Supporting Information

NF_3 for Difluoroamination of Tertiary Lithium Reagents

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Contents

1. General remark

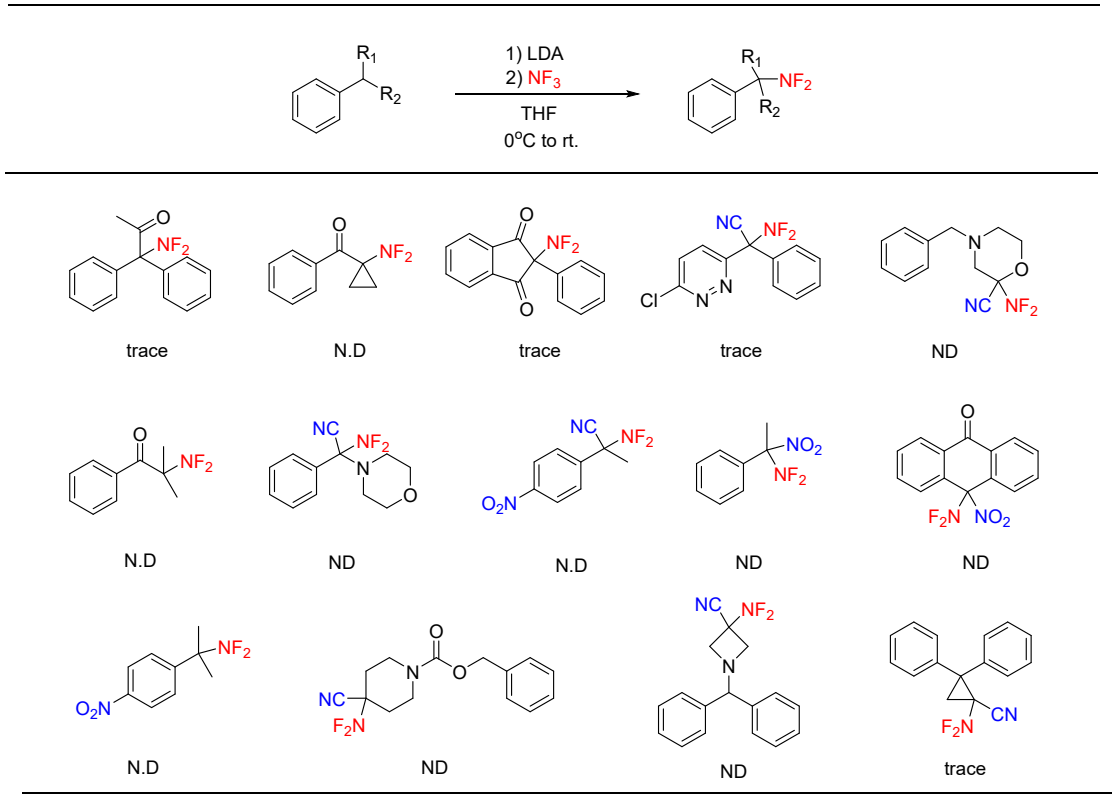
All reagents were commercially available and used without further purification unless indicated otherwise. ^{1}H, ^{13}C and ^{19}F NMR spectra were detected on a 500 MHz, 400 MHz or 300 MHz NMR spectrometer. Data for ^{1}H NMR, ^{13}C NMR and ^{19}F NMR were recorded as follows: chemical shift (δ, ppm), multiplicity (br = broad, s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet, quin = quintet, coupling constant(s) in Hz). All reactions were monitored by ^{19}F NMR. Flash column chromatography was carried out using 300-400 mesh silica gel at medium pressure. High resolution mass spectrometry (HRMS) was performed on a Waters Premier GC-TOF MS instrument with electron impact (EI) ionization mode, or on a Thermo Scientific Q Exactive HF Orbitrap-FTMS instrument with electrospray ionization (ESI) mode. Unless otherwise noted, all reagents and solvents were obtained commercially and used without further purification.

Warning

It is worth noting that NF_3 is a potent greenhouse gas, with a global warming potential (GWP) of approximately 17,200 [^30] [^31] over a 100-year time horizon, significantly higher than that of carbon dioxide. Therefore, during experimental operations, the rate of bubbling should be minimized to reduce the emission of NF_3 into the atmosphere as much as possible.

2. The synthesis of NF_2-containing compounds

2. 1. The non reactive substrates



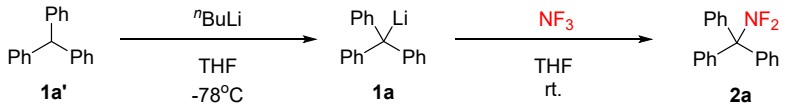
Scheme S1： The table of non reactive substrates

The reaction conditions and operations are the same as those for the preparation of **2b-2o**

2. 2. General procedure for the reactions

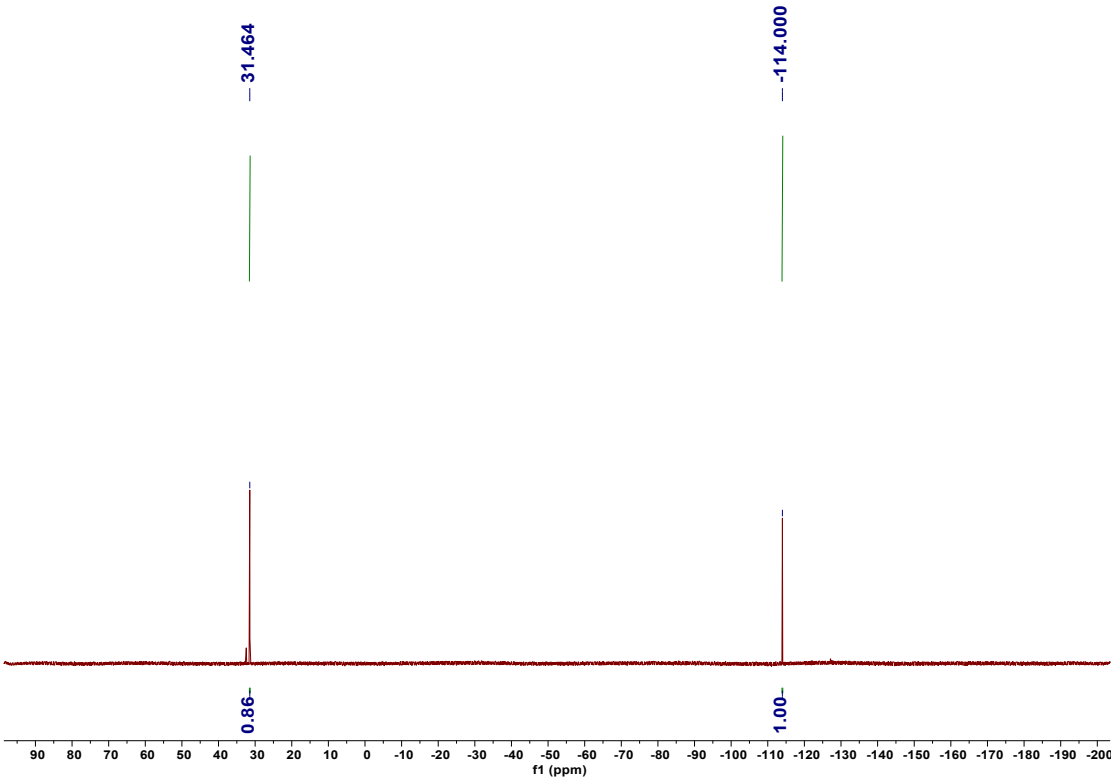
The stability of the obtained difluoroamination products was also systematically investigated. Most products exhibited good short-term stability when stored at room temperature under inert atmosphere. Specifically, representative products including **2a**, **2c** and **2g** showed no obvious decomposition after being stored in air at room temperature for more than 1 month, indicating excellent long-term stability. Most of the products are easily adsorbed by acidic silica gel, and require the use of an eluent containing 1% triethylamine for separation

2. 2. 1 The synthesis of **2a**



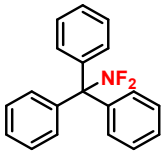
^{n}BuLi (2.4 M, 0.41 mL, 1.0 mmol, 2 equiv) was added into a solution of substrate **1a'** (0.5 mmol) in THF (10 mL) at -78 ℃ in a 25 mL Schlenk flask (flask A), and the reaction mixture was stirred at the same temperature under an Ar atmosphere for 60 minutes. A second 25 mL Schlenk flask (flask B) was charged with nitrogen trifluoride (NF_3) and fitted with a needle connected to a 200 mL NF_3-filled balloon as a reserve gas. The reaction mixture in flask A was then transferred dropwise into flask B at room temperature via syringe pump at a flow rate of 20 mL/h, while NF_3 in the balloon was simultaneously bubbled through the solution in flask B. When the dropwise addition is complete, the reaction is finished. Upon completion of the reaction, the solvent was removed by concentration under vacuum and the residue was subjected to flash column chromatography with petroleum ether/ethyl acetate (100:1, 1% Et_3N) as the eluent to afford product **2a**.

Method for ^{19}F Yield Determination



Figure：^{19}F NMR spectrum of the crude reaction mixture for the synthesis of **2a**

Upon completion of the reaction, 1.0 mmol of fluorobenzene (96.1 mg) was precisely added to the reaction system as an internal standard. The ^{19}F NMR yield of the reaction was calculated via the integral area ratio between the characteristic peak of the target product's difluoroamino group and the characteristic peak of fluorobenzene (δ 114.00 ppm, s). Taking the test of product **2a** as an example: its characteristic difluoroamino peak is located at δ = 31.46 ppm (s), and the integral ratio to the internal standard peak is 0.86:1, corresponding to an ^{19}F NMR yield of 86%.

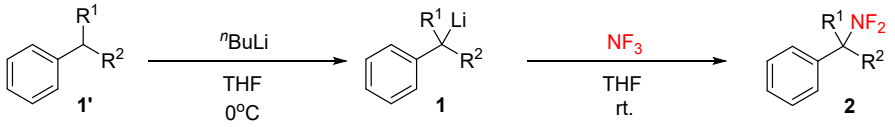


2a

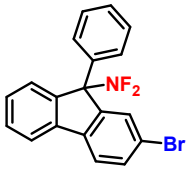
N,N-difluoro-1,1,1-triphenylmethanamin (2a)[1] (110.7 mg, 75%)

^1H NMR (400 MHz, $CDCl_3$): δ 7.45 – 7.39 (m, 6H), 7.38 – 7.30 (m, 9H); ^{19}F NMR (376 MHz, $CDCl_3$) δ 32.15 (s, 2F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.5, 129.8, 128.02, 128.05, 87.0 (t, $^2J_{C\text{-}F}$ = 8.7 Hz); LRMS (ESI) Calcd for $C_{19}H_{16}F_2N^+$ $[M+H]^+$: 296.1, Found: 296.1.

2. 2. 2 The synthesis of **2b-2o**



LDA (2.0 M, 0.5 mL, 1.0 mmol, 2 equiv) was added into a solution of substrate **1'** (0.5 mmol) in THF (10 mL) at 0 °C in a 25 mL Schlenk flask (flask A), and the reaction mixture was stirred at the same temperature under an Ar atmosphere for 30 minutes. A second 25 mL Schlenk flask (flask B) was charged with nitrogen trifluoride (NF_3) and fitted with a needle connected to a 200 mL NF_3-filled balloon as a reserve gas. The reaction mixture in flask A was then transferred dropwise into flask B at room temperature via syringe pump at a flow rate of 20 mL/h, while NF_3 in the balloon was simultaneously bubbled through the solution in flask B. When the dropwise addition is complete, the reaction is finished. Upon completion of the reaction, the solvent was removed by concentration under vacuum and the residue was subjected to flash column chromatography with petroleum ether/ethyl acetate (50:1 to 30:1, 1% Et_3N) as the eluent to afford product **2**.



2b

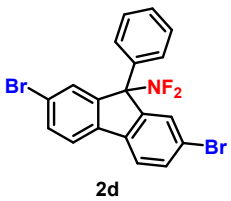
2-bromo-N,N-difluoro-9-phenyl-9H-fluoren-9-amine (2b) (116.7 mg, 63%)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, $^{3}J_{H\text{-}H}$ = 6.7 Hz, 1H), 7.68 (s, 1H), 7.60 (t, $^{3}J_{H\text{-}H}$ = 1.0 Hz, 3H), 7.54 (d, $^{3}J_{H\text{-}H}$ = 7.8 Hz, 1H), 7.48 (t, $^{3}J_{H\text{-}H}$ = 7.6 Hz, 1H), 7.42 – 7.37 (m, 2H), 7.37 – 7.32 (m, 4H); ^{19}F NMR (376 MHz, $CDCl_3$): AB system, δ 35.87 (d, $^{2}J_{F\text{-}F}$ = 563.3 Hz, 1F), 34.26 (d, $^{2}J_{F\text{-}F}$ = 565.7 Hz, 1F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 143.8 (t, *J* = 5.9 Hz), 141.7 (t, *J* = 5.4 Hz), 140.7, 140.6, 137.3 (t, *J* = 3.6 Hz), 133.3, 130.4, 130.3, 129.1, 128.8, 128.7, 127.2, 126.4, 121.9, 121.7, 120.5, 87.1 (t, $^{2}J_{C\text{-}F}$ = 9.1 Hz); IR (neat) ν = 3063, 2960, 2926, 1719, 1664, 1645, 1599, 1496, 1483, 1465, 1450, 1406, 1262, 1162, 1066, 1034, 905, 857, 758, 728, 698, 649 cm^{-1}; HRMS (DART) Calcd for $C_{19}H_{12}BrFN^{+}$ [M-F]$^{+}$: 352.0132, Found: 352.0129.

2c

N,N-difluoro-9-phenyl-9H-fluoren-9-amine (2c) (104.1 mg, 71%)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, $^{3}J_{H\text{-}H}$ = 6.7 Hz, 2H), 7.56 (d, $^{3}J_{H\text{-}H}$ = 7.6 Hz, 2H), 7.47 (tt, $^{3}J_{H\text{-}H}$ = 7.5, $^{4}J_{H\text{-}H}$ = 1.1 Hz, 2H), 7.45 – 7.41 (m, 2H), 7.36 – 7.30 (m, 5H); ^{19}F NMR (376 MHz, $CDCl_3$): δ 34.35 (s, 2F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 141.9 (t, *J* = 5.9 Hz), 141.7, 138.1 (t, *J* = 4.1 Hz), 130.1, 128.9, 128.5, 128.3, 127.2, 126.6, 120.4, 87.3 (t, $^{2}J_{C\text{-}F}$ = 9.3 Hz); IR (neat) ν = 3058, 3029, 2923, 2852, 1957, 1605, 1584, 1494, 1475, 1450, 1289, 1155, 1082, 1032, 999, 976, 917, 894, 852, 755, 746, 697, 645, 619 cm^{-1}; HRMS (FI) Calcd for $C_{19}H_{13}F_2N^{+}$ [M]$^{+}$:293.1011, Found: 293.1007.



2d

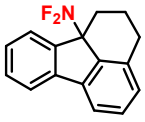
2,7-dibromo-N,N-difluoro-9-phenyl-9H-fluoren-9-amine (2d) (51.6 mg, 23%)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (s, 2H), 7.63 – 7.55 (m, 4H), 7.39 – 7.34 (m, 5H); ^{19}F NMR (376 MHz, $CDCl_3$): δ 35.21 (s, 2F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 143.5 (t, J = 6.1 Hz), 139.6, 136.6 (t, J = 6.3 Hz), 133.6, 130.4, 129.3, 129.1, 127.4 , 126.3, 122.4, 121.8; IR (neat) ν = 3060, 2922, 2851, 1654, 1576, 1598, 1495, 1455, 1413, 1252, 1174, 1061, 980, 970, 861, 813, 734, 698, 651 cm^{-1}; HRMS (DART) Calcd for $C_{19}H_{11}Br_2FN^+$ $[M\text{-}F]^+$: 429.9237, Found: 429.9233.

2e

N,N-difluoro-9-methyl-9H-fluoren-9-amine (2e) (47.4 mg, 41%)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, $^{3}J_{H\text{-}H}$ = 7.5 Hz, 2H), 7.62 (d, $^{3}J_{H\text{-}H}$ = 7.6 Hz, 2H), 7.46 (t, $^{3}J_{H\text{-}H}$ = 7.5 Hz, 2H), 7.35 (t, $^{3}J_{H\text{-}H}$ = 7.5 Hz, 2H), 1.91 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ 38.85 (s, 2F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 141.9 (t, J = 6.0 Hz), 141.2, 130.1, 128.2, 125.8, 120.4, 81.5 (t, $^{2}J_{C\text{-}F}$ = 7.8 Hz), 18.5 (t, $^{3}J_{C\text{-}F}$ = 7.5 Hz); IR (neat) ν = 3064, 2991, 2935, 2854, 1608, 1478, 1452, 1375, 1300, 1252, 1216, 1111, 962, 930, 860, 815, 758, 733, 657, 595, 559 cm^{-1}; HRMS (ESI) Calcd for $C_{14}H_{11}FN^+$ $[M\text{-}F]^+$: 212.0870, Found: 212.0863.

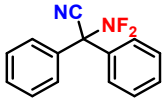


2f

N,N-difluoro-5,6-dihydrofluoranthen-6a(4H)-amine (2f) (68.1 mg, 53%)

This compound is particularly challenging to purify, as it slowly decomposes during flash column chromatography, leading to contamination with unknown byproducts.^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, $^{3}J_{H\text{-}H}$ = 7.5 Hz, 2H), 7.50 – 7.42 (m, 2H), 7.38 (t, $^{3}J_{H\text{-}H}$ = 8.0 Hz, 1H), 7.31 (t, $^{3}J_{H\text{-}H}$ = 7.5 Hz, 1H), 7.09 (d, $^{3}J_{H\text{-}H}$ = 7.4 Hz, 1H), 3.19 – 3.06 (m, 1H), 2.92 – 2.82 (m, 1H), 2.82 – 2.73 (m, 1H), 2.52 – 2.36 (m, 1H), 1.97 – 1.85 (m, 1H), 1.71 – 1.62 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$): AB system, δ 35.48 (d, $^{2}J_{F\text{-}F}$ = 565.1 Hz, 1F), 31.53 (d, $^{2}J_{F\text{-}F}$ = 563.3 Hz, 1F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 142.9, 141.4 (t, J = 6.4 Hz), 140.6, 138.2 (t, J = 7.9 Hz), 137.8, 130.7, 129.9, 127.5, 126.9, 126.83, 126.79, 120.6, 117.8, 79.8 (t, $^{2}J_{C\text{-}F}$ = 8.6 Hz), 26.7 (t, $^{3}J_{C\text{-}F}$ = 5.1 Hz), 25.3, 18.5; IR (neat) ν = 3056, 2917, 2848, 1688, 1645, 1607, 1485, 1451, 1337, 1303, 1261, 1064,

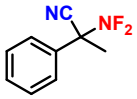
1035, 967, 858, 830, 758, 592 cm^{-1}; HRMS (ESI) Calcd for $C_{16}H_{13}FN^+$ $[M-F]^+$: 238.1027, Found: 238.1018.



2g

2-(difluoroamino)-2,2-diphenylacetonitrile (2g) (98.9 mg, 81%)

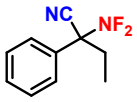
^1H NMR (400 MHz, $CDCl_3$): δ 7.64 – 7.53 (m, 4H), 7.52 – 7.39 (m, 6H); ^{19}F NMR (376 MHz, $CDCl_3$): δ 45.38 (s, 2F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 133.5 (t, J = 2.5 Hz), 130.2, 129.4, 127.2, 114.6 (t, J = 11.8 Hz), 82.1 (t, $^2J_{C-F}$ = 7.5 Hz); IR (neat) ν = 3060, 3037, 2928, 2854, 1958, 1813, 1597, 1493, 1450, 1341, 1225, 1193, 1159, 1086, 1036, 999, 967, 953, 927, 888, 866, 776, 758, 746, 698, 658, 642, 619, 596, 543, 474 cm^{-1}; HRMS (EI) Calcd for $C_{14}H_{10}N^+$ $[M-NF_2]^+$: 193.0886, Found: 193.0889.



2h

2-(difluoroamino)-2-phenylpropanenitrile (2h) (65.5 mg, 72%)

^1H NMR (400 MHz, $CDCl_3$): δ 7.65 – 7.56 (m, 2H), 7.53 – 7.44 (m, 3H), 2.07 – 2.00 (m, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): AB system, δ 47.18 (d, $^2J_{F-F}$ = 567.4 Hz, 1F), 42.62 (d, $^2J_{F-F}$ = 567.4 Hz, 1F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 132.2 (d, J = 5.5 Hz), 130.7, 129.5, 126.7, 115.0 (t, J = 11.5 Hz), 75.3 (t, $^2J_{C-F}$ = 7.1 Hz), 24.3 (dd, J = 4.5, 2.3 Hz); IR (neat) ν = 3067, 3012, 2928, 2855, 1602, 1495, 1452, 1382, 1334, 1241, 1176, 1098, 1080, 1029, 978, 934, 878, 835, 721, 696, 665, 606, 505, 460, 412 cm^{-1}; HRMS (FI) Calcd for $C_9H_8F_2N_2^+$ $[M]^+$: 182.0650, Found: 186.0646.

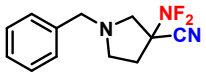


2i

2-(difluoroamino)-2-phenylbutanenitrile (2i) (66.7 mg, 68%)

^1H NMR (400 MHz, $CDCl_3$): δ 7.60 – 7.52 (m, 2H), 7.51 – 7.46 (m, 3H), 2.47 – 2.34 (m, 1H), 2.33 – 2.22 (m, 1H), 0.95 (t, $^3J_{H-H}$ = 7.4 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): AB system, δ 47.36 (d, $^2J_{F-F}$ = 571.0 Hz, 1F), 41.71 (d, $^2J_{F-F}$ = 569.2 Hz, 1F); ^{13}C NMR

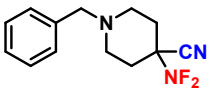
(101 MHz, $CDCl_3$): δ 130.6（t, J = 0.6 Hz）, 130.5, 129.4, 127.1, 114.1 (t, J = 12.1 Hz), 81.1 (t, $^2J_{C\text{-}F}$ = 6.2 Hz), 30.3 (t, $^3J_{C\text{-}F}$ = 2.6 Hz), 8.4; IR (neat) ν = 3067, 3036, 2986, 2944, 2886, 2851, 1959, 1886, 1812, 1665, 1601, 1493, 1453, 1388, 1334, 1305, 1261, 1219, 1157, 1103, 1081, 1003, 978, 957, 869, 800, 756, 721, 697, 674, 601, 585, 540, 505, 458, 418, 409 cm^{-1}; HRMS (FI) Calcd for $C_{10}H_{10}F_2N_2^+$ $[M]^+$: 196.0807, Found: 196.0806.



2j

1-benzyl-3-(difluoroamino)pyrrolidine-3-carbonitrile (2j) (32.1 mg, 27%)

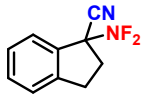
^1H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.27 (m, 5H), 3.68 (s, 2H), 3.15 (dd, J = 11.3, 3.3 Hz, 1H), 3.03 (d, J = 10.8 Hz, 1H), 2.92 – 2.67 (m, 2H), 2.59 – 2.48 (m, 1H), 2.47 – 2.37 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$): AB system, δ 52.10 (d, $^2J_{F\text{-}F}$ = 575.8 Hz, 1F), 47.38 (d, $^2J_{F\text{-}F}$ = 575.2 Hz, 1F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.2, 128.74, 128.67, 127.8, 115.7 (t, J = 14.1 Hz), 74.7 (t, $^2J_{C\text{-}F}$ = 6.4 Hz), 60.1 (d, $^3J_{C\text{-}F}$ = 5.4 Hz), 58.7, 52.2, 34.2 (d, $^3J_{C\text{-}F}$ = 4.1 Hz); IR (neat) ν = 3064, 3030, 2926, 2811, 1495, 1479, 1454, 1443, 1382, 1354, 1333, 1306, 1260, 1208, 1154, 1102, 1065, 1028, 963, 914, 869, 738, 699, 481, 460 cm^{-1}; HRMS (DART) Calcd for $C_{12}H_{14}F_2N_3^+$ $[M+H]^+$: 238.1150, Found: 238.1148.



2k

1-benzyl-4-(difluoroamino)piperidine-4-carbonitrile (2k) (51.5 mg, 41%)

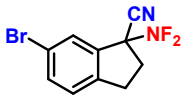
^1H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.26 (m, 5H), 3.57 (s, 2H), 3.01 – 2.92 (m, 2H), 2.37 (td, $^3J_{H\text{-}H}$ = 12.3, $^4J_{F\text{-}H}$ = 3.1 Hz, 2H), 2.17 – 2.01 (m, 4H); ^{19}F NMR (376 MHz, $CDCl_3$): δ 42.37 (s, 2F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.6, 129.1, 128.6, 127.6, 114.8 (t, J = 11.9 Hz), 71.9 (t, $^2J_{C\text{-}F}$ = 6.6 Hz), 62.4, 48.6, 31.0 (t, $^3J_{C\text{-}F}$ = 3.2 Hz); IR (neat) ν = 3031, 2962, 2854, 1723, 1676, 1603, 1520, 1496, 1454, 1355, 1261, 1029, 867, 800, 703 cm^{-1}; HRMS (ESI) Calcd for $C_{13}H_{16}F_2N_3^+$ $[M+H]^+$: 252.1307, Found: 252.1306.



2l

1-(difluoroamino)-2,3-dihydro-1H-indene-1-carbonitrile (2l) (43.7 mg, 45%)

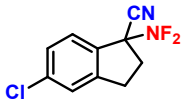
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, $^{3}J_{H-H}$ = 7.8 Hz, 1H), 7.48 (td, $^{3}J_{H-H}$ = 7.5, $^{4}J_{F-H}$ = 0.9 Hz, 1H), 7.41 – 7.33 (m, 2H), 3.30 – 3.16 (m, 1H), 3.16 – 3.05 (m, 1H), 2.91 – 2.70 (m, 2H); ^{19}F NMR (376 MHz, $CDCl_3$): AB system, δ 49.40 (d, $^{2}J_{F-F}$ = 574.6 Hz, 1F), 43.28 (d, $^{2}J_{F-F}$ = 574.6 Hz, 1F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.5, 133.0 (d, *J* = 5.5 Hz), 132.0, 128.1, 127.0 (d, *J* = 2.9 Hz), 125.6, 115.1 (t, *J* = 12.7 Hz), 79.5 (t, $^{2}J_{C-F}$ = 7.2 Hz), 34.9 (dd, *J* = 5.7, 0.8 Hz), 30.1; IR (neat) ν = 3077, 2961, 2857, 1479, 1461, 1437, 1412, 1314, 1260, 1029, 978, 897, 870, 801, 775, 760, 735, 709, 670, 481, 433 cm^{-1}; HRMS (ESI) Calcd for $C_{10}H_8N^+$ $[M\text{-}NF_2]^+$: 142.0651, Found: 142.0653.



2m

6-bromo-1-(difluoroamino)-2,3-dihydro-1H-indene-1-carbonitrile (2m) (48.9 mg, 36%)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (s, 1H), 7.60 (d, $^{3}J_{H-H}$ = 8.2 Hz, 1H), 7.24 (d, $^{3}J_{H-H}$ = 8.3 Hz, 1H), 3.22 – 3.00 (m, 2H), 2.90 – 2.73 (m, 2H); ^{19}F NMR (376 MHz, $CDCl_3$): AB system, δ 47.89 (d, $^{2}J_{F-F}$ = 578.2 Hz, 1F), 42.32 (d, $^{2}J_{F-F}$ = 578.8 Hz, 1F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 144.4, 135.2, 134.9 (d, *J* = 5.6 Hz), 130.0 (d, *J* = 2.7 Hz), 127.0, 121.6, 114.6 (t, *J* = 12.5 Hz), 79.0 (t, $^{2}J_{C-F}$ = 7.9 Hz), 35.1 (dd, *J* = 5.4, 1.2 Hz), 29.7; IR (neat) ν = 3063, 2925, 2853, 1475, 1449, 1437, 1408, 1247, 1164, 1065, 977, 902, 867, 821, 738, 682, 651, 566, 481, 442, 415 cm^{-1}; HRMS (FI) Calcd for $C_{10}H_7BrF_2N_2^+$ $[M]^+$: 271.9755, Found: 271.9753.

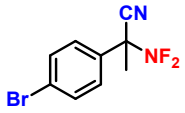


2n

5-chloro-1-(difluoroamino)-2,3-dihydro-1H-indene-1-carbonitrile (2n) (53.6 mg, 47%)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, $^{3}J_{H-H}$ = 7.5 Hz, 1H), 7.40 – 7.33 (m, 2H), 3.28 – 3.14 (m, 1H), 3.14 – 3.03 (m, 1H), 2.91 – 2.72 (m, 2H); ^{19}F NMR (376 MHz, $CDCl_3$):

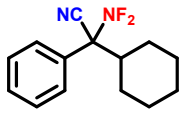
AB system, δ 48.02 (d, $^{2}J_{F\text{-}F}$ = 577.0 Hz, 1F), 41.81 (d, $^{2}J_{F\text{-}F}$ = 577.0 Hz, 1F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 147.3, 138.5, 131.5 (d, *J* = 5.9 Hz), 128.6, 128.0 (d, *J* = 2.7 Hz), 125.9, 114.7 (t, *J* = 12.3 Hz), 78.8 (dd, $^{2}J_{C\text{-}F}$ = 7.2, 2.0 Hz), 35.0 (dd, *J* = 6.8, 1.3 Hz), 29.9; IR (neat) ν = 3083, 2960, 2928, 2855, 1899, 1720, 1600, 1580, 1474, 1452, 1436, 1417, 1319, 1300, 1256, 1209, 1096, 1071, 979, 897, 872, 819, 739, 718, 696, 653, 598, 559, 483, 447, 419, 410 cm^{-1}; HRMS (FI) Calcd for $C_{10}H_7ClF_2N_2^+$ $[M]^+$: 228.0260, Found: 228.0262.



2o

2-(4-bromophenyl)-2-(difluoroamino)propanenitrile (2o) (57.2 mg, 44%)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, $^{3}J_{H\text{-}H}$ = 8.9 Hz, 2H), 7.47 (d, $^{3}J_{H\text{-}H}$ = 8.9 Hz, 2H), 2.02 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): AB system, δ 47.14 (d, $^{2}J_{F\text{-}F}$ = 569.2 Hz, 1F), 42.65 (d, $^{2}J_{F\text{-}F}$ = 569.8 Hz, 1F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 132.8, 131.3 (d, *J* = 5.4 Hz), 128.4, 125.3, 114.6 (t, *J* = 12.3 Hz), 74.8 (t, $^{2}J_{C\text{-}F}$ = 7.7 Hz), 24.17 (dd, *J* = 2.4, 1.0 Hz); IR (neat) ν = 3093, 3010, 2960, 2851, 2258, 1908, 1685, 1590, 1491, 1456, 1403, 1381, 1249, 1173, 1095, 1080, 1011, 979, 930, 876, 840, 813, 729, 714, 695, 608, 538, 509, 427 cm^{-1}; HRMS (FI) Calcd for $C_9H_7BrF_2N_2^+$ $[M]^+$: 259.9755, Found: 259.9756.



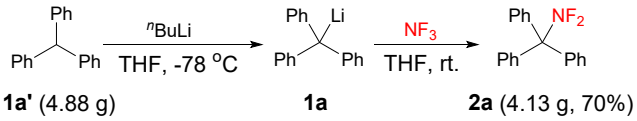
2p

2-cyclohexyl-2-(difluoroamino)-2-phenylacetonitrile (2p) (97.6mg, 78%)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 – 7.40 (m, 5H), 2.41 – 2.30 (m, 1H), 2.09 (d, *J* = 12.6 Hz, 1H), 1.85 – 1.70 (m, 2H), 1.65 (d, *J* = 14.0 Hz, 1H), 1.41 – 1.15 (m, 3H), 1.12 – 0.91 (m, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): AB system, δ 43.90 (d, $^{2}J_{F\text{-}F}$ = 572.2 Hz, 1F), 38.87 (d, $^{2}J_{F\text{-}F}$ = 572.8 Hz, 1F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 130.1, 129.9 (dd, *J* = 6.8, 1.6 Hz), 128.8, 127.6, 125.4 (d, *J* = 5.9 Hz), 114.6 (dd, *J* = 10.9, 1.9 Hz), 83.5 (t, $^{2}J_{C\text{-}F}$ = 5.5 Hz), 45.1 (t, $^{3}J_{C\text{-}F}$ = 2.0 Hz), 28.5 (d, *J* = 2.3 Hz), 26.9, 25.9, 25.8 (d, *J* = 2.7 Hz); IR (neat) ν = 3065.1, 2937.0, 2859.2, 2675.3, 1960.9, 1889.9, 1811.9, 1811.9, 1601.8, 1494.6, 1452.0, 1372.8, 1327.3, 1278.2, 1254.3, 1216.8, 1074.9, 1028.1,

1006.3, 974.3, 915.7, 879.2, 806.9, 762.4, 707.9, 659.7, 644.3, 517.2, 471.3 cm^{-1}; HRMS (DART) Calcd for $C_{14}H_{20}F_2N_3^+$ $[M + NH_4]^+$: 268.1620, Found: 268.1617.

3. A large-scale reaction

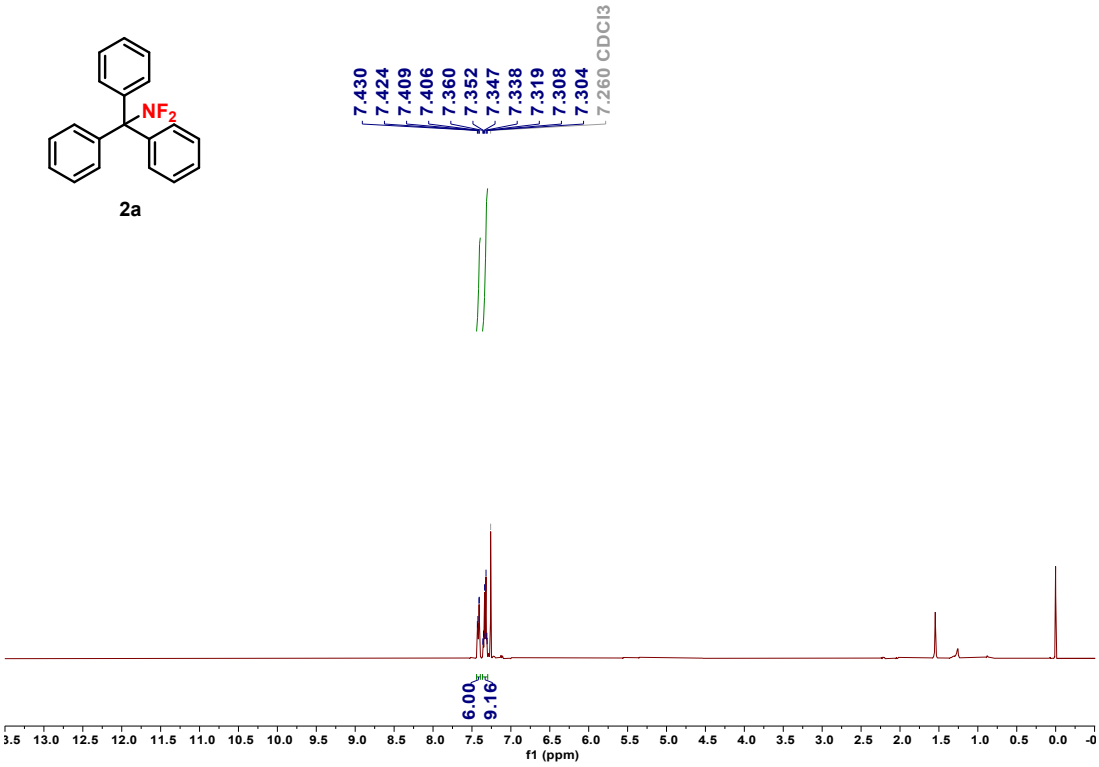


1a' (4.88 g) **1a** **2a** (4.13 g, 70%)

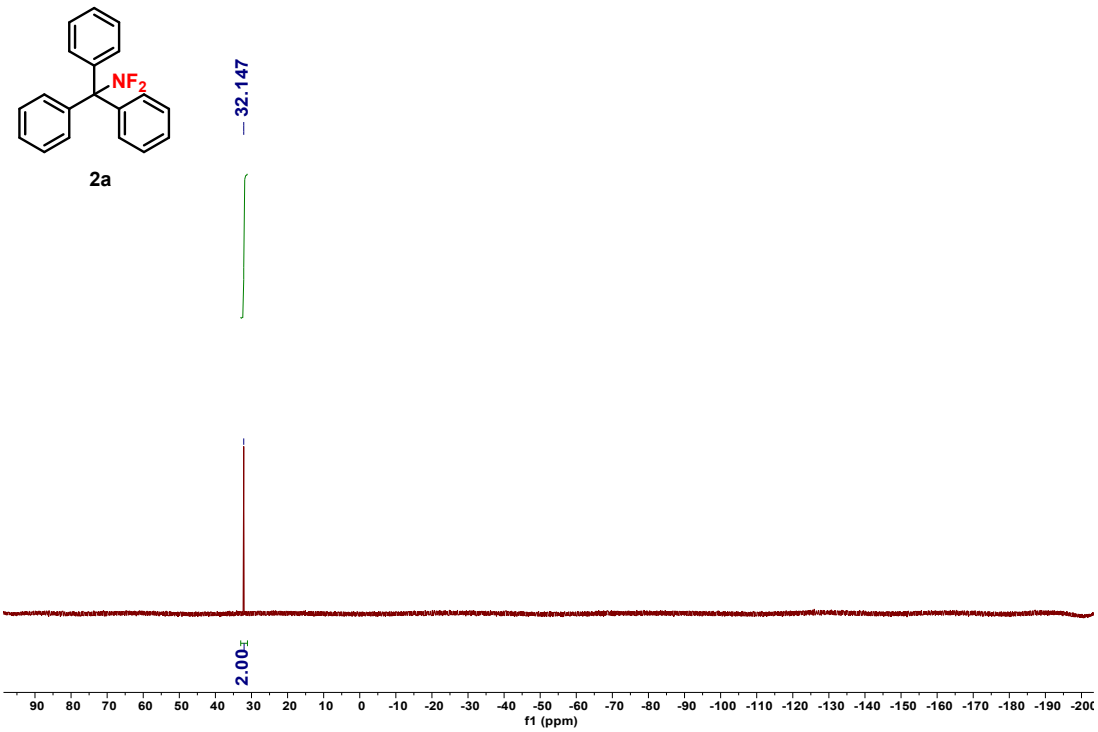
^{n}BuLi (2.4 M, 12.5 mL, 30 mmol, 1.5 equiv) was added into a solution of substrate **1a'** (20 mmol, 4.88 g) in THF (40 mL) at -78 ℃ in a 100 mL Schlenk flask (flask A), and the reaction mixture was stirred at the same temperature under an Ar atmosphere for 60 minutes. A second 250 mL Schlenk flask (flask B) was charged with nitrogen trifluoride (NF_3) and fitted with a needle connected to a 300 mL NF_3-filled balloon as a reserve gas. The reaction mixture in flask A was then transferred dropwise into flask B at room temperature via syringe pump at a flow rate of 20 mL/h, while NF_3 in the balloon was simultaneously bubbled through the solution in flask B. When the dropwise addition is complete, the reaction is finished. Upon completion of the reaction, the solvent was removed by concentration under vacuum and the residue was subjected to flash column chromatography with petroleum ether/ethyl acetate (100:1, 1% Et_3N) as the eluent to afford product **2a** as a light brown solid (4.13 g, 70% yield).

4. Copies of ^{1}H NMR, ^{19}F NMR, ^{13}C NMR spectra

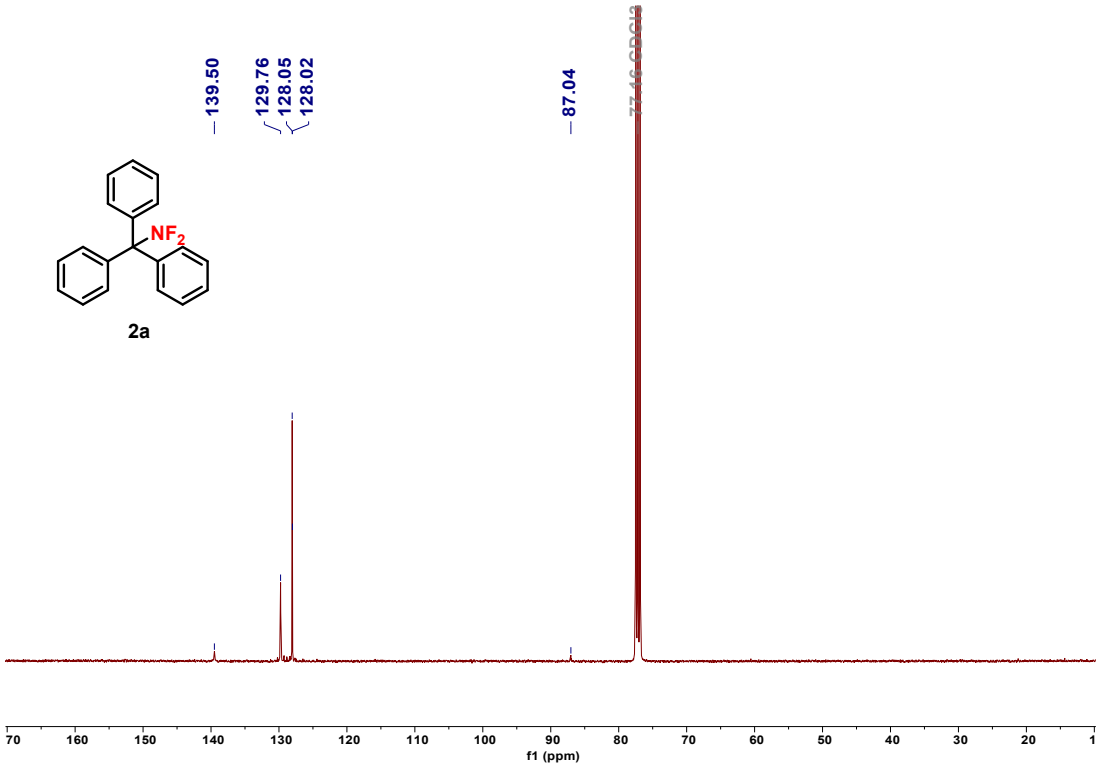
^{1}H NMR of **2a** (400 MHz, $CDCl_3$):



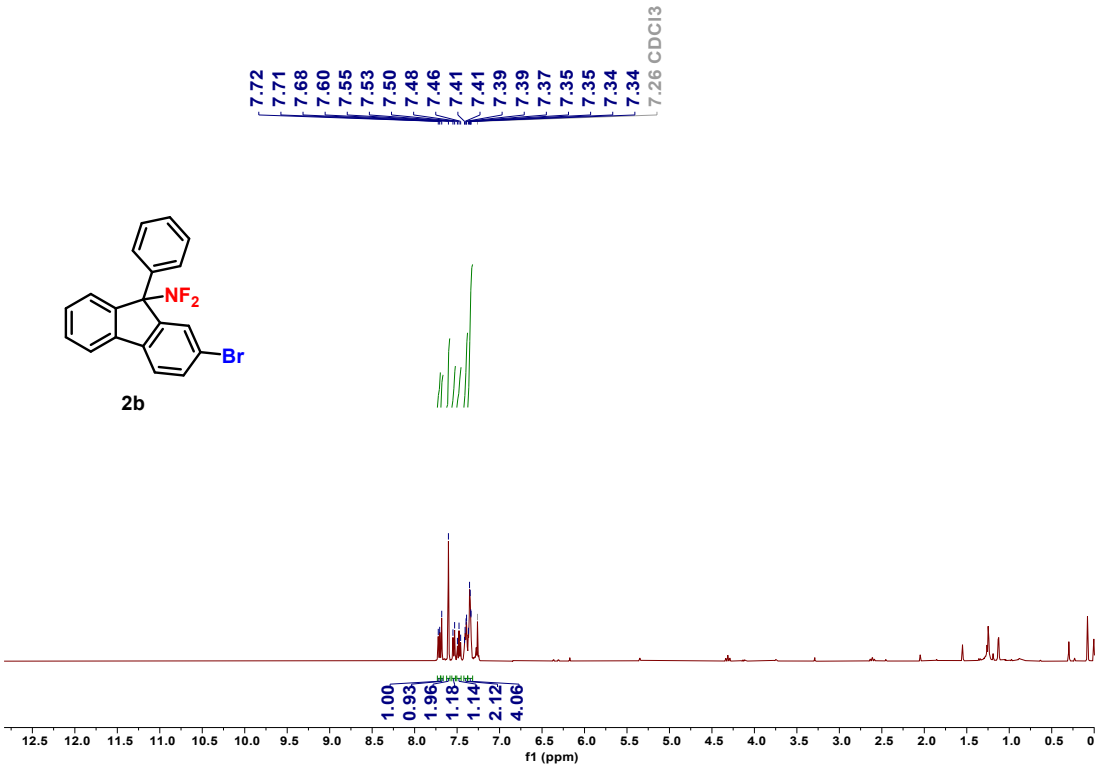
^{19}F NMR of **2a** (376 MHz, $CDCl_3$):



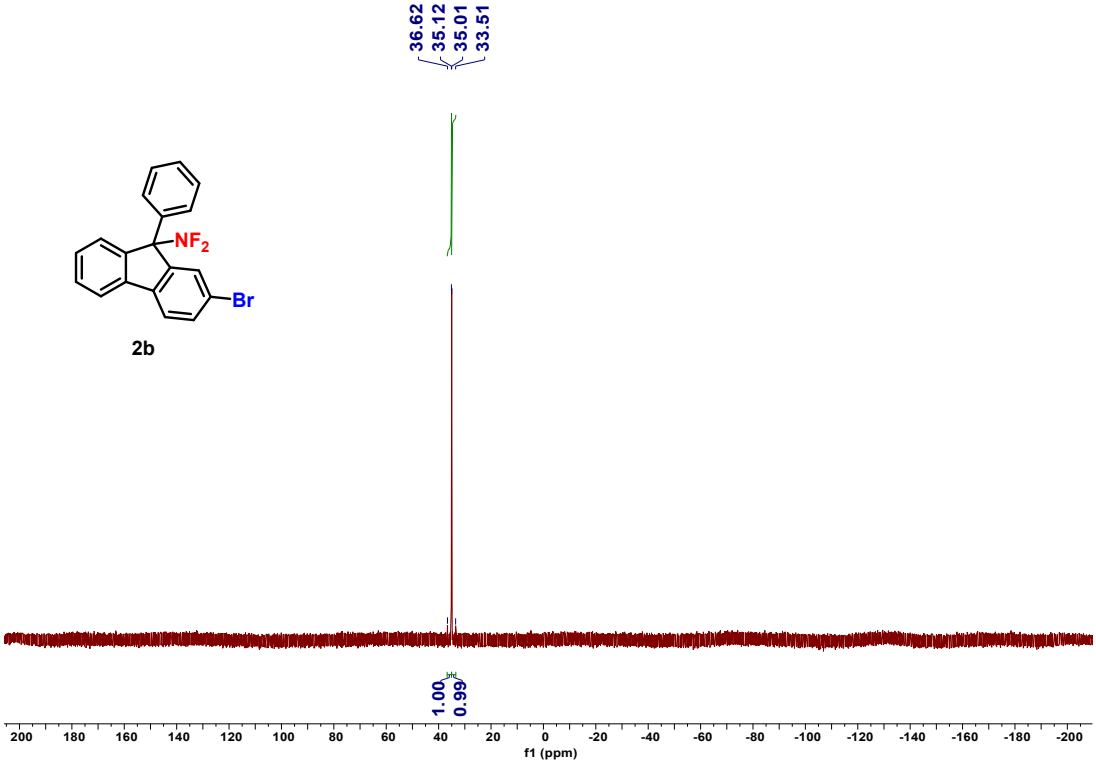
^{13}C NMR of **2a** (101 MHz, $CDCl_3$):



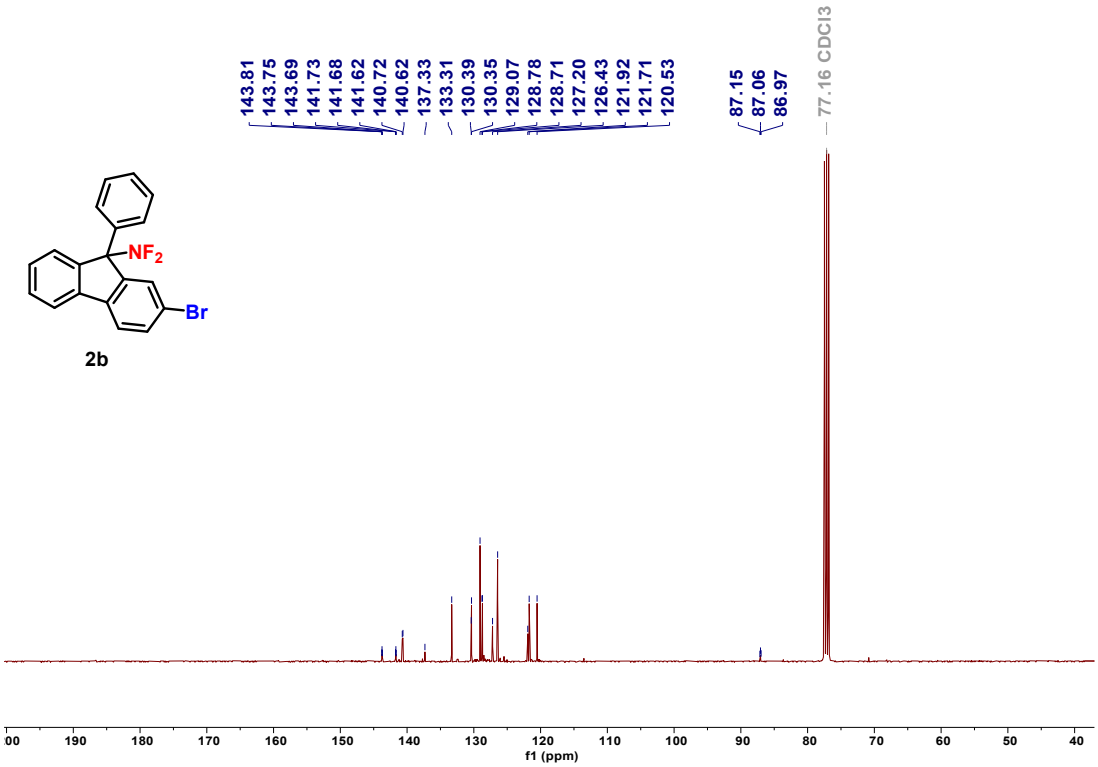
^{1}H NMR of **2b** (400 MHz, $CDCl_3$):



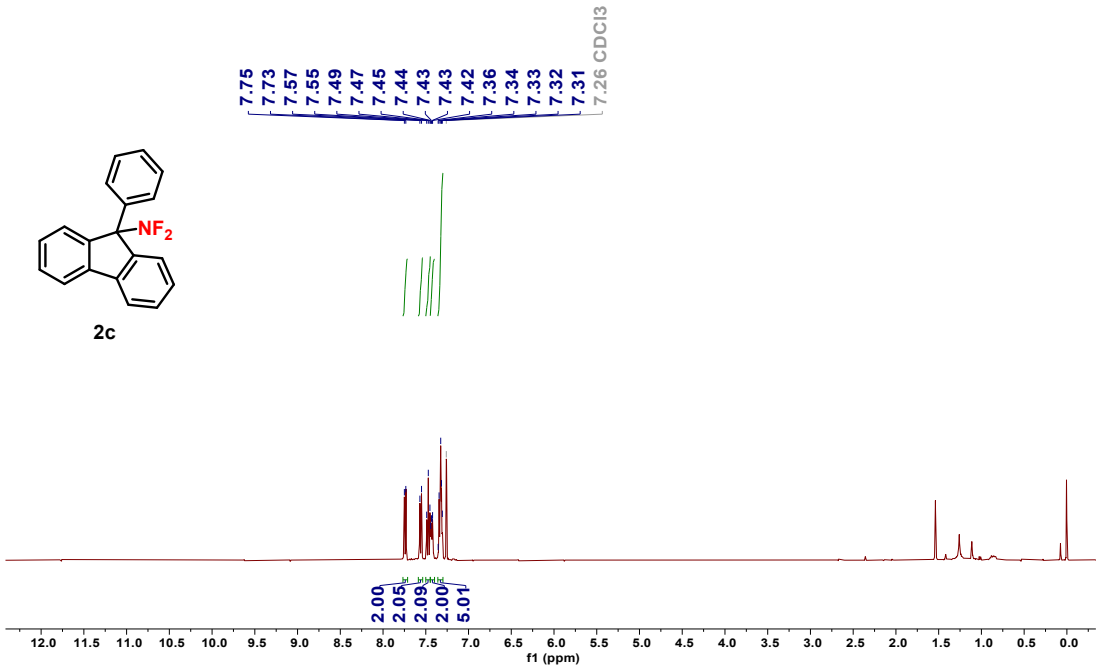
^{19}F NMR of **2b** (376 MHz, $CDCl_3$):



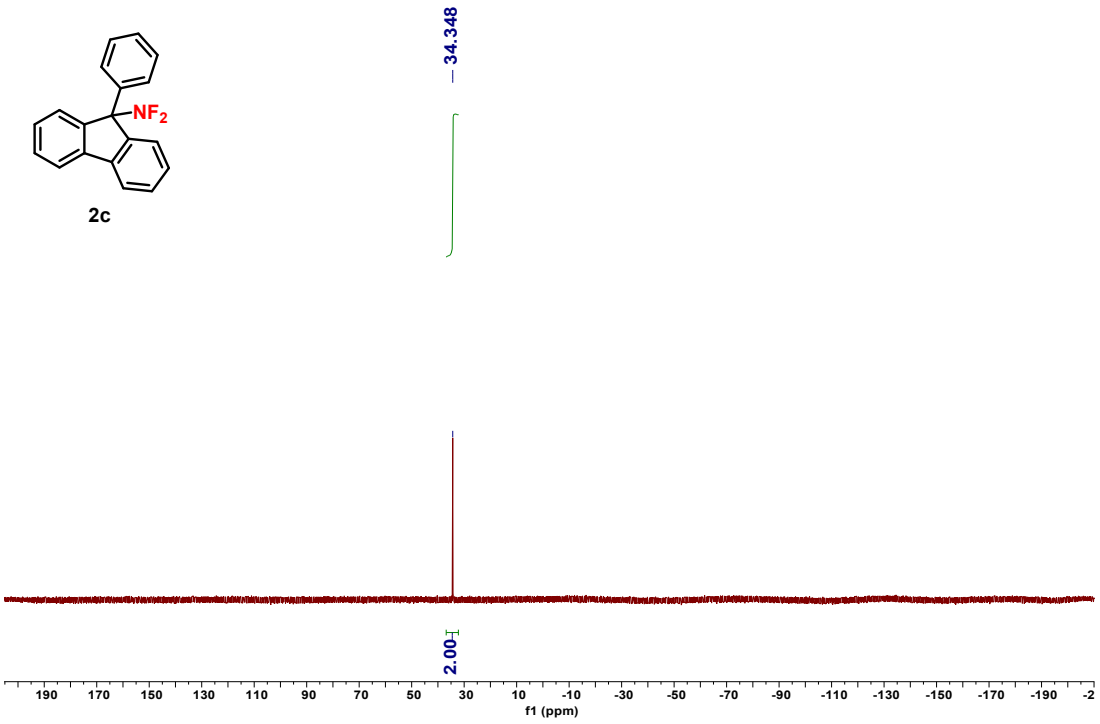
^{13}C NMR of **2b** (101 MHz, $CDCl_3$):



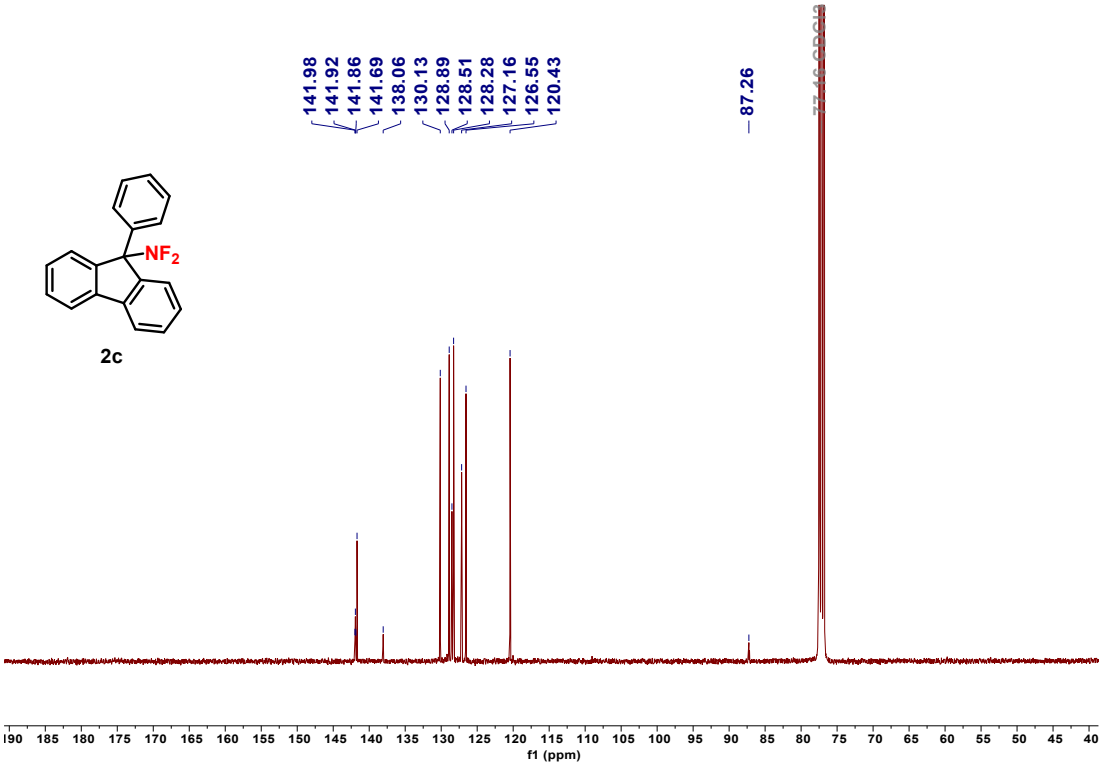
^{1}H NMR of **2c** (400 MHz, $CDCl_3$):



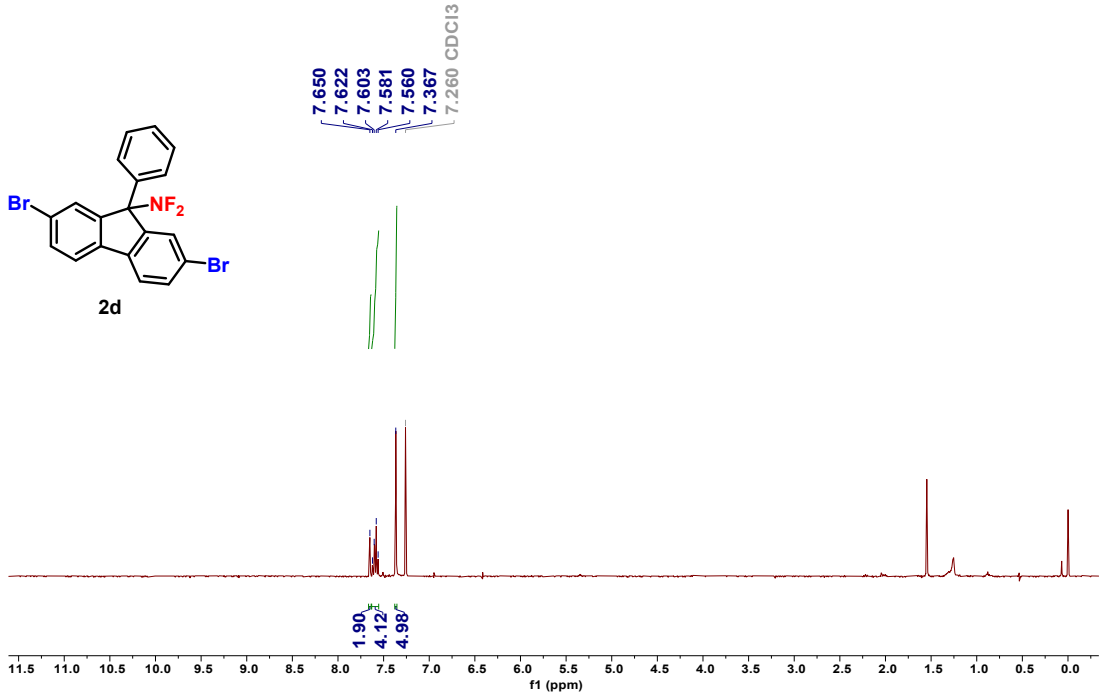
^{19}F NMR of **2c** (376 MHz, $CDCl_3$):



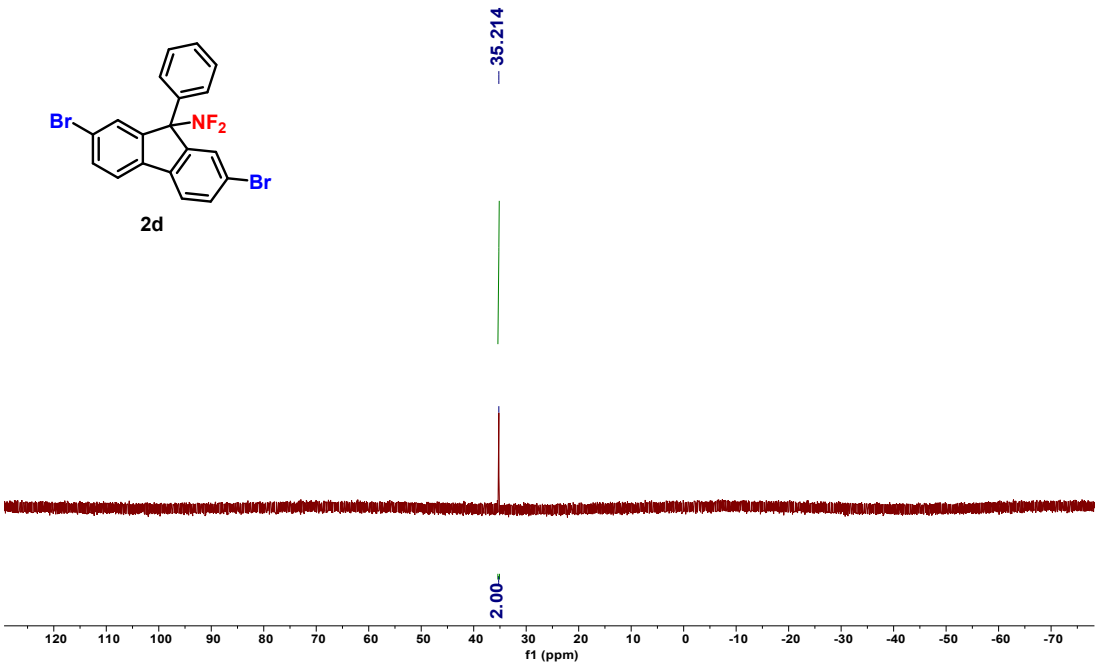
^{13}C NMR of **2c** (101 MHz, $CDCl_3$):



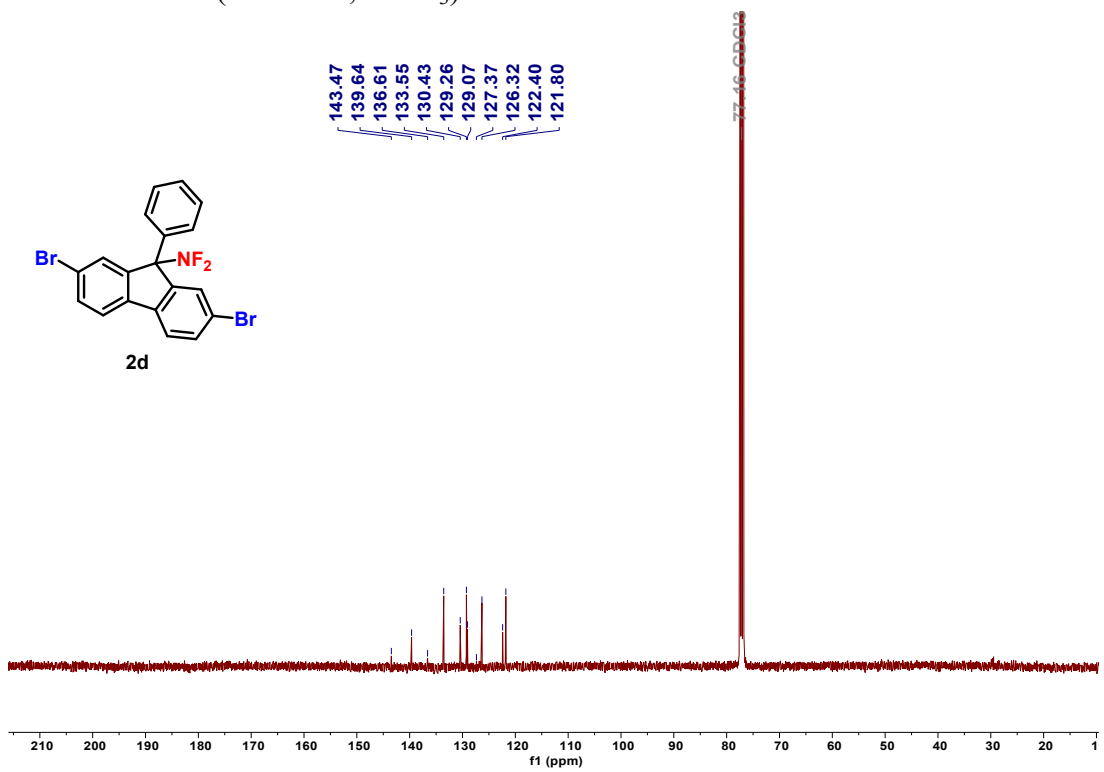
^{1}H NMR of **2d** (400 MHz, $CDCl_3$):



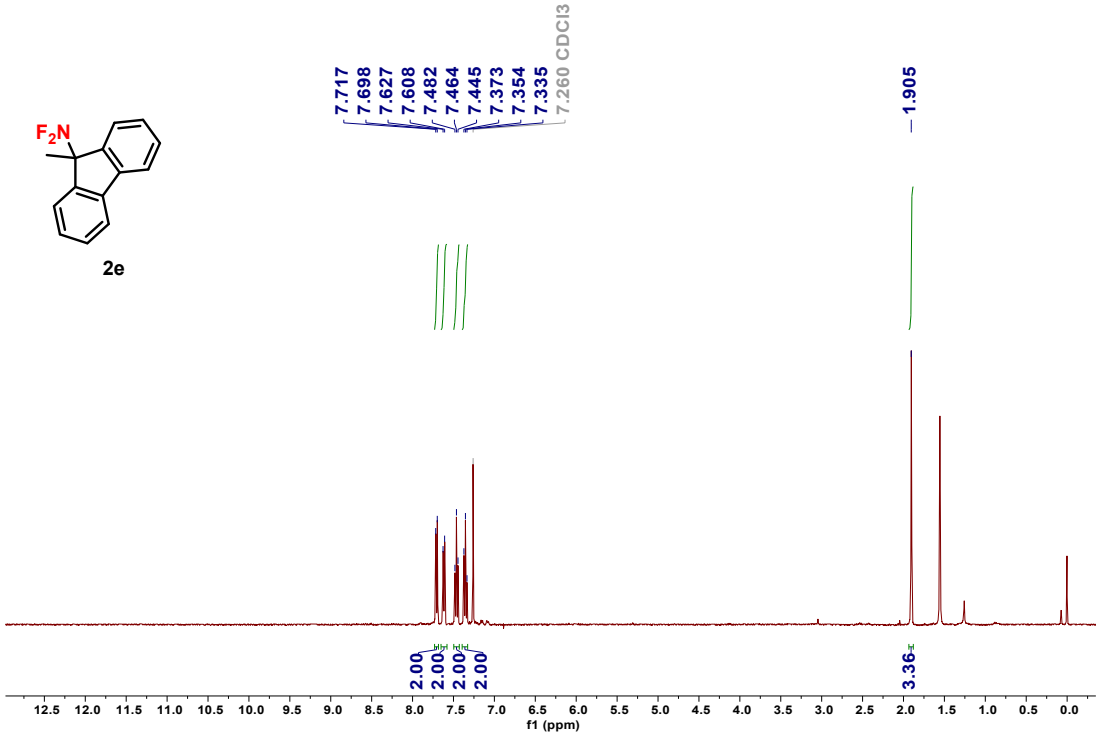
^{19}F NMR of **2d** (376 MHz, $CDCl_3$):



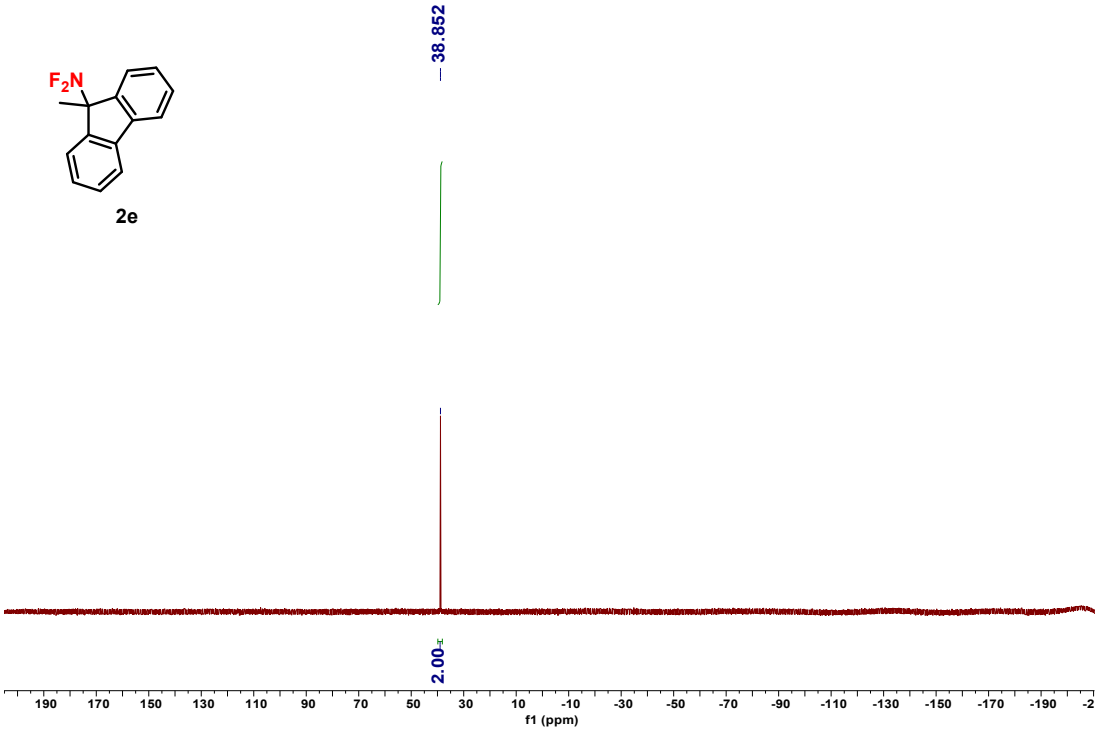
^{13}C NMR of **2d** (101 MHz, $CDCl_3$):



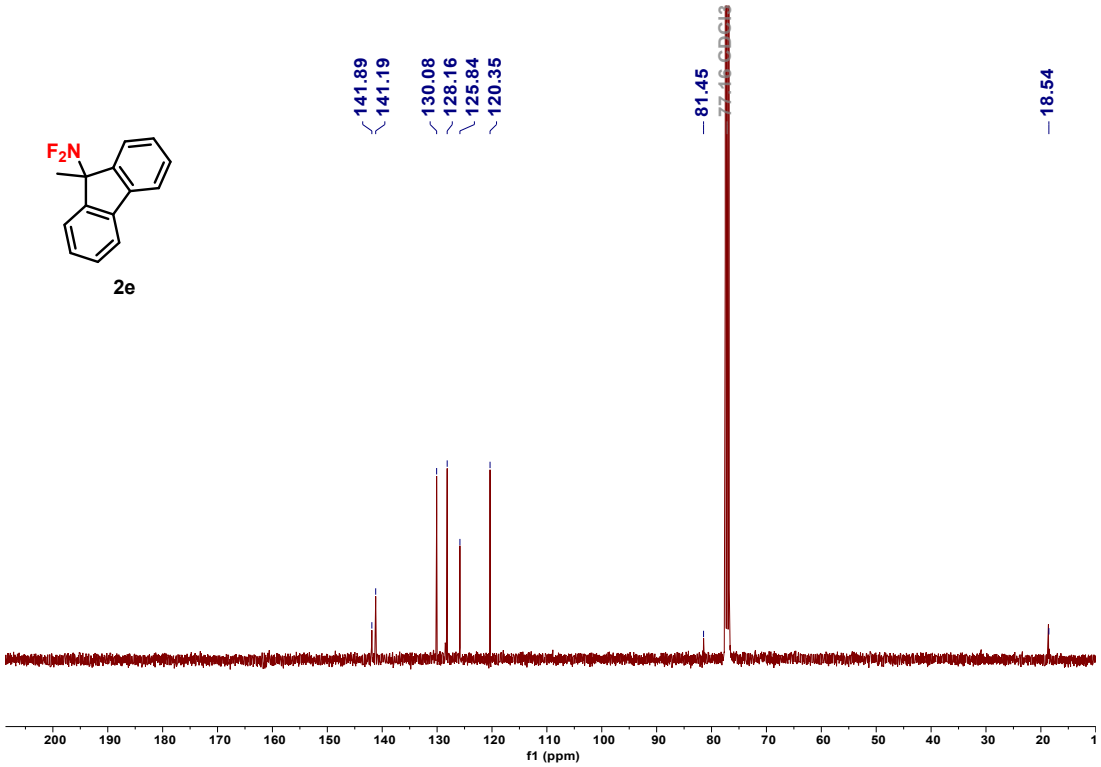
^{1}H NMR of **2e** (400 MHz, $CDCl_3$):



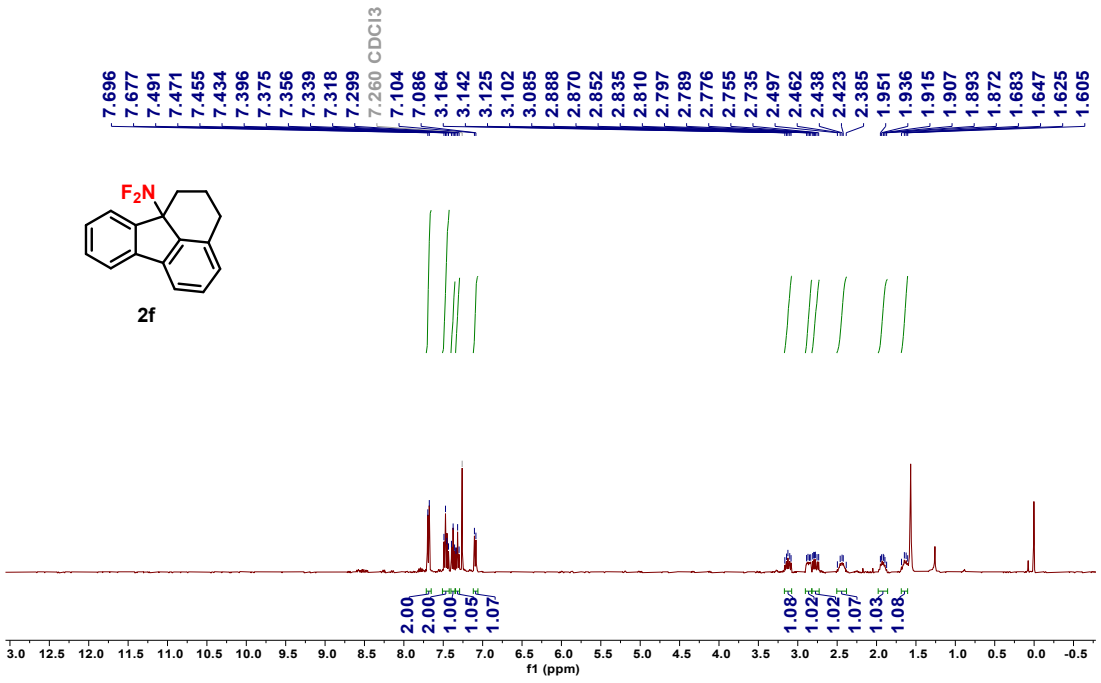
^{19}F NMR of **2e** (376 MHz, $CDCl_3$):



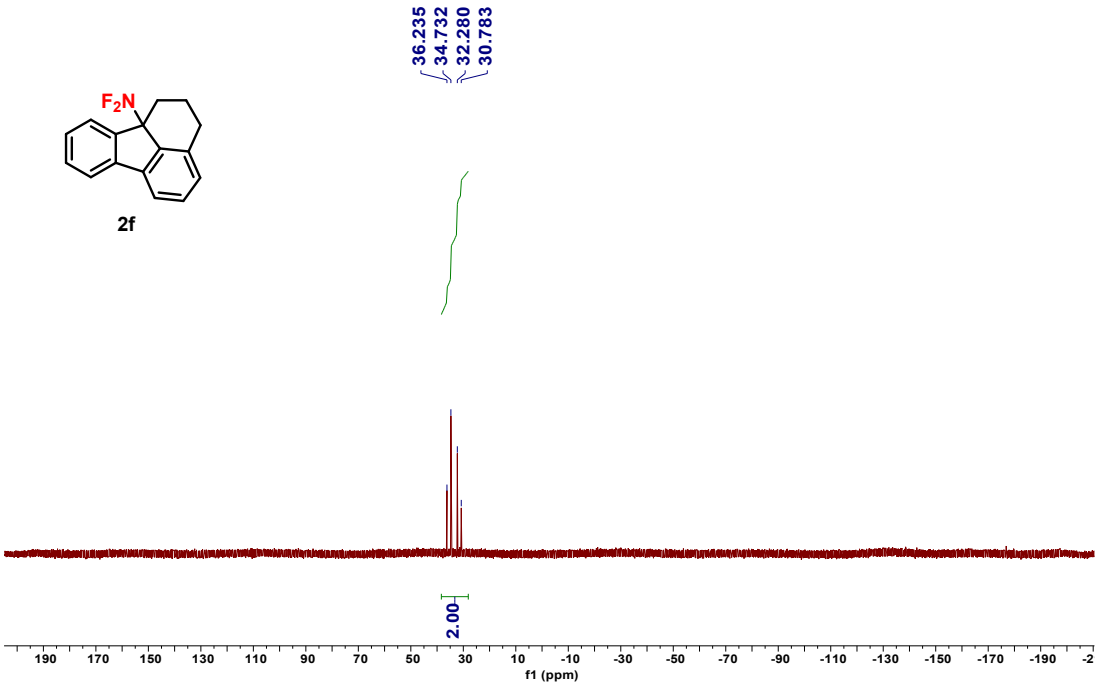
^{13}C NMR of **2e** (101 MHz, $CDCl_3$):



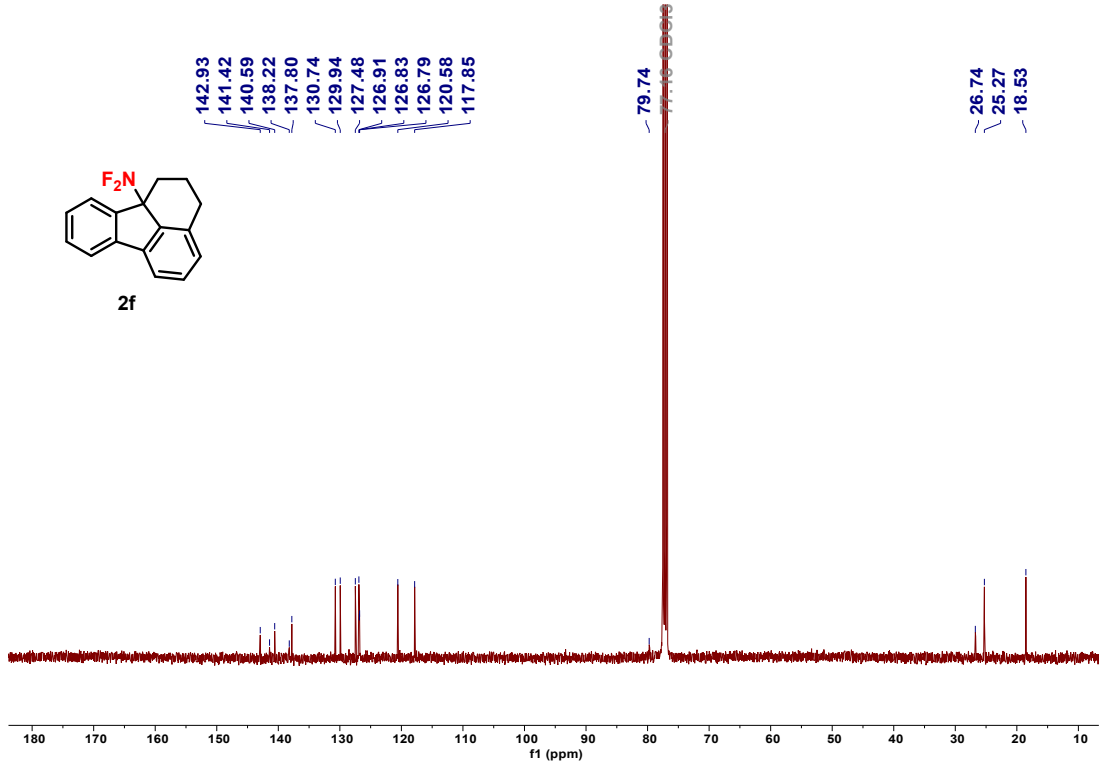
^{1}H NMR of **2f** (400 MHz, $CDCl_3$):



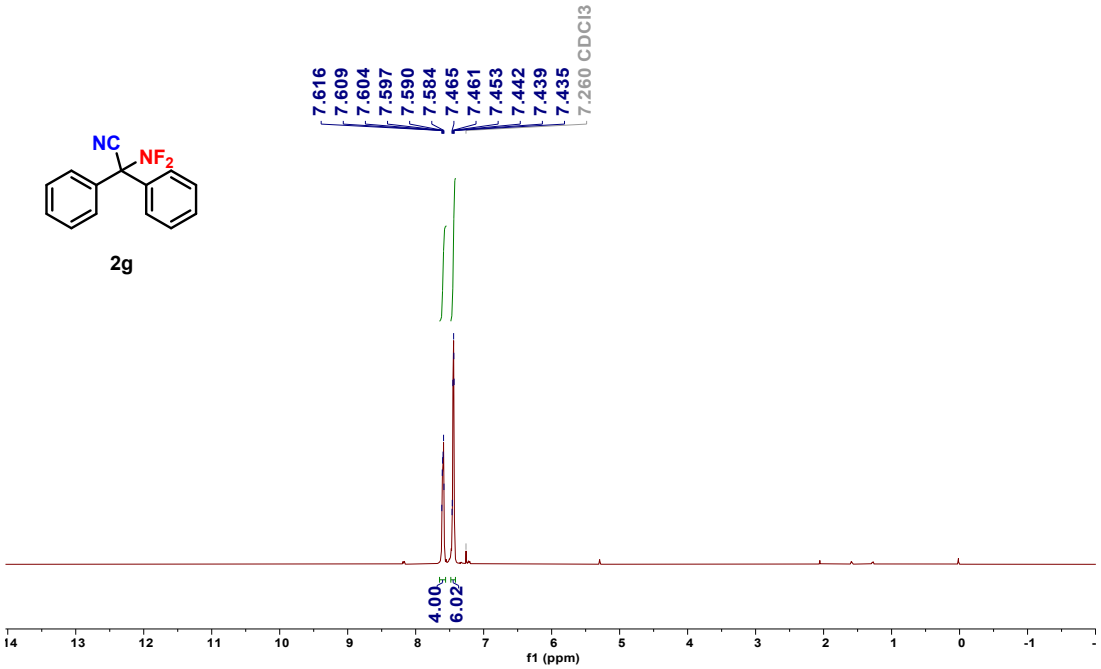
^{19}F NMR of **2f** (376 MHz, $CDCl_3$):



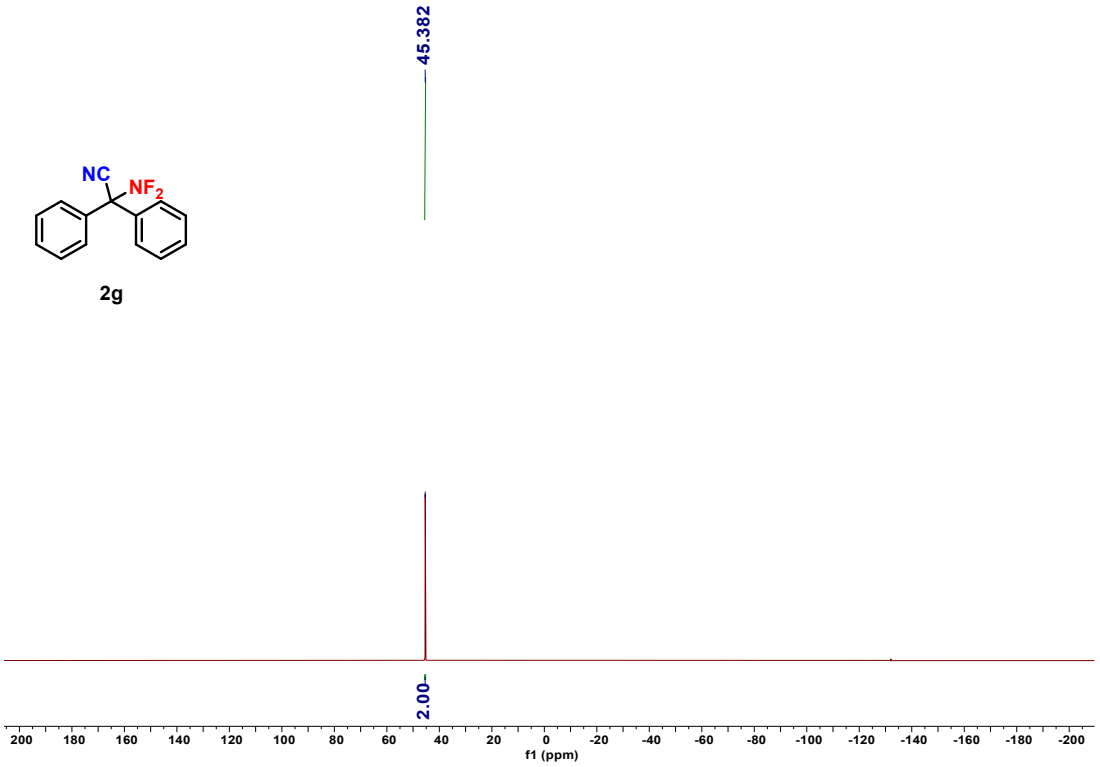
^{13}C NMR of **2f** (101 MHz, $CDCl_3$):



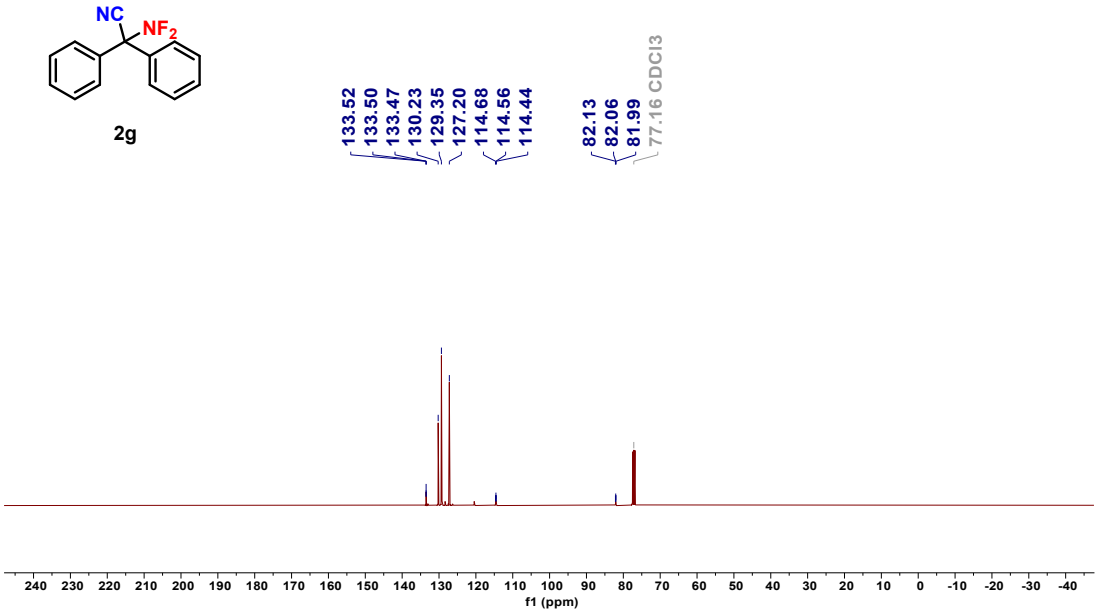
^{1}H NMR of **2g** (400 MHz, $CDCl_3$):



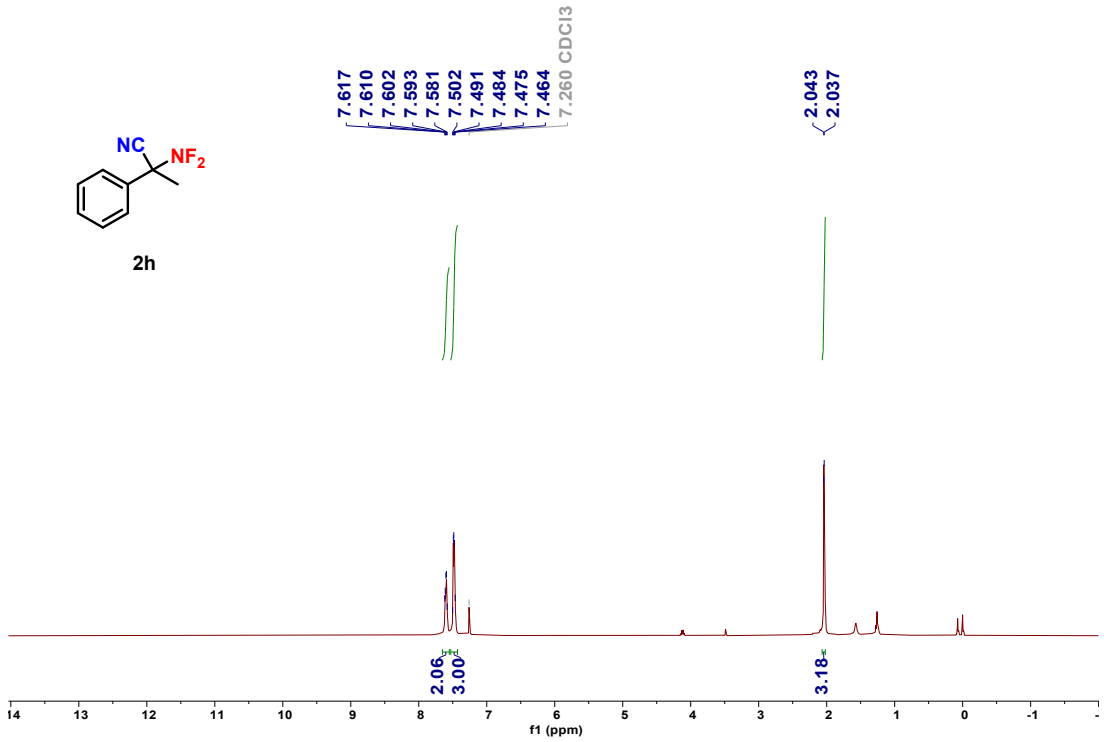
^{19}F NMR of **2g** (376 MHz, $CDCl_3$):



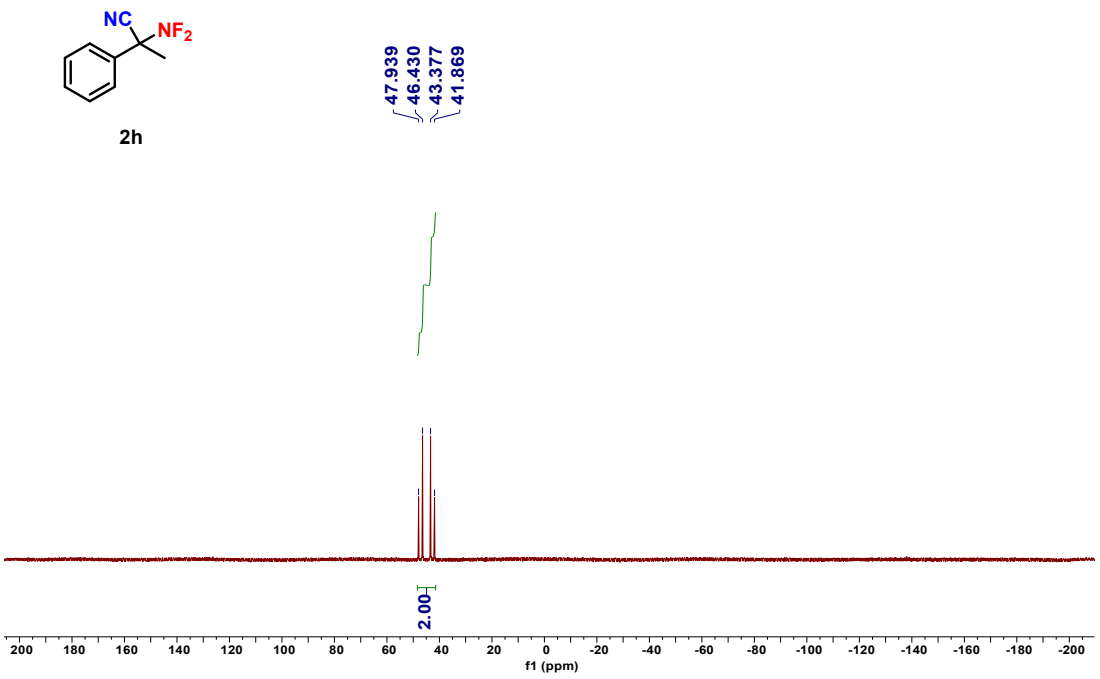
^{13}C NMR of **2g** (101 MHz, $CDCl_3$):



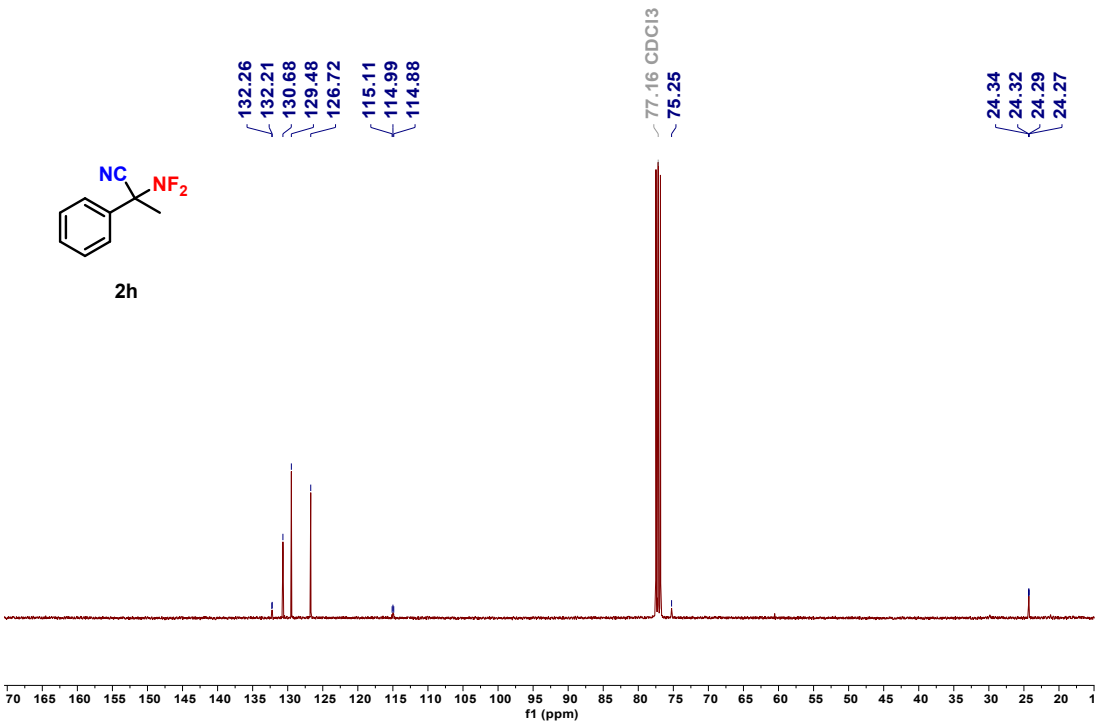
^{1}H NMR of **2h** (400 MHz, $CDCl_3$):



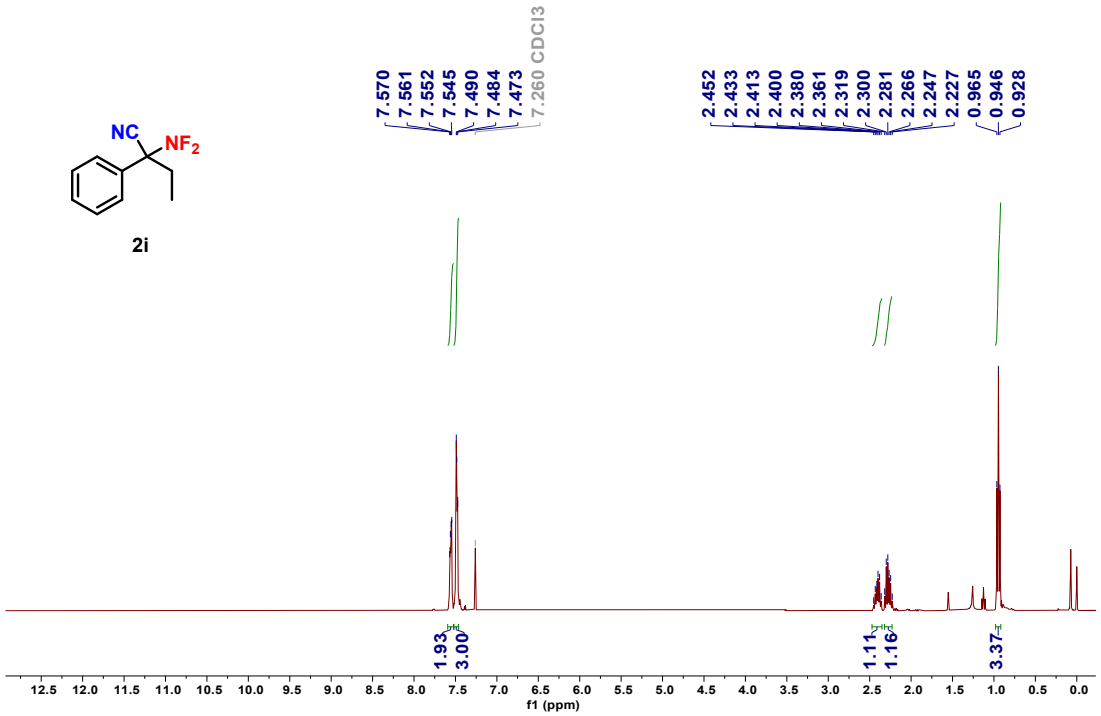
^{19}F NMR of **2h** (376 MHz, $CDCl_3$):



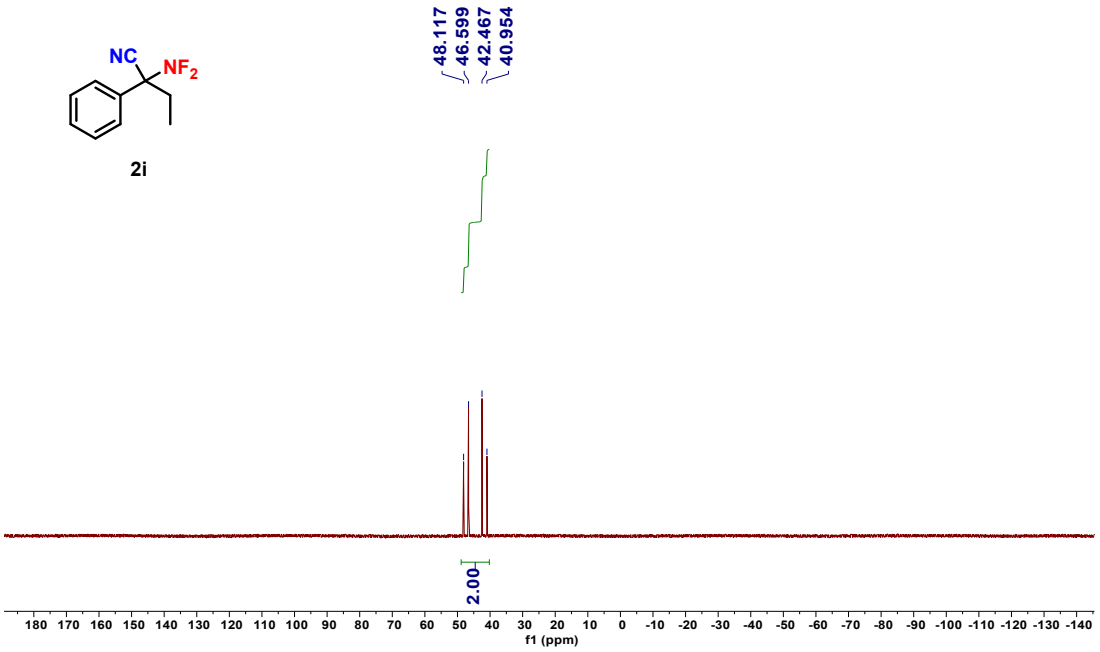
^{13}C NMR of **2h** (101 MHz, $CDCl_3$):



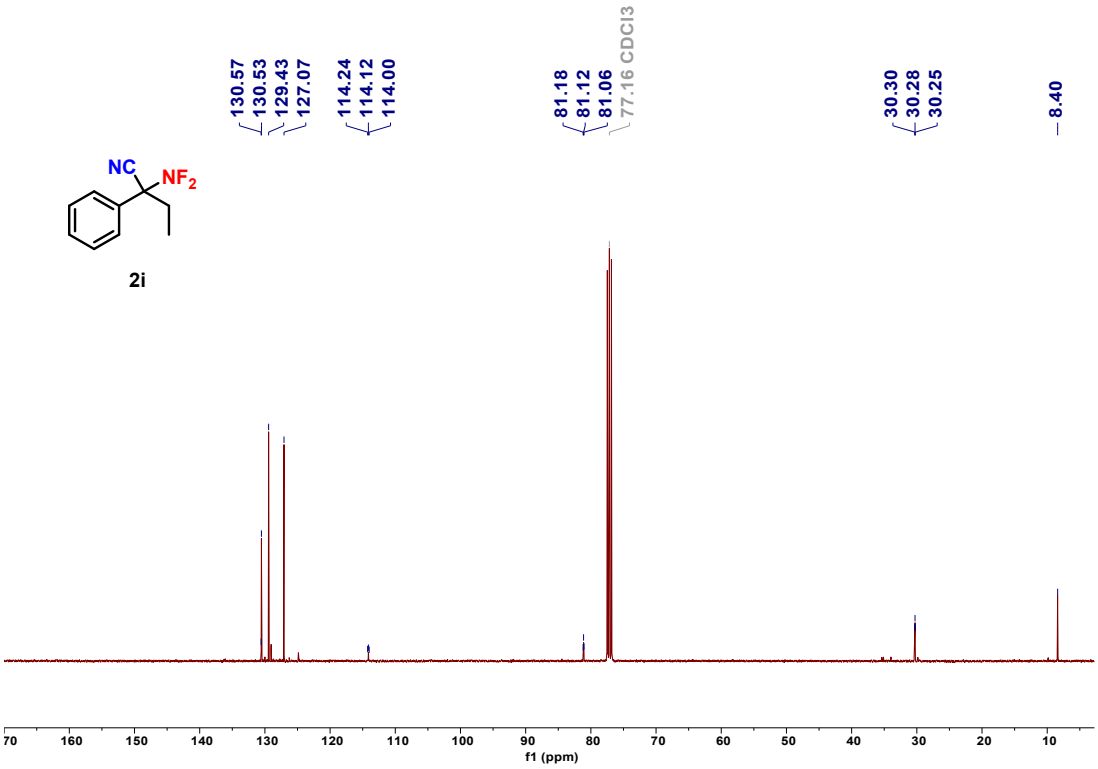
^{1}H NMR of **2i** (400 MHz, $CDCl_3$):



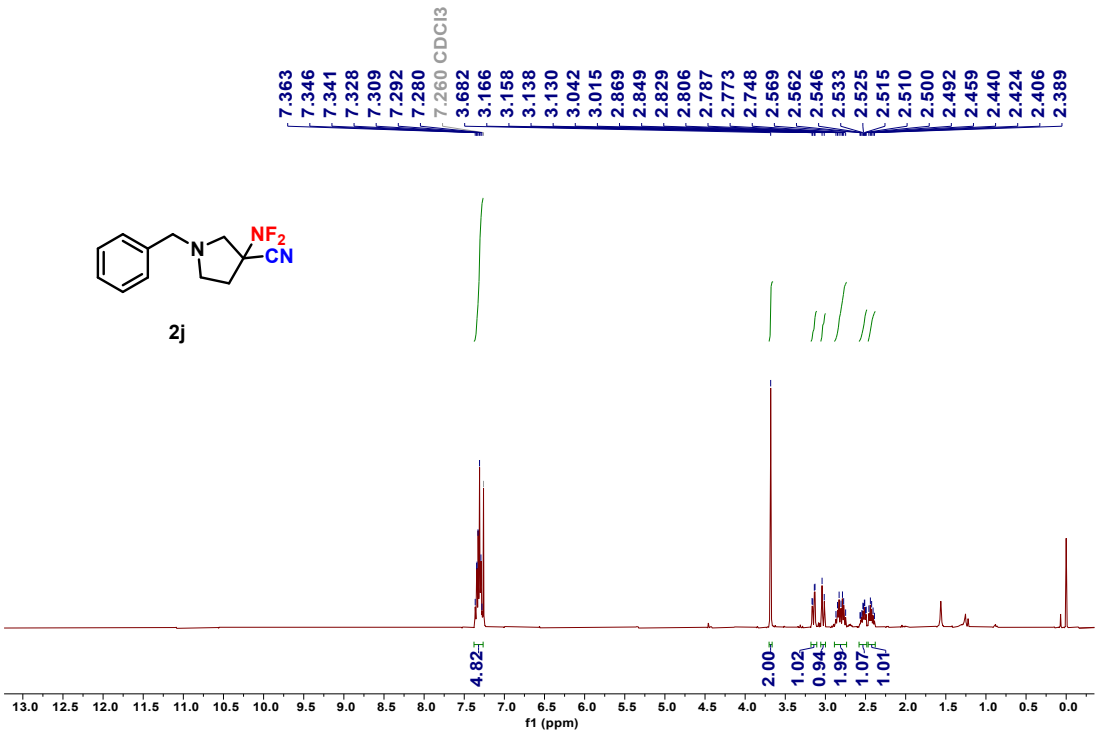
^{19}F NMR of **2i** (376 MHz, $CDCl_3$):



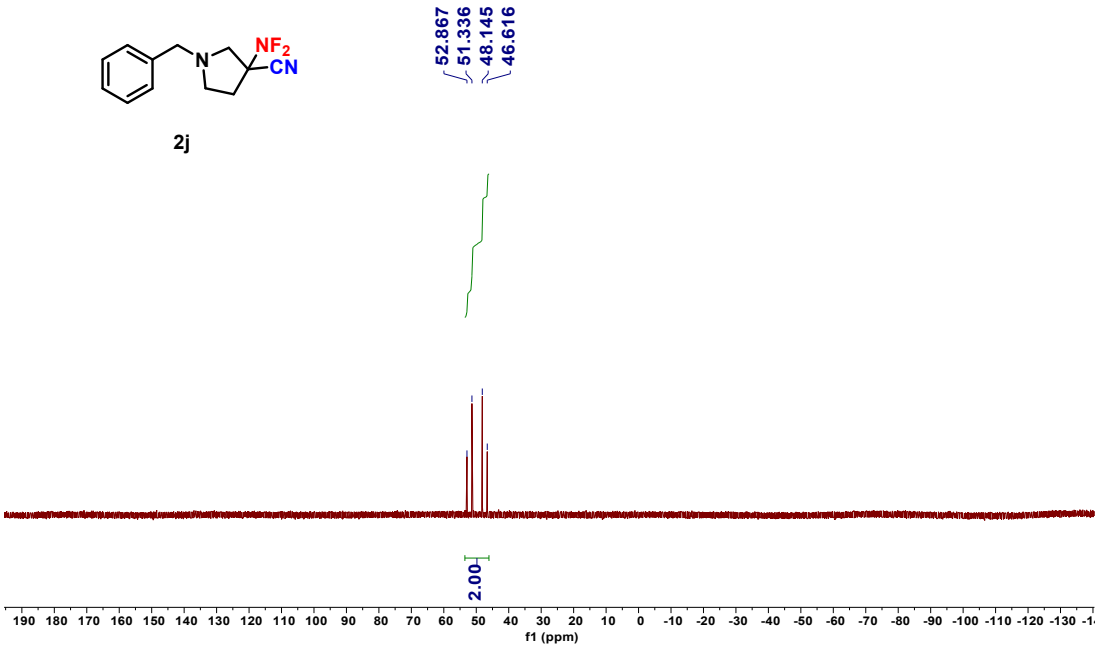
^{13}C NMR of **2i** (101 MHz, $CDCl_3$):



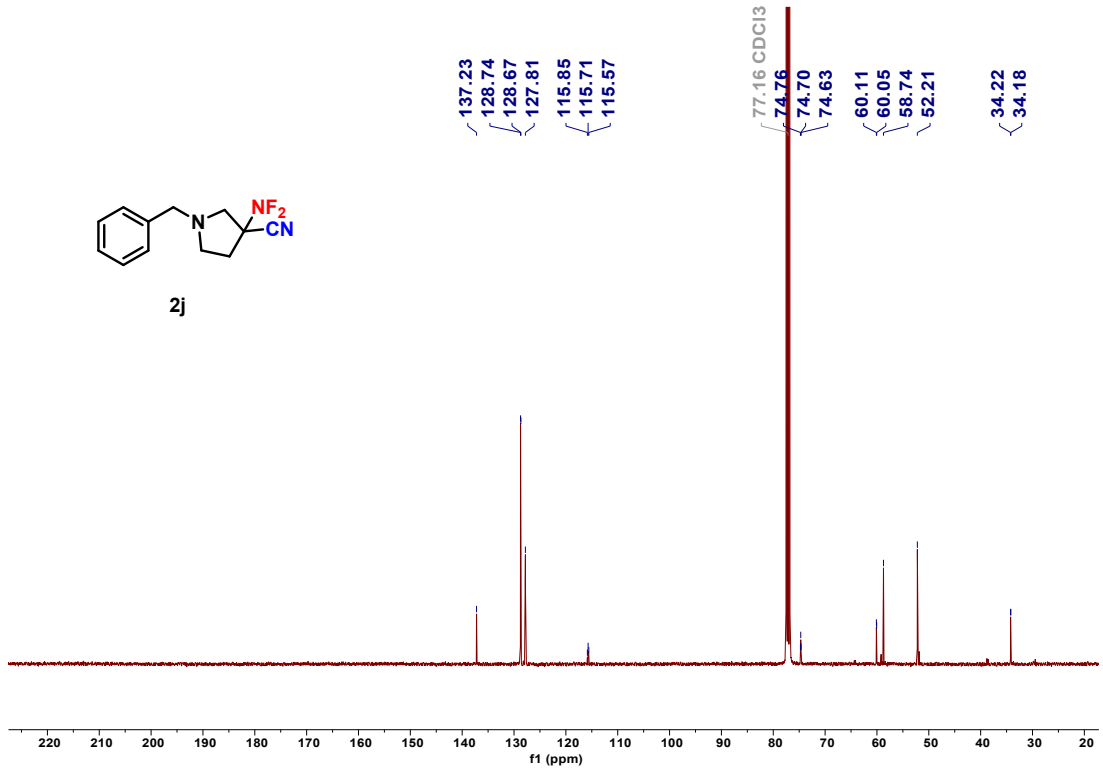
^{1}H NMR of **2j** (400 MHz, $CDCl_3$):



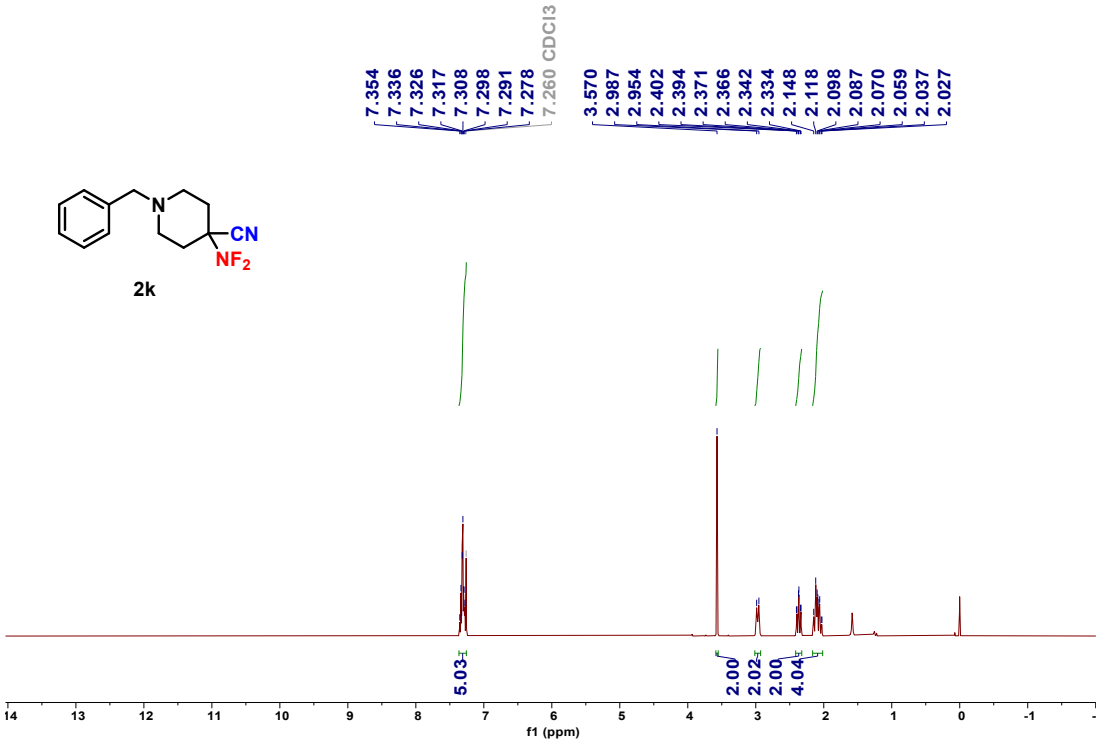
^{19}F NMR of **2j** (376 MHz, $CDCl_3$):



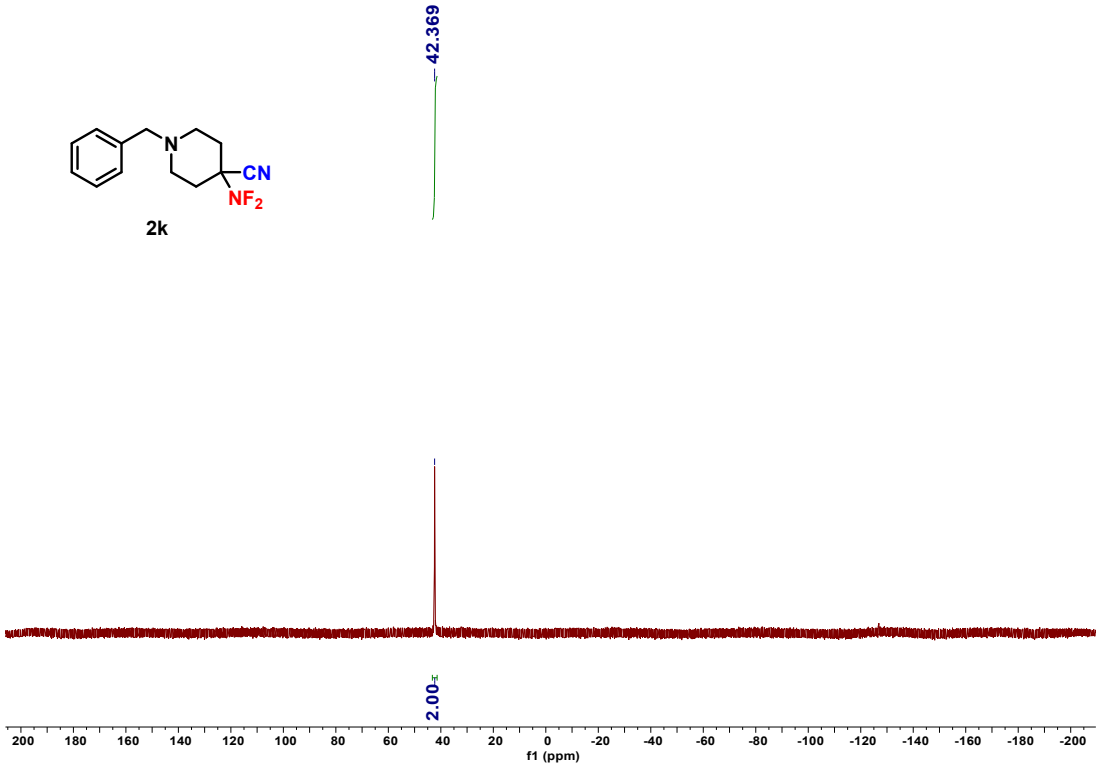
^{13}C NMR of **2j** (101 MHz, $CDCl_3$):



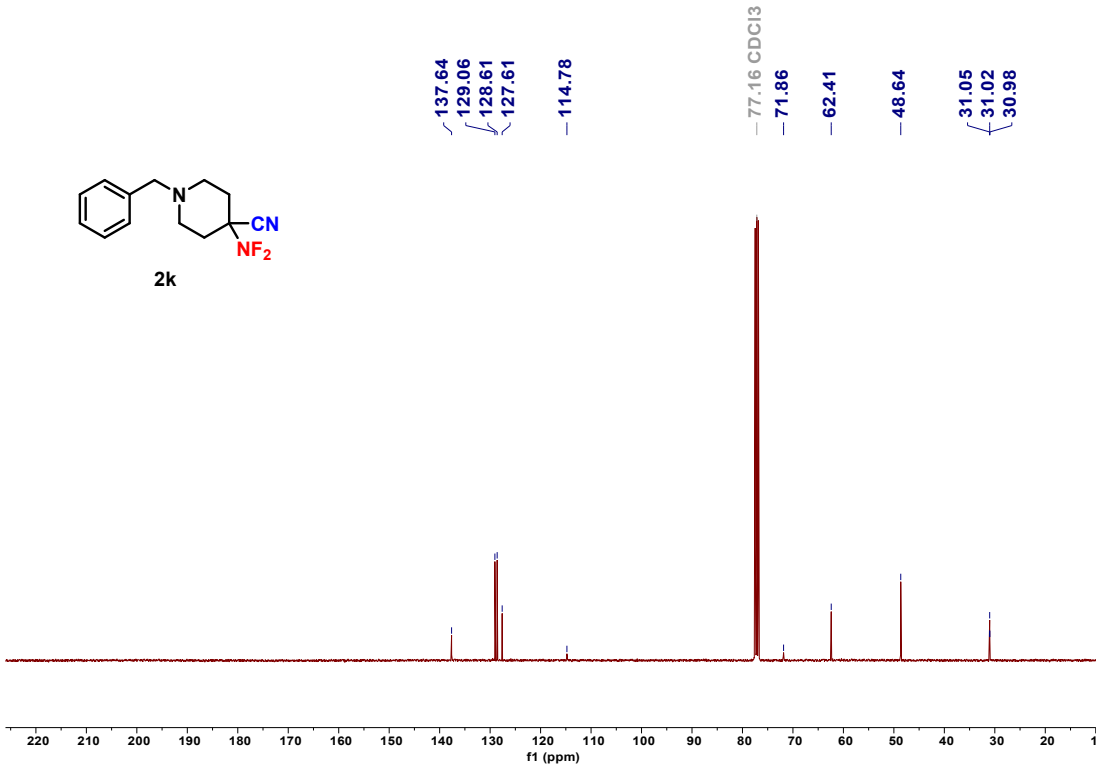
^{1}H NMR of **2k** (400 MHz, $CDCl_3$):



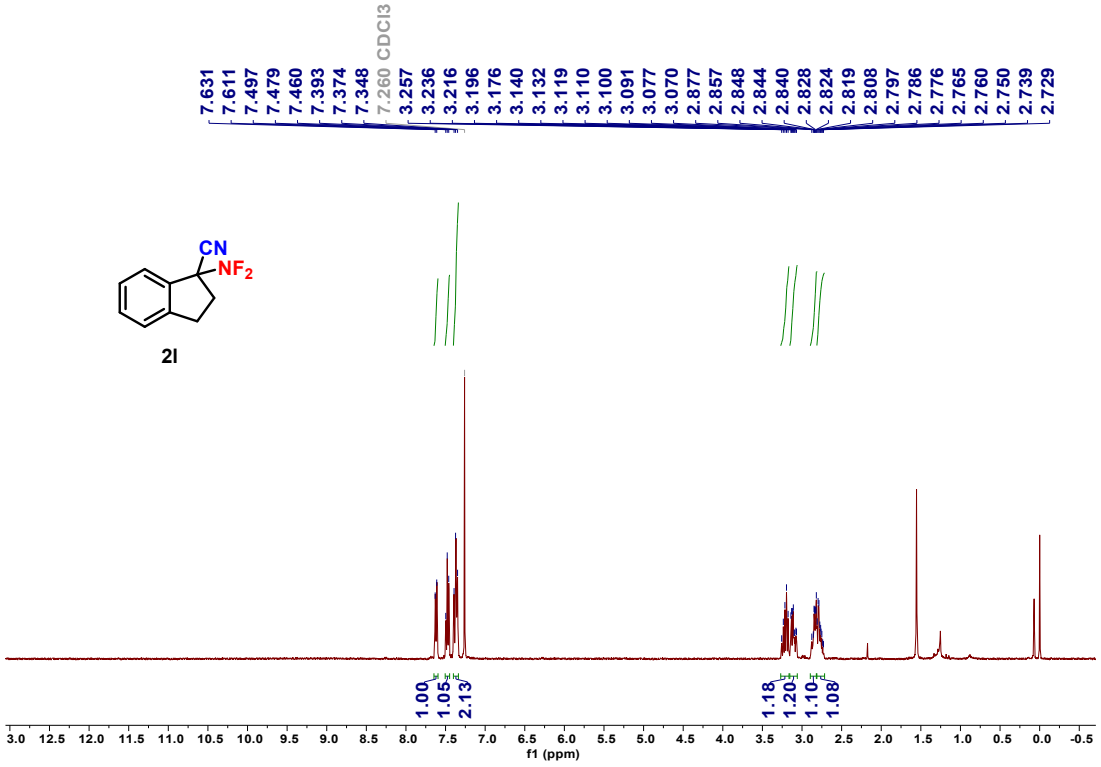
^{19}F NMR of **2k** (376 MHz, $CDCl_3$):



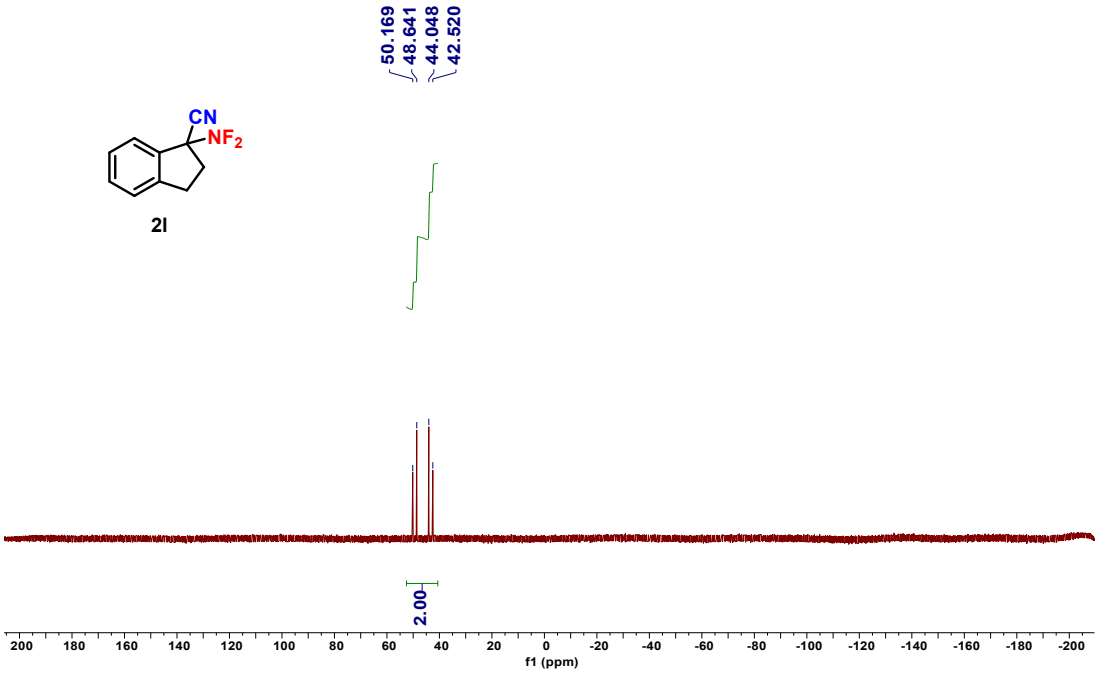
^{13}C NMR of **2k** (101 MHz, $CDCl_3$):



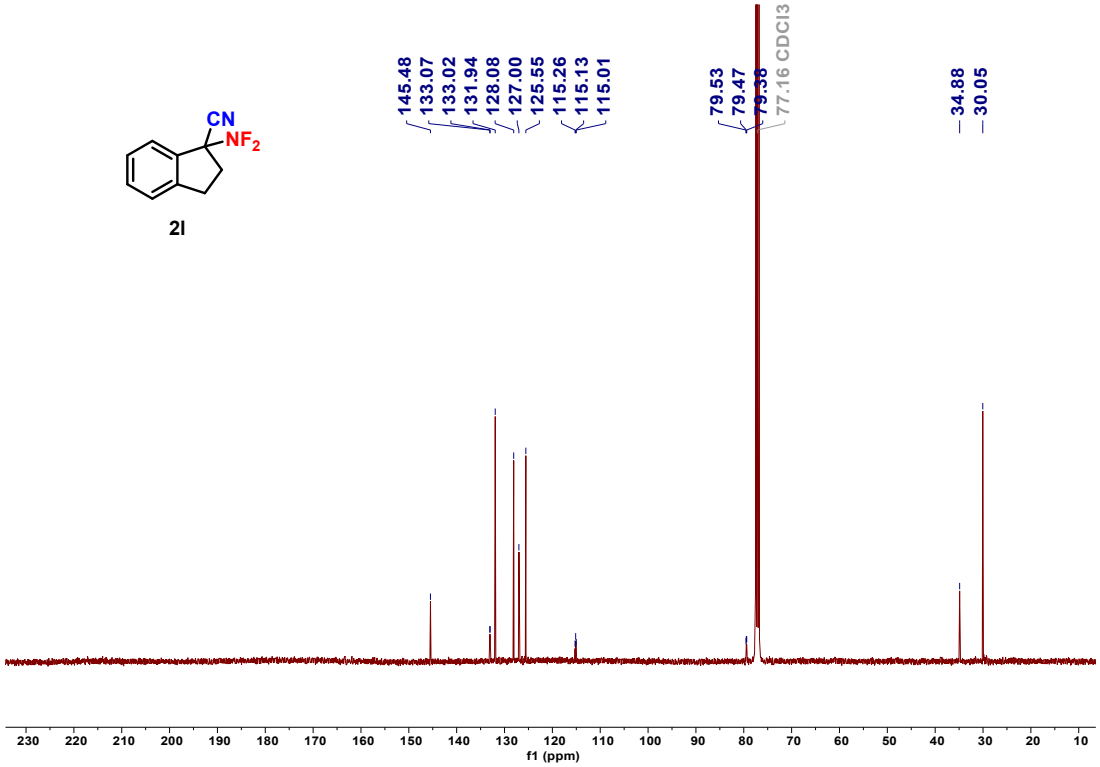
^{1}H NMR of **2l** (400 MHz, $CDCl_3$):



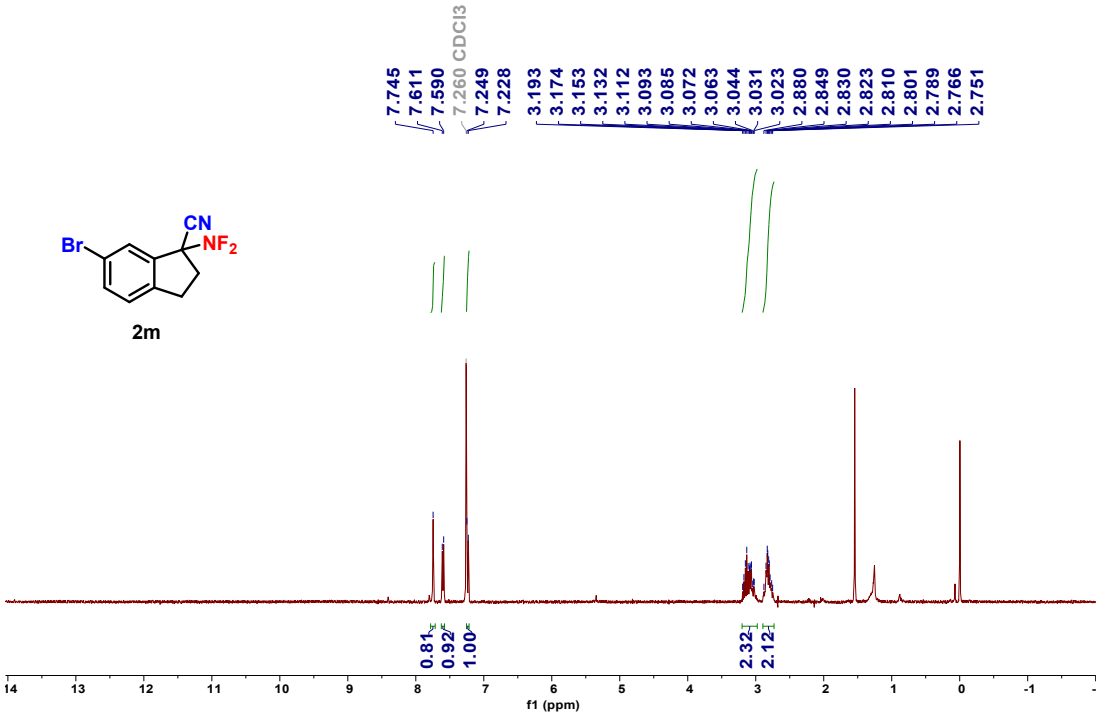
^{19}F NMR of **2l** (376 MHz, $CDCl_3$):



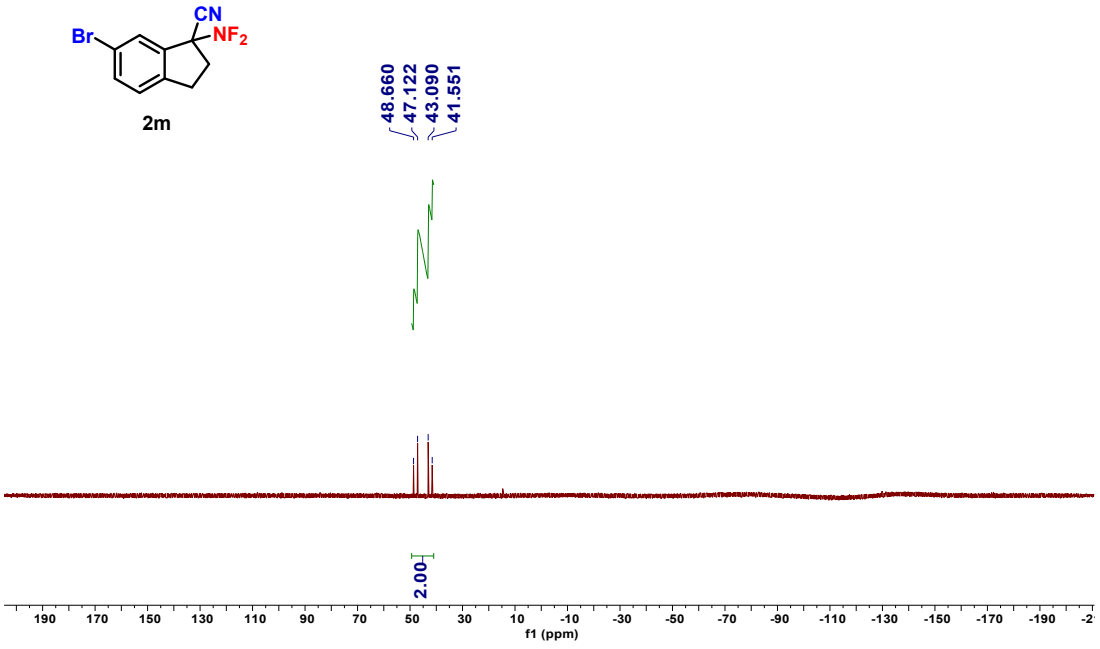
^{13}C NMR of **2l** (101 MHz, $CDCl_3$):



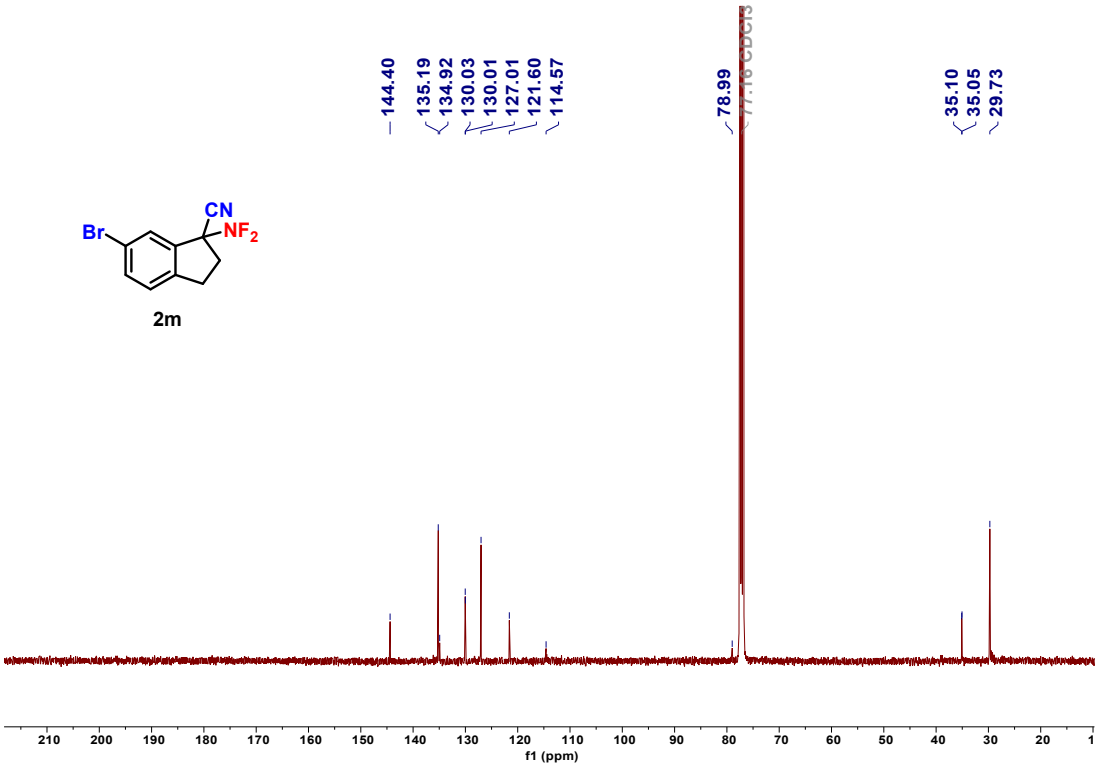
^{1}H NMR of **2m** (400 MHz, $CDCl_3$):



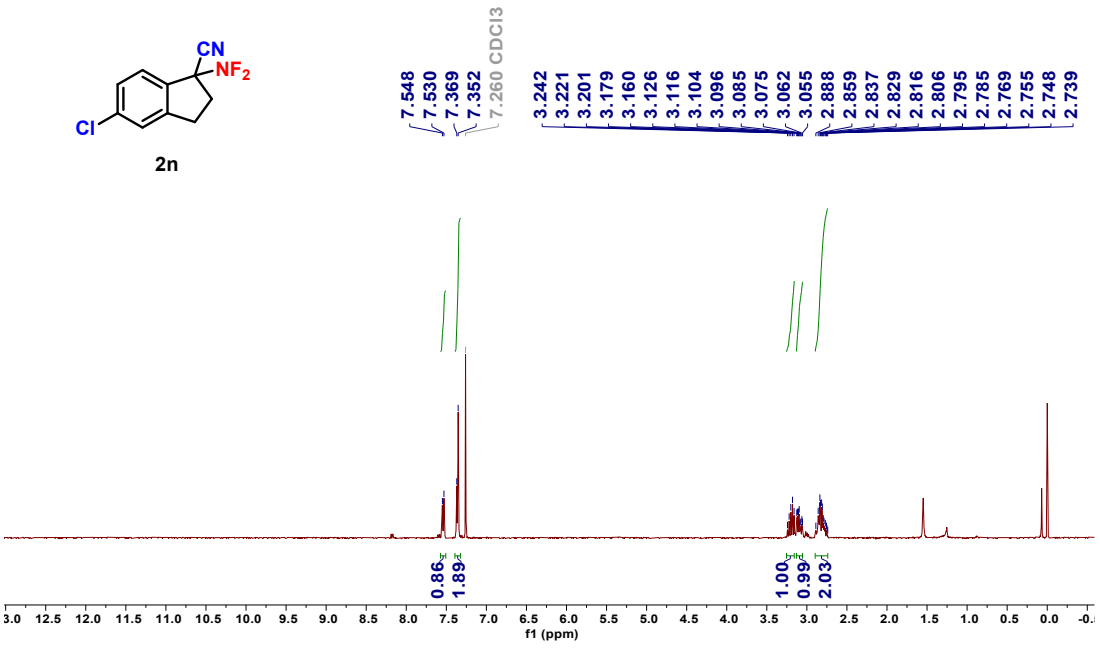
^{19}F NMR of **2m** (376 MHz, $CDCl_3$):



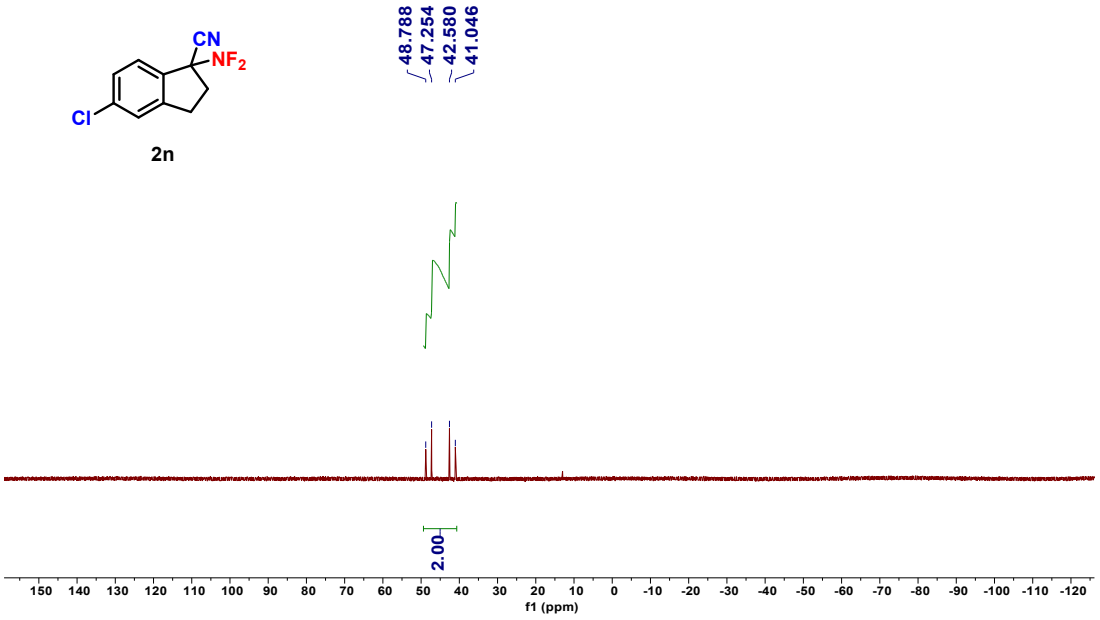
^{13}C NMR of **2m** (101 MHz, $CDCl_3$):



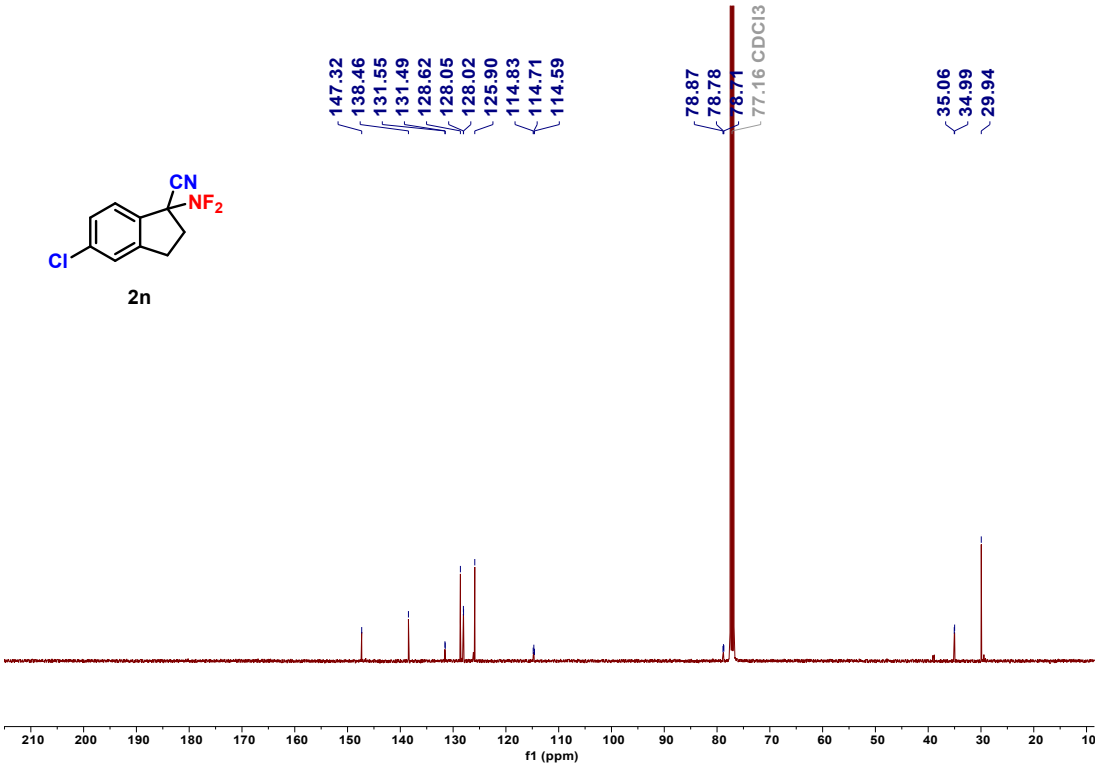
^{1}H NMR of **2n** (400 MHz, $CDCl_3$):



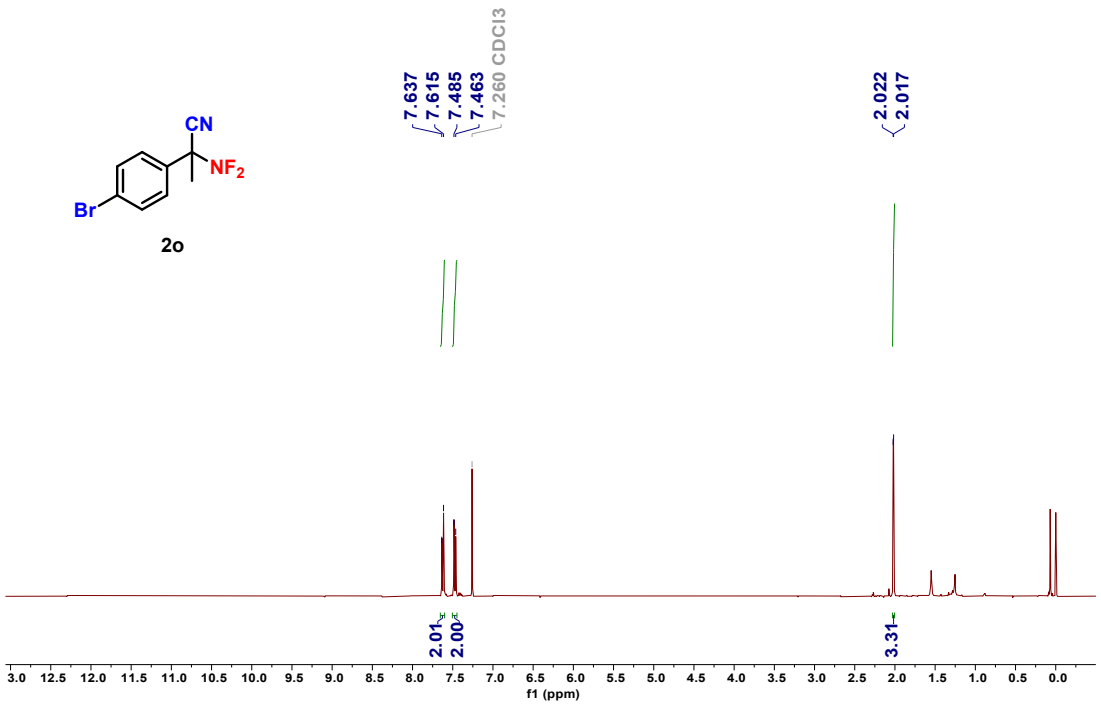
^{19}F NMR of **2n** (376 MHz, $CDCl_3$):



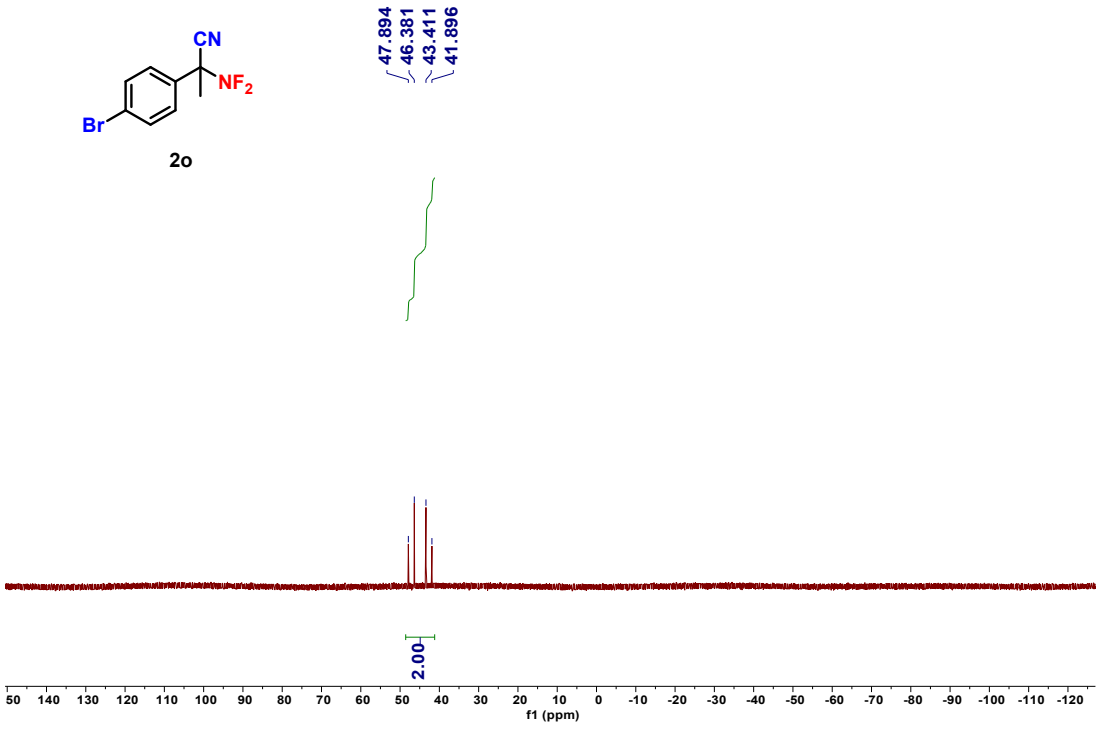
^{13}C NMR of **2n** (101 MHz, $CDCl_3$):



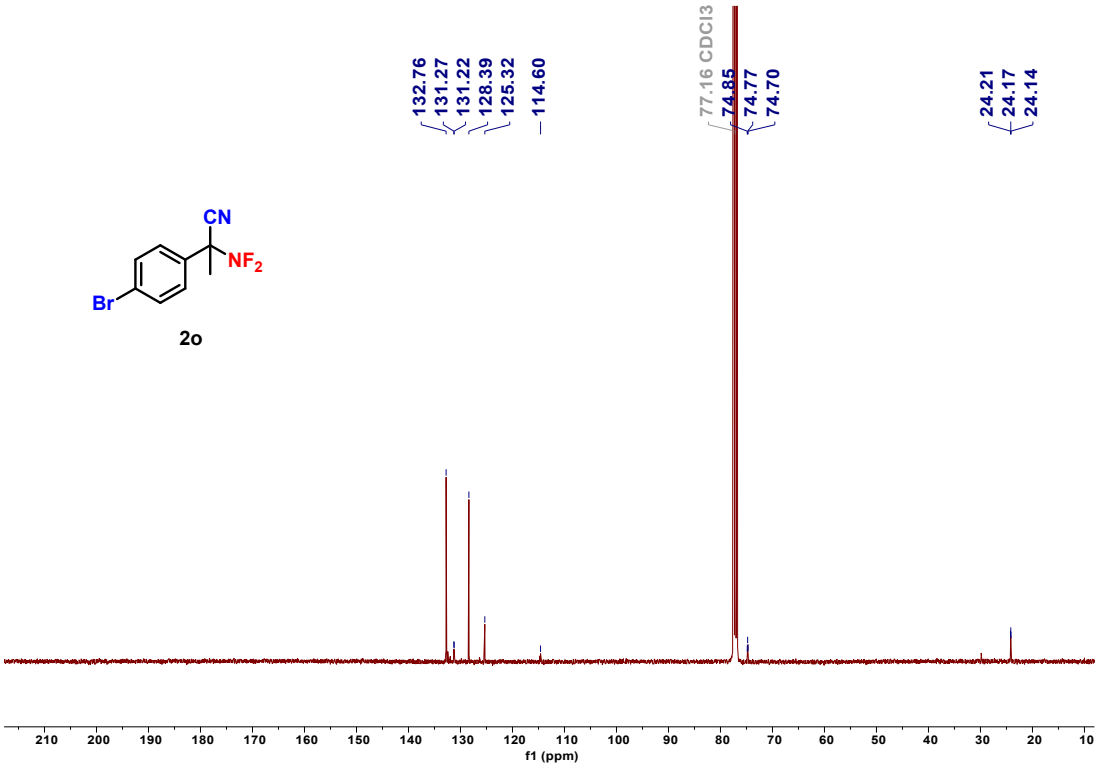
^{1}H NMR of **2o** (400 MHz, $CDCl_3$):



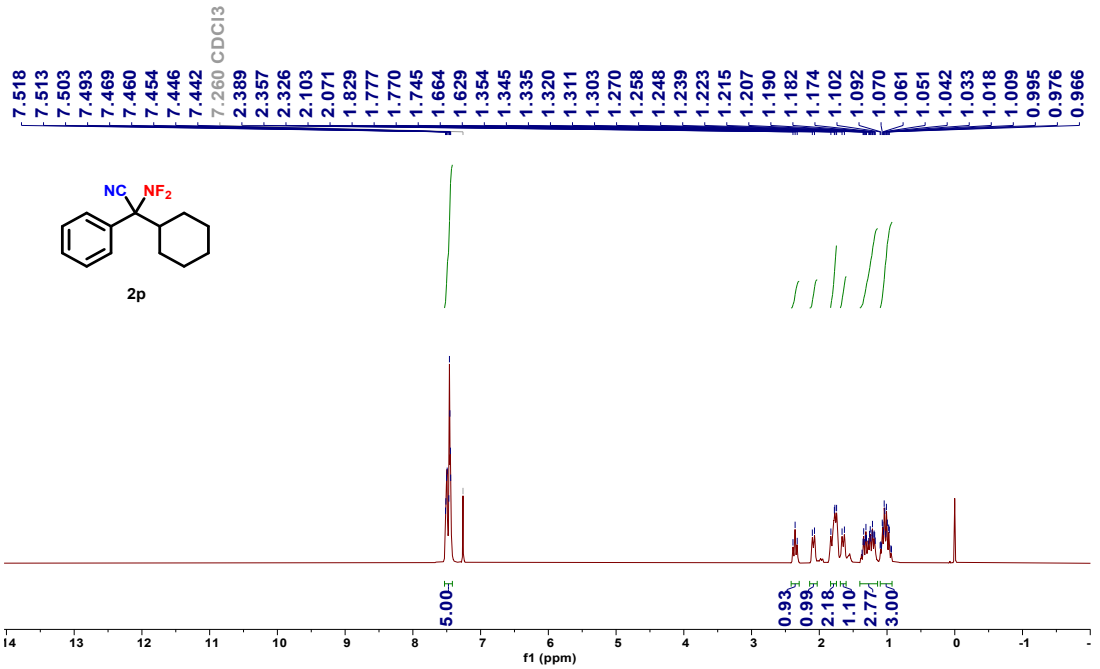
^{19}F NMR of **2o** (376 MHz, $CDCl_3$):



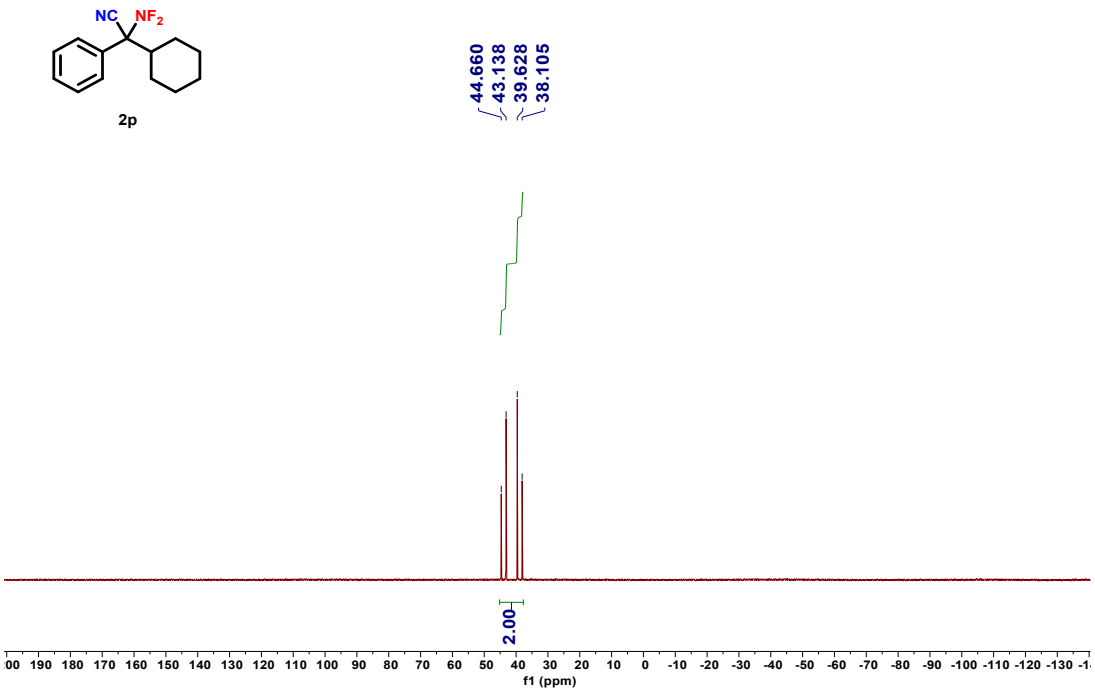
^{13}C NMR of **2o** (101 MHz, $CDCl_3$):



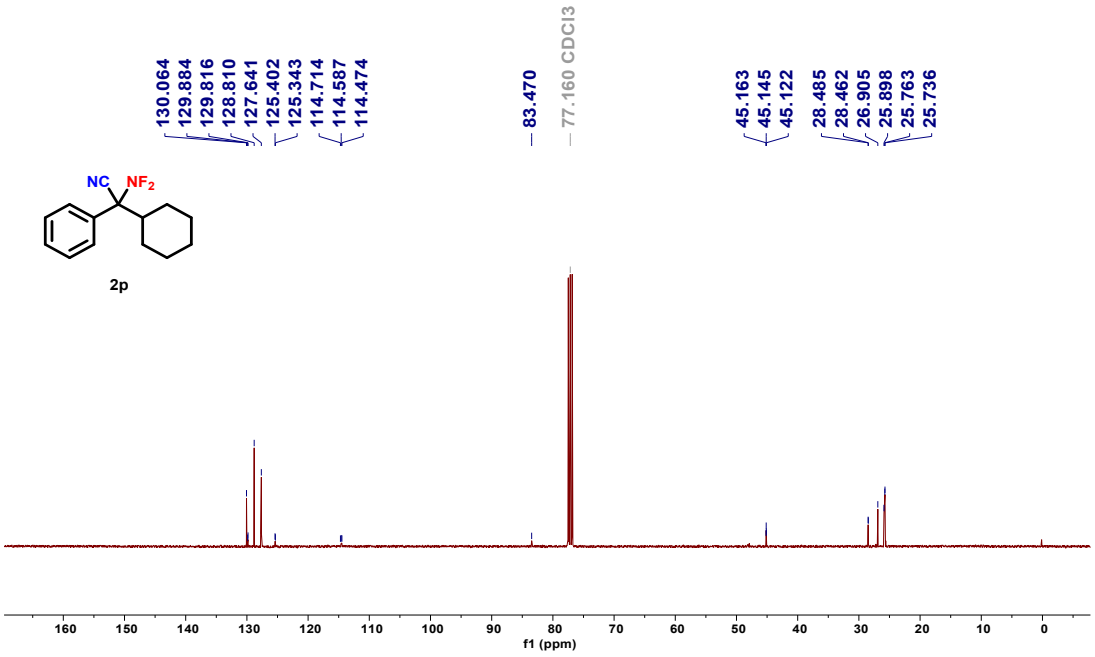
^{1}H NMR of **2p** (400 MHz, $CDCl_3$):



^{19}F NMR of **2p** (376 MHz, $CDCl_3$):



^{13}C NMR of **2p** (101 MHz, $CDCl_3$):



5. References

[1] Prakash, G. K. S.; Etzkorn, M.; Olah, G. A.; Christe, K. O.; Schneider, S.; Vij, A. Triphenylmethyldifluoramine: a Stable Reagent for the Synthesis of Gem-Bis(difluoramines). *Chem. Commun.* **2002**, 1712–1713.