Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Copper(II)-Catalyzed Trifluoromethylation of *N*-Aryl Imines

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Supporting Material

A . General Information

General Procedures. All reactions were performed in oven-dried or flame-dried round-bottom flasks and vials. Stainless steel syringes and cannula were used to transfer air- and moisture-sensitive liquids. Flash chromatography was performed using silica gel 60 (230-400 mesh) from Sigma Aldrich.

Materials. Commercial reagents were purchased from Sigma Aldrich, Fluka, EM Science, and Lancaster and used as received. All solvents were used after being freshly distilled unless otherwise noted.

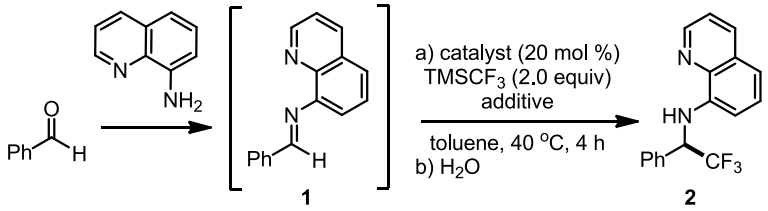
Instrumentation. Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on Bruker UltraShield-400 (400 MHz). Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to the NMR solvent residual peak ($CHCl_3$: δ 7.26). Chemical shifts for carbons are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the NMR solvent ($CDCl_3$: δ 77.0). For those complicated spin-spin splitting patterns, coupling constants were obtained by 2D J-resolve experiments. Data are represented as follows: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), coupling constants in Hertz (Hz), and integration.

The mass spectroscopic data were obtained at the Georgia State University mass spectrometry facility using a Micromass Platform II single quadrupole instrument. Infrared (IR) spectra were obtained by using a Perkin Elmer Spectrum 100 FT-IR spectrometer. Data are represented as follows: frequency of absorption (cm^{-1}).

Abbreviations used: EtOH – ethanol, EtOAc – ethyl acetate, THF – tetrahydrofuran, MeOH – methanol, Et_2O – diethyl ether, DCM – dichloromethane, TEA – triethylamine, MS – molecular sieves, TLC – thin layer chromatography.

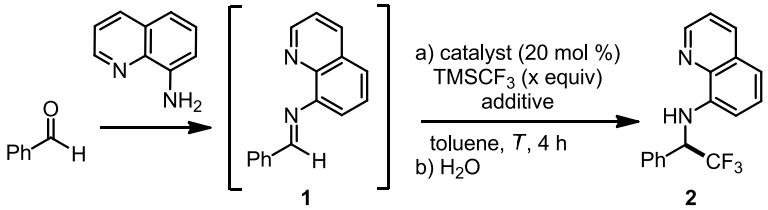
B. Catalyst Discovery for Copper(II)-Catalyzed Trifluoromethylation of *N*-Aryl Imines

Table S1. Catalyst Discovery for Trifluoromethylation of *N*-Aryl Imines



entry	catalyst	additive (equiv)	conversion	yield
1	none	KF (3.0)	<5%	NA
2	CuI	KF (3.0)	<5%	NA
3	$CuBr_2$	KF (3.0)	<5%	NA
4	CuOAc	KF (3.0)	35%	23%
5	$Cu(OAc)_2$	KF (3.0)	>95%	65%
6	$Cu(TFA)_2$	KF (3.0)	43%	24%
7	$Cu(OTf)_2$	KF (3.0)	<5%	NA
8	$CuSO_4$	KF (3.0)	<5%	NA
9	$Cu(OAc)_2$	LiOAc (1.0)	>95%	78%
10	$Cu(OAc)_2$	none	>95%	81%

Table S2. Temperature and $TMSCF_3$ Quantity Screen



entry	***T***	***x*** (equiv)	yield
1	40 °C	1.0	55%
2	40 °C	2.0	81%
3	40 °C	3.0	82%
4	RT	2.0	57%

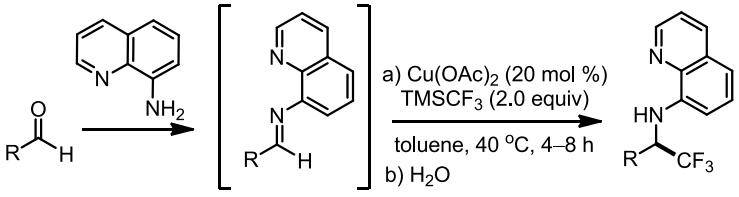
General Procedure

To a flame-dried sealable 2-dram vial equipped with a stir bar were added 43.2 mg of 8-aminoquinoline (0.3 mmol, 1.0 equiv), 37 µL of freshly distilled benzaldehyde (0.36 mmol, 1.2 equiv), 0.1 g of freshly activated molecular sieves (4 Å) and 2 mL of toluene and the mixture was stirred for 1 h at room temperature to afford the imine (note: the progress of imine formation was monitored by ^1H NMR in $CDCl_3$ (pretreated with K_2CO_3). The solution was then added to a vial that was charged with copper salts (0.06 mmol, 20 mol %) and additives (not in the case of entry

10) under argon. The mixture was stirred at room temperature for 10 minutes, and 88 μL $TMSCF_3$ (0.6 mmol, 2.0 equiv) was added. The reaction was warmed to 40 °C for 4 h and quenched with saturated aqueous $NaHCO_3$ solution. The mixture was first filtered through a short pad of celite (to remove the molecular sieves) and then extracted with EtOAc. The organic phase was concentrated and the crude product was purified by flash column chromatography.

C. Procedure for $Cu(OAc)_2$-Catalyzed *N*-Aryl Imine Trifluoromethylation

Table S3. $Cu(OAc)_2$-Catalyzed *N*-Aryl Imine Trifluoromethylation

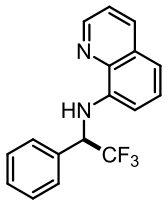


entry	R	product	yield
1	phenyl	**2**	81%
2	3-Cl-phenyl	**S1a**	70%
3	4-F-phenyl	**S2a**	71%
4	4-Cl-phenyl	**S3a**	78%
5	4-NO_2-phenyl	**S4a**	72%
6	4-Br-phenyl	**S5a**	71%
7	4-Me-phenyl	**S6a**	67%
8	4-MeO-phenyl	**S7a**	69%
9	3,4-$(Me)_2$-phenyl	**S8a**	63%
10	2-furyl	**S9a**	61%
11	3-pyridyl	**S10a**	72%
12	2-pyridyl	**S11a**	61%
13	cyclohexyl	**S12a**	62%
14	*iso*-butyl	**S13a**	47%
15	cinnamyl	**S14a**	53%

General Procedure

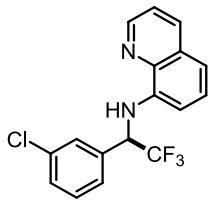
To a flame-dried sealable 2-dram vial equipped with a stir bar were added 43.2 mg of 8-aminoquinoline (0.3 mmol, 1.0 equiv), 37 μL of freshly distilled aldehyde (0.36 mmol, 1.2 equiv), 0.1 g of freshly activated molecular sieves (4 Å) and 2 mL of toluene and the mixture was stirred for 1–12 h at room temperature to afford the imine (note: the progress of imine formation was monitored by ^1H NMR in $CDCl_3$ (pretreated with K_2CO_3). The solution was then added to a vial that was charged with $Cu(OAc)_2$ (0.06 mmol, 10.9 mg, 20 mol %) under argon. The mixture was

stirred at room temperature for 10 minutes, and 88 μL $TMSCF_3$ (0.6 mmol, 2.0 equiv) was added. The reaction was warmed to 40 ^oC for 4 h (monitoring by TLC until all the 8-aminoquinoline disappears). Then it was quenched with saturated aqueous $NaHCO_3$ solution. The mixture was first filtered through a short pad of celite (to remove the molecular sieves) and then extracted with EtOAc. The organic phase was concentrated and the crude product was purified by flash column chromatography.



2

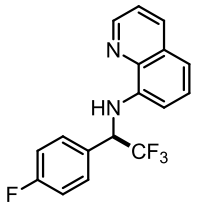
***N*-(2,2,2-trifluoro-1-phenylethyl)quinolin-8-amine** (**2**) : ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.80 (d, J = 2.8 Hz, 1H), 8.07 (d, J = 8.1 Hz, 1H), 7.59 (d, J = 6.5 Hz, 2H), 7.46-7.35 (m, 4H), 7.31 (t, J = 7.9 Hz, 1H), 7.15 (t, J = 7.1 Hz, 2H), 6.65 (d, J = 7.6 Hz, 1H), 5.17-5.13 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 147.47, 142.26, 138.26, 135.99, 133.96, 129.06, 128.83, 128.49, 128.04, 127.26, 125.19 (q, J = 281 Hz), 121.65, 116.00, 106.20, 60.13 (q, J = 30 Hz). ^{19}F NMR (377 MHz, $CDCl_3$, ppm): δ -73.82 (d, J = 7.2 Hz). IR ν_{max} (neat)/cm^{-1}: 3362, 2940, 1594, 1520, 1467, 1204, 1148, 1067, 818,702. HRMS (ESI, m/z): calcd for $C_{17}H_{14}F_3N_2^+$ [M+H^+]: 303.1109; Found: 301.1114.



S1a

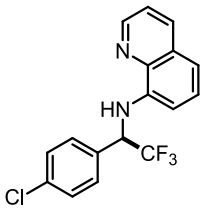
***N*-(1-(3-chlorophenyl)-2,2,2-trifluoroethyl)quinolin-8-amine** (**S1a**) : ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.80 (d, J = 2.0 Hz, 1H), 8.08 (d, J = 8.0 Hz, 1H), 7.58 (s, 1H), 7.51-7.39 (m, 2H), 7.39-7.24 (m, 3H), 7.14 (dd, J = 13.3 Hz, 7.8 Hz, 2H), 6.58 (d, J = 7.2 Hz, 1H), 5.12-5.09 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 147.60, 141.90, 138.21, 136.04, 134.84, 130.12, 129.39, 128.50, 128.28,

127.19, 126.23, 124.8 (q, J = 281 Hz), 121.77, 116.37, 106.22, 59.83 (q, J = 30 Hz). ^{19}F NMR (377 MHz, $CDCl_3$, ppm): δ -73.75 (d, J = 7.1 Hz). IR ν_{max} (neat)/cm^{-1}: 3358, 3006, 1578, 1520, 1275, 1260, 1175, 1126, 765, 744. HRMS (ESI, m/z): calcd for $C_{17}H_{13}ClF_3N_2^+$ [M+H$^+$]: 337.0719; Found: 337.0724.



S2a

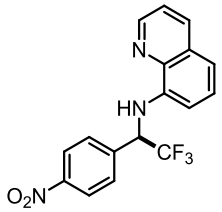
***N*-(2,2,2-trifluoro-1-(4-fluorophenyl)ethyl)quinolin-8-amine** (**S2a**) : ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.80 (s, 1H), 8.08 (d, J = 8.0 Hz, 1H), 7.56-7.53 (m, 2H), 7.43-7.41 (m, 1H), 7.29 (t, J = 7.7 Hz, 1H), 7.16-7.06 (m, 4H), 6.58 (d, J = 7.5 Hz, 1H), 5.15-5.08 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 164.37, 161.91, 147.56, 142.07, 138.28, 136.04, 129.85, 129.77, 128.53, 127.21, 124.0 (q, J = 280 Hz), 121.74, 116.23, 116.00, 115.78, 106.28, 59.61 (q, J = 30 Hz). ^{19}F NMR (377 MHz, $CDCl_3$, ppm) δ -74.11 (d, J = 7.1 Hz), -112.58 (t, J = 4.5 Hz). IR ν_{max} (neat)/cm^{-1}: 3345, 2989, 1578, 1510, 1275, 1260, 1173, 1124, 768, 743. HRMS (ESI, m/z): calcd for $C_{17}H_{13}F_4N_2^+$ [M+H$^+$]:321.1051; Found: 321.1013.



S3a

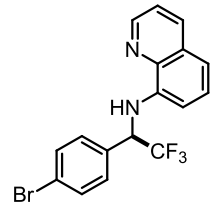
***N*-(1-(4-chlorophenyl)-2,2,2-trifluoroethyl)quinolin-8-amine** (**S3a**) : ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.79 (d, J = 3.2 Hz, 1H), 8.08 (d, J = 8.0 Hz, 1H), 7.51 (d, J = 8.4 Hz, 2H), 7.42 (dd, J = 8.2 Hz, 4.2 Hz, 1H), 7.37 (d, J = 8.4 Hz, 2H), 7.29 (t, J = 8.0 Hz, 1H), 7.15 (d, J = 8.4 Hz, 1H), 7.12 (d, J = 7.6 Hz, 1H), 6.57 (d, J = 7.6 Hz, 1H), 5.13-5.08 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 147.58, 141.93, 138.23, 136.06, 135.11, 132.48, 129.41, 129.10, 128.50, 127.18, 124.9 (q, J = 280 Hz), 121.76, 116.32, 106.30, 59.68 (q, J = 30.0 Hz). ^{19}F NMR (377 MHz, $CDCl_3$, , ppm) δ -73.95 (d,

J = 7.1 Hz). IR ν_{max} (neat)/cm^{-1}: 3356, 2892, 1521, 1251, 1172, 1126, 817, 764, 748. HRMS (ESI, m/z): calcd for $C_{17}H_{13}ClF_3N_2^+$ [M+H^+]: 337.0719; Found: 337.0715.



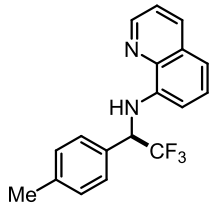
S4a

***N*-(2,2,2-trifluoro-1-(4-nitrophenyl)ethyl)quinolin-8-amine** (**S4a**) : ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.77 (d, *J* = 2.0 Hz, 1H), 8.21 (d, *J* = 8.8 Hz, 2H), 8.06 (d, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.41 (dd, *J* = 7.9 Hz, 4.0 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 1H), 7.15 (t, *J* = 8.4 Hz, 2H), 6.47 (d, *J* = 7.2 Hz, 1H), 5.23-5.18 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 147.78, 141.50, 141.09, 138.20, 136.13, 129.19, 128.53, 127.07, 124.5 (q, *J* = 280 Hz), 124.03, 121.93, 116.85, 106.35, 59.89 (q, *J* = 31 Hz). ^{19}F NMR (377 MHz, $CDCl_3$, ppm) δ -73.48 (d, *J* = 6.8 Hz). IR ν_{max} (neat)/cm^{-1}: 3362, 2990, 1578, 1521, 1347, 1275, 1260, 1127, 767, 745. HRMS (ESI, m/z): calcd for $C_{17}H_{13}F_3N_3O_2^+$ [M+H^+]: 348.0960; Found: 348.0955.



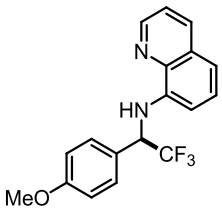
S5a

***N*-(1-(4-bromophenyl)-2,2,2-trifluoroethyl)quinolin-8-amine** (**S5a**) : ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.79 (d, *J* = 2.8 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.46-7.40 (m, 3H), 7.29 (t, *J* = 8.0 Hz, 1H), 7.13 (dd, *J* = 15.6 Hz, 7.8 Hz, 2H), 6.57 (d, *J* = 7.6 Hz, 1H), 5.13-5.06 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 147.58, 141.93, 138.24, 136.05, 133.02, 132.06, 129.72, 128.50, 127.18, 124.8 (q, *J* = 280 Hz), 123.29, 121.76, 116.34, 106.31, 59.77 (q, *J* = 30 Hz). ^{19}F NMR (377 MHz, $CDCl_3$, ppm) δ -73.92 (d, *J* = 7.0 Hz). IR ν_{max} (neat)/cm^{-1}: 3351, 3005, 1520, 1479, 1275, 1260, 1126, 756, 743. HRMS (ESI, m/z): calcd for $C_{17}H_{13}BrF_3N_2^+$ [M+H^+]: 381.0214; Found: 381.0216.



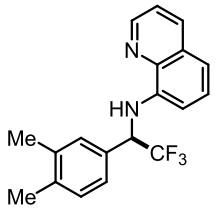
S6a

***N*-(2,2,2-trifluoro-1-p-tolylethyl)quinolin-8-amine** (**S6a**) : ^{1}HNMR (400 MHz, $CDCl_3$, ppm) δ 8.78 (d, J = 3.2 Hz, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.45 (d, J = 8.0 Hz, 2H), 7.40 (dd, J = 8.2 Hz, 4.2 Hz, 1H), 7.30 (t, J = 8.0 Hz, 1H), 7.20 (d, J = 8.0 Hz, 2H), 7.14-7.09 (m, 2H), 6.64 (d, J = 7.6 Hz, 1H), 5.11-5.07 (m, 1H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 147.43, 142.34, 138.95, 138.27, 135.98, 130.95, 129.53, 128.49, 127.90, 127.28, 125.2 (q, J = 280 Hz), 121.63, 115.90, 106.19, 59.74 (q, J = 30.0 Hz), 21.16. ^{19}F NMR (377 MHz, $CDCl_3$, ppm) δ -73.96 (d, J = 7.2 Hz). IR ν_{max} (neat)/cm^{-1}: 3335, 2923, 1578, 1521, 1253, 1170, 1124, 818, 790. HRMS (ESI, m/z): calcd for $C_{18}H_{16}F_3N_2^+$ [M+H$^+$]: 3171266; Found: 317.1267.



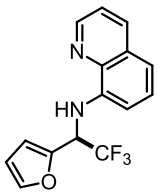
S7a

***N*-(2,2,2-trifluoro-1-(4-methoxyphenyl)ethyl)quinolin-8-amine** (**S7a**) : ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.78 (d, J = 2.8 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 7.48 (d, J = 8.0 Hz, 2H), 7.40 (dd, J = 8.1 Hz, 4.1 Hz, 1H), 7.30 (t, J = 7.6 Hz, 1H), 7.13 (d, J = 8.0 Hz, 1H), 7.08 (d, J = 7.2 Hz, 1H), 6.92 (d, J = 8.8 Hz, 2H), 6.64 (d, J = 7.2 Hz, 1H), 5.11-5.04 (m, 1H), 3.80 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 160.12, 147.44, 142.35, 138.29, 135.99, 129.20, 128.50, 127.28, 125.91, 125.2 (q, J = 280 Hz), 121.63, 115.91, 114.25, 106.25, 59.61 (q, J = 30 Hz), 55.25. ^{19}F NMR (377 MHz, $CDCl_3$, ppm) δ -74.15 (d, J = 7.1 Hz). IR ν_{max} (neat)/cm^{-1}: 3339, 3006, 1614, 1513, 1275, 1260, 1123, 760, 741. HRMS (ESI, m/z): calcd for $C_{18}H_{16}F_3N_2O^+$ [M+H$^+$]: 333.1215; Found: 333.1216.



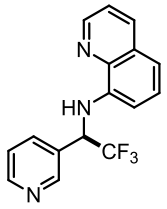
S8a

***N*-(1-(3,4-dimethylphenyl)-2,2,2-trifluoroethyl)quinolin-8-amine** (**S8a**): ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.79-8.78 (m, 1H), 8.07 (d, J = 8.4 Hz, 1H), 7.40 (dd, J = 8.2 Hz, 4.2 Hz, 1H), 7.32-7.28 (m, 3H), 7.14 (t, J = 9.6 Hz, 2H), 7.07 (d, J = 7.2 Hz, 1H), 6.67 (d, J = 7.6 Hz, 1H), 5.07-5.02 (m, 1H), 2.27 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 147.42, 142.50, 138.31, 137.64, 137.14, 135.99, 131.39, 130.07, 129.18, 128.52, 127.34, 125.39, 125.3 (q, J = 280 Hz), 121.63, 115.84, 106.16, 59.96 (q, J = 31 Hz), 19.86, 19.52. ^{19}F NMR (377 MHz, $CDCl_3$, ppm) δ -73.87 (d, J = 7.2 Hz). IR ν_{max} (neat)/cm^{-1}: 3341, 2989, 1578, 1520, 1275, 1260, 1123, 763, 751. HRMS (ESI, m/z): calcd for $C_{19}H_{18}F_3N_2^+$ [M+H$^+$]: 331.1422; Found: 331.1410.



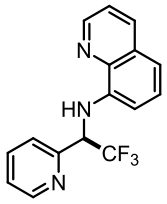
S9a

***N*-(2,2,2-trifluoro-1-(furan-2-yl)ethyl)quinolin-8-amine** (**S9a**) : ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.78 (d, J = 3.2 Hz, 1H), 8.08 (d, J = 8.0 Hz, 1H), 7.47 (s, 1H), 7.46-7.38 (m, 2H), 7.19 (d, J = 8.0 Hz, 1H), 7.01 (d, J = 8.8 Hz, 1H), 6.84 (d, J = 7.6 Hz, 1H), 6.55 (d, J = 3.2 Hz, 1H), 6.40 (s, 1H), 5.36-5.29 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 147.55, 143.33, 142.22, 138.29, 136.00, 128.59, 127.24, 124.50 (q, J = 281 Hz), 121.68, 116.42, 110.62, 109.49, 106.02, 54.46 (q, J = 32 Hz). ^{19}F NMR (377 MHz, $CDCl_3$, ppm) δ -74.27 (d, J = 6.6 Hz). IR ν_{max} (neat)/cm^{-1}: 3348, 2989, 1579, 1520, 1280, 1275, 1151, 770, 759. HRMS (ESI, m/z): calcd for $C_{15}H_{12}F_3N_2^+$ [M+H$^+$]: 293.0902; Found: 293.0906.



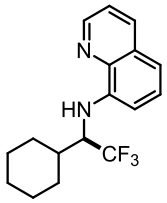
S10a

***N*-(2,2,2-trifluoro-1-(pyridin-3-yl)ethyl)quinolin-8-amine** (**S10a**) : ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.81-8.79 (m, 2H), 8.63 (s, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.91 (d, J = 7.6 Hz, 1H), 7.42 (dd, J = 7.8 Hz, 3.9 Hz, 1H), 7.32-7.26 (m, 2H), 7.17-7.13 (m, 2H), 6.61 (d, J = 7.2 Hz, 1H), 5.21-5.18 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 150.50, 149.81, 147.67, 141.74, 138.27, 136.08, 135.31, 129.97, 128.55, 127.17, 124.8 (q, J = 280 Hz), 123.80, 121.83, 116.63, 106.37, 58.31 (q, J = 31 Hz). ^{19}F NMR (377 MHz, $CDCl_3$, ppm) δ -73.90 (d, J = 6.9 Hz). IR ν_{max} (neat)/cm^{-1}: 3341, 3006, 1579, 1521, 1275, 1260, 1127, 756, 741. HRMS (ESI, m/z): calcd for $C_{16}H_{13}F_3N_3^+$ [M+H$^+$]: 304.1062; Found: 304.1051.



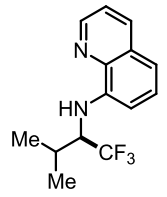
S11a

***N*-(2,2,2-trifluoro-1-(pyridin-2-yl)ethyl)quinolin-8-amine** (**S11a**) : ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.82 (s, 1H), 8.73 (d, J = 2.0 Hz, 1H), 8.06 (d, J = 8.0 Hz, 1H), 7.76 (d, J = 7.2 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H), 7.53 (d, J = 7.6 Hz, 1H), 7.41-7.29 (m, 3H), 7.15 (d, J = 8.0 Hz, 1H), 6.81 (d, J = 7.2 Hz, 1H), 5.33-5.29 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 153.06, 149.70, 147.58, 142.66, 138.44, 136.85, 135.92, 128.62, 127.30, 125.2 (q, J = 282 Hz), 123.85, 123.06, 121.62, 116.01, 106.17, 60.74 (q, J = 30 Hz). ^{19}F NMR (377 MHz, $CDCl_3$, ppm) δ -73.28 (d, J = 6.7 Hz). IR ν_{max} (neat)/cm^{-1}: 3363, 3006, 1579, 1514, 1275, 1260, 1121, 765, 746. HRMS (ESI, m/z): calcd for $C_{16}H_{13}F_3N_3^+$ [M+H$^+$]: 304.1062; Found: 304.1065.



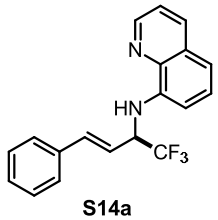
S12a

***N*-(1-cyclohexyl-2,2,2-trifluoroethyl)quinolin-8-amine** (**S12a**) : ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.78 (dd, J = 4.4, 2.0 Hz, 1H), 8.10 (d, J = 4.4 Hz, 2.0 Hz, 1H), 7.43-7.28 (m, 2H), 7.14 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 6.80 (d, J = 3.6 Hz, 1H), 6.60 (d, J = 6.0 Hz, 1H), 4.00-3.95 (m, 1H), 2.17-2.02 (m, 2H), 1.84-1.68 (m, 4H), 1.38-1.29 (m, 4H), 1.20-1.17 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 147.24, 144.01, 138.08, 136.02, 130.68, 128.70, 127.85, 127.47, 125.02, 122.19, 121.57, 115.10, 105.29, 59.72 (q, J = 28 Hz), 38.67, 30.38, 27.44, 26.16, 25.98, 25.92. ^{19}F NMR (377 MHz, $CDCl_3$, ppm): δ -71.57 (d, J = 8.0 Hz). IR ν_{max} (neat)/cm^{-1}: 3388, 3006, 1579, 1521, 1275, 1260, 1127, 756, 741. HRMS (ESI, m/z): calcd for $C_{17}H_{20}F_3N_2^+$ [M+H$^+$]: 309.1579; Found: 309. 1569.



S13a

***N*-(1,1,1-trifluoro-3-methylbutan-2-yl)quinolin-8-amine** (**S13a**) : ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.77 (d, J = 3.2 Hz, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.43-7.39 (m, 2H), 7.15 (d, J = 8.4 Hz, 1H), 6.82 (d, J = 7.6 Hz, 1H), 6.60 (d, J = 9.2 Hz, 1H) 4.03-3.94 (m, 1H), 2.43-2.35 (m, 1H), 1.20 (d, J = 6.8 Hz, 3H), 1.11 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 147.25, 144.04, 138.12, 136.01, 130.67, 128.67, 127.46, 126.43(q, J = 283 Hz), 121.58, 115.21, 105.43, 59.83 (q, J = 28 Hz), 28.73, 20.34, 17.19. ^{19}F NMR (377 MHz, $CDCl_3$, ppm): δ -72.16 (d, J = 7.8 Hz). IR ν_{max} (neat)/cm^{-1}: 3372, 3006, 1579, 1521, 1275, 1260, 1127, 756, 741. HRMS (ESI, m/z): calcd for $C_{14}H_{16}F_3N_2^+$ [M+H$^+$]: 269.1266; Found: 269.1260.

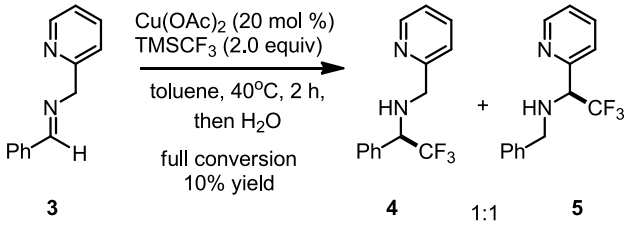


S14a

(*E*)-*N*-(1,1,1-trifluoro-4-phenylbut-3-en-2-yl)quinolin-8-amine (**S14a**): ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.81 (d, J = 2.0 Hz, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.46-7.42 (m, 4H), 7.37-7.28 (m, 3H), 7.21 (d, J = 8.0 Hz, 1H), 6.92 (d, J = 16 Hz, 1H), 6.88 (d, J = 8.0 Hz, 1H), 6.78 (d, J = 8.0 Hz, 1H), 6.37 (dd, J = 16 Hz, 6.4, Hz, 1H), 4.92-4.83 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 147.40, 142.46, 138.20, 136.04, 135.60, 135.44, 129.58, 128.60, 128.41, 127.34, 126.78, 123.96, 121.65, 120.57, 116.00, 105.94, 57.82 (q, J = 31 Hz). ^{19}F NMR (377 MHz, $CDCl_3$, ppm): δ -74.85 (d, J = 6.9 Hz). IR ν_{max} (neat)/cm^{-1}: 3362, 2940, 1594, 1520, 1467, 1204, 1148, 1067, 818, 702. HRMS (ESI, m/z): calcd for $C_{19}H_{16}F_3N_2$ [M+H$^+$]: 329.1266; Found: 329.1262.

D. Control Experiments for Mechanistic Studies

Scheme S1. Imine Trifluoromethylation with a Picolylamine-Derived Imine

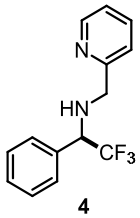


3 **4** 1:1 **5**

a. Procedure for Imine Trifluoromethylation with a Picolylamine-Derived Imine

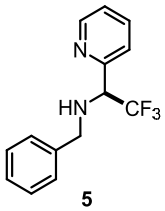
To a flame-dried sealable 2-dram vial equipped with a stir bar were added 33 mg of picolylamine (0.3 mmol, 1.0 equiv), 37 µL of freshly distilled benzaldehyde (0.36 mmol, 1.2 equiv), 0.1 g of activated 4 Å molecular sieves and 2 mL of toluene and the mixture was stirred for 1 h at room temperature to afford imines *in situ*. The imine solution was added to a vial which was charged with 11 mg of $Cu(OAc)_2$ (0.06 mmol, 20 mol%) under argon, and then 88 µL of $TMSCF_3$ (0.6 mmol, 2.0 equiv) was added. The reaction mixture was stirred at 40 ^{o}C for 2 h (monitoring by TLC, until the imine disappears). Then the reaction was quenched with saturated aqueous $NaHCO_3$ solution. The mixture was first filtered through a short pad of celite (to remove the molecular sieves) and then

extracted with EtOAc. The organic phase was concentrated and the crude product was purified by flash column chromatography to afford **4** and **5**.



4

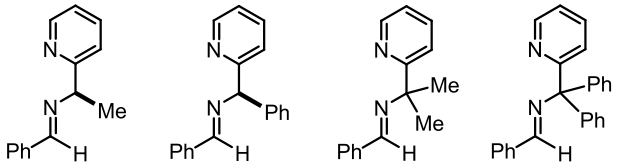
2,2,2-Trifluoro-1-phenyl-*N*-(pyridin-2-ylmethyl)ethanamine (**4**) : ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.55 (d, J = 4.8 Hz, 1H), 7.63 (t, J = 7.6 Hz, 1H), 7.42-7.38 (m, 5H), 7.22-7.16 (m, 2H), 4.19 (q, J = 7.2 Hz, 1H), 3.86 (AB, J = 14.4 Hz, 2H), 3.13 (br, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 158.36, 149.36, 136.52, 134.02, 129.04, 128.73, 128.68, 126.79, 123.99, 122.35, 122.22, 64.11 (q, J = 29 Hz), 52.39. ^{19}F NMR (377 MHz, $CDCl_3$, ppm): δ -73.21 (d, J = 7.4 Hz). IR ν_{max} (neat)/cm^{-1}: 3383, 2955, 1577, 1521, 1482, 1267, 1194, 1086, 816, 742. HRMS (ESI, m/z): calcd for $C_{14}H_{14}F_3N_2^+$ [M+H$^+$]: 267.1109; Found: 267.1111.



5

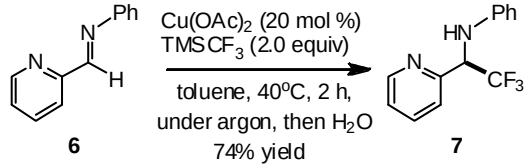
***N*-benzyl-2,2,2-trifluoro-1-(pyridin-2-yl)ethanamine** (**5**) : ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.67 (d, J = 4.4 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H), 7.34-7.25 (m, 7H), 4.24 (q, J = 7.2 Hz, 1H), 3.80 (AB, J = 13.2 Hz, 2H), 3.00 (br, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 153.57, 149.58, 138.97, 136.55, 129.26, 128.40, 128.15, 127.21, 126.46, 124.21, 123.64, 63.64 (q, J = 28 Hz), 51.46. ^{19}F NMR (377 MHz, $CDCl_3$, ppm): δ -73.27 (d, J = 7.5 Hz). IR ν_{max} (neat)/cm^{-1}: 3321, 3068, 2931, 2854, 1591, 1263, 1165, 1154, 997, 892, 747, 698. HRMS (ESI, m/z): calcd for $C_{14}H_{14}F_3N_2$ [M+H$^+$]: 267.1109; Found: 267.1113.

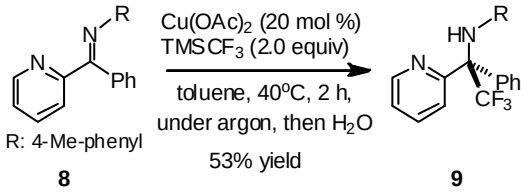
Scheme S2. Exploration of Imine Trifluoromethylation with Other Picolylamine-Derived Imines

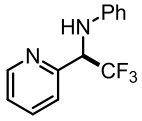


A series of mono- and di-α-substituted picolylamine derived imines were tested; however, none of them are suitable substrates for imine trifluoromethylation.

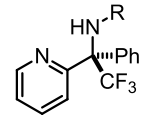
Scheme S3. Imine Trifluoromethylation without the quinolinyl directing group







***N*-(2,2,2-trifluoro-1-(pyridin-2-yl)ethyl)aniline (7)** : ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.68 (d, J = 4.8 Hz, 1H), 7.74 (t, J = 7.6 Hz, 1H), 7.43 (d, J = 7.6 Hz, 1H), 7.34 (t, J = 6.0 Hz, 1H), 7.22 (t, J = 7.6 Hz, 2H), 6.83-6.79 (m, 3H), 5.60 (d, J = 7.2 Hz, 1H), 5.05 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 152.05, 149.42, 146.23, 136.81, 129.34, 125.05 (q, J = 281 Hz), 123.95, 123.79, 119.05, 114.12, 60.53 (q, J = 30 Hz). ^{19}F NMR (377 MHz, $CDCl_3$, ppm): δ -73.87 (d, J = 37 Hz). IR ν_{max} (neat)/cm^{-1}: 3402, 1605, 1508, 1434, 1269, 1248, 1167, 999, 749, 693. calcd for $C_{13}H_{12}F_3N_2$ [M+H$^+$]: 253.0953; Found: 253.0951.



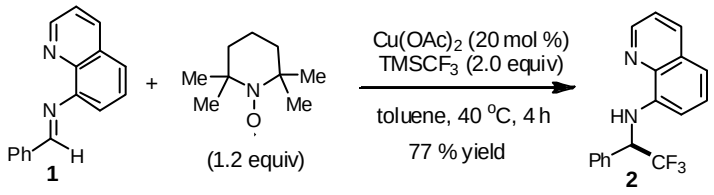
R = 4-Me-phenyl

9

4-Methyl-*N*-(2,2,2-trifluoro-1-phenyl-1-(pyridin-2-yl)ethyl)aniline (9) : ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.75 (d, J = 4.4 Hz, 1H), 7.67 (d, J = 6.8 Hz, 2H), 7.61 (t, J = 7.6 Hz, 1H), 7.47-7.43 (m, 3H), 7.33-7.30 (m, 1H), 7.19 (s, 1H), 7.06 (d, J = 8.0 Hz, 1H), 6.90 (d, J = 8.0 Hz, 2H), 6.90 (d, J = 8.0 Hz, 2H), 6.53 (d, J = 8.0 Hz, 2H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 156.47, 147.21, 141.66, 137.79, 136.57, 128.99, 128.77, 128.42, 128.40, 128.16, 127.22, 126.30 (q, J = 290 Hz), 125.03, 123.26, 116.30, 68.79 (q, J = 26 Hz), 20.28. ^{19}F NMR (377 MHz, $CDCl_3$, ppm): δ -66.88. . IR ν_{max} (neat)/cm^{-1}: 3346, 1615, 1516, 1257, 1146, 932, 699. HRMS (ESI, m/z): calcd for $C_{20}H_{18}F_3N_2$ [M+H$^+$]: 343.1422; Found: 343.1419.

b. Procedure for Imine Trifluoromethylation in the presence of TEMPO

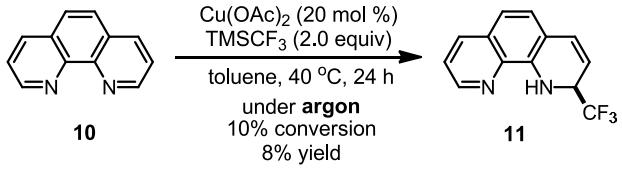
Scheme S4. Imine Trifluoromethylation in the presence of TEMPO



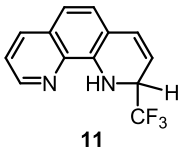
To a flame-dried sealable 2-dram vial equipped with a stir bar were added 8-aminoquinoline (43.2 mg, 0.3 mmol, 1.0 equiv), freshly distilled benzaldehyde (37 µL, 0.36 mmol, 1.2 equiv), activated molecular sieves (4 Å, 0.1 g) and 2 mL toluene and the mixture was stirred for 1 h at room temperature to afford the imine. Without purification, the imine was added to a vial which was charged with $Cu(OAc)_2$ (10.9 mg, 0.06 mmol, 20 mol%) and TEMPO (57 mg, 0.36 mmol, 1.2 equiv) under argon, then the mixture was stirred at room temperature for 10 minutes before $TMSCF_3$ (88 µL, 0.6 mmol, 2.0 equiv) was added. The reaction mixture was stirred at 40 ^{o}C for 4 h and monitored by TLC. Then the reaction was quenched with saturated aqueous $NaHCO_3$ solution. The mixture was first filtered through a short pad of celite (to remove the molecular sieves) and then extracted with EtOAc. The organic phase was concentrated and the crude product was purified by flash column chromatography to afford **2**.

c. Procedure for Cu(II)-Catalyzed Trifluoromethylation of 1,10-Phenanthroline

Scheme S5. Cu(II)-Catalyzed Trifluoromethylation of 1,10-Phenanthroline to Afford 1,2-Dihydrophenanthroline

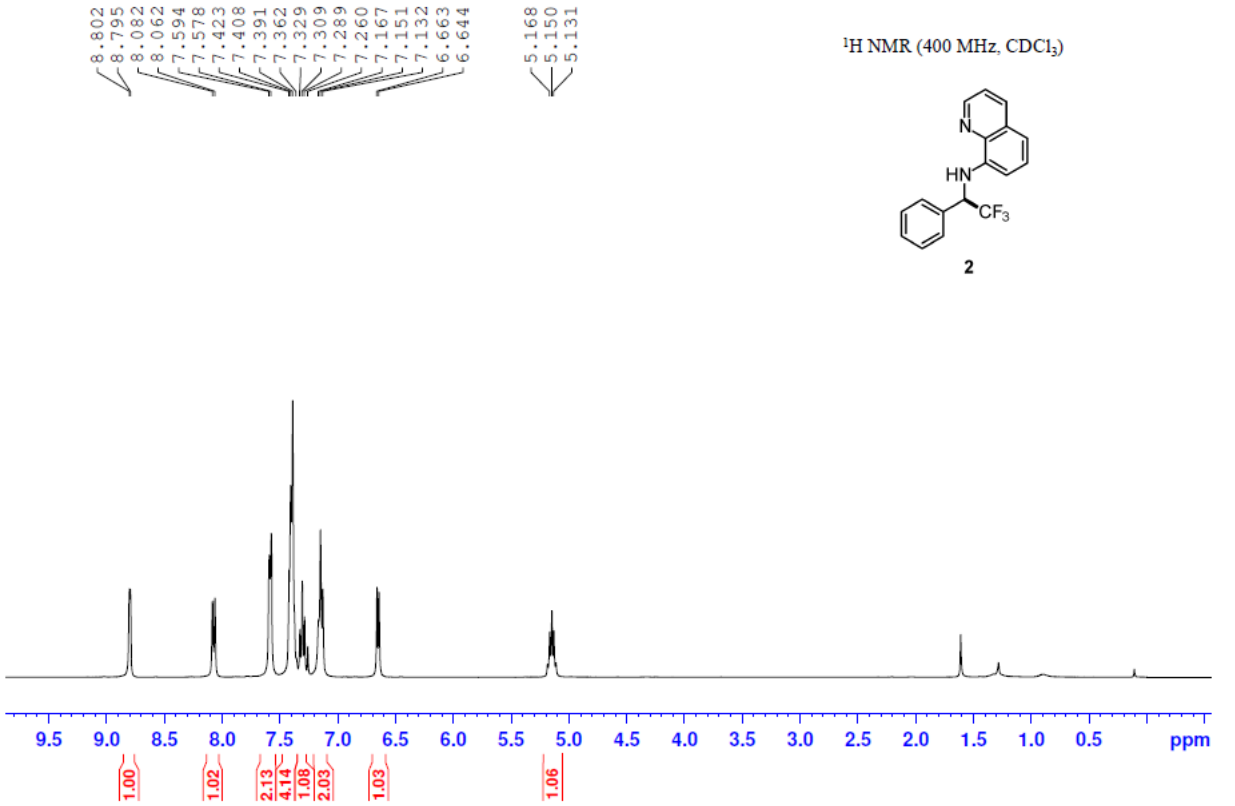


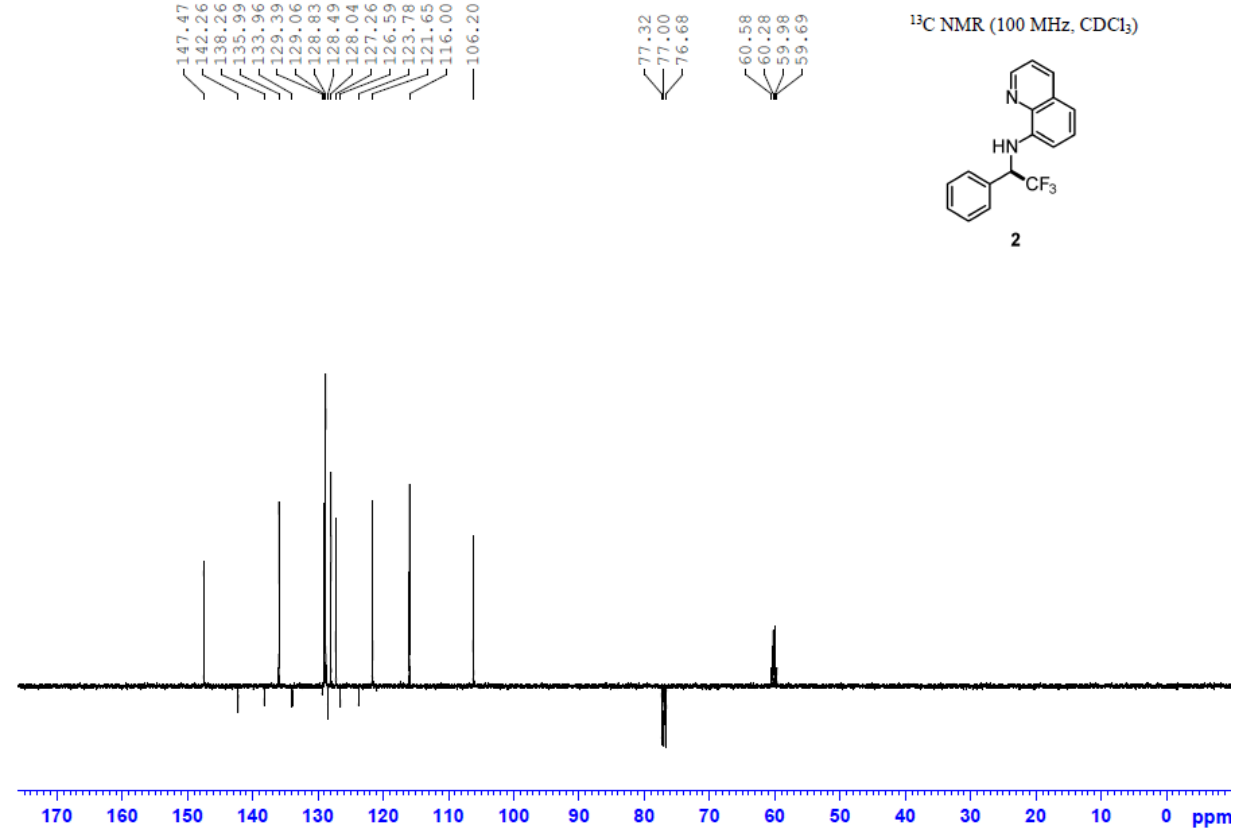
Under argon, to a mixture of **10** (18mg, 0.1 mmol), $Cu(OAc)_2$ (3.7 mg, 0.02 mmol), KOAc (9.8 mg, 0.1 mmol) and HOAc (6 μL, 0.1 mmol) in toluene (2.0 mL), $TMSCF_3$ (15 μL, 0.1 mmol) was added at room temperature. The reaction mixture was allowed to stir at 40 °C for 3 hours. Another portion of $TMSCF_3$ (15 μL, 0.1 mmol) was added and continue stirring at 40 °C. After 24 hours, the reaction was quenched by H_2O and extracted with ethyl acetate for three times. The organic layer was washed by brine, dried over Na_2SO_4 and concentrated under vacuum. The residue was purified with flash silica gel column chromatography (40% ethyl acetate in petroleum ether).

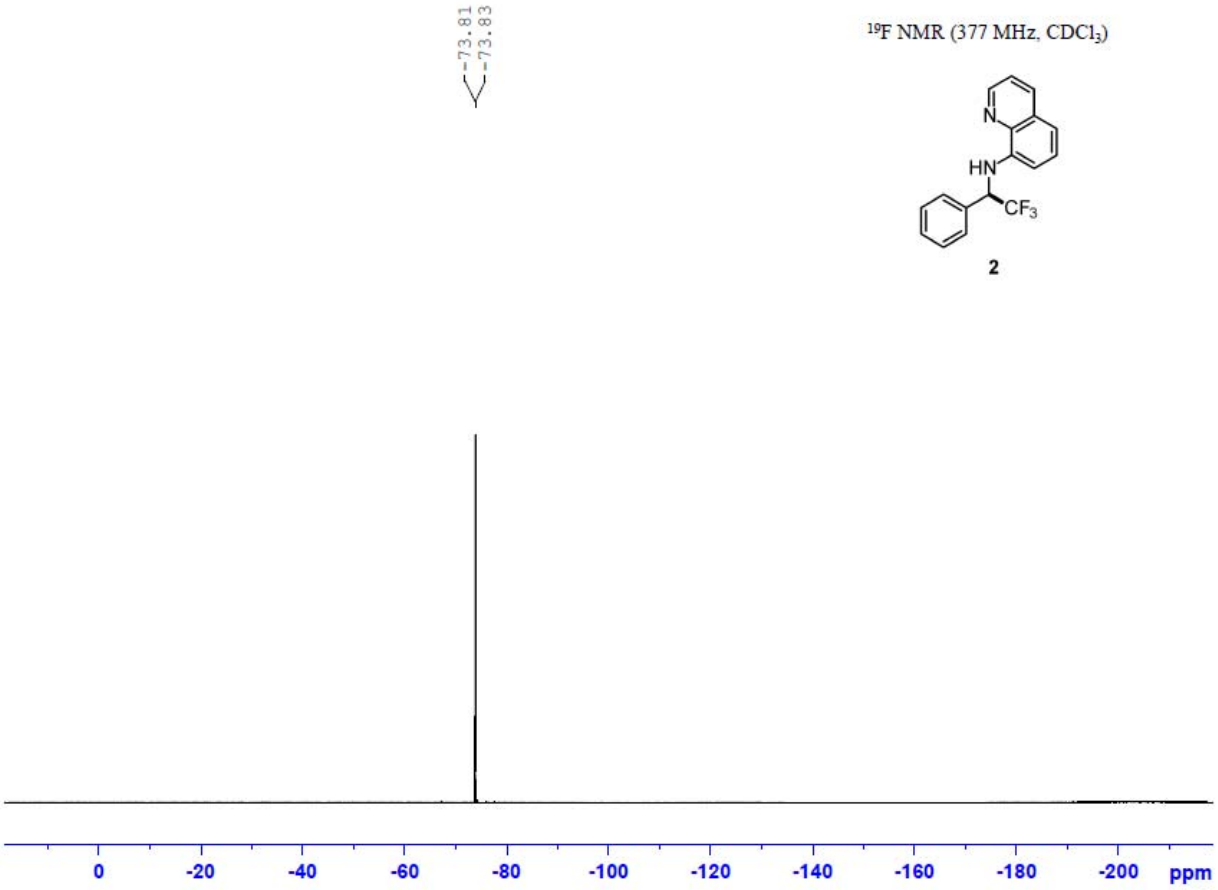


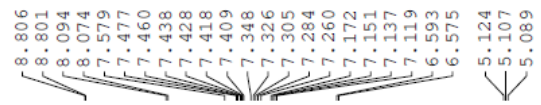
2-(Trifluoromethyl)-1,2-dihydro-1,10-phenanthroline (11) : ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.72 (d, J = 3.2 Hz, 1H), 8.01 (d, J = 8.4 Hz, 1H), 7.34 (q, J = 4.0 Hz, 1H), 7.14 (d, J = 8.0 Hz, 1H), 7.04 (d, J = 8.4 Hz, 1H), 6.77 (d, J = 10.0 Hz, 1H), 6.41 (s, 1H), 5.63 (td, J = 7.6 Hz, 2.0 Hz, 1H), 5.12 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 147.9, 138.5, 136.6, 136.0, 129.0, 126.0, 125.2, 123.7 (q, J = 264 Hz), 121.6, 115.1, 114.2, 113.4, 55.0 (q, J = 31 Hz); ^{19}F NMR (377 MHz, $CDCl_3$, ppm): δ -81.24 (d, J = 7.5 Hz). IR ν_{max} (neat)/cm^{-1}: 3672, 2928, 2513, 2159, 2029, 1977, 1384, 1120, 1067. HRMS (ESI, m/z): calcd for $C_{13}H_{10}N_2F_3^+$ [M+H$^+$]: 251.0796, found: 251.0791.

E. NMR Spectra

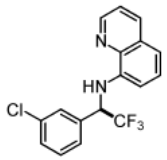




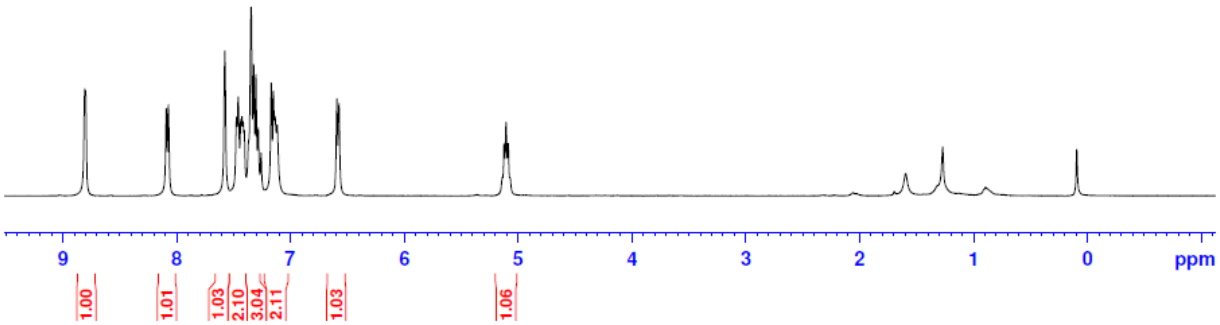




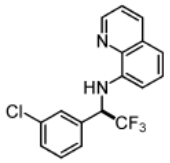
^{1}H NMR (400 MHz, $CDCl_3$)



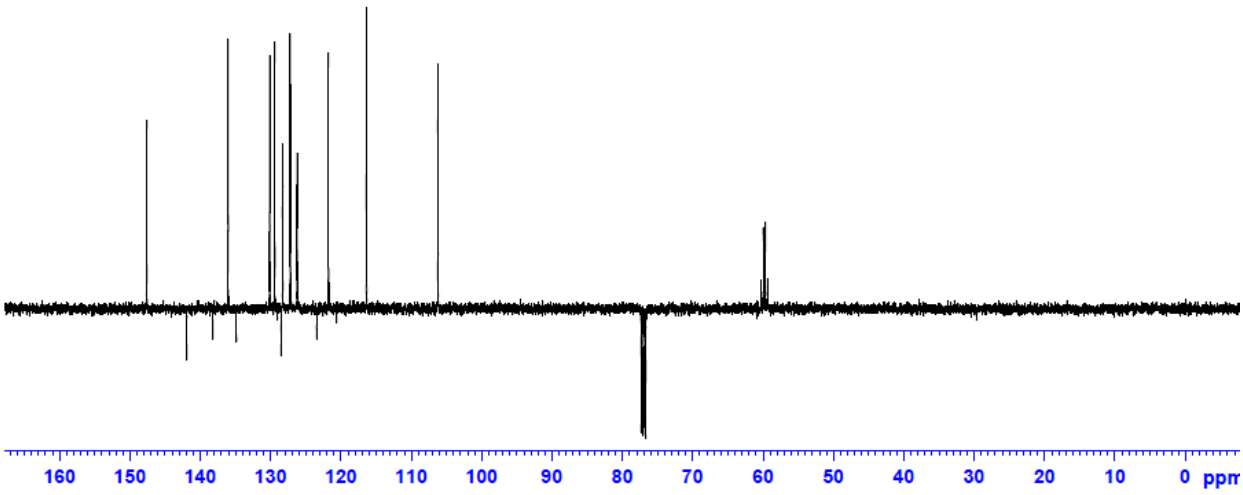
S1a

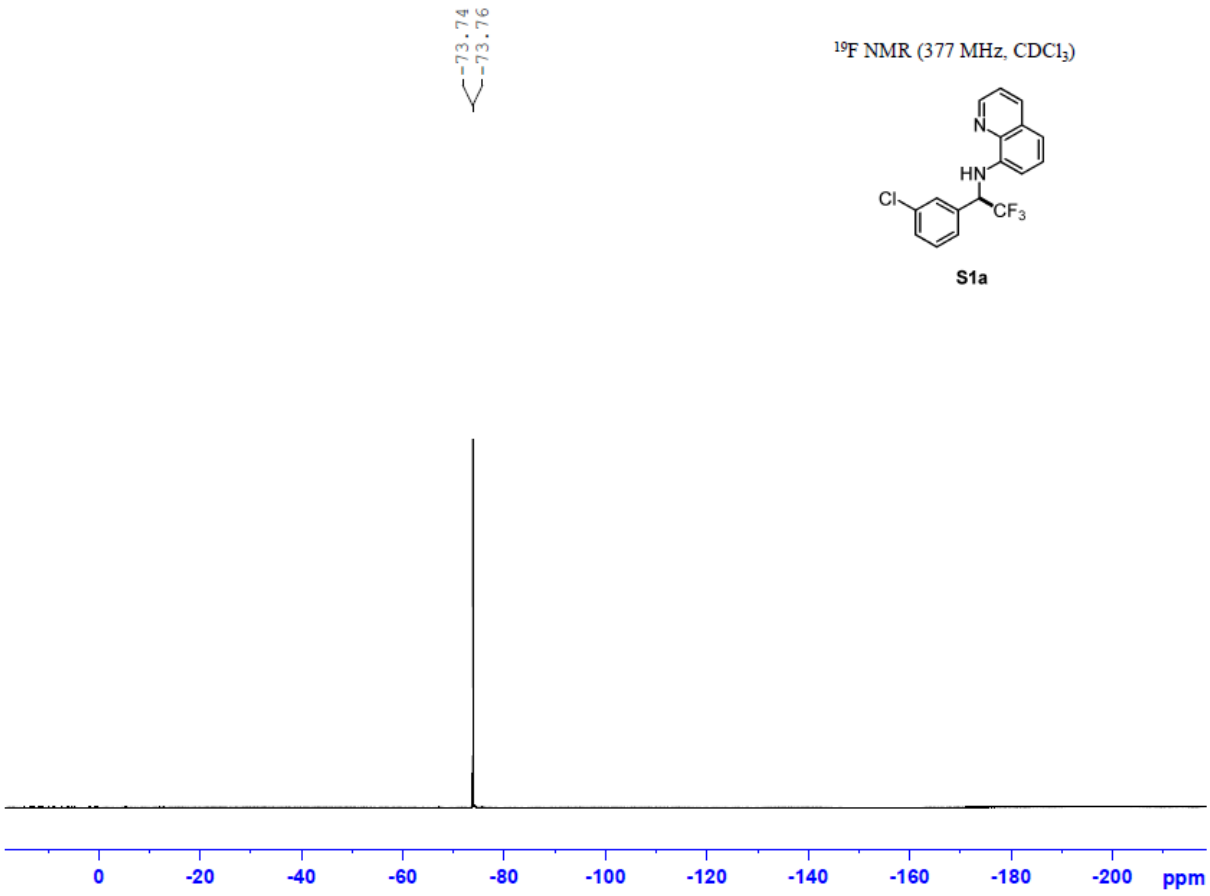


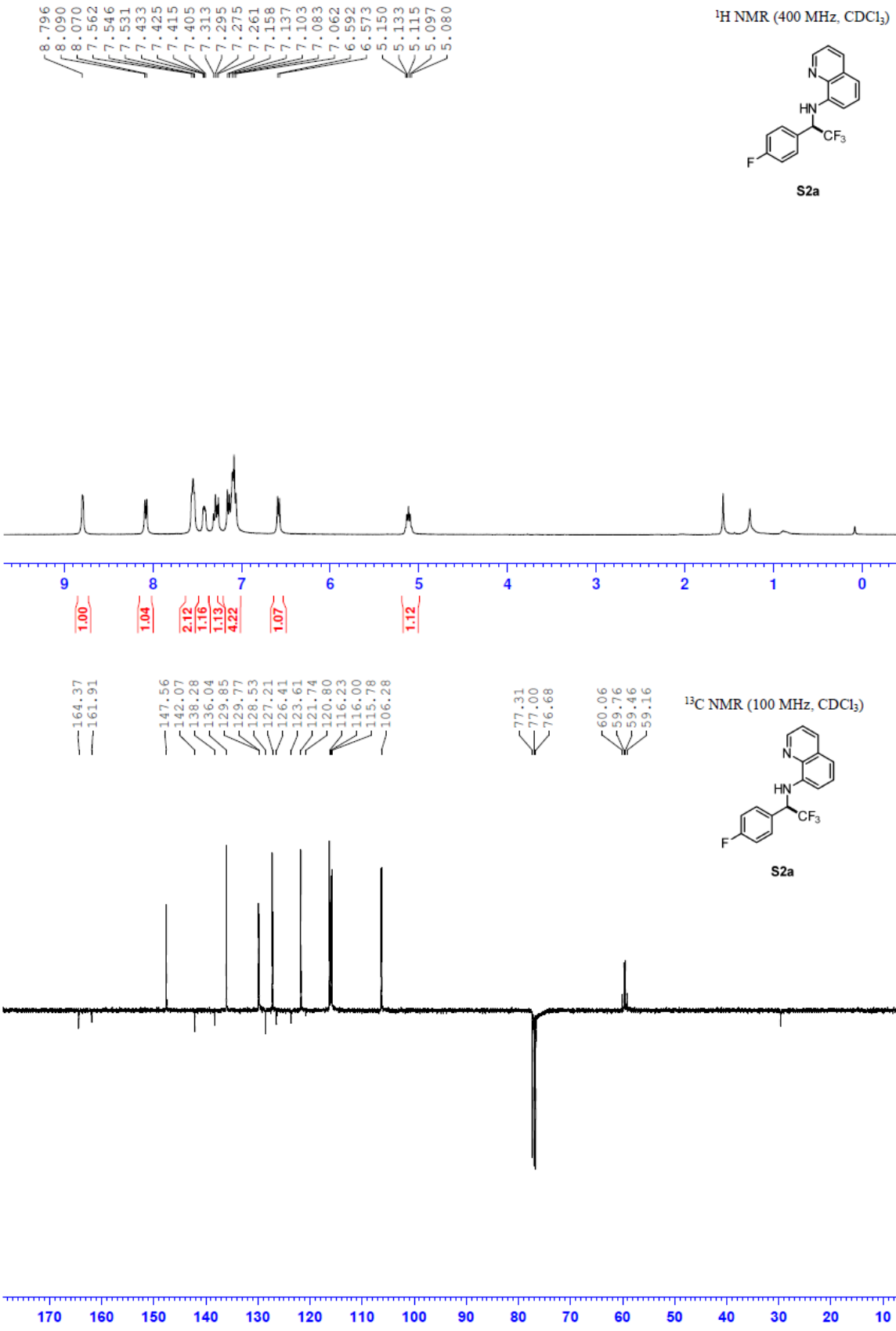
^{13}C NMR (100 MHz, $CDCl_3$)



S1a



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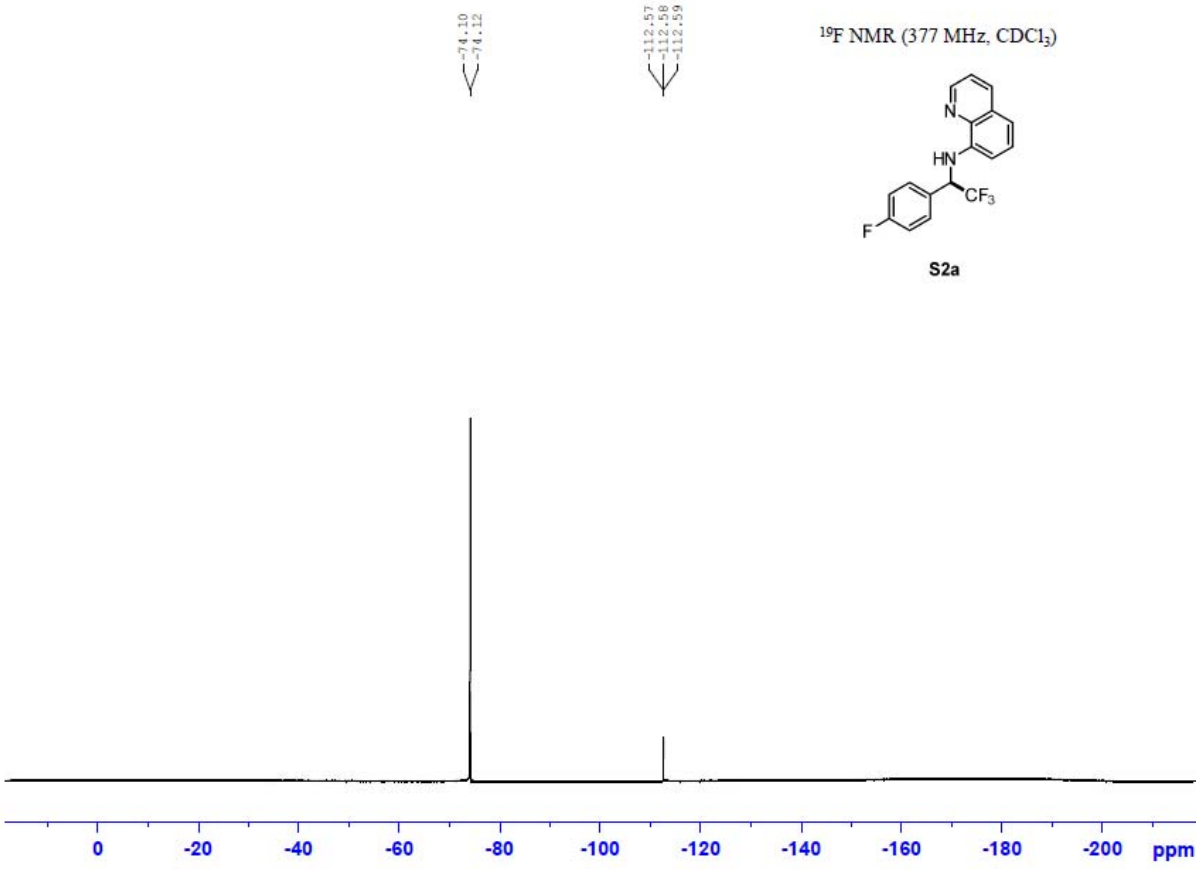
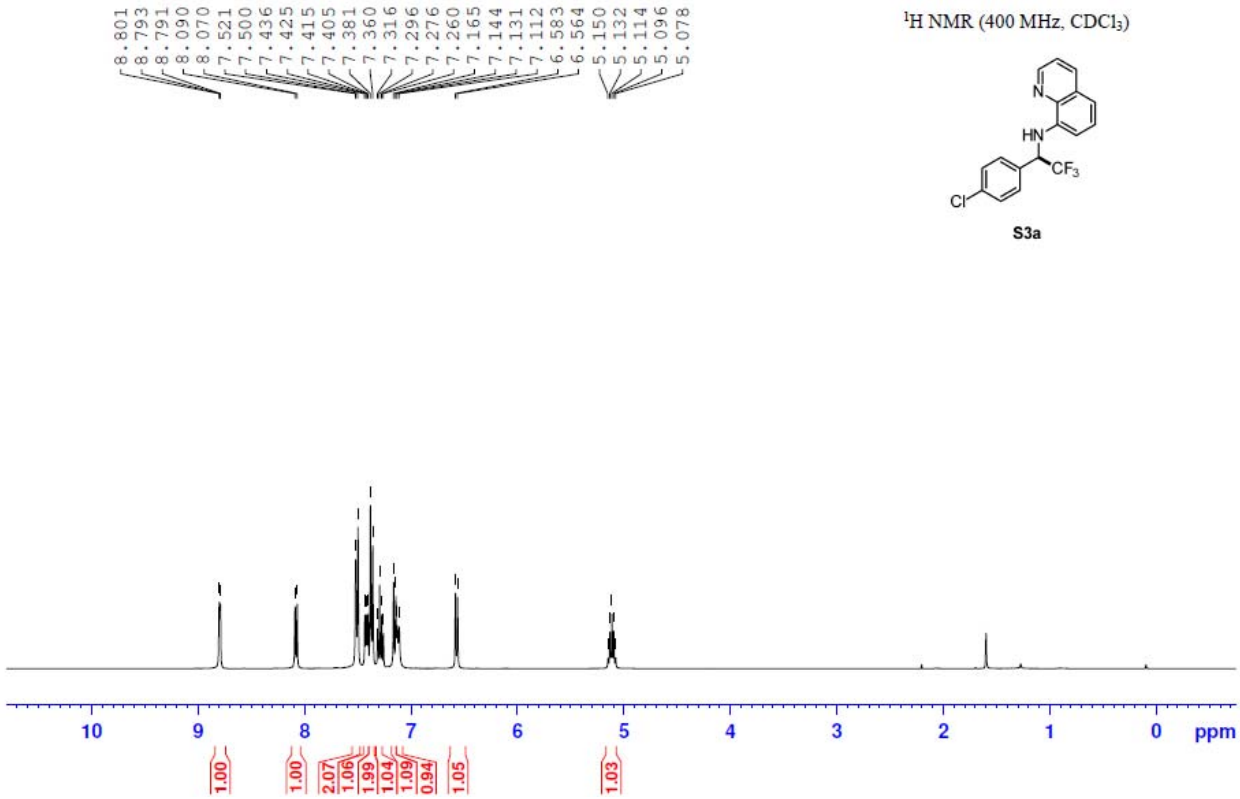
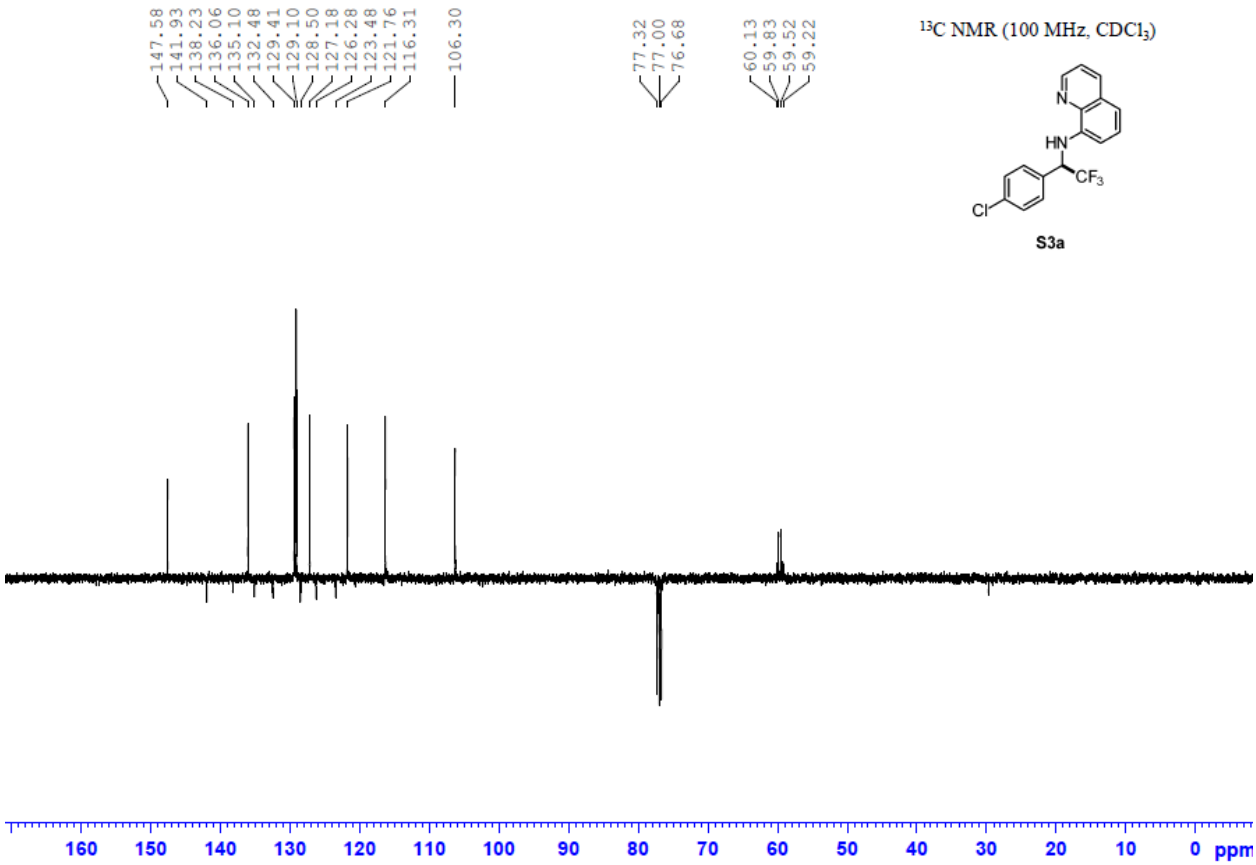
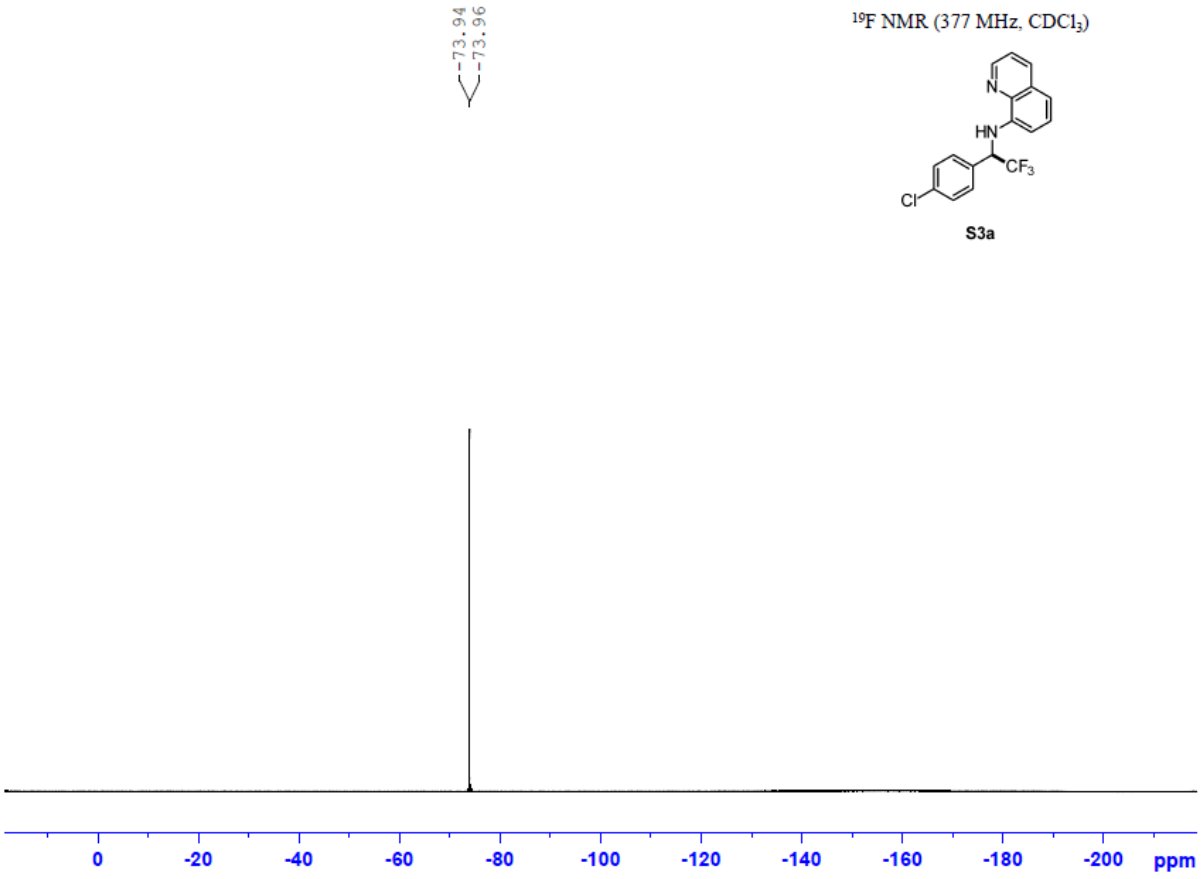
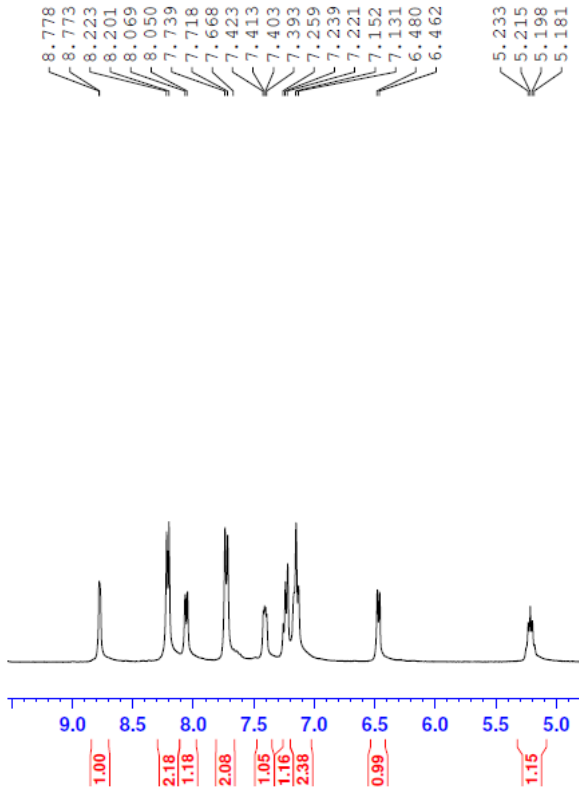
8.090
8.070
7.562
7.546
7.531
7.433
7.425
7.415
7.405
7.313
7.295
7.275
7.261
7.158
7.137
7.103
7.083
7.062
6.592
6.573
5.150
5.133
5.115
5.097
5.080
1H NMR (400 MHz, CDCl3)
S2a
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.04
2.12
1.16
1.13
4.22
1.07
1.12
164.37
161.91
147.56
142.07
138.28
136.04
129.85
129.77
128.53
127.21
126.41
123.61
121.74
120.80
116.23
116.00
115.78
106.28
77.31
77.00
76.68
60.06
59.76
59.46
59.16
13C NMR (100 MHz, CDCl3)
S2a
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm



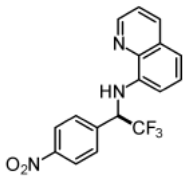




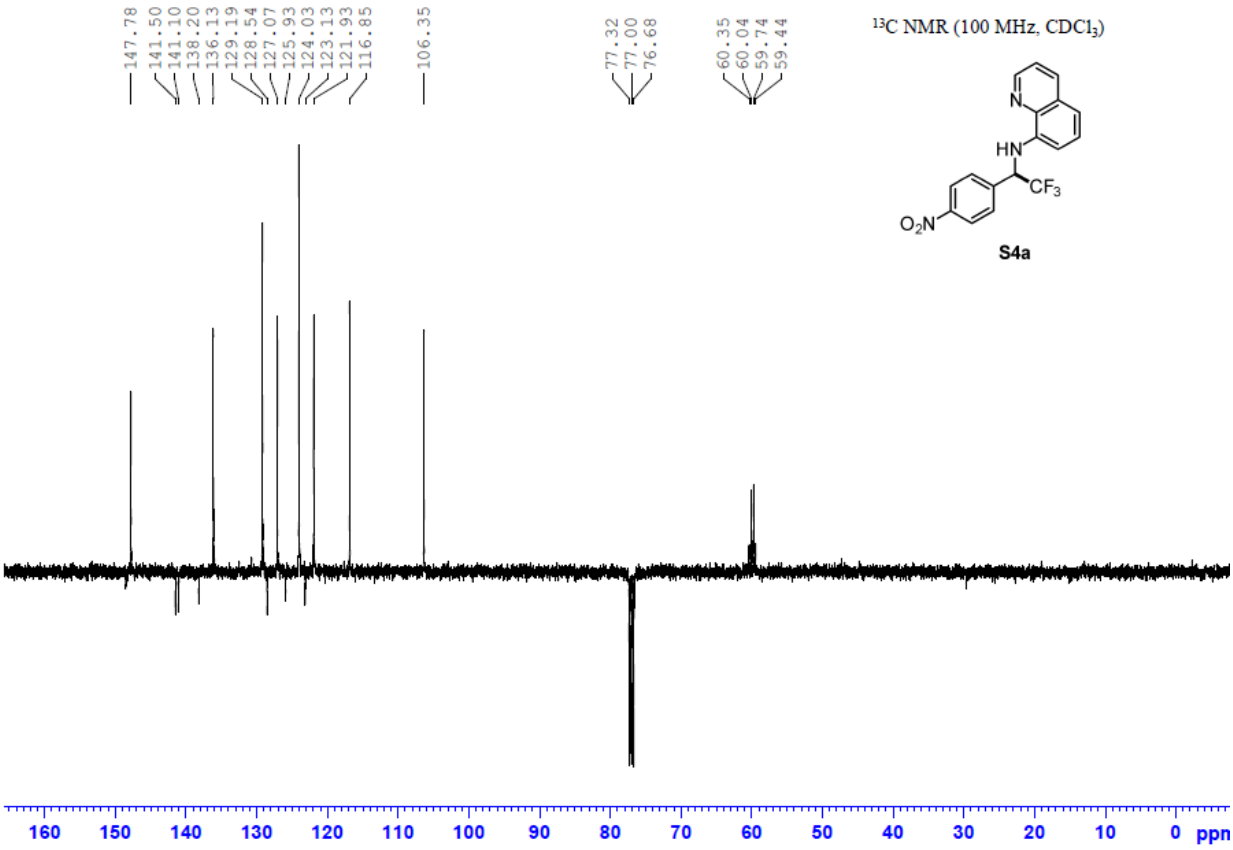




^{1}H NMR (400 MHz, $CDCl_3$)

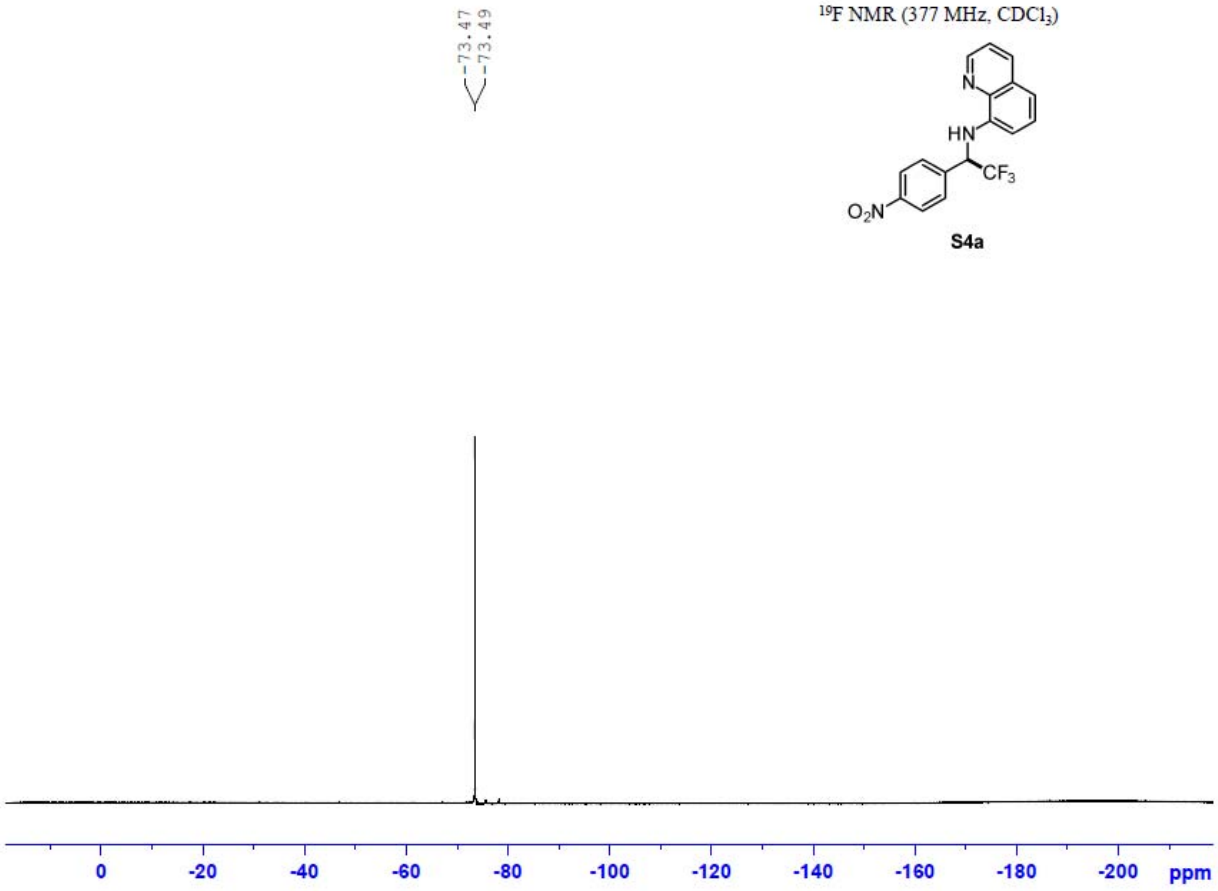


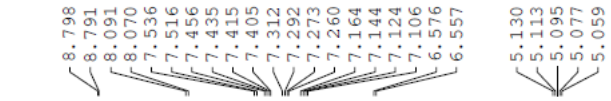
S4a



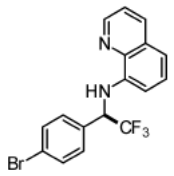
^{13}C NMR (100 MHz, $CDCl_3$)

S4a

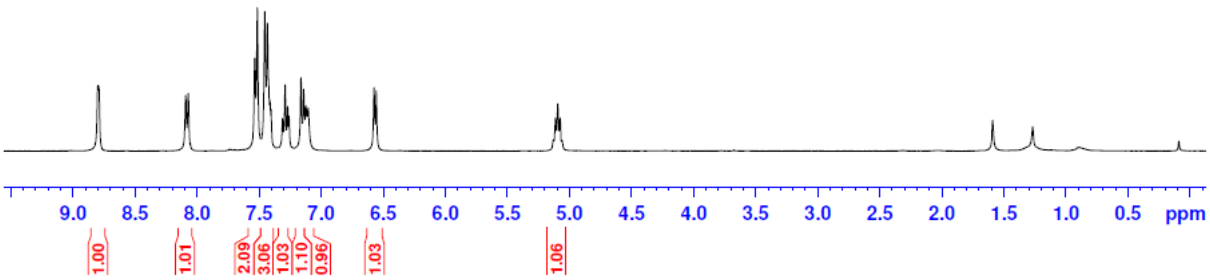




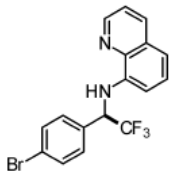
^{1}H NMR (400 MHz, $CDCl_3$)



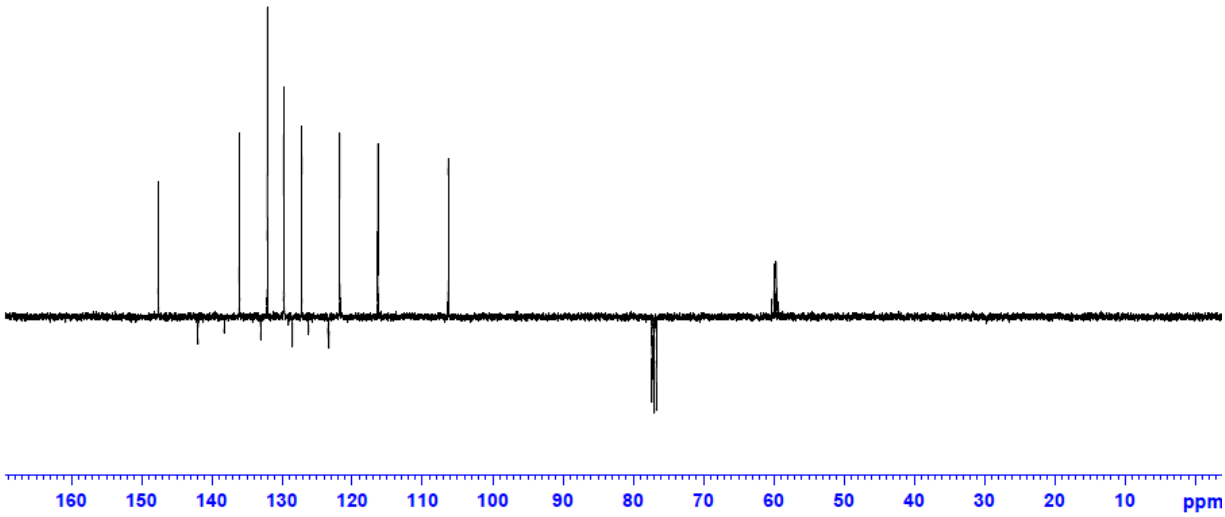
S5a

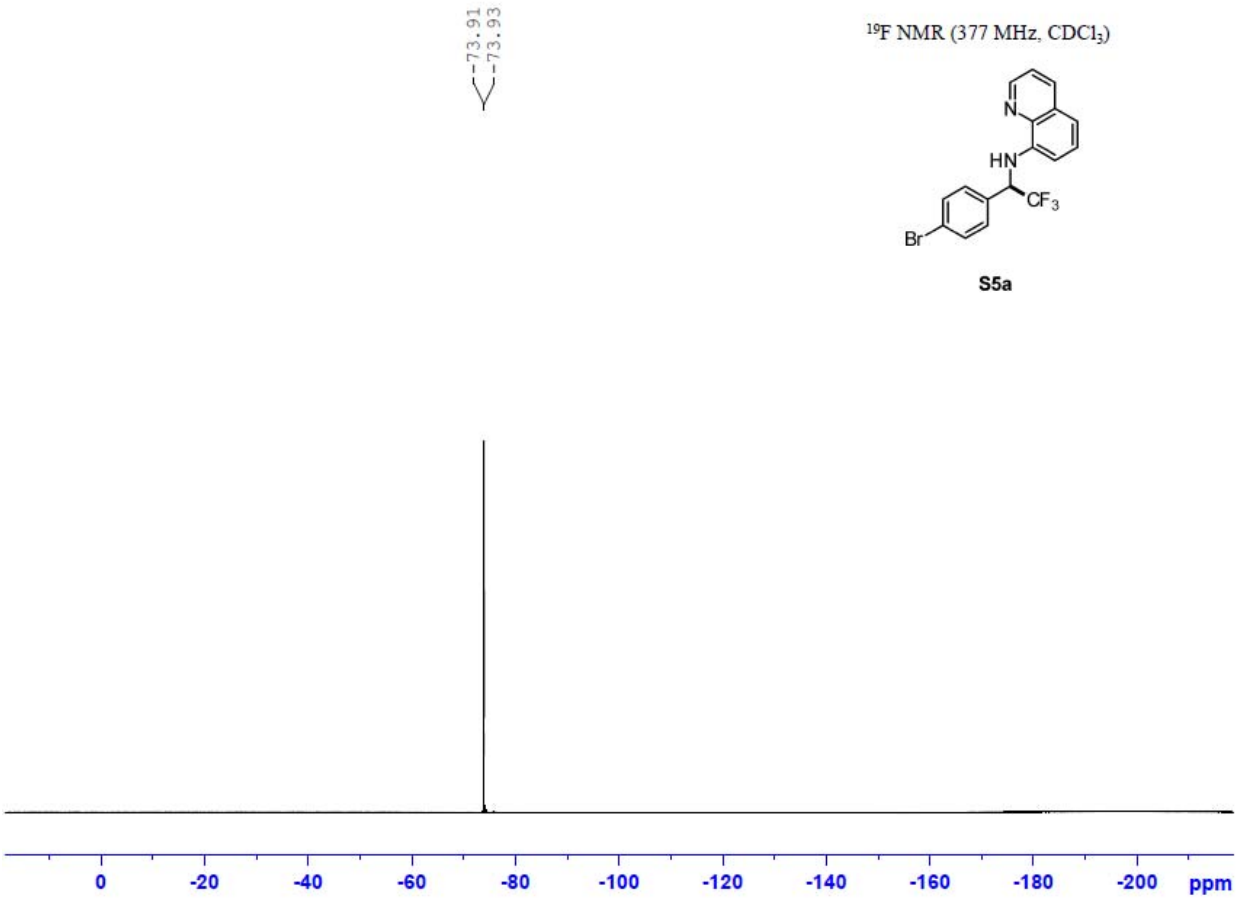


^{13}C NMR (100 MHz, $CDCl_3$)

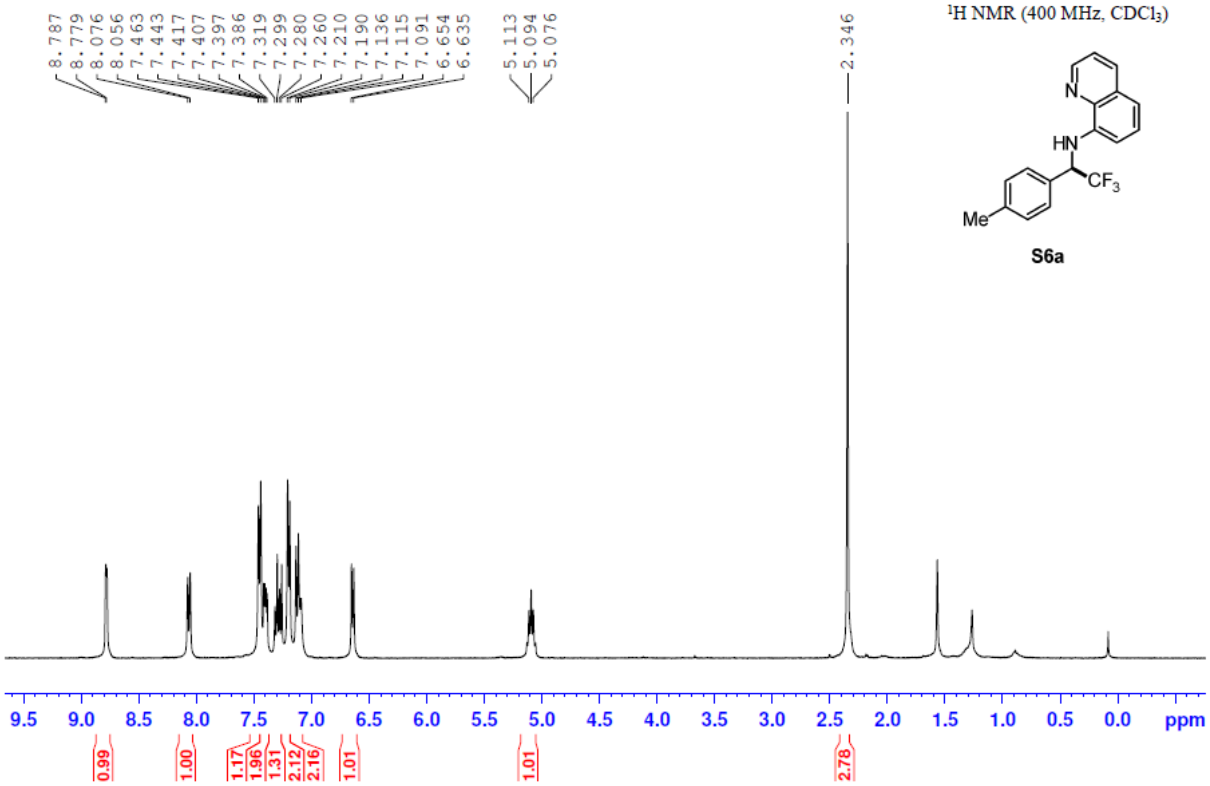


S5a



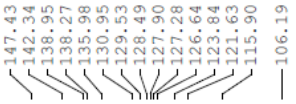


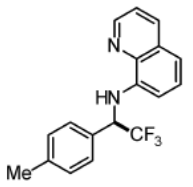
^{1}H NMR (400 MHz, $CDCl_3$)



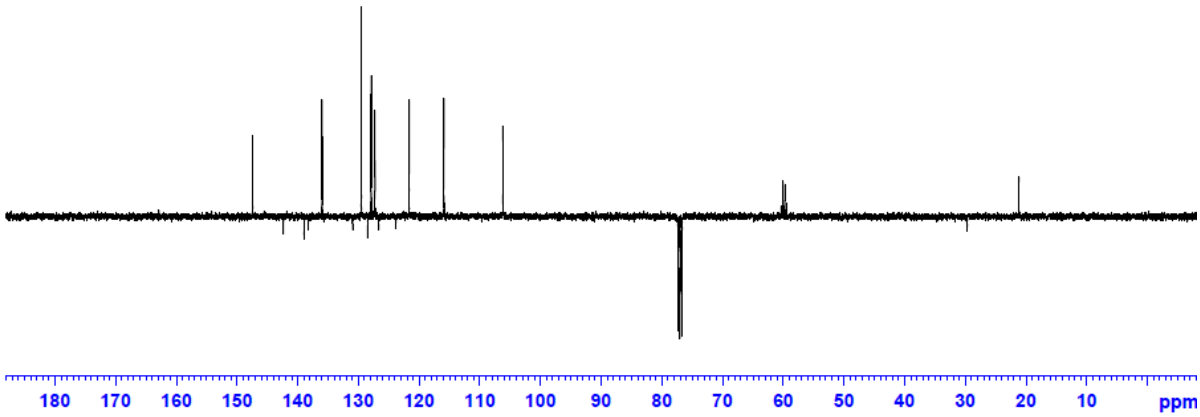
S6a

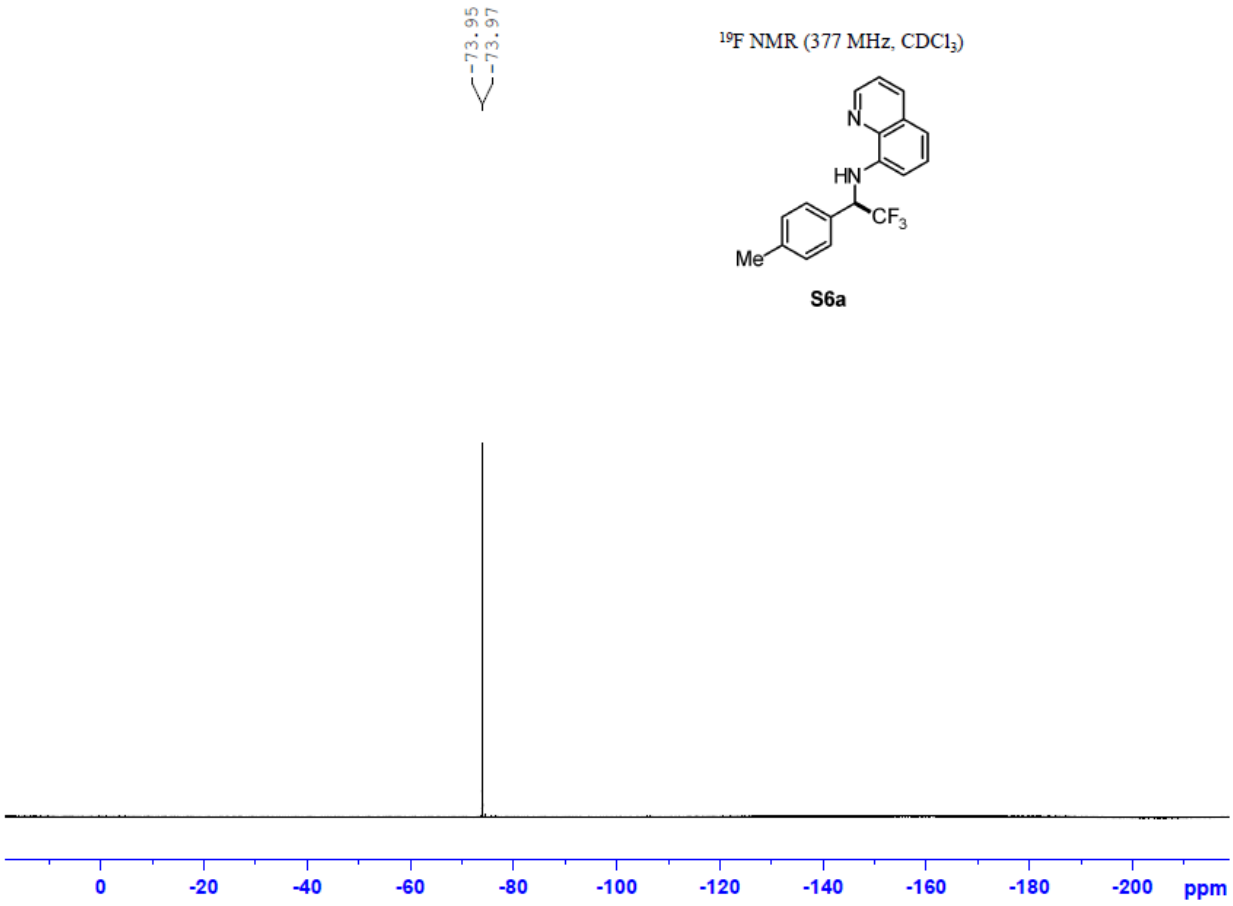
^{13}C NMR (100 MHz, $CDCl_3$)





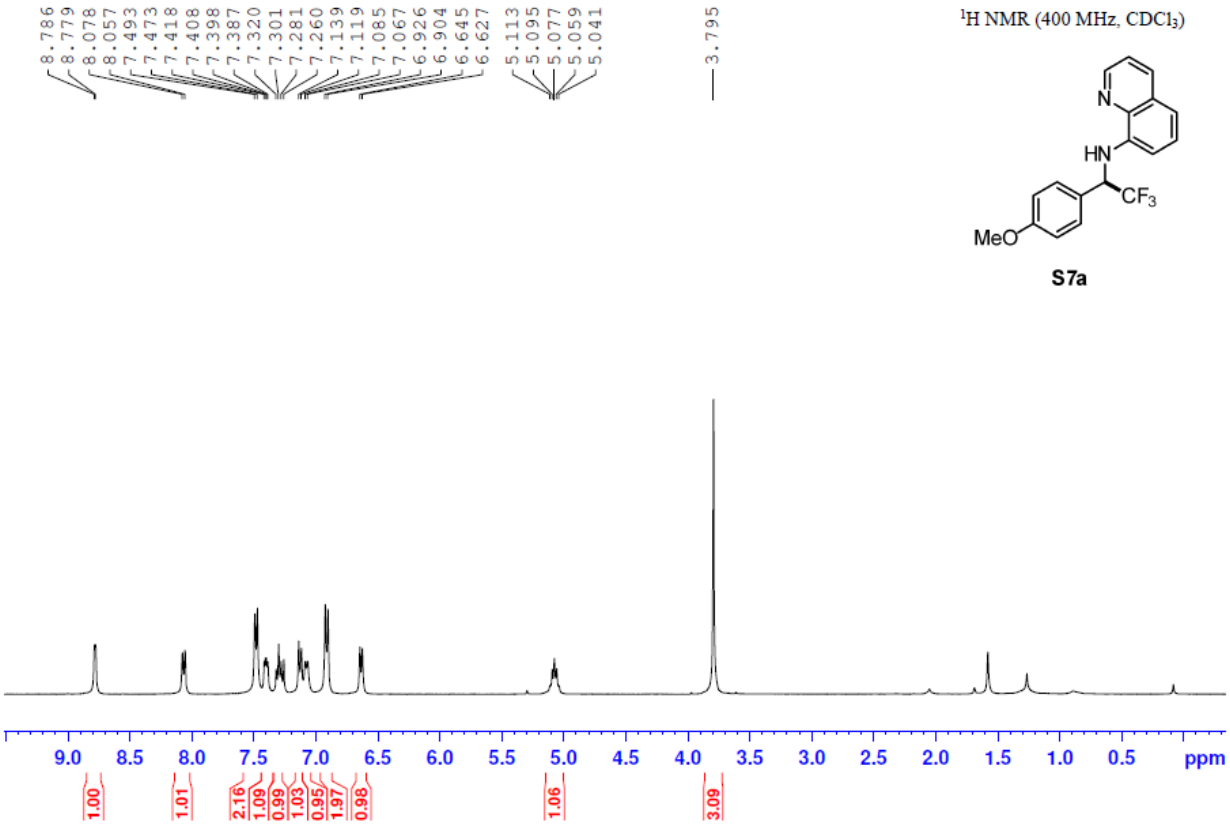
S6a





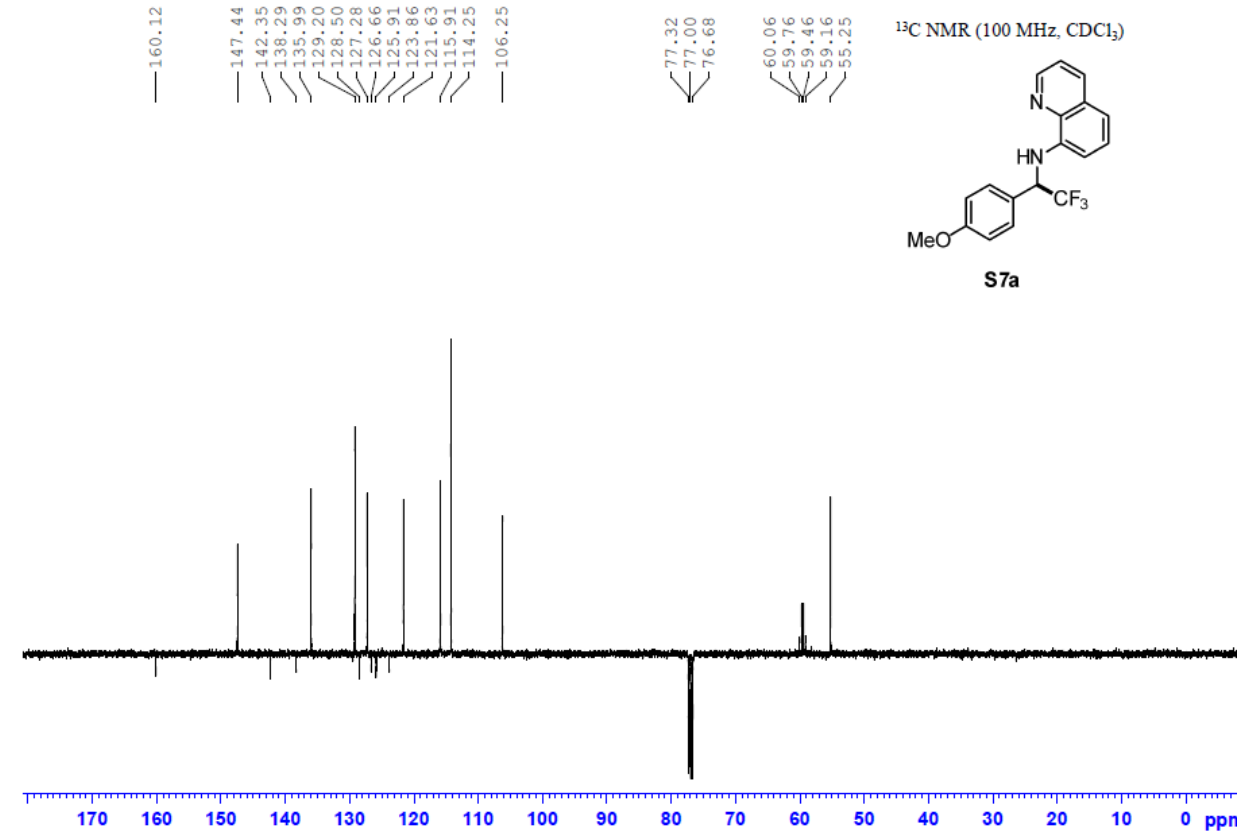
^{19}F NMR (377 MHz, $CDCl_3$)

S6a



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

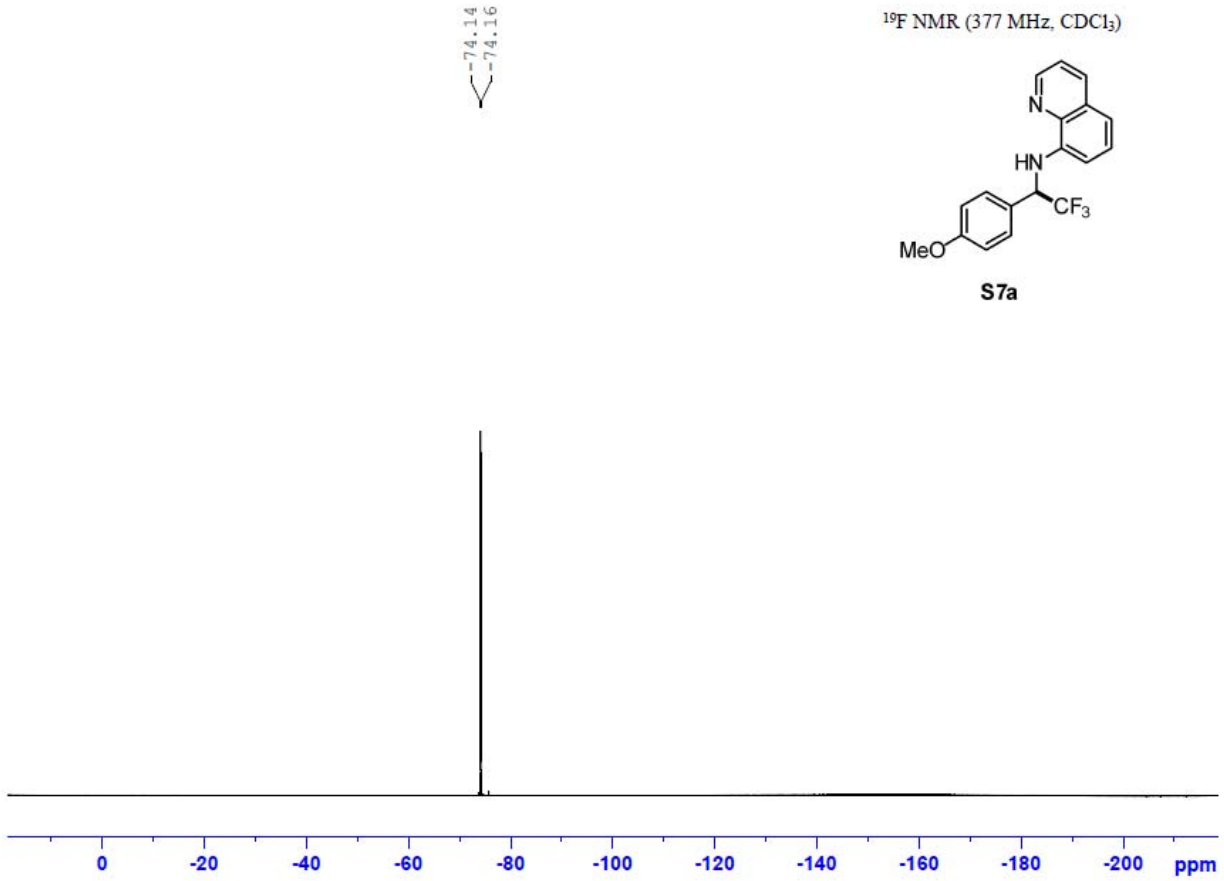
S7a



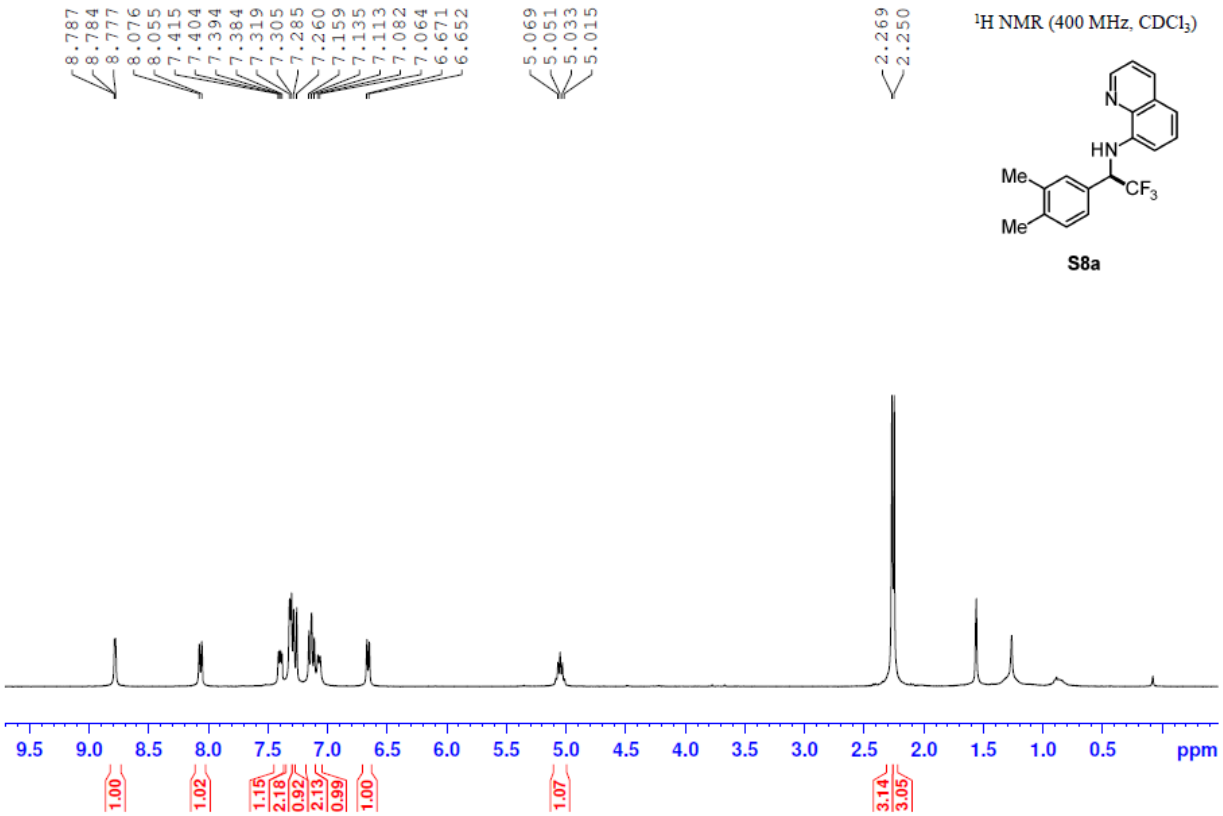
^{13}C NMR (100 MHz, $CDCl_3$)

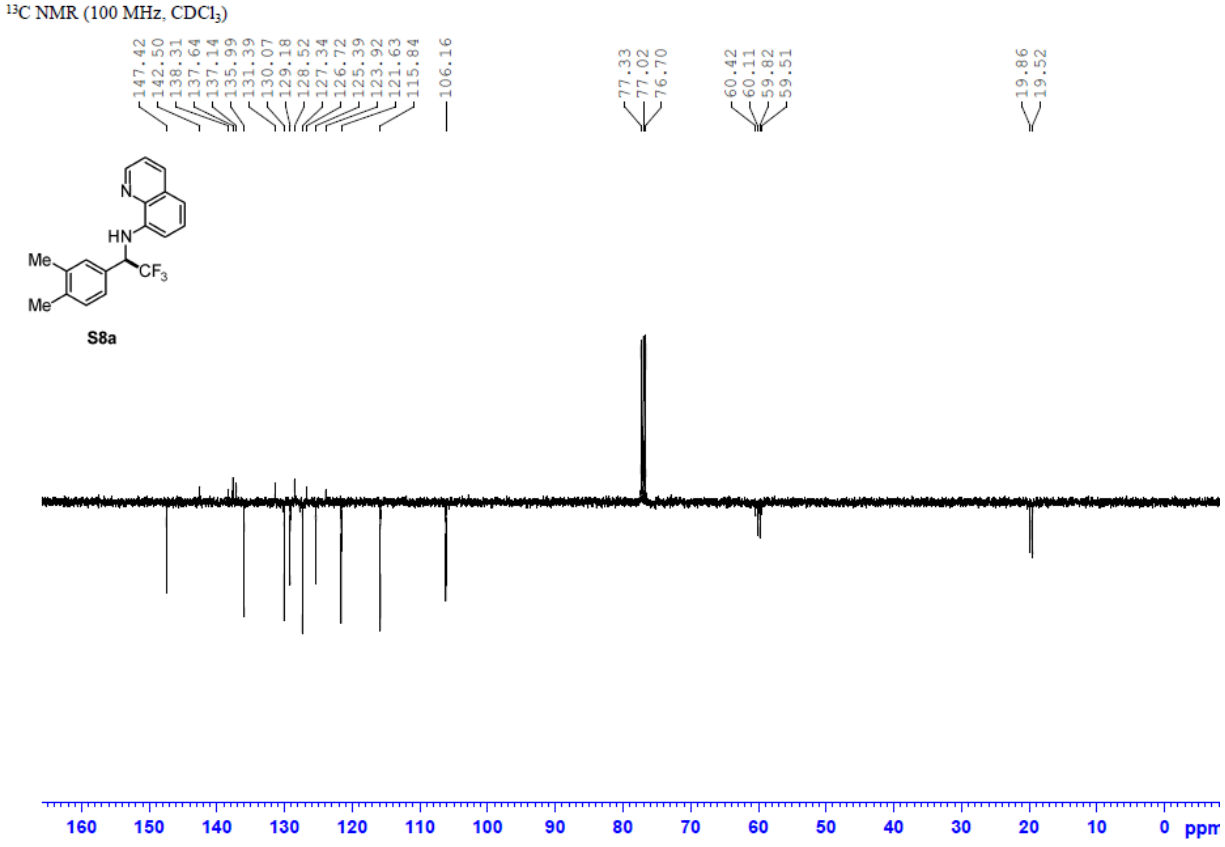
S7a

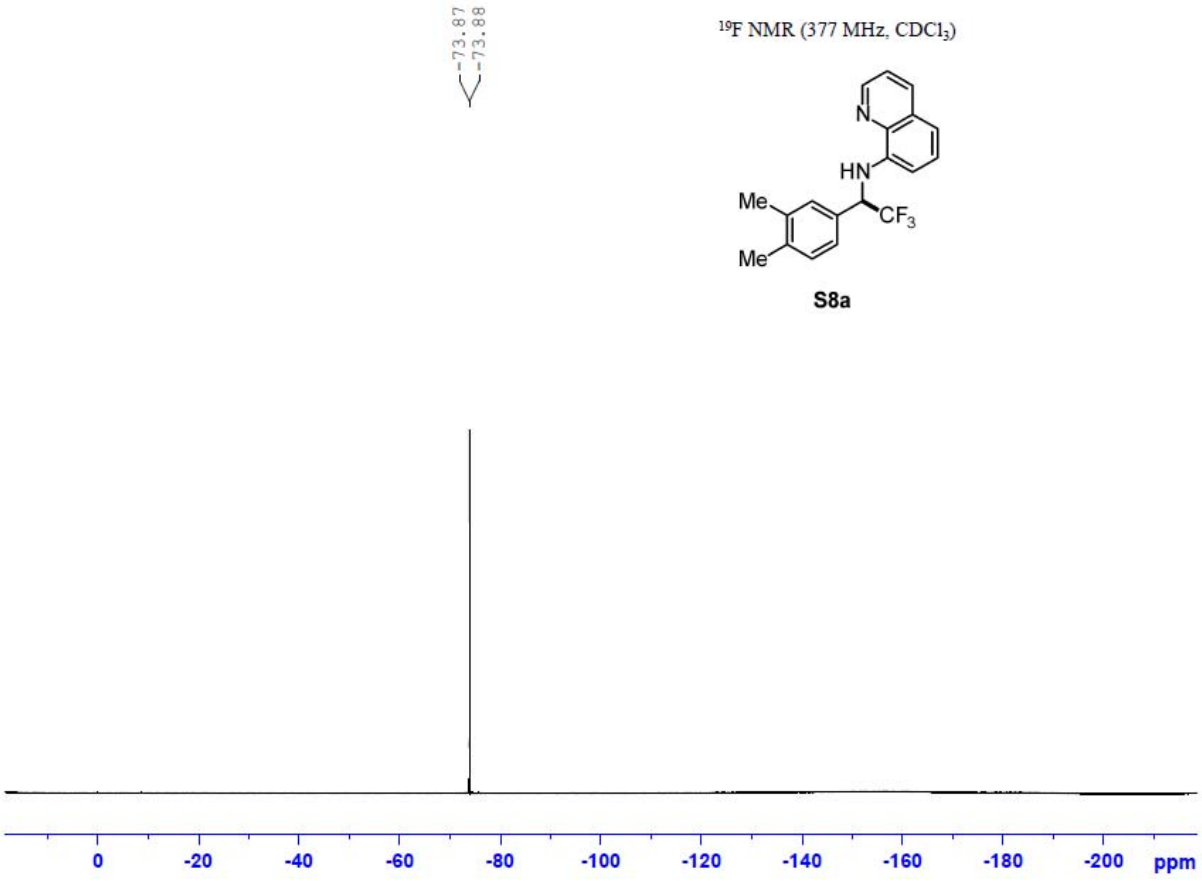
^{19}F NMR (377 MHz, $CDCl_3$)

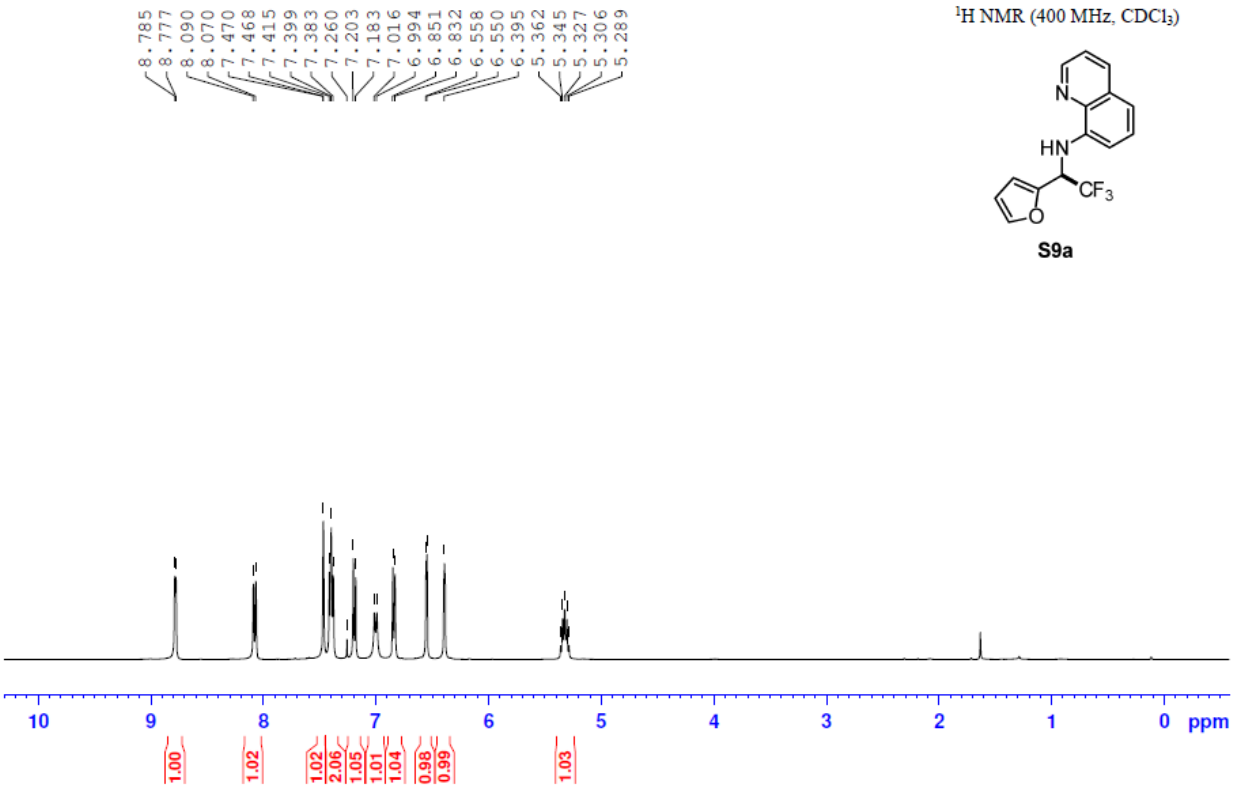


S7a


8.787
8.784
8.777
8.076
8.055
7.415
7.404
7.394
7.384
7.319
7.305
7.285
7.260
7.159
7.135
7.113
7.082
7.064
6.671
6.652
5.069
5.051
5.033
5.015
2.269
2.250
1H NMR (400 MHz, CDCl3)
N
HN
Me
Me
CF3
S8a
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 ppm
1.00
1.02
1.15
2.18
0.92
2.13
0.99
1.00
1.07
3.14
3.05

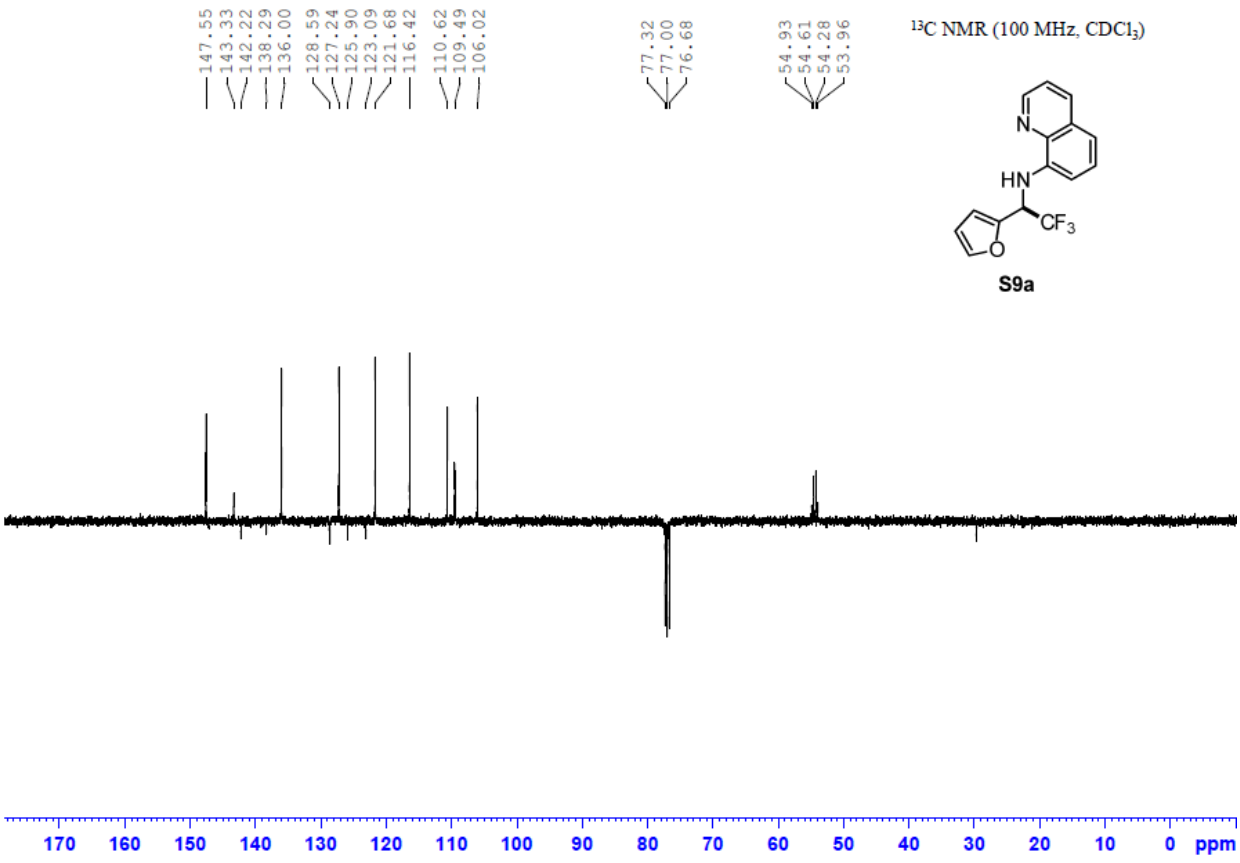

13C NMR (100 MHz, CDCl3)
147.42
142.50
138.31
137.64
137.14
135.99
131.39
130.07
129.18
128.52
127.34
126.72
125.39
123.92
121.63
115.84
106.16
77.33
77.02
76.70
60.42
60.11
59.82
59.51
19.86
19.52
N
HN
Me
Me
CF3
S8a
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm





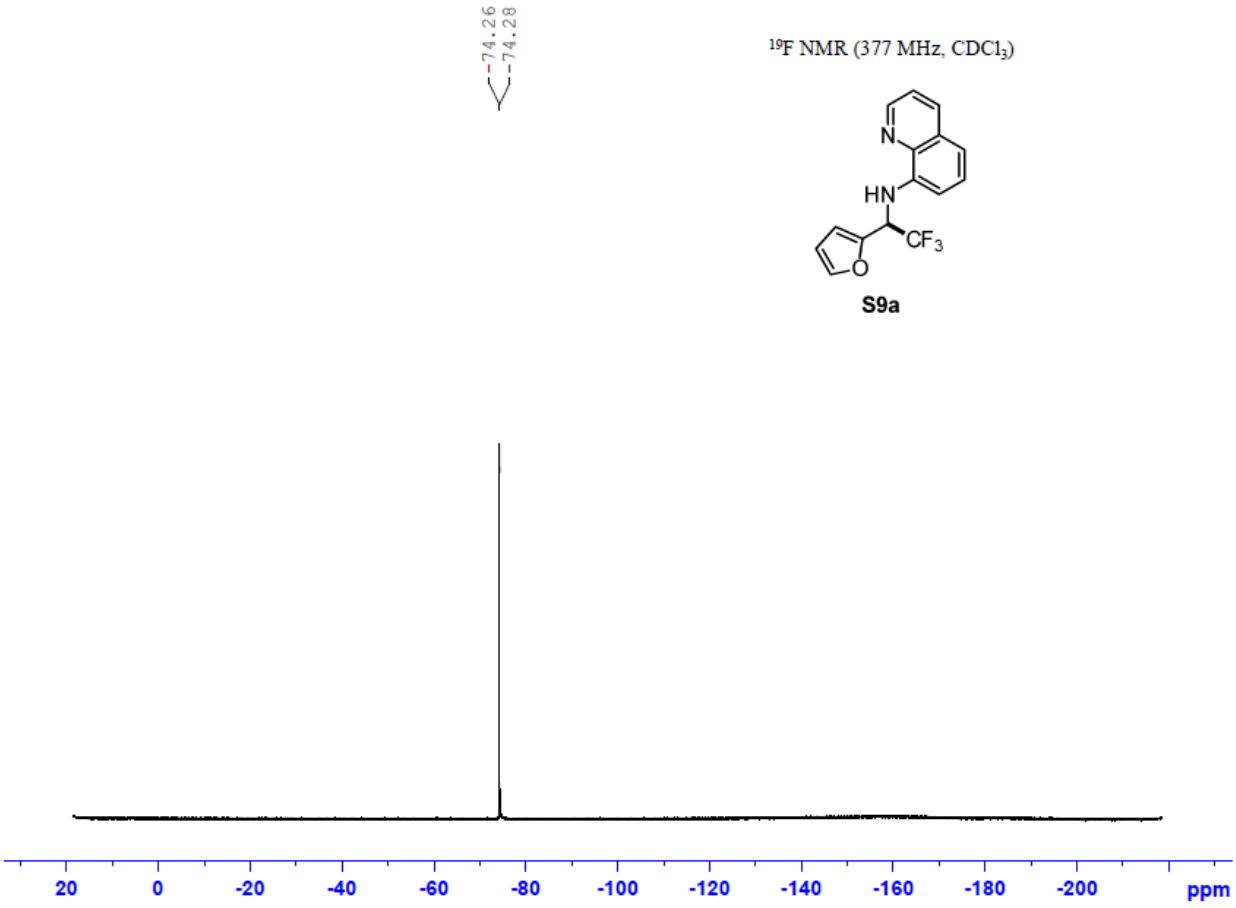
^{1}H NMR (400 MHz, $CDCl_3$)

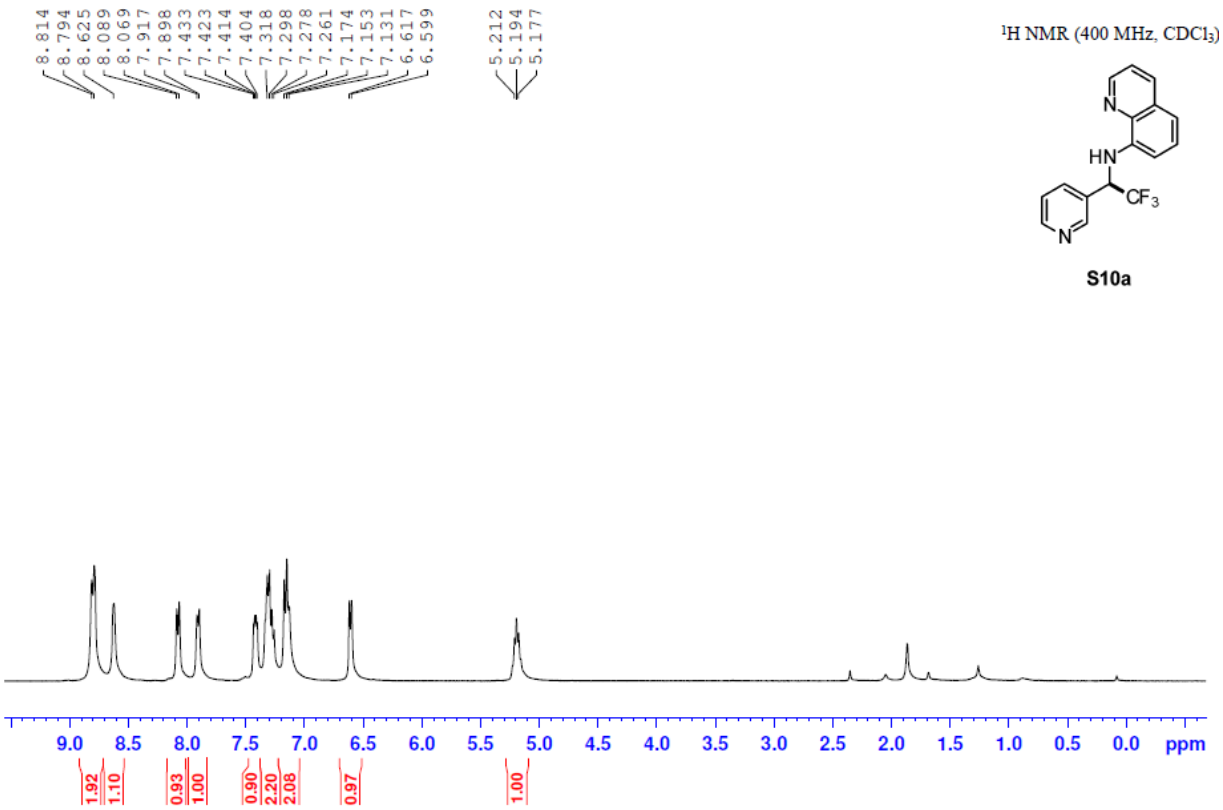
S9a



^{13}C NMR (100 MHz, $CDCl_3$)

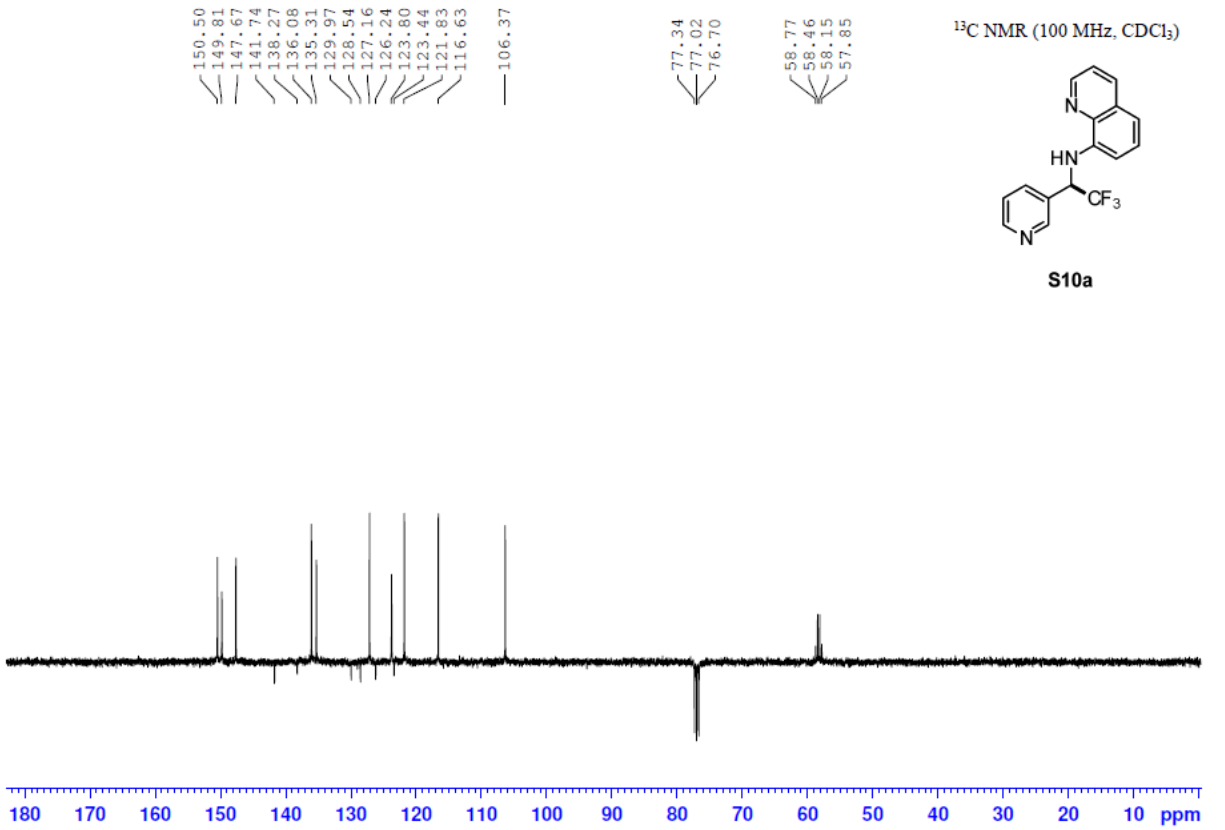
S9a





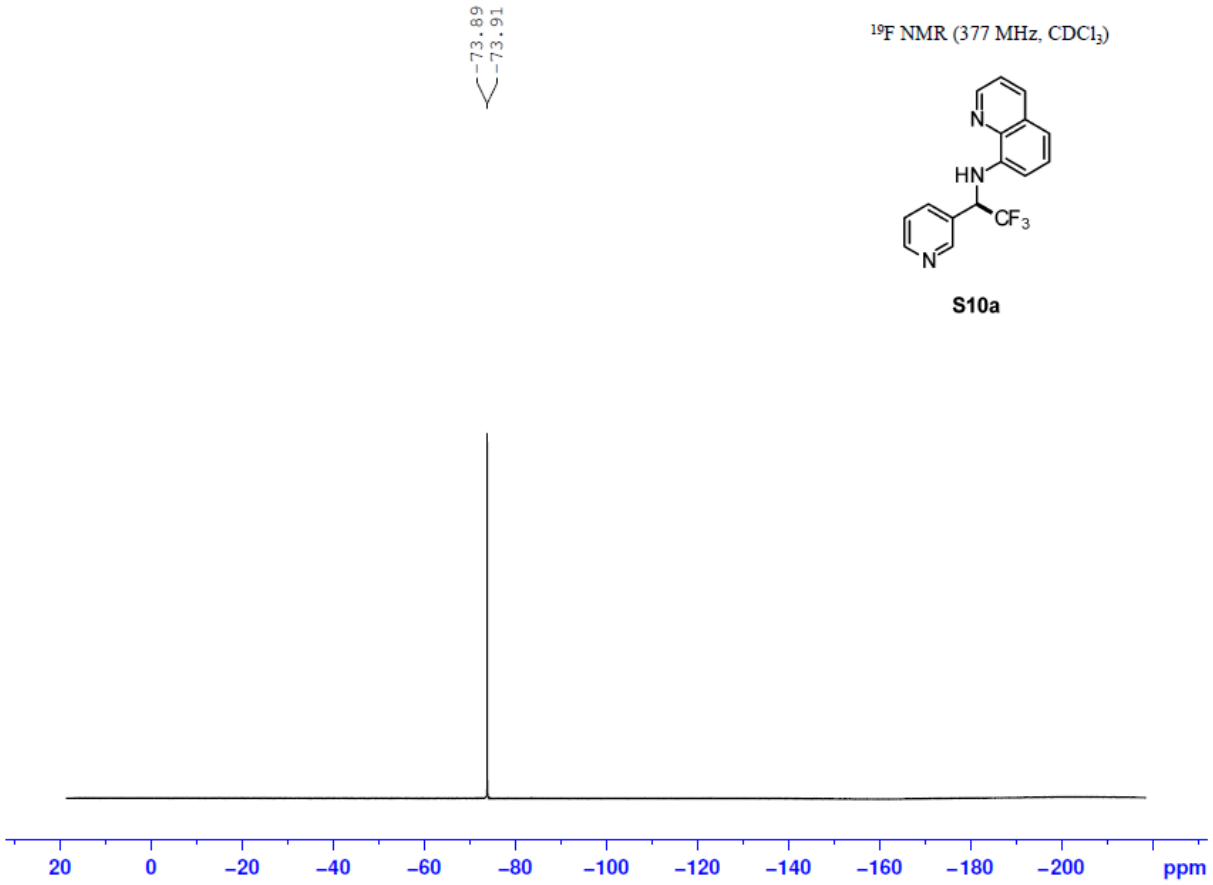
^{1}H NMR (400 MHz, $CDCl_3$)

S10a



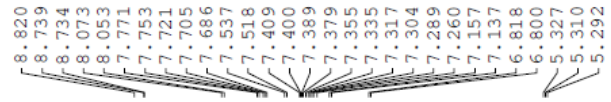
^{13}C NMR (100 MHz, $CDCl_3$)

S10a

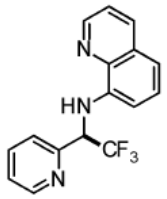


^{19}F NMR (377 MHz, $CDCl_3$)

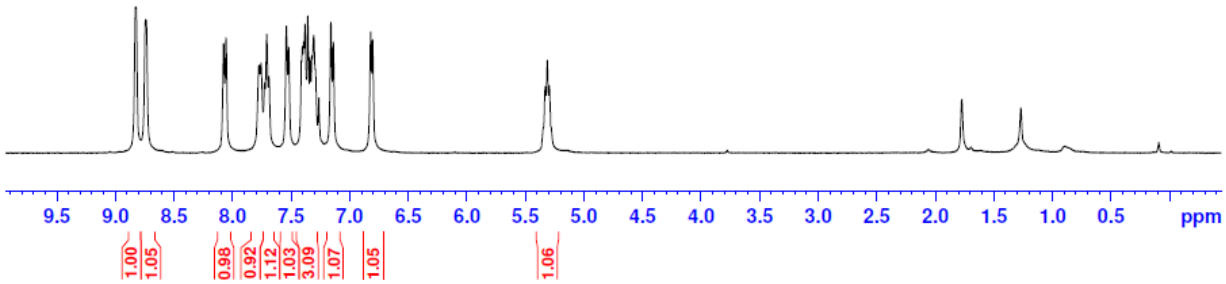
S10a

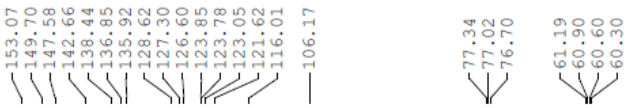


^{1}H NMR (400 MHz, $CDCl_3$)

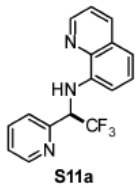


S11a

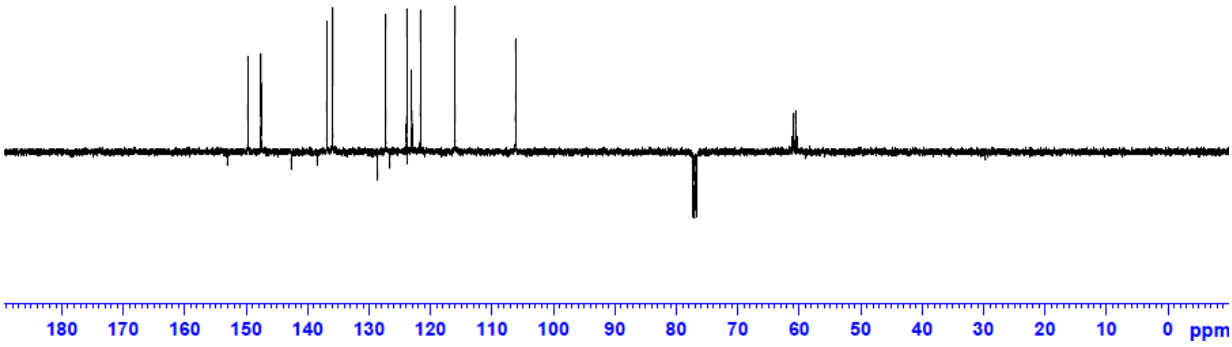




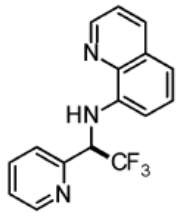
^{13}C NMR (100 MHz, $CDCl_3$)



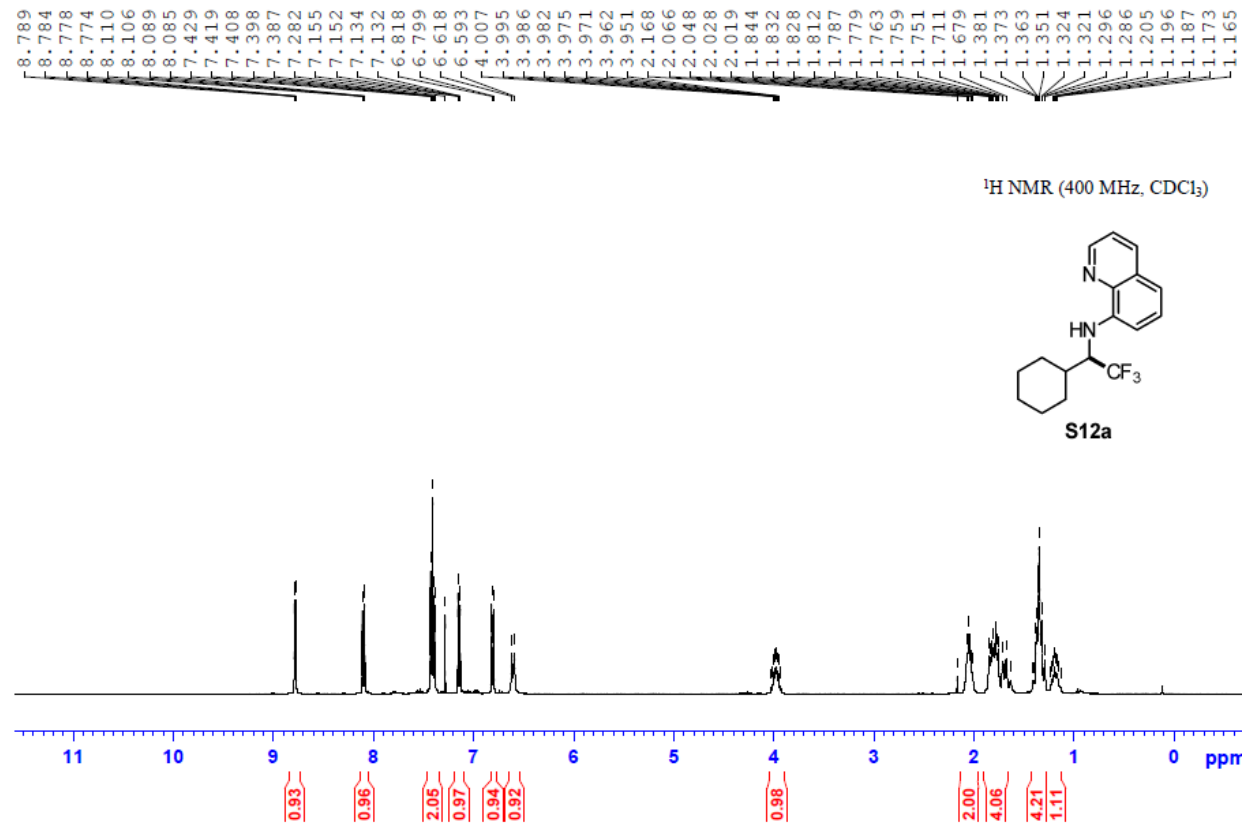
S11a

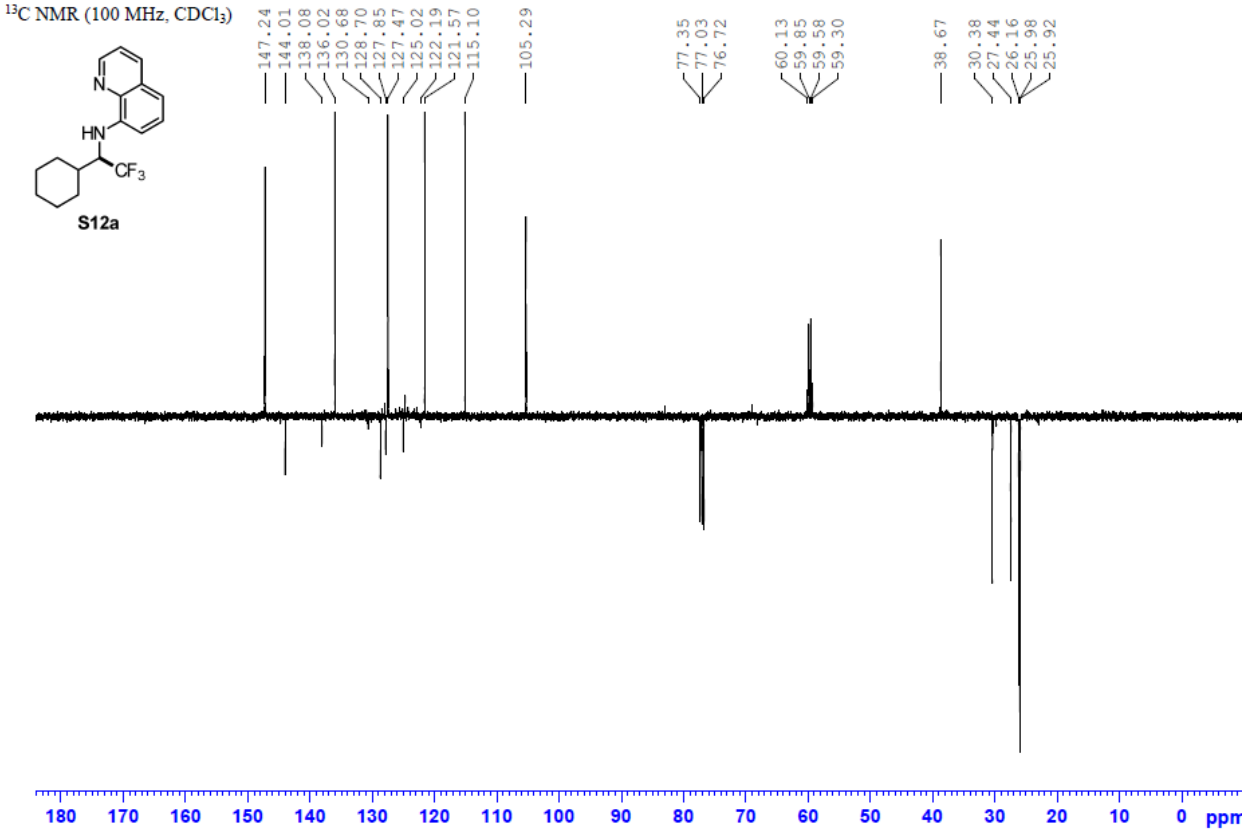


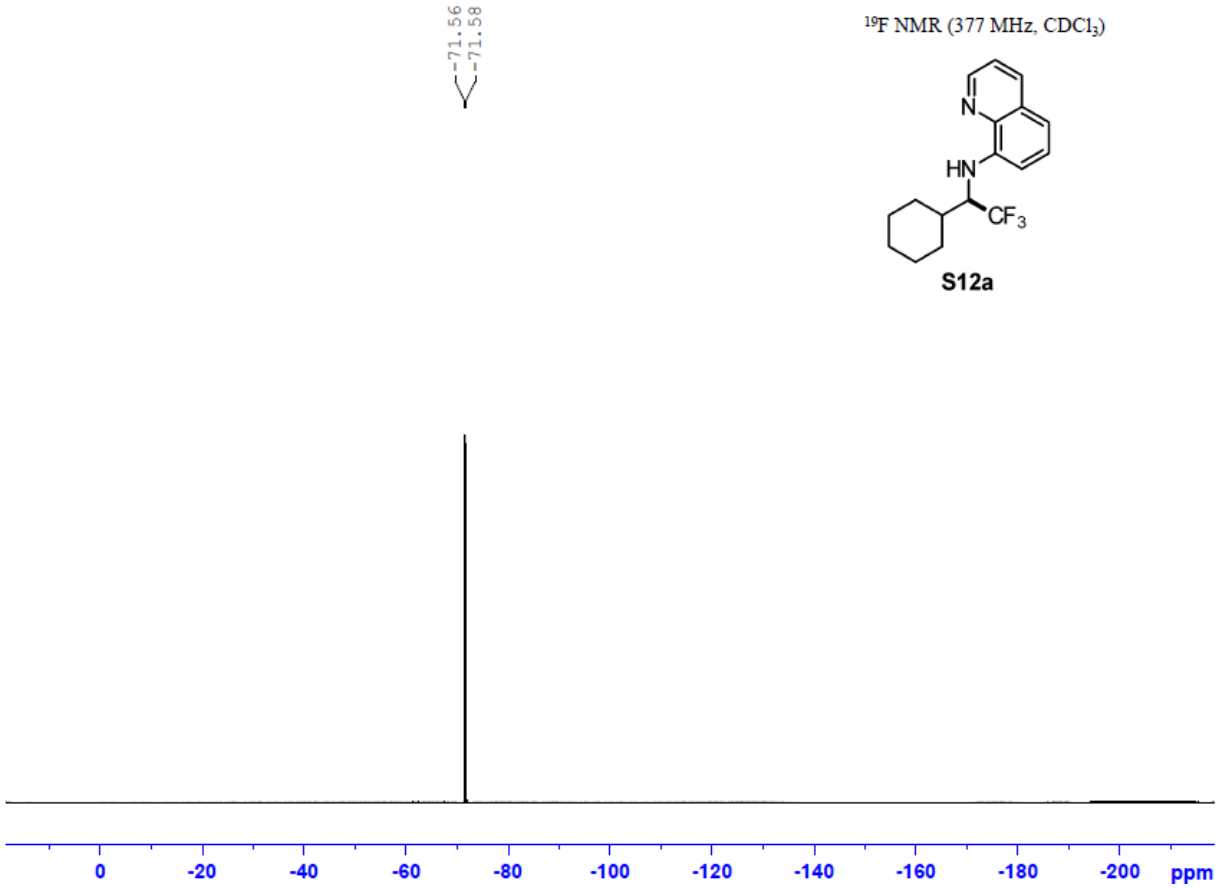
^{19}F NMR (377 MHz, $CDCl_3$)

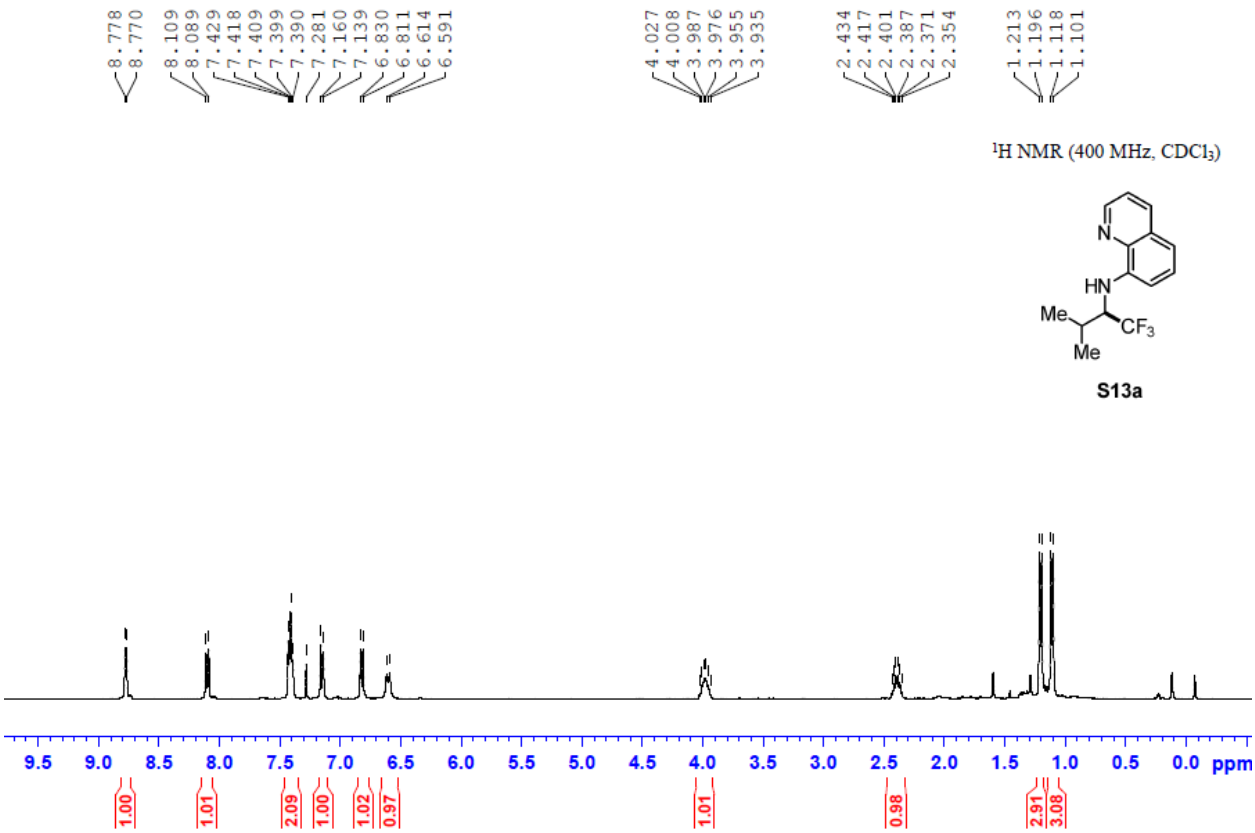


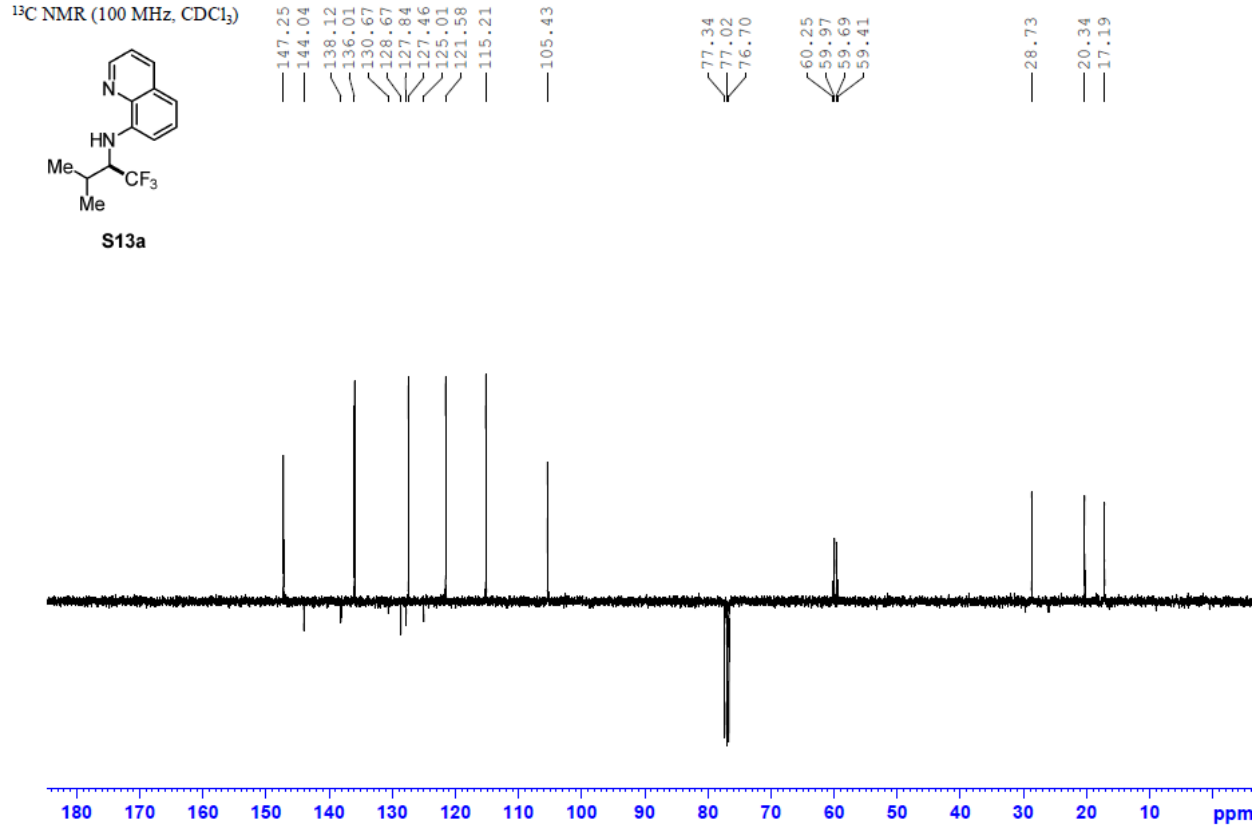
S11a

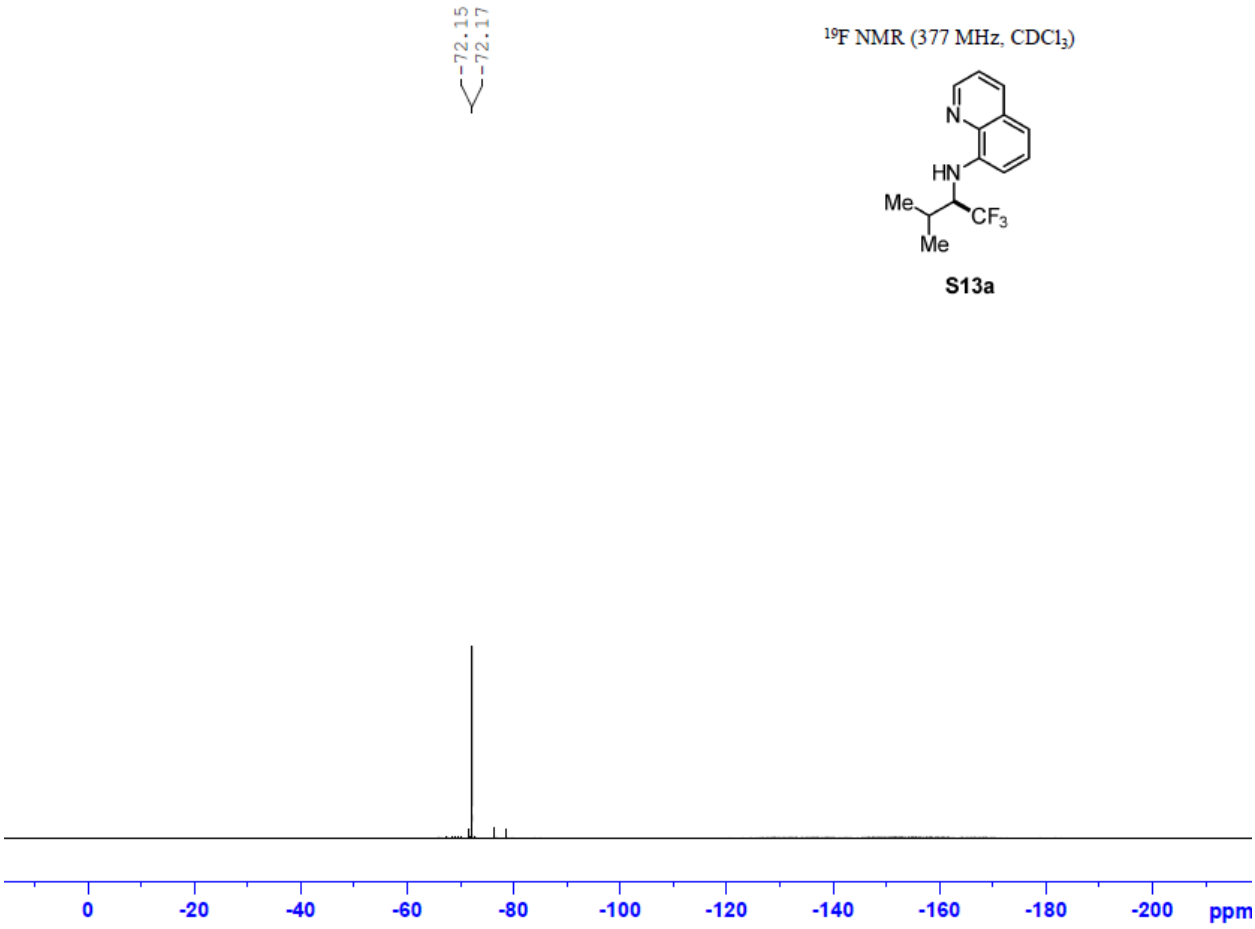




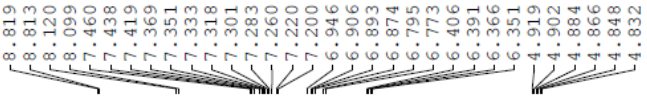




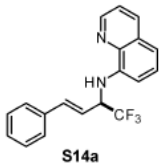




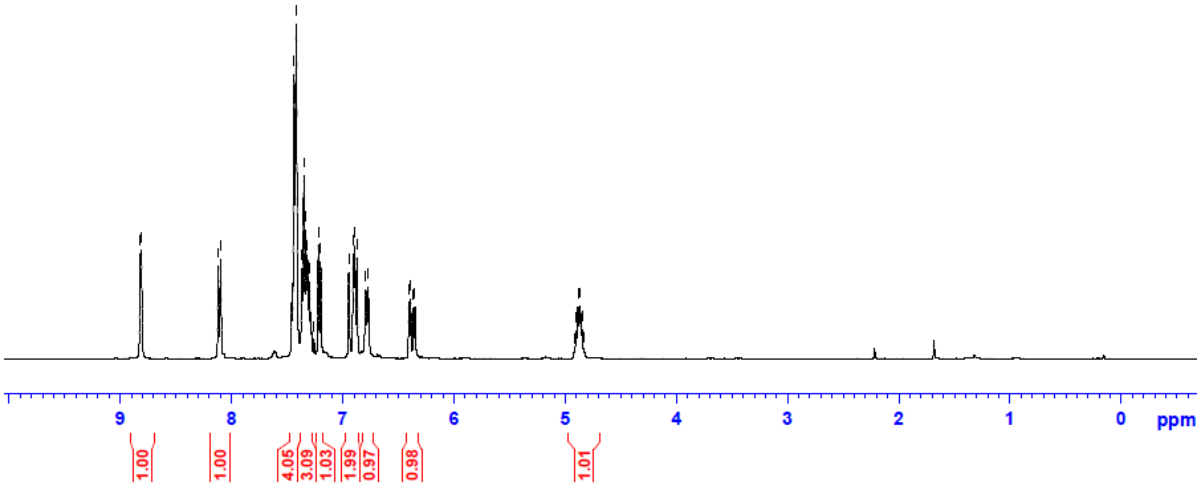
S13a

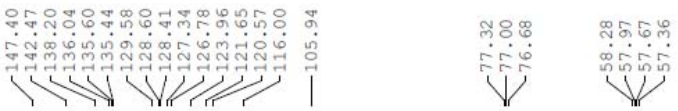


^{1}H NMR (400 MHz, $CDCl_3$)

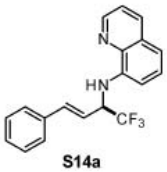


S14a

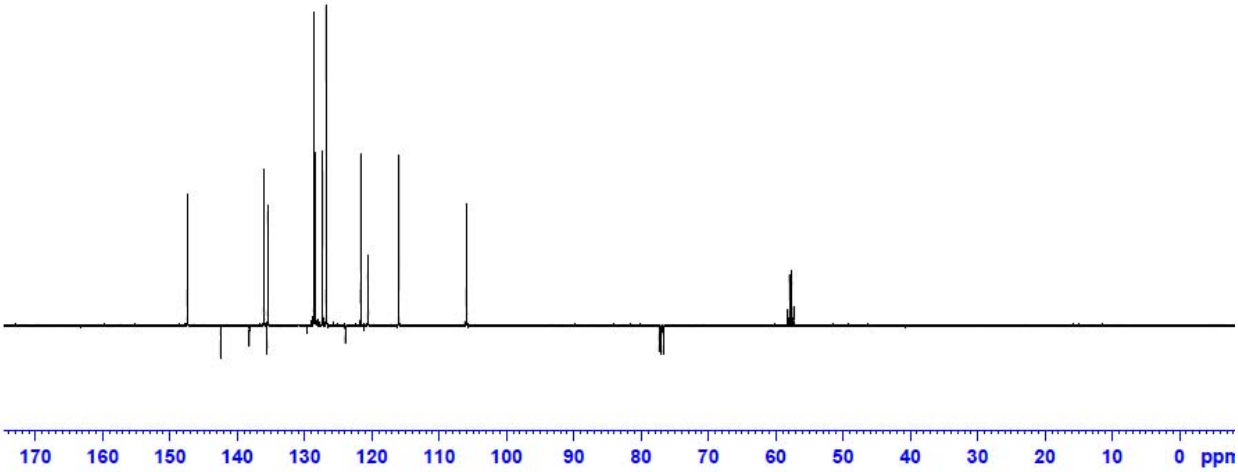


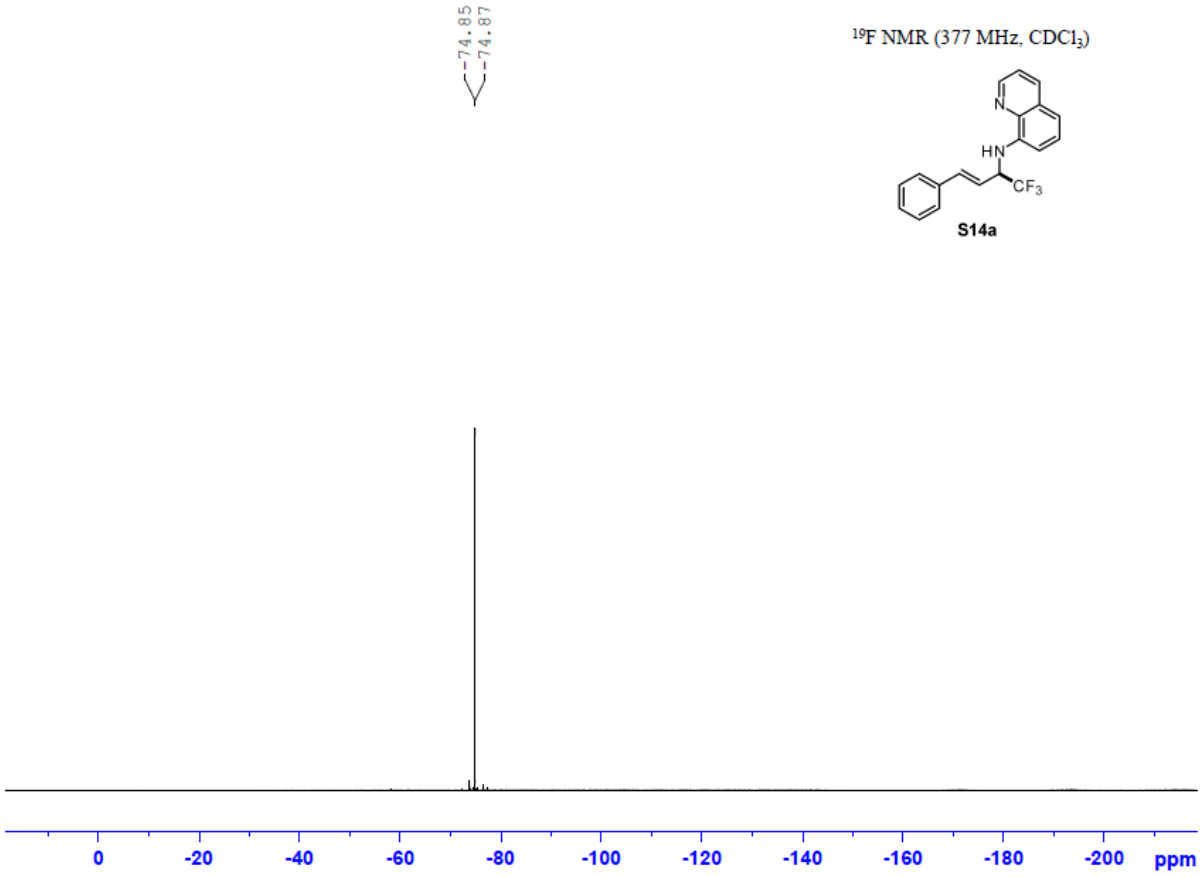


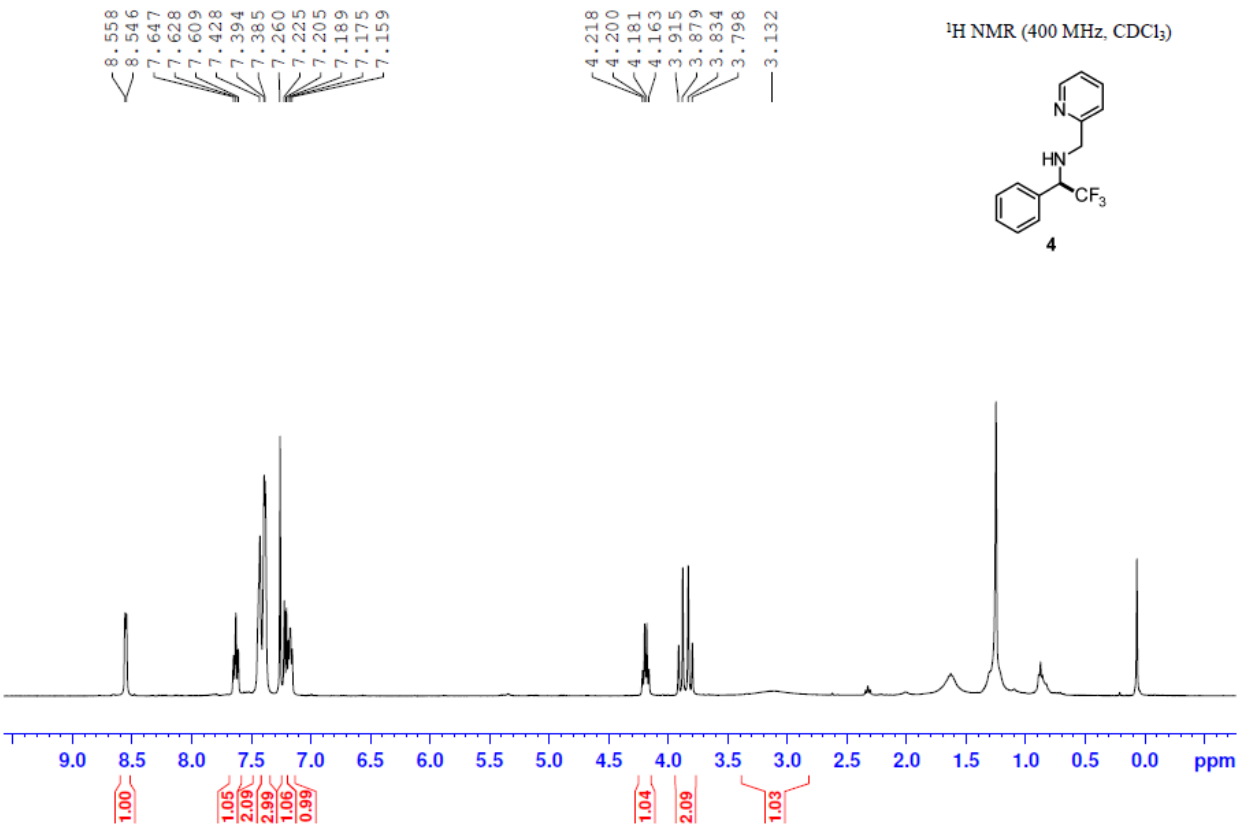
^{13}C NMR (100 MHz, $CDCl_3$)

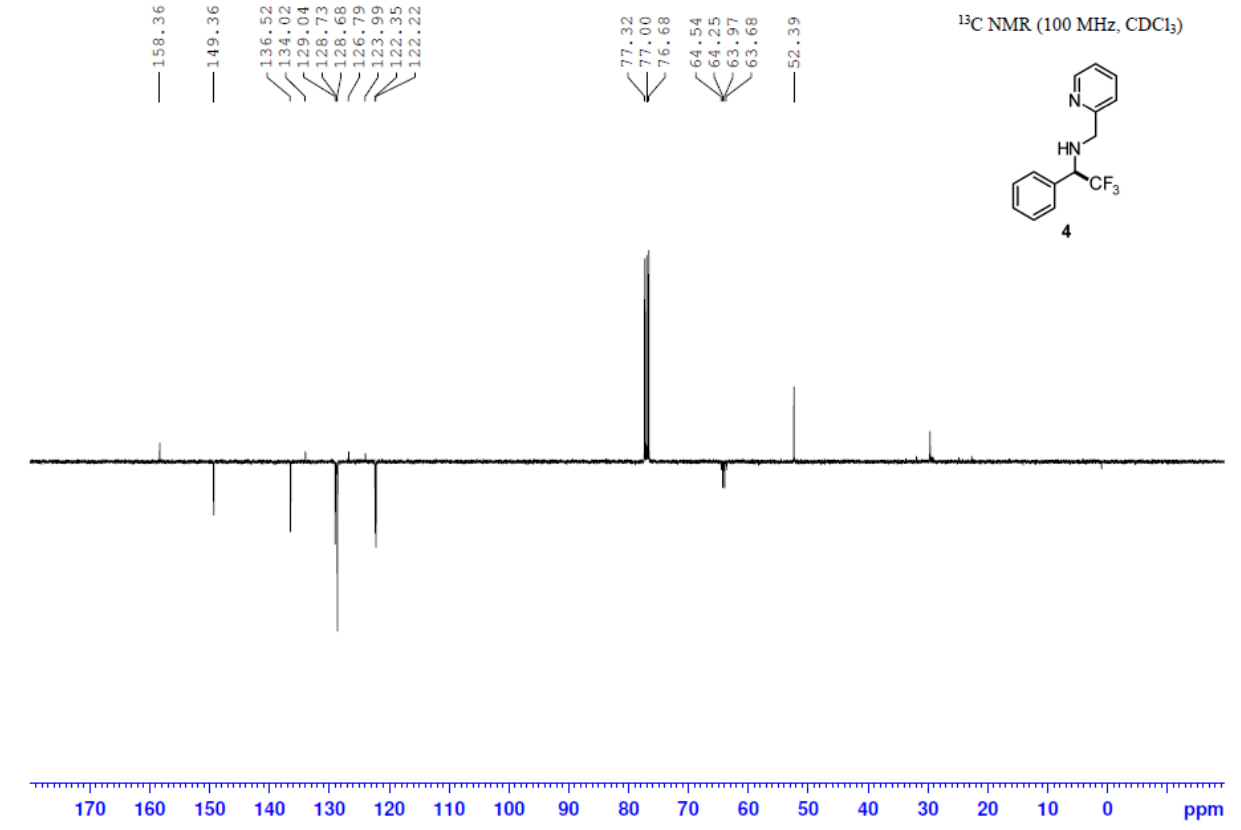


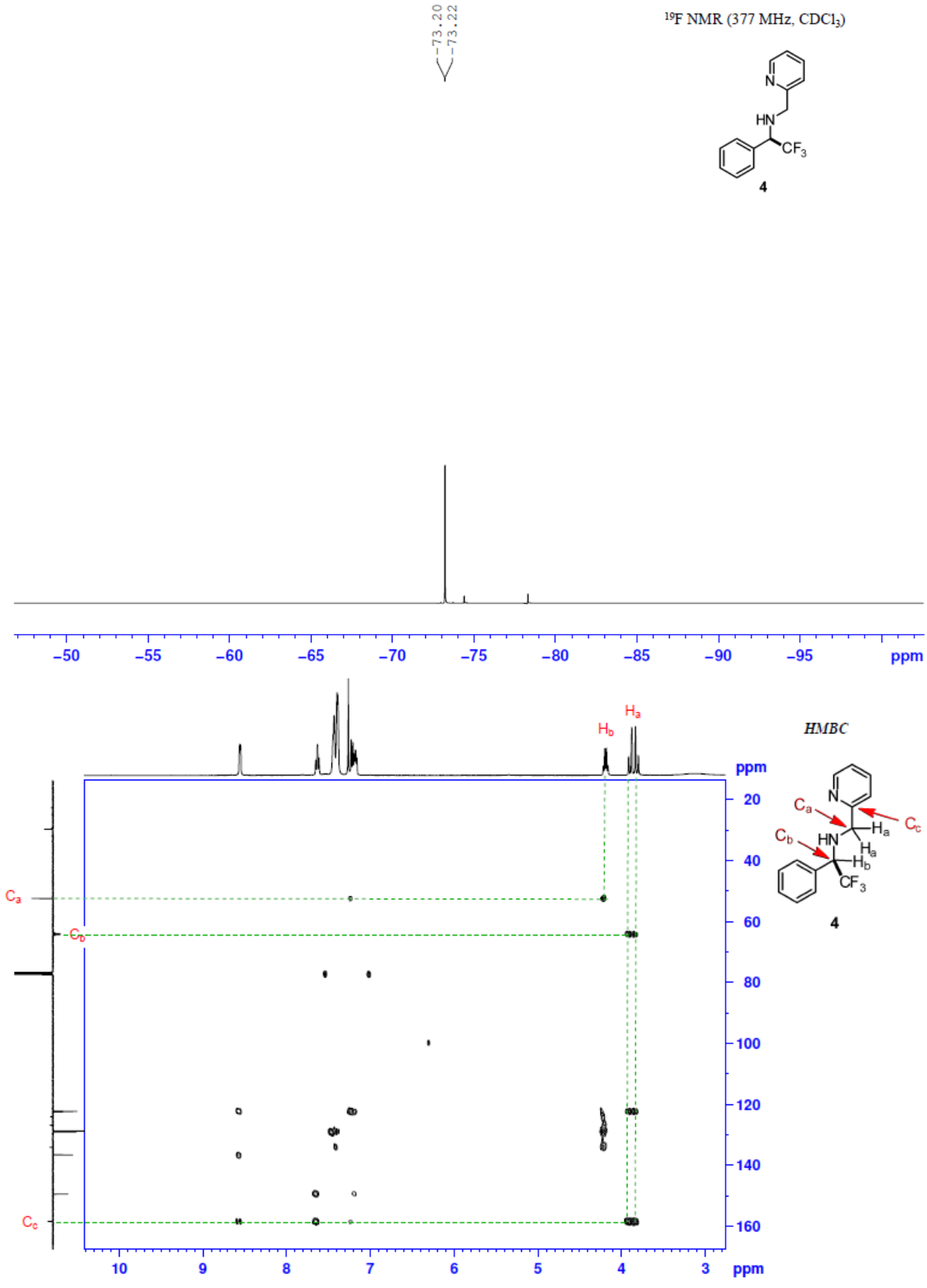
S14a

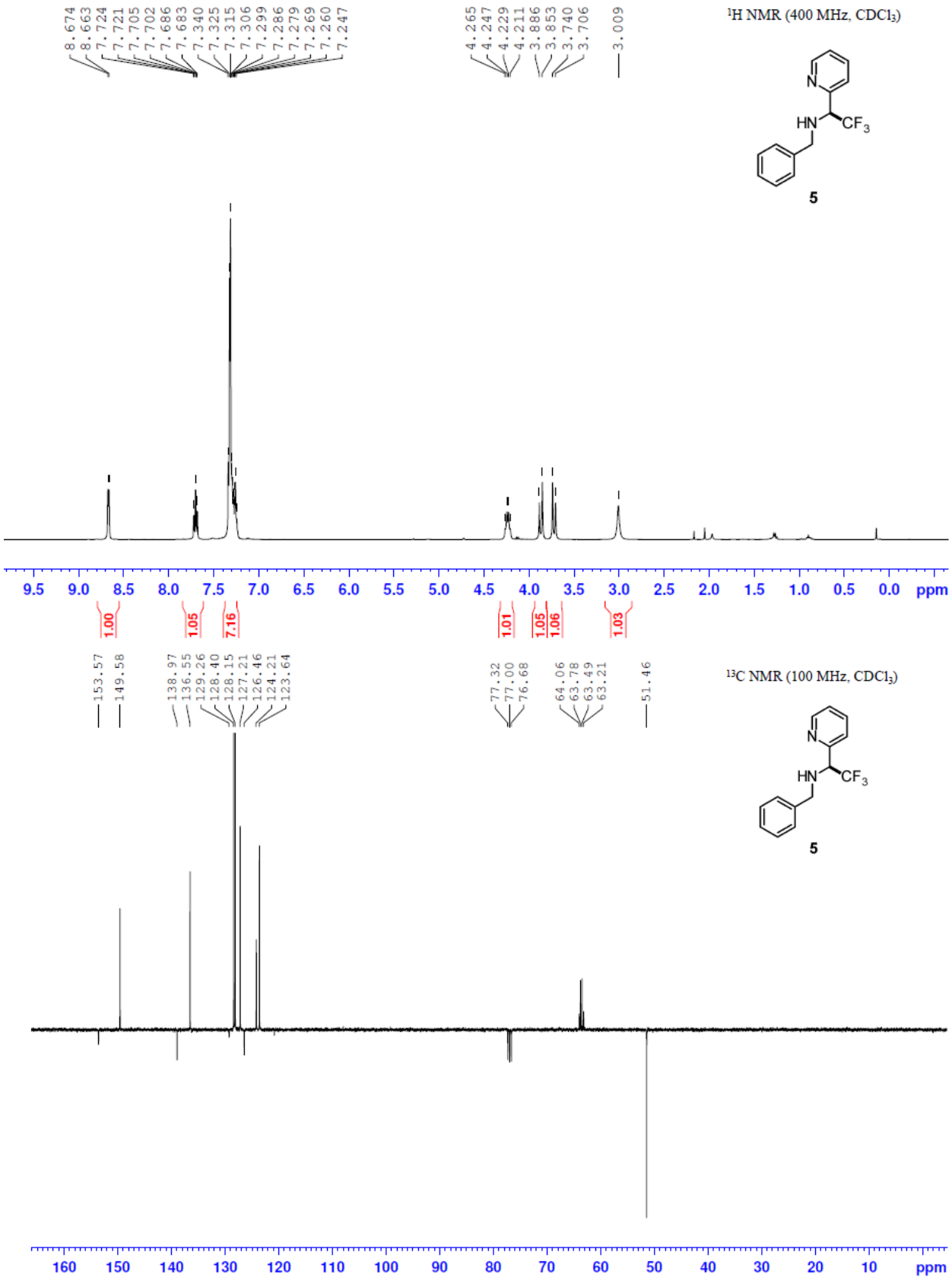


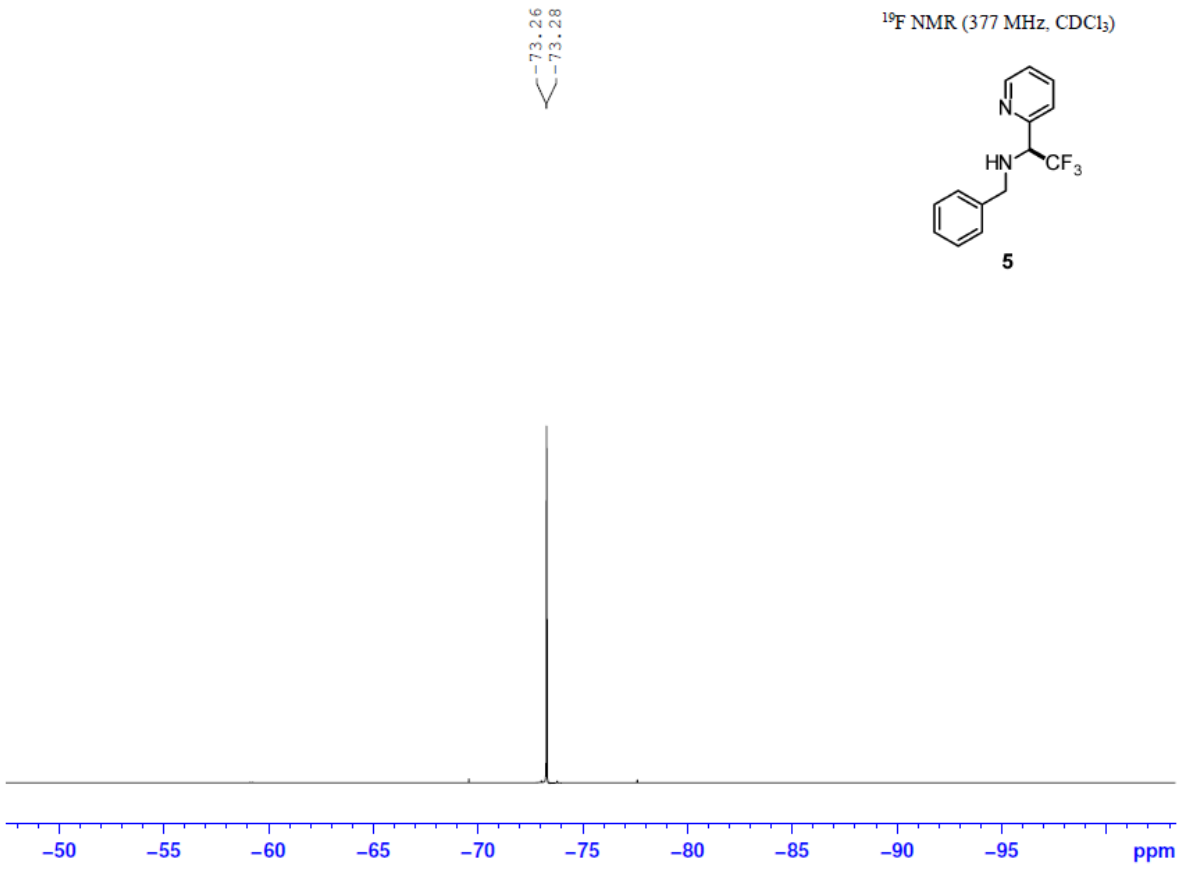


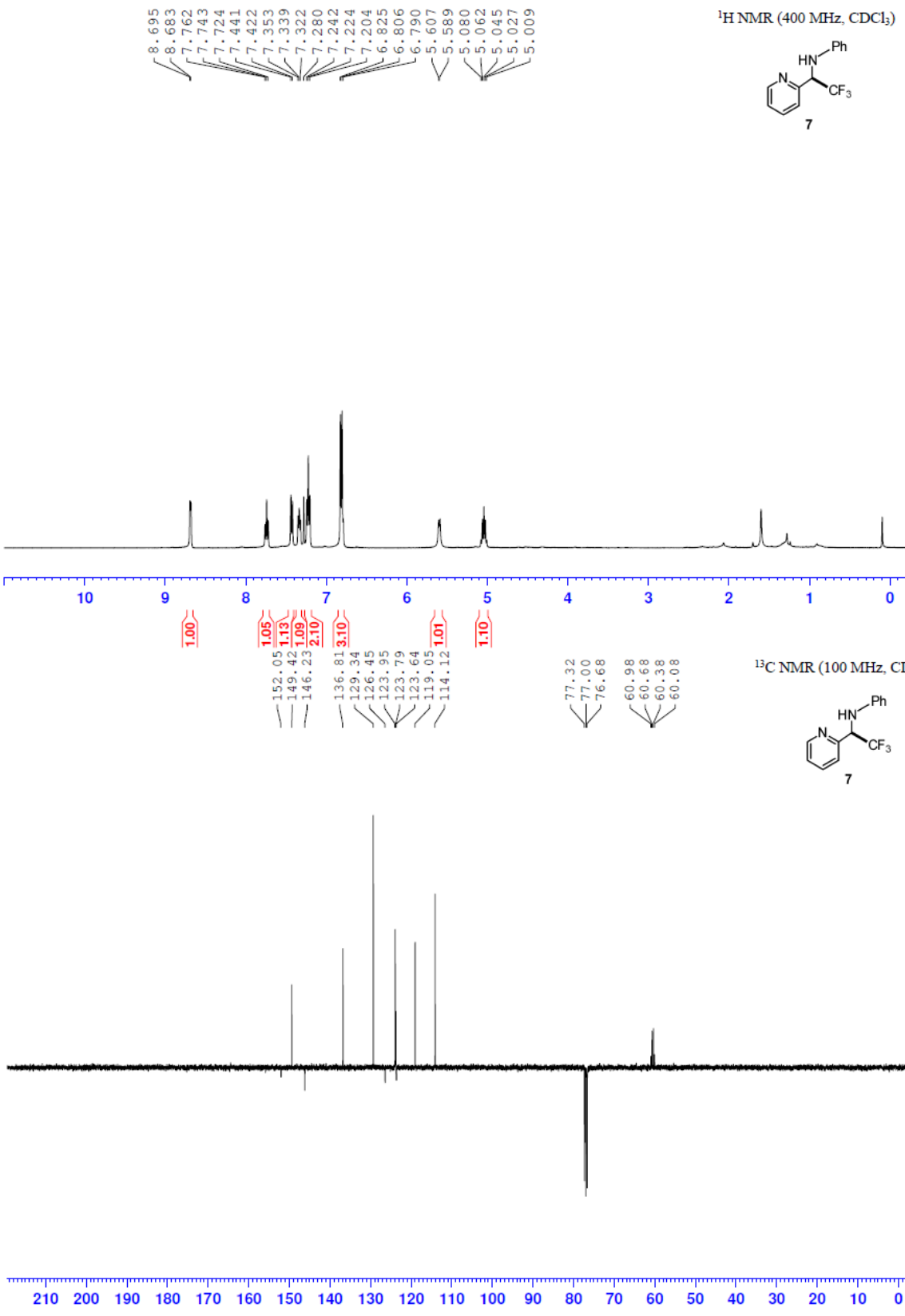


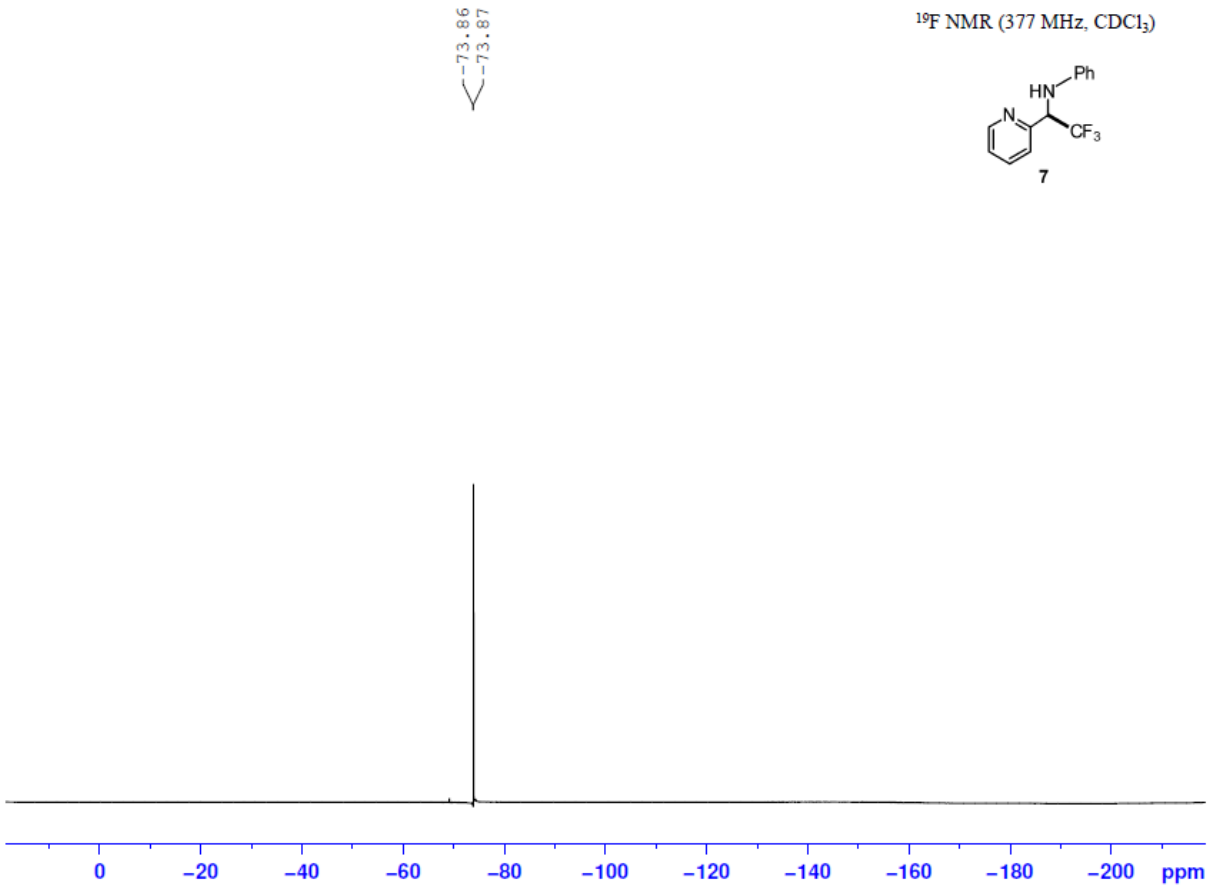


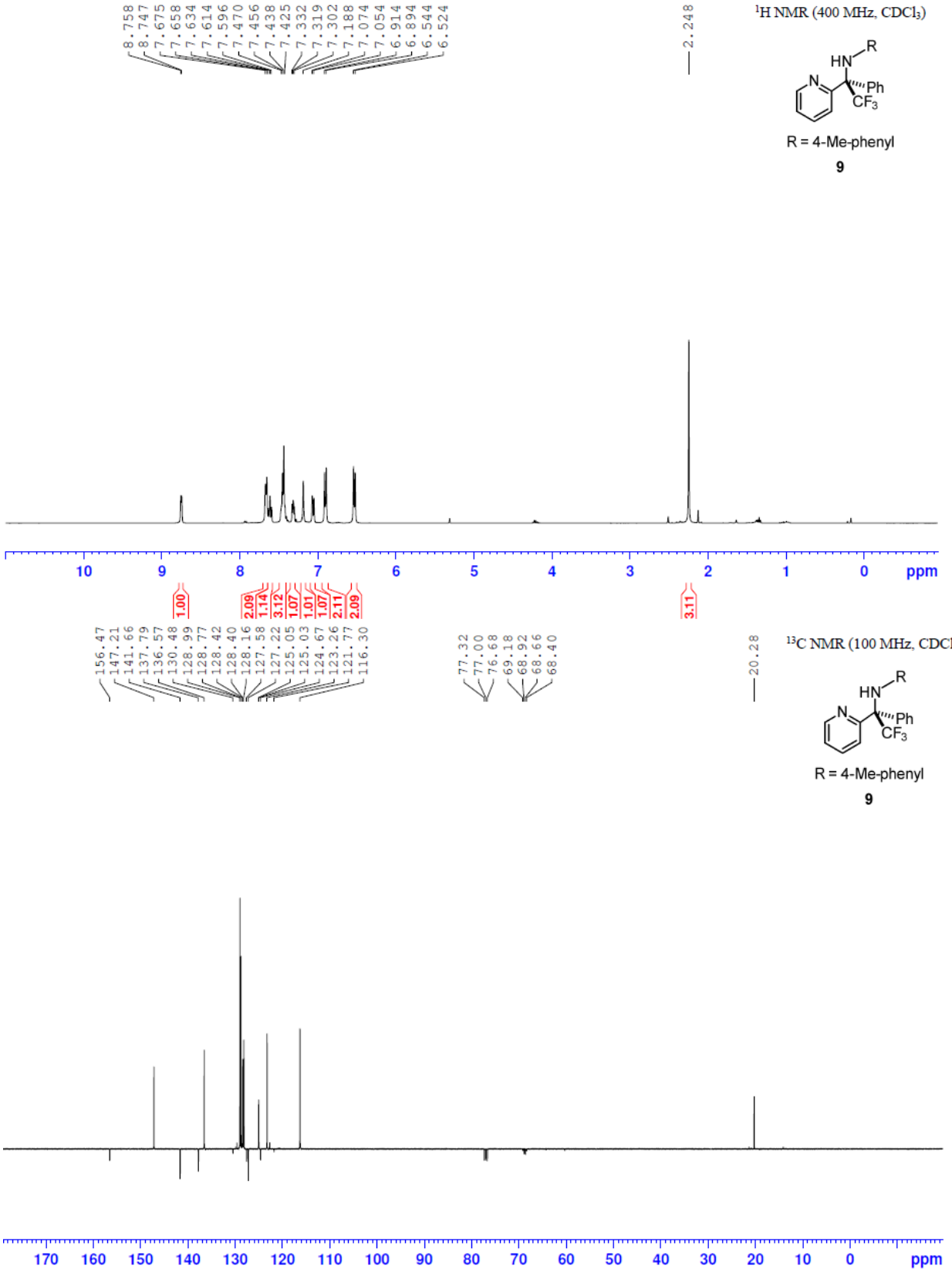


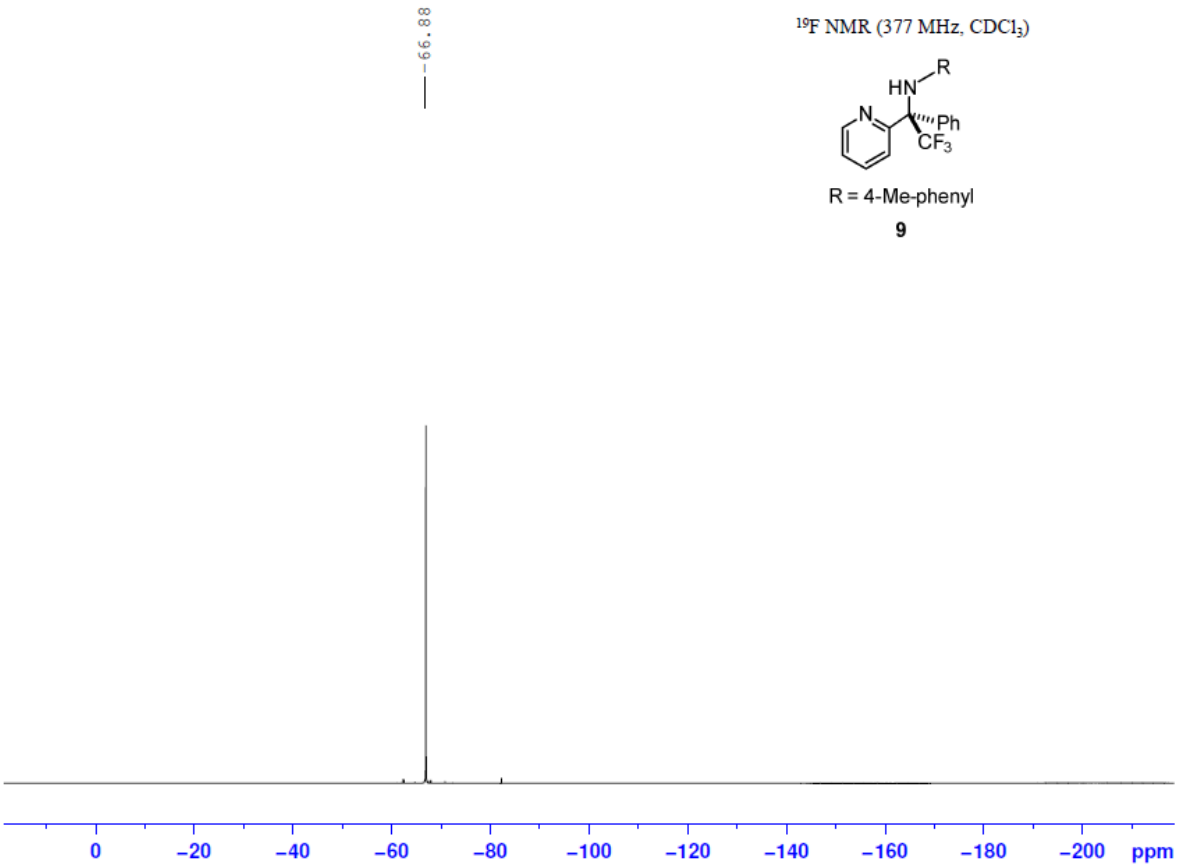

8.674
8.663
7.724
7.721
7.705
7.702
7.686
7.683
7.340
7.325
7.315
7.306
7.299
7.286
7.279
7.269
7.260
7.247
4.265
4.247
4.229
4.211
3.886
3.853
3.740
3.706
3.009
1H NMR (400 MHz, CDCl3)
N
HN
CF3
5
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00
1.05
7.16
1.01
1.05
1.06
1.03
153.57
149.58
138.97
136.55
129.26
128.40
128.15
127.21
126.46
124.21
123.64
77.32
77.00
76.68
64.06
63.78
63.49
63.21
51.46
13C NMR (100 MHz, CDCl3)
N
HN
CF3
5
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

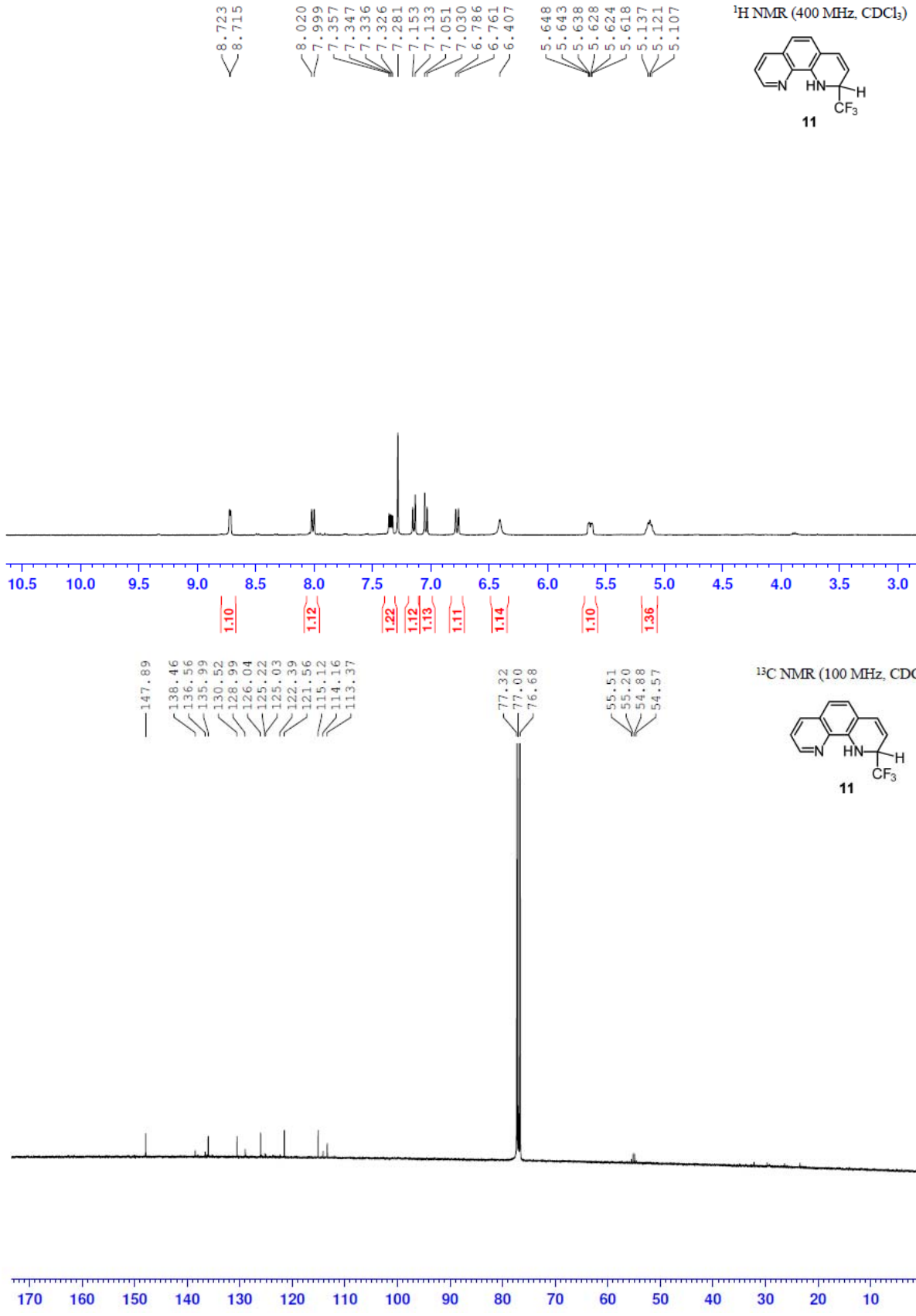



8.695
8.683
7.762
7.743
7.724
7.441
7.422
7.353
7.339
7.322
7.280
7.242
7.224
7.204
6.825
6.806
6.790
5.607
5.589
5.080
5.062
5.045
5.027
5.009
1H NMR (400 MHz, CDCl3)
Ph
HN
N
CF3
7
10 9 8 7 6 5 4 3 2 1 0 ppm
1.00
1.05
1.13
1.09
2.10
3.10
1.01
1.10
152.05
149.42
146.23
136.81
129.34
126.45
123.95
123.79
123.64
119.05
114.12
77.32
77.00
76.68
60.98
60.68
60.38
60.08
13C NMR (100 MHz, CDCl3)
Ph
HN
N
CF3
7
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm




8.758
8.747
7.675
7.658
7.634
7.614
7.596
7.470
7.456
7.438
7.425
7.332
7.319
7.302
7.188
7.074
7.054
6.914
6.894
6.544
6.524
2.248
1H NMR (400 MHz, CDCl3)
HN
R
N
Ph
CF3
R = 4-Me-phenyl
9
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
2.09
1.14
3.12
1.07
1.01
1.07
2.11
2.09
3.11
156.47
147.21
141.66
137.79
136.57
130.48
128.99
128.77
128.42
128.40
128.16
127.58
127.22
125.05
125.03
124.67
123.26
121.77
116.30
77.32
77.00
76.68
69.18
68.92
68.66
68.40
20.28
13C NMR (100 MHz, CDCl3)
HN
R
N
Ph
CF3
R = 4-Me-phenyl
9
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm




8.723
8.715
8.020
7.999
7.357
7.347
7.336
7.326
7.281
7.153
7.133
7.051
7.030
6.786
6.761
6.407
5.648
5.643
5.638
5.628
5.624
5.618
5.137
5.121
5.107
1H NMR (400 MHz, CDCl3)
N
HN
H
CF3
11
10.5 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 ppm
1.10
1.12
1.22
1.12
1.13
1.11
1.14
1.10
1.36
147.89
138.46
136.56
135.99
130.52
128.99
126.04
125.22
125.03
122.39
121.56
115.12
114.16
113.37
77.32
77.00
76.68
55.51
55.20
54.88
54.57
13C NMR (100 MHz, CDCl3)
N
HN
H
CF3
11
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm