Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

for

Z-Selective Pd-Catalyzed 2,2,2-Trifluoroethylation of Acrylamides at Room Temperature

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1. General information

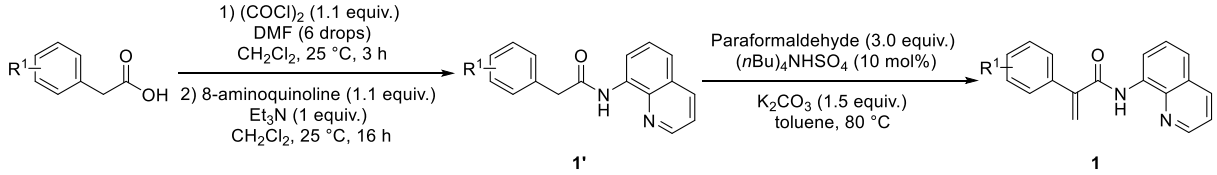
All reactions were carried out using oven-dried glassware and magnetic stirring under argon at 25 °C unless otherwise stated. Analytical thin layer chromatography was performed on silica gel aluminum plates with F-254 indicator and visualized by UV light (254 nm) and/or chemical staining with a $KMnO_4$ solution, *p*-anisaldehyde or a phosphomolybdic acid solution. Silica gel column chromatography was performed using 0.040-0.063 nm silica gel. ^{1}H NMR spectra were recorded on a Bruker DXP 300 MHz spectrometer at 300.1 MHz, ^{13}C NMR spectra at 75.5 MHz and ^{19}F NMR spectra at 282.4 MHz. Chemical shifts (δ) are quoted in parts per million (ppm) relative to residual solvent peak for $CDCl_3$ (δ_H = 7.26 ppm, δ_C = 77.00 ppm) and relative to external $CFCl_3$ (δ_F = 0 ppm). Coupling constants (*J*) are quoted in Hz. The following abbreviations were used to show the multiplicities: s: singlet, d: doublet, t: triplet, q: quadruplet, dd: doublet of doublet, qd: quartet of doublets, m: multiplet. High-Resolution Mass Spectra (HRMS) were recorded with a Waters LCT Premier mass spectrometer with a micro-TOF analyzer. IR spectra were recorded on a PerkinElmer Spectrometer Pargon 100 (ATR). The wave numbers (n) of recorded IR-signals are quoted in cm^{-1}. Melting points were recorded on a Heizbank system Kofler WME and were uncorrected.

2. Materials

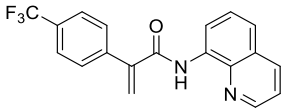
Acetonitrile (MeCN) and dichloromethane (CH_2Cl_2) were distilled over CaH_2 prior to use. Analytical reagent grade toluene was used from Fisher Scientific. Anhydrous *N*,*N*-dimethylformamide (DMF) over molecular sieve from Acros Organics (Solvent extra dry over molecular sieves, Acroseal®) was used. Oxalyl chloride, 8-aminoquinoline, triethylamine and palladium(II) acetate were purchased from Acros Organics or Sigma Aldrich. Acrylamides **1a**,[1] **[D]-1a**,[1] **1b**,[2] **1c**,[1] **1d**,[1] **1f**,[2] **1g**,[1] **1h**,[1] **1i**,[1] **1j**,[2] **1l**,[1] **1m**,[1] **1n**,[1] **1o**,[1] **1p**,[1] **1q**,[2] **1r**,[1] and **1s**,[2] were prepared according to the procedures described in the literature.

3. General procedure for the synthesis of amides 1

3.1 Preparation of amides 1b-d and 1f-q



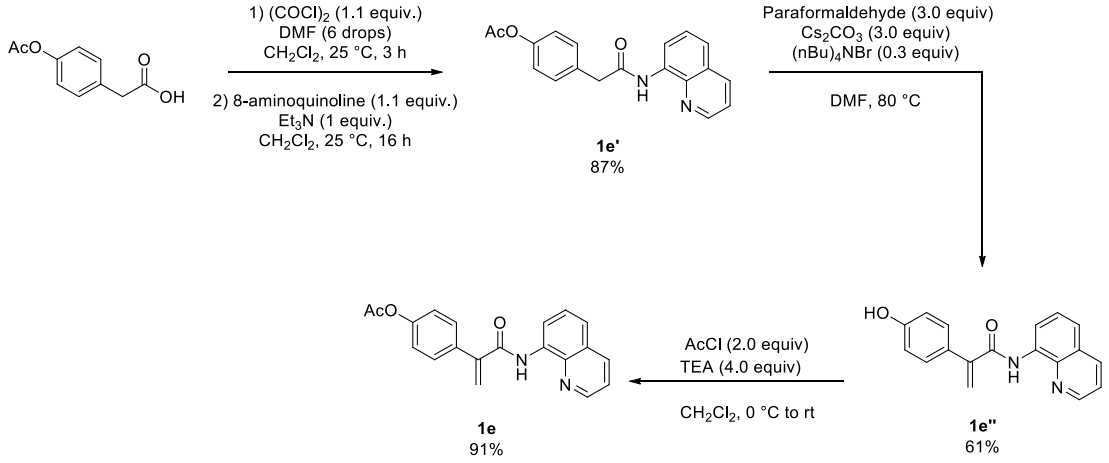
In an oven-dried round bottom Schlenk under argon, oxalyl chloride (1.9 mL, 22.0 mmol, 1.1 equiv.) was slowly added at 0 °C to a solution of the acid (20.0 mmol, 1.0 equiv.) and DMF (6 drops) in dried CH_2Cl_2 (30 mL). After stirring at room temperature for 3 hours, the solvent was removed under vacuum and the residue was dissolved in dried CH_2Cl_2 (100 mL). Et_3N (2.8 mL, 20 mmol, 1.0 equiv.) and 8-aminoquinoline (3.17 g, 22.0 mmol, 1.1 equiv.) were added and the reaction was followed by TLC until it was completed. Water (200 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 × 300 mL). The combined organic layers were dried over $MgSO_4$. Removal of the solvent under vacuum and purification of the residue by silica gel column chromatography afforded the desired intermediate **1'**.
An oven-dried round bottom flask, equipped with a reflux condenser under argon, was charged with **1'** (10.0 mmol, 1.0 equiv), paraformaldehyde (900.0 mg, 30.0 mmol, 3.0 equiv.), (nBu)$_4$NHSO$_4$ (34.0 mg, 0.10 mmol, 0.1 equiv.) and K_2CO_3 (2.07 g, 15.0 mmol, 1.5 equiv), followed by toluene (80 mL). The reaction mixture was stirred at 80 °C and the reaction was followed by TLC until completion. Water (200 mL) was added and the aqueous layer was extracted with Et_2O (3 × 300 mL). The combined organic layers were dried over Na_2SO_4. Removal of the solvent under vacuum and purification of the residue by silica gel column chromatography afforded the desired product **1**.



1k

***N*-(quinolin-8-yl)-2-(4-(trifluoromethyl)phenyl)acrylamide 1k**. Prepared in a 10 mmol scale. Purification by silica gel column chromatography (height 8 cm, width 3.5 cm, eluent: Petroleum ether/CH_2Cl_2, from 50:50 to 20:80). The titled compound was obtained as a white solid (1.30 g, **67%**). **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 10.26 (s, 1H), 8.91 – 8.81 (m, 1H), 8.67 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.74 – 7.65 (m, 4H), 7.62 – 7.52 (m, 2H), 7.43 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.38 (s, 1H), 5.92 (s, 1H).**^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 165.0, 148.2, 144.8, 140.2, 138.5, 136.1, 134.1, 130.4 (q, *J* = 32.5 Hz), 128.6, 127.8, 127.2, 125.4 (q, *J* =3.8 Hz), 124.0 (q, *J* = 272.6 Hz), 122.9, 122.0, 121.6, 116.5. *NMR data are in accordance with the literature data*.[3]

3.2 Preparation of the amide 1e



Compound **1e'** was prepared following the procedure described in the section 3.1 starting from 2-(4-acetoxyphenyl)acetic acid, which was previously synthetized according to a procedure already reported in the literature.[4] After purification by silica gel column chromatography (height 13 cm, width 5.0 cm, eluent: Petroleum ether/EtOAc, from 90:10 to 50:50) the titled compound was obtained as a brownish solid (5.58 g, **87%**). **R_f** (Petroleum ether/ EtOAc, 50:50):0.44. **m.p.**: 103 – 104 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 9.92 (s, 1H), 8.78 – 8.66 (m, 2H), 8.16 – 8.07 (m, 1H), 7.56 – 7.36 (m, 5H), 7.17 – 7.09 (m, 2H), 3.88 (s, 2H), 2.31 (s, 3H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 169.4, 169.1, 149.9, 148.2, 138.2, 136.1, 134.2, 132.2, 130.5, 127.7, 127.1, 122.0, 121.6, 121.5, 116.2, 44.5, 21.1. **IR** (neat, cm^{-1}) ν: 3319, 1758, 1688, 1522, 1484, 1180, 1161, 909, 830. **HRMS** (ESI^+) calcd. for $C_{19}H_{17}N_2O_3$ m/z 321.1239 $[M + H]^+$, found 321.1239 (0 ppm).

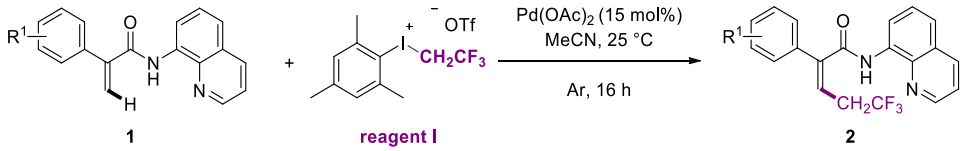
Compound **1e''** was obtained following a procedure adapted from the literature.[5] In an oven-dried round bottom flask under argon, Cs_2CO_3 (2.93 g, 9.0 mmol, 3.0 equiv.), (nBu)$_4$NBr (290 mg, 0.90 mmol, 0.3 equiv.) and paraformaldehyde (270 mg, 9.0 mmol, 3.0 equiv.) were added to a solution of **1e'** (961 mg, 3.0 mmol, 1.0 equiv.) in dried DMF (15 mL). The reaction mixture was stirred for 4 hours at 80 °C. Upon cooling down to room temperature, water (20 mL) was added followed by EtOAc (20 mL). The aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (3 × 20 mL), dried over Na_2SO_4 and concentrated under vacuum. The crude material was purified by silica gel column chromatography (Petroleum ether/EtOAc, from 90:10 to 50:50) affording the intermediate **1e''** (530 mg, **61%**), in which the acetyl group was cleaved.

Et_3N (0.94 mL, 6.88 mmol, 4 equiv.) and acetyl chloride (0.25 mL, 4 equiv., 3.44 mmol) were added dropwise to a solution of the intermediate **1e''** (500 mg, 1.0 equiv., 1.72 mmol) in CH_2Cl_2 at 0 °C. The reaction mixture was stirred for 4 hours at 25 °C. Water (20 mL) was then added. The organic layer was

washed with water (2 x 10 mL), dried over Na_2SO_4 and concentrated under vacuum. Purification by silica gel column chromatography (height 13 cm, width 3 cm, eluent: Petroleum ether/EtOAc, from 90:10 to 70:30) furnished **1e** (521 mg, **91%**) as a pale brown solid. $\mathbf{R_f}$ (Petroleum ether/EtOAc, 50:50):0.42. **m.p.**: 112 – 113 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 10.27 (s, 1H), 8.87 (dd, *J* = 7.1, 1.9 Hz, 1H), 8.69 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.63 – 7.48 (m, 4H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.22 – 7.14 (m, 2H), 6.32 (s, 1H), 5.84 (s, 1H), 2.34 (s, 3H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 169.3, 165.5, 150.9, 148.4, 145.0, 138.6, 136.2, 134.3, 129.5, 127.8, 127.2, 122.3, 122.0, 121.9, 121.6, 116.5, 21.2. One carbon is overlapped. **IR** (neat, cm^{-1}) ν 3374, 1749, 1668, 1528, 1509, 1487, 1204, 1172, 915, 788. **HRMS** (ESI^+) calcd. for $C_{20}H_{17}N_2O_3$ m/z 333.1239 $[M + H]^+$, found 333.1235 (-1.2 ppm).

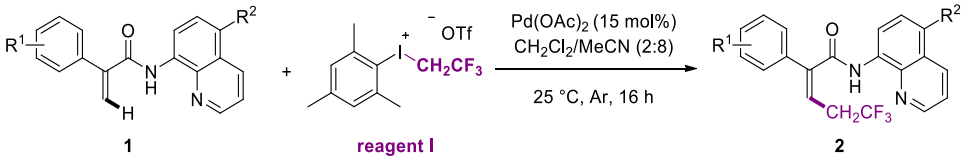
4. General procedure for the synthesis of the trifluoroethylated acrylamides 2

Procedure 1:



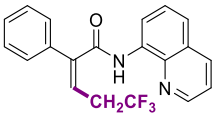
An oven-dried sealed tube equipped with a stirring bar under argon was charged with $Pd(OAc)_2$ (13.5 mg, 0.06 mmol, 15 mol%), amide **1** (0.80 mmol, 2.0 equiv.), the 2,2,2-trifluoroethyl(mesityl)iodonium trifluoromethanesulfonate (191.2 mg, 0.40 mmol, 1.0 equiv.), followed by dried acetonitrile (2 mL). The mixture was stirred at 25 °C for 16 hours. The solvent was removed under vacuum and the resulting crude material was purified by silica gel column chromatography to afford the desired trifluoroethylated product **2**.

Procedure 2:



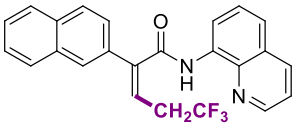
An oven-dried sealed tube equipped with a stirring bar under argon was charged with $Pd(OAc)_2$ (13.5 mg, 0.06 mmol, 15 mol%), amide **1** (0.80 mmol, 2.0 equiv.), the 2,2,2-trifluoroethyl(mesityl)iodonium trifluoromethanesulfonate (191.2 mg, 0.40 mmol, 1.0 equiv.), followed by dried acetonitrile (1.6 mL) and dried CH_2Cl_2 (0.4 mL). The mixture was stirred at 25 °C for 16 hours. The solvent was removed under vacuum and the resulting crude material was purified by silica gel column chromatography to afford the desired trifluoroethylated product **2**.

5. Purification and characterization of the trifluoroethylated acrylamides 2



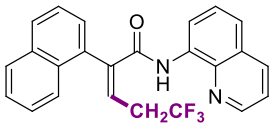
2a

(*Z*)-5,5,5-trifluoro-2-phenyl-*N*-(quinolin-8-yl)pent-2-enamide 2a was prepared according to the general procedure 1. Purification by silica gel column chromatography (height 12 cm, width 3.0 cm, eluent: *n*-Pentane/Et_2O, from 100:0 to 90:10) afforded the titled compound as a white solid (89.7 mg, **63%**). **R_f** (Cyclohexane/Et_2O, 80:20):0.46. **m.p.**: 84 – 85 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 10.03 (s, 1H), 8.94 – 8.84 (m, 1H), 8.66 – 8.59 (m, 1H), 8.18 – 8.10 (m, 1H), 7.63 – 7.49 (m, 4H), 7.48 – 7.35 (m, 4H), 6.17 (t, *J* = 7.2 Hz, 1H), 3.52 (qd, *J* = 10.8, 7.2 Hz, 2H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 165.7, 148.5, 143.2, 138.6, 136.7, 136.3, 134.1, 129.0, 129.0, 128.00, 127.7, 127.3, 126.1 (q, *J* = 276.9 Hz), 123.9 (q, *J* = 3.8 Hz), 122.4, 121.8, 116.8, 34.8 (q, *J* = 30.0 Hz). **^{19}F NMR** (282.4 MHz, $CDCl_3$) δ -66.4 (t, *J* = 10.8 Hz). **IR** (neat, cm^{-1}) ν: 3339, 2922, 1671, 1527, 1486, 1251, 1138, 1120, 887, 822, 786, 752. **HRMS** (ESI^+) calcd. for $C_{20}H_{16}F_3N_2O$ m/z 357.1215 $[M + H]^+$, found 357.1219 (1.1 ppm).



2b

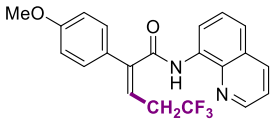
***(Z)*-5,5,5-trifluoro-2-(naphtalen-2-yl)-*N*-(quinolin-8-yl)pent-2-enamide 2b** was prepared according to the general procedure 2. Purification by silica gel column chromatography (height 10 cm, width 3.0 cm, eluent: Cyclohexane/Et_2O, from 98:2 to 95:5) afforded the titled compound as a white solid (63.3 mg, **39%**). **R_f** (Cyclohexane/Et_2O, 80:20):0.38. **m.p.**: 85 – 86 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 10.09 (s, 1H), 8.93 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.53 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.13 (dd, *J* = 8.3, 1.5 Hz, 1H), 8.01 (s, 1H), 7.94 –7.80 (m, 3H), 7.67–7.49 (m, 5H), 7.36 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.29 (t, *J* = 7.2 Hz, 1H), 3.54 (qd, *J* = 10.8, 7.3 Hz, 2H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 165.7, 148.3, 143.2, 138.5, 136.1, 134.0, 133.7, 133.3, 133.2, 128.6, 128.3, 127.8, 127.6, 127.14, 127.07, 126.6, 126.5, 125.9 (q, *J* = 277.0 Hz), 124.7, 123.6 (q, *J* = 3.9 Hz), 122.3, 121.6, 116.7, 34.7 (q, *J* = 30.0 Hz).**^{19}F NMR** (282.4 MHz, $CDCl_3$) δ -66.2 (t, *J* = 10.8 Hz). **IR** (neat, cm^{-1}) ν: 3348, 3065, 1667, 1534, 1487, 1251, 1144, 1127, 1115, 822, 479. **HRMS** (ESI^+) calcd. for $C_{24}H_{18}F_3N_2O$ m/z 407.1371 $[M + H]^+$, found 407.1376 (1.2 ppm).



2c

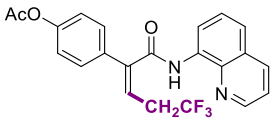
***(Z)*-5,5,5-trifluoro-2-(naphtalen-1-yl)-*N*-(quinolin-8-yl)pent-2-enamide 2c** was prepared according to the general procedure 2. Purification by silica gel column chromatography (height 10 cm, width 3.0 cm, eluent: Cyclohexane/Et_2O, from 98:2 to 90:10) afforded the titled compound as a white solid (26.1 mg, **16%**). **R_f** (Cyclohexane/Et_2O 80:20):0.46. **m.p.**: 145 – 146 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 9.76 (s, 1H), 8.63 (dd, *J* = 7.5, 1.1 Hz, 1H), 8.12 (dd, *J* =4.2, 1.5 Hz, 1H), 7.88 – 7.75 (m, 4H), 7.51–

7.44 (m, 2H), 7.39 – 7.28 (m, 4H), 7.13 – 7.05 (m, 1H), 6.10 (t, *J* = 6.8 Hz, 1H), 3.79 (qd, *J* = 11.1, 6.9 Hz, 2H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 164.8, 148.0, 140.3, 138.4, 135.9, 135.4, 134.1, 133.8, 132.1, 131.3 (q, *J* = 4.0 Hz), 129.4, 128.4, 127.9, 127.7, 126.3, 126.2 (q, *J* = 276.9 Hz), 125.6, 125.2, 121.9, 121.4, 116.2, 34.4 (q, *J* = 29.8 Hz). Two carbons are overlapped. **^{19}F NMR** (282.4 MHz, $CDCl_3$) δ -66.5 (t, *J* = 11.1 Hz). **IR** (neat, cm^{-1}) ν: 3327, 2924, 1668, 1521, 1326, 1256, 1139, 786, 756, 454. **HRMS** (ESI^+) calcd. for $C_{24}H_{18}F_3N_2O$ m/z 407.1371 $[M + H]^+$, found 407.1368 (-0.7 ppm).



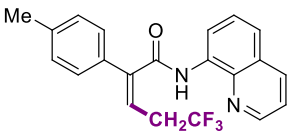
2d

(*Z*)-5,5,5-trifluoro-2-(4-methoxyphenyl)-*N*-(quinolin-8-yl)pent-2-enamide 2d was prepared according to the general procedure 1. Purification by silica gel column chromatography (height 13 cm, width 3.0 cm, eluent: *n*-Pentane/Et_2O, from 100/0 to 80/20) afforded the titled compound as a white solid (80.3 mg, **52%**). **R_f** (*n*-Pentane /Et_2O, 80/20):0.36. **m.p.**: 96 – 97 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 10.02 (s, 1H), 8.89 (dd, *J* = 6.8, 2.2 Hz, 1H), 8.66 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.62 – 7.52 (m, 2H), 7.49 – 7.37 (m, 3H), 6.98 – 6.89 (m, 2H), 6.07 (t, *J* = 7.2 Hz, 1H), 3.84 (s, 3H), 3.46 (qd, *J* = 10.8, 7.2 Hz, 2H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 166.1, 160.2, 148.5, 142.8, 138.6, 136.3, 134.2, 129.1, 129.0, 128.0, 127.3, 126.1 (q, *J* = 276.8 Hz), 122.3, 121.8 (q, *J* = 4.0 Hz), 121.8, 116.8, 114.4, 55.5, 34.7 (q, *J* = 29.9 Hz). **^{19}F NMR** (282.4 MHz, $CDCl_3$) δ -66.4 (t, *J* = 10.8 Hz). **IR** (neat, cm^{-1}) ν: 3333, 2964, 1663, 1531, 1279, 1244, 1133, 1105, 928, 826, 795. **HRMS** (ESI^+) calcd. for $C_{21}H_{18}F_3N_2O_2$ m/z 387.1320 $[M + H]^+$, found 387.1325 (1.3 ppm).



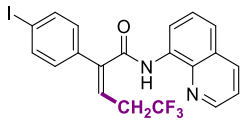
2e

(*Z*)-4-(5,5,5-trifluoro-2-(4-acetoxypehnyl)-*N*-(quinolin-8-yl)pent-2-enamide 2e was prepared according to the general procedure 1. Purification by silica gel column chromatography (height 13 cm, width 3.0 cm, eluent: *n*-Pentane/Et_2O, from 90:10 to 65:35) afforded the titled compound as a pale white solid (102.0 mg, **62**%). **R_f** (*n*-Pentane /Et_2O, 60:40):0.33. **m.p.**:128 – 129 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 10.04 (s, 1H), 8.92 – 8.81 (m, 1H), 8.66 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.63 – 7.48 (m, 4H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.21 – 7.11 (m, 2H), 6.15 (t, *J* = 7.2 Hz, 1H), 3.51 (qd, *J* = 10.8, 7.2 Hz, 2H), 2.32 (s, 3H).**^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 169.3, 165.4, 151.2, 148.6, 142.3, 138.5, 136.2, 134.3, 134.0, 128.9, 127.9, 127.2, 126.0 (q, *J* = 276.8 Hz), 124.1 (q, *J* = 4.0 Hz), 122.4, 122.2, 121.8, 116.7, 34.7 (q, *J* = 30.0 Hz), 21.2. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -66.4 (t, *J* = 10.7 Hz). **IR** (neat, cm^{-1}) ν: 3337, 1752, 1667, 1530, 1490, 1366, 1337, 1225, 1146, 918, 826. **HRMS** (ESI^+) calcd. for $C_{22}H_{18}F_3N_2O_3$ m/z 415.1270 $[M + H]^+$, found 415.1284 (3.4 ppm).



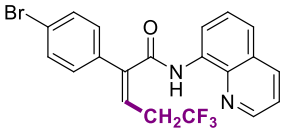
2f

***(Z)*-5,5,5-trifluoro-2-(4-methylphenyl)-*N*-(quinolin-8-yl)pent-2-enamide 2f** was prepared according to the general procedure 1. Purification by silica gel column chromatography (height 13 cm, width 3.0 cm, eluent: Cyclohexane/Et_2O, from 98:2 to 95:5) afforded the titled compound as a white solid (68.2 mg, **46**%). $\mathbf{R_f}$ (Cyclohexane/Et_2O, 80:20):0.36. **m.p.**: 115 – 116 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 10.05 (s, 1H), 8.92 (dd, *J* = 7.1, 1.5 Hz, 1H), 8.65 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.13 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.63 – 7.52 (m, 2H), 7.47 – 7.36 (m, 3H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.14 (t, *J* = 7.2 Hz, 1H), 3.50 (qd, *J* = 10.8, 7.2 Hz, 2H), 2.40 (s, 3H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 165.8, 148.3, 143.0, 138.8, 138.5, 136.1, 134.0, 133.6, 129.5, 127.8, 127.4, 127.2, 125.9 (q, *J* = 277.1), 122.6 (q, *J* = 3.8 Hz), 122.2, 121.6, 116.6, 34.6 (q, *J* = 30.0 Hz), 21.2. **^{19}F NMR** (282.4 MHz, $CDCl_3$) δ -66.3 (t, *J* = 10.8 Hz). **IR** (neat, cm^{-1}) ν: 3347, 2925, 1670, 1529, 1486, 1251, 1117, 825, 786. **HRMS** (ESI^+) calcd. for $C_{21}H_{18}F_3N_2O$ m/z 371.1371 $[M + H]^+$, found 371.1368 (-0.8 ppm).



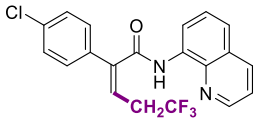
2g

(*Z*)-5,5,5-trifluoro-2-(4-iodophenyl)-*N*-(quinolin-8-yl)pent-2-enamide 2g was prepared according to the general procedure 1. Purification by silica gel column chromatography (height 13 cm, width 3.0 cm, eluent: *n*-Pentane/Et_2O, from 100:0 to 90:10) afforded the titled compound as a white solid (106.0 mg, **55%**). $\mathbf{R_f}$ (*n*-Pentane /Et_2O, 80:20):0.45. White solid. **m.p.**: 157 – 159 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 10.00 (s, 1H), 8.90-8.81 (m, 1H), 8.67 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.78 – 7.72 (m, 2H), 7.63 – 7.53 (m, 2H), 7.43 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.32 – 7.23 (m, 2H), 6.16 (t, *J* = 7.2 Hz, 1H), 3.47 (qd, *J* = 10.8, 7.2 Hz, 2H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 165.2, 148.6, 142.4, 138.5, 138.1, 136.4, 136.1, 133.9, 129.4, 128.0, 127.3, 125.9 (q, *J* = 276.8 Hz), 124.0 (q, *J* = 3.7 Hz), 122.5, 121.9, 116.9, 95.0, 34.8 (q, *J* = 30.1 Hz). **^{19}F NMR** (282.4 MHz, $CDCl_3$) -66.3 (t, *J* = 10.8 Hz). **IR** (neat, cm^{-1}) ν: 3342, 2922, 1667, 1530, 1489, 1337, 1245, 1138, 929, 828, 795. **HRMS** (ESI^+) calcd. for $C_{20}H_{15}F_3IN_2O$ m/z 483.0181 $[M + H]^+$, found 483.0196 (3.1 ppm).



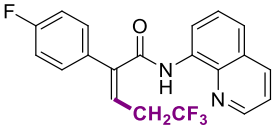
2h

***(Z)*-5,5,5-trifluoro-2-(4-bromophenyl)-*N*-(quinolin-8-yl)pent-2-enamide 2h** was prepared according to the general procedure 1. Purification by silica gel column chromatography (height 10 cm, width 3.0 cm, eluent: Cyclohexane/Et_2O, from 98:2 to 94:6) afforded the titled compound as a white solid (127.0 mg, **73**%). This reaction was scaled up to 1.40 mmol according to the general procedure 1. Purification by silica gel column chromatography (height 10 cm, width 4.0 cm, eluent: Cyclohexane/Et_2O, from 100:0 to 95:5) afforded the titled compound as a white solid (379.2 mg, **62%**). $\mathbf{R_f}$ (Cyclohexane/Et_2O 80:20):0.38. **m.p.**: 154 – 155 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 10.03 (s, 1H), 8.91 – 8.83 (m, 1H), 8.67 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.67 – 7.37 (m, 7H), 6.17 (t, *J* = 7.2 Hz, 1H), 3.50 (qd, *J* = 10.8, 7.2 Hz, 2H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 165.0, 148.4, 142.1, 138.4, 136.2, 135.4, 133.8, 132.0, 129.1, 127.8, 127.1, 125.7 (q, *J* =277.1 Hz), 123.9 (q, *J* = 3.8 Hz), 123.1, 122.4, 121.7, 116.7, 34.6 (q, *J* = 30.2 Hz). **^{19}F NMR** (282.4 MHz, $CDCl_3$) δ -66.2 (t, *J* = 10.8 Hz). **IR** (neat, cm^{-1}) ν: 3350, 3047, 1670, 1531, 1486, 1250, 1139, 1122, 1053, 828, 787, 504. **HRMS** (ESI^+) calcd. for $C_{20}H_{15}F_3N_2O^{81}Br$ m/z 437.0299 $[M + H]^+$, found 437.0289 (-1.0 ppm).



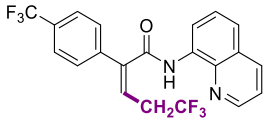
2i

(*Z*)- 5,5,5-trifluoro-2-(4-chlorophenyl)-*N*-(quinolin-8-yl)pent-2-enamide 2i was prepared according to the general procedure 1. Purification by silica gel column chromatography (height 13 cm, width 3.0 cm, eluent: *n*-Pentane/Et_2O, from 100:0 to 90:10) afforded the titled compound as a white solid (91.2 mg, **58%**). $\mathbf{R_f}$ (*n*-Pentane/Et_2O, 80:20): 0.45. **m.p.**: 138 – 139 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 10.01 (s, 1H), 8.91 – 8.82 (m, 1H), 8.67 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.62 – 7.53 (m, 2H), 7.51 – 7.35 (m, 5H), 6.15 (t, *J* = 7.2 Hz, 1H), 3.48 (qd, *J* = 10.8, 7.2 Hz, 2H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 165.3, 148.6, 142.2, 138.6, 136.4, 135.1, 135.0, 134.0, 129.2, 129.0, 128.0, 127.3, 125.9 (q, *J* = 276.9 Hz), 124.1 (q, *J* = 4.0 Hz), 122.6, 121.9, 116.9, 34.8 (q, *J* = 30.1 Hz). **^{19}F NMR** (282.4 MHz, $CDCl_3$) δ -66.3 (t, *J* = 10.8 Hz). **IR** (neat, cm^{-1}) ν: 3357, 1670, 1533, 1486, 1253, 1142, 1123, 1094, 832, 787. **HRMS** (ESI^+) calcd. for $C_{20}H_{15}{}^{35}ClF_3N_2O$ m/z 391.0794 $[M + H]^+$, found 391.0803 (2.3 ppm).



2j

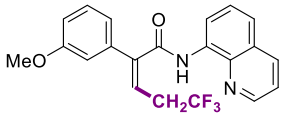
(*Z*)-5,5,5-trifluoro-2-(4-fluorophenyl)-*N*-(quinolin-8-yl)pent-2-enamide 2j was prepared according to the general procedure 1. Purification by silica gel column chromatography (height 13 cm, width 3.0 cm, eluent: *n*-Pentane/Et_2O, from 100:0 to 90:10) afforded the titled compound as a white solid (104.0 mg, **70**%). $\mathbf{R_f}$ (*n*-Pentane /Et_2O, 80/20):0.47. **m.p.**: 91 – 93 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 10.01 (s, 1H), 8.92 – 8.82 (m, 1H), 8.68 – 8.62 (m, 1H), 8.18 – 8.11 (m, 1H), 7.65 – 7.45 (m, 4H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.16 – 7.06 (m, 2H), 6.12 (t, *J* = 7.1 Hz, 1H), 3.50 (qd, *J* = 10.8, 7.1 Hz, 2H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 165.4, 163.2 (d, *J* = 248.9 Hz), 148.5, 142.2, 138.6, 136.3, 134.0, 132.8 (d, *J* = 3.4 Hz), 129.6 (d, *J* = 8.3 Hz), 128.0, 127.3, 126.0 (q, *J* = 276.9 Hz), 124.1 – 123.8 (m), 122.5, 121.8, 116.8, 116.0 (d, *J* = 21.8 Hz), 34.7 (q, *J* = 30.0 Hz). **^{19}F NMR** (282.4 MHz, $CDCl_3$) δ -66.4 (t, *J* = 10.8 Hz), -112.9 – -113.1 (m). **IR** (neat, cm^{-1}) ν: 3357, 1667, 1531, 1486, 1379, 1251, 1152, 1087, 825, 789, 757. **HRMS** (ESI^+) calcd. for $C_{20}H_{15}F_4N_2O$ m/z 375.1121 $[M + H]^+$, found 375.1116 (-1.3 ppm).



2k

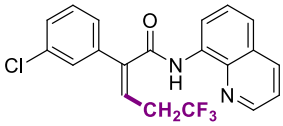
(*Z*)-5,5,5-trifluoro-)-2-(4-(trifluoromethyl)phenyl)-*N*-(quinolin-8-yl)pent-2-enamide 2k was prepared according to the general procedure 1. Purification by silica gel column chromatography (height 12 cm, width 3.0 cm, eluent: *n*-Pentane/Et_2O, from 100:0 to 90:10) afforded the titled compound as a white solid (111.0 mg, **65%**). $\mathbf{R_f}$ (*n*-Pentane /Et_2O, 80:20):0.58. **m.p.**: 119 – 120 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 10.00 (s, 1H), 8.90 – 8.81 (m 1H), 8.64 (dd, *J* = 4.3, 1.6 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.72 – 7.62 (m, 4H), 7.62 – 7.54 (m, 2H), 7.42 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.23 (t, *J* = 7.2 Hz, 1H), 3.52 (qd, *J* = 10.7, 7.2 Hz, 2H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 164.9, 148.6, 142.2, 140.2, 138.6, 136.4, 133.9, 131.0 (q, *J* = 32.7 Hz), 128.1, 128.0, 127.3, 126.0 (q, *J* = 3.8 Hz), 125.9 (q, *J* = 276.9 Hz), 125.5 (q, *J* = 3.5 Hz), 124.1 (q, *J* = 272.2 Hz), 122.7, 121.9, 116.9, 34.8 (q, *J* = 30.2 Hz). **^{19}F NMR**

(282.4 MHz, $CDCl_3$) δ -63.2 (s), -66.3 (t, *J* = 10.7 Hz). IR (neat, cm^{-1}) ν: 3355, 1665, 1528, 1487, 1325, 1251, 1150, 1117, 1072, 845. **HRMS** (ESI^+) calcd. for $C_{21}H_{15}F_6N_2O$ m/z 425.1089 $[M + H]^+$, found 425.1102(3.1 ppm).



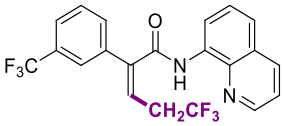
2l

(*Z*)-5,5,5-trifluoro-2-(3-methoxyphenyl)-*N*-(quinolin-8-yl)pent-2-enamide 2l was prepared according to the general procedure 1. Purification by silica gel column chromatography (height 13 cm, width 3.0 cm, eluent: Cyclohexane/Et_2O, from 100:0 to 87.5:12.5) afforded the titled compound as a pale yellow solid (89.9 mg, **58**%). $\mathbf{R_f}$ (Cyclohexane/Et_2O, 80:20):0.39. **m.p.**: 69 – 71 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 10.05 (s, 1H), 8.87 (dd, *J* = 6.7, 2.3 Hz, 1H), 8.65 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.63 – 7.51 (m, 2H), 7.40 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.37 – 7.31 (m, 1H), 7.14 – 7.08 (m, 1H), 7.08 – 7.04 (m, 1H), 6.99 – 6.93 (m, 1H), 6.16 (t, *J* = 7.1 Hz, 1H), 3.83 (s, 3H), 3.52 (qd, *J* = 10.8, 7.1 Hz, 2H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 165.5, 160.0, 148.5, 142.9, 138.7, 138.1, 136.3, 134.2, 130.1, 128.0, 127.3, 126.1 (q, *J* = 276.8 Hz), 124.5 (q, *J* = 3.9 Hz), 122.4, 121.8, 120.3, 116.8, 114.6, 113.3, 55.5, 34.8 (q, *J* = 30.0 Hz). **^{19}F NMR** (282.4 MHz, $CDCl_3$) δ -66.4 (t, *J* = 10.8 Hz). **IR** (neat, cm^{-1}) ν: 3327, 2928, 1662, 1527, 1486, 1254, 1119, 1083, 1048, 900, 827, 780. **HRMS** (ESI^+) calcd. for $C_{21}H_{18}F_3N_2O_2$ m/z 387.2928 $[M + H]^+$, found 387.1308(-3.1 ppm).



2m

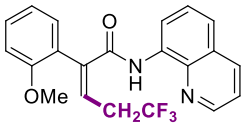
***(Z)*-5,5,5-trifluoro-2-(3-chlorophenyl)-*N*-(quinolin-8-yl)pent-2-enamide 2m** was prepared according to the general procedure 1. Purification by silica gel column chromatography (height 10 cm, width 3.0 cm, eluent: Cyclohexane/Et_2O, from 98:2 to 90:10) afforded the titled compound as a white solid (92.8 mg, **60**%). $\mathbf{R_f}$ (Cyclohexane/Et_2O, 80:20):0.39. **m.p.**: 43 – 44 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 9.99 (s, 1H), 8.82 (dd, *J* = 6.6, 2.4 Hz, 1H), 8.61 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.07 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.58 – 7.25 (m, 7H), 6.13 (t, *J* = 7.2 Hz, 1H), 3.47 (qd, *J* = 10.8, 7.2 Hz, 2H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 164.8, 148.5, 141.9, 138.5, 138.3, 136.2, 134.9, 133.8, 130.1, 129.0, 127.9, 127.6, 127.2, 125.9, 125.7 (q, *J* = 277.1 Hz), 124.9 (q, *J* = 3.9 Hz), 122.4, 121.8, 116.8, 34.7 (q, *J* = 30.1 Hz).**^{19}F NMR** (282.4 MHz, $CDCl_3$) δ -66.2 (t, *J* = 10.7 Hz). **IR** (neat, cm^{-1}) ν: 3331, 3059, 1665, 1528, 1334, 1244, 1143, 788, 453. **HRMS** (ESI^+) calcd. for $C_{20}H_{15}F_3N_2O^{35}Cl$ m/z 391.0825 $[M + H]^+$, found 391.0818 (-0.7 ppm).



2n

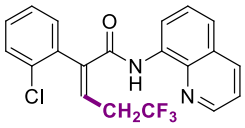
***(Z)*-5,5,5-trifluoro-2-(3-trifluoromethylphenyl)-*N*-(quinolin-8-yl)pent-2-enamide 2n** was prepared according to the general procedure 1. Purification by silica gel column chromatography (height 10 cm, width 3.0 cm, eluent: Cyclohexane/Et_2O, from 98:2 to 95:5) afforded the titled compound as a white

solid (84.5 mg, **50**%). $\mathbf{R_f}$ (Cyclohexane/Et_2O, 80:20):0.22. **m.p.**: 105– 106 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 10.06 (s, 1H), 8.89 – 8.84 (m, 1H), 8.64 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.83 (s, 1H), 7.75 – 7.65 (m, 2H), 7.63 – 7.52 (m, 3H), 7.45 – 7.34 (m, 1H), 6.23 (t, *J* = 7.2 Hz, 1H), 3.56 (qd, *J* = 10.7, 7.2 Hz, 2H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 164.6, 148.4, 141.9, 138.5, 137.5, 136.2, 133.7, 131.3 (q, *J* = 32.5 Hz), 131.08, 131.07, 129.5, 127.9, 127.1, 125.7 (q, *J* = 277.0 Hz), 125.5 (q, *J* = 3.6 Hz), 124.3 (q, *J* = 3.9 Hz), 123.8 (q, *J* = 272.5 Hz), 122.5, 121.8, 116.8, 34.7 (q, *J* = 30.2 Hz).**^{19}F NMR** (282.4 MHz, $CDCl_3$) δ -63.1 (s), -66.2 (dt, *J* = 10.7, 1.9 Hz). **IR** (neat, cm^{-1}) ν: 3352, 2922, 1662, 1527, 1487, 1327, 1244, 1145, 1123, 1078, 787. **HRMS** (ESI^+) calcd. for $C_{21}H_{15}F_6N_2O$ m/z 425.1089 $[M + H]^+$, found 425.1093 (0.9 ppm).



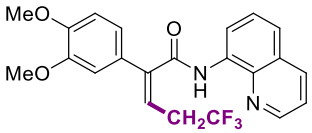
2o

***(Z)*-5,5,5-trifluoro-2-(2-methoxyphenyl)-*N*-(quinolin-8-yl)pent-2-enamide 2o** was prepared according to the general procedure 2. Purification by silica gel column chromatography (height 10 cm, width 3.0 cm, eluent: Cyclohexane/Et_2O, from 98:2 to 95:5) afforded the titled compound as a white solid (55.1 mg, **36**%). $\mathbf{R_f}$ (Cyclohexane/Et_2O, 80:20):0.31. **m.p.**: 99 – 100 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 10.11 (s, 1H), 8.83 (dd, *J* = 7.4, 1.5 Hz, 1H), 8.59 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.60 – 7.32 (m, 5H), 7.11 – 7.05 (m, 1H), 6.95 (d, *J* = 8.2 Hz, 1H), 6.08 (t, *J* = 6.9 Hz, 1H), 3.77 – 3.61 (m, 5H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 165.3, 157.0, 148.1, 139.9, 138.6, 136.1, 134.5, 131.1, 130.4, 128.0 (q, *J* =3.9 Hz), 127.8, 127.2, 127.0, 126.1 (q, *J* = 276.9 Hz), 121.7, 121.4, 121.2, 116.5, 111.1, 55.6, 34.3 (q, *J* = 29.7 Hz).**^{19}F NMR** (282.4 MHz, $CDCl_3$) δ -66.5 (t, *J* = 11.1 Hz). **IR** (neat, cm^{-1}) ν: 3345, 2922, 1684, 1524, 1484, 1330, 1252, 1131, 1045, 756. **HRMS** (ESI^+) calcd. for $C_{21}H_{18}F_3N_2O_2$ m/z 387.1320 $[M + H]^+$, found 391.1326 (1.5 ppm).



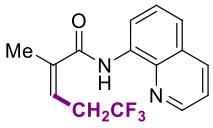
2p

***(Z)*-5,5,5-trifluoro-2-(2-chlorophenyl)-*N*-(quinolin-8-yl)pent-2-enamide 2p** was prepared according to the general procedure 2. Purification by silica gel column chromatography (height 10 cm, width 3.0 cm, eluent: Cyclohexane/Et_2O, from 98:2 to 93:7) afforded the titled compound as a white solid (98.4 mg, **63**%). $\mathbf{R_f}$ (Cyclohexane/Et_2O, 80:20):0.26. **m.p**.: 84 – 85 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.79 (dd, *J* = 7.2, 1.8 Hz, 1H), 8.51 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.08 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.57 – 7.32 (m, 7H), 6.13 (t, *J* = 6.9 Hz, 1H), 3.83 (qd, *J* = 11.1, 6.8 Hz, 2H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 163.6, 148.2, 139.5, 138.6, 136.7, 136.1, 134.09, 134.07, 131.7, 131.2 (q, *J* = 4.0 Hz), 130.3, 130.0, 127.8, 127.5, 127.2, 126.0 (q, *J* = 276.8 Hz), 122.0, 121.5, 116.4, 34.2 (q, *J* = 30.0 Hz).**^{19}F NMR** (282.4 MHz, $CDCl_3$) δ -66.6 (t, *J* = 11.1 Hz). **IR** (neat, cm^{-1}) ν: 3333, 3315, 2922, 1681, 1521, 1483, 1251, 1139, 825; 576, 470. **HRMS** (ESI^+) calcd. for $C_{20}H_{15}F_3N_2O^{35}Cl$ m/z 391.0825 $[M + H]^+$, found 391.0829 (1.0 ppm).



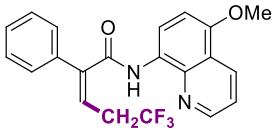
2q

***(Z)*-5,5,5-trifluoro-2-(3,4-dimethoxyphenyl)-*N*-(quinolin-8-yl)pent-2-enamide 2q** was prepared according to the general procedure 2. Purification by silica gel column chromatography (height 10 cm, width 3.0 cm, eluent: Cyclohexane/Et_2O, from 98:2 to 90:10) afforded the titled compound as a white solid (32.7 mg, **20**%). $\mathbf{R_f}$ (Cyclohexane/Et_2O, 80:20):0.39. **m.p.**: 99 – 100 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 10.06 (s, 1H), 8.88 (dd, *J* = 6.7, 2.2 Hz, 1H), 8.65 (dd, *J* = 4.1, 1.6 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.64 – 7.51 (m, 2H), 7.45–7.37 (m, 1H), 7.13–7.01 (m, 2H), 6.90 (d, *J* = 7.1 Hz, 1H), 6.09 (t, *J* = 8.3 Hz, 1H), 3.92 (s, 3H), 3.89 (s, 3H), 3.51 (qd, *J* = 10.9, 7.2 Hz, 2H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 165.7, 149.6, 149.1, 148.4, 142.5, 138.6, 136.2, 134.0, 129.4, 127.9, 127.2, 126.0 (q, *J* = 276.9 Hz), 123.1 (q, *J* = 3.9 Hz), 122.2, 121.7, 120.7, 116.7, 111.2, 110.5, 56.0, 55.9, 34.6 (q, *J* = 30.0 Hz). **^{19}F NMR** (282.4 MHz, $CDCl_3$) δ -66.4 (t, *J* = 10.9 Hz). **IR** (neat, cm^{-1}) ν: 3335, 2934, 1662, 1536, 1514, 1486, 1250, 1142, 1024, 789. **HRMS** (ESI^+) calcd. for $C_{22}H_{20}F_3N_2O_3$ m/z 417.1426 $[M + H]^+$, found 417.1429 (0.7 ppm).



2r

***(Z)*-5,5,5-trifluoro-2-methyl-*N*-(quinolin-8-yl)pent-2-enamide 2r** was prepared according to the general procedure 2 on a 0.20 mmol scale. Purification by silica gel column chromatography (height 10 cm, width 3.0 cm, eluent: Cyclohexane/Et_2O, from 100:0 to 97:3) afforded the titled compound as a white solid (31.3 mg, **53%**). $\mathbf{R_f}$ (Cyclohexane/Et_2O, 80:20):0.40. **m.p.**: 66 – 67 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 10.17 (s, 1H), 8.87–8.73 (m, 2H), 8.17 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.60–7.43 (m, 3H), 5.83 (td, *J* = 7.0, 1.5 Hz, 1H), 3.50–3.35 (m, 2H), 2.25 (s, 3H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 166.2, 148.4, 138.6, 136.4, 136.3, 134.0, 127.9, 127.3, 126.0 (q, *J* = 276.9 Hz) 124.6 (q, *J* = 3.9 Hz), 122.0, 121.7, 116.7, 34.3 (q, *J* = 29.7 Hz), 21.1. **^{19}F NMR** (282.4 MHz, $CDCl_3$) δ -66.8 (t, *J* = 11.0 Hz). **IR** (neat, cm^{-1}) ν: 3347, 2926, 1678, 1538, 1488, 1338, 1251, 1242, 788. **HRMS** (ESI^+) calcd. for $C_{15}H_{14}F_3N_2O$ m/z 295.1058 $[M + H]^+$, found 295.1065 (2.4 ppm).



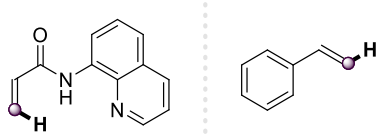
2s

***(Z)*-5,5,5-trifluoro-2-phenyl-*N*-(5-methoxy-quinolin-8-yl)pent-2-enamide 2s** was prepared according to the general procedure 2. Purification by silica gel column chromatography (height 10 cm, width 3.0 cm, eluent: *n*-Pentane/Et_2O, from 95:5 to 90:10) afforded the titled compound as a white solid (27.5 mg, **18%**). $\mathbf{R_f}$ (Cyclohexane/Et_2O, 80:20):0.19. **m.p.**: 107 – 108 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.80 (d, *J* = 8.5 Hz, 1H), 8.64 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.54 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.59–7.35 (m, 6H), 6.86 (d, *J* = 8.6 Hz, 1H), 6.14 (t, *J* = 7.2 Hz, 1H), 4.00 (s, 3H), 3.52 (qd, *J* = 10.8, 7.2 Hz, 2H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 165.2, 150.8, 148.8, 143.2, 139.3, 136.7, 131.1, 128.8, 128.7, 127.6, 127.4, 126.0 (q, *J* = 276.9 Hz), 123.3 (q, *J* = 3.9 Hz), 120.8, 120.4, 116.9, 104.1, 55.8, 34.6 (q, *J* = 30.0 Hz).**^{19}F NMR** (282.4 MHz, $CDCl_3$) δ -66.4 (t, *J* = 10.8 Hz). **IR** (neat, cm^{-1}) ν: 3351,

2928, 1668, 1233, 1495, 1245, 1148, 1088. **HRMS** (ESI$^+$) calcd. for $C_{21}H_{18}F_3N_2O_2$ m/z 387.1320 [M + H]$^+$, found 387.1324 (1.0 ppm).

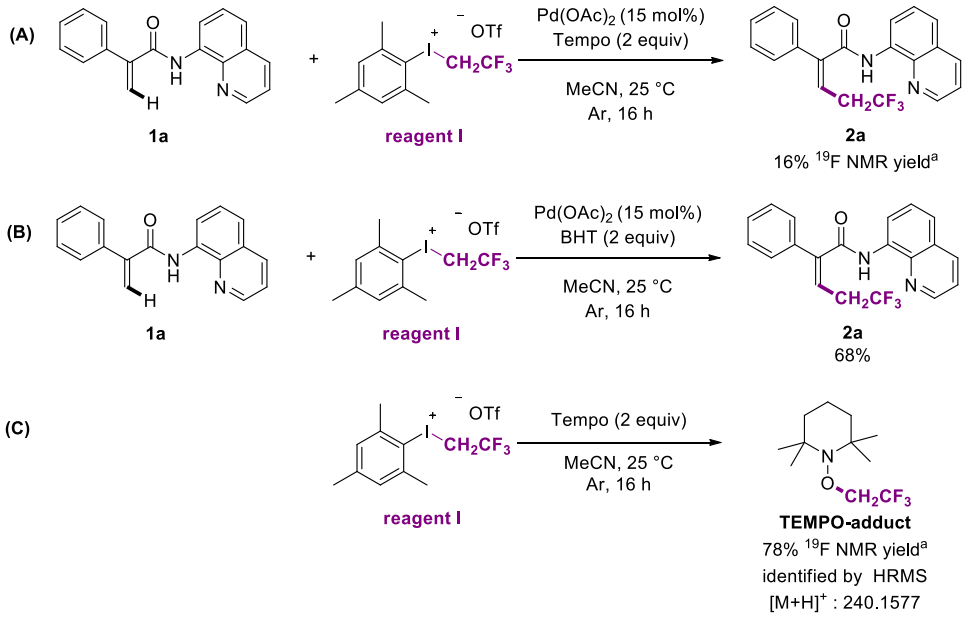
6. Reluctant Substrates

Despite all our efforts, in our standard reaction conditions, the acrylic amide was a reluctant substrate. In addition, when styrene was used, no reaction occurred, showing the importance of the directing group in the transformation.



7. Mechanistic studies

7.1 Experiments with radical scavengers



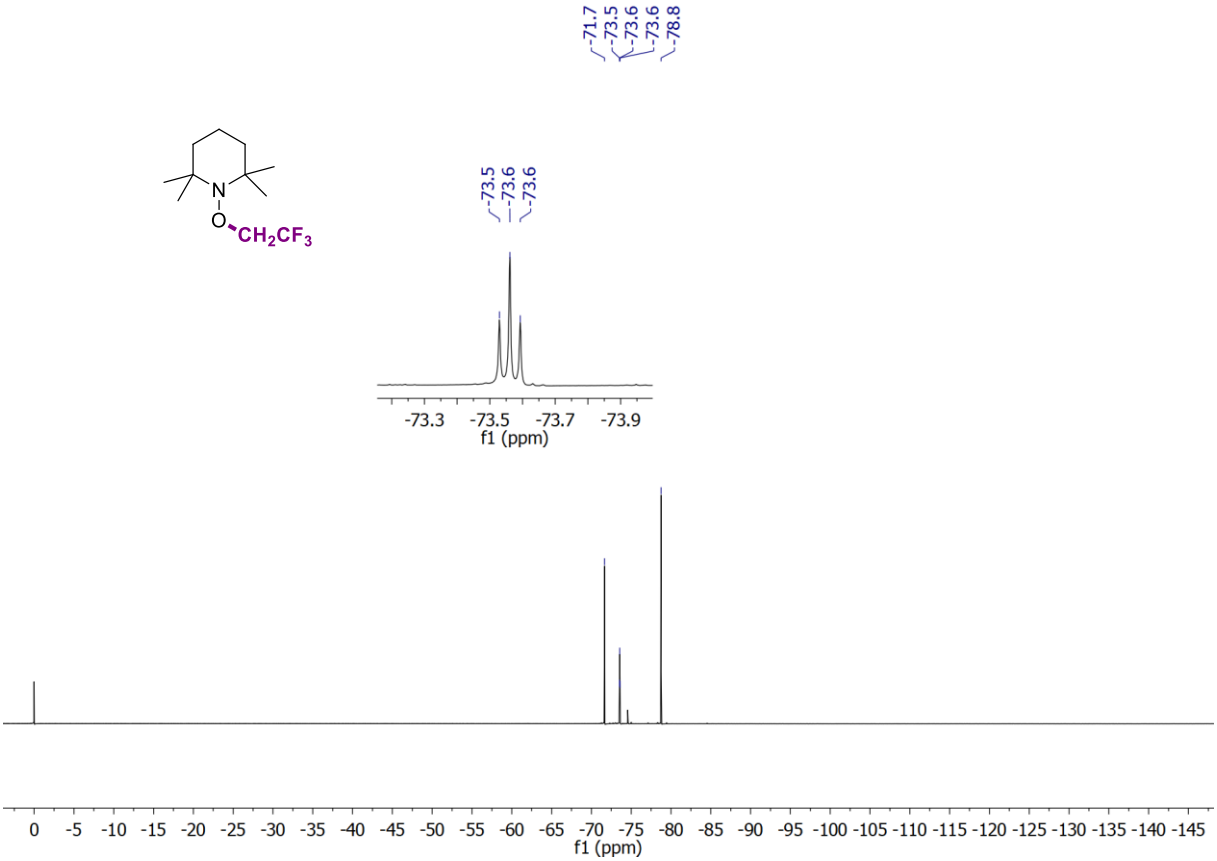
[a] ^{19}F Yields were determined by ^{19}F NMR using α,α,α-trifluoroacetophenone as an internal standard

(A): An oven-dried sealed tube equipped with a stirring bar under argon was charged with $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 15 mol%), **1a** (54.9 mg, 0.20 mmol, 2.0 equiv.), the 2,2,2-trifluoroethyl(mesityl)iodonium trifluoromethanesulfonate (47.8 mg, 0.10 mmol, 1.0 equiv.), Tempo (31.3 mg, 0.20 mmol, 2.0 equiv.) followed by dried acetonitrile (0.5 mL). The mixture was stirred at 25 °C for 16 hours. α,α,α-trifluoroacetophenone (14 µL, 0.10 mmol, 1.0 equiv.) was added as an internal standard for determining the ^{19}F NMR yield.

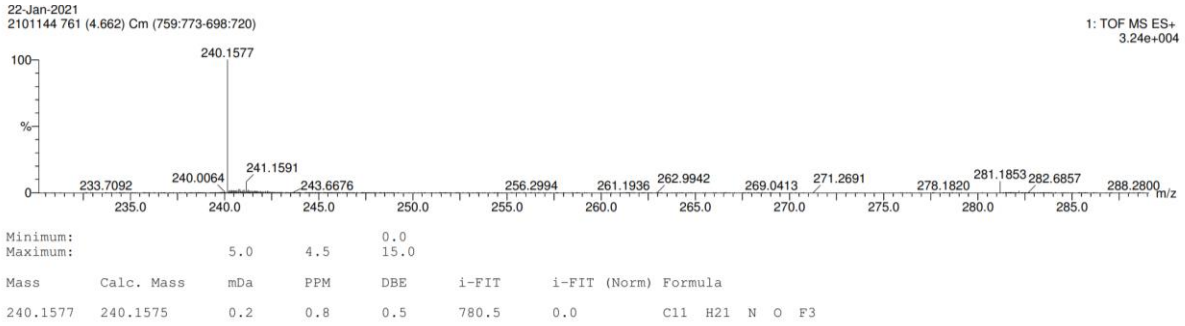
(B): An oven-dried sealed tube equipped with a stirring bar under argon was charged with $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 15 mol%), **1a** (54.9 mg, 0.20 mmol, 2.0 equiv.), the 2,2,2-trifluoroethyl(mesityl)iodonium trifluoromethanesulfonate (47.8 mg, 0.10 mmol, 1.0 equiv.), BHT (44.1 mg, 0.20 mmol, 2.0 equiv.) followed by dried acetonitrile (0.5 mL). The mixture was stirred at 25 °C

for 16 hours. α,α,α-trifluoroacetophenone (14 µL, 1.0 equiv., 0.10 mmol) was added as an internal standard for determining the ^{19}F NMR yield. The solvent was removed under vacuum and the resulting crude material was purified by silica gel column chromatography to afford the desired product **2a** (24.1 mg, **68%**).

(C) An oven-dried sealed tube equipped with a stirring bar under argon was charged with the 2,2,2-trifluoroethyl(mesityl)iodonium trifluoromethanesulfonate (47.8 mg, 0.10 mmol, 1.0 equiv.) and TEMPO (31.3 mg, 0.20 mmol, 2.0 equiv.) followed by dried acetonitrile (0.5 mL). The mixture was stirred at 25 °C for 16 hours. α,α,α-trifluoroacetophenone (14 µL, 0.10 mmol, 1.0 equiv.) was added as an internal standard for the ^{19}F NMR yield. A peak was observed at -73.6 ppm (t, J = 9.0 Hz) and is in agreement with the data described in the literature for that compound.[6] A small fraction of the crude material was analyzed by GC-MS identifying a peak at m/z 239.2 corresponding to the TEMPO-adduct. The molecular formula of this product was confirmed by HRMS (ESI$^+$): calcd. for $C_{11}H_{21}F_3NO$ m/z 240.1575 $[M + H]^+$, found 240.1577 (0.8 ppm).

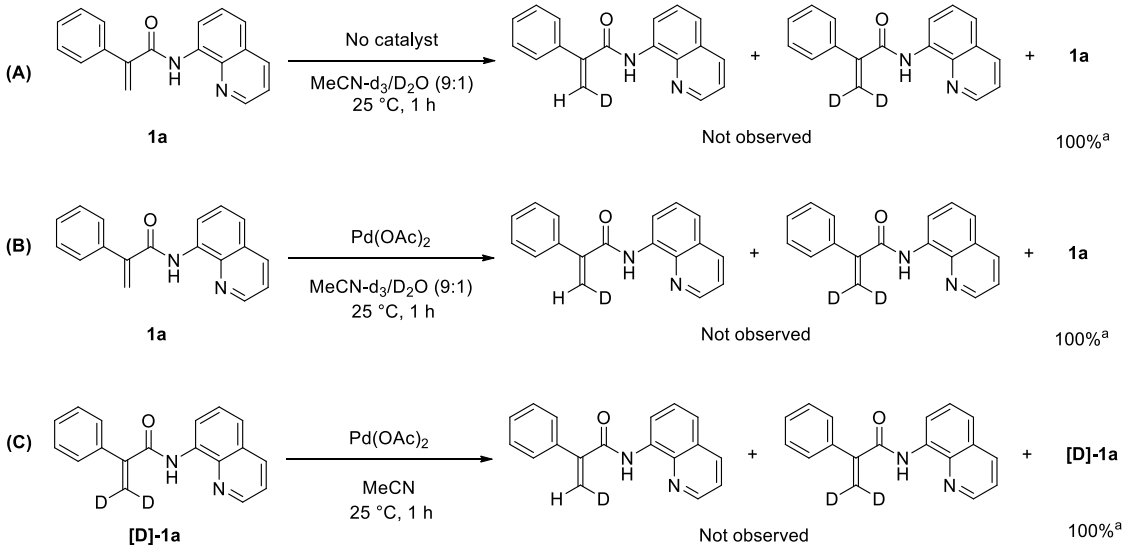


^{19}F NMR (282.4 MHz, $CDCl_3$) NMR of the crude material corresponding to the reaction of the reagent **I** with TEMPO (equation c)



HRMS (ESI^+) of the crude material corresponding to the reaction of the reagent **I** with TEMPO (equation c)

7.2 Scrambling experiments



[a] ^{1}H NMR Yields were determined using 1,1,2,2-tetrachloroethane as an internal standard

Experimental procedure

(A) An oven-dried sealed tube equipped with a stirring bar under argon was charged with **1a** (54.9 mg, 0.20 mmol, 1.0 equiv.), followed by a mixture of MeCN-d_3/D_2O (9:1, 0.5 mL). The mixture was stirred at 25 °C for 1 hour. 1,1,2,2-tetrachloroethane (21 µL, 0.20 mmol, 1.0 equiv.) was added as an internal standard for determining the ^{1}H NMR yield.

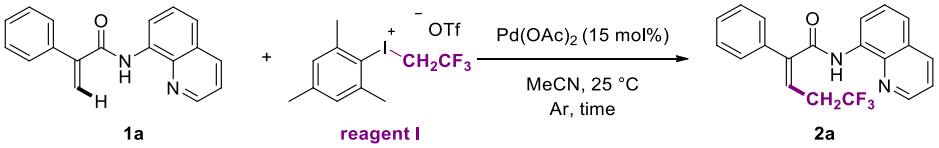
(B) An oven-dried sealed tube equipped with a stirring bar under argon was charged with **1a** (54.9 mg, 0.20 mmol, 1.0 equiv.), $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 7.5 mol%) followed by a mixture of MeCN-d_3/D_2O (9:1, 0.5 mL). The mixture was stirred at 25 °C for 1 hour. 1,1,2,2-tetrachloroethane (21 µL, 0.20 mmol, 1.0 equiv.) was added as an internal standard for determining the ^{1}H NMR yield.

(C) An oven-dried sealed tube equipped with a stirring bar under argon was charged with **[D]-1a** (54.9 mg, 0.20 mmol, 1.0 equiv.), $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 7.5 mol%) followed by dried MeCN (0.5 mL). The mixture was stirred at 25 °C for 1 hour. 1,1,2,2-tetrachloroethane (21 µL, 0.20 mmol, 1.0 equiv.) was added as an internal standard for determining the ^{1}H NMR yield.

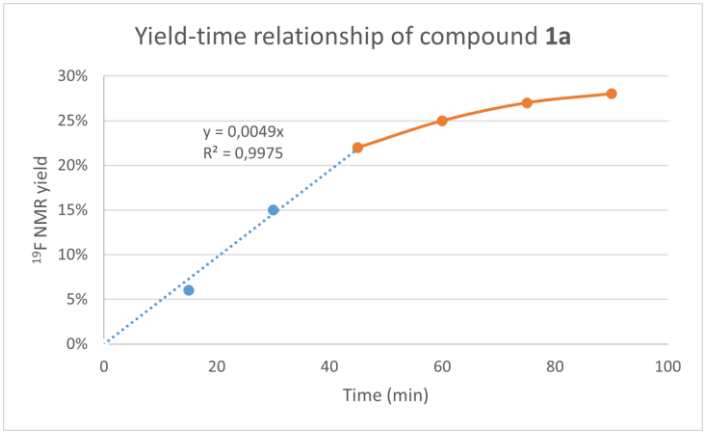
The reactions **(A)**, **(B)** and **(C)**, with and without palladium catalyst, with **1a** and **[D]-1a**, show that there is no exchange H/D or vice versa. Therefore, the C–H bond activation step is not reversible.

7.3 Kinetic Isotope effect (KIE) measurements

Yield-time relationship of compound 1a

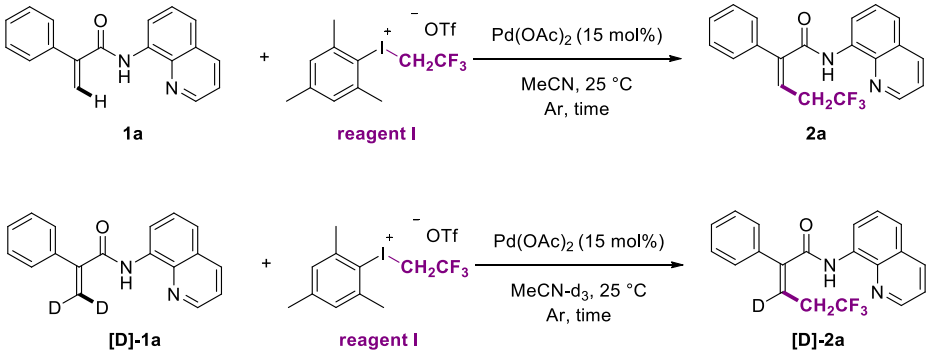


Different oven-dried sealed tubes equipped with a stirring bar under argon were charged with $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 15 mol%), **1a** (54.9 mg, 0.20 mmol, 2.0 equiv.), the trifluoroethyl(mesityl)iodonium trifluoromethanesulfonate (47.8 mg, 0.10 mmol, 1.0 equiv.), followed by dried acetonitrile (0.5 mL). The mixture was stirred at 25 °C for either 15, 30, 45, 60 or 90 minutes. α,α,α-trifluoroacetophenone (14 µL, 0.10 mmol, 1.0 equiv.) was added as an internal standard for determining the ^{19}F NMR yield.

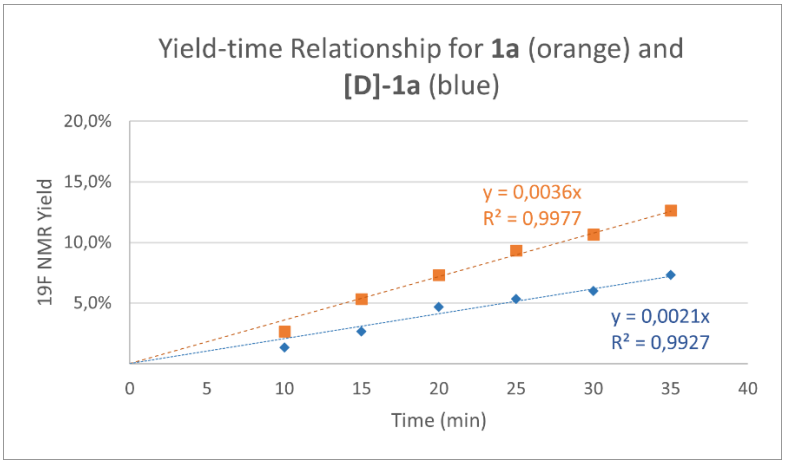


The yield-time relationship is linear until 45 minutes.

Parallel reactions

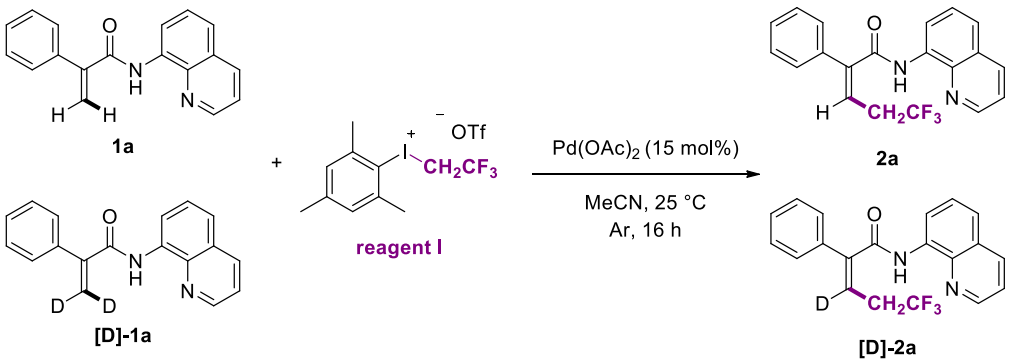


Different oven-dried sealed tubes equipped with a stirring bar under argon were charged with $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 15 mol%), **1a** (54.9 mg, 0.20 mmol, 2.0 equiv.), the trifluoroethyl(mesityl)iodonium trifluoromethanesulfonate (47.8 mg, 0.10 mmol, 1.0 equiv.), followed by dried acetonitrile (0.5 mL). The mixture was stirred at 25 °C for either 10, 15, 20, 25, 30 or 35 minutes. α,α,α-trifluoroacetophenone (14 µL, 0.10 mmol, 1.0 equiv.) was added as an internal standard for determining the ^{19}F NMR yield.



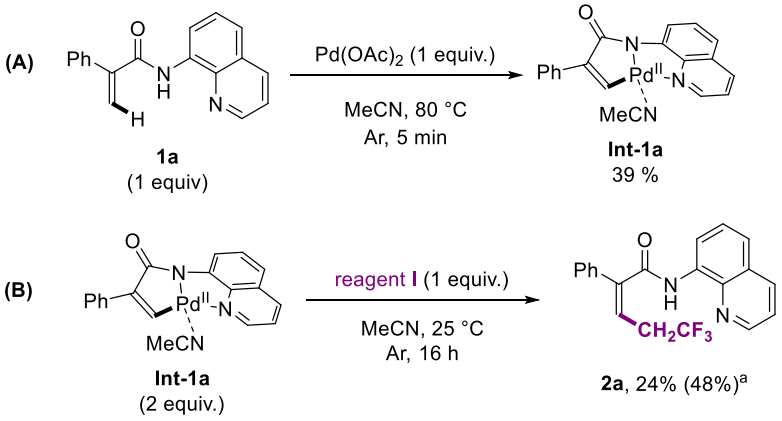
The yield time relationship of the parallel reactions provided a KIE value of k_H/k_D = 1.8.

Competition experiments



An oven-dried sealed tube equipped with a stirring bar under argon was charged with $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 15 mol%), **1a** (54.9 mg, 0.20 mmol, 2.0 equiv.), **[D]-1a** (55.2 mg, 0.20 mmol, 2.0 equiv.), the trifluoroethyl(mesityl)iodonium trifluoromethanesulfonate (47.8 mg, 0.10 mmol, 1.0 equiv.), followed by dried acetonitrile (0.5 mL). The mixture was stirred at 25 °C for 16 hours. The solvent was removed under vacuum and the resulting crude material was purified by silica gel column chromatography to afford the desired trifluoroethylated products **2a** and **[D]-2a** (18.4 mg, H/D: 0.71/0.29). The competition experiment provided the following KIE value, calculated based on the ^{1}H NMR product ratio: P_H/P_D = 2.4.[7]

6.4 Preparation of the palladacycle Int-1a

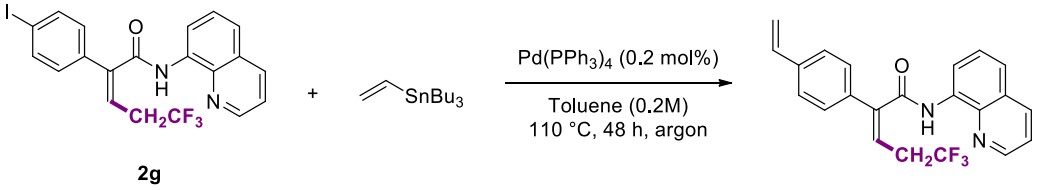


(A) According to Zhang's procedure,[3] an oven-dried 30 mL sealed tube equipped with a stirring bar under argon was charged with **1a** (200.0 mg, 0.73 mmol, 1.0 equiv.), $Pd(OAc)_2$ (164.0 mg, 0.73 mmol, 1.0 equiv.) followed by dried acetonitrile (6 mL). After sealing the tube with a screw cap, the reaction was stirred at 80 °C for 5 minutes (monitored by TLC). The yellow precipitate was filtered and washed with MeCN (5 mL). The solid was then dried under vacuum to afford the desired product **Int-1a** as a yellow powder (120.0 mg, **39%**). **m.p.**: burnt at 280°C. **^{1}H NMR** (300.1 MHz, CD_3CN) δ 8.88 (d, *J* = 8.1 Hz, 1H), 8.54 (d, *J* = 4.7 Hz, 1H), 8.38 (d, *J* = 8.0 Hz, 1H), 7.62 (s, 1H), 7.59−7.48 (m, 4H), 7.38−7.23 (m, 4iH), 1.99 (s, 3H). **^{13}C NMR** (75.5 MHz, CD_3CN): the product was not soluble enough to do a ^{13}C NMR. **IR** (neat, cm^{-1}) ν: 3047, 1602, 1463, 1374, 1342, 776, 700. **HRMS** (ESI^+) calcd. for $C_{20}H_{16}N_3O^{106}Pd$ m/z 420.0328 $[M + H]^+$, found 422.0337 (2.1 ppm).

(B) An oven-dried sealed tube equipped with a stirring bar under argon was charged with **Int-1a** (83.8 mg, 0.20 mmol, 2.0 equiv.), the trifluoroethyl(mesityl)iodonium trifluoromethanesulfonate (47.8 mg, 0.10 mmol, 1.0 equiv.), followed by dried acetonitrile (0.5 mL). The mixture was stirred at 25 °C for 16 hours. α,α,α-Trifluoroacetophenone (14 µL, 0.10 mmol, 1.0 equiv.) was added as an internal standard for the ^{19}F NMR yield (48%). Then CH_2Cl_2 was added (10 mL) followed by water (10 mL). The organic layer was washed with water (1 × 10 mL), dried over Na_2SO_4 and concentrated under vacuum. The resulting crude material was purified by silica gel column chromatography to afford product **2a** (8.4 mg, **24%**).

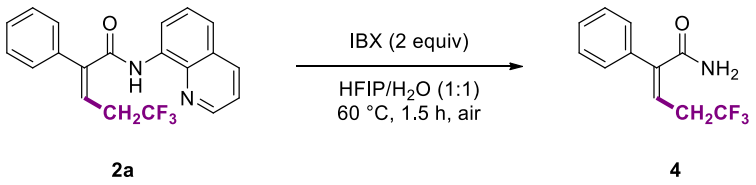
8. Post-Functionalization reactions

7.1. Stille reaction[8]



An oven-dried 1 mL sealed tube equipped with a stirring bar under air was charged with (*Z*)-5,5,5-trifluoro-2-(4-iodophenyl)-*N*-(quinoline-8-yl)pent-2-enamide **2g** (24.1 mg, 0.05 mmol, 1.0 equiv.). Then, 0.25 mL of stock solution of $Pd(PPh_3)_4$ in toluene (0.4. 10^{-3} M) was added, followed by tributylvinyltin (14.6 µL, 0.05 mmol, 1.0 equiv.). The reaction mixture was heated at 100 °C for 48 hours. The solvent was evaporated under vacuum. The resulting crude material was purified by silica gel column chromatography (height 7 cm, width 1.5 cm, eluent: *n*-Pentane/Et_2O, from 98:2 to 95:5) to afford the titled compound **5** as a white solid (7.1 mg, **37%**). $\mathbf{R_f}$ (Cyclohexane/Et_2O, 90:10):0.22. **m.p.**: 86 – 87 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 10.04 (s, 1H), 8.83 (d, *J* = 7.4 Hz, 1H), 8.52-8.46 (m, 1H), 8.08 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.64-7.46 (m, 4H), 7.40-7.31 (m, 3H), 7.14 (t, *J* = 7.5 Hz, 1H), 6.84 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.89 (d, *J* = 17.6 Hz, 1H), 5.39 (d, *J* = 10.9 Hz, 1H), 3.01-2.83 (m, 2H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 163.6, 148.2, 142.5, 138.7, 138.2, 136.2, 136.1, 134.3, 133.1, 129.9, 127.9 (q, *J* = 3.0 Hz), 127.8, 127.3, 127.1, 125.6 (q, *J* = 271.0 Hz), 122.0, 121.5, 116.5, 115.1, 34.5 (q, *J* = 30.2 Hz) **^{19}F NMR** (282.4 MHz, $CDCl_3$) δ -65.5 (t, *J* = 10.6 Hz). **IR** (neat, cm^{-1}) ν: 3323, 2923, 2853, 1686, 1525, 1486, 1252, 1141, 1122, 828. **HRMS** (ESI^+) calcd. for $C_{22}H_{18}F_3N_2O$ m/z 383.1371 $[M + H]^+$, found 383.1375 (1.0 ppm).

7.2. Removal of the directing group[9]

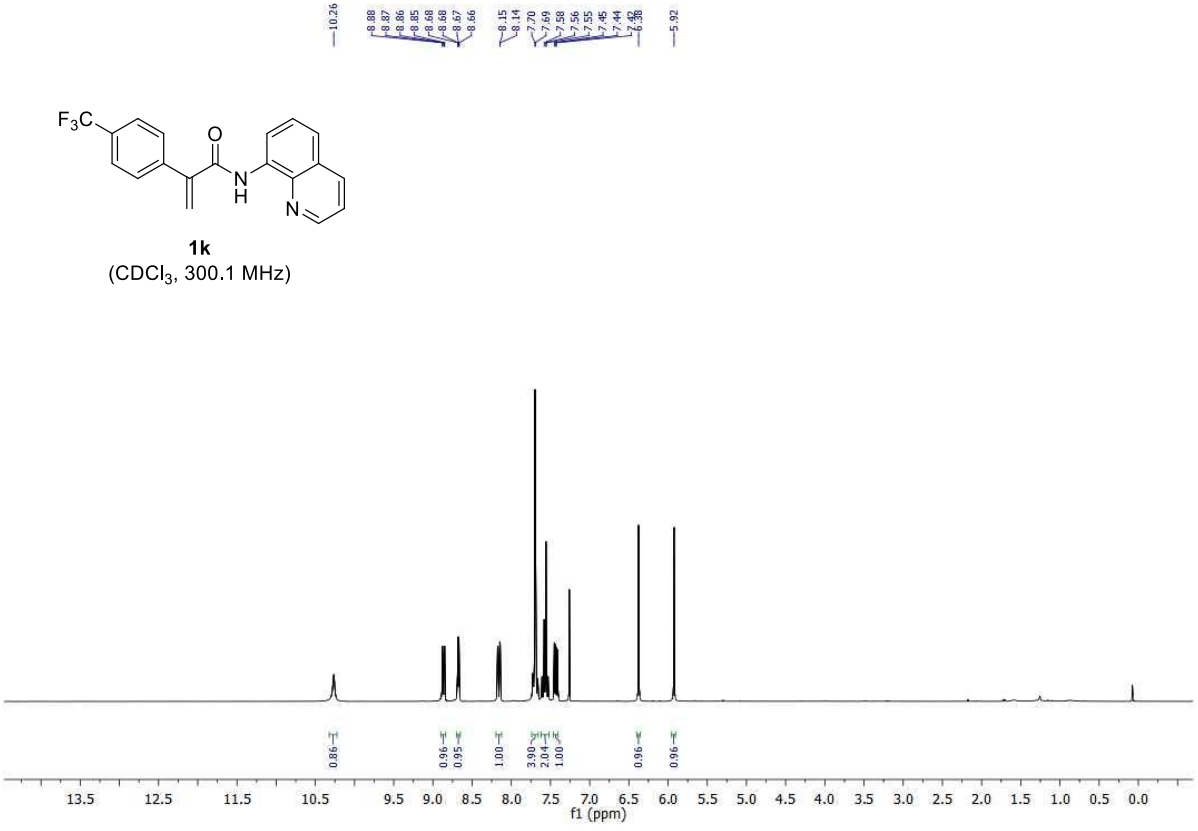


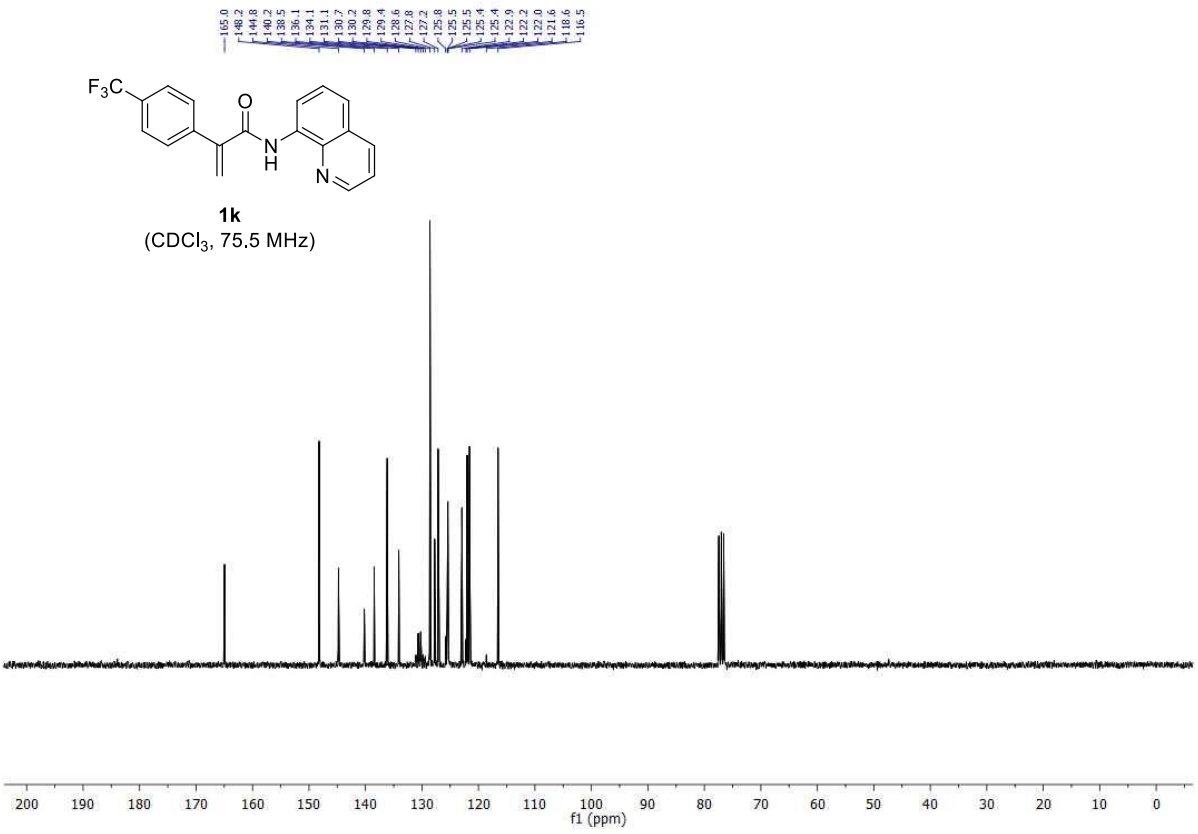
An oven-dried sealed tube equipped with a stirring bar under air was charged with (*Z*)-5,5,5-trifluoro-2-phenyl-*N*-(quinoline-8-yl)pent-2-enamide **2a** (71.2 mg, 0.20 mmol, 1.0 equiv.), IBX (112.0 mg, 0.40 mmol, 2.0 equiv.), followed by HFIP (0.65 mL) and H_2O (0.65 mL). The mixture was stirred at 60 °C for 1.5 hours (monitored by TLC). An aqueous saturated solution of $NaHCO_3$ (10 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The resulting crude material was purified by silica gel column chromatography (height 10 cm, width 3.0 cm, eluent: Cyclohexane/Et_2O, from 70:30 to 60:40) to afford the titled compound **4** as a white solid (38.6 mg, **84%**). $\mathbf{R_f}$ (Cyclohexane/Et_2O, 70:20):0.32. **m.p.**: 142 – 143 °C. **^{1}H NMR** (300.1 MHz, $CDCl_3$) δ 7.50–7.29 (m, 5H), 6.44 (s, 1H), 6.01 (m, 1H), 5.63 (s, 1H), 3.52–3.30 (m, 2H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 169.3, 141.7, 136.7, 128.9, 128.8, 127.4, 125.9 (q, *J* = 276.9 Hz), 124.0 (q, *J* = 4.1 Hz), 34.5 (q, *J* = 30.0 Hz).**^{19}F NMR** (282.4 MHz, $CDCl_3$) δ -65.9 (t, *J* = 10.9 Hz). **IR** (neat, cm^{-1}) ν: 3377, 3183, 1654, 1632, 1247, 1134, 1064, 694, 610. **HRMS** (ESI^+) calcd. for $C_{11}H_{11}F_3NO$ m/z 230.0793 $[M + H]^+$, found 230.0786 (-3.0 ppm).

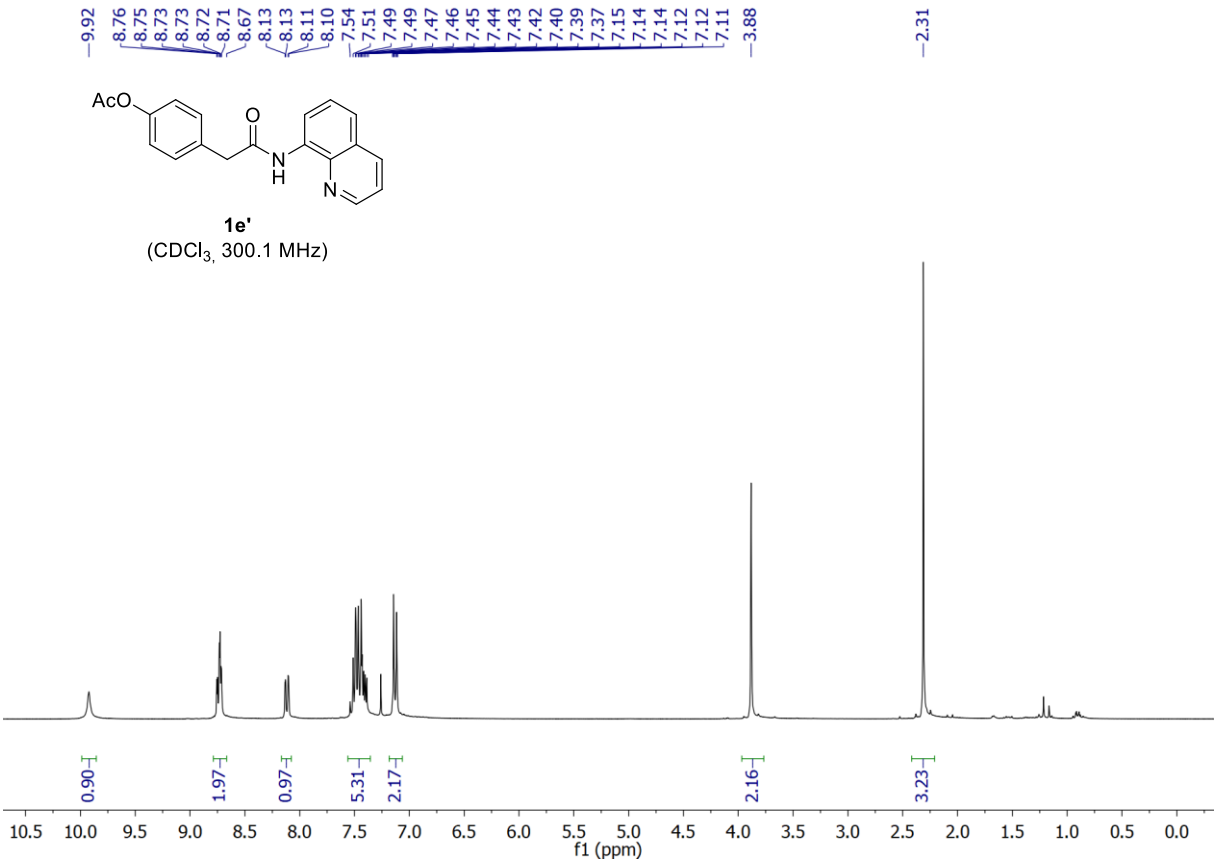
9. References

[1] Q. Zhao, T. Poisson, X. Pannecoucke, J.-P. Bouillon and T. Besset, *Org. Lett.*, 2017, **19**, 5106–5109.
[2] Q. Zhao, M.-Y. Chen, T. Poisson, X. Pannecoucke, J.-P. Bouillon and T. Besset, *Eur. J. Org. Chem*., 2018, **44**, 6167–6175.
[3] J.-L. Pan, C. Chen, Z.-G. Ma, J. Zhou, L.-R. Wang and S.-Y. Zhang, *Org. Lett*., 2017, **19**, 5216–5219.
[4] M. Mastihubová and M. Poláková, *Beilstein J. Org. Chem*., 2016, **12**, 524–530.
[5] T. Piou, A. Bunescu, Q. Wang, L. Neuville and J. Zhu, *Angew. Chem. Int. Ed.*, 2013, **52**, 12385–12389.
[6] Y. Zhu, J. Gong and Y. Wang, *J. Org. Chem*., 2017, **82**, 7428–7436.
[7] C. Wu, J. Zhou, G. He, H. Li, Q. Yang, R. Wang and Y. Zhou, *Org. Chem. Front.*, 2019, **6**, 1183–1188.
[8] M. E. Krolski, A. F. Renaldo, D. E. Rudisill and J. K. Stille, *J. Org. Chem.*, 1988, **53**, 1170–1176.
[9] Z. Zhang, X. Li, M. Song, Y. Wan, D. Zheng, G. Zhang and G. Chen, *J. Org. Chem.*, 2019, **84**, 12792–12799.

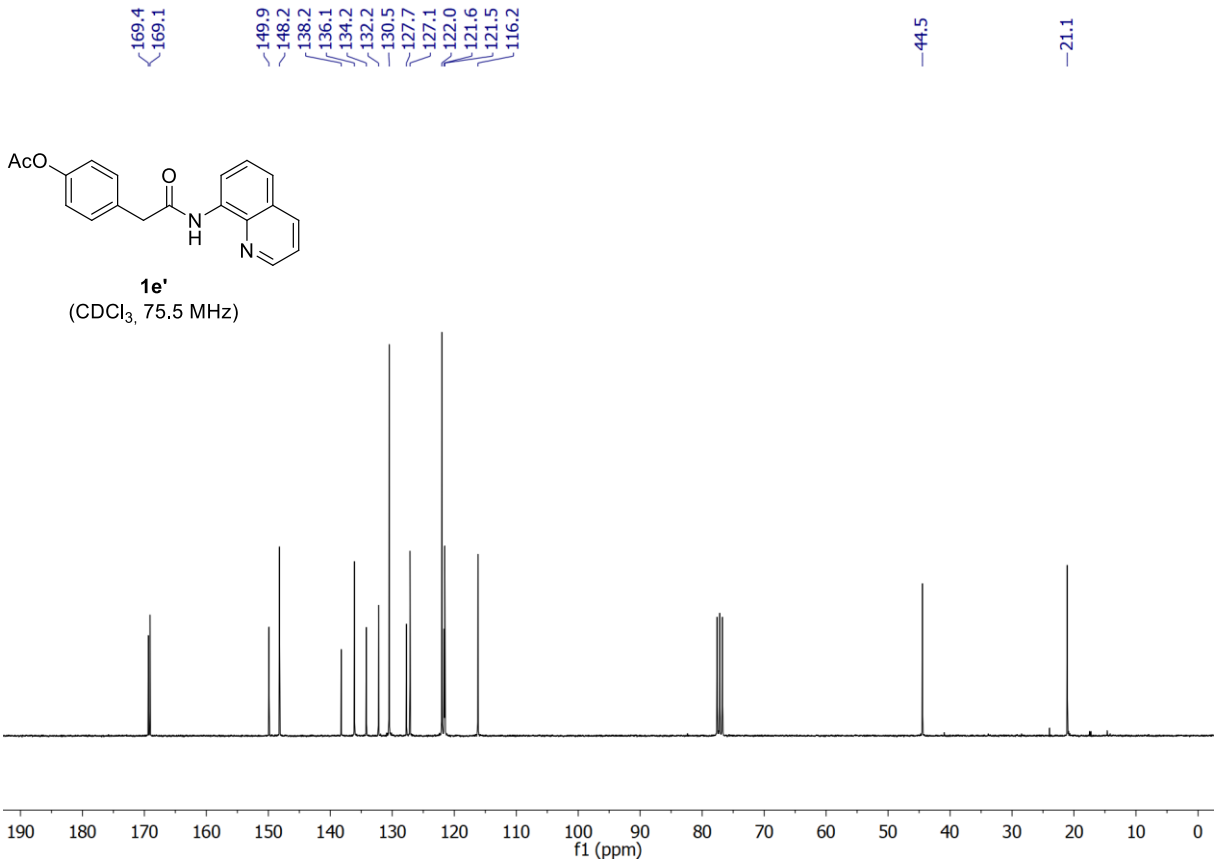
10.NMR Spectra







1e'
($CDCl_3$, 300.1 MHz)



1e'
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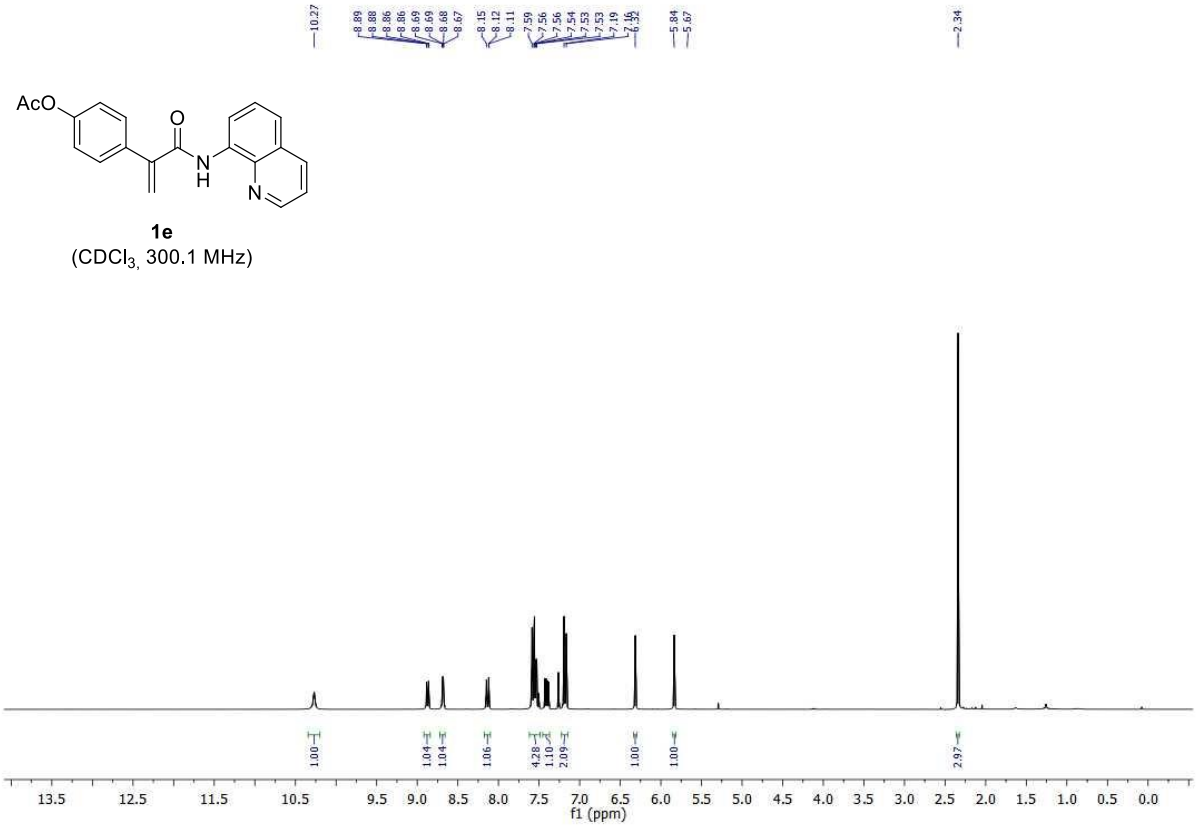

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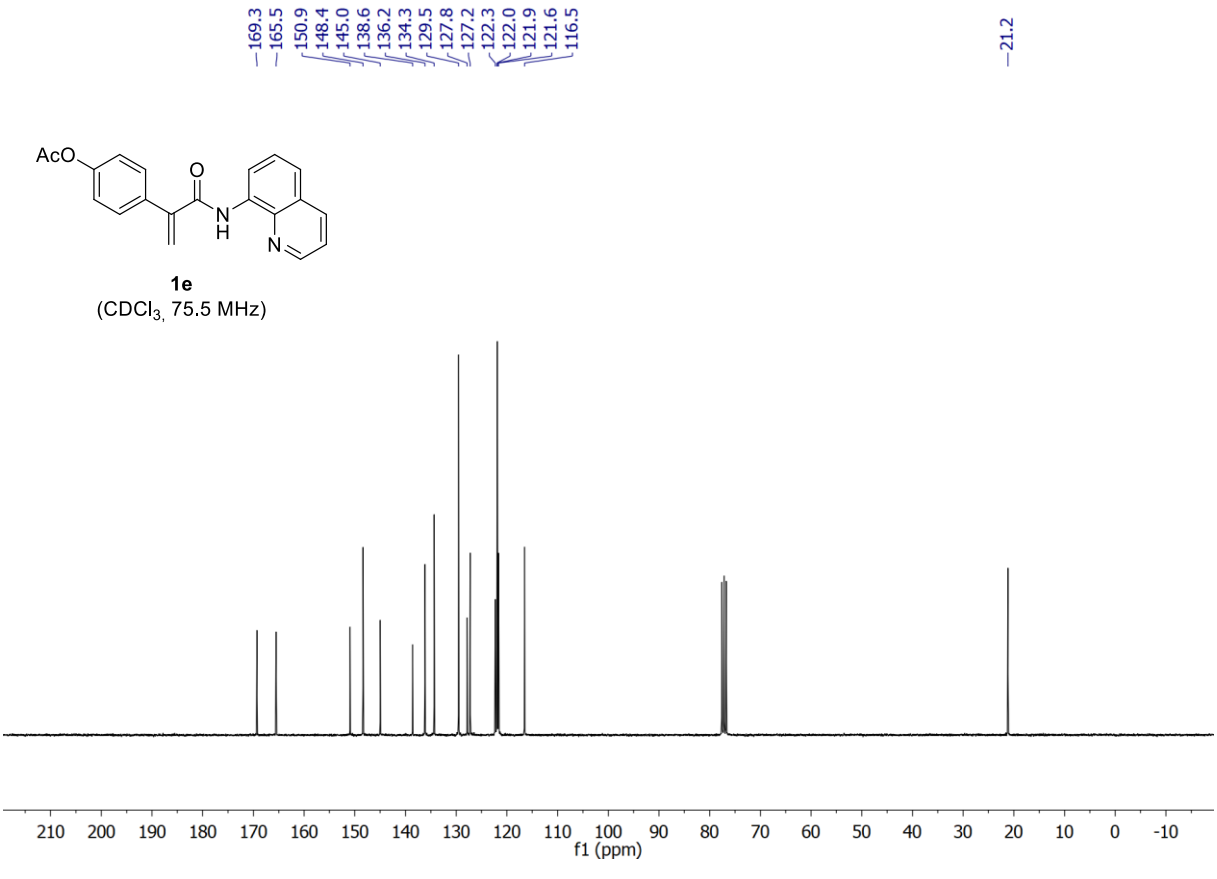

1e
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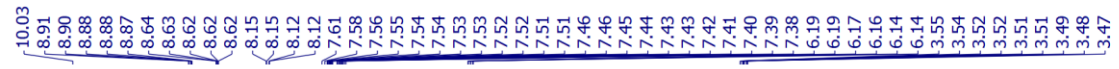
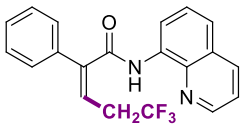
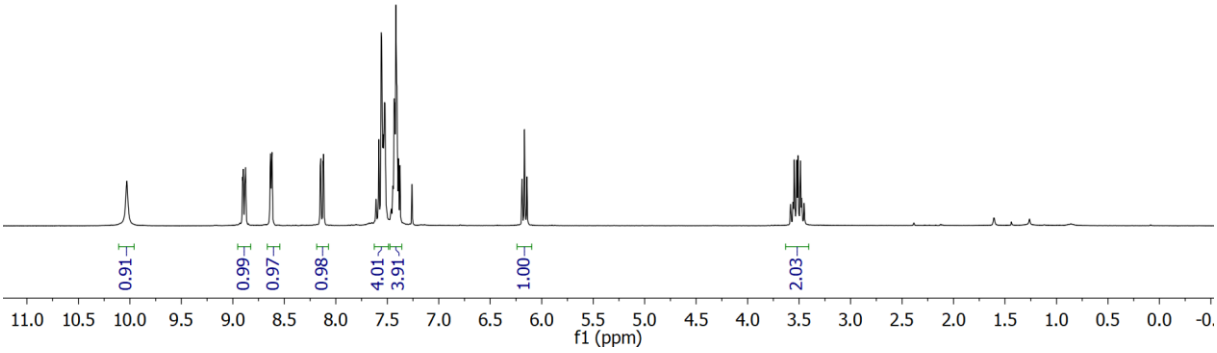
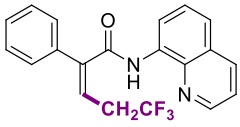




2a
($CDCl_3$, 300.1 MHz)





2a
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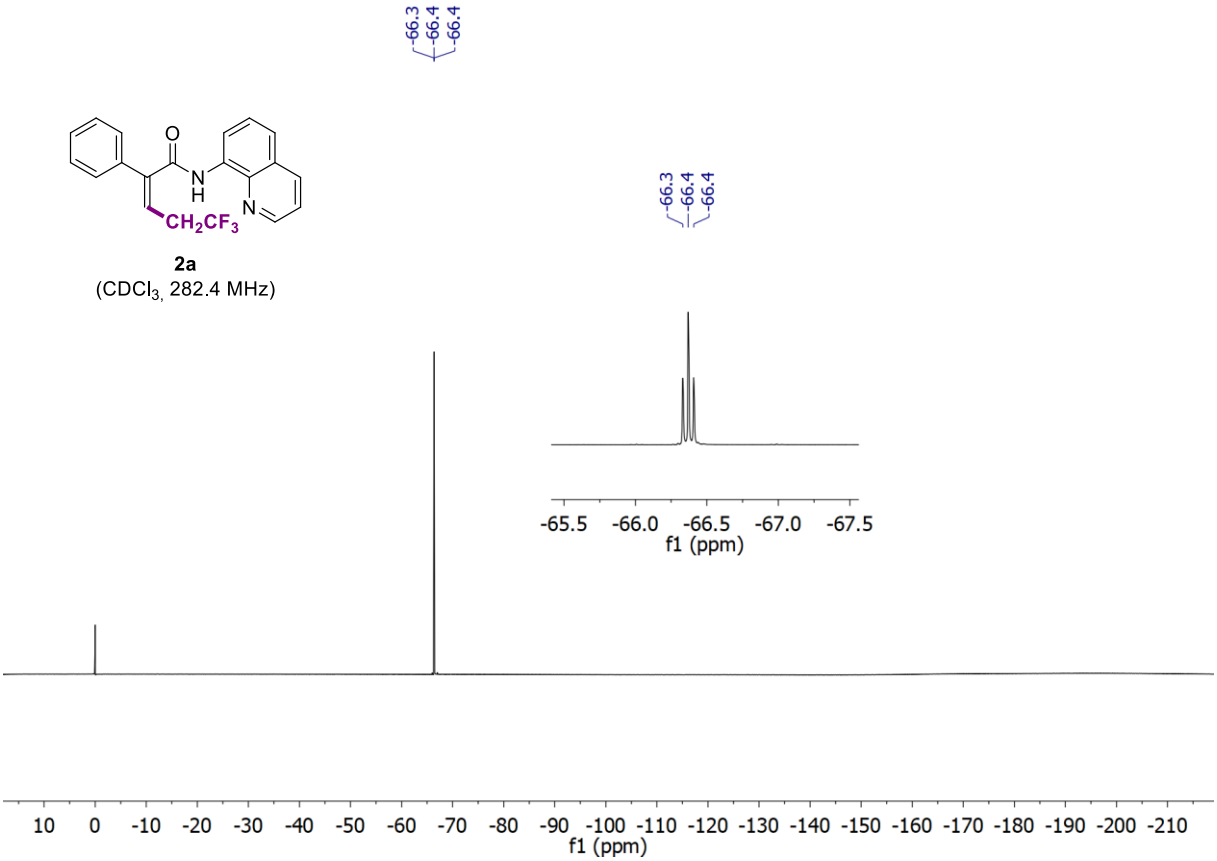

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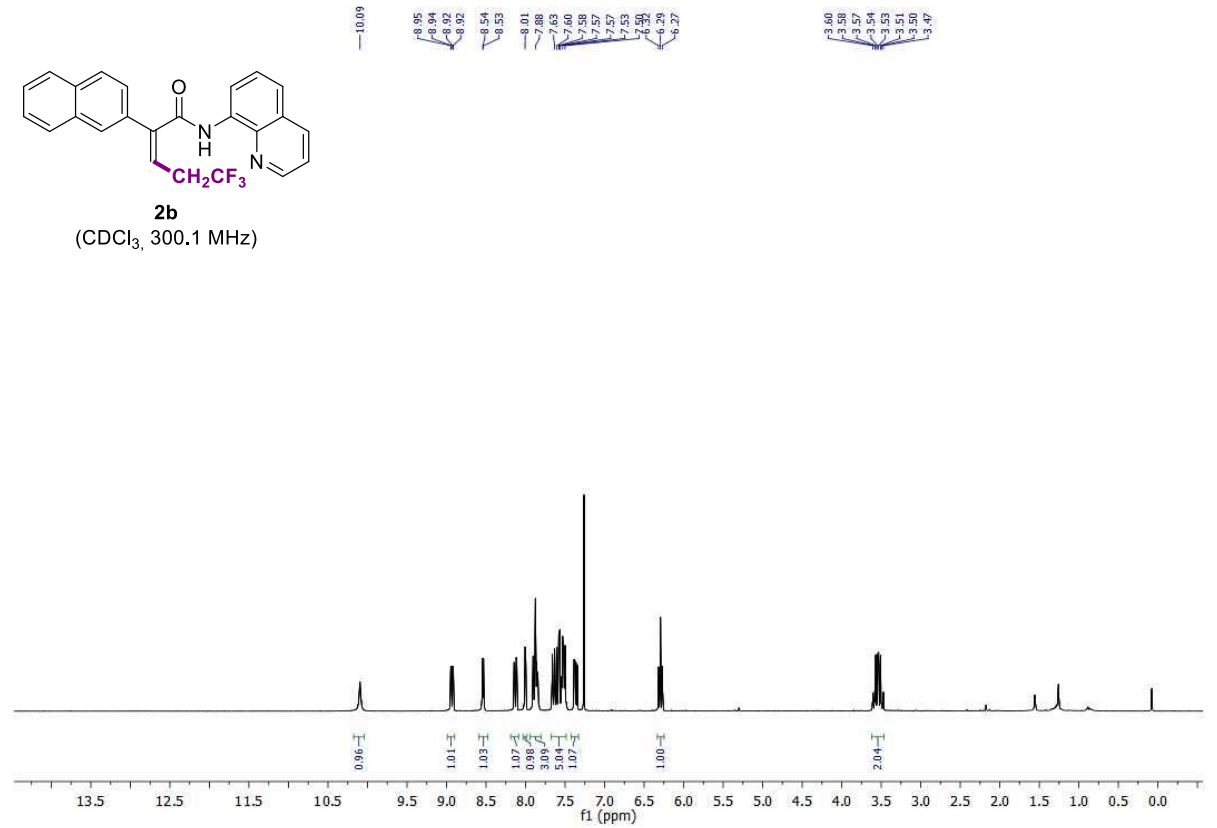
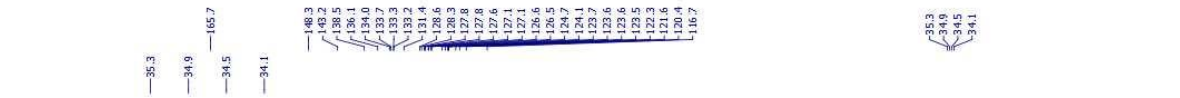
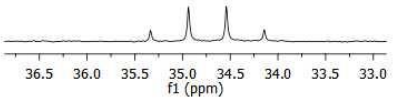
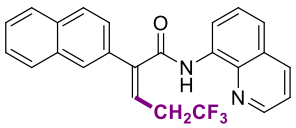


2b
($CDCl_3$, 300.1 MHz)

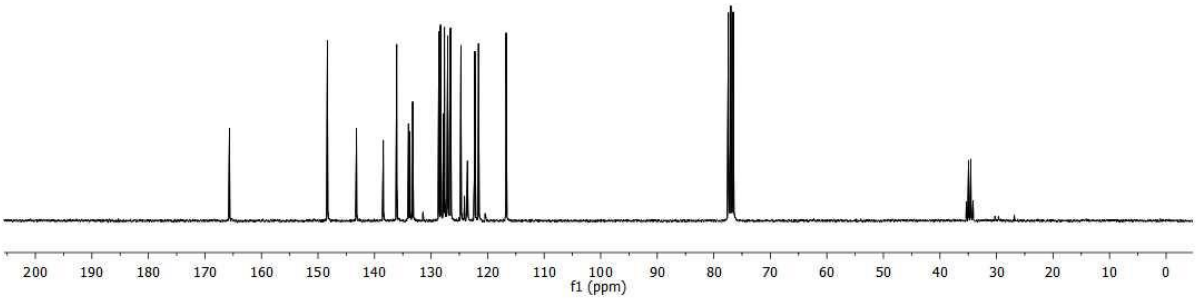


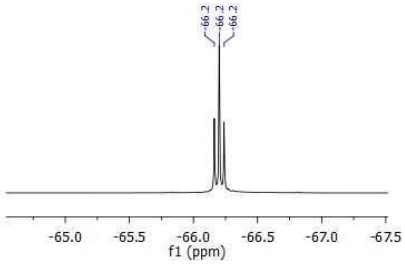


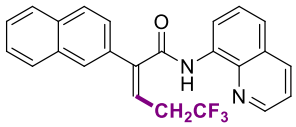


2b

($CDCl_3$, 75.5 MHz)

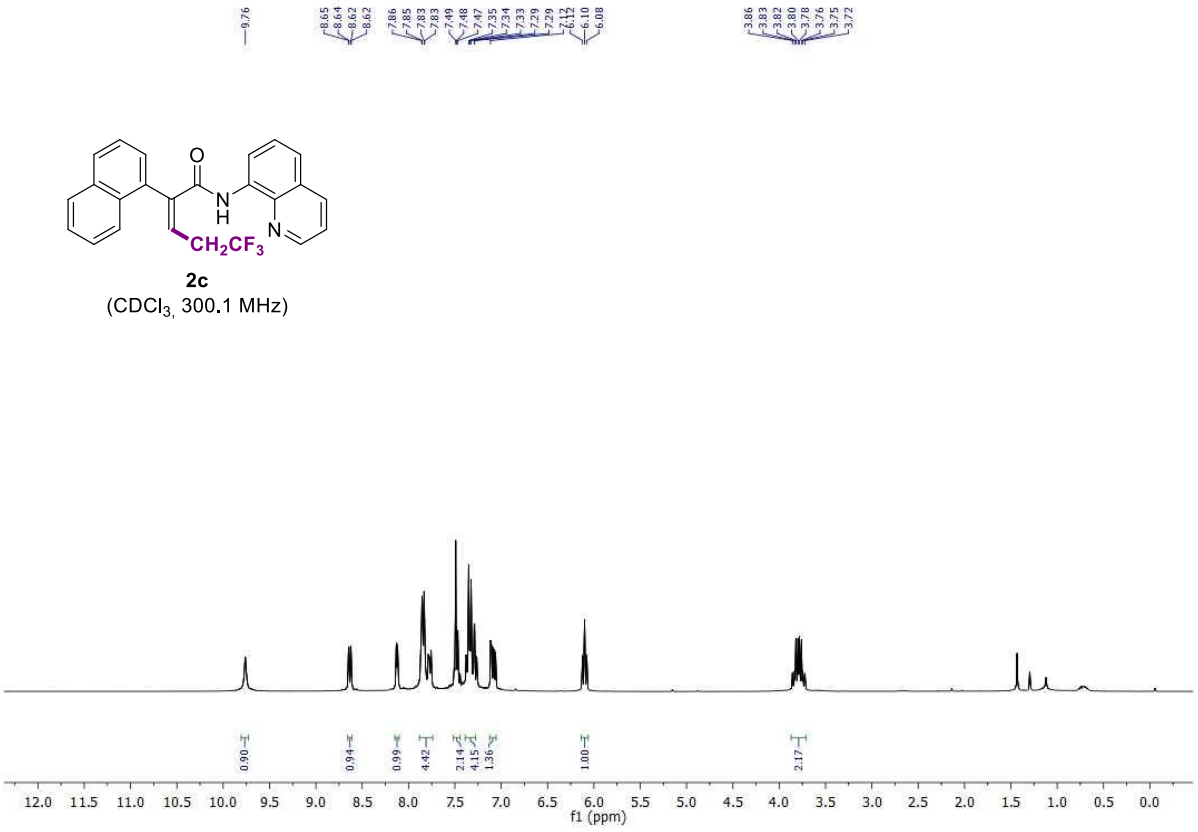




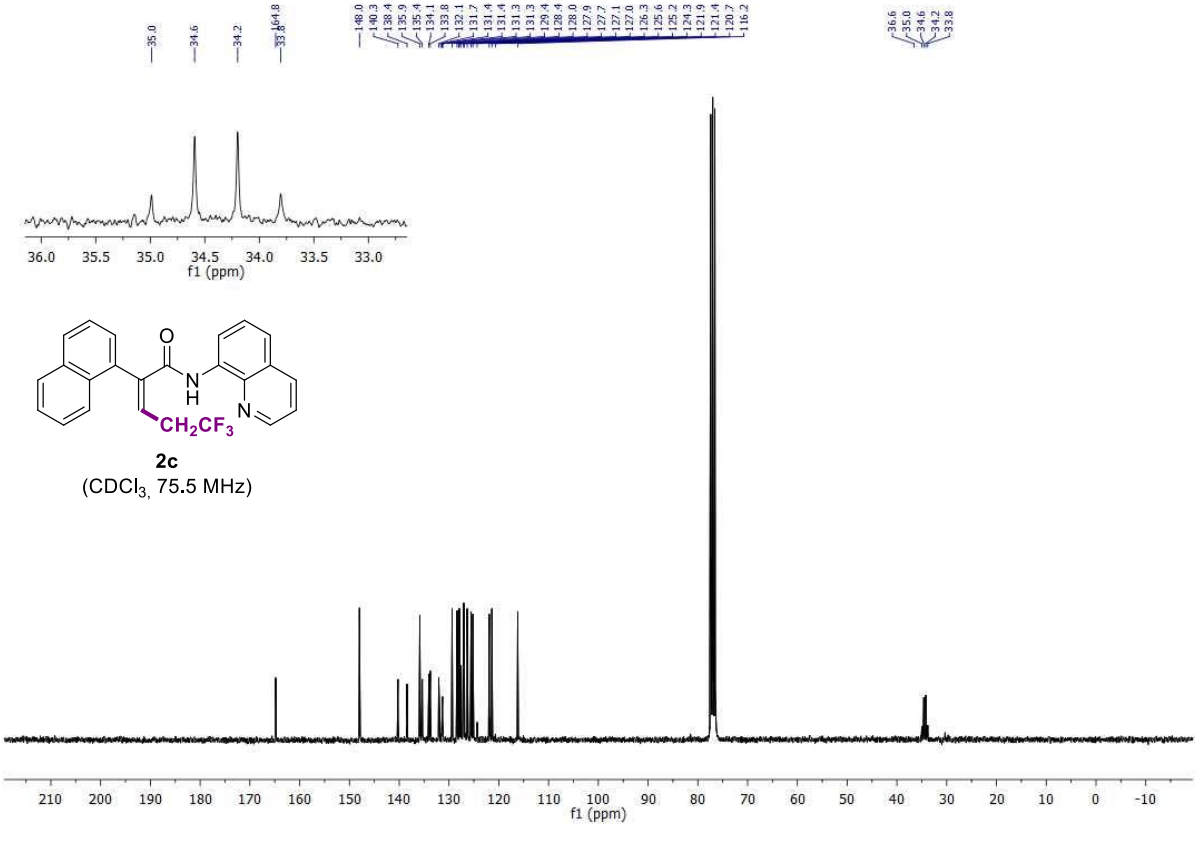


2b

($CDCl_3$, 282.4 MHz)



2c
($CDCl_3$, 300.1 MHz)



2c
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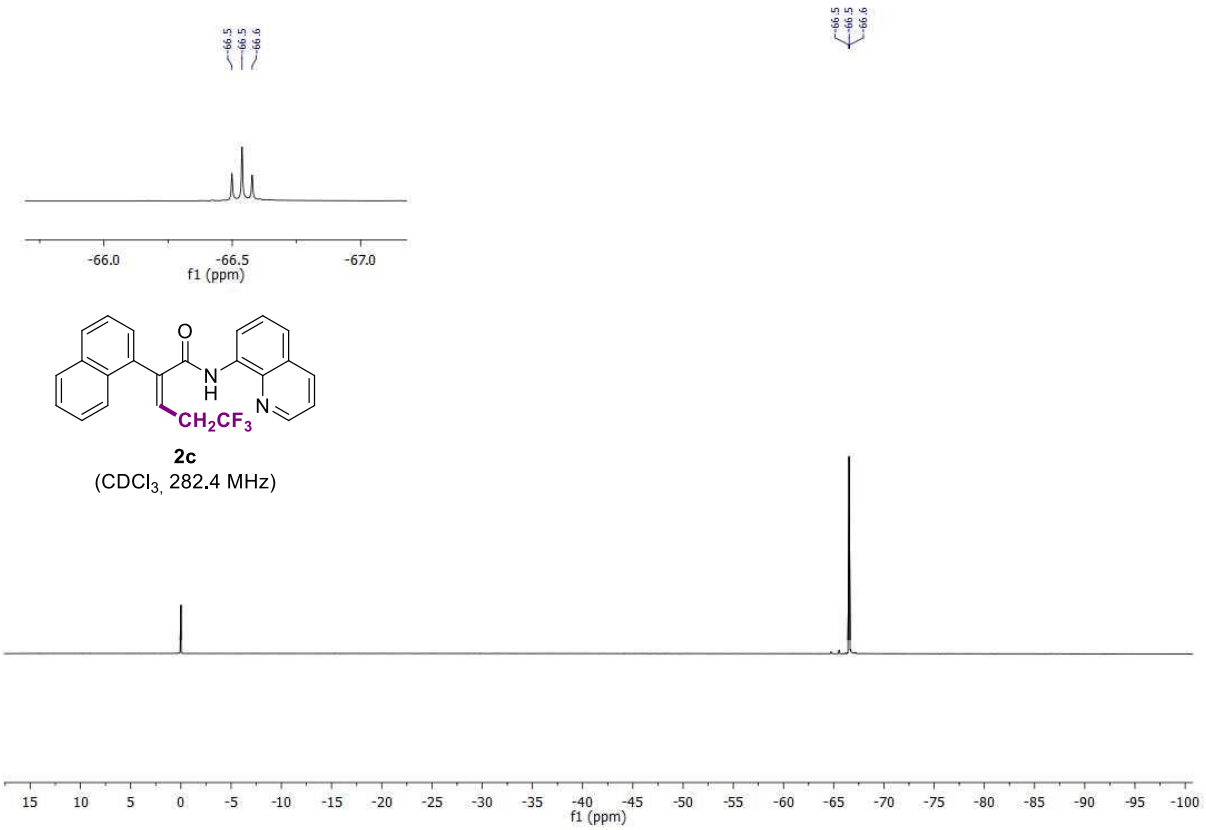

2c
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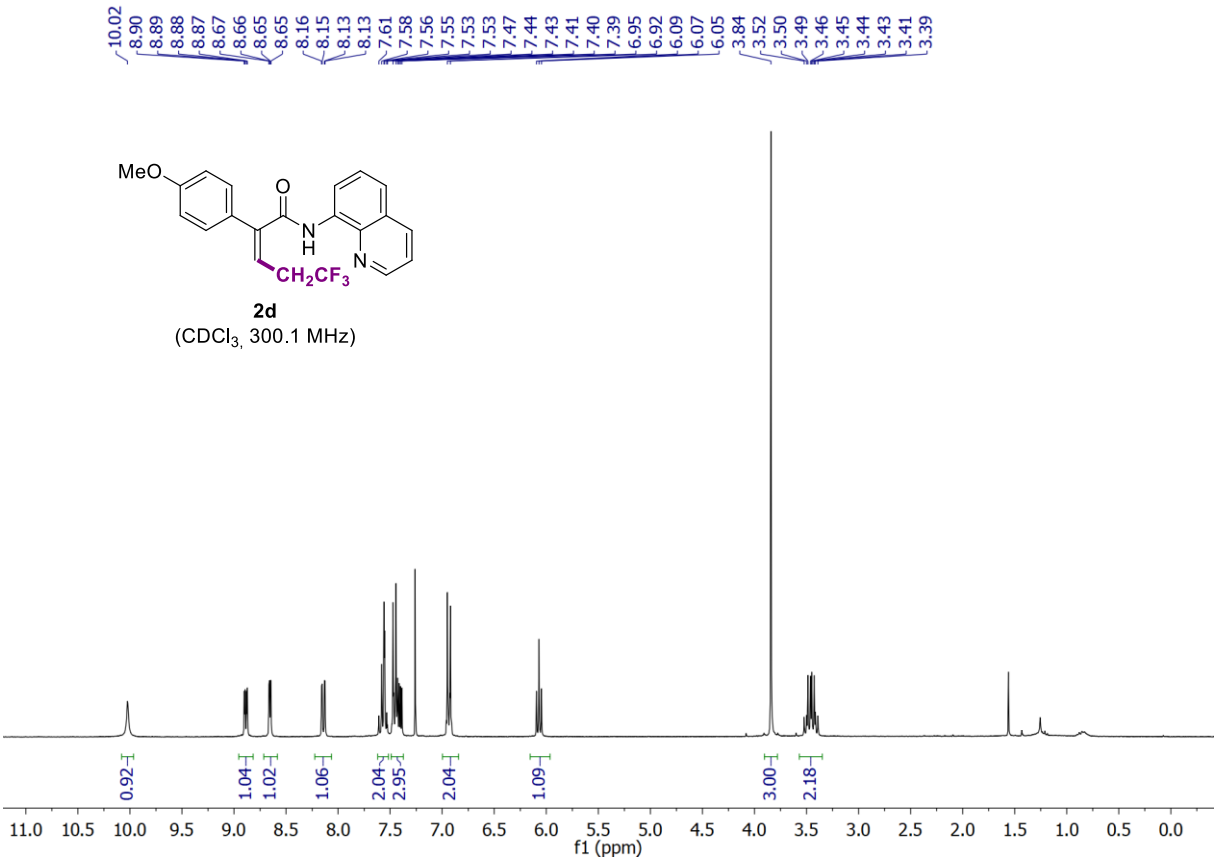
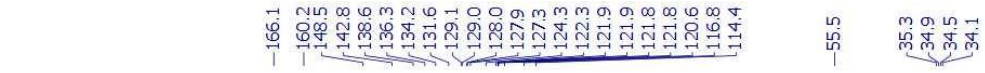
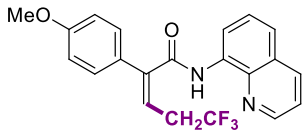
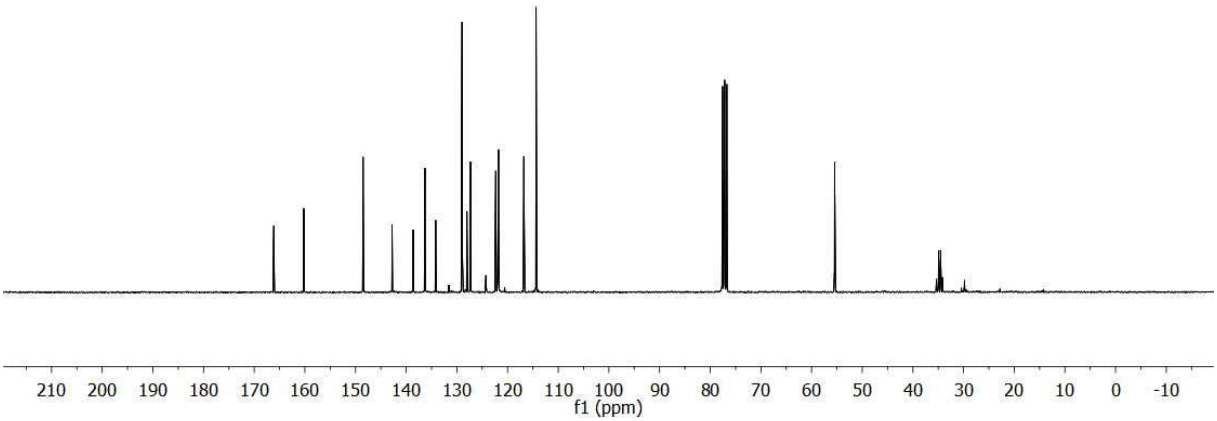


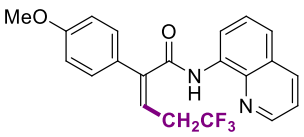
2d
($CDCl_3$, 300.1 MHz)



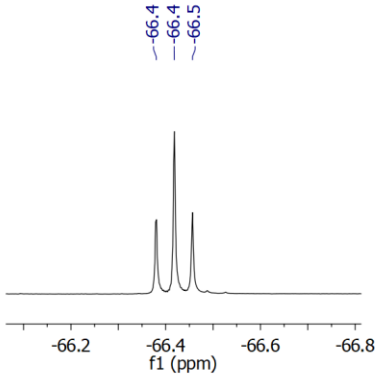


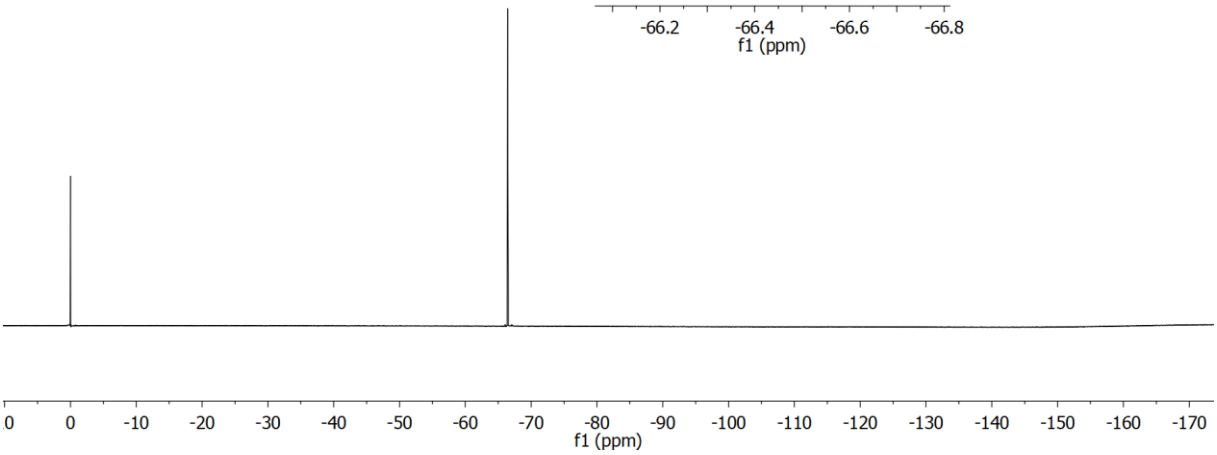
2d
($CDCl_3$, 75.5 MHz)



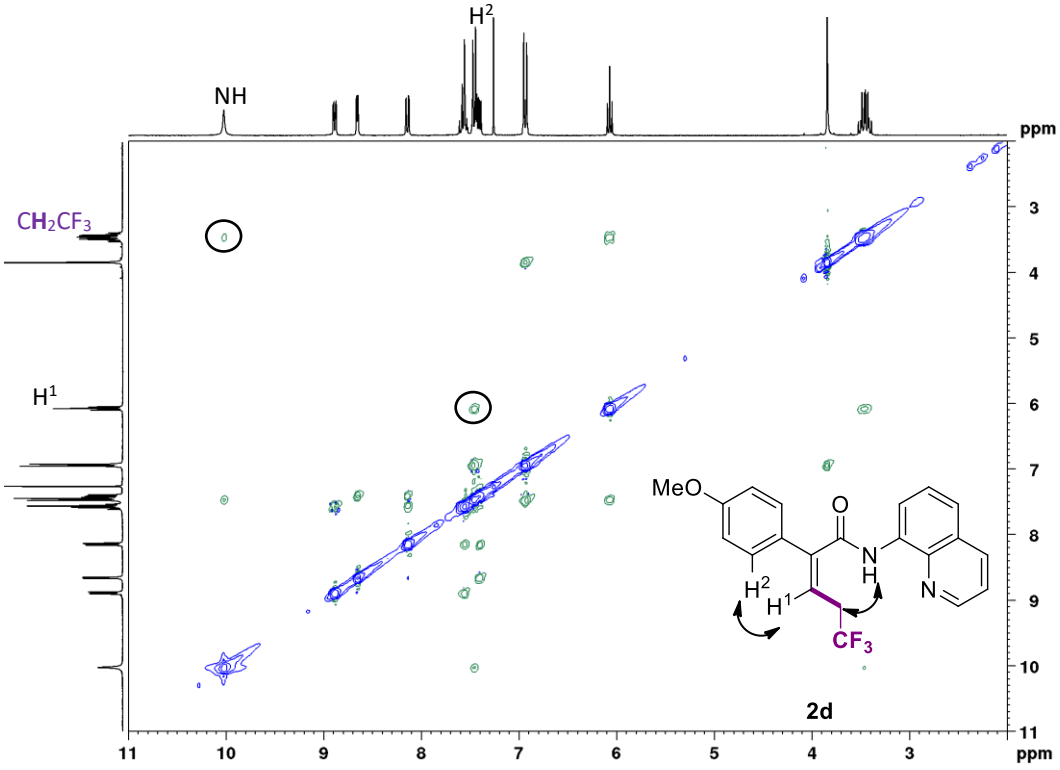


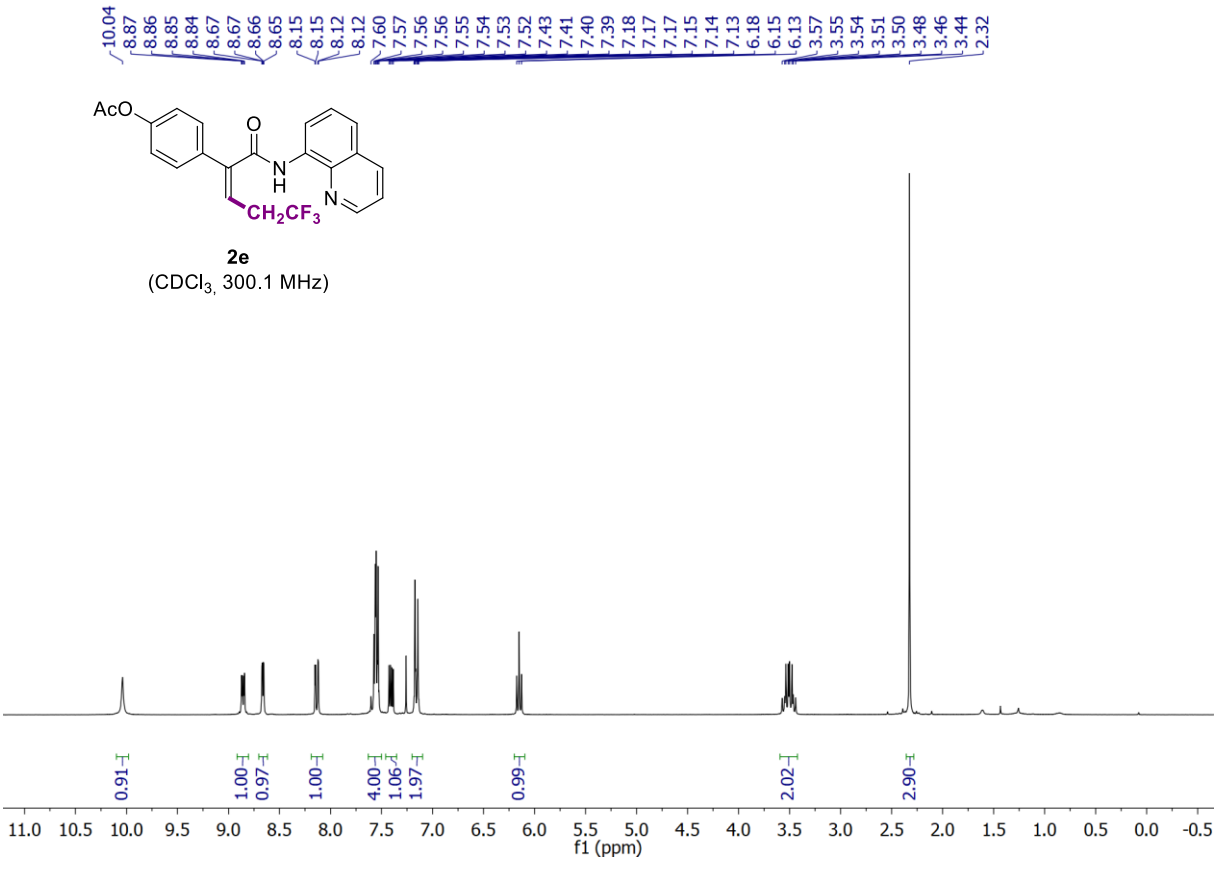
2d
($CDCl_3$, 282.4 MHz)

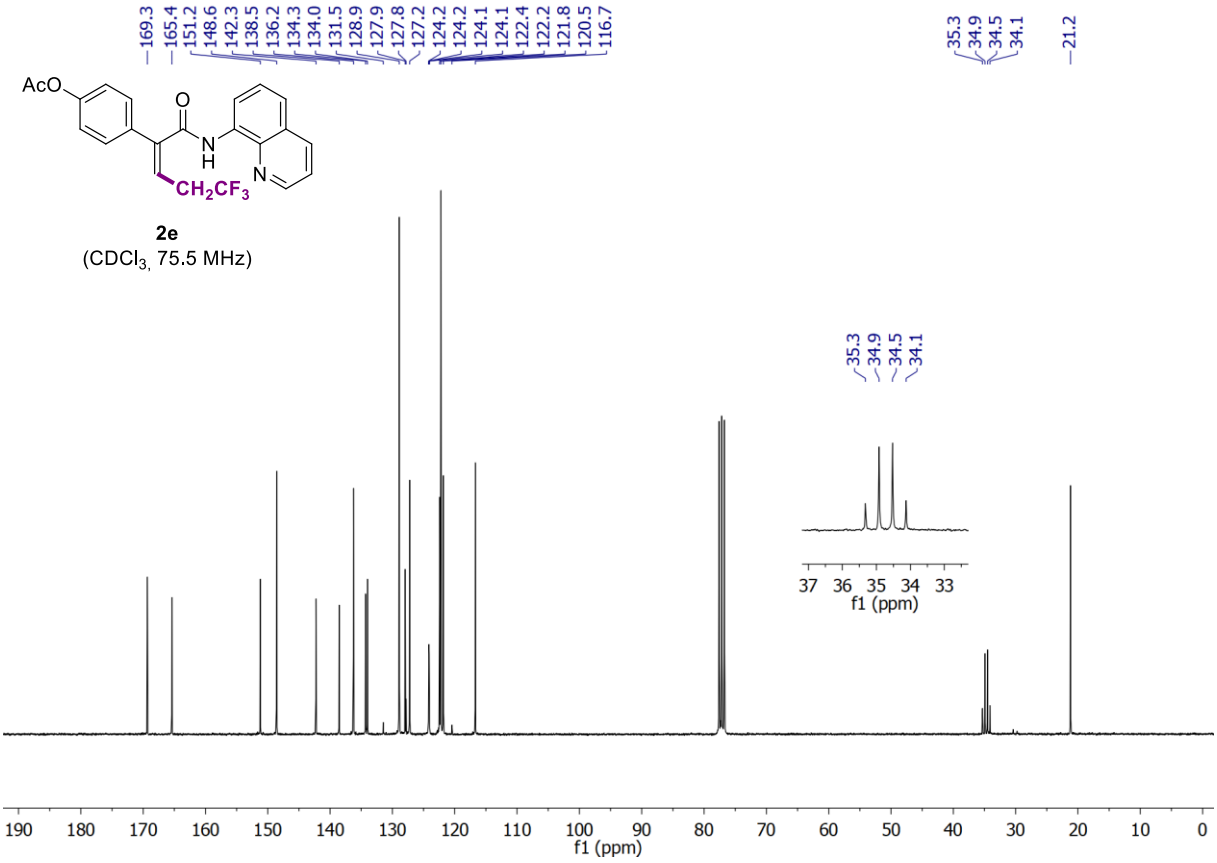


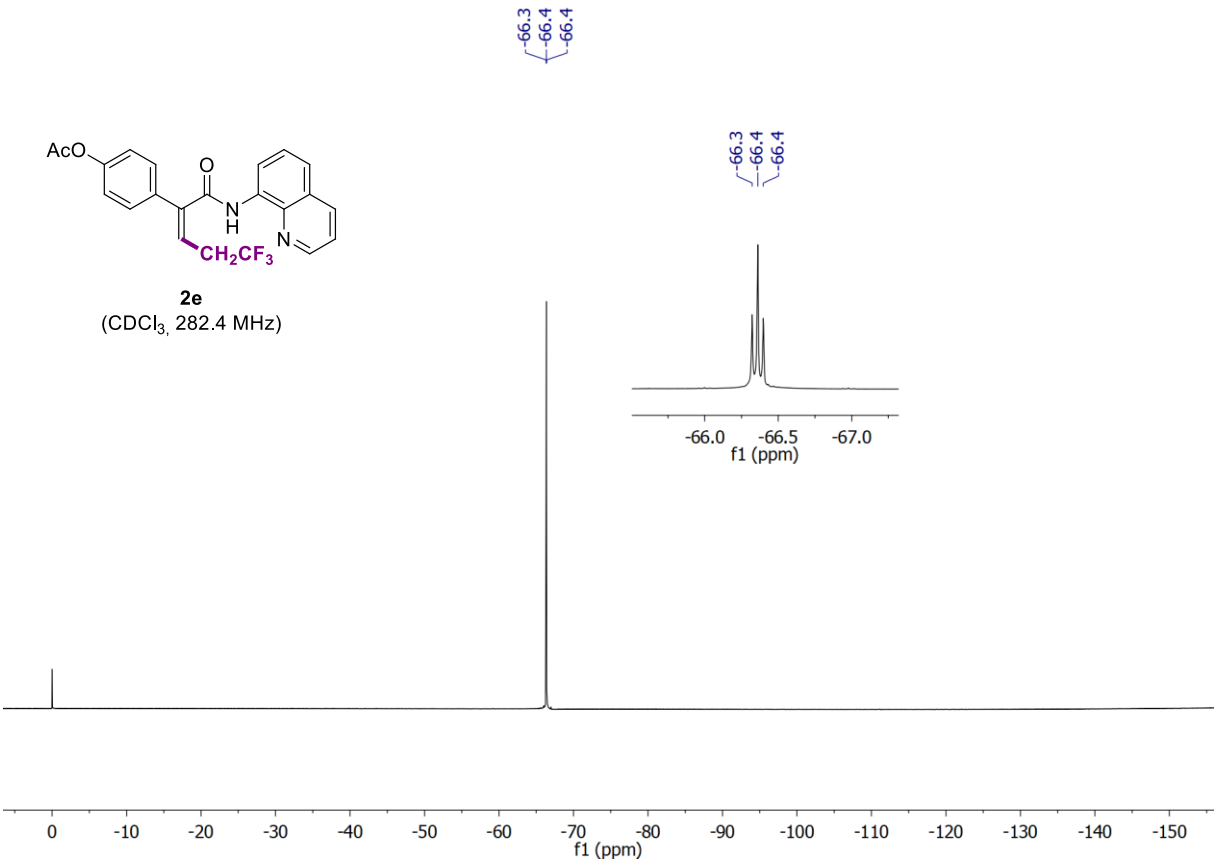


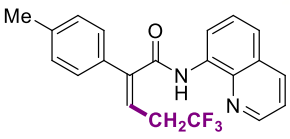
NOESY 2D spectra of compound **2d**





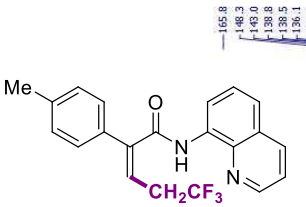

169.3
165.4
151.2
148.6
142.3
138.5
136.2
134.3
134.0
131.5
128.9
127.9
127.8
127.2
124.2
124.2
124.1
124.1
122.4
122.2
121.8
120.5
116.7
35.3
34.9
34.5
34.1
21.2
AcO
O
N
H
N
CH2CF3
2e
(CDCl3, 75.5 MHz)
35.3
34.9
34.5
34.1
37 36 35 34 33
f1 (ppm)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-66.3
-66.4
-66.4
AcO
O
N
H
N
CH2CF3
2e
(CDCl3, 282.4 MHz)
-66.3
-66.4
-66.4
-66.0 -66.5 -67.0
f1 (ppm)
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150
f1 (ppm)



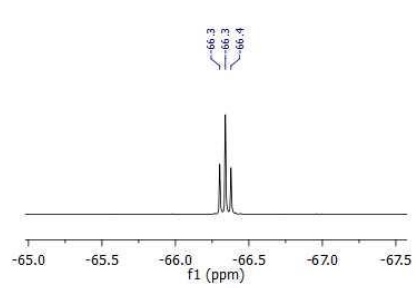
2f

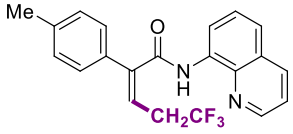
($CDCl_3$, 300.1 MHz)



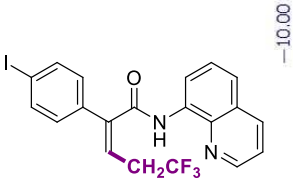
2f

($CDCl_3$, 75.5 MHz)

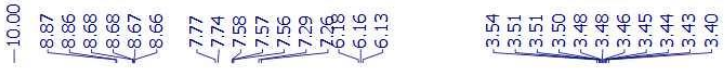


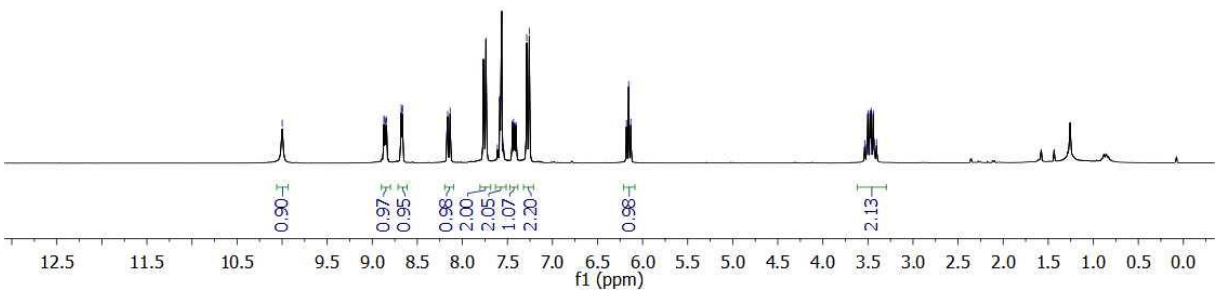


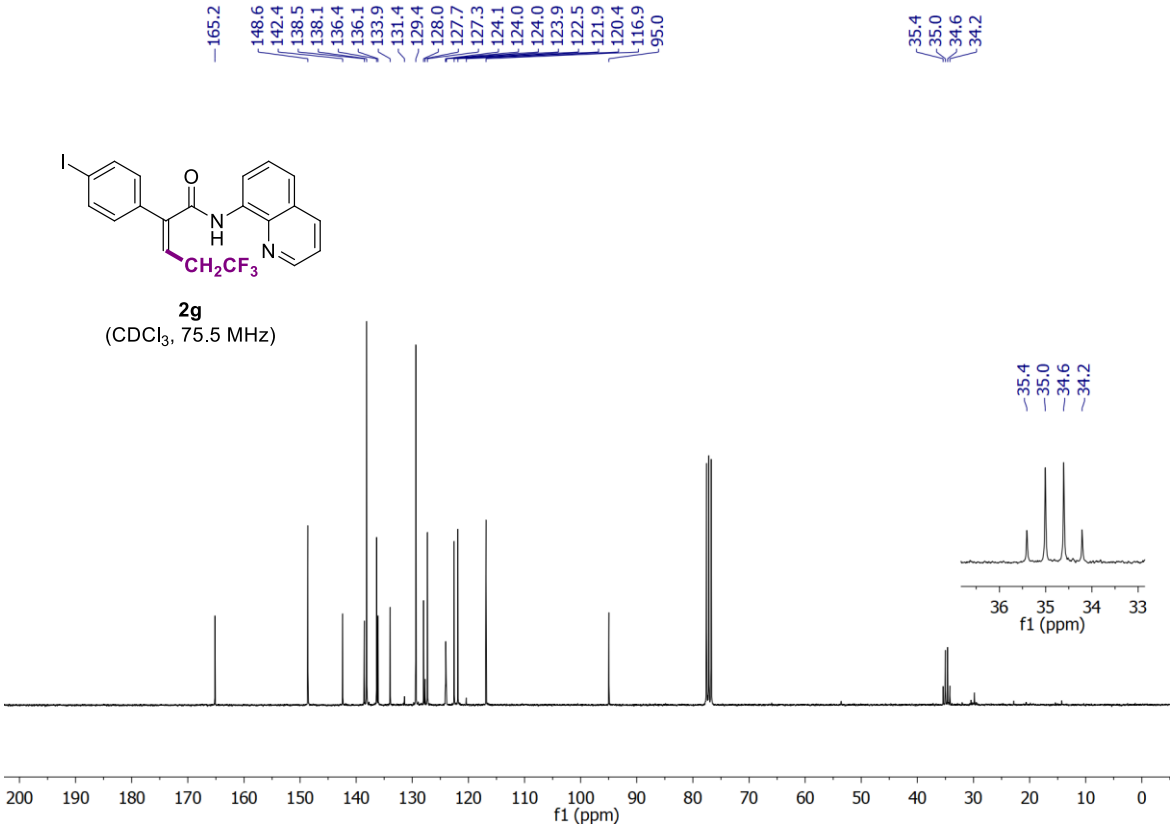
2f
($CDCl_3$, 282.4 MHz)

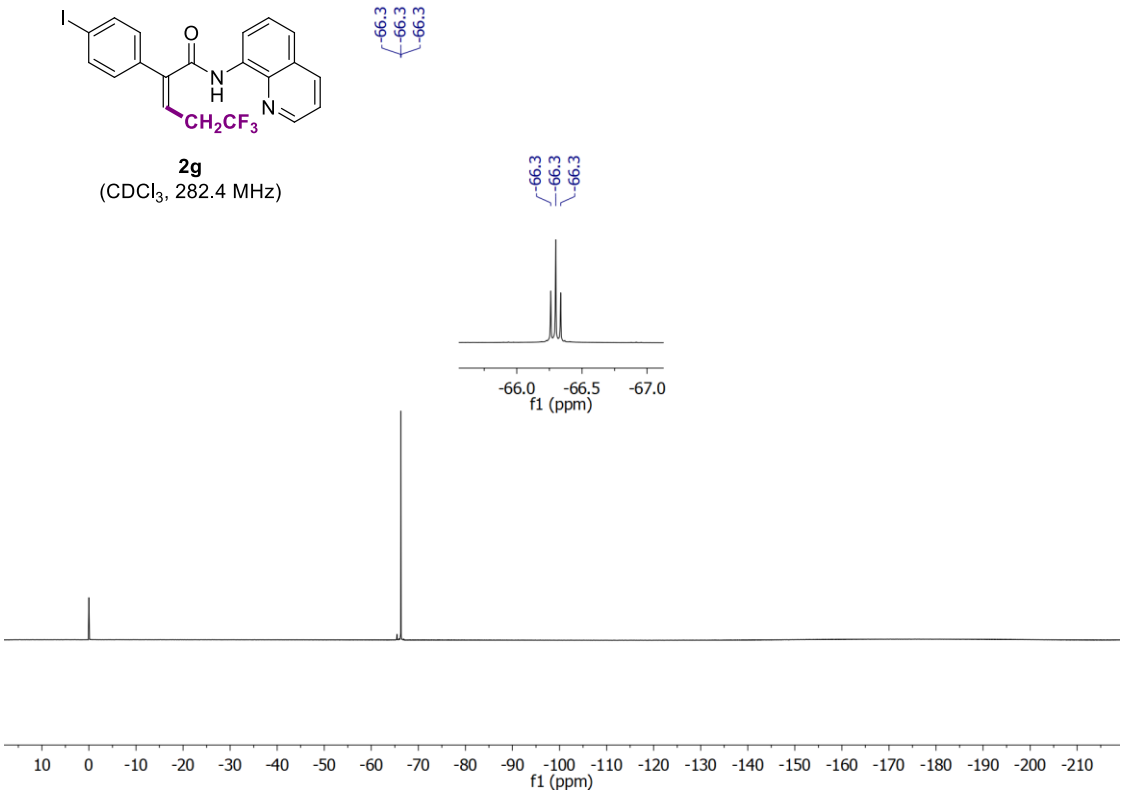


2g
($CDCl_3$, 300.1 MHz)

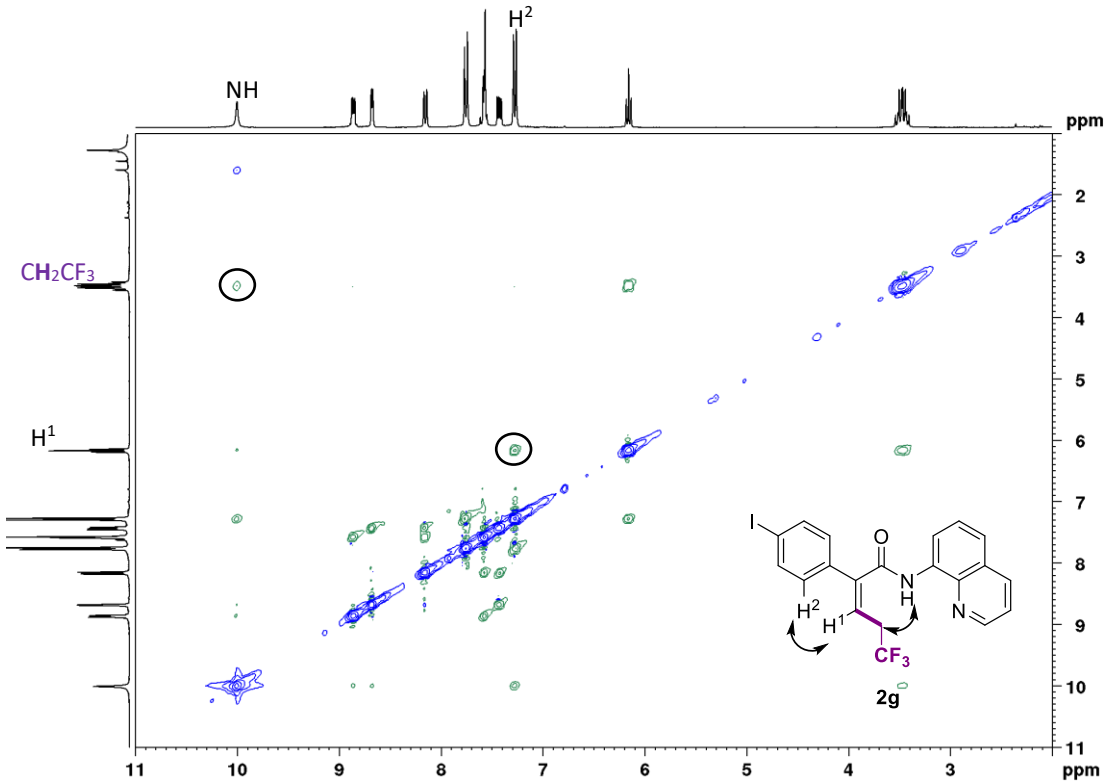


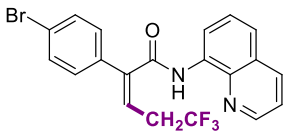



165.2
148.6
142.4
138.5
138.1
136.4
136.1
133.9
131.4
129.4
128.0
127.7
127.3
124.1
124.0
124.0
123.9
122.5
121.9
120.4
116.9
95.0
35.4
35.0
34.6
34.2
I
O
N
H
N
CH2CF3
2g
(CDCl3, 75.5 MHz)
35.4
35.0
34.6
34.2
36 35 34 33
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

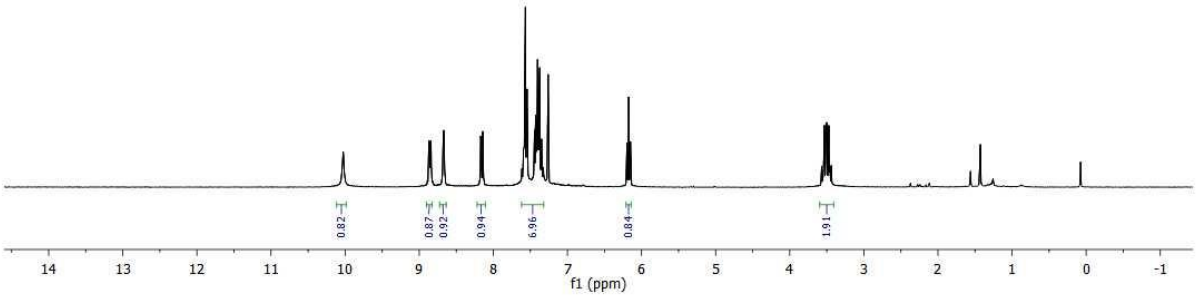

66.3
66.3
66.3
I
O
N
H
N
CH2CF3
2g
(CDCl3, 282.4 MHz)
66.3
66.3
66.3
-66.0 -66.5 -67.0
f1 (ppm)
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

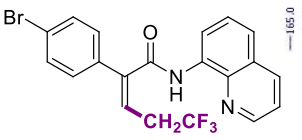
NOESY 2D spectra of compound **2g**





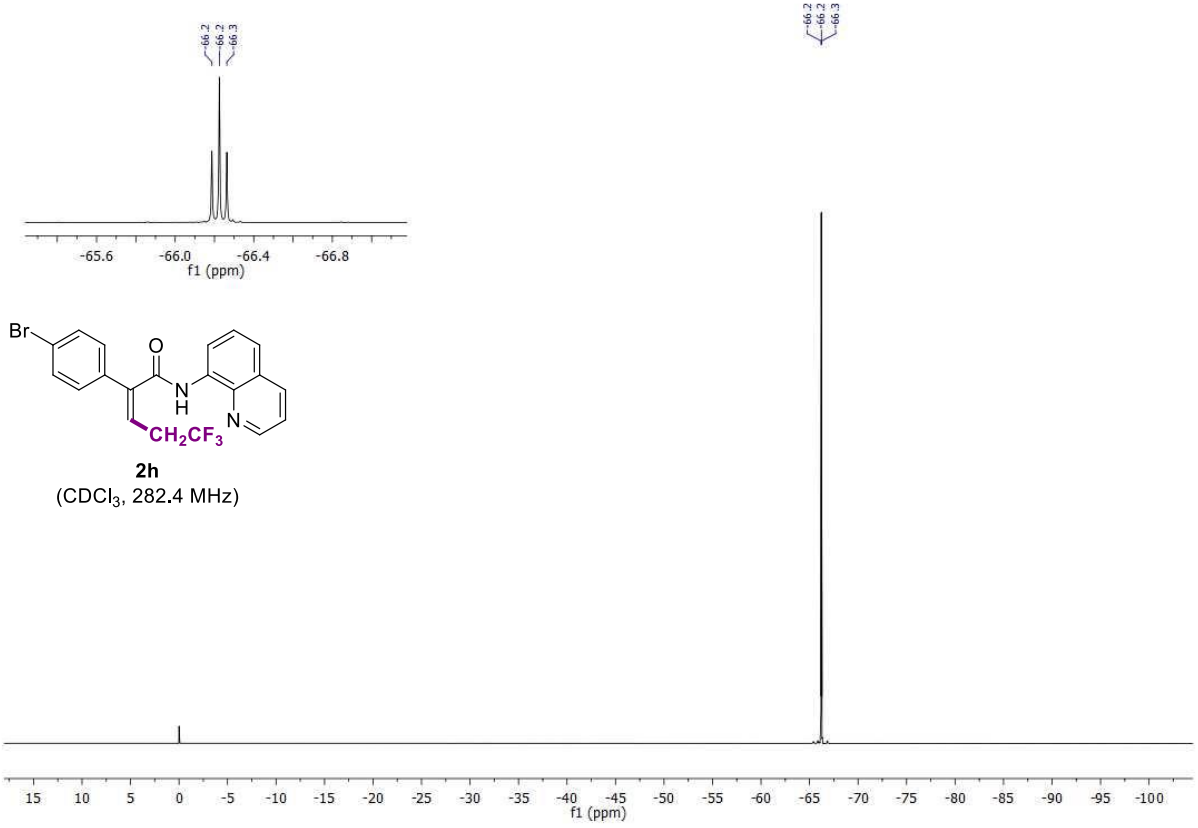
2h
($CDCl_3$, 300.1 MHz)





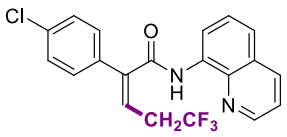
2h

($CDCl_3$, 75.5 MHz)

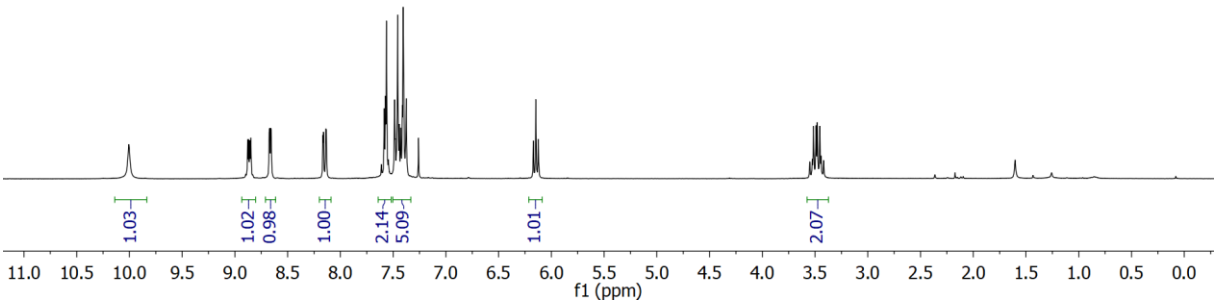


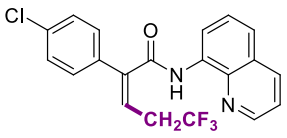
2h

($CDCl_3$, 282.4 MHz)

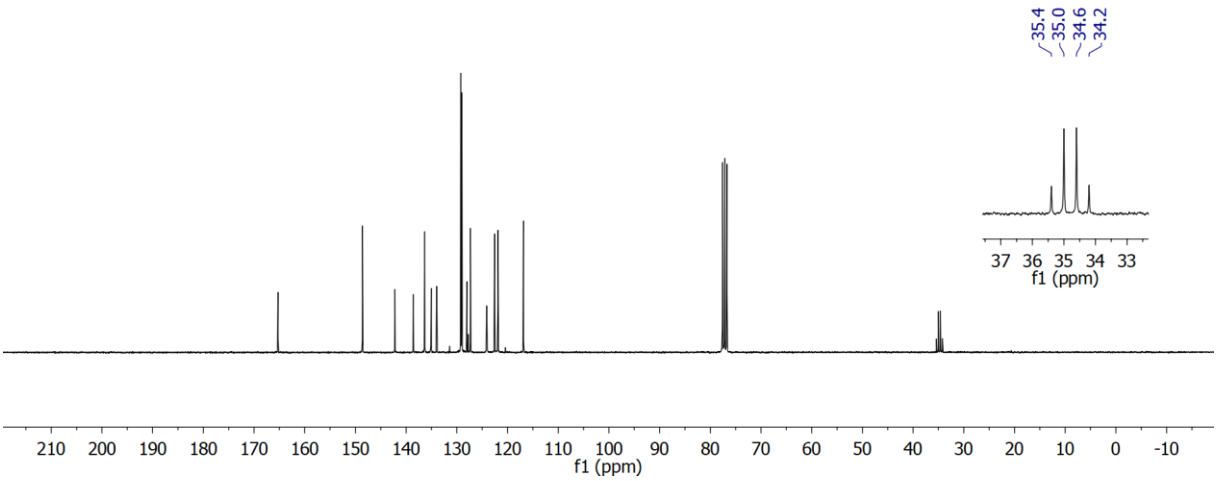


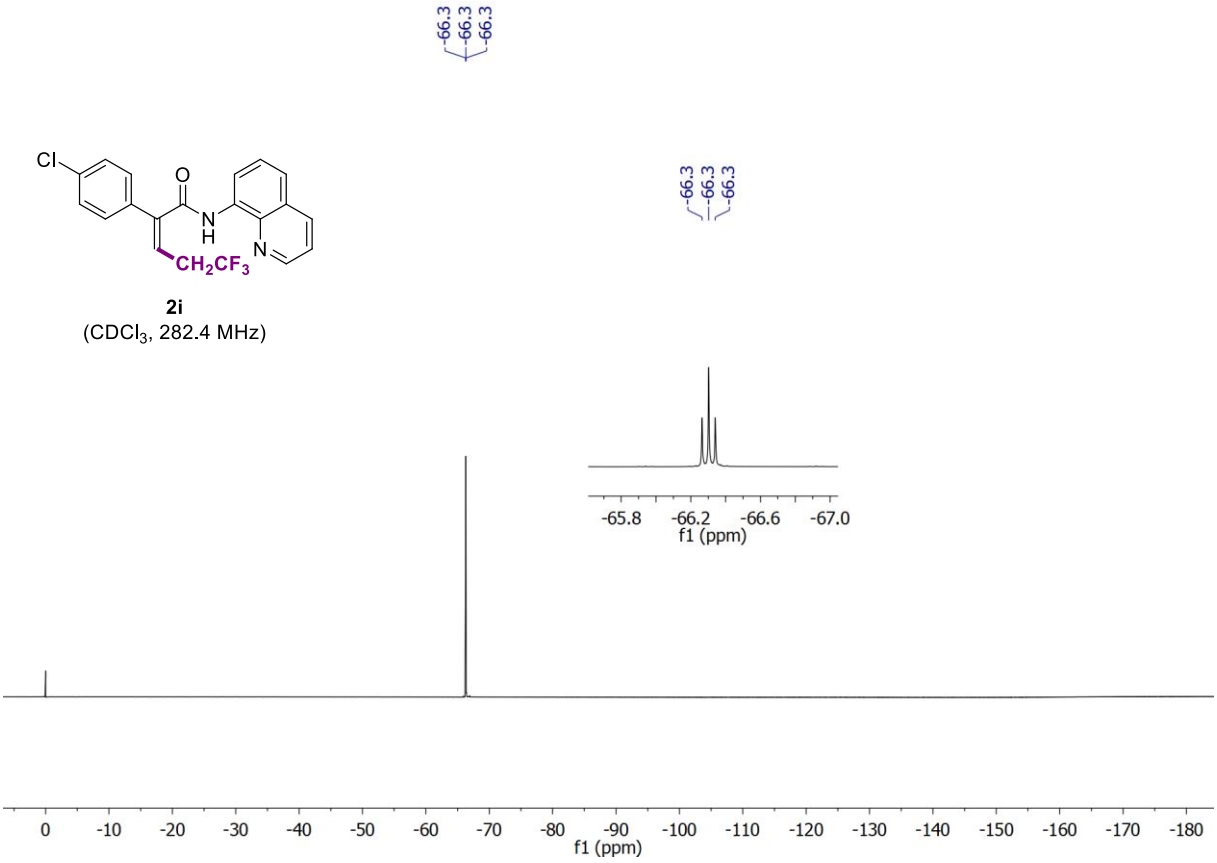
2i
($CDCl_3$, 300.1 MHz)



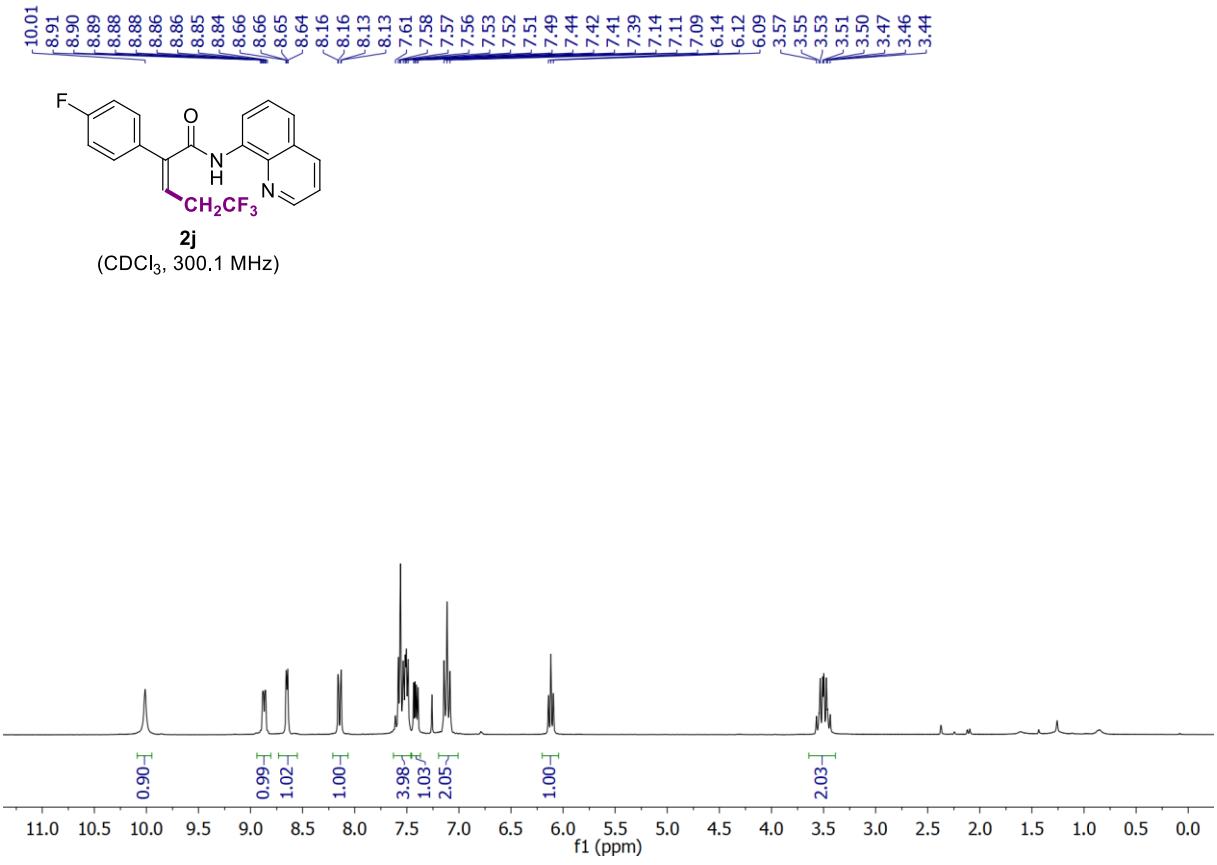


2i
($CDCl_3$, 75.5 MHz)

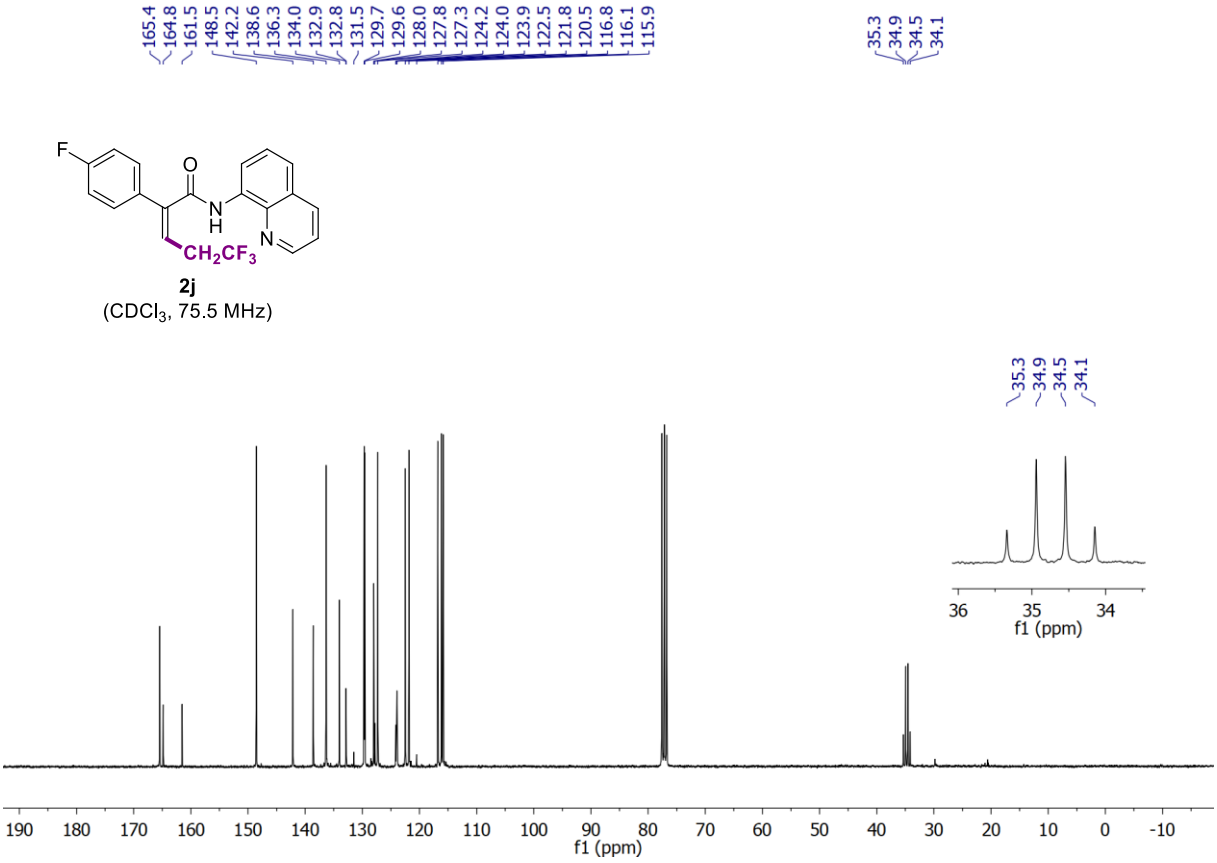


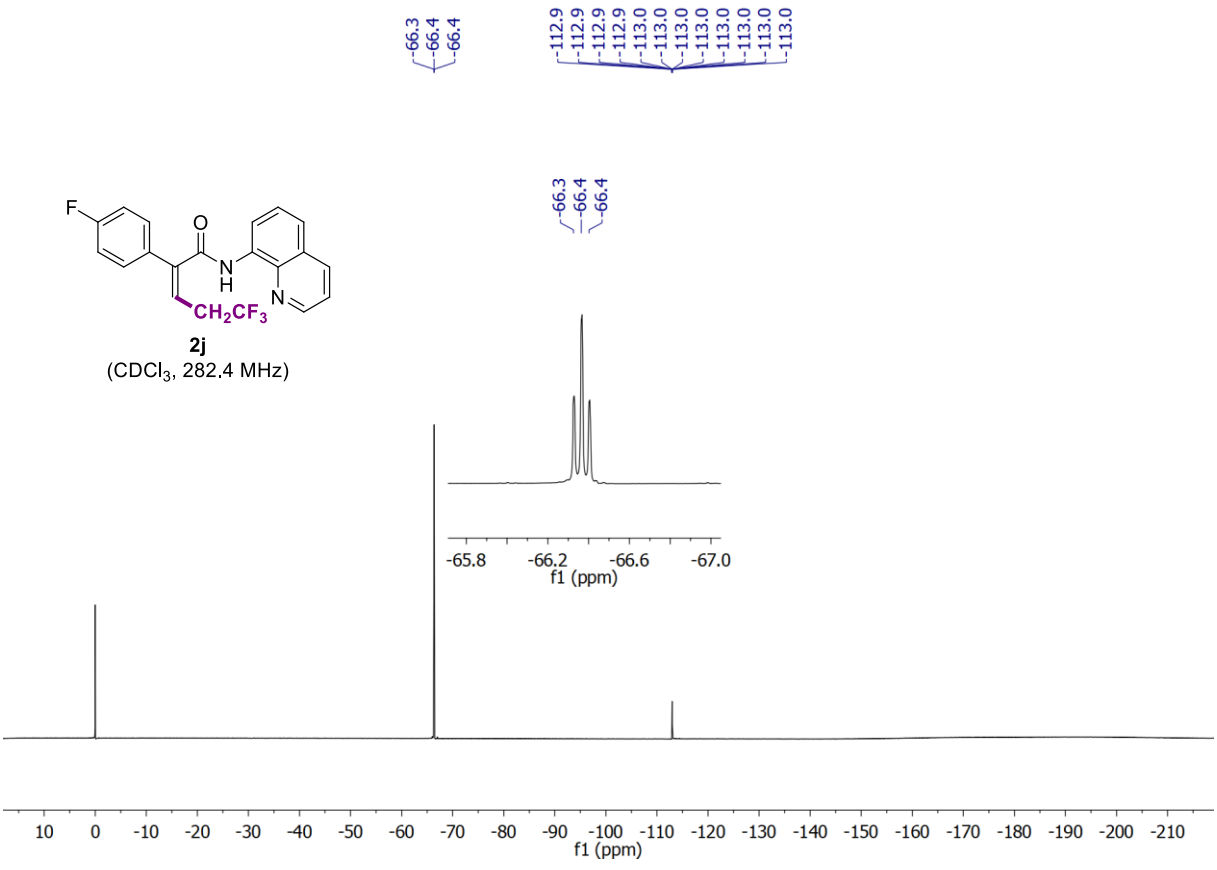


2i
($CDCl_3$, 282.4 MHz)



2j
($CDCl_3$, 300.1 MHz)


165.4
164.8
161.5
148.5
142.2
138.6
136.3
134.0
132.9
132.8
131.5
129.7
129.6
128.0
127.8
127.3
124.2
124.0
123.9
122.5
121.8
120.5
116.8
116.1
115.9
35.3
34.9
34.5
34.1
F
O
N
H
N
CH2CF3
2j
(CDCl3, 75.5 MHz)
f1 (ppm)


-66.3
-66.4
-66.4
-112.9
-112.9
-112.9
-112.9
-113.0
-113.0
-113.0
-113.0
-113.0
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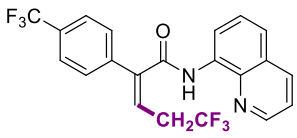
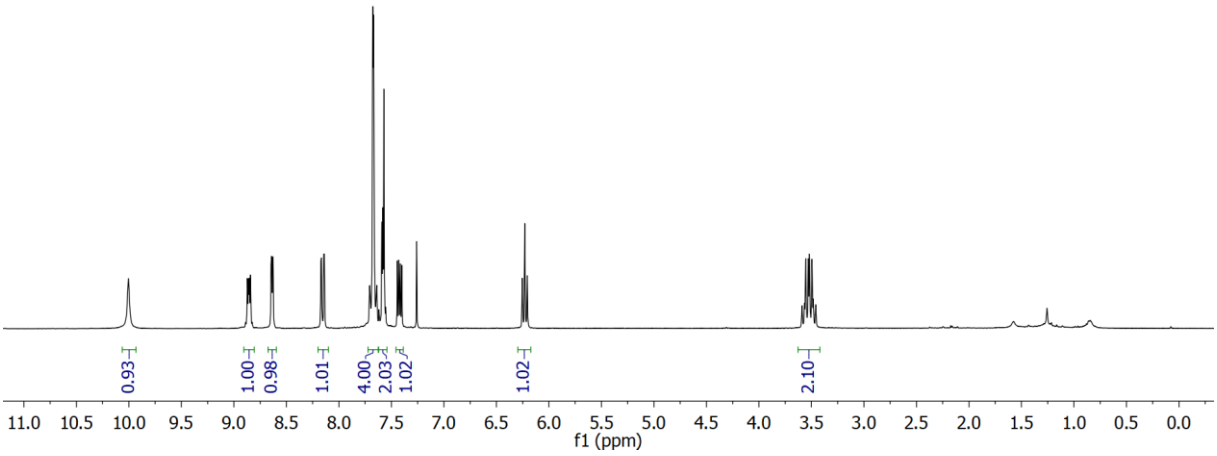
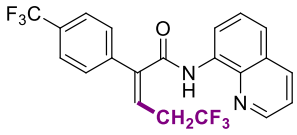
-113.0
-113.0
F
O
N
H
N
CH2CF3
2j
(CDCl3, 282.4 MHz)
f1 (ppm)

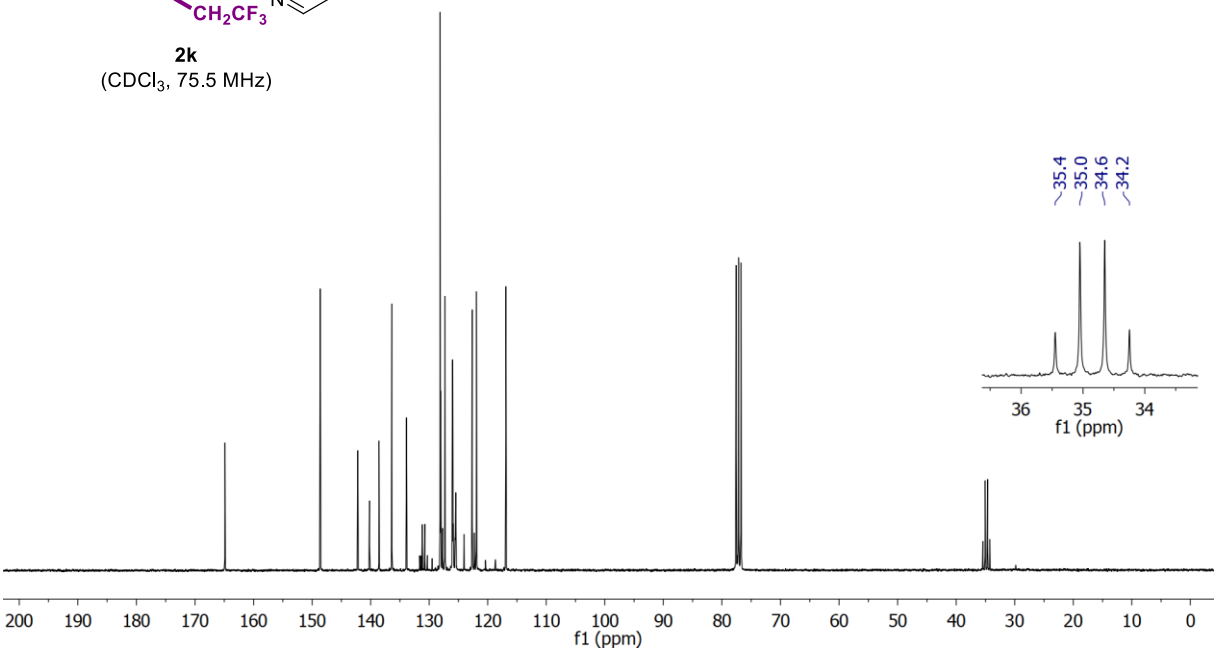


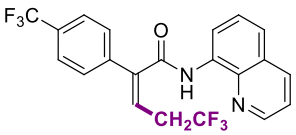
2k
($CDCl_3$, 300.1 MHz)



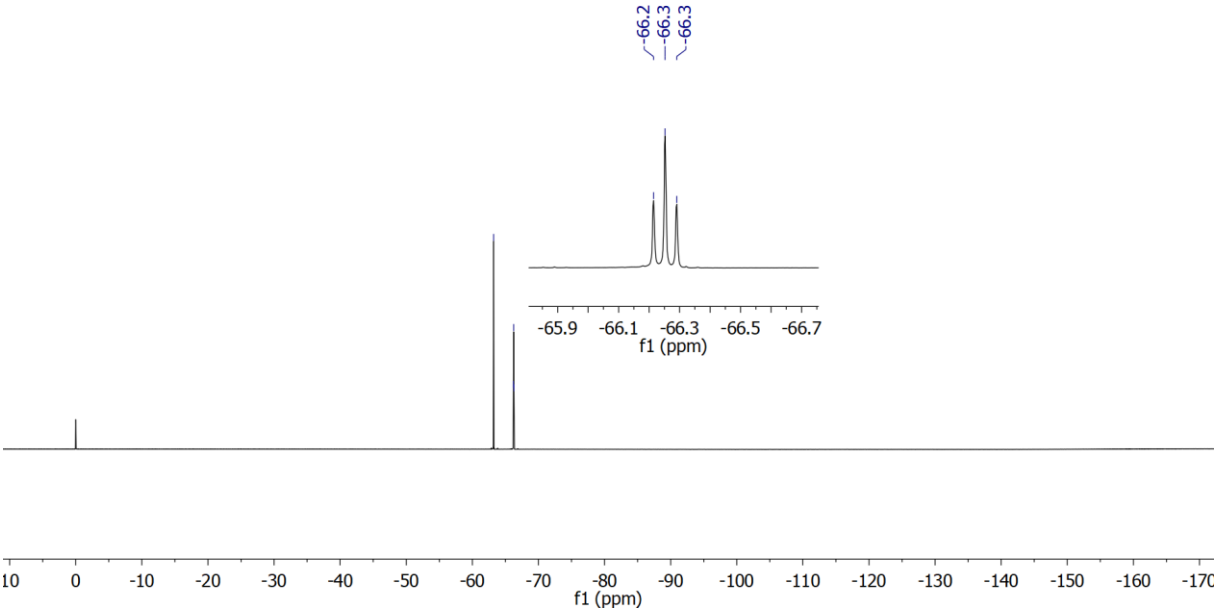


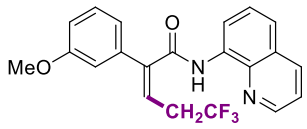
2k
($CDCl_3$, 75.5 MHz)



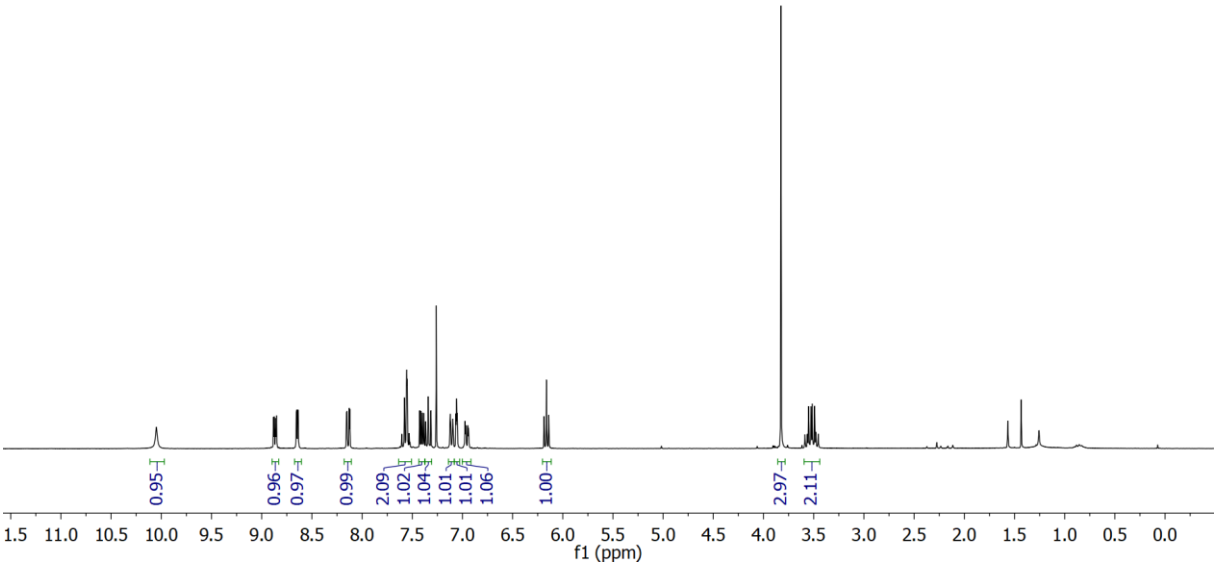


2k
($CDCl_3$, 282.4 MHz)



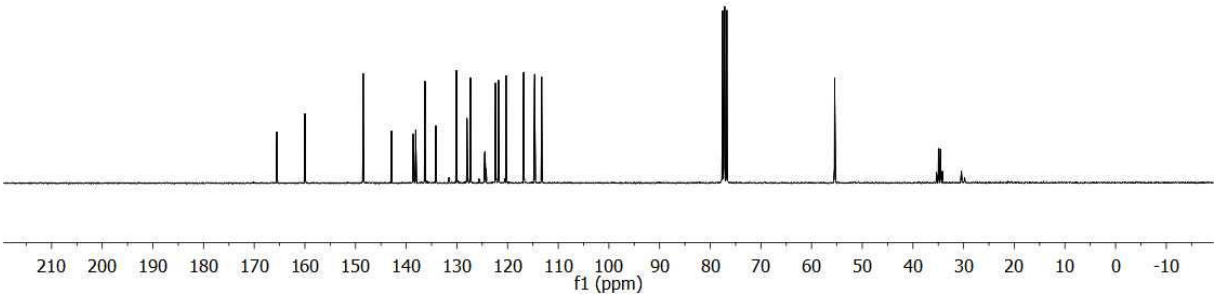


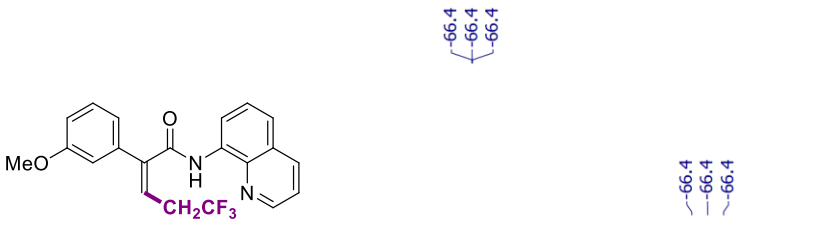
2l
($CDCl_3$, 300.1 MHz)



2l

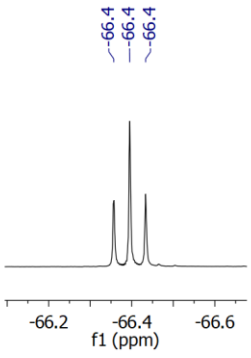
($CDCl_3$, 75.5 MHz)

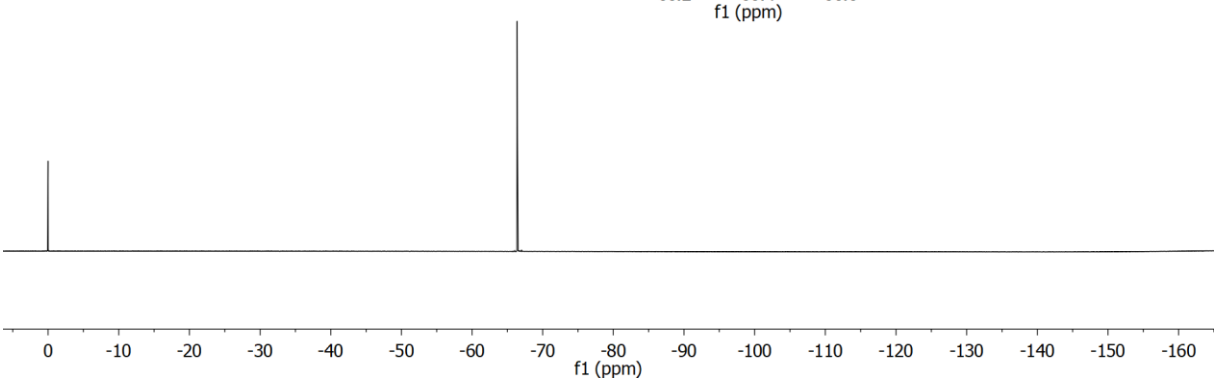


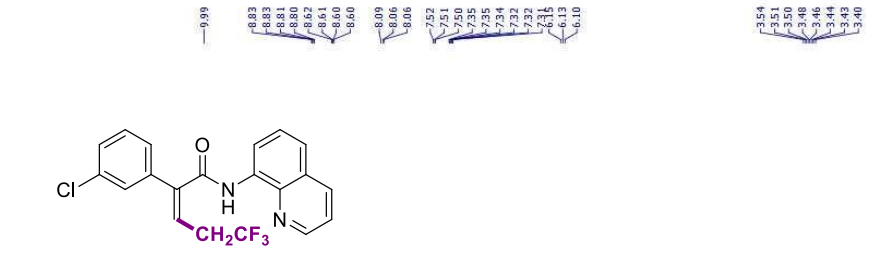


2l

($CDCl_3$, 282.4 MHz)

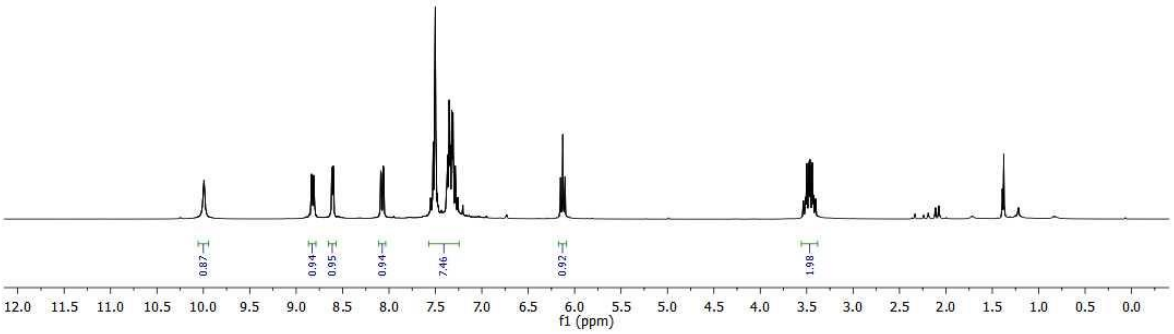


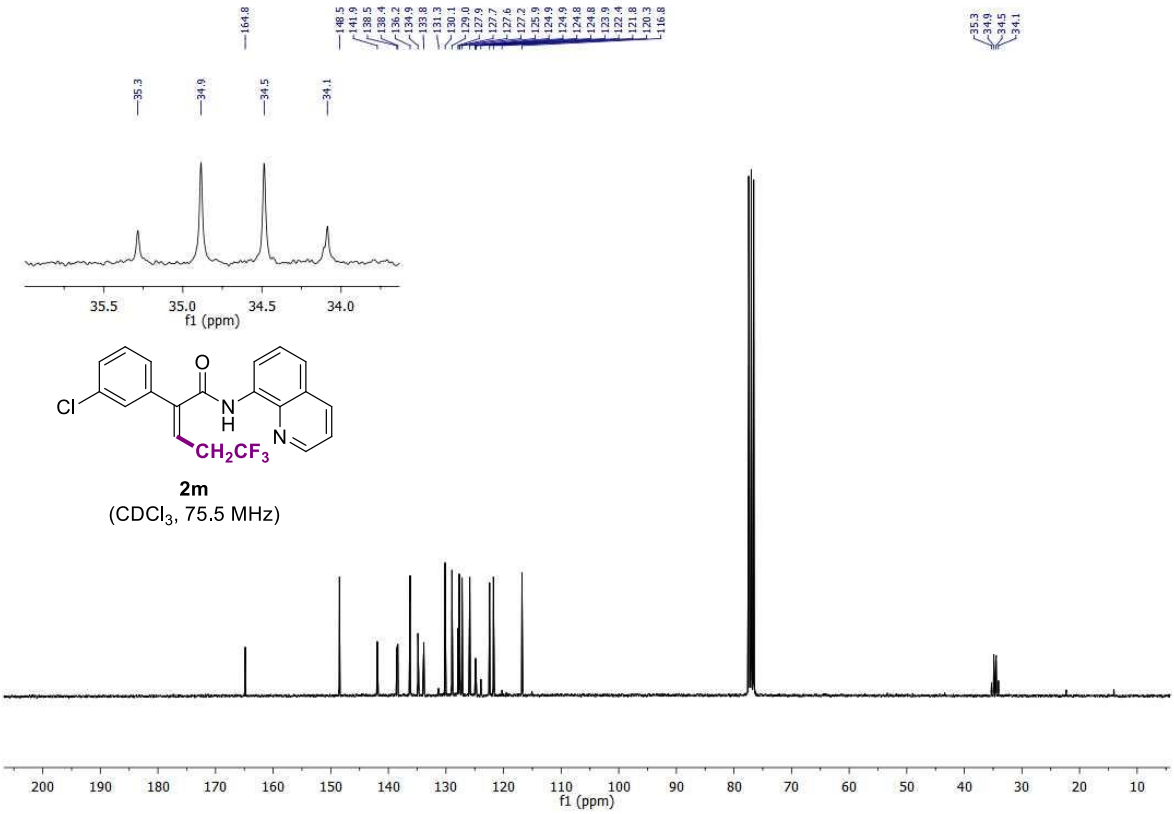




2m

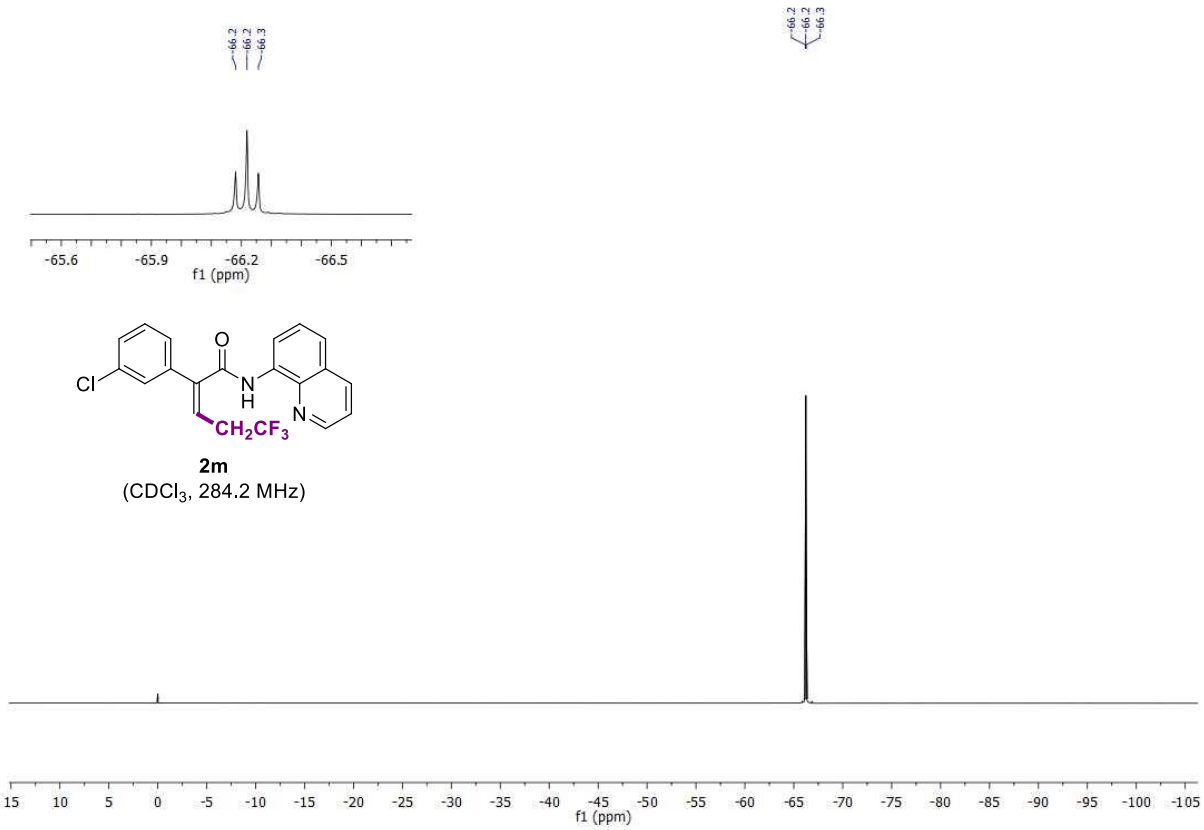
($CDCl_3$, 300.1 MHz)



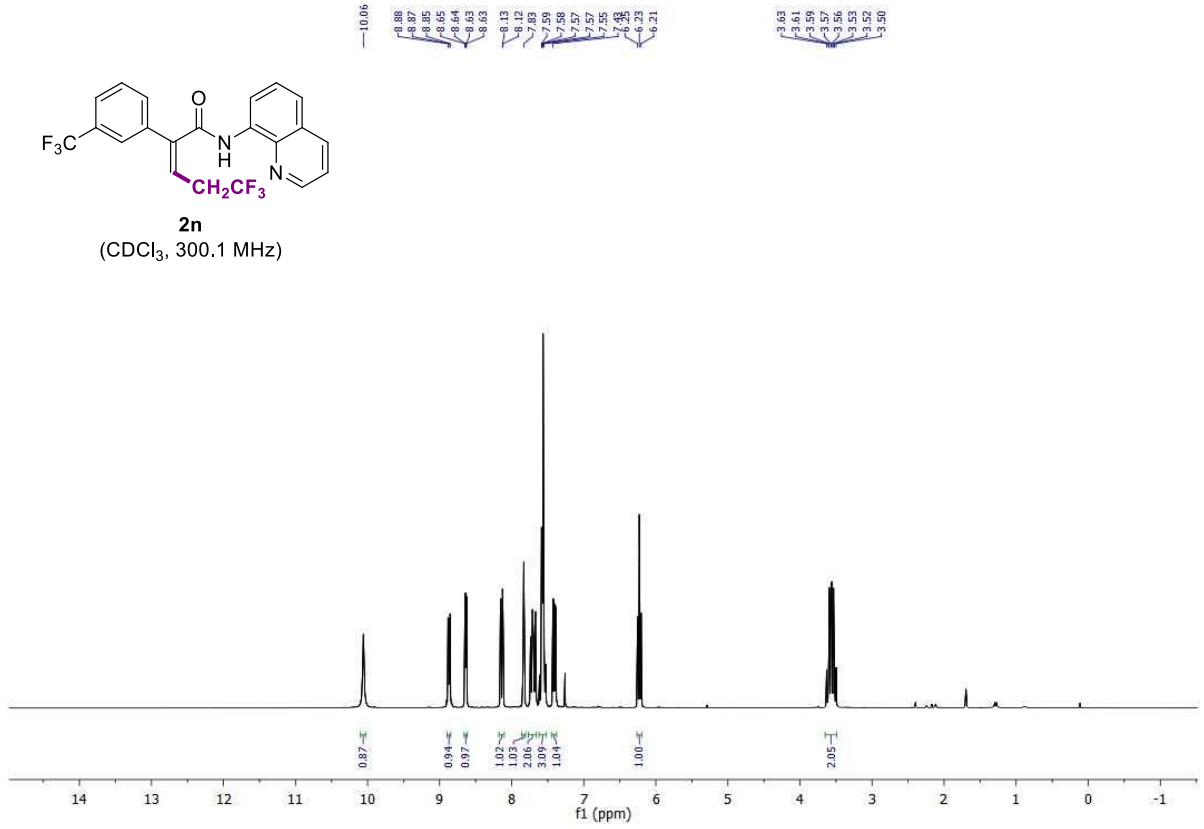


2m

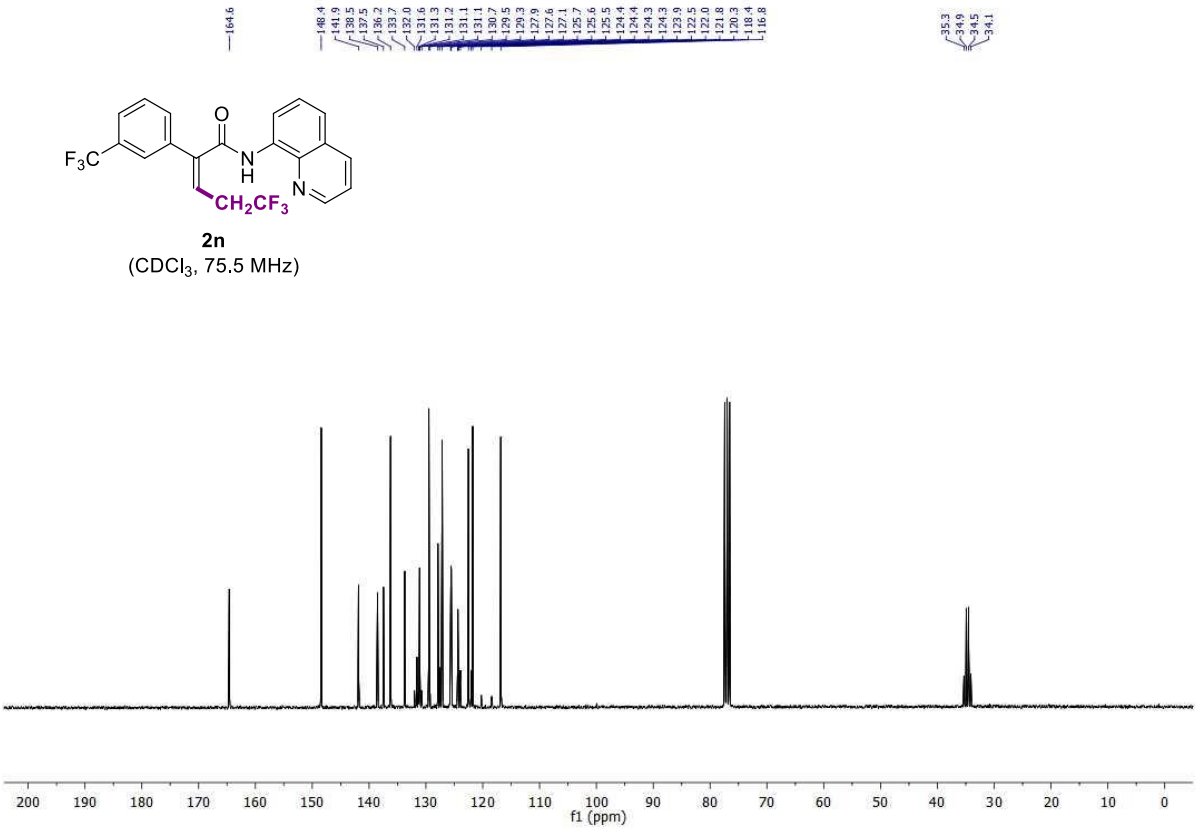
($CDCl_3$, 75.5 MHz)



2m
($CDCl_3$, 284.2 MHz)

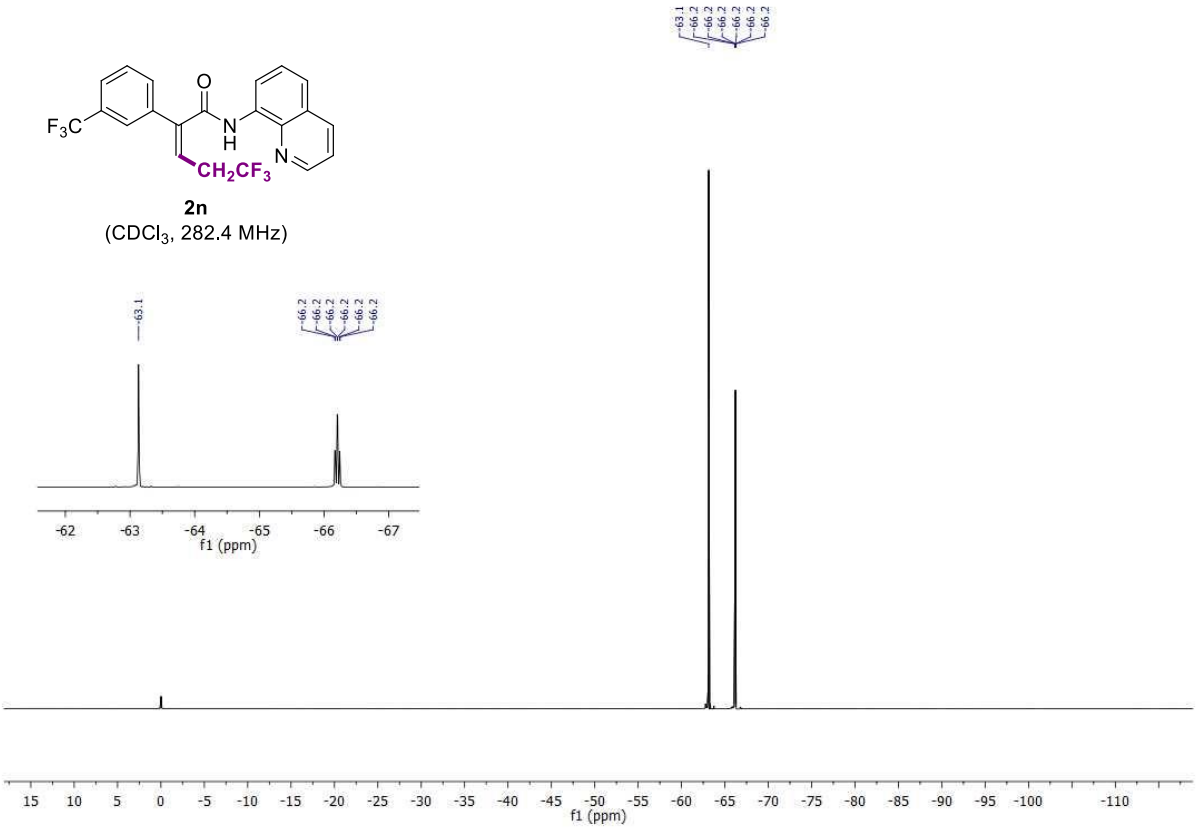


2n
($CDCl_3$, 300.1 MHz)



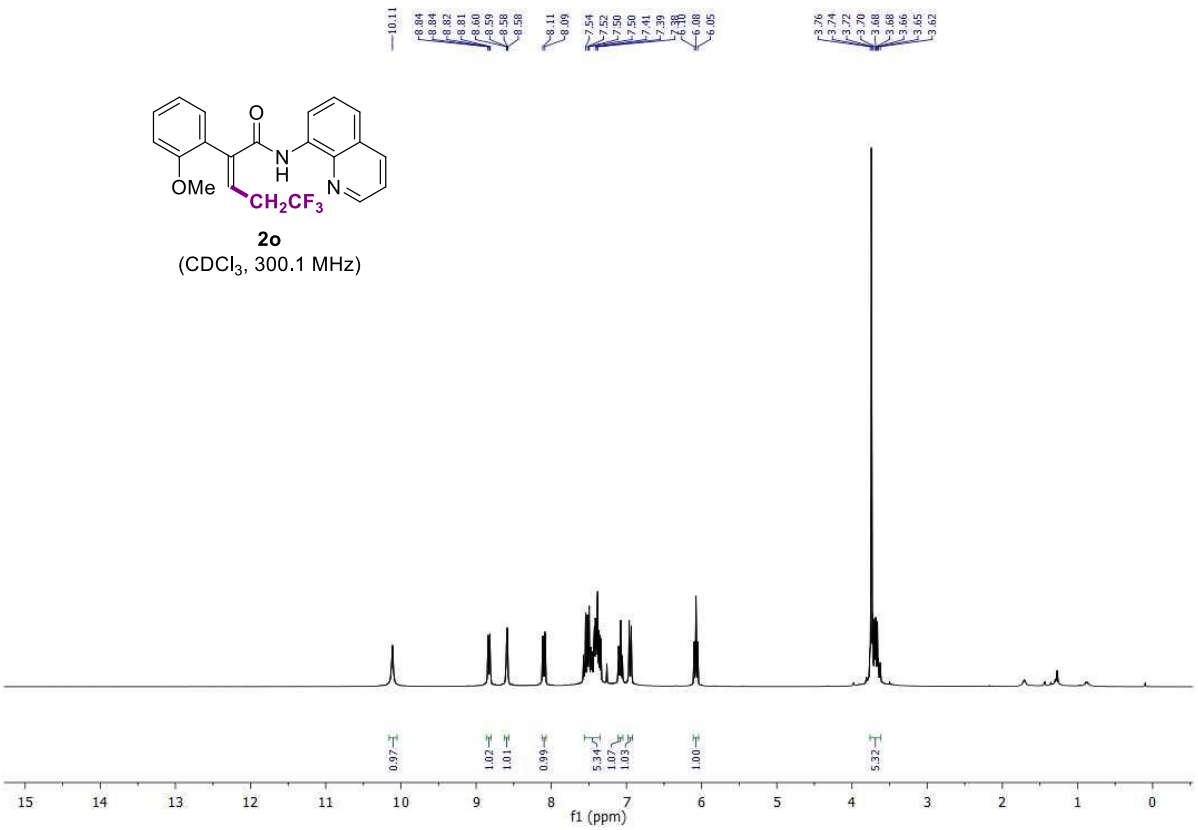
2n

($CDCl_3$, 75.5 MHz)

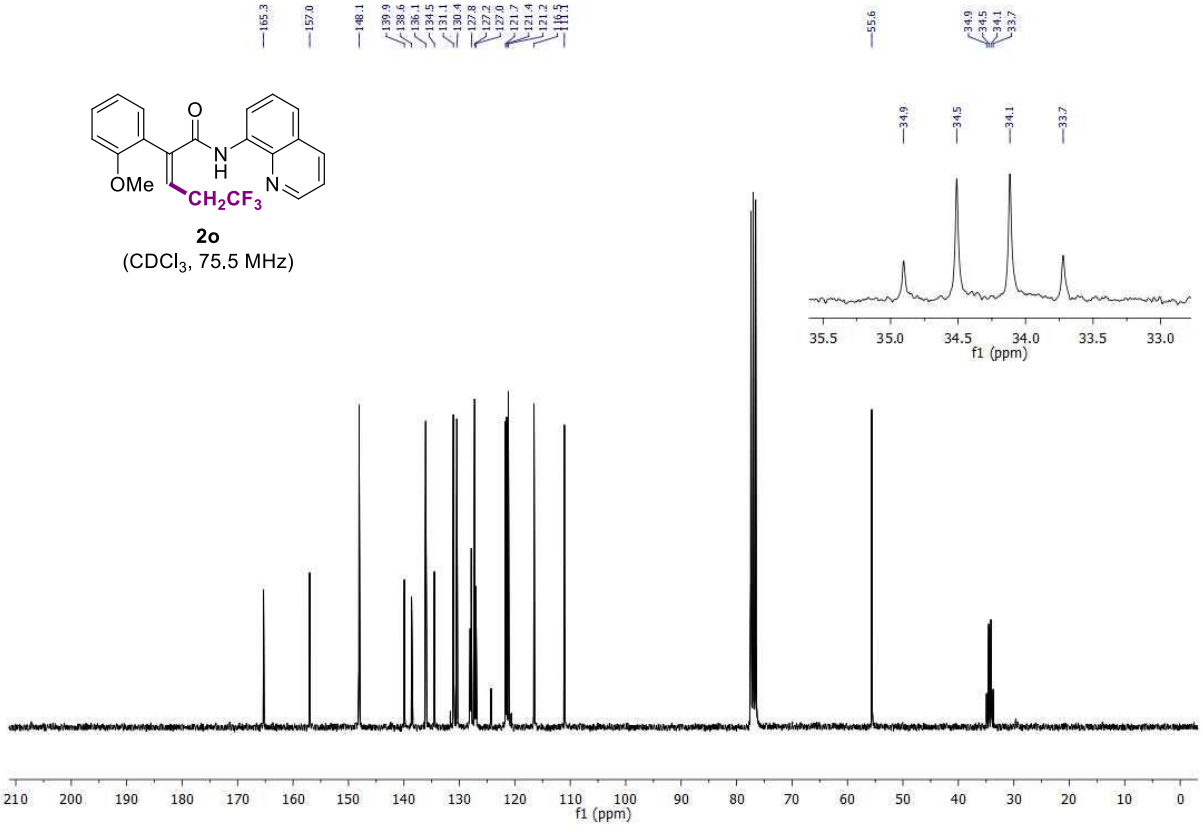


2n

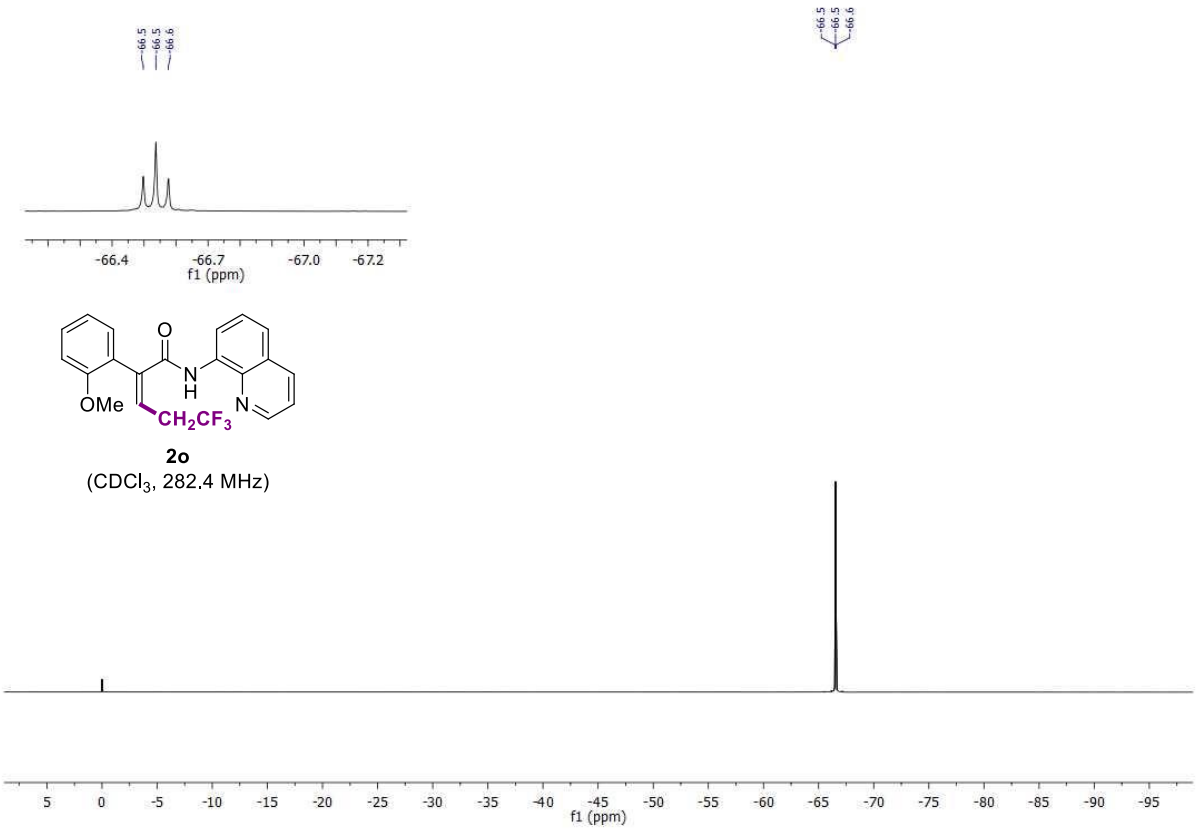
($CDCl_3$, 282.4 MHz)



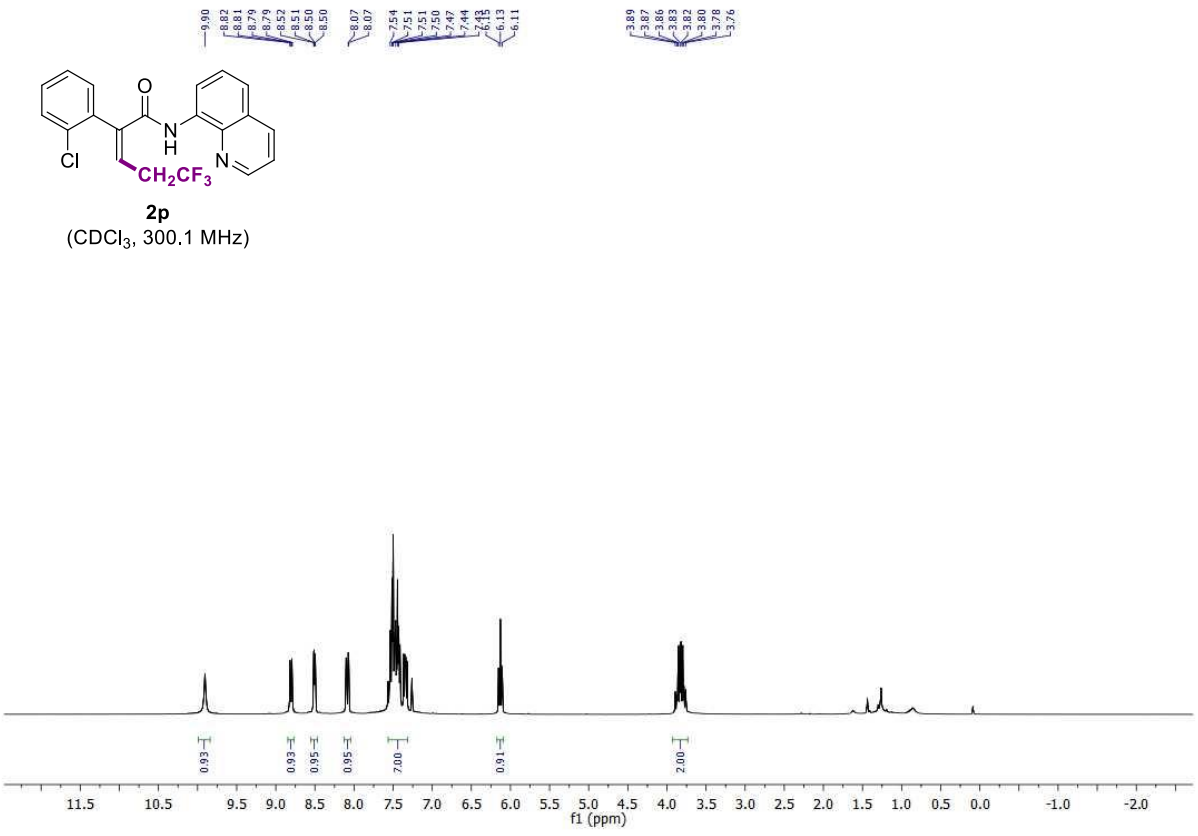
2o
($CDCl_3$, 300.1 MHz)



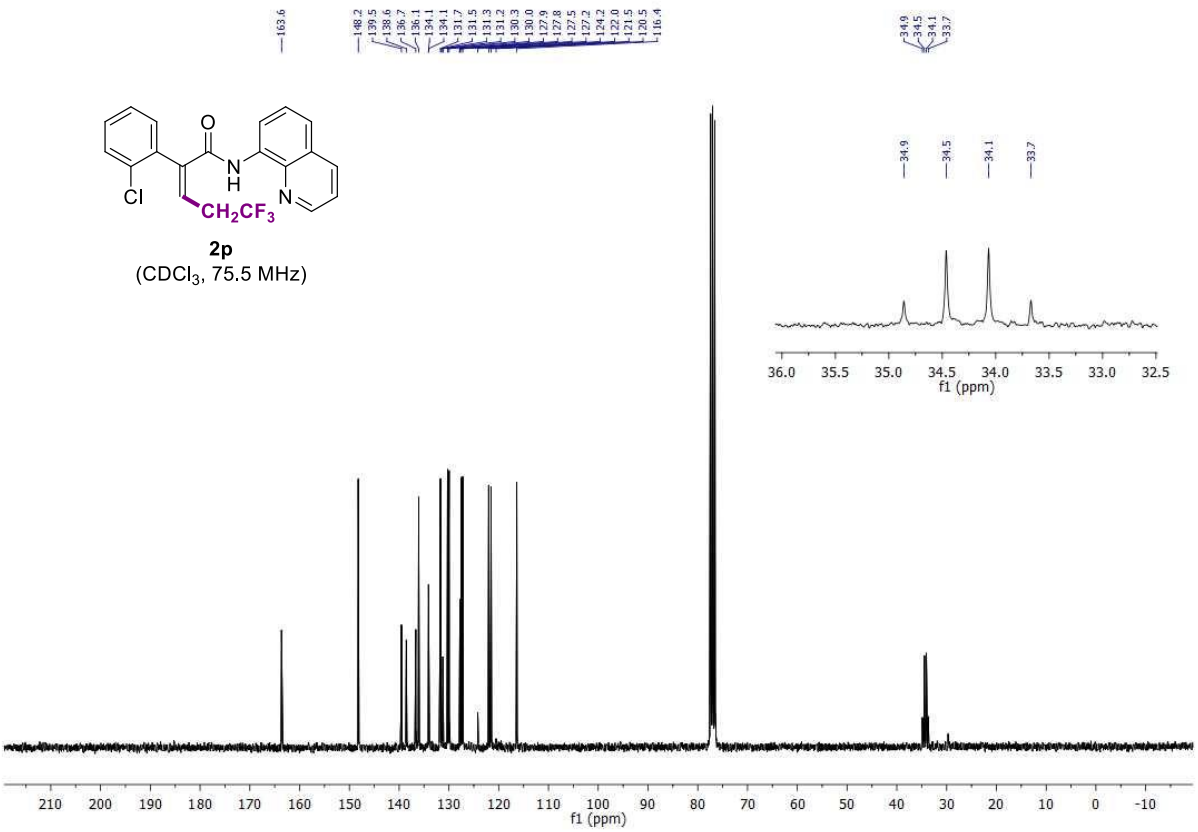
2o
($CDCl_3$, 75.5 MHz)

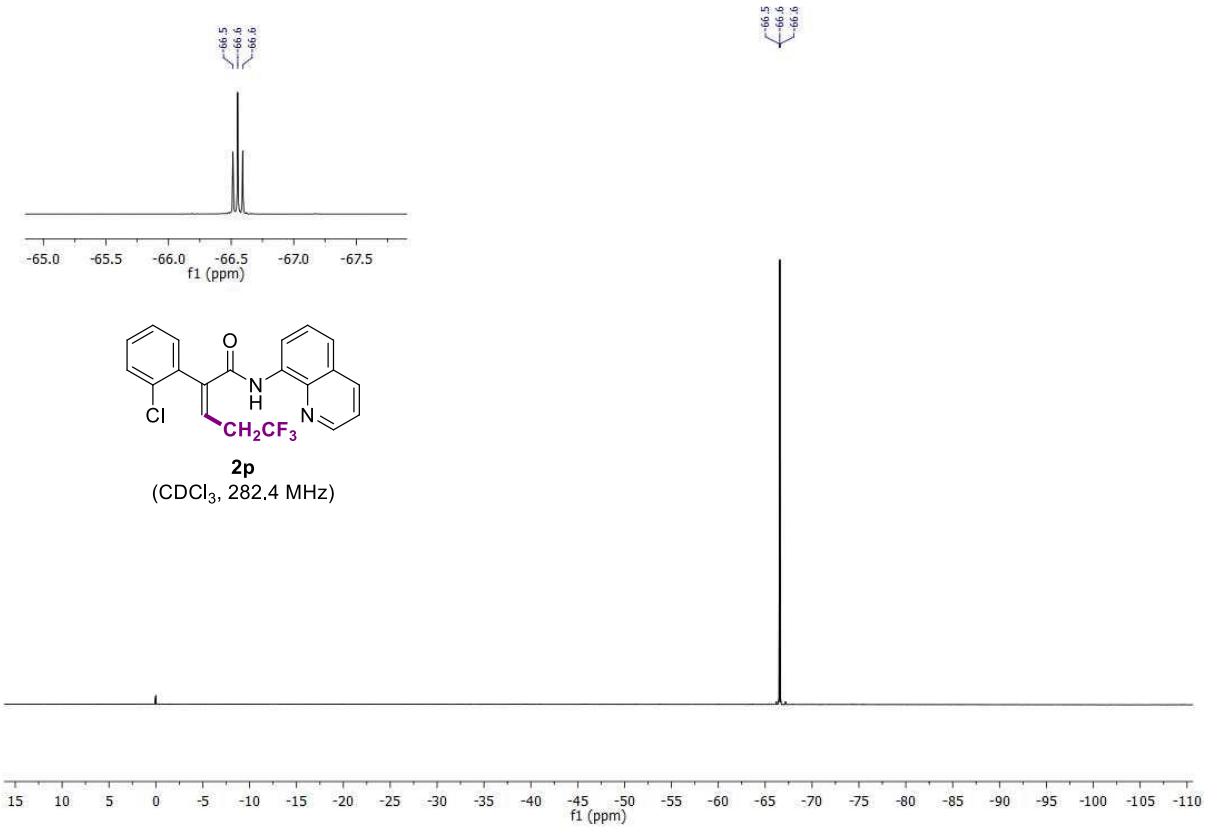


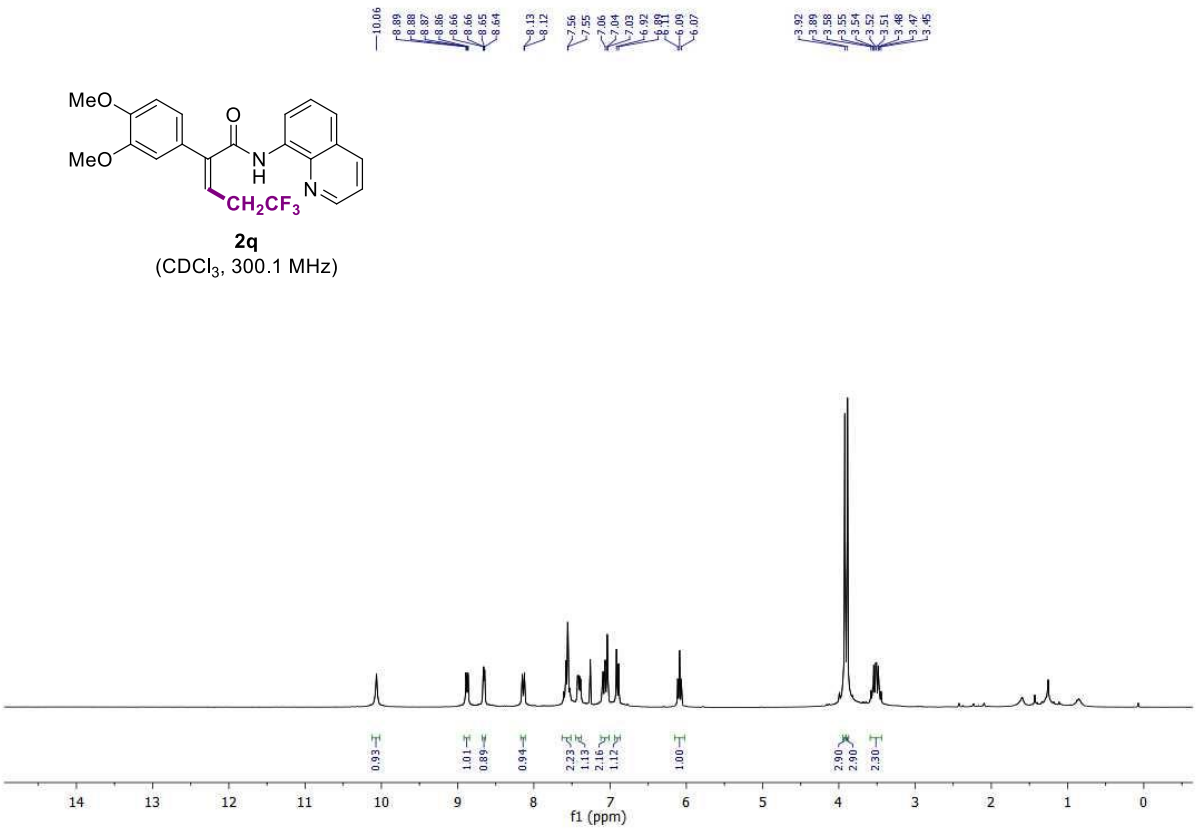
2o
($CDCl_3$, 282.4 MHz)



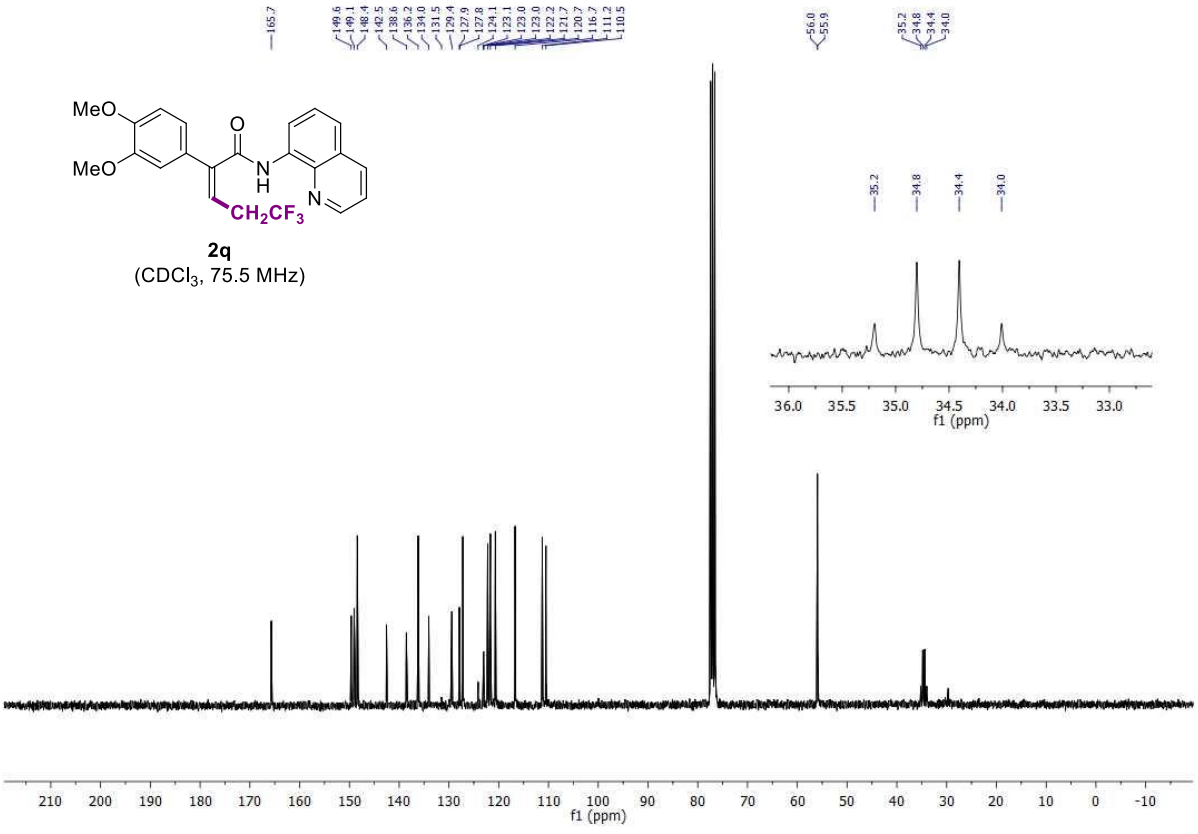
2p
($CDCl_3$, 300.1 MHz)


Cl
O
N
H
N
CH2CF3
2p
(CDCl3, 75.5 MHz)
f1 (ppm)

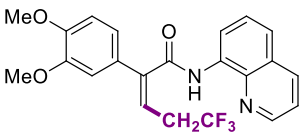

Cl
O
N
H
N
CH2CF3
2p
(CDCl3, 282.4 MHz)
f1 (ppm)



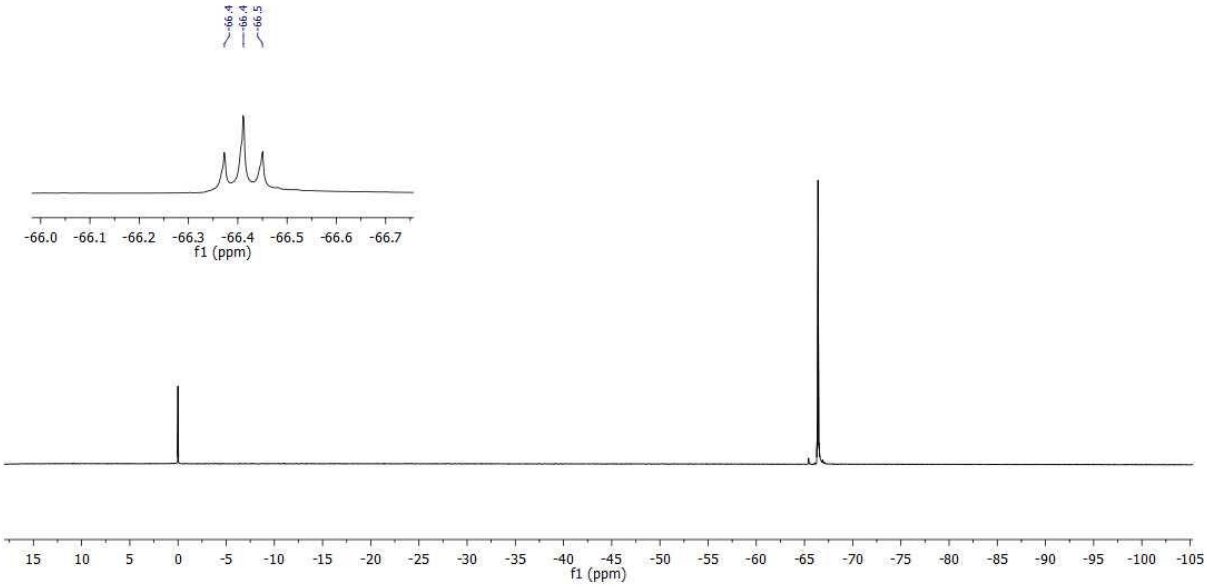
2q
($CDCl_3$, 300.1 MHz)

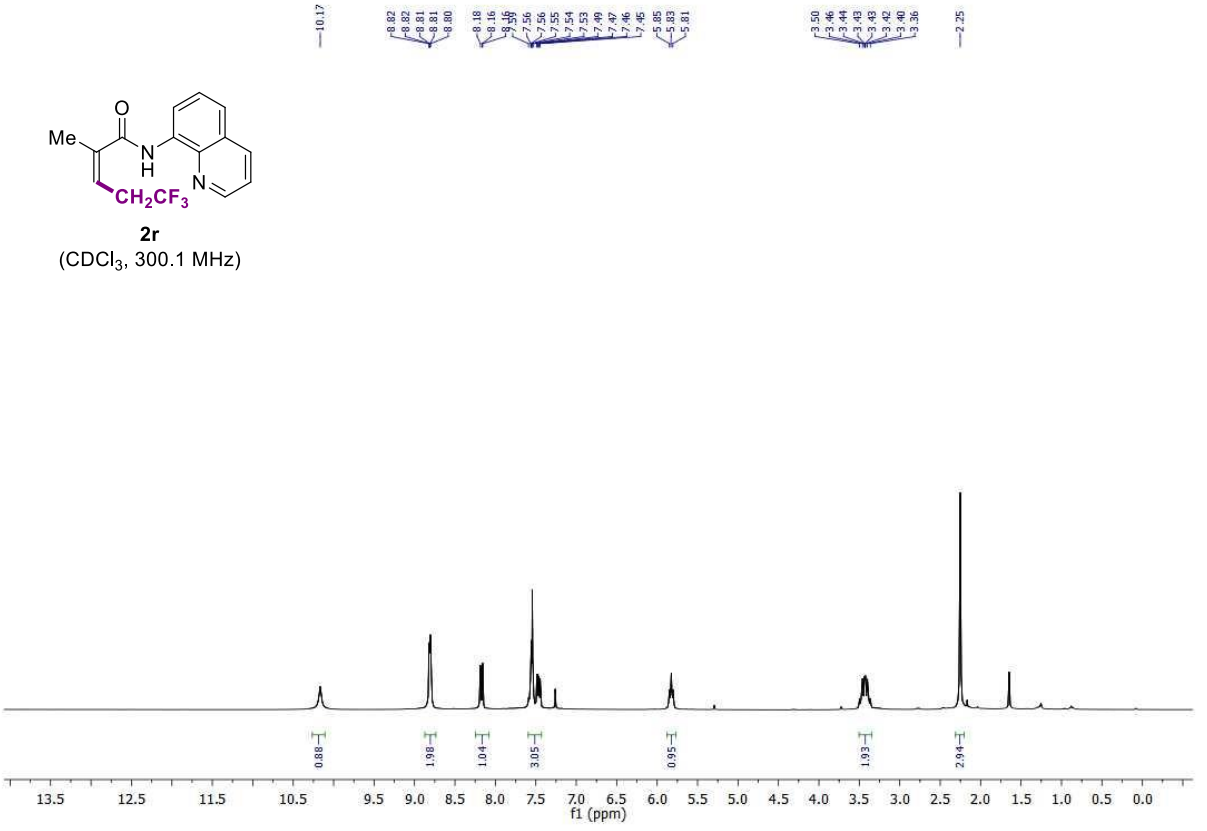


2q
($CDCl_3$, 75.5 MHz)

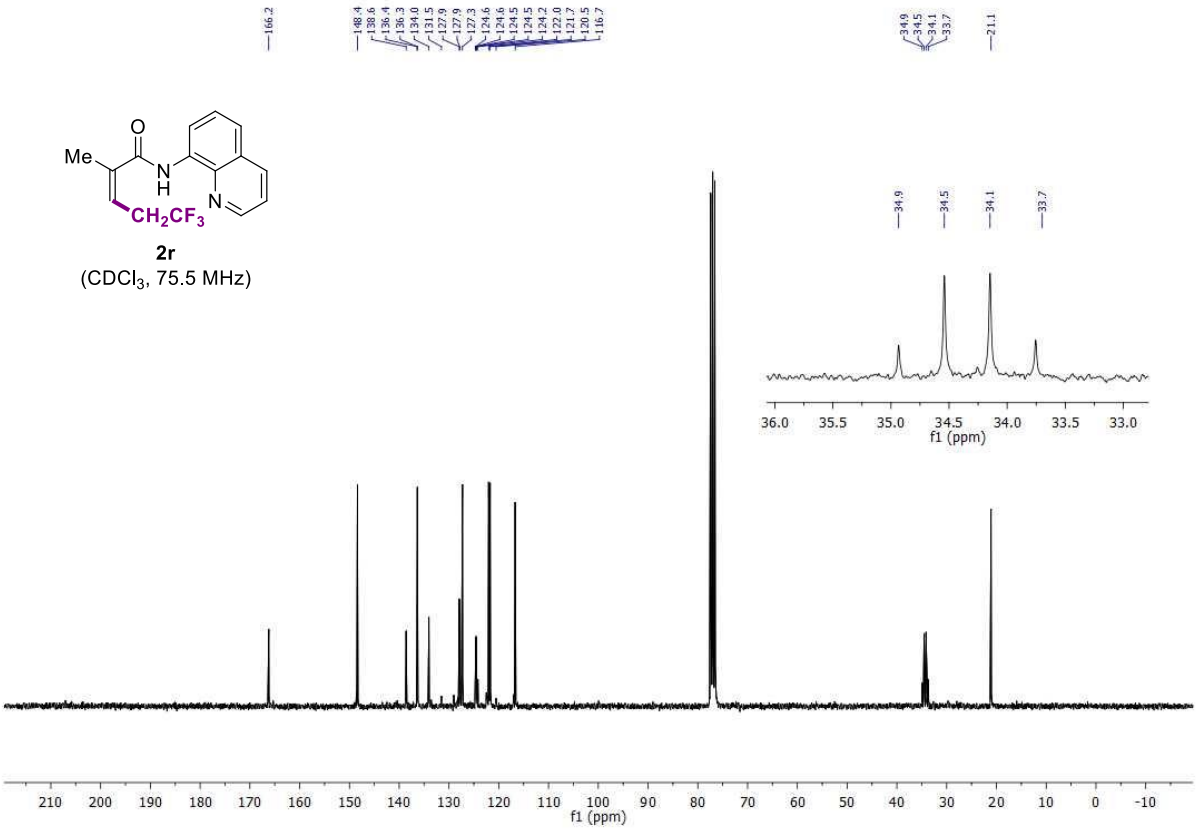


2q
($CDCl_3$, 282.4 MHz)

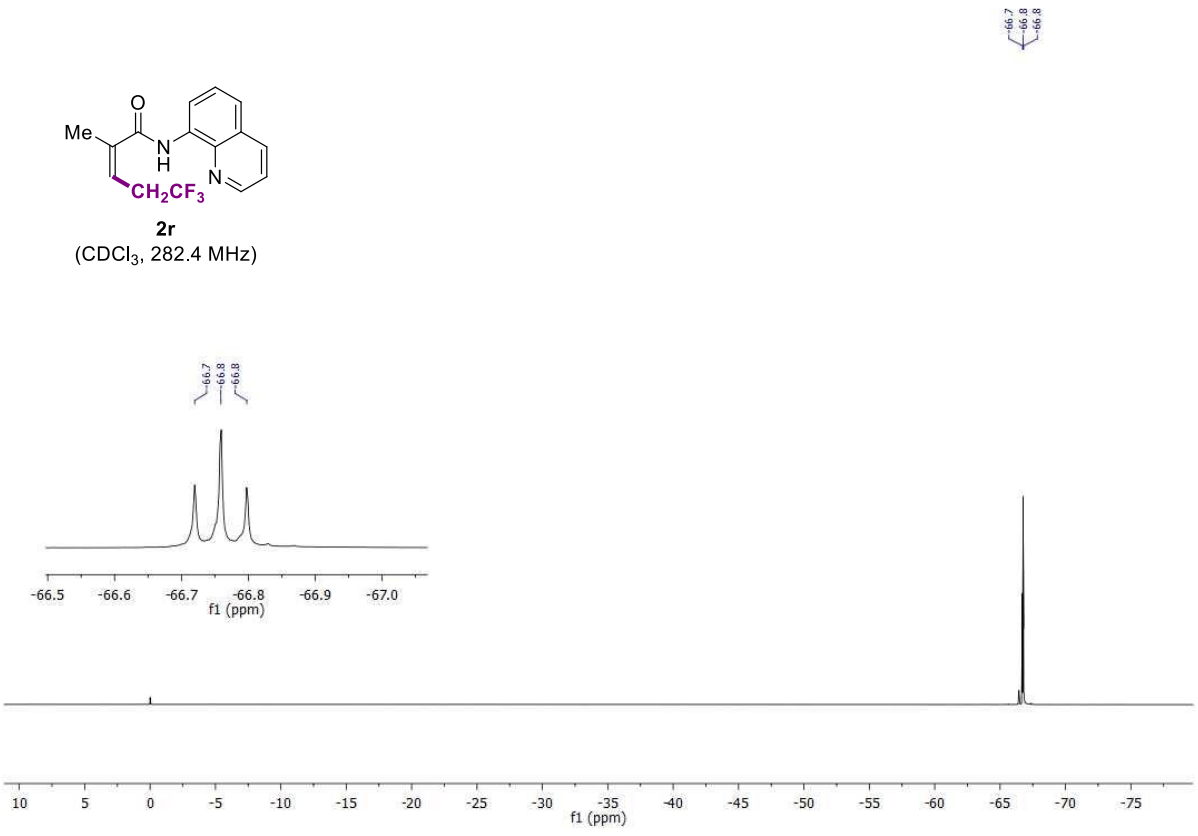




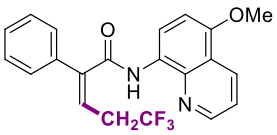
2r
($CDCl_3$, 300.1 MHz)



2r
($CDCl_3$, 75.5 MHz)

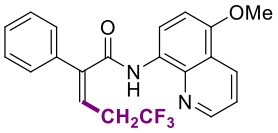


2r
($CDCl_3$, 282.4 MHz)



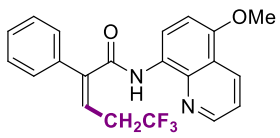
2s

($CDCl_3$, 300.1 MHz)

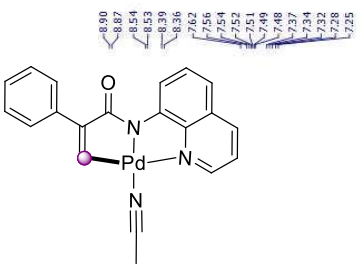


2s

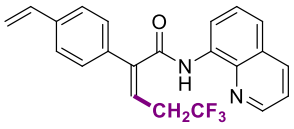
($CDCl_3$, 75.5 MHz)



2s
($CDCl_3$, 282.4 MHz)

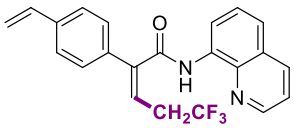


Int-1a
(CD_3CN, 300.1 MHz)



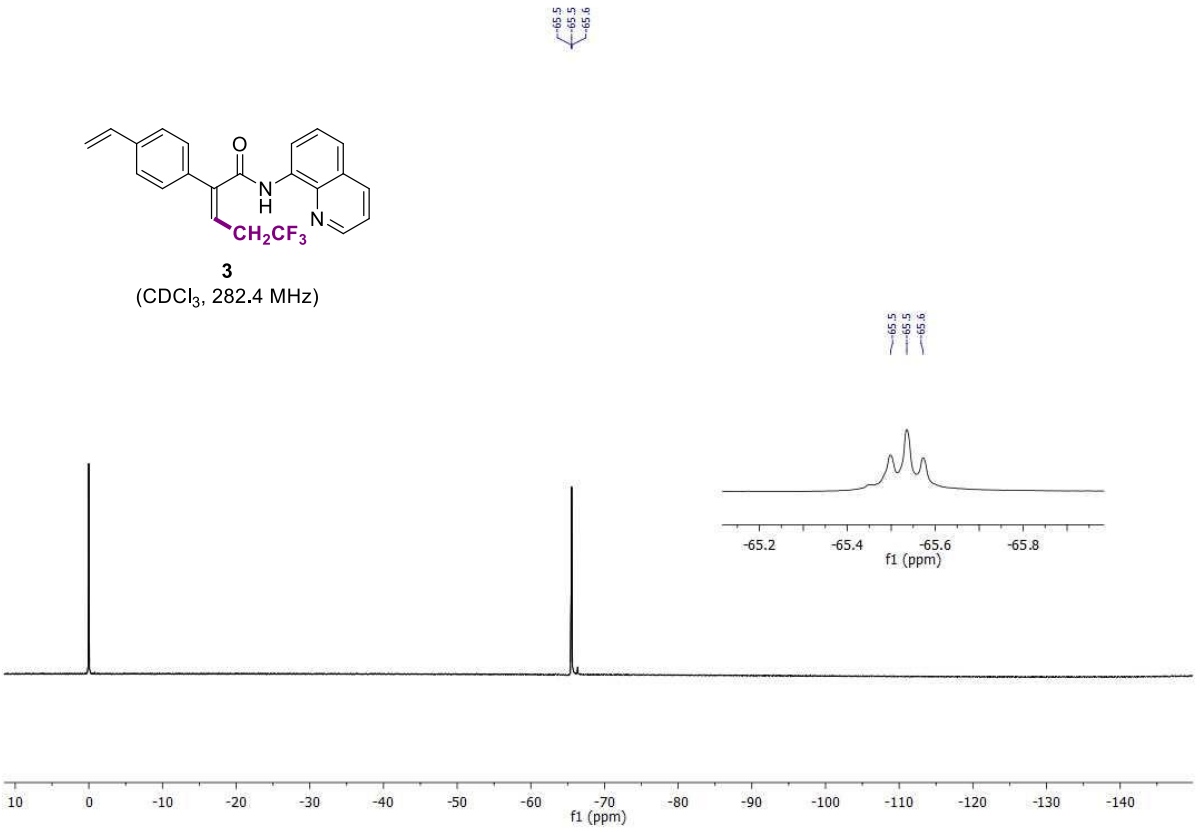
3

($CDCl_3$, 300.1 MHz)



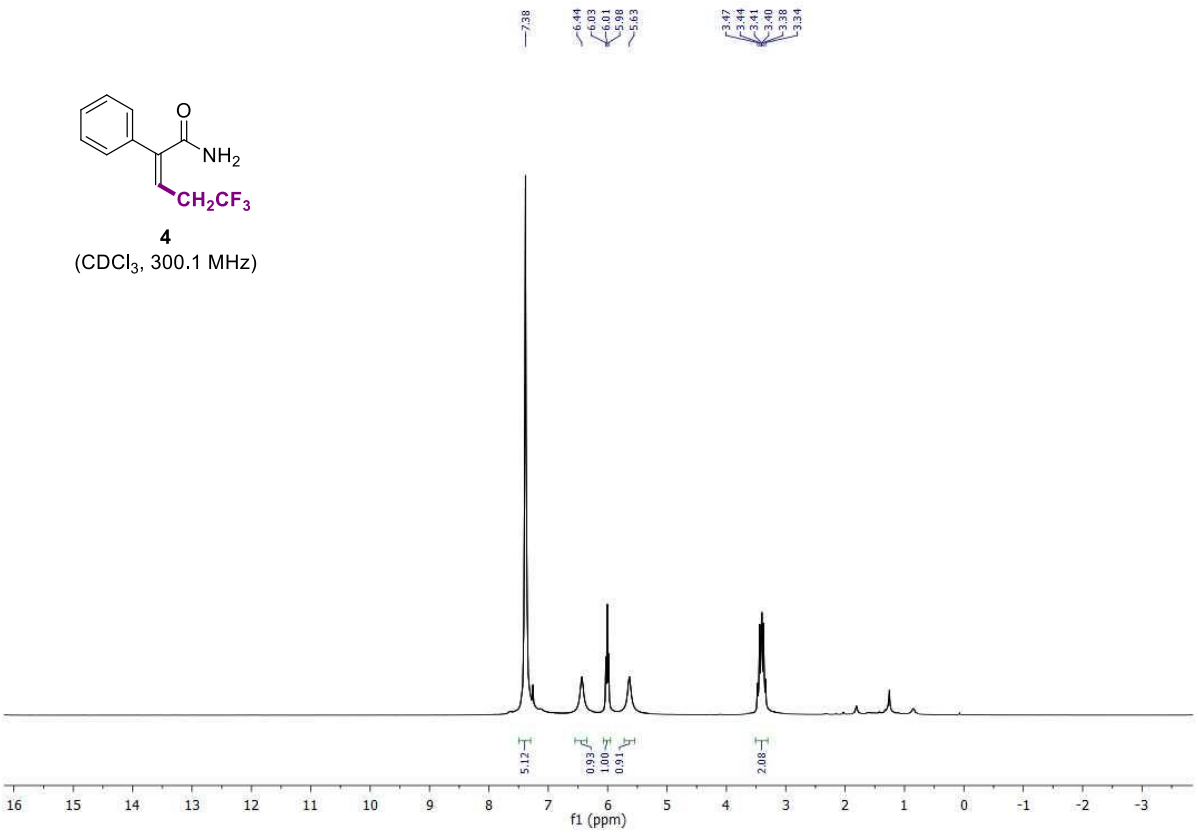
3

($CDCl_3$, 75.5 MHz)



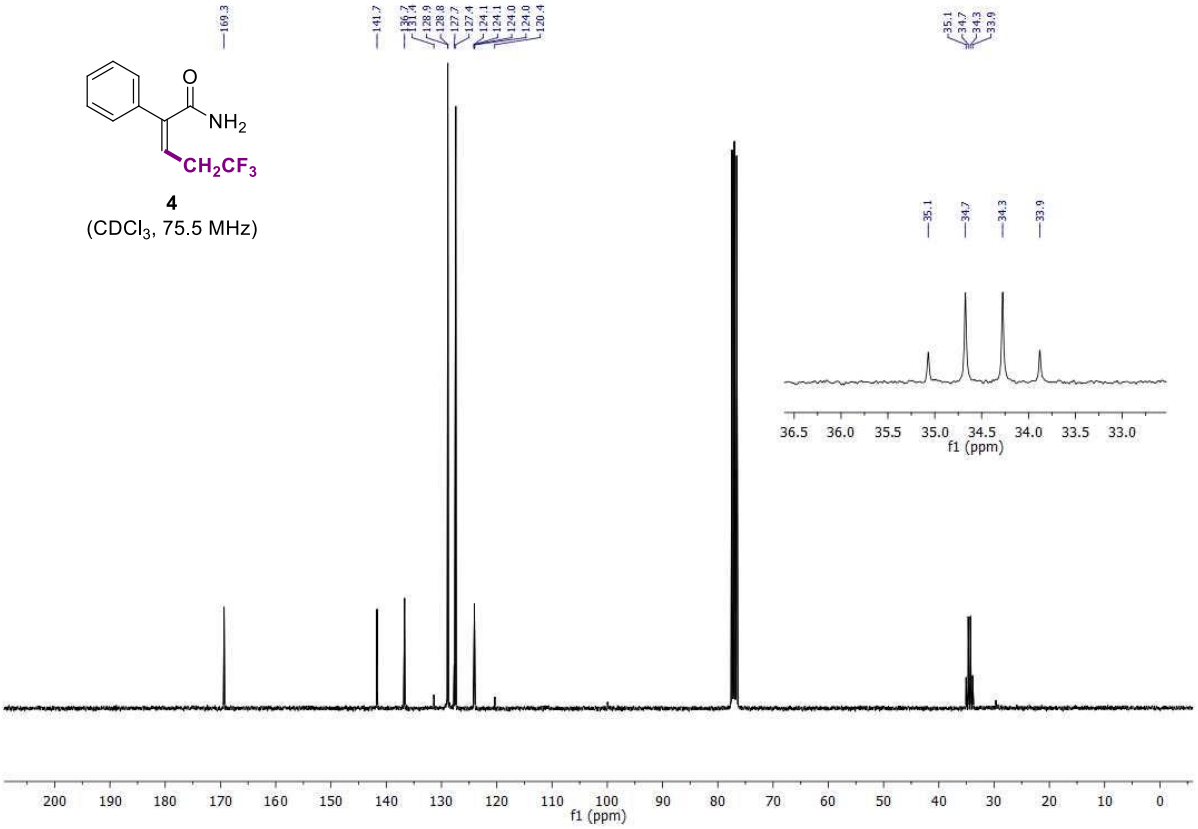
3

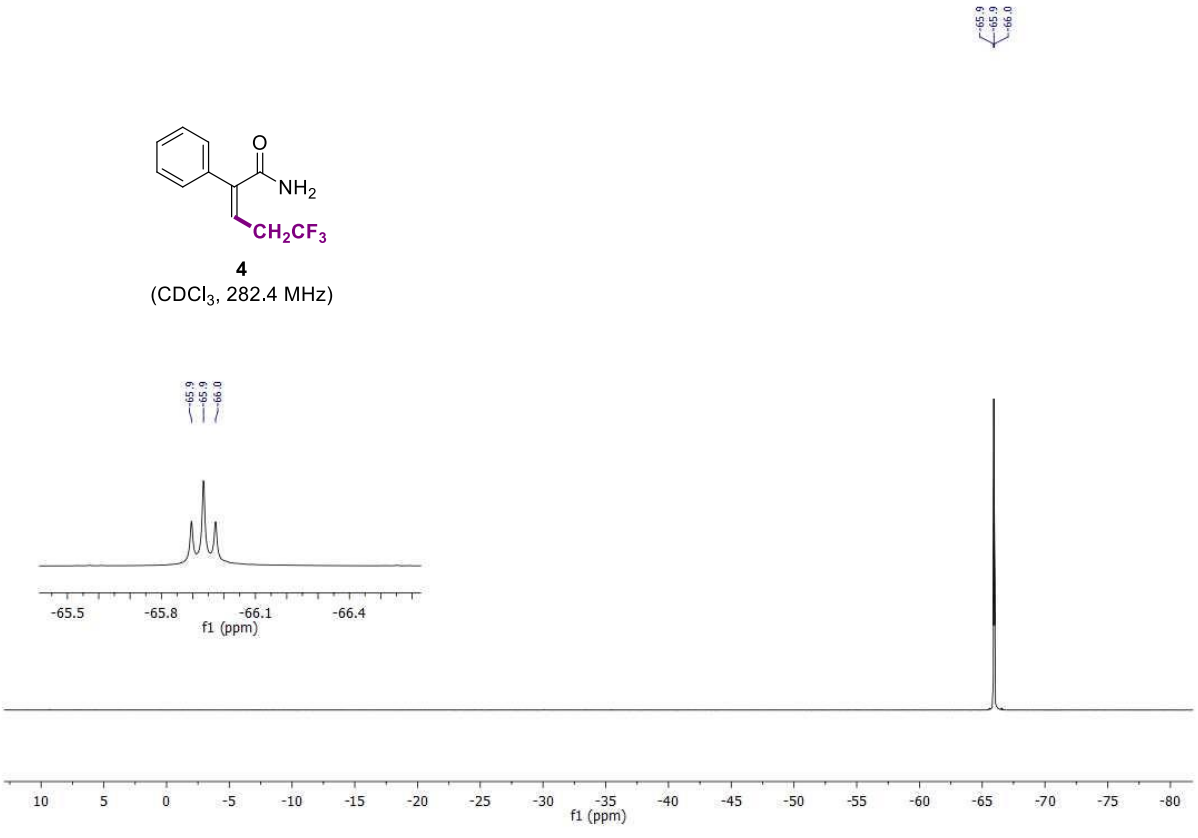
($CDCl_3$, 282.4 MHz)



4

($CDCl_3$, 300.1 MHz)


O
NH2
CH2CF3
4
(CDCl3, 75.5 MHz)
f1 (ppm)


O
NH2
CH2CF3
4
(CDCl3, 282.4 MHz)
f1 (ppm)