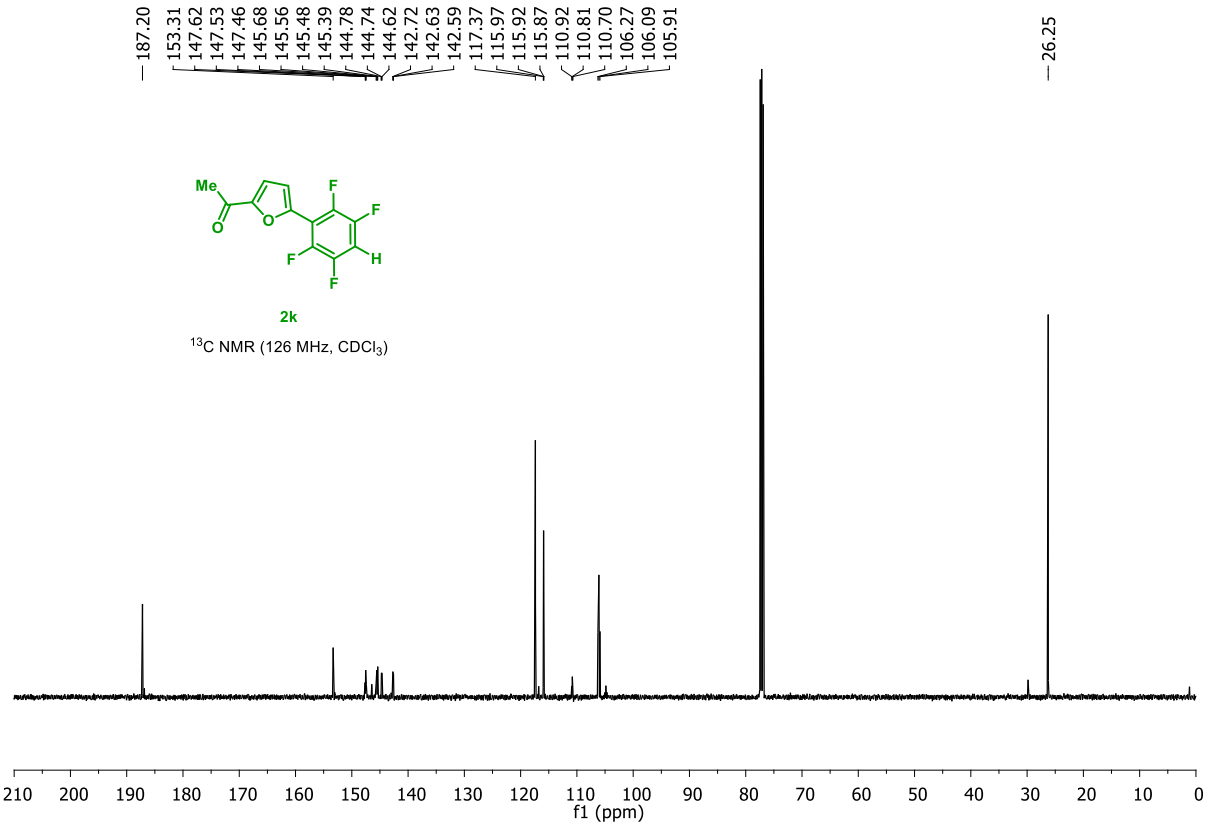
2j

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



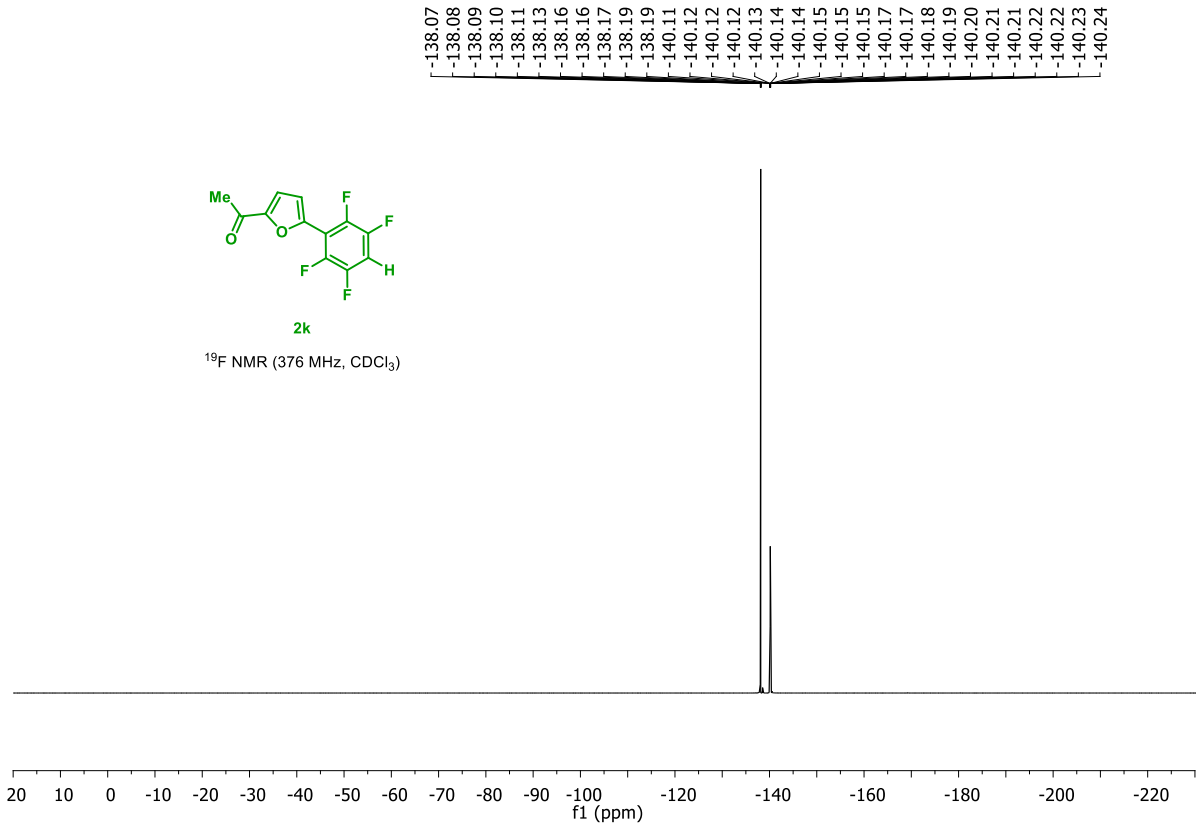
2k

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



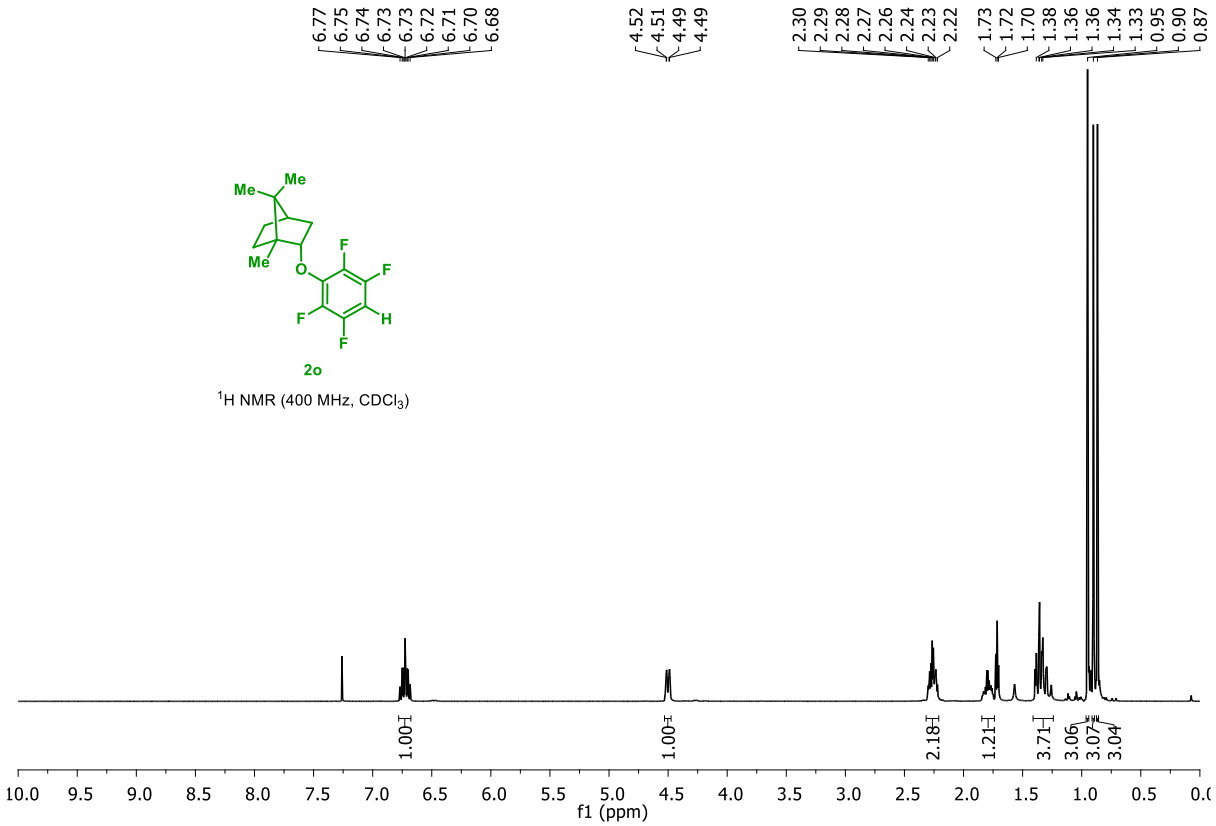
2k

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



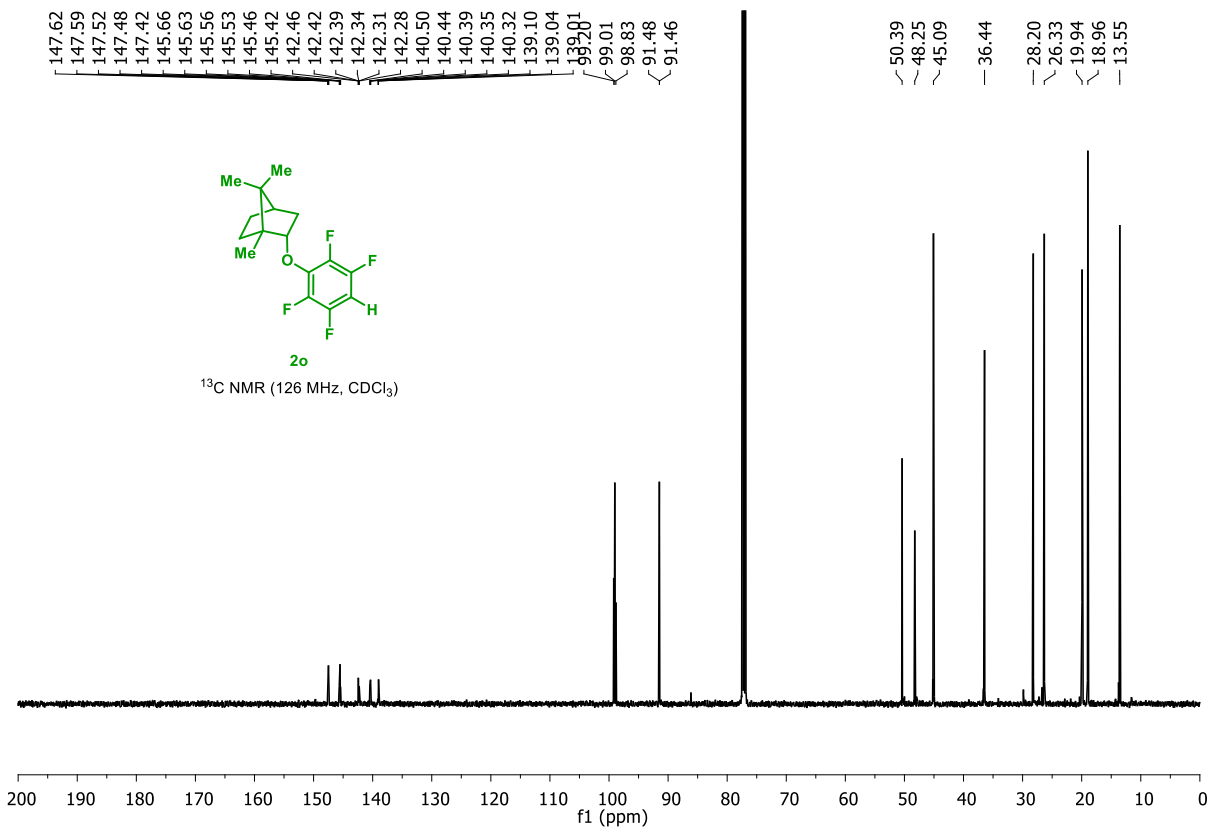
2k

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



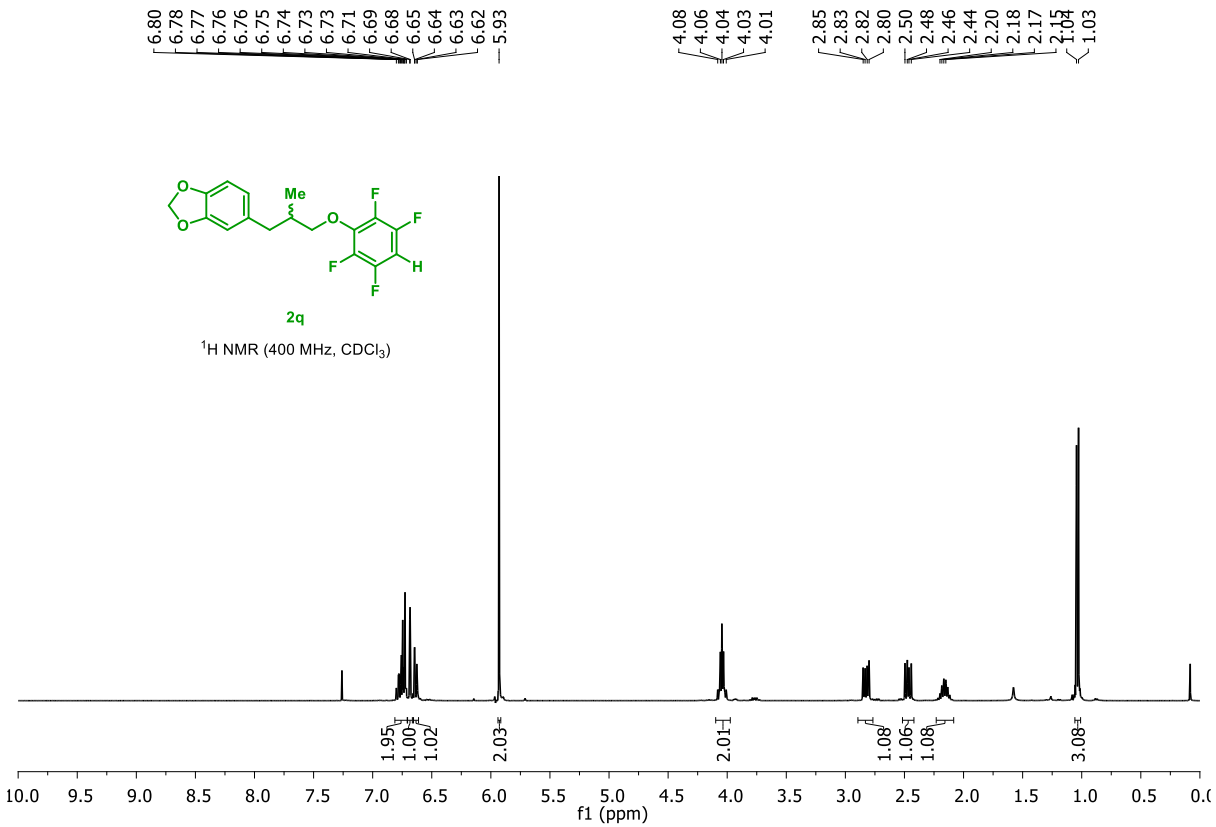
2o

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



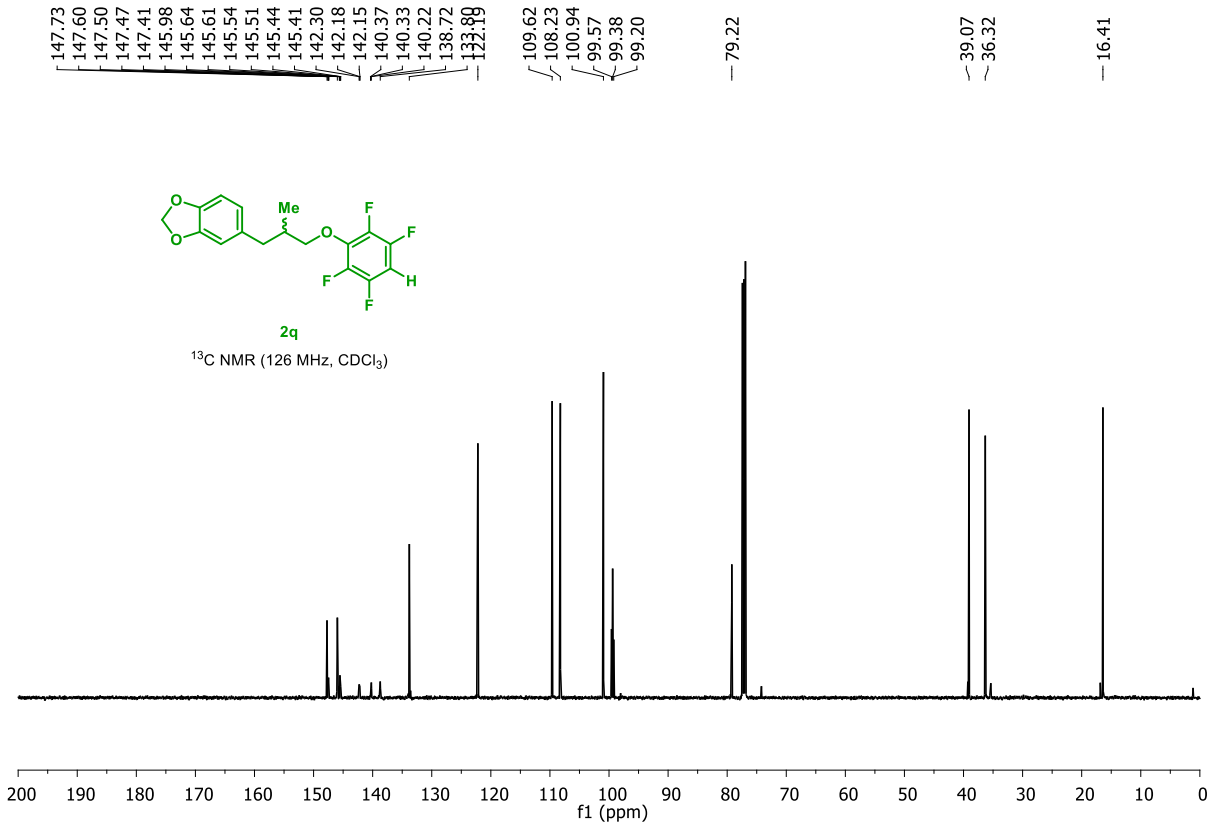
2o

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



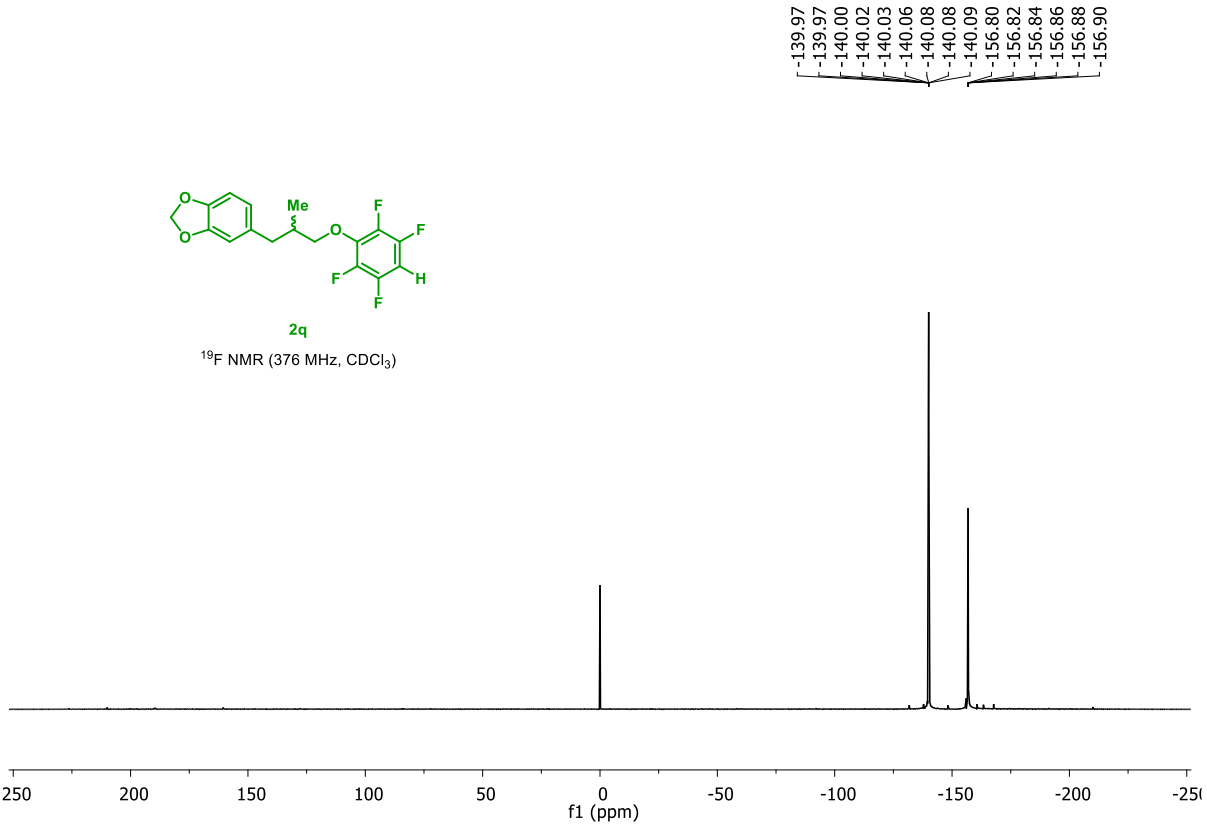
2q

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



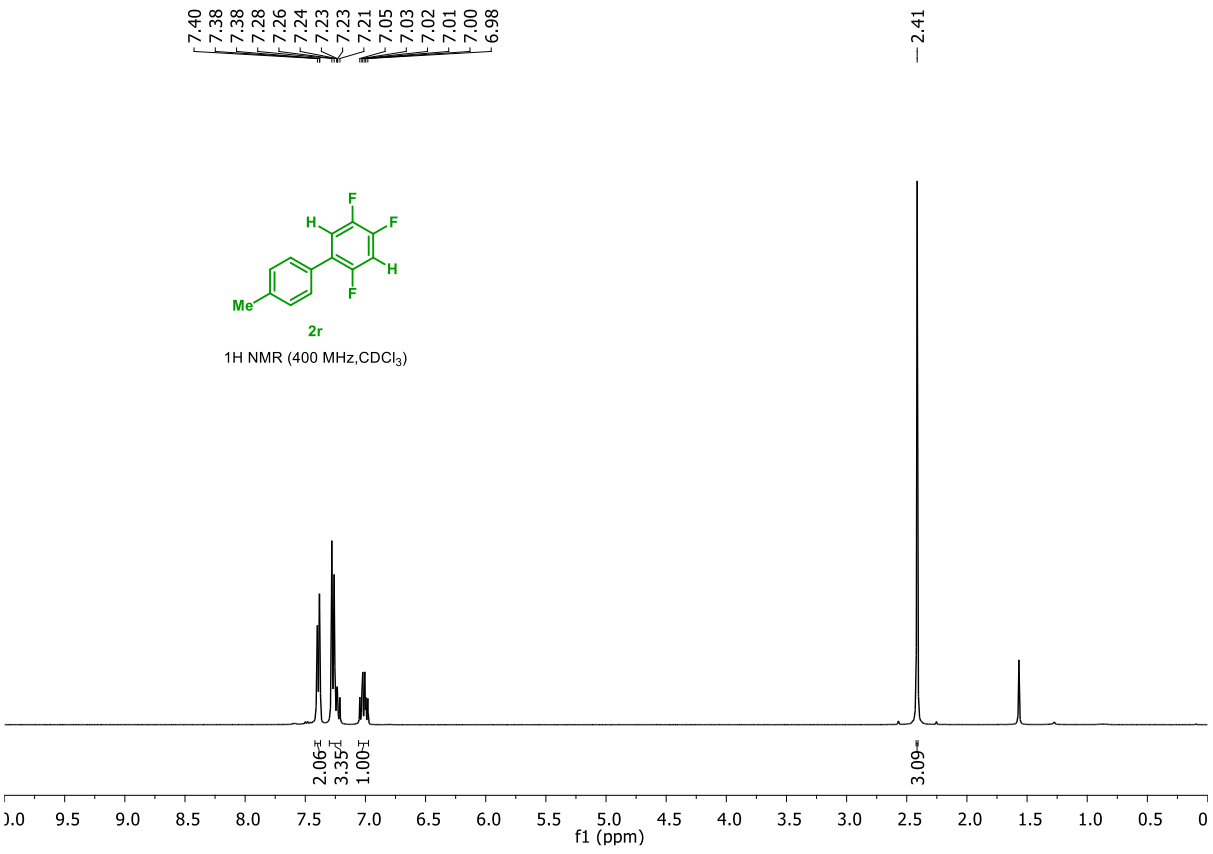
2q

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



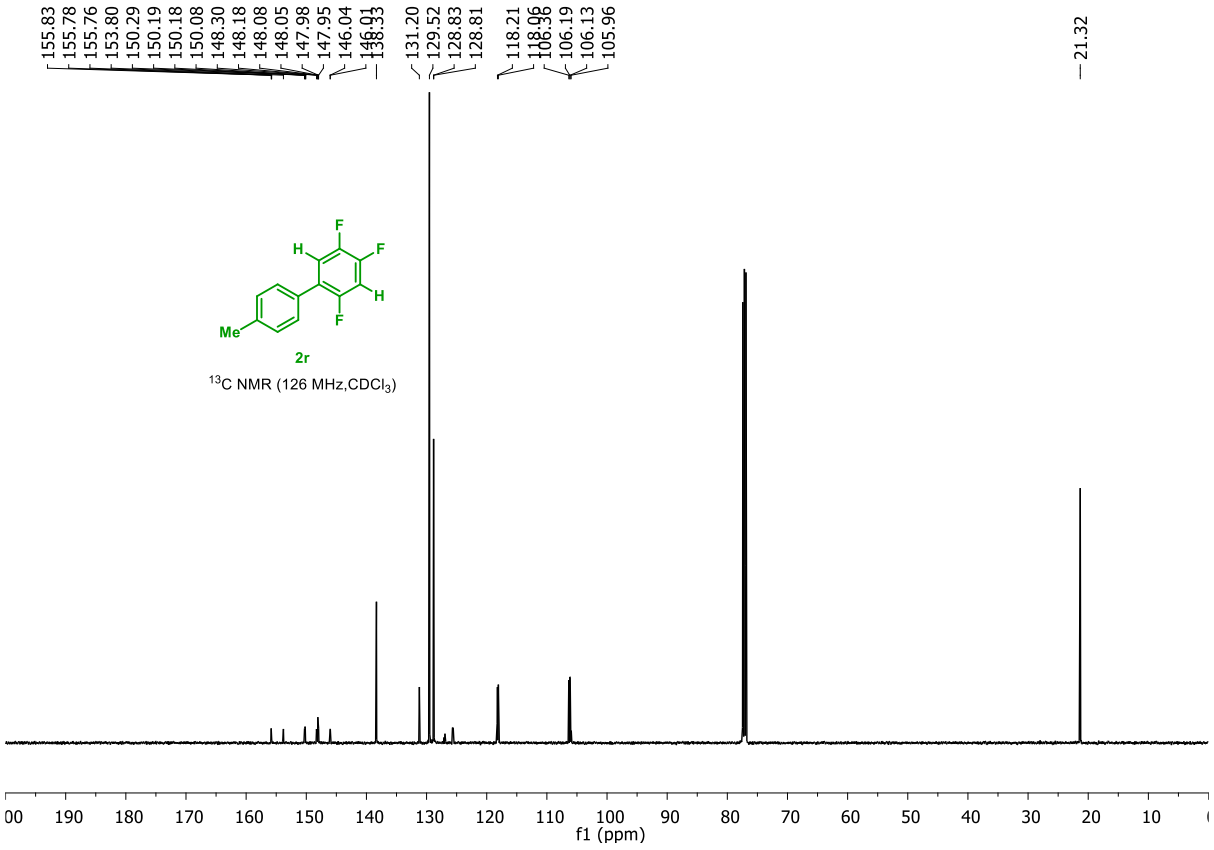
2q

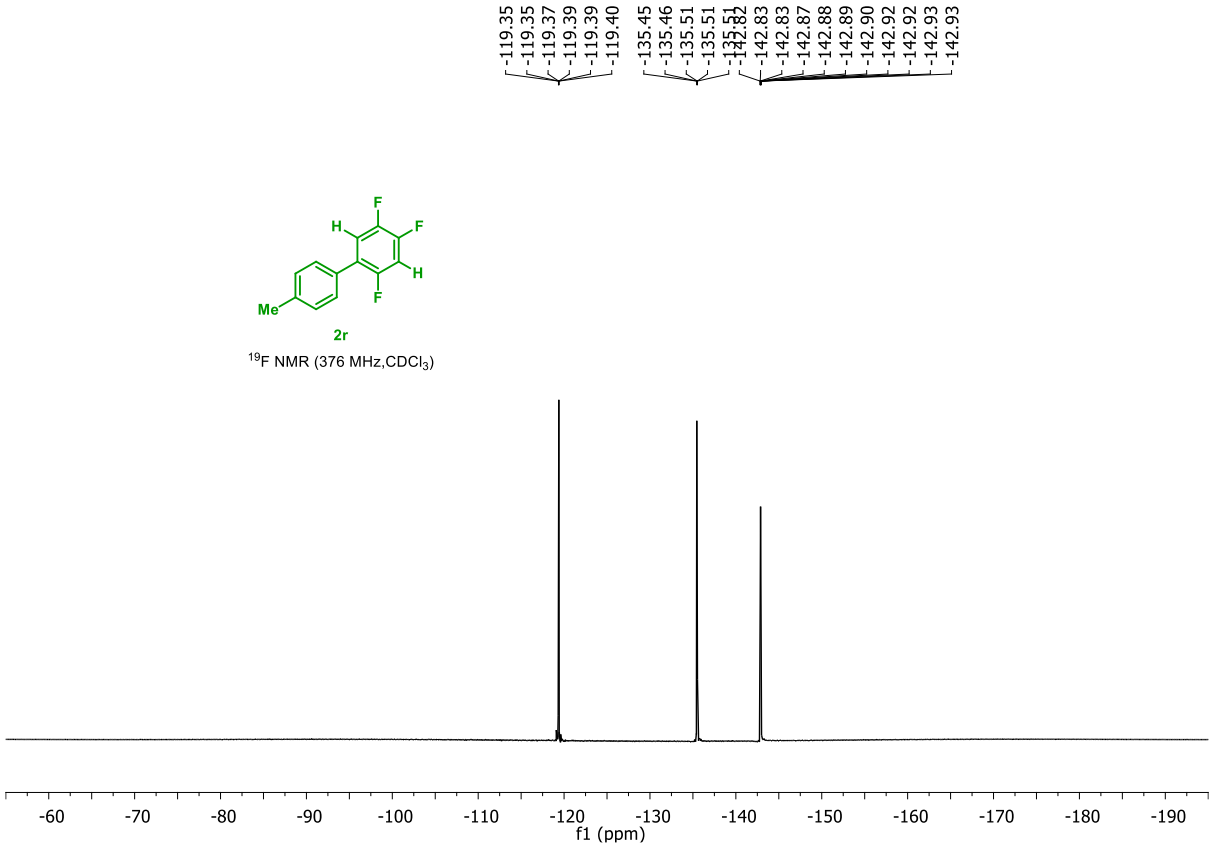
^{19}F NMR (376 MHz, $CDCl_3$)

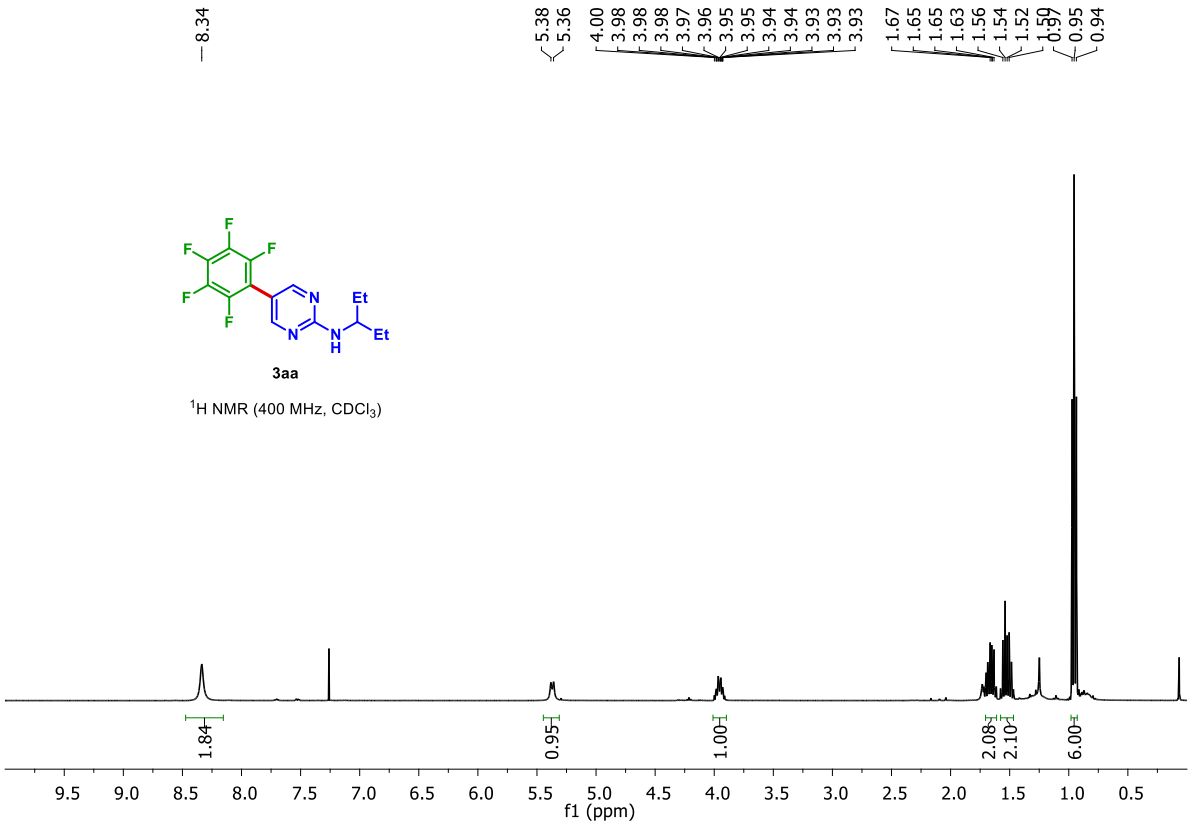


2r

1H NMR (400 MHz,$CDCl_3$)

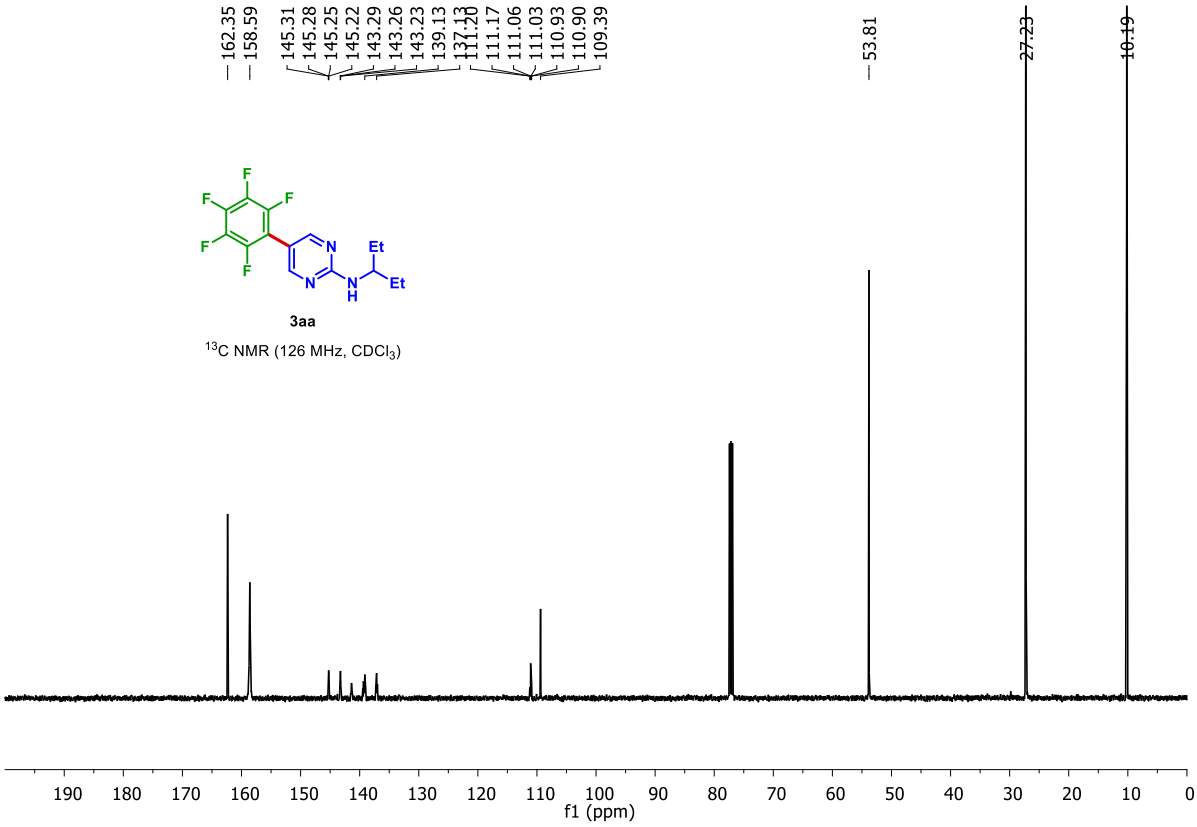

155.83
155.78
155.76
153.80
150.29
150.19
150.18
150.08
148.30
148.18
148.08
148.05
147.98
147.95
146.04
146.01
138.33
131.20
129.52
128.83
128.81
118.21
118.06
106.36
106.19
106.13
105.96
21.32
F
H
F
H
F
Me
2r
13C NMR (126 MHz,CDCl3)
f1 (ppm)


-119.35
-119.35
-119.37
-119.39
-119.39
-119.40
-135.45
-135.46
-135.51
-135.51
-142.83
-142.83
-142.87
-142.88
-142.89
-142.90
-142.92
-142.92
-142.93
-142.93
F
H
F
H
F
Me
2r
19F NMR (376 MHz,CDCl3)
f1 (ppm)



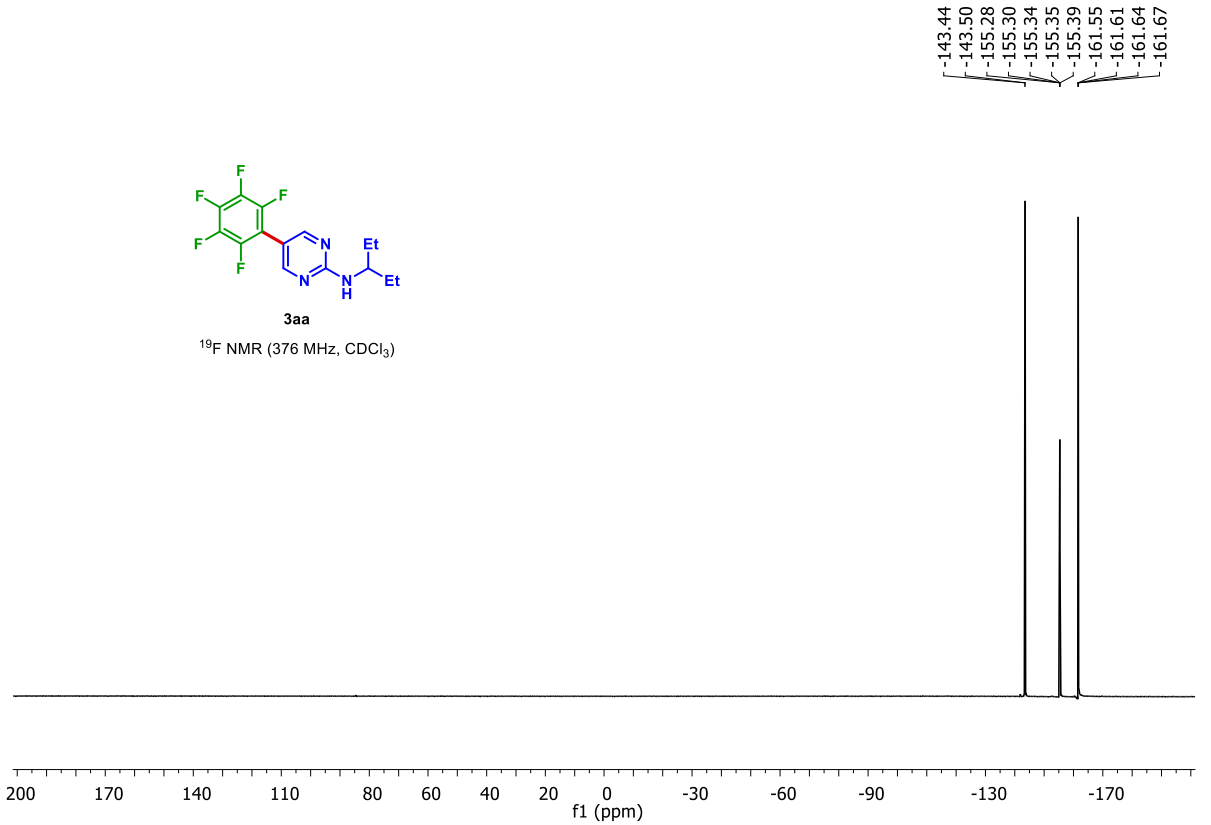
3aa

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



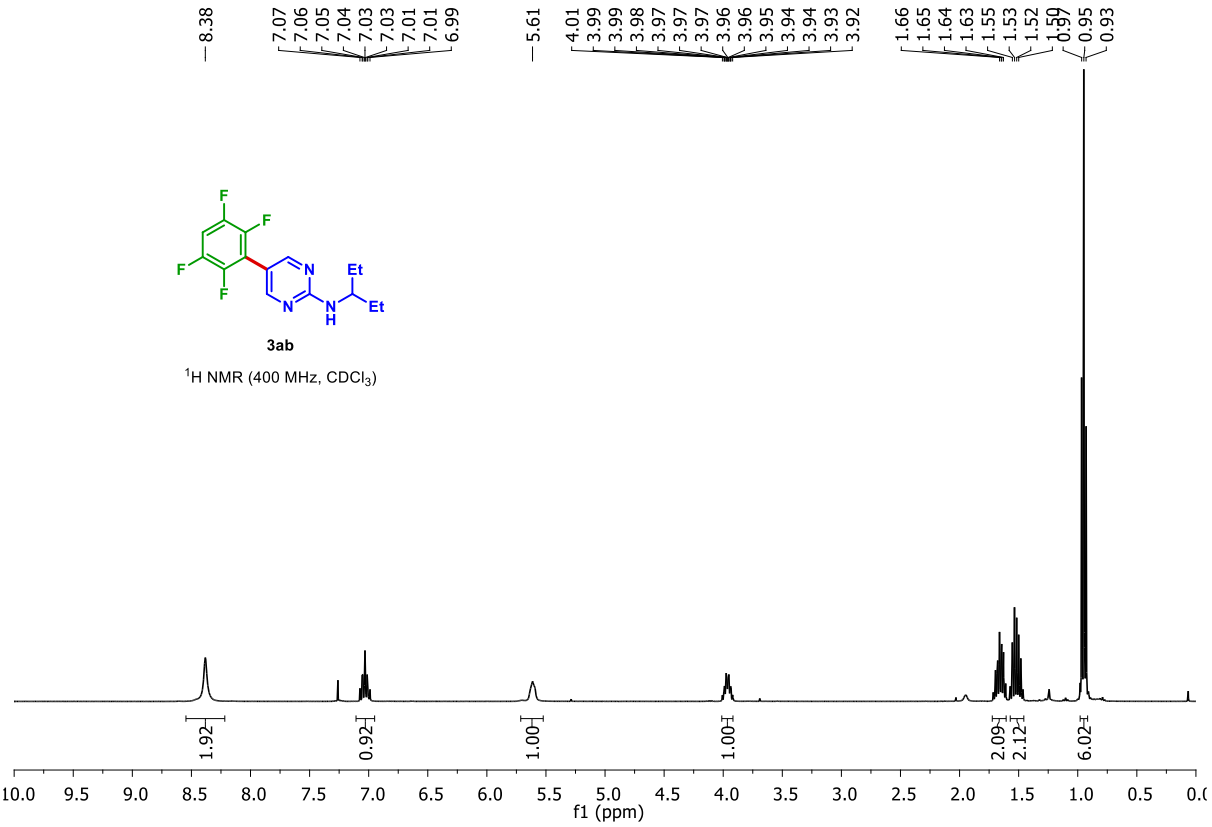
3aa

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



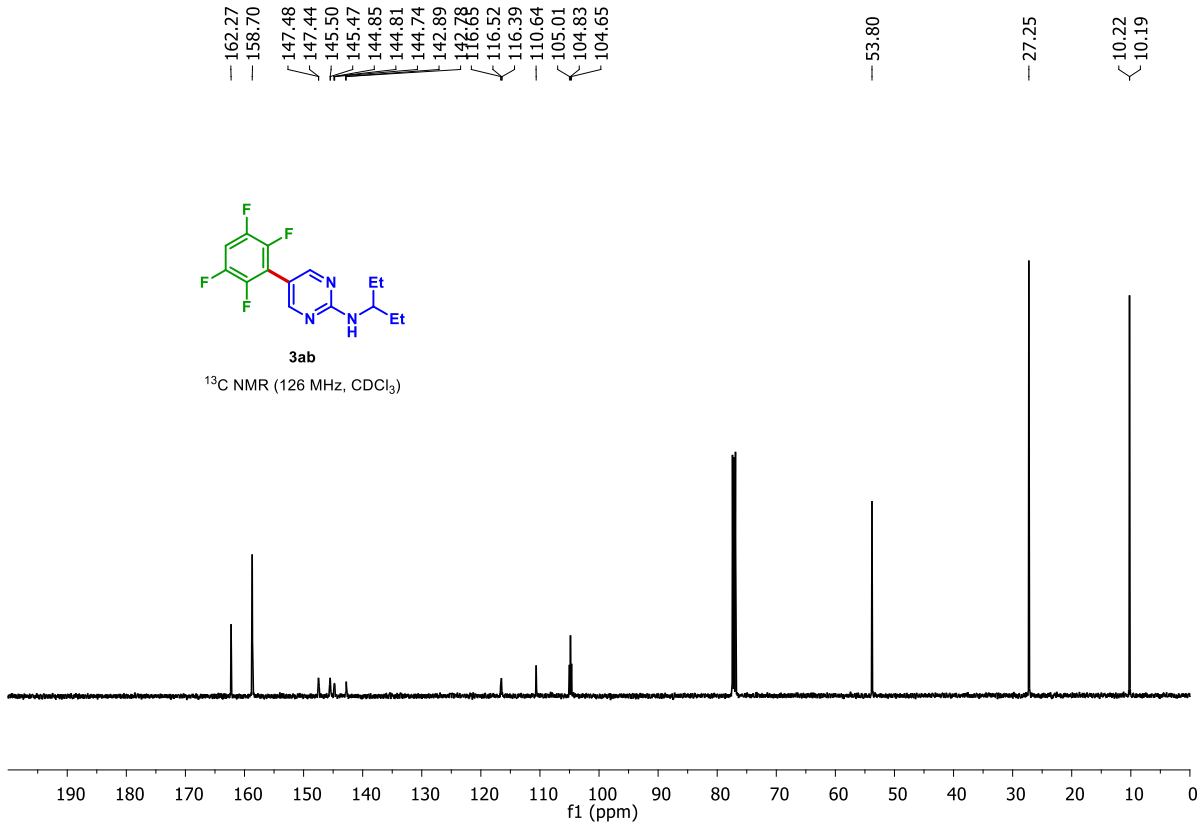
3aa

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



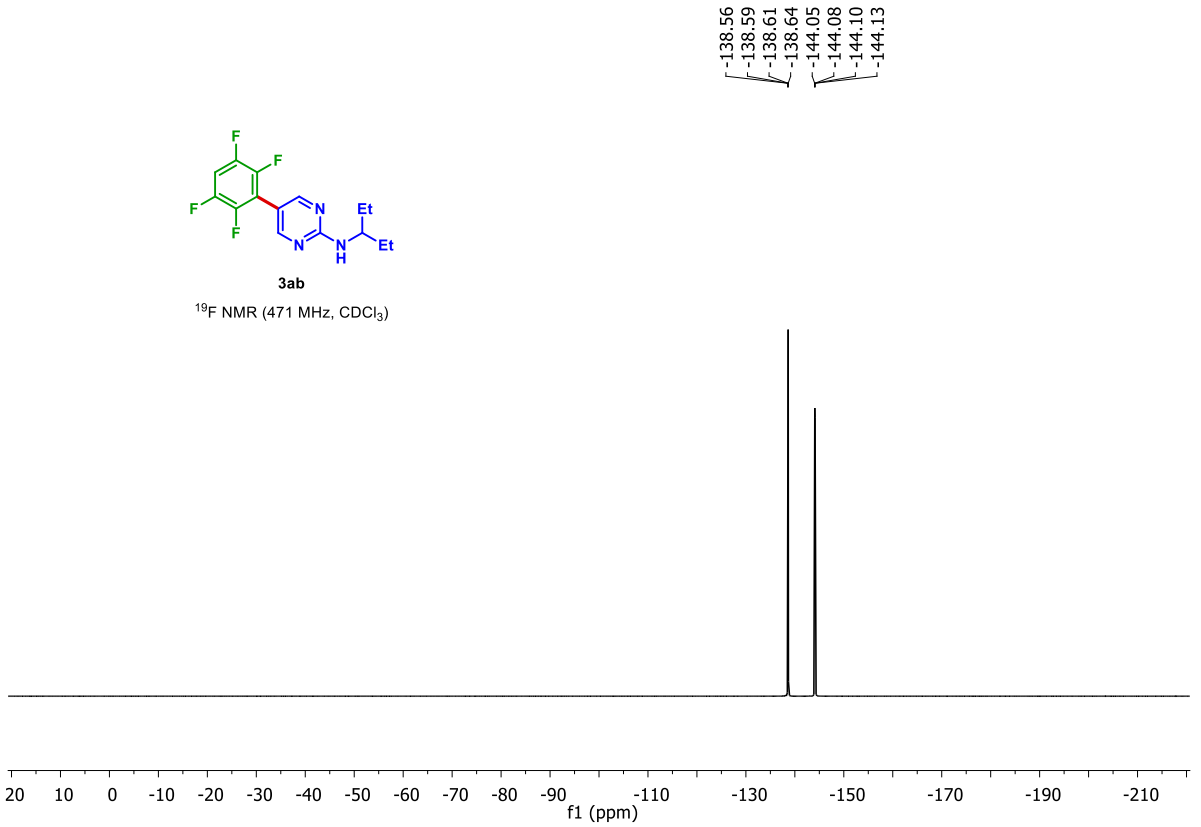
3ab

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



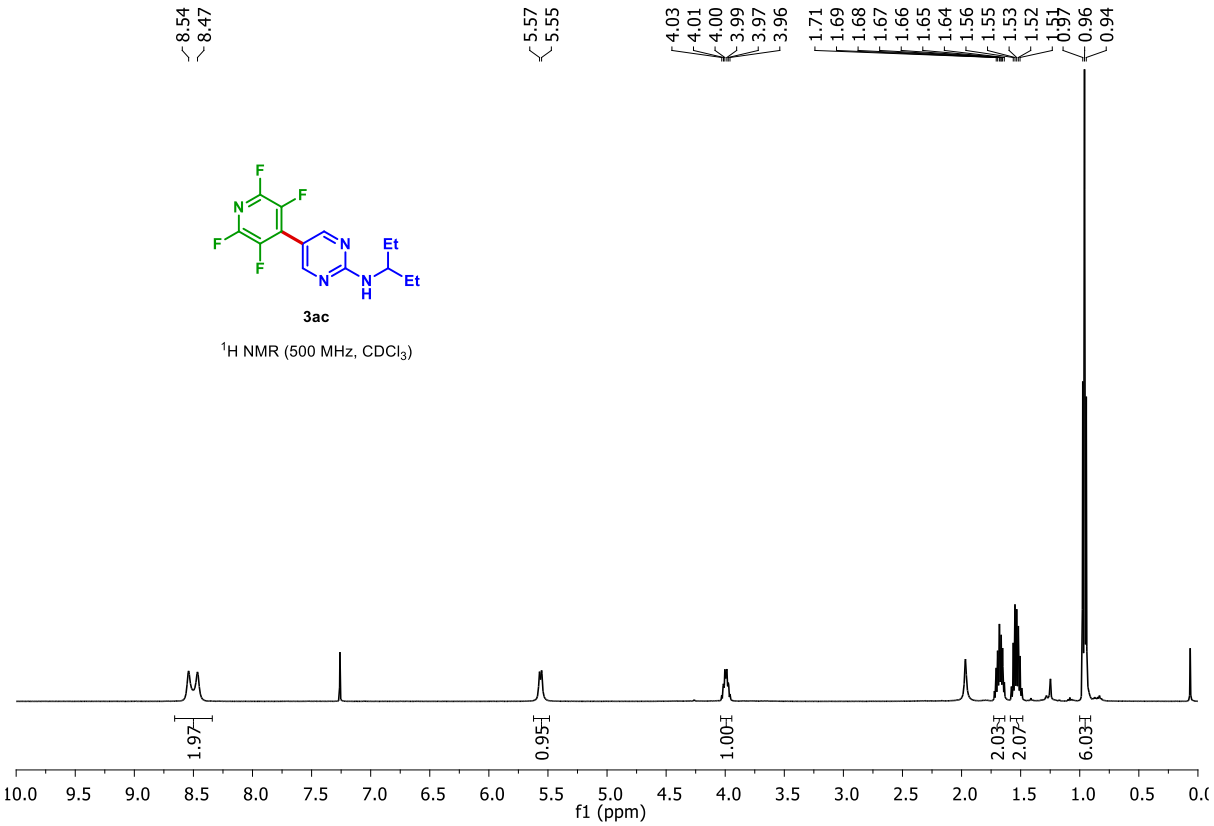
3ab

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



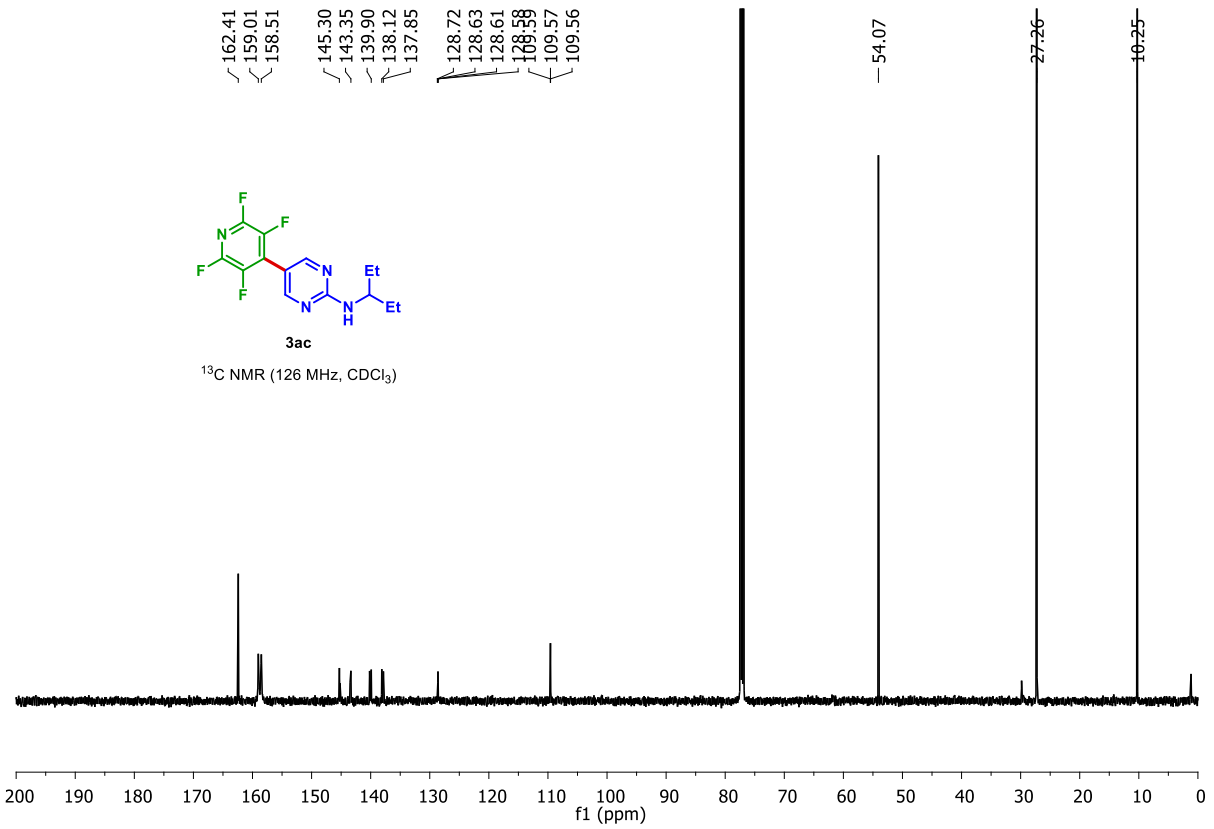
3ab

^{19}F NMR (471 MHz, $CDCl_3$)



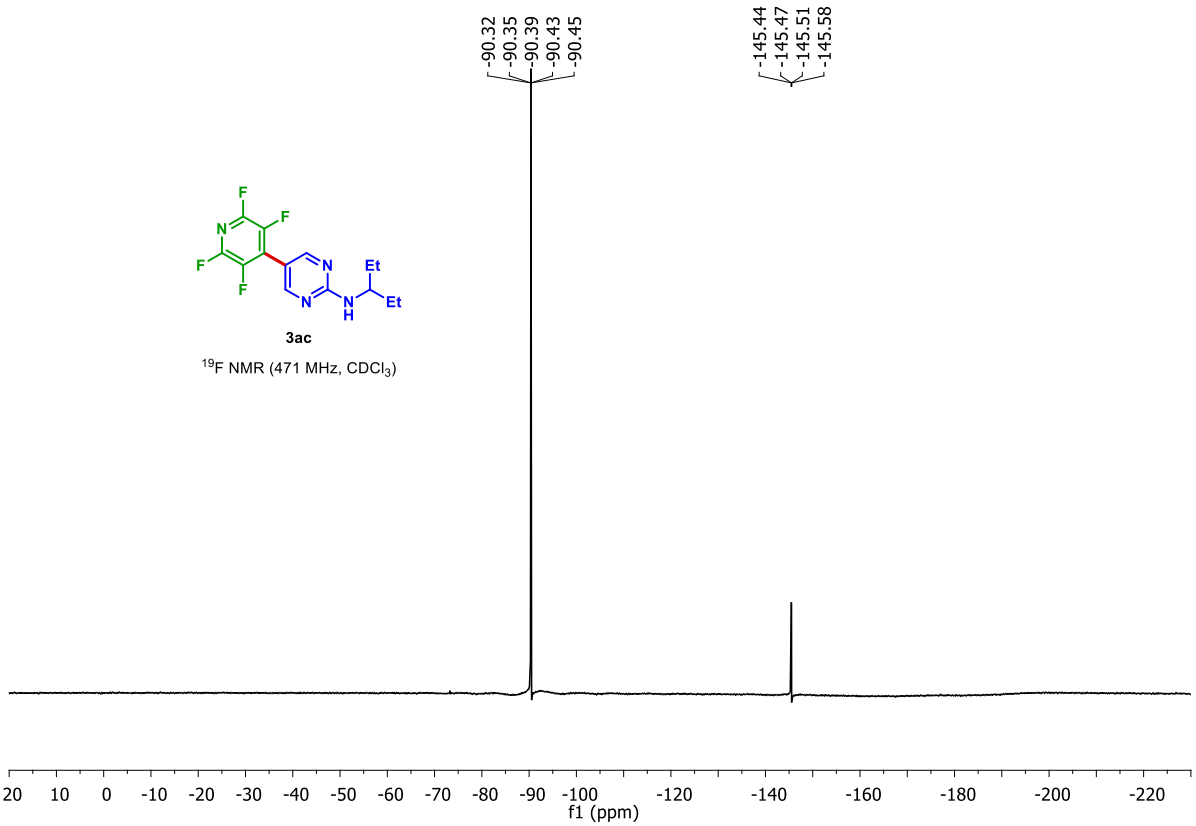
3ac

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



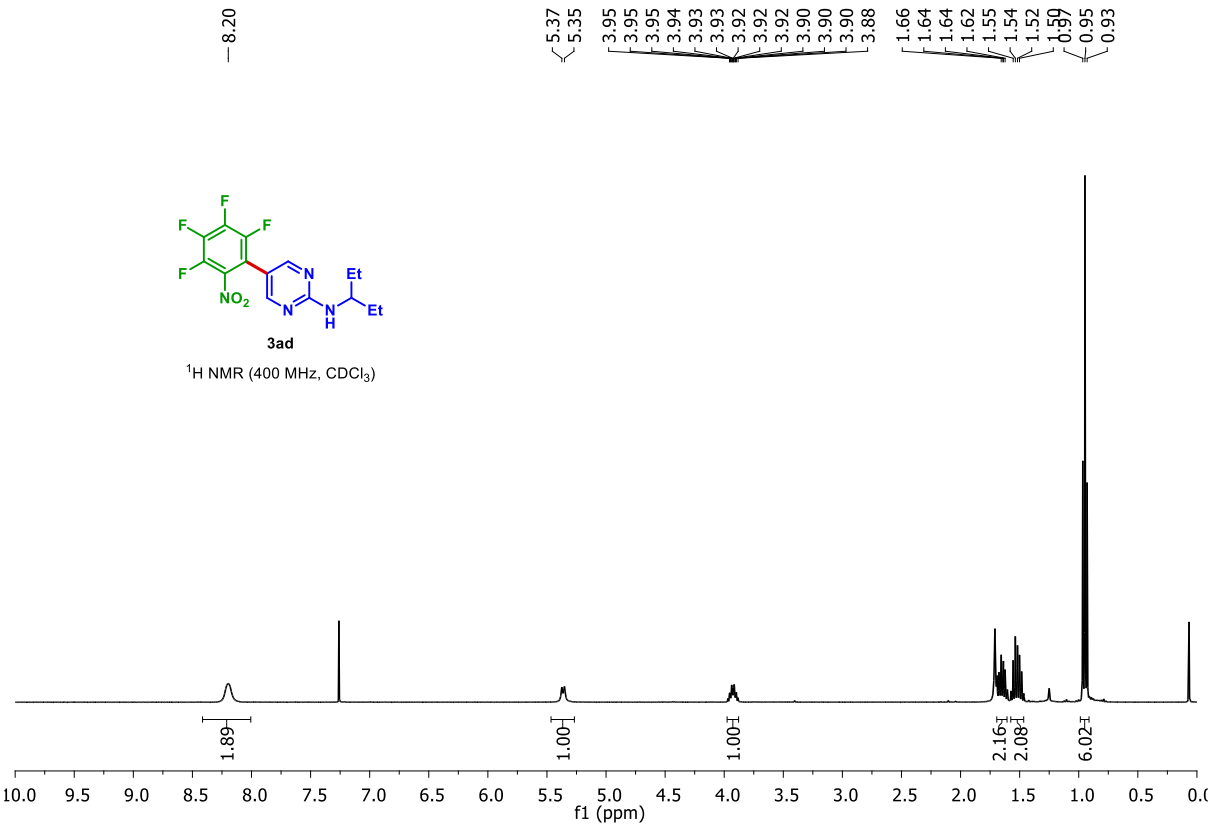
3ac

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



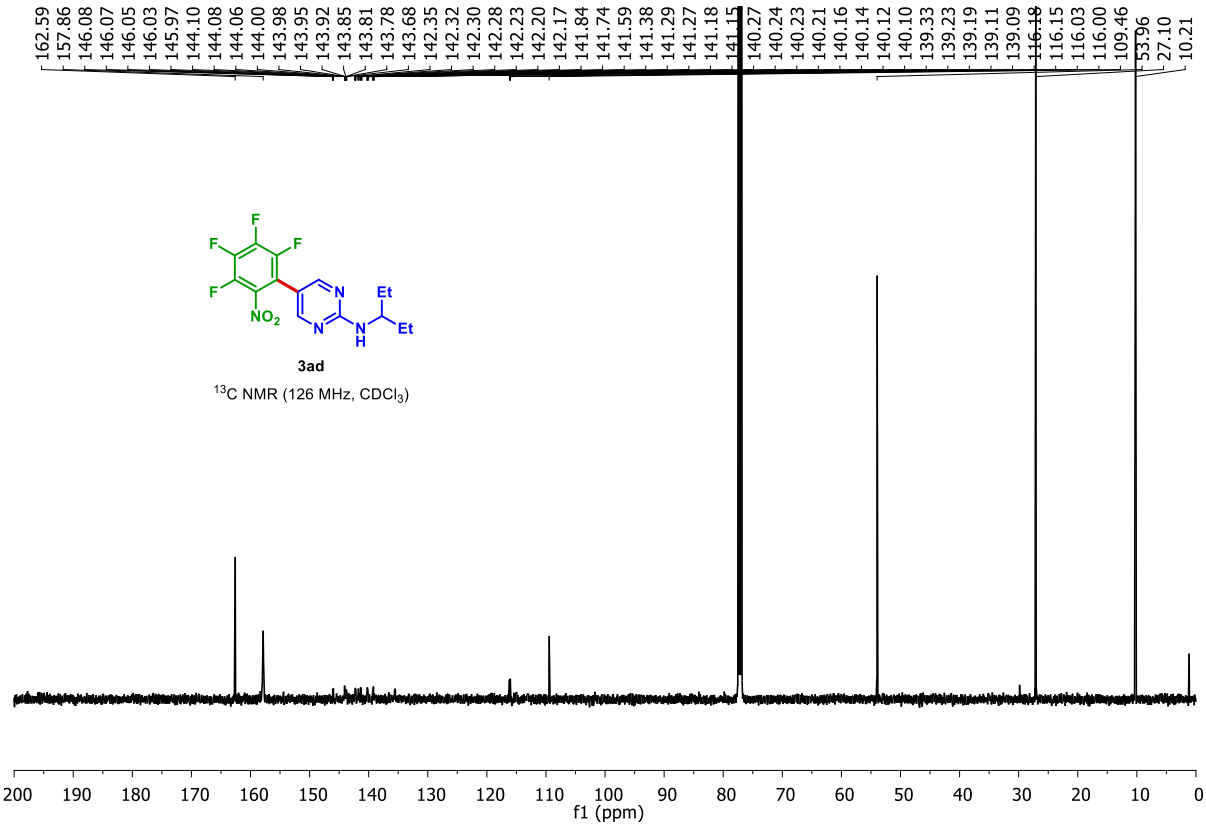
3ac

^{19}F NMR (471 MHz, $CDCl_3$)



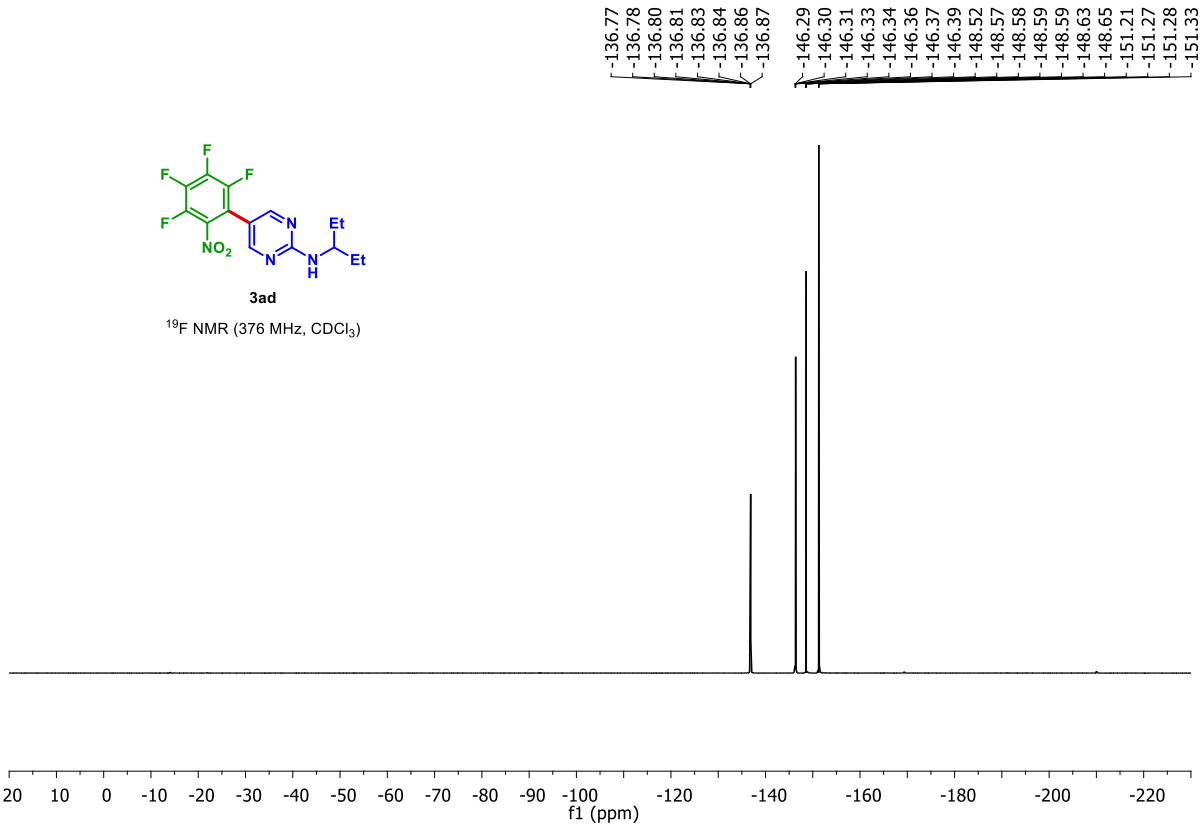
3ad

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



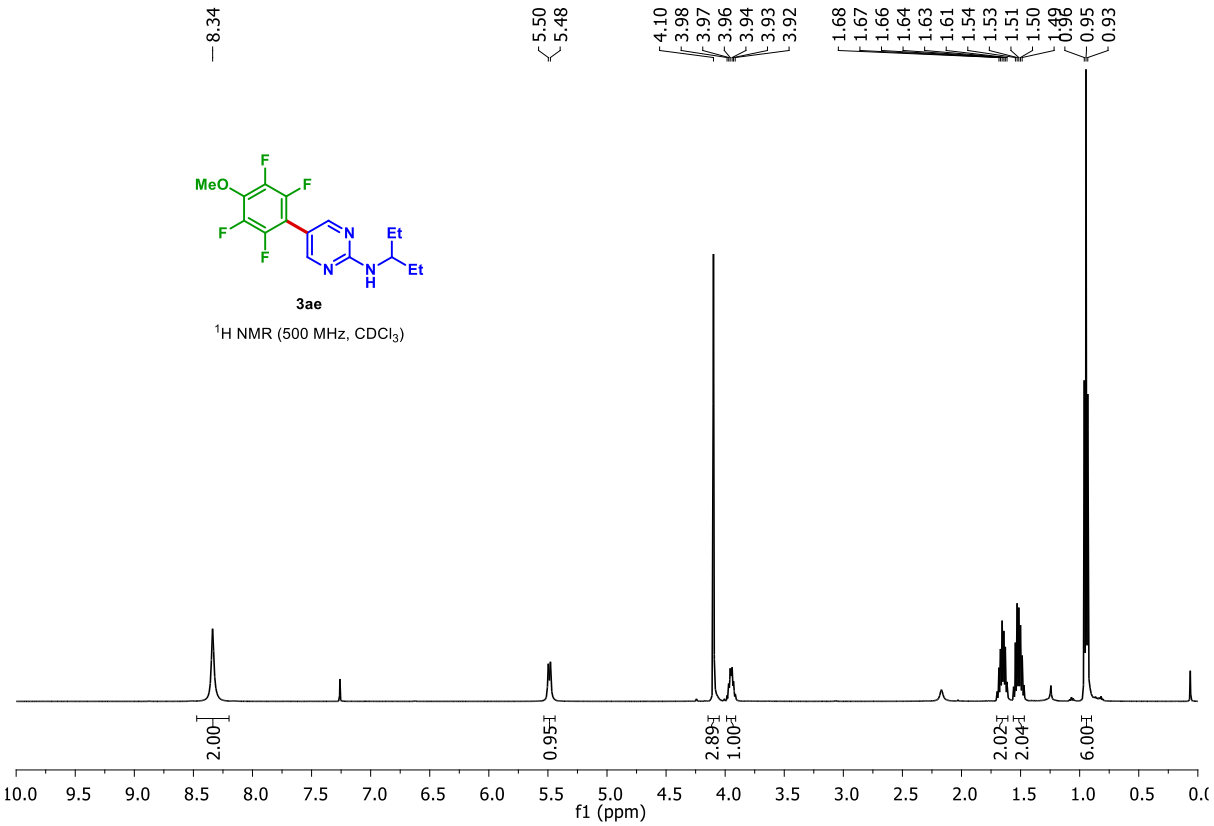
3ad

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



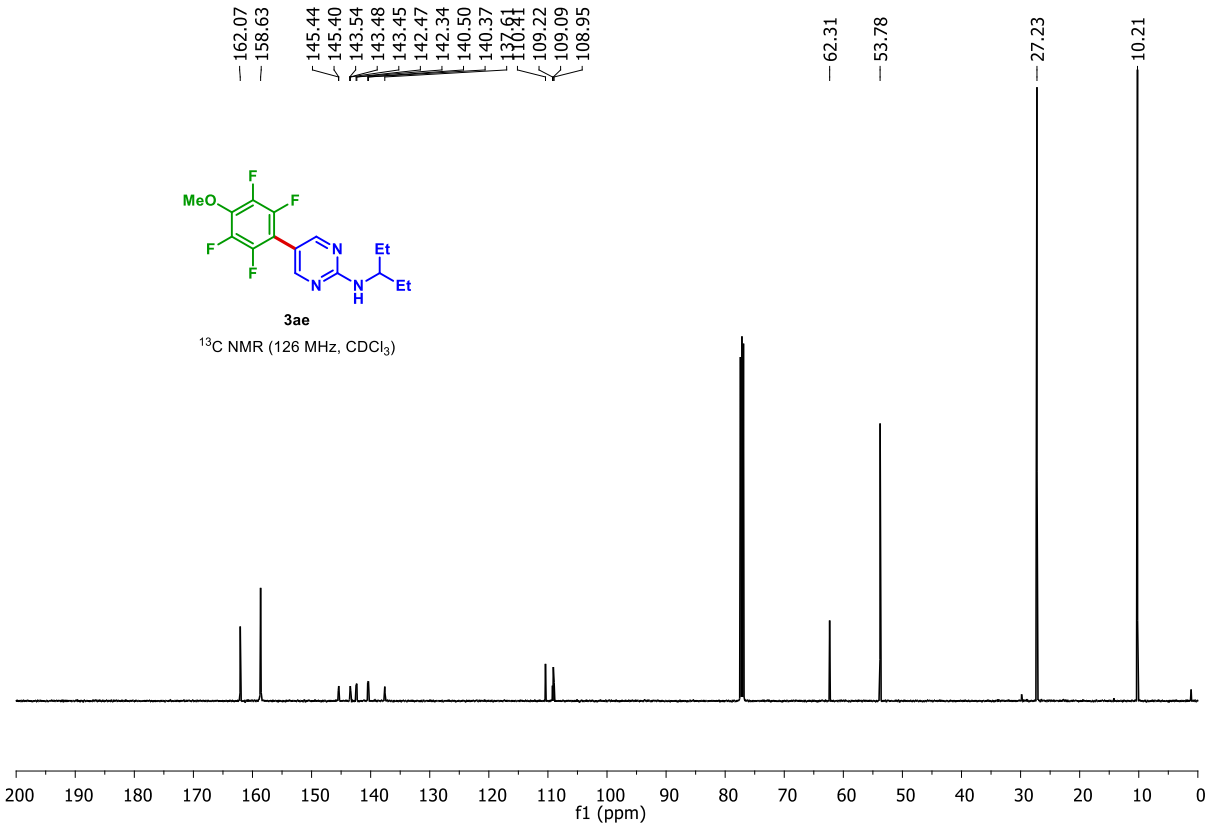
3ad

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



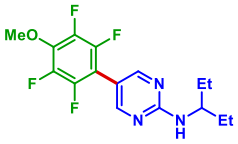
3ae

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



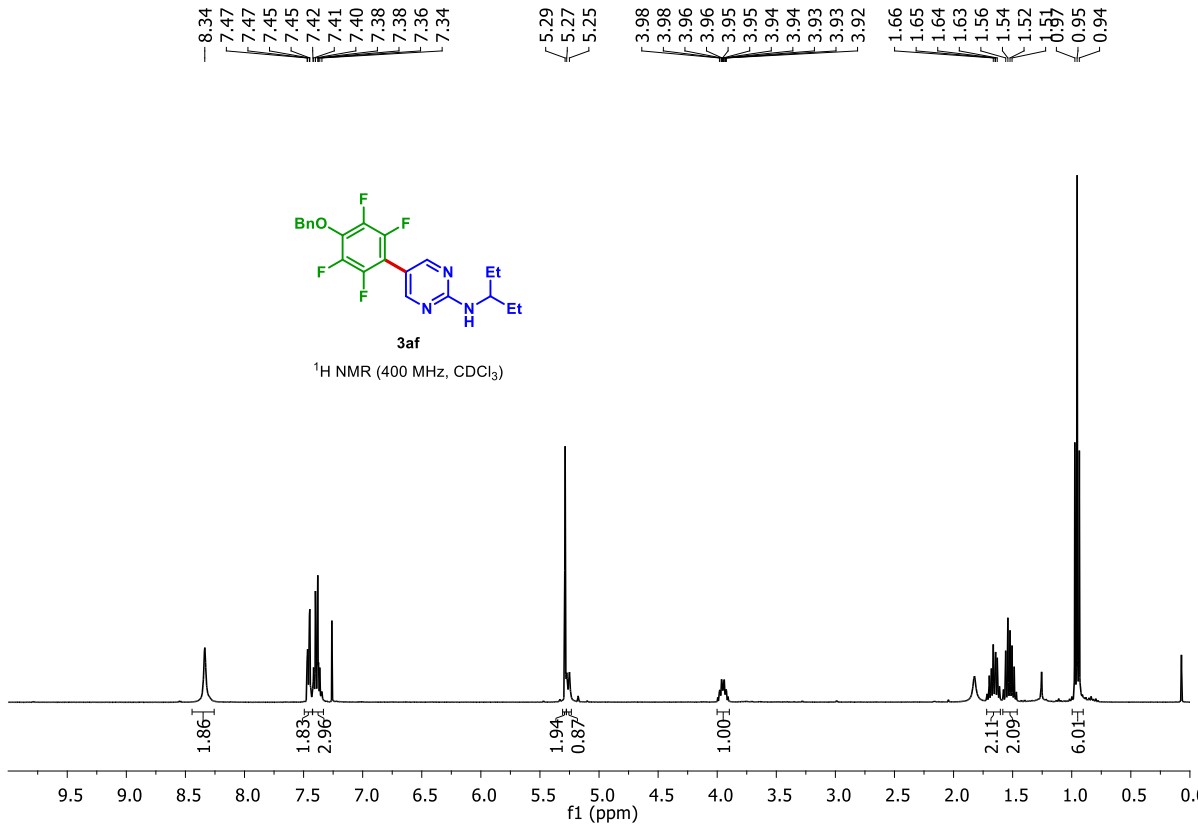
3ae

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



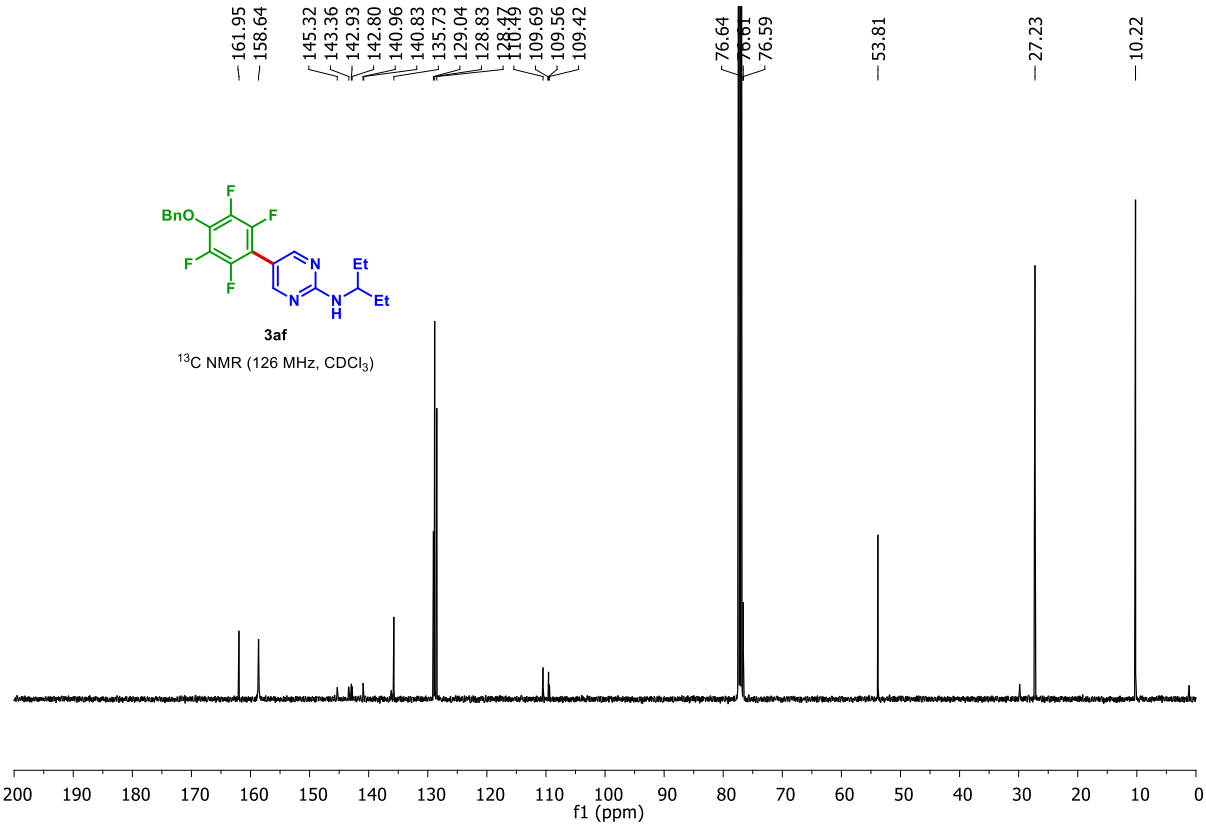
3ae

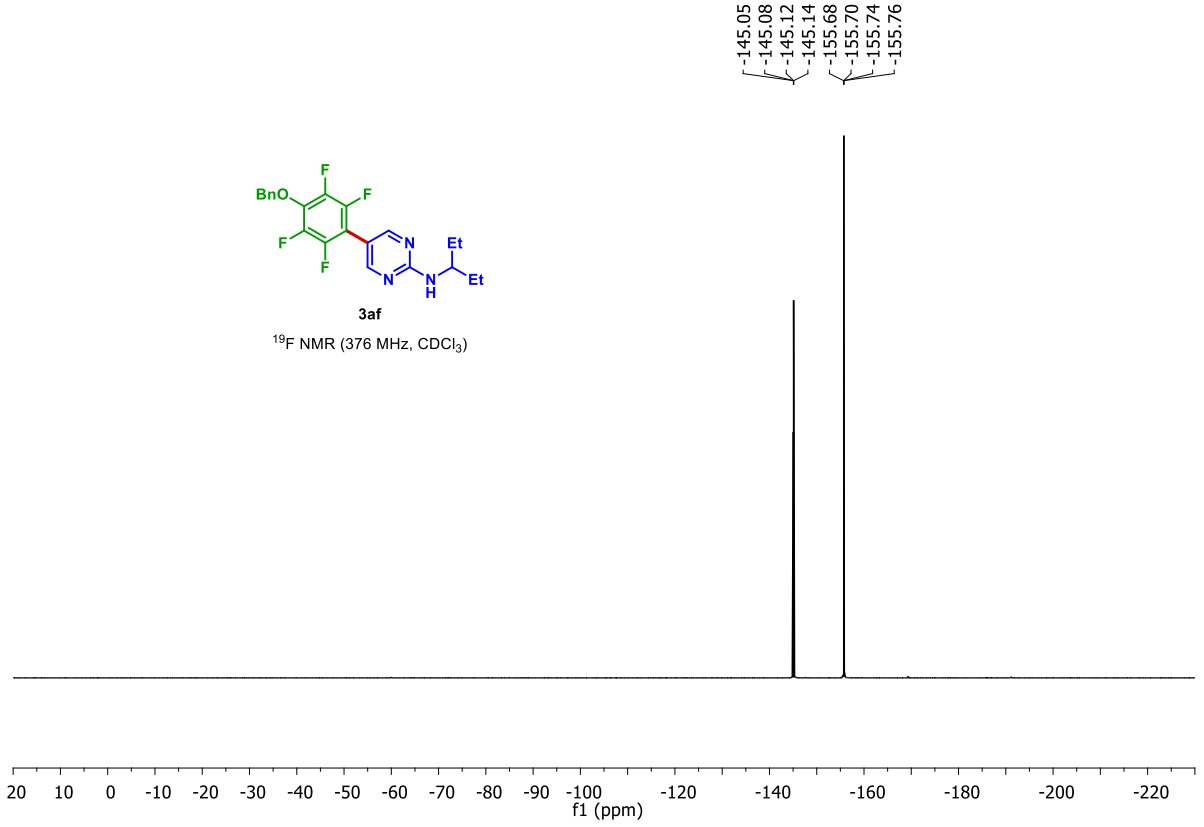
^{19}F NMR (471 MHz, $CDCl_3$)

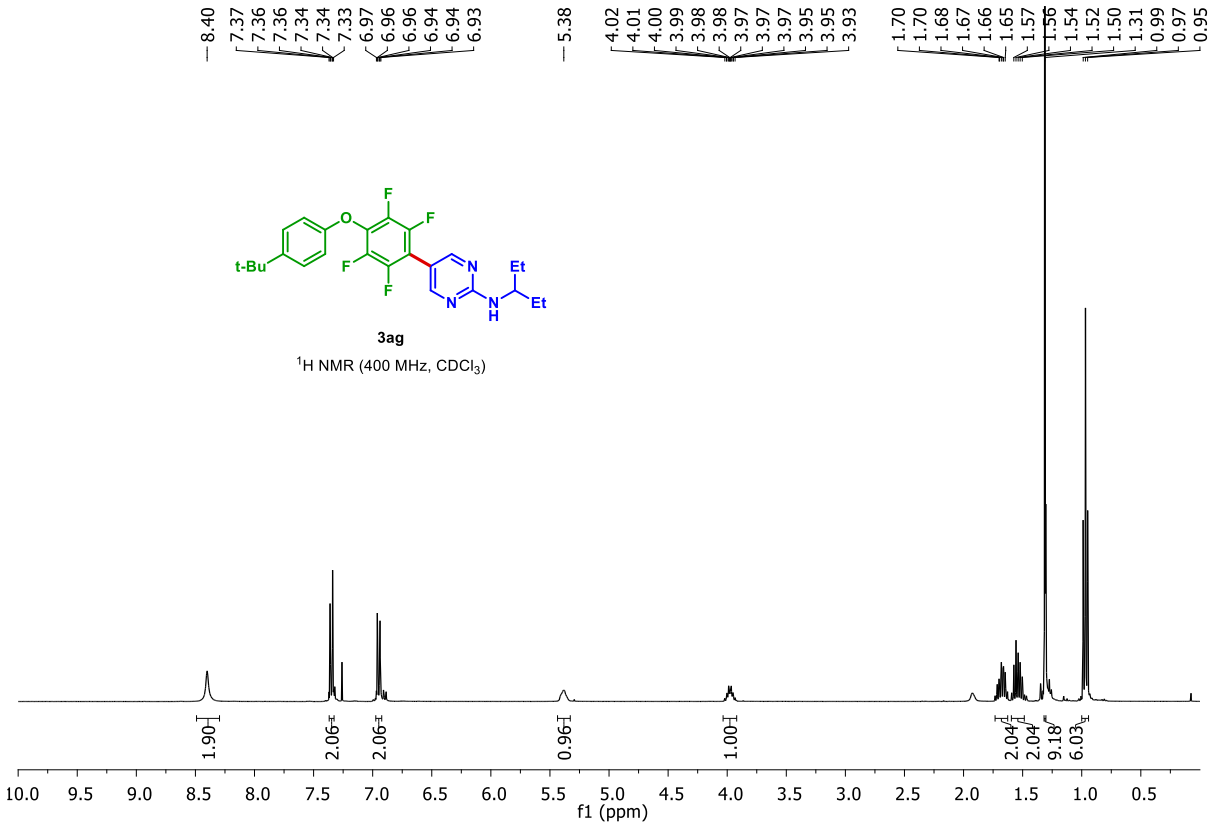


3af

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

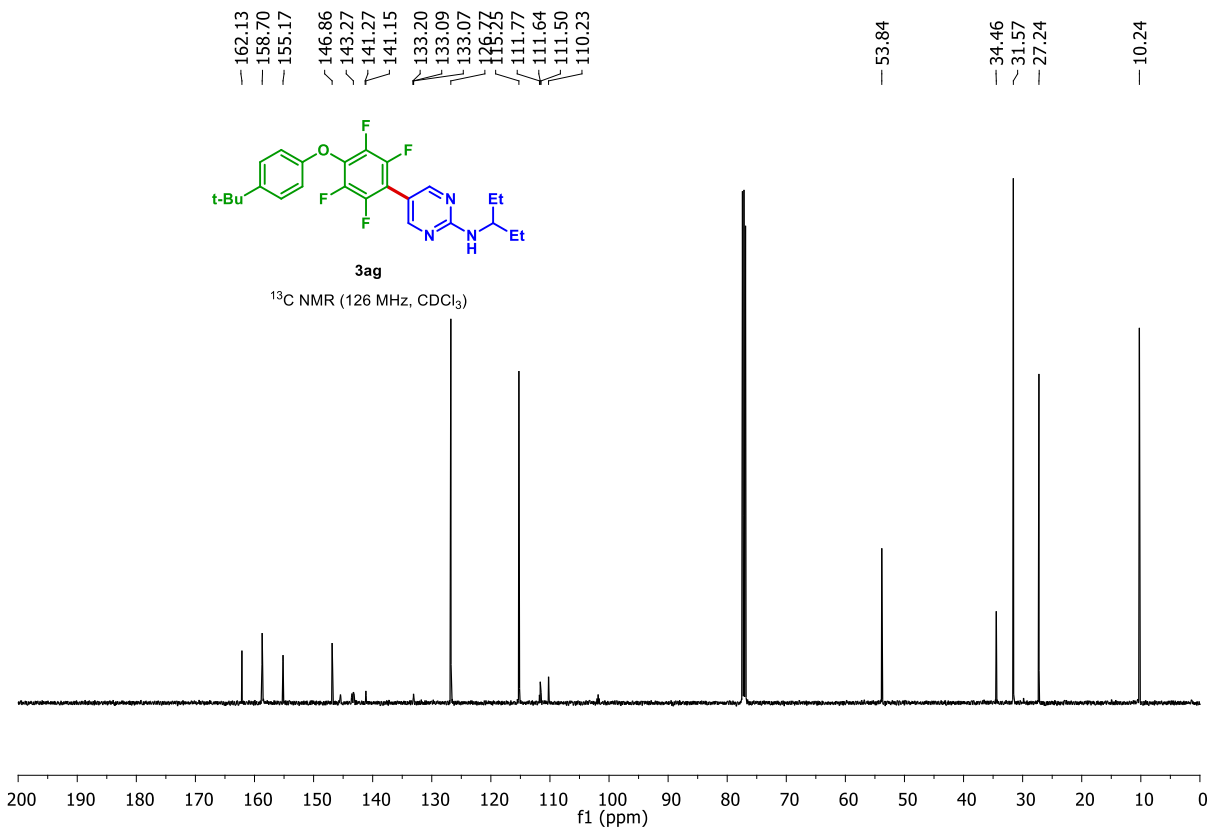

161.95
158.64
145.32
143.36
142.93
142.80
140.96
140.83
135.73
129.04
128.83
109.69
109.56
109.42
76.64
76.61
76.59
53.81
27.23
10.22
BnO
F
F
F
F
N
N
N
H
Et
Et
3af
13C NMR (126 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-145.05
-145.08
-145.12
-145.14
-155.68
-155.70
-155.74
-155.76
BnO
F
F
F
F
N
N
N
H
Et
Et
3af
19F NMR (376 MHz, CDCl3)
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
-220
f1 (ppm)



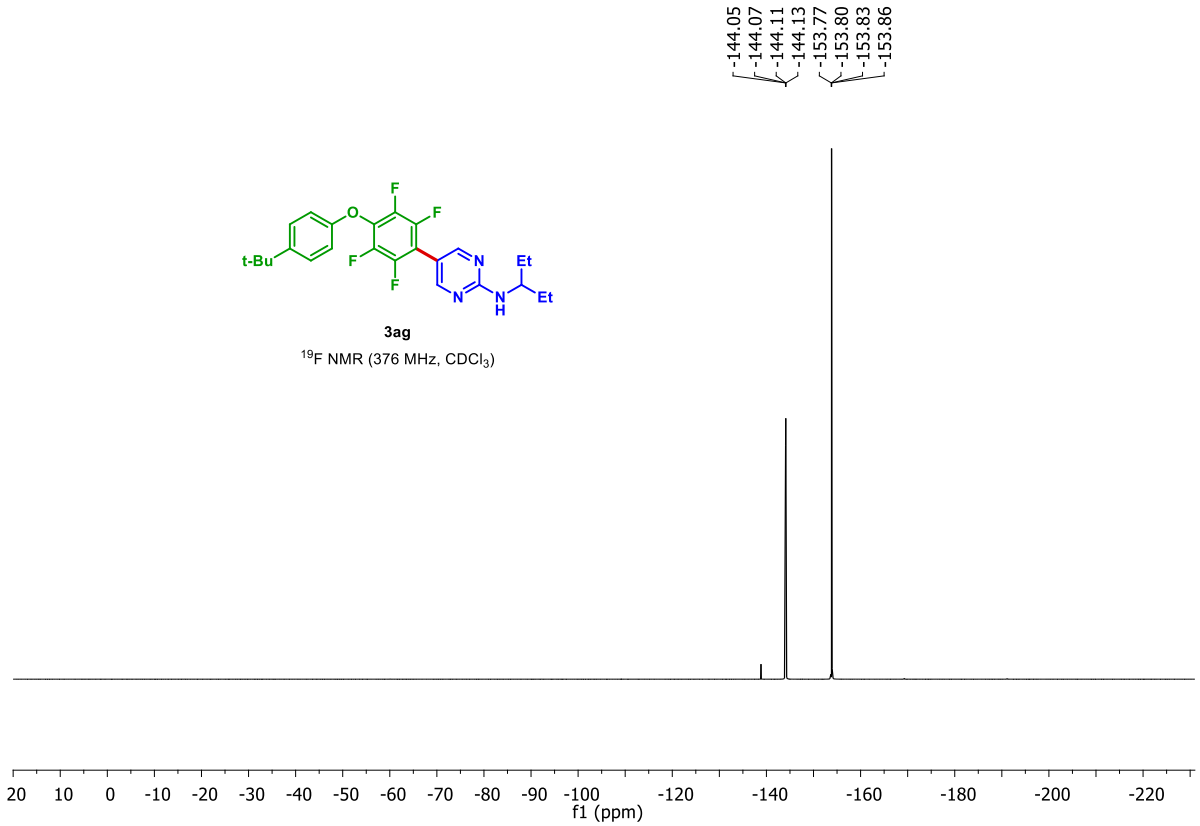
3ag

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



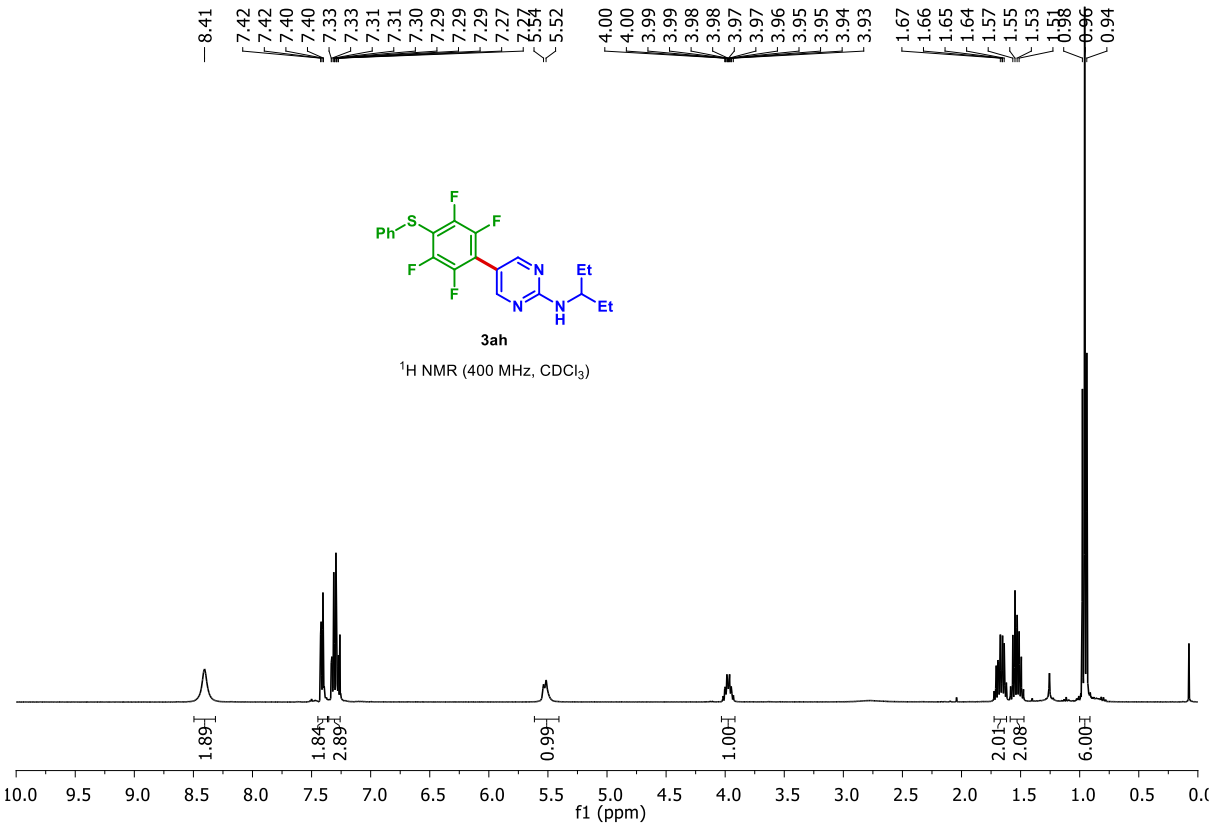
3ag

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



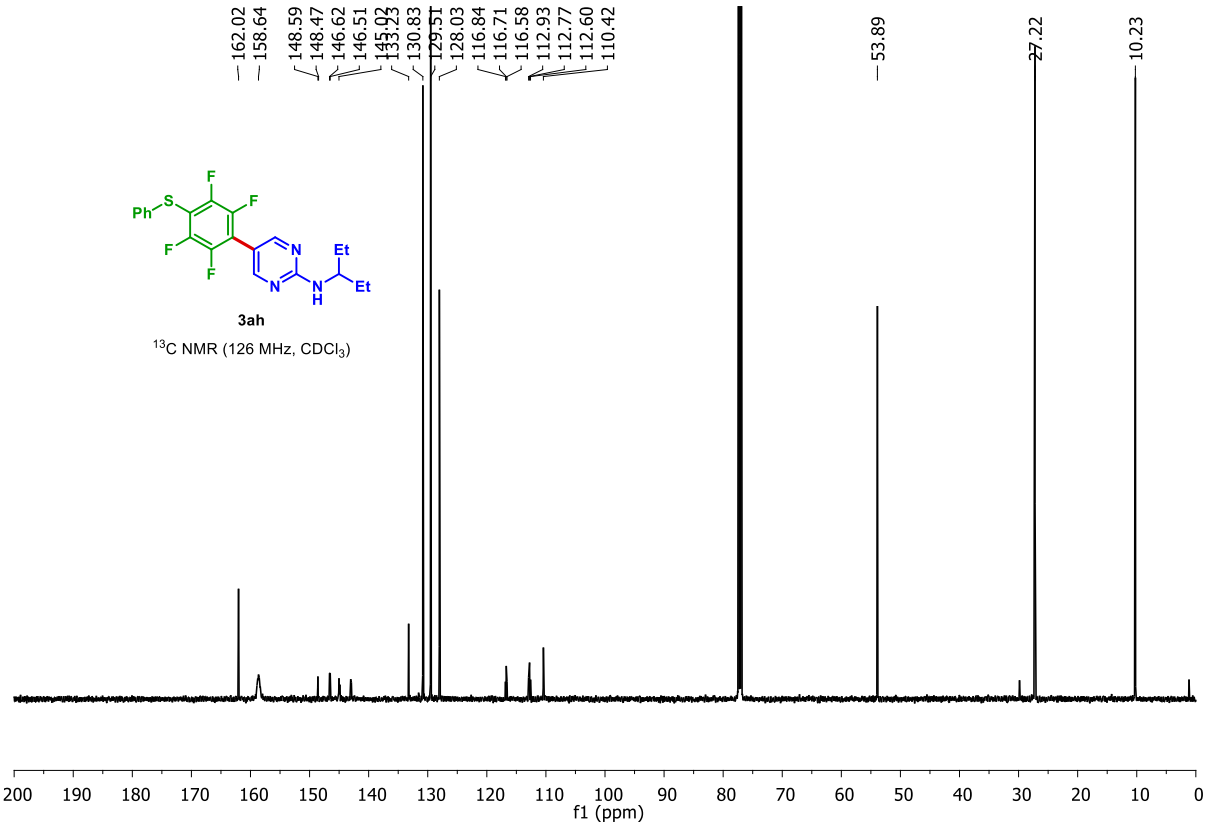
3ag

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



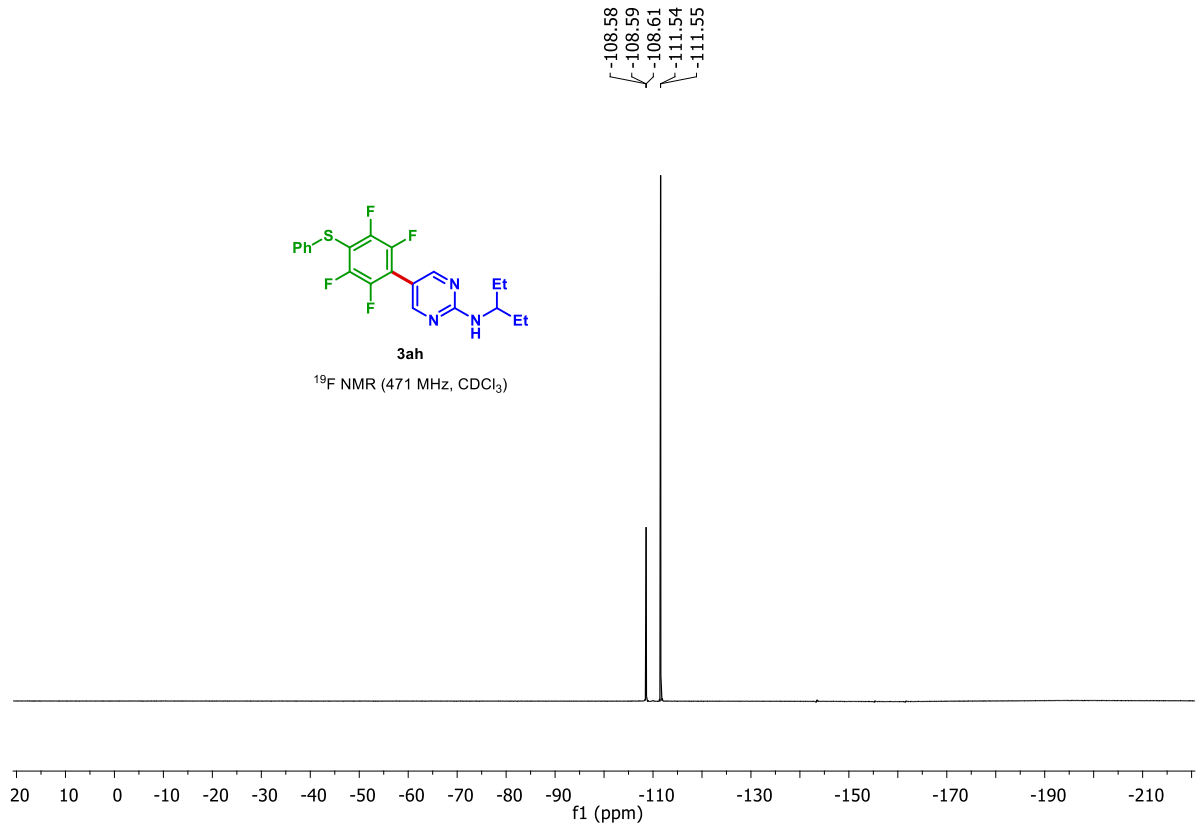
3ah

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



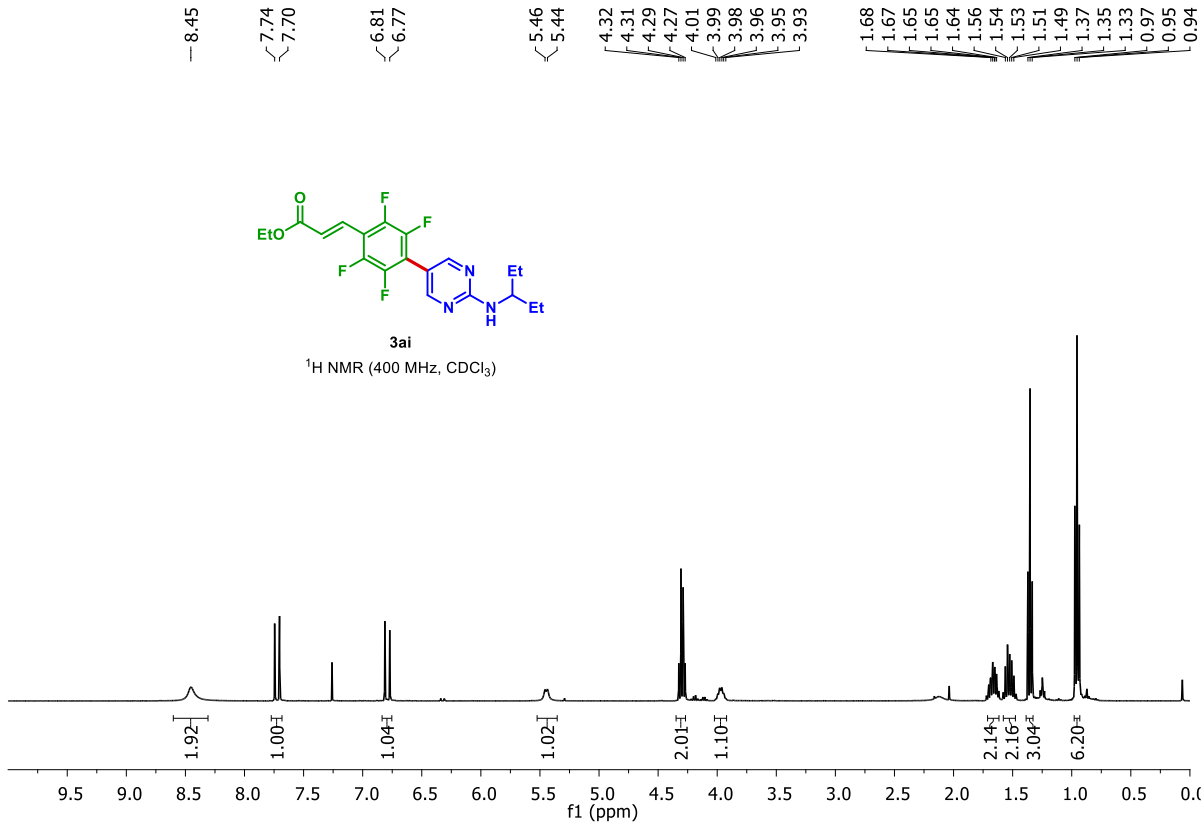
3ah

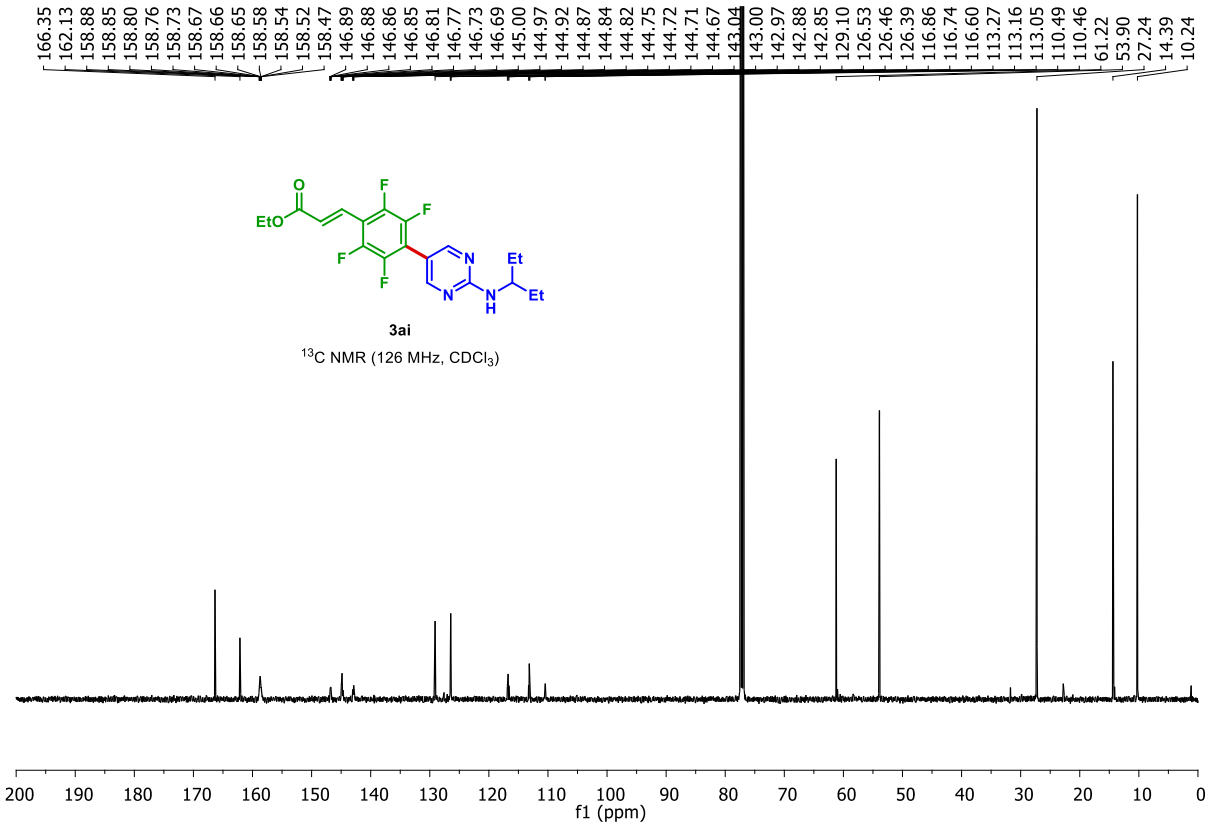
^{13}C NMR (126 MHz, $CDCl_3$)

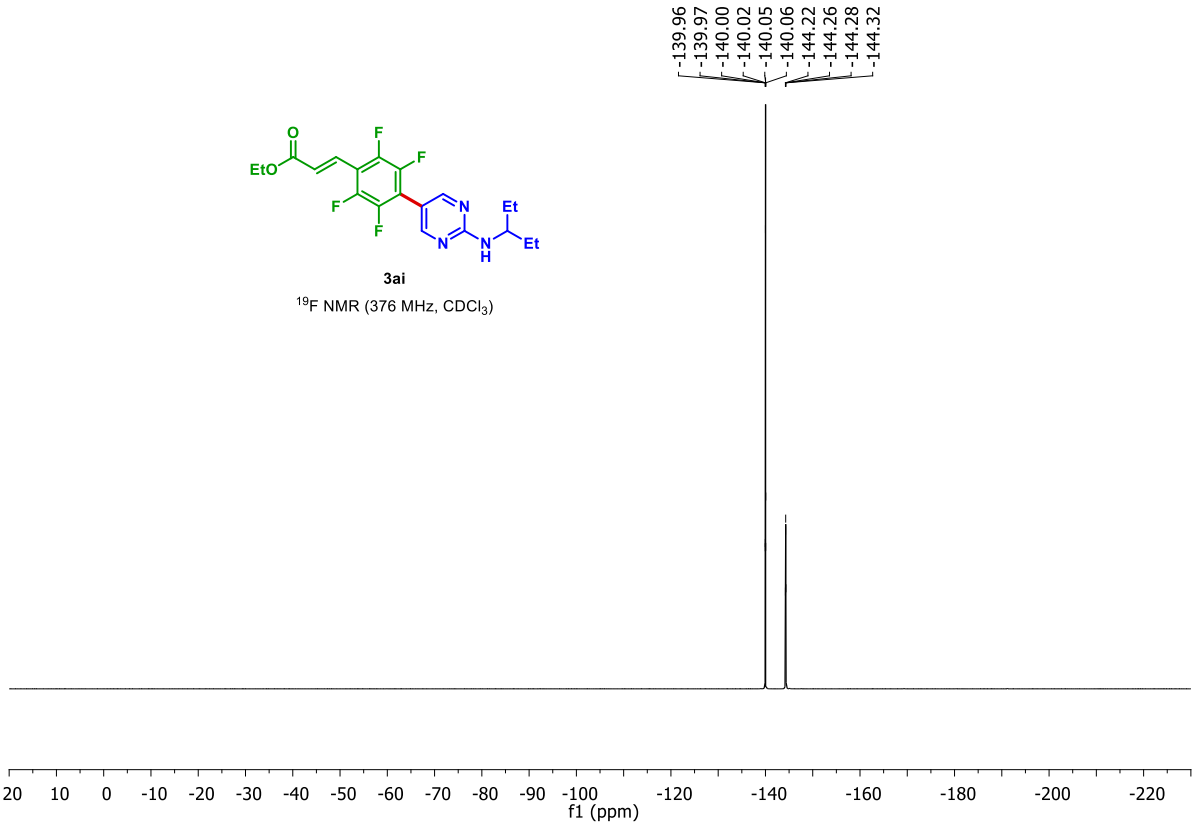


3ah

^{19}F NMR (471 MHz, $CDCl_3$)

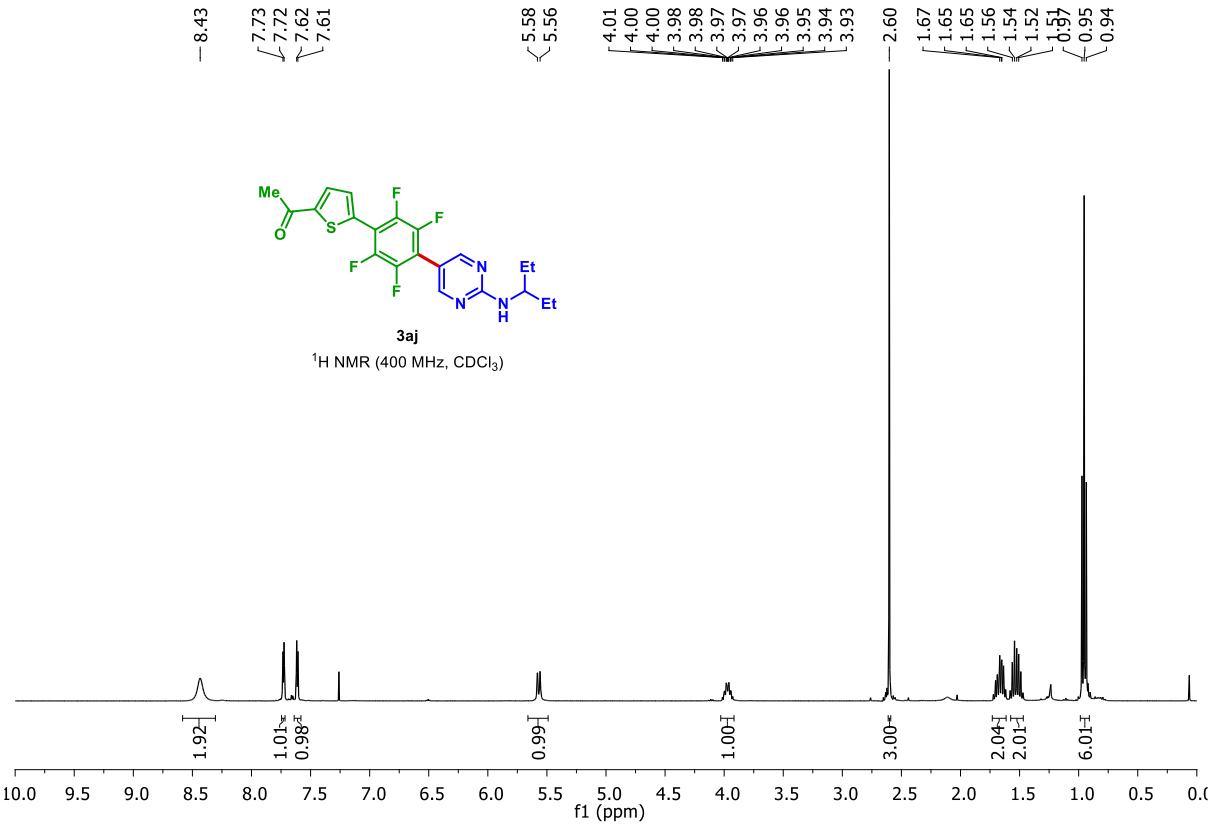

8.45
7.74
7.70
6.81
6.77
5.46
5.44
4.32
4.31
4.29
4.27
4.01
3.99
3.98
3.96
3.95
3.93
1.68
1.67
1.65
1.65
1.64
1.56
1.54
1.53
1.51
1.49
1.37
1.35
1.33
0.97
0.95
0.94
3ai
1H NMR (400 MHz, CDCl3)
1.92
1.00
1.04
1.02
2.01
1.10
2.14
2.16
3.04
6.20
f1 (ppm)


166.35
162.13
158.88
158.85
158.80
158.76
158.73
158.67
158.66
158.65
158.58
158.54
158.52
158.47
146.89
146.88
146.86
146.85
146.81
146.77
146.73
146.69
145.00
144.97
144.92
144.87
144.84
144.82
144.75
144.72
144.71
144.67
143.04
143.00
142.97
142.88
142.85
129.10
126.53
126.46
126.39
116.86
116.74
116.60
113.27
113.16
113.05
110.49
110.46
61.22
53.90
27.24
14.39
10.24
3ai
13C NMR (126 MHz, CDCl3)
f1 (ppm)



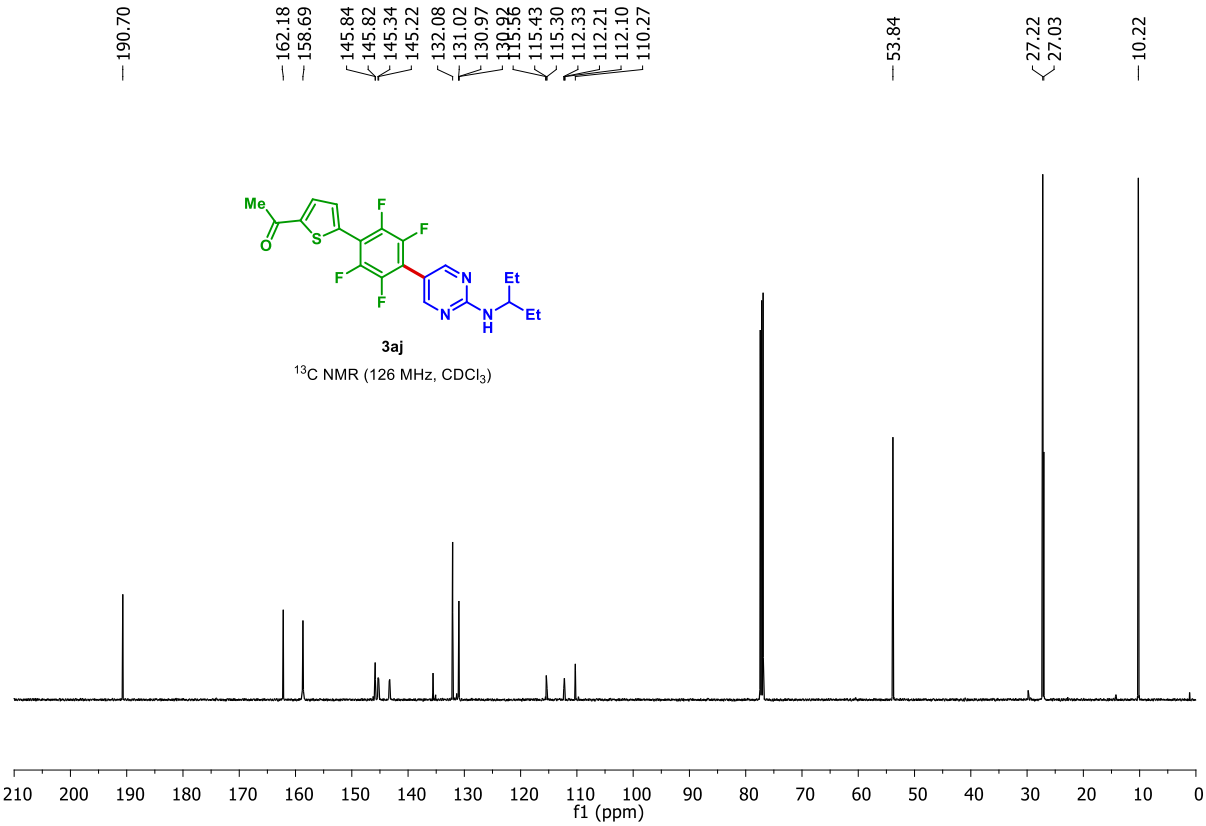
3ai

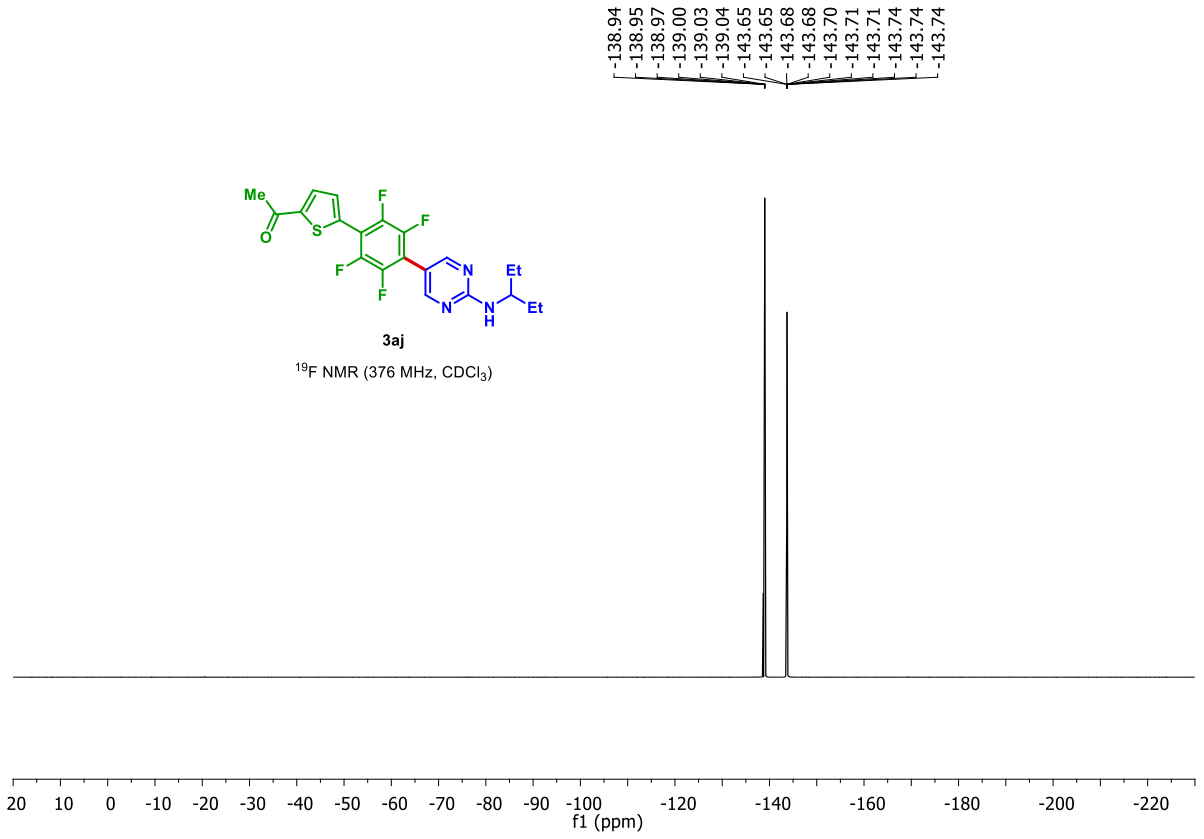
^{19}F NMR (376 MHz, $CDCl_3$)

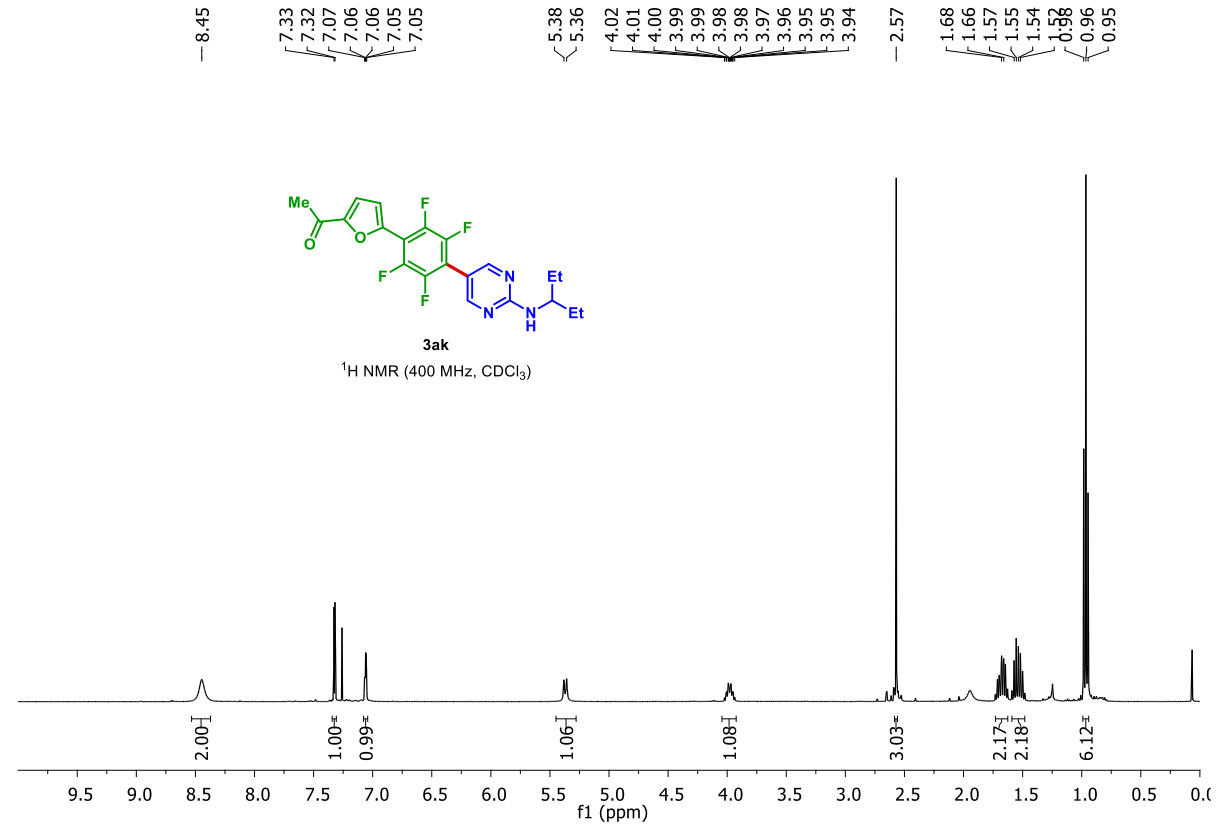


3aj

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

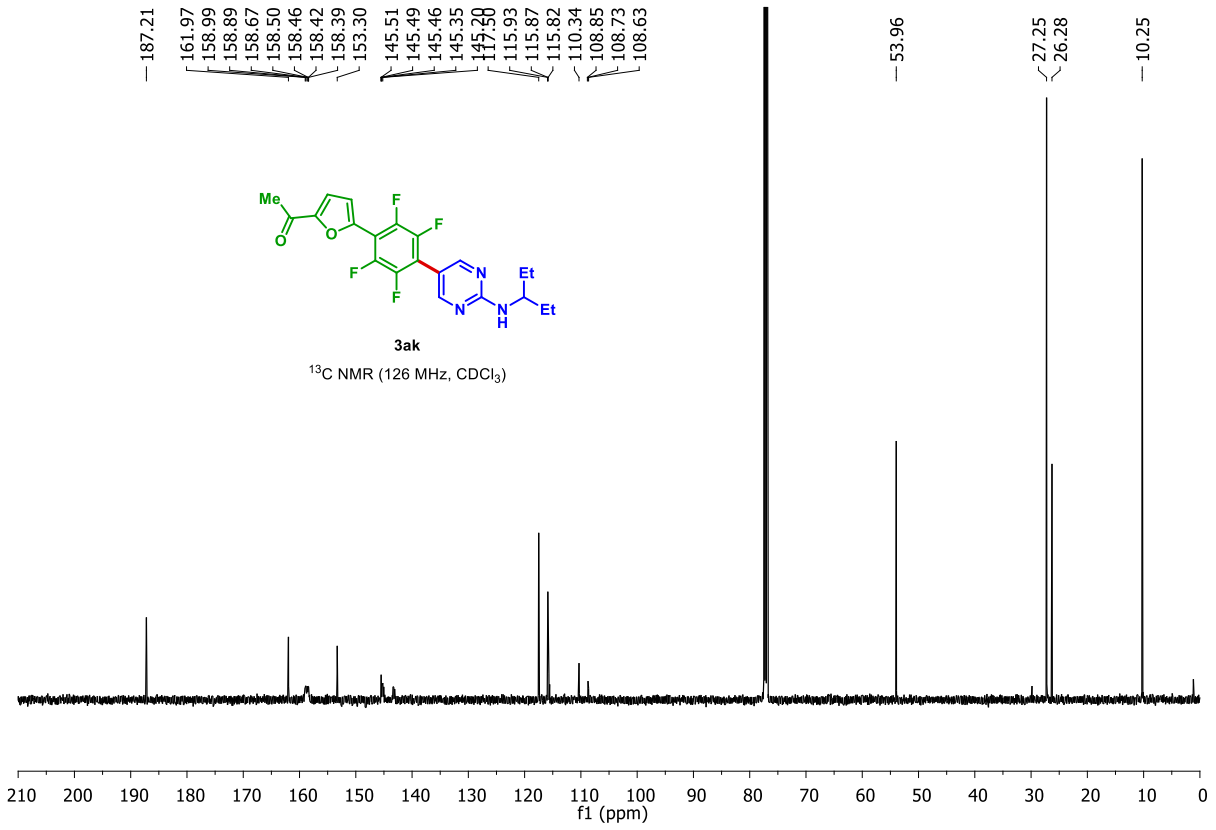

190.70
162.18
158.69
145.84
145.82
145.34
145.22
132.08
131.02
130.97
130.92
115.56
115.43
115.30
112.33
112.21
112.10
110.27
53.84
27.22
27.03
10.22
Me
O
S
F
F
F
F
N
N
H
Et
Et
3aj
13C NMR (126 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-138.94
-138.95
-138.97
-139.00
-139.03
-139.04
-143.65
-143.65
-143.68
-143.68
-143.70
-143.71
-143.71
-143.74
-143.74
-143.74
Me
O
S
F
F
F
F
N
N
H
Et
Et
3aj
19F NMR (376 MHz, CDCl3)
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200 -220
f1 (ppm)



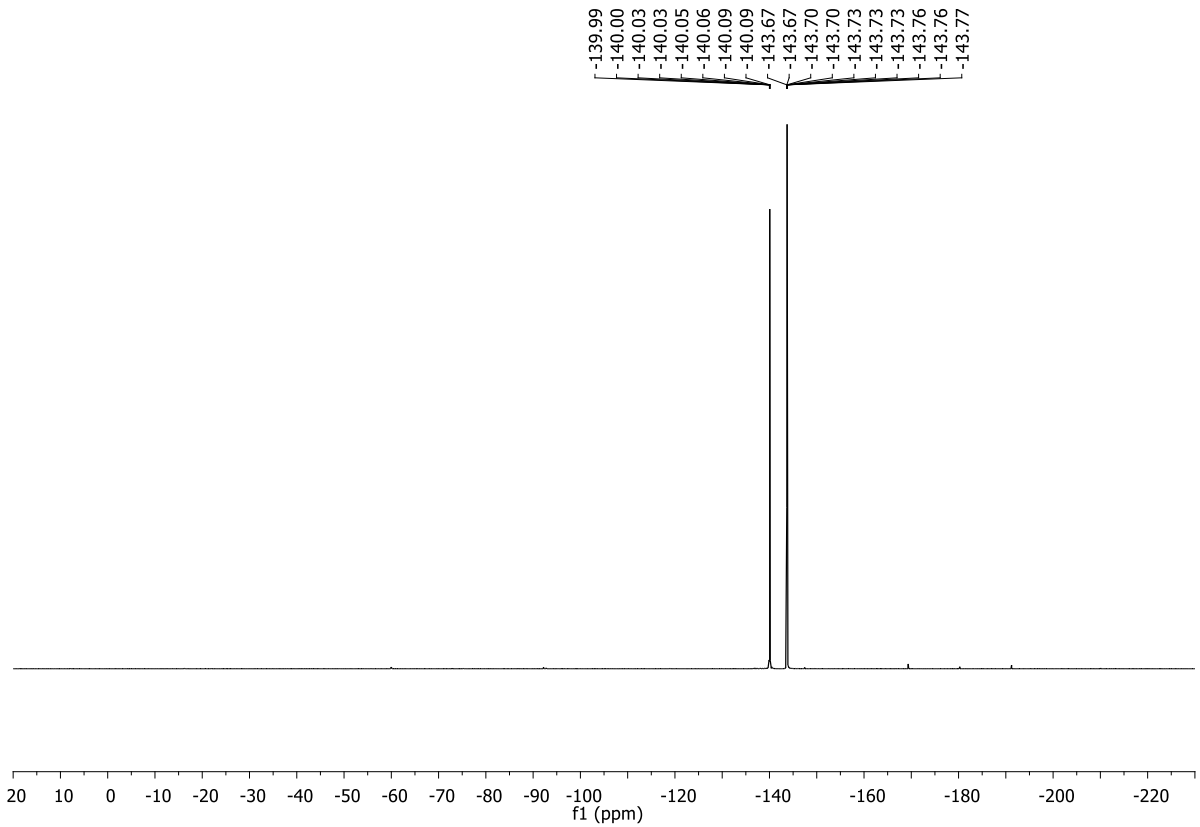
3ak

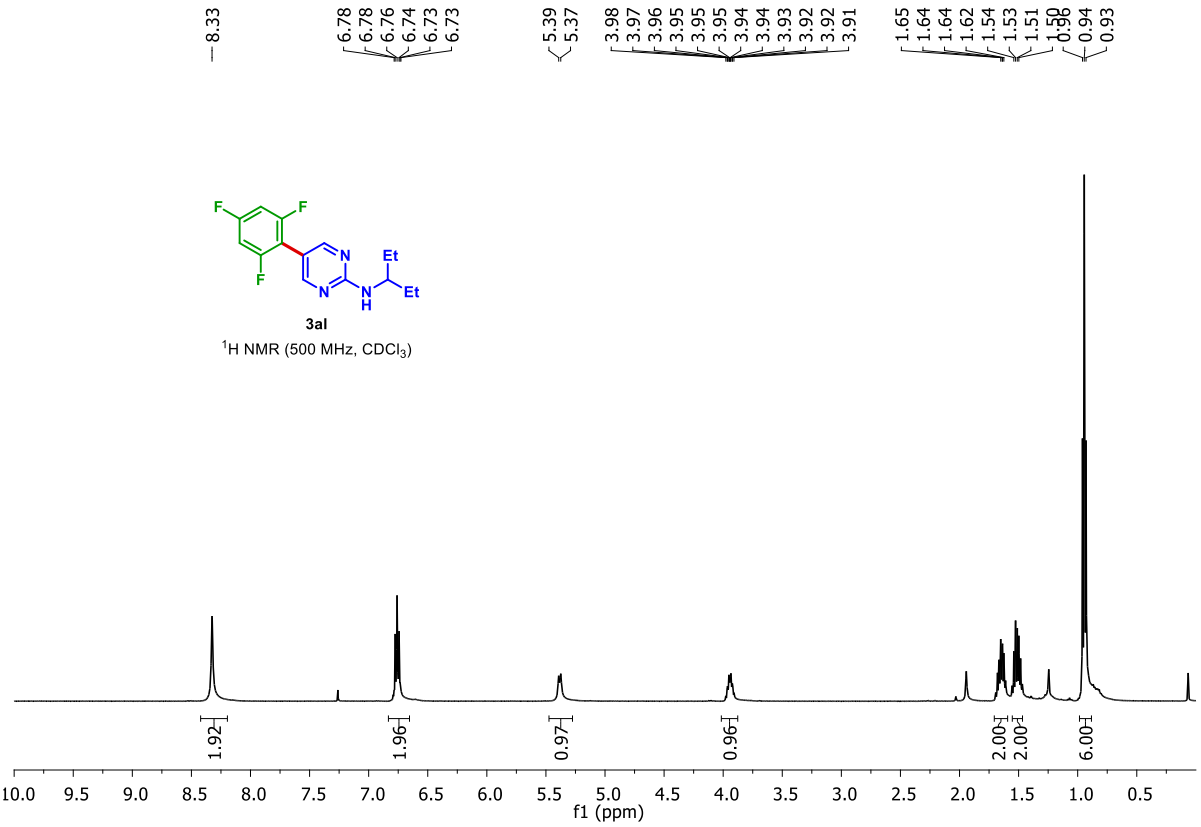
^{1}H NMR (400 MHz, $CDCl_3$)



3ak

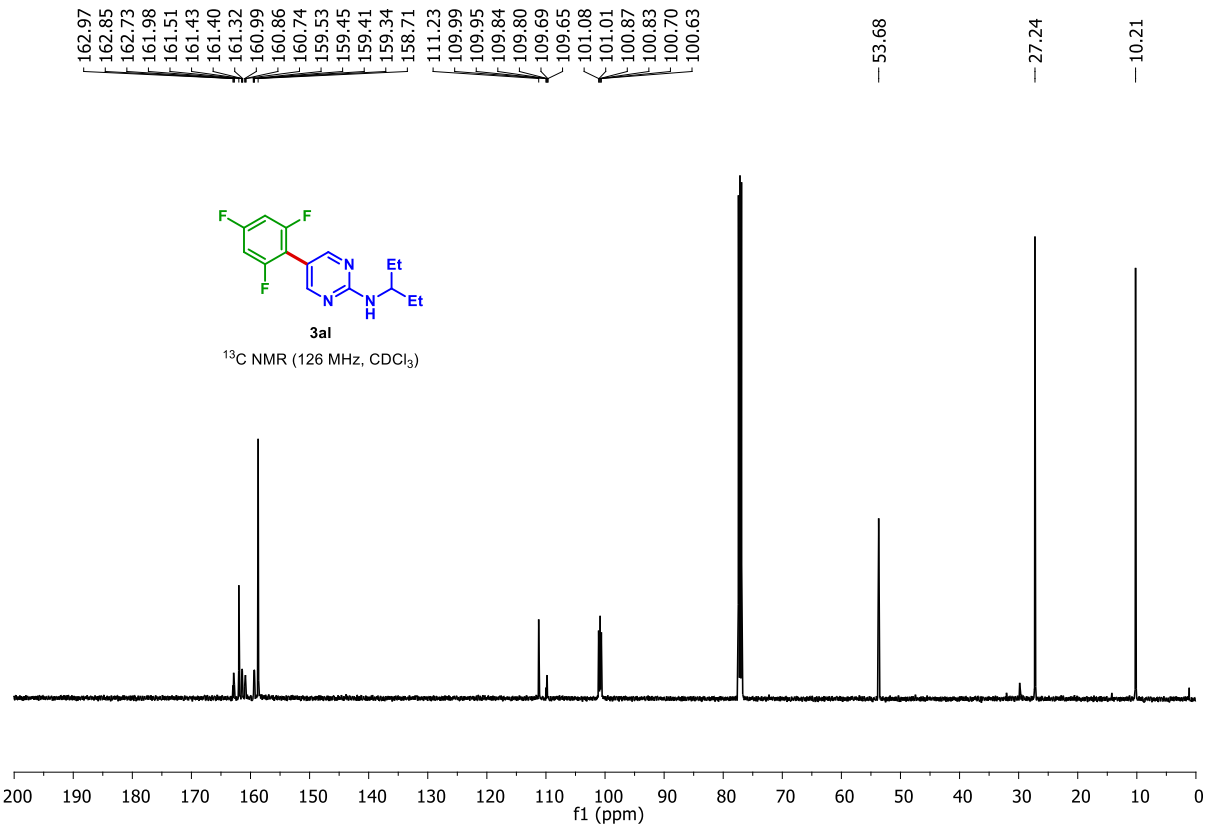
^{13}C NMR (126 MHz, $CDCl_3$)

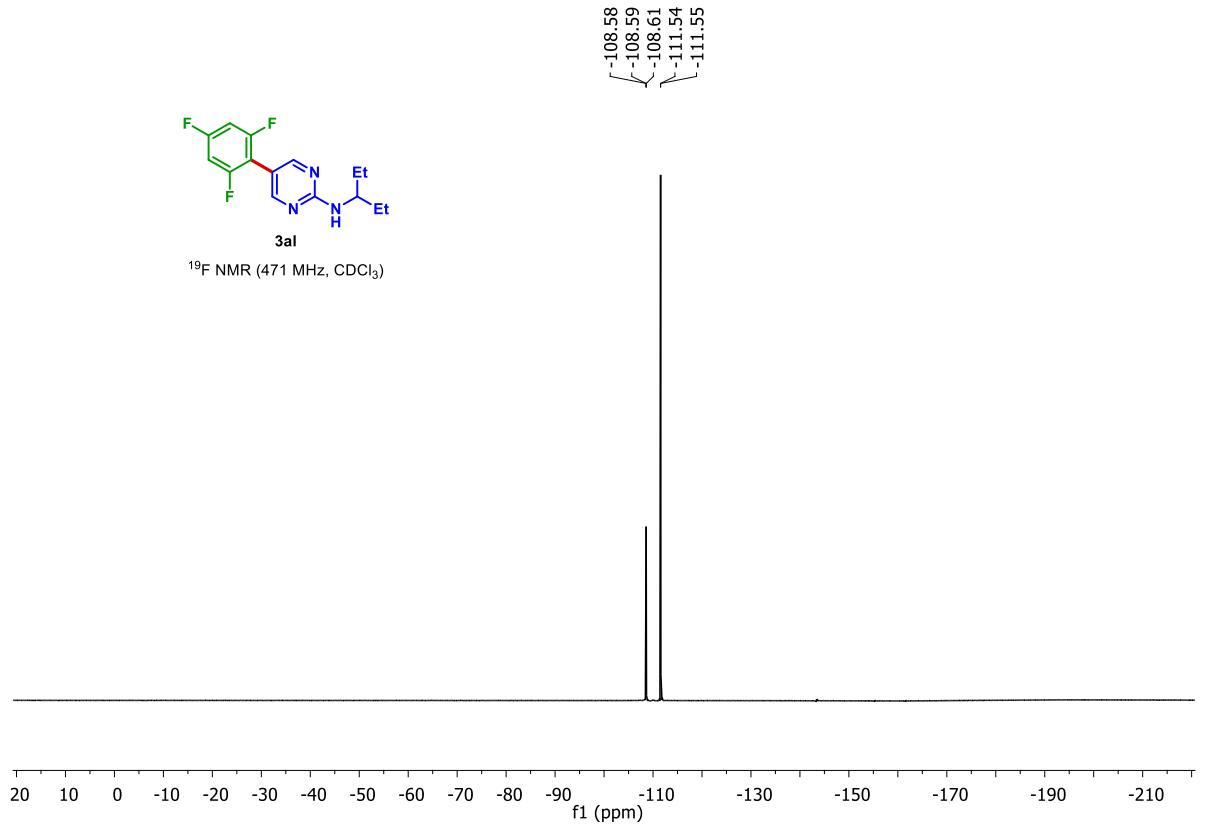


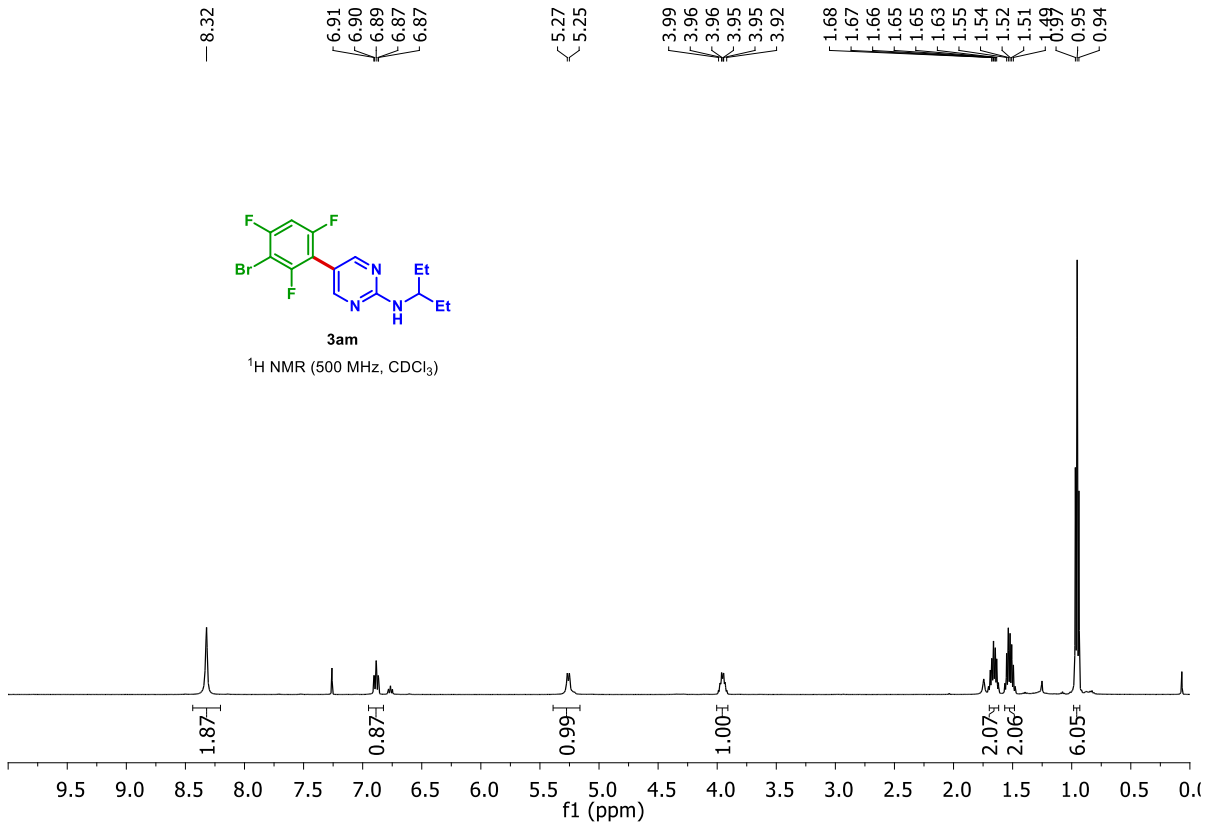


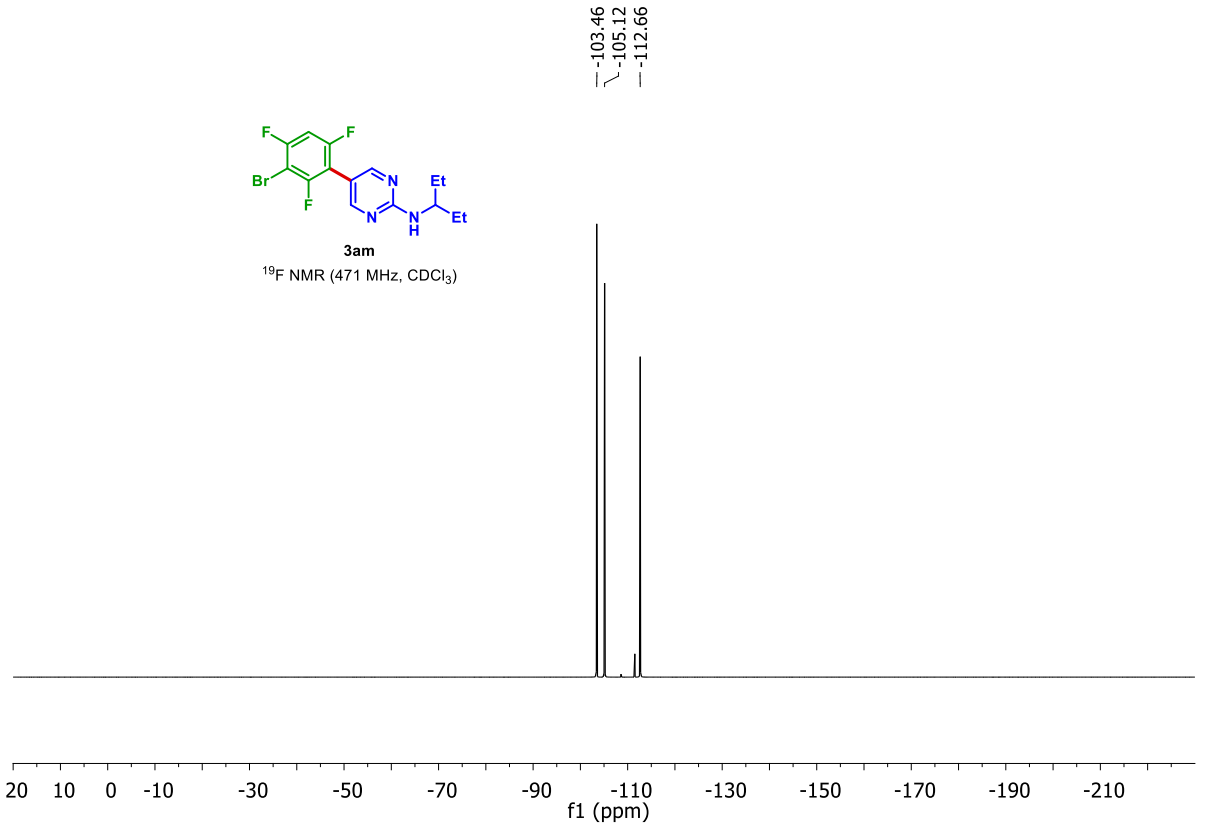
3al

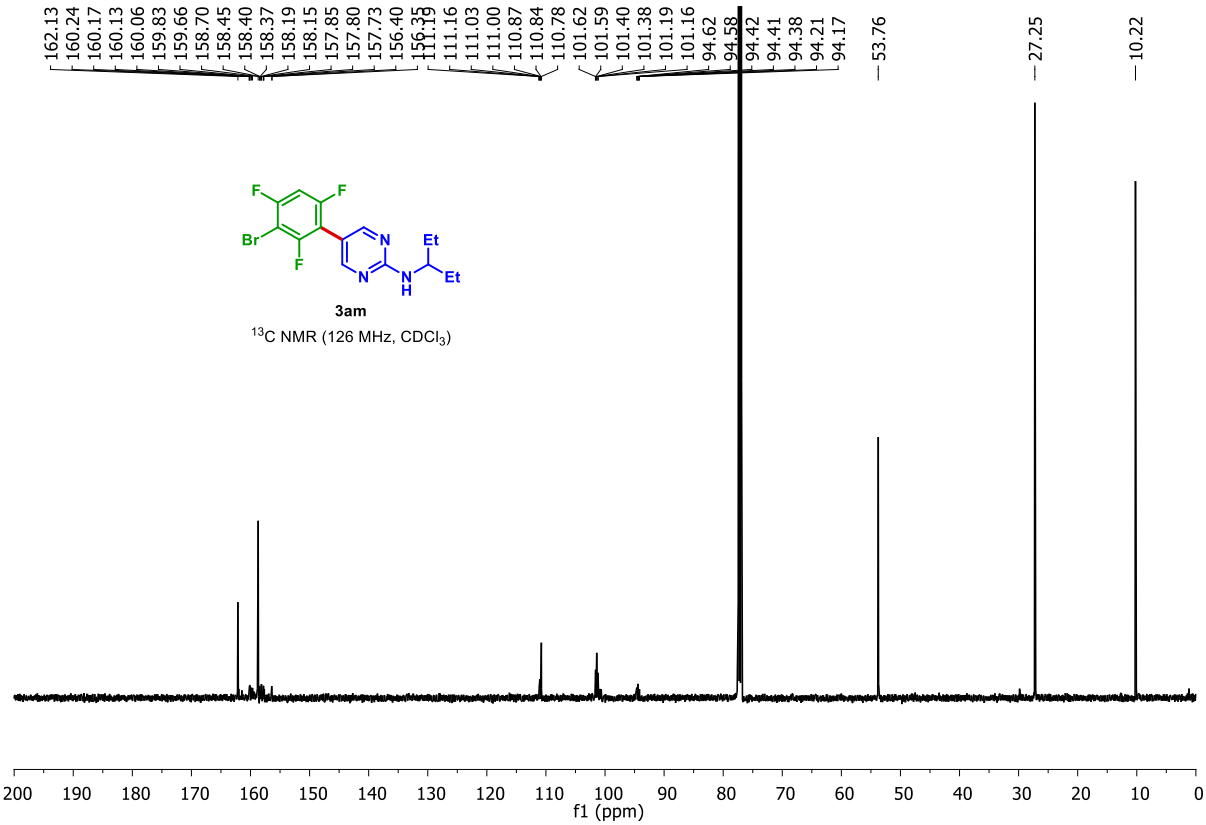
^{1}H NMR (500 MHz, $CDCl_3$)

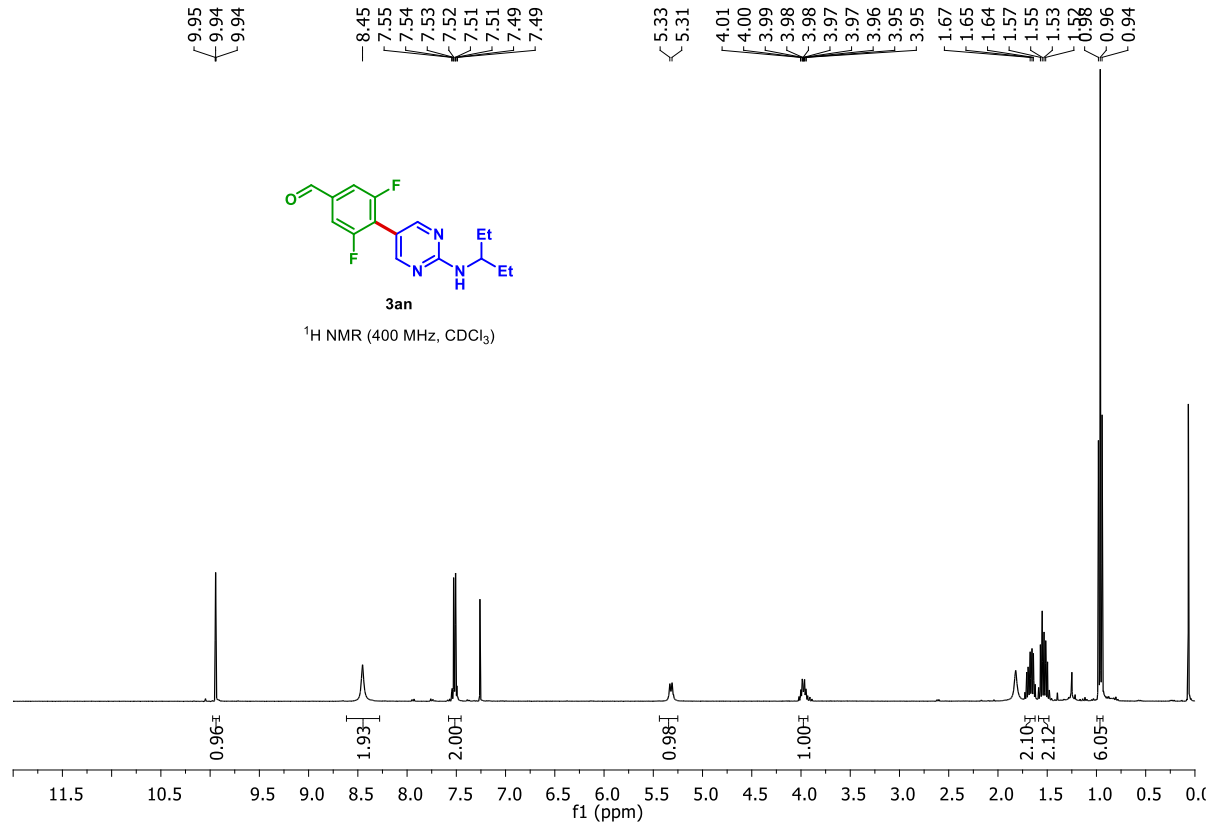

162.97
162.85
162.73
161.98
161.51
161.43
161.40
161.32
160.99
160.86
160.74
159.53
159.45
159.41
159.34
158.71
111.23
109.99
109.95
109.84
109.80
109.69
109.65
101.08
101.01
100.87
100.83
100.70
100.63
53.68
27.24
10.21
F
F
F
N
N
N
H
Et
Et
3al
13C NMR (126 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

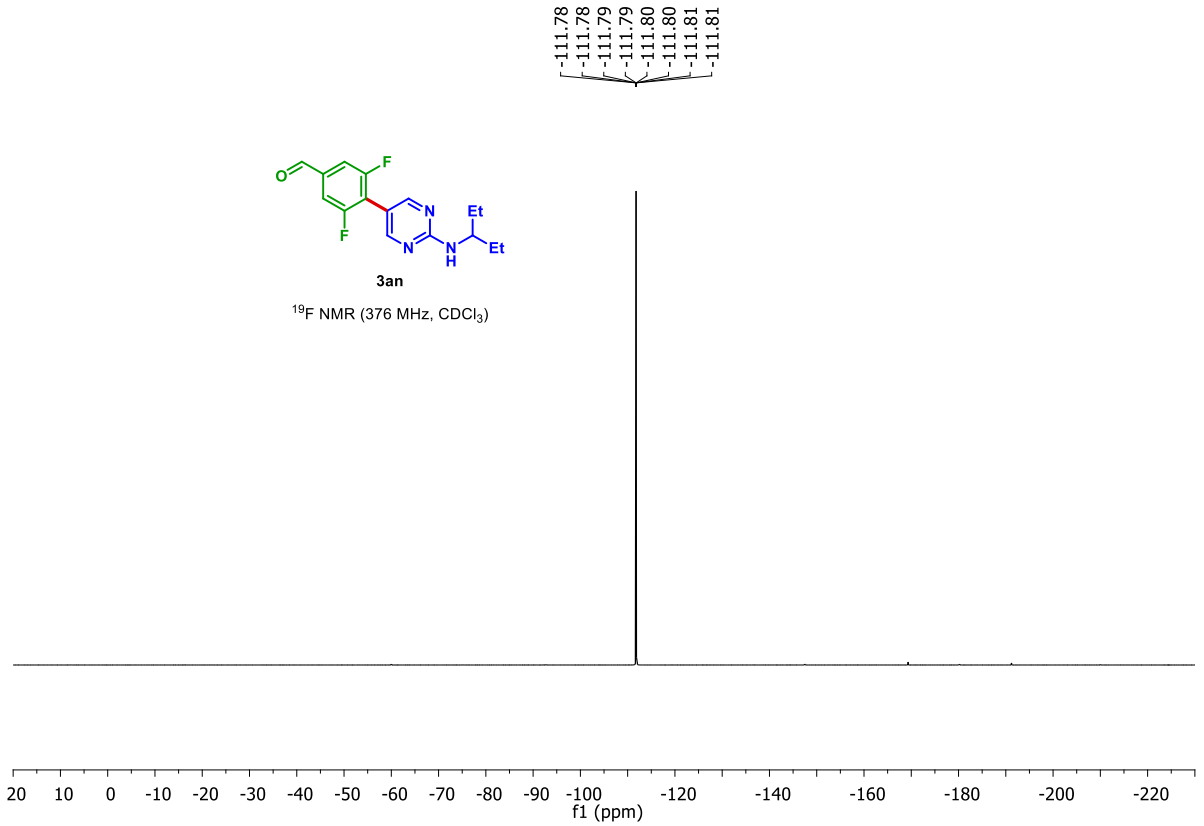

-108.58
-108.59
-108.61
-111.54
-111.55
F
F
F
N
N
N
H
Et
Et
3al
19F NMR (471 MHz, CDCl3)
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

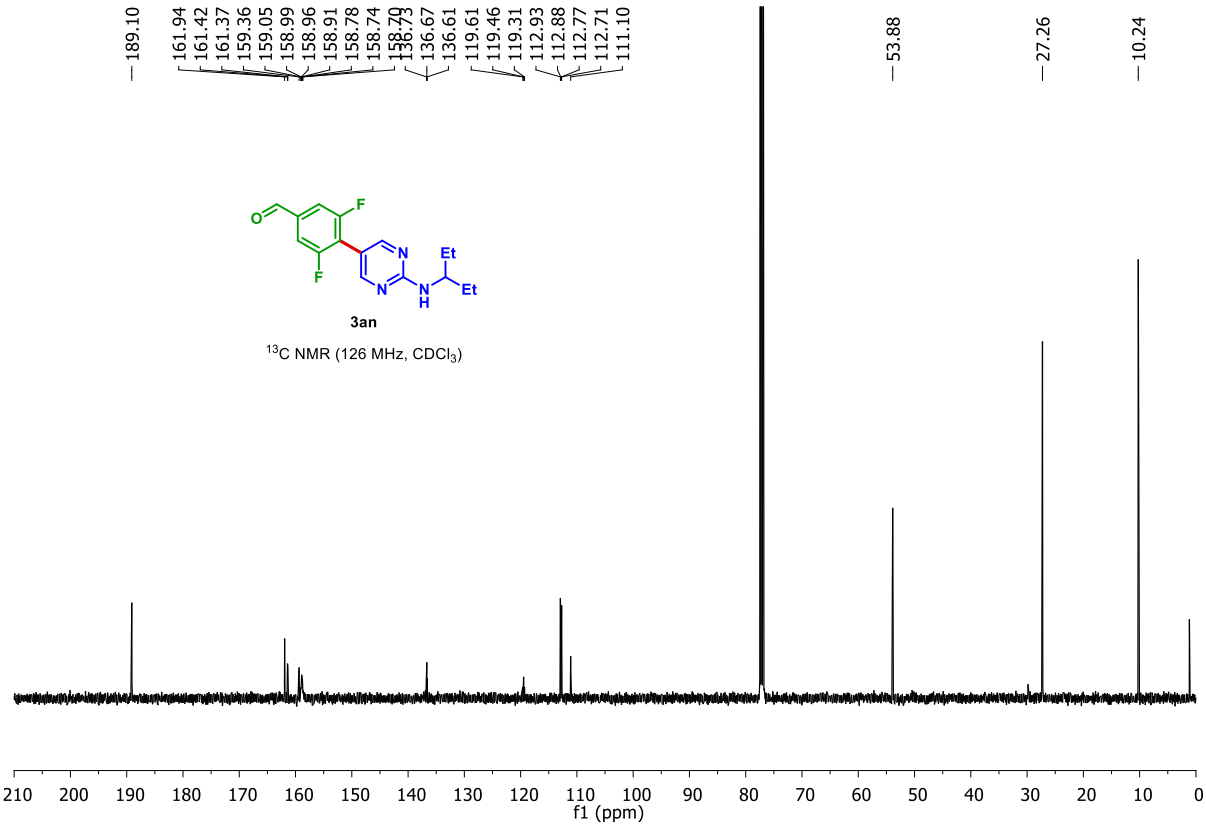

8.32
6.91
6.90
6.89
6.87
6.87
5.27
5.25
3.99
3.96
3.96
3.95
3.95
3.92
1.68
1.67
1.66
1.65
1.65
1.63
1.55
1.54
1.52
1.51
1.49
0.97
0.95
0.94
F
F
Br
F
N
Et
N
N
H
Et
3am
1H NMR (500 MHz, CDCl3)
1.87
0.87
0.99
1.00
2.07
2.06
6.05
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

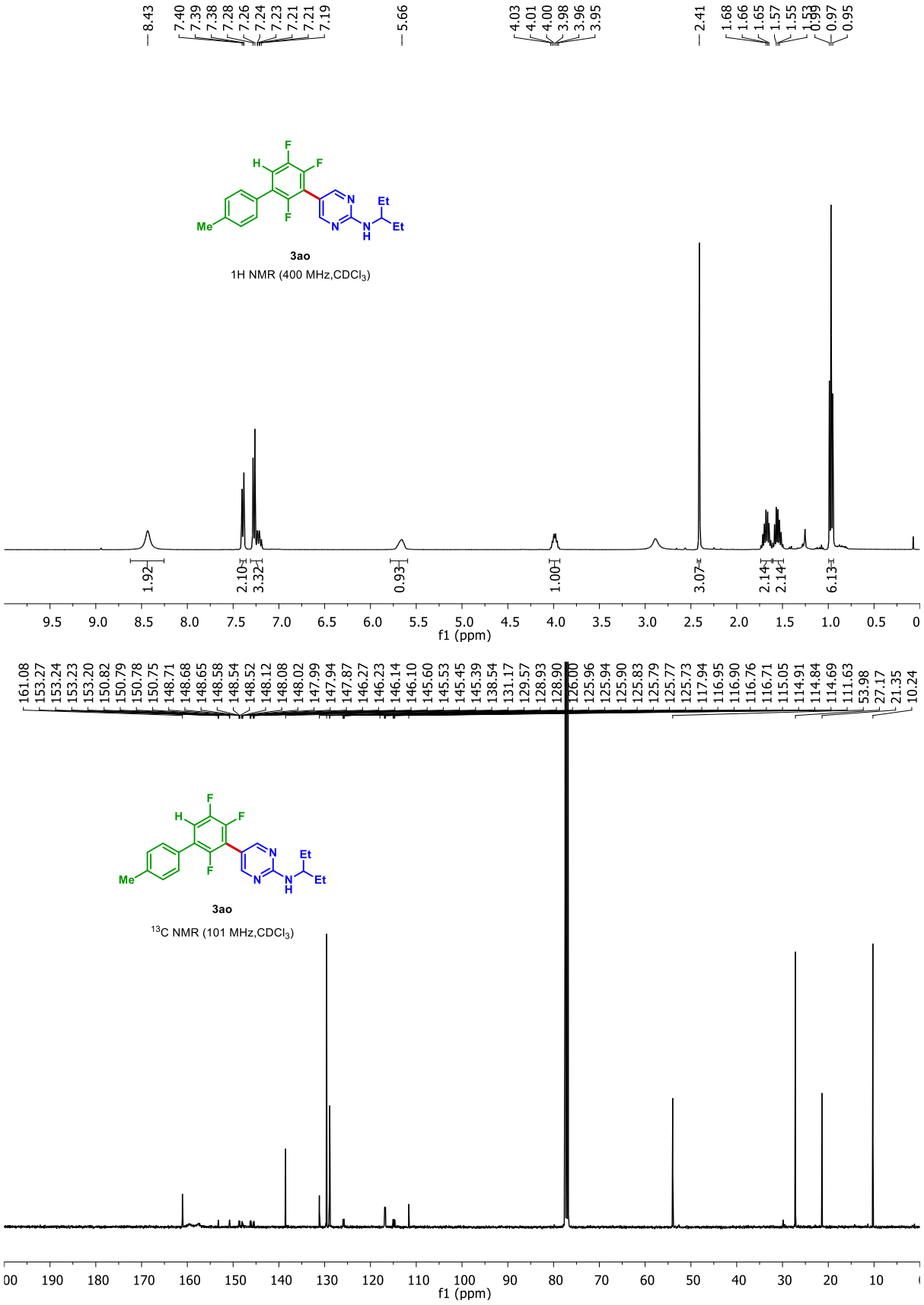

-103.46
-105.12
-112.66
F
F
Br
F
N
Et
N
N
H
Et
3am
19F NMR (471 MHz, CDCl3)
20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190 -210
f1 (ppm)

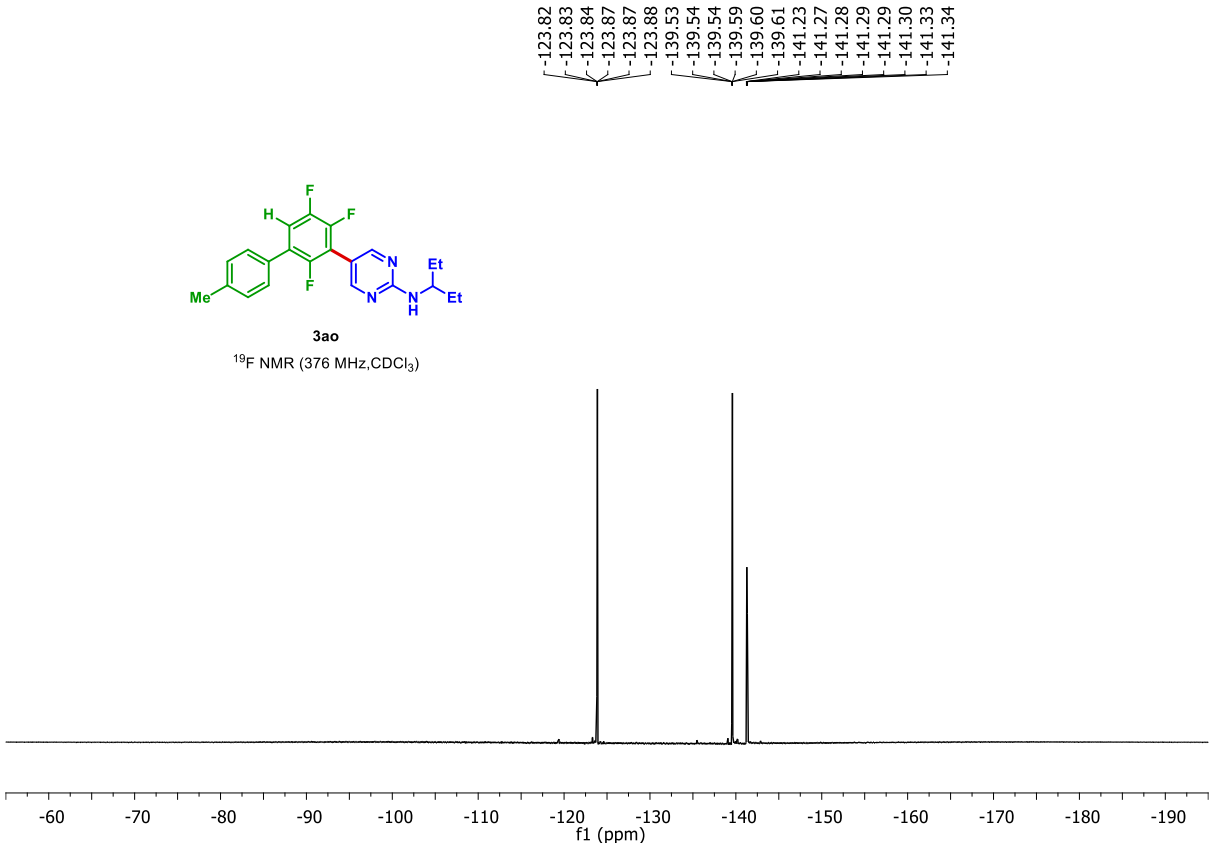

162.13
160.24
160.17
160.13
160.06
159.83
159.66
158.70
158.45
158.40
158.37
158.19
158.15
157.85
157.80
157.73
156.40
111.16
111.03
111.00
110.87
110.84
110.78
101.62
101.59
101.40
101.38
101.19
101.16
94.62
94.58
94.42
94.41
94.38
94.21
94.17
53.76
27.25
10.22
F
F
Br
F
N
Et
N
N
H
Et
3am
13C NMR (126 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.95
9.94
9.94
8.45
7.55
7.54
7.53
7.52
7.51
7.51
7.49
7.49
5.33
5.31
4.01
4.00
3.99
3.98
3.98
3.97
3.97
3.96
3.95
3.95
1.67
1.65
1.64
1.57
1.55
1.53
0.98
0.96
0.94
O
F
F
N
Et
N
N
H
Et
3an
1H NMR (400 MHz, CDCl3)
0.96
1.93
2.00
0.98
1.00
2.10
2.12
6.05
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


-111.78
-111.78
-111.79
-111.79
-111.80
-111.80
-111.81
-111.81
O
F
F
N
N
Et
N
H
Et
3an
^{19}F NMR (376 MHz, CDCl$_3$)
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200 -220
f1 (ppm)

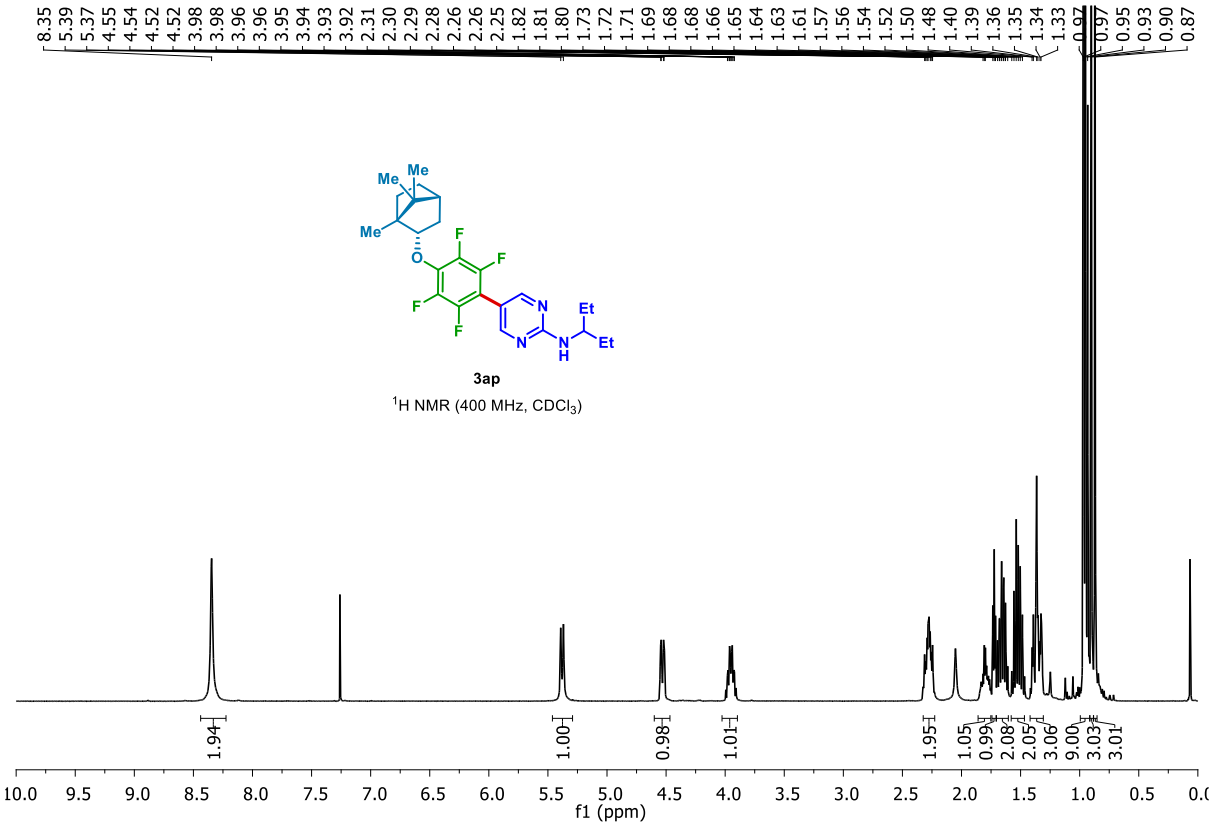

189.10
161.94
161.42
161.37
159.36
159.05
158.99
158.96
158.91
158.78
158.74
158.70
136.73
136.67
136.61
119.61
119.46
119.31
112.93
112.88
112.77
112.71
111.10
53.88
27.26
10.24
O
F
F
N
N
Et
N
H
Et
3an
^{13}C NMR (126 MHz, CDCl$_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.43
7.40
7.39
7.38
7.28
7.26
7.24
7.23
7.21
7.21
7.19
5.66
4.03
4.01
4.00
3.98
3.96
3.95
2.41
1.68
1.66
1.65
1.57
1.55
1.53
0.99
0.97
0.95
F
H
F
Me
F
N
N
Et
N
H
Et
3ao
1H NMR (400 MHz,CDCl3)
1.92
2.10
3.32
0.93
1.00
3.07
2.14
2.14
6.13
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)
161.08
153.27
153.24
153.23
153.20
150.82
150.79
150.78
150.75
148.71
148.68
148.65
148.58
148.54
148.52
148.12
148.08
148.02
147.99
147.94
147.87
146.27
146.23
146.14
146.10
145.60
145.53
145.45
145.39
138.54
131.17
129.57
128.93
128.90
126.00
125.96
125.94
125.90
125.83
125.79
125.77
125.73
117.94
116.95
116.90
116.76
116.71
115.05
114.91
114.84
114.69
111.63
53.98
27.17
21.35
10.24
F
H
F
Me
F
N
N
Et
N
H
Et
3ao
13C NMR (101 MHz,CDCl3)
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)



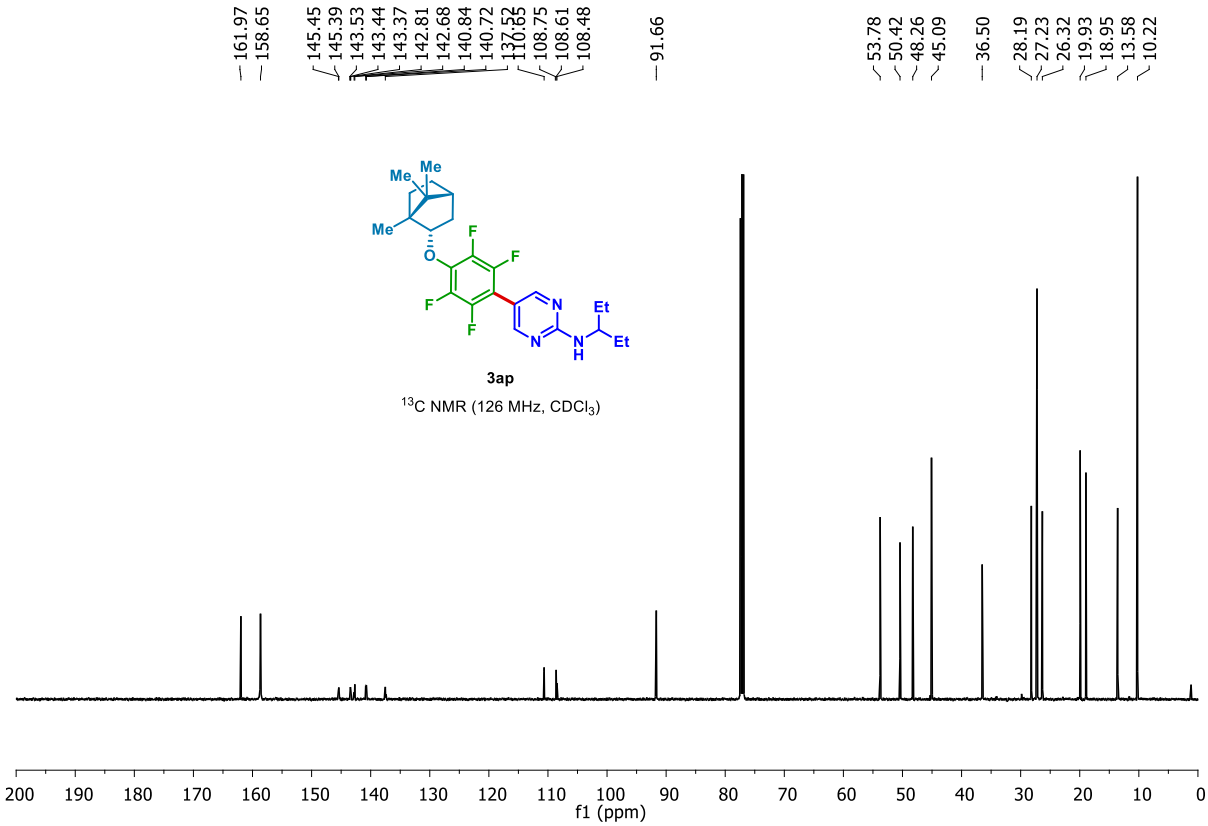
3ao

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



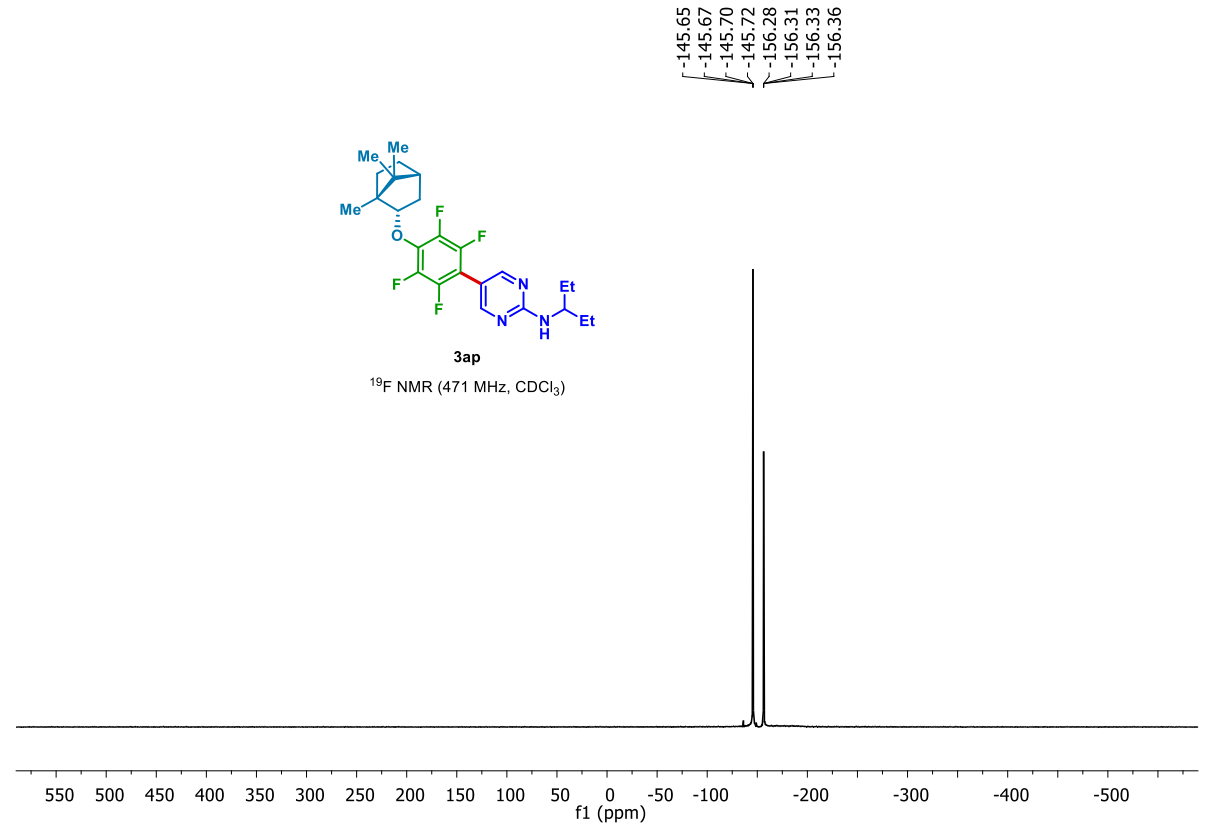
3ap

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



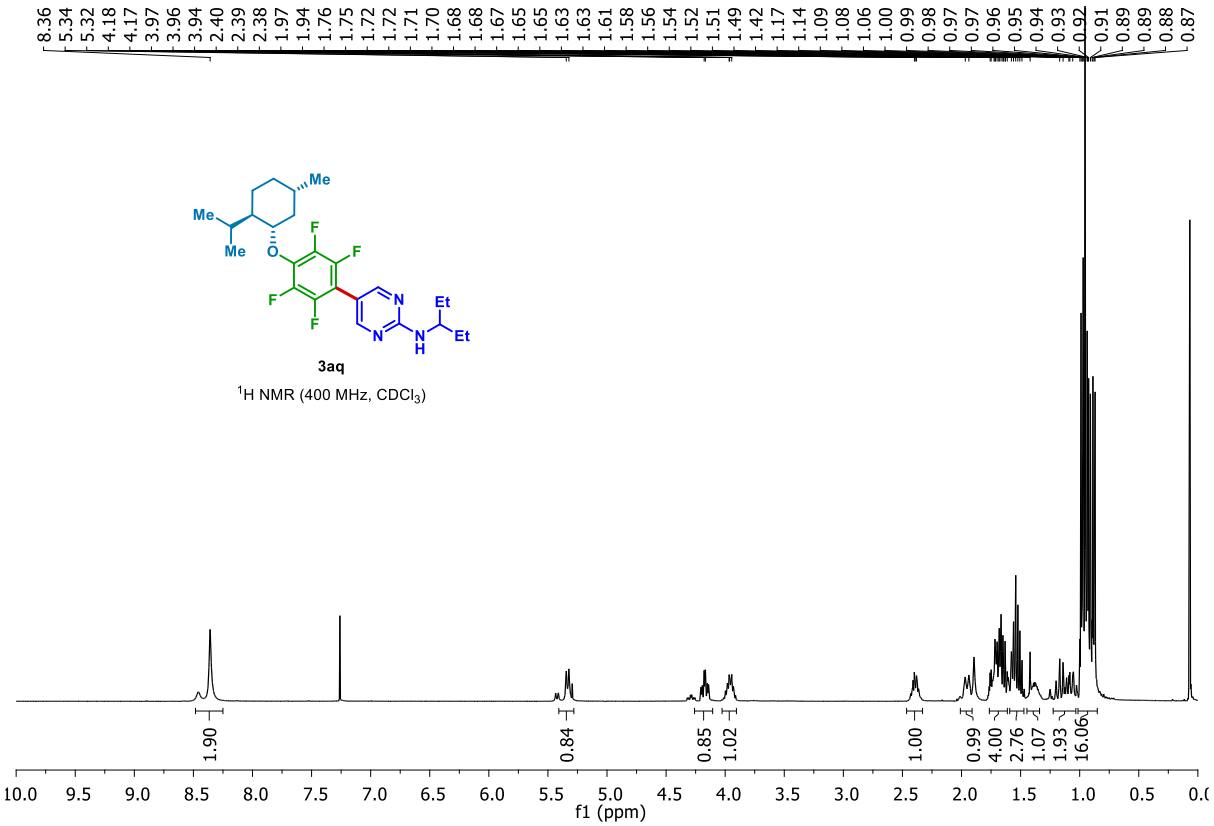
3ap

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



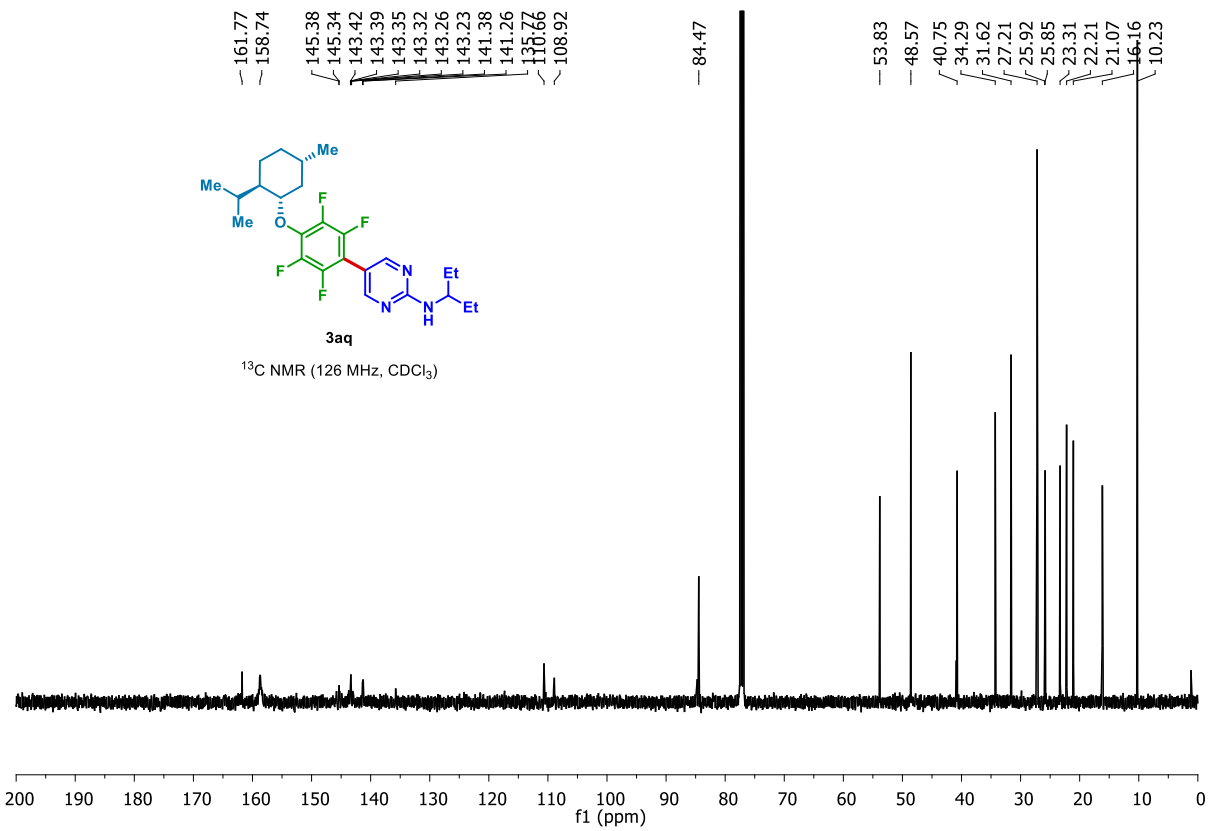
3ap

^{19}F NMR (471 MHz, $CDCl_3$)



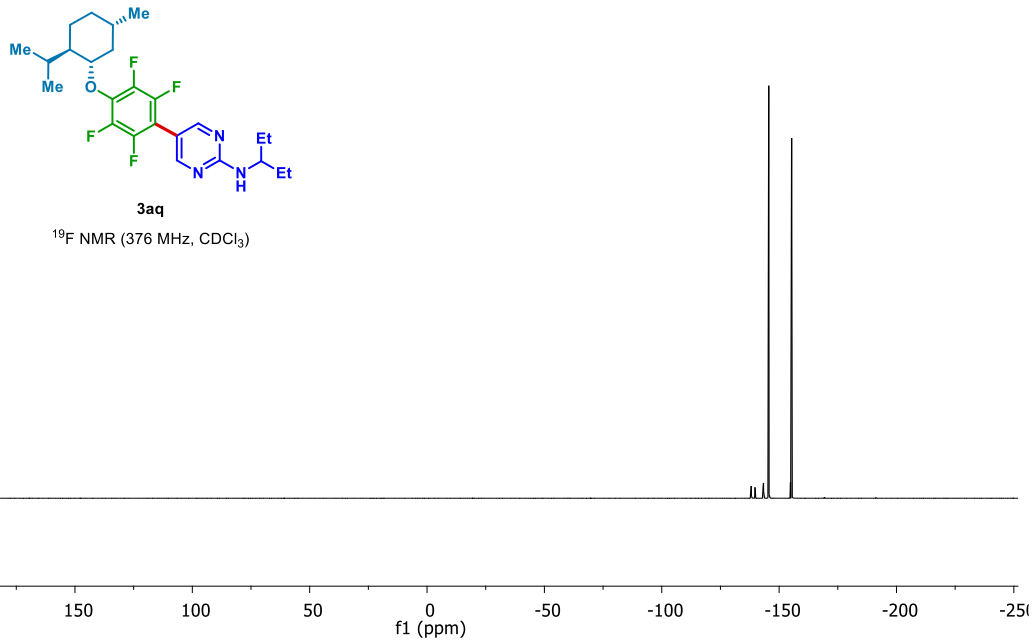
3aq

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



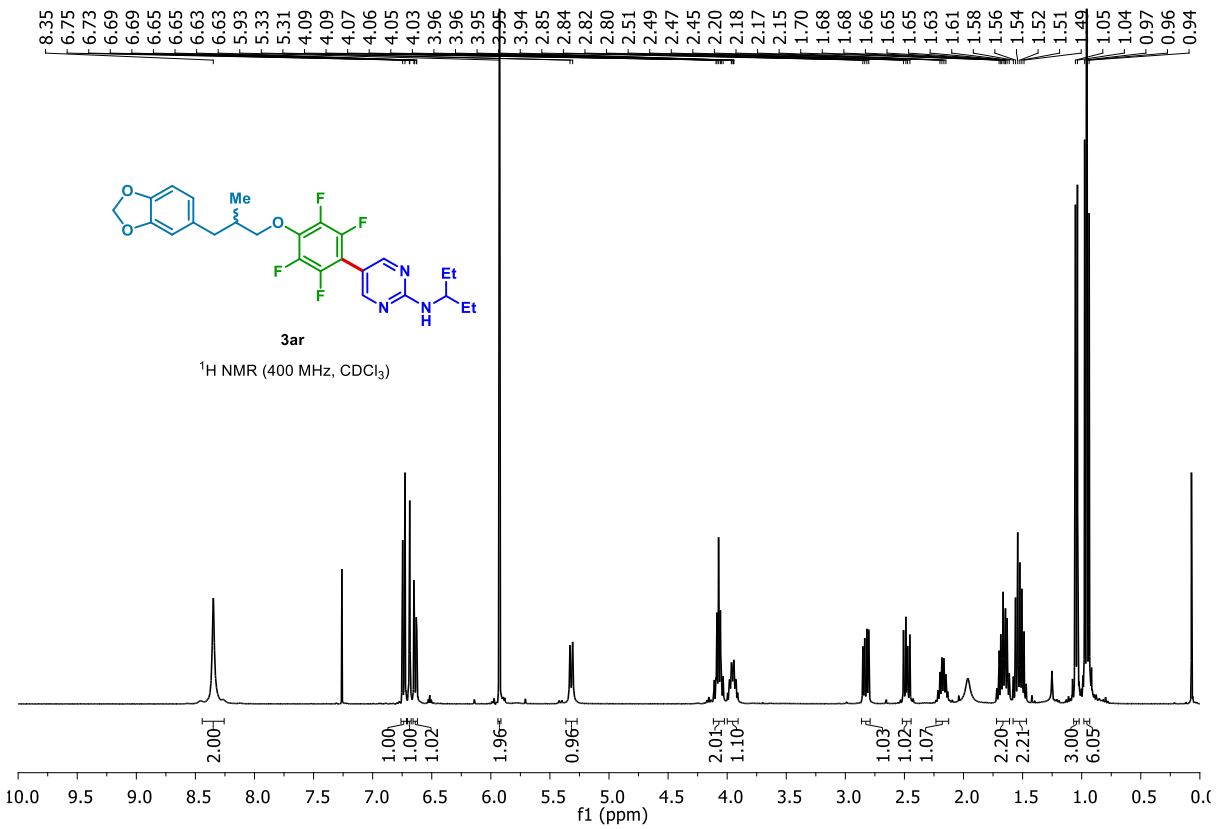
3aq

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



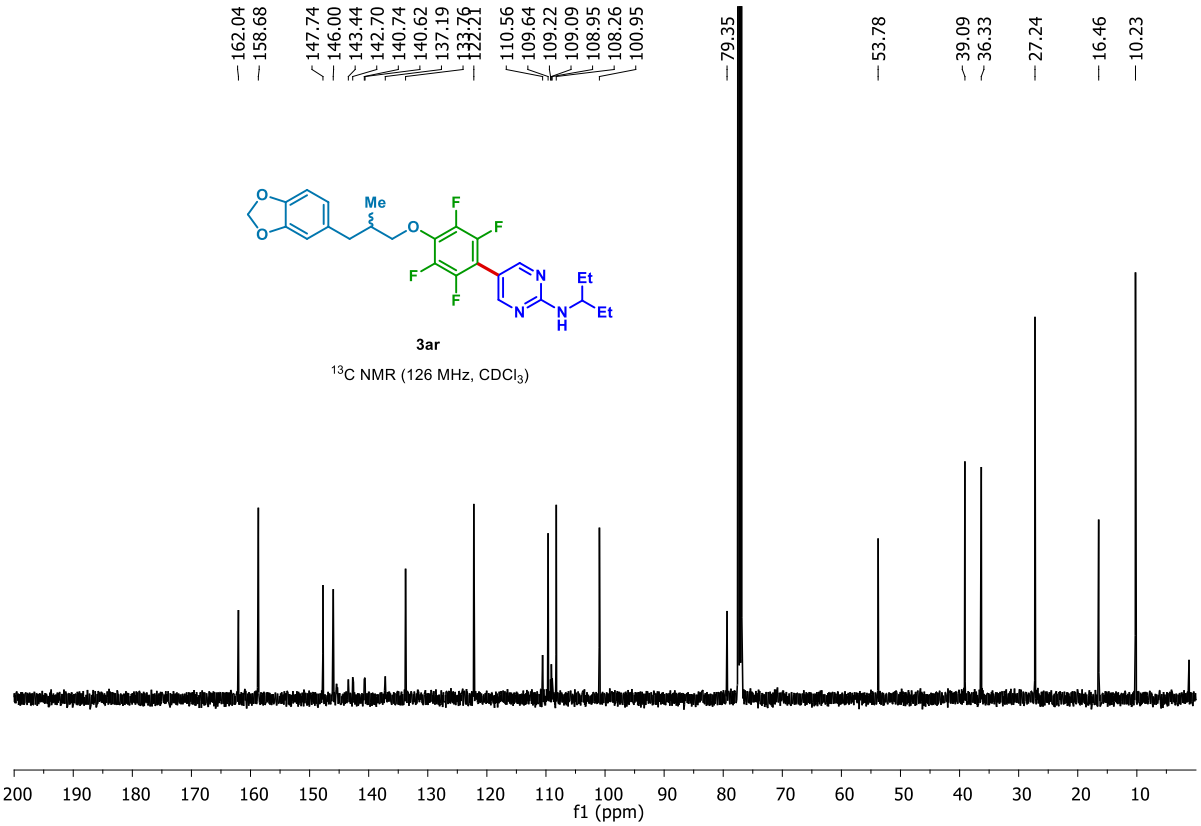
3aq

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



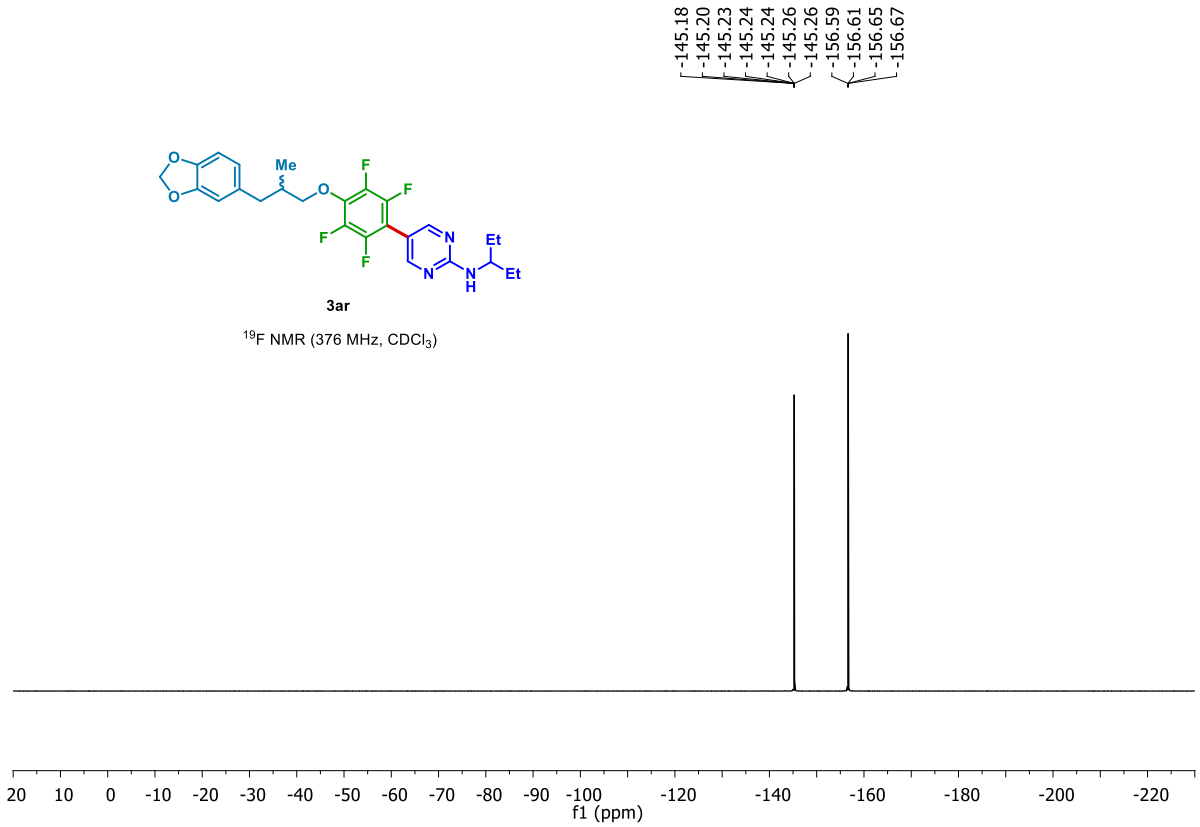
3ar

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



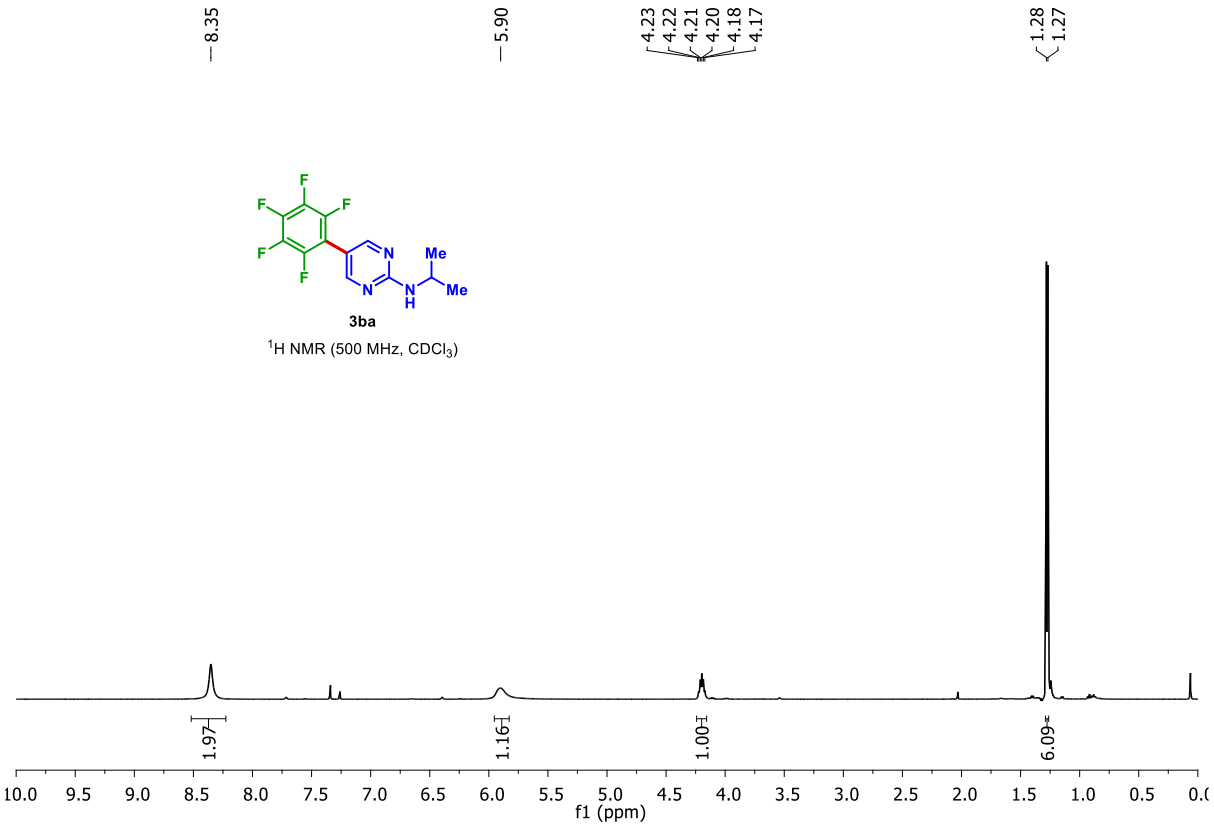
3ar

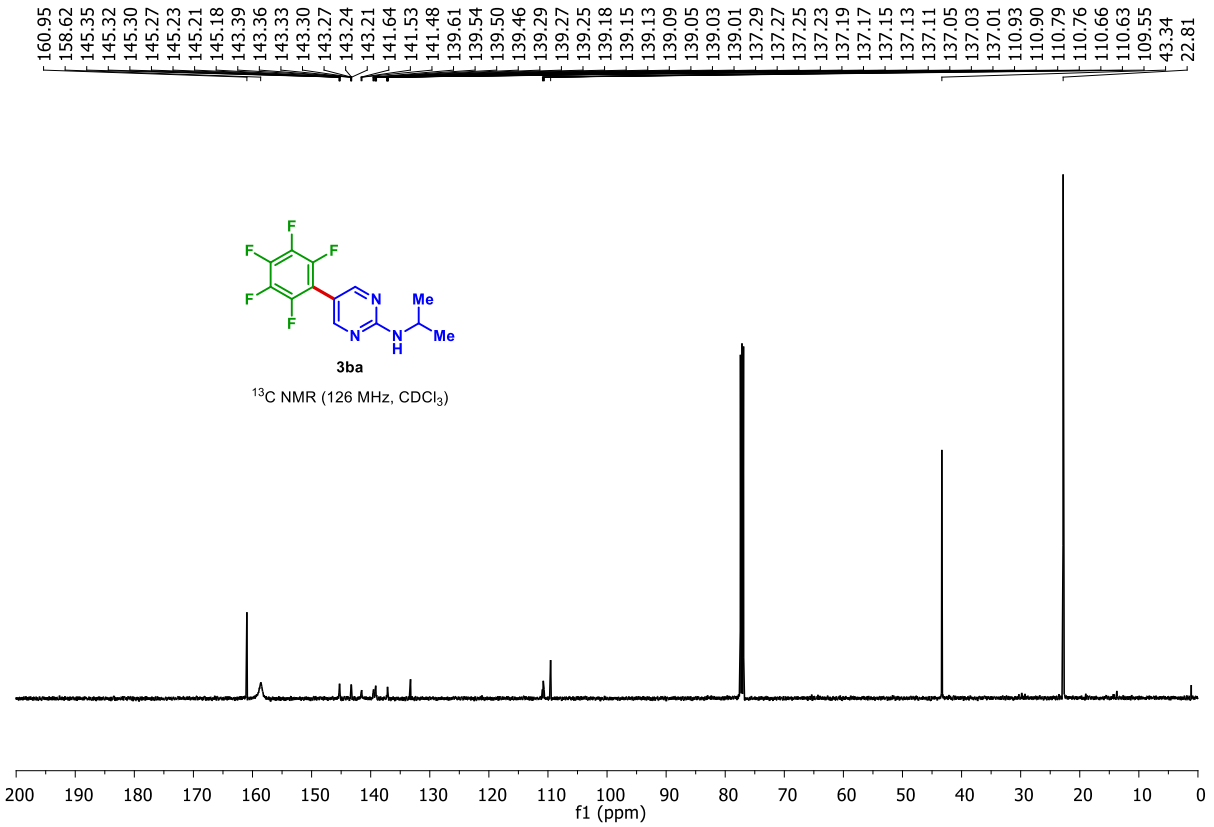
^{13}C NMR (126 MHz, $CDCl_3$)

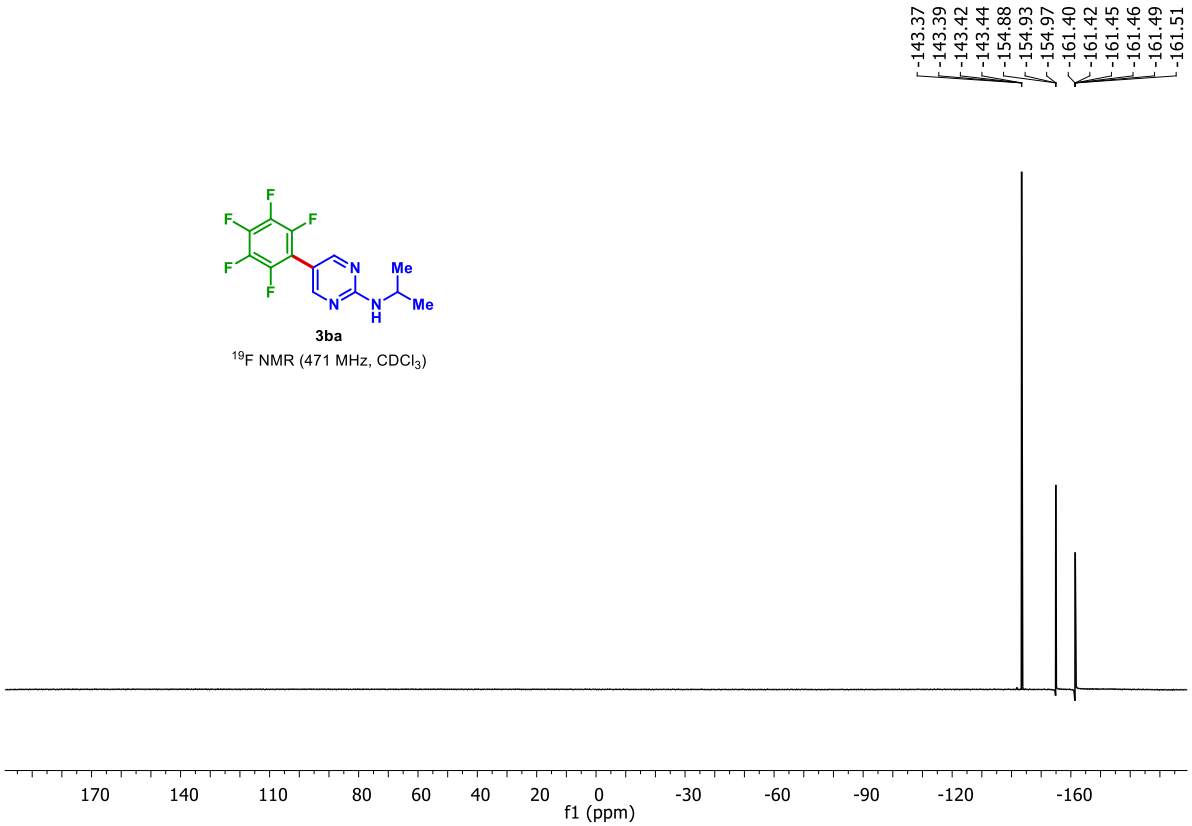


3ar

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

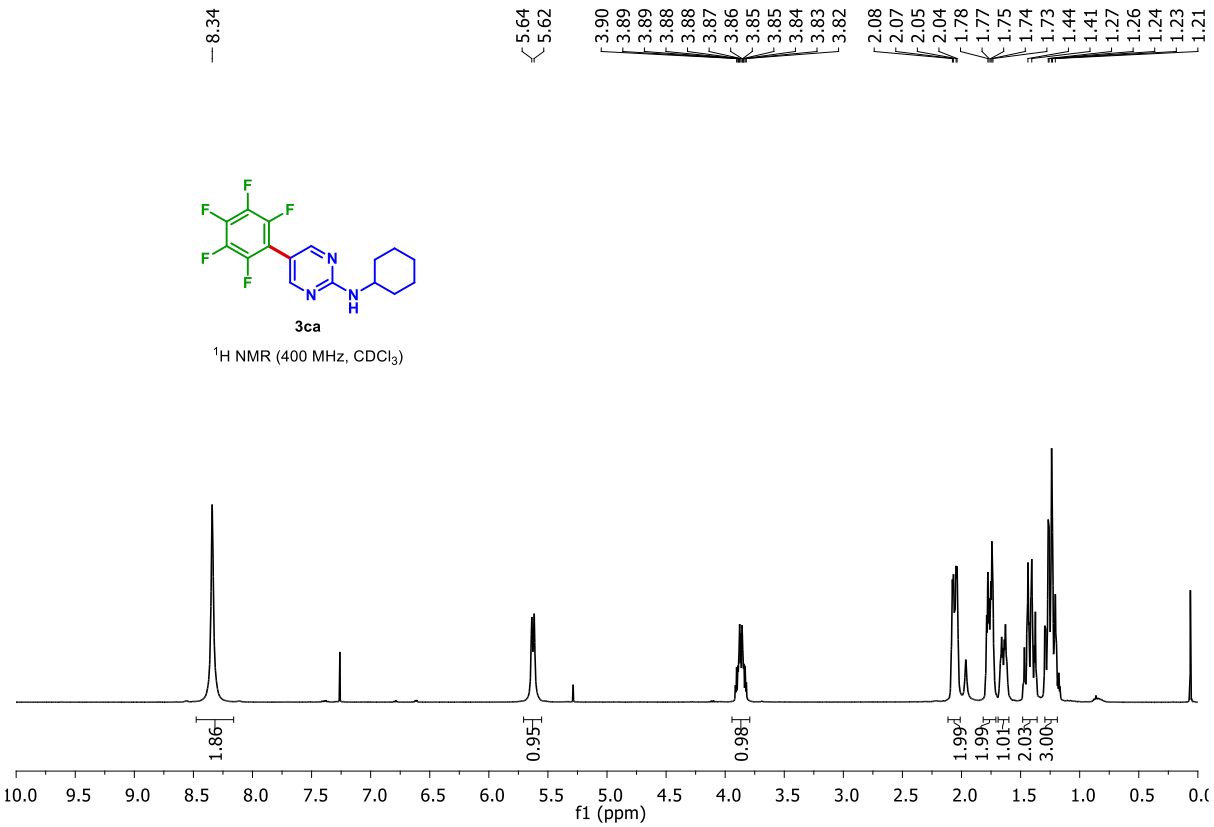

8.35
5.90
4.23
4.22
4.21
4.20
4.18
4.17
1.28
1.27
3ba
1H NMR (500 MHz, CDCl3)
1.97
1.16
1.00
6.09
f1 (ppm)


160.95
158.62
145.35
145.32
145.30
145.27
145.23
145.21
145.18
143.39
143.36
143.33
143.30
143.27
143.24
143.21
141.64
141.53
141.48
139.61
139.54
139.50
139.46
139.29
139.27
139.25
139.18
139.15
139.13
139.09
139.05
139.03
139.01
137.29
137.27
137.25
137.23
137.19
137.17
137.15
137.13
137.11
137.05
137.03
137.01
110.93
110.90
110.79
110.76
110.66
110.63
109.55
43.34
22.81
3ba
13C NMR (126 MHz, CDCl3)
f1 (ppm)



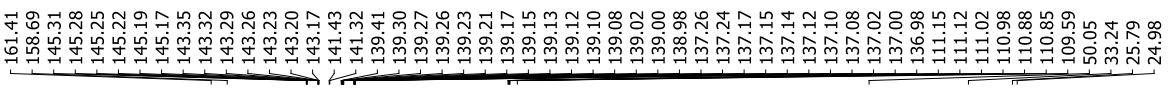
3ba

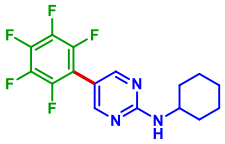
^{19}F NMR (471 MHz, $CDCl_3$)



3ca

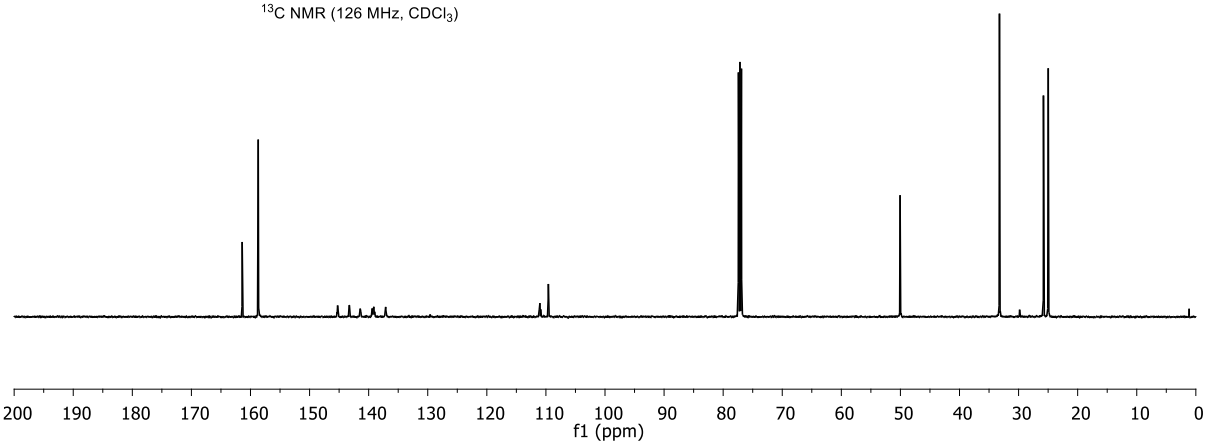
^{1}H NMR (400 MHz, $CDCl_3$)

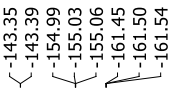


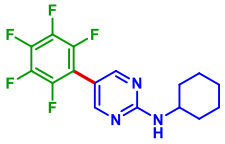


3ca

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

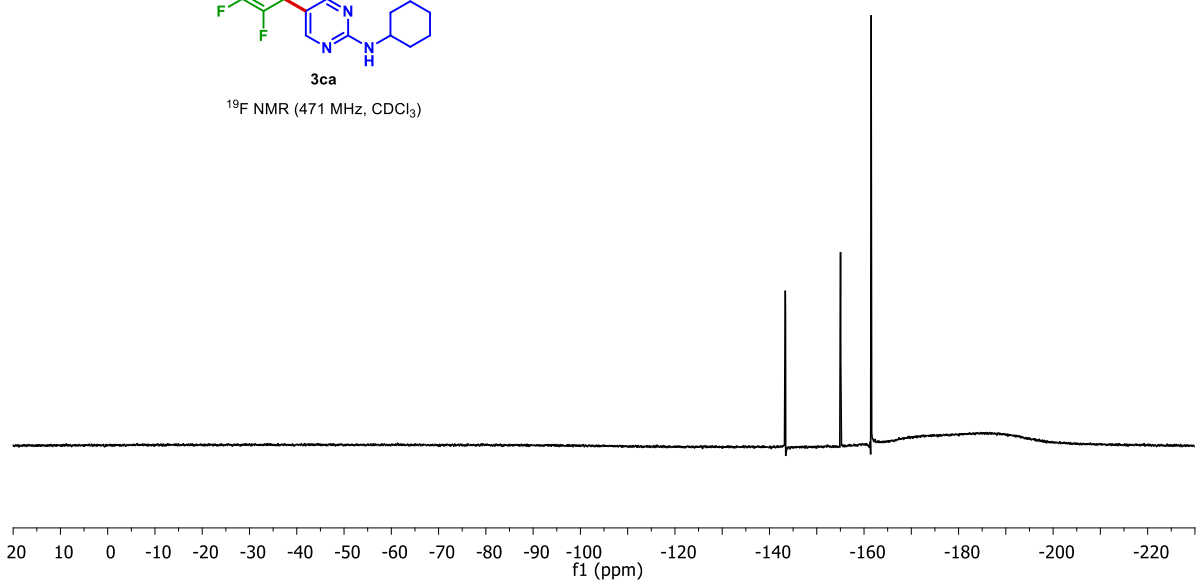


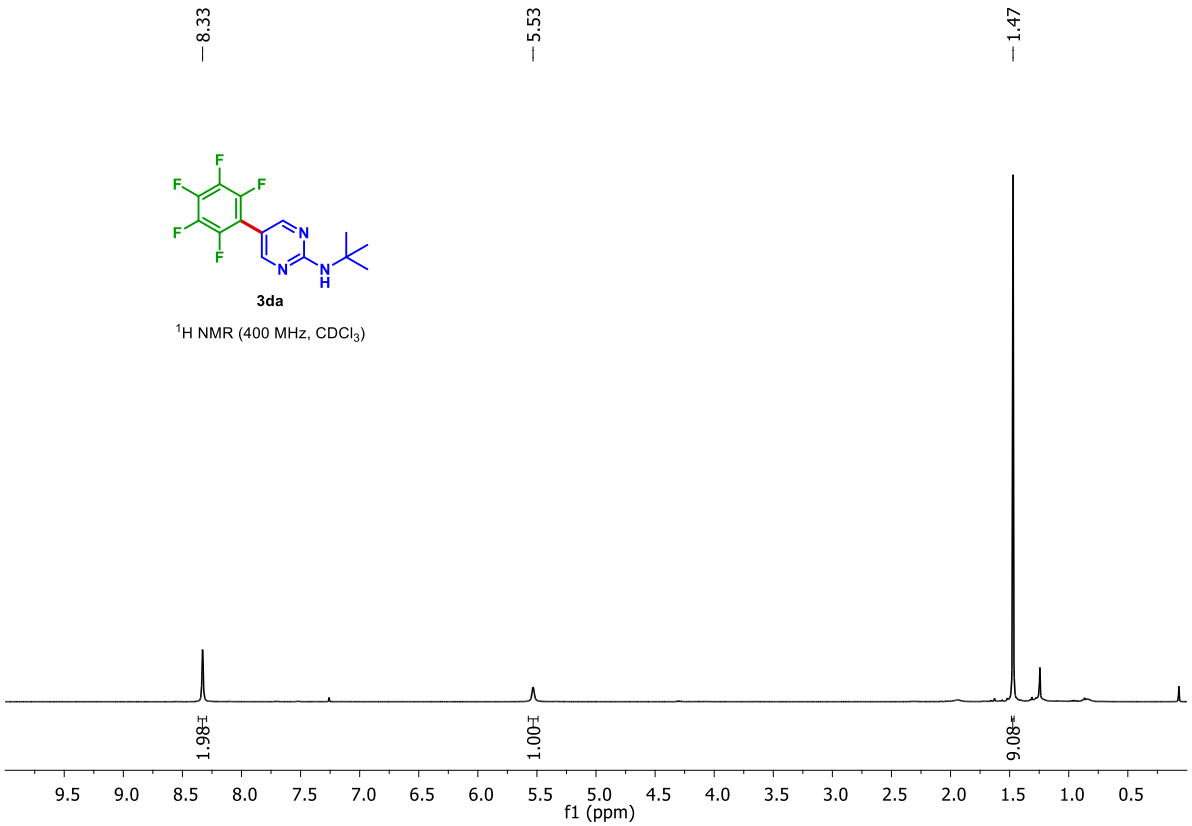


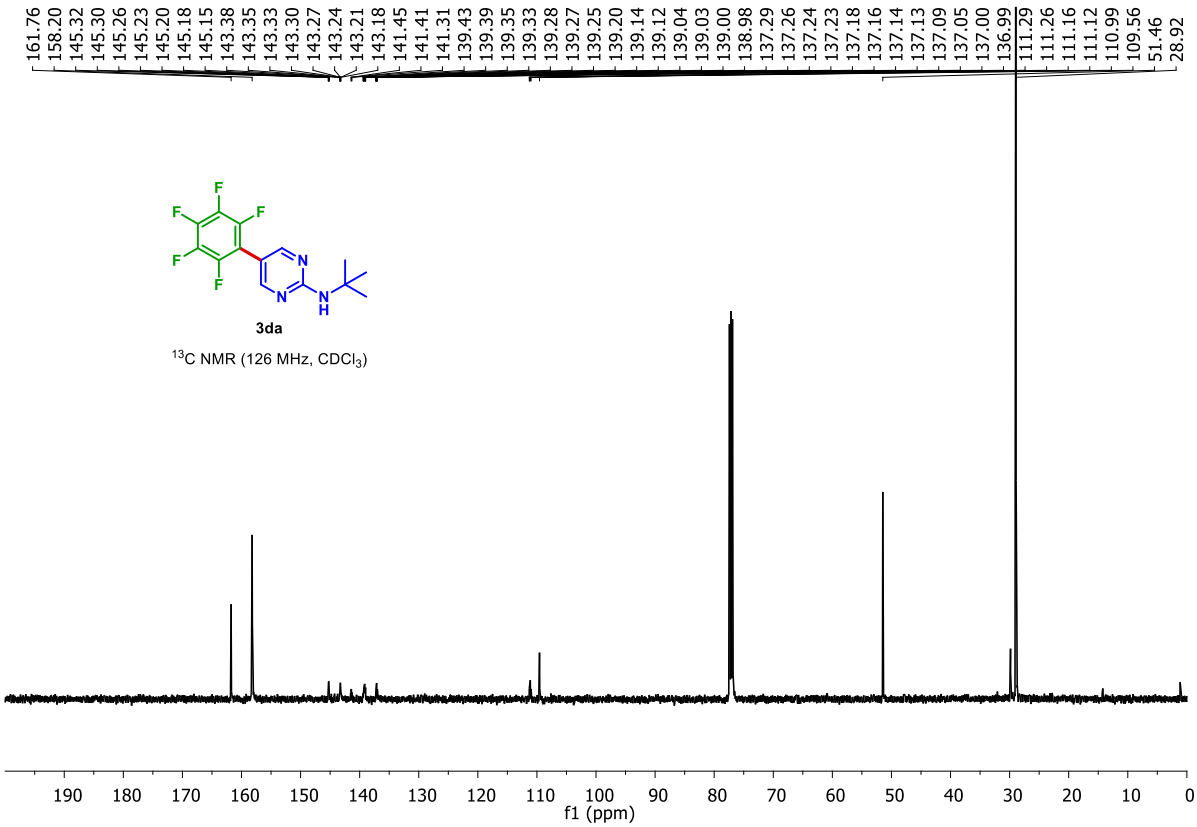


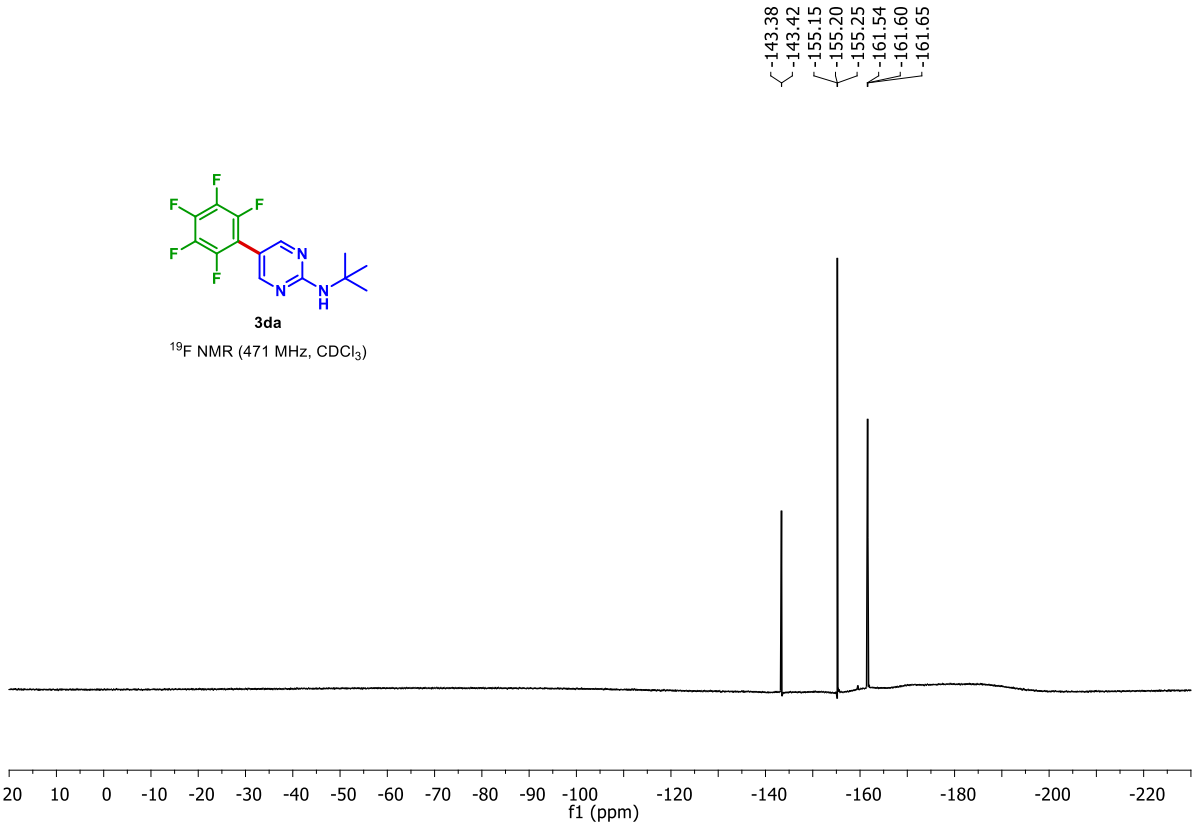
3ca

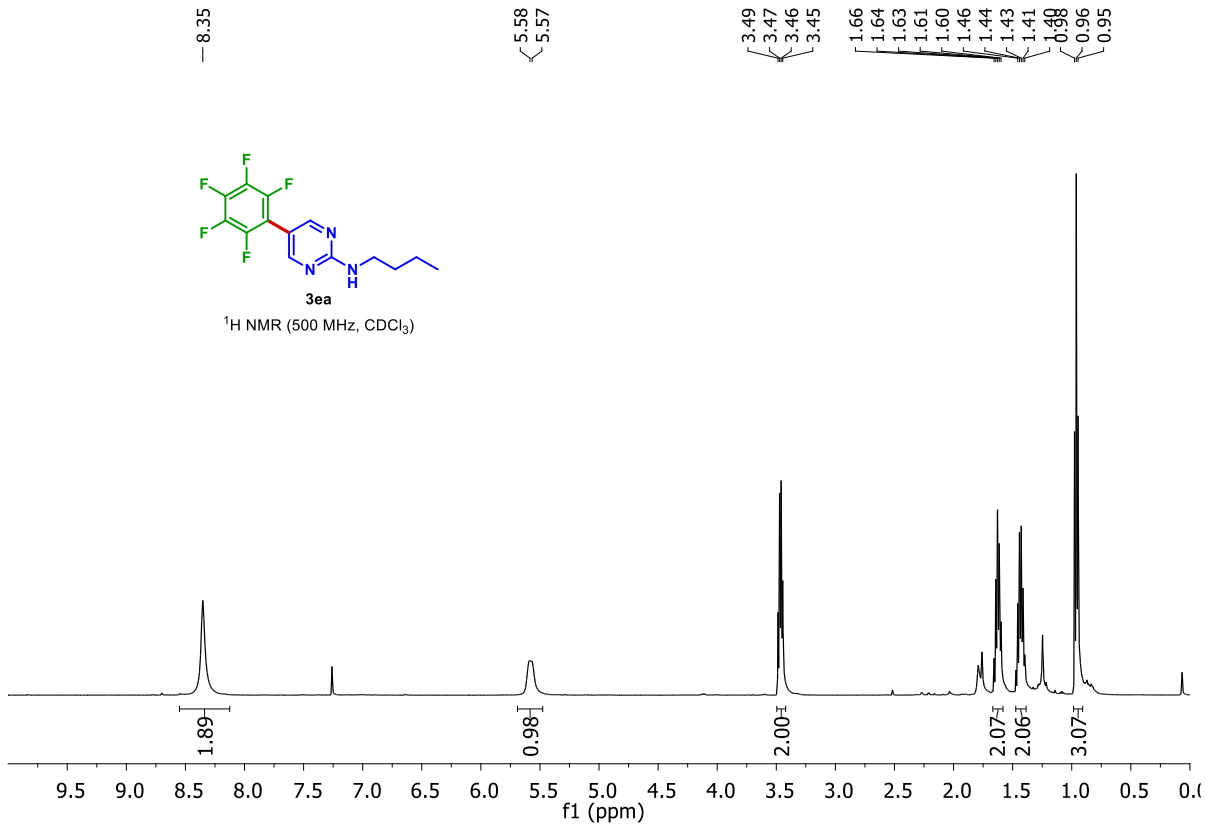
^{19}F NMR (471 MHz, $CDCl_3$)

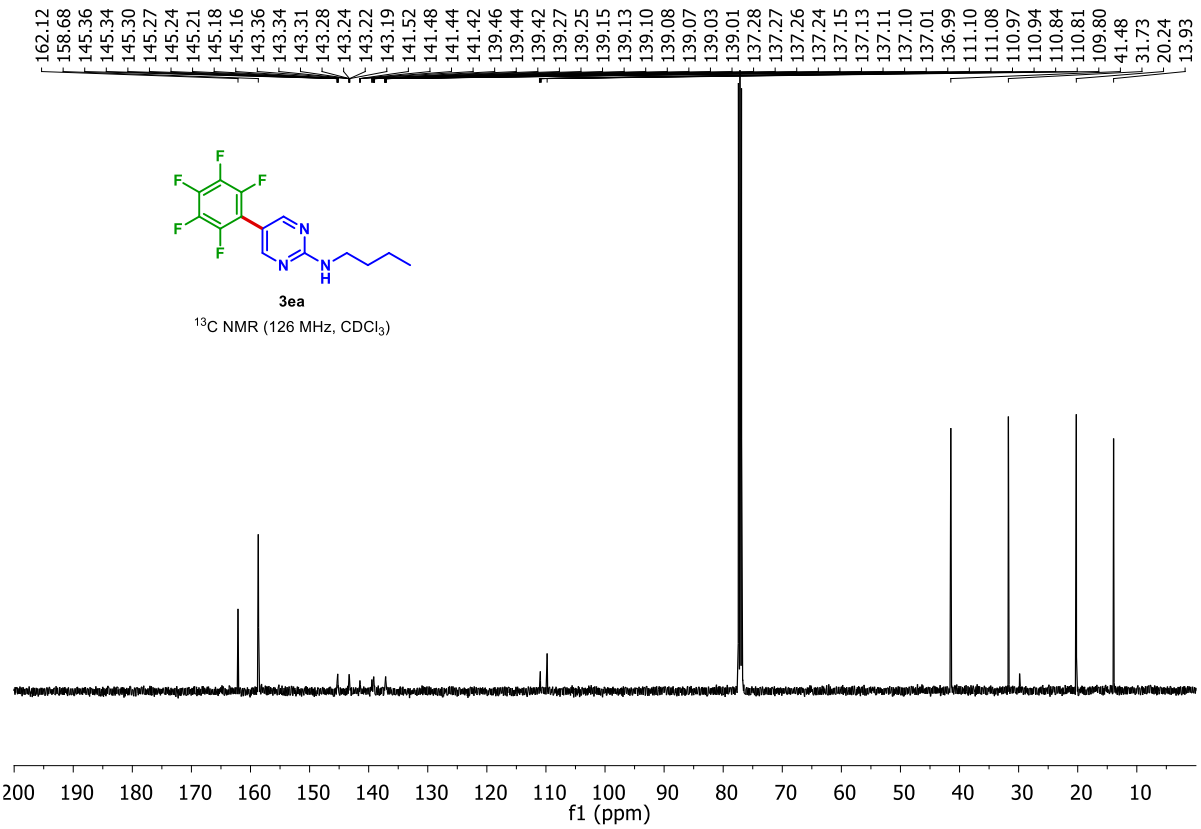



8.33
5.53
1.47
3da
1H NMR (400 MHz, CDCl3)
1.98
1.00
9.08
f1 (ppm)


161.76
158.20
145.32
145.30
145.26
145.23
145.20
145.18
145.15
143.38
143.35
143.33
143.30
143.27
143.24
143.21
143.18
141.45
141.41
141.31
139.43
139.39
139.35
139.33
139.28
139.27
139.25
139.20
139.14
139.12
139.04
139.03
139.00
138.98
137.29
137.26
137.24
137.23
137.18
137.16
137.14
137.13
137.09
137.05
137.00
136.99
111.29
111.26
111.16
111.12
110.99
109.56
51.46
28.92
3da
13C NMR (126 MHz, CDCl3)
f1 (ppm)

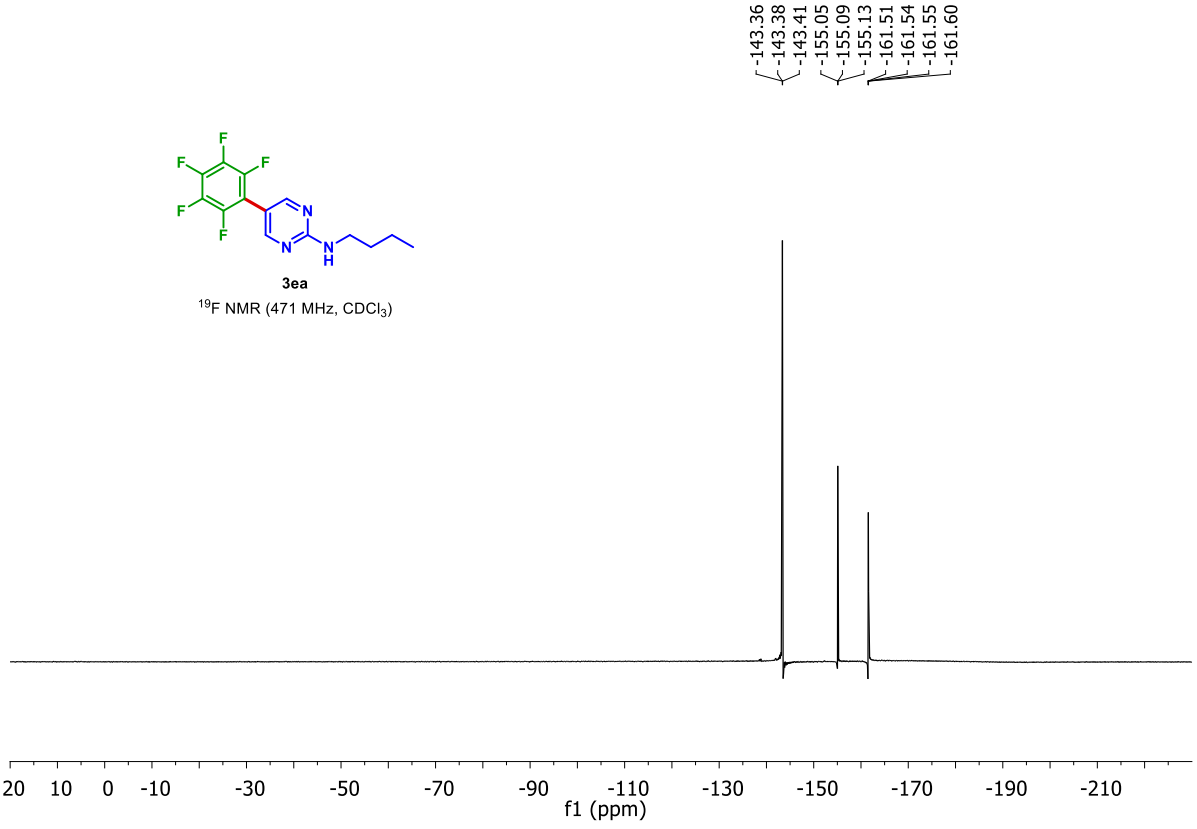

-143.38
-143.42
-155.15
-155.20
-155.25
-161.54
-161.60
-161.65
3da
19F NMR (471 MHz, CDCl3)
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200 -220
f1 (ppm)


8.35
5.58
5.57
3.49
3.47
3.46
3.45
1.66
1.64
1.63
1.61
1.60
1.46
1.44
1.43
1.41
1.40
0.98
0.96
0.95
3ea
1H NMR (500 MHz, CDCl3)
1.89
0.98
2.00
2.07
2.06
3.07
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)



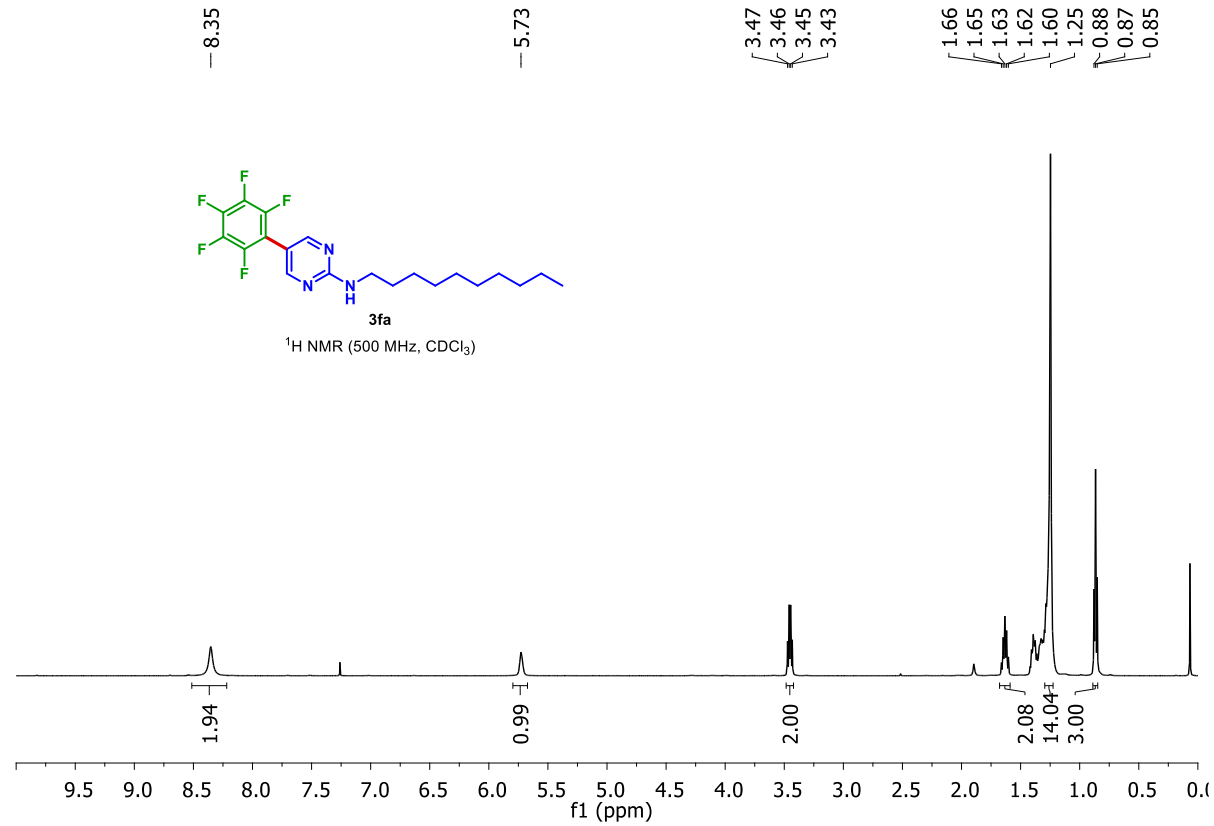
3ea

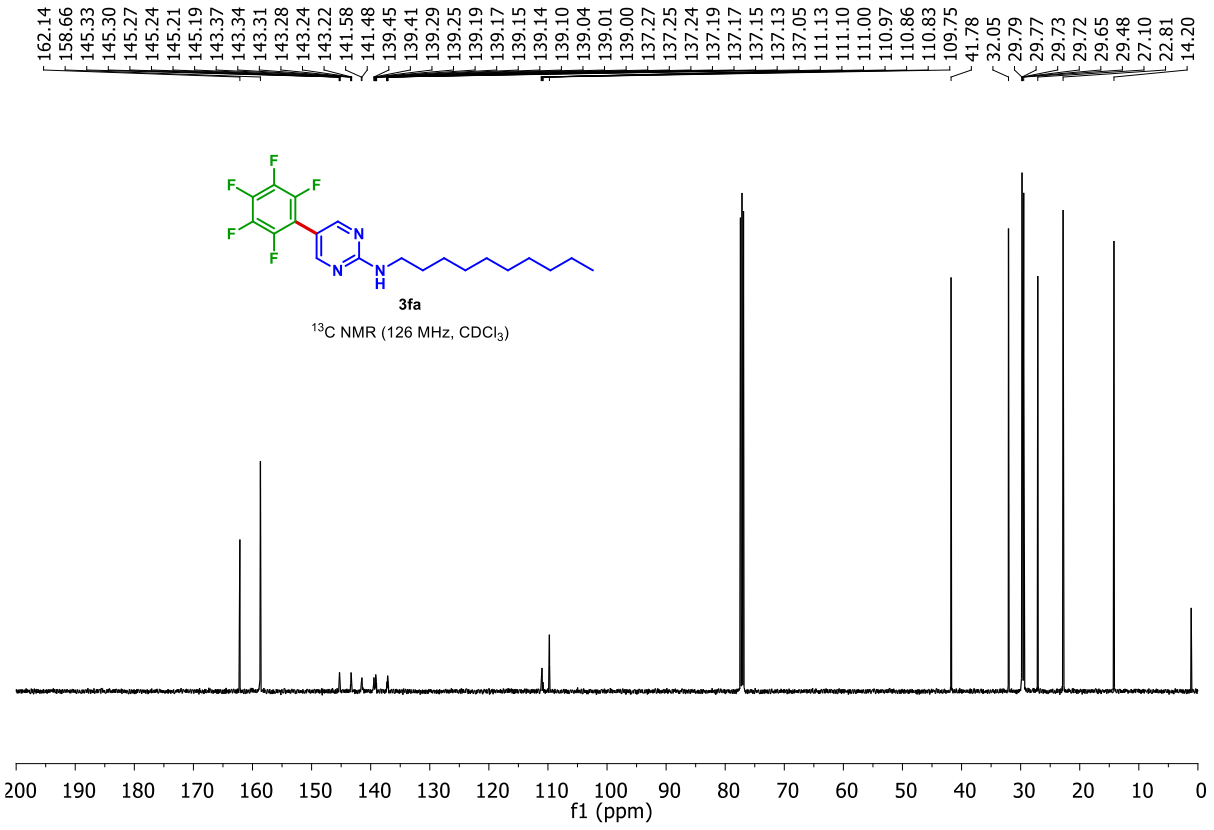
^{13}C NMR (126 MHz, $CDCl_3$)

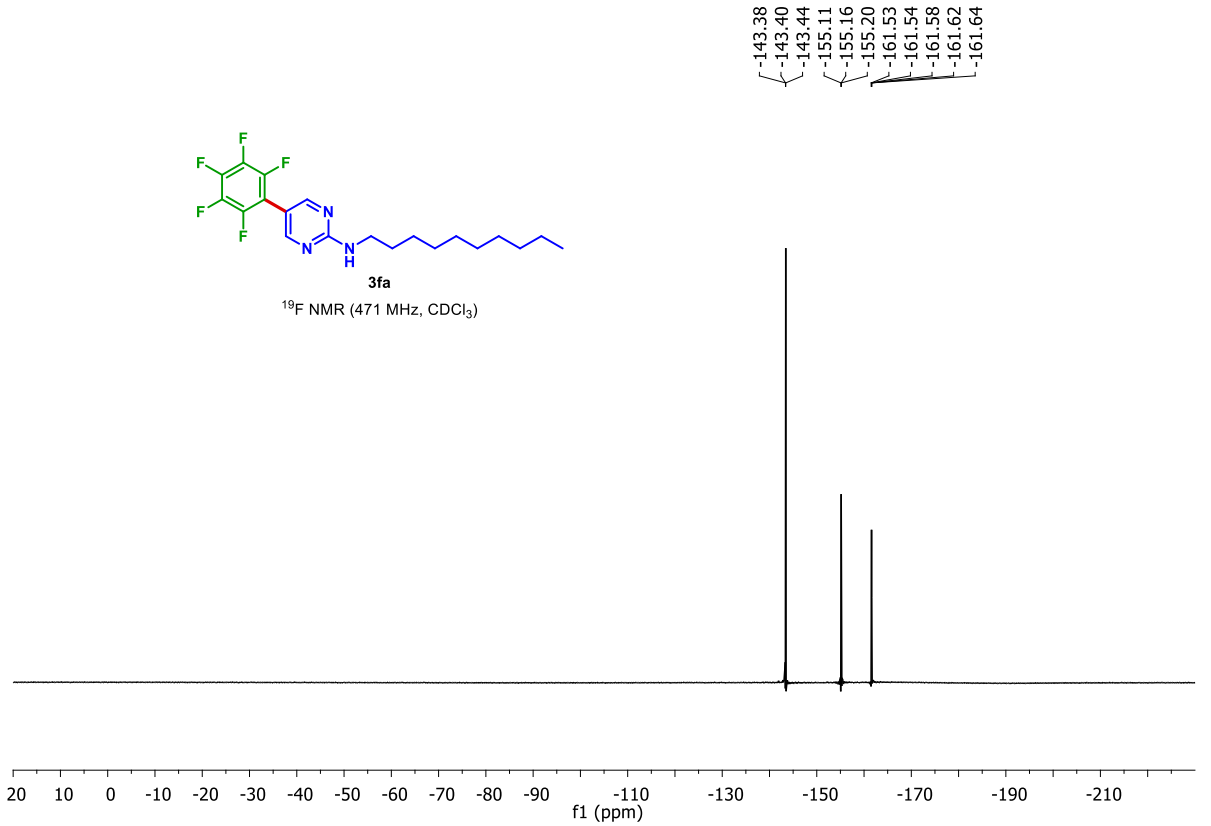


3ea

^{19}F NMR (471 MHz, $CDCl_3$)

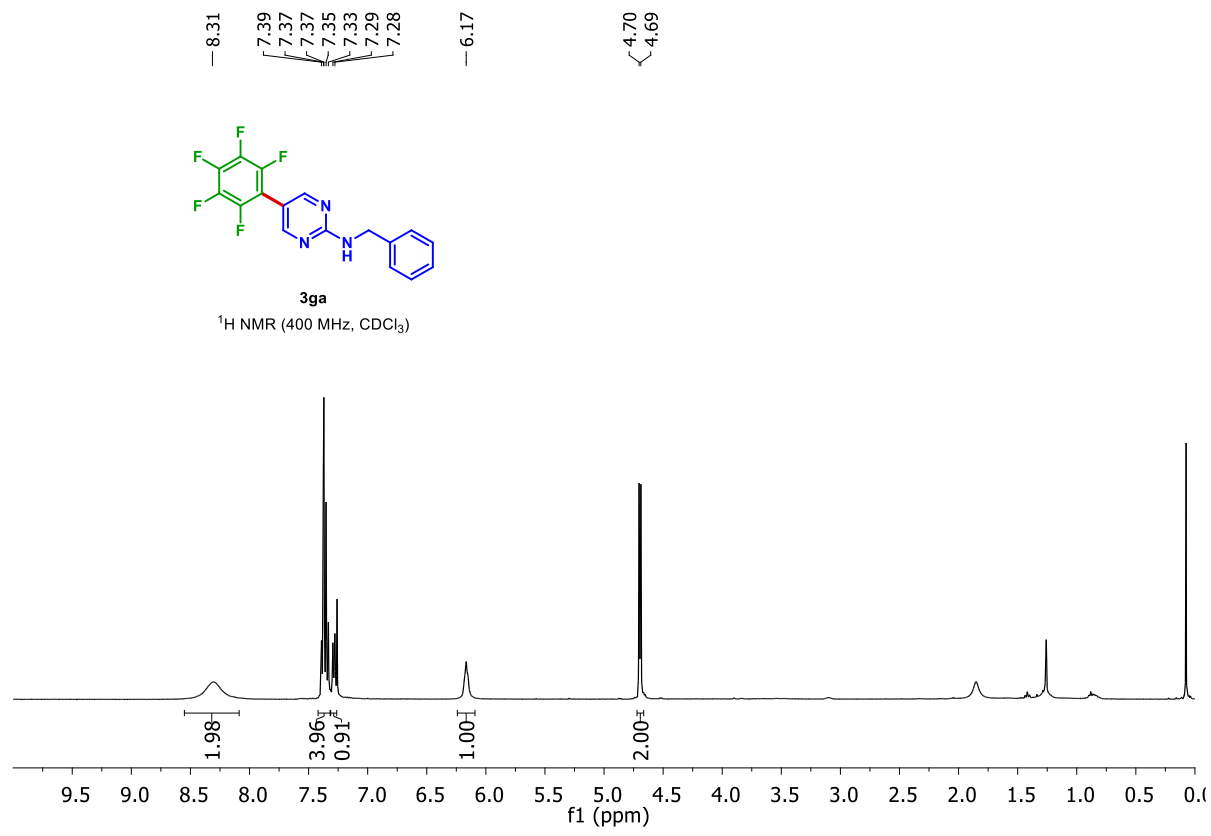

8.35
5.73
3.47
3.46
3.45
3.43
1.66
1.65
1.63
1.62
1.60
1.25
0.88
0.87
0.85
F
F
F
F
F
N
N
N
H
3fa
1H NMR (500 MHz, CDCl3)
1.94
0.99
2.00
2.08
14.04
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


162.14
158.66
145.33
145.30
145.27
145.24
145.21
145.19
143.37
143.34
143.31
143.28
143.24
143.22
141.58
141.48
139.45
139.41
139.29
139.25
139.19
139.17
139.15
139.14
139.10
139.04
139.01
139.00
137.27
137.25
137.24
137.19
137.17
137.15
137.13
137.05
111.13
111.10
111.00
110.97
110.86
110.83
109.75
41.78
32.05
29.79
29.77
29.73
29.72
29.65
29.48
27.10
22.81
14.20
F
F
F
F
F
N
N
N
H
3fa
13C NMR (126 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



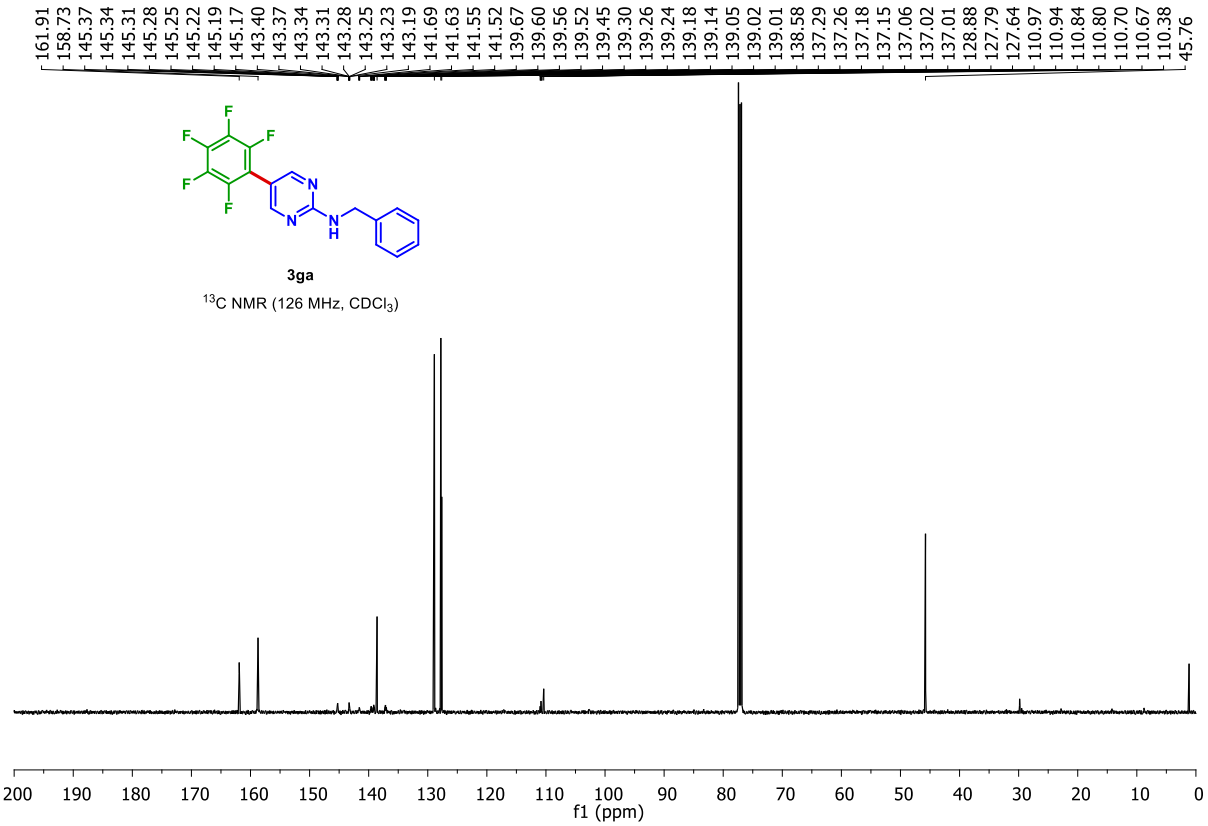
3fa

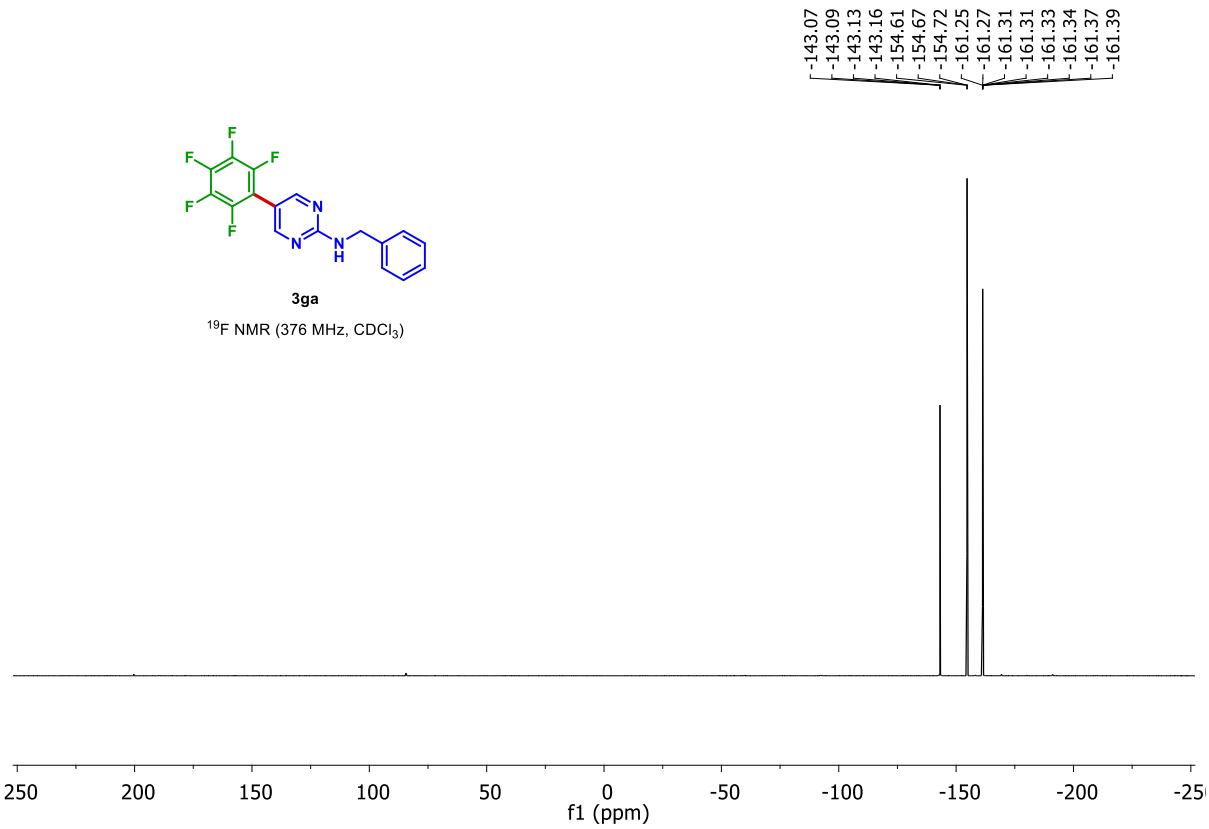
^{19}F NMR (471 MHz, $CDCl_3$)

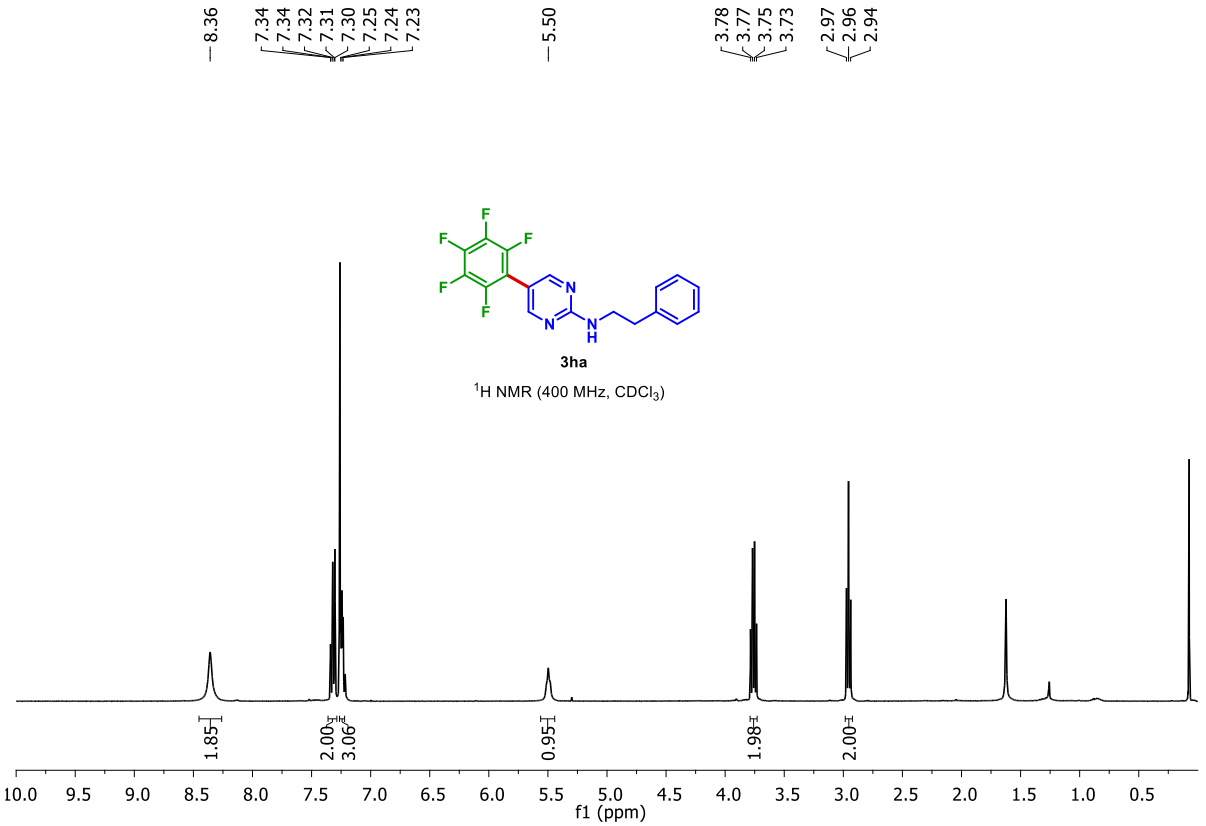


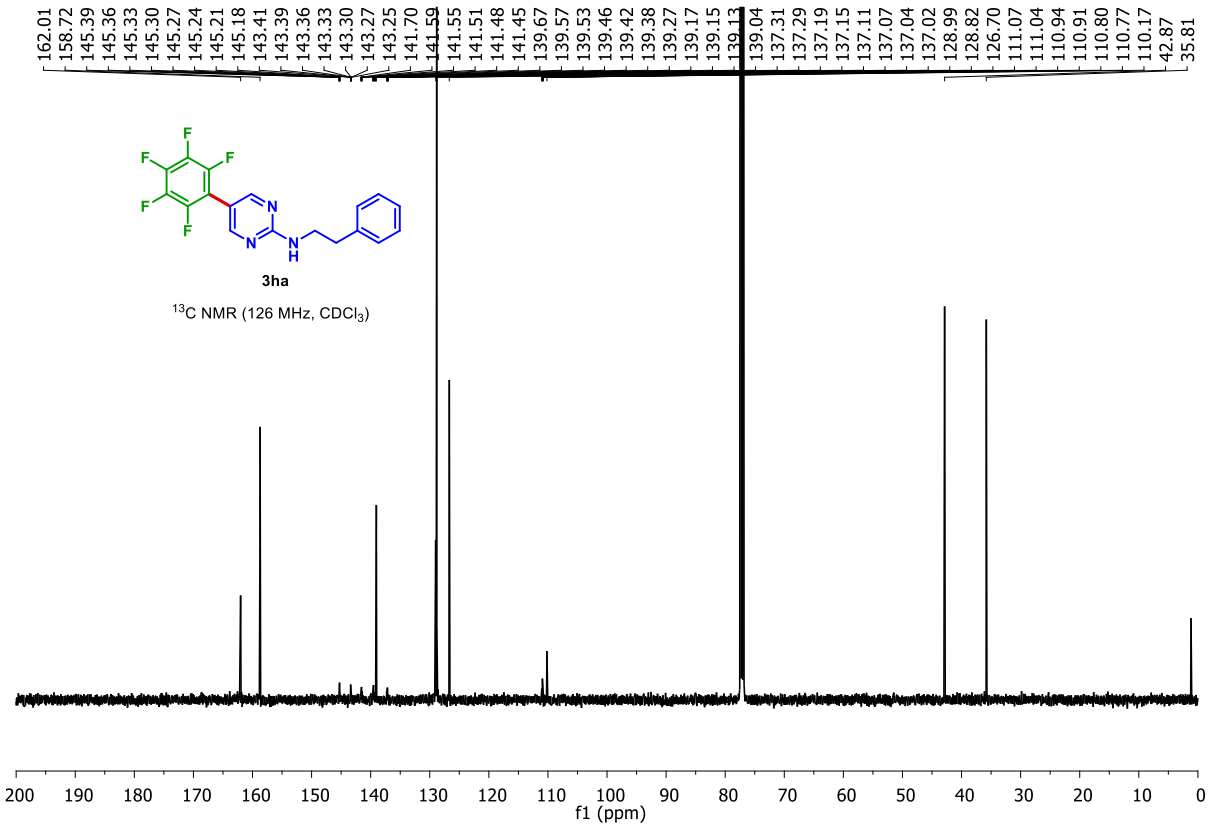
3ga

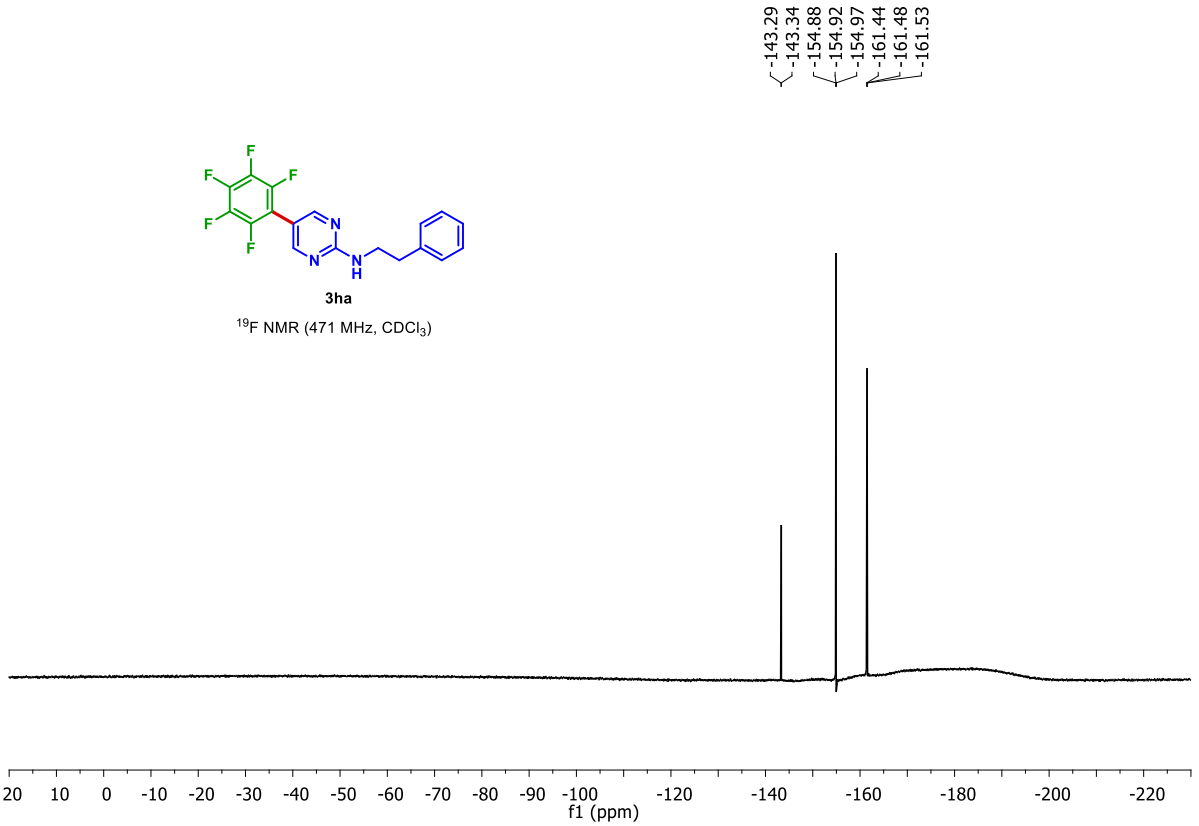
^{1}H NMR (400 MHz, $CDCl_3$)

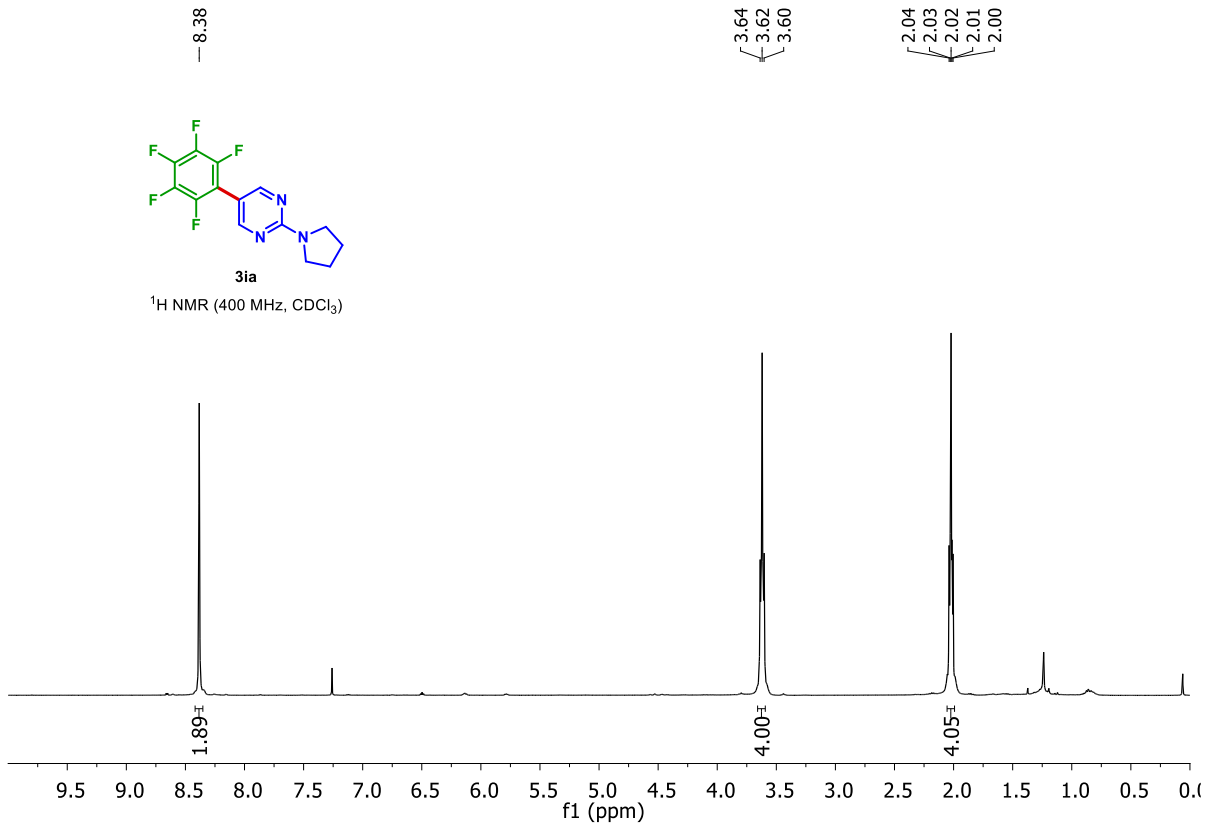

161.91
158.73
145.37
145.34
145.31
145.28
145.25
145.22
145.19
145.17
143.40
143.37
143.34
143.31
143.28
143.25
143.23
143.19
141.69
141.63
141.55
141.52
139.67
139.60
139.56
139.52
139.45
139.30
139.26
139.24
139.18
139.14
139.05
139.02
139.01
138.58
137.29
137.26
137.18
137.15
137.06
137.02
137.01
128.88
127.79
127.64
110.97
110.94
110.84
110.80
110.70
110.67
110.38
45.76
F
F
F
F
F
N
N
H
3ga
^{13}C NMR (126 MHz, $CDCl_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

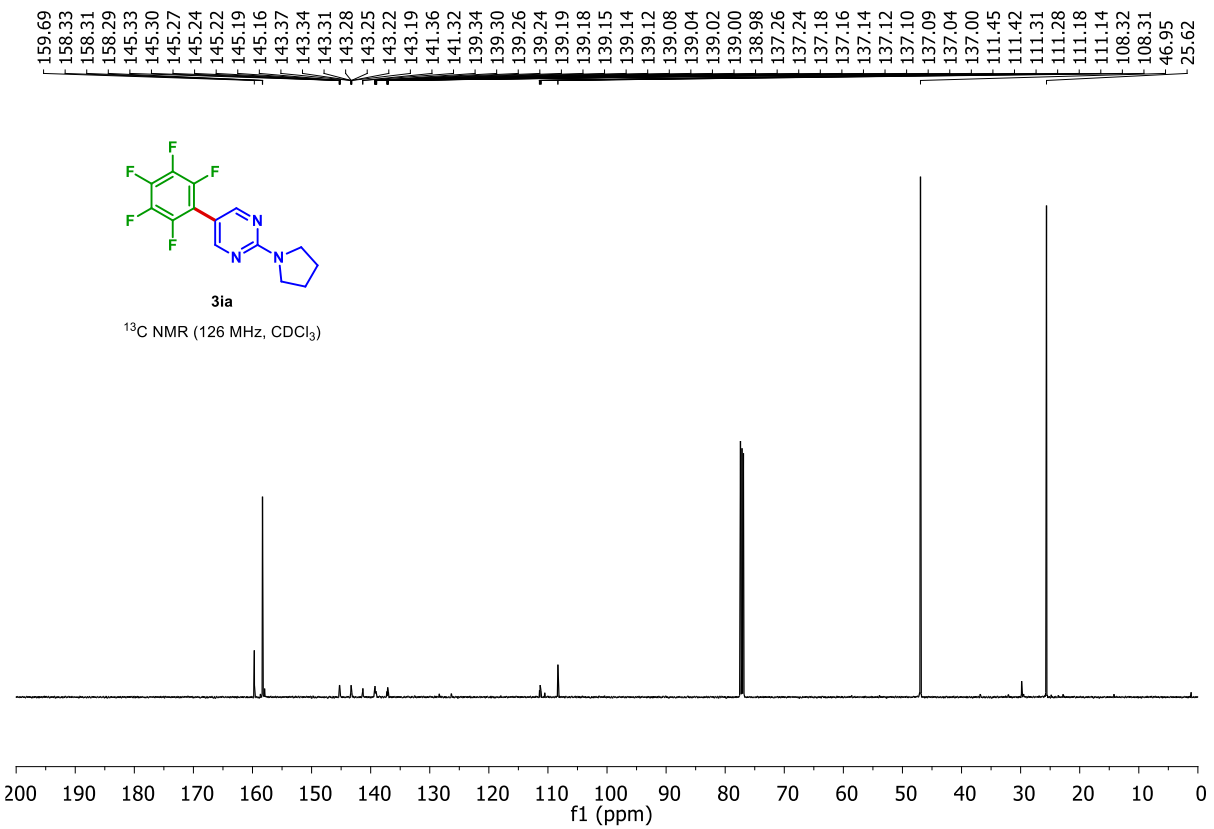

-143.07
-143.09
-143.13
-143.16
-154.61
-154.67
-154.72
-161.25
-161.27
-161.31
-161.31
-161.33
-161.34
-161.37
-161.39
F
F
F
F
F
N
N
H
3ga
^{19}F NMR (376 MHz, $CDCl_3$)
250
200
150
100
50
0
-50
-100
-150
-200
f1 (ppm)

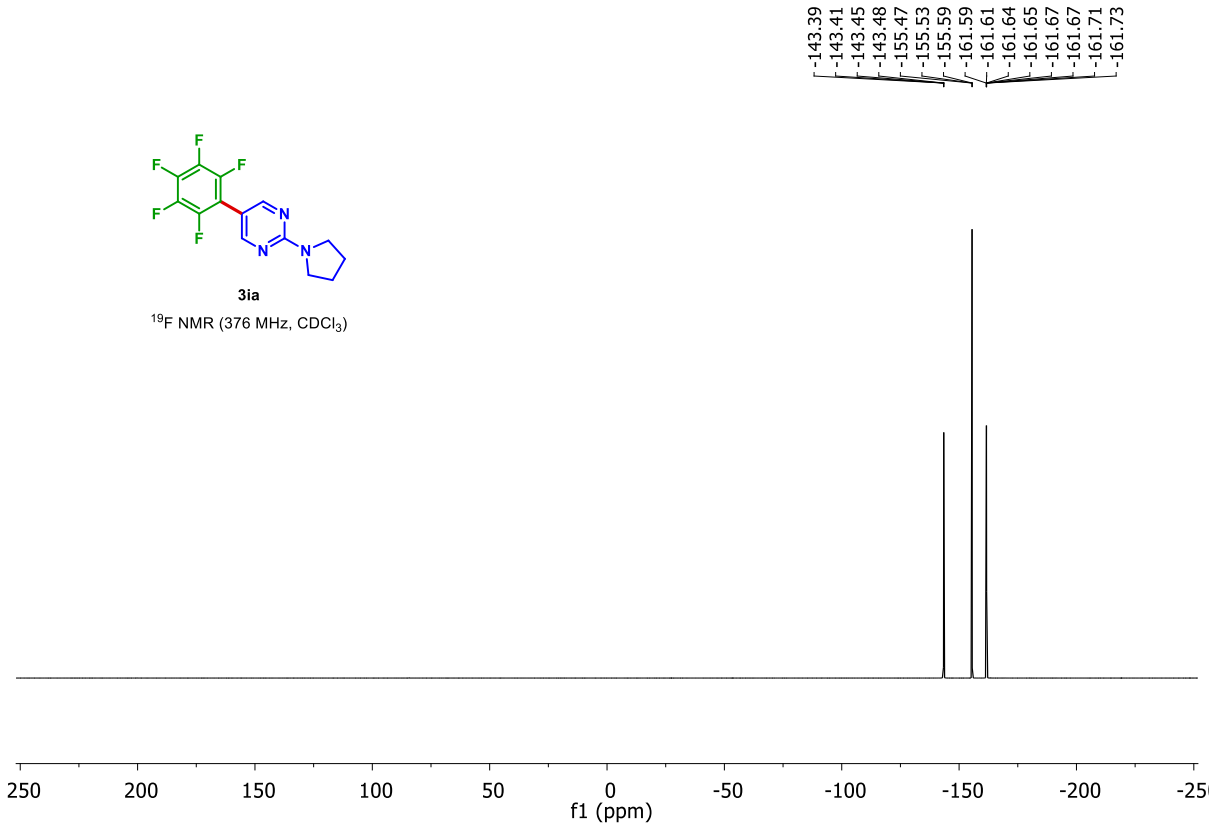

8.36
7.34
7.34
7.32
7.31
7.30
7.25
7.24
7.23
5.50
3.78
3.77
3.75
3.73
2.97
2.96
2.94
3ha
1H NMR (400 MHz, CDCl3)
1.85
2.00
3.06
0.95
1.98
2.00
f1 (ppm)

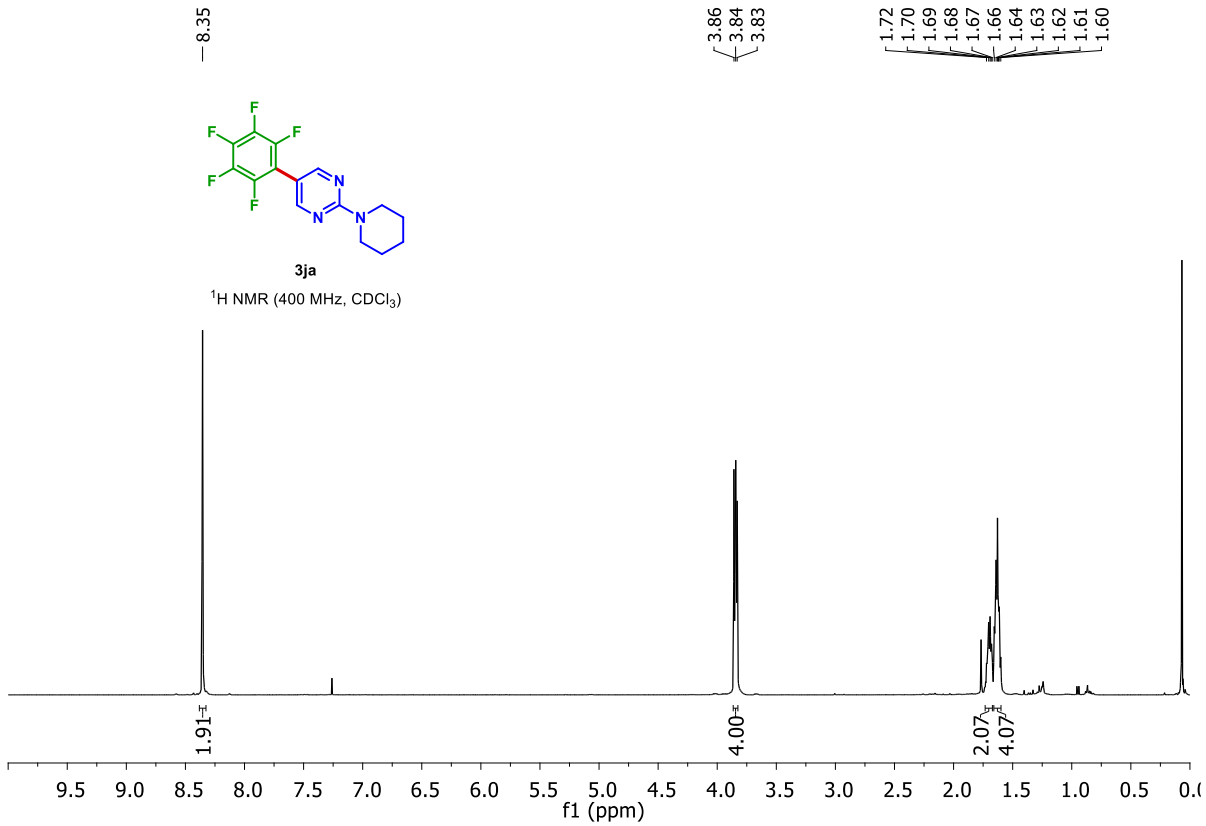

162.01
158.72
145.39
145.36
145.33
145.30
145.27
145.24
145.21
145.18
143.41
143.39
143.36
143.33
143.30
143.27
143.25
141.70
141.59
141.55
141.51
141.48
141.45
139.67
139.57
139.53
139.46
139.42
139.38
139.27
139.17
139.15
139.13
139.04
137.31
137.29
137.19
137.15
137.11
137.07
137.04
137.02
128.99
128.82
126.70
111.07
111.04
110.94
110.91
110.80
110.77
110.17
42.87
35.81
3ha
13C NMR (126 MHz, CDCl3)
f1 (ppm)

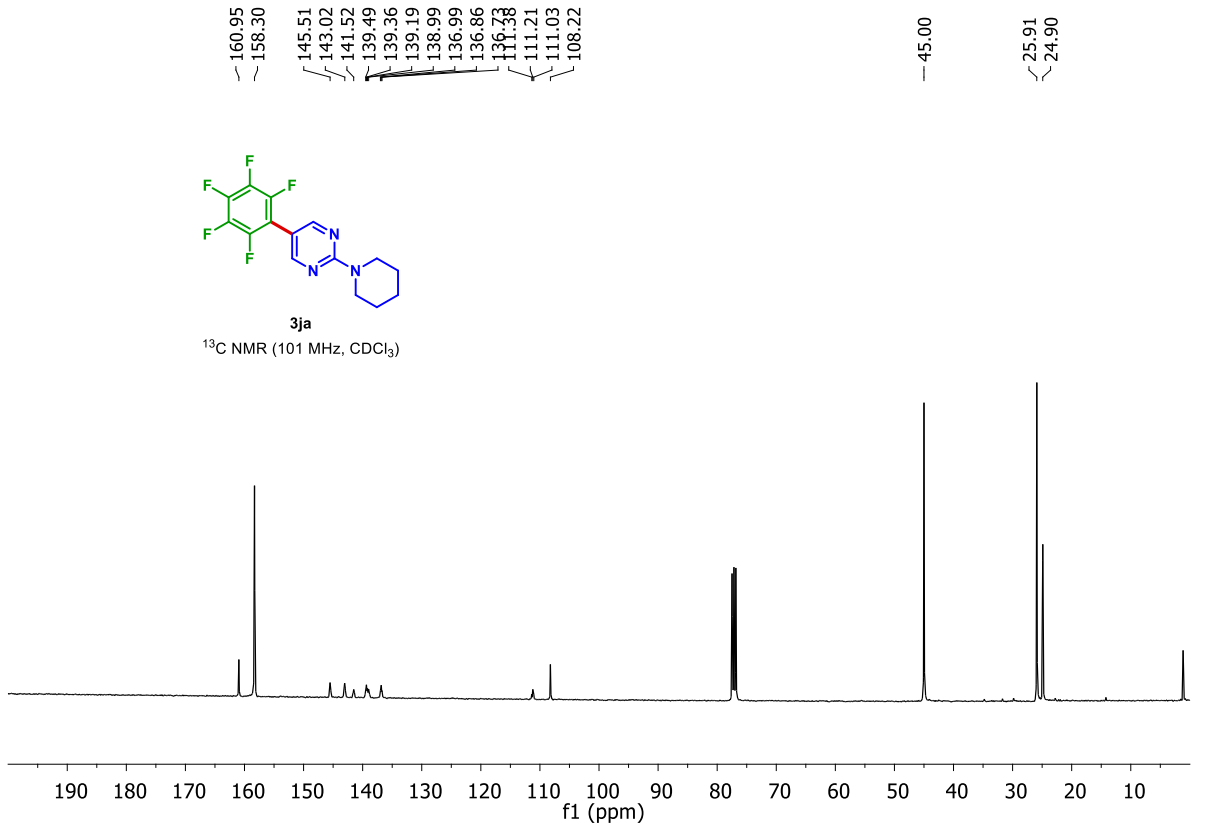

-143.29
-143.34
-154.88
-154.92
-154.97
-161.44
-161.48
-161.53
3ha
19F NMR (471 MHz, CDCl3)
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200 -220
f1 (ppm)

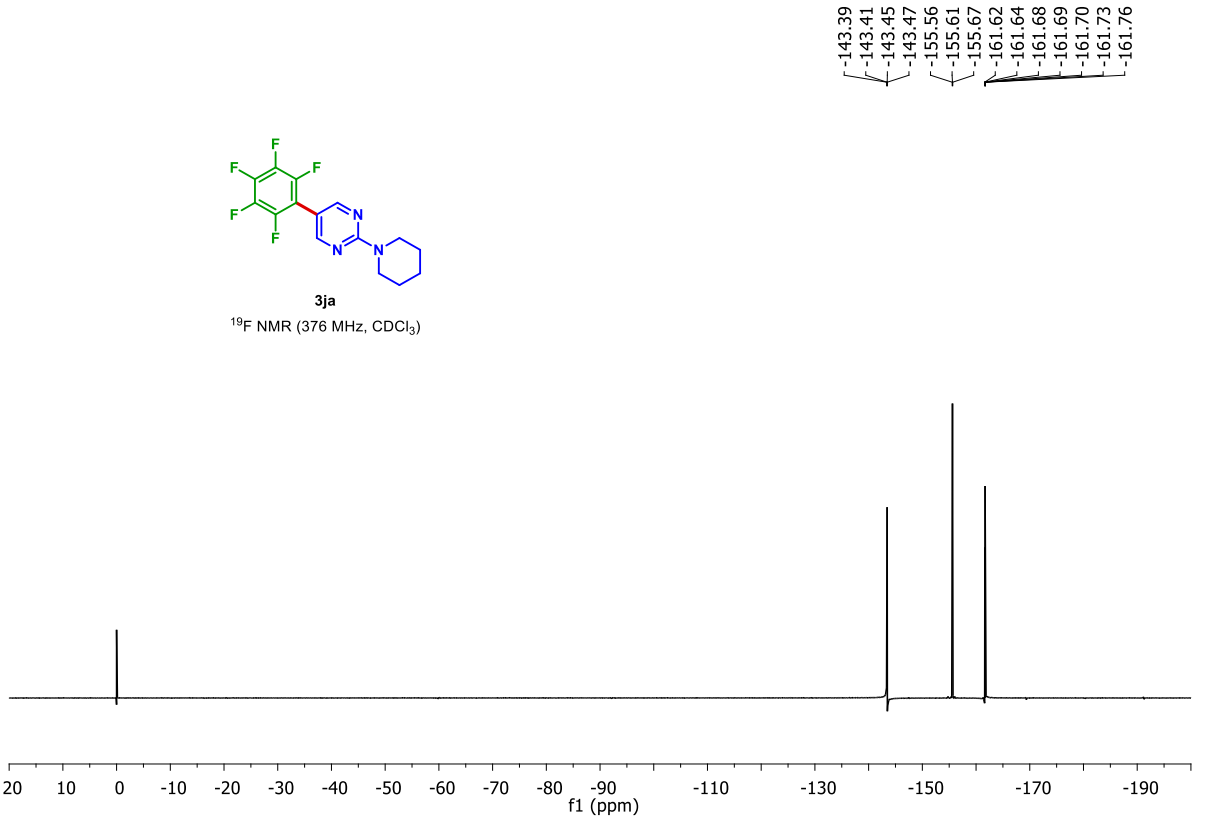

8.38
3.64
3.62
3.60
2.04
2.03
2.02
2.01
2.00
3ia
1H NMR (400 MHz, CDCl3)
1.89
4.00
4.05
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

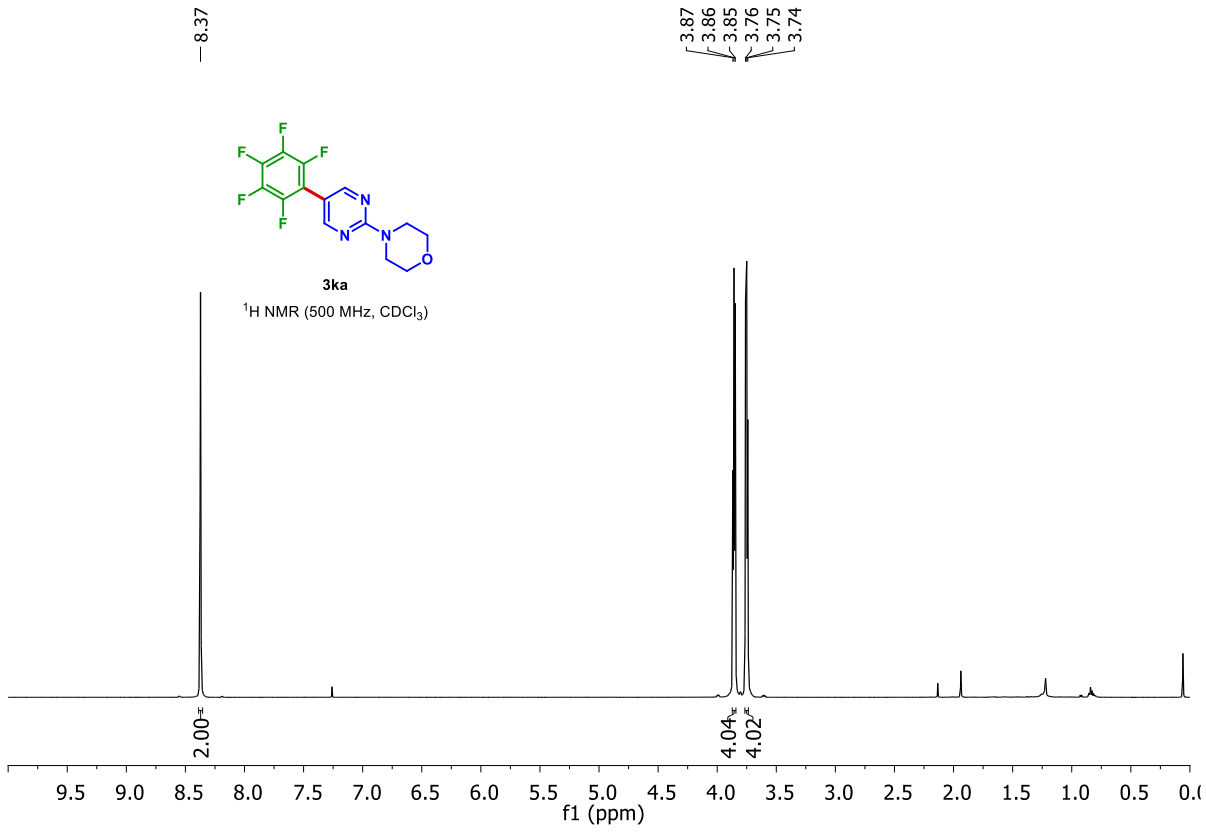

159.69
158.33
158.31
158.29
145.33
145.30
145.27
145.24
145.22
145.19
145.16
143.37
143.34
143.31
143.28
143.25
143.22
143.19
141.36
141.32
139.34
139.30
139.26
139.24
139.19
139.18
139.15
139.14
139.12
139.08
139.04
139.02
139.00
138.98
137.26
137.24
137.18
137.16
137.14
137.12
137.10
137.09
137.04
137.00
111.45
111.42
111.31
111.28
111.18
111.14
108.32
108.31
46.95
25.62
3ia
13C NMR (126 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

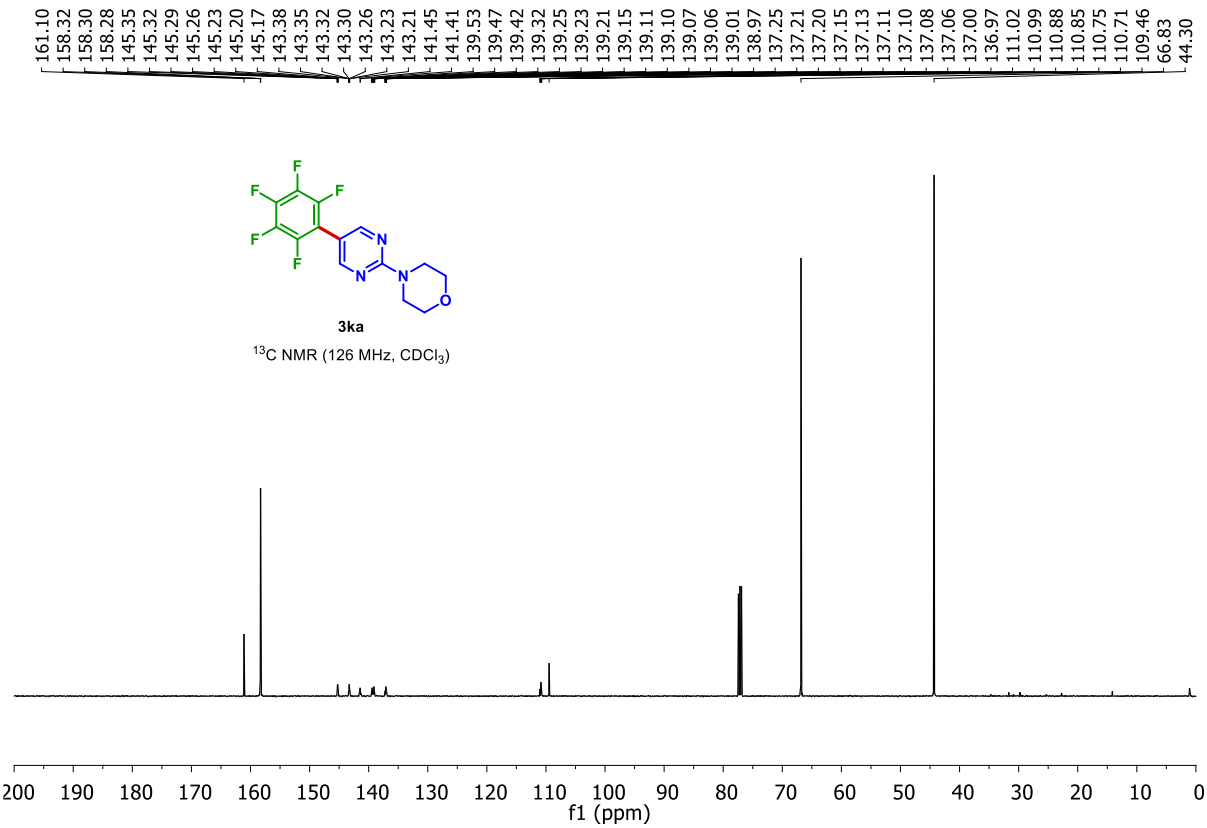

-143.39
-143.41
-143.45
-143.48
-155.47
-155.53
-155.59
-161.59
-161.61
-161.64
-161.65
-161.67
-161.67
-161.71
-161.73
3ia
19F NMR (376 MHz, CDCl3)
250 200 150 100 50 0 -50 -100 -150 -200
f1 (ppm)

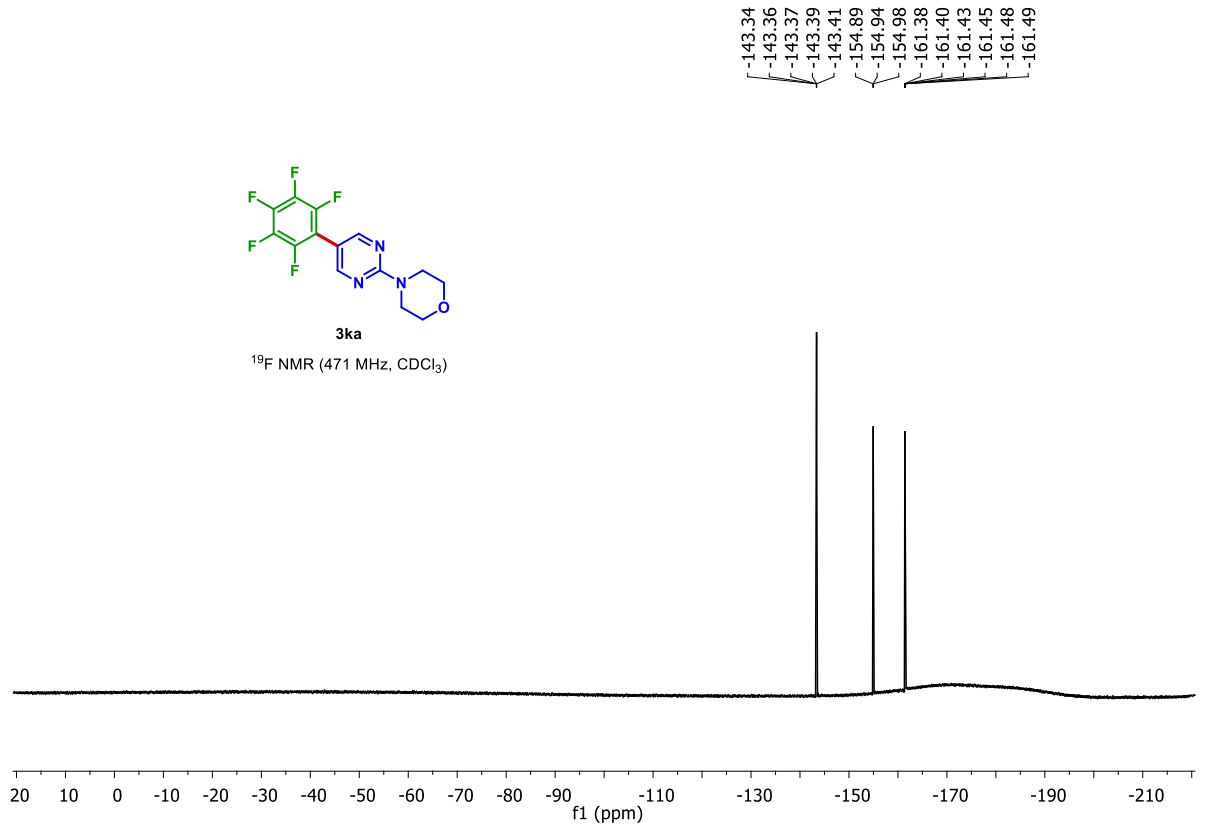

8.35
3.86
3.84
3.83
1.72
1.70
1.69
1.68
1.67
1.66
1.64
1.63
1.62
1.61
1.60
F
F
F
F
F
N
N
N
3ja
1H NMR (400 MHz, CDCl3)
1.91
4.00
2.07
4.07
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

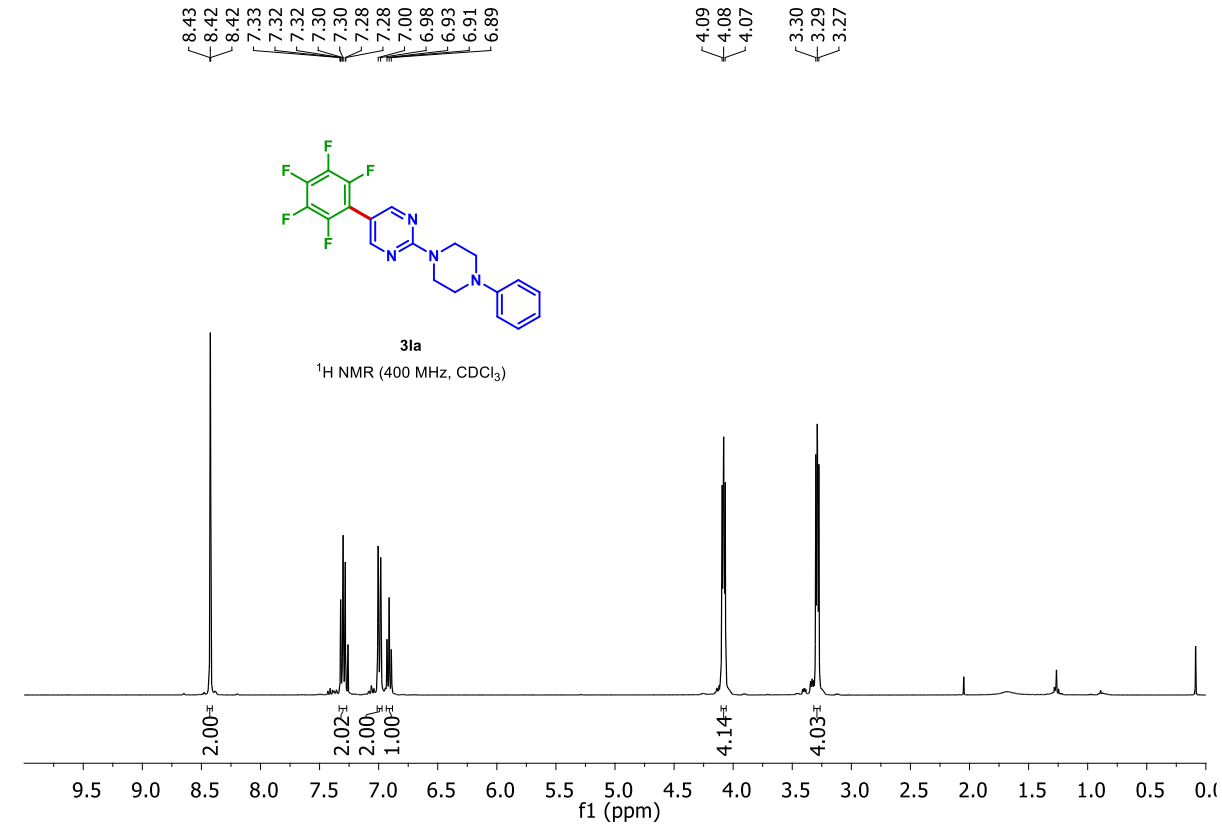

160.95
158.30
145.51
143.02
141.52
139.49
139.36
139.19
138.99
136.99
136.86
136.73
111.38
111.21
111.03
108.22
45.00
25.91
24.90
F
F
F
F
F
N
N
N
3ja
13C NMR (101 MHz, CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

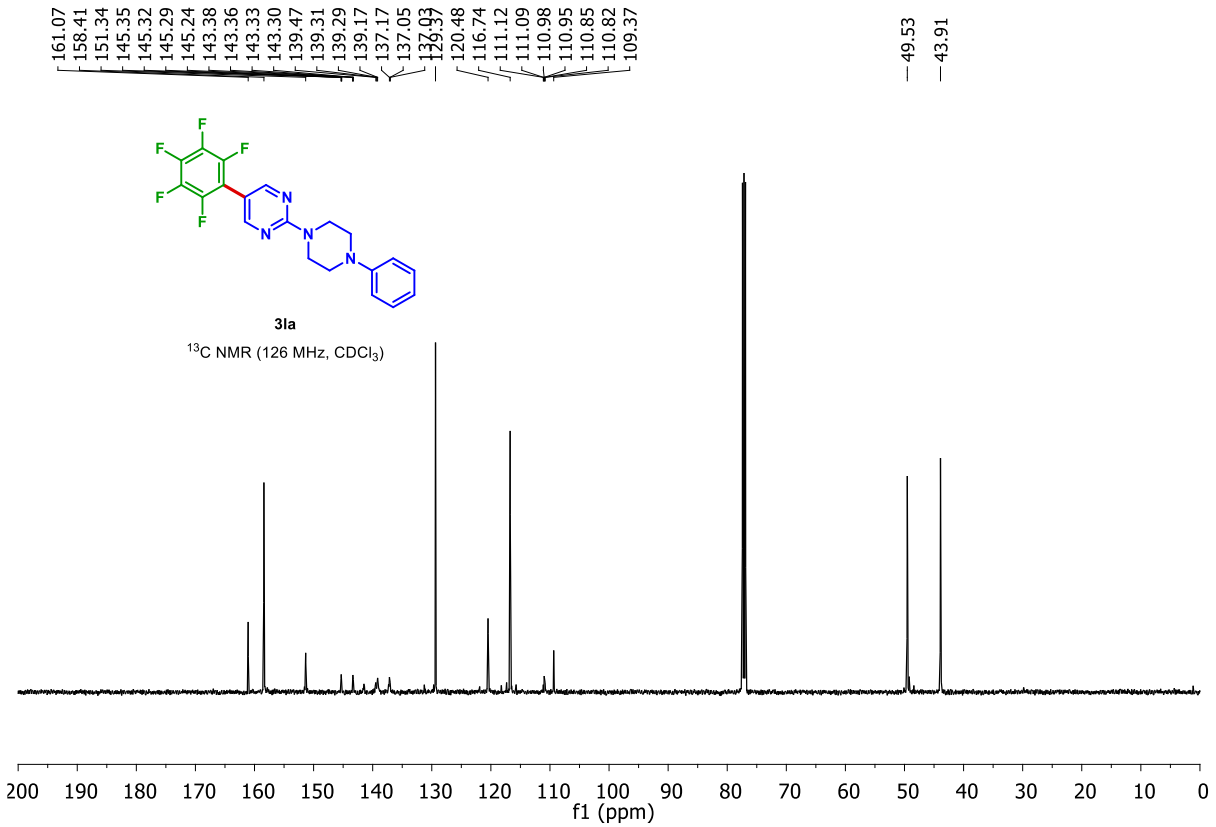

-143.39
-143.41
-143.45
-143.47
-155.56
-155.61
-155.67
-161.62
-161.64
-161.68
-161.69
-161.70
-161.73
-161.76
F
F
F
F
F
N
N
N
3ja
19F NMR (376 MHz, CDCl3)
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-110
-130
-150
-170
-190
f1 (ppm)

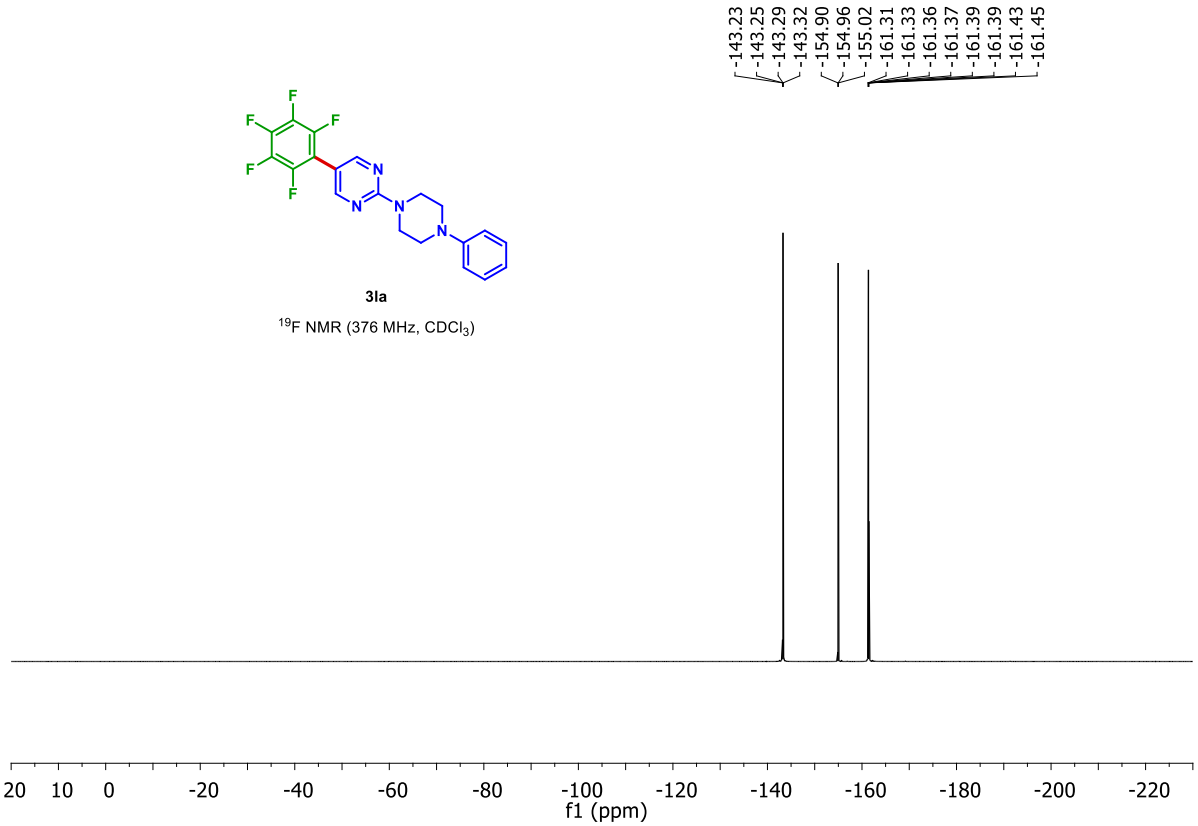

8.37
3.87
3.86
3.85
3.76
3.75
3.74
F
F
F
F
F
N
N
N
O
3ka
1H NMR (500 MHz, CDCl3)
2.00
4.04
4.02
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


161.10
158.32
158.30
158.28
145.35
145.32
145.29
145.26
145.23
145.20
145.17
143.38
143.35
143.32
143.30
143.26
143.23
143.21
141.45
141.41
139.53
139.47
139.42
139.32
139.25
139.23
139.21
139.15
139.11
139.10
139.07
139.06
139.01
138.97
137.25
137.21
137.20
137.15
137.13
137.11
137.10
137.08
137.06
137.00
136.97
111.02
110.99
110.88
110.85
110.75
110.71
109.46
66.83
44.30
F
F
F
F
F
N
N
N
O
3ka
^{13}C NMR (126 MHz, CDCl$_3$)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-143.34
-143.36
-143.37
-143.39
-143.41
-154.89
-154.94
-154.98
-161.38
-161.40
-161.43
-161.45
-161.48
-161.49
F
F
F
F
F
N
N
N
O
3ka
^{19}F NMR (471 MHz, CDCl$_3$)
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190 -210
f1 (ppm)

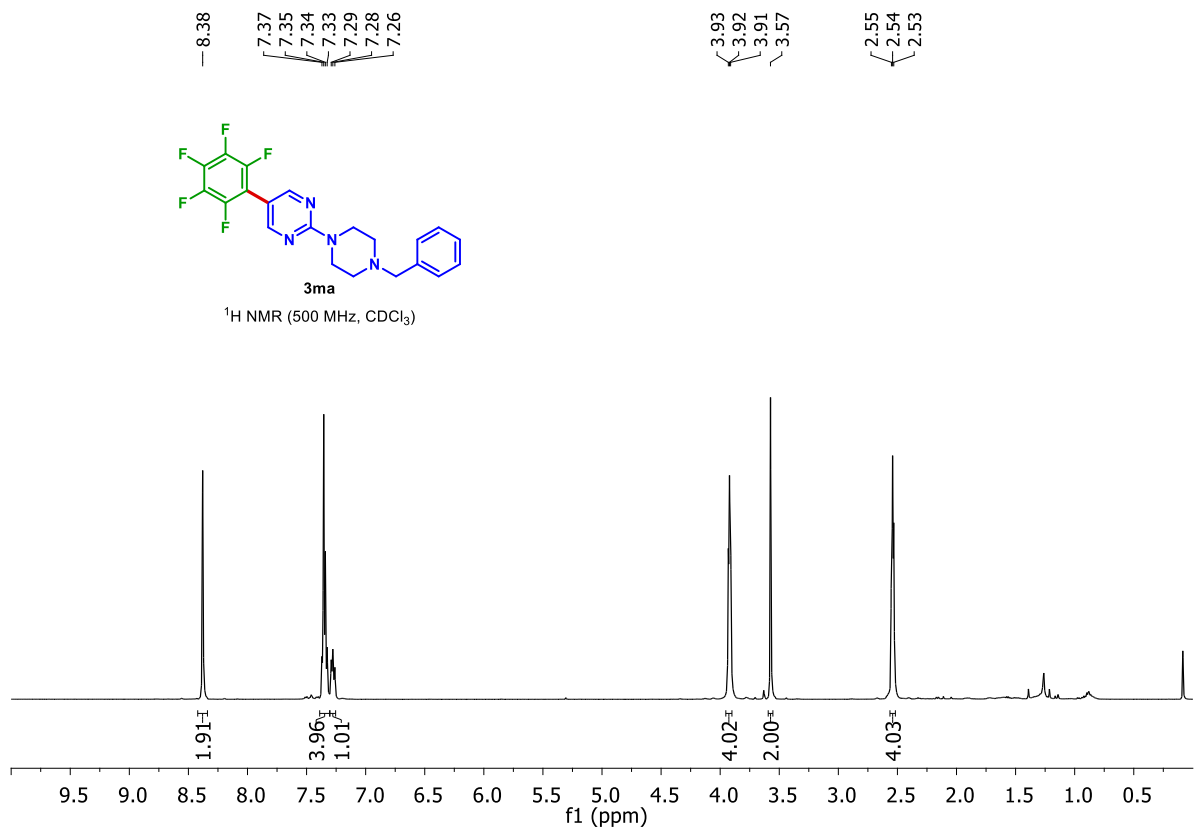

8.43
8.42
8.42
7.33
7.32
7.32
7.30
7.30
7.28
7.28
7.00
6.98
6.93
6.91
6.89
4.09
4.08
4.07
3.30
3.29
3.27
3la
^{1}H NMR (400 MHz, $CDCl_3$)
2.00
2.02
2.00
1.00
4.14
4.03
f1 (ppm)


161.07
158.41
151.34
145.35
145.32
145.29
145.24
143.38
143.36
143.33
143.30
139.47
139.31
139.29
139.17
137.17
137.05
120.48
116.74
111.12
111.09
110.98
110.95
110.85
110.82
109.37
49.53
43.91
3la
^{13}C NMR (126 MHz, $CDCl_3$)
f1 (ppm)



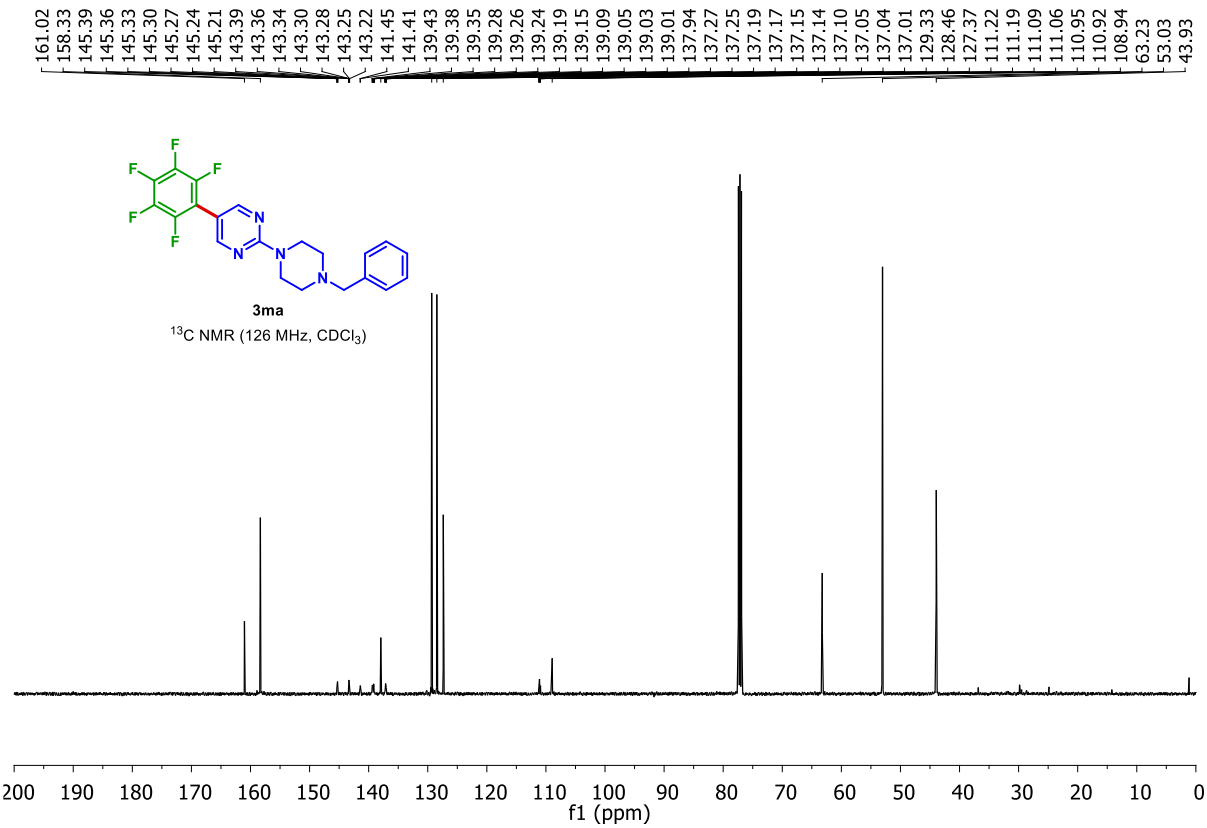
3la

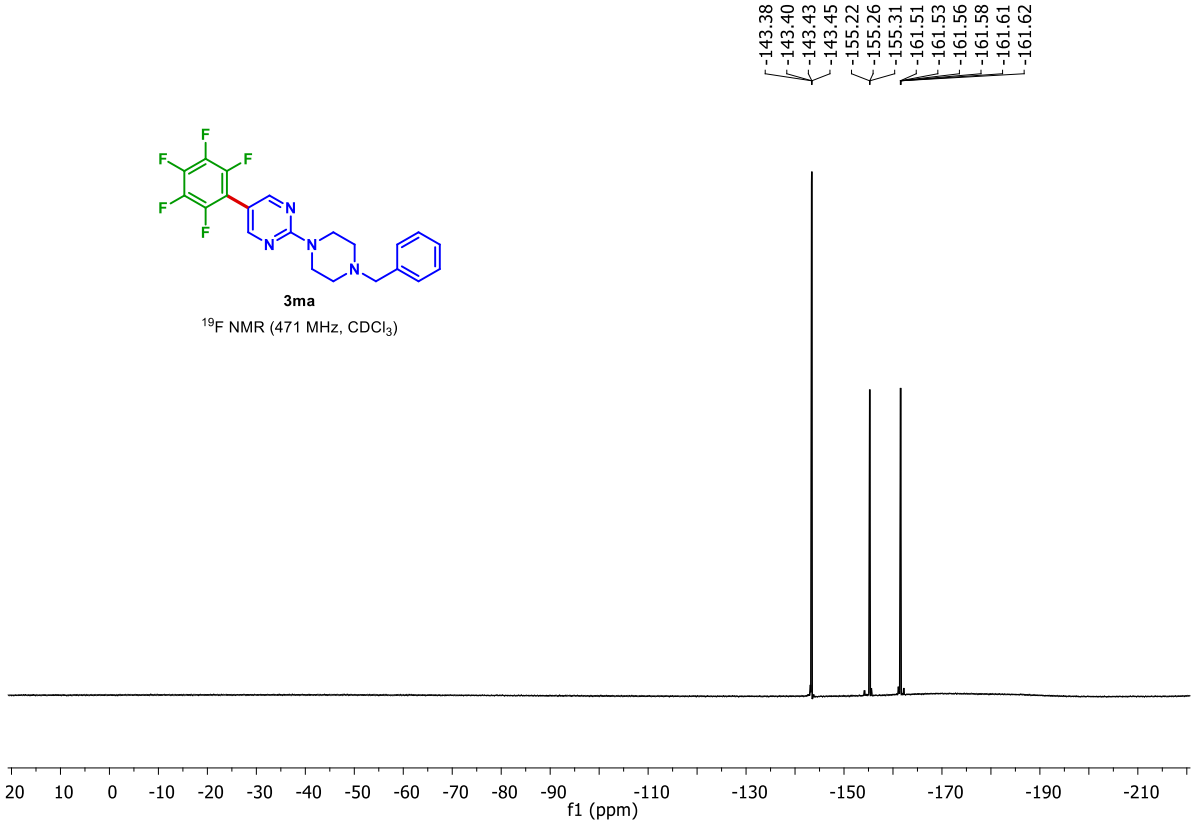
^{19}F NMR (376 MHz, $CDCl_3$)

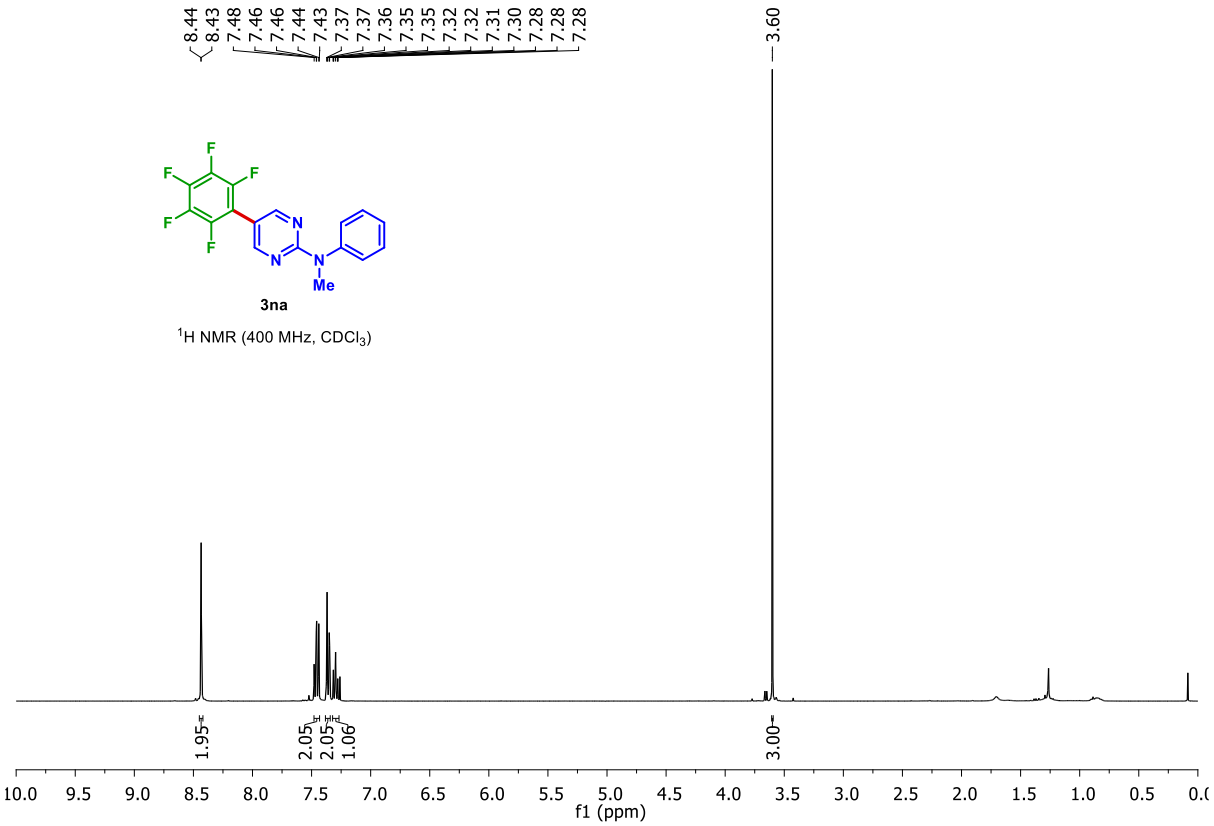


3ma

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

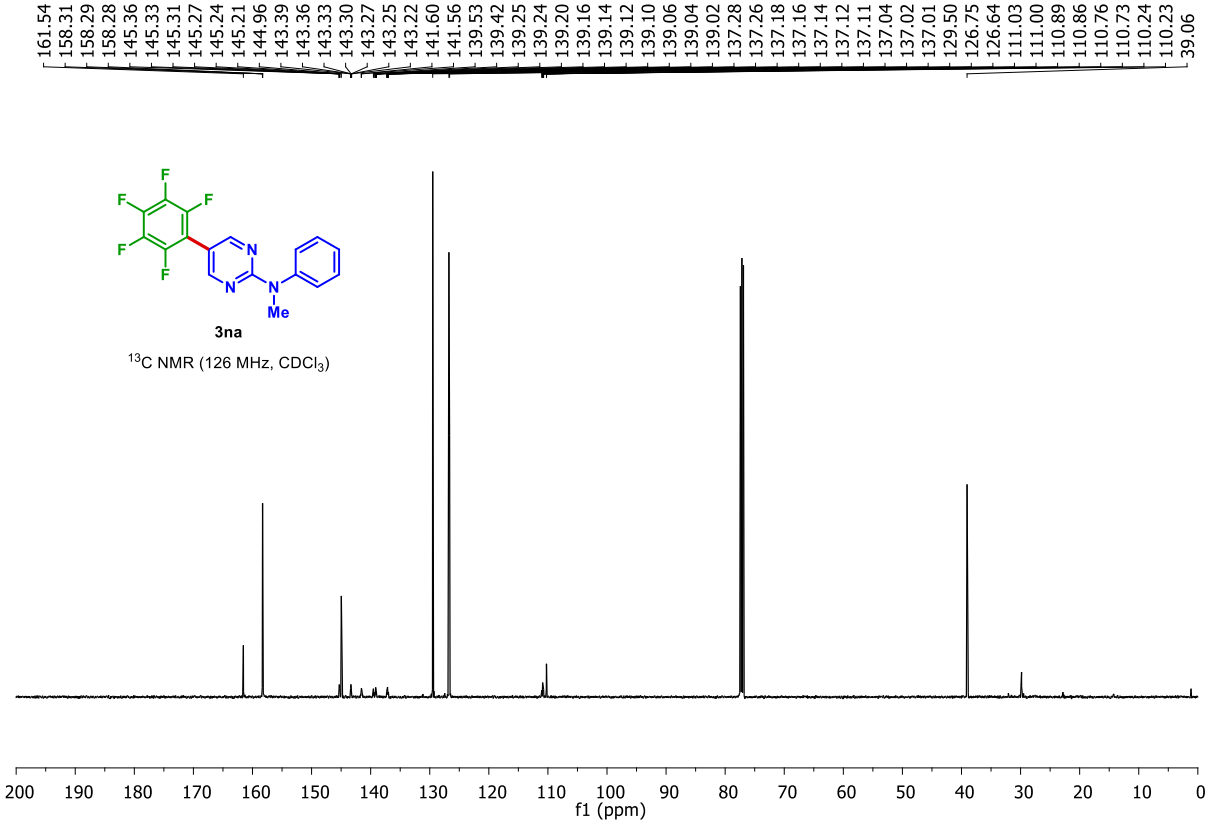

161.02
158.33
145.39
145.36
145.33
145.30
145.27
145.24
145.21
143.39
143.36
143.34
143.30
143.28
143.25
143.22
141.45
141.41
139.43
139.38
139.35
139.28
139.26
139.24
139.19
139.15
139.09
139.05
139.03
139.01
137.94
137.27
137.25
137.19
137.17
137.15
137.14
137.10
137.05
137.04
137.01
129.33
128.46
127.37
111.22
111.19
111.09
111.06
110.95
110.92
108.94
63.23
53.03
43.93
3ma
13C NMR (126 MHz, CDCl3)
f1 (ppm)


-143.38
-143.40
-143.43
-143.45
-155.22
-155.26
-155.31
-161.51
-161.53
-161.56
-161.58
-161.61
-161.62
3ma
19F NMR (471 MHz, CDCl3)
f1 (ppm)



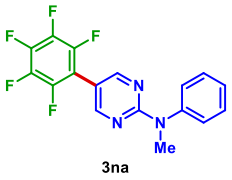
3na

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



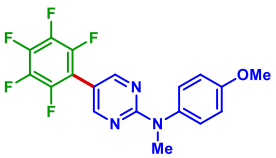
3na

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



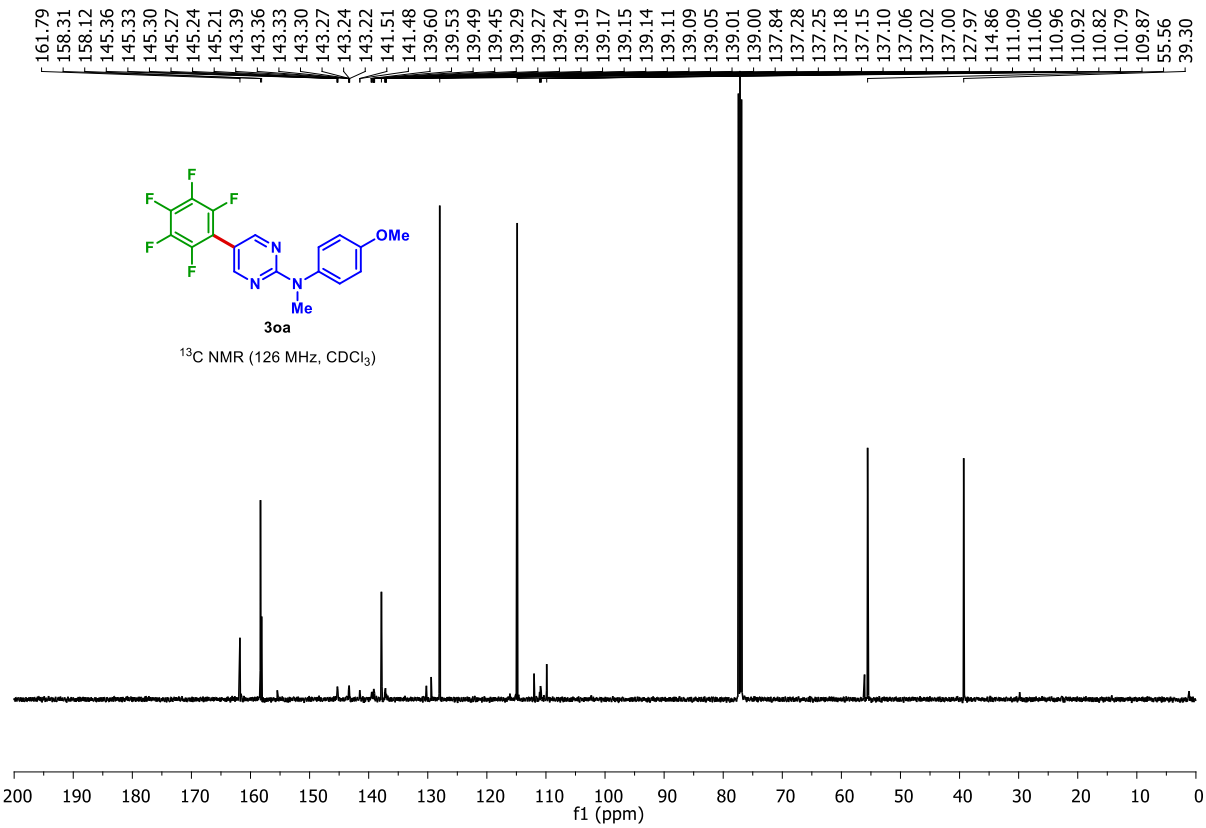
3na

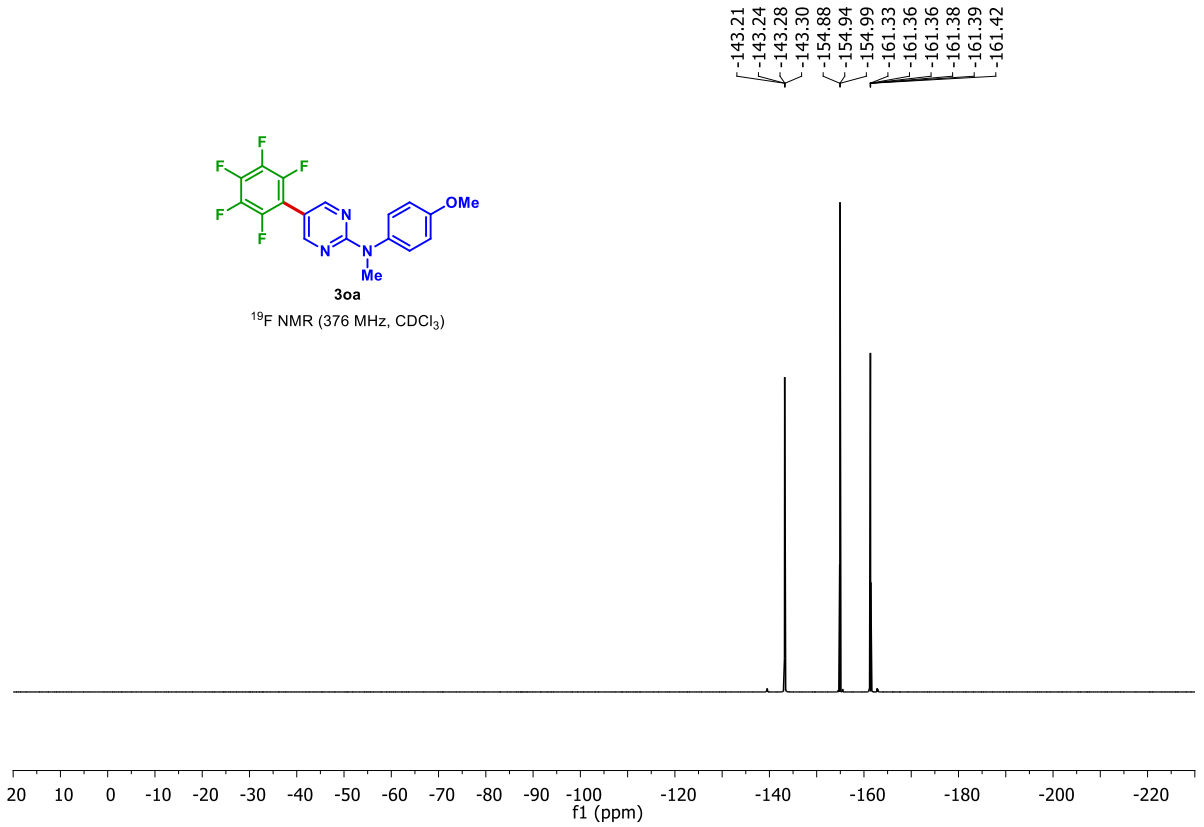
^{19}F NMR (376 MHz, $CDCl_3$)

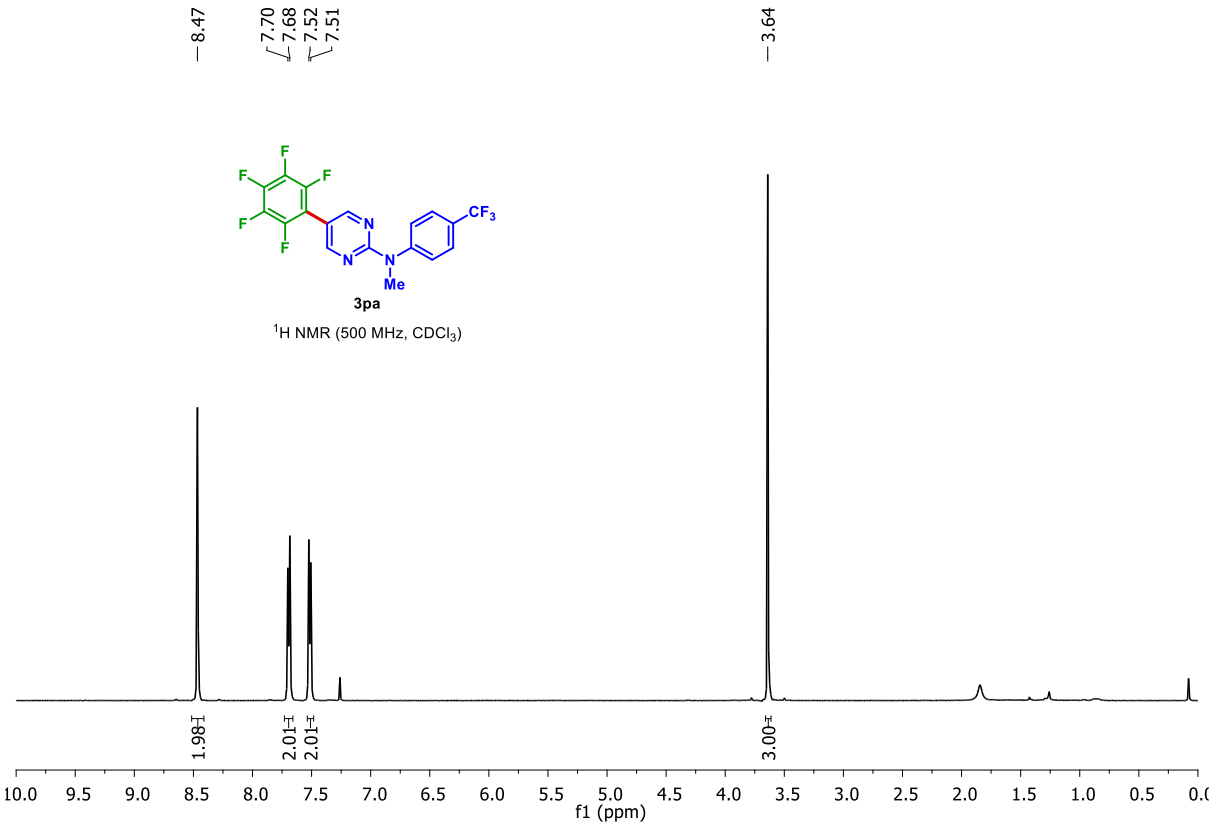


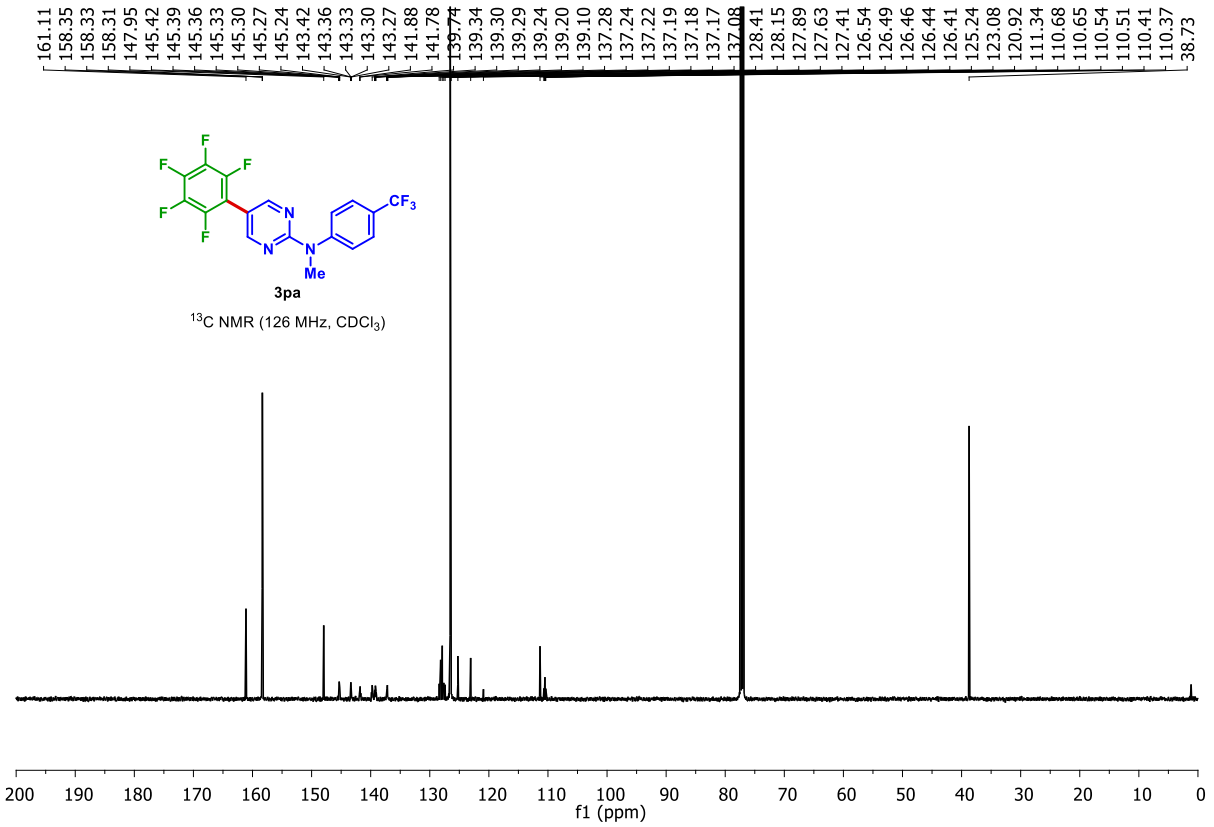
3oa

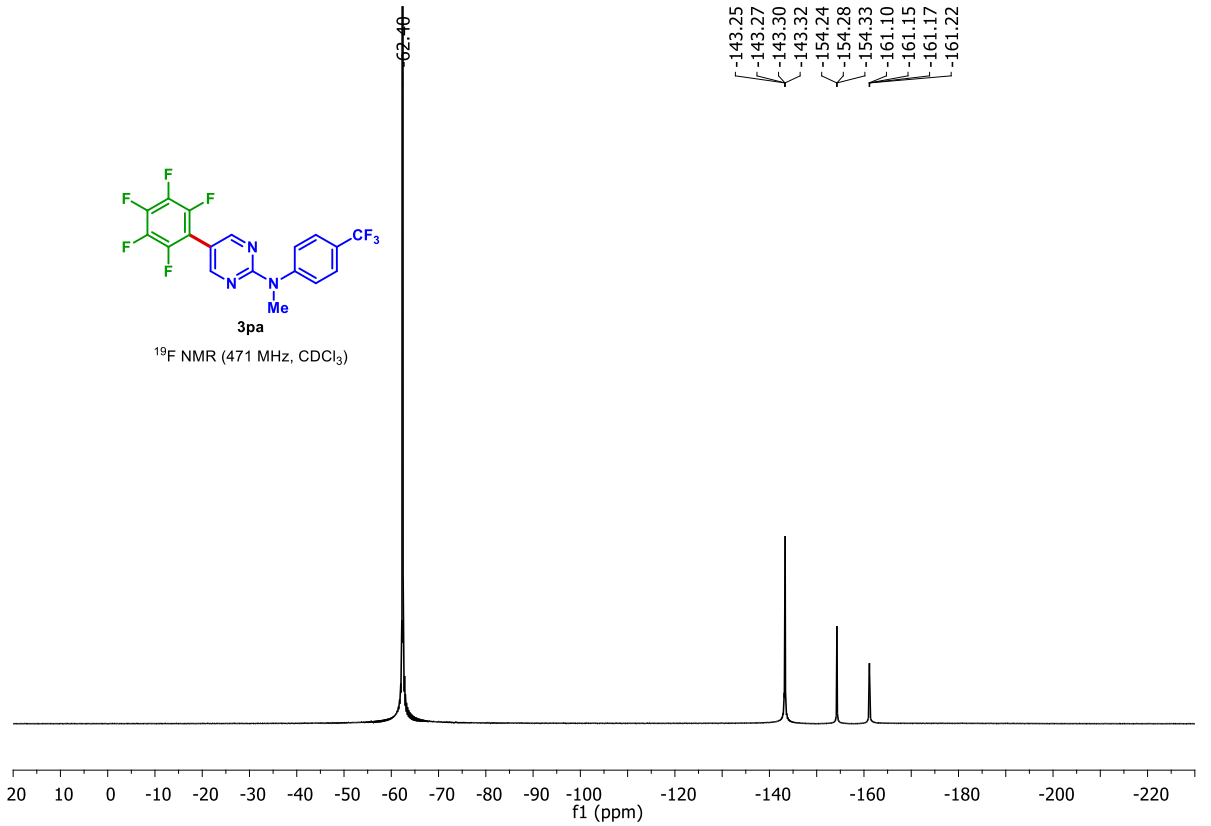
^{1}H NMR (400 MHz, $CDCl_3$)


161.79
158.31
158.12
145.36
145.33
145.30
145.27
145.24
145.21
143.39
143.36
143.33
143.30
143.27
143.24
143.22
141.51
141.48
139.60
139.53
139.49
139.45
139.29
139.27
139.24
139.19
139.17
139.15
139.14
139.11
139.09
139.05
139.01
139.00
137.84
137.28
137.25
137.18
137.15
137.10
137.06
137.02
137.00
127.97
114.86
111.09
111.06
110.96
110.92
110.82
110.79
109.87
55.56
39.30
F
F
F
F
F
N
N
N
Me
OMe
3oa
^{13}C NMR (126 MHz, CDCl$_3$)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-143.21
-143.24
-143.28
-143.30
-154.88
-154.94
-154.99
-161.33
-161.36
-161.36
-161.38
-161.39
-161.42
F
F
F
F
F
N
N
N
Me
OMe
3oa
^{19}F NMR (376 MHz, CDCl$_3$)
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200 -220
f1 (ppm)

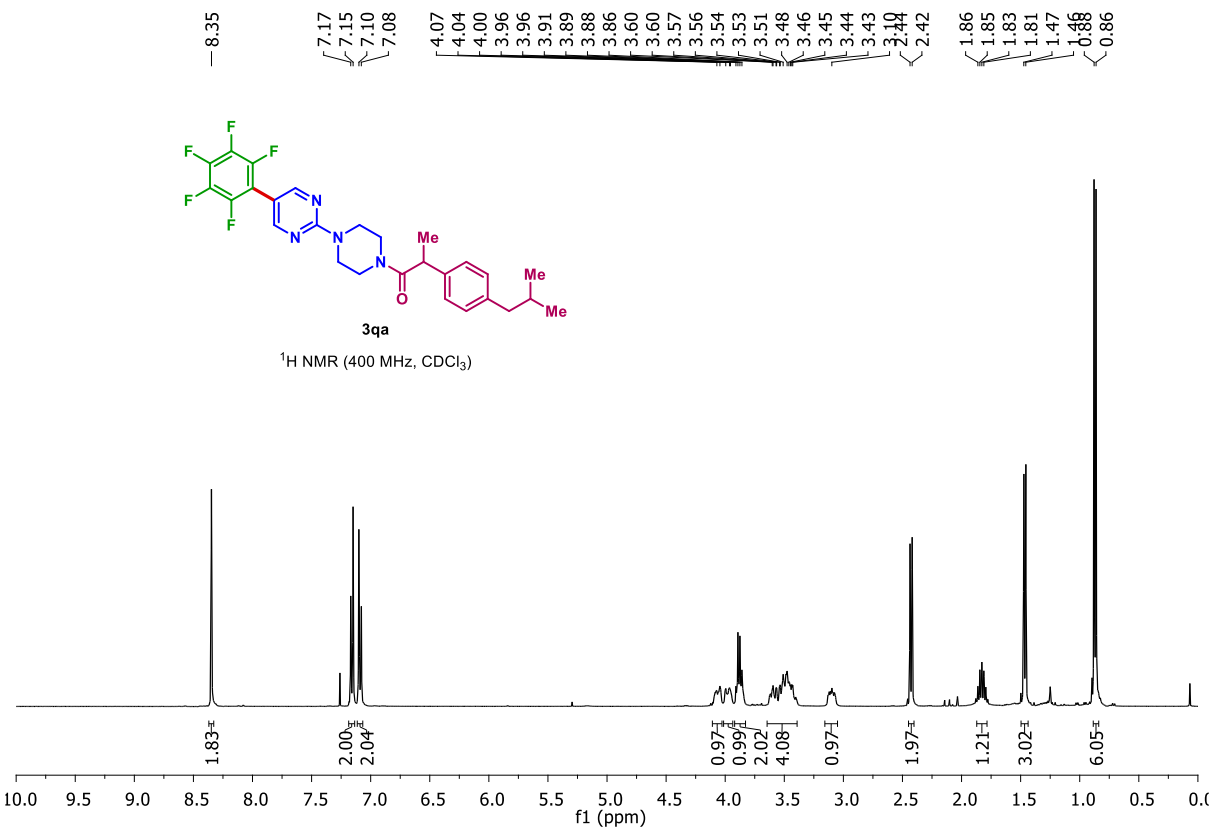

8.47
7.70
7.68
7.52
7.51
3.64
F
F
F
F
F
N
N
N
Me
CF3
3pa
1H NMR (500 MHz, CDCl3)
1.98
2.01
2.01
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


161.11
158.35
158.33
158.31
147.95
145.42
145.39
145.36
145.33
145.30
145.27
145.24
143.42
143.36
143.33
143.30
143.27
141.88
141.78
139.74
139.34
139.30
139.29
139.24
139.20
139.10
137.28
137.24
137.22
137.19
137.18
137.17
137.08
128.41
128.15
127.89
127.63
127.41
126.54
126.49
126.46
126.44
126.41
125.24
123.08
120.92
111.34
110.68
110.65
110.54
110.51
110.41
110.37
38.73
F
F
F
F
F
N
N
N
Me
CF3
3pa
13C NMR (126 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



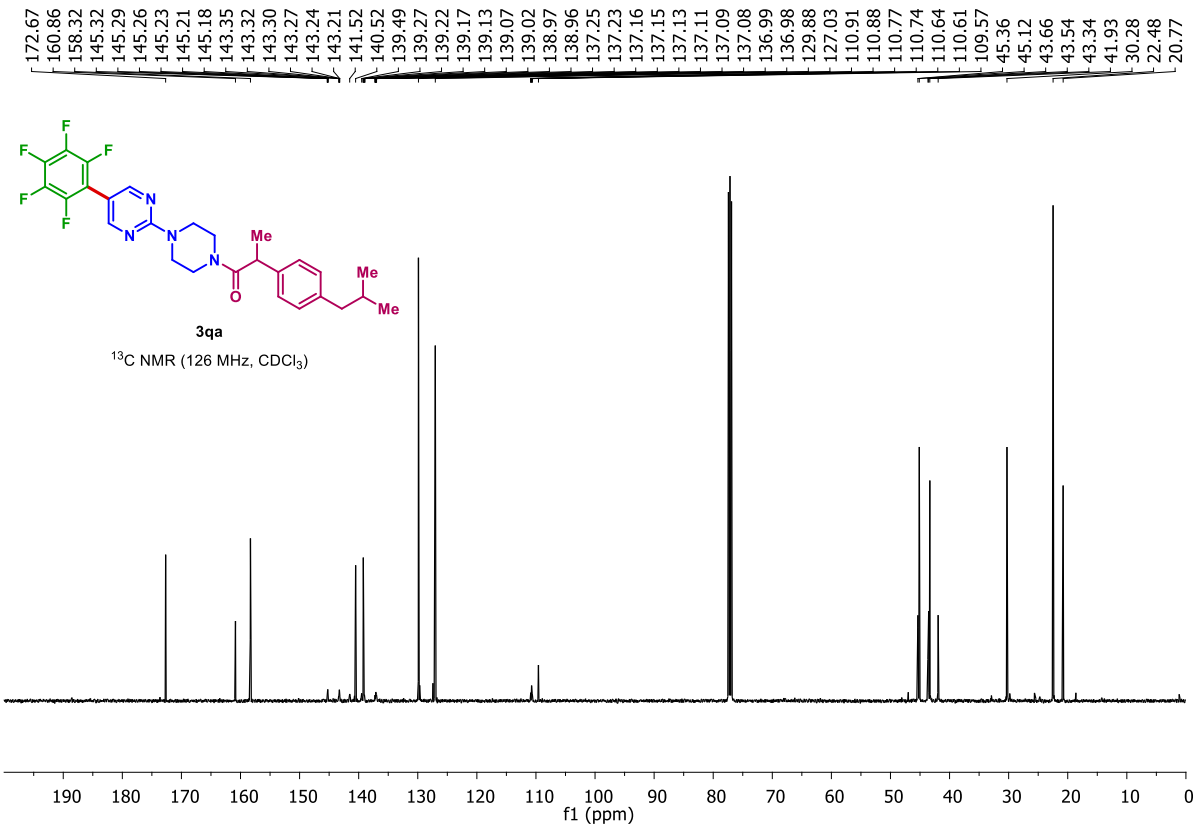
3pa

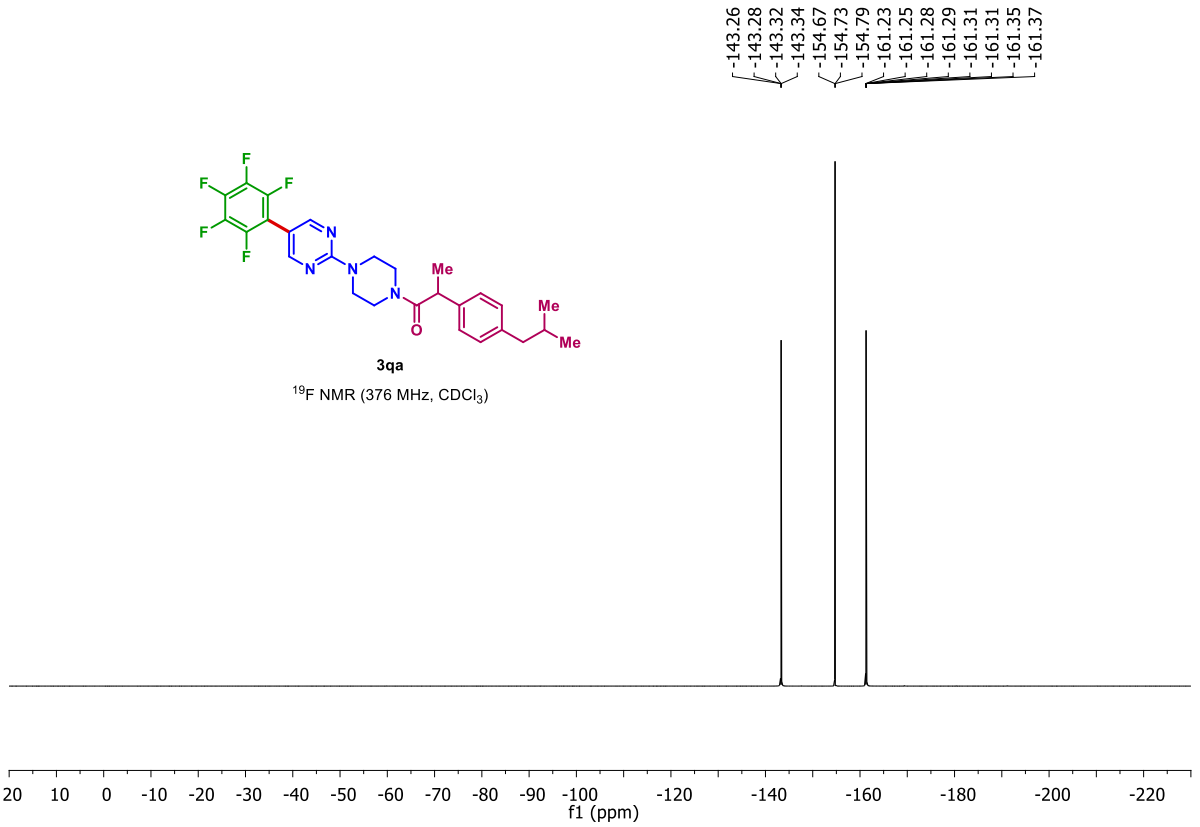
^{19}F NMR (471 MHz, $CDCl_3$)

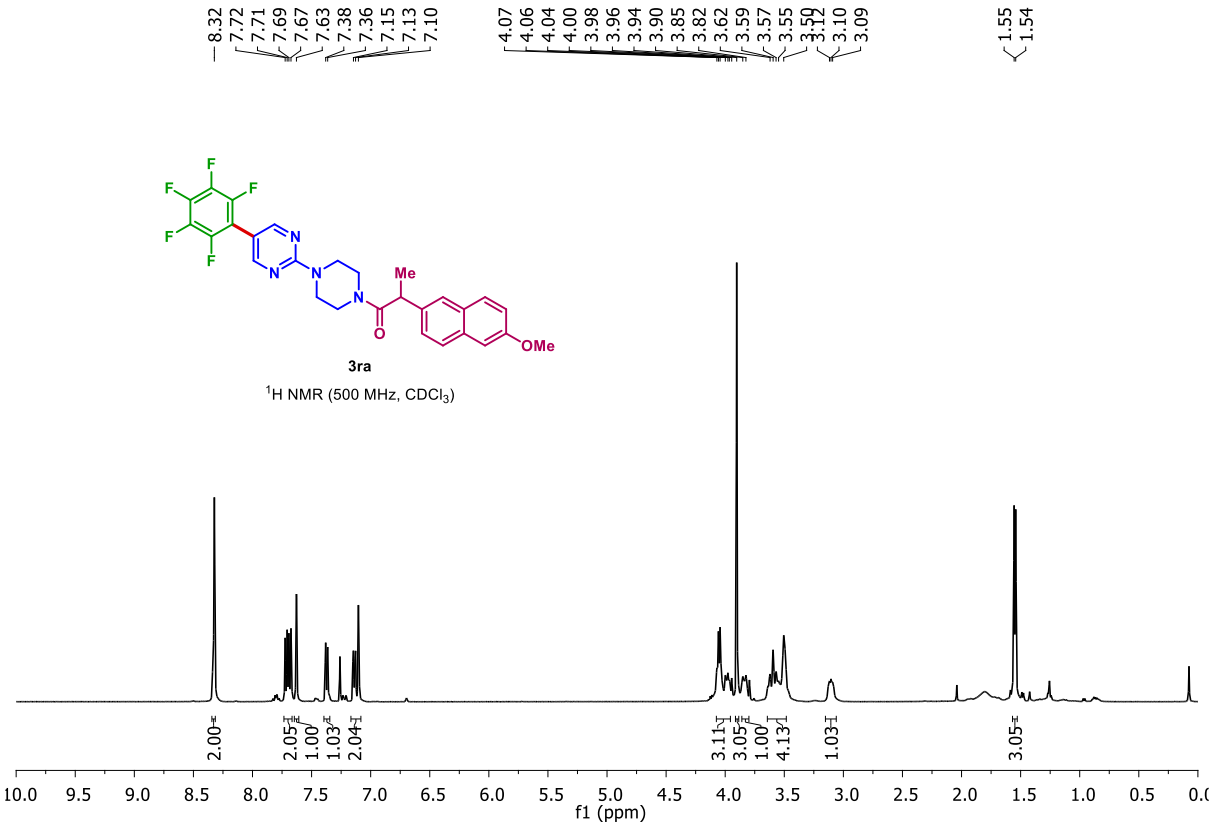


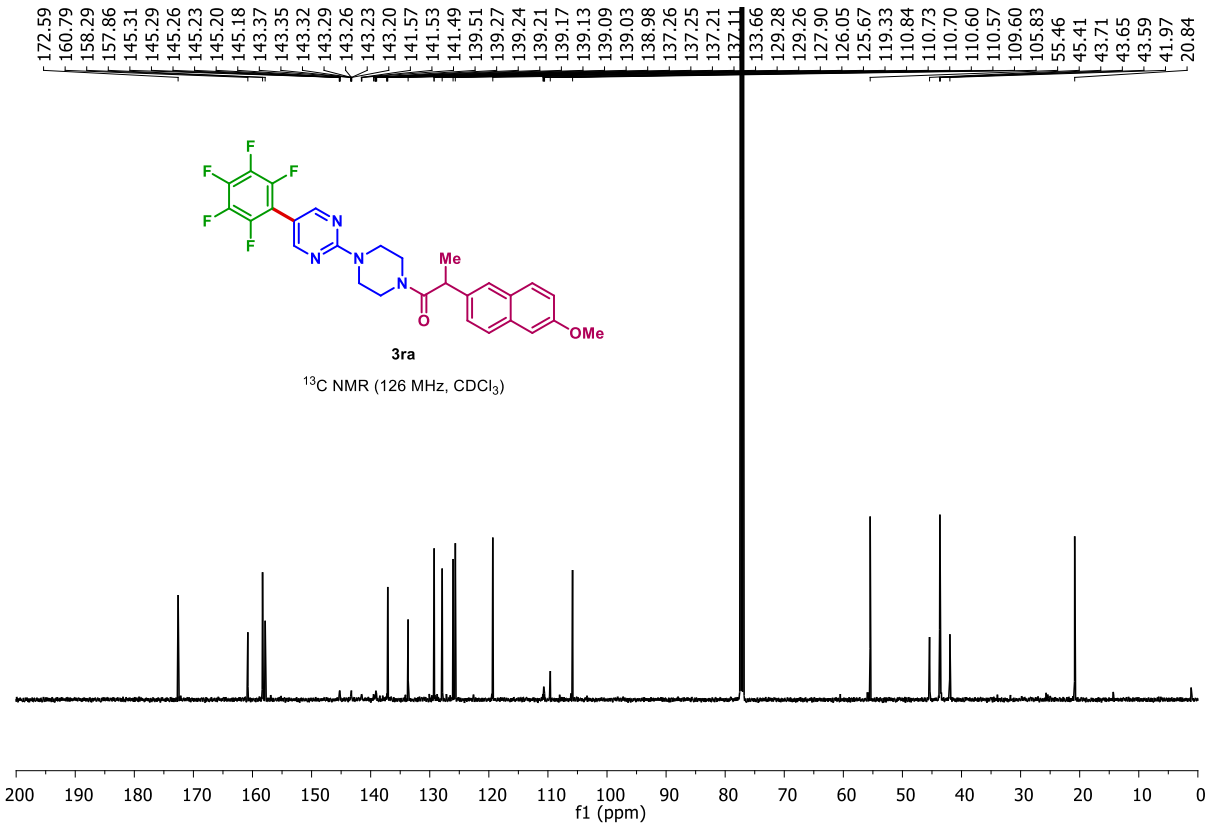
3qa

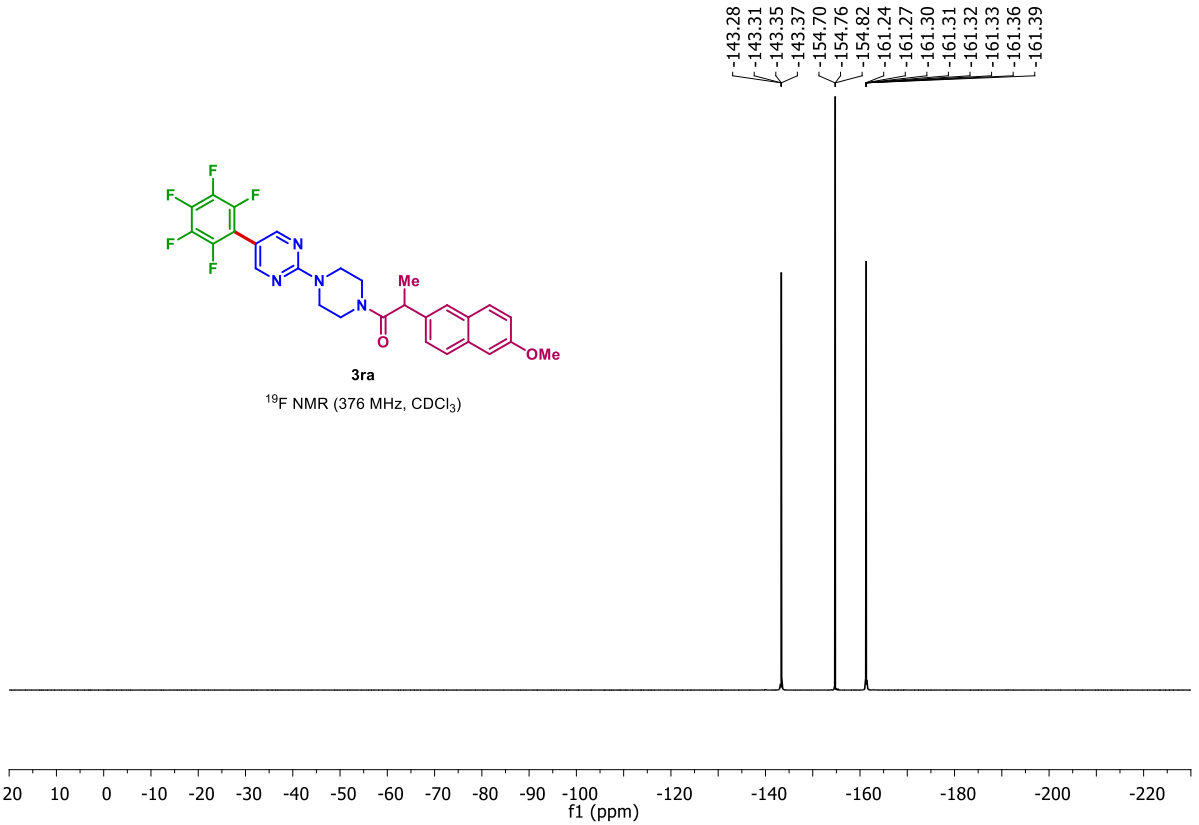
^{1}H NMR (400 MHz, $CDCl_3$)


172.67
160.86
158.32
145.32
145.29
145.26
145.23
145.21
145.18
143.35
143.32
143.30
143.27
143.24
143.21
141.52
140.52
139.49
139.27
139.22
139.17
139.13
139.07
139.02
138.97
138.96
137.25
137.23
137.16
137.15
137.13
137.11
137.09
137.08
136.99
136.98
129.88
127.03
110.91
110.88
110.77
110.74
110.64
110.61
109.57
45.36
45.12
43.66
43.54
43.34
41.93
30.28
22.48
20.77
F
F
F
F
N
N
N
O
Me
Me
Me
3qa
^{13}C NMR (126 MHz, CDCl$_3$)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-143.26
-143.28
-143.32
-143.34
-154.67
-154.73
-154.79
-161.23
-161.25
-161.28
-161.29
-161.31
-161.31
-161.35
-161.37
F
F
F
F
F
N
N
N
O
Me
Me
Me
3qa
^{19}F NMR (376 MHz, CDCl$_3$)
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
-220
f1 (ppm)

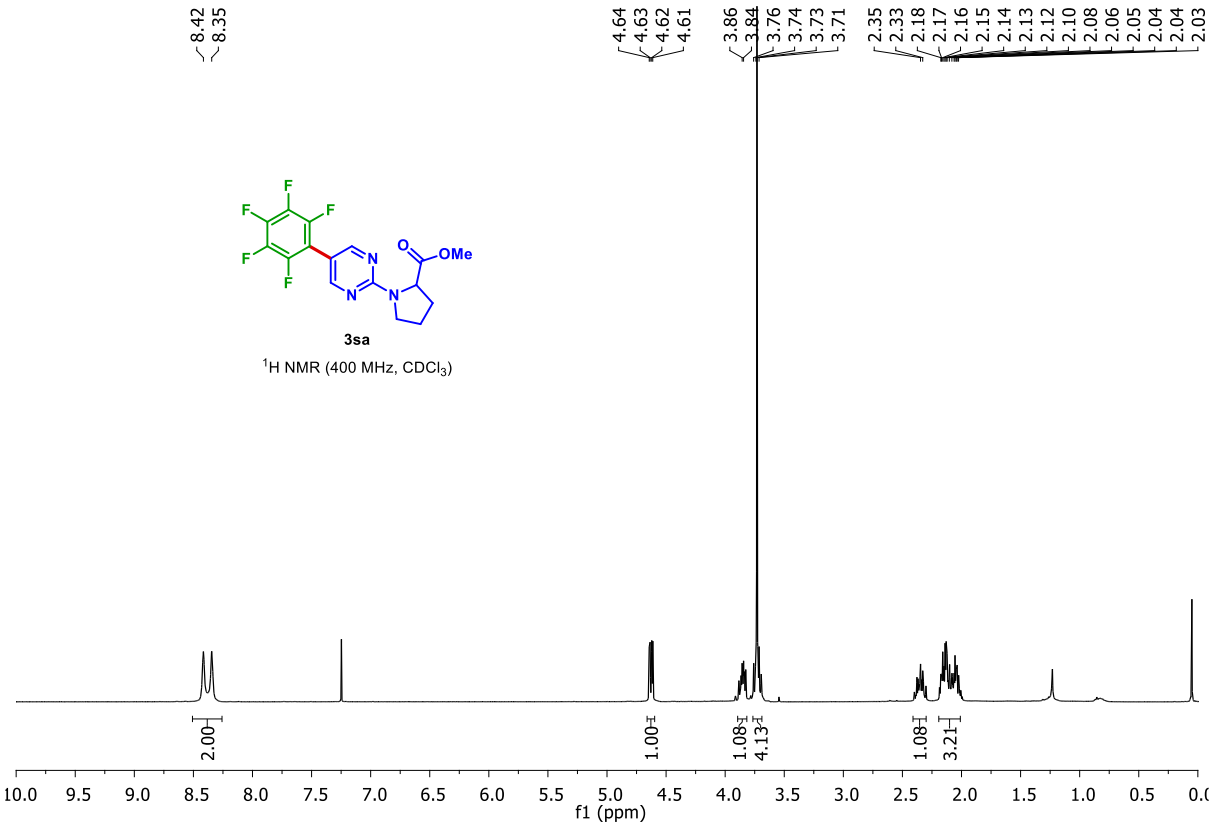

8.32
7.72
7.71
7.69
7.67
7.63
7.38
7.36
7.15
7.13
7.10
4.07
4.06
4.04
4.00
3.98
3.96
3.94
3.90
3.85
3.82
3.62
3.59
3.57
3.55
3.52
3.10
3.09
1.55
1.54
F
F
F
F
F
N
N
N
N
Me
O
OMe
3ra
1H NMR (500 MHz, CDCl3)
2.00
2.05
1.00
1.03
2.04
3.11
3.05
1.00
4.13
1.03
3.05
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


172.59
160.79
158.29
157.86
145.31
145.29
145.26
145.23
145.20
145.18
143.37
143.35
143.32
143.29
143.26
143.23
143.20
141.57
141.53
141.49
139.51
139.27
139.24
139.21
139.17
139.13
139.09
139.03
138.98
137.26
137.25
137.21
137.11
133.66
129.28
129.26
127.90
126.05
125.67
119.33
110.84
110.73
110.70
110.60
110.57
109.60
105.83
55.46
45.41
43.71
43.65
43.59
41.97
20.84
F
F
F
F
F
N
N
N
N
Me
O
OMe
3ra
13C NMR (126 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



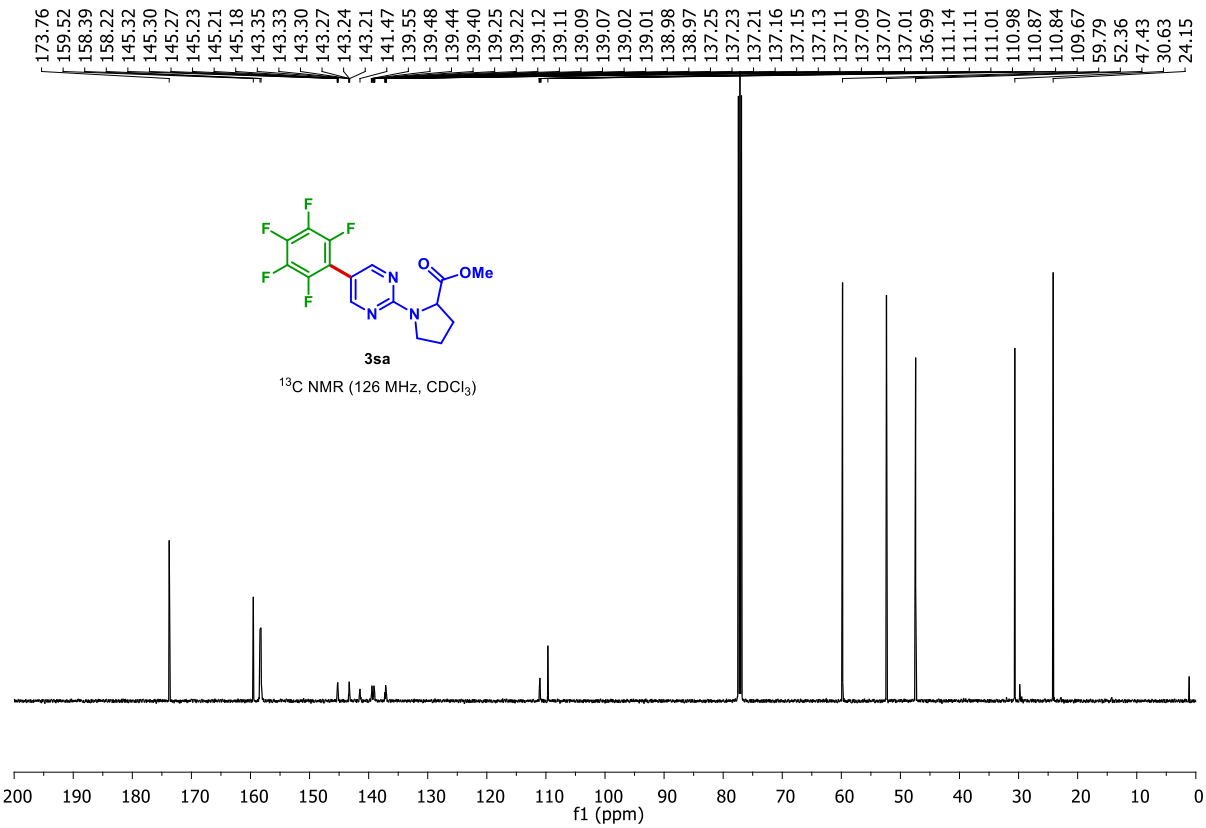
3ra

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



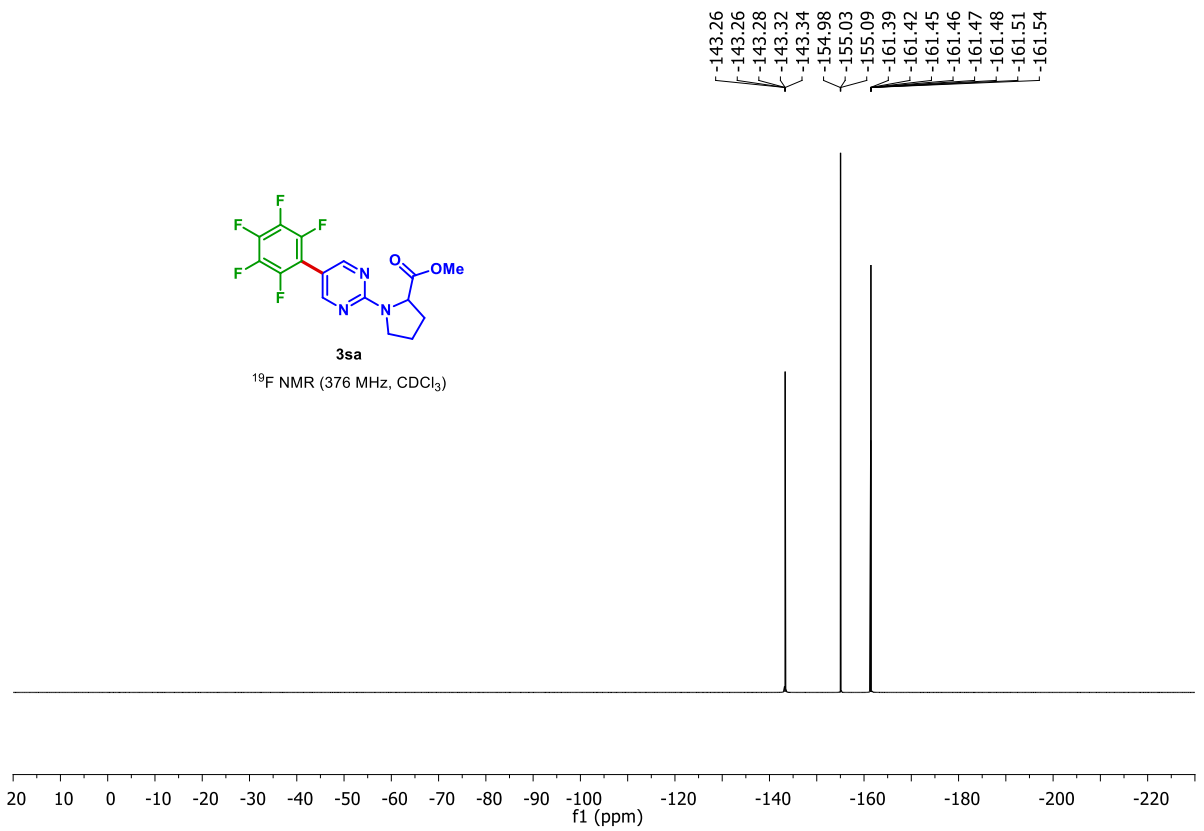
3sa

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



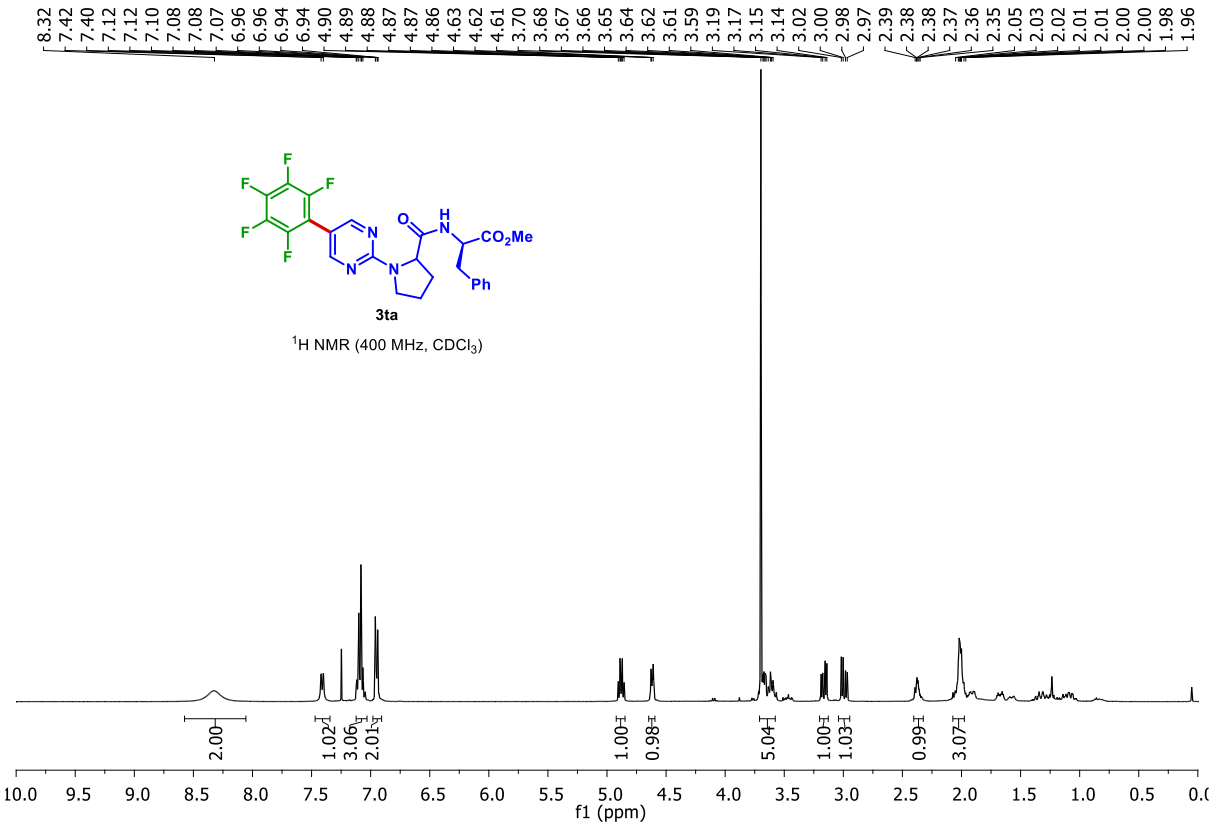
3sa

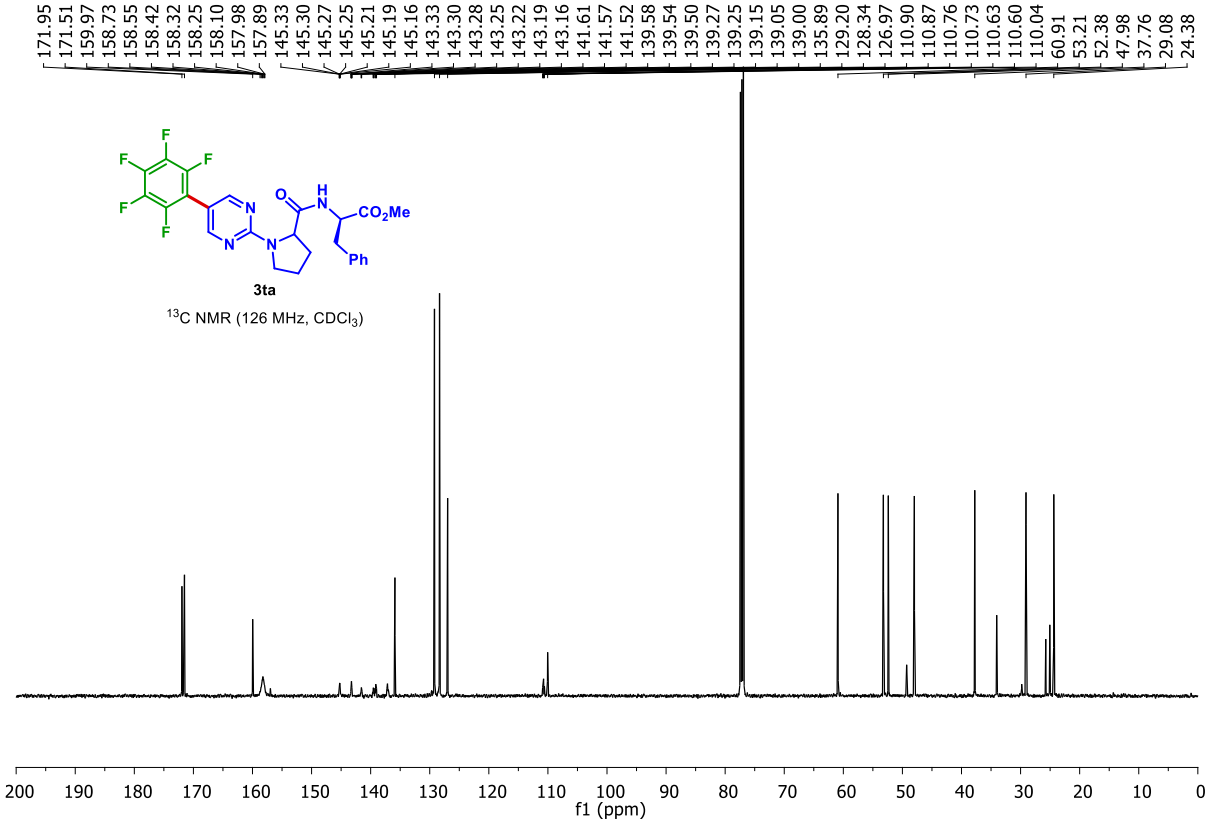
^{13}C NMR (126 MHz, $CDCl_3$)

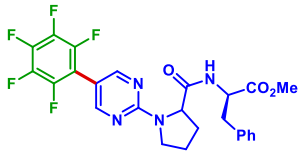


3sa

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

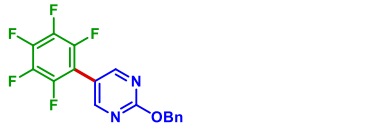

3ta
^{1}H NMR (400 MHz, $CDCl_3$)
f1 (ppm)


3ta
^{13}C NMR (126 MHz, $CDCl_3$)
f1 (ppm)



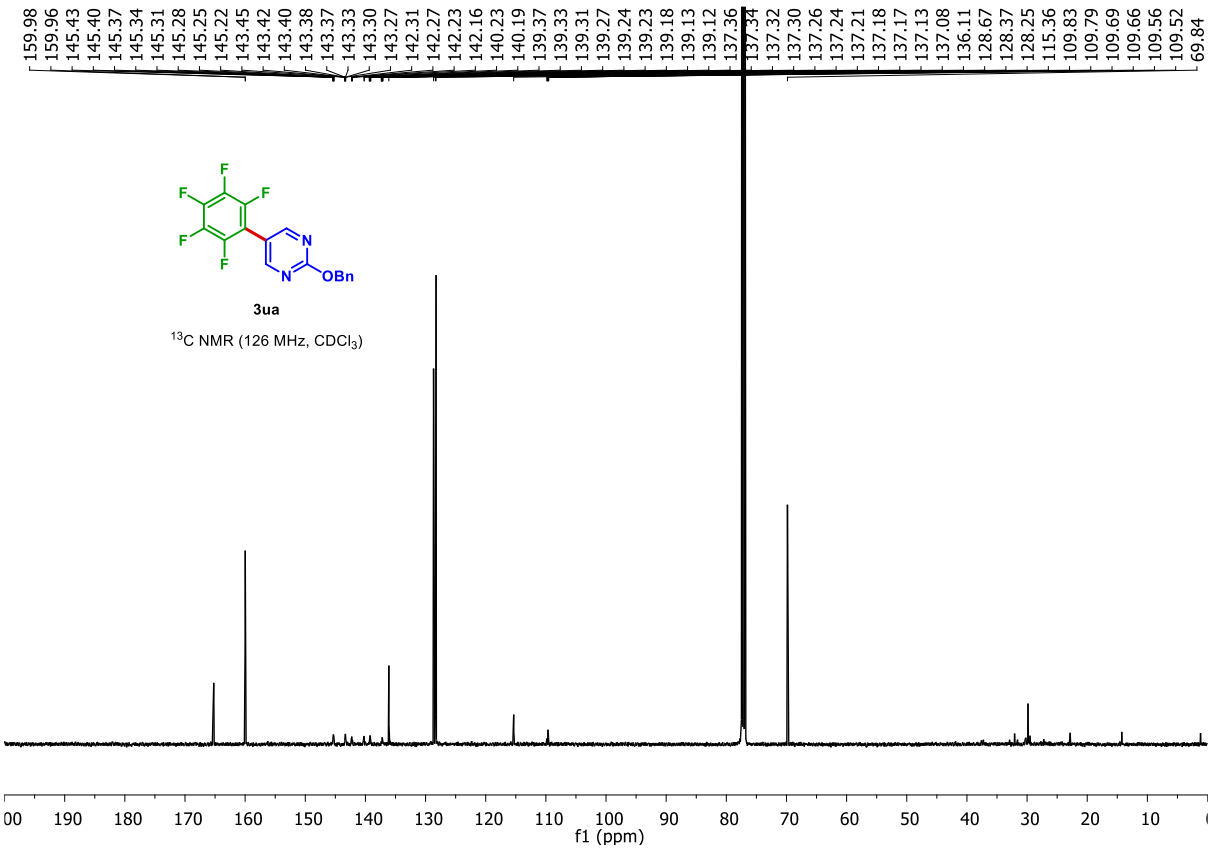
3ta

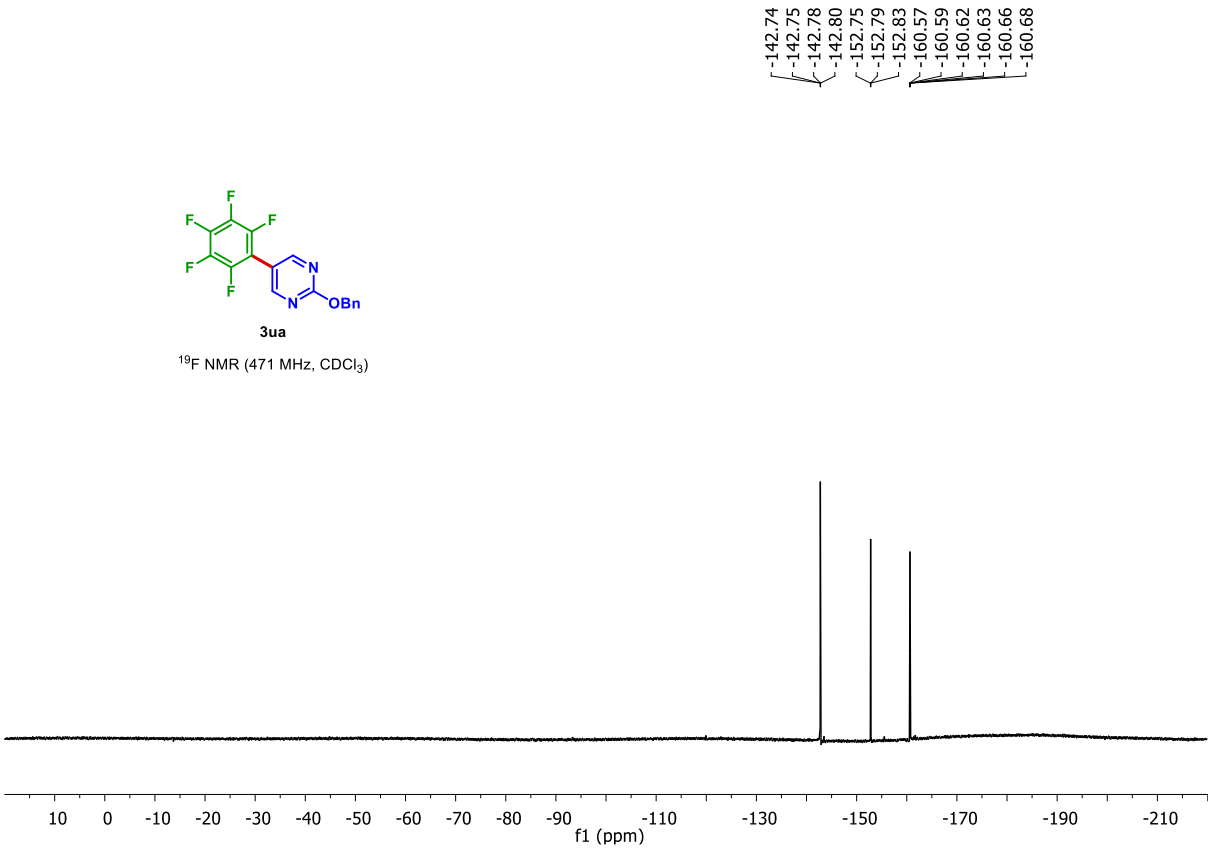
^{19}F NMR (376 MHz, $CDCl_3$)

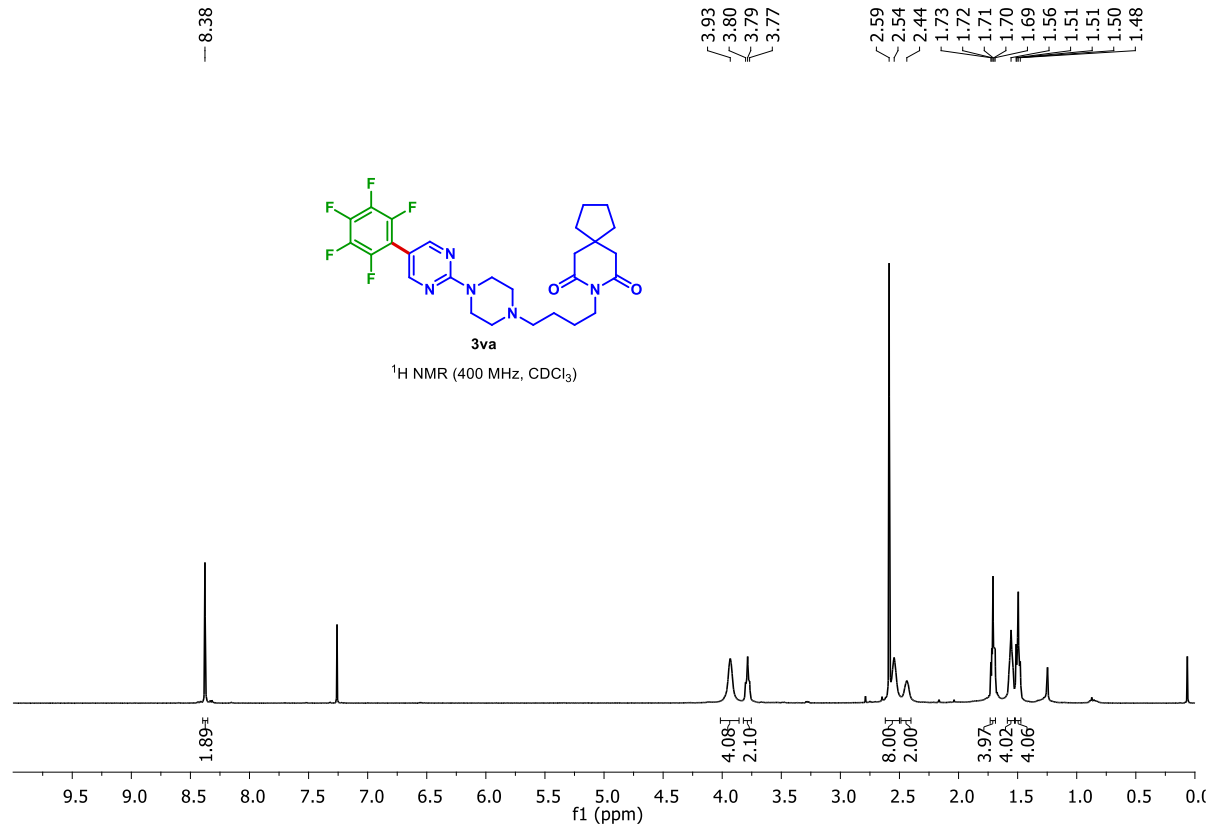


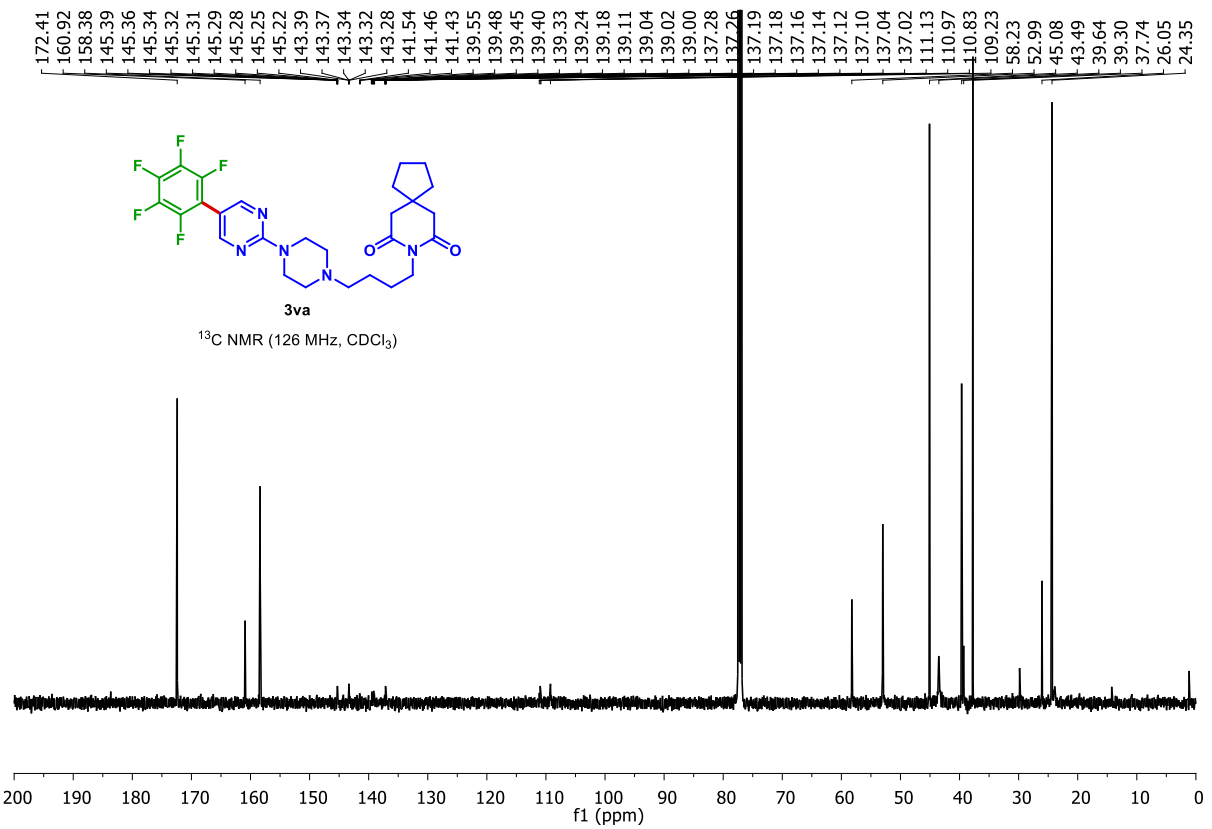
3ua

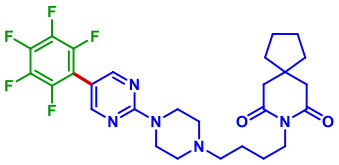
^{1}H NMR (500 MHz, $CDCl_3$)


159.98
159.96
145.43
145.40
145.37
145.34
145.31
145.28
145.25
145.22
143.45
143.42
143.40
143.38
143.37
143.33
143.30
143.27
142.31
142.27
142.23
142.16
140.23
140.19
139.37
139.33
139.31
139.27
139.24
139.23
139.18
139.13
139.12
137.36
137.34
137.32
137.30
137.26
137.24
137.21
137.18
137.17
137.13
137.08
136.11
128.67
128.37
128.25
115.36
109.83
109.79
109.69
109.66
109.56
109.52
69.84
F
F
F
F
F
N
N
OBn
3ua
13C NMR (126 MHz, CDCl3)
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


-142.74
-142.75
-142.78
-142.80
-152.75
-152.79
-152.83
-160.57
-160.59
-160.62
-160.63
-160.66
-160.68
F
F
F
F
F
N
N
OBn
3ua
19F NMR (471 MHz, CDCl3)
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

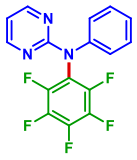

8.38
3.93
3.80
3.79
3.77
2.59
2.54
2.44
1.73
1.72
1.71
1.70
1.69
1.56
1.51
1.51
1.50
1.48
3va
1H NMR (400 MHz, CDCl3)
1.89
4.08
2.10
8.00
2.00
3.97
4.02
4.06
f1 (ppm)


172.41
160.92
158.38
145.39
145.36
145.34
145.32
145.31
145.29
145.28
145.25
145.22
143.39
143.37
143.34
143.32
143.28
141.54
141.46
141.43
139.55
139.48
139.45
139.40
139.33
139.24
139.18
139.11
139.04
139.02
139.00
137.28
137.26
137.19
137.18
137.16
137.14
137.12
137.10
137.04
137.02
111.13
110.97
110.83
109.23
58.23
52.99
45.08
43.49
39.64
39.30
37.74
26.05
24.35
3va
13C NMR (126 MHz, CDCl3)
f1 (ppm)



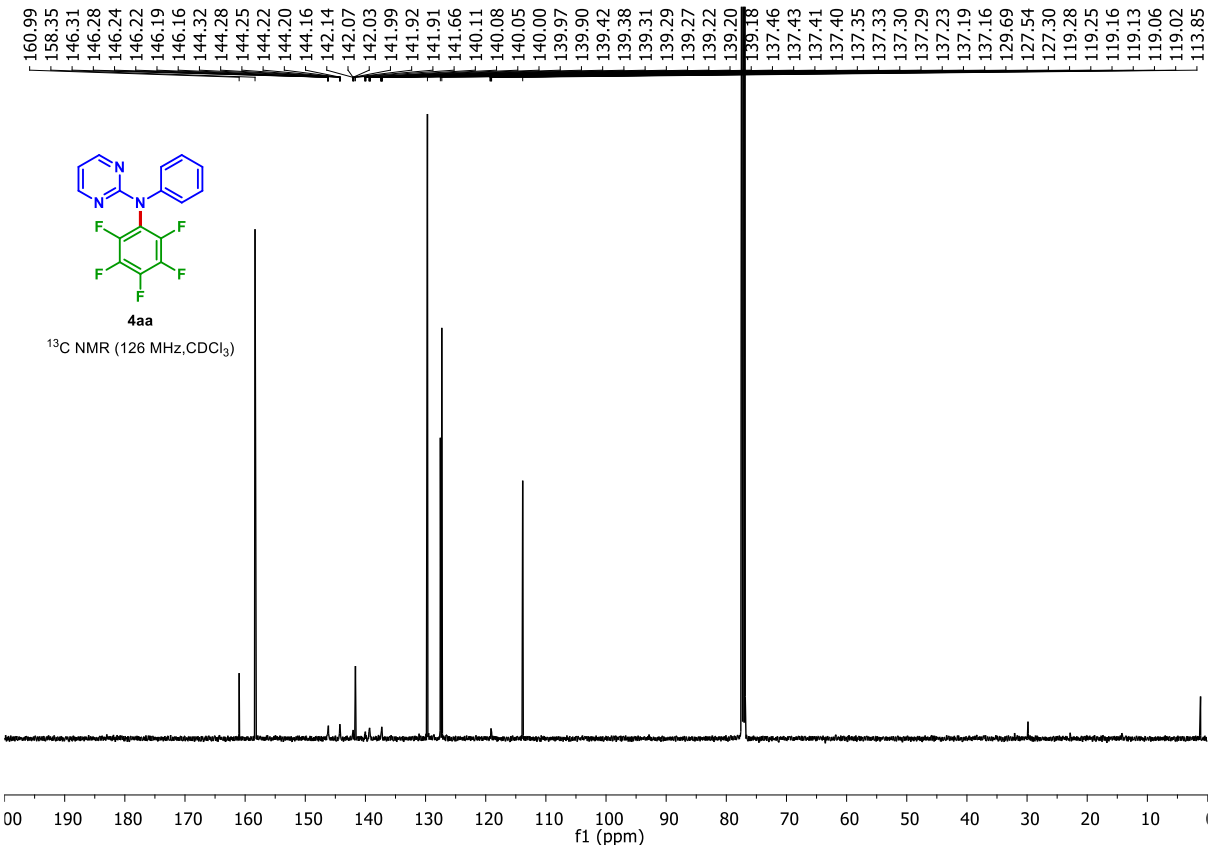
3va

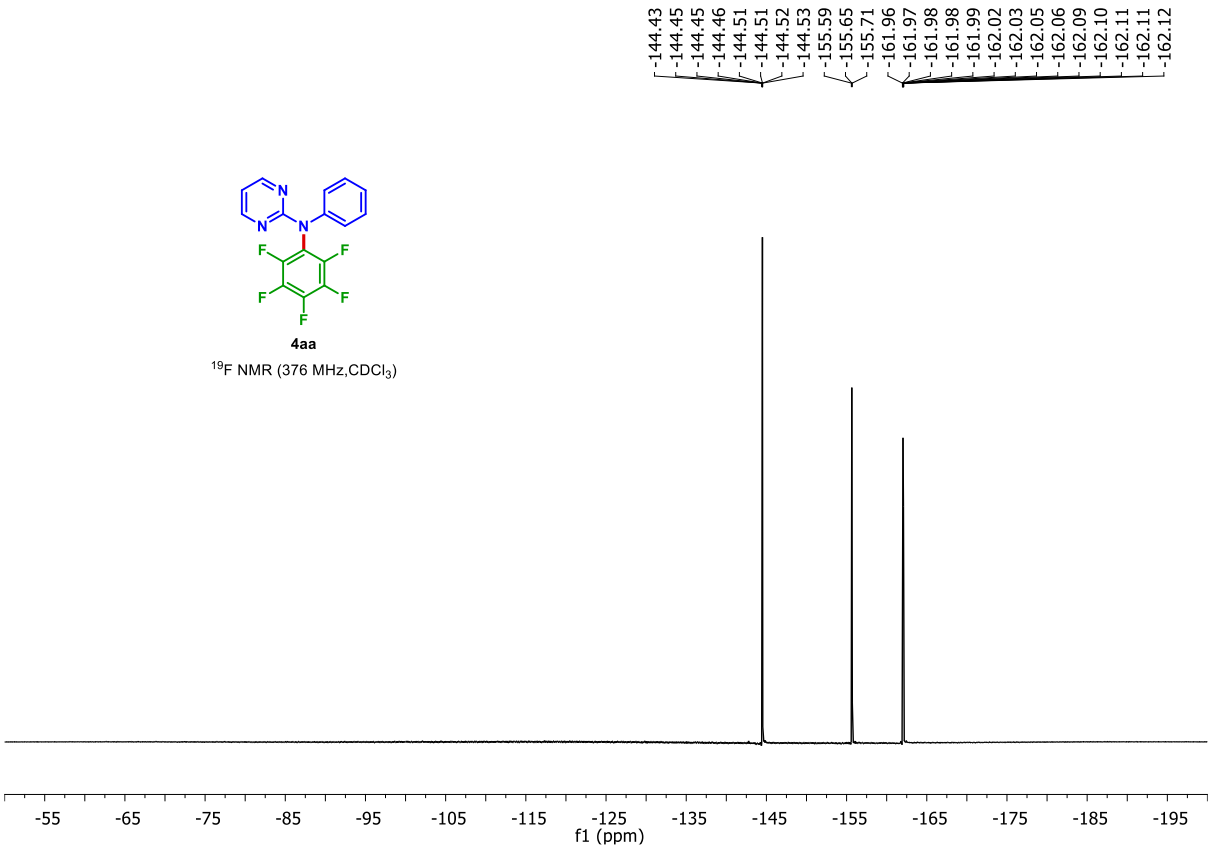
^{19}F NMR (471 MHz, $CDCl_3$)

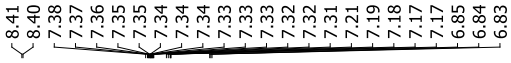


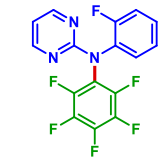
4aa

1H NMR (500 MHz,$CDCl_3$)


160.99
158.35
146.31
146.28
146.24
146.22
146.19
146.16
144.32
144.28
144.25
144.22
144.20
144.16
142.14
142.07
142.03
141.99
141.92
141.91
141.66
140.11
140.08
140.05
140.00
139.97
139.90
139.42
139.38
139.31
139.29
139.27
139.22
139.20
139.18
137.46
137.43
137.41
137.40
137.35
137.33
137.30
137.29
137.23
137.19
137.16
129.69
127.54
127.30
119.28
119.25
119.16
119.13
119.06
119.02
113.85
4aa
13C NMR (126 MHz,CDCl3)
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

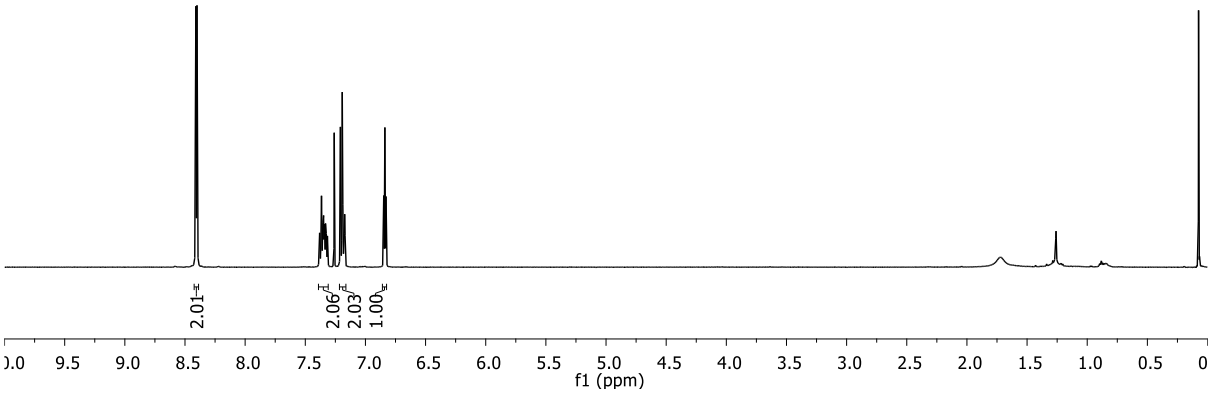

-144.43
-144.45
-144.45
-144.46
-144.51
-144.51
-144.52
-144.53
-155.59
-155.65
-155.71
-161.96
-161.97
-161.98
-161.98
-161.99
-162.02
-162.03
-162.05
-162.06
-162.09
-162.10
-162.11
-162.11
-162.12
4aa
19F NMR (376 MHz,CDCl3)
-55 -65 -75 -85 -95 -105 -115 -125 -135 -145 -155 -165 -175 -185 -195
f1 (ppm)

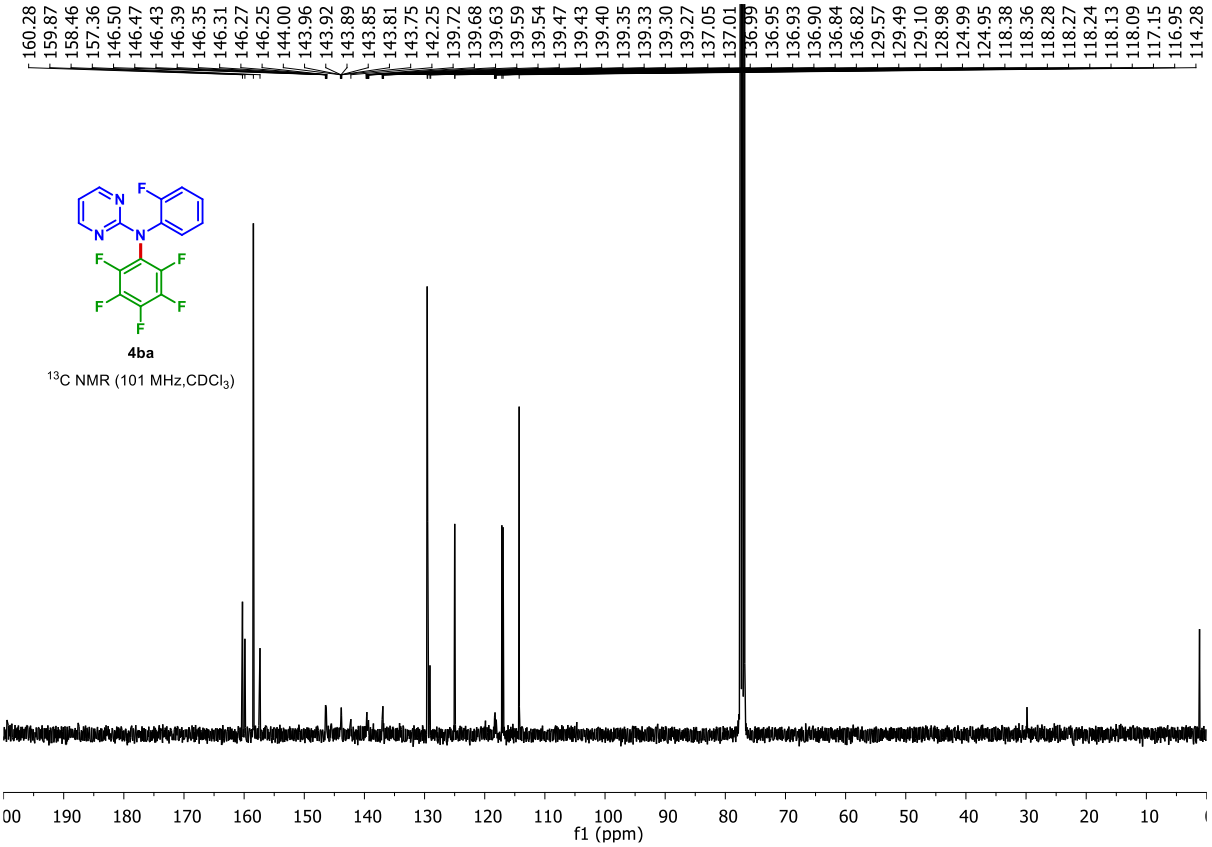




4ba

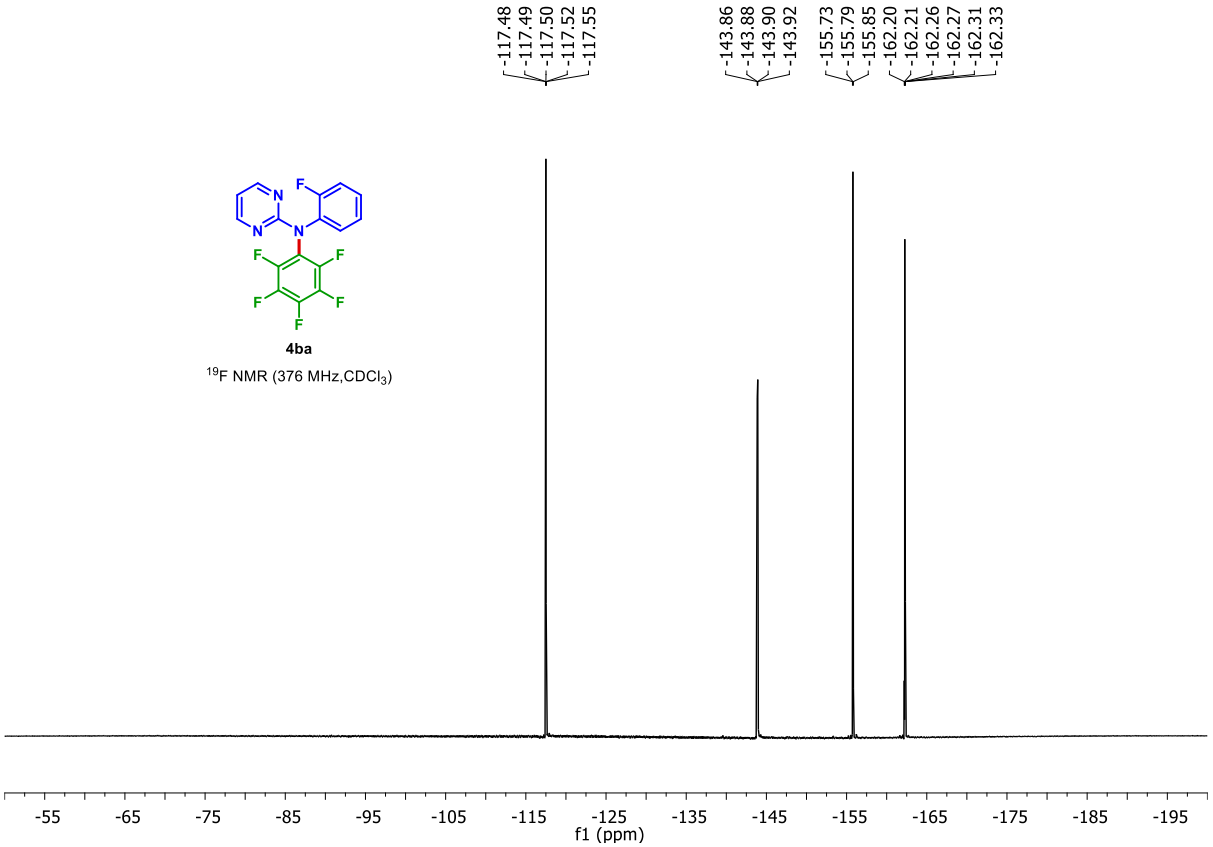
1H NMR (500 MHz,$CDCl_3$)

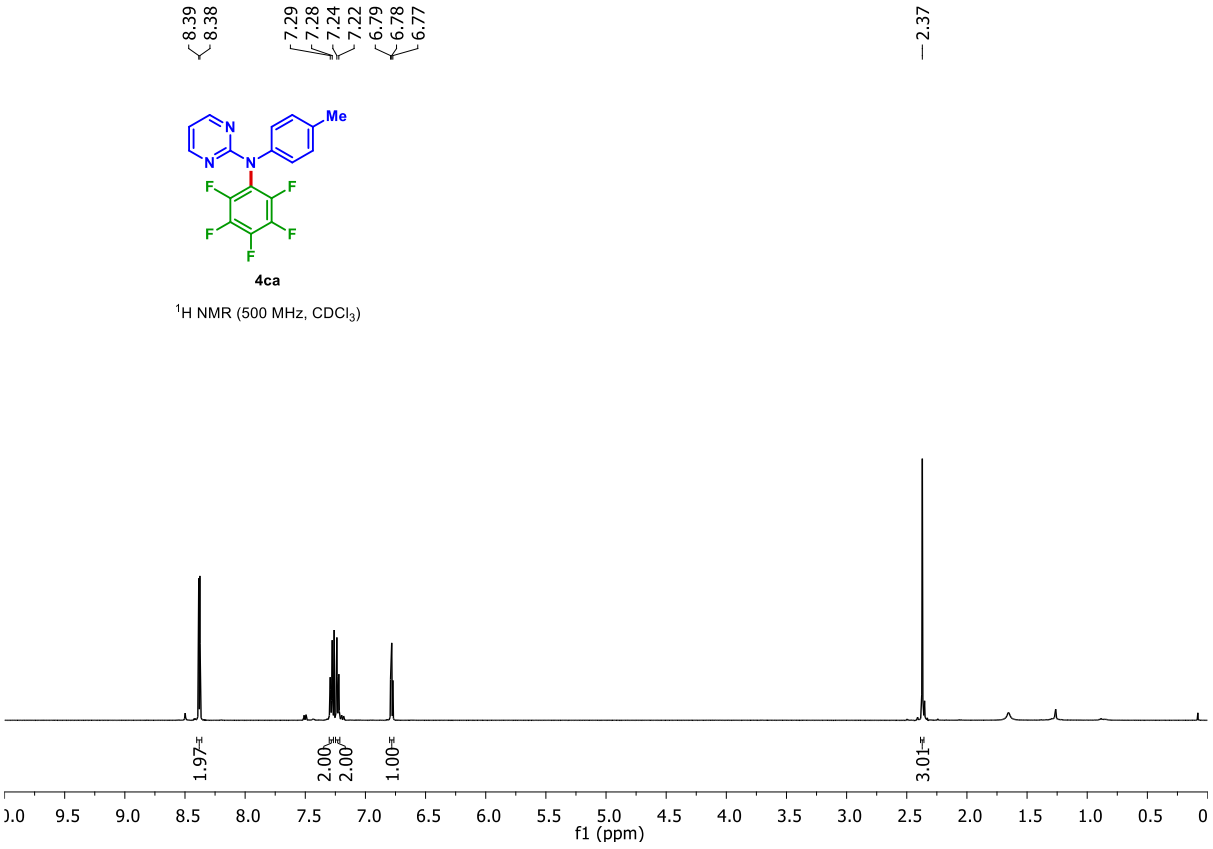


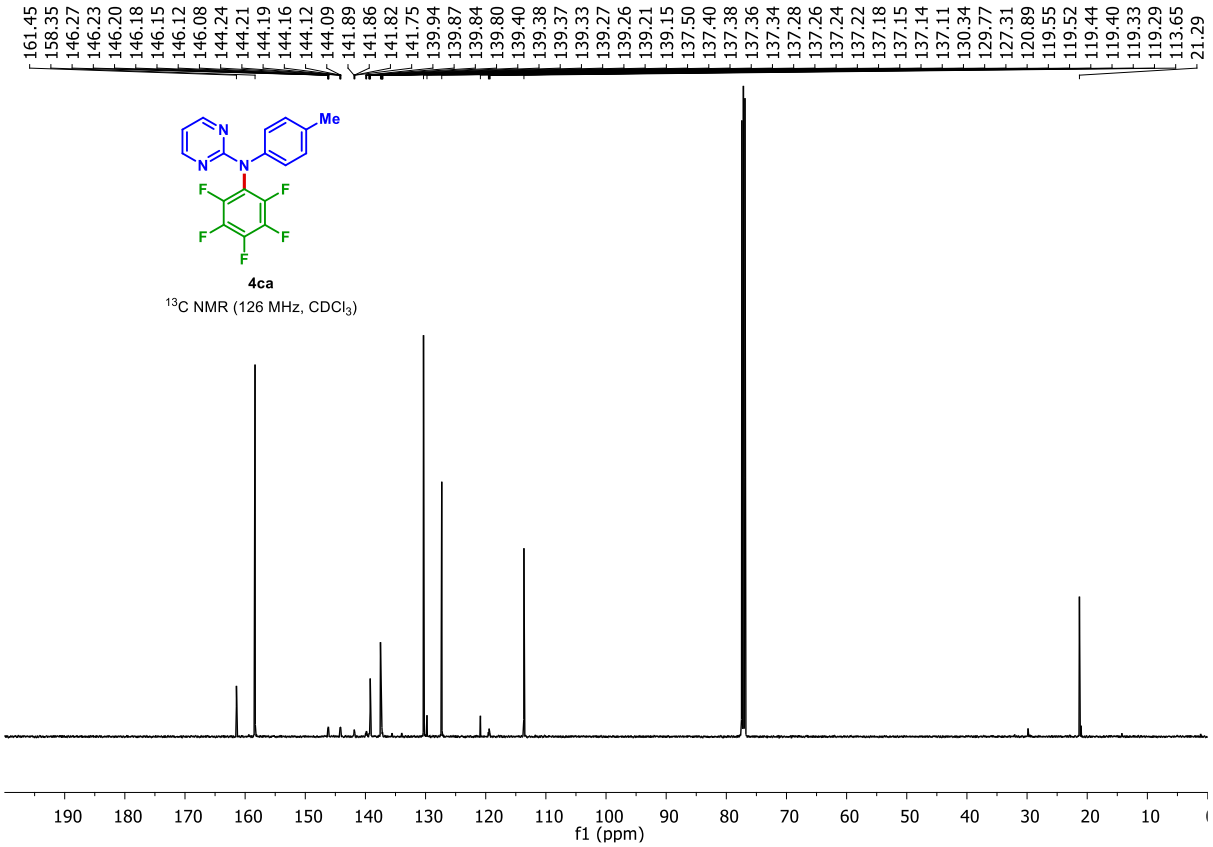


4ba

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

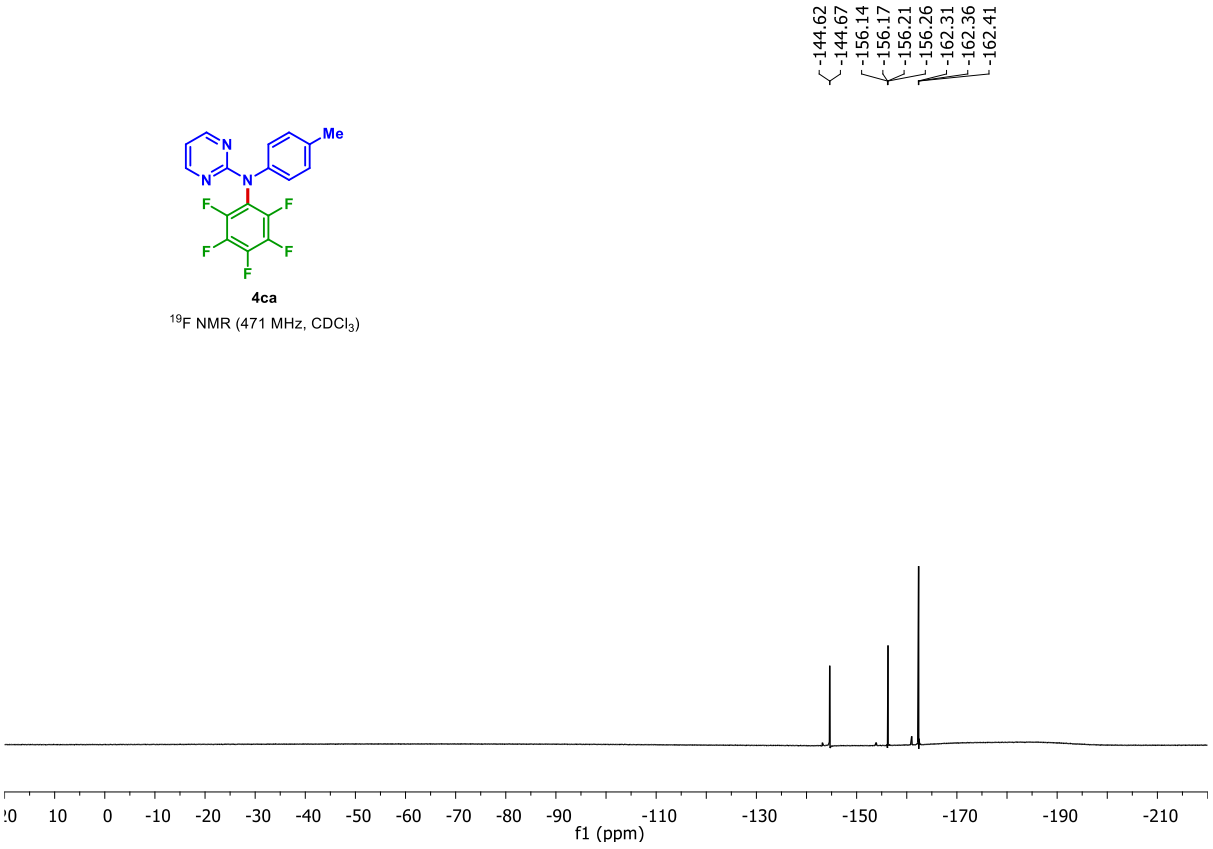

-117.48
-117.49
-117.50
-117.52
-117.55
-143.86
-143.88
-143.90
-143.92
-155.73
-155.79
-155.85
-162.20
-162.21
-162.26
-162.27
-162.31
-162.33
F
N
N
N
F
F
F
F
F
4ba
^{19}F NMR (376 MHz,CDCl$_3$)
-55
-65
-75
-85
-95
-105
-115
-125
-135
-145
-155
-165
-175
-185
-195
f1 (ppm)


8.39
8.38
7.29
7.28
7.24
7.22
6.79
6.78
6.77
2.37
N
N
N
Me
F
F
F
F
F
4ca
^{1}H NMR (500 MHz, CDCl$_3$)
1.97
2.00
2.00
1.00
3.01
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)



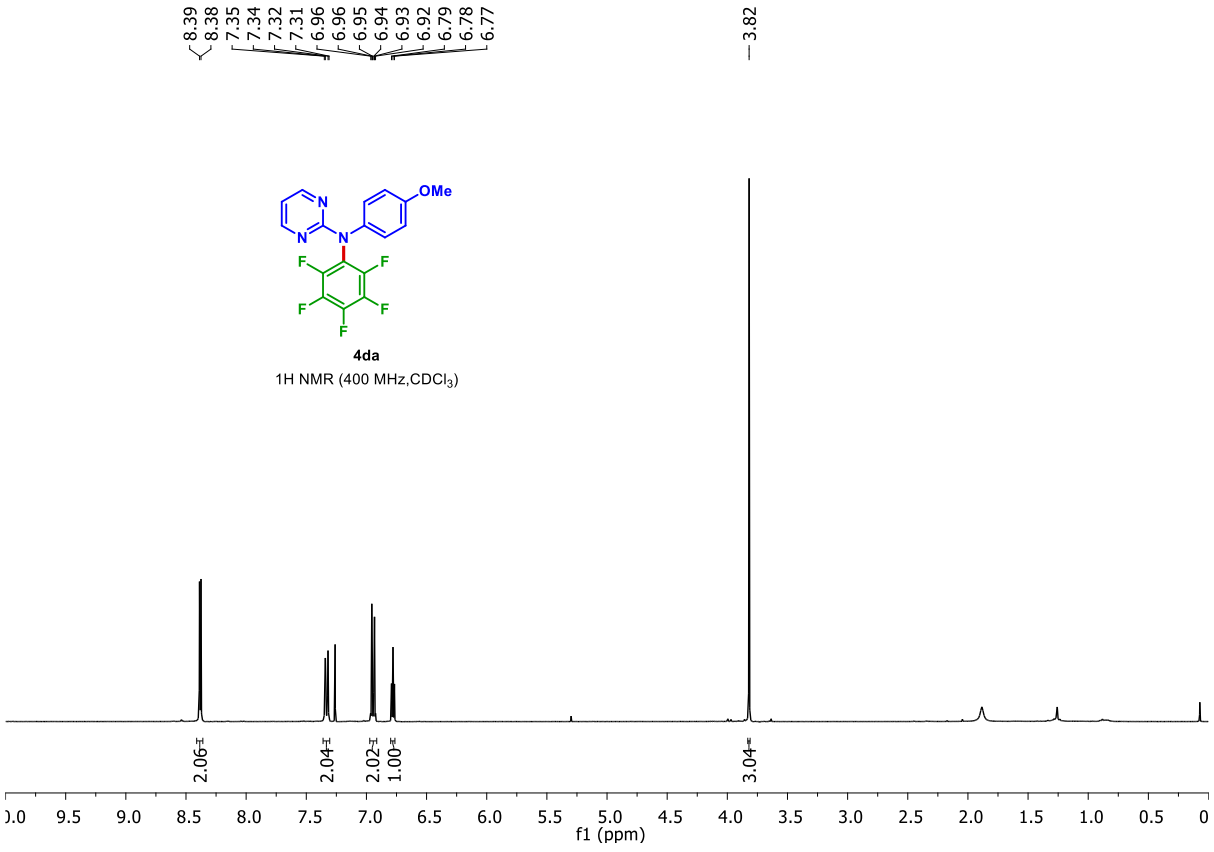
4ca

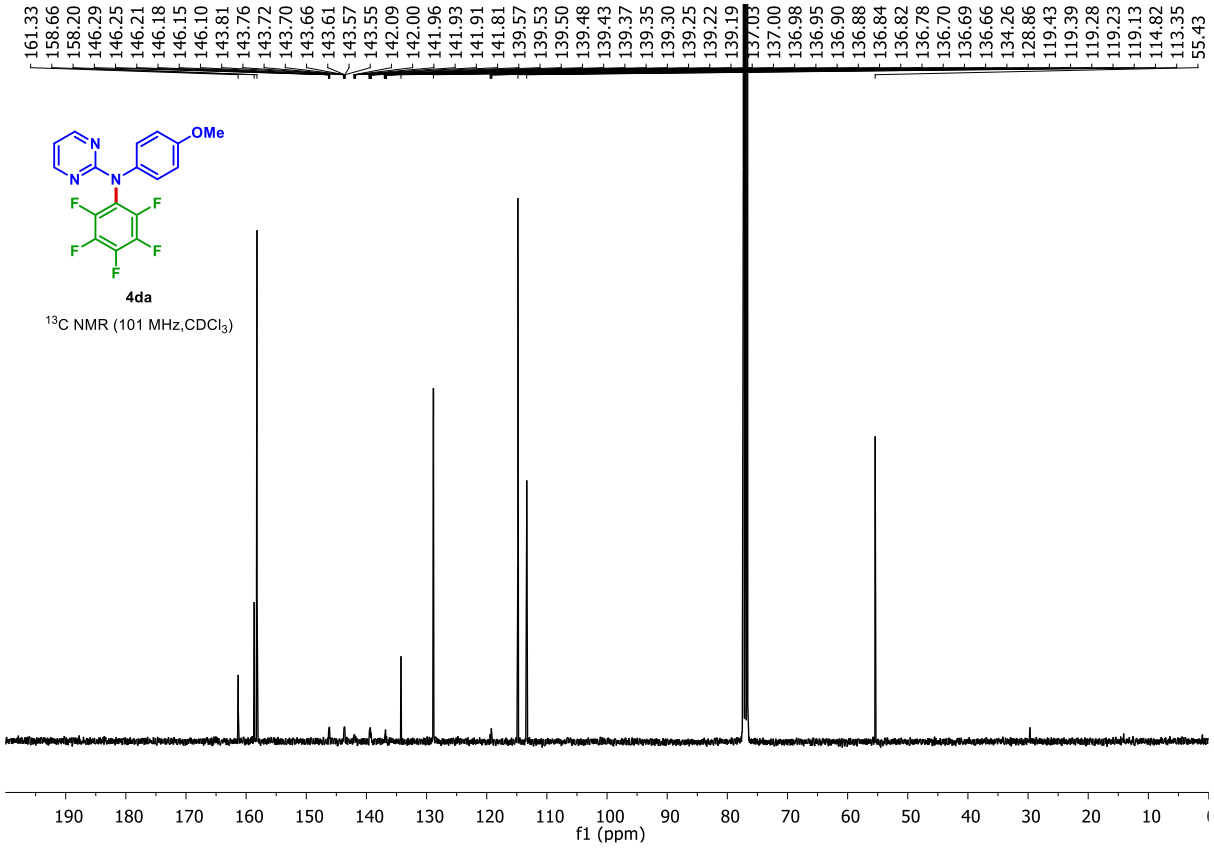
^{13}C NMR (126 MHz, $CDCl_3$)

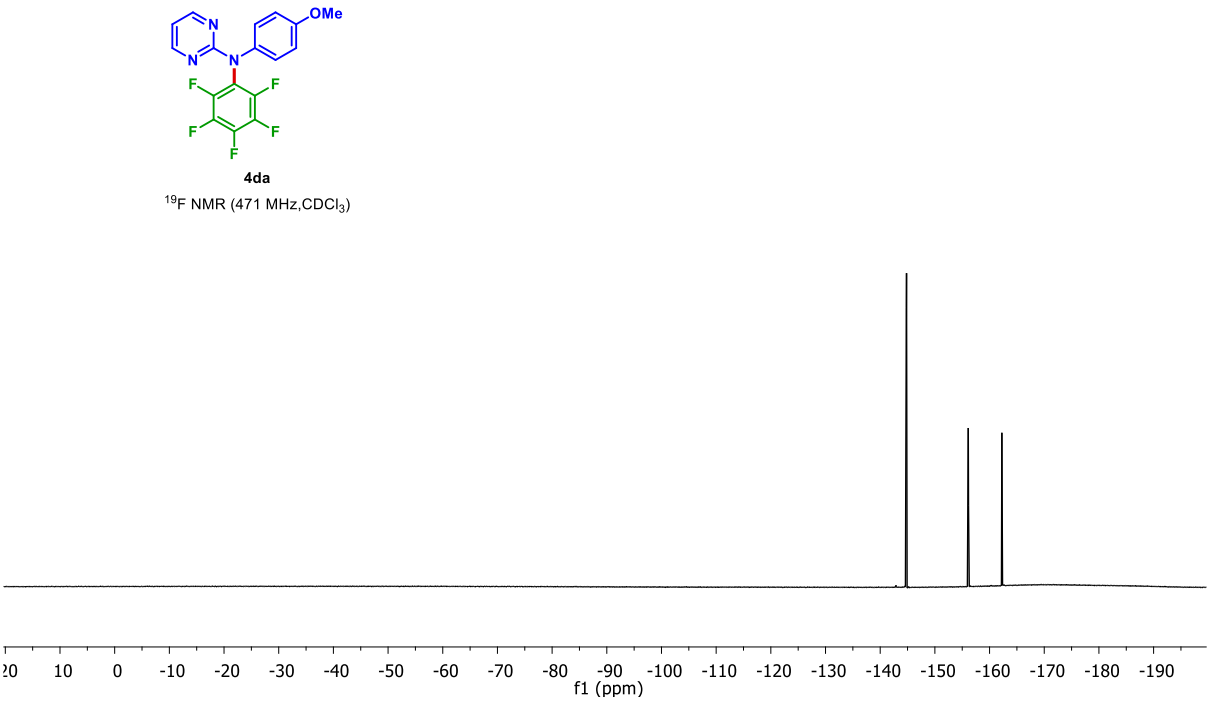


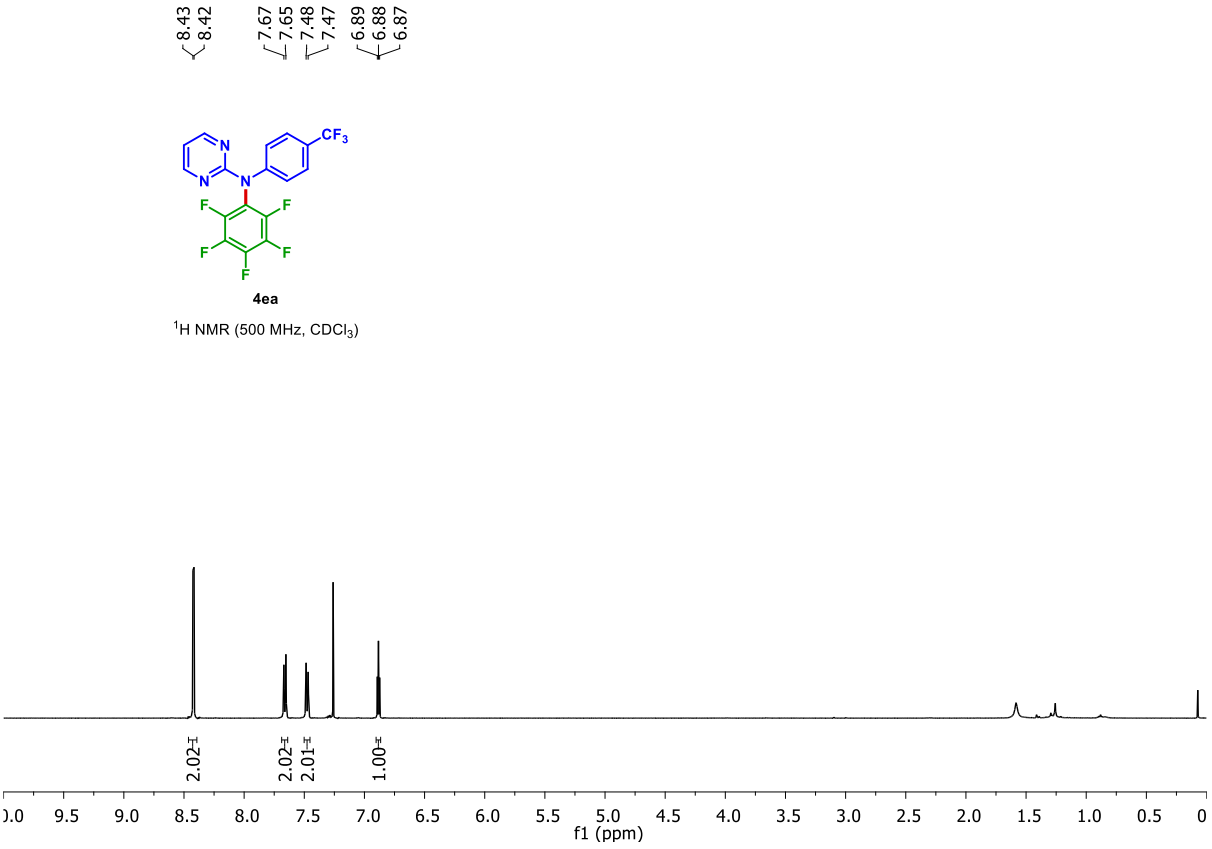
4ca

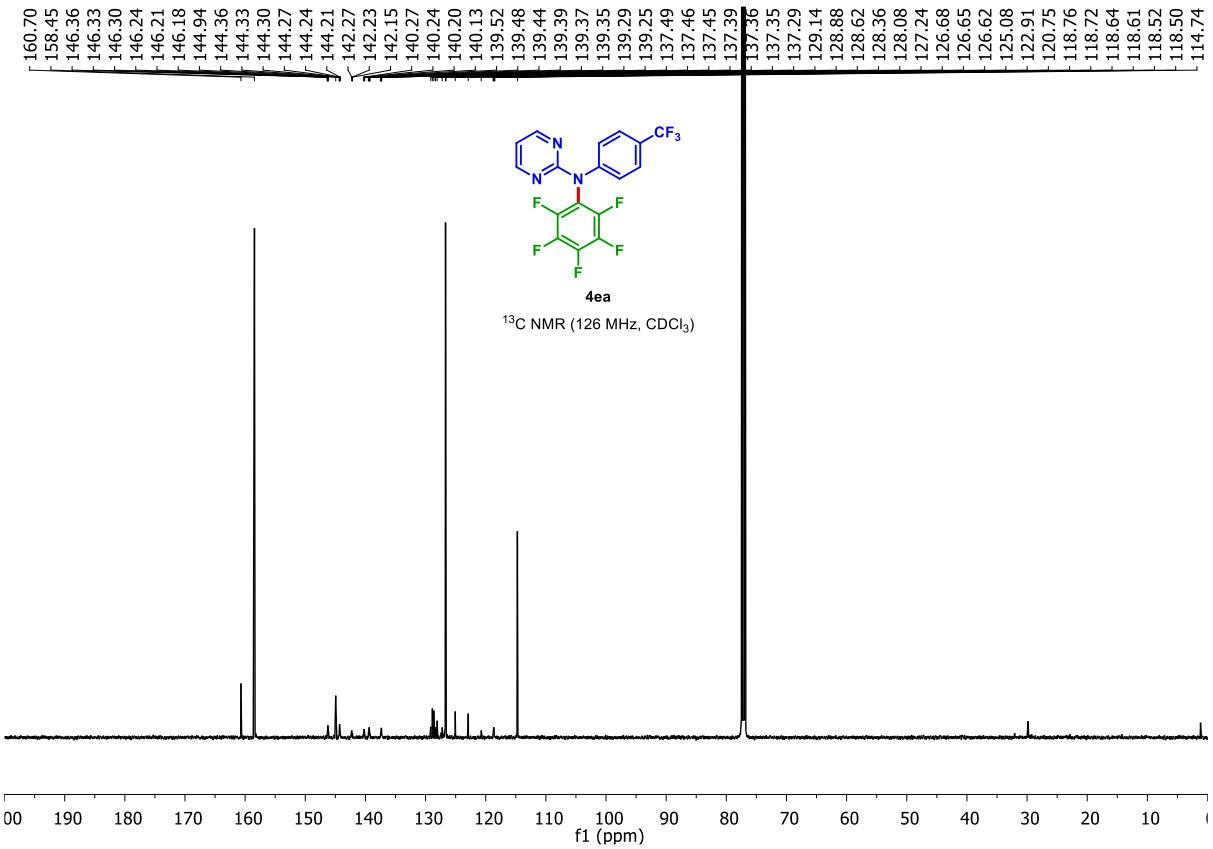
^{19}F NMR (471 MHz, $CDCl_3$)

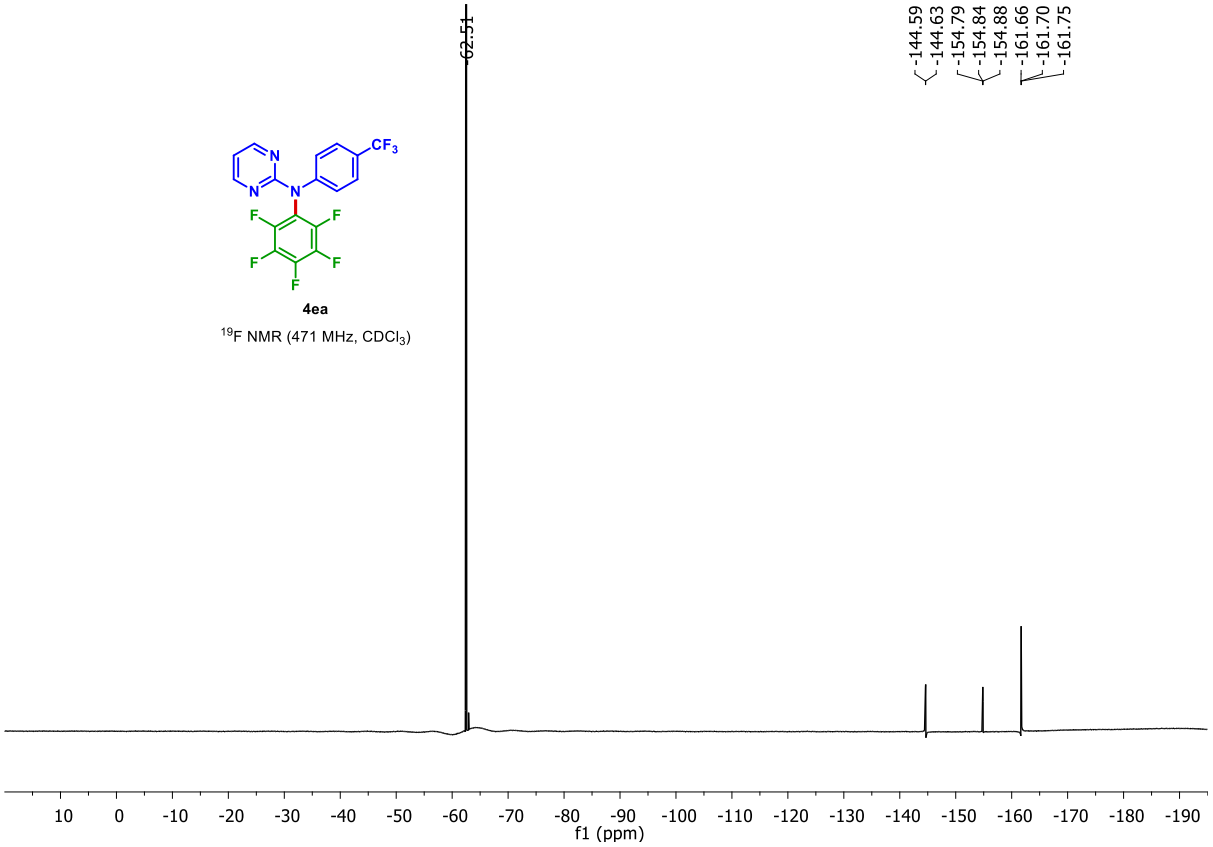

8.39
8.38
7.35
7.34
7.32
7.31
6.96
6.96
6.95
6.94
6.93
6.92
6.79
6.78
6.77
3.82
OMe
N
N
N
F
F
F
F
F
4da
1H NMR (400 MHz,CDCl3)
2.06
2.04
2.02
1.00
3.04
f1 (ppm)

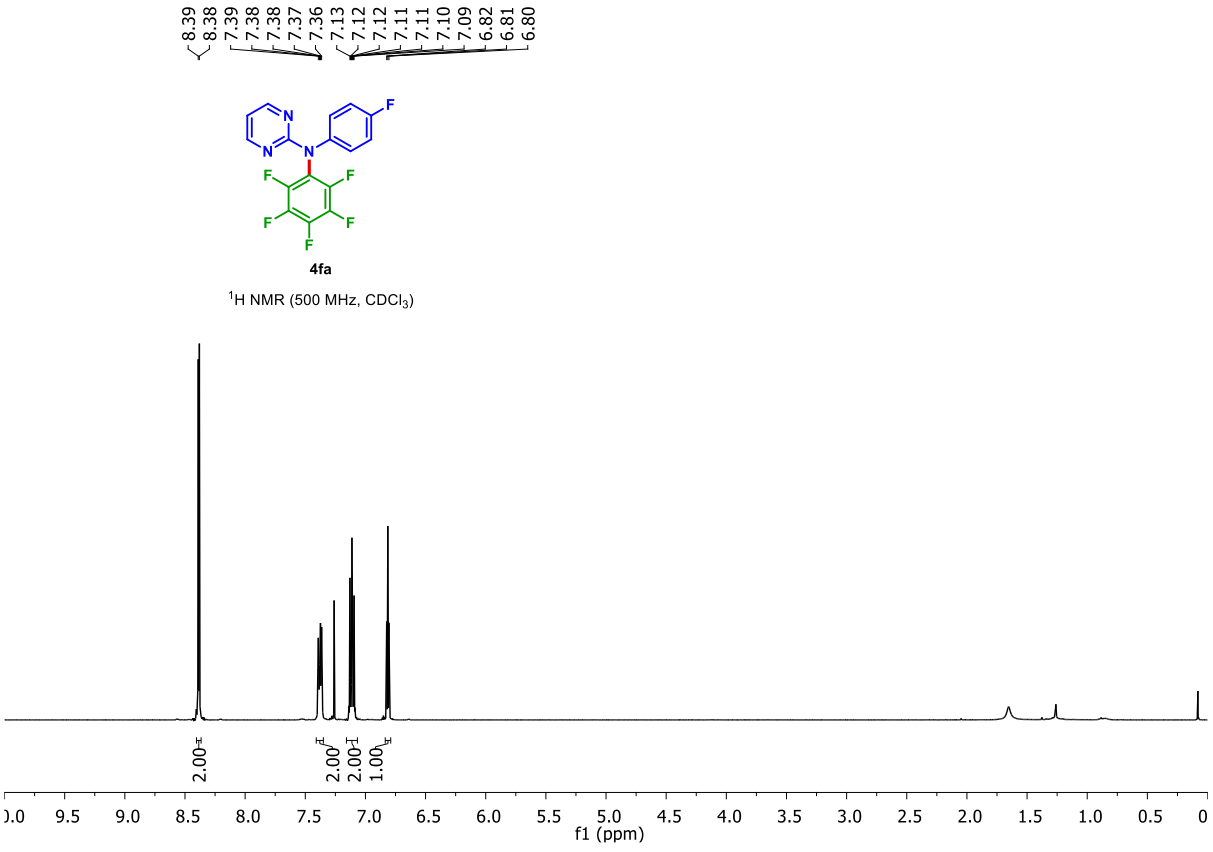

161.33
158.66
158.20
146.25
146.21
146.18
146.15
146.10
143.81
143.76
143.72
143.70
143.66
143.61
143.57
143.55
142.09
142.00
141.96
141.93
141.91
141.81
139.57
139.53
139.50
139.48
139.43
139.37
139.35
139.30
139.25
139.22
139.19
137.03
137.00
136.98
136.95
136.90
136.88
136.84
136.82
136.78
136.70
136.69
136.66
134.26
128.86
119.43
119.39
119.28
119.23
119.13
114.82
113.35
55.43
OMe
N
N
N
F
F
F
F
F
4da
13C NMR (101 MHz,CDCl3)
f1 (ppm)

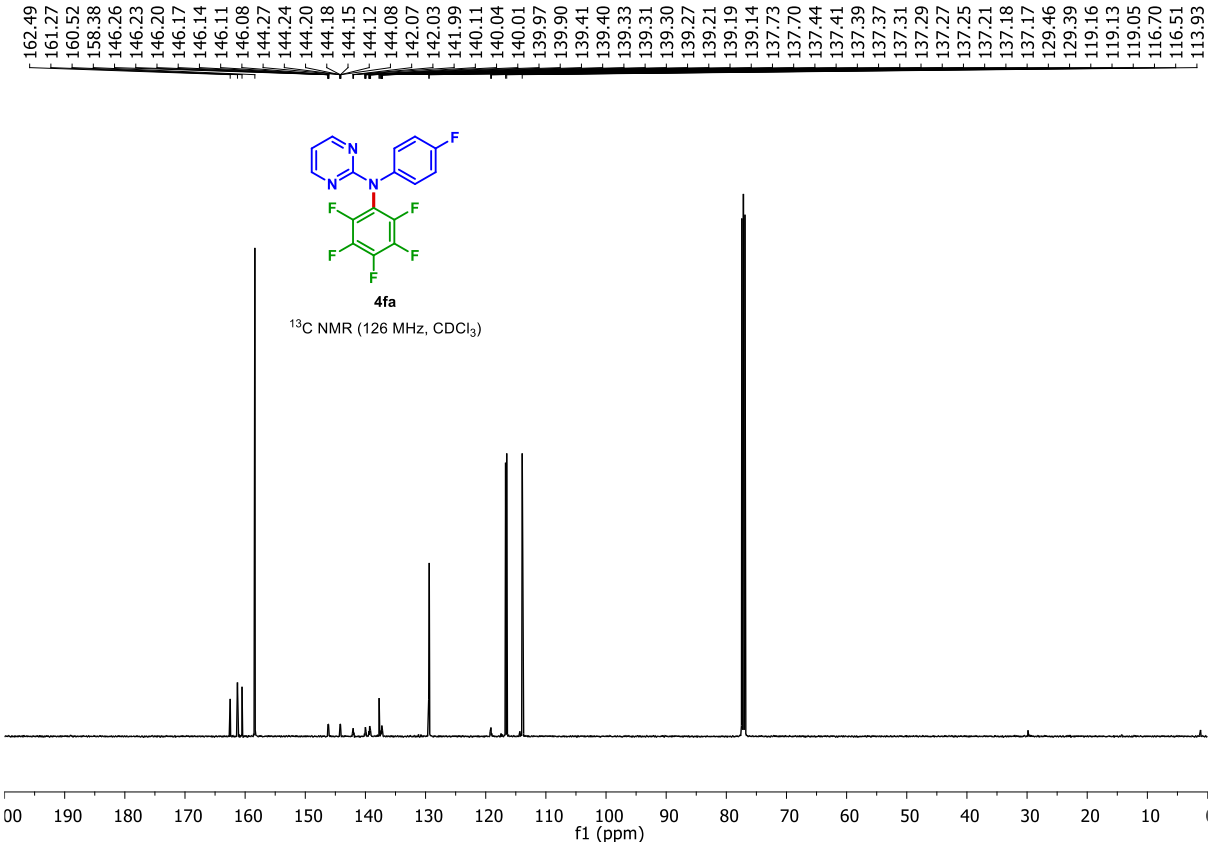

-144.77
-144.78
-144.81
-144.83
-156.06
-156.11
-156.15
-162.19
-162.20
-162.24
-162.25
-162.29
-162.30
OMe
N
N
N
F
F
F
F
F
4da
19F NMR (471 MHz,CDCl3)
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

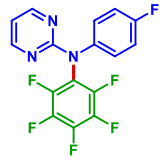

8.43
8.42
7.67
7.65
7.48
7.47
6.89
6.88
6.87
CF3
N
N
N
F
F
F
F
F
4ea
1H NMR (500 MHz, CDCl3)
2.02
2.02
2.01
1.00
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)


160.70
158.45
146.36
146.33
146.30
146.24
146.21
146.18
144.94
144.36
144.33
144.30
144.27
144.24
144.21
142.27
142.23
142.15
140.27
140.24
140.20
140.13
139.52
139.48
139.44
139.39
139.37
139.35
139.29
139.25
137.49
137.46
137.45
137.39
137.36
137.35
137.29
129.14
128.88
128.62
128.36
128.08
127.24
126.68
126.65
126.62
125.08
122.91
120.75
118.76
118.72
118.64
118.61
118.52
118.50
114.74
CF3
N
N
N
F
F
F
F
F
4ea
13C NMR (126 MHz, CDCl3)
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


62.51
-144.59
-144.63
-154.79
-154.84
-154.88
-161.66
-161.70
-161.75
CF3
N
N
N
F
F
F
F
F
4ea
19F NMR (471 MHz, CDCl3)
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

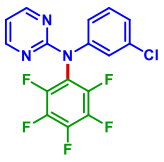

8.39
8.38
7.39
7.38
7.38
7.37
7.36
7.13
7.12
7.12
7.11
7.11
7.10
7.09
6.82
6.81
6.80
4fa
1H NMR (500 MHz, CDCl3)
2.00
2.00
2.00
1.00
f1 (ppm)


162.49
161.27
160.52
158.38
146.26
146.23
146.20
146.17
146.14
146.11
146.08
144.27
144.24
144.20
144.18
144.15
144.12
144.08
142.07
142.03
141.99
140.11
140.04
140.01
139.97
139.90
139.41
139.40
139.33
139.31
139.30
139.27
139.21
139.19
139.14
137.73
137.70
137.44
137.41
137.39
137.37
137.31
137.29
137.27
137.25
137.21
137.18
137.17
129.46
129.39
119.16
119.13
119.05
116.70
116.51
113.93
4fa
13C NMR (126 MHz, CDCl3)
f1 (ppm)



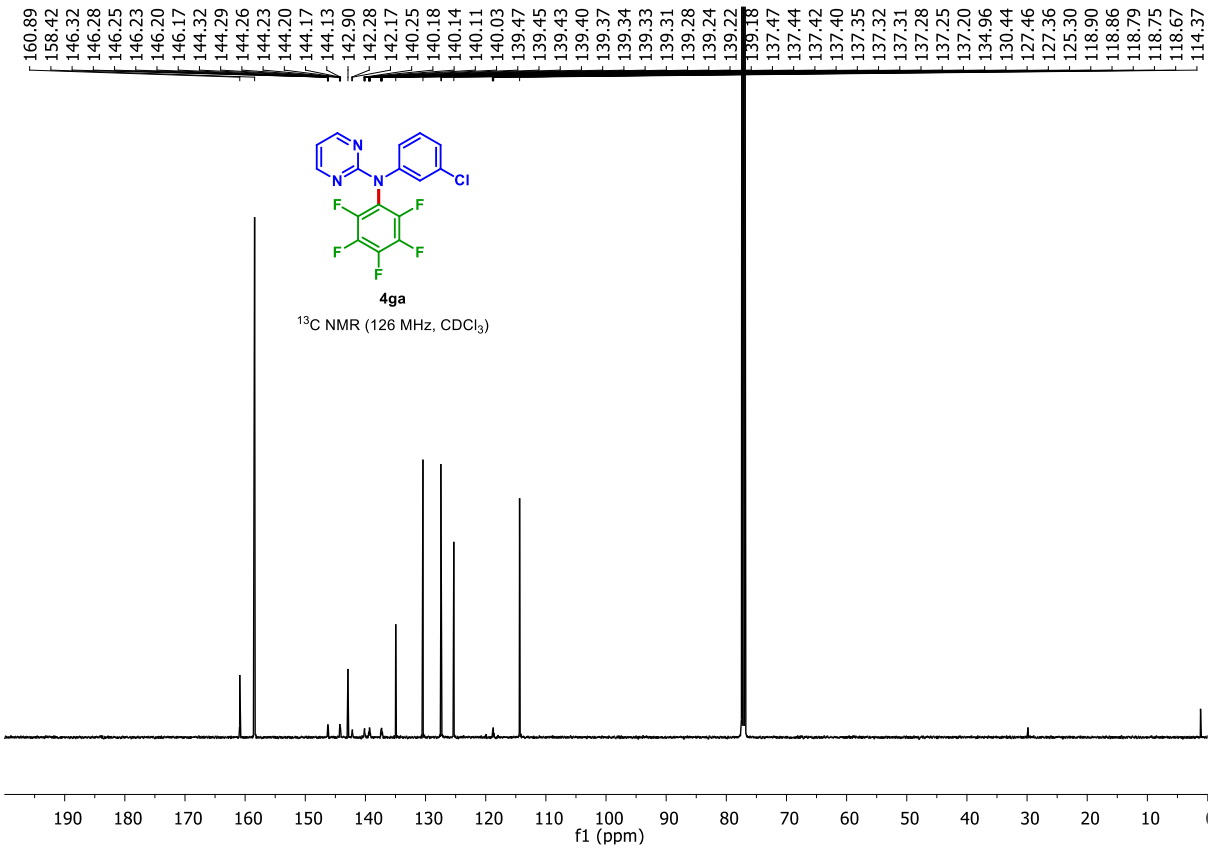
4fa

^{19}F NMR (471 MHz, $CDCl_3$)



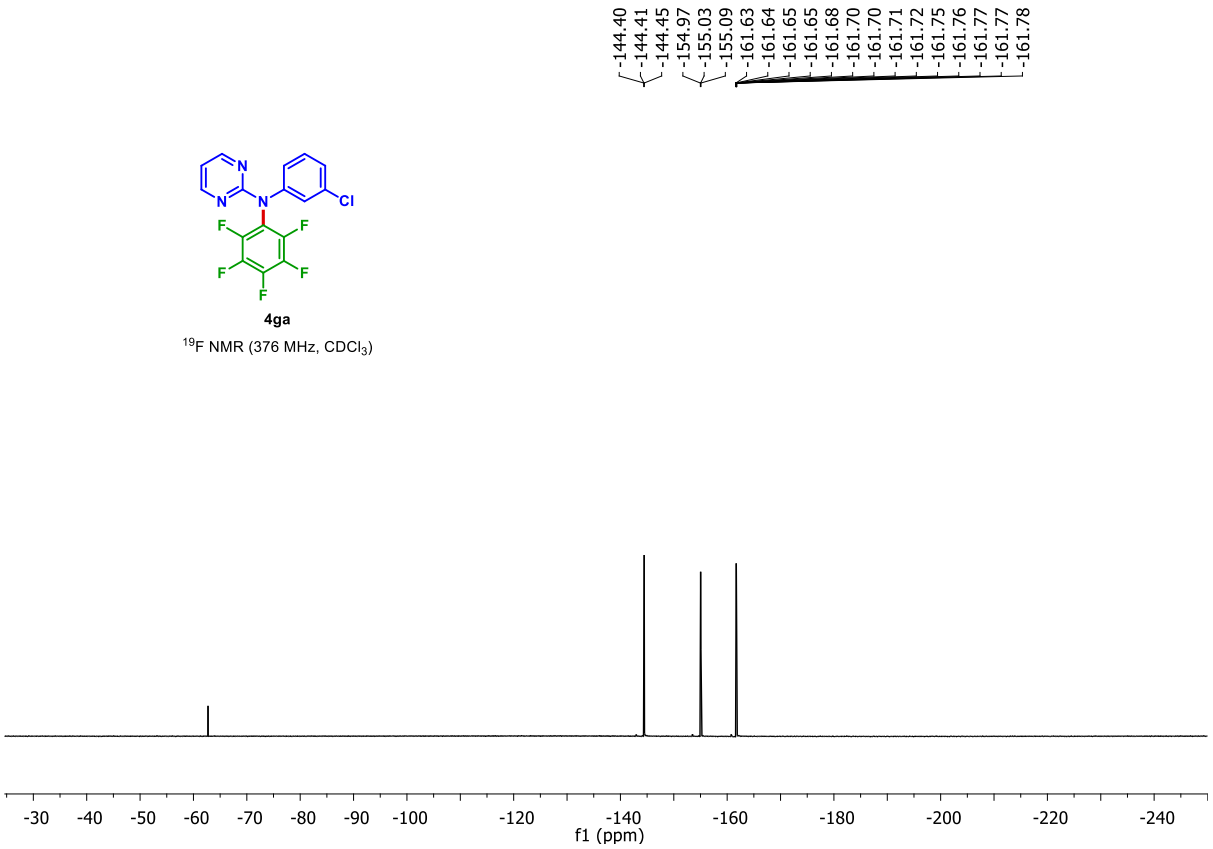
4ga

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



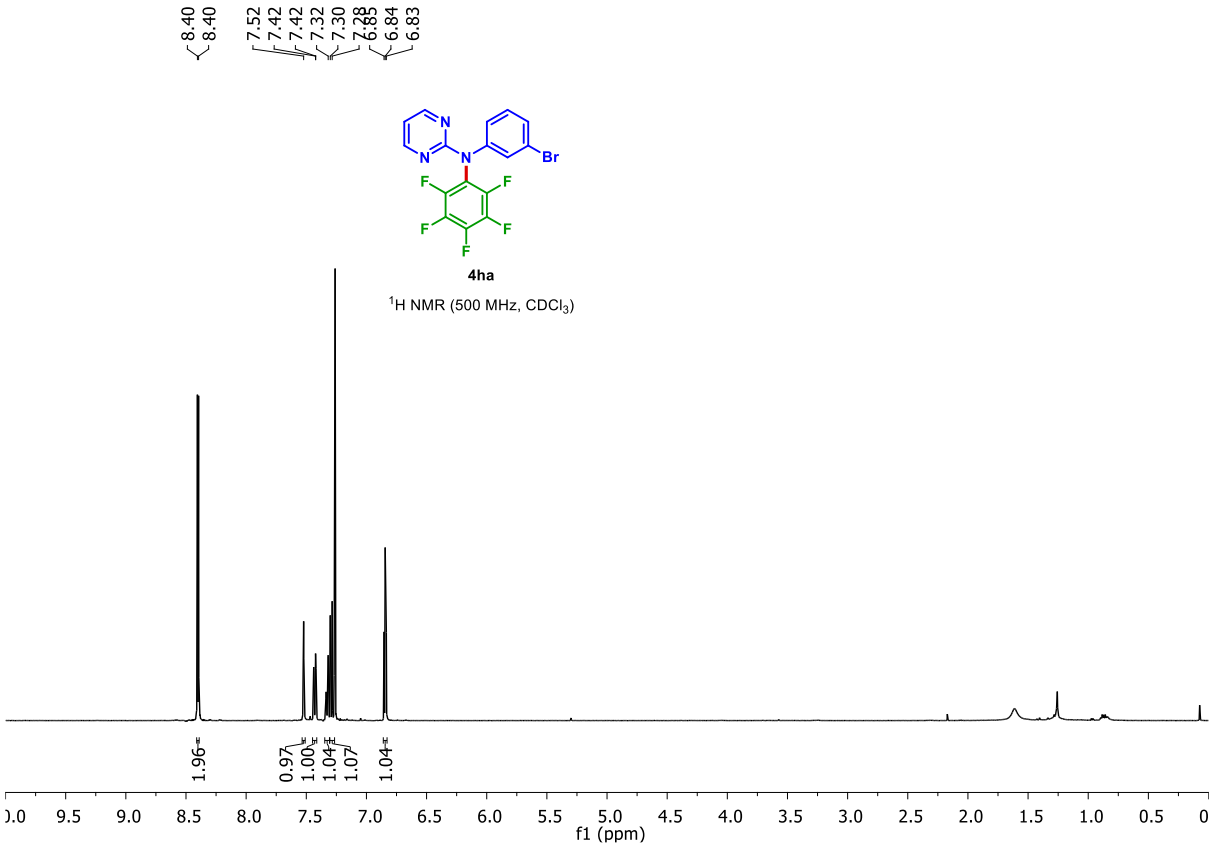
4ga

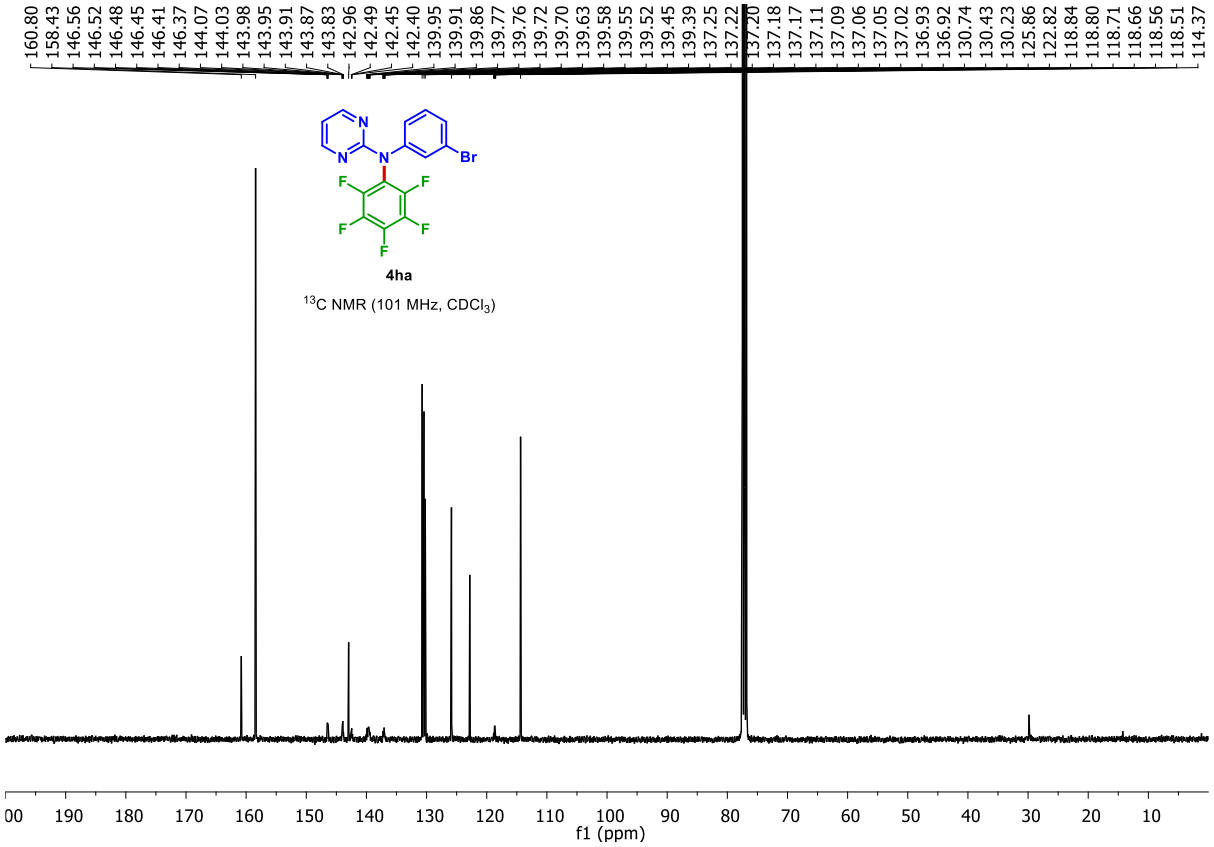
^{13}C NMR (126 MHz, $CDCl_3$)

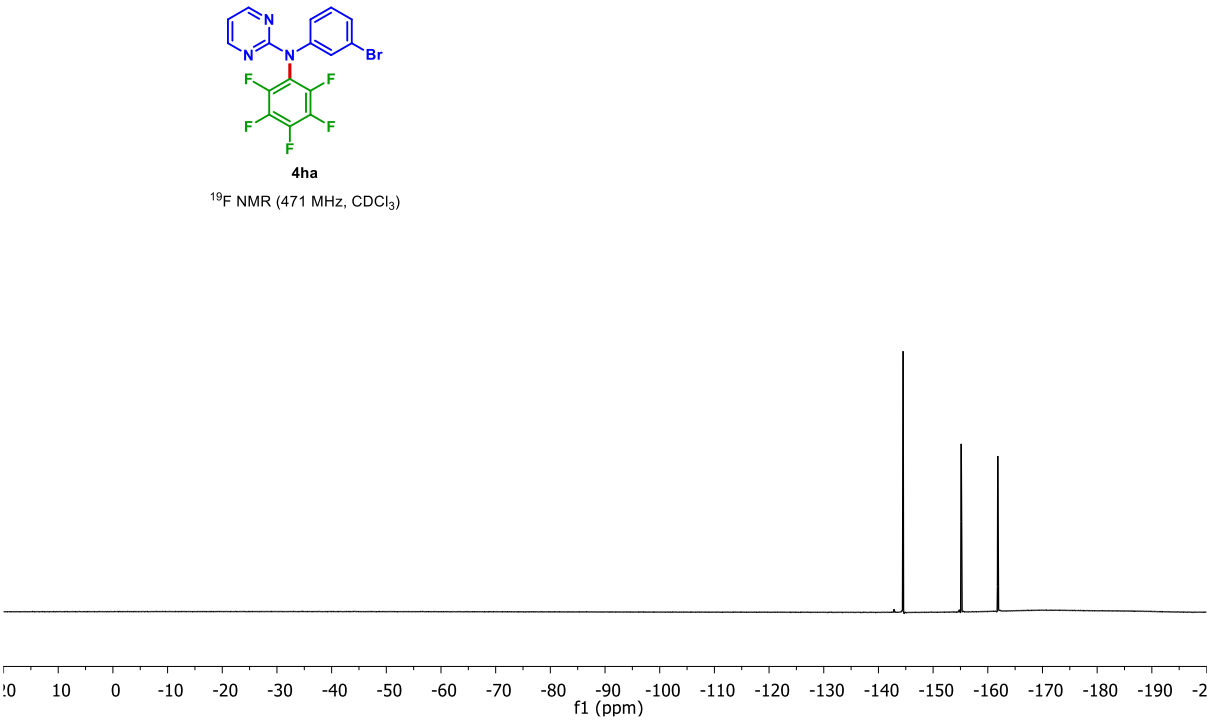


4ga

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

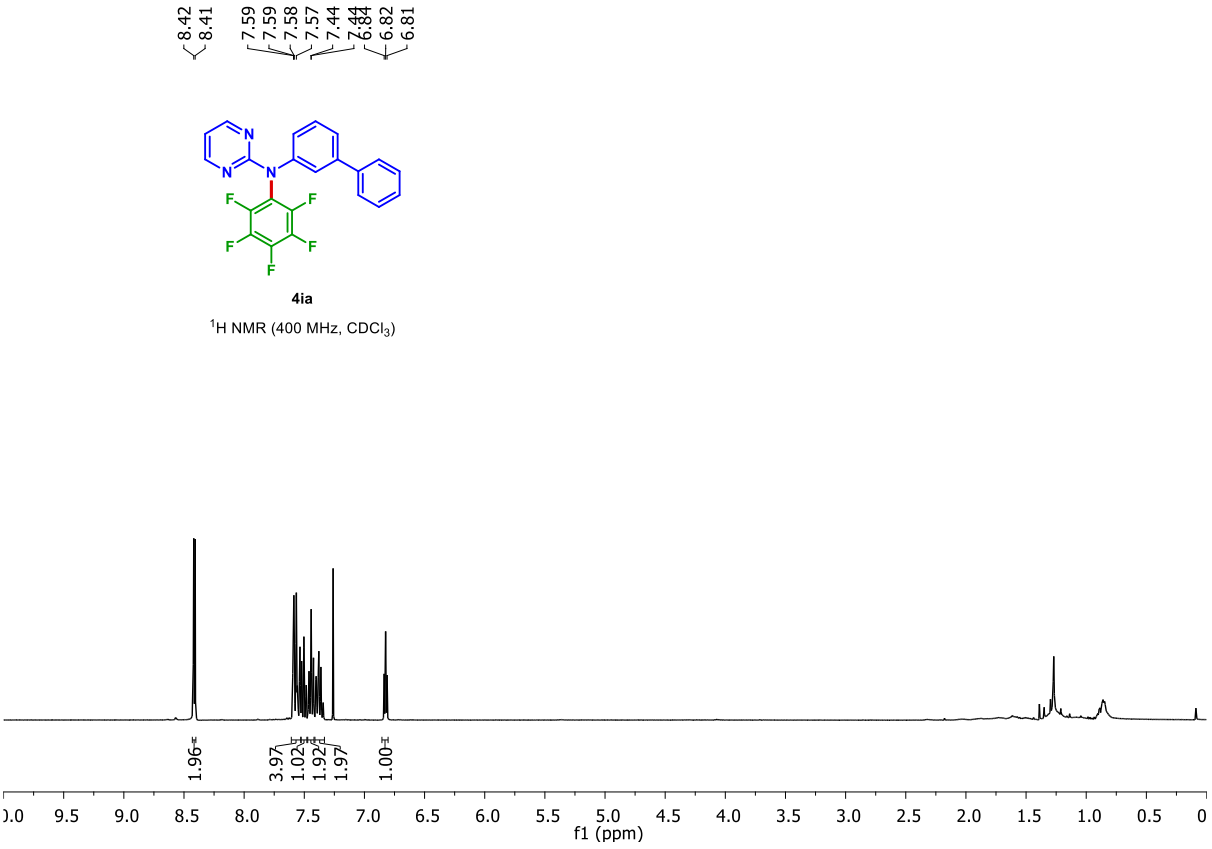

8.40
8.40
7.52
7.42
7.42
7.32
7.30
7.28
6.85
6.84
6.83
4ha
^{1}H NMR (500 MHz, $CDCl_3$)
1.96
0.97
1.00
1.04
1.07
1.04
f1 (ppm)


160.80
158.43
146.56
146.52
146.48
146.45
146.41
146.37
144.07
144.03
143.98
143.95
143.91
143.87
143.83
142.96
142.49
142.45
142.40
139.95
139.91
139.86
139.77
139.76
139.72
139.70
139.63
139.58
139.55
139.52
139.45
139.39
137.25
137.22
137.20
137.18
137.17
137.11
137.09
137.06
137.05
137.02
136.93
136.92
130.74
130.43
130.23
125.86
122.82
118.84
118.80
118.71
118.66
118.56
118.51
114.37
4ha
^{13}C NMR (101 MHz, $CDCl_3$)
f1 (ppm)



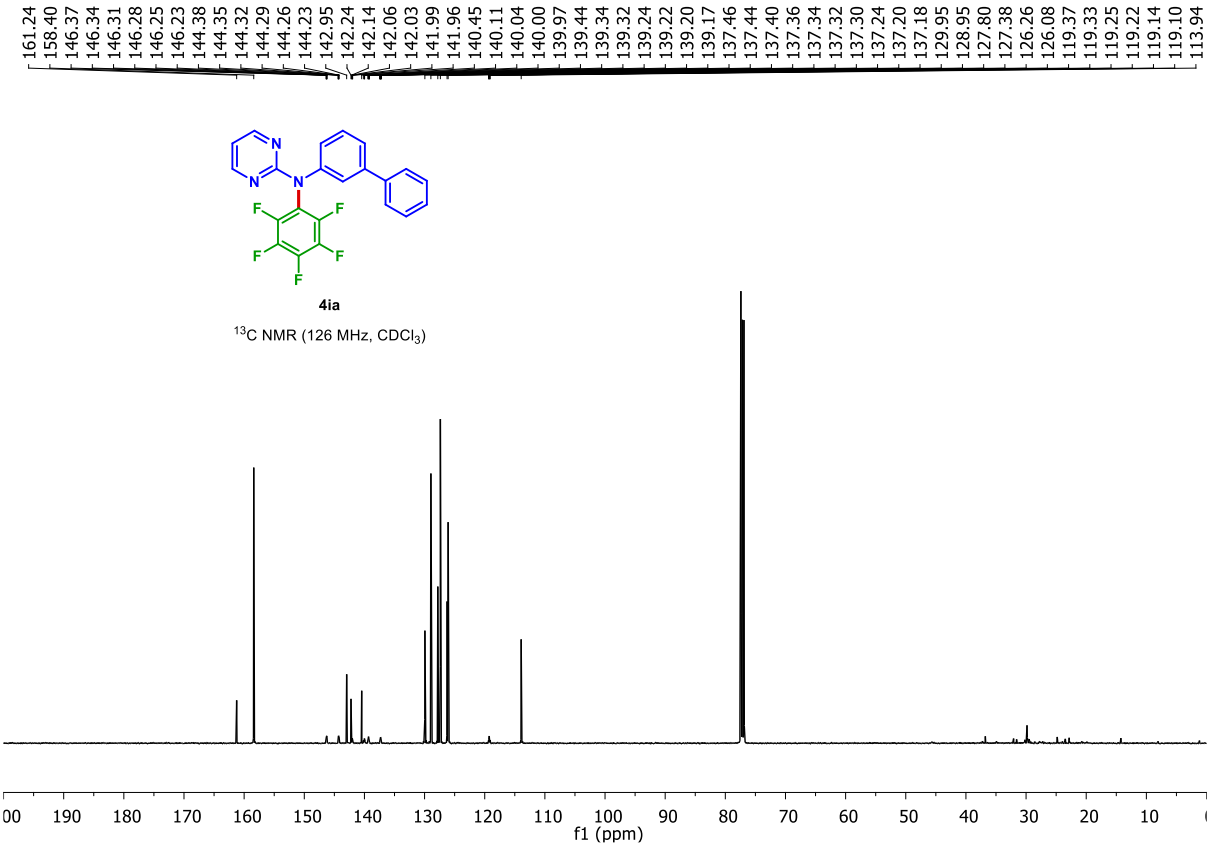
4ha

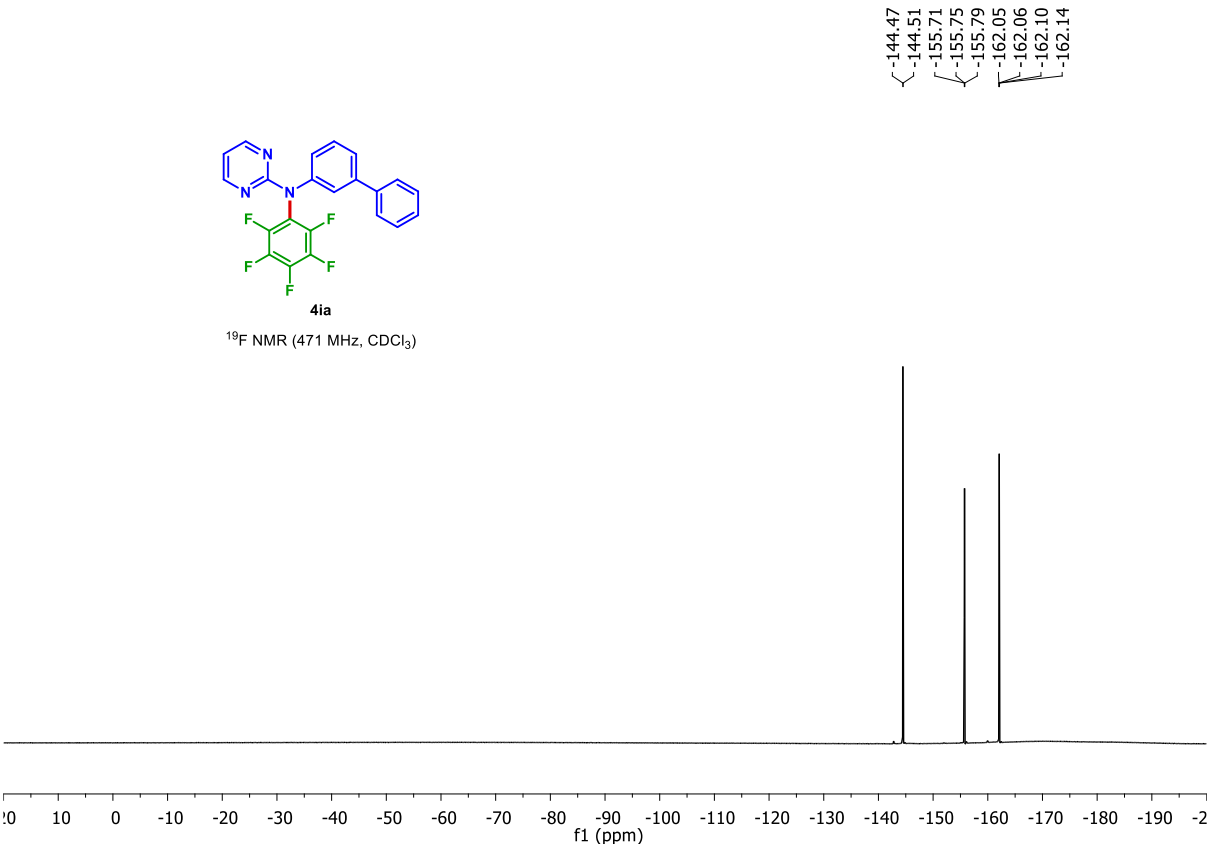
^{19}F NMR (471 MHz, $CDCl_3$)

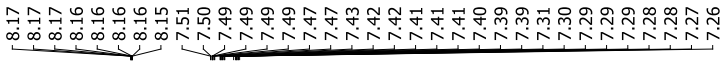


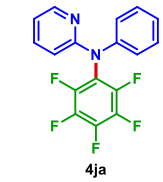
4ia

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


161.24
158.40
146.37
146.34
146.31
146.28
146.25
146.23
144.38
144.35
144.32
144.29
144.26
144.23
142.95
142.24
142.14
142.06
142.03
141.99
141.96
140.45
140.11
140.04
140.00
139.97
139.44
139.34
139.32
139.24
139.22
139.20
139.17
137.46
137.44
137.40
137.36
137.34
137.32
137.30
137.24
137.20
137.18
129.95
128.95
127.80
127.38
126.26
126.08
119.37
119.33
119.25
119.22
119.14
119.10
113.94
4ia
^{13}C NMR (126 MHz, CDCl$_3$)
f1 (ppm)

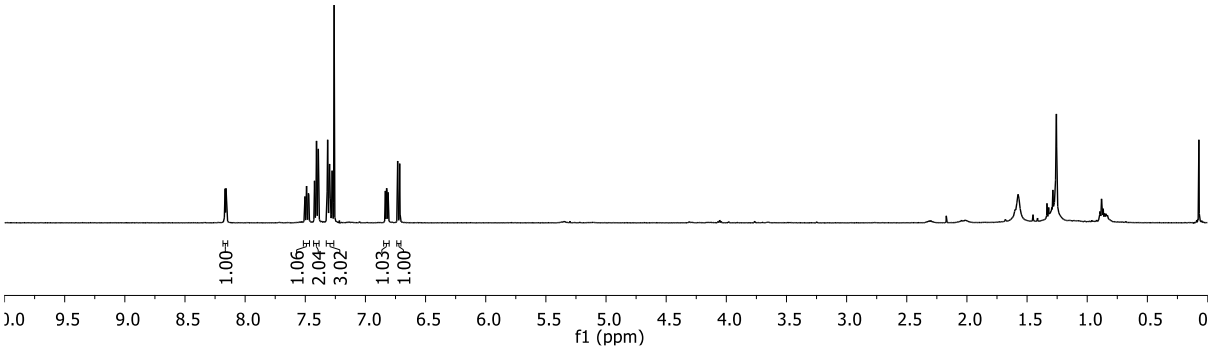

-144.47
-144.51
-155.71
-155.75
-155.79
-162.05
-162.06
-162.10
-162.14
4ia
^{19}F NMR (471 MHz, CDCl$_3$)
f1 (ppm)

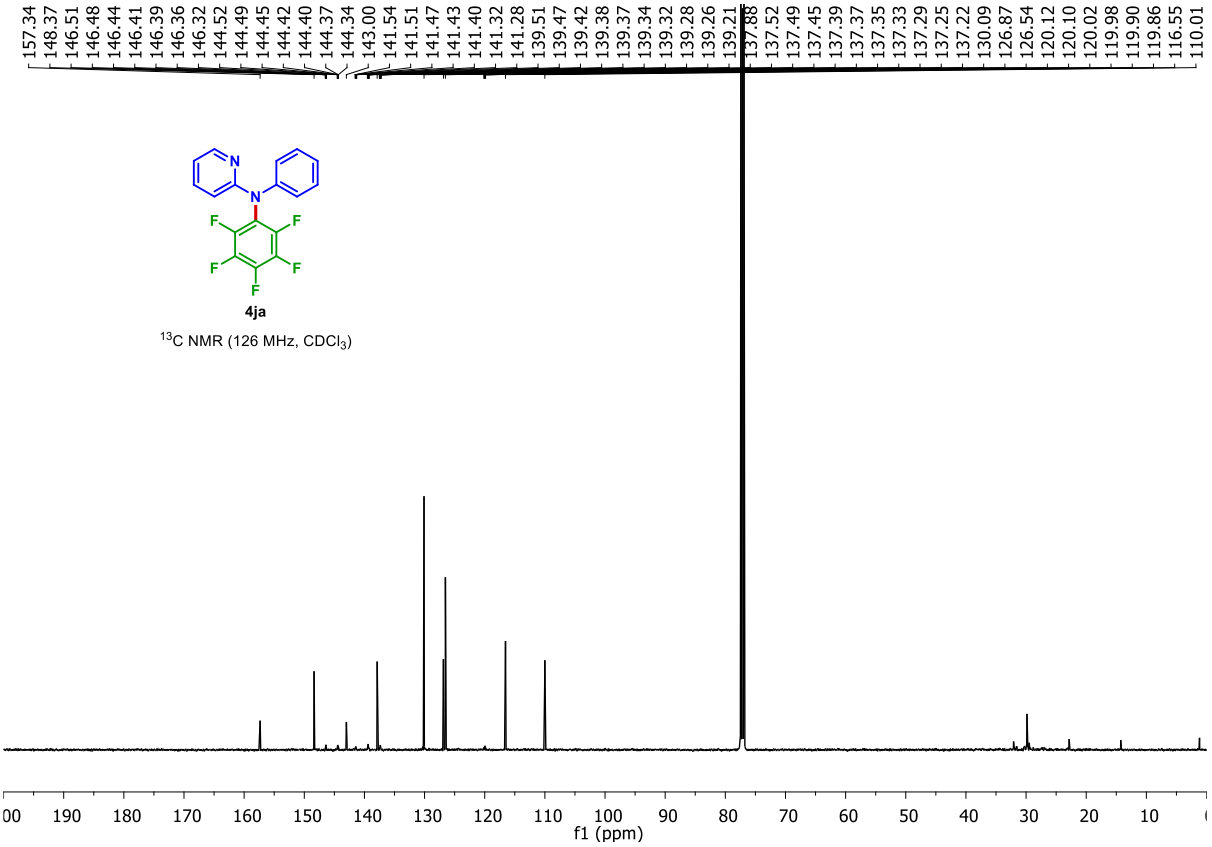




4ja

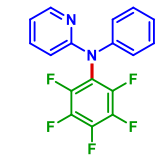
^{1}H NMR (500 MHz, $CDCl_3$)





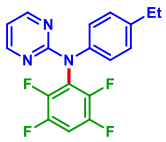
4ja

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



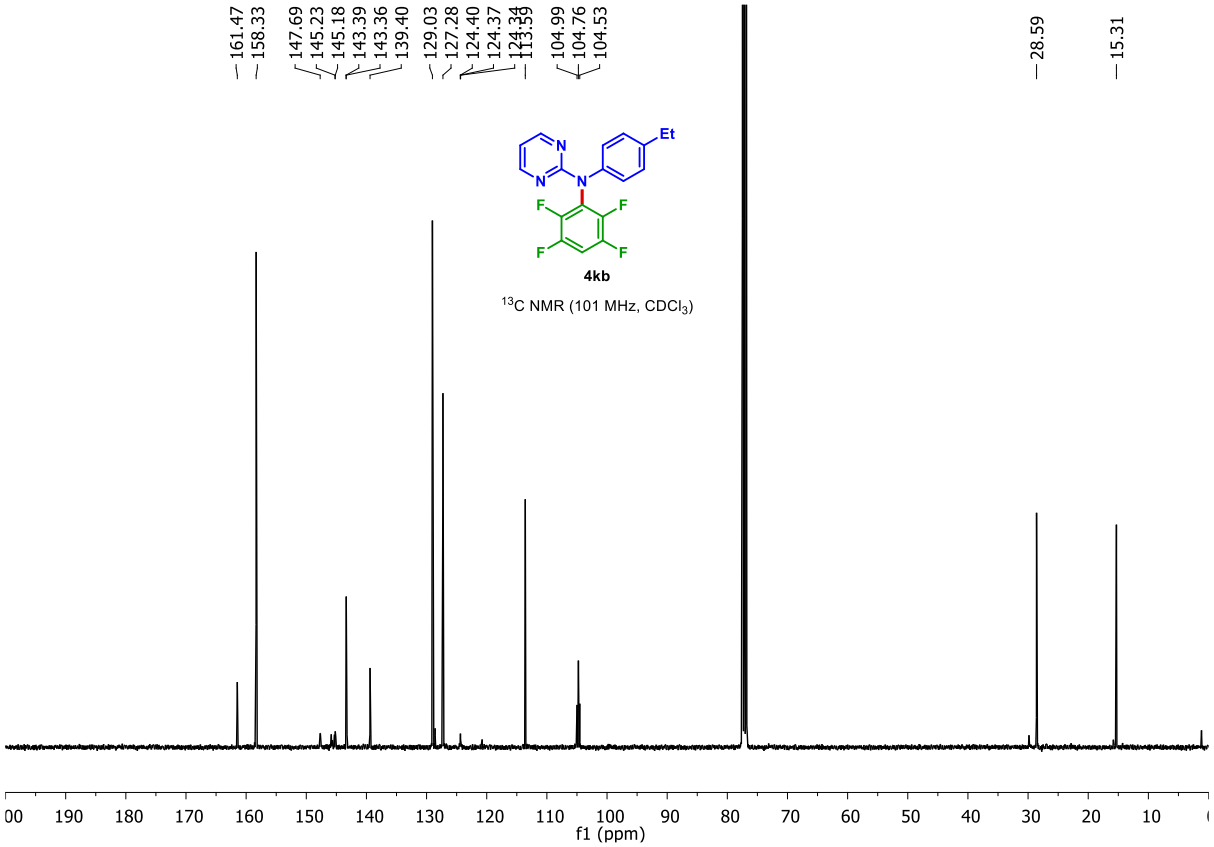
4ja

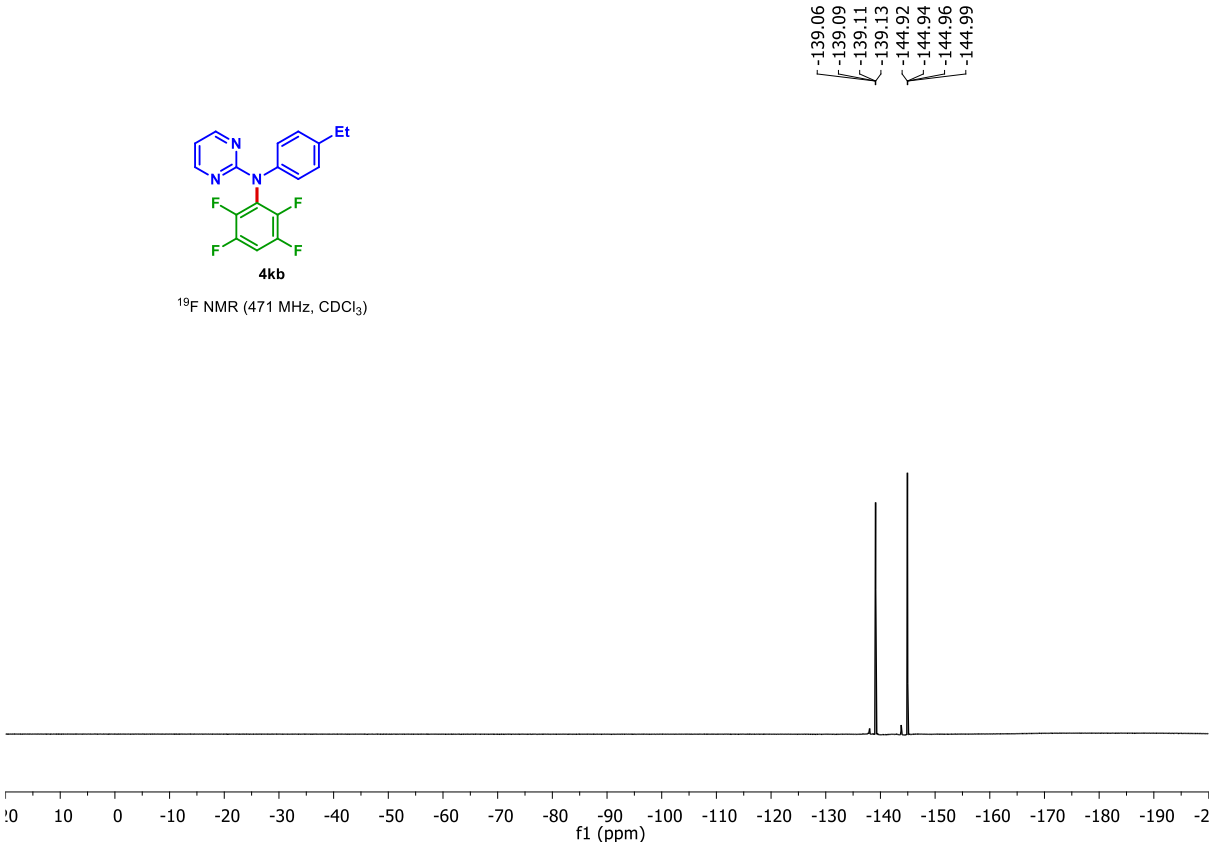
^{19}F NMR (471 MHz, $CDCl_3$)

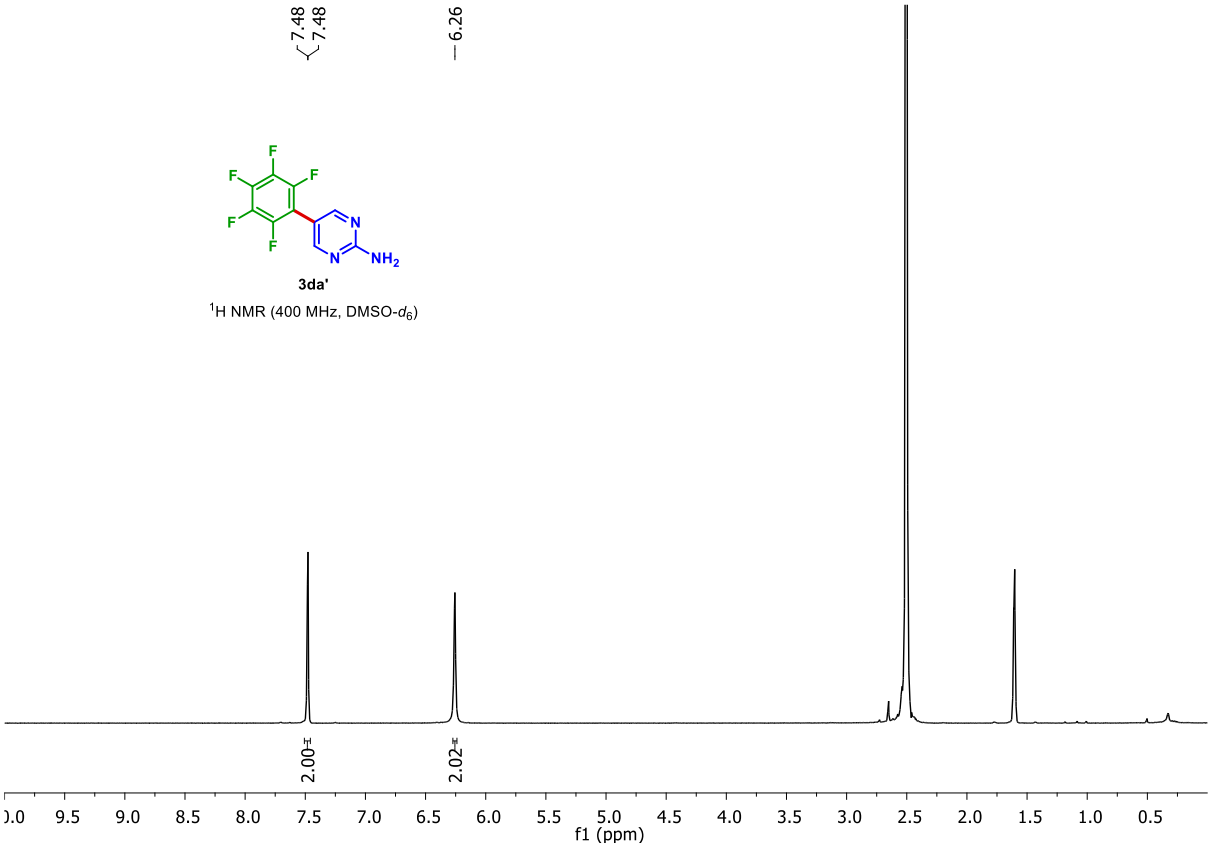


4kb

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

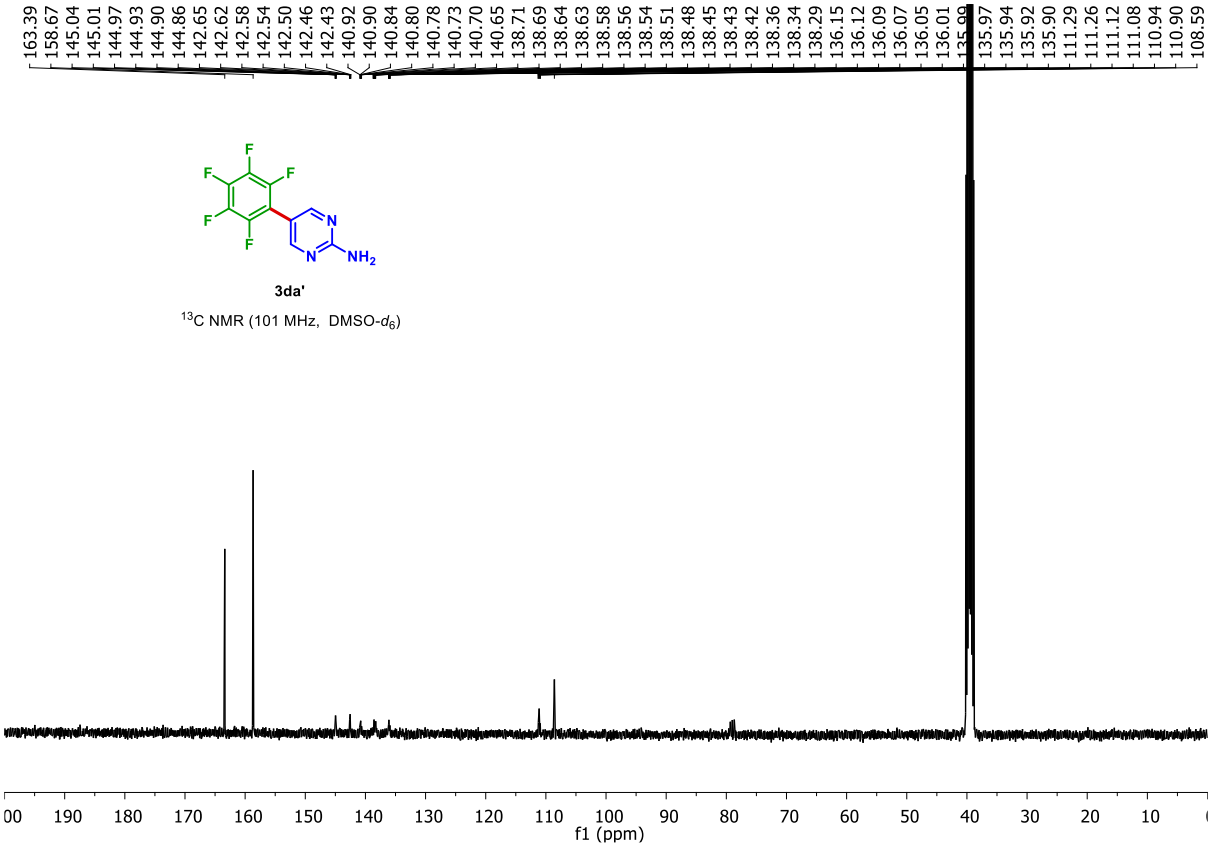

161.47
158.33
147.69
145.23
145.18
143.39
143.36
139.40
129.03
127.28
124.40
124.37
124.34
113.39
104.99
104.76
104.53
28.59
15.31
Et
N
N
N
F
F
F
F
4kb
13C NMR (101 MHz, CDCl3)
f1 (ppm)


-139.06
-139.09
-139.11
-139.13
-144.92
-144.94
-144.96
-144.99
Et
N
N
N
F
F
F
F
4kb
19F NMR (471 MHz, CDCl3)
f1 (ppm)



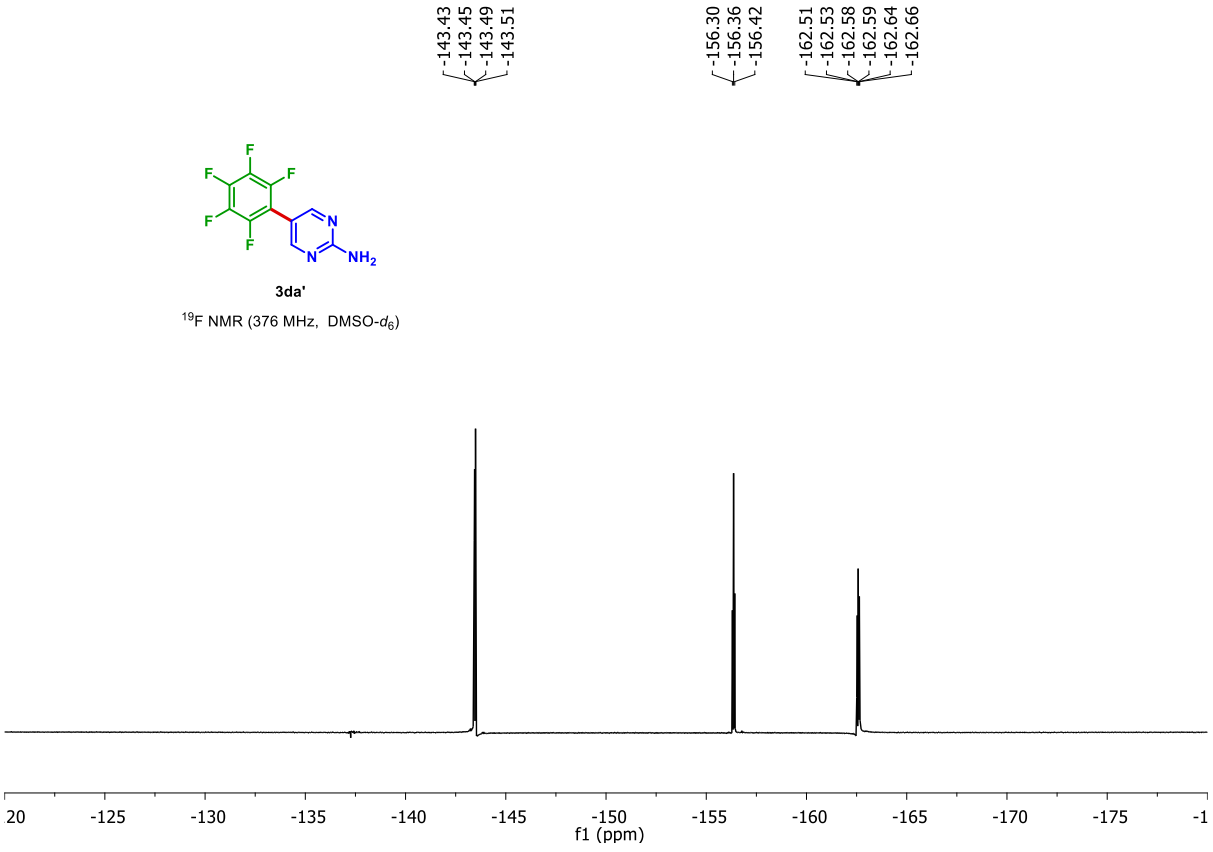
3da'

^{1}H NMR (400 MHz, DMSO-d_6)



3da'

^{13}C NMR (101 MHz, DMSO-d_6)


-143.43
-143.45
-143.49
-143.51
-156.30
-156.36
-156.42
-162.51
-162.53
-162.58
-162.59
-162.64
-162.66
F
F
F
F
F
N
N
NH2
3da'
19F NMR (376 MHz, DMSO-d6)
20
-125
-130
-135
-140
-145
-150
-155
-160
-165
-170
-175
-1
f1 (ppm)