

Supporting Information

Cobalt-Catalyzed Selective Functionalization of Aniline Derivatives with Hexafluoroisopropanol

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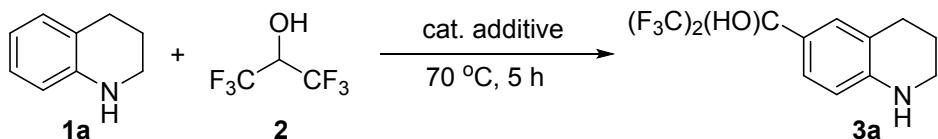
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General methods

The NMR spectra were recorded on Bruker spectrometers (^1H at 400 MHz, ^{13}C at 100 MHz and ^{19}F at 376 MHz). Chemical shifts (δ) were given in ppm with reference to solvent signals [^1H NMR: CDCl_3 (7.26); ^{13}C NMR: CDCl_3 (77.02); ^1H NMR: $\text{DMSO}-d_6$ (2.50); ^{13}C NMR: $\text{DMSO}-d_6$ (40.01)]. ^1H NMR data are reported as follows: chemical shift, multiplicity (s = singlet, br s = broad singlet, d = doublet, br d = broad doublet, t = triplet, br t = broad triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. The high resolution mass spectrums were recorded on a Bruker maXis impact mass spectrometer. Fourier transform infrared spectroscopy tests (FTIR) were carried out on a Bruker Tensor 27 spectrometer using KBr pellets. Melting points (m.p.) were performed using a Büchi AG M-565. Column chromatography was performed on silica gel (200-300 mesh). Reactions were monitored by using thin layer chromatography (TLC) (Qingdao Jiyida silica gel reagent factory GF254). All solvents and reagents were used as obtained from commercial sources without further purification. X-Ray diffraction data of one these crystals were collected on a Bruker SMART diffractometer. And the structures were solved by direct methods SHELXS-2014. Cyclic voltammograms was recorded at scan rates of 50, 100, 200 and 500 mV s^{-1} from a solution of A1 and A3 (10^{-3} mol dm^{-3}) in HFIP containing 0.1 mol dm^{-3} tetrabutylammonium hexafluorophosphate (TBAPF₆), using a disc Pt electrode (2 mm diameter) and a platinum wire as working and counter electrodes, respectively. The working electrode potentials were measured versus SCE reference electrode.

Screening of optimal conditions

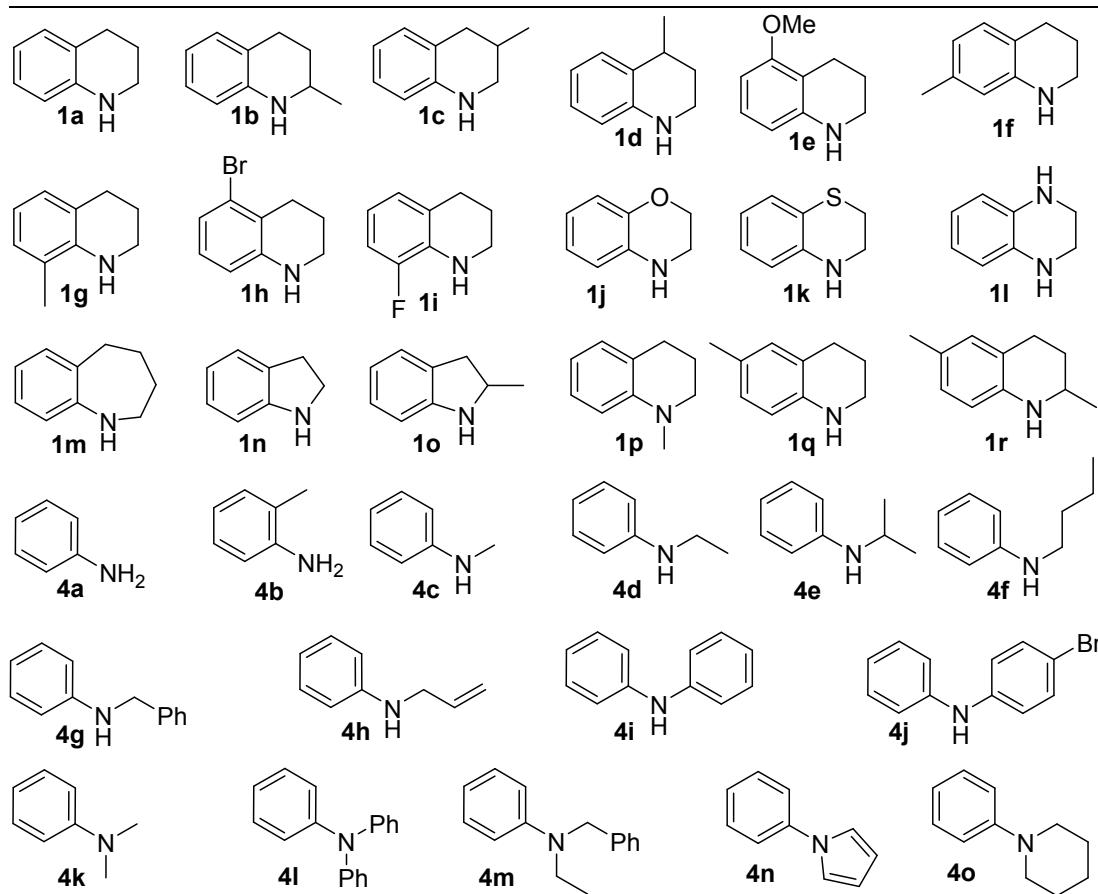
Table S1. Optimization of reaction conditions^a



Entry	Cat.	Additive	Yield of 3aa (%) ^b
1	Co(OAc) ₂ ·4H ₂ O	A1	98
2	CoCl ₂ ·6H ₂ O	A1	64
3	CuCl	A1	60
4	CuI	A1	57
5	CuCl ₂	A1	63
6	Ni(OAc) ₂ ·4H ₂ O	A1	73
7	PdCl ₂	A1	32
8	Pd(OAc) ₂	A1	63

^aReaction conditions: **1a** (0.25 mmol), additive (0.25 mmol), Cat. (2 mol %), HFIP **2** (0.5 mL), 70 °C, under air, 5 h. ^bIsolated yield

Scheme S1. Substrates employed for the transformation.



Typical procedure for the synthesis of product 3

Under air atmosphere, a mixture of aniline derivative **1** (0.25 mmol), *O*-benzoyl piperidine (0.25 mmol), Co(OAc)₂·4H₂O (2 mol %) and 0.25 mL HFIP (**2**) was stirred at 70 °C for 5 h. Then, the mixture was extracted with EtOAc for three times, and the combined organic layer were washed with aq. NaCl for three times, dried over Na₂SO₄, and concentrated in vacuo. The residue was purified by column chromatography on silica gel to give the desired product (petroleum ether : ethyl acetate = 5:1, v/v).

In vitro cytotoxicity

All the cell lines, HepG2, Hela, A549 and HSF, used in this study were obtained from the Shanghai Cell Bank, China Academy of Sciences. The cells were supplemented with 10% heat-inactivated fetal bovine serum in a cell incubator including 5% CO₂ /95% air at 37°C. Assays of cytotoxicity were determined in 96-well, flat bottomed microtiter plates, and the supplemented culture medium with cell lines was added to the wells. Compounds 4, aa and AB-AD were dissolved in the culture medium with 1% DMSO as different concentrations (2.5, 5, 10, 20, 30, 40, 50 μM respectively). The resulted solutions were subsequently added to a set of wells and control wells contained supplemented media with 1% DMSO. The plates were incubated at 37°C in a cell incubator including 5% CO₂ /95% air for a further 48h. Cytotoxic screening was conducted by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetra- zolum bromide (MTT) assay after indicated incubating time. The MTT solution (10 μL, 5 mg/mL) was added into each well and incubated for another 4 h (for the time-dependent cytotoxic effects studies, the treatment time is 24, 48, 72 h, respectively) at 37°C in a cell incubator including 5% CO₂ /95% air. After removal of the supernatant, DMSO (150 mL) was added to dissolve the formazan crystals, then the absorbance was read by enzyme labeling instrument with 570 nm wavelength measurement. The cytotoxicity was calculated based on the percentage cell survival in a dose dependent manner relative to the negative control, and final IC₅₀ values were calculated by the Bliss method (n = 5). All the tests were repeated in at least three independent experiments.

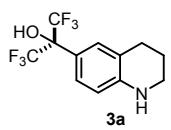
Table S2. IC₅₀ values of all compounds towards three selected tumor cell lines and normal cell line for 24 h.^a

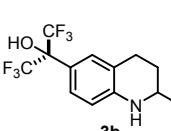
Compounds	IC ₅₀ (μ M)			
	HepG-2	HeLa	A549	HSF
3a	> 50	> 50	> 50	> 50
3b	> 50	> 50	> 50	> 50
3c	> 50	> 50	> 50	> 50
3d	> 50	> 50	> 50	> 50
3e	> 50	> 50	> 50	> 50
3f	> 50	> 50	> 50	> 50
3g	> 50	> 50	> 50	> 50
3h	26.091+0.67	23+0.59	27.59+0.57	22.6+1.44
3i	> 50	26.24+0.41	> 50	38.04+0.855
3j	> 50	> 50	> 50	> 50
3k	> 50	> 50	> 50	> 50
3l	> 50	> 50	> 50	> 50
3m	> 50	> 50	> 50	> 50
3n	> 50	> 50	> 50	> 50
3o	> 50	11.36+1.04	14.03+2.31	12.52+0.97
3p	> 50	> 50	> 50	36.99+1.47
3q	> 50	> 50	> 50	> 50
3r	> 50	> 50	> 50	> 50
5a	> 50	> 50	> 50	> 50
5b	> 50	> 50	> 50	> 50

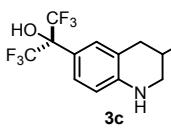
5c	> 50	> 50	> 50	> 50
5d	> 50	44+1.46	> 50	> 50
5e	41.69+0.77	> 50	> 50	> 50
5f	18.94+0.205	22.7+1.35	29.6+2.01	24.05+0.64
5g	6.718+0.99	24.26+0.49	34.86+0.84	28.57+1.26
5h	> 50	26.95+0.689	38.63+1.374	26.14+1.68
5i	11.731+1.032	31.32+1.17	3.96+0.55	42.25+2.02
5j	25.32+0.934	> 50	> 50	11.37+0.73
5k	> 50	> 50	> 50	> 50
5l	> 50	> 50	> 50	> 50
5m	> 50	> 50	> 50	> 50

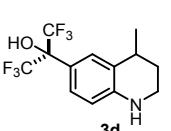
^aIC50 values are presented as the mean ± SD (standard error of the mean) from three separated experiments.

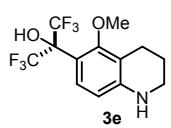
Characterization of the obtained products

 Known compound, white solid, 98% yield (73.3 mg), m.p.: 111.0 – 111.1 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.30 – 7.15 (m, 2H), 6.45 (d, *J* = 8.8 Hz, 1H), 3.60 (s, 1H), 3.31 (t, *J*₁ = 5.6 Hz, *J*₂ = 11.2 Hz, 2H), 2.77 (t, *J*₁ = 6.4 Hz, *J*₂ = 12.8 Hz, 2H), 1.99 – 1.88 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 146.0, 127.6, 125.0, 124.4, 121.5, 121.2, 117.1, 113.7, 41.7, 27.1, 21.6; ¹⁹F NMR (376 MHz, CDCl₃): δ -75.72 (s, 6F); IR (neat): ν = 3430, 2928, 2852, 1611, 1518, 1470, 1391, 1266, 1202, 1144, 960, 822, 709 cm⁻¹; MS (EI): m/z 299.1 [M]⁺.

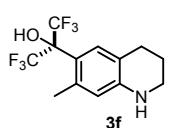
 Unknown compound, white solid, 94% yield (73.6 mg), m.p.: 81.0 – 81.1 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.24 – 7.18 (m, 2H), 6.45 (d, *J* = 8.4 Hz, 1H), 3.67 (s, 1H), 3.49 – 3.38 (m, 1H), 2.88 – 2.70 (m, 2H), 1.98 – 1.91 (m, 1H), 1.64 – 1.53 (m, 1H), 1.21 (d, *J* = 6.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 146.1, 127.3, 125.0, 124.3, 121.5, 120.7, 116.9, 113.4, 47.1, 29.6, 26.6, 22.5; ¹⁹F NMR (376 MHz, CDCl₃): δ -75.71 (s, 6F); IR (neat): ν = 3445, 2993, 2826, 2064, 1603, 1475, 1395, 1188, 960, 822, 709 cm⁻¹; HRMS (ESI): calcd for [M+H]⁺: 314.0974; found: m/z 314.0976.

 Unknown compound, pale pink solid, 93% yield (72.8 mg), m.p.: 117.8 – 117.9 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.30 – 7.19 (m, 2H), 6.47 (d, *J* = 9.2 Hz, 1H), 3.34 – 3.24 (m, 1H), 2.96 – 2.86 (m, 1H), 2.83 – 2.73 (m, 1H), 2.48 – 2.38 (m, 1H), 2.11 – 1.98 (m, 1H), 1.05 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 145.7, 127.6, 125.0, 124.3, 121.5, 120.8, 116.8, 113.3, 48.6, 35.5, 26.7, 18.9; ¹⁹F NMR (376 MHz, CDCl₃): δ -75.78 (s, 6F); IR (neat): ν = 3468, 2921, 1602, 1471, 1392, 1349, 1269, 1199, 1143, 822 cm⁻¹; HRMS (ESI): calcd for [M+H]⁺: 314.0974; found: m/z 314.0975.

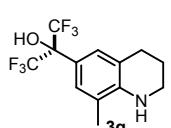
 Unknown compound, white solid, 92% yield (72.8 mg), m.p.: 155.4 – 155.5 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.33 (s, 1H), 7.28 – 7.16 (m, 1H), 6.48 (d, *J* = 8.6 Hz, 1H), 3.58 – 3.18 (m, 3H), 3.98 – 2.98 (m, 1H), 2.02 – 1.91 (m, 1H), 1.75 – 1.63 (m, 1H), 1.29 (d, *J* = 7.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 145.5, 126.6, 126.2, 124.9, 124.3, 121.5, 116.9, 113.7, 38.7, 30.4, 29.2, 22.3; ¹⁹F NMR (376 MHz, CDCl₃): δ -74.22 (s, 6F); IR (neat): ν = 3450, 2922, 2852, 1645, 1471, 1394, 1194, 1031, 822 cm⁻¹; HRMS (ESI): calcd for [M+H]⁺: 314.0974; found: m/z 314.0975.



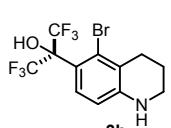
Unknown compound, white solid, 95% yield (78.1 mg), m.p.: 92.8 – 92.9 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.39 (d, *J* = 8.8 Hz, 1H), 6.65 (d, *J* = 8.8 Hz, 1H), 3.84 (s, 3H), 3.28 – 3.06 (m, 2H), 2.75 (t, *J*₁ = 6.7 Hz, *J*₂ = 13.4 Hz, 2H), 2.00 – 1.76 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 158.4, 142.9, 126.6, 125.1, 122.2, 119.8, 113.6, 105.4, 55.5, 42.0, 22.2, 20.8; ¹⁹F NMR (376 MHz, CDCl₃): δ -75.24 (s, 6F); IR (neat): ν = 3450, 2925, 2849, 1596, 1469, 1393, 1349, 1262, 1195, 1125, 1034, 958, 820 cm⁻¹; HRMS (ESI): calcd for [M+H]⁺: 330.0923; found: m/z 330.0924.



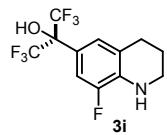
Unknown compound, white solid, 97% yield (75.9 mg), m.p.: 137.8 – 137.9 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.07 (s, 1H), 6.26 (s, 1H), 3.29 (t, *J*₁ = 5.6 Hz, *J*₂ = 11.2 Hz, 2H), 2.71 (t, *J*₁ = 6.4 Hz, *J*₂ = 12.8 Hz, 2H), 2.43 (s, 3H), 1.99 – 1.80 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 145.3, 137.4, 128.8, 124.8, 122.0, 118.5, 118.5, 115.0, 41.7, 26.5, 22.4, 21.9; ¹⁹F NMR (376 MHz, CDCl₃): δ -74.66 (s, 6F); IR (neat): ν = 3428, 2995, 2849, 2062, 1762, 1597, 1472, 1393, 1244, 1188, 1139, 1062 cm⁻¹; HRMS (ESI): calcd for [M+H]⁺: 314.0974; found: m/z 314.0972.



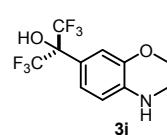
Unknown compound, white solid, 98% yield (76.7 mg), m.p.: 134.1 – 134.2 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.13 (d, *J* = 8.4 Hz, 1H), 3.81 (s, 1H), 3.43 – 3.11 (m, 3H), 2.79 (t, *J*₁ = 6.4 Hz, *J*₂ = 12.8 Hz, 1H), 2.08 (s, 2H), 2.01 – 1.85 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 144.2, 125.7, 125.4, 124.36, 121.5, 120.8, 120.5, 116.2, 42.1, 27.4, 21.6, 17.3; ¹⁹F NMR (376 MHz, CDCl₃): δ -75.72 (s, 6F); IR (neat): ν = 3451, 2826, 1599, 1472, 1394, 1355, 1204, 1188, 1139, 1062 cm⁻¹; HRMS (ESI): calcd for [M+H]⁺: 314.0974; found: m/z 314.0975.



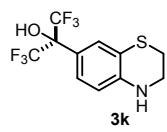
Unknown compound, white solid, 89% yield (83.9 mg), m.p.: 106.7 – 106.8 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.34 (d, *J* = 8.7 Hz, 1H), 7.25 (d, *J* = 8.7 Hz, 1H), 3.19 (t, *J*₁ = 5.2 Hz, *J*₂ = 10.4 Hz, 2H), 2.87 (t, *J*₁ = 6.8 Hz, *J*₂ = 13.6 Hz, 2H), 1.99 – 1.85 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 144.1, 130.4, 128.2, 127.3, 127.0, 124.7, 121.9, 119.8, 41.9, 28.2, 22.7; ¹⁹F NMR (376 MHz, CDCl₃): δ -74.89 (s, 6F); IR (neat): ν = 3447, 2993, 2821, 1600, 1476, 1395, 1355, 1182, 1002, 779 cm⁻¹; HRMS (ESI): calcd for [M+H]⁺: 377.9923; found: m/z 377.9918.



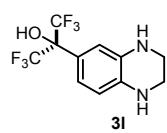
Unknown compound, white soild, 72% yield (57.1 mg), m.p.: 80.7 – 80.8 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.13 (d, *J* = 12.6 Hz, 1H), 7.05 (s, 1H), 3.55 (br s, 1H), 3.36 (t, *J*₁ = 5.6 Hz, *J*₂ = 11.2 Hz, 2H), 2.79 (t, *J*₁ = 6.4 Hz, *J*₂ = 12.8 Hz, 2H), 2.01 – 1.86 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 151.3, 148.9, 134.7 (d, *J* = 12.1 Hz), 124.2, 123.1 (d, *J* = 4.2 Hz), 122.7, 121.3, 115.7 (d, *J* = 7.4 Hz), 111.0 (d, *J* = 20.5 Hz), 41.0, 26.7 (d, *J* = 2.9 Hz), 21.3; ¹⁹F NMR (376 MHz, CDCl₃): δ -75.89 (s, 6F), -138.47 (s, 1F); IR (neat): ν = 3446, 3001, 2851, 1596, 1471, 1393, 1348, 1269, 1203, 1152, 962, 752 cm⁻¹; HRMS (ESI): calcd for [M+H]⁺: 318.0723; found: m/z 318.0724.



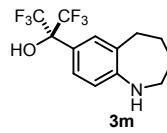
Known compound, white soild, 87% yield (65.5 mg), m.p.: 119.3 – 111.1 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.22 (s, 1H), 7.01 – 6.82 (m, 2H), 6.62 (d, *J* = 8.4 Hz, 1H), 6.14 (s, 1H), 4.13 (t, *J*₁ = 4.0 Hz, *J*₂ = 8.0 Hz, 2H), 3.31 (t, *J*₁ = 4.0 Hz, *J*₂ = 8.0 Hz, 2H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 142.7, 136.9, 125.0, 122.2, 120.1, 118.2, 115.0, 114.3, 64.9, 40.1; ¹⁹F NMR (376 MHz, DMSO-*d*₆): δ -75.74 (s, 6F); IR (neat): ν = 3440, 2992, 2085, 1762, 1595, 1470, 1388, 1243, 1052, 958 cm⁻¹; MS (EI): m/z 301.0 [M]⁺.



Known compound, white soild, 95% yield (75.3 mg), m.p.: 98.9 – 90.0 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.31 (s, 1H), 7.16 (d, *J* = 8.4 Hz, 1H), 6.48 (d, *J* = 8.6 Hz, 1H), 3.67 (t, *J*₁ = 4.8 Hz, *J*₂ = 9.6 Hz, 2H), 3.26 (s, 1H), 3.04 (t, *J*₁ = 4.8 Hz, *J*₂ = 9.6 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 143.0, 126.1, 124.2, 123.8, 121.3, 118.4, 115.9, 114.8, 42.3, 25.5; ¹⁹F NMR (376 MHz, CDCl₃): δ -75.74 (s, 6F); IR (neat): ν = 3452, 2998, 2839, 1600, 1472, 1394, 1355, 1267, 1187, 958, 753 cm⁻¹; MS (EI): m/z 317.0 [M]⁺.

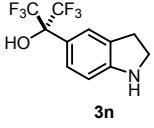


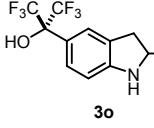
Unknown compound, yellow soild, 80% yield (60.0 mg), m.p.: 143.8 – 143.9 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.99 (s, 1H), 6.69 (s, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 6.38 (d, *J* = 8.4 Hz, 1H), 5.59 (s, 2H), 3.21 (d, *J* = 6.4 Hz, 4H); ¹³C NMR (100 MHz, DMSO-*d*₆) 136.0, 134.6, 134.0, 125.2, 122.3, 118.3, 117.3, 116.0, 113.8, 112.6, 112.0; ¹⁹F NMR (376 MHz, DMSO-*d*₆): δ -74.07 (s, 6F); IR (neat): ν = 3448, 2807, 1594, 1470, 1393, 1347, 1243, 1033, 821 cm⁻¹; HRMS (ESI): calcd for [M+H]⁺: 301.0770; found: m/z 301.0768.

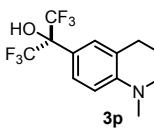


Known compound, white soild, 60% yield (47.0 mg), m.p.: 115.1 – 115.2 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.49 – 7.19 (m, 2H), 6.67 (s, 1H), 4.08 (br s, 2H), 3.06 (s, 2H), 2.78 (s, 2H), 1.90 – 1.58 (m, 4H);

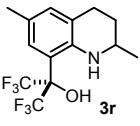
¹³C NMR (100 MHz, CDCl₃) δ 151.4, 133.3, 129.1, 124.9, 124.3, 121.8, 121.5, 119.3, 48.5, 36.1, 31.2, 26.5; ¹⁹F NMR (376 MHz, CDCl₃): δ -75.53 (s, 6F); IR (neat): ν = 3450, 2993, 2820, 2066, 1599, 1476, 1393, 1355, 1244, 1184, 1003 cm⁻¹; MS (EI): m/z 313.1 [M]⁺.

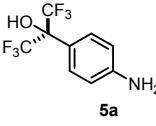
 Known compound, white solid, 80% yield (51.6 mg), m.p.: 160.1 – 160.2 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.18 (s, 1H), 7.27 (s, 1H), 7.21 (d, *J* = 8.0 Hz, 1H), 6.53 (d, *J* = 8.0 Hz, 1H), 5.81 (s, 1H), 3.47 (t, *J*₁ = 8.4 Hz, *J*₂ = 16.8 Hz, 2H), 2.94 (t, *J*₁ = 8.4 Hz, *J*₂ = 16.8 Hz, 2H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 154.3, 129.4, 126.6, 125.2, 122.9, 122.3, 118.5, 107.7, 46.9, 29.4; ¹⁹F NMR (376 MHz, DMSO-*d*₆): δ -74.19 (s, 6F); IR (neat): ν = 3435, 2998, 2851, 1597, 1472, 1393, 1352, 1259, 1190, 1092, 752 cm⁻¹; MS (EI): m/z 285.1 [M]⁺.

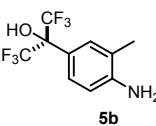
 Known compound, white solid, 96% yield (71.8 mg), m.p.: 110.6 – 110.7 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.38 – 7.28 (m, 2H), 6.56 (d, *J* = 8.4 Hz, 1H), 4.13 – 4.02 (m, 1H), 3.25 – 3.14 (m, 1H), 2.74 – 2.64 (m, 1H), 1.32 (d, *J* = 6.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 151.9, 129.3, 126.2, 124.4, 122.9, 121.5, 119.7, 108.9, 55.5, 37.4, 22.1; ¹⁹F NMR (376 MHz, CDCl₃): δ -75.64 (s, 6F); IR (neat): ν = 3448, 2805, 1762, 1593, 1468, 1390, 1345, 1245, 1051, 960, 821, 750 cm⁻¹; MS (EI): m/z 299.1 [M]⁺.

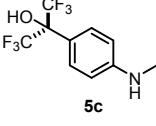
 Unknown compound, yellow oil, 98% yield (76.7 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.33 (d, *J* = 8.8 Hz, 1H), 7.22 (d, *J* = 6.0 Hz, 1H), 6.57 (d, *J* = 8.8 Hz, 1H), 3.41 (s, 1H), 3.26 (t, *J*₁ = 5.6 Hz, *J*₂ = 11.2 Hz, 2H), 2.90 (s, 3H), 2.77 (t, *J*₁ = 6.4 Hz, *J*₂ = 12.8 Hz, 2H), 1.97 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 147.7, 126.6, 125.4, 124.4, 122.5, 121.5, 115.8, 110.2, 51.0, 38.8, 28.0, 22.0; ¹⁹F NMR (376 MHz, CDCl₃): δ -75.76 (s, 6F); IR (neat): ν = 3604, 3523, 3444, 3313, 2930, 1662, 1520, 1267, 1204, 964, 718 cm⁻¹; HRMS (ESI): calcd for [M+H]⁺: 314.0974; found: m/z 314.0975.

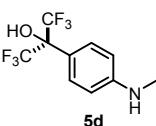
 Unknown compound, yellow solid, 90% yield (70.4 mg), m.p.: 74.5 – 74.6 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.20 (s, 1H), 6.98 (s, 1H), 3.16 (t, *J*₁ = 5.6 Hz, *J*₂ = 11.2 Hz, 2H), 2.86 (t, *J*₁ = 6.8 Hz, *J*₂ = 13.6 Hz, 2H), 2.30 (s, 3H), 1.97 – 1.81 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 139.2, 133.9, 131.9, 131.6, 129.0, 126.7, 125.0, 122.1, 42.6, 26.6, 22.9, 21.0; ¹⁹F NMR (376 MHz, CDCl₃): δ -74.99 (s, 6F); IR (neat): ν = 3453, 2807, 1596, 1469, 1393, 1348, 1265, 1198, 1141, 1041, 959 cm⁻¹; HRMS (ESI): calcd for [M+H]⁺: 314.0974; found: m/z 314.0972.


 Unknown compound, white solid, 92% yield (75.2 mg), m.p.: 83.3 – 83.4 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.12 (s, 1H), 6.90 (s, 1H), 3.13 – 2.98 (m, 1H), 2.89 – 2.72 (m, 2H), 2.20 (s, 2H), 1.95 – 1.85 (m, 1H), 1.47 – 1.33 (m, 1H), 1.18 (d, $J = 6.5$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) 138.9, 133.9, 131.6, 131.3, 126.7, 125.3, 124.8, 122.4, 122.1, 48.6, 30.2, 26.6, 21.4, 21.0; ^{19}F NMR (376 MHz, CDCl_3): δ -73.72 (s, 3F), -76.32 (s, 3F); IR (neat): ν = 3451, 2928, 1596, 1469, 1392, 1351, 1266, 1198, 1140, 960 cm^{-1} ; HRMS (ESI): calcd for $[\text{M}+\text{H}]^+$: 328.1131; found: m/z 328.1133.


 Known compound, white solid, 45% yield (29.1 mg), m.p.: 149.4 – 149.5 °C; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.16 (s, 1H), 7.30 (s, 2H), 6.63 (s, 2H), 5.41 (s, 2H); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ 150.5, 128.0, 125.1, 122.3, 117.2, 113.7; ^{19}F NMR (376 MHz, $\text{DMSO}-d_6$): δ -74.35 (s, 6F); IR (neat): ν = 3445, 2806, 1595, 1470, 1393, 1345, 1245, 1034, 823 cm^{-1} ; MS (EI): m/z 259.0 $[\text{M}]^+$.

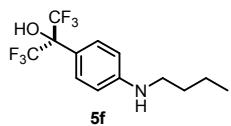

 Known compound, white solid, 45% yield (30.7 mg), m.p.: 131.8 – 131.9 °C; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.12 (s, 1H), 7.28 – 7.10 (m, 2H), 6.66 (d, $J = 8.4$ Hz, 1H), 5.17 (s, 2H), 2.09 (s, 3H); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ 148.5, 128.7, 125.5, 125.2, 122.3, 120.9, 117.5, 113.7, 18.1; ^{19}F NMR (376 MHz, $\text{DMSO}-d_6$): δ -74.24 (s, 6F); IR (neat): ν = 3445, 1596, 1472, 1393, 1349, 1196, 823 cm^{-1} ; MS (EI): m/z 273.1 $[\text{M}]^+$.


 Known compound, white solid, 85% yield (58.0 mg), m.p.: 84.7 – 84.8 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.47 (d, $J = 8.4$ Hz, 2H), 6.62 (d, $J = 8.4$ Hz, 2H), 3.68 (s, 1H), 2.84 (s, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 150.4, 127.6, 124.3, 121.5, 117.5, 112.1, 30.4; ^{19}F NMR (376 MHz, CDCl_3): δ -75.83 (s, 6F); IR (neat): ν = 3453, 2807, 1596, 1469, 1393, 1345, 1192, 1135, 822 cm^{-1} ; MS (EI): m/z 273.1 $[\text{M}]^+$.

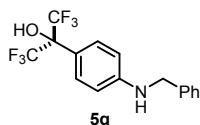

 Known compound, white solid, 65% yield (46.6 mg), m.p.: 88.6 – 88.7 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.46 (d, $J = 8.4$ Hz, 2H), 6.60 (d, $J = 8.8$ Hz, 2H), 3.69 (br s, 2H), 3.26 – 3.10 (m, 2H), 1.26 (t, $J_1 = 7.2$ Hz, $J_2 = 14.4$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 149.6, 127.6, 124.3, 121.5, 117.3, 112.3, 38.2, 14.7; ^{19}F NMR (376 MHz, CDCl_3): δ -75.84 (s, 6F); IR (neat): ν = 3455, 2806, 1613, 1590, 1462, 1384, 1337, 1256, 1182, 1108, 956, 926, 828 cm^{-1} ; MS (EI): m/z 287.1 $[\text{M}]^+$.



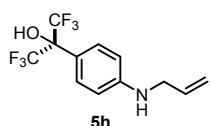
Unknown compound, white soild, 60% yield (45.2 mg), m.p.: 107.8 – 107.9 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.44 (d, *J* = 8.6 Hz, 2H), 6.58 (d, *J* = 8.8 Hz, 2H), 3.77 – 3.40 (m, 3H), 1.22 (d, *J* = 6.3 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) 148.7, 127.6, 124.3, 121.5, 116.9, 112.6, 44.1, 22.9; ¹⁹F NMR (376 MHz, CDCl₃): δ -75.82 (s, 6F); IR (neat): ν = 3456, 2805, 1596, 1468, 1393, 1343, 1262, 1106, 821 cm⁻¹; HRMS (ESI): calcd for [M+H]⁺: 302.0974; found: m/z 302.0973.



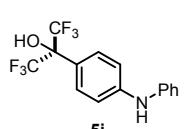
Known compound, white soild, 55% yield (43.3 mg), m.p.: 71.4 – 71.5 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.45 (d, *J* = 8.4 Hz, 2H), 6.60 (d, *J* = 8.8 Hz, 2H), 3.66 (s, 1H), 3.12 (t, *J*₁ = 7.2 Hz, *J*₂ = 14.4 Hz, 2H), 1.67 – 1.54 (m, 2H), 1.49 – 1.37 (m, 2H), 0.96 (t, *J*₁ = 7.2 Hz, *J*₂ = 14.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 149.7, 127.6, 124.3, 121.5, 117.1, 112.2, 43.3, 31.5, 20.2, 13.8; ¹⁹F NMR (376 MHz, CDCl₃): δ -75.88 (s, 6F); IR (neat): ν = 3445, 1601, 1471, 1392, 1350, 1265, 1186, 929, 822, 751 cm⁻¹; MS (EI): m/z 315.1 [M]⁺.



Known compound, white soild, 60% yield (50.3 mg), m.p.: 101.6 – 101.7 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.46 (d, *J* = 8.8 Hz, 2H), 7.41 – 7.20 (m, 5H), 6.64 (d, *J* = 8.8 Hz, 2H), 4.33 (s, 2H), 4.16 (s, 1H), 3.54 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) 149.37, 138.77, 128.78, 127.66, 127.51, 124.32, 121.46, 117.69, 112.40, 48.03; ¹⁹F NMR (376 MHz, CDCl₃): δ -75.84 (s, 6F); IR (neat): ν = 3449, 2814, 1599, 1470, 1393, 1352, 1187 cm⁻¹; MS (EI): m/z 335.1 [M]⁺.

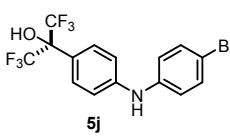


Unknown compound, white soild, 80% yield (59.8 mg), m.p.: 131.8 – 131.9 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.39 (d, *J* = 8.4 Hz, 2H), 6.55 (d, *J* = 8.8 Hz, 2H), 5.97 – 5.78 (m, 1H), 5.35 – 5.04 (m, 2H), 4.01 – 3.29 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) 149.3, 134.8, 127.6, 124.3, 121.4, 117.7, 116.7, 112.5, 46.2; ¹⁹F NMR (376 MHz, CDCl₃): δ -75.82 (s, 6F); IR (neat): ν = 3441, 2997, 2807, 1762, 1597, 1471, 1393, 1348, 1242, 1188, 1047 cm⁻¹; HRMS (ESI): calcd for [M+H]⁺: 300.0818; found: m/z 300.0819.

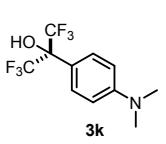


Unknown compound, brown oil, 70% yield (62.1 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.45 (d, *J* = 8.4 Hz, 2H), 7.20 (t, *J*₁ = 7.6 Hz, *J*₂ = 14.2 Hz, 2H), 7.02 (d, *J* = 8.4 Hz, 2H), 6.98 – 6.88 (m, 3H), 5.71 (s, 1H), 3.37 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 145.4, 141.7, 129.5, 127.8, 124.3, 122.5,

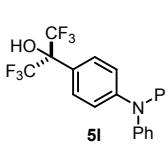
121.4, 120.5, 119.6, 115.9; ^{19}F NMR (376 MHz, CDCl_3): δ -75.70 (s, 6F); IR (neat): ν = 3418, 2805, 1597, 1526, 1392, 1338, 1266, 1192, 1108, 932, 824, 748, 699 cm^{-1} ; HRMS (ESI): calcd for $[\text{M}+\text{H}]^+$: 336.0818; found: m/z 336.0820.



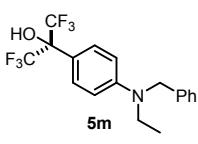
Unknown compound, brown soild, 35% yield (36.1 mg), m.p.: 81.2 – 81.3 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 7.62 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 8.4 Hz, 2H), 7.06 (dd, J_1 = 8.4 Hz, J_2 = 19.2 Hz, 4H), 5.86 (s, 1H), 3.63 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 144.7, 140.9, 132.4, 127.9, 124.2, 121.1, 120.8, 116.3, 114.3; ^{19}F NMR (376 MHz, CDCl_3): δ -75.73 (s, 6F); IR (neat): ν = 3607, 3524, 3442, 3304, 1663, 1590, 1520, 1268, 1217, 1104, 927, 815, 704 cm^{-1} ; HRMS (ESI): calcd for $[\text{M}+\text{H}]^+$: 413.9923; found: m/z 413.9918.



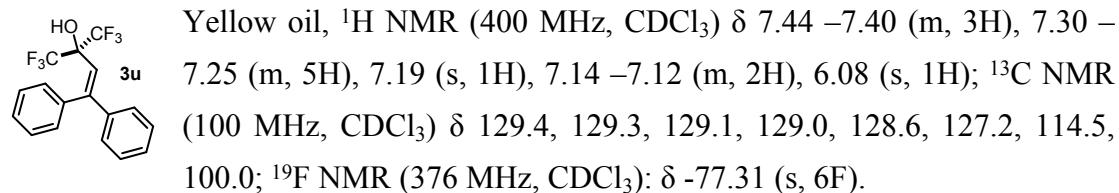
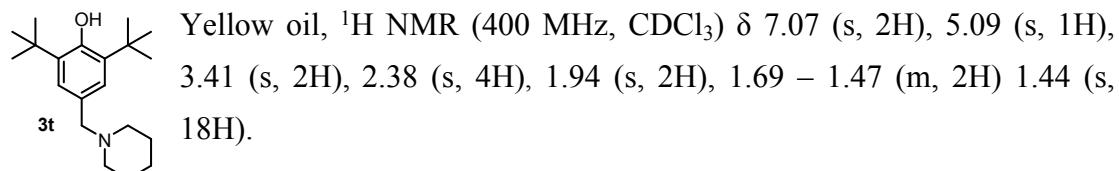
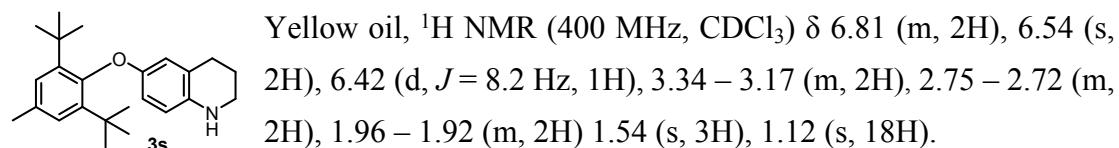
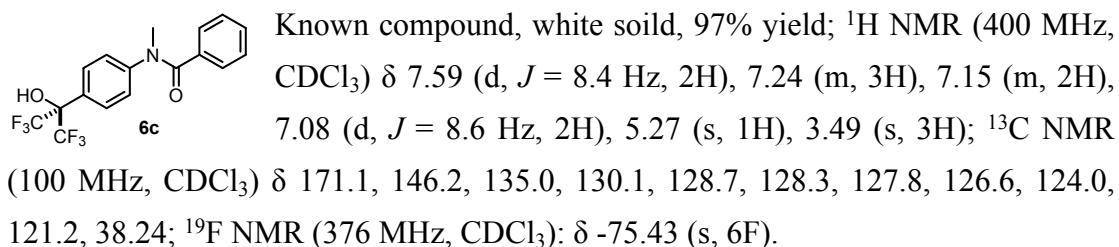
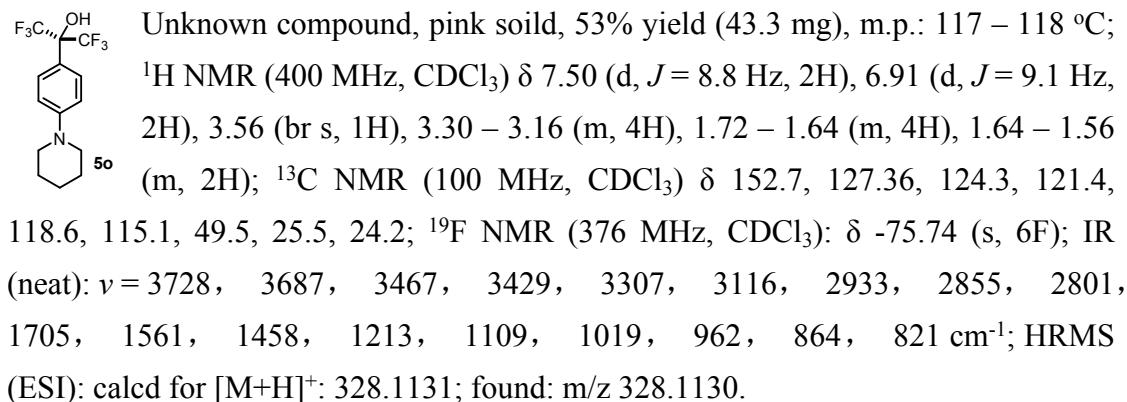
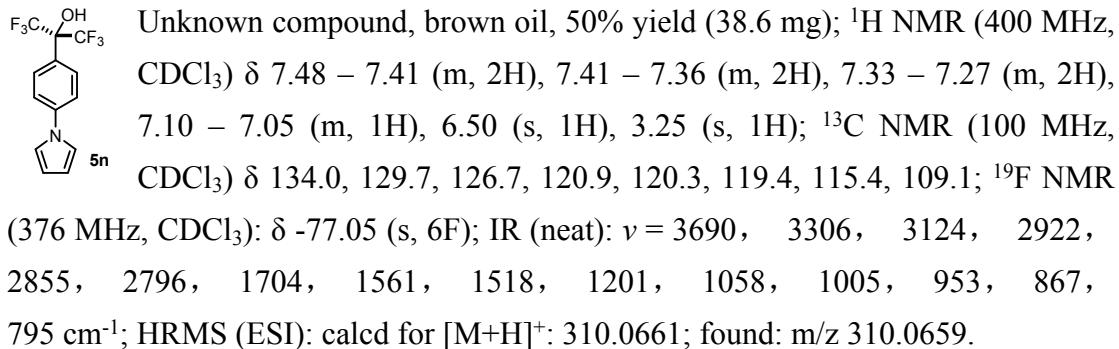
Known compound, white soild, 80% yield (50.3 mg), m.p.: 76.8 – 76.9 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) 7.52 (d, J = 8.0 Hz, 2H), 6.72 (d, J = 8.2 Hz, 2H), 3.48 (s, 1H), 2.97 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 151.3, 127.3, 124.4, 121.5, 116.4, 111.8, 40.2; ^{19}F NMR (376 MHz, CDCl_3): δ -75.83 (s, 6F); IR (neat): ν = 3447, 2922, 2807, 1605, 1529, 1470, 1392, 1350, 1269, 1191, 931, 819 cm^{-1} ; MS (EI): m/z 287.1 $[\text{M}]^+$.



Unknown compound, brown oil, 60% yield (61.7 mg); ^1H NMR (400 MHz, CDCl_3) δ 7.38 (d, J = 8.4 Hz, 2H), 7.17 (t, J_1 = 7.6 Hz, J_2 = 15.2 Hz, 4H), 7.07 – 6.91 (m, 8H), 3.15 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 149.6, 147.1, 129.6, 127.4, 125.5, 124.2, 124.0, 121.4, 121.4, 121.3; ^{19}F NMR (376 MHz, CDCl_3): δ -75.64 (s, 6F); IR (neat): ν = 3521, 2925, 1733, 1593, 1499, 1268, 1218, 1105, 930, 831, 752, 700 cm^{-1} ; HRMS (ESI): calcd for $[\text{M}+\text{H}]^+$: 412.1131; found: m/z 412.1129.



Known compound, white soild, 85% yield (80.1 mg), m.p.: 76.8 – 76.9 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 7.59 (d, J = 8.8 Hz, 2H), 7.45 – 7.39 (m, 2H), 7.38 – 7.32 (m, 3H), 6.82 (d, J = 8.8 Hz, 2H), 4.64 (s, 2H), 3.60 (q, J = 7.0 Hz, 2H), 1.33 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 149.6, 138.6, 128.8, 127.6, 127.1, 126.5, 124.5, 121.6, 116.1, 111.5, 53.8, 45.2, 12.0; ^{19}F NMR (376 MHz, CDCl_3): δ -75.68 (s, 6F); IR (neat): ν = 3648, 3499, 2967, 1609, 1526, 1402, 1265, 1168, 969, 922, 811, 738 cm^{-1} ; MS (EI): m/z 377.1 $[\text{M}]^+$.



Single crystal X-ray diffraction data of **3a**

Colorless and transparent block-like single crystals of **3a** were grown by layering a chloroform solution at ambient temperature. X-Ray diffraction data of one these crystals were collected on a Bruker P4 diffractometer. The measurements were performed with Mo-K α radiation ($\lambda = 0.71073 \text{ \AA}$). Data were collected at 293 K, using the ω - and φ - scans to a maximum θ value of 27.374°. The data were refined by full-matrix least-squares techniques on F^2 with SHELXTL-2014. And the structures were solved by direct methods SHELXS-2014. All the non-hydrogen atoms were refined anisotropically. The hydrogen atoms were included at geometrically idealized positions. An ORTEP representation of the structure is shown below.

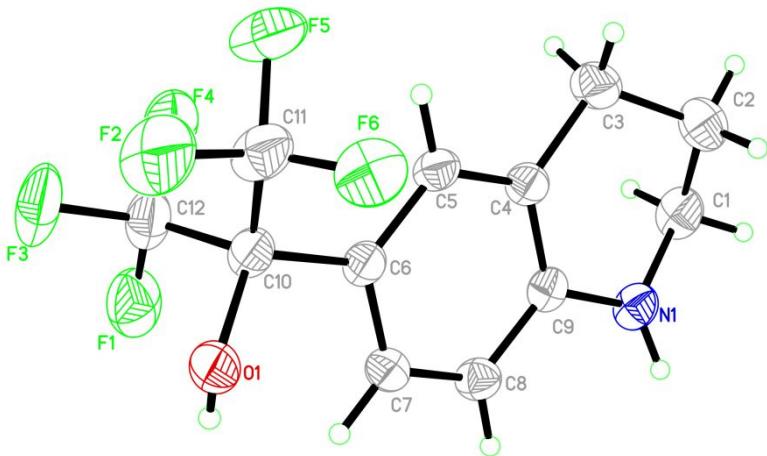


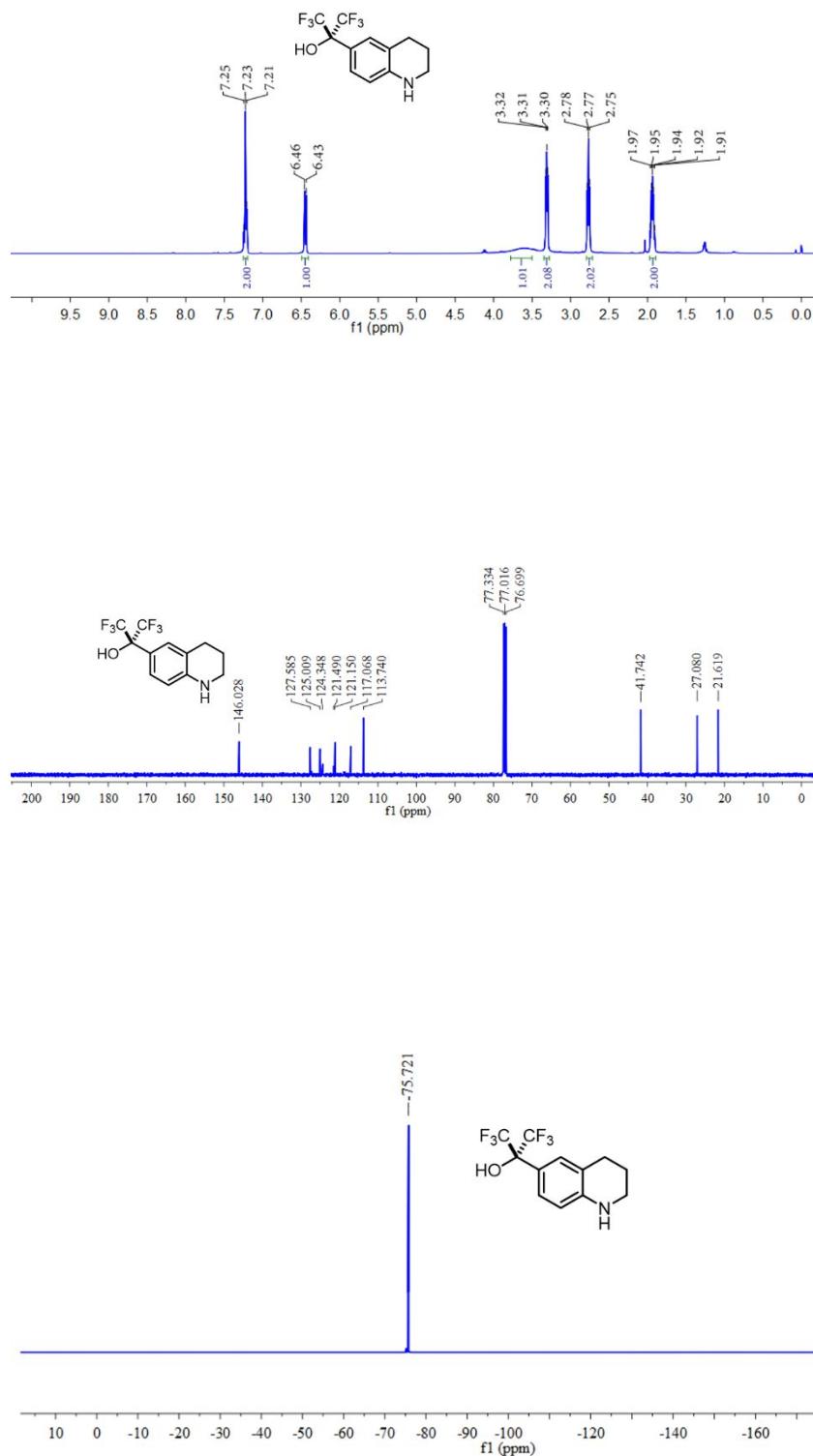
Figure S1. ORTEP drawing of **3a** with the numbering scheme.

Table S3 Crystal data and structure refinement for **3a**.

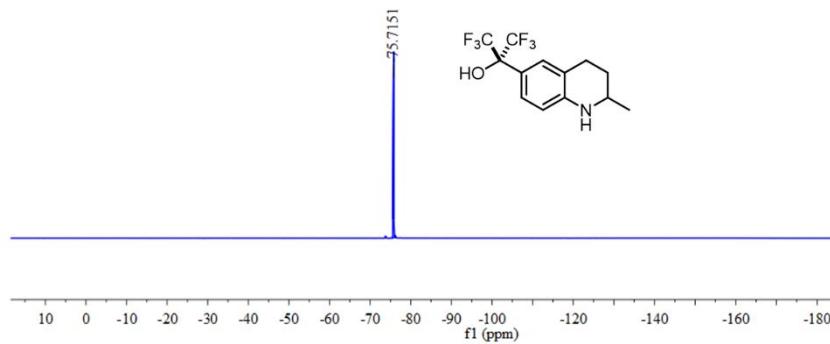
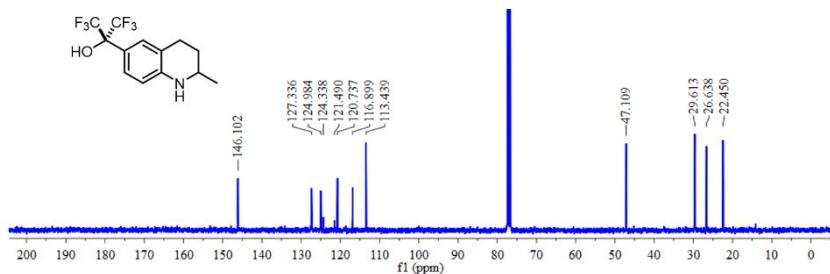
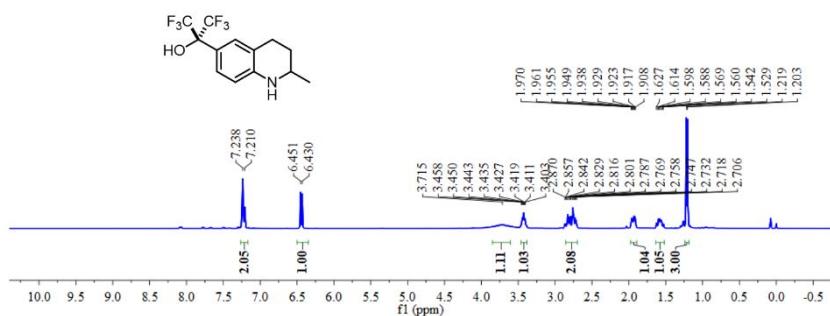
Identification code	3a	
Empirical formula	C ₁₂ H ₁₁ F ₆ NO	
Formula weight	299.22	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2 1/c	
Unit cell dimensions	a = 10.812(2) Å b = 14.506(3) Å c = 10.197(2) Å	α = 90°. β = 115.15(3)°. γ = 90°.
Volume	1447.7(6) Å ³	
Z	4	
Density (calculated)	1.373 Mg/m ³	
Absorption coefficient	0.140 mm ⁻¹	
F(000)	608	
Crystal size	0.22 x 0.20 x 0.18 mm ³	
Theta range for data collection	2.081 to 27.374°.	
Index ranges	-13<=h<=13, -18<=k<=18, -13<=l<=13	
Reflections collected	15864	
Independent reflections	3253 [R(int) = 0.0206]	
Completeness to theta = 25.242°	100.0 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	3253 / 0 / 181	
Goodness-of-fit on F ²	1.038	
Final R indices [I>2sigma(I)]	R1 = 0.0557, wR2 = 0.1681	
R indices (all data)	R1 = 0.0656, wR2 = 0.1775	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.435 and -0.402 e Å ⁻³	

NMR Spectra for All Products

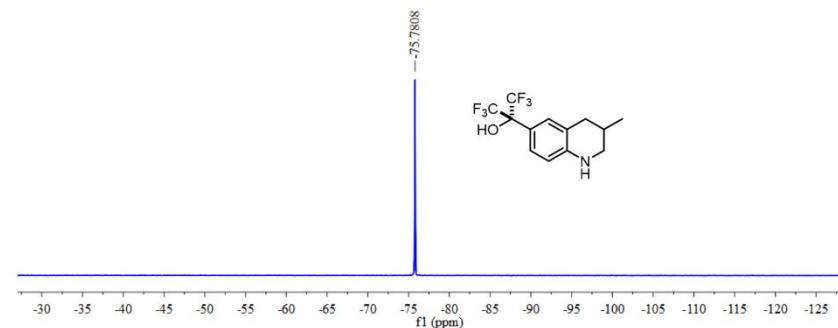
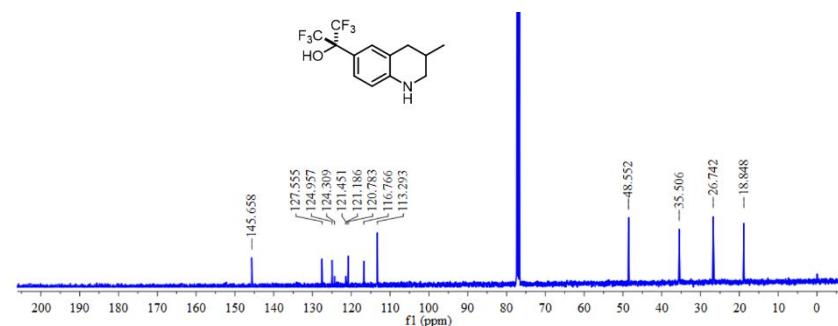
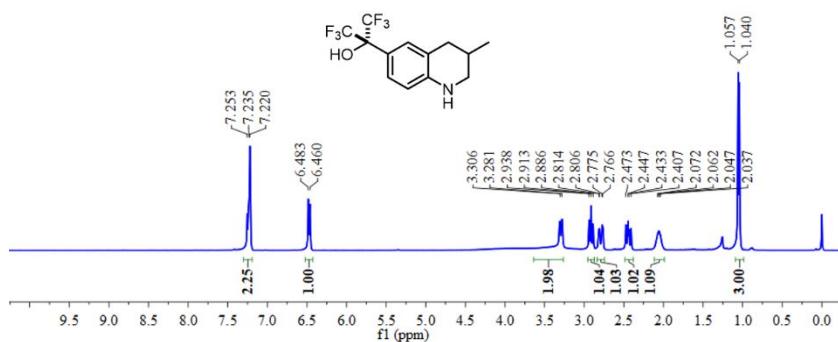
^1H , ^{13}C and ^{19}F NMR Spectra of 3a



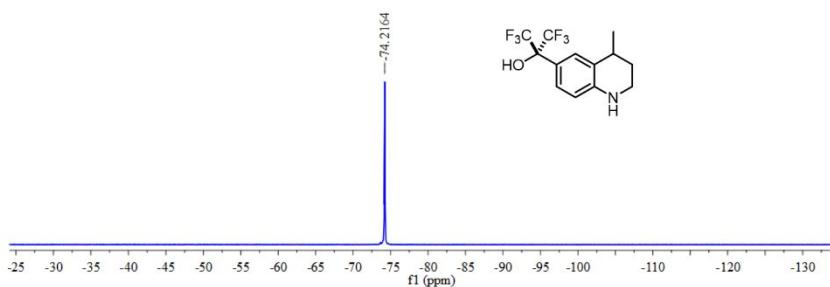
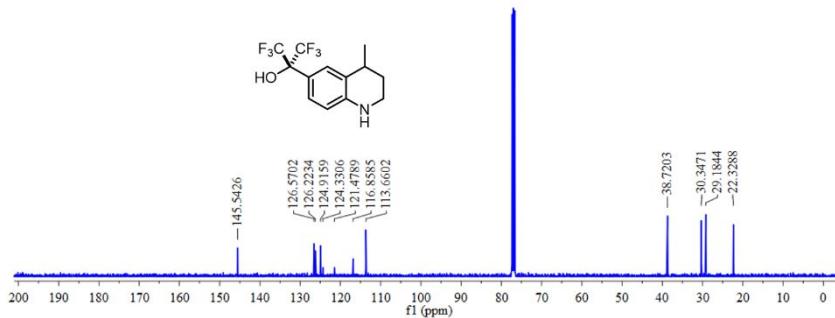
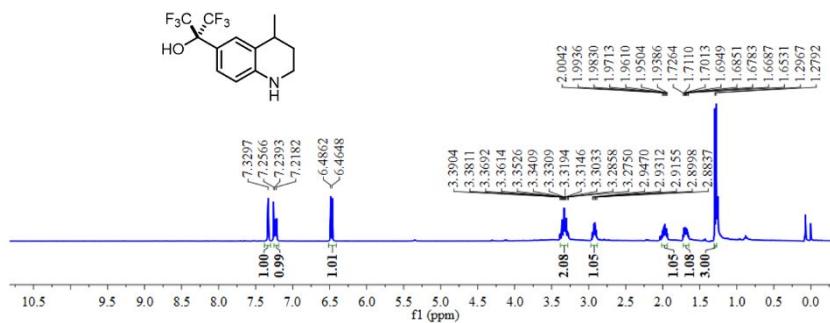
¹H, ¹³C and ¹⁹F NMR Spectra of 3b



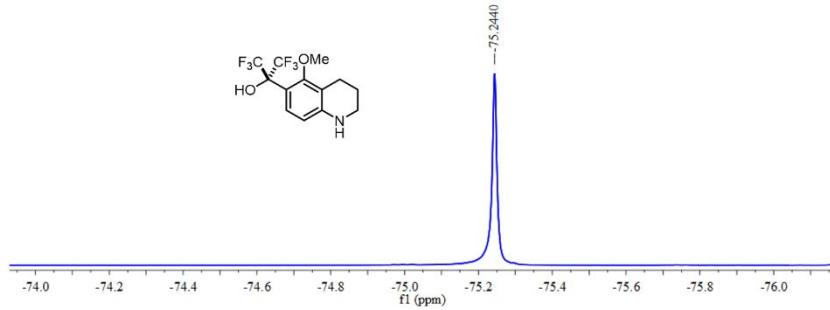
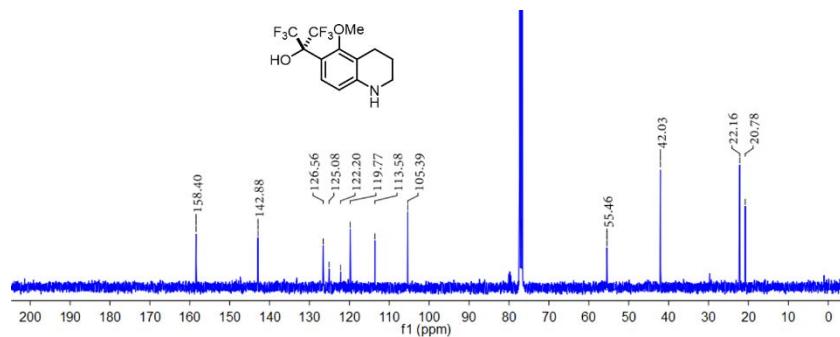
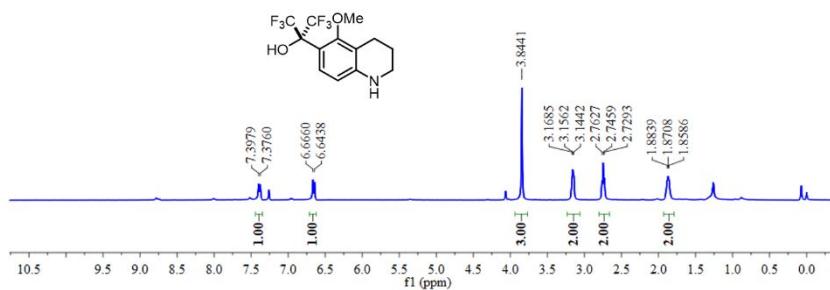
¹H, ¹³C and ¹⁹F NMR Spectra of 3c



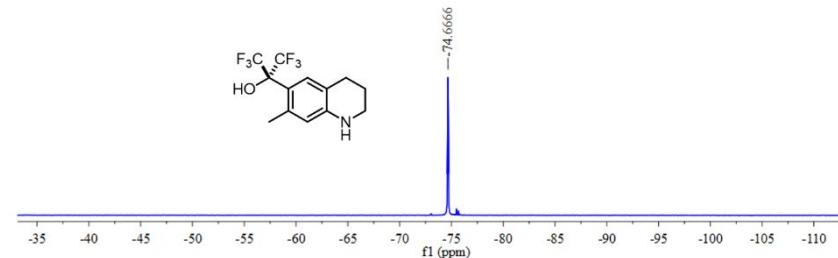
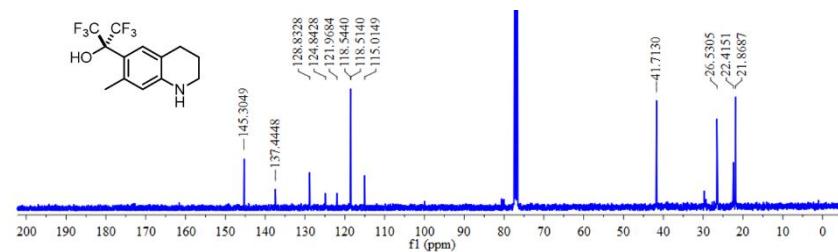
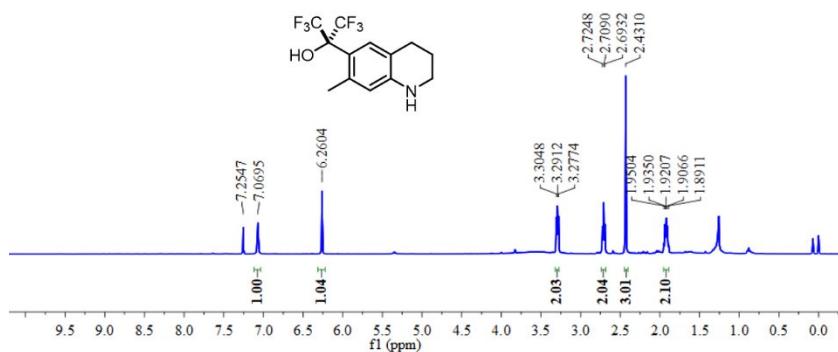
¹H, ¹³C and ¹⁹F NMR Spectra of 3d



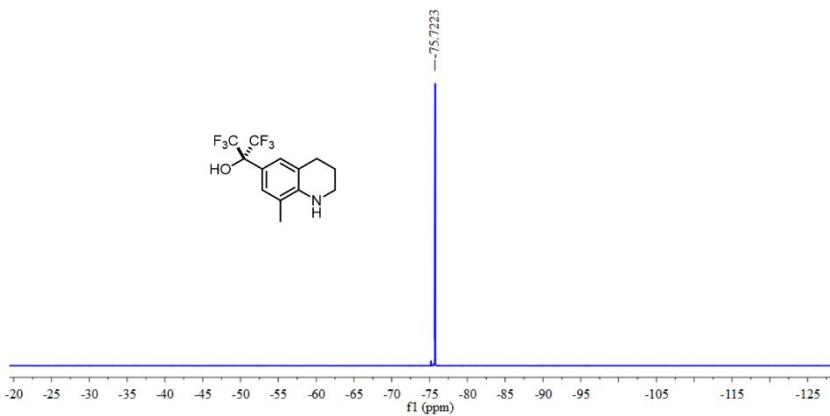
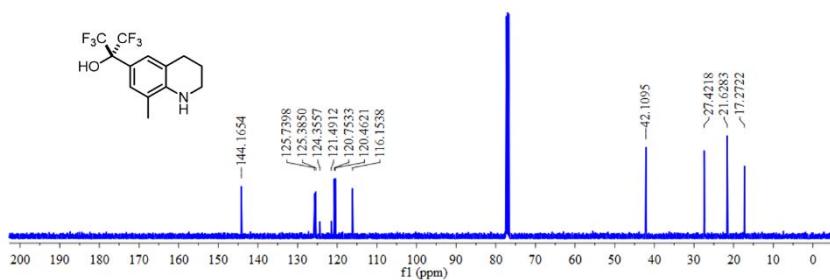
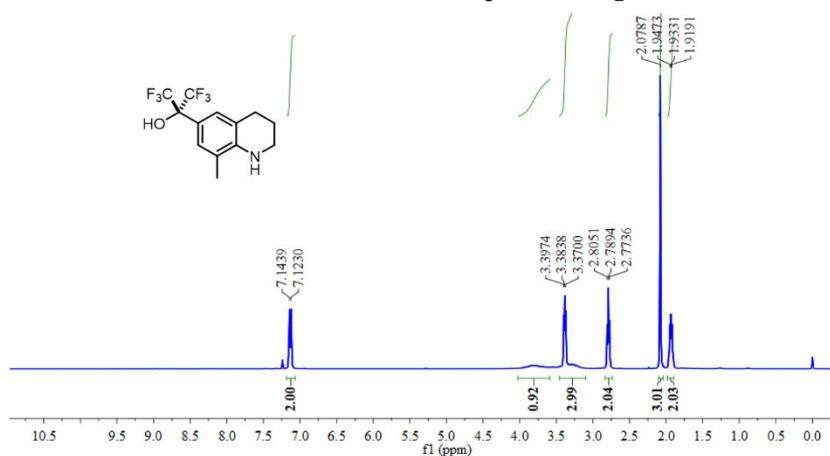
¹H, ¹³C and ¹⁹F NMR Spectra of 3e



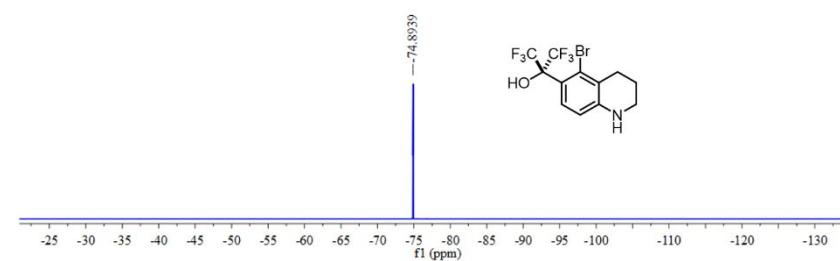
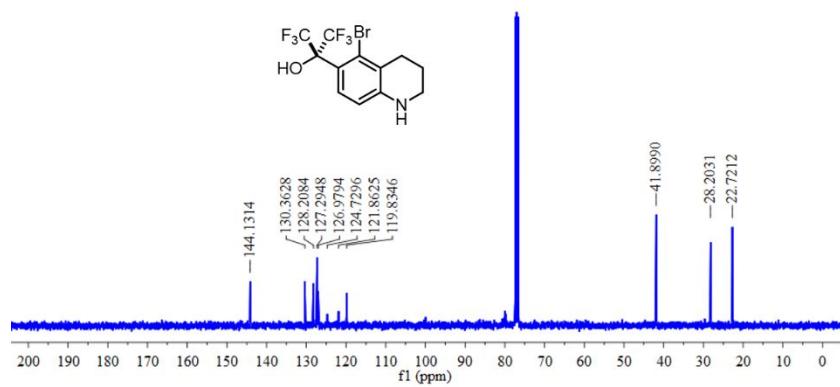
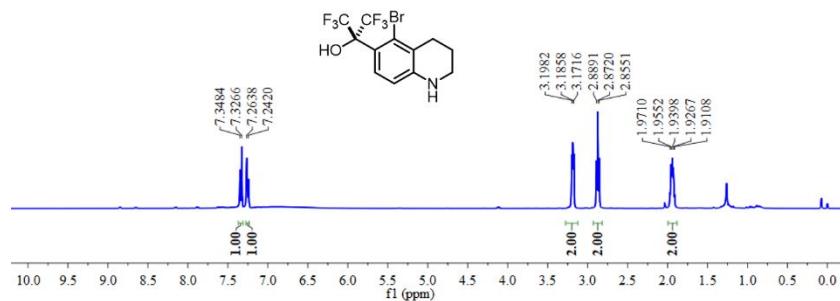
¹H, ¹³C and ¹⁹F NMR Spectra of 3f



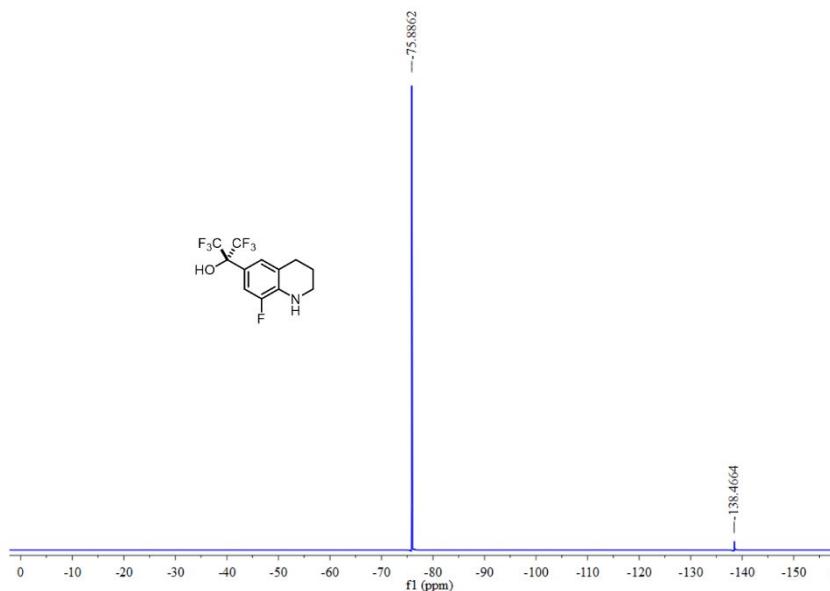
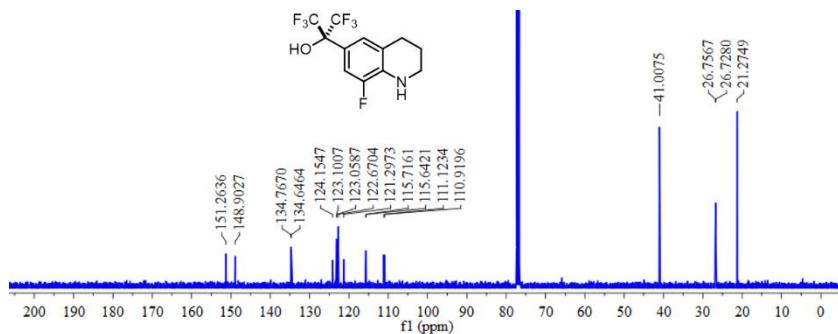
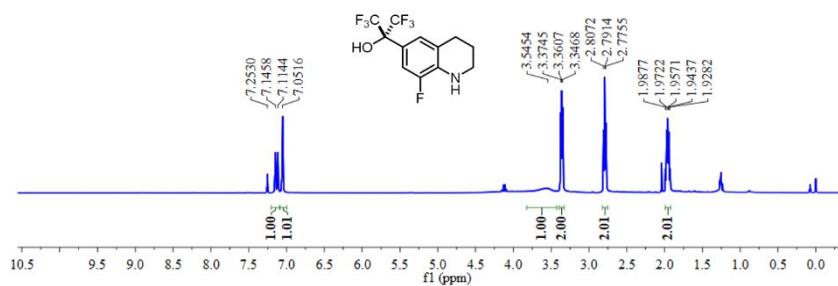
¹H, ¹³C and ¹⁹F NMR Spectra of 3g



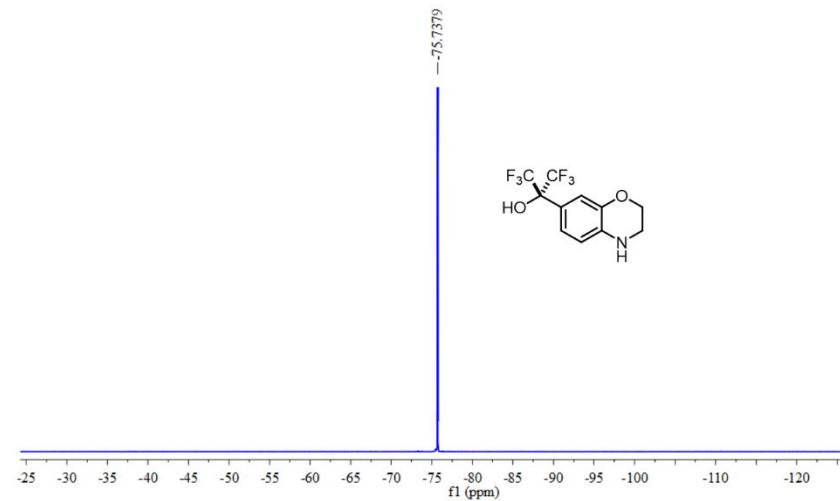
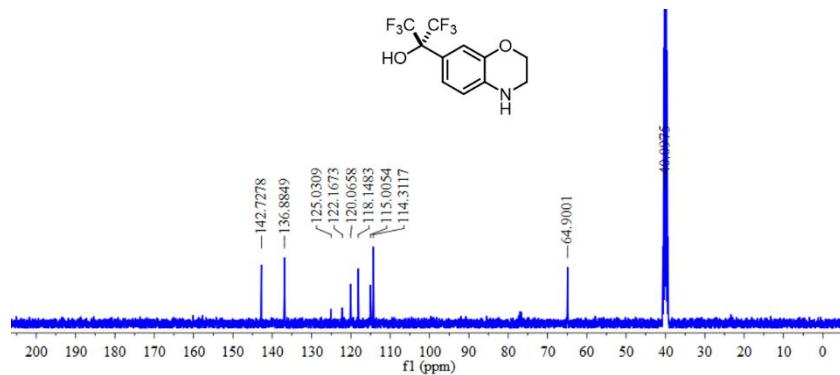
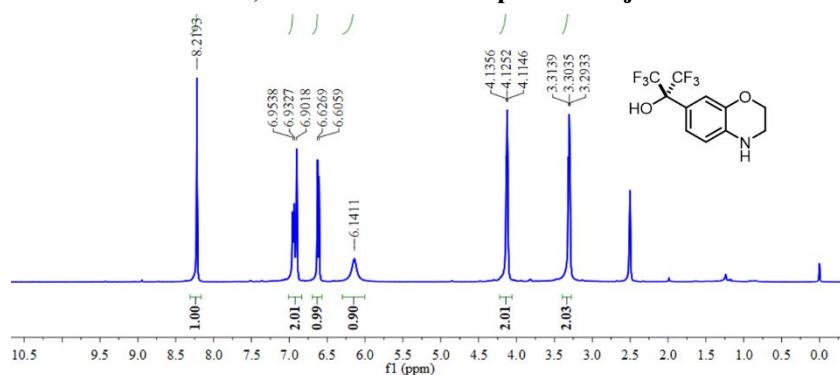
¹H, ¹³C and ¹⁹F NMR Spectra of 3h



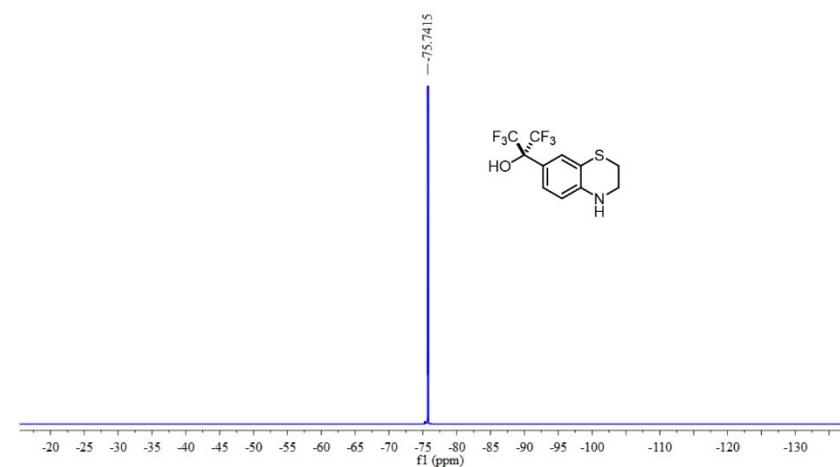
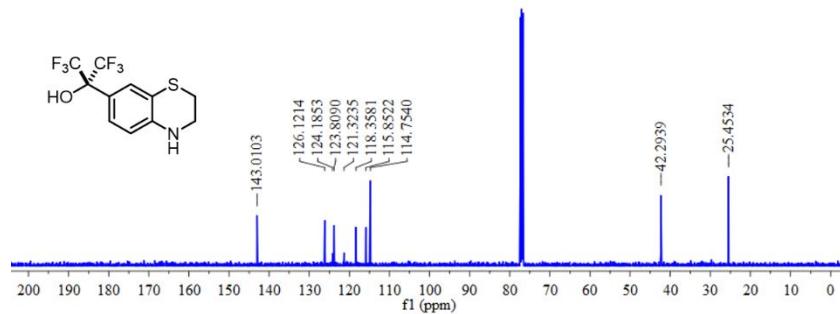
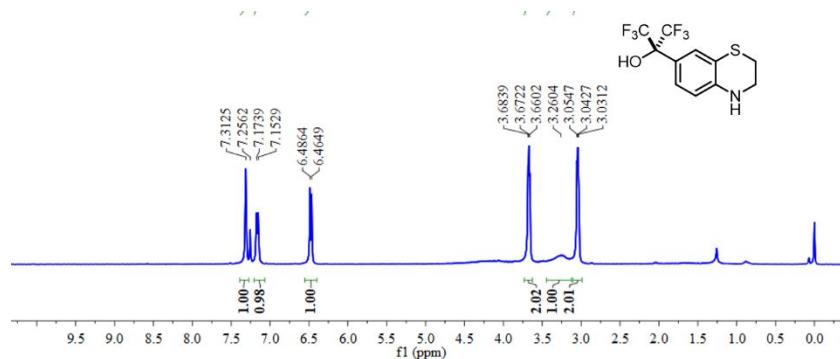
¹H, ¹³C and ¹⁹F NMR Spectra of 3i



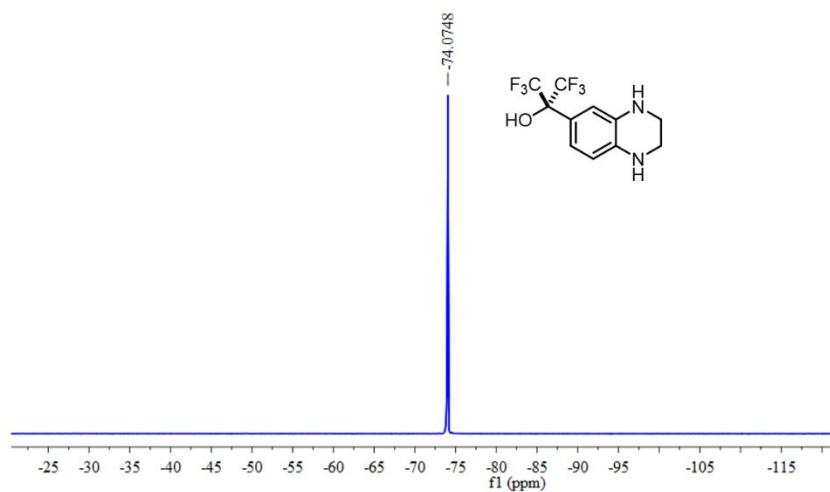
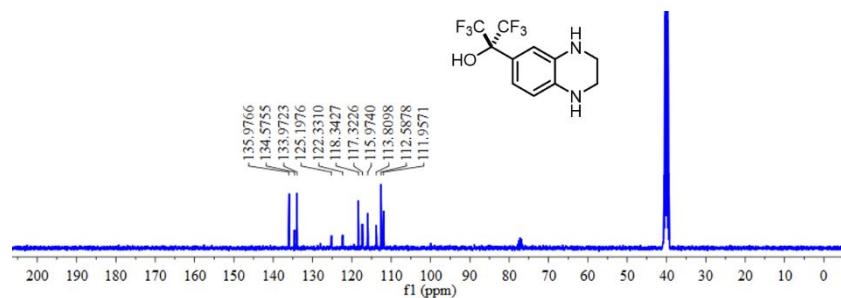
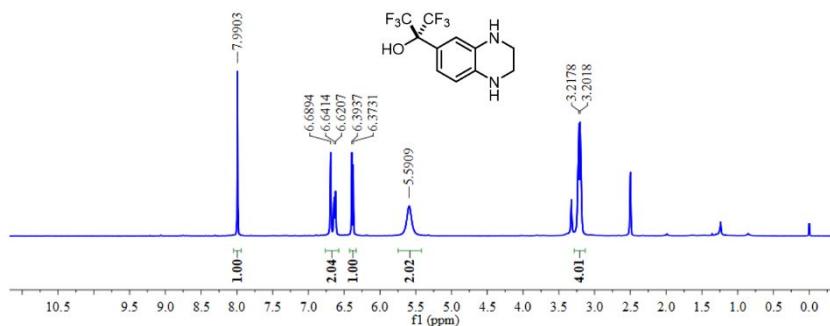
¹H, ¹³C and ¹⁹F NMR Spectra of 3j



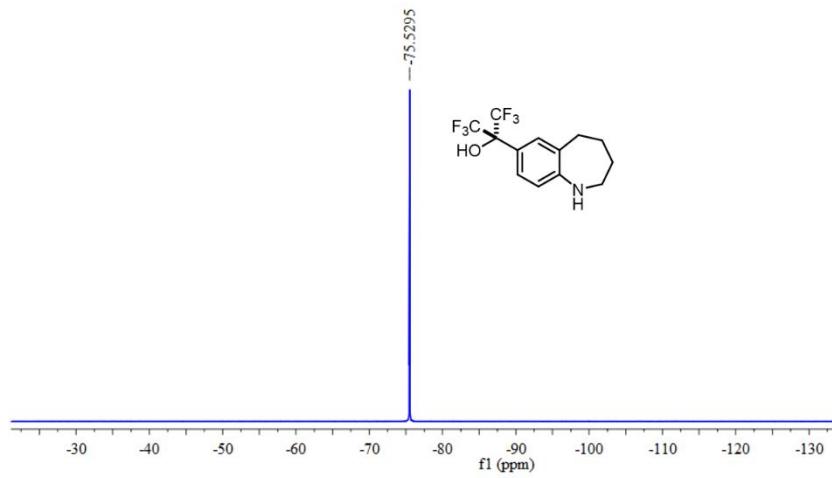
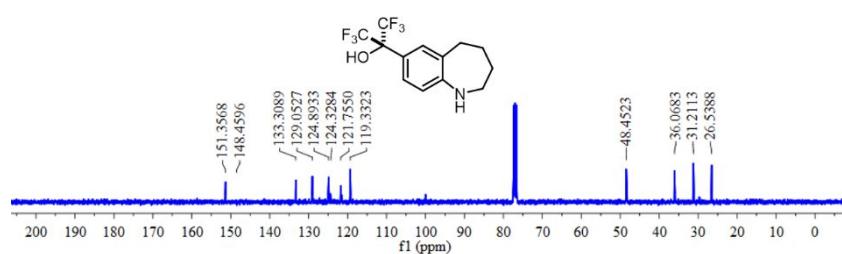
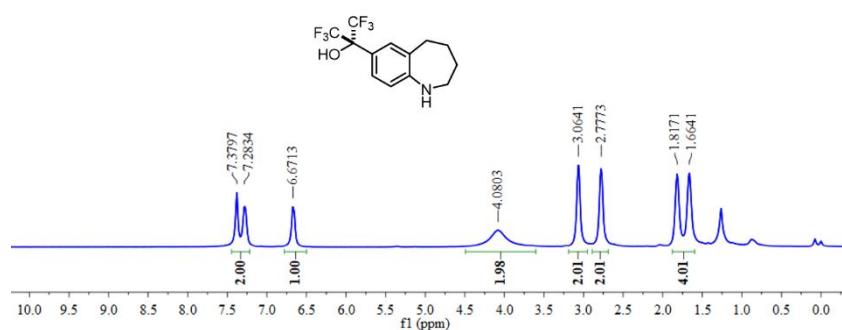
¹H, ¹³C and ¹⁹F NMR Spectra of 3k



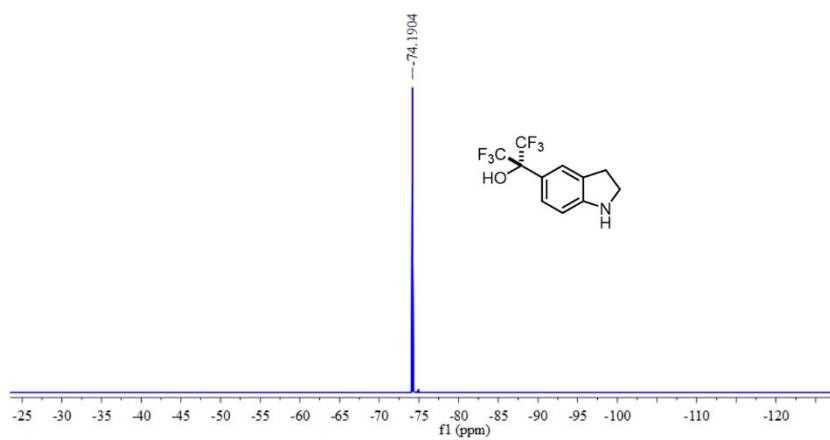
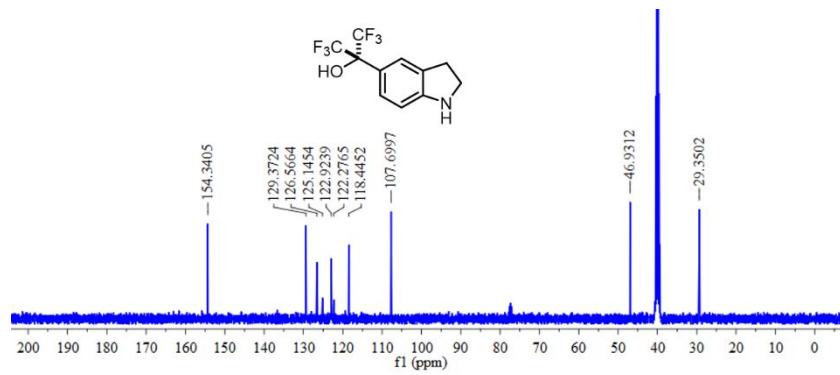
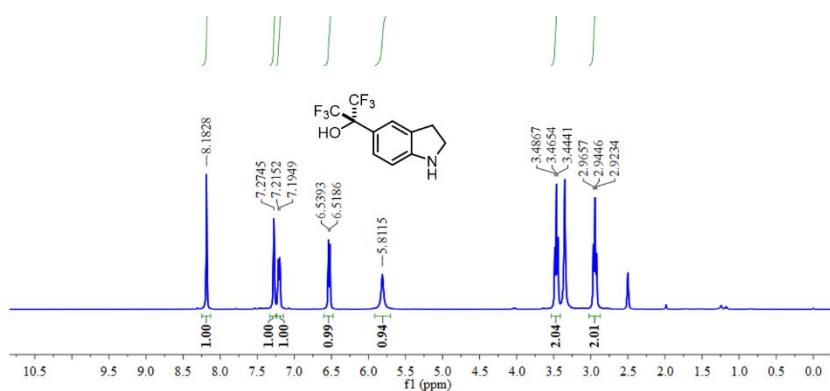
¹H, ¹³C and ¹⁹F NMR Spectra of 3l



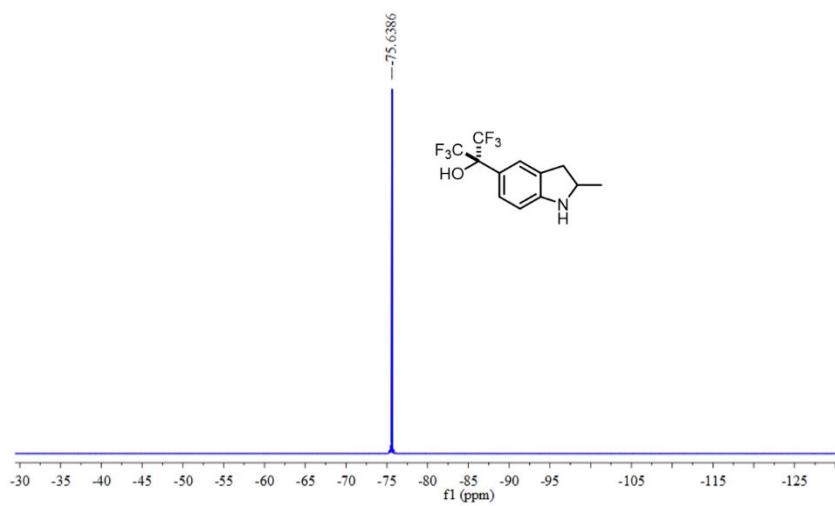
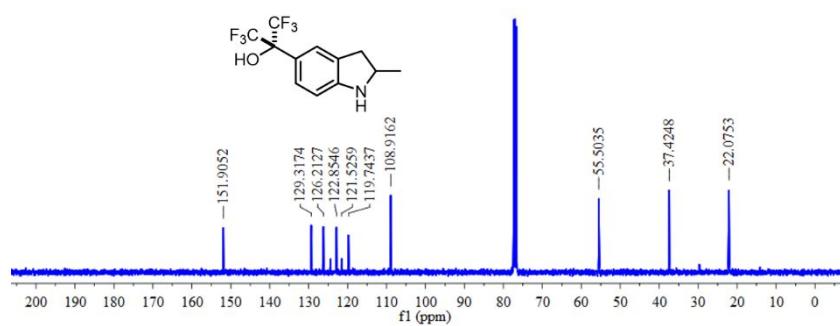
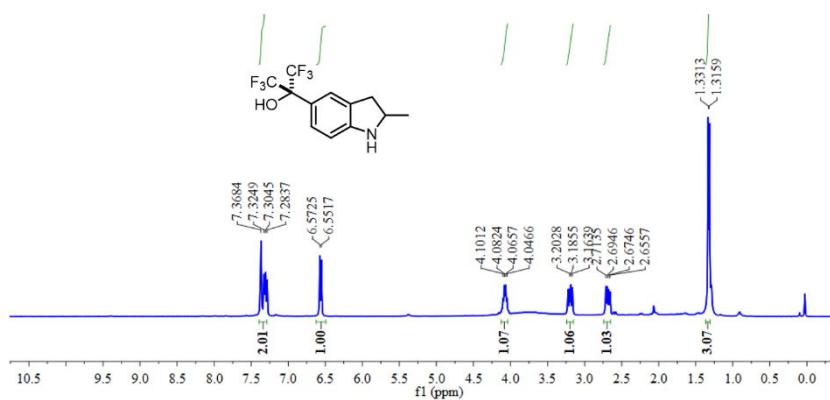
¹H, ¹³C and ¹⁹F NMR Spectra of 3m



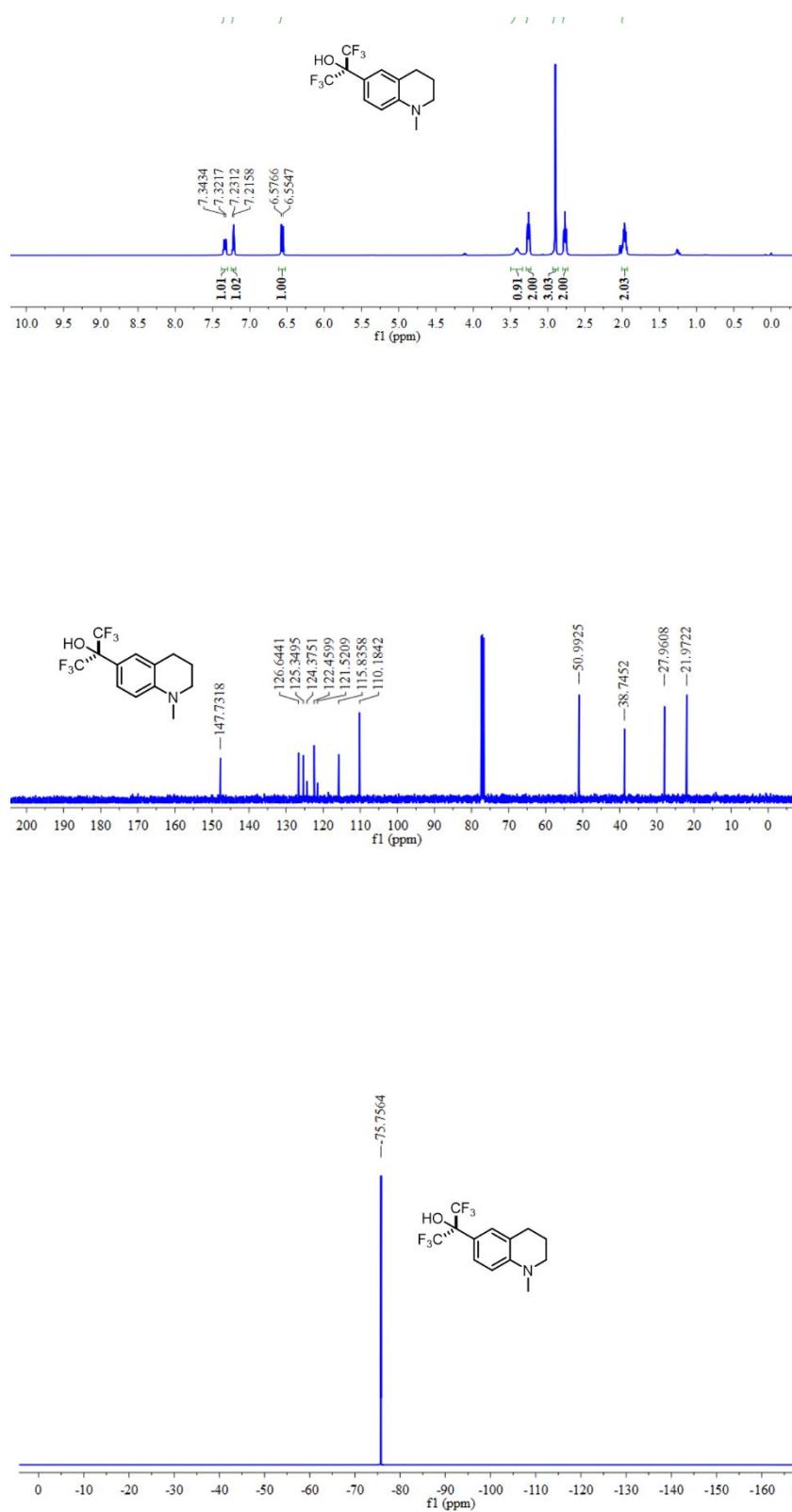
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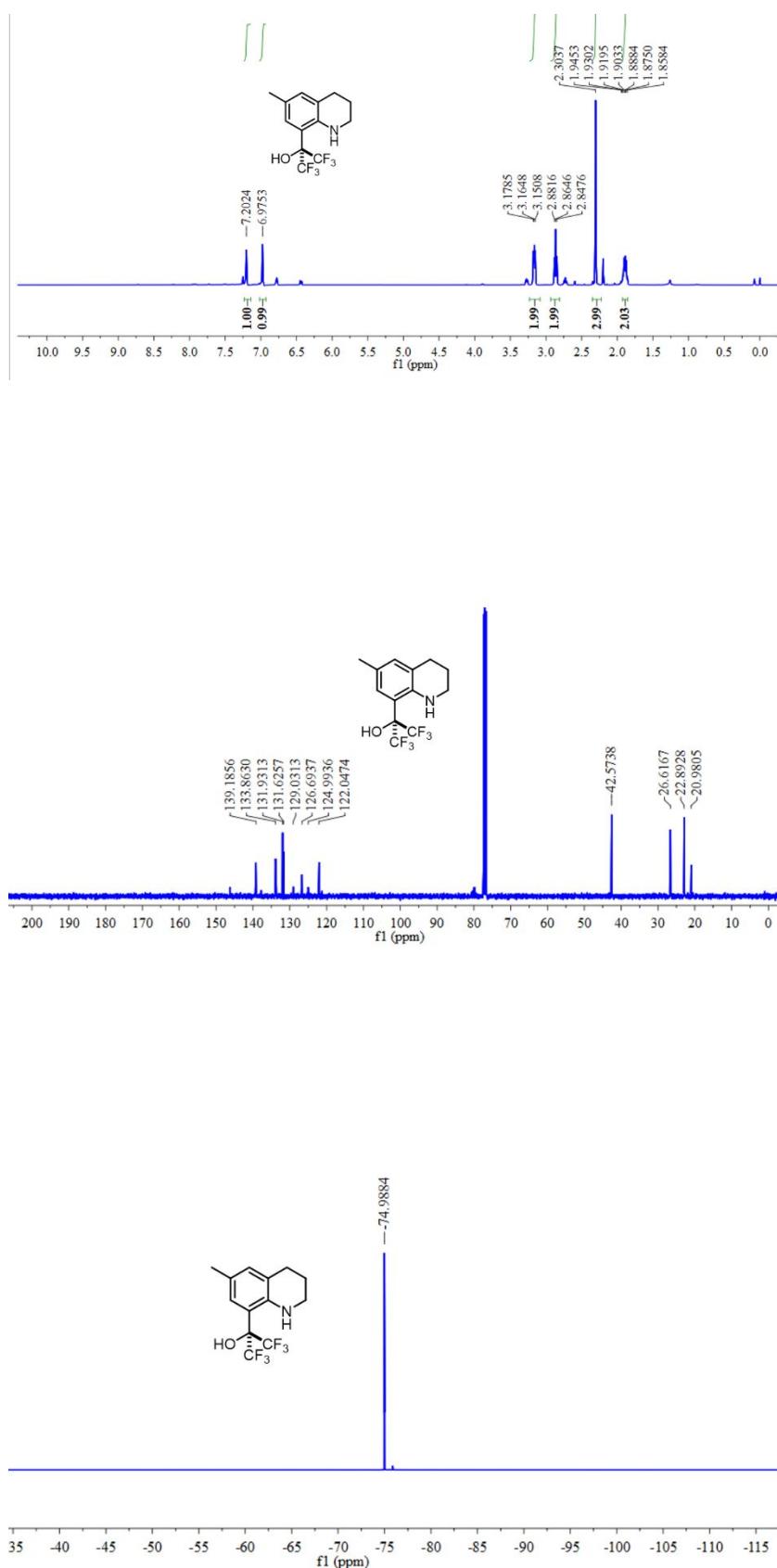
¹H, ¹³C and ¹⁹F NMR Spectra of 3o



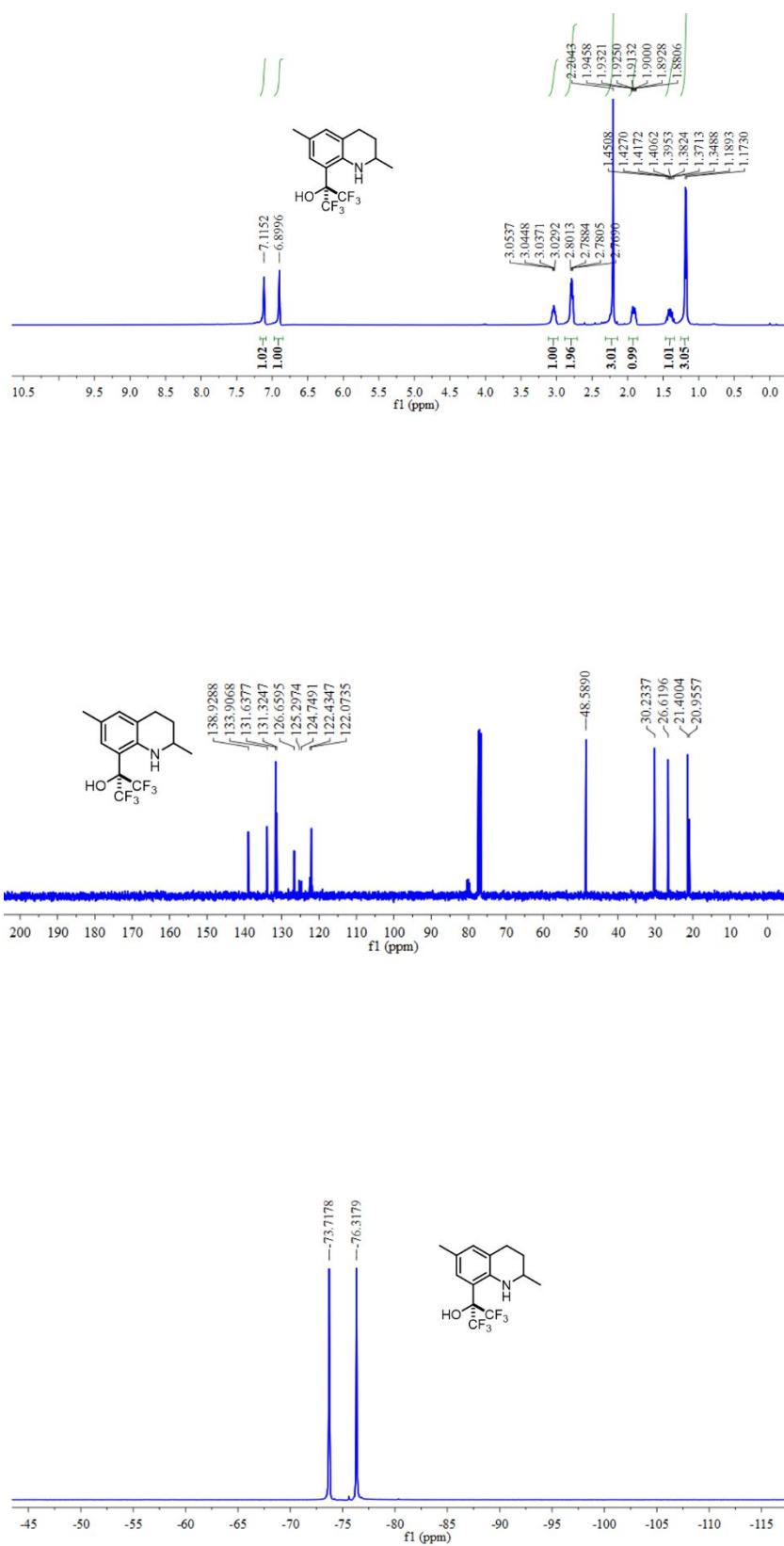
¹H, ¹³C and ¹⁹F NMR Spectra of 3p



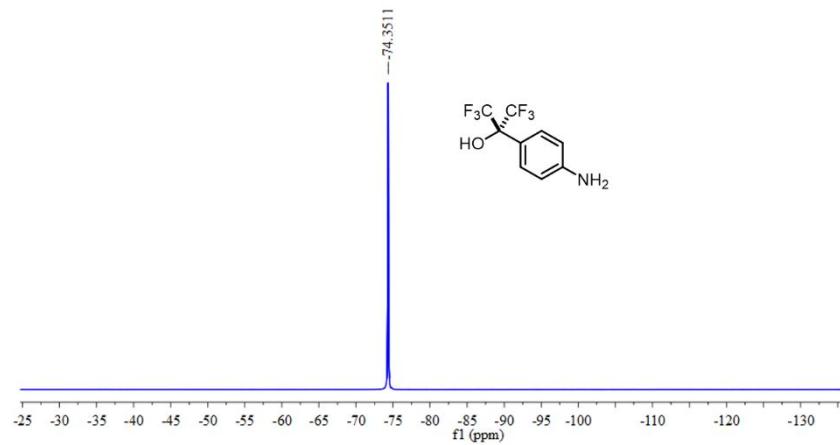
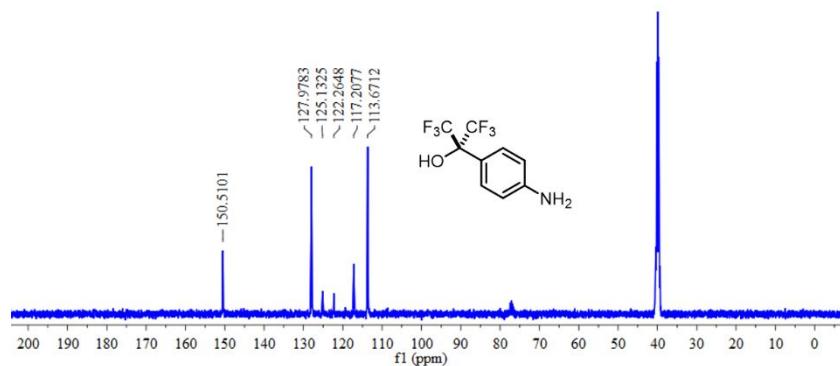
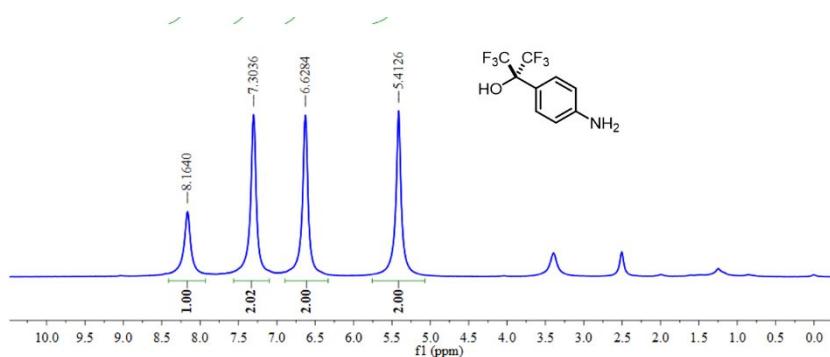
¹H, ¹³C and ¹⁹F NMR Spectra of 3q



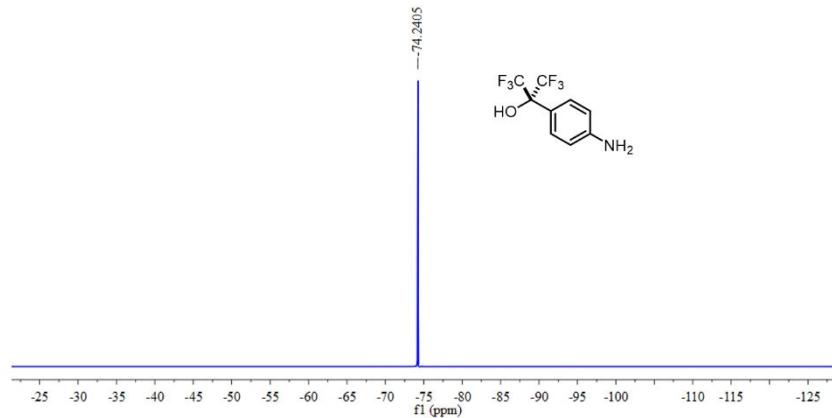
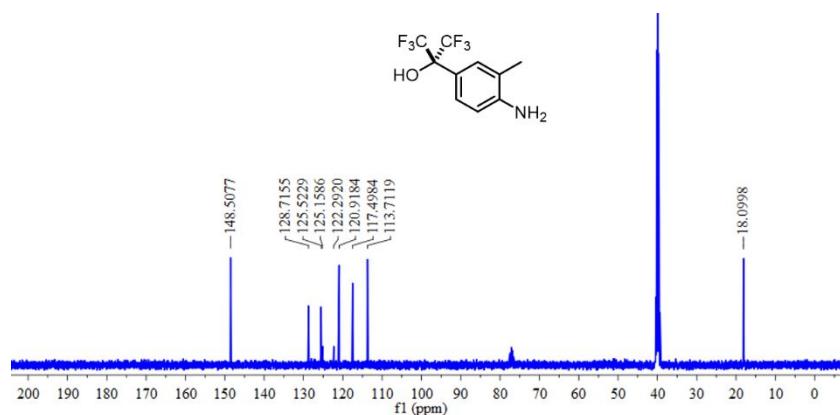
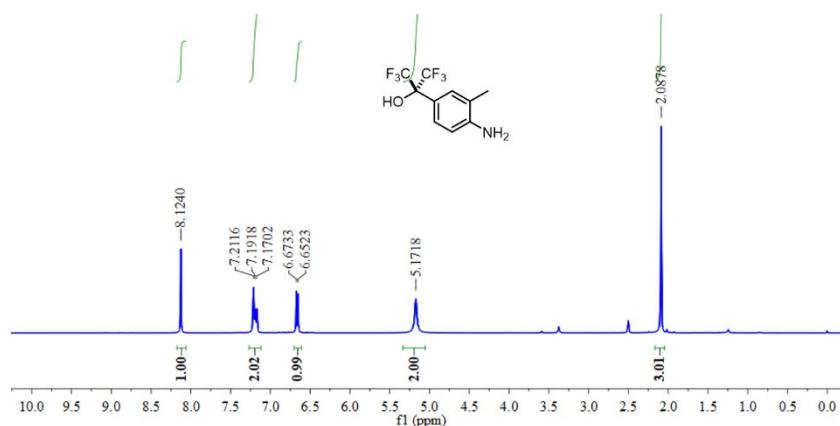
¹H, ¹³C and ¹⁹F NMR Spectra of 3r



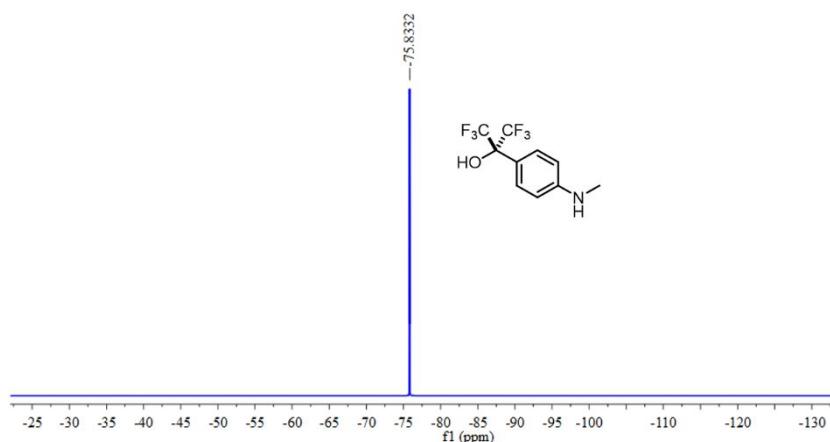
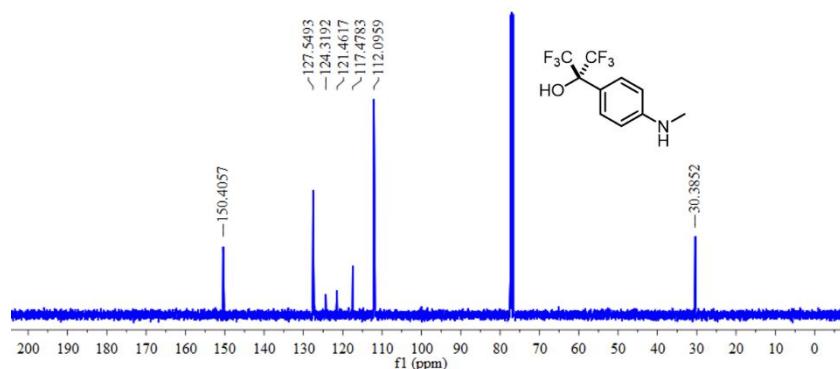
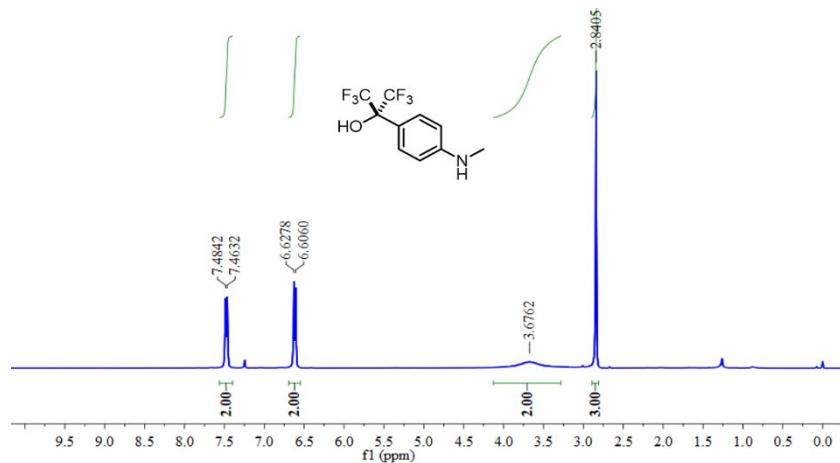
¹H, ¹³C and ¹⁹F NMR Spectra of 5a



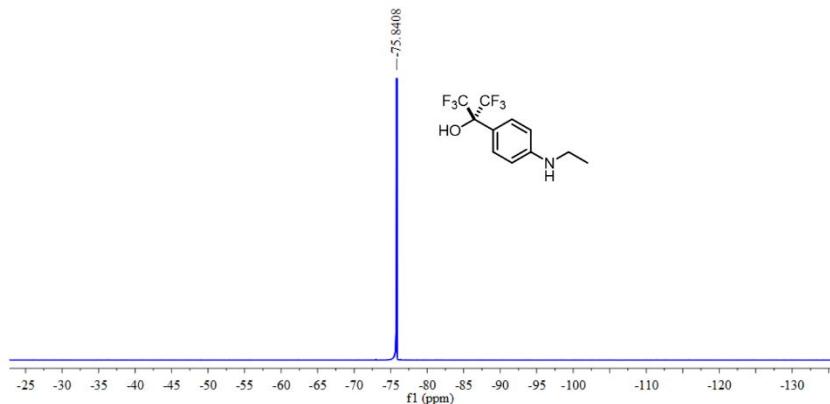
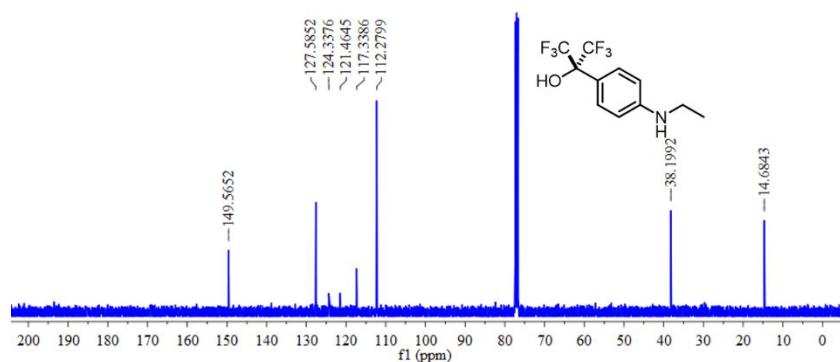
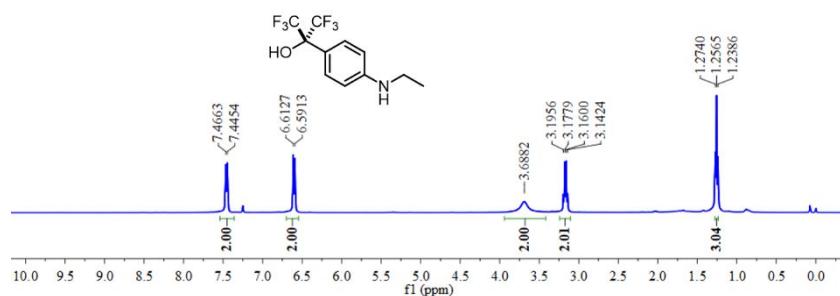
¹H, ¹³C and ¹⁹F NMR Spectra of 5b



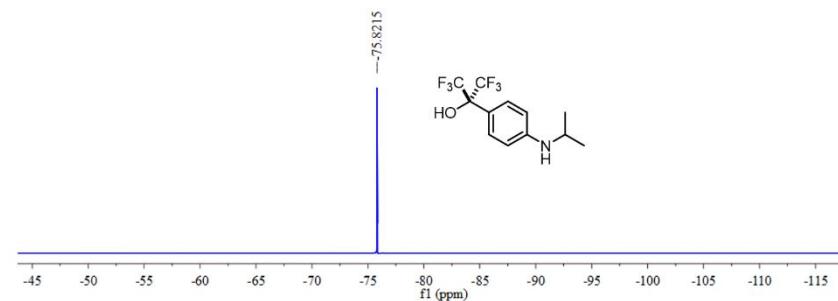
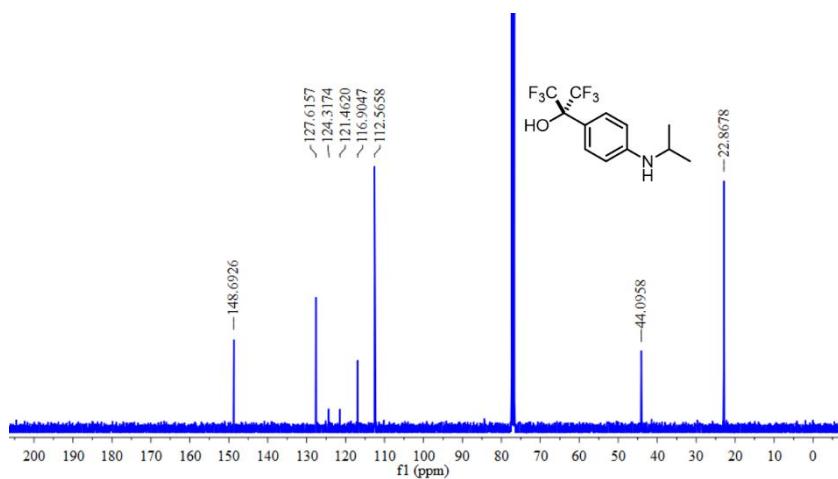
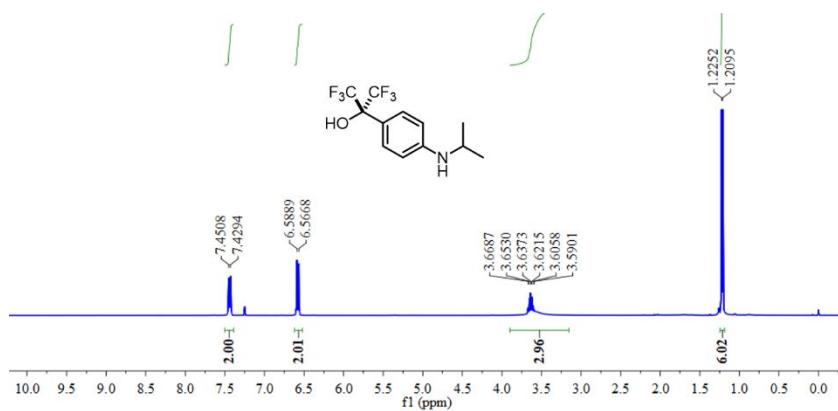
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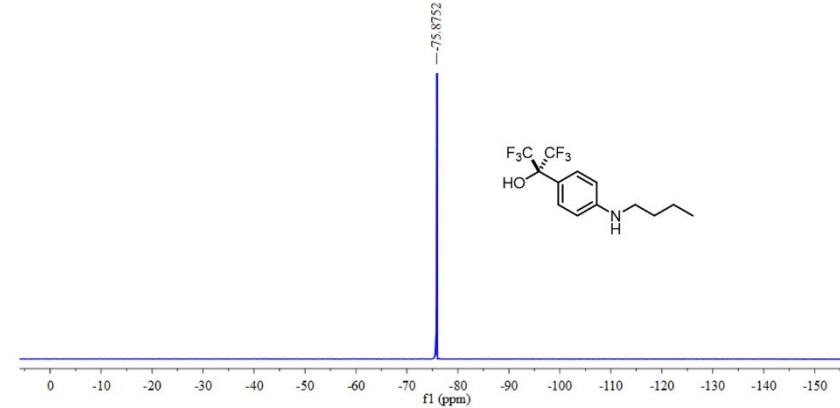
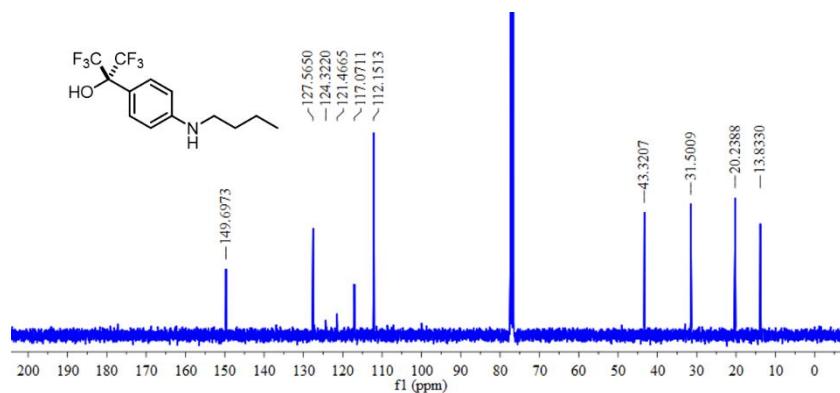
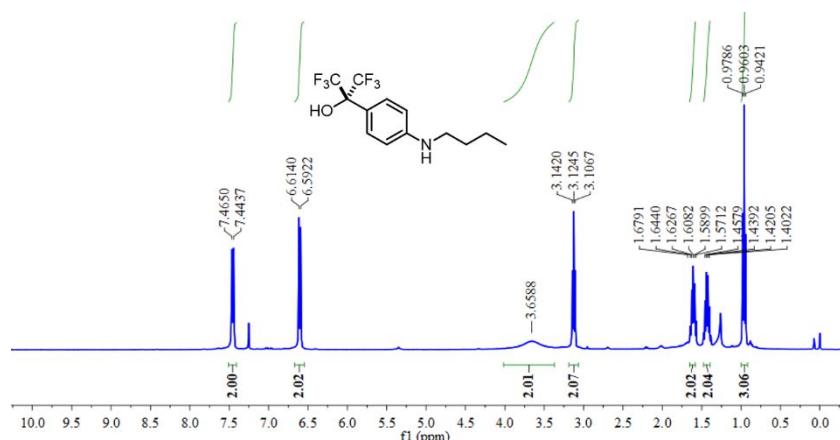
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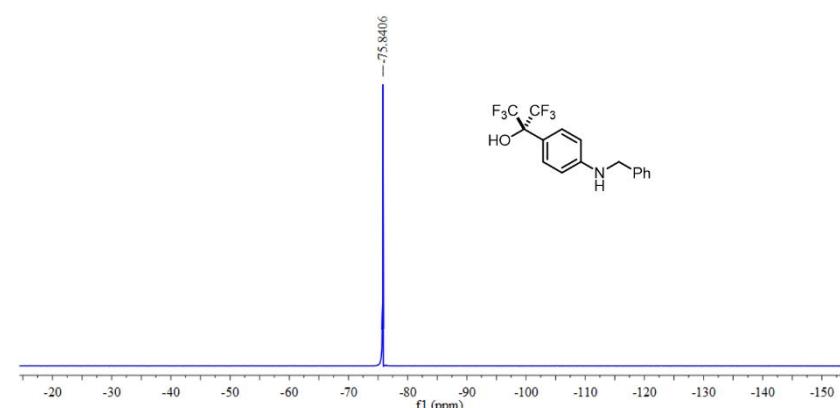
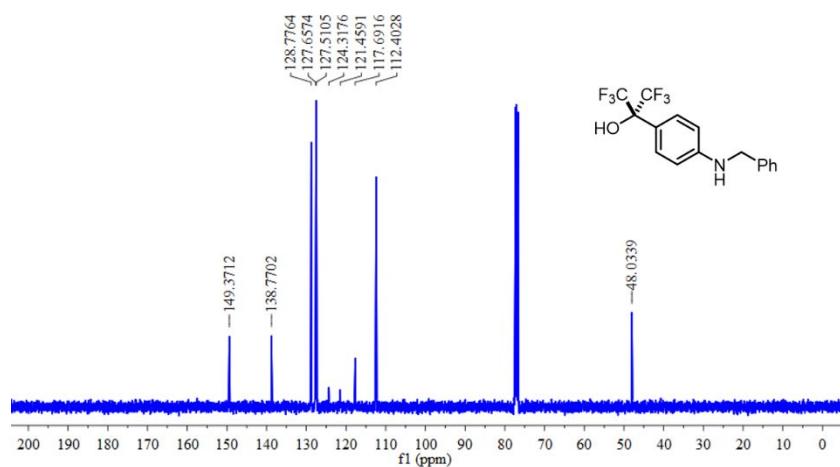
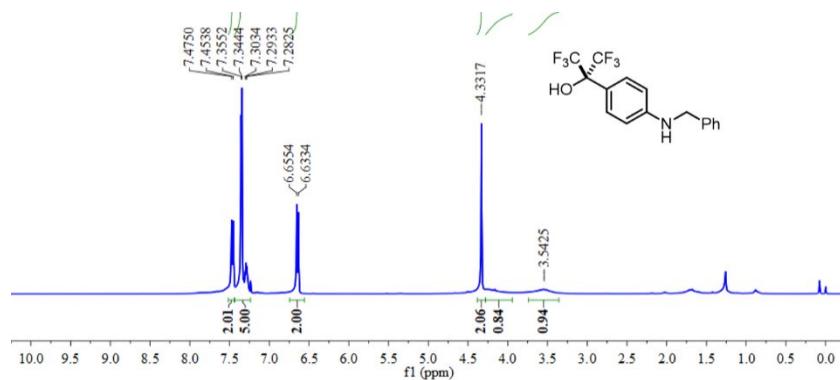
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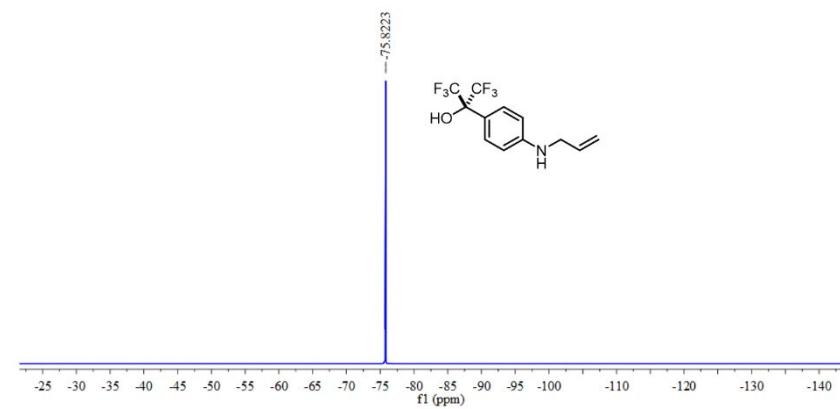
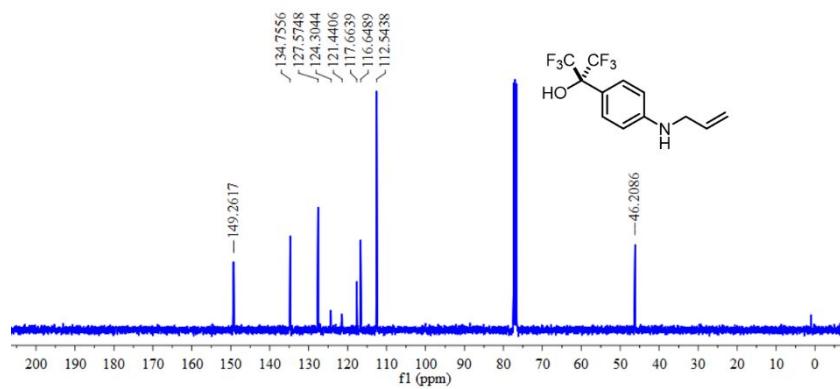
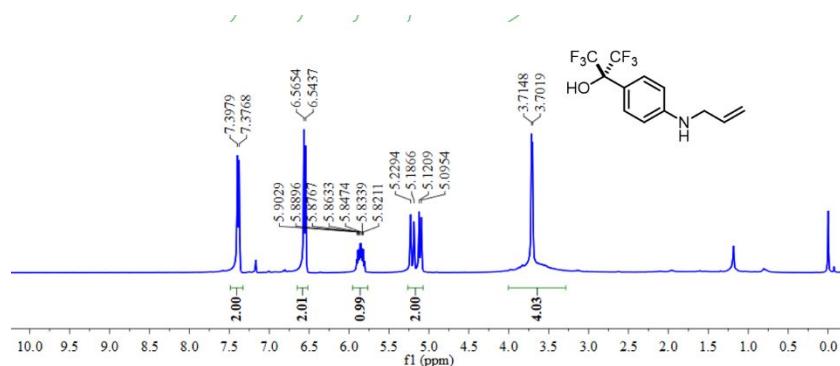
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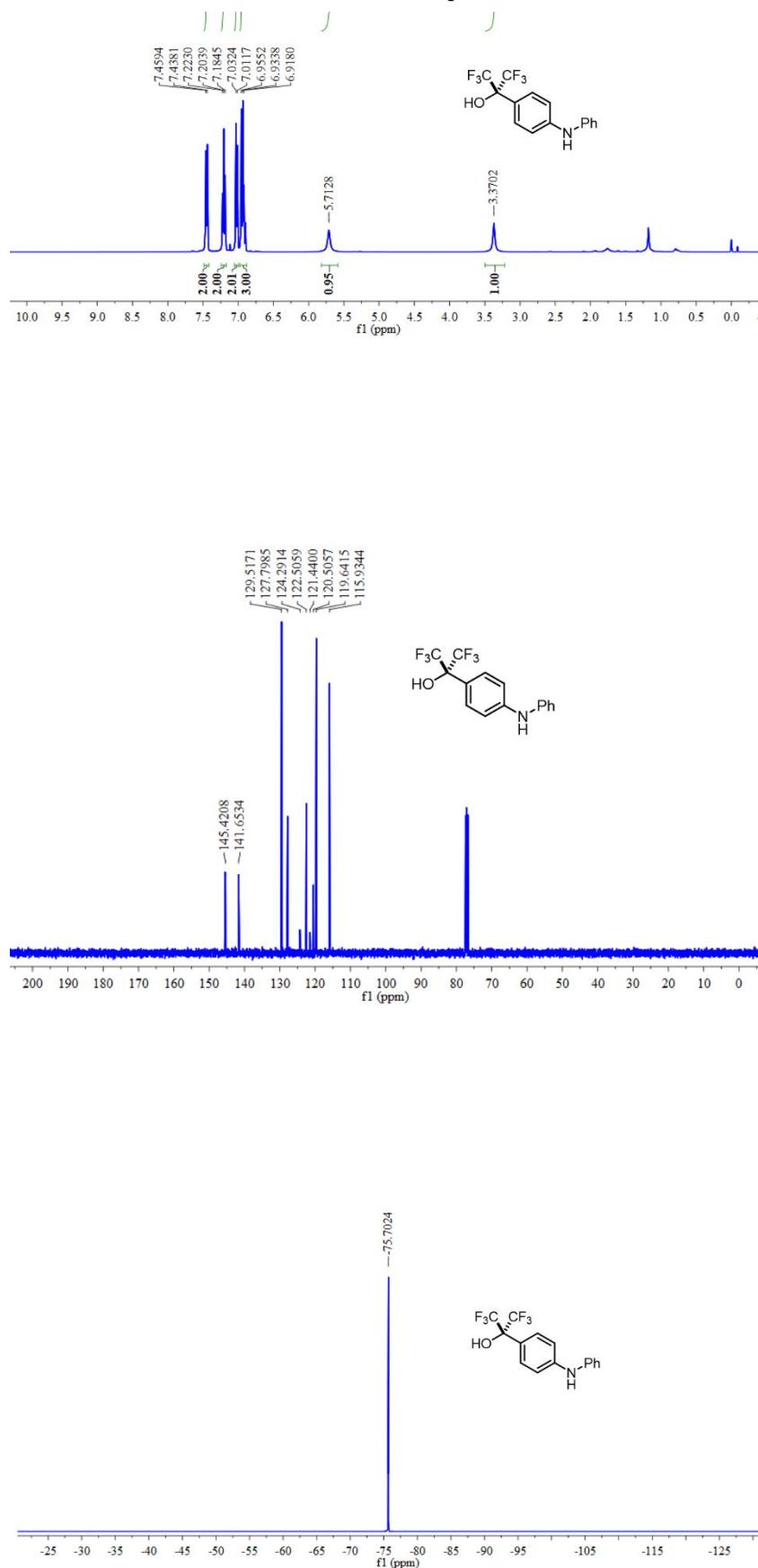
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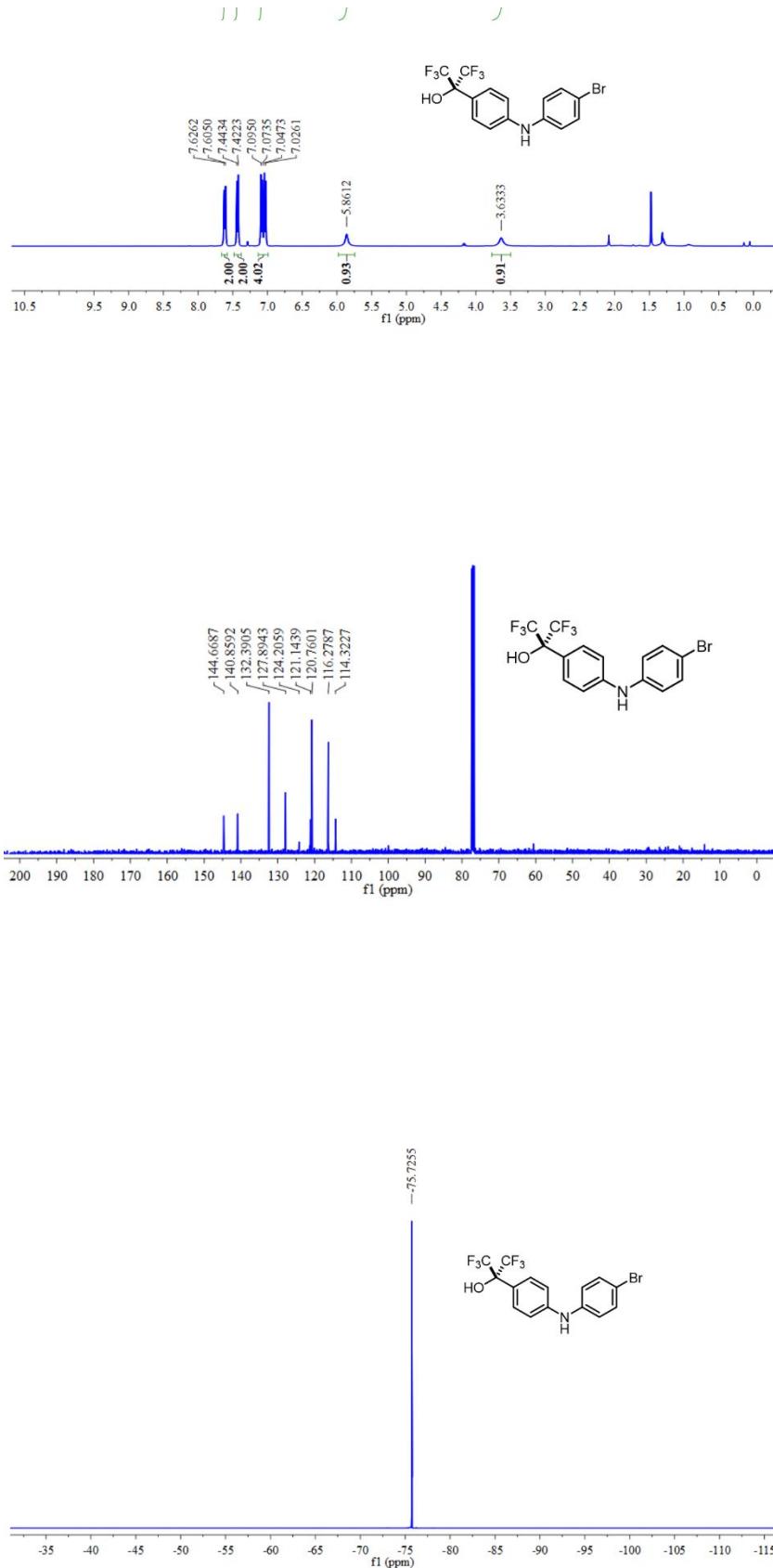
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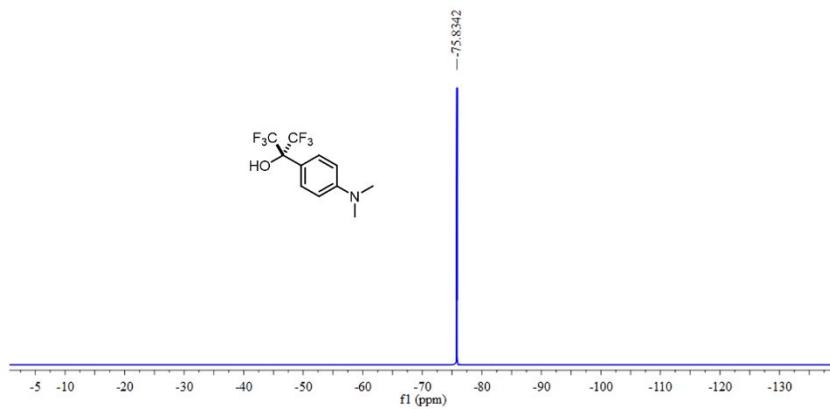
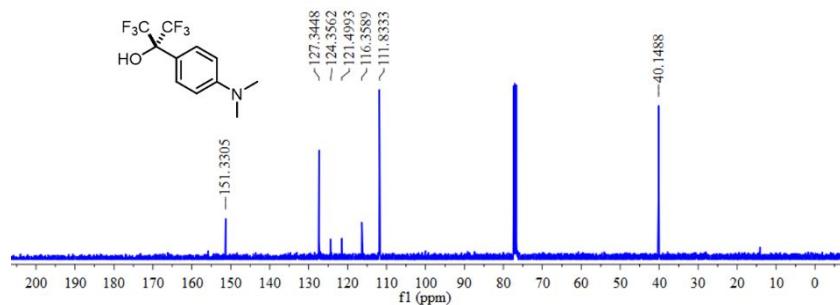
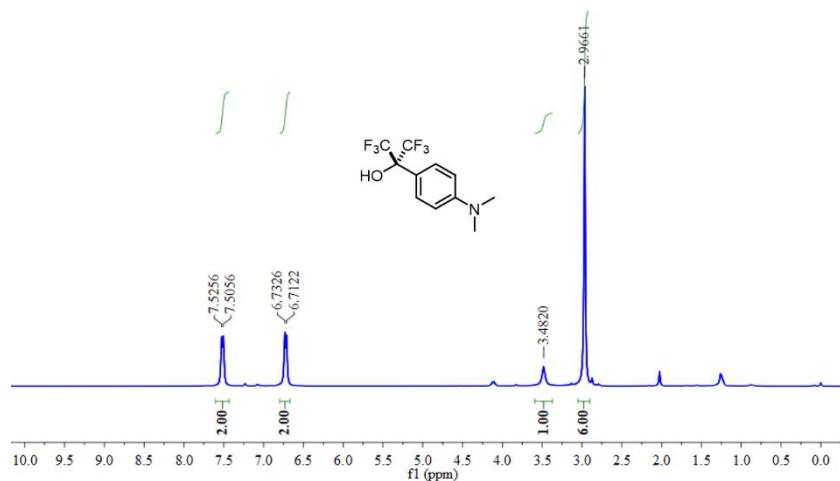
¹H, ¹³C and ¹⁹F NMR Spectra of 5i



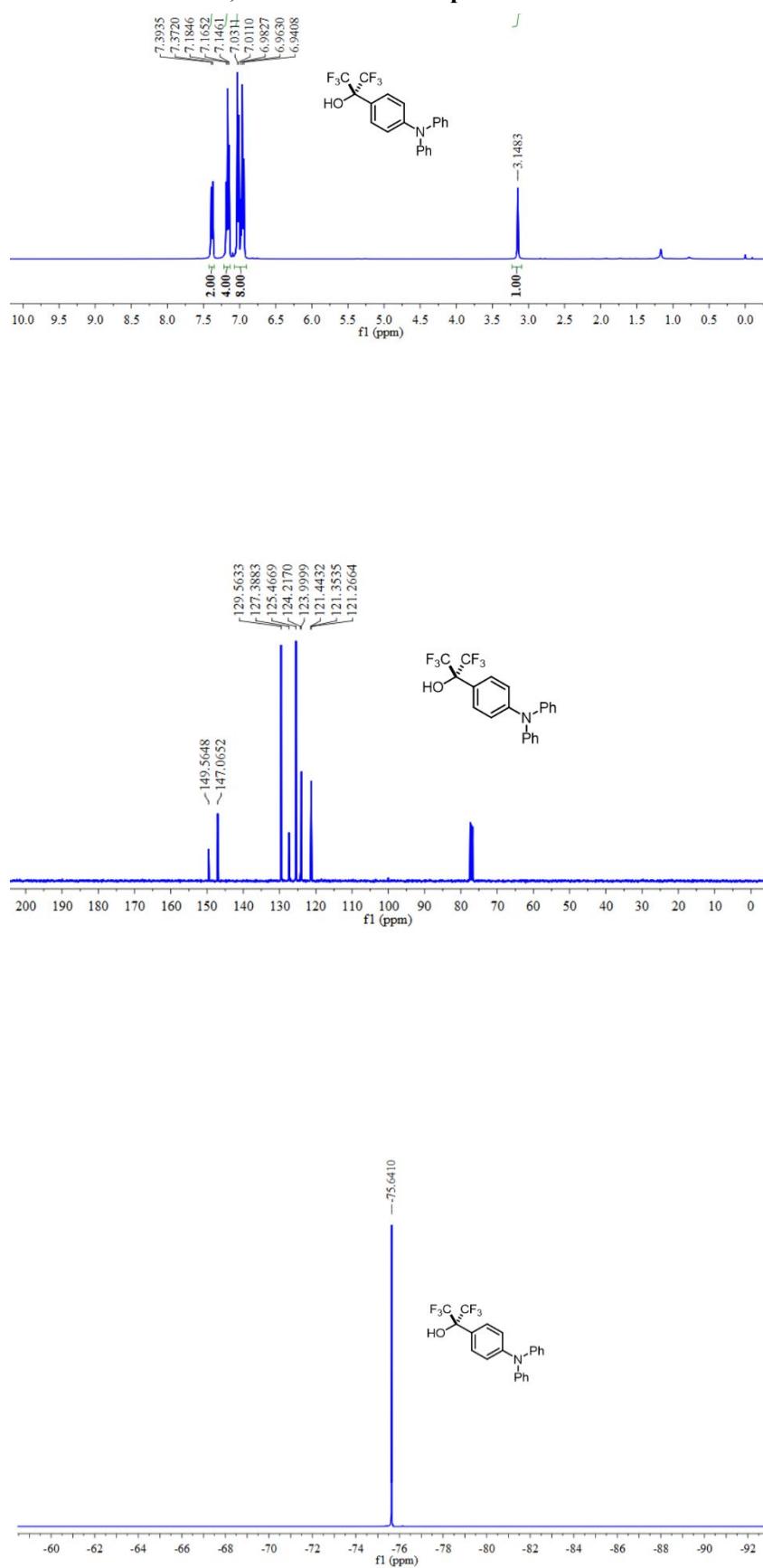
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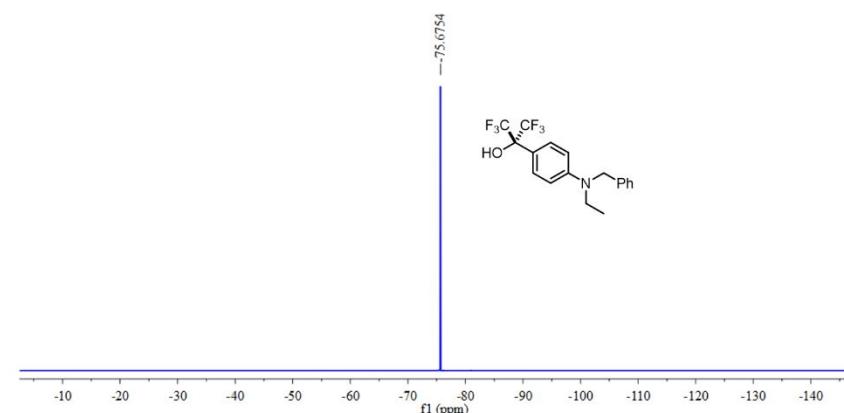
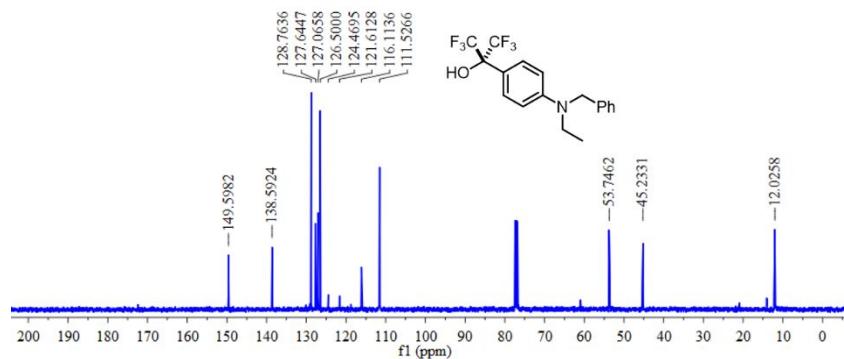
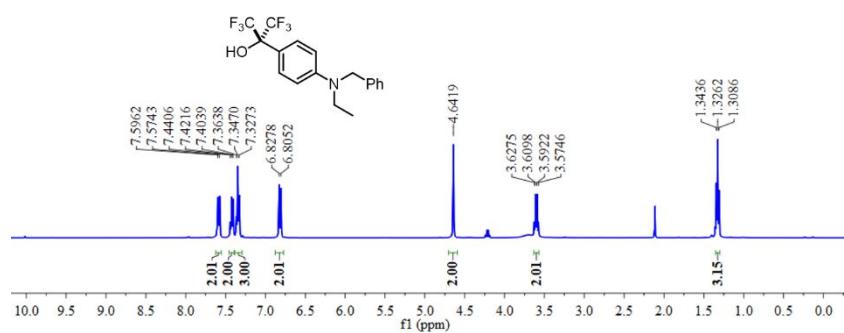
¹H, ¹³C and ¹⁹F NMR Spectra of 5k



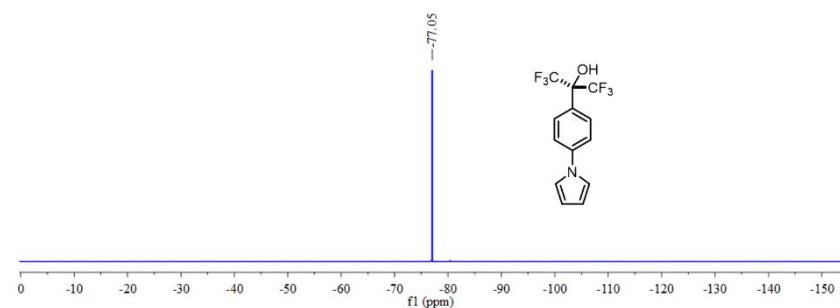
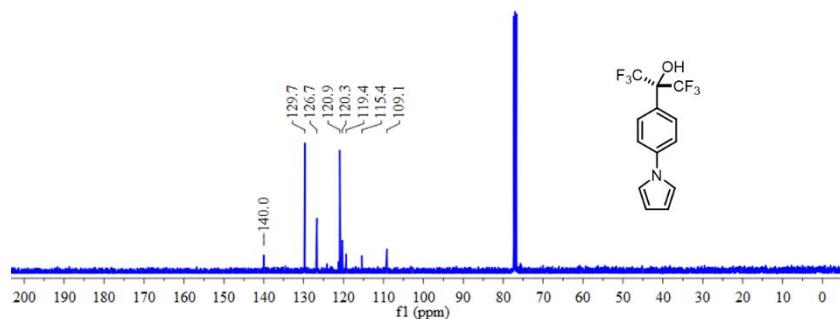
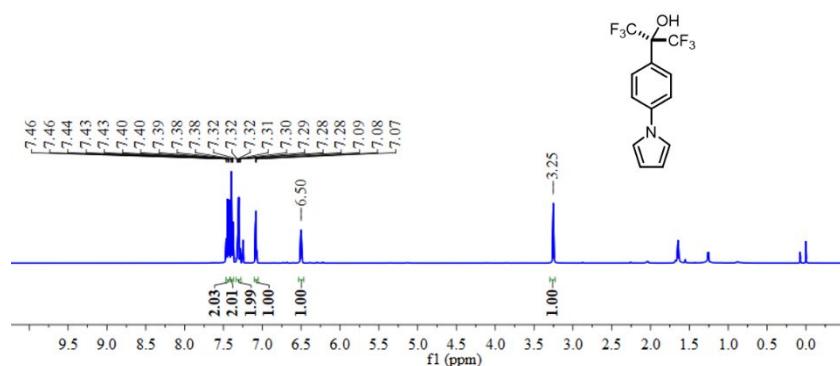
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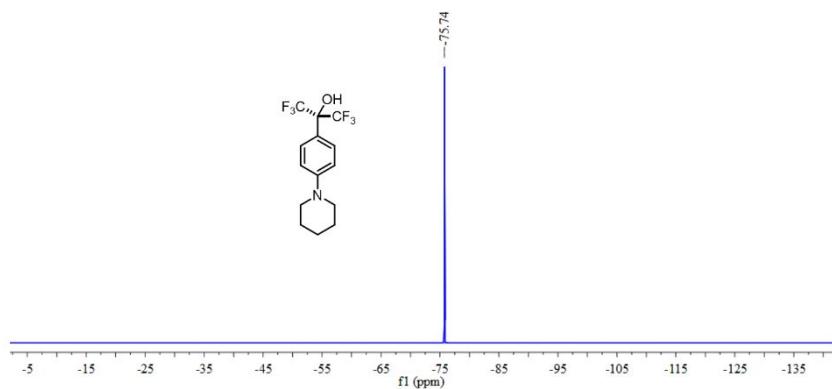
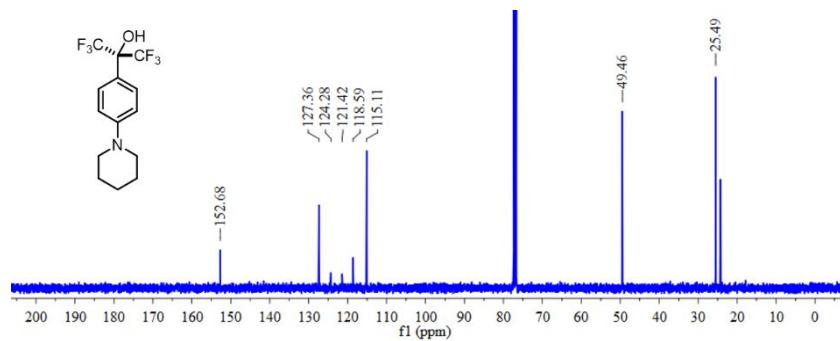
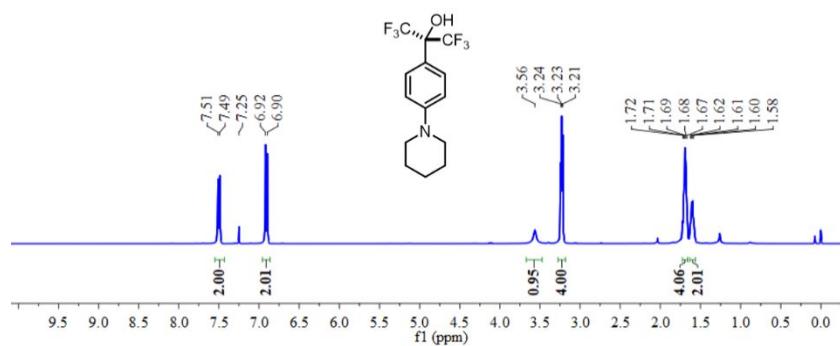
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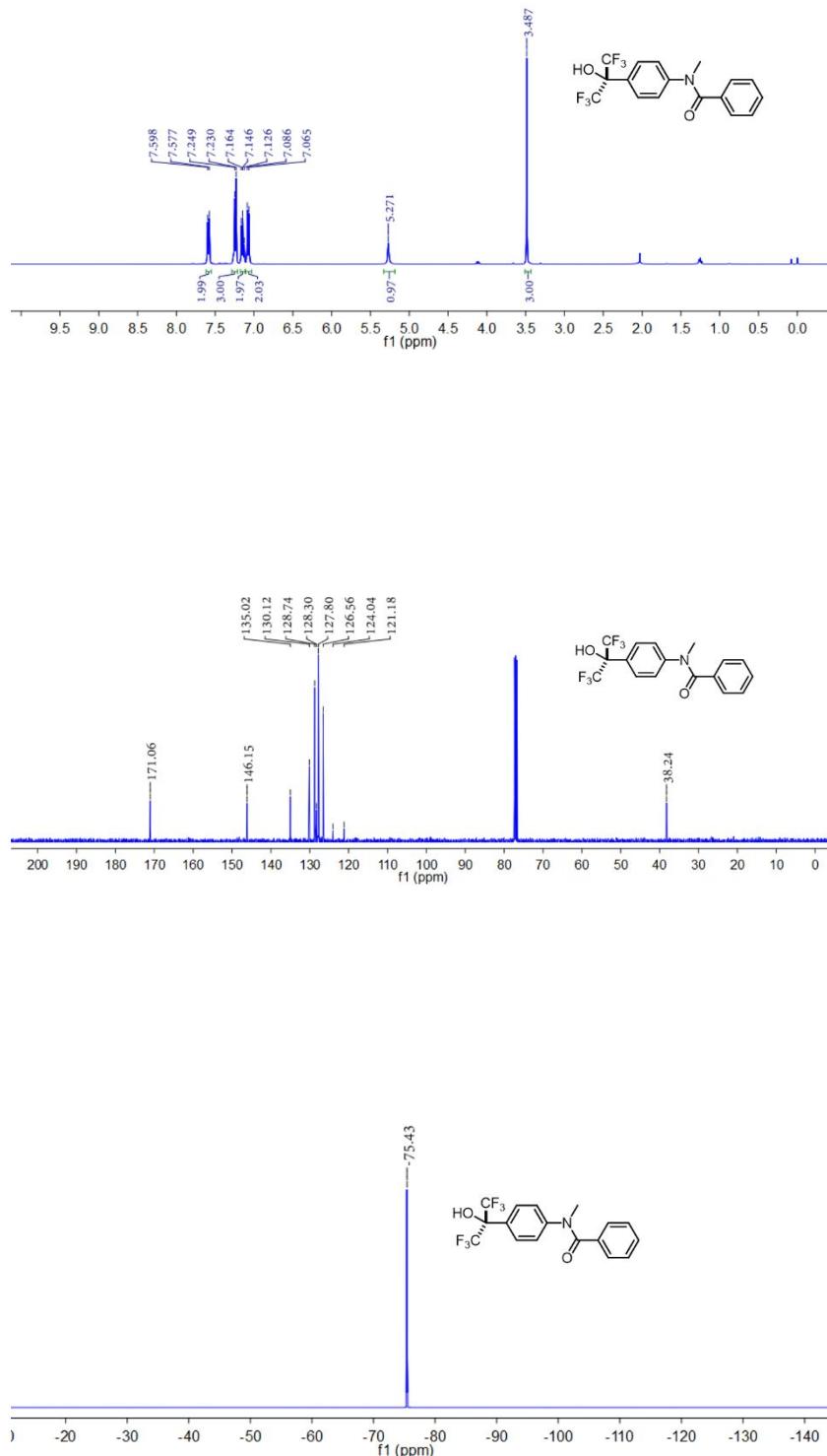
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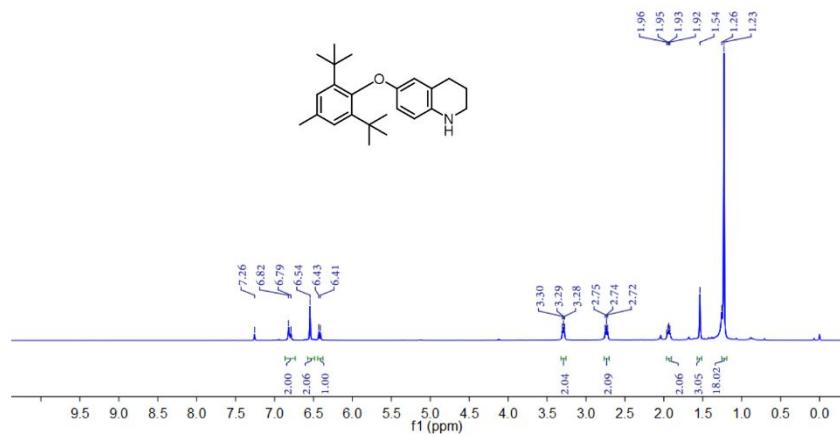
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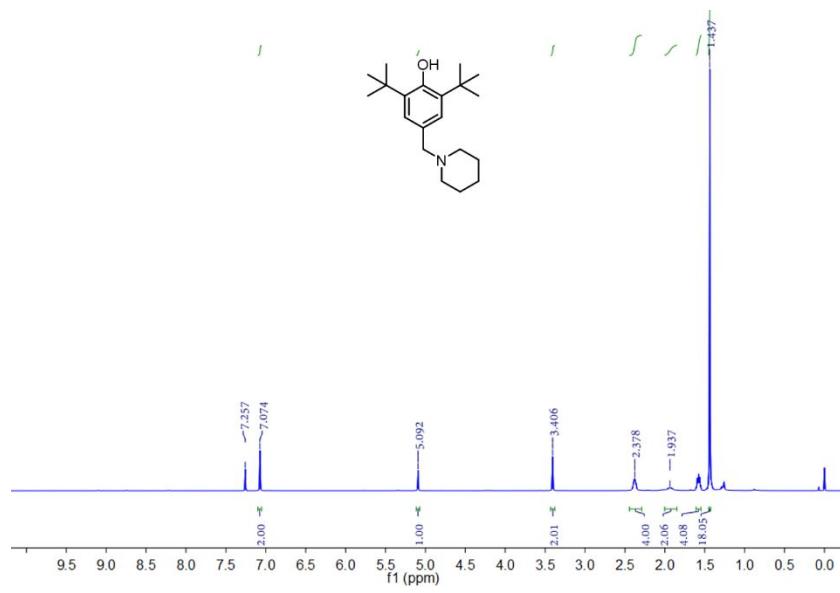
¹H, ¹³C and ¹⁹F NMR Spectra of 6c



¹H NMR Spectra of 3s



¹H NMR Spectra of 3t



¹H, ¹³C and ¹⁹F NMR Spectra of 3u

