Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information for

Inverse-Electron-Demand [4+2] Cycloaddition of Photogenerated Aza-*ortho*-Quinone Methides with 1,3,5-Triazinanes: Access to Perfluoroalkylated Tetrahydroquinazolines

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1. General Information

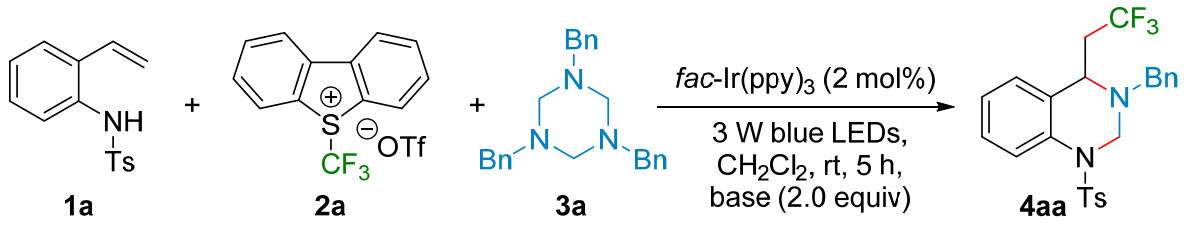
Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. All the solvents were treated according to standard methods. Flash column chromatography was performed using 200-300 mesh silica gel. **^{1}H NMR** spectra were recorded on 400 spectrophotometers. Chemical shifts (δ (ppm)) are reported in ppm from the resonance of tetramethyl silane as the internal standard (TMS: 0.00 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, dd = doublet of doublets, m = multiplet), coupling constants (Hz) and integration. **^{13}C NMR** spectra were recorded on 100 MHz with complete proton decoupling spectrophotometers ($CDCl_3$: 77.0 ppm). **^{19}F NMR** spectra were recorded on 376 MHz with complete proton decoupling spectrophotometers. The high resolution mass spectra (HRMS) were measured on Bruker micrOTOF-II mass spectrometer by ESI. IR spectra were recorded on an IR spectrophotometer.

2. Preparation of Starting Materials

N-Ts-2-alkenylanilines **1**[1] and hexahydro-1,3,5-triazines **3**[2] were prepared according to the reported methods, Umemoto reagents are commercially available. Perfluoroalkyl substituted Umemoto reagents were prepared according to the known procedure.[3]

3. Detailed Condition Optimization

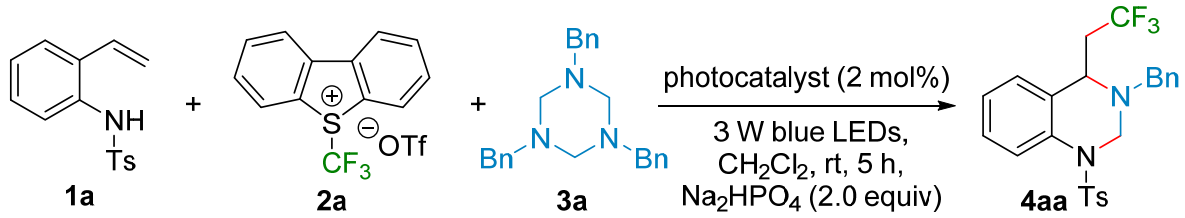
Table S1. Screen of bases.[a]

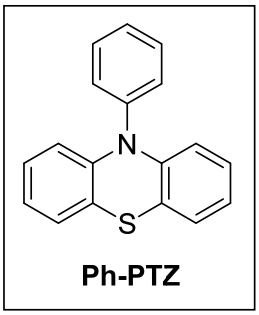


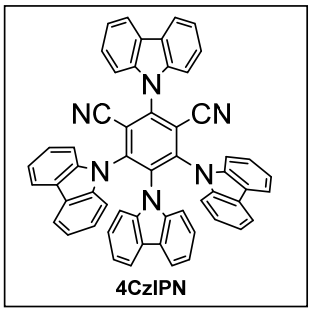
Entry	Base	Yield (%)[b]	Entry	Base	Yield (%)[b]
1	-	6	5	$NaHCO_3$	62
2	Cs_2CO_3	34	6	$KHCO_3$	50
3	Na_2CO_3	45	7	NaOAc	34
4	K_2CO_3	50	**8**	**Na_2HPO_4**	**69**

[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.12 mmol, 1.2 equiv), **3a** (0.1 mmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (0.02mmol, 2.0 mol %), base (0.2 mmol, 2.0 equiv), CH_2Cl_2 (1.0 mL), rt, 5 h, irradiation with 3 W blue LEDs. [b] Yields determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as the internal standard.

Table S2. Screen of photocatalysts.[a]



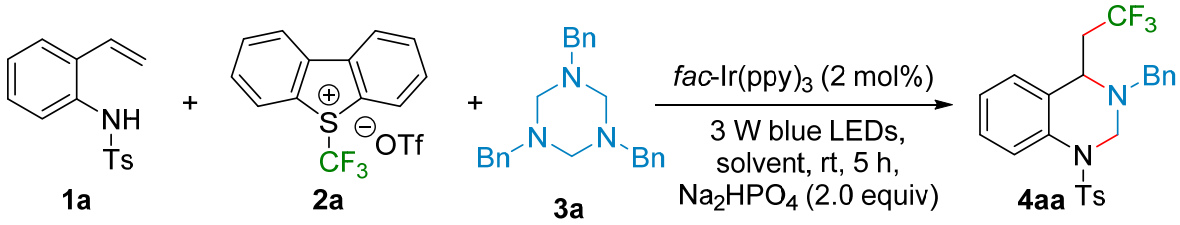




Entry	Photocatalyst	Yield (%)[b]
1	***fac*-Ir(ppy)$_3$**	**69**
2	[Ir(ppy)$_2$(dtbbpy)]PF$_6$	18
3	Ru(phen)$_3$Cl$_2$	15
4	4C$_Z$IPN	16
5	Ph-PTZ[c]	64

[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.12 mmol, 1.2 equiv), **3a** (0.10 mmol, 1.0 equiv), photocatalyst (0.02mmol, 2.0 mol %), Na_2HPO_4 (0.2 mmol, 2.0 equiv), CH_2Cl_2 (1.0 mL), rt, 5 h, irradiation with 3 W blue LEDs. [b] Yields determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as the internal standard. [c] Under the irradiation of 2 x 3 W purple LEDs.

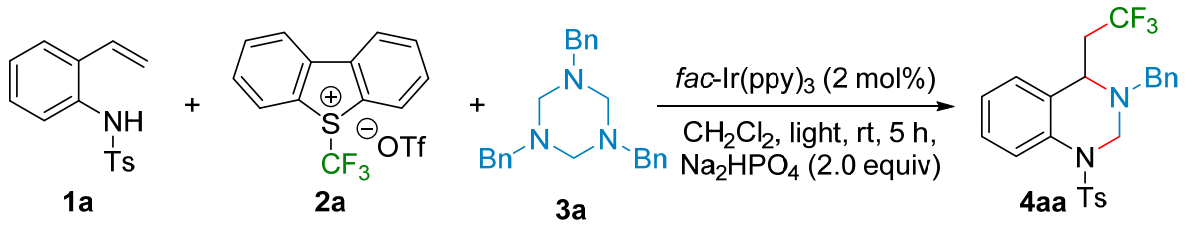
Table S3. Screen of the solvents.[a]



Entry	Solvent	Yield (%)[b]	Entry	Solvent	Yield (%)[b]
1	**CH_2Cl_2**	**69**	5	Toluene	21
2	CH_3CN	50	6	THF	37
3	DCE	65	7	CH_3Cl	54
4	DMF	32	8	PhCl	37

[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.12 mmol, 1.2 equiv), **3a** (0.1 mmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (0.02mmol, 2.0 mol %), Na_2HPO_4 (0.2 mmol, 2.0 equiv), solvent (1.0 mL), rt, 5 h, irradiation with 3 W blue LEDs. [b] Yields determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as the internal standard.

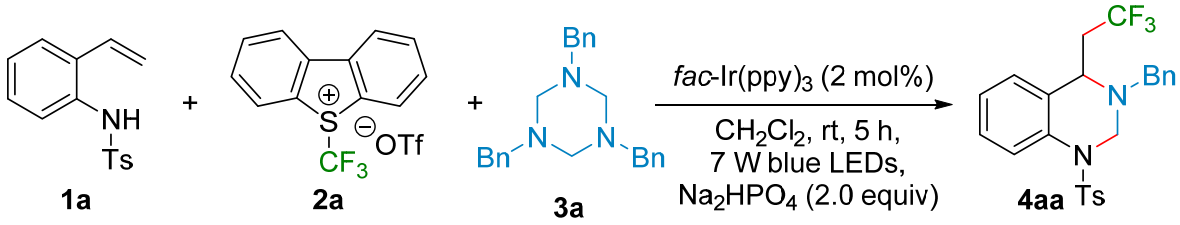
Table S4. Screen of the light sources.[a]



Entry	Light	Yield (%)[b]
1	3 W blue LEDs	69
2	2*3 W blue LEDs	*68*
3	**7 W blue LEDs**	**84**
4	7 W white LEDs	72
5	18 W white LEDs	75

[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.12 mmol, 1.2 equiv), **3a** (0.1 mmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (0.02mmol, 2.0 mol %), Na_2HPO_4 (0.2 mmol, 2.0 equiv), CH_2Cl_2 (1.0 mL), rt, 5 h, irradiation with light. [b] Yields determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as the internal standard.

Table S5. Control experiments.[a]



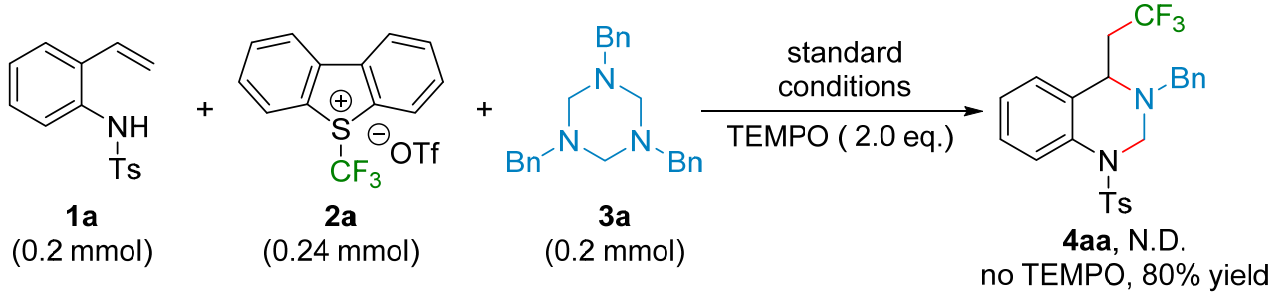
Entry[a]	Condition	Yield (%)[b]
1	-	84 (80) [c]
2	No PC	8
3	No light	-
4	No degass	-

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.24 mmol, 1.2 equiv), **3a** (0.2 mmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (0.04 mmol, 2.0 mol %), Na_2HPO_4 (0.4 mmol, 2.0 equiv), CH_2Cl_2 (2.0 mL), rt, 5 h, irradiation with 7 W blue LEDs. [b] Yields determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as the internal standard. [c] Isolated yield.

4. Mechanistic Studies

4.1 TEMPO-quenching experiment.

In the presence of stoichiometric radical quenchers, such as TEMPO, significant inhibition of the reactivity was observed, which supports that the process involves radical steps. (Scheme S1).



Scheme S1. TEMPO-quenching experiment.

4.2 Luminescence quenching experiments.

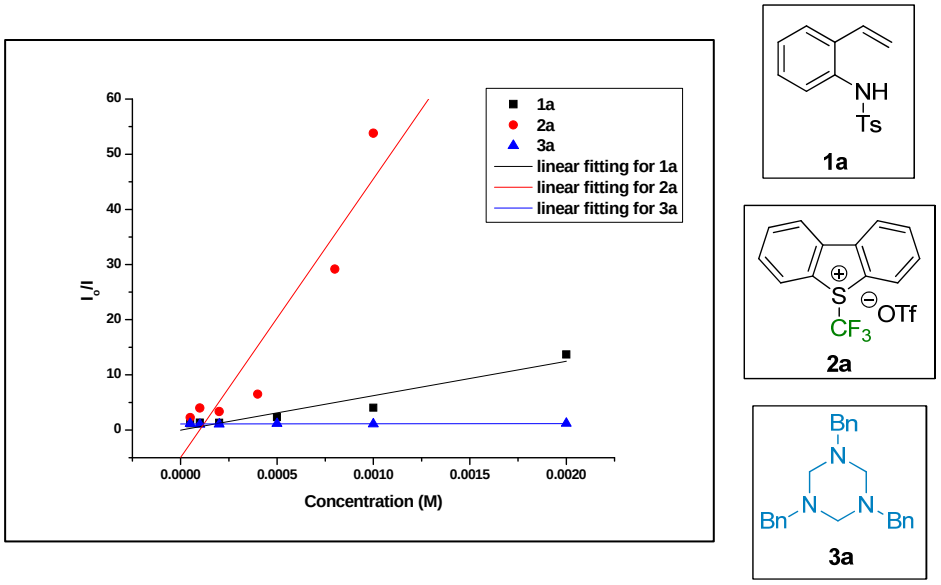
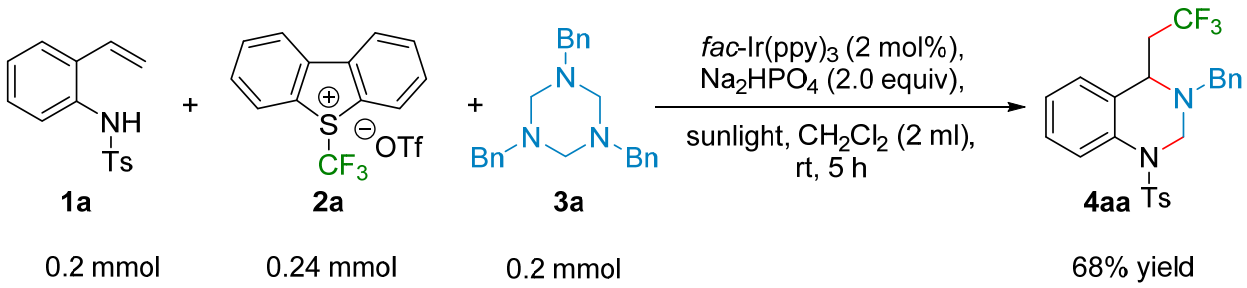


Figure S1. *fac*-Ir(ppy)$_3$ emission quenching by **1a**, **2a** and **3a**.

Fluorescence spectra was collected on Agilent Fluorescence Spectrophotometer G9800AS24 for all experiments. All *fac*-Ir(ppy)$_3$ solutions were excited at 350 nm and the emission intensity was collected at 510 nm. In a typical experiment, the emission spectrum of a 1×10^{-5} M solution of *fac*-Ir(ppy)$_3$ in CH_2Cl_2 was collected. The significant decrease of *fac*-Ir(ppy)$_3$ luminescence could be observed in the presence of substrate **2a**. And a slightly decrease of *fac*-Ir(ppy)$_3$ luminescence was observed in the presence of substrate **1a**. The decrease of *fac*-Ir(ppy)$_3$ luminescence couldn't be observed in the presence of substrate **3a** (Figure S1).

5. Synthetic Application of the Reactions

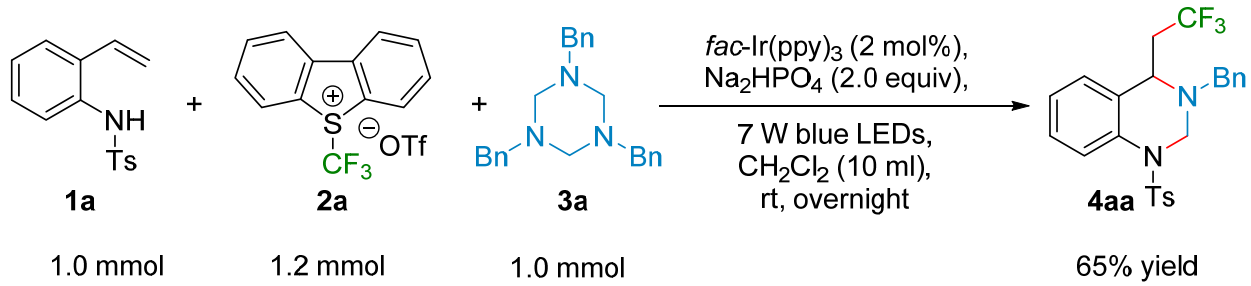
5.1 Sun-light-driven reaction



1a (54.6 mg, 0.2 mmol), **2a** (96.6 mg, 1.2 eq.), **3a** (71.5 mg, 1.0 eq.), *fac*-Ir(ppy)$_3$ (2.6 mg, 2.0 mol%), Na_2HPO_4 (56.8 mg, 2.0 eq.) and anhydrous CH_2Cl_2 (2.0 mL) were added to a 10 mL Schlenk flask equipped with a magnetic stir bar. The resulting

mixture was degassed by a “freeze-pump-thaw” procedure (3 times) under argon atmosphere. Then the solution was stirring under sun light for 5 h. Upon the completion of reaction as monitored by TLC, the solvent was removed by vacuum and the crude reaction mixture was purified by flash chromatography on silica gel (silica: 200–300; eluent: petroleum ether/ethyl acetate (20 : 1–10 : 1) to provide the pure product **4aa** as a white solid in 68 % yield.

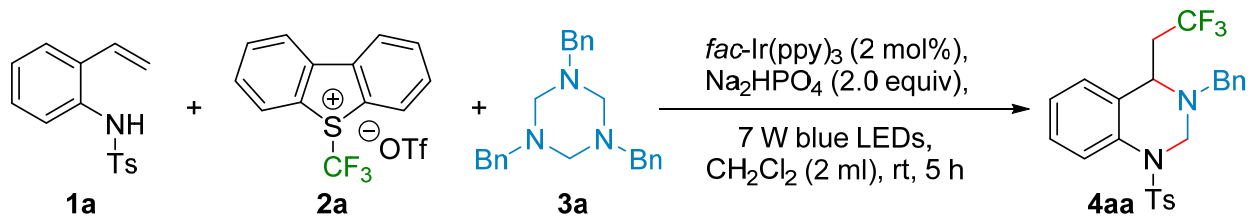
5.2 1.0 mmol scale reaction



1a (273.4 mg, 1.0 mmol), **2a** (482.8 mg, 1.2 eq.), **3a** (357.5 mg, 1.0 eq.), *fac*-Ir(ppy)$_3$ (13.0 mg, 2.0 mol%), Na_2HPO_4 (283.9 mg, 2.0 eq.) and anhydrous CH_2Cl_2 (10.0 mL) were added to a 50 mL Schlenk flask equipped with a magnetic stir bar. The resulting mixture was degassed by a “freeze-pump-thaw” procedure (3 times) under argon atmosphere. Then the solution was stirred at a distance of ca. 5 cm from two 7 W blue LEDs. Upon the completion of reaction as monitored by TLC, the solvent was removed by vacuum and the crude reaction mixture was purified by flash chromatography on silica gel (silica: 200–300; eluent: petroleum ether/ethyl acetate (20 : 1–10 : 1) to provide the pure product **4aa** as a white solid in 65 % yield.

6. General Procedure and Spectral Data of Products

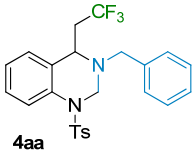
6.1 Representative procedure for visible-light induced compound 4aa synthesis



1a (54.6 mg, 0.2 mmol), **2a** (96.6 mg, 1.2 eq.), **3a** (71.5 mg, 1.0 eq.), *fac*-Ir(ppy)$_3$ (2.6 mg, 2.0 mol%), Na_2HPO_4 (56.8 mg, 2.0 eq.) and anhydrous CH_2Cl_2 (2.0 mL) were added to a 10 mL Schlenk flask equipped with a magnetic stir bar. The resulting mixture was degassed by a “freeze-pump-thaw” procedure (3 times) under argon atmosphere. Then the solution was stirred at a distance of ca. 5 cm from a 7 W blue LEDs. Upon the completion of reaction as monitored by TLC, the solvent was removed by vacuum and the crude reaction mixture was purified by flash chromatography on silica gel (silica: 200–300; eluent: petroleum ether/ethyl acetate (20 : 1–10 : 1) to provide the pure product **4aa** as a white solid in 80 % yield.

6.2 Spectral data of products

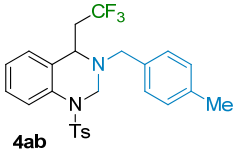
3-benzyl-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (4aa)



4aa

73.7 mg, white solid, 80% yield in 5 h. **^{1}H NMR** (400 MHz, CDCl3) δ (ppm) 7.71 – 7.68 (m, 3H), 7.34 – 7.23 (m, 7H), 7.20 (t, *J* = 7.8 Hz, 1H), 7.02 (t, *J* = 7.4 Hz, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 5.03 (d, *J* = 12.7 Hz, 1H), 4.60 (d, *J* = 12.7 Hz, 1H), 3.96 – 3.93 (m, 1H), 3.86 (d, *J* = 13.5 Hz, 1H), 3.55 (d, *J* = 13.5 Hz, 1H), 2.38 (s, 3H), 2.34 – 2.22 (m, 1H), 2.13 – 2.00 (m, 1H). **^{13}C NMR** (101 MHz, CDCl3) δ (ppm) 144.0, 136.9, 136.6, 135.5, 129.7, 129.1, 128.3, 128.0, 127.6, 126.8, 125.5 (q, *J* = 278.8 Hz), 125.0, 123.6, 120.0, 62.3, 57.1, 54.2 (q, *J* = 3.0 Hz), 40.8 (q, *J* = 26.8 Hz), 21.4. **^{19}F NMR** (376 MHz, CDCl3) δ (ppm) -63.37. **IR** (in KBr): 3418, 3127, 1604, 1492, 1333, 1153, 1121, 1009, 917, 676, 575 cm^{-1}. **HRMS** (ESI) for: $C_{24}H_{24}F_3N_2O_2S$ [M + H]$^+$: calcd: 461.1505, found: 461.1517.

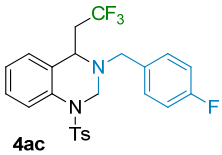
3-(4-methylbenzyl)-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (4ab)



4ab

66.4 mg, colorless liquid, 70% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.71 – 7.66 (m, 3H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.22 – 7.12 (m, 5H), 7.03 (t, *J* = 7.4 Hz, 1H), 6.95 (d, *J* = 8.0 Hz, 1H), 5.02 (d, *J* = 12.6 Hz, 1H), 4.60 (d, *J* = 12.6 Hz, 1H), 3.96 – 3.92 (m, 1H), 3.82 (d, *J* = 13.3 Hz, 1H), 3.51 (d, *J* = 13.3 Hz, 1H), 2.39 (s, 3H), 2.34 (s, 3H), 2.31 – 2.22 (m, 1H), 2.12 – 1.99 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 144.0, 137.2, 136.6, 135.5, 133.8, 129.7, 129.1, 129.0, 128.2, 128.0, 126.9, 125.5 (q, *J* = 278.8 Hz), 125.1, 123.6, 120.0, 62.3, 56.9, 54.1 (q, *J* = 3.0 Hz), 40.8 (q, *J* = 26.7 Hz), 21.5, 21.1. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.26. **IR** (in KBr): 3445, 3129, 1602, 1400, 1251, 1162, 1121, 1096, 814, 757, 673, 581, 565 cm^{-1}. **HRMS** (ESI) for: $C_{25}H_{26}F_3N_2O_2S$ [M + H]$^+$: calcd: 475.1662, found: 475.1664.

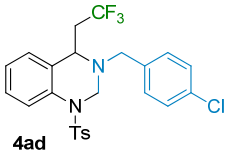
3-(4-fluorobenzyl)-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (4ac)



4ac

72.7 mg, white solid, 76% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.68 (d, *J* = 8.2 Hz, 2H), 7.65 (d, *J* = 8.5 Hz, 1H), 7.30 – 7.25 (m, 4H), 7.19 (t, *J* = 7.7 Hz, 1H), 7.05 – 6.96 (m, 4H), 5.04 (d, *J* = 12.7 Hz, 1H), 4.58 (d, *J* = 12.7 Hz, 1H), 3.96 – 3.93 (m, 1H), 3.87 (d, *J* = 13.5 Hz, 1H), 3.54 (d, *J* = 13.4 Hz, 1H), 2.40 (s, 3H), 2.37 – 2.29 (m, 1H), 2.19 – 2.06 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 162.3 (d, *J* = 245.5 Hz), 144.1, 136.8, 135.6, 132.7 (d, *J* = 3.1 Hz), 130.8 (d, *J* = 8.1 Hz), 129.8, 128.2, 128.1, 126.8, 125.5 (q, *J* = 278.8 Hz), 124.8, 123.7, 119.8, 115.1 (d, *J* = 21.3 Hz), 61.9, 56.4, 54.3 (q, *J* = 3.0 Hz), 41.0 (q, *J* = 26.7 Hz), 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.36, -114.98. **IR** (in KBr): 3446, 3127, 1604, 1511, 1339, 1250, 1231, 1098, 961, 818, 672, 580, 561 cm^{-1}. **HRMS** (ESI) for: $C_{24}H_{23}F_4N_2O_2S$ [M + H]$^+$: calcd: 479.1411, found: 490.1420.

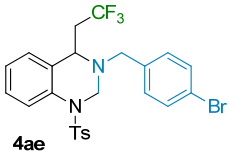
3-(4-chlorobenzyl)-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (4ad)



4ad

76.2 mg, white solid, 77% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.68 (d, *J* = 8.1 Hz, 2H), 7.64 (d, *J* = 8.5 Hz, 1H), 7.30 – 7.24 (m, 6H), 7.19 (t, *J* = 7.7 Hz, 1H), 7.03 (t, *J* = 7.4 Hz, 1H), 6.96 (d, *J* = 7.4 Hz, 1H), 5.03 (d, *J* = 12.7 Hz, 1H), 4.57 (d, *J* = 12.8 Hz, 1H), 3.95 – 3.92 (m, 1H), 3.88 (d, *J* = 13.6 Hz, 1H), 3.54 (d, *J* = 13.6 Hz, 1H), 2.40 (s, 3H), 2.36 – 2.27 (m, 1H), 2.20 – 2.07 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 144.1, 136.8, 135.6, 135.5, 133.3, 130.5, 129.8, 128.4, 128.2, 128.1, 126.8, 125.5 (q, *J* = 278.8 Hz), 124.7, 123.7, 119.8, 61.9, 56.4, 54.4 (q, *J* = 3.0 Hz), 41.0 (q, *J* = 26.8 Hz), 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.29. **IR** (in KBr): 3444, 3128, 1603, 1492, 1401, 1342, 1257, 1172, 1117, 1096, 1011, 657, 579 cm^{-1}. **HRMS** (ESI) for: $C_{24}H_{23}ClF_3N_2O_2S$ [M + H]$^+$: calcd: 495.1115, found: 495.1106.

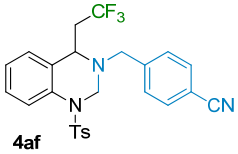
3-(4-bromobenzyl)-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (4ae)



4ae

78.8 mg, white solid, 73% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.68 (d, *J* = 8.2 Hz, 2H), 7.64 (d, *J* = 8.5 Hz, 1H), 7.44 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.19 (d, *J* = 8.2 Hz, 3H), 7.03 (t, *J* = 7.4 Hz, 1H), 6.96 (d, *J* = 7.3 Hz, 1H), 5.03 (d, *J* = 12.8 Hz, 1H), 4.57 (d, *J* = 12.8 Hz, 1H), 3.95 – 3.92 (m, 1H), 3.86 (d, *J* = 13.7 Hz, 1H), 3.52 (d, *J* = 13.7 Hz, 1H), 2.40 (s, 3H), 2.37 – 2.27 (m, 1H), 2.20 – 2.07 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 144.1, 136.8, 136.0, 135.5, 131.4, 130.8, 129.8, 128.2, 128.1, 126.8, 125.5 (q, *J* = 278.8 Hz), 124.7, 123.7, 121.5, 119.8, 61.9, 56.5, 54.5 (q, *J* = 3.0 Hz), 41.0 (q, *J* = 26.8 Hz), 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.27. **IR** (in KBr): 3452, 3128, 1603, 1401, 1341, 1253, 1170, 1150, 1095, 1006, 757, 677 cm^{-1}. **HRMS** (ESI) for: $C_{24}H_{23}BrF_3N_2O_2S$ $[M + H]^+$: calcd: 539.0610, found: 539.0617.

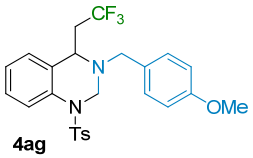
4-((1-tosyl-4-(2,2,2-trifluoroethyl)-1,2-dihydroquinazolin-3(4H)-yl)methyl)benzonitrile (4af)



4af

72.8 mg, white solid, 75% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.69 (d, *J* = 8.2 Hz, 2H), 7.63 (d, *J* = 8.1 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.20 (t, *J* = 7.4 Hz, 1H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.99 (d, *J* = 7.3 Hz, 1H), 5.04 (d, *J* = 12.9 Hz, 1H), 4.57 (d, *J* = 12.9 Hz, 1H), 4.03 (d, *J* = 14.2 Hz, 1H), 3.97 – 3.94 (m, 1H), 3.66 (d, *J* = 14.2 Hz, 1H), 2.48 – 2.34 (m, 4H), 2.29 – 2.16 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 144.2, 142.7, 137.0, 135.6, 132.1, 129.9, 129.7, 128.2, 126.7, 125.4 (q, *J* = 278.8 Hz), 124.4, 123.8, 119.7, 118.9, 111.4, 61.6, 56.7, 55.1 (q, *J* = 3.0 Hz), 41.2 (q, *J* = 26.7 Hz), 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.30. **IR** (in KBr): 3442, 3128, 1606, 1400, 1339, 1169, 1096, 1008, 907, 814, 760, 673, 544 cm^{-1}. **HRMS** (ESI) for: $C_{25}H_{23}F_3N_3O_2S$ $[M + H]^+$: calcd: 486.1458, found: 486.1463.

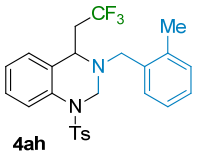
3-(4-methoxybenzyl)-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (4ag)



4ag

71.6 mg, colorless liquid, 73% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.68 (t, *J* = 7.7 Hz, 3H), 7.29 – 7.25 (m, 2H), 7.20 (t, *J* = 8.0 Hz, 3H), 7.03 (t, *J* = 7.4 Hz, 1H), 6.96 (d, *J* = 7.5 Hz, 1H), 6.86 (d, *J* = 8.4 Hz, 2H), 5.03 (d, *J* = 12.6 Hz, 1H), 4.58 (d, *J* = 12.6 Hz, 1H), 3.96 – 3.93 (m, 1H), 3.82 – 3.79 (m, 4H), 3.50 (d, *J* = 13.2 Hz, 1H), 2.39 (s, 3H), 2.33 – 2.22 (m, 1H), 2.13 – 2.00 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 159.0, 144.0, 136.7, 135.6, 130.4, 129.8, 128.9, 128.2, 128.0, 126.9, 125.5 (q, *J* = 278.8 Hz), 125.1, 123.6, 120.0, 113.6, 62.2, 56.5, 55.2, 54.0 (q, *J* = 2.7 Hz), 40.9 (q, *J* = 26.8 Hz), 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.29. **IR** (in KBr): 3443, 3130, 1614, 1400, 1250, 1164, 1095, 673, 580, 543 cm^{-1}. **HRMS** (ESI) for: $C_{25}H_{26}F_3N_2O_3S$ $[M + H]^+$: calcd: 491.1611, found: 491.1617.

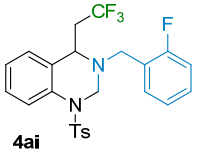
3-(2-methylbenzyl)-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (4ah)



4ah

71.2 mg, white solid, 75% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.76 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 7.24 – 7.06 (m, 5H), 7.04 (t, *J* = 7.4 Hz, 1H), 6.96 (d, *J* = 7.4 Hz, 1H), 5.10 (d, *J* = 12.7 Hz, 1H), 4.60 (d, *J* = 12.7 Hz, 1H), 3.94 – 3.90 (m, 1H), 3.84 (d, *J* = 13.1 Hz, 1H), 3.48 (d, *J* = 13.1 Hz, 1H), 2.38 (s, 3H), 2.28 (s, 3H), 2.26 – 2.16 (m, 1H), 2.07 – 1.94 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 144.1, 138.1, 136.4, 135.5, 134.5, 130.4, 130.2, 129.8, 128.3, 128.2, 127.8, 126.9, 125.6, 125.3 (q, *J* = 278.8 Hz), 124.8, 123.6, 120.0, 62.6, 55.2, 53.2 (q, *J* = 3.0 Hz), 40.5 (q, *J* = 26.9 Hz), 21.5, 18.9. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.68. **IR** (in KBr): 3446, 3129, 1636, 1604, 1400, 1153, 1121, 1095, 1005, 751, 704, 577, 543 cm^{-1}. **HRMS** (ESI) for: $C_{25}H_{26}F_3N_2O_2S$ $[M + H]^+$: calcd: 475.1662, found: 475.1656.

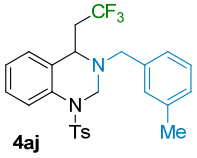
3-(2-fluorobenzyl)-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (4ai)



4ai

78.5 mg, white solid, 82% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.70 (d, *J* = 8.4 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 3H), 7.20 (t, *J* = 7.8 Hz, 1H), 7.12 (t, *J* = 7.4 Hz, 1H), 7.06 – 6.99 (m, 3H), 5.03 (d, *J* = 12.7 Hz, 1H), 4.62 (d, *J* = 12.7 Hz, 1H), 3.97 – 3.94 (m, 1H), 3.88 (d, *J* = 13.8 Hz, 1H), 3.62 (d, *J* = 13.8 Hz, 1H), 2.39 (s, 3H), 2.34 – 2.22 (m, 1H), 2.11 – 1.98 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 161.4 (d, *J* = 247.7 Hz), 144.1, 136.5, 135.5, 131.2 (d, *J* = 4.0 Hz), 129.7, 129.4 (d, *J* = 8.2 Hz), 128.2, 128.1, 126.9, 125.4 (q, *J* = 278.8 Hz), 125.3, 124.0 (d, *J* = 3.7 Hz), 123.9, 123.8, 120.3, 115.3 (d, *J* = 21.7 Hz), 62.5, 54.30 (q, *J* = 2.7 Hz), 50.2 (d, *J* = 2.6 Hz), 41.0 (q, *J* = 26.8 Hz), 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.62, -117.59. **IR** (in KBr): 3446, 3129, 1605, 1492, 1400, 1332, 1151, 1124, 1008, 757, 674, 577, 545 cm^{-1}. **HRMS** (ESI) for: $C_{24}H_{23}F_4N_2O_2S$ $[M + H]^+$: calcd: 479.1411, found: 479.1420.

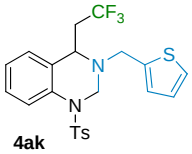
3-(3-methylbenzyl)-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (4aj)



4aj

72.1 mg, colorless liquid, 76% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.72 (d, *J* = 8.5 Hz, 1H), 7.67 (d, *J* = 8.1 Hz, 2H), 7.28 – 7.24 (m, 2H), 7.20 (t, *J* = 7.5 Hz, 2H), 7.11 – 7.01 (m, 4H), 6.95 (d, *J* = 7.5 Hz, 1H), 5.02 (d, *J* = 12.6 Hz, 1H), 4.61 (d, *J* = 12.7 Hz, 1H), 3.95 – 3.91 (m, 1H), 3.82 (d, *J* = 13.5 Hz, 1H), 3.51 (d, *J* = 13.5 Hz, 1H), 2.39 (s, 3H), 2.34 (s, 3H), 2.31 – 2.22 (m, 1H), 2.11 – 1.98 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 144.0, 137.9, 136.7, 136.6, 135.5, 129.8, 129.7, 128.3, 128.3, 128.1, 128.1, 126.9, 126.1, 125.5 (q, *J* = 278.8 Hz), 125.1, 123.6, 120.1, 62.4, 57.2, 54.1 (q, *J* = 2.7 Hz), 40.9 (q, *J* = 26.9 Hz), 21.5, 21.3. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.32. **IR** (in KBr): 3444, 3127, 1606, 1491, 1333, 1152, 1120, 1010, 758, 675, 576, 546 cm^{-1}. **HRMS** (ESI) for: $C_{25}H_{26}F_3N_2O_2S$ $[M + H]^+$: calcd: 475.1662, found: 475.1660.

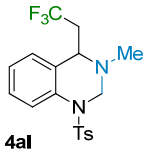
3-(thiophen-2-ylmethyl)-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (4ak)



4ak

56.9 mg, colorless liquid, 61% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.68 (t, *J* = 7.8 Hz, 3H), 7.28 (d, *J* = 7.7 Hz, 3H), 7.21 (t, *J* = 7.8 Hz, 1H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.99 – 6.92 (m, 3H), 5.04 (d, *J* = 12.7 Hz, 1H), 4.59 (d, *J* = 12.7 Hz, 1H), 4.06 – 4.01 (m, 2H), 3.76 (d, *J* = 14.1 Hz, 1H), 2.40 (s, 3H), 2.35 – 2.19 (m, 1H), 2.09 – 1.96 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 144.1, 140.3, 136.5, 135.4, 129.8, 128.3, 128.1, 127.0, 126.9, 126.5, 125.8, 125.5 (q, *J* = 278.8 Hz), 125.2, 123.9, 120.4, 62.1, 54.1 (q, *J* = 3.0 Hz), 51.9, 41.0 (q, J = 26.9 Hz), 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.35. **IR** (in KBr): 3445, 3123, 1601, 1491, 1400, 1270, 1162, 1122, 1096, 757, 578, 543 cm^{-1}. **HRMS** (ESI) for: $C_{22}H_{22}F_3N_2O_2S_2$ $[M + H]^+$: calcd: 467.1069, found: 467.1064.

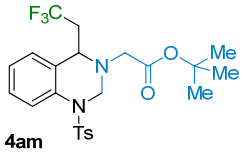
3-methyl-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (4al)



4al

58.4 mg, white solid, 76% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.66 (d, *J* = 8.2 Hz, 2H), 7.63 (d, *J* = 8.4 Hz, 1H), 7.26 (d, *J* = 8.1 Hz, 2H), 7.18 (t, *J* = 7.7 Hz, 1H), 7.08 – 7.00 (m, 2H), 4.84 (d, *J* = 12.7 Hz, 1H), 4.60 (d, *J* = 12.7 Hz, 1H), 3.80 – 3.77 (m, 1H), 2.42 (s, 3H), 2.39 (s, 3H), 2.29 – 2.04 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 143.9, 137.0, 135.5, 129.6, 128.1, 127.8, 127.2, 126.2, 125.8 (q, *J* = 278.8 Hz), 124.2, 121.0, 64.5, 56.5 (q, *J* = 2.8 Hz), 41.5 (q, *J* = 26.6 Hz), 40.9, 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.81. **IR** (in KBr): 3419, 3129, 1602, 1401, 1337, 1255, 1123, 1005, 1010, 659, 546 cm^{-1}. **HRMS** (ESI) for: $C_{18}H_{19}F_3N_2NaO_2S$ $[M + Na]^+$: calcd: 407.1012, found: 407.1022.

Tert-butyl 2-(1-tosyl-4-(2,2,2-trifluoroethyl)-1,2-dihydroquinazolin-3(4H)-yl)acetate (4am)

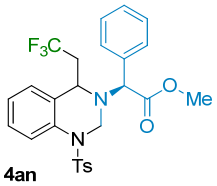


4am

61.2 mg, colorless liquid, 63% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.60 (d, *J* = 8.1 Hz, 2H), 7.26 – 7.20 (m, 3H), 7.10 (t, *J* = 7.5 Hz, 1H), 7.02 (d, *J* = 7.6 Hz, 1H), 4.98 (d, *J* = 12.8 Hz, 1H), 4.65 (d, *J* = 12.8 Hz, 1H), 4.16 – 4.13 (m, 1H), 3.41 (d, *J* = 17.1 Hz, 1H), 3.20 (d, *J* = 17.1 Hz, 1H),

2.38 (s, 3H), 2.17 – 1.90 (m, 2H), 1.45 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 168.9, 144.0, 136.7, 135.6, 129.5, 128.0, 127.8, 127.8, 127.3, 125.8 (q, *J* = 278.8 Hz), 124.8, 122.3, 81.7, 63.5, 54.6 (q, *J* = 2.8 Hz), 54.2, 41.6 (q, *J* = 26.9 Hz), 28.0, 21.4. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.67. **IR** (in KBr): 3444, 3129, 1736, 1633, 1400, 1161, 1092, 659, 575 cm^{-1}. **HRMS** (ESI) for: $C_{23}H_{28}F_3N_2O_4S$ $[M + H]^+$: calcd: 485.1716, found: 485.1727.

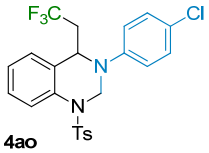
(2S)-methyl 2-phenyl-2-(1-tosyl-4-(2,2,2-trifluoroethyl)-1,2-dihydroquinazolin-3(4H)-yl)acetate (4an)



4an

67.4 mg, colorless liquid, 65% yield in 5 h, d.r. = 2:1. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.73 (d, *J* = 8.5 Hz, 1H, minor), 7.69 (d, *J* = 8.1 Hz, 2H, major), 7.62 (d, *J* = 8.4 Hz, 1H, major), 7.54 (d, *J* = 8.1 Hz, 2H, minor), 7.46 – 7.29 (m, 6H, major + minor), 7.26 – 7.17 (m, 2H, major + minor), 7.05 (t, *J* = 8.0 Hz, 1H, minor), 7.01 (d, *J* = 7.5 Hz, 1H, minor), 6.99 (t, *J* = 8.0 Hz, 1H, major), 6.75 (d, *J* = 7.6 Hz, 1H, major), 5.40 (d, *J* = 13.2 Hz, 1H, major), 4.72 (d, *J* = 12.8 Hz, 1H, minor), 4.65 (d, *J* = 13.2 Hz, 1H, major), 4.47 (d, *J* = 12.8 Hz, 1H, minor), 4.37 (s, 1H, major + minor), 4.18 (t, *J* = 6.5 Hz, 1H, minor), 3.78 (t, *J* = 6.8 Hz, 1H, major), 3.69 (s, 3H, major), 3.63 (s, 3H, minor), 2.41 (s, 3H, major), 2.37 (s, 3H, minor), 2.34 – 2.23 (m, 1H, major + minor), 1.99 – 1.84 (m, 1H, major + minor). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) (major + minor) 171.0, 144.2, 136.7, 135.8, 135.5, 135.2, 134.5, 134.4, 129.9, 129.7, 129.2, 129.2, 128.8, 128.7, 128.5, 128.4, 128.1, 126.9, 126.8, 125.3 (q, *J* = 278.8 Hz), 125.0, 124.9, 123.8, 123.7, 120.2, 120.1, 68.0, 66.8, 60.7, 59.7, 53.5 (q, *J* = 3.0 Hz), 52.4, 52.3, 51.4 (q, *J* = 3.0 Hz), 41.4 (q, *J* = 27.3 Hz), 40.8 (q, *J* = 27.3 Hz), 21.5, 21.4. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.35. **IR** (in KBr): 3444, 3129, 1746, 1400, 1169, 1119, 1096, 757, 702, 615, 577 cm^{-1}. **HRMS** (ESI) for: $C_{26}H_{25}F_3N_2NaO_4S$ $[M + Na]^+$: calcd: 541.1379, found: 541.1381.

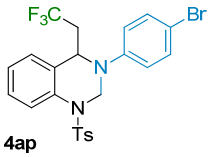
3-(4-chlorophenyl)-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (4ao)



4ao

50.0 mg, white solid, 52% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.91 (d, *J* = 8.4 Hz, 1H), 7.26 (t, *J* = 7.8 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.14 – 7.07 (m, 4H), 7.01 (d, *J* = 8.0 Hz, 2H), 6.75 (d, *J* = 8.7 Hz, 2H), 5.77 (d, *J* = 13.7 Hz, 1H), 4.81 (d, *J* = 13.7 Hz, 1H), 4.78 – 4.75 (m, 1H), 2.58 – 2.45 (m, 1H), 2.32 (s, 3H), 2.30 – 2.24 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 146.2, 143.9, 135.8, 135.5, 129.4, 129.3, 128.4, 127.4, 127.0, 127.0, 126.2, 125.4 (q, *J* = 278.8 Hz), 124.6, 121.9, 120.1, 60.5, 53.3 (q, *J* = 3.0 Hz), 40.5 (q, J = 26.9 Hz), 21.4. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.37. **IR** (in KBr): 3446, 3128, 1596, 1494, 1398, 1205, 1160, 1002, 968, 656, 581, 534 cm^{-1}. **HRMS** (ESI) for: $C_{23}H_{21}ClF_3N_2O_2S$ $[M + H]^+$: calcd: 481.0959, found: 481.0952.

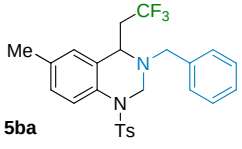
3-(4-bromophenyl)-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (4ap)



4ap

57.8 mg, white solid, 55% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.92 (d, *J* = 8.4 Hz, 1H), 7.25 (d, *J* = 8.5 Hz, 3H), 7.20 (d, *J* = 8.1 Hz, 2H), 7.14 – 7.07 (m, 2H), 7.01 (d, *J* = 8.1 Hz, 2H), 6.69 (d, *J* = 8.7 Hz, 2H), 5.78 (d, *J* = 13.8 Hz, 1H), 4.82 – 4.75 (m, 2H), 2.59 – 2.45 (m, 1H), 2.37 – 2.24 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 146.7, 143.9, 135.8, 135.5, 132.2, 129.3, 128.4, 127.4, 126.9, 126.2, 125.4 (q, *J* = 278.8 Hz), 124.7, 121.9, 120.4, 114.3, 60.3, 53.1 (q, *J* = 3.0 Hz), 40.4 (q, *J* = 26.9 Hz), 21.4. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.33. **IR** (in KBr): 3420, 3128, 1590, 1492, 1399, 1160, 1126, 1003, 830, 581 cm^{-1}. **HRMS** (ESI) for: $C_{23}H_{20}BrF_3N_2NaO_2S$ $[M + Na]^+$: calcd: 547.0273, found: 547.0266.

3-benzyl-6-methyl-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (5ba)

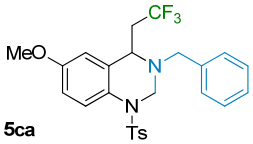


5ba

64.5 mg, colorless liquid, 68% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.66 (d, *J* = 8.1 Hz, 2H), 7.59 (d, *J* = 8.6 Hz, 1H), 7.34 – 7.26 (m, 7H), 7.01 (d, *J* = 8.0 Hz, 1H), 6.75 (s, 1H), 5.00 (d, *J* = 12.6 Hz, 1H), 4.57 (d, *J* = 12.7 Hz, 1H), 3.91 – 3.84 (m, 2H), 3.54 (d, *J* = 13.5 Hz, 1H), 2.39 (s, 3H),

2.32 – 2.19 (m, 4H), 2.12 – 1.99 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 143.9, 137.0, 136.6, 133.3, 132.9, 129.7, 129.1, 128.8, 128.6, 128.3, 127.6, 126.9, 125.6 (q, *J* = 278.8 Hz), 125.0, 120.0, 62.3, 57.2, 54.2 (q, *J* = 2.7 Hz), 40.9 (q, *J* = 26.7 Hz), 21.5, 20.6. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.36. **IR** (in KBr): 3446, 3128, 1622, 1499, 1400, 1254, 1160, 1122, 1096, 812, 662, 547 cm^{-1}. **HRMS** (ESI) for: $C_{25}H_{26}F_3N_2O_2S$ $[M + H]^+$: calcd: 475.1662, found: 475.1667.

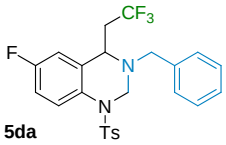
3-benzyl-6-methoxy-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (5ca)



5ca

60.8 mg, white solid, 62% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.69 (d, *J* = 9.2 Hz, 1H), 7.60 (d, *J* = 8.1 Hz, 2H), 7.34 – 7.29 (m, 2H), 7.26 (d, *J* = 6.2 Hz, 5H), 6.81 – 6.79 (m, 1H), 6.46 (d, *J* = 2.2 Hz, 1H), 4.89 (d, *J* = 12.0 Hz, 1H), 4.55 (d, *J* = 12.6 Hz, 1H), 3.87 – 3.83 (m, 1H), 3.79 (d, *J* = 13.6 Hz, 1H), 3.75 (s, 3H), 3.52 (d, *J* = 13.5 Hz, 1H), 2.39 (s, 3H), 2.23 – 2.04 (m, 1H), 1.98 – 1.85 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 155.9, 144.0, 136.9, 136.2, 129.7, 129.1, 128.4, 128.3, 127.6, 127.3, 127.0, 125.5 (q, *J* = 278.8 Hz), 122.4, 113.8, 112.9, 62.6, 57.3, 55.4, 54.3 (q, *J* = 2.8 Hz), 40.5 (q, *J* = 27.0 Hz), 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.38. **IR** (in KBr): 3419, 3129, 1619, 1500, 1400, 1257, 1157, 1095, 1003, 754, 574 cm^{-1}. **HRMS** (ESI) for: $C_{25}H_{26}F_3N_2O_3S$ $[M + H]^+$: calcd: 491.1611, found: 491.1620.

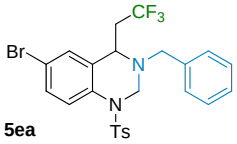
3-benzyl-6-fluoro-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (5da)



5da

66.0 mg, colorless liquid, 69% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.75 – 7.71 (m, 1H), 7.62 (d, *J* = 8.1 Hz, 2H), 7.34 – 7.25 (m, 7H), 6.97 – 6.92 (m, 1H), 6.69 – 6.67 (m, 1H), 4.95 (d, *J* = 12.7 Hz, 1H), 4.56 (d, *J* = 12.7 Hz, 1H), 3.89 – 3.86 (m, 1H), 3.81 (d, *J* = 13.4 Hz, 1H), 3.51 (d, *J* = 13.4 Hz, 1H), 2.40 (s, 3H), 2.26 – 2.13 (m, 1H), 2.00 – 1.87 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 158.8 (d, *J* = 245.6 Hz), 144.3, 136.5, 136.1, 131.5 (d, *J* = 2.8 Hz), 129.8, 129.1, 128.4, 127.7, 127.5 (d, *J* = 6.3 Hz), 126.9, 125.3 (q, *J* = 278.8 Hz), 122.5 (d, *J* = 7.7 Hz), 115.3 (d, *J* = 22.2 Hz), 114.5 (d, *J* = 22.5 Hz), 62.5, 57.3, 54.1 (q, *J* = 3,0 Hz), 40.4 (q, *J* = 27.2 Hz), 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.39, -118.00. **IR** (in KBr): 3445, 3128, 1597, 1497, 1399, 1336, 1155, 1015, 899, 810, 546 cm^{-1}. **HRMS** (ESI) for: $C_{24}H_{23}F_4N_2O_2S$ $[M + H]^+$: calcd: 479.1411, found: 479.1419.

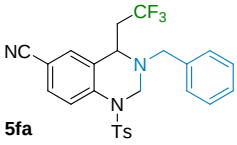
3-benzyl-6-bromo-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (5ea)



5ea

75.5 mg, colorless liquid, 70% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.66 – 7.64 (m, 3H), 7.35 – 7.26 (m, 8H), 7.08 (d, *J* = 2.2 Hz, 1H), 5.03 (d, *J* = 12.7 Hz, 1H), 4.57 (d, *J* = 12.7 Hz, 1H), 3.91 – 3.88 (m, 1H), 3.83 (d, *J* = 13.4 Hz, 1H), 3.51 (d, *J* = 13.4 Hz, 1H), 2.41 (s, 3H), 2.33 – 2.20 (m, 1H), 2.10 – 1.97 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 144.4, 136.5, 136.1, 134.7, 131.2, 130.8, 129.9, 129.1, 128.4, 127.8, 127.0, 126.9, 125.3 (q, *J* = 278.8 Hz), 121.8, 116.5, 62.3, 57.3, 53.9 (q, *J* = 2.9 Hz), 40.6 (q, *J* = 27.2 Hz), 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.34. **IR** (in KBr): 3444, 3128, 1634, 1400, 1162, 1095, 1008, 811, 662, 543 cm^{-1}. **HRMS** (ESI) for: $C_{24}H_{23}BrF_3N_2O_2S$ $[M + H]^+$: calcd: 539.0610, found: 539.0618.

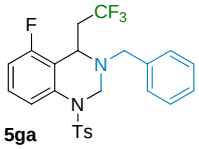
3-benzyl-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline-6-carbonitrile (5fa)



5fa

72.8 mg, colorless liquid, 75% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.89 (d, *J* = 8.8 Hz, 1H), 7.74 (d, *J* = 8.2 Hz, 2H), 7.52 (d, *J* = 8.8 Hz, 1H), 7.40 – 7.35 (m, 5H), 7.31 (d, *J* = 5.8 Hz, 3H), 5.19 (d, *J* = 12.0 Hz, 1H), 4.70 (d, *J* = 12.0 Hz, 1H), 4.04 – 4.01 (m, 1H),, 3.89 (d, *J* = 13.4 Hz, 1H), 3.55 (d, *J* = 13.4 Hz, 1H), 2.25 – 2.39 (m, 4H), 2.23 – 2.11 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 144.9, 139.6, 136.0, 135.8, 132.1, 131.8, 130.1, 129.0, 128.5, 127.9, 126.8, 125.1 (q, *J* = 278.8 Hz), 125.0, 119.7, 118.1, 106.5, 62.4, 57.2, 53.7 (q, *J* = 2.9 Hz), 40.5 (q, *J* = 27.4 Hz), 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.24. **IR** (in KBr): 3446, 3129, 1609, 1495, 1400, 1168, 1099, 814, 664, 572, 545 cm^{-1}. **HRMS** (ESI) for: $C_{25}H_{23}F_3N_3O_2S$ $[M + H]^+$: calcd: 486.1458, found: 486.1456.

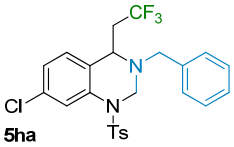
3-benzyl-5-fluoro-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (5ga)



5ga

77.5 mg, colorless liquid, 81% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.71 (d, *J* = 7.9 Hz, 2H), 7.48 (d, *J* = 8.6 Hz, 1H), 7.32 – 7.25 (m, 7H), 7.17 (q, *J* = 8.0 Hz, 1H), 6.75 (t, *J* = 6.6 Hz, 1H), 5.15 (d, *J* = 12.8 Hz, 1H), 4.59 (d, *J* = 12.9 Hz, 1H), 4.25 (t, *J* = 6.6 Hz, 1H), 3.88 (d, *J* = 13.4 Hz, 1H), 3.56 (d, *J* = 13.4 Hz, 1H), 2.41 (s, 3H), 2.37 – 2.25 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 159.9 (d, *J* = 243.8 Hz), 144.3, 137.0 (d, *J* = 6.6 Hz), 136.6 (d, *J* = 2.0 Hz), 129.9, 129.2, 128.7, 128.6, 128.3, 127.7, 126.8, 125.3 (q, *J* = 278.8 Hz), 114.8 (d, *J* = 3.1 Hz), 112.2 (d, *J* = 20.1 Hz), 109.8 (d, *J* = 21.8 Hz), 61.5, 57.2, 49.7 – 49.6 (m), 38.7 (d, *J* = 27.1 Hz), 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.23, -116.00. **IR** (in KBr): 3445, 3128, 1619, 1474, 1400, 1164, 1095, 814, 665, 587, 542 cm^{-1}. **HRMS** (ESI) for: $C_{24}H_{23}F_4N_2O_2S$ $[M + H]^+$: calcd: 479.1411, found: 479.1420.

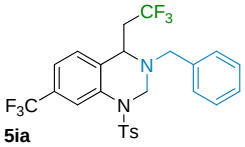
3-benzyl-7-chloro-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (5ha)



5ha

82.2 mg, white solid, 83% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.81 (d, *J* = 1.8 Hz, 1H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.34 – 7.26 (m, 7H), 7.02 – 7.00 (m, 1H), 6.88 (d, *J* = 8.2 Hz, 1H), 5.03 (d, *J* = 12.7 Hz, 1H), 4.57 (d, *J* = 12.7 Hz, 1H), 3.92 – 3.88 (m, 7H), 3.83 (d, *J* = 13.4 Hz, 1H), 3.50 (d, *J* = 13.4 Hz, 1H), 2.41 (s, 3H), 2.37 – 2.21 (m, 1H), 2.07 – 1.94 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 144.5, 136.5, 136.0, 133.8, 129.9, 129.3, 129.1, 128.4, 127.7, 127.0, 125.3 (q, *J* = 278.8 Hz), 123.7, 123.1, 119.9, 62.3, 57.2, 53.7 (q, *J* = 2.8 Hz), 40.7 (q, *J* = 27.0 Hz), 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.34. **IR** (in KBr): 3445, 3128, 1597, 1401, 1340, 1166, 1126, 1017, 908, 665, 541 cm^{-1}. **HRMS** (ESI) for: $C_{24}H_{23}ClF_3N_2O_2S$ $[M + H]^+$: calcd: 495.1115, found: 495.1111.

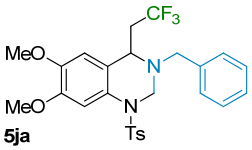
3-benzyl-1-tosyl-4-(2,2,2-trifluoroethyl)-7-(trifluoromethyl)-1,2,3,4-tetrahydroquinazoline (5ia)



5ia

74.0 mg, white solid,70% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 8.07 (s, 1H), 7.69 (d, *J* = 8.3 Hz, 2H), 7.36 – 7.26 (m, 8H), 7.08 (d, *J* = 8.0 Hz, 1H), 5.10 (d, *J* = 12.7 Hz, 1H), 4.61 (d, *J* = 12.8 Hz, 1H), 4.00 – 3.97 (m, 1H), 3.86 (d, *J* = 13.4 Hz, 1H), 3.52 (d, *J* = 13.4 Hz, 1H), 2.41 (s, 3H), 2.39 – 2.28 (m, 1H), 2.14 – 2.01 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 144.7, 136.4, 136.0, 135.8, 130.4 (q, *J* = 32.0 Hz), 130.0, 129.1, 128.9, 128.4, 127.8, 127.0, 125.3 (q, *J* = 278.8 Hz), 123.6 (q, *J* = 273.7 Hz), 119.8 (q, *J* = 3.6 Hz), 116.7 (q, *J* = 4.1 Hz), 62.2, 57.3, 54.0 (q, *J* = 3.0 Hz), 40.6 (q, *J* = 27.4 Hz), 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -62.88, -63.34. **IR** (in KBr): 3442, 3129, 1631, 1400, 1167, 1096, 542 cm^{-1}. **HRMS** (ESI) for: $C_{25}H_{22}F_6N_2NaO_2S$ $[M + Na]^+$: calcd: 551.1198, found: 551.1208.

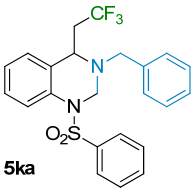
3-benzyl-6,7-dimethoxy-1-tosyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (5ja)



5ja

56.2 mg, colorless liquid, 54% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.61 (d, *J* = 7.7 Hz, 2H), 7.38 (s, 1H), 7.33 – 7.26 (m, 7H), 6.38 (s, 1H), 4.85 (d, *J* = 12.5 Hz, 1H), 4.54 (d, *J* = 12.6 Hz, 1H), 3.87 (s, 3H), 3.80 – 3.75 (m, 5H), 3.52 (d, *J* = 13.5 Hz, 1H), 2.40 (s, 3H), 2.17 – 2.03 (m, 1H), 1.92 – 1.79 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 148.3, 145.8, 144.1, 136.9, 136.1, 129.6, 129.0, 128.4, 128.3, 127.6, 127.1, 125.5 (q, *J* = 278.8 Hz), 117.9, 110.1, 105.1, 62.6, 57.3, 56.0, 56.0, 53.8 (d, *J* = 2.8 Hz), 40.6 (q, J = 26.6 Hz), 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -62.27. **IR** (in KBr): 3445, 3127, 1617, 1526, 1400, 1244, 1166, 1110, 907, 657, 543 cm^{-1}. **HRMS** (ESI) for: $C_{26}H_{28}F_3N_2O_4S$ $[M + H]^+$: calcd: 521.1716, found: 521.1700.

3-benzyl-1-(phenylsulfonyl)-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (5ka)

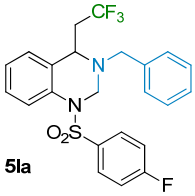


5ka

71.4 mg, colorless liquid, 80% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.79 (d, *J* = 8.1 Hz, 2H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.34 – 7.25 (m, 5H), 7.21 (t, *J* =

7.8 Hz, 1H), 7.04 (t, *J* = 7.4 Hz, 1H), 6.97 (d, *J* = 7.5 Hz, 1H), 5.05 (d, *J* = 12.7 Hz, 1H), 4.64 (d, *J* = 12.0 Hz, 1H), 3.97 – 3.94 (m, 1H), 3.87 (d, *J* = 13.5 Hz, 1H), 3.56 (d, *J* = 13.5 Hz, 1H), 2.38 – 2.24 (m, 1H), 2.16 – 2.03 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 139.7, 136.8, 135.5, 133.1, 129.2, 129.1, 128.3, 128.1, 127.6, 126.8, 125.4 (q, *J* = 278.8 Hz), 125.1, 123.8, 120.0, 62.4, 57.1, 54.2 (q, *J* = 2.7 Hz), 40.9 (q, *J* = 26.8 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.27. **IR** (in KBr): 3443, 3128, 1604, 1492, 1400, 1253, 1163, 914, 755, 588 cm^{-1}. **HRMS** (ESI) for: $C_{23}H_{22}F_3N_2O_2S$ $[M + H]^+$: calcd: 447.1349, found: 447.1356.

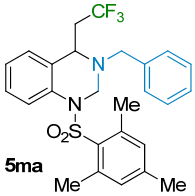
3-benzyl-1-((4-fluorophenyl)sulfonyl)-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (5la)



5la

69.7 mg, white solid, 75% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.82 – 7.79 (m, 2H), 7.66 (d, *J* = 8.4 Hz, 1H), 7.34 – 7.28 (m, 5H), 7.24 – 7.14 (m, 3H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.99 (d, *J* = 7.5 Hz, 1H), 5.03 (d, *J* = 12.7 Hz, 1H), 4.63 (d, *J* = 12.7 Hz, 1H), 3.99 – 3.96 (m, 1H), 3.86 (d, *J* = 13.4 Hz, 1H), 3.57 (d, *J* = 13.4 Hz, 1H), 2.44 – 2.30 (m, 1H), 2.23 – 2.10 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 165.2 (d, *J* = 255.9 Hz), 135.8 (d, *J* = 3.3 Hz), 129.6 (d, *J* = 9.4 Hz), 125.3 (q, *J* = 278.8 Hz), 116.5 (d, *J* = 22.7 Hz), 54.3 (q, *J* = 2.7 Hz), 41.0 (q, *J* = 26.9 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.23, -104.12. **IR** (in KBr): 3443, 3125, 1592, 1400, 1249, 1152, 837, 577 cm^{-1}. **HRMS** (ESI) for: $C_{23}H_{21}F_4N_2O_2S$ $[M + H]^+$: calcd: 465.1254, found: 465.1248.

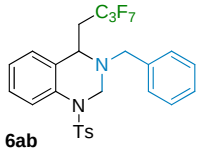
3-benzyl-1-(mesitylsulfonyl)-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydroquinazoline (5ma)



5ma

62.5 mg, white solid, 64% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.40 (d, *J* = 7.2 Hz, 2H), 7.34 – 7.25 (m, 3H), 7.07 – 7.01 (m, 5H), 6.77 (d, *J* = 7.7 Hz, 1H), 5.27 (d, *J* = 13.3 Hz, 1H), 4.61 (d, *J* = 13.3 Hz, 1H), 4.09 (d, *J* = 13.2 Hz, 2H), 3.72 (d, *J* = 13.6 Hz, 1H), 2.66 – 2.57 (m, 7H), 2.43 – 2.26 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 142.8, 138.7, 137.2, 136.6, 132.5, 129.4, 128.4, 128.1, 127.7, 127.4, 125.6 (q, *J* = 278.8 Hz), 125.0, 123.7, 119.1, 61.3, 57.1, 54.0 (q, *J* = 2.8 Hz), 41.9 (q, *J* = 26.6 Hz), 22.6, 21.0. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -63.16. **IR** (in KBr): 3444, 3128, 1604, 1400, 1152, 993, 755, 663, 602, 529 cm^{-1}. **HRMS** (ESI) for: $C_{26}H_{28}F_3N_2O_2S$ $[M + H]^+$: calcd: 489.1818, found: 489.1829.

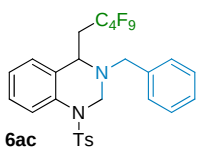
3-benzyl-4-(2,2,3,3,4,4,4-heptafluorobutyl)-1-tosyl-1,2,3,4-tetrahydroquinazoline (6ab)



6ab

84.1 mg, colorless liquid, 75% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.75 (d, *J* = 8.4 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.33 – 7.20 (m, 8H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.96 (d, *J* = 7.5 Hz, 1H), 4.98 (d, *J* = 12.6 Hz, 1H), 4.61 (d, *J* = 12.6 Hz, 1H), 4.10 – 4.07 (m, 1H), 3.84 (d, *J* = 13.4 Hz, 1H), 3.59 (d, *J* = 13.4 Hz, 1H), 2.38 (s, 3H), 2.30 – 2.15 (m, 1H), 2.06 – 1.94 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 144.1, 136.8, 136.4, 135.6, 129.7, 129.1, 128.3, 128.2, 127.6, 126.9, 125.6, 123.8, 120.4, 62.2, 57.2, 53.4 (d, *J* = 3.0 Hz), 37.4 (t, *J* = 20.5 Hz), 21.4. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -80.30 (t, *J* = 10.3 Hz, 3F), -112.58 – -115.31 (m, 2F), -127.79 (t, *J* = 7.5 Hz, 2F). **IR** (in KBr): 3415, 3129, 1638, 1400, 1220, 1169, 1093, 911, 671, 578 cm^{-1}. **HRMS** (ESI) for: $C_{26}H_{24}F_7N_2O_2S$ $[M + H]^+$: calcd: 561.1441, found: 561.1440.

3-benzyl-4-(2,2,3,3,4,4,5,5,5-nonafluoropentyl)-1-tosyl-1,2,3,4-tetrahydroquinazoline (6ac)

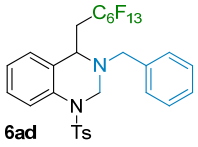


6ac

95.2 mg, colorless liquid, 78% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.75 (d, *J* = 8.4 Hz, 1H), 7.64 (d, *J* = 8.1 Hz, 2H), 7.35 – 7.21 (m, 8H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 4.99 (d, *J* = 12.6 Hz, 1H), 4.60 (d, *J* = 12.6 Hz, 1H), 4.10 – 4.07 (m, 1H), 3.85 (d, *J* = 13.4 Hz, 1H), 3.59 (d, *J* = 13.4 Hz, 1H), 2.38 (s, 3H), 2.31 – 2.15 (m, 1H), 2.06 – 1.94 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 144.1, 136.8, 136.4, 135.6, 129.7, 129.1, 128.3, 128.2, 127.6, 126.9, 125.6, 123.8, 120.4, 62.2, 57.2, 53.4 (d, *J* = 3.0 Hz), 37.6 (t, *J* = 20.5 Hz), 21.4. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -81.07 (t, *J* = 10.2 Hz, 3F), -111.80 – -114.50 (m, 2F), -124.43 – -

124.52 (m, 2F), -125.85 – -125.97 (m, 2F). **IR** (in KBr): 3442, 3127, 1603, 1400, 1236, 1168, 1000, 755, 672, 578 cm^{-1}. **HRMS** (ESI) for: $C_{27}H_{24}F_9N_2O_2S$ $[M + H]^+$: calcd: 611.1409, found: 611.1414.

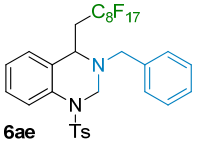
3-benzyl-1-tosyl-4-(2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptyl)-1,2,3,4-tetrahydroquinazoline (6ad)



6ad

93.8 mg, colorless liquid, 66% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.76 (d, *J* = 8.4 Hz, 1H), 7.64 (d, *J* = 8.1 Hz, 2H), 7.34 – 7.21 (m, 8H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.96 (d, *J* = 7.5 Hz, 1H), 4.98 (d, *J* = 12.6 Hz, 1H), 4.61 (d, *J* = 12.6 Hz, 1H), 4.10 – 4.07 (m, 1H), 3.84 (d, *J* = 13.4 Hz, 1H), 3.59 (d, *J* = 13.4 Hz, 1H), 2.37 (s, 3H), 2.31 – 2.16 (m, 1H), 2.06 – 1.95 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 144.1, 136.8, 136.4, 135.6, 129.7, 129.1, 128.3, 128.2, 127.6, 126.9, 125.7, 123.9, 120.4, 62.3, 57.3, 53.5 (d, *J* = 2.7 Hz), 37.7 (t, *J* = 20.5 Hz), 21.4. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -80.79 (t, *J* = 11.3 Hz, 3F), -111.62 – -114.24 (m, 2F), -121.80 (s, 2F), -122.91 (s, 2F), -123.50 – -123.58 (m, 2F), -126.13 – -126.21 (m, 2F). **IR** (in KBr): 3445, 3128, 1604, 1492, 1400, 1240, 1168, 913, 752, 578 cm^{-1}. **HRMS** (ESI) for: $C_{29}H_{24}F_{13}N_2O_2S$ $[M + H]^+$: calcd: 711.1345, found: 711.1343.

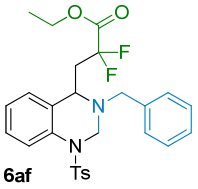
3-benzyl-4-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-heptadecafluorononyl)-1-tosyl-1,2,3,4-tetrahydroquinazoline (6ae)



6ae

105.4 mg, colorless liquid, 65% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.75 (d, *J* = 8.4 Hz, 1H), 7.64 (d, *J* = 8.1 Hz, 2H), 7.35 – 7.21 (m, 8H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.96 (d, *J* = 7.5 Hz, 1H), 4.98 (d, *J* = 12.6 Hz, 1H), 4.61 (d, *J* = 12.6 Hz, 1H), 4.10 – 4.07 (m, 1H), 3.85 (d, *J* = 13.4 Hz, 1H), 3.59 (d, *J* = 13.4 Hz, 1H), 2.37 (s, 3H), 2.31 – 2.15 (m, 1H), 2.06 – 1.94 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 144.1, 136.8, 136.4, 135.6, 129.7, 129.2, 128.3, 128.2, 127.6, 126.9, 125.7, 123.9, 120.4, 62.3, 57.3, 53.5 (d, *J* = 2.9 Hz), 37.7 (t, *J* = 20.5 Hz), 21.3. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -80.83 (t, *J* = 9.9 Hz, 3F), -111.63 – -114.22 (m, 2F), -121.62 (s, 2F), -121.99 (s, 4F), -122.76 (s, 2F), -123.50 (s, 2F), -126.18 (s, 2F). **IR** (in KBr): 3444, 3125, 1603, 1493, 1349, 1202, 1149, 1007, 753, 670, 578 cm^{-1}. **HRMS** (ESI) for: $C_{31}H_{23}F_{17}N_2NaO_2S$ $[M + Na]^+$: calcd: 833.1101, found: 833.1098.

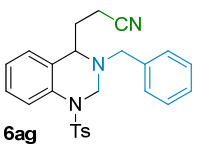
Ethyl 3-(3-benzyl-1-tosyl-1,2,3,4-tetrahydroquinazolin-4-yl)-2,2-difluoropropanoate (6af)



6af

77.2 mg, white solid, 75% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.69 (d, *J* = 8.1 Hz, 2H), 7.63 (d, *J* = 8.5 Hz, 1H), 7.35 – 7.26 (m, 7H), 7.17 (t, *J* = 7.5 Hz, 1H), 7.01 (q, *J* = 6.9, 6.2 Hz, 2H), 4.96 (d, *J* = 12.7 Hz, 1H), 4.58 (d, *J* = 12.7 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 4.00 – 3.96 (m, 1H), 3.83 (d, *J* = 13.0 Hz, 1H), 3.55 (d, *J* = 13.0 Hz, 1H), 2.68 – 2.53 (m, 1H), 2.40 (s, 3H), 2.24 – 2.10 (m, 1H), 1.34 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 164.0 – 163.3 (m), 144.0, 136.8, 136.4, 135.5, 129.8, 128.3, 128.2, 127.9, 127.7, 126.8, 124.4, 123.4, 119.2, 117.1 – 112.1 (m), 62.8, 61.1, 57.2, 55.0 – 54.9 (m), 40.9 (t, *J* = 22.7 Hz), 21.5, 13.9. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -99.34 (d, *J* = 269.9 Hz, 1F), -109.78 (d, *J* = 270.0 Hz, 1F). **IR** (in KBr): 3446, 3128, 1773, 1492, 1336, 1170, 1001, 674, 544 cm^{-1}. **HRMS** (ESI) for: $C_{27}H_{29}F_2N_2O_4S$ $[M + H]^+$: calcd: 515.1811, found: 515.1818.

3-(3-benzyl-1-tosyl-1,2,3,4-tetrahydroquinazolin-4-yl)propanenitrile (6ag)

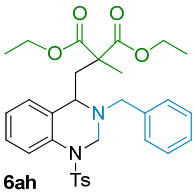


6ag

44.9 mg, colorless liquid, 52% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.68 (d, *J* = 8.4 Hz, 1H), 7.63 (d, *J* = 8.1 Hz, 2H), 7.39 – 7.31 (m, 3H), 7.27 (d, *J* = 7.8 Hz, 4H), 7.19 (t, *J* = 7.8 Hz, 1H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.98 (d, *J* = 7.5 Hz, 1H), 4.90 (d, *J* = 12.6 Hz, 1H), 4.69 (d, *J* = 12.6 Hz, 1H), 3.82 (d, *J* = 13.3 Hz, 1H), 3.62 – 3.59 (m, 1H), 3.56 (d, *J* = 13.3 Hz, 1H), 2.42 (s, 3H), 2.06 – 1.79 (m, 4H). **^{13}C NMR**

(101 MHz, $CDCl_3$) δ (ppm) 144.1, 137.0, 136.9, 135.8, 129.8, 129.4, 128.5, 128.0, 127.9, 127.7, 127.1, 126.1, 124.0, 120.5, 119.5, 63.0, 57.7, 57.0, 31.6, 21.5, 12.8. **IR** (in KBr): 3443, 3129, 1633, 1400, 1167, 1079, 889, 671, 571 cm^{-1}. **HRMS** (ESI) for: $C_{25}H_{26}N_3O_2S$ $[M + H]^+$: calcd: 432.1740, found: 432.1740.

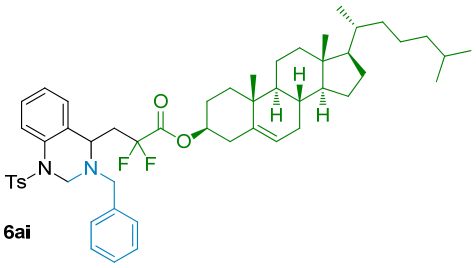
Diethyl 2-((3-benzyl-1-tosyl-1,2,3,4-tetrahydroquinazolin-4-yl)methyl)-2-methylmalonate (6ah)



6ah

65.5 mg, colorless liquid, 58% yield in 5 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.69 (d, *J* = 8.0 Hz, 2H), 7.58 (d, *J* = 8.5 Hz, 1H), 7.36 – 7.26 (m, 7H), 7.12 (t, *J* = 7.6 Hz, 1H), 7.03 – 6.96 (m, 2H), 4.94 (d, *J* = 12.5 Hz, 1H), 4.67 (d, *J* = 12.5 Hz, 1H), 4.23 – 4.07 (m, 4H), 3.84 – 3.76 (m, 2H), 3.50 (d, *J* = 12.8 Hz, 1H), 2.47 – 2.41 (m, 1H), 2.39 (s, 3H), 2.02 – 1.97 (m, 1H), 1.30 – 1.27 (m, 6H), 1.20 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 172.3, 171.4, 143.8, 137.0, 136.7, 135.4, 130.1, 129.7, 128.6, 128.1, 127.5, 127.3, 126.7, 125.8, 122.9, 118.5, 61.4, 61.2, 61.1, 57.2, 56.2, 52.1, 41.2, 21.4, 19.1, 14.0, 13.9. **IR** (in KBr): 3422, 3127, 1730, 1400, 1235, 1167, 1095, 917, 671, 596 cm^{-1}. **HRMS** (ESI) for: $C_{31}H_{37}N_2O_6S$ $[M + H]^+$: calcd: 565.2367, found: 565.2384.

(3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl-3-(3-benzyl-1-tosyl-1,2,3,4-tetrahydroquinazolin-4-yl)-2,2-difluoropropanoate (6ai)

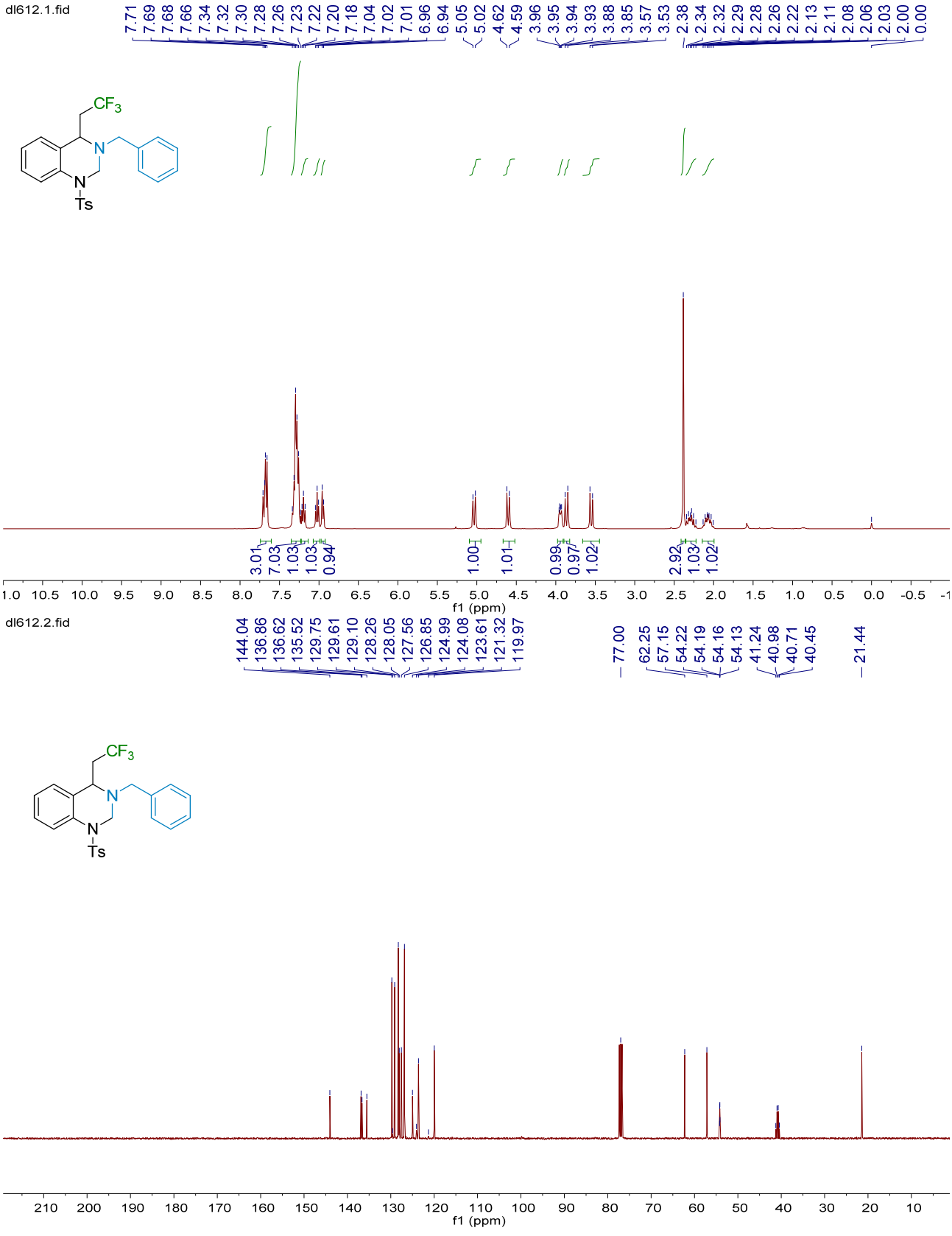


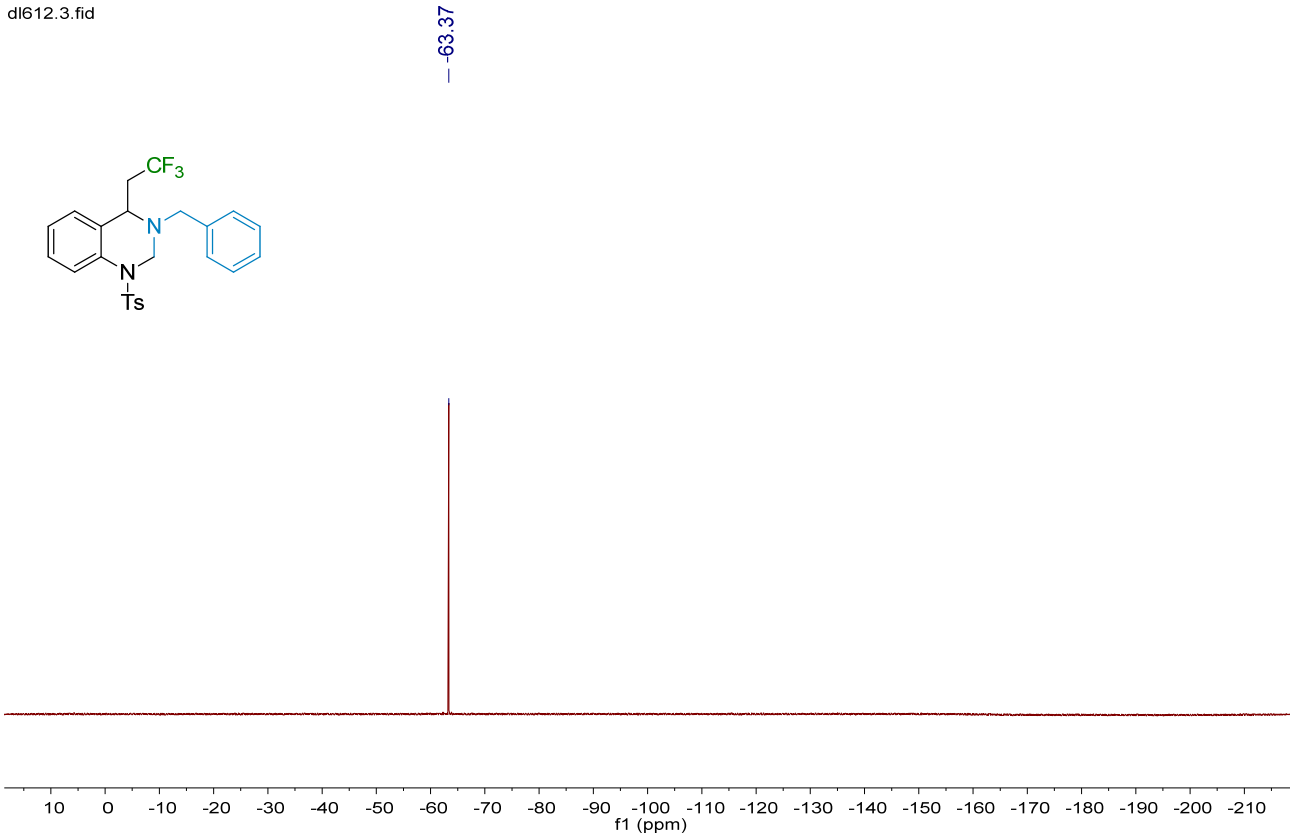
6ai

100.9 mg, colorless liquid, 59% yield in 5 h, d.r. > 19:1. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.70 – 7.65 (m, 3H), 7.34 – 7.25 (m, 7H), 7.17 (t, *J* = 8.3 Hz, 1H), 7.00 (q, *J* = 8.8, 8.1 Hz, 2H), 5.42 – 5.35 (m, 1H), 4.99 – 4.94 (m, 1H), 4.77 – 4.67 (m, 1H), 4.61 (d, *J* = 12.6 Hz, 1H), 3.96 (d, *J* = 8.5 Hz, 1H), 3.85 – 3.80 (m, 1H), 3.55 (d, *J* = 13.1 Hz, 1H), 2.64 – 2.48 (m, 1H), 2.39 (s, 3H), 2.36 – 2.27 (m, 1H), 2.18 – 1.80 (m, 6H), 1.72 – 1.26 (m, 13H), 1.19 – 1.07 (m, 7H), 1.03 (s, 4H), 0.92 (d, *J* = 6.4 Hz, 3H), 0.87 (d, *J* = 6.4 Hz, 7H), 0.69 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm) 163.4 – 162.7 (m), 144.0 (d, *J* = 1.6 Hz), 138. 7 (d, *J* = 12.3 Hz), 136.8 (d, *J* = 4.5 Hz), 136.4, 135.5 (d, *J* = 2.7 Hz), 129.8, 129.7 (d, *J* = 1.7 Hz), 128.3, 128.2, 127.9, 127.6 (d, *J* = 3.1 Hz), 126.8, 124.5, 123.5 (d, *J* = 6.4 Hz), 123.3, 119.2, 117.1 – 112.1 (m), 61.5 (d, *J* = 9.5 Hz), 57.2, 56.6, 56.1, 54.8 – 54.6 (m), 49.9 (d, *J* = 2.0 Hz), 42.3, 41.2 – 40.7 (m), 39.7, 39.5, 37.6, 36.8 (d, *J* = 5.7 Hz), 36.5, 36.1, 35.8, 31.9, 31.8, 28.2, 28.0, 27.4 (d, *J* = 5.0 Hz), 24.3, 23.8, 22.8, 22.5, 21.5, 21.0, 19.3 (d, *J* = 1.2 Hz), 18.7, 11.8. **^{19}F NMR** (376 MHz, $CDCl_3$) δ (ppm) -98.81 – -99.70 (m, 1F), -108.17 – -109.28 (m, 1F). **IR** (in KBr): 3443, 3129, 2951, 1767, 1400, 1168, 1090, 752, 576 cm^{-1}. **HRMS** (ESI) for: $C_{52}H_{68}F_2N_2NaO_4S$ $[M + Na]^+$: calcd: 877.4760, found: 877.4750.

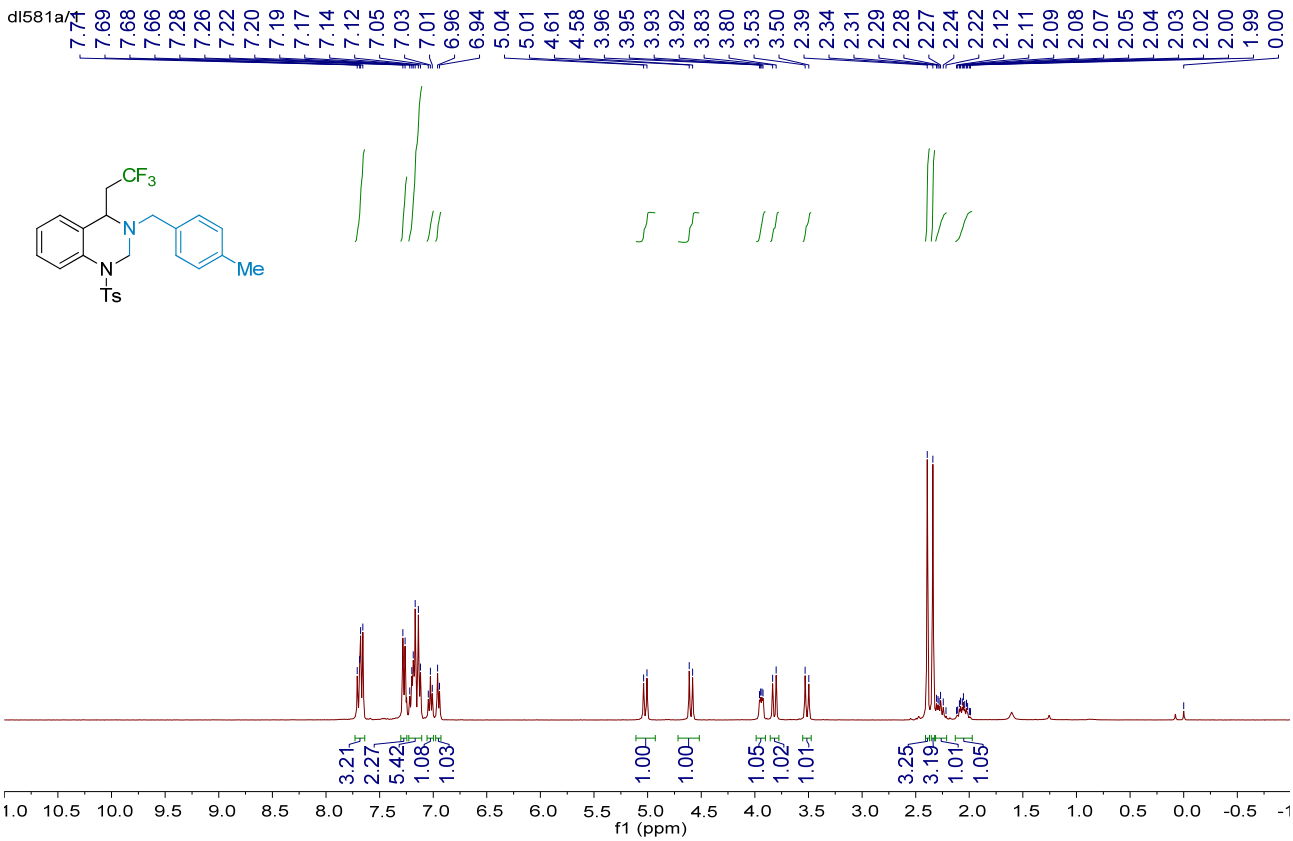
7. Copies of ^{1}H NMR, ^{13}C NMR and ^{19}F NMR Spectra

^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 4aa





^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 4ab



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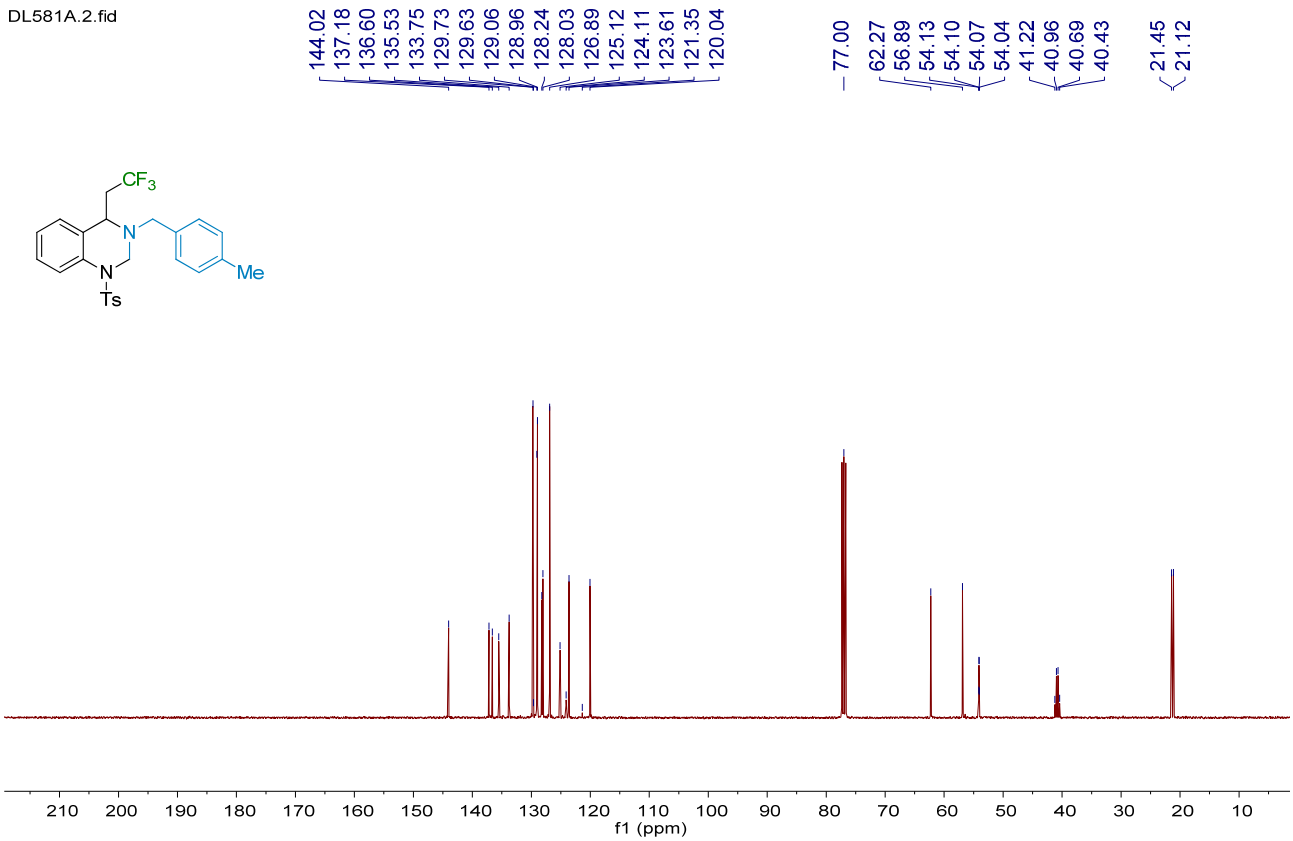
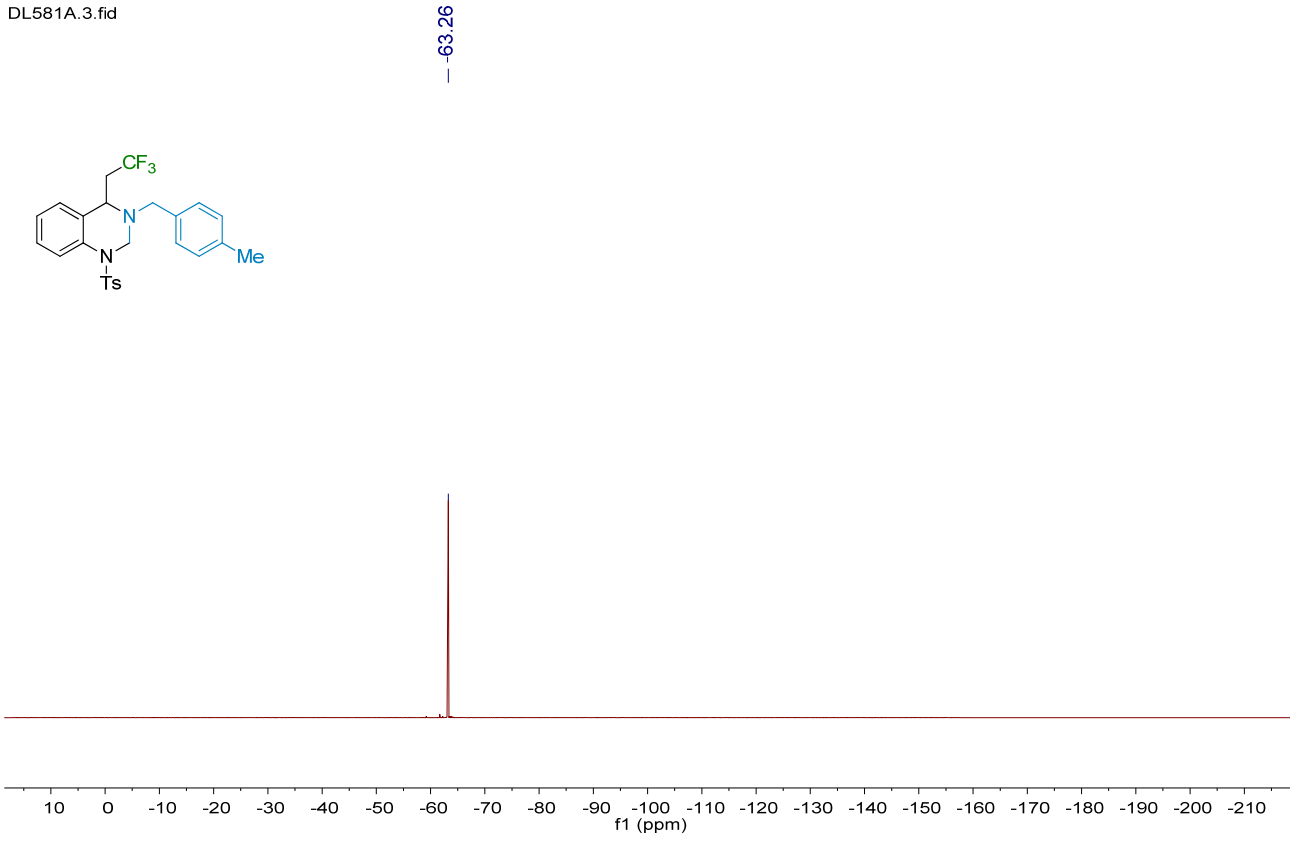
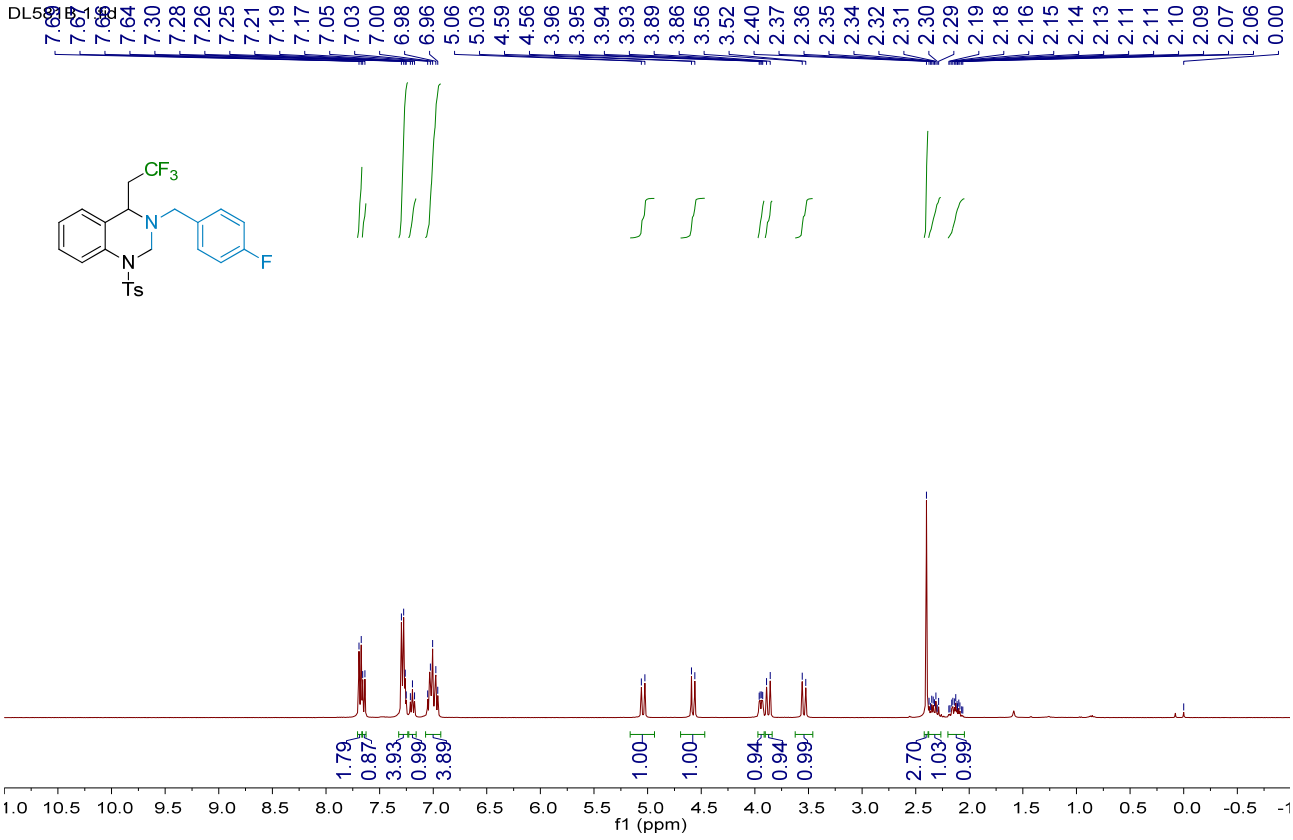
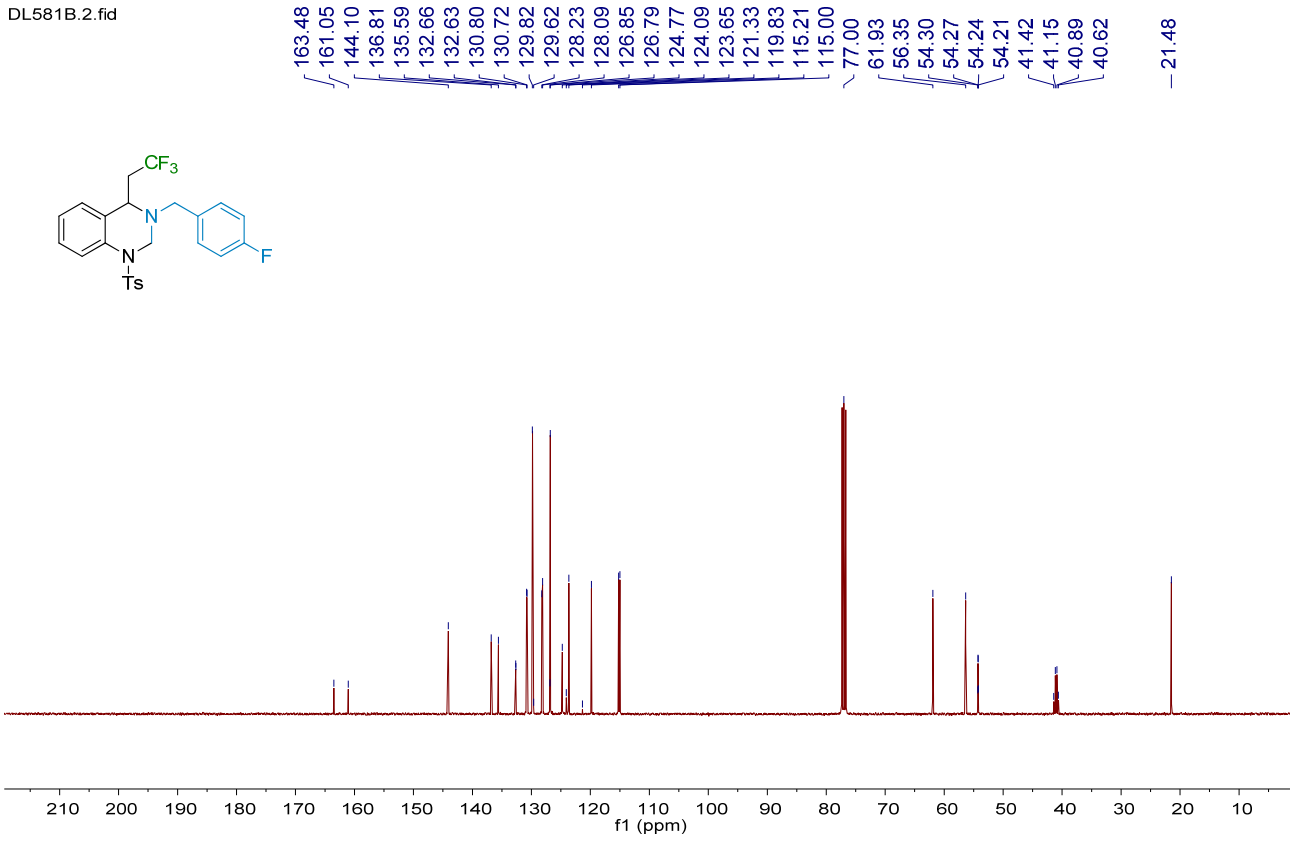


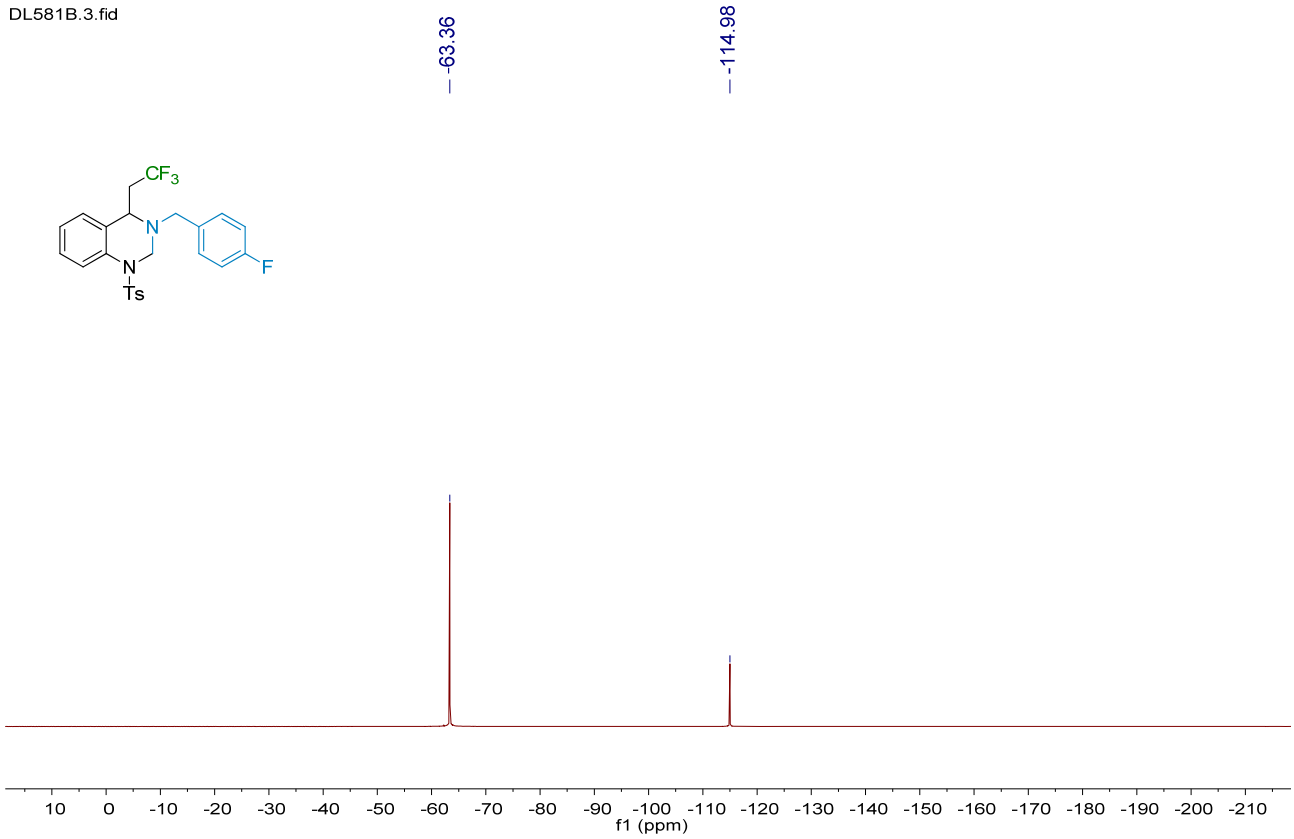
DL581A.3.fid



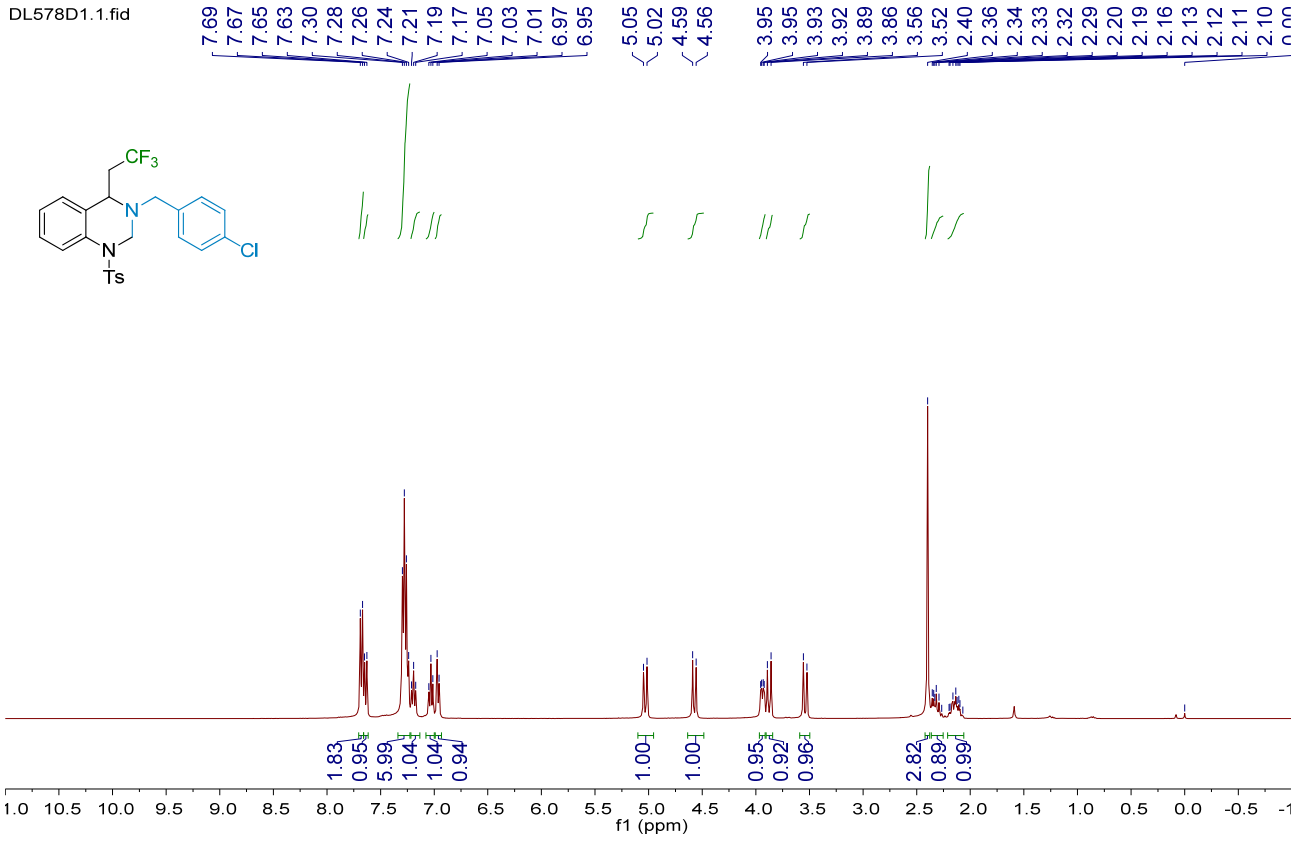
^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 4ac







^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 4ad



DL578D1.2.fid

144.11
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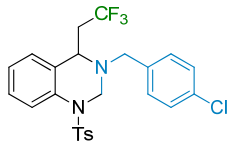
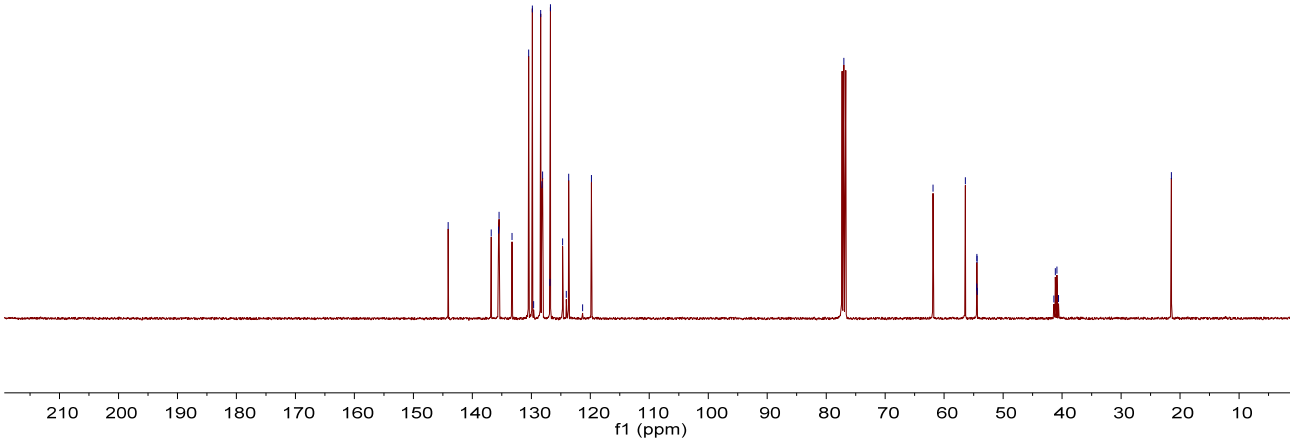
21.47





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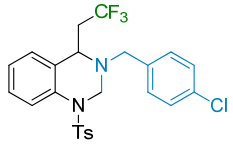
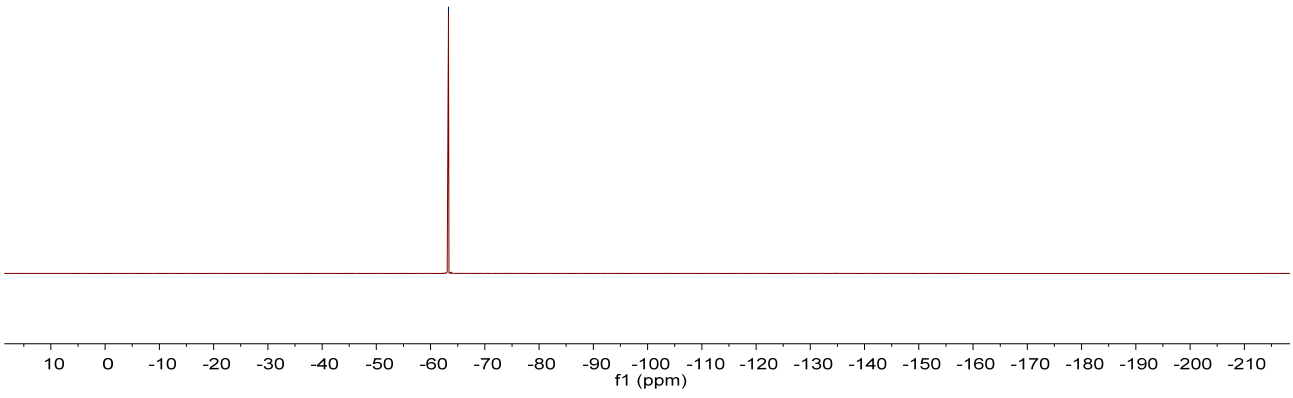
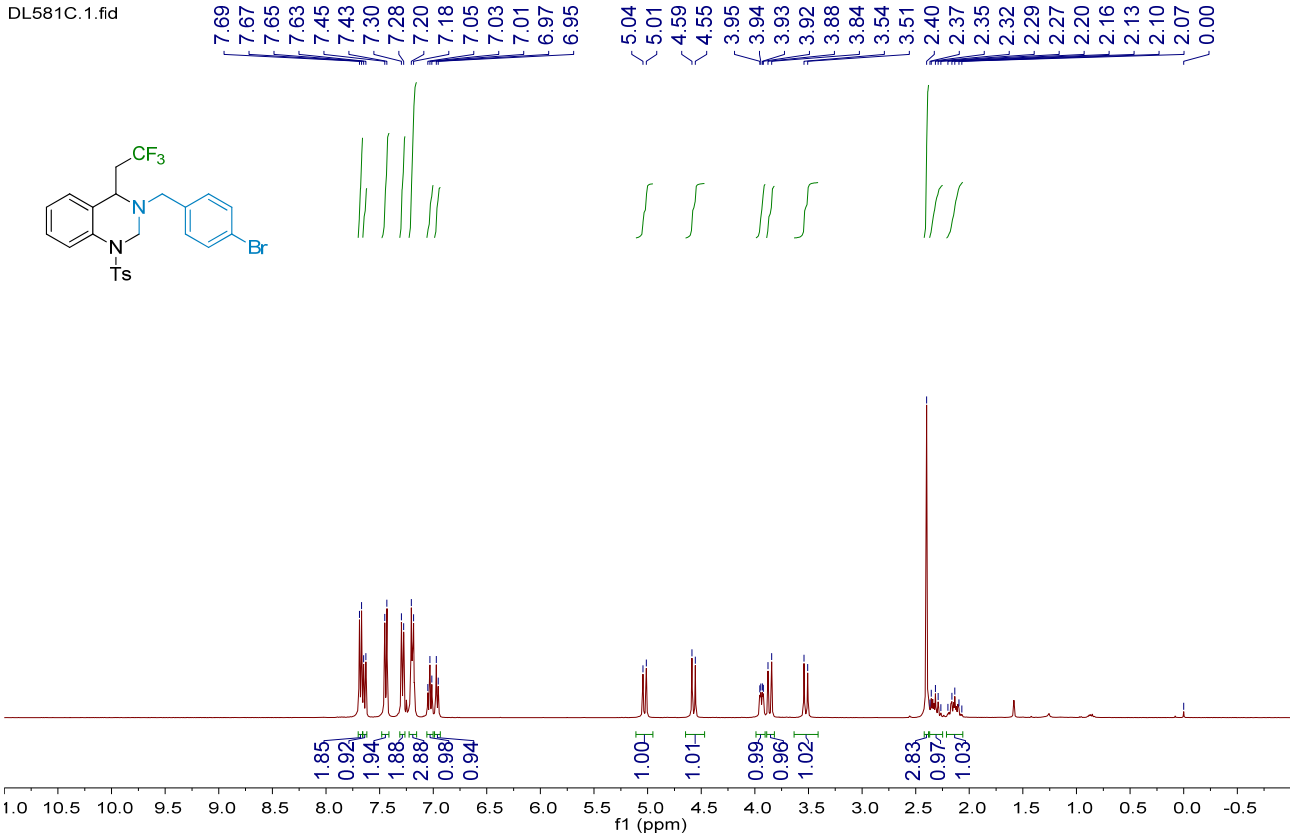
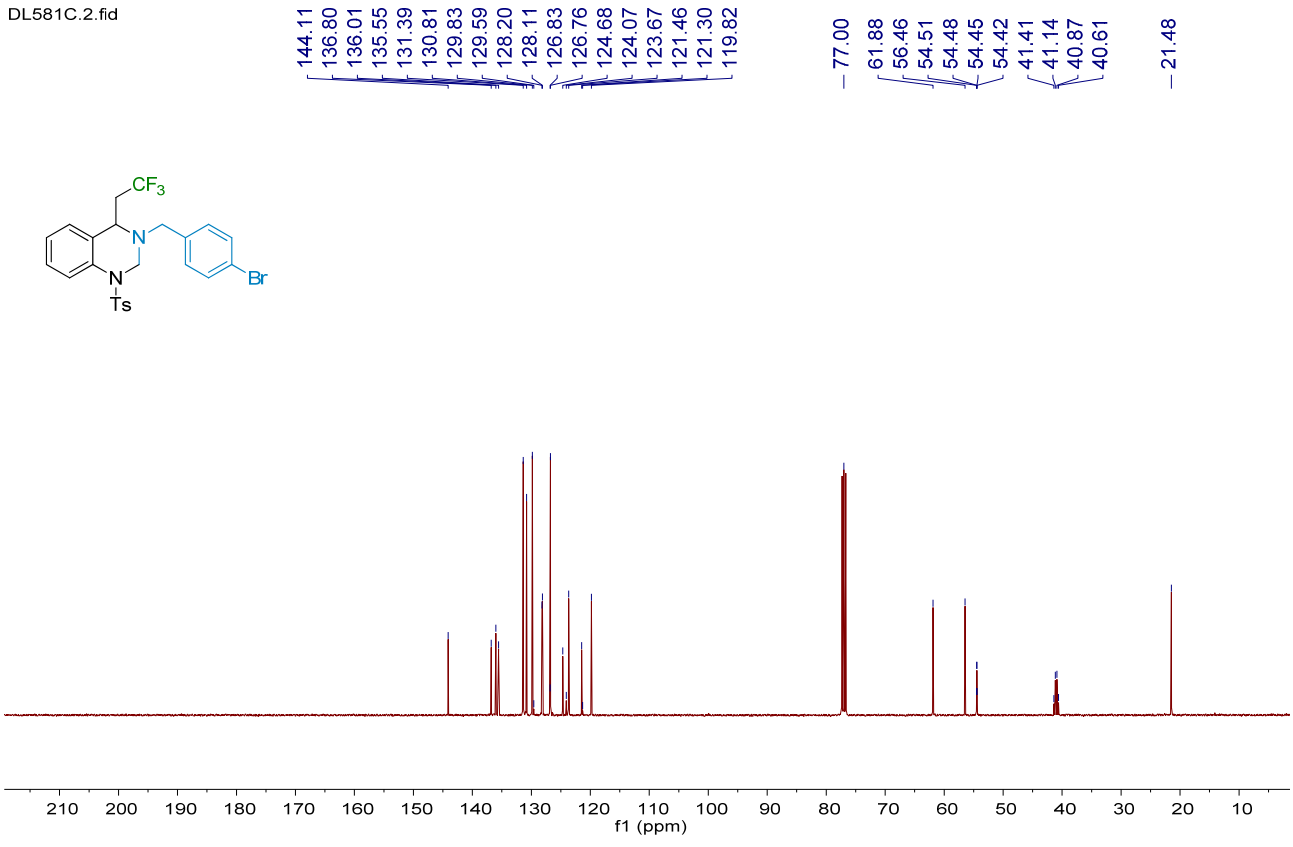
-63.29

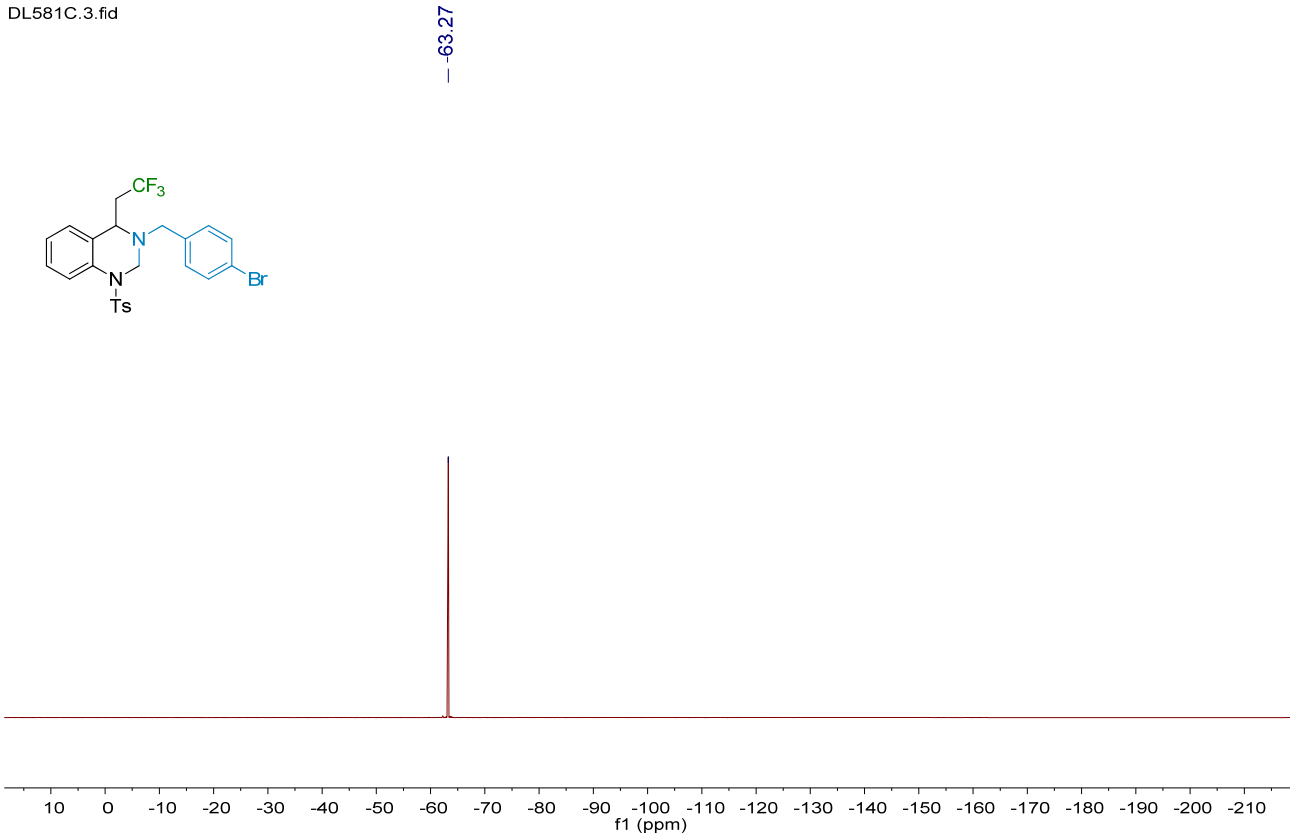




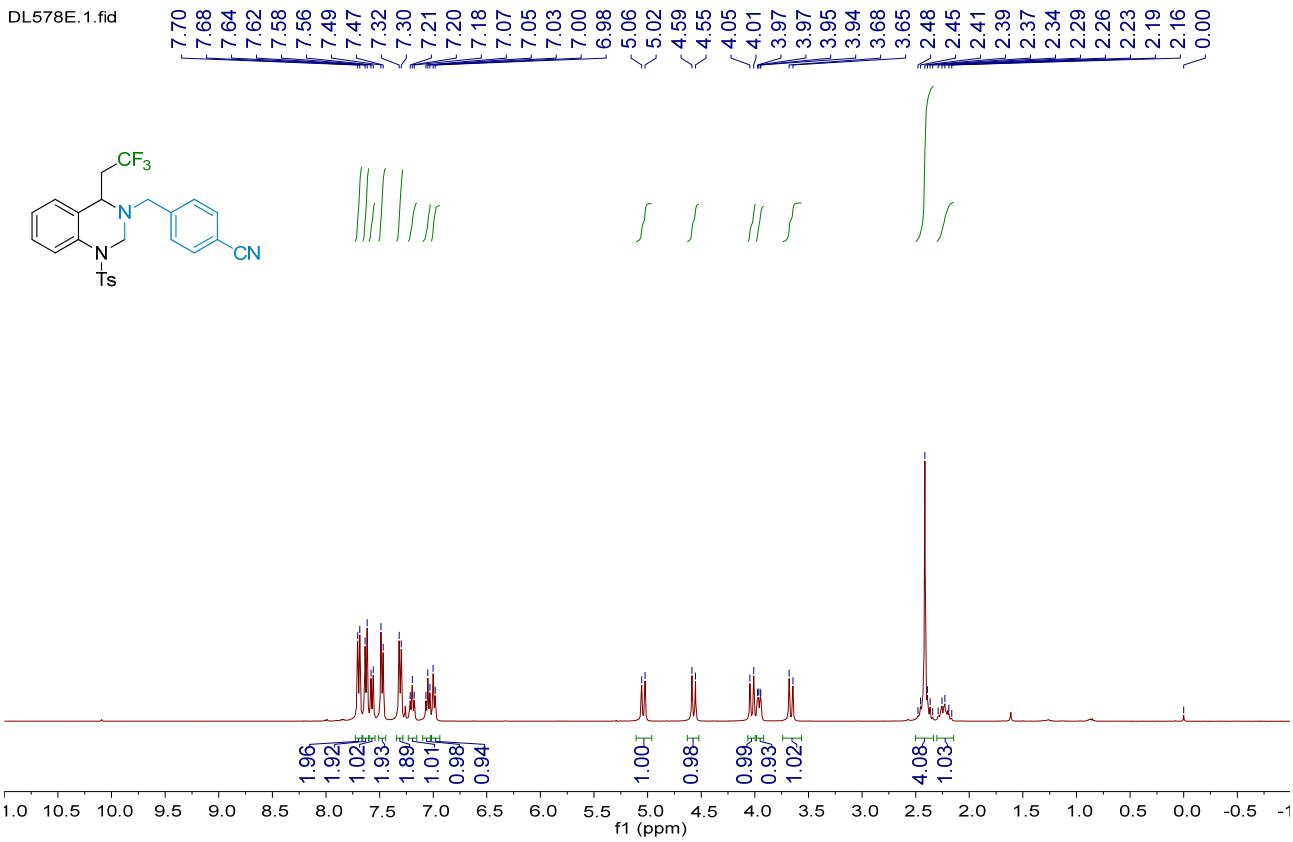
^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 4ae







^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 4af



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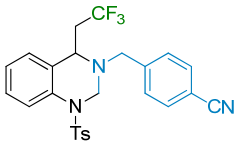

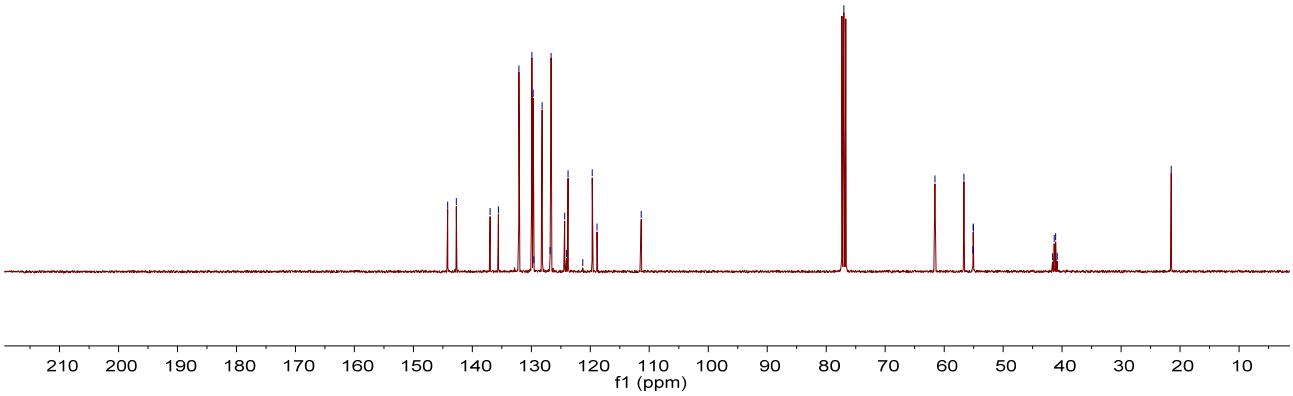

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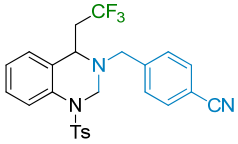
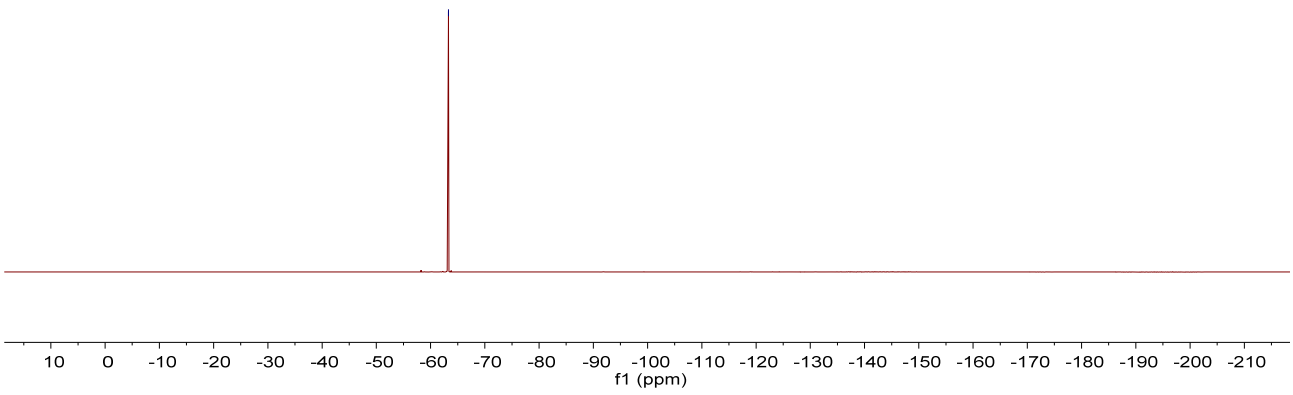
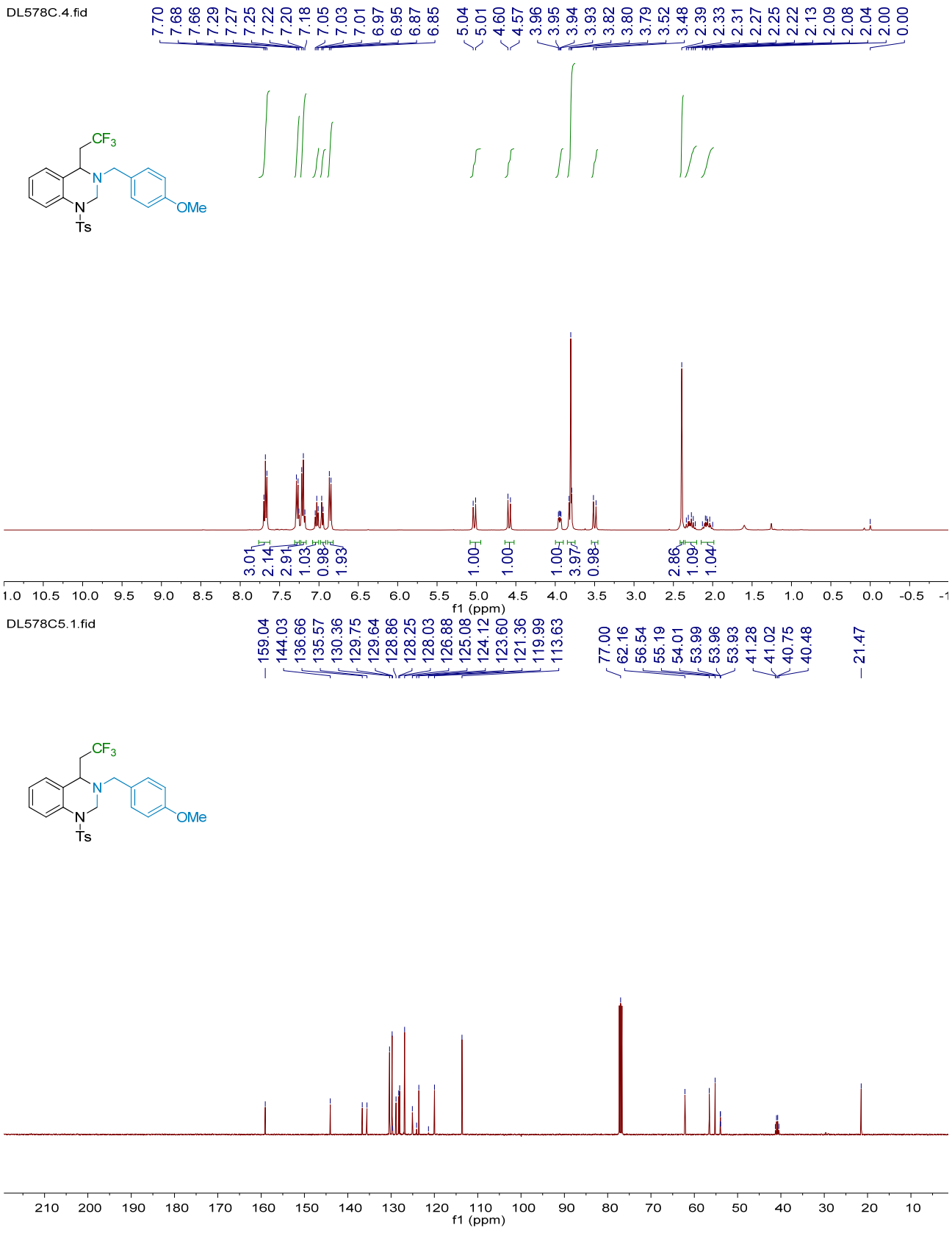
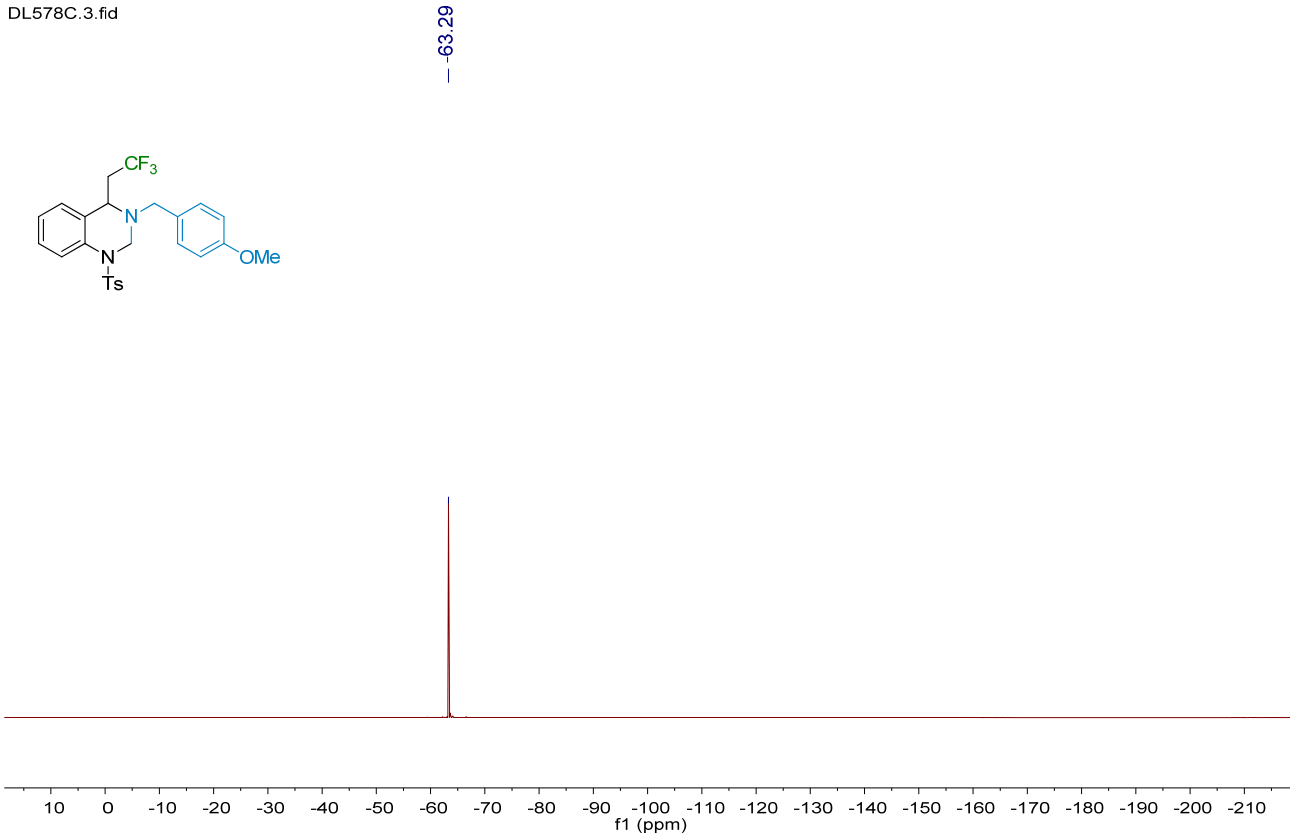


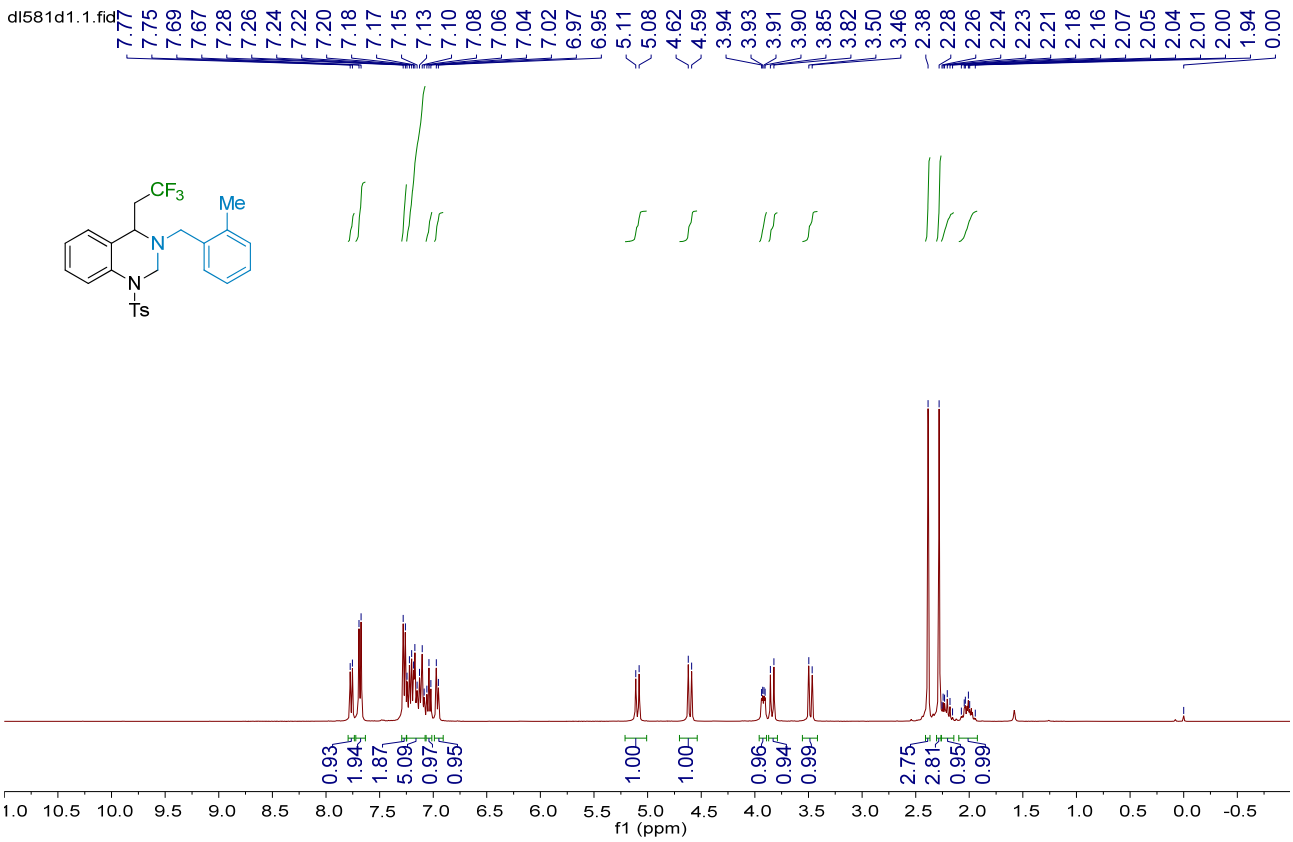


^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 4ag





^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 4ah



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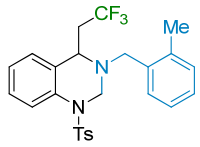

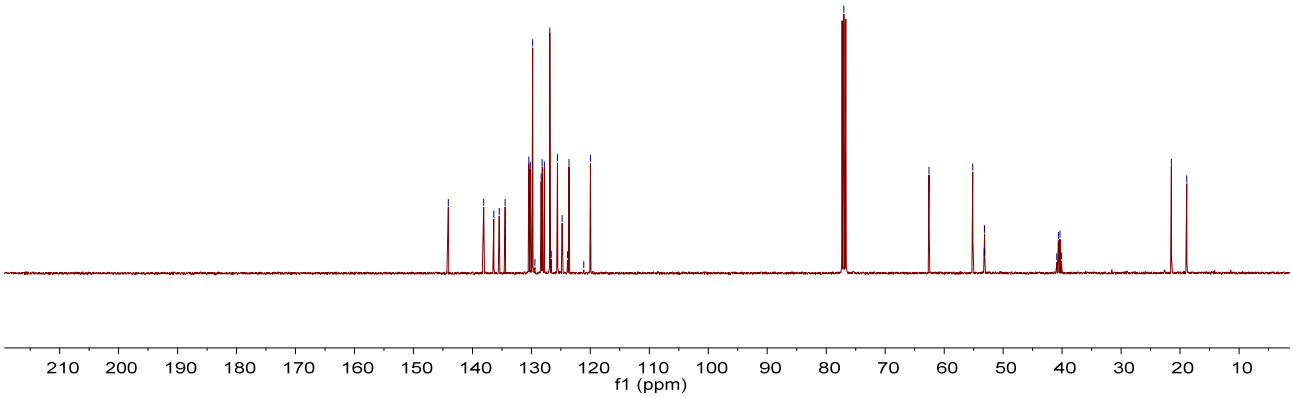

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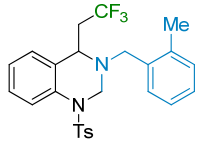
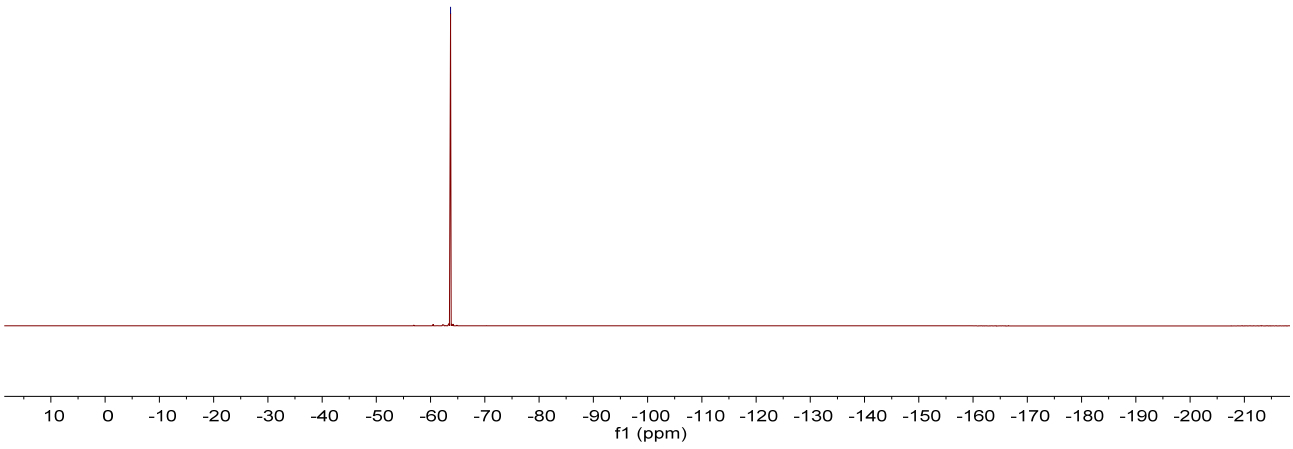
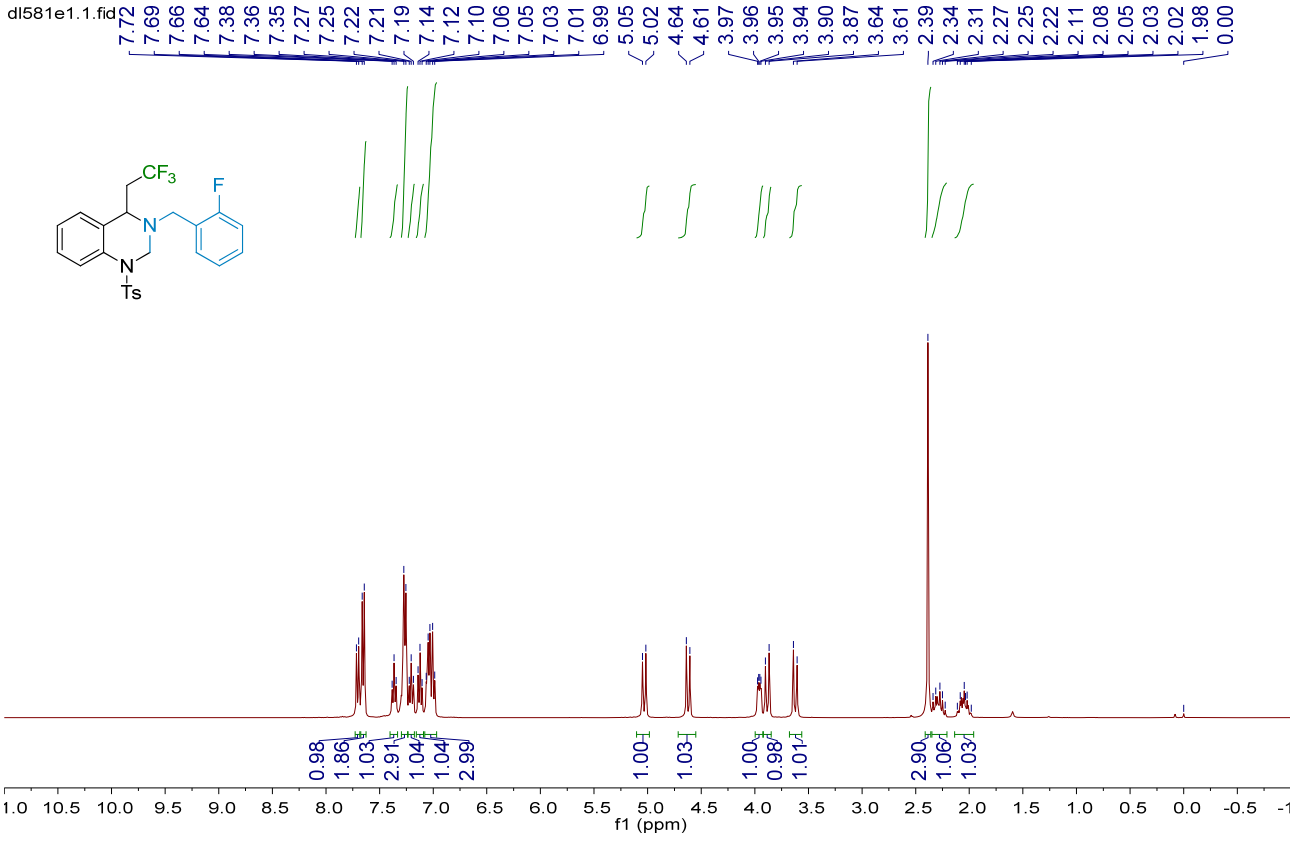
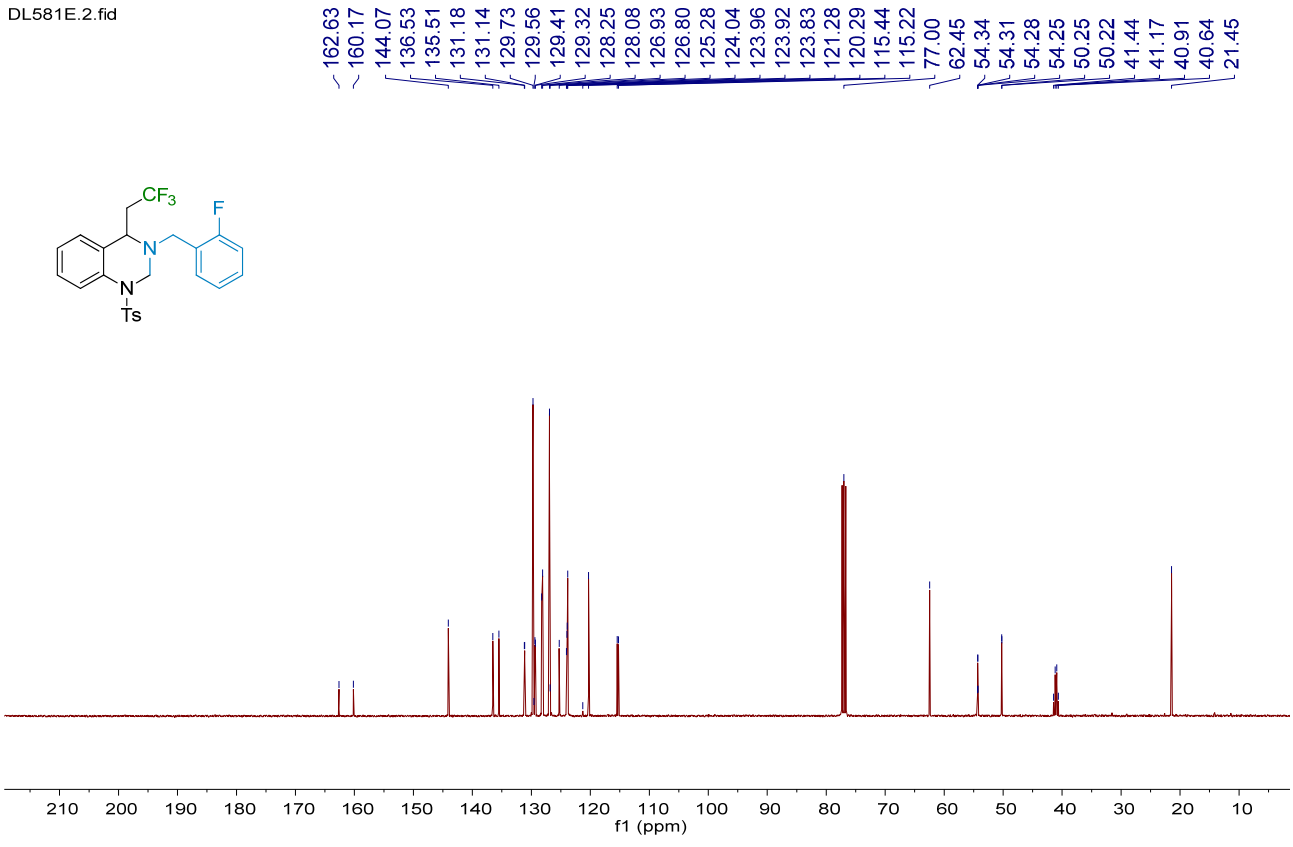




^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 4ai





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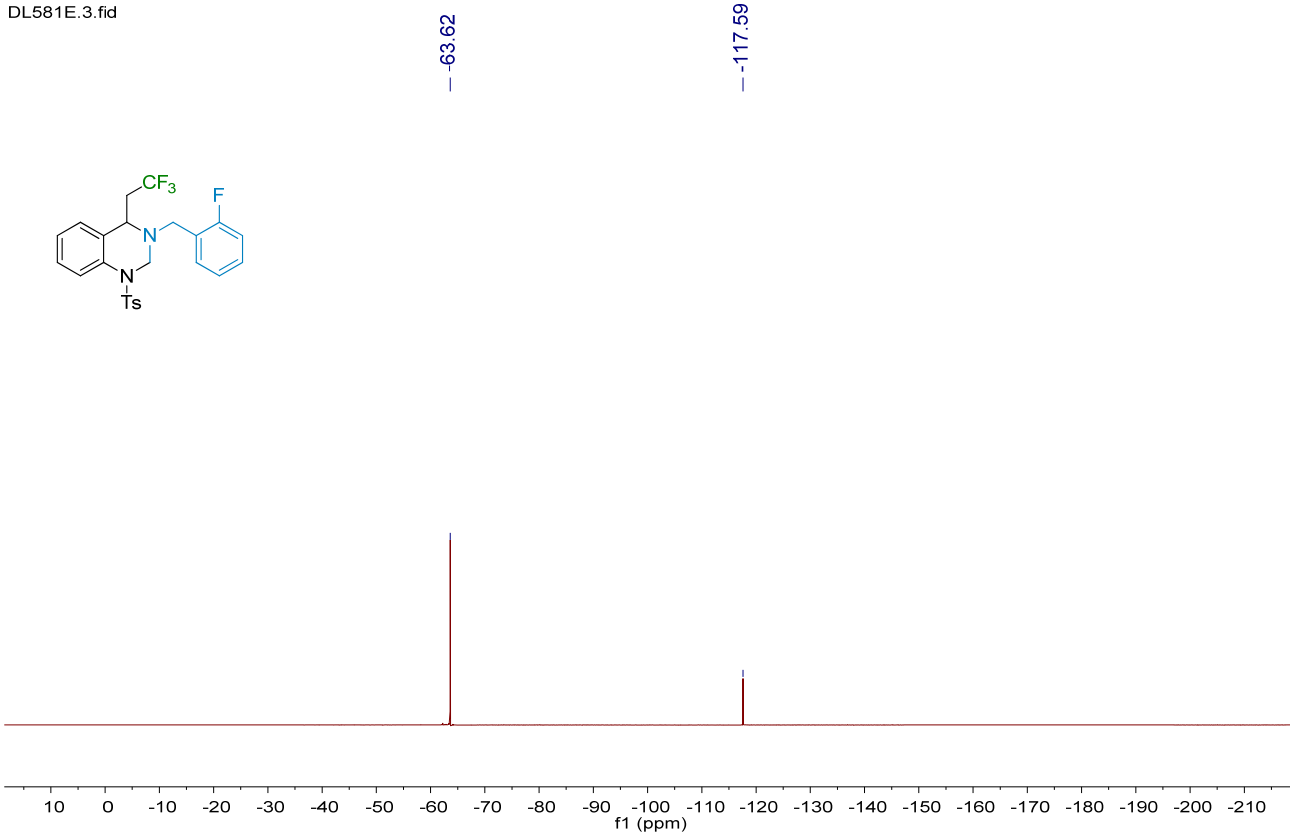
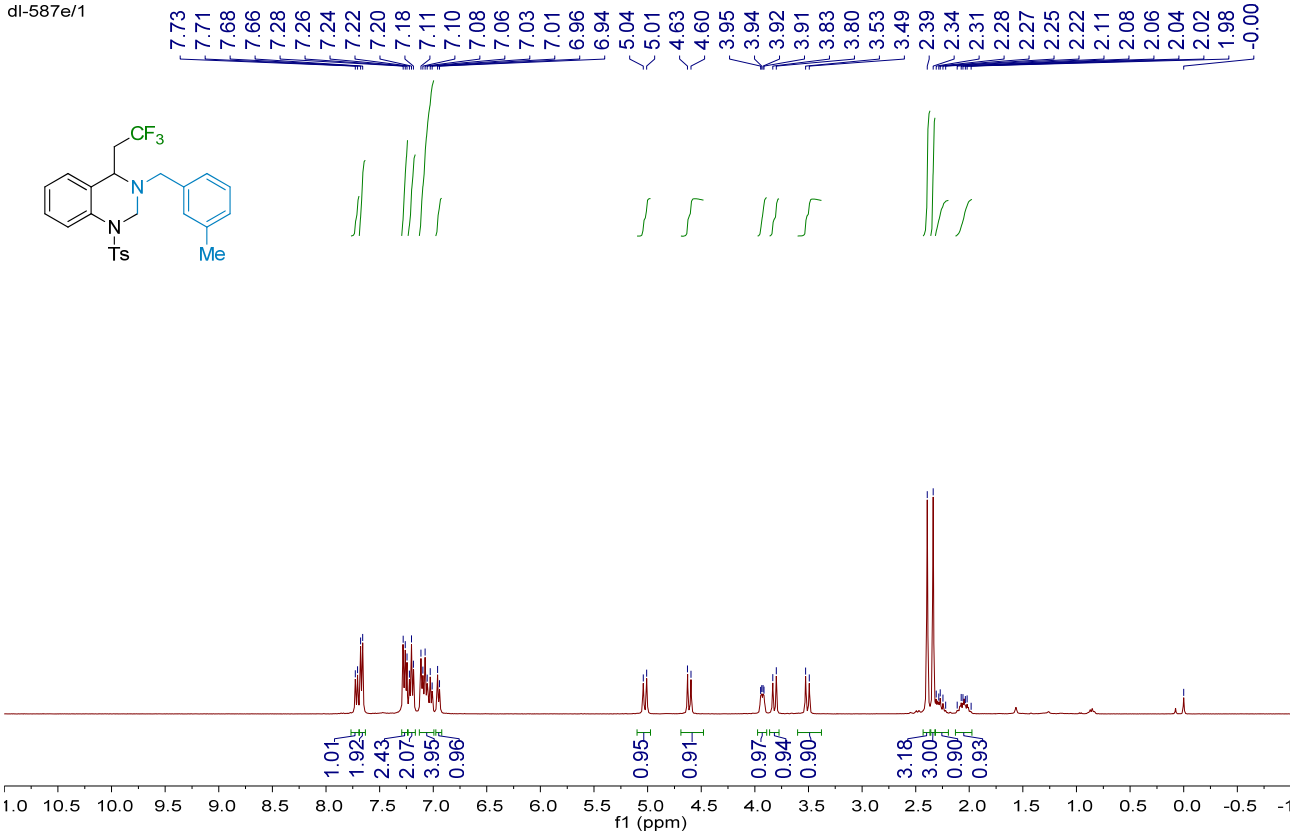


^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 4aj

dl-587e/1



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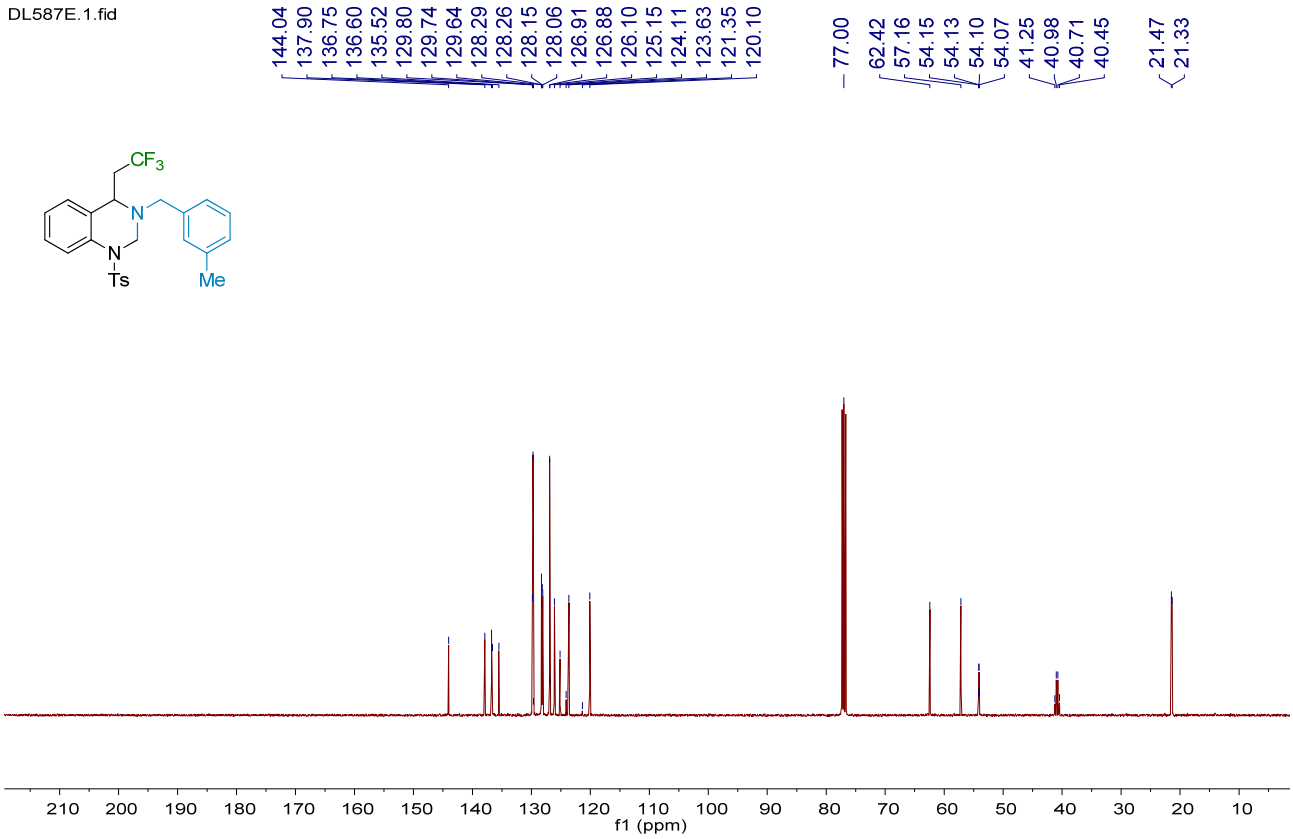

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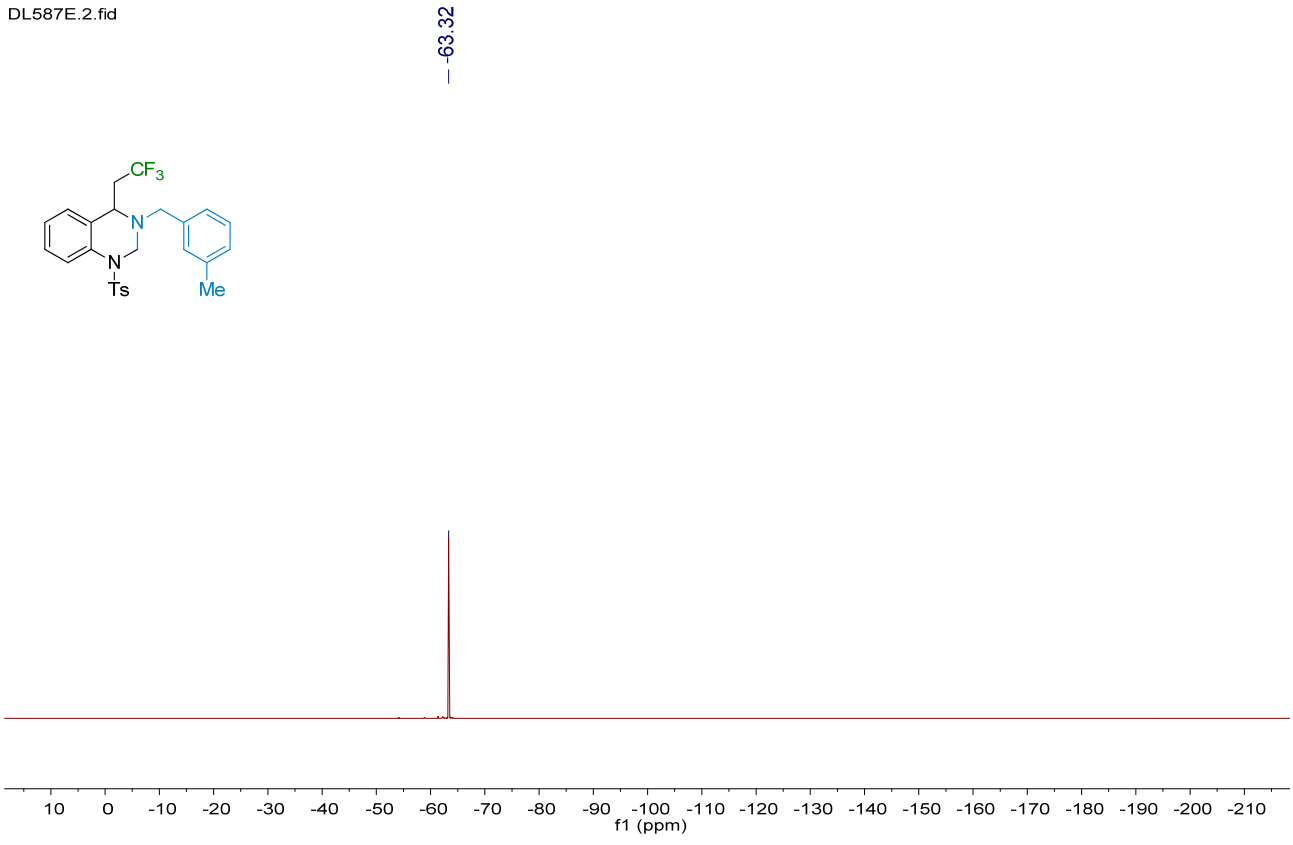
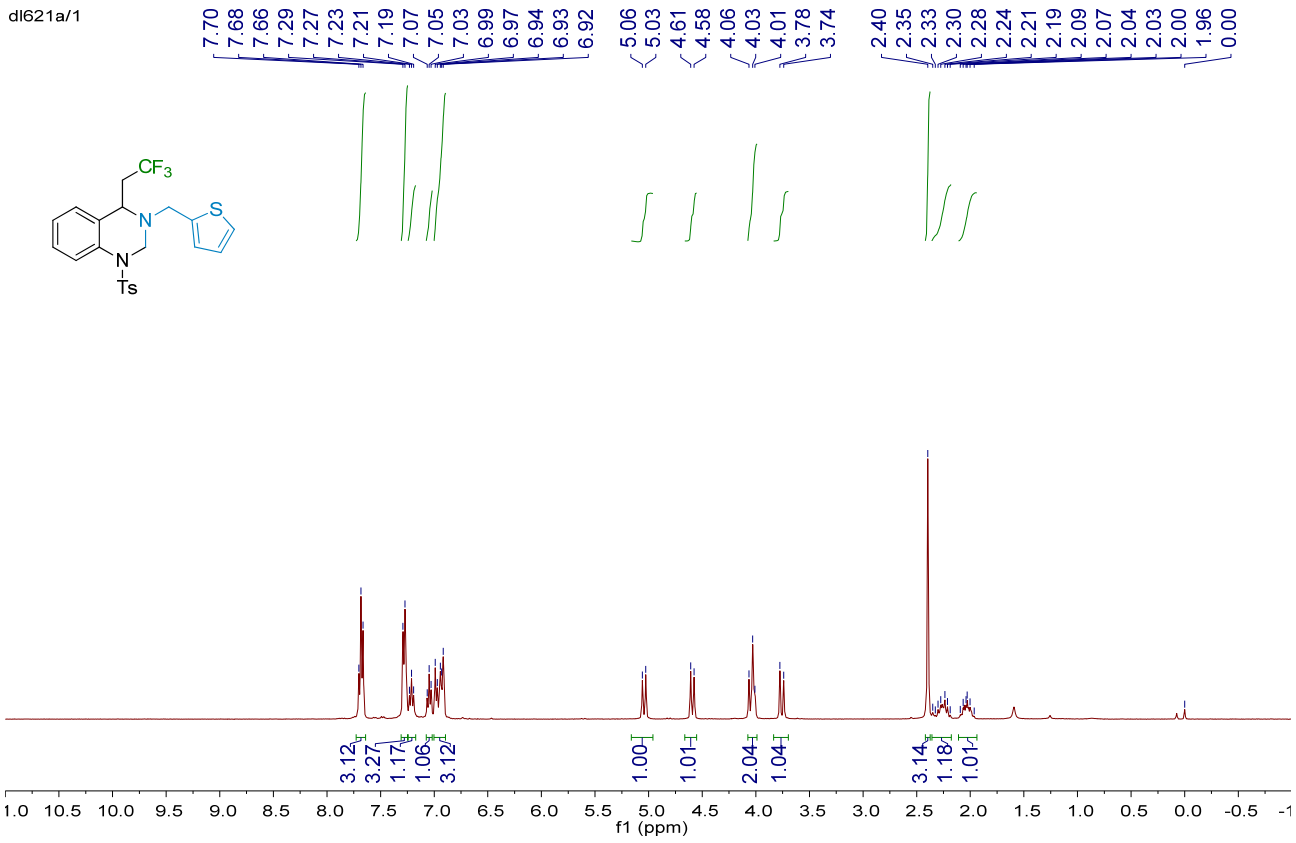
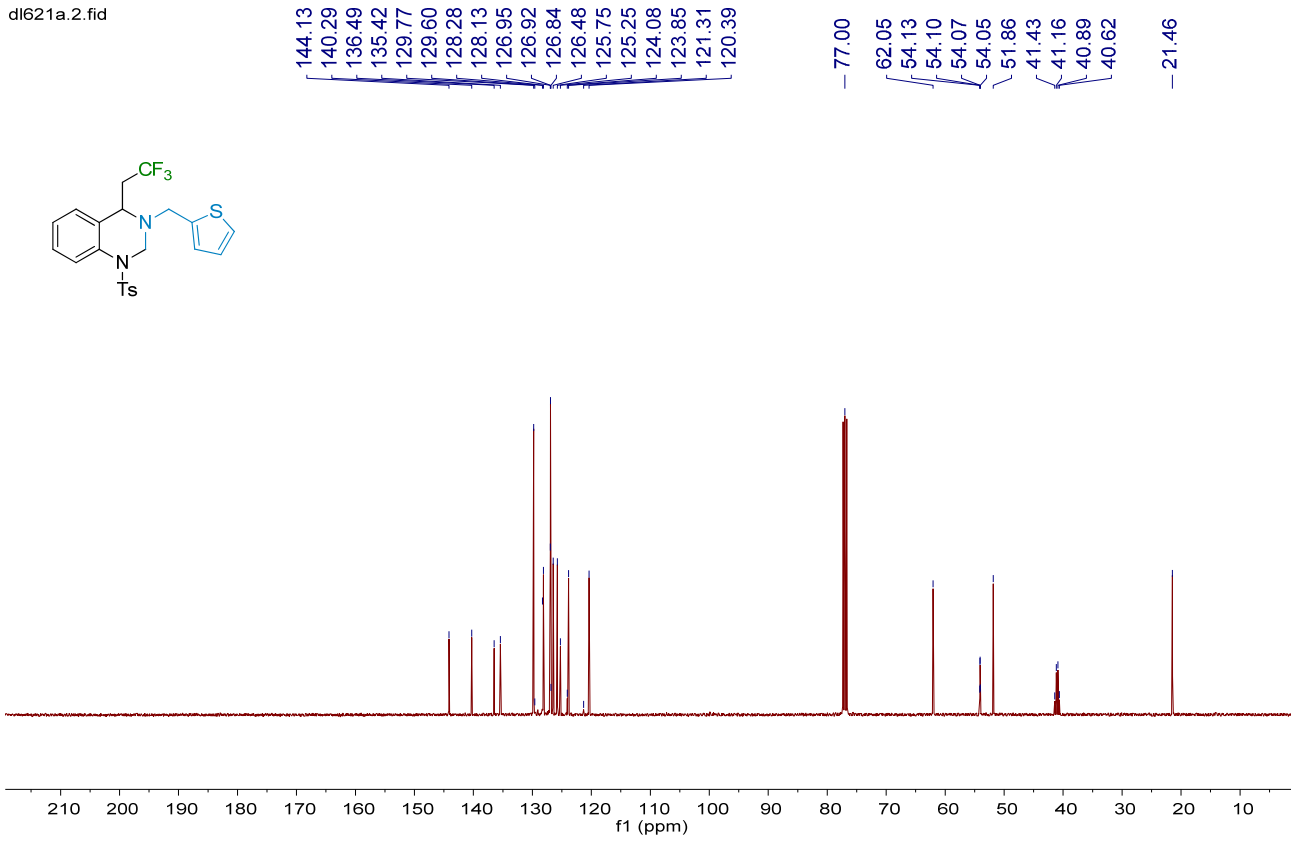
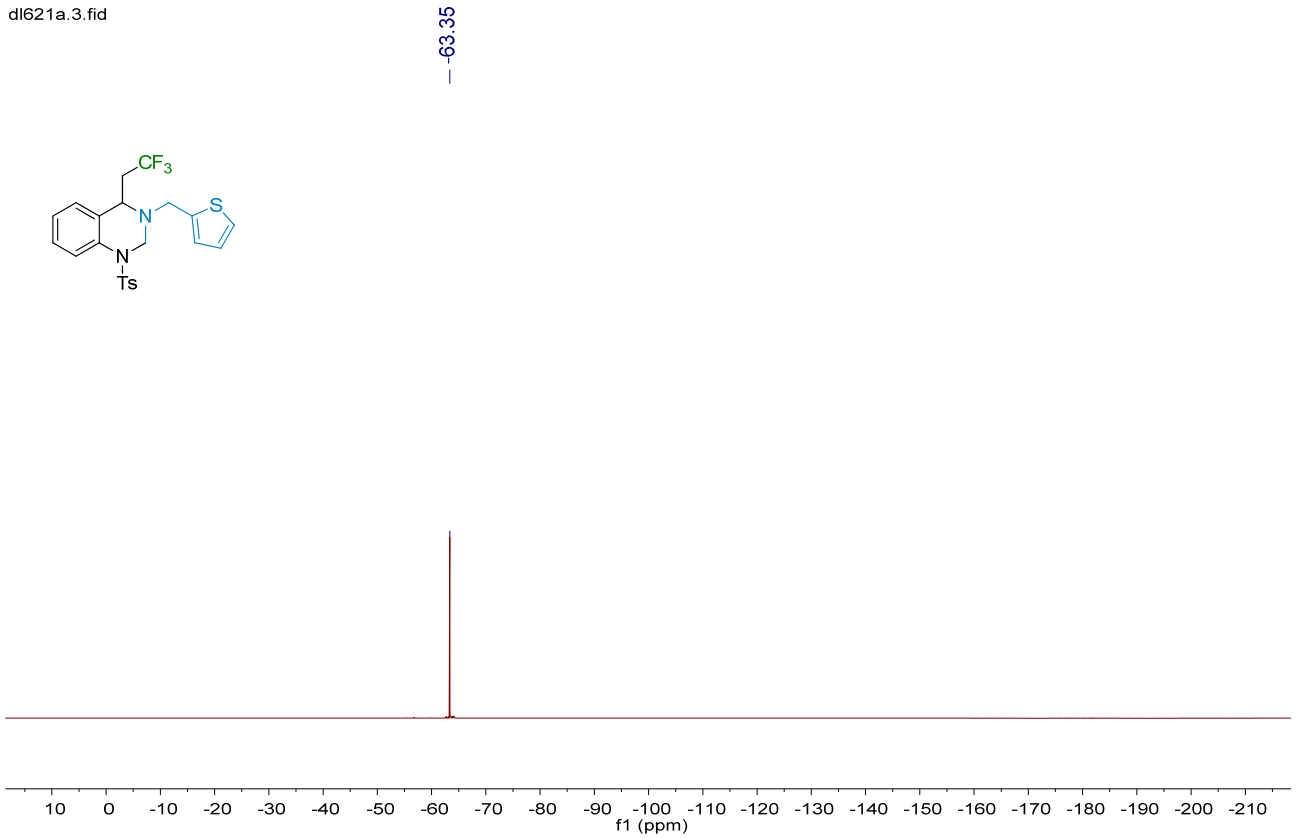


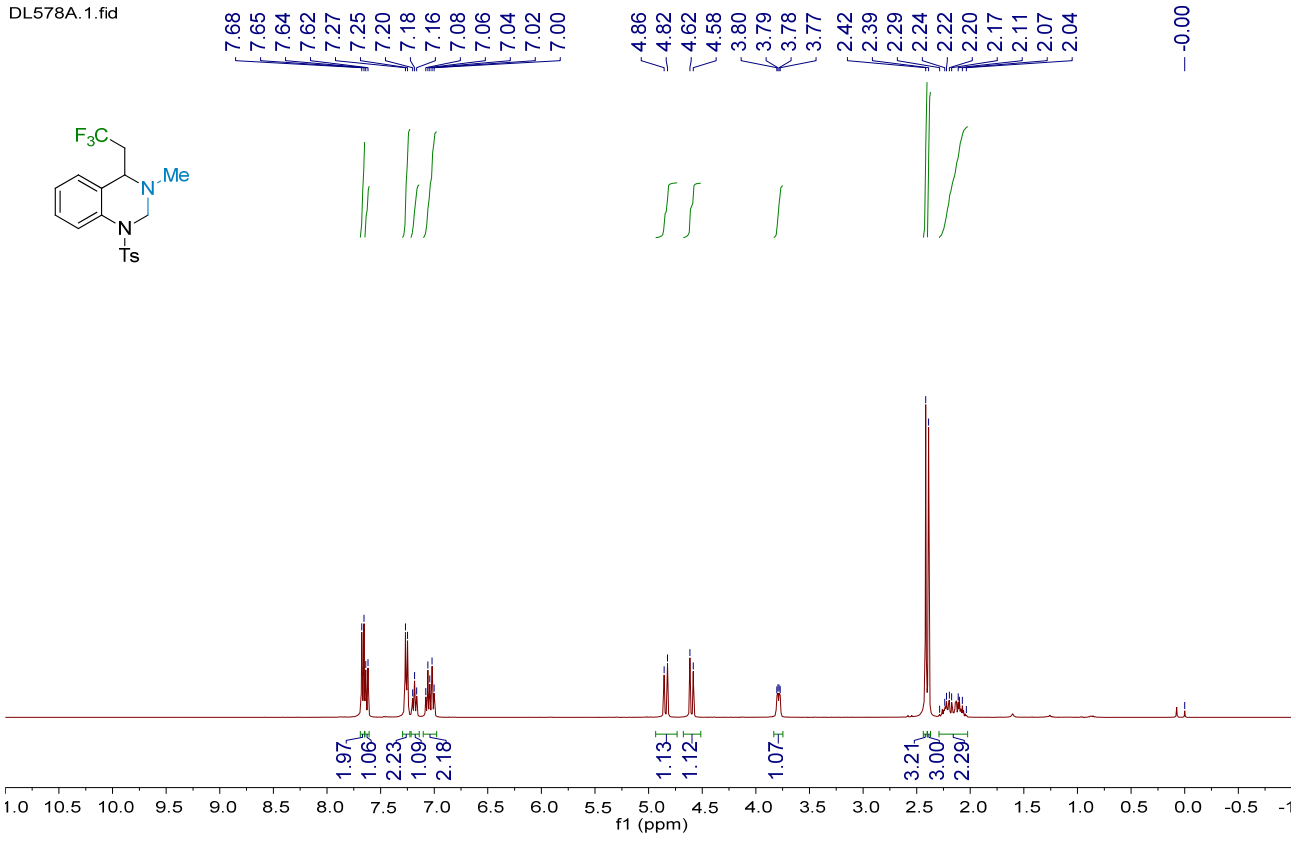
^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 4ak







^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 4al



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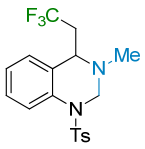

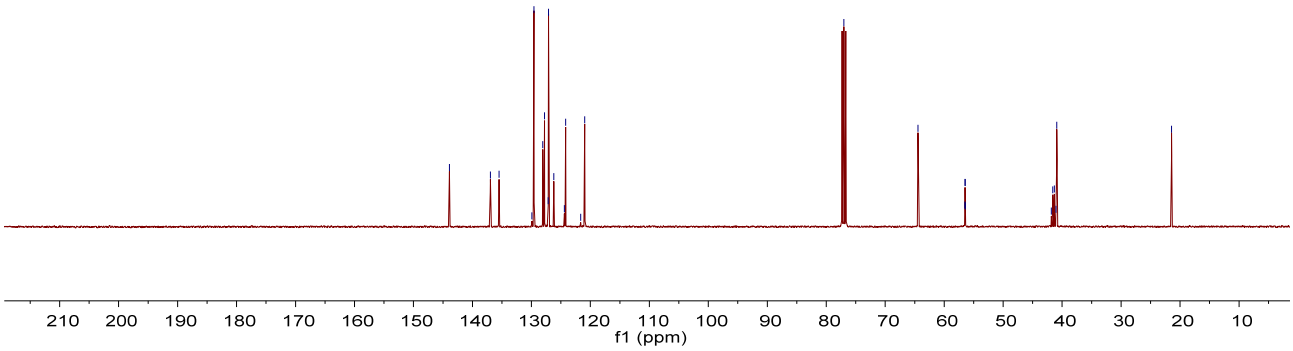

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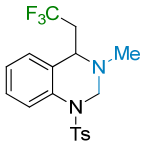
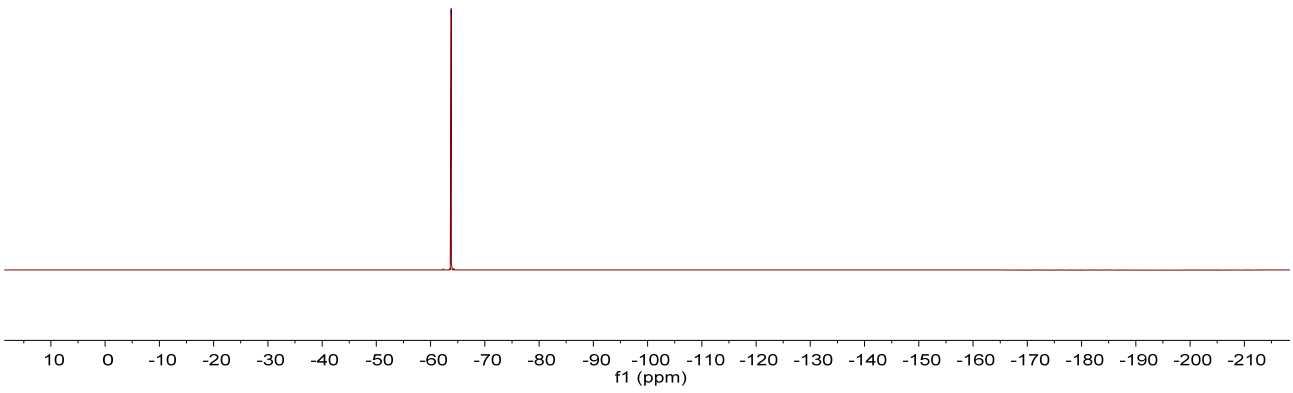
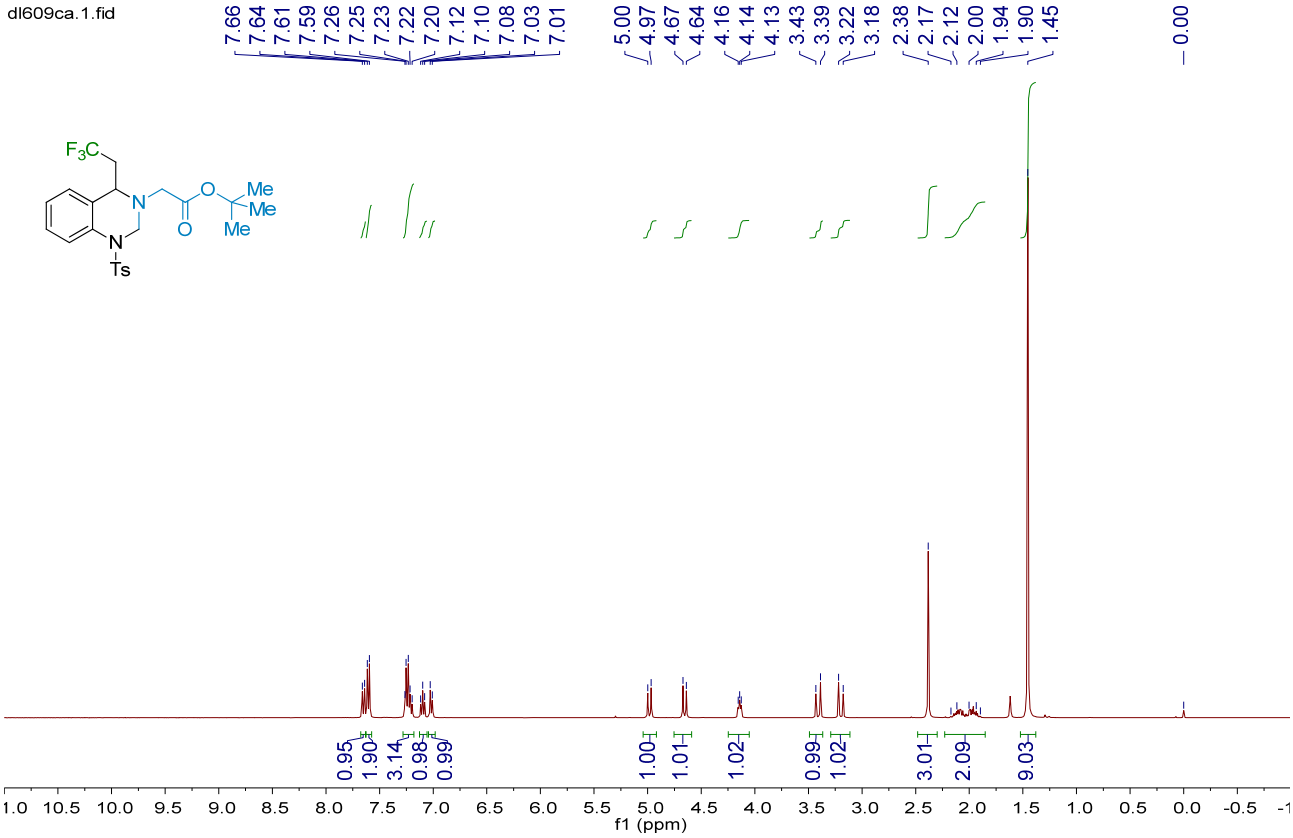
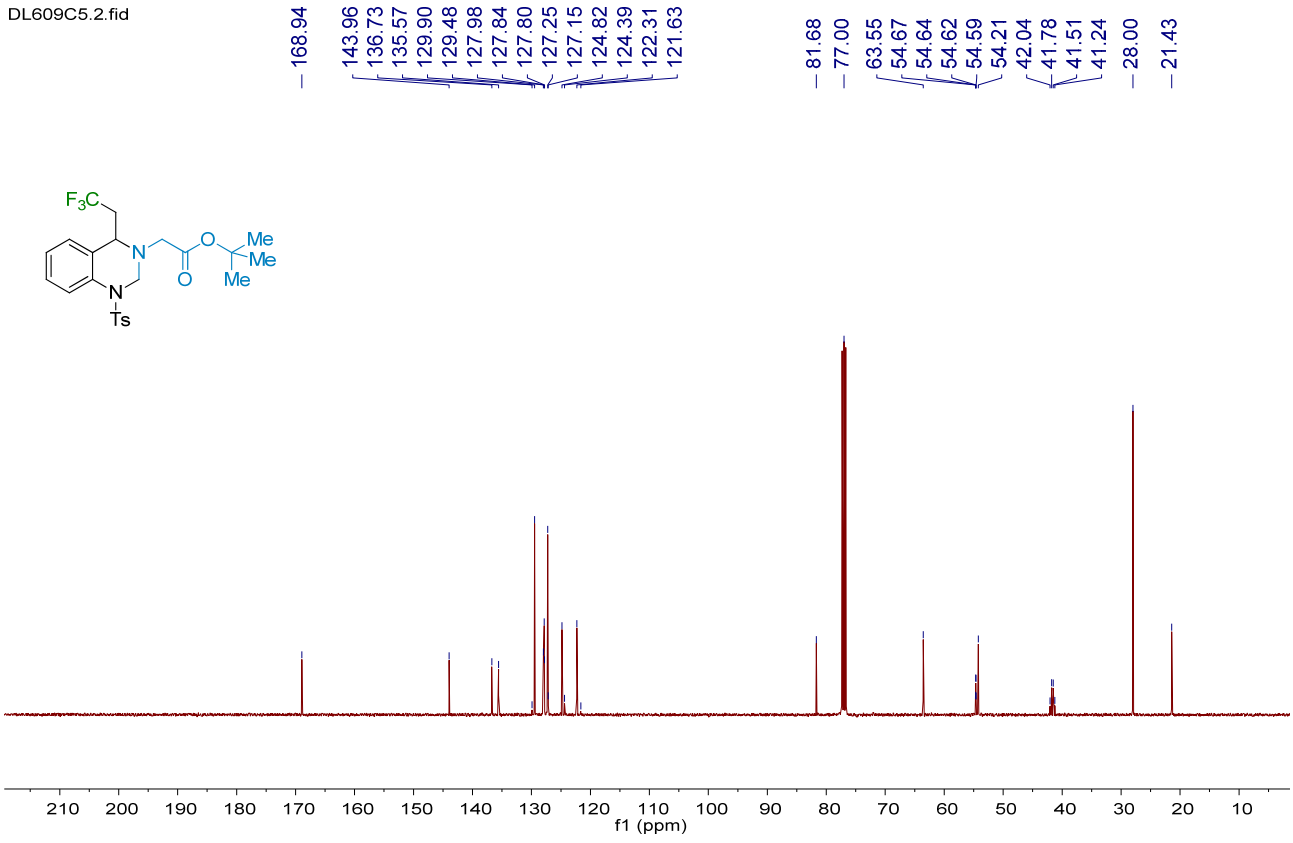
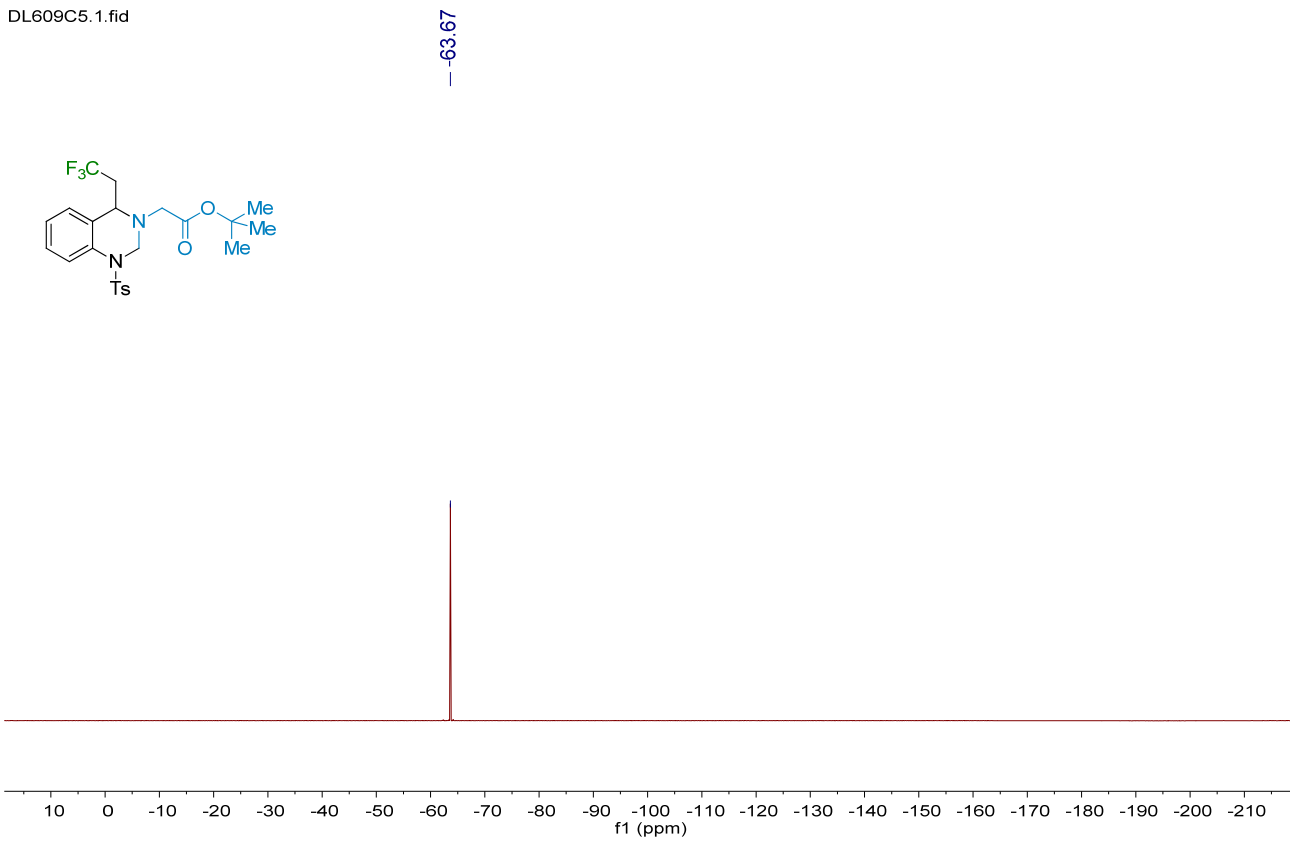




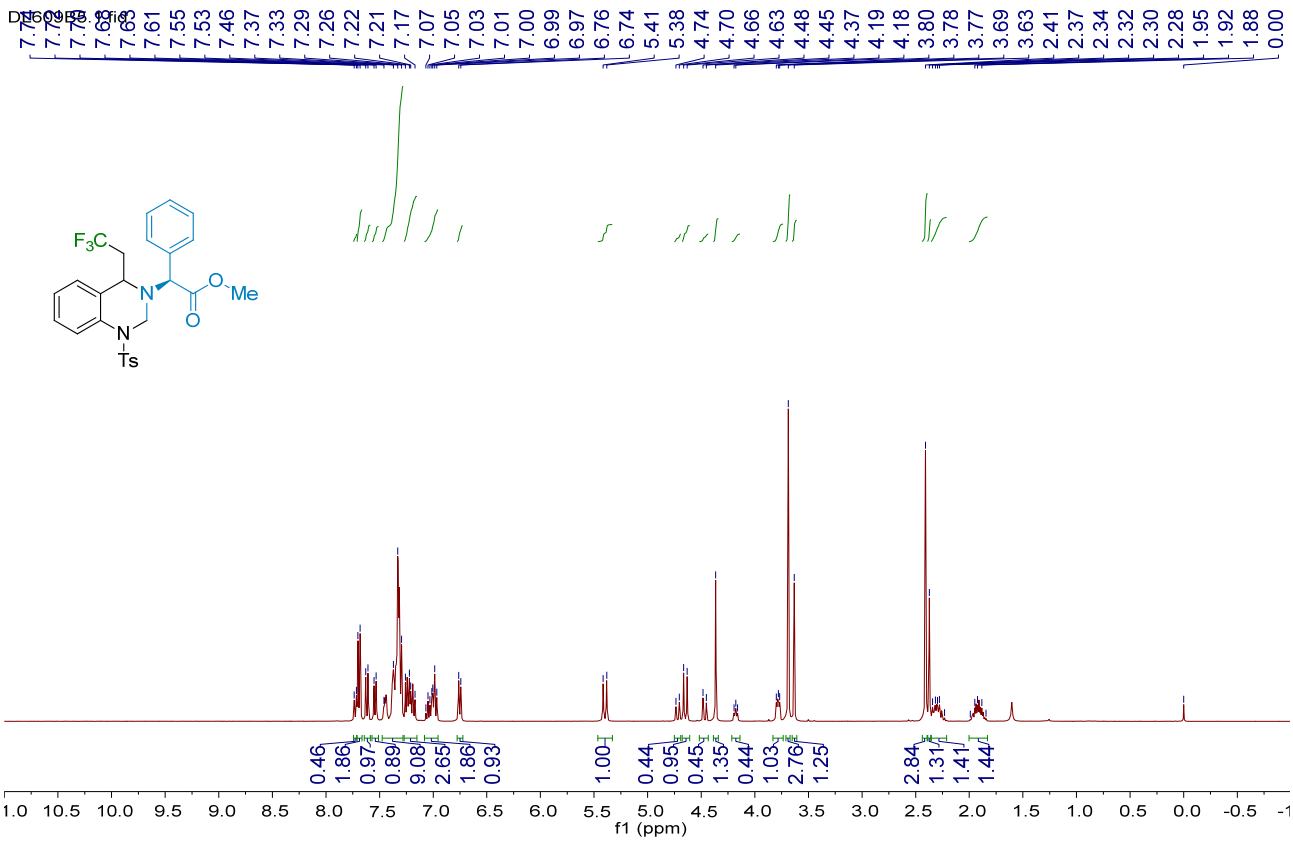
^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 4am







^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 4an



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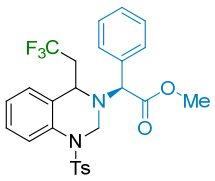

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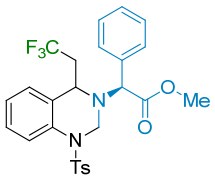
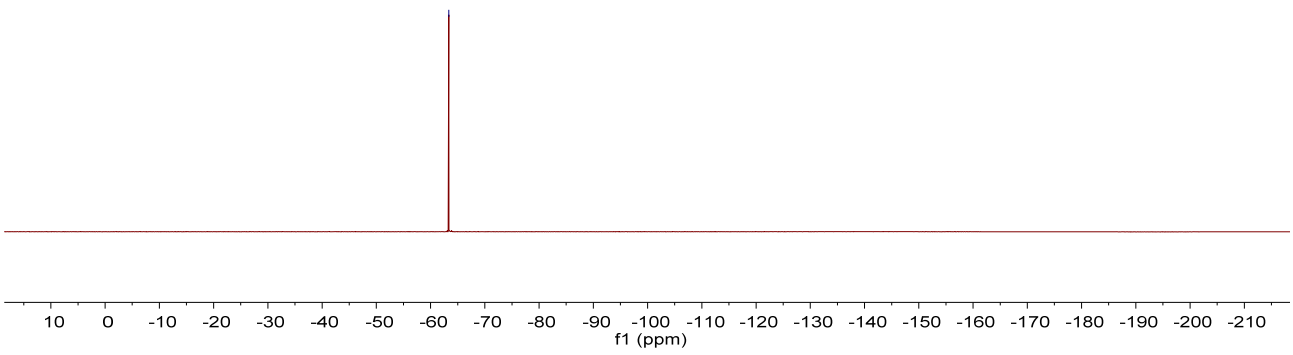
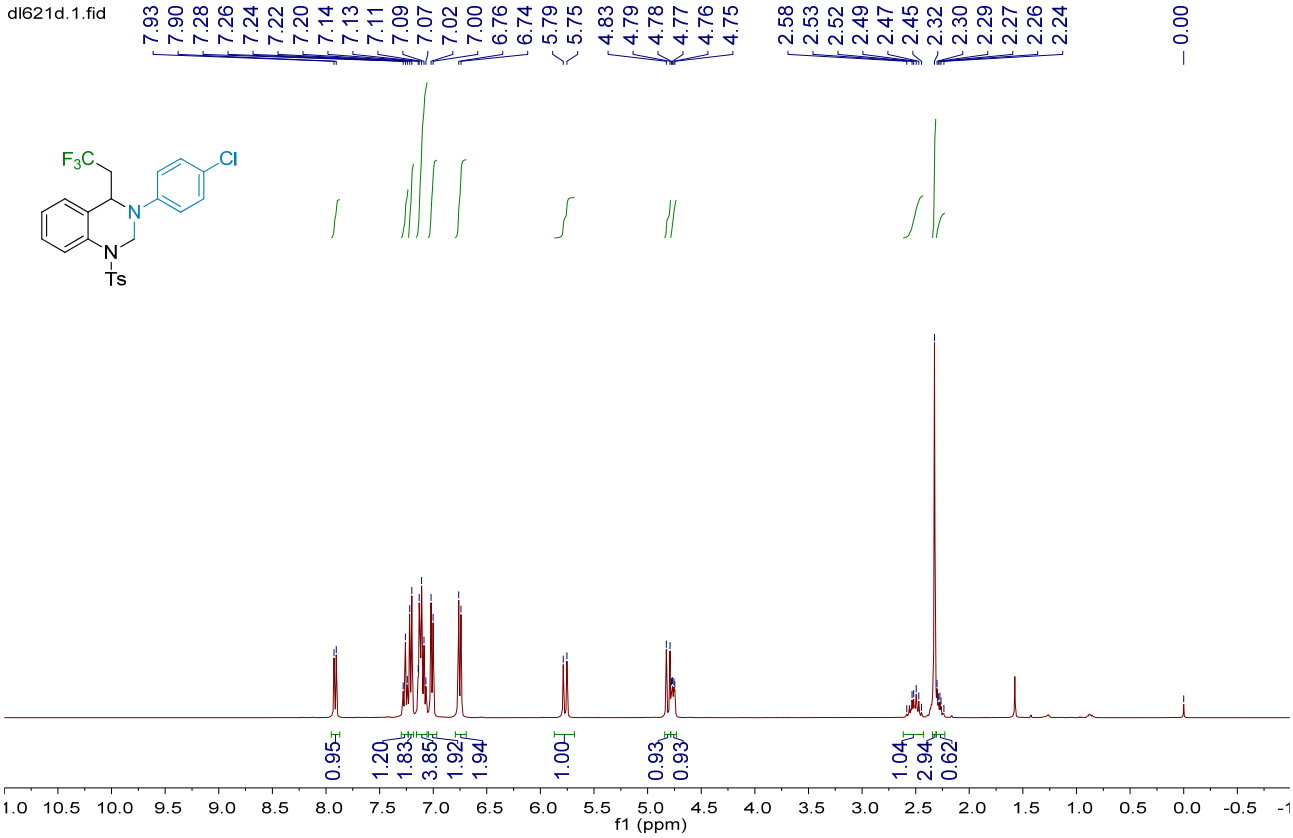
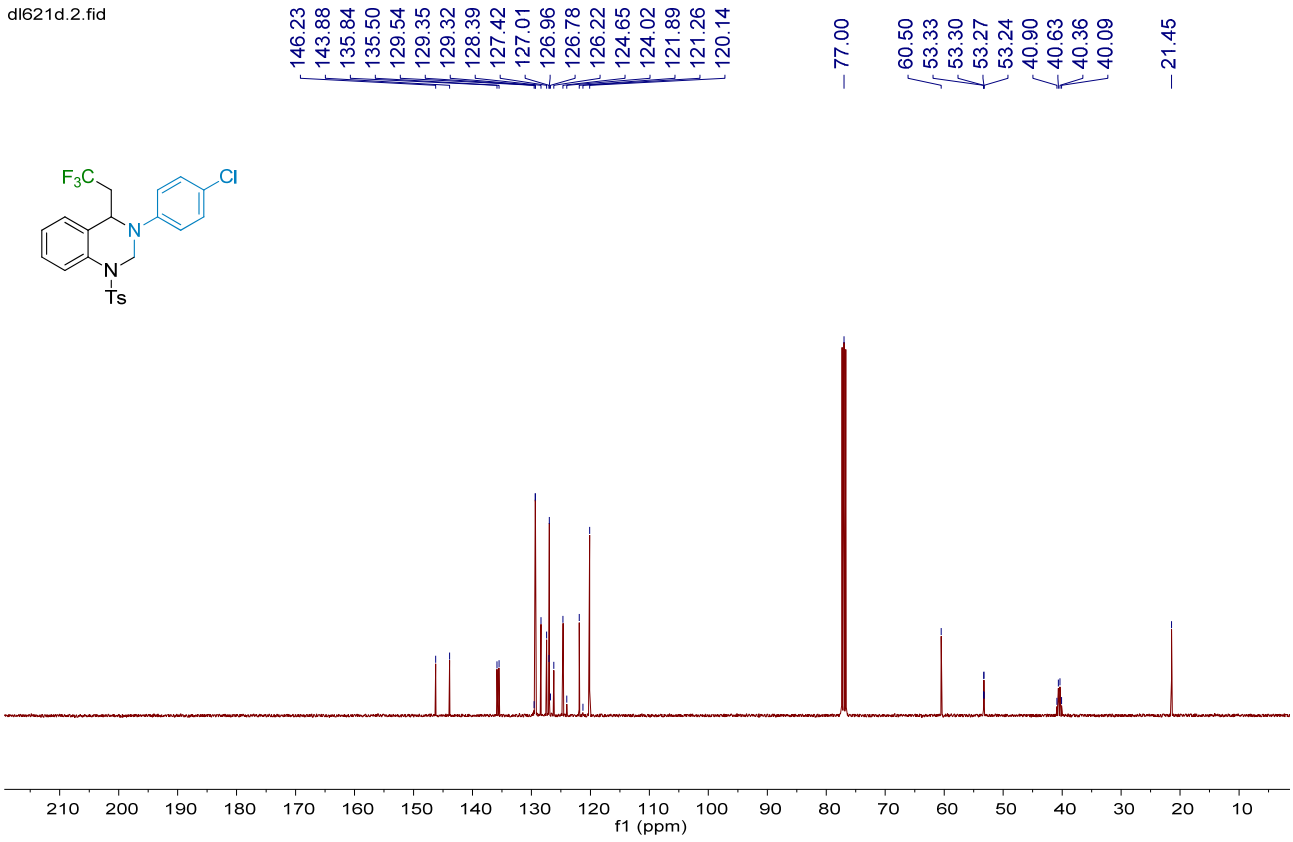
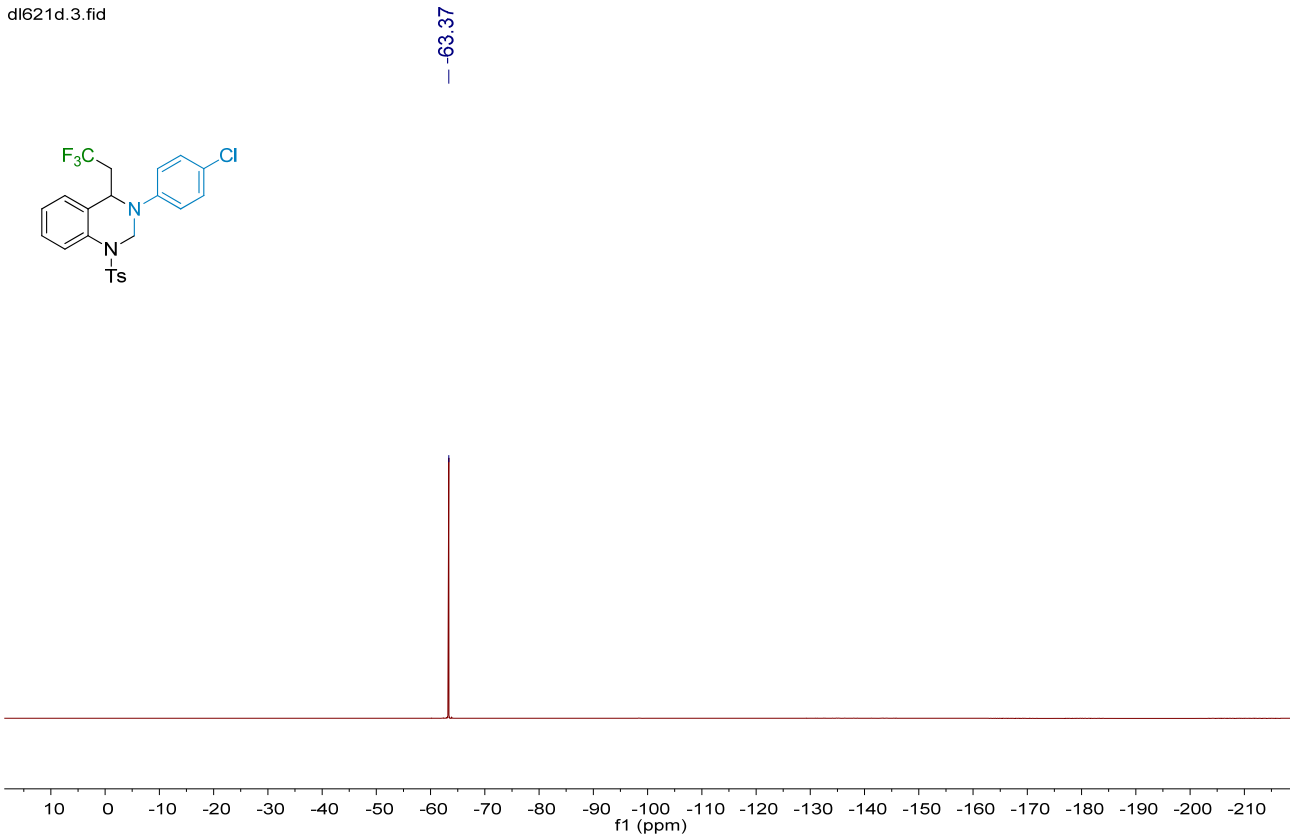




^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 4ao







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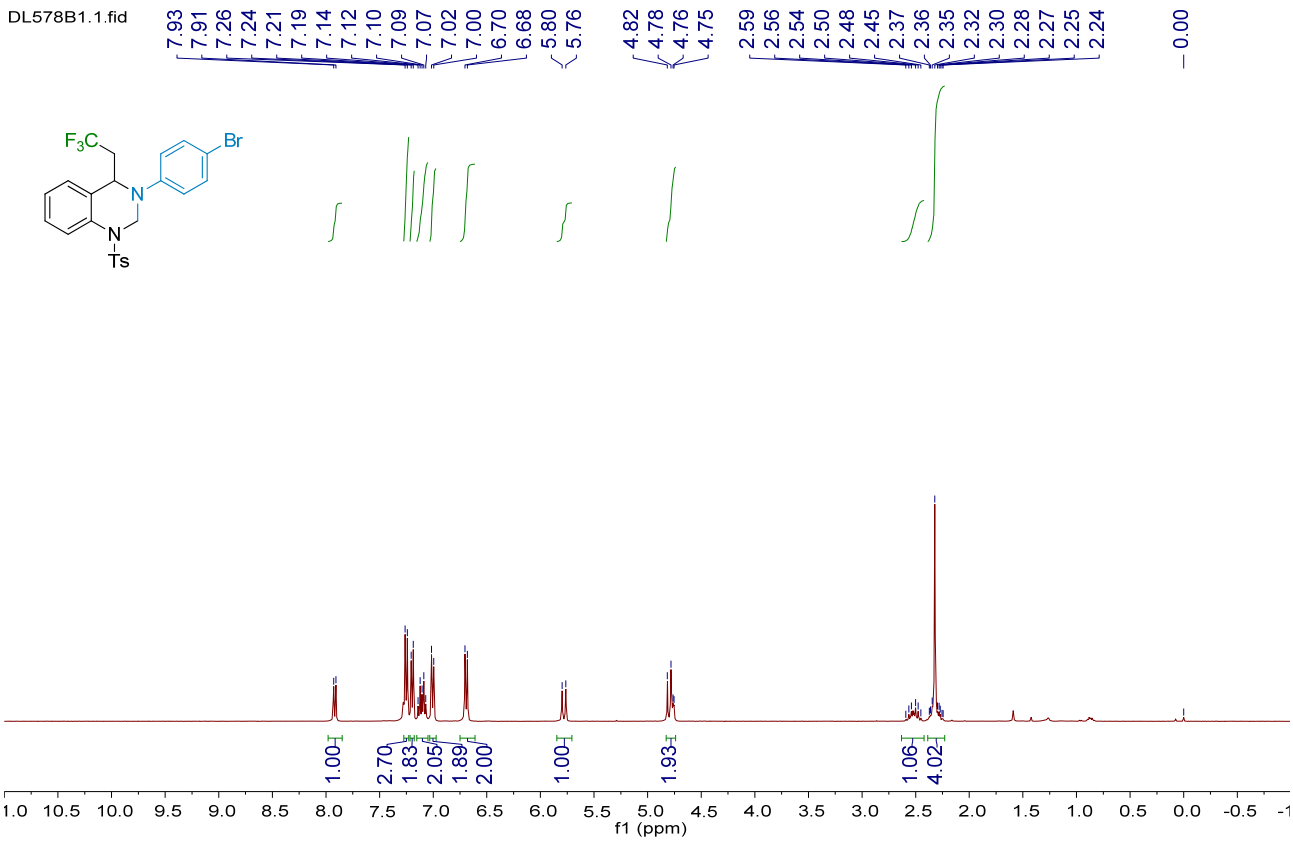

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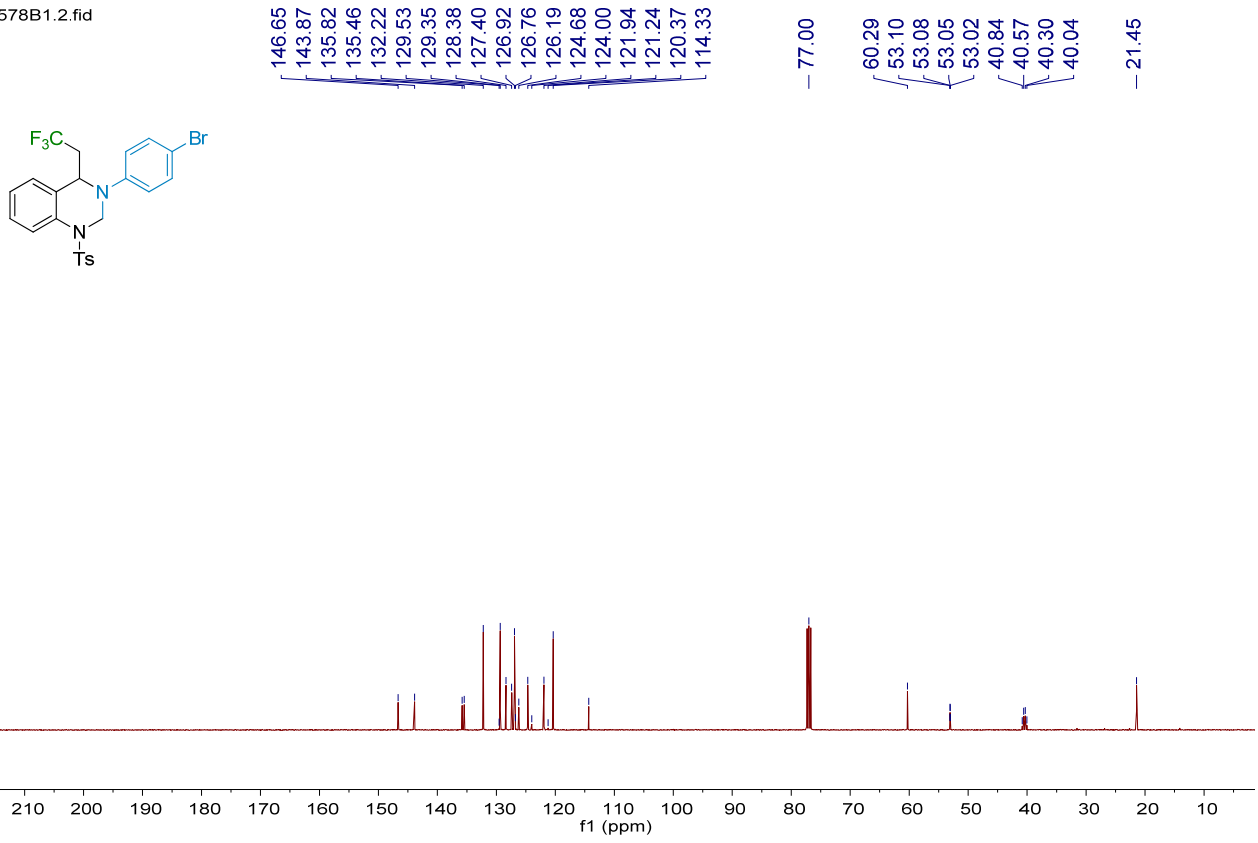

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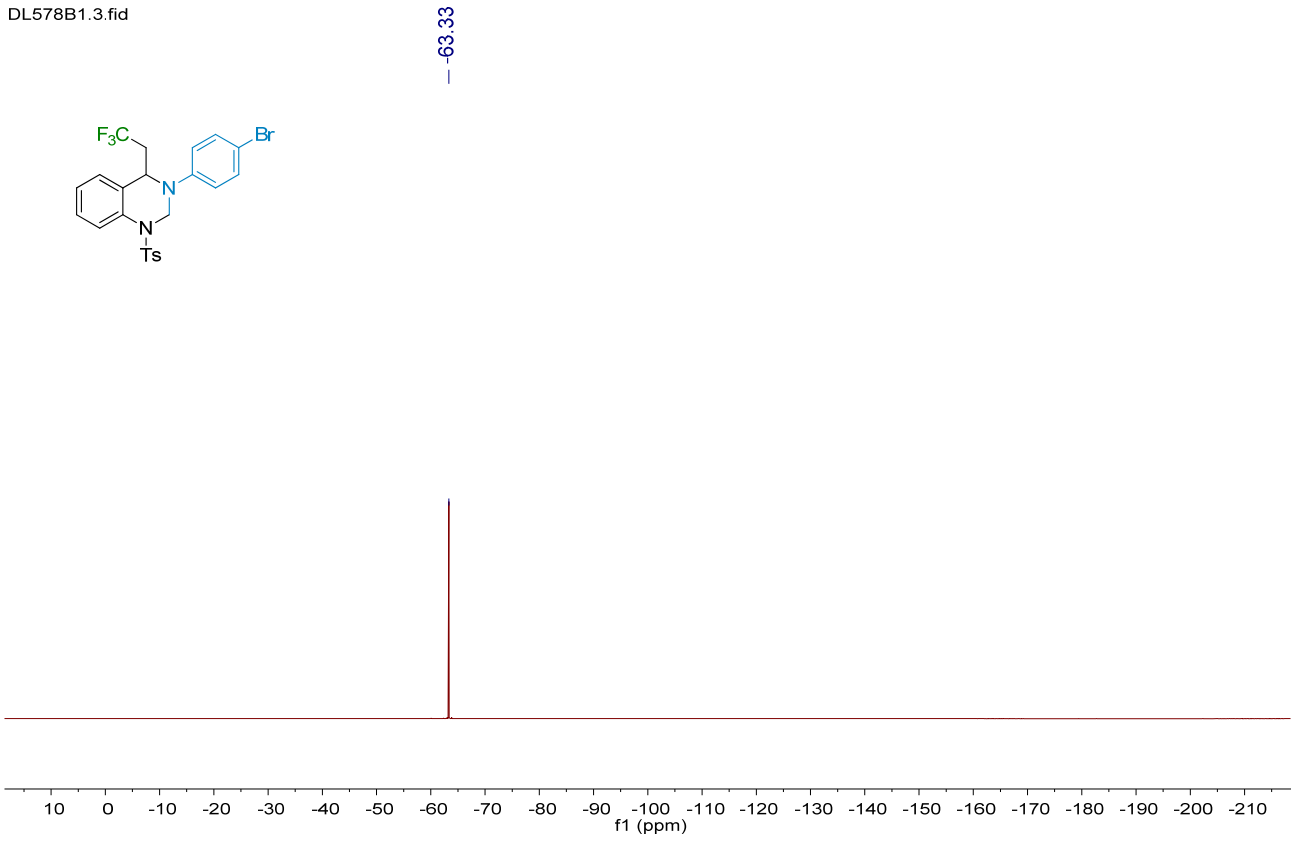
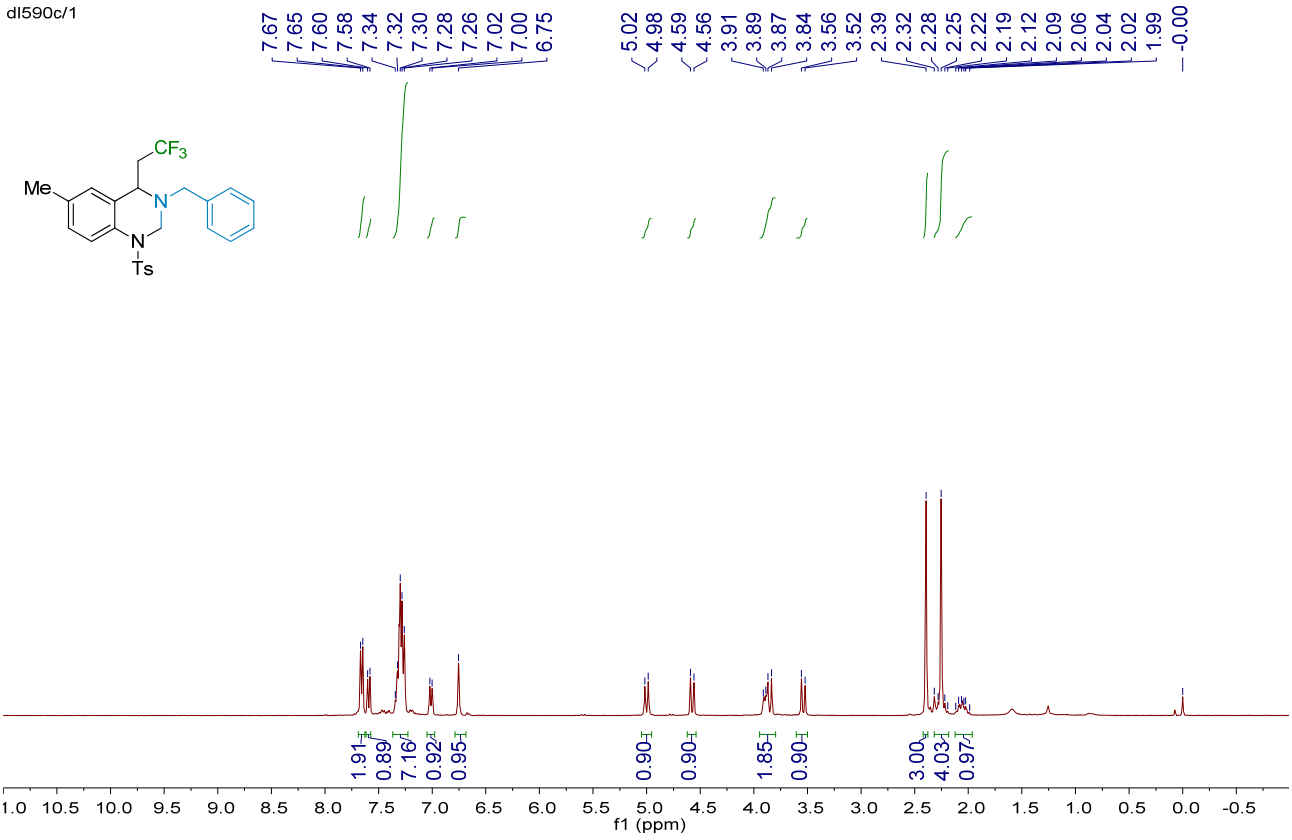
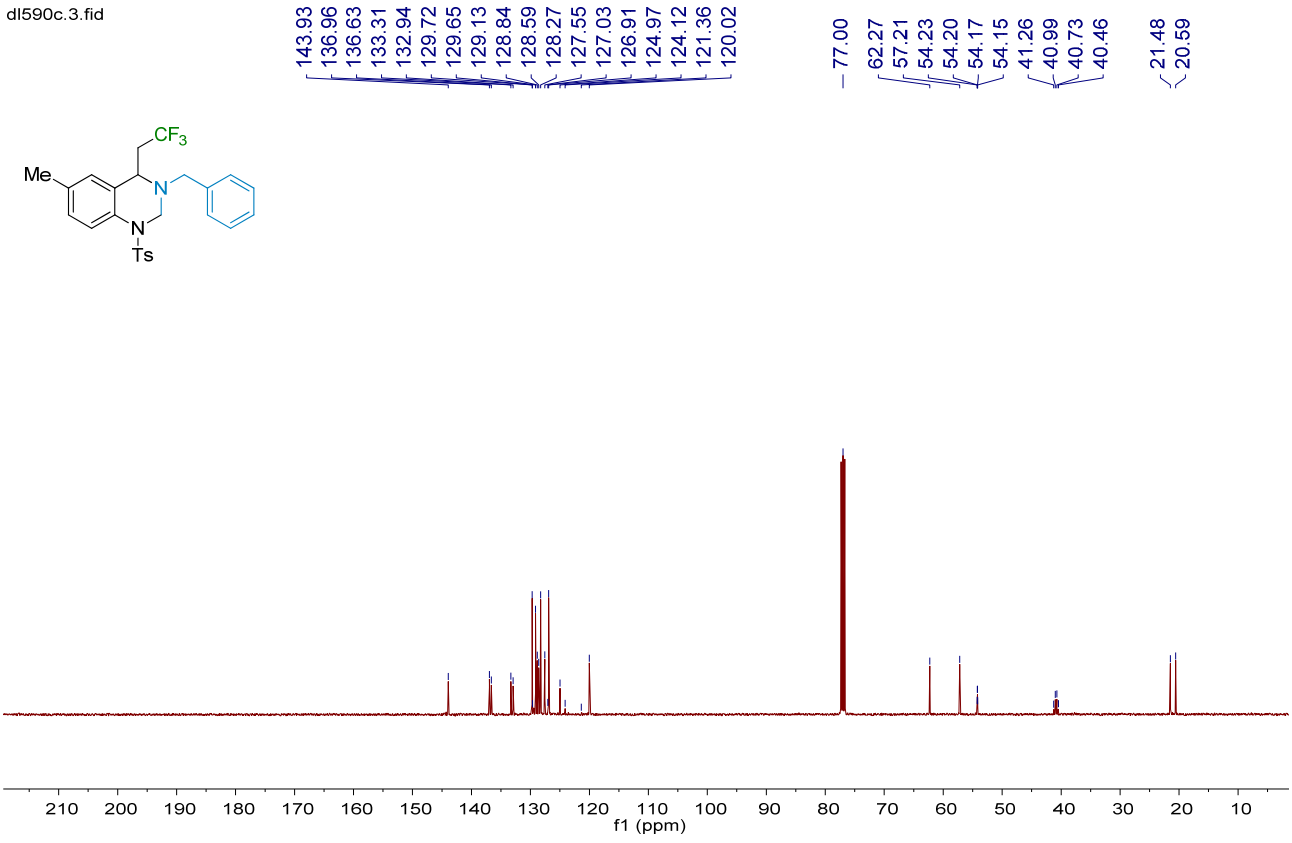
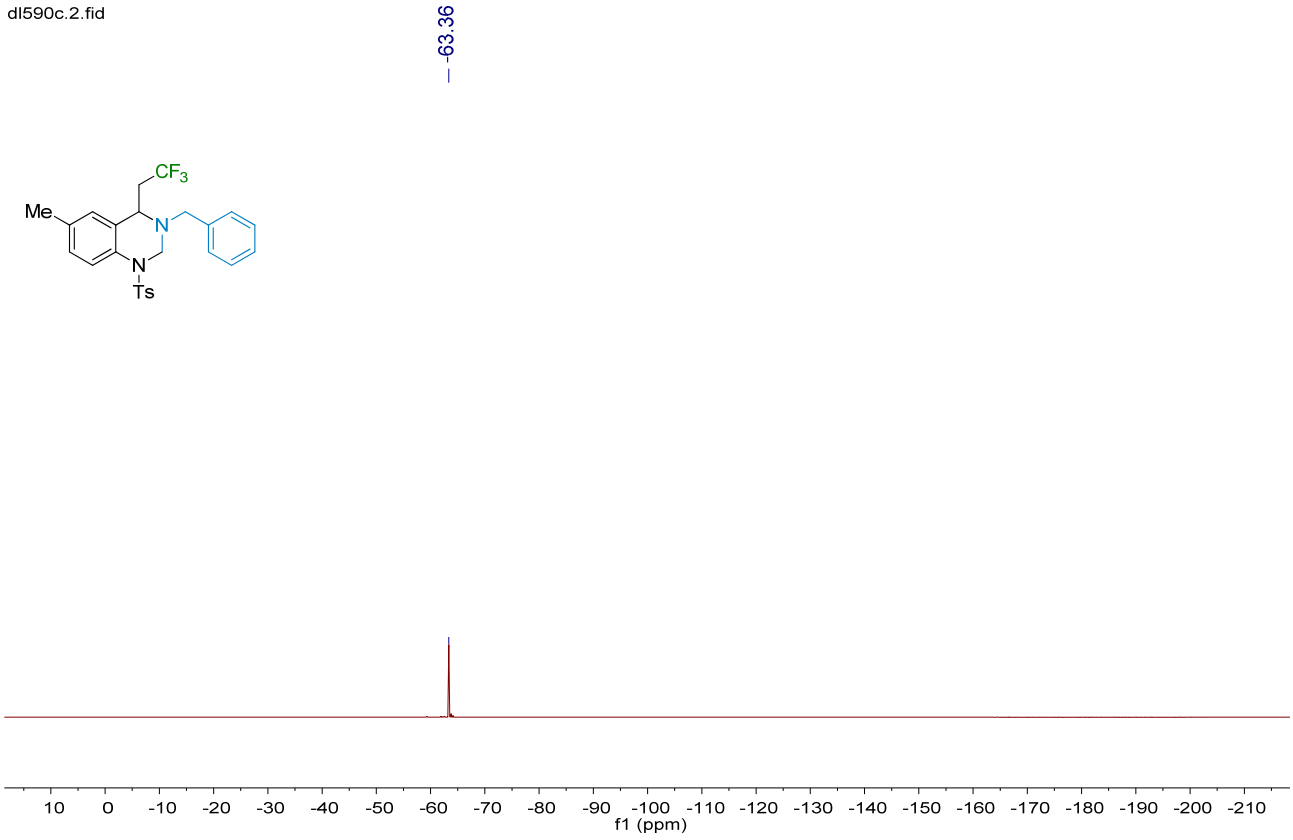


^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 5ba







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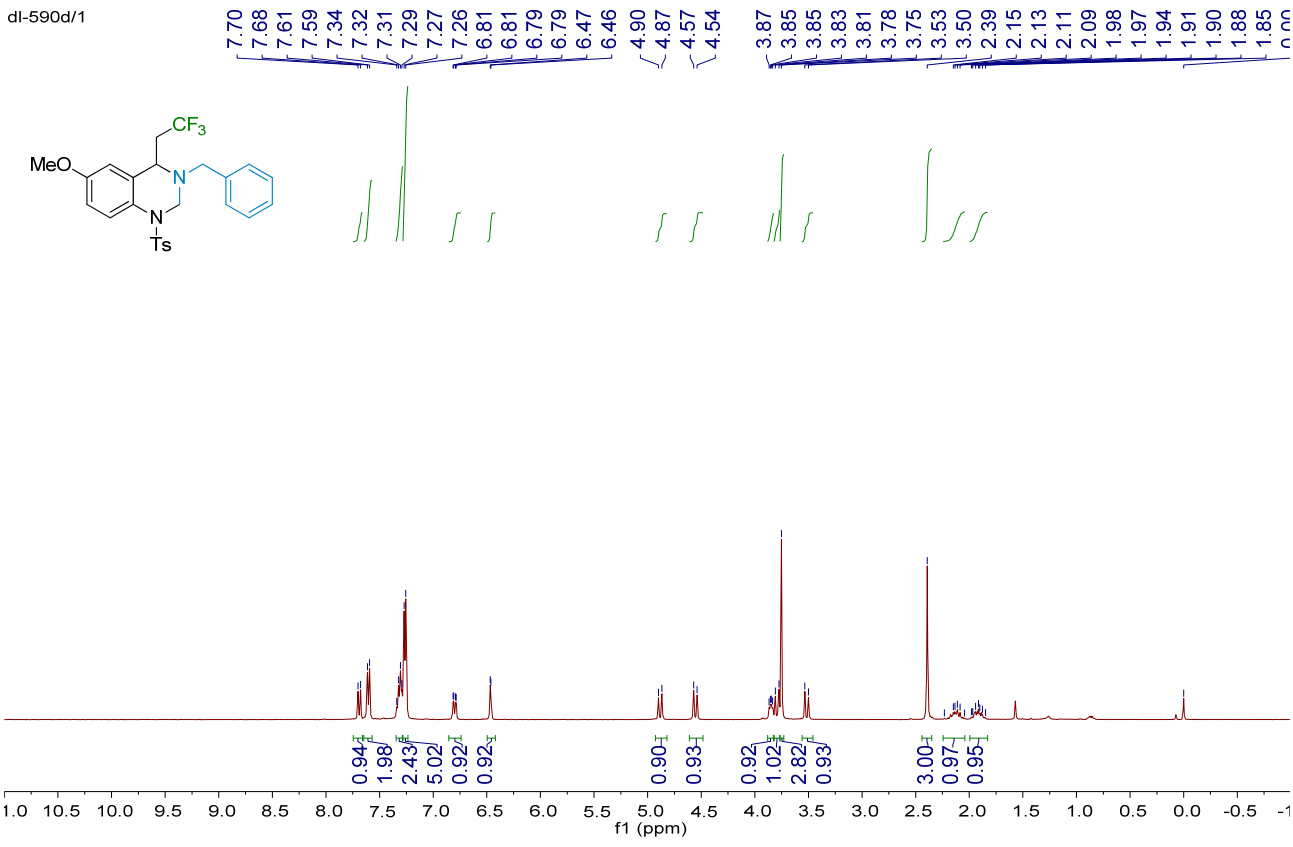

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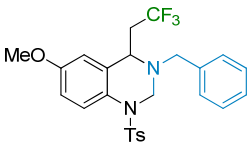

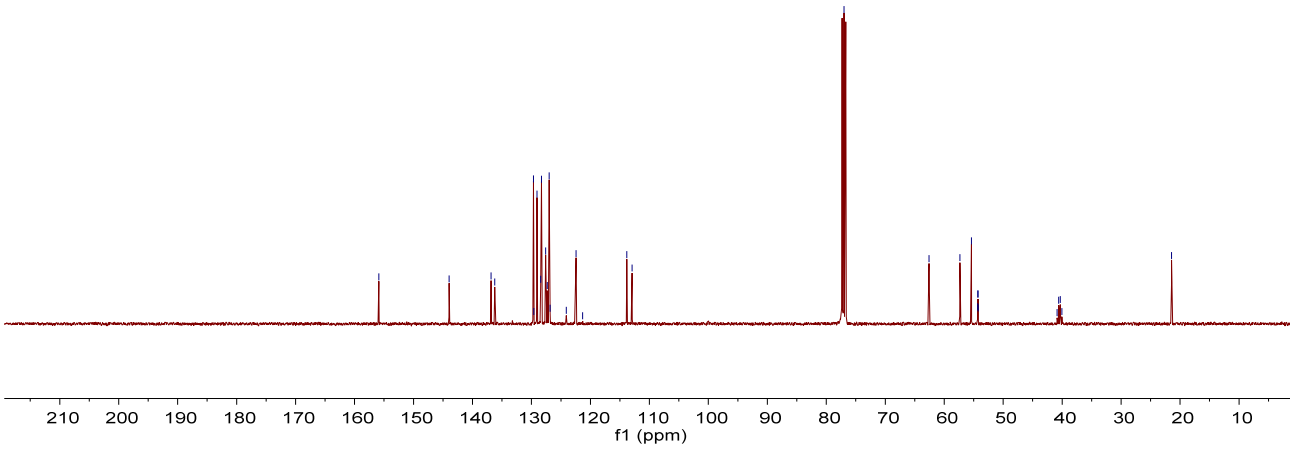

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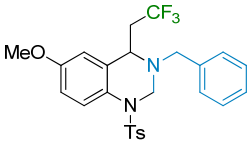
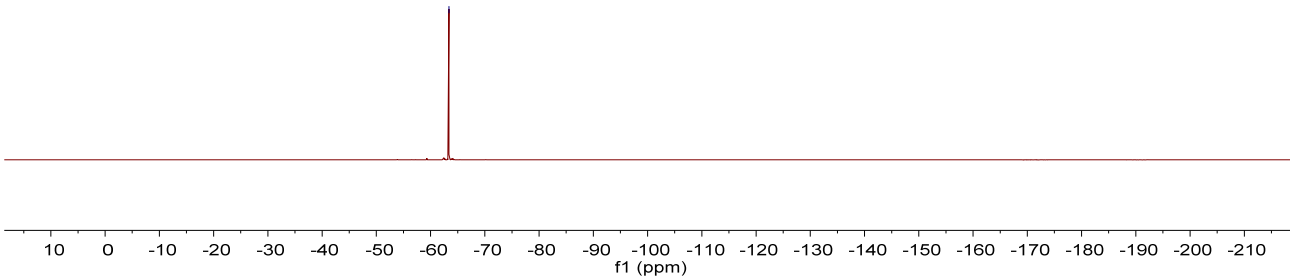
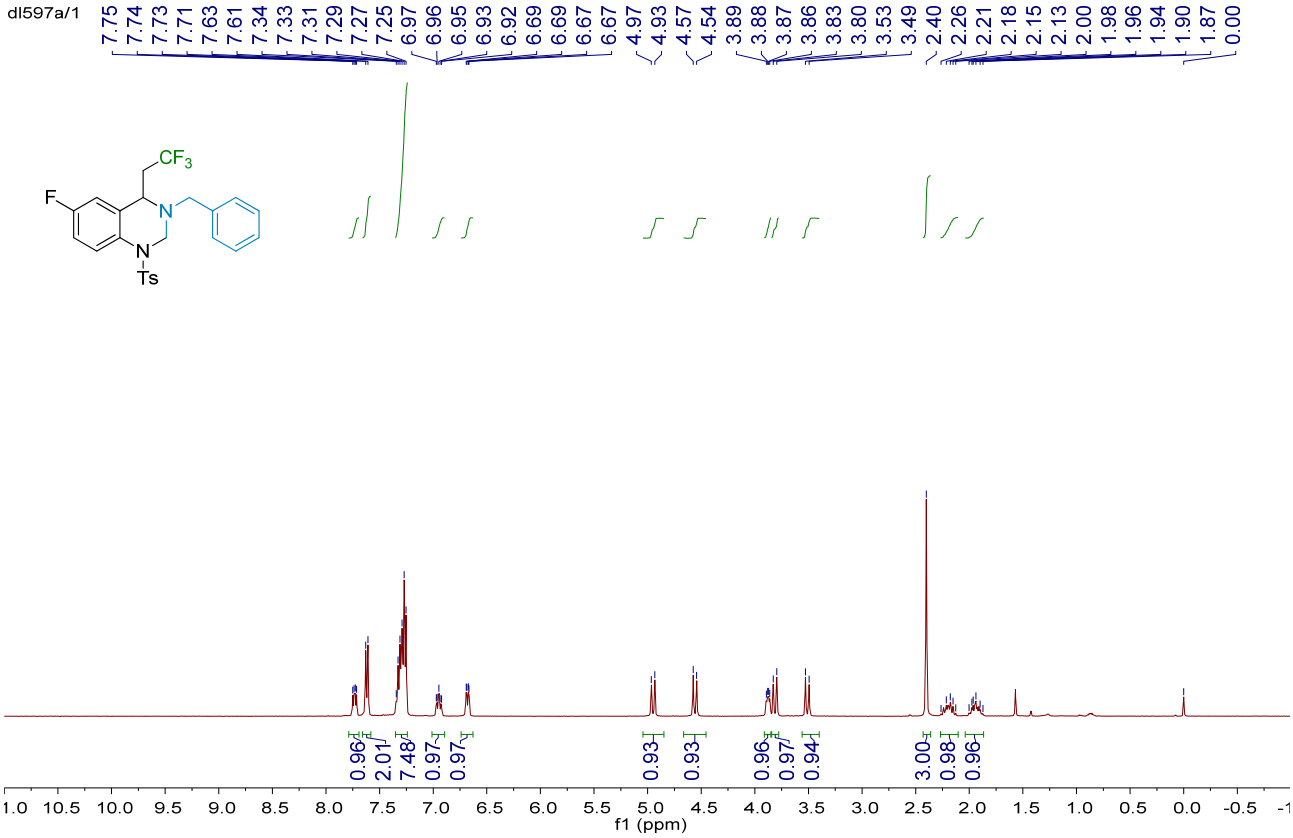
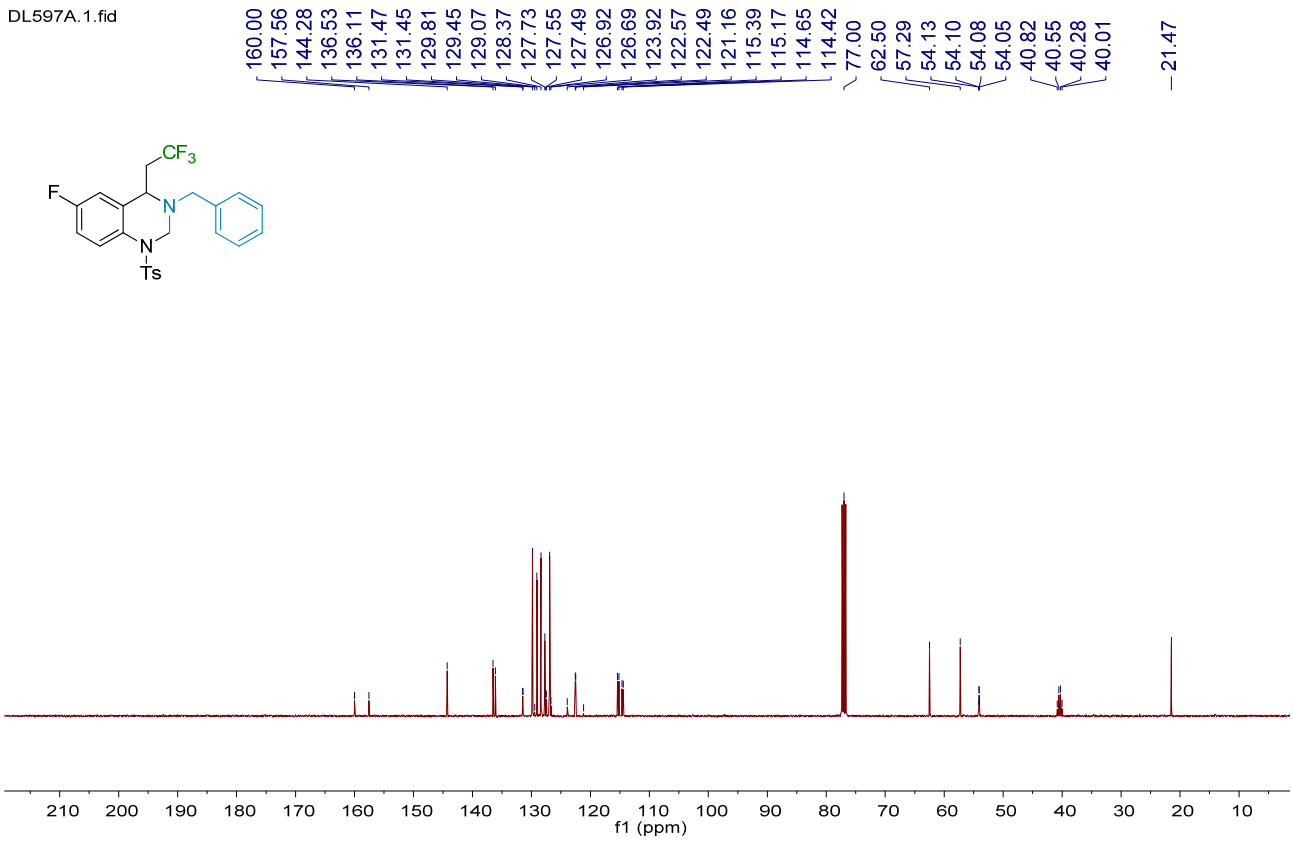
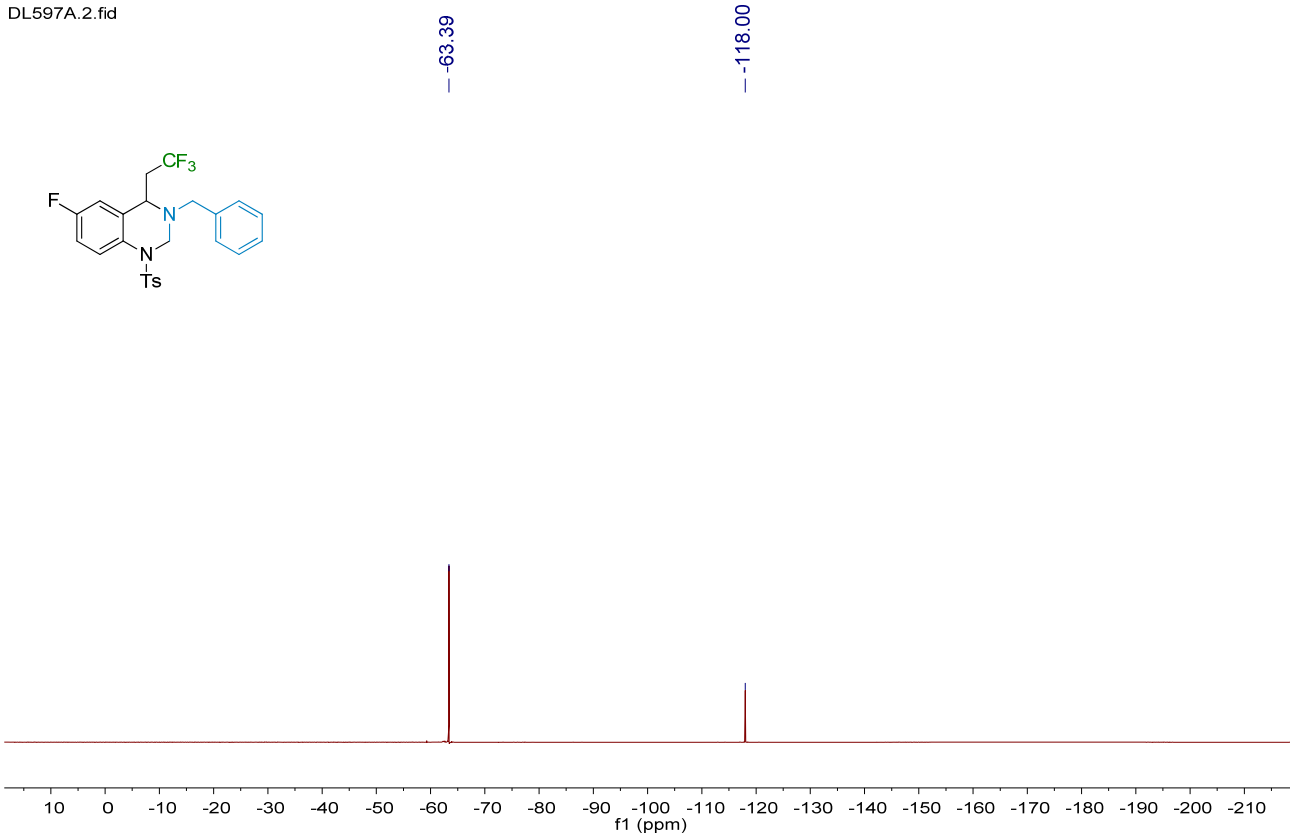




^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 5da







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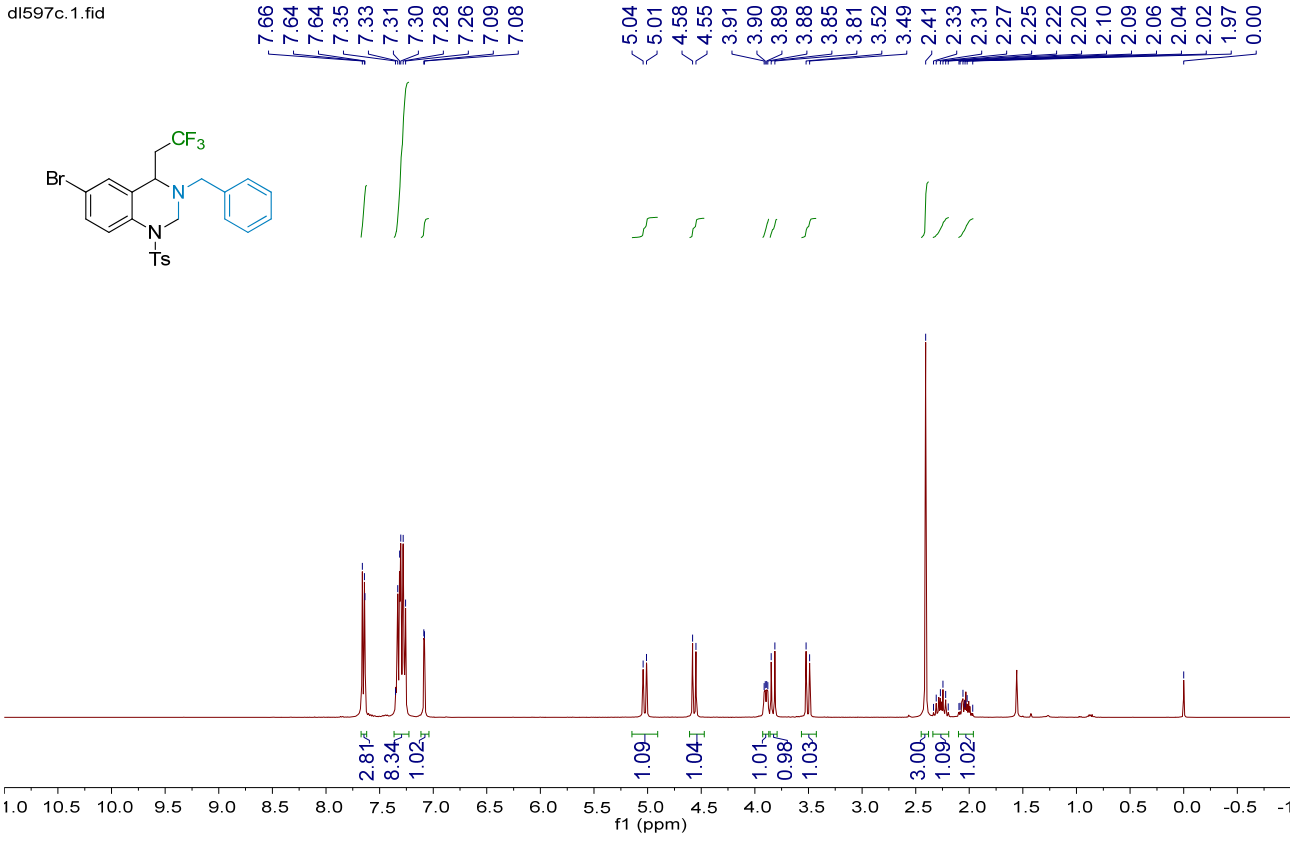

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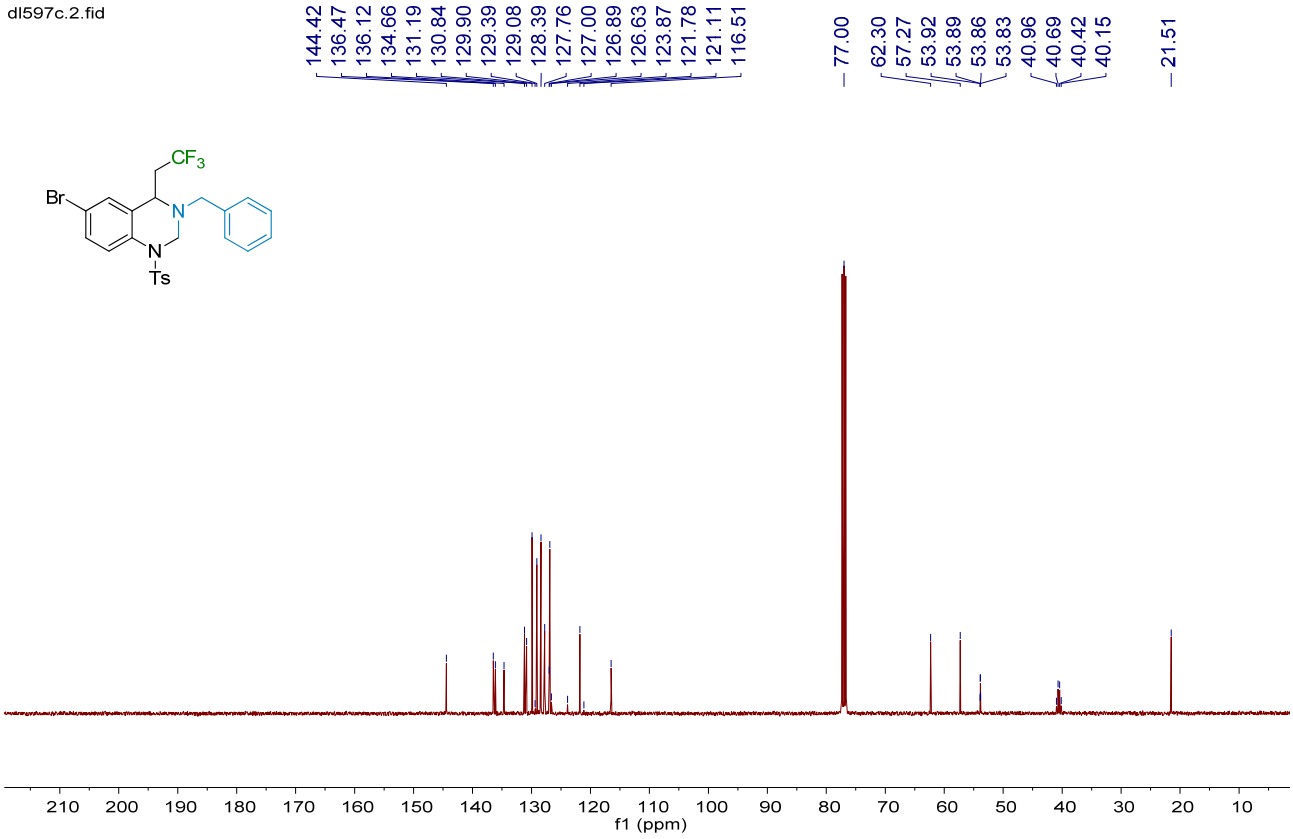

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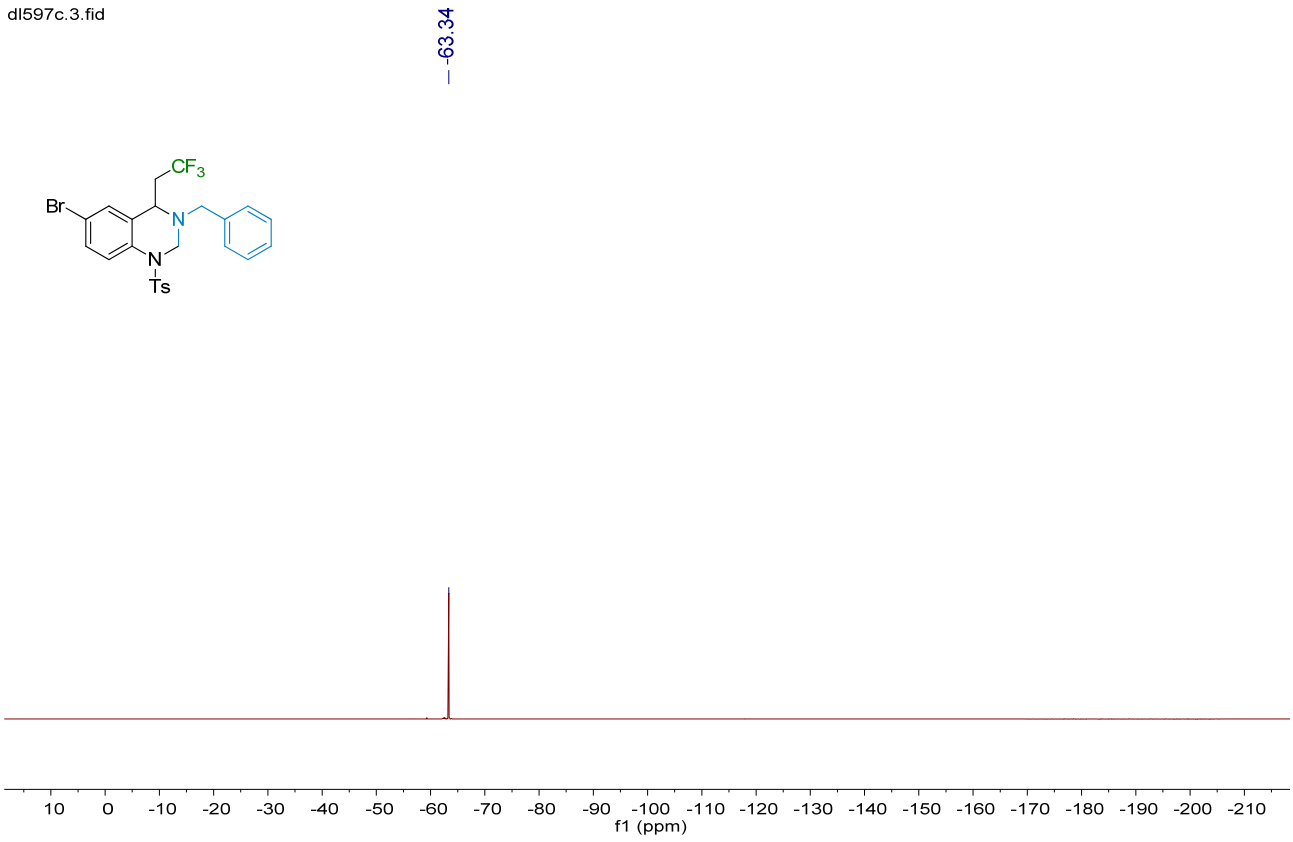

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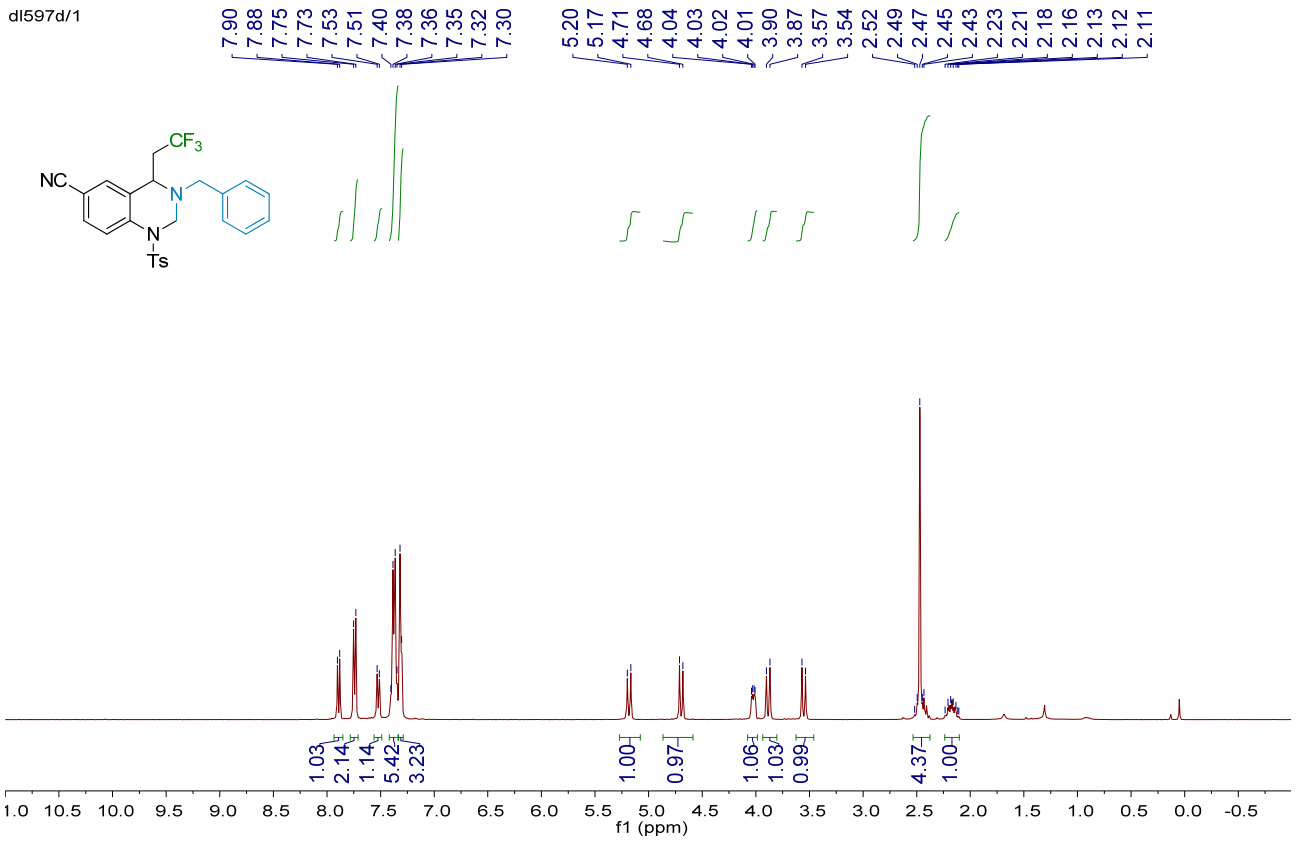

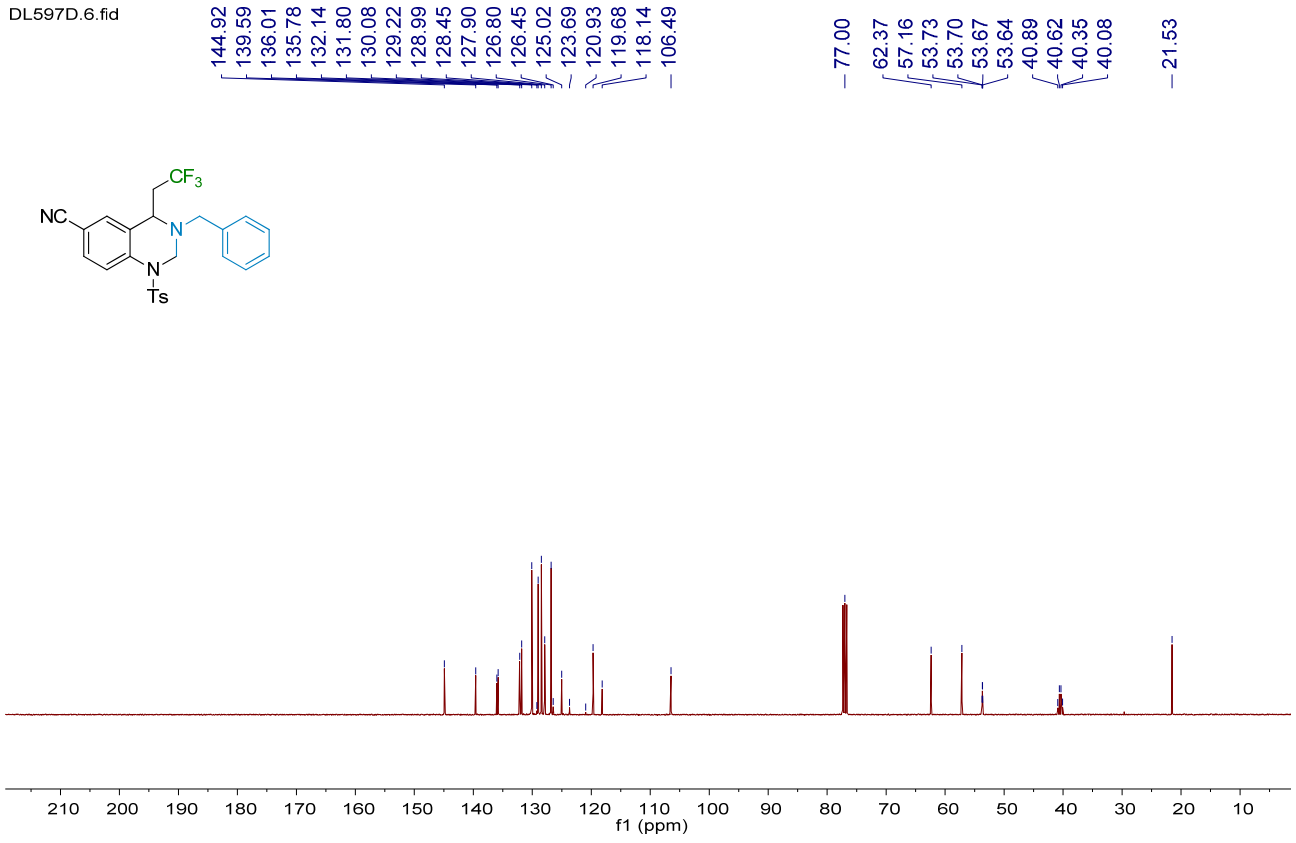

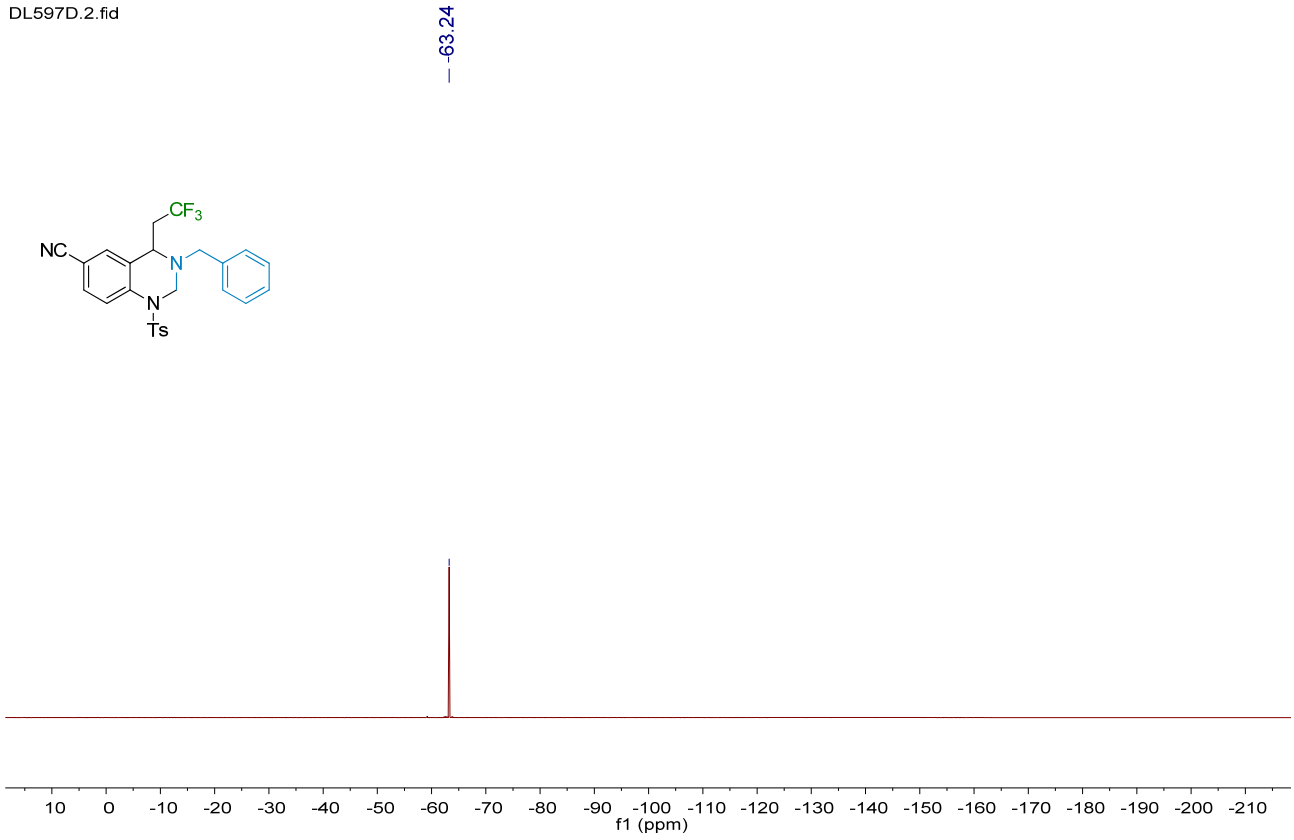

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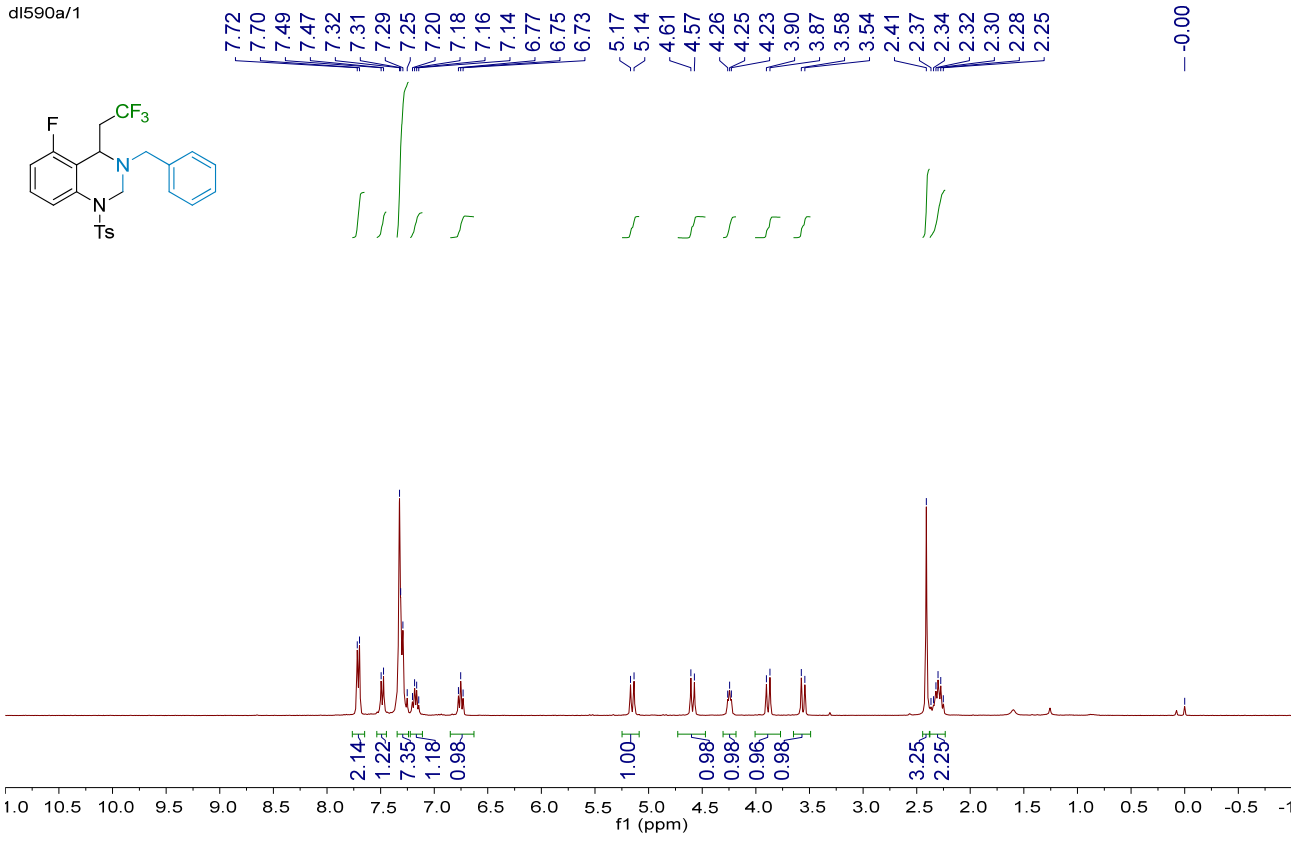

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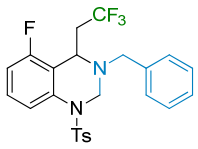

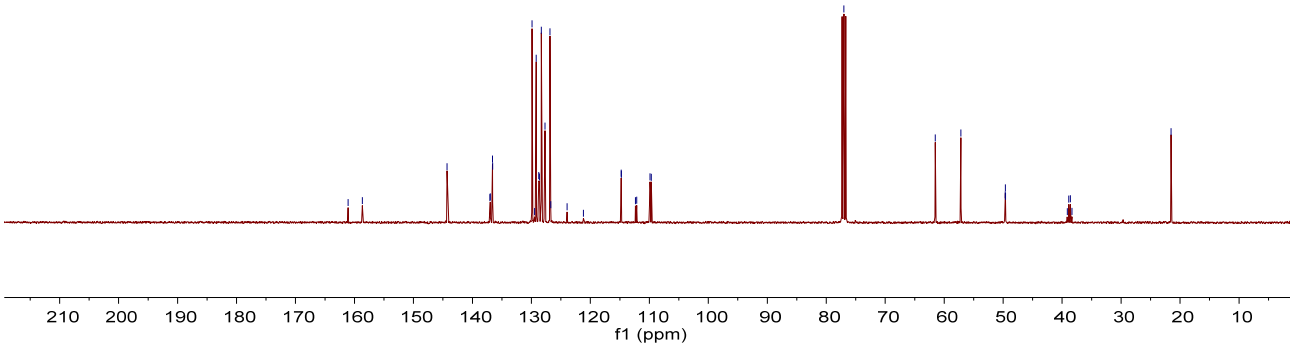

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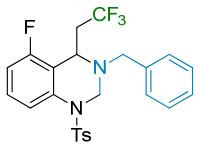
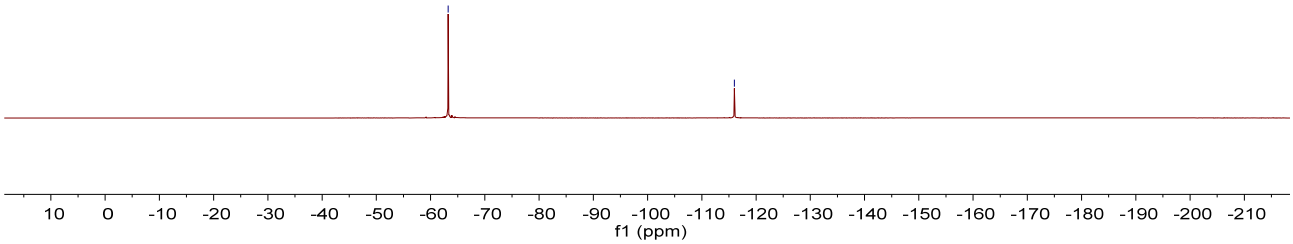
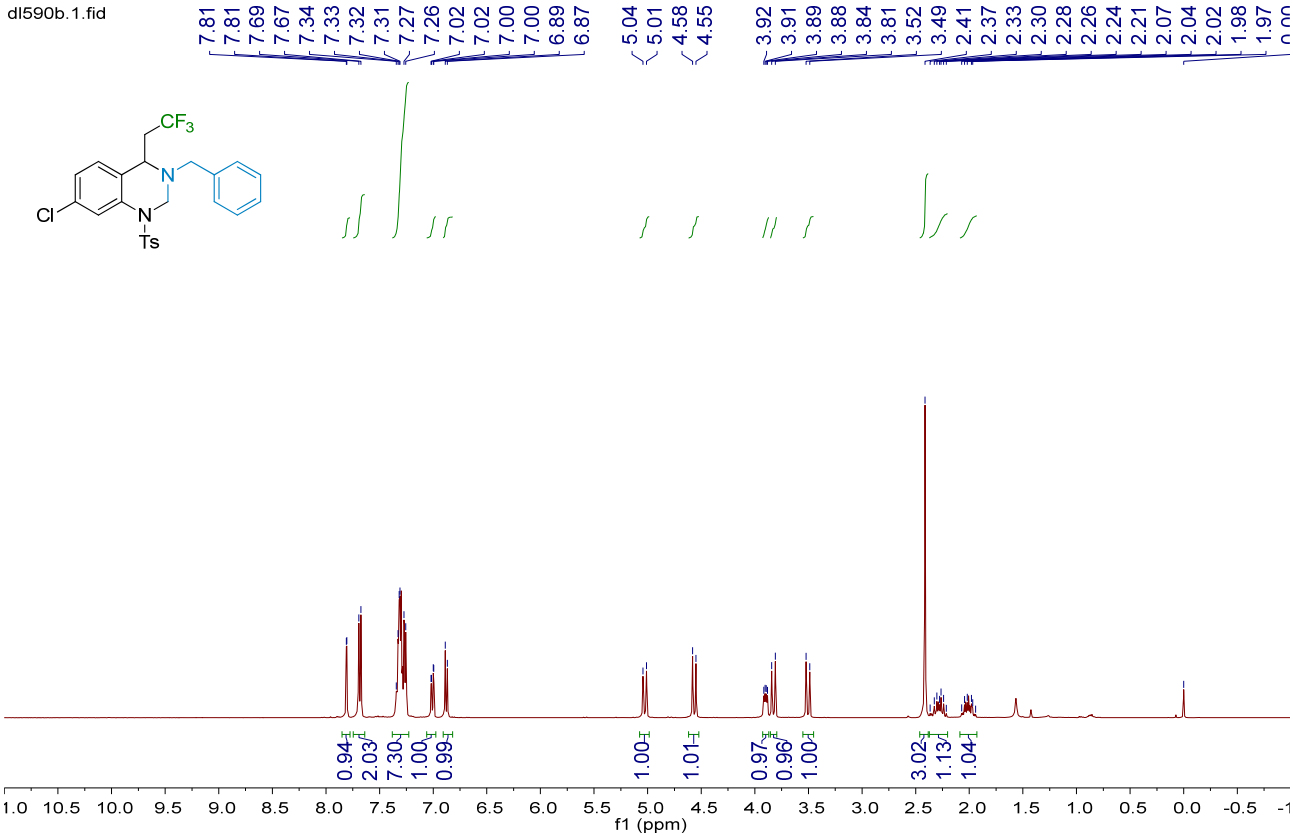
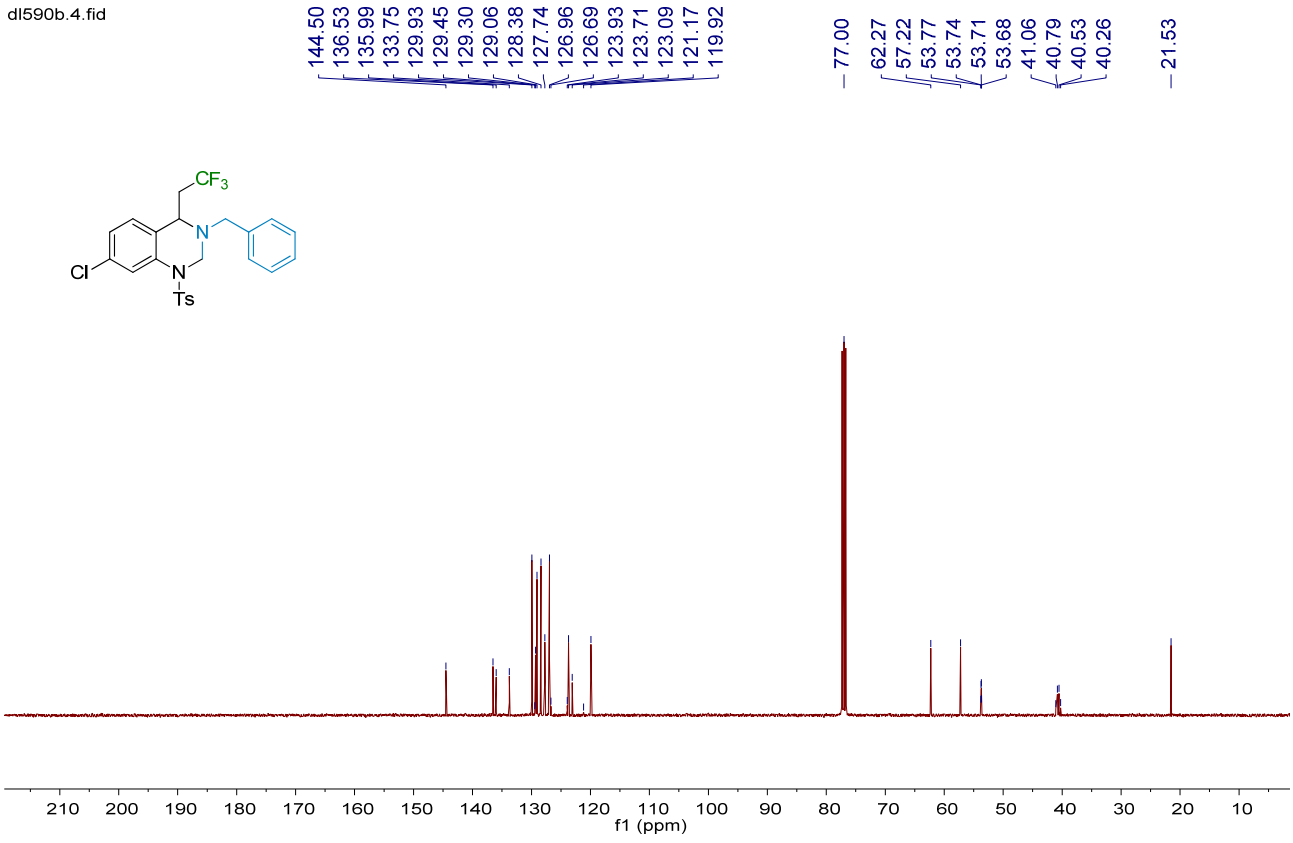
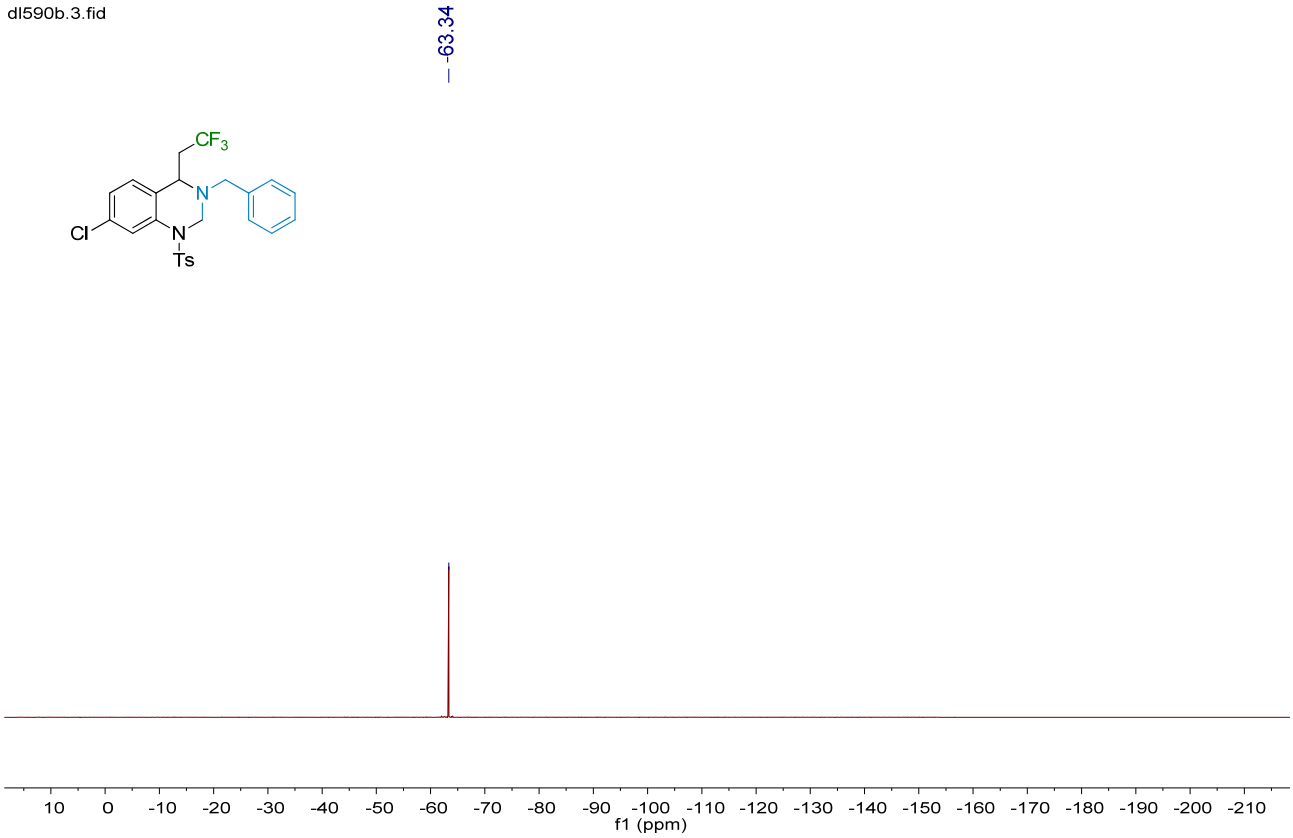




^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 5ha







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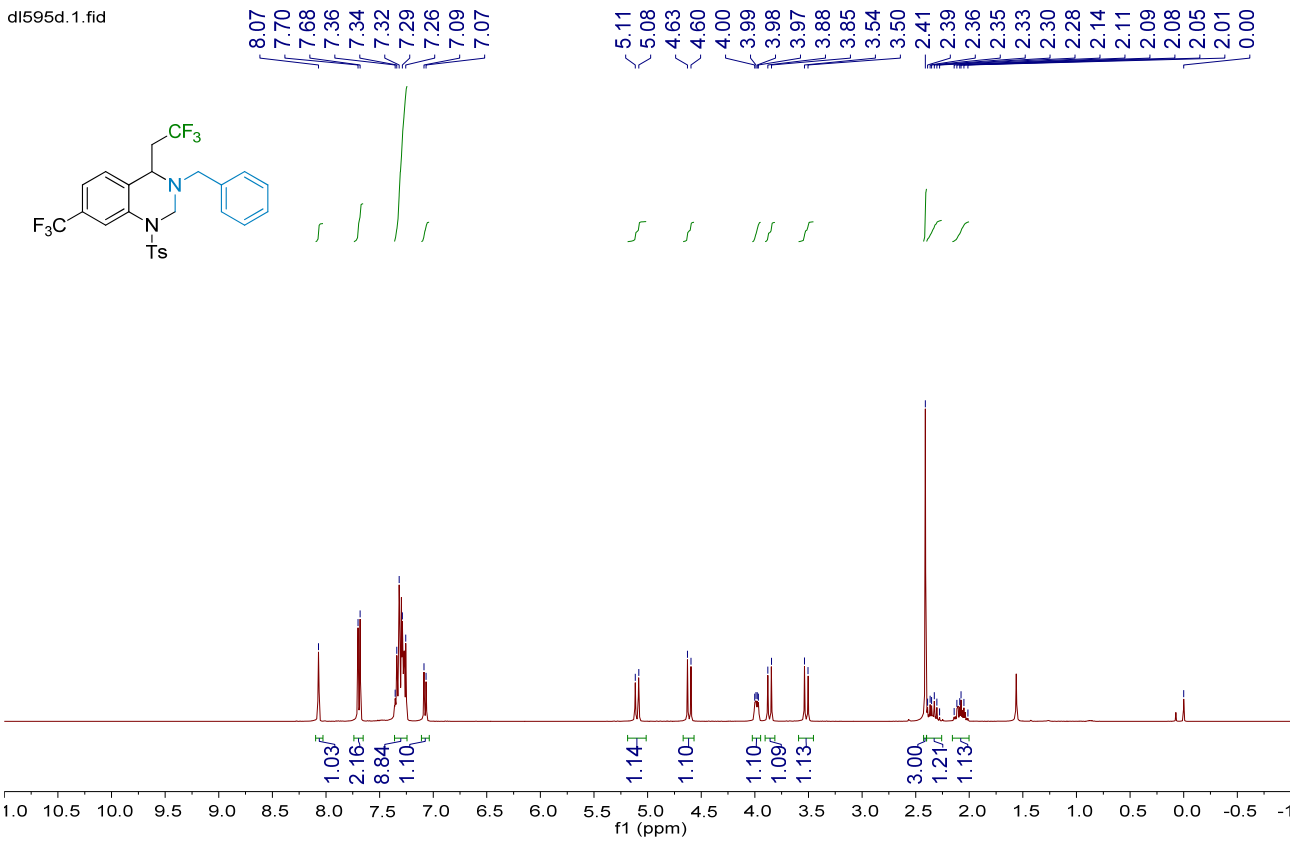

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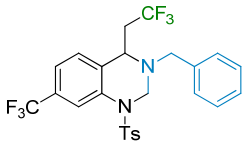

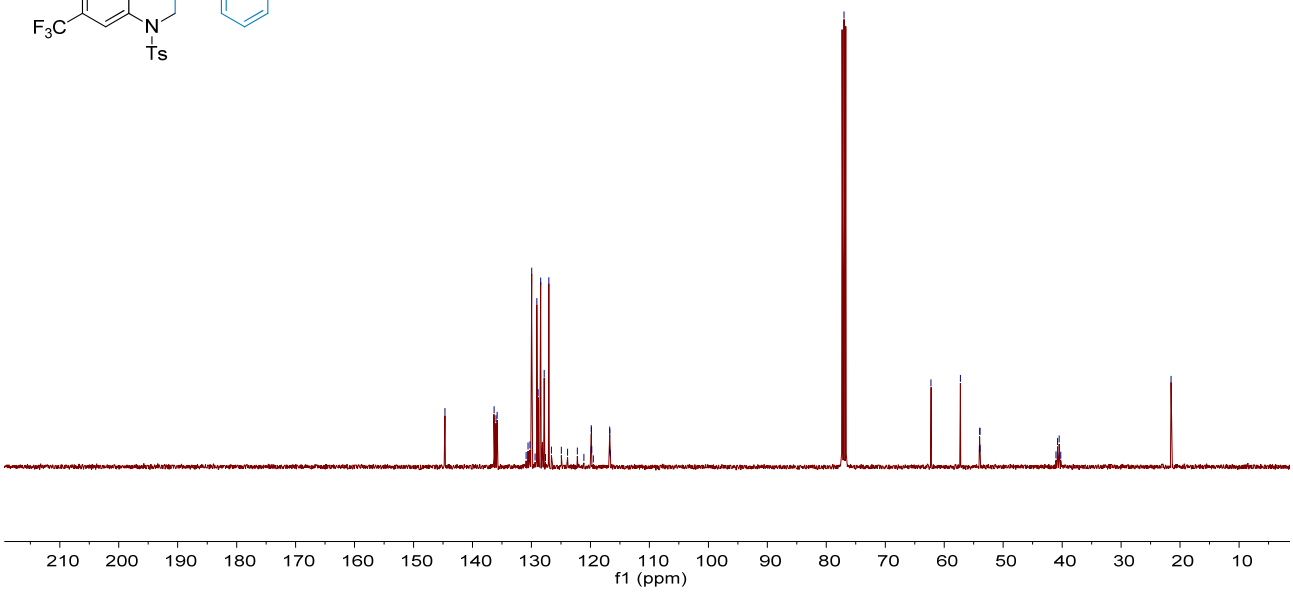

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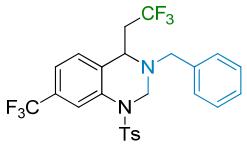

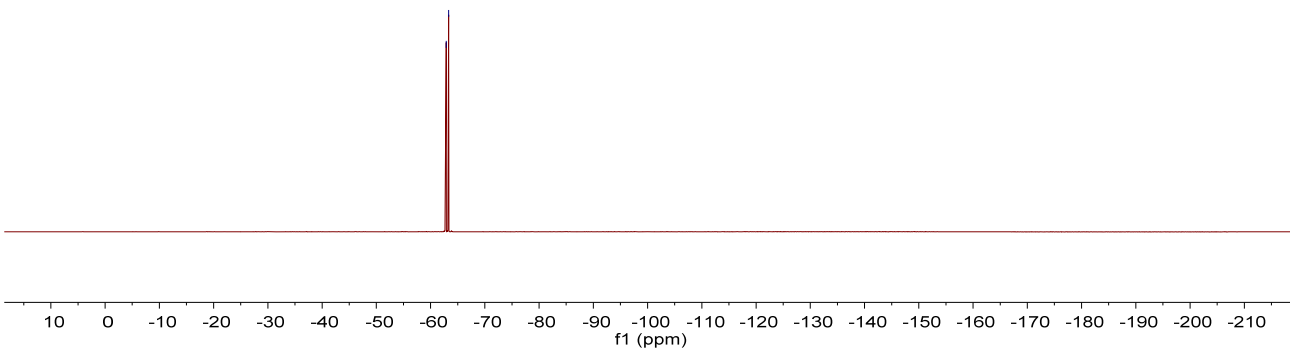

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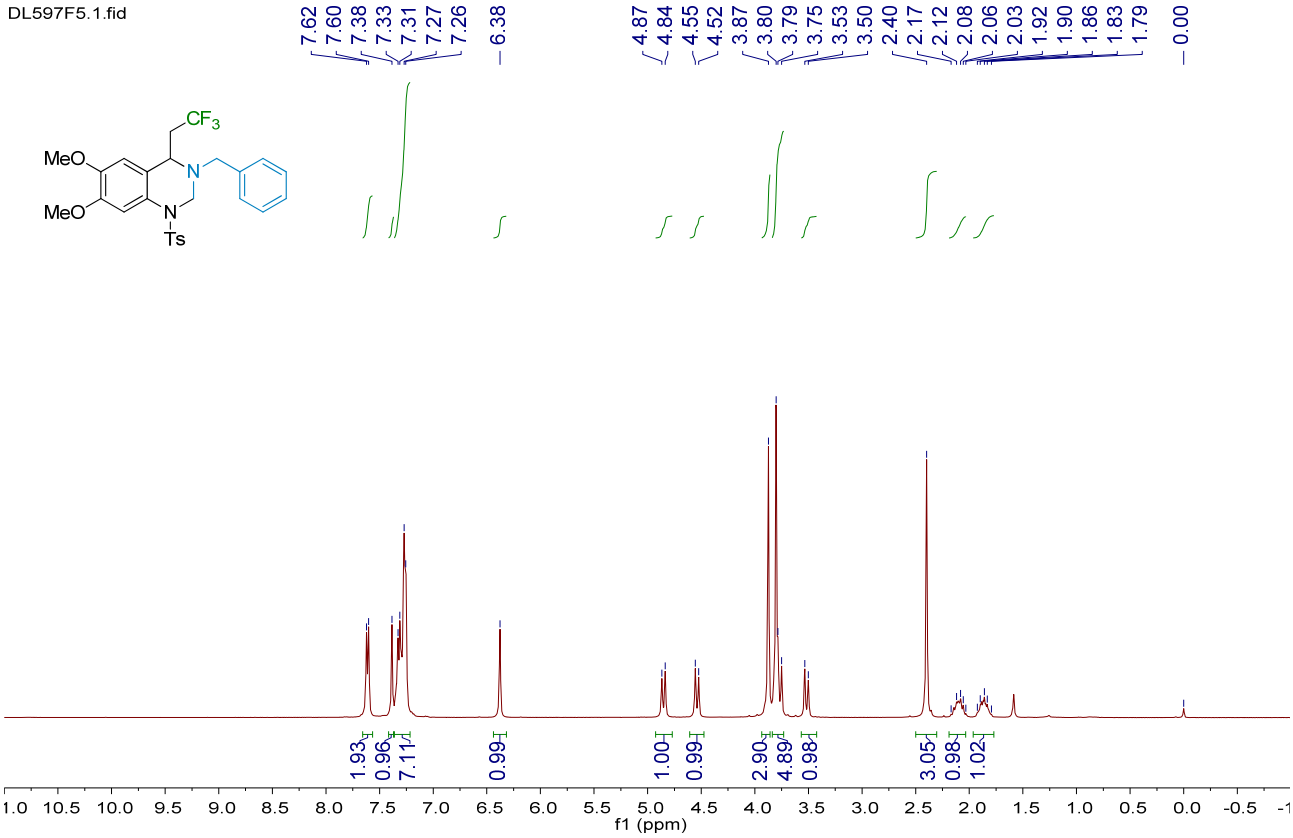

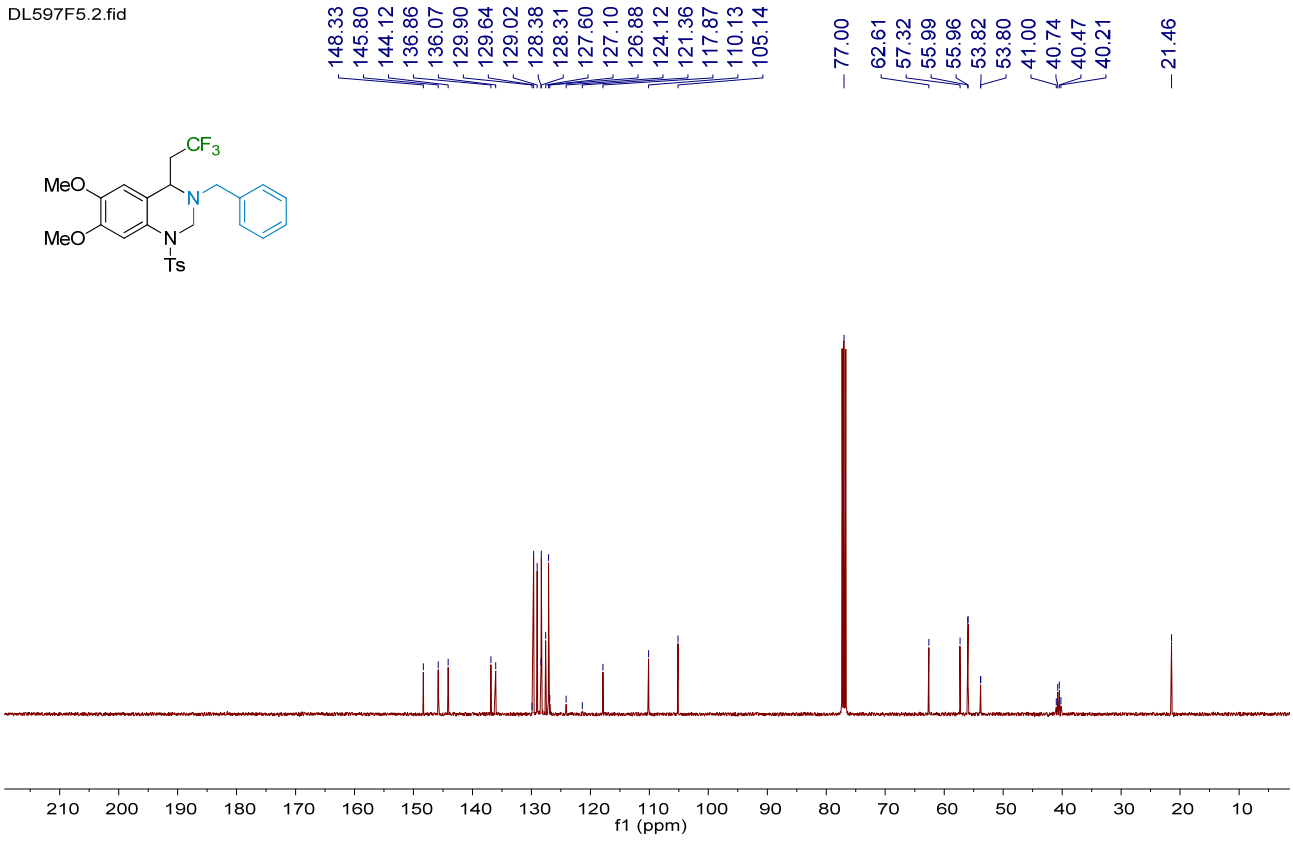

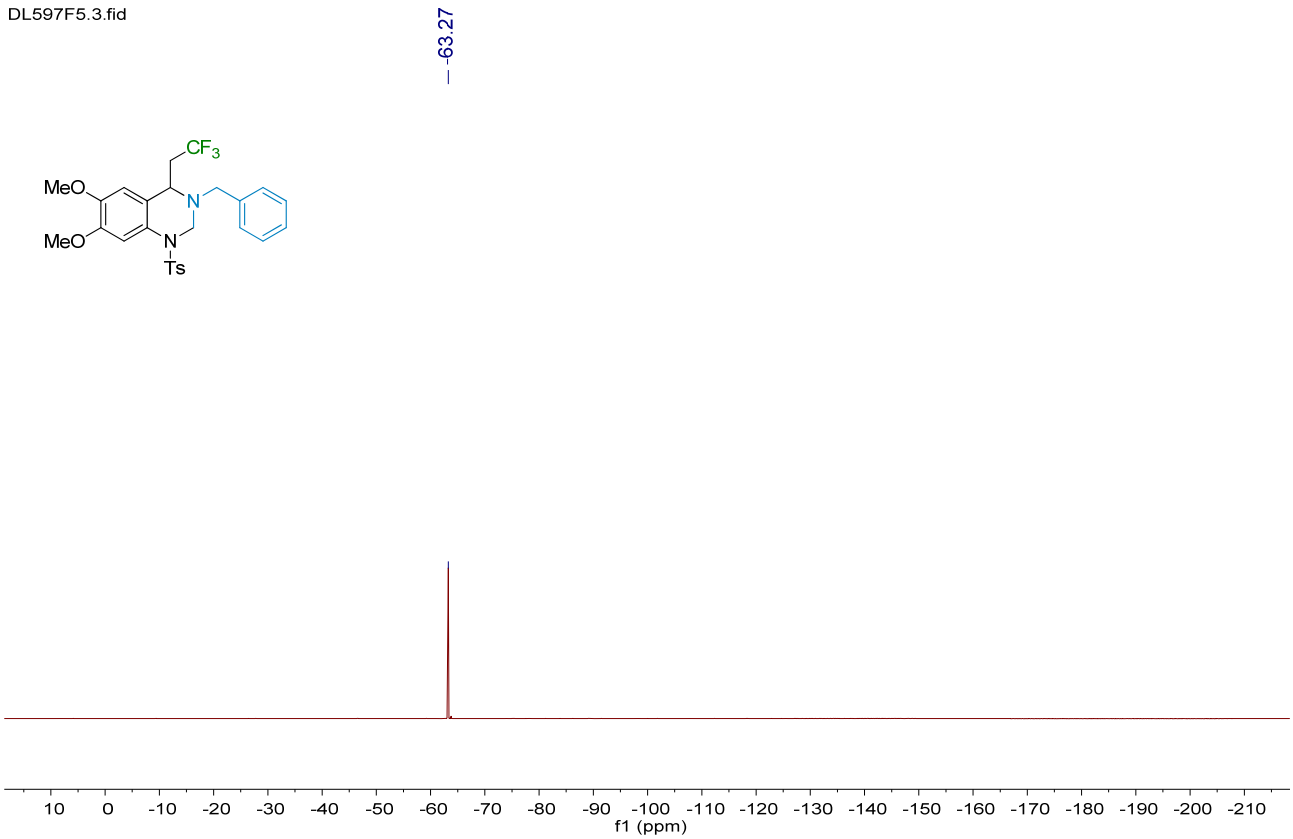

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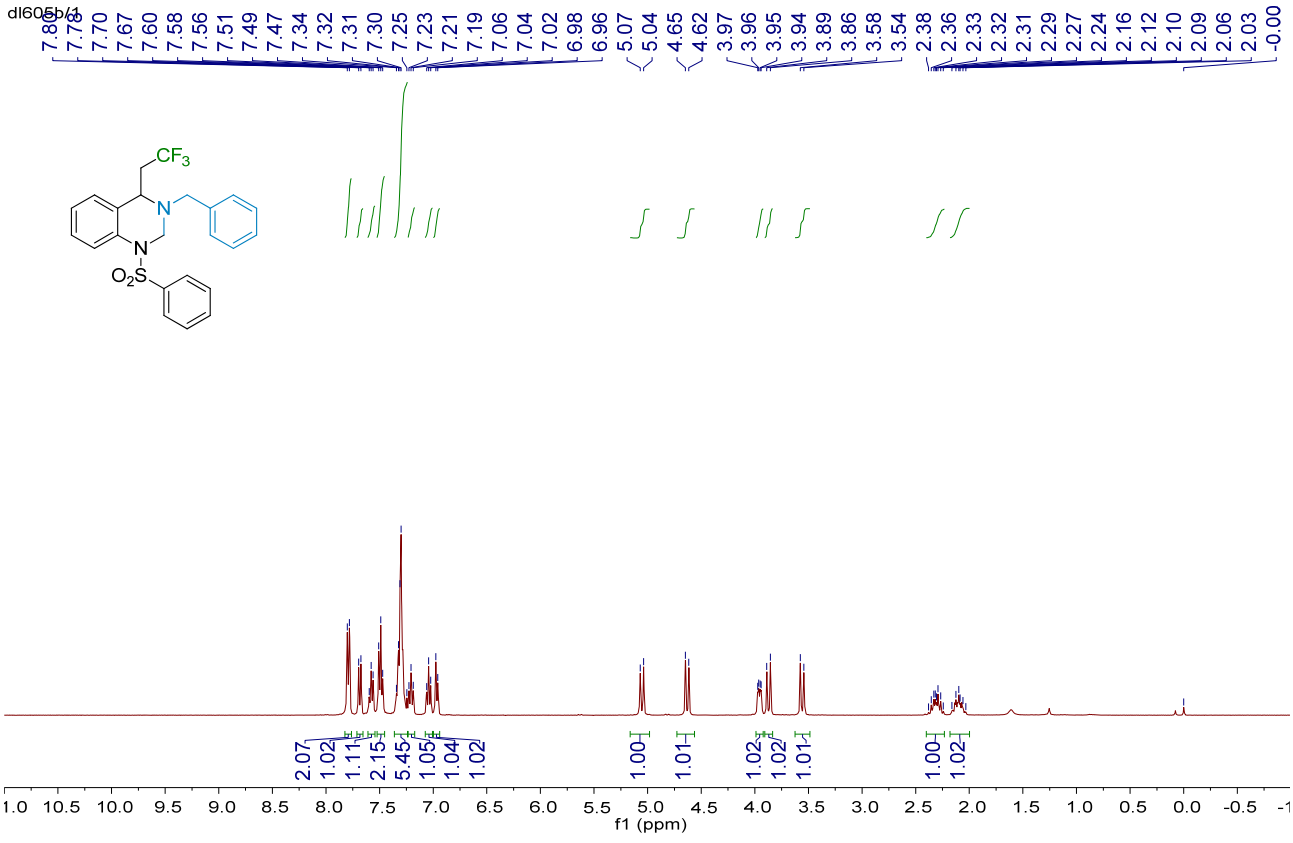

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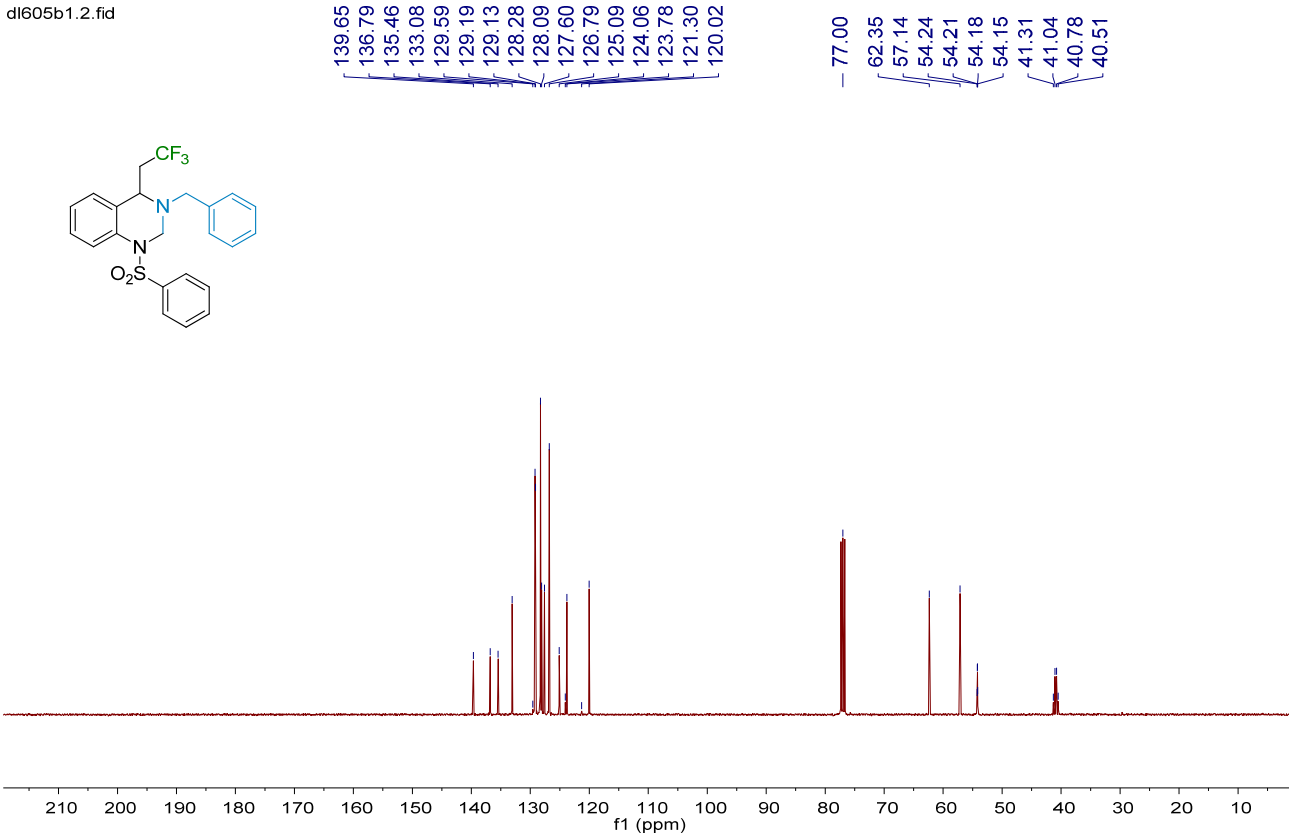

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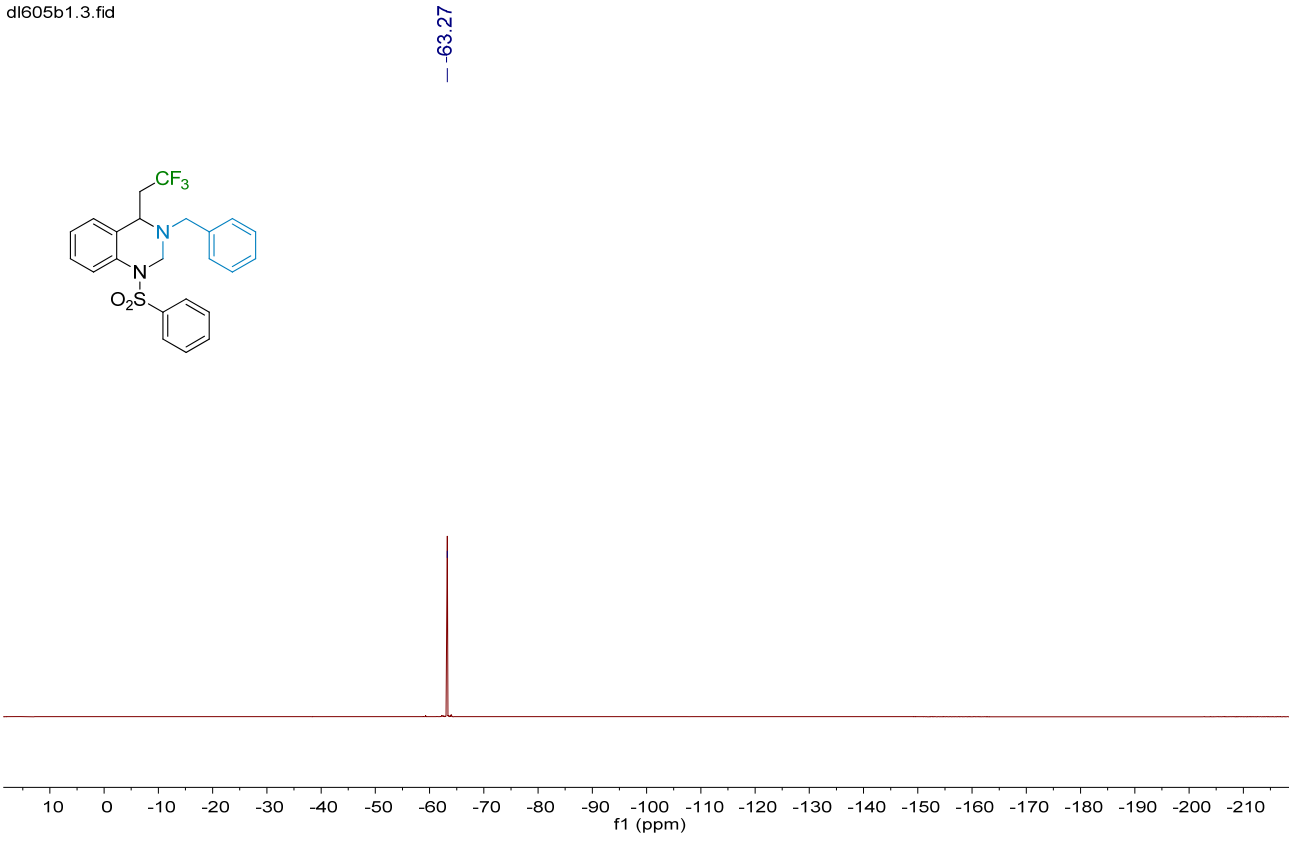
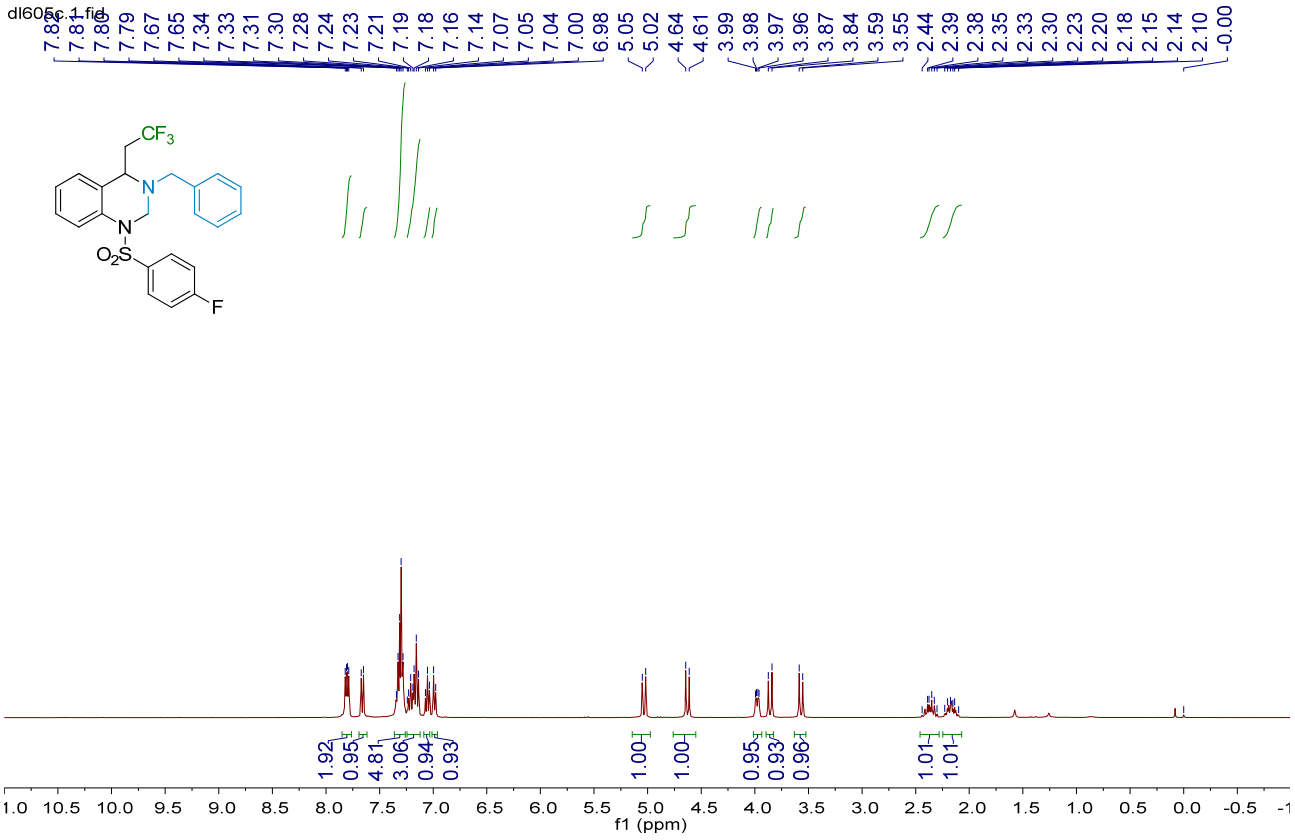
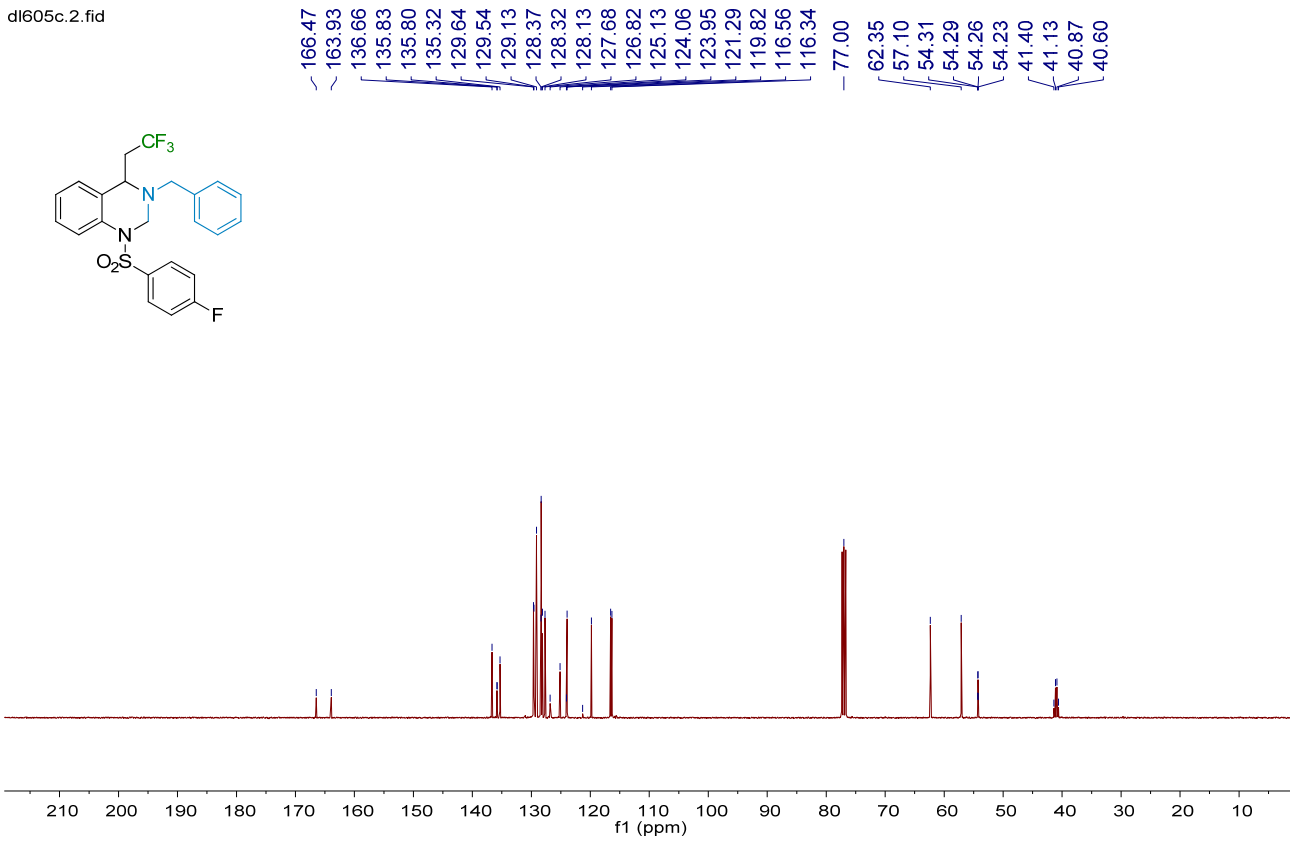
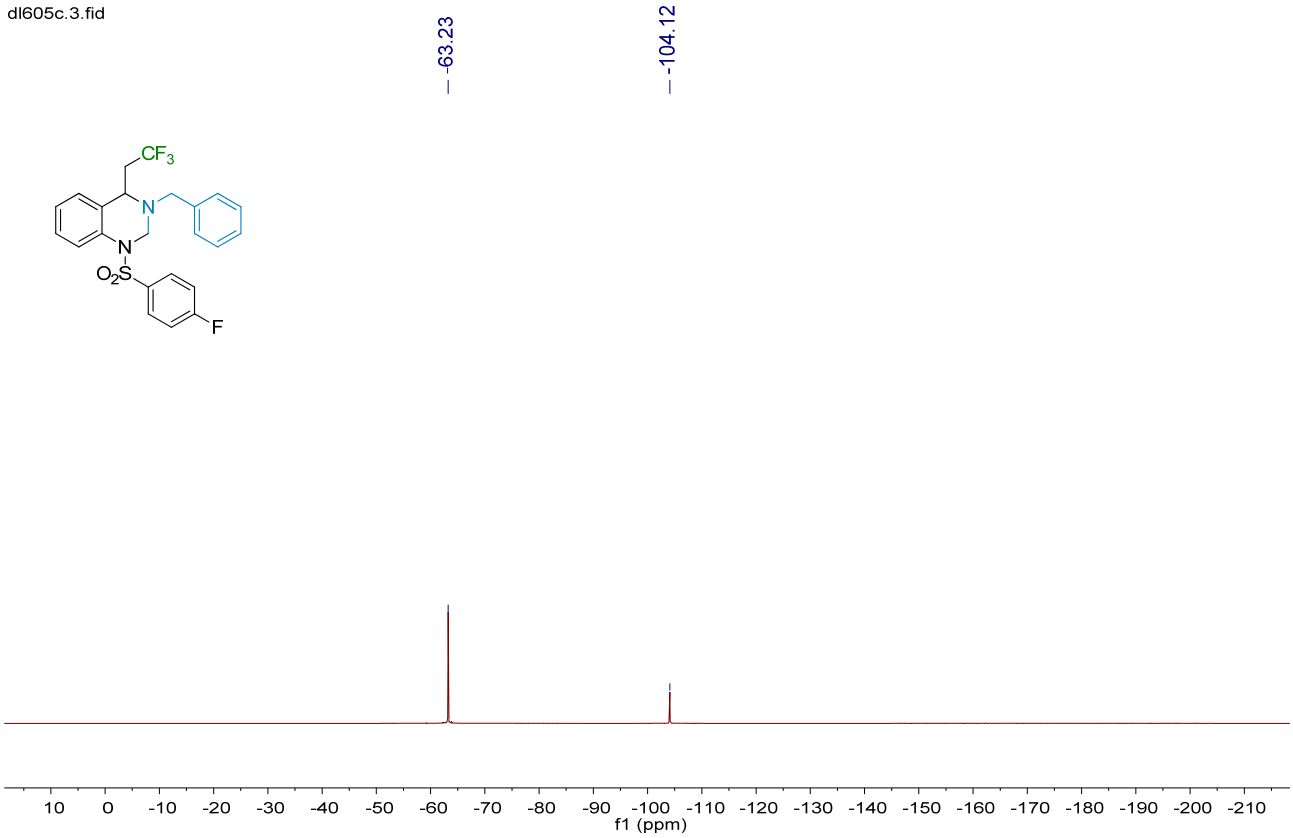


^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 5la







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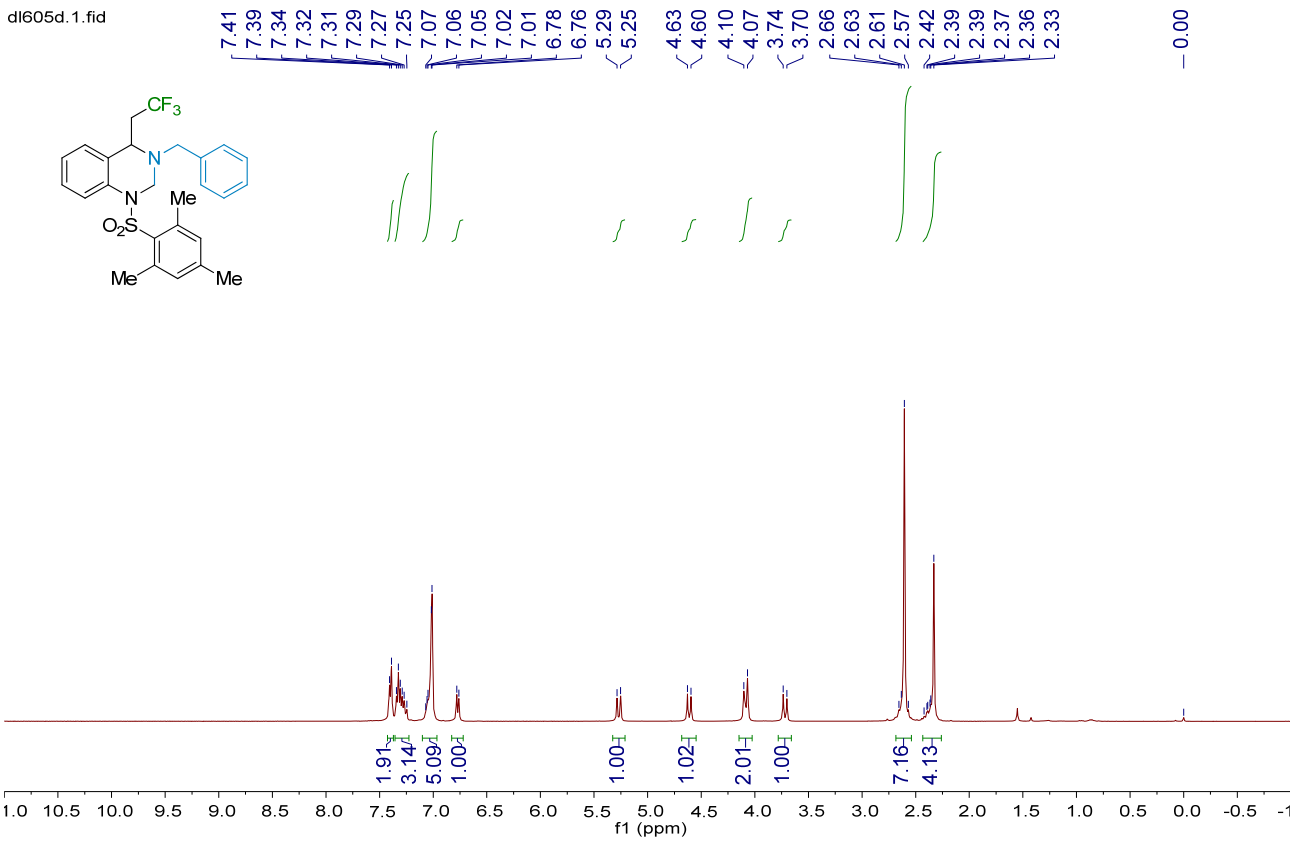

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77.00

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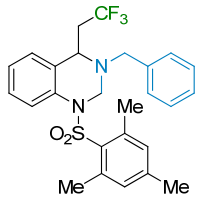

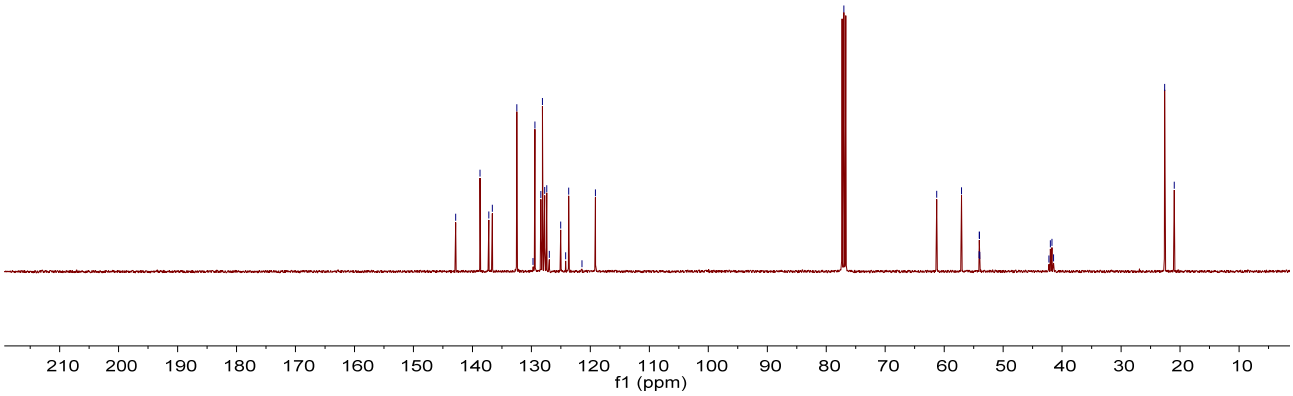

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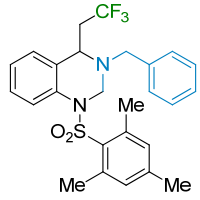
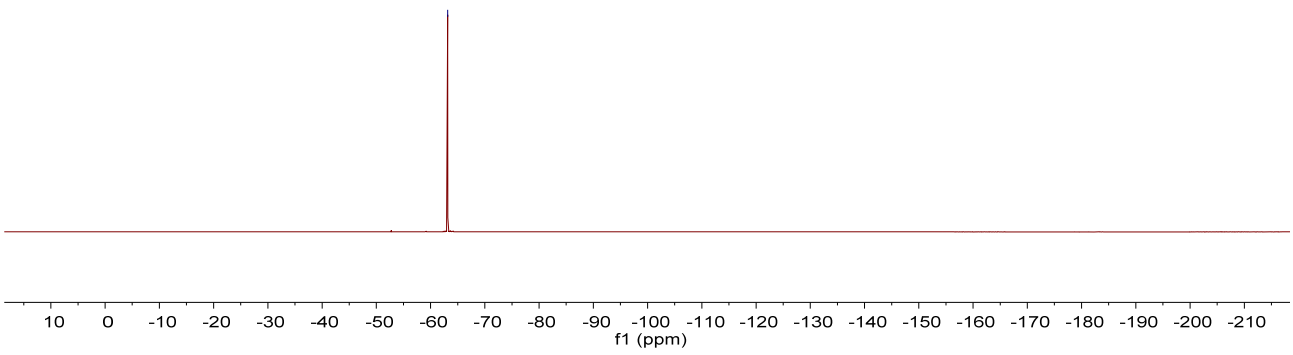
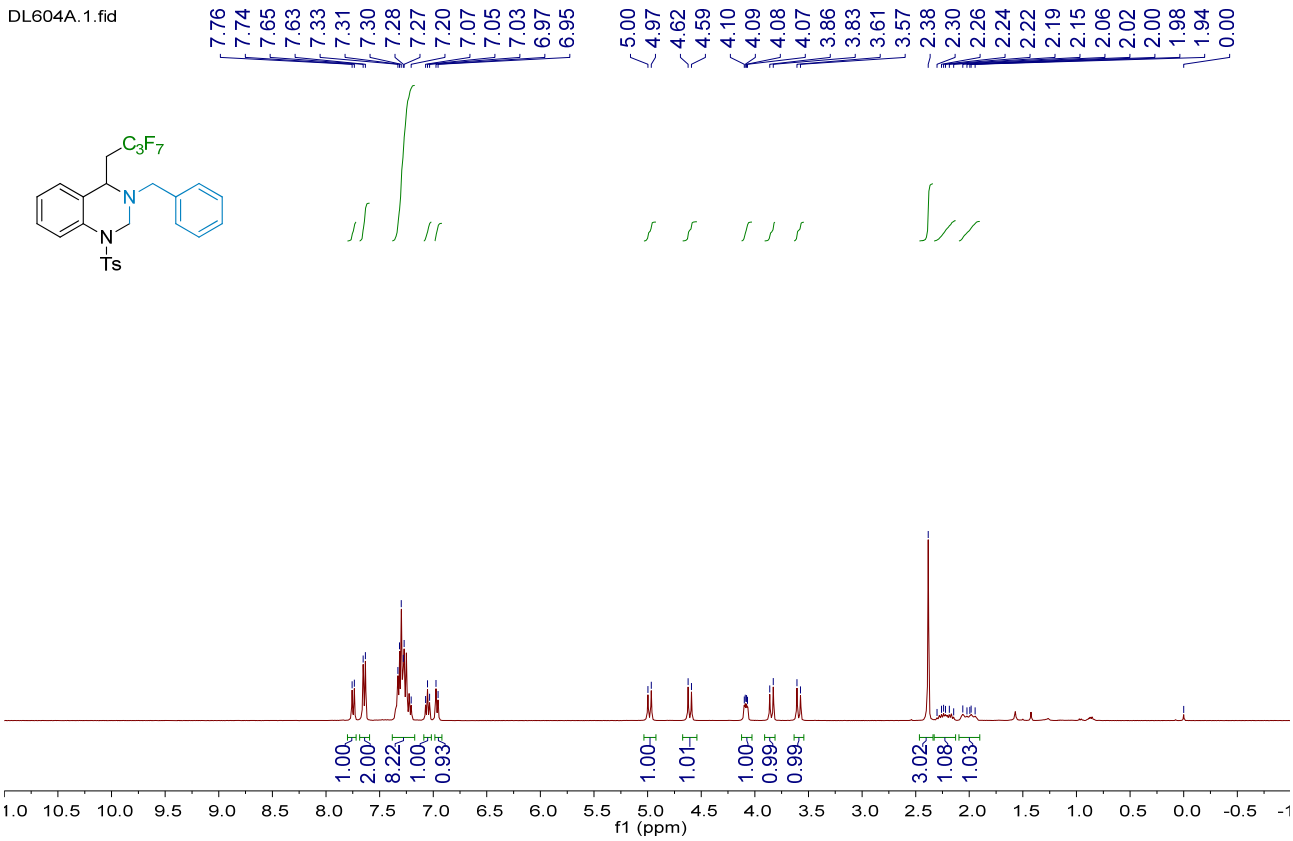
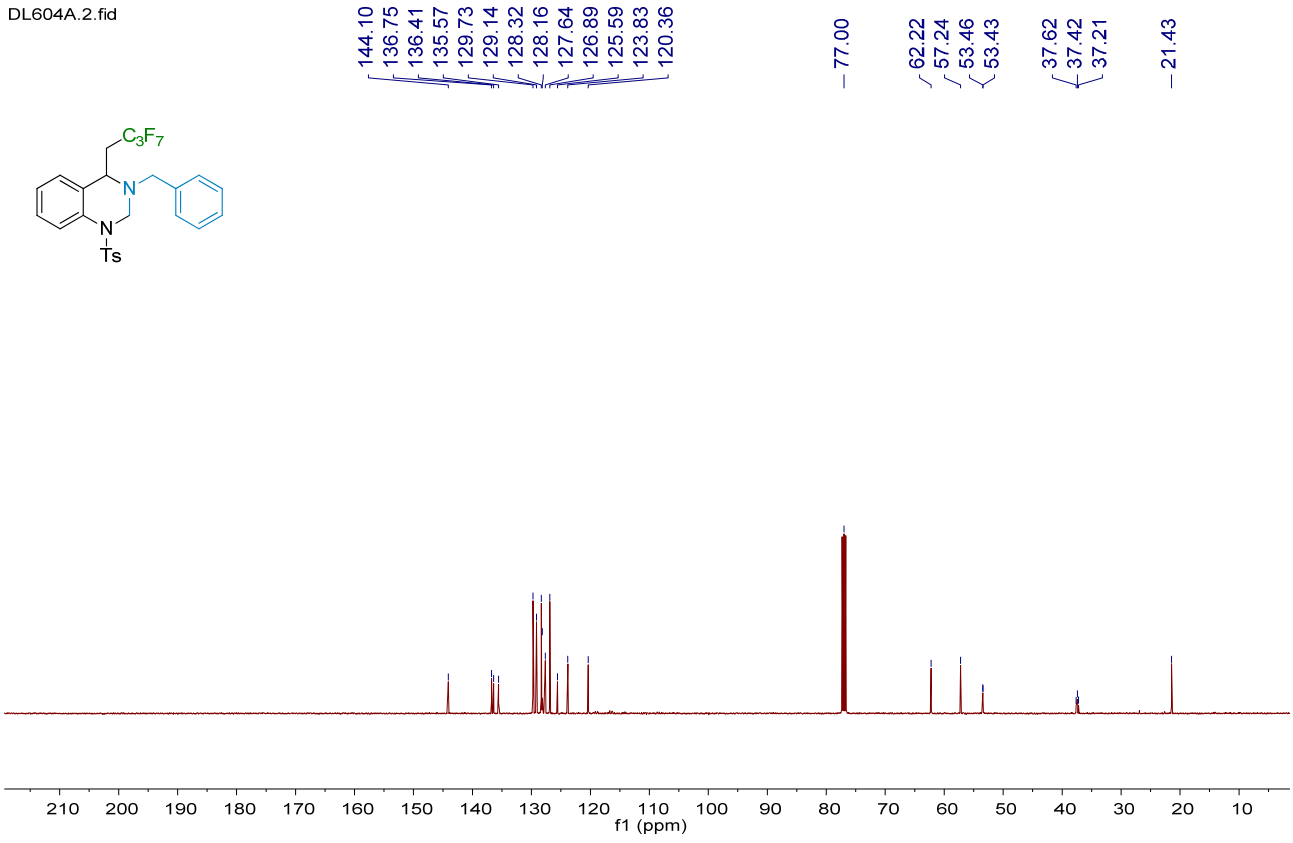
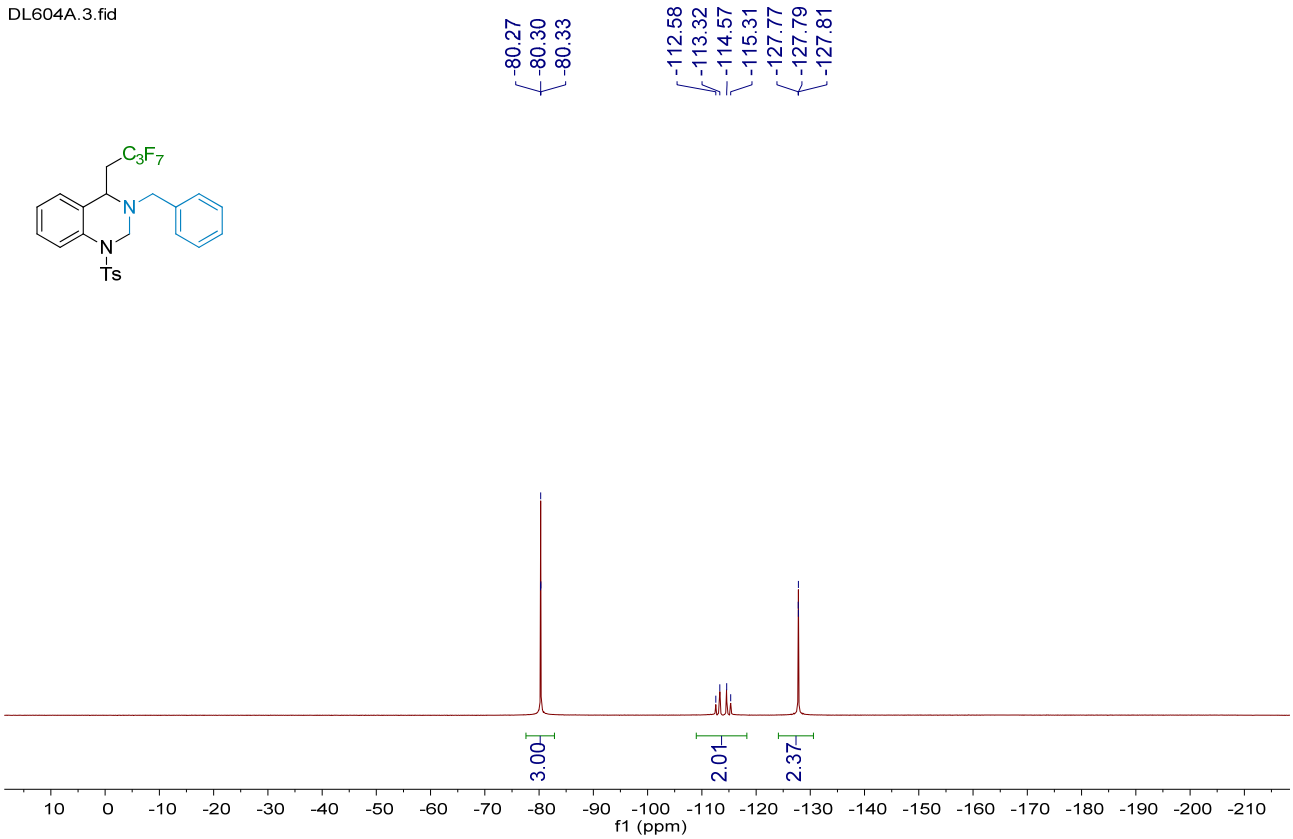




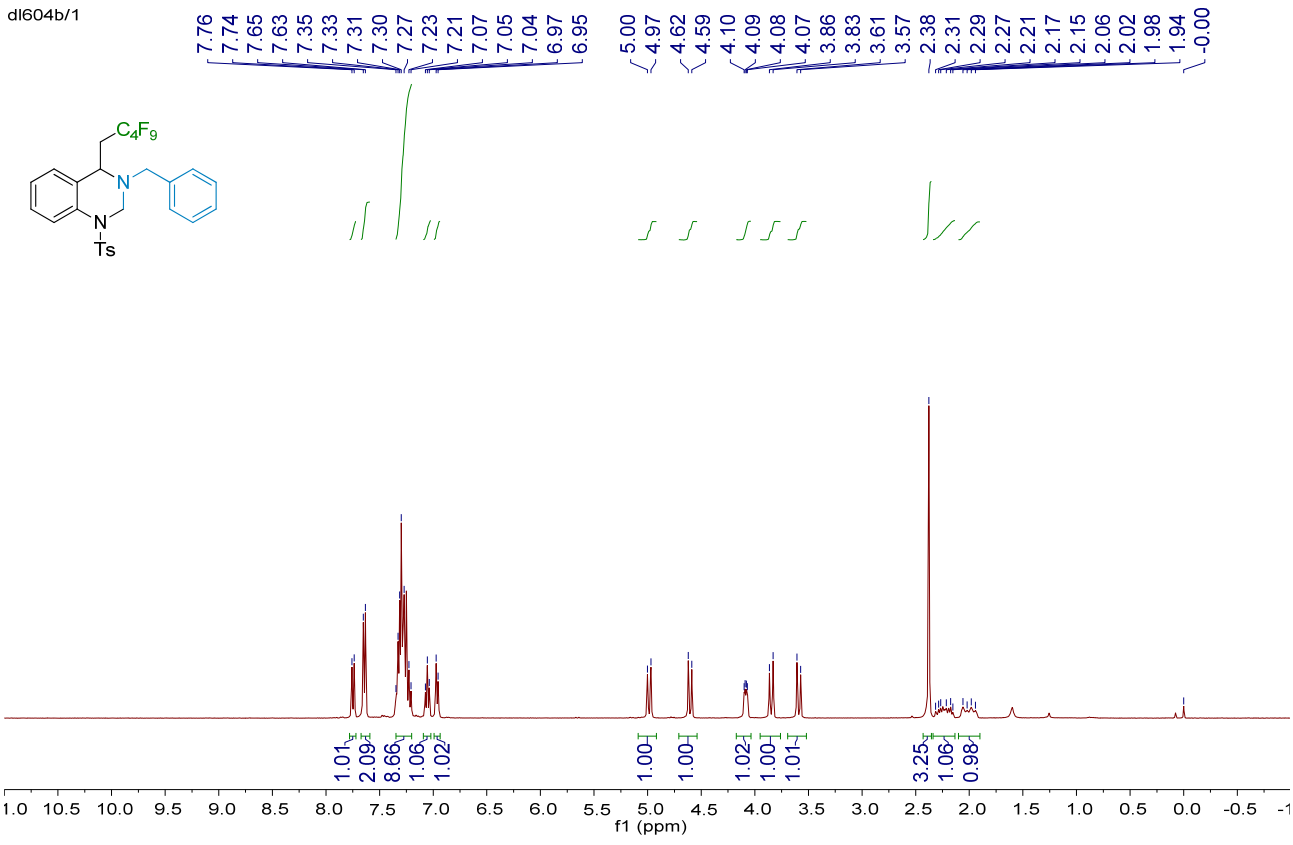
^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 6ab







^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 6ac



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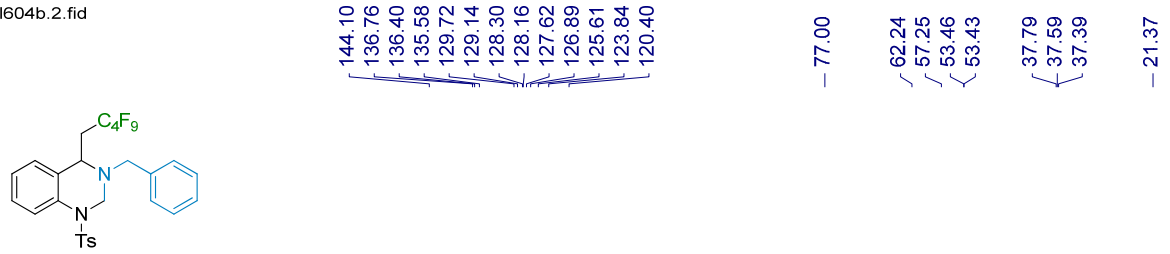

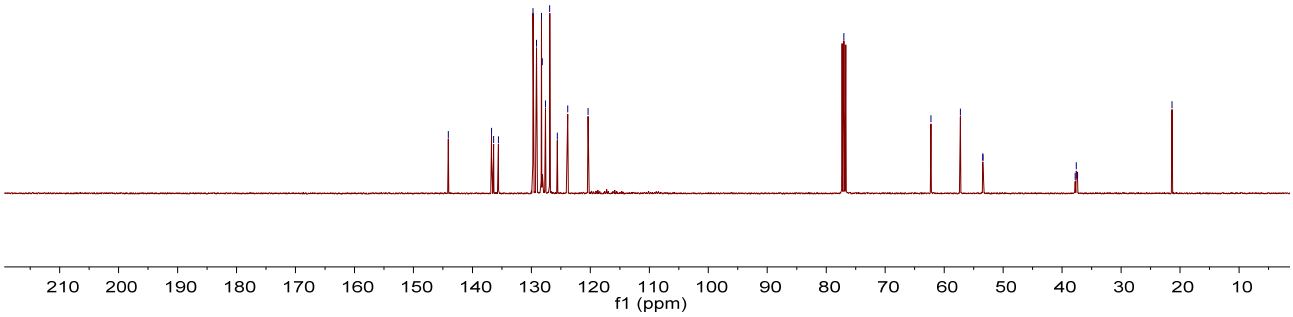

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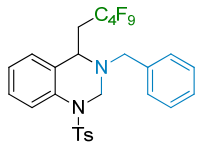
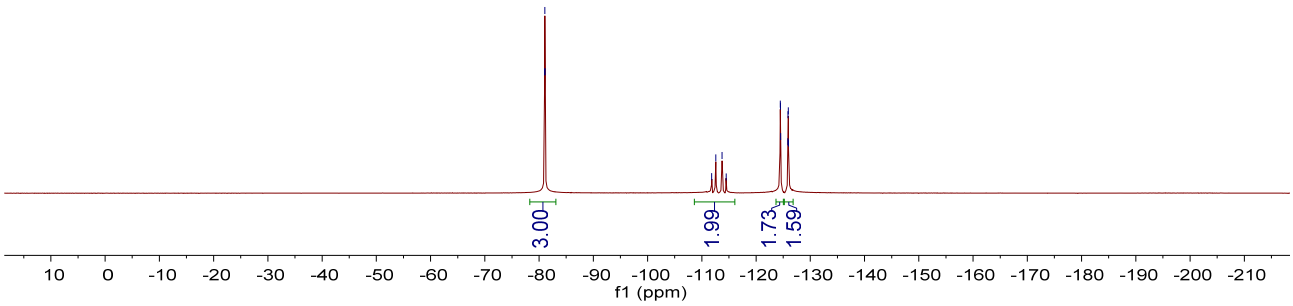
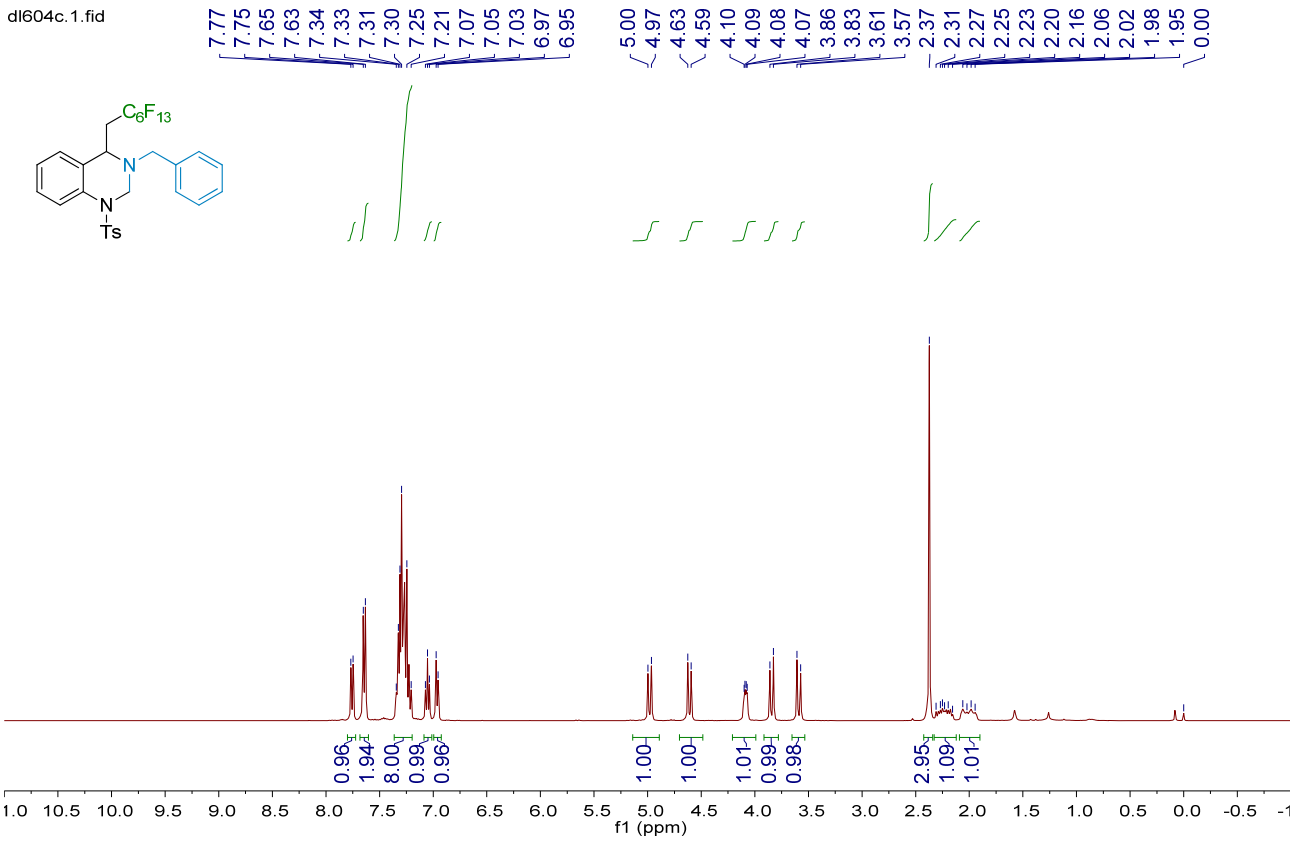
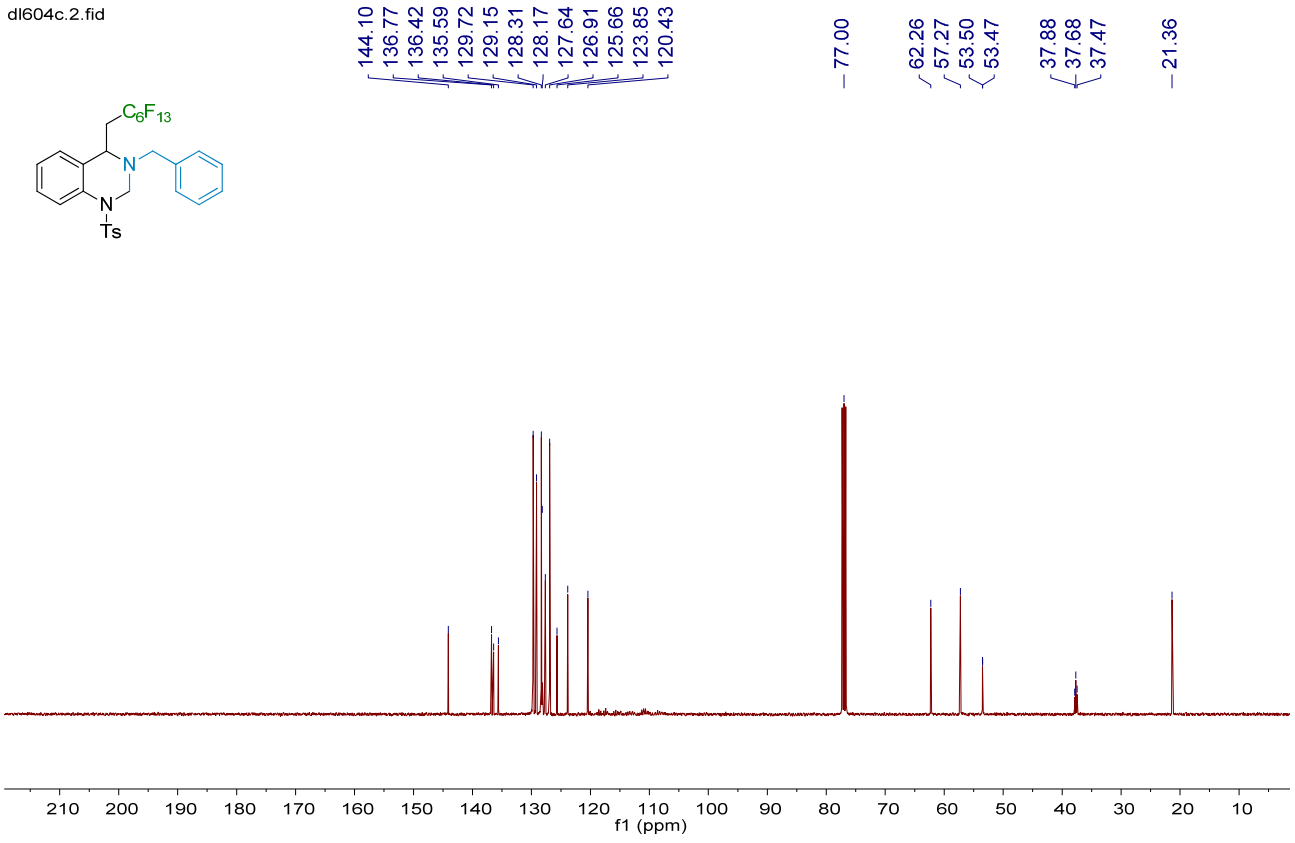
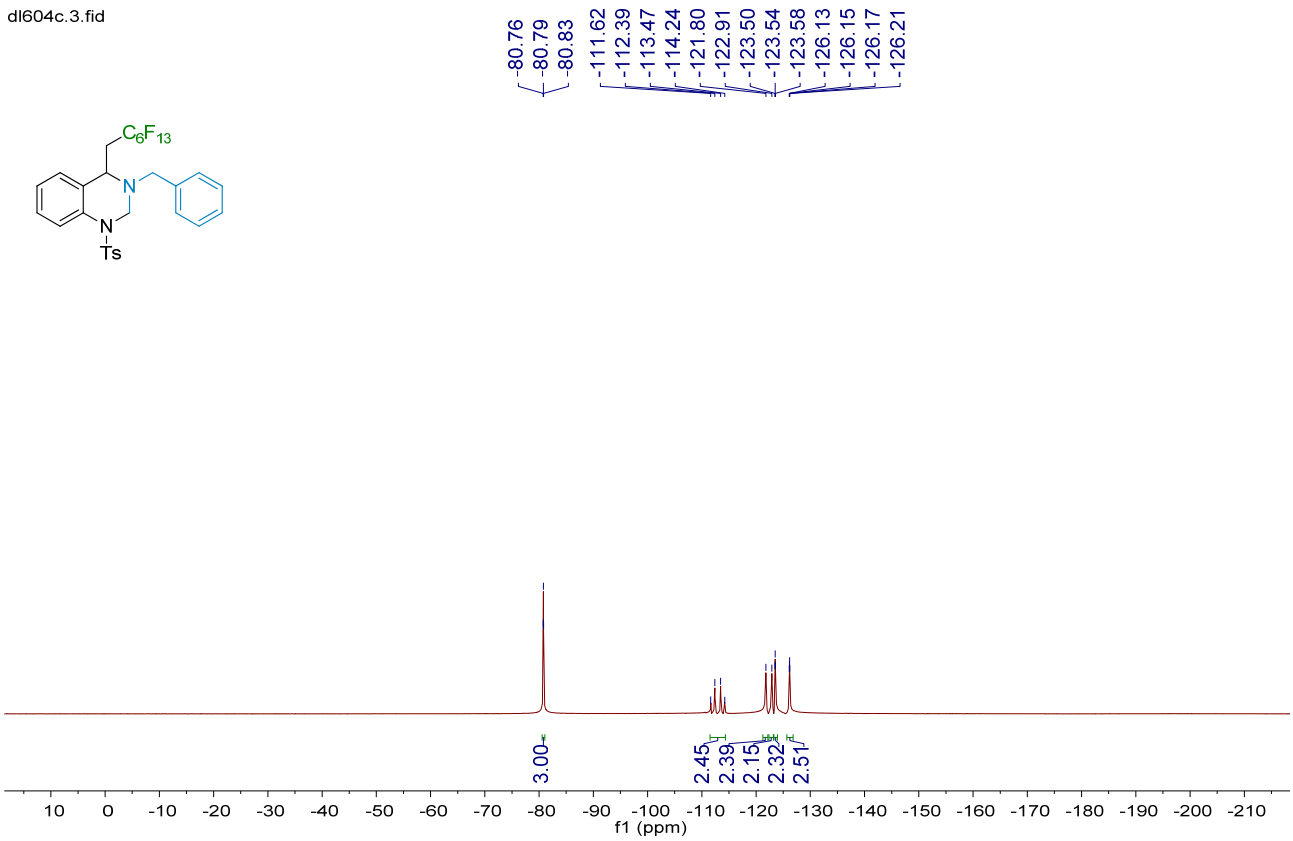




^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 6ad







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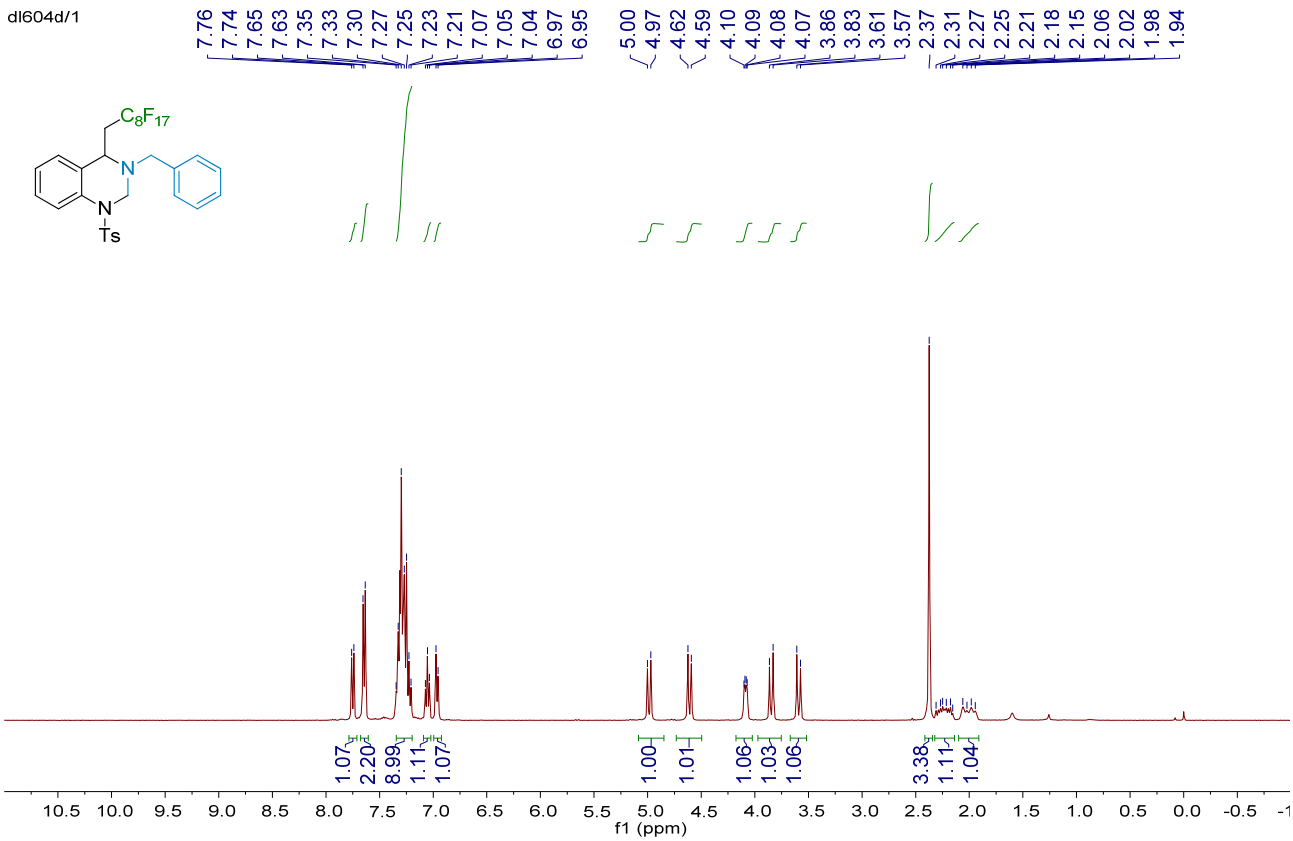

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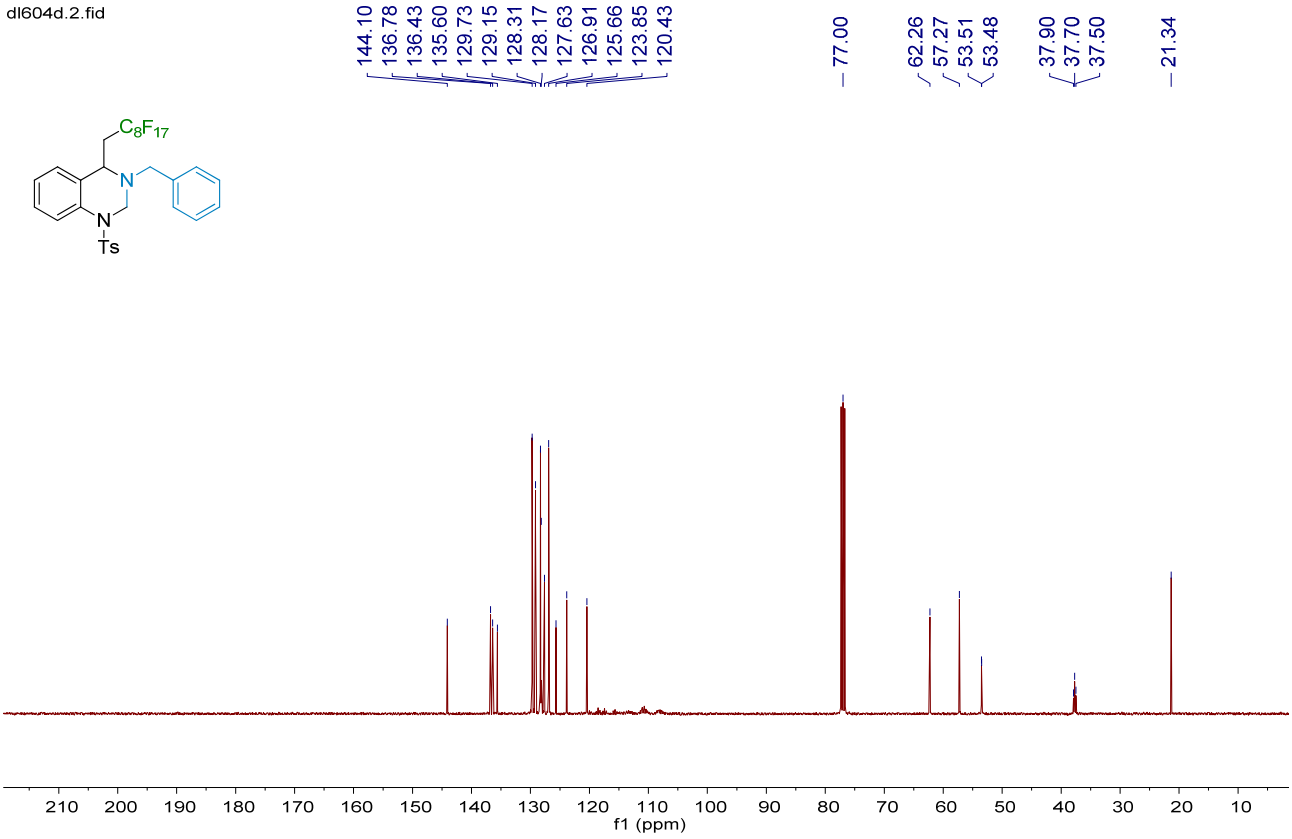

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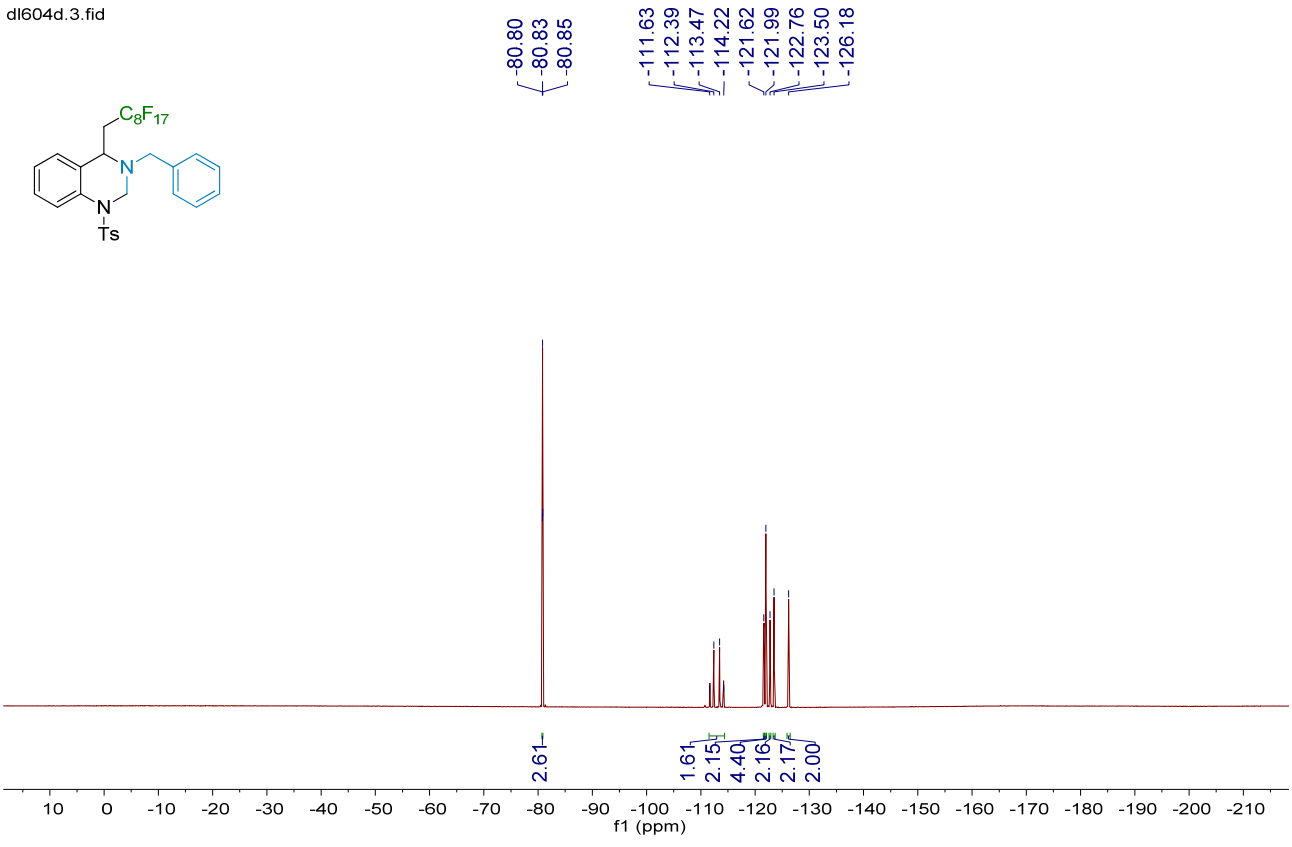
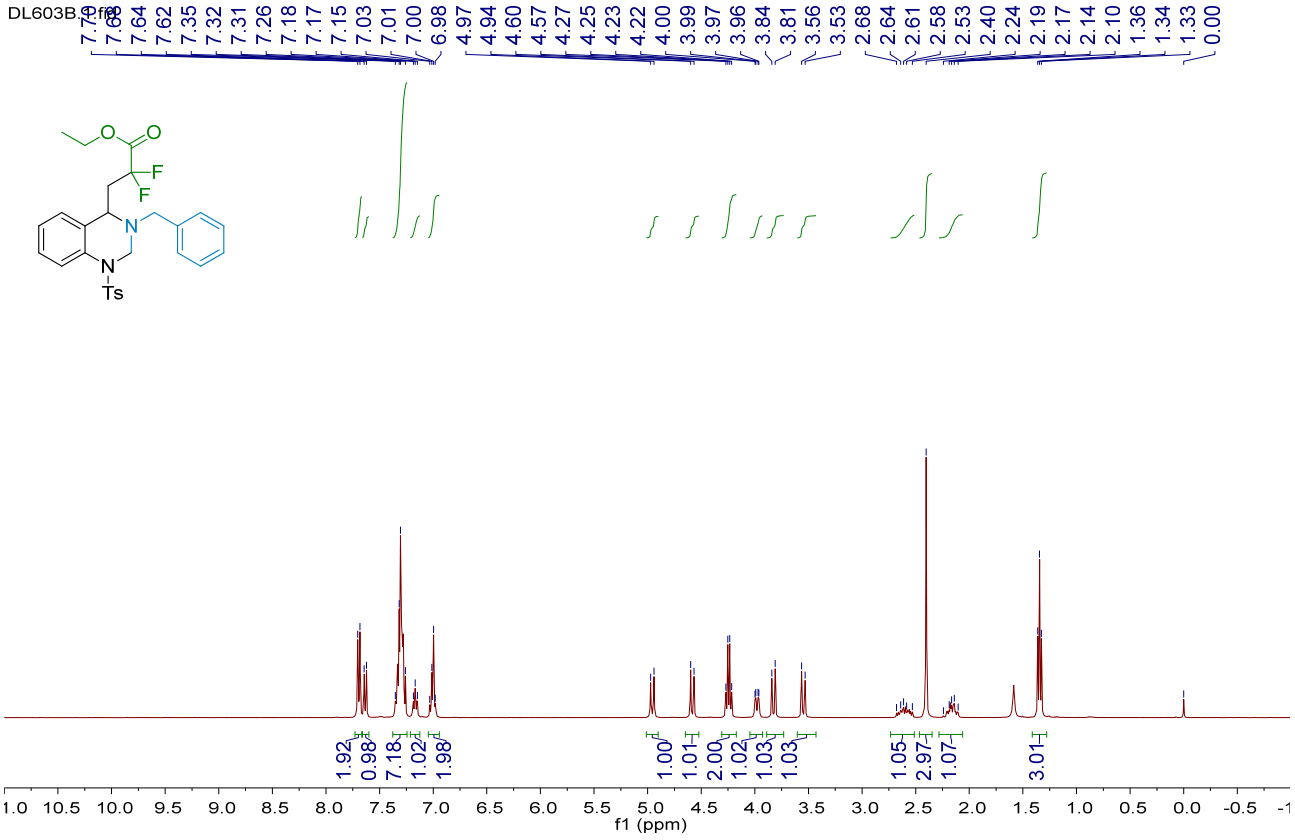
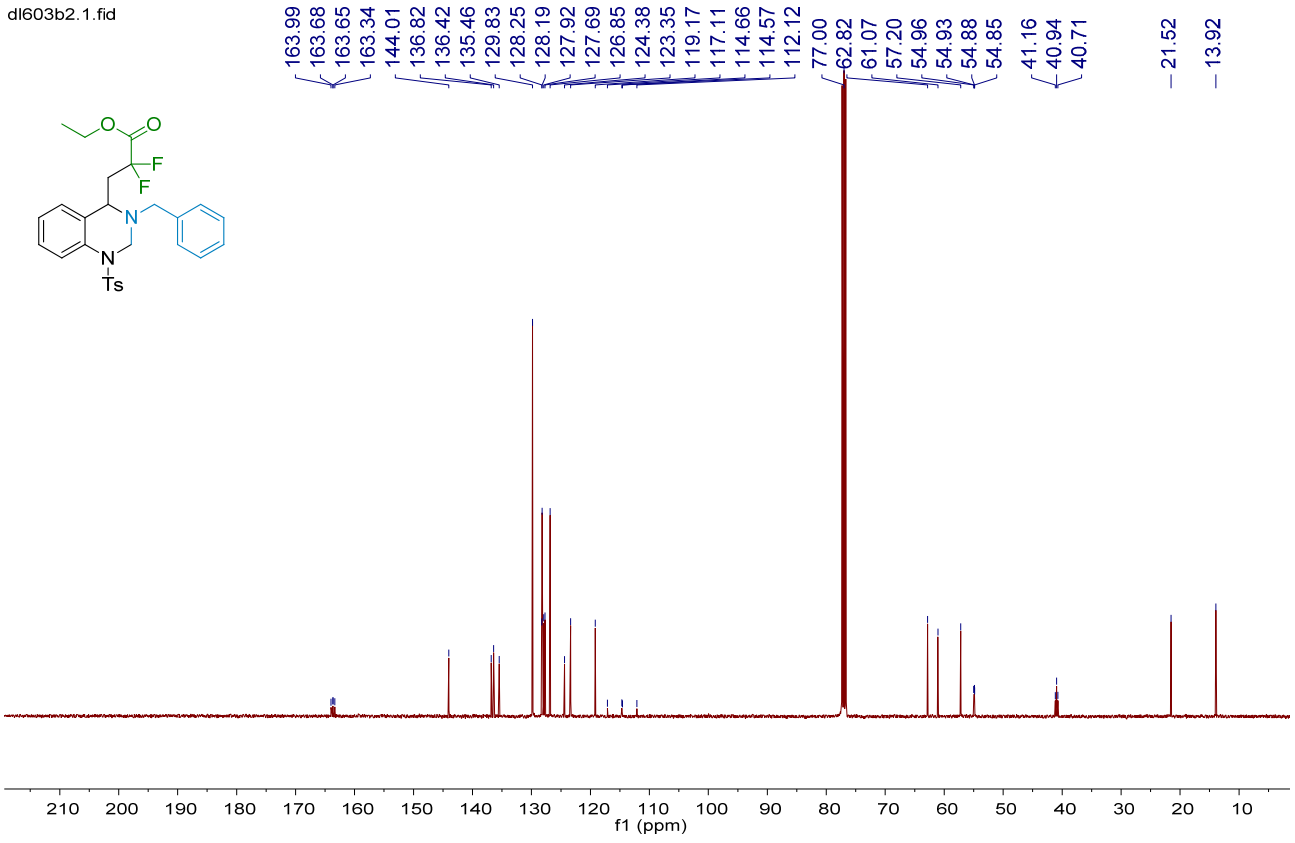
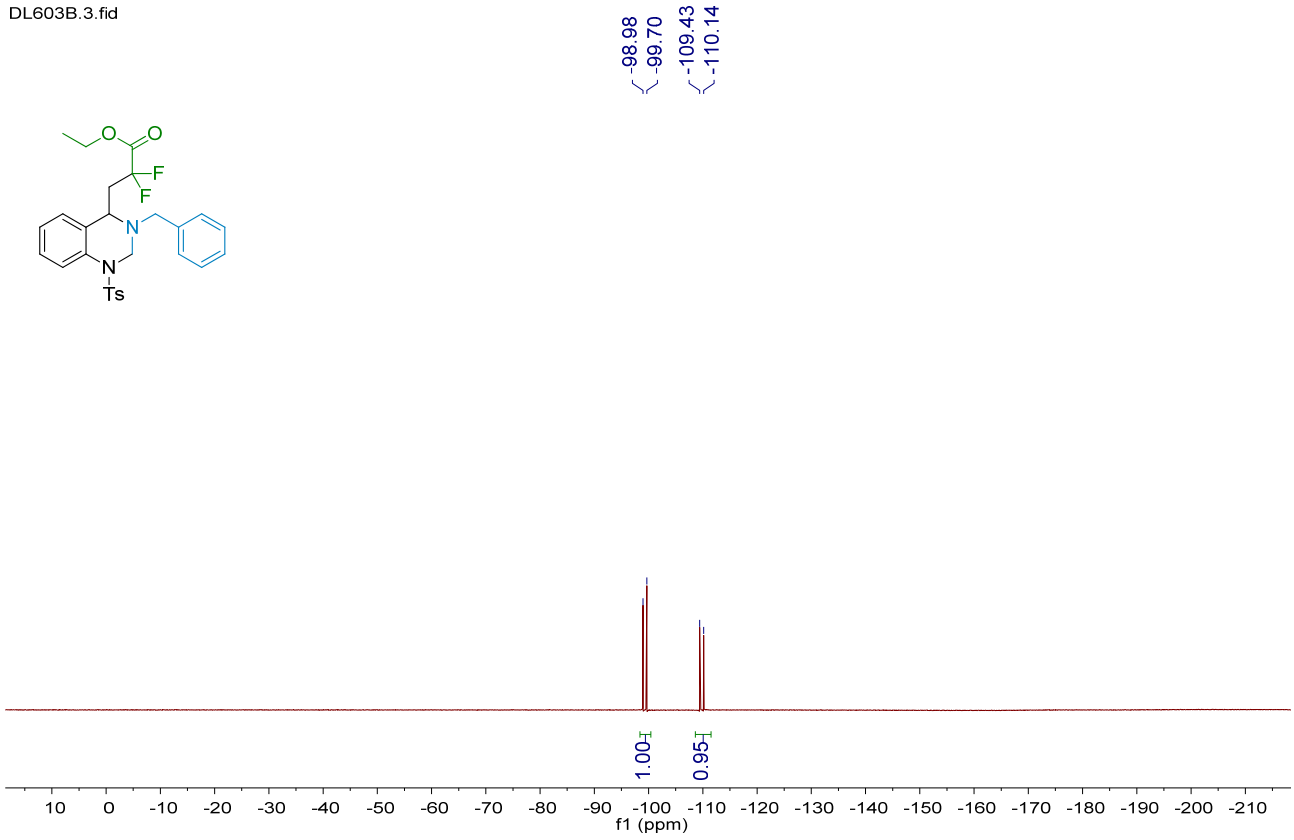


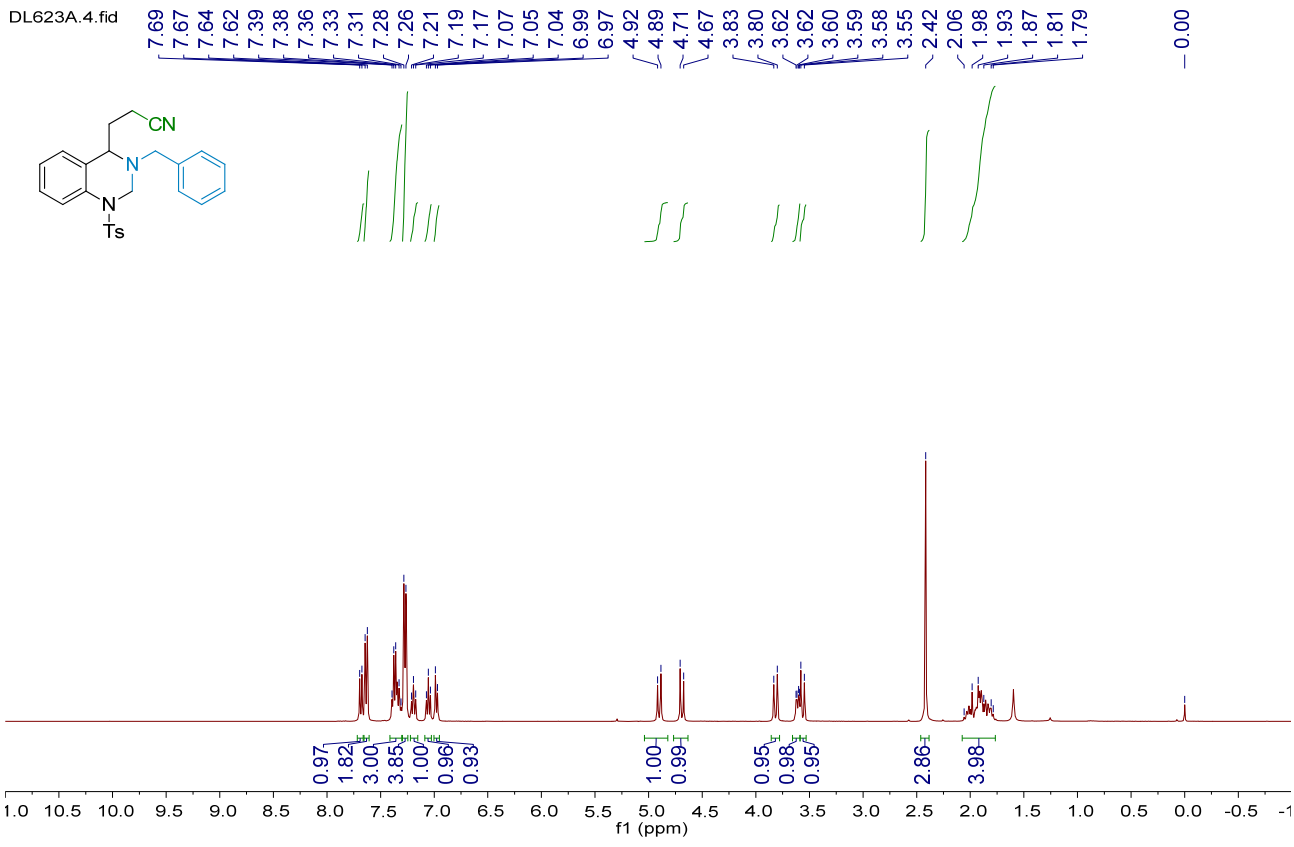
^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 6af

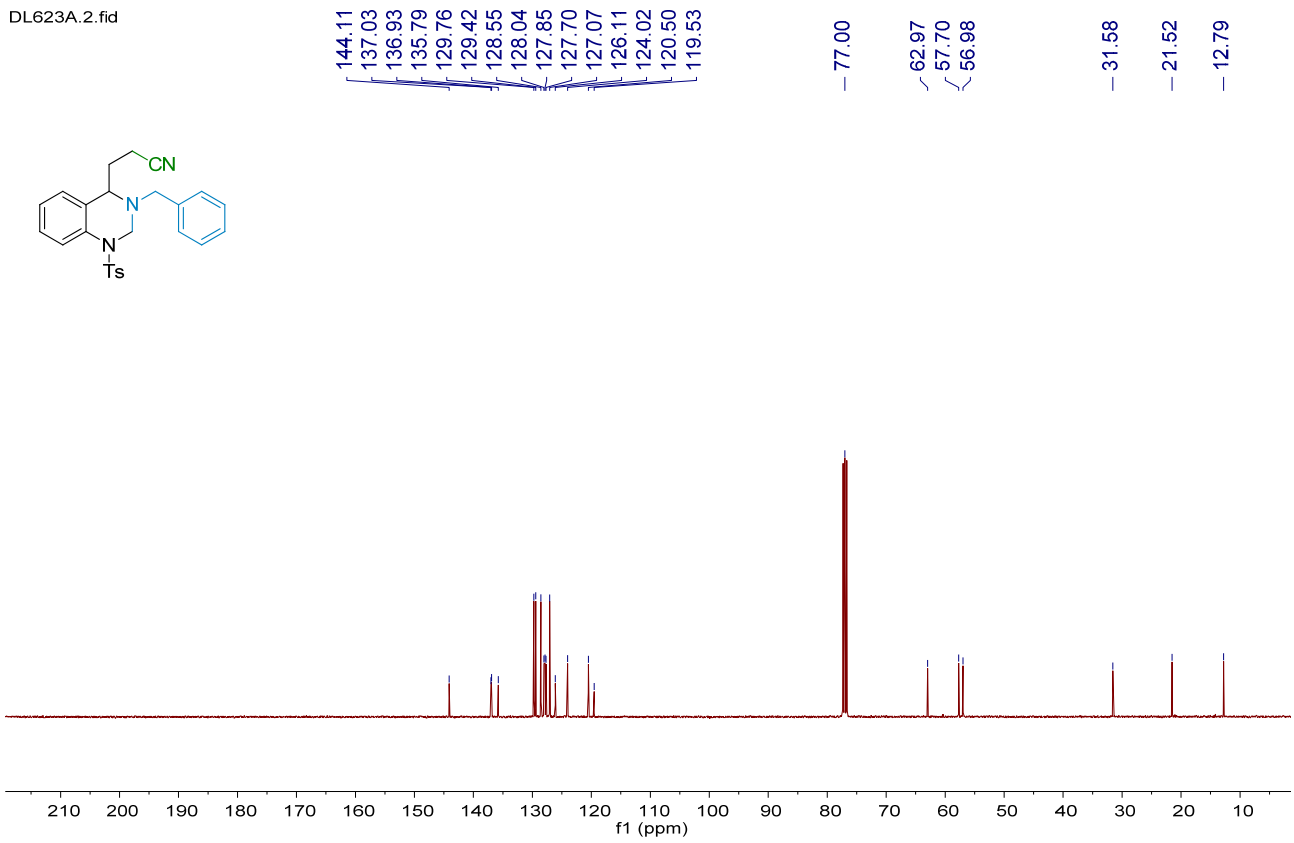




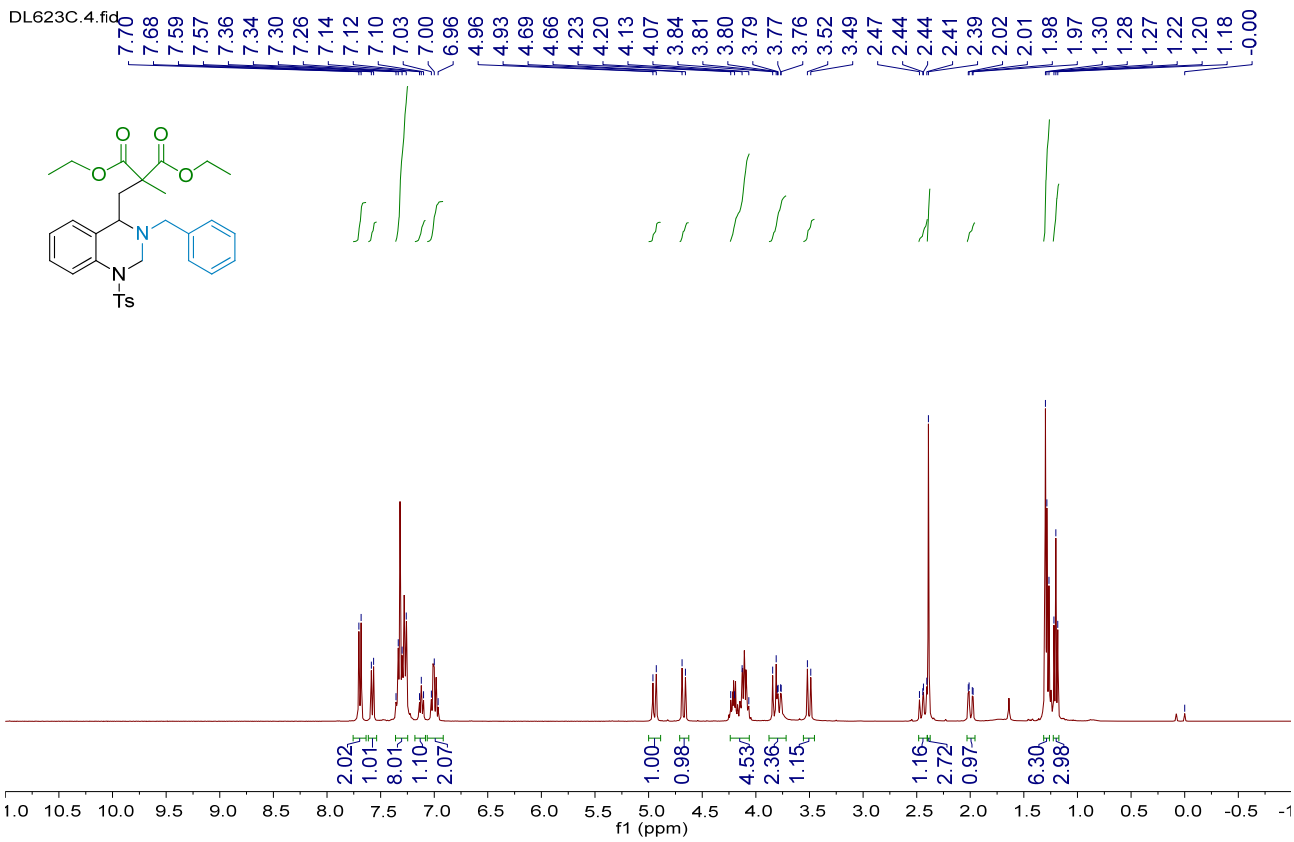


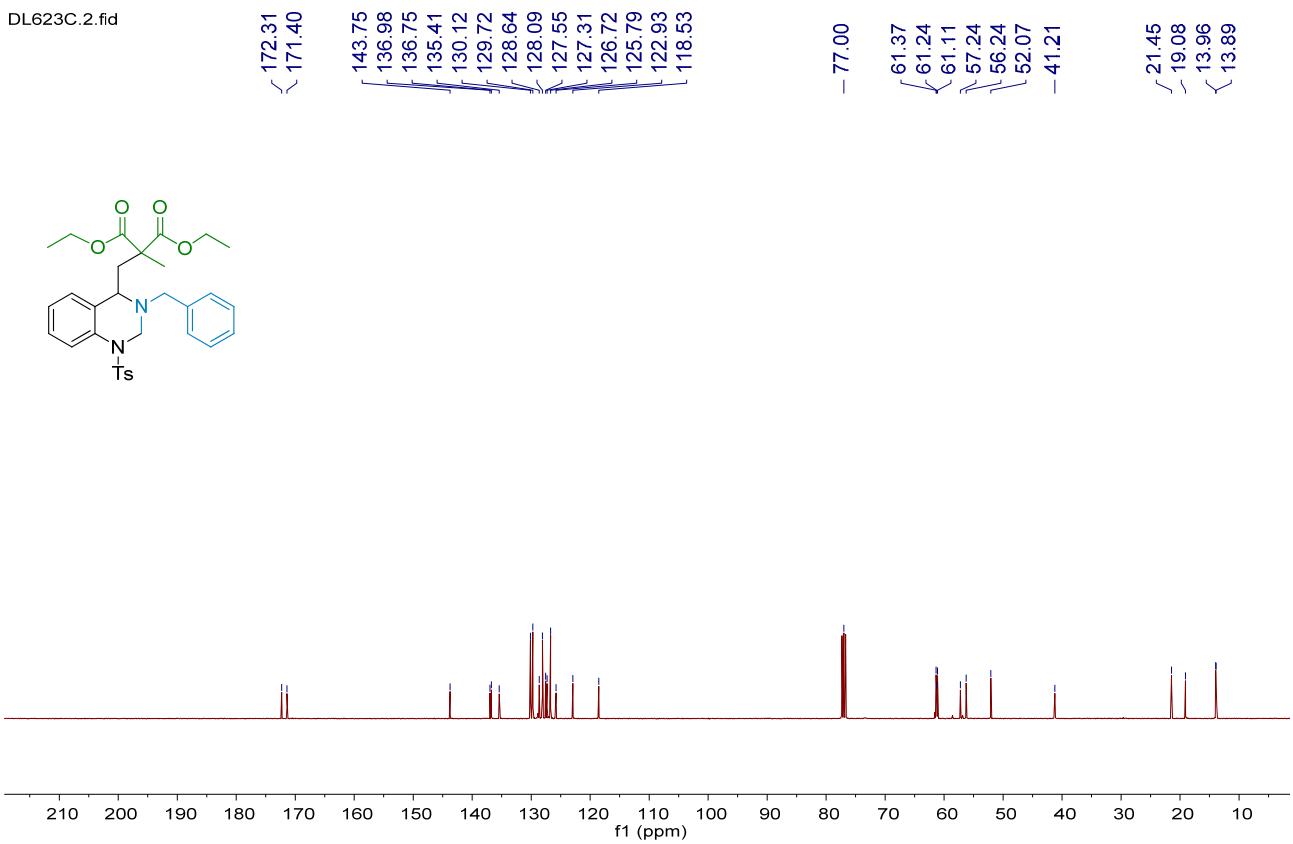
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of 6ag



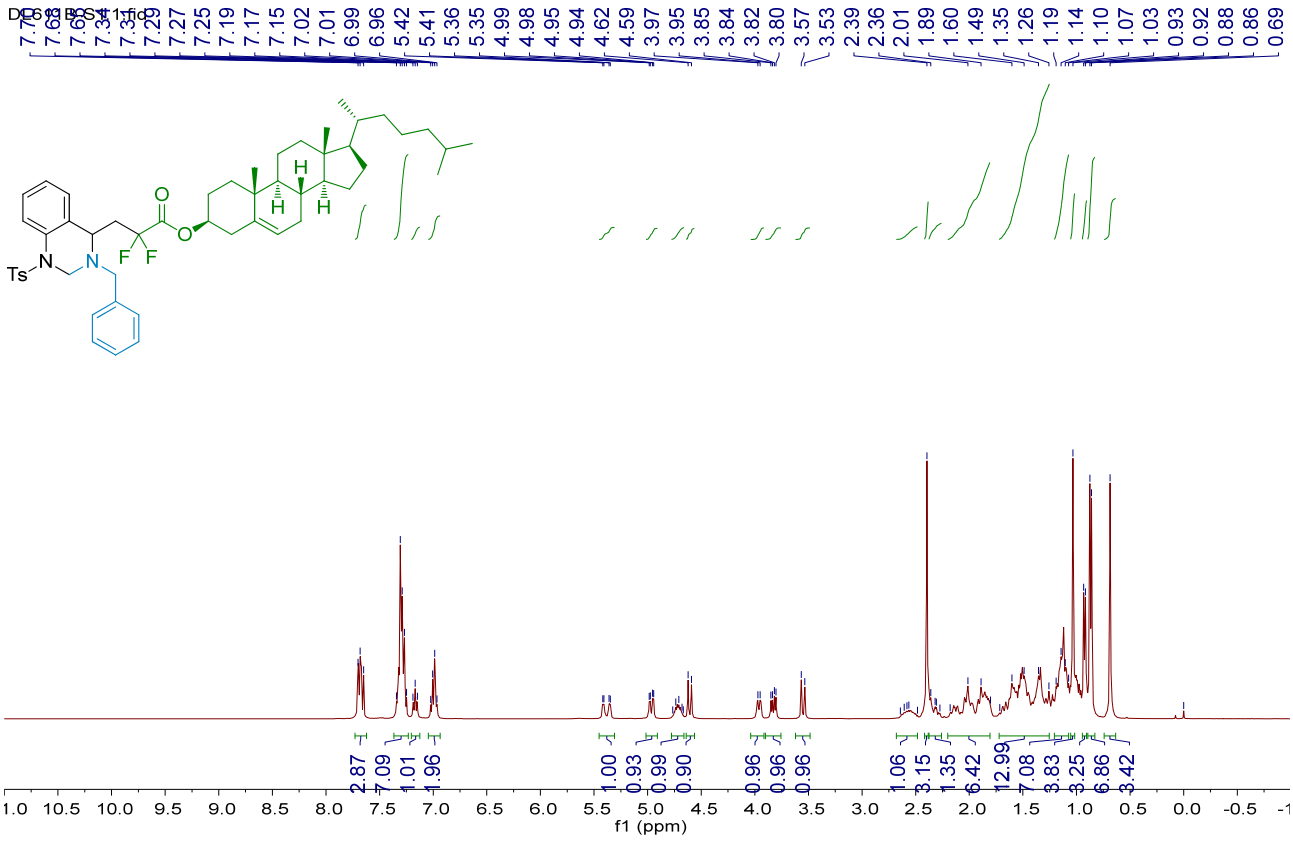


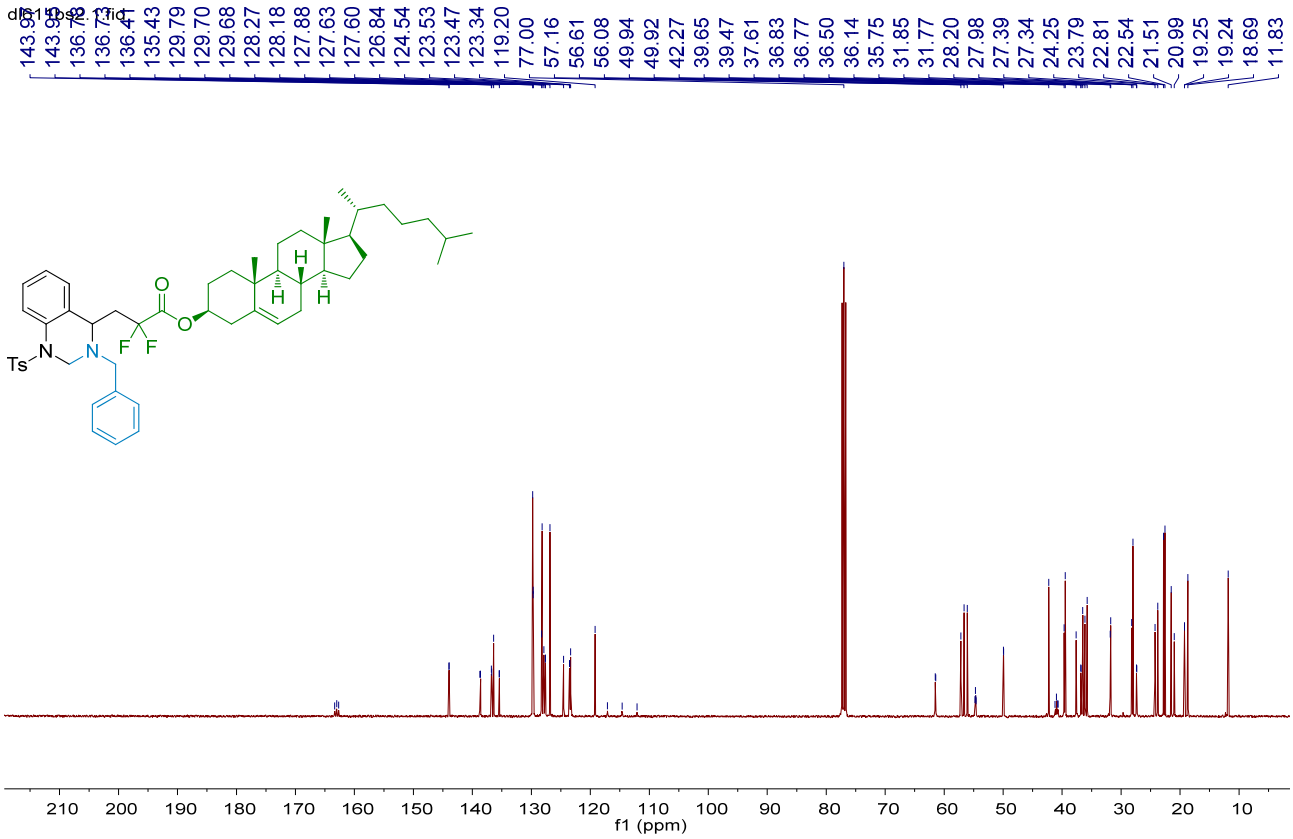
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of 6ah





^{1}H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$) and ^{19}F NMR (376 MHz, $CDCl_3$) spectra of 6ai

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136.72
136.71
136.41
135.43
129.79
129.70
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128.27
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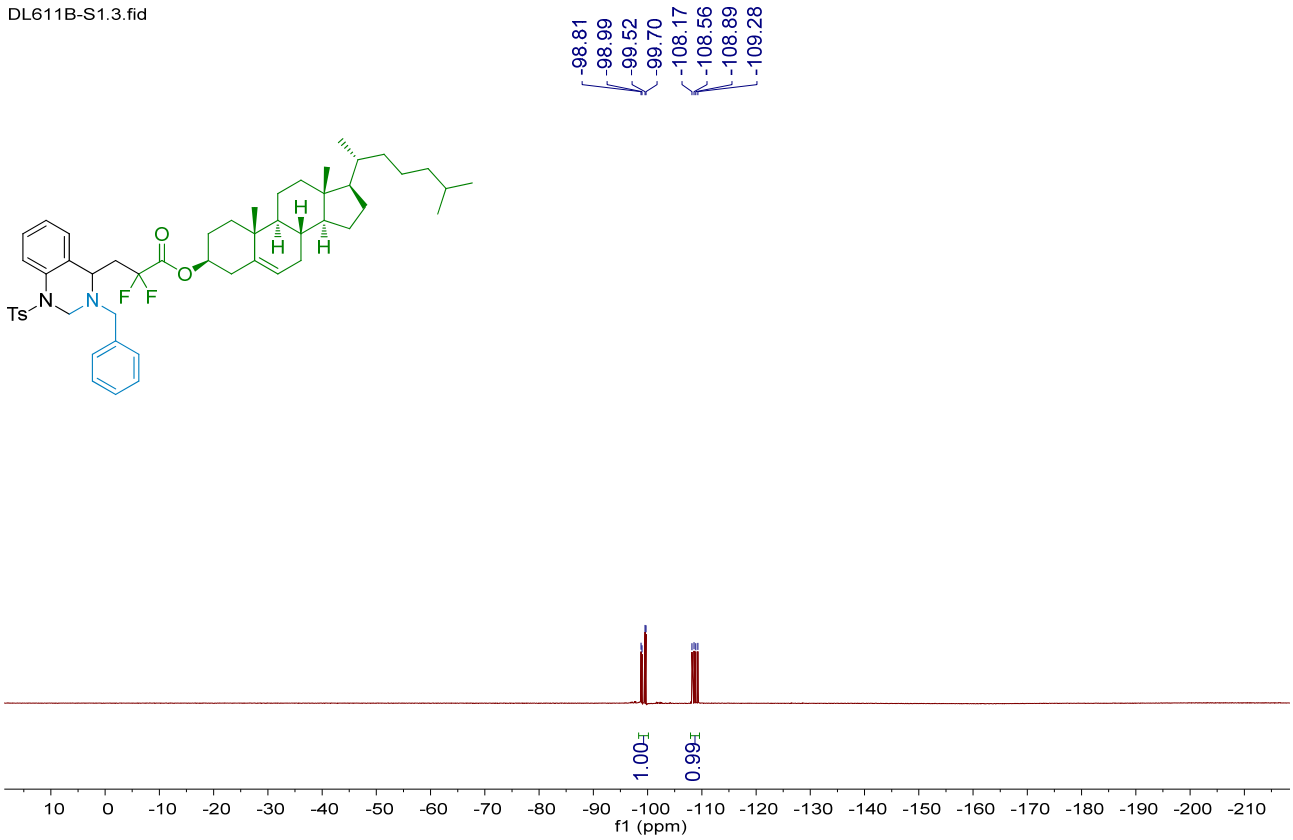
127.88
127.63
127.60
126.84
124.54
123.53
123.47
123.34
119.20
77.00
57.16
56.61
56.08
49.94
49.92
42.27
39.65
39.47
37.61
36.83
36.77
36.50
36.14
35.75
31.85
31.77
28.20
27.98
27.39
27.34
24.25
23.79
22.81
22.54
21.51
20.99
19.25
19.24
18.69
11.83
Ts
N
N
F
F
O
O
H
H
H
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


DL611B-S1.3.fid
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-99.52
-99.70
-108.17
-108.56
-108.89
-109.28
Ts
N
N
F
F
O
O
H
H
H
1.00
0.99
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

8. References

1. (a) L. Fra, A. Millán, J. A. Souto and K. Muňiz, *Angew. Chem. Int. Ed.,* 2014, **53**, 7349-7353; (b) L. Y. Liu and Z. Y. Wang, *Green Chem.,* 2017, **19**, 2076-2079.
2. (a) T. L. Richard and W. B. Motherwell, *Tetrahedron,* 1992, **48**, 1465-1484; (b) R. E. Ruscoe, M. Callingham, J. A. Baker, S. E. Korkis and H. W. Lam, *Chem. Commun.,* 2019, **55**, 838-841.
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