Defluorinative Multicomponent Cascade Reaction of Trifluoromethylarenes via Photoexcited Palladium Catalysis

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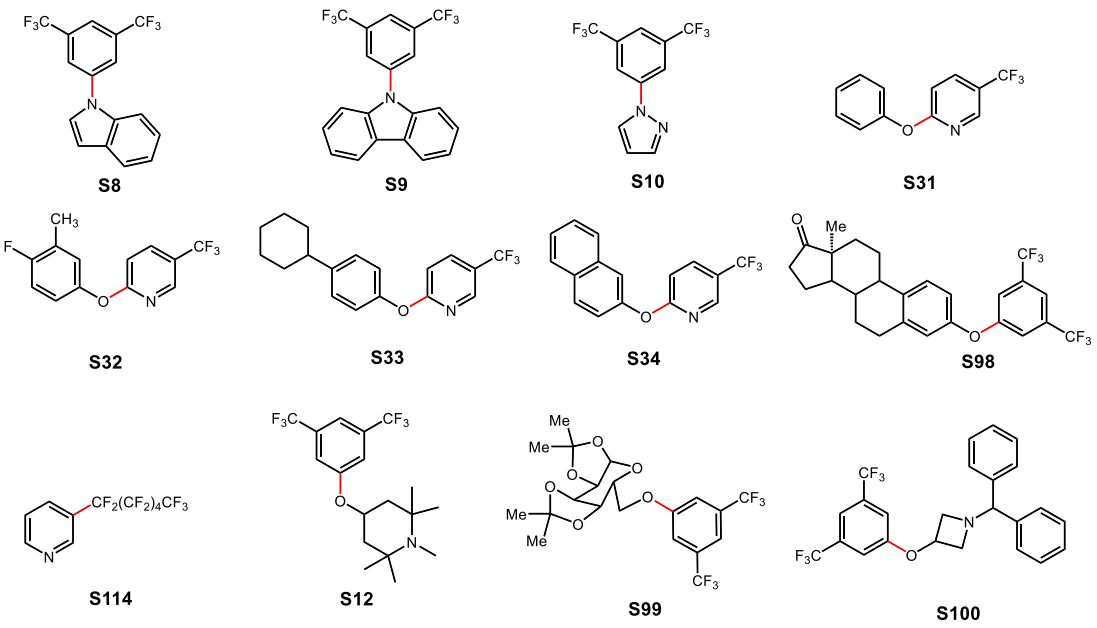
1. General Information

Commercial reagents were purchased from Adamas-Beta, Bide Pharmatech, J&K, Energy Chemical. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator using a water bath. Chromatographic purification of products was accomplished using forced-flow chromatography on silica gel (Fluka, 230–400 mesh). Thin-layer chromatography (TLC) was performed on Huanghai 0.25 mm silica gel F-254 plates. ^{1}H NMR spectra were recorded on a Bruker UltraShield Plus Avance III 400 MHz and are internally referenced to residual protic $CDCl_3$ (7.26 ppm) (Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets), coupling constant (Hz), and integration. ^{13}C NMR spectra were recorded on a Bruker UltraShield Plus Avance III 400 MHz (101 MHz) and data are reported in terms of chemical shift relative to $CDCl_3$ (77.16 ppm). ^{19}F NMR spectra were recorded on a Bruker UltraShield Plus Avance III 400 MHz (376 MHz). ^{31}P NMR spectra were recorded on a Bruker UltraShield Plus Avance III 400 MHz (162 MHz). High Resolution Mass Spectra were obtained on Thermo Fisher Exactive Plus Orbitrap Mass Spectrum (ESI), Orbitrap Exploris GC Mass Spectrum (EI) or Waters Synapt-G2-Si Mass Spectrum (APCI). Ultraviolet-Visible absorption spectra was acquired using Agilent Cary 60. Steady-state emission spectra and Quantum yield were acquired using a Hitachi F-4700.

2. Synthesis and characterization of starting materials

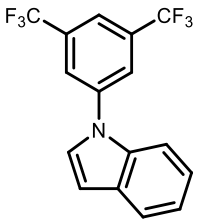


Scheme S1. (Het)Aromatic Fluoroalkyl-Contained Structures.

The corresponding (het)aromatic fluoroalkyl-contained compounds S**8**-S**10** were synthesized according to the literature.[1] To an 40 mL vial equipped with a stir bar was added 1-bromo-3,5-bis(trifluoromethyl)benzene (2.9 g, 10 mmol, 1.0 equiv.),

N-heterocycle (1.8 g, 15 mmol, 1.5 equiv.), Cu_2O (42.9 mg, 0.3 mmol, 0.03 equiv.), *N*,*N*'-bis(furan-2-ylmethyl)oxamide (BFMO) (74.5 mg, 0.3 mmol, 0.03 equiv.), K_3PO_4 (4.23 g, 20 mmol, 2.0 equiv.) and 10 mL DMSO followed by bubbling with N_2 for 10 min at room temperature. After sealing the vial with parafilm, the reaction was carried out in 120℃ with vigorous stirring for 24 h. The reaction mixture was cooled to ambient temperature and diluted with 50 mL water followed by the extraction with ethyl acetate (15 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography on silica gel to afford the products.

1-(3,5-bis(trifluoromethyl)phenyl)-1*H*-indole (S8)



Purified by flash chromatography (PE:EA = 20:1) on silica gel to afford the title compound (2.5 g, 75% yield) as a white solid.

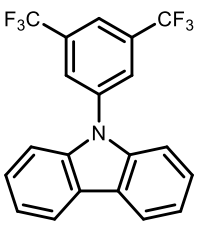
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 2H), 7.84 (s, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.53 (d, *J* = 8.2 Hz, 1H), 7.35 (d, *J* = 3.4 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.23 (t, *J* = 7.4 Hz, 1H), 6.77 (d, *J* = 3.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 141.45, 135.55, 133.51 (q, *J* = 33.9 Hz), 129.95, 127.24, 124.06 – 123.98 (m), 123.64, 123.07 (q, *J* = 274.7 Hz), 121.86, 121.65, 120.28 – 119.48 (m), 109.90, 106.05.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.96.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{10}F_6N$ ($[M+H]^+$): 330.0712, found: 330.0708.

9-(3,5-bis(trifluoromethyl)phenyl)-9*H*-carbazole (S9)



Purified by flash chromatography (PE:EA = 20:1) on silica gel to afford the title compound (2.1 g, 56% yield) as a white solid.

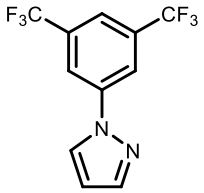
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (dt, *J* = 7.7, 1.0 Hz, 2H), 8.10 (s, 2H), 7.98 (s, 1H), 7.50 – 7.46 (m, 2H), 7.41 – 7.35 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 140.20, 139.81, 133.79 (q, *J* = 34.0 Hz), 127.15, 126.74, 124.14, 123.06 (q, *J* = 274.7 Hz), 121.35, 120.95 – 120.86 (m), 109.22.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.88.

HRMS (ESI-TOF) m/z calcd. for $C_{20}H_{12}F_6N$ ($[M+H]^+$): 380.0868, found: 380.0865.

1-(3,5-bis(trifluoromethyl)phenyl)-1*H*-pyrazole (S10)



Purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (1.8 g, 80% yield) as a yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 1.6 Hz, 2H), 8.03 (d, *J* = 2.6 Hz, 1H), 7.86 – 7.70 (m, 2H), 6.56 (t, *J* = 2.2 Hz, 1H).

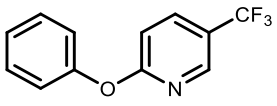
^{13}C NMR (101 MHz, $CDCl_3$) δ 142.64, 141.26, 133.24 (q, *J* = 33.9 Hz), 126.95, 123.07 (q, *J* = 273.7 Hz), 119.68 (p, *J* = 3.8 Hz), 118.90 – 118.82 (m), 109.36.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.09.

HRMS (ESI-TOF) m/z calcd. for $C_{11}H_7F_6N_2$ ($[M+H]^+$): 281.0508, found: 281.0499.

The corresponding (het)aromatic fluoroalkyl-contained compounds **31**-**34**, **98** were synthesized according to the literature.[2] To an 40 mL vial equipped with a stir bar was added (het)aromatic bromine (10 mmol, 1.0 equiv.), phenol (15 mmol, 1.5 equiv.), CuI (19.0 mg, 0.1 mmol, 0.01 equiv.), *N*,*N*'-bis([1,1'-biphenyl]-2-yl)ethanediamide (BPPO) (39.2 mg, 0.1 mmol, 0.01 equiv.), K_3PO_4 (4.23 g, 20 mmol, 2.0 equiv.) and 10 mL DMF followed by bubbling with N_2 for 10 min at room temperature. After sealing the vial with parafilm, the reaction was carried out in 110℃ with vigorous stirring for 24 h. The reaction mixture was cooled to ambient temperature and diluted with 50 mL water followed by the extraction with ethyl acetate (15 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography on silica gel to afford the products.

2-phenoxy-5-(trifluoromethyl)pyridine (S31)



Purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (1.9 g, 80% yield) as a pale yellow oil.

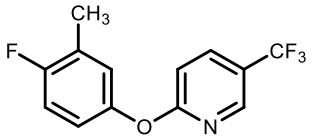
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.83 (dd, *J* = 8.8, 2.6 Hz, 1H), 7.42 – 7.37 (m, 2H), 7.22 (td, *J* = 7.5, 1.6 Hz, 1H), 7.15 – 7.12 (m, 2H), 6.95 (d, *J* = 8.7 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.93, 153.31, 145.51 (q, *J* = 4.4 Hz), 136.68 (q, *J* = 3.2 Hz), 129.84, 125.51, 123.84 (q, *J* = 272.7 Hz), 121.55, 121.54 (q, *J* = 33.2 Hz), 111.37.

^{19}F NMR (376 MHz, $CDCl_3$) δ -61.66.

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_9F_3NO$ ($[M+H]^+$): 240.0631, found: 240.0625.

2-(4-fluoro-3-methylphenoxy)-5-(trifluoromethyl)pyridine (S32)



Purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (2.4 g, 88% yield) as a yellow solid.

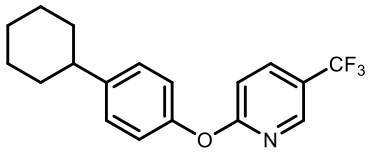
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1H), 7.90 (dd, *J* = 8.7, 2.6 Hz, 1H), 7.07 – 6.97 (m, 3H), 6.95 – 6.91 (m, 1H), 2.30 (d, *J* = 2.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.05, 158.77 (d, *J* = 242.6 Hz), 148.65 (d, *J* = 3.0 Hz), 145.61 (q, *J* = 4.4 Hz), 136.84 (q, *J* = 3.3 Hz), 126.64 (d, *J* = 19.2 Hz), 124.39 (d, *J* = 5.4 Hz), 123.83 (q, *J* = 272.7 Hz), 121.69 (q, *J* = 33.4 Hz), 120.25 (d, *J* = 8.4 Hz), 116.09 (d, *J* = 24.5 Hz), 111.41, 14.89 (d, *J* = 3.4 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -61.68, -121.35 – -121.40 (m).

HRMS (ESI-TOF) m/z calcd. for $C_{13}H_{10}F_4NO$ ($[M+H]^+$): 272.0693, found: 272.0690.

2-(4-cyclohexylphenoxy)-5-(trifluoromethyl)pyridine (S33)



Purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (2.7 g, 85% yield) as a pale yellow solid.

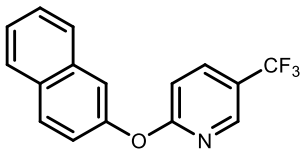
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 – 8.45 (m, 1H), 7.86 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.25 (d, *J* = 8.5 Hz, 2H), 7.07 – 7.05 (m, 2H), 6.97 (d, *J* = 8.7 Hz, 1H), 2.53 (tt, *J* = 8.5, 3.8 Hz, 1H), 1.92 – 1.84 (m, 4H), 1.78 – 1.73 (m, 1H), 1.47 – 1.34 (m, 4H), 1.30 – 1.23 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.19, 151.18, 145.67 (q, *J* = 4.3 Hz), 145.38, 136.70 (q, *J* = 3.2 Hz), 128.24, 123.88 (q, *J* = 272.7 Hz), 121.45 (q, *J* = 33.2 Hz), 121.18, 111.33, 44.13, 34.66, 27.01, 26.26.

^{19}F NMR (376 MHz, $CDCl_3$) δ -61.64.

HRMS (ESI-TOF) m/z calcd. for $C_{18}H_{19}F_3NO$ ($[M+H]^+$): 322.1413, found: 322.1409.

2-(naphthalen-2-yloxy)-5-(trifluoromethyl)pyridine (S34)



Purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (2.1 g, 72% yield) as a pale yellow solid.

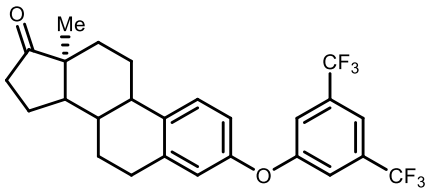
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.94– 7.87 (m, 3H), 7.82 (d, *J* = 7.3 Hz, 1H), 7.62 (d, *J* = 2.5 Hz, 1H), 7.54 – 7.47 (m, 2H), 7.31 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.07 (d, *J* = 8.7 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.09, 150.93, 145.69 (q, *J* = 4.3 Hz), 136.86 (q, *J* = 3.2 Hz), 134.27, 131.47, 129.98, 128.01, 127.70, 126.80, 125.79, 123.85 (q, *J* = 272.7 Hz), 121.76 (q, *J* = 33.2 Hz), 121.39, 118.25, 111.51.

^{19}F NMR (376 MHz, $CDCl_3$) δ -61.61.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{11}F_3NO$ ($[M+H]^+$): 290.0787, found: 290.0782.

(13*S*)-2-(3,5-bis(trifluoromethyl)phenoxy)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[a]phenanthren-17-one (S98)



Purified by flash chromatography (PE:EA = 10:1) on silica gel to afford the title compound (3.6 g, 80% yield) as a pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (s, 1H), 7.37 (s, 2H), 7.33 (d, *J* = 8.5 Hz, 1H), 6.84 (dd, *J* = 8.5, 2.7 Hz, 1H), 6.80 (d, *J* = 2.5 Hz, 1H), 2.94 – 2.90 (m, 2H), 2.53 (dd, *J* = 18.8, 8.7 Hz, 1H), 2.46 – 2.41 (m, 1H), 2.33 (td, *J* = 10.8, 4.2 Hz, 1H), 2.21 – 1.97 (m, 4H), 1.70 – 1.46 (m, 6H), 0.95 (s, 3H).

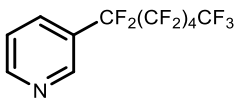
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.21, 152.92, 139.25, 137.04, 133.19 (q, *J* = 33.7 Hz), 127.41, 123.14 (q, *J* = 272.7 Hz), 120.15, 117.81 (d, *J* = 3.7 Hz), 117.35, 116.47 – 115.21 (m), 50.60, 48.11, 44.29, 38.19, 35.99, 31.71, 29.61, 26.46, 25.95, 21.74, 14.00.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.96.

HRMS (ESI-TOF) m/z calcd. for $C_{26}H_{24}F_6NaO_2$ ($[M+Na]^+$): 505.1578, found: 505.1573.

The corresponding (het)aromatic fluoroalkyl-contained compounds **114** were synthesized as the following procedure: to an 40 mL vial equipped with a stir bar was added 3-iodopyridine (2.1 g, 10 mmol, 1.0 equiv.), Cu powder (1.3 g, 20 mmol, 2.0 equiv.), 2,2'-bipyridine (124.9 mg, 0.8 mmol, 0.08 equiv.) and 10 mL DMSO followed by bubbling with N_2 for 10 min at room temperature. Perfluoro-1-iodohexane (6.9 g, 15 mmol, 1.5 equiv.) was syringed into the reaction vessel before sealing with parafilm. The reaction was carried out in 100℃ for 54 h. The reaction mixture was cooled to ambient temperature and diluted with 50 mL water followed by the extraction with ethyl acetate (15 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography on silica gel to afford the products.

3-(perfluorohexyl)pyridine (S114)



Purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (3.0 g, 75% yield) as a pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 – 8.76 (m, 2H), 7.85 – 7.81 (m, 1H), 7.41 – 7.36 (m, 1H).

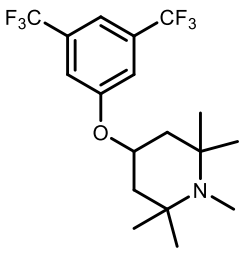
^{13}C NMR (101 MHz, $CDCl_3$) δ 153.21 (t, *J* = 1.9 Hz), 148.13 (td, *J* = 7.0, 3.6 Hz), 134.66 (t, *J* = 6.5 Hz), 125.45 (t, *J* = 24.5 Hz), 123.58 – 121.64 (m), 123.33, 118.40 (dt, *J* = 74.4, 32.7 Hz), 115.69 (dt, *J* = 43.5, 32.7 Hz), 114.09 – 112.59 (m), 111.70 – 110.14 (m), 109.16 – 107.44 (m).

^{19}F NMR (376 MHz, $CDCl_3$) δ -81.49 (t, *J* = 10.2 Hz), -112.04 (t, *J* = 14.8 Hz), -121.73 – -121.88 (m), -122.22 – -122.33 (m), -123.16 – -123.29 (m), -126.57 – -126.74 (m).

HRMS (ESI-TOF) m/z calcd. for $C_{11}H_5F_{13}N$ ($[M+H]^+$): 398.0209, found: 398.0203.

The corresponding (het)aromatic fluoroalkyl-contained compounds **12, 99, 100** were synthesized according to the literature.[4] To an 40 mL vial equipped with a stir bar was added 1-bromo-3,5-bis(trifluoromethyl)benzene (2.9 g, 10 mmol, 1.0 equiv.), alcohol (20 mmol, 2.0 equiv.), CuI (95.2 mg, 0.5 mmol, 0.05 equiv.), *N*,*N*'-bis(2-phenylethyl)ethanediamide (148.2 mg, 0.5 mmol, 0.05 equiv.), ^{t}BuONa (1.2 g, 12 mmol, 1.2 equiv.) and 10 mL DMF followed by bubbling with N_2 for 10 min at room temperature. After sealing the vial with parafilm, the reaction was carried out in 100℃ with vigorous stirring for 24 h. The reaction mixture was cooled to ambient temperature and diluted with 50 mL water followed by the extraction with ethyl acetate (15 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography on silica gel to afford the products.

4-(3,5-bis(trifluoromethyl)phenoxy)-1,2,2,6,6-pentamethylpiperidine (S12)



Purified by flash chromatography (PE:EA:Et_3N = 4:1:0.03) on silica gel to afford the title compound (2.5 g, 65% yield) as a pale yellow solid.

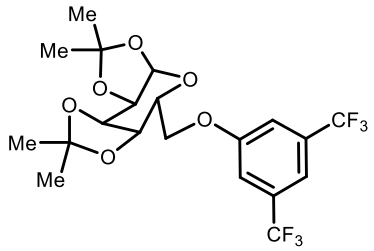
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (s, 1H), 7.28 (s, 2H), 4.60 (tt, *J* = 11.2, 4.0 Hz, 1H), 2.28 (s, 3H), 1.98 (dd, *J* = 12.3, 3.9 Hz, 2H), 1.61 (t, *J* = 11.7 Hz, 2H), 1.21 (s, 6H), 1.14 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.53, 133.00 (q, *J* = 33.2 Hz), 123.36 (q, *J* = 272.6 Hz), 115.82 (d, *J* = 4.2 Hz), 114.99 – 112.89 (m), 71.38, 55.41, 45.95, 33.10, 28.21, 21.21.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.13.

HRMS (ESI-TOF) m/z calcd. for $C_{18}H_{24}F_6NO$ ($[M+H]^+$): 384.1757, found: 384.1751.

(3a*S*,5*S*,5a*S*,8a*R*,8b*S*)-5-((3,5-bis(trifluoromethyl)phenoxy)methyl)-2,2,7,7-tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran (S99)



Purified by flash chromatography (PE:EA = 6:1) on silica gel to afford the title compound (2.9 g, 61% yield) as a pale yellow solid.

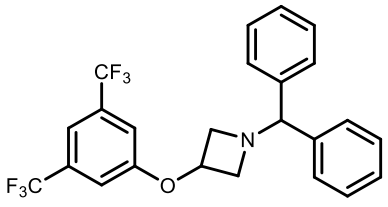
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.38 (s, 2H), 5.58 (d, *J* = 5.0 Hz, 1H), 4.68 (dd, *J* = 7.9, 2.5 Hz, 1H), 4.38 – 4.34 (m, 2H), 4.26 – 4.19 (m, 3H), 1.54 (s, 3H), 1.49 (s, 3H), 1.37 (s, 3H), 1.36 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.37, 132.89 (q, *J* = 33.4 Hz), 123.31 (q, *J* = 272.7 Hz), 115.33 (q, *J* = 4.0 Hz), 114.69 – 114.62 (m), 109.85, 109.03, 96.50, 71.03, 70.80, 70.64, 67.73, 66.31, 26.16, 26.11, 25.02, 24.55.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.04.

HRMS (ESI-TOF) m/z calcd. for $C_{20}H_{23}F_6O_6$ ($[M+H]^+$): 473.1393, found: 473.1387.

1-benzhydryl-3-(3,5-bis(trifluoromethyl)phenoxy)azetidine (S100)



Purified by flash chromatography (PE:EA:Et_3N = 4:1:0.03) on silica gel to afford the title compound (3.1 g, 69% yield) as a pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.42 (m, 5H), 7.28 (t, *J* = 7.5 Hz, 4H), 7.22 – 7.18 (m, 2H), 7.15 (s, 2H), 4.85 (p, *J* = 5.6 Hz, 1H), 4.43 (s, 1H), 3.75 – 3.71 (m, 2H), 3.16 – 3.13 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.91, 141.80, 133.14 (q, *J* = 33.5 Hz), 128.75, 127.54, 127.53, 123.19 (q, *J* = 272.8 Hz), 115.10 (q, *J* = 4.0 Hz), 114.84 (p, *J* = 3.9 Hz), 78.46, 67.12, 60.14.

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.06.

HRMS (ESI-TOF) m/z calcd. for $C_{24}H_{20}F_6NO$ ($[M+H]^+$): 452.1444, found: 452.1440.

3. General Procedure for Three Components Coupling

Procedure A: To an 8 mL vial equipped with a stir bar was added $Pd(PPh_3)_4$ (5.2 mg, 4.6 μmol, 0.015 equiv.), XantPhos (14.0 mg, 0.024 mmol, 0.08 equiv.), bis(2-methoxyphenyl)phenylphosphine (7.8 mg, 0.024 mmol, 0.08 equiv.), substituted trifluoromethylbenzene (0.90 mmol, 3.0 equiv.), amine or 1,3-dicarbonyl compound (if solid or high boiling point liquid, 0.30 mmol, 1.0 equiv.), LiOH (7.2 mg, 0.30 mmol, 1.0 equiv.) and THF (3.0 mL). The solution was degassed by bubbling with nitrogen for 8 minutes and 1,3-butadiene (2.0 mol/L in THF, 300 μL, 0.60 mmol, 2.0 equiv.) was syringed into the reaction vessel before sealing with parafilm. The reaction was carried out in a steel chamber under the irradiation at room temperature via blue LEDs (40 W, λ_{max} = 440 nm) for 12 h. The reaction mixture was removed from the light, cooled to ambient temperature, quenched by exposure to air. After the removal of solvent, the residue was purified by flash chromatography on silica gel to afford the desired product.

Procedure B: To an 8 mL vial equipped with a stir bar was added $Pd(PPh_3)_4$ (5.2 mg, 4.6 μmol, 0.015 equiv.), XantPhos (14.0 mg, 0.024 mmol, 0.08 equiv.), $Mg(OTf)_2$ (10.6 mg, 0.06 mmol, 0.2 equiv.), substituted (het)trifluoromethylbenzene (0.90 mmol, 3.0 equiv.), amine (if solid or high boiling point liquid, 0.30 mmol, 1.0 equiv.), LiOH (7.2 mg, 0.30 mmol, 1.0 equiv.) and THF (3.0 mL). The solution was degassed by bubbling with nitrogen for 8 minutes and 1,3-butadiene (2.0 mol/L in THF, 300 μL, 0.60 mmol, 2.0 equiv.) was syringed into the reaction vessel before sealing with parafilm. The reaction was carried out in a steel chamber under the irradiation at room temperature via blue LEDs (40 W, λ_{max} = 440 nm) for 24 h. The reaction mixture was removed from the light, cooled to ambient temperature, quenched by exposure to air. After the removal of solvent, the residue was purified by flash chromatography on silica gel to afford the desired product.

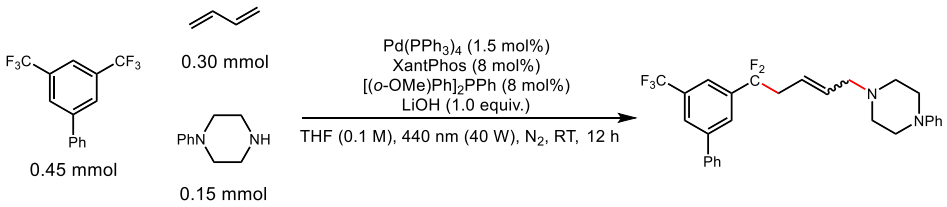
4. General Procedure for Hydrogenation of 1,4-Addition Product

Procedure C: To an 8 mL vial equipped with a stir bar was added $Pd(OH)_2/C$ (20 wt%), alkene (0.1 mmol, 1.0 equiv.), THF (1.0 mL) and 1,1,1,3,3,3-hexafluoro-2-propanol (1.0 mL). The reaction was carried out at room temperature with continuously bubbling of H_2 (balloon) for 1 h. The reaction mixture was quenched by exposure to air. After the removal of solvent, the residue was purified by flash chromatography on silica gel to afford the desired product.

Procedure D: To an 8 mL vial equipped with a stir bar was added $Pd(OH)_2/C$ (20 wt%), alkene (0.1 mmol, 1.0 equiv.), THF (1.0 mL) and 1,1,1,3,3,3-hexafluoro-2-propanol (1.0 mL). The reaction was carried out at 55℃ with continuously bubbling of H_2 (balloon) for 1 h. The reaction mixture was cooled to ambient temperature, quenched by exposure to air. After the removal of solvent, the residue was purified by flash chromatography on silica gel to afford the desired product.

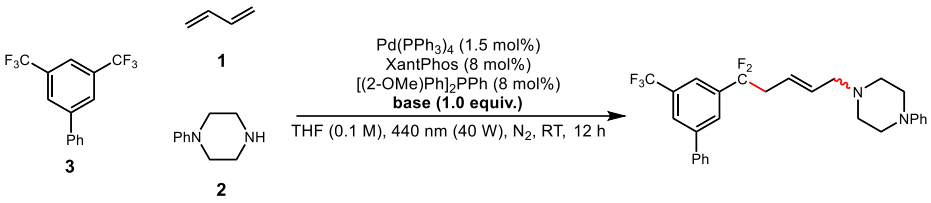
Procedure E: To an 8 mL vial equipped with a stir bar was added $Pd(OH)_2/C$ (20 wt%), alkene (0.1 mmol, 1.0 equiv.), (2-CH_3)THF (1.0 mL) and 1,1,1,3,3,3-hexafluoro-2-propanol (1.0 mL). The reaction was carried out at 70℃ with continuously bubbling of H_2 (balloon) for 1 h. The reaction mixture was cooled to ambient temperature, quenched by exposure to air. After the removal of solvent, the residue was purified by flash chromatography on silica gel to afford the desired product.

5. Reaction Optimization



Entry	Variation of standard condition	Yield
1	None	85% (*E*/*Z* = 1:2)
2	5 mol% $Pd(PPh_3)_4$	18%
3	4 mol% XantPhos	35%
4	2.0 equivalent of $ArCF_3$	61%
5	no $Pd(PPh_3)_4$	ND.
6	no XantPhos	28%
7	no $[(o\text{-OMe})Ph]_2PPh$	72%
8	no LiOH	2%
9	no irradiation	ND.
10	0.3 mmol scale	91% (*E*/*Z* = 1:2)

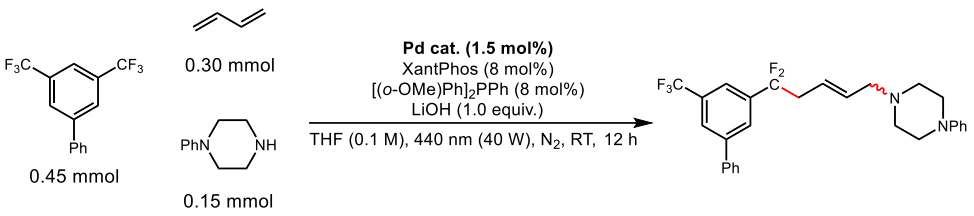
Table S1. Optimization of Standard Condition.



Entry	Base	Yield
1	$Me_4NOH•5H_2O$	7% (75%)
2	NaOH	<5% (69%)
3	KOH	<5% (45%)
4	$CsOH•H_2O$	16% (72%)
5	K_2CO_3	29% (35%)
6	K_3PO_4	10% (<5%)
7	^{t}BuOK	13% (33%)
8	^{t}BuCO$_2$K	19% (23%)
9	DABCO	10%(<5%)
10	Li_2CO_3	ND. (ND.)
11	DBU	61% (69%)
12	TMG	72% (58%)

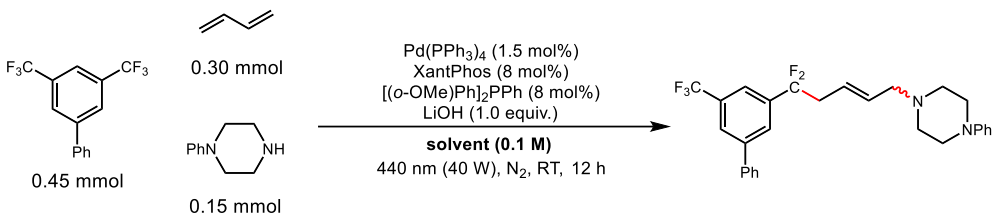
Reaction conditions: **1** (0.30 mmol), **2** (0.15 mmol), **3** (0.45 mmol), $Pd(PPh_3)_4$ (1.5 mol%), XantPhos (8 mol%), $[(o\text{-OMe})Ph]_2PPh$ (8 mol%), base (0.15 mmol), THF (0.1 M), λ_{max} = 440 nm Kessil (40 W), N_2, RT, 6 h. GC yield with 1,3,5-trimethylbenzene as internal standard. When 1.0 equiv. of LiOTf was added, the yield was shown in parenthesis.

Table S2. Optimization of Different Bases.



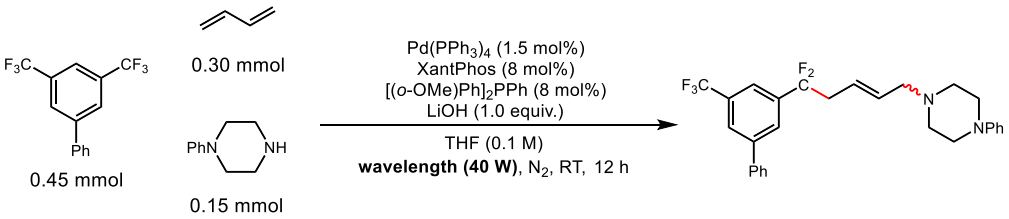
Entry	Pd cat.	Yield
1	$Pd(PPh_3)_2Cl_2$	79%
2	$Pd(dppf)Cl_2$	33%
3	$Pd(acac)_2$	71%
4	$Pd_2(dba)_3$	19%
5	Pd(^{t}Bu$_2$PhP)Cl$_2$	78%
6	Pd(XantPhos)Cl$_2$	76%
7	Pd[^{t}Bu$_2$(p-NMe$_2$)PhP]Cl$_2$	79%
8	$Pd(OAc)_2$	2%

Table S3. Optimization of Different Palladium Catalysts.



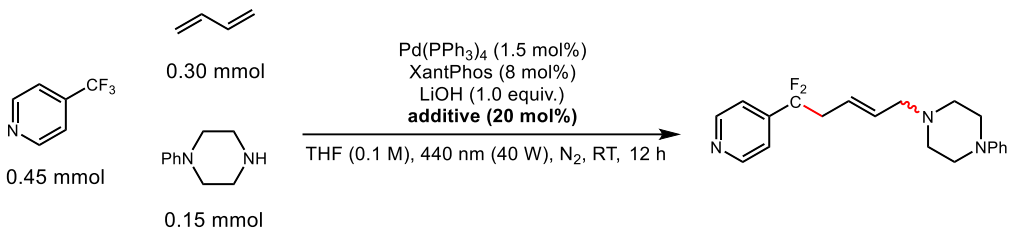
Entry	Solvent	Yield
1	MeCN	43%
2	EtOAc	12%
3	DCM	10%
4	dioxane	17%
5	THP	<1%
6	TBME	<1%
7	(2-CH_3)THF	39%
8	DMF	29%

Table S4. Optimization of Different Solvents.



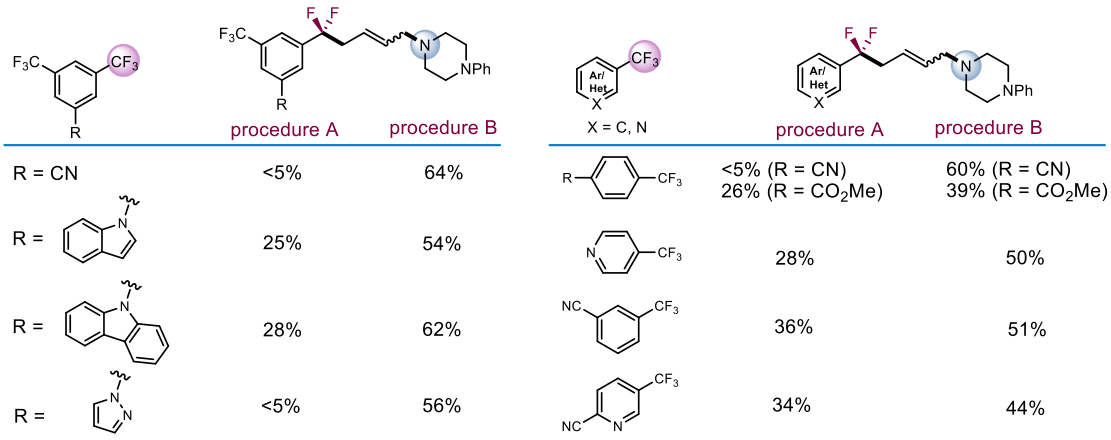
Entry	Wavelength	Yield
1	370 nm	53%
2	390 nm	73%
3	425 nm	84%
4	440 nm	85%
5	467 nm	65%
6	525 nm	ND.

Table S5. Optimization of Different Wavelengths.



Entry	additive	Yield
1	None	28%
2	$In(OTf)_3$	17%
3	$Bi(OTf)_3$	13%
4	$Sc(OTf)_3$	23%
5	$Mg(OTf)_2$	50%
6	$Zn(OTf)_2$	28%

Table S6. Optimization of Different Additives.



	procedure A	procedure B
R = CN	<5%	64%
R =	25%	54%
R =	28%	62%
R =	<5%	56%

X = C, N	procedure A	procedure B
	<5% (R = CN) 26% (R = CO_2Me)	60% (R = CN) 39% (R = CO_2Me)
	28%	50%
	36%	51%
	34%	44%

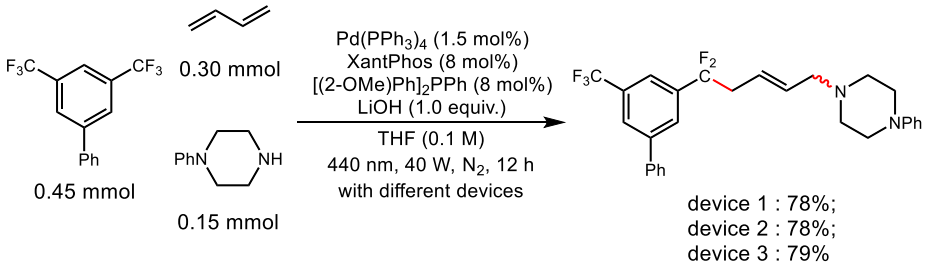
Procedure A: (Het)ArCF_3 (0.9 mmol), 1,3-butadiene (0.6 mmol), 1-phenylpiperazine (0.3 mmol), $Pd(PPh_3)_4$ (1.5 mol%), XantPhos (8 mol%), (*o*-OMe)Ph_2PPh (8 mol%), LiOH (0.3 mmol), THF (0.1 M), λ_{max} = 440 nm Kessil (40 W), N_2, RT, 12 h. Procedure B: (Het)ArCF_3 (0.9 mmol), 1,3-butadiene (0.6 mmol), 1-phenylpiperazine (0.3 mmol), $Pd(PPh_3)_4$ (1.5 mol%), XantPhos (8 mol%), $Mg(OTf)_2$ (20 mol%), LiOH (0.3 mmol), THF (0.1 M), λ_{max} = 440 nm Kessil (40 W), N_2, RT, 12 h.

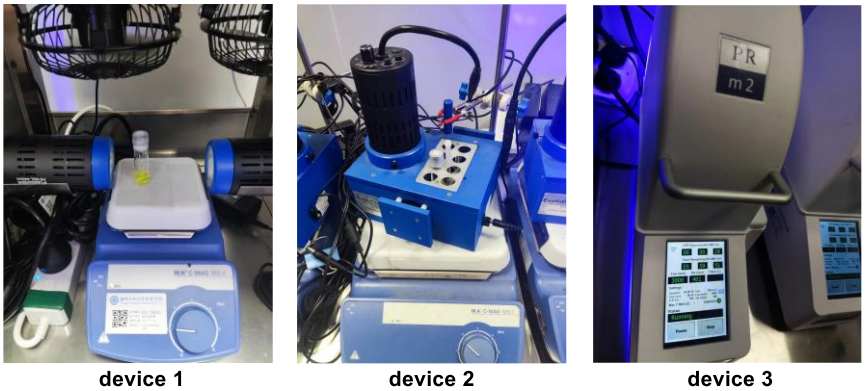
Table S7. $Mg(OTf)_2$ as Additive to Improve Yields for Some Sorts of (Het)ArCF_3 Substrates.

Figure S1. Photochemical Reaction Device.

Figure S2. Three Types of THF.

I. Superdry, stabilizer free, with molecular sieves, *J&K*; **II**. Superdry, stabilized with 250 ppm BHT, without molecular sieves, *J&K*; **III**. Regular, AR, *Sinopharm*. (from left to right). THF **II** is the most effective solvent and is preferentially used in most situations.





device 1 **device 2** **device 3**

device 1 : 25℃ (before irradiation), 34℃ (after irradiation);

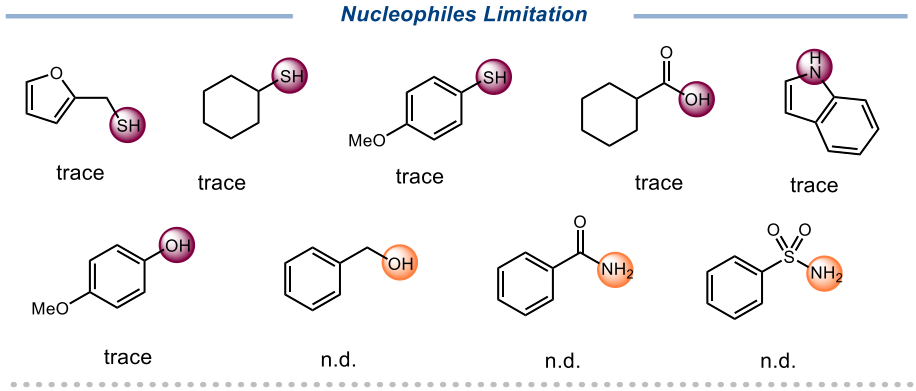
device 2 : 25℃ (before irradiation), 25℃ (after irradiation);

device 3 : 25℃ (before irradiation), 25℃ (after irradiation).

Figure S3. Three Types of Photocatalytic Devices.

Two different types of photocatalytic devices (devices 2 and 3) in our lab were applied besides the standard reaction setup (device 1). The results indicated that

altering both the temperature and the device used for the reaction had a negligible impact on reproducibility.



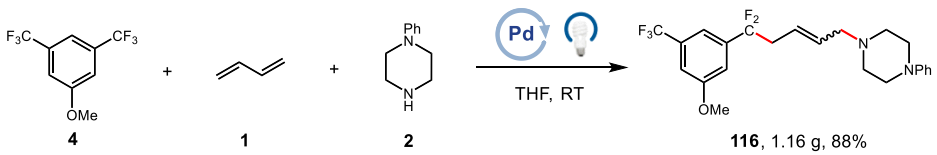
Scheme S2. Nucleophiles Limitation.

Some nucleophiles other than amines and 1,3-dicarbonyl compounds were applied under standard condition. In the case of thiol, thiophenol, carboxylic acid, indole and phenol, only trace amount of desire product was detected by GCMS. Benzenesulfonamide, benzyl alcohol and benzamide did not give any target products.

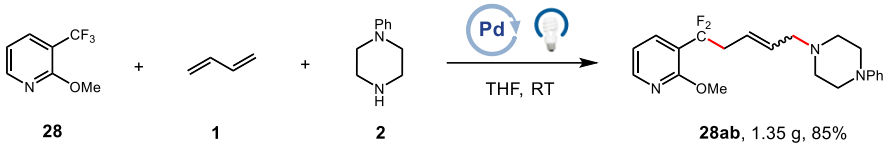
6. Synthetic Applications

Gram-scale Synthesis

To an 100 mL round-bottom flask equipped with a stir bar was added $Pd(PPh_3)_4$ (52 mg, 0.045 mmol, 0.015 equiv.), XantPhos (140 mg, 0.24 mmol, 0.08 equiv.), bis(2-methoxyphenyl)phenylphosphine (78 mg, 0.24 mmol, 0.08 equiv.), 1-phenylpiperazine (487 mg, 3.0 mmol, 1.0 equiv.), LiOH (72 mg, 3.0 mmol, 1.0 equiv.) and THF (30 mL). The solution was degassed by bubbling with nitrogen for 10 minutes. Then 1-methoxy-3,5-bis(trifluoromethyl)benzene (2.2 g, 9.0 mmol, 3.0 equiv.) and 1,3-butadiene (2.0 mol/L in THF, 3 mL, 6.0 mmol, 2.0 equiv.) was syringed into the reaction vessel before sealing with parafilm. The reaction was carried out in a steel chamber under the irradiation at room temperature via blue LEDs (40 W × 2, λ_{max} = 440 nm) for 12 h.. The reaction mixture was removed from the light, cooled to ambient temperature, quenched by exposure to air. After the removal of solvent, the residue was purified by flash chromatography on silica gel to afford the desired product.



To an 100 mL round-bottom flask equipped with a stir bar was added $Pd(PPh_3)_4$ (69 mg, 0.06 mmol, 0.015 equiv.), XantPhos (185 mg, 0.32 mmol, 0.08 equiv.), $Mg(OTf)_2$ (141 mg, 0.8 mmol, 0.2 equiv.), 1-phenylpiperazine (649 mg, 4.0 mmol, 1.0 equiv.), LiOH (96 mg, 4.0 mmol, 1.0 equiv.) and THF (40 mL). The solution was degassed by bubbling with nitrogen for 10 minutes. Then 2-methoxy-3-(trifluoromethyl)pyridine (2.1 g, 12.0 mmol, 3.0 equiv.) and 1,3-butadiene (2.0 mol/L in THF, 4 mL, 8.0 mmol, 2.0 equiv.) was syringed into the reaction vessel before sealing with parafilm. The reaction was carried out in a steel chamber under the irradiation at room temperature via blue LEDs (40 W × 2, λ_{max} = 440 nm) for 24 h. The reaction mixture was removed from the light, cooled to ambient temperature, quenched by exposure to air. After the removal of solvent, the residue was purified by flash chromatography on silica gel to afford the desired product.



Scheme S3. Gram-scale Synthesis.

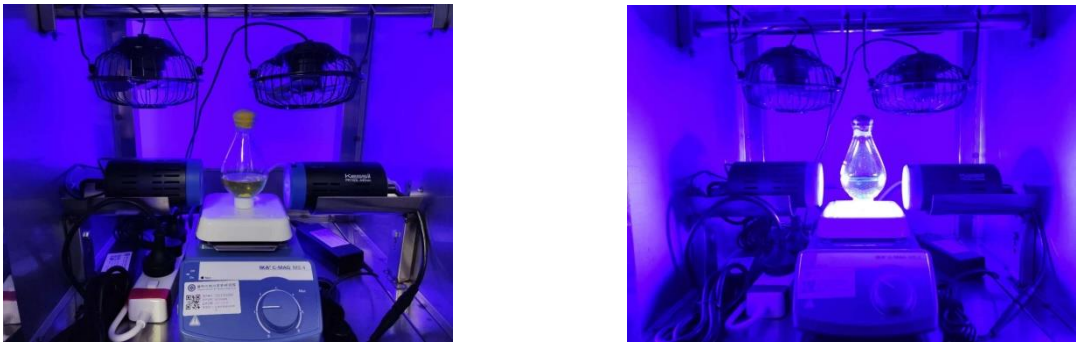


Figure S4. Gram-scale Setup.

Piperazine as Nucleophile (Procedure F)

To an 8 mL vial equipped with a stir bar was added $Pd(PPh_3)_4$ (5.2 mg, 4.6 μmol, 0.03 equiv.), XantPhos (14.0 mg, 0.024 mmol, 0.16 equiv.), bis(2-methoxyphenyl)phenylphosphine (7.8 mg, 0.024 mmol, 0.16 equiv.), 3,5-bis(trifluoromethyl)-1,1'-biphenyl (261 mg, 0.90 mmol, 6.0 equiv.), piperazine dihydrochloride (24.4 mg, 0.15 mmol, 1.0 equiv.), LiOH (14.4 mg, 0.60 mmol, 4.0 equiv.) and THF (3.0 mL). The solution was degassed by bubbling with nitrogen for 8 minutes and 1,3-butadiene (2.0 mol/L in THF, 300 μL, 0.60 mmol, 4.0 equiv.) was syringed into the reaction vessel before sealing with parafilm. The reaction was carried out in a steel chamber under the irradiation at room temperature via blue LEDs (40 W, λ_{max} = 440 nm) for 12 h. The reaction mixture was removed from the light, cooled to ambient temperature, quenched by exposure to air. After the removal of

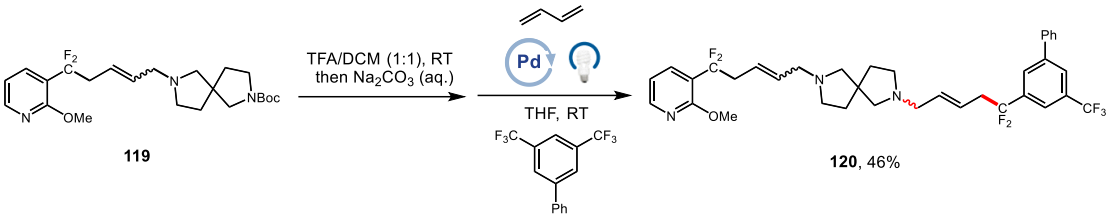
solvent, the residue was purified by flash chromatography on silica gel to afford the desired product.

2,2-Dimethyl-1,3-dioxane-4,6-dione as Nucleophile (Procedure G)

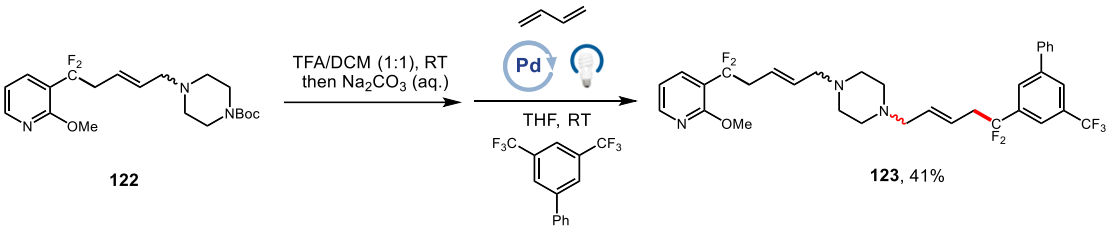
To an 8 mL vial equipped with a stir bar was added $Pd(PPh_3)_4$ (5.2 mg, 4.6 μmol, 0.03 equiv.), XantPhos (14.0 mg, 0.024 mmol, 0.16 equiv.), bis(2-methoxyphenyl)phenylphosphine (7.8 mg, 0.024 mmol, 0.16 equiv.), 3,5-bis(trifluoromethyl)-1,1'-biphenyl (261 mg, 0.90 mmol, 6.0 equiv.), 2,2-dimethyl-1,3-dioxane-4,6-dione (21.6 mg, 0.15 mmol, 1.0 equiv.), LiOH (7.2 mg, 0.30 mmol, 2.0 equiv.) and THF (3.0 mL). The solution was degassed by bubbling with nitrogen for 8 minutes and 1,3-butadiene (2.0 mol/L in THF, 300 μL, 0.60 mmol, 4.0 equiv.) was syringed into the reaction vessel before sealing with parafilm. The reaction was carried out in a steel chamber under the irradiation at room temperature via blue LEDs (40 W, λ_{max} = 440 nm) for 12 h. The reaction mixture was removed from the light, cooled to ambient temperature, quenched by exposure to air. After the removal of solvent, the residue was purified by flash chromatography on silica gel to afford the desired product.

Different aromatic trifluoromethyls connected by diamine (Procedure H)

Substrate **119** or **122** was prepared via procedure A. To an 8 mL vial equipped with a stir bar was added **119** or **122** (131 mg, 0.3 mmol, 1.0 equiv.), TFA (1 mL) and DCM (1 mL). The reaction was stirring under room temperature for 6 h followed by quenching with saturated Na_2CO_3 (aq.). Then the aqueous layer was extracted with three portions of DCM. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residue was used on the next step without further purification. To another 8 mL vial contained the residue that mention previously and equipped with a stir bar was added $Pd(PPh_3)_4$ (5.2 mg, 4.6 μmol, 0.015 equiv.), XantPhos (14.0 mg, 0.024 mmol, 0.08 equiv.), bis(2-methoxyphenyl)phenylphosphine (7.8 mg, 0.024 mmol, 0.08 equiv.), 3,5-bis(trifluoromethyl)-1,1'-biphenyl (261 mg, 0.90 mmol, 3.0 equiv.), LiOH (7.2 mg, 0.30 mmol, 1.0 equiv.) and THF (3.0 mL). The solution was degassed by bubbling with nitrogen for 8 minutes and 1,3-butadiene (2.0 mol/L in THF, 300 μL, 0.60 mmol, 2.0 equiv.) was syringed into the reaction vessel before sealing with parafilm. The reaction was carried out in a steel chamber under the irradiation at room temperature via blue LEDs (40 W, λ_{max} = 440 nm) for 12 h. The reaction mixture was removed from the light, cooled to ambient temperature, quenched by exposure to air. After the removal of solvent, the residue was purified by flash chromatography on silica gel to afford the desired product.



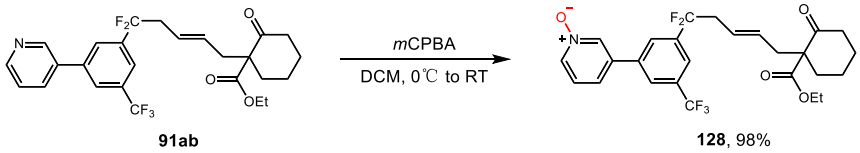
Scheme S4. Different Aromatic Trifluoromethyls Connected by 2,7-Diazaspiro[4.4]nonane Motif.



Scheme S5. Different Aromatic Trifluoromethyls Connected by Piperazine Motif.

Treated with Oxidant (Procedure I)

Substrate **91a** was prepared via procedure A. To an 8 mL vial equipped with a stir bar was added **91a** (51.1 mg, 0.1 mmol, 1.0 equiv.), *m*CPBA (25.9 mg, 0.15 mmol, 1.5 equiv.) and DCM (2 mL). The reaction was stirring at 0℃ for 0.5 h and moved to room temperature for another 3 h followed by quenching with saturated Na_2CO_3 (aq.). Then the aqueous layer was extracted with three portions of DCM. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography on silica gel to afford the desired product.



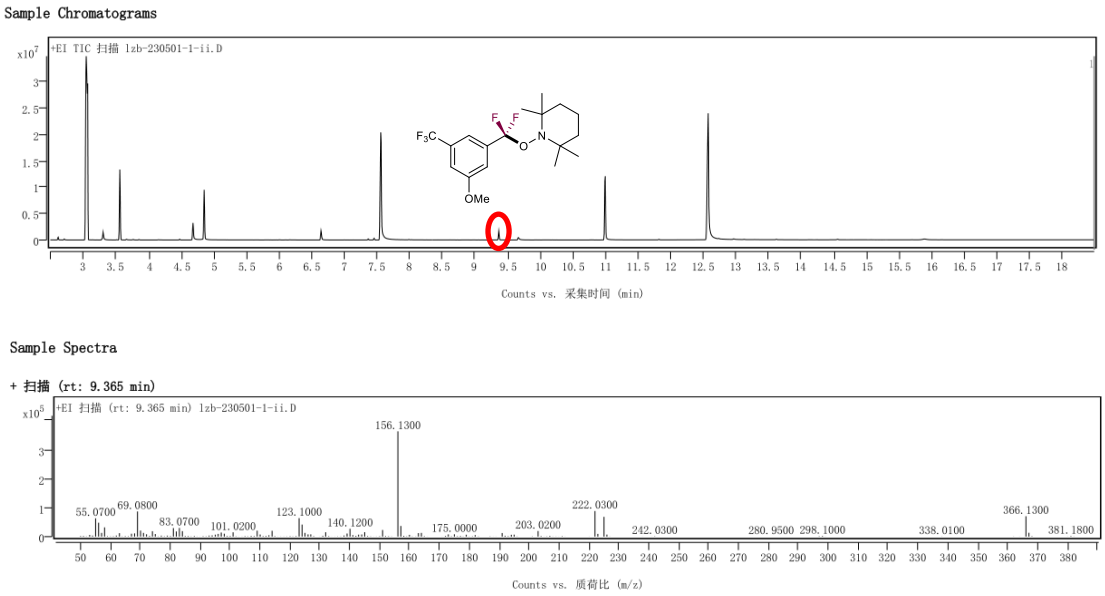
Scheme S6. Oxidative Transformation.

7. Preliminary Mechanistic Experiments

Radical Trapping Experiment

To an 8 mL vial equipped with a stir bar was added $Pd(PPh_3)_4$ (5.2 mg, 4.6 μmol, 0.015 equiv.), XantPhos (14.0 mg, 0.024 mmol, 0.08 equiv.), bis(2-methoxyphenyl)phenylphosphine (7.8 mg, 0.024 mmol, 0.08 equiv.), 1-phenylpiperazine (50.1 mg, 0.30 mmol, 1.0 equiv.), LiOH (7.2 mg, 0.30 mmol, 1.0 equiv.), TEMPO (93.4 mg, 0.6 mmol, 2.0 equiv.) or BHT (132.2 mg, 0.6 mmol, 2.0 equiv.) and THF (3.0 mL). The solution was degassed by bubbling with nitrogen for 8 minutes. Then 1-methoxy-3,5-bis(trifluoromethyl)benzene (219.7 mg, 0.90 mmol, 3.0

equiv.) and 1,3-butadiene (2.0 mol/L in THF, 300 μL, 0.60 mmol, 2.0 equiv.) was syringed into the reaction vessel before sealing with parafilm. The reaction was carried out in a steel chamber under the irradiation at room temperature via blue LEDs (40 W, λ_{max} = 440 nm) for 12 h. The reaction mixture was removed from the light, cooled to ambient temperature, quenched by exposure to air. After the removal of solvent, the residue was dissolved in 1 mL $CDCl_3$ followed by the addition of $MeNO_2$ (0.37 mmol) as internal standard, then the solution was analyzed by ^{1}H NMR and GCMS.



Scheme S7. TEMPO-radical Intermediate Detected by GCMS.

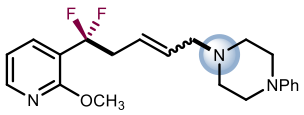
Radical Clock Experiment (Procedure J)

To an 8 mL vial equipped with a stir bar was added $Pd(PPh_3)_4$ (5.2 mg, 4.6 μmol, 0.015 equiv.), XantPhos (14.0 mg, 0.024 mmol, 0.08 equiv.), bis(2-methoxyphenyl)phenylphosphine (7.8 mg, 0.024 mmol, 0.08 equiv.), 1-phenylpiperazine (50.1 mg, 0.30 mmol, 1.0 equiv.), LiOH (7.2 mg, 0.30 mmol, 1.0 equiv.) and THF (3.0 mL). The solution was degassed by bubbling with nitrogen for 8 minutes. Then 1-methoxy-3,5-bis(trifluoromethyl)benzene (219.7 mg, 0.90 mmol, 3.0 equiv.) and (1-cyclopropylvinyl)benzene (86.4 mg, 0.60 mmol, 2.0 equiv.) was syringed into the reaction vessel before sealing with parafilm. The reaction was carried out in a steel chamber under the irradiation at room temperature via blue LEDs (40 W, λ_{max} = 440 nm) for 12 h. The reaction mixture was removed from the light, cooled to ambient temperature, quenched by exposure to air. After the removal of solvent, the residue was purified by flash chromatography on silica gel to afford the desired product.

Tracking Experiment

To an 8 mL vial equipped with a stir bar was added $Pd(PPh_3)_4$ (2.6 mg, 2.3 μmol, 0.015 equiv.), XantPhos (7.0 mg, 0.012 mmol, 0.08 equiv.), bis(2-methoxyphenyl)phenylphosphine (3.9 mg, 0.012 mmol, 0.08 equiv.), 1-phenylpiperazine (25.1 mg, 0.15 mmol, 1.0 equiv.), LiOH (3.6 mg, 0.15 mmol, 1.0 equiv.) and THF (1.5 mL). The solution was degassed by bubbling with nitrogen for 8 minutes. Then 1,3-bis(trifluoromethyl)benzene (94 mg, 0.45 mmol, 3.0 equiv.) and 1,3-butadiene (2.0 mol/L in THF, 150 μL, 0.30 mmol, 2.0 equiv.) was syringed into the reaction vessel before sealing with parafilm. The reaction was carried out in a steel chamber under the irradiation via blue LEDs (40 W, λ_{max} = 440 nm) for six parallel setups. The temperature in these setups was approx. 40℃. The reaction mixture was removed from the light in sequence, cooled to ambient temperature, quenched by exposure to air. After the removal of solvent, the residue was analyzed by ^1H NMR with $MeNO_2$ as internal standard.

To an 8 mL vial equipped with a stir bar was added $Pd(PPh_3)_4$ (5.2 mg, 4.6 μmol, 0.015 equiv.), XantPhos (14.0 mg, 0.024 mmol, 0.08 equiv.), $Mg(OTf)_2$ (10.6 mg, 0.06 mmol, 0.2 equiv.), 1-phenylpiperazine (50.1 mg, 0.30 mmol, 1.0 equiv.), LiOH (7.2 mg, 0.30 mmol, 1.0 equiv.) and THF (3.0 mL). The solution was degassed by bubbling with nitrogen for 8 minutes. Then 2-methoxy-3-(trifluoromethyl)pyridine (160 mg, 0.90 mmol, 3.0 equiv.), mesitylene (internal standard, 14 μL, 0.1 mmol) and 1,3-butadiene (2.0 mol/L in THF, 300 μL, 0.60 mmol, 2.0 equiv.) was syringed into the reaction vessel before sealing with parafilm. The reaction was carried out in a steel chamber under the irradiation at room temperature via blue LEDs (40 W, λ_{max} = 440 nm). Samples (100μL) were taken out from the vial via microsyringe without stopping irradiation followed by the GC analysis.



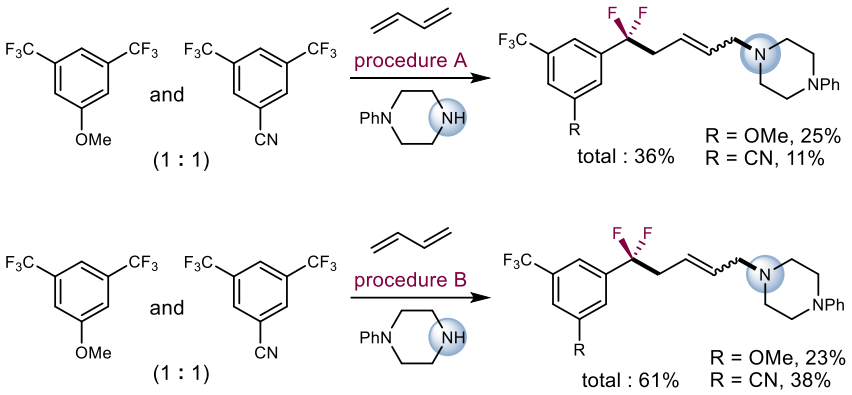
28ab (*E*, *Z*)

Time/h	*E* : *Z* ratio	Yield/%
1.0	3.0 : 1	16
1.5	3.0 : 1	31
2.0	3.1 : 1	49
3.0	3.2 : 1	62
4.0	3.2 : 1	68
5.0	3.1 : 1	70
6.0	3.1 : 1	72
7.0	3.1 : 1	73
8.0	3.2 : 1	74
18.0	3.2 : 1	76

Table S8. Tracking Experiment of *E/Z* Ratio.

Competitive Experiment

To an 8 mL vial equipped with a stir bar was added $Pd(PPh_3)_4$ (5.2 mg, 4.6 μmol, 0.015 equiv.), XantPhos (14.0 mg, 0.024 mmol, 0.08 equiv.), bis(2-methoxyphenyl)phenylphosphine (7.8 mg, 0.024 mmol, 0.08 equiv.) or $Mg(OTf)_2$ (10.6 mg, 0.06 mmol, 0.2 equiv.), 1-phenylpiperazine (50.1 mg, 0.30 mmol, 1.0 equiv.), LiOH (7.2 mg, 0.30 mmol, 1.0 equiv.) and THF (3.0 mL). The solution was degassed by bubbling with nitrogen for 8 minutes. Then 1-methoxy-3,5-bis(trifluoromethyl)benzene (183 mg, 0.75 mmol, 2.5 equiv.), 3,5-bis(trifluoromethyl)benzonitrile (179 mg, 0.75 mmol, 2.5 equiv.) and 1,3-butadiene (2.0 mol/L in THF, 300 μL, 0.60 mmol, 2.0 equiv.) was syringed into the reaction vessel before sealing with parafilm. The reaction was carried out in a steel chamber under the irradiation at room temperature via blue LEDs (40 W, λ_{max} = 440 nm). The reaction mixture was removed from the light, cooled to ambient temperature, quenched by exposure to air. After the removal of solvent, the residue was purified by flash chromatography on silica gel to afford the desired product.



Scheme S8. Competitive Experiment via Procedure A and B.

UV-vis absorption spectra

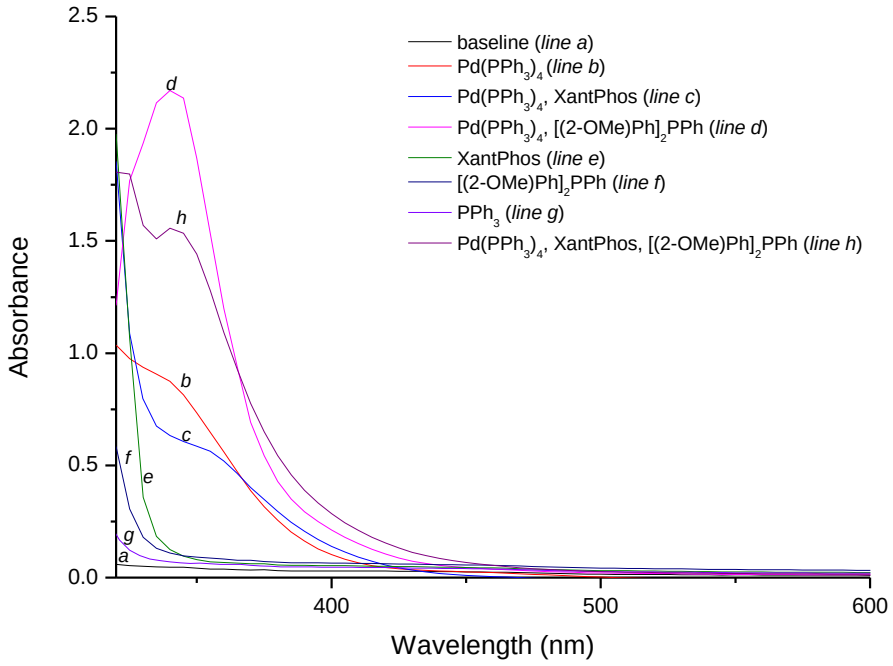


Figure S5. UV-vis Absorption Spectra of Reaction Mixture. The Concentration of Each Component is 1/8 of the Reaction Conditions of Table 1, Entry 1.

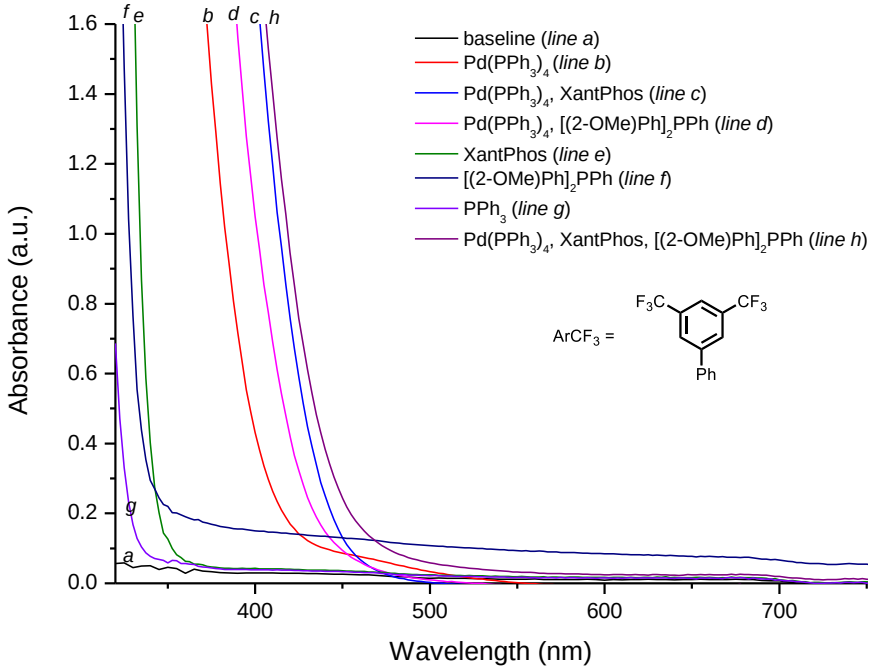


Figure S6. UV-vis Absorption Spectra of Reaction Mixture. The Concentration of Each Component is Equal with the Reaction Conditions of Table 1, entry 1.

Luminescence Quenching spectra

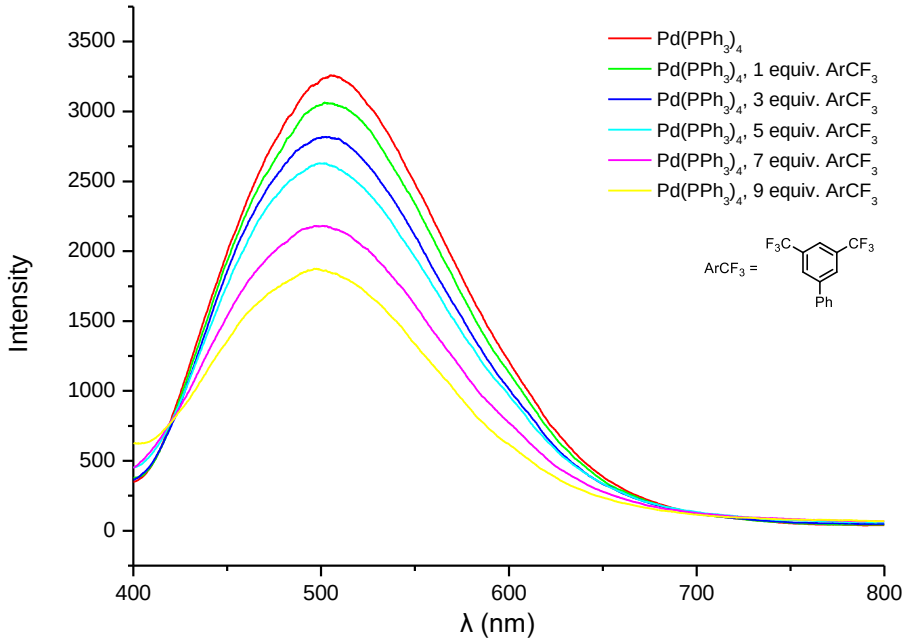


Figure S7. Emission Quenching of $Pd(PPh_3)_4$ by $ArCF_3$.

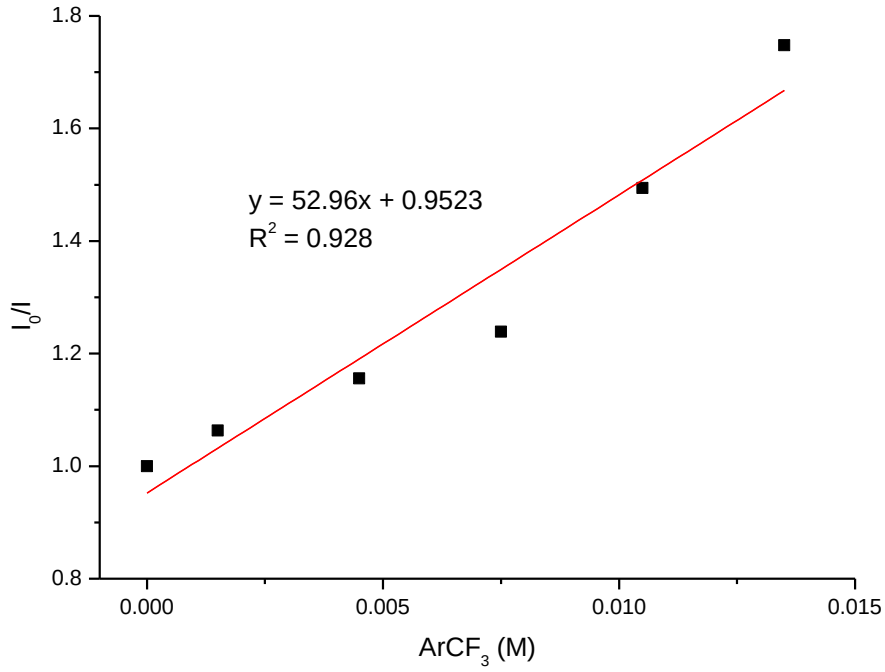


Figure S8. Stern-Volmer Luminescence Quenching of $Pd(PPh_3)_4$ by $ArCF_3$.

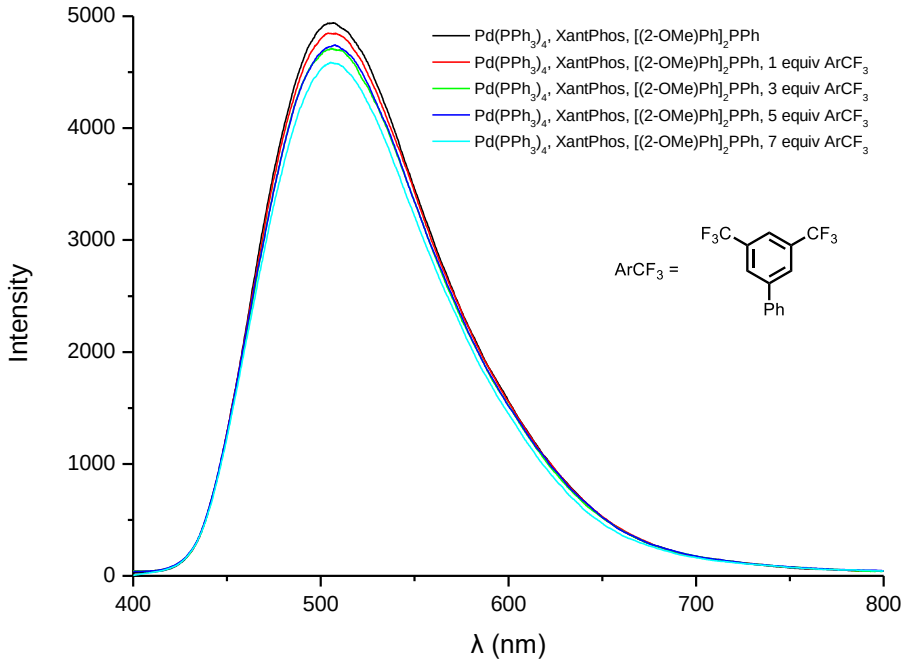


Figure S9. Emission Quenching of $Pd(PPh_3)_4$-XantPhos-$[(2\text{-}OMe)Ph]_2PPh$ by $ArCF_3$.

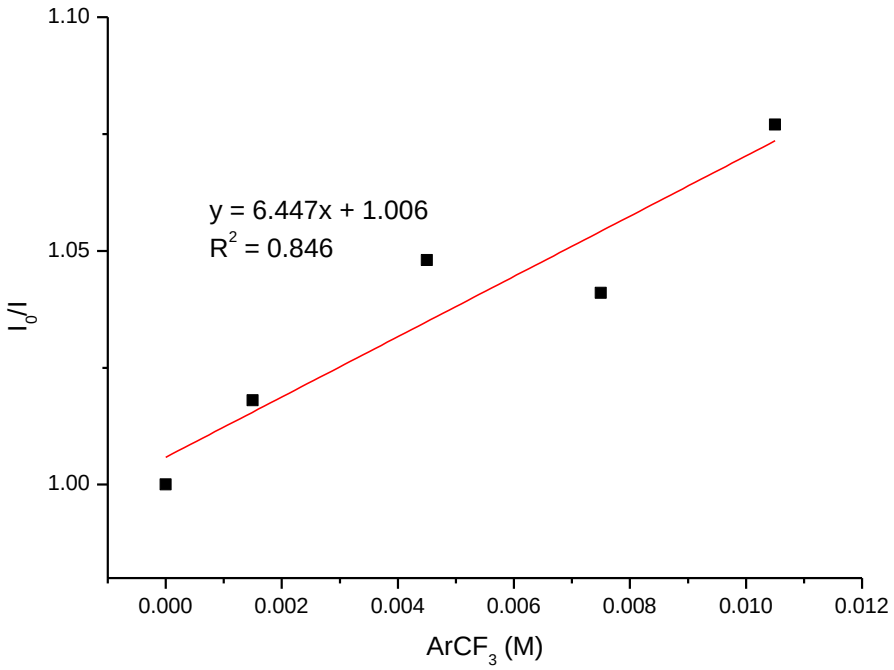


Figure S10. Stern-Volmer Luminescence Quenching of $Pd(PPh_3)_4$-XantPhos-$[(2\text{-}OMe)Ph]_2PPh$ by $ArCF_3$.

^{31}P NMR Spectra

To a NMR tube were added $Pd(PPh_3)_4$ (5.2 mg, 4.6 μmol, 1.0 equiv), Xantphos (14 mg, 24 μmol, 5.3 equiv), $[(2\text{-OMe})Ph]_2PPh$ (7.8 mg, 24 μmol, 5.3 equiv), PPh_3 (4.8 mg, 18.4 μmol, 4.0 equiv) and $CDCl_3$ (0.5 mL). Then the reaction mixture was shaked for 5 min at room temperature and analyzed by ^{31}P NMR.

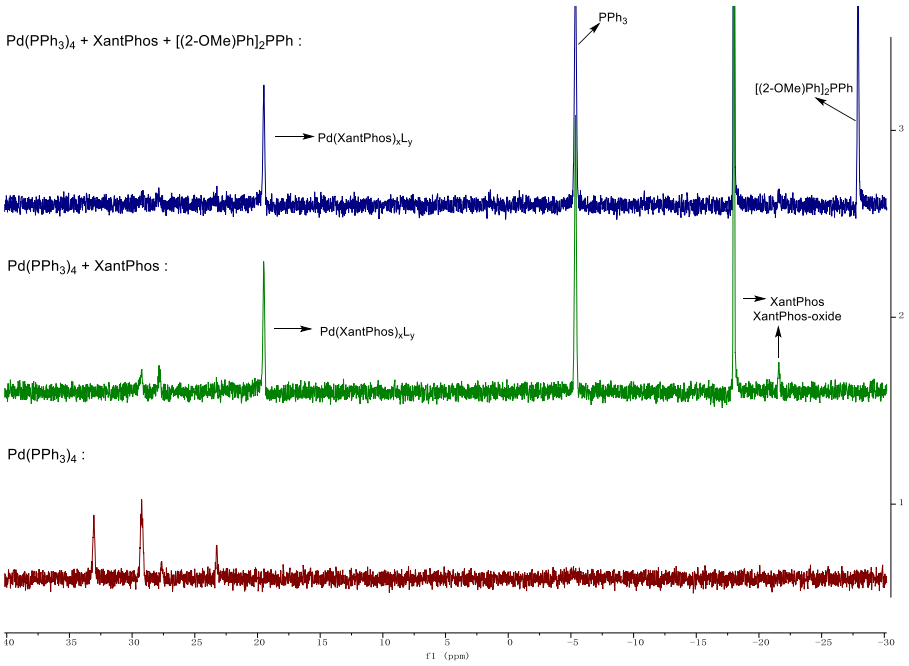


Figure S11. ^{31}P NMR Spectra of $Pd(PPh_3)_4$, $Pd(PPh_3)_4$ + XantPhos and $Pd(PPh_3)_4$ + $[(2\text{-OMe})Ph]_2PPh$ + XantPhos.

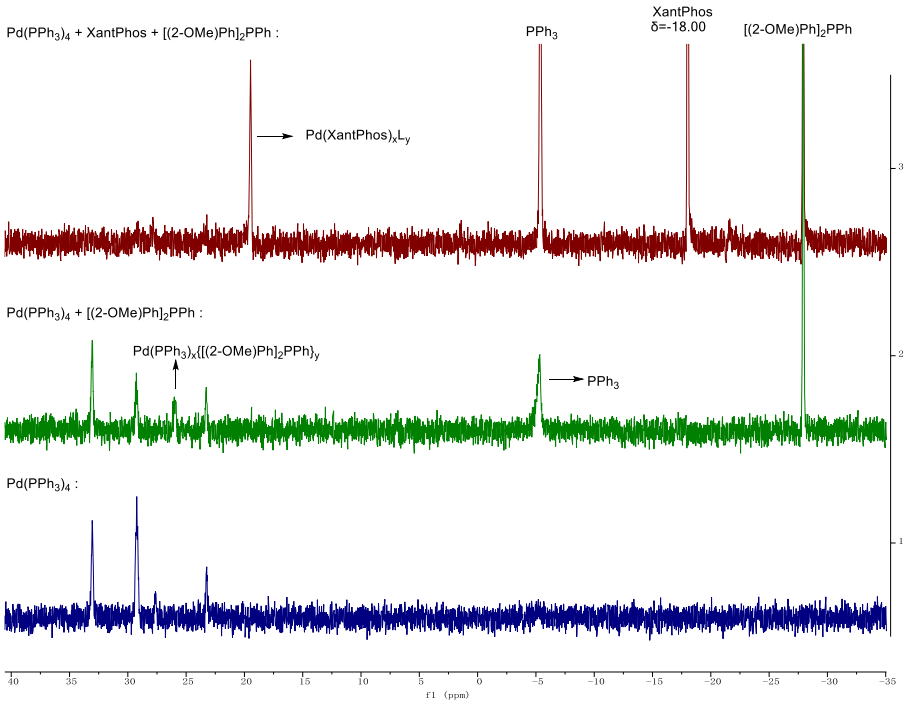


Figure S12. ^{31}P NMR Spectra of $Pd(PPh_3)_4$, $Pd(PPh_3)_4$ + $[(2\text{-}OMe)Ph]_2PPh$ and $Pd(PPh_3)_4$ + $[(2\text{-}OMe)Ph]_2PPh$ + XantPhos.

8. Computation data

Energies and Cartesian coordinates at 298.15 K and 1 atm for all structures (Energies are given in Hartree and coordinates in angstroms).

E-IM

B3LYP-D3/6-31G* (for C H O F P) & LanL2DZ (for Pd) SCF energy in vacuum:

-3352.049272

B3LYP-D3/6-311G** (for C H O F P) & LanL2DZ (for Pd) SCF energy in THF:

-3353.5713775

B3LYP-D3/6-311G** (for C H O F P) & LanL2DZ (for Pd) free energy in THF:

-3352.862043

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C	2.26791200	-4.84348700	-1.37667000
C	2.98455400	-3.68532500	-1.06692600
C	2.26716900	-2.63510500	-0.48897300
C	0.89398800	-2.66903600	-0.24808800
C	0.21051700	-3.85615200	-0.55377200
C	3.91131100	-1.07247800	-1.00956800
C	4.71559300	-2.02344700	-1.63670300
C	5.70382800	-1.53999300	-2.49966700
H	6.35387300	-2.23374300	-3.02075900
C	5.88005700	-0.16690000	-2.69090800
C	5.06460300	0.75690000	-2.03722000
C	4.04237300	0.30512900	-1.19142800
H	0.36365300	-5.84613700	-1.34690500
H	2.77475100	-5.68868400	-1.82822200
H	-0.85619200	-3.92878500	-0.37917000
H	6.66497700	0.18590200	-3.35207700
H	5.21878700	1.81847300	-2.18687300
O	2.91868800	-1.47093500	-0.14153800
C	4.49166400	-3.49273700	-1.26520900

C	5.19715300	-3.75445400	0.09366900
H	4.82028600	-3.08186100	0.87035300
H	5.02299600	-4.78632400	0.41611100
H	6.27615000	-3.59557800	-0.00497300
C	5.05997300	-4.44790700	-2.32193600
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H	6.13831300	-4.30342900	-2.43180800
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C	1.15566500	-1.99409600	2.81717300
C	-0.62810100	-0.36351100	2.94011100
C	1.28805900	-1.94334700	4.20548800
H	1.79963500	-2.64686000	2.23860000
C	-0.50571100	-0.32880800	4.32683100
H	-1.37709800	0.25156000	2.44990500
C	0.45697800	-1.11802800	4.96251000
H	2.03930500	-2.55572000	4.69467500
H	-1.15973000	0.31132000	4.91186800
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C	-1.68390400	-1.56546000	-0.04128900
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H	-2.27858200	-2.29460800	1.90296400
C	-3.32150200	-1.83931700	-1.80936400
H	-1.39659300	-0.91528100	-2.08137700
C	-4.19811800	-2.44369500	-0.90391800
H	-4.52903200	-3.01853300	1.14350200
H	-3.61228000	-1.71161900	-2.84755800
H	-5.17229900	-2.78407400	-1.23556600
C	3.32801700	1.11908300	1.48453300
C	4.58011600	0.60852500	1.85308400

C	2.39957500	1.45438700	2.47977900
C	4.89247900	0.43302900	3.20075700
H	5.30719000	0.34703100	1.09142100
C	2.71928600	1.28834400	3.82532700
H	1.42076100	1.83103600	2.19926900
C	3.96445000	0.77223200	4.18721400
H	5.86297400	0.03365500	3.47970700
H	1.98907700	1.54083300	4.58632800
H	4.21068500	0.63251400	5.23549100
C	3.46742300	3.06047000	-0.67229500
C	4.03694200	3.89290900	0.29833200
C	3.31769100	3.53447300	-1.98675600
C	4.45226800	5.18228700	-0.04346400
H	4.16161600	3.53767800	1.31529800
C	3.74565100	4.81563700	-2.32566800
H	2.87175200	2.89591800	-2.74548600
C	4.31089600	5.64406300	-1.35141100
H	4.89198000	5.82217100	0.71559600
H	3.63396300	5.16999600	-3.34592600
H	4.63788500	6.64549500	-1.61374200
Pd	0.54718300	1.09515900	-0.39436800
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H	-1.60310700	2.71276200	-1.78950000
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H	0.64679200	3.66869400	0.12758300
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C	-4.06485500	2.12996600	-0.71396100
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F	-3.93623200	3.47981900	-0.93793300
F	-3.67328800	1.50192400	-1.88131400
C	-6.34079000	2.75963900	0.17930500

C	-5.97302200	0.51061500	-0.62787400
C	-7.64407100	2.41673200	0.53555700
H	-5.97557800	3.76791600	0.34036200
C	-7.27338100	0.16944600	-0.25465100
H	-5.32884900	-0.22288800	-1.09248400
C	-8.11346300	1.11893500	0.32752500
H	-8.29763800	3.16249100	0.97641200
C	-7.72626800	-1.25172400	-0.44540600
H	-9.12450500	0.84723900	0.60857700
F	-7.37867500	-1.72432400	-1.66718300
F	-7.14047500	-2.07761600	0.46121700
F	-9.05528500	-1.39218300	-0.31336100
C	-1.70587700	2.25099000	0.29223200
H	-1.19535500	2.39631600	1.24402600

***Z*-IM**

B3LYP-D3/6-31G* (for C H O F P) & LanL2DZ (for Pd) SCF energy in vacuum: -3352.054655

B3LYP-D3/6-311G** (for C H O F P) & LanL2DZ (for Pd) SCF energy in THF: -3353.5811755

B3LYP-D3/6-311G** (for C H O F P) & LanL2DZ (for Pd) free energy in THF: -3352.865688

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C	-1.60240000	0.90713800	3.28921700
C	-1.04008900	1.09111800	2.02599600
C	-1.71352200	1.65971300	0.94470700
C	-2.99075800	2.18915800	1.17895000
C	0.70533400	-0.41979500	2.42419800
C	0.19718200	-0.77676300	3.67054100
C	0.71118400	-1.95153800	4.23123700
H	0.34913000	-2.29306400	5.19435500
C	1.70441400	-2.68967700	3.57944300
C	2.22220000	-2.27158100	2.35204200

C	1.71123100	-1.11724200	1.74961900
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H	-0.55991600	1.99314900	5.58900200
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C	0.14819100	4.05849900	0.21905100
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C	0.81743200	5.27123900	0.04708500
H	-0.23543200	3.78533200	1.19585600
C	1.12265000	4.77977800	-2.30025600
H	0.34093900	2.89436200	-2.97675300
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H	1.49488300	5.06110300	-3.28103800
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C	-2.39278000	1.81534400	-1.79557600
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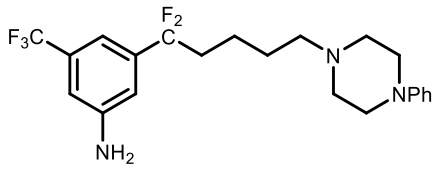
C	-3.93035400	3.11904700	-3.13848100
H	-2.18878300	3.93270600	-2.16907000

C	-4.32797100	0.75893900	-2.80569200
H	-2.88599100	-0.27377400	-1.59601600
C	-4.70519200	1.98196800	-3.36794300
H	-4.22176000	4.07247300	-3.56881900
H	-4.92739200	-0.13052100	-2.97485300
H	-5.59929200	2.04761500	-3.98042200
C	2.83971100	1.25765800	0.50828500
C	3.15916000	1.67328900	1.80619800
C	3.08966100	2.11479400	-0.57206900
C	3.71551500	2.93465000	2.01857600
H	2.98463400	1.01219400	2.64826400
C	3.66694300	3.36426600	-0.35914300
H	2.83782600	1.79974200	-1.58054900
C	3.97486400	3.77865500	0.93758100
H	3.95712900	3.25220900	3.02858000
H	3.85737200	4.01931100	-1.20189400
H	4.41570600	4.75676100	1.10477600
C	3.76278200	-1.31798600	-0.30235800
C	5.00400600	-0.66411600	-0.24191700
C	3.72962800	-2.66774400	-0.69278700
C	6.17801000	-1.34324300	-0.57093800
H	5.06238500	0.37207400	0.06547200
C	4.90686000	-3.34336800	-1.01100000
H	2.78929600	-3.19761300	-0.73413200
C	6.13508700	-2.68233900	-0.95651300
H	7.12824300	-0.82034700	-0.51901200
H	4.86146200	-4.38882800	-1.30177800
H	7.05053300	-3.20824400	-1.20988100
Pd	0.48774100	-0.18540700	-1.51601200
C	-4.07960800	-2.49446600	-0.82517100
C	-3.73496900	-2.91758000	-2.10711700
C	-2.40328800	-3.19889400	-2.41335000
C	-1.40650600	-3.03302000	-1.44632500
C	-1.74497500	-2.58465400	-0.16705500

C	-3.08078600	-2.33080000	0.13835000
H	-5.11572400	-2.29801600	-0.56957100
H	-4.50458900	-3.05752300	-2.85923400
H	-2.15115800	-3.58518800	-3.39634000
H	-0.98162200	-2.47334900	0.59130900
C	-0.00648800	-3.52567300	-1.73782200
C	-3.48658900	-1.90843400	1.52258000
F	-2.42560200	-1.83032400	2.35899900
F	-4.08685000	-0.69946800	1.50375700
F	-4.36502500	-2.77443300	2.06464000
F	0.76708600	-3.35037100	-0.60815500
F	-0.09228400	-4.88615900	-1.92916500
C	0.90351000	-0.49643700	-3.64345600
H	1.60502000	0.26141700	-3.98638600
C	-0.46072900	-0.18627100	-3.59024000
H	-0.82771500	0.75364400	-3.98589300
H	-1.20960200	-0.95500500	-3.42968600
C	1.41016500	-1.62120500	-2.93712700
H	2.48792400	-1.66787800	-2.82222100
C	0.72528100	-2.98067400	-2.96878400
H	1.49398200	-3.72839200	-3.18919700
H	0.01396800	-3.01306400	-3.79922800

9. Experimental Data

3-(1,1-difluoro-5-(4-phenylpiperazin-1-yl)pentyl)-5-(trifluoromethyl)aniline (5a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 2:1:0.03) on silica gel to afford the title compound (91.0 mg, 71% yield; 33.5 mg, 78% yield) as a colorless oil.

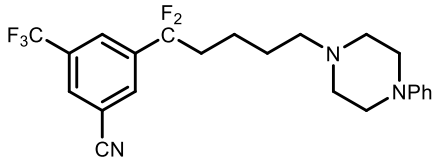
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (dd, *J* = 9.2, 6.4 Hz, 2H), 6.97 (s, 1H), 6.91 – 6.70 (m, 5H), 3.90 (s, 2H), 3.11 (t, *J* = 8.0 Hz, 4H), 2.49 (t, *J* = 8.0 Hz, 4H), 2.29 (t, *J* = 8.0 Hz, 2H), 2.04 (tdd, *J* = 16.1, 9.3, 6.7 Hz, 2H), 1.63 – 1.30 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.43, 147.21, 139.63 (t, *J* = 27.2 Hz), 132.13 (q, *J* = 32.3 Hz), 129.21, 123.91 (q, J = 273.7 Hz), 122.50 (t, *J* = 242.9 Hz), 119.79, 116.14, 114.38 (t, *J* = 6.1 Hz), 112.43, 111.58, 58.29, 53.35 49.20, 38.86 (t, *J* = 27.2 Hz), 26.50, 20.58 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.93, -96.04 (t, *J* = 15.0 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{22}H_{27}F_5N_3$ ($[M+H]^+$): 428.2120, found: 428.2111.

3-(1,1-difluoro-5-(4-phenylpiperazin-1-yl)pentyl)-5-(trifluoromethyl)benzonitrile (6a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (83.9 mg, 64% yield; 23.7 mg, 54% yield) as a colorless oil.

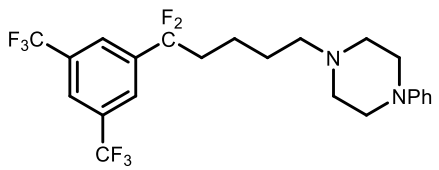
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.88 (d, *J* = 1.8 Hz, 2H), 7.21 – 7.16 (m, 2H), 6.86 – 6.84 (m, 2H), 6.78 (t, *J* = 8.0, 1H), 3.13 – 3.11 (m, 4H), 2.53 – 2.50 (m, 4H), 2.32 (dd, *J* = 8.2, 6.5 Hz, 2H), 2.17 – 2.04 (m, 2H), 1.56 – 1.39 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.16, 140.49 (t, *J* = 28.7 Hz), 132.77 (q, *J* = 34.2 Hz), 132.15 (t, *J* = 6.1 Hz), 130.31, 129.23, 126.35, 122.63 (q, *J* = 273.7 Hz), 121.38 (t, *J* = 245.4 Hz), 119.89, 116.75, 116.19, 114.28, 58.11, 53.37, 49.21, 38.75 (t, *J* = 26.6 Hz), 26.34, 20.37 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.08, -96.60 (td, *J* = 16.6, 3.2 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{23}H_{25}F_5N_3$ ($[M+H]^+$): 438.1963, found: 438.1953.

1-(5-(3,5-bis(trifluoromethyl)phenyl)-5,5-difluoropentyl)-4-phenylpiperazine (7a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (85.0 mg, 59% yield; 38.4 mg, 80% yield) as a white solid.

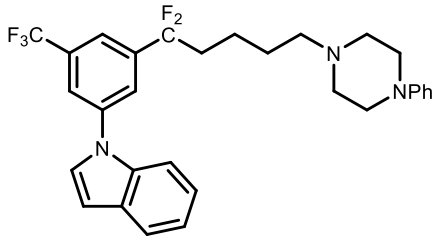
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.96 (s, 2H), 7.31 – 7.28 (m, 2H), 6.96 (d, *J* = 8.2 Hz, 2H), 6.89 (t, *J* = 7.3 Hz, 1H), 3.22 (t, *J* = 5.0 Hz, 4H), 2.61 (t, *J* = 5.0 Hz, 4H), 2.42 (t, *J* = 7.2 Hz, 2H), 2.23 (tt, *J* = 16.2, 7.7 Hz, 2H), 1.67 – 1.51 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.41, 140.12 (t, *J* = 28.3 Hz), 132.33 (q, *J* = 33.9 Hz), 129.22, 125.63, 123.90, 123.05 (q, *J* = 273.7 Hz), 121.73 (t, *J* = 243.9 Hz), 119.85, 116.18, 58.18, 53.39, 49.24, 38.86 (t, *J* = 26.6 Hz), 26.43, 20.40.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.92, -96.44 (t, *J* = 16.5 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{23}H_{25}F_8N_2$ ($[M+H]^+$): 481.1885, found: 481.1869.

1-(3-(1,1-difluoro-5-(4-phenylpiperazin-1-yl)pentyl)-5-(trifluoromethyl)phenyl)-1*H*-indole (8a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (85.4 mg, 54 % yield; 34.4 mg, 65% yield) as a pale yellow solid.

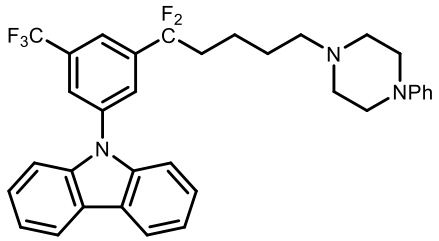
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.74 (s, 1H), 7.63 – 7.61 (m, 2H), 7.45 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.26 (d, *J* = 3.4 Hz, 1H), 7.21 – 7.11 (m, 4H), 6.84 – 6.81 (m, 2H), 6.76 (tt, *J* = 7.3, 1.2 Hz, 1H), 6.66 (dd, *J* = 3.4, 0.9 Hz, 1H), 3.09 (dd, *J* = 6.1, 4.0 Hz, 4H), 2.49 (t, *J* = 5.0 Hz, 4H), 2.31 (t, *J* = 7.0 Hz, 2H), 2.20 – 2.08 (m, 2H), 1.54 – 1.44 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.38, 140.89, 140.58 (t, *J* = 28.0 Hz), 135.57, 132.86 (q, *J* = 33.3 Hz), 129.80, 129.21, 127.42, 126.00 (q, *J* = 273.3 Hz), 124.47 (t, *J* = 239.2 Hz), 123.96 (t, *J* = 6.1 Hz), 123.34, 122.05, 121.71, 121.35, 119.84, 119.61 – 119.57 (m), 116.16, 110.01, 105.45, 58.22, 53.37, 49.20, 38.93 (t, *J* = 26.9 Hz), 26.46, 20.54 (d, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.66 (d, *J* = 3.7 Hz), -95.95 (td, *J* = 16.5, 3.9 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{30}H_{31}F_5N_3$ ($[M+H]^+$): 528.2433, found: 528.2421.

9-(3-(1,1-difluoro-5-(4-phenylpiperazin-1-yl)pentyl)-5-(trifluoromethyl)phenyl)-9*H*-carbazole (9a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (107.4 mg, 62% yield; 38.1 mg, 66% yield) as a white solid.

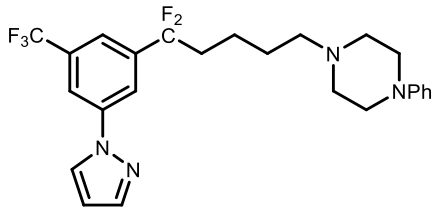
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.6 Hz, 1H), 7.83 (d, *J* = 14.9 Hz, 0H), 7.73 (s, 0H), 7.36 – 7.20 (m, 3H), 7.17 – 7.12 (m, 1H), 6.81 – 6.73 (m, 2H), 3.06 (t, *J* = 5.1 Hz, 2H), 2.46 (t, *J* = 5.1 Hz, 2H), 2.30 (t, *J* = 6.6 Hz, 1H), 2.21 – 2.09 (m, 1H), 1.50 – 1.48 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.37, 140.88 (t, *J* = 28.0 Hz), 140.30, 139.11, 133.14 (q, *J* = 33.4 Hz), 129.21, 127.04, 126.56, 125.06, 123.94, 121.40 (q, *J* = 273.7 Hz), 122.03 (t, *J* = 244.4 Hz), 121.02, 120.76, 120.72, 119.82, 116.14, 109.32, 58.24, 53.38, 49.19, 38.92 (t, *J* = 26.8 Hz), 26.47, 20.60 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.55, -95.79 (t).

HRMS (ESI-TOF) m/z calcd. for $C_{34}H_{33}F_5N_3$ ($[M+H]^+$): 578.2589, found: 578.2576.

1-(5-(3-(1*H*-pyrazol-1-yl)-5-(trifluoromethyl)phenyl)-5,5-difluoropentyl)-4-phenylpiperazine (10a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (80.3 mg, 56% yield; 37.4 mg, 78% yield) as a pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 3.8, 1.7 Hz, 2H), 7.91 (d, *J* = 2.5 Hz, 1H), 7.68 (d, *J* = 1.7 Hz, 1H), 7.54 (s, 1H), 7.17 (t, *J* = 8.0 Hz, 2H), 6.83 (d, *J* = 7.6 Hz, 2H), 6.78 – 6.75 (m, 1H), 6.44 (dd, *J* = 2.6, 1.8 Hz, 1H), 3.10 (t, *J* = 5.2 Hz, 4H),

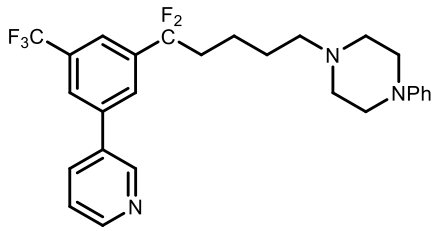
2.49 (t, *J* = 5.2 Hz, 4H), 2.30 (t, *J* = 6.8 Hz, 2H), 2.14 (tt, *J* = 16.4, 8.4 Hz, 2H), 1.55 – 1.40 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.40, 142.26, 140.91, 140.37 (t, *J* = 28.0 Hz), 132.61 (q, *J* = 33.3 Hz), 129.20, 126.98, 123.39 (q, *J* = 273.7 Hz), 122.07 (t, *J* = 244.4 Hz), 119.80, 119.56 – 119.53 (m), 118.82 (t, *J* = 6.3 Hz), 117.02, 116.15, 108.94, 58.19, 53.35, 49.18, 38.86 (t, *J* = 26.8 Hz), 26.42, 20.49 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.77 (d, *J* = 3.1 Hz), -96.10 (td, *J* = 16.6, 3.8 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{25}H_{28}F_5N_4$ ($[M+H]^+$): 479.2229, found: 479.2218.

1-(5,5-difluoro-5-(3-(pyridin-3-yl)-5-(trifluoromethyl)phenyl)pentyl)-4-phenylpiperazine (11a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (101.3 mg, 69% yield; 37.1 mg, 76% yield) as a pale yellow solid.

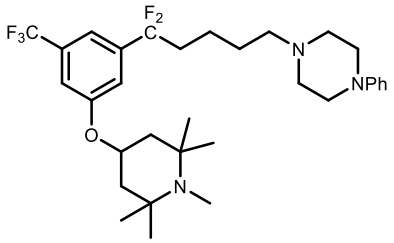
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (d, *J* = 2.4 Hz, 1H), 8.67 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.91 – 7.86 (m, 3H), 7.77 (s, 1H), 7.41 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.25 (dd, *J* = 8.5, 7.1 Hz, 2H), 6.91 (d, *J* = 8.1 Hz, 2H), 6.85 (t, *J* = 7.3 Hz, 1H), 3.17 (t, *J* = 5.2 Hz, 4H), 2.57 (t, *J* = 5.0 Hz, 4H), 2.39 (t, *J* = 7.1 Hz, 2H), 2.23 (tt, *J* = 16.0, 7.4 Hz, 2H), 1.64 – 1.50 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.38, 149.80, 148.35, 139.70 (t, *J* = 27.7 Hz), 139.52, 134.69, 132.16 (q, *J* = 32.9 Hz), 129.19, 127.19 (t, *J* = 6.3 Hz), 125.36, 123.90, 123.67 (q, *J* = 273.7 Hz), 122.27 (t, *J* = 244.4 Hz), 121.68, 119.80, 116.13, 58.19, 53.35, 49.19, 38.96 (t, *J* = 27.0 Hz), 26.45, 20.52 (t, *J* = 3.9 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.62, -95.96 (t, *J* = 16.5 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{27}H_{29}F_5N_3$ ($[M+H]^+$): 490.2276, found: 490.2280.

1-(5,5-difluoro-5-(3-((1,2,2,6,6-pentamethylpiperidin-4-yl)oxy)-5-(trifluoromethyl)phenyl)pentyl)-4-phenylpiperazine (12a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (155.2 mg, 89% yield; 57.1 mg, 98% yield) as a colorless oil.

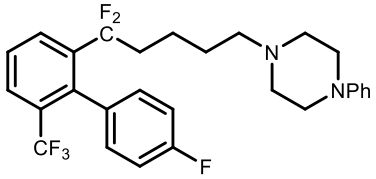
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.13 (m, 3H), 7.08 (s, 2H), 6.84 (d, *J* = 8.2 Hz, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 4.51 (tt, *J* = 11.2, 3.9 Hz, 1H), 3.10 (t, *J* = 4.9 Hz, 4H), 2.49 (t, *J* = 5.0 Hz, 4H), 2.29 (t, *J* = 7.3 Hz, 2H), 2.20 (s, 3H), 2.07 (tt, *J* = 15.9, 8.2 Hz, 2H), 1.91 (dd, *J* = 11.8, 3.3 Hz, 2H), 1.64 – 1.37 (m, 6H), 1.12 (s, 6H), 1.06 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.19, 151.41, 140.07 (t, *J* = 27.4 Hz), 132.41 (q, *J* = 32.7 Hz), 129.22, 123.71 (q, *J* = 272.6 Hz), 121.05 (t, *J* = 244.4 Hz), 119.84, 116.17, 116.08 (t, *J* = 7.1 Hz), 113.99, 113.39, 70.92, 58.30, 55.43, 53.37, 49.21, 45.99, 38.86 (t, *J* = 27.1 Hz), 33.04, 29.83, 28.19, 26.48, 21.21, 20.60 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.81, -95.88 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{32}H_{45}F_5N_3O$ ($[M+H]^+$): 582.3477, found: 582.3461.

1-(5,5-difluoro-5-(4'-fluoro-6-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)pentyl)-4-phenylpiperazine (13a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (129.1 mg, 85% yield; 39.6 mg, 78% yield) as a colorless oil.

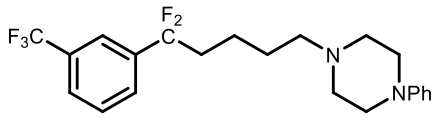
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (t, *J* = 7.9 Hz, 2H), 7.47 (t, *J* = 8.0 Hz, 1H), 7.20 – 7.12 (m, 4H), 6.98 (t, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.1 Hz, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 3.10 (t, *J* = 4.9 Hz, 4H), 2.45 (t, *J* = 5.0 Hz, 4H), 2.18 (t, *J* = 7.6 Hz, 2H), 1.66 (tt, *J* = 16.8, 7.9 Hz, 2H), 1.32 (p, *J* = 7.4 Hz, 2H), 1.19 (p, *J* = 7.8 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.69 (d, *J* = 247.7 Hz), 151.38, 138.30, 137.65 (t, *J* = 24.7 Hz), 132.41 (d, *J* = 8.1 Hz), 131.16 (q, *J* = 28.9 Hz), 130.98, 129.65 (t, *J* = 9.7 Hz), 129.22, 128.00, 127.57 – 127.51 (m), 123.66 (q, *J* = 275.7 Hz), 122.81 (t, *J* = 245.4 Hz), 119.83, 116.14, 114.00 (d, *J* = 21.5 Hz), 58.17, 53.34, 49.19, 38.12 (t, *J* = 26.4 Hz), 26.37, 20.62 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -57.05, -87.29 (t, *J* = 17.0 Hz), -101.17 – -125.45 (m).

HRMS (ESI-TOF) m/z calcd. for $C_{28}H_{29}F_6N_2$ ($[M+H]^+$): 507.2229, found: 507.2220.

1-(5,5-difluoro-5-(3-(trifluoromethyl)phenyl)pentyl)-4-phenylpiperazine (14a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (94.0 mg, 76% yield; 33.5 mg, 81% yield) as a pink oil.

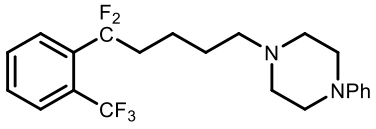
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.60 (dd, *J* = 11.8, 7.9 Hz, 2H), 7.47 (t, *J* = 7.8 Hz, 1H), 7.18 (dd, *J* = 8.5, 7.1 Hz, 2H), 6.84 (d, *J* = 8.2 Hz, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 3.11 (t, *J* = 5.2 Hz, 4H), 2.49 (t, *J* = 5.2 Hz, 4H), 2.29 (t, *J* = 5.2 Hz, 2H), 2.10 (tt, *J* = 16.8, 7.6 Hz, 2H), 1.53 – 1.37 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.43, 138.57 (t, *J* = 27.5 Hz), 131.16 (q, *J* = 32.8 Hz), 129.24, 129.22, 128.56 (t, *J* = 6.0 Hz), 126.69 – 126.65 (m), 122.89 (q, *J* = 273.7 Hz), 122.42 (t, *J* = 243.4 Hz), 122.22 – 122.12 (m), 119.83, 116.17, 58.26, 53.37, 49.22, 38.94 (t, *J* = 27.2 Hz), 26.48, 20.56.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.70, -95.96 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{22}H_{26}F_5N_2$ ($[M+H]^+$): 413.2011, found: 413.1999.

1-(5,5-difluoro-5-(2-(trifluoromethyl)phenyl)pentyl)-4-phenylpiperazine (15a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (111.3 mg, 95% yield; 36.8 mg, 89% yield) as a pink oil.

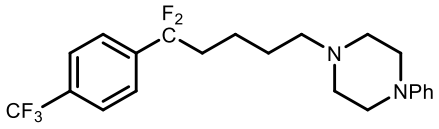
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.9 Hz, 1H), 7.59 – 7.49 (m, 1H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.18 (dd, *J* = 8.5, 7.1 Hz, 2H), 6.84 (d, *J* = 8.2 Hz, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 3.11 (t, *J* = 5.2 Hz, 4H), 2.50 (t, *J* = 5.2 Hz, 4H), 2.30 (t, *J* = 7.2 Hz, 2H), 2.12 (td, *J* = 17.2, 7.2 Hz, 2H), 1.52 – 1.48 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.44, 136.29 (t, *J* = 27.8 Hz), 131.87, 129.93, 129.21, 128.20 (t, *J* = 9.2 Hz), 127.66 (q, *J* = 6.4 Hz), 127.26 (qt, *J* = 32.3, 2.4 Hz), 123.74 (q, *J* = 274.7 Hz), 122.54 (t, *J* = 246.4 Hz), 119.80, 116.16, 58.32, 53.36, 49.21, 42.18 – 36.68 (m), 26.48, 20.44 (t, *J* = 3.7 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -57.65 (td, *J* = 15.9, 2.7 Hz), -93.20 – -93.43 (m).

HRMS (ESI-TOF) m/z calcd. for $C_{22}H_{26}F_5N_2$ ($[M+H]^+$): 413.2011, found: 413.1996.

1-(5,5-difluoro-5-(4-(trifluoromethyl)phenyl)pentyl)-4-phenylpiperazine (16a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (70.5 mg, 57% yield; 38.5 mg, 93% yield) as a colorless oil.

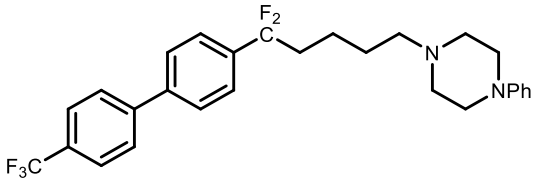
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.1 Hz, 2H), 7.51 (d, *J* = 8.1 Hz, 2H), 7.17 (t, *J* = 7.7 Hz, 2H), 6.84 (d, *J* = 8.1 Hz, 2H), 6.76 (t, *J* = 7.3 Hz, 1H), 3.10 (t, 4H), 2.48 (t, 4H), 2.28 (t, 2H), 2.18 – 1.98 (m, 2H), 1.55 – 1.31 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.44, 141.15 (t, *J* = 27.1 Hz), 132.02 (q, *J* = 32.4 Hz), 129.23, 128.81, 125.90 – 125.31 (m), 123.88 (q, *J* = 273.7 Hz), 122.47 (t, *J* = 242.9 Hz), 119.84, 116.17, 58.28, 53.38, 49.25, 38.95 (t, *J* = 27.1 Hz), 26.52, 20.58 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.83, -96.27 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{22}H_{26}F_5N_2$ ($[M+H]^+$): 413.2011, found: 413.1996.

1-(5,5-difluoro-5-(4'-(trifluoromethyl)-[1,1'-biphenyl]-4-yl)pentyl)-4-phenylpiperazine (17a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (90.8 mg, 62% yield; 39.0 mg, 80% yield) as a white solid.

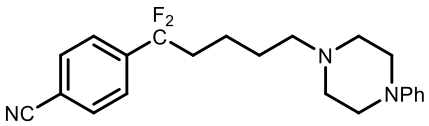
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.56 (m, 6H), 7.49 (d, *J* = 8.3 Hz, 2H), 7.17 (dd, *J* = 8.8, 7.2 Hz, 2H), 6.83 (d, *J* = 8.2 Hz, 2H), 6.76 (t, *J* = 7.3 Hz, 1H), 3.09 (t, *J* = 4.8 Hz, 4H), 2.49 (t, *J* = 5.2 Hz, 4H), 2.30 (t, *J* = 7.2 Hz, 2H), 2.12 (tt, *J* = 15.9, 7.7 Hz, 2H), 1.53 – 1.39 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.44, 143.86, 141.20, 137.37 (t, *J* = 27.1 Hz), 129.96 (q, *J* = 32.5 Hz), 129.22, 127.62, 127.44, 126.02 – 125.78 (m), 124.33 (q, *J* = 272.7 Hz), 123.04 (t, *J* = 244.4 Hz), 119.82, 116.14, 58.27, 53.36, 49.23, 38.97 (t, *J* = 27.5 Hz), 26.54, 20.71 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.44, -95.24 (t, *J* = 16.2 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{28}H_{30}F_5N_2$ ($[M+H]^+$): 489.2324, found: 489.2316.

4-(1,1-difluoro-5-(4-phenylpiperazin-1-yl)pentyl)benzonitrile (18a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (66.5 mg, 60% yield; 29.5 mg, 80% yield) as a pink solid.

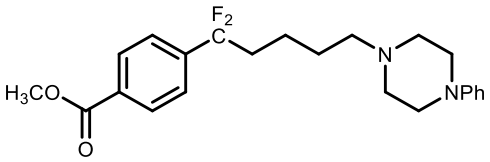
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.1 Hz, 2H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.21 – 7.16 (m, 2H), 6.86 – 6.83 (m, 2H), 6.77 (tt, *J* = 7.3, 1.1 Hz, 1H), 3.11 (t, *J* = 5.2 Hz, 4H), 2.50 (t, *J* = 5.2 Hz, 4H), 2.29 (t, *J* = 7.2 Hz 2H), 2.07 (tt, *J* = 16.8, 7.6 Hz 2H), 1.53 – 1.35 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.36, 142.01 (t, *J* = 27.3 Hz), 132.48, 129.22, 126.02, 122.17 (t, *J* = 243.4 Hz), 119.86, 118.16, 116.16, 113.94 (t, *J* = 1.9 Hz), 58.21, 53.34, 49.20, 38.80 (t, *J* = 26.9 Hz), 26.43, 20.50 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -96.87 (t, *J* = 16.4 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{22}H_{26}F_2N_3$ ($[M+H]^+$): 370.2089, found: 370.2080.

methyl 4-(1,1-difluoro-5-(4-phenylpiperazin-1-yl)pentyl)benzoate (19a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 5:1:0.03) on silica gel to afford the title compound (47.1 mg, 39% yield; 33.8 mg, 84% yield) as a white solid.

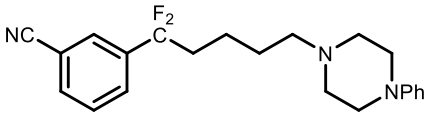
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 2H), 7.18 (t, *J* = 8.0 Hz, 2H), 6.84 (d, *J* = 7.9 Hz, 2H), 6.77 (t, *J* = 7.4 Hz, 1H), 3.85 (s, 3H), 3.10 (t, *J* = 5.2 Hz, 4H), 2.48 (t, *J* = 5.0 Hz, 4H), 2.28 (t, *J* = 7.2 Hz, 2H), 2.07 (tt, *J* = 16.0, 8.0 Hz, 2H), 1.51 – 1.35 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.46, 151.41, 141.82 (t, *J* = 26.8 Hz), 131.51, 129.83, 129.19, 125.20 (d, *J* = 6.2 Hz), 122.69 (t, *J* = 242.8 Hz), 119.78, 116.13, 58.26, 53.34, 52.41, 49.21, 38.91 (t, *J* = 27.1 Hz), 26.50, 20.59 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -96.25 (t, *J* = 16.2 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{23}H_{29}F_2N_2O_2$ ($[M+H]^+$): 403.2192, found: 403.2182.

3-(1,1-difluoro-5-(4-phenylpiperazin-1-yl)pentyl)benzonitrile (20a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (56.5 mg, 51% yield; 25.6 mg, 70% yield) as a pink solid.

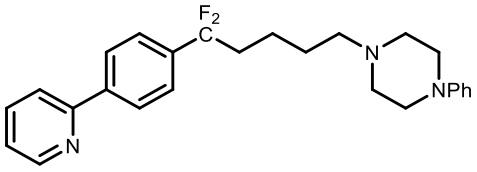
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.63 (t, *J* = 6.6 Hz, 2H), 7.47 (t, *J* = 7.8 Hz, 1H), 7.18 (t, *J* = 7.9 Hz, 2H), 6.85 (d, *J* = 8.1 Hz, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 3.11 (t, *J* = 5.0 Hz, 4H), 2.50 (t, *J* = 5.0 Hz, 4H), 2.30 (t, *J* = 7.4 Hz, 2H), 2.08 (tt, *J* = 16.2, 7.9 Hz, 2H), 1.54 – 1.35 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.38, 139.04 (t, *J* = 27.8 Hz), 133.39, 129.61, 129.49 (t, *J* = 6.0 Hz), 129.21, 128.94 (t, *J* = 6.4 Hz), 122.00 (t, *J* = 243.4 Hz), 119.82, 118.18, 116.15, 113.04, 58.18, 53.35, 49.19, 38.81 (t, *J* = 26.9 Hz), 26.41, 20.51 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -96.24 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{22}H_{26}F_2N_3$ ($[M+H]^+$): 370.2089, found: 370.2079.

1-(5,5-difluoro-5-(4-(pyridin-2-yl)phenyl)pentyl)-4-phenylpiperazine (21a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (75.8 mg, 60% yield; 40.2 mg, 95% yield) as a white solid.

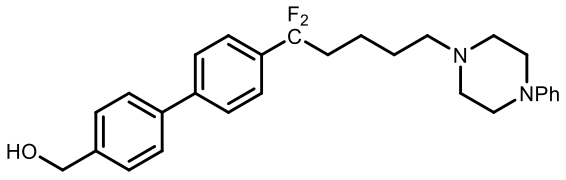
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, *J* = 5.5 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 2H), 7.69 – 7.61 (m, 2H), 7.49 (d, *J* = 8.1 Hz, 2H), 7.18 – 7.14 (m, 3H), 6.83 (d, *J* = 8.1 Hz, 2H), 6.76 (t, *J* = 7.3 Hz, 1H), 3.09 (t, *J* = 5.1 Hz, 4H), 2.49 – 2.46 (m, 4H), 2.28 (t, *J* = 7.4 Hz, 2H), 2.11 (tt, *J* = 15.9, 7.7 Hz, 2H), 1.52 – 1.36 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.60, 151.42, 149.91, 140.79, 137.87 (t, *J* = 26.9 Hz), 136.97, 129.18, 127.05, 125.26 (t, *J* = 6.1 Hz), 122.65, 123.13 (t, *J* = 242.2 Hz), 120.79, 119.73, 116.11, 58.31, 53.33, 49.19, 38.99 (t, *J* = 27.4 Hz), 26.53, 20.74 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -95.31 (t, *J* = 16.1 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{26}H_{30}F_2N_3$ ($[M+H]^+$): 422.2402, found: 422.2392.

(4'-(1,1-difluoro-5-(4-phenylpiperazin-1-yl)pentyl)-[1,1'-biphenyl]-4-yl)methanol (22a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 1:1:0.03) on silica gel to afford the title compound (68.9 mg, 51% yield; 30.5 mg, 68% yield) as a white solid.

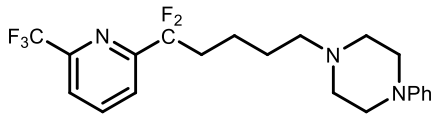
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.44 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 7.9 Hz, 2H), 7.16 (t, *J* = 8.0 Hz, 2H), 6.82 (d, *J* = 8.1 Hz, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 4.63 (s, 2H), 3.08 (t, *J* = 5.0 Hz, 4H), 2.48 (t, *J* = 5.0 Hz, 4H), 2.33 (s, 1H), 2.27 (t, *J* = 7.4 Hz, 2H), 2.16 – 2.04 (m, 4H), 1.52 – 1.37 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.36, 142.27, 140.82, 139.54, 136.36 (t, *J* = 26.9 Hz), 129.20, 127.58, 127.38, 127.14, 125.58 (t, *J* = 6.1 Hz), 123.14 (t, *J* = 242.4 Hz), 119.86, 116.19, 64.84, 58.33, 53.30, 49.14, 38.97 (t, *J* = 27.6 Hz), 26.45, 20.73 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -95.00 (t, *J* = 16.2 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{28}H_{33}F_2N_2O$ ($[M+H]^+$): 451.2555, found: 451.2545.

1-(5,5-difluoro-5-(6-(trifluoromethyl)pyridin-2-yl)pentyl)-4-phenylpiperazine(23 a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (83.1 mg, 67% yield; 39.4 mg, 95% yield) as a white solid.

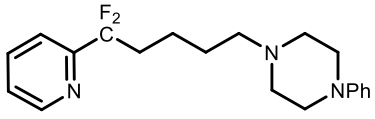
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (t, *J* = 7.9 Hz, 1H), 7.76 (d, *J* = 7.9 Hz, 1H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.19 – 7.16 (m, 2H), 6.84 (d, *J* = 8.2 Hz, 2H), 6.76 (t, *J* = 7.3 Hz, 1H), 3.11 (t, 4H), 2.50 (t, 4H), 2.39 – 2.26 (m, 4H), 1.56 – 1.40 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.62 (t, *J* = 30.9 Hz), 151.43, 148.04 (q, *J* = 35.3 Hz), 138.84, 129.20, 122.87 (t, *J* = 4.4 Hz), 121.46 – 121.43 (m), 121.30 (t, *J* = 242.4 Hz), 121.23 (q, *J* = 274.7 Hz), 119.76, 116.12, 58.31, 53.33, 49.19, 35.64 (t, *J* = 24.6 Hz), 26.56, 20.21 (t, *J* = 4.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.97, -98.08 (t, *J* = 17.0 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{21}H_{25}F_5N_3$ ($[M+H]^+$): 414.1963, found: 414.1952.

1-(5,5-difluoro-5-(pyridin-2-yl)pentyl)-4-phenylpiperazine (24a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (66.3 mg, 64% yield; 31.2 mg, 90% yield) as a pink solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.71 (td, *J* = 7.8, 1.8 Hz, 1H), 7.55 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.27 (dd, *J* = 7.7, 4.9 Hz, 1H), 7.20 – 7.16 (m,

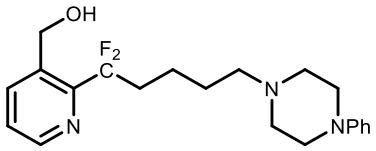
2H), 6.84 (d, *J* = 7.7 Hz, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 3.11 (t, *J* = 5.2 Hz, 4H), 2.50 (t, *J* = 5.2 Hz, 4H), 2.35 – 2.22 (m, 4H), 1.55 – 1.38 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.05 (t, *J* = 29.4 Hz), 151.42, 149.49, 137.10, 129.19, 124.68, 121.78 (t, *J* = 241.7 Hz), 120.01 (t, *J* = 4.6 Hz), 119.75, 116.12, 58.36, 53.33, 49.18, 36.31 (t, *J* = 25.3 Hz), 26.58, 20.32 (t, *J* = 4.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -99.05 (t, *J* = 16.9 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{20}H_{26}F_2N_3$ ($[M+H]^+$): 346.2089, found: 346.2080.

(2-(1,1-difluoro-5-(4-phenylpiperazin-1-yl)pentyl)pyridin-3-yl)methanol (25a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 1:1:0.03) on silica gel to afford the title compound (85.5 mg, 76% yield; 33.4 mg, 89% yield) as a white solid.

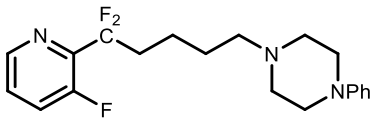
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 4.6 Hz, 1H), 7.97 (d, *J* = 7.9 Hz, 1H), 7.28 (dd, *J* = 7.9, 4.7 Hz, 1H), 7.18 (t, *J* = 7.7 Hz, 2H), 6.84 (d, *J* = 8.1 Hz, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 4.85 (s, 2H), 3.11 (t, *J* = 5.0 Hz, 4H), 2.85 (s, 1H), 2.52 (t, *J* = 5.0 Hz, 4H), 2.53 – 2.29 (m, 4H), 1.55 – 1.51 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.35, 150.81 (t, *J* = 30.7 Hz), 146.91, 137.04, 135.94, 129.19, 124.99, 124.02 (t, *J* = 240.8 Hz), 119.85, 116.17, 60,42, 58.43, 53.31, 49.12, 35.95 (t, *J* = 24.5 Hz), 26.61, 20.20 (t, *J* = 4.5 Hz).

^{19}F NMR (376 MHz, **$CDCl_3$**) δ -93.70 (t, *J* = 17.6 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{21}H_{28}F_2N_3O$ ($[M+H]^+$): 376.2195, found: 376.2185.

1-(5,5-difluoro-5-(3-fluoropyridin-2-yl)pentyl)-4-phenylpiperazine (26a)



The title product was prepared via procedure B & C, purified by flash chromatography (PE:EA:Et_3N = 5:1:0.03) on silica gel to afford the title compound (76.3 mg, 70% yield; 35.4 mg, 97% yield) as a colorless oil.

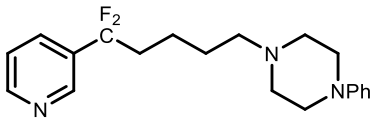
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 4.5 Hz, 1H), 7.42 (ddd, *J* = 10.1, 8.4, 1.3 Hz, 1H), 7.33 (dt, *J* = 8.4, 4.2 Hz, 1H), 7.20 – 7.16 (m, 2H), 6.85 (d, *J* = 7.9 Hz, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 3.13 – 3.10 (m, 4H), 2.52 – 2.50 (m, 4H), 2.37 – 2.25 (m, 4H), 1.57 – 1.50 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.45 (d, *J* = 265.8 Hz), 151.42, 144.53 (d, *J* = 5.2 Hz), 142.51 (td, *J* = 29.7, 10.6 Hz), 129.19, 126.66 (d, *J* = 4.2 Hz), 125.16 (d, *J* = 19.5 Hz), 121.21 (td, *J* = 242.4, 4.2 Hz), 119.74, 116.11, 58.33, 53.34, 49.19, 36.09 (t, *J* = 24.6 Hz), 26.61, 20.10 (t, *J* = 4.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -97.64 (qd, *J* = 17.5, 5.8 Hz), -121.38 (tdd, *J* = 20.1, 10.5, 3.9 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{20}H_{25}F_3N_3$ ($[M+H]^+$): 364.1995, found: 364.1982.

1-(5,5-difluoro-5-(pyridin-3-yl)pentyl)-4-phenylpiperazine (27a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (75.6 mg, 73% yield; 27.0 mg, 78% yield) as a colorless oil.

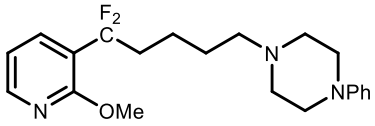
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, *J* = 2.3 Hz, 1H), 8.61 (d, *J* = 4.8 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.29 (dd, *J* = 7.9, 4.9 Hz, 1H), 7.19 (t, *J* = 7.7 Hz, 2H), 6.85 (d, *J* = 8.2 Hz, 2H), 6.78 (t, *J* = 7.3 Hz, 1H), 3.11 (t, *J* = 5.0 Hz, 4H), 2.50 (t, *J* = 5.0 Hz, 4H), 2.30 (t, *J* = 7.4 Hz, 2H), 2.11 (tt, *J* = 16.1, 7.7 Hz, 2H), 1.54 – 1.38 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.37, 151.08, 146.78 (t, *J* = 6.6 Hz), 133.14 (t, *J* = 27.3 Hz), 132.91 (t, *J* = 5.9 Hz), 129.20, 123.30, 122.15 (t, *J* = 243.4 Hz), 119.80, 116.13, 58.22, 53.34, 49.19, 38.91 (t, *J* = 26.9 Hz), 26.44, 20.51 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -96.00 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{20}H_{26}F_2N_3$ ($[M+H]^+$): 346.2089, found: 346.2081.

1-(5,5-difluoro-5-(2-methoxypyridin-3-yl)pentyl)-4-phenylpiperazine (28a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (91.2 mg, 81% yield; 36.9 mg, 98% yield) as a white solid.

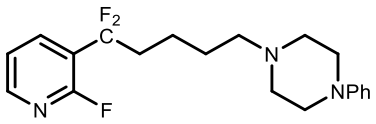
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (dd, *J* = 5.1, 1.9 Hz, 1H), 7.69 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.20 – 7.16 (m, 2H), 6.86 – 6.83 (m, 3H), 6.77 (t, *J* = 7.3 Hz, 1H), 3.92 (s, 3H), 3.10 (t, 4H), 2.49 (t, *J* = 5.0 Hz, 4H), 2.33 – 2.21 (m, 4H), 1.51 – 1.44 (m, 2H), 1.37 – 1.29 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.58 (t, *J* = 4.4 Hz), 151.41, 148.38 (t, *J* = 1.7 Hz), 135.90 (t, *J* = 8.3 Hz), 129.19, 121.91 (t, *J* = 243.4 Hz), 119.78, 119.50 (t, *J* = 28.3 Hz), 116.45, 116.13, 58.37, 53.76, 53.34, 49.19, 36.28 (t, *J* = 26.0 Hz), 26.53, 20.73 (t, *J* = 4.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -96.14 (t, *J* = 17.0 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{21}H_{28}F_2N_3O$ ($[M+H]^+$): 376.2195, found: 376.2182.

1-(5,5-difluoro-5-(2-fluoropyridin-3-yl)pentyl)-4-phenylpiperazine (29a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (58.8 mg, 54% yield; 30.7 mg, 84% yield) as a white solid.

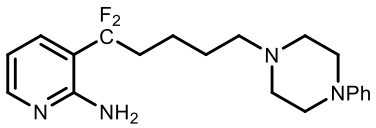
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 4.8 Hz, 1H), 7.91 – 7.86 (m, 1H), 7.21 – 7.16 (m, 3H), 6.85 (d, *J* = 7.9 Hz, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 3.11 (t, *J* = 5.0 Hz , 4H), 2.50 (t, *J* = 5.0 Hz, 4H), 2.32 – 2.16 (m, 4H), 1.54 – 1.47 (m, 2H), 1.43 – 1.35 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.84 (dt, *J* = 242.4, 5.1 Hz), 151.39, 149.29 (dt, *J* = 13.1, 2.0 Hz), 138.29 (td, *J* = 7.2, 3.4 Hz), 129.19, 121.48 (d, *J* = 4.6 Hz), 120.68 (td, *J* = 244.4, 7.1 Hz), 119.78, 120.17 – 119.31 (m), 116.13, 58.17, 53.33, 49.18, 37.19 (td, *J* = 26.0, 3.3 Hz), 26.37, 20.48 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -66.64 – -66.72 (m), -95.80 – -95.93 (m).

HRMS (ESI-TOF) m/z calcd. for $C_{20}H_{25}F_3N_3$ ($[M+H]^+$): 364.1995, found: 364.1982.

3-(1,1-difluoro-5-(4-phenylpiperazin-1-yl)pentyl)pyridin-2-amine (30a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 2:1:0.03) on silica gel to afford the title compound (86.4 mg, 80% yield; 27.1 mg, 75% yield) as a white solid.

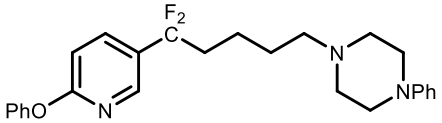
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 8.03 (m, 1H), 7.47 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.20 – 7.16 (m, 2H), 6.86 – 6.84 (m, 2H), 6.78 (tt, *J* = 7.3, 1.1 Hz, 1H), 6.63 (dd, *J* = 7.6, 5.0 Hz, 1H), 4.84 (s, 2H), 3.12 (t, *J* = 5.2 Hz, 4H), 2.50 (t, *J* = 5.2 Hz, 4H), 2.30 (t, *J* = 7.2 Hz, 2H), 2.23 – 2.11 (m, 2H), 1.54 – 1.37 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.17, 151.38, 149.78, 135.10 (t, *J* = 7.5 Hz), 129.20, 123.62 (t, *J* = 241.6 Hz), 119.81, 116.14, 115.75 (t, *J* = 26.6 Hz), 113.77, 58.24, 53.34, 49.18, 36.03 (t, *J* = 26.7 Hz), 26.41, 20.52 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -96.79 (t, *J* = 16.7 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{20}H_{27}F_2N_4$ ($[M+H]^+$): 361.2198, found: 361.2187.

1-(5,5-difluoro-5-(6-phenoxypyridin-3-yl)pentyl)-4-phenylpiperazine (31a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (93.1 mg, 71% yield; 23.2 mg, 53% yield) as a white solid.

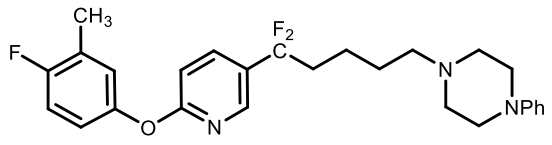
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 2.5 Hz, 1H), 7.69 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.34 (t, *J* = 7.9 Hz, 2H), 7.21 – 7.14 (m, 3H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.86 (dd, *J* = 8.4, 6.4 Hz, 3H), 6.78 (t, *J* = 7.3 Hz, 1H), 3.12 (t, *J* = 5.0 Hz, 4H), 2.51 (t, *J* = 5.0 Hz, 4H), 2.30 (dd, *J* = 8.4, 6.4 Hz, 2H), 2.14 – 2.02 (m, 2H), 1.54 – 1.37 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.74, 153.70, 151.39, 145.12 (t, *J* = 6.9 Hz), 136.73 (t, *J* = 5.5 Hz), 129.91, 129.23, 127.97 (t, *J* = 27.7 Hz), 125.31, 122.33 (t, *J* = 242.4 Hz), 121.52, 119.85, 116.18, 111.08, 58.26, 53.36, 49.21, 38.85 (t, *J* = 27.3 Hz), 26.46, 20.62 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -94.29 (td, *J* = 16.1, 4.6 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{26}H_{30}F_2N_3O$ ($[M+H]^+$): 438.2351, found: 438.2340.

1-(5,5-difluoro-5-(6-(4-fluoro-3-methylphenoxy)pyridin-3-yl)pentyl)-4-phenylpiperazine (32a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (56.3 mg, 40% yield; 37.2 mg, 79% yield) as a pink solid.

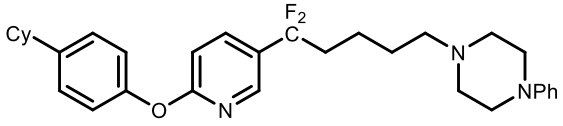
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 2.4 Hz, 1H), 7.68 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.18 (dd, *J* = 8.7, 7.2 Hz, 2H), 6.94 (t, *J* = 8.9 Hz, 1H), 6.90 – 6.81 (m, 5H), 6.77 (t, *J* = 7.3 Hz, 1H), 3.11 (t, *J* = 5.2 Hz, 4H), 2.50 (t, *J* = 5.2 Hz, 4H), 2.30 (t, *J* = 7.2 Hz, 2H), 2.20 (d, *J* = 2.0 Hz, 3H), 2.08 (tt, *J* = 16.0, 7.7 Hz, 2H), 1.53 – 1.37 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.79, 158.55 (d, *J* = 242.1 Hz), 151.39, 149.02 (d, *J* = 2.9 Hz), 145.02 (t, *J* = 6.8 Hz), 136.74, 129.21, 127.97 (t, *J* = 27.8 Hz), 126.45 (d, *J* = 19.2 Hz), 124.31 (d, *J* = 5.4 Hz), 122.29 (t, *J* = 242.2 Hz), 120.17 (d, *J* = 8.4 Hz), 119.83, 116.15, 115.95 (d, *J* = 24.4 Hz), 110.97, 58.22, 53.34, 49.20, 38.81 (t, *J* = 27.3 Hz), 26.44, 20.60 (t, *J* = 4.0 Hz), 14.85 (d, *J* = 3.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -94.22 (t, *J* = 16.2 Hz), -121.84 – -121.89 (m).

HRMS (ESI-TOF) m/z calcd. for $C_{27}H_{31}F_3N_3O$ ($[M+H]^+$): 470.2414, found: 470.2410.

1-(5-(6-(4-cyclohexylphenoxy)pyridin-3-yl)-5,5-difluoropentyl)-4-phenylpiperazine (33a)



The title product was prepared via procedure B & C, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (109.1 mg, 70% yield; 47.4 mg, 91% yield) as a pink solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 2.6 Hz, 1H), 7.65 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.15 (dd, *J* = 8.0, 4.8 Hz, 4H), 6.97 (d, *J* = 8.2 Hz, 2H), 6.83 (dd, *J* = 8.6, 4.1 Hz,

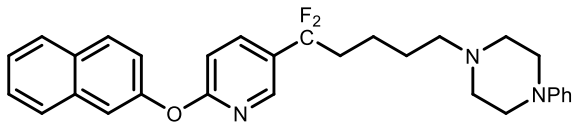
3H), 6.76 (t, *J* = 7.3 Hz, 1H), 3.10 (t, *J* = 4.8 Hz, 4H), 2.50 – 2.40 (m, 5H), 2.28 (t, *J* = 7.3 Hz, 2H), 2.07 (tt, *J* = 16.0, 7.6 Hz, 2H), 1.83 – 1.74 (m, 4H), 1.69 – 1.65 (m, 1H), 1.50 – 1.29 (m, 8H), 1.21 – 1.13 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.89, 151.51, 151.37, 145.08 (t, *J* = 6.8 Hz), 144.95, 136.61 (t, *J* = 5.5 Hz), 129.18, 128.14, 127.72 (t, *J* = 27.5 Hz), 122.33 (t, *J* = 242.2 Hz), 121.09, 119.78, 116.12, 110.94, 58.22, 53.32, 49.17, 44.06, 38.81 (t, *J* = 27.4 Hz), 34.62, 26.98, 26.43, 26.22, 20.60 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -94.18 (td, *J* = 16.2, 5.1 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{32}H_{40}F_2N_3O$ ($[M+H]^+$): 520.3134, found: 520.3124.

1-(5,5-difluoro-5-(6-(naphthalen-2-yloxy)pyridin-3-yl)pentyl)-4-phenylpiperazine (34a)



The title product was prepared via procedure B & C, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (90.6 mg, 62% yield; 41.6 mg, 85% yield) as a white solid.

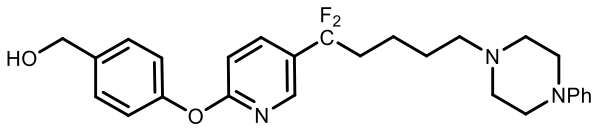
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 2.6 Hz, 1H), 7.81 – 7.76 (m, 2H), 7.70 (dd, *J* = 8.4, 2.8 Hz, 2H), 7.50 (d, *J* = 2.4 Hz, 1H), 7.42 – 7.35 (m, 2H), 7.22 – 7.17 (m, 3H), 6.91 (d, *J* = 8.6 Hz, 1H), 6.85 – 6.83 (m, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 3.10 (t, *J* = 5.0 Hz, 4H), 2.48 (t, *J* = 5.0 Hz, 4H), 2.30 – 2.27 (m, 2H), 2.08 (tt, *J* = 16.0, 7.8 Hz, 2H), 1.52 – 1.36 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.79, 151.37, 151.28, 145.12 (t, *J* = 6.9 Hz), 136.78 (t, *J* = 5.5 Hz), 134.26, 131.27, 129.87, 129.20, 128.06 (t, *J* = 27.7 Hz), 127.94, 127.62, 126.67, 125.57, 122.31 (t, *J* = 242.2 Hz), 121.46, 119.80, 118.00, 116.13, 111.14, 58.24, 53.34, 49.18, 38.84 (t, *J* = 27.2 Hz), 26.46, 20.60 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -94.25 (t, *J* = 16.1 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{30}H_{32}F_2N_3O$ ($[M+H]^+$): 488.2508, found: 488.2498.

(4-((5-(1,1-difluoro-5-(4-phenylpiperazin-1-yl)pentyl)pyridin-2-yl)oxy)phenyl)methanol (35a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 1:1:0.03) on silica gel to afford the title compound (58.9 mg, 42% yield; 35.9 mg, 77% yield) as a white solid.

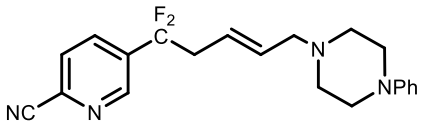
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (dd, *J* = 2.4, 1.0 Hz, 1H), 7.68 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.20 – 7.15 (m, 3H), 7.05 – 7.02 (m, 2H), 6.87 – 6.82 (m, 3H), 6.77 (tt, *J* = 7.2, 1.1 Hz, 1H), 4.59 (s, 2H), 3.10 (t, *J* = 5.2 Hz, 3H), 2.49 (t, *J* = 5.2 Hz, 3H), 2.28 (t, *J* = 6.8 Hz, 2H), 2.13 – 2.01 (m, 2H), 1.53 – 1.36 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.70, 153.05, 151.38, 145.05 (t, *J* = 6.9 Hz), 138.09, 136.75 (t, *J* = 5.6 Hz), 129.20, 128.52, 128.06 (t, *J* = 27.7 Hz), 122.29 (t, *J* = 242.4 Hz), 121.55, 119.85, 116.18, 111.11, 64.71, 58.22, 53.32, 49.18, 38.80 (t, *J* = 27.3 Hz), 26.39, 20.60 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -94.25 (t, *J* = 16.2 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{27}H_{32}F_2N_3O_2$ ($[M+H]^+$): 468.2457, found: 468.2447.

(*E*)-5-(1,1-difluoro-5-(4-phenylpiperazin-1-yl)pent-3-en-1-yl)picolinonitrile (36ab)



The title product was prepared via procedure B, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (48.6 mg, 44% yield; 38.8 mg, 35% yield for *E* isomer) as a yellow solid.

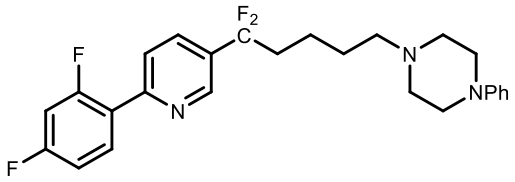
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.83 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.68 (d, *J* = 8.1 Hz, 1H), 7.18 (dd, *J* = 8.7, 6.9 Hz, 2H), 6.84 (d, *J* = 8.1 Hz, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 5.58 (dt, *J* = 13.6, 6.4 Hz, 1H), 5.46 (dt, *J* = 15.0, 6.9 Hz, 1H), 3.09 (t, *J* = 5.1 Hz, 4H), 2.93 – 2.80 (m, 4H), 2.43 (t, *J* = 5.1 Hz, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.21, 148.23 (t, *J* = 6.3 Hz), 135.85 (t, *J* = 27.6 Hz), 135.13, 134.66, 134.25 (t, *J* = 5.9 Hz), 129.17, 128.06, 122.68 (t, *J* = 4.9 Hz), 120.29 (*J* = 246.44 Hz), 119.80, 116.62, 116.08, 60.30, 53.03, 49.04, 42.19 (t, *J* = 27.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -96.37 (t, *J* = 15.8 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{21}H_{23}F_2N_4$ ($[M+H]^+$): 369.1885, found: 369.1879.

1-(5,5-difluoro-5-(6-(4-fluoro-3-methylphenoxy)pyridin-3-yl)pentyl)-4-phenylpiperazine (37a)



The title product was prepared via procedure B & C, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (82.3 mg, 60% yield; 30.8 mg, 67% yield) as a white solid.

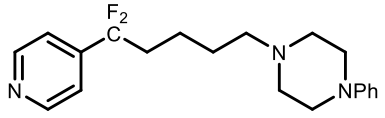
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, *J* = 2.0 Hz, 1H), 7.97 (td, *J* = 8.8, 6.6 Hz, 1H), 7.78 – 7.73 (m, 2H), 7.19 – 7.15 (m, 2H), 6.93 (td, *J* = 8.3, 2.5 Hz, 1H), 6.87 – 6.81 (m, 3H), 6.77 (t, *J* = 7.3 Hz, 1H), 3.11 (t, 4H), 2.50 (t, *J* = 5.0 Hz, 4H), 2.31 (t, *J* = 7.3 Hz, 2H), 2.14 (tt, *J* = 15.9, 7.7 Hz, 2H), 1.56 – 1.41 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.65 (dd, *J* = 251.9, 12.1 Hz), 160.88 (dd, *J* = 253.0, 12.0 Hz), 153.85, 151.36, 146.71 (t, *J* = 6.4 Hz), 133.60 (t, *J* = 5.8 Hz), 132.36 (dd, *J* = 9.8, 4.3 Hz), 131.70 (t, *J* = 27.5 Hz), 129.20, 123.65 (d, *J* = 10.1 Hz), 123.00 (dd, *J* = 11.3, 3.6 Hz), 122.26 (t, *J* = 243.4 Hz), 119.84, 116.16, 112.21 (dd, *J* = 21.2, 3.7 Hz), 104.62 (dd, *J* = 27.0, 25.4 Hz), 58.16, 53.33, 49.17, 38.85 (t, *J* = 26.9 Hz), 26.39, 20.53 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -95.70 (t, *J* = 16.2 Hz), -108.12 (p, *J* = 8.3 Hz), -112.40 (q, *J* = 9.7 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{26}H_{28}F_4N_3$ ($[M+H]^+$): 458.2214, found: 458.2211.

1-(5,5-difluoro-5-(pyridin-4-yl)pentyl)-4-phenylpiperazine (38a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (57.0 mg, 55% yield; 28.3 mg, 82% yield) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, *J* = 5.1 Hz, 2H), 7.29 (d, *J* = 5.0 Hz, 2H), 7.20 – 7.16 (m, 2H), 6.85 (d, *J* = 8.1 Hz, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 3.11 (t, *J* = 4.4

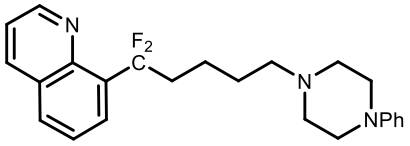
Hz, 4H), 2.49 (t, *J* = 5.1 Hz, 4H), 2.29 (t, *J* = 7.7 Hz, 2H), 2.06 (tt, *J* = 16.2, 7.7 Hz, 2H), 1.53 – 1.36 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.38, 150.38, 145.52 (t, *J* = 28.1 Hz), 129.19, 121.75 (t, *J* = 242.9 Hz), 119.81, 119.69 (t, *J* = 5.9 Hz), 116.13, 58.20, 53.35, 49.21, 38.47 (t, *J* = 26.5 Hz), 26.45, 20.41 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -98.52 (t, *J* = 16.4 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{20}H_{26}F_2N_3$ ($[M+H]^+$): 346.2089, found: 346.2080.

8-(1,1-difluoro-5-(4-phenylpiperazin-1-yl)pentyl)quinolone (39a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (48.6 mg, 41% yield; 20.5 mg, 52% yield) as a pink solid.

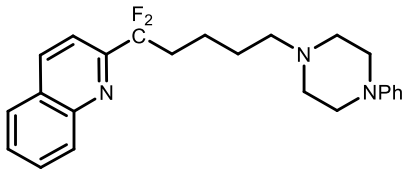
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.10 (dd, *J* = 8.4, 1.9 Hz, 1H), 7.91 (dd, *J* = 7.3, 1.4 Hz, 1H), 7.81 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 1H), 7.37 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.19 – 7.15 (m, 2H), 6.82 (d, *J* = 7.7 Hz, 2H), 6.76 (tt, *J* = 7.3, 1.1 Hz, 1H), 3.07 (t, *J* = 5.2 Hz, 4H), 2.75 (tt, *J* = 16.8, 8.0 Hz, 2H), 2.45 (t, *J* = 5.2 Hz, 4H), 2.25 (t, *J* = 7.2 Hz, 2H), 1.50 – 1.43 (m, 2H), 1.40 – 1.32 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.41, 150.19, 145.18 (t, *J* = 3.5 Hz), 136.50, 134.08 (t, *J* = 24.2 Hz), 130.55, 129.20, 128.85, 127.34 (t, *J* = 9.7 Hz), 125.74, 123.62 (t, *J* = 243.0 Hz), 121.39, 119.78, 116.14, 58.38, 53.28, 49.14, 37.95 (t, *J* = 25.3 Hz), 26.51, 20.99 (t, *J* = 4.4 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -92.19 (t, *J* = 17.0 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{24}H_{28}F_2N_3$ ($[M+H]^+$): 396.2246, found: 396.2238.

2-(1,1-difluoro-5-(4-phenylpiperazin-1-yl)pentyl)quinoline (40a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (56.9 mg, 48% yield; 30.0 mg, 76% yield) as a pink solid.

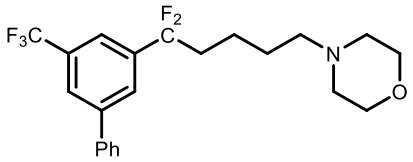
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.6 Hz, 1H), 8.08 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.77 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.69 – 7.63 (m, 2H), 7.51 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.19 – 7.15 (m, 2H), 6.84 – 6.81 (m, 2H), 6.76 (t, *J* = 7.3 Hz, 1H), 3.10 – 3.07 (m, 4H), 2.50 – 2.29 (m, 8H), 1.56 – 1.47 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.07 (t, *J* = 29.7 Hz), 151.44, 147.39, 137.47, 130.18, 129.98, 129.19, 128.30, 127.71, 127.67, 122.02 (t, *J* = 242.1 Hz), 119.75, 117.24 (t, *J* = 4.0 Hz), 116.13, 58.36, 53.32, 49.18, 36.25 (t, *J* = 25.0 Hz), 26.65, 20.37 (t, *J* = 4.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -97.88 (t, *J* = 17.5 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{24}H_{28}F_2N_3$ ($[M+H]^+$): 396.2246, found: 396.2238.

4-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)morpholine (41a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 10:1:0.03) on silica gel to afford the title compound (99.2 mg, 80% yield; 38.6 mg, 93% yield) as a colorless oil.

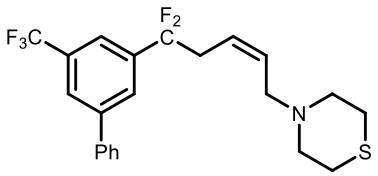
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.85 (s, 1H), 7.69 (s, 1H), 7.61 – 7.59 (m, 2H), 7.51 – 7.47 (m, 2H), 7.45 – 7.40 (m, 1H), 3.68 (t, *J* = 4.7 Hz, 4H), 2.40 (t, *J* = 4.6 Hz, 4H), 2.31 (t, *J* = 7.0 Hz, 2H), 2.19 (tt, *J* = 16.0, 7.4 Hz, 2H), 1.56 – 1.48 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.79, 139.16 (t, *J* = 27.4 Hz), 139.06, 131.71 (q, *J* = 32.6 Hz), 129.27, 128.65, 127.36, 127.17 (t, *J* = 5.9 Hz), 125.33 (d, *J* = 3.8 Hz), 123.89 (q, *J* = 273.7 Hz), 122.46 (t, *J* = 243.4 Hz), 120.84 – 120.74 (m), 67.04, 58.63, 53.82, 39.00 (t, *J* = 27.1 Hz), 26.15, 20.47 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.59, -95.92 (td, *J* = 16.7, 3.5 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{22}H_{25}F_5NO$ ($[M+H]^+$): 414.1851, found: 414.1837.

(*Z*)-4-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pent-2-en-1-yl)thio morpholine (42ab)



The title product was prepared via procedure A, purified by flash chromatography (PE:EA:Et_3N = 10:1:0.03) on silica gel to afford the title compound (102.5 mg, 80% yield; 69.2 mg, 54% yield for *Z* isomer) as a yellow oil.

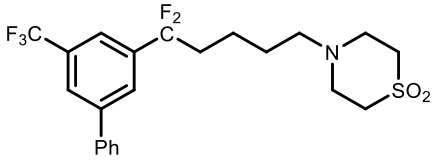
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.84 (s, 1H), 7.69 (s, 1H), 7.61 – 7.58 (m, 3H), 7.52 – 7.47 (m, 3H), 7.46 – 7.41 (m, 1H), 5.73 – 5.66 (m, 1H), 5.61 – 5.54 (m, 1H), 3.00 (td, *J* = 15.6, 7.5 Hz, 1H), 2.90 (d, *J* = 6.6 Hz, 1H), 2.62 – 2.59 (m, 6H), 2.57 – 2.54 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.81, 138.97, 138.59 (t, *J* = 27.2 Hz), 132.27, 131.72 (q, *J* = 32.7 Hz), 129.30, 128.71, 127.35, 125.42 (d, *J* = 3.9 Hz), 123.84 (q, J = 273.7 Hz), 122.58, 122.53, 121.49 (t, *J* = 246.4 Hz), 120.92 (q, *J* = 6.1 Hz), 55.95, 54.92, 37.75 (t, *J* = 28.3 Hz), 28.04.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.61, -94.96 (t, *J* = 15.5 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{22}H_{23}F_5NS$ ($[M+H]^+$): 428.1466, found: 428.1460.

4-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)thiomorpholine 1,1-dioxide (43a)



The title product was prepared via procedure A & C, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (77.5 mg, 56% yield; 40.7 mg, 88% yield) as a white solid.

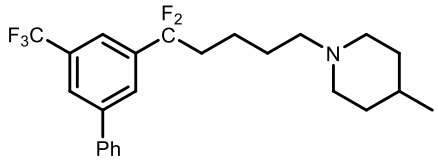
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.85 (s, 1H), 7.69 (s, 1H), 7.62 – 7.60 (m, 2H), 7.52 – 7.48 (m, 2H), 7.46 – 7.42 (m, 1H), 3.04 – 2.94 (m, 8H), 2.51 – 2.48 (m, 2H), 2.19 (tt, *J* = 15.9, 7.5 Hz, 2H), 1.54 – 1.50 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.83, 139.04 (t, *J* = 27.4 Hz), 138.95, 131.73 (q, *J* = 32.7 Hz), 129.30, 128.71, 127.33, 127.09 (t, *J* = 5.9 Hz), 125.40 – 125.37 (m), 123.85 (q, *J* = 273.7 Hz), 122.34 (t, *J* = 244.4 Hz), 120.70 – 120.68 (m), 56.55, 51.37, 50.80, 38.87 (t, *J* = 27.1 Hz), 26.66, 20.19 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.56 (d, *J* = 2.1 Hz), -96.07 (td, *J* = 16.5, 4.0 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{22}H_{25}F_5NO_2S$ ($[M+H]^+$): 462.1521, found: 462.1510.

1-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-4-methylpiperidine (44a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 10:1:0.03) on silica gel to afford the title compound (118.6 mg, 93% yield; 32.9 mg, 77% yield) as a pale yellow oil.

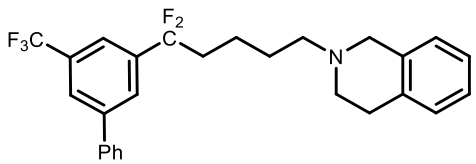
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.85 (s, 1H), 7.69 (s, 1H), 7.61 – 7.58 (m, 2H), 7.51 – 7.47 (m, 2H), 7.44 – 7.40 (m, 1H), 2.84 (dt, *J* = 11.1, 2.5 Hz, 2H), 2.28 (dd, *J* = 8.6, 6.3 Hz, 2H), 2.23 – 2.13 (m, 2H), 1.86 (td, *J* = 11.6, 2.5 Hz, 2H), 1.62 – 1.44 (m, 6H), 1.40 – 1.28 (m, 1H), 1.26 – 1.16 (m, 2H), 0.90 (d, *J* = 6.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.80, 139.26 (t, *J* = 27.5 Hz), 139.14, 131.74 (q, *J* = 32.7 Hz), 129.27, 128.62, 127.40, 127.20 (t, *J* = 6.1 Hz), 125.33 – 125.28 (m), 123.93 (q, *J* = 273.7 Hz), 122.51 (t, *J* = 243.2 Hz), 120.89 – 120.79 (m), 58.75, 54.20, 39.07 (t, *J* = 27.1 Hz), 34.42, 30.95, 26.77, 21.99, 20.74.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.61, -95.82 (t, *J* = 16.5 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{24}H_{29}F_5N$ ($[M+H]^+$): 426.2215, found: 426.2204.

2-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-1,2,3,4-tetrahydroisoquinoline (45a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (113.0 mg, 82% yield; 33.6 mg, 73% yield) as a yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.88 (s, 1H), 7.73 (s, 1H), 7.63 – 7.61 (m, 2H), 7.52 – 7.48 (m, 2H), 7.46 – 7.42 (m, 1H), 7.14 – 7.08 (m, 3H), 7.02 – 7.00 (m,

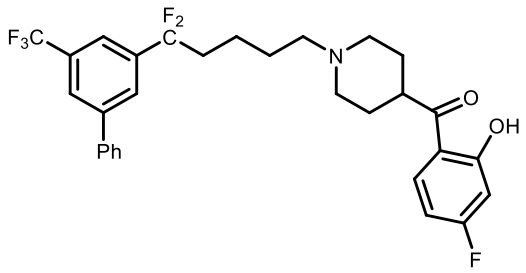
1H), 3.62 (s, 2H), 2.90 (t, *J* = 6.0 Hz, 2H), 2.72 (t, *J* = 6.0 Hz, 2H), 2.52 (dd, *J* = 8.1, 6.5 Hz, 2H), 2.31 – 2.19 (m, 2H), 1.72 – 1.54 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.81, 139.22 (t, *J* = 27.5 Hz), 139.10, 134.73, 134.35, 131.74 (q, *J* = 32.7 Hz), 129.26, 128.77, 128.62, 127.39, 127.20 (t, *J* = 6.1 Hz), 126.69, 126.27, 125.74, 125.33, 123.92 (q, *J* = 273.7 Hz), 122.50 (t, *J* = 243.3 Hz), 120.80 – 120.77 (m), 58.03, 56.27, 51.05, 39.08 (t, *J* = 27.1 Hz), 29.10, 26.86, 20.61 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.56, -95.80 (t, *J* = 16.4 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{27}H_{27}F_5N$ ($[M+H]^+$): 460.2058, found: 460.2054.

3-(1-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)piperidin-4-yl)-6-fluoro-2,3-dihydrobenzo[d]isoxazole (46a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 2:1:0.03) on silica gel to afford the title compound (153.5 mg, 94% yield; 33.9 mg, 62% yield) as a yellow solid.

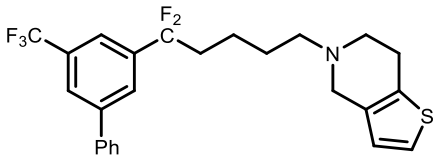
^{1}H NMR (400 MHz, $CDCl_3$) δ 12.82 (s, 1H), 7.90 (s, 1H), 7.86 (s, 1H), 7.76 (dd, *J* = 8.9, 6.5 Hz, 1H), 7.70 (s, 1H), 7.61 (d, *J* = 7.5 Hz, 2H), 7.50 (t, *J* = 7.5 Hz, 2H), 7.43 (t, *J* = 7.3 Hz, 1H), 6.66 (dd, *J* = 10.4, 2.6 Hz, 1H), 6.60 (td, *J* = 8.5, 2.5 Hz, 1H), 3.18 (tt, *J* = 10.4, 4.4 Hz, 1H), 2.99 (d, *J* = 11.1 Hz, 2H), 2.36 (t, *J* = 7.1 Hz, 2H), 2.21 (tt, *J* = 15.8, 7.5 Hz, 2H), 2.06 (td, *J* = 11.4, 3.3 Hz, 2H), 1.92 – 1.79 (m, 4H), 1.59 – 1.49 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.70, 167.39 (d, *J* = 256.7 Hz), 165.82 (d, *J* = 14.3 Hz), 142.79, 139.17 (t, *J* = 27.4 Hz), 139.06, 132.09 (d, *J* = 11.7 Hz), 131.70 (q, *J* = 32.3 Hz), 129.28, 128.65, 127.38, 127.18 (t, *J* = 6.0 Hz), 125.34, 123.90 (q, *J* = 273.7 Hz), 122.49 (t, *J* = 244.4 Hz), 120.76 (d, *J* = 3.8 Hz), 115.41 (d, *J* = 2.3 Hz), 107.20 (d, *J* = 22.8 Hz), 105.45 (d, *J* = 23.4 Hz), 58.40, 53.24, 43.68, 39.02 (t, *J* = 27.1 Hz), 28.90, 26.62, 20.59 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.55, -95.89 (t, *J* = 16.4 Hz), -98.54 – -101.81 (m).

HRMS (ESI-TOF) m/z calcd. for $C_{30}H_{30}F_6NO_2$ ($[M+H]^+$): 550.2175, found: 550.2177.

5-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine (47a)



The title product was prepared via procedure A & E, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (125.1 mg, 90% yield; 20.1 mg, 43% yield) as a pale yellow oil.

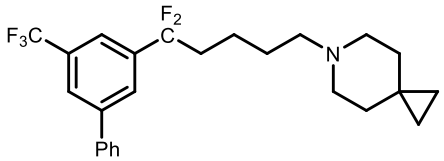
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.86 (s, 1H), 7.71 (s, 1H), 7.61 (d, *J* = 7.6 Hz, 2H), 7.50 (t, *J* = 7.4 Hz, 2H), 7.44 (t, *J* = 7.3 Hz, 1H), 7.07 (d, *J* = 5.1 Hz, 1H), 6.72 (d, *J* = 5.1 Hz, 1H), 3.54 (s, 2H), 2.87 (t, *J* = 5.7 Hz, 2H), 2.77 (t, *J* = 5.8 Hz, 2H), 2.54 (t, *J* = 7.4 Hz, 2H), 2.29 – 2.17 (m, 2H), 1.69 – 1.52 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.79, 139.18 (t, *J* = 27.4 Hz), 139.09, 133.84, 133.50, 131.72 (q, *J* = 32.6 Hz), 129.28, 128.64, 127.40, 127.19, 125.34, 123.90 (q, *J* = 274.7 Hz), 122.83, 122.48 (t, *J* = 244.4 Hz), 120.79, 57.55, 53.27, 51.08, 39.11 (t, *J* = 27.1 Hz), 27.10, 25.53, 20.59 (t, *J* = 3.9 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.55, -95.86 (t, *J* = 16.4 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{25}H_{25}F_5NS$ ($[M+H]^+$): 466.1622, found: 466.1614.

6-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-6-azaspiro[2.5]octane (48a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (108.9 mg, 83% yield; 43.0 mg, 96% yield) as a pink solid.

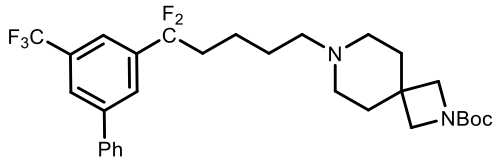
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.85 (s, 1H), 7.69 (s, 1H), 7.60 (d, *J* = 7.0 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 2H), 7.42 (t, *J* = 7.3 Hz, 1H), 2.54 (s, 4H), 2.44 (dd, *J* = 9.1, 6.3 Hz, 2H), 2.27 – 2.15 (m, 2H), 1.67 – 1.59 (m, 2H), 1.54 – 1.42 (m, 6H), 0.27 (s, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.81, 139.13 (t, *J* = 27.4 Hz), 139.05, 131.71 (q, *J* = 32.7 Hz), 129.25, 128.62, 127.37, 127.17 (t, *J* = 5.9 Hz), 125.33, 123.89 (q, *J* = 273.7 Hz), 122.42 (t, *J* = 243.2 Hz), 120.73 (d, *J* = 3.1 Hz), 58.35, 53.25, 38.93 (t, *J* = 27.0 Hz), 34.53, 26.16, 20.59 (t, *J* = 4.0 Hz), 17.36, 11.56.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.61, -95.81 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{25}H_{29}F_5N$ ($[M+H]^+$): 438.2215, found: 438.2202.

***tert*-butyl-7-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-2,7-diazaspiro[3.5]nonane-2-carboxylate (49a)**



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (99.4 mg, 60% yield; 53.7 mg, 97% yield) as a yellow solid.

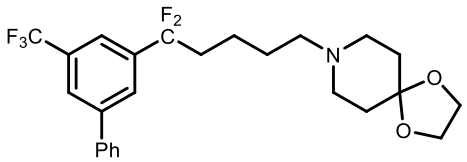
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.83 (s, 1H), 7.68 (s, 1H), 7.60 – 7.57 (m, 2H), 7.49 – 7.45 (m, 2H), 7.43 – 7.38 (m, 1H), 3.57 (s, 4H), 2.43 – 2.09 (m, 8H), 1.70 (t, *J* = 5.4 Hz, 4H), 1.53 – 1.40 (m, 13H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.59, 142.78, 139.18 (t, *J* = 27.5 Hz), 139.06, 131.71 (q, *J* = 32.7 Hz), 129.25, 128.63, 127.35, 127.16 (t, *J* = 5.9 Hz), 125.29, 123.89 (q, *J* = 273.7 Hz), 122.45 (t, *J* = 243.1 Hz), 120.75, 79.38, 58.28, 50.61, 38.92 (t, *J* = 27.0 Hz), 35.53, 33.46, 28.52, 26.56, 20.55 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.60, -95.80 (t, *J* = 16.4 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{30}H_{38}F_5N_2O_2$ ($[M+H]^+$): 553.2848, found: 553.2841.

8-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-1,4-dioxa-8-azaspiro[4.5]decane (50a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 10:1:0.03) on silica gel to afford the title compound (90.1 mg, 64% yield; 38.6 mg, 82% yield) as a colorless oil.

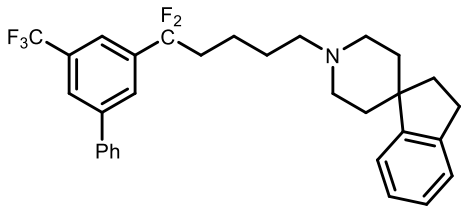
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.84 (s, 1H), 7.69 (s, 1H), 7.61 – 7.58 (m, 2H), 7.51 – 7.47 (m, 2H), 7.42 – 7.40 (m, 1H), 3.94 (s, 4H), 2.51 – 2.48 (m, 4H), 2.35 (t, *J* = 7.2 Hz, 2H), 2.25 – 2.13 (m, 2H), 1.73 (t, *J* = 5.7 Hz, 4H), 1.57 – 1.46 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.81, 139.23 (t, *J* = 27.5 Hz), 139.11, 131.74 (q, *J* = 32.7 Hz), 129.27, 128.63, 127.39, 127.19 (t, *J* = 5.7 Hz), 125.33, 123.91 (q, *J* = 274.7 Hz), 122.47 (t, *J* = 243.1 Hz), 120.79 – 120.76 (d, *J* = 3.3 Hz), 107.34, 64.33, 57.88, 51.49, 39.04 (t, *J* = 27.1 Hz), 34.90, 26.92, 20.65.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.62, -95.85 (t, *J* = 16.4 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{25}H_{29}F_5NO_2$ ($[M+H]^+$): 470.2113, found: 470.2108.

1'-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-2,3-dihydrospiro[indene-1,4'-piperidine] (51a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 5:1:0.03) on silica gel to afford the title compound (123.2 mg, 80% yield; 36.4 mg, 71% yield) as a white solid.

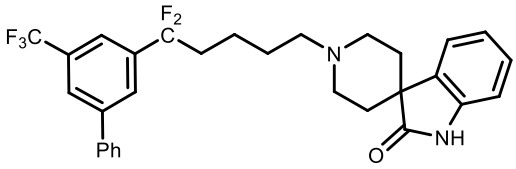
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.89 (s, 1H), 7.73 (s, 1H), 7.63 (d, *J* = 7.8 Hz, 2H), 7.51 (t, *J* = 7.5 Hz, 2H), 7.45 (t, *J* = 7.3 Hz, 1H), 7.23 – 7.17 (m, 4H), 2.92 – 2.86 (m, 4H), 2.39 (t, *J* = 7.4 Hz, 2H), 2.30 – 2.11 (m, 4H), 2.02 – 1.91 (m, 4H), 1.63 – 1.53 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.41, 143.21, 142.79, 139.23 (t, *J* = 27.5 Hz), 139.09, 131.72 (q, *J* = 32.7 Hz), 129.27, 128.63, 127.38, 127.19, 126.78, 126.53, 125.32, 124.66, 123.91 (q, *J* = 273.7 Hz), 122.65, 122.49 (t, *J* = 244.4 Hz), 120.79, 58.87, 51.42, 46.52, 39.10 (t, *J* = 27.1 Hz), 36.93, 35.03, 29.98, 26.80, 20.75 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.53, -95.85 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{31}H_{33}F_5N$ ($[M+H]^+$):514.2528, found: 514.2521.

1'-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)spiro[isoindoline-1,4'-piperidin]-3-one (52a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (112.5 mg, 71% yield; 50.3 mg, 95% yield) as a white solid.

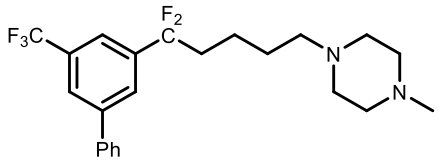
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.10 (s, 1H), 7.91 (s, 1H), 7.88 (s, 1H), 7.73 (s, 1H), 7.64 – 7.60 (m, 2H), 7.52 – 7.48 (m, 2H), 7.45 – 7.41 (m, 1H), 7.35 (d, *J* = 7.5 Hz, 1H), 7.20 (td, *J* = 7.7, 1.2 Hz, 1H), 7.01 (td, *J* = 7.6, 1.0 Hz, 1H), 6.92 (d, *J* = 7.7 Hz, 1H), 2.97 – 2.91 (m, 2H), 2.73 – 2.68 (m, 2H), 2.53 (t, *J* = 7.3 Hz, 2H), 2.24 (tt, *J* = 16.2, 7.6 Hz, 2H), 2.01 – 1.85 (m, 4H), 1.69 – 1.53 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 182.87, 142.81, 140.31, 139.24 (t, *J* = 27.4 Hz), 139.09, 135.17, 131.73 (q, *J* = 32.7 Hz), 129.26, 128.62, 127.81, 127.38, 127.18 (t, *J* = 5.9 Hz), 125.35 –125.30 (m), 123.92 (q, *J* = 273.7 Hz), 123.81, 122.48 (t, *J* = 244.4 Hz), 122.20, 120.80 – 120.78 (m), 109.83, 58.48, 48.63, 45.63, 39.07 (t, *J* = 27.0 Hz), 33.08, 26.62, 20.66 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.55, -95.85 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{30}H_{30}F_5N_2O$ ($[M+H]^+$): 529.2273, found: 529.2265.

1-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-4-methylpiperazine (53a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 5:1:0.03) on silica gel to afford the title compound (111.2 mg, 87% yield; 35.2 mg, 83% yield) as a pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.84 (s, 1H), 7.68 (s, 1H), 7.60 – 7.58 (m, 2H), 7.50 – 7.46 (m, 2H), 7.43 – 7.39 (m, 1H), 2.43 – 2.13 (m, 15H), 1.57 – 1.44 (m, 4H).

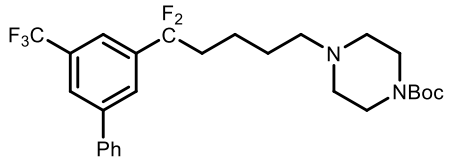
^{13}C NMR (101 MHz, $CDCl_3$) δ 142.77, 139.18 (t, *J* = 27.4 Hz), 139.08, 131.71 (q, *J* = 32.6 Hz), 129.25, 128.62, 127.37, 127.17 (t, *J* = 6.1 Hz), 125.31, 123.89 (q, *J* =

273.7 Hz), 122.46 (t, J = 244.4 Hz), 120.79 – 120.75 (m), 58.19, 55.17, 53.24, 46.09, 39.00 (t, *J* = 27.1 Hz), 26.49, 20.56 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.59, -95.89 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{23}H_{28}F_5N_2$ ($[M+H]^+$): 427.2167, found: 427.2159.

***tert*-butyl-4-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)piperazine-1-carboxylate (54a)**



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (107.6 mg, 70% yield; 38.0 mg, 74% yield) as a colorless oil.

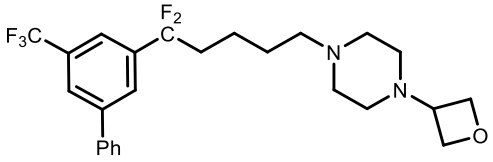
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.85 (s, 1H), 7.69 (s, 1H), 7.62 – 7.59 (m, 2H), 7.49 (t, *J* = 7.4 Hz, 2H), 7.45 – 7.41 (m, 1H), 3.41 (t, *J* = 5.0 Hz, 4H), 2.36 – 2.31 (m, 6H), 2.20 (tt, *J* = 15.9, 7.5 Hz, 2H), 1.59 – 1.49 (m, 4H), 1.45 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 154.85, 142.80, 139.15 (t, *J* = 27.5 Hz), 139.06, 131.71 (q, *J* = 32.7 Hz), 129.27, 128.65, 127.36, 127.17 (t, *J* = 5.7 Hz), 125.34, 123.88 (q, *J* = 273.7 Hz), 122.44 (t, *J* = 244.4 Hz), 121.31 – 120.46 (m), 79.75, 58.22, 53.09, 38.98 (t, *J* = 27.1 Hz), 28.53, 26.37, 20.49 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.59, -95.95 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{27}H_{34}F_5N_2O_2$ ($[M+H]^+$): 513.2535, found: 513.2525.

1-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-4-(oxetan-3-yl)piperazine (55a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (102.5 mg, 73% yield; 35.7 mg, 76% yield) as a pink solid.

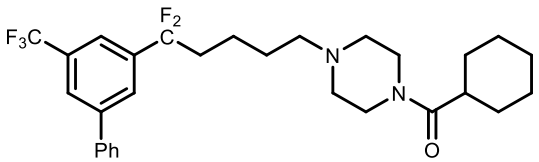
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.84 (s, 1H), 7.68 (s, 1H), 7.61 – 7.58 (m, 2H), 7.50 – 7.46 (m, 2H), 7.44 – 7.40 (m, 1H), 4.61 (dt, *J* = 16.9, 6.3 Hz, 4H), 3.46 (p, *J* = 6.4 Hz, 1H), 2.47 – 2.13 (m, 12H), 1.56 – 1.46 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.79, 139.18 (t, *J* = 27.5 Hz), 139.08, 131.73 (q, *J* = 32.7 Hz), 129.26, 128.64, 127.36, 127.16 (t, *J* = 6.0 Hz), 125.31, 123.89 (q, *J* = 273.7 Hz), 122.45 (t, *J* = 243.2 Hz), 120.93 – 120.59 (m), 75.56, 59.34, 58.13, 52.79, 49.60, 38.97 (t, *J* = 27.0 Hz), 26.40, 20.53 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.62, -95.83 (t, *J* = 16.4 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{25}H_{30}F_5N_2O$ ($[M+H]^+$): 469.2273, found: 469.2263.

cyclohexyl(4-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)piperazin-1-yl)methanone (56a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (131.6 mg, 84% yield; 38.2 mg, 73% yield) as a pale yellow solid.

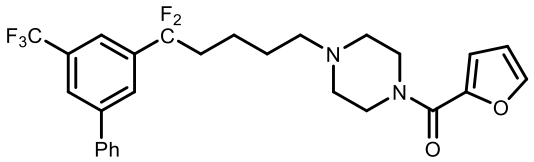
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.85 (s, 1H), 7.68 (s, 1H), 7.61 – 7.58 (m, 2H), 7.50 – 7.46 (m, 2H), 7.44 – 7.40 (m, 1H), 3.58 (t, *J* = 5.1 Hz, 2H), 3.46 (t, *J* = 4.9 Hz, 2H), 2.46 – 2.31 (m, 7H), 2.19 (tt, *J* = 15.9, 7.5 Hz, 2H), 1.81 – 1.77 (m, 2H), 1.71 – 1.67 (m, 3H), 1.56 – 1.46 (m, 6H), 1.31 – 1.20 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.62, 142.80, 139.12 (t, *J* = 27.4 Hz), 139.03, 131.71 (q, *J* = 32.7 Hz), 129.27, 128.65, 127.34, 127.14, 125.33, 123.87 (q, *J* = 273.7 Hz), 122.42 (t, *J* = 243.1 Hz), 120.72, 58.01, 53.79, 53.00, 45.34, 41.51, 40.46, 38.93 (t, *J* = 27.0 Hz), 29.47, 26.30, 25.94, 20.45 (d, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.58, -95.94 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{29}H_{36}F_5N_2O$ ($[M+H]^+$): 523.2742, found: 523.2737.

(4-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)piperazin-1-yl)(furan-2-yl)methanone (57a)



The title product was prepared via procedure A & C, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (59.2 mg, 39% yield; 42.7 mg, 84% yield) as a pale yellow solid.

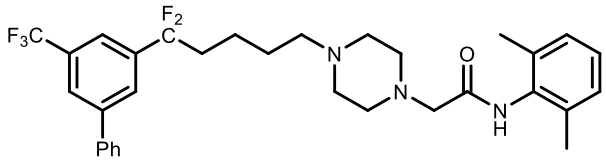
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.85 (s, 1H), 7.70 (s, 1H), 7.62 – 7.59 (m, 2H), 7.51 – 7.40 (m, 4H), 6.98 (d, *J* = 3.5 Hz, 1H), 6.47 (dd, *J* = 3.5, 1.8 Hz, 1H), 3.78 (s, 4H), 2.45 (t, *J* = 5.1 Hz, 4H), 2.36 (t, *J* = 6.8 Hz, 2H), 2.21 (tt, *J* = 15.8, 7.4 Hz, 2H), 1.60 – 1.48 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.12, 148.03, 143.73, 142.79, 139.12 (t, *J* = 27.4 Hz), 139.02, 131.70 (q, *J* = 32.7 Hz), 129.27, 128.65, 127.35, 127.15 (t, *J* = 6.2 Hz), 125.35 – 125.31 (m), 123.87 (q, *J* = 273.7 Hz), 122.43 (t, *J* = 244.4 Hz), 120.82 – 120.72 (m), 116.40, 111.34, 58.00, 53.35, 38.95 (t, *J* = 27.1 Hz), 26.36, 20.43 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.57, -95.92 (t, *J* = 16.4 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{27}H_{28}F_5N_2O_2$ ($[M+H]^+$): 507.2065, found: 507.2059.

2-(4-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)piperazin-1-yl)-*N*-(2,6-dimethylphenyl)acetamide (58a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (68.8 mg, 40% yield; 47.7 mg, 83% yield) as a pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (s, 1H), 7.90 (s, 1H), 7.86 (s, 1H), 7.70 (s, 1H), 7.62 – 7.59 (m, 2H), 7.52 – 7.48 (m, 2H), 7.45 – 7.41 (m, 1H), 7.10 – 7.08 (m, 3H), 3.18 (s, 2H), 2.70 (s, 4H), 2.51 (s, 4H), 2.35 (t, *J* = 7.0 Hz, 2H), 2.27 – 2.15 (m, 8H), 1.60 – 1.47 (m, 4H).

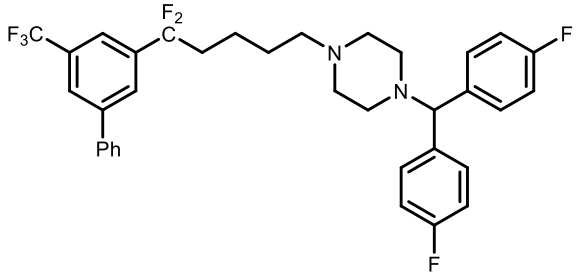
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.57, 142.80, 139.15 (t, *J* = 27.4 Hz), 139.03, 135.06, 133.76, 131.71 (q, *J* = 32.7 Hz), 129.26, 128.65, 128.38, 127.33, 127.24, 127.15 (t, *J* = 6.1 Hz), 125.30, 123.88 (q, *J* = 273.7 Hz), 122.44 (t, *J* = 243.2 Hz),

120.74 – 120.72 (m), 61.74, 57.99, 53.84, 53.42, 38.92 (t, *J* = 27.1 Hz), 26.41, 20.46, 18.71.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.56, -95.77 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{32}H_{37}F_5N_3O$ ($[M+H]^+$): 574.2851, found: 574.2846.

1-(bis(4-fluorophenyl)methyl)-4-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)piperazine (59a)



The title product was prepared via procedure A & C, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (94.0 mg, 51% yield; 52.9 mg, 86% yield) as a pale yellow solid.

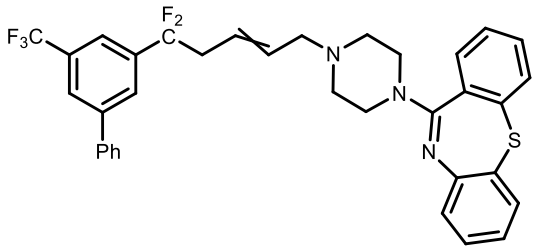
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.86 (s, 1H), 7.71 (s, 1H), 7.62 – 7.60 (m, 2H), 7.52 – 7.48 (m, 2H), 7.46 – 7.42 (m, 1H), 7.36 – 7.32 (m, 4H), 6.97 (t, *J* = 8.7 Hz, 4H), 4.20 (s, 1H), 2.45 – 2.16 (m, 12H), 1.56 – 1.48 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.91 (d, *J* = 245.4 Hz), 142.77, 139.18 (t, *J* = 27.4 Hz), 139.06, 138.37 (d, *J* = 3.2 Hz), 131.70 (q, *J* = 32.7 Hz), 129.35 (d, *J* = 7.8 Hz), 129.26, 128.63, 127.37, 127.16 (t, *J* = 6.0 Hz), 125.32, 123.90 (q, *J* = 273.7 Hz), 122.46 (t, *J* = 244.4 Hz), 120.78, 115.48 (d, *J* = 21.2 Hz), 74.62, 58.17, 53.50, 51.79, 38.98 (t, *J* = 27.0 Hz), 26.43, 20.57 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.58, -95.86 (t, *J* = 16.4 Hz), -115.71 – -115.78 (m).

HRMS (ESI-TOF) m/z calcd. for $C_{35}H_{34}F_7N_2$ ($[M+H]^+$): 615.2605, found: 615.2596.

(*E*/*Z*)11-(4-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pent-2-en-1-yl)piperazin-1-yl)dibenzo[b,f][1,4]thiazepine (60ab)



The title product was prepared via procedure A, purified by flash chromatography (PE:EA:Et_3N = 1:1:0.03) on silica gel to afford the title compound (176.4 mg, 95% yield) as a pale yellow solid.

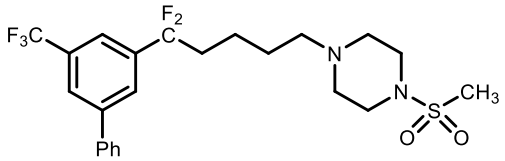
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.72 (m, 2H), 7.59 (d, *J* = 10.5 Hz, 1H), 7.48 – 7.44 (m, 2H), 7.41 – 7.31 (m, 3H), 7.30 – 7.26 (m, 2H), 7.22 – 7.14 (m, 3H), 7.06 (td, *J* = 7.6, 1.6 Hz, 1H), 6.97 (dd, *J* = 8.0, 1.5 Hz, 1H), 6.77 (td, *J* = 7.4, 1.5 Hz, 1H), 5.67 – 5.43 (m, 2H), 3.37 (s, 4H), 2.96 – 2.79 (m, 4H), 2.31 – 2.20 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.75, 148.99, 148.95, 142.76, 142.72, 139.96, 139.92, 138.84, 138.78, 138.61 (t, *J* = 27.3 Hz), 138.57 (t, *J* = 27.3 Hz), 134.17, 133.67, 132.21, 132.18, 131.61 (q, *J* = 32.3 Hz), 131.59 (q, *J* = 33.3 Hz), 130.80, 129.23, 129.22, 129.13, 129.02, 128.62, 128.27, 128.01, 127.26, 127.20, 125.40, 125.26 – 125.22 (m, *J* = 4.9 Hz), 123.83 (t, *J* = 5.1 Hz), 123.81 (q, *J* = 273.7 Hz), 122.86, 122.83, 122.39 (t, *J* = 5.1 Hz), 121.45 (t, *J* = 245.4 Hz), 121.36 (t, *J* = 245.4 Hz), 120.83, 60.50, 55.13, 52.80, 42.44 (t, *J* = 28.1 Hz), 37.72 (t, *J* = 28.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.42, -62.43, -94.75 – -94.84 (m), -94.96 – -95.10 (m).

HRMS (ESI-TOF) m/z calcd. for $C_{35}H_{31}F_5N_3S$ ($[M+H]^+$): 620.2153, found: 620.2156.

1-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-4-(methylsulfonyl)piperazine (61a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (104.4 mg, 71% yield; 32.5 mg, 66% yield) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.84 (s, 1H), 7.68 (s, 1H), 7.68 – 7.58 (m, 2H), 7.51 – 7.47 (m, 2H), 7.45 – 7.41 (m, 1H), 3.20 (t, *J* = 4.9 Hz, 4H), 2.75 (s, 3H),

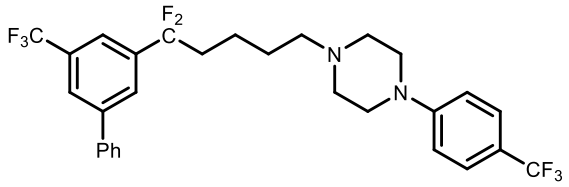
2.50 (t, *J* = 5.0 Hz, 4H), 2.37 (t, *J* = 6.7 Hz, 2H), 2.19 (tt, *J* = 15.9, 7.4 Hz, 2H), 1.56 – 1.48 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.80, 139.11 (t, *J* = 27.4 Hz), 139.00, 131.70 (q, *J* = 32.7 Hz), 129.29, 128.69, 127.34, 127.14 (t, *J* = 6.1 Hz), 125.33, 123.88 (q, *J* = 273.7 Hz), 122.42 (t, *J* = 243.4 Hz), 120.75 – 120.72 (m), 57.67, 52.46, 45.93, 38.92 (t, *J* = 27.1 Hz), 34.07, 26.32, 20.35 (t, *J* = 3.9 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.56, -95.95 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{23}H_{28}F_5N_2O_2S$ ($[M+H]^+$): 491.1786, found: 491.1775.

1-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-4-(4-(trifluoro methyl)phenyl)piperazine (62a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (133.0 mg, 80% yield; 40.7 mg, 73% yield) as a white solid.

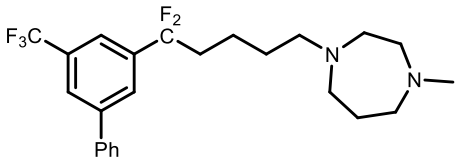
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.88 (s, 1H), 7.73 (s, 1H), 7.63 – 7.61 (m, 2H), 7.52 – 7.42 (m, 5H), 6.91 (d, *J* = 8.6 Hz, 2H), 3.26 (t, *J* = 5.2 Hz, 4H), 2.57 (t, *J* = 5.2 Hz, 4H), 2.40 (t, *J* = 7.0 Hz, 2H), 2.30 – 2.18 (m, 2H), 1.65 – 1.51 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.42, 142.85, 139.22 (t, *J* = 27.4 Hz), 139.08, 131.78 (q, *J* = 32.6 Hz), 129.30, 128.68, 127.38, 127.20 (t, *J* = 6.1 Hz), 126.50 (q, *J* = 3.7 Hz), 125.37, 124.93 (q, *J* = 271.7 Hz), 123.94 (q, *J* = 273.7 Hz), 122.51 (t, *J* = 243.4 Hz), 120.74 (t, *J* = 32.3 Hz), 120.82 – 120.79 (m), 114.59, 58.12, 53.04, 48.04, 38.98 (t, *J* = 27.0 Hz), 26.44, 20.54 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -61.29, -62.57, -95.82 (t, *J* = 16.5 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{29}H_{29}F_8N_2$ ($[M+H]^+$): 557.2198, found: 557.2190.

1-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-4-methyl-1,4-di azepane (63a)



The title product was prepared via procedure A & C, purified by flash chromatography (PE:EA:Et_3N = 1:1:4%) on silica gel to afford the title compound (112.3 mg, 85% yield; 60.1 mg, 68% yield) as a yellow oil.

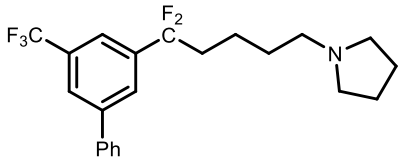
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.84 (s, 1H), 7.68 (d, *J* = 1.9 Hz, 1H), 7.60 – 7.58 (m, 2H), 7.49 – 7.44 (m, 2H), 7.43 – 7.38 (m, 1H), 2.67 – 2.64 (m, 4H), 2.59 – 2.54 (m, 4H), 2.43 (t, *J* = 6.8 Hz, 2H), 2.31 (s, 3H), 2.18 (tt, *J* = 15.8, 7.5 Hz, 2H), 1.75 (p, *J* = 6.0 Hz, 2H), 1.51 – 1.45 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.75, 139.23 (t, *J* = 27.5 Hz), 139.06, 131.68 (q, *J* = 32.6 Hz), 129.22, 128.58, 127.34, 127.15 (t, *J* = 5.9 Hz), 125.27 – 125.23 (m), 123.88 (q, *J* = 274.7 Hz), 122.50 (t, *J* = 243.1 Hz), 120.84 – 120.73 (m), 58.07, 58.02, 56.95, 54.77, 54.25, 47.08, 38.99 (t, *J* = 27.0 Hz), 27.41, 27.19, 20.43 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.59, -95.78 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{24}H_{30}F_5N_2$ ($[M+H]^+$): 441.2324, found: 441.2313.

1-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)pyrrolidine (64a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 10:1:0.03) on silica gel to afford the title compound (102.5 mg, 86% yield; 31.9 mg, 80% yield) as a colorless oil.

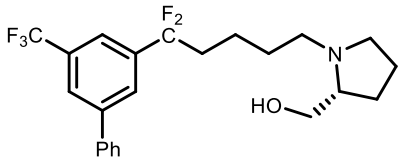
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.85 (s, 1H), 7.69 (s, 1H), 7.61 – 7.59 (m, 2H), 7.51 – 7.47 (m, 2H), 7.44 – 7.40 (m, 1H), 2.48 – 2.40 (m, 6H), 2.26 – 2.14 (m, 2H), 1.77 – 1.74 (m, 4H), 1.59 – 1.49 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.78, 139.22 (t, *J* = 27.4 Hz), 139.10, 131.70 (q, *J* = 32.6 Hz), 129.26, 128.62, 127.39, 127.20 (t, *J* = 6.1 Hz), 125.33 – 125.29 (m), 123.91 (q, *J* = 273.7 Hz), 122.49 (t, *J* = 243.4 Hz), 120.79 (d, *J* = 4.1 Hz), 56.28, 54.33, 39.10 (t, *J* = 27.1 Hz), 28.71, 23.48, 20.71 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.59, -95.89 (t, *J* = 16.4 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{22}H_{25}F_5N$ ($[M+H]^+$): 398.1902, found: 398.1891.

(*R*)-(1-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)pyrrolidin-2-yl)methanol (65a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 2:1:0.03) on silica gel to afford the title compound (117.4 mg, 92% yield; 18.4 mg, 43% yield) as a yellow oil.

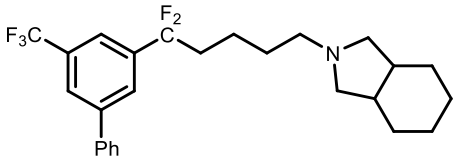
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.86 (s, 1H), 7.70 (s, 1H), 7.61 (d, *J* = 7.6 Hz, 2H), 7.50 (t, *J* = 7.5 Hz, 2H), 7.43 (t, *J* = 7.3 Hz, 1H), 3.60 (dd, *J* = 10.7, 3.6 Hz, 1H), 3.38 (dd, *J* = 10.8, 2.4 Hz, 1H), 3.14 (dt, *J* = 9.1, 4.1 Hz, 1H), 2.75 – 2.68 (m, 1H), 2.56 – 2.54 (m, 1H), 2.29 – 2.15 (m, 4H), 1.91 – 1.82 (m, 1H), 1.78 – 1.69 (m, 3H), 1.58 – 1.49 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.83, 139.22 (t, *J* = 27.6 Hz), 139.10, 131.58 (t, *J* = 32.8 Hz), 129.28, 128.64, 127.40, 127.20 (d, *J* = 6.1 Hz), 125.36, 123.91 (q, *J* = 273.7 Hz), 122.45 (t, *J* = 243.1 Hz), 120.77, 65.02, 61.94, 54.26, 54.19, 39.05 (t, *J* = 27.2 Hz), 28.66, 27.71, 23.67, 20.38 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.61, -96.08 (t, *J* = 16.4 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{23}H_{27}F_5NO$ ($[M+H]^+$): 428.2007, found: 428.2001.

2-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)octahydro-1*H*-isoindole (66a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (102.9 mg, 76% yield; 35.8 mg, 79% yield) as a pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.85 (s, 1H), 7.69 (s, 1H), 7.61 – 7.58 (m, 2H), 7.51 – 7.46 (m, 2H), 7.44 – 7.40 (m, 1H), 2.73 (dd, *J* = 9.2, 6.9 Hz, 2H), 2.50 (t,

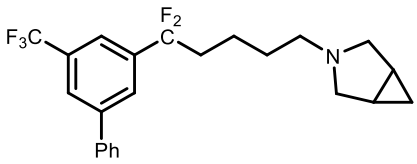
J = 7.1 Hz, 2H), 2.44 (dd, *J* = 9.3, 5.6 Hz, 2H), 2.26 – 2.07 (m, 4H), 1.56 – 1.36 (m, 10H), 1.33 – 1.27 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.80, 139.27 (t, *J* = 27.5 Hz), 139.14, 131.73 (q, *J* = 32.7 Hz), 129.26, 128.62, 127.39, 127.21 (t, *J* = 5.9 Hz), 125.33 – 125.29 (m), 123.94 (q, *J* = 273.7 Hz), 122.52 (t, *J* = 243.2 Hz), 120.89 – 120.73 (m), 58.52, 57.33, 39.06 (t, *J* = 27.1 Hz), 37.19, 28.64, 26.98, 22.98, 20.54.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.63, -95.84 (t, *J* = 16.4 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{26}H_{31}F_5N$ ($[M+H]^+$): 452.2371, found: 452.2364.

3-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-3-azabicyclo[3.1.0]hexane (67a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (73.7 mg, 60% yield; 25.8 mg, 63% yield) as a colorless oil.

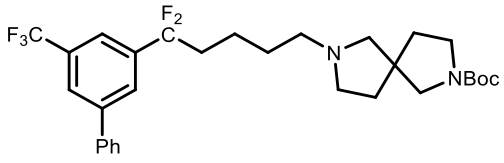
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.85 (s, 1H), 7.70 (s, 1H), 7.61 (d, *J* = 7.2 Hz, 2H), 7.50 (t, *J* = 7.3 Hz, 2H), 7.43 (t, *J* = 7.4 Hz, 1H), 2.96 (d, *J* = 8.5 Hz, 2H), 2.38 (t, *J* = 6.8 Hz, 2H), 2.26 – 1.12 (m, 4H), 1.48 (p, *J* = 3.5 Hz, 4H), 1.33 – 1.29 (m, 2H), 0.63 (q, *J* = 4.0 Hz, 1H), 0.31 (td, *J* = 7.7, 4.2 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.77, 139.25 (t, *J* = 27.5 Hz), 139.14, 131.70 (q, *J* = 32.8 Hz), 129.27, 128.62, 127.41, 127.21 (t, *J* = 6.0 Hz), 125.28, 123.93 (q, J = 273.7 Hz), 122.56 (t, *J* = 244.4 Hz), 120.83 – 120.72 (m), 55.21, 55.08, 38.98 (t, *J* = 27.0 Hz), 28.39, 20.43, 15.39, 7.06.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.59, -95.87 (t, *J* = 16.5 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{23}H_{25}F_5N$ ($[M+H]^+$): 410.1902, found: 410.1888.

***tert*-butyl-7-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-2,7-diazaspiro[4.4]nonane-2-carboxylate (68a)**



The title product was prepared via procedure A & E, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (96.1 mg, 58% yield; 43.2 mg, 78% yield) as a colorless oil.

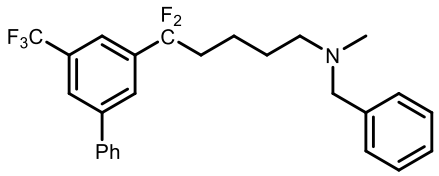
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.84 (s, 1H), 7.68 (s, 1H), 7.60 (d, *J* = 7.4 Hz, 2H), 7.48 (t, *J* = 7.4 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 1H), 3.39 – 3.15 (m, 4H), 2.63 (dt, *J* = 13.6, 6.3 Hz, 1H), 2.49 (dd, *J* = 9.4, 3.9 Hz, 2H), 2.41 – 2.33 (m, 3H), 2.19 (td, *J* = 16.2, 8.6 Hz, 2H), 1.81 – 1.69 (m, 4H), 1.52 (s, 4H), 1.44 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 154.86, 154.76, 142.78, 139.21 (t, *J* = 27.4 Hz), 139.07, 131.70 (q, *J* = 32.7 Hz), 129.27, 128.63, 127.37, 127.17 (t, *J* = 6.2 Hz), 125.31, 123.89 (q, *J* = 273.7 Hz), 122.46 (t, *J* = 244.4 Hz), 120.77 (d, *J* = 3.7 Hz), 79.25, 79.18, 64.45, 64.29, 58.06, 57.12, 56.11, 54.06, 48.11, 47.30, 45.54, 45.13, 39.02 (t, *J* = 27.1 Hz), 38.38, 37.37, 35.77, 35.61, 28.64, 28.35, 20.55 (t, *J* = 4.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.59, -95.87 – -96.01 (m).

HRMS (ESI-TOF) m/z calcd. for $C_{30}H_{38}F_5N_2O_2$ ($[M+H]^+$): 553.2848, found: 553.2839.

***N*-benzyl-5,5-difluoro-*N*-methyl-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentan-1-amine (69a)**



The title product was prepared via procedure A & C, purified by flash chromatography (PE:EA:Et_3N = 10:1:0.03) on silica gel to afford the title compound (104.6 mg, 78% yield; 23.8 mg, 53% yield) as a colorless oil.

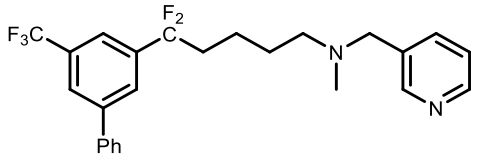
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.76 (s, 1H), 7.61 (s, 1H), 7.53 – 7.51 (m, 2H), 7.43 – 7.39 (m, 2H), 7.37 – 7.32 (m, 1H), 7.23 – 7.11 (m, 5H), 3.36 (s, 2H), 2.26 (t, *J* = 6.7 Hz, 2H), 2.13 – 2.01 (m, 5H), 1.51 – 1.39 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.76, 139.28 (t, *J* = 27.5 Hz), 139.22, 139.14, 131.69 (q, *J* = 32.7 Hz), 129.28, 129.10, 128.63, 128.34, 127.41, 127.21 (t, *J* = 6.0 Hz), 127.08, 125.31, 122.55 (t, *J* = 244.4 Hz), 120.81 – 120.79 (m), 62.58, 56.82, 42.35, 39.02 (t, *J* = 27.1 Hz), 27.02, 20.31.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.54, -95.88 (t, *J* = 16.5 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{26}H_{27}F_5N$ ($[M+H]^+$): 448.2058, found: 448.2048.

5,5-difluoro-*N*-methyl-*N*-(pyridin-3-ylmethyl)-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentan-1-amine (70a)



The title product was prepared via procedure A & E, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (95.5 mg, 71% yield; 17.1 mg, 38% yield) as a colorless oil.

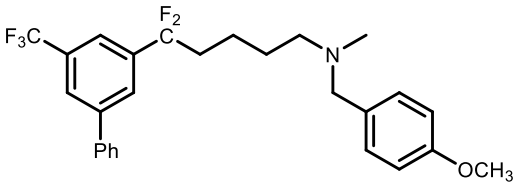
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 – 8.46 (m, 2H), 7.88 (s, 1H), 7.84 (s, 1H), 7.68 (s, 1H), 7.63 – 7.59 (m, 3H), 7.49 (t, *J* = 7.4 Hz, 2H), 7.45 – 7.41 (m, 1H), 7.20 (dd, *J* = 7.8, 4.8 Hz, 1H), 3.45 (s, 2H), 2.35 (t, *J* = 6.7 Hz, 2H), 2.22 – 2.10 (m, 5H), 1.55 – 1.50 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 150.40, 148.69, 142.80, 139.24 (t, *J* = 27.3 Hz), 139.11, 136.68, 134.63, 131.73 (q, *J* = 32.5 Hz), 129.29, 128.66, 127.40 127.18 (t, *J* = 6.1 Hz), 125.34, 123.92 (q, *J* = 273.7 Hz), 123.47, 122.49 (t, *J* = 244.4 Hz), 120.78, 59.73, 56.91, 42.18, 39.02 (t, *J* = 27.1 Hz), 27.01, 20.27 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.59, -95.98 (t, *J* = 16.5 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{25}H_{26}F_5N_2$ ($[M+H]^+$): 449.2011, found: 449.2005.

5,5-difluoro-*N*-(4-methoxybenzyl)-*N*-methyl-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentan-1-amine (71a)



The title product was prepared via procedure A & C, purified by flash chromatography (PE:EA:Et_3N = 10:1:0.03) on silica gel to afford the title compound (117.4 mg, 82% yield; 41.7 mg, 87% yield) as a colorless oil.

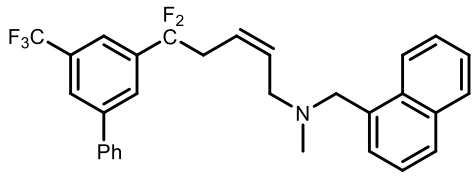
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.87 (s, 1H), 7.71 (s, 1H), 7.62 (d, *J* = 7.8 Hz, 2H), 7.50 (t, *J* = 7.5 Hz, 2H), 7.46 – 7.42 (m, 1H), 7.20 – 7.18 (m, 2H), 6.85 – 6.82 (m, 2H), 3.79 (s, 3H), 3.40 (s, 2H), 2.36 – 2.32 (m, 2H), 2.25 – 2.13 (m, 5H), 1.58 – 1.51 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.72, 142.75, 139.26 (t, *J* = 27.4 Hz), 139.10, 131.68 (q, J = 33.3 Hz), 131.18, 130.22, 129.27, 128.62, 127.39, 127.19 (t, *J* = 5.9 Hz), 125.32 – 125.28 (m), 122.55 (t, *J* = 244.4 Hz), 120.81 – 120.78 (m), 113.66, 61.88, 56.70, 55.31, 42.18, 39.02 (t, *J* = 27.0 Hz), 27.02, 20.36 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.53 (d, *J* = 3.1 Hz), -95.77 (td, *J* = 15.7, 4.1 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{27}H_{29}F_5NO$ ($[M+H]^+$): 478.2164, found: 478.2153.

(*Z*)-5,5-difluoro-*N*-methyl-*N*-(naphthalen-1-ylmethyl)-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pent-2-en-1-amine (72ab)



The title product was prepared via procedure A, purified by flash chromatography (PE:EA = 10:1) on silica gel to afford the title compound (89.1 mg, 60% yield; 62.2 mg, 42% yield for *Z* isomer) as a pale yellow solid.

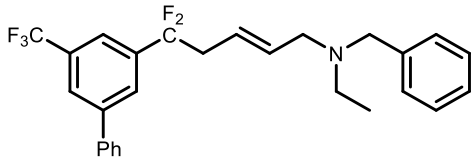
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 – 8.25 (m, 1H), 7.90 (s, 1H), 7.87 – 7.85 (m, 2H), 7.79 (dd, *J* = 7.2, 2.3 Hz, 1H), 7.75 (s, 1H), 7.58 – 7.56 (m, 2H), 7.51 – 7.45 (m, 5H), 7.42 – 7.38 (m, 2H), 5.91 (dt, *J* = 12.3, 6.8 Hz, 1H), 5.68 – 5.61 (m, 1H), 3.81 (s, 2H), 3.09 – 2.99 (m, 4H), 2.17 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.73, 138.98, 138.67 (t, *J* = 27.3 Hz), 134.65, 133.97, 133.09, 132.53, 131.65 (q, *J* = 32.7 Hz), 130.24, 129.22, 128.59, 128.51, 127.62, 127.33, 125.93, 125.71, 125.40 – 125.36 (m), 125.16, 124.69, 123.90 (q, *J* = 273.7 Hz), 122.20 (t, *J* = 5.2 Hz), 121.61 (t, *J* = 245.4 Hz), 121.06, 121.03 – 120.74 (m), 60.37, 54.37, 42.46, 37.73 (t, *J* = 28.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.48, -94.95 (t, *J* = 15.6 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{30}H_{27}F_5N$ ($[M+H]^+$): 496.2058, found: 496.2051.

(*E*)-*N*-benzyl-*N*-ethyl-5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pent-2-en-1-amine (73ab)



The title product was prepared via procedure A, purified by flash chromatography (PE:EA:Et_3N = 10:1:0.03) on silica gel to afford the title compound (107.5 mg, 78% yield; 41.3 mg, 30% yield for *E* isomer) as a pale yellow oil.

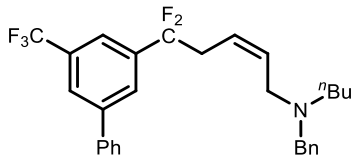
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.86 (s, 1H), 7.73 (s, 1H), 7.60 (d, *J* = 7.9 Hz, 2H), 7.55 – 7.45 (m, 3H), 7.31 – 7.29 (m, 4H), 7.27 – 7.23 (m, 1H), 5.82 (dt, *J* = 12.3, 6.3 Hz, 1H), 5.59 (dt, *J* = 11.1, 6.9 Hz, 1H), 3.47 (s, 2H), 3.04 – 2.96 (m, 4H), 2.44 (q, *J* = 7.2 Hz, 2H), 1.03 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.72, 139.41, 139.06, 138.69 (t, *J* = 27.3 Hz), 133.54, 131.66 (q, *J* = 32.8 Hz), 129.26, 129.00, 128.63, 128.29, 127.38, 126.99, 125.39, 123.90 (q, *J* = 273.7 Hz), 121.61 (t, *J* = 245.4 Hz), 121.72, 121.67, 121.17 – 120.68 (m), 57.87, 50.05, 47.48, 37.78 (t, *J* = 28.1 Hz), 12.00.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.56, -95.01 (t, *J* = 15.6 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{27}H_{27}F_5N$ ($[M+H]^+$): 460.2058, found: 460.2048.

(*Z*)-*N*-benzyl-*N*-butyl-5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pent-2-en-1-amine (74ab)



The title product was prepared via procedure A, purified by flash chromatography (PE:EA = 20:1) on silica gel to afford the title compound (61.4 mg, 42% yield; 38.0 mg, 26% yield for *Z* isomer) as a yellow solid.

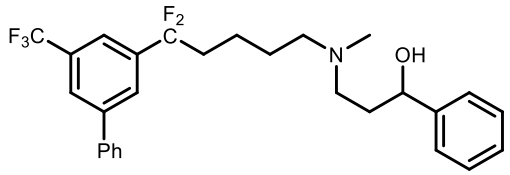
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.71 (s, 1H), 7.57 (s, 1H), 7.46 (dd, *J* = 7.5, 2.3 Hz, 2H), 7.40 – 7.36 (m, 2H), 7.34 – 7.30 (m, 1H), 7.16 – 7.13 (m, 4H), 7.11 – 7.07 (m, 1H), 5.67 (dt, *J* = 12.3, 6.6 Hz, 1H), 5.47 – 5.40 (m, 1H), 3.31 (s, 2H), 2.88 – 2.78 (m, 4H), 2.21 (t, *J* = 7.2 Hz, 2H), 1.33 – 1.26 (m, 2H), 1.16 (h, *J* = 7.2 Hz, 2H), 0.74 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.70, 139.66, 139.06, 138.71 (t, *J* = 27.3 Hz), 133.76, 131.65 (q, *J* = 32.7 Hz), 129.25, 128.94, 128.63, 128.25, 127.38, 127.31, 126.92, 125.39 – 125.35 (m), 123.90 (q, *J* = 273.7 Hz), 121.63 (t, *J* = 244.5 Hz), 121.54 (t, *J* = 5.2 Hz), 121.03 – 120.93 (m), 58.39, 53.56, 50.55, 37.78 (t, *J* = 28.1 Hz), 29.37, 20.61, 14.09.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.56, -95.04 (t, *J* = 15.6 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{29}H_{31}F_5N$ ($[M+H]^+$): 488.2371, found: 488.2363.

3-((5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)(methyl)amino)-1-phenylpropan-1-ol (75a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 2:1:0.03) on silica gel to afford the title compound (105.7 mg, 72% yield; 36.0 mg, 73% yield) as a pale yellow solid.

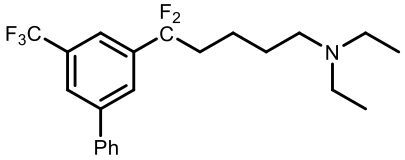
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.78 (s, 1H), 7.62 (s, 1H), 7.52 – 7.49 (m, 2H), 7.39 – 7.29 (m, 3H), 7.24 (dt, *J* = 15.1, 7.5 Hz, 4H), 7.15 – 7.11 (m, 1H), 4.80 (t, *J* = 5.8 Hz, 1H), 2.60 (dt, *J* = 13.0, 6.6 Hz, 1H), 2.45 – 2.31 (m, 2H), 2.29 – 2.22 (m, 1H), 2.21 – 2.07 (m, 5H), 1.73 (q, *J* = 6.0 Hz, 2H), 1.53 – 1.40 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.17, 142.87, 139.23 (t, *J* = 27.4 Hz), 139.08, 131.77 (q, *J* = 32.6 Hz), 129.25, 128.61, 128.29, 127.40, 127.19 (t, *J* = 5.9 Hz), 126.99, 125.67, 125.35, 123.93 (q, *J* = 273.7 Hz), 122.42 (t, *J* = 243.4 Hz), 120.75, 75.74, 57.76, 57.13, 41.89, 39.06 (t, *J* = 27.2 Hz), 34.59, 26.95, 20.42 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.57, -95.96 (t, *J* = 16.5 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{28}H_{31}F_5NO$ ($[M+H]^+$): 492.2320, found: 492.2313.

***N,N*-diethyl-5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentan-1-amine (76a)**



The title product was prepared via procedure A & C, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (103.0 mg, 86% yield; 20.1 mg, 50% yield) as a pale yellow oil.

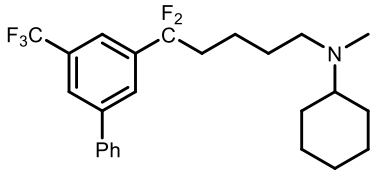
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.85 (s, 1H), 7.70 (s, 1H), 7.61 (d, *J* = 8.1 Hz, 2H), 7.50 (t, *J* = 7.4 Hz, 2H), 7.45 – 7.41 (m, 1H), 2.50 (q, *J* = 7.6, 7.1 Hz, 4H), 2.40 (t, *J* = 6.8 Hz, 2H), 2.26 – 2.14 (m, 2H), 1.50 – 1.47 (m, 4H), 0.99 (t, *J* = 7.1 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.83, 139.31 (t, *J* = 28.3 Hz), 139.19, 131.78 (q, *J* = 32.3 Hz), 129.28, 128.66, 127.41, 127.23, 125.31, 122.55 (t, *J* = 244.4 Hz), 120.84, 52.69, 47.07, 39.12 (t, *J* = 27.1 Hz), 26.94, 20.70, 11.79.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.62, -95.81 (t, *J* = 16.4 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{22}H_{27}F_5N$ ($[M+H]^+$): 400.2058, found: 400.2049.

***N*-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-*N*-methylcyclohexanamine (77a)**



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (118.6 mg, 90% yield; 17.6 mg, 40% yield) as a colorless oil.

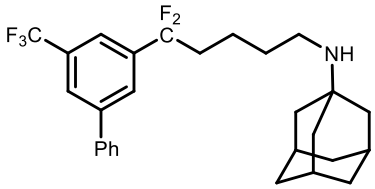
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.85 (s, 1H), 7.70 (s, 1H), 7.61 (d, *J* = 8.2 Hz, 2H), 7.52 – 7.48 (m, 2H), 7.45 – 7.41 (m, 1H), 2.42 – 2.14 (m, 8H), 1.77 – 1.75 (m, 4H), 1.61 (d, *J* = 12.5 Hz, 1H), 1.49 – 1.47 (m, 4H), 1.28 – 1.15 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.78, 139.29 (t, *J* = 27.4 Hz), 139.16, 131.73 (q, *J* = 32.7 Hz), 129.27, 128.62, 127.40, 127.23, 125.30, 122.56 (t, *J* = 244.4 Hz), 120.83, 62.90, 53.27, 39.13 (t, *J* = 27.0 Hz), 37.95, 28.71, 27.74, 26.51, 26.17, 20.61 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.63, -95.74 (t, *J* = 16.4 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{25}H_{31}F_5N$ ($[M+H]^+$): 440.2371, found: 440.2364.

***N*-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)adamantan-1-amine (78a)**



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (51.3 mg, 36% yield; 44.8 mg, 94% yield) as a white solid.

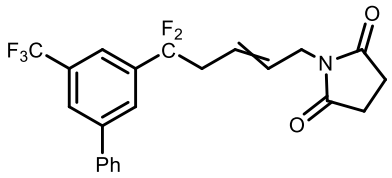
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.85 (s, 1H), 7.69 (s, 1H), 7.60 (d, *J* = 7.6 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 2H), 7.42 (t, 1H), 2.56 (t, *J* = 6.6 Hz, 2H), 2.19 (tt, *J* = 15.9, 7.2 Hz, 4H), 2.04 (t, *J* = 3.3 Hz, 3H), 1.67 – 1.47 (m, 17H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.77, 139.22 (t, *J* = 27.4 Hz), 139.10, 131.71 (q, *J* = 32.6 Hz), 129.25, 128.61, 127.38, 127.18 (t, *J* = 6.0 Hz), 125.30 – 125.25 (m), 123.91 (q, *J* = 274.7 Hz), 122.49 (t, *J* = 243.4 Hz), 120.78, 50.48, 42.90, 40.09, 39.09 (t, *J* = 27.1 Hz), 36.86, 30.84, 29.69, 20.51 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.59, -95.88 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{28}H_{33}F_5N$ ($[M+H]^+$): 478.2528, found: 478.2519.

(*E/Z*)-1-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pent-2-en-1-yl)pyrrolidine-2,5-dione (80ab)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA: Et_3N = 10:1:2%) on silica gel to afford the title compound (35.5 mg, 28% yield) as a pale yellow oil.

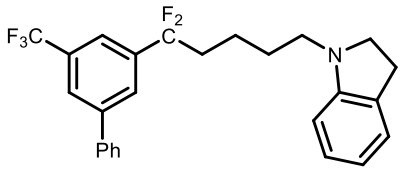
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90, 7.81 (s, s, 2H), 7.73, 7.65 – 7.60 (s, m, 3H), 7.52 – 7.48 (m, 2H), 7.45 – 7.41 (m, 1H), 5.73 – 5.55 (m, 2H), 4.06 – 4.04 (m, 2H), 3.20, 2.90 (td, *J* = 16.2, 6.7 Hz, td, *J* = 15.6, 6.6 Hz, 2H), 2.66, 2.63 (s, s, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.75, 176.71, 142.74, 142.69, 138.94, 138.49 (t, *J* = 27.1 Hz), 138.42, 131.65 (q, *J* = 32.8 Hz), 131.61 (q, *J* = 32.3 Hz), 129.32, 129.27, 129.26, 128.66, 128.64, 127.68, 127.38, 125.47, 125.07 (t, *J* = 5.2 Hz), 124.80 (t, *J* = 4.8 Hz), 123.83 (q, *J* = 273.7 Hz), 121.37 (t, *J* = 245.4 Hz), 120.90, 42.27 (t, *J* = 28.4 Hz), 40.06, 37.36 (t, *J* = 28.1 Hz), 35.25, 28.27, 28.18.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.56, -62.57, -95.20 (t, *J* = 16.0 Hz).

MS (EI) m/z calcd. for $C_{22}H_{18}F_5NO_2$ ($[M]^+$): 423.1258 found: 422.99.

1-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)indoline (81a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA = 20:1) on silica gel to afford the title compound (74.5 mg, 56% yield; 29.8 mg, 67% yield) as a colorless oil.

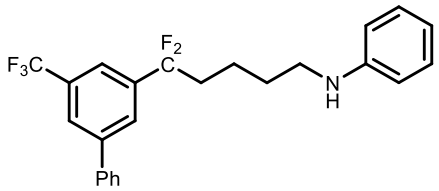
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.88 (s, 1H), 7.73 (s, 1H), 7.62 (d, *J* = 7.0 Hz, 2H), 7.53 – 7.49 (m, 2H), 7.47 – 7.43 (m, 1H), 7.09 – 7.04 (m, 2H), 6.68 – 6.64 (m, 1H), 6.45 (d, *J* = 7.8 Hz, 1H), 3.32 (t, *J* = 8.2 Hz, 2H), 3.07 (t, *J* = 6.9 Hz, 2H), 2.96 (t, *J* = 8.3 Hz, 2H), 2.32 – 2.20 (m, 2H), 1.71 – 1.60 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.64, 142.83, 139.16 (t, *J* = 27.4 Hz), 139.08, 131.75 (q, *J* = 32.7 Hz), 130.11, 129.29, 128.65, 127.42, 127.40, 127.20 (t, *J* = 6.1 Hz), 125.39, 124.56, 123.92 (q, *J* = 273.7 Hz), 122.48 (t, *J* = 243.4 Hz), 120.80, 117.67, 106.98, 53.33, 49.20, 39.05 (t, *J* = 27.1 Hz), 28.67, 27.17, 20.35.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.56, -95.90 (t, *J* = 16.6 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{26}H_{25}F_5N$ ($[M+H]^+$): 446.1902, found: 446.1896.

***N*-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)aniline (82a)**



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA = 10:1) on silica gel to afford the title compound (72.6 mg, 58% yield; 29.9 mg, 71% yield) as a pale yellow oil.

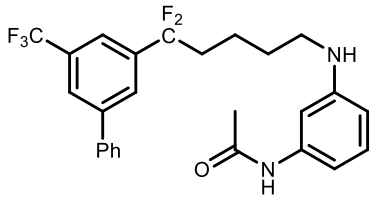
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.88 (s, 1H), 7.73 (s, 1H), 7.62 (d, *J* = 8.2 Hz, 2H), 7.51 (t, *J* = 7.5 Hz, 2H), 7.47 – 7.43 (m, 1H), 7.20 – 7.16 (m, 2H), 6.71 (td, *J* = 7.3, 1.2 Hz, 1H), 6.62 – 6.59 (m, 2H), 3.14 (t, *J* = 6.6 Hz, 2H), 2.30 – 2.18 (m, 2H), 1.72 – 1.60 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 148.28, 142.84, 139.11 (t, *J* = 27.4 Hz), 139.04, 131.76 (q, *J* = 32.7 Hz), 129.40, 129.29, 128.66, 127.40, 127.15 (t, *J* = 6.0 Hz), 125.41, 123.89 (q, *J* = 272.7 Hz), 122.40 (t, *J* = 244.4 Hz), 120.74 (q, *J* = 6.4 Hz), 117.49, 112.84, 43.69, 39.01 (t, *J* = 27.2 Hz), 29.20, 20.23 (t, *J* = 3.9 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.53, -96.05 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{24}H_{23}F_5N$ ($[M+H]^+$): 420.1745, found: 420.1736.

_N_-(3-((5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)amino)phenyl)acetamide (83a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA = 5:1) on silica gel to afford the title compound (88.2 mg, 62% yield; 23.8 mg, 50% yield) as a green yellow solid.

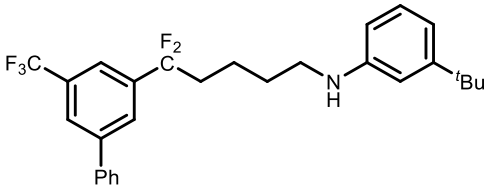
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.86 (s, 1H), 7.70 (s, 1H), 7.63 – 7.60 (m, 2H), 7.52 – 7.47 (m, 2H), 7.46 – 7.41 (m, 1H), 7.32 (s, 1H), 7.08 – 7.04 (m, 2H), 6.61 (dd, *J* = 7.9, 2.0 Hz, 1H), 6.32 (dd, *J* = 8.1, 2.3 Hz, 1H), 3.10 (t, *J* = 6.7 Hz, 2H), 2.27 – 2.13 (m, 5H), 1.68 – 1.57 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.51, 148.99, 142.85, 139.03, 139.10 (t, *J* = 28.3 Hz), 131.73 (q, *J* = 33.3 Hz), 129.72, 129.27, 128.64, 127.39, 127.14, 125.41, 123.88 (q, *J* = 273.7 Hz), 122.37 (t, *J* = 244.4 Hz), 120.72, 108.73, 108.69, 104.44, 43.66, 38.96 (t, *J* = 27.1 Hz), 29.10, 24.82, 20.16.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.54, -96.08 (t, *J* = 16.4 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{26}H_{26}F_5N_2O$ ($[M+H]^+$): 477.1960, found: 477.1951.

3-(*tert*-butyl)-_N_-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)aniline (84a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA = 10:1) on silica gel to afford the title compound (74.1mg, 52% yield; 32.9 mg, 69% yield) as a yellow oil.

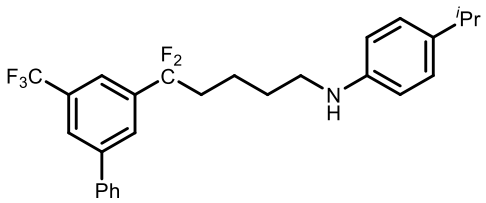
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.88 (s, 1H), 7.73 (s, 1H), 7.63 (dt, *J* = 8.6, 2.1 Hz, 2H), 7.51 (td, *J* = 8.3, 7.7, 2.2 Hz, 2H), 7.47 – 7.43 (m, 1H), 7.14 (td, *J* = 8.0, 2.8 Hz, 1H), 6.79 – 6.76 (m, 1H), 6.64 (q, *J* = 2.3 Hz, 1H), 6.44 (ddd, *J* = 7.9, 2.4, 1.0 Hz, 1H), 3.15 (t, *J* = 6.6 Hz, 2H), 2.31 – 2.19 (m, 2H), 1.72 – 1.62 (m, 4H), 1.31 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.45, 148.09, 142.85, 139.14 (t, *J* = 27.5 Hz), 139.07, 131.77 (q, *J* = 32.7 Hz), 129.29, 129.08, 128.66, 127.40, 127.17 (t, *J* = 6.1 Hz), 125.41, 123.90 (q, *J* = 273.7 Hz), 122.41 (t, *J* = 244.4 Hz), 120.75, 114.95, 110.61, 109.65, 43.85, 39.05 (t, *J* = 27.2 Hz), 34.73, 31.45, 29.33, 20.29 (t, *J* = 3.9 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.53, -96.03 (t, *J* = 16.5 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{28}H_{31}F_5N$ ($[M+H]^+$): 476.2371, found: 476.2365.

***N*-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-4-isopropylaniline (85a)**



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA = 10:1) on silica gel to afford the title compound (62.0 mg, 45% yield; 34.7 mg, 75% yield) as a yellow oil.

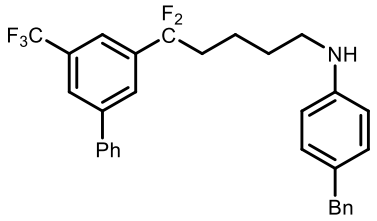
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.89 (s, 1H), 7.74 (s, 1H), 7.64 (dt, *J* = 8.5, 2.6 Hz, 2H), 7.54 – 7.49 (m, 2H), 7.48 – 7.43 (m, 1H), 7.07 (d, *J* = 8.5 Hz, 2H), 6.57 (d, *J* = 8.5 Hz, 2H), 3.13 (t, *J* = 6.6 Hz, 2H), 2.83 (hept, *J* = 6.9 Hz, 1H), 2.31 – 2.19 (m, 2H), 1.71 – 1.61 (m, 4H), 1.23 (d, *J* = 6.9 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 146.32, 142.85, 139.15 (t, *J* = 27.3 Hz), 139.07, 138.10, 131.77 (q, *J* = 32.7 Hz), 129.29, 128.65, 127.40, 127.24, 127.16 (t, *J* = 8.1 Hz), 125.40, 123.91 (q, *J* = 273.7 Hz), 122.41 (t, *J* = 244.4 Hz), 120.76, 112.95, 43.02, 39.01 (t, *J* = 27.1 Hz), 33.28, 29.29, 24.37, 20.24 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.54, -95.99 (t, *J* = 16.4 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{27}H_{29}F_5N$ ($[M+H]^+$): 462.2215, found: 462.2210.

4-benzyl-*N*-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)aniline (86a)



The title product was prepared via procedure B & D, purified by flash chromatography (PE:EA = 10:1) on silica gel to afford the title compound (83.7 mg, 55% yield; 32.7 mg, 64% yield) as a yellow solid.

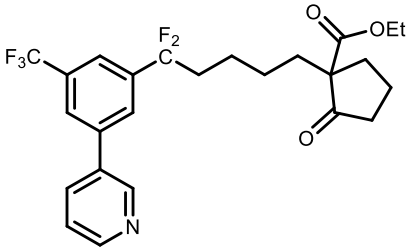
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.89 (s, 1H), 7.74 (s, 1H), 7.65 – 7.62 (m, 2H), 7.54 – 7.50 (m, 2H), 7.48 – 7.44 (m, 1H), 7.32 – 7.28 (m, 2H), 7.22 – 7.19 (m, 3H), 7.04 – 7.01 (m, 2H), 6.58 – 6.56 (m, 2H), 3.90 (s, 2H), 3.13 (t, *J* = 6.6 Hz, 2H), 2.31 – 2.19 (m, 2H), 1.72 – 1.61 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 146.41, 142.84, 142.14, 139.04, 139.12 (t, *J* = 27.3 Hz), 131.76 (q, *J* = 32.6 Hz), 130.28, 129.88, 129.28, 128.91, 128.65, 128.47, 127.39, 127.15, 125.94, 125.40, 123.90 (q, *J* = 273.7 Hz), 122.39 (t, *J* = 244.4 Hz), 120.75 – 120.72 (m), 113.15, 44.02, 41.14, 38.99 (t, *J* = 27.2 Hz), 29.18, 20.22.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.52 (d, *J* = 2.6 Hz), -96.02 (td, *J* = 16.3, 2.7 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{31}H_{29}F_5N$ ($[M+H]^+$): 510.2215, found: 510.2209.

Ethyl-1-(5,5-difluoro-5-(3-(pyridin-3-yl)-5-(trifluoromethyl)phenyl)pentyl)-2-oxo cyclopentane-1-carboxylate (87a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 5:1:0.03) on silica gel to afford the title compound (96.7 mg, 67% yield; 42.0 mg, 87% yield) as a colorless oil.

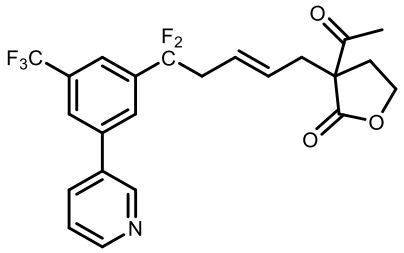
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (d, *J* = 2.4 Hz, 1H), 8.66 (dd, *J* = 4.9, 1.5 Hz, 1H), 7.90 (dt, *J* = 8.0, 2.0 Hz, 1H), 7.87 (s, 1H), 7.81 (s, 1H), 7.72 (s, 1H), 7.42 (dd, *J* = 8.0, 4.9 Hz, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 2.49 – 2.35 (m, 2H), 2.25 – 2.10 (m, 3H), 2.02 – 1.80 (m, 4H), 1.58 – 1.36 (m, 4H), 1.30 – 1.19 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 214.88, 171.08, 149.78, 148.34, 139.67 (t, *J* = 27.6 Hz), 139.53, 134.74, 132.14 (q, *J* = 33.0 Hz), 127.15 (t, *J* = 6.4 Hz), 125.35, 123.90, 123.65 (q, *J* = 273.7 Hz), 122.20 (t, *J* = 244.4 Hz), 121.64 – 121.60 (m), 61.49, 60.28, 38.83 (t, *J* = 27.1 Hz), 38.01, 33.46, 33.02, 24.44, 22.71 (t, *J* = 3.9 Hz), 19.69, 14.16.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.69, -96.20 (t, *J* = 16.4 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{25}H_{27}F_5NO_3$ ($[M+H]^+$): 484.1906, found: 484.1896.

(*E*)-3-acetyl-3-(5,5-difluoro-5-(3-(pyridin-3-yl)-5-(trifluoromethyl)phenyl)pent-2-en-1-yl)dihydrofuran-2(3*H*)-one (88ab)



The title product was prepared via procedure A, purified by flash chromatography (PE:EA:Et_3N = 5:1:0.03) on silica gel to afford the title compound (78.8 mg, 58% yield) as a colorless oil.

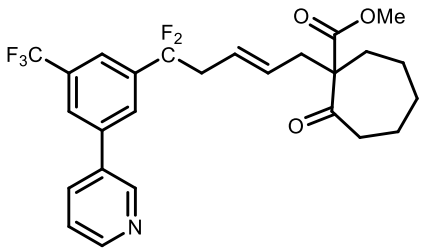
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (d, *J* = 2.4 Hz, 1H), 8.65 (dd, *J* = 4.9, 1.6 Hz, 1H), 7.92 – 7.88 (m, 2H), 7.81 (s, 1H), 7.70 (s, 1H), 7.42 (dd, *J* = 7.9, 4.8 Hz, 1H), 5.58 – 5.51 (m, 1H), 5.40 (dt, *J* = 15.0, 7.2 Hz, 1H), 4.18 – 4.06 (m, 2H), 2.90 (td, *J* = 16.0, 7.0 Hz, 2H), 2.74 – 2.65 (m, 2H), 2.60 – 2.55 (m, 1H), 2.24 (s, 3H), 1.96 (dt, *J* = 13.0, 8.8 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 201.84, 175.01, 149.79, 148.27, 139.64, 138.96 (t, *J* = 27.3 Hz), 134.73, 134.55, 132.11 (q, *J* = 33.0 Hz), 130.16, 127.20 (t, *J* = 6.1 Hz), 125.64 – 125.51 (m), 123.91, 123.58 (q, *J* = 273.7 Hz), 121.70 – 121.54 (m), 120.90 (t, *J* = 244.4 Hz), 66.25, 60.93, 42.48 (t, *J* = 28.0 Hz), 37.62, 28.75, 25.66.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.69, -95.62 (t, *J* = 15.9 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{23}H_{21}F_5NO_3$ ($[M+H]^+$): 454.1436, found: 454.1429.

Methyl-(*E*)-1-(5,5-difluoro-5-(3-(pyridin-3-yl)-5-(trifluoromethyl)phenyl)pent-2-en-1-yl)-2-oxocycloheptane-1-carboxylate (89ab)



The title product was prepared via procedure A, purified by flash chromatography (PE:EA:Et_3N = 4:1:0.03) on silica gel to afford the title compound (111.2 mg, 73% yield) as a colorless oil.

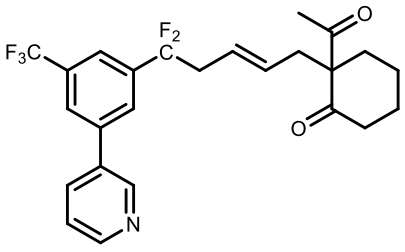
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (d, *J* = 2.4 Hz, 1H), 8.62 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.89 (dt, *J* = 7.9, 2.1 Hz, 1H), 7.84 (s, 1H), 7.79 (s, 1H), 7.69 (s, 1H), 7.39 (dd, *J* = 7.9, 4.8 Hz, 1H), 5.53 – 5.46 (m, 1H), 5.37 (dt, *J* = 14.8, 6.9 Hz, 1H), 3.60 (s, 3H), 2.86 (td, *J* = 15.9, 6.9 Hz, 2H), 2.63 (dd, *J* = 14.0, 6.4 Hz, 1H), 2.58 – 2.52 (m, 1H), 2.38 – 2.32 (m, 1H), 2.24 (dd, *J* = 14.1, 7.9 Hz, 1H), 1.98 – 1.91 (m, 1H), 1.66 – 1.44 (m, 6H), 1.31 – 1.23 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.96, 172.29, 149.66, 148.22, 139.41, 139.13 (t, *J* = 27.1 Hz), 134.67, 134.59, 132.50, 131.98 (q, *J* = 33.3 Hz), 127.28 (t, *J* = 5.9 Hz), 125.30, 123.82, 123.68 (t, *J* = 4.9 Hz), 123.57 (q, *J* = 273.7 Hz), 121.69 – 121.61 (m), 121.05 (t, *J* = 245.4 Hz), 62.81, 52.19, 42.42 (t, *J* = 27.8 Hz), 42.10, 38.43, 32.19, 29.84, 25.52, 24.54.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.71, -94.63 (t, *J* = 15.9 Hz), -94.98 – -95.09 (m), -95.28 (t, *J* = 15.9 Hz), -95.44 (t, *J* = 16.0 Hz), -96.10 (t, *J* = 16.0 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{26}H_{26}F_5NO_3$ ($[M+H]^+$): 496.1906, found: 496.1895.

(*E*)-2-acetyl-2-(5,5-difluoro-5-(3-(pyridin-3-yl)-5-(trifluoromethyl)phenyl)pent-2-en-1-yl)cyclohexan-1-one (90ab)



The title product was prepared via procedure A, purified by flash chromatography (PE:EA:Et_3N = 5:1:0.03) on silica gel to afford the title compound (71.1 mg, 51% yield) as a colorless oil.

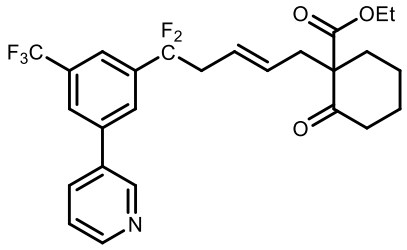
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (d, *J* = 2.4 Hz, 1H), 8.65 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.90 (dt, *J* = 8.0, 2.0 Hz, 1H), 7.86 (s, 1H), 7.79 (s, 1H), 7.69 (s, 1H), 7.41 (dd, *J* = 7.9, 4.9 Hz, 1H), 5.44 – 5.32 (m, 2H), 2.86 (td, *J* = 15.9, 5.3 Hz, 2H), 2.51 – 2.16 (m, 5H), 2.01 – 1.88 (m, 4H), 1.65 – 1.51 (m, 3H), 1.33 – 1.26 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 209.48, 205.90, 149.73, 148.29, 139.51, 139.12 (t, *J* = 27.3 Hz), 134.74, 134.66, 132.05 (q, *J* = 33.0 Hz), 131.84, 127.30 (t, *J* = 5.8 Hz), 125.40 – 125.36 (m), 123.89, 123.66 (t, *J* = 5.0 Hz), 123.62 (q, *J* = 273.7 Hz), 121.79 – 121.65 (m), 121.09 (t, *J* = 245.4 Hz), 67.45, 42.45 (t, *J* = 27.9 Hz), 41.73, 37.41, 34.05, 27.09, 26.21, 22.10.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.69, -95.32 (td, *J* = 15.8, 8.7 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{25}H_{25}F_5NO_2$ $([M+H]^+)$: 466.1800, found: 466.1792.

Ethyl-(*E*)-1-(5,5-difluoro-5-(3-(pyridin-3-yl)-5-(trifluoromethyl)phenyl)pent-2-en-1-yl)-2-oxocyclohexane-1-carboxylate (91ab)



The title product was prepared via procedure A, purified by flash chromatography (PE:EA:Et_3N = 5:1:0.03) on silica gel to afford the title compound (78.7 mg, 53% yield) as a pale yellow oil.

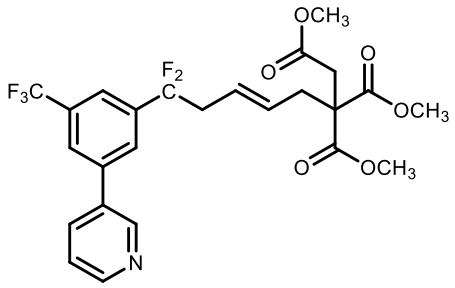
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (d, *J* = 2.4 Hz, 1H), 8.64 (dd, *J* = 4.9, 1.6 Hz, 1H), 7.89 (dt, *J* = 8.0, 1.9 Hz, 1H), 7.85 (s, 1H), 7.80 (s, 1H), 7.70 (s, 1H), 7.40 (dd, *J* = 7.9, 4.9 Hz, 1H), 5.52 (dt, *J* = 15.0, 7.4 Hz, 1H), 5.36 (dt, *J* = 14.9, 7.0 Hz, 1H), 4.13 – 4.05 (m, 2H), 2.86 (td, *J* = 15.9, 7.0 Hz, 2H), 2.48 (dd, *J* = 14.0, 6.8 Hz, 1H), 2.40 – 2.35 (m, 2H), 2.30 – 2.25 (m, 2H), 1.96 – 1.92 (m, 1H), 1.65 – 1.48 (m, 3H), 1.31 – 1.23 (m, 1H), 1.18 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.42, 171.38, 149.74, 148.31, 139.46, 139.20 (t, *J* = 27.3 Hz), 134.69, 134.65, 132.33, 132.03 (q, *J* = 32.9 Hz), 127.33 (t, *J* = 5.7 Hz), 125.34 – 125.29 (m), 123.85, 123.63 (q, *J* = 273.7 Hz), 123.42 (t, *J* = 5.0 Hz), 121.83 – 121.68 (m), 121.12 (t, *J* = 244.4 Hz), 61.31, 60.80, 42.44 (t, *J* = 27.8 Hz), 41.08, 38.02, 35.77, 27.45, 22.45, 14.14.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.72, -95.31 (td, *J* = 15.9, 4.0 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{26}H_{27}F_5NO_3$ ($[M+H]^+$): 496.1906, found: 496.1897.

Trimethyl-(*E*)-7,7-difluoro-7-(3-(pyridin-3-yl)-5-(trifluoromethyl)phenyl)hept-4-ene-1,2,2-tricarboxylate (92ab)



The title product was prepared via procedure A, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (91.4 mg, 57% yield) as a colorless oil.

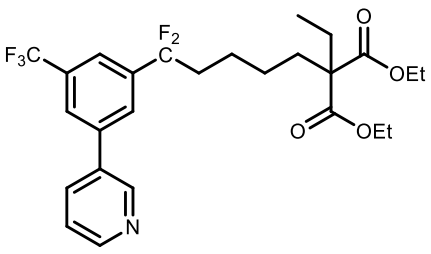
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (d, *J* = 2.4 Hz, 1H), 8.64 (dd, *J* = 4.9, 1.6 Hz, 1H), 7.90 (dt, *J* = 8.0, 2.1 Hz, 1H), 7.86 (s, 1H), 7.81 (s, 1H), 7.71 (s, 1H), 7.40 (dd, *J* = 7.9, 4.8 Hz, 1H), 5.47 – 5.45 (m, 2H), 3.67 (s, 6H), 3.59 (s, 3H), 2.93 – 2.83 (m, 2H), 2.79 (s, 2H), 2.69 (d, *J* = 6.0 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.69, 170.26, 149.74, 148.31, 139.56, 139.07 (t, *J* = 27.3 Hz), 134.71, 134.62, 132.11 (q, *J* = 33.0 Hz), 130.96, 127.25 (t, *J* = 6.0 Hz), 125.46, 125.11 (t, *J* = 4.7 Hz), 123.86, 123.60 (q, *J* = 273.7 Hz), 121.68, 120.93 (t, *J* = 244.4 Hz), 55.38, 52.86, 51.84, 42.38 (t, *J* = 27.9 Hz), 37.13, 36.54.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.73, -95.50 (t, *J* = 16.0 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{25}H_{25}F_5NO_6$ ($[M+H]^+$): 530.1597, found: 530.1594.

Diethyl-2-(5,5-difluoro-5-(3-(pyridin-3-yl)-5-(trifluoromethyl)phenyl)pentyl)-2-ethylmalonate (93a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 4:1:0.03) on silica gel to afford the title compound (55.4 mg, 36% yield; 38.0 mg, 74% yield) as a colorless oil.

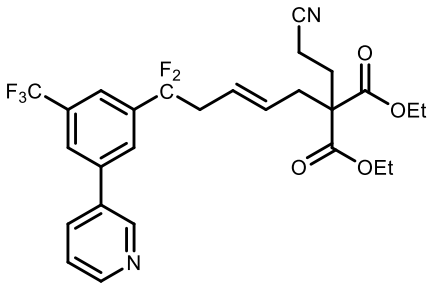
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (d, *J* = 2.4 Hz, 1H), 8.67 (dd, *J* = 4.8, 1.7 Hz, 1H), 7.90 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.87 (s, 1H), 7.82 (s, 1H), 7.73 (s, 1H), 7.42 (dd, *J* = 7.9, 4.9 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 4H), 2.22 – 2.10 (m, 2H), 1.92 – 1.82 (m, 4H), 1.48 (p, *J* = 7.8 Hz, 2H), 1.21 (t, *J* = 7.0 Hz, 9H), 0.78 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.77, 149.79, 148.36, 139.70 (t, *J* = 27.6 Hz), 139.54, 134.74, 132.17 (q, *J* = 33.0 Hz), 127.18, 125.36, 123.90, 123.66 (q, *J* = 273.7 Hz), 122.21 (t, *J* = 244.4 Hz), 121.63, 61.14, 57.88, 38.91 (t, *J* = 27.1 Hz), 31.53, 25.46, 23.73, 22.73 (t, *J* = 4.2 Hz), 14.18, 8.52.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.70, -96.18 (t, *J* = 16.5 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{28}H_{31}F_5NO_4$ ($[M+H]^+$): 516.2168, found: 516.2166.

Diethyl-(*E*)-2-(2-cyanoethyl)-2-(5,5-difluoro-5-(3-(pyridin-3-yl)-5-(trifluoromethyl)phenyl)pent-2-en-1-yl)malonate (94ab)



The title product was prepared via procedure A, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (121.3 mg, 75% yield) as a colorless oil.

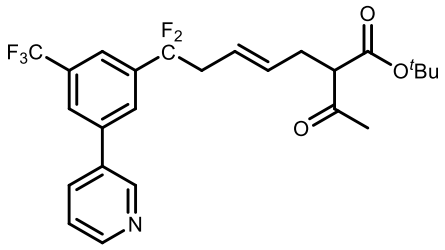
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (d, *J* = 2.4 Hz, 1H), 8.63 (dd, *J* = 4.9, 1.6 Hz, 1H), 7.91 – 7.87 (m, 2H), 7.81 (s, 1H), 7.70 (s, 1H), 7.40 (dd, *J* = 7.9, 4.8 Hz, 1H), 5.52 (dt, *J* = 15.1, 6.7 Hz, 1H), 5.43 (dt, *J* = 14.9, 7.0 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 4H), 2.88 (td, *J* = 16.2, 6.7 Hz, 2H), 2.60 (d, *J* = 7.0 Hz, 2H), 2.34 (dd, *J* = 8.7, 7.0 Hz, 2H), 2.08 (dd, *J* = 8.7, 7.0 Hz, 2H), 1.20 (t, *J* = 7.1 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.79, 149.72, 148.23, 139.54, 138.98 (t, *J* = 27.3 Hz), 134.65, 134.49, 132.02 (q, *J* = 32.9 Hz), 130.23, 127.15 (t, *J* = 5.7 Hz), 125.48, 125.21 (t, *J* = 4.6 Hz), 123.83, 123.55 (q, *J* = 273.7 Hz), 121.59, 120.82 (t, *J* = 244.4 Hz), 118.93, 61.84, 56.28, 42.29 (t, *J* = 27.8 Hz), 36.62, 28.74, 13.94, 12.80.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.69, -95.60 (t, *J* = 16.2 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{27}H_{28}F_5N_2O_4$ ($[M+H]^+$): 539.1964, found: 539.1959.

***tert*-butyl-(*E*)-2-acetyl-7,7-difluoro-7-(3-(pyridin-3-yl)-5-(trifluoromethyl)phenyl) hept-4-enoate (95ab)**



The title product was prepared via procedure A, purified by flash chromatography (PE:EA:Et_3N = 4:1:0.03) on silica gel to afford the title compound (44.3 mg, 31% yield) as a colorless oil.

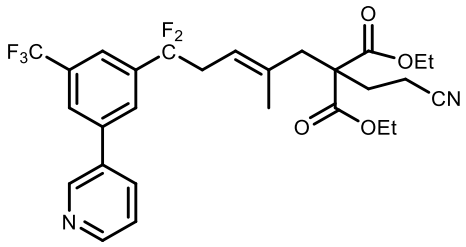
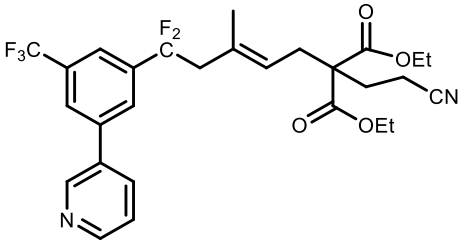
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.67 (d, *J* = 4.3 Hz, 1H), 7.91 (dt, *J* = 8.0, 2.0 Hz, 1H), 7.87 (s, 1H), 7.81 (s, 1H), 7.71 (s, 1H), 7.42 (dd, *J* = 7.9, 4.8 Hz, 1H), 5.53 (dt, *J* = 15.4, 6.4 Hz, 1H), 5.44 (dt, *J* = 15.6, 6.6 Hz, 1H), 3.32 (t, *J* = 7.3 Hz, 1H), 2.86 (td, *J* = 15.9, 6.6 Hz, 2H), 2.48 (t, *J* = 6.9 Hz, 2H), 2.15 (s, 3H), 1.41 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 202.55, 168.25, 149.78, 148.34, 139.49, 139.20 (t, J = 27.3 Hz), 134.77, 134.70, 133.38, 132.08 (q, *J* = 33.0 Hz), 127.33 (t, *J* = 6.8 Hz), 125.41, 123.92, 123.65 (q, *J* = 273.7 Hz), 122.57 (t, *J* = 4.9 Hz), 121.81, 121.07 (t, *J* = 245.4 Hz), 82.26, 60.27, 42.48 (t, *J* = 28.0 Hz), 30.98, 29.06, 27.95.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.69, -95.20 (dt, *J* = 33.0, 16.0 Hz), -95.50 (dt, *J* = 20.4, 15.9 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{25}H_{27}F_5NO_3$ ($[M+H]^+$): 484.1906, found: 484.1898.

Diethyl-(*E*)-2-(2-cyanoethyl)-2-(5,5-difluoro-2-methyl-5-(3-(pyridin-3-yl)-5-(trifluoromethyl)phenyl)pent-2-en-1-yl)malonate
Diethyl-(*E*)-2-(2-cyanoethyl)-2-(5,5-difluoro-3-methyl-5-(3-(pyridin-3-yl)-5-(trifluoromethyl)phenyl)pent-2-en-1-yl)malonate (96)

The title product was prepared via procedure A, purified by flash chromatography (PE:EA: Et_3N = 3:1:4%) on silica gel to afford the title compound (109 mg, 66% yield, 1:3) as a pale yellow solid.

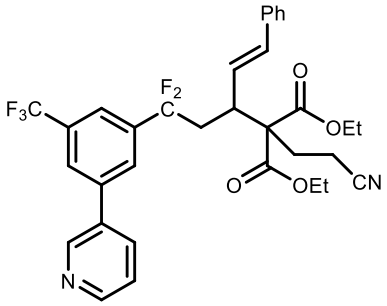
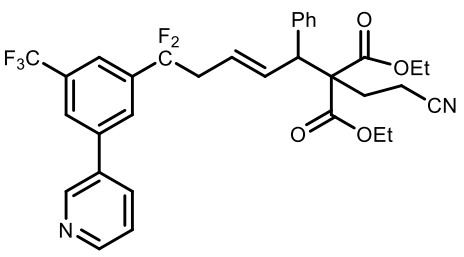
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (d, *J* = 2.4 Hz, 1H), 8.64 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.95 – 7.85 (m, 2H), 7.83, 7.81 (s, s, 1H), 7.72, 7.69 (s, s, 1H), 7.40 (dd, *J* = 7.9, 4.8 Hz, 1H), 5.34 – 5.19, 5.14 – 4.87 (m, 1H), 4.12 (q, *J* = 7.1 Hz, 4H), 2.84 (t, *J* = 16.6 Hz, 2H), 2.69, 2.58 (s, d, *J* = 7.4 Hz, 2H), 2.30 (dd, *J* = 8.7, 7.0 Hz, 2H), 2.03 (dd, *J* = 8.7, 6.9 Hz, 2H), 1.68, 1.48 (s, s, 3H), 1.35 – 1.07 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.22, 169.96, 149.74, 148.26, 139.52, 139.46, 139.27 (t, *J* = 27.4 Hz), 135.91, 134.65, 134.50, 132.00 (q, *J* = 33.3 Hz), 131.93 (q, *J* = 33.3 Hz), 131.47 (t, *J* = 3.0 Hz), 127.09, 125.40, 124.94, 123.83, 123.57 (q, *J* = 273.7 Hz), 121.57, 121.42, 120.24, 118.94, 61.86, 61.81, 56.21, 55.98, 48.76 (t, *J* = 26.8 Hz), 43.17, 37.94 (t, *J* = 27.7 Hz), 32.09, 28.76, 28.69, 17.70, 17.09, 13.93, 13.90, 12.98, 12.90.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.66, -62.67, -94.43 (t, *J* = 16.6 Hz), -95.21 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{28}H_{30}F_5N_2O_4$ ($[M+H]^+$): 553.2120, found: 553.2117.

Diethyl-(*E*)-2-(2-cyanoethyl)-2-(5,5-difluoro-1-phenyl-5-(3-(pyridin-3-yl)-5-(trifluoromethyl)phenyl)pent-1-en-3-yl)malonate
Diethyl-(*E*)-2-(2-cyanoethyl)-2-(5,5-difluoro-1-phenyl-5-(3-(pyridin-3-yl)-5-(trifluoromethyl)phenyl)pent-2-en-1-yl)malonate (97)

The title product was prepared via procedure A, purified by flash chromatography (PE:EA: Et_3N = 3:1:4%) on silica gel to afford the title compound (54.1 mg, 29% yield, 2:1) as a pale yellow solid.

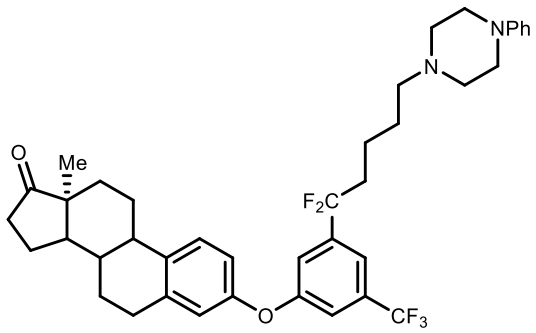
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73, 8.62, 8.60, 8.57 (d, *J* = 2.4 Hz, d, *J* = 2.4 Hz, dd, *J* = 4.9, 1.5 Hz, dd, *J* = 4.9, 1.5 Hz, 2H), 7.77 – 7.61 (m, 4H), 7.34, 7.29 (dd, *J* = 7.9, 4.9 Hz, dd, *J* = 7.9, 4.8 Hz, 1H), 7.19 – 7.12 (m, 3H), 7.05 – 6.96 (m, 2H), 6.11, 6.03 (dd, *J* = 15.3, 8.6 Hz, d, *J* = 15.8 Hz, 1H), 5.67, 5.34 (dd, *J* = 15.8, 10.1 Hz, dt, *J* = 14.8, 7.1 Hz, 1H), 4.22 – 4.04, 3.86 (m, d, *J* = 8.6 Hz, 4H), 2.88 – 2.78 (m, 1H), 2.63 – 2.36 (m, 3H), 2.24 – 2.15 (m, 1H), 2.10 – 1.94 (m, 2H), 1.25 – 1.12 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.46, 169.43, 169.09, 168.96, 149.73, 149.70, 148.29, 148.23, 139.56, 139.40, 138.83 (t, *J* = 27.0 Hz), 137.87, 135.84, 135.81, 135.11, 134.68, 134.65, 134.55, 134.50, 132.04 (q, *J* = 32.7 Hz), 128.96, 128.68, 128.65, 128.21, 127.80, 127.64, 127.22, 126.31, 125.88, 125.57, 125.36, 123.85, 123.79, 123.57 (q, *J* = 273.7 Hz), 123.18, 121.76, 121.06, 119.25, 119.11, 62.36, 62.12, 62.03, 61.80, 61.42, 60.43, 54.32, 44.10, 42.49 (t, *J* = 28.1 Hz), 40.69 (t, *J* = 26.6 Hz), 30.50, 29.76 (t, *J* = 78.5 Hz), 14.15, 14.09, 13.97, 13.70 (d, *J* = 1.5 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.63, -62.70, -89.57 (t, *J* = 14.6 Hz), -90.23 (t, *J* = 14.6 Hz), -93.94 (dd, *J* = 16.3, 13.7 Hz), -94.59 (t, *J* = 15.1 Hz), -95.46 (t, *J* = 16.9 Hz), -95.98 – -96.17 (m), -96.68 (t, *J* = 16.7 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{33}H_{32}F_5N_2O_4$ ($[M+H]^+$): 615.2277 found: 615.2270.

(*13S*)-2-(3-(1,1-difluoro-5-(4-phenylpiperazin-1-yl)pentyl)-5-(trifluoromethyl)phenoxy)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[a]phenanthren-17-one (98a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (122.1 mg, 60% yield; 42.3 mg, 87% yield) as a pink solid.

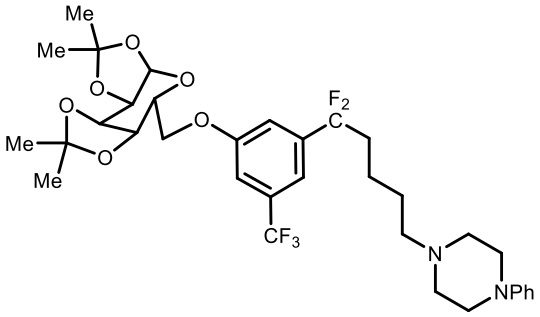
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (s, 1H), 7.21 – 7.14 (m, 5H), 6.83 (d, *J* = 7.8 Hz, 2H), 6.77 – 6.69 (m, 3H), 3.11 – 3.08 (m, 4H), 2.83 – 2.79 (m, 2H), 2.50 – 2.39 (m, 5H), 2.35 – 2.18 (m, 4H), 2.12 – 1.87 (m, 6H), 1.60 – 1.34 (m, 10H), 0.85 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.62, 153.36, 151.35, 140.35 (t, *J* = 27.7 Hz), 138.95, 136.43, 132.54 (q, *J* = 33.0 Hz), 129.16, 127.18, 123.43 (q, *J* = 274.7 Hz), 122.08 (t, *J* = 244.4 Hz), 119.78, 119.75, 118.06 (t, J = 6.1 Hz), 116.98, 116.08, 115.94 –115.81 (m), 58.18, 53.32, 50.48, 49.14, 48.01, 44.18, 38.75 (t, *J* = 27.0 Hz), 38.12, 35.90, 31.64, 29.54, 26.41, 26.39, 25.88, 21.65, 20.47 (t, *J* = 3.9 Hz), 13.93.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.62 (d, *J* = 4.1 Hz), -95.79 (td, *J* = 16.6, 5.4 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{40}H_{46}F_5N_2O_2$ ($[M+H]^+$): 681.3474, found: 681.3464.

1-(5,5-difluoro-5-(3-(((3a*R*,5*R*,5a*R*,8a*S*,8b*R*)-2,2,7,7-tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-5-yl)methoxy)-5-(trifluoromethyl)phenyl)pentyl)-4-phenylpiperazine (99a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (164.4 mg, 82% yield; 65.2 mg, 97% yield) as a colorless oil.

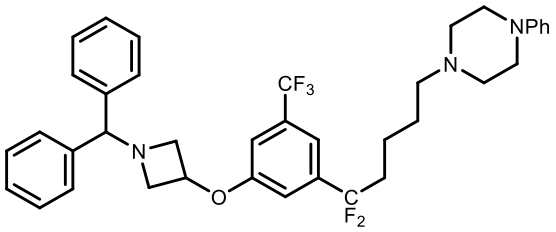
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (s, 1H), 7.19 – 7.15 (m, 4H), 6.84 (d, *J* = 7.7 Hz, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 5.50 (d, *J* = 4.9 Hz, 1H), 4.59 (dd, *J* = 7.9, 2.4 Hz, 1H), 4.30 – 4.26 (m, 2H), 4.15 – 4.08 (m, 3H), 3.11 (t, *J* = 5.2 Hz, 4H), 2.50 (t, *J* = 5.2 Hz, 4H), 2.30 (t, *J* = 7.2 Hz, 2H), 2.07 (tt, *J* = 16.1, 7.8 Hz, 2H), 1.53 – 1.35 (m, 10H), 1.29 – 1.27 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.11, 151.42, 139.99 (t, *J* = 27.5 Hz), 132.29 (q, *J* = 32.9 Hz), 129.19, 123.66 (q, *J* = 272.5 Hz), 122.25 (t, *J* = 244.4 Hz), 119.78, 116.14, 115.36 (t, *J* = 6.5 Hz), 114.43, 112.85, 109.76, 108.96, 96.47, 71.04, 70.77, 70.63, 67.48, 66.35, 58.27, 53.35, 49.19, 38.87 (t, *J* = 27.1 Hz), 26.47, 26.16, 26.10, 25.01, 24.53, 20.55 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.72, -87.33 – -106.50 (m).

HRMS (ESI-TOF) m/z calcd. for $C_{34}H_{44}F_5N_2O_6$ ($[M+H]^+$): 671.3114, found: 671.3107.

1-(5-(3-((1-benzhydrylazetidin-3-yl)oxy)-5-(trifluoromethyl)phenyl)-5,5-difluoropentyl)-4-phenylpiperazine (100a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (137.9 mg, 71% yield; 35.8 mg, 55% yield) as a white solid.

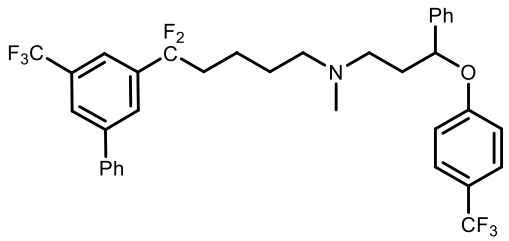
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (dt, *J* = 8.2, 1.9 Hz, 4H), 7.22 – 7.10 (m, 9H), 6.94 (d, *J* = 10.6 Hz, 2H), 6.84 (d, *J* = 7.9 Hz, 2H), 6.77 (td, *J* = 7.3, 1.1 Hz, 1H), 4.76 (p, *J* = 5.7 Hz, 1H), 4.35 (s, 1H), 3.66 – 3.62 (m, 2H), 3.12 – 3.04 (m, 6H), 2.49 (t, *J* = 5.0 Hz, 4H), 2.28 (t, *J* = 7.4 Hz, 2H), 2.09 – 1.97 (m, 2H), 1.52 – 1.33 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.62, 151.38, 141.82, 140.24 (t, *J* = 27.4 Hz), 132.52 (q, *J* = 32.8 Hz), 129.24, 128.70, 127.50, 123.54 (q, *J* = 273.7 Hz), 122.12 (t, *J* = 243.3 Hz), 119.87, 116.18, 115.15, 114.65, 112.63, 78.43, 66.83, 60.25, 58.22, 53.33, 49.17, 38.83 (t, *J* = 27.0 Hz), 26.39, 20.51.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.75, -96.01 (t, *J* = 16.4 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{38}H_{41}F_5N_3O$ ($[M+H]^+$): 650.3164, found: 650.3157.

5,5-difluoro-*N*-methyl-*N*-(3-phenyl-3-(4-(trifluoromethyl)phenoxy)propyl)-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentan-1-amine (101a)



The title product was prepared via procedure A & C, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (102.6 mg, 54% yield; 40.1 mg, 63% yield) as a pale yellow oil.

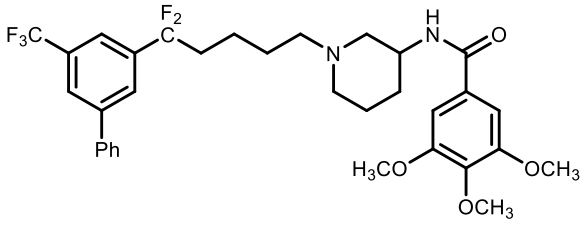
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.83 (s, 1H), 7.68 (s, 1H), 7.59 (d, *J* = 7.5 Hz, 2H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.41 (dd, *J* = 11.0, 7.9 Hz, 3H), 7.32 (d, *J* = 4.4 Hz, 4H), 7.27 – 7.23 (m, 1H), 6.88 (d, *J* = 8.5 Hz, 2H), 5.26 (dd, *J* = 8.4, 4.7 Hz, 1H), 2.52 (dt, *J* = 12.4, 7.3 Hz, 1H), 2.45 – 2.38 (m, 1H), 2.32 – 2.29 (m, 2H), 2.21 – 2.09 (m, 6H), 1.99 – 1.90 (m, 1H), 1.48 – 1.44 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.84, 142.82, 141.35, 139.26 (t, *J* = 27.6 Hz), 139.11, 131.75 (q, *J* = 32.7 Hz), 129.29, 128.88, 128.65, 127.93, 127.39, 127.17, 126.85 (q, *J* = 3.8 Hz), 125.99, 125.34, 124.53 (q, *J* = 272.7 Hz), 123.93 (q, *J* = 274.7 Hz), 122.85 (q, *J* = 32.3 Hz), 122.46 (t, *J* = 244.4 Hz), 120.78, 115.87, 78.57, 57.58, 53.81, 42.27, 39.05 (t, *J* = 27.0 Hz), 36.64, 27.08, 20.50 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -61.54, -62.59, -95.91 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{35}H_{34}F_8NO$ ($[M+H]^+$): 636.2507, found: 636.2500.

***N*-(1-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)piperidin-3-yl)-3,4,5-trimethoxybenzamide (102a)**



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 2:1:0.03) on silica gel to afford the title compound (152.1 mg, 82% yield; 49.0 mg, 79% yield) as a pale yellow solid.

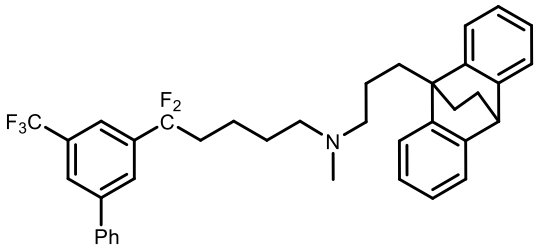
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.83 (s, 1H), 7.67 (s, 1H), 7.59 (d, *J* = 7.6 Hz, 2H), 7.49 – 7.39 (m, 3H), 7.04 (s, 2H), 6.90 (s, 1H), 4.27 (s, 1H), 3.89 – 3.86 (m, 9H), 2.61 – 2.49 (m, 4H), 2.34 (s, 2H), 2.21 – 2.12 (m, 2H), 1.73 – 1.53 (m, 8H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.29, 153.20, 142.80, 140.85, 139.13 (t, *J* = 27.4 Hz), 138.94, 132.10, 131.67 (q, *J* = 32.6 Hz), 130.31, 129.24, 128.63, 127.31, 127.04, 125.33, 123.82 (q, *J* = 273.7 Hz), 122.32 (t, *J* = 243.4 Hz), 120.61, 104.51, 60.96, 58.24, 56.38, 53.95, 45.52, 39.01 (t, *J* = 27.1 Hz), 29.06, 26.41, 21.99, 20.28.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.58, -96.36 – -96.49 (m).

HRMS (ESI-TOF) m/z calcd. for $C_{33}H_{38}F_5N_2O_4$ ($[M+H]^+$): 621.2746, found: 621.2742.

_N_-(3-(9,10-ethanoanthracen-9(10_H_)-yl)propyl)-5,5-difluoro-_N_-methyl-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentan-1-amine (103a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (173.2 mg, 96% yield; 42.3 mg, 70% yield) as a white solid.

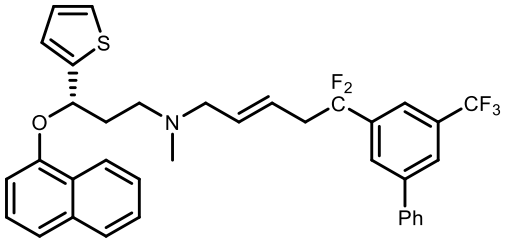
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 9.2 Hz, 2H), 7.63 (s, 1H), 7.50 (d, *J* = 7.5 Hz, 2H), 7.37 (t, *J* = 7.4 Hz, 2H), 7.31 (t, *J* = 7.1 Hz, 1H), 7.17 – 7.13 (m, 4H), 7.02 – 6.94 (m, 4H), 4.17 (s, 1H), 2.53 (t, *J* = 7.5 Hz, 2H), 2.34 (t, *J* = 7.2 Hz, 4H), 2.21 – 2.09 (m, 5H), 1.87 – 1.80 (m, 2H), 1.74 – 1.69 (m, 2H), 1.54 – 1.45 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.59, 145.13, 142.79, 139.26 (t, *J* = 27.3 Hz), 139.08, 131.72 (q, *J* = 32.5 Hz), 129.25, 128.61, 127.38, 127.19, 125.36, 125.32, 123.45, 122.50 (t, *J* = 243.4 Hz), 121.40, 120.80, 59.09, 57.62, 44.94, 44.66, 42.48, 39.16 (t, *J* = 27.0 Hz), 29.81, 29.01, 27.79, 27.18, 22.81, 20.61 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.50, -95.82 (t, *J* = 16.5 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{38}H_{39}F_5N$ ($[M+H]^+$): 604.2997, found: 604.3000.

(_S_,_E_)-5,5-difluoro-_N_-methyl-_N_-(3-(naphthalen-1-yloxy)-3-(thiophen-2-yl)propyl)-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pent-2-en-1-amine (104ab)



The title product was prepared via procedure A, purified by flash chromatography (PE:EA = 8:1) on silica gel to afford the title compound (173.3 mg, 93% yield; 109.1 mg, 59% yield for *E* isomer) as a yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.88 (s, 1H), 7.77 (s, 1H), 7.70 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.63 (s, 1H), 7.58 (dd, *J* = 7.0, 1.6 Hz, 2H), 7.49 –

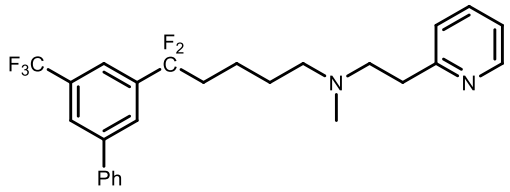
7.39 (m, 5H), 7.34 (d, *J* = 8.2 Hz, 1H), 7.23 (d, *J* = 7.2 Hz, 1H), 7.18 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.03 (d, *J* = 4.2 Hz, 1H), 6.91 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.84 (d, *J* = 7.6 Hz, 1H), 5.76 (dd, *J* = 7.8, 5.0 Hz, 1H), 5.52 – 5.42 (m, 2H), 2.99 – 2.87 (m, 2H), 2.65 – 2.54 (m, 3H), 2.48 – 2.33 (m, 2H), 2.19 – 2.10 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.63, 145.52, 142.72, 139.05, 138.79 (t, *J* = 27.3 Hz), 134.72, 134.47, 131.61 (q, *J* = 32.7 Hz), 129.27, 128.65, 127.56, 127.35, 127.28 (t, *J* = 7.1 Hz), 126.64, 126.38, 126.22, 125.89, 125.32, 125.28, 124.76, 124.65, 123.93 (q, *J* = 273.7 Hz), 123.09 (t, *J* = 4.9 Hz), 122.27, 121.31 (t, *J* = 245.4 Hz), 120.91 – 120.89 (m), 120.57, 106.95, 74.35, 59.89, 52.91, 42.23 (t, *J* = 28.0 Hz), 42.12, 36.97.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.49, -95.63 (t, *J* = 16.1 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{36}H_{33}F_5NOS$ ($[M+H]^+$): 622.2198, found: 622.2193.

5,5-difluoro-*N*-methyl-*N*-(2-(pyridin-2-yl)ethyl)-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentan-1-amine (105a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (99.4 mg, 72% yield; 36.2 mg, 78% yield) as a yellow oil.

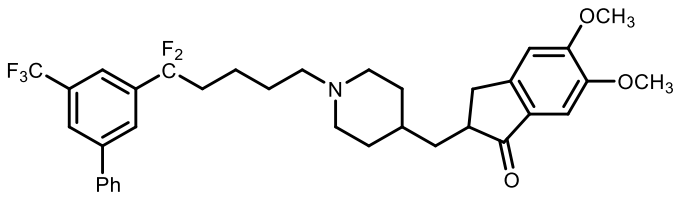
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 5.0 Hz, 1H), 7.88 (s, 1H), 7.84 (s, 1H), 7.69 (s, 1H), 7.61 – 7.53 (m, 3H), 7.48 (t, *J* = 7.4 Hz, 2H), 7.42 (t, *J* = 7.3 Hz, 1H), 7.14 (d, *J* = 7.8 Hz, 1H), 7.09 – 7.06 (m, 1H), 2.93 (t, *J* = 7.2 Hz, 2H), 2.75 (t, *J* = 6.4 Hz, 2H), 2.40 (t, *J* = 7.0 Hz, 2H), 2.28 (s, 3H), 2.17 (tt, *J* = 15.7, 7.4 Hz, 2H), 1.56 – 1.42 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.56, 149.33, 142.76, 139.23 (t, *J* = 27.5 Hz), 139.09, 136.41, 131.69 (q, *J* = 32.7 Hz), 129.24, 128.60, 127.37, 127.18 (t, *J* = 6.0 Hz), 125.28, 123.90 (q, *J* = 273.7 Hz), 123.34, 122.46 (t, *J* = 243.2 Hz), 121.25, 120.77 (d, *J* = 3.6 Hz), 57.57, 57.20, 42.21, 39.01 (t, *J* = 27.0 Hz), 36.01, 26.93, 20.43 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.58, -95.83 (t, *J* = 16.5 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{26}H_{28}F_5N_2$ ($[M+H]^+$): 463.2167, found: 463.2163.

2-((1-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)piperidin-4-yl)methyl)-5,6-dimethoxy-2,3-dihydro-1*H*-inden-1-one (106a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (119.6 mg, 65% yield; 43.8 mg, 71% yield) as a white solid.

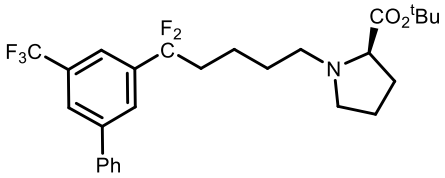
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.84 (s, 1H), 7.68 (s, 1H), 7.59 (dd, *J* = 7.0, 1.7 Hz, 2H), 7.47 (t, *J* = 7.4 Hz, 2H), 7.41 (t, *J* = 7.3 Hz, 1H), 7.45 (s, 1H), 6.84 (s, 1H), 3.94 (s, 3H), 3.88 (s, 3H), 3.22 (dd, *J* = 17.6, 8.2 Hz, 1H), 2.88 (dd, *J* = 10.7, 7.0 Hz, 2H), 2.70 – 2.65 (m, 2H), 2.31 – 2.13 (m, 4H), 1.92 – 1.85 (m, 3H), 1.74 – 1.64 (m, 2H), 1.56 – 1.45 (m, 5H), 1.33 – 1.24 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.81, 155.57, 149.55, 148.82, 142.76, 139.19 (t, *J* = 27.4 Hz), 139.05, 131.68 (q, *J* = 33.3 Hz), 129.41, 129.23, 128.59, 127.34, 127.15 (t, *J* = 6.3 Hz), 125.25, 123.88 (q, *J* = 273.7 Hz), 122.46 (t, *J* = 243.1 Hz), 120.74, 107.46, 104.49, 58.64, 56.28, 56.17, 54.06, 54.02, 45.49, 39.00 (t, *J* = 27.1 Hz), 38.80, 34.57, 33.48, 33.01, 31.89, 26.68, 20.67 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.58, -95.81 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{35}H_{39}F_5NO_3$ ($[M+H]^+$): 616.2845, found: 616.2841.

***tert*-butyl-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-*D*-proli nate (107a)**



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (114.4 mg, 77% yield; 32.4 mg, 65% yield) as a pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.86 (s, 1H), 7.70 (s, 1H), 7.60 (d, *J* = 8.5 Hz, 2H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.42 (t, *J* = 6.6 Hz, 1H), 3.10 (td, *J* = 8.2, 3.4 Hz,

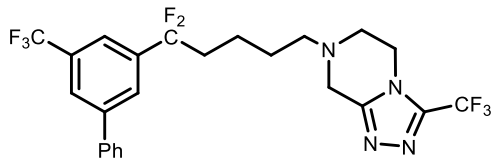
1H), 3.01 (dd, *J* = 8.9, 5.3 Hz, 1H), 2.73 – 2.67 (m, 1H), 2.40 – 2.14 (m, 4H), 2.08 – 2.00 (m, 1H), 1.91 – 1.83 (m, 2H), 1.79 – 1.71 (m, 1H), 1.59 – 1.48 (m, 4H), 1.43 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.57, 142.79, 139.29 (t, *J* = 27.4 Hz), 139.16, 131.72 (q, *J* = 32.7 Hz), 129.25, 128.59, 127.41, 127.25 (t, *J* = 6.2 Hz), 125.29, 123.94 (q, *J* = 273.7 Hz), 122.55 (t, *J* = 243.2 Hz), 120.84 – 120.80 (m), 80.62, 66.76, 54.40, 53.51, 38.93 (t, *J* = 27.0 Hz), 29.29, 28.45, 28.21, 23.13, 20.54 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.61, -94.86 – -96.54 (m).

HRMS (ESI-TOF) m/z calcd. for $C_{27}H_{33}F_5NO_2$ ($[M+H]^+$): 498.2426, found: 498.2420.

7-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-3-(trifluoromethyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine (108a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA: Et_3N = 2:1:4%) on silica gel to afford the title compound (145.5 mg, 94% yield; 46.6 mg, 90% yield) as a colorless oil.

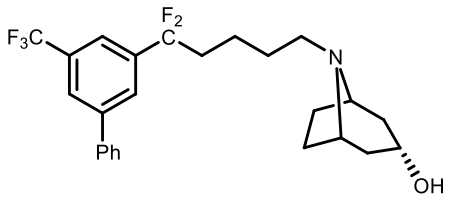
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.85 (s, 1H), 7.68 (s, 1H), 7.61 – 7.58 (m, 2H), 7.50 – 7.47 (m, 2H), 7.44 – 7.40 (m, 1H), 4.10 (t, *J* = 5.5 Hz, 2H), 3.84 (s, 2H), 2.91 (t, *J* = 5.5 Hz, 2H), 2.61 (t, *J* = 6.9 Hz, 2H), 2.21 (tt, *J* = 15.9, 7.5 Hz, 2H), 1.64 – 1.54 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.25, 143.38 (q, *J* = 39.4 Hz), 142.85, 139.04 (t, *J* = 27.4 Hz), 138.93, 131.73 (q, *J* = 32.7 Hz), 129.27, 128.69, 127.31, 127.08 (t, *J* = 6.1 Hz), 125.38, 123.84 (q, *J* = 273.7 Hz), 122.31 (t, *J* = 244.4 Hz), 120.66 (d, *J* = 3.7 Hz), 118.49 (q, *J* = 270.7 Hz), 56.85, 49.26, 48.92, 43.52 (d, *J* = 1.7 Hz), 38.87 (t, *J* = 27.2 Hz), 26.52, 20.10 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.62, -63.17, -96.13 (t, *J* = 16.4 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{24}H_{23}F_8N_4$ ($[M+H]^+$): 519.1789 found: 519.1788.

(1*R*,3*r*,5*S*)-8-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-8-azabicyclo[3.2.1]octan-3-ol (109a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 2:1:0.03) on silica gel to afford the title compound (94.7 mg, 70% yield; 35.0 mg, 77% yield) as a white solid.

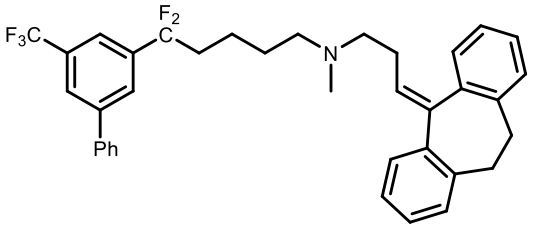
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.85 (s, 1H), 7.69 (s, 1H), 7.62 – 7.59 (m, 2H), 7.49 (td, *J* = 7.3, 1.1 Hz, 2H), 7.45 – 7.41 (m, 1H), 4.01 – 3.98 (m, 1H), 3.12 (t, *J* = 3.7 Hz, 2H), 2.95 – 2.88 (m, 1H), 2.31 (t, *J* = 7.0 Hz, 2H), 2.19 (tt, *J* = 16.0, 7.7 Hz, 2H), 2.06 – 2.00 (m, 4H), 1.89 – 1.85 (m, 2H), 1.63 (s, 1H), 1.60 (s, 1H), 1.51 – 1.49 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.76, 139.22 (t, *J* = 27.5 Hz), 139.10, 131.70 (q, *J* = 32.6 Hz), 129.26, 128.63, 127.37, 127.20 (t, *J* = 6.1 Hz), 125.28, 123.91 (q, *J* = 273.7 Hz), 122.54 (*t*, J = 244.4 Hz), 120.79 – 120.78 (m), 65.09, 58.14, 51.92, 39.26, 39.04 (t, *J* = 26.8 Hz), 28.49, 26.31, 20.62 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.60, -95.79 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{25}H_{29}F_5NO$ ($[M+H]^+$): 454.2164, found: 454.2159.

***N*-(3-(10,11-dihydro-5*H*-dibenzo[a,d][7]annulen-5-ylidene)propyl)-5,5-difluoro-*N*-methyl-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentan-1-amine (110a)**



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 10:1:0.03) on silica gel to afford the title compound (149.7 mg, 85% yield; 31.8 mg, 54% yield) as a yellow solid.

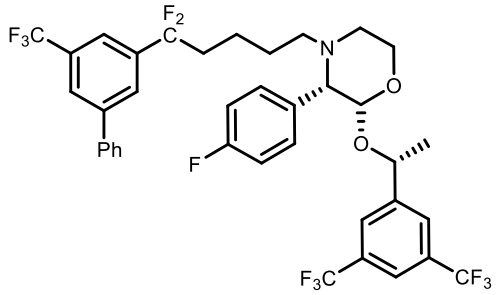
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.86 (s, 1H), 7.71 (s, 1H), 7.62 (dd, *J* = 7.5, 1.9 Hz, 2H), 7.50 (t, *J* = 7.4 Hz, 2H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.29 – 7.27 (m, 1H), 7.20 – 7.11 (m, 6H), 7.05 – 7.02 (m, 1H), 5.86 (t, *J* = 7.3 Hz, 1H), 3.34 (d, *J* = 41.0 Hz, 2H), 2.97 (s, 1H), 2.77 (s, 1H), 2.44 (t, *J* = 7.5 Hz, 2H), 2.30 – 2.14 (m, 9H), 1.48 – 1.44 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.68, 142.81, 141.42, 140.22, 139.46, 139.28 (t, *J* = 27.4 Hz), 139.13, 137.18, 131.74 (q, *J* = 32.7 Hz), 130.09, 129.49, 129.28, 128.71, 128.64, 128.33, 128.08, 127.50, 127.40, 127.20, 127.13, 126.11, 125.83, 125.30, 123.94 (q, *J* = 273.7 Hz), 122.47 (t, *J* = 244.4 Hz), 120.81, 57.43, 57.02, 42.18, 39.07 (t, *J* = 27.0 Hz), 33.91, 32.17, 27.30, 26.93, 20.50 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.55, -95.80 (t, *J* = 16.5 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{37}H_{37}F_5N$ ($[M+H]^+$): 590.2841, found: 590.2838.

(2*R*,3*S*)-2-((*R*)-1-(3,5-bis(trifluoromethyl)phenyl)ethoxy)-4-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-3-(4-fluorophenyl)morpholine (111a)



The title product was prepared via procedure A & C, purified by flash chromatography (PE:EA:Et_3N = 10:1:0.03) on silica gel to afford the title compound (212.4 mg, 93 % yield; 24.2 mg, 32% yield) as a pale yellow solid.

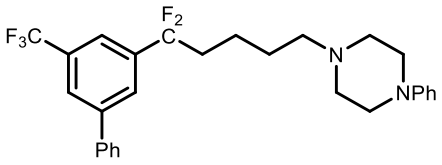
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.84 (s, 1H), 7.69 (s, 1H), 7.64 – 7.60 (m, 3H), 7.52 – 7.48 (m, 2H), 7.46 – 7.42 (m, 1H), 7.32 (s, 2H), 7.15 (s, 2H), 6.98 (t, *J* = 8.5 Hz, 2H), 4.86 (q, *J* = 6.5 Hz, 1H), 4.29 – 4.26 (m, 2H), 3.67 (d, *J* = 11.1 Hz, 1H), 3.31 (s, 1H), 3.04 (d, *J* = 11.6 Hz, 1H), 2.47 – 2.35 (m, 2H), 2.12 (dt, *J* = 16.6, 8.6 Hz, 2H), 1.88 (s, 1H), 1.55 – 1.31 (m, 7H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.38, 145.83, 142.85, 139.24 (t, *J* = 27.1 Hz), 139.07, 131.76 (d, *J* = 32.3 Hz), 131.70 (q, *J* = 33.3 Hz), 130.86 (d, *J* = 7.9 Hz), 129.31, 128.69, 127.37, 127.14, 126.42, 125.33, 123.23 (q, *J* = 273.7 Hz), 122.46 (t, *J* = 244.3 Hz), 121.52, 120.74, 115.09 (d, *J* = 21.4 Hz), 95.79, 72.43, 69.68, 59.75, 54.96, 51.79, 39.06 (t, *J* = 27.2 Hz), 25.17, 24.54, 20.34.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.63, -62.92, -96.00 (t, *J* = 16.3 Hz), -114.54 – -114.62 (m).

HRMS (ESI-TOF) m/z calcd. for $C_{38}H_{34}F_{12}NO_2$ ($[M+H]^+$): 764.2392, found: 764.2396.

1-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-4-phenylpiperazine (112a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (133.3 mg, 91% yield; 46.0 mg, 92% yield) as a colorless oil.

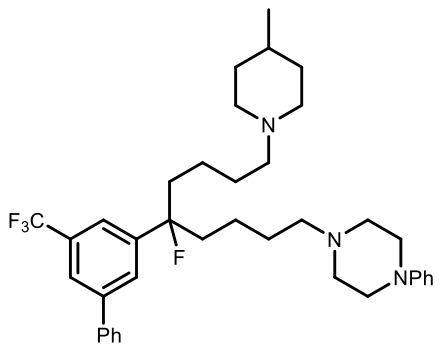
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.77 (s, 1H), 7.62 (s, 1H), 7.51 (d, *J* = 7.5 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.33 (t, *J* = 7.3 Hz, 1H), 7.17 (t, *J* = 7.6 Hz, 2H), 6.82 (d, *J* = 8.1 Hz, 2H), 6.76 (t, *J* = 7.3 Hz, 1H), 3.08 (t, *J* = 5.0 Hz, 4H), 2.48 (t, *J* = 4.9 Hz, 4H), 2.29 (t, *J* = 7.1 Hz, 2H), 2.13 (tt, *J* = 15.9, 7.4 Hz, 2H), 1.58 – 1.37 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.43, 142.81, 139.20 (t, *J* = 27.4 Hz), 139.08, 131.74 (q, *J* = 32.7 Hz), 129.27, 129.21, 128.64, 127.38, 127.19 (t, *J* = 5.9 Hz), 125.34, 123.91 (q, *J* = 274.7 Hz), 122.49 (t, *J* = 243.3 Hz), 120.79 (d, *J* = 4.1 Hz), 119.80, 116.15, 58.25, 53.38, 49.22, 39.02 (t, *J* = 27.1 Hz), 26.50, 20.58 (t, *J* = 3.9 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.54, -95.81 (t, *J* = 16.4 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{28}H_{30}F_5N_2$ ($[M+H]^+$): 489.2324, found: 489.2321.

1-(5-fluoro-9-(4-methylpiperidin-1-yl)-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)nonyl)-4-phenylpiperazine (113a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 2:1:0.03) on silica gel to afford the title compound (76.2 mg, 41% yield; 43.8 mg, 70% yield) as a white solid.

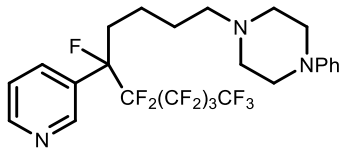
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.57 (s, 1H), 7.52 (d, *J* = 7.6 Hz, 2H), 7.42 – 7.30 (m, 3H), 7.32 (t, *J* = 7.3 Hz, 1H), 7.17 (t, *J* = 7.8 Hz, 2H), 6.82 (d, *J* = 8.2 Hz, 2H), 6.76 (t, *J* = 7.3 Hz, 1H), 3.07 (t, *J* = 5.0 Hz, 4H), 2.77 – 2.72 (m, 2H), 2.45 (t, *J* = 5.0 Hz, 4H), 2.23 (t, *J* = 7.4 Hz, 2H), 2.14 (t, *J* = 7.6 Hz, 2H), 1.98 – 1.82 (m, 4H), 1.75 (t, *J* = 11.6 Hz, 2H), 1.52 – 1.31 (m, 8H), 1.17 – 1.02 (m, 5H), 0.81 (d, *J* = 6.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.40, 145.06 (d, *J* = 22.9 Hz), 142.19 (d, *J* = 1.8 Hz), 139.74, 131.77 – 130.82 (m), 129.15 (d, *J* = 4.0 Hz), 128.29, 127.38, 126.69 (d, *J* = 10.5 Hz), 124.26 (q, *J* = 273.7 Hz), 122.78 (d, *J* = 3.9 Hz), 120.32 – 120.20 (m), 119.73, 116.10, 99.67 (d, *J* = 177.8 Hz), 58.91, 58.42, 54.13 (d, *J* = 2.7 Hz), 53.33, 49.17, 40.91 (d, *J* = 10.6 Hz), 40.67 (d, *J* = 10.7 Hz), 34.36, 30.91, 27.22, 26.99, 22.00, 21.48 (d, *J* = 3.5 Hz), 21.32 (d, *J* = 3.6 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.29, -160.65 – -161.92 (m).

HRMS (ESI-TOF) m/z calcd. for $C_{38}H_{50}F_4N_3$ ($[M+H]^+$): 624.3935, found: 624.3931.

1-(5,6,6,7,7,8,8,9,9,10,10,10-dodecafluoro-5-(pyridin-3-yl)decyl)-4-phenylpiperazine (115a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (98.2 mg, 55% yield; 49.6 mg, 83% yield) as a pale yellow solid.

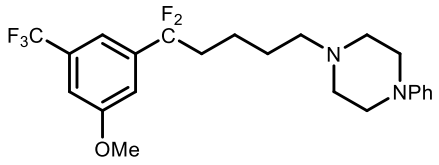
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 – 8.58 (m, 2H), 7.69 (dd, *J* = 7.9, 2.5 Hz, 1H), 7.29 (dd, *J* = 8.1, 4.8 Hz, 1H), 7.20 – 7.16 (m, 2H), 6.84 (d, *J* = 7.7 Hz, 2H), 6.77 (tt, *J* = 7.3, 1.0 Hz, 1H), 3.08 (dd, *J* = 6.5, 3.6 Hz, 4H), 2.47 – 2.08 (m, 8H), 1.54 – 1.26 (m, 3H), 0.98 – 0.87 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.38, 150.54, 147.28 (d, *J* = 10.3 Hz), 133.81 (d, *J* = 10.7 Hz), 129.79 (d, *J* = 21.5 Hz), 129.21, 123.30 (d, *J* = 2.5 Hz), 119.82, 116.14, 96.94 (dt, *J* = 191.9, 27.3 Hz), 57.96, 53.27, 49.17, 32.52 (d, *J* = 20.5 Hz), 26.46, 20.03 (d, *J* = 2.9 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -80.87 (t, *J* = 9.9 Hz), -117.65 – -126.31 (m), -176.53 – -176.75.

HRMS (ESI-TOF) m/z calcd. for $C_{25}H_{26}F_{12}N_3$ ($[M+H]^+$): 596.1930, found: 596.1925.

1-(5,5-difluoro-5-(3-methoxy-5-(trifluoromethyl)phenyl)pentyl)-4-phenylpiperazine (116a)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (122.0 mg, 92% yield; 42.6 mg, 96% yield) as a pale yellow oil.

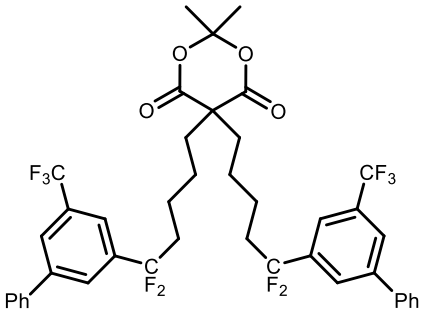
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (s, 1H), 7.20 – 7.14 (m, 2H), 7.09 (s, 2H), 6.84 (d, *J* = 8.2 Hz, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 3.78 (s, 3H), 3.10 (t, 4H), 2.49 (t, 4H), 2.29 (t, *J* = 7.3 Hz, 2H), 2.07 (tt, *J* = 16.1, 7.5 Hz, 2H), 1.58 – 1.26 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.06, 151.42, 140.05 (t, *J* = 27.5 Hz), 132.39 (q, *J* = 32.7 Hz), 129.22, 123.71 (q, *J* = 272.7 Hz), 122.28 (t, *J* = 244.4 Hz), 119.83, 116.16, 114.62 (t, *J* = 6.3 Hz), 114.38 – 113.93 (m), 111.95 (d, *J* = 4.0 Hz), 58.25, 55.83, 53.36, 49.20, 38.86 (t, *J* = 27.0 Hz), 26.44, 20.55 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.75, -95.86 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{23}H_{28}F_5N_2O$ ($[M+H]^+$): 443.2116, found: 443.2103.

5,5-bis(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (117a)



The title product was prepared via procedure G & D, purified by flash chromatography (PE:EA = 20:1) on silica gel to afford the title compound (101.0 mg, 85% yield; 75.6 mg, 95% yield) as a white solid.

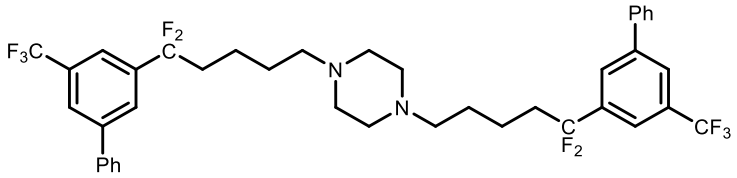
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 2H), 7.83 (s, 2H), 7.68 (s, 2H), 7.62 – 7.59 (m, 4H), 7.52 – 7.48 (m, 4H), 7.45 – 7.41 (m, 2H), 2.22 – 2.10 (m, 4H), 2.01 – 1.97 (m, 4H), 1.70 (s, 6H), 1.54 – 1.46 (m, 4H), 1.40 – 1.32 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.22, 142.90, 139.02, 138.98 (t, *J* = 27.3 Hz), 131.79 (q, *J* = 32.6 Hz), 129.26, 128.65, 127.39, 127.09 (t, *J* = 5.7 Hz), 125.44, 123.87 (q, *J* = 273.7 Hz), 122.19 (t, *J* = 244.4 Hz), 120.70 – 120.64 (m), 105.75, 54.50, 38.90, 38.76 (t, *J* = 27.4 Hz), 29.85, 25.24, 22.37 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.60, -96.29 (t, *J* = 16.3 Hz).

MS (ESI) m/z calculated for $C_{42}H_{39}F_{10}O_4$ ($[M + H]^+$): 797.2683, found 797.1.

1,4-bis(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)piperazine (118a)



The title product was prepared via procedure F & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (82.8 mg, 75% yield; 56.1 mg, 76% yield) as a colorless oil.

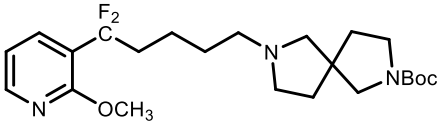
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 2H), 7.85 (s, 2H), 7.69 (s, 2H), 7.62 – 7.59 (m, 4H), 7.49 (t, *J* = 7.4 Hz, 4H), 7.42 (t, *J* = 7.3 Hz, 2H), 2.43 – 2.13 (m, 16H), 1.55 – 1.44 (m, 8H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.78, 139.19 (t, *J* = 27.5 Hz), 139.08, 131.72 (q, *J* = 32.7 Hz), 129.26, 128.62, 127.37, 127.17 (t, *J* = 5.9 Hz), 125.31, 123.91 (q, *J* = 273.7 Hz), 122.47 (t, *J* = 244.4 Hz), 120.78, 58.22, 53.22, 39.00 (t, *J* = 27.1 Hz), 26.45, 20.58.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.58, -95.85 (t, *J* = 16.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{40}H_{41}F_{10}N_2$ ($[M+H]^+$): 739.3105, found: 739.3102.

***tert*-butyl-7-(5,5-difluoro-5-(2-methoxypyridin-3-yl)pentyl)-2,7-diazaspiro[4.4]nonane-2-carboxylate (119a)**



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (66.9 mg, 51% yield; 35.8 mg, 82% yield) as a white solid.

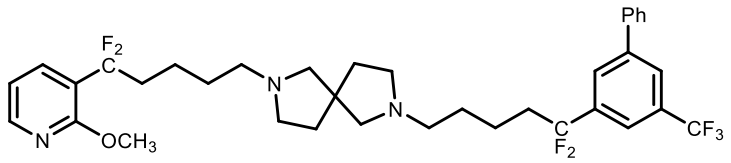
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19, 7.97 (dd, *J* = 5.1, 1.8 Hz, dd, *J* = 5.0, 1.9 Hz, 1H), 7.74, 7.33 (dd, *J* = 7.5, 1.9 Hz, dd, *J* = 7.1, 1.9 Hz, 1H), 6.91, 6.77 (dd, *J* = 7.5, 5.0 Hz, dd, *J* = 7.2, 5.0 Hz, 1H), 3.97, 3.92 (s, s, 3H), 3.38 – 3.13 (m, 4H), 2.65 – 2.43 (m, 4H), 2.40 – 2.24 (m, 4H), 1.83 – 1.67 (m, 4H), 1.59 – 1.31 (m, 13H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.24, 160.56 (t, *J* = 4.2 Hz), 154.84, 154.74, 148.35, 144.09, 137.56, 135.89 (t, *J* = 8.1 Hz), 125.17, 121.91 (t, *J* = 243.4 Hz), 119.50 (t, *J* = 27.3 Hz), 116.70, 116.43, 79.22, 79.16, 64.54, 64.46, 64.29, 58.15, 58.09, 57.24, 57.17, 56.67, 56.20, 54.18, 54.06, 53.73, 53.29, 48.08, 47.28, 45.54, 45.13, 38.37, 37.42, 37.36, 36.26 (t, *J* = 26.1 Hz), 35.78, 35.67, 35.61, 29.83, 28.92, 28.63, 28.40, 27.46, 20.71 (t, *J* = 4.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.59, -75.61, -96.07 – -96.24 (m).

HRMS (ESI-TOF) m/z calcd. for $C_{23}H_{36}F_2N_3O_3$ ($[M+H]^+$): 440.2719, found: 440.2715.

2-(5,5-difluoro-5-(2-methoxypyridin-3-yl)pentyl)-7-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)-2,7-diazaspiro[4.4]nonane (120a)



The title product was prepared via procedure H & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (91.5 mg, 46% yield; 51.7 mg, 78% yield) as a pale yellow solid.

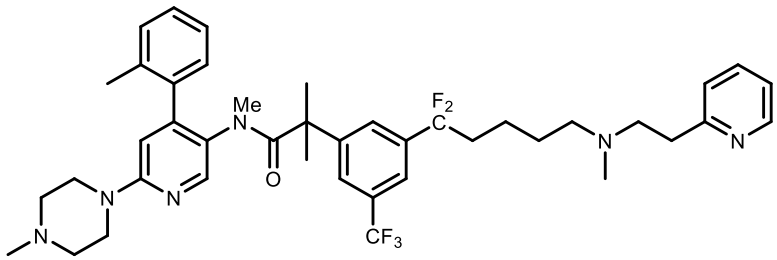
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (dd, *J* = 5.0, 1.8 Hz, 1H), 7.88 (s, 1H), 7.84 (s, 1H), 7.75 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.68 (s, 1H), 7.60 (dd, *J* = 7.4, 1.8 Hz, 2H), 7.48 (t, *J* = 7.4 Hz, 2H), 7.44 – 7.40 (m, 1H), 6.91 (dd, *J* = 7.5, 5.0 Hz, 1H), 3.98 (s, 3H), 2.57 – 2.46 (m, 6H), 2.39 – 2.13 (m, 10H), 1.85 – 1.70 (m, 4H), 1.52 – 1.44 (m, 6H), 1.40 – 1.32 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.58 (t, *J* = 4.4 Hz), 148.34, 142.75, 139.23 (t, *J* = 27.4 Hz), 139.07, 135.91 (t, *J* = 8.2 Hz), 132.16 (t, *J* = 9.1 Hz), 131.68 (q, *J* = 32.3 Hz), 129.25, 128.61, 127.36, 127.17, 125.27, 123.89 (q, *J* = 273.7 Hz), 122.49 (t, *J* = 244.4 Hz), 121.96 (t, *J* = 243.4 Hz), 120.75, 119.54 (t, *J* = 27.7 Hz), 116.43, 67.86, 67.83, 56.38, 56.27, 54.16, 53.74, 47.46, 39.30, 39.03 (t, *J* = 27.0 Hz), 36.29 (t, *J* = 26.0 Hz), 28.49, 28.43, 20.77 (t, *J* = 4.1 Hz), 20.59 (t, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.57, -95.88 (td, *J* = 16.4, 4.2 Hz), -96.12 (t, *J* = 17.0 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{36}H_{43}F_7N_3O$ ($[M+H]^+$): 666.3289, found: 666.3286.

2-(3-(1,1-difluoro-5-(methyl(2-(pyridin-2-yl)ethyl)amino)pentyl)-5-(trifluoromethyl)phenyl)-N,2-dimethyl-N-(6-(4-methylpiperazin-1-yl)-4-(o-tolyl)pyridin-3-yl)propanamide (121)



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 1:1:5%) on silica gel to afford the title compound (220.0 mg, 98% yield; 45.0 mg, 60% yield) as a yellow solid.

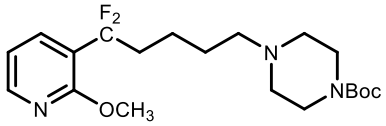
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, *J* = 5.0 Hz, 1H), 7.93 (s, 1H), 7.53 – 7.42 (m, 5H), 7.24 – 7.05 (m, 5H), 7.02 (dd, *J* = 7.5, 5.0 Hz, 1H), 6.43 (s, 1H), 3.49 (t, *J* = 5.0 Hz, 4H), 2.84 (dd, *J* = 9.3, 6.1 Hz, 2H), 2.67 (dd, *J* = 9.5, 6.0 Hz, 2H), 2.43 (t, *J* = 5.1 Hz, 5H), 2.34 – 2.16 (m, 8H), 2.11 – 1.87 (m, 3H), 1.55 – 1.19 (m, 13H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.53, 158.20, 149.29, 148.16, 147.35, 139.60 (t, *J* = 27.5 Hz), 136.84, 136.40, 131.91 (q, *J* = 32.9 Hz), 130.29, 129.11, 128.32, 125.52, 125.05, 124.62, 123.31, 122.82, 122.29, 122.21, 121.23, 120.29, 119.79, 108.25, 57.53, 57.16, 54.89, 47.38, 46.26, 45.40, 42.15, 38.95 (t, *J* = 27.1 Hz), 35.95, 31.92, 26.88, 23.40, 20.36 (t, *J* = 4.0 Hz), 20.02.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.53, -95.08 – -96.84 (m).

HRMS (ESI-TOF) m/z calcd. for $C_{42}H_{52}F_5N_6O$ ($[M+H]^+$): 751.4117, found: 751.4113.

***tert*-butyl-4-(5,5-difluoro-5-(2-methoxypyridin-3-yl)pentyl)piperazine-1-carboxylate (122)**



The title product was prepared via procedure A & D, purified by flash chromatography (PE:EA:Et_3N = 6:1:0.03) on silica gel to afford the title compound (59.6 mg, 50% yield; 37.3 mg, 93% yield) as a colorless oil.

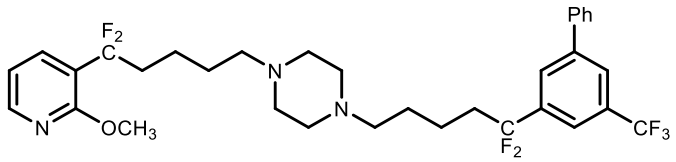
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (dd, *J* = 5.1, 1.8 Hz, 1H), 7.74 (dd, *J* = 7.5, 1.9 Hz, 1H), 6.91 (dd, *J* = 7.5, 5.0 Hz, 1H), 3.97 (s, 3H), 3.38 (t, *J* = 5.1 Hz, 4H), 2.36 – 2.24 (m, 8H), 1.52 – 1.32 (m, 13H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.57 (t, *J* = 4.4 Hz), 154.84, 148.38 (t, *J* = 1.9 Hz), 135.88 (t, *J* = 8.3 Hz), 121.88 (t, *J* = 243.4 Hz), 119.48 (t, *J* = 27.4 Hz), 116.44, 79.68, 58.33, 53.74, 53.09, 36.23 (t, *J* = 26.0 Hz), 28.52, 26.44, 20.64 (t, *J* = 4.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -96.20 (t, *J* = 17.0 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{20}H_{32}F_2N_3O_3$ $([M+H]^+)$: 400.2406, found: 400.2400.

1-(5,5-difluoro-5-(2-methoxypyridin-3-yl)pentyl)-4-(5,5-difluoro-5-(5-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)pentyl)piperazine (123)



The title product was prepared via procedure H & D, purified by flash chromatography (PE:EA:Et_3N = 3:1:0.03) on silica gel to afford the title compound (76.7 mg, 41% yield; 43.2 mg, 69% yield) as a colorless oil.

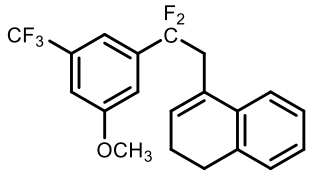
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (dd, *J* = 5.0, 1.8 Hz, 1H), 7.87 (s, 1H), 7.83 (s, 1H), 7.75 (dd, *J* = 7.4, 1.9 Hz, 1H), 7.68 (s, 1H), 7.59 (dd, *J* = 7.1, 1.6 Hz, 2H), 7.50 – 7.46 (m, 2H), 7.43 – 7.39 (m, 1H), 6.91 (dd, *J* = 7.4, 5.0 Hz, 1H), 3.98 (s, 3H), 2.42 – 2.12 (m, 16H), 1.52 – 1.45 (m, 6H), 1.39 – 1.31 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.59 (t, *J* = 4.5 Hz), 148.38 (t, *J* = 2.0 Hz), 142.78, 139.19 (t, *J* = 27.4 Hz), 139.07, 135.91 (t, *J* = 8.3 Hz), 131.71 (q, *J* = 32.6 Hz), 129.25, 128.62, 127.37, 127.17, 125.30, 123.89 (q, *J* = 274.7 Hz), 122.46 (t, *J* = 244.4 Hz), 121.91 (t, *J* = 243.4 Hz), 120.77, 119.52 (t, *J* = 27.4 Hz), 116.44, 58.33, 58.22, 53.75, 53.20, 38.99 (t, *J* = 27.1 Hz), 36.28 (t, *J* = 26.0 Hz), 26.49, 26.44, 20.74 (t, *J* = 4.2 Hz), 20.57 (t, *J* = 4.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.60, -95.86 (t, *J* = 16.3 Hz), -96.15 (t, *J* = 17.0 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{33}H_{39}F_7N_3O$ ($[M+H]^+$): 626.2976, found: 626.2971.

4-(2,2-difluoro-2-(3-methoxy-5-(trifluoromethyl)phenyl)ethyl)-1,2-dihydronaphthalene (127)



The title product was prepared via procedure J & D, purified by flash chromatography (PE:EA = 20:1) on silica gel to afford the title compound (33.1 mg, 30% yield) as a colorless oil.

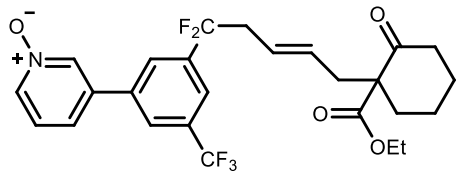
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (s, 1H), 7.01 – 6.96 (m, 6H), 5.75 (t, *J* = 4.7 Hz, 1H), 3.67 (s, 3H), 3.17 (t, *J* = 15.1 Hz, 2H), 2.57 (t, *J* = 8.0 Hz, 2H), 2.09 (td, *J* = 8.0, 4.7 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.76, 139.62 (t, *J* = 27.5 Hz), 136.32, 134.18, 132.05, 131.95 (q, *J* = 32.7 Hz), 128.67 (t, *J* = 4.4 Hz), 127.66, 127.05, 126.27, 123.71 (q, *J* = 273.7 Hz), 123.11 (t, *J* = 1.8 Hz), 121.70 (t, *J* = 247.5 Hz), 114.78 – 114.55 (m), 112.08 – 112.04 (m), 55.75, 42.13 (t, *J* = 28.3 Hz), 28.20, 23.27.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.83, -93.70 (t, *J* = 15.2 Hz).

MS (EI) m/z calculated for $C_{20}H_{17}F_5O$ ($[M]^+$): 368.1200, found 368.01.

(*E*)-3-(3-(5-(1-(ethoxycarbonyl)-2-oxocyclohexyl)-1,1-difluoropent-3-en-1-yl)-5-(trifluoromethyl)phenyl)pyridine 1-oxide (128)



The title product was prepared via procedure I & D, purified by flash chromatography (PE:EA:Et_3N = 1:5:5%) on silica gel to afford the title compound (50.6 mg, 99% yield) as a pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.25 (d, *J* = 6.4 Hz, 1H), 7.83 (s, 1H), 7.78 (s, 1H), 7.75 (s, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.40 (dd, *J* = 8.0, 6.4 Hz, 1H), 5.52 (dt, *J* = 14.9, 7.3 Hz, 1H), 5.35 (dt, *J* = 14.9, 7.0 Hz, 1H), 4.13 – 4.07 (m, 2H),

2.85 (td, *J* = 15.9, 7.0 Hz, 2H), 2.52 – 2.34 (m, 3H), 2.30 – 2.23 (m, 2H), 1.97 – 1.93 (m, 1H), 1.67 – 1.50 (m, 3H), 1.33 – 1.16 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.48, 171.38, 139.64 (t, *J* = 27.6 Hz), 138.79, 138.36, 137.89, 136.82, 132.58, 132.42 (q, *J* = 33.7 Hz), 127.29 (t, *J* = 6.2 Hz), 126.38, 125.23, 124.60, 123.37 (q, *J* = 273.7 Hz), 123.23 – 123.01 (m), 120.93 (t, *J* = 245.4 Hz), 61.36, 60.81, 42.38 (t, *J* = 27.8 Hz), 41.12, 38.03, 35.89, 27.49, 22.48, 14.18.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.81, -95.34 (td, *J* = 15.9, 4.6 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{26}H_{27}F_5NO_4$ ($[M+H]^+$): 512.1855, found: 512.1852.

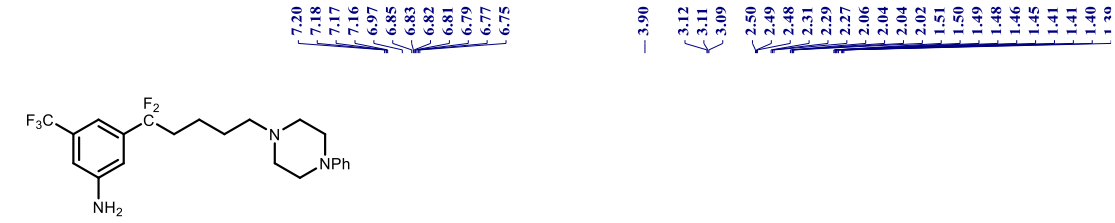
10. References

1. Pawar, G. G.; Wu, H.; De, S.; Ma, D. Copper(I) oxide/*N*,*N*'-bis[(2-furyl)methyl]oxalamide-catalyzed coupling of (hetero)aryl halides and nitrogen heterocycles at low catalytic loading. *Adv. Synth. Catal.* **2017**, *359*, 1631–1636.

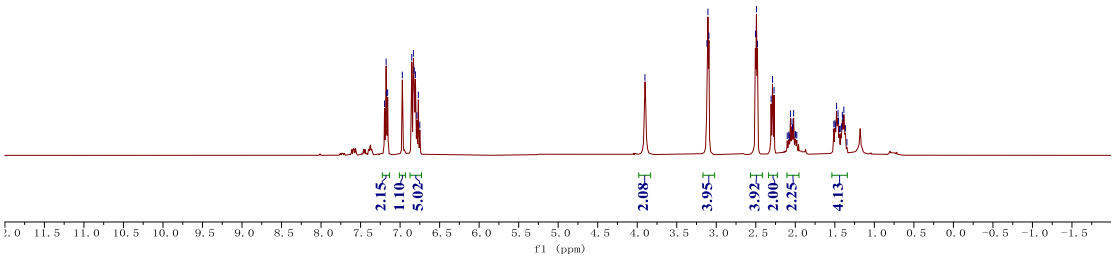
2. Zhai, Y.; Chen, X.; Zhou, W.; Fan, M.; Lai, Y.; Ma, D. Copper-catalyzed diaryl ether formation from (hetero)aryl halides at low catalytic loadings. *J. Org. Chem*. **2017**, *82*, 4964–4969.

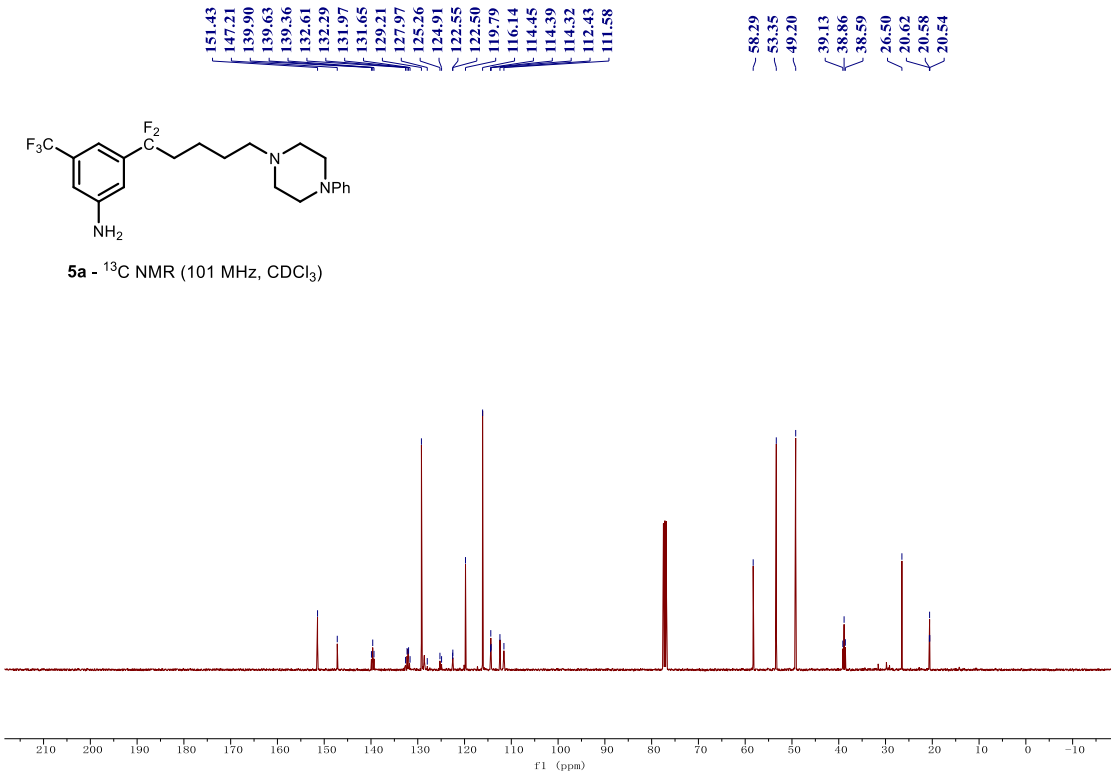
3. Chen, Z.; Jiang, Y.; Zhang, L.; Guo, Y.; Ma, D. Oxalic diamides and *tert*-butoxide: two types of ligands enabling practical access to alkyl aryl ethers via Cu-catalyzed coupling reaction. *J. Am. Chem. Soc*. **2019**, *141*, 3541–3549.

11. NMR Spectra

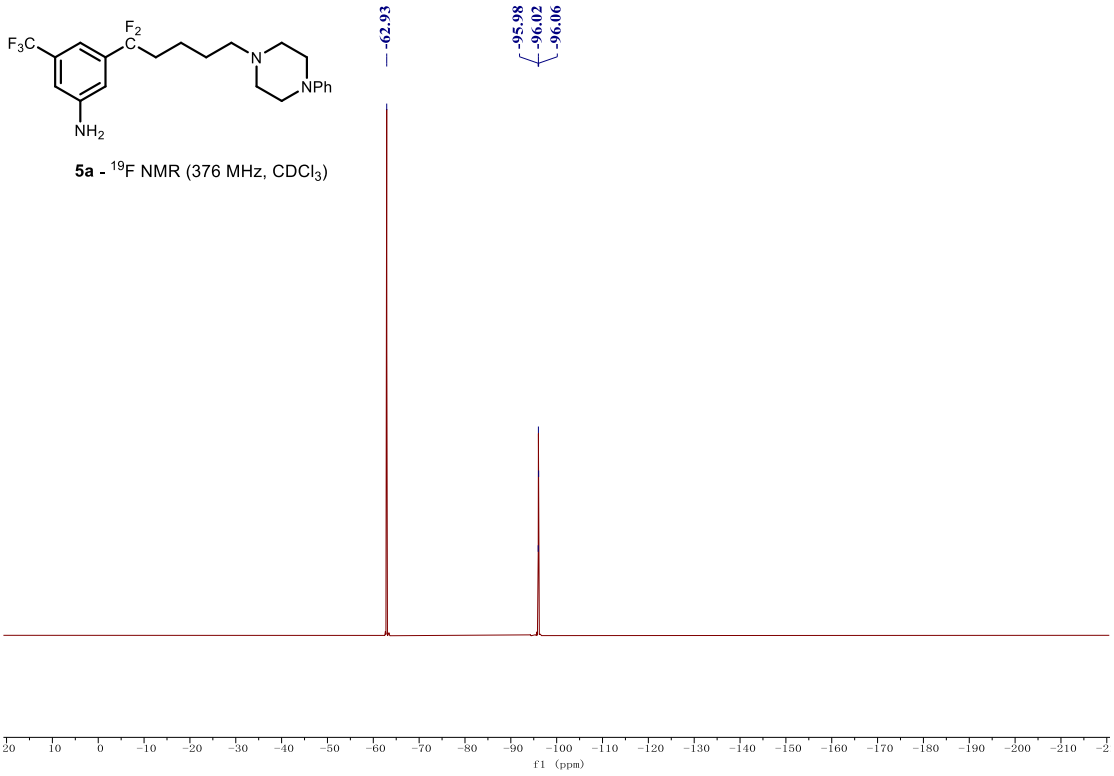


5a - ^{1}H NMR (400 MHz, $CDCl_3$)

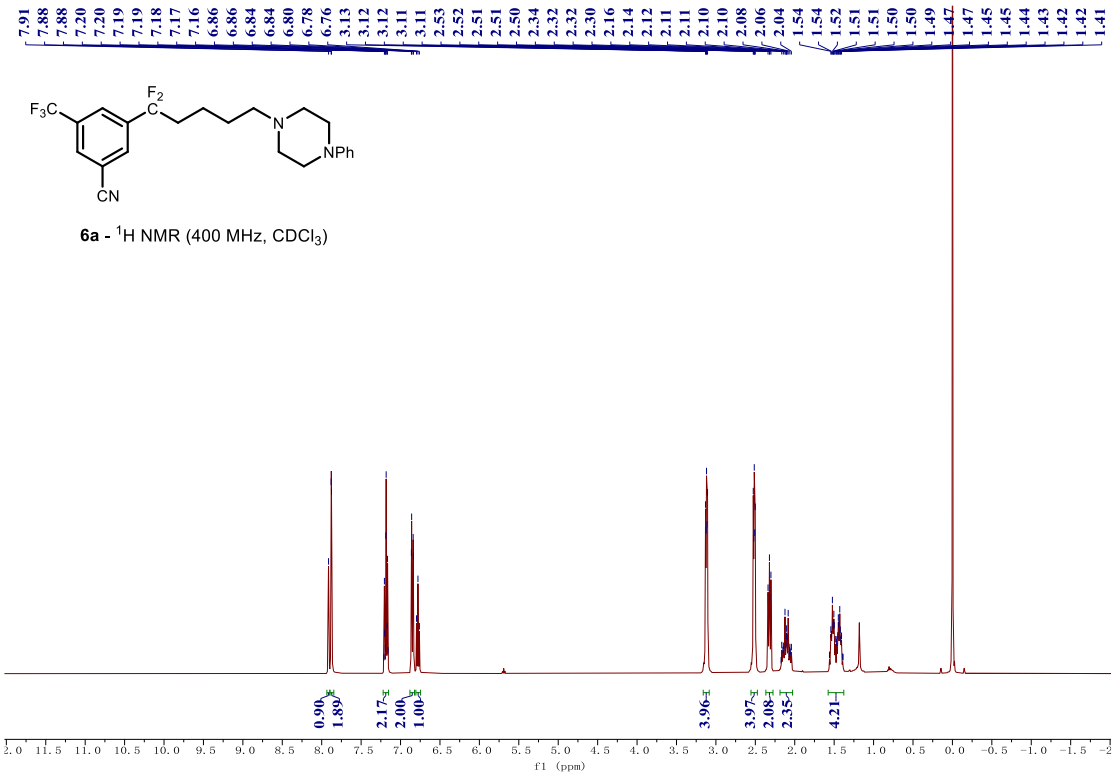




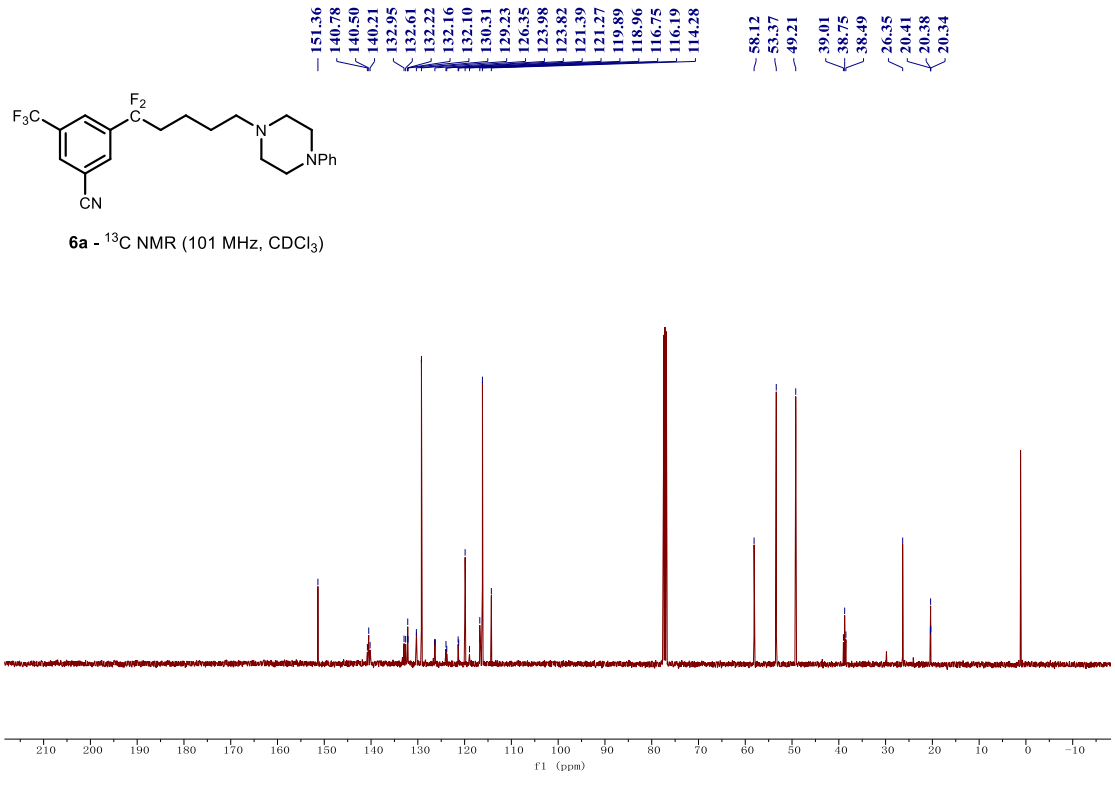
5a - ^{13}C NMR (101 MHz, $CDCl_3$)



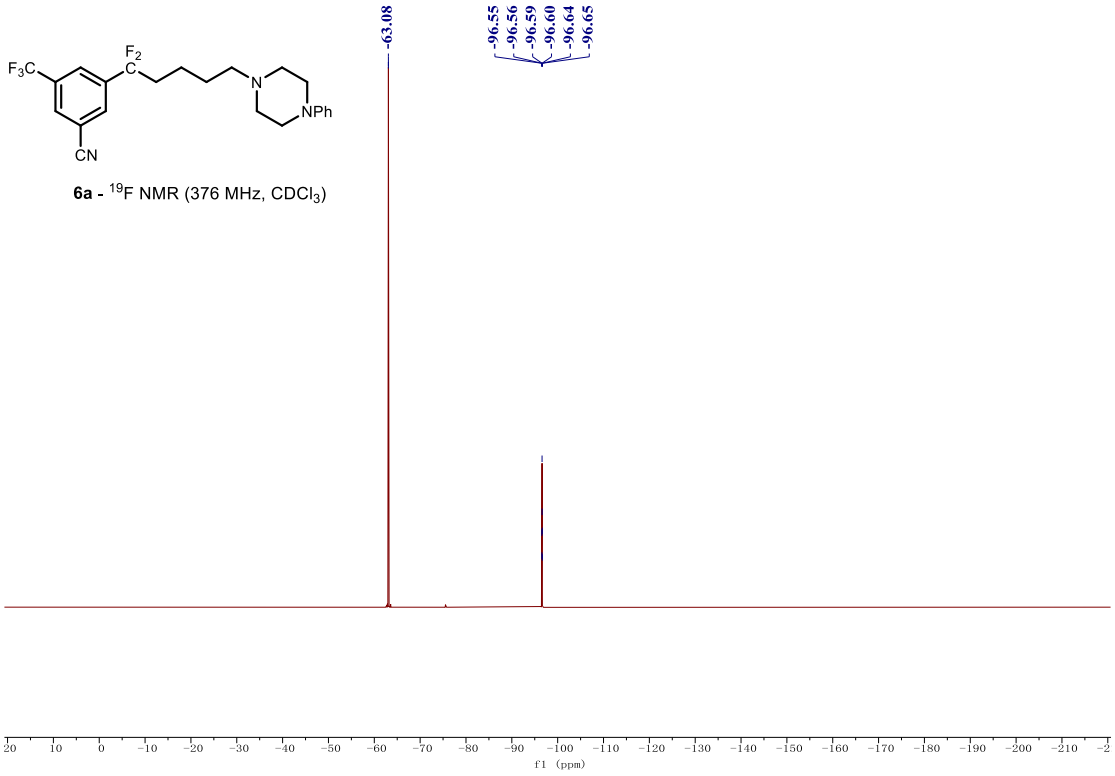
5a - ^{19}F NMR (376 MHz, $CDCl_3$)



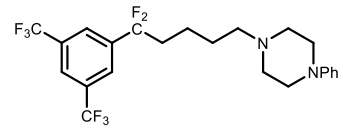
6a - ^{1}H NMR (400 MHz, $CDCl_3$)



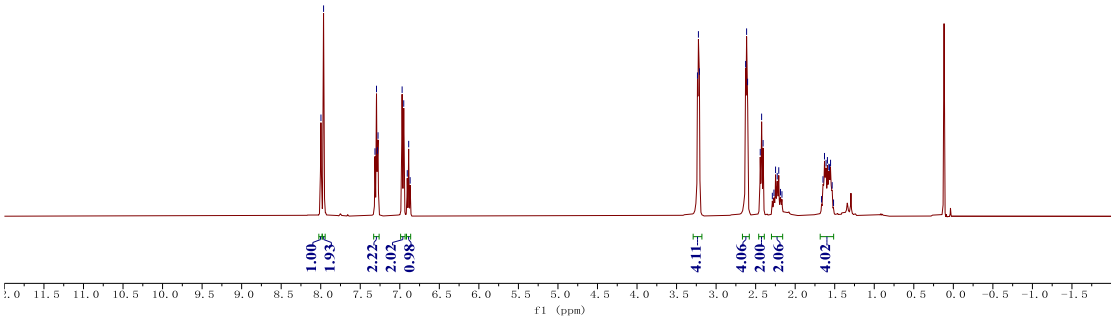
6a - ^{13}C NMR (101 MHz, $CDCl_3$)

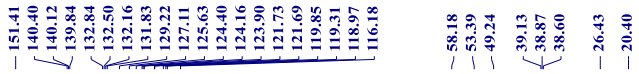


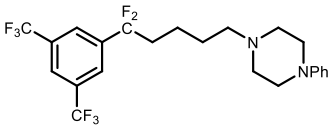
6a - ^{19}F NMR (376 MHz, $CDCl_3$)



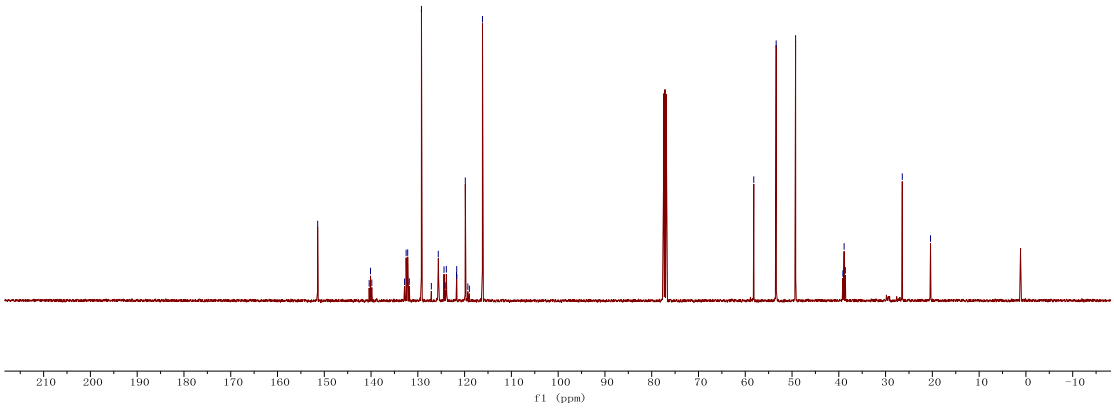
7a - ^{1}H NMR (400 MHz, $CDCl_3$)

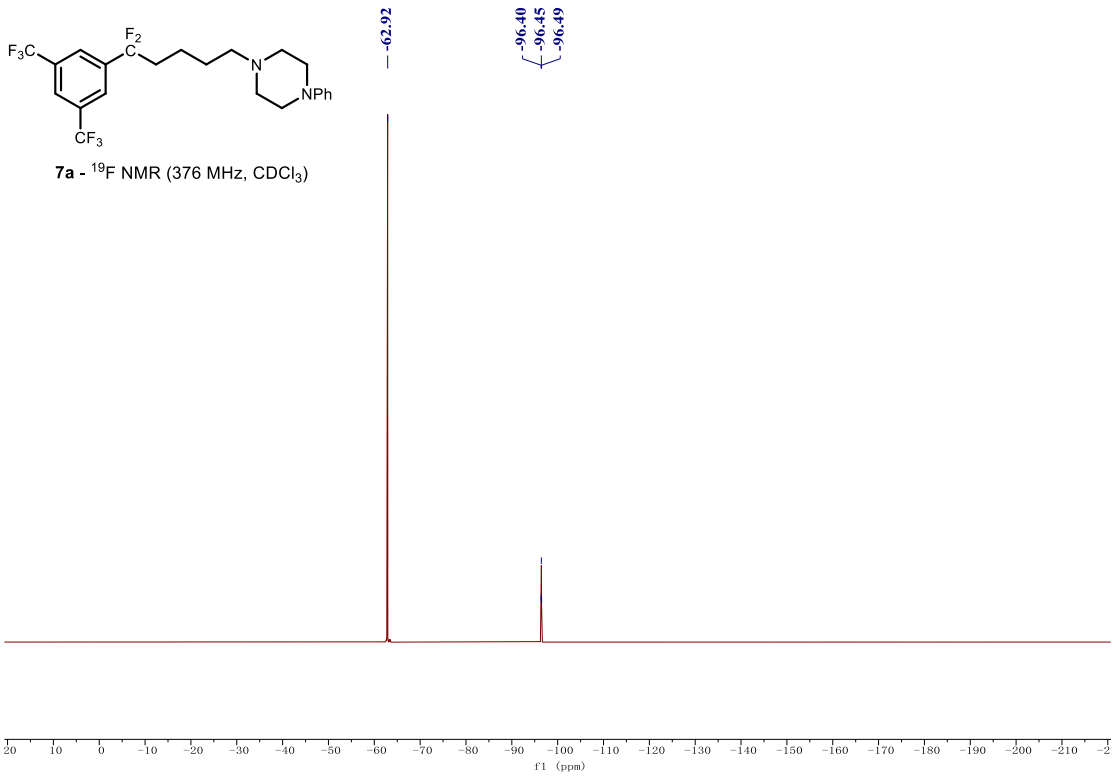




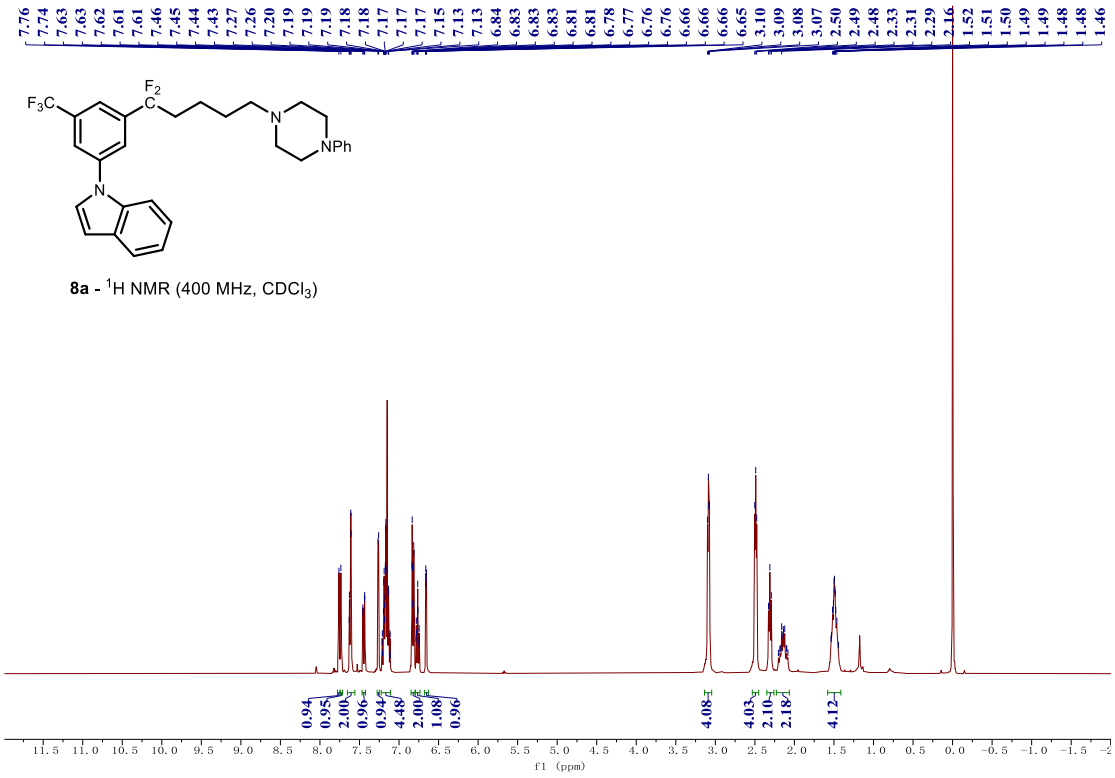


7a - ^{13}C NMR (101 MHz, $CDCl_3$)

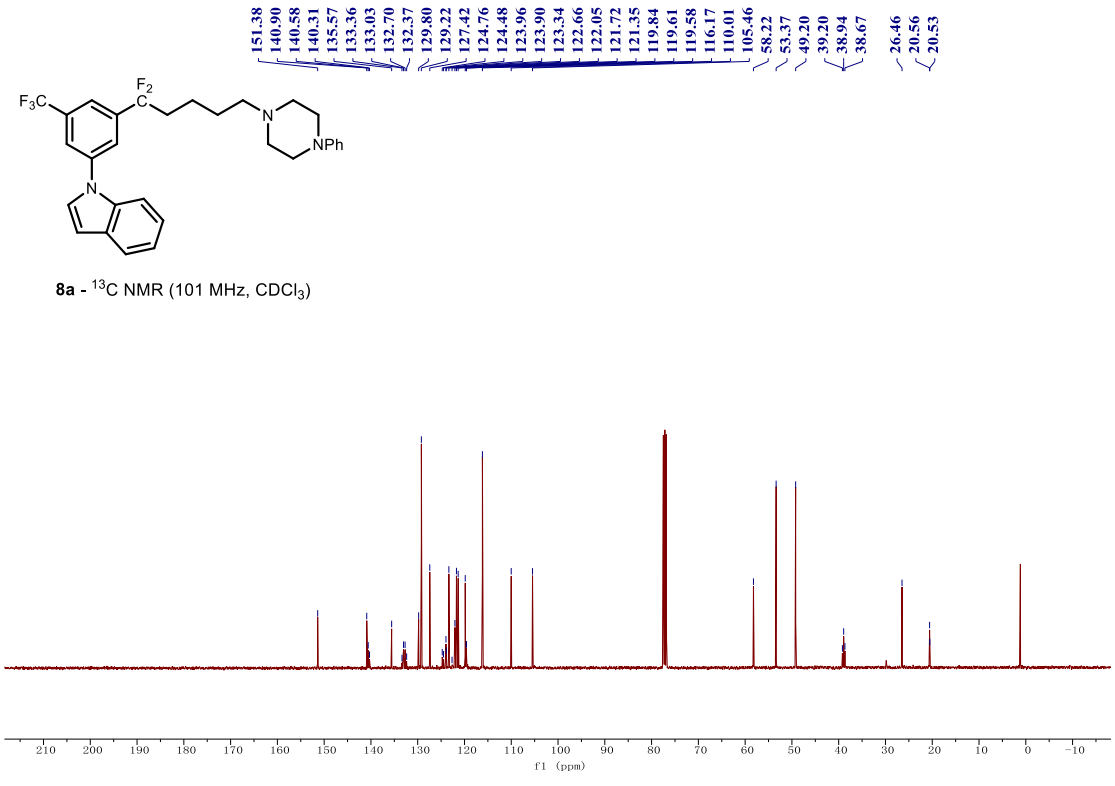




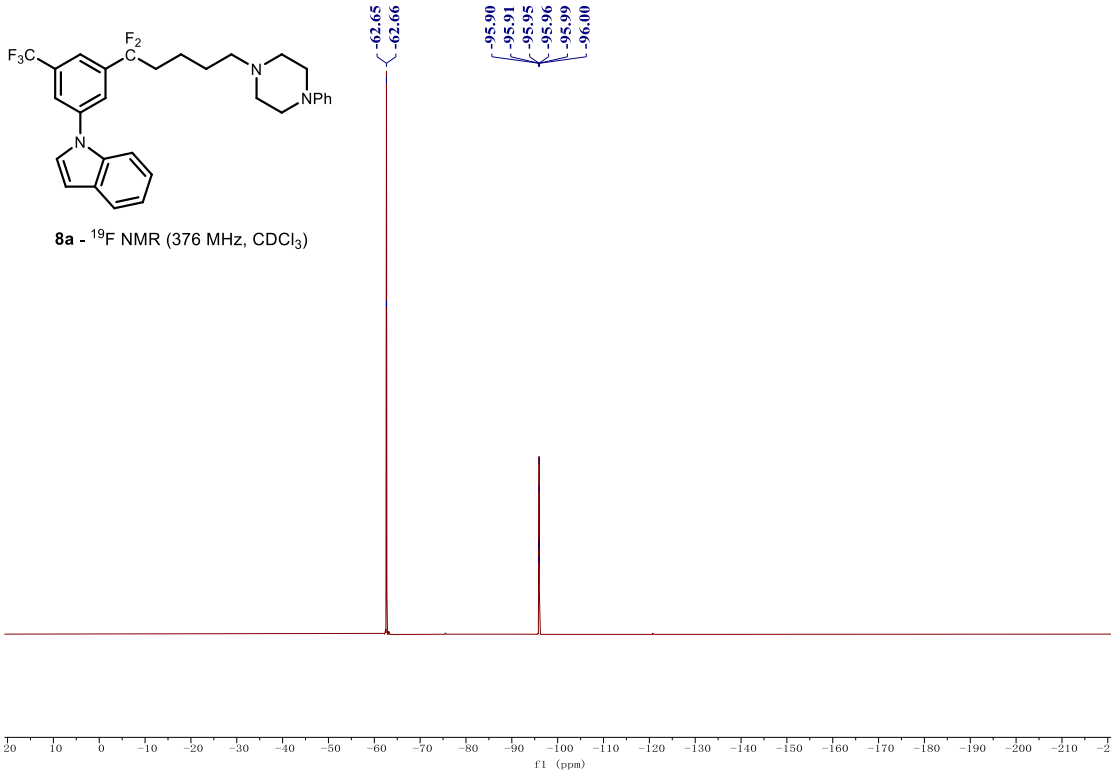
7a - ^{19}F NMR (376 MHz, $CDCl_3$)



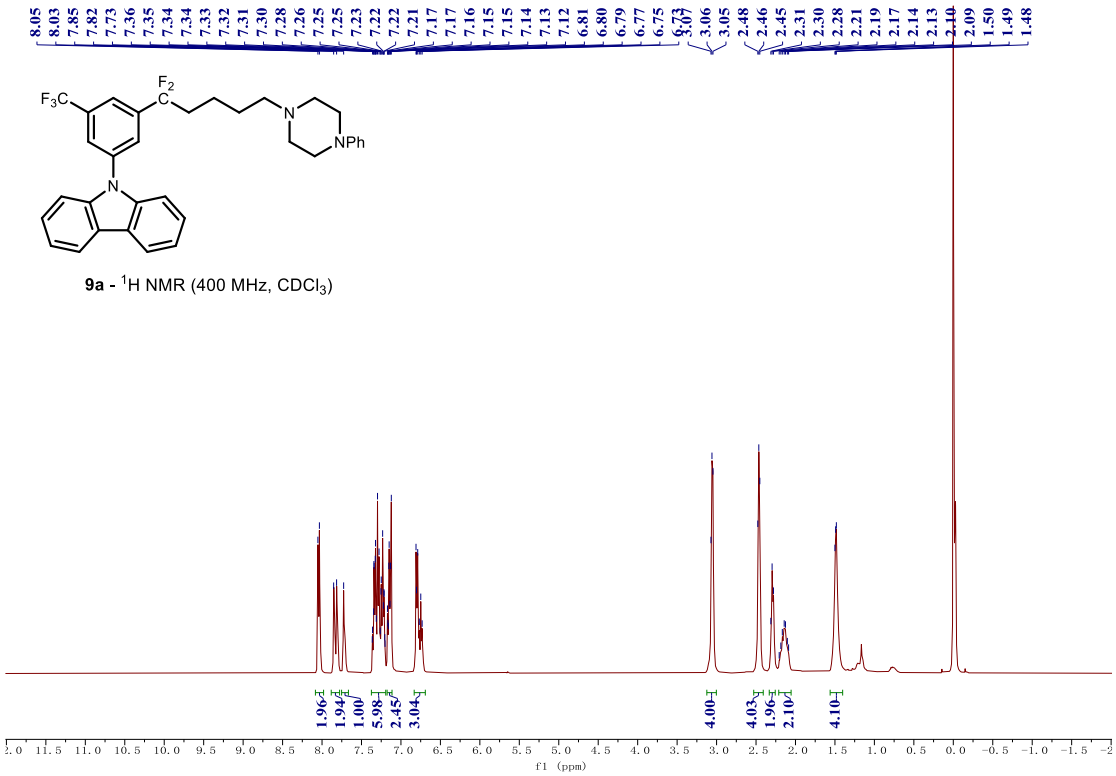
8a - ^{1}H NMR (400 MHz, $CDCl_3$)



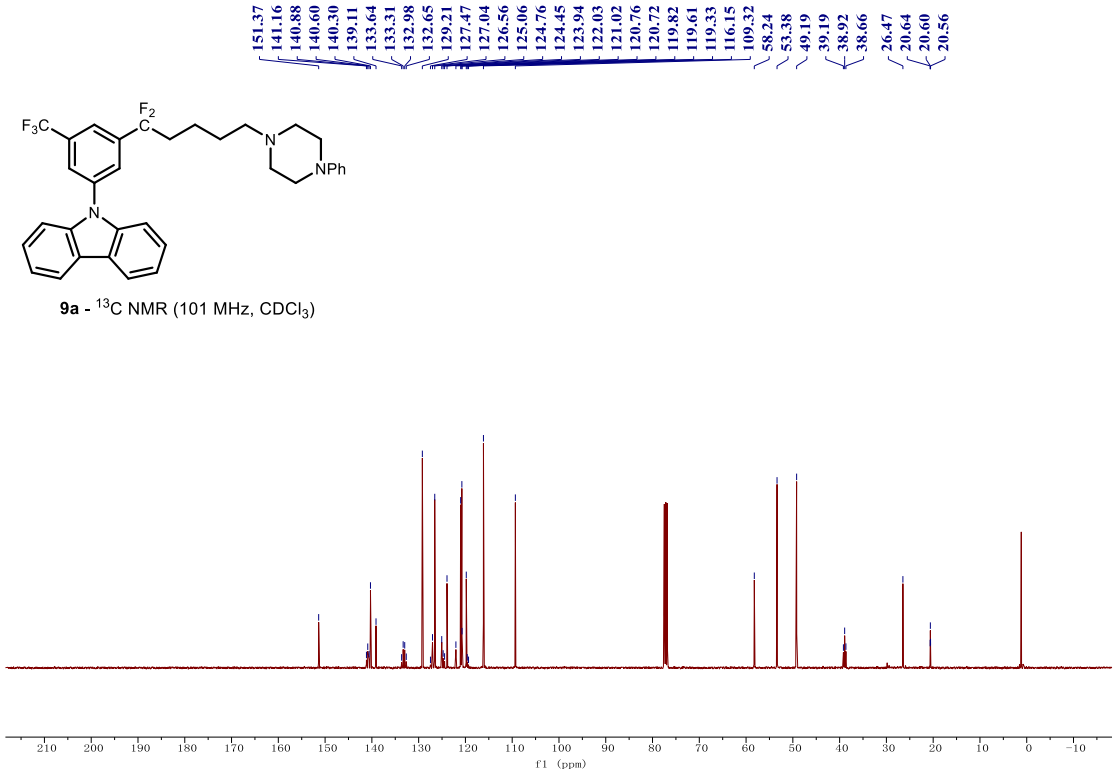
8a - ^{13}C NMR (101 MHz, $CDCl_3$)



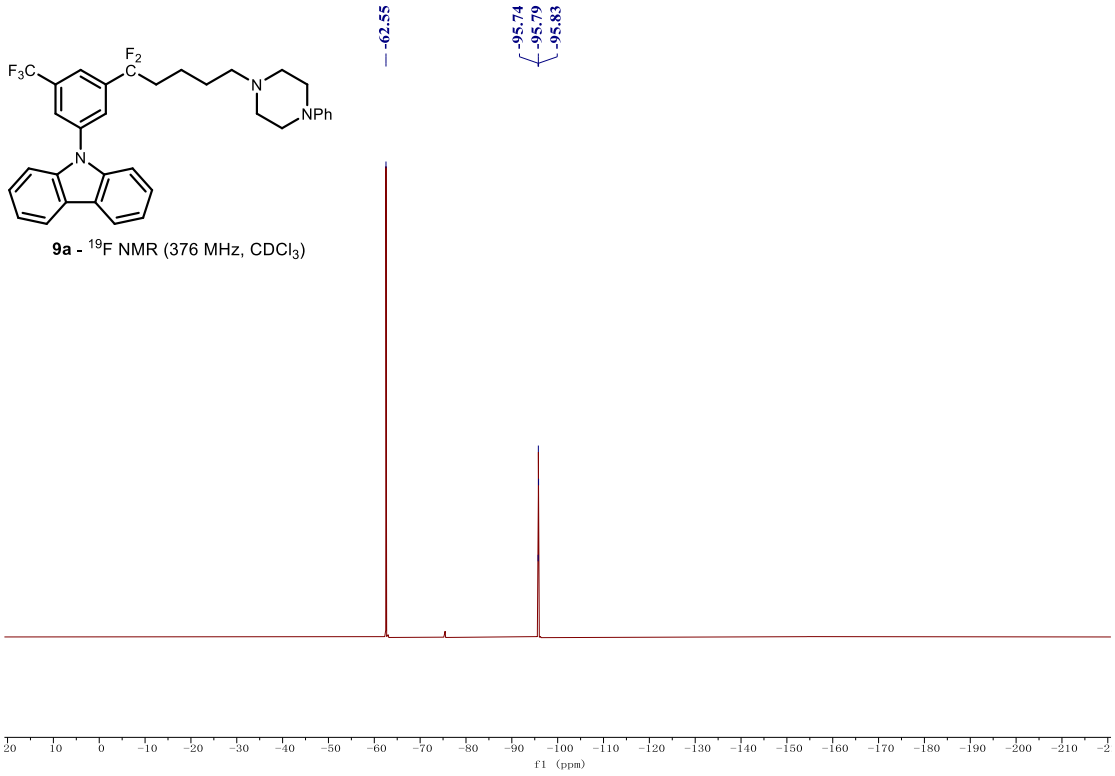
8a - ^{19}F NMR (376 MHz, $CDCl_3$)



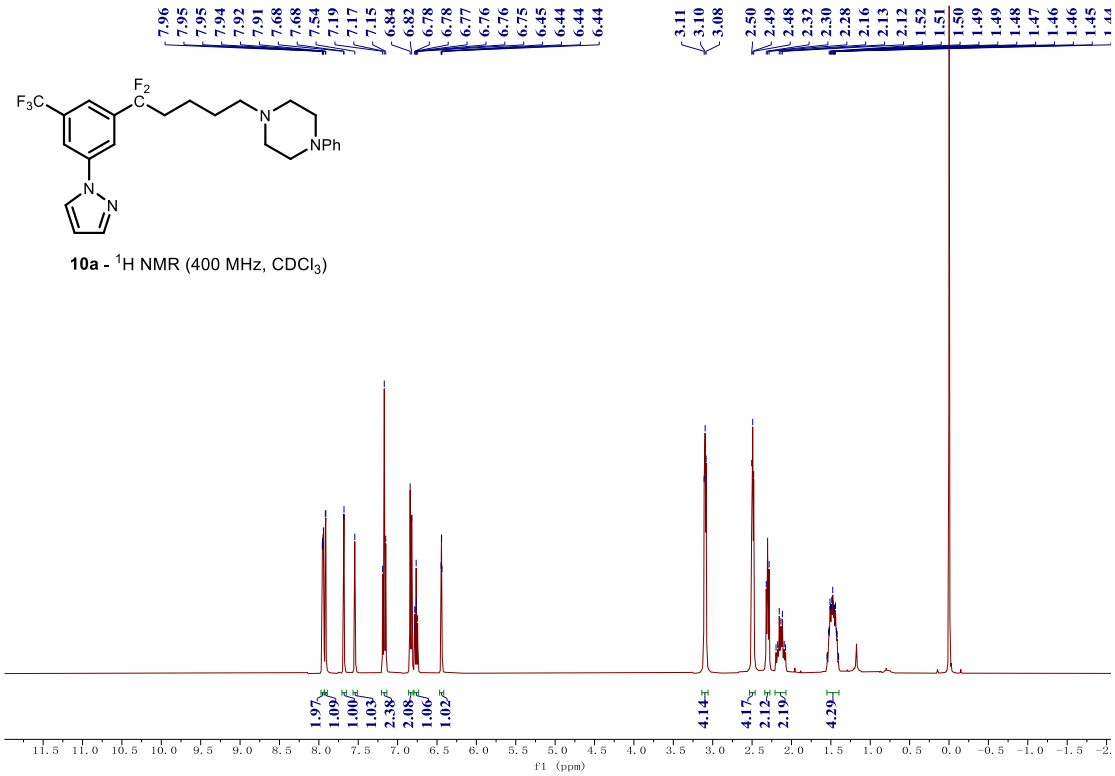
9a - ^{1}H NMR (400 MHz, $CDCl_3$)



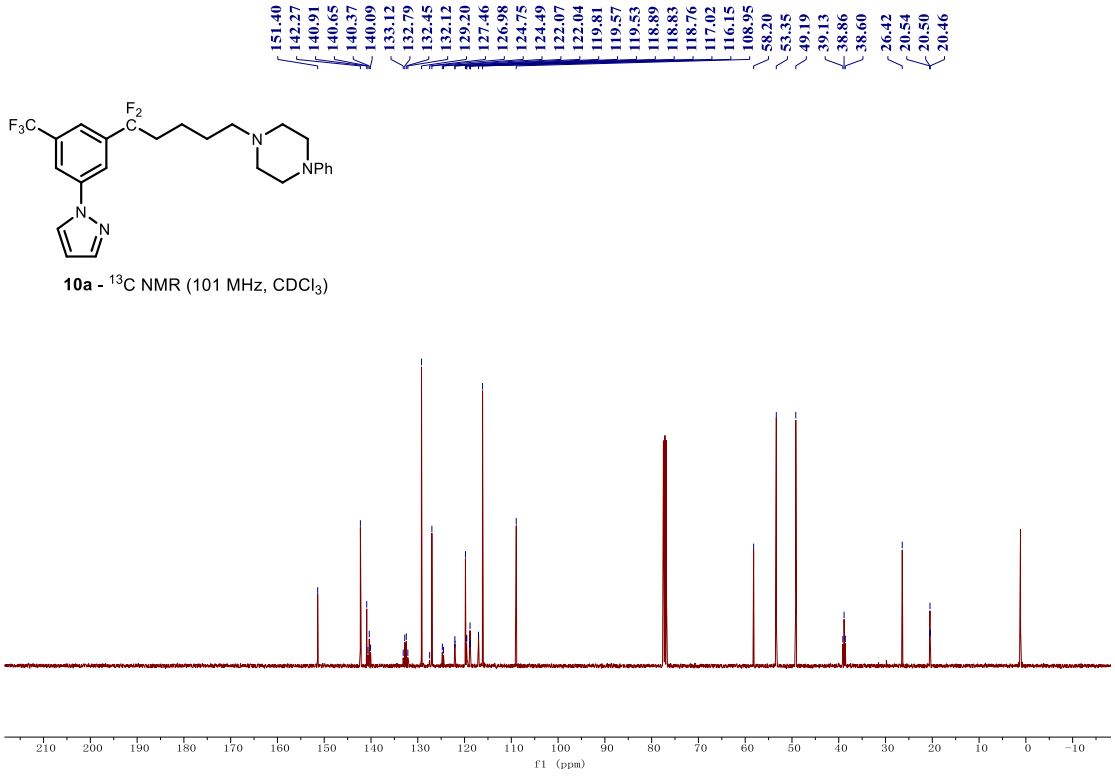
9a - ^{13}C NMR (101 MHz, $CDCl_3$)



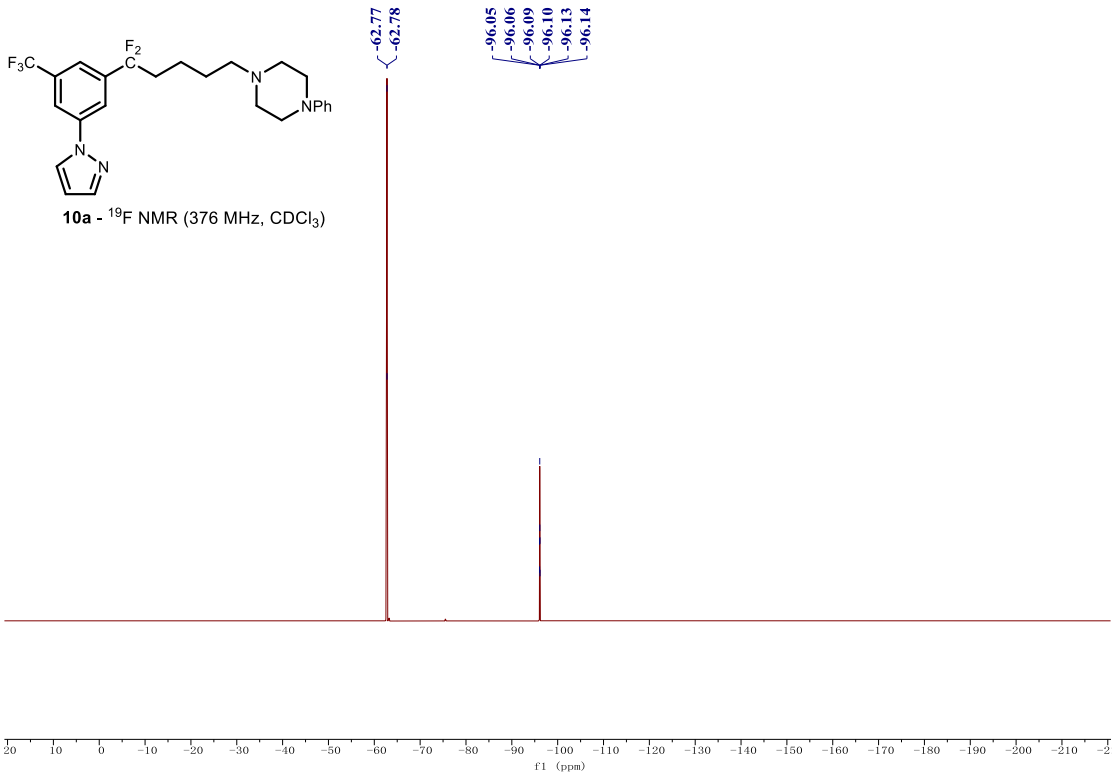
9a - ^{19}F NMR (376 MHz, $CDCl_3$)



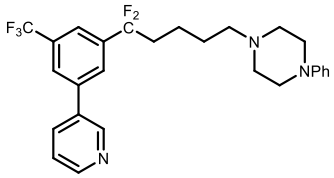
10a - ^{1}H NMR (400 MHz, $CDCl_3$)



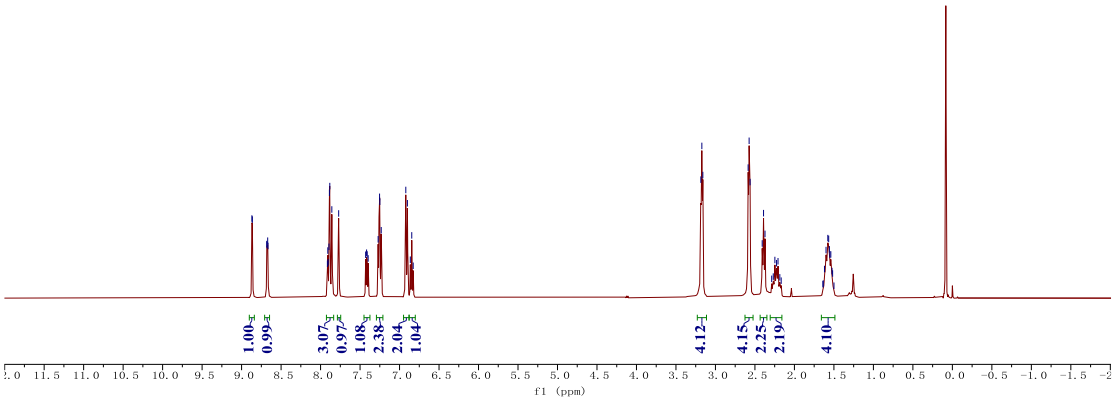
10a - ^{13}C NMR (101 MHz, $CDCl_3$)

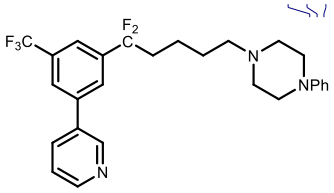


10a - ^{19}F NMR (376 MHz, $CDCl_3$)

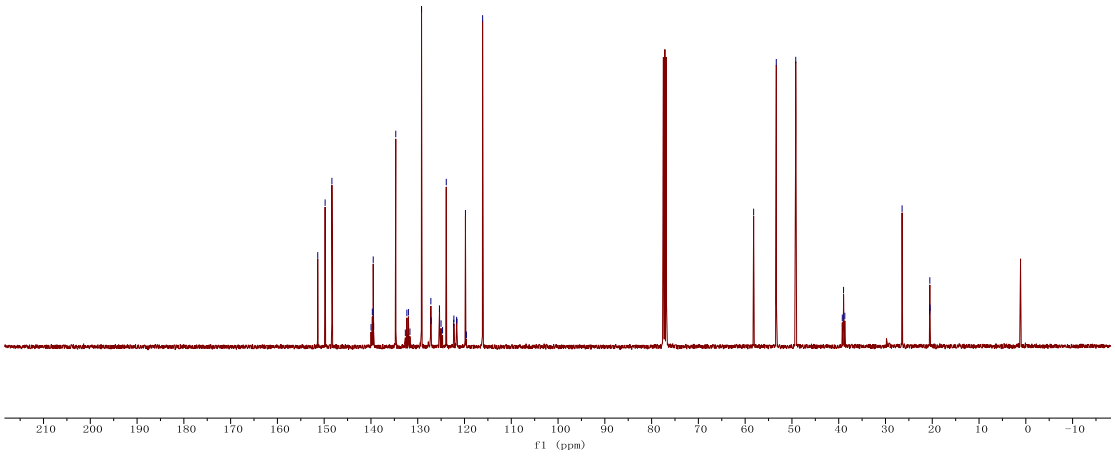


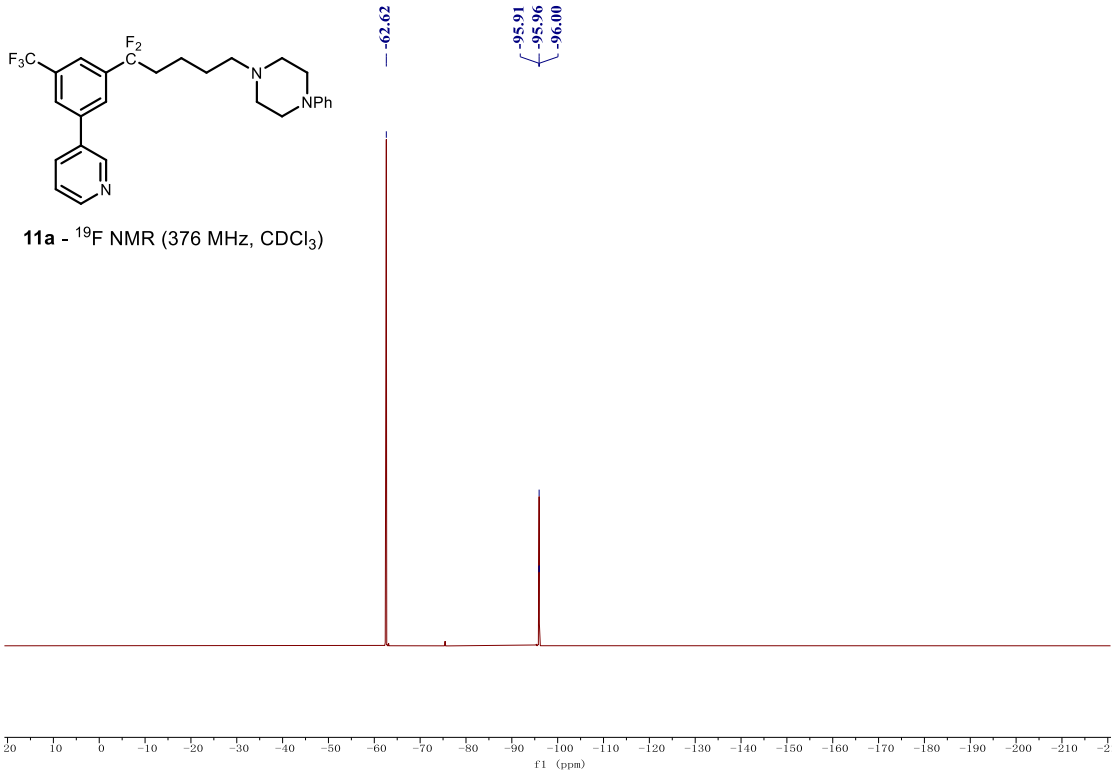
11a - ^{1}H NMR (400 MHz, $CDCl_3$)



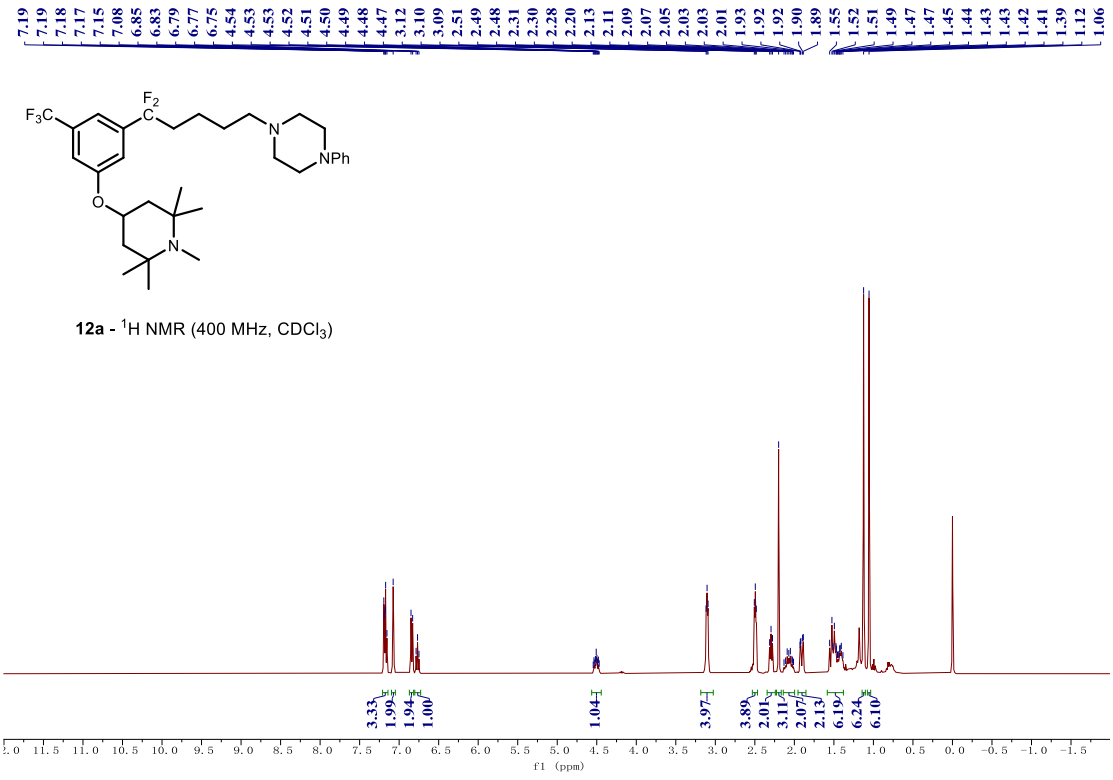


11a - ^{13}C NMR (101 MHz, $CDCl_3$)



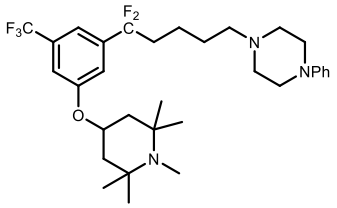


11a - ^{19}F NMR (376 MHz, $CDCl_3$)

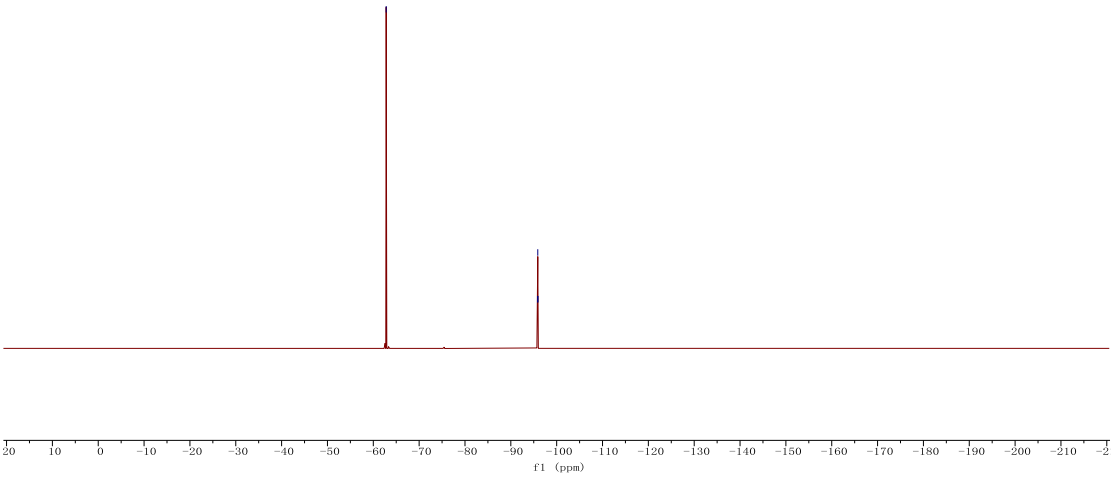


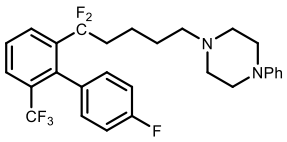
12a - ^{1}H NMR (400 MHz, $CDCl_3$)

12a - ^{13}C NMR (101 MHz, $CDCl_3$)

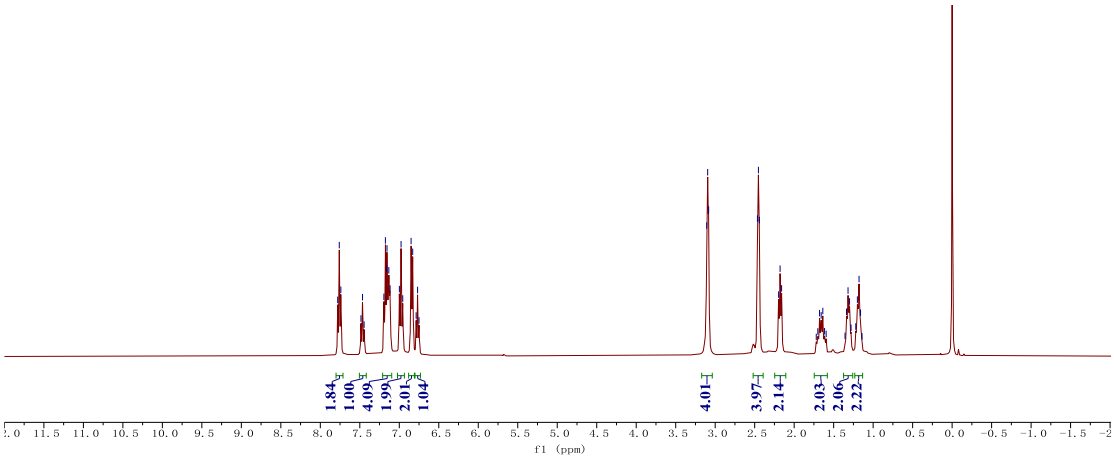


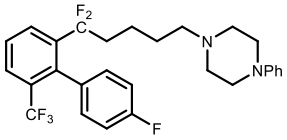
12a - ^{19}F NMR (376 MHz, $CDCl_3$)



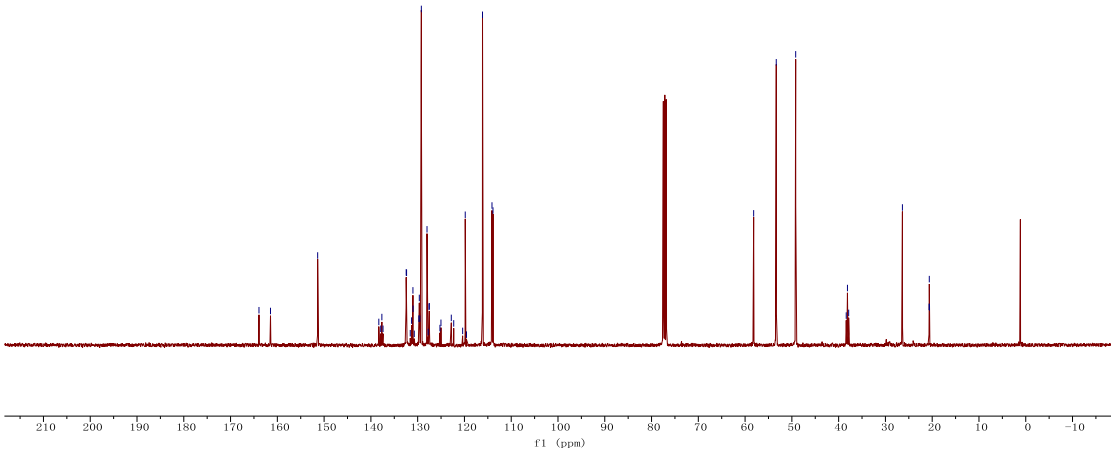


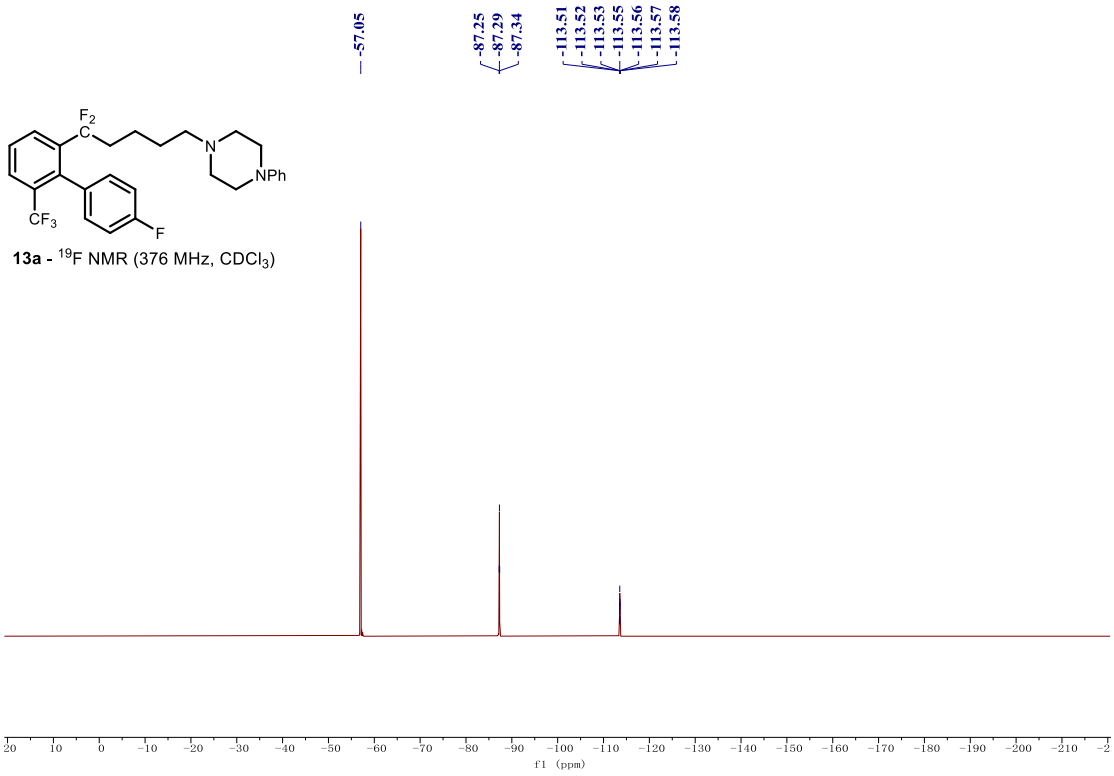
13a - ^{1}H NMR (400 MHz, $CDCl_3$)



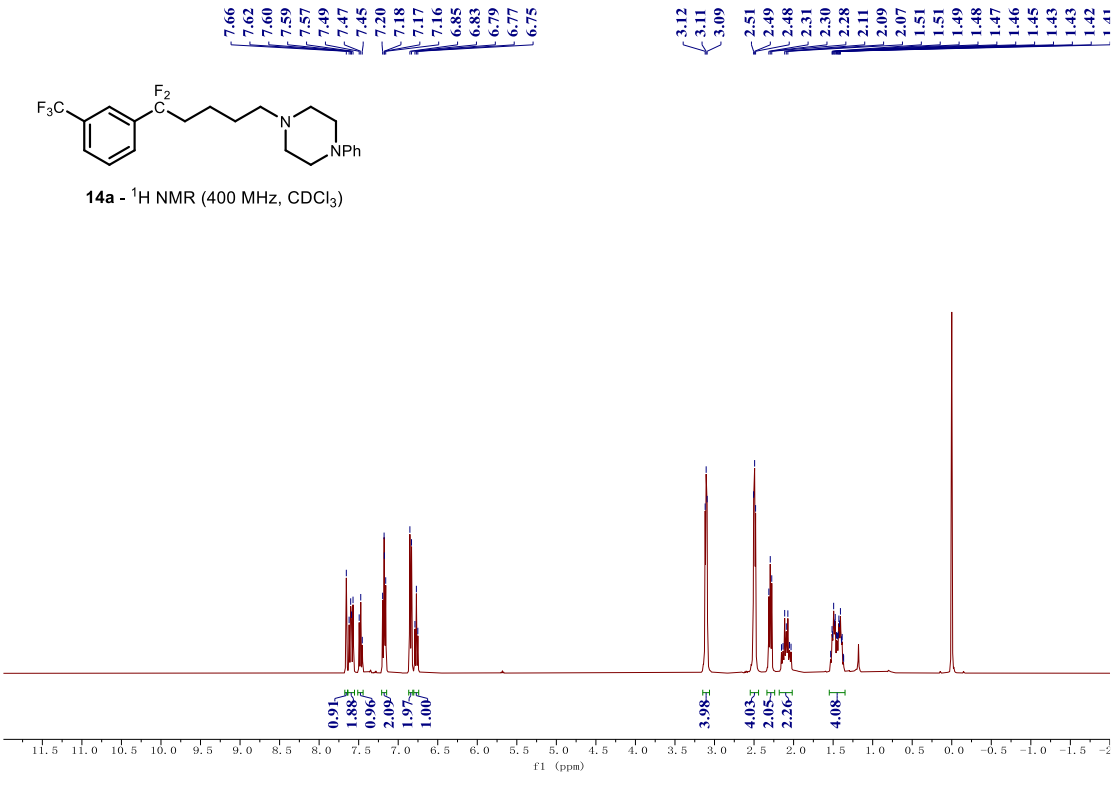


13a - ^{13}C NMR (101 MHz, $CDCl_3$)

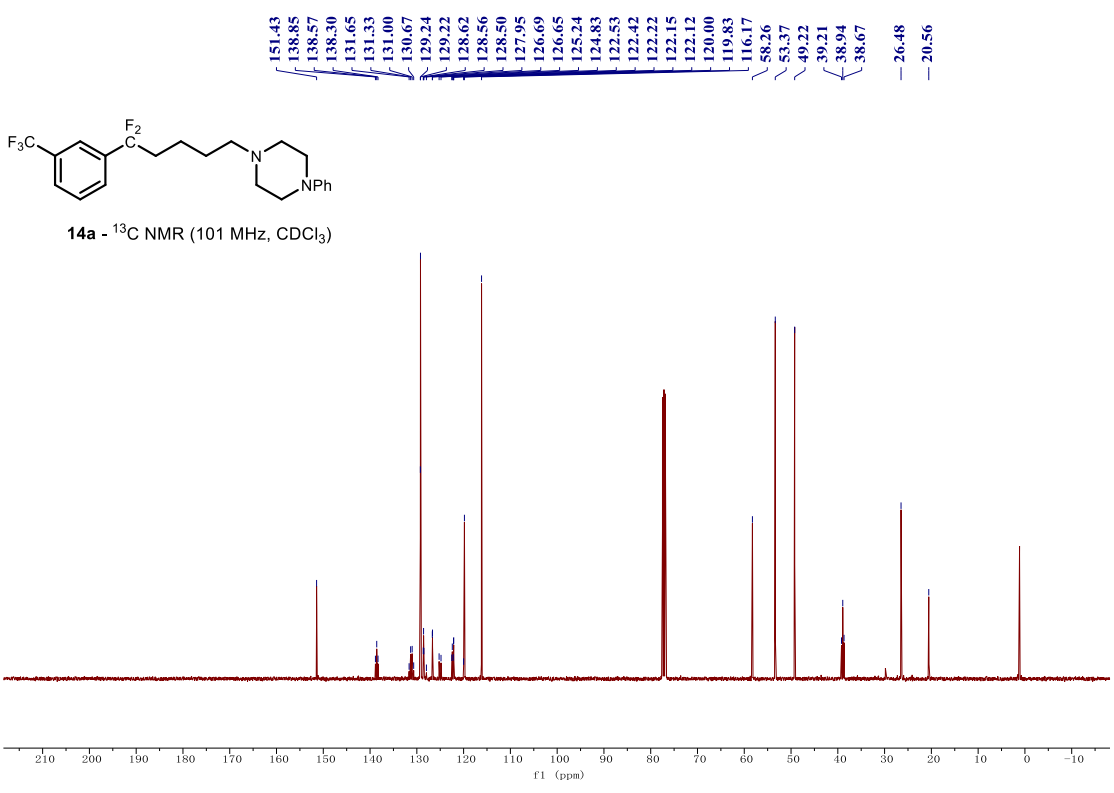




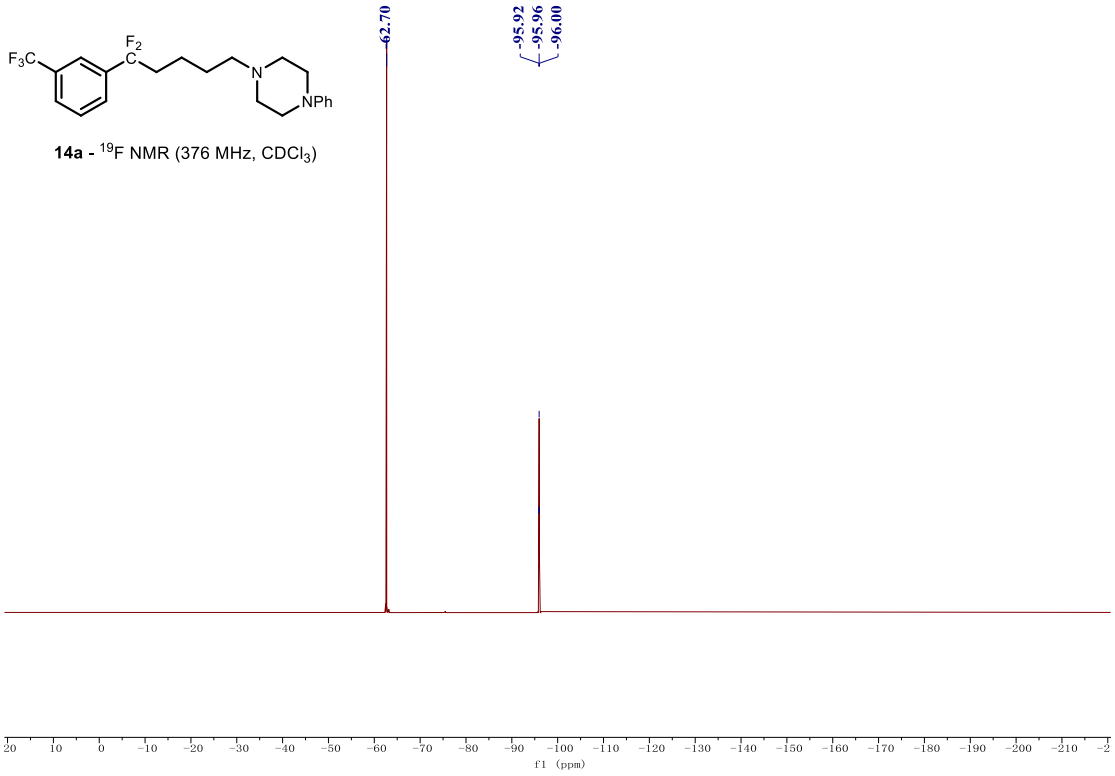
13a - ^{19}F NMR (376 MHz, $CDCl_3$)



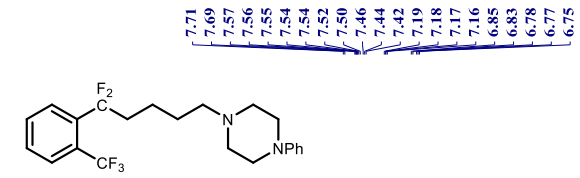
14a - ^{1}H NMR (400 MHz, $CDCl_3$)



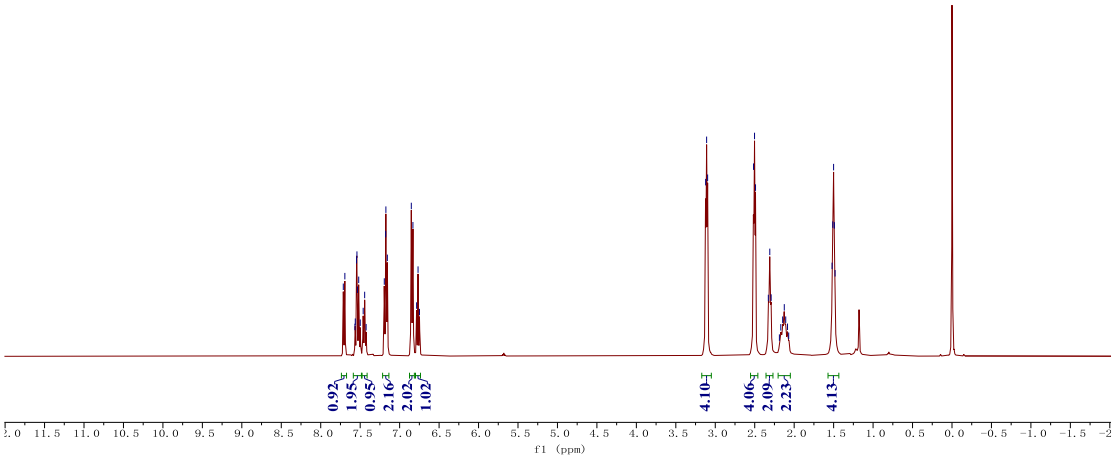
14a - ^{13}C NMR (101 MHz, $CDCl_3$)

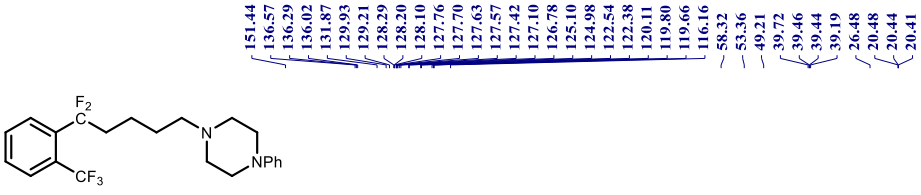


14a - ^{19}F NMR (376 MHz, $CDCl_3$)

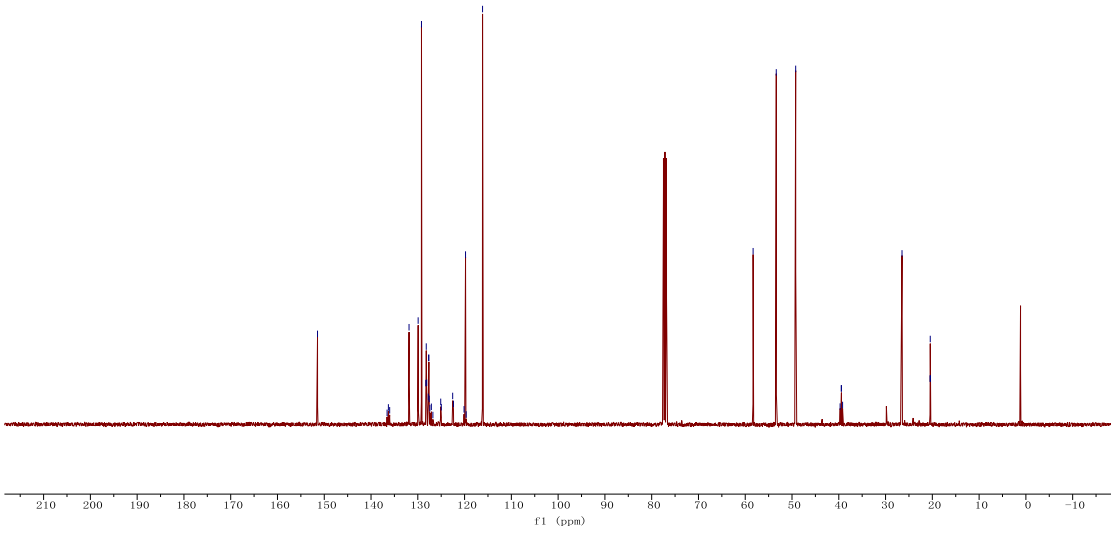


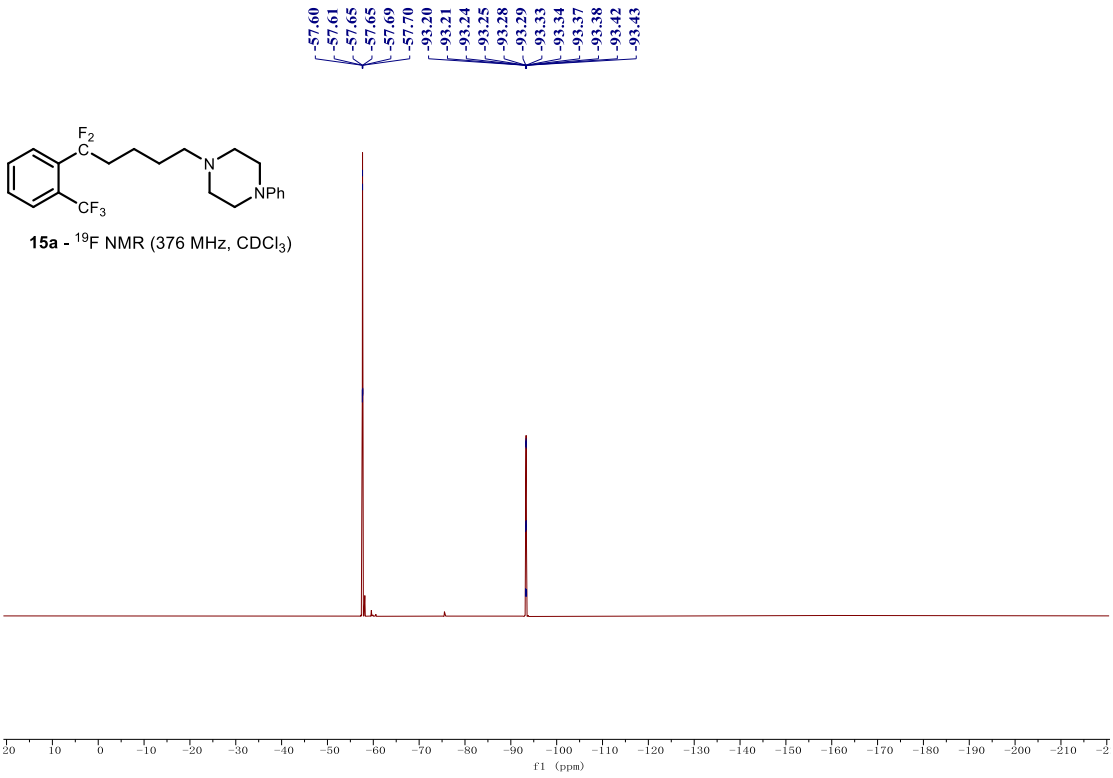
15a - ^{1}H NMR (400 MHz, $CDCl_3$)



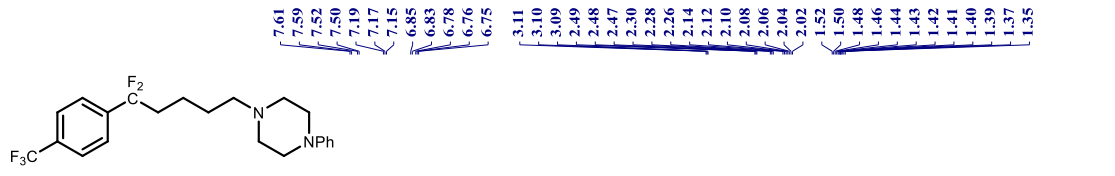


15a - ^{13}C NMR (101 MHz, $CDCl_3$)

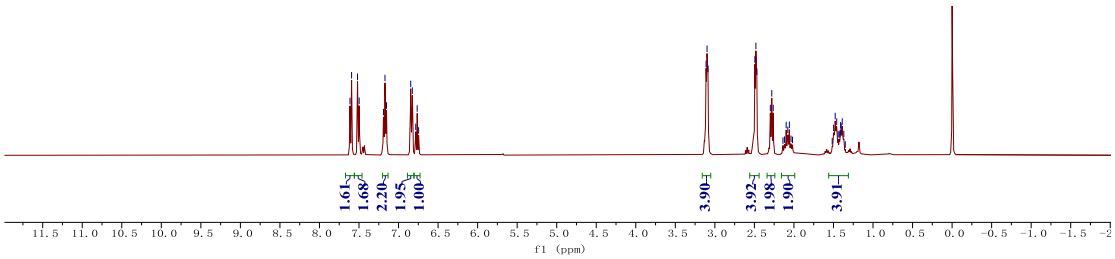


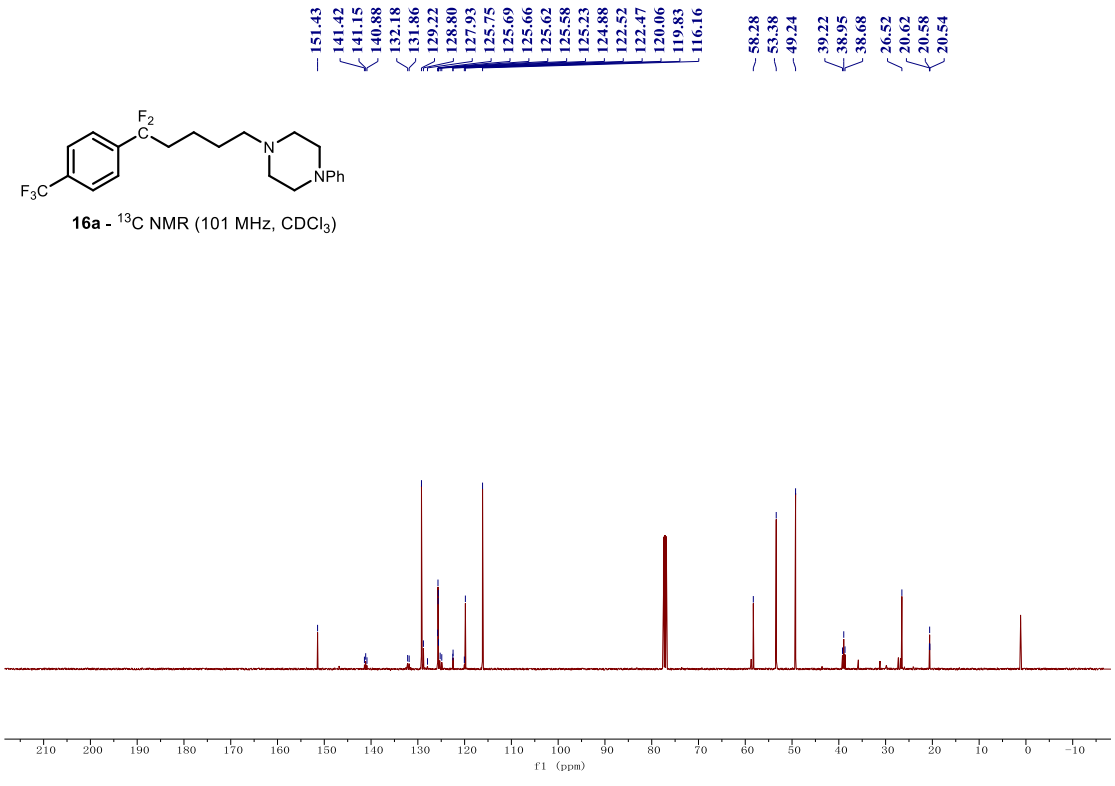


15a - ^{19}F NMR (376 MHz, $CDCl_3$)

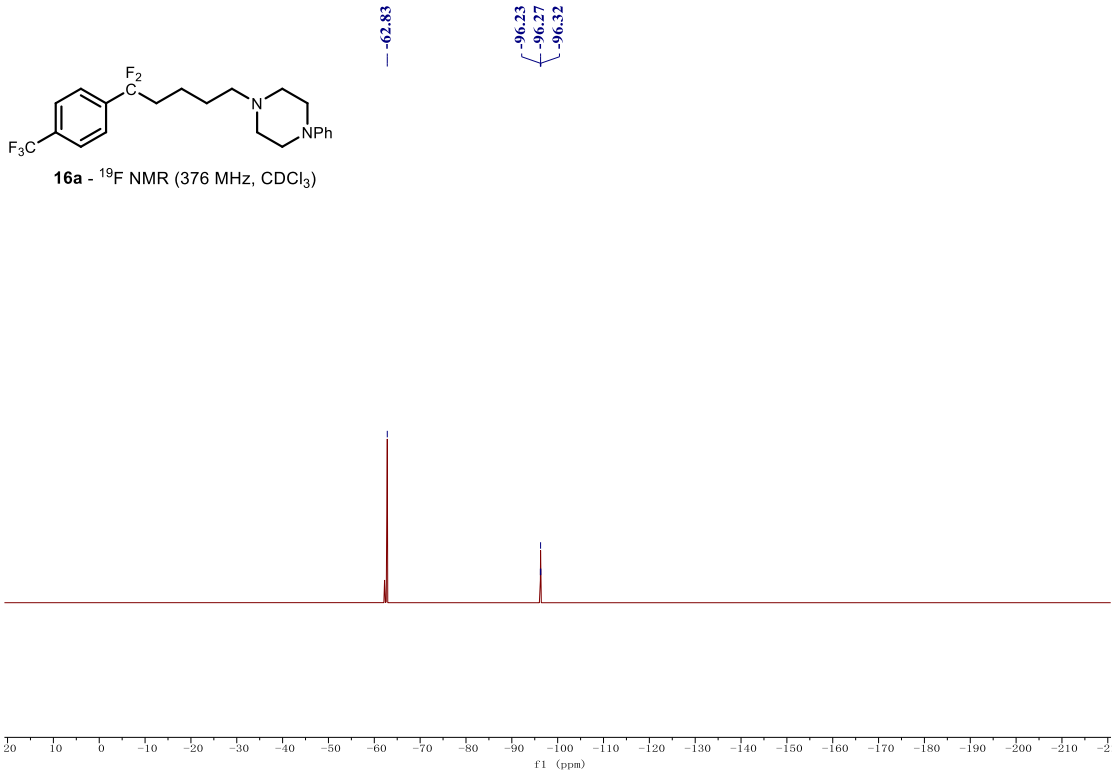


16a - ^{1}H NMR (400 MHz, $CDCl_3$)

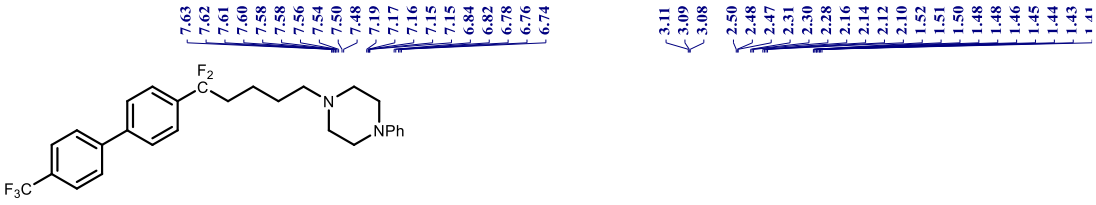




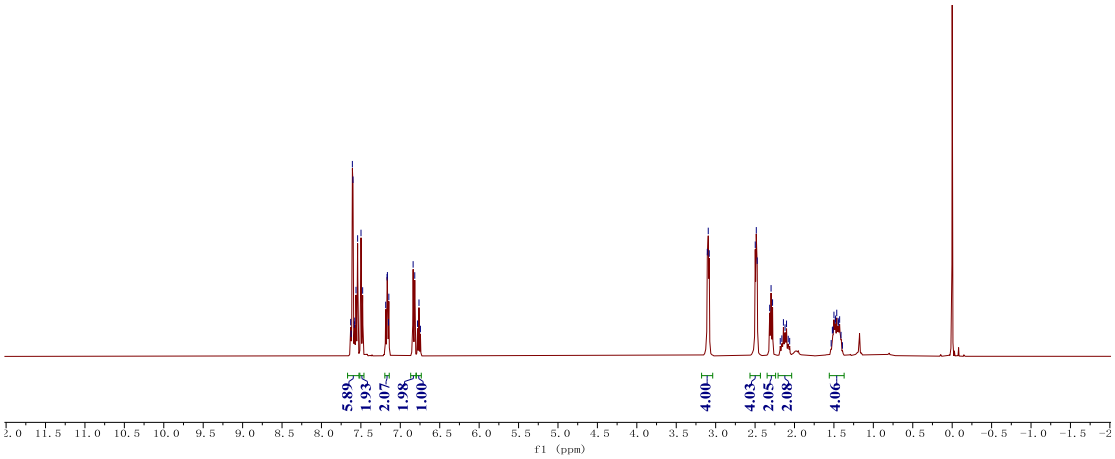
16a - ^{13}C NMR (101 MHz, $CDCl_3$)

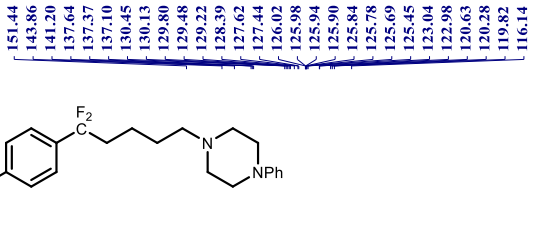


16a - ^{19}F NMR (376 MHz, $CDCl_3$)

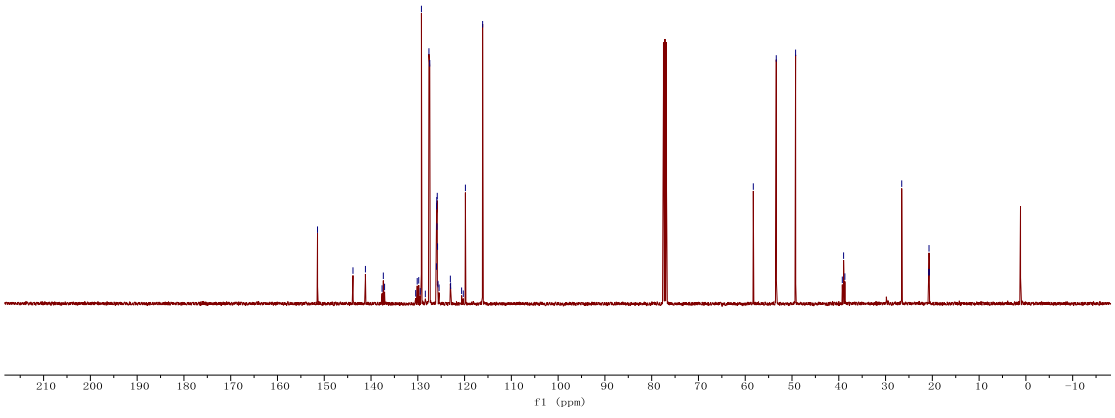


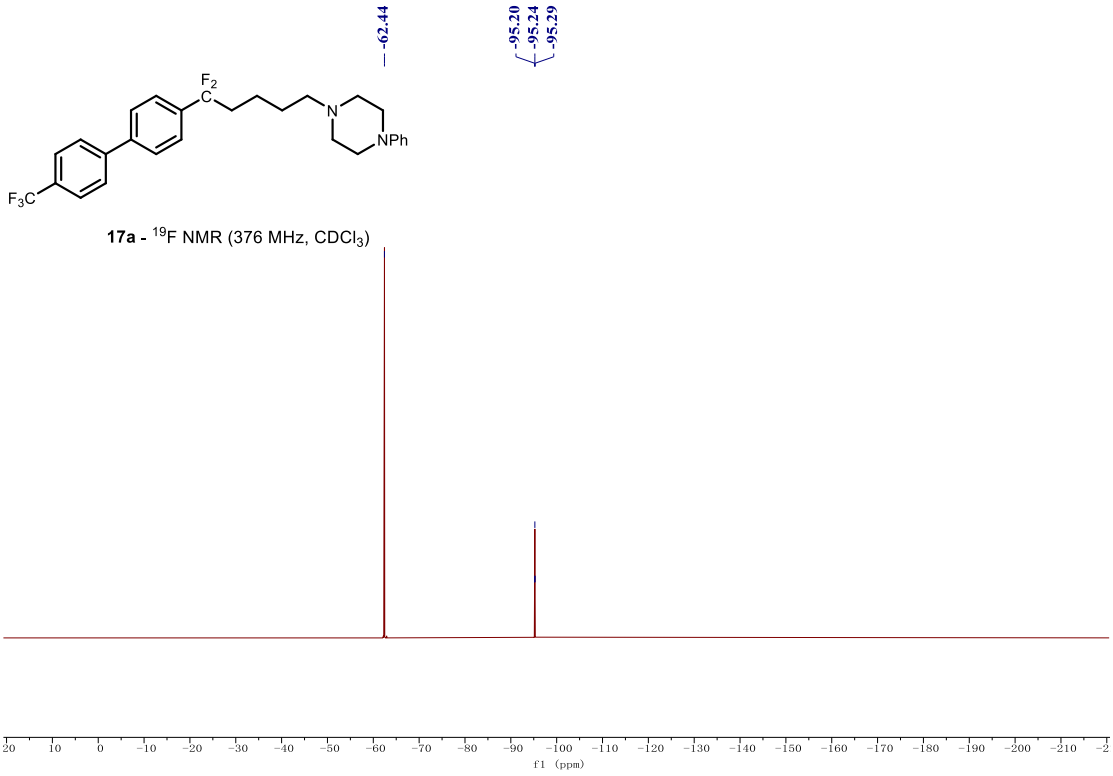
17a - ^{1}H NMR (400 MHz, $CDCl_3$)



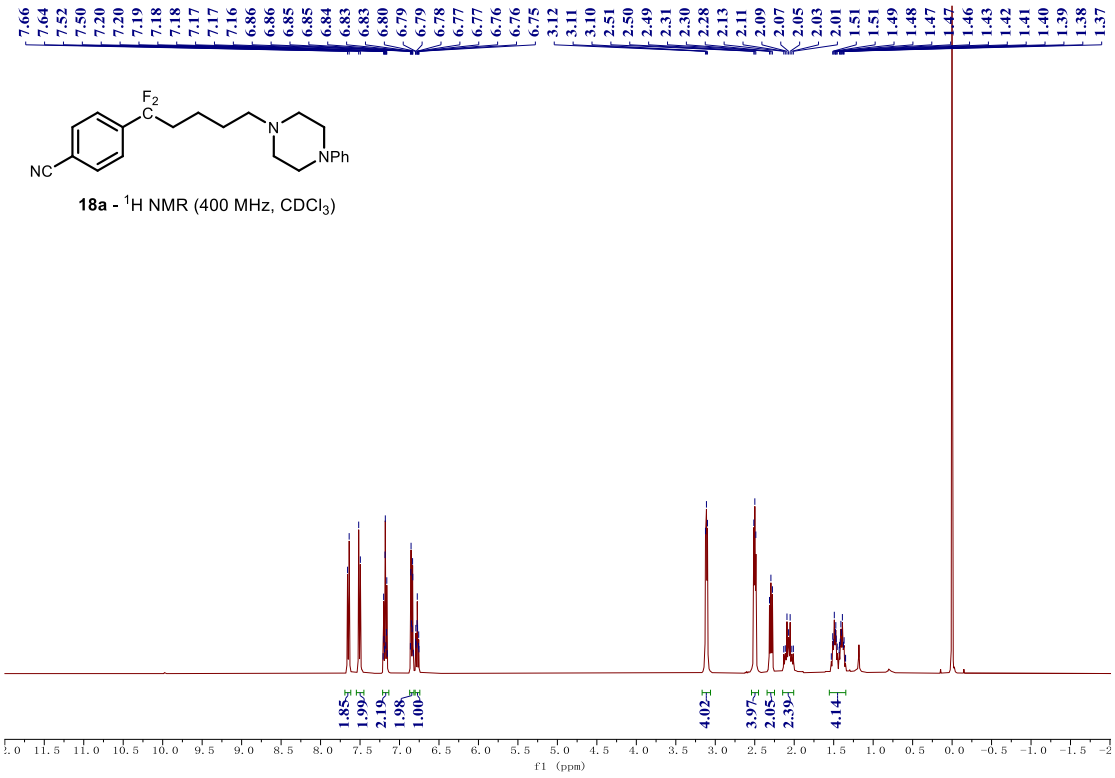


17a - ^{13}C NMR (101 MHz, $CDCl_3$)

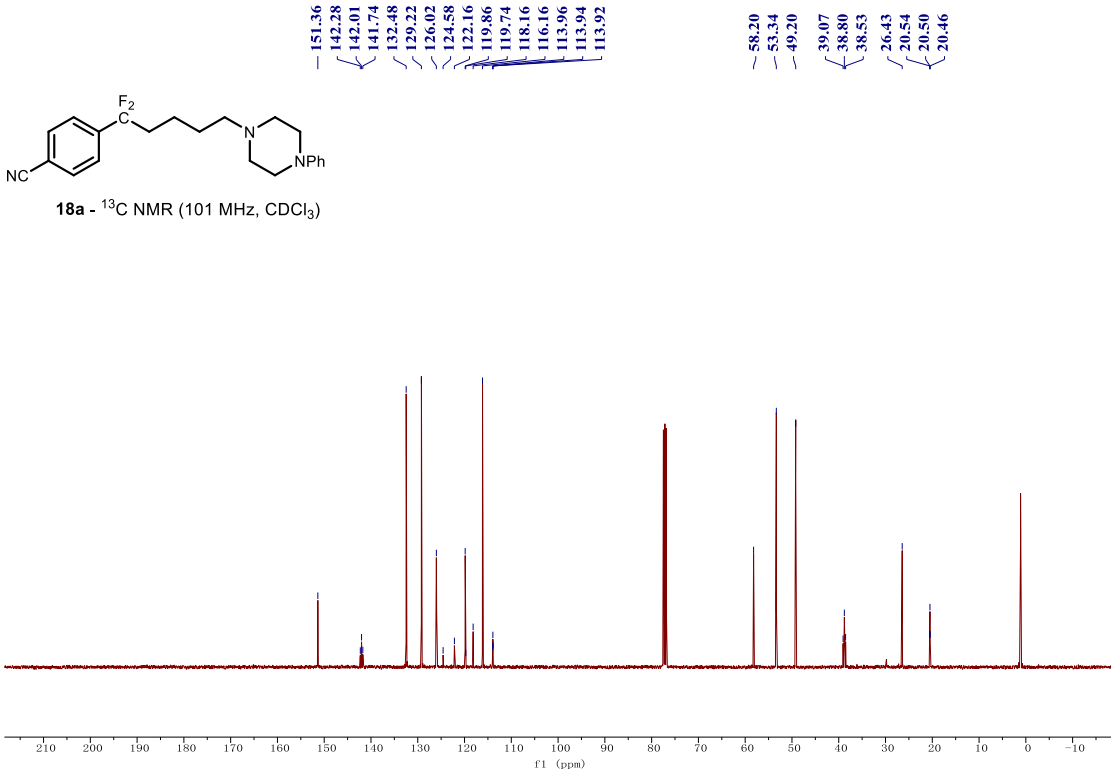




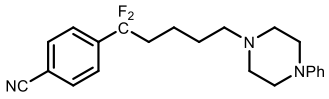
17a - ^{19}F NMR (376 MHz, $CDCl_3$)



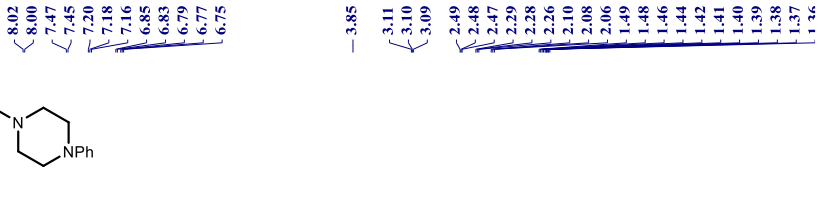
18a - ^{1}H NMR (400 MHz, $CDCl_3$)

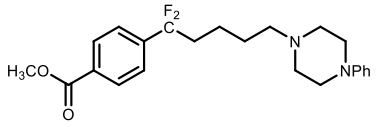


18a - ^{13}C NMR (101 MHz, $CDCl_3$)

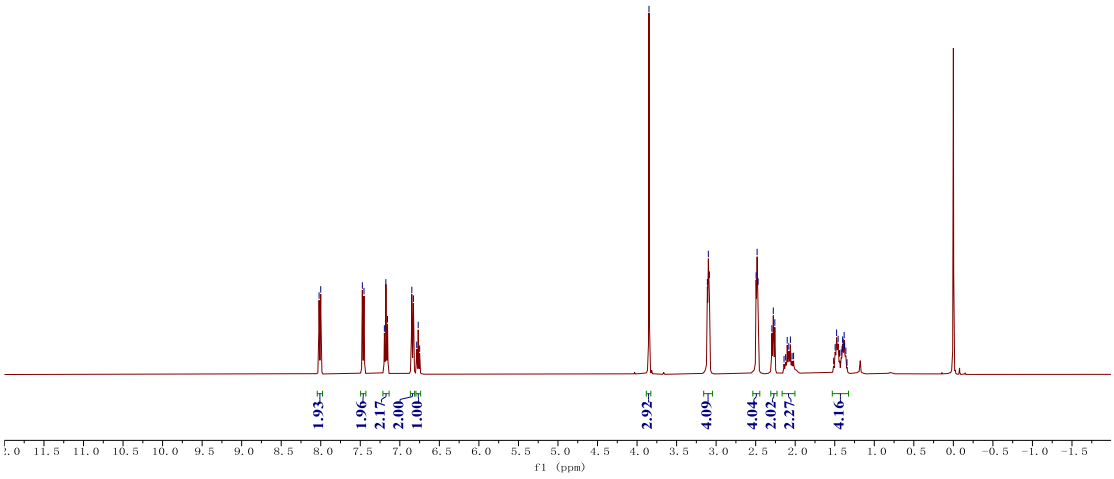


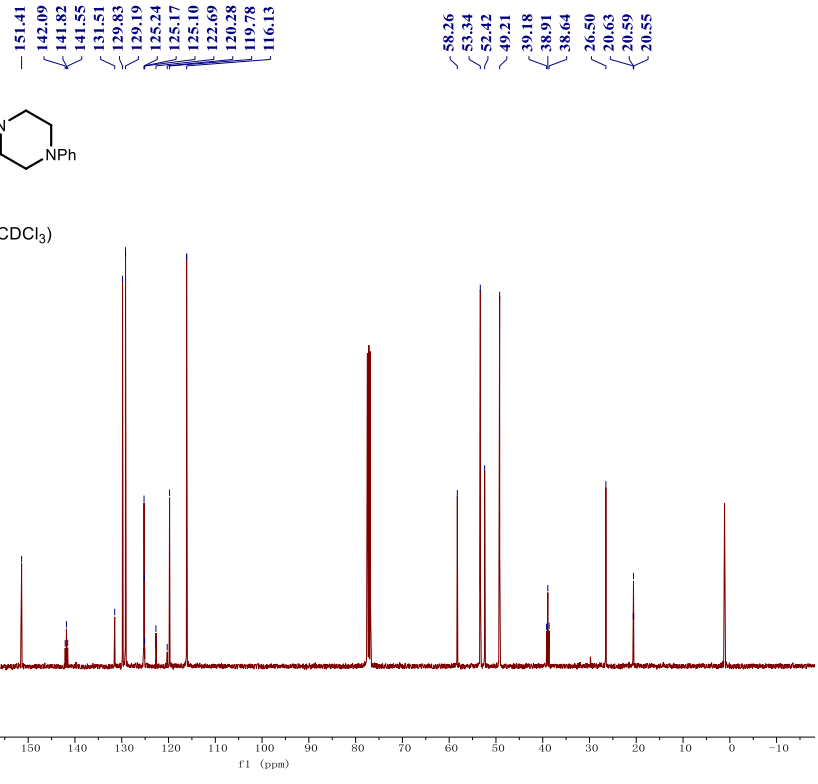
18a - ^{19}F NMR (376 MHz, $CDCl_3$)

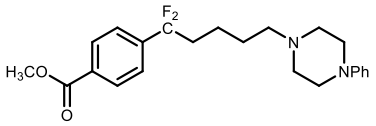




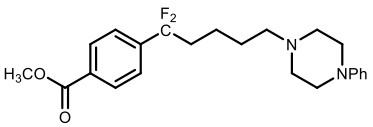
19a - ^{1}H NMR (400 MHz, $CDCl_3$)



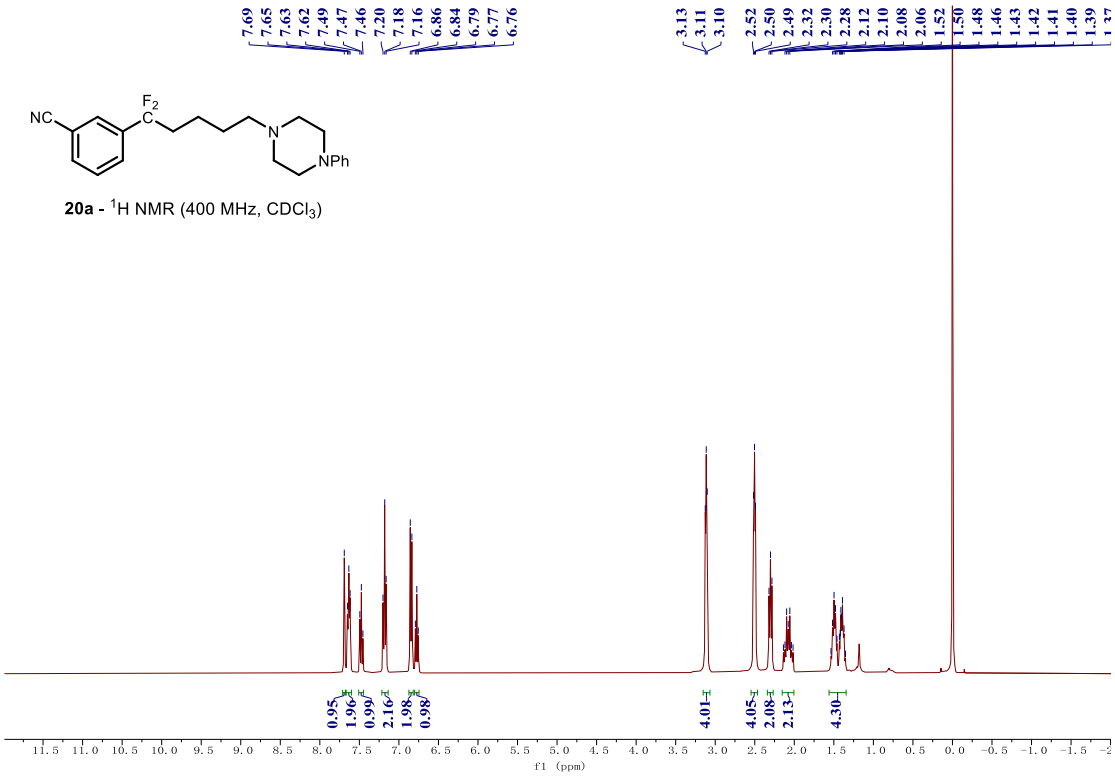




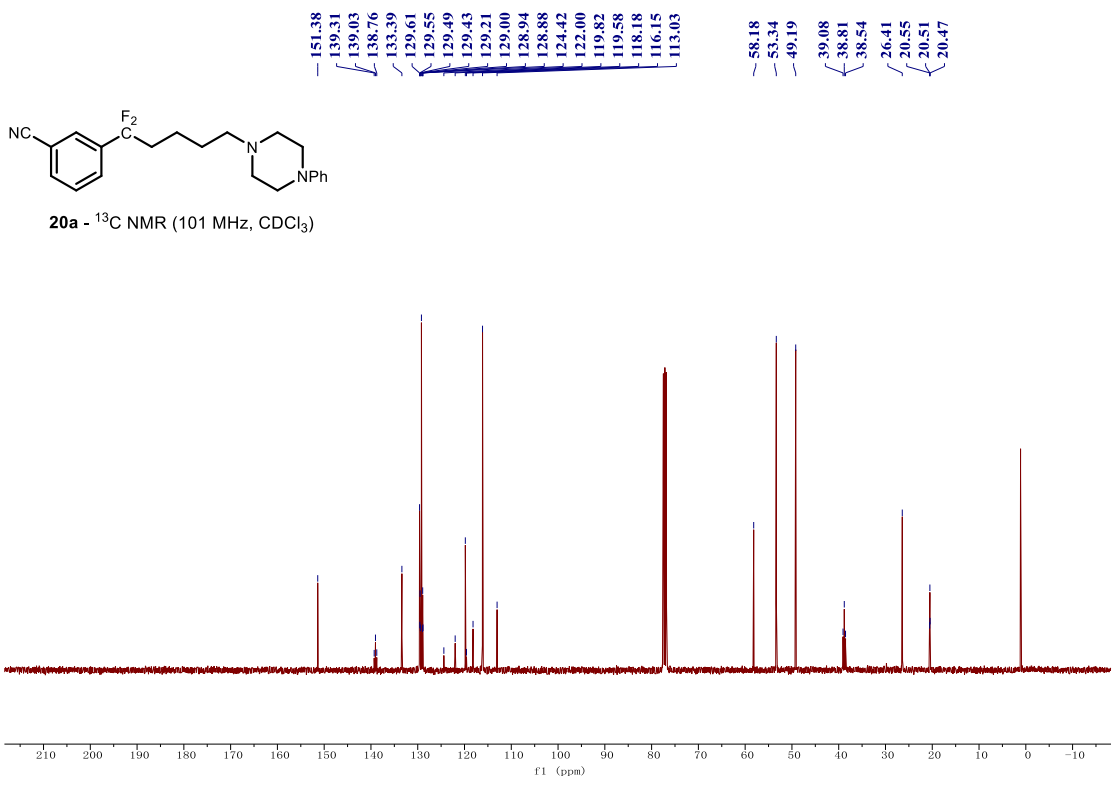
19a - ^{13}C NMR (101 MHz, $CDCl_3$)



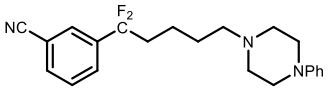
19a - ^{19}F NMR (376 MHz, $CDCl_3$)



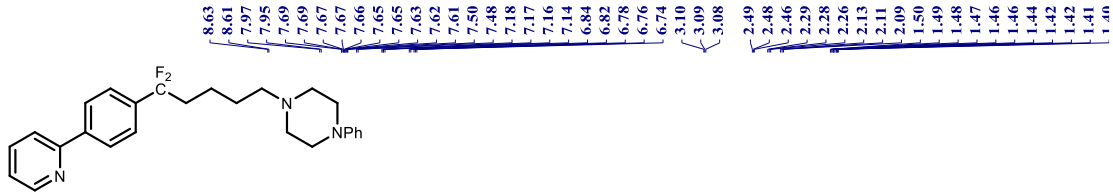
20a - ^{1}H NMR (400 MHz, $CDCl_3$)



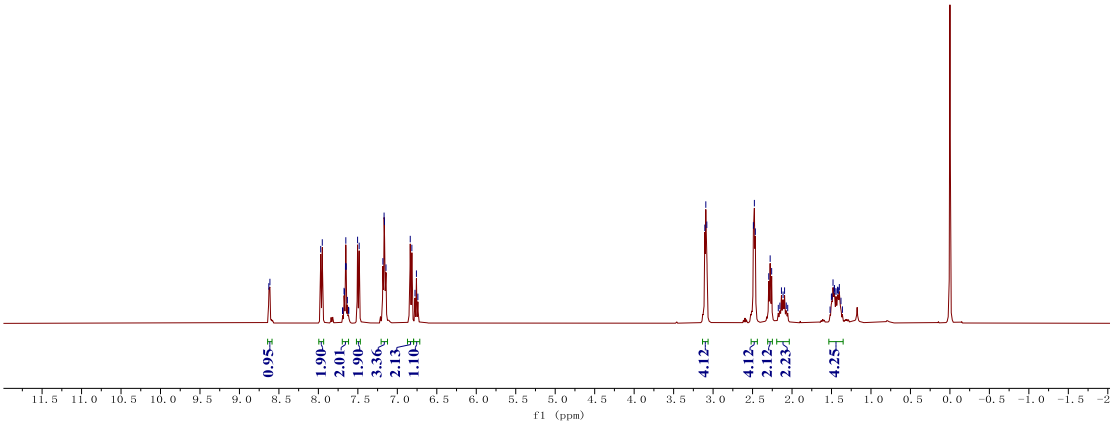
20a - ^{13}C NMR (101 MHz, $CDCl_3$)



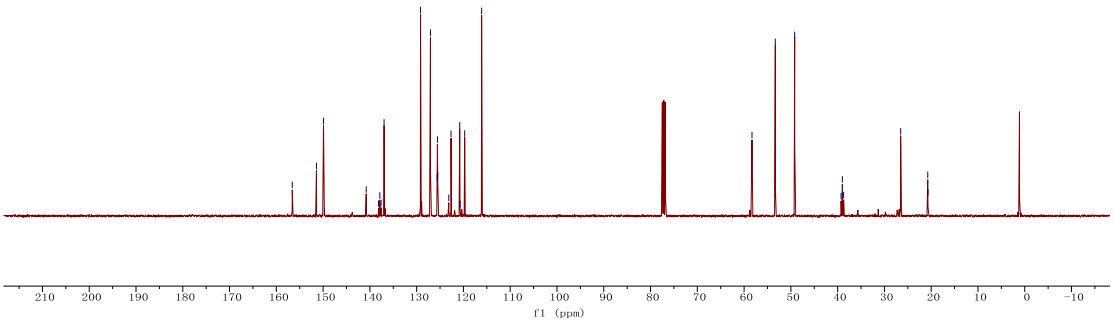
20a - ^{19}F NMR (376 MHz, $CDCl_3$)

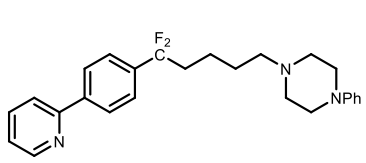


21a - ^{1}H NMR (400 MHz, $CDCl_3$)

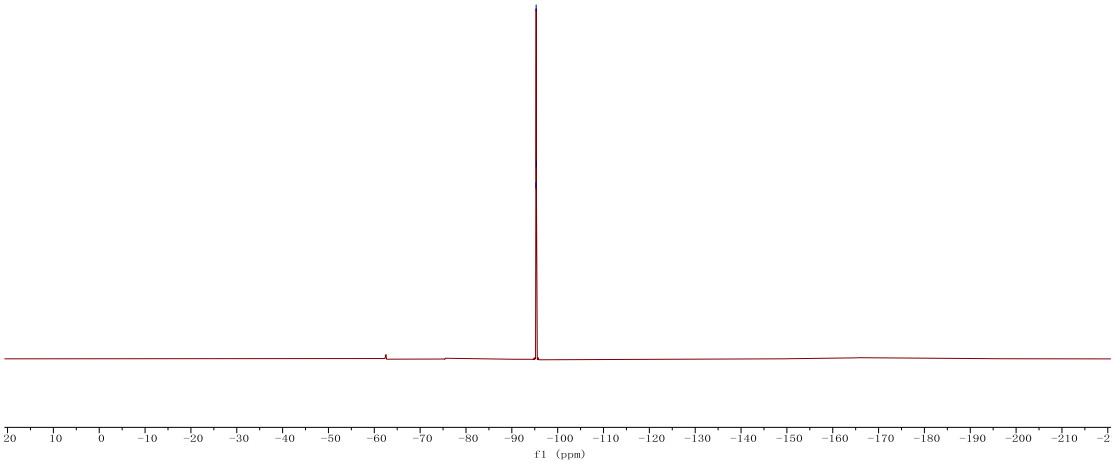


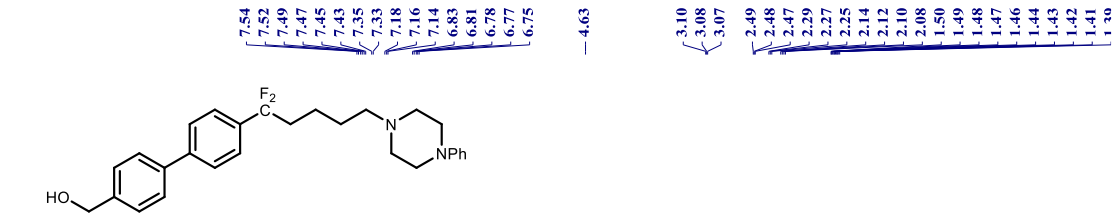
21a - ^{13}C NMR (101 MHz, $CDCl_3$)



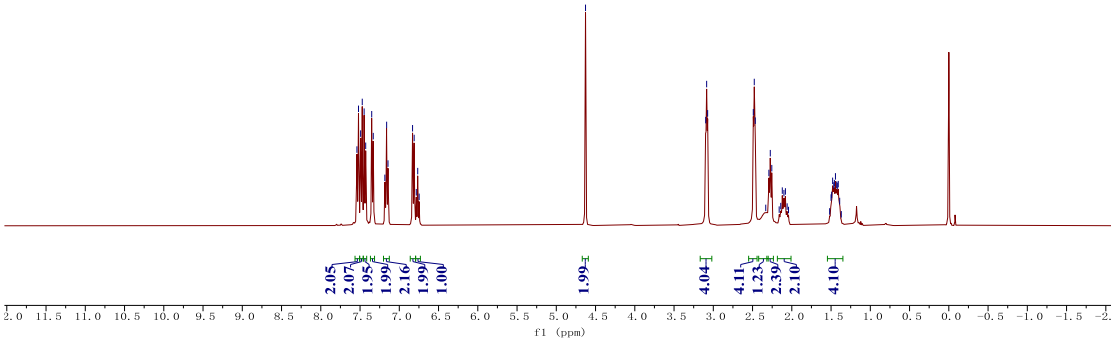


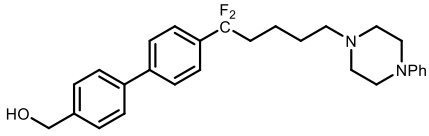
21a - ^{19}F NMR (376 MHz, $CDCl_3$)



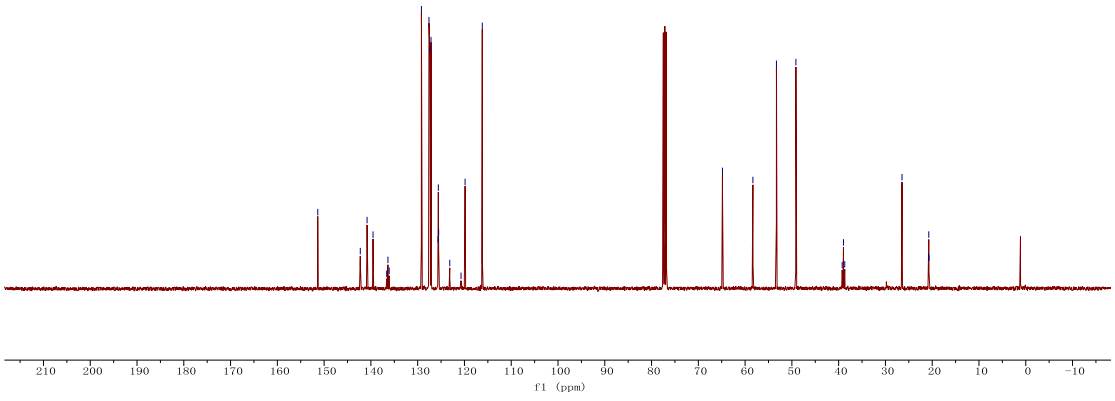


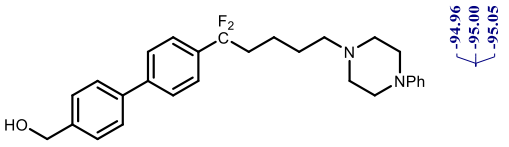
22a - ^{1}H NMR (400 MHz, $CDCl_3$)



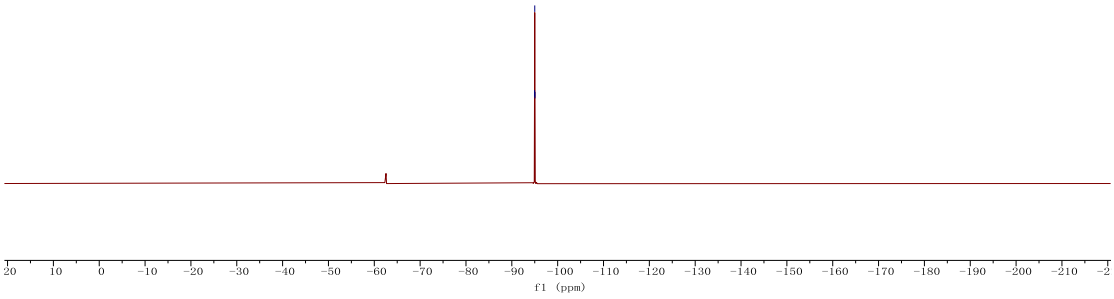


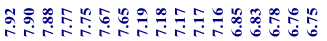
22a - ^{13}C NMR (101 MHz, $CDCl_3$)

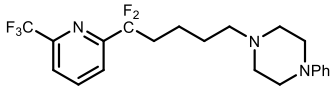




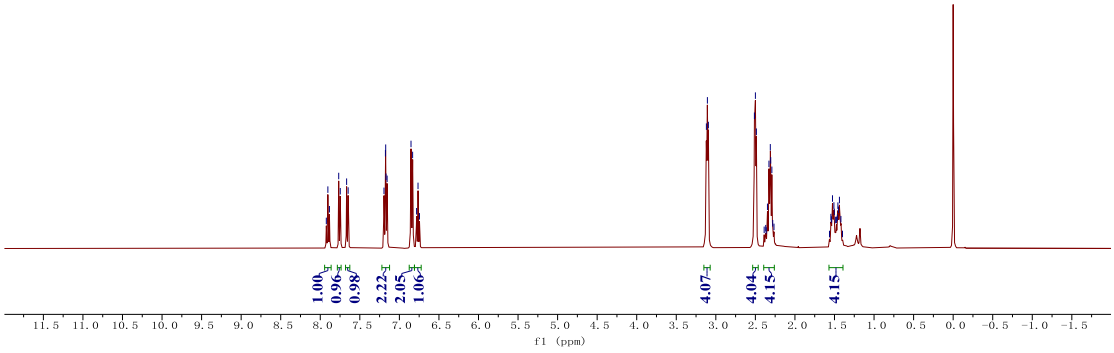
22a - ^{19}F NMR (376 MHz, $CDCl_3$)

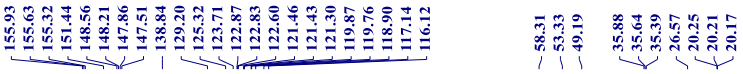


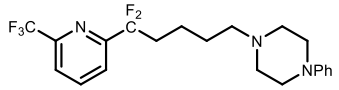




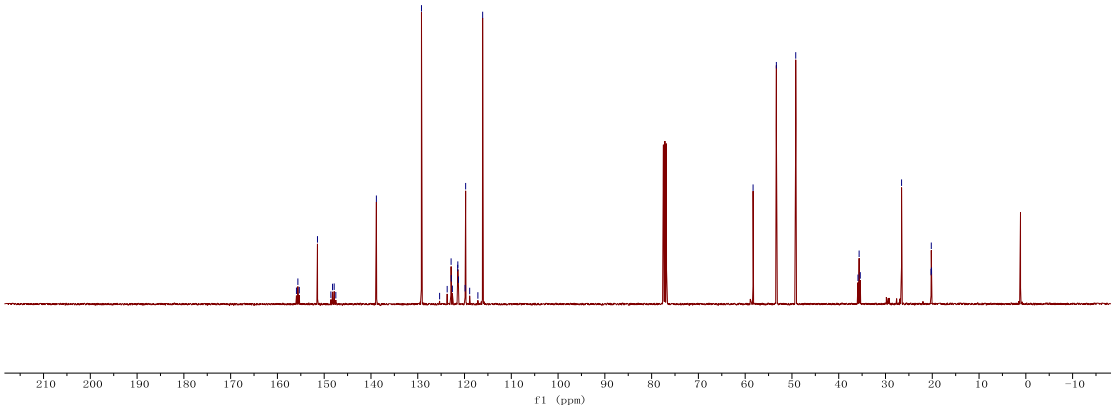
23a - ^{1}H NMR (400 MHz, $CDCl_3$)

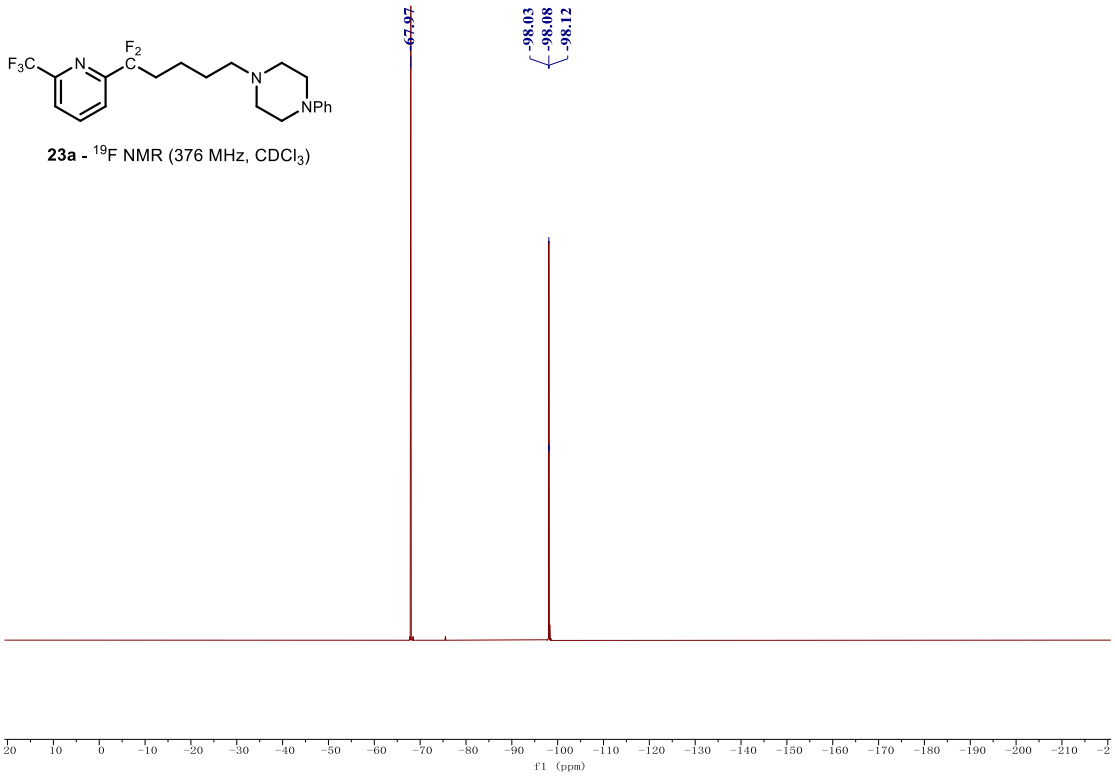




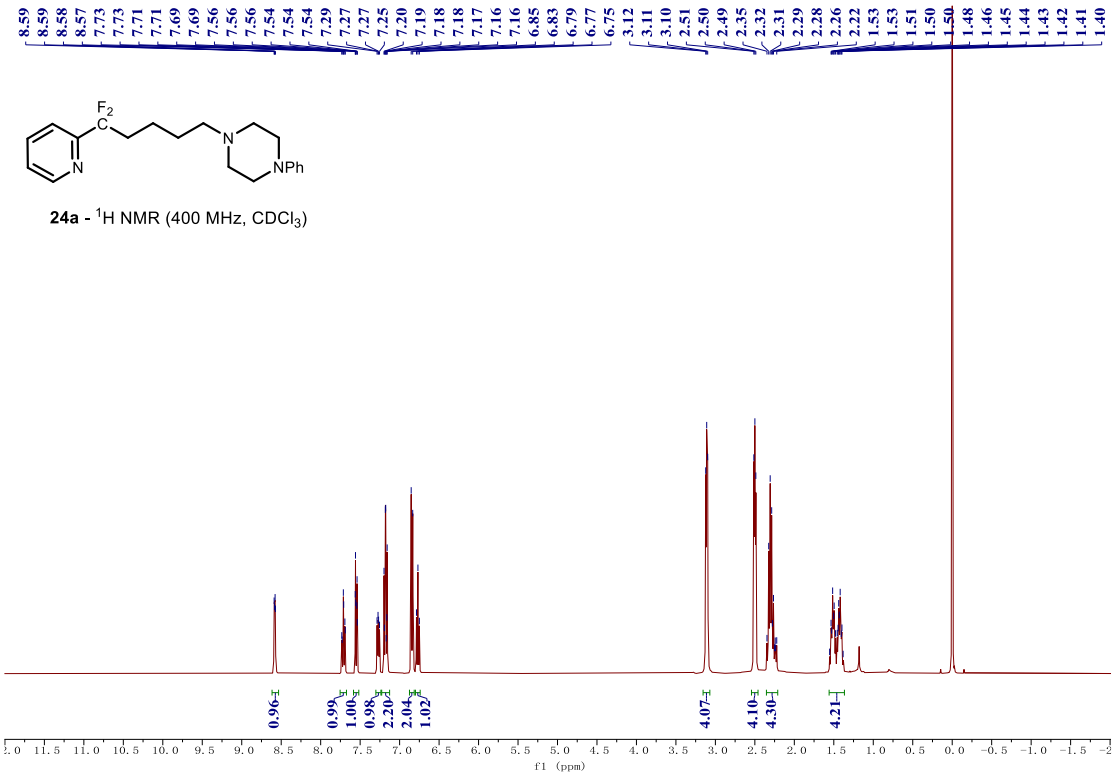


23a - ^{13}C NMR (101 MHz, $CDCl_3$)

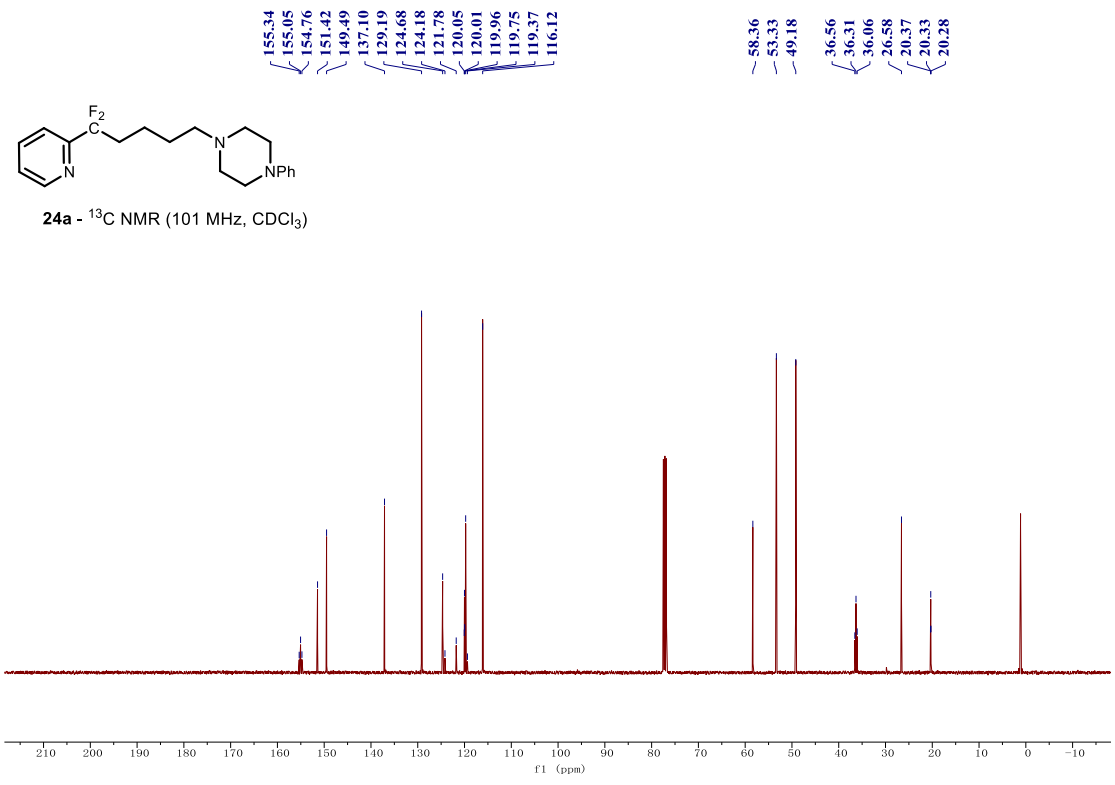




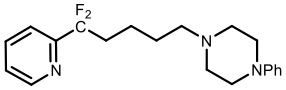
23a - ^{19}F NMR (376 MHz, $CDCl_3$)



24a - ^{1}H NMR (400 MHz, $CDCl_3$)

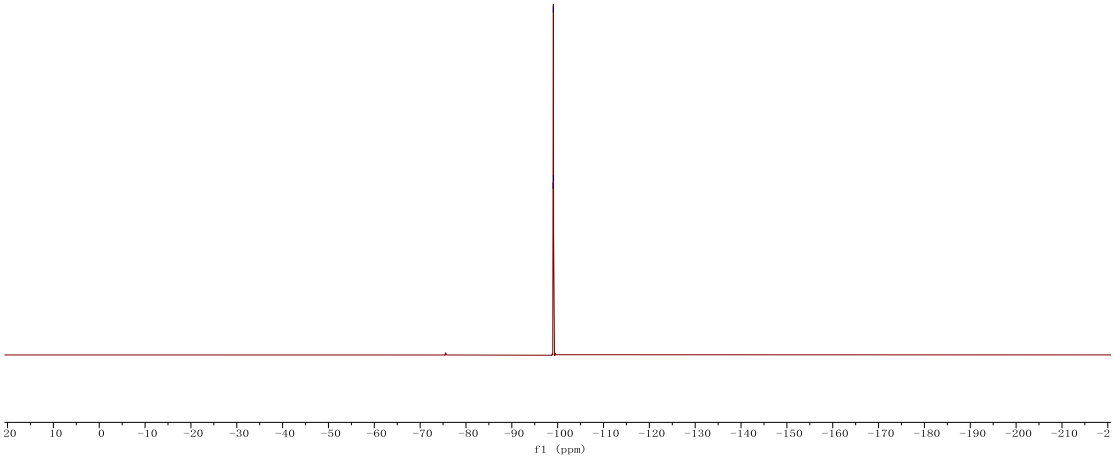


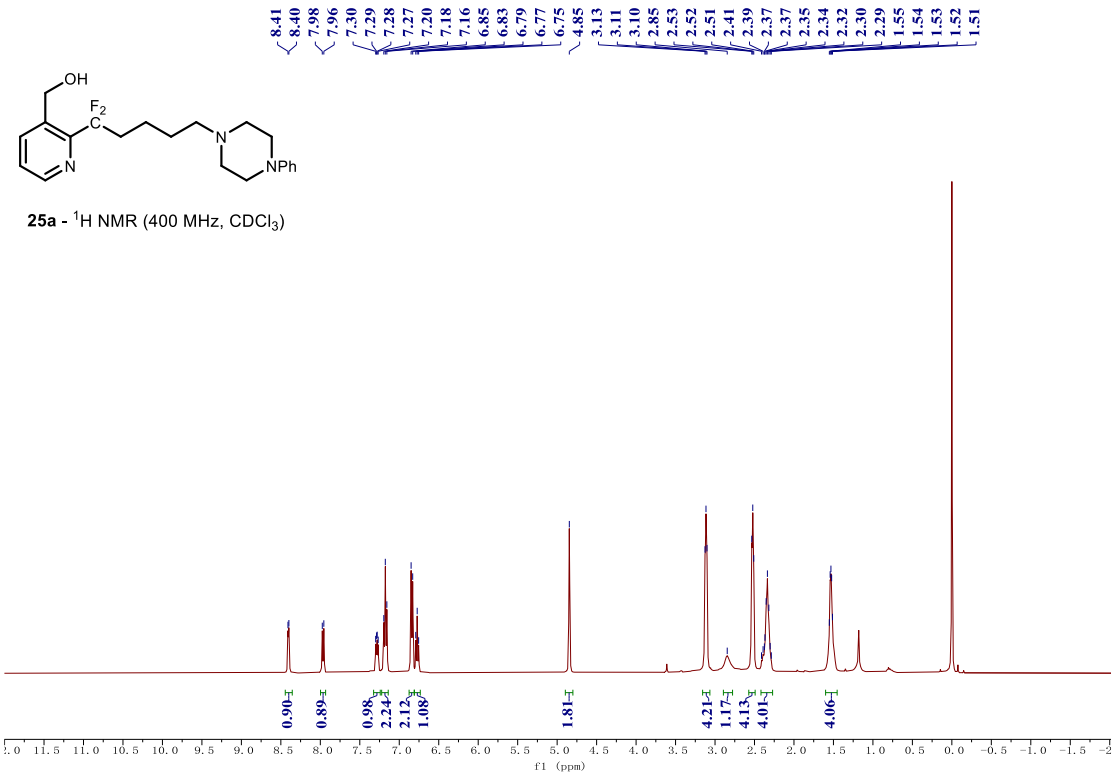
24a - ^{13}C NMR (101 MHz, $CDCl_3$)



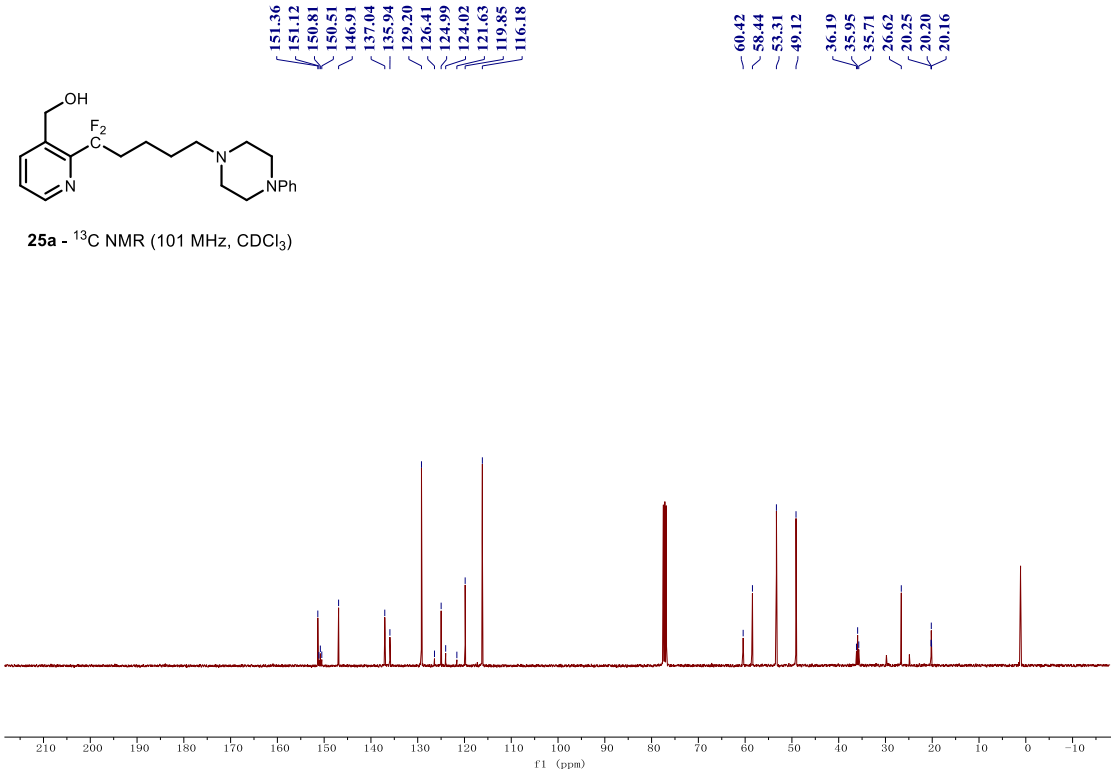
-99.01
-99.05
-99.10

24a - ^{19}F NMR (376 MHz, $CDCl_3$)

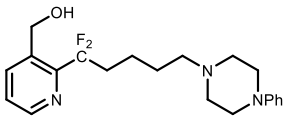




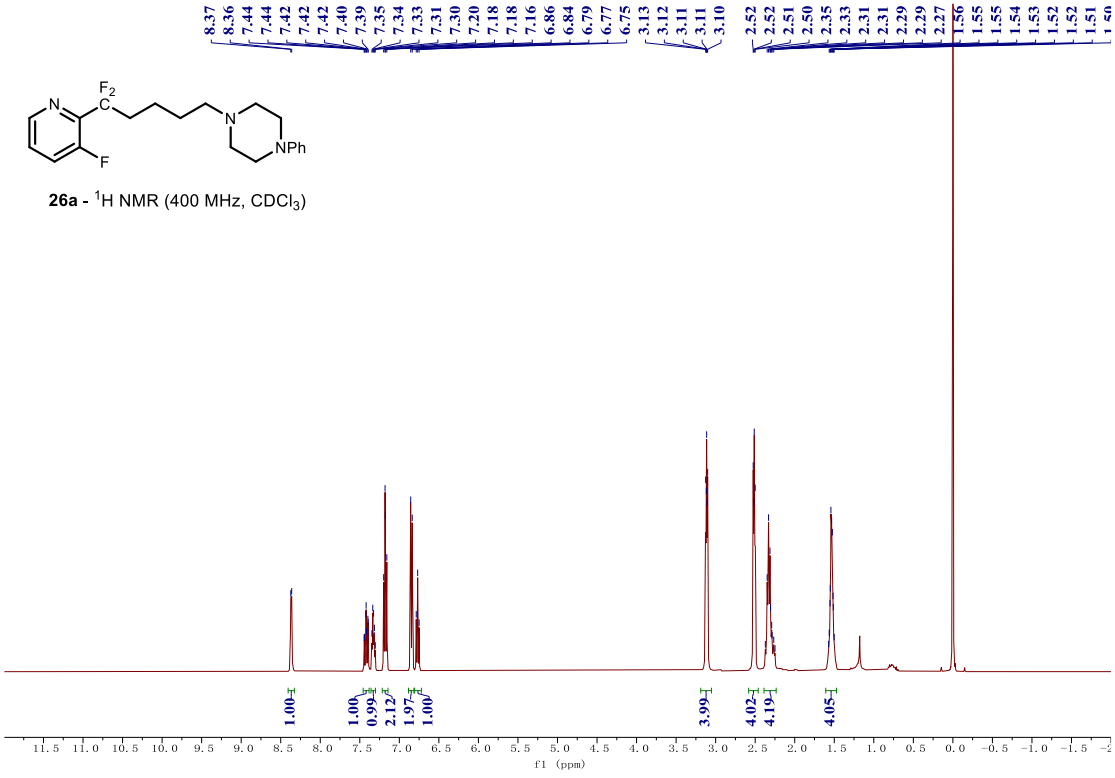
25a - ^{1}H NMR (400 MHz, $CDCl_3$)



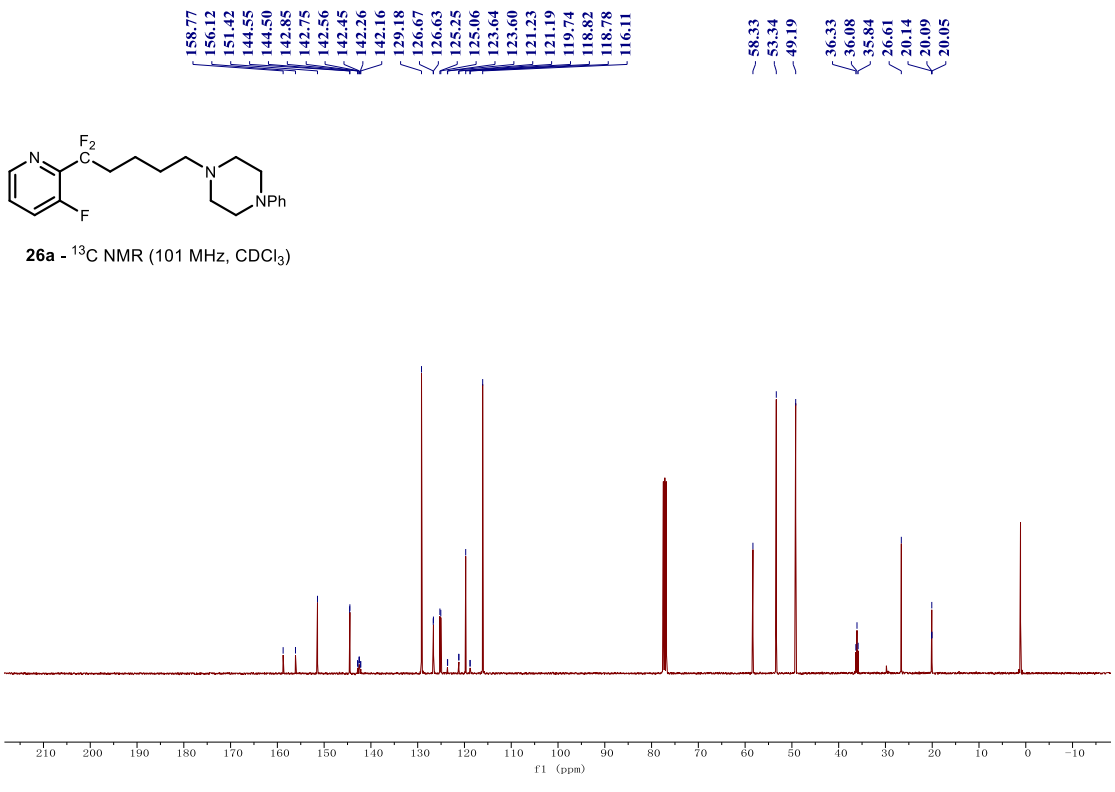
25a - ^{13}C NMR (101 MHz, $CDCl_3$)



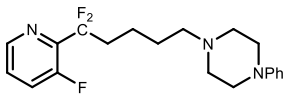
25a - ^{19}F NMR (376 MHz, $CDCl_3$)



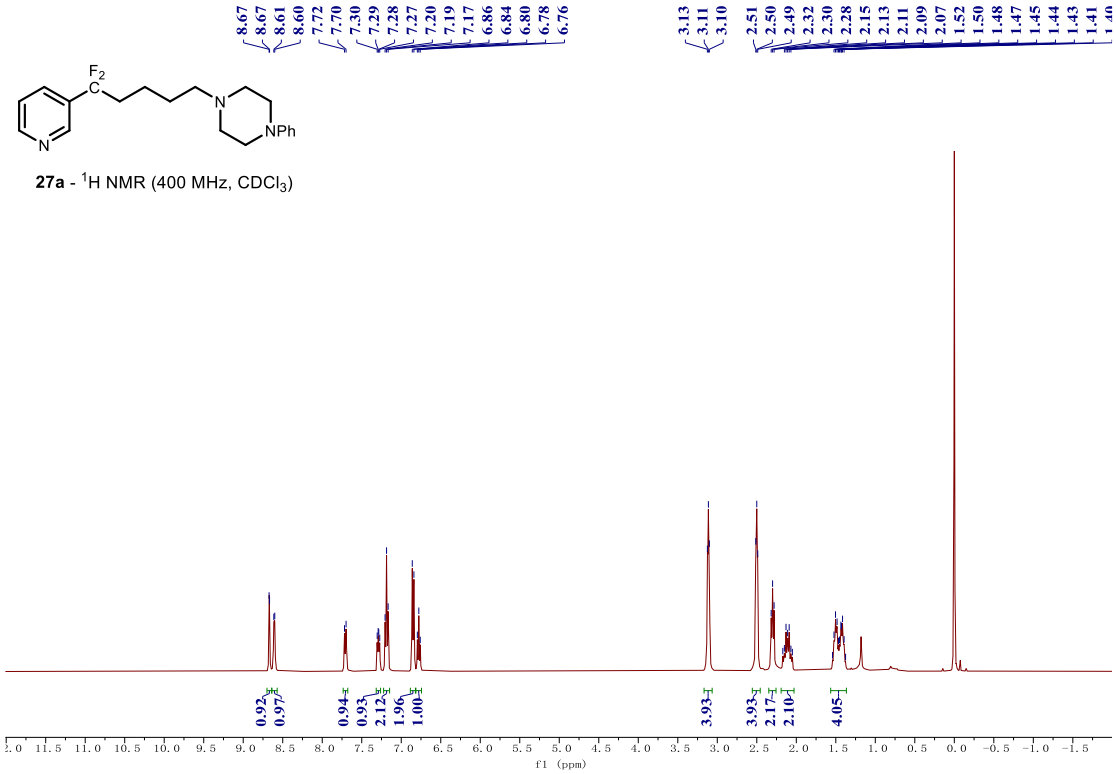
26a - ^{1}H NMR (400 MHz, $CDCl_3$)



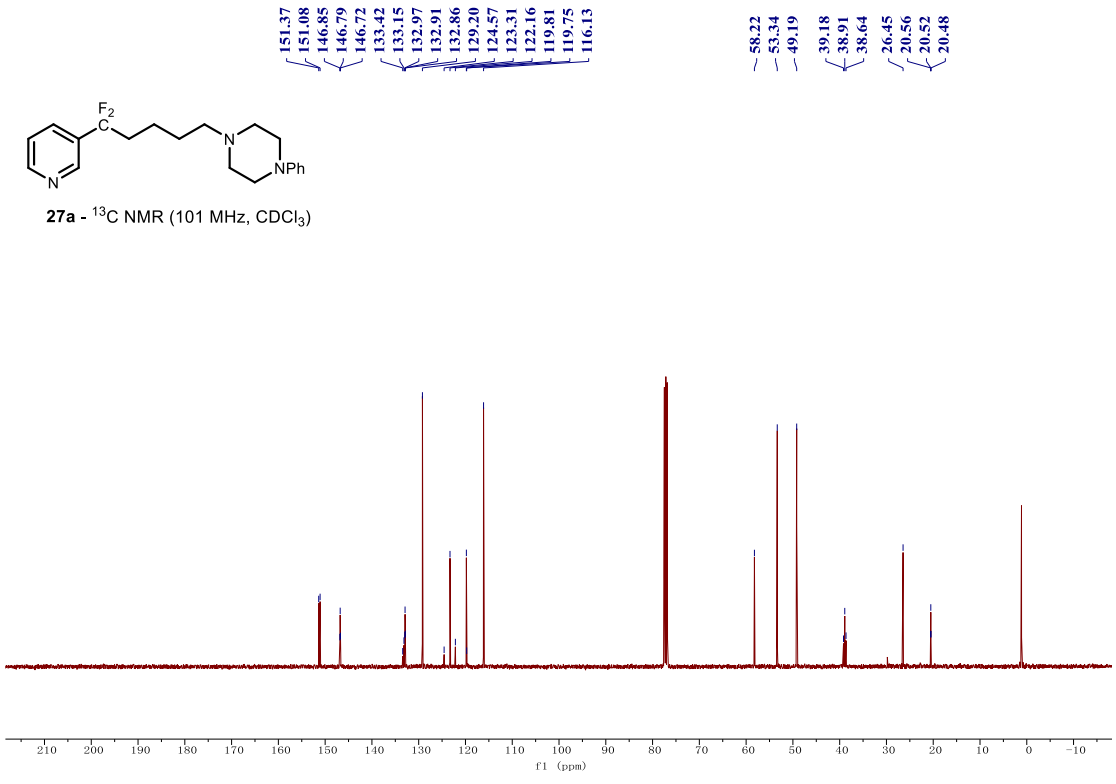
26a - ^{13}C NMR (101 MHz, $CDCl_3$)



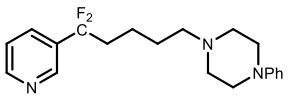
26a - ^{19}F NMR (376 MHz, $CDCl_3$)



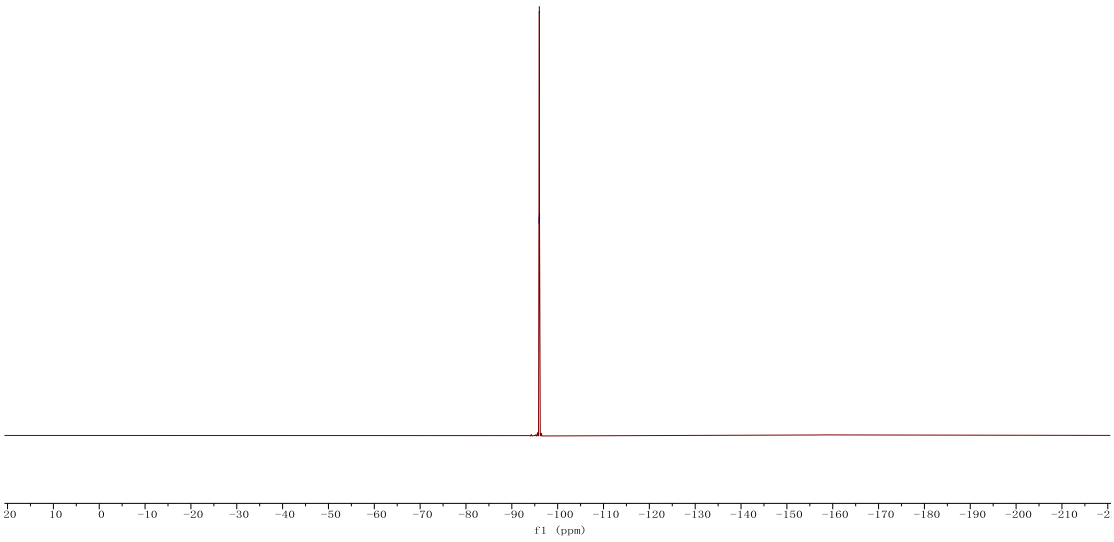
27a - ^{1}H NMR (400 MHz, $CDCl_3$)

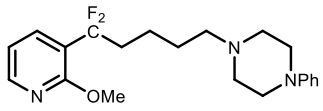


27a - ^{13}C NMR (101 MHz, $CDCl_3$)

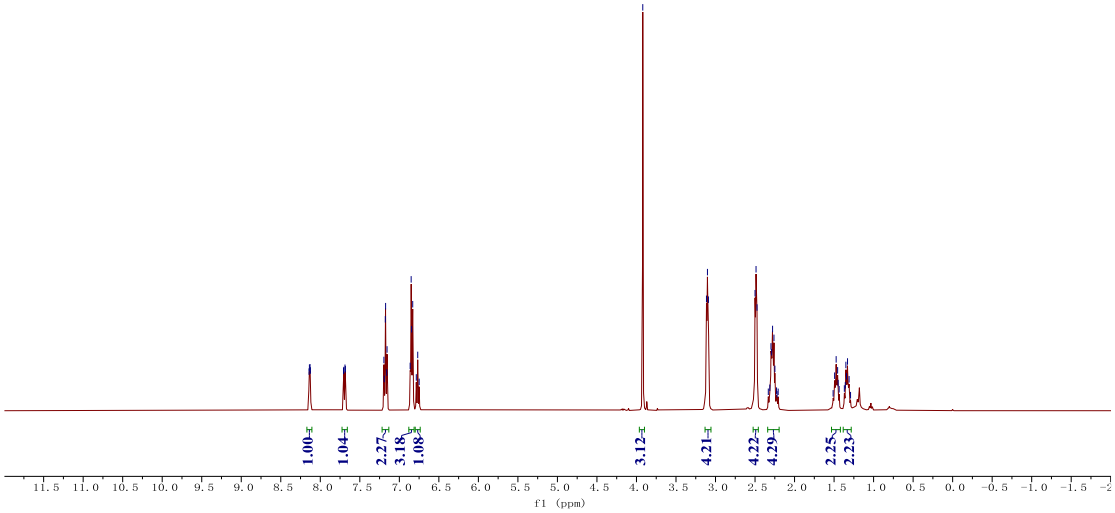


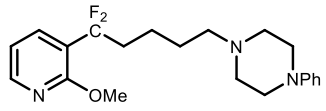
27a - ^{19}F NMR (376 MHz, $CDCl_3$)



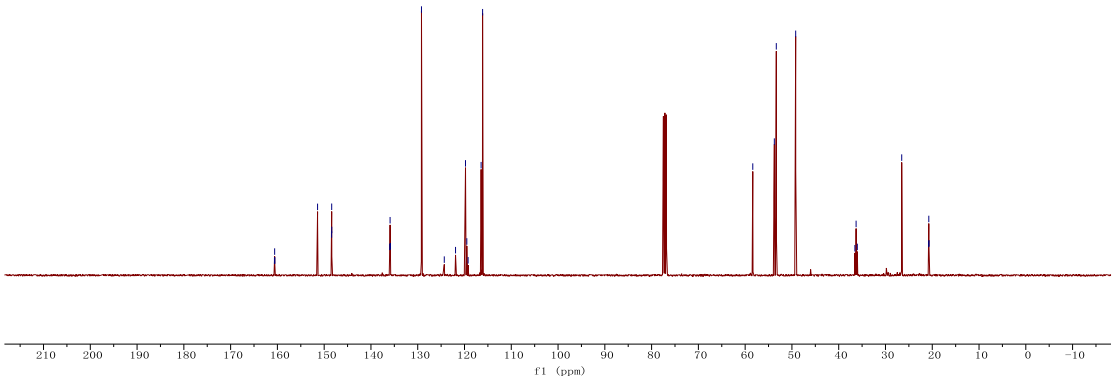


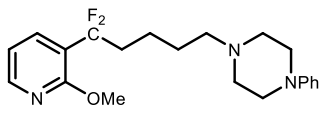
28a - ^{1}H NMR (400 MHz, $CDCl_3$)



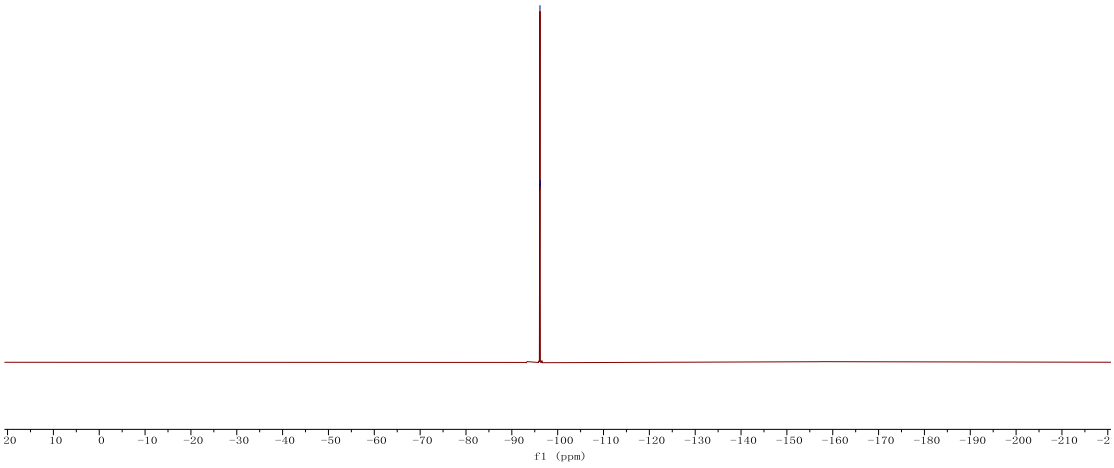


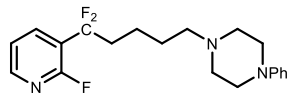
28a - ^{13}C NMR (101 MHz, $CDCl_3$)



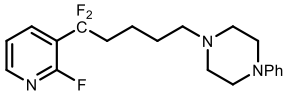


28a - ^{19}F NMR (376 MHz, $CDCl_3$)

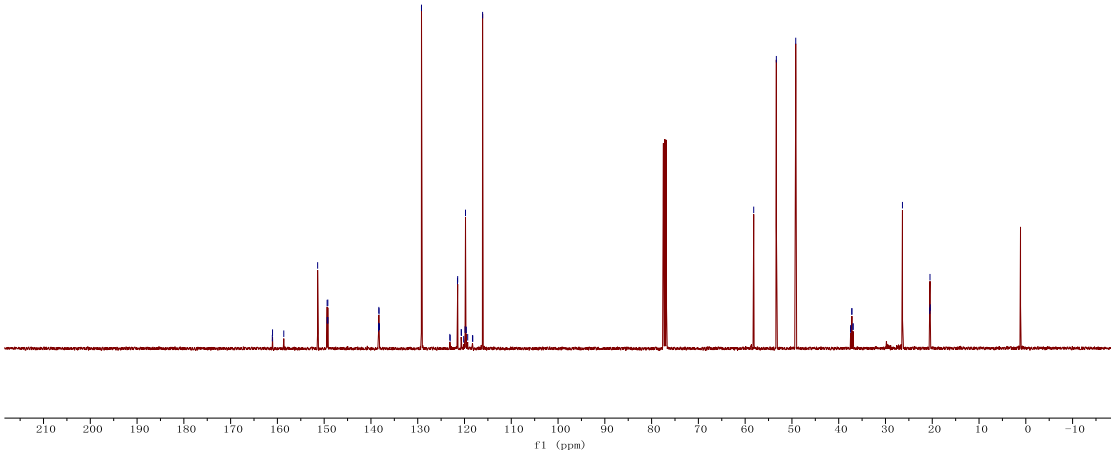


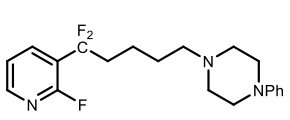


29a - ^{1}H NMR (400 MHz, $CDCl_3$)



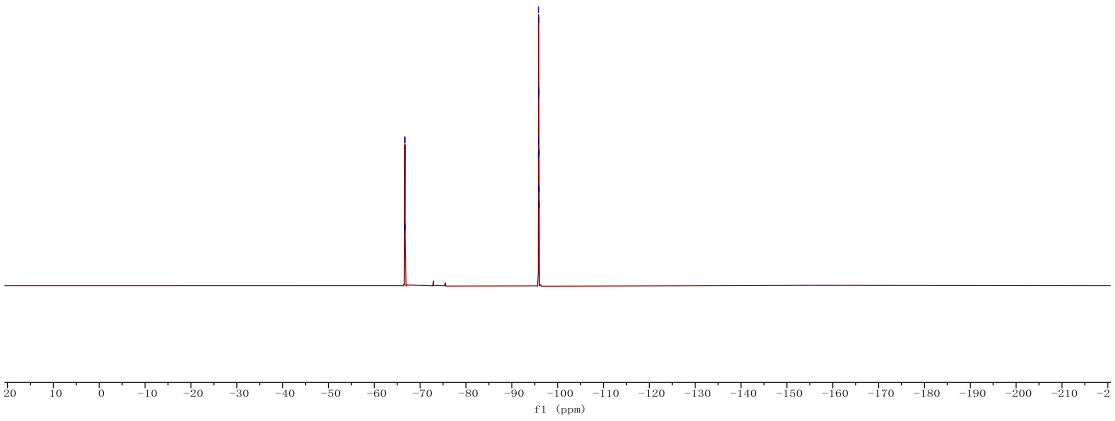
29a - ^{13}C NMR (101 MHz, $CDCl_3$)

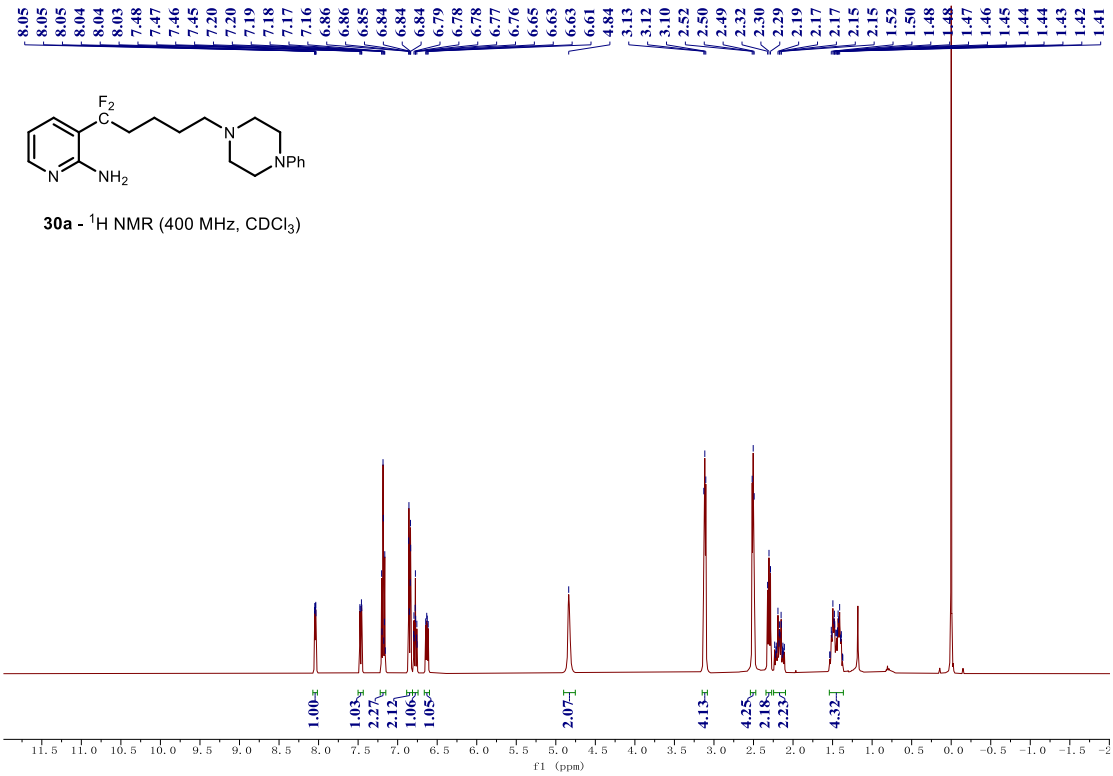




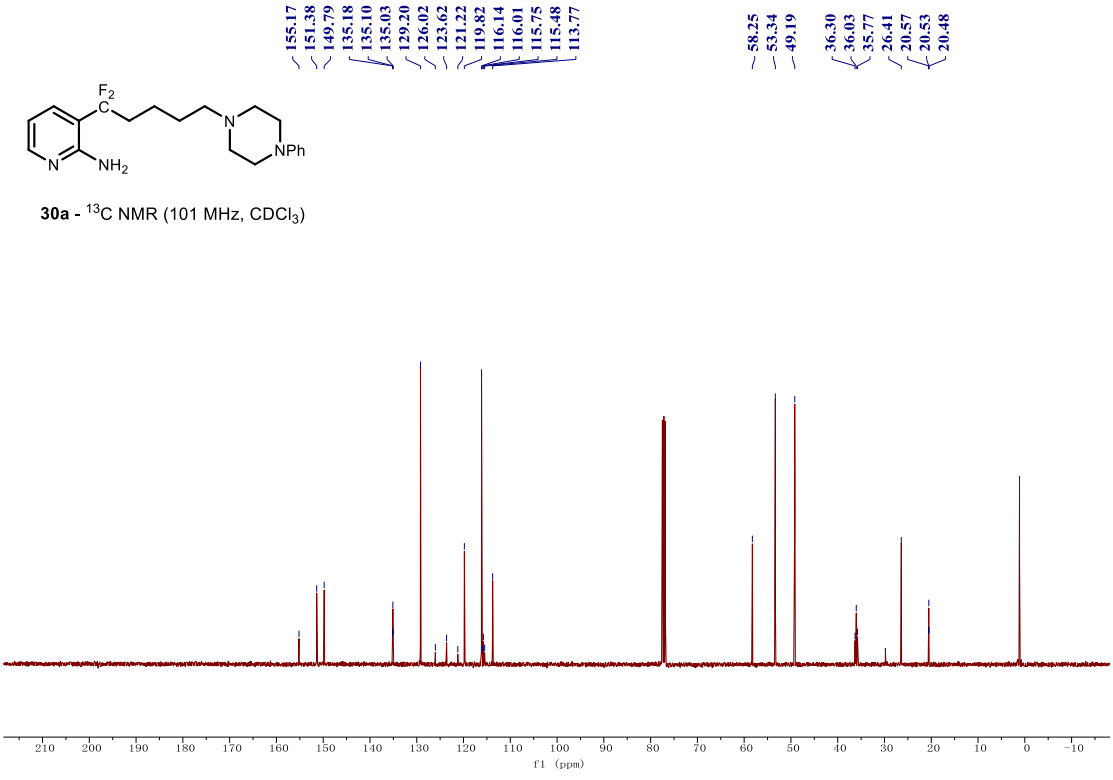
-66.64
-66.66
-66.69
-66.72
-95.80
-95.81
-95.82
-95.84
-95.85
-95.87
-95.88
-95.90
-95.91
-95.93

29a - ^{19}F NMR (376 MHz, $CDCl_3$)

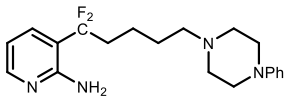




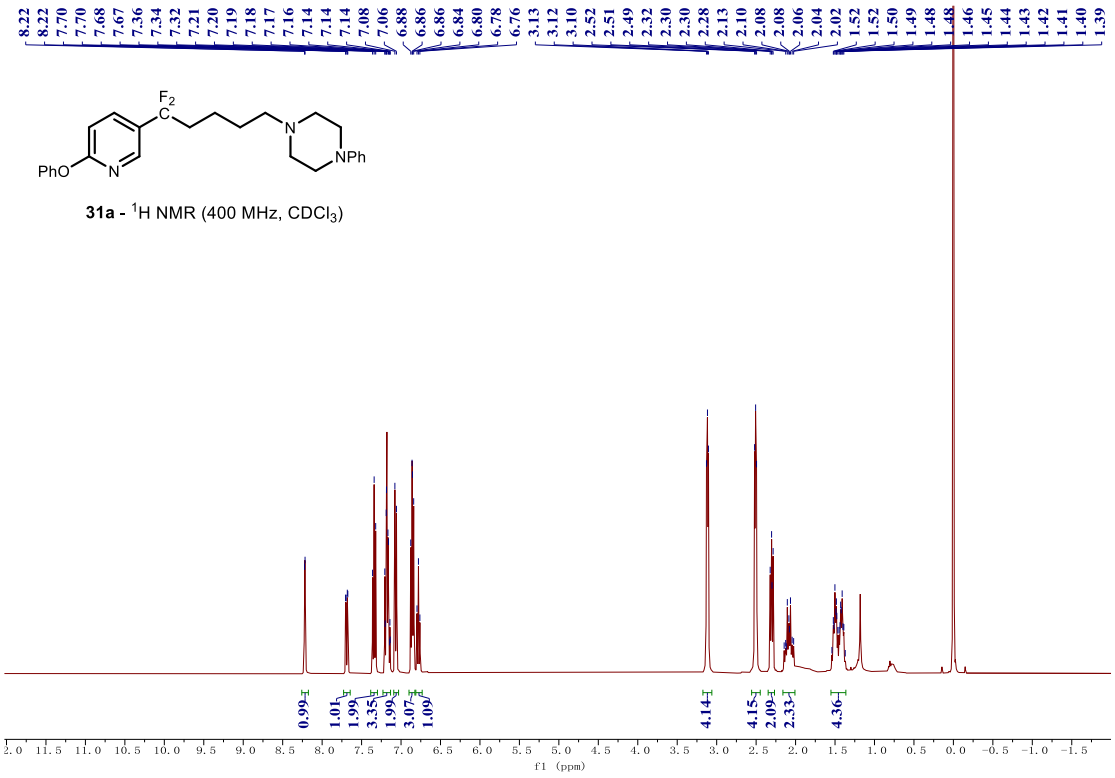
30a - ^{1}H NMR (400 MHz, $CDCl_3$)



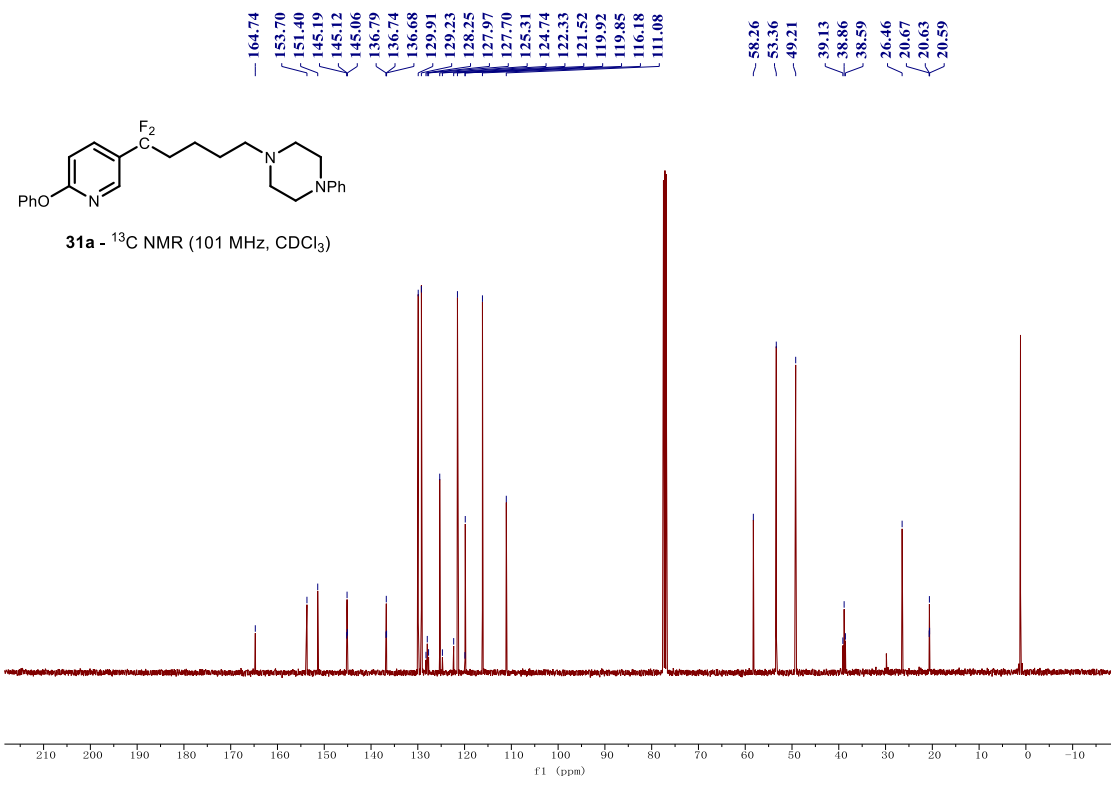
30a - ^{13}C NMR (101 MHz, $CDCl_3$)



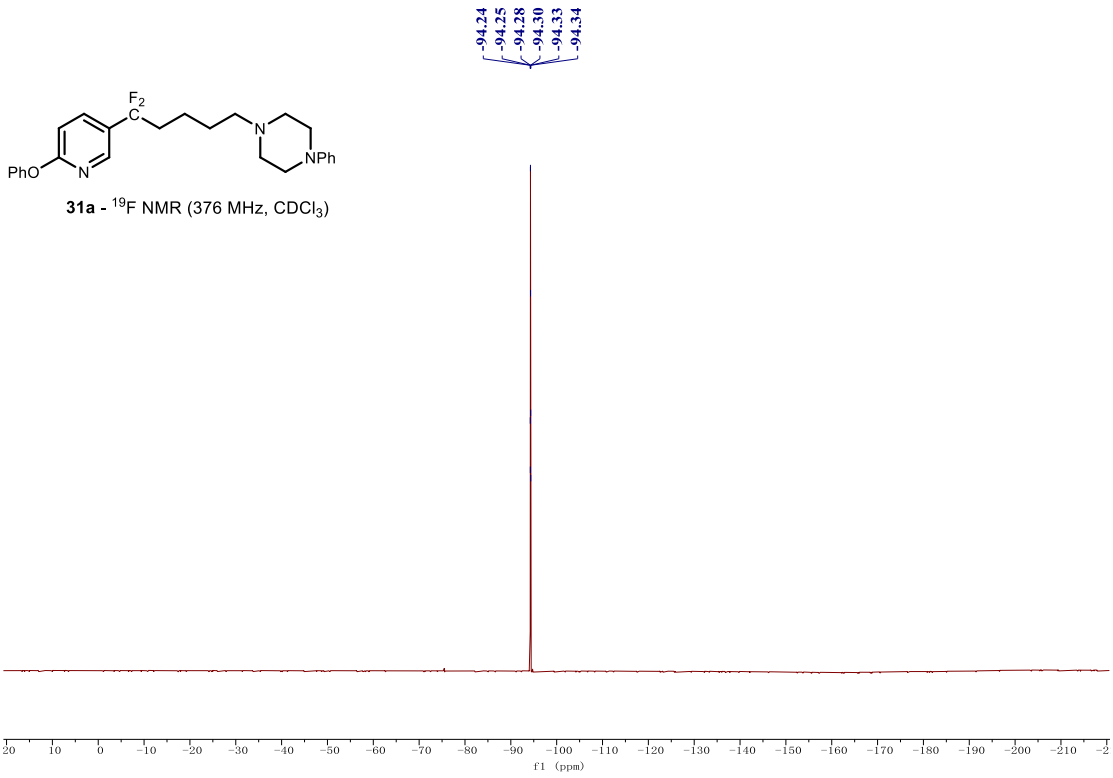
30a - ^{19}F NMR (376 MHz, $CDCl_3$)



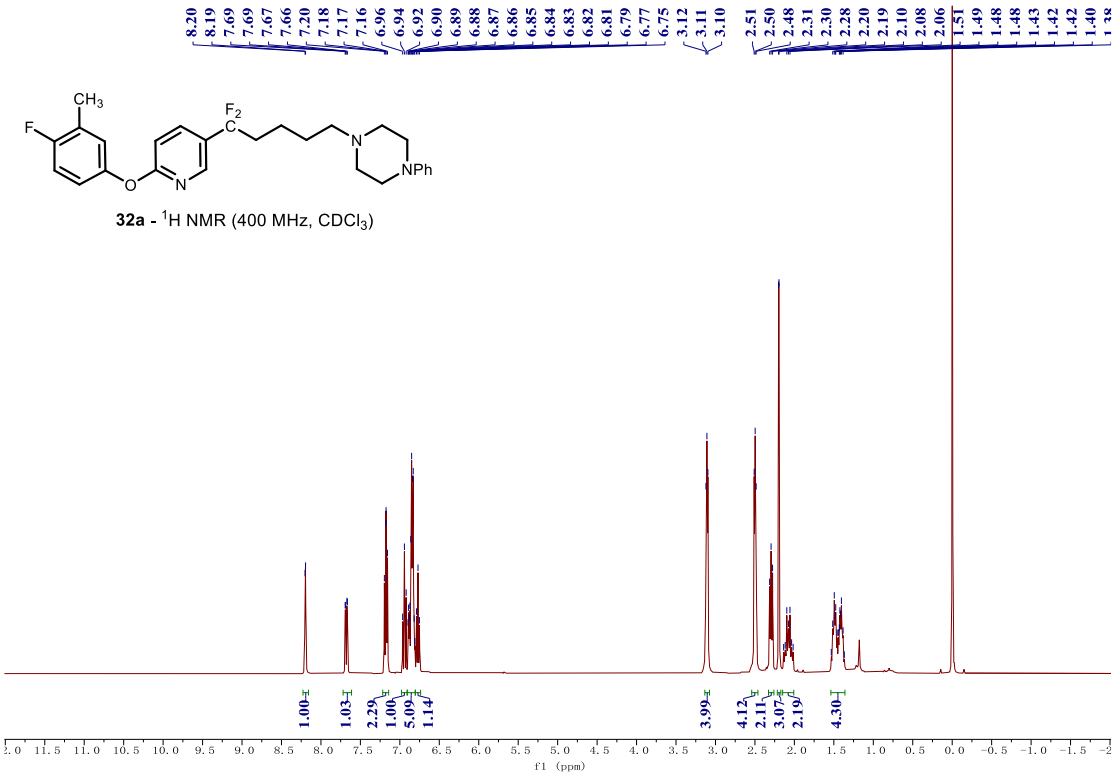
31a - ^{1}H NMR (400 MHz, $CDCl_3$)



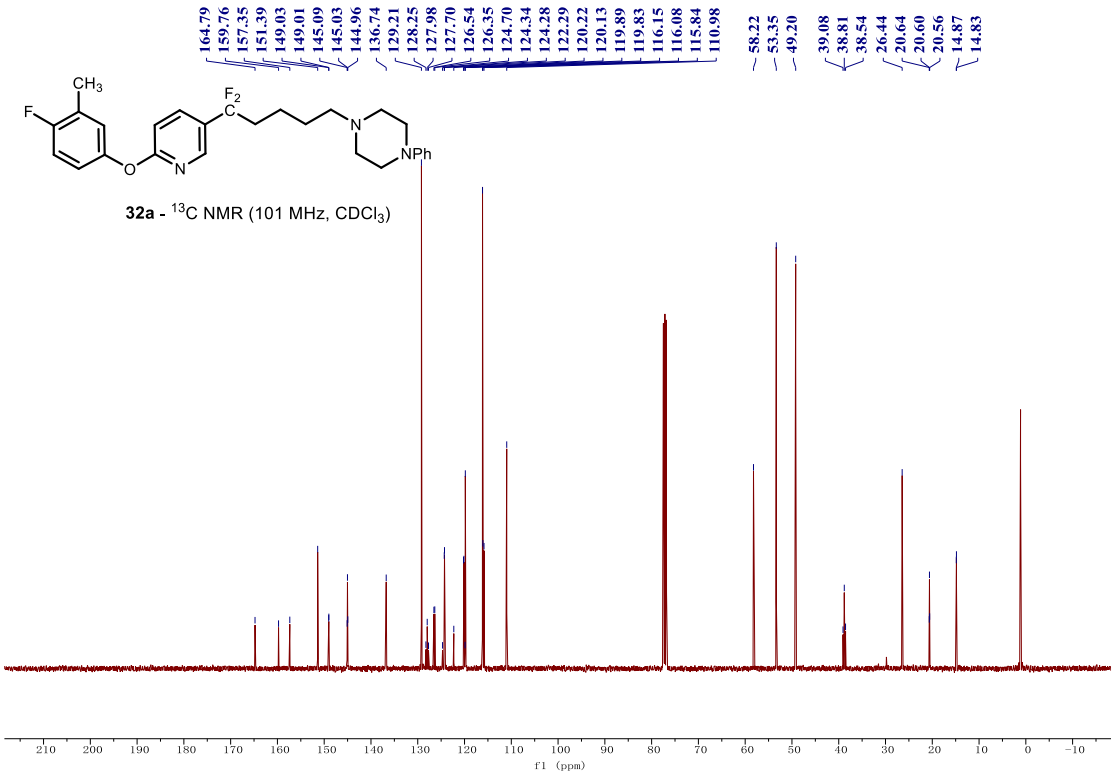
31a - ^{13}C NMR (101 MHz, $CDCl_3$)



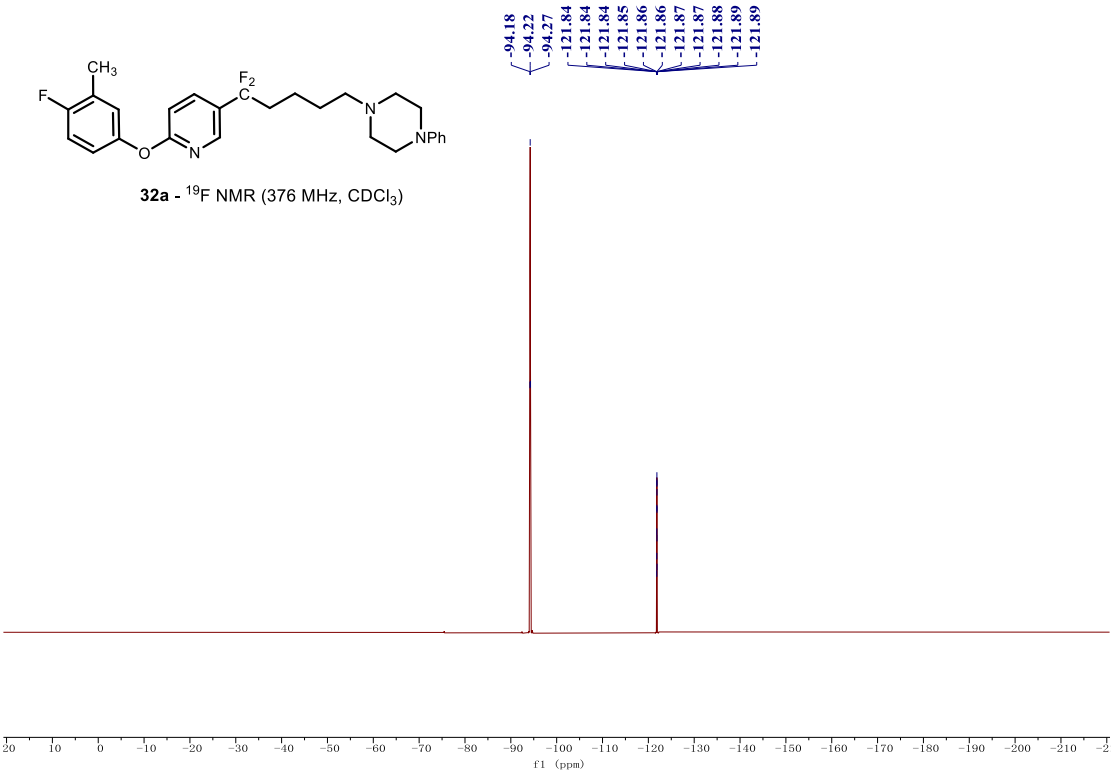
31a - ^{19}F NMR (376 MHz, $CDCl_3$)



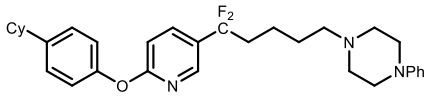
32a - ^{1}H NMR (400 MHz, $CDCl_3$)



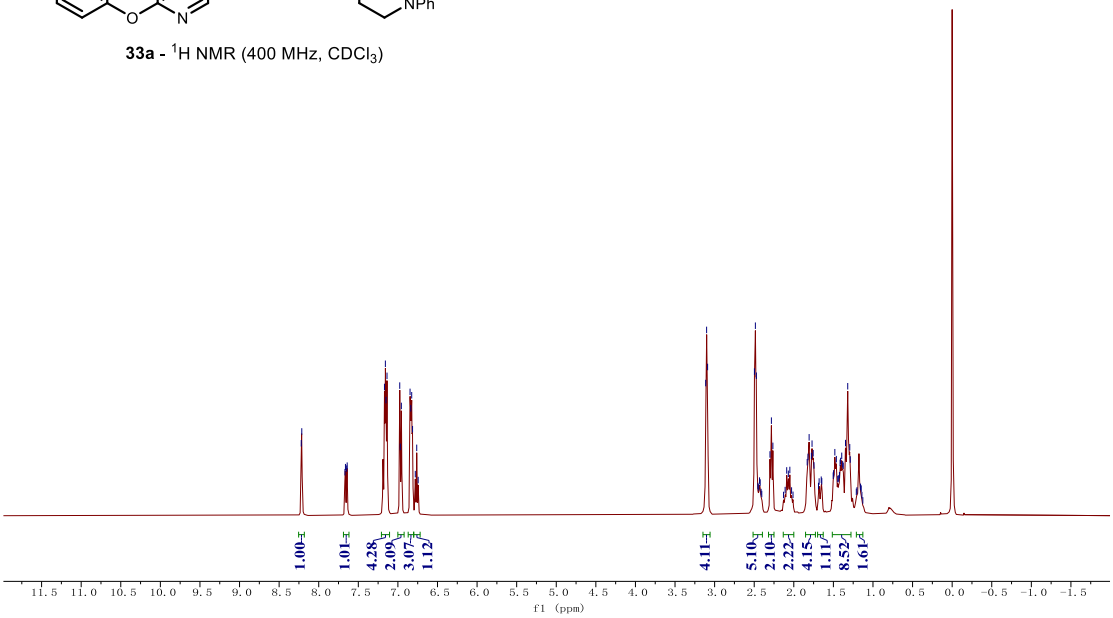
32a - ^{13}C NMR (101 MHz, $CDCl_3$)

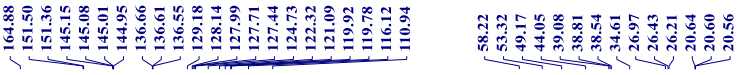


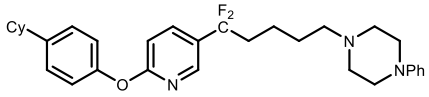
32a - ^{19}F NMR (376 MHz, $CDCl_3$)



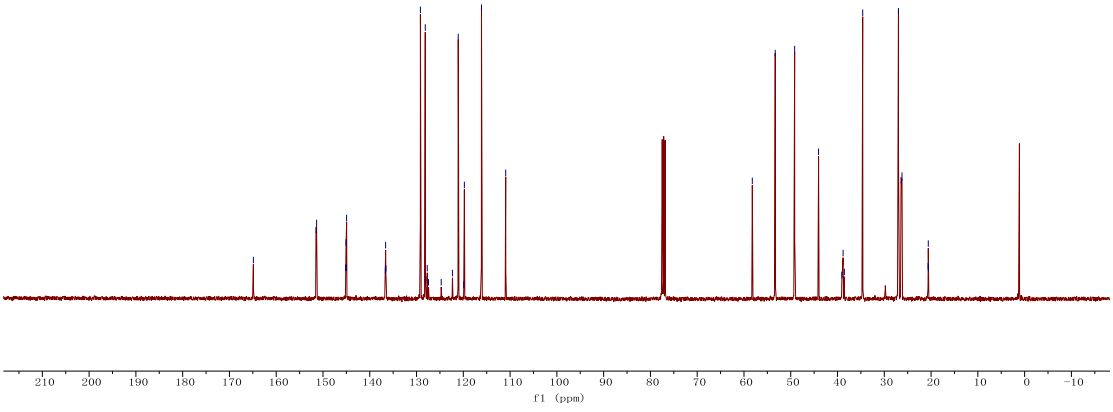
33a - ^{1}H NMR (400 MHz, $CDCl_3$)

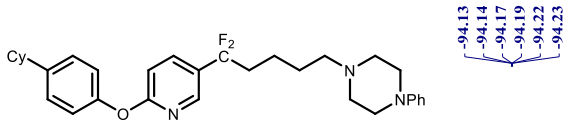




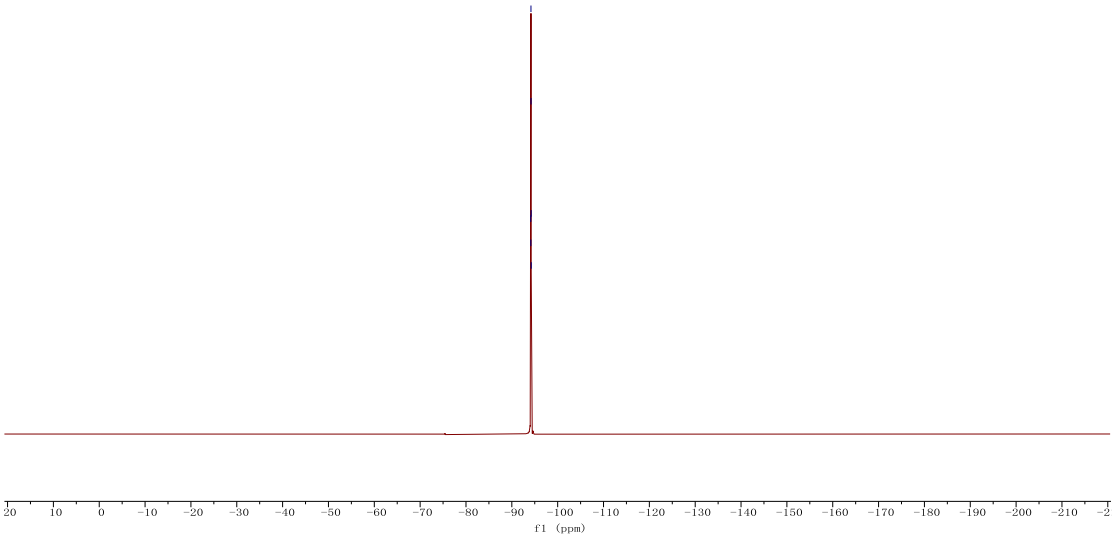


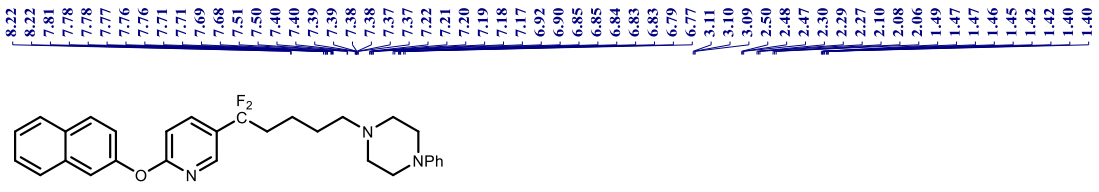
33a - ^{13}C NMR (101 MHz, $CDCl_3$)



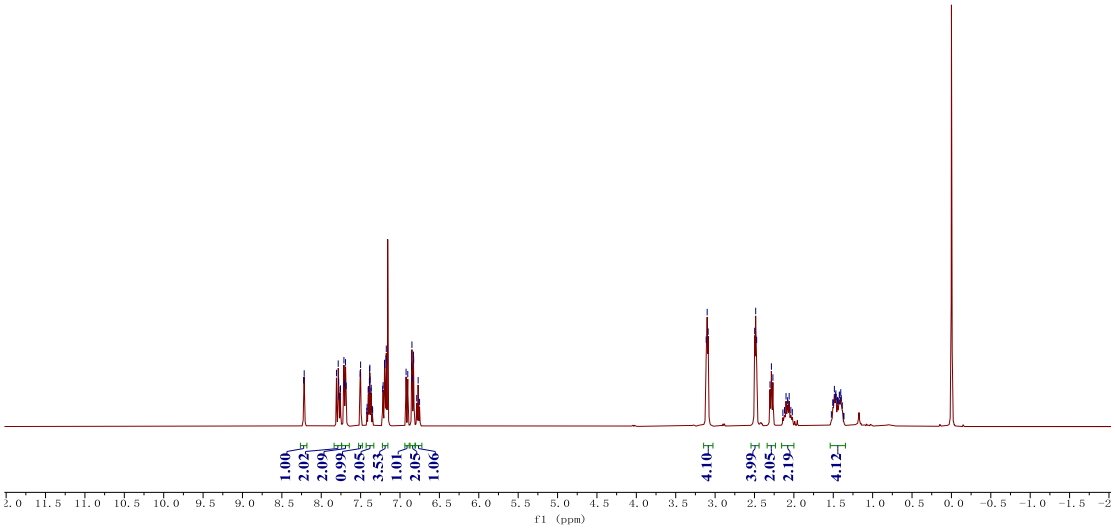


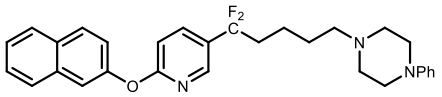
33a - ^{19}F NMR (376 MHz, $CDCl_3$)



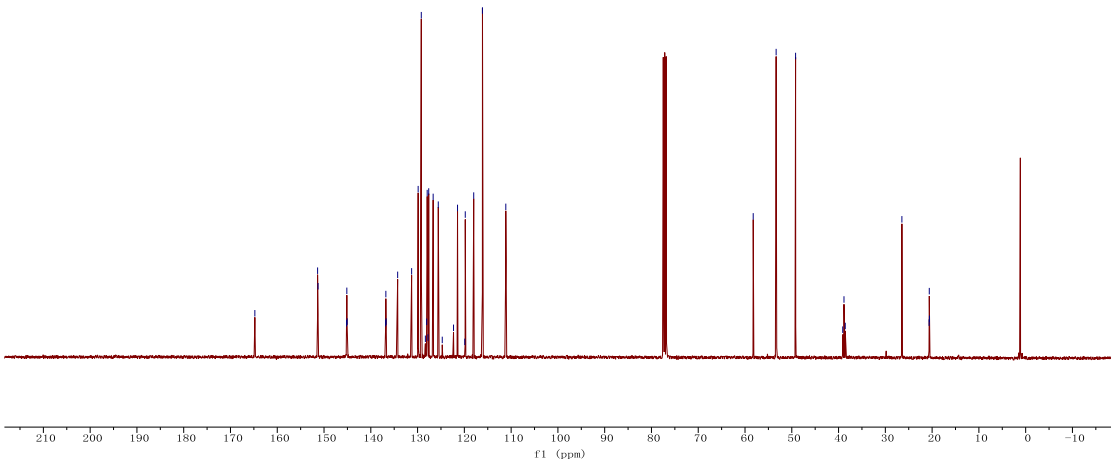


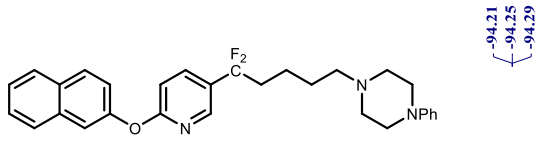
34a - ^{1}H NMR (400 MHz, $CDCl_3$)



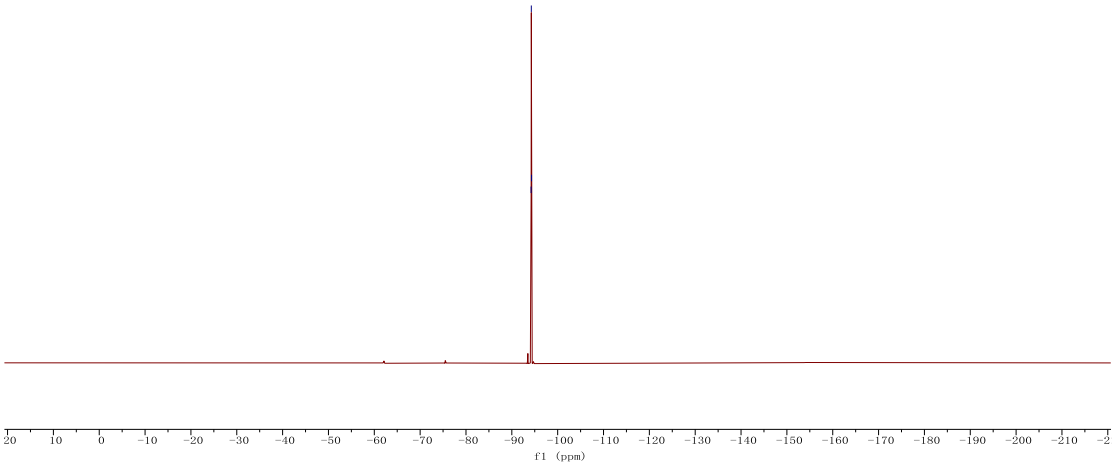


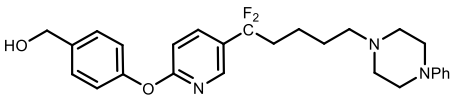
34a - ^{13}C NMR (101 MHz, $CDCl_3$)



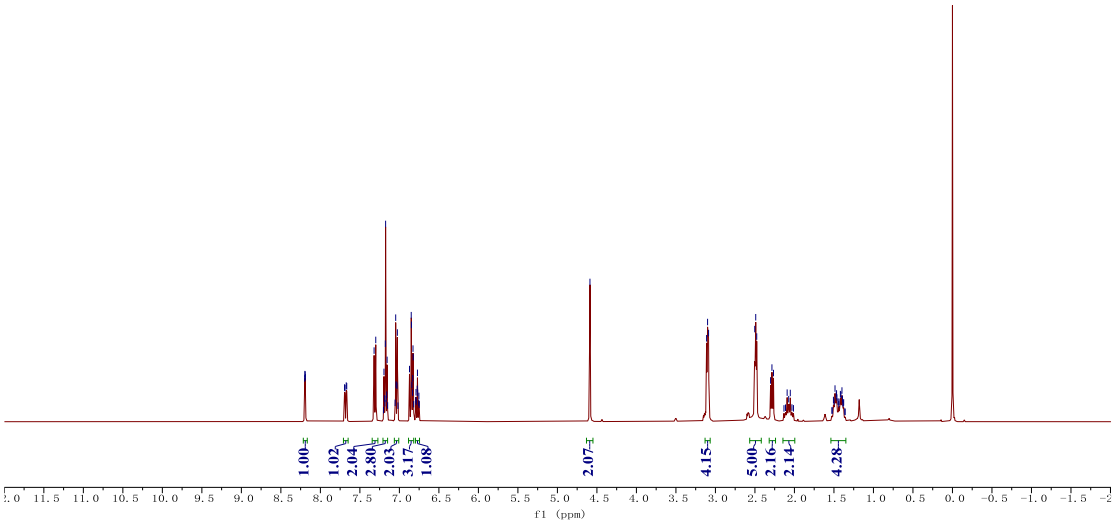


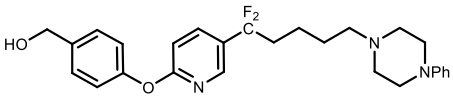
34a - ^{19}F NMR (376 MHz, $CDCl_3$)



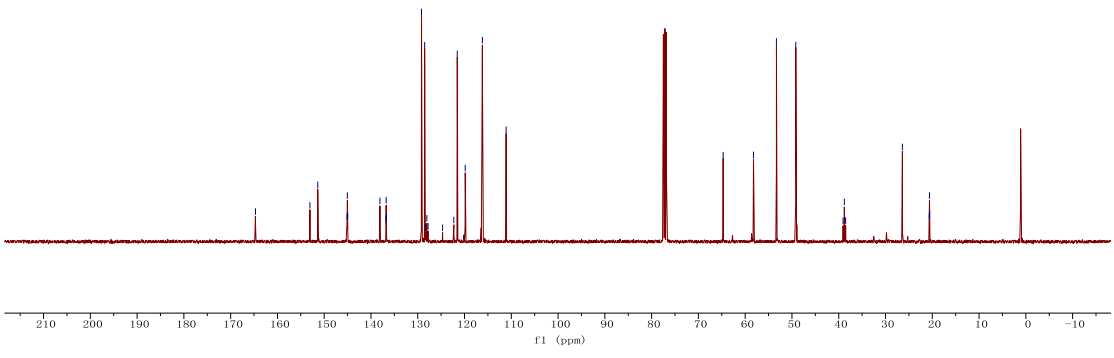


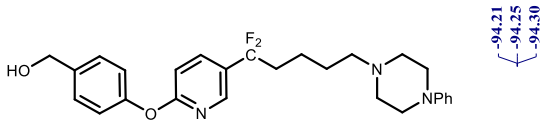
35a - ^{1}H NMR (400 MHz, $CDCl_3$)



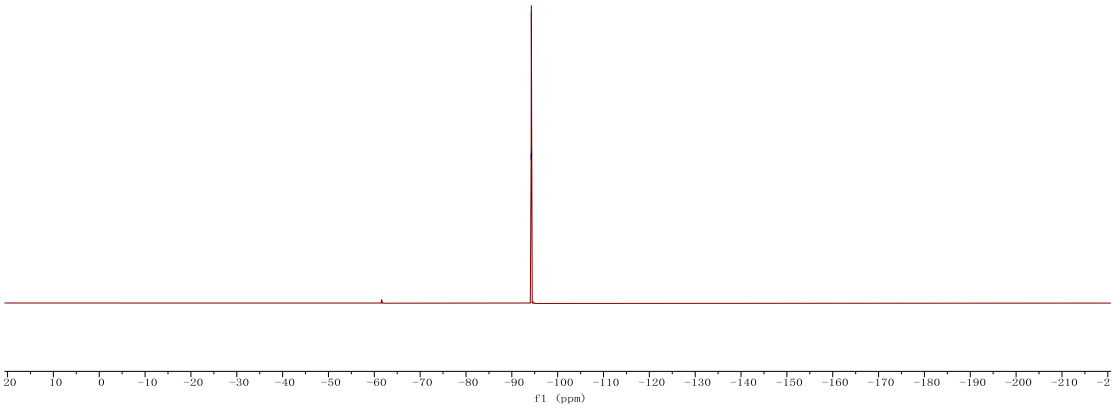


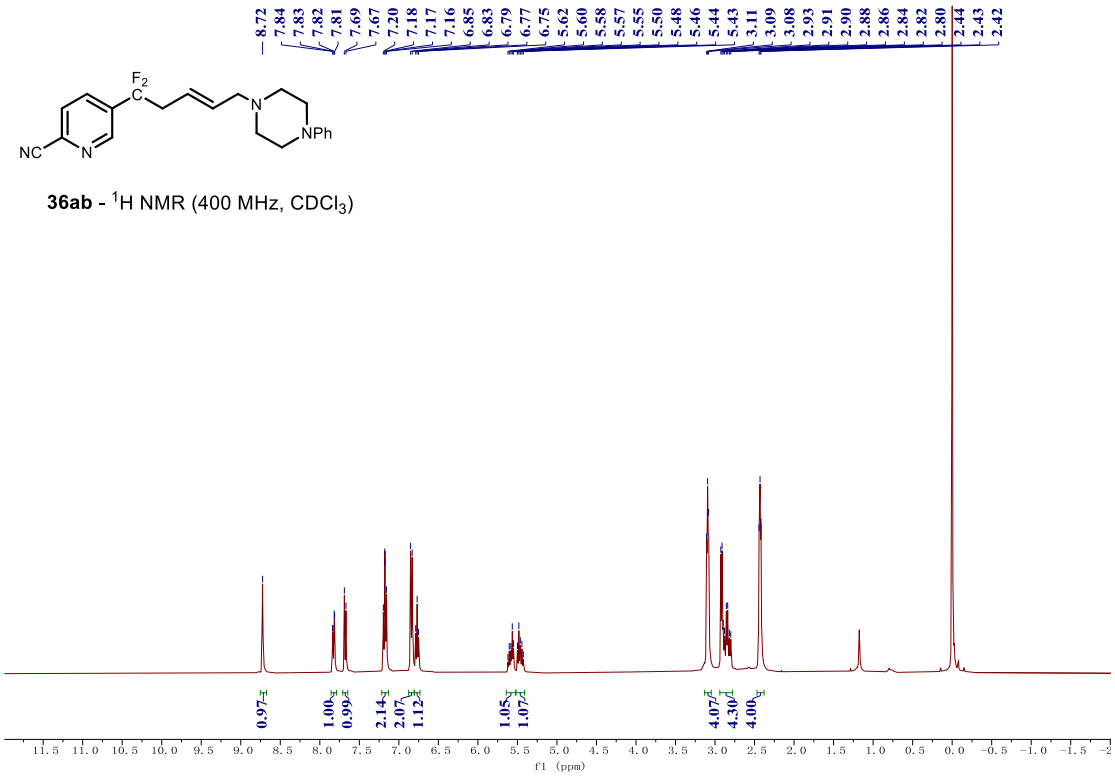
35a - ^{13}C NMR (101 MHz, $CDCl_3$)



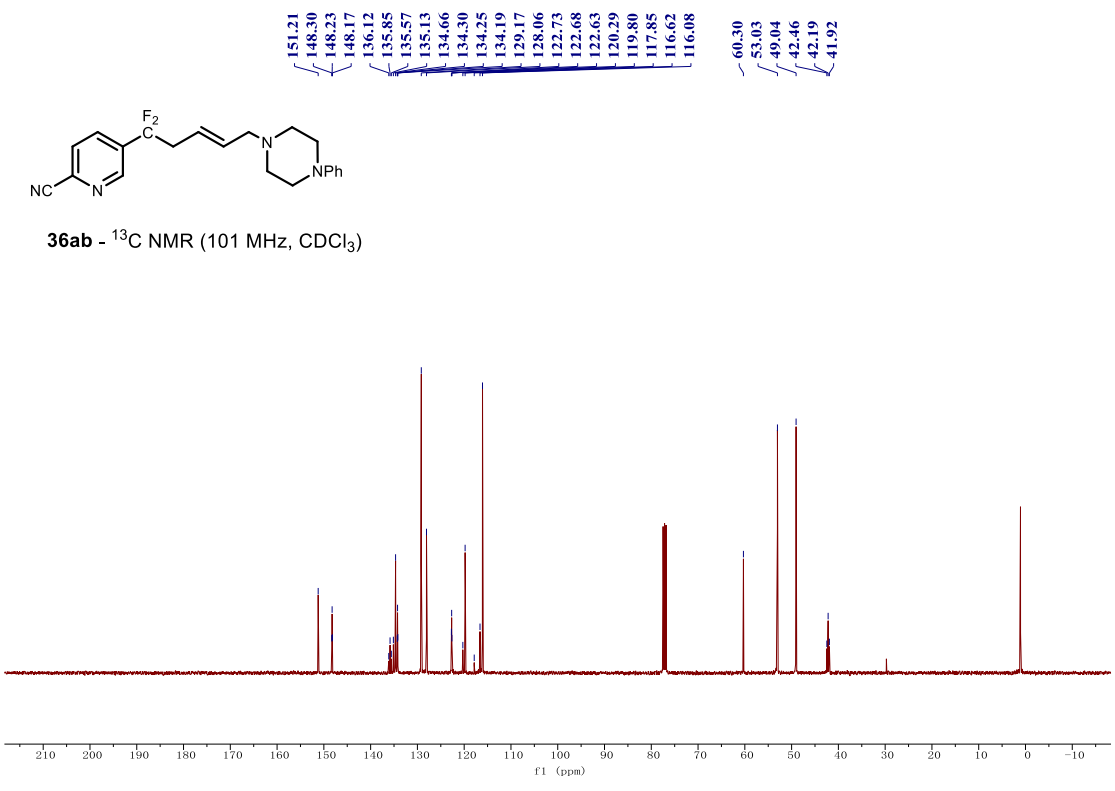


35a - ^{19}F NMR (376 MHz, $CDCl_3$)

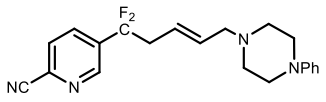




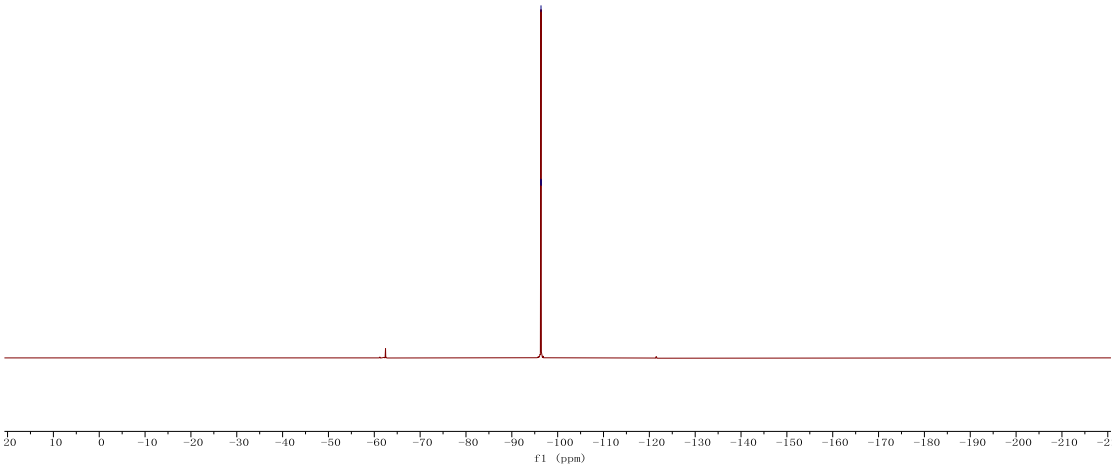
36ab - ^{1}H NMR (400 MHz, $CDCl_3$)

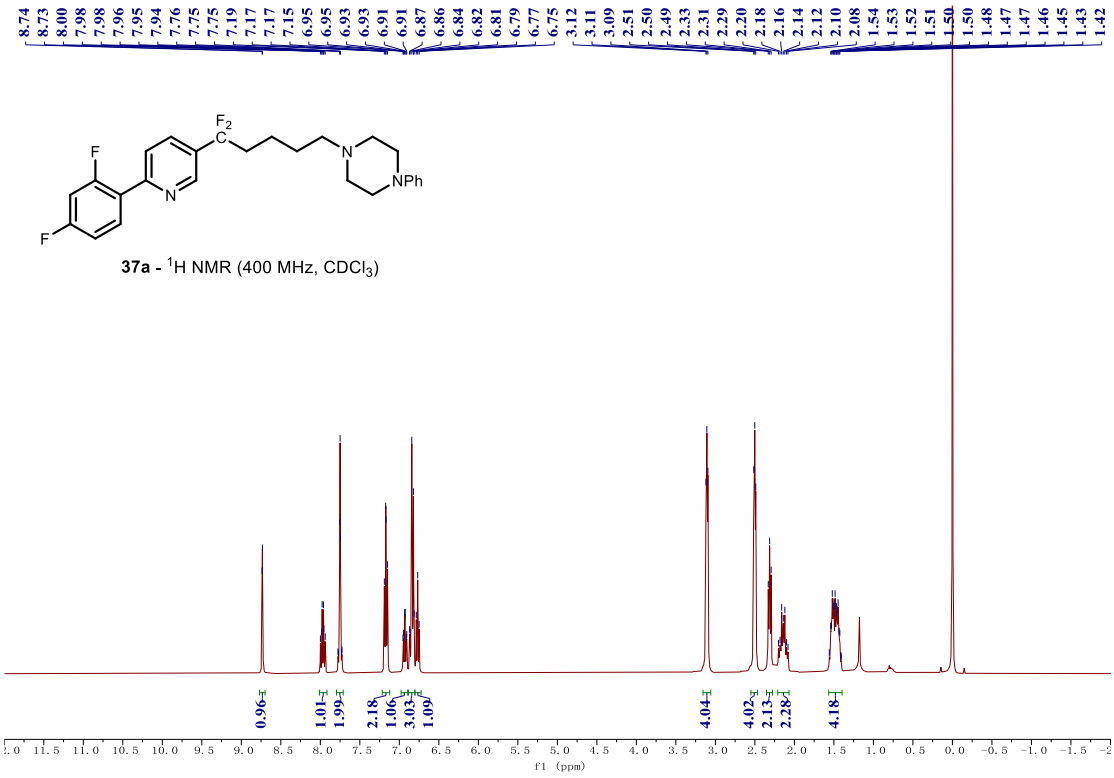


36ab - ^{13}C NMR (101 MHz, $CDCl_3$)

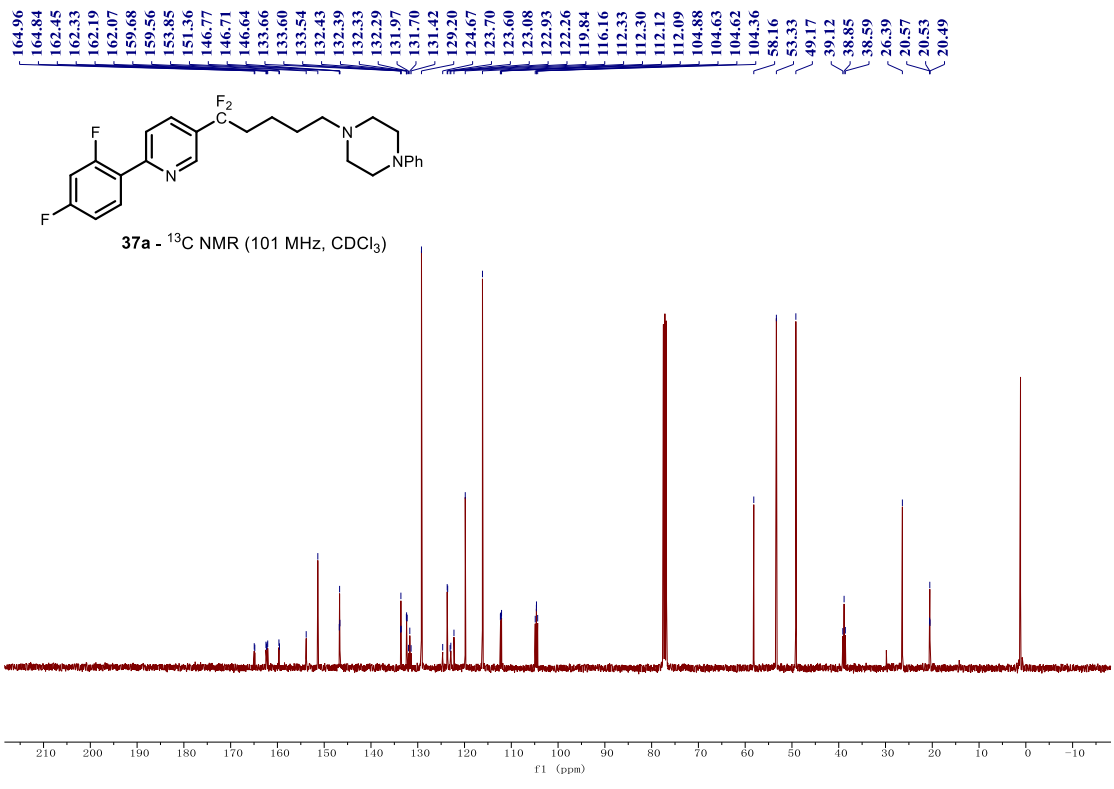


36ab - ^{19}F NMR (376 MHz, $CDCl_3$)

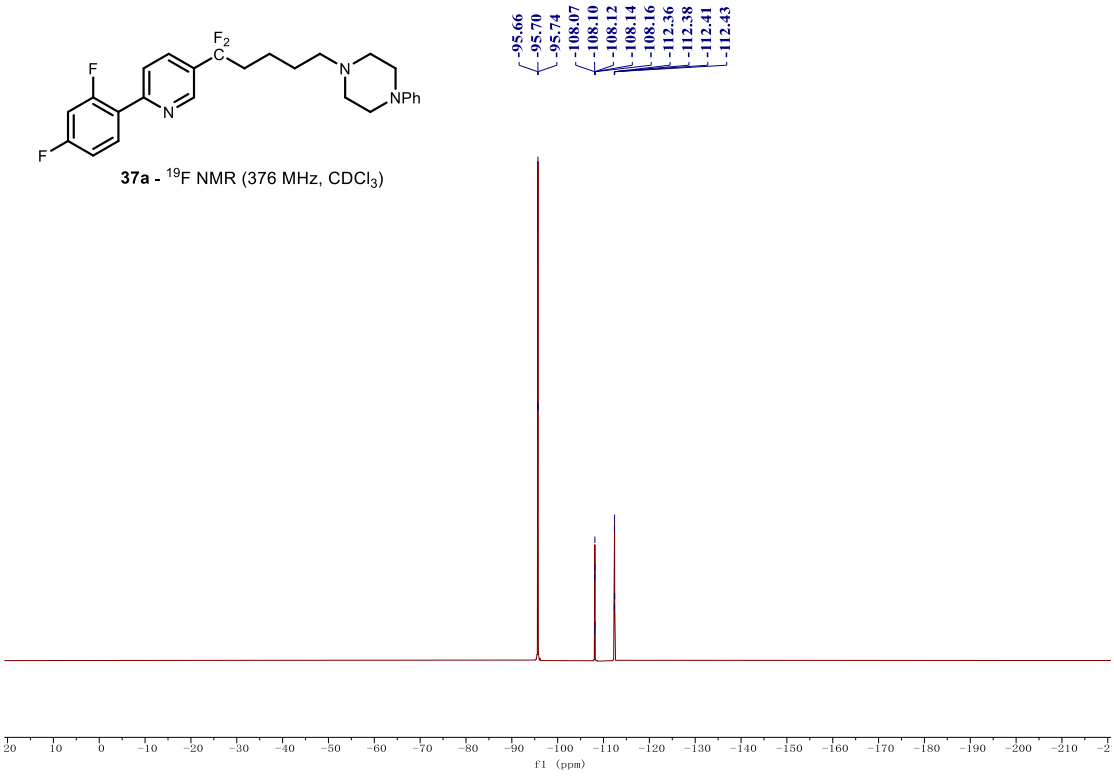




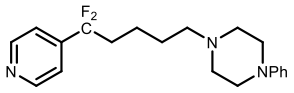
37a - ^{1}H NMR (400 MHz, $CDCl_3$)



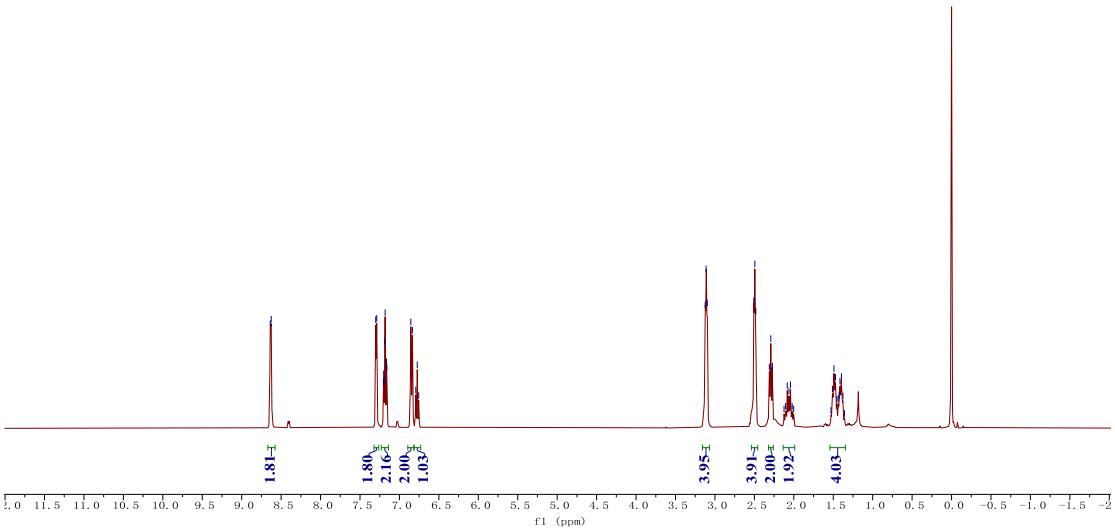
37a - ^{13}C NMR (101 MHz, $CDCl_3$)

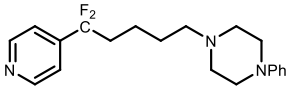


37a - ^{19}F NMR (376 MHz, $CDCl_3$)

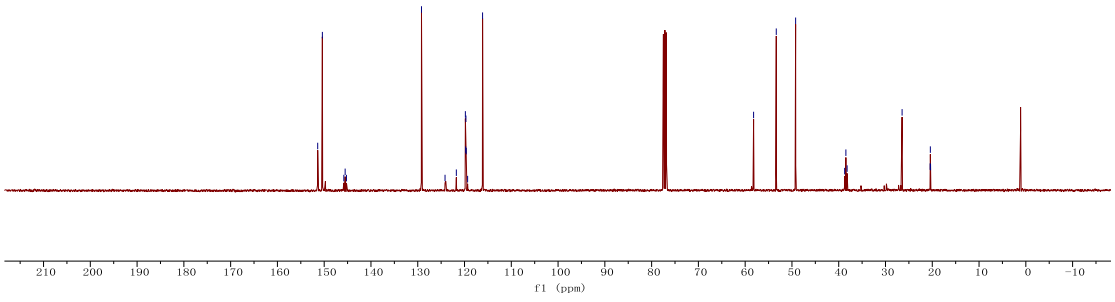


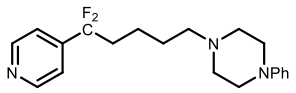
38a - ^{1}H NMR (400 MHz, $CDCl_3$)



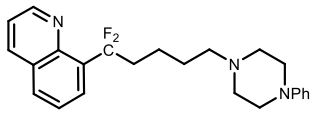


38a - ^{13}C NMR (101 MHz, $CDCl_3$)

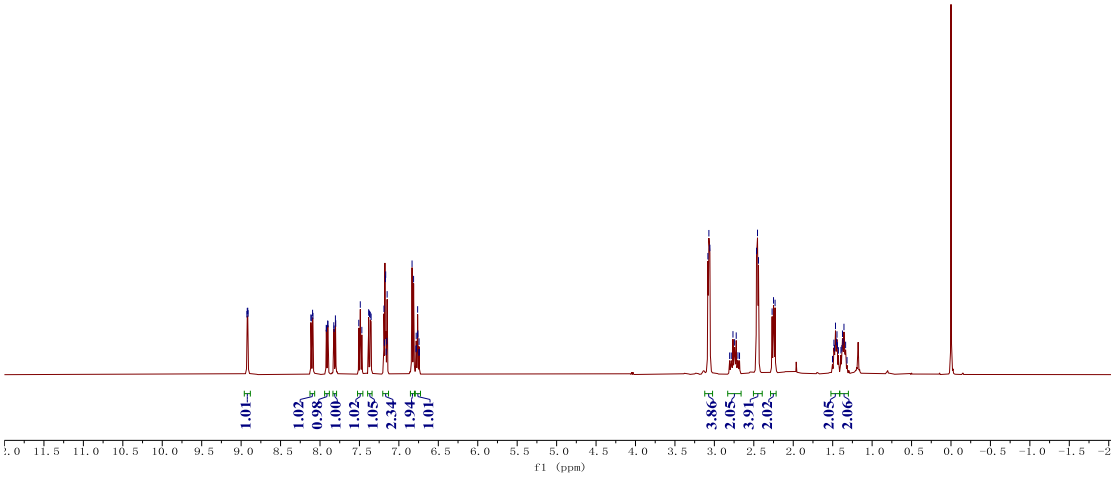


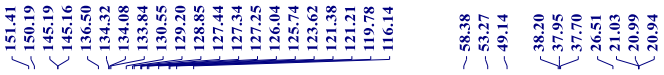


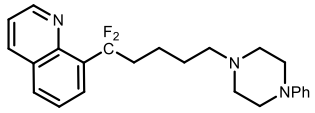
38a - ^{19}F NMR (376 MHz, $CDCl_3$)



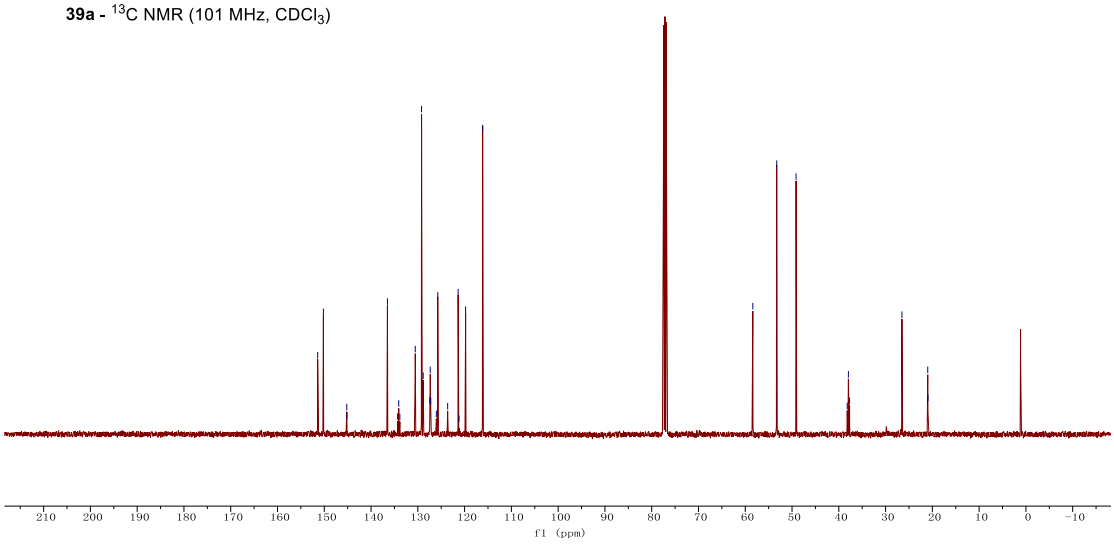
39a - ^{1}H NMR (400 MHz, $CDCl_3$)

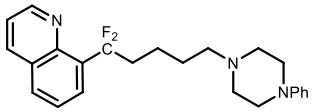






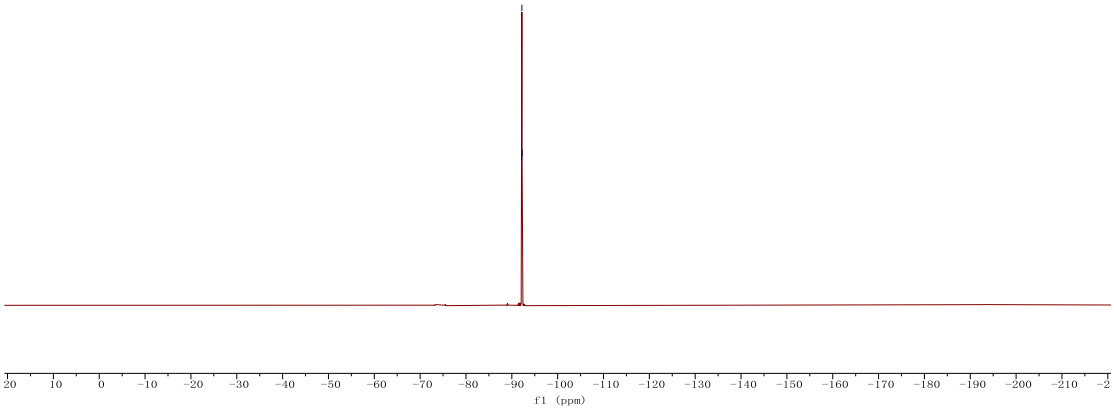
39a - ^{13}C NMR (101 MHz, $CDCl_3$)

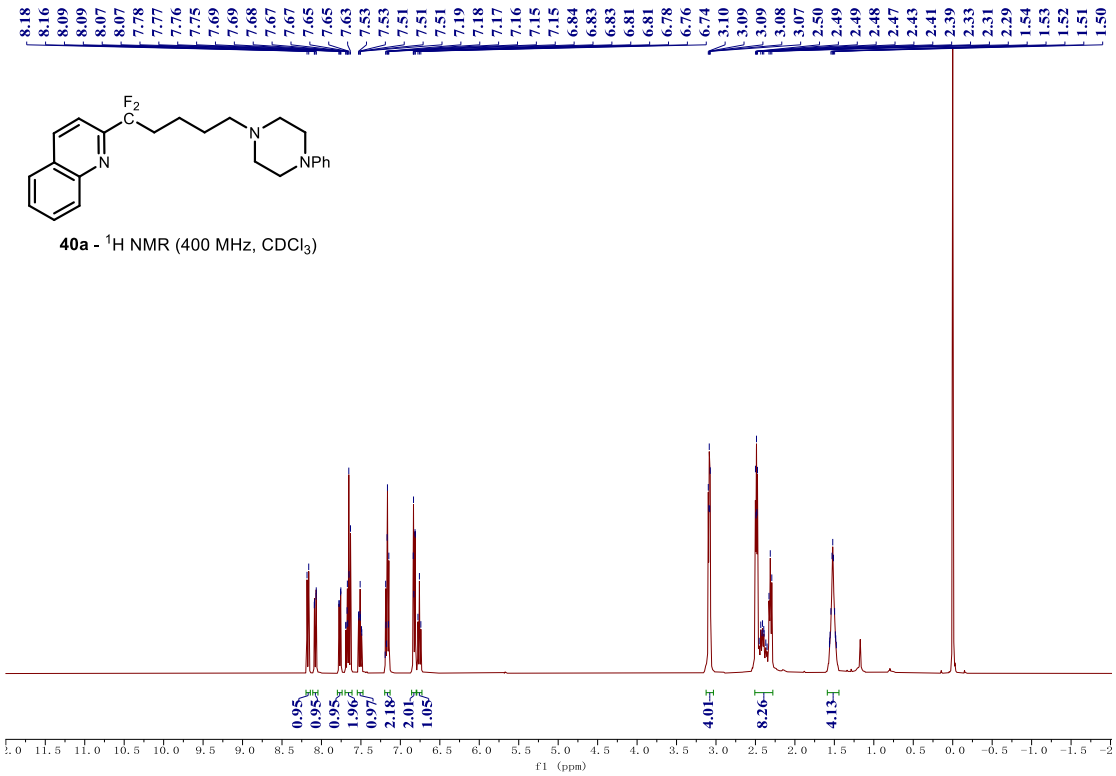




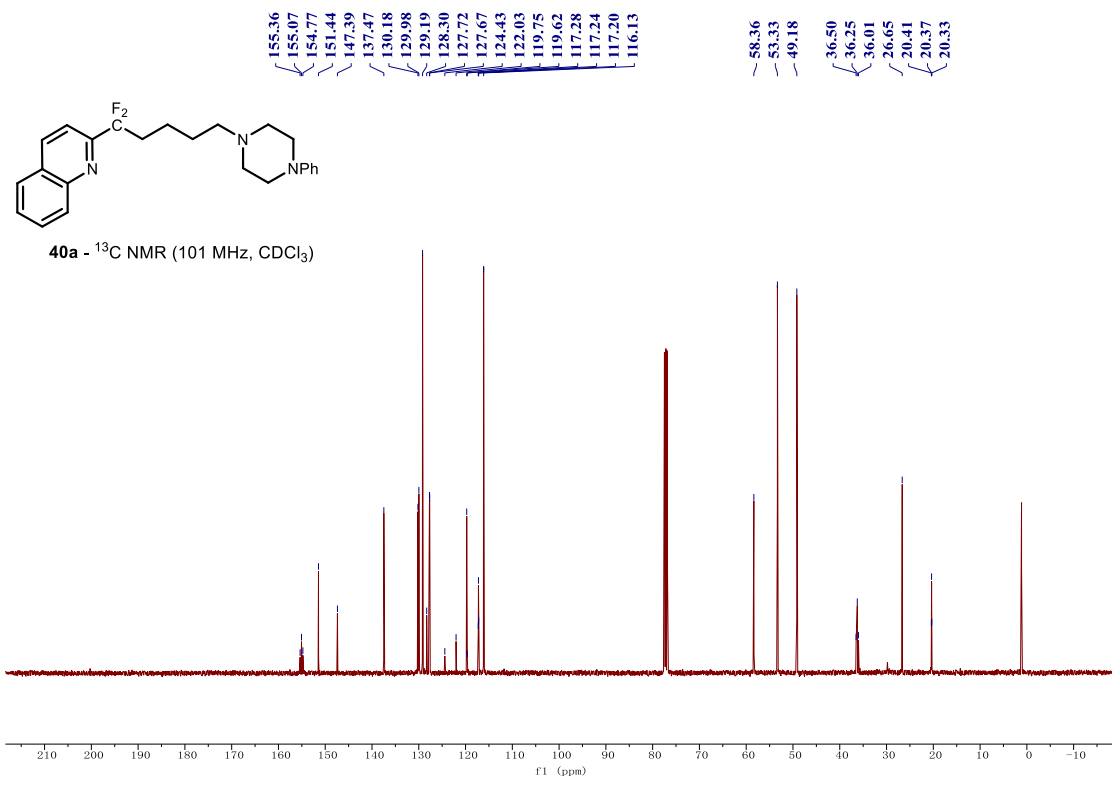
-92.15
-92.19
-92.24

39a - ^{19}F NMR (376 MHz, $CDCl_3$)

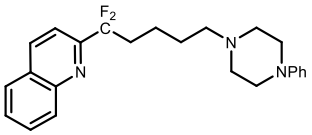




40a - ^{1}H NMR (400 MHz, $CDCl_3$)

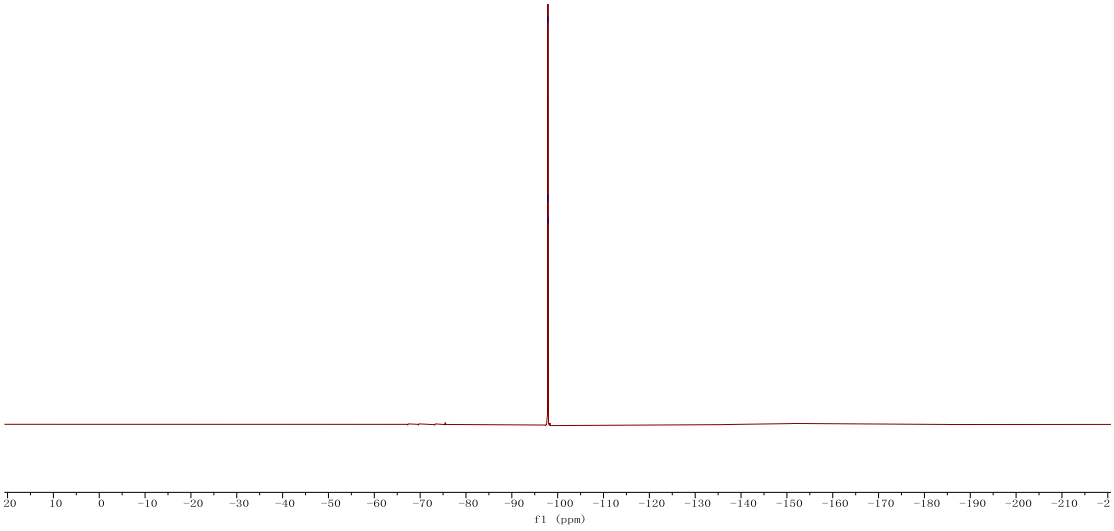


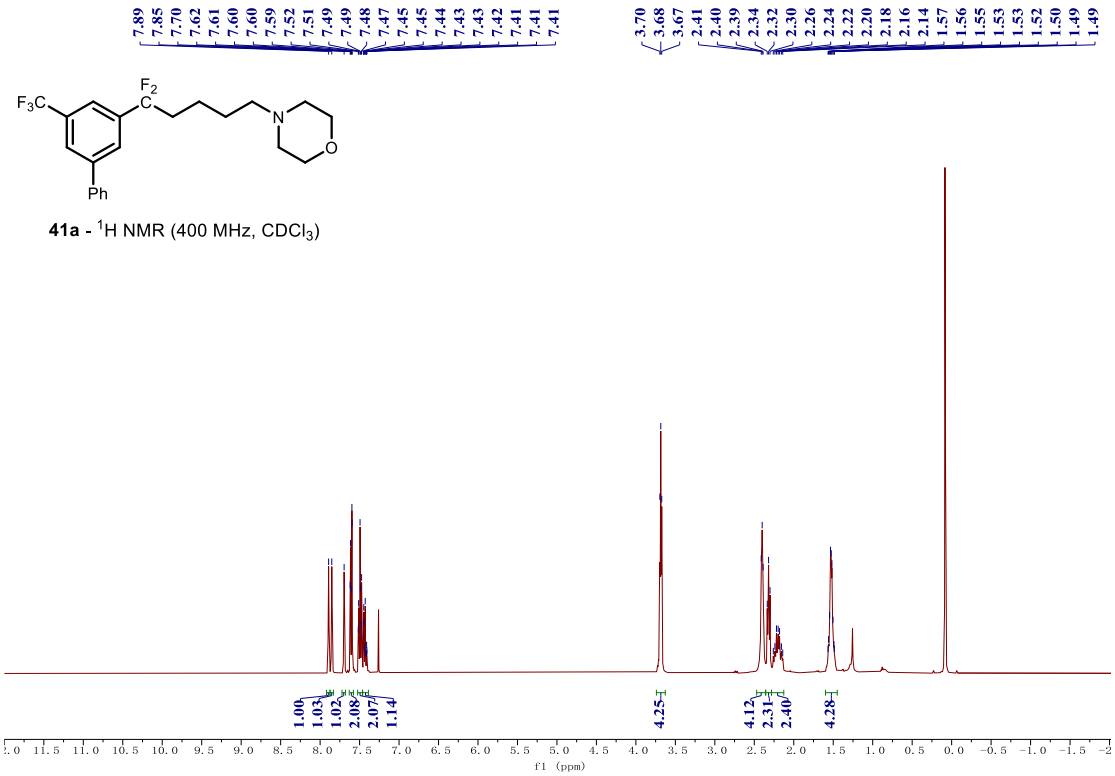
40a - ^{13}C NMR (101 MHz, $CDCl_3$)



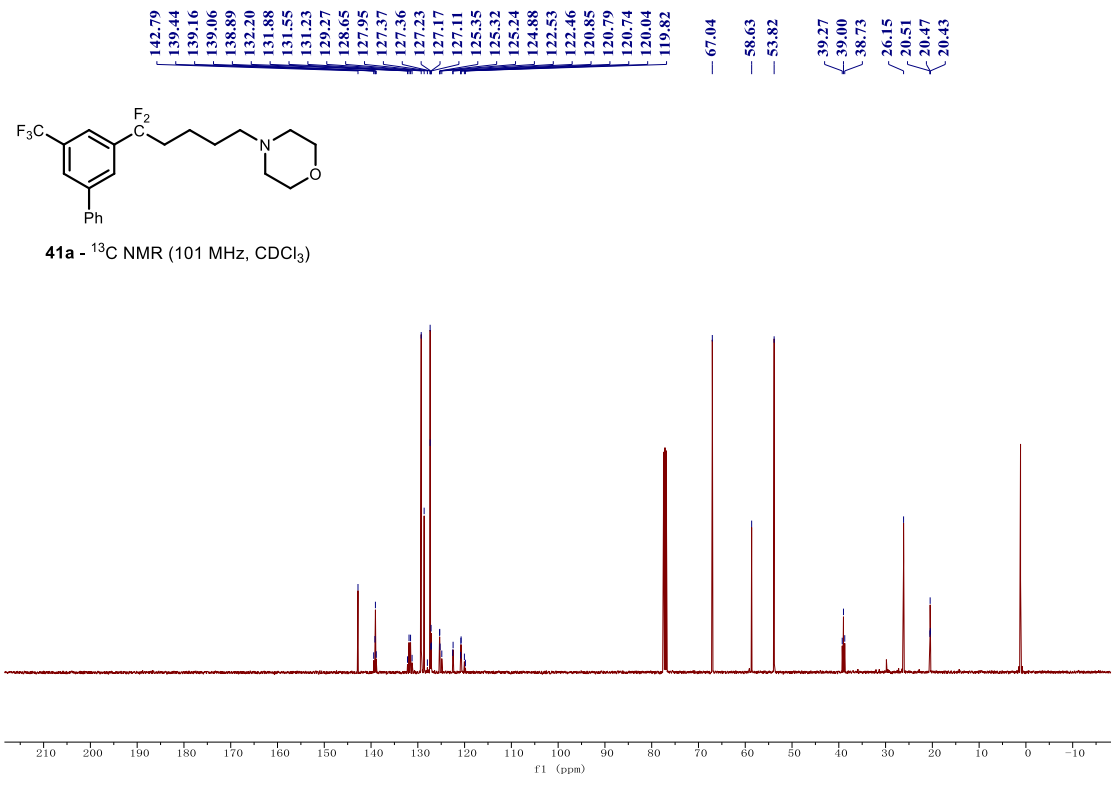
-97.83
-97.88
-97.93

40a - ^{19}F NMR (376 MHz, $CDCl_3$)

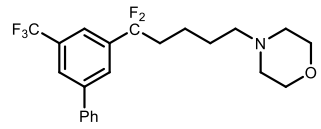




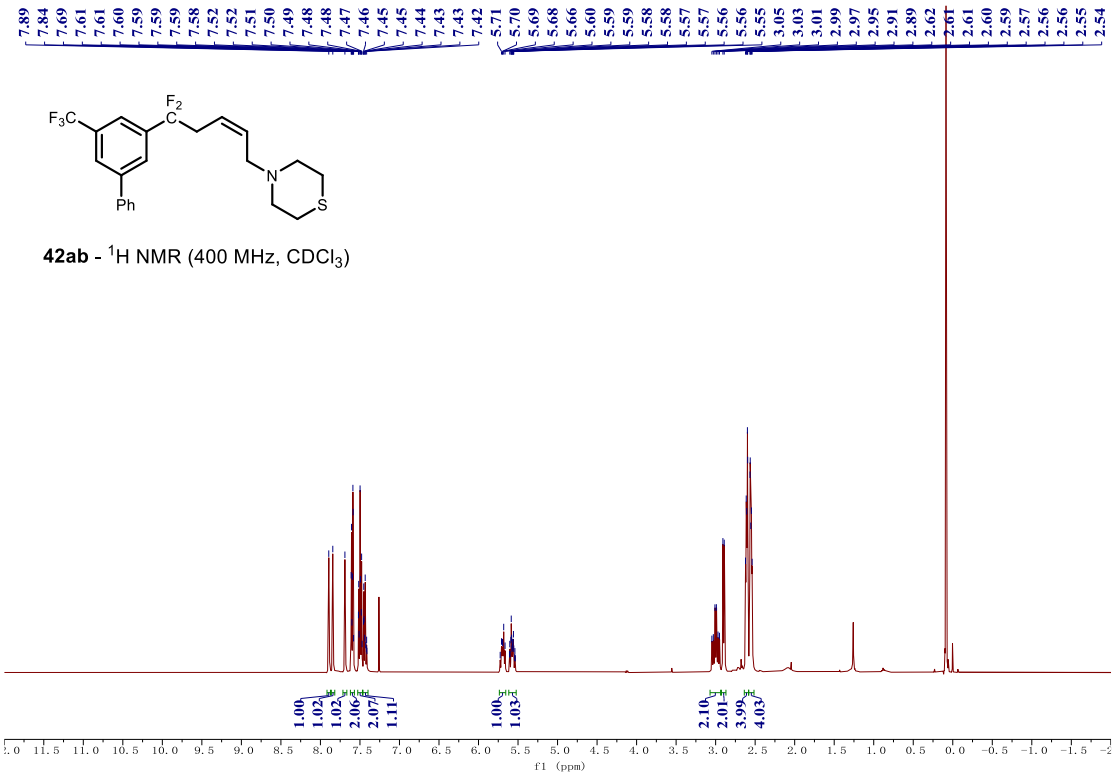
41a - ^{1}H NMR (400 MHz, $CDCl_3$)



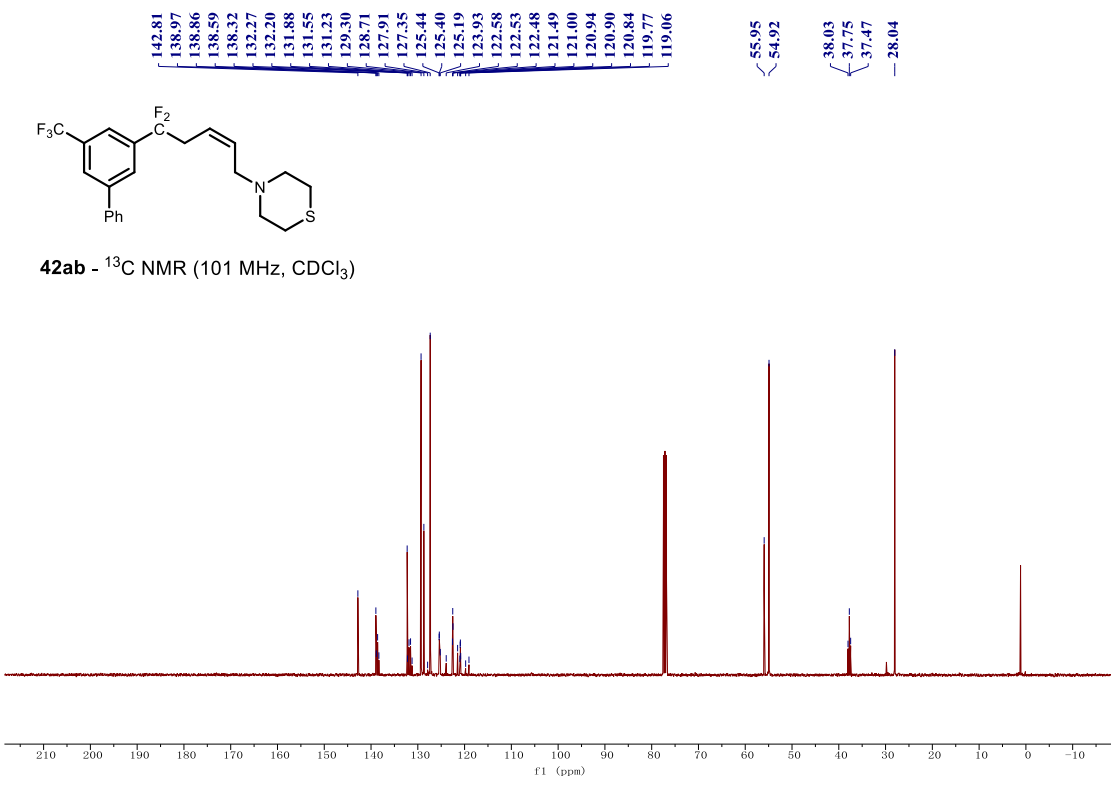
41a - ^{13}C NMR (101 MHz, $CDCl_3$)



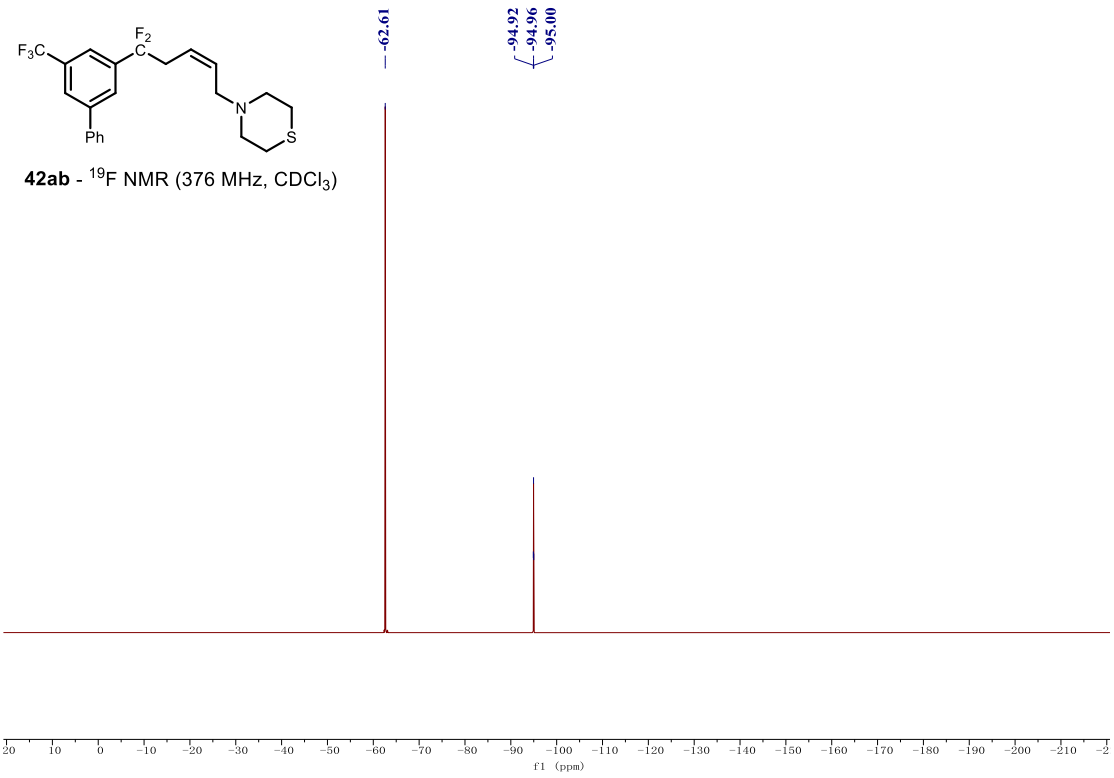
41a - ^{19}F NMR (376 MHz, $CDCl_3$)



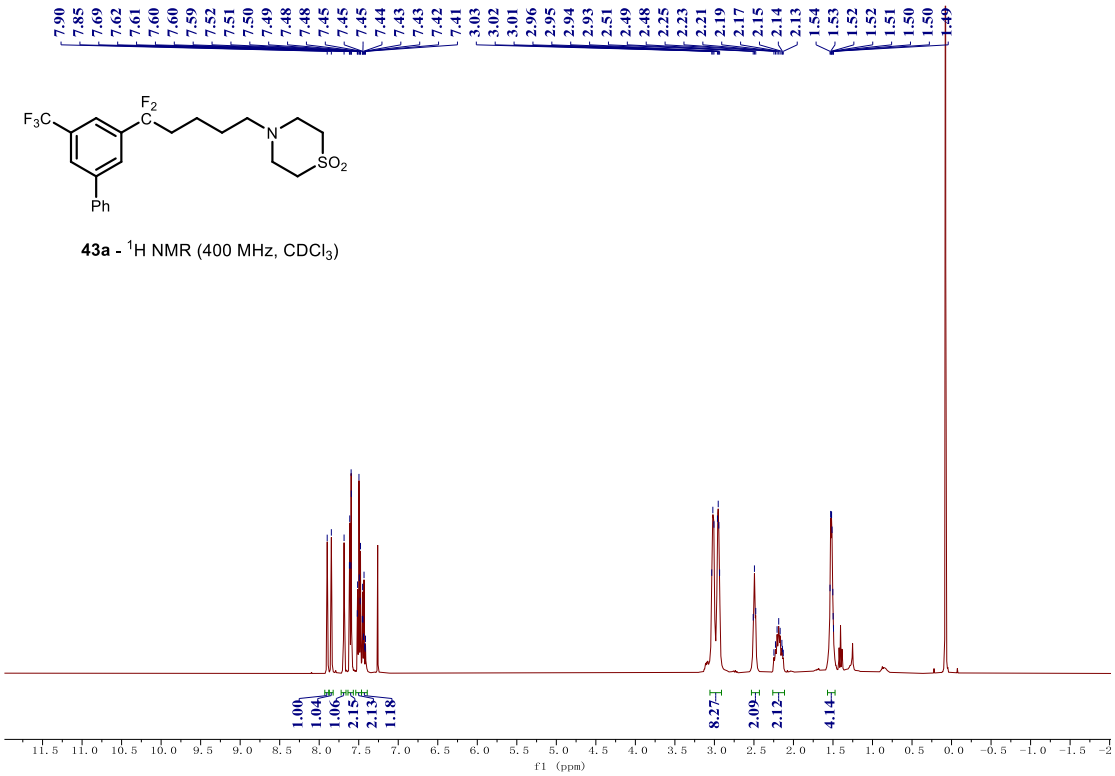
42ab - ^{1}H NMR (400 MHz, $CDCl_3$)



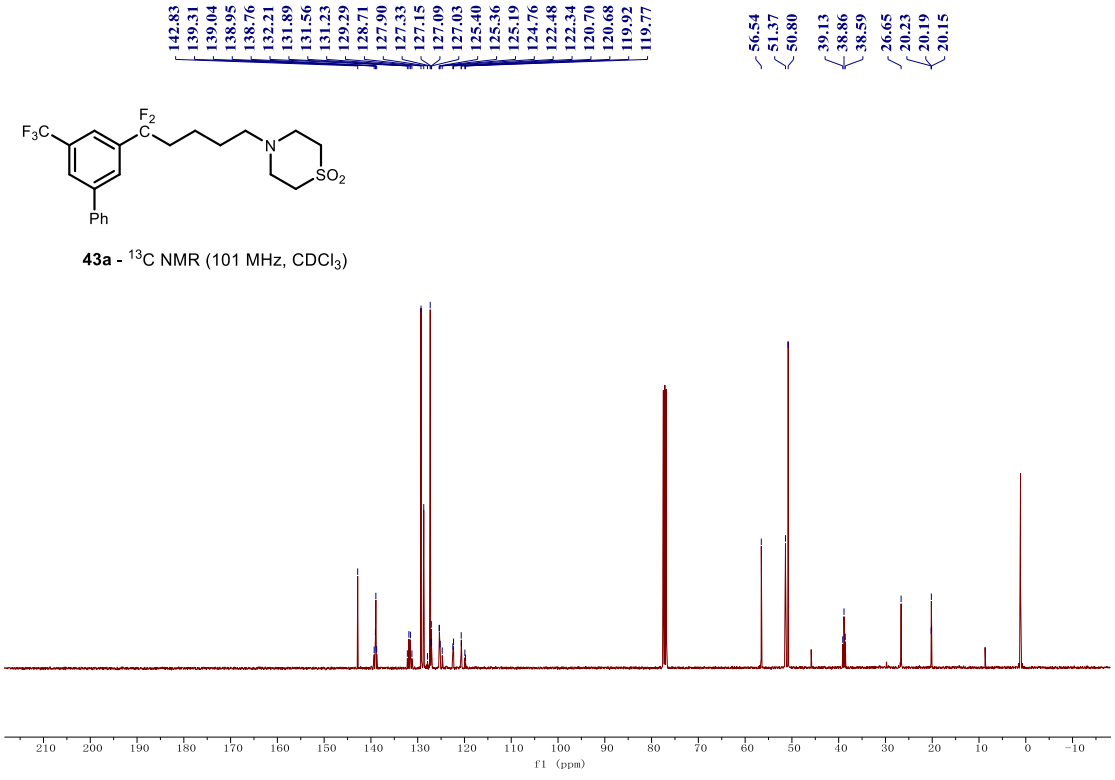
42ab - ^{13}C NMR (101 MHz, $CDCl_3$)



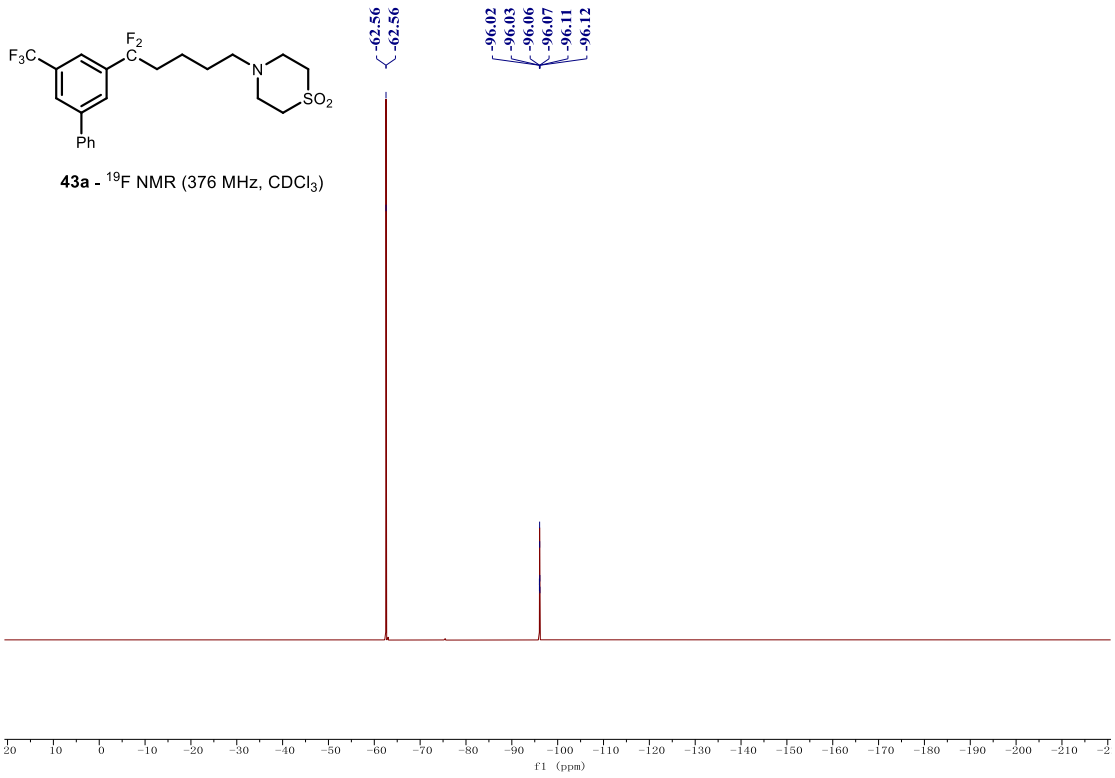
42ab - ^{19}F NMR (376 MHz, $CDCl_3$)



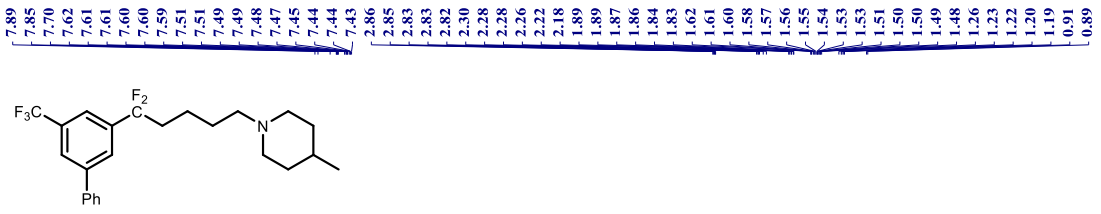
43a - ^{1}H NMR (400 MHz, $CDCl_3$)



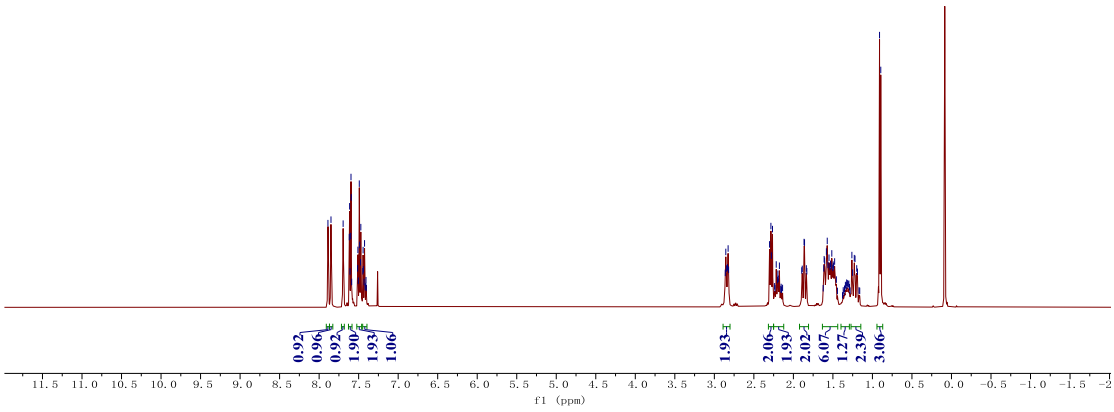
43a - ^{13}C NMR (101 MHz, $CDCl_3$)

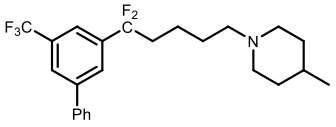


43a - ^{19}F NMR (376 MHz, $CDCl_3$)

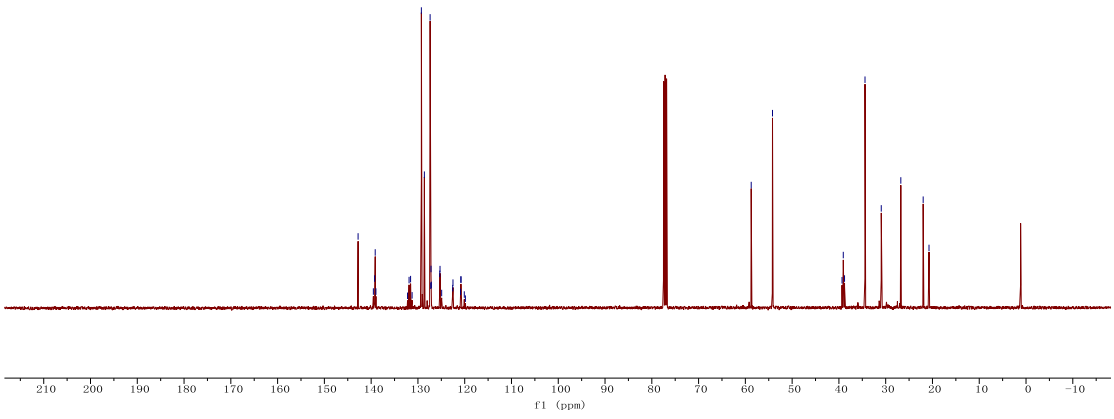


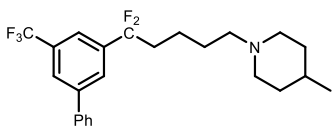
44a - ^{1}H NMR (400 MHz, $CDCl_3$)



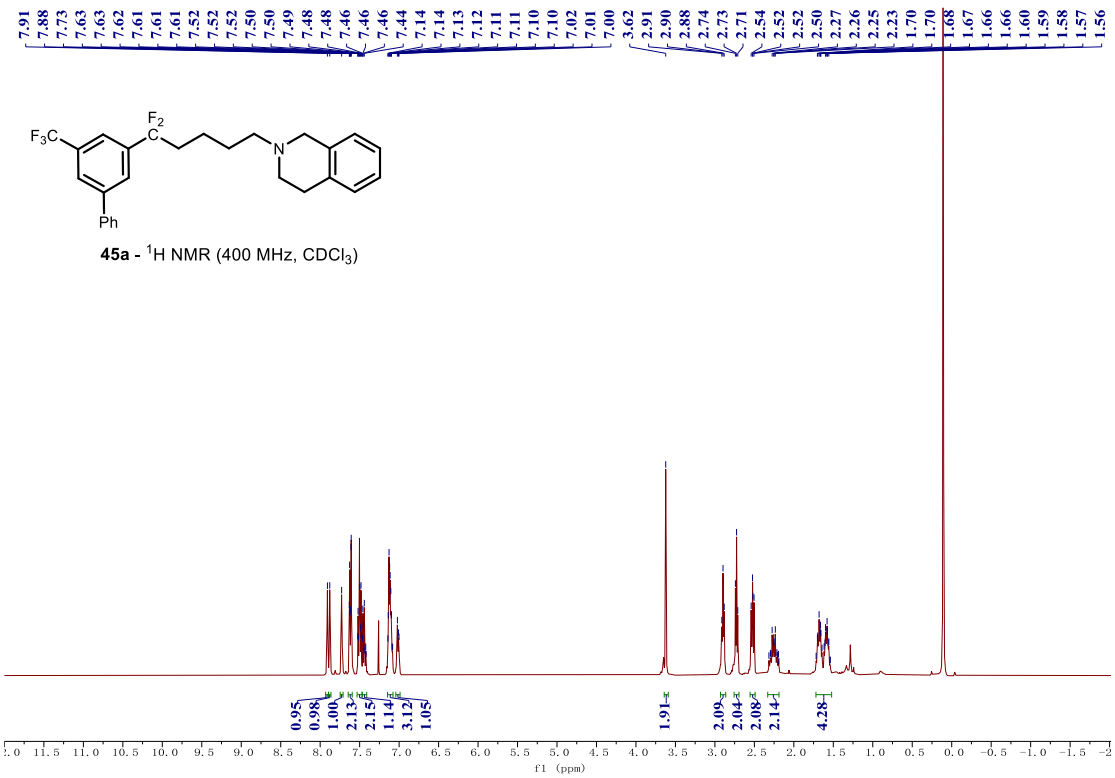


44a - ^{13}C NMR (101 MHz, $CDCl_3$)

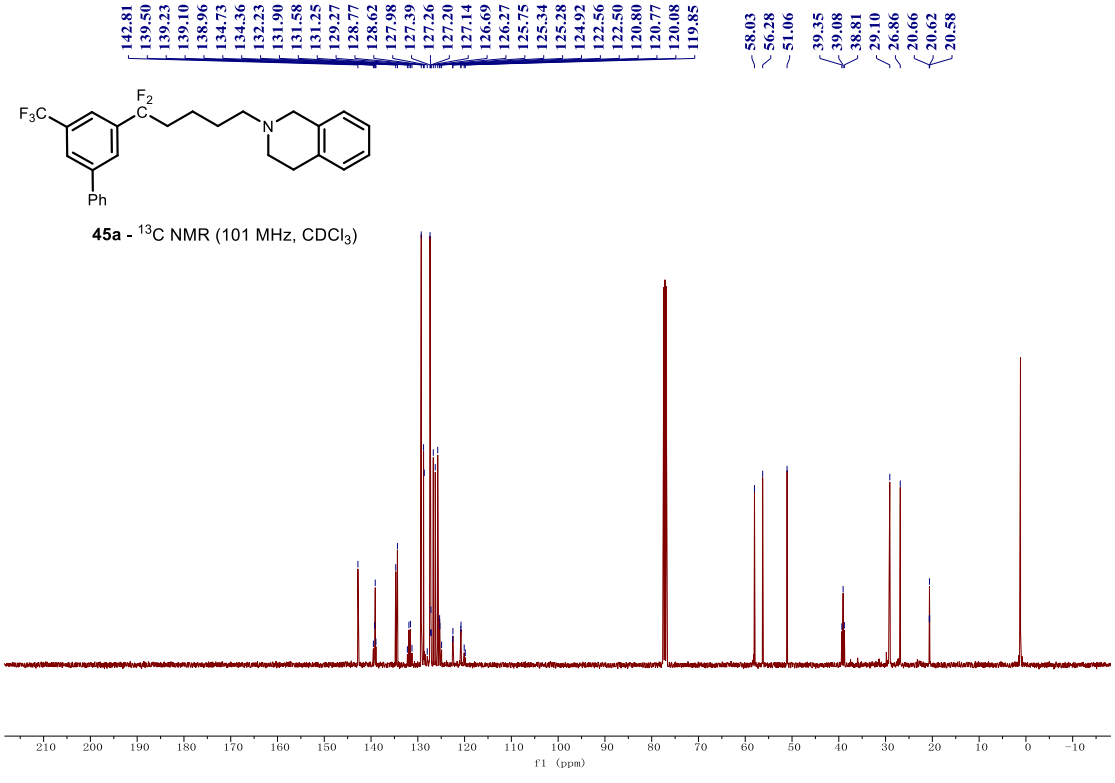




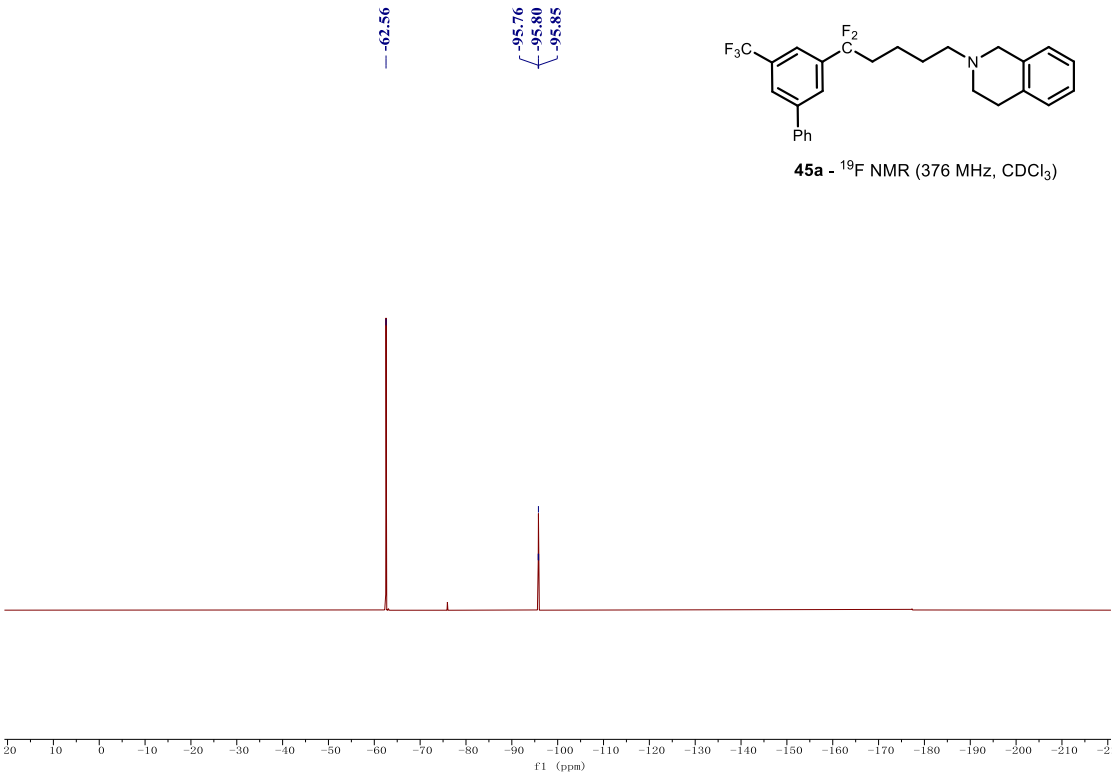
44a - ^{19}F NMR (376 MHz, $CDCl_3$)



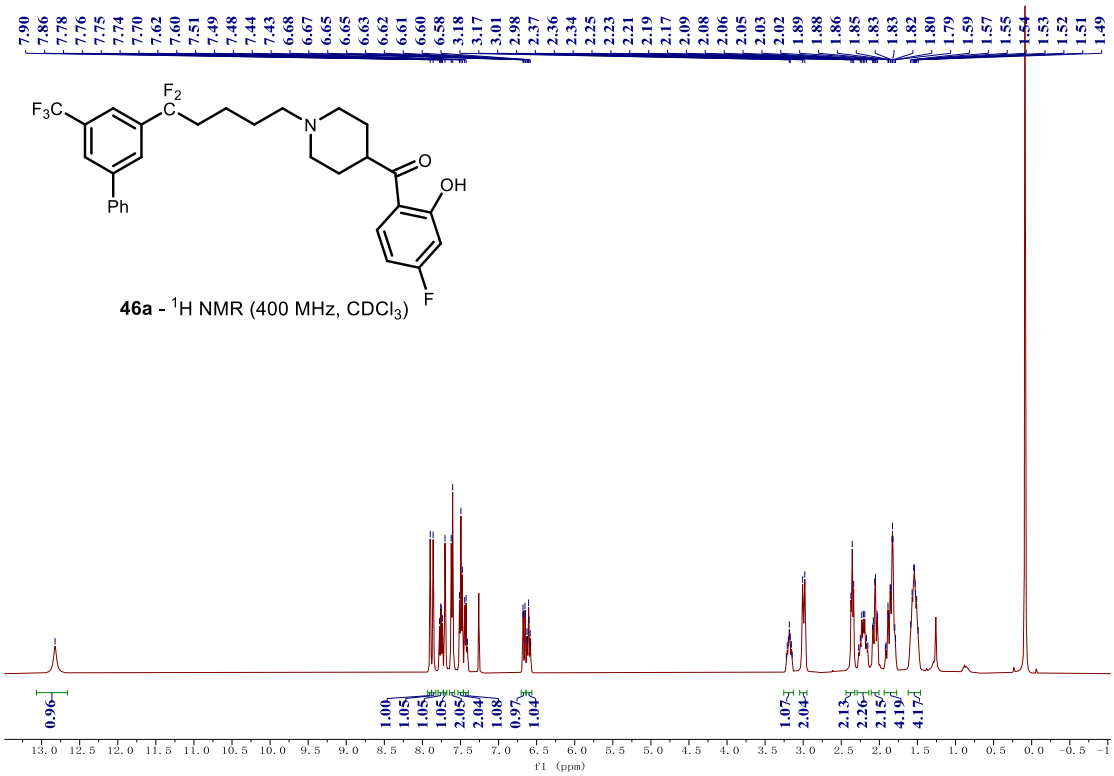
45a - ^{1}H NMR (400 MHz, $CDCl_3$)



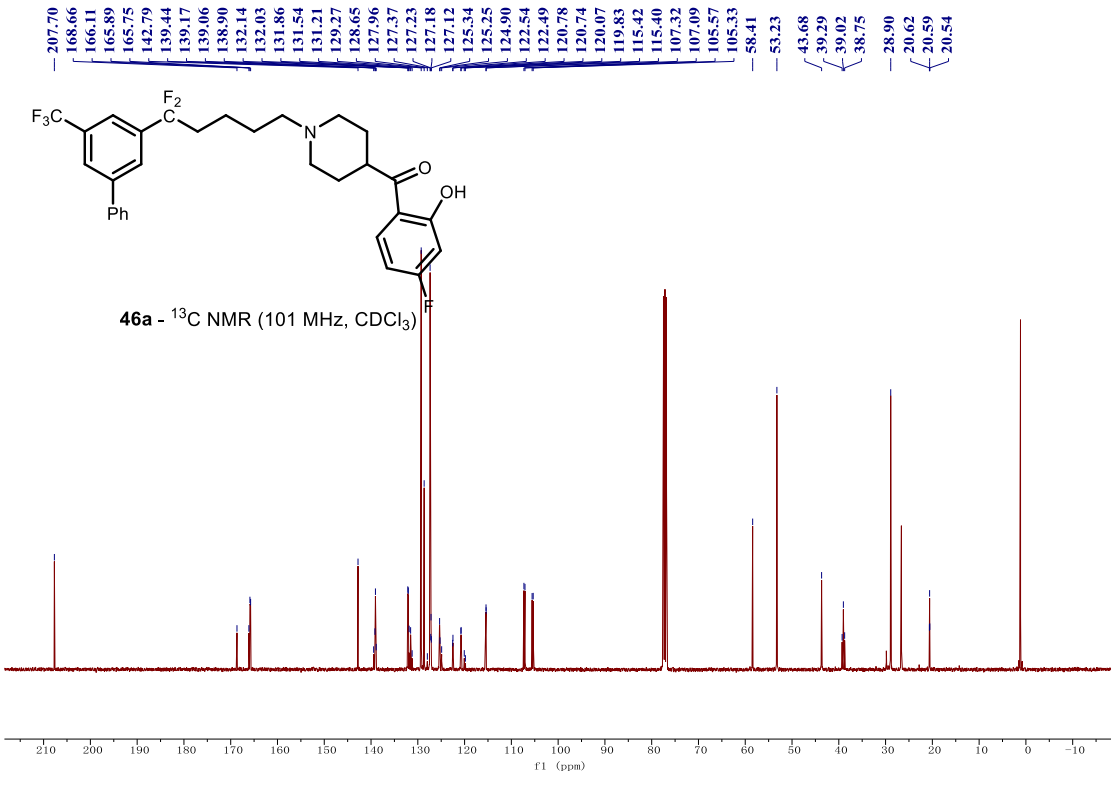
45a - ^{13}C NMR (101 MHz, $CDCl_3$)



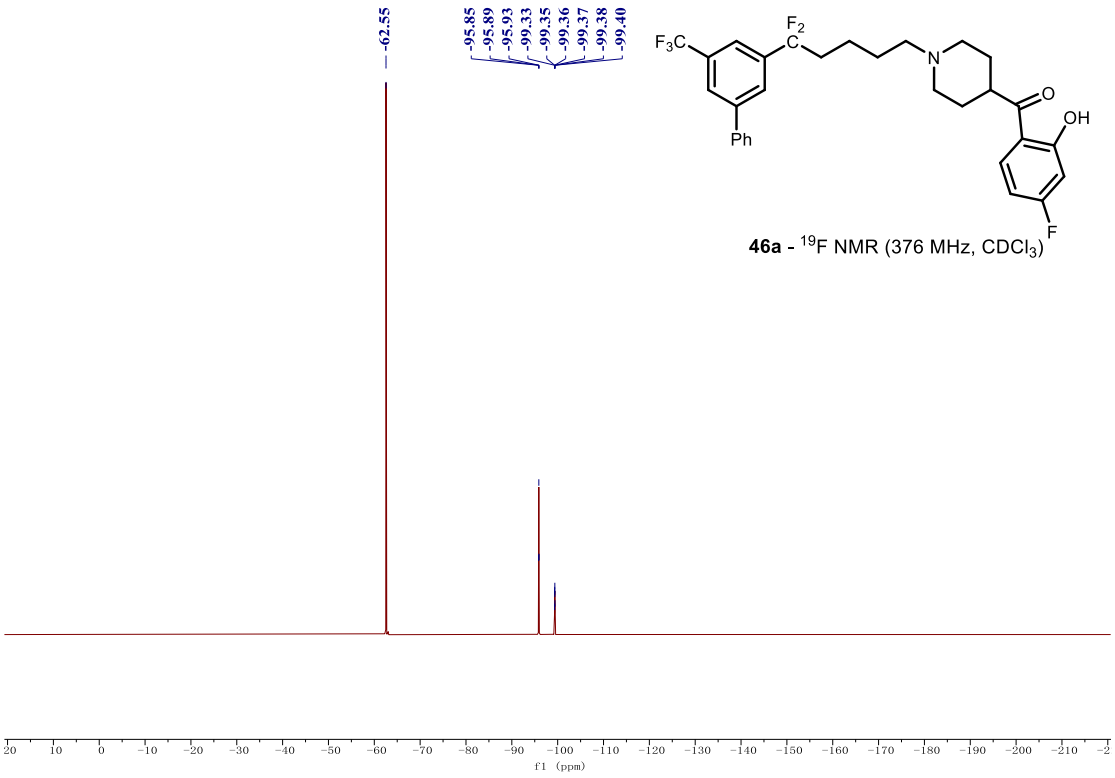
45a - ^{19}F NMR (376 MHz, $CDCl_3$)



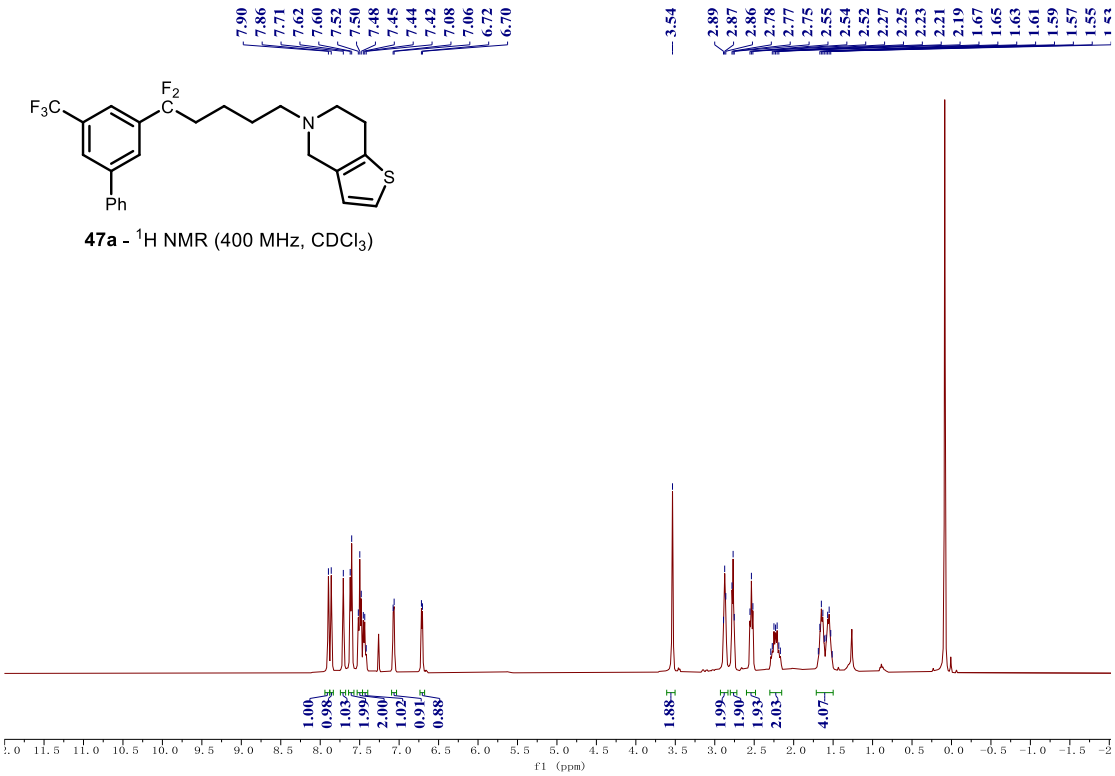
46a - ^{1}H NMR (400 MHz, $CDCl_3$)



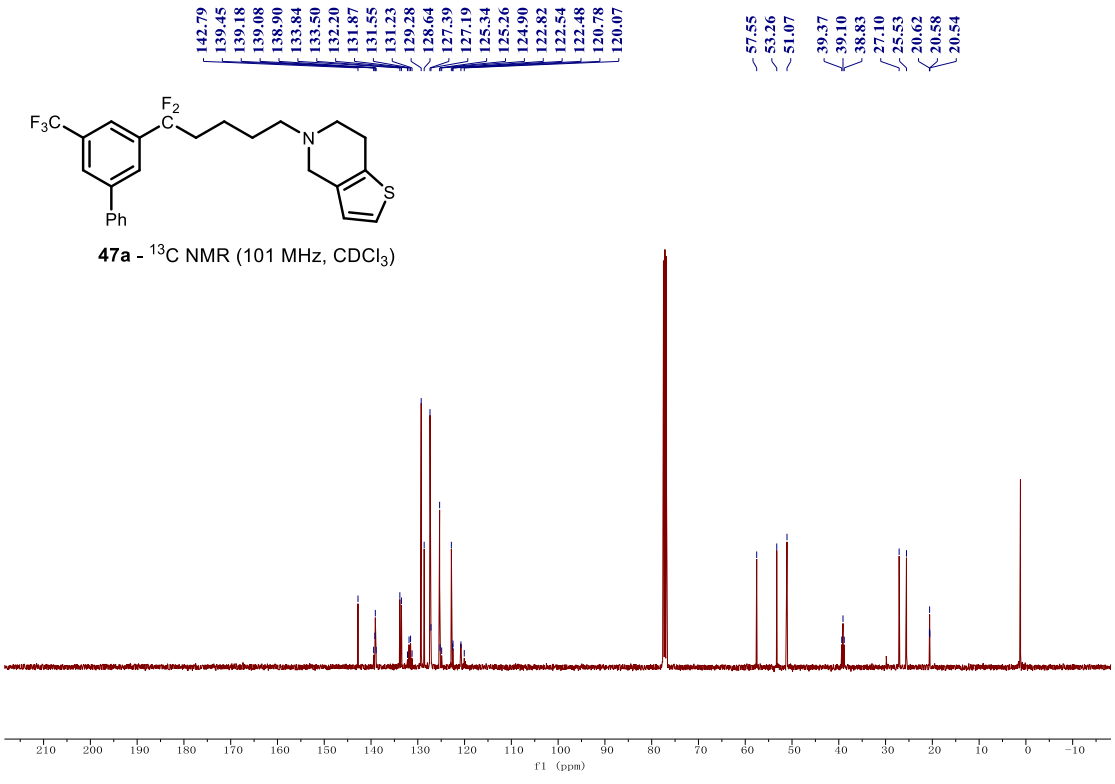
46a - ^{13}C NMR (101 MHz, $CDCl_3$)



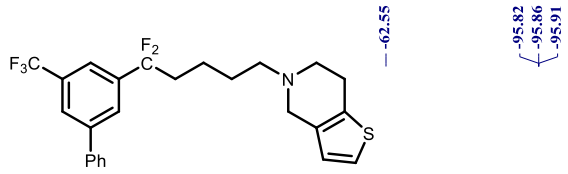
46a - ^{19}F NMR (376 MHz, $CDCl_3$)



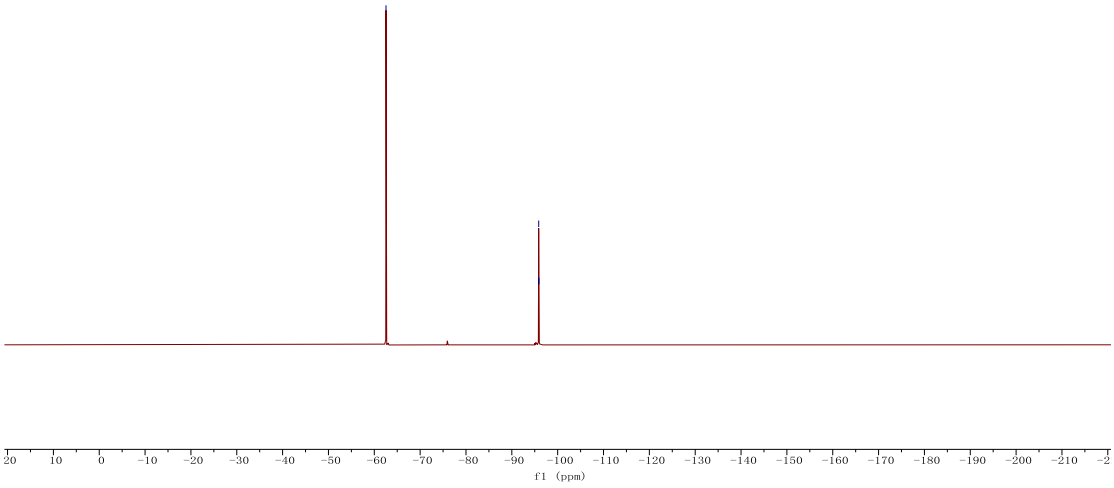
47a - ^{1}H NMR (400 MHz, $CDCl_3$)

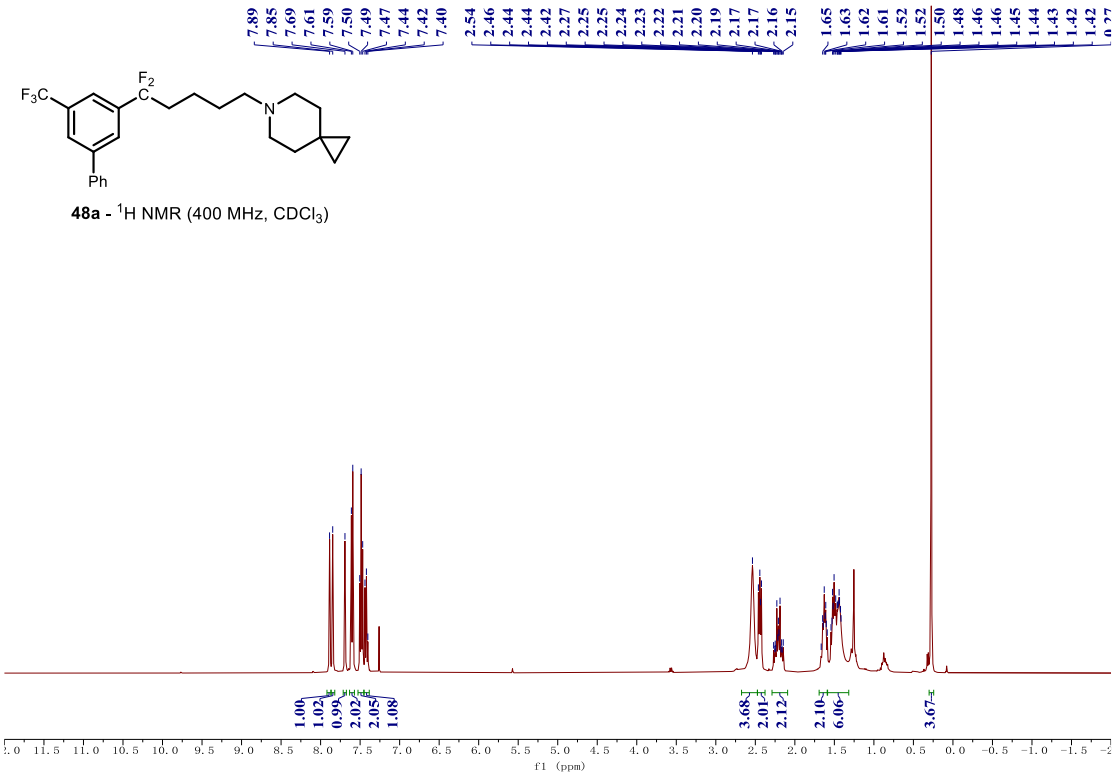


47a - ^{13}C NMR (101 MHz, $CDCl_3$)

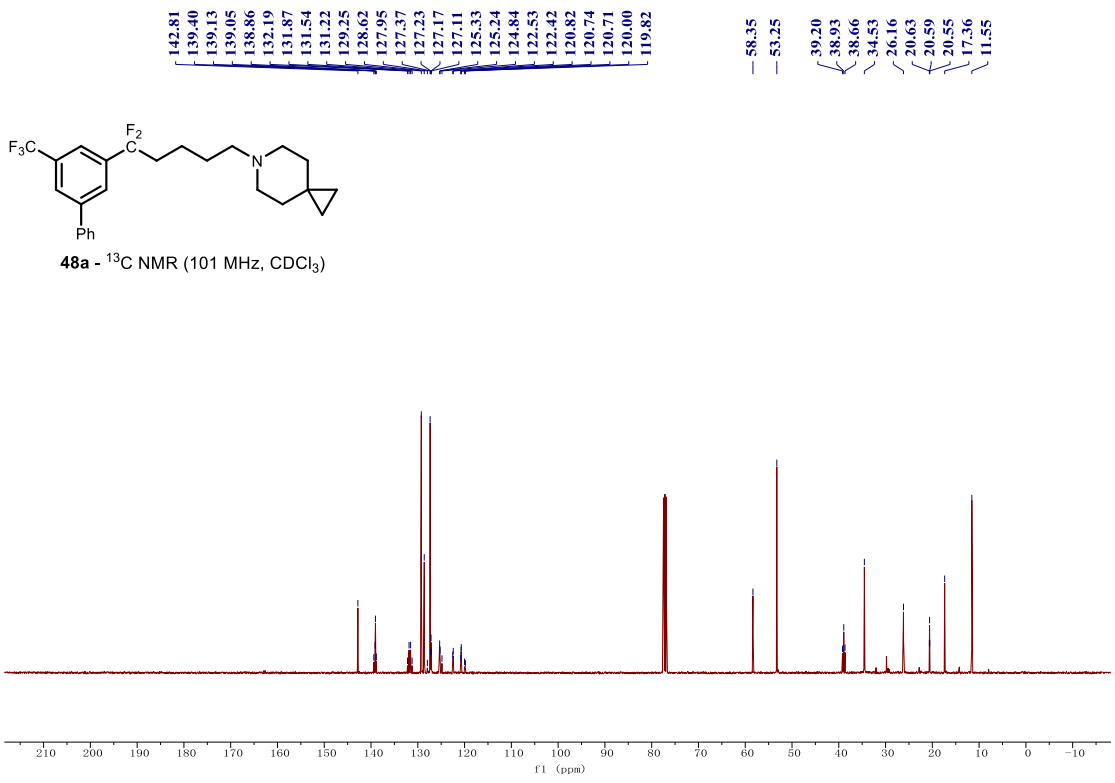


47a - ^{19}F NMR (376 MHz, $CDCl_3$)

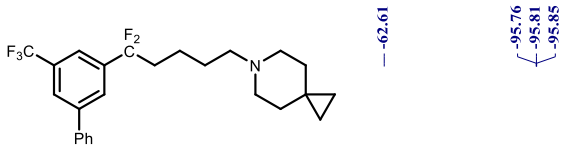




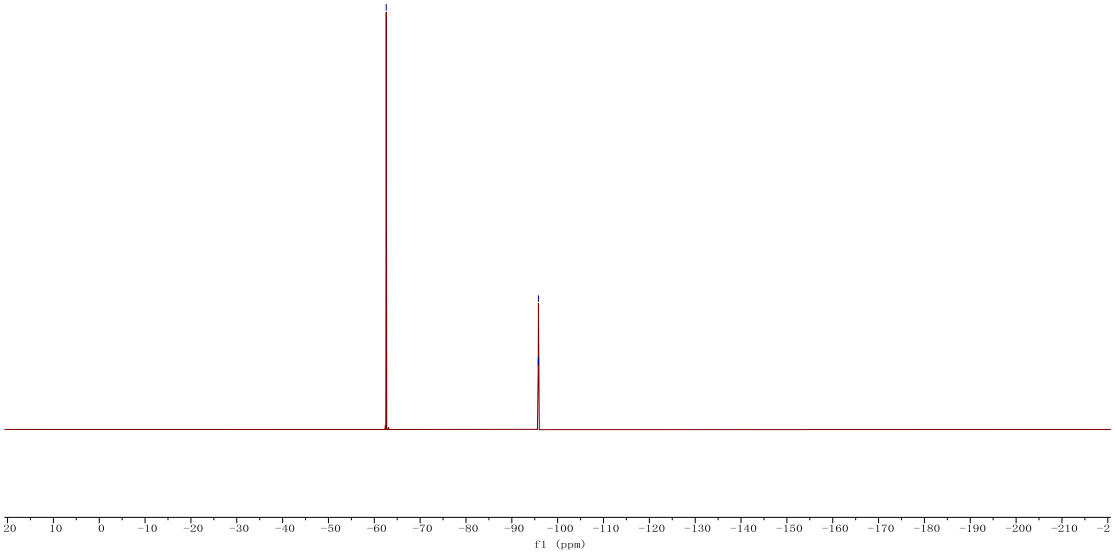
48a - ^{1}H NMR (400 MHz, $CDCl_3$)

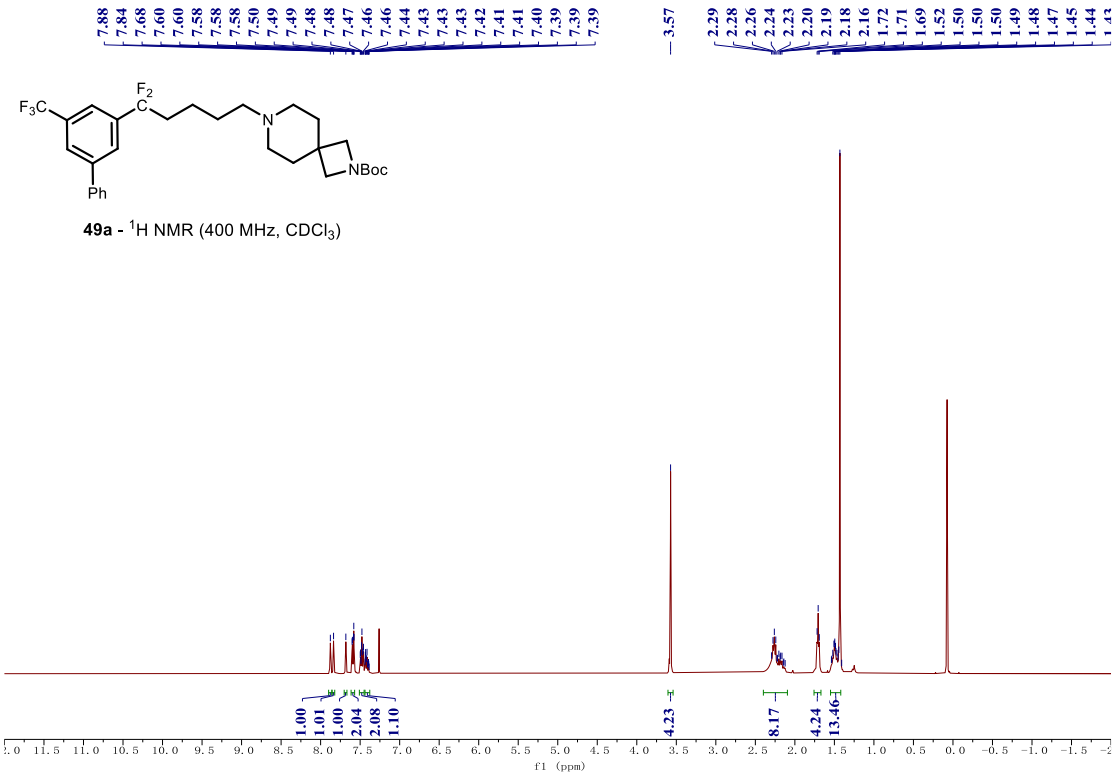


48a - ^{13}C NMR (101 MHz, $CDCl_3$)

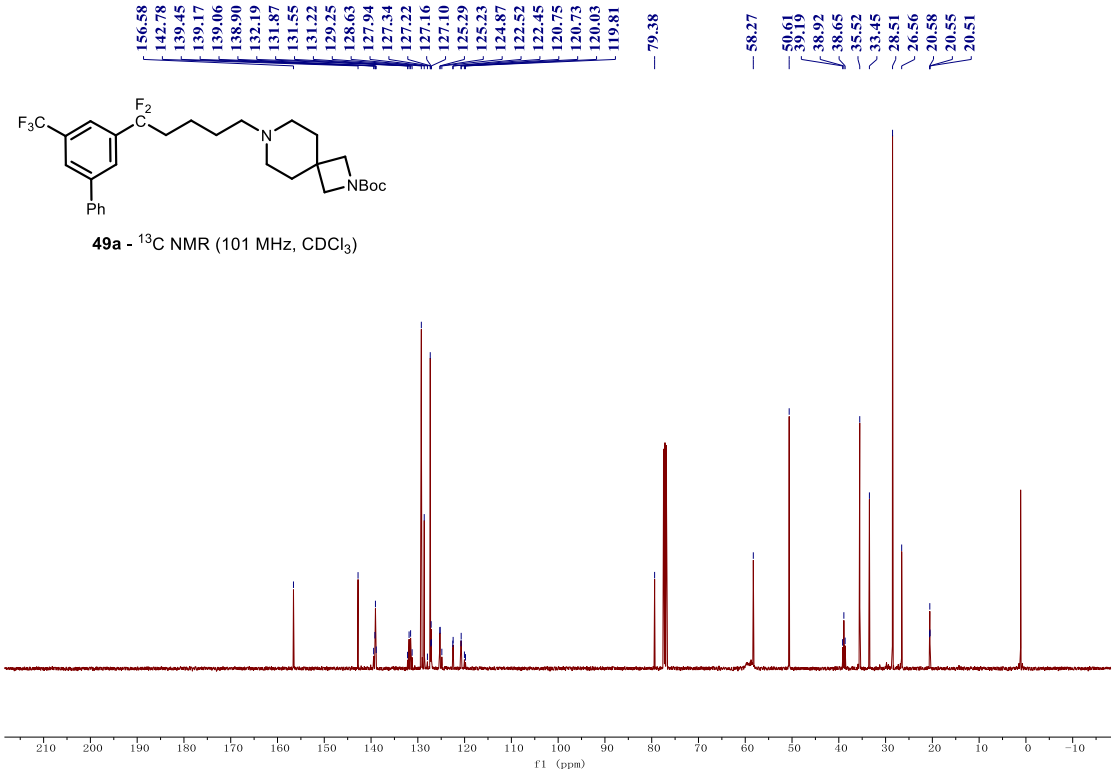


48a - ^{19}F NMR (376 MHz, $CDCl_3$)

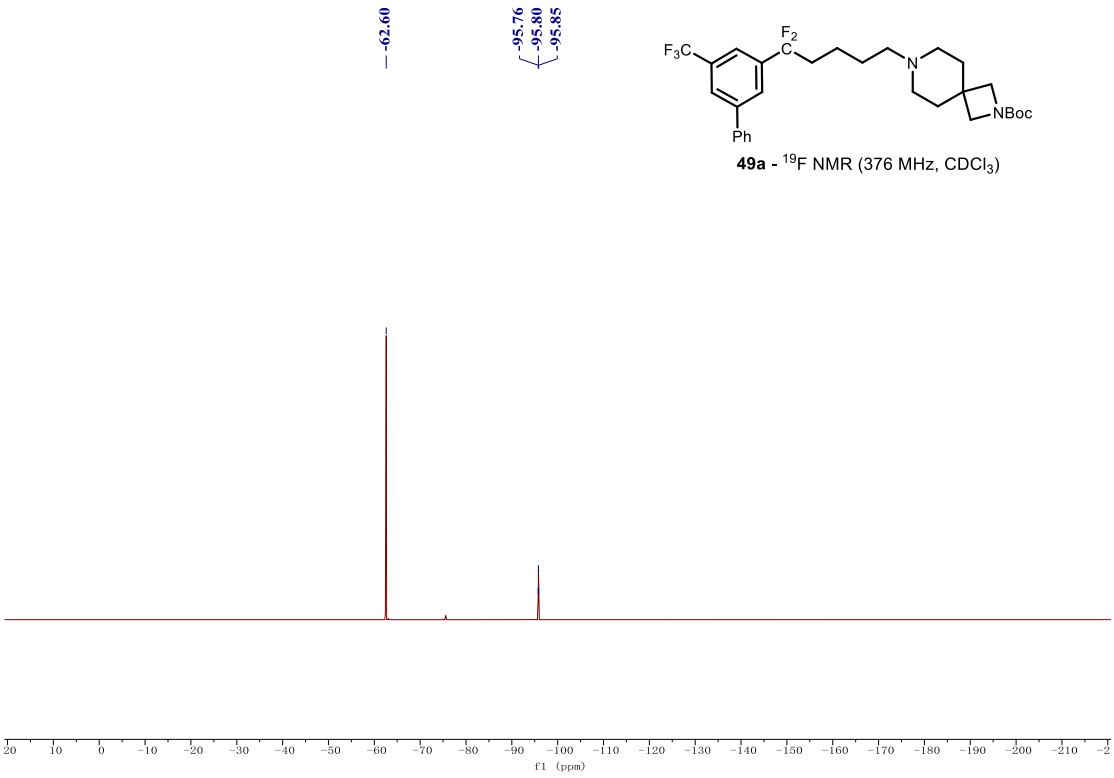




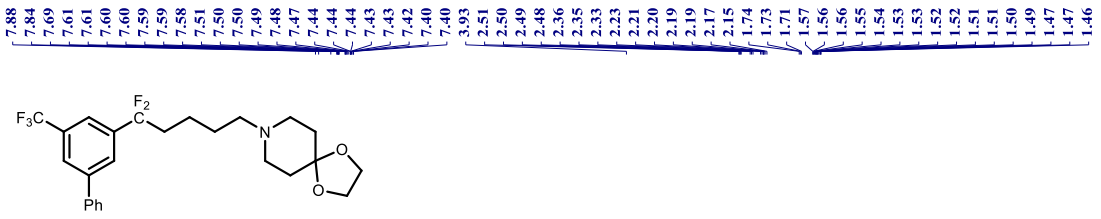
49a - ^{1}H NMR (400 MHz, $CDCl_3$)



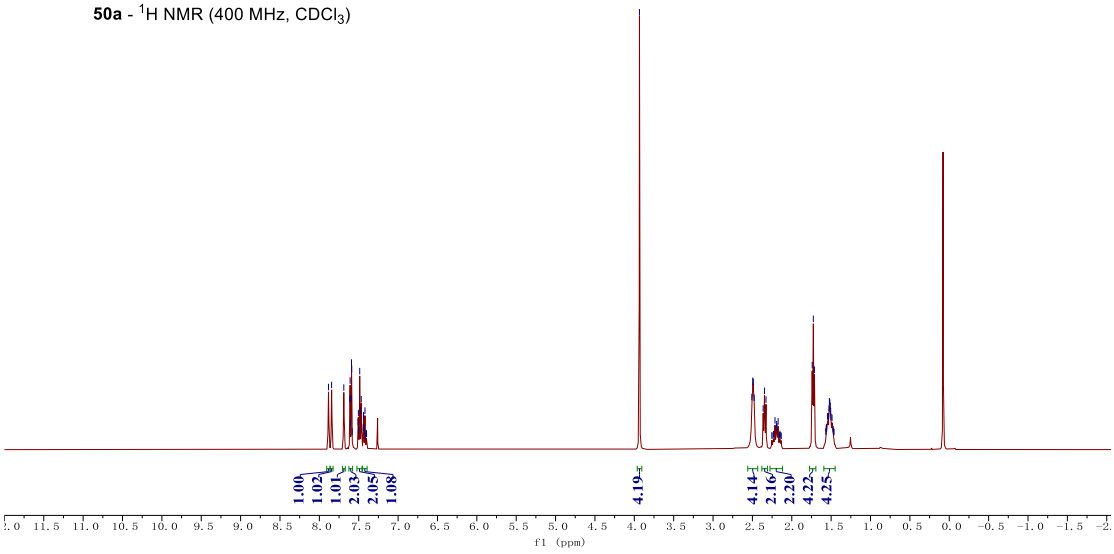
49a - ^{13}C NMR (101 MHz, $CDCl_3$)

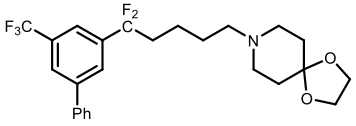


49a - ^{19}F NMR (376 MHz, $CDCl_3$)

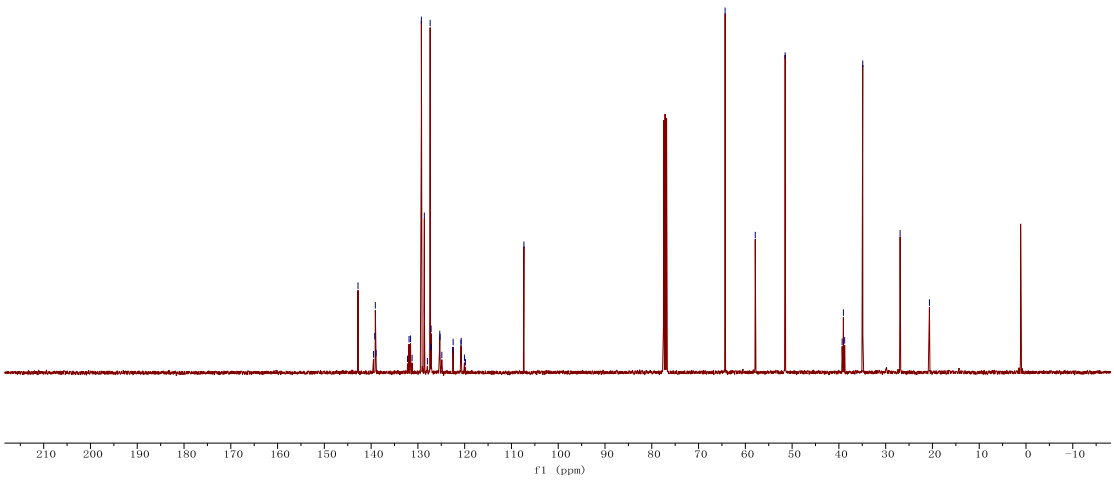


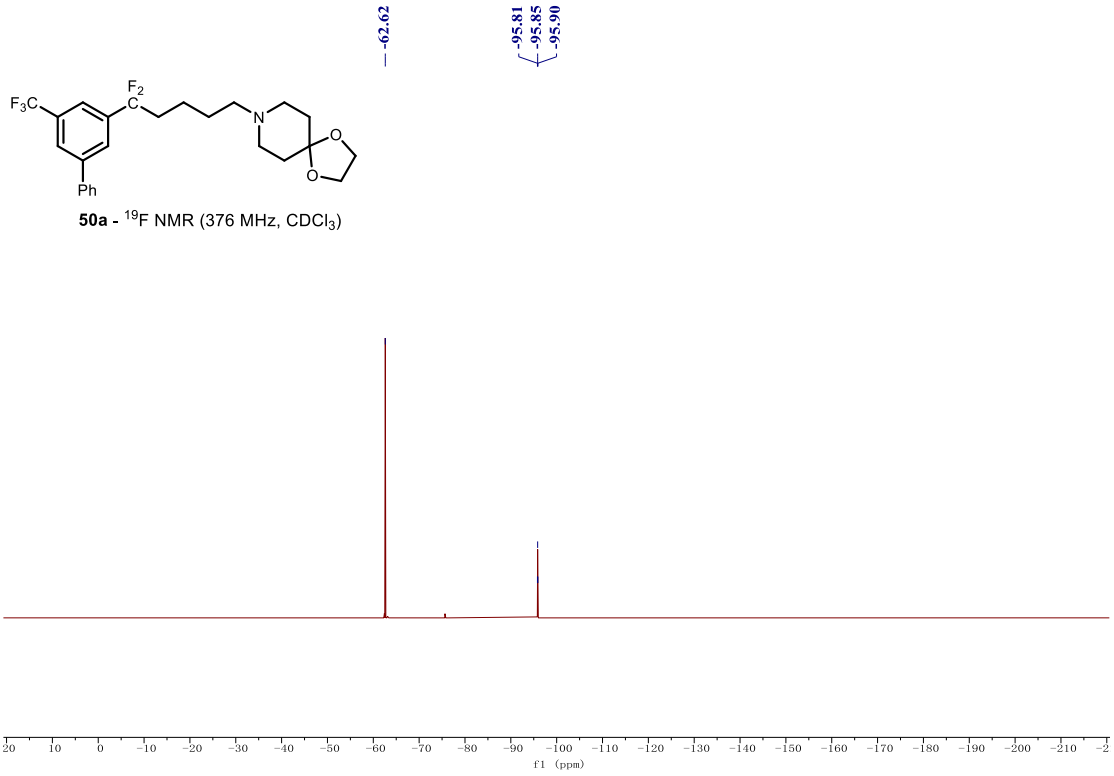
50a - ^{1}H NMR (400 MHz, $CDCl_3$)



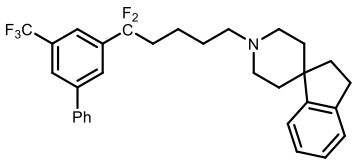


50a - ^{13}C NMR (101 MHz, $CDCl_3$)

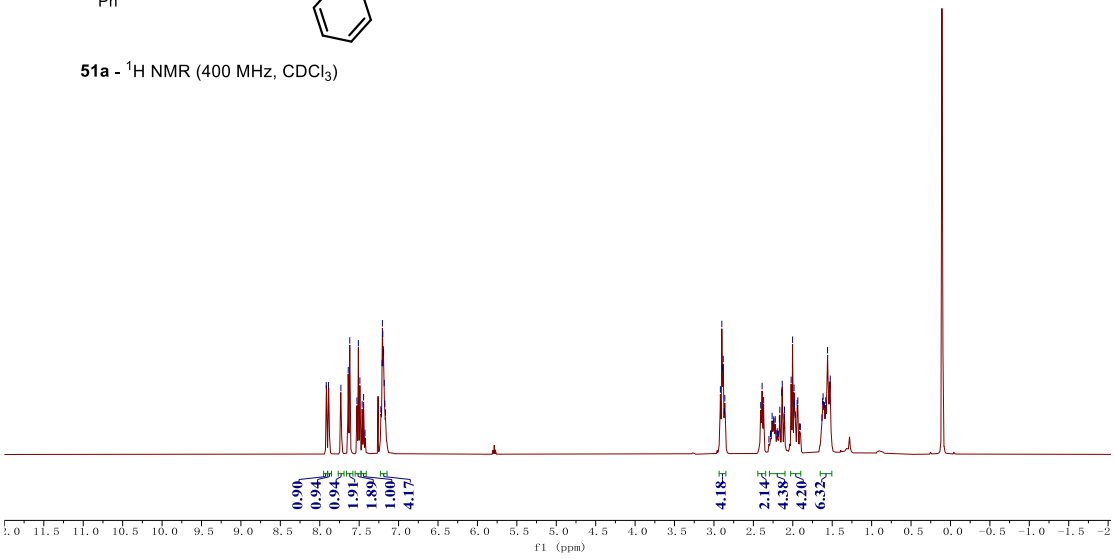


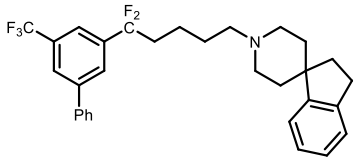


50a - ^{19}F NMR (376 MHz, $CDCl_3$)

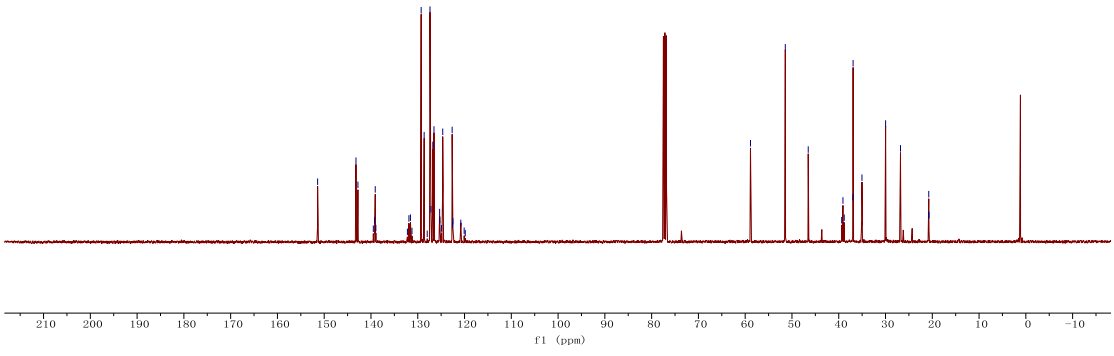


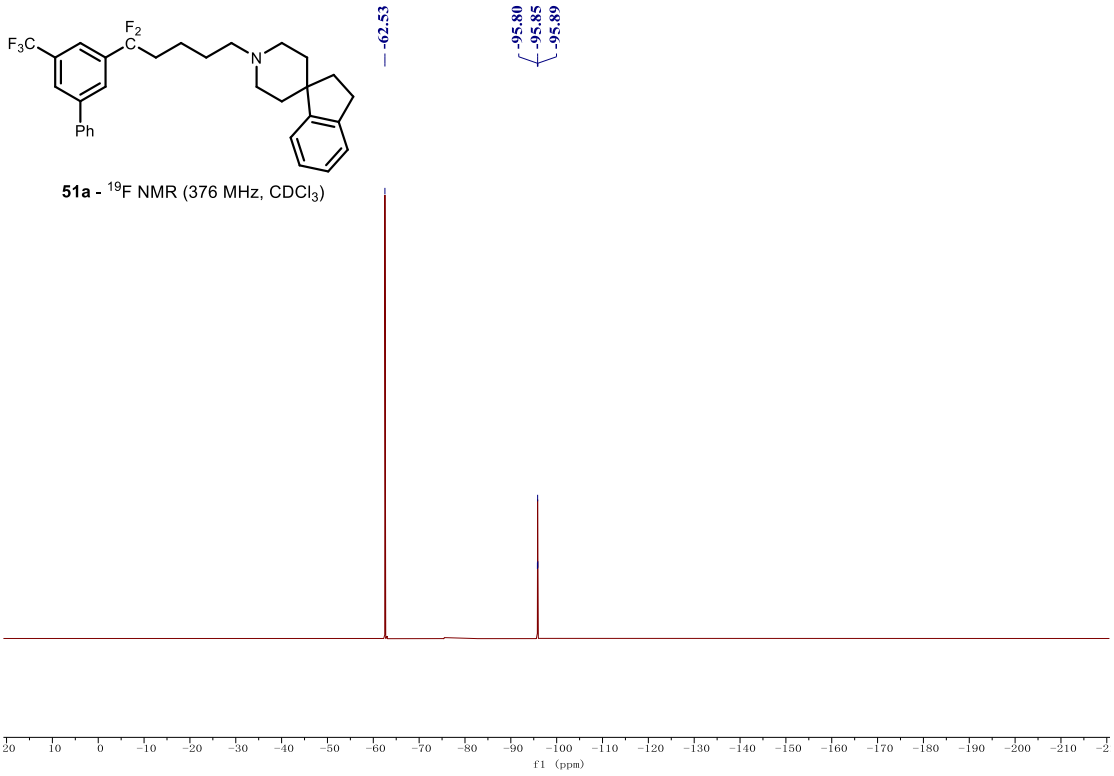
51a - ^{1}H NMR (400 MHz, $CDCl_3$)



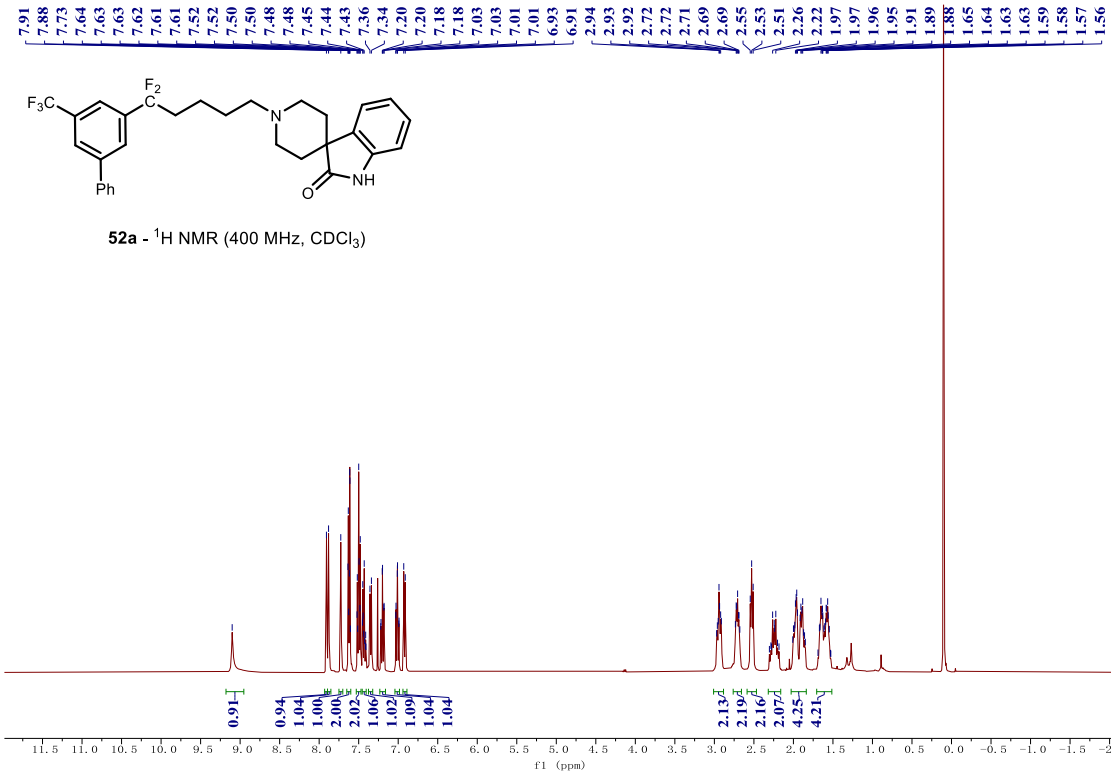


51a - ^{13}C NMR (101 MHz, $CDCl_3$)

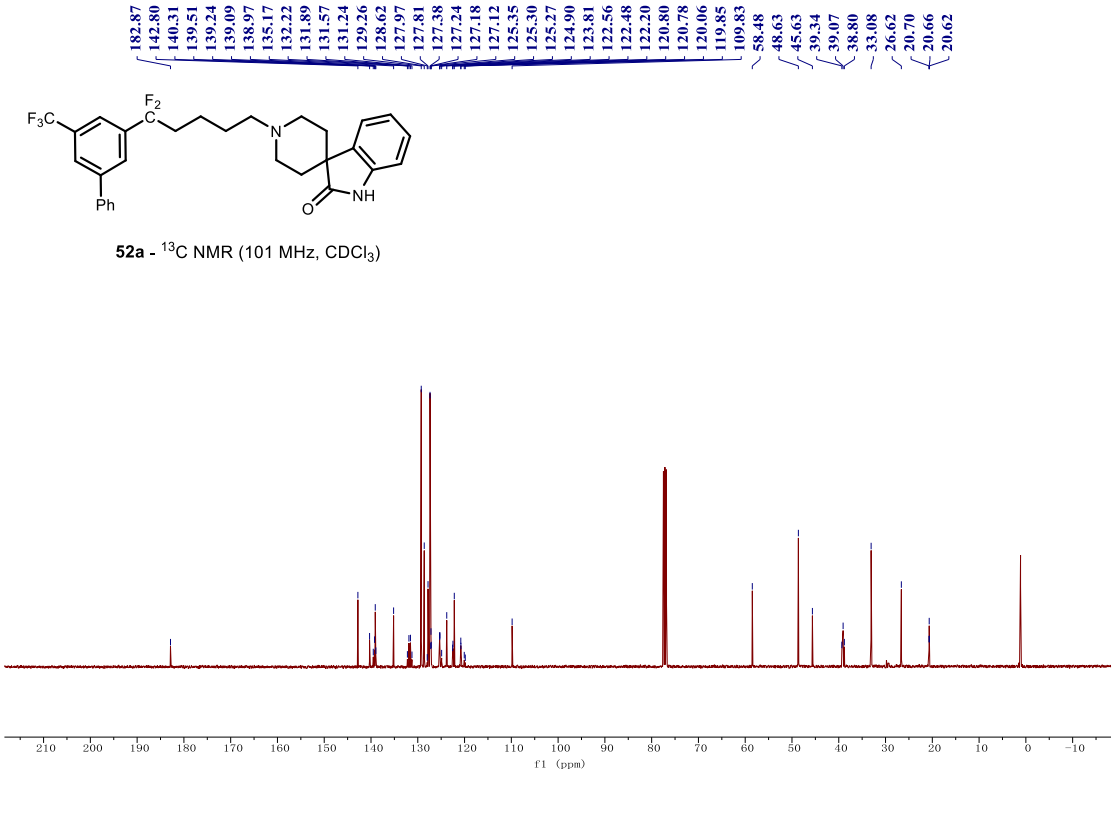




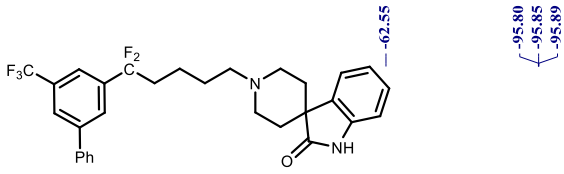
51a - ^{19}F NMR (376 MHz, $CDCl_3$)



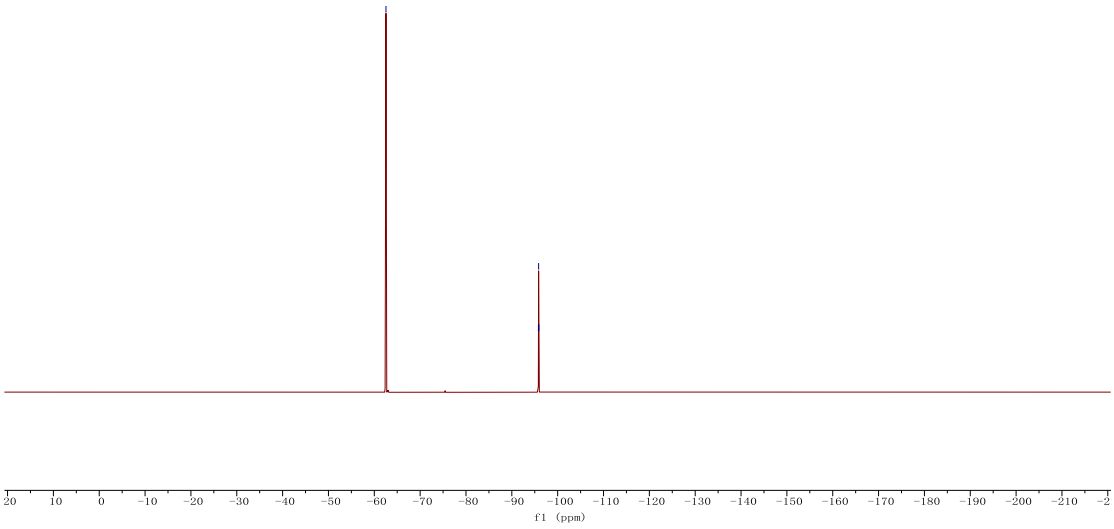
52a - ^{1}H NMR (400 MHz, $CDCl_3$)

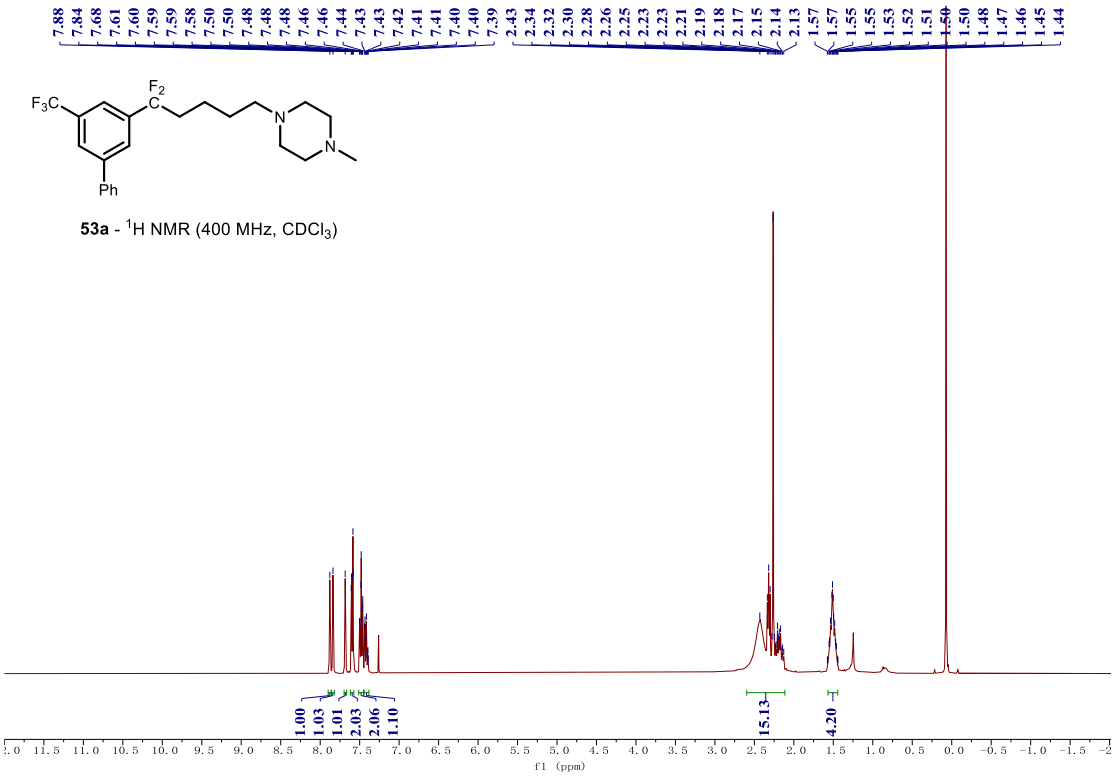


52a - ^{13}C NMR (101 MHz, $CDCl_3$)

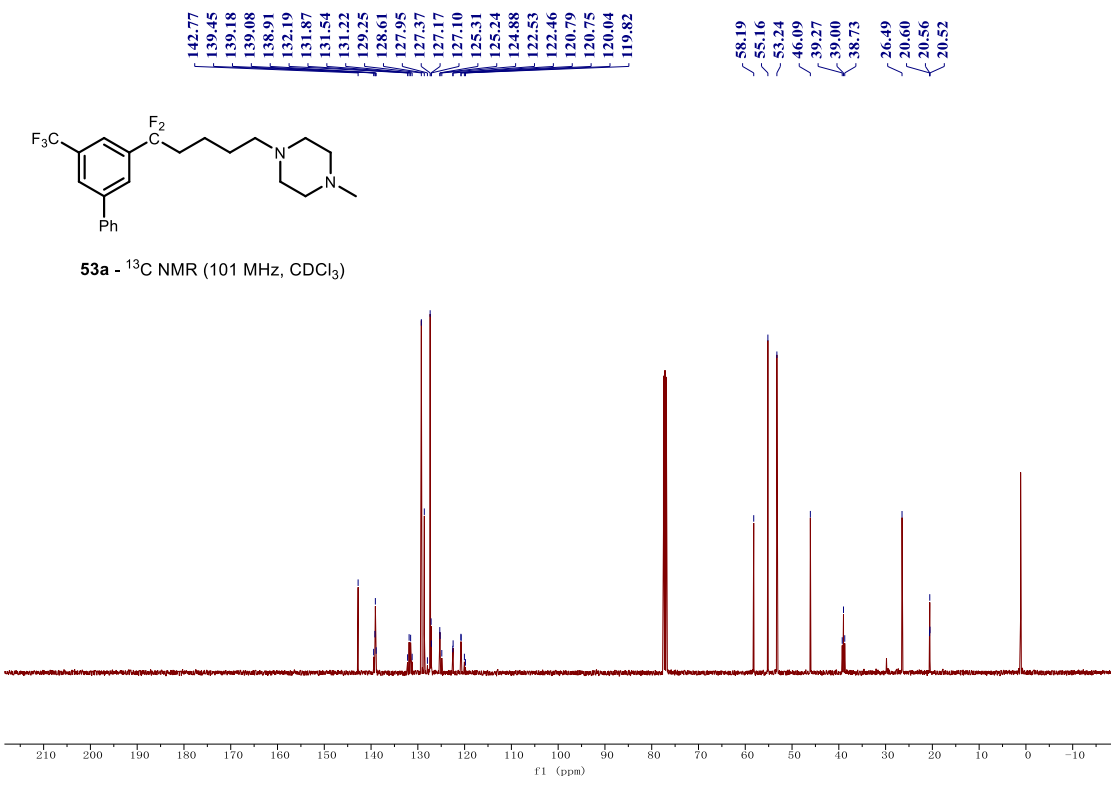


52a - ^{19}F NMR (376 MHz, $CDCl_3$)

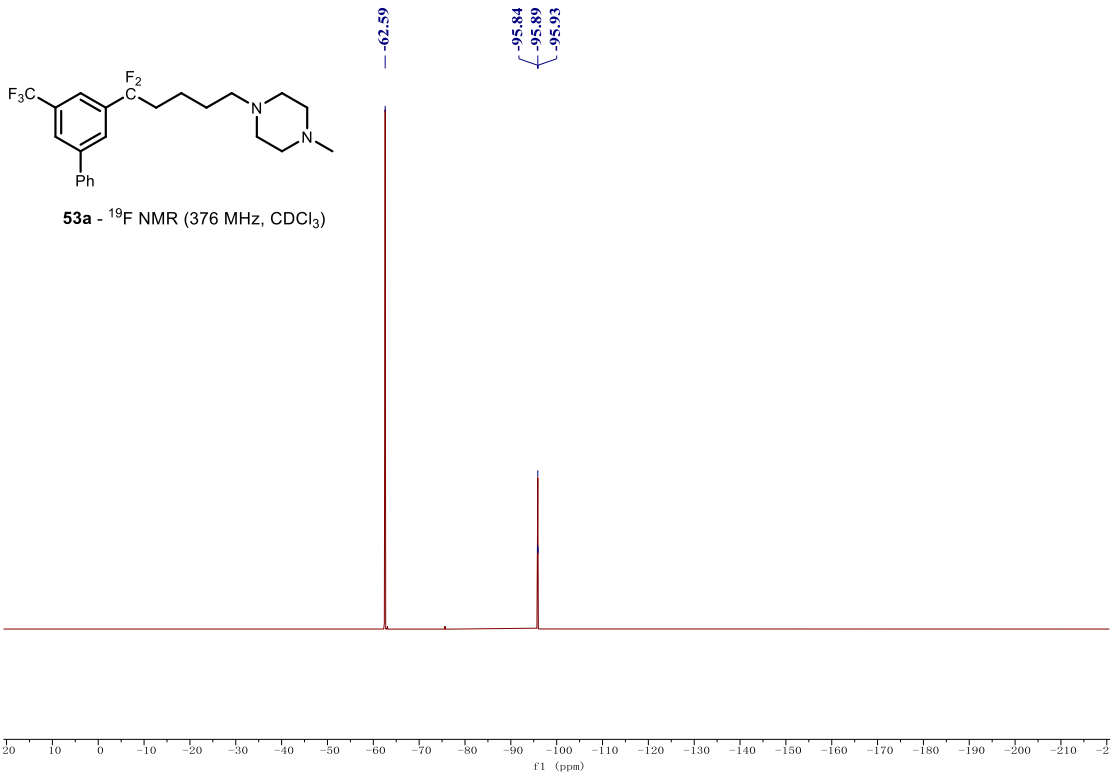




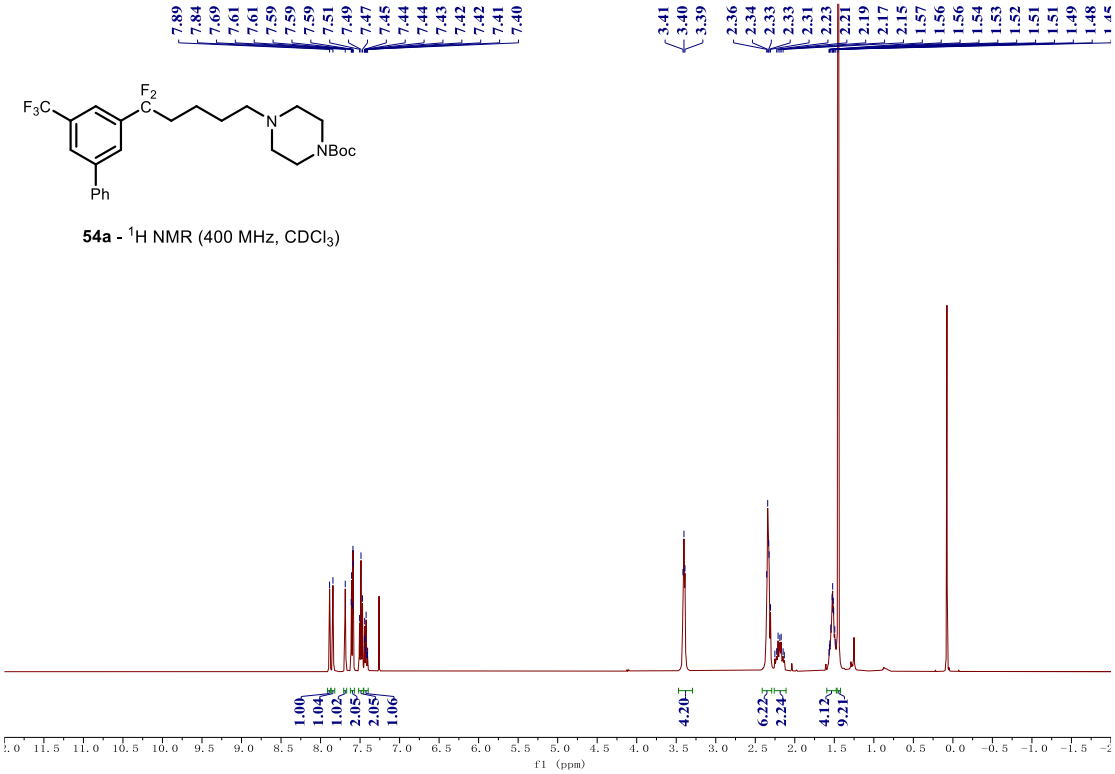
53a - ^{1}H NMR (400 MHz, $CDCl_3$)



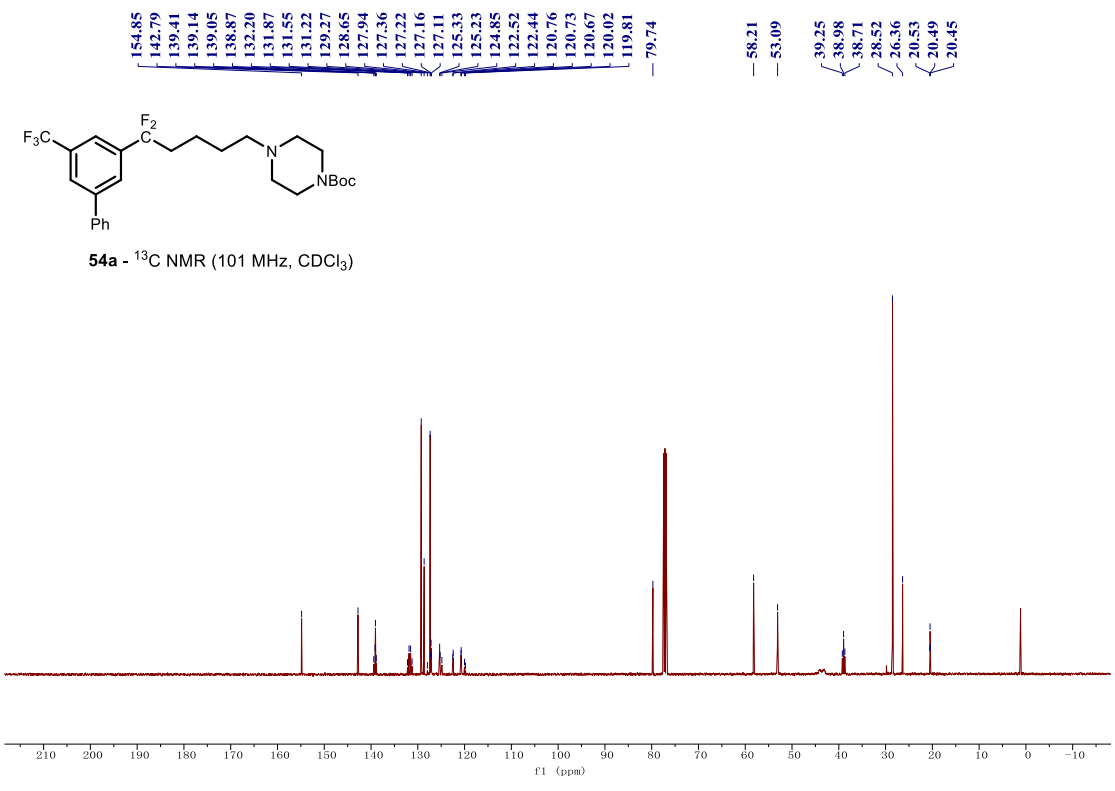
53a - ^{13}C NMR (101 MHz, $CDCl_3$)



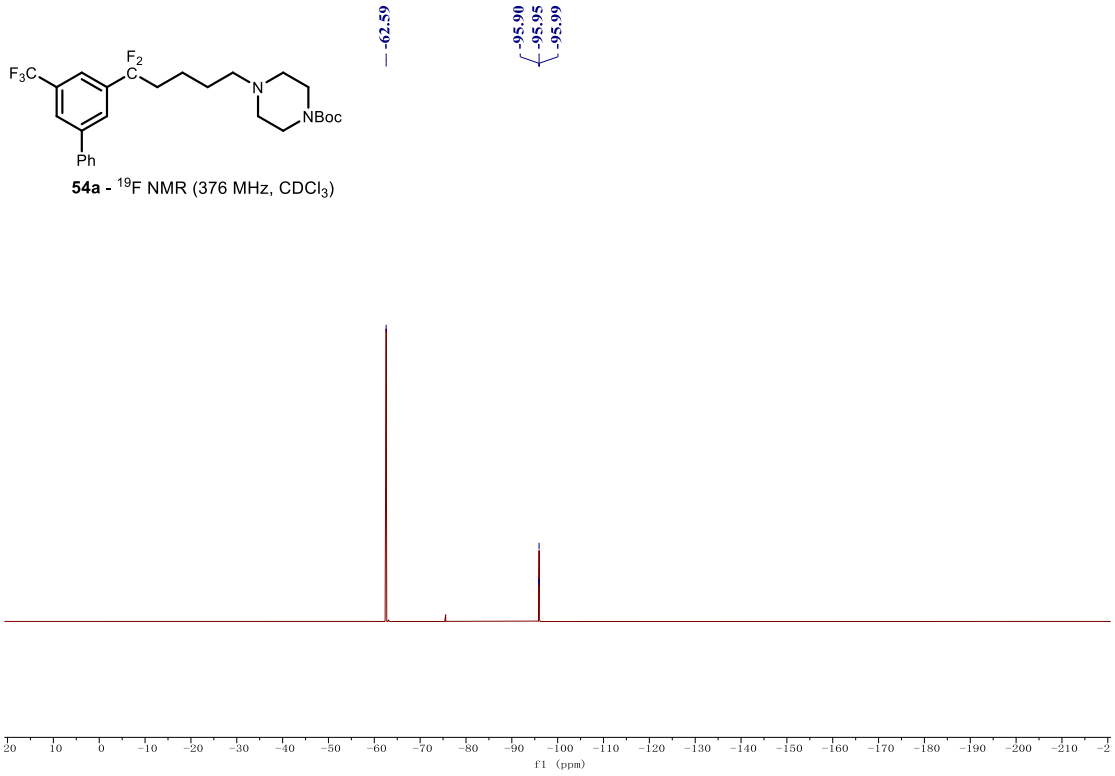
53a - ^{19}F NMR (376 MHz, $CDCl_3$)



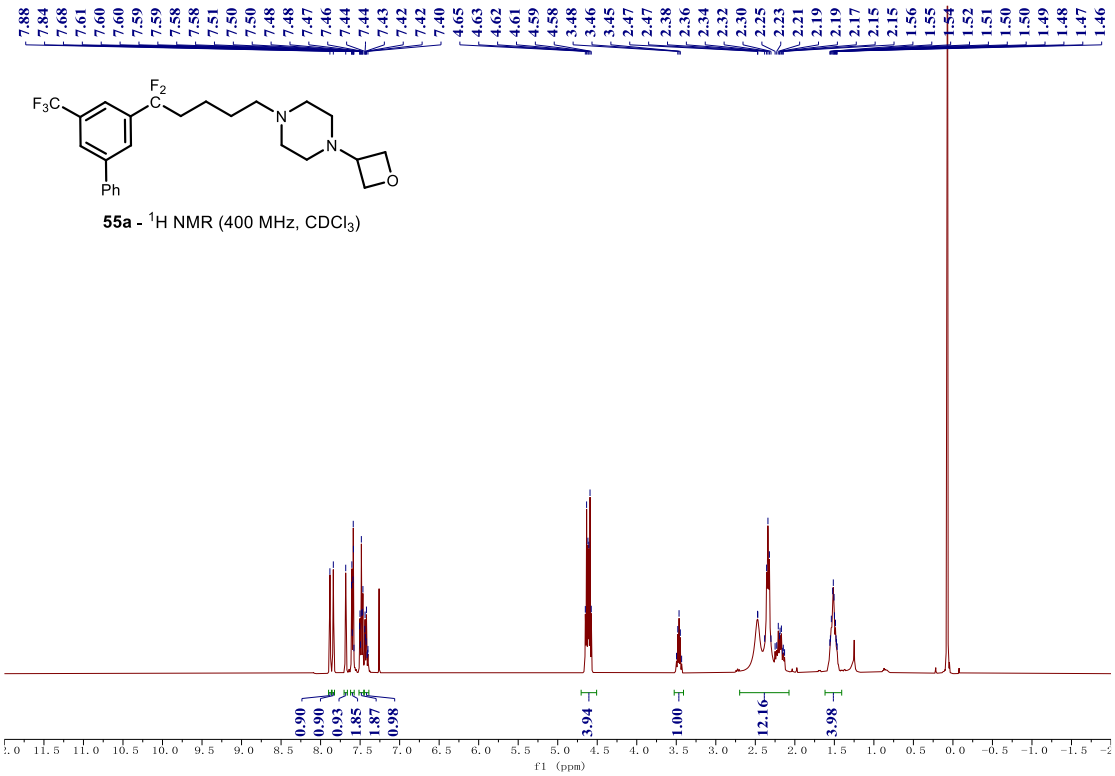
54a - ^{1}H NMR (400 MHz, $CDCl_3$)



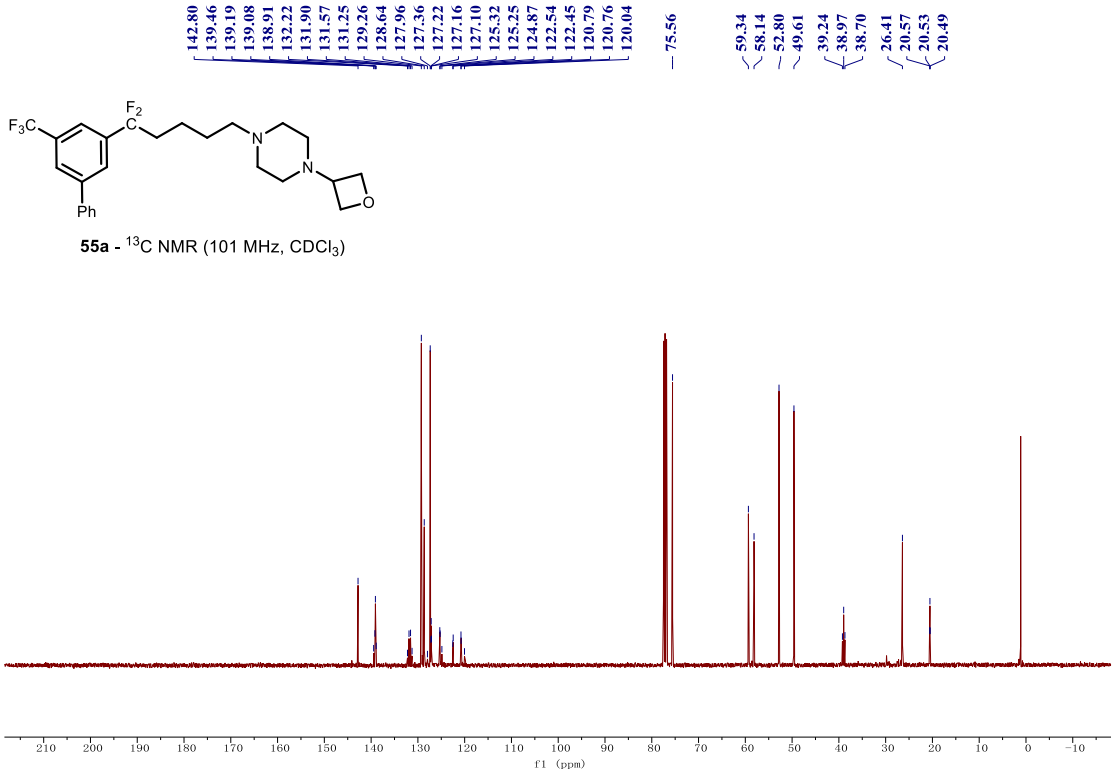
54a - ^{13}C NMR (101 MHz, $CDCl_3$)



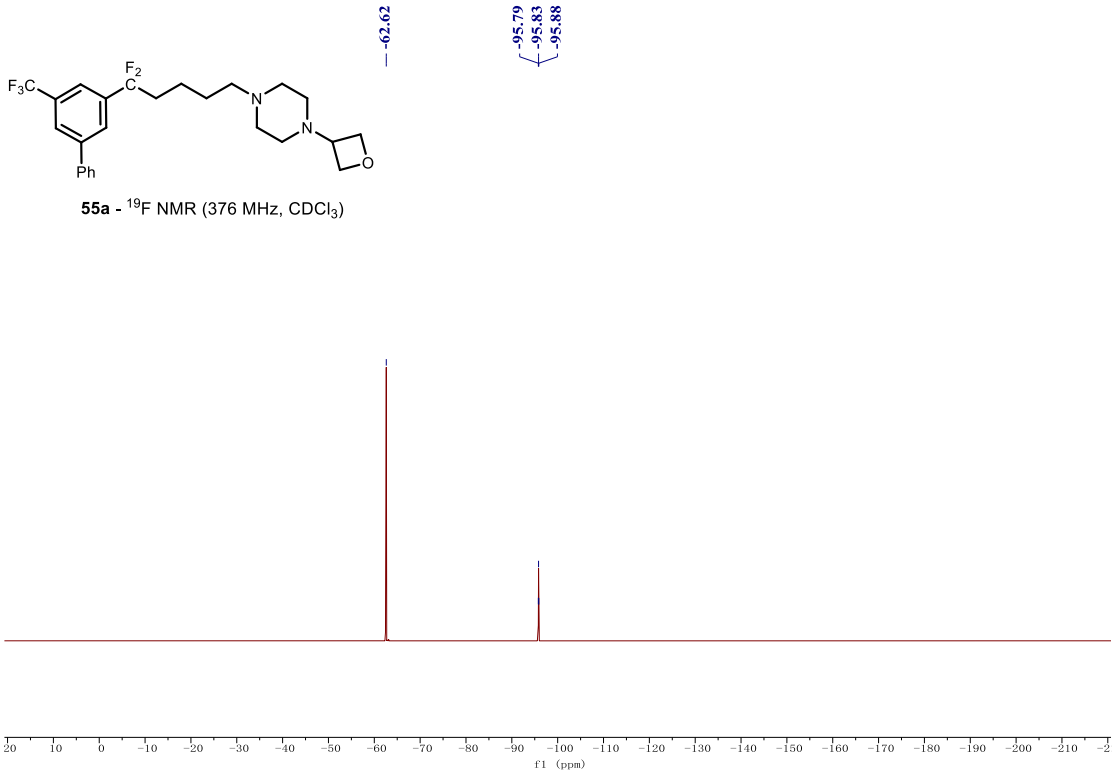
54a - ^{19}F NMR (376 MHz, $CDCl_3$)



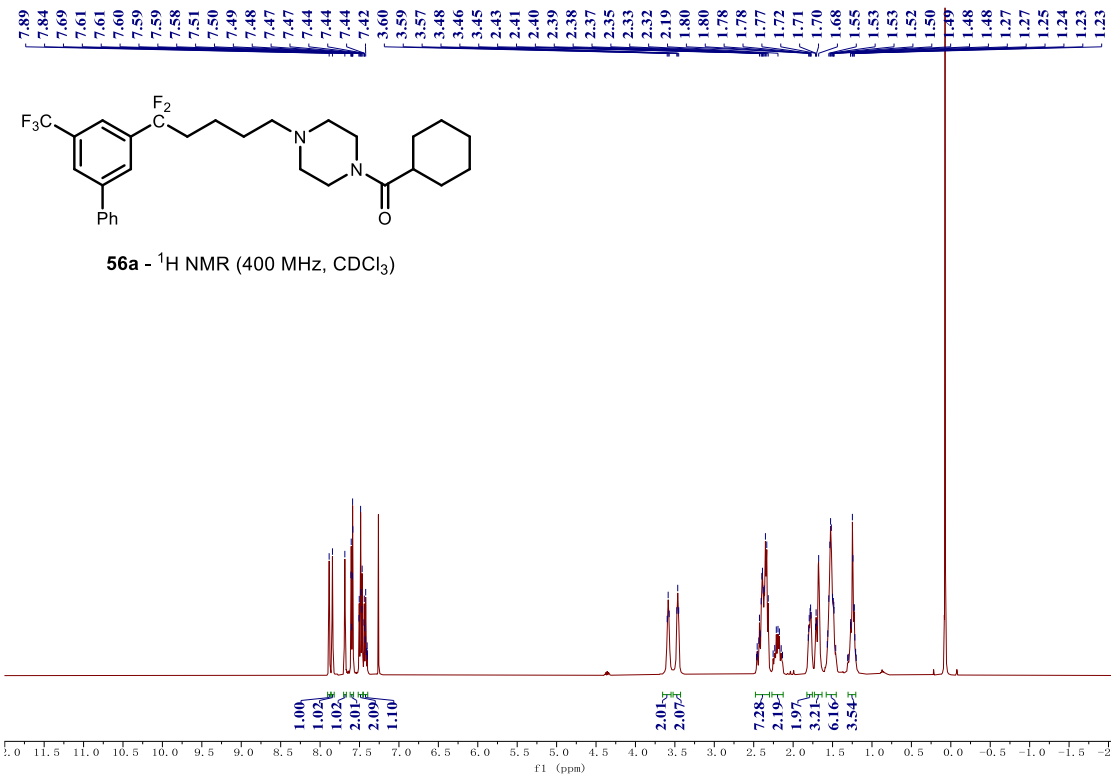
55a - ^{1}H NMR (400 MHz, $CDCl_3$)



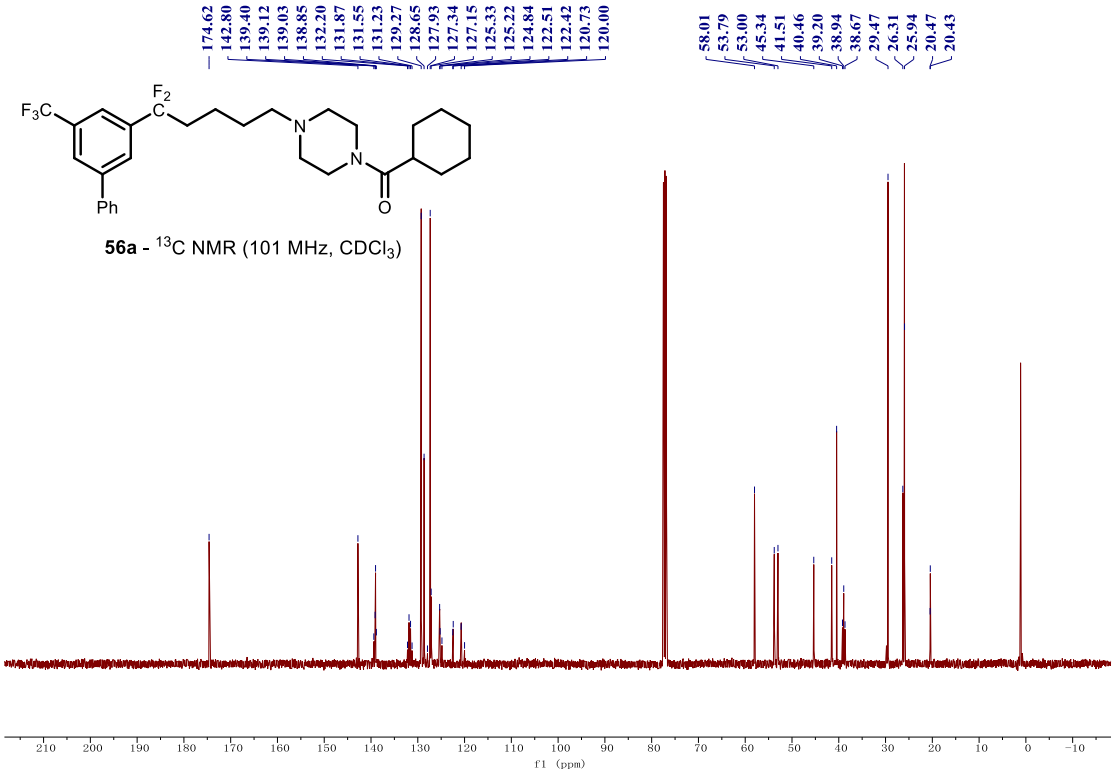
55a - ^{13}C NMR (101 MHz, $CDCl_3$)



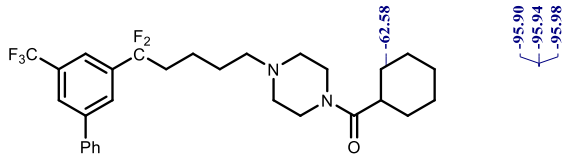
55a - ^{19}F NMR (376 MHz, $CDCl_3$)



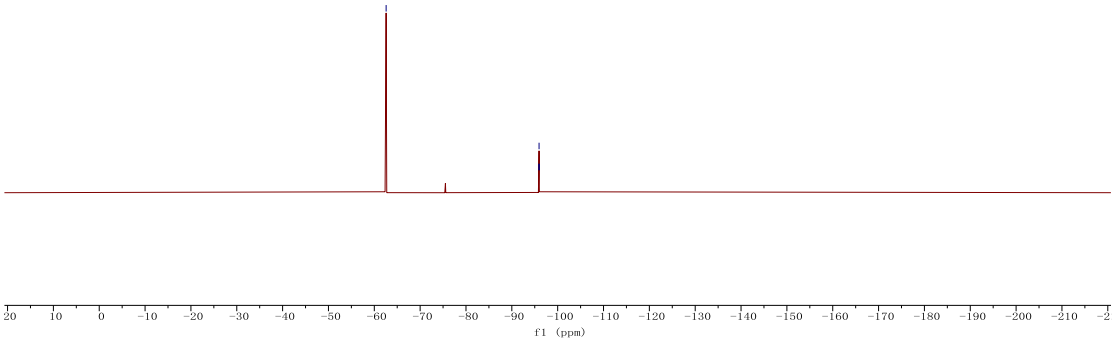
56a - ^{1}H NMR (400 MHz, $CDCl_3$)

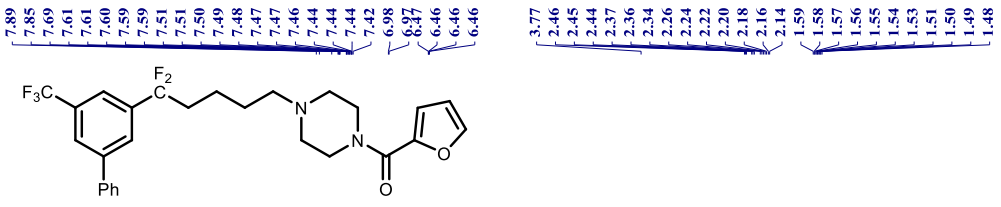


56a - ^{13}C NMR (101 MHz, $CDCl_3$)

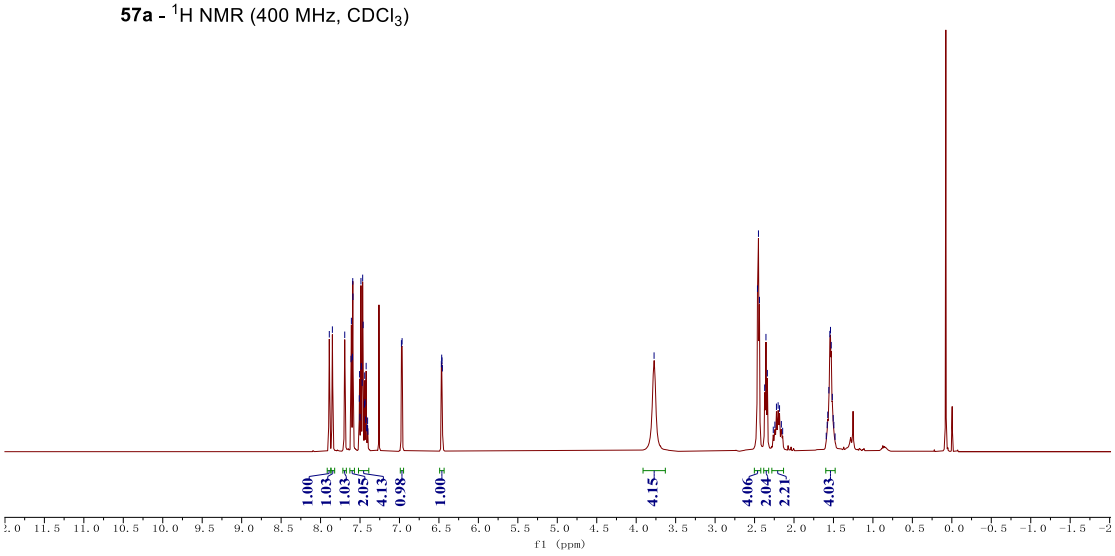


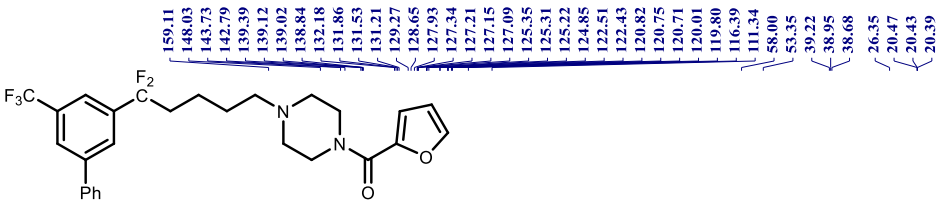
56a - ^{19}F NMR (376 MHz, $CDCl_3$)



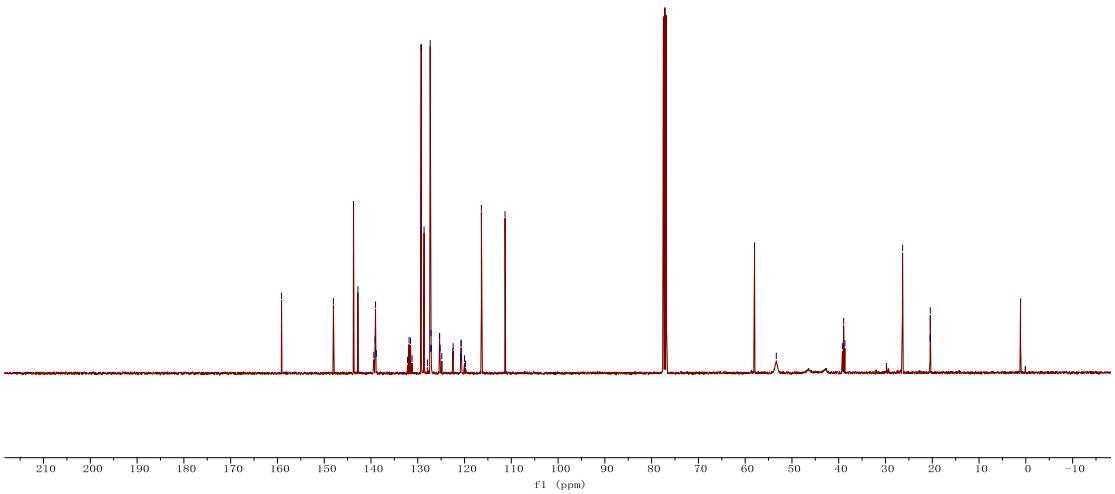


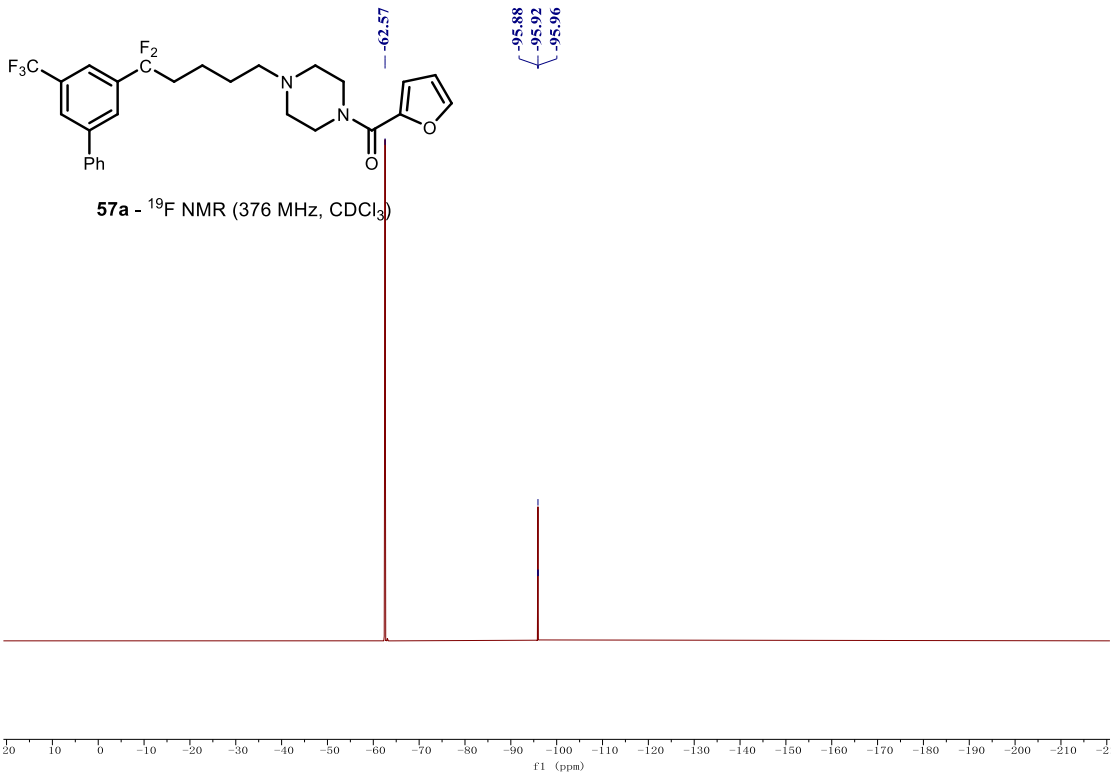
57a - ^{1}H NMR (400 MHz, $CDCl_3$)



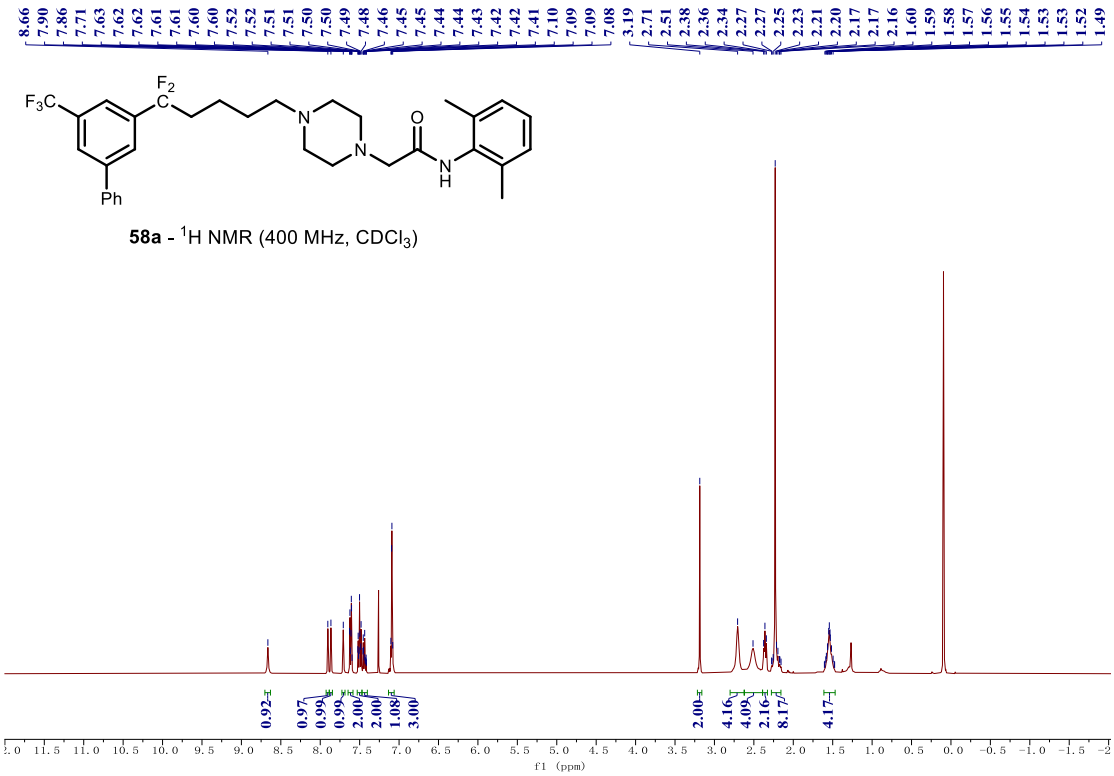


57a - ^{13}C NMR (101 MHz, $CDCl_3$)

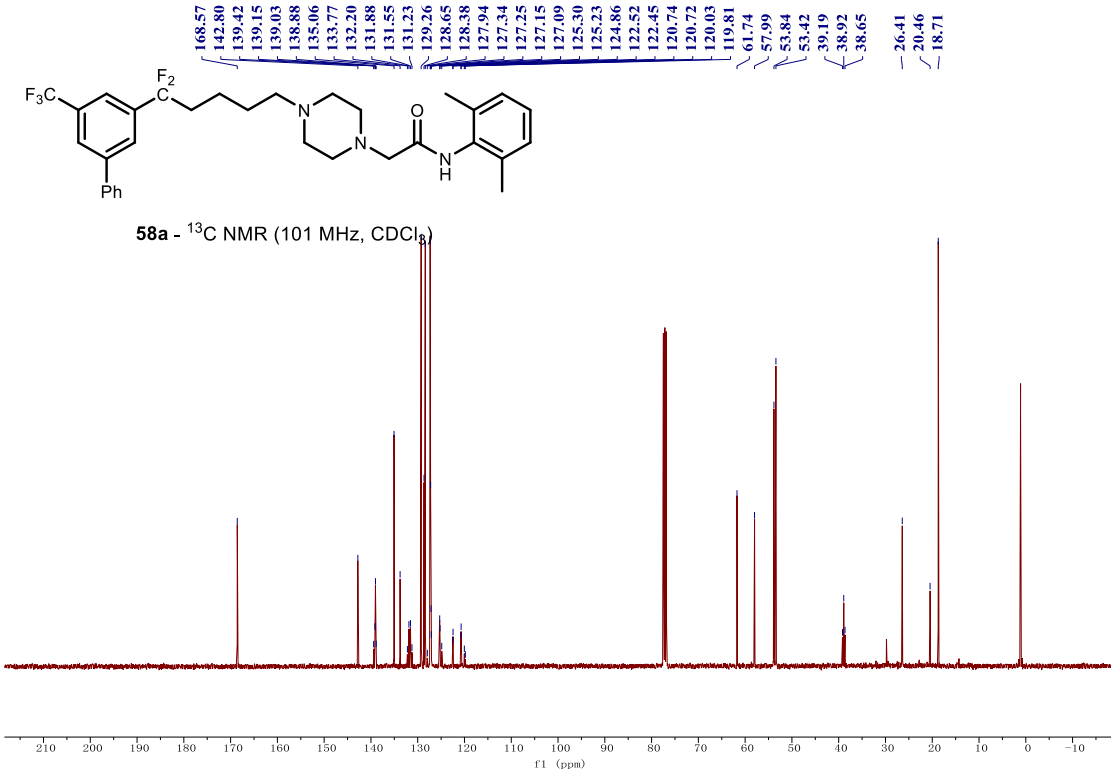




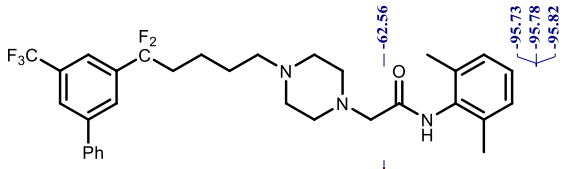
57a - ^{19}F NMR (376 MHz, $CDCl_3$)



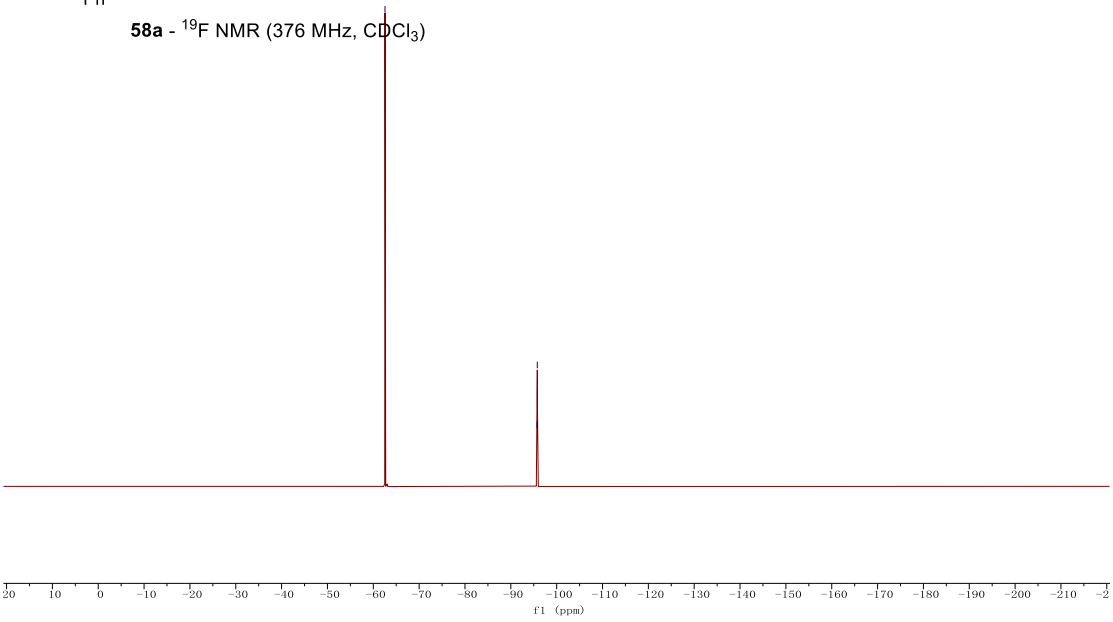
58a - ^{1}H NMR (400 MHz, $CDCl_3$)

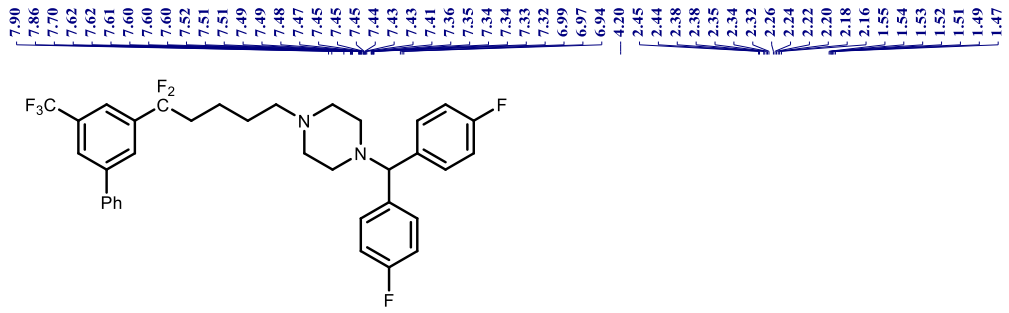


58a - ^{13}C NMR (101 MHz, $CDCl_3$)

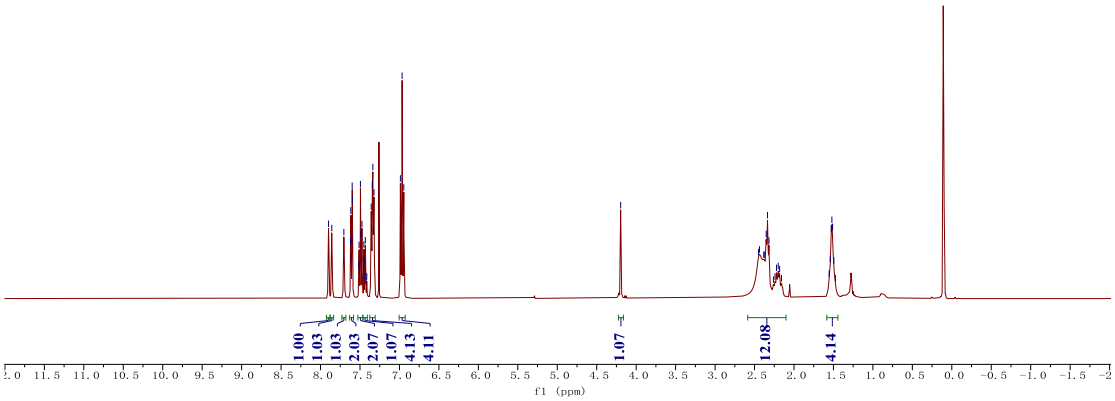


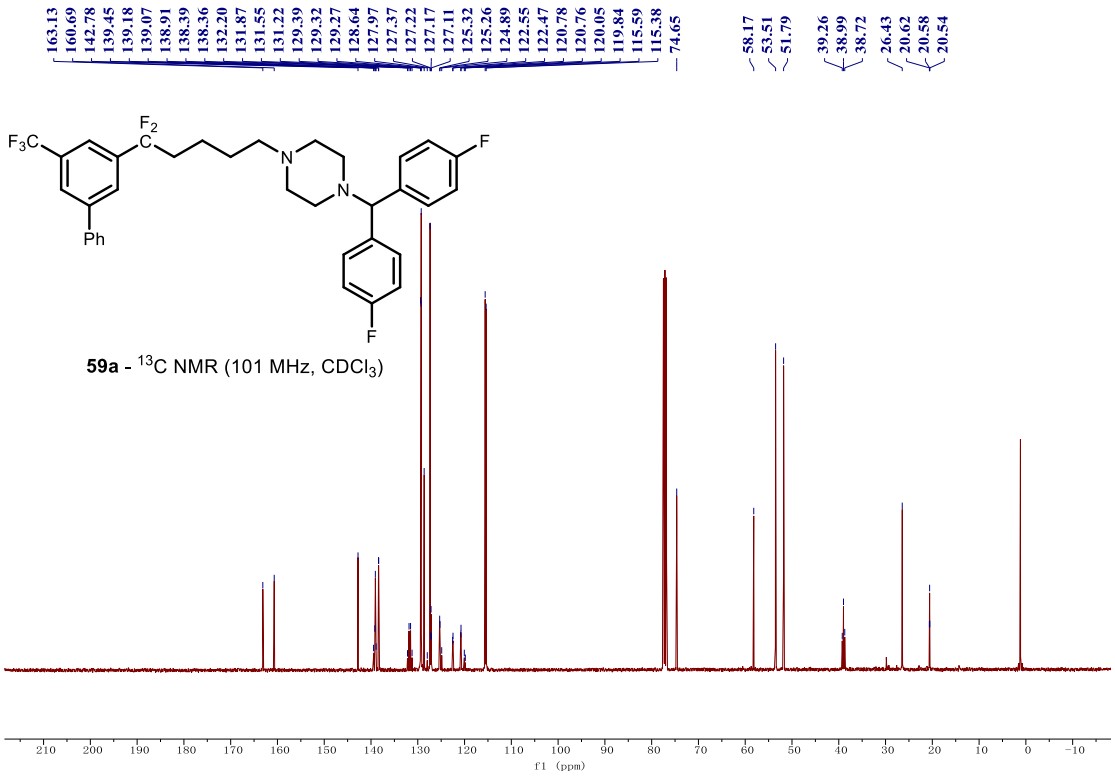
58a - ^{19}F NMR (376 MHz, $CDCl_3$)



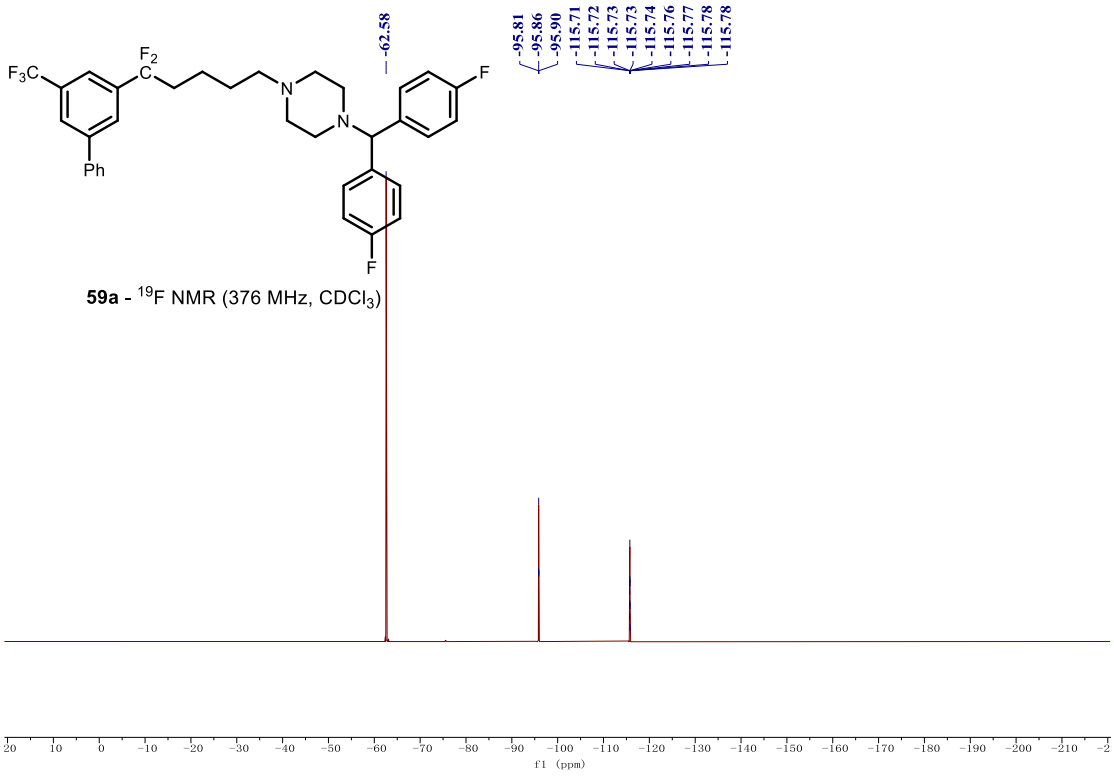


59a - ^{1}H NMR (400 MHz, $CDCl_3$)



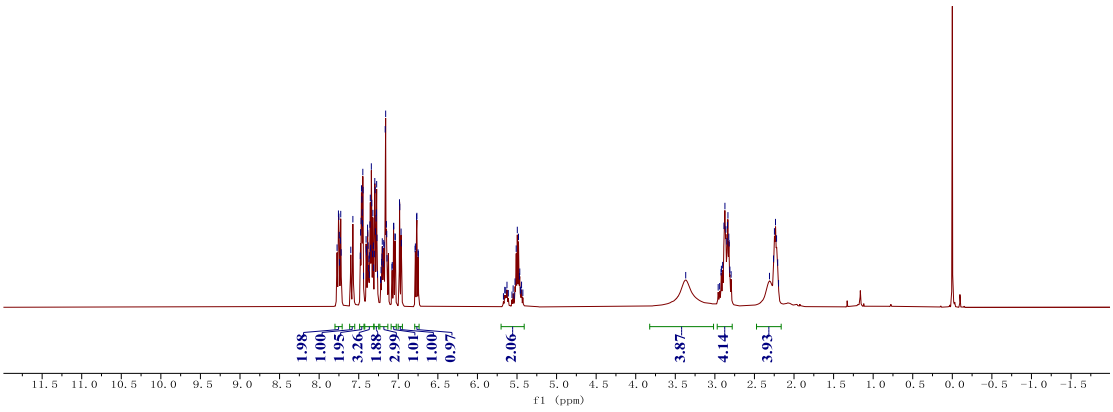


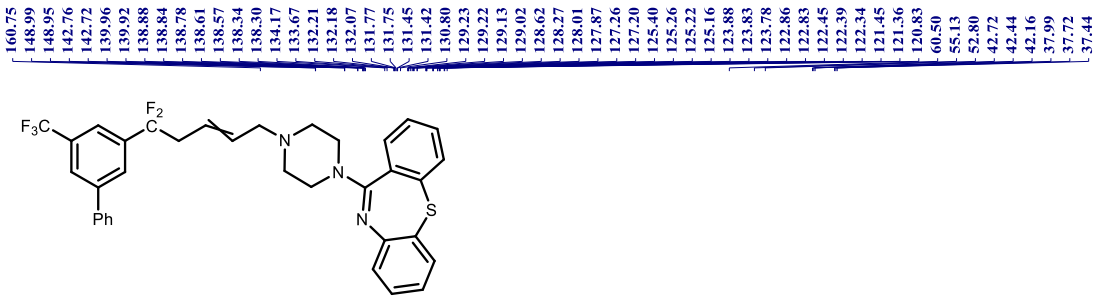
59a - ^{13}C NMR (101 MHz, $CDCl_3$)



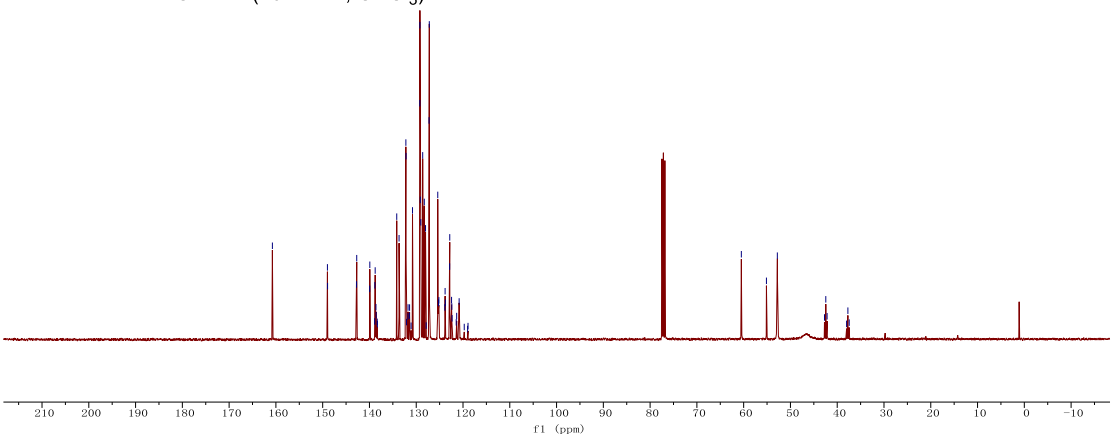
59a - ^{19}F NMR (376 MHz, $CDCl_3$)

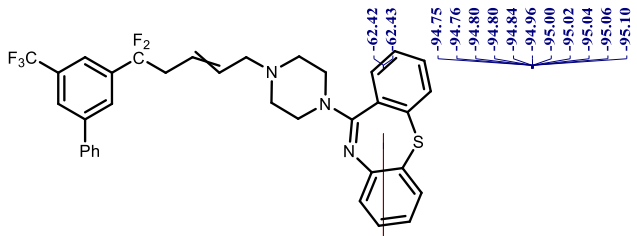
60a - ^{1}H NMR (400 MHz, $CDCl_3$)



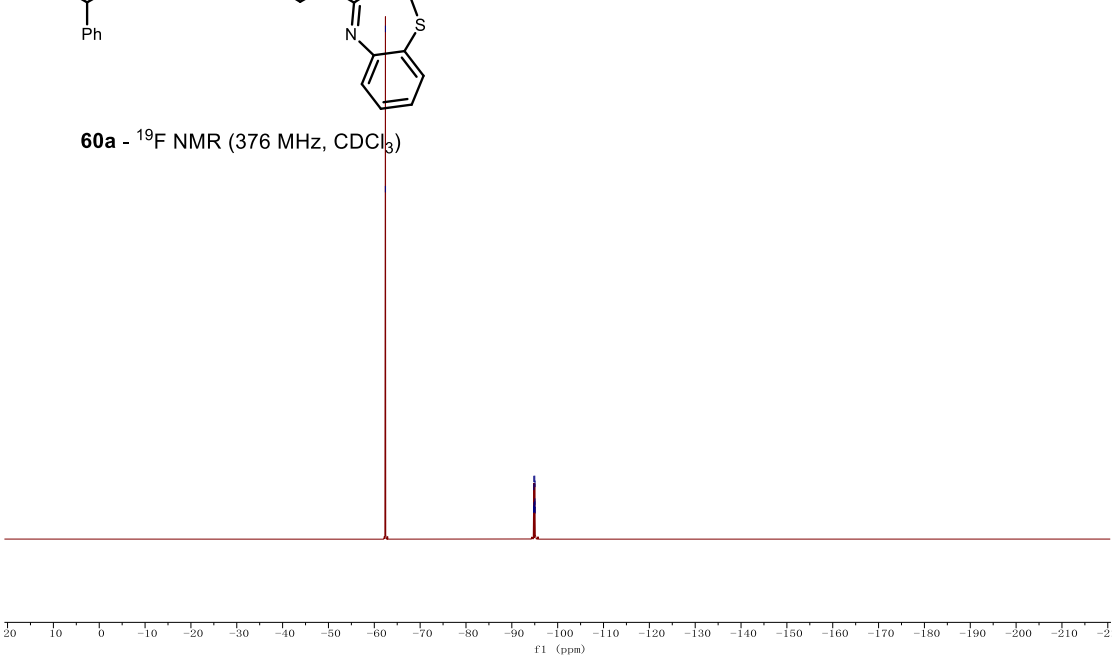


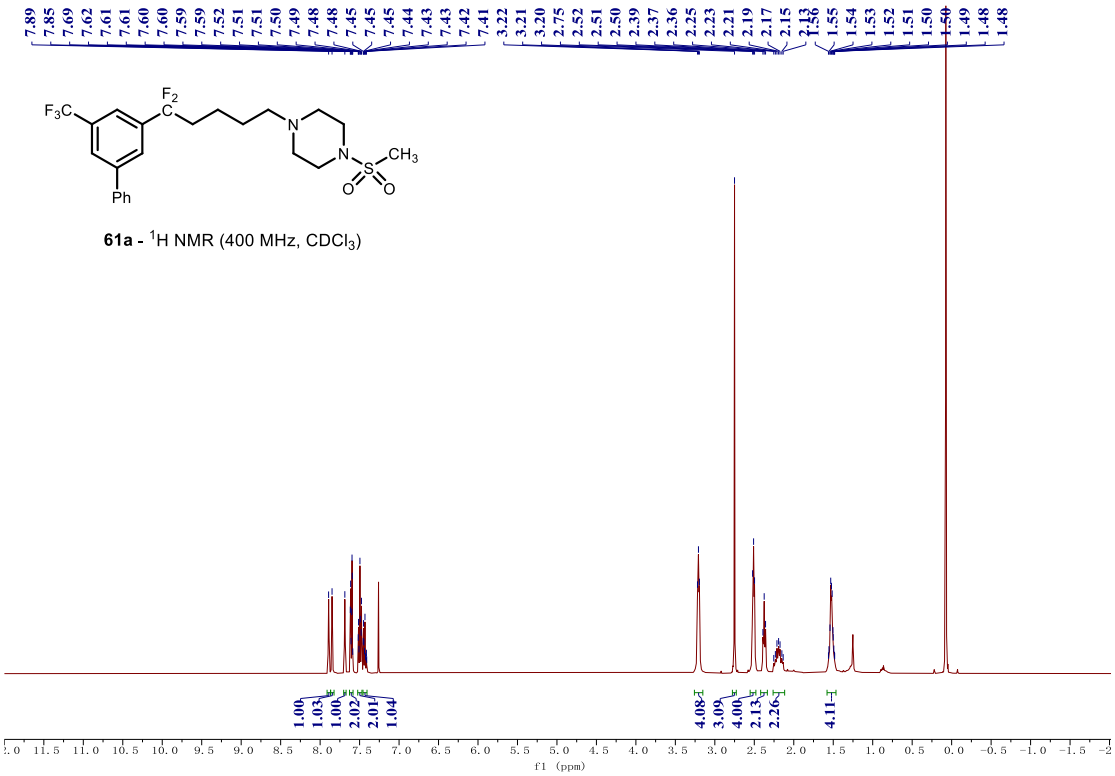
60a - ^{13}C NMR (101 MHz, $CDCl_3$)



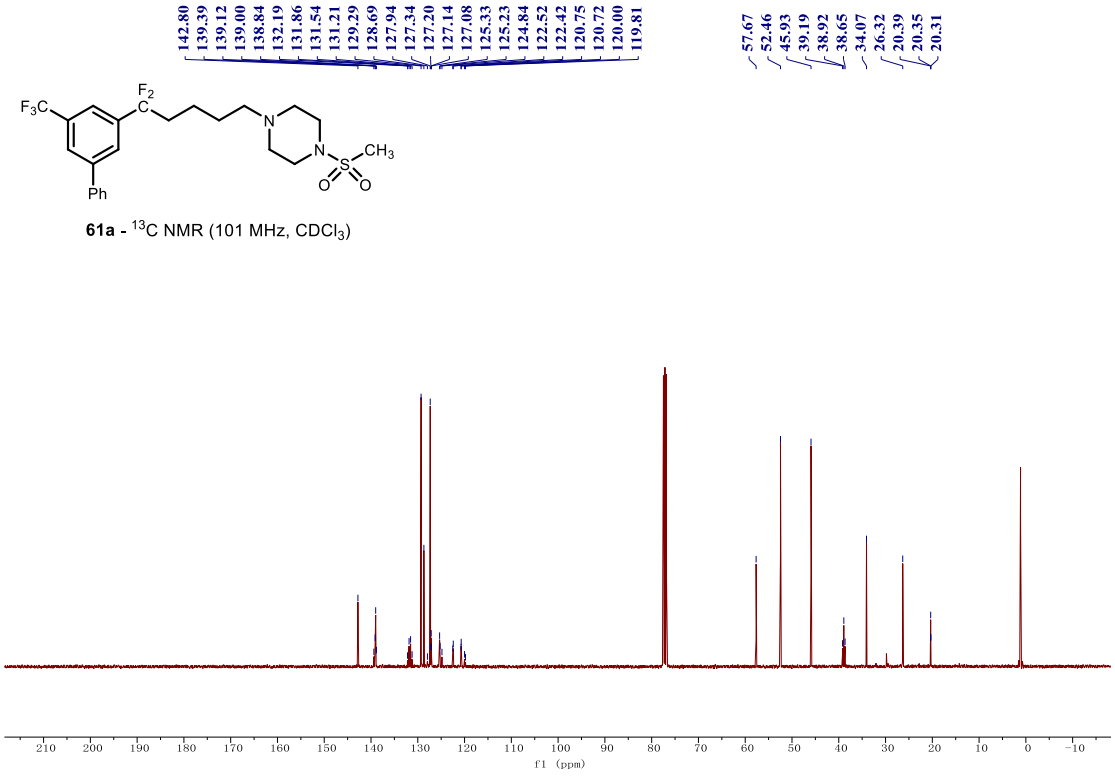


60a - ^{19}F NMR (376 MHz, $CDCl_3$)

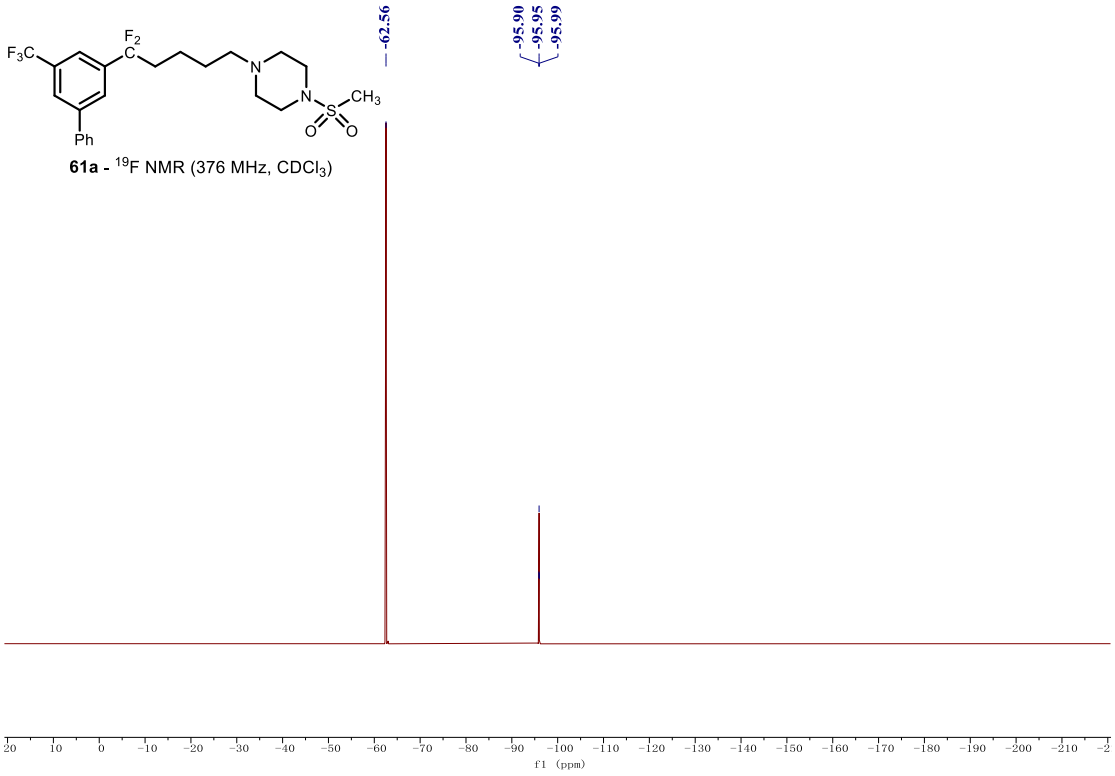




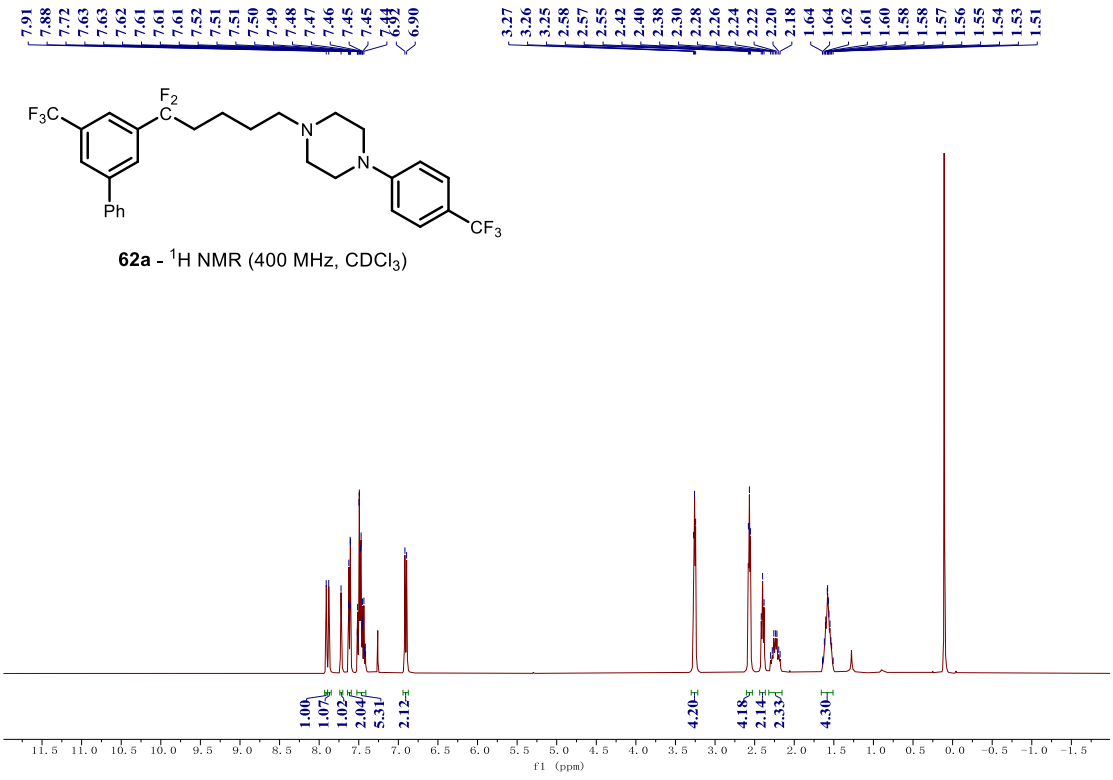
61a - ^{1}H NMR (400 MHz, $CDCl_3$)



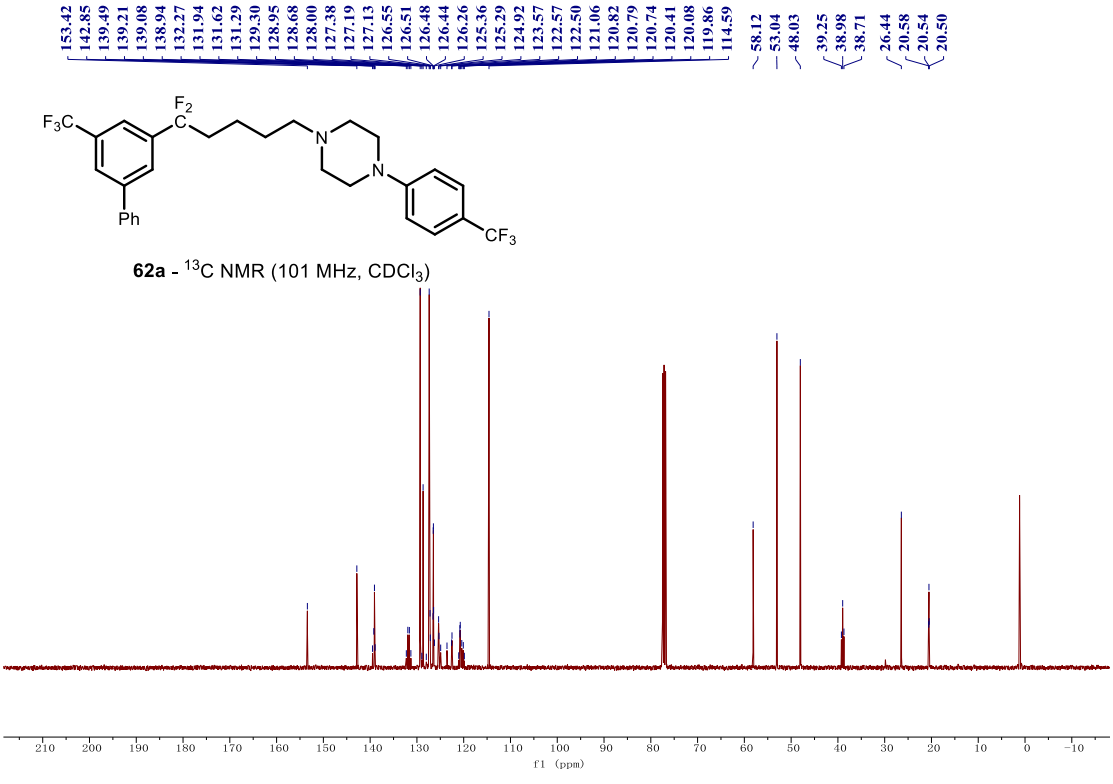
61a - ^{13}C NMR (101 MHz, $CDCl_3$)



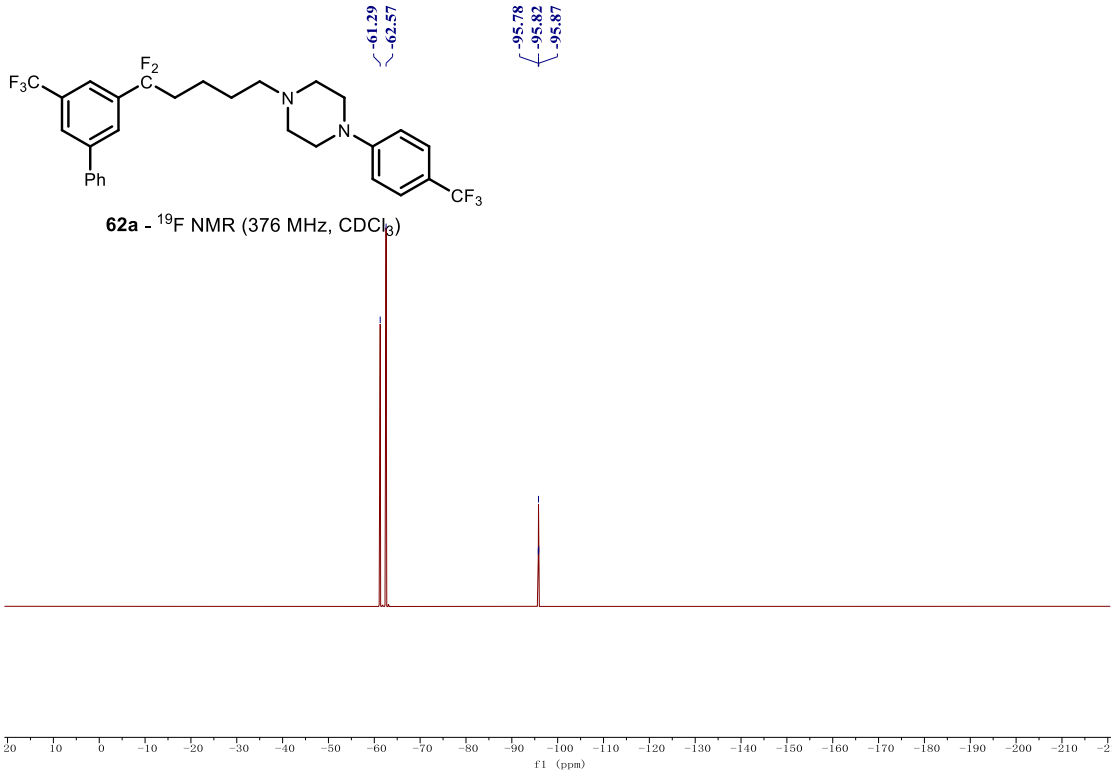
61a - ^{19}F NMR (376 MHz, $CDCl_3$)



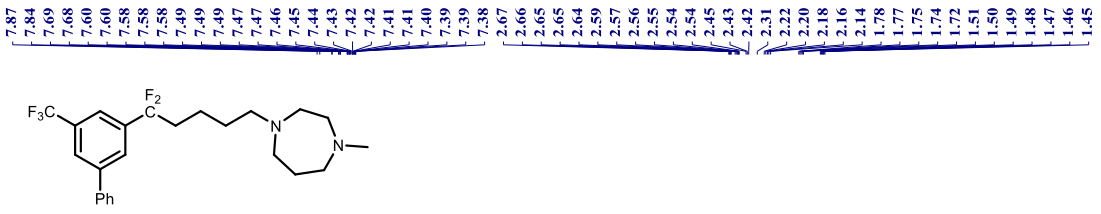
62a - ^{1}H NMR (400 MHz, $CDCl_3$)



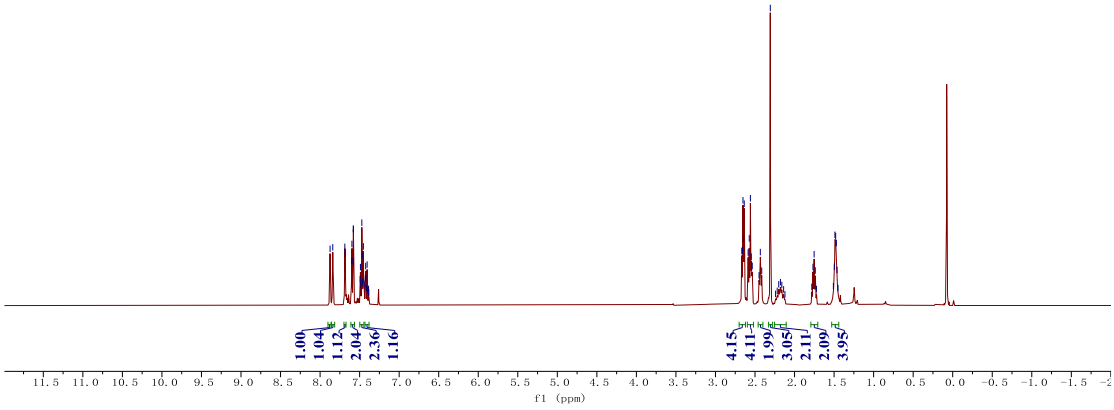
62a - ^{13}C NMR (101 MHz, $CDCl_3$)

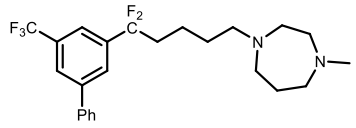


62a - ^{19}F NMR (376 MHz, $CDCl_3$)

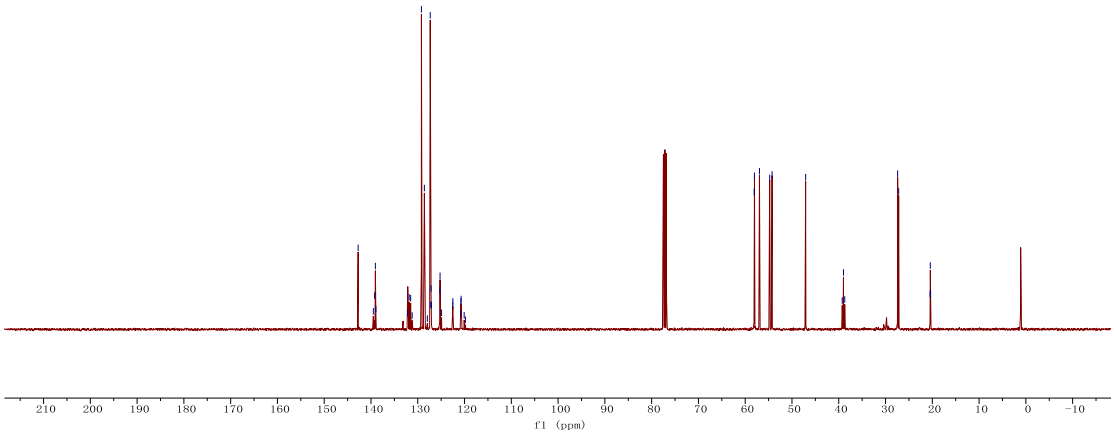


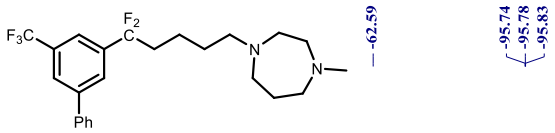
63a - ^{1}H NMR (400 MHz, $CDCl_3$)



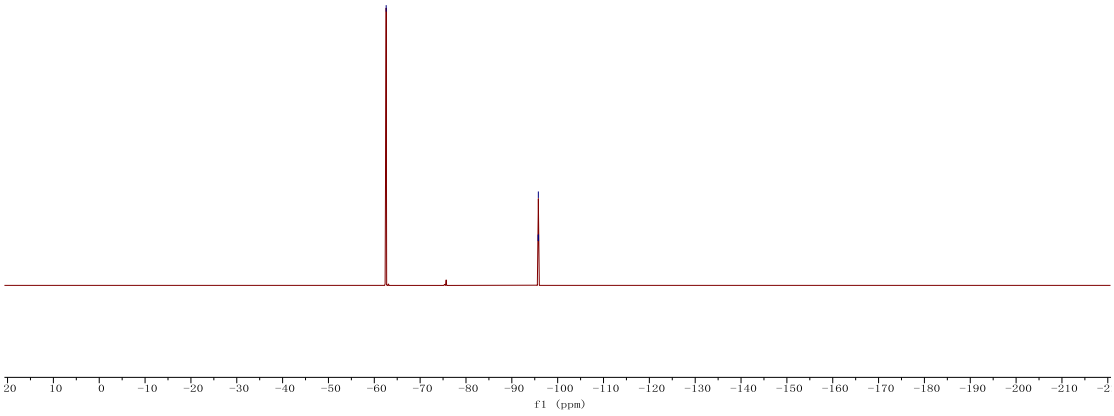


63a - ^{13}C NMR (101 MHz, $CDCl_3$)

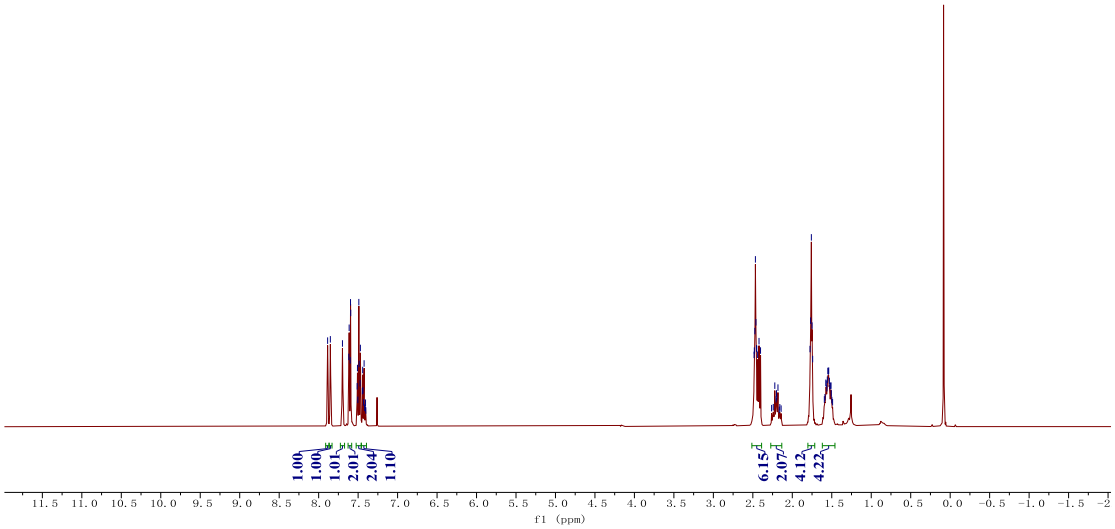


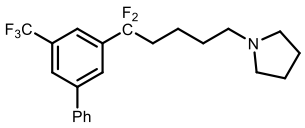


63a - ^{19}F NMR (376 MHz, $CDCl_3$)

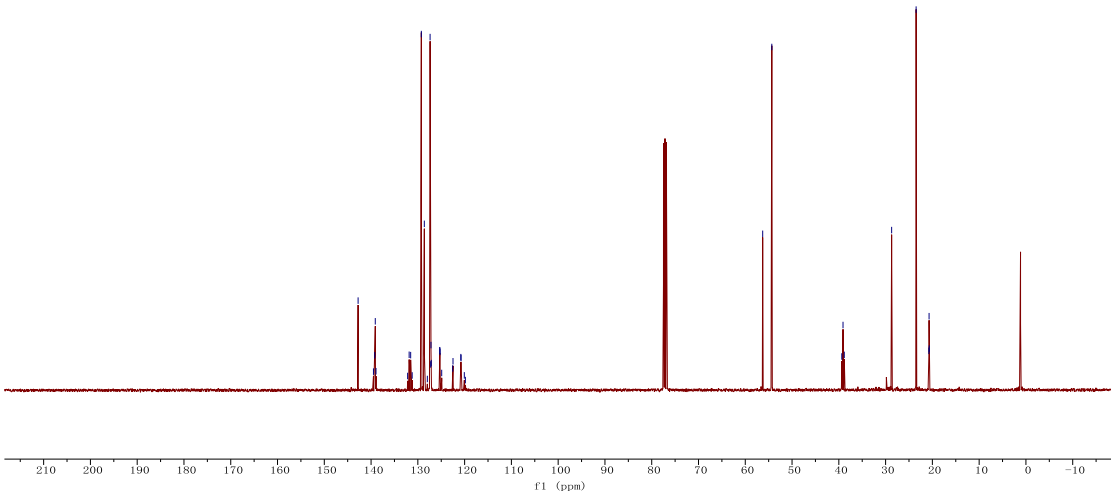


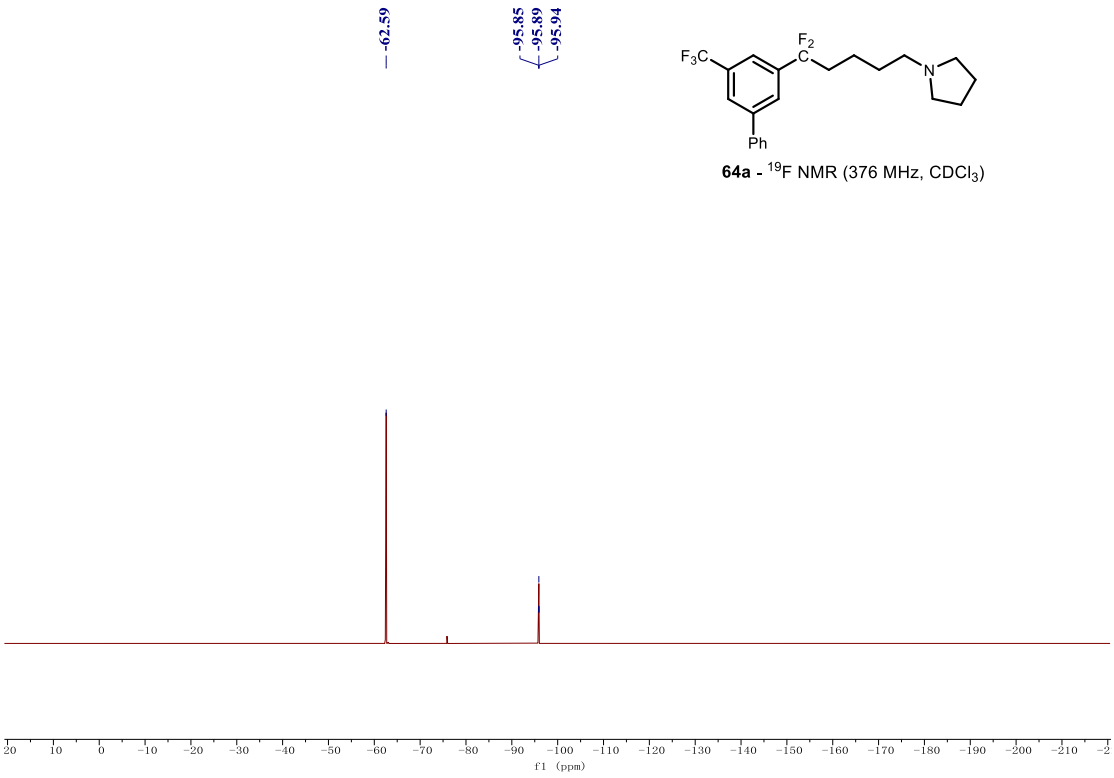
64a - ^{1}H NMR (400 MHz, $CDCl_3$)



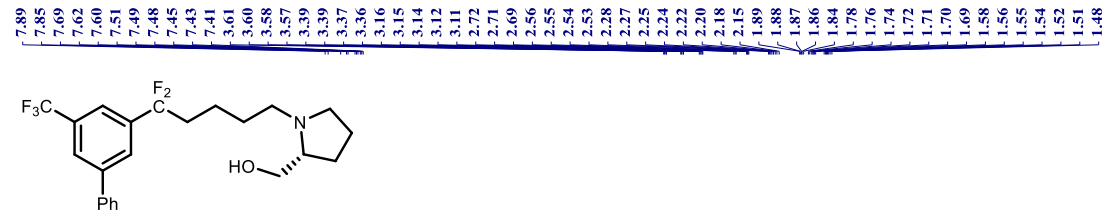


64a - ^{13}C NMR (101 MHz, $CDCl_3$)

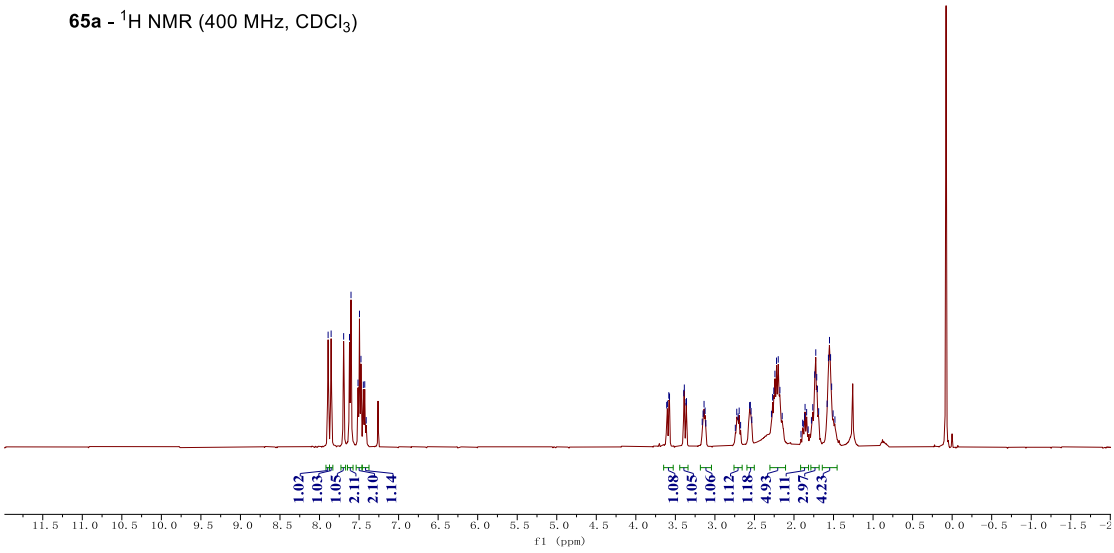


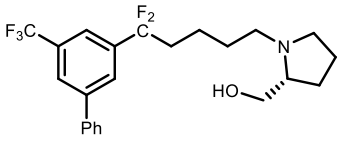


64a - ^{19}F NMR (376 MHz, $CDCl_3$)

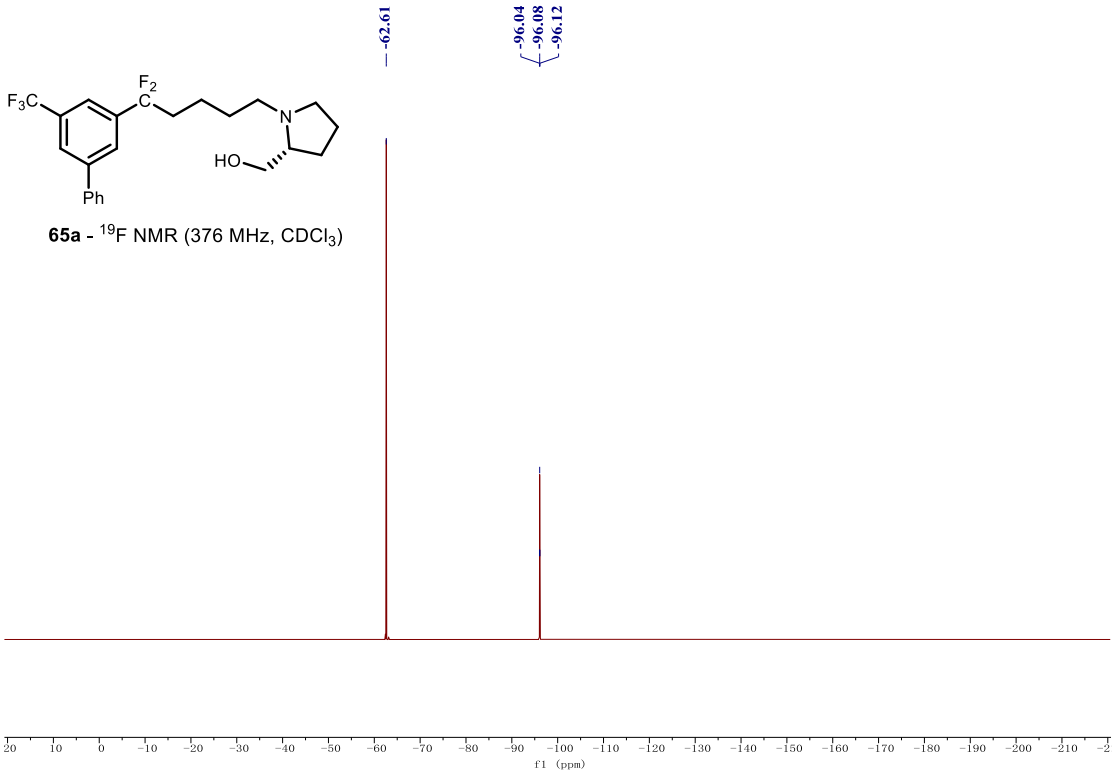


65a - ^{1}H NMR (400 MHz, $CDCl_3$)

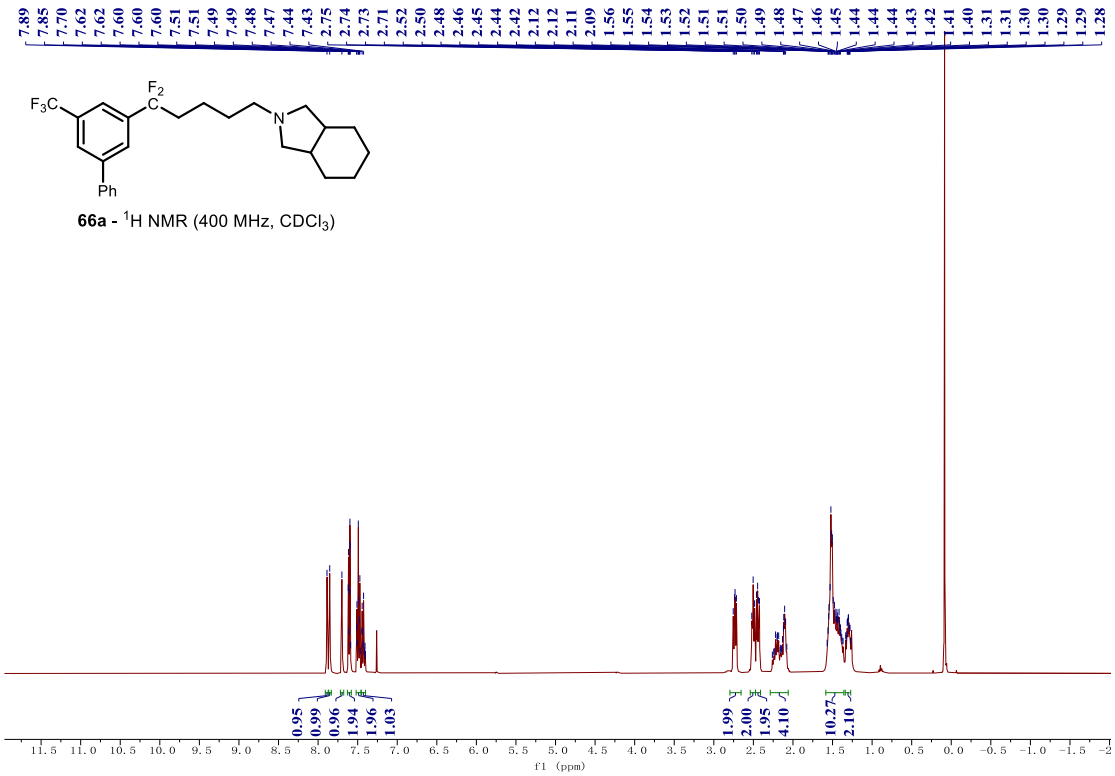




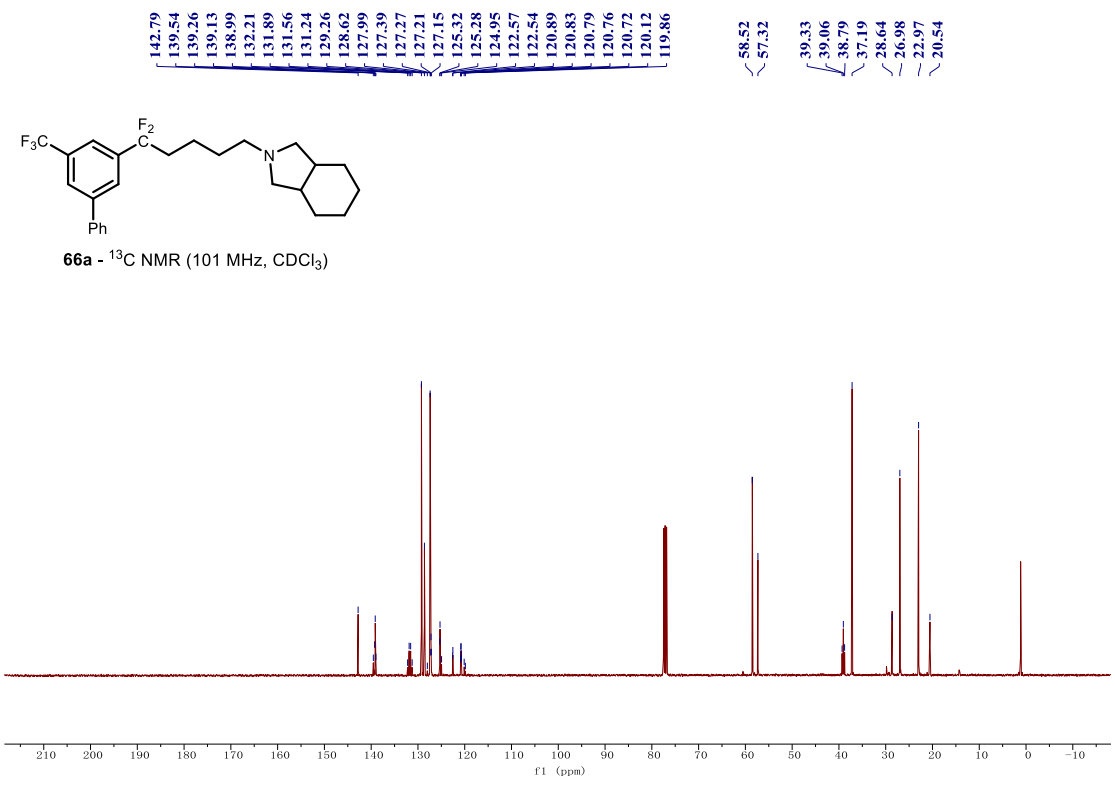
65a - ^{13}C NMR (101 MHz, $CDCl_3$)



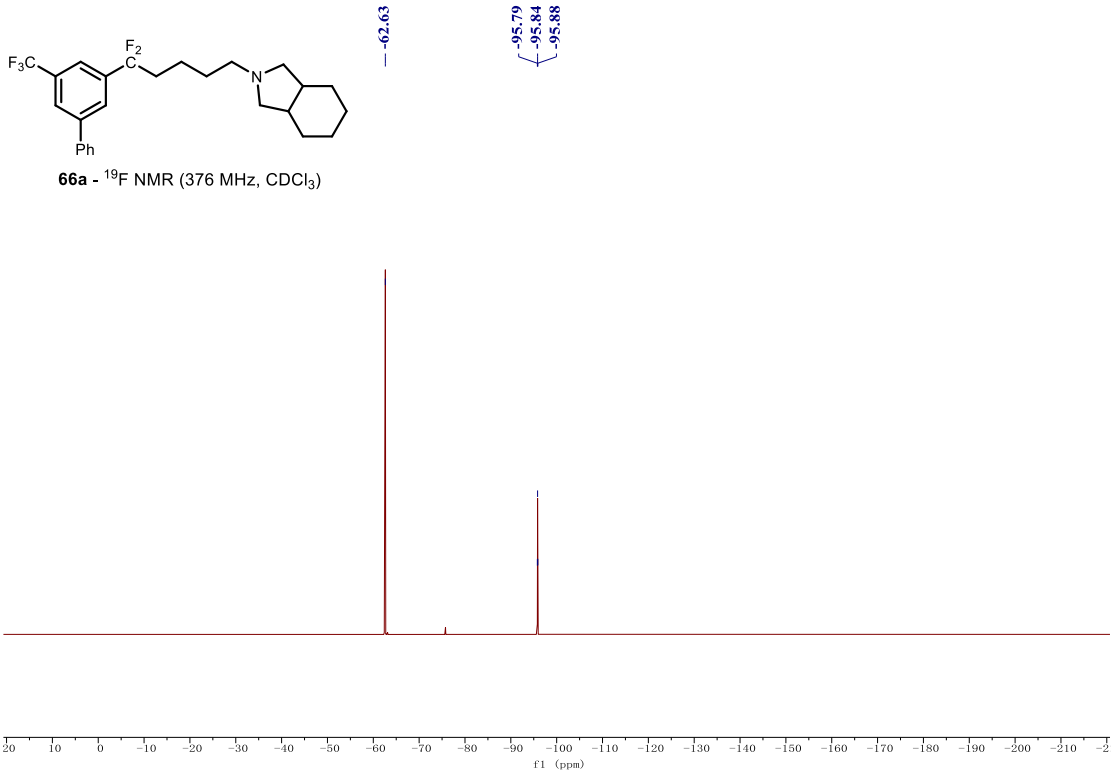
65a - ^{19}F NMR (376 MHz, $CDCl_3$)



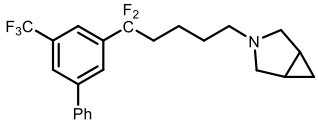
66a - ^{1}H NMR (400 MHz, $CDCl_3$)



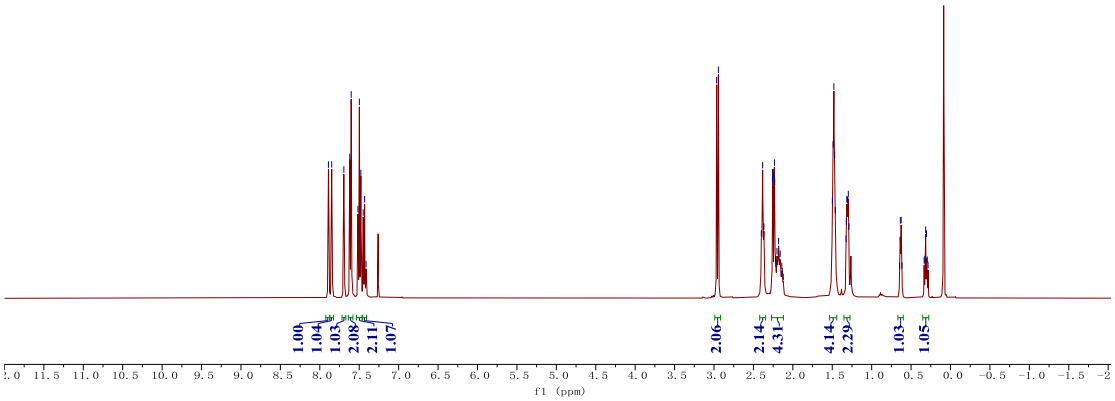
66a - ^{13}C NMR (101 MHz, $CDCl_3$)

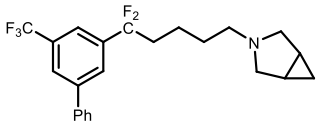


66a - ^{19}F NMR (376 MHz, $CDCl_3$)

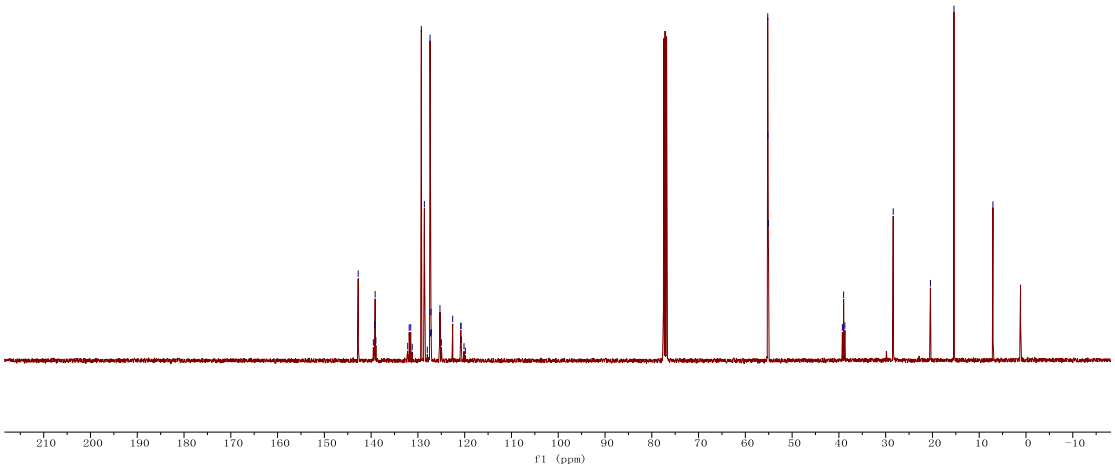


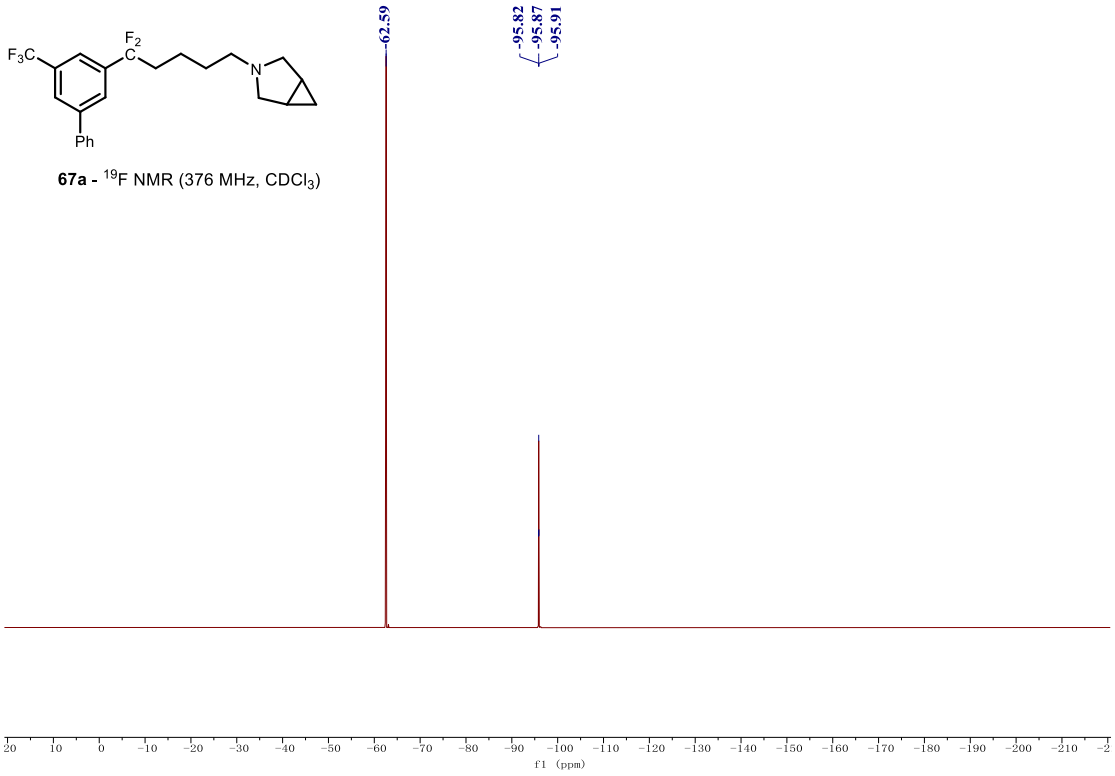
67a - ^{1}H NMR (400 MHz, $CDCl_3$)



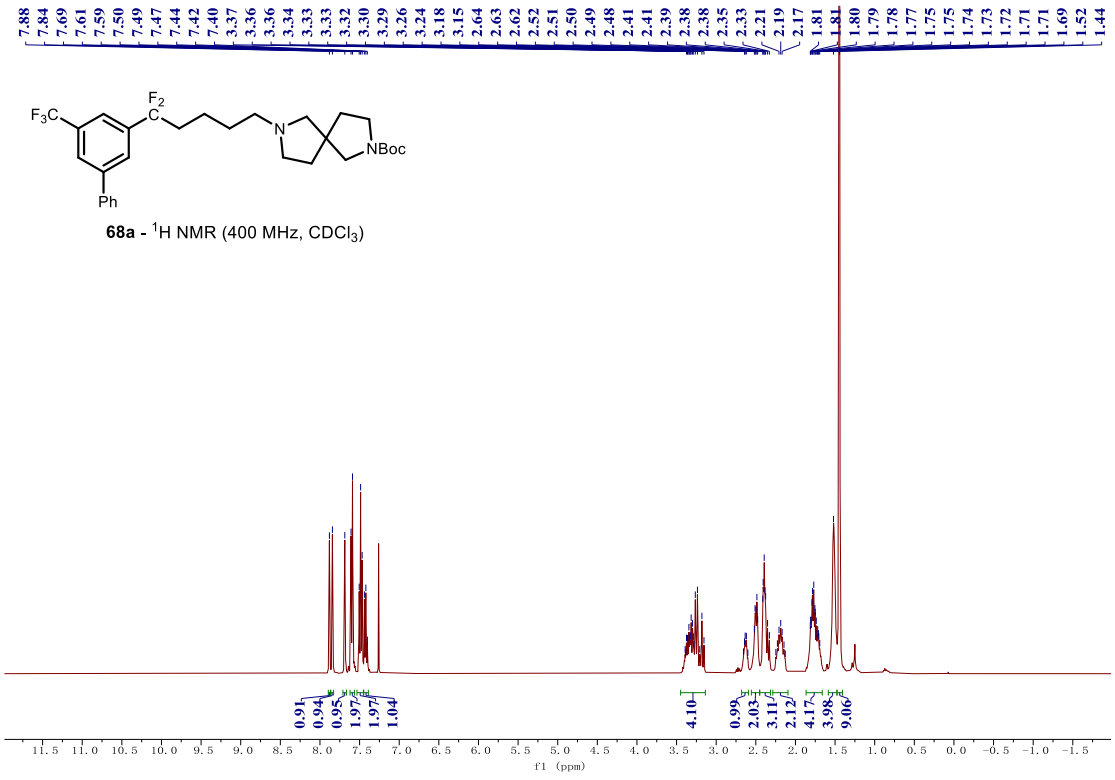


67a - ^{13}C NMR (101 MHz, $CDCl_3$)

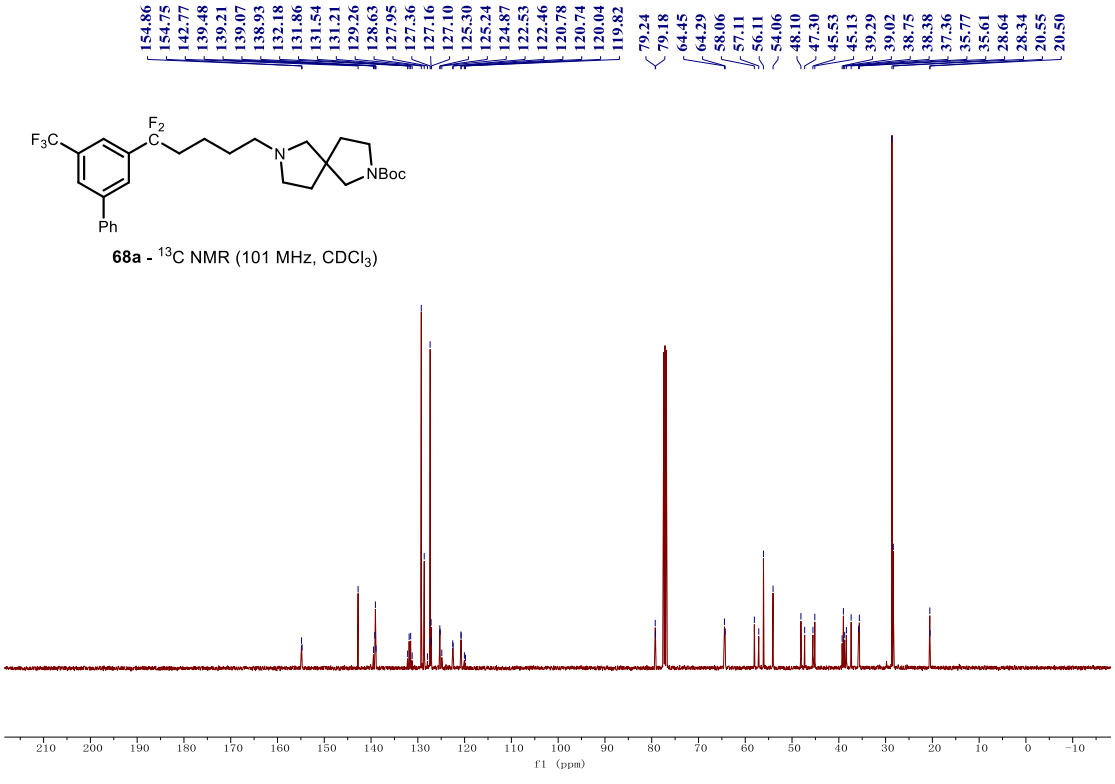




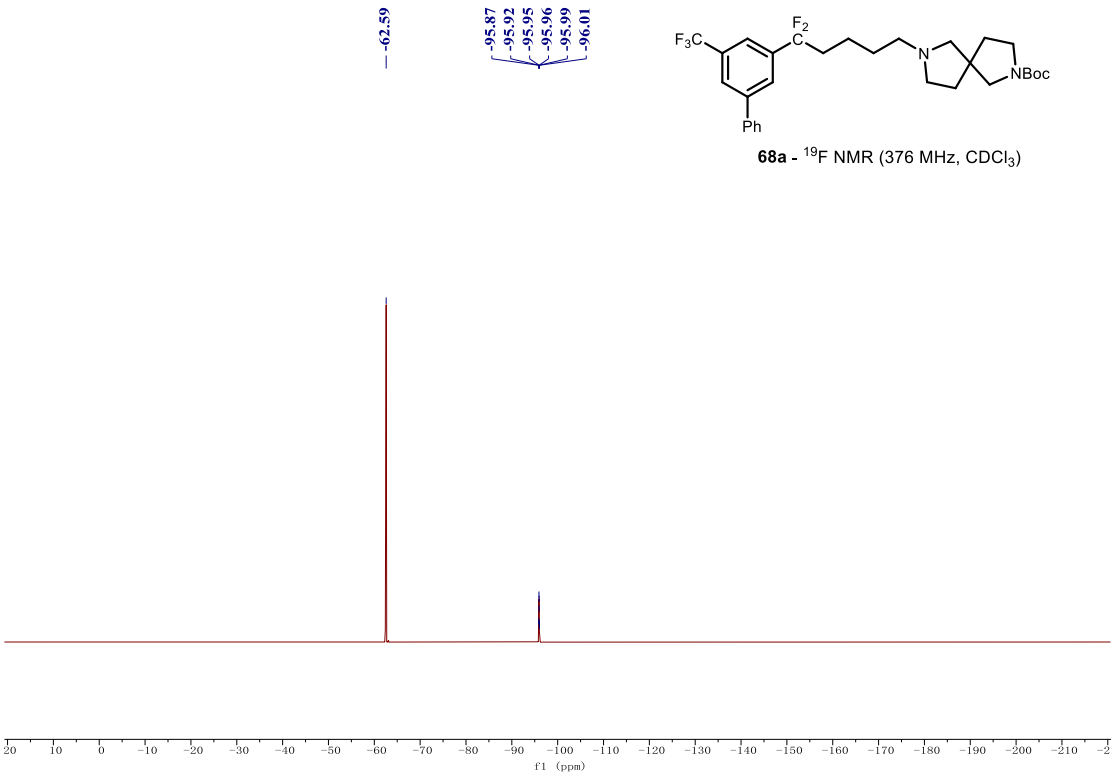
67a - ^{19}F NMR (376 MHz, $CDCl_3$)



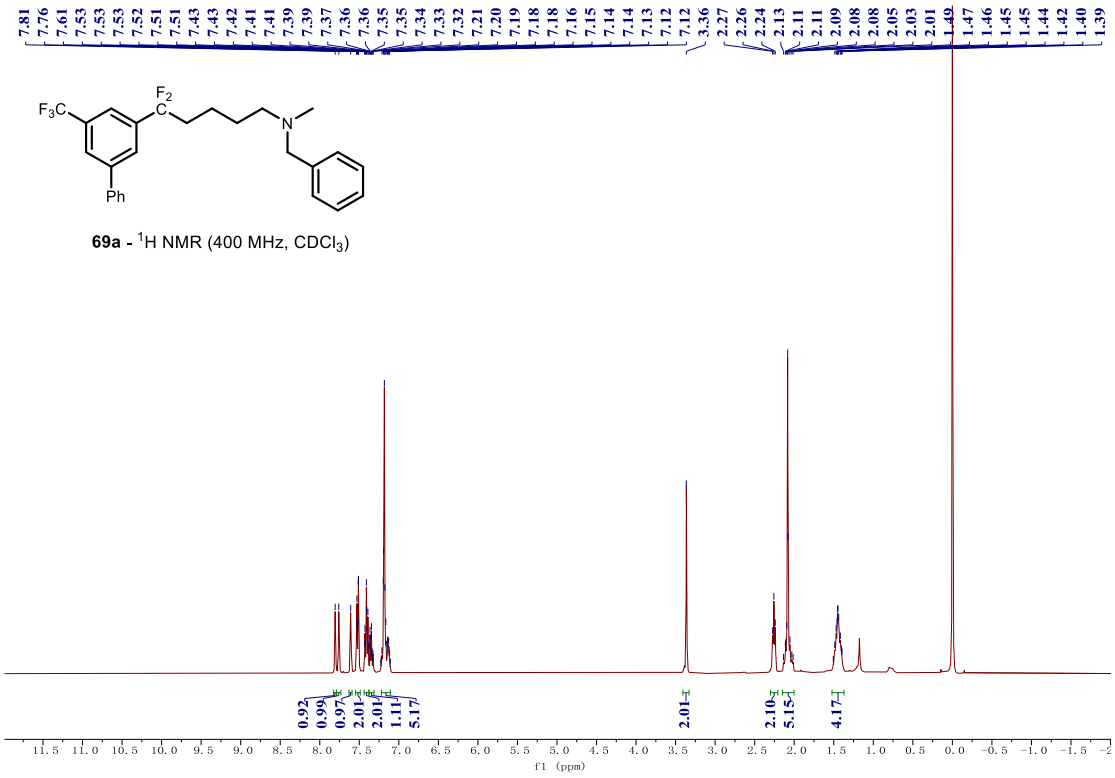
68a - ^{1}H NMR (400 MHz, $CDCl_3$)



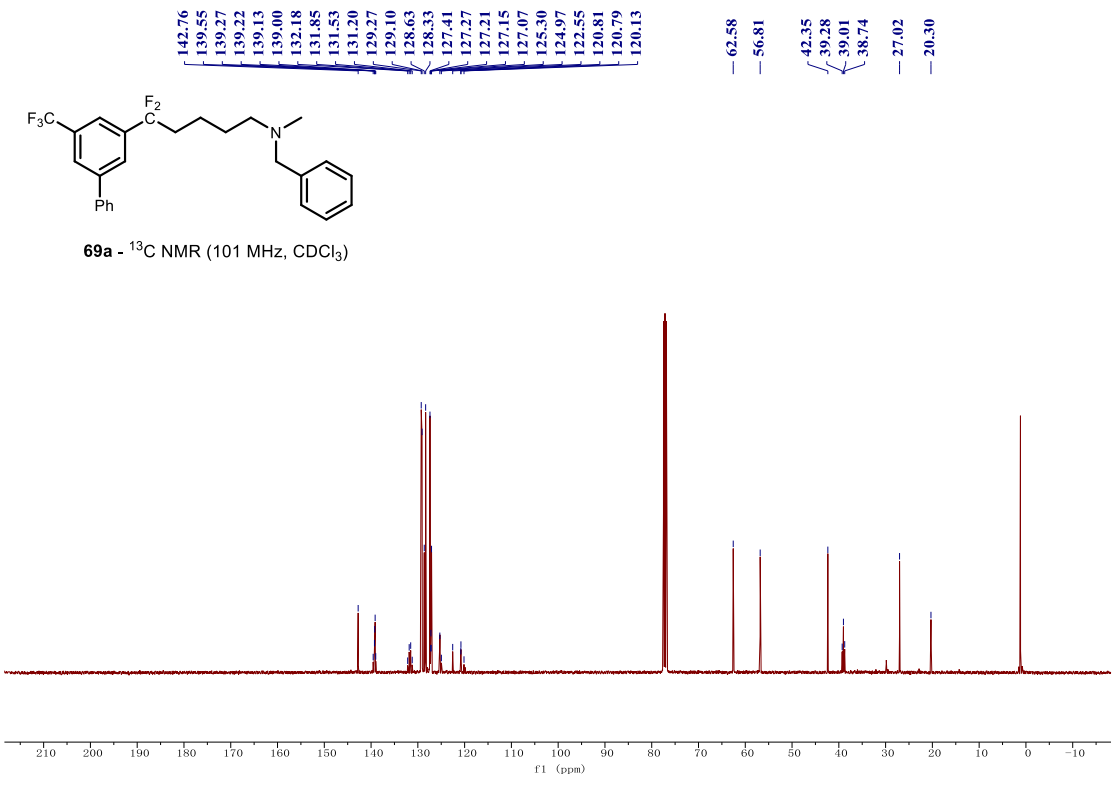
68a - ^{13}C NMR (101 MHz, $CDCl_3$)



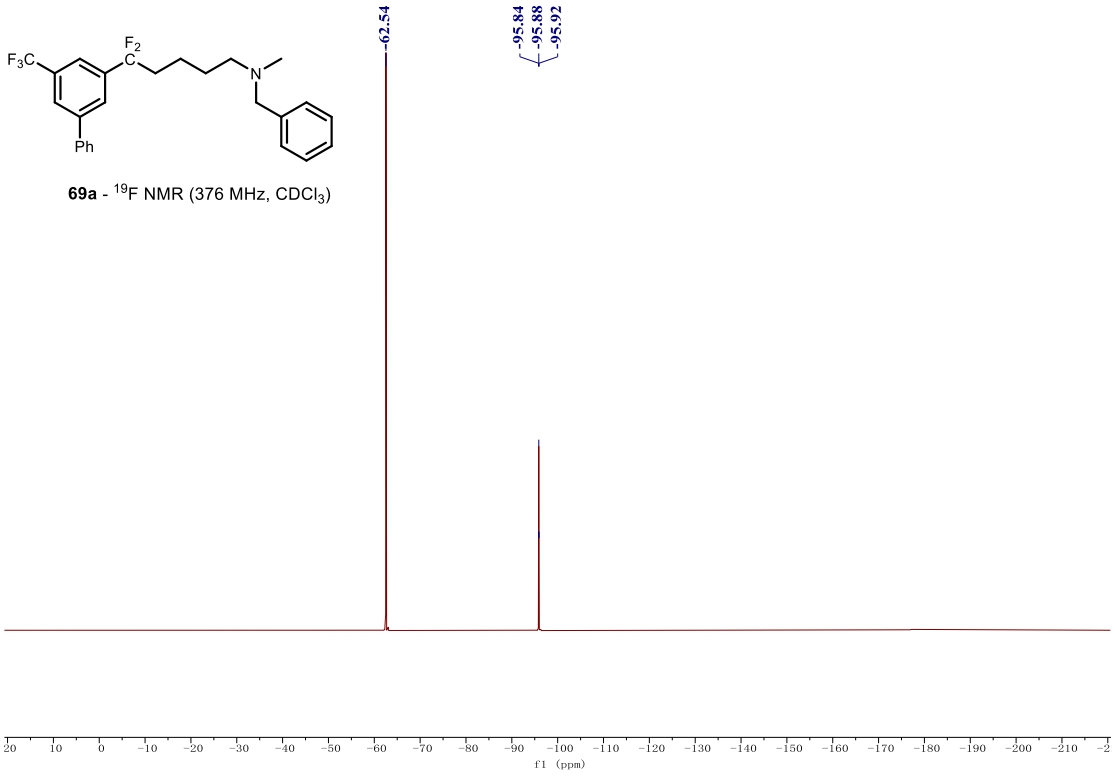
68a - ^{19}F NMR (376 MHz, $CDCl_3$)



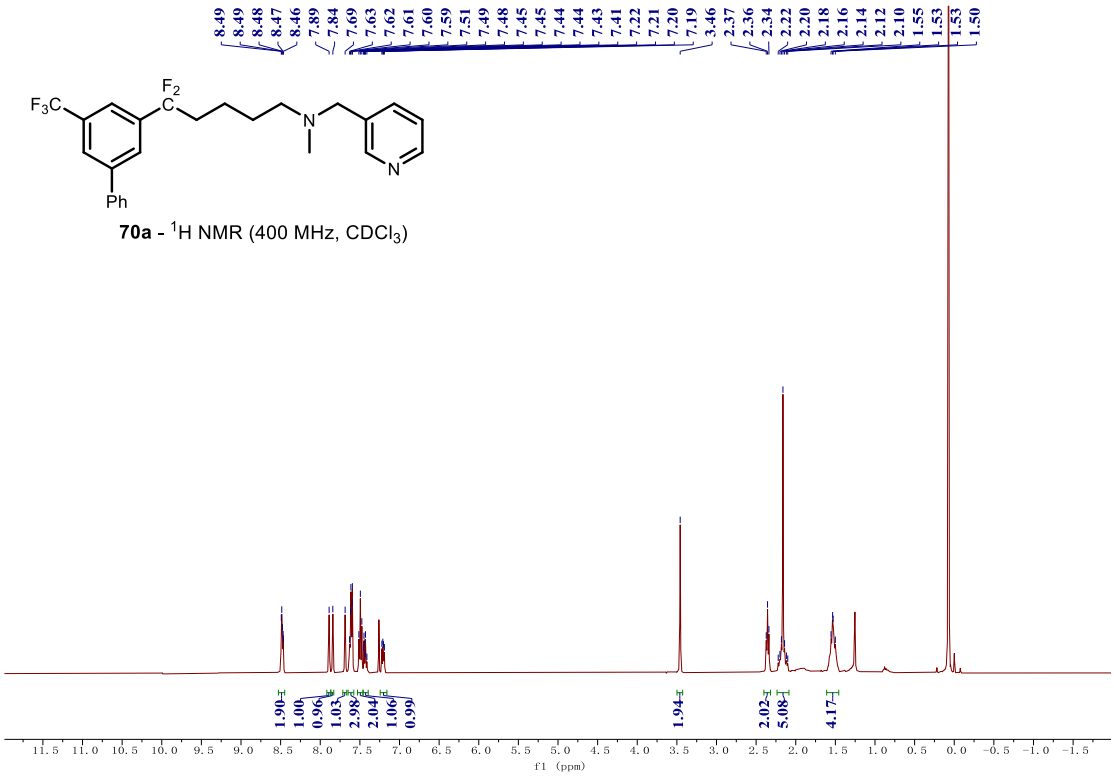
69a - ^{1}H NMR (400 MHz, $CDCl_3$)



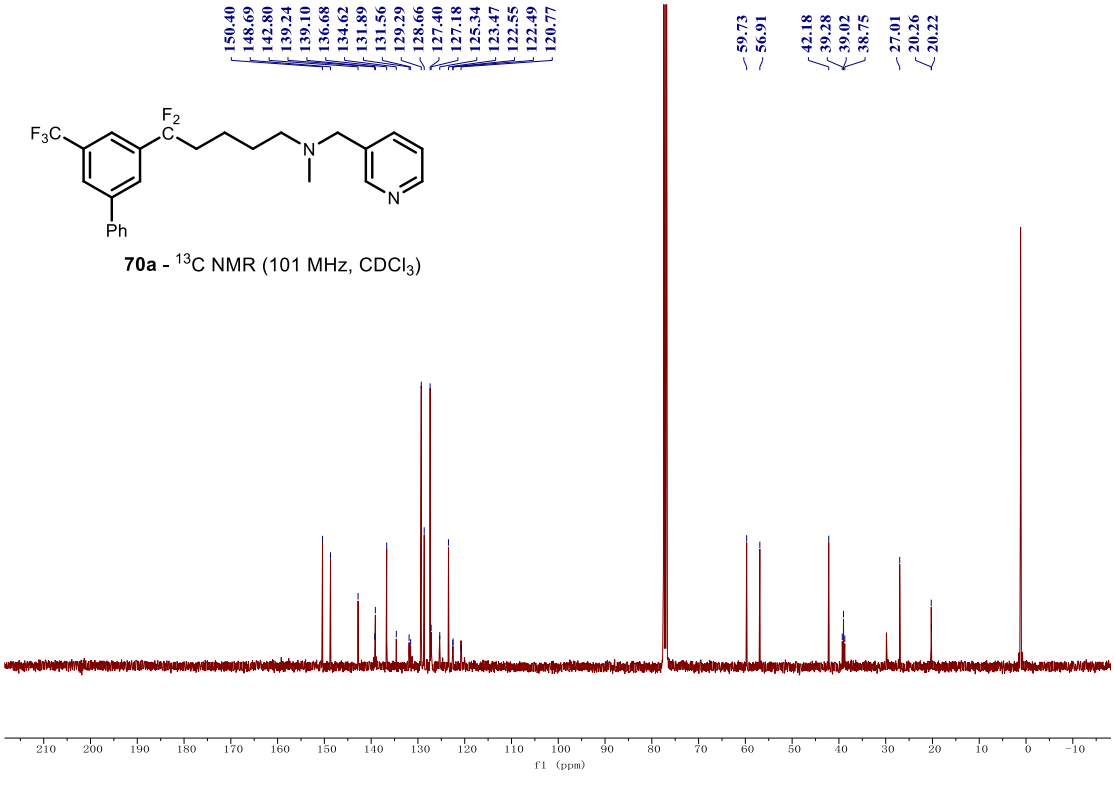
69a - ^{13}C NMR (101 MHz, $CDCl_3$)



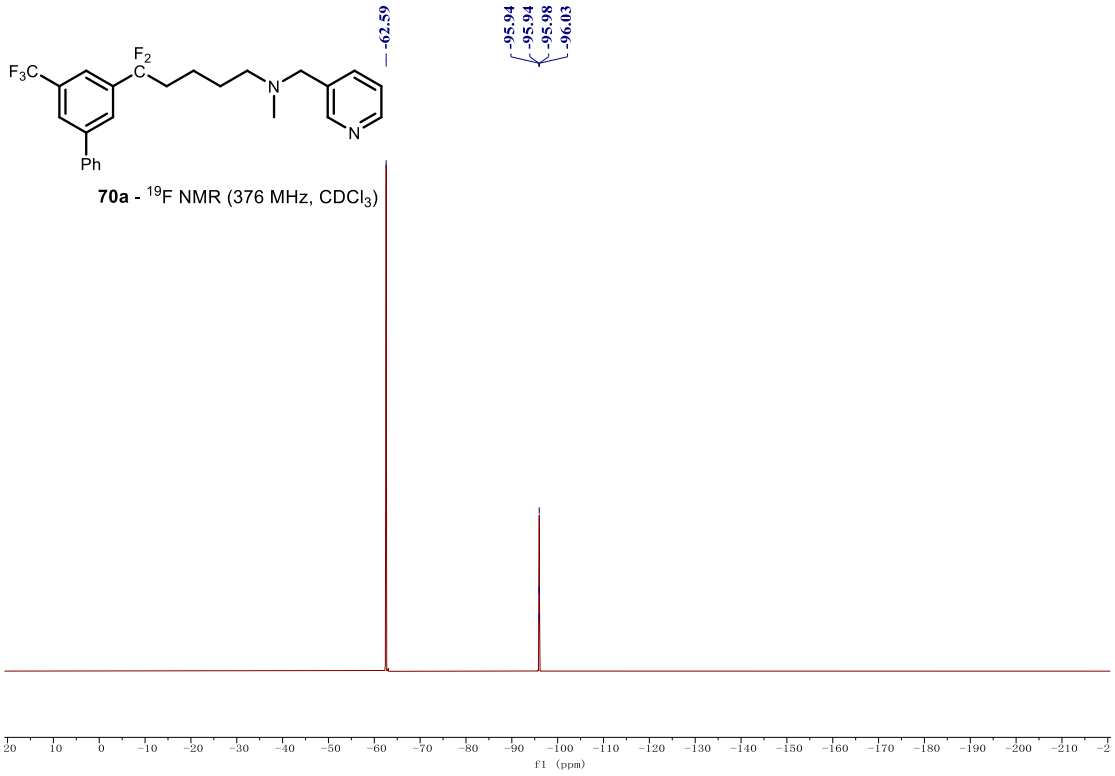
69a - ^{19}F NMR (376 MHz, $CDCl_3$)



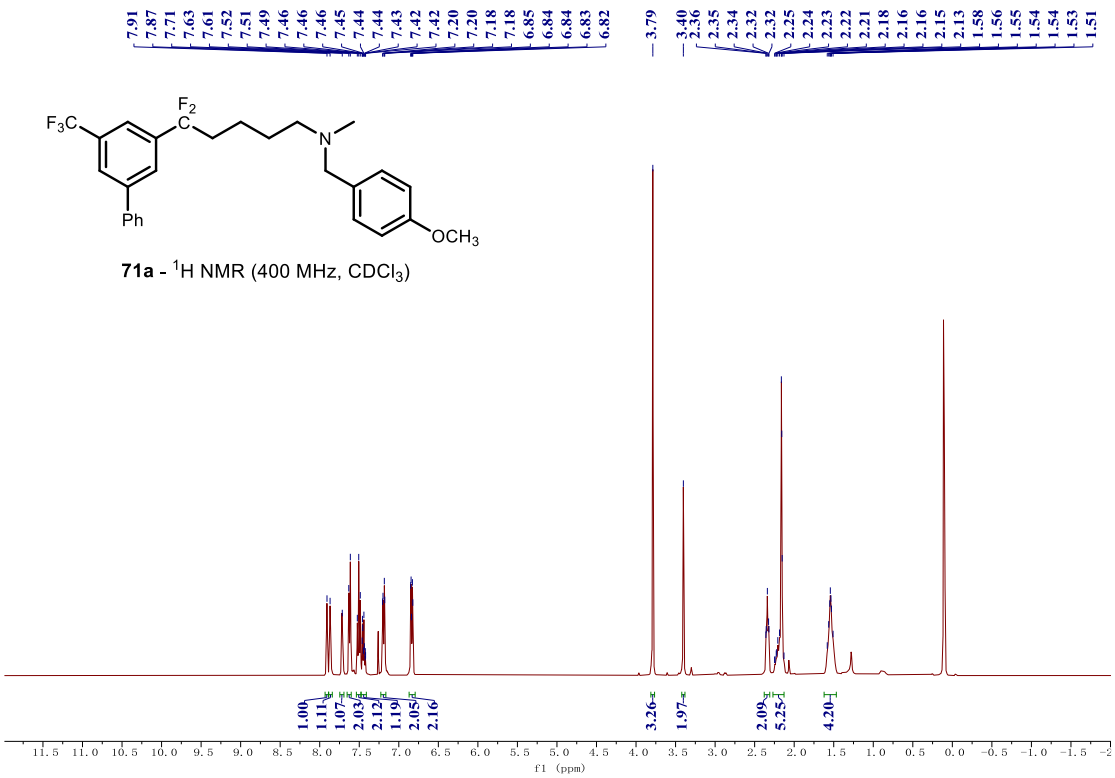
70a - ^{1}H NMR (400 MHz, $CDCl_3$)



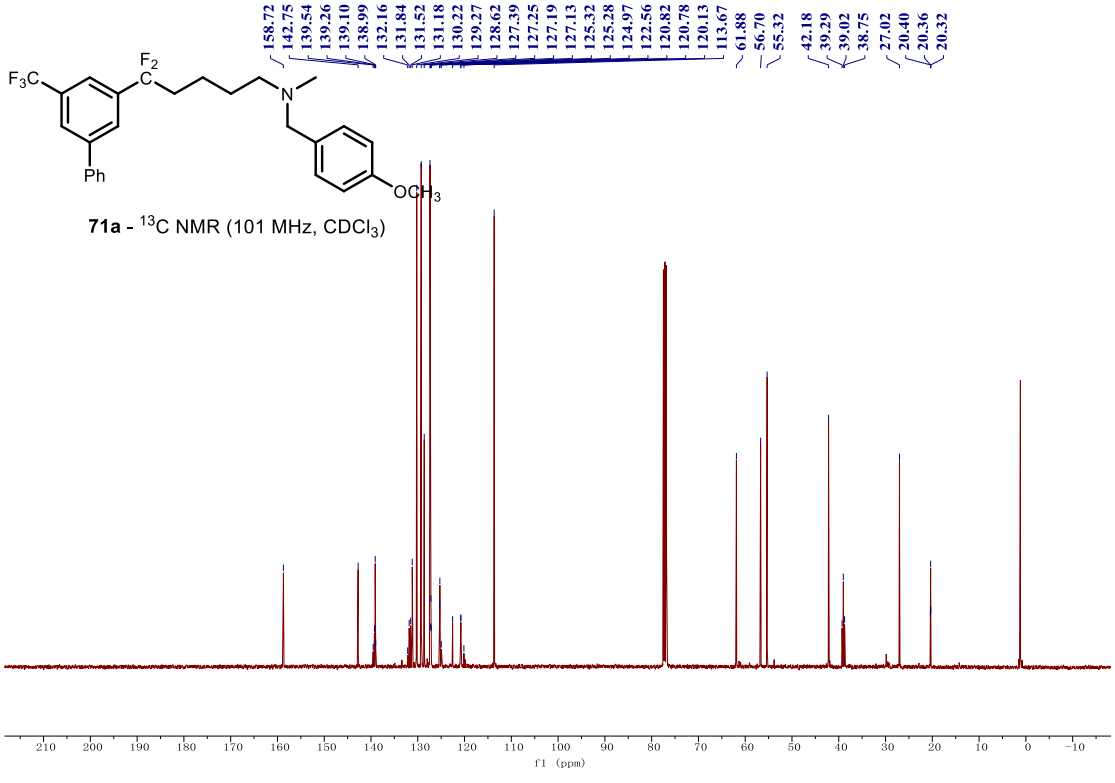
70a - ^{13}C NMR (101 MHz, $CDCl_3$)



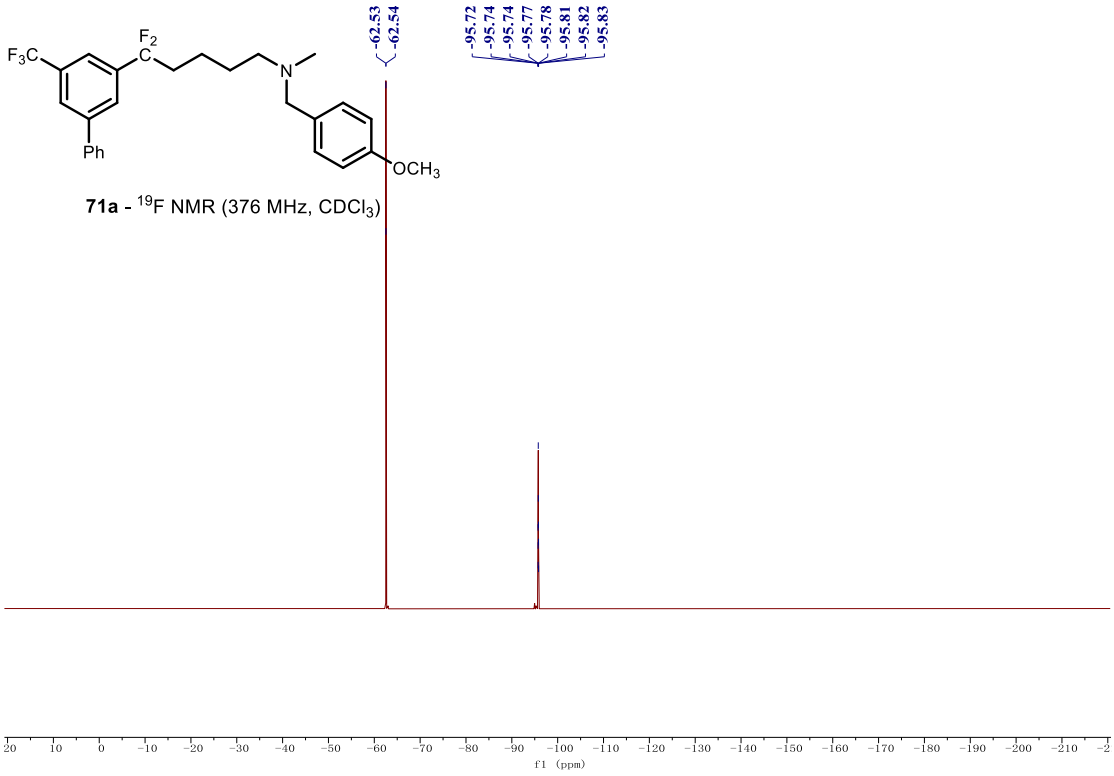
70a - ^{19}F NMR (376 MHz, $CDCl_3$)



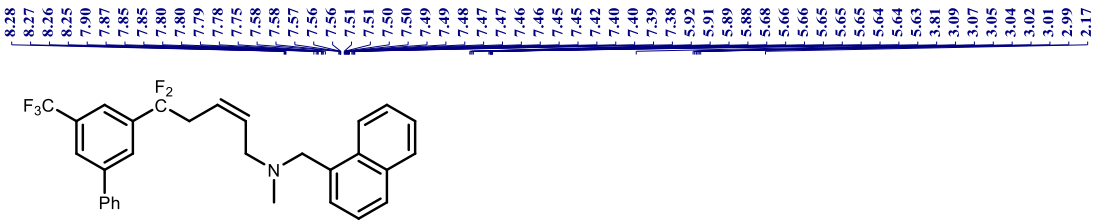
71a - ^{1}H NMR (400 MHz, $CDCl_3$)



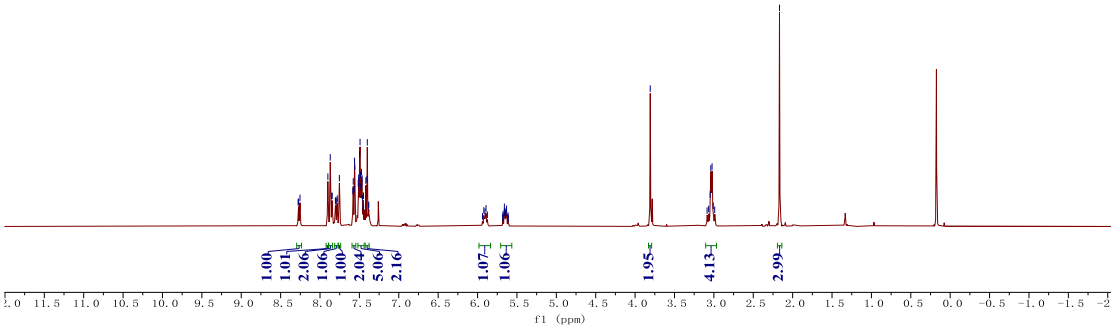
71a - ^{13}C NMR (101 MHz, $CDCl_3$)



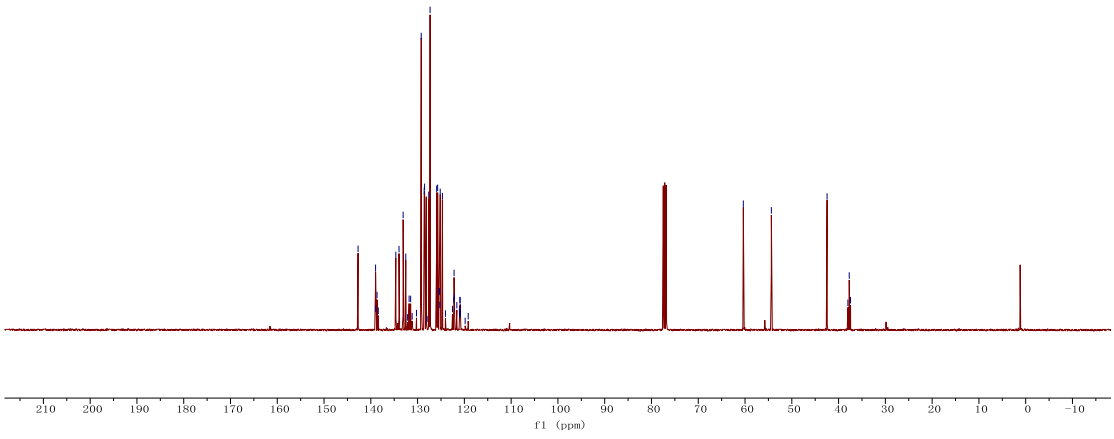
71a - ^{19}F NMR (376 MHz, $CDCl_3$)

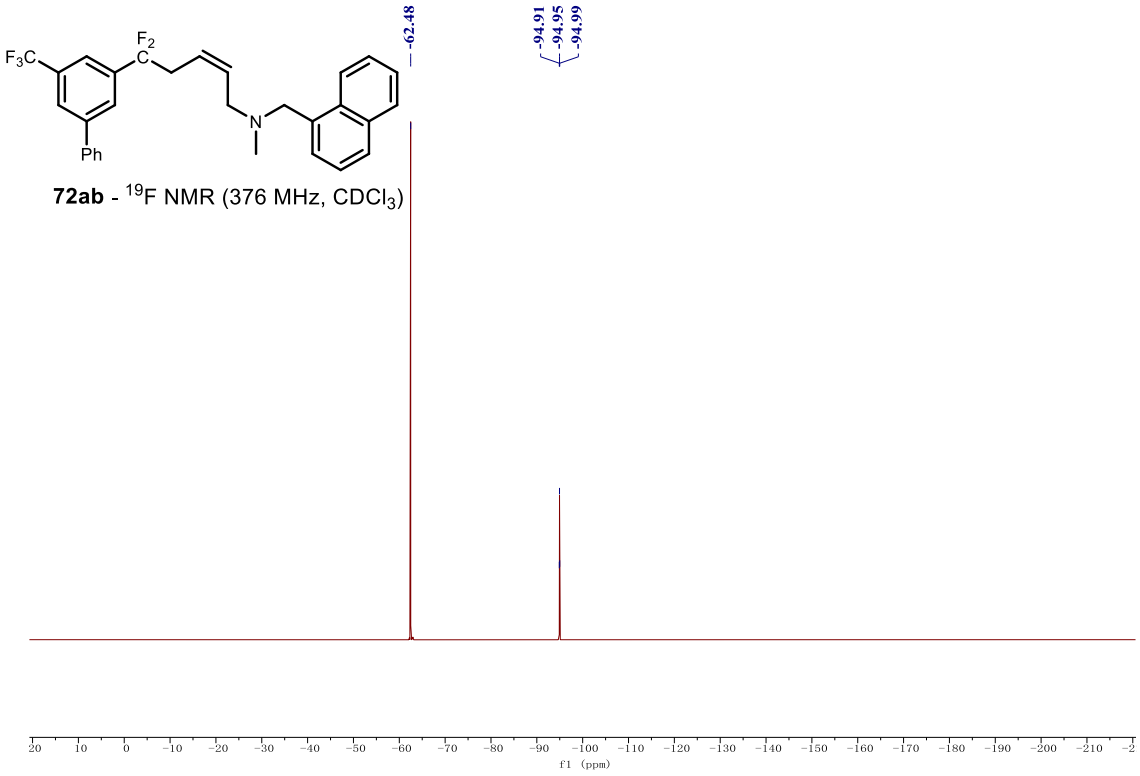


72ab - ^{1}H NMR (400 MHz, $CDCl_3$)

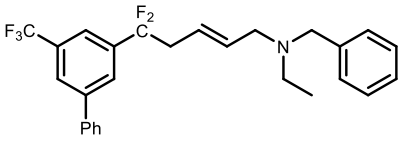


72ab - ^{13}C NMR (101 MHz, $CDCl_3$)

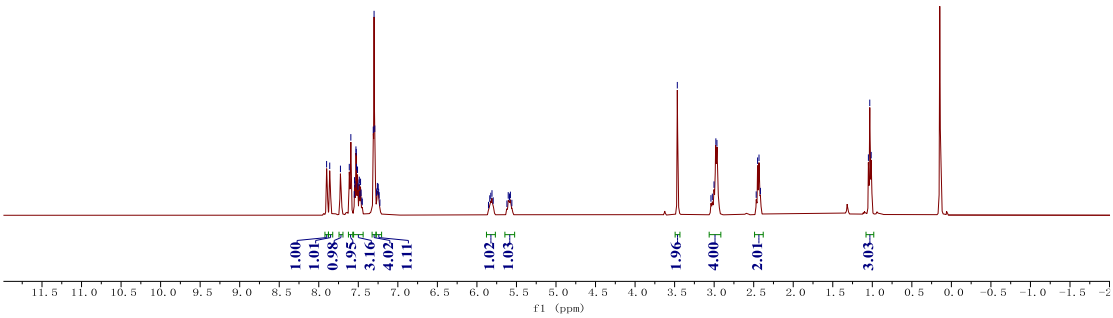


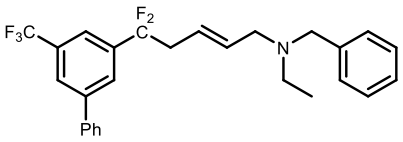


72ab - ^{19}F NMR (376 MHz, $CDCl_3$)

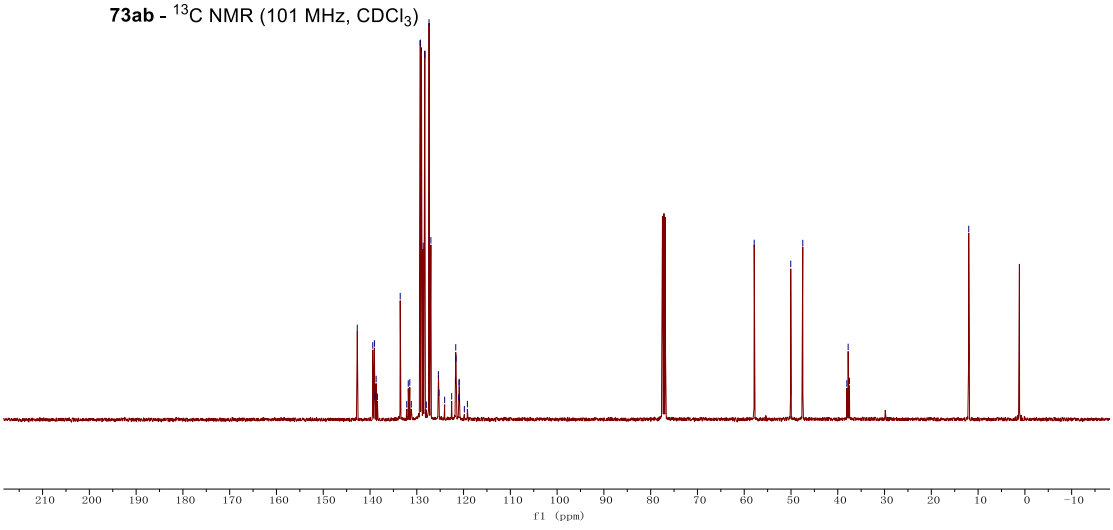


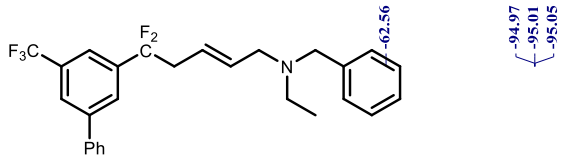
73ab - ^{1}H NMR (400 MHz, $CDCl_3$)



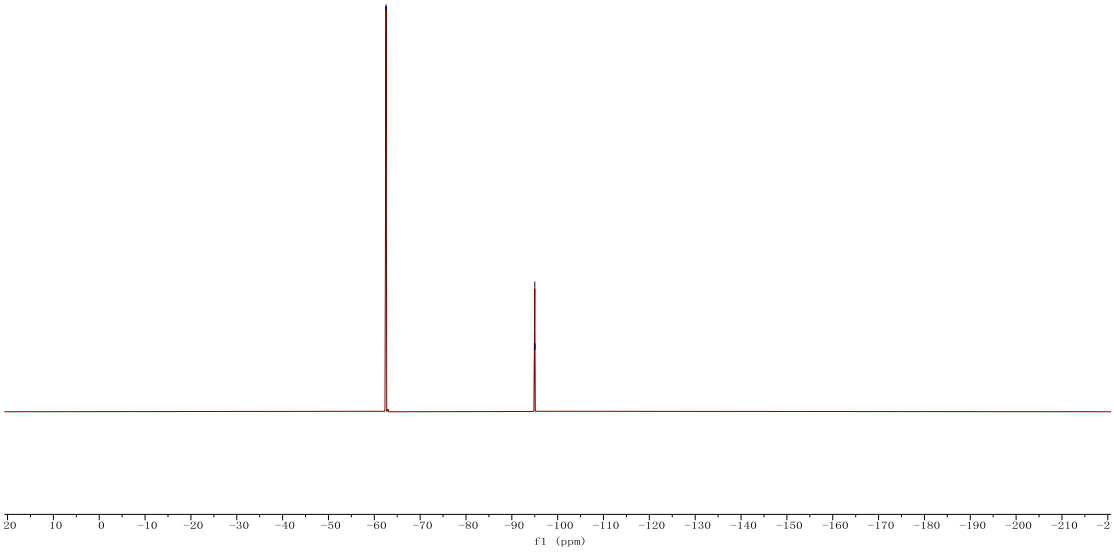


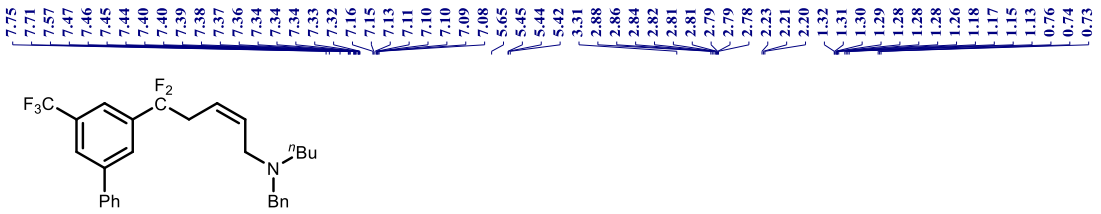
73ab - ^{13}C NMR (101 MHz, $CDCl_3$)



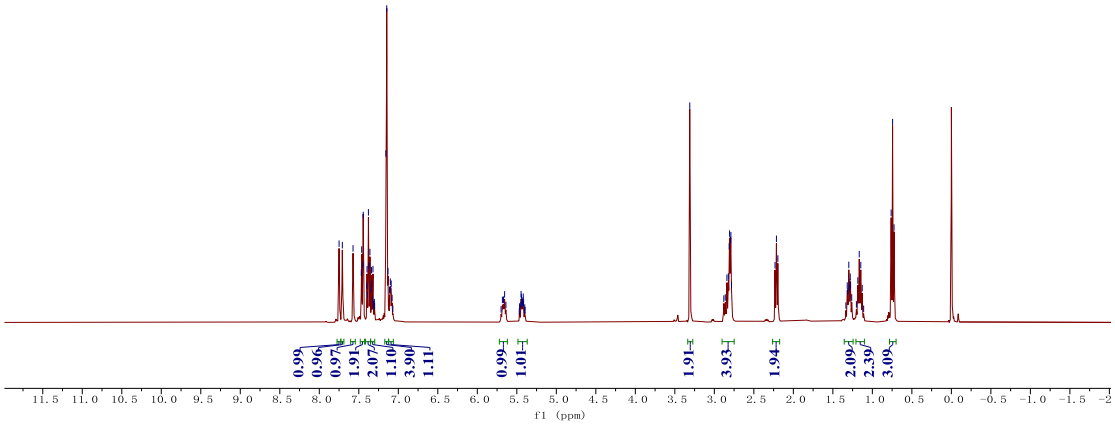


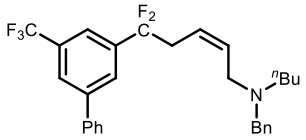
73ab - ^{19}F NMR (376 MHz, $CDCl_3$)



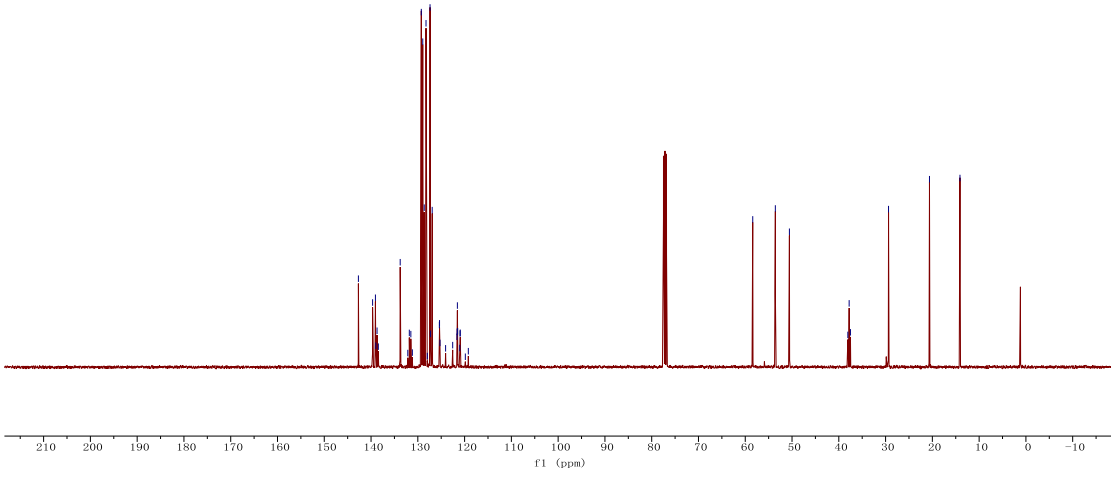


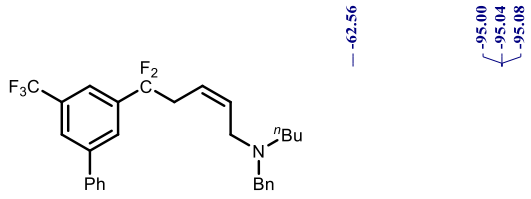
74ab - ^{1}H NMR (400 MHz, $CDCl_3$)



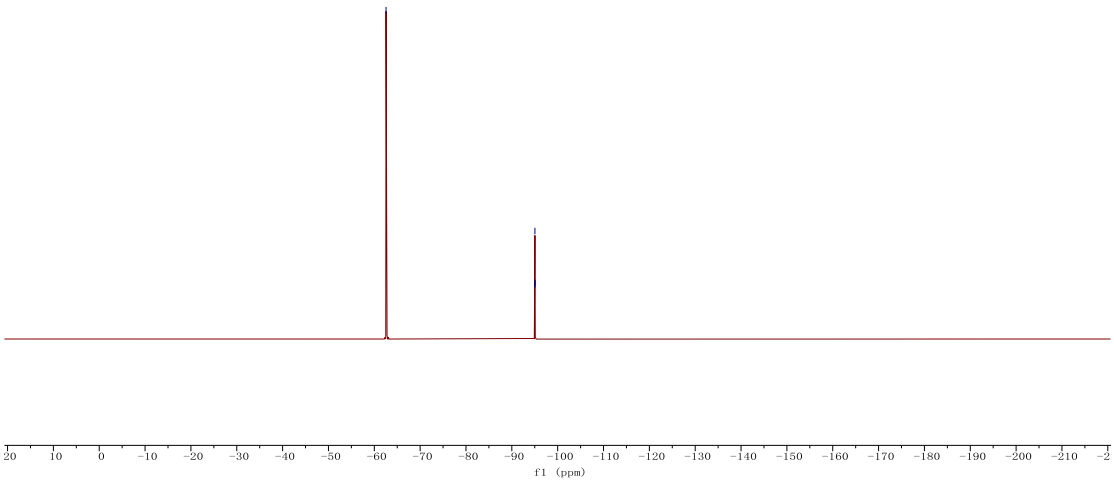


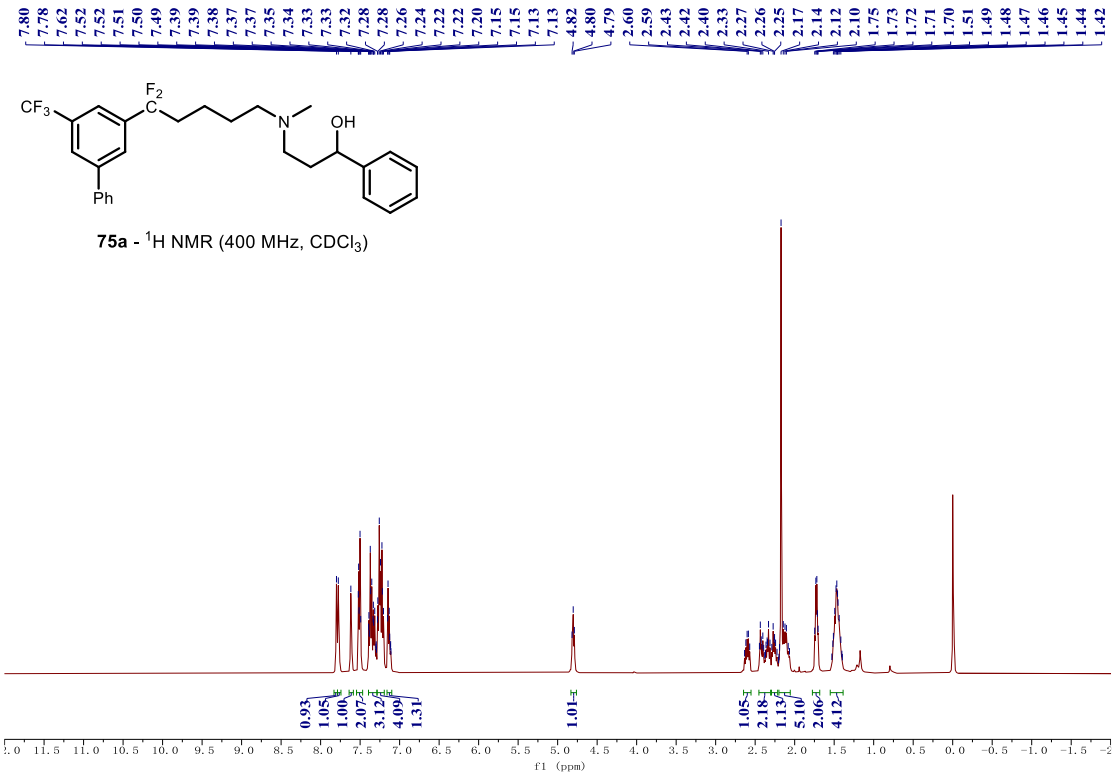
74ab - ^{13}C NMR (101 MHz, $CDCl_3$)



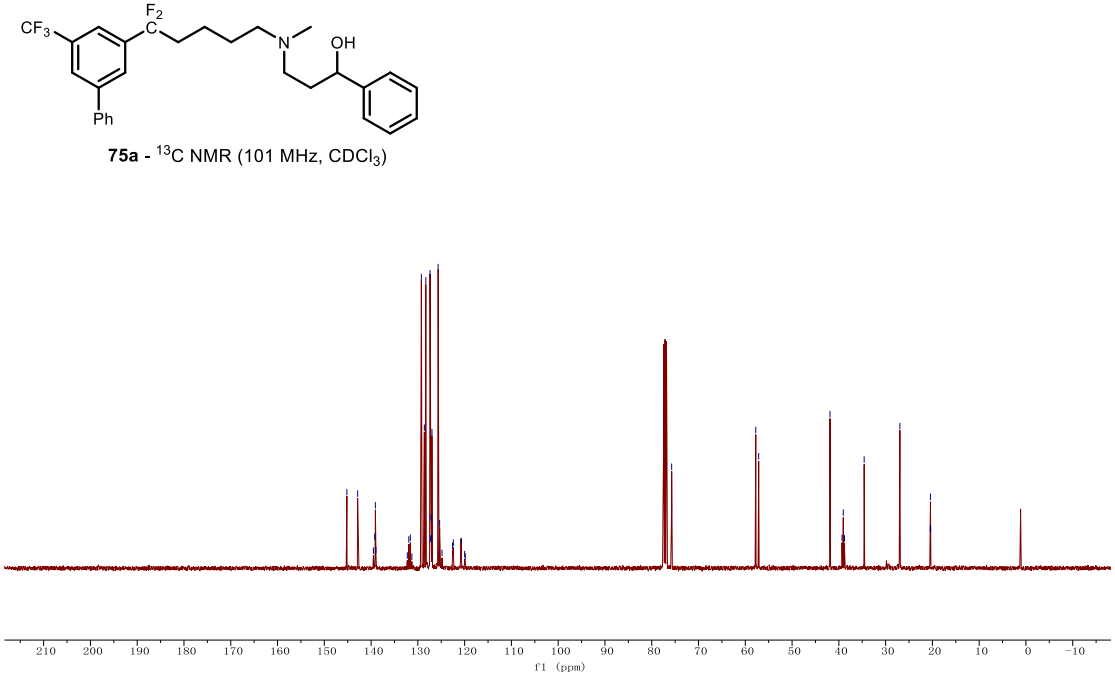


74ab - ^{19}F NMR (376 MHz, $CDCl_3$)

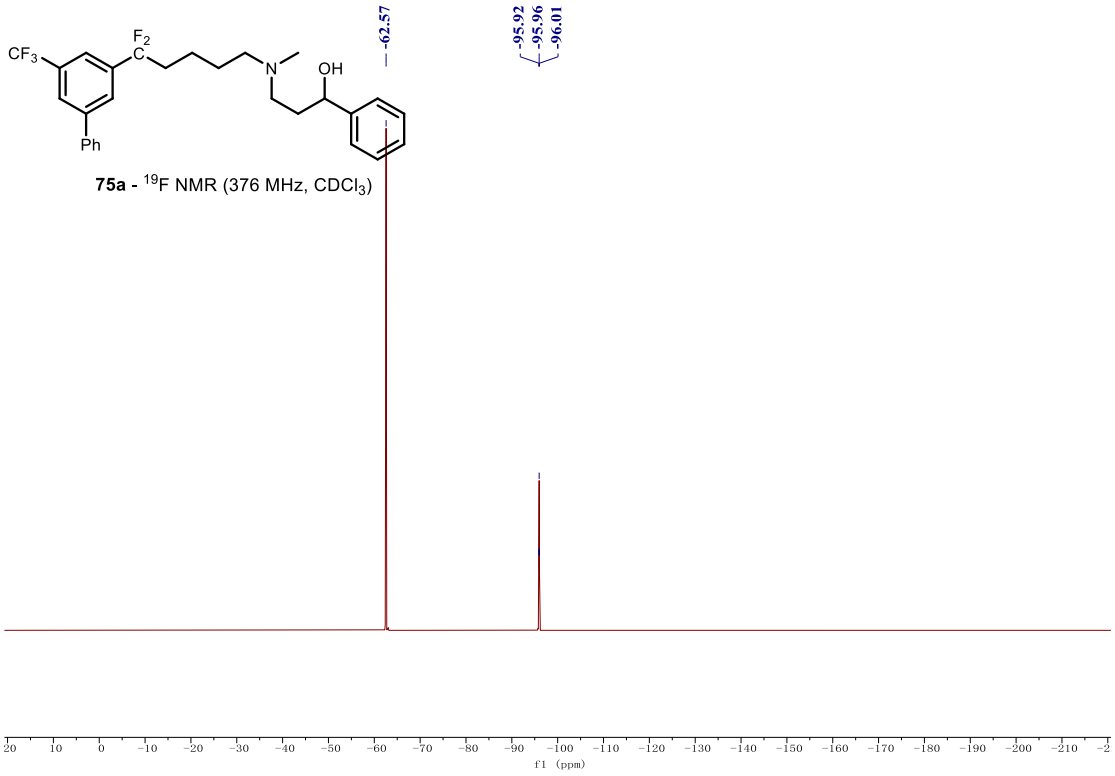




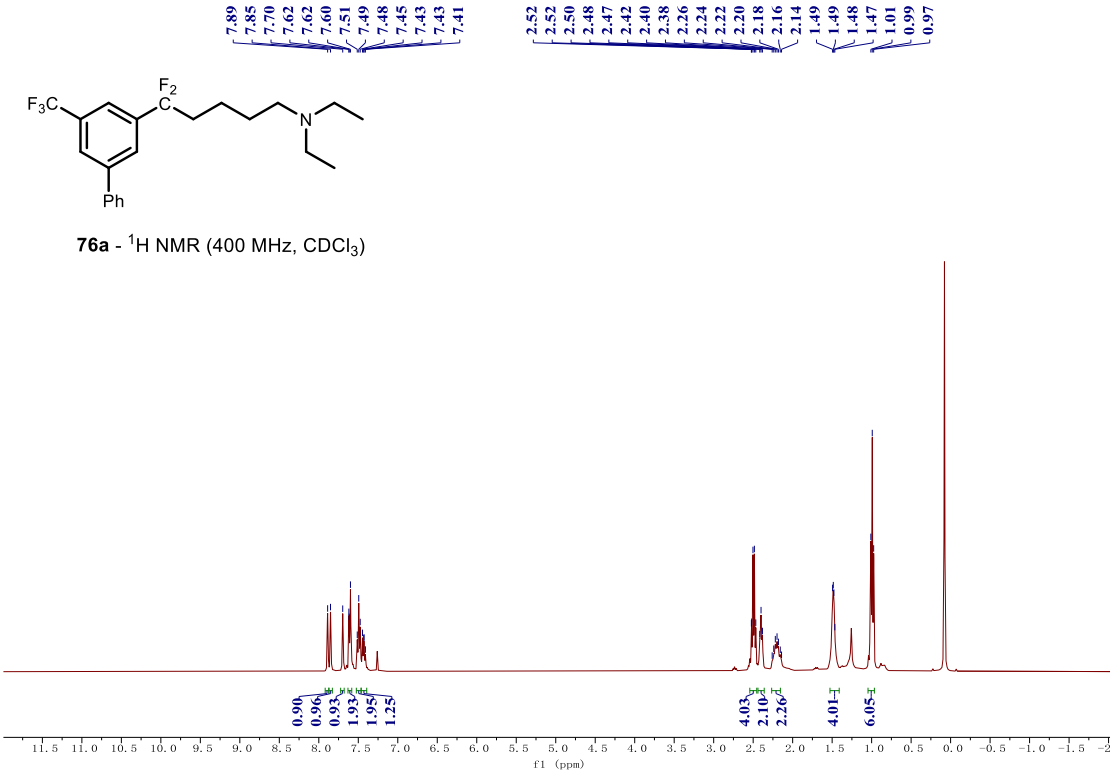
75a - ^{1}H NMR (400 MHz, $CDCl_3$)



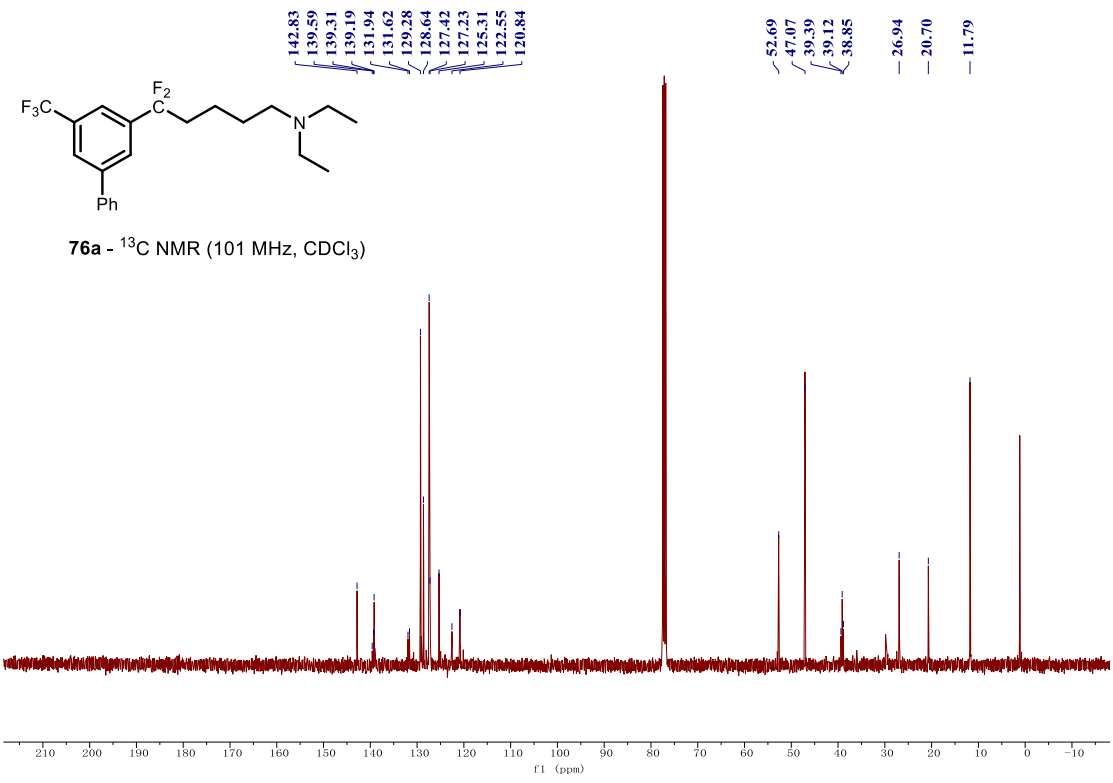
75a - ^{13}C NMR (101 MHz, $CDCl_3$)



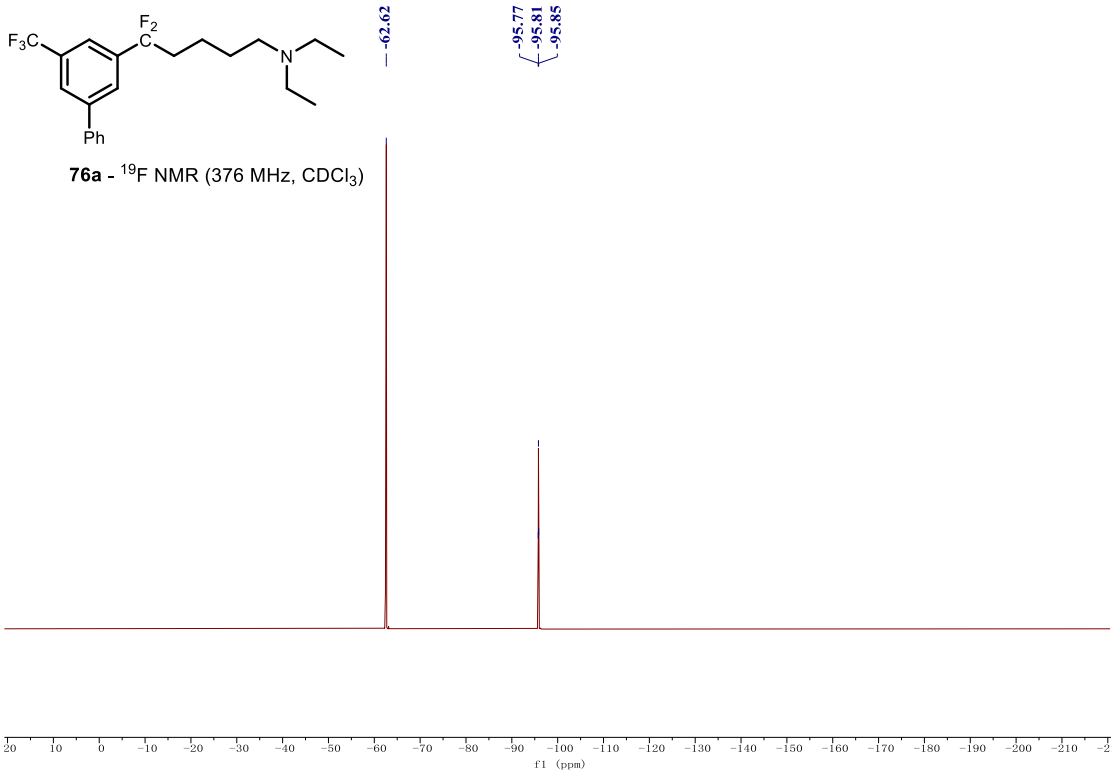
75a - ^{19}F NMR (376 MHz, $CDCl_3$)



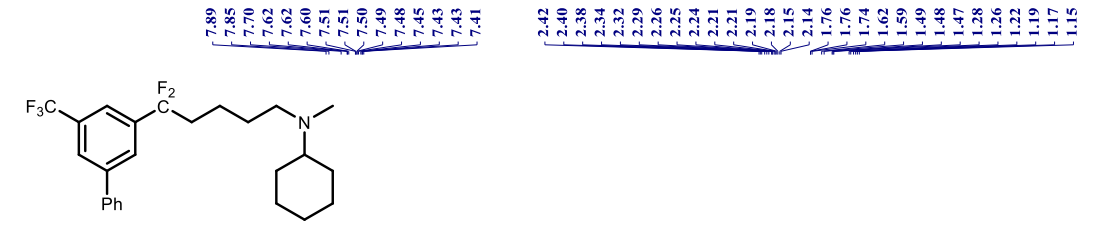
76a - ^{1}H NMR (400 MHz, $CDCl_3$)



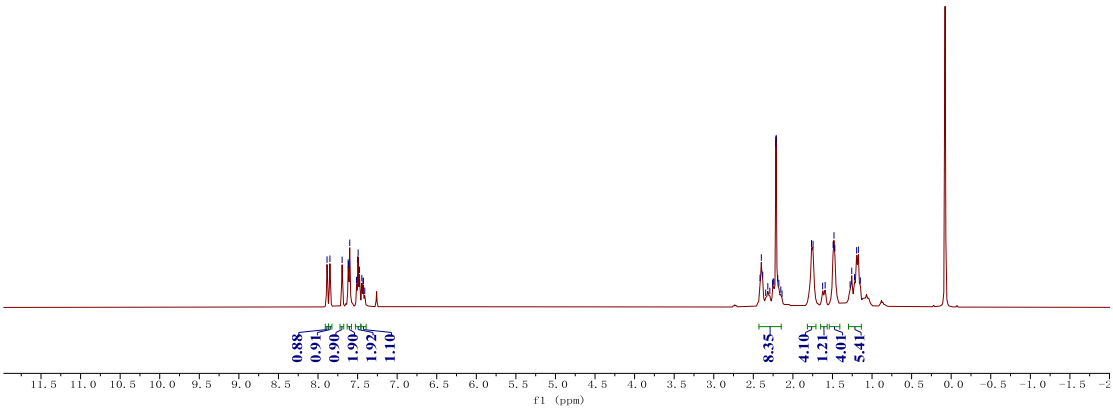
76a - ^{13}C NMR (101 MHz, $CDCl_3$)

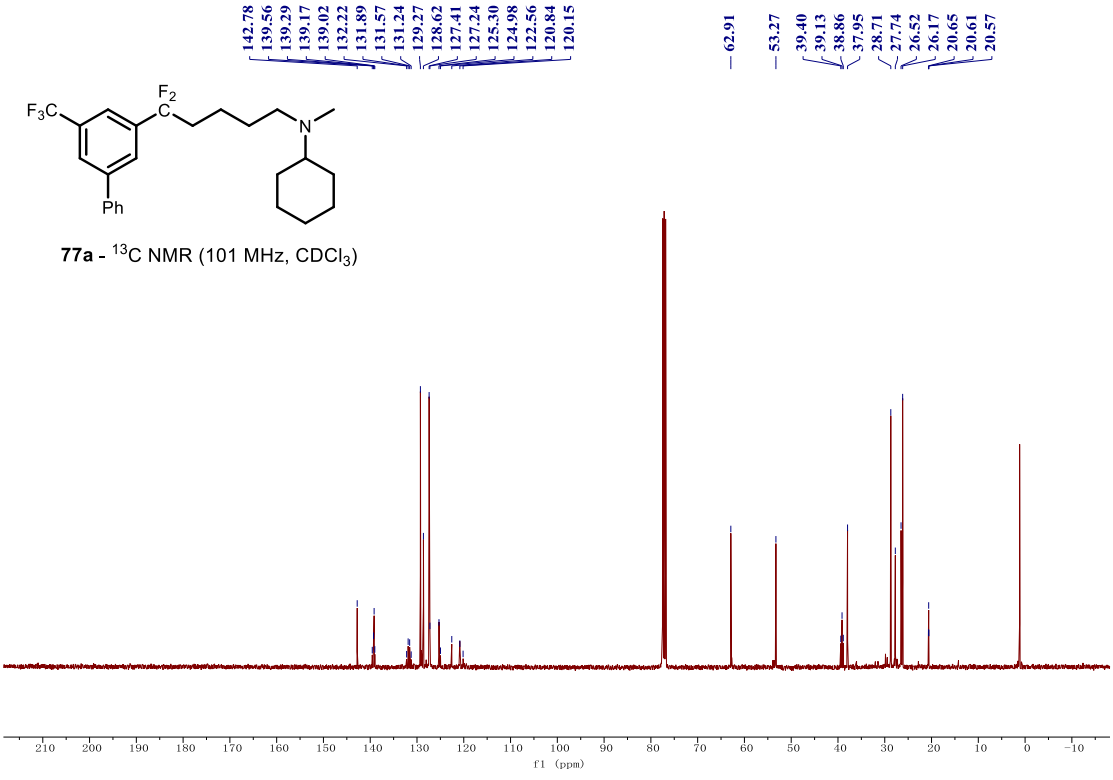


76a - ^{19}F NMR (376 MHz, $CDCl_3$)

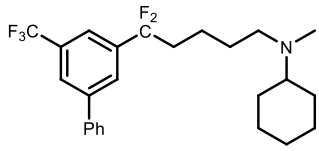


77a - ^{1}H NMR (400 MHz, $CDCl_3$)

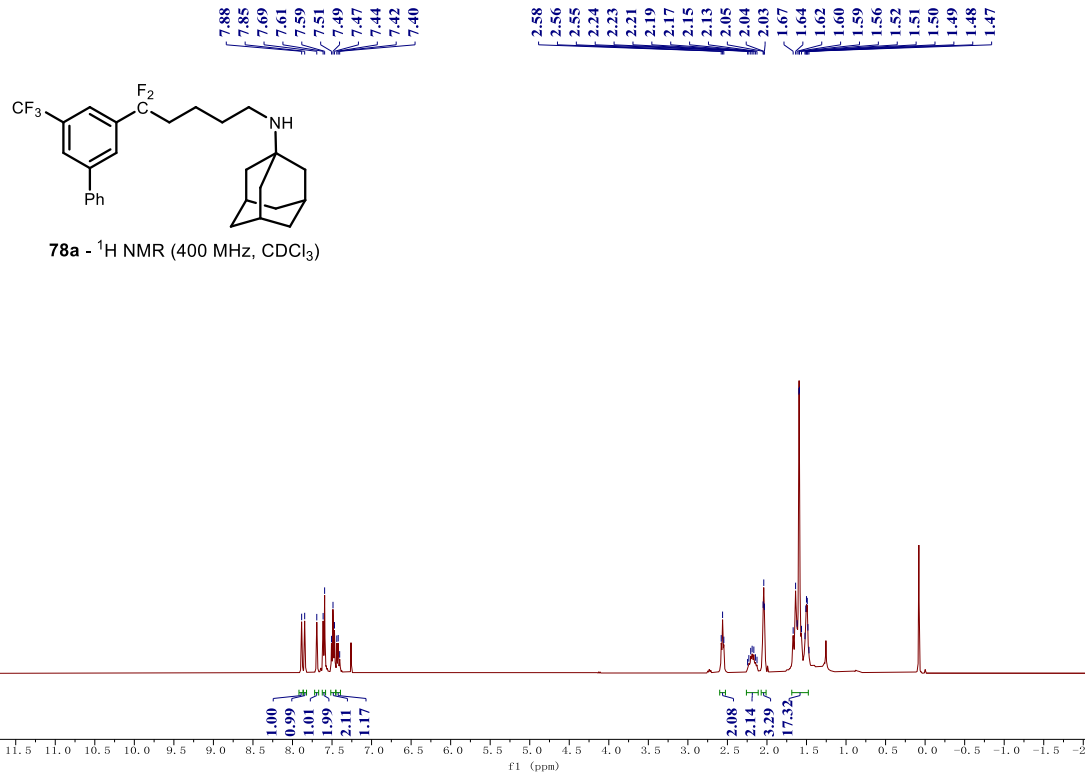




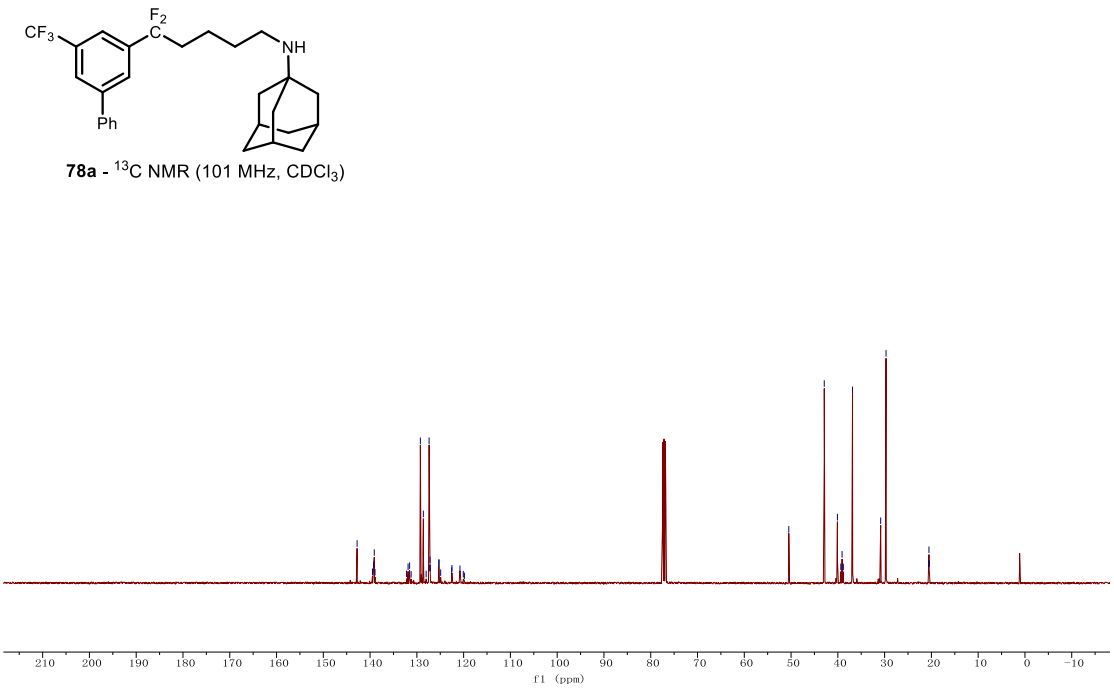
77a - ^{13}C NMR (101 MHz, $CDCl_3$)



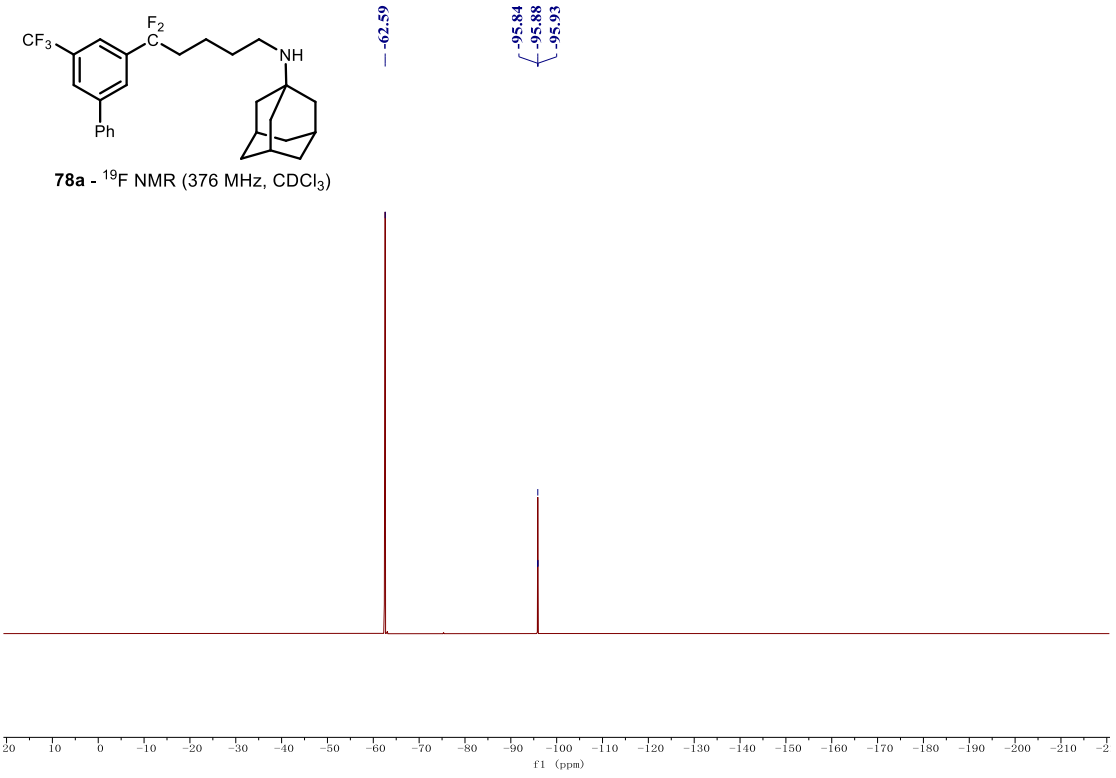
77a - ^{19}F NMR (376 MHz, $CDCl_3$)



78a - ^{1}H NMR (400 MHz, $CDCl_3$)

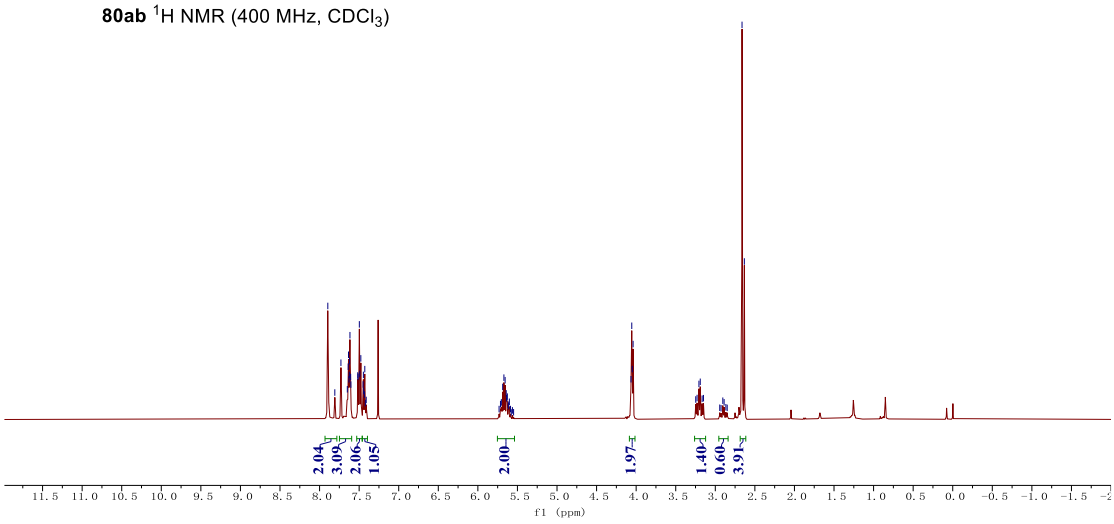


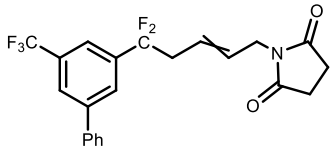
78a - ^{13}C NMR (101 MHz, $CDCl_3$)



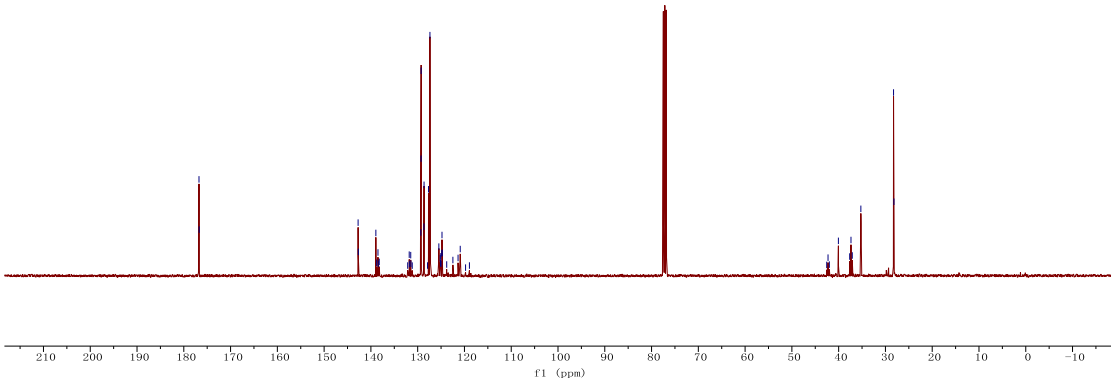
78a - ^{19}F NMR (376 MHz, $CDCl_3$)

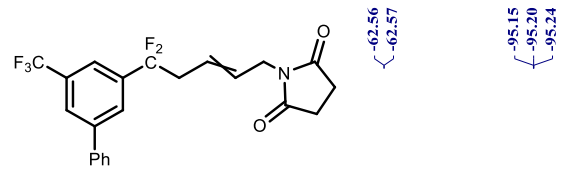
80ab ^{1}H NMR (400 MHz, $CDCl_3$)



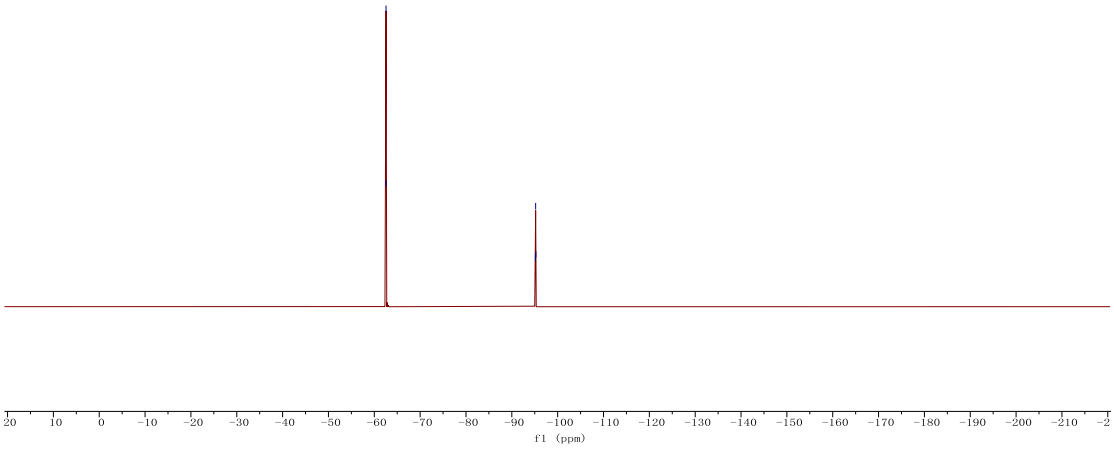


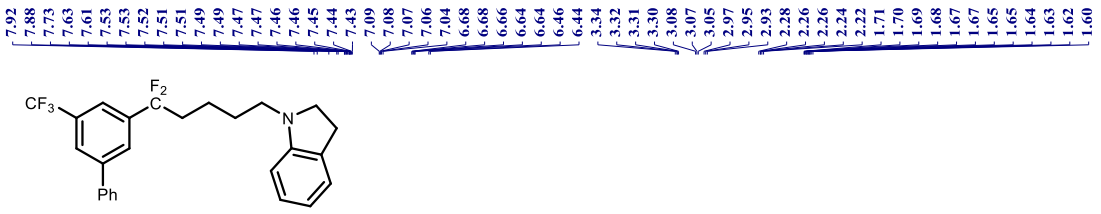
80ab ^{13}C NMR (101 MHz, $CDCl_3$)



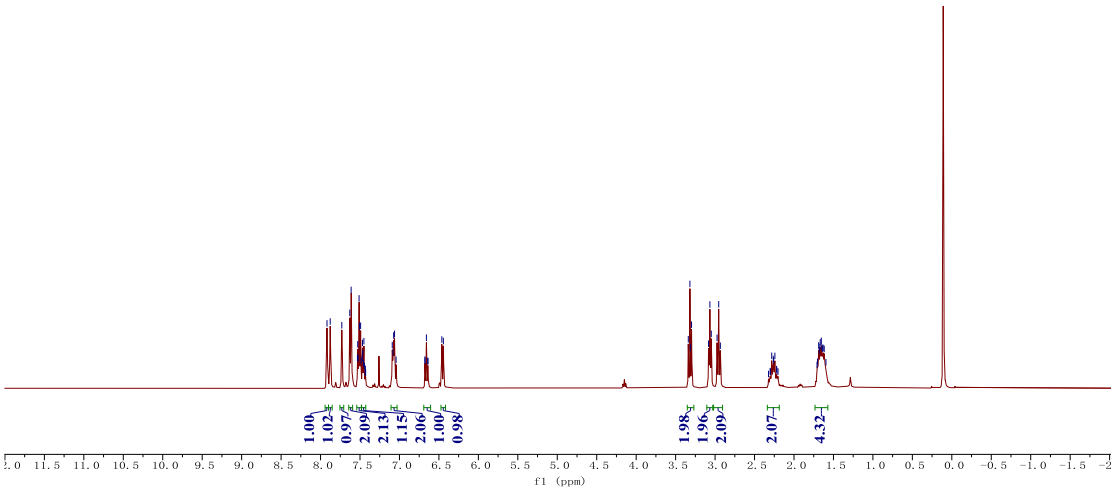


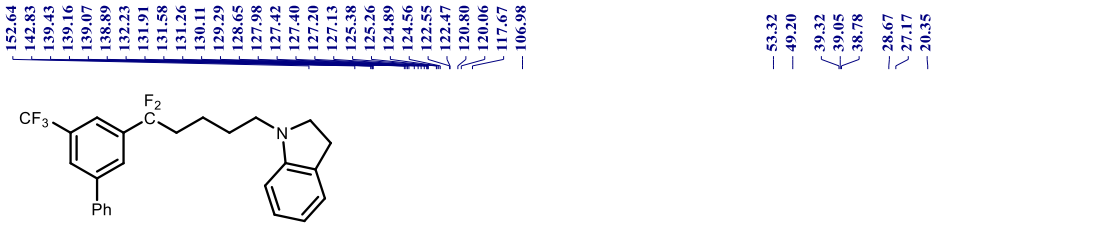
80ab ^{19}F NMR (376 MHz, $CDCl_3$)



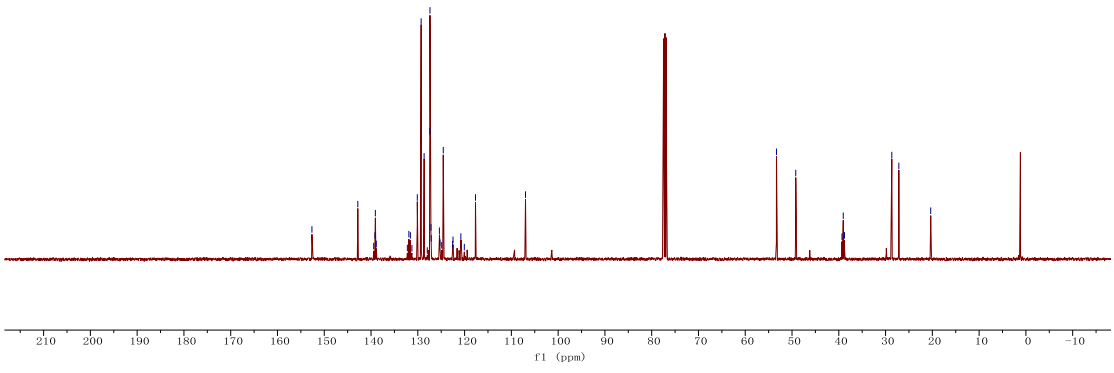


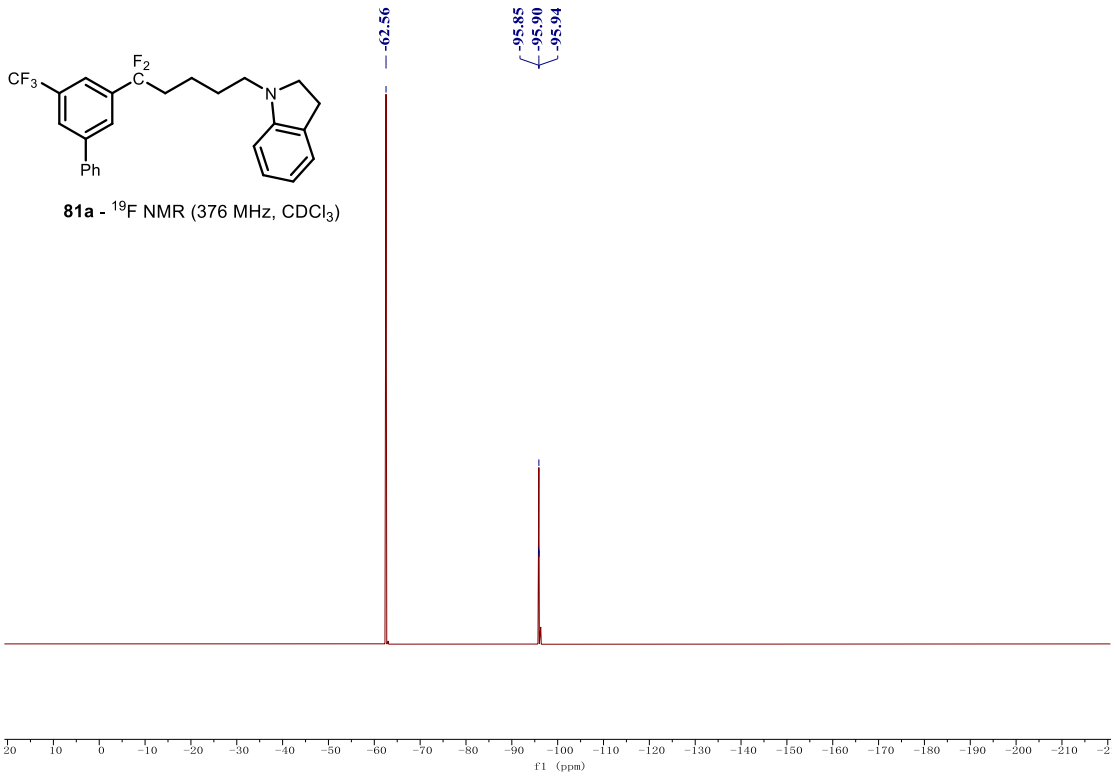
81a - ^{1}H NMR (400 MHz, $CDCl_3$)



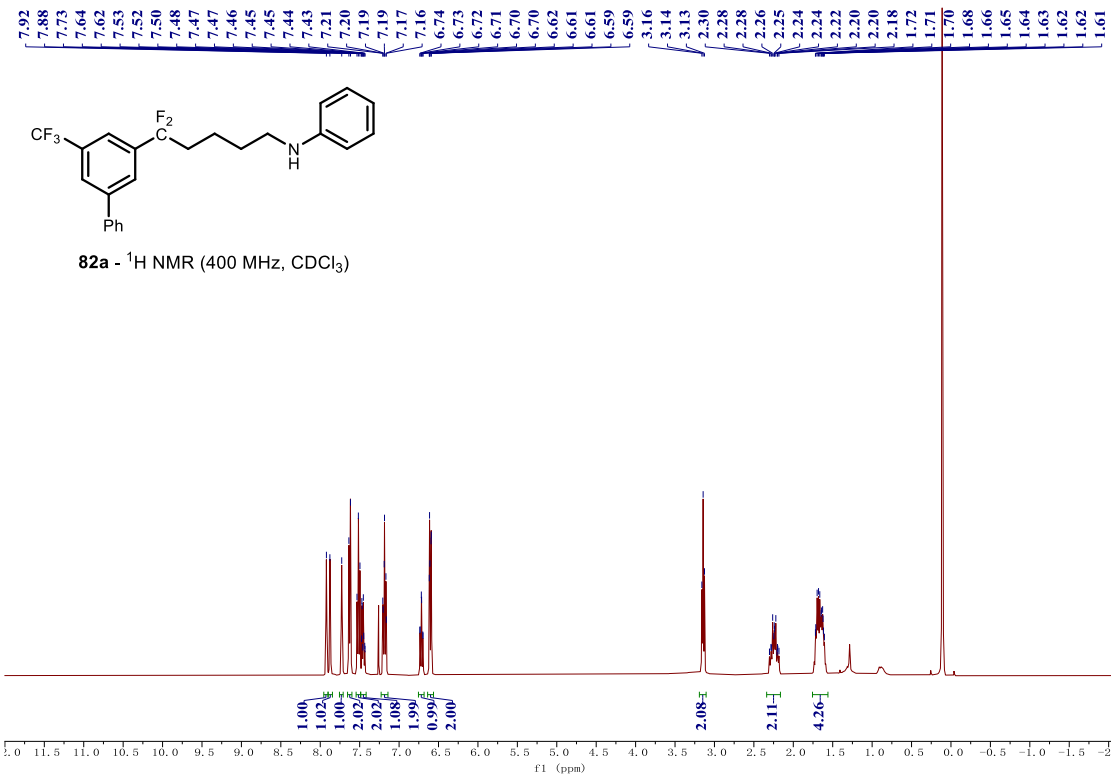


81a - ^{13}C NMR (101 MHz, $CDCl_3$)

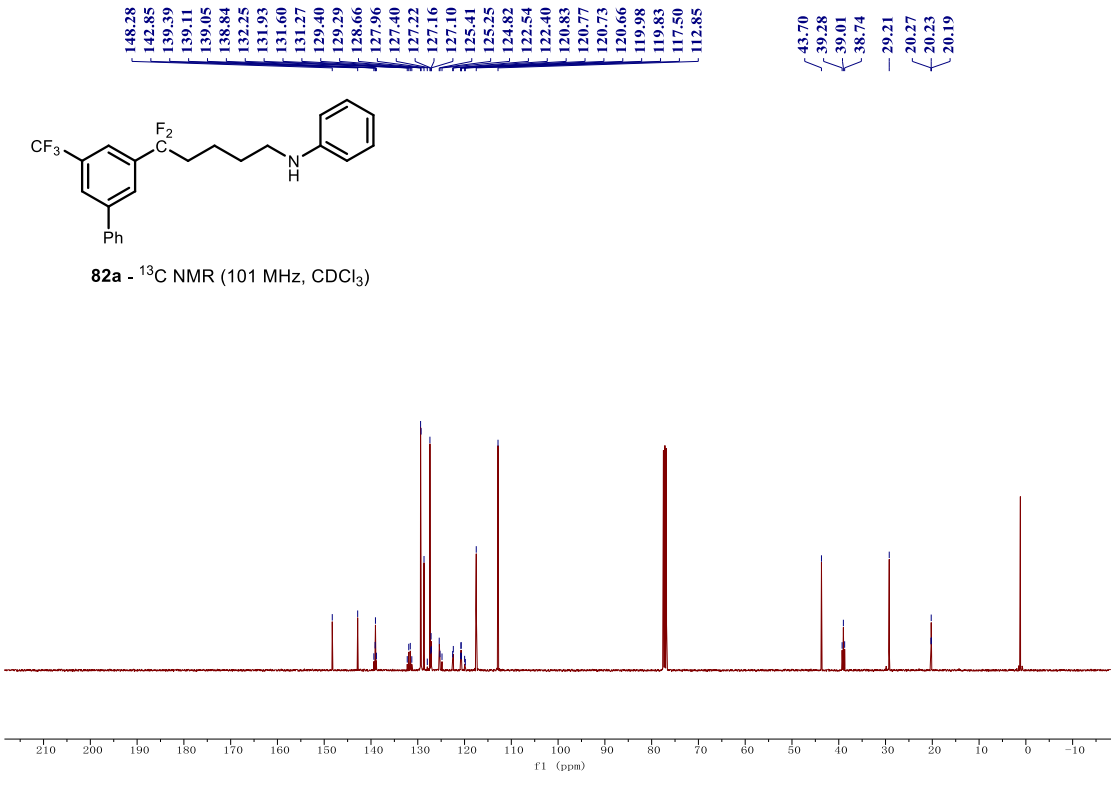




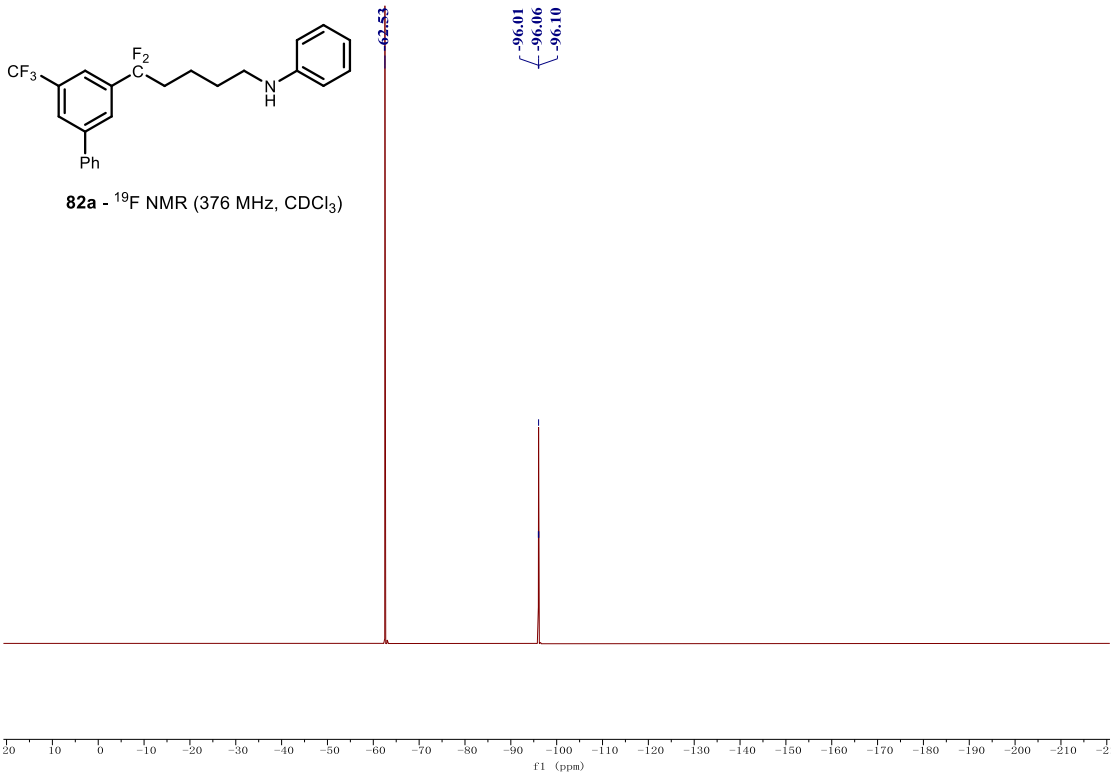
81a - ^{19}F NMR (376 MHz, $CDCl_3$)



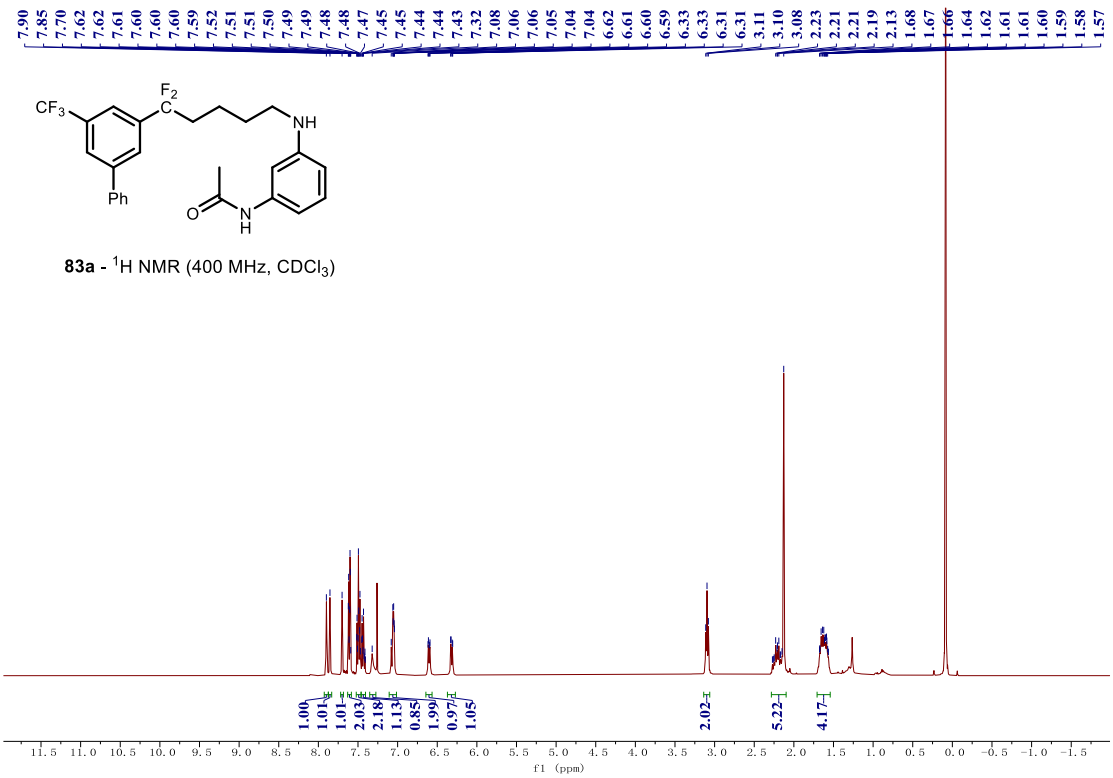
82a - ^{1}H NMR (400 MHz, $CDCl_3$)



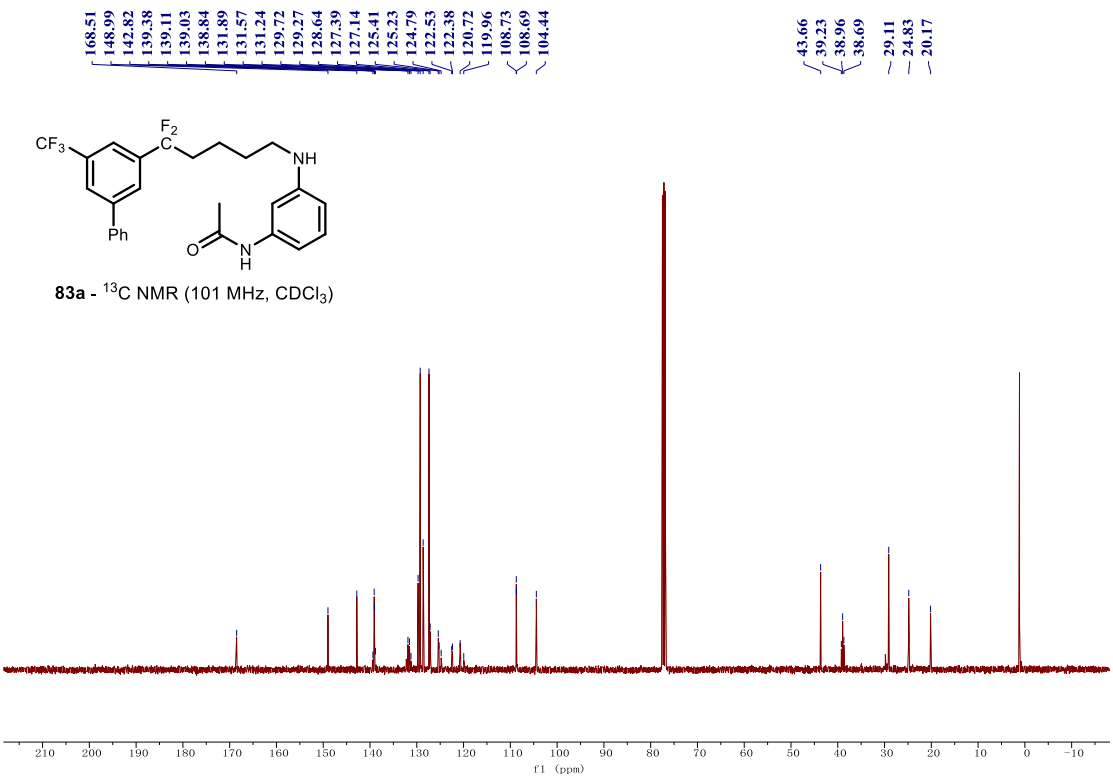
82a - ^{13}C NMR (101 MHz, $CDCl_3$)



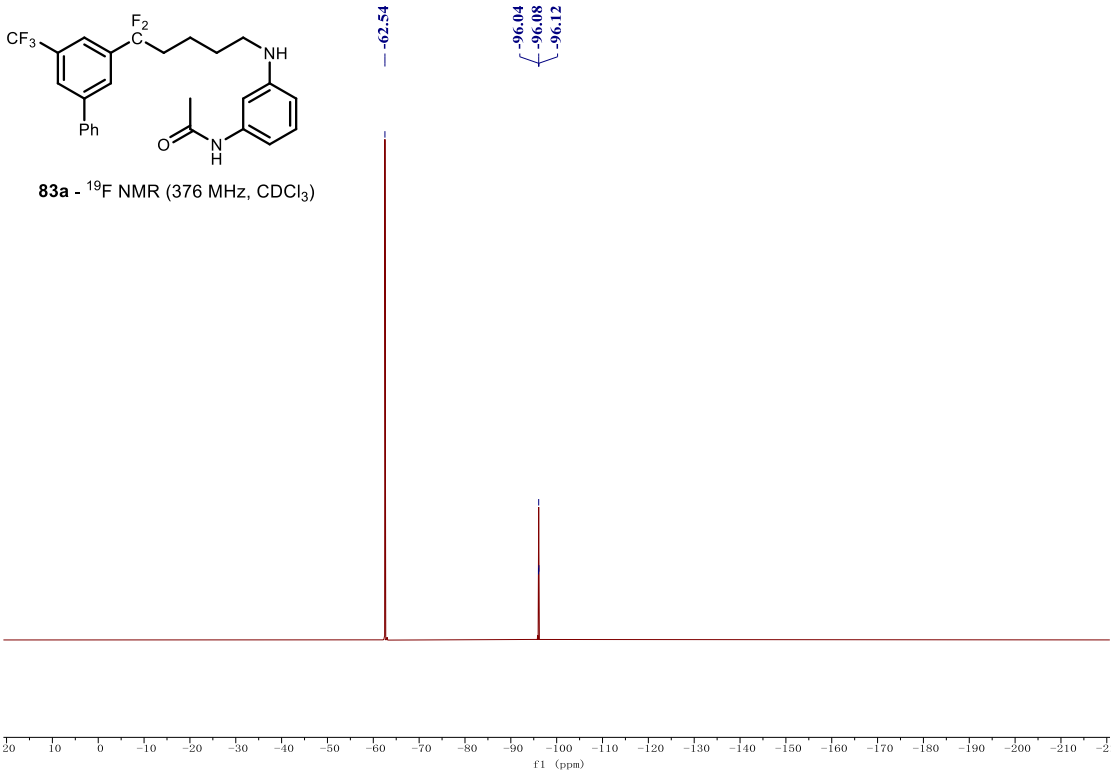
82a - ^{19}F NMR (376 MHz, $CDCl_3$)



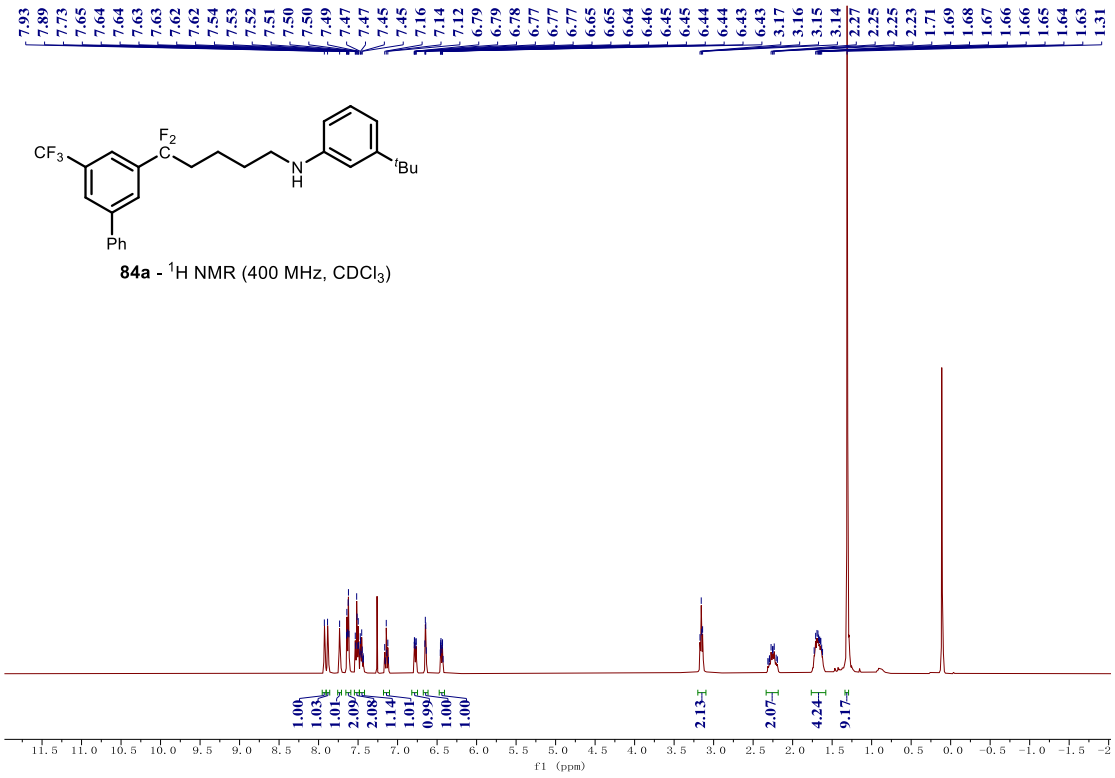
83a - ^{1}H NMR (400 MHz, $CDCl_3$)



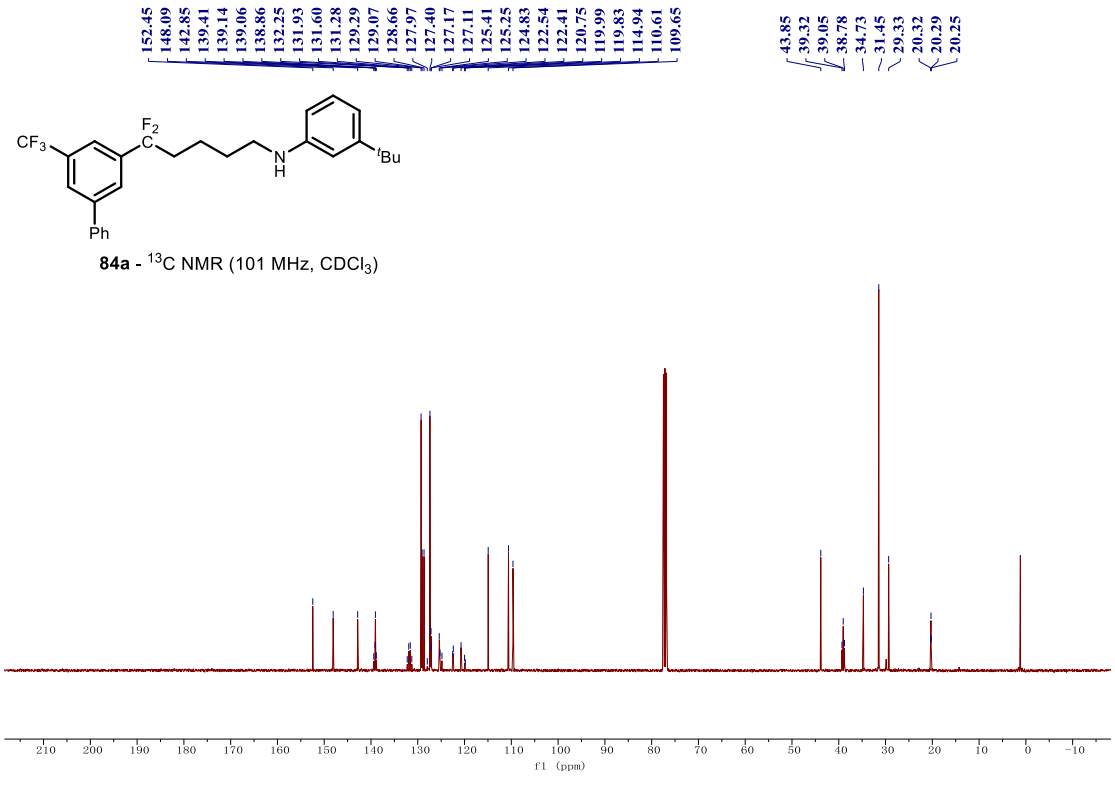
83a - ^{13}C NMR (101 MHz, $CDCl_3$)



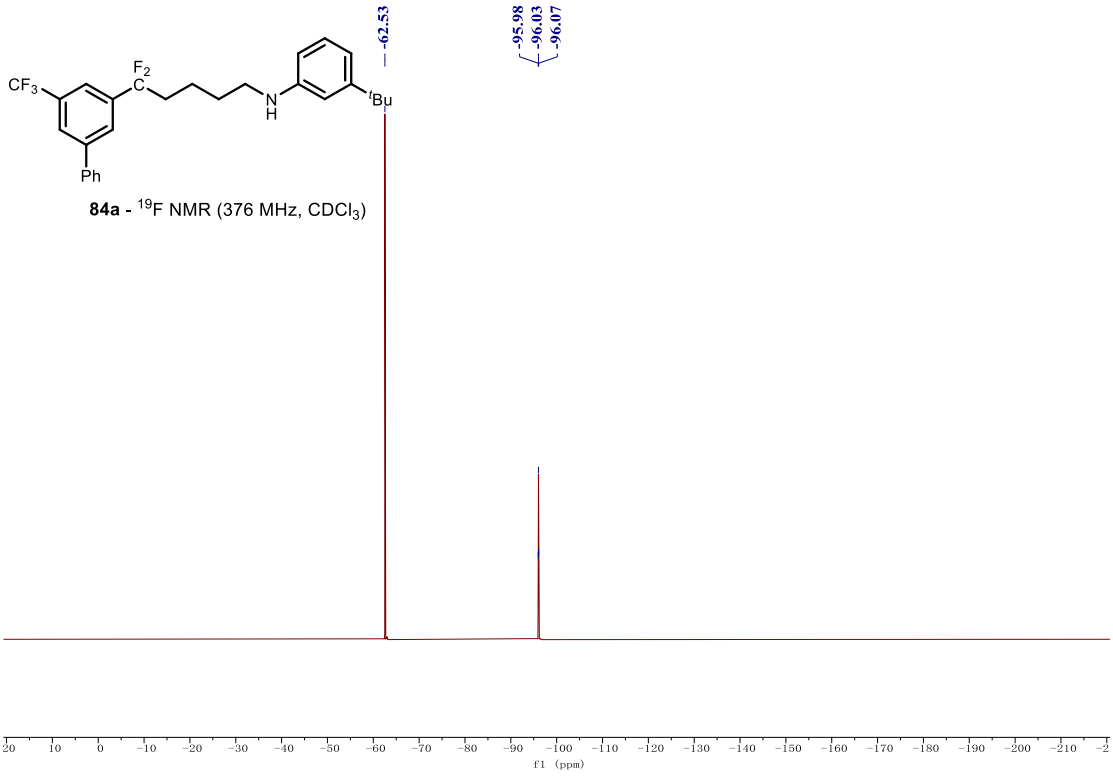
83a - ^{19}F NMR (376 MHz, $CDCl_3$)



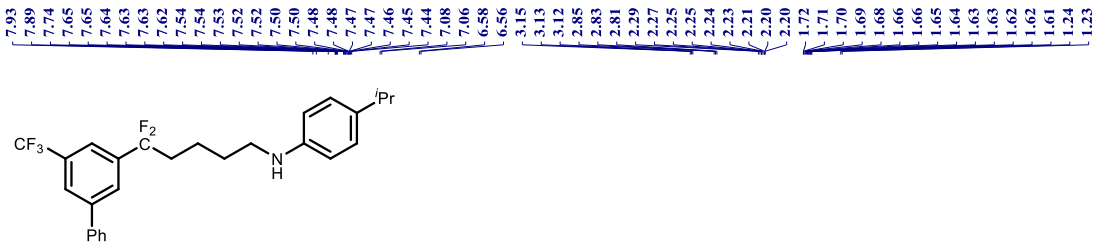
84a - ^{1}H NMR (400 MHz, $CDCl_3$)



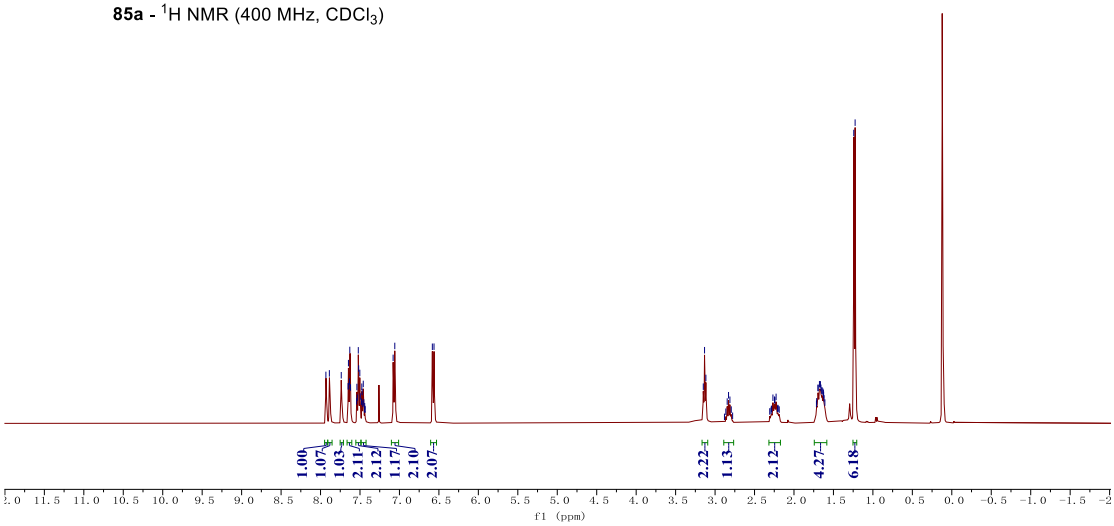
84a - ^{13}C NMR (101 MHz, $CDCl_3$)

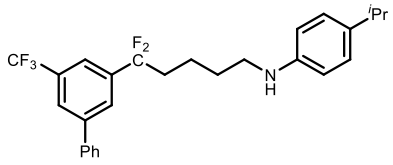


84a - ^{19}F NMR (376 MHz, $CDCl_3$)

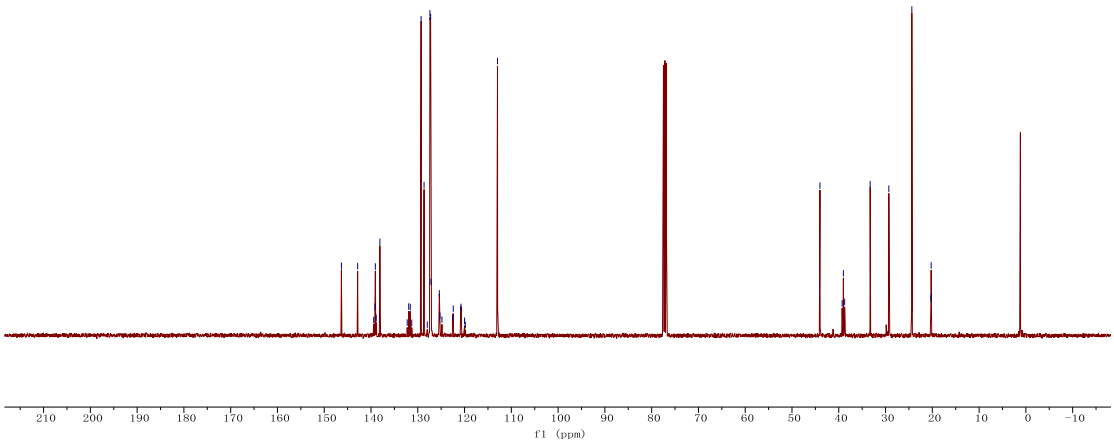


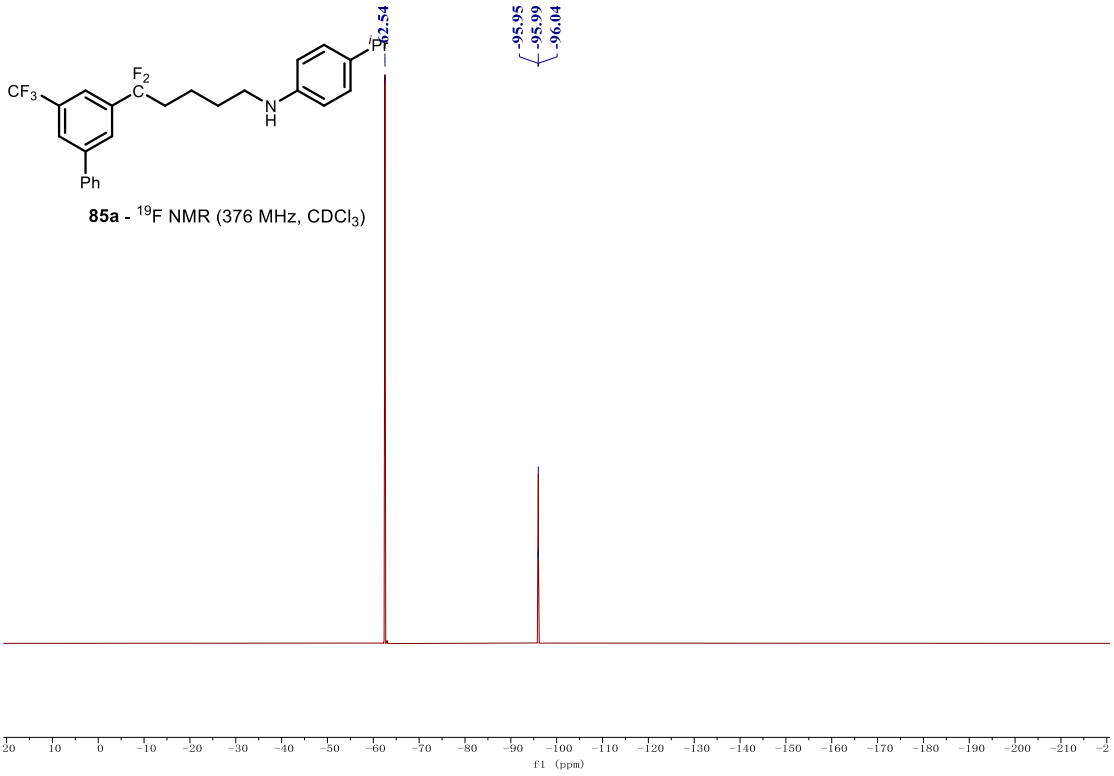
85a - ^{1}H NMR (400 MHz, $CDCl_3$)



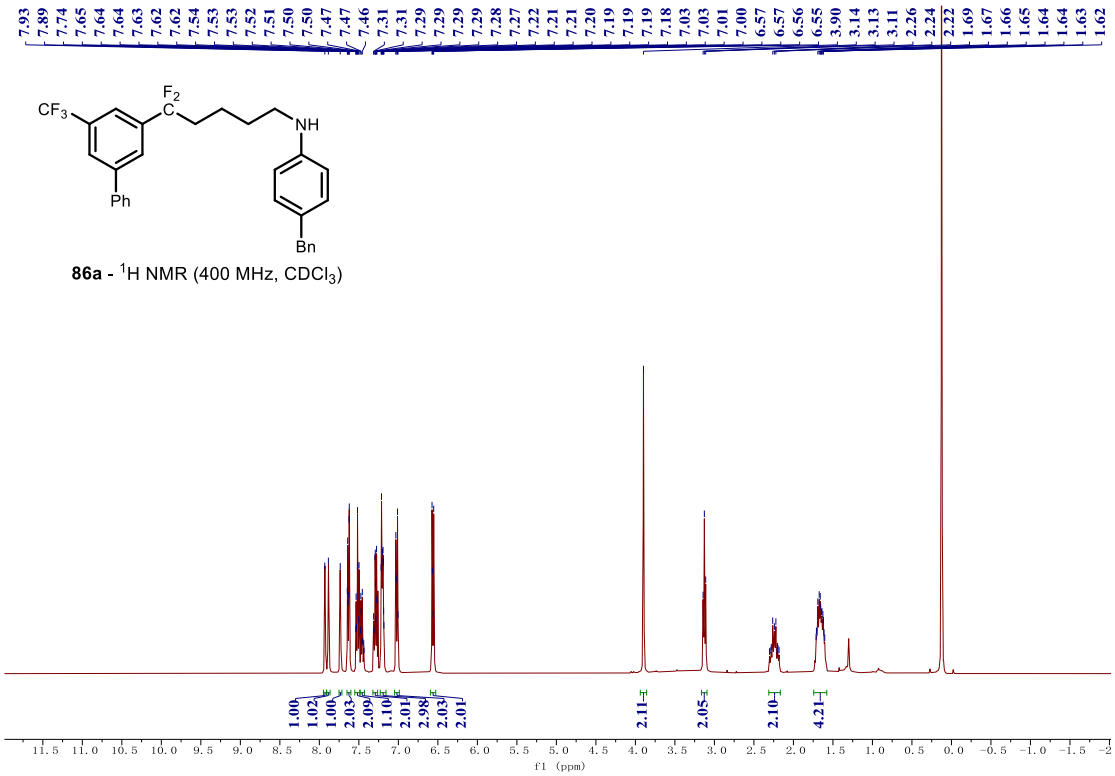


85a - ^{13}C NMR (101 MHz, $CDCl_3$)

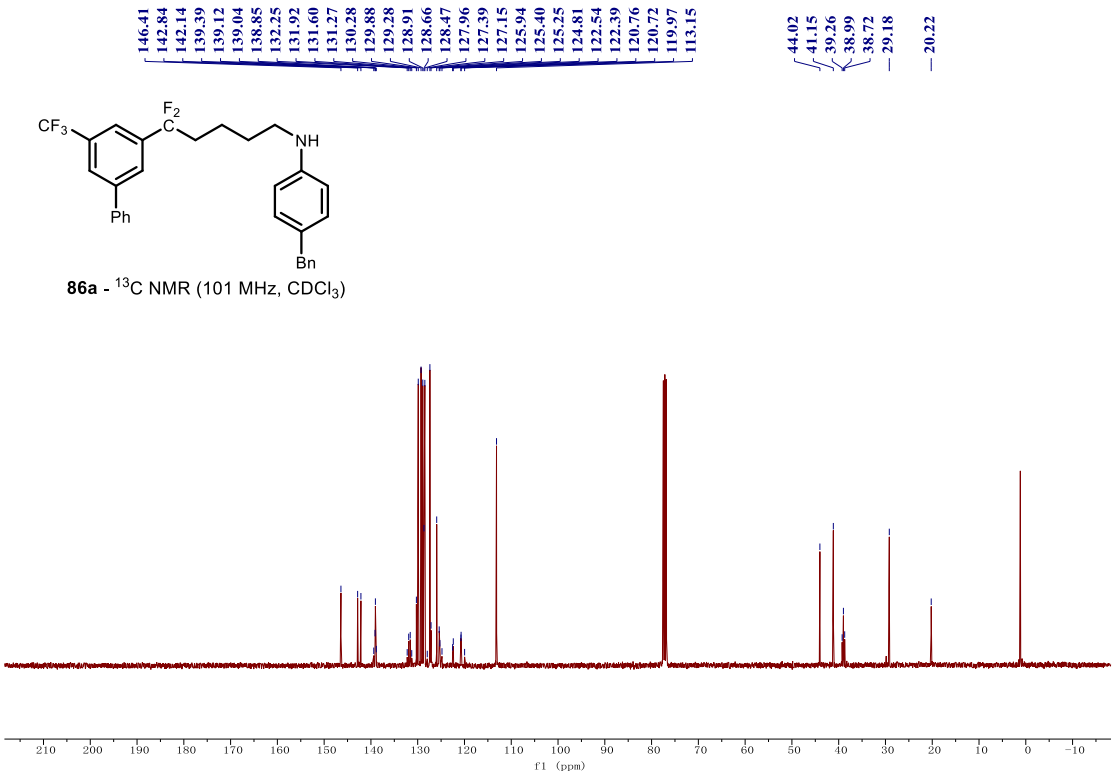




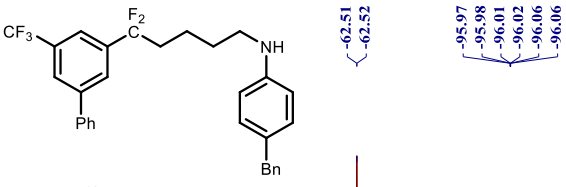
85a - ^{19}F NMR (376 MHz, $CDCl_3$)



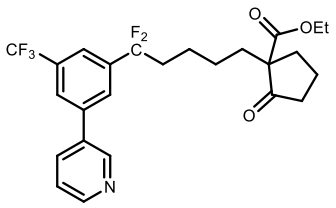
86a - ^{1}H NMR (400 MHz, $CDCl_3$)



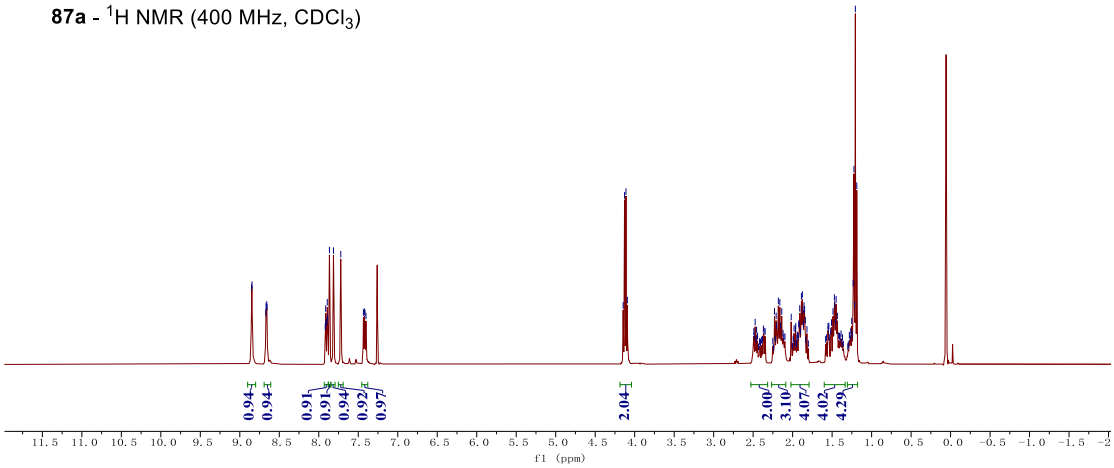
86a - ^{13}C NMR (101 MHz, $CDCl_3$)

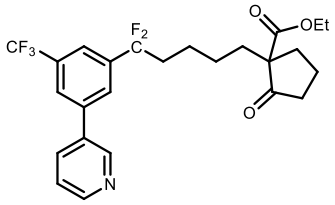


86a - ^{19}F NMR (376 MHz, $CDCl_3$)

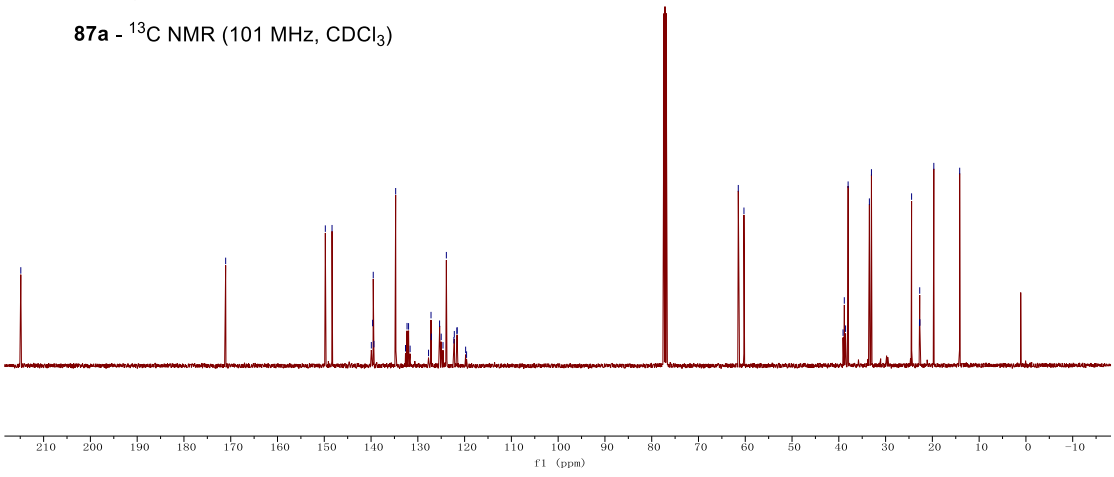


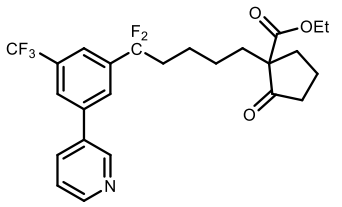
87a - ^{1}H NMR (400 MHz, $CDCl_3$)



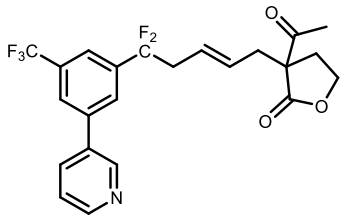


87a - ^{13}C NMR (101 MHz, $CDCl_3$)

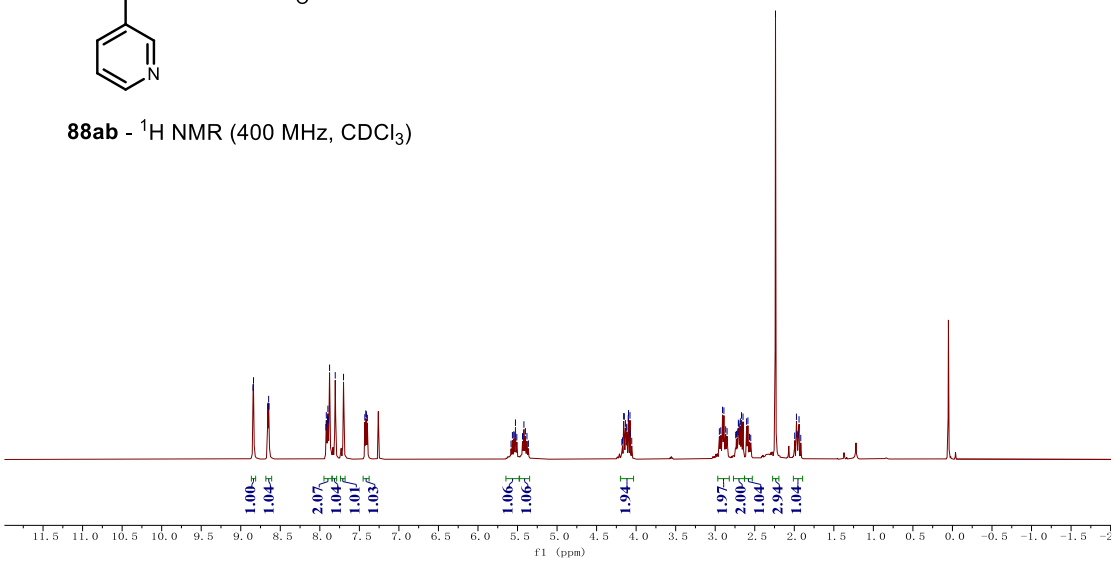


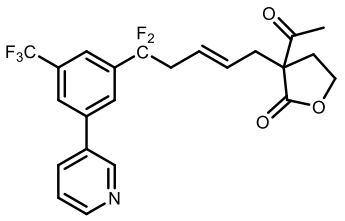


87a - ^{19}F NMR (376 MHz, $CDCl_3$)

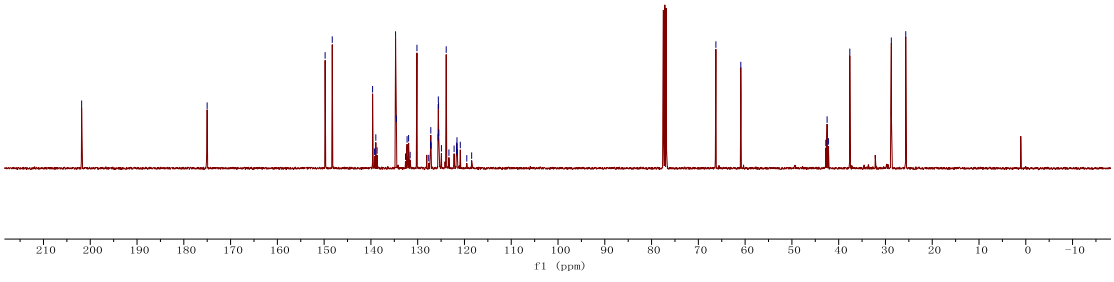


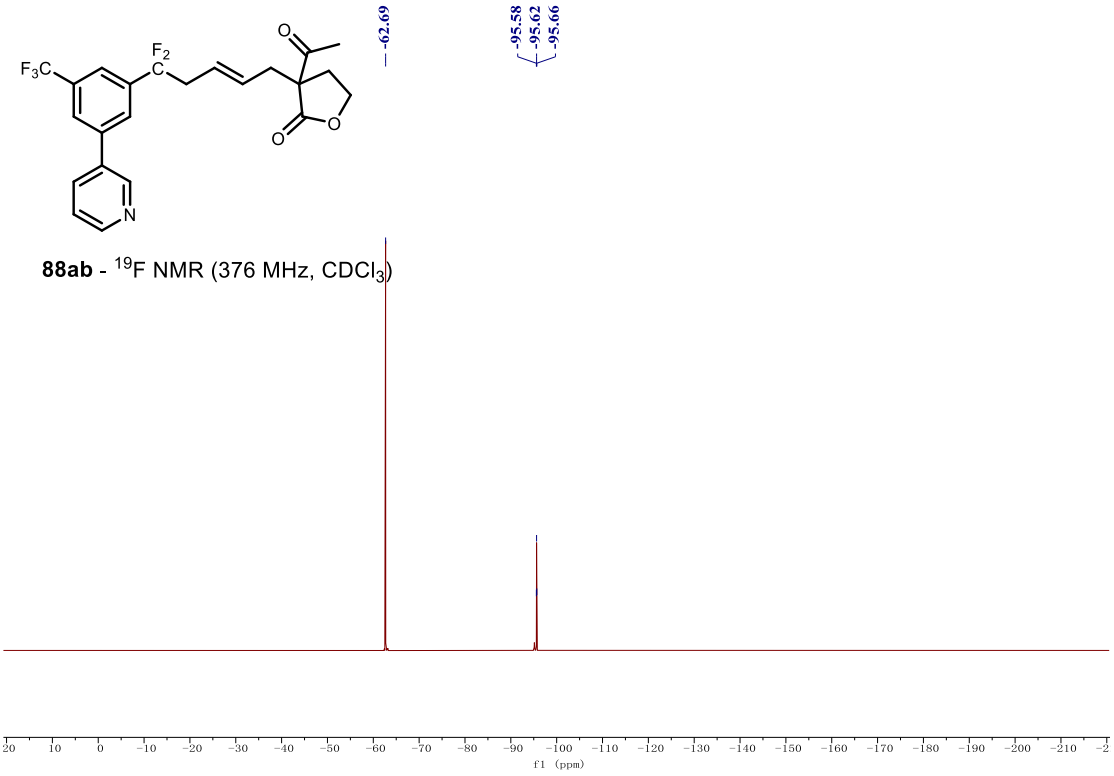
88ab - ^{1}H NMR (400 MHz, $CDCl_3$)



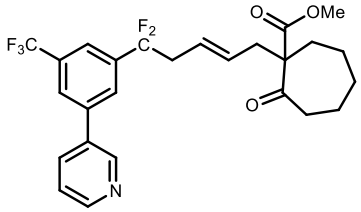


88ab - ^{13}C NMR (101 MHz, $CDCl_3$)

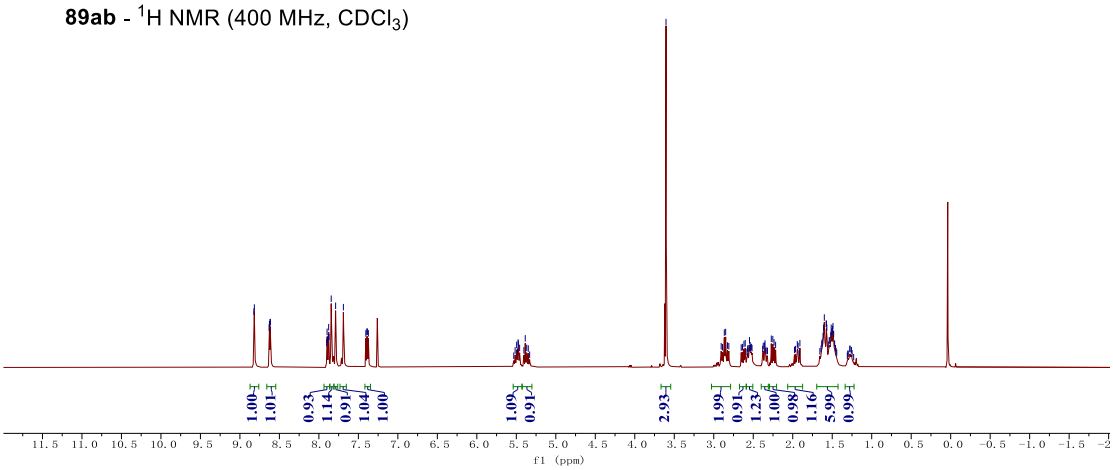


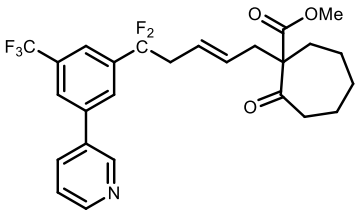


88ab - ^{19}F NMR (376 MHz, $CDCl_3$)

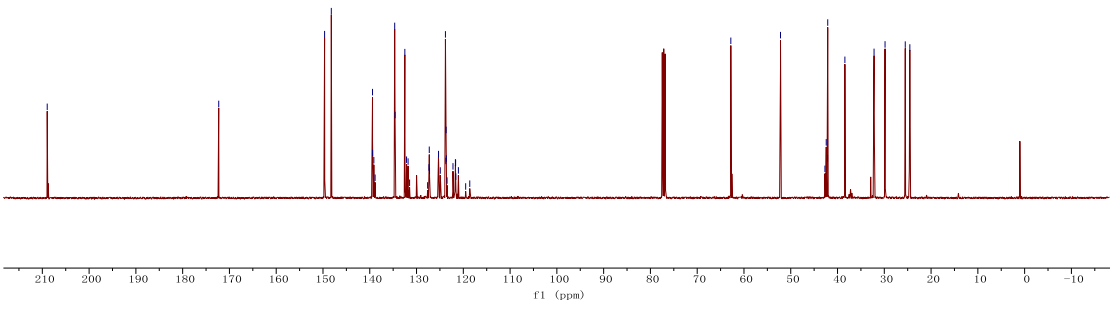


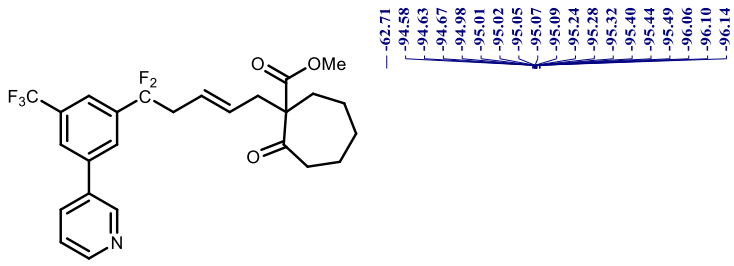
89ab - ^{1}H NMR (400 MHz, $CDCl_3$)



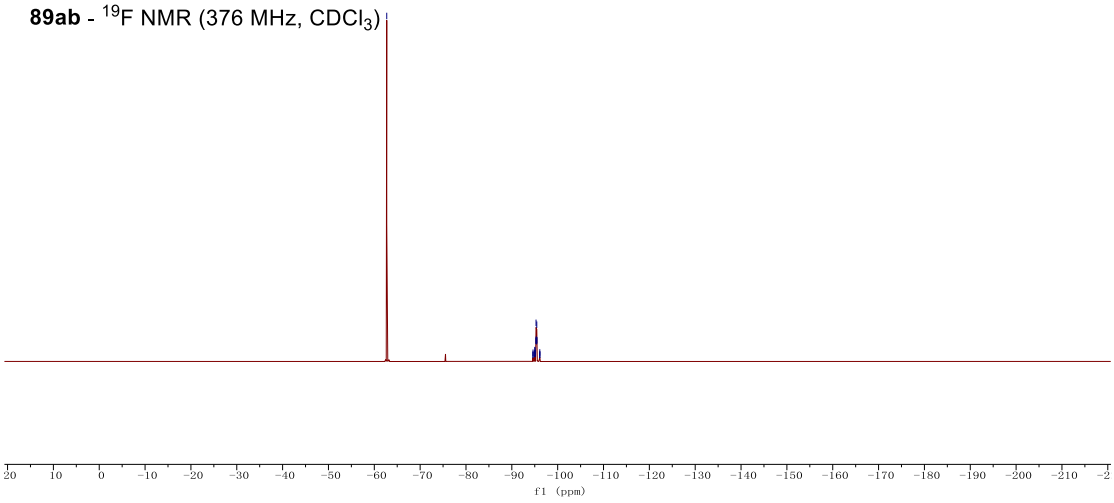


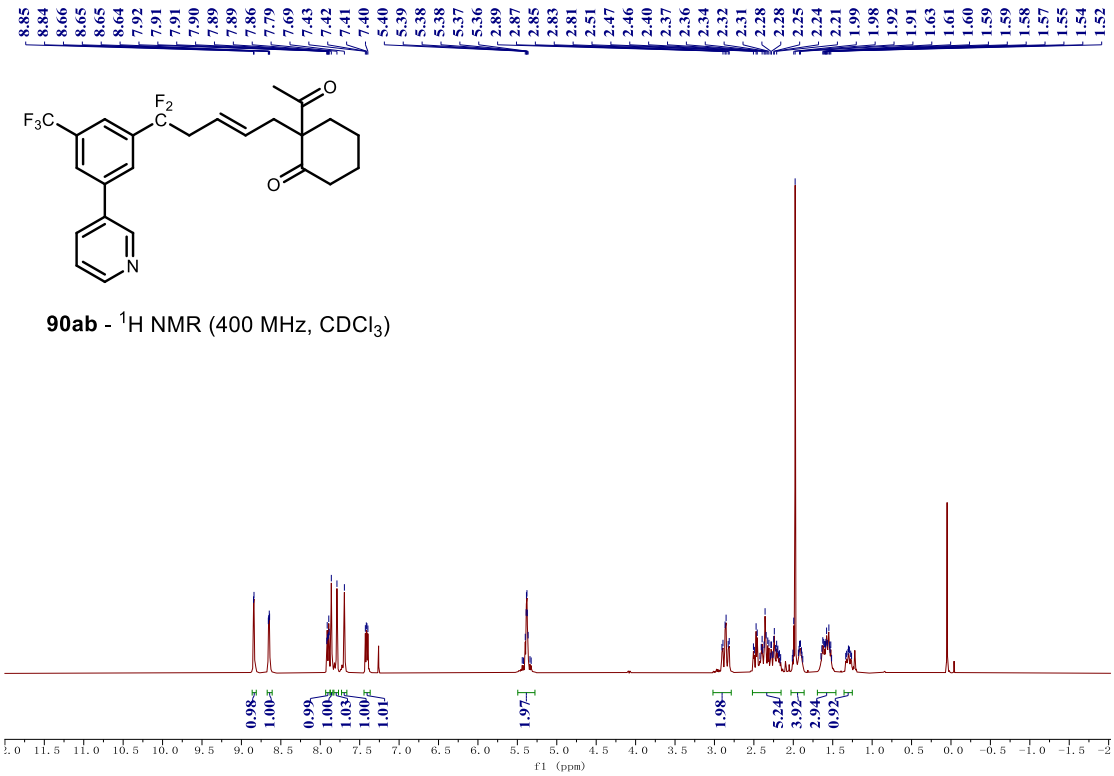
89ab - ^{13}C NMR (101 MHz, $CDCl_3$)



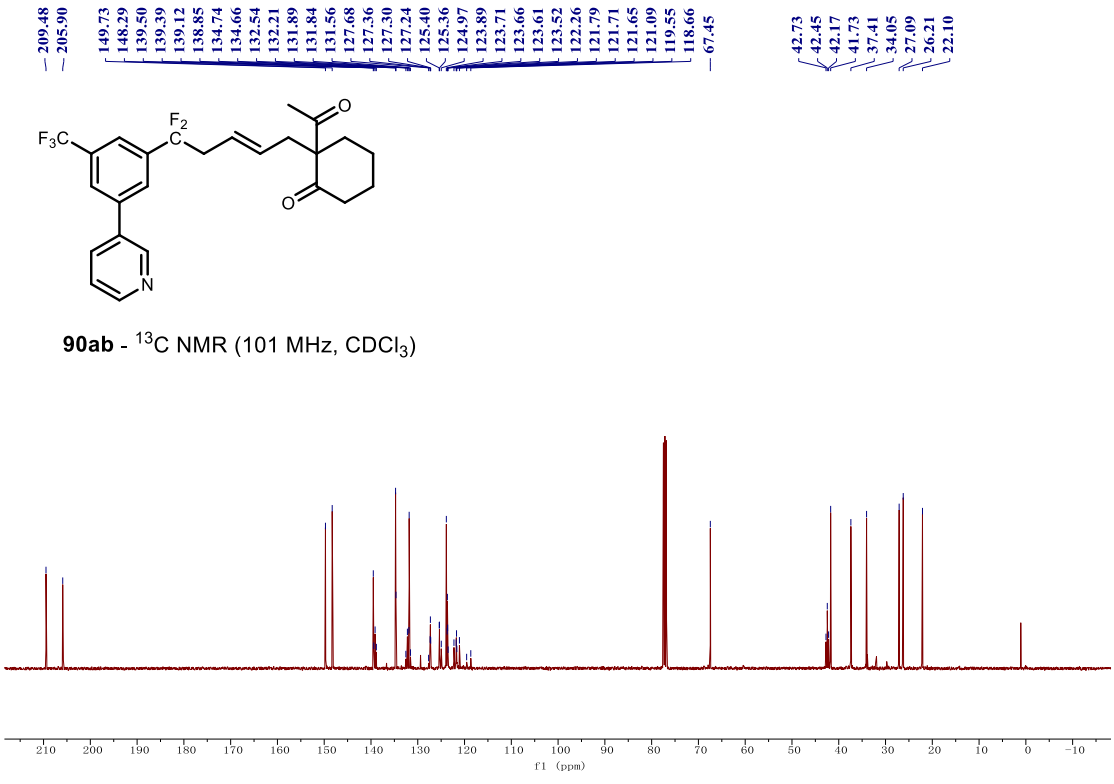


89ab - ^{19}F NMR (376 MHz, $CDCl_3$)

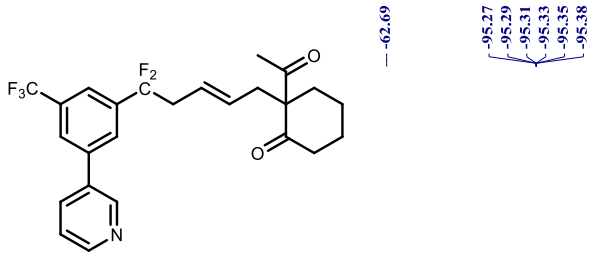




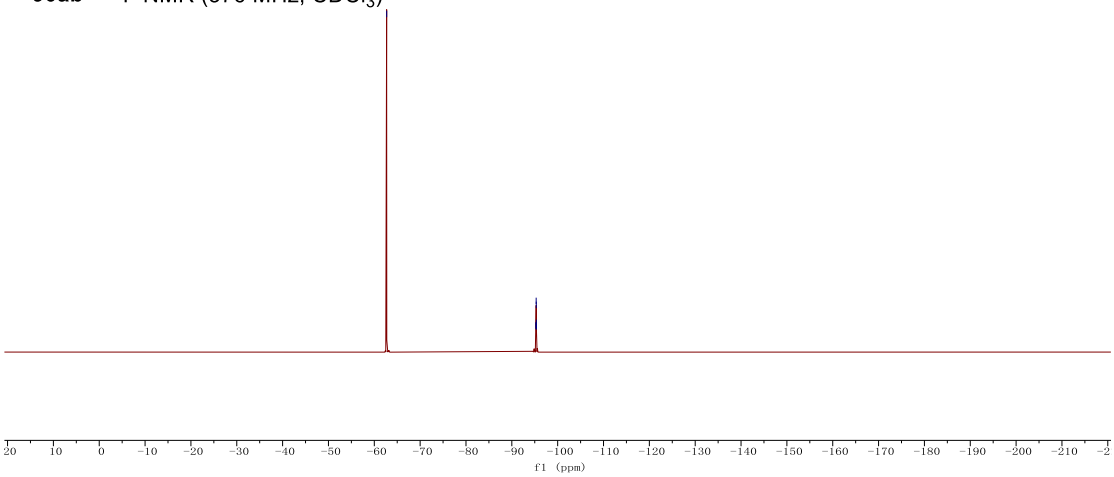
90ab - ^{1}H NMR (400 MHz, $CDCl_3$)

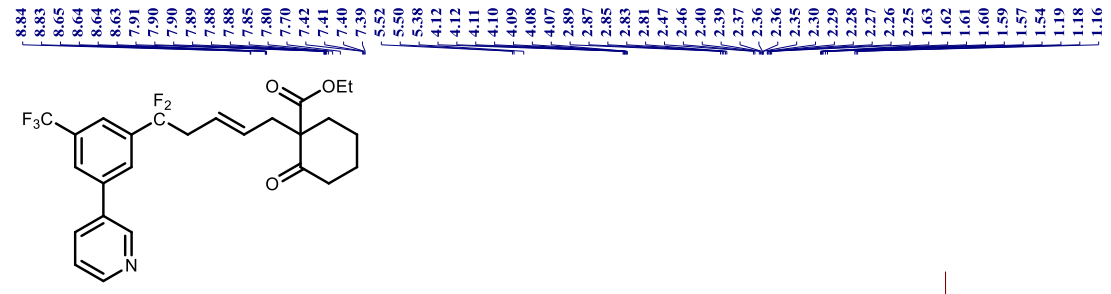


90ab - ^{13}C NMR (101 MHz, $CDCl_3$)

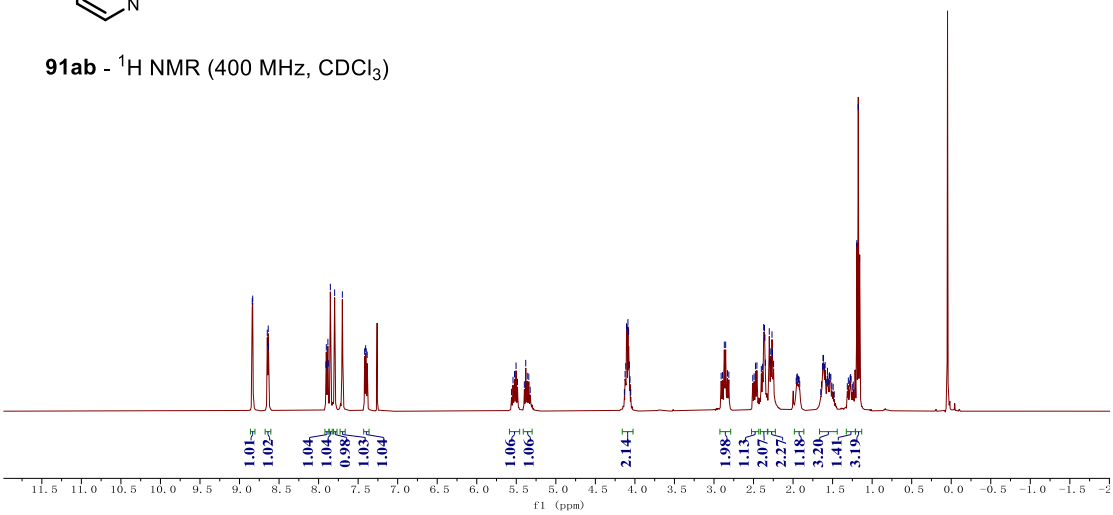


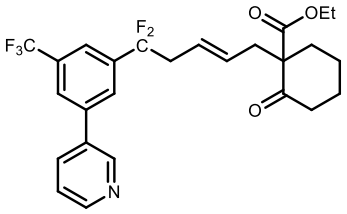
90ab - ^{19}F NMR (376 MHz, $CDCl_3$)



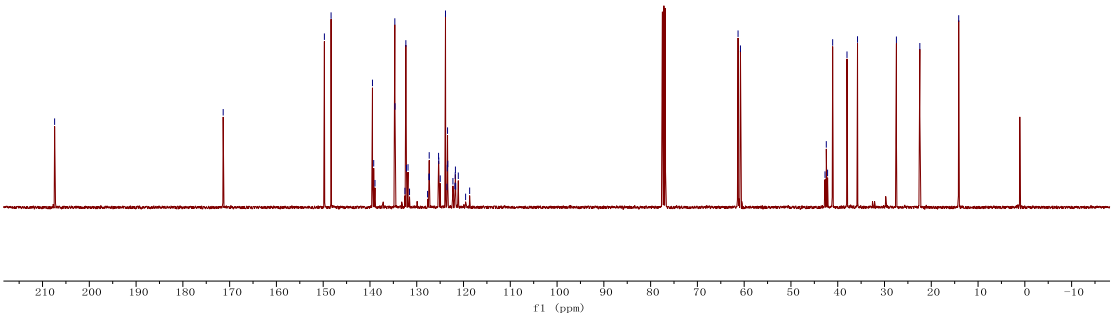


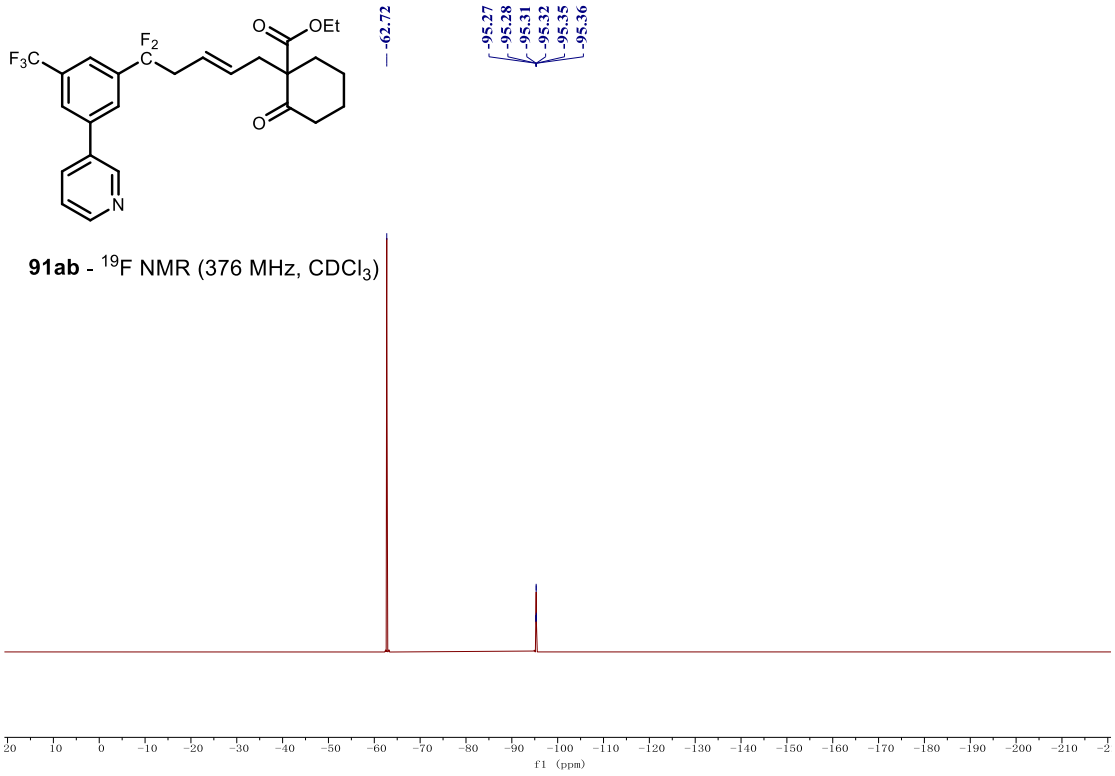
91ab - ^{1}H NMR (400 MHz, $CDCl_3$)



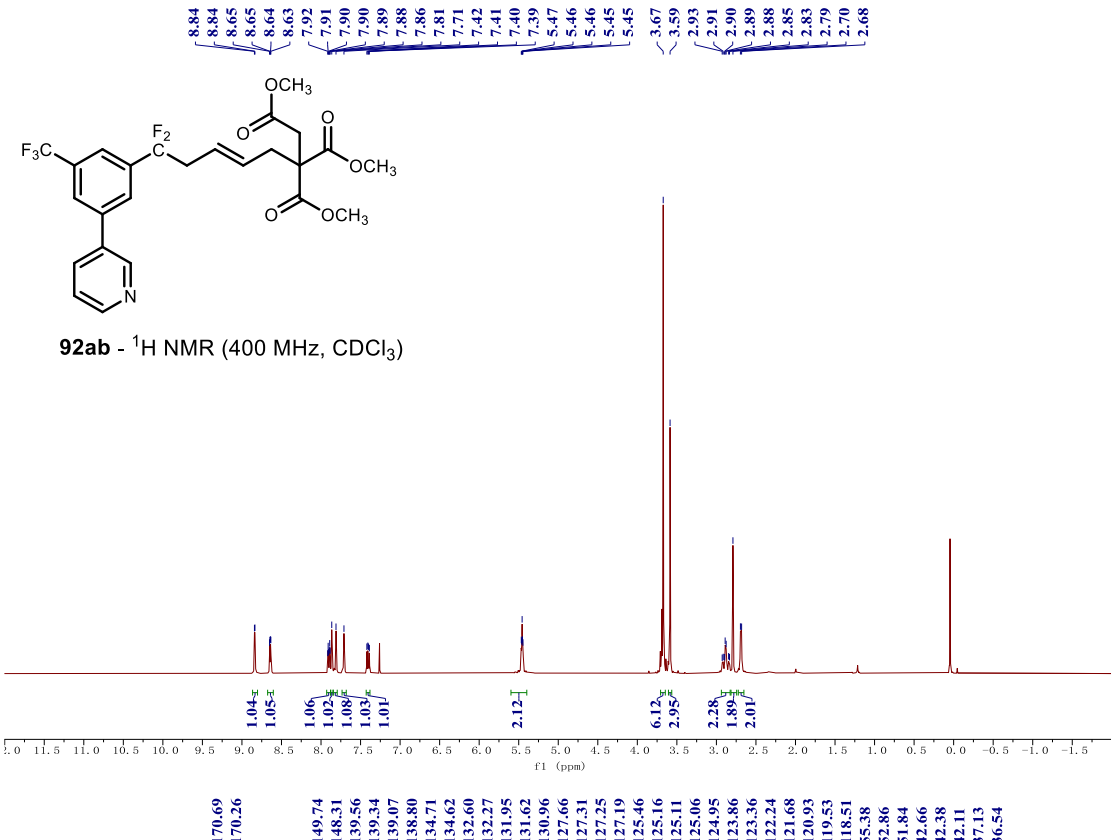


91ab - ^{13}C NMR (101 MHz, $CDCl_3$)

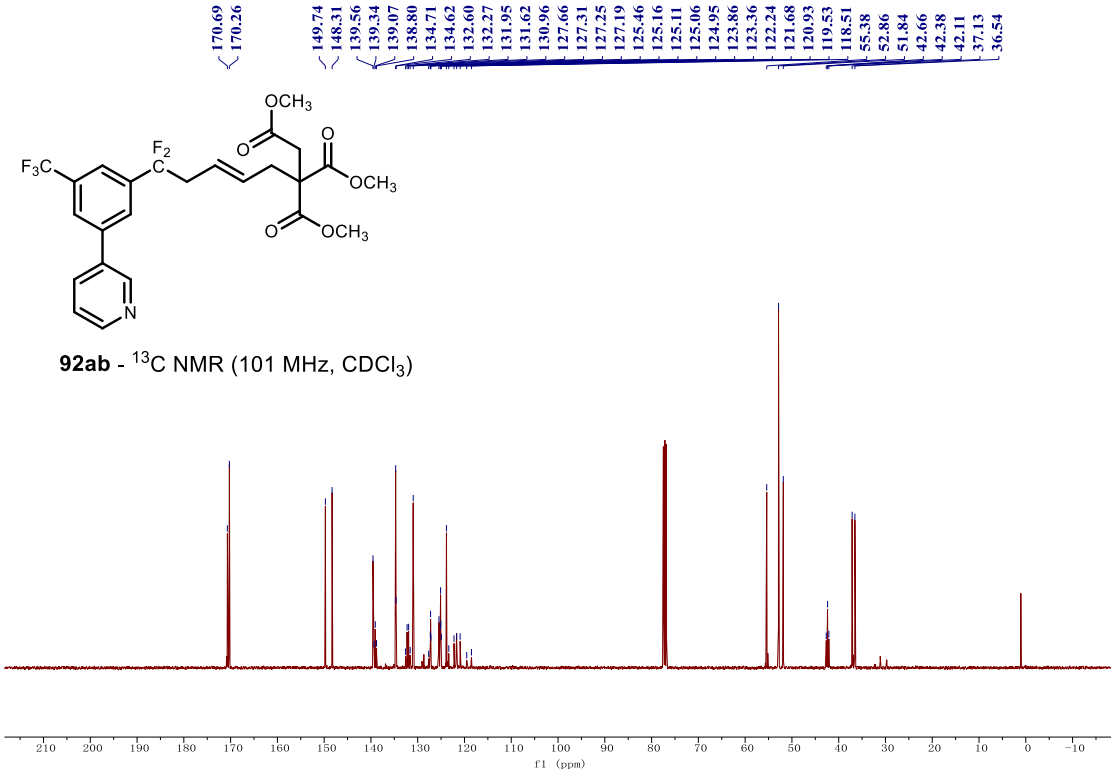




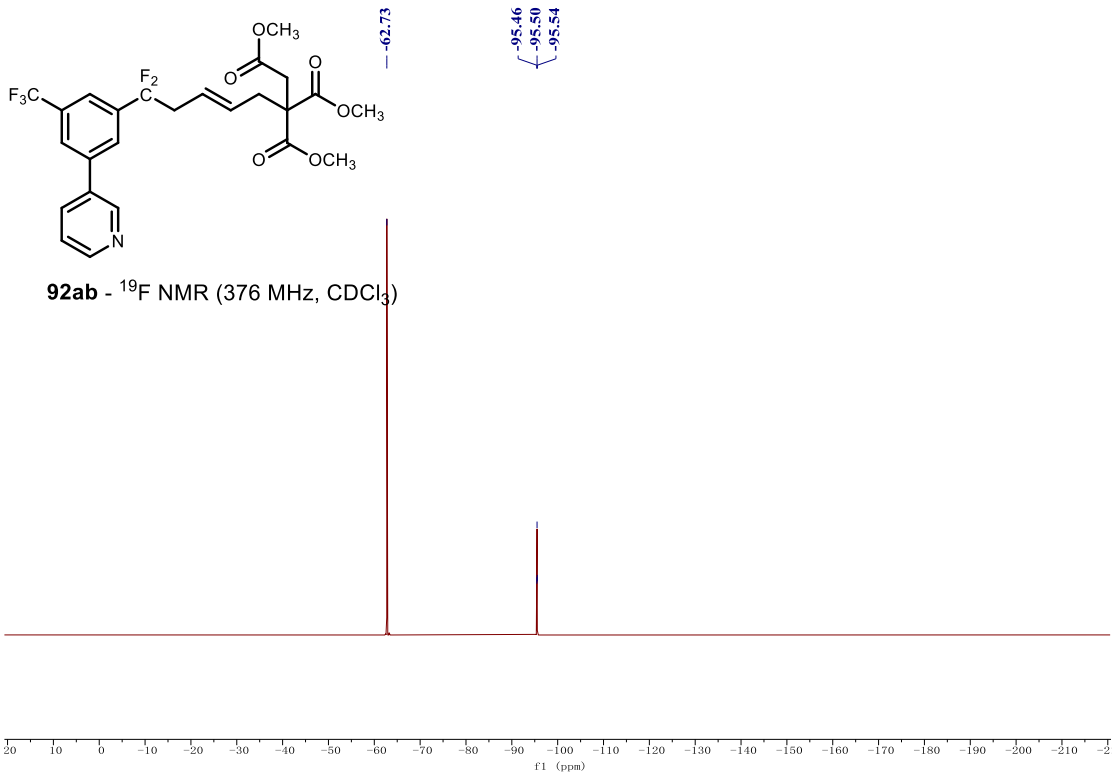
91ab - ^{19}F NMR (376 MHz, $CDCl_3$)



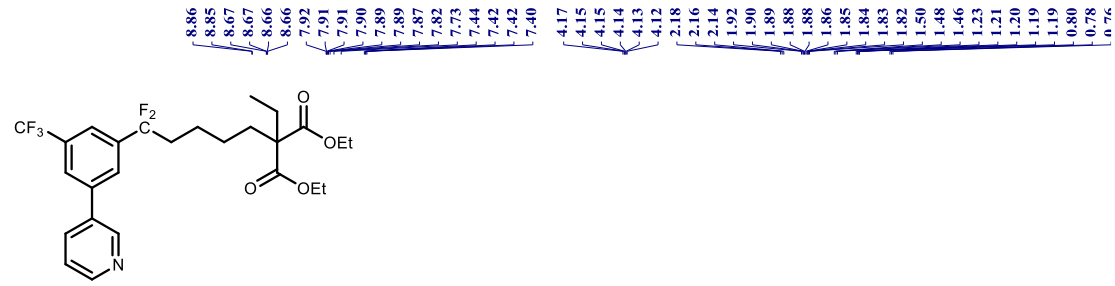
92ab - ^{1}H NMR (400 MHz, $CDCl_3$)



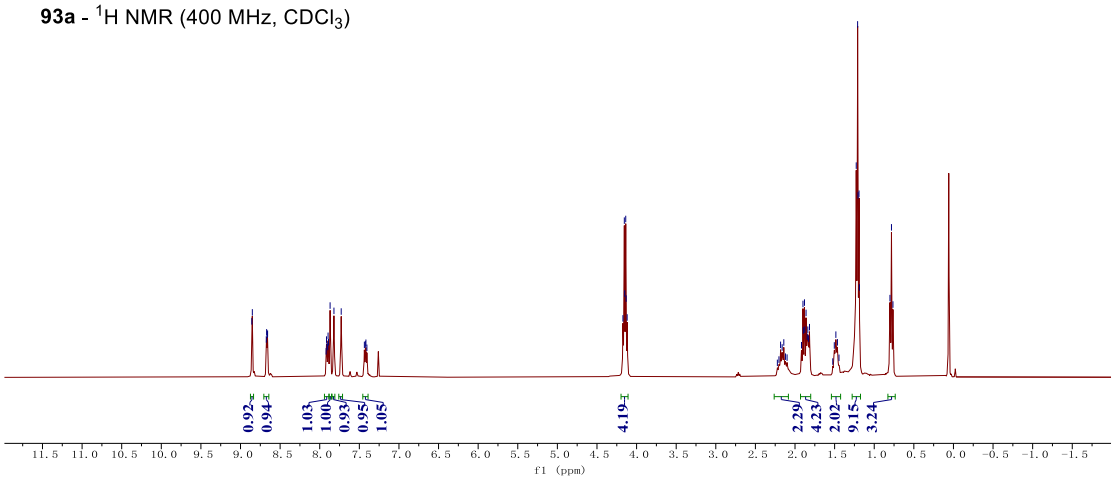
92ab - ^{13}C NMR (101 MHz, $CDCl_3$)

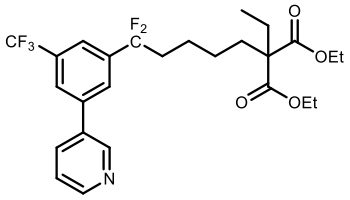


92ab - ^{19}F NMR (376 MHz, $CDCl_3$)

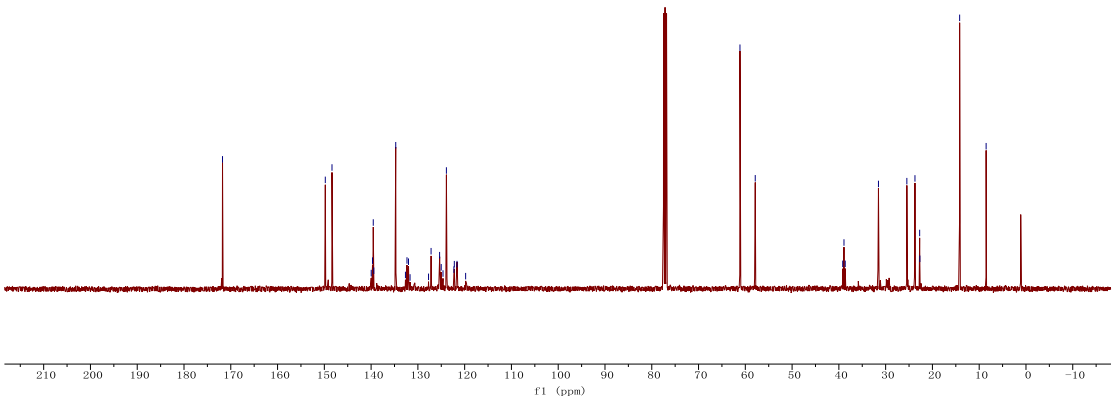


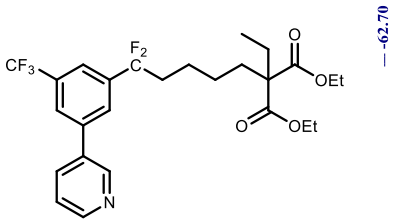
93a - ^{1}H NMR (400 MHz, $CDCl_3$)



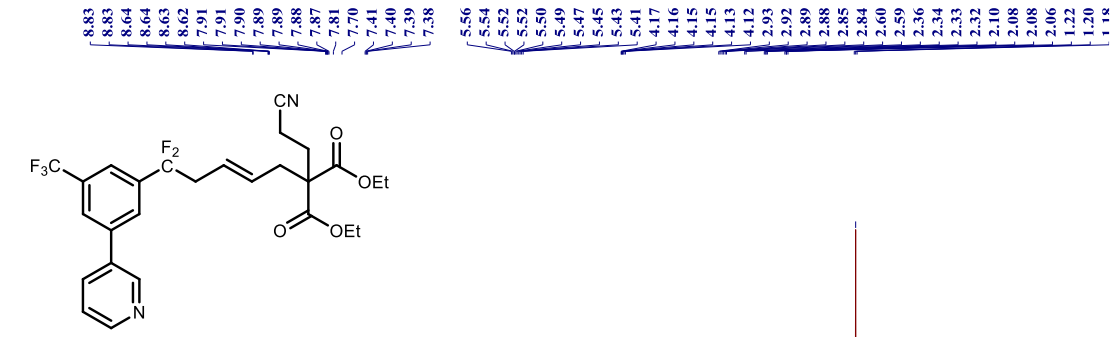


93a - ^{13}C NMR (101 MHz, $CDCl_3$)

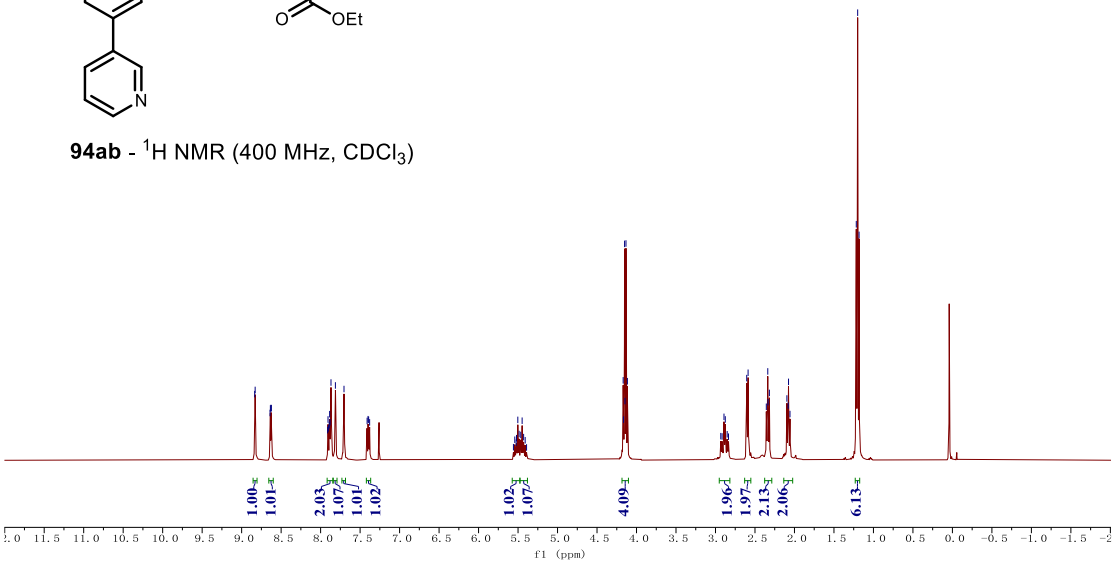


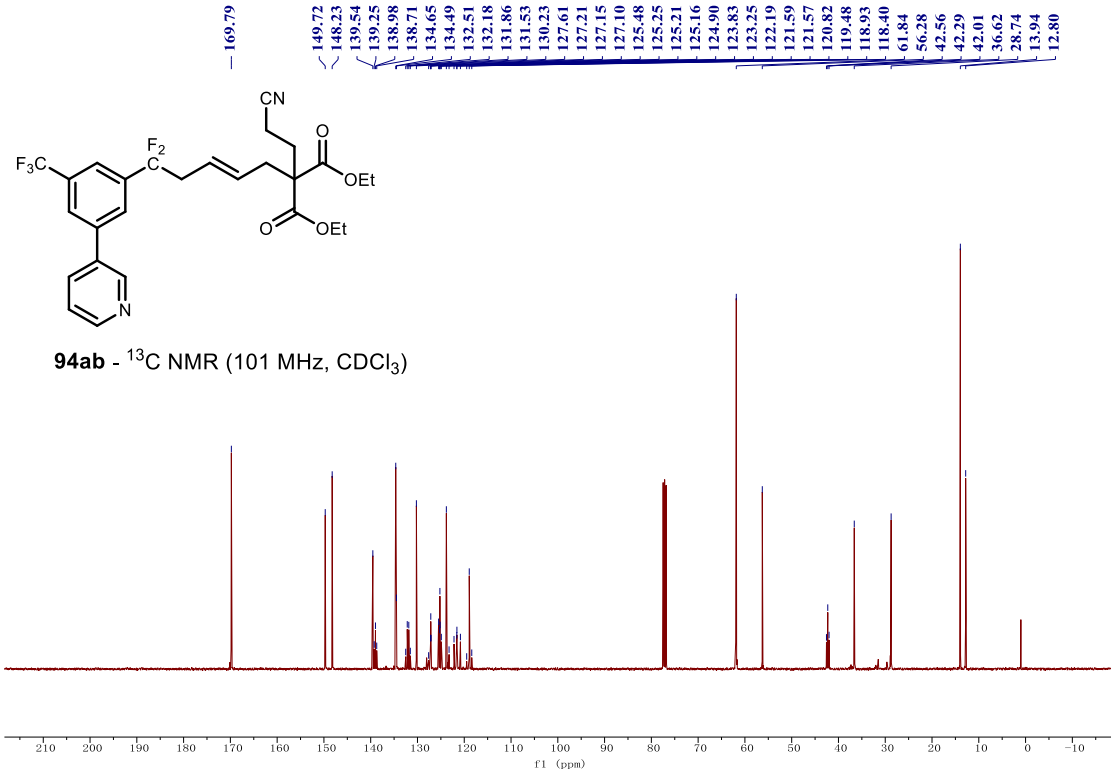


93a - ^{19}F NMR (376 MHz, $CDCl_3$)

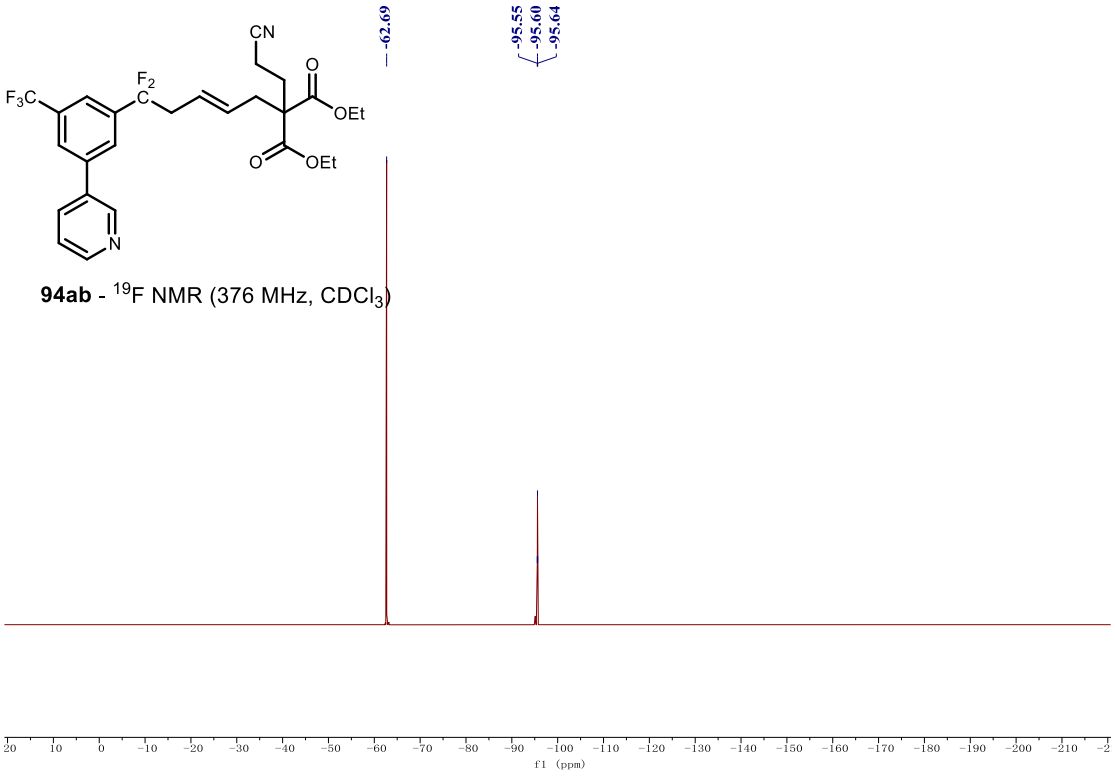


94ab - ^{1}H NMR (400 MHz, $CDCl_3$)

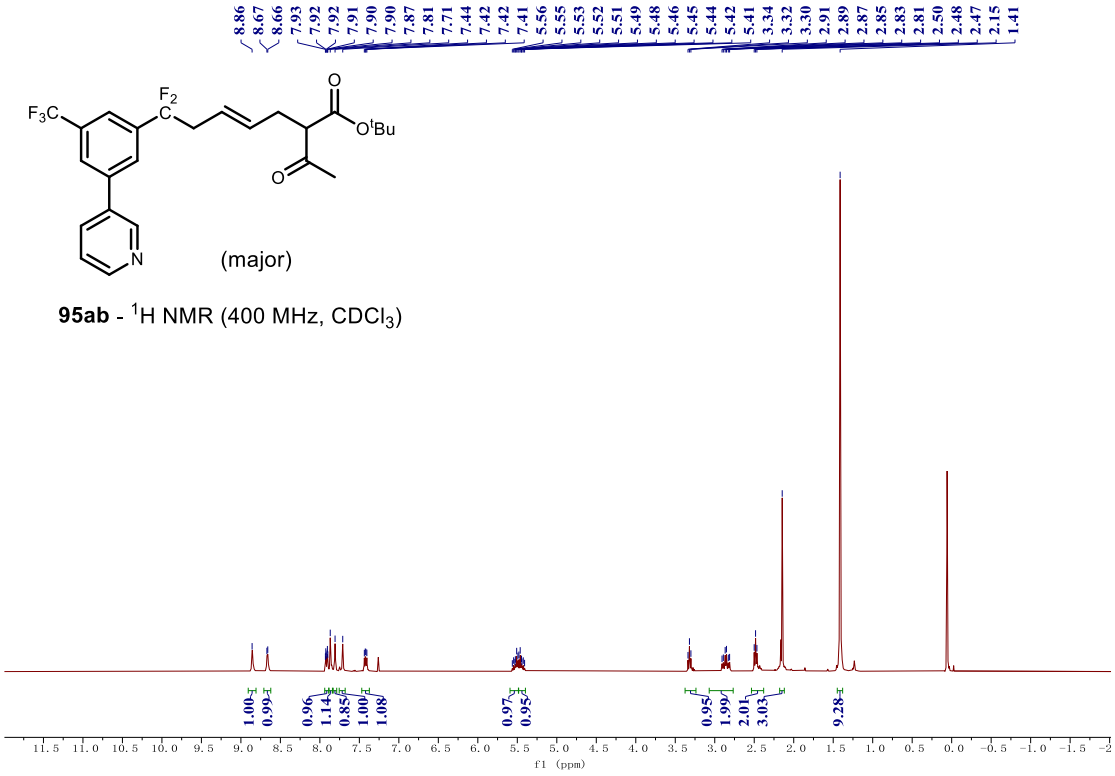




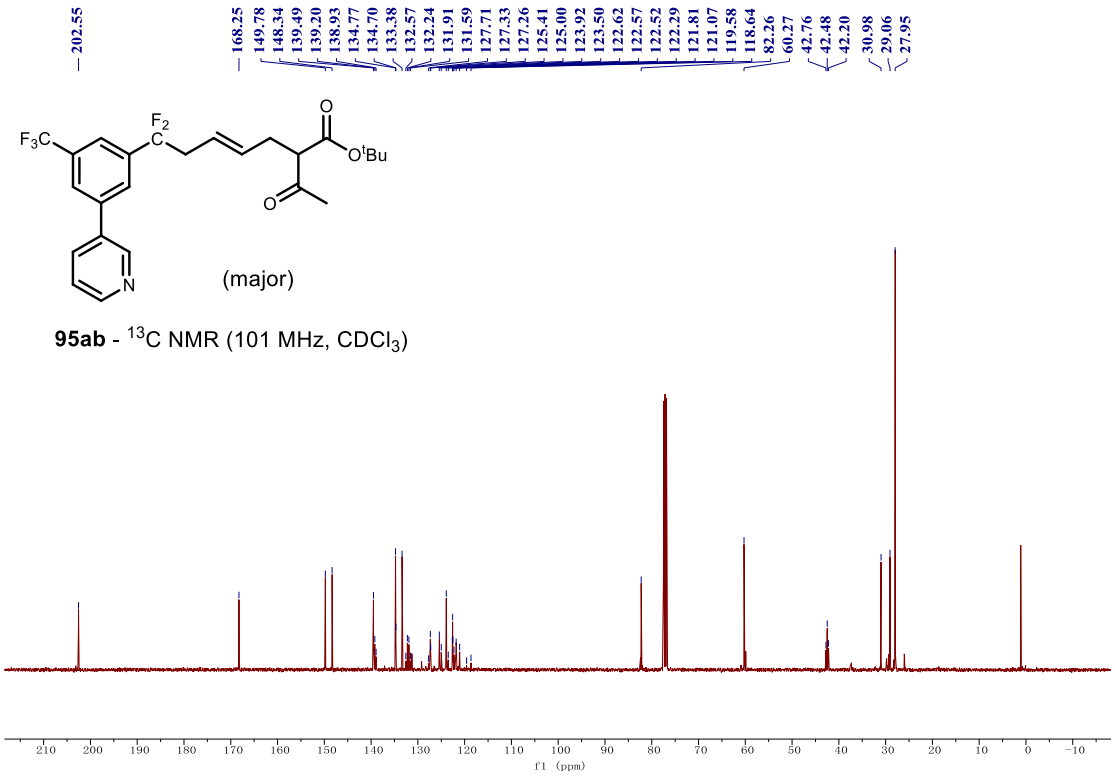
94ab - ^{13}C NMR (101 MHz, $CDCl_3$)



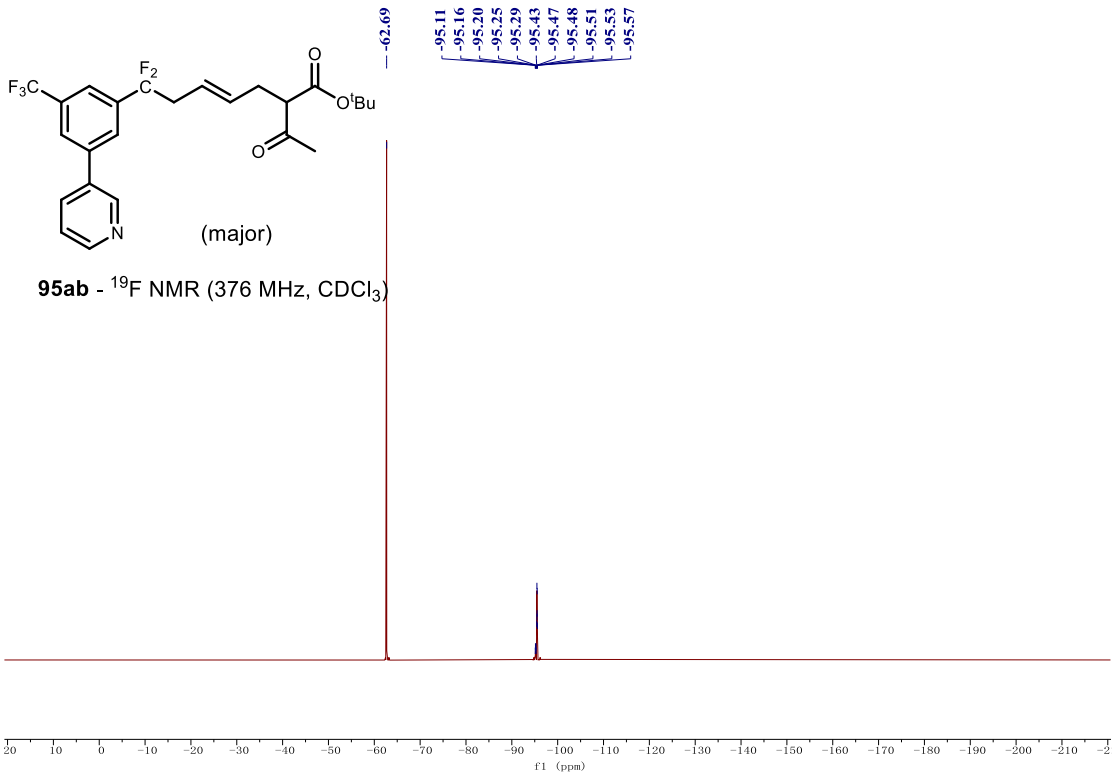
94ab - ^{19}F NMR (376 MHz, $CDCl_3$)



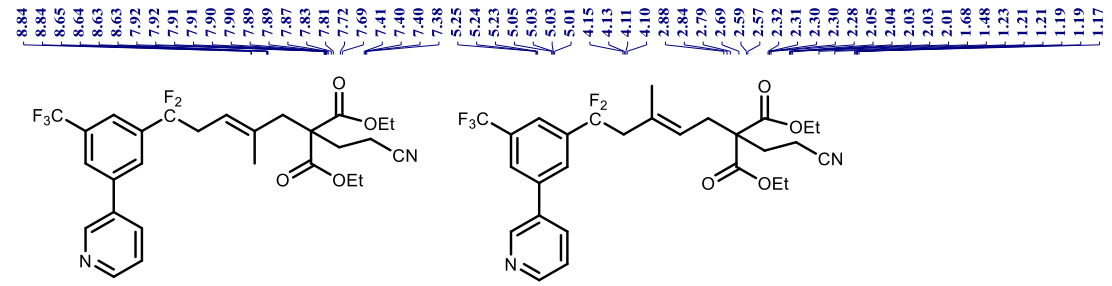
95ab - ^{1}H NMR (400 MHz, $CDCl_3$)



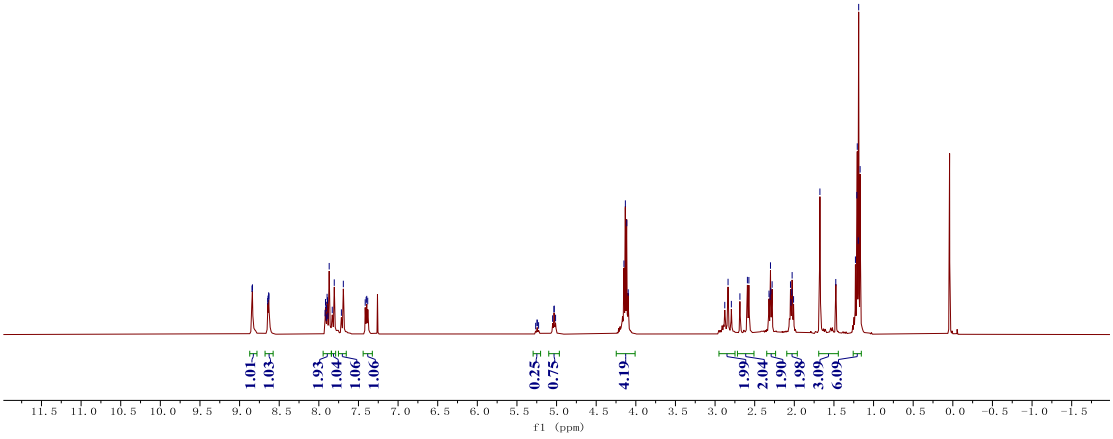
95ab - ^{13}C NMR (101 MHz, $CDCl_3$)

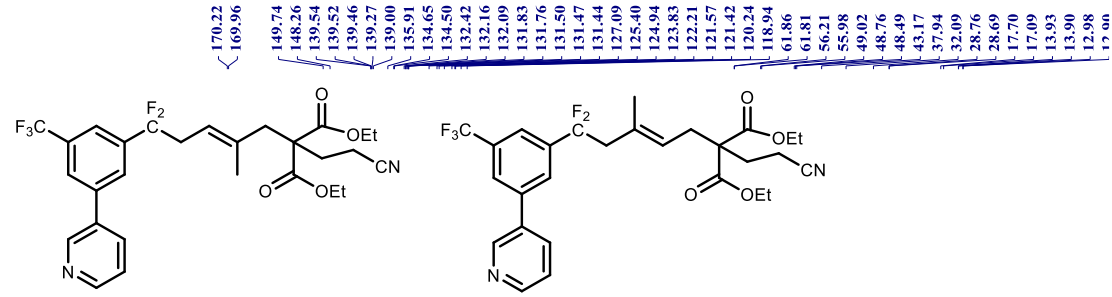


95ab - ^{19}F NMR (376 MHz, $CDCl_3$)

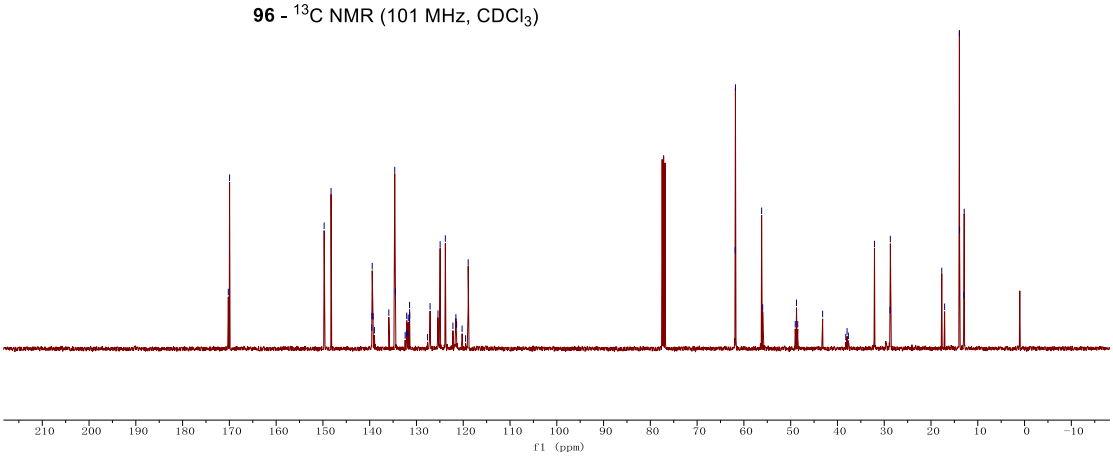


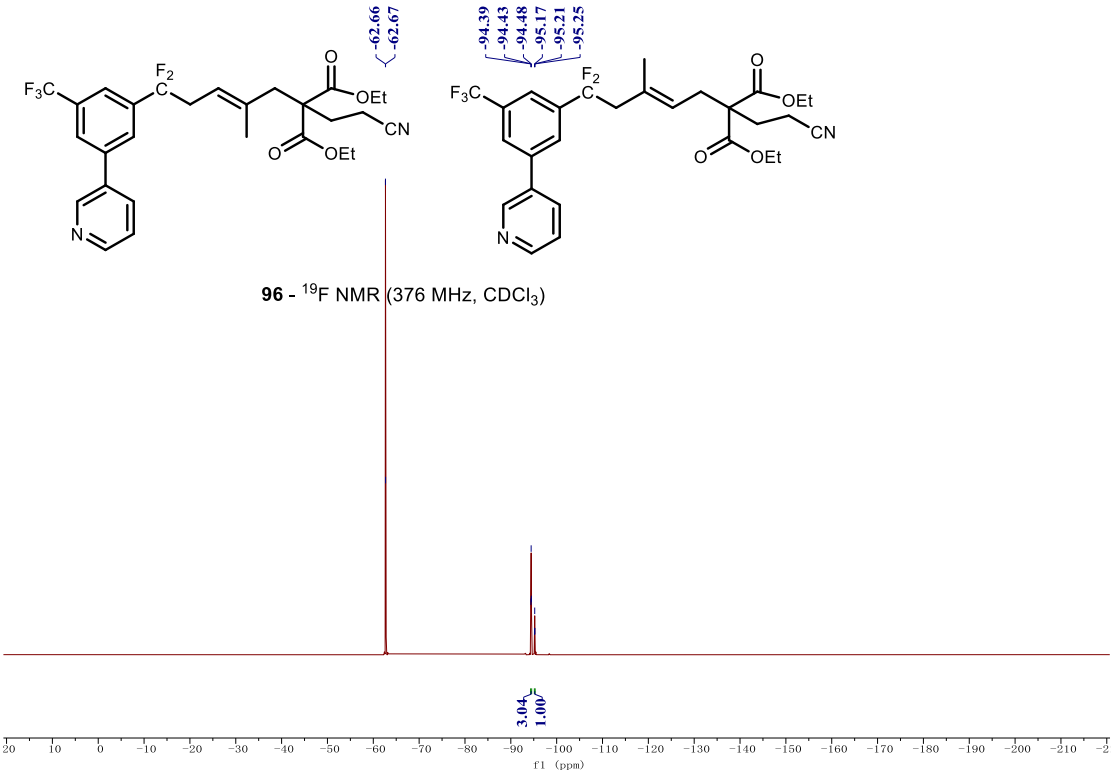
96 - ^{1}H NMR (400 MHz, $CDCl_3$)



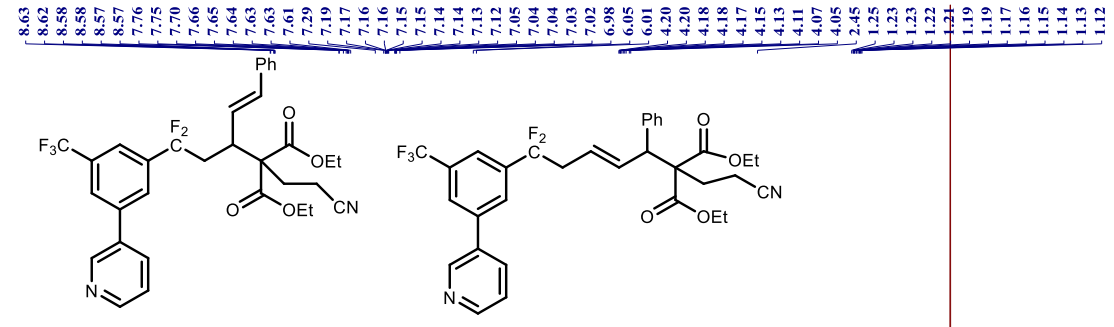


96 - ^{13}C NMR (101 MHz, $CDCl_3$)

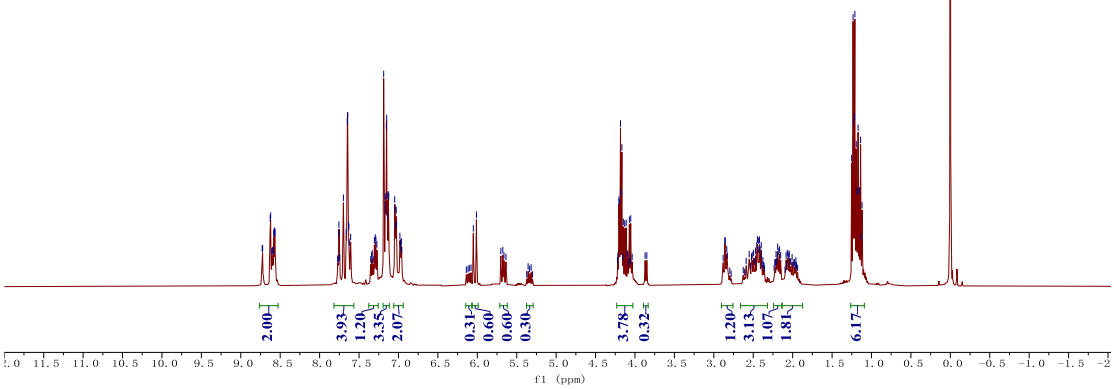


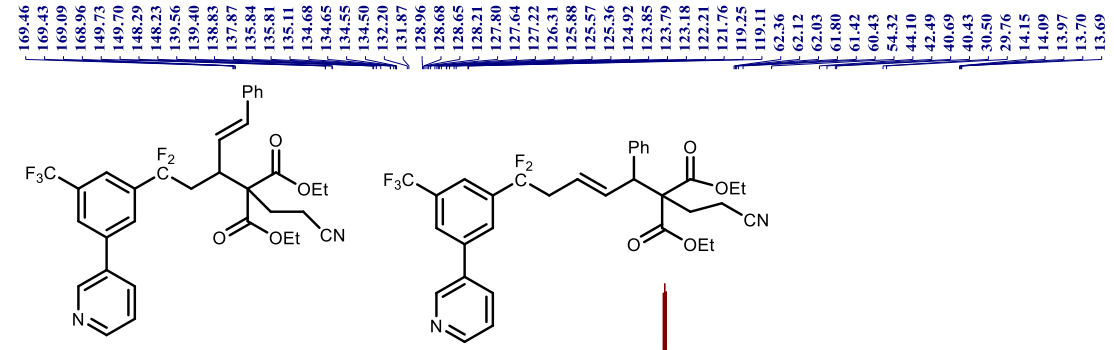


96 - ^{19}F NMR (376 MHz, $CDCl_3$)

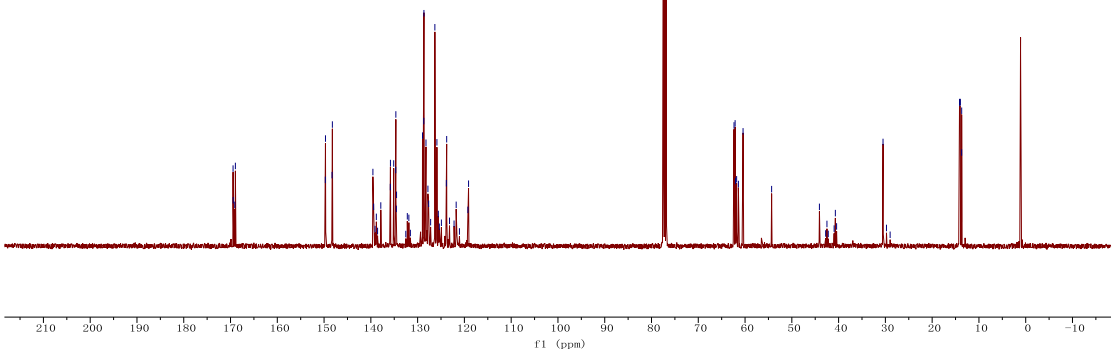


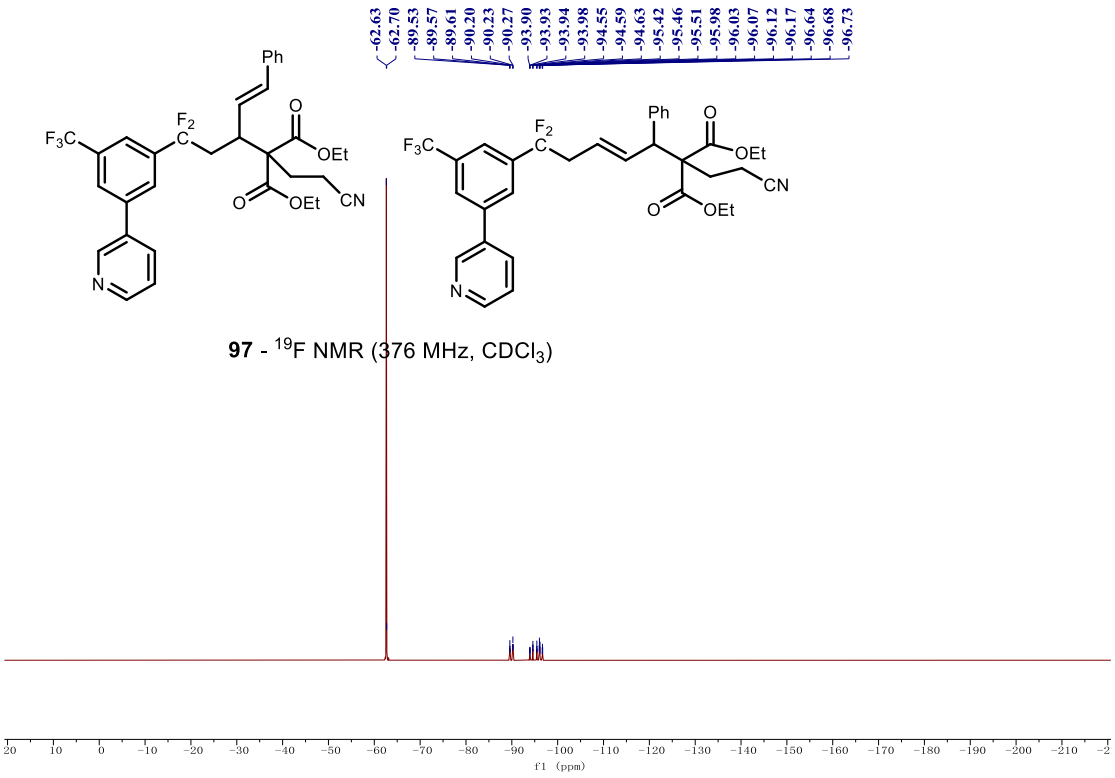
97 - ^{1}H NMR (400 MHz, $CDCl_3$)



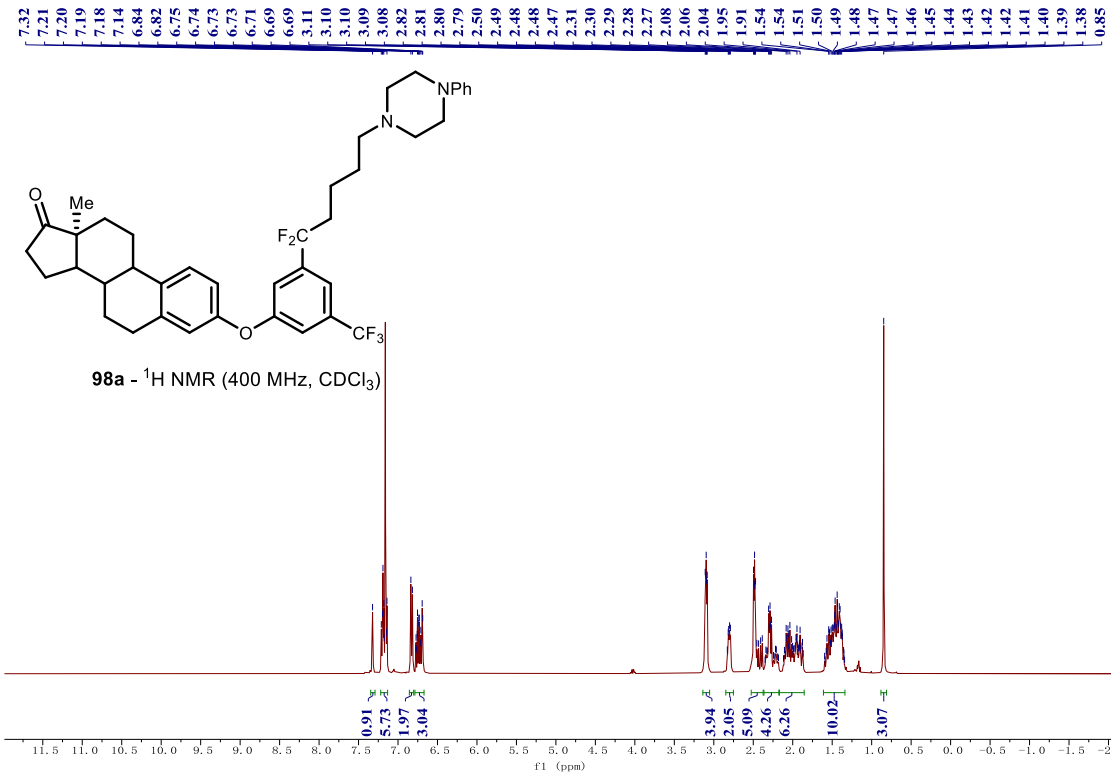


97 - ^{13}C NMR (101 MHz, $CDCl_3$)

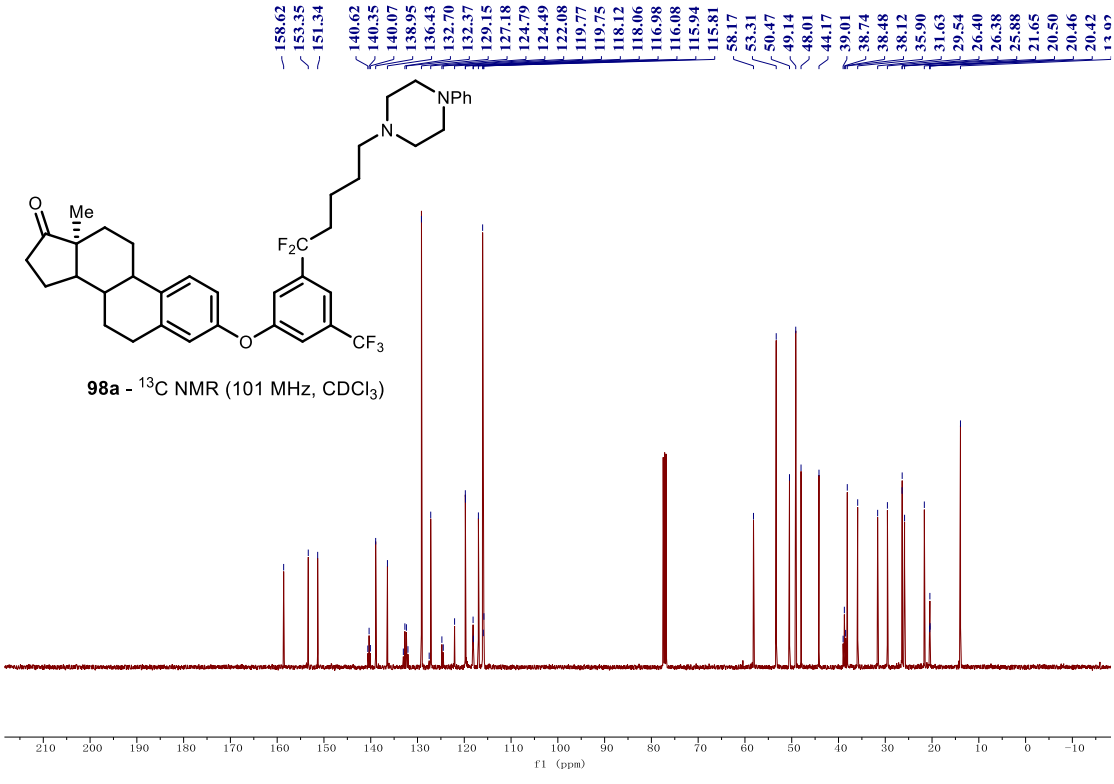




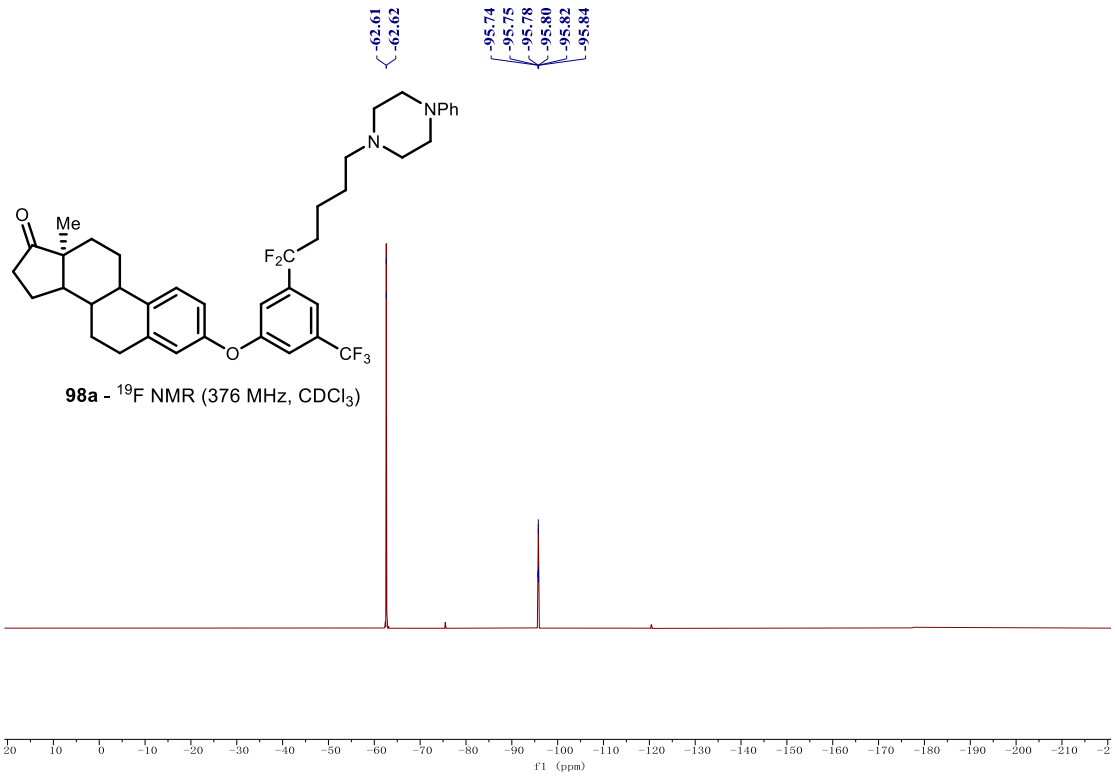
97 - ^{19}F NMR (376 MHz, $CDCl_3$)



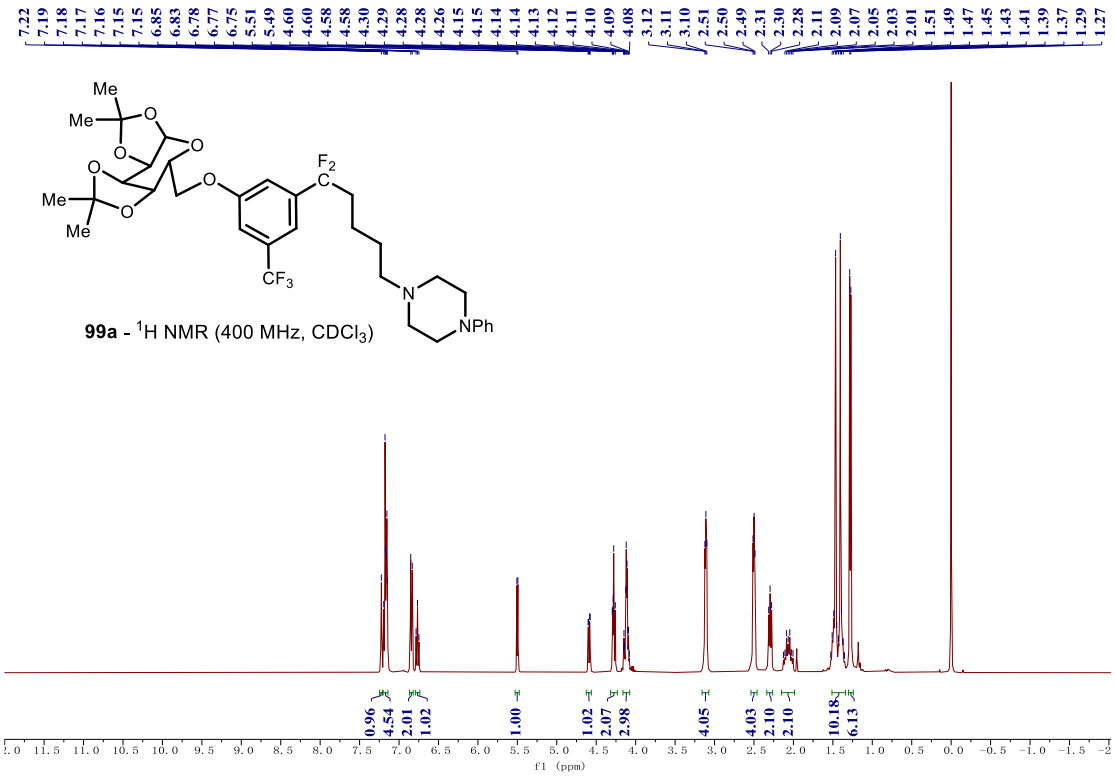
98a - ^{1}H NMR (400 MHz, $CDCl_3$)



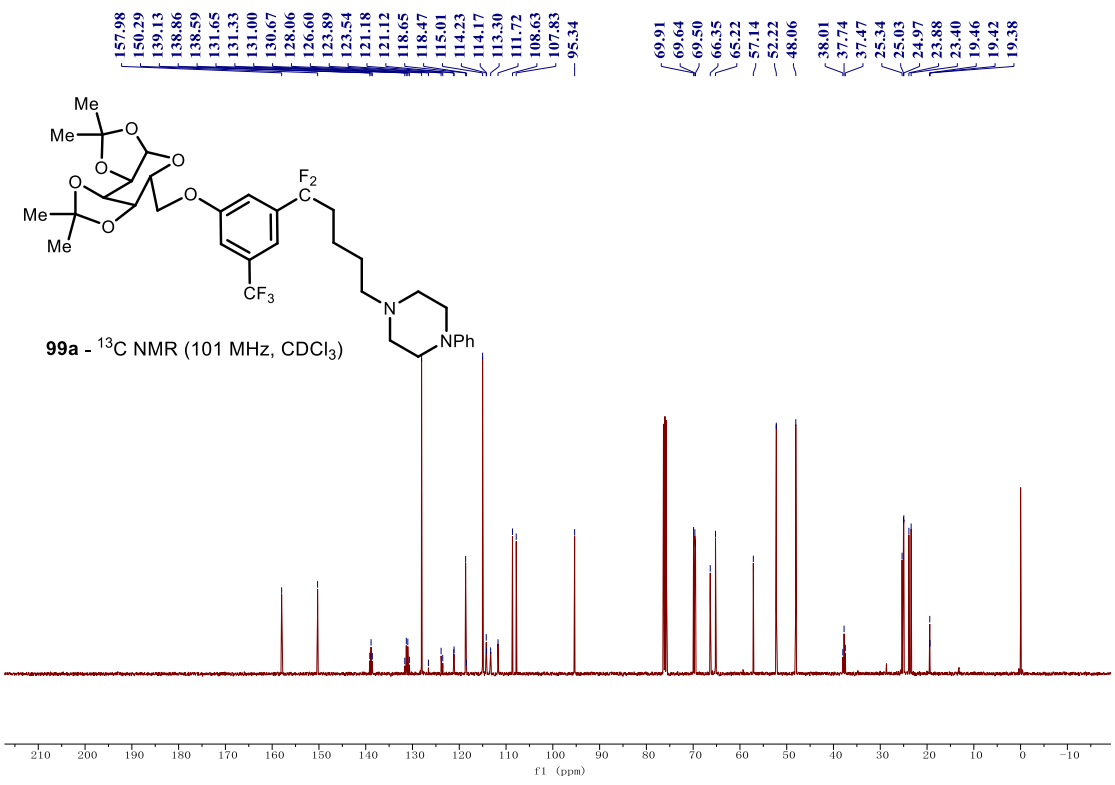
98a - ^{13}C NMR (101 MHz, $CDCl_3$)



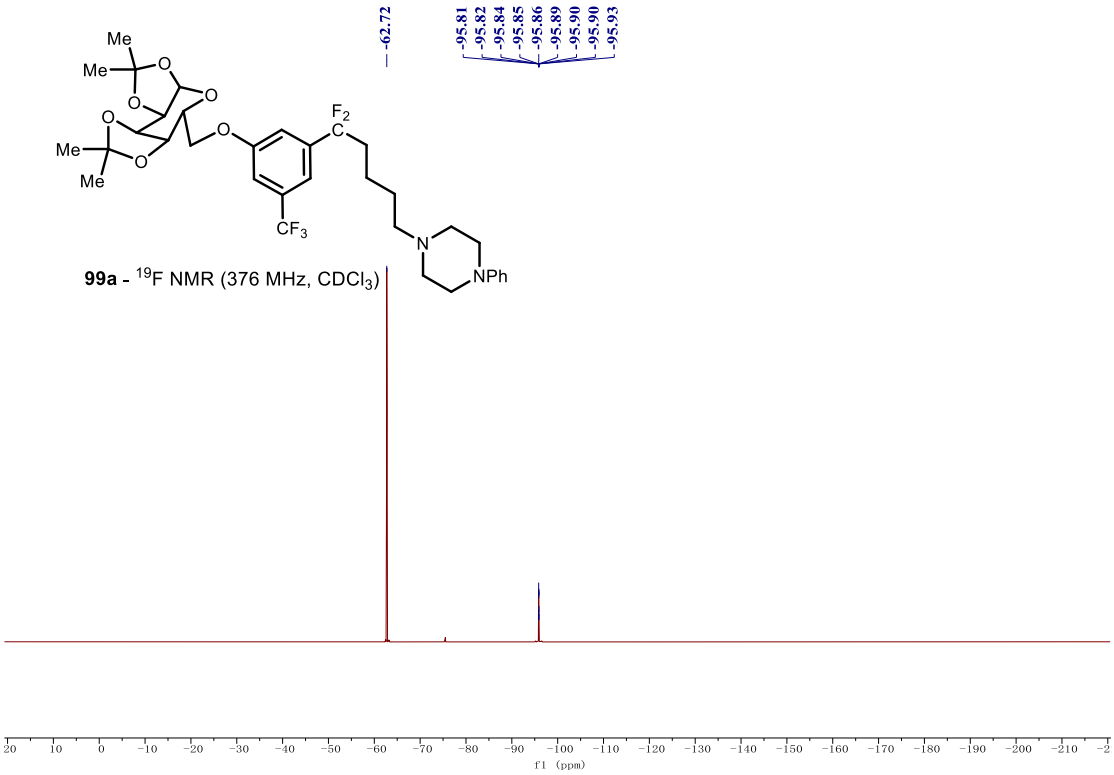
98a - ^{19}F NMR (376 MHz, $CDCl_3$)

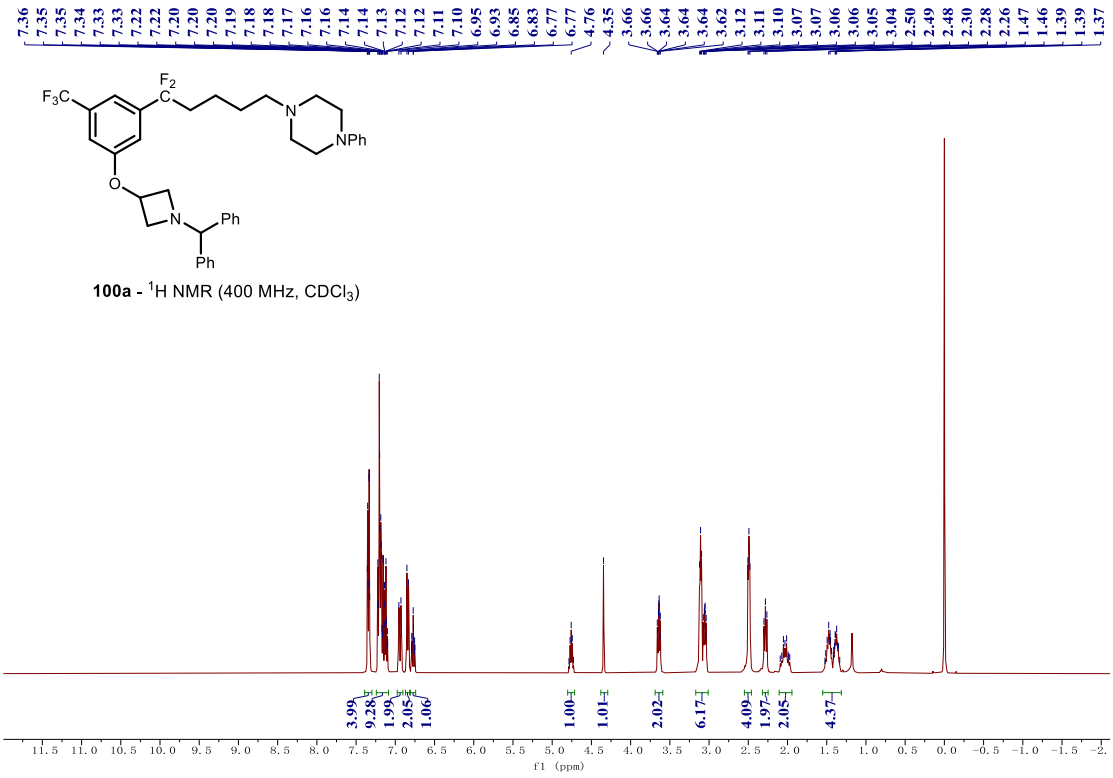


99a - ^{1}H NMR (400 MHz, $CDCl_3$)

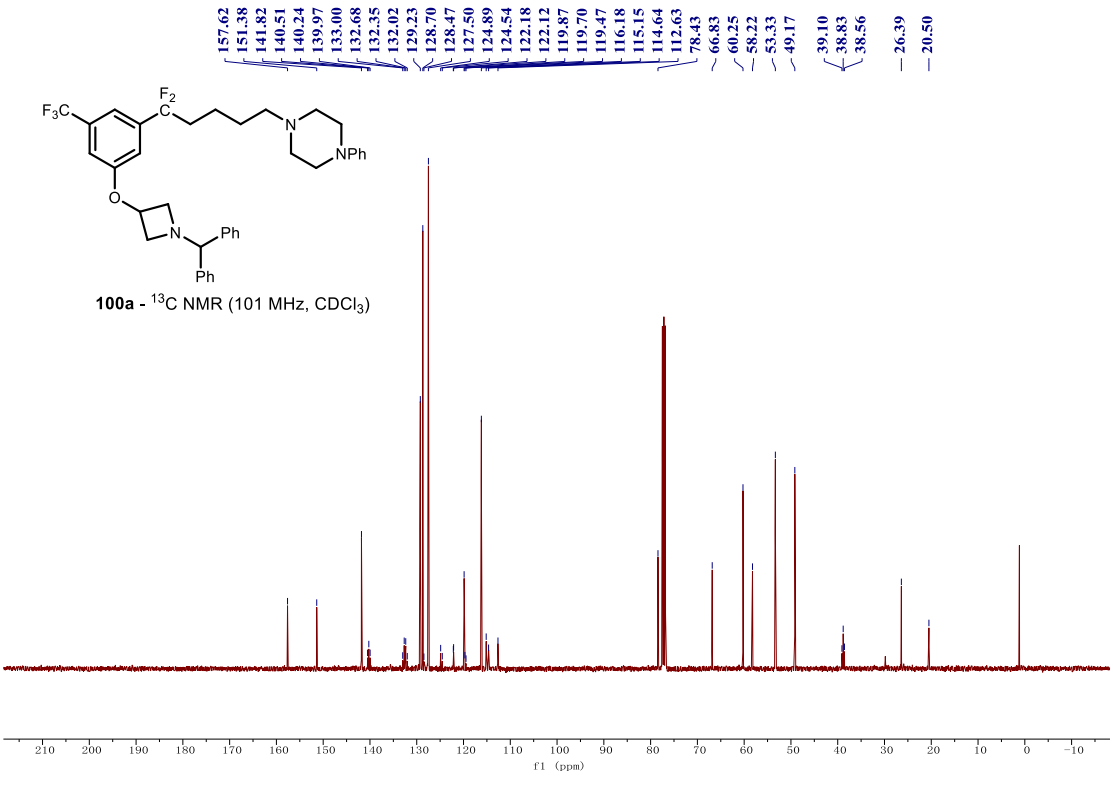


99a - ^{13}C NMR (101 MHz, $CDCl_3$)

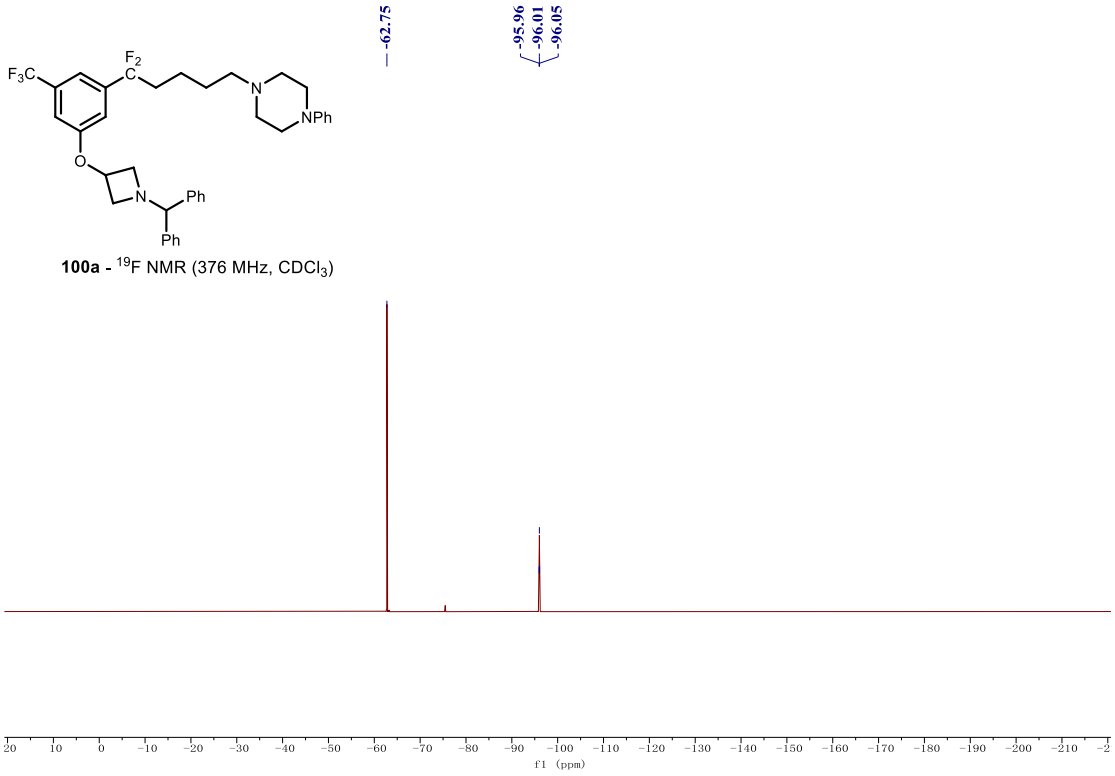

-62.72
-95.81
-95.82
-95.84
-95.85
-95.86
-95.89
-95.90
-95.90
-95.93
Me
Me
O
O
O
O
Me
Me
O
O
F2
C
CF3
N
NPh
99a - 19F NMR (376 MHz, CDCl3)
20
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)



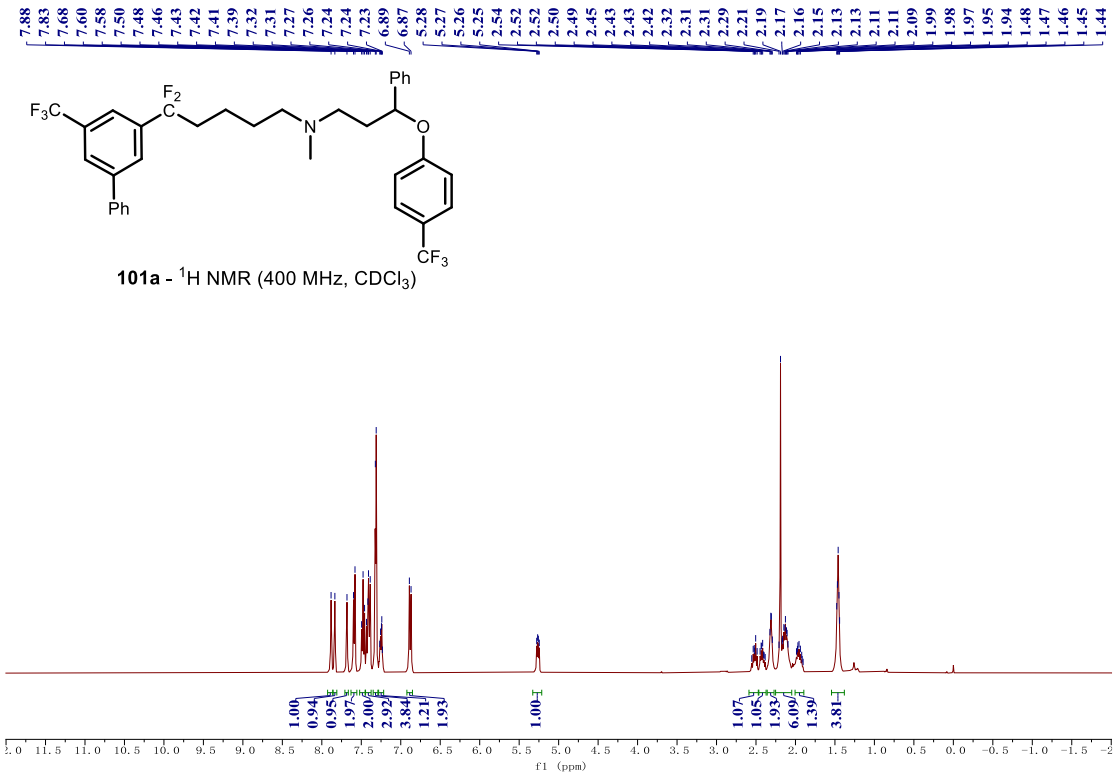
100a - ^{1}H NMR (400 MHz, $CDCl_3$)



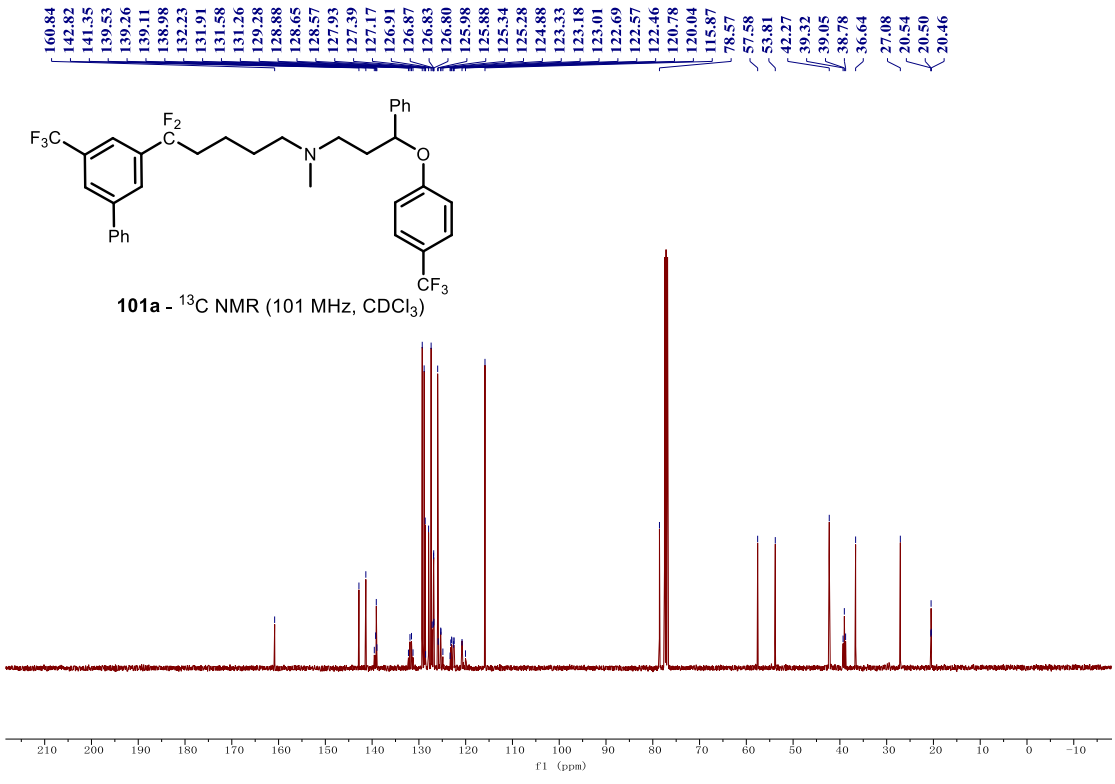
100a - ^{13}C NMR (101 MHz, $CDCl_3$)



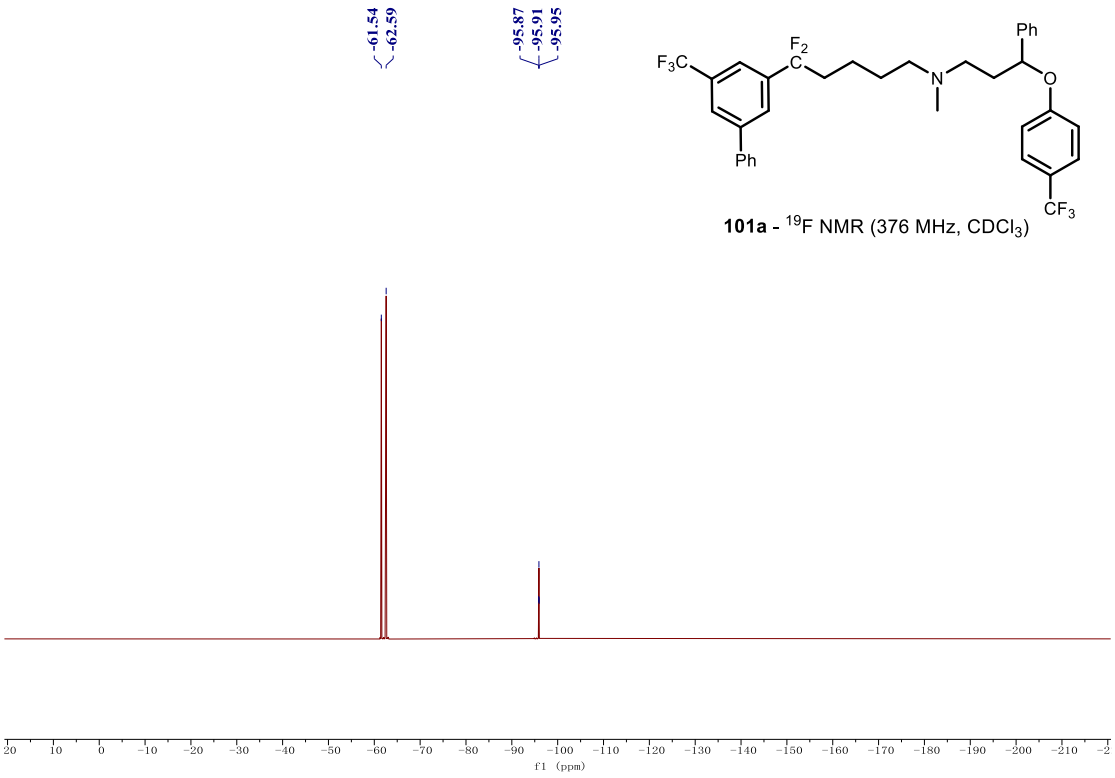
100a - ^{19}F NMR (376 MHz, $CDCl_3$)



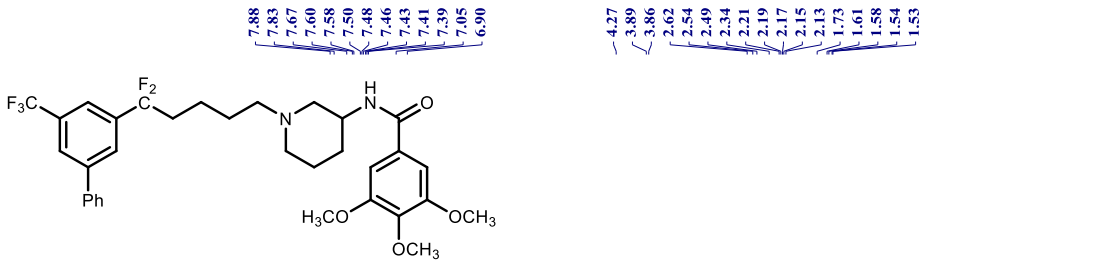
101a - ^{1}H NMR (400 MHz, $CDCl_3$)



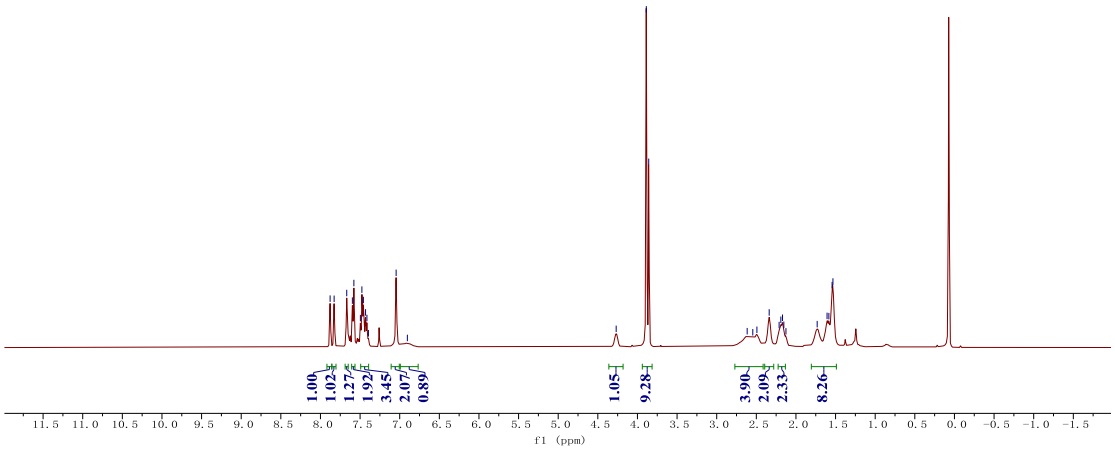
101a - ^{13}C NMR (101 MHz, $CDCl_3$)

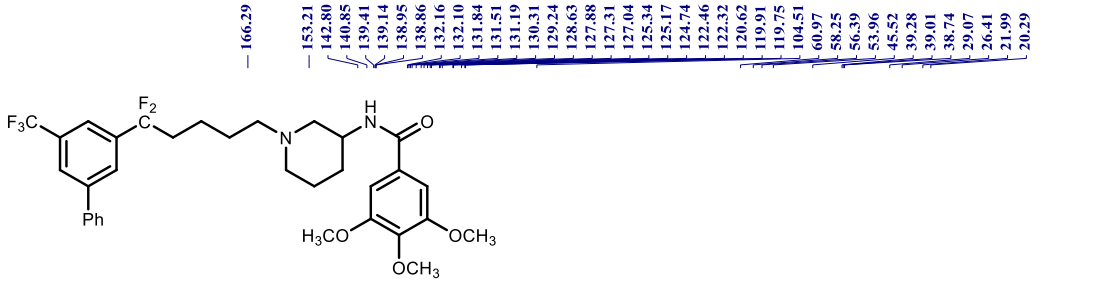


101a - ^{19}F NMR (376 MHz, $CDCl_3$)

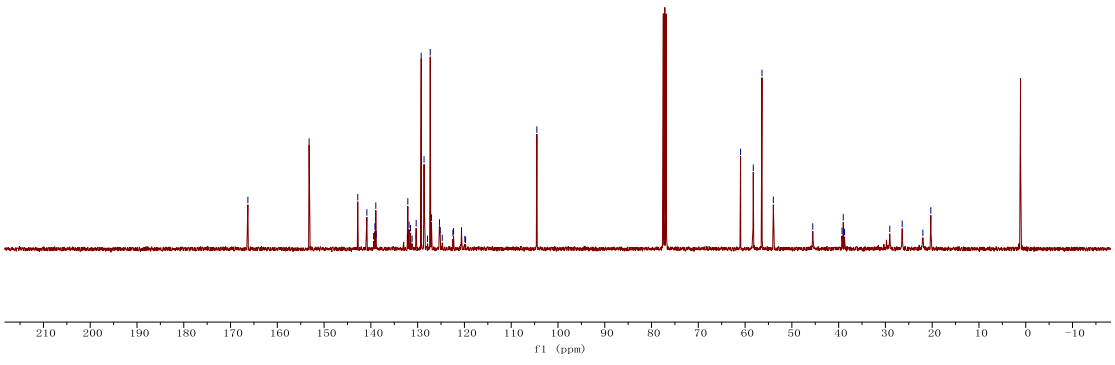


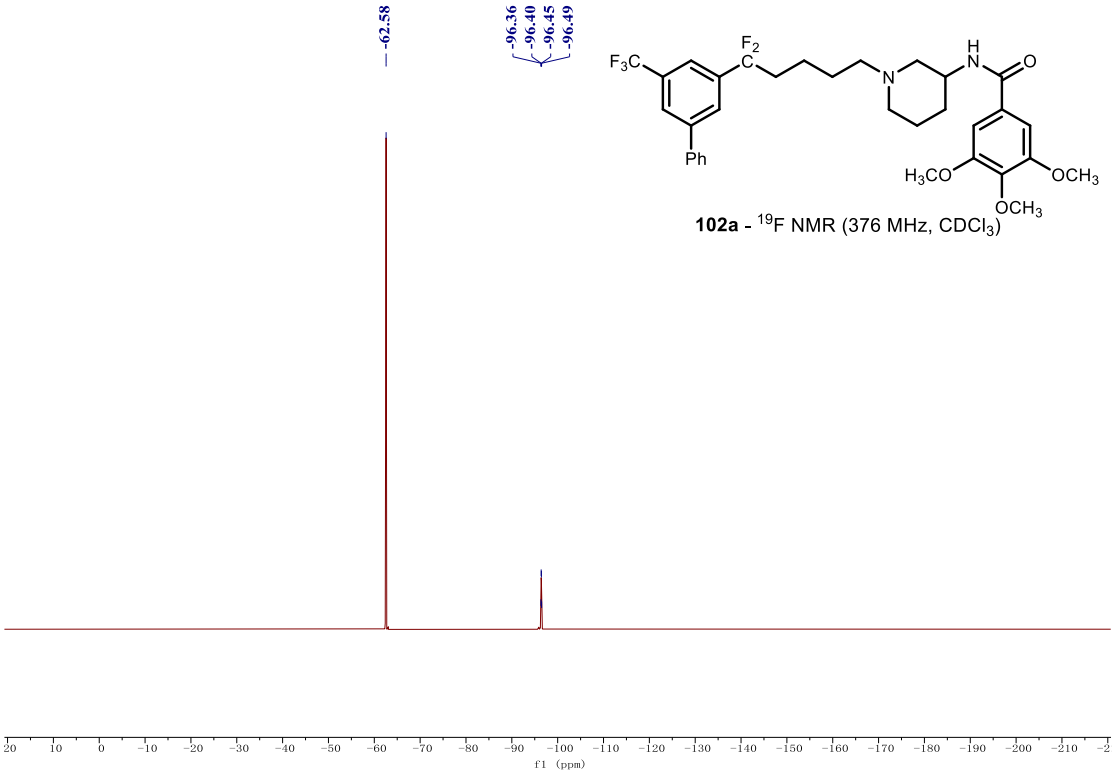
102a - ^{1}H NMR (400 MHz, $CDCl_3$)



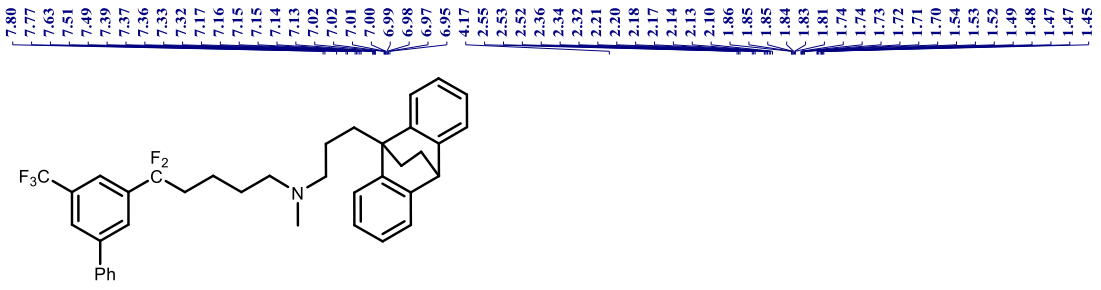


102a - ^{13}C NMR (101 MHz, $CDCl_3$)

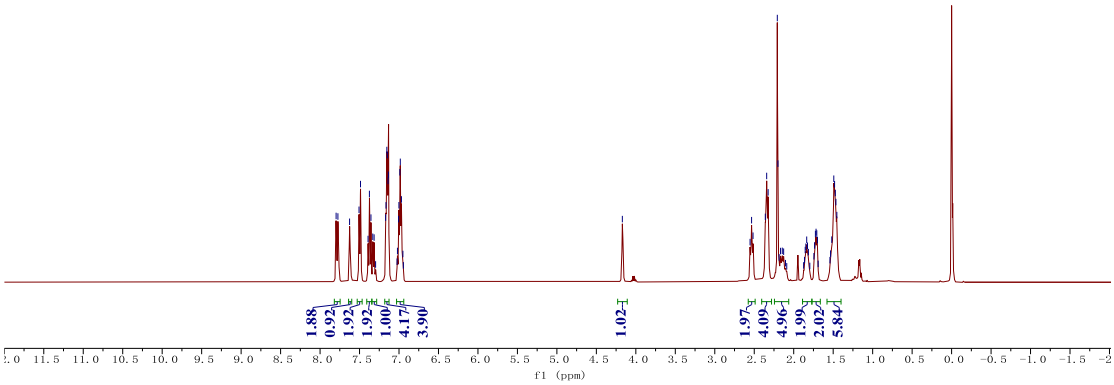


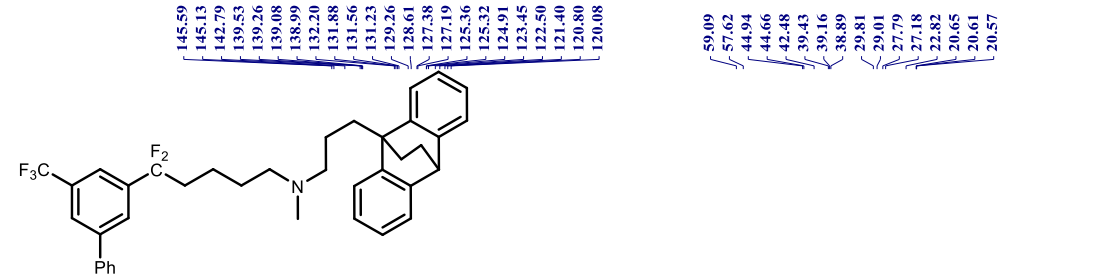


102a - ^{19}F NMR (376 MHz, $CDCl_3$)

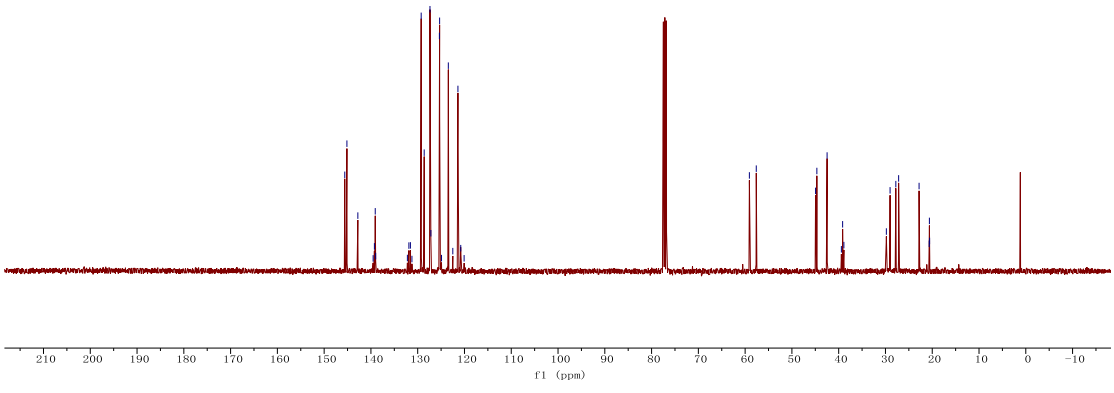


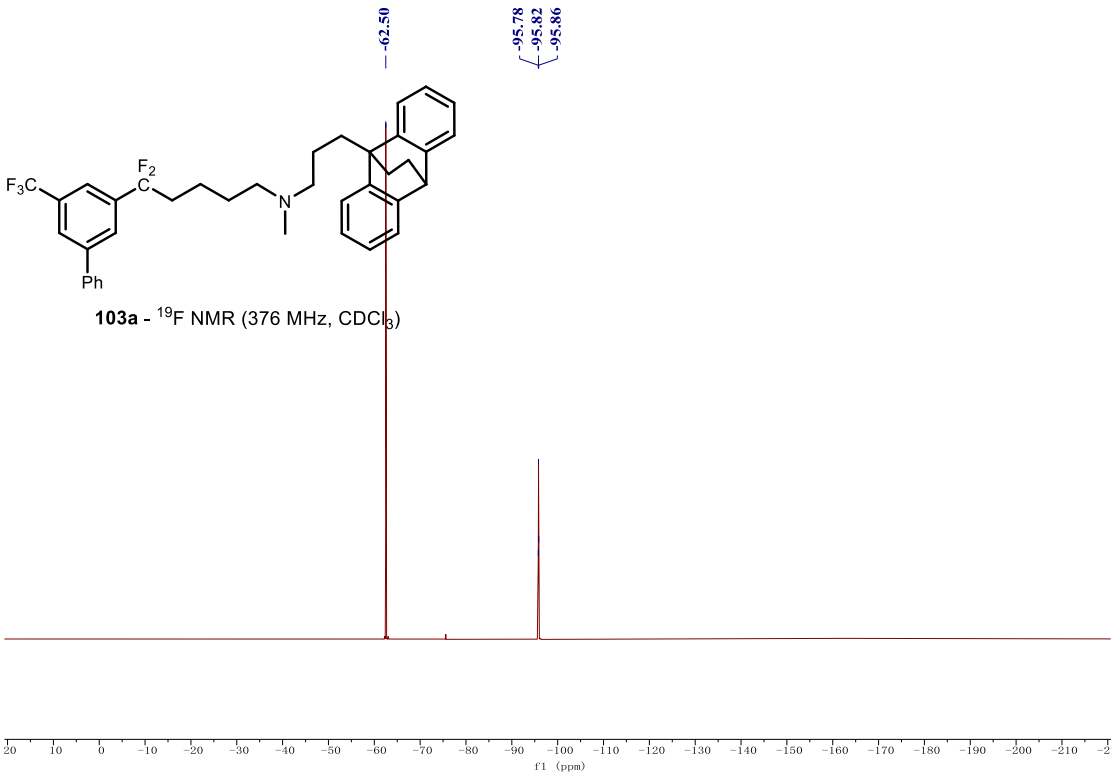
103a - ^{1}H NMR (400 MHz, $CDCl_3$)



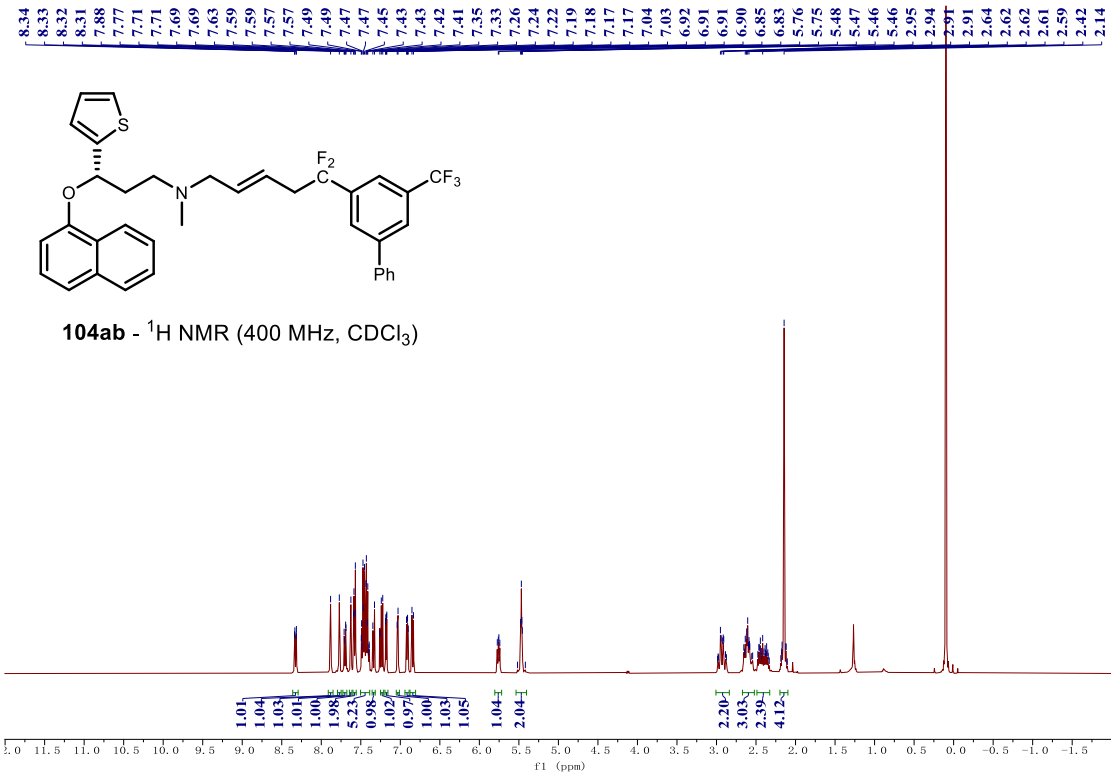


103a - ^{13}C NMR (101 MHz, $CDCl_3$)

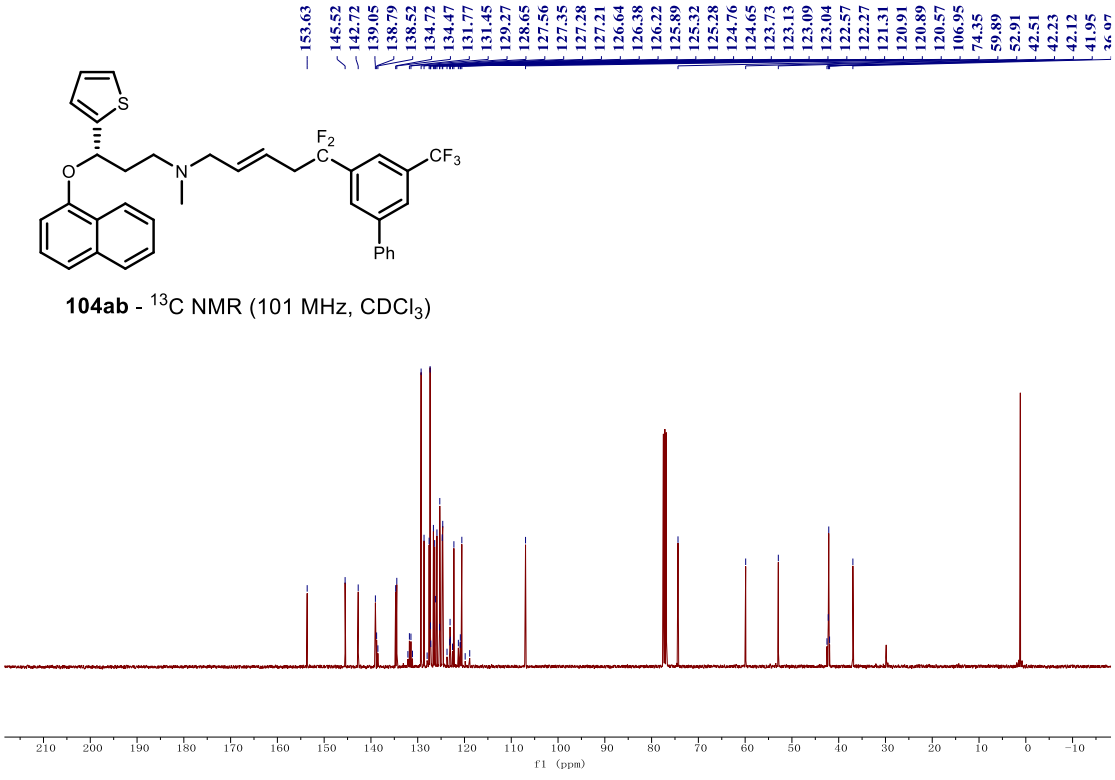




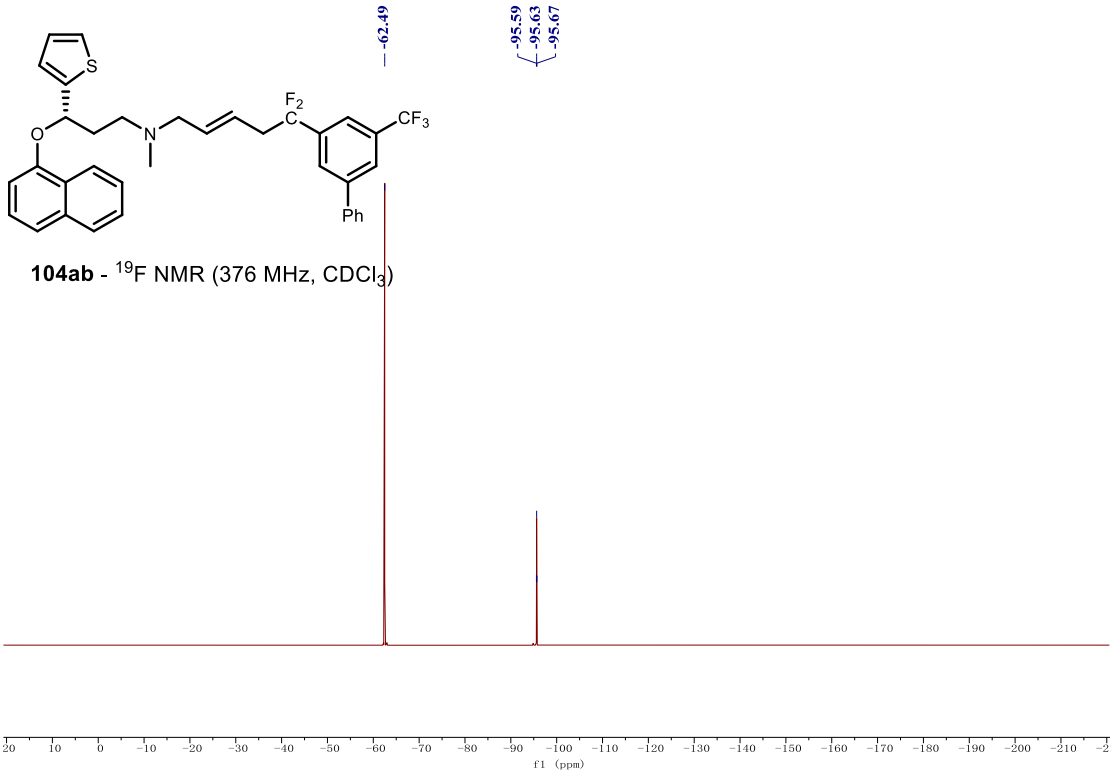
103a - ^{19}F NMR (376 MHz, $CDCl_3$)



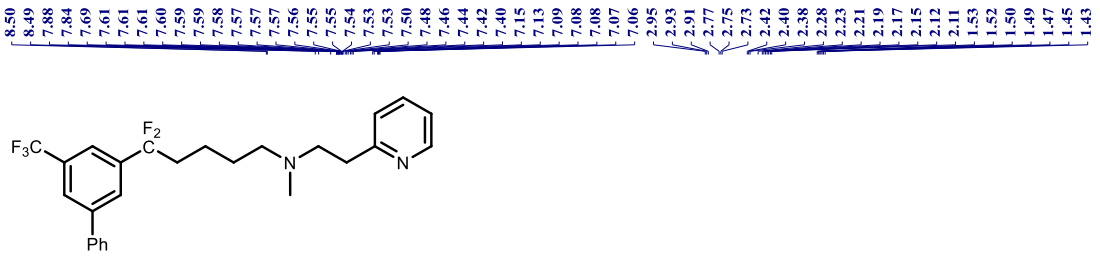
104ab - ^{1}H NMR (400 MHz, $CDCl_3$)



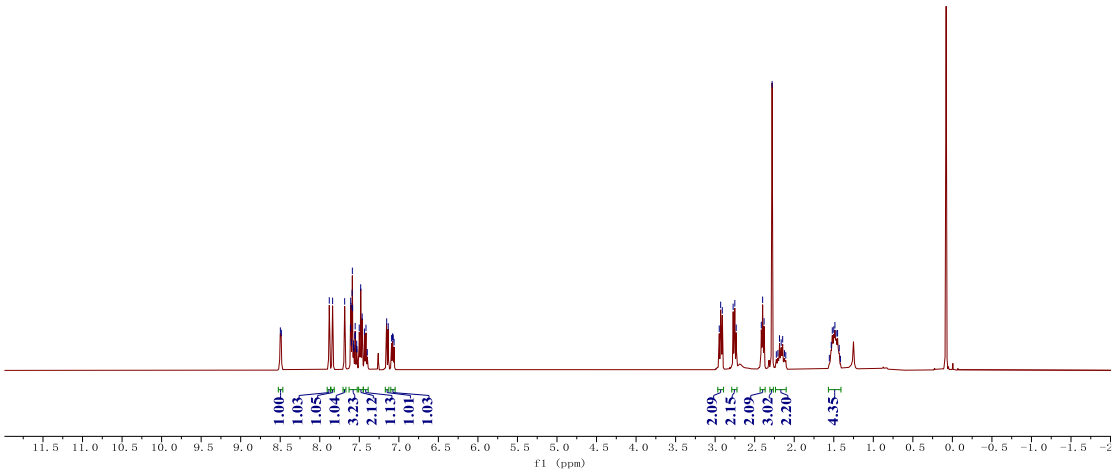
104ab - ^{13}C NMR (101 MHz, $CDCl_3$)

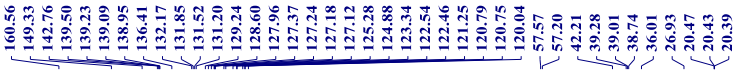


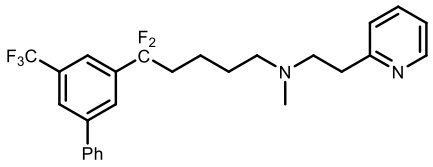
104ab - ^{19}F NMR (376 MHz, $CDCl_3$)



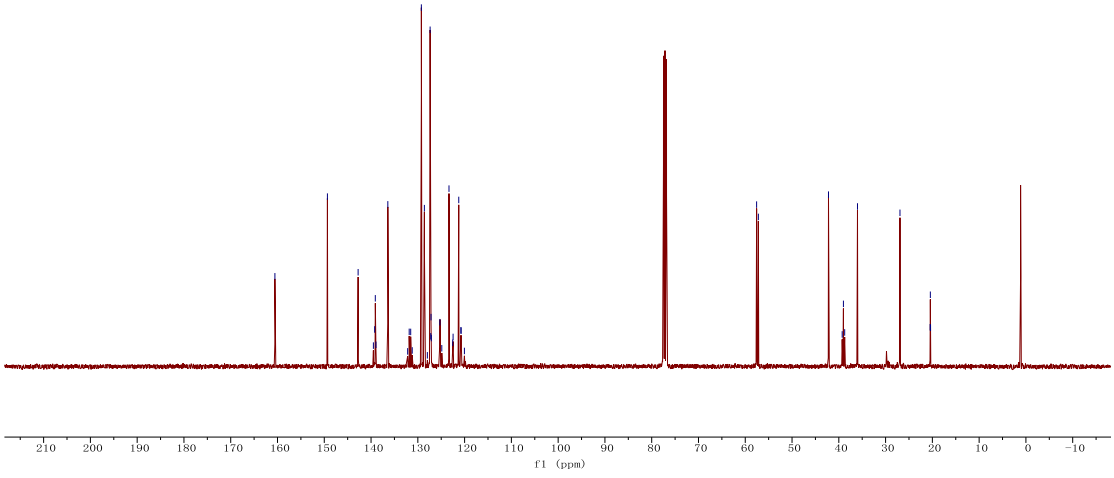
105a - ^{1}H NMR (400 MHz, $CDCl_3$)

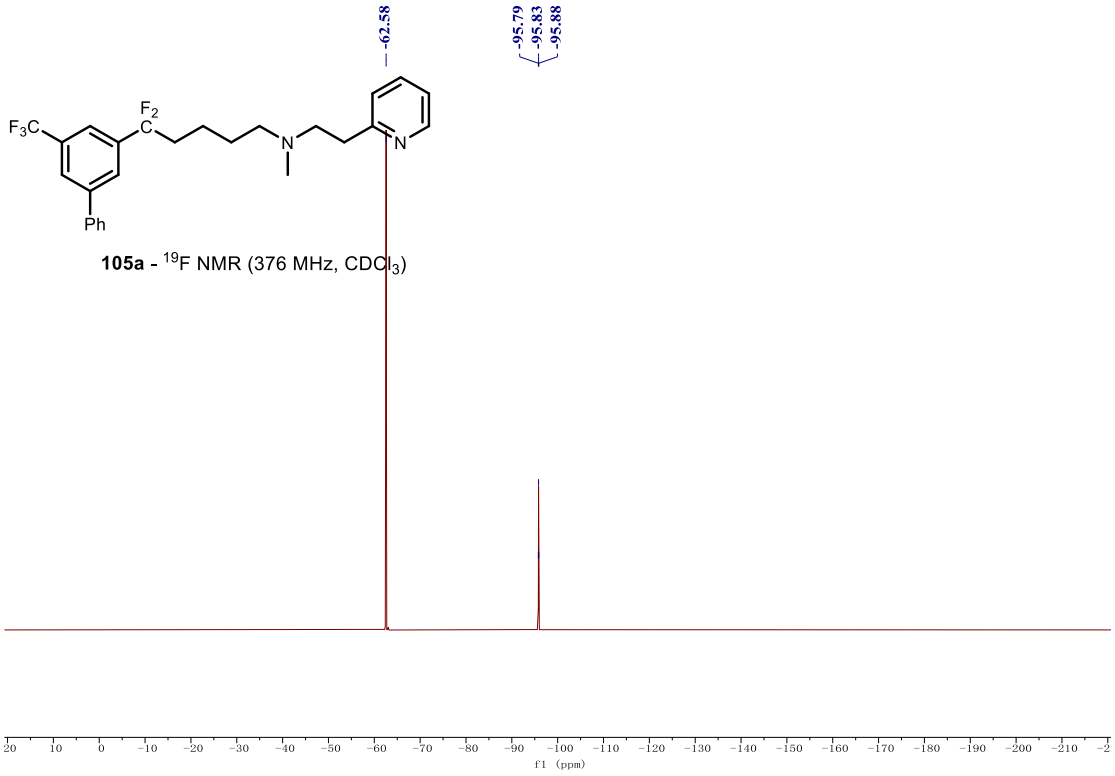




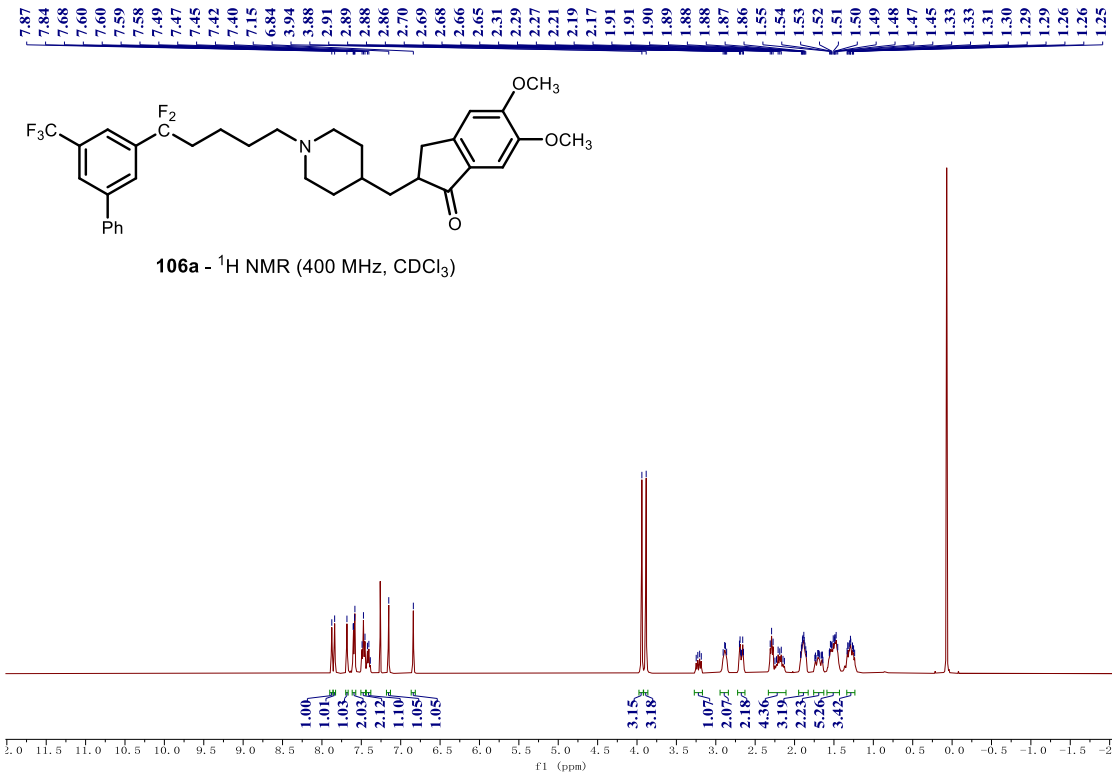


105a - ^{13}C NMR (101 MHz, $CDCl_3$)

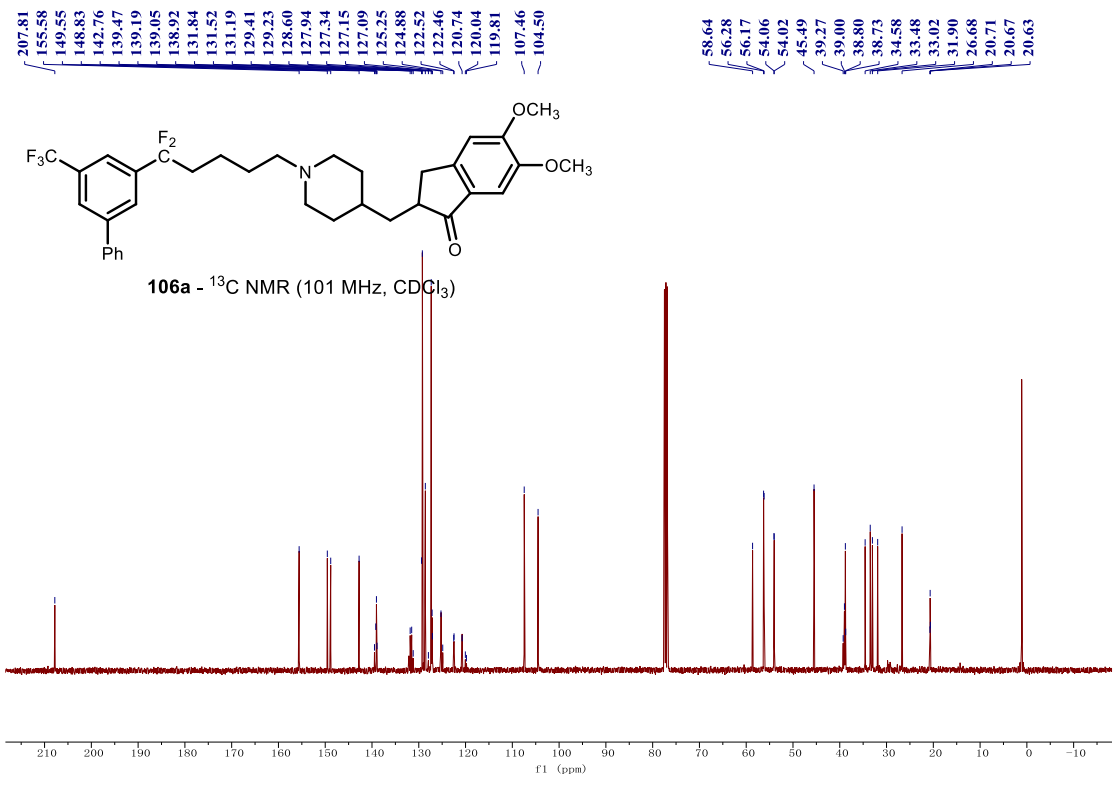




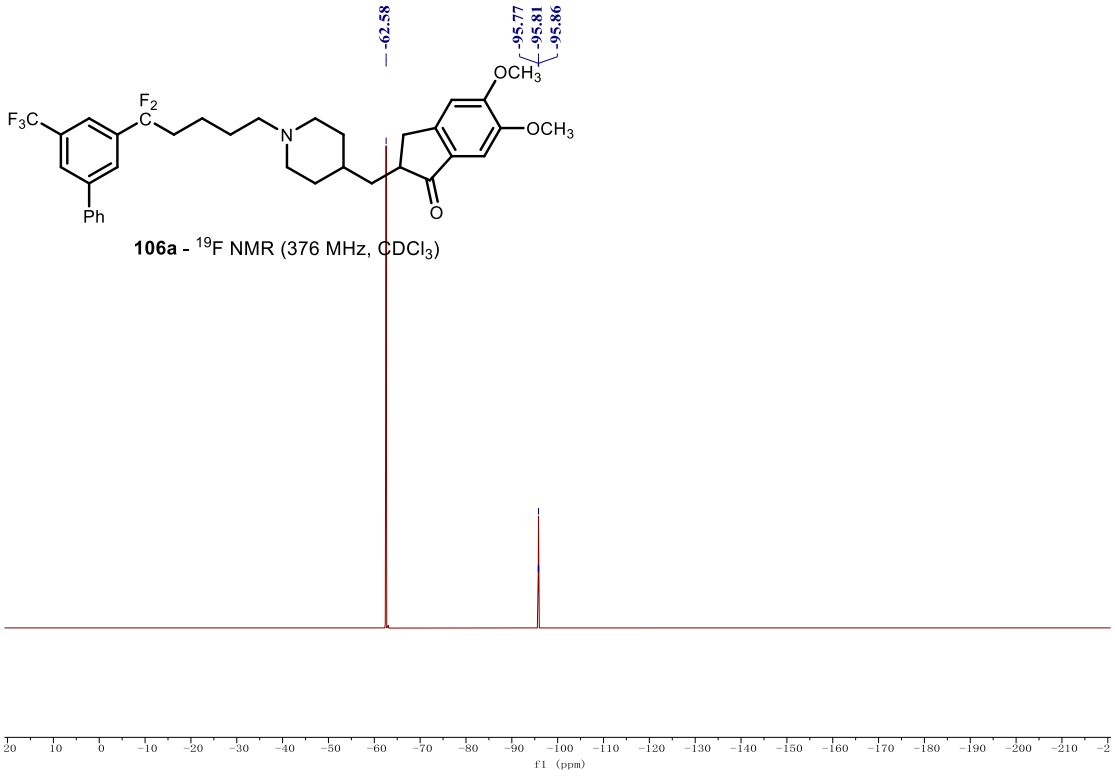
105a - ^{19}F NMR (376 MHz, $CDCl_3$)



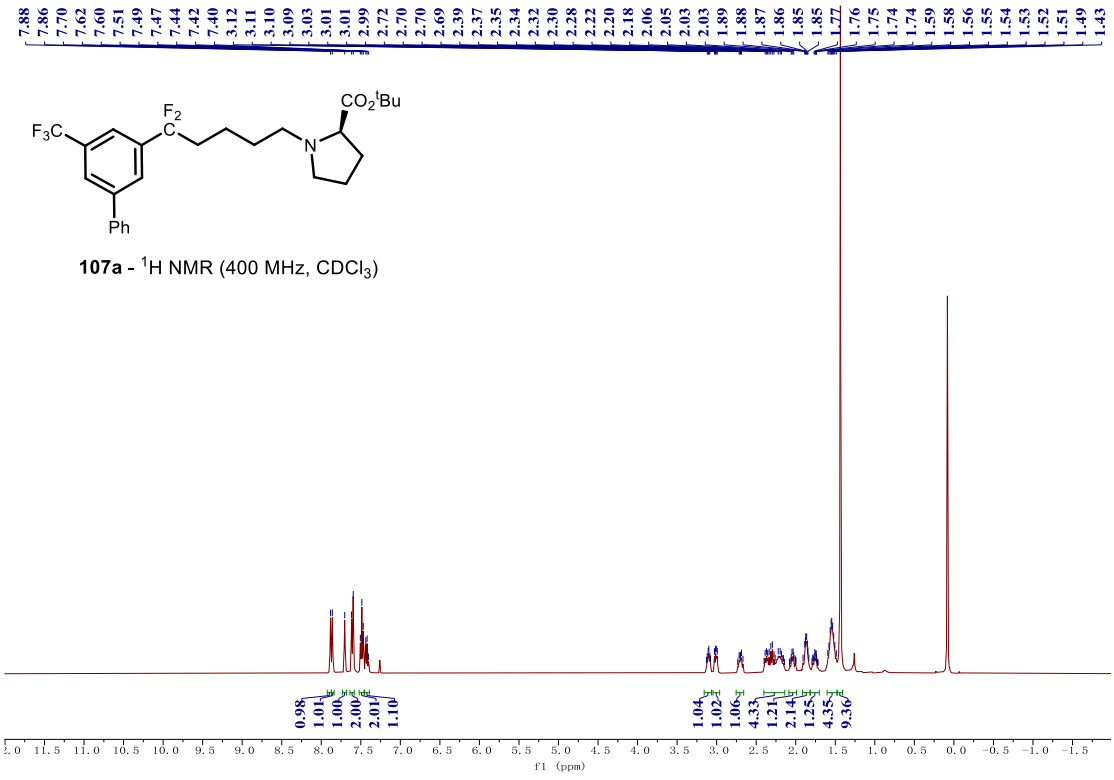
106a - ^{1}H NMR (400 MHz, $CDCl_3$)



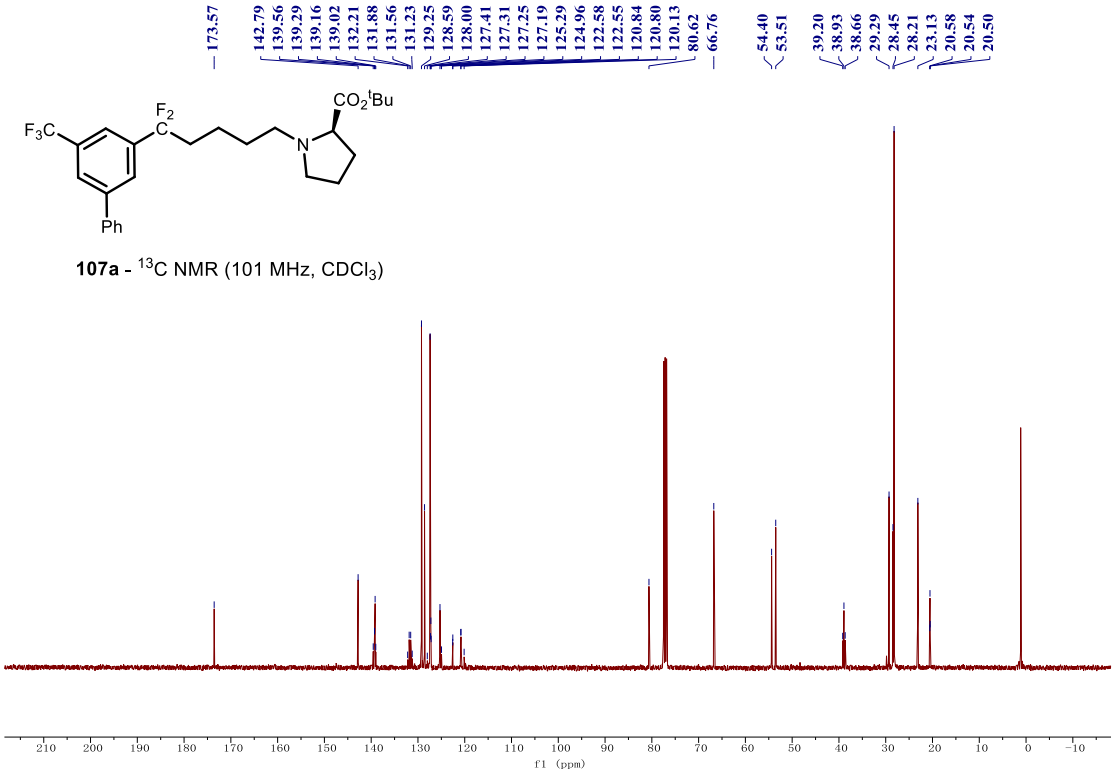
106a - ^{13}C NMR (101 MHz, $CDCl_3$)



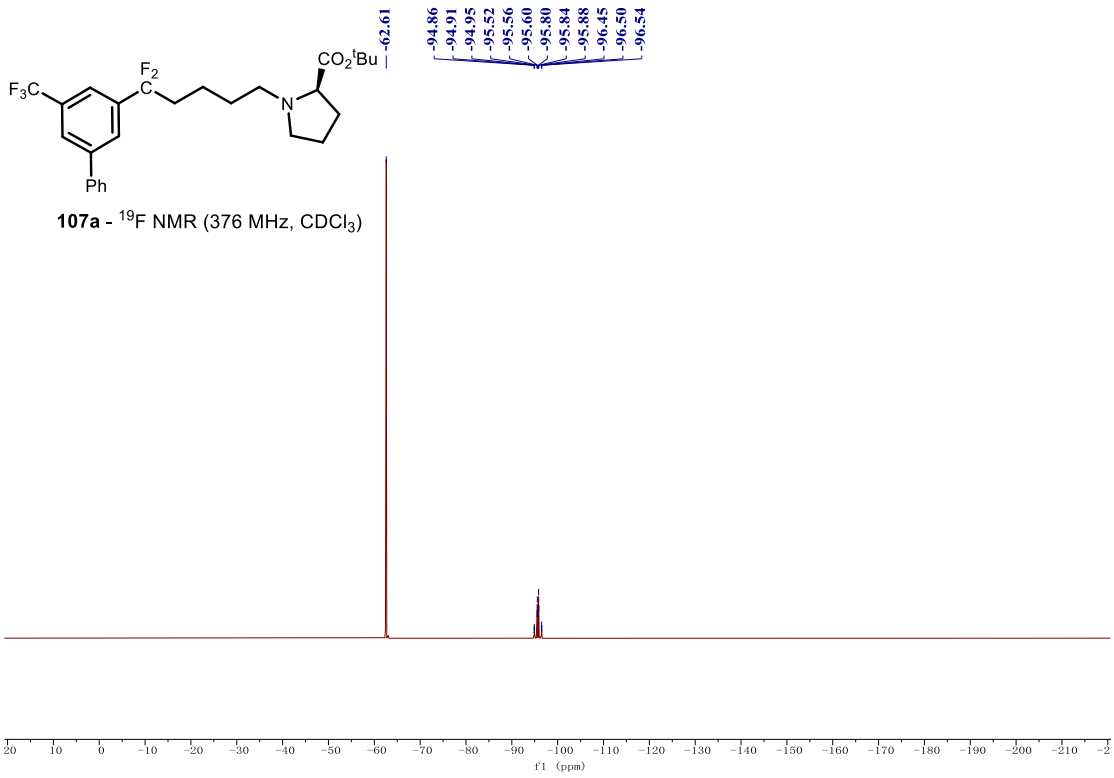
106a - ^{19}F NMR (376 MHz, $CDCl_3$)



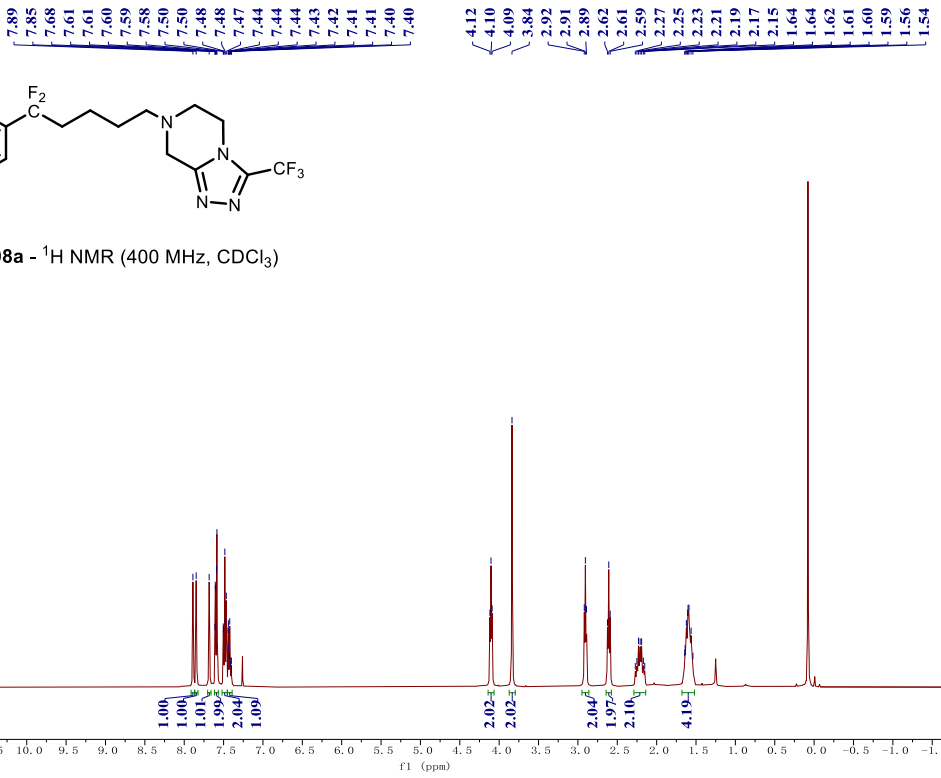
107a - ^{1}H NMR (400 MHz, $CDCl_3$)



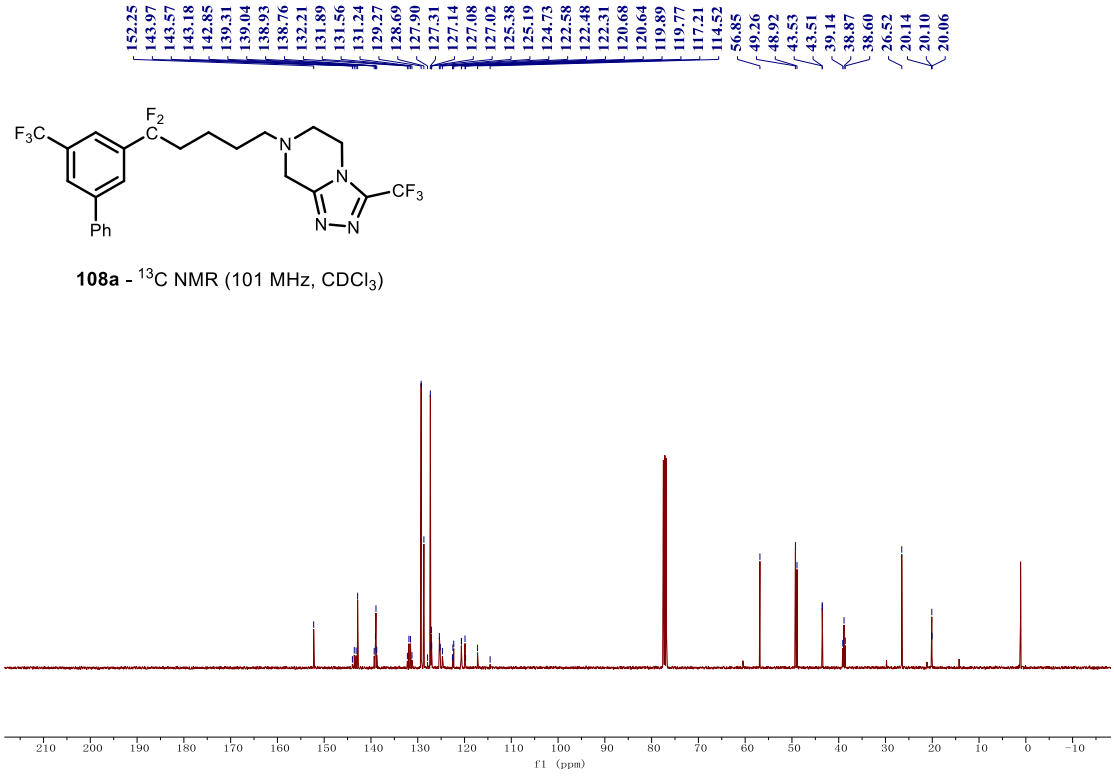
107a - ^{13}C NMR (101 MHz, $CDCl_3$)



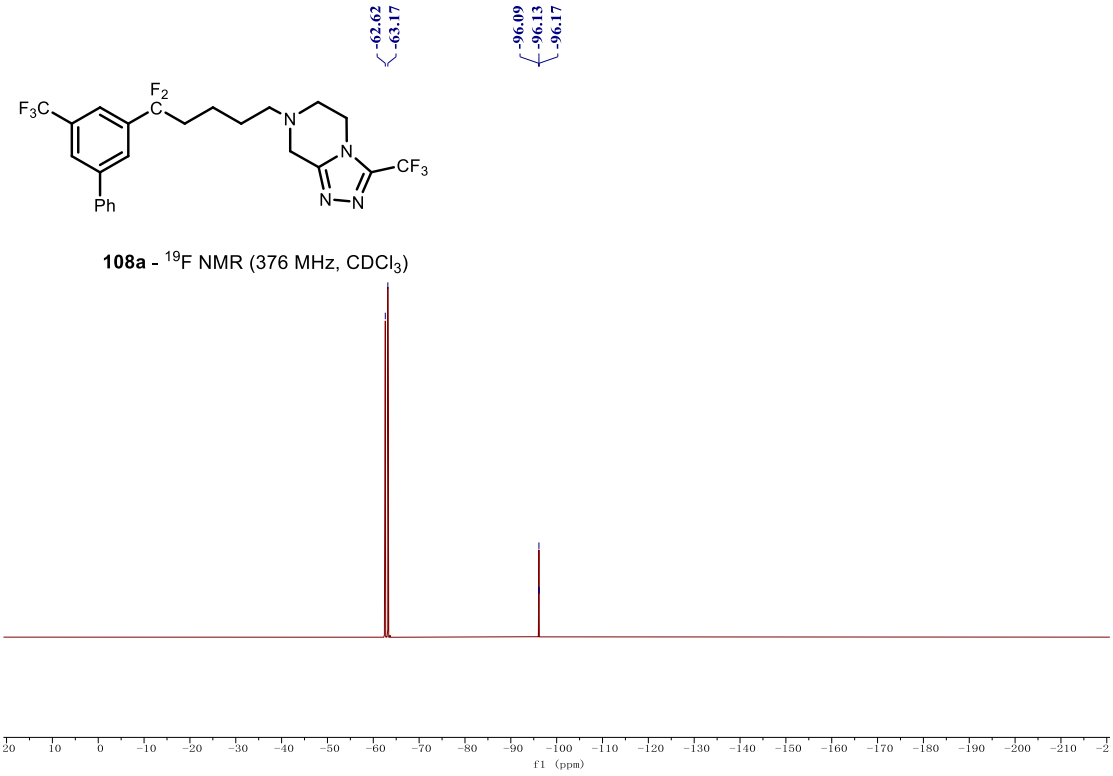
107a - ^{19}F NMR (376 MHz, $CDCl_3$)



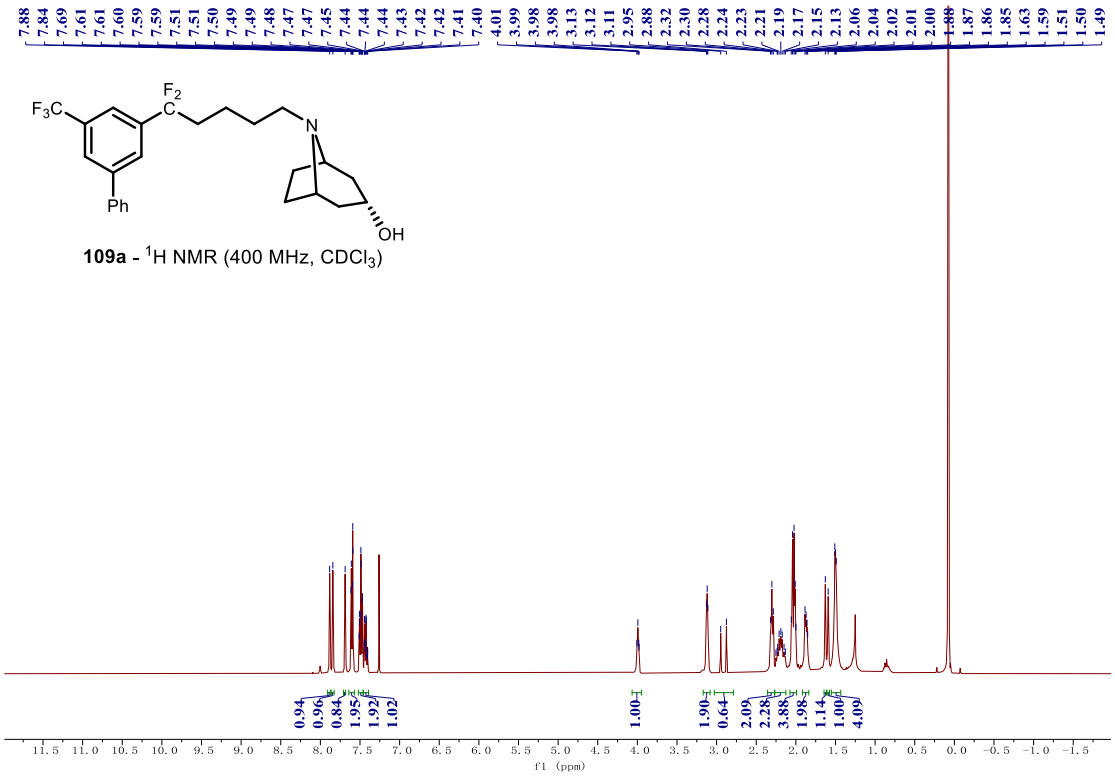
108a - ^{1}H NMR (400 MHz, $CDCl_3$)



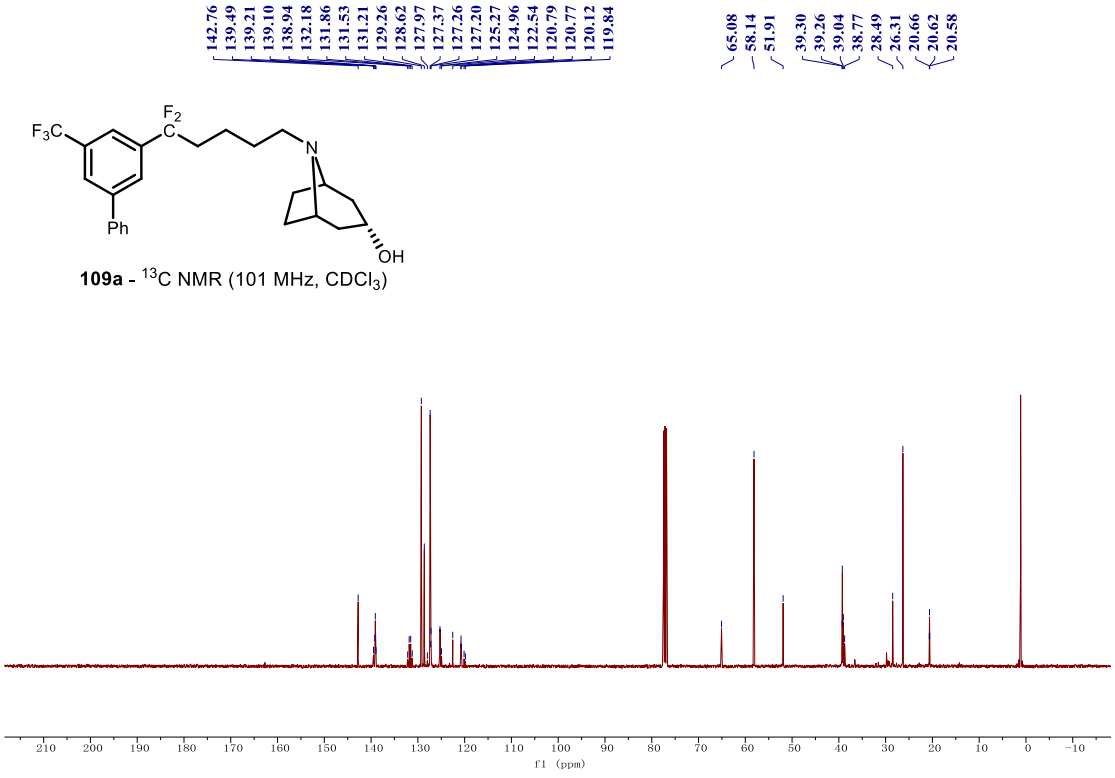
108a - ^{13}C NMR (101 MHz, $CDCl_3$)



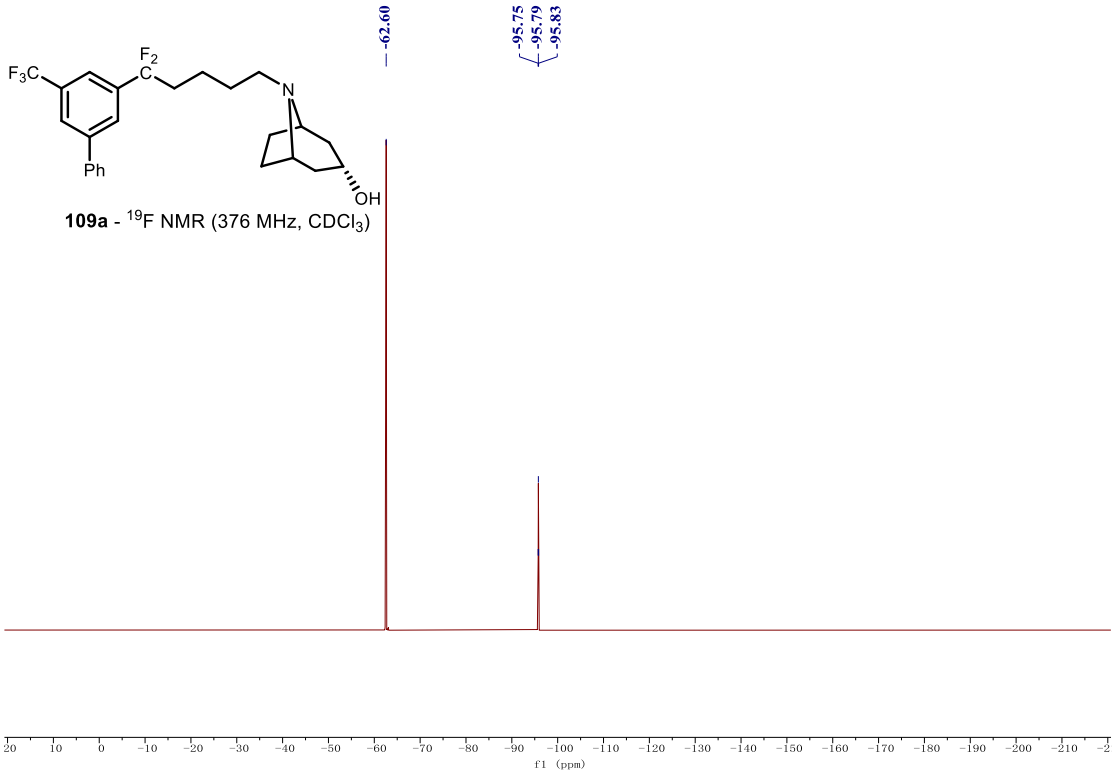
108a - ^{19}F NMR (376 MHz, $CDCl_3$)



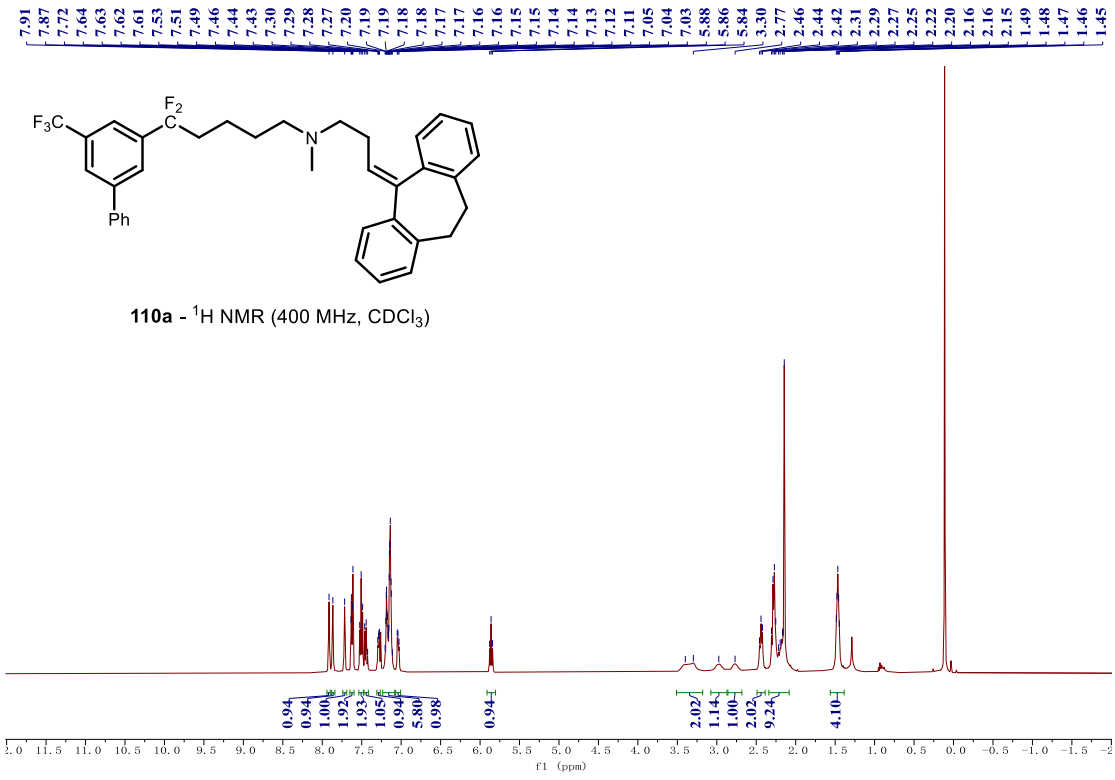
109a - ^{1}H NMR (400 MHz, $CDCl_3$)



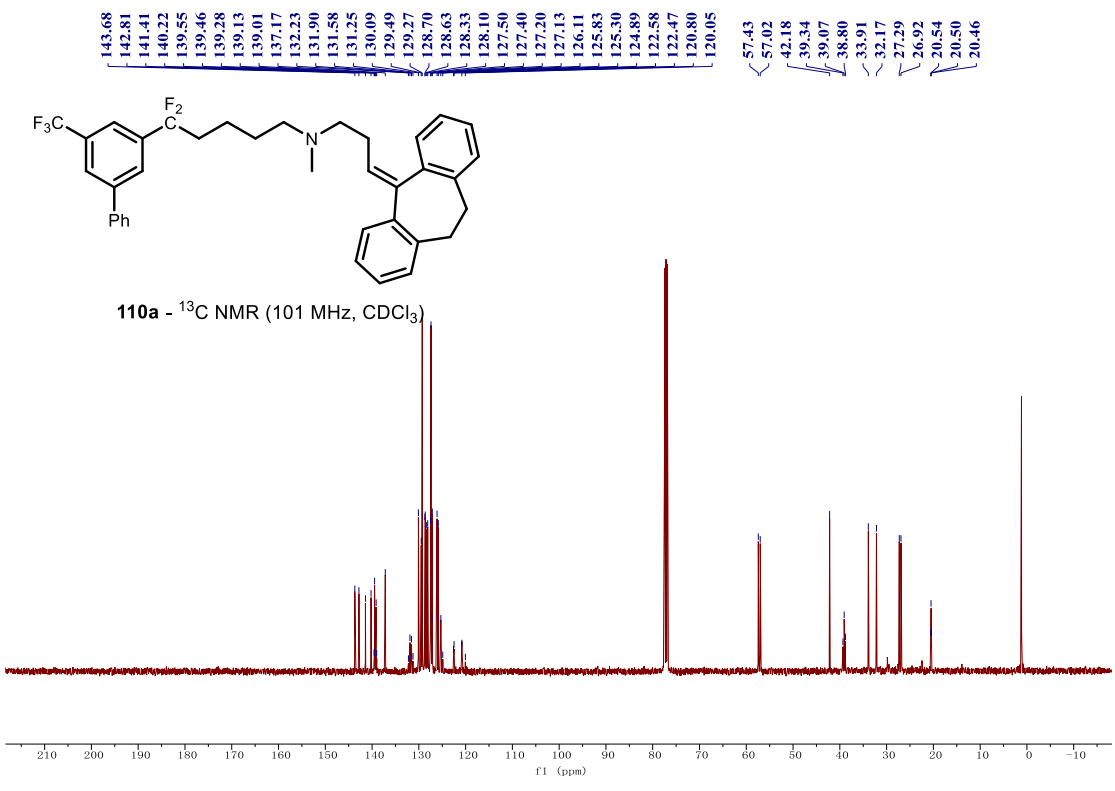
109a - ^{13}C NMR (101 MHz, $CDCl_3$)



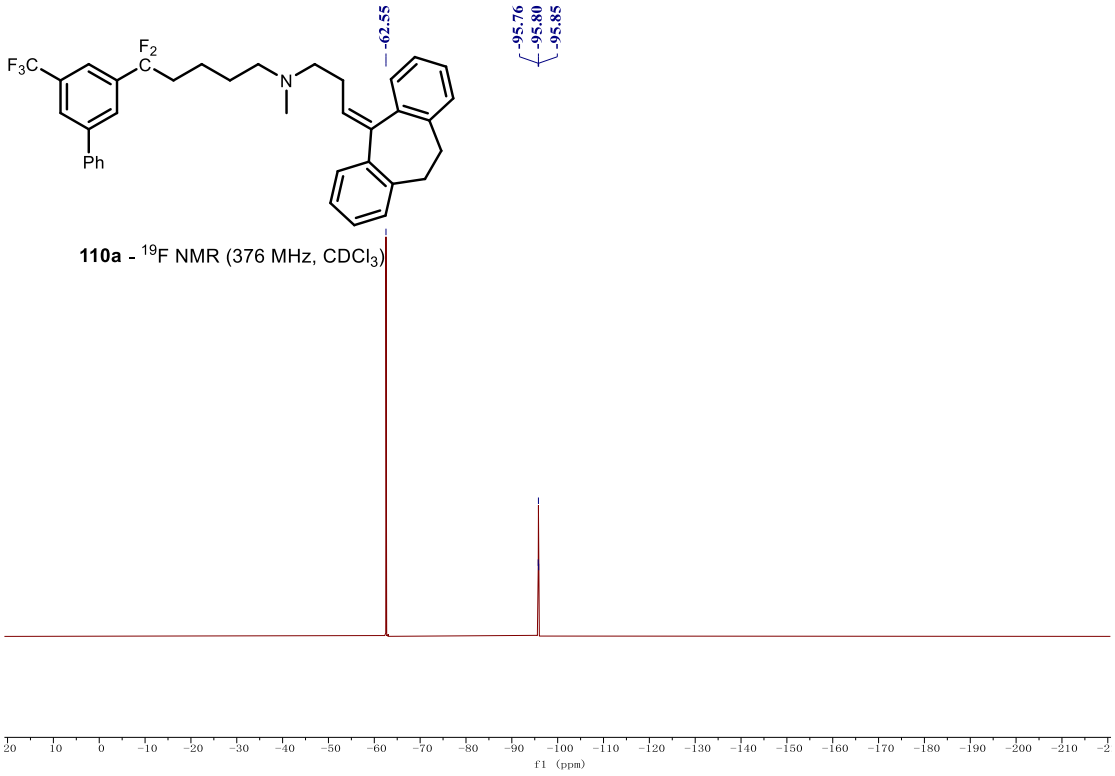
109a - ^{19}F NMR (376 MHz, $CDCl_3$)



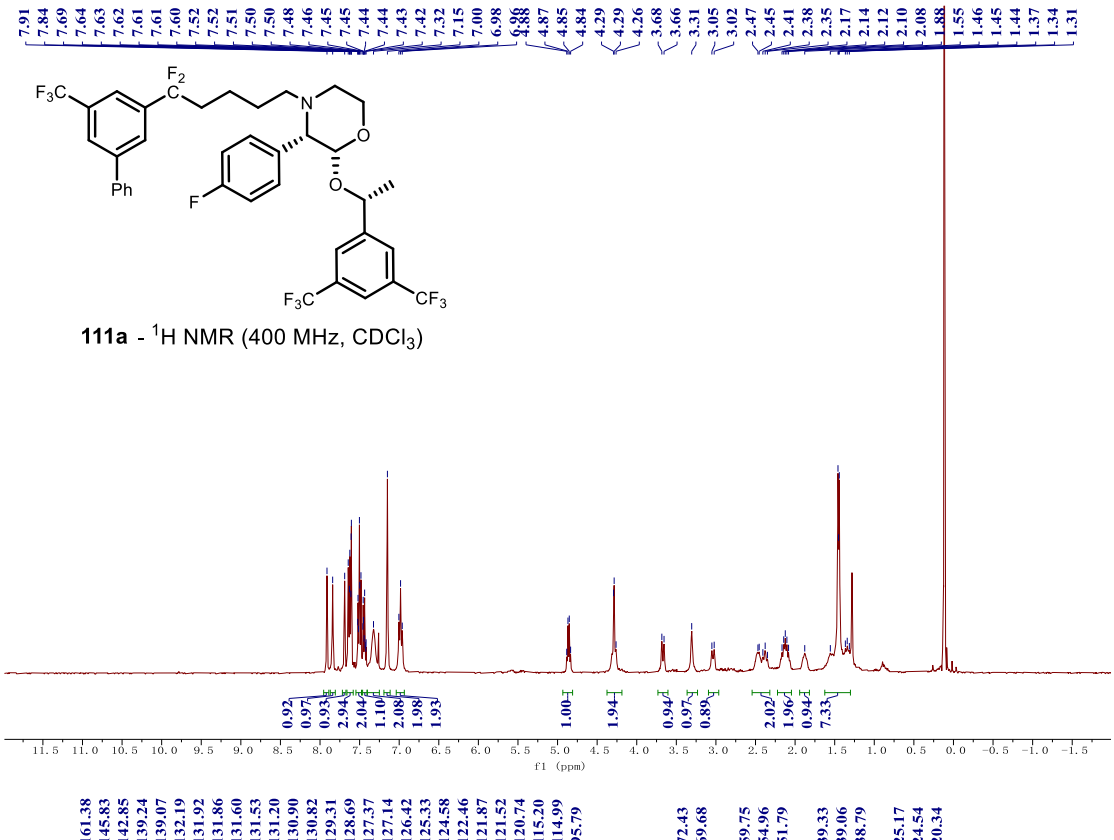
110a - ^{1}H NMR (400 MHz, $CDCl_3$)



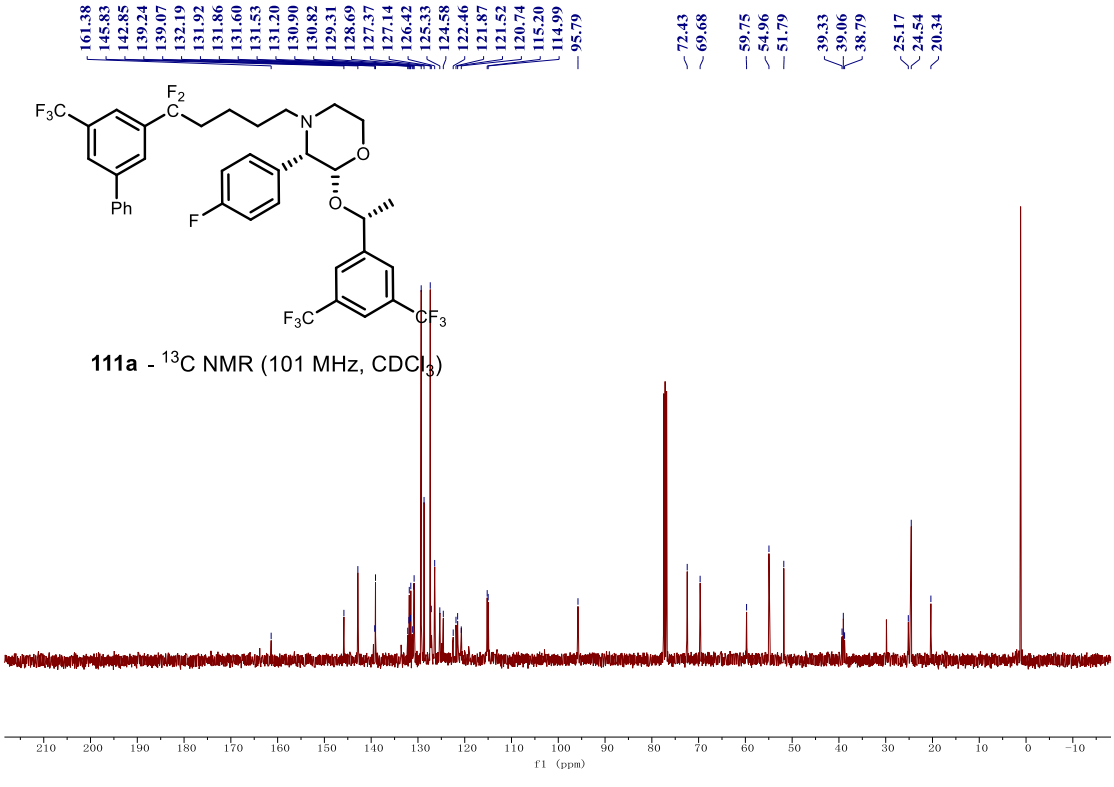
110a - ^{13}C NMR (101 MHz, $CDCl_3$)



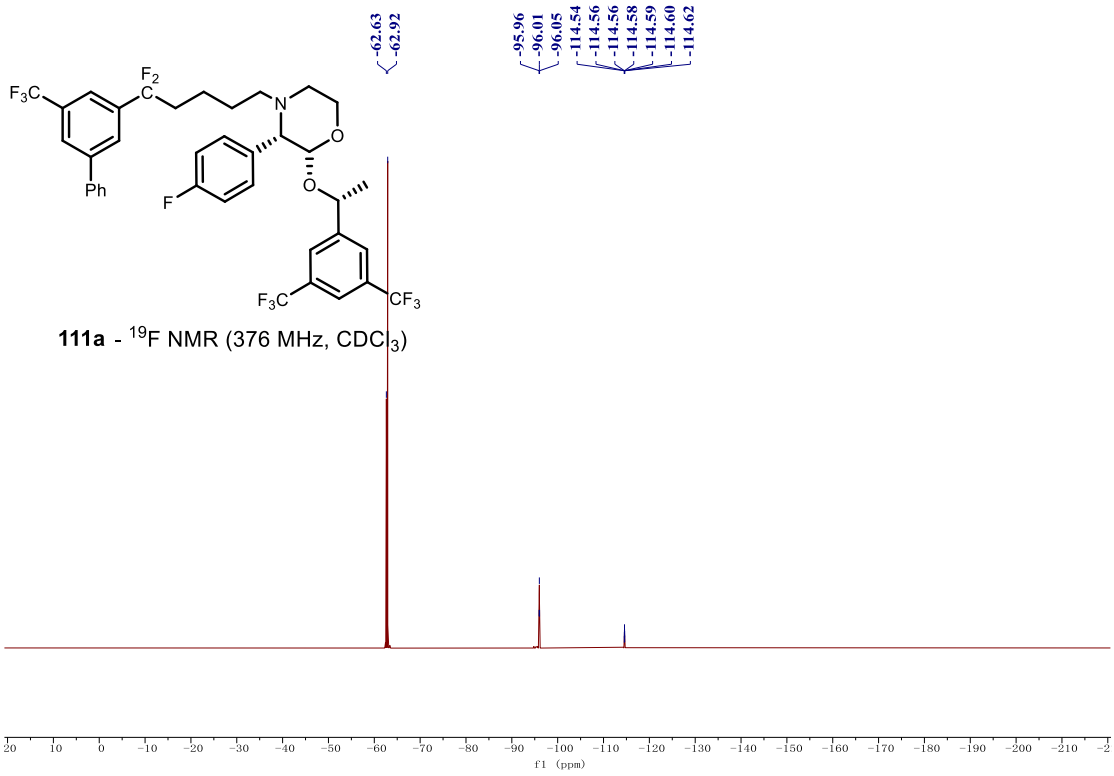
110a - ^{19}F NMR (376 MHz, $CDCl_3$)



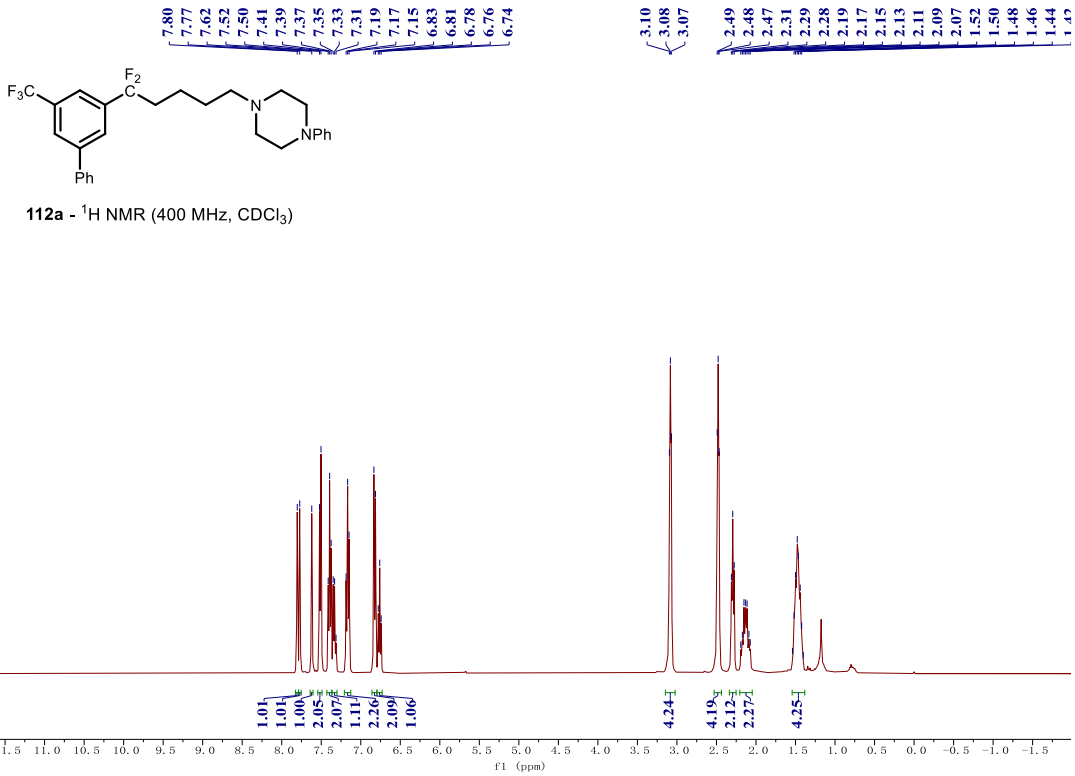
111a - ^{1}H NMR (400 MHz, $CDCl_3$)



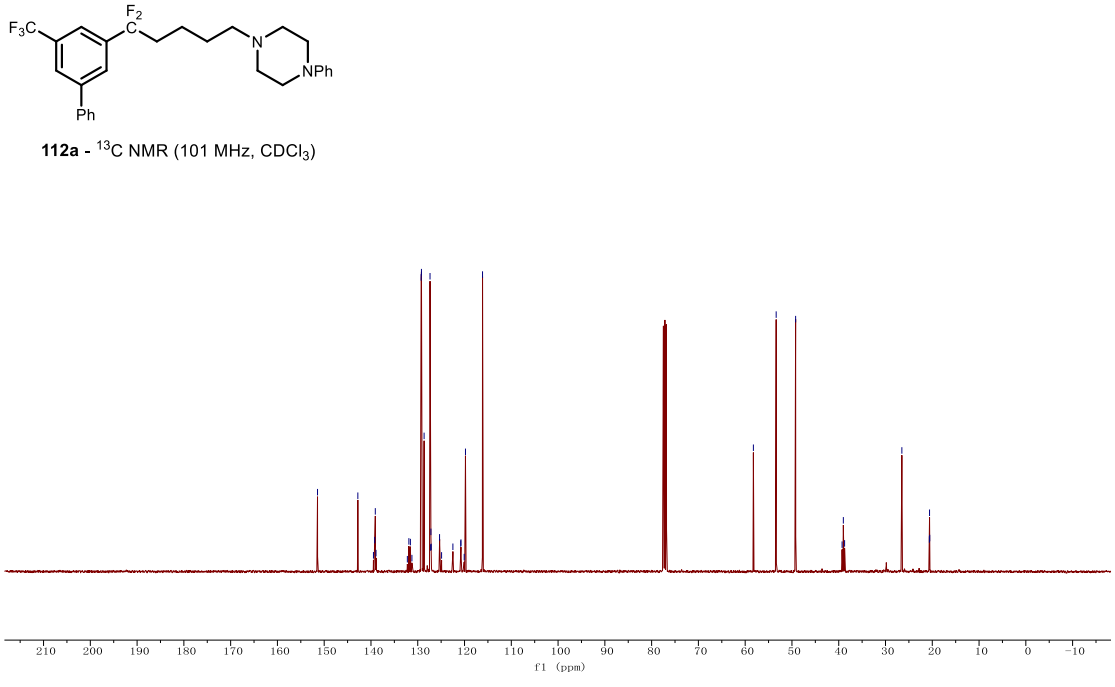
111a - ^{13}C NMR (101 MHz, $CDCl_3$)



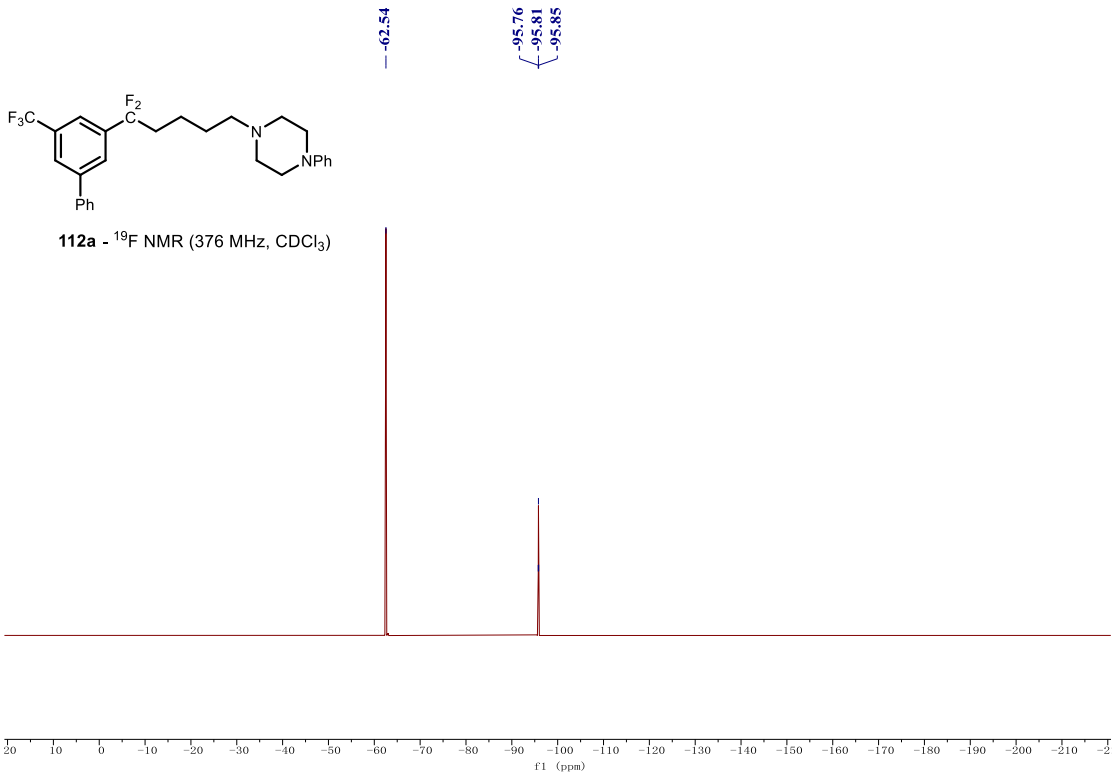
111a - ^{19}F NMR (376 MHz, CDC_3)



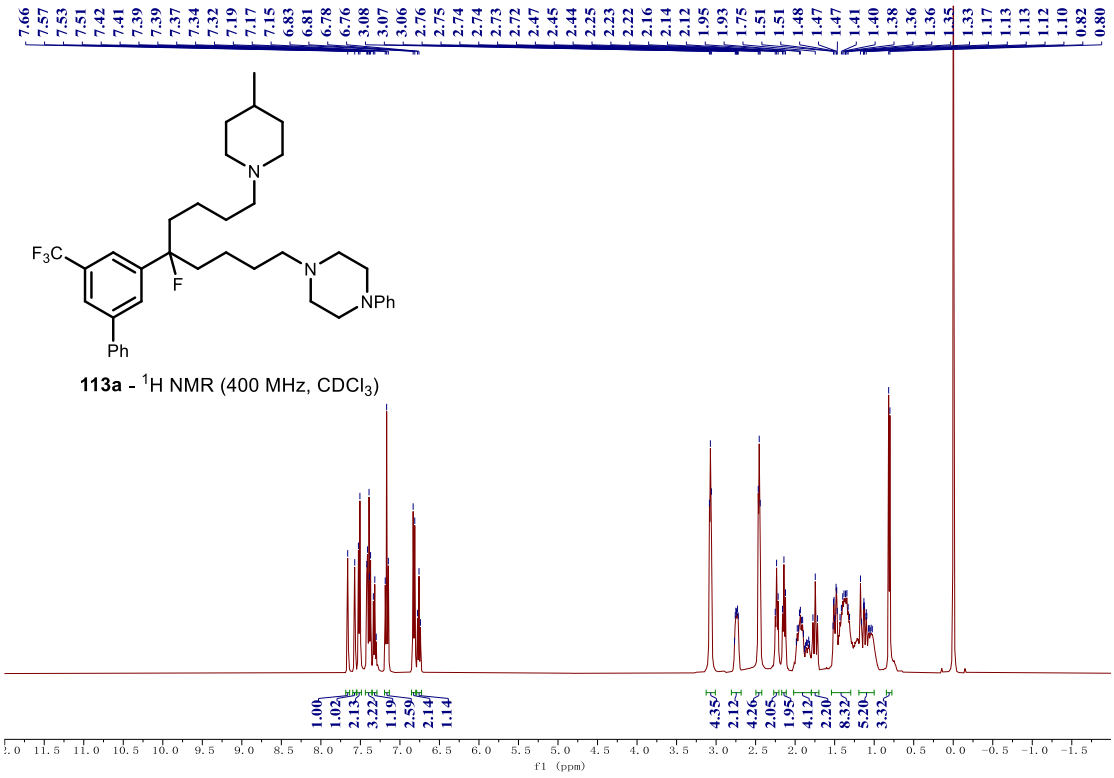
112a - ^{1}H NMR (400 MHz, $CDCl_3$)



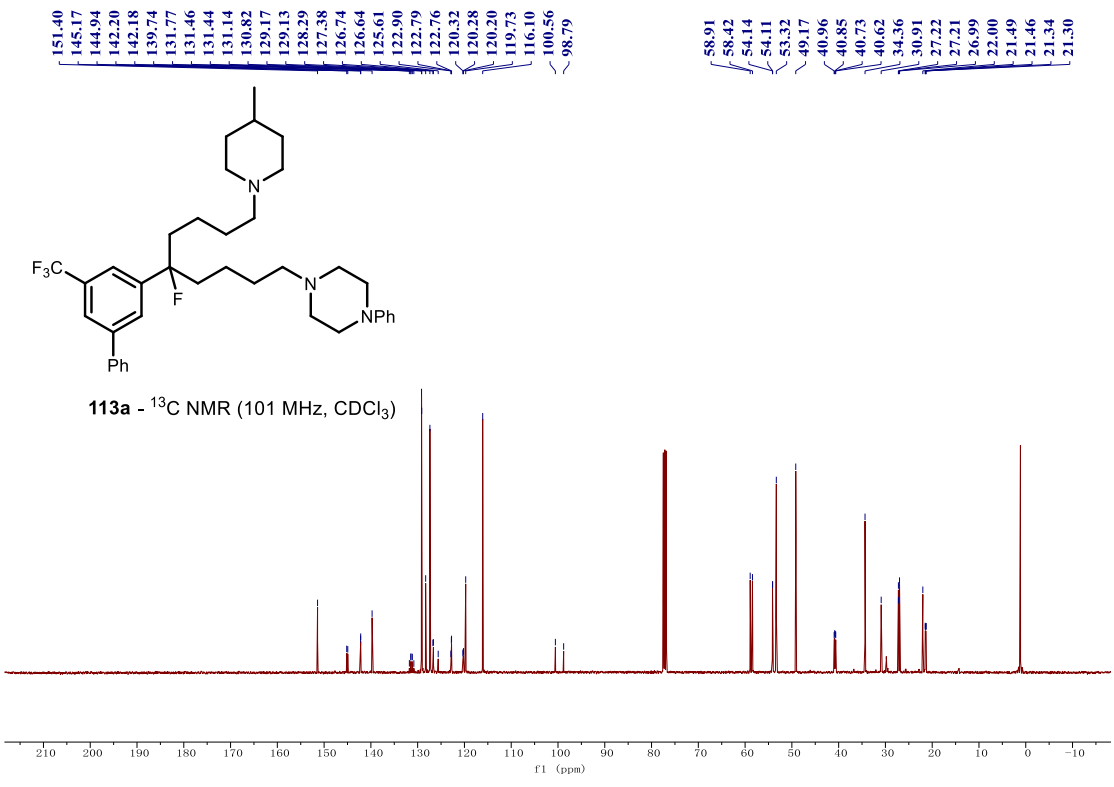
112a - ^{13}C NMR (101 MHz, $CDCl_3$)



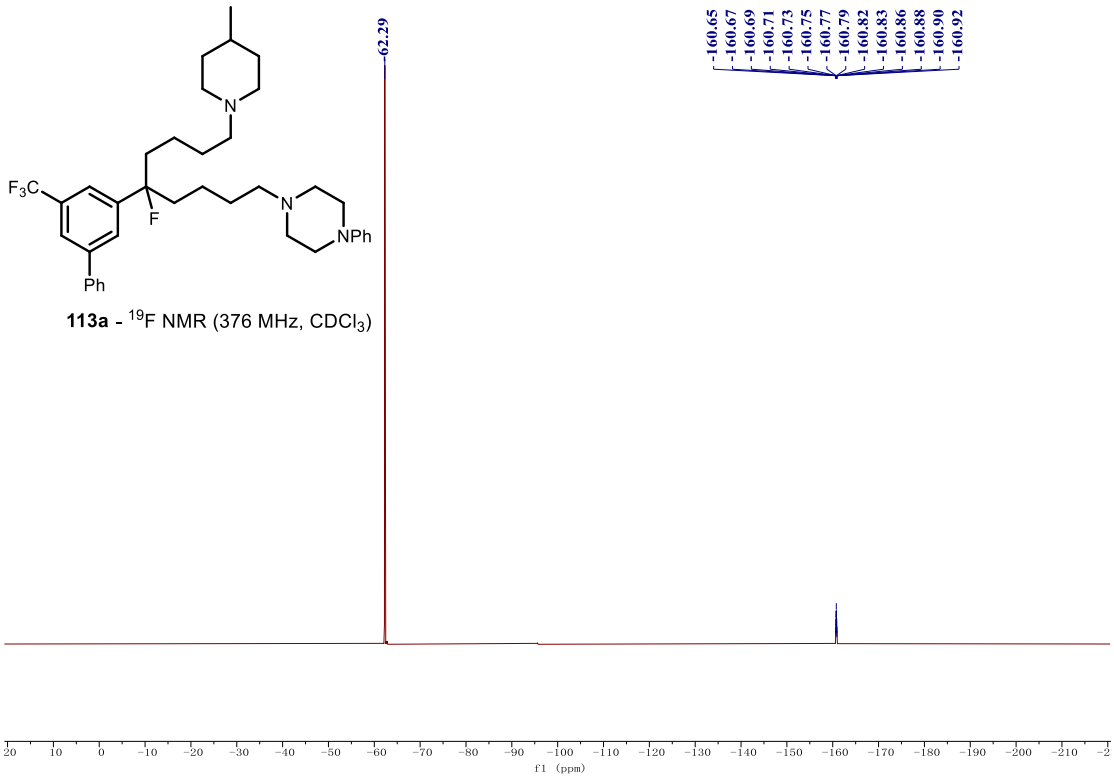
112a - ^{19}F NMR (376 MHz, $CDCl_3$)



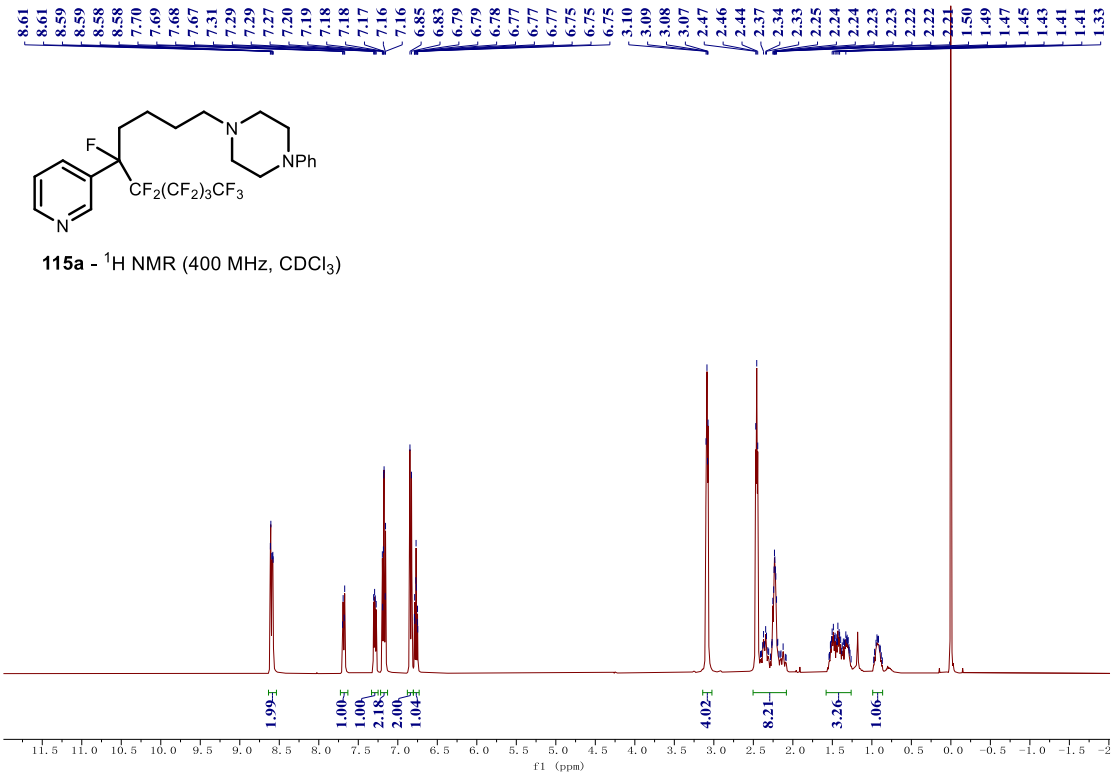
113a - ^{1}H NMR (400 MHz, $CDCl_3$)



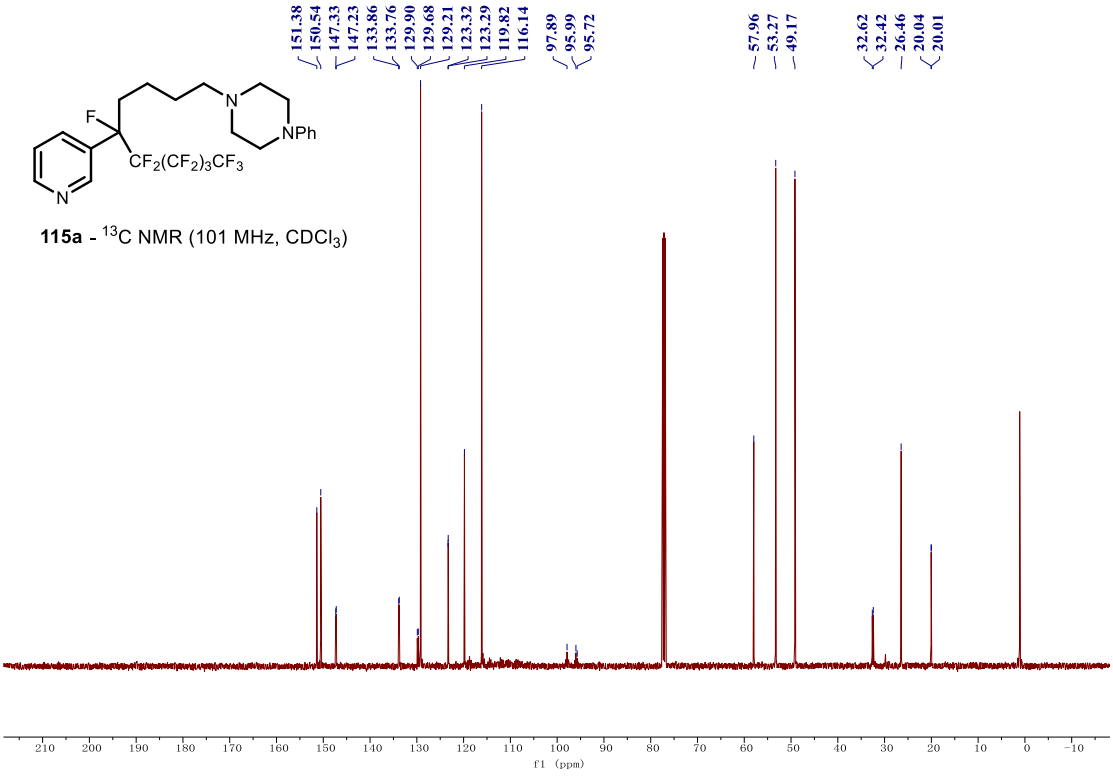
113a - ^{13}C NMR (101 MHz, $CDCl_3$)



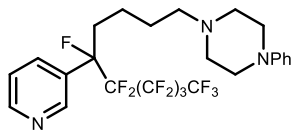
113a - ^{19}F NMR (376 MHz, $CDCl_3$)



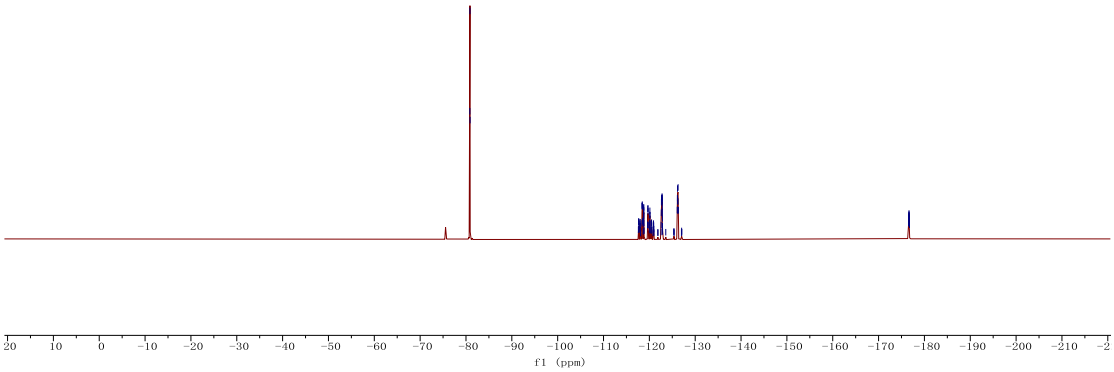
115a - ^{1}H NMR (400 MHz, $CDCl_3$)

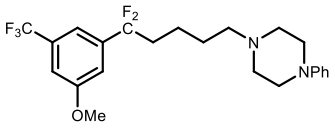


115a - ^{13}C NMR (101 MHz, $CDCl_3$)

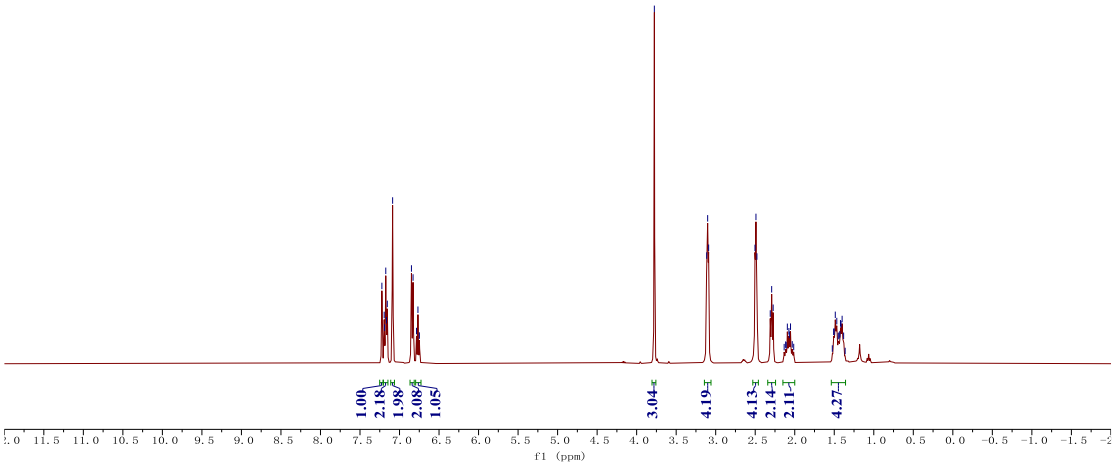


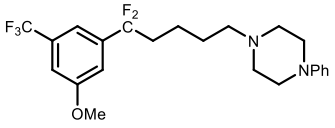
115a - ^{19}F NMR (376 MHz, $CDCl_3$)



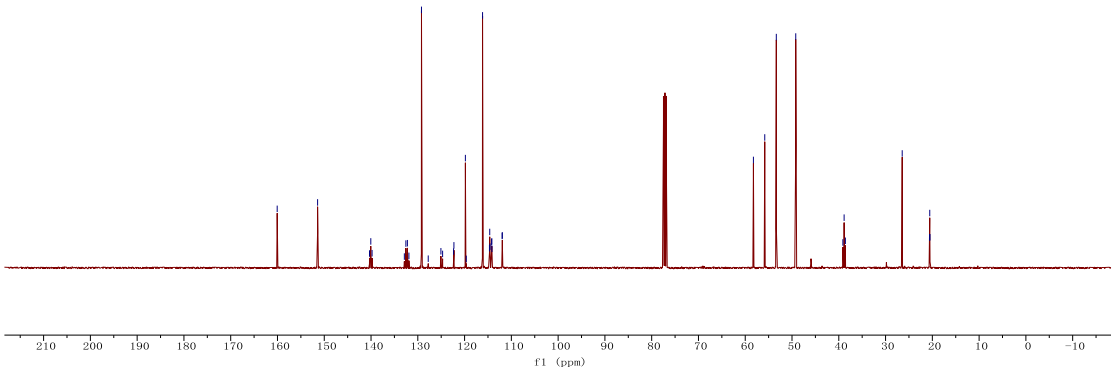


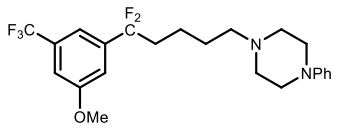
116a - ^{1}H NMR (400 MHz, $CDCl_3$)



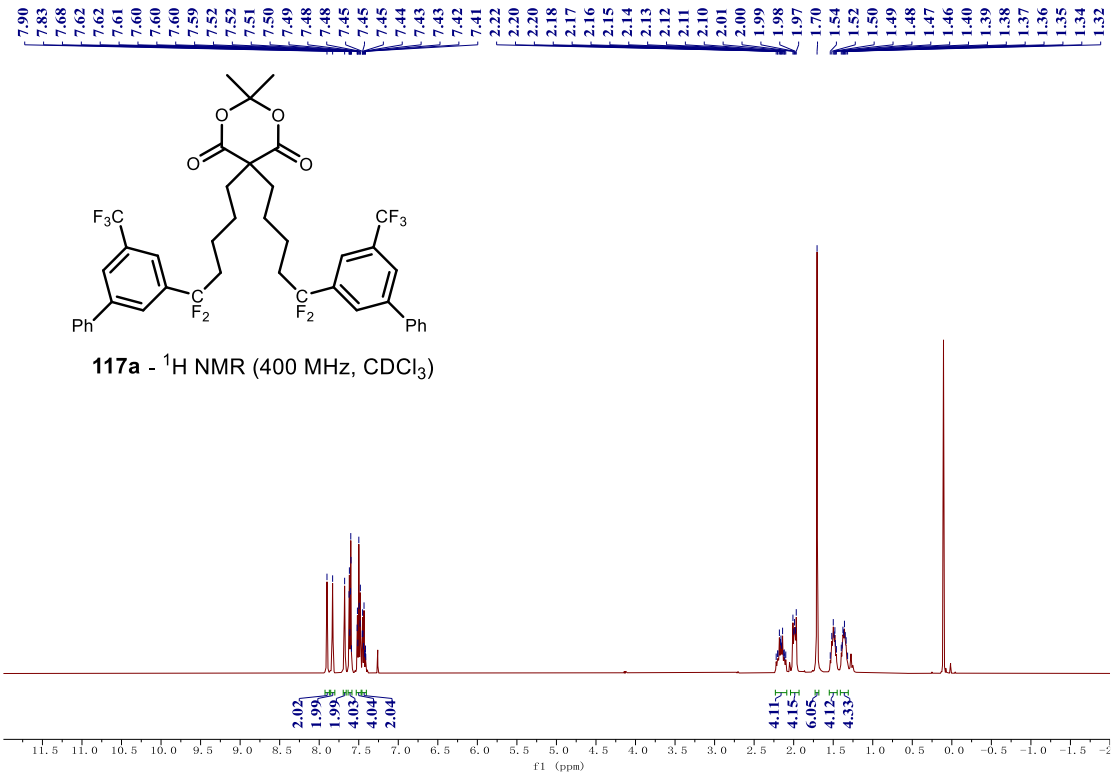


116a - ^{13}C NMR (101 MHz, $CDCl_3$)

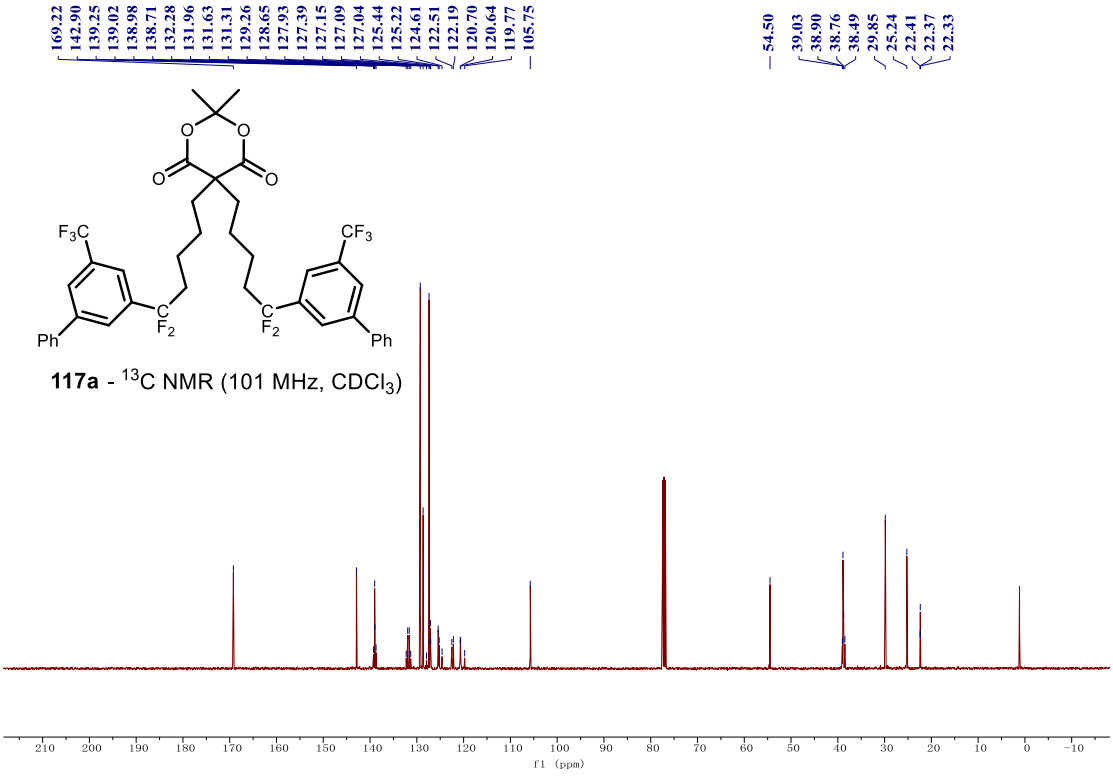




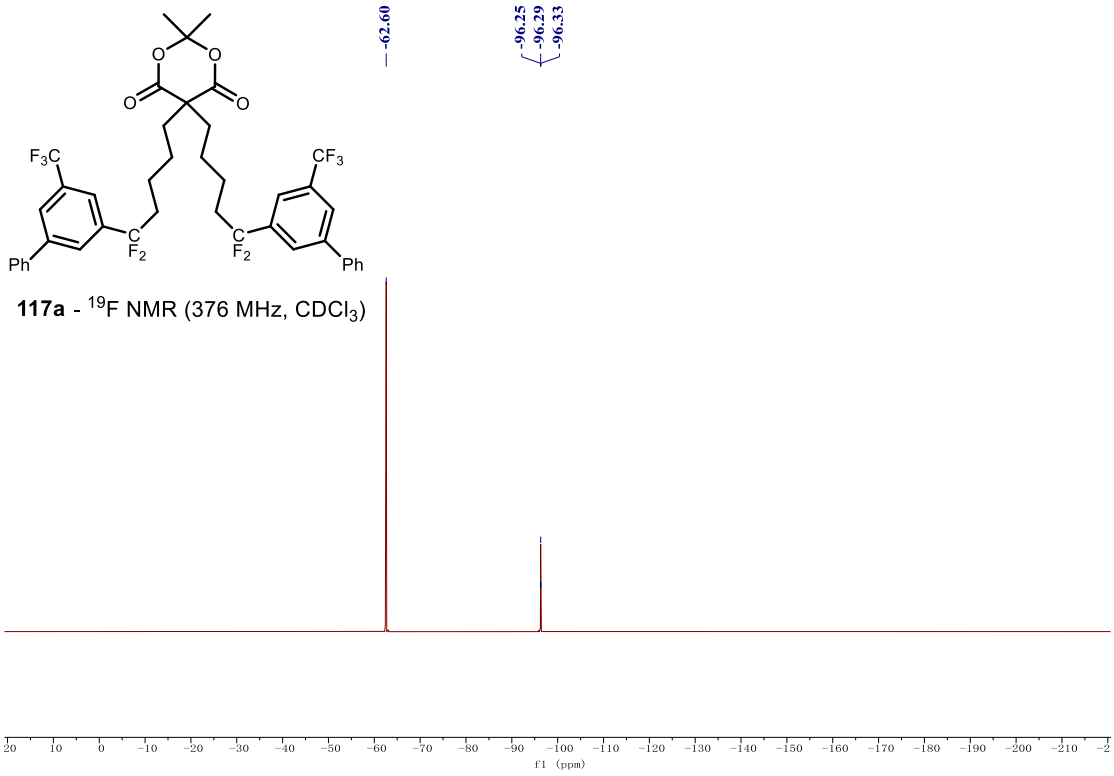
116a - ^{19}F NMR (376 MHz, $CDCl_3$)



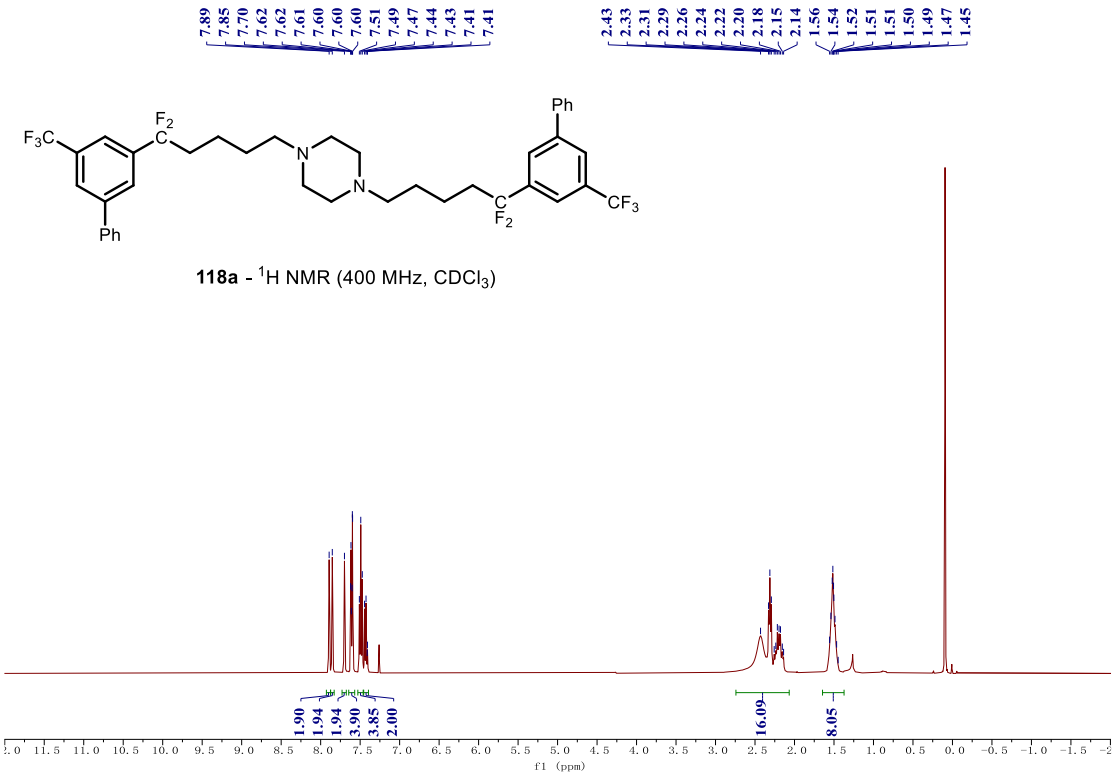
117a - ^{1}H NMR (400 MHz, $CDCl_3$)



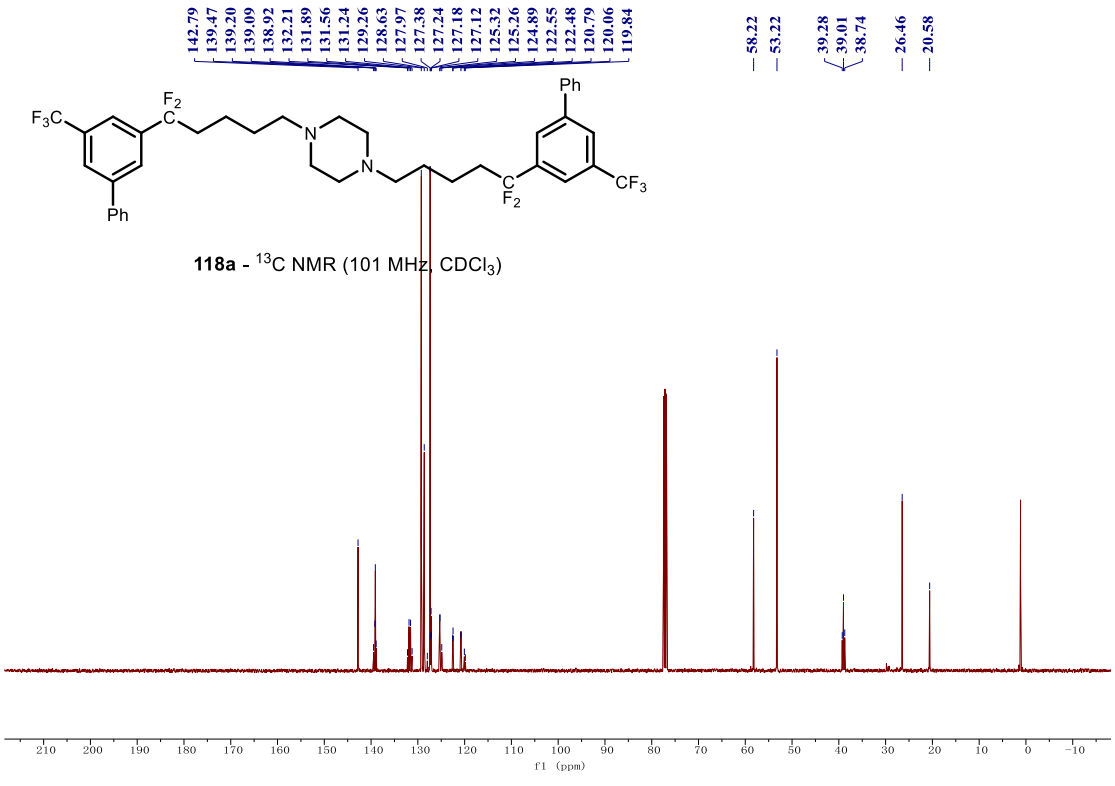
117a - ^{13}C NMR (101 MHz, $CDCl_3$)



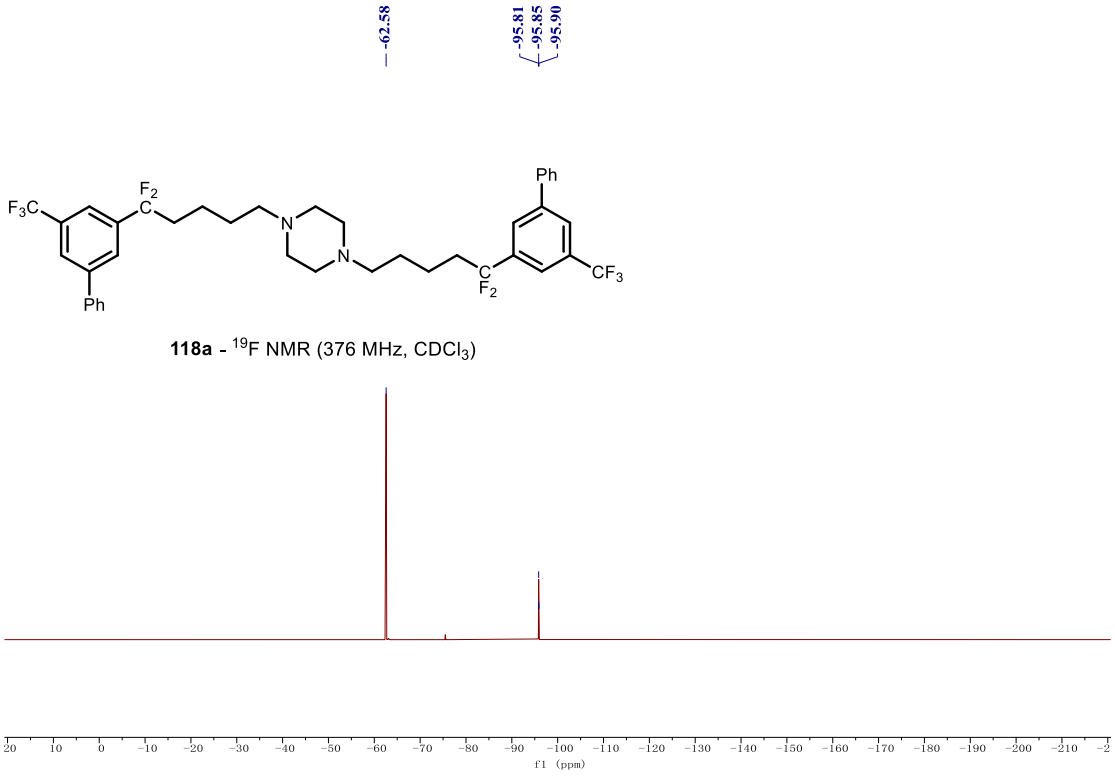
117a - ^{19}F NMR (376 MHz, $CDCl_3$)



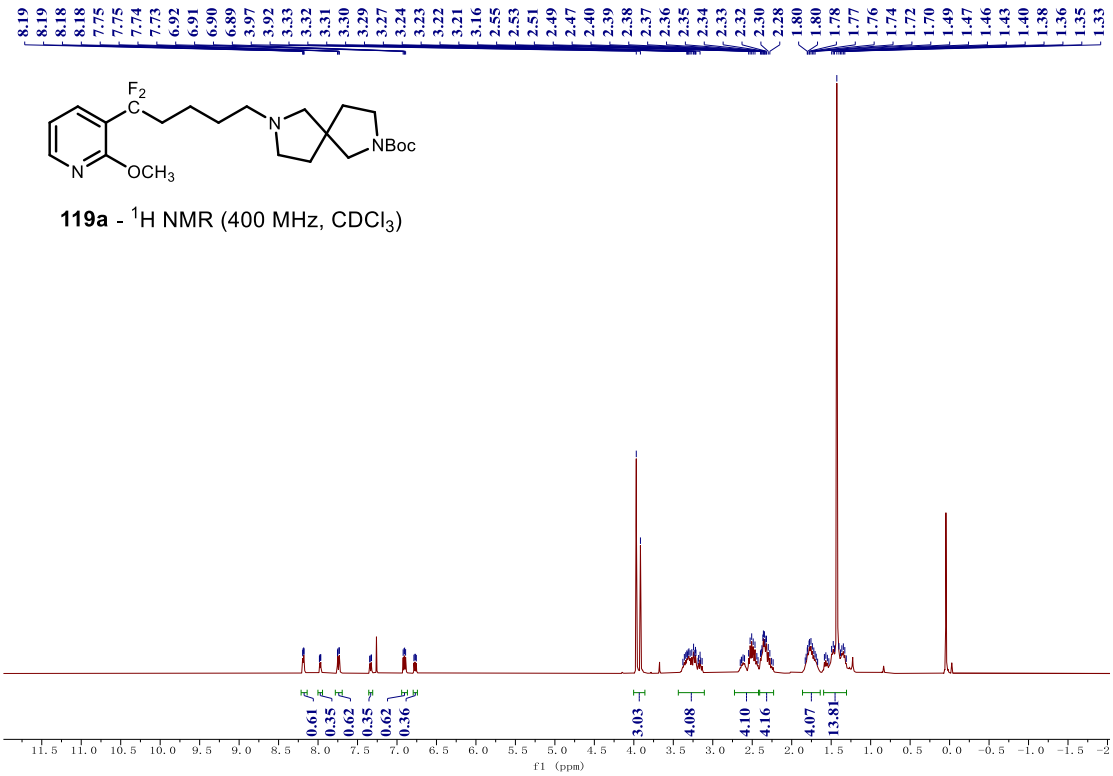
118a - ^{1}H NMR (400 MHz, $CDCl_3$)



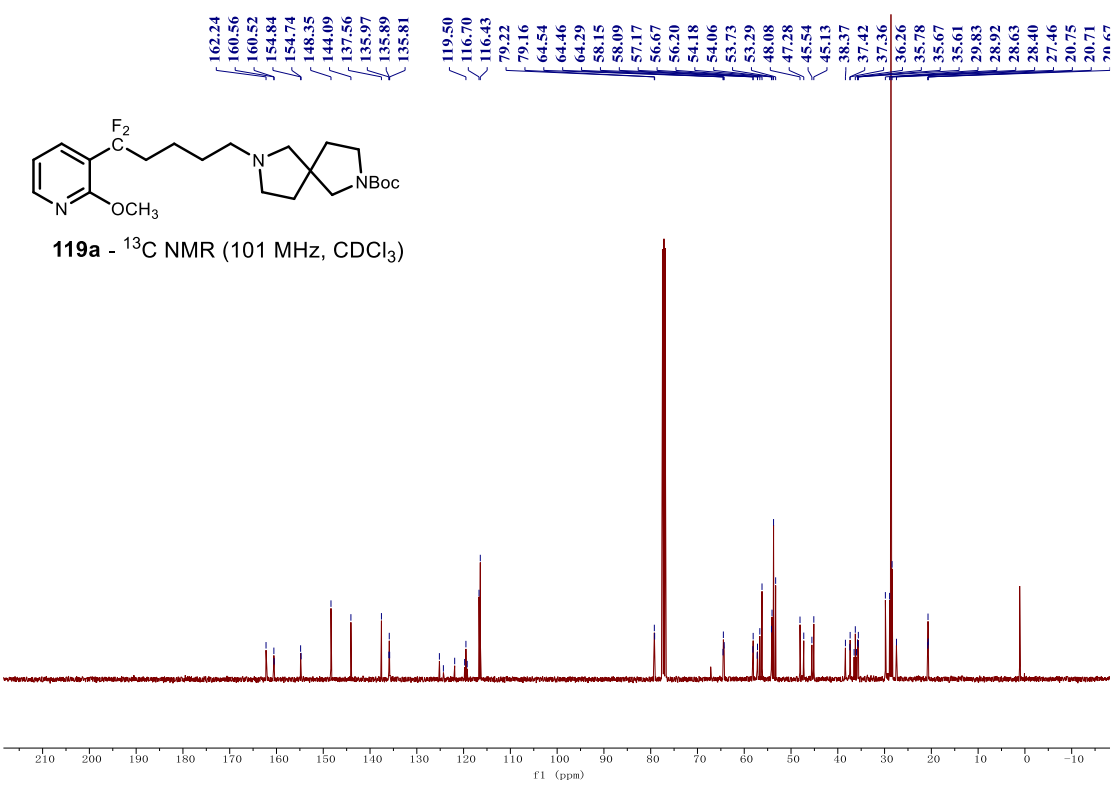
118a - ^{13}C NMR (101 MHz, $CDCl_3$)



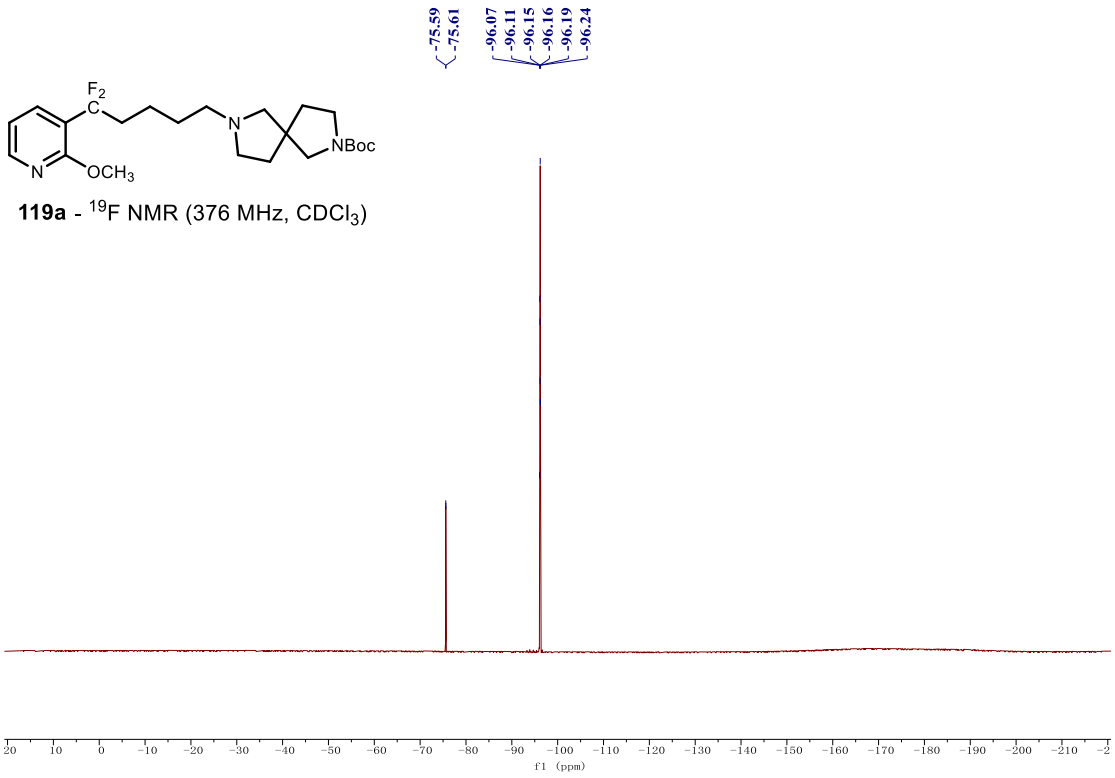
118a - ^{19}F NMR (376 MHz, $CDCl_3$)



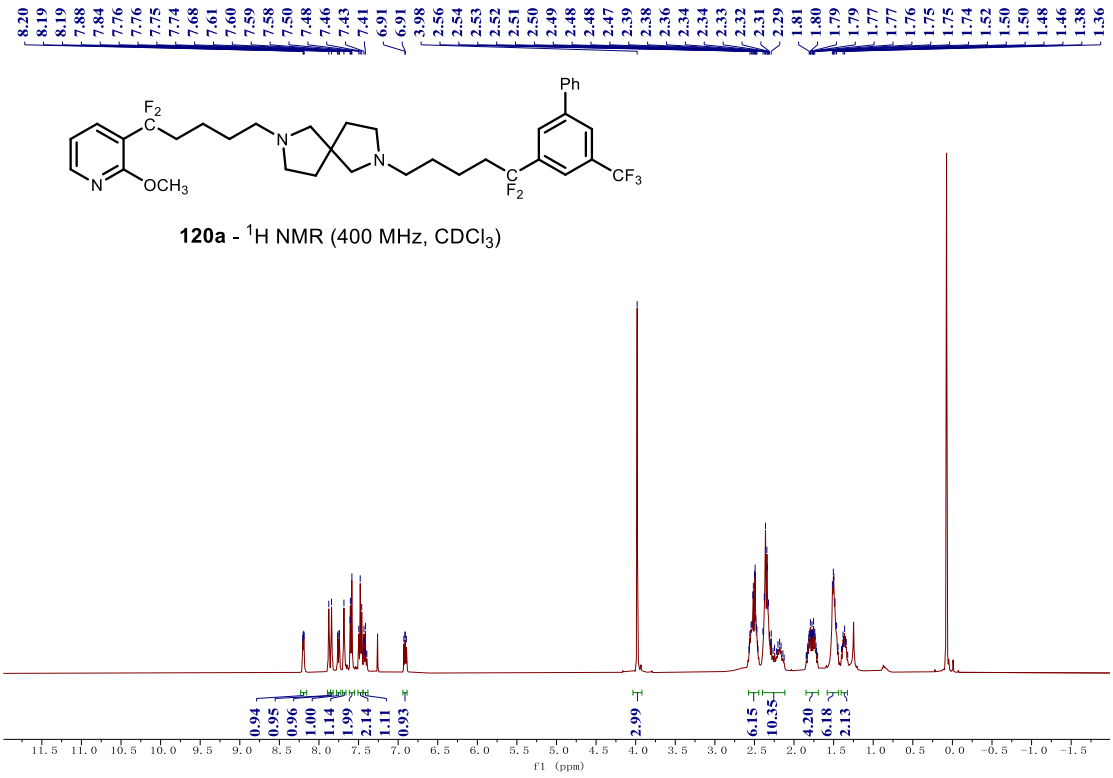
119a - ^{1}H NMR (400 MHz, $CDCl_3$)



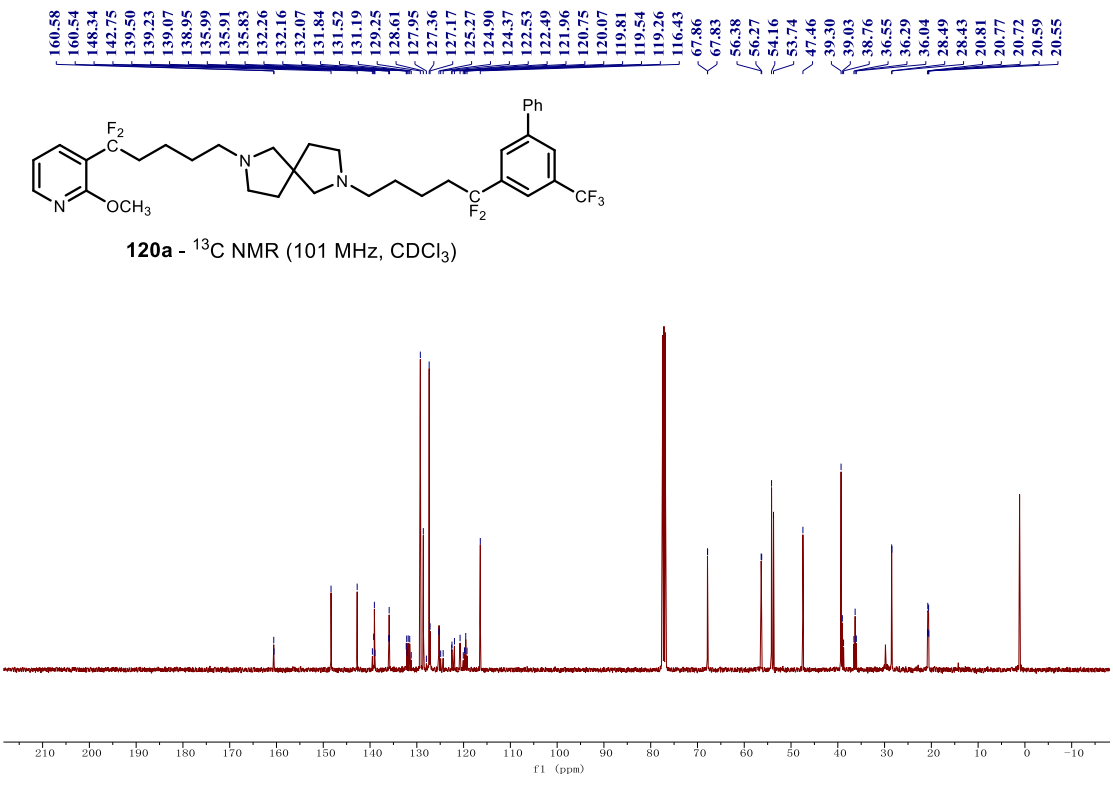
119a - ^{13}C NMR (101 MHz, $CDCl_3$)



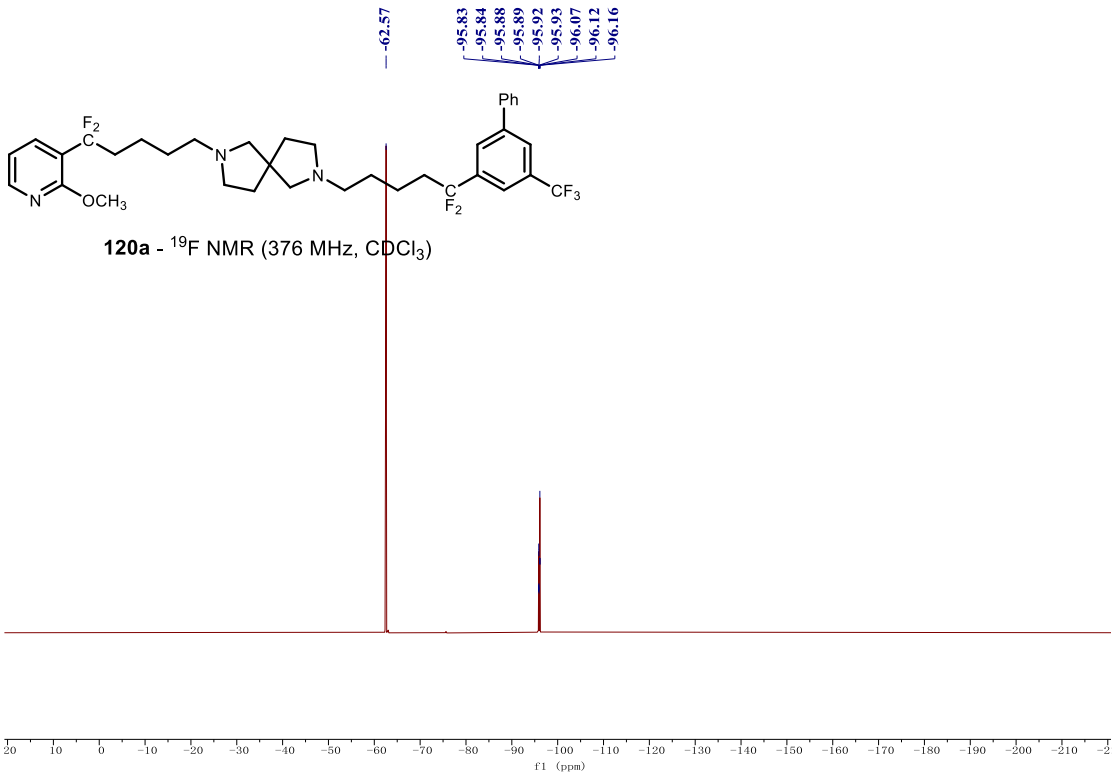
119a - ^{19}F NMR (376 MHz, $CDCl_3$)



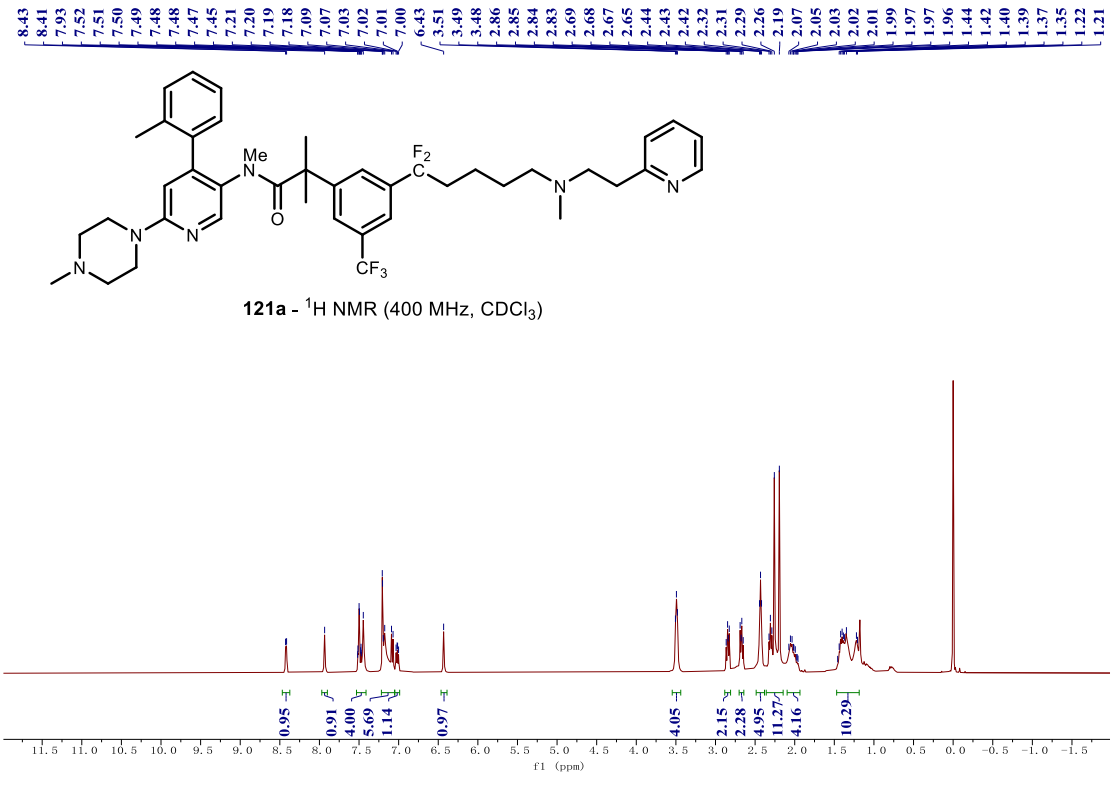
120a - ^{1}H NMR (400 MHz, $CDCl_3$)



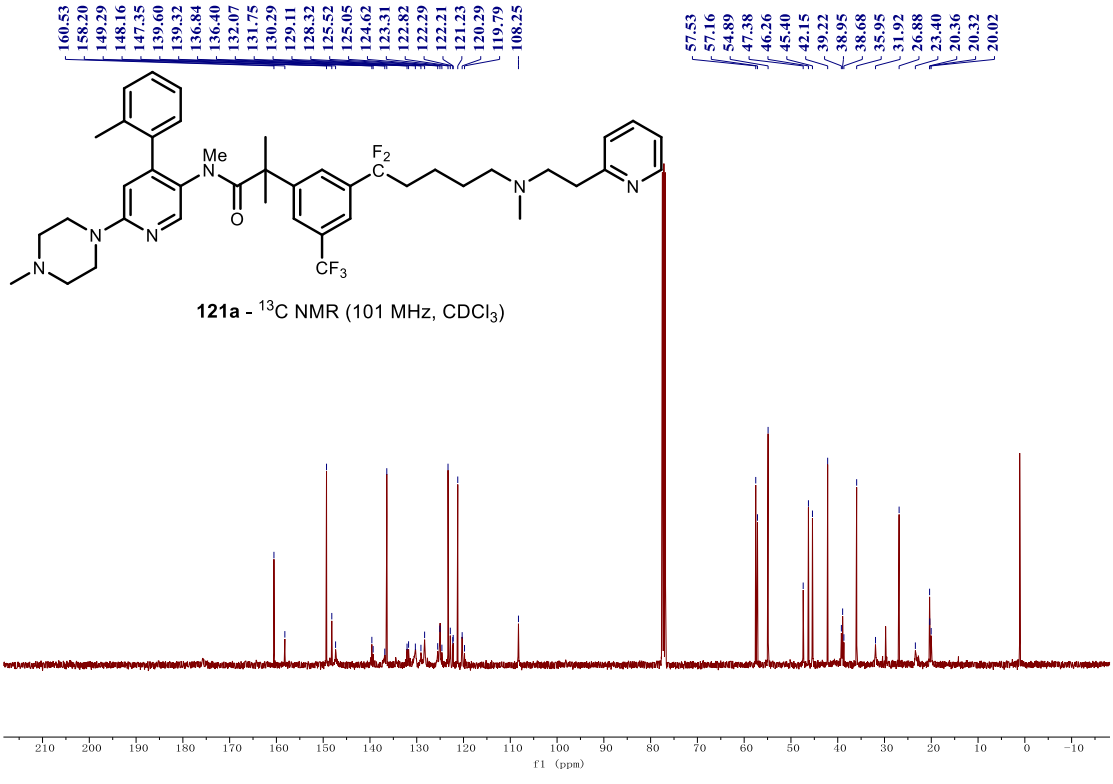
120a - ^{13}C NMR (101 MHz, $CDCl_3$)



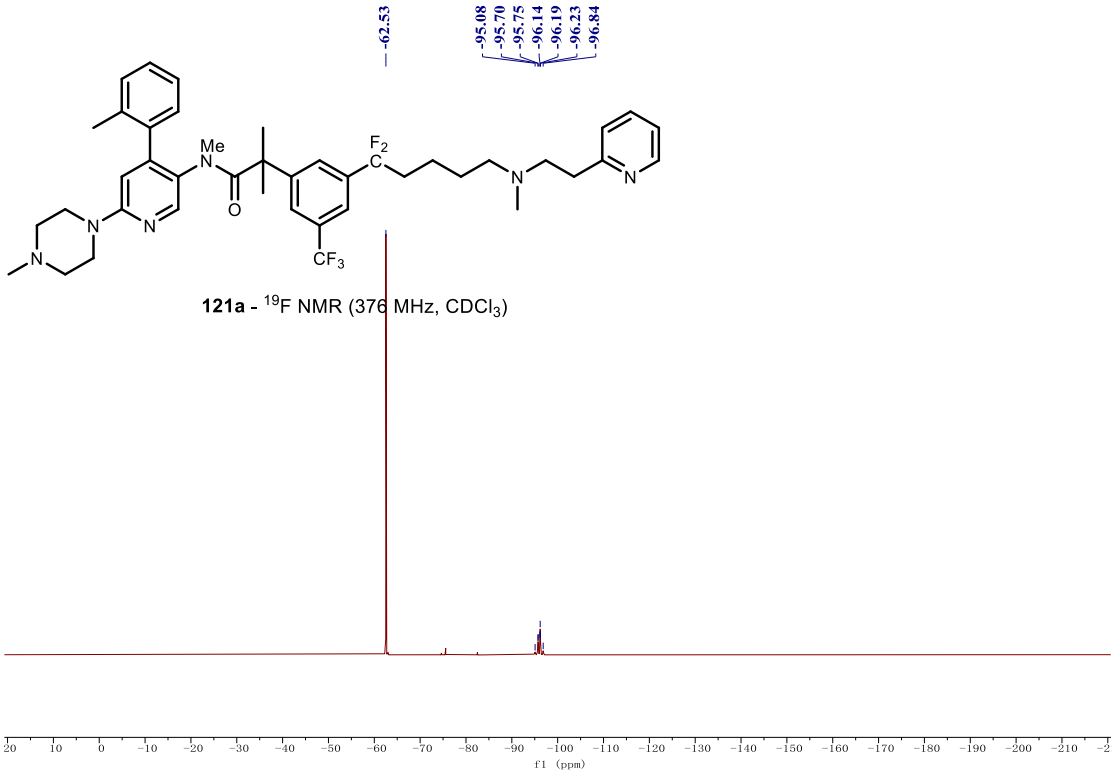
120a - ^{19}F NMR (376 MHz, $CDCl_3$)



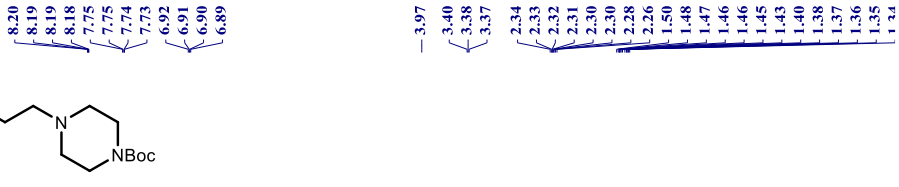
121a - ^{1}H NMR (400 MHz, $CDCl_3$)

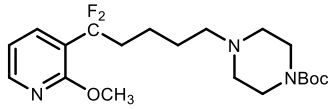


121a - ^{13}C NMR (101 MHz, $CDCl_3$)

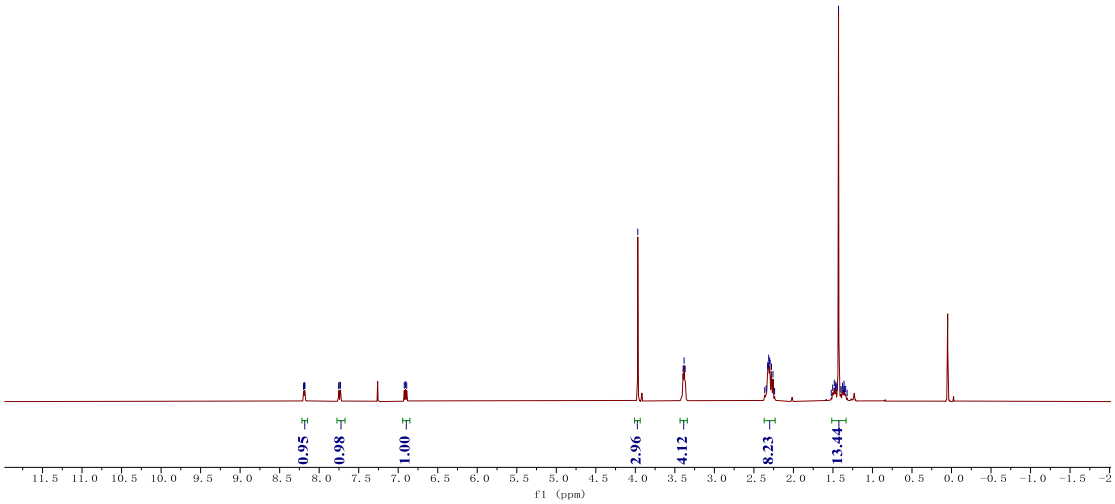


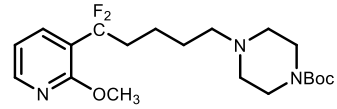
121a - ^{19}F NMR (376 MHz, $CDCl_3$)



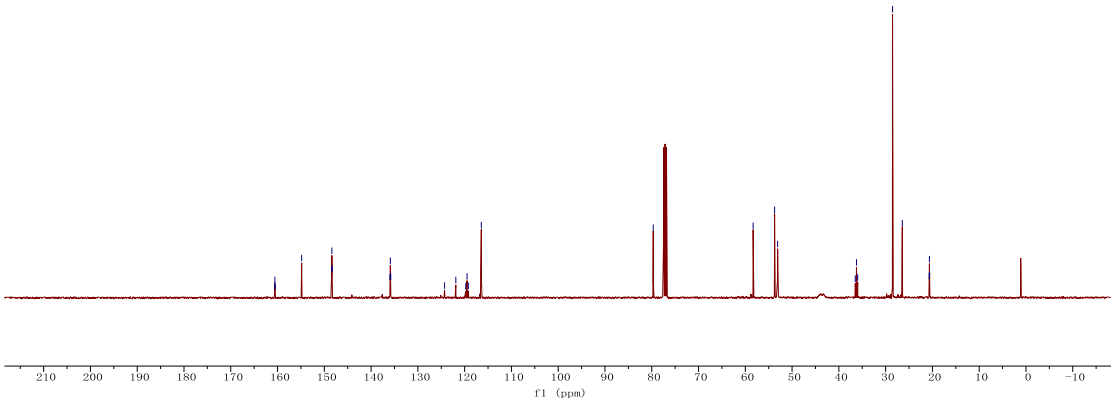


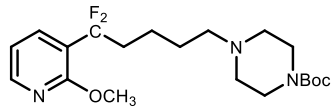
122a - ^{1}H NMR (400 MHz, $CDCl_3$)



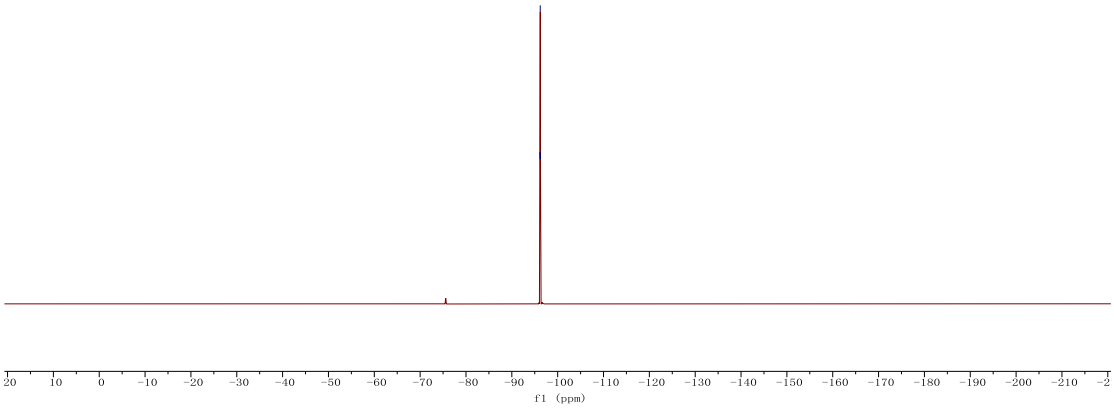


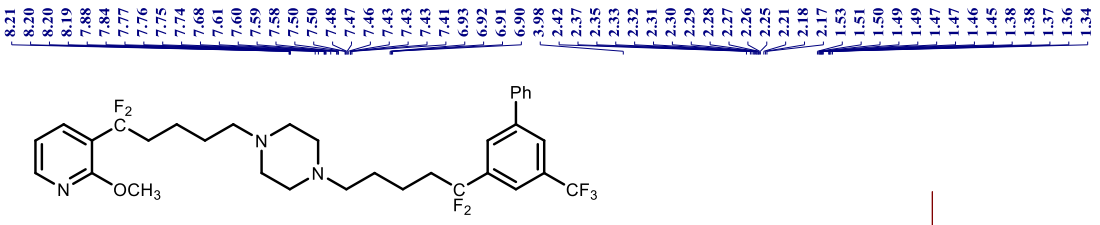
122a - ^{13}C NMR (101 MHz, $CDCl_3$)



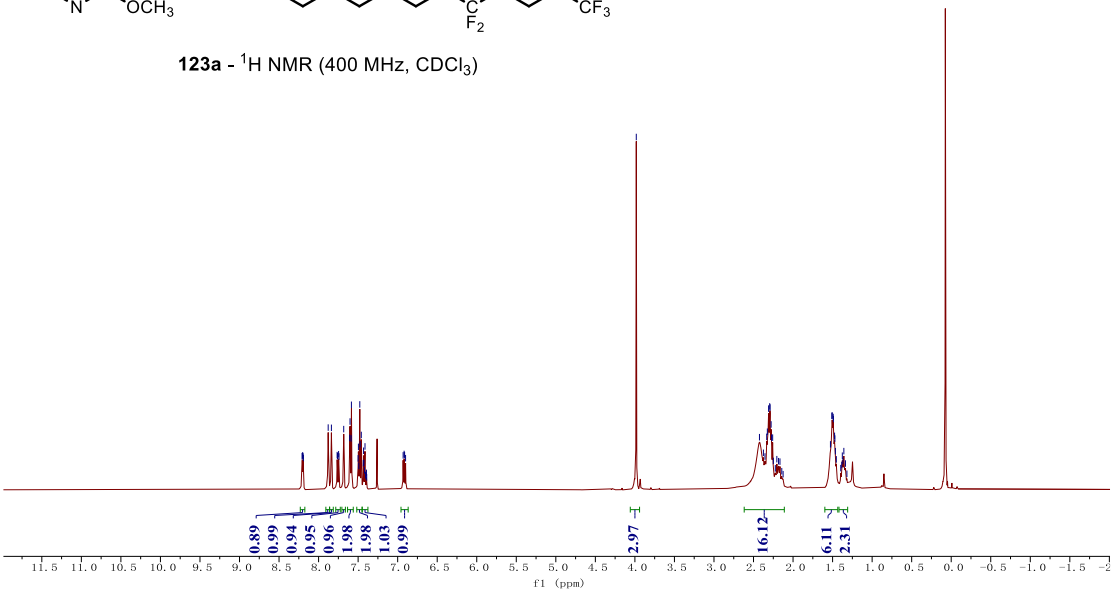


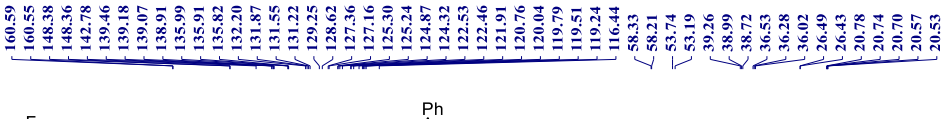
122a - ^{19}F NMR (376 MHz, $CDCl_3$)

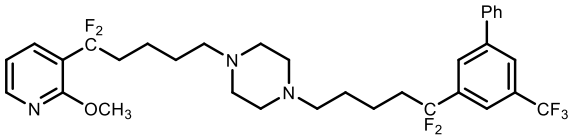




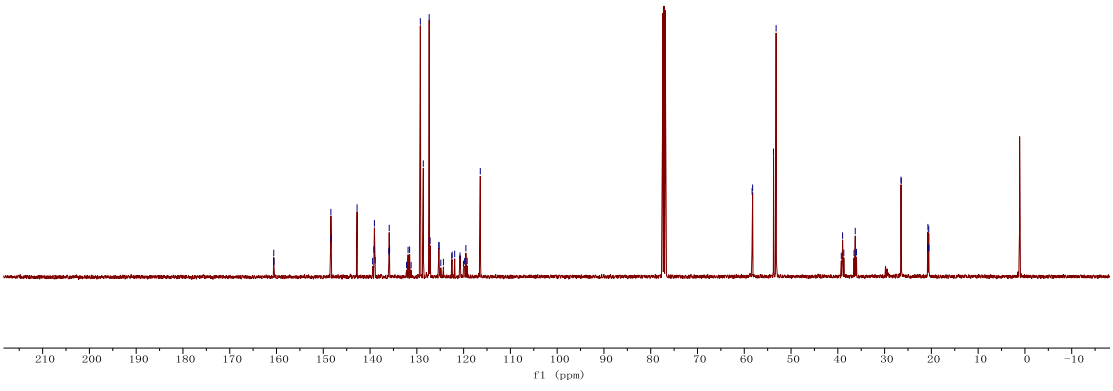
123a - ^{1}H NMR (400 MHz, $CDCl_3$)

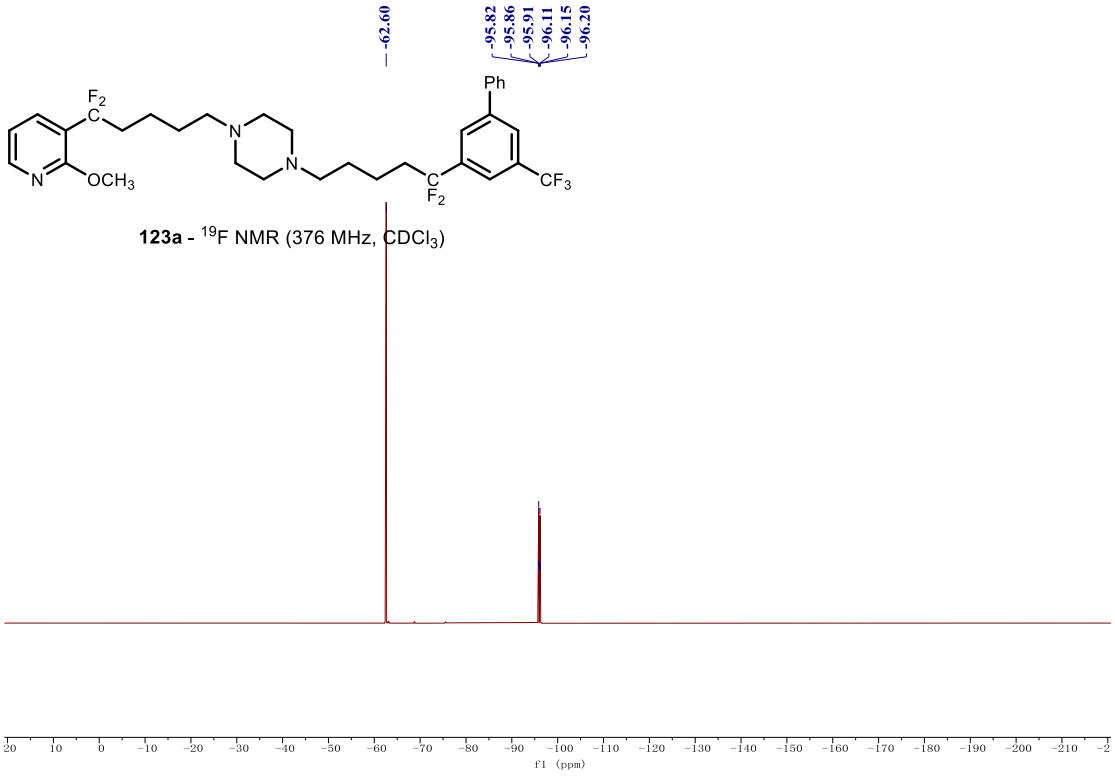




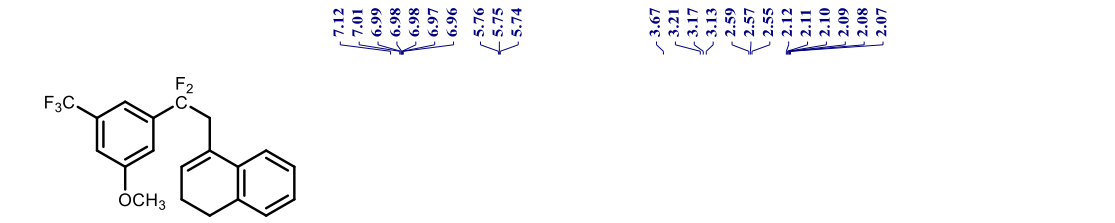


123a - ^{13}C NMR (101 MHz, $CDCl_3$)

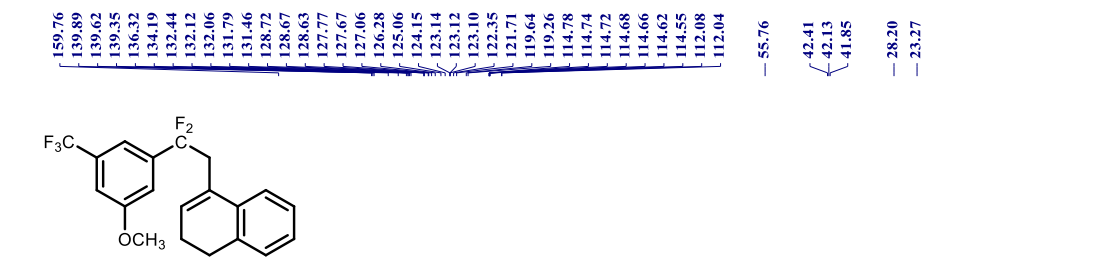




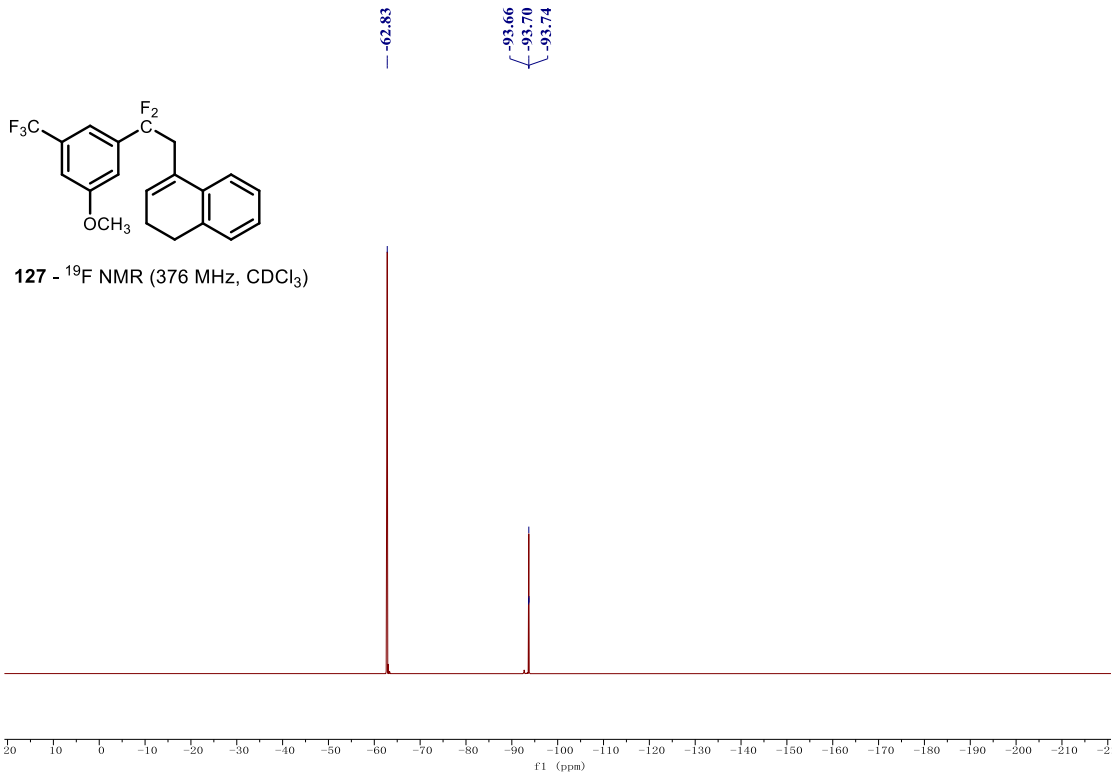
123a - ^{19}F NMR (376 MHz, $CDCl_3$)



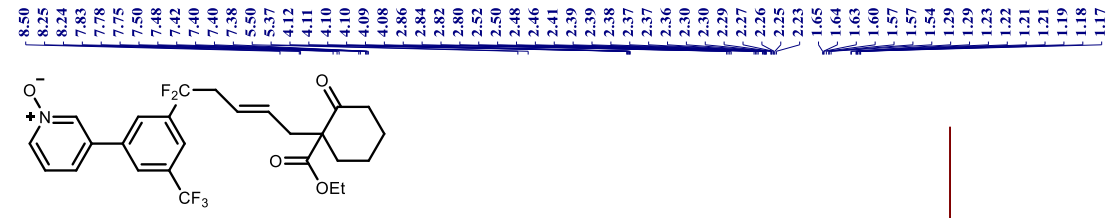
127 - ^{1}H NMR (400 MHz, $CDCl_3$)



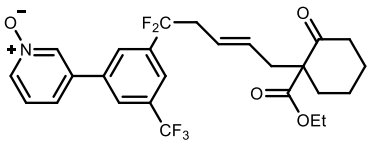
127 - ^{13}C NMR (101 MHz, $CDCl_3$)



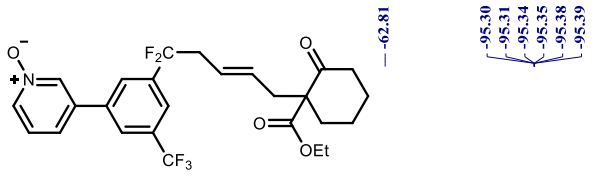
127 - ^{19}F NMR (376 MHz, $CDCl_3$)



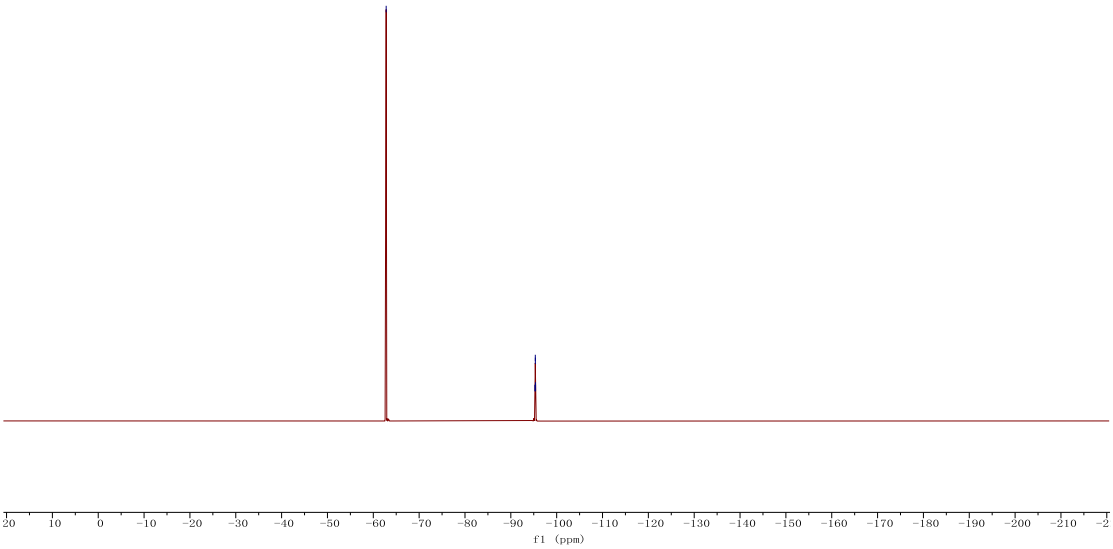
128 - ^{1}H NMR (400 MHz, $CDCl_3$)

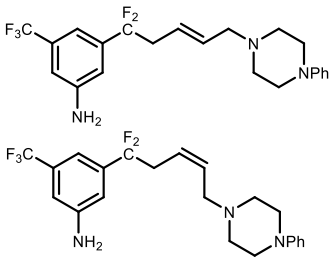


128 - ^{13}C NMR (101 MHz, $CDCl_3$)



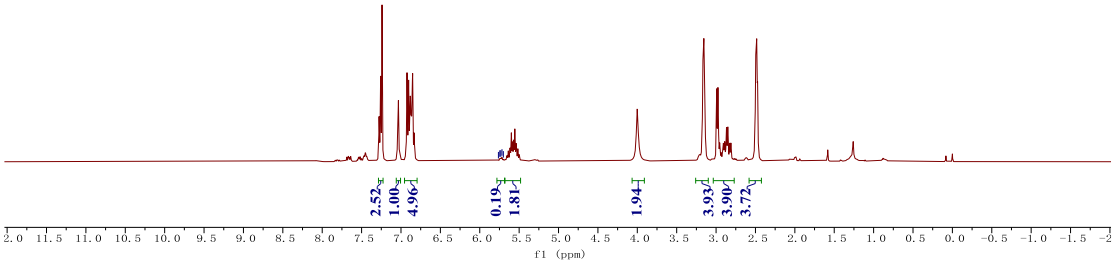
128 - ^{19}F NMR (376 MHz, $CDCl_3$)

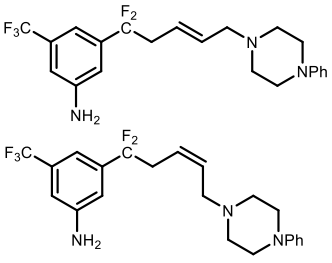




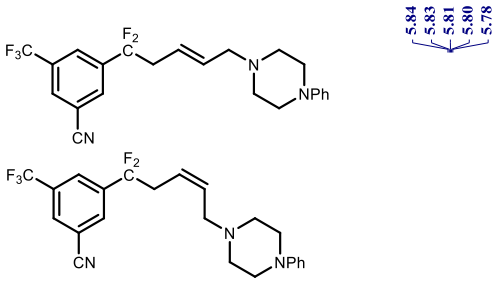
5ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 4.3 : 1



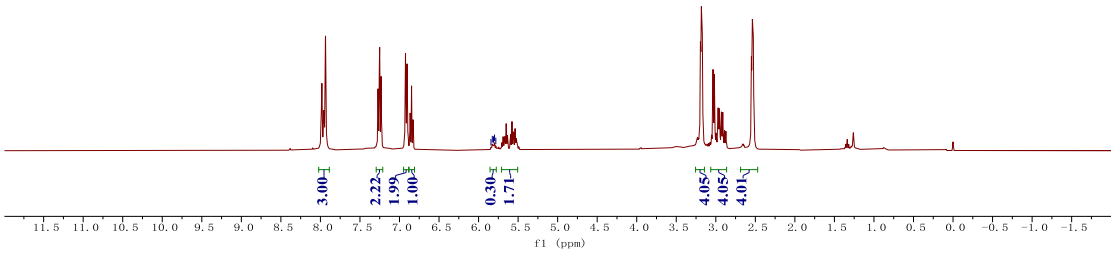


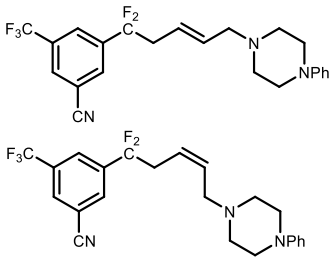
5ab - ^{19}F NMR (376 MHz, $CDCl_3$)



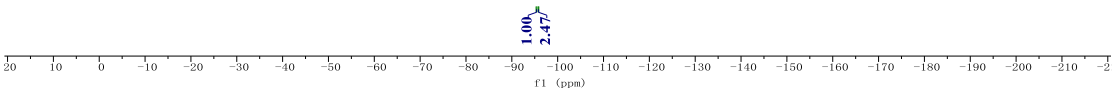
6ab - ^{1}H NMR (400 MHz, $CDCl_3$)

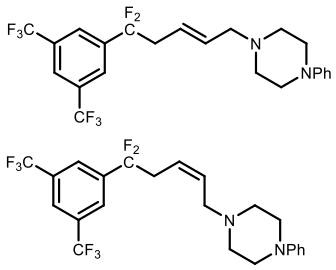
E / Z = 2.5 : 1





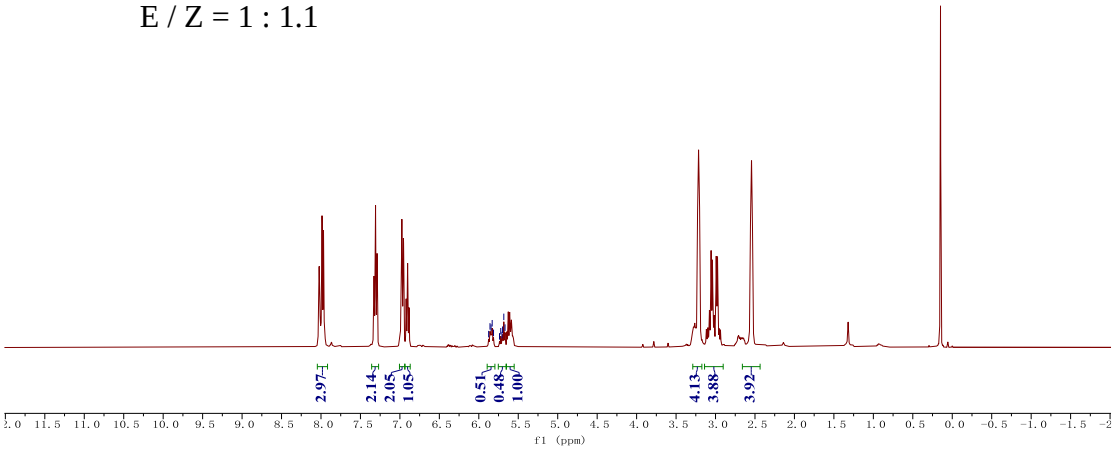
6ab - ^{19}F NMR (376 MHz, $CDCl_3$)

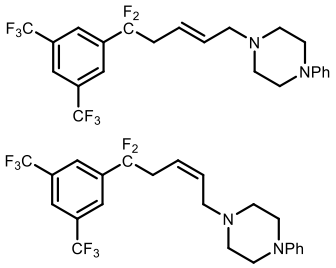




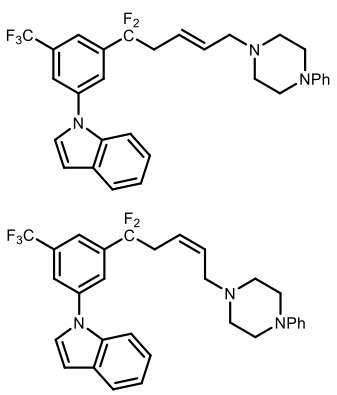
7ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 1.1



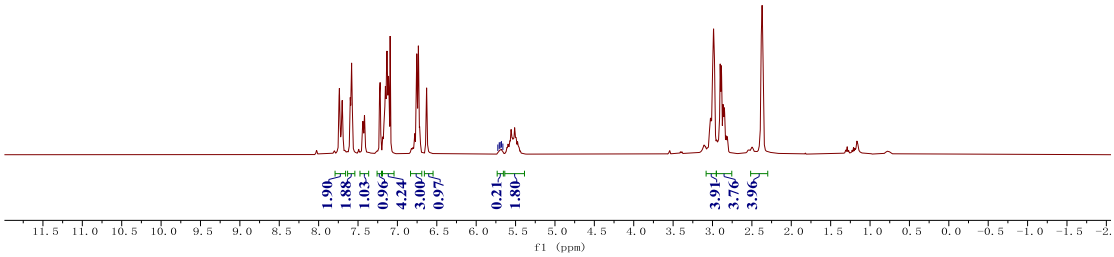


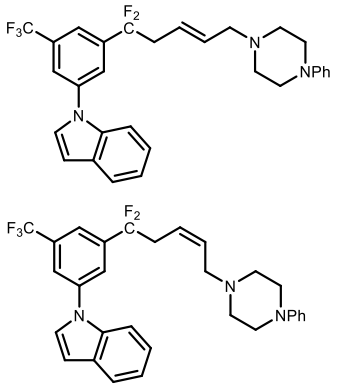
7ab - ^{19}F NMR (376 MHz, $CDCl_3$)



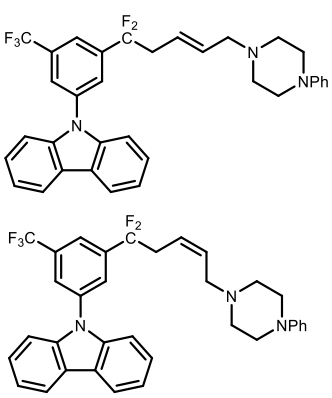
8ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 4.0 : 1



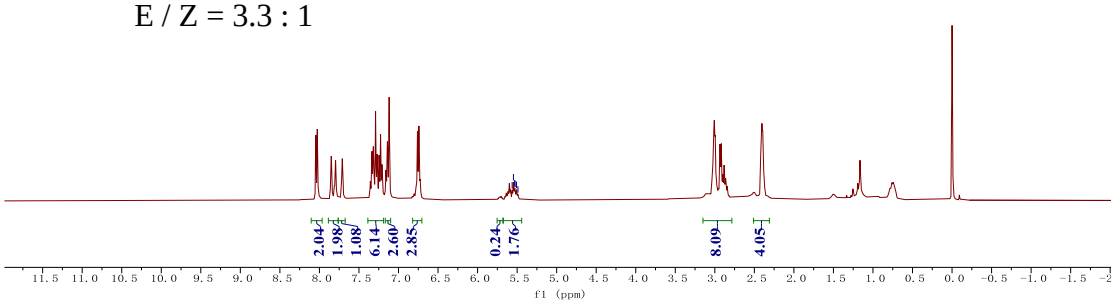


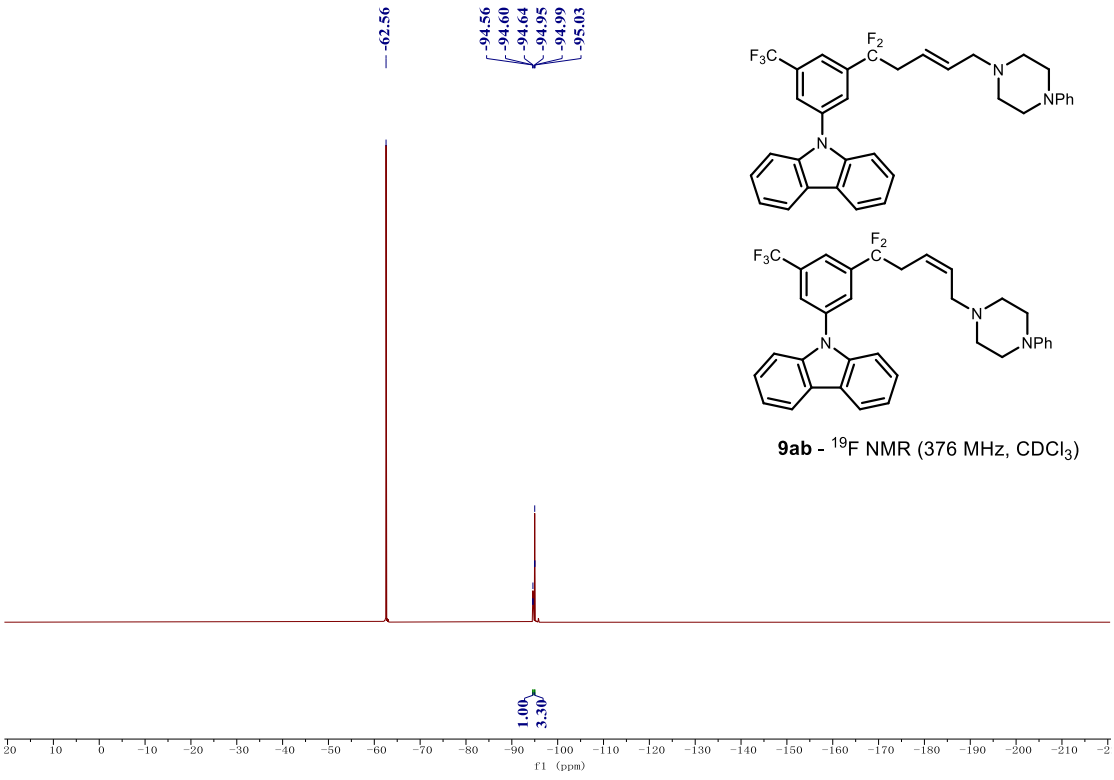
8ab - ^{19}F NMR (376 MHz, $CDCl_3$)



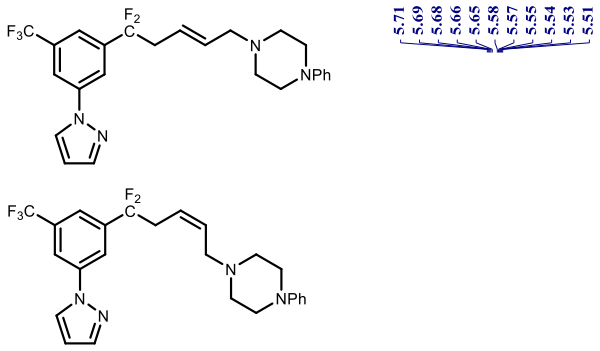
9ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 3.3 : 1



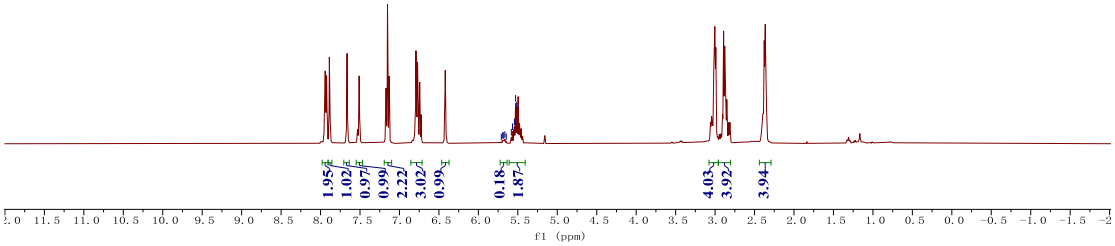


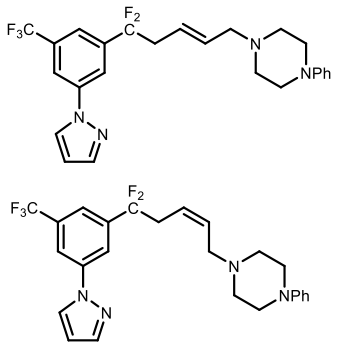
9ab - ^{19}F NMR (376 MHz, $CDCl_3$)



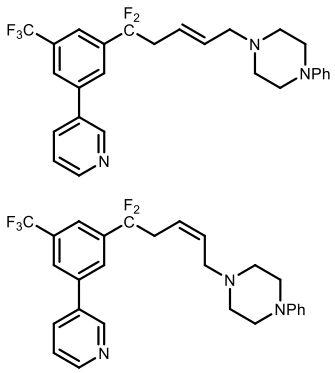
10ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 4.9 : 1



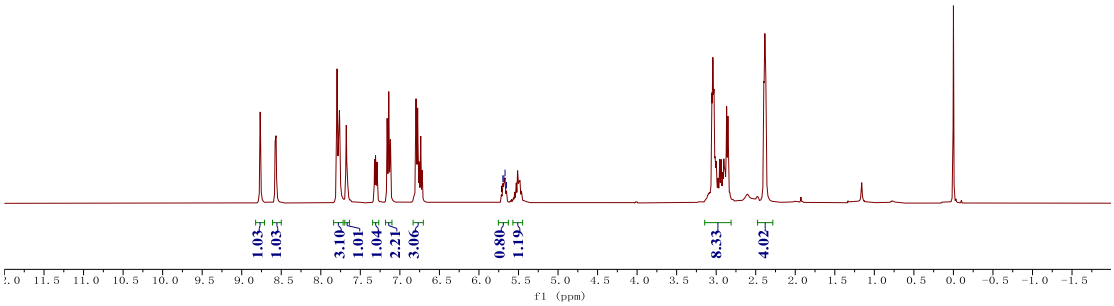


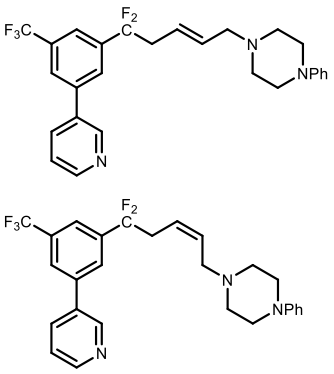
10ab - ^{19}F NMR (376 MHz, $CDCl_3$)



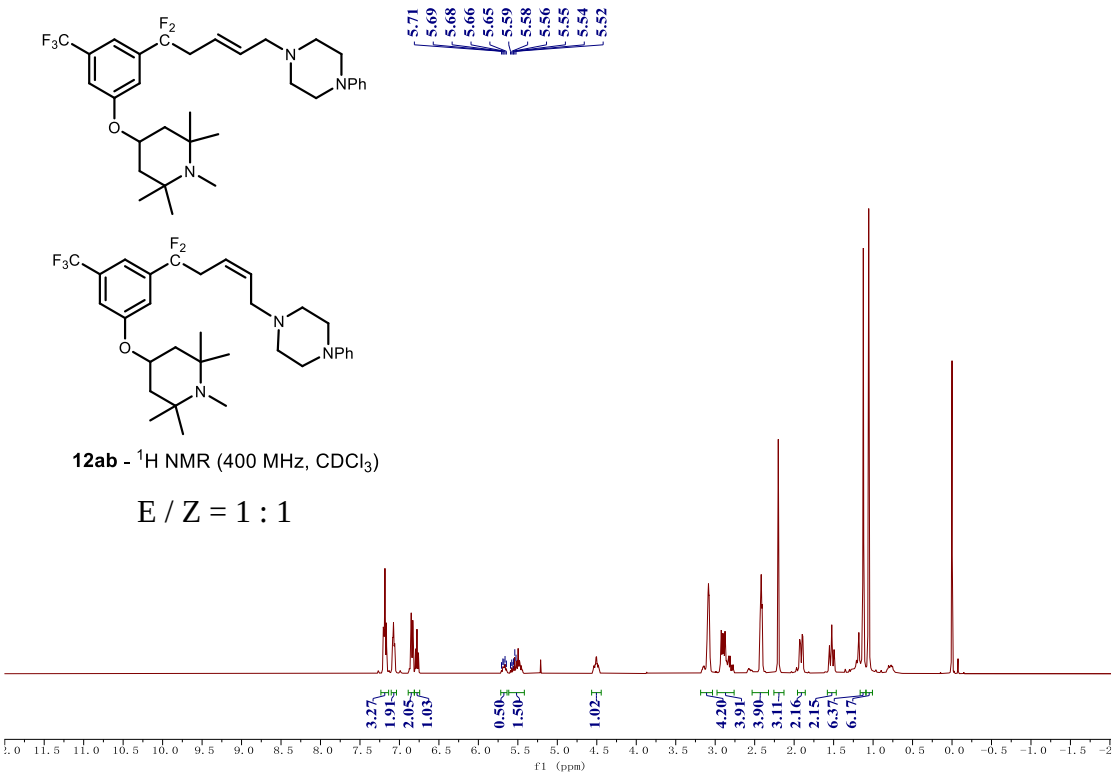
11ab - ^{1}H NMR (400 MHz. $CDCl_3$)

E / Z = 1 : 4.1



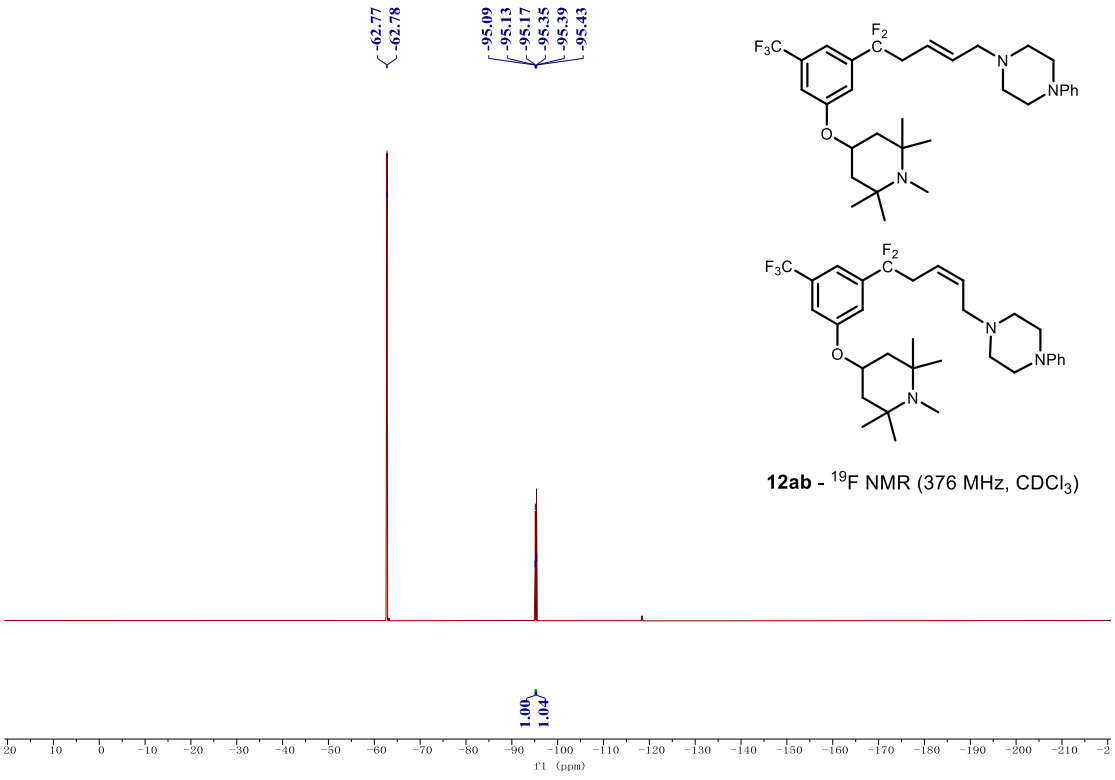


11ab - ^{19}F NMR (376 MHz, $CDCl_3$)

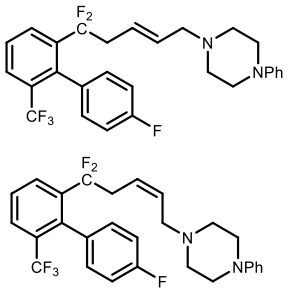


12ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 1

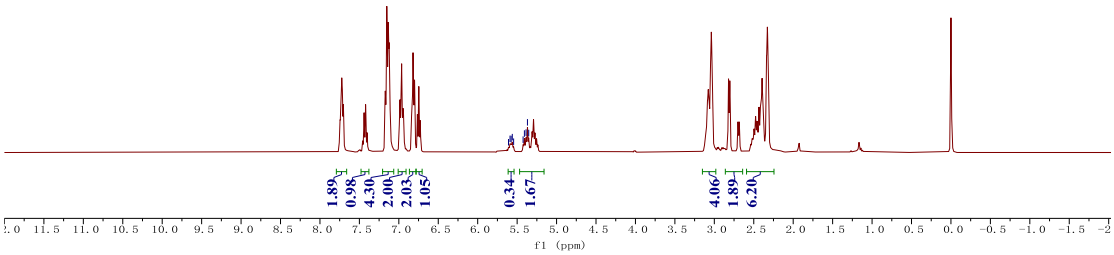


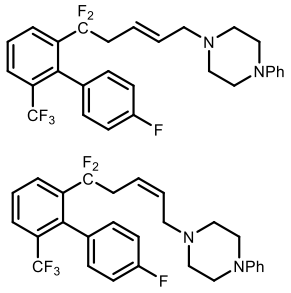
12ab - ^{19}F NMR (376 MHz, $CDCl_3$)



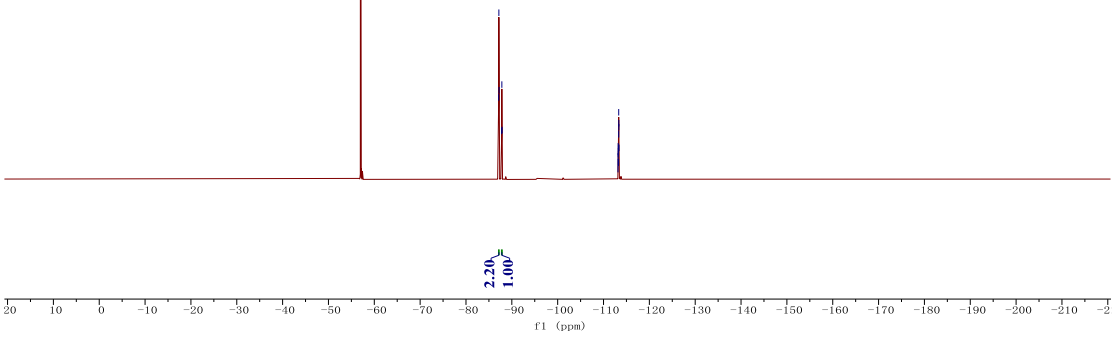
13ab - ^{1}H NMR (400 MHz, $CDCl_3$)

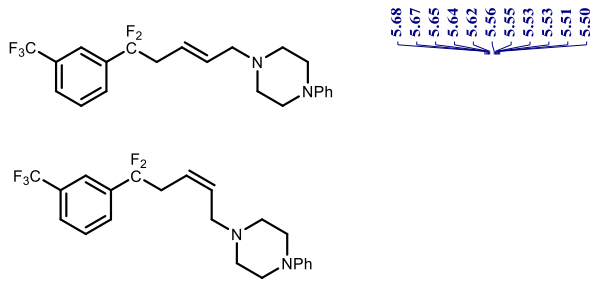
E / Z = 2.2 : 1





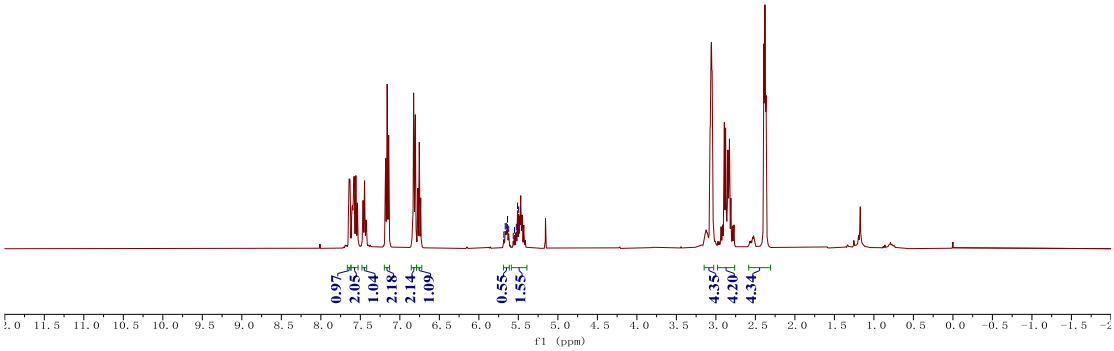
13ab - ^{19}F NMR (376 MHz, $CDCl_3$)

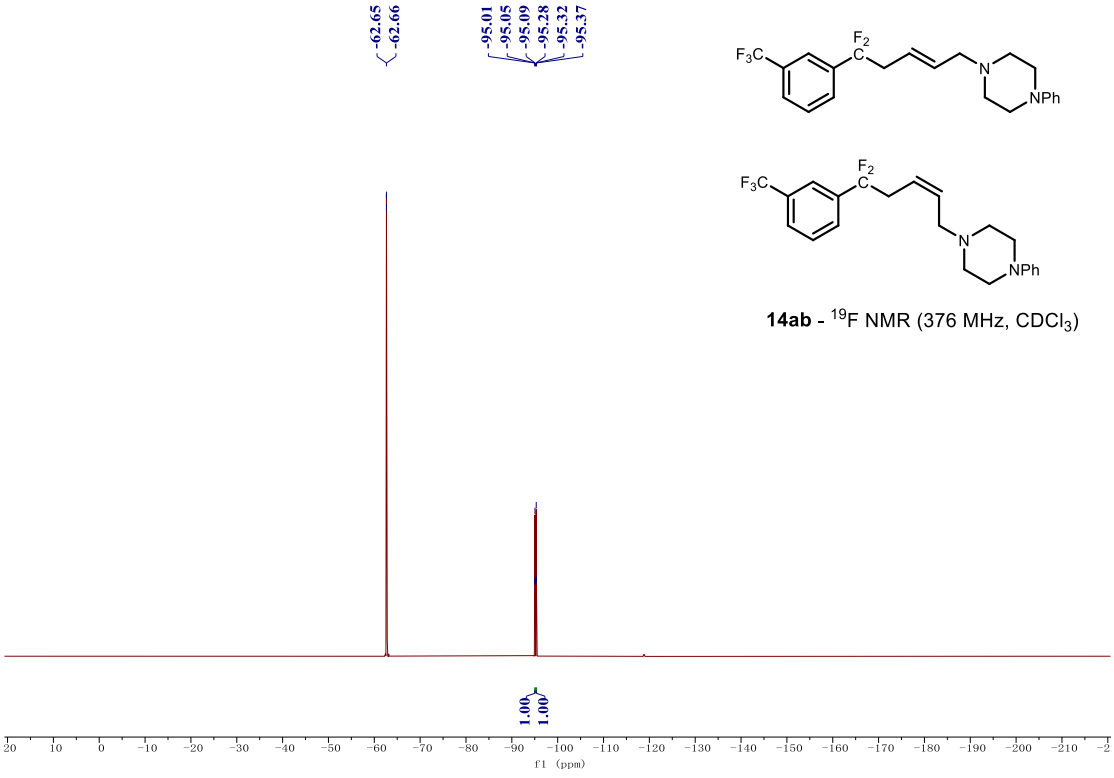




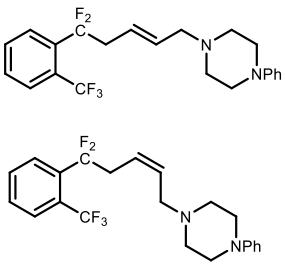
14ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 1



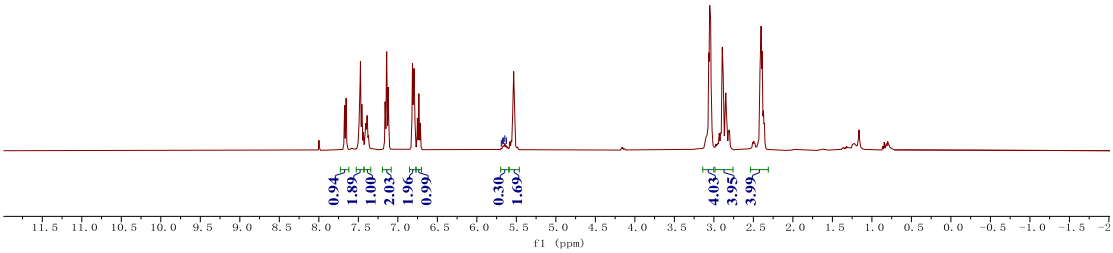


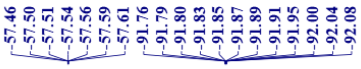
14ab - ^{19}F NMR (376 MHz, $CDCl_3$)

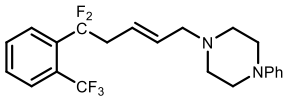


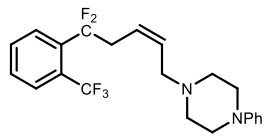
15ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 2.2 : 1

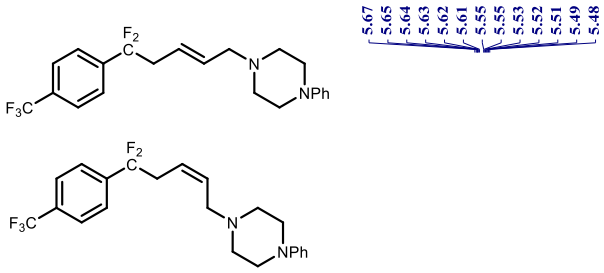






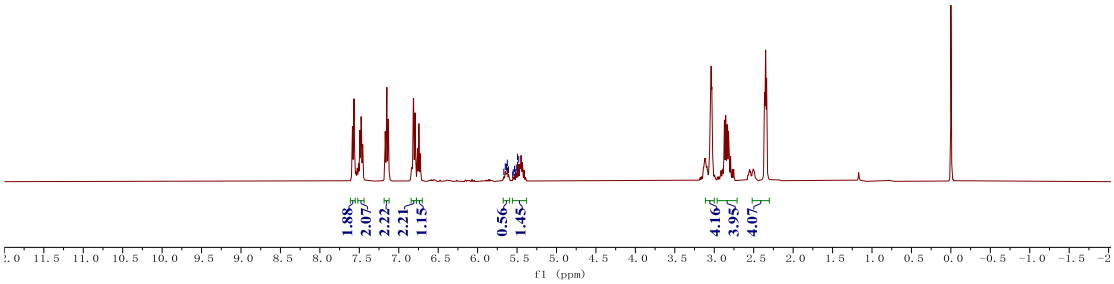


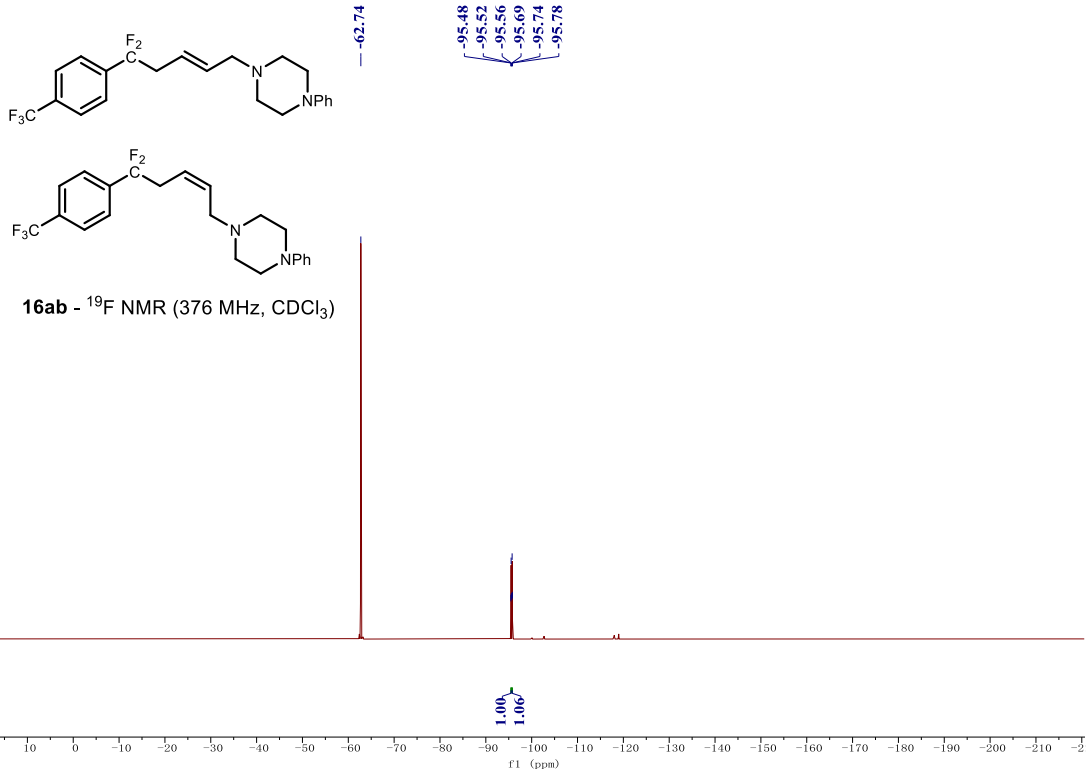
15ab - ^{19}F NMR (376 MHz, $CDCl_3$)



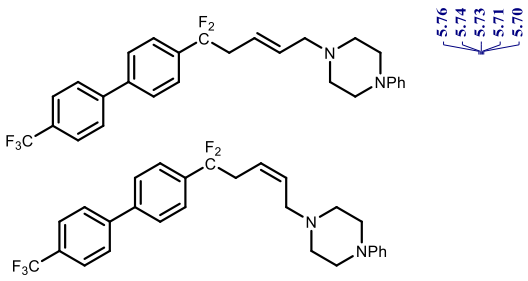
16ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 1.1



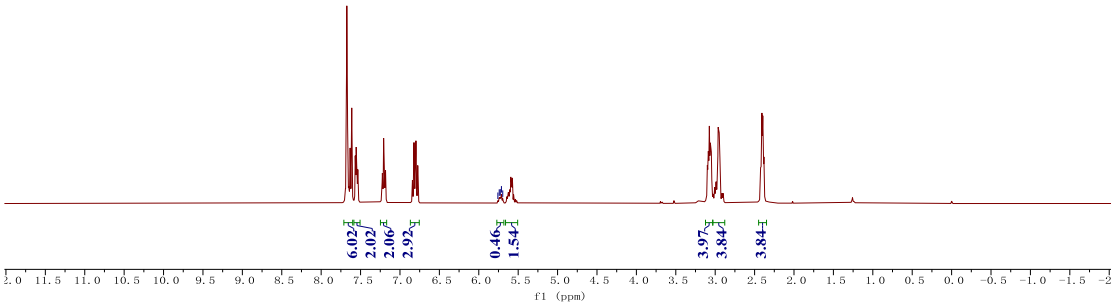


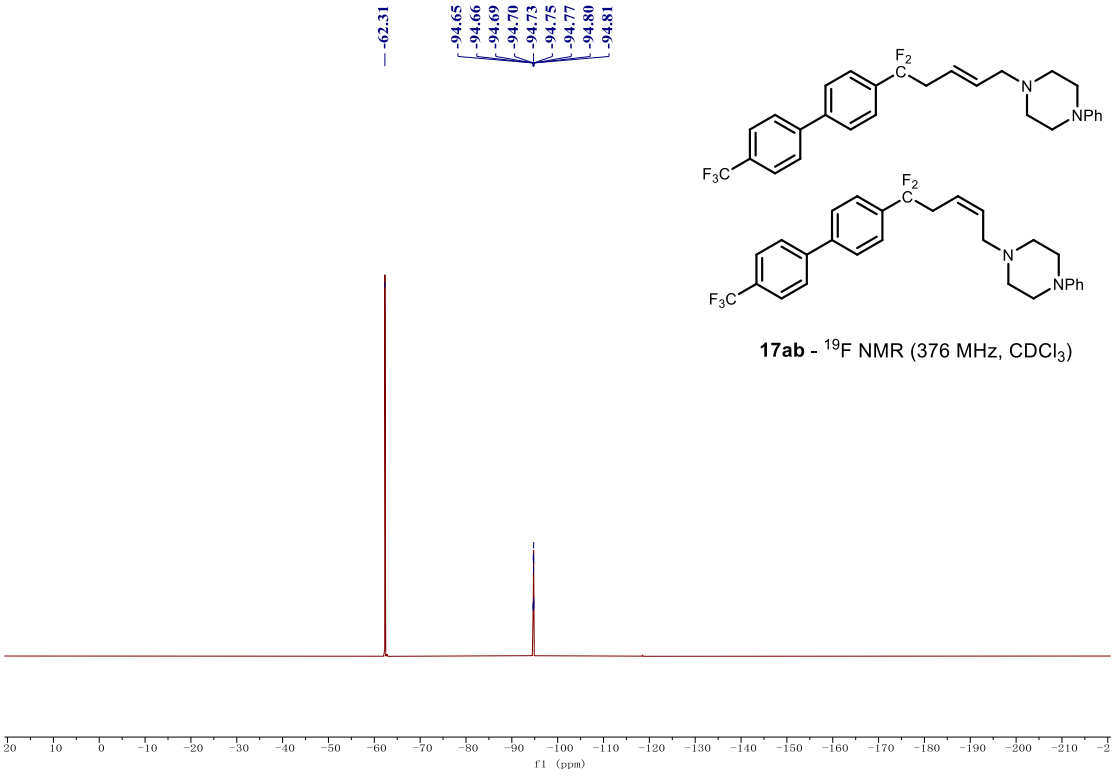
16ab - ^{19}F NMR (376 MHz, $CDCl_3$)



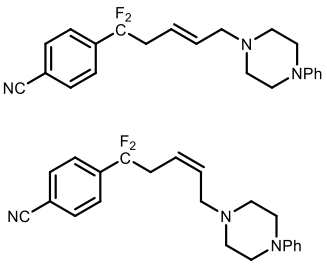
17ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1.2 : 1



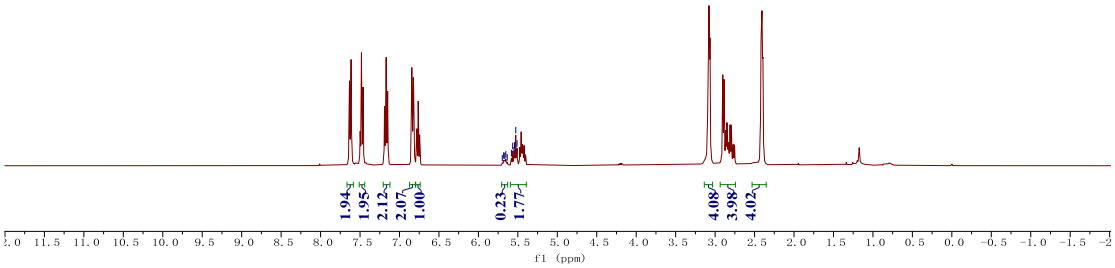


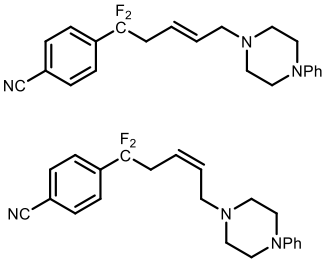
17ab - ^{19}F NMR (376 MHz, $CDCl_3$)



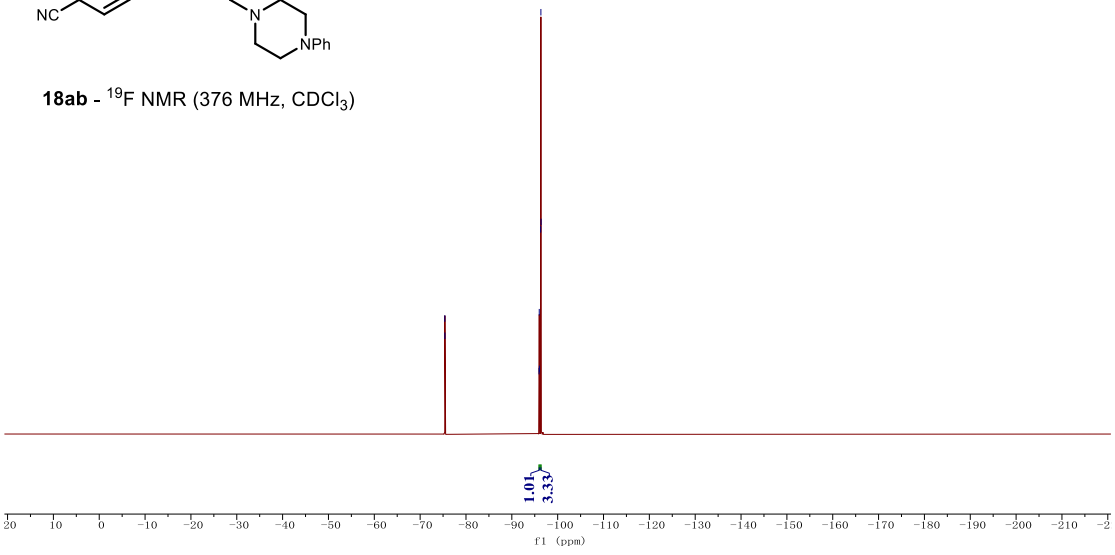
18ab - ^{1}H NMR (400 MHz, $CDCl_3$)

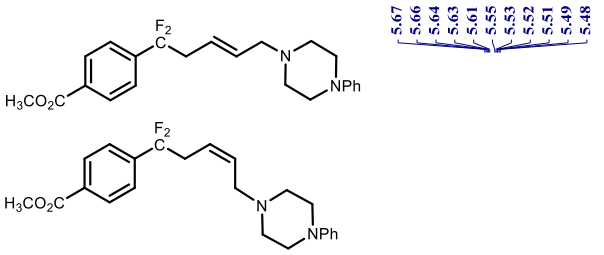
E / Z = 3.3 : 1





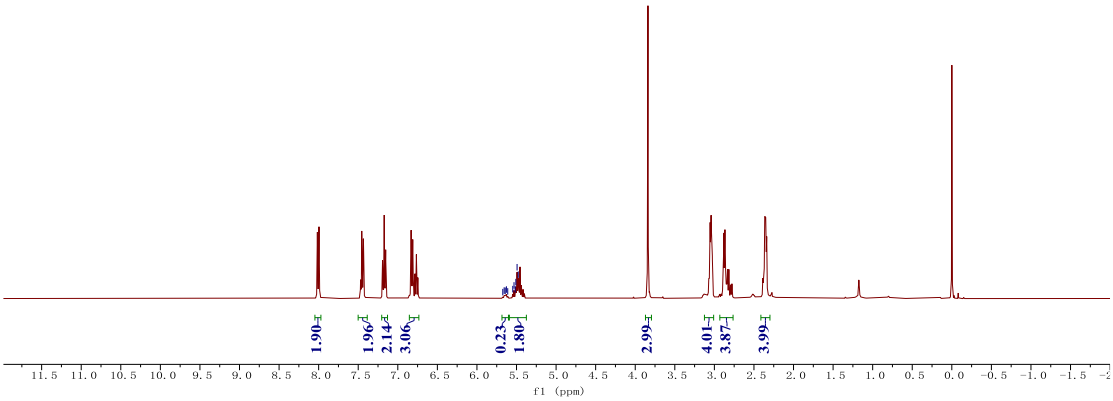
18ab - ^{19}F NMR (376 MHz, $CDCl_3$)

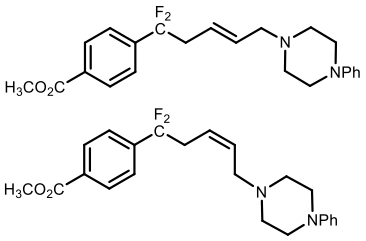




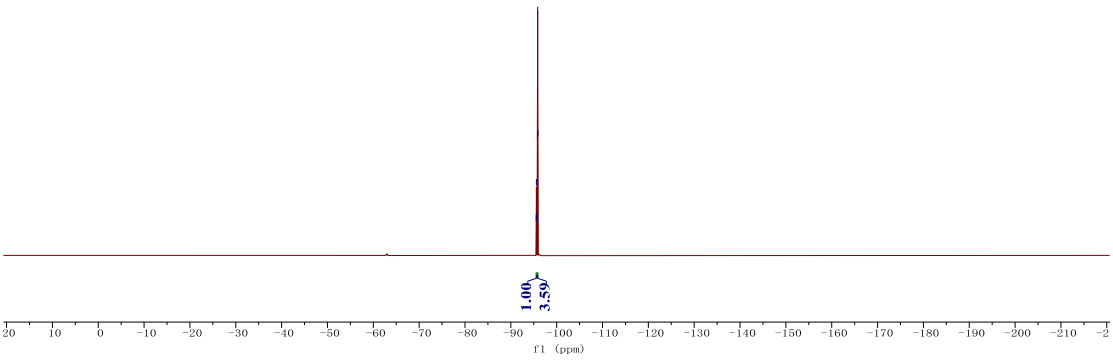
19aa - ^{1}H NMR (400 MHz, $CDCl_3$)

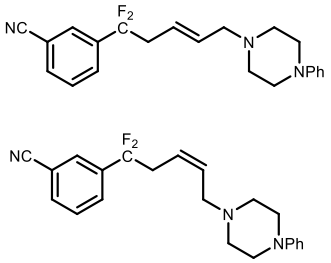
E / Z = 3.6 : 1





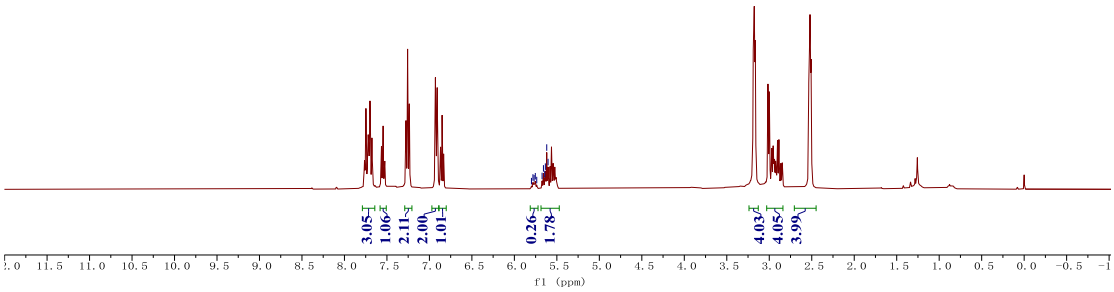
19aa - ^{19}F NMR (376 MHz, $CDCl_3$)

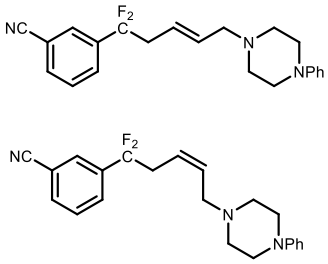




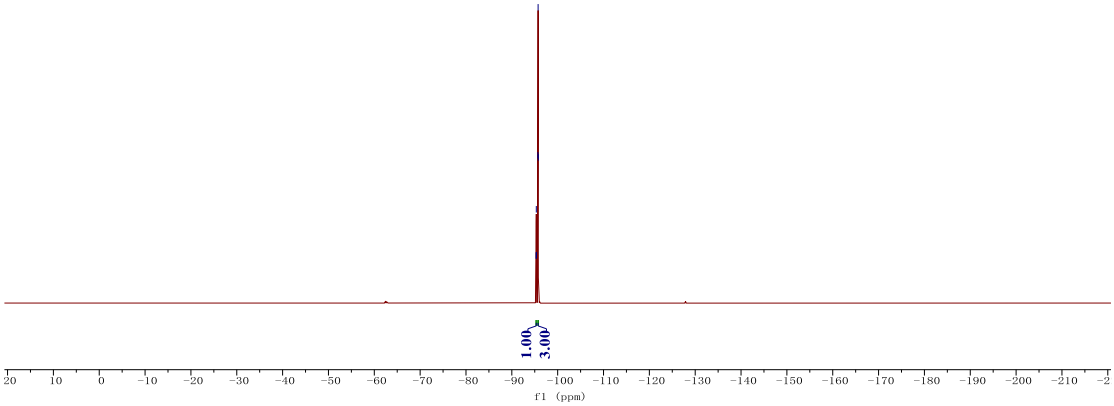
20ab - ^{1}H NMR (400 MHz, $CDCl_3$)

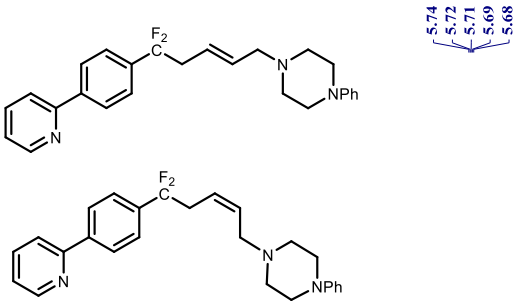
E / Z = 3.0 : 1





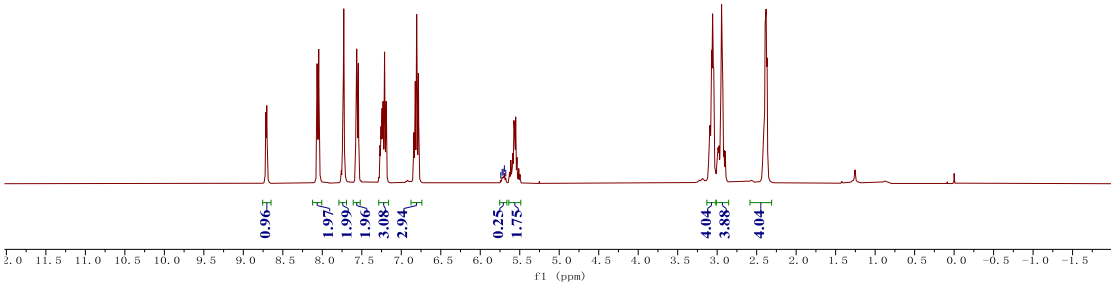
20ab - ^{19}F NMR (376 MHz, $CDCl_3$)

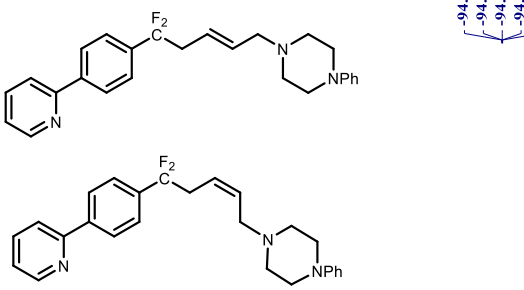




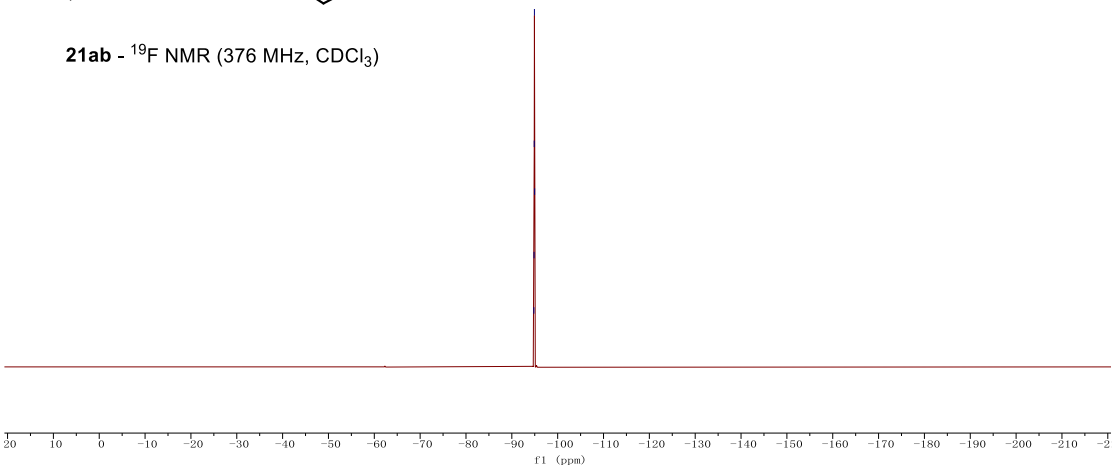
21ab - ^{1}H NMR (400 MHz, $CDCl_3$)

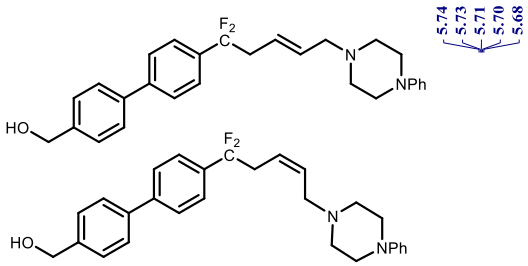
E / Z = 3.0 : 1





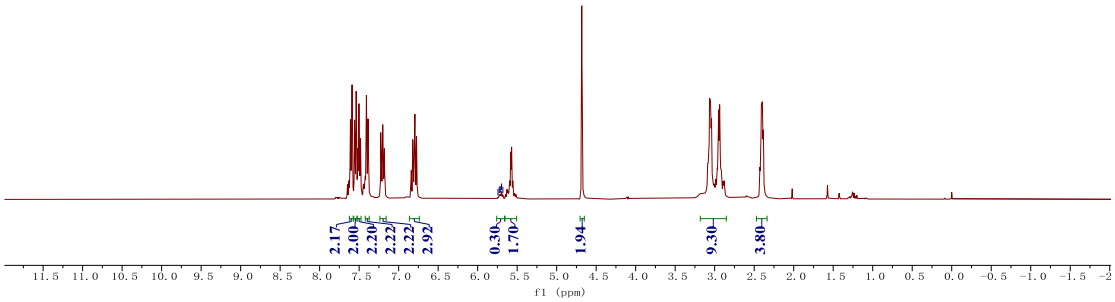
21ab - ^{19}F NMR (376 MHz, $CDCl_3$)

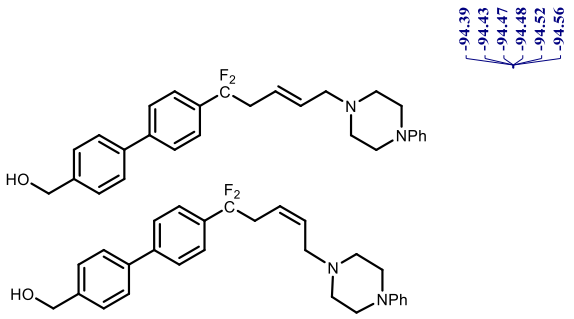




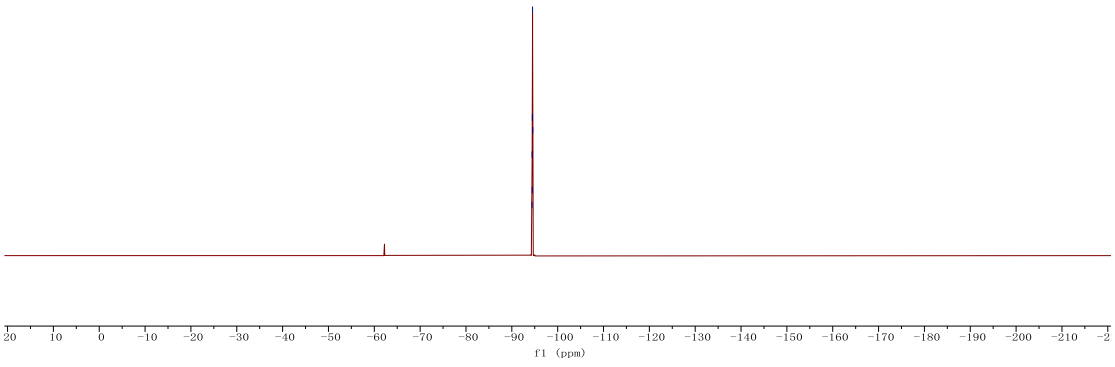
22ab - ^{1}H NMR (400 MHz, $CDCl_3$)

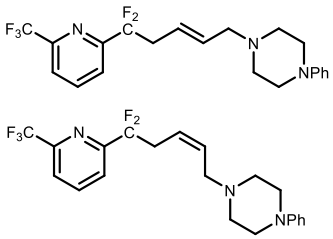
E / Z = 2.3 : 1





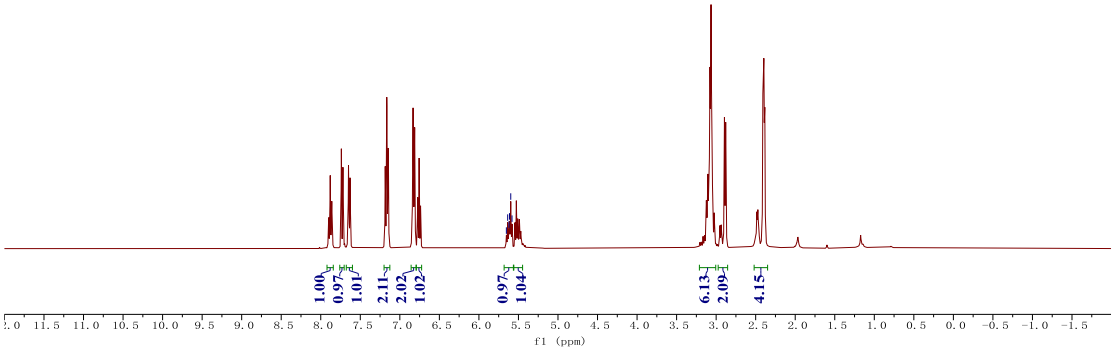
22ab - ^{19}F NMR (376 MHz, $CDCl_3$)

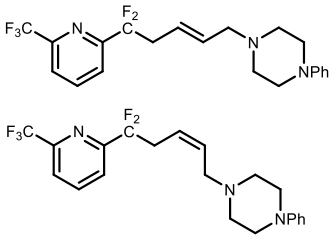




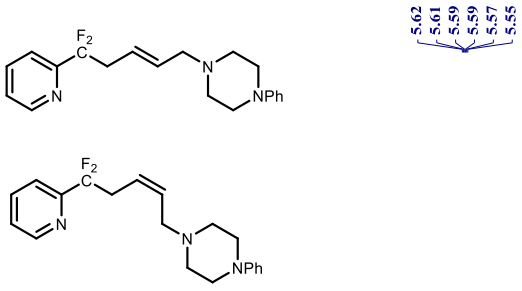
23ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 5.7 : 1



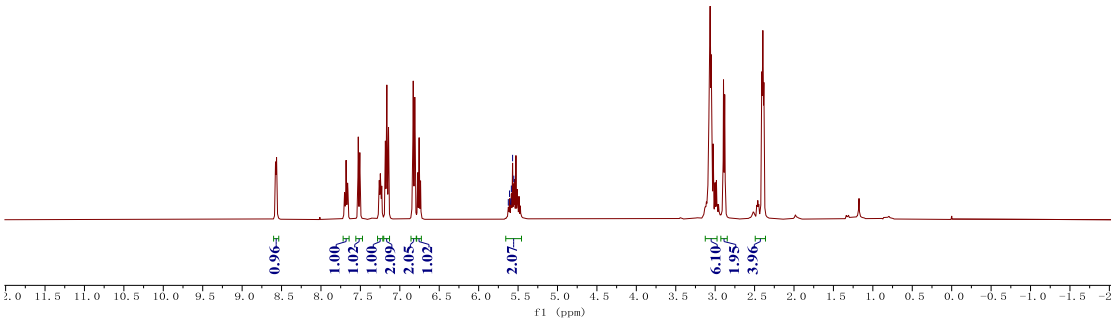


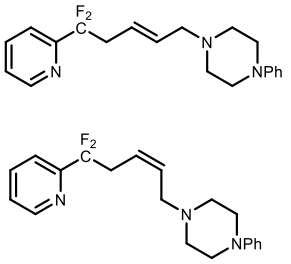
23ab - ^{19}F NMR (376 MHz, $CDCl_3$)



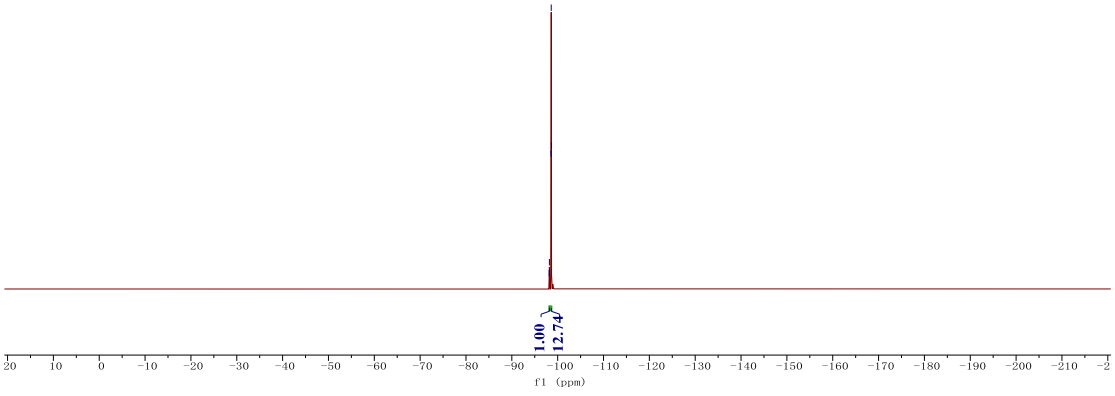
24ab - ^{1}H NMR (400 MHz, $CDCl_3$)

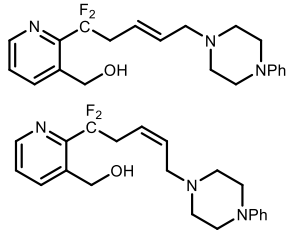
E / Z = 12.7 : 1





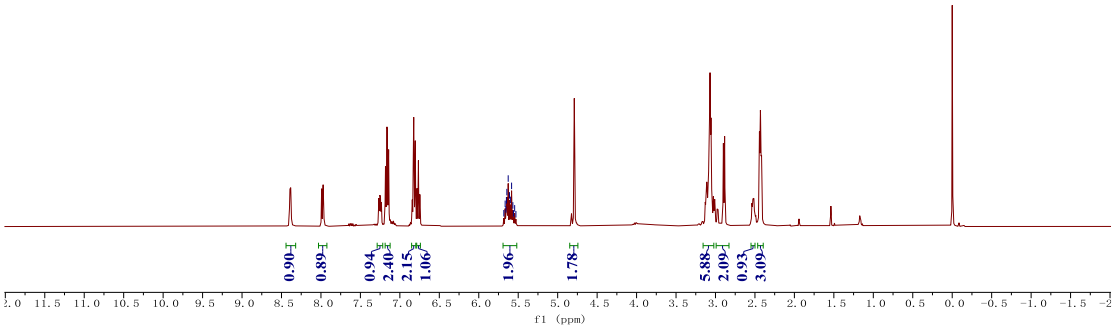
24ab - ^{19}F NMR (376 MHz, $CDCl_3$)

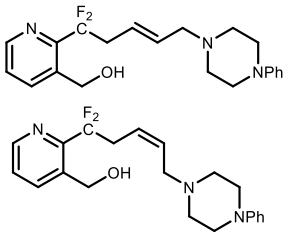




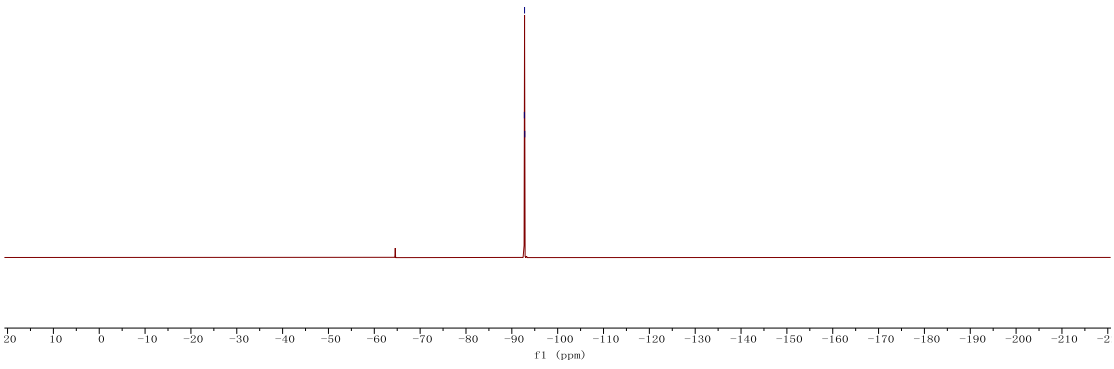
25ab - ^{1}H NMR (400 MHz, $CDCl_3$)

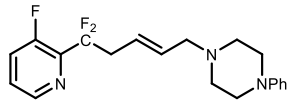
E / Z = 3.3 : 1

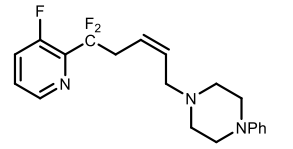




25ab - ^{19}F NMR (376 MHz, $CDCl_3$)

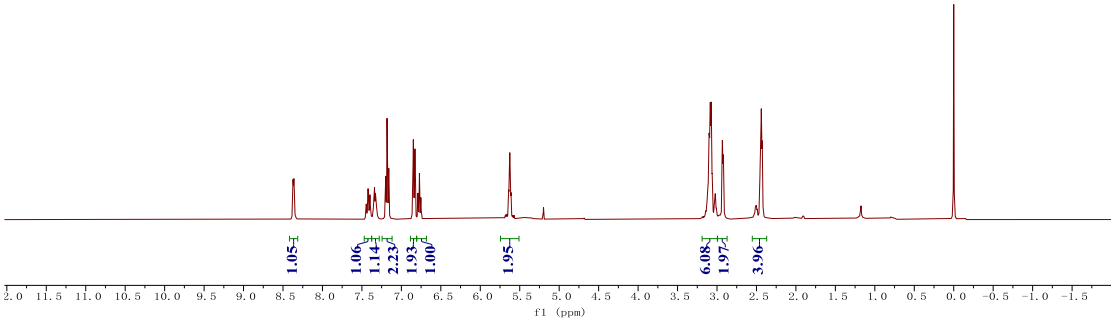


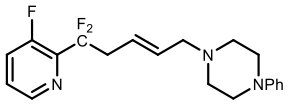


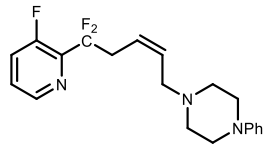


26ab - ^{1}H NMR (400 MHz, $CDCl_3$)

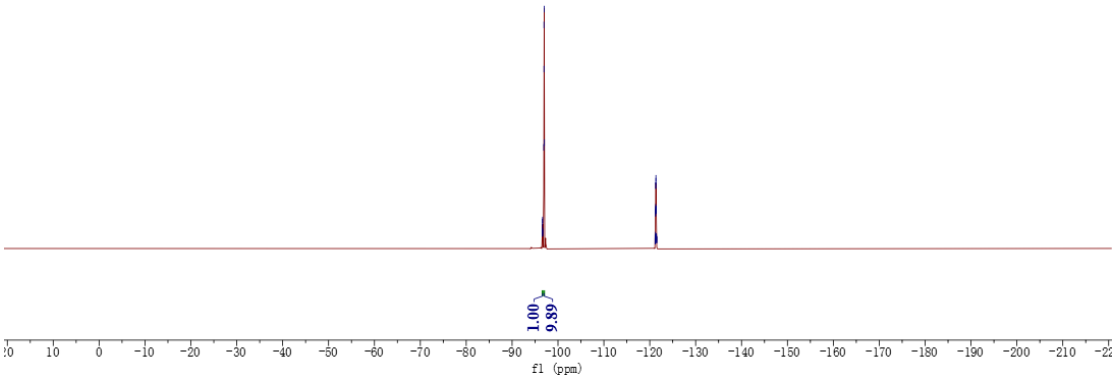
E / Z = 9.9 : 1

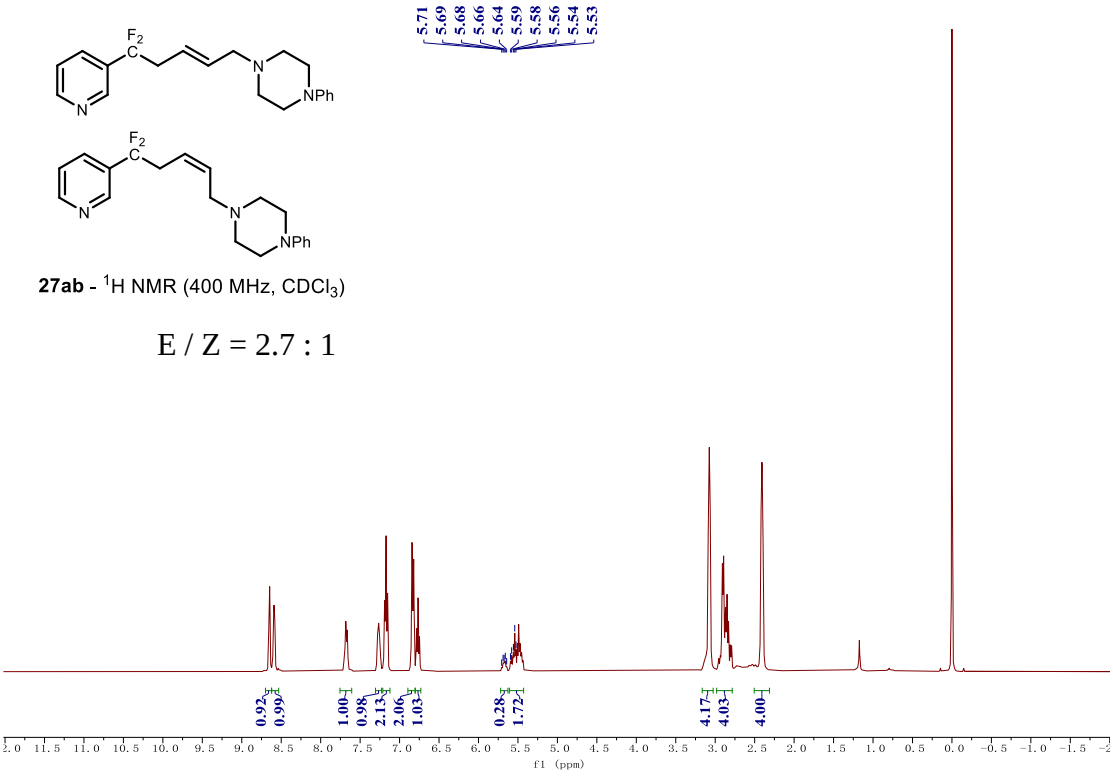






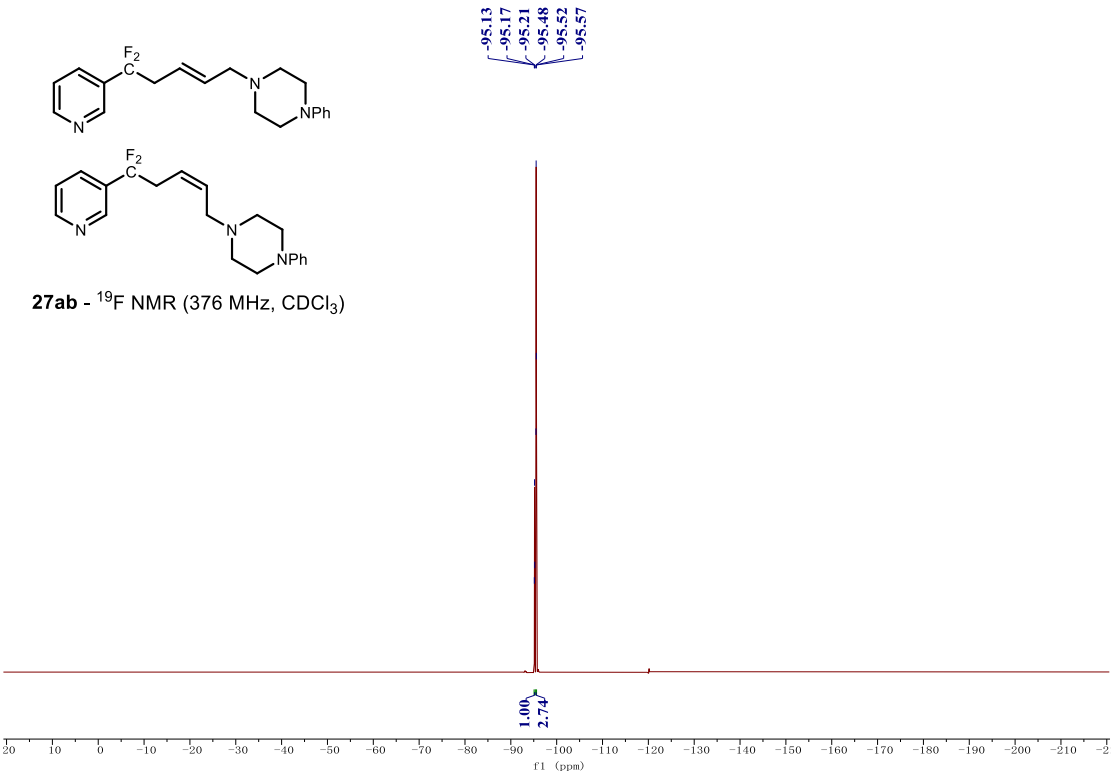
26ab - ^{19}F NMR (376 MHz, $CDCl_3$)



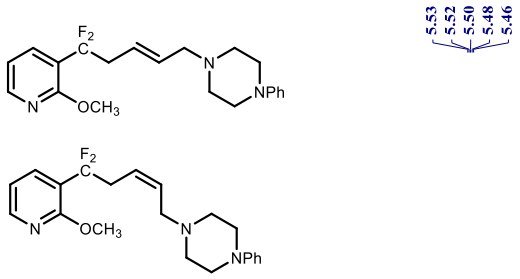


27ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 2.7 : 1

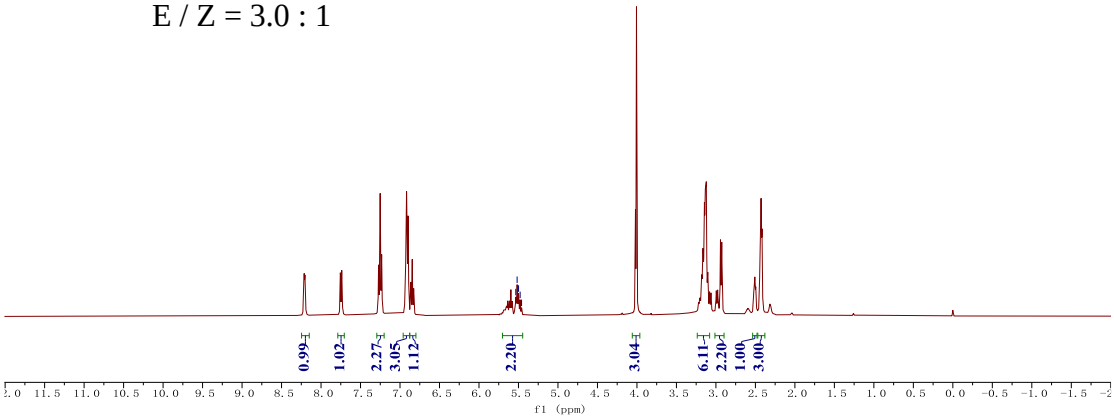


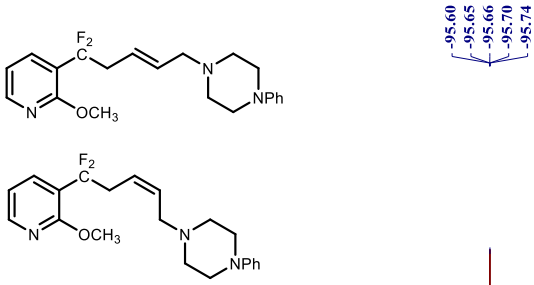
27ab - ^{19}F NMR (376 MHz, $CDCl_3$)



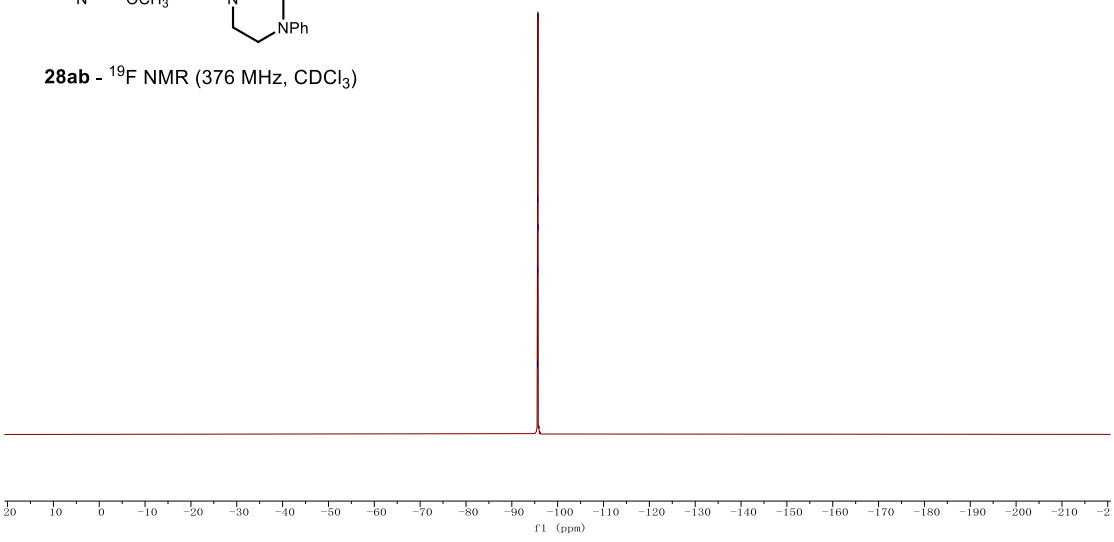
28ab - ^{1}H NMR (400 MHz, $CDCl_3$)

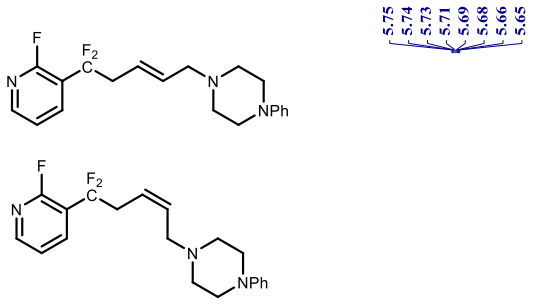
E / Z = 3.0 : 1





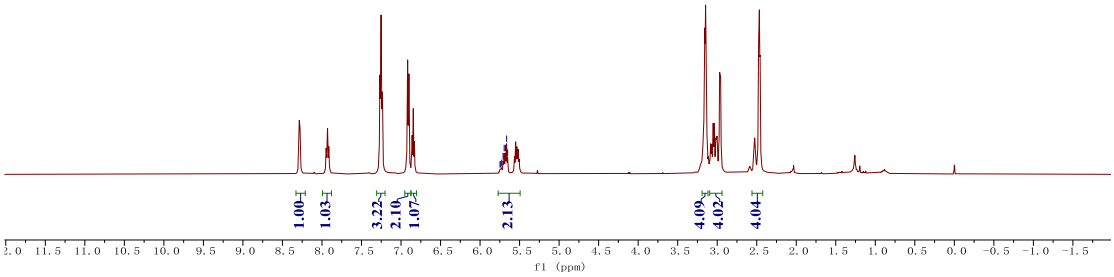
28ab - ^{19}F NMR (376 MHz, $CDCl_3$)

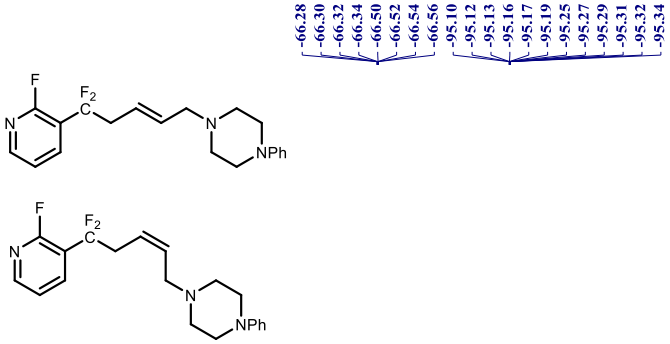




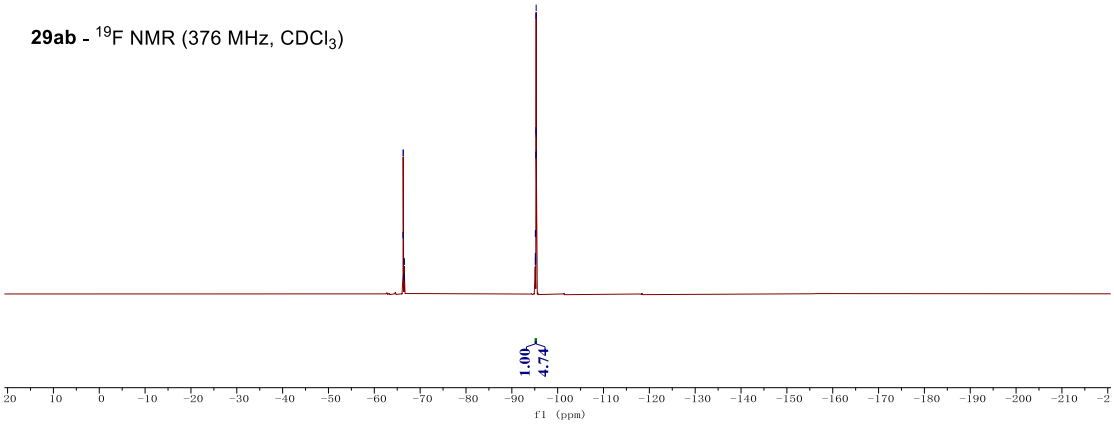
29ab - ^{1}H NMR (400 MHz, $CDCl_3$)

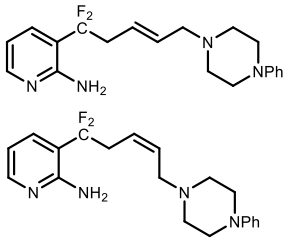
E / Z = 4.7 : 1





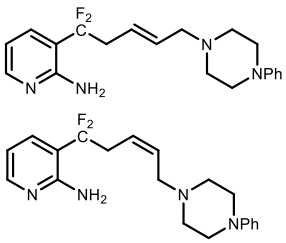
29ab - ^{19}F NMR (376 MHz, $CDCl_3$)



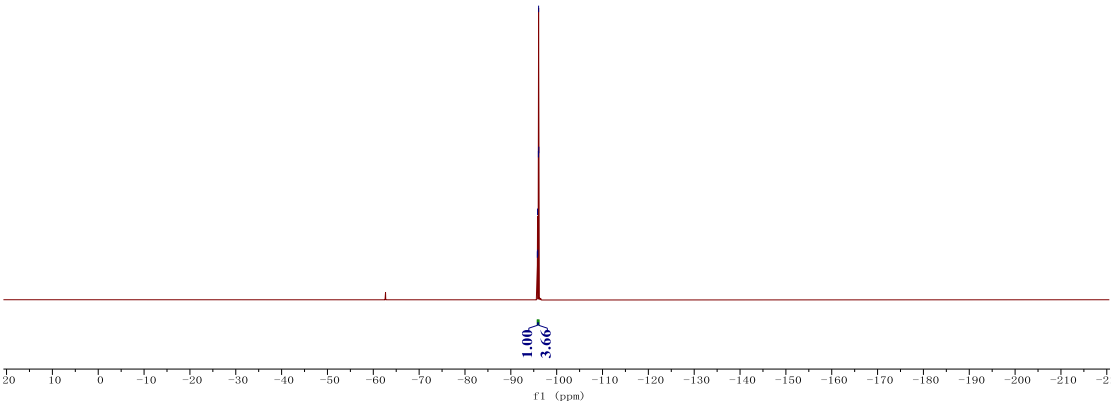


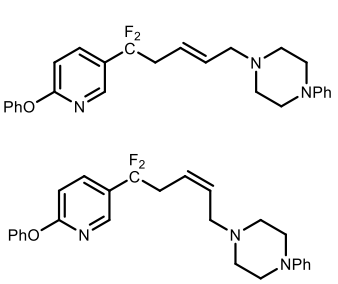
30ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 3.7 : 1



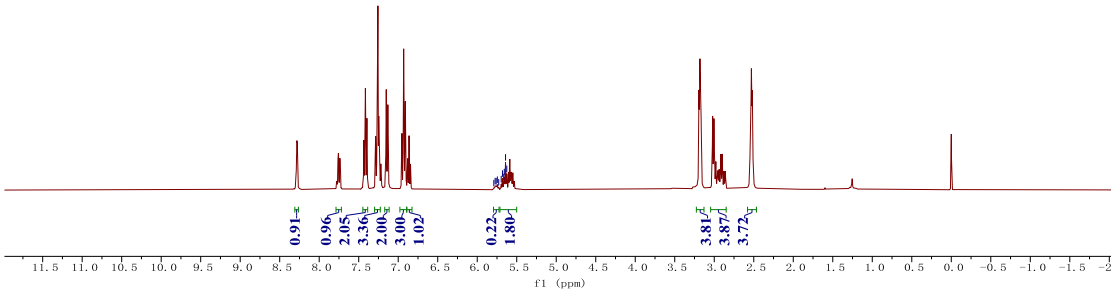
30ab - ^{19}F NMR (376 MHz, $CDCl_3$)

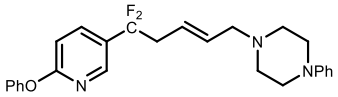


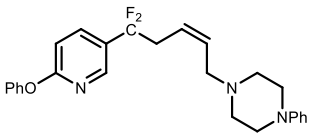


31ab - ^{1}H NMR (400 MHz, $CDCl_3$)

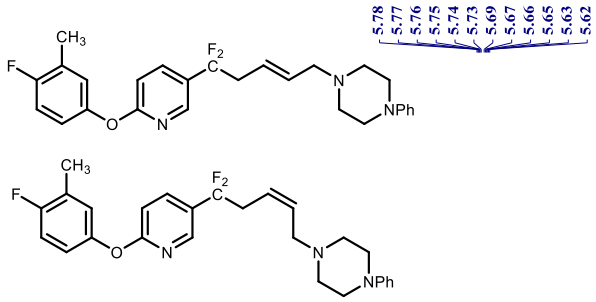
E / Z = 3.6 : 1





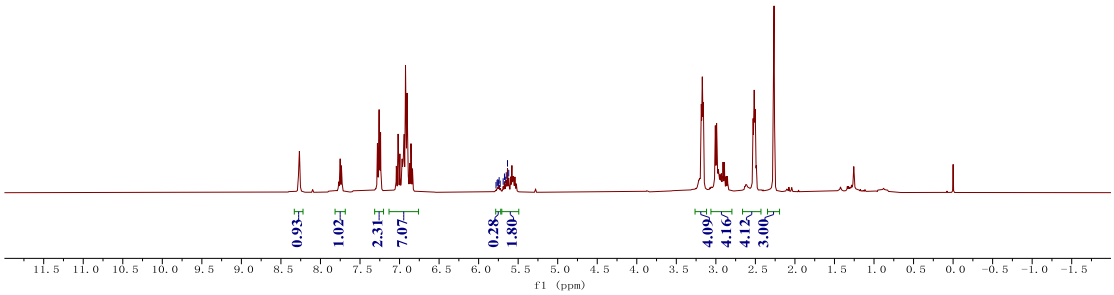


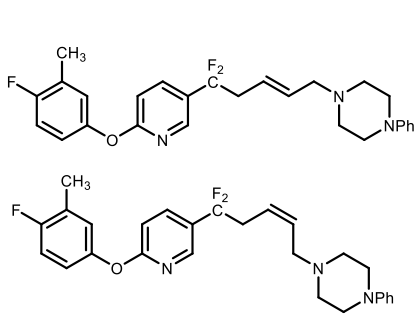
31ab - ^{19}F NMR (376 MHz, $CDCl_3$)

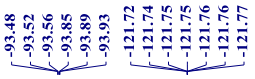


32ab - ^{1}H NMR (400 MHz, $CDCl_3$)

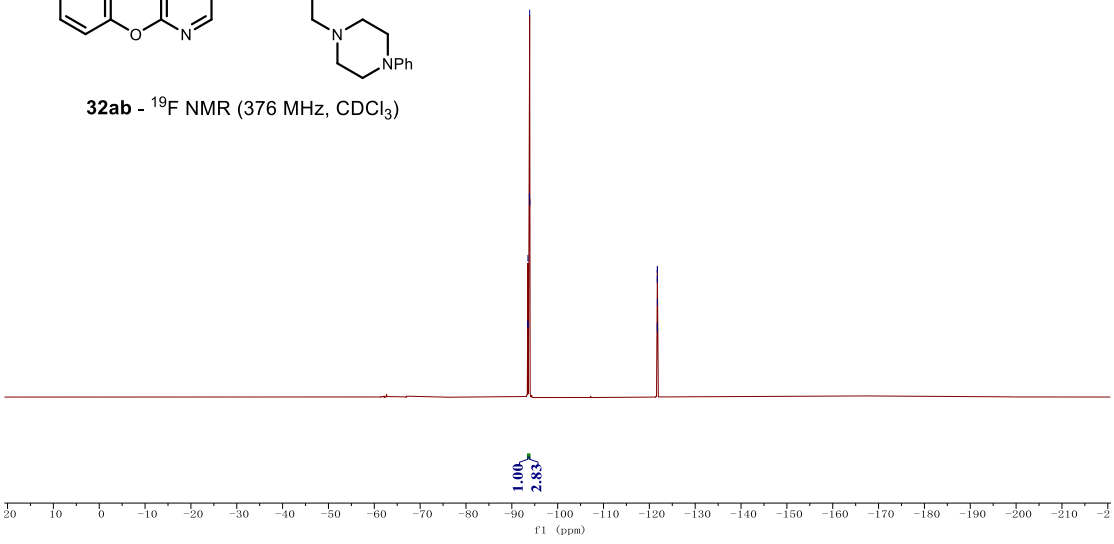
E / Z = 2.8 : 1

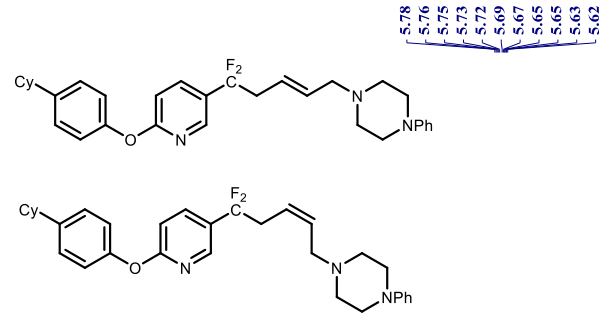






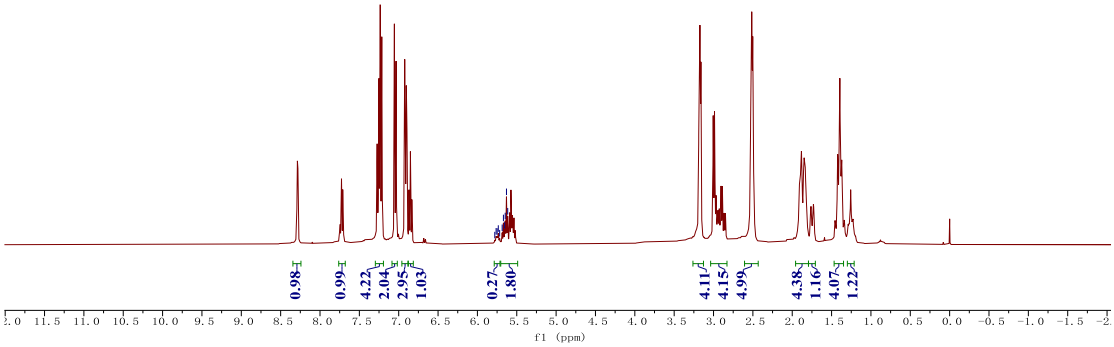
32ab - ^{19}F NMR (376 MHz, $CDCl_3$)

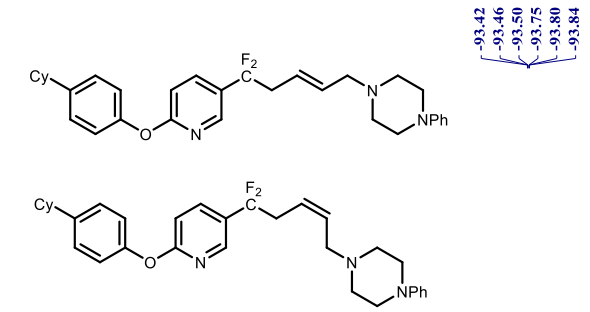




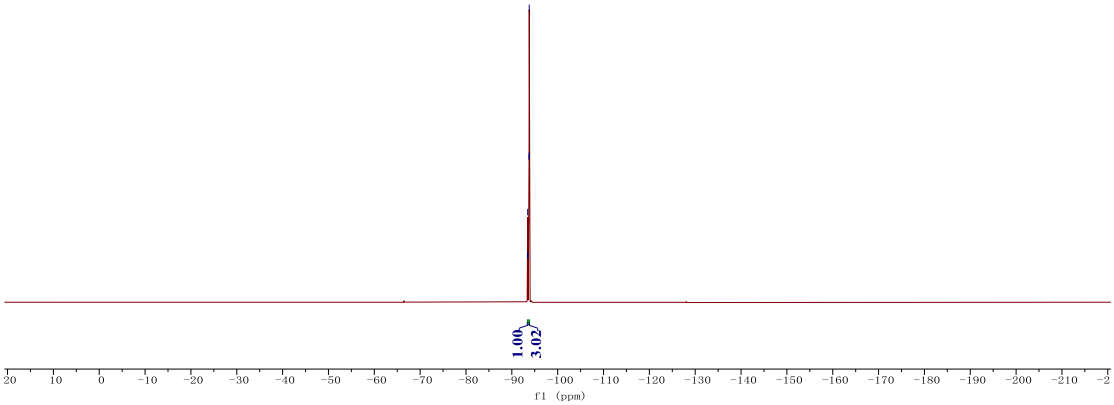
33ab - ^{1}H NMR (400 MHz, $CDCl_3$)

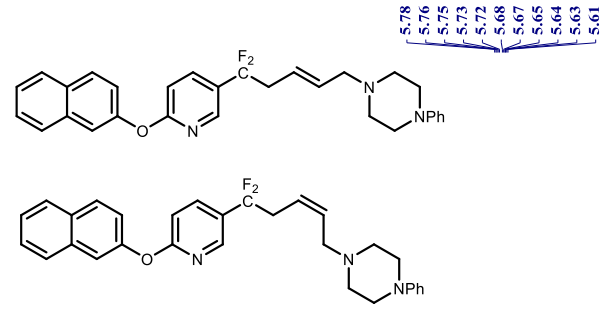
E / Z = 3.0 : 1





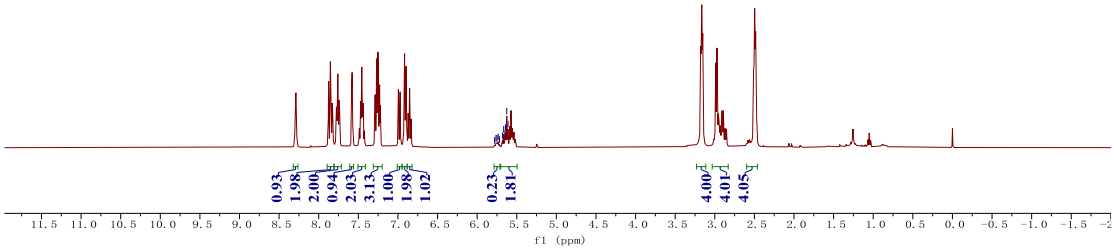
33ab - ^{19}F NMR (376 MHz, $CDCl_3$)

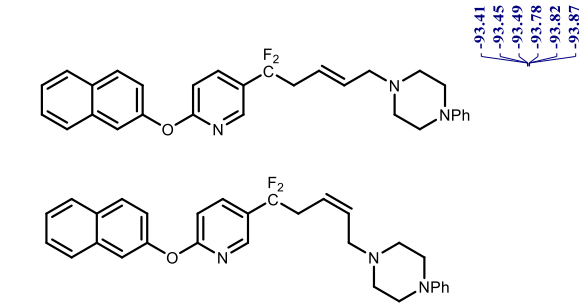




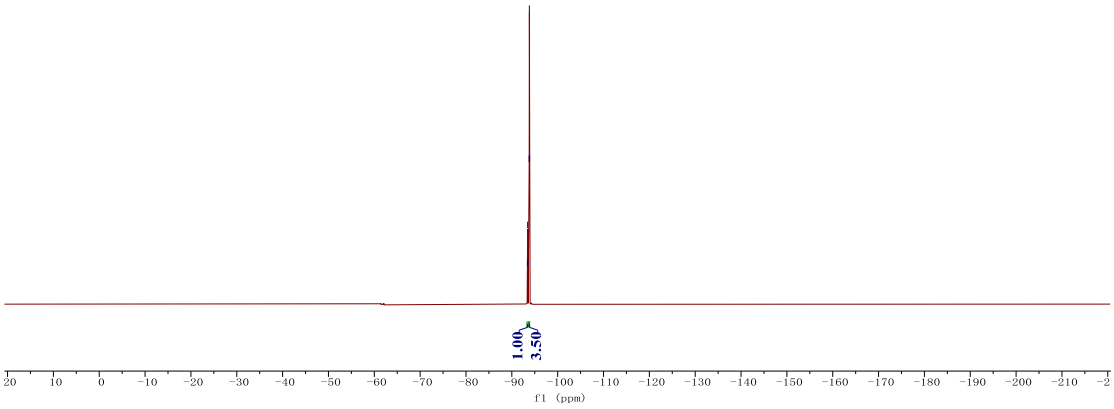
34ab - ^{1}H NMR (400 MHz, $CDCl_3$)

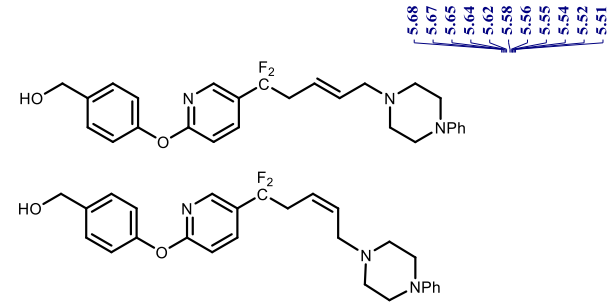
E / Z = 3.5 : 1





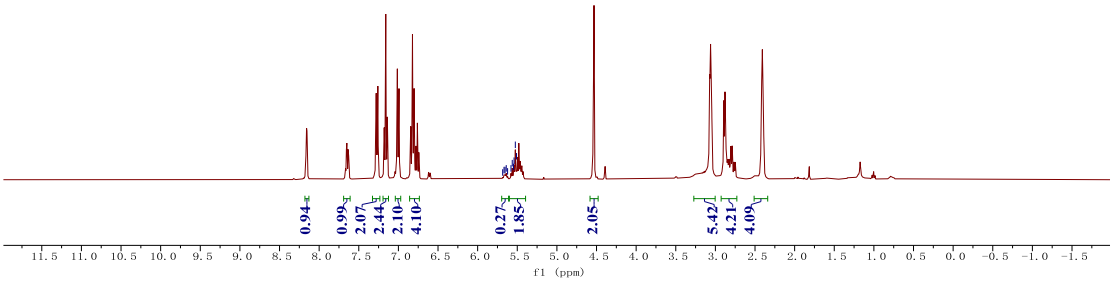
34ab - ^{19}F NMR (376 MHz, $CDCl_3$)

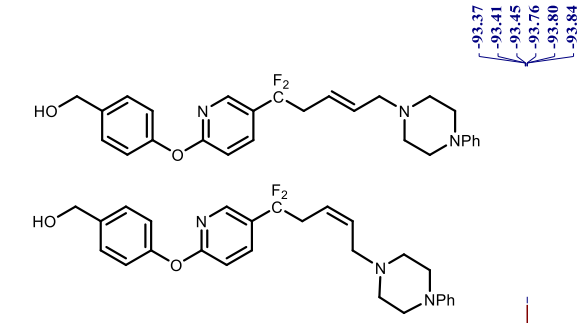




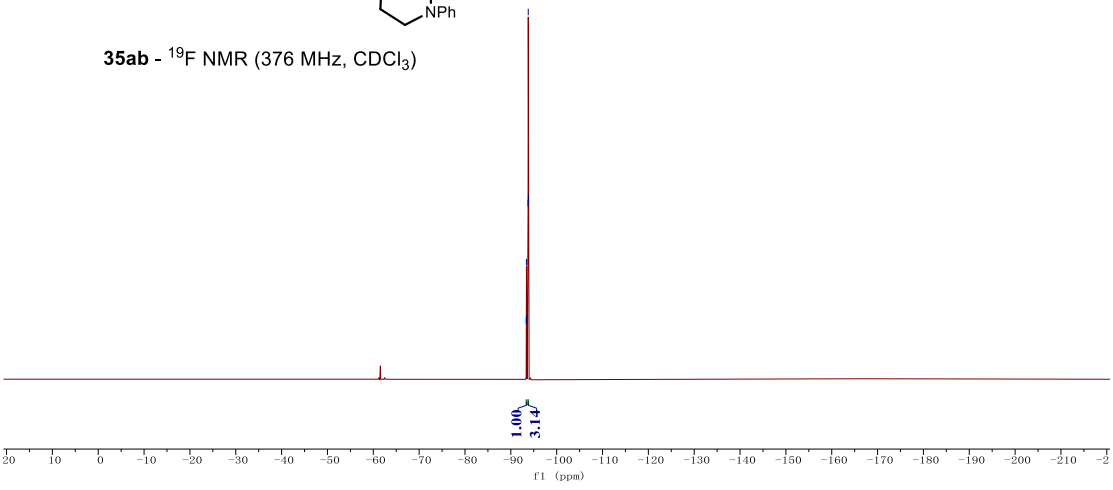
35ab - ^{1}H NMR (400 MHz, $CDCl_3$)

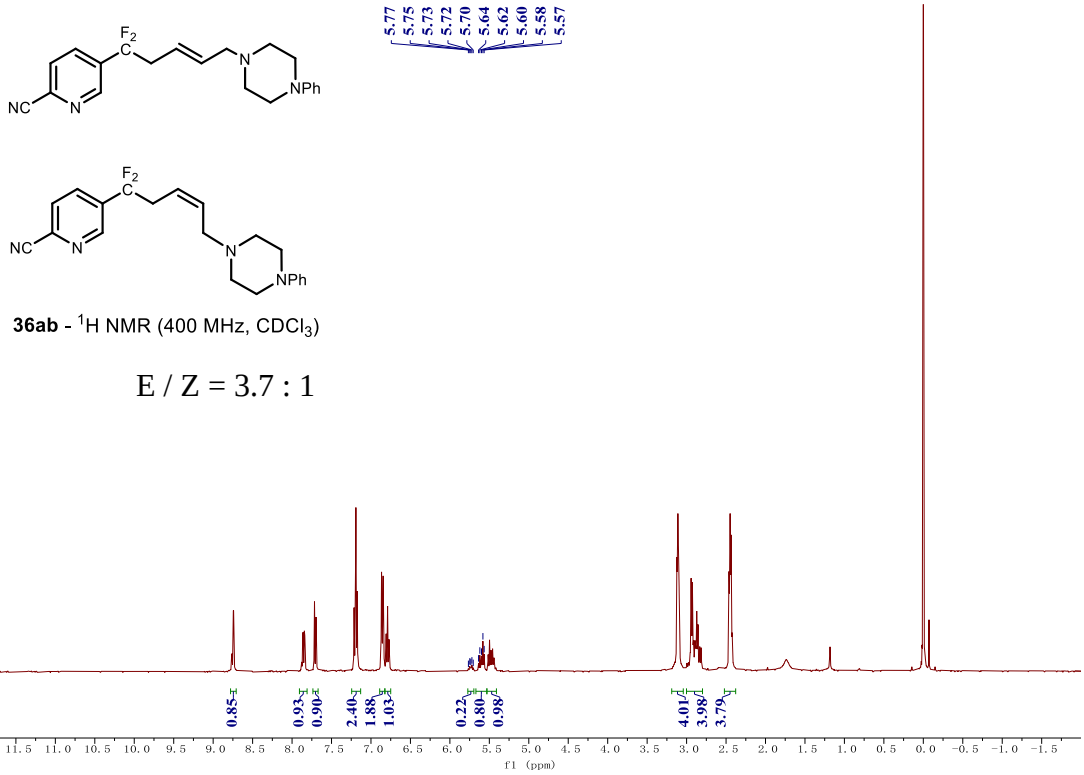
E / Z = 3.1 : 1





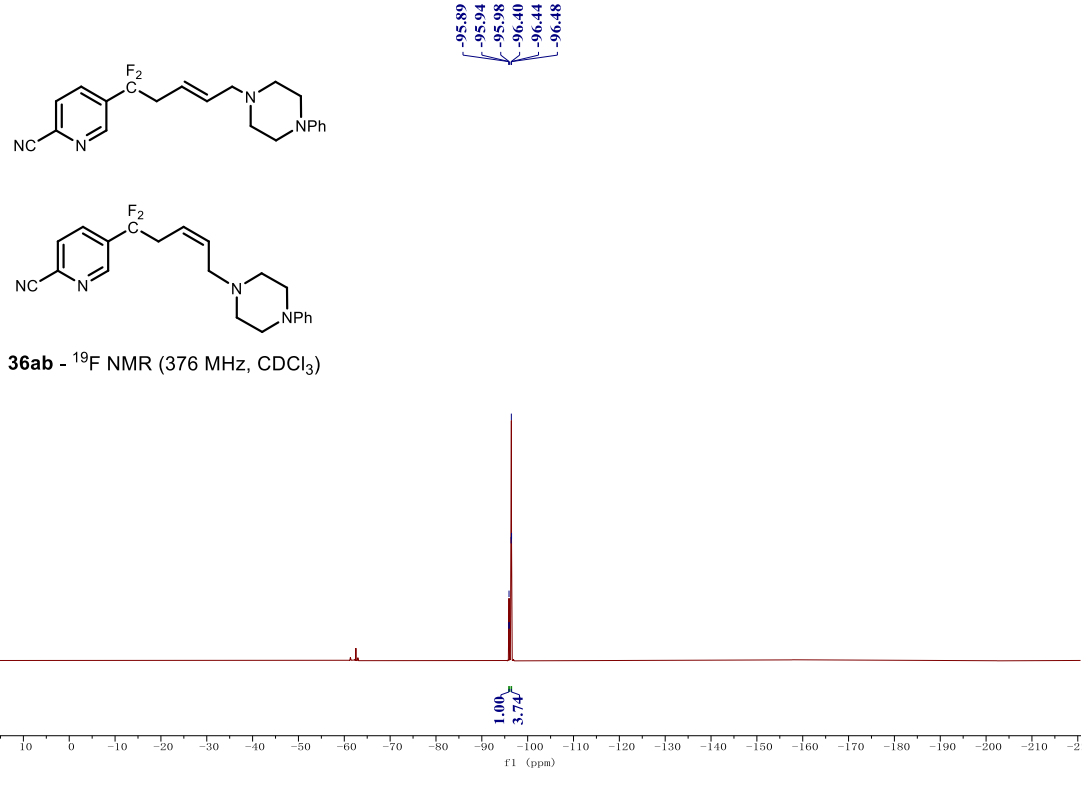
35ab - ^{19}F NMR (376 MHz, $CDCl_3$)



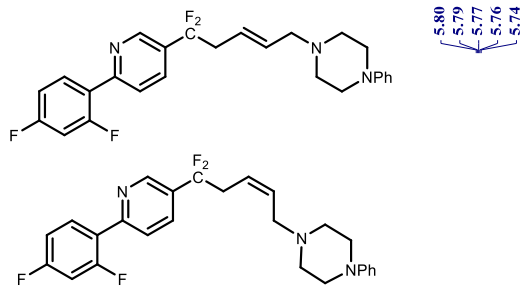


36ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 3.7 : 1

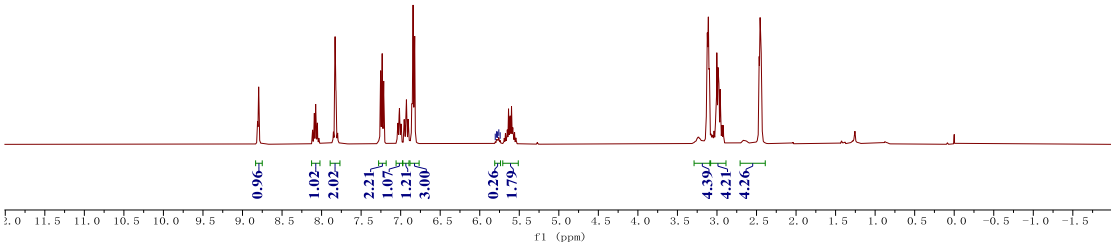


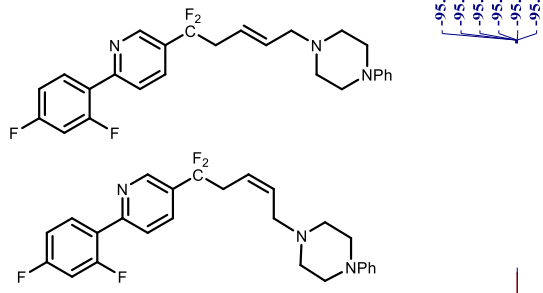
36ab - ^{19}F NMR (376 MHz, $CDCl_3$)



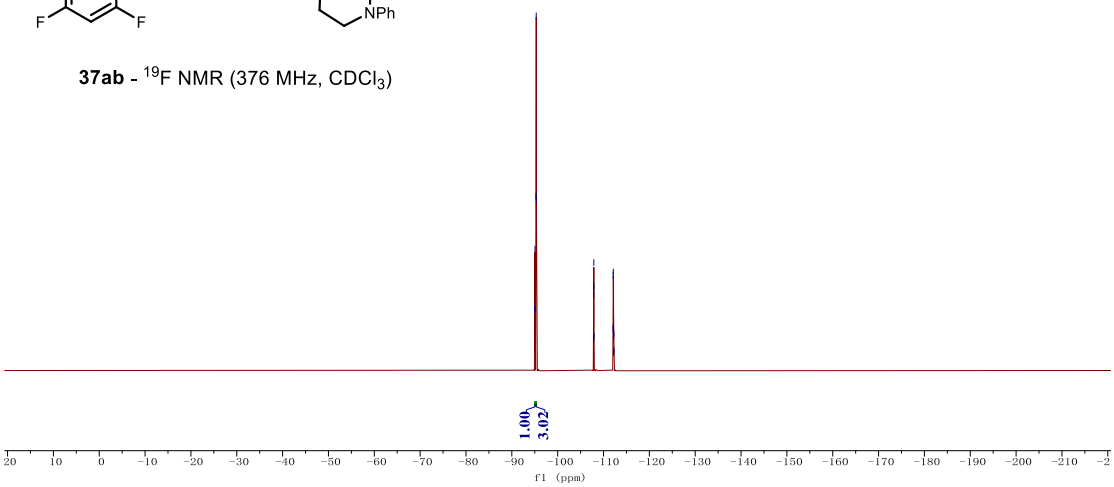
37ab - ^{1}H NMR (400 MHz, $CDCl_3$)

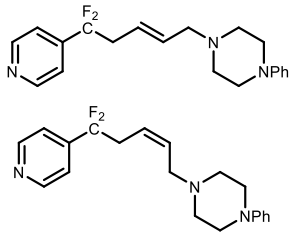
E / Z = 3.0 : 1





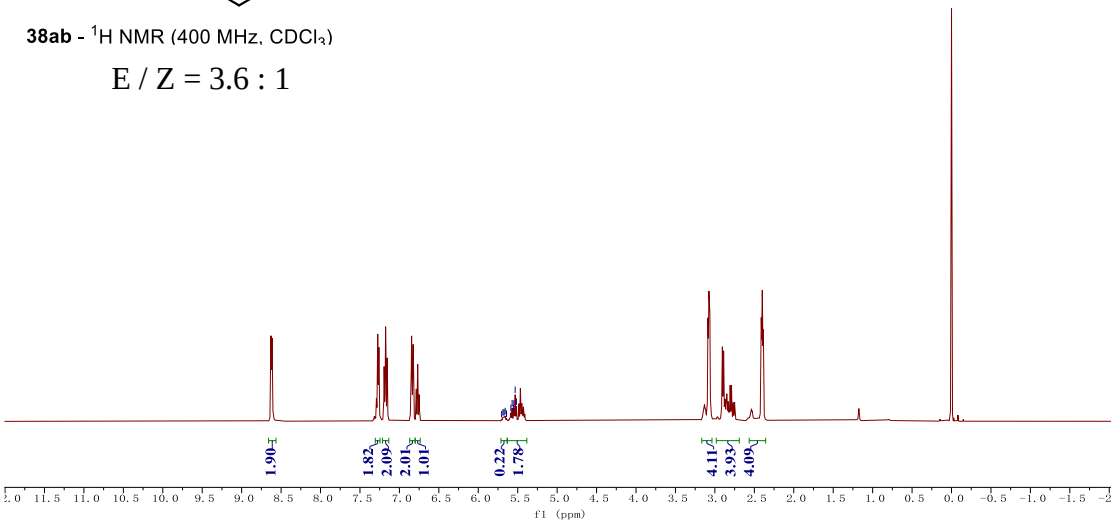
37ab - ^{19}F NMR (376 MHz, $CDCl_3$)

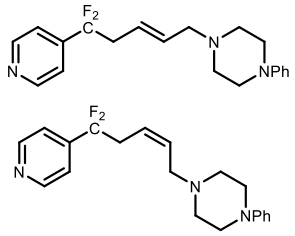




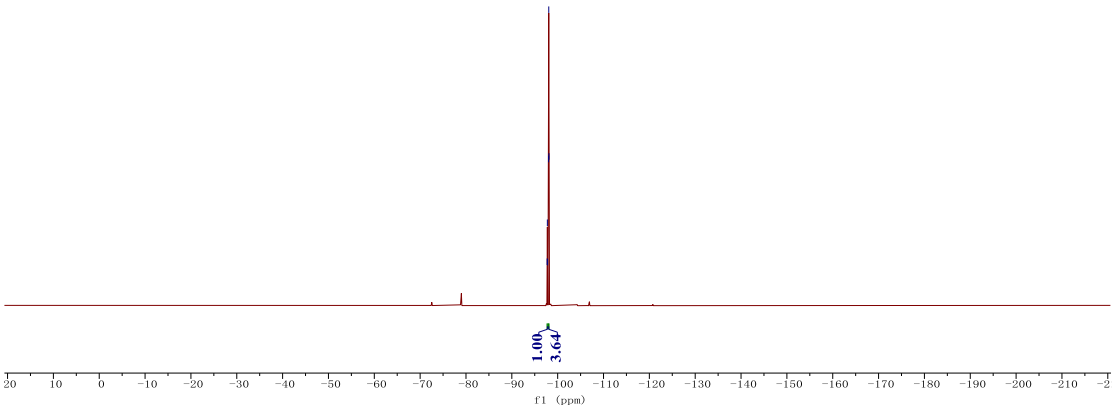
38ab - ^{1}H NMR (400 MHz, $CDCl_3$)

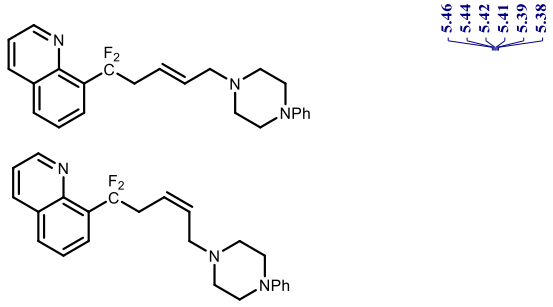
E / Z = 3.6 : 1





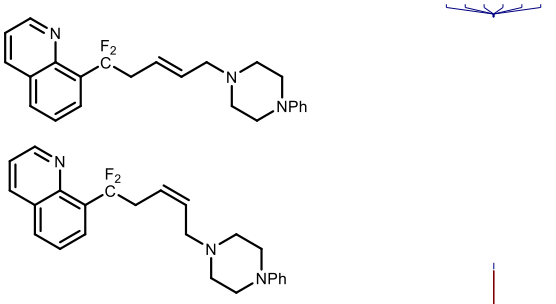
38ab - ^{19}F NMR (376 MHz, $CDCl_3$)



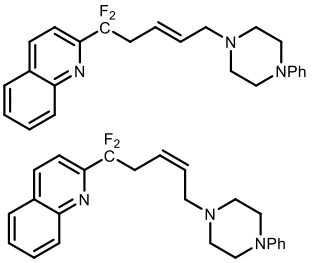


39ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 2.5 : 1

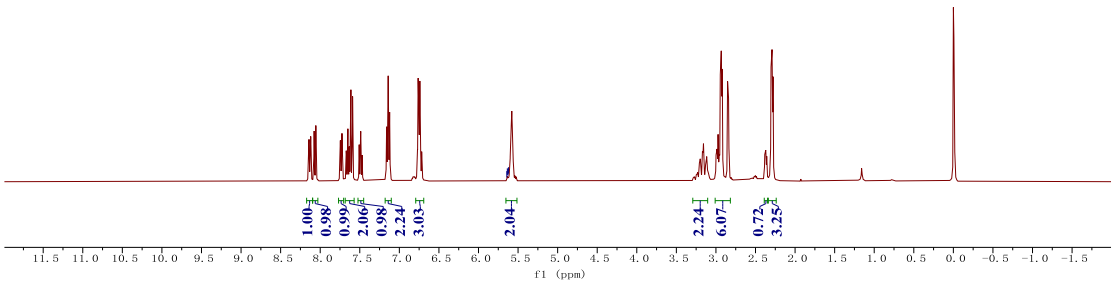


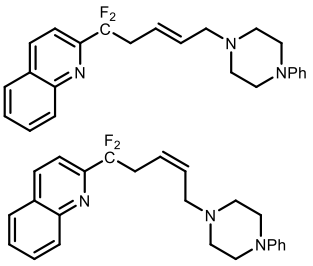
39ab - ^{19}F NMR (376 MHz, $CDCl_3$)



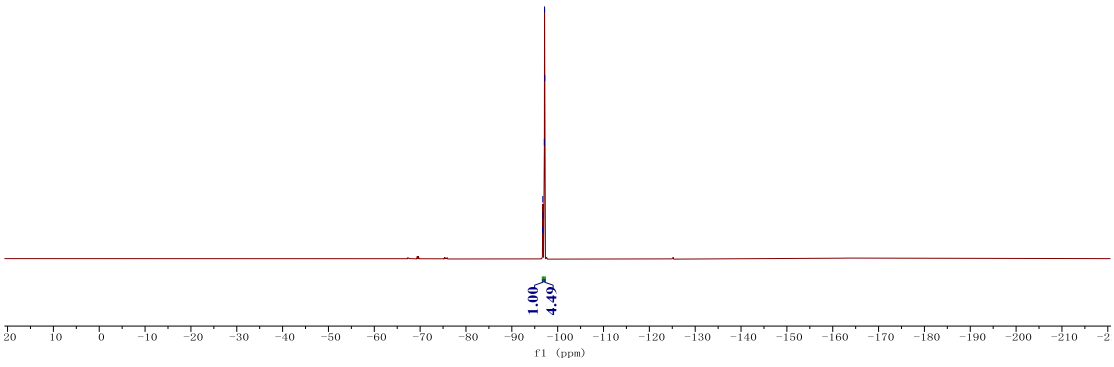
40ab - ^{1}H NMR (400 MHz, $CDCl_3$)

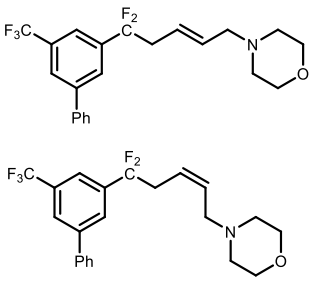
E / Z = 4.5 : 1





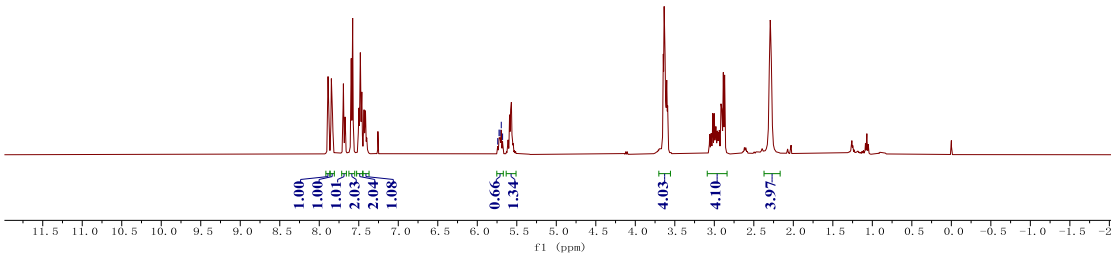
40ab - ^{19}F NMR (376 MHz, $CDCl_3$)

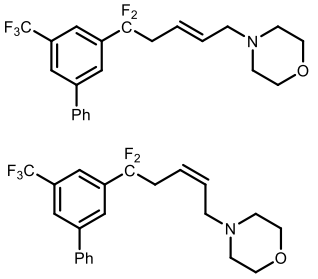




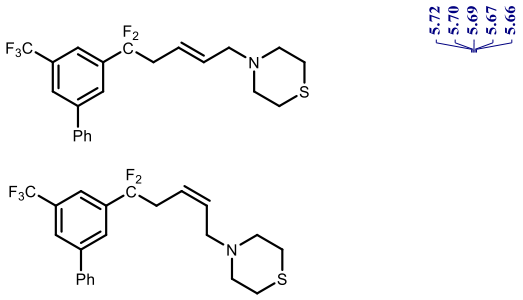
41ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 2.0



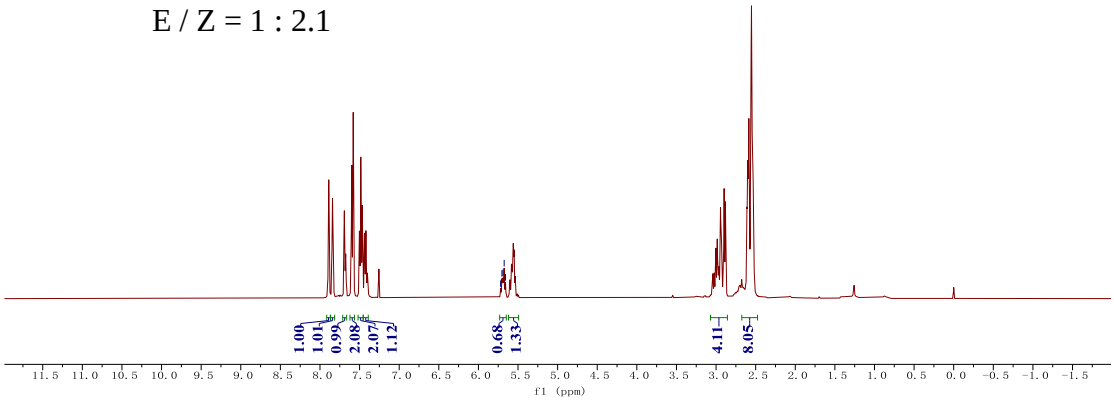


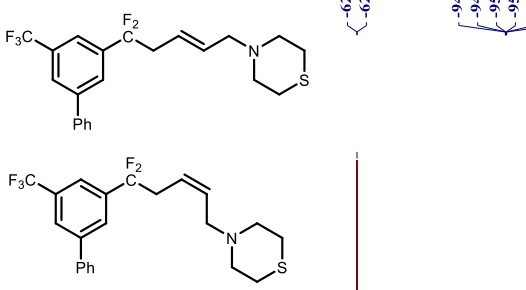
41ab - ^{19}F NMR (376 MHz, $CDCl_3$)



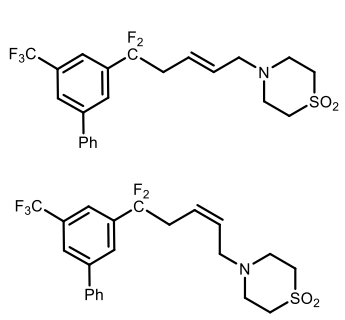
42ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 2.1



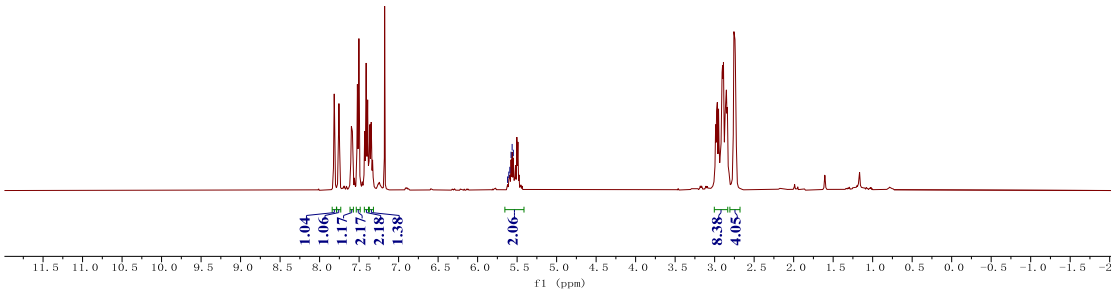


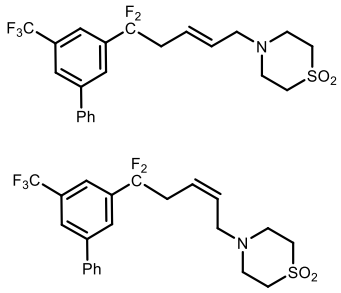
42ab - ^{19}F NMR (376 MHz, $CDCl_3$)



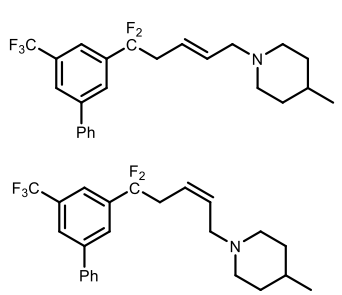
43ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 1.2



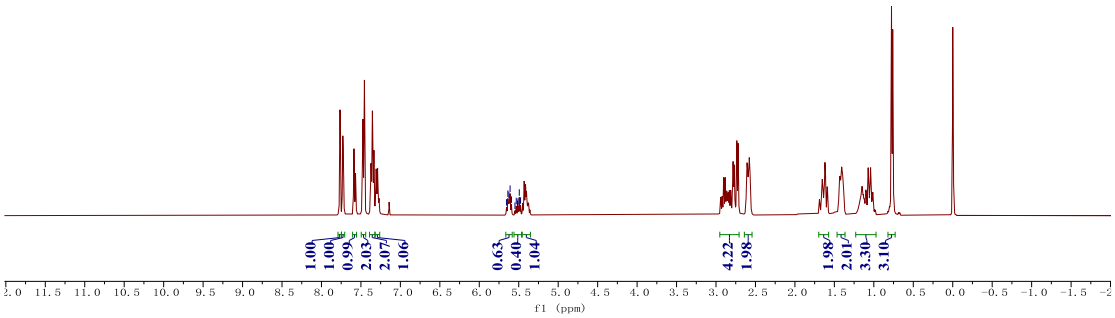


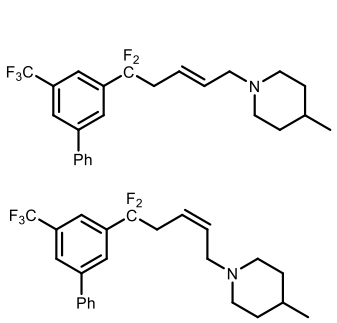
43ab - ^{19}F NMR (376 MHz, $CDCl_3$)



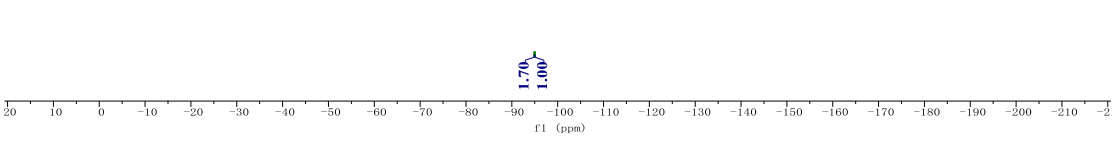
44ab - ^{1}H NMR (400 MHz, $CDCl_3$)

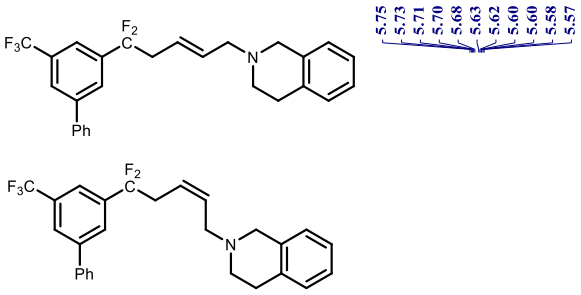
E / Z = 1 : 1.7





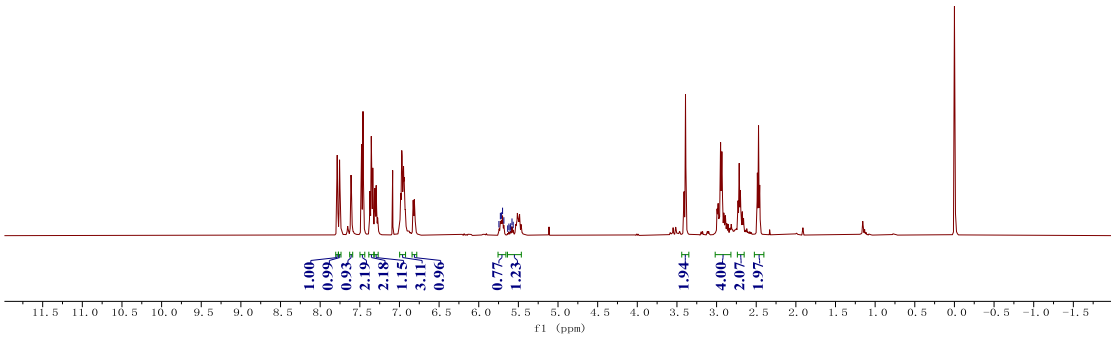
44ab - ^{19}F NMR (376 MHz, $CDCl_3$)

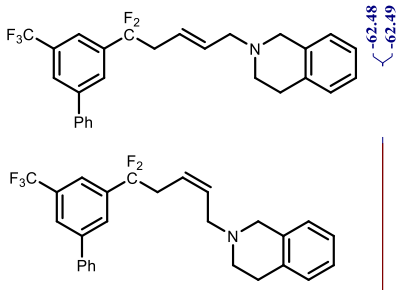




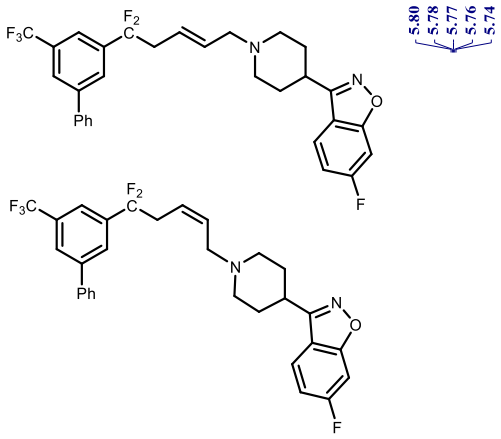
45ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 3.3



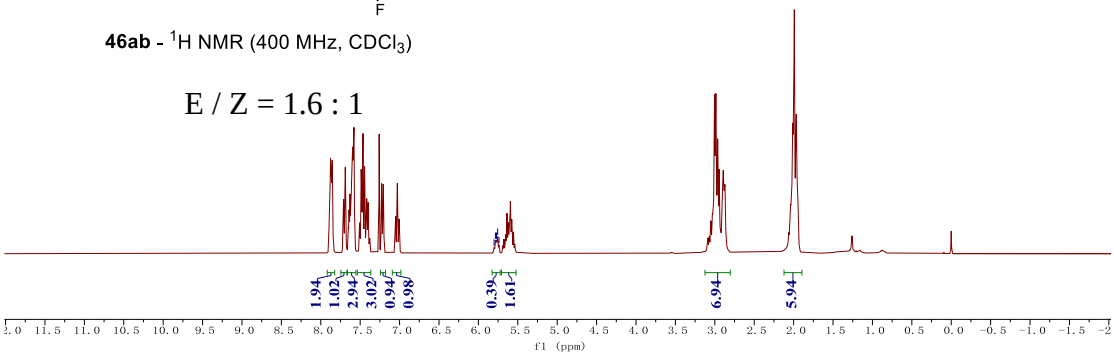


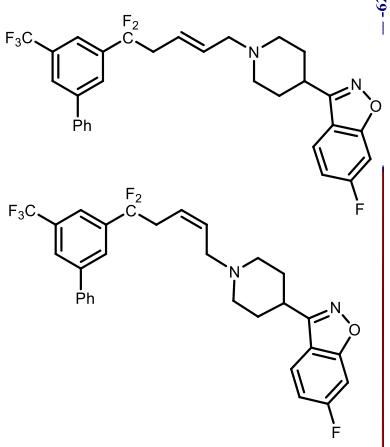
45ab - ^{19}F NMR (376 MHz, $CDCl_3$)



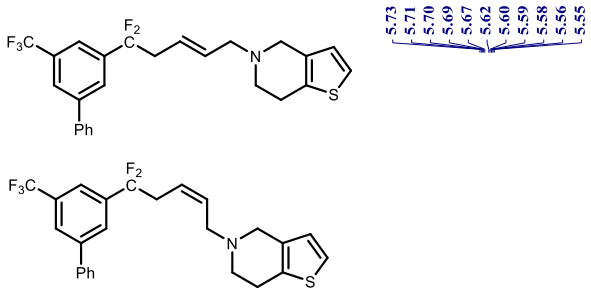
46ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1.6 : 1



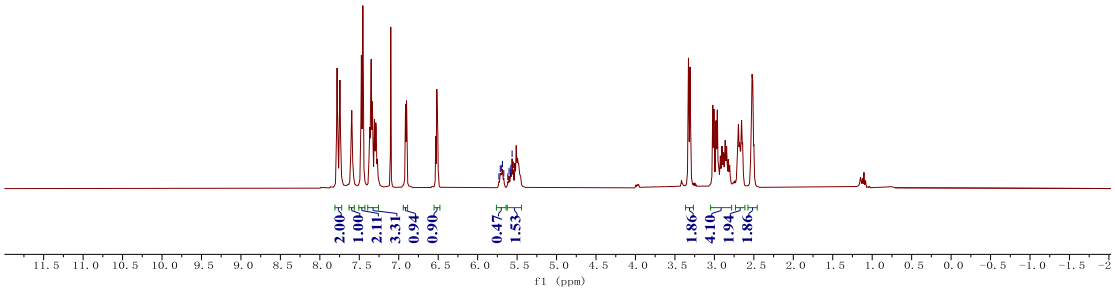


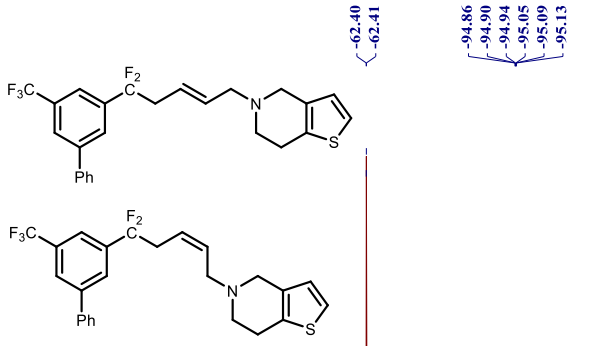
46ab- ^{19}F NMR (376 MHz, $CDCl_3$)



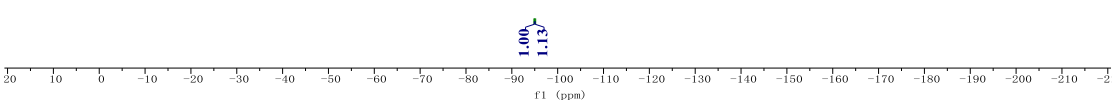
47ab - ^{1}H NMR (400 MHz, $CDCl_3$)

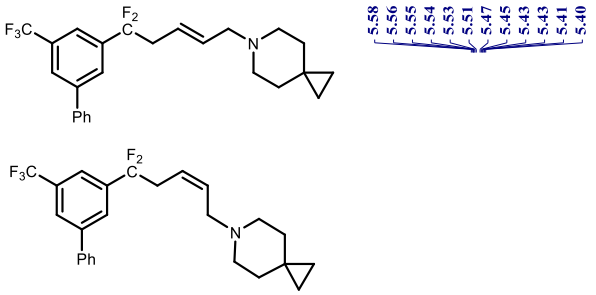
E / Z = 1.2 : 1





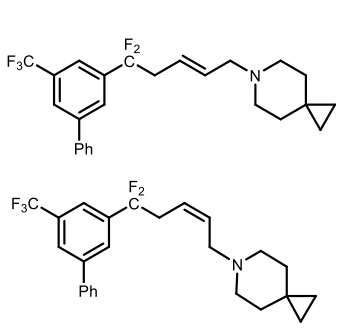
47ab - ^{19}F NMR (376 MHz, $CDCl_3$)



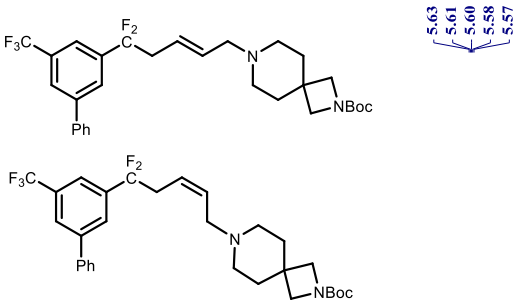


48ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1.5 : 1

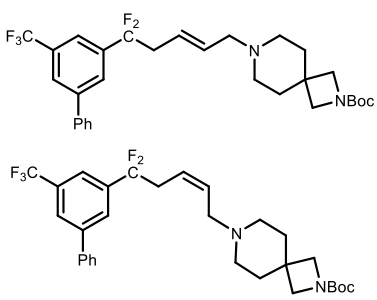


48ab - ^{19}F NMR (376 MHz, $CDCl_3$)

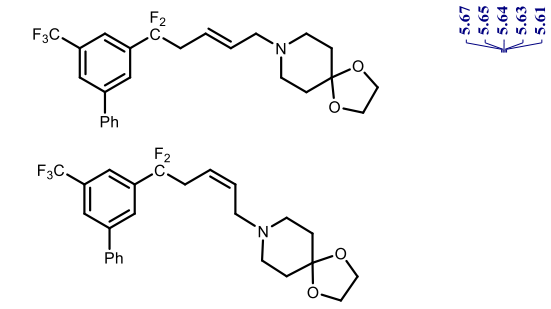


49ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 2.4

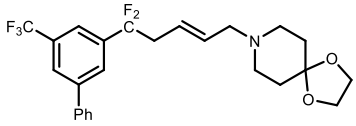


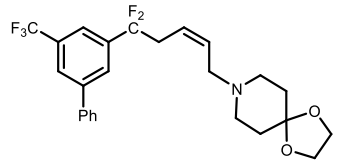
49ab - ^{19}F NMR (376 MHz, $CDCl_3$)



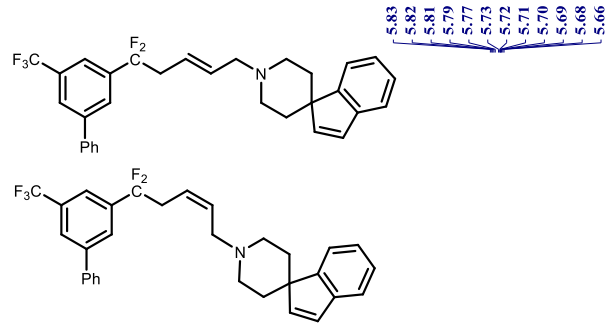
50ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 3.0



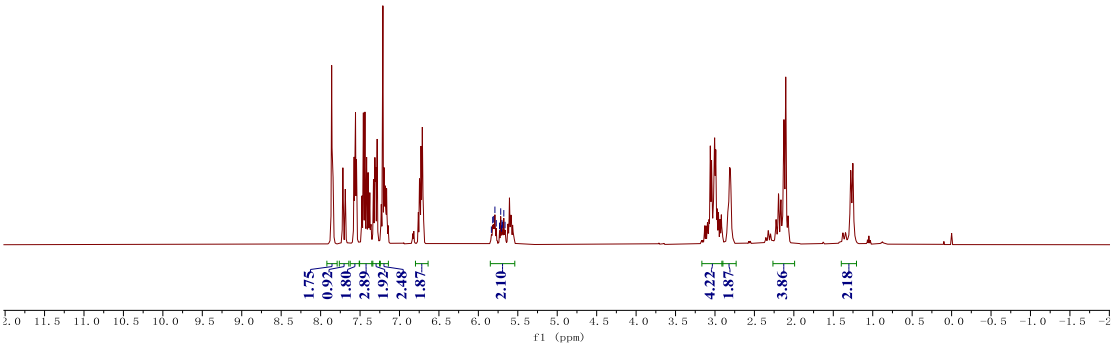


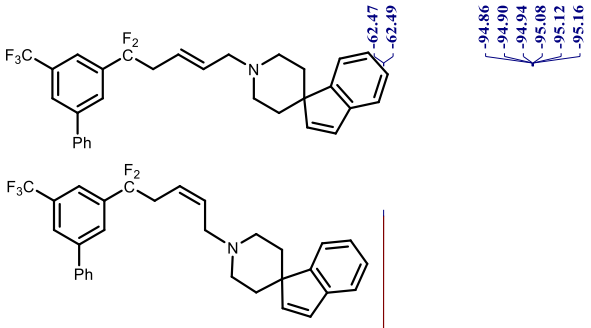
50ab - ^{19}F NMR (376 MHz, $CDCl_3$)



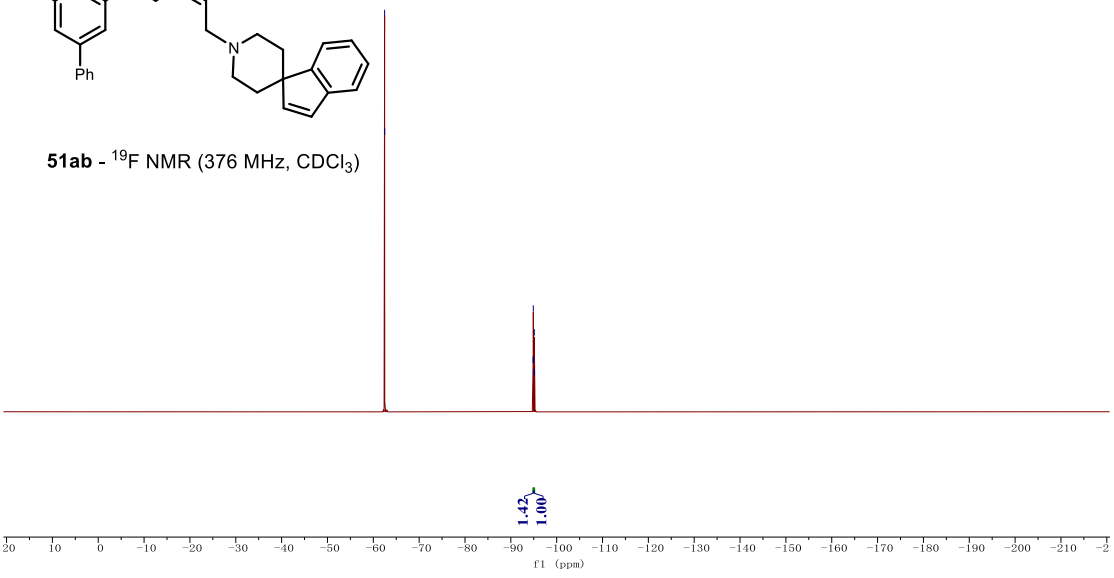
51ab - ^{1}H NMR (400 MHz, $CDCl_3$)

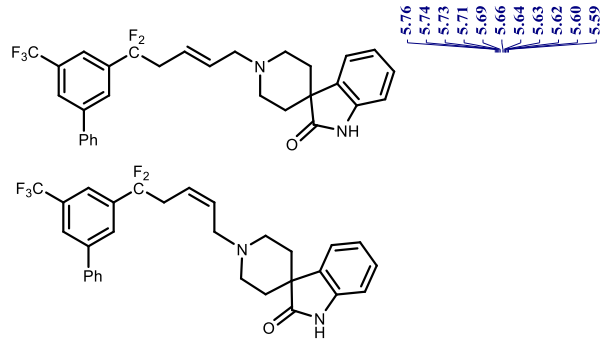
E / Z = 1 : 1.4





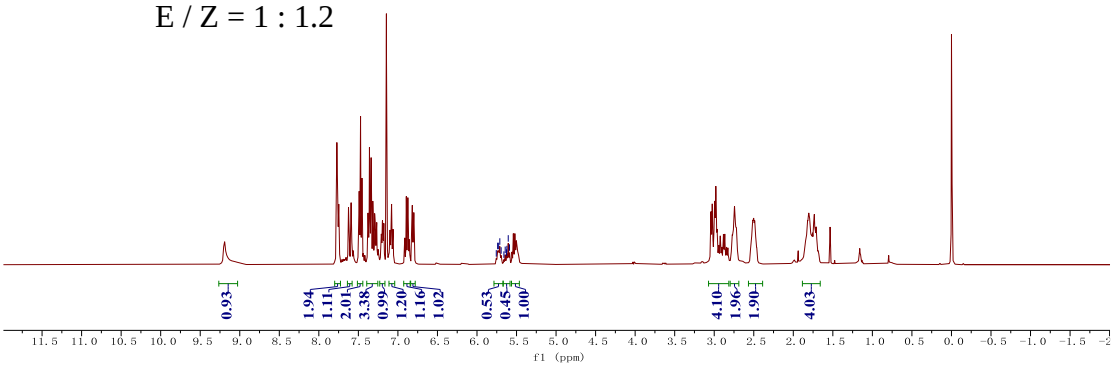
51ab - ^{19}F NMR (376 MHz, $CDCl_3$)

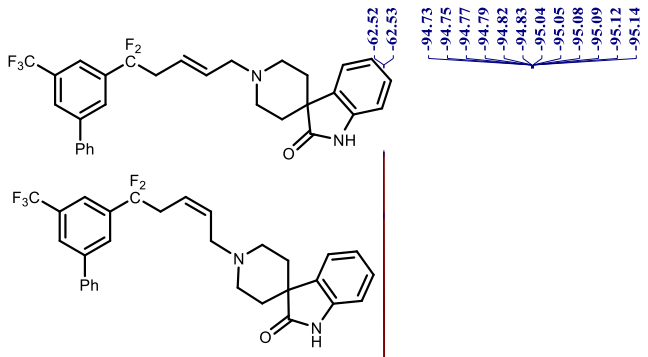




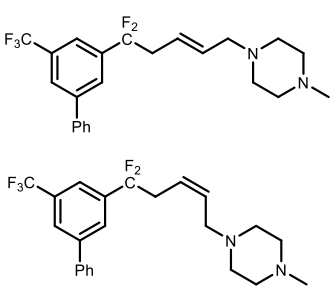
52ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 1.2



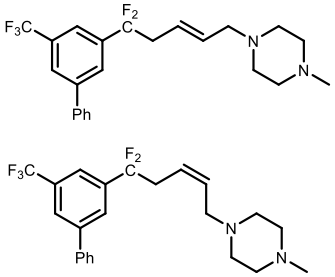


52ab - ^{19}F NMR (376 MHz, $CDCl_3$)

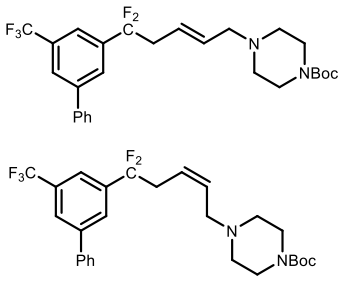


53ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 2.4

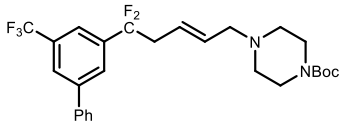


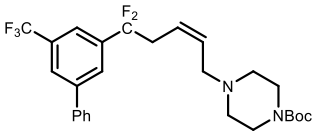
53ab - ^{19}F NMR (376 MHz, $CDCl_3$)



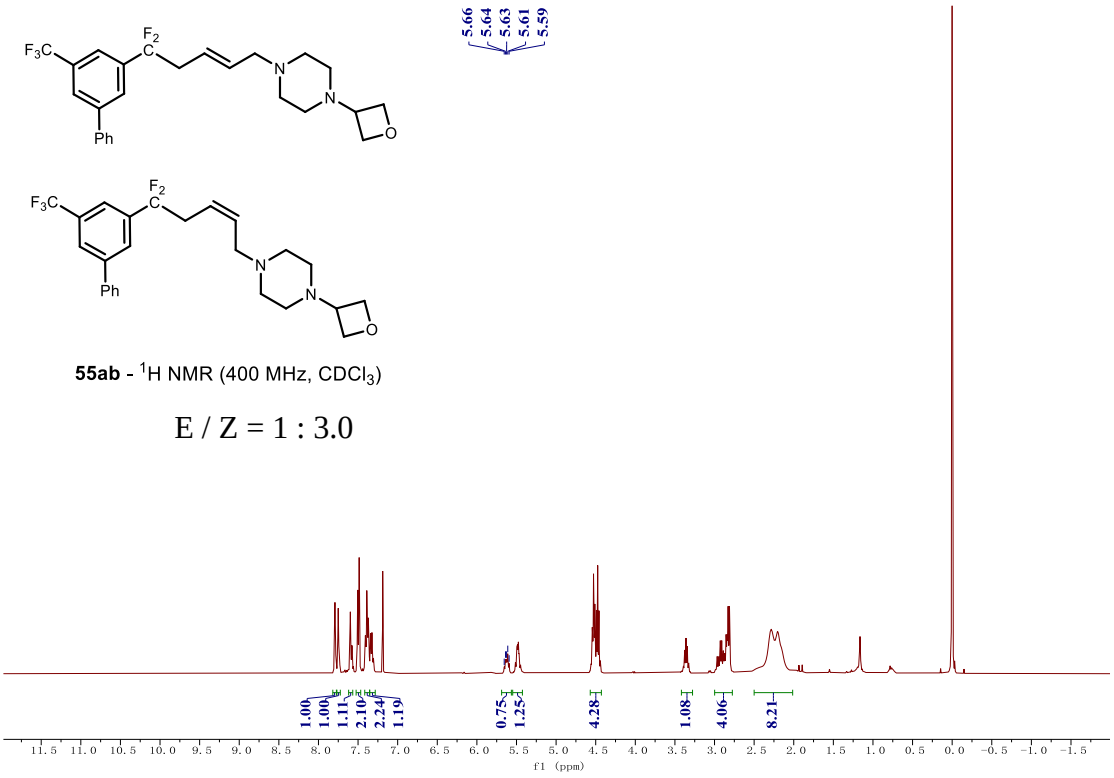
54ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 2.3



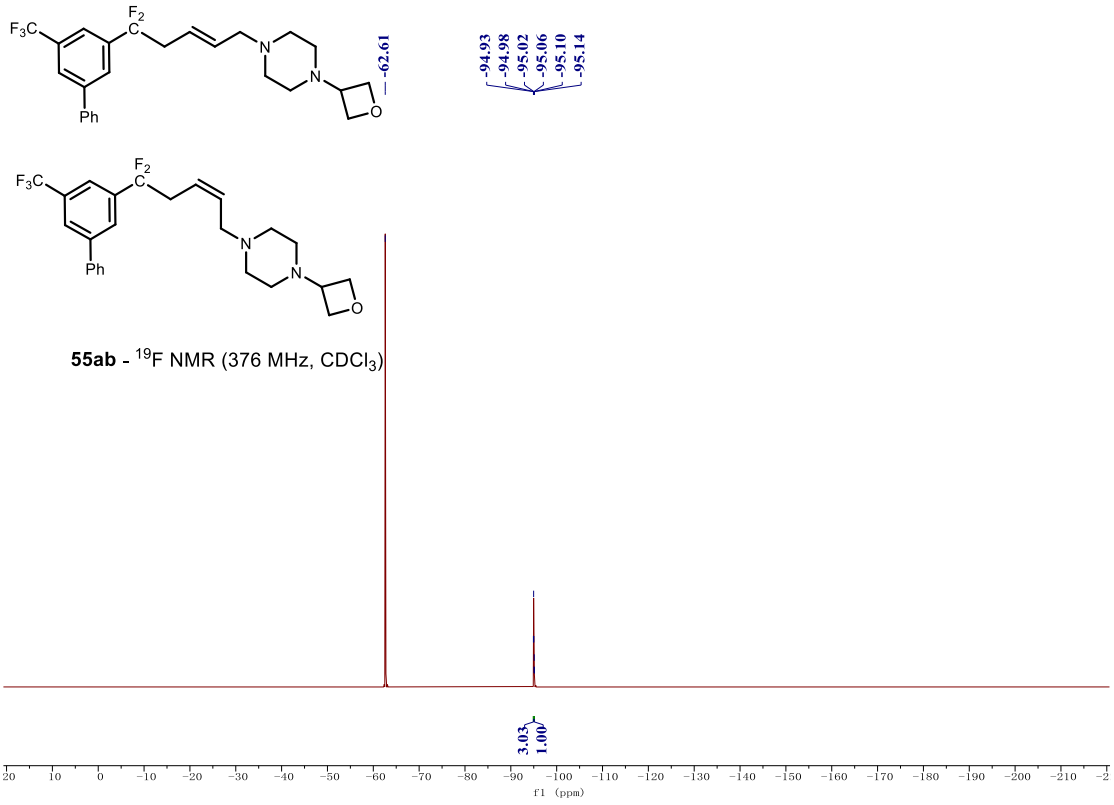


54ab - ^{19}F NMR (376 MHz, $CDCl_3$)

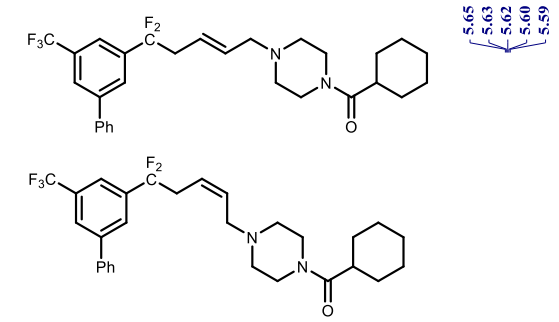


55ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 3.0

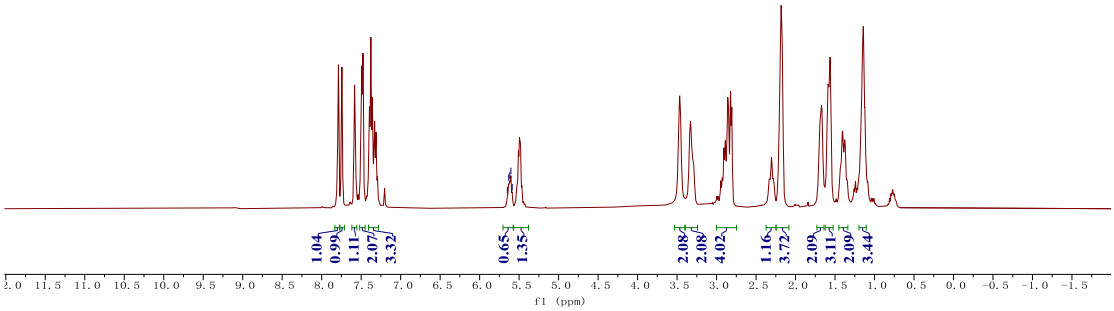


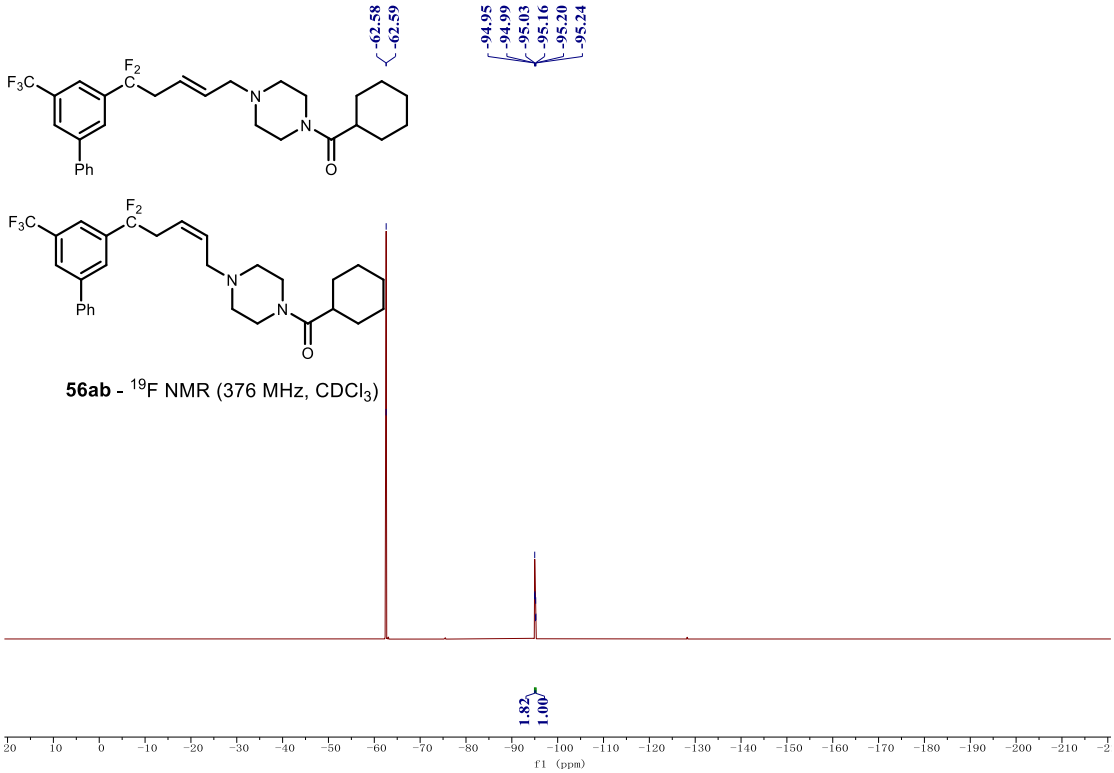
55ab - ^{19}F NMR (376 MHz, $CDCl_3$)



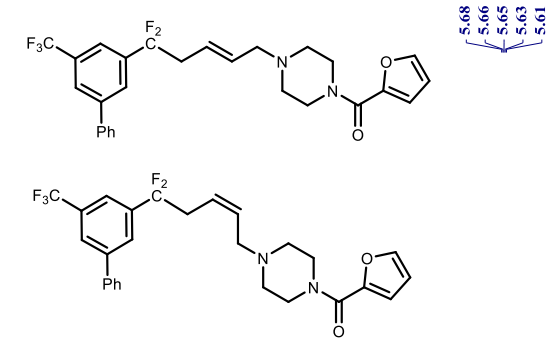
56ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 1.8



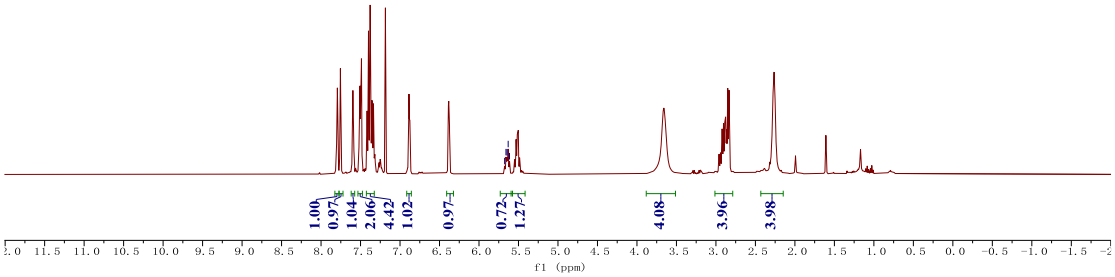


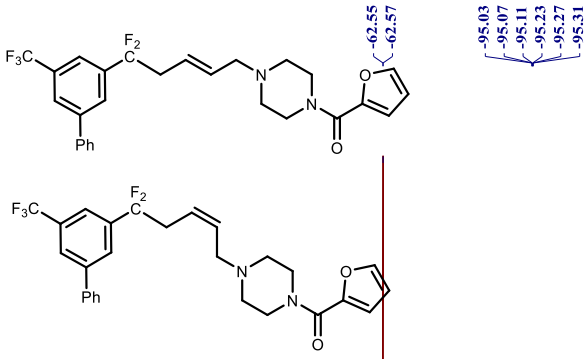
56ab - ^{19}F NMR (376 MHz, $CDCl_3$)

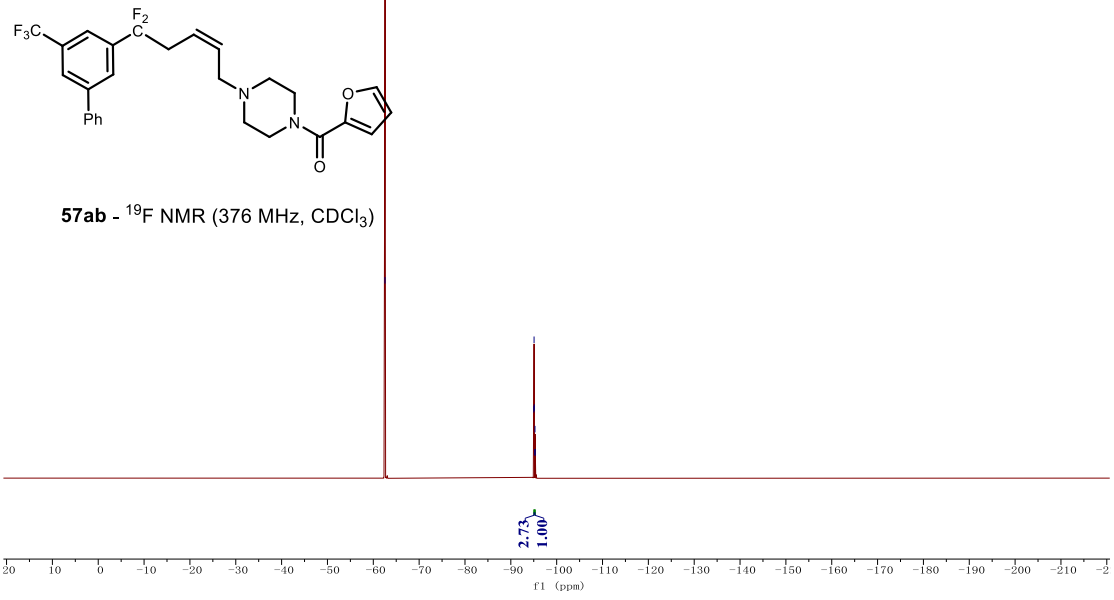


57ab - ^{1}H NMR (400 MHz, $CDCl_3$)

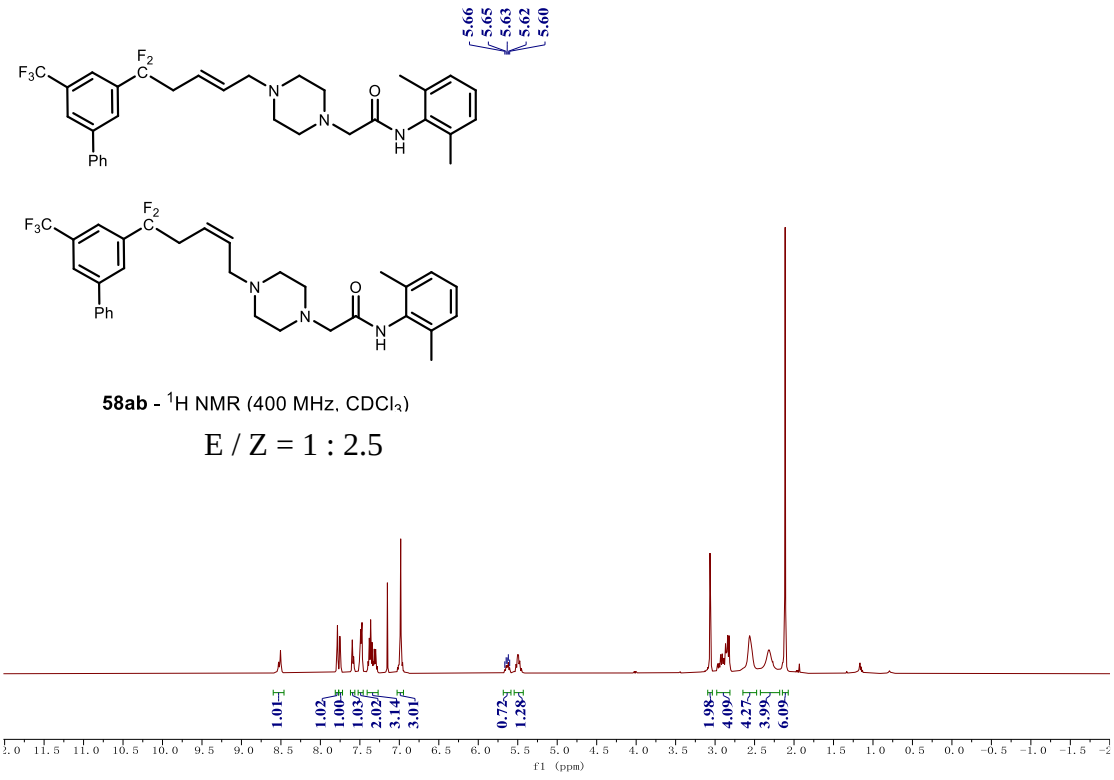
E / Z = 1 : 2.7





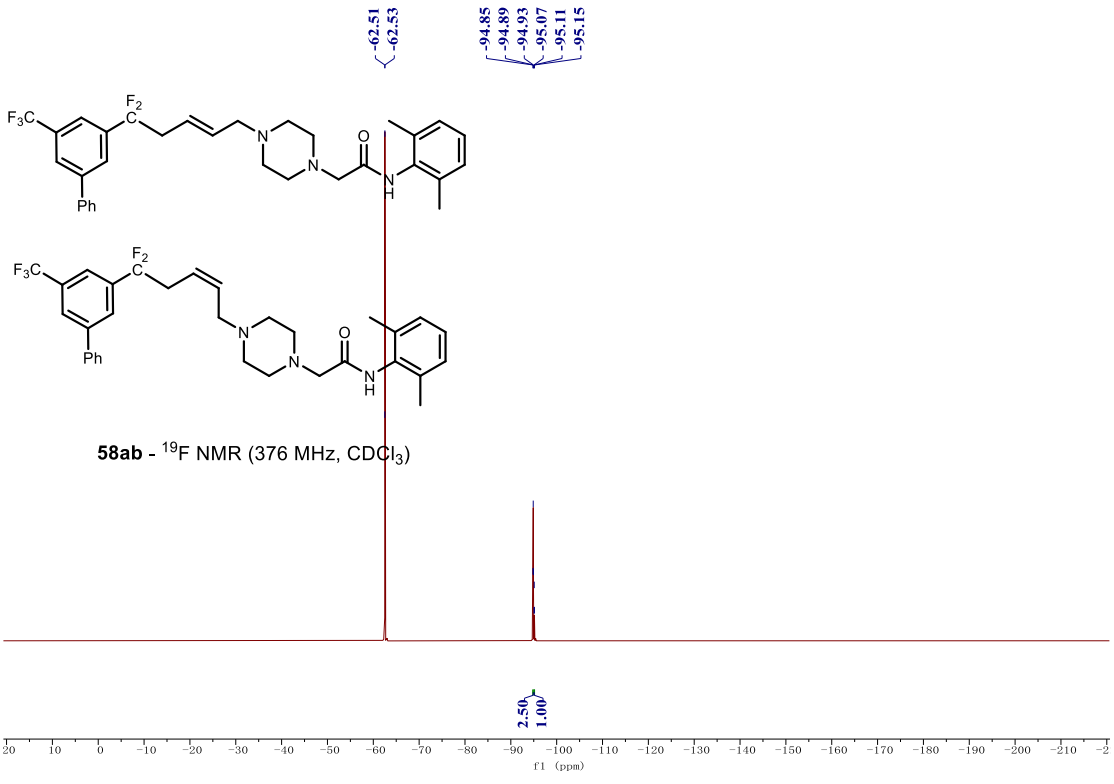


57ab - ^{19}F NMR (376 MHz, $CDCl_3$)

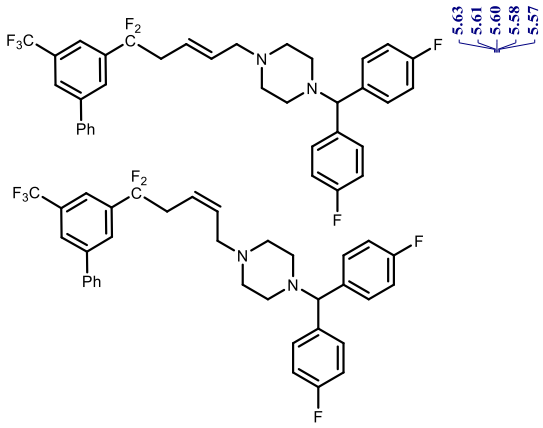


58ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 2.5

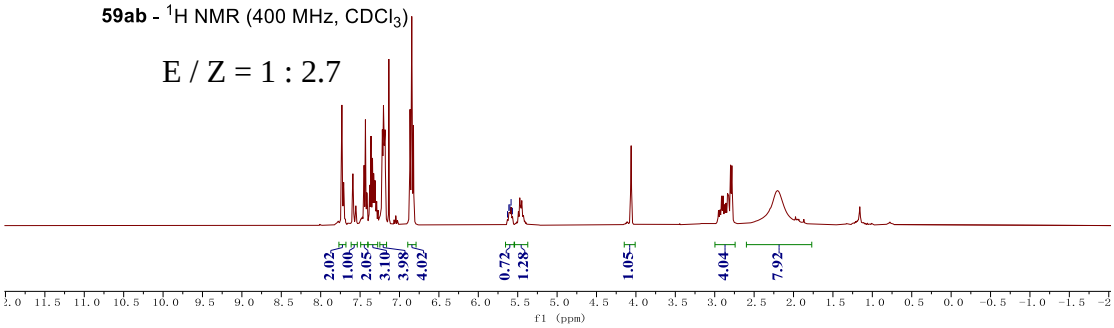


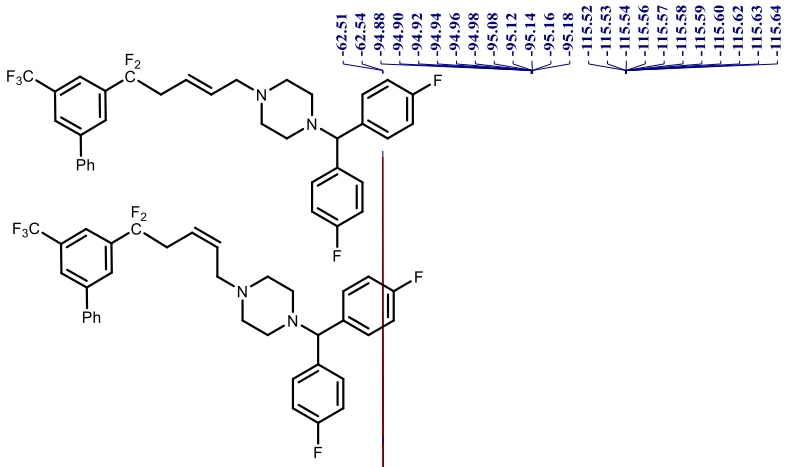
58ab - ^{19}F NMR (376 MHz, $CDCl_3$)



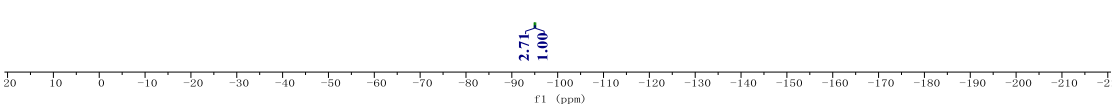
59ab - ^{1}H NMR (400 MHz, $CDCl_3$)

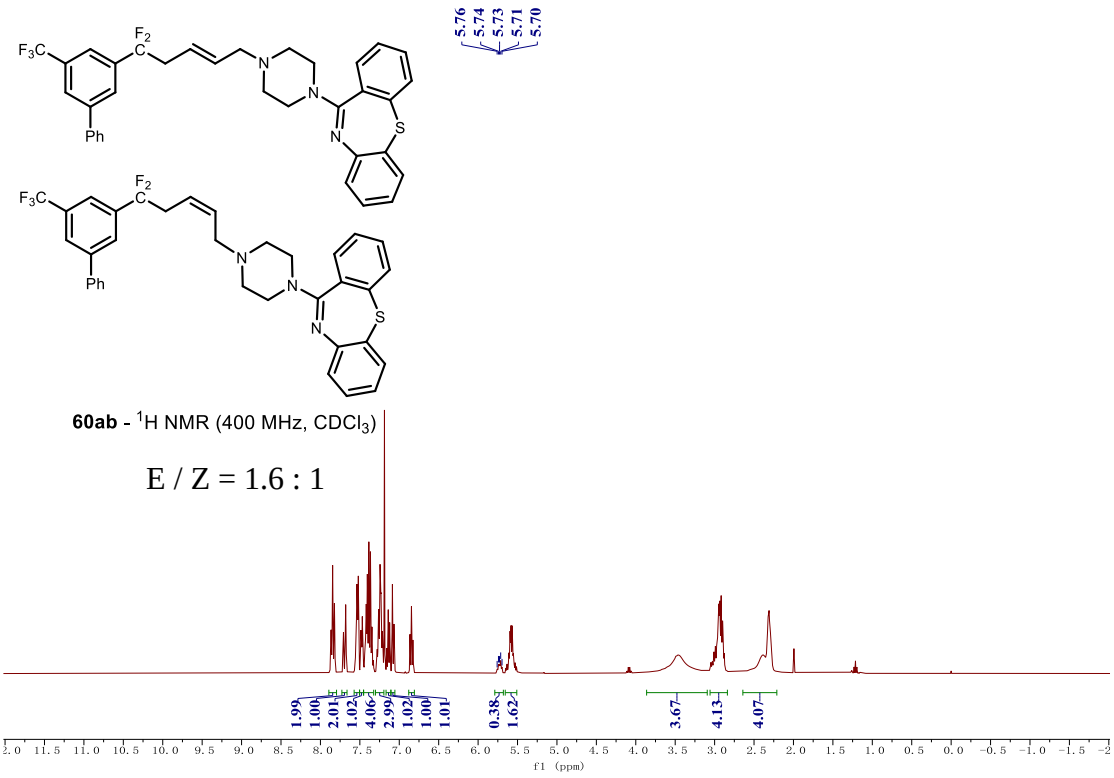
E / Z = 1 : 2.7





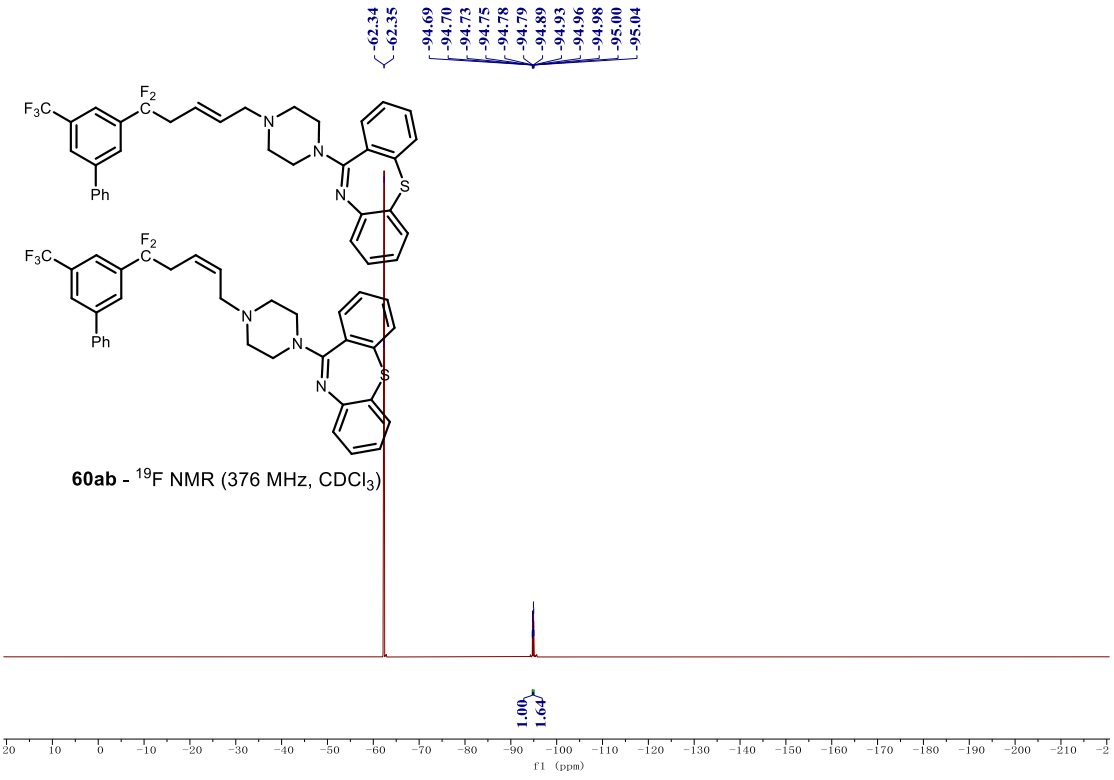
59ab - ^{19}F NMR (376 MHz, $CDCl_3$)



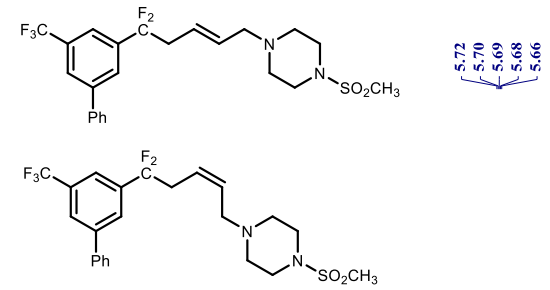


60ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1.6 : 1

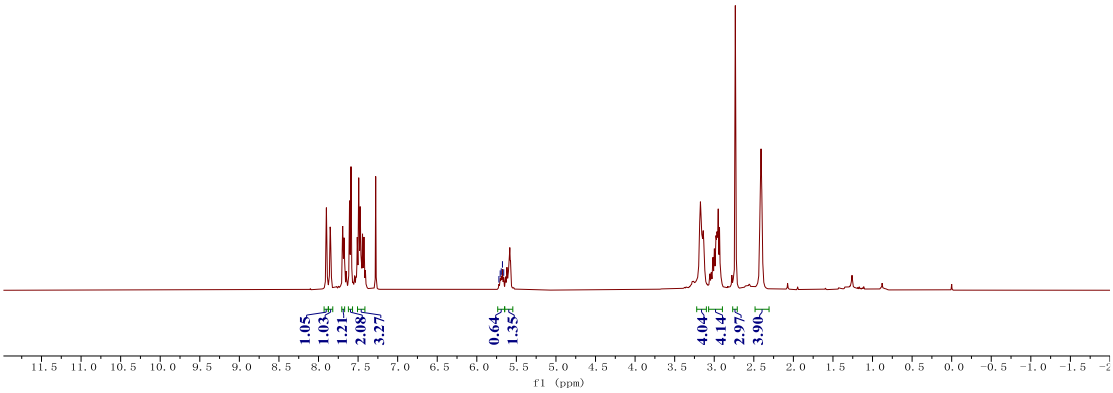


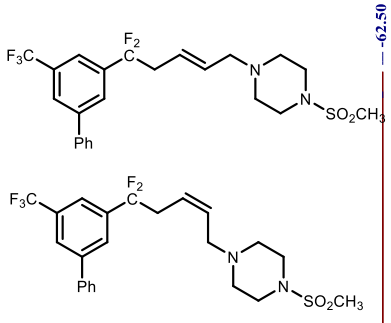
60ab - ^{19}F NMR (376 MHz, $CDCl_3$)



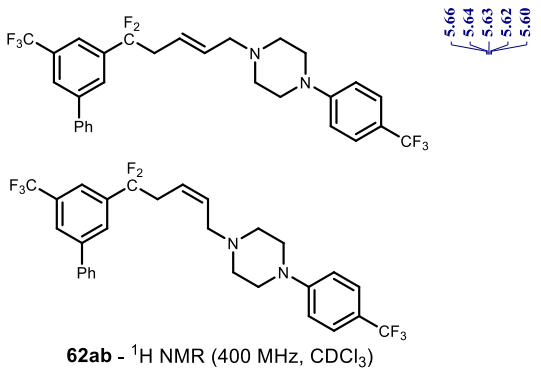
61ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 1.9



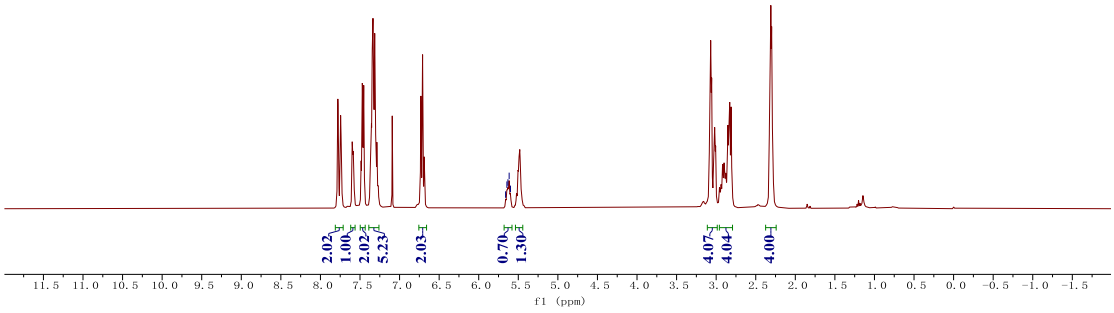


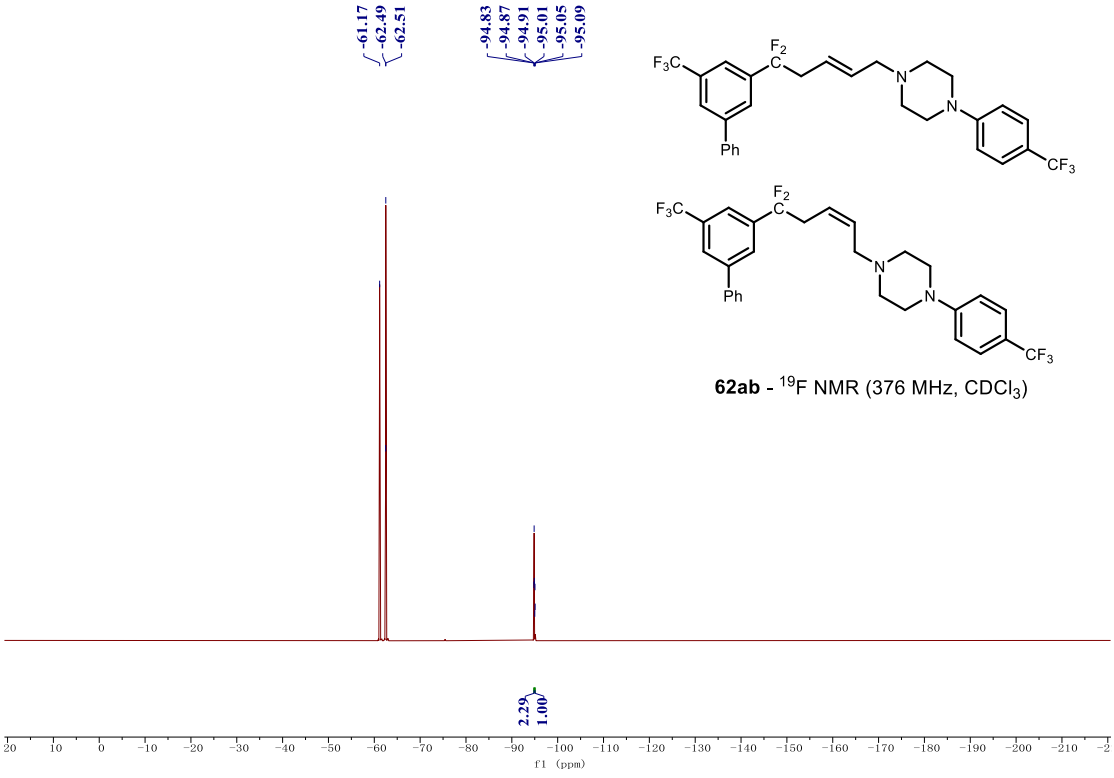
61ab - ^{19}F NMR (376 MHz, $CDCl_3$)



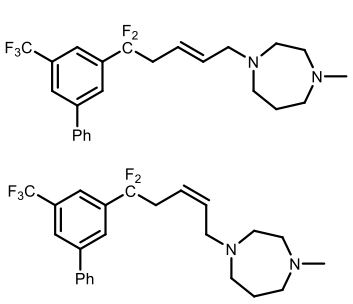
62ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 2.3



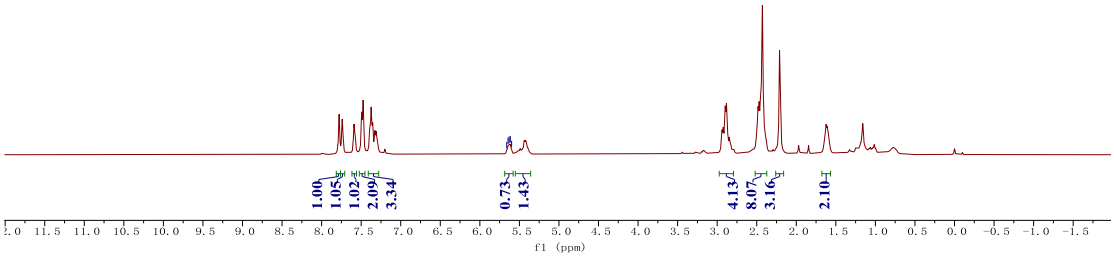


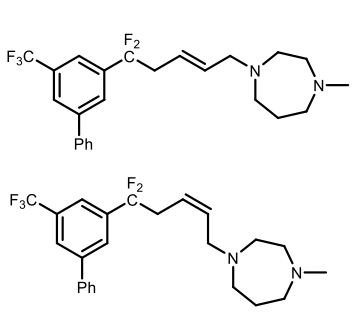
62ab - ^{19}F NMR (376 MHz, $CDCl_3$)

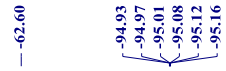


63ab - ^{1}H NMR (400 MHz, $CDCl_3$)

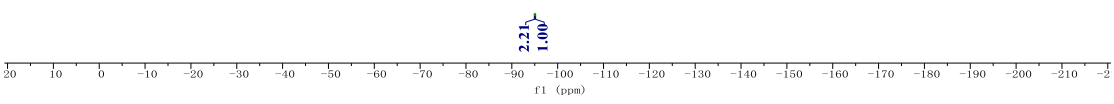
E / Z = 1 : 2.2

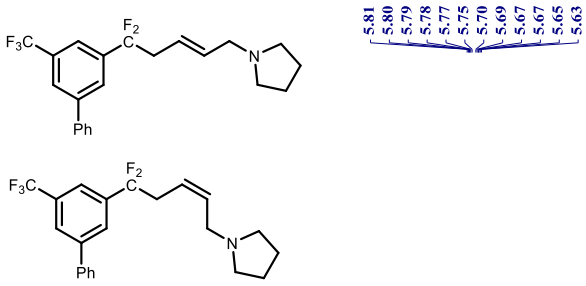






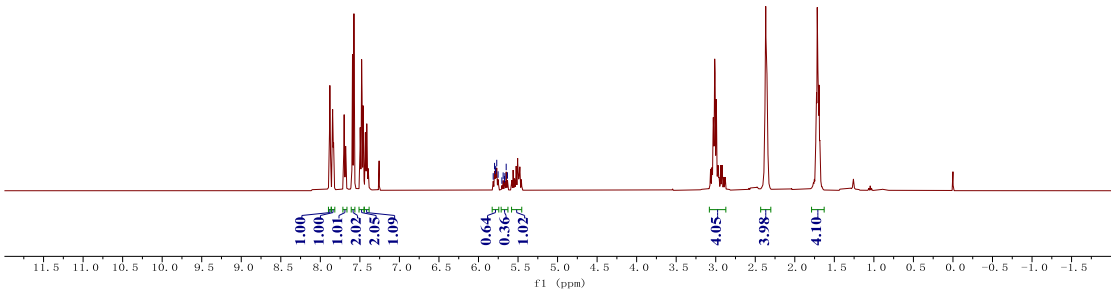
63ab - ^{19}F NMR (376 MHz, $CDCl_3$)

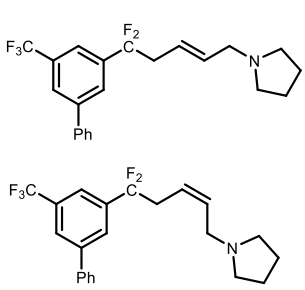




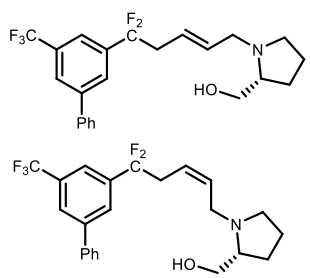
64ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 1.8



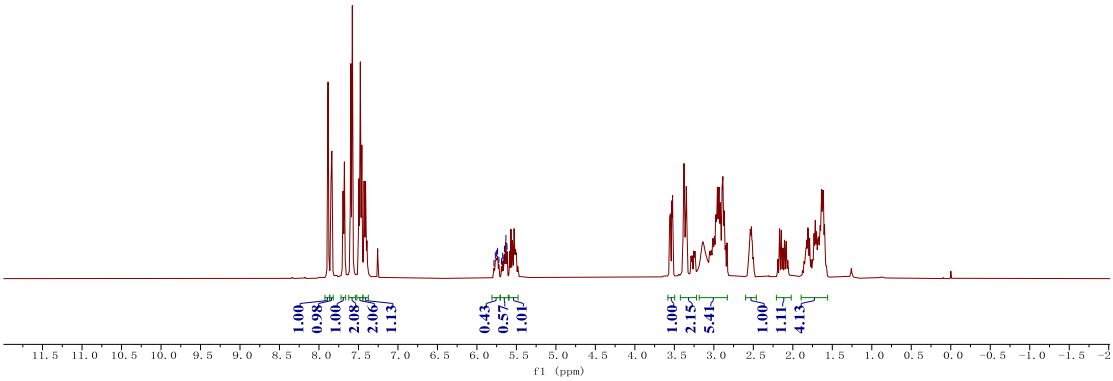


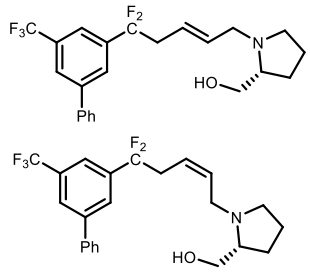
64ab - ^{19}F NMR (376 MHz, $CDCl_3$)



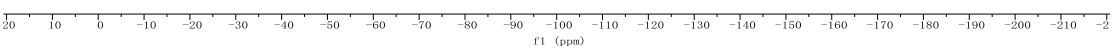
65ab - ^{1}H NMR (400 MHz, $CDCl_3$)

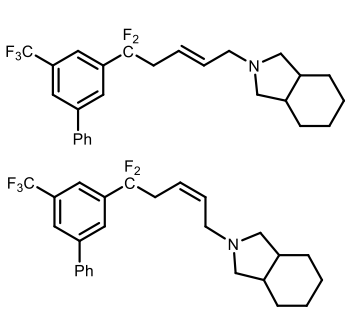
E / Z = 1.3 : 1





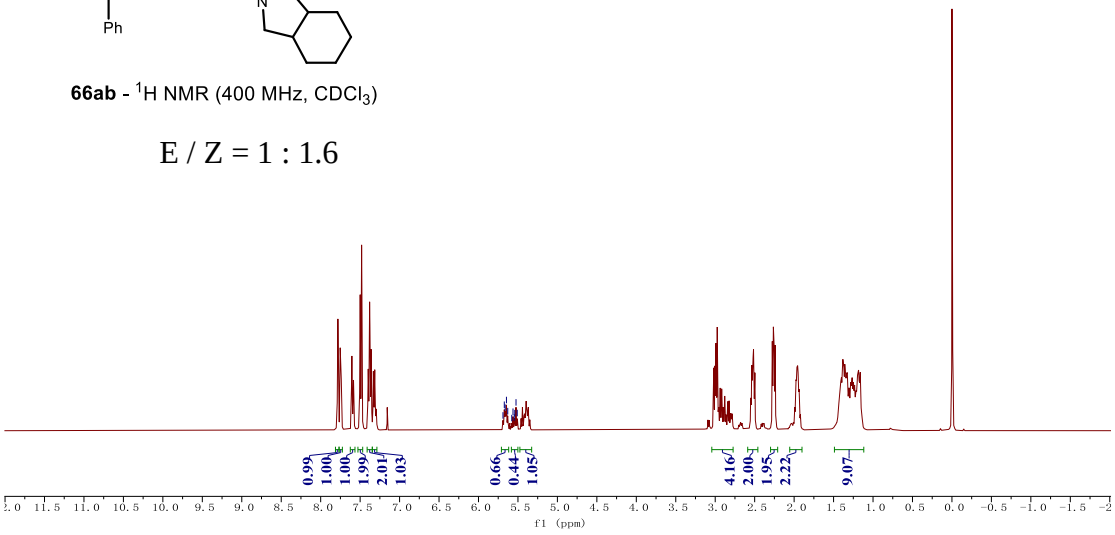
65ab - ^{19}F NMR (376 MHz, $CDCl_3$)

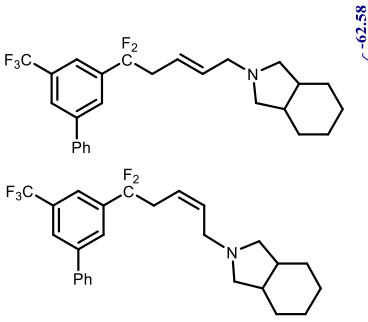




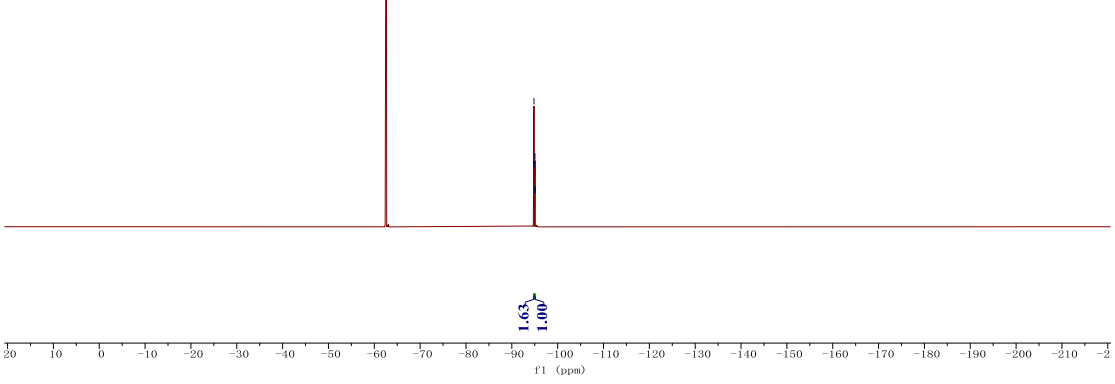
66ab - ^{1}H NMR (400 MHz, $CDCl_3$)

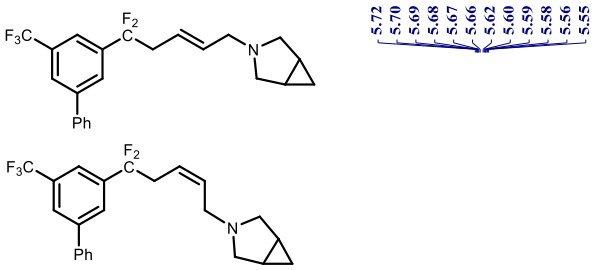
E / Z = 1 : 1.6





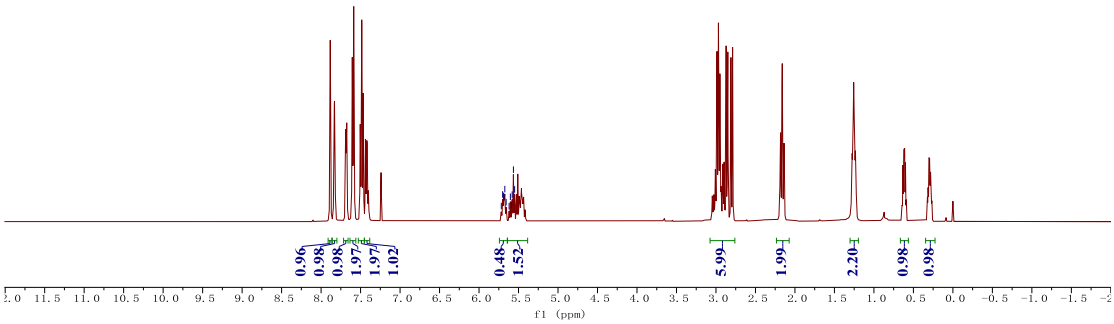
66ab - ^{19}F NMR (376 MHz, $CDCl_3$)

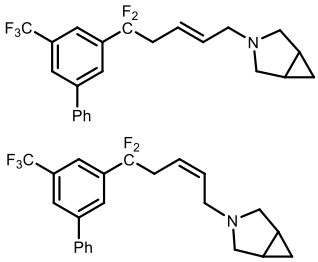




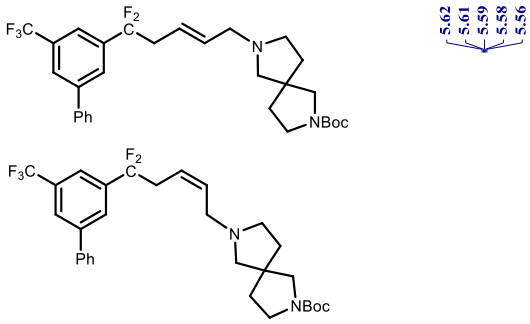
67ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1.1 : 1



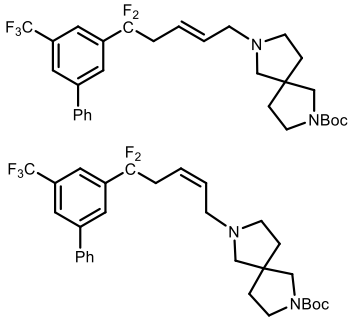


67ab - ^{19}F NMR (376 MHz, $CDCl_3$)

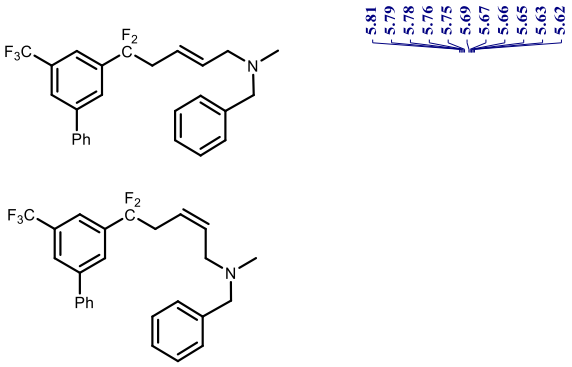


68ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 3.0

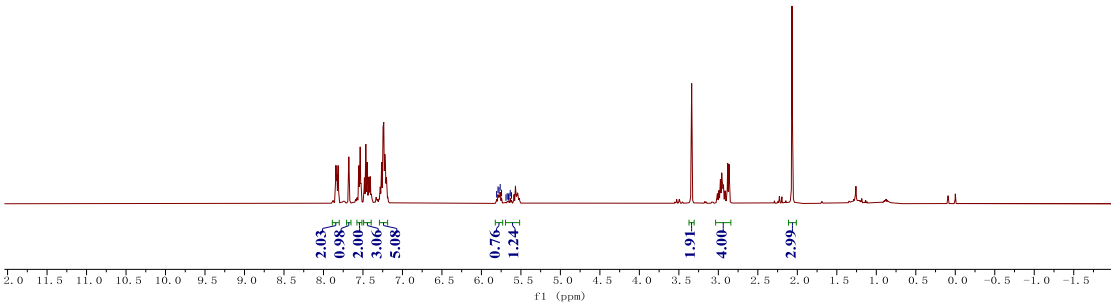


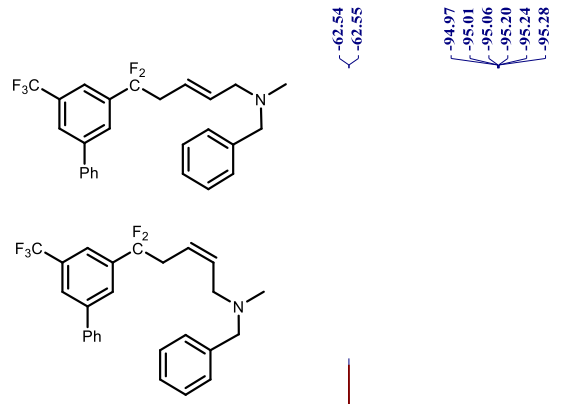
68ab - ^{19}F NMR (376 MHz, $CDCl_3$)



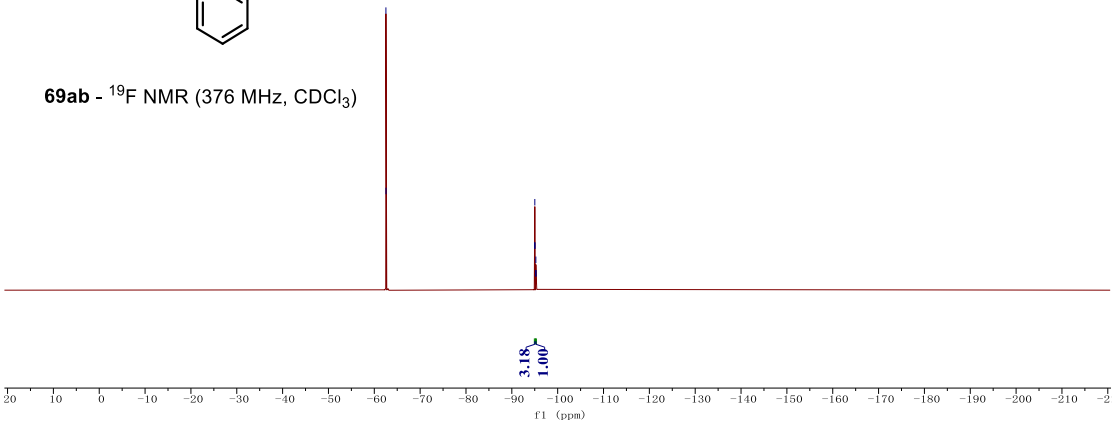
69ab - ^{1}H NMR (400 MHz, $CDCl_3$)

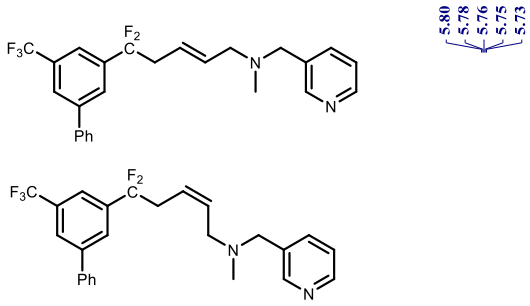
E / Z = 1 : 3.2





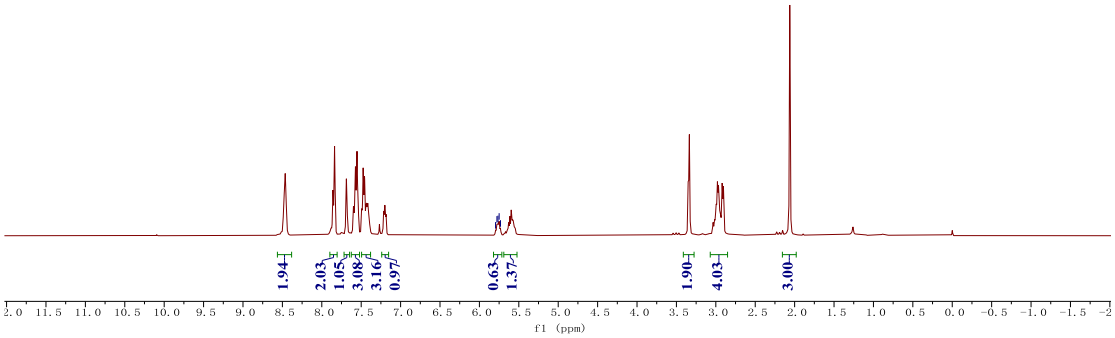
69ab - ^{19}F NMR (376 MHz, $CDCl_3$)

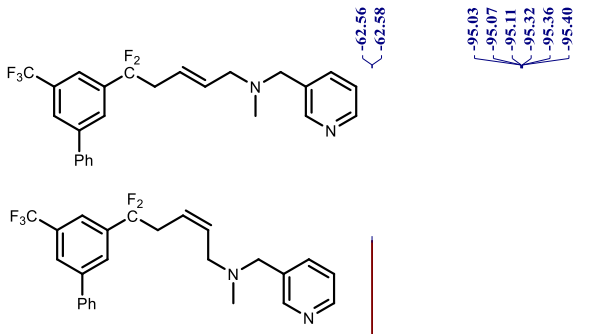


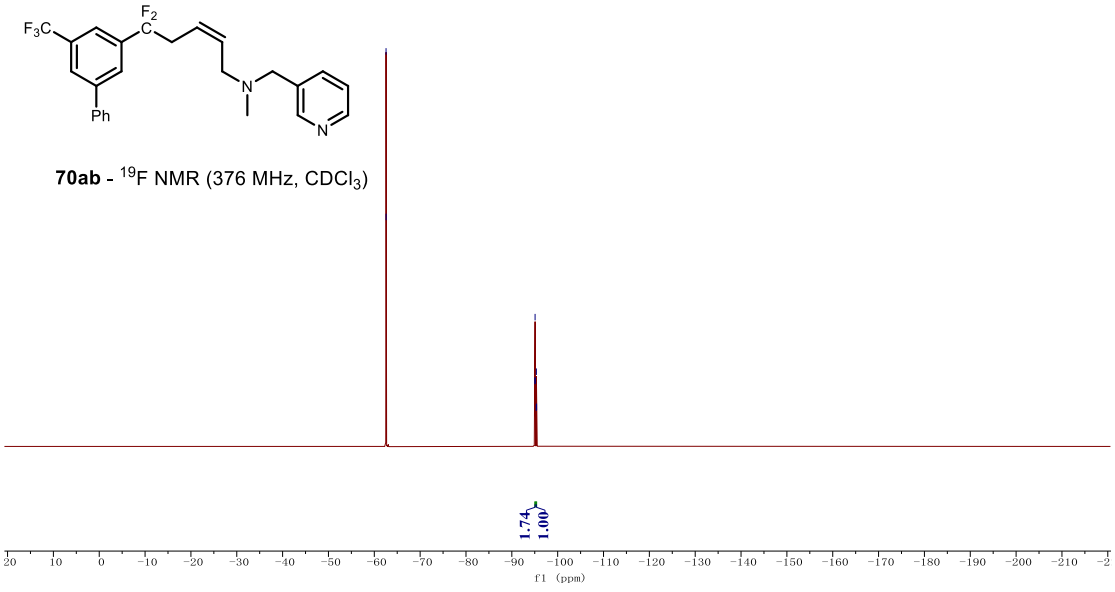


70ab - ^{1}H NMR (400 MHz, $CDCl_3$)

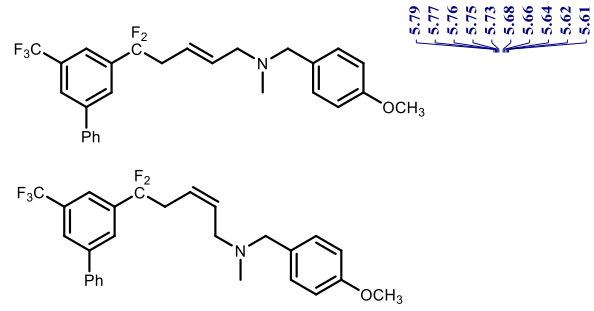
E / Z = 1 : 1.7





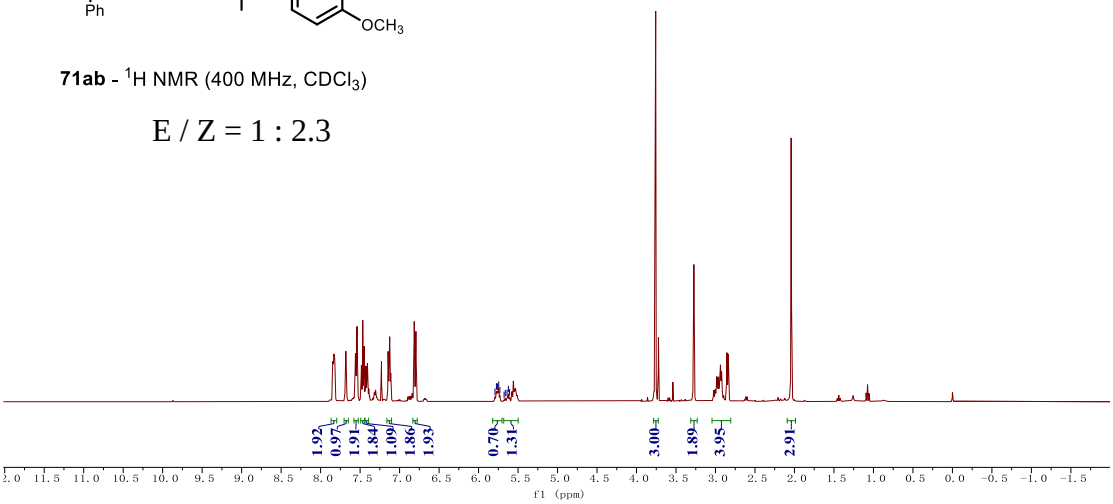


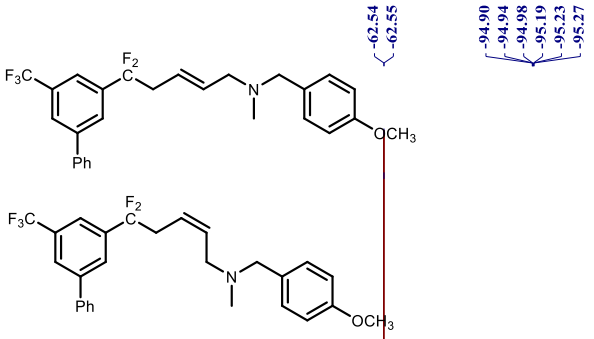
70ab - ^{19}F NMR (376 MHz, $CDCl_3$)



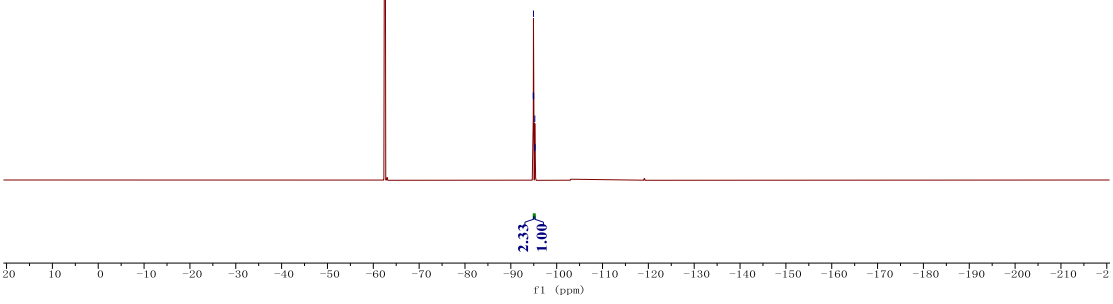
71ab - ^{1}H NMR (400 MHz, $CDCl_3$)

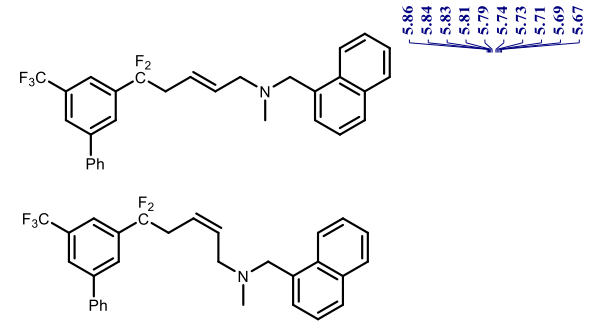
E / Z = 1 : 2.3





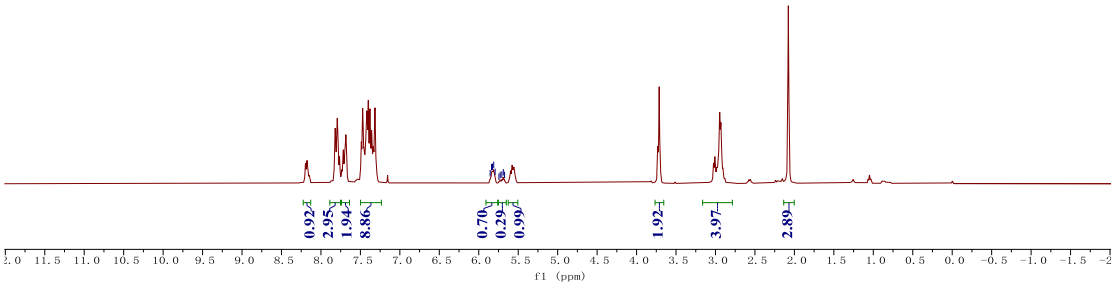
71ab - ^{19}F NMR (376 MHz, $CDCl_3$)

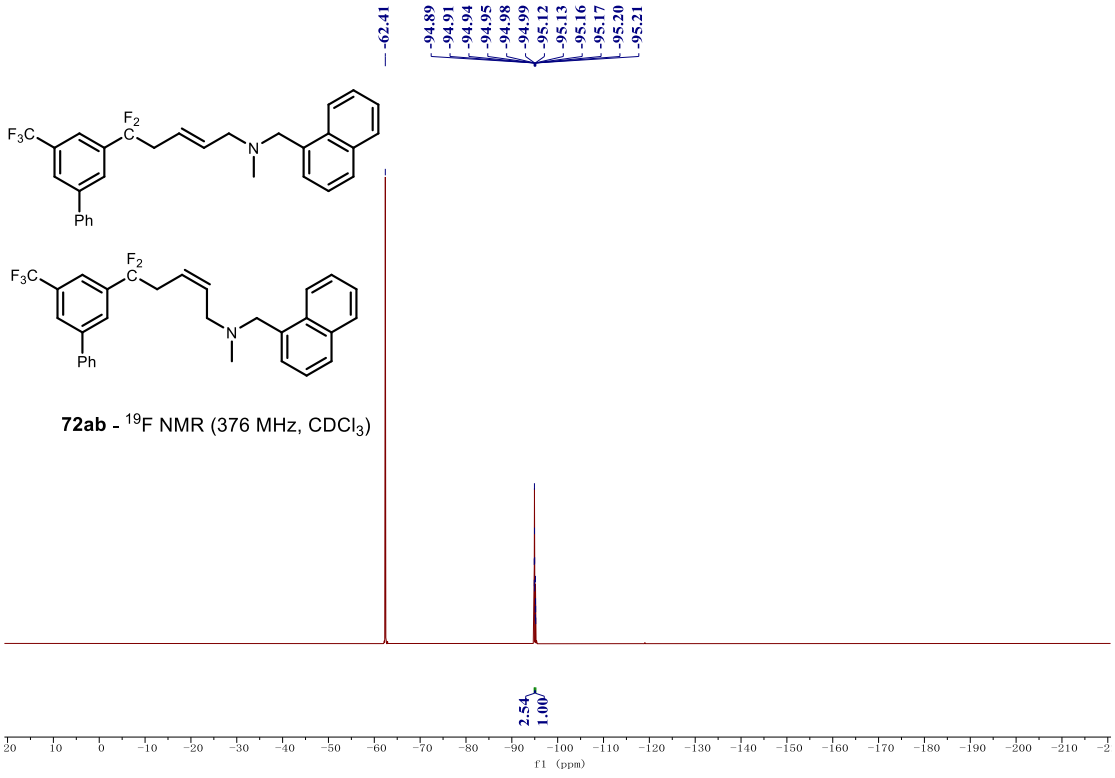




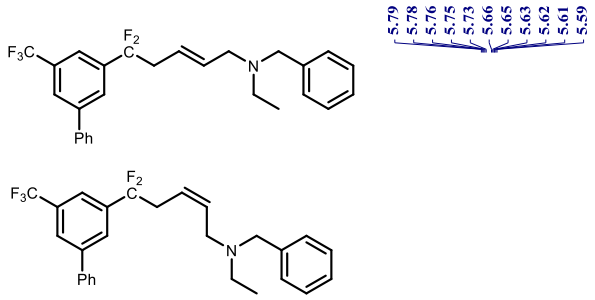
72ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 2.5



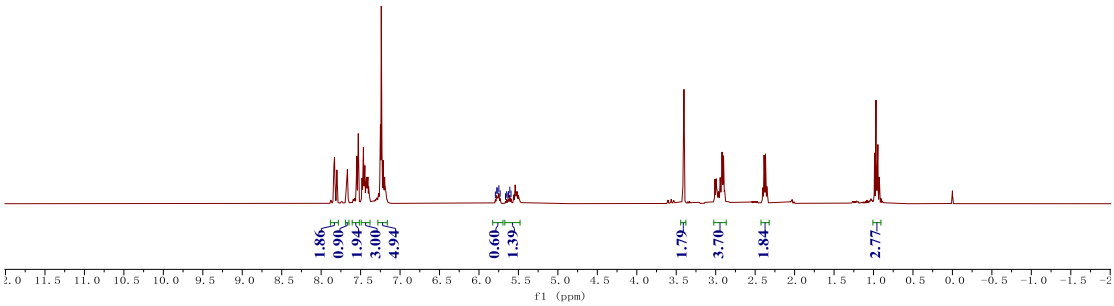


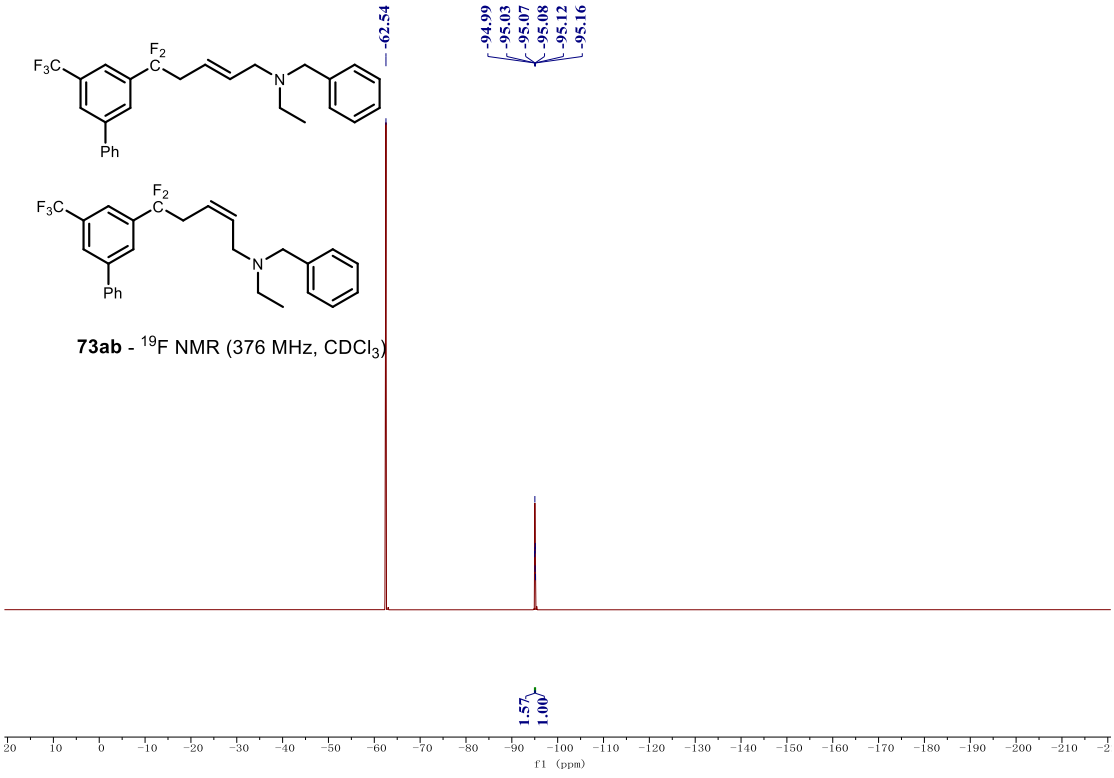
72ab - ^{19}F NMR (376 MHz, $CDCl_3$)



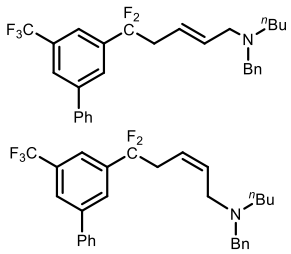
73ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 1.6



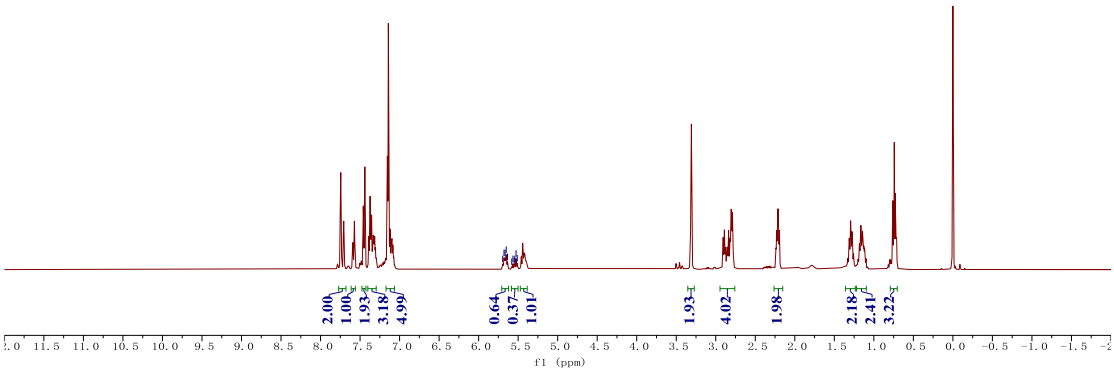


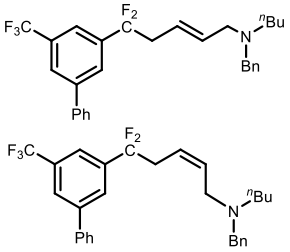
73ab - ^{19}F NMR (376 MHz, $CDCl_3$)



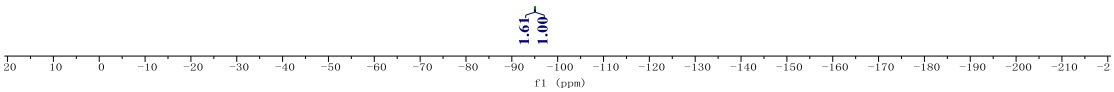
74ab - ^{1}H NMR (400 MHz, $CDCl_3$)

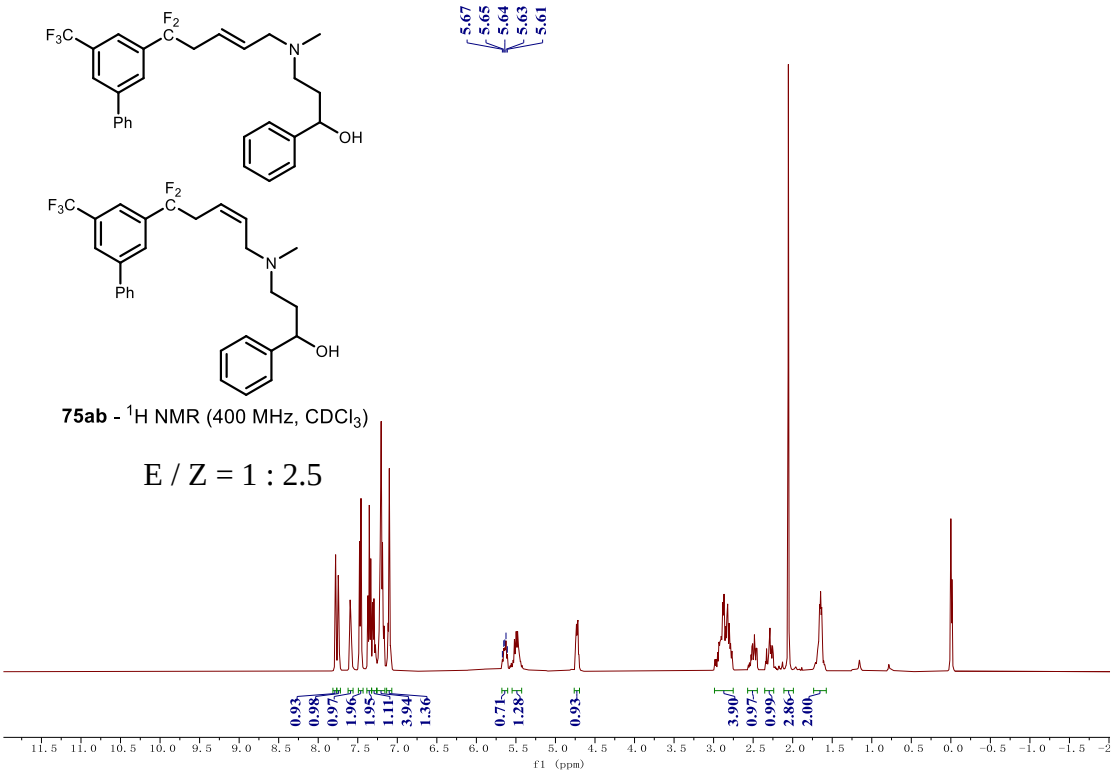
E / Z = 1 : 1.6





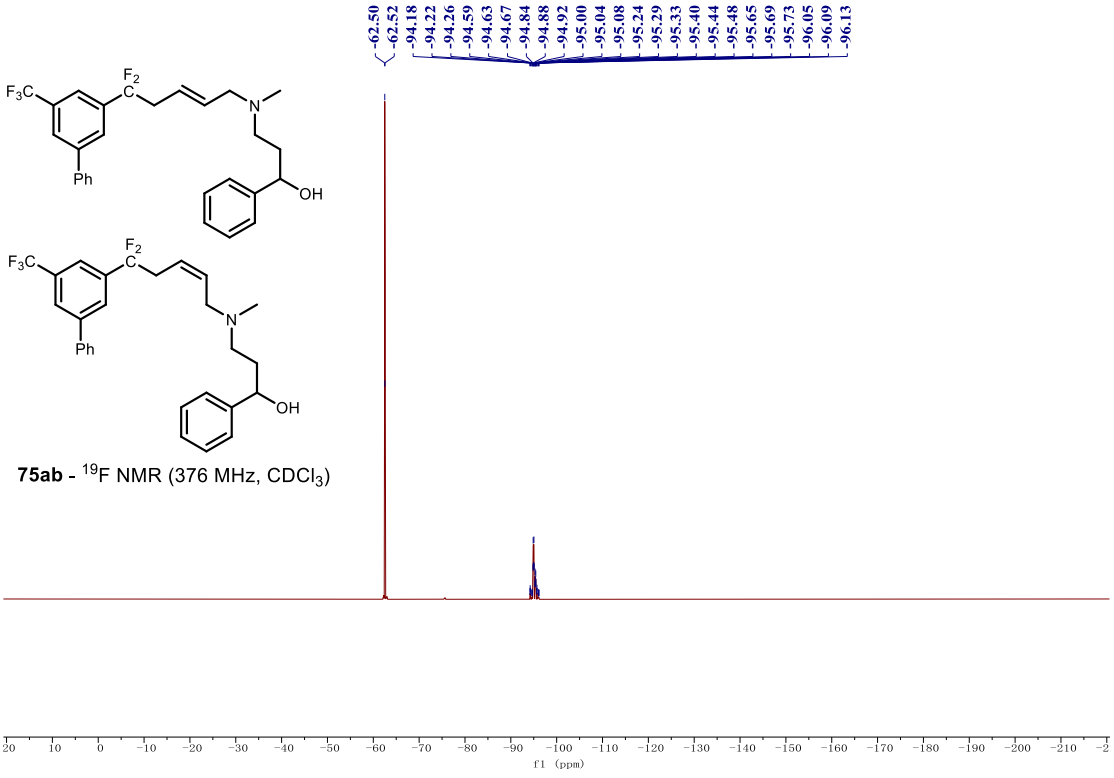
74ab - ^{19}F NMR (376 MHz, $CDCl_3$)



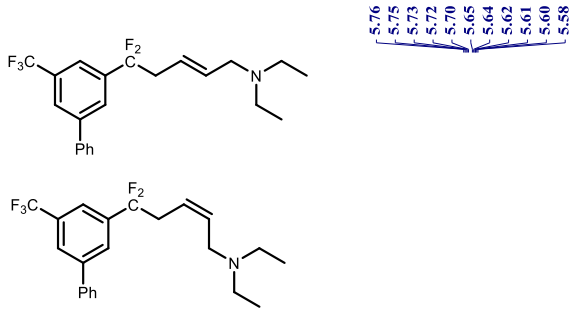


75ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 2.5

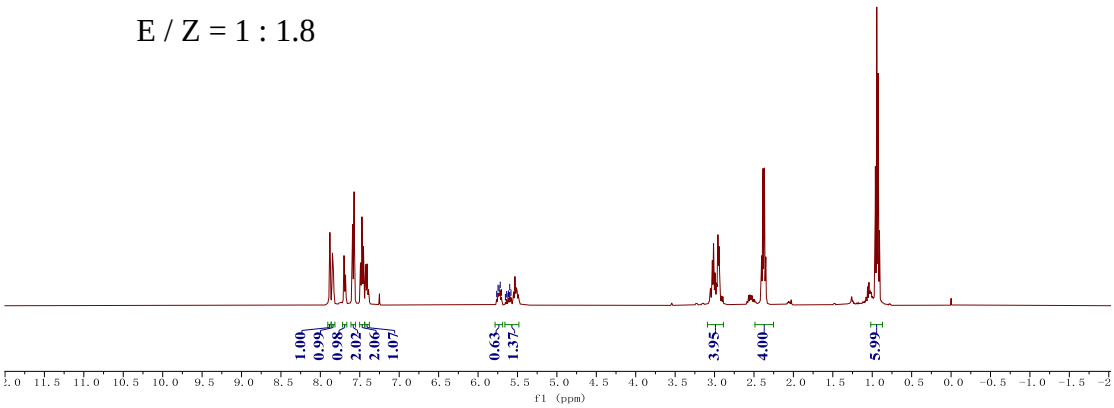


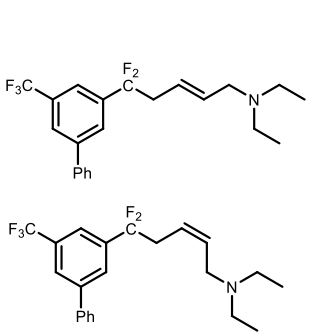
75ab - ^{19}F NMR (376 MHz, $CDCl_3$)



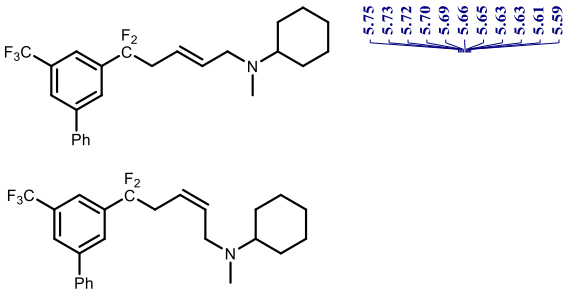
76ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 1.8



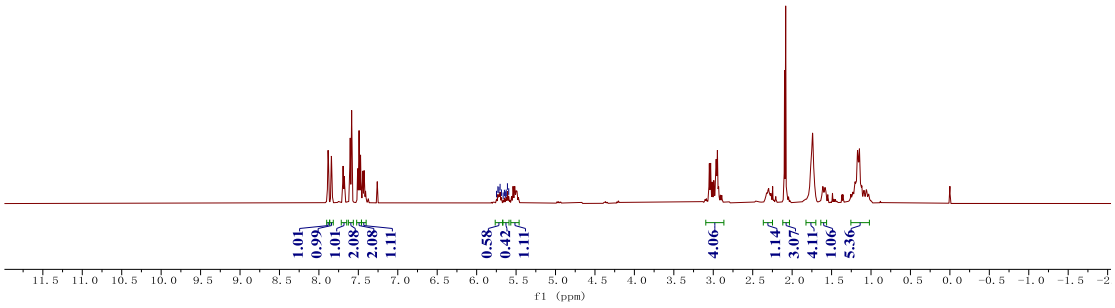


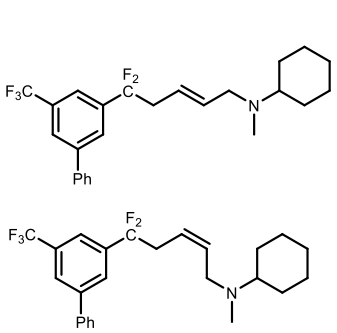
76ab - ^{19}F NMR (376 MHz, $CDCl_3$)



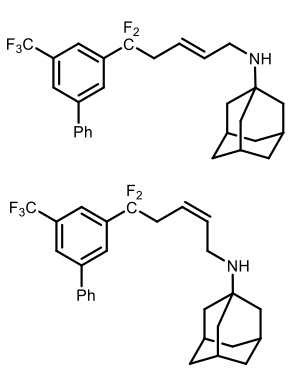
77ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 1.4



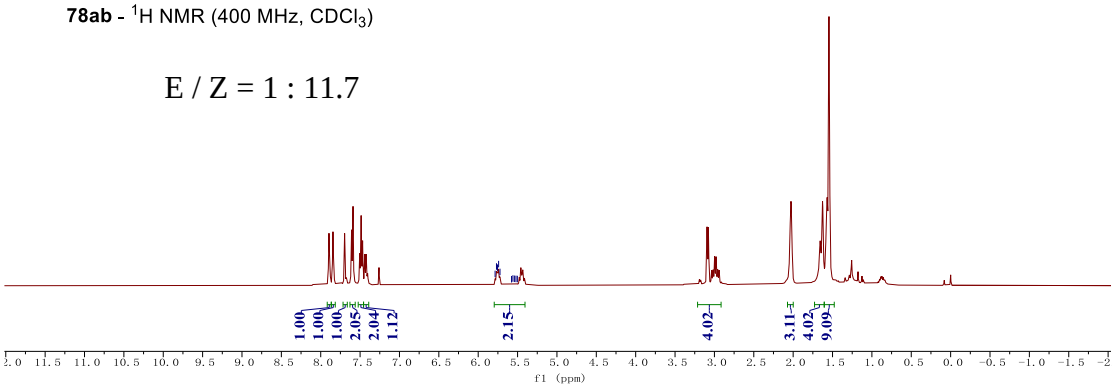


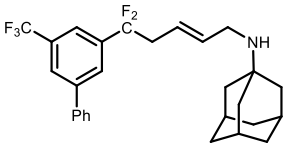
77ab - ^{19}F NMR (376 MHz, $CDCl_3$)

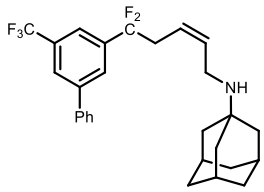


78ab - ^{1}H NMR (400 MHz, $CDCl_3$)

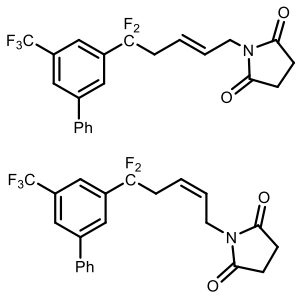
E / Z = 1 : 11.7





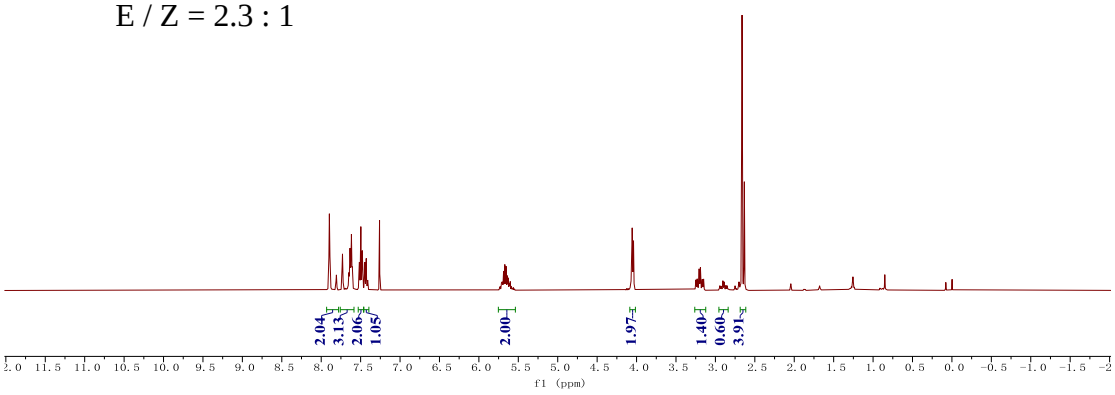


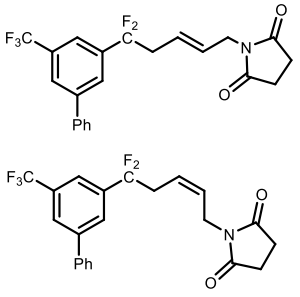
78ab - ^{19}F NMR (376 MHz, $CDCl_3$)



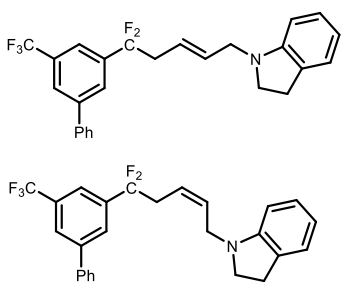
80ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 2.3 : 1



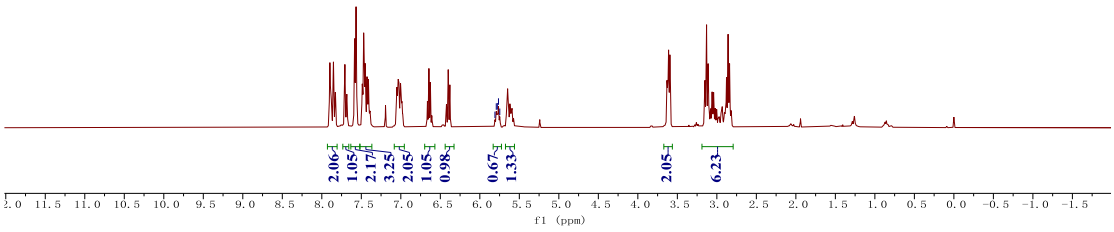


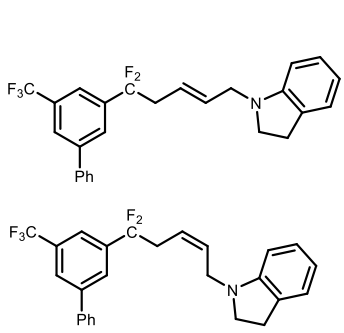
80ab - ^{19}F NMR (376 MHz, $CDCl_3$)



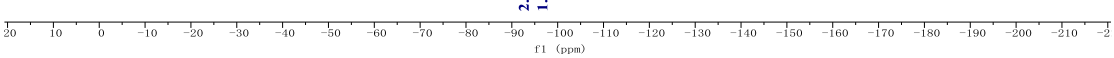
81ab - ^{1}H NMR (400 MHz, $CDCl_3$)

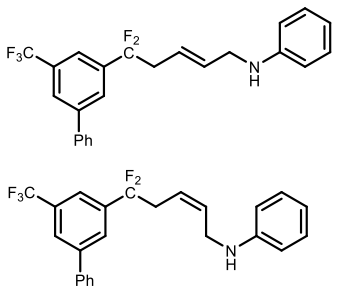
E / Z = 1 : 2.0





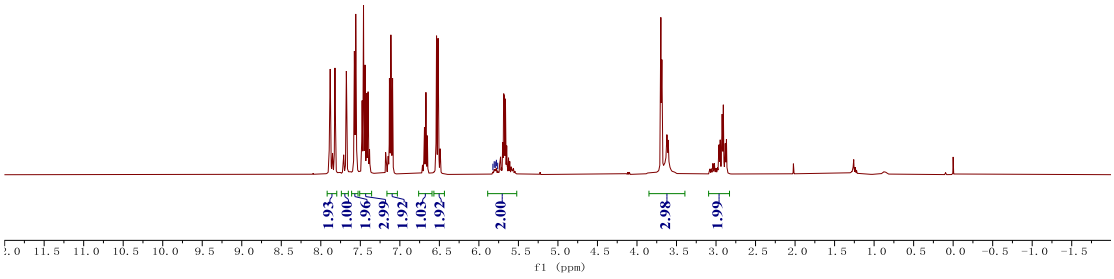
81ab - ^{19}F NMR (376 MHz, $CDCl_3$)

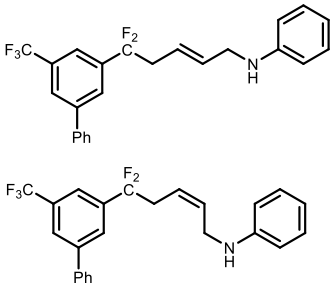




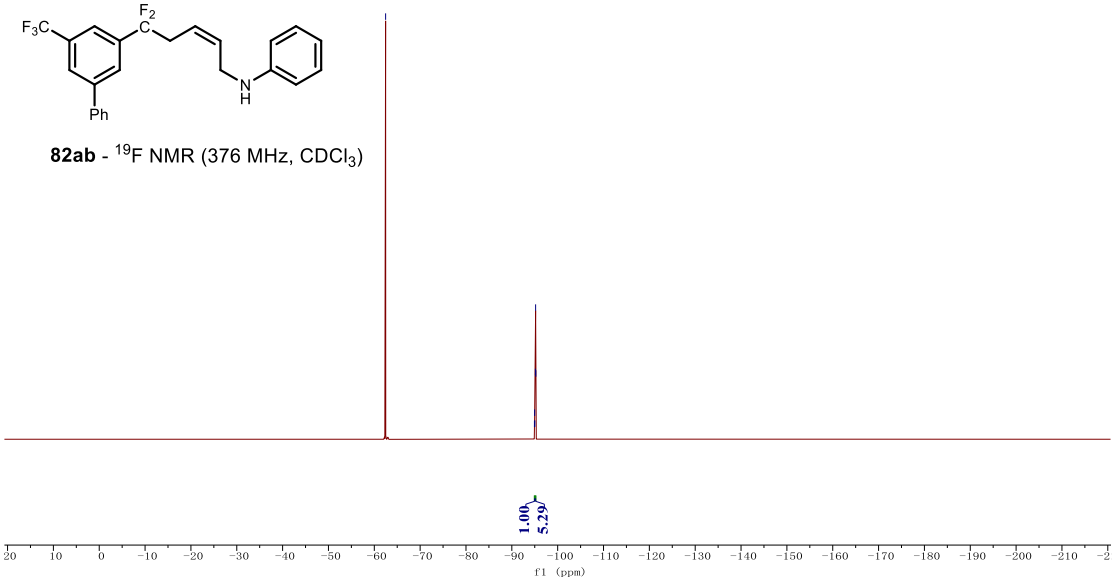
82ab - ^{1}H NMR (400 MHz, $CDCl_3$)

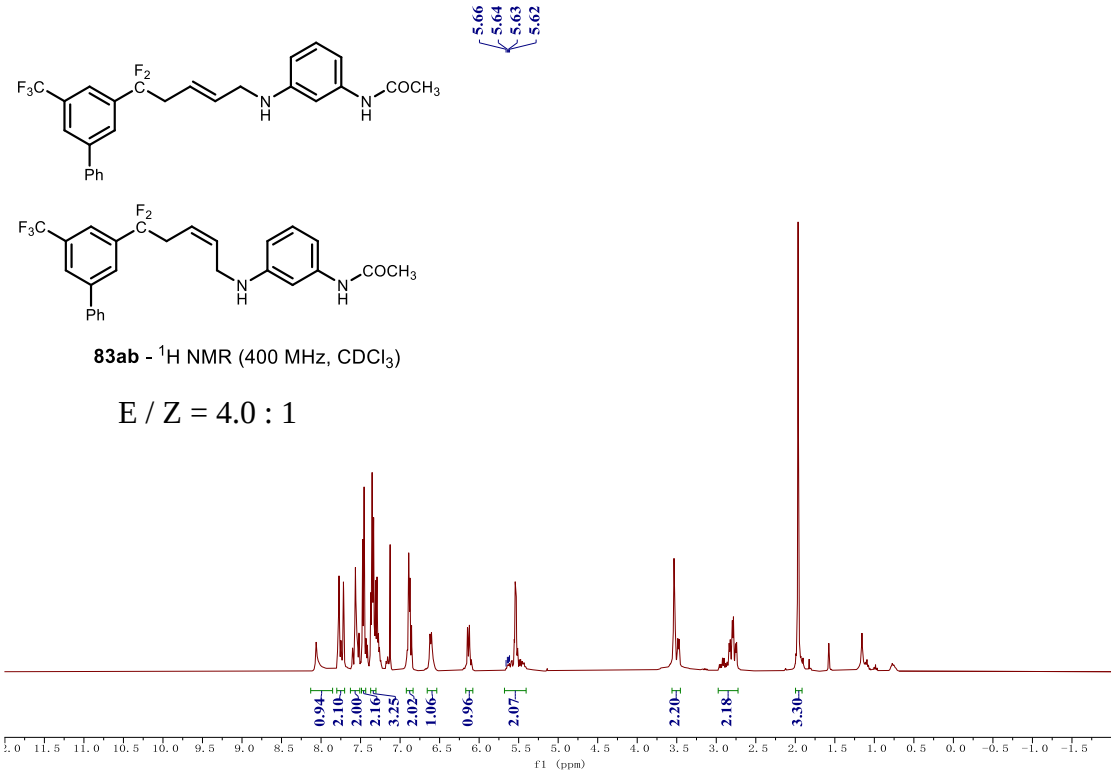
E / Z = 5.3 : 1





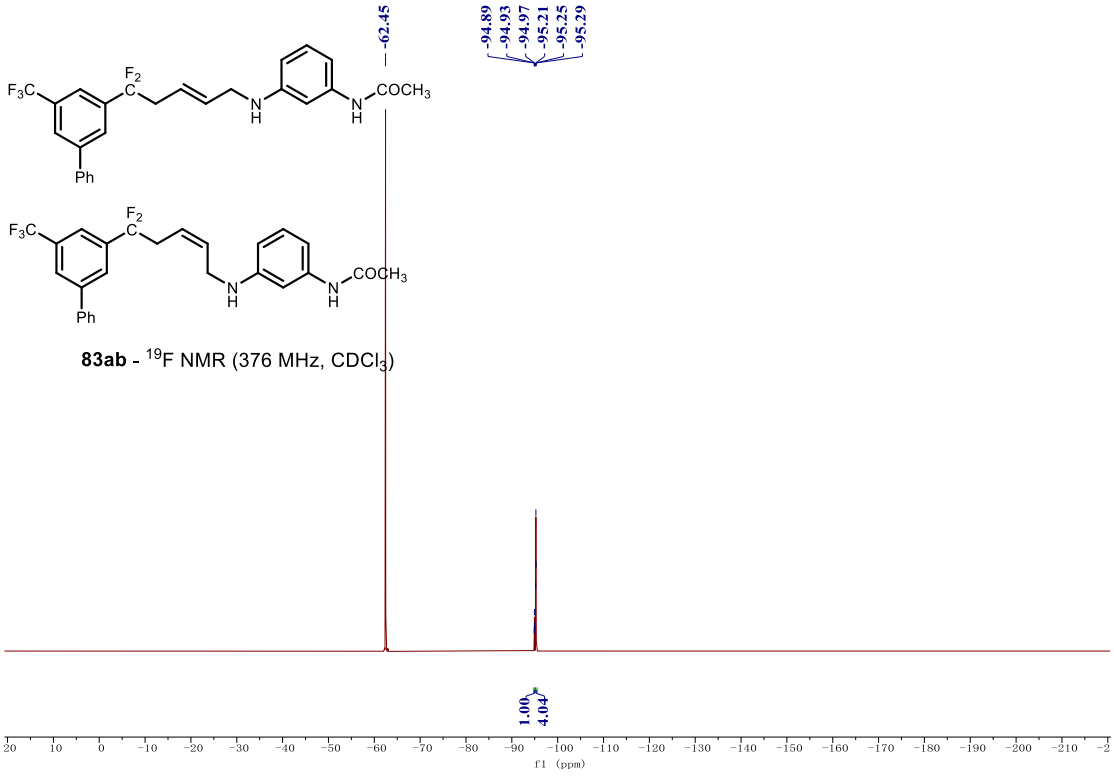
82ab - ^{19}F NMR (376 MHz, $CDCl_3$)



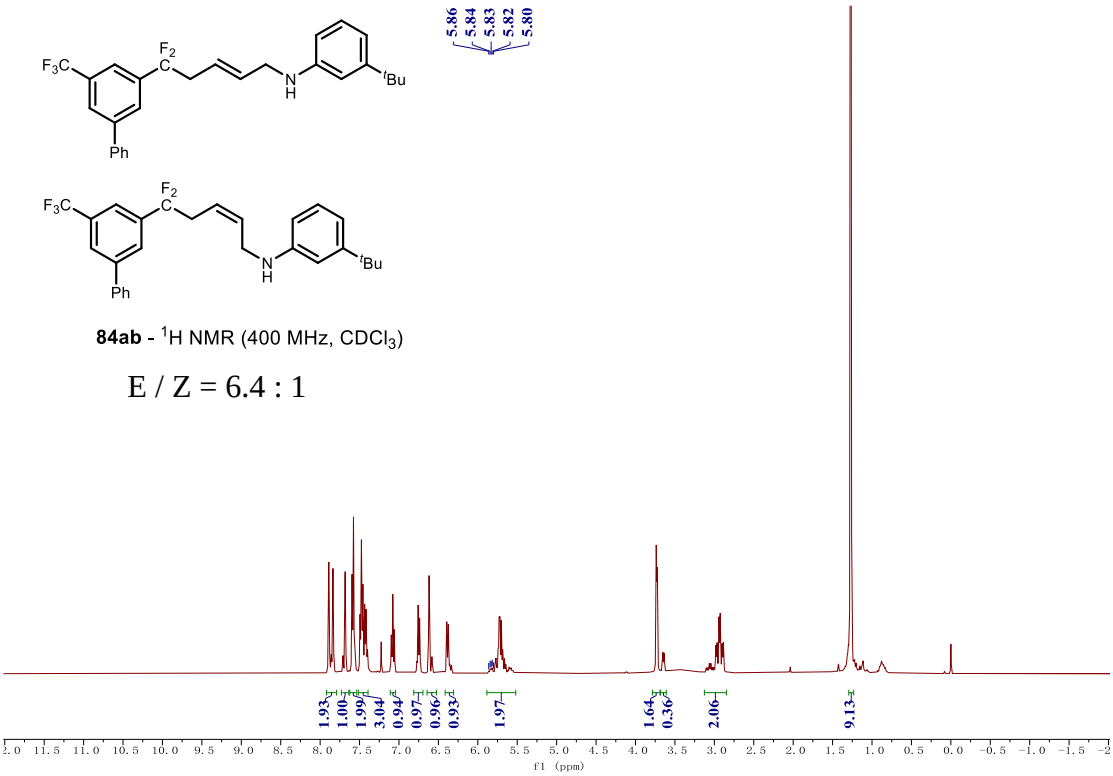


83ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 4.0 : 1

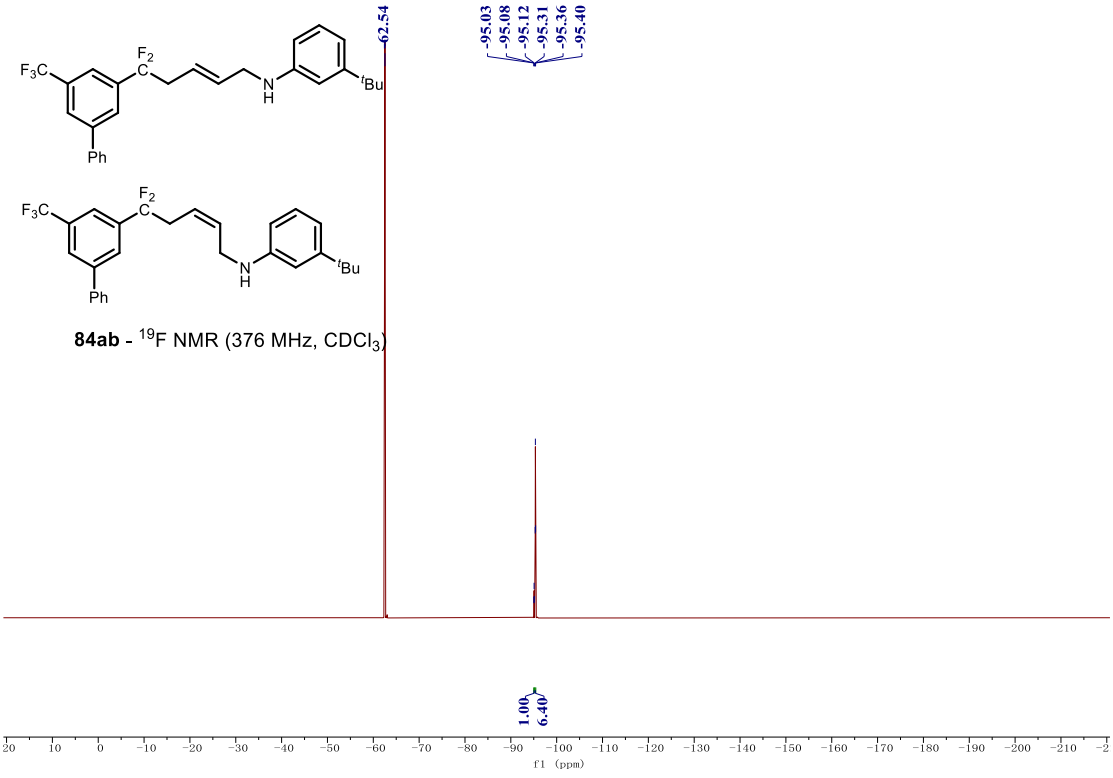


83ab - ^{19}F NMR (376 MHz, $CDCl_3$)

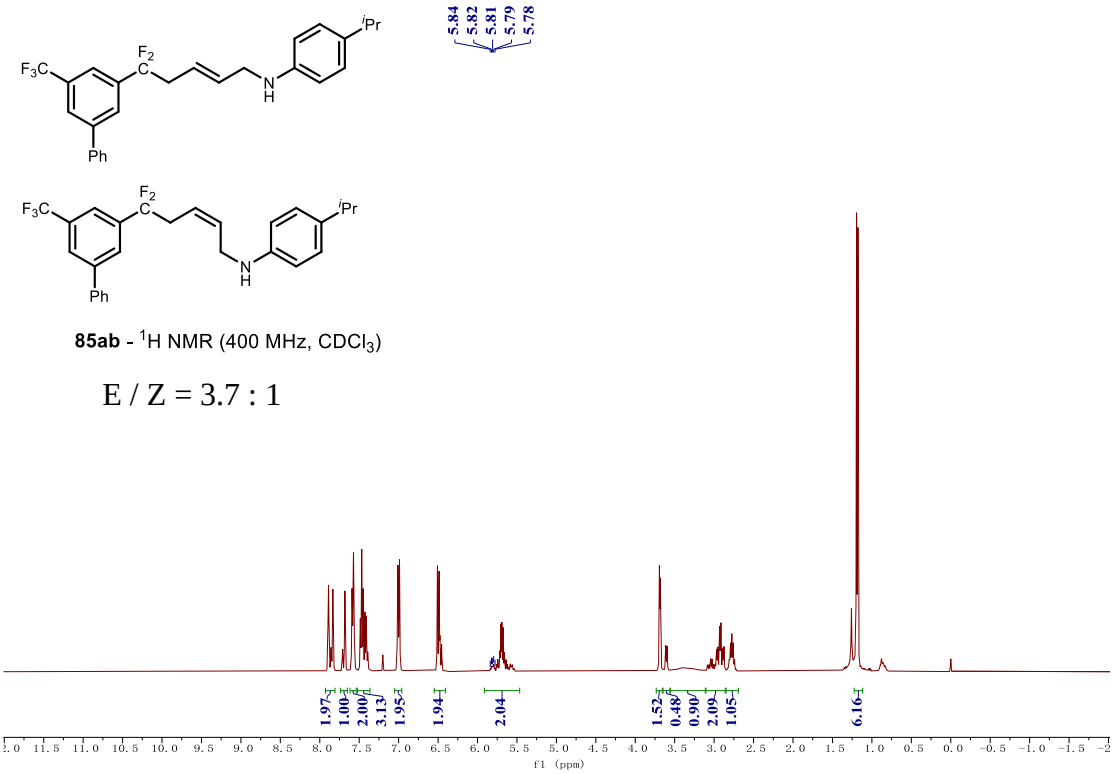


84ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 6.4 : 1

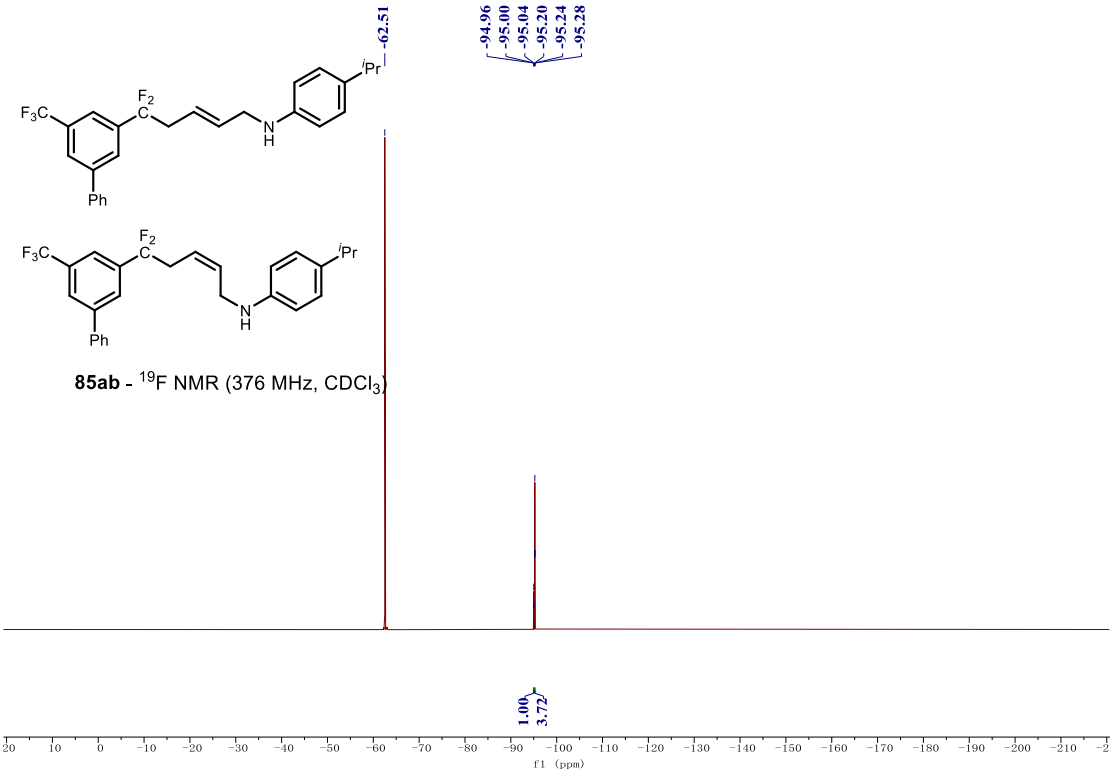


84ab - ^{19}F NMR (376 MHz, $CDCl_3$)

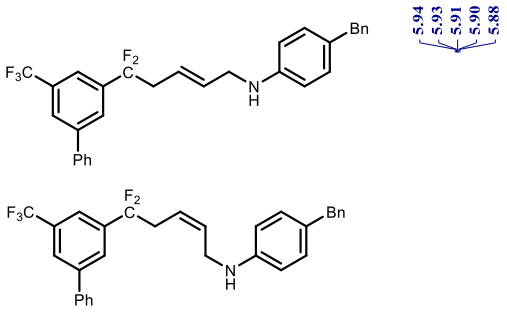


85ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 3.7 : 1

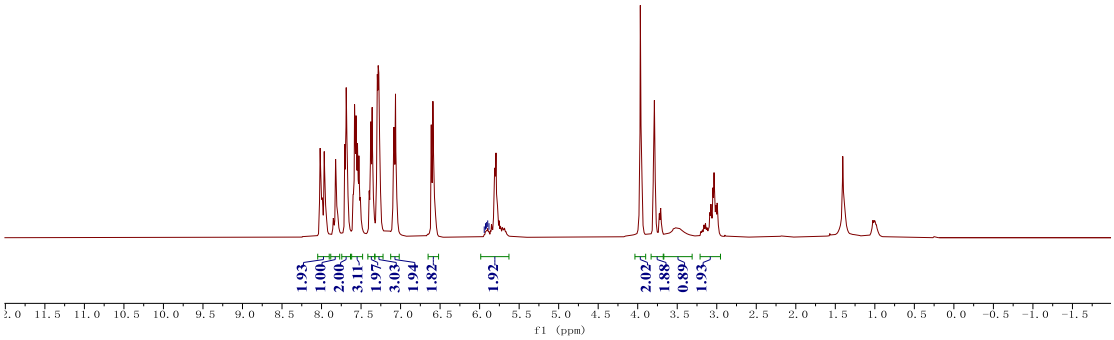


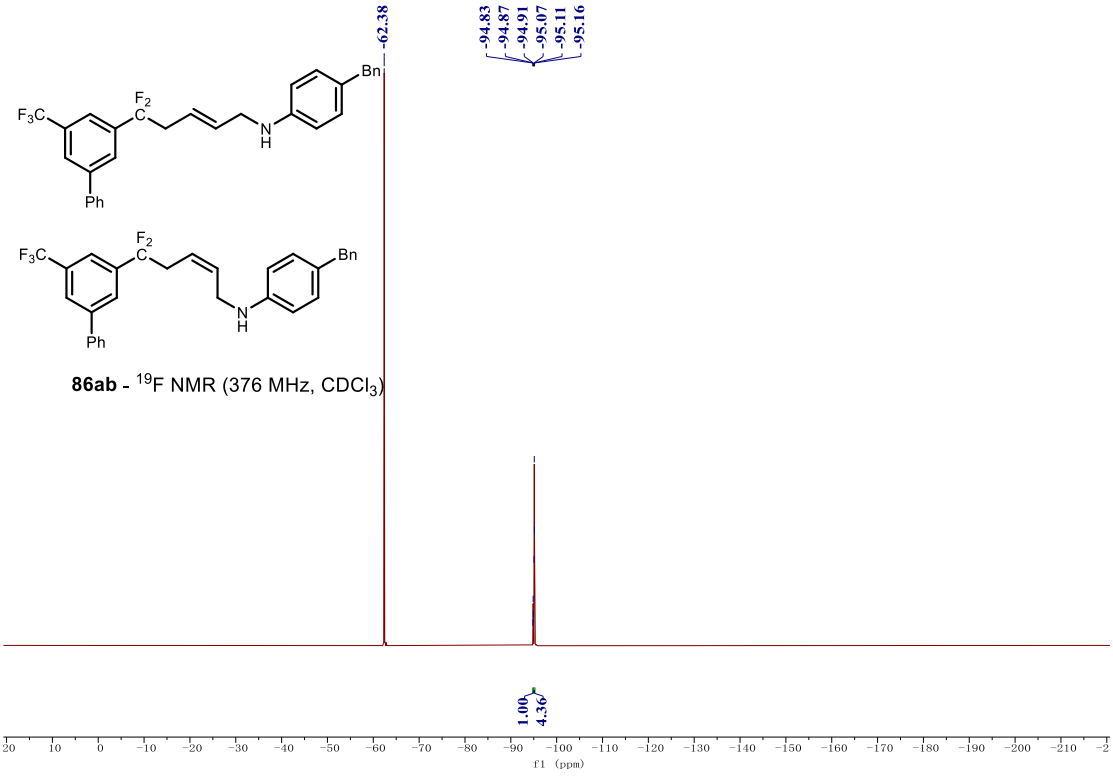
85ab - ^{19}F NMR (376 MHz, $CDCl_3$)



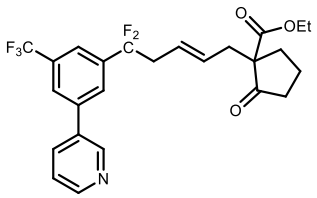
86ab - ^{1}H NMR (400 MHz, $CDCl_3$)

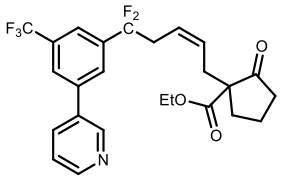
E / Z = 4.4 : 1





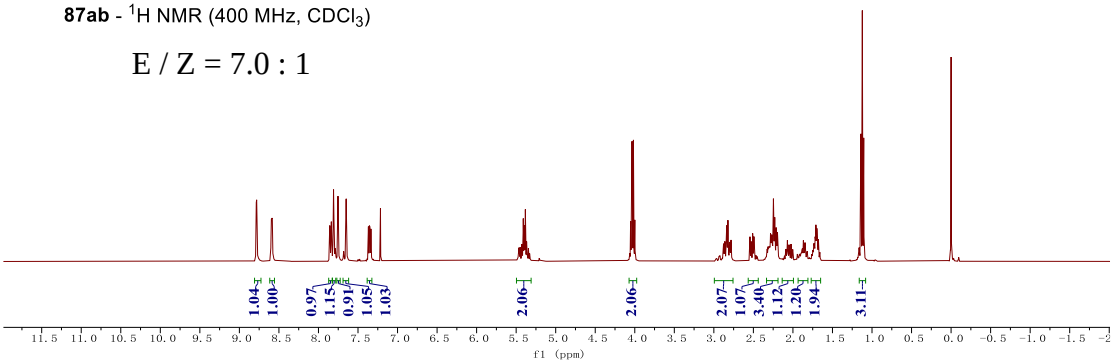
86ab - ^{19}F NMR (376 MHz, $CDCl_3$)

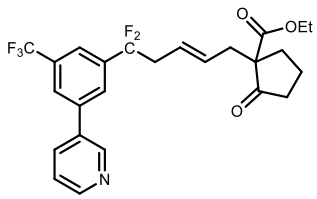


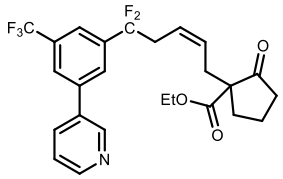


87ab - ^{1}H NMR (400 MHz, $CDCl_3$)

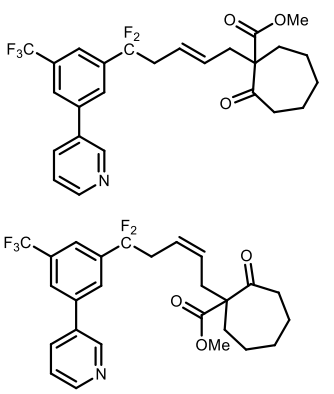
E / Z = 7.0 : 1





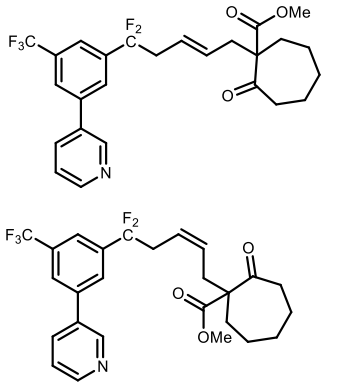


87ab - ^{19}F NMR (376 MHz, $CDCl_3$)

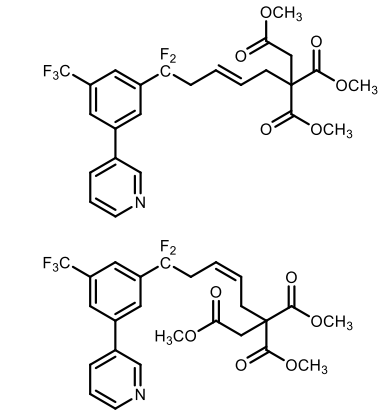


89ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 10.1 : 1

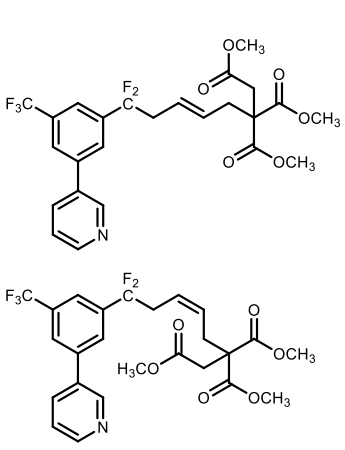


89ab - ^{19}F NMR (376 MHz, $CDCl_3$)

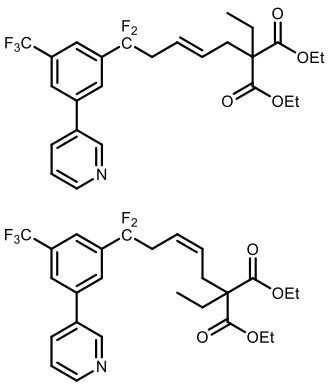


92ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = > 15 : 1

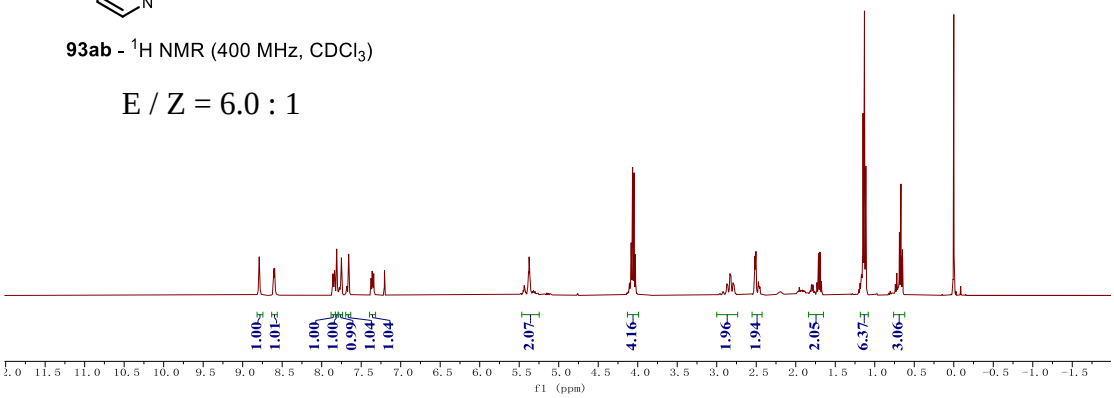


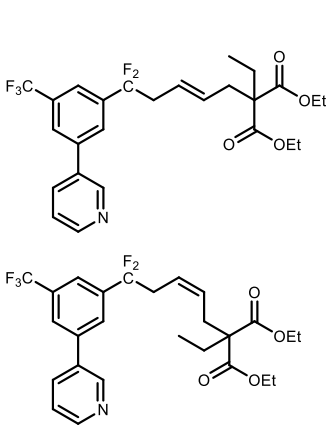
92ab - ^{19}F NMR (376 MHz, $CDCl_3$)



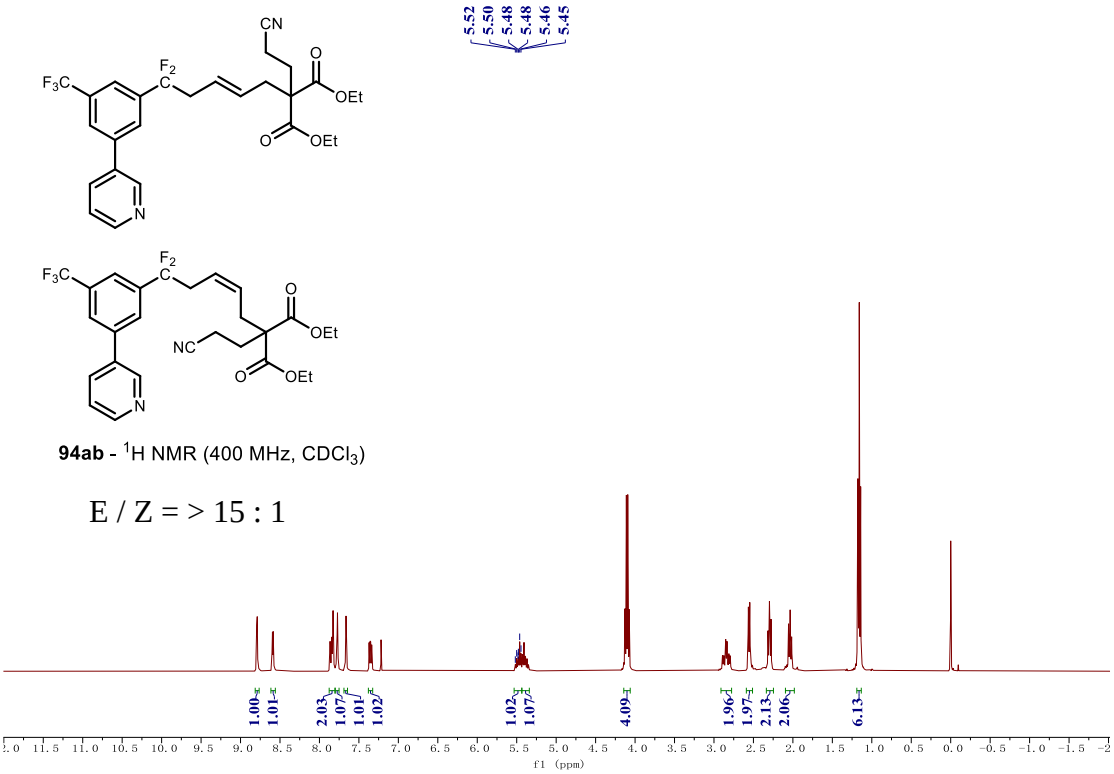
93ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 6.0 : 1



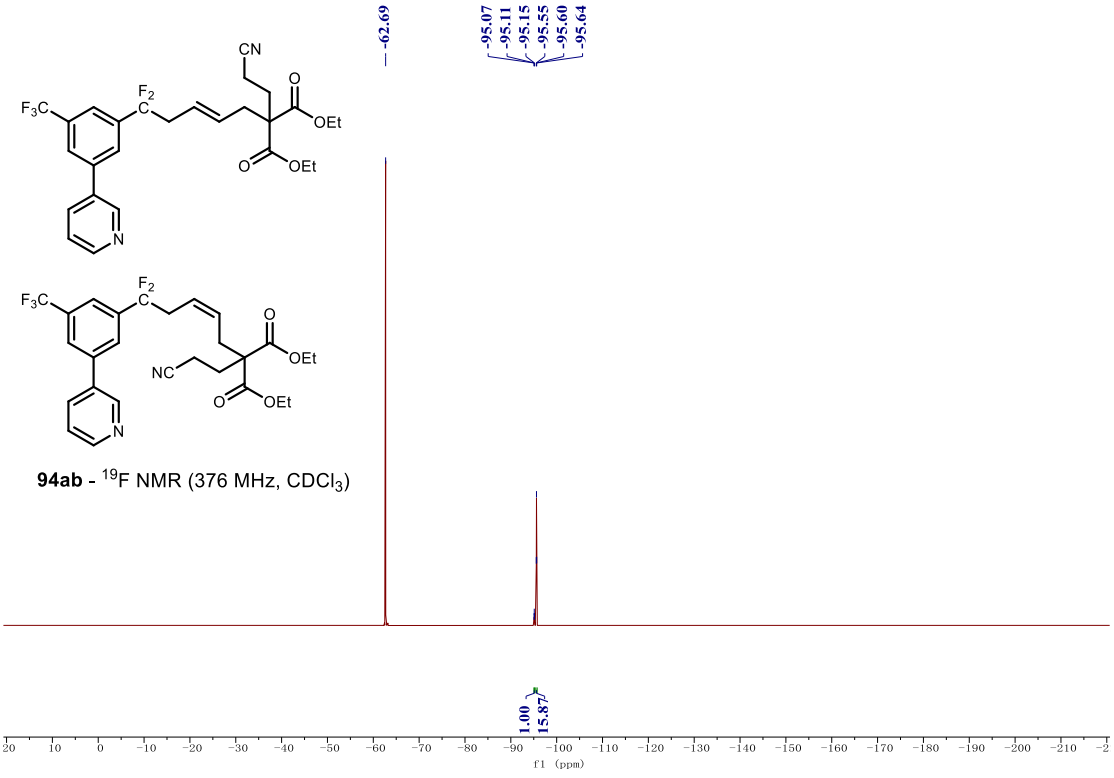


93ab - ^{19}F NMR (376 MHz, $CDCl_3$)

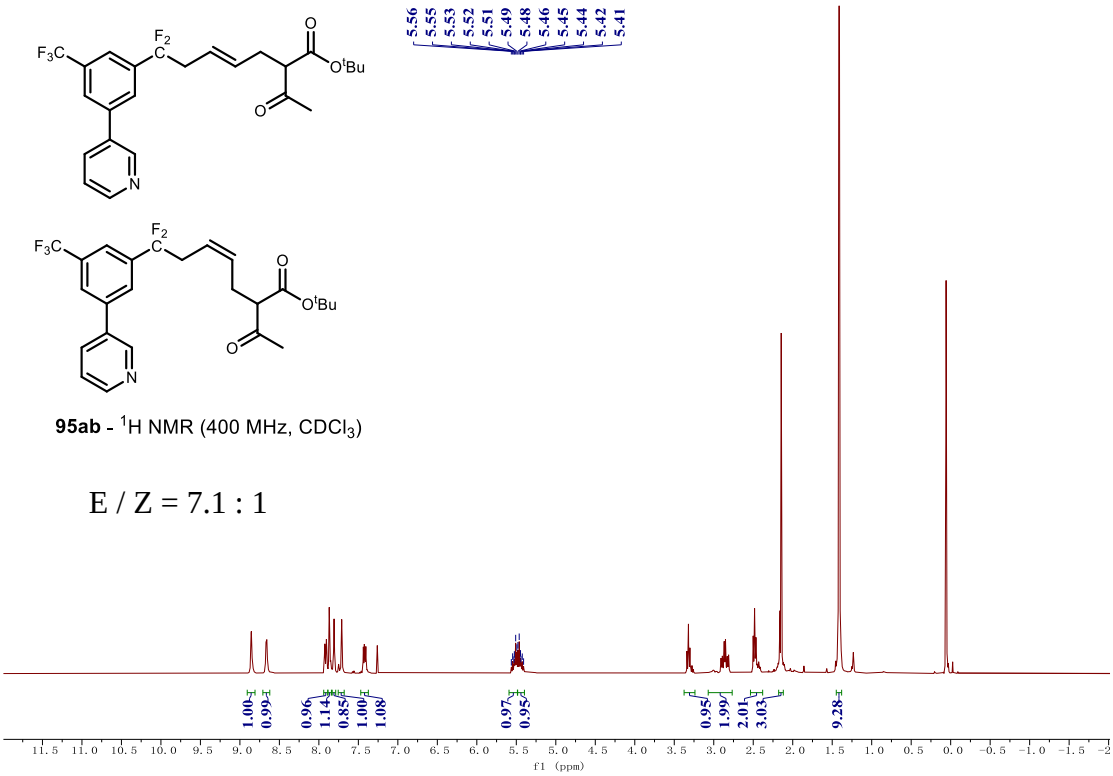


94ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = > 15 : 1

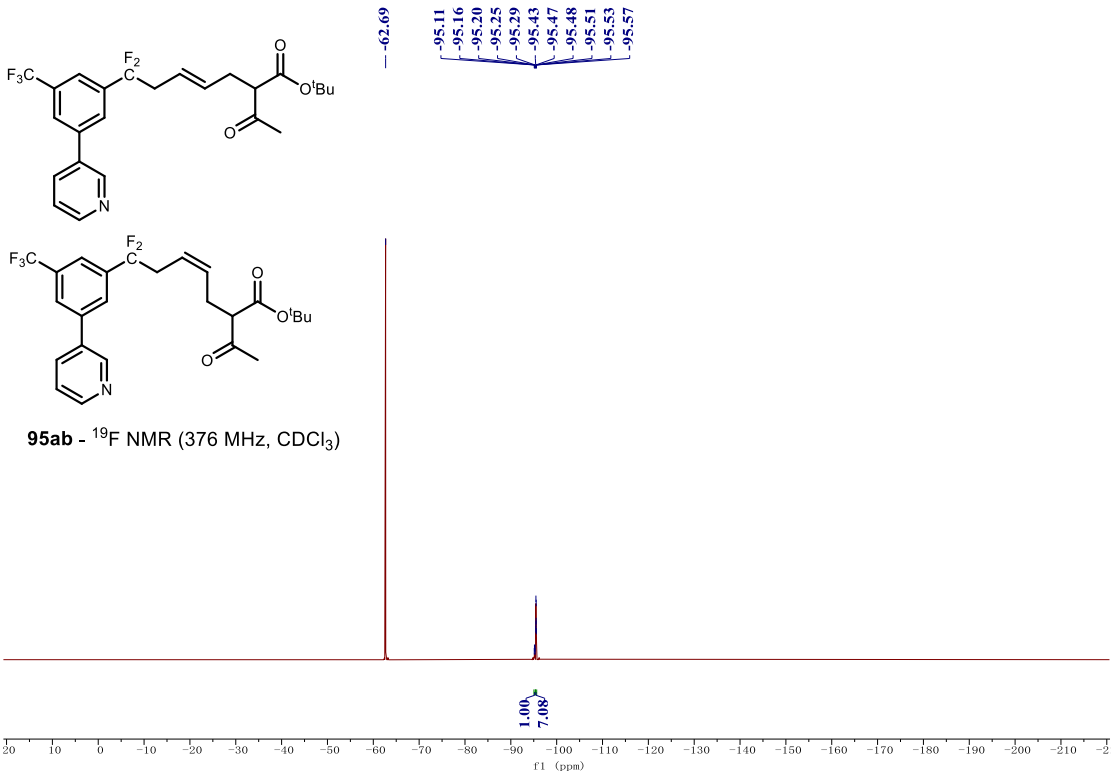


94ab - ^{19}F NMR (376 MHz, $CDCl_3$)

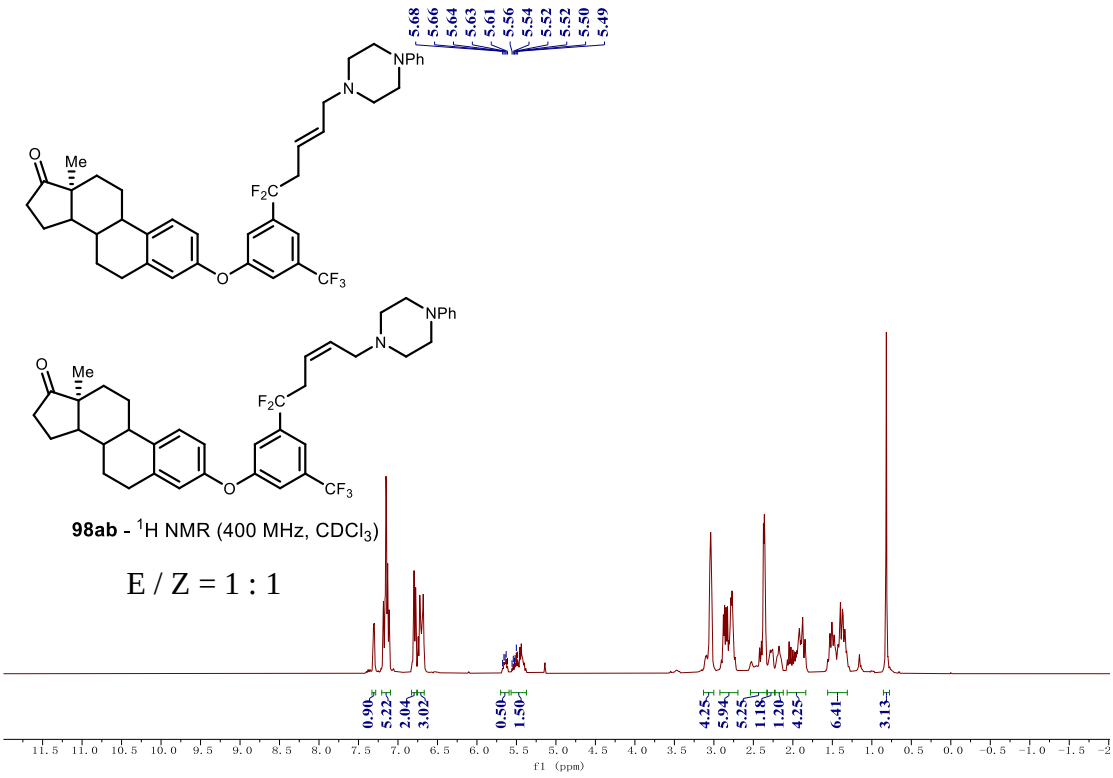


95ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 7.1 : 1

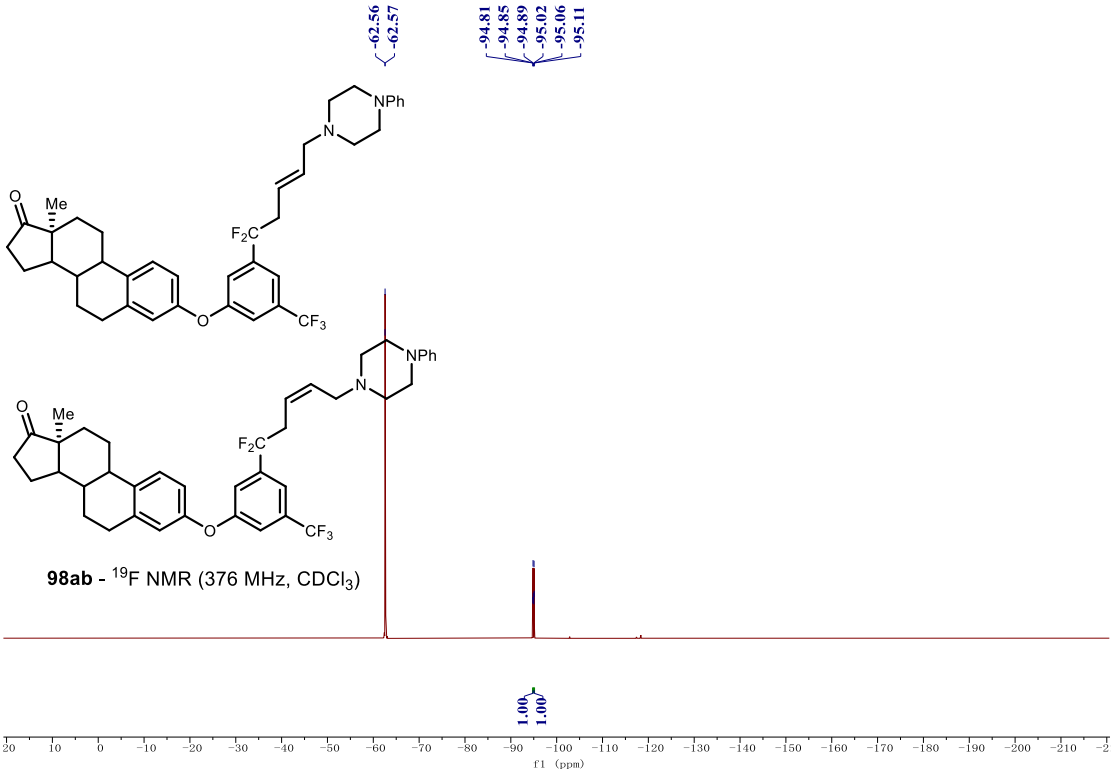


95ab - ^{19}F NMR (376 MHz, $CDCl_3$)

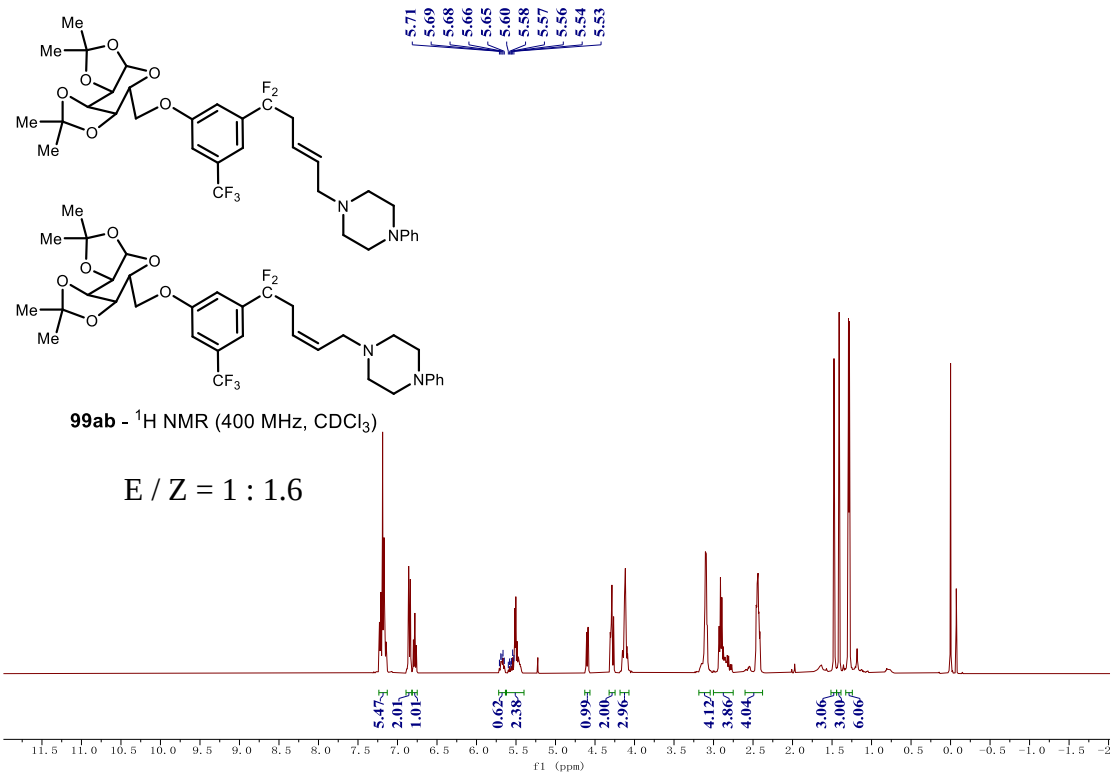


98ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 1

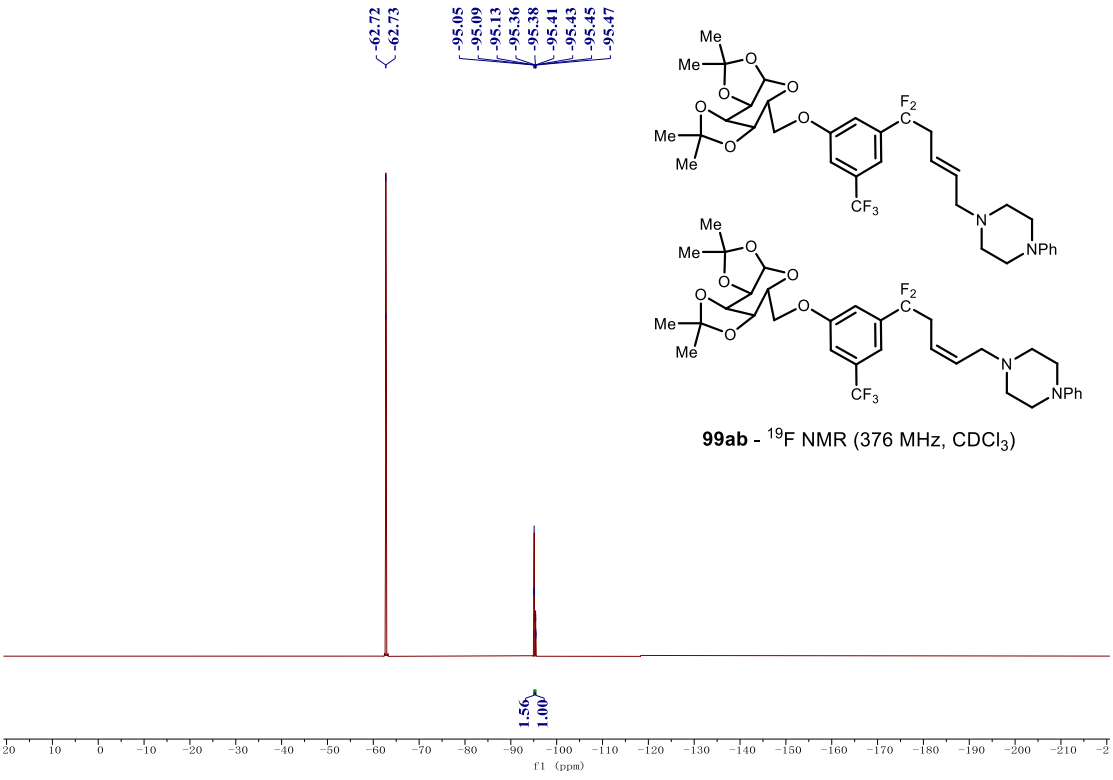


98ab - ^{19}F NMR (376 MHz, $CDCl_3$)

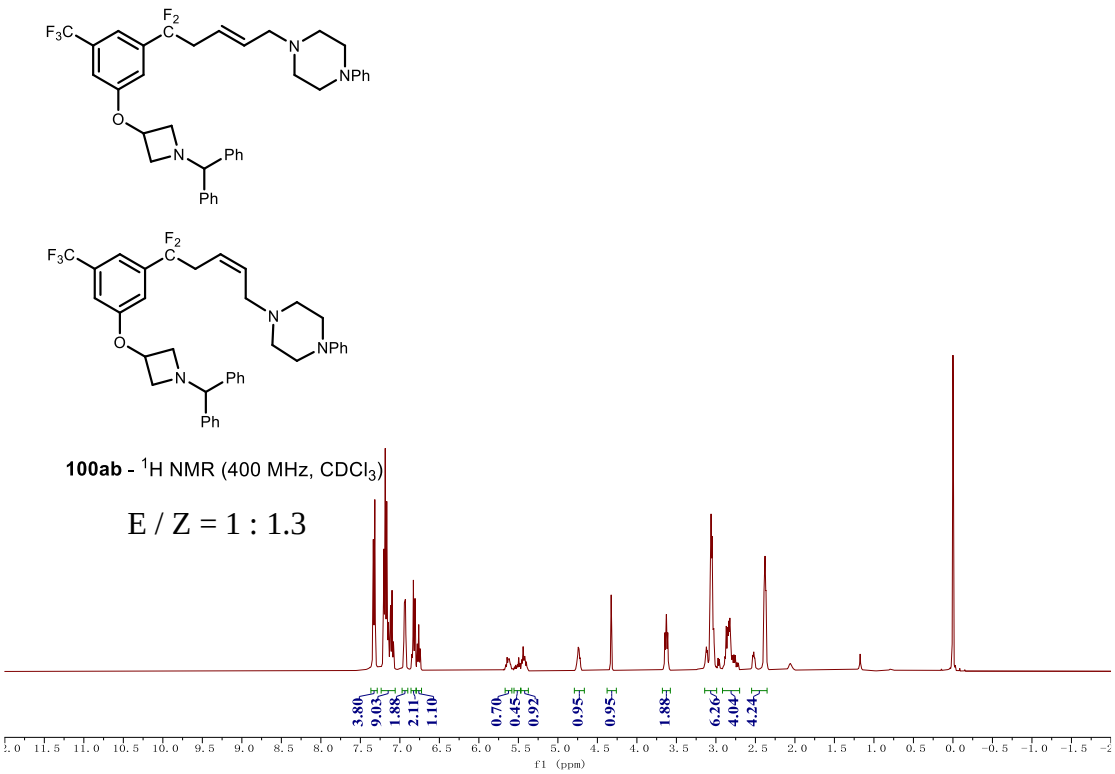


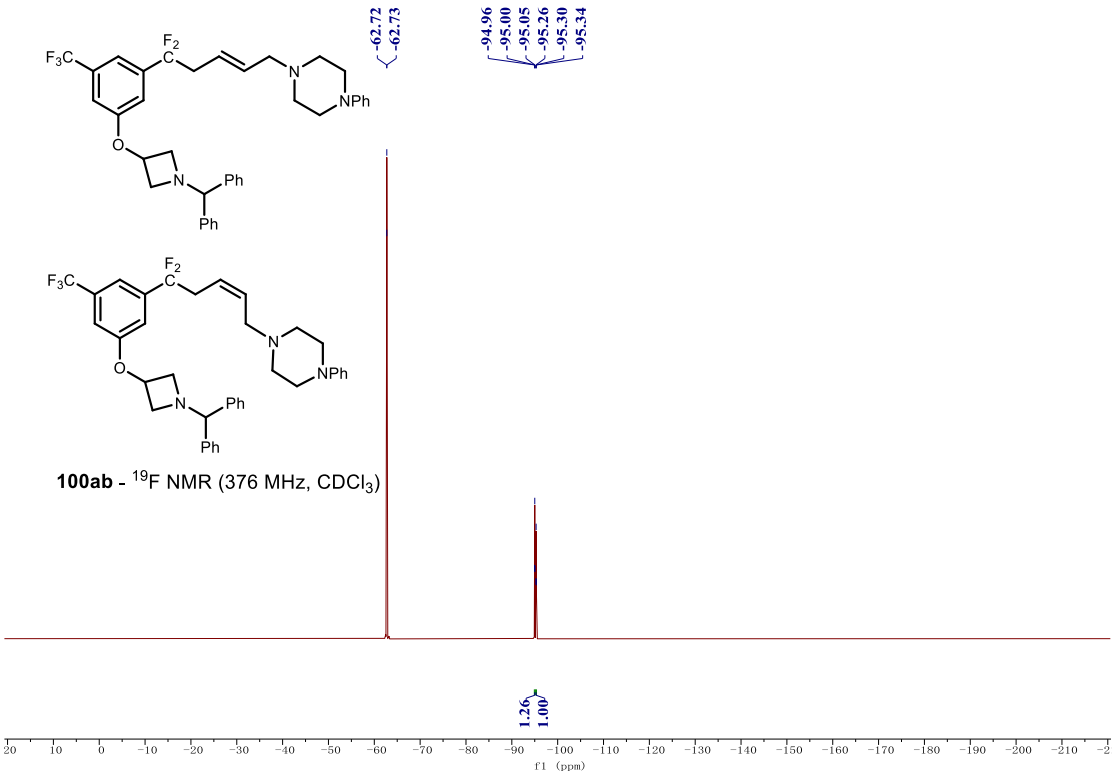
99ab - ^{1}H NMR (400 MHz, $CDCl_3$)

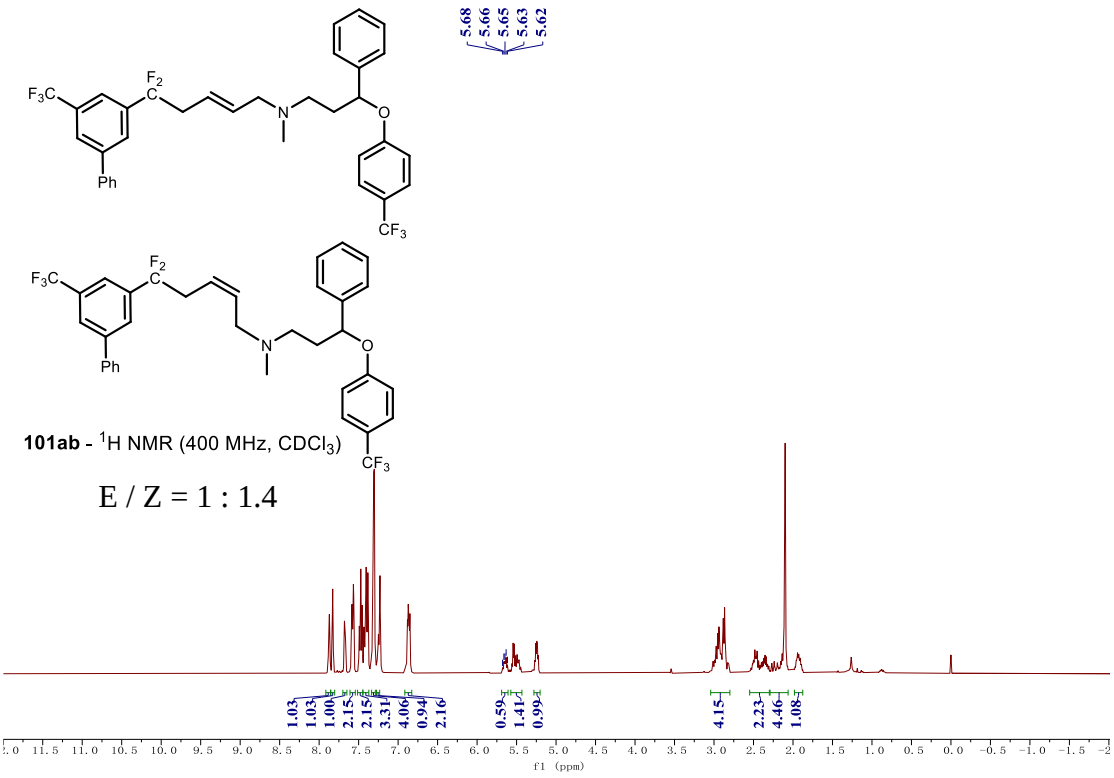
E / Z = 1 : 1.6



99ab - ^{19}F NMR (376 MHz, $CDCl_3$)

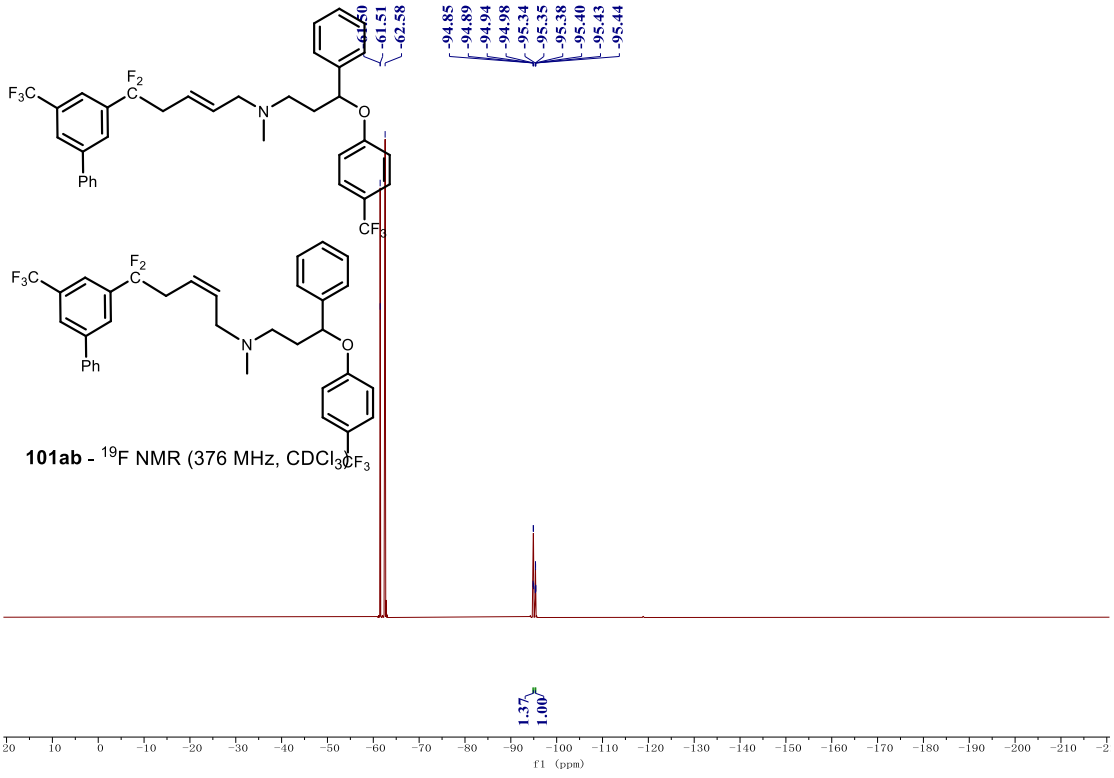

F2
F3C
N
NPh
O
N
Ph
Ph
100ab - 1H NMR (400 MHz, CDCl3)
E / Z = 1 : 1.3
3.80
9.03
1.88
2.11
1.10
0.70
0.45
0.92
0.95
0.95
1.88
6.26
4.04
4.24
f1 (ppm)


-62.72
-62.73
-94.96
-95.00
-95.05
-95.26
-95.30
-95.34
F2
F3C
N
NPh
O
N
Ph
Ph
100ab - 19F NMR (376 MHz, CDCl3)
1.26
1.00
f1 (ppm)

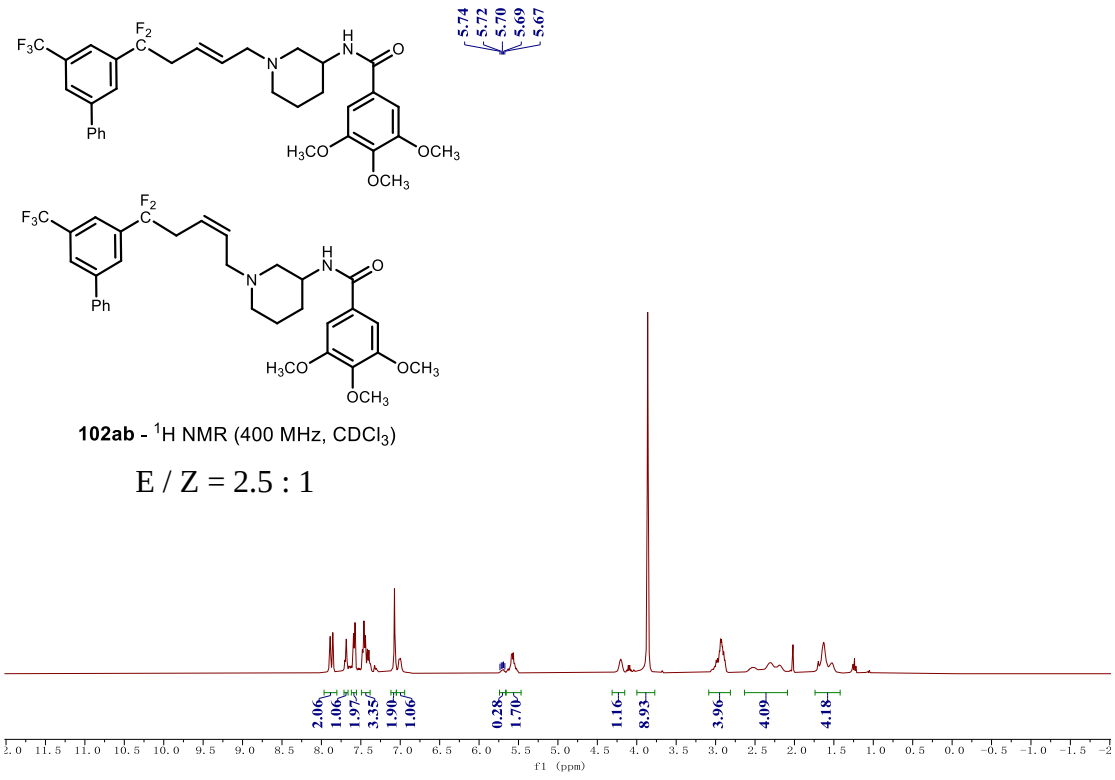


101ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 1.4

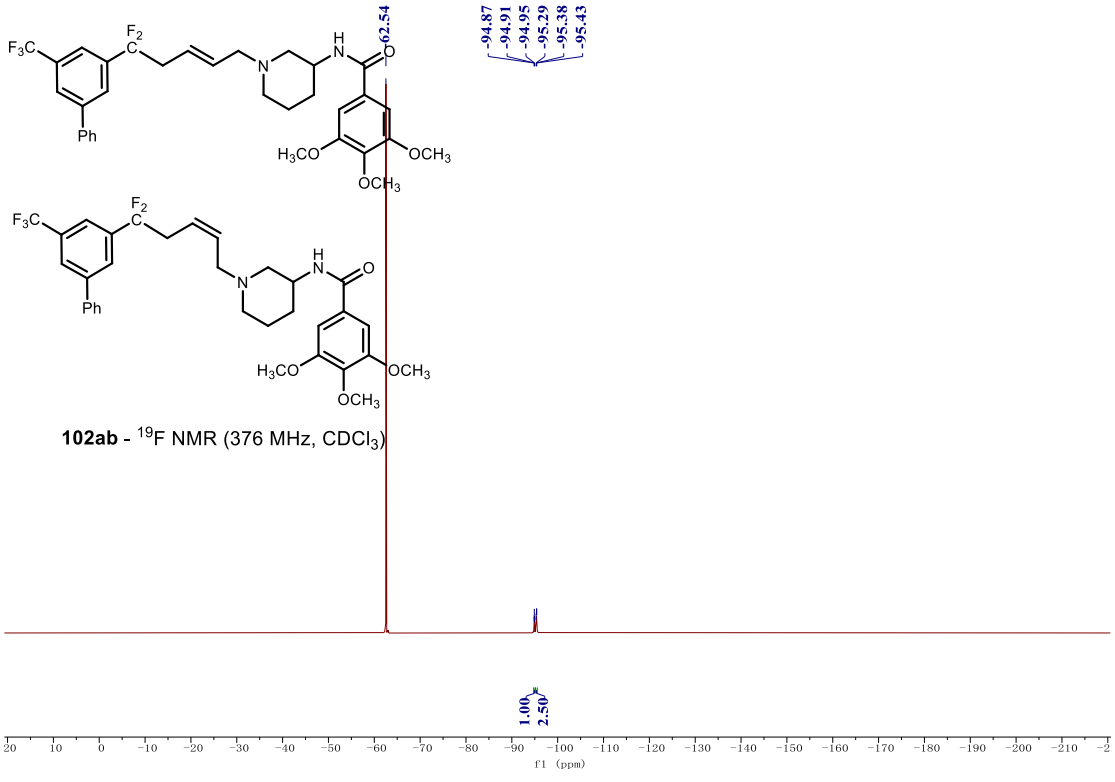


101ab - ^{19}F NMR (376 MHz, $CDCl_3$)

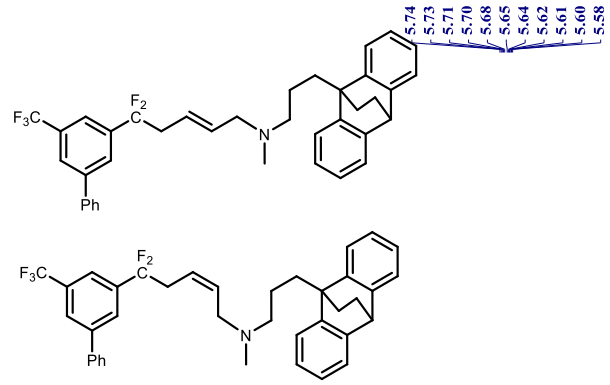


102ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 2.5 : 1

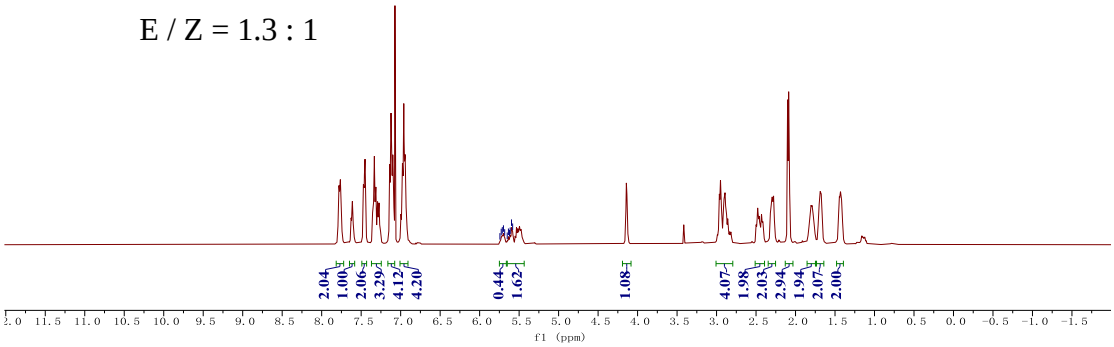


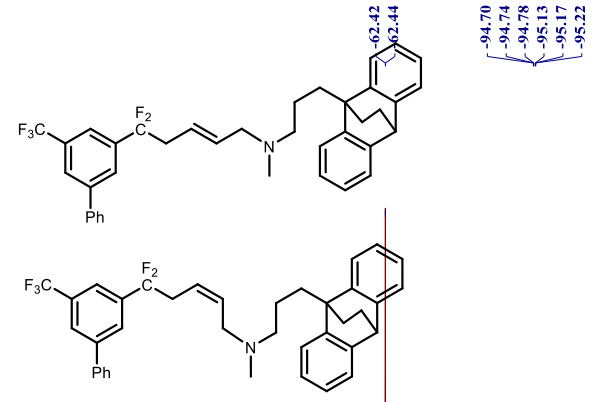
102ab - ^{19}F NMR (376 MHz, $CDCl_3$)



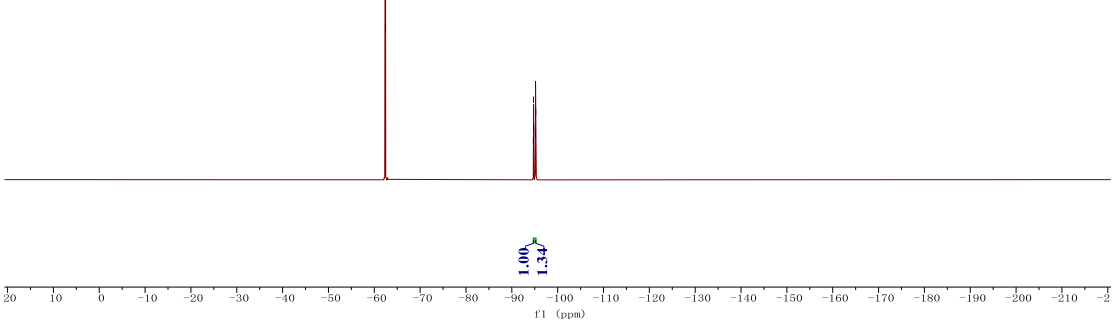
103ab - ^{1}H NMR (400 MHz, $CDCl_3$)

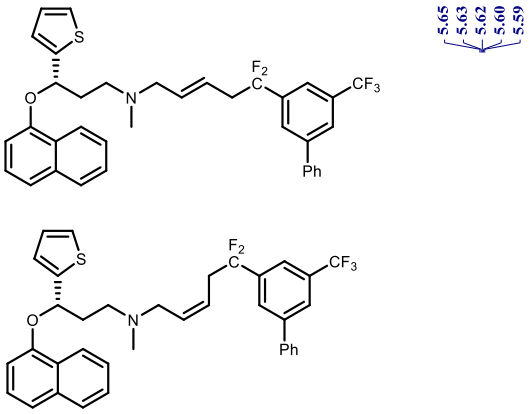
E / Z = 1.3 : 1





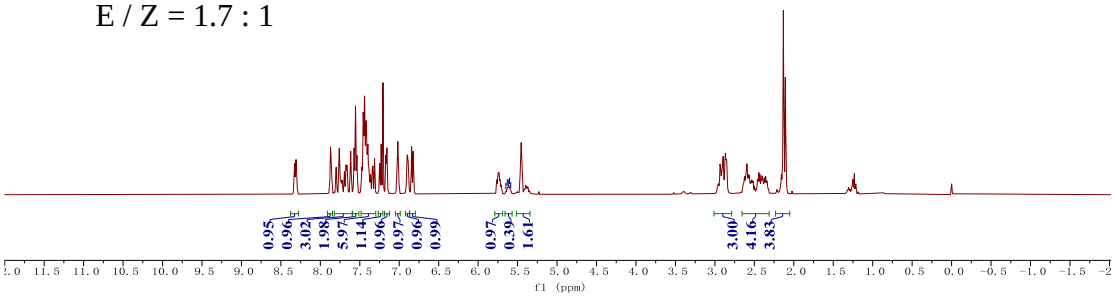
103ab - ^{19}F NMR (376 MHz, $CDCl_3$)

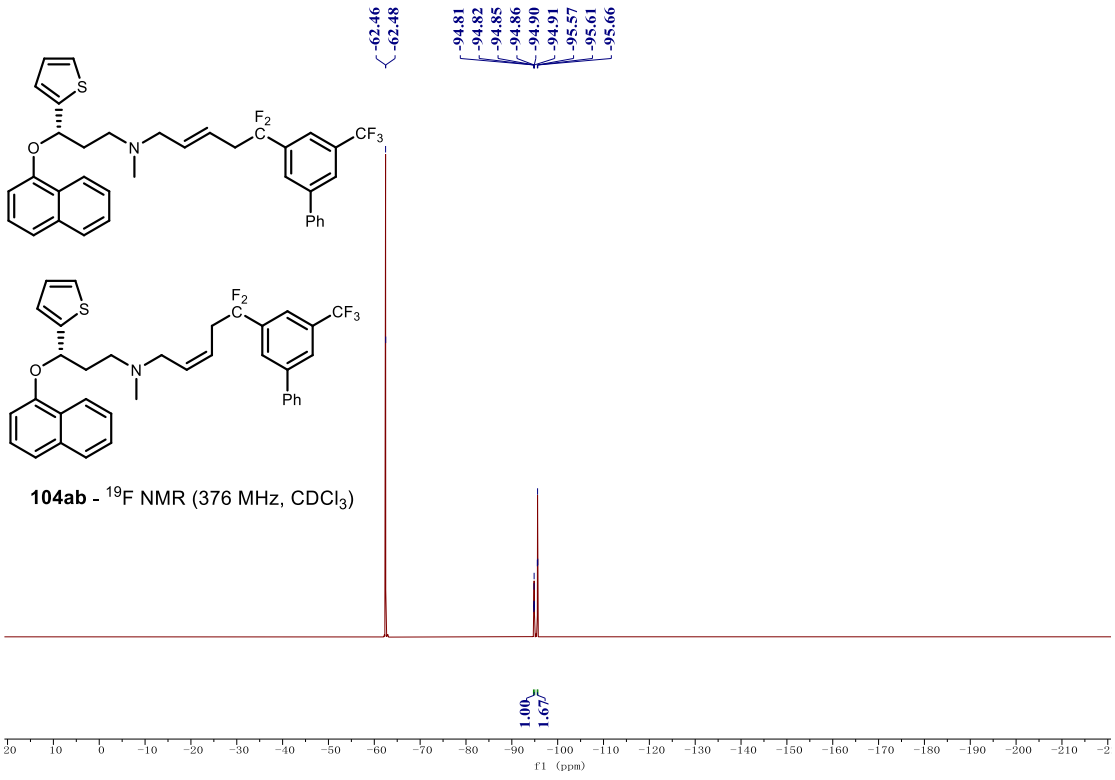




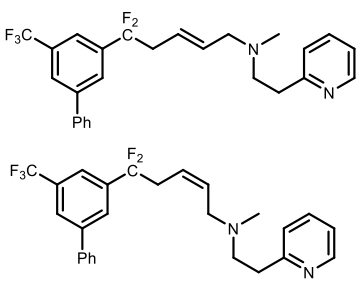
104ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1.7 : 1



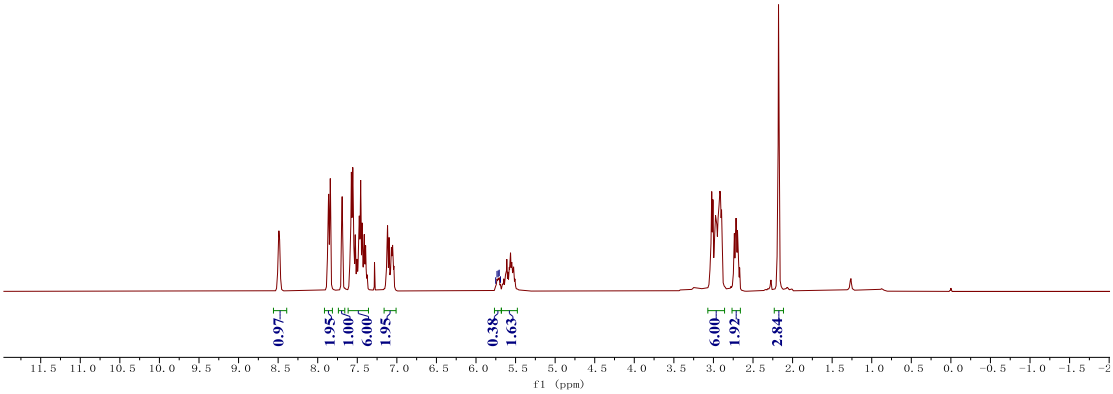


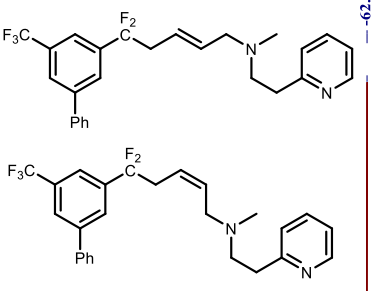
104ab - ^{19}F NMR (376 MHz, $CDCl_3$)



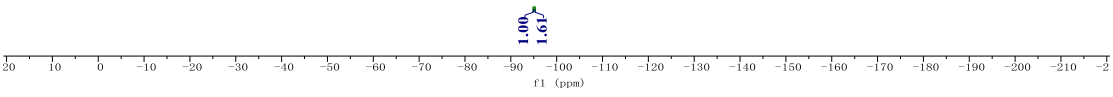
105ab - ^{1}H NMR (400 MHz. $CDCl_3$)

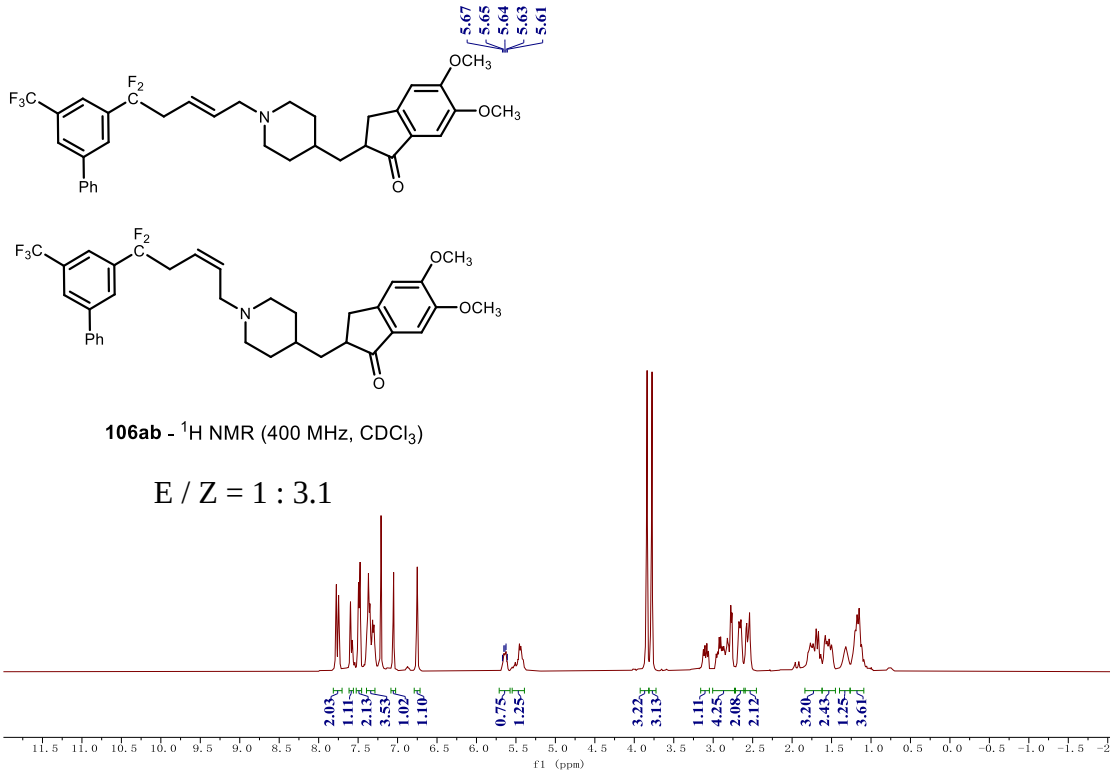
E / Z = 1.6 : 1





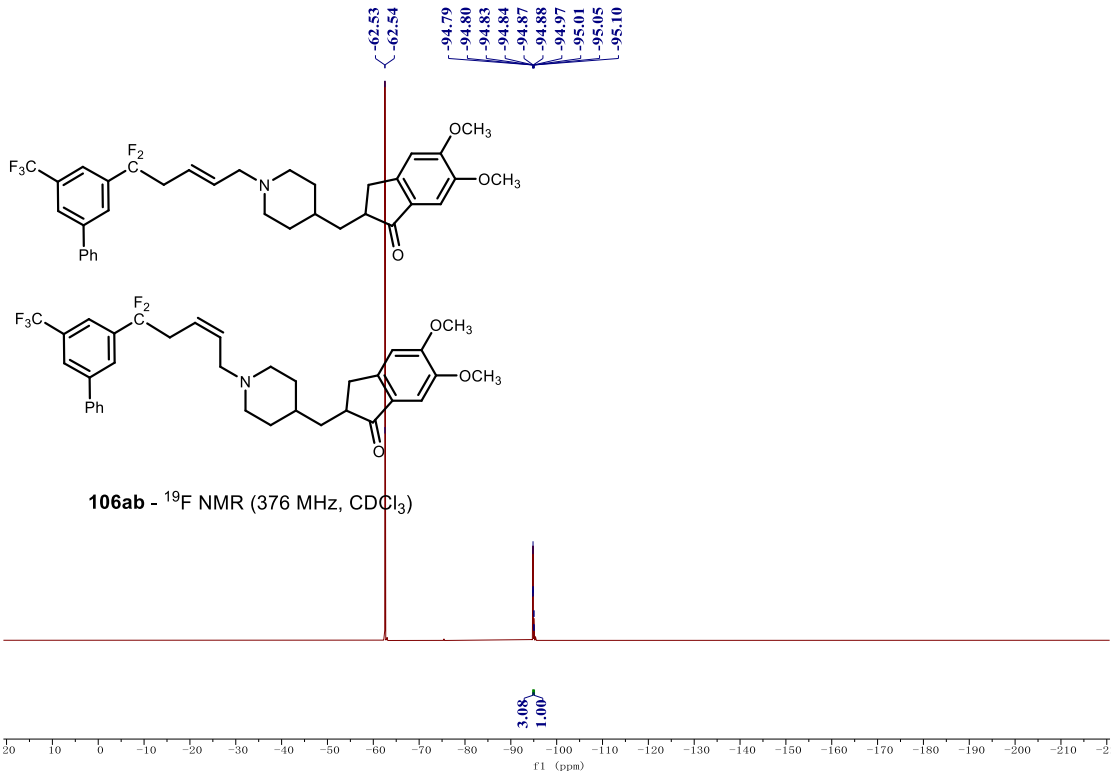
105ab - ^{19}F NMR (376 MHz, $CDCl_3$)



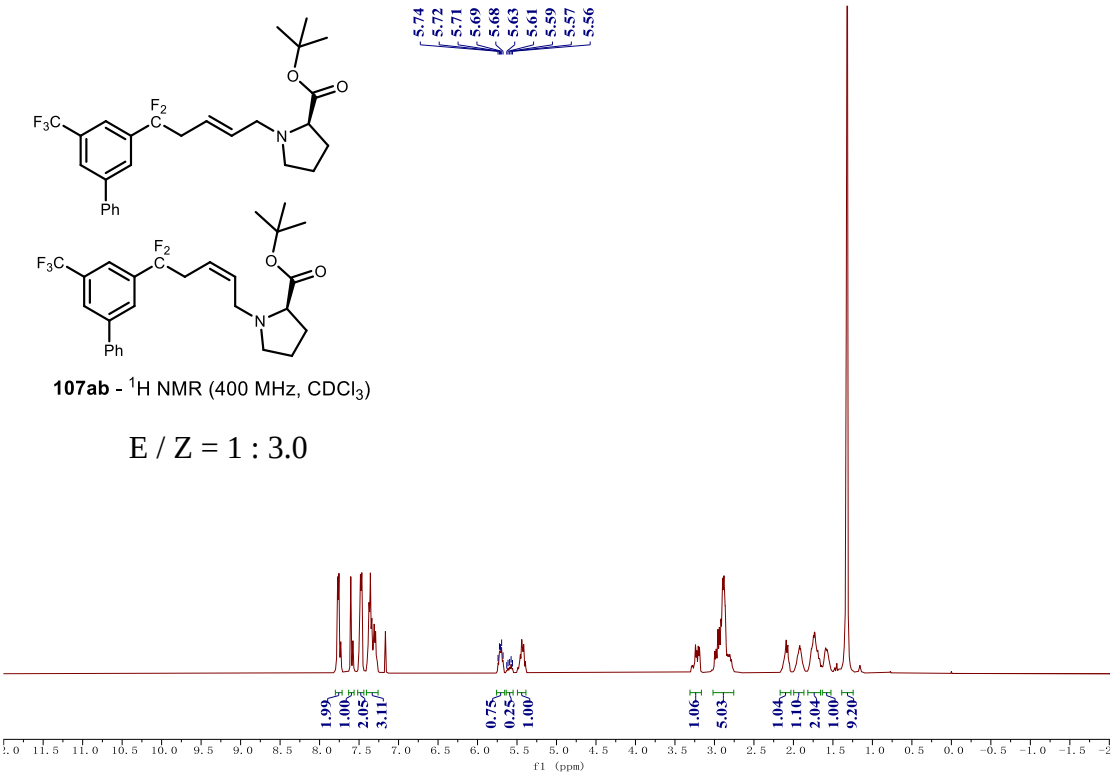


106ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 3.1

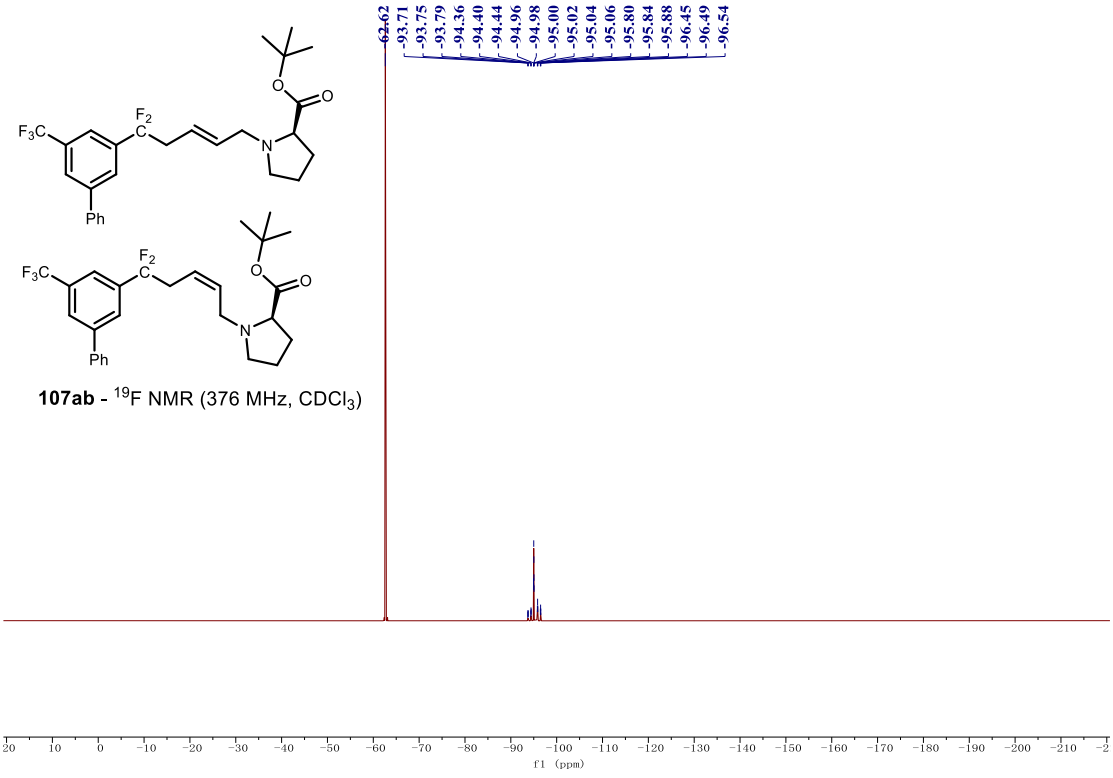


106ab - ^{19}F NMR (376 MHz, $CDCl_3$)

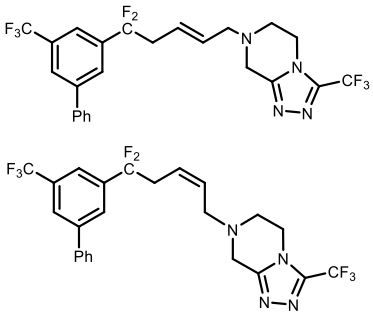


107ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 3.0

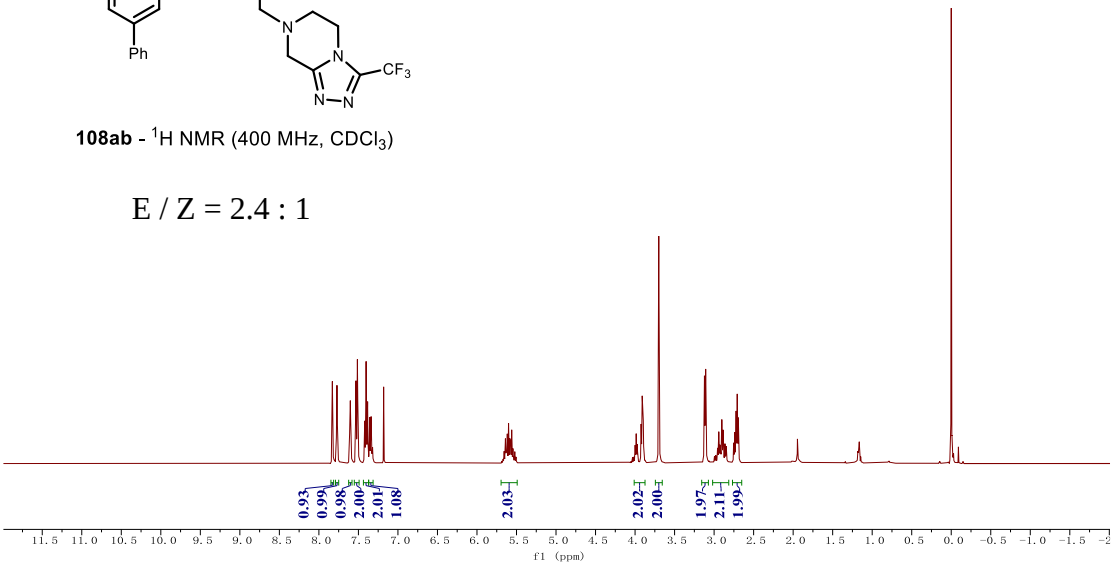


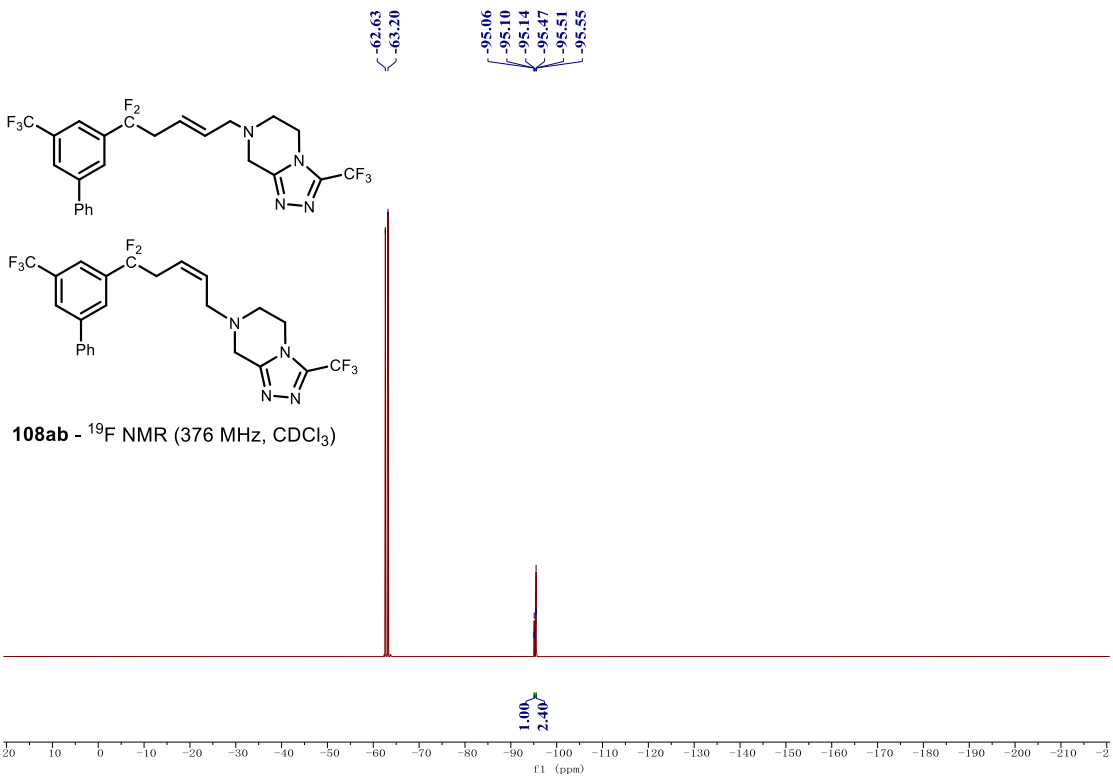
107ab - ^{19}F NMR (376 MHz, $CDCl_3$)



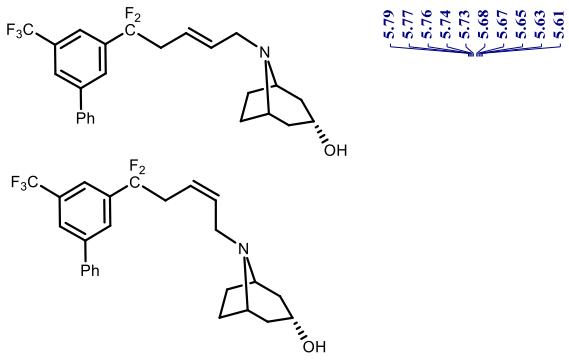
108ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 2.4 : 1



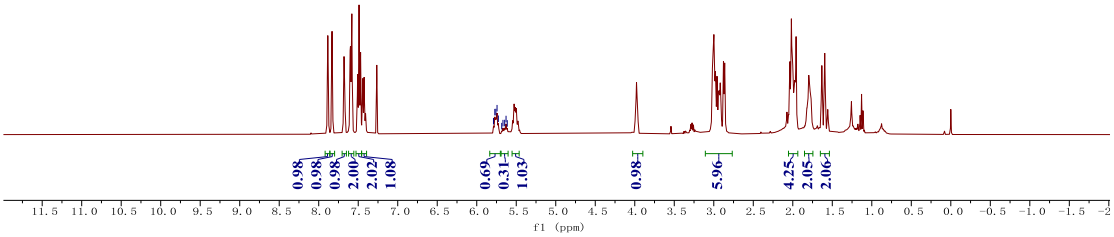


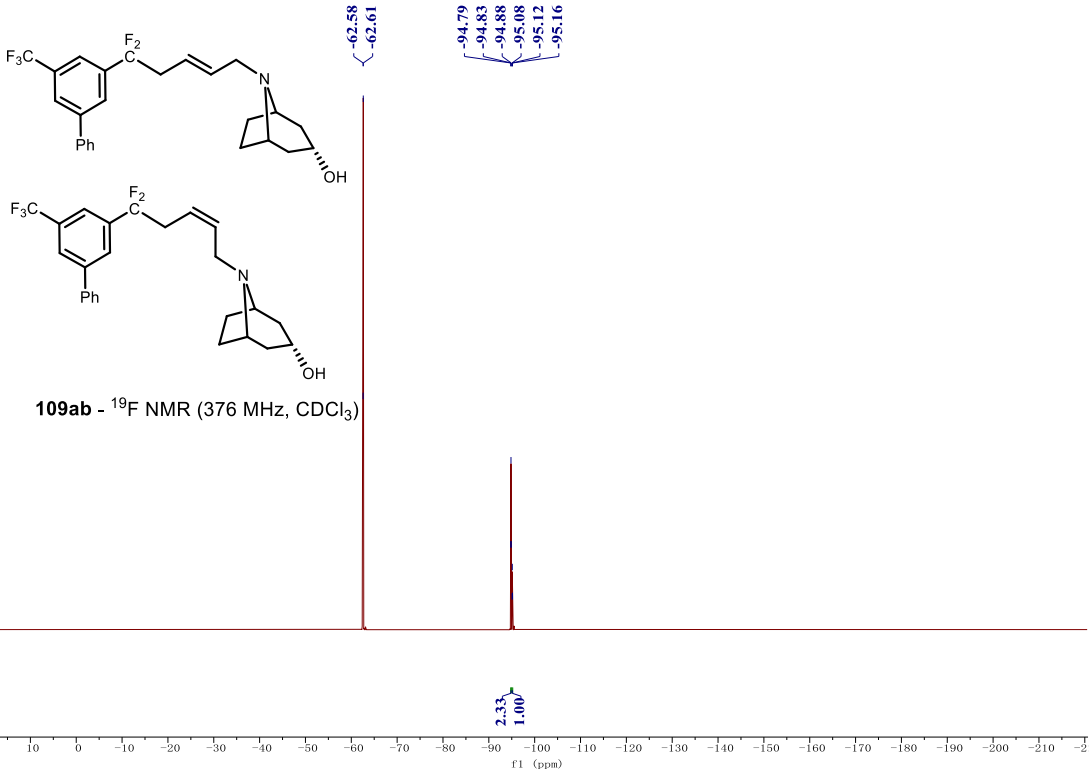
108ab - ^{19}F NMR (376 MHz, $CDCl_3$)



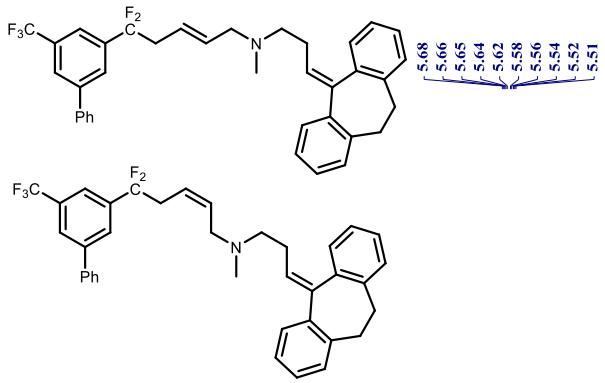
109ab - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 2.3



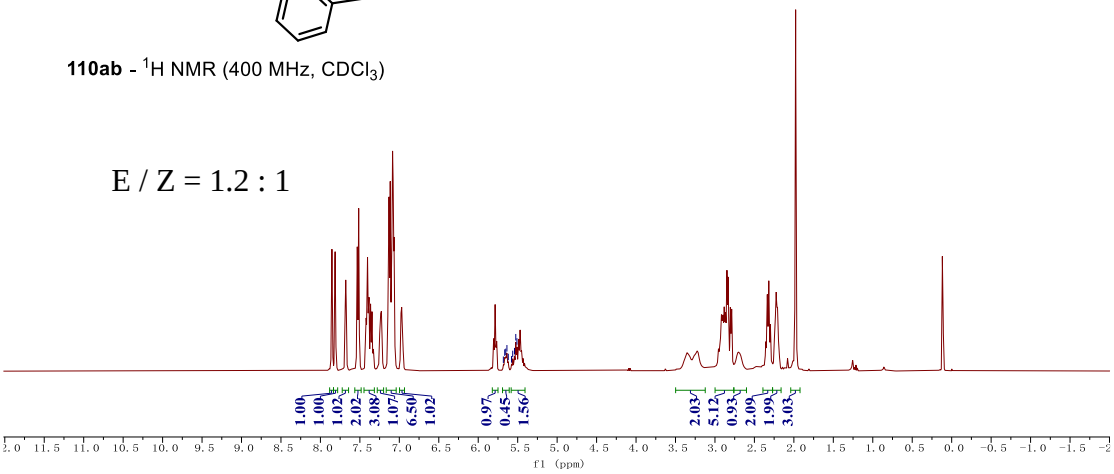


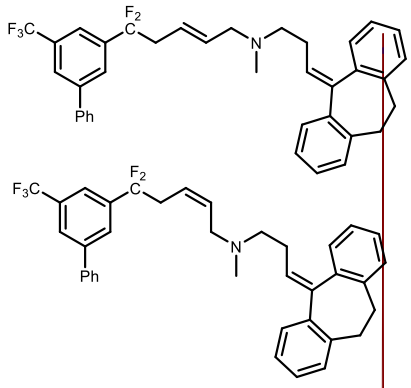
109ab - ^{19}F NMR (376 MHz, $CDCl_3$)



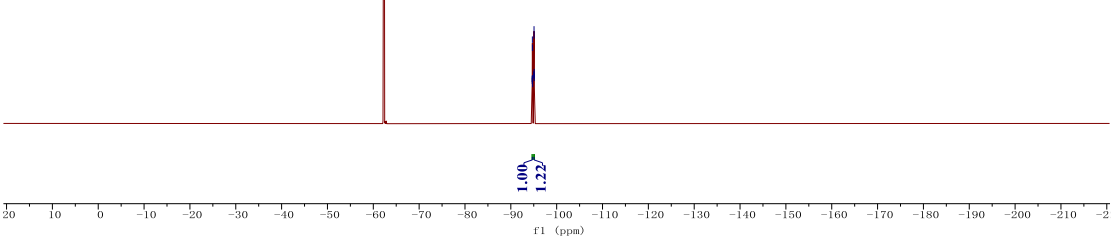
110ab - ^{1}H NMR (400 MHz, $CDCl_3$)

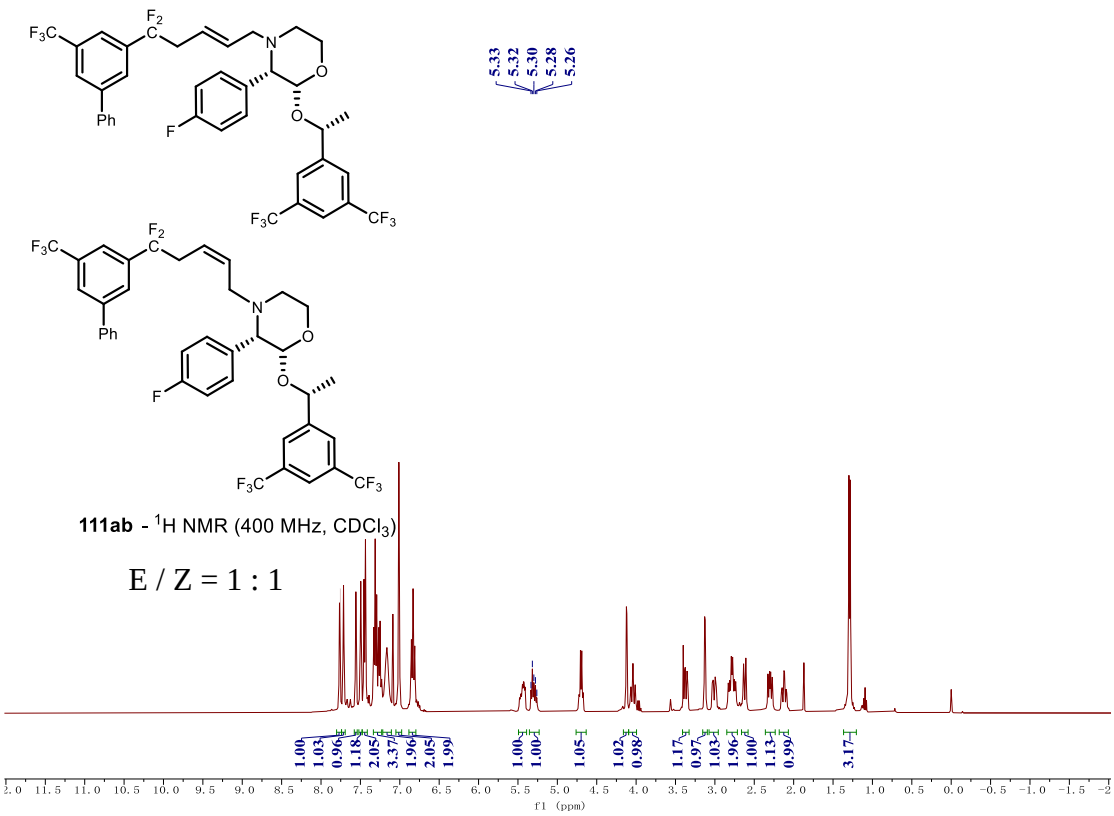
E / Z = 1.2 : 1

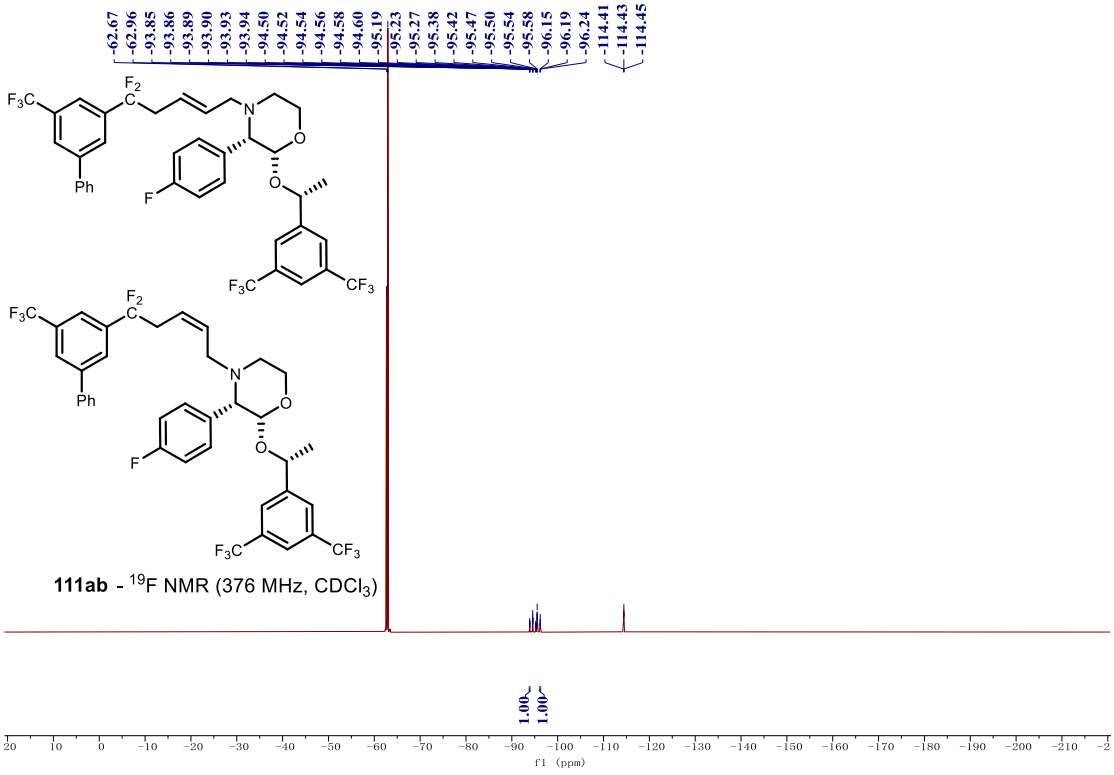


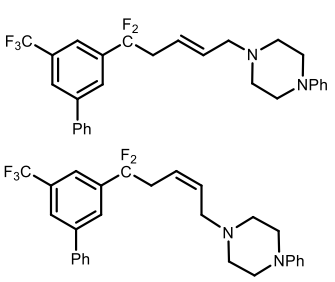


110ab - ^{19}F NMR (376 MHz, $CDCl_3$)



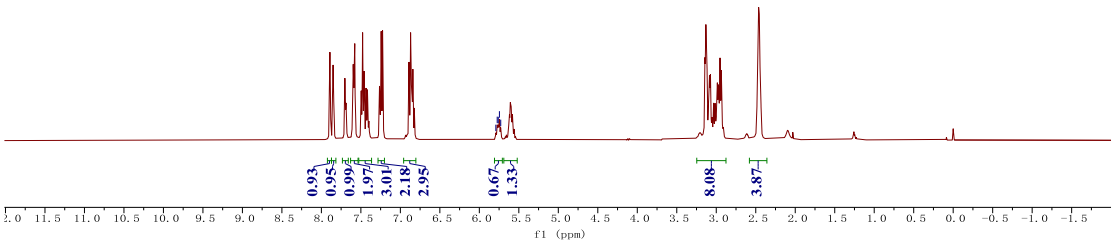

111ab - 1H NMR (400 MHz, CDCl3)
E / Z = 1 : 1

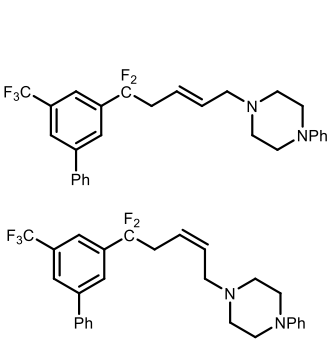

111ab - 19F NMR (376 MHz, CDCl3)



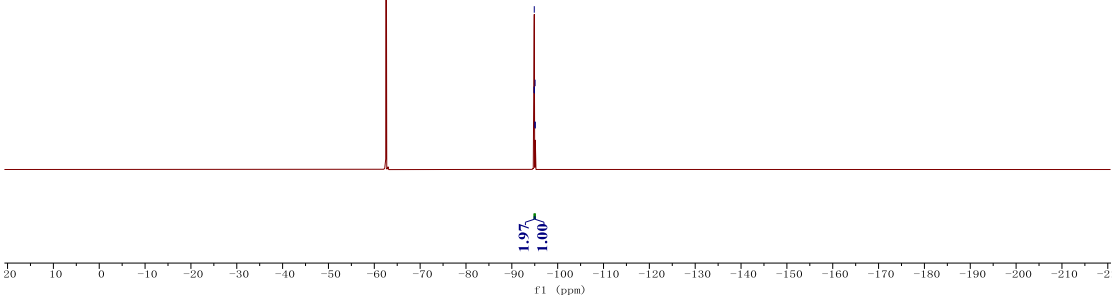
112 - ^{1}H NMR (400 MHz, $CDCl_3$)

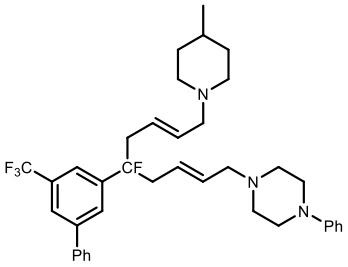
E / Z = 1 : 2.0





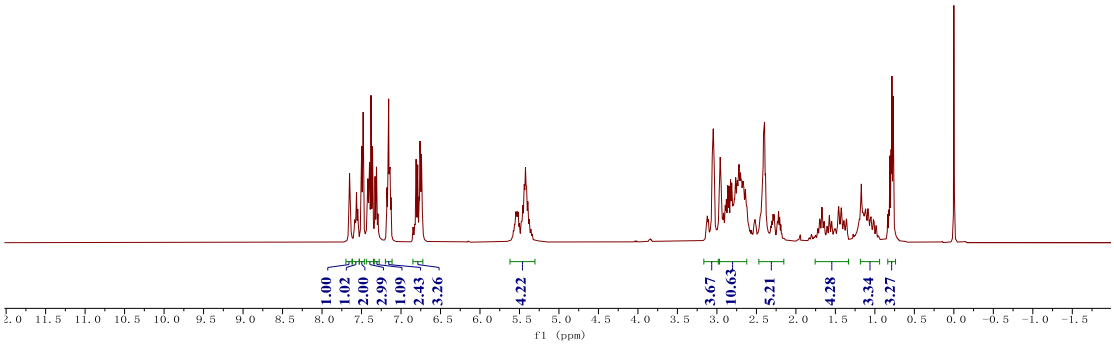
112 - ^{19}F NMR (376 MHz, $CDCl_3$)

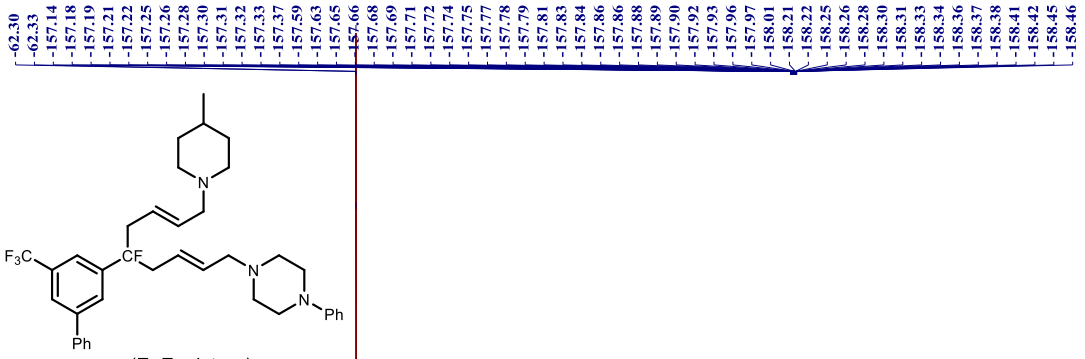




(E, Z mixture)

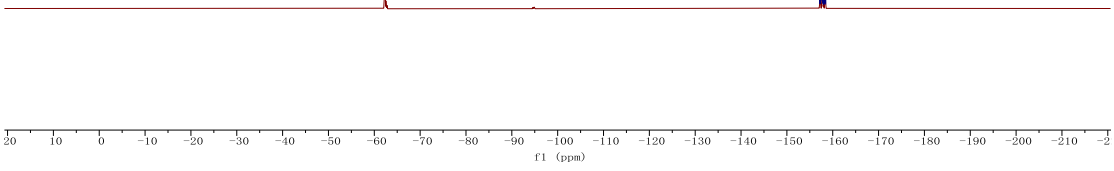
113 - ^{1}H NMR (400 MHz, $CDCl_3$)

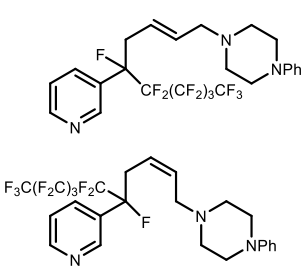




(E, Z mixture)

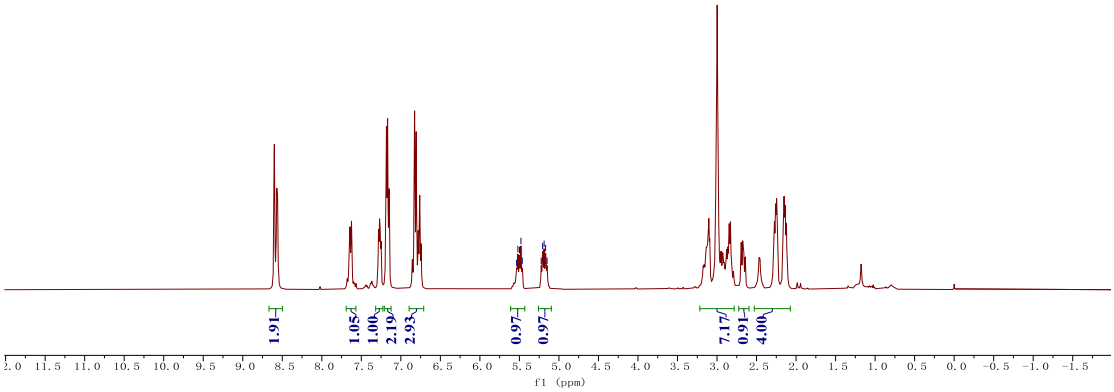
113 - ^{19}F NMR (376 MHz, $CDCl_3$)

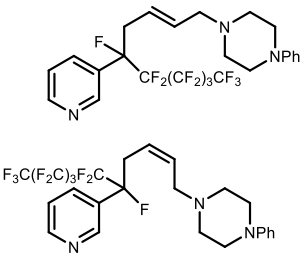




115 - ^{1}H NMR (400 MHz, $CDCl_3$)

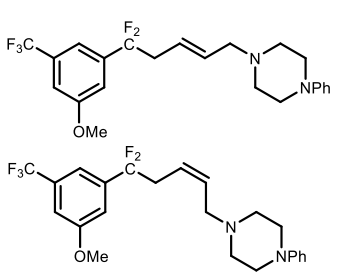
(E, Z mixtures)





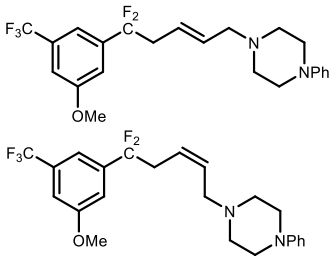
115 - ^{19}F NMR (376 MHz, $CDCl_3$)

(E, Z mixtures)

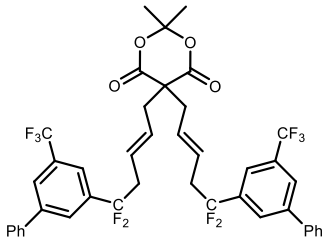


116 - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 1 : 3.0

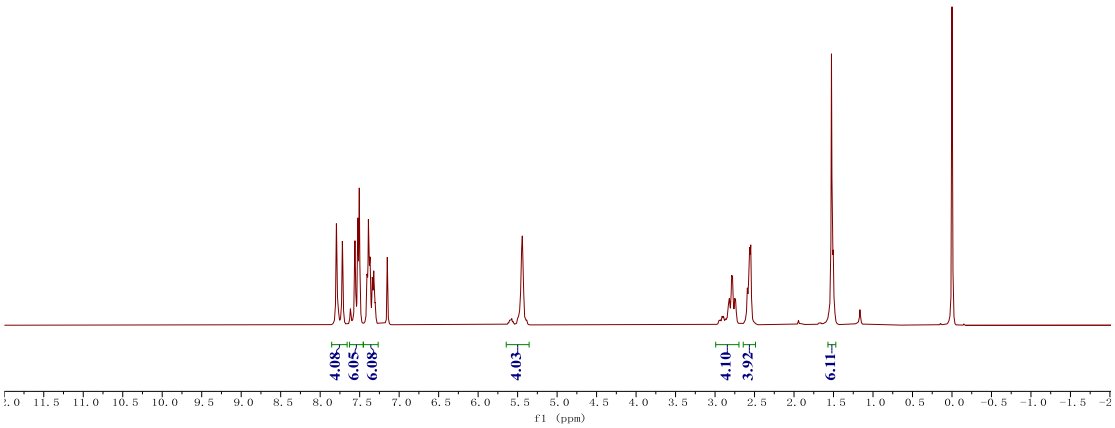


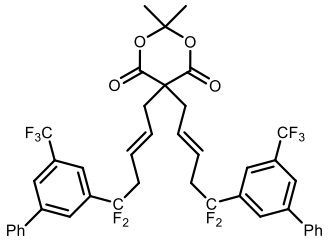
116 - ^{19}F NMR (376 MHz, $CDCl_3$)



(E, Z mixture)

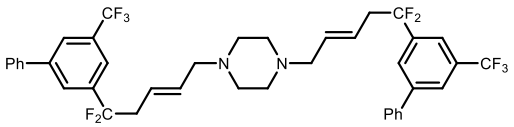
117 - ^{1}H NMR (400 MHz, $CDCl_3$)





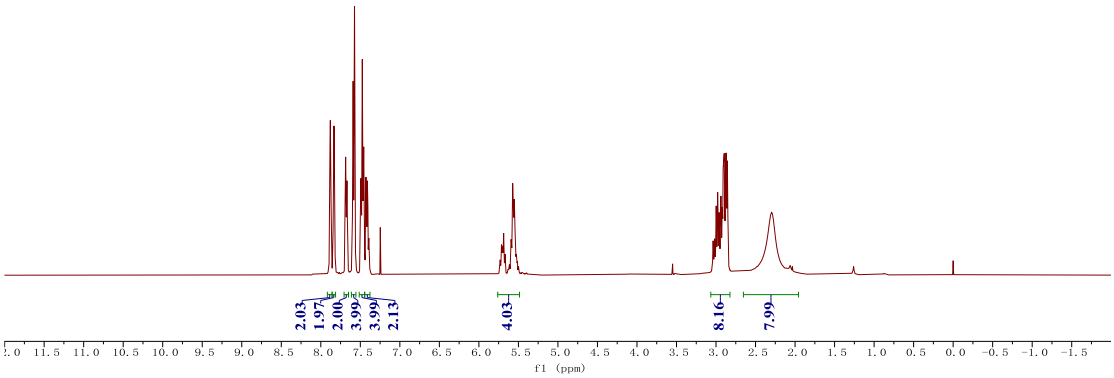
(E, Z mixture)

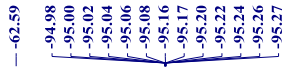
117 - ^{19}F NMR (376 MHz, $CDCl_3$)

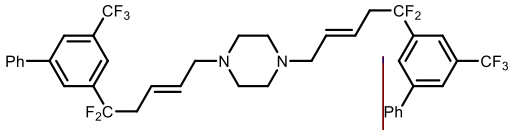


(E, Z mixtures)

118 - ^{1}H NMR (400 MHz, $CDCl_3$)

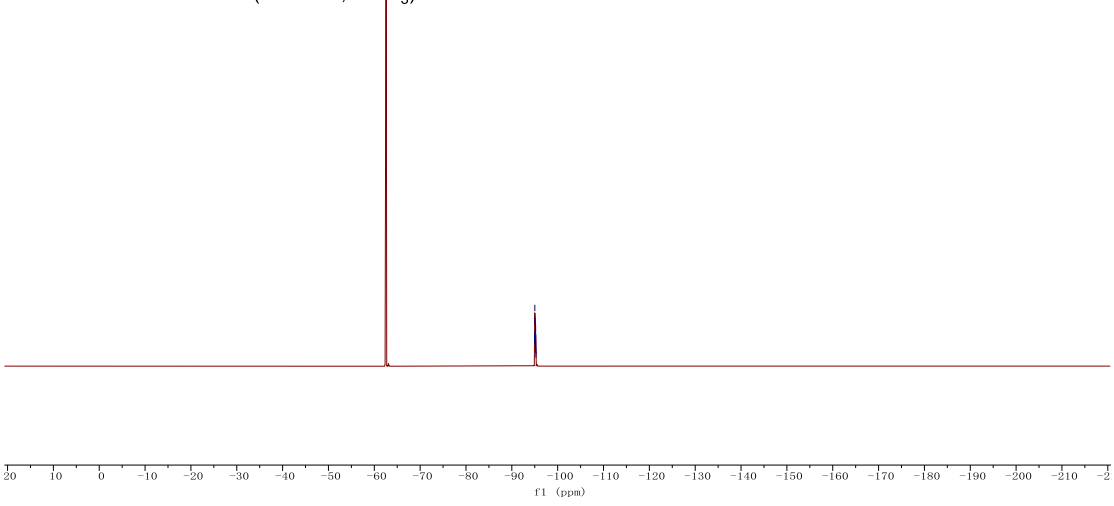


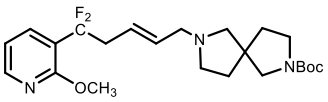


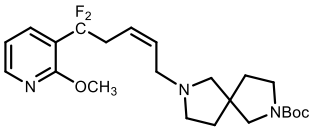


(E, Z mixtures)

118 - ^{19}F NMR (376 MHz, $CDCl_3$)

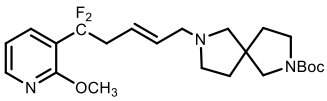


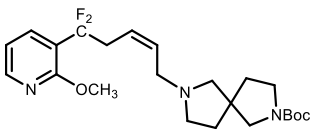




(E, Z mixture)

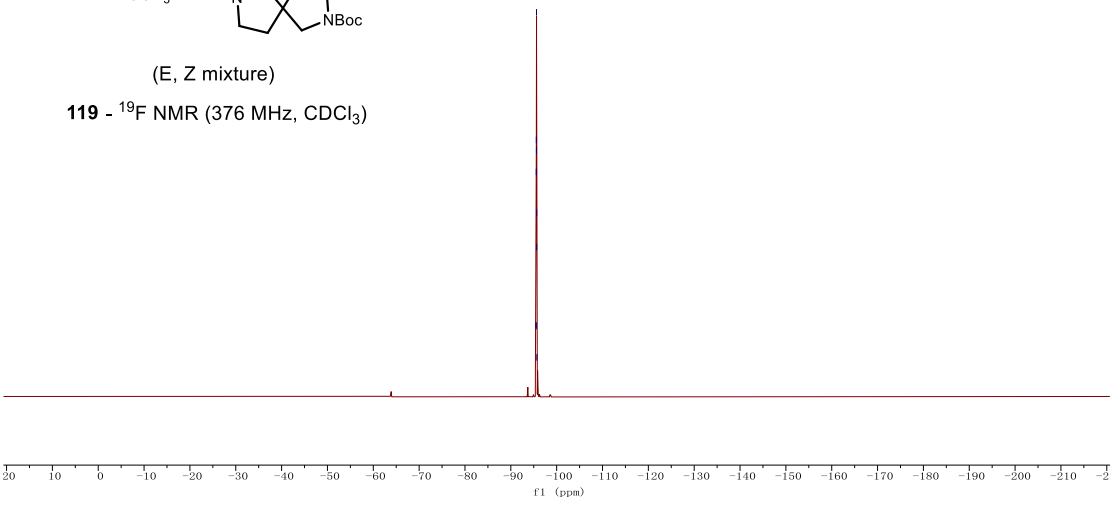
119 - ^{1}H NMR (400 MHz, $CDCl_3$)

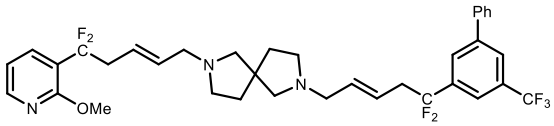




(E, Z mixture)

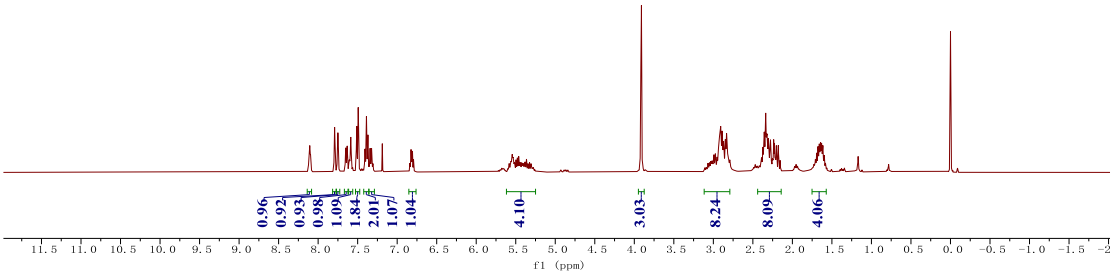
119 - ^{19}F NMR (376 MHz, $CDCl_3$)

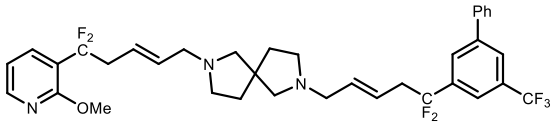




(E, Z mixture)

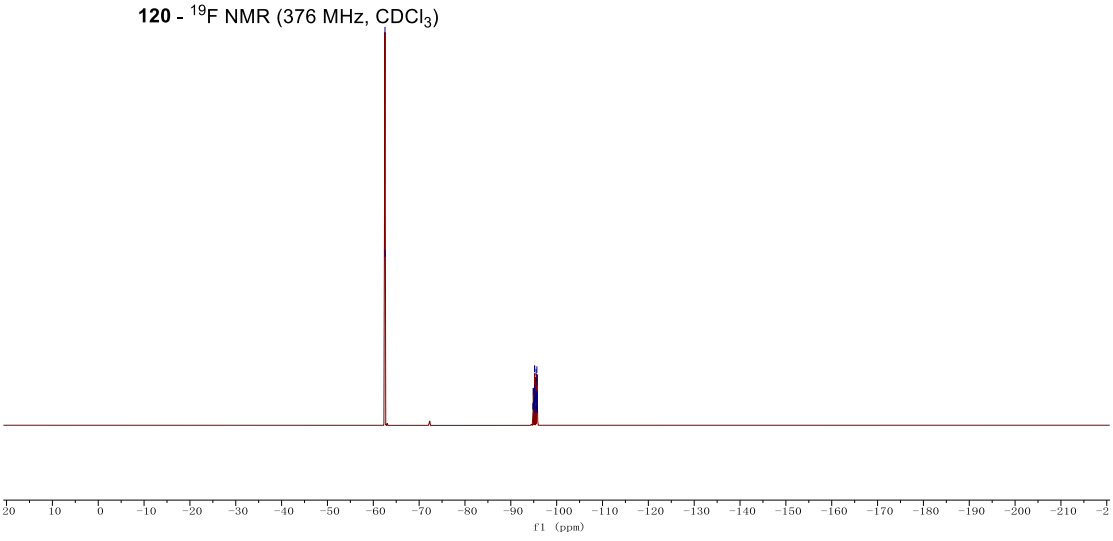
120 - ^{1}H NMR (400 MHz, $CDCl_3$)

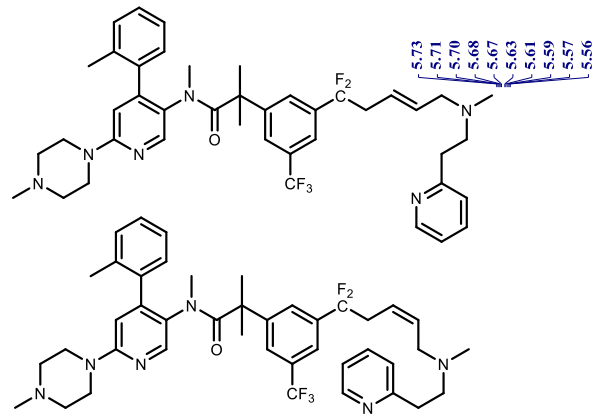




(E, Z mixture)

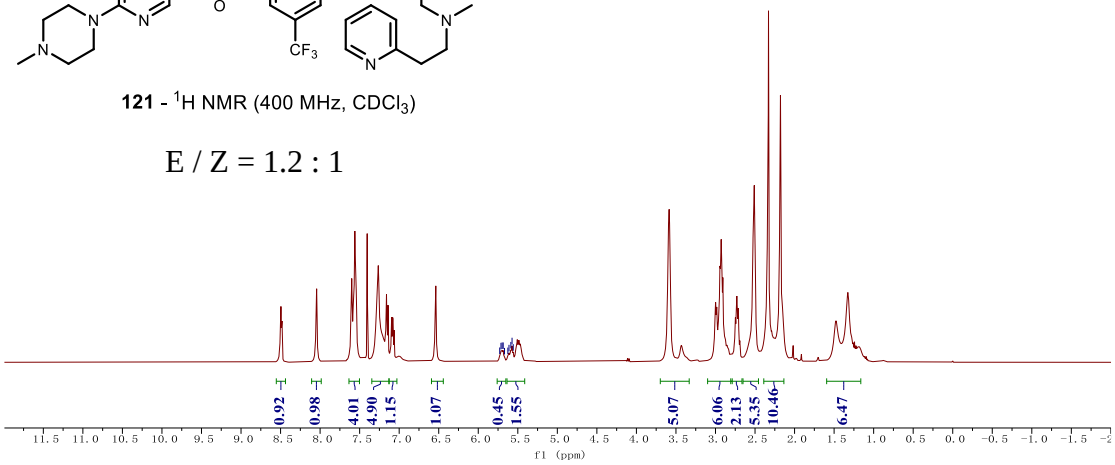
120 - ^{19}F NMR (376 MHz, $CDCl_3$)

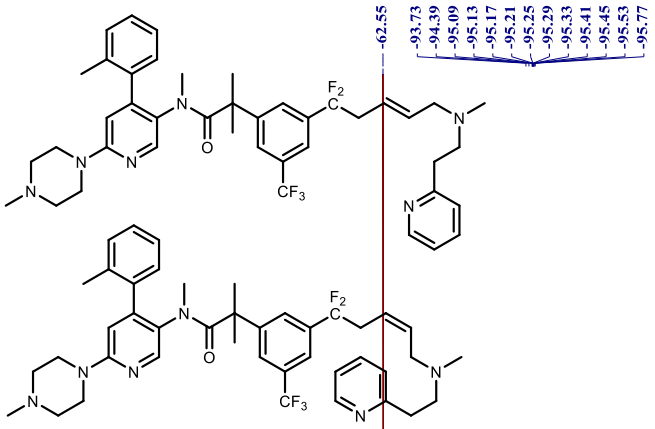




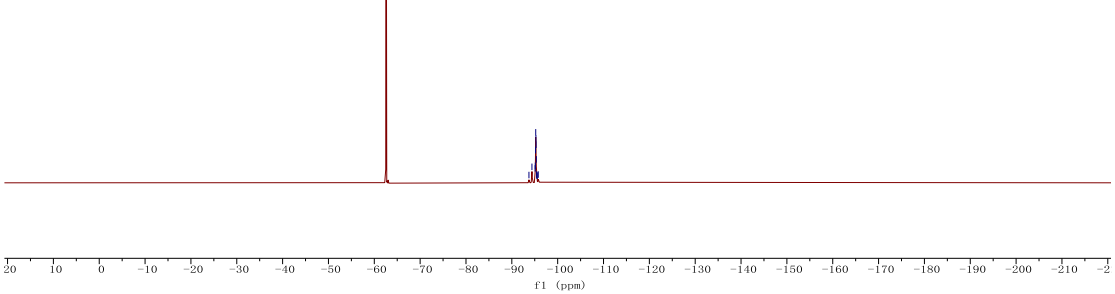
121 - ^{1}H NMR (400 MHz, $CDCl_3$)

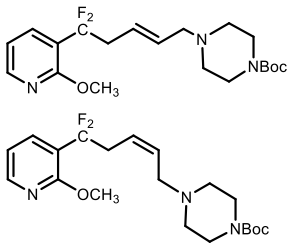
E / Z = 1.2 : 1





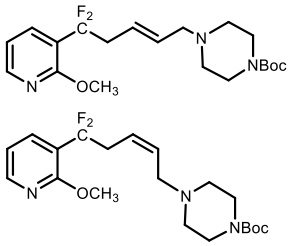
121 - ^{19}F NMR (376 MHz, $CDCl_3$)



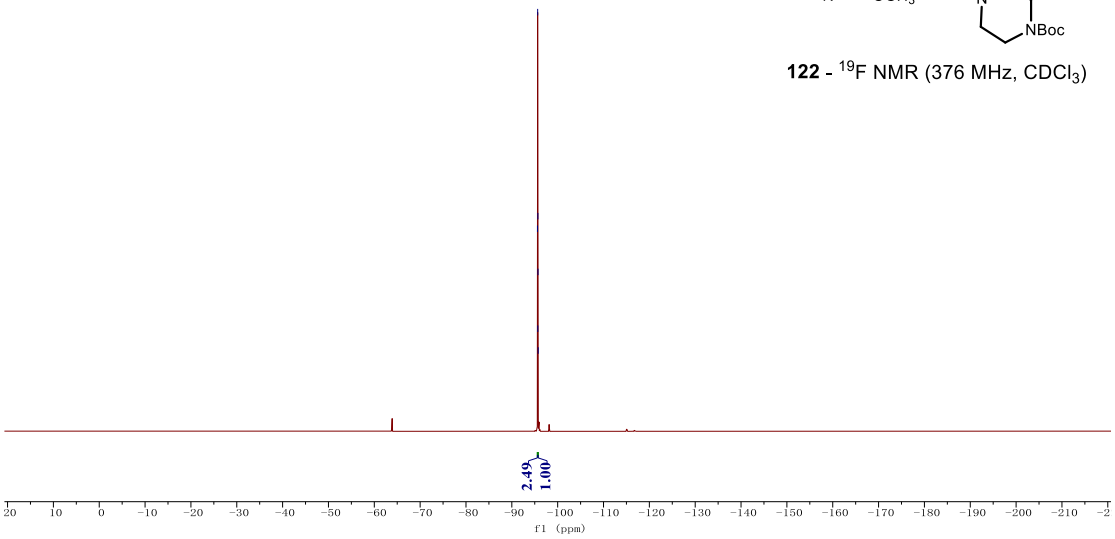


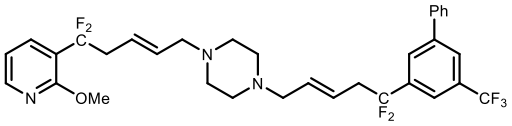
122 - ^{1}H NMR (400 MHz, $CDCl_3$)

E / Z = 2.5 : 1



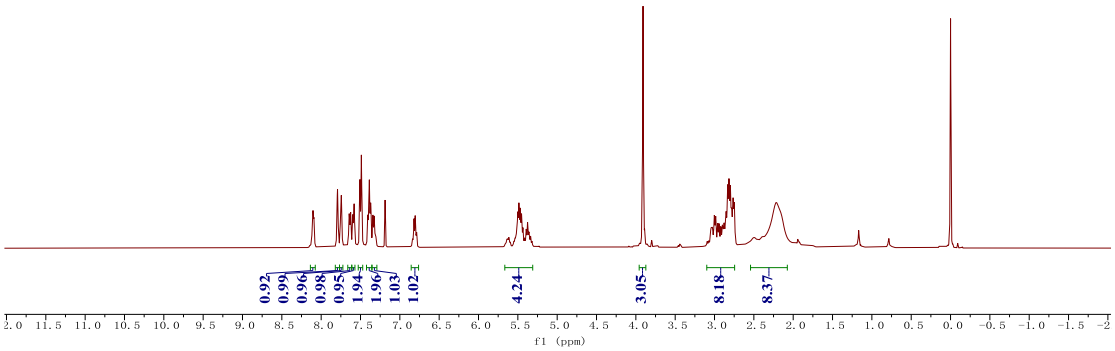
122 - ^{19}F NMR (376 MHz, $CDCl_3$)

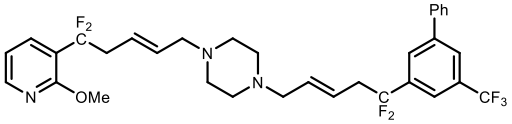




(E, Z mixture)

123 - ^{1}H NMR (400 MHz, $CDCl_3$)





(E, Z mixture)

123 - ^{19}F NMR (376 MHz, $CDCl_3$)