Vanadium-Catalyzed C(sp^3)–H Fluorination Reactions

Ji-Bao Xia, Yuyong Ma, and Chuo Chen*

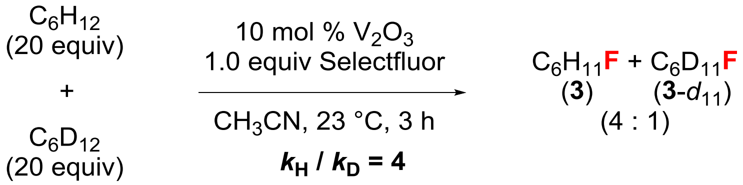
Electronic Supplementary Information

Materials and Methods

General Information. All reactions were performed in glassware under argon. Organic solutions were concentrated by rotary evaporator at ca. 30 mmHg unless otherwise noted. Flash column chromatography was performed as described by Still[1], employing EMD silica gel 60 (230–400 mesh ASTM). TLC analyses were performed on EMD 250 μm Silica Gel 60 F_{254} plates and visualized by quenching of UV fluorescence (λ_{max}= 254 nm), or by staining ceric ammonium molybdate. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Inova-500 or Inova-400. Chemical shifts for ^{1}H and ^{13}C NMR spectra are reported in ppm (δ) relative to the ^{1}H and ^{13}C signals in the solvent ($CDCl_3$: 7.26, 77.00 ppm; C_6D_6: δ 7.16, 128.06 ppm; CD_3CN: δ 1.94, 1.32 ppm) and the multiplicities are presented as follows: s = singlet, d = doublet, t = triplet, q = quartet, hept = heptet, m = multiplet. Crude ^{1}H and ^{19}F NMR spectra were recorded on an Inova-400 in CD_3CN using fluorobenzene (^{19}F NMR δ –114.930) as an external standard. Mass spectra were acquired on an Agilent 6120 Single Quadrupole LC/MS or Agilent 7820A GC/5975 MSD.

Materials. Acetonitrile (anhydrous, 99.8%) was purchased from Sigma-Aldrich. Selectfluor (98+%) was purchased from Alfa Aesar. Vanadium(III) Oxide (95%) was purchased from Strem Chemicals Inc. Fluorobenzene (≥99.5%) was purchased from Fluka. Acetonitrile-*d*3 (D, 99.8%) was purchased from Cambridge Isotope Laboratories, Inc.

General procedure for the V_2O_3-catalyzed C(sp^3)–H fluorination reaction. To a 4 mL clear vial charged with vanadium(III) oxide (3.0 mg, 0.02 mmol, 10 mol%), Selectfluor (106.3 mg, 0.3 mmol, 1.5 equiv) was added anhydrous acetonitrile (2.0 mL), and the reaction substrate (0.2 mmol, 1.0 equiv). The reaction mixture was degassed three times by *Freeze-Pump-Thaw* cycles and stirred at room temperature for 6-48 h. The crude yield was determined by NMR using fluorobenzene as an external standard. Upon completion, the reaction mixture was poured into diethyl ether (20 mL), filtrated, concentrated and purified by silica gel flash column chromatography using diethyl ether/pentane as the eluent.

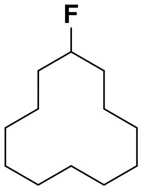


The intermolecular kinetic isotope effect study. To a 4 mL clear vial charged with vanadium(III) oxide (1.5 mg, 0.01 mmol) and Selectfluor (35.4 mg, 0.1 mmol, 1.0 equiv) was added acetonitrile (1.0 mL), cyclohexane (168.4 mg, 20.0 mmol, 20.0 equiv), and cyclohexane-d_{12} (192.5 mg, 1.0 mmol, 20.0 equiv). The reaction mixture was then degassed three times by *freeze-pump-thaw* cycles and stirred at room temperature for 3 h. The ratio of **3**:**3**-d_{11} was determined by ^{19}F NMR on a Varian Inova-400 NMR instrument to be 81:19.

---

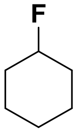
[1] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

Characterization Data



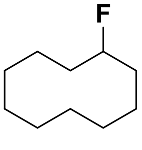
2

Fluorocyclododecane (2).[2] Prepared from cyclododecane (33.6 mg, 0.2 mmol, 1.0 equiv) according to the general procedure (24 h), purified by flash column chromatography (pentane), and concentrated by rotary evaporator at ca. 100 mm Hg to give **2** (24.0 mg, 65% yield) as a colorless oil: R_f = 0.5 (pentane). ^{1}H NMR (400 MHz, C_6D_6) δ 4.59 (dddd, J = 47.3, 11.5, 7.2, 4.6 Hz, 1H), 1.47–1.73 (m, 4H), 1.33–1.38 (m, 2H), 1.10–1.27 (m, 16H); ^{13}C NMR (100 MHz, C_6D_6) δ 91.8 (d, J = 167.0 Hz), 30.3 (d, J = 21.2 Hz), 24.4, 24.1, 23.5, 23.4, 20.8 (d, J = 6.7 Hz); ^{19}F NMR (376 MHz, C_6D_6) δ –176.12 (dtt, J = 47.4, 23.7, 15.5 Hz, 1F).



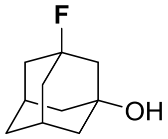
3

Fluorocyclohexane (3).[3] Prepared from cyclohexane (84.2 mg, 1.0 mmol, 5.0 equiv) according to the general procedure (20 h) to give **3** (70% NMR yield). ^{19}F NMR (376 MHz, CD_3CN) δ –172.30 (brs, 1F).



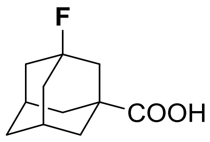
4

Fluorocyclodecane (4).[4] Prepared from cyclodecane (140.3 mg, 1.0 mmol, 5.0 equiv) according to the general procedure (20 h) to give **4** (19.2 mg, 61% yield). ^{1}H NMR (400 MHz, C_6D_6) δ 4.66 (dtt, J = 46.4, 7.7, 4.1 Hz, 1H), 1.63–1.87 (m, 4H), 1.41–1.51 (m, 2H), 1.26–1.37 (m, 12H); ^{13}C NMR (100 MHz, C_6D_6) δ 93.5 (d, J = 165.7 Hz), 31.1 (d, J = 21.9 Hz), 25.3, 25.1, 24.0, 21.8 (d, J = 7.7 Hz); ^{19}F NMR (376 MHz, C_6D_6) δ –165.56 (dtt, J = 46.6, 26.6, 13.7 Hz, 1F).



5

3-Fluoroadamantan-1-ol (5).[2] Prepared from 1-adamantanol (30.4 mg, 0.2 mmol, 1.0 equiv) according to the general procedure (20 h) and purified by flash column chromatography (15% ethyl acetate/hexanes) to give **5** (25.1 mg, 74% yield) as a colorless solid: R_f = 0.3 (30% ethyl acetate/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36–2.38 (m, 2H), 1.89–1.91 (m, 2H), 1.80–1.83 (m, 4H), 1.60–1.69 (m, 5H), 1.49–1.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 93.3 (d, J = 185.7 Hz), 71.0 (d, J = 11.8 Hz), 50.4 (d, J = 17.1 Hz), 43.8 (d, J = 1.6 Hz), 41.3 (d, J = 17.5 Hz), 34.4 (d, J = 2.1 Hz), 31.4 (d, J = 10.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ –133.24 (m, 1F).



6

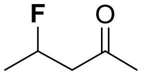
3-Fluoroadamantan-1-carboxylic acid (6).[2] Prepared from 1-Adamantanecarboxylic acid (36.0 mg, 0.2 mmol, 1.0 equiv) according to the general procedure (20 h) and purified by flash column chromatography (15% ethyl acetate/hexanes) to give **6** (27.9 mg, 70% yield) as a colorless solid: R_f = 0.2 (30% ethyl acetate/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.7 (brs, 1H), 2.36–2.37 (m, 2H), 2.03–2.05 (m, 2H), 1.79–1.89 (m, 8H), 1.60–1.62 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.5, 91.0 (d, J = 184.2 Hz), 43.7 (d, J = 10.4 Hz), 42.3 (d, J = 20.3 Hz), 40.7 (d, J = 17.5 Hz), 36.3 (d, J = 1.9 Hz), 33.7 (d, J = 1.9 Hz), 29.7 (d, J = 10.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ –132.83 (s, 1F).

---

[2] Amaoka, Y.; Nagatomo, M.; Inoue, M. *Org. Lett.* **2013**, *15*, 2160.

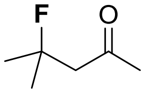
[3] Chambers, R. D.; Kenwright, A. M.; Parsons, M.; Sandford, G.; Moilliet, J. S. *J. Chem. Soc. Perkin Trans. 1*, 2002, 2190.

[4] Bloom, S.; Pitts, C. R.; Miller, D. C.; Haselton, N.; Holl, M. G.; Urheim, E.; Lectka, T. *Angew. Chem. Int. Ed.* **2012**, *51*, 10580.



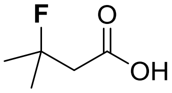
7

4-Fluoropentan-2-one (7). Prepared from 2-pentanone (17.2 mg, 0.2 mmol, 1.0 equiv) according to the general procedure (20 h) to give **7** (47% NMR yield). ^{1}H NMR (400 MHz, CD_3CN) δ 4.95-5.14 (m, 1H), 2.81 (ddd, *J* = 16.8, 15.2, 7.9 Hz, 1H), 2.62 (ddd, *J* = 30.4, 16.8, 4.3 Hz, 1H), 2.09 (s, 3H), 1.29 (dd, *J* = 24.2, 6.2 Hz, 3H); ^{19}F NMR (376 MHz, CD_3CN) δ –173.37 (ddqd, *J* = 48.3, 30.4, 24.2, 15.2 Hz, 1F).



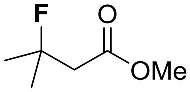
8

4-Fluoro-4-methylpentan-2-one (8).[5] Prepared from 4-methylpentan-2-one (20.0 mg, 0.2 mmol, 1.0 equiv) according to the general procedure (20 h) to give **8** (78% NMR yield). ^{1}H NMR (400 MHz, CD_3CN) δ 2.75 (d, *J* = 17.5 Hz, 2H), 2.10 (s, 3H), 1.37 (d, *J* = 22.0 Hz, 6H); ^{19}F NMR (376 MHz, CD_3CN) δ –133.28 (heptt, *J* = 22.0, 17.5 Hz, 1F).



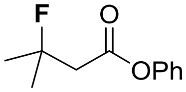
9

3-Fluoro-3-methylbutanoic acid (9). Prepared from methyl 3-methylbutanoic acid (20.4 mg, 0.2 mmol, 1.0 equiv) according to the general procedure (20 h), purified by flash column chromatography (20% ethyl acetate/hexanes), and concentrated by rotary evaporator at ca. 100 mm Hg to give **9** (15.2 mg, 63% yield) as a colorless oil: R_f = 0.2 (30% ethyl acetate/hexanes). ^{1}H NMR (400 MHz, C_6D_6) δ 2.33 (d, *J* = 15.6 Hz, 2H), 1.21 (d, *J* = 21.3 Hz, 6H); ^{13}C NMR (100 MHz, C_6D_6) δ 176.0 (d, *J* = 10.3 Hz), 92.4 (d, *J* = 170.2 Hz), 45.6 (d, *J* = 26.3 Hz), 26.6 (d, *J* = 24.0 Hz); ^{19}F NMR (376 MHz, C_6D_6) δ –134.40 (heptt, *J* = 21.7, 16.2 Hz, 1F); MS(ESI) calcd for $C_5H_9FO_2Na$ $(M+Na)^+$ 143.1, found 143.1.



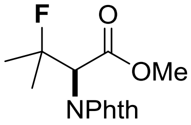
10

Methyl 3-fluoro-3-methylbutanoate (10). Prepared from methyl 3-methylbutanoate (23.2 mg, 0.2 mmol, 1.0 equiv) according to the general procedure (20 h) to give **10** (85% NMR yield). ^{1}H NMR (400 MHz, CD_3CN) δ 3.61 (s, 3H), 2.63 (d, *J* = 17.7 Hz, 2H), 1.42 (d, *J* = 21.7 Hz, 6H); ^{19}F NMR (376 MHz, CD_3CN) δ –134.91 (heptt, *J* = 21.7, 17.7 Hz, 1F).



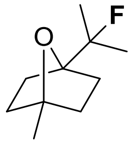
11

Phenyl 3-fluoro-3-methylbutanoate (11). Prepared from phenyl 3-methylbutanoate (35.3 mg, 0.2 mmol, 1.0 equiv) according to the general procedure (20 h) to give **11** (12% NMR yield). ^{19}F NMR (376 MHz, CD_3CN) δ –135.27 (heptt, *J* = 21.6, 17.7 Hz, 1F).



12

(2*R*)-*N*-Phthaloyl-3-fluorovaline methyl ester (12). Prepared from (*S*)-*N*-phthaloylvaline methyl ester (52.2 mg, 0.2 mmol, 1.0 equiv) according to the general procedure (18 h) and purified by flash column chromatography (10% ethyl acetate/hexanes) to give **12** (25.5 mg, 46% yield) as a colorless oil: R_f = 0.2 (20% ethyl acetate/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.76 (dd, *J* = 5.5, 3.1 Hz, 2H), 4.99 (d, *J* = 10.2 Hz, 1H), 3.72 (s, 3H), 1.69 (d, *J* = 22.8 Hz, 3H), 1.55 (d, *J* = 22.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 166.7 (d, *J* = 10.5 Hz), 134.3, 131.7, 123.7, 95.6 (d, *J* = 173.0 Hz), 57.7 (d, *J* = 25.9 Hz), 52.5, 26.3 (d, *J* = 22.8 Hz), 23.8 (d, *J* = 23.7 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ –136.52 (dqq, *J* = 10.2, 22.5, 22.8 Hz, 1F); $MS(ESI)^+$ calcd for $C_{14}H_{14}FNO_4Na$ $(M+Na)^+$ 302.1, found 302.1.



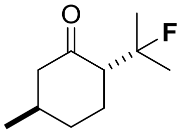
13

1-(2-Fluoropropan-2-yl)-4-methyl-7-oxabicyclo[2.2.1]heptane (13). Prepared from 1,4-cineole (30.9 mg, 0.2 mmol, 1.0 equiv) according to the general procedure (24 h), purified by flash column chromatography (2% diethyl ether/pentane), and concentrated by rotary evaporator at ca. 100 mm Hg to give **13** (18.1 mg, 53% yield) as a colorless oil: R_f = 0.4

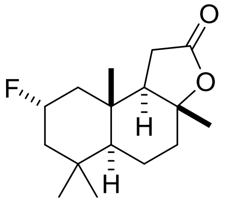
---

[5] Shellhamer, D. F.; Anstine, D. T.; Gallego, K. M.; Ganesh, B. R.; Hanson, A. A.; Hanson, K. A.; Henderson, R. D.; Prince, J. M.; Heasley, V. L. *J. Chem. Soc., Perkin Trans. 2,* **1995**, 861.

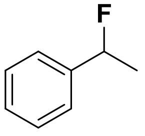
(5% diethyl ether/pentane). ^{1}H NMR (400 MHz, C_6D_6) δ 1.76–1.84 (m, 2H), 1.24–1.46 (m, 15H); ^{13}C NMR (100 MHz, C_6D_6) δ 94.9 (d, *J* = 172.0 Hz), 89.6 (d, *J* = 21.1 Hz), 83.7, 37.2, 32.5 (d, *J* = 5.3 Hz), 23.5 (d, *J* = 25.6 Hz), 21.3; ^{19}F NMR (376 MHz, C_6D_6) δ –146.24 (hept, *J* = 21.5 Hz, 1F); MS(EI) calcd for $C_{12}H_{17}FO$ $(M)^+$ 172.1, found 172.2.


14

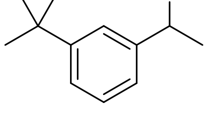
(2*R*,5*R*)-2-(2-Fluoropropan-2-yl)-5-methylcyclohexanone (14). Prepared from (−)-menthone (30.9 mg, 0.2 mmol, 1.0 equiv) according to the general procedure (30 h), purified by preparative TLC [(the plate was pretreated with ammonium (1 mL, 7M in methanol) in hexane (50 mL)] (5% ethyl acetate/hexanes), and concentrated by rotary evaporator at ca. 100 mm Hg to give **14** (26.0 mg, 75% yield) as a colorless oil: R_f = 0.4 (5% ethyl acetate/hexanes). ^{1}H NMR (400 MHz, C_6D_6) δ 2.27-2.33 (m, 1H), 2.09–2.19 (m, 2H), 1.55 (d, *J* = 23.2 Hz, 3H), 1.44 (d, *J* = 22.8 Hz, 3H), 1.31–1.45 (m, 3H), 1.18–1.29 (m, 1H), 0.78–0.88 (m, 1H), 0.62 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 207.9 (d, *J* = 11.0 Hz), 95.3 (d, *J* = 165.5 Hz), 58.8 (d, *J* = 22.5 Hz), 51.2 (d, *J* = 4.2 Hz), 35.7, 33.6, 27.7 (d, *J* = 4.8 Hz), 27.5 (d, *J* = 23.3 Hz), 22.3 (d, *J* = 23.3 Hz), 22.1; ^{19}F NMR (376 MHz, C_6D_6) δ –133.75 (heptd, *J* = 23.0, 7.5 Hz, 1F); MS(ESI) calcd for $C_{10}H_{17}FONa$ $(M+Na)^+$ 195.1, found 195.1.


15a

2α-Fluorosclareolide (15a).[6] Prepared from sclareolide (50.1 mg, 0.2 mmol, 1.5 equiv) according to the general procedure (48 h) to give 2α-fluorosclareolide **15a** (56% NMR yield), 2β-fluorosclareolide **15b** (6% NMR yield) and 3α-fluorosclareolide **15c** (16% NMR yield). Purified by flash column chromatography (10% ethyl acetate/hexanes) to give a mixture of all three isomers (40.6 mg, 76% yield) as a colorless solid: R_f = 0.3 (20% ethyl acetate/hexanes). **15a**: ^{19}F NMR (376 MHz, CD_3CN) δ –179.22 (ddddd, *J* = 48.0, 11.1, 11.1, 5.5, 5.5 Hz, 1F); **15b**: ^{19}F NMR (376 MHz, CD_3CN) δ –172.05 (m, 1F); **15c**: ^{19}F NMR (376 MHz, CD_3CN) δ –187.44 (ddd, *J* = 47.8, 47.7, 11.9 Hz, 1F).


16

(1-Fluoroethyl)benzene (16).[7] Prepared from ethylbenzene (21.2 mg, 0.2 mmol, 1.0 equiv) according to the general procedure (24 h) to give **2** (67% NMR yield). ^{19}F NMR (376 MHz, CD_3CN) δ –166.38 (dq, *J* = 47.8, 23.9 Hz, 1F).

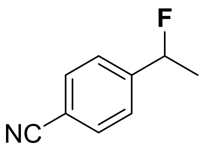

17

1-(*tert*-Butyl)-3-(1-fluoroethyl)benzene (17).[7] Prepared from 1-(*tert*-butyl)-3-ethylbenzene (32.5 mg, 0.2 mmol, 1.0 equiv) according to the general procedure (48 h) and purified by flash column chromatography (1% diethyl ether/pentane) to give **3** (17.0 mg, 47% yield) as a colorless oil: R_f = 0.3 (1% diethyl ether/pentane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.39 (m, 2H), 7.29–7.34 (m, 1H), 7.17–7.20 (m, 1H), 5.64 (dq, *J* = 47.7, 6.4 Hz, 1H), 1.67 (dd, *J* = 23.9, 6.4 Hz, 3H), 1.33 (s, 9H); ^{19}F NMR (376 MHz, $CDCl_3$) δ –165.97 (dq, *J* = 47.8, 23.9 Hz, 1F).

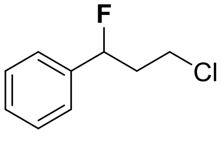
---

[6] Liu, W.; Huang, X.; Cheng, M.-J.; Nielsen, R. J.; Goddard III, W. A.; Groves, J. T. *Science* **2012**, *337*, 1322.

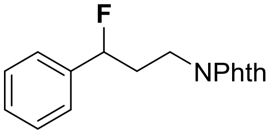
[7] Xia, J.-B.; Zhu, C.; Chen, C. *J. Am. Chem. Soc.*, 2013, **135**, 17494.


18

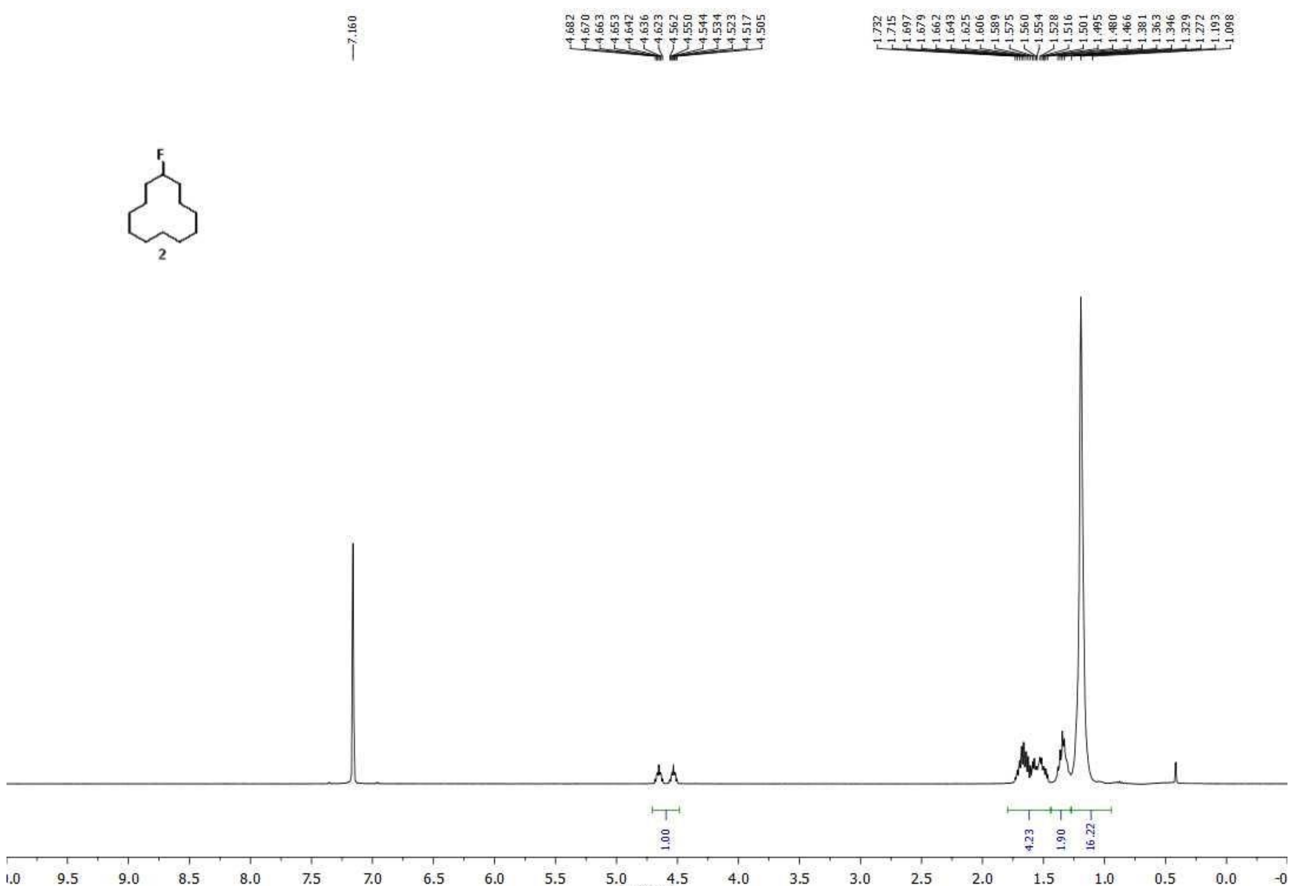
4-(1-Fluoroethyl)benzonitrile (18).[7] Prepared from 4-ethylbenzonitrile (26.2 mg, 0.2 mmol, 1.0 equiv) according to the general procedure (24 h) and purified by flash column chromatography (3% diethyl ether/pentane) to give **18** (7.2 mg, 24% yield) as a colorless oil: R_f = 0.3 (3% diethyl ether/pentane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.0 Hz, 2H), 7.45 (d, *J* = 8.0 Hz, 2H), 5.67 (dq, *J* = 47.4, 6.5 Hz, 1H), 1.64 (dd, *J* = 24.0, 6.5 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ –172.73 (dq, *J* = 47.9, 24.0 Hz, 1F).

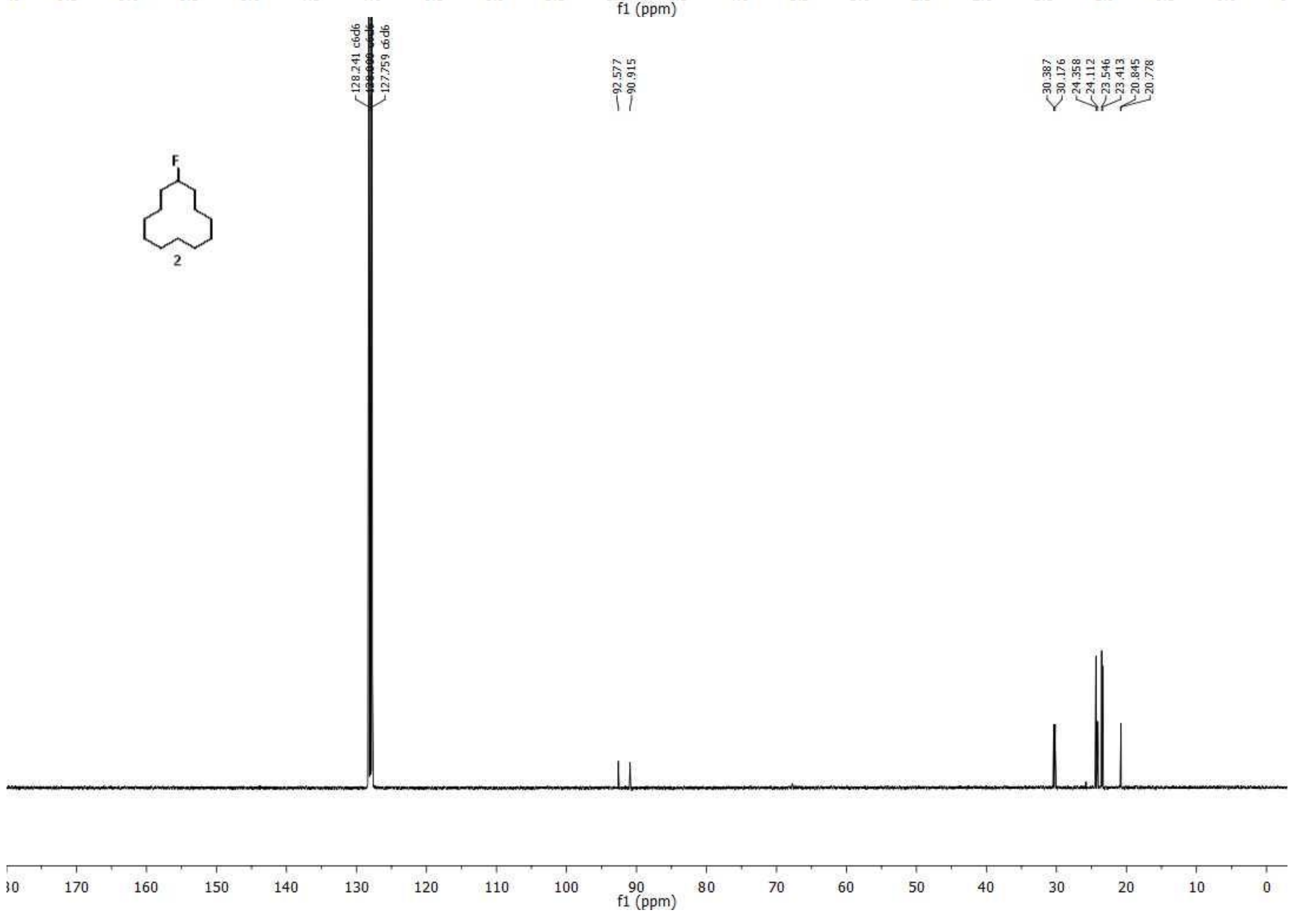

19

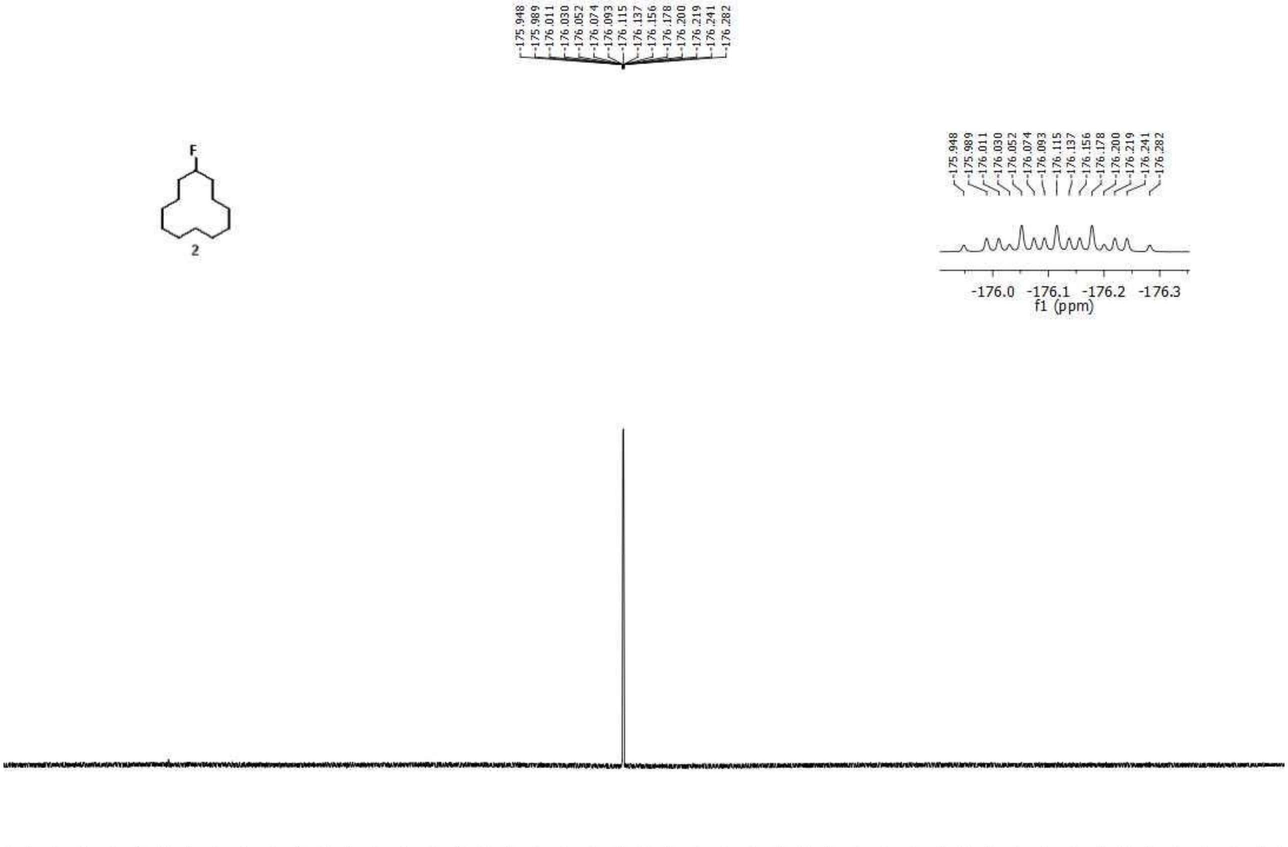
(3-Chloro-1-fluoropropyl)benzene (19).[7] Prepared from (3-chloropropyl)benzene (30.9 mg, 0.2 mmol, 1.0 equiv) according to the general procedure (24 h) and purified by preparative TLC (1% ethyl acetate/hexanes) to give **19** (12.0 mg, 35% yield) as a colorless oil: R_f = 0.4 (1% ethyl acetate/hexanes). ^{1}H NMR (400 MHz, C_6D_6) δ 7.03–7.07 (m, 5H), 5.42 (ddd, *J* = 48.0, 9.0, 3.9 Hz, 1H), 3.26–3.33 (m, 1H), 3.04–3.09 (m, 1H), 1.92–2.04 (m, 1H), 1.64–1.80 (m, 1H); ^{19}F NMR (376 MHz, C_6D_6) δ –179.53 (ddd, *J* = 48.2, 31.0, 13.5 Hz, 1F).

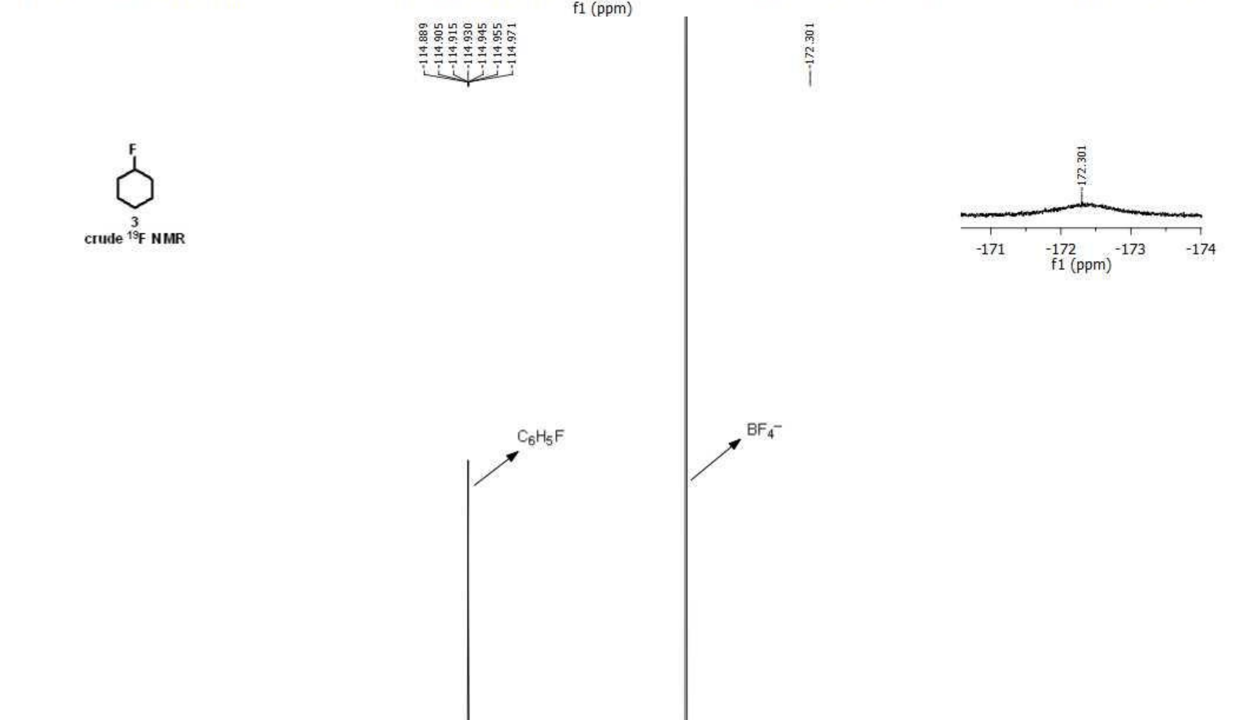

20

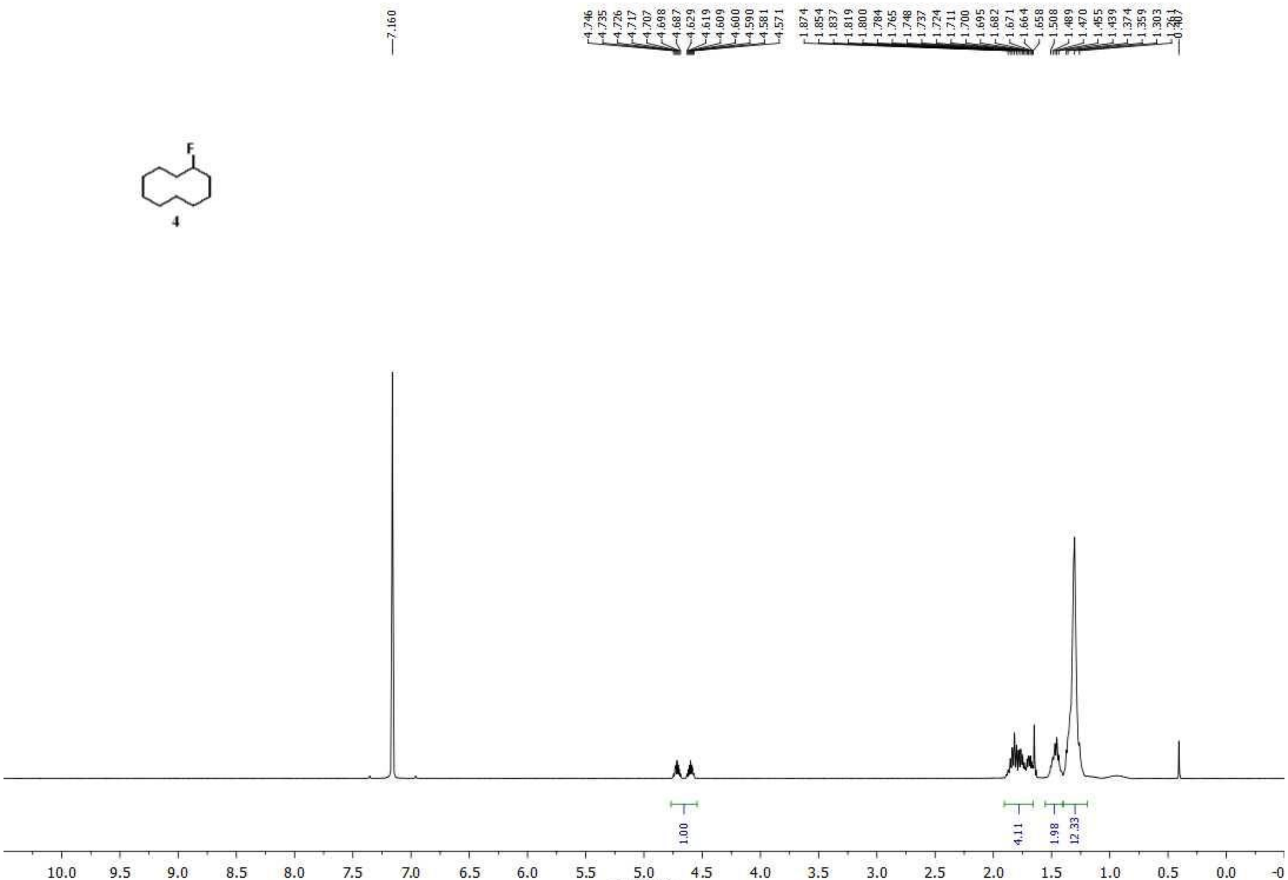
***N*-Phthaloyl 3-fluoro-3-phenylpropylamine (20).**[7] Prepared from 2-(3-phenylpropyl)isoindoline-1,3-dione (53.0 mg, 0.2 mmol, 1.0 equiv) according to the general procedure (6 h) and purified by preparative TLC (20% ethyl acetate/hexanes) to give **20** (24.5 mg, 43% yield) as a colorless oil: R_f = 0.4 (20% ethyl acetate/hexanes). ^{1}H NMR (400 MHz, C_6D_6) δ 7.43–7.45 (m, 2H), 6.96–7.11 (m, 5H), 6.88–6.90 (m, 2H), 5.28 (ddd, *J* = 48.1, 9.2, 4.0 Hz, 1H), 3.61–3.76 (m, 2H), 2.12–2.25 (m, 1H), 1.87–2.02 (m, 1H); ^{19}F NMR (376 MHz, C_6D_6) δ -176.15 (ddd, *J* = 47.4, 30.7, 16.2 Hz, 1F).

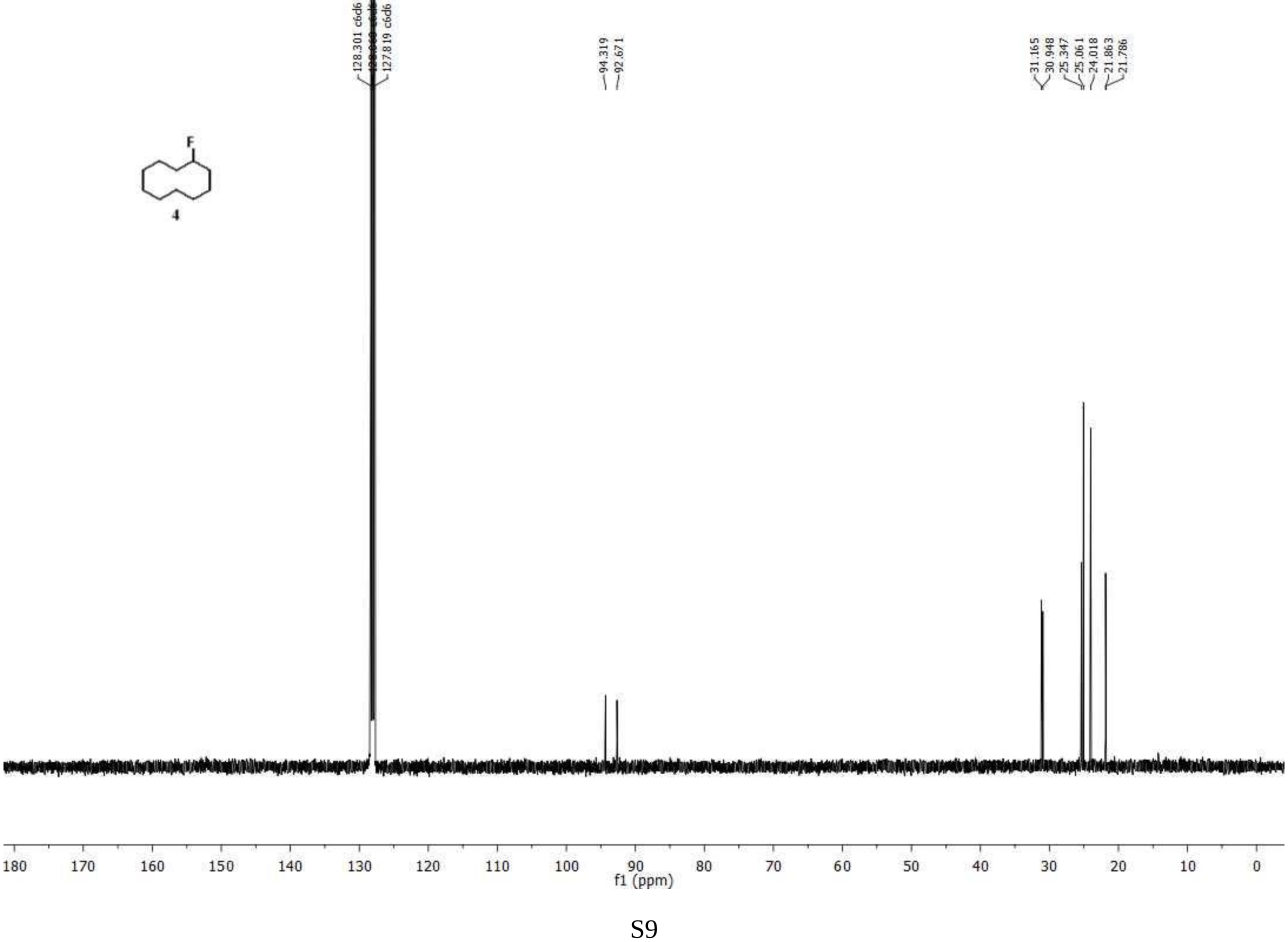

7.160
4.682
4.670
4.663
4.653
4.642
4.636
4.623
4.562
4.550
4.544
4.534
4.523
4.517
4.505
1.732
1.715
1.697
1.679
1.662
1.643
1.625
1.606
1.589
1.575
1.560
1.554
1.528
1.516
1.501
1.495
1.480
1.466
1.381
1.363
1.346
1.329
1.272
1.193
1.098
F
2
1.00
4.23
1.90
16.22
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

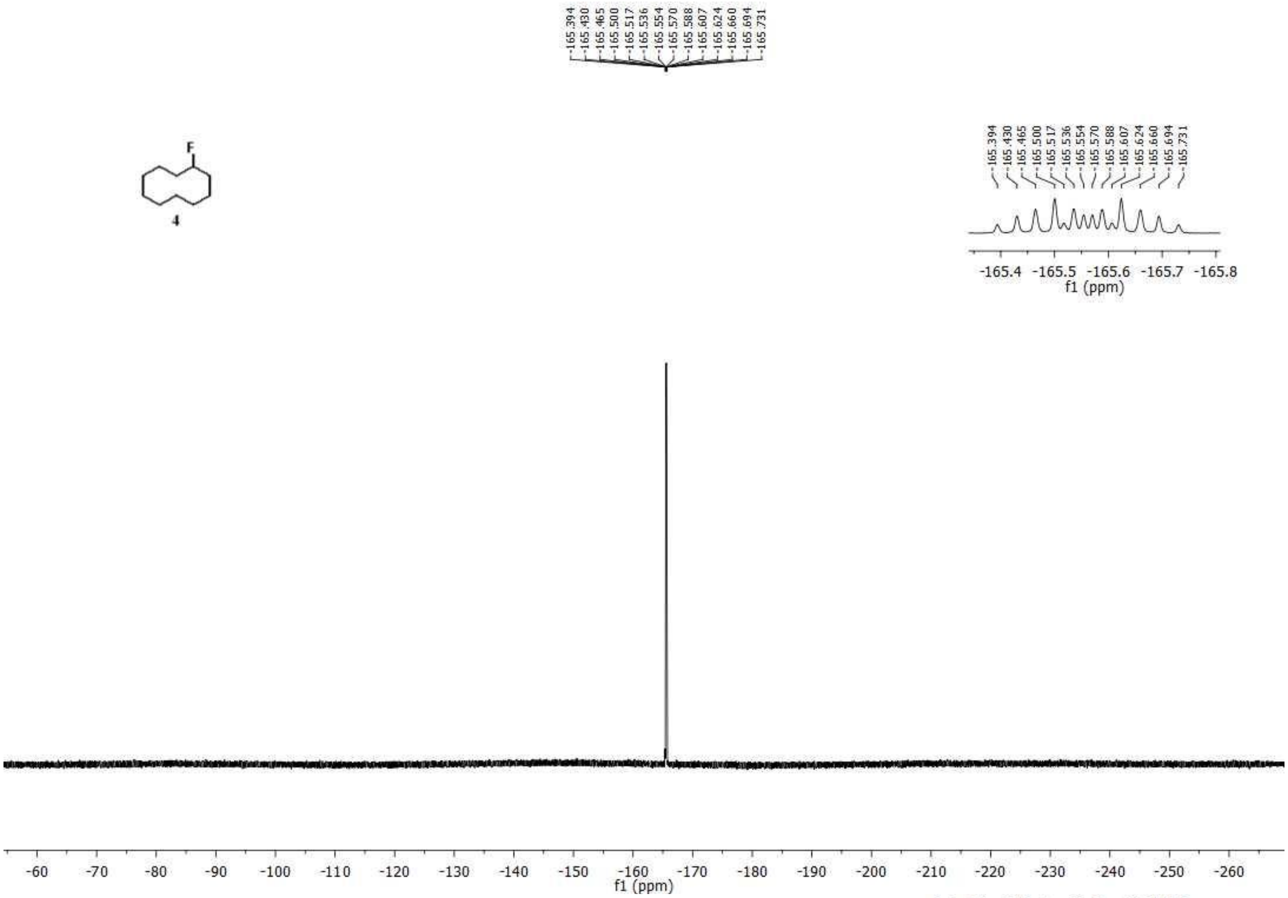

128.241 c6d6
128.000 c6d6
127.759 c6d6
92.577
90.915
30.387
30.176
24.358
24.112
23.546
23.413
20.845
20.778
F
2
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

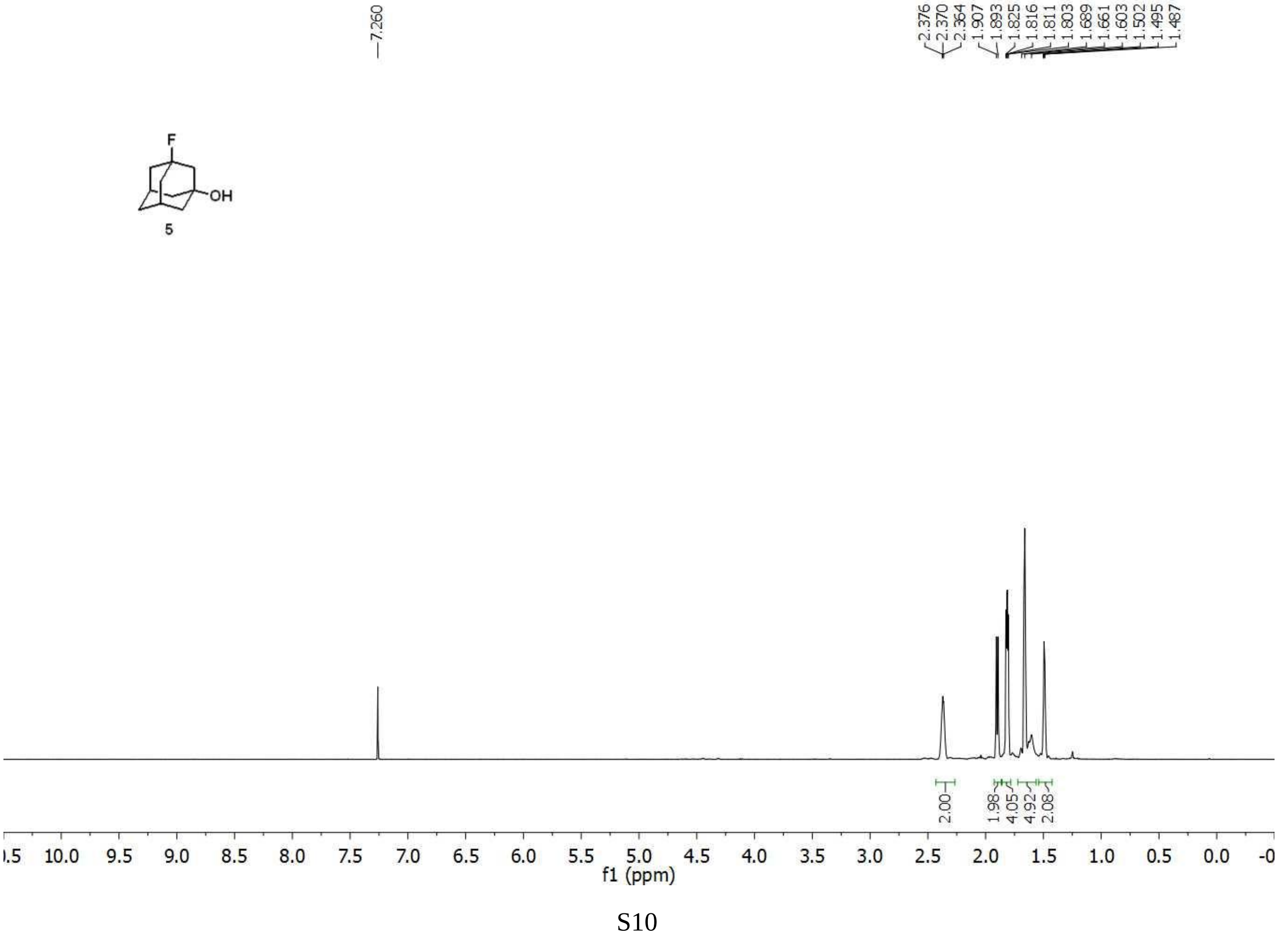

-175.948
-175.989
-176.011
-176.030
-176.052
-176.074
-176.093
-176.115
-176.137
-176.156
-176.178
-176.200
-176.219
-176.241
-176.282
F
2
-176.0 -176.1 -176.2 -176.3
f1 (ppm)
-70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240 -250 -260 -270 -280 -290
f1 (ppm)

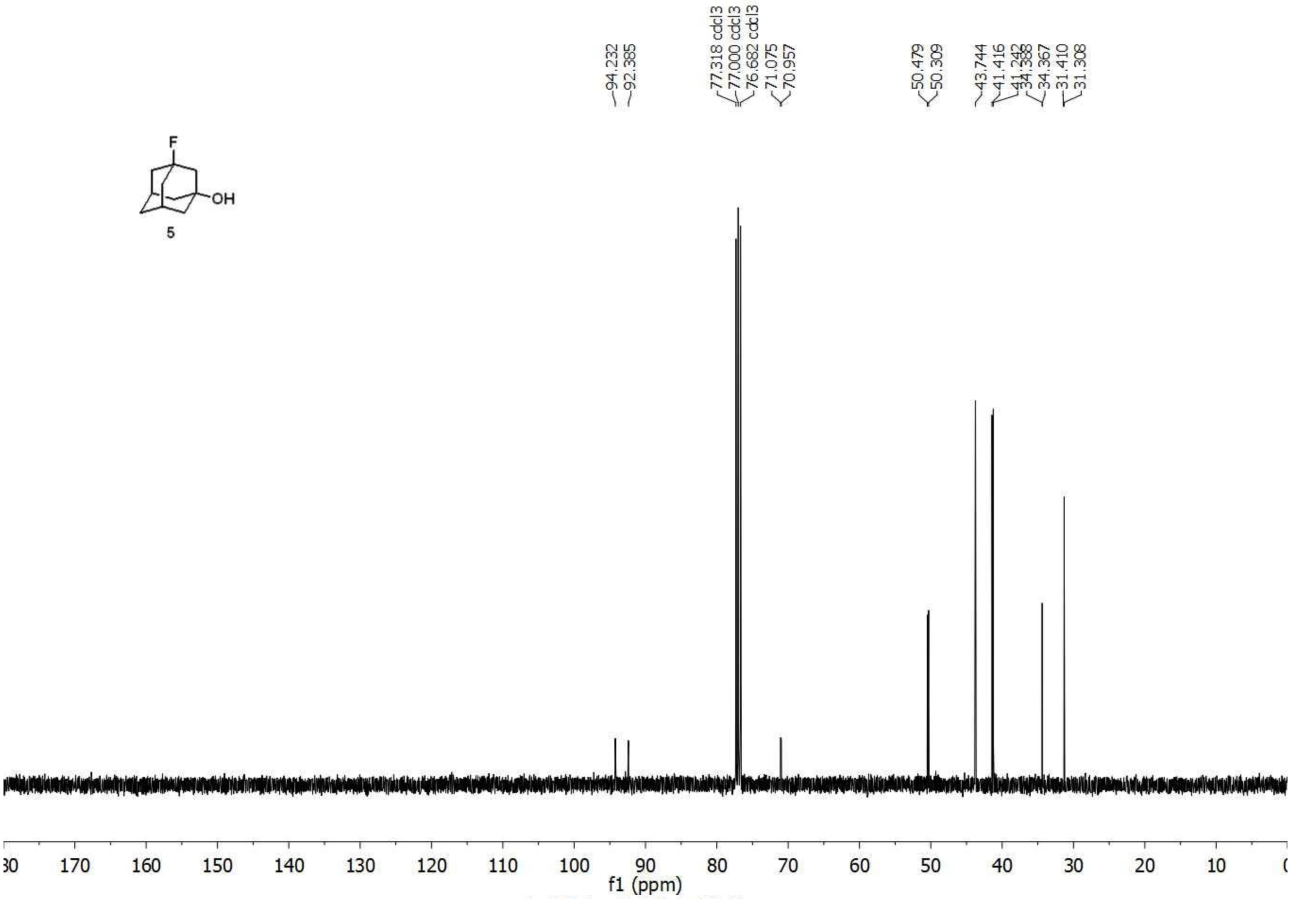

-114.889
-114.905
-114.915
-114.930
-114.945
-114.955
-114.971
-172.301
F
3
crude ^{19}F NMR
-172.301
-171 -172 -173 -174
f1 (ppm)
C_6H_5F
BF_4^-
-40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

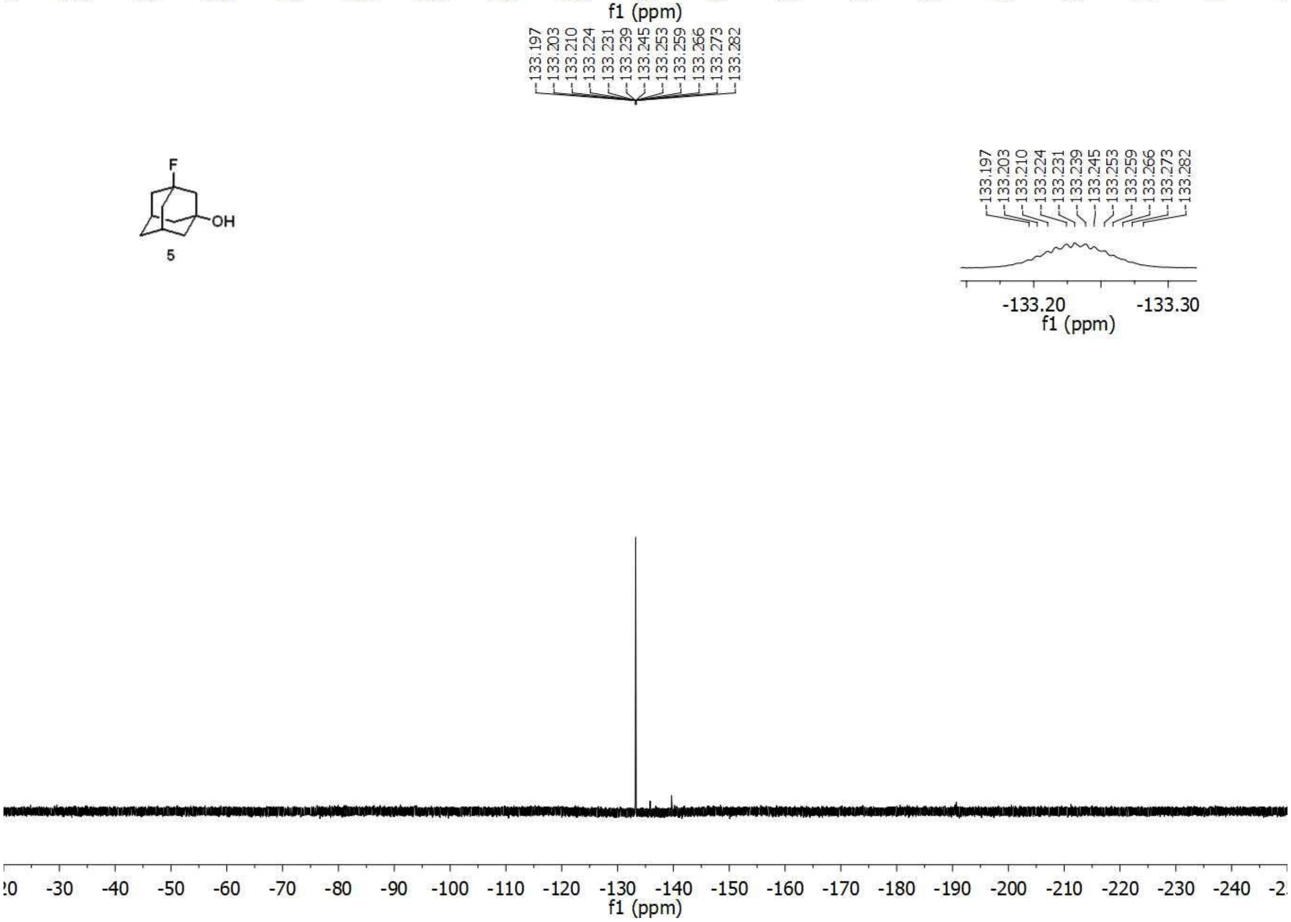

7.160
4.746
4.735
4.726
4.717
4.707
4.698
4.687
4.629
4.619
4.609
4.600
4.590
4.581
4.571
1.874
1.854
1.837
1.819
1.800
1.784
1.765
1.748
1.737
1.724
1.711
1.700
1.695
1.682
1.671
1.664
1.658
1.508
1.489
1.470
1.455
1.439
1.374
1.359
1.303
1.281
0.407
F
4
1.00
4.11
1.98
12.33
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

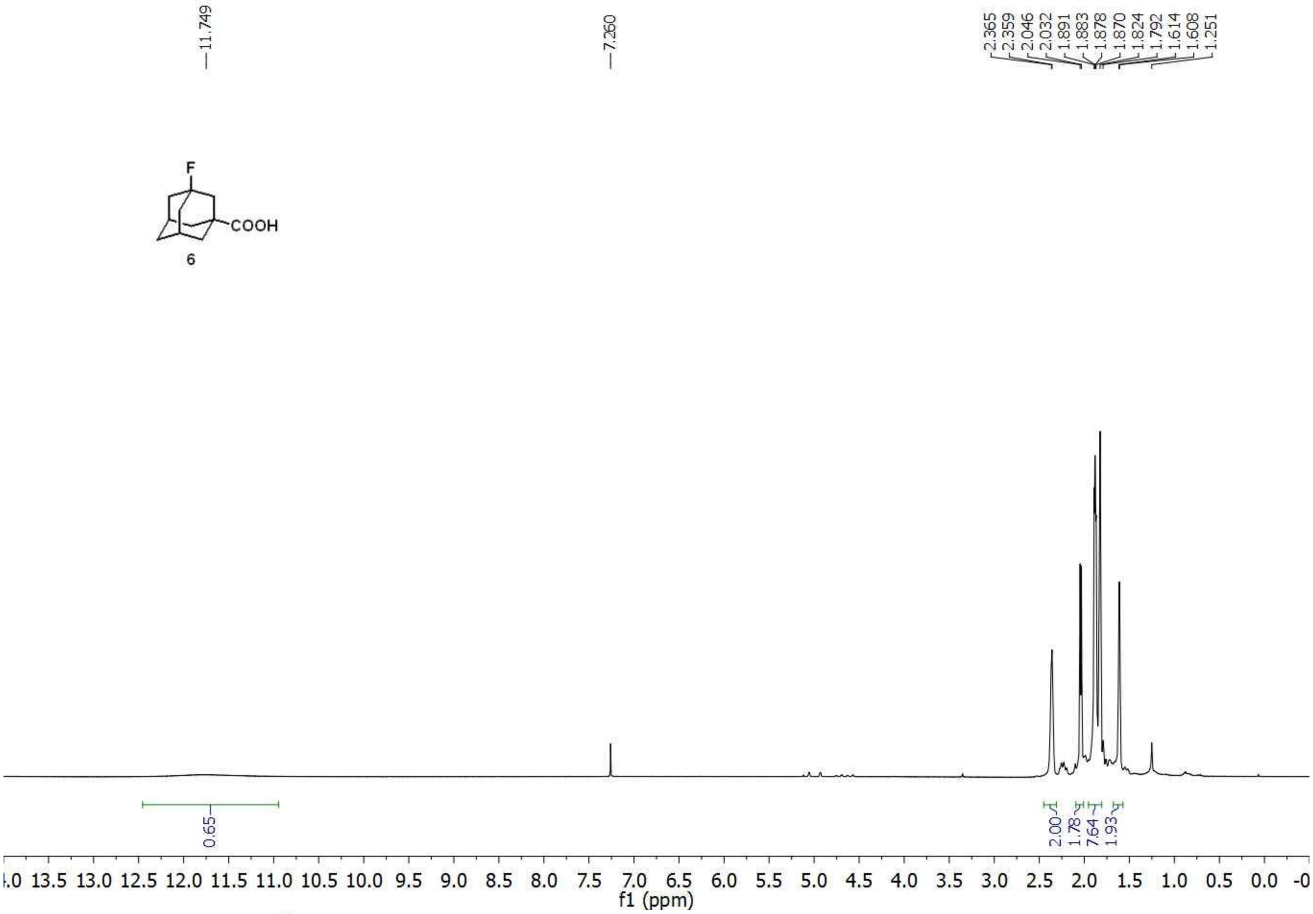

128.301 c6d6
127.819 c6d6
94.319
92.671
31.165
30.948
25.347
25.061
24.018
21.863
21.786
F
4
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-165.394
-165.430
-165.465
-165.500
-165.517
-165.536
-165.554
-165.570
-165.588
-165.607
-165.624
-165.660
-165.694
-165.731
F
4
-165.4 -165.5 -165.6 -165.7 -165.8
f1 (ppm)
-60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240 -250 -260
f1 (ppm)

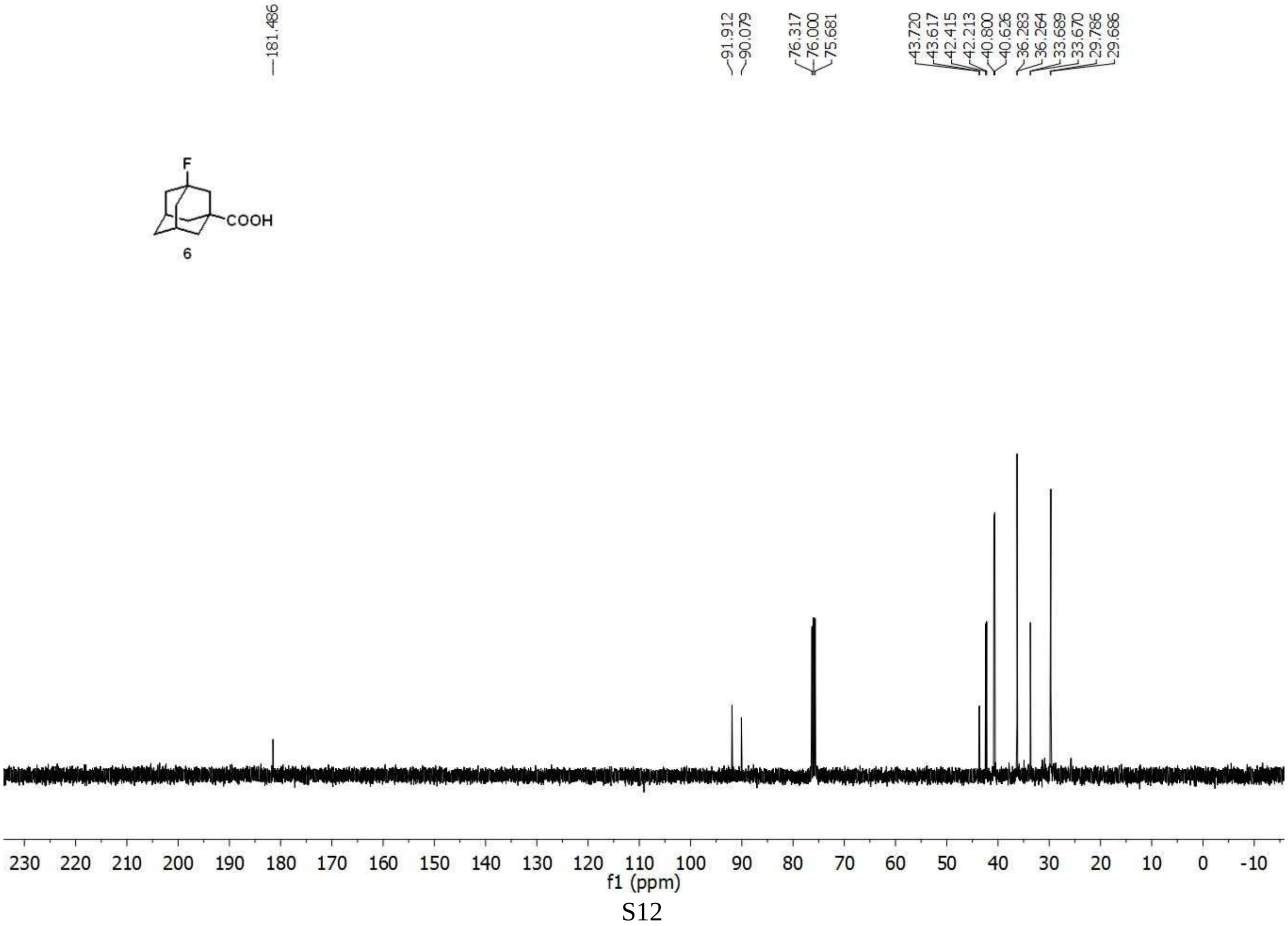

7.260
2.376
2.370
2.364
1.907
1.893
1.825
1.816
1.811
1.803
1.689
1.661
1.603
1.502
1.495
1.487
F
OH
5
2.00
1.98
4.05
4.92
2.08
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


94.232
92.385
77.318 cdcl3
77.000 cdcl3
76.682 cdcl3
71.075
70.957
50.479
50.309
43.744
41.416
41.242
34.388
34.367
31.410
31.308
F
OH
5
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

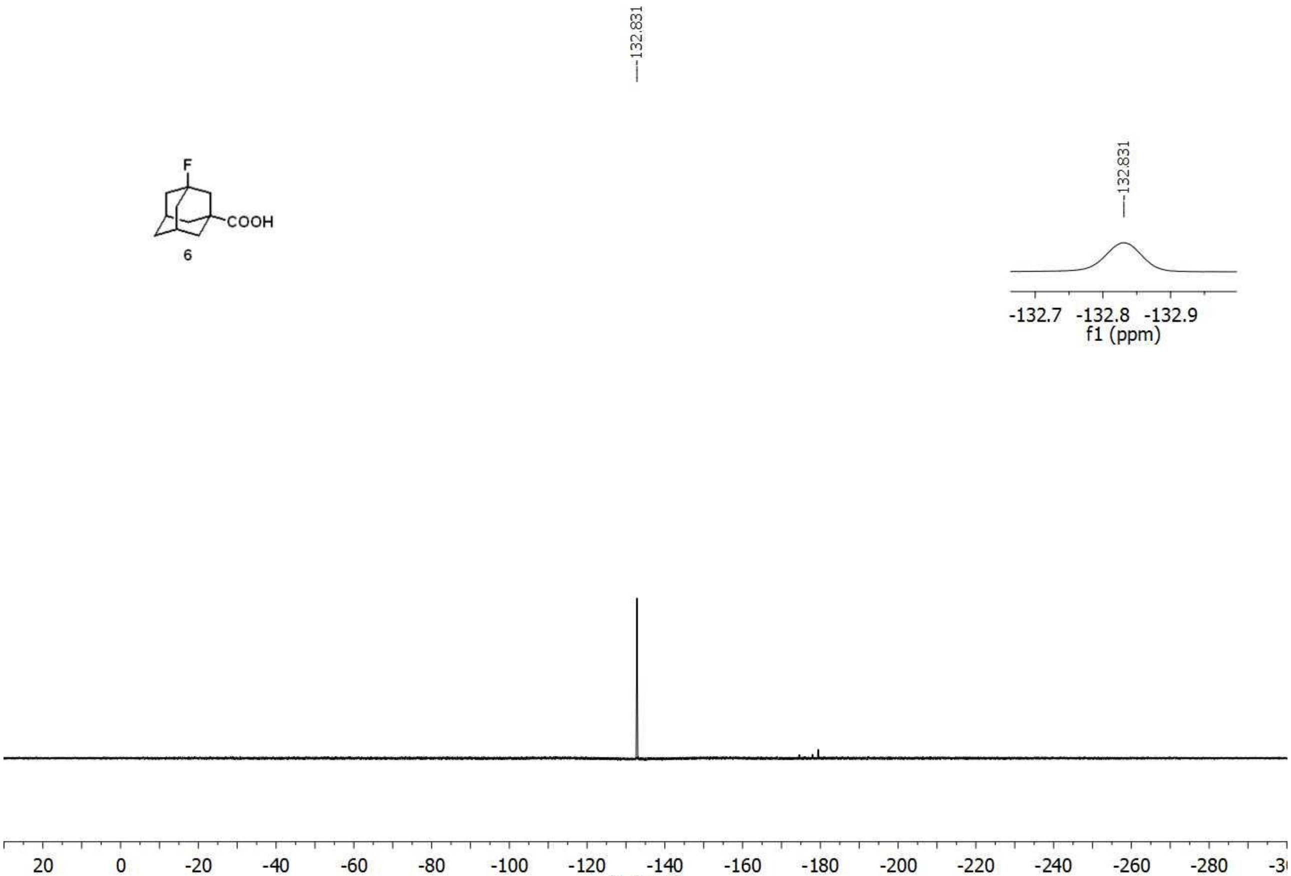

133.197
133.203
133.210
133.224
133.231
133.239
133.245
133.253
133.259
133.266
133.273
133.282
F
OH
5
-133.20
-133.30
f1 (ppm)
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
-240
f1 (ppm)

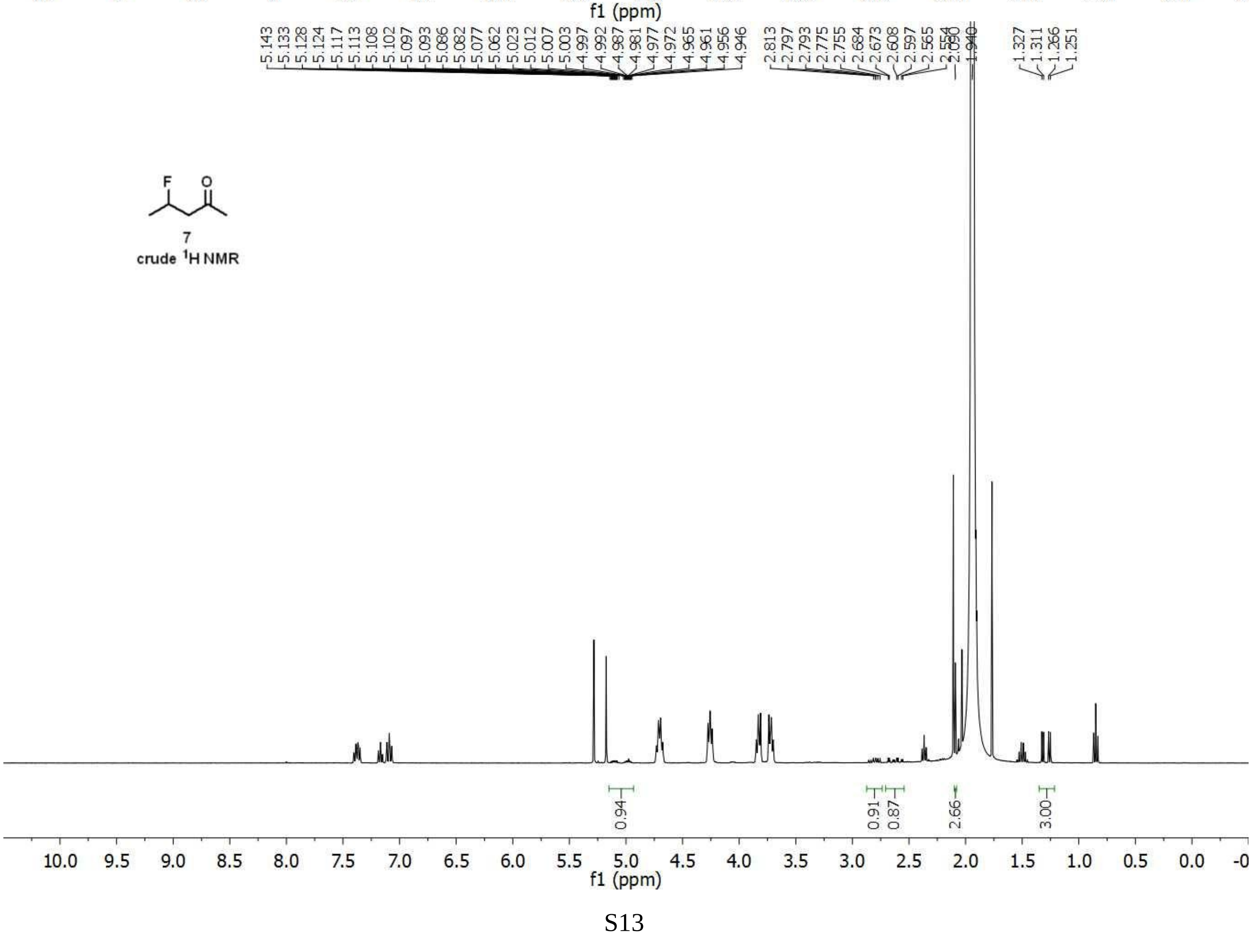


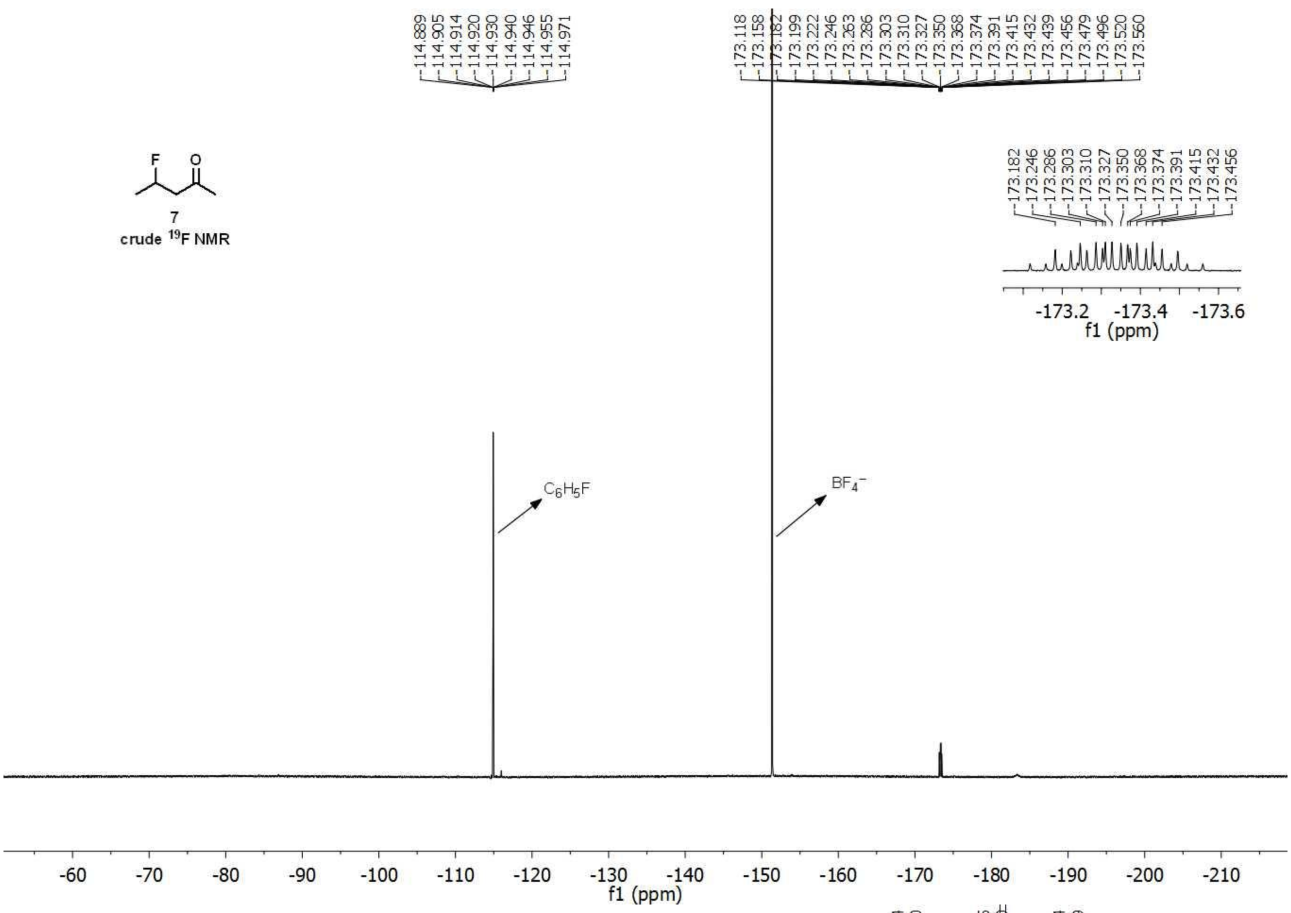
11.749
7.260
2.365
2.359
2.046
2.032
1.891
1.883
1.878
1.870
1.824
1.792
1.614
1.608
1.251
F
COOH
6
0.65
2.00
1.78
7.64
1.93
.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)



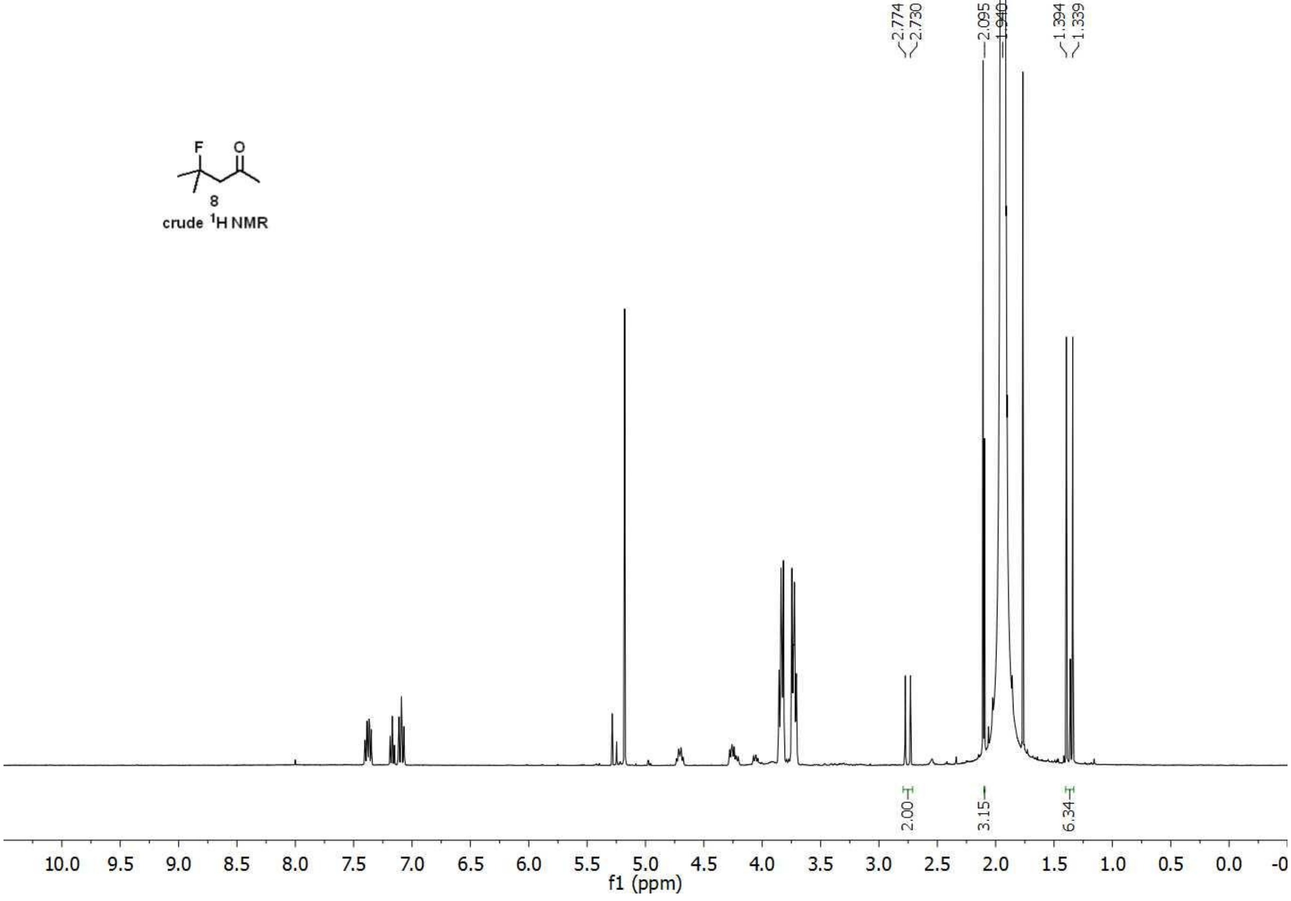
181.486
91.912
90.079
76.317
76.000
75.681
43.720
43.617
42.415
42.213
40.800
40.626
36.283
36.264
33.689
33.670
29.786
29.686
F
COOH
6
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-132.831
F
COOH
6
-132.831
-132.7
-132.8
-132.9
f1 (ppm)
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
-260
-280
-3
f1 (ppm)

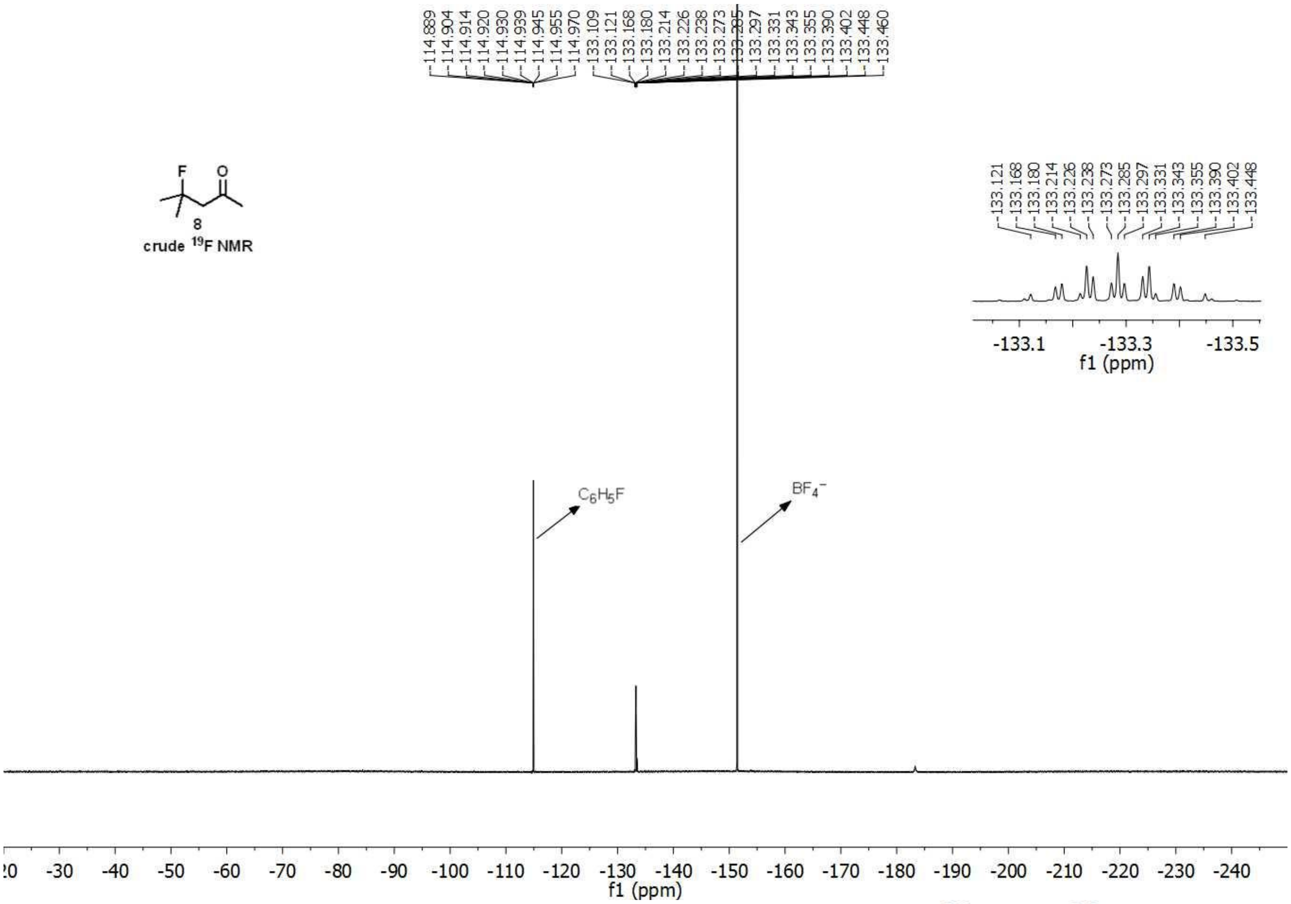

5.143
5.133
5.128
5.124
5.117
5.113
5.108
5.102
5.097
5.093
5.086
5.082
5.077
5.062
5.023
5.012
5.007
5.003
4.997
4.992
4.987
4.981
4.977
4.972
4.965
4.961
4.956
4.946
2.813
2.797
2.793
2.775
2.755
2.684
2.673
2.608
2.597
2.565
2.554
2.090
1.940
1.327
1.311
1.266
1.251
F
O
7
crude ^{1}H NMR
0.94
0.91
0.87
2.66
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

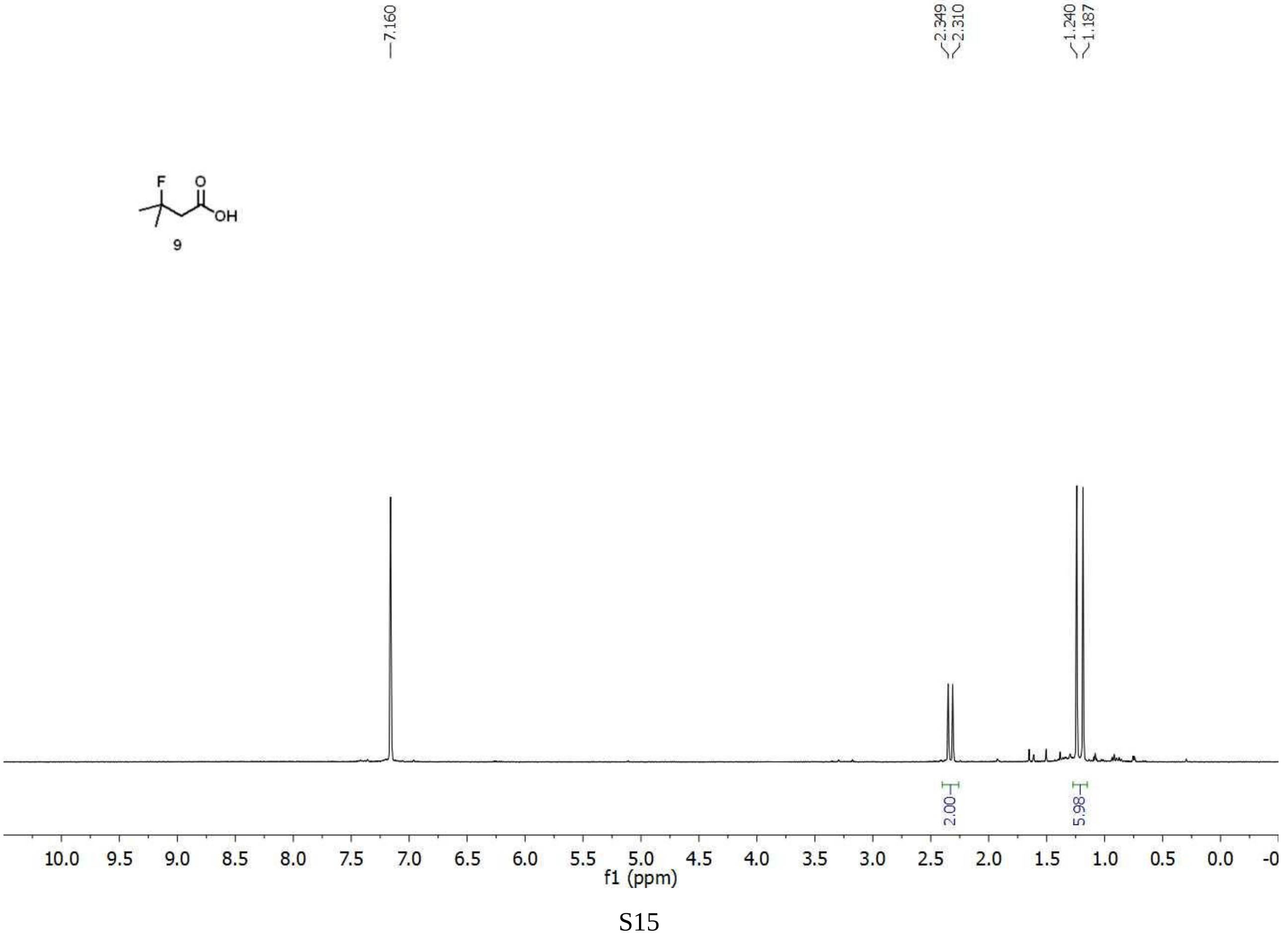

7

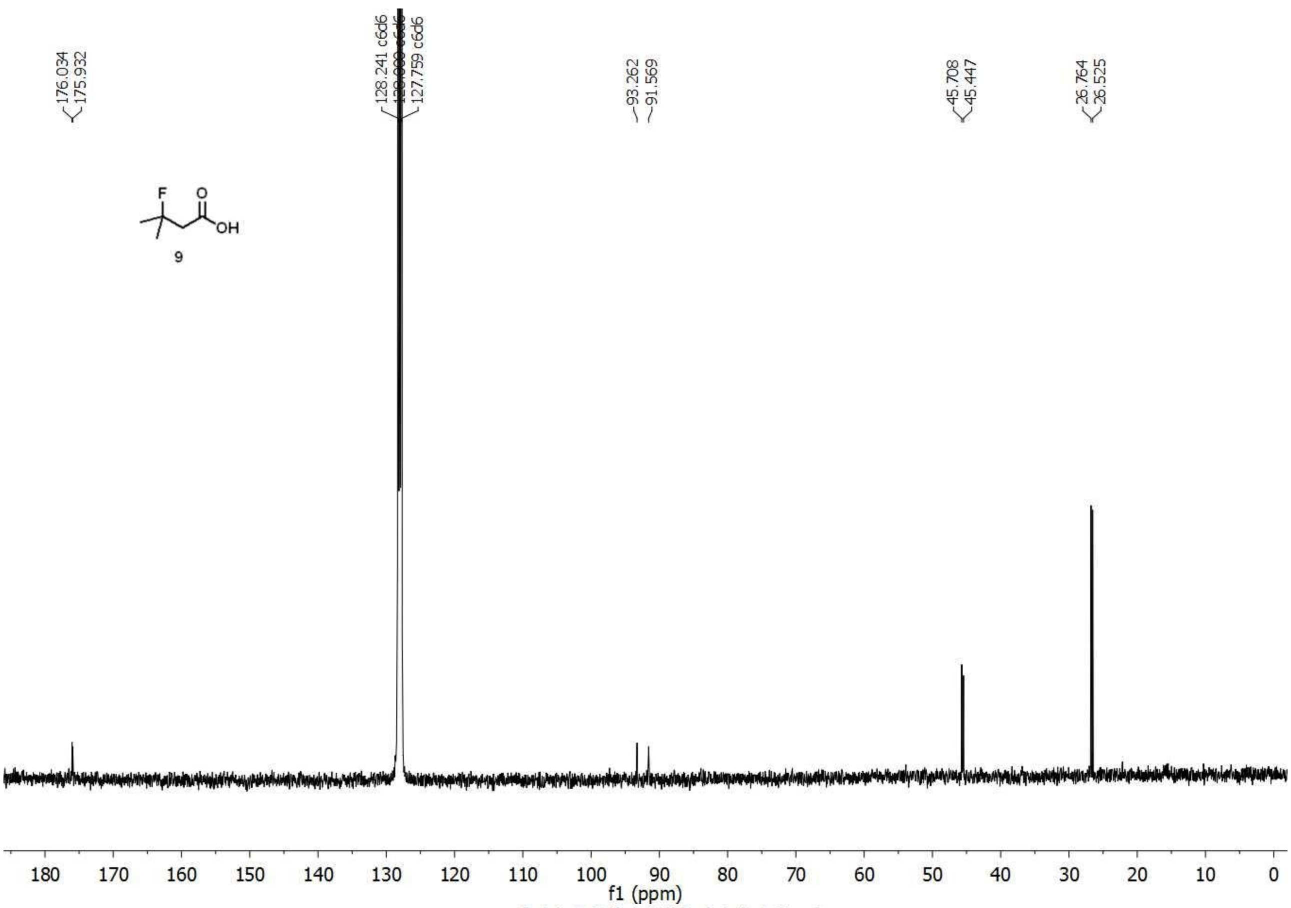
crude ^{19}F NMR

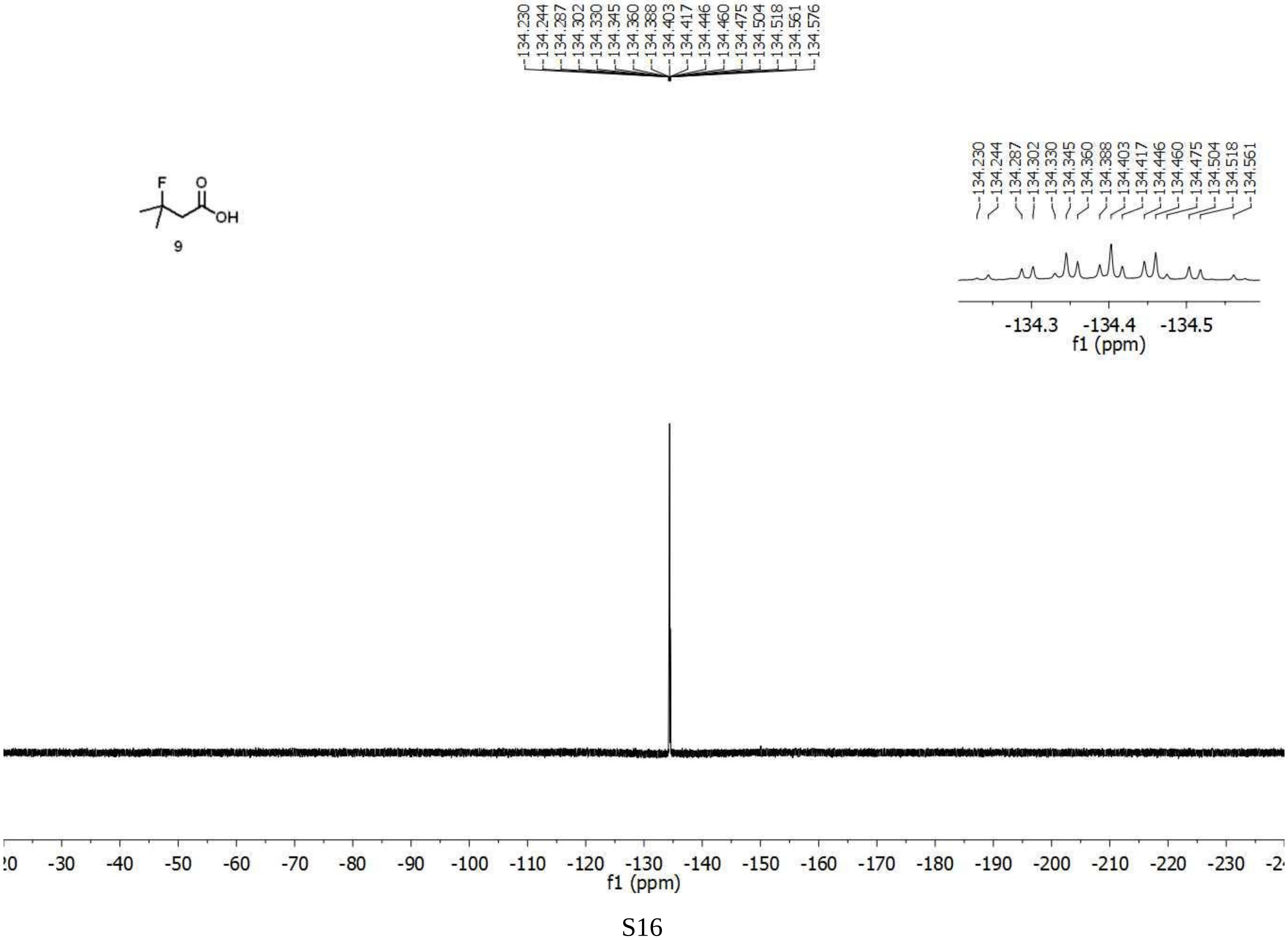

8

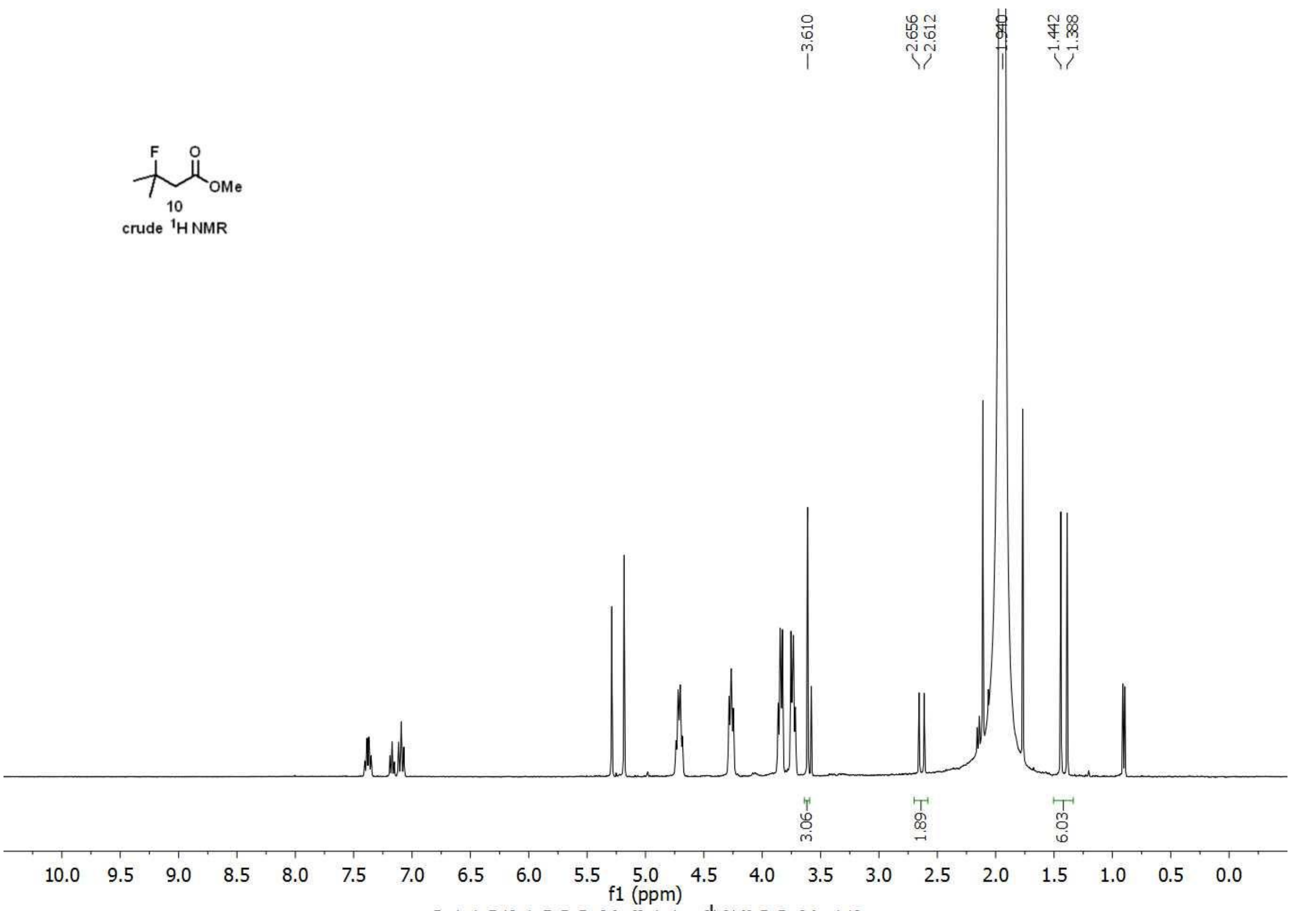
crude ^{1}H NMR

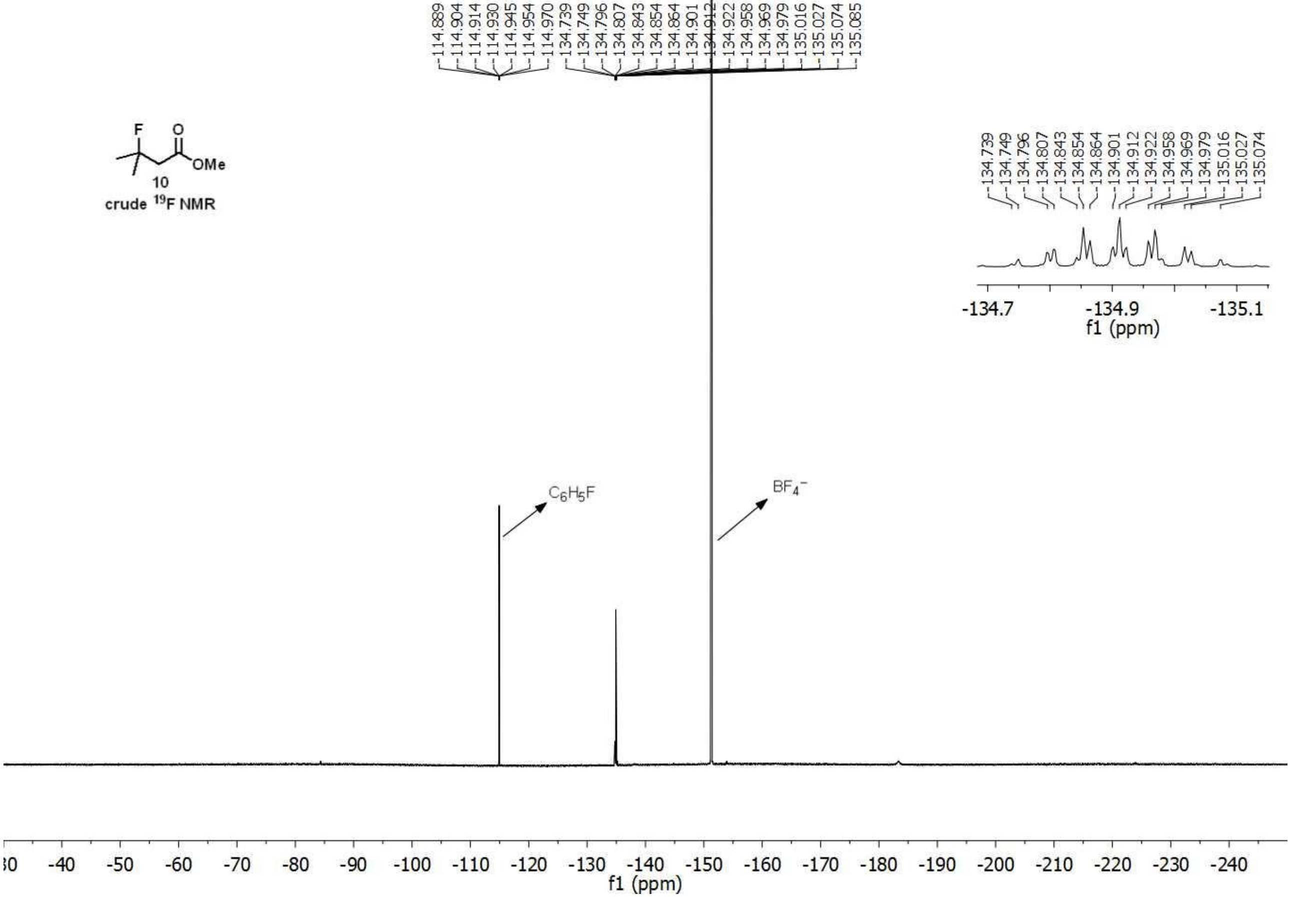

-114.889
-114.904
-114.914
-114.920
-114.930
-114.939
-114.945
-114.955
-114.970
-133.109
-133.121
-133.168
-133.180
-133.214
-133.226
-133.238
-133.273
-133.285
-133.297
-133.331
-133.343
-133.355
-133.390
-133.402
-133.448
-133.460
F
O
8
crude ^{19}F NMR
-133.121
-133.168
-133.180
-133.214
-133.226
-133.238
-133.273
-133.285
-133.297
-133.331
-133.343
-133.355
-133.390
-133.402
-133.448
-133.1
-133.3
-133.5
f1 (ppm)
C_6H_5F
BF_4^-
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
-240
f1 (ppm)

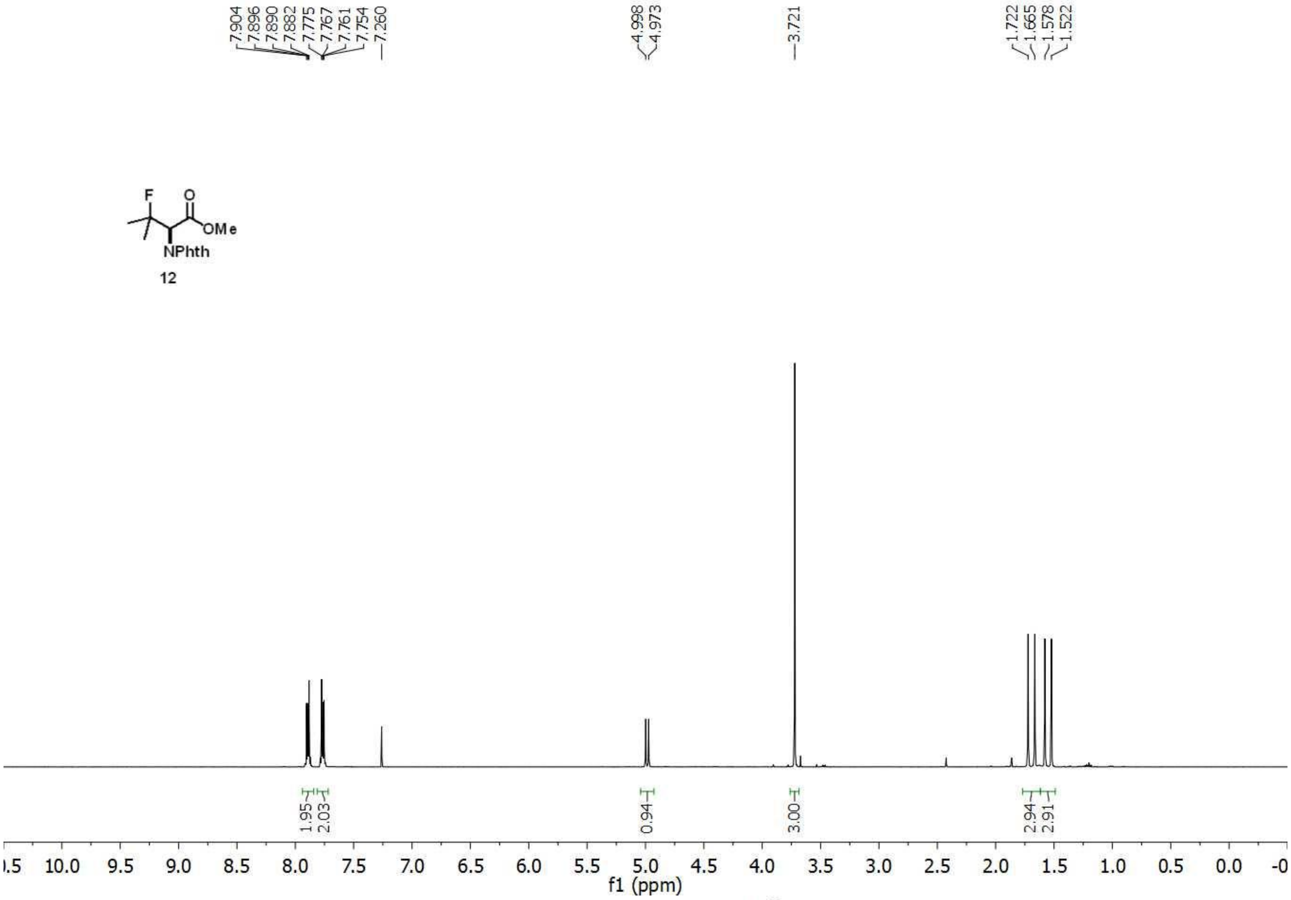

7.160
2.349
2.310
1.240
1.187
F
O
OH
9
2.00
5.98
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

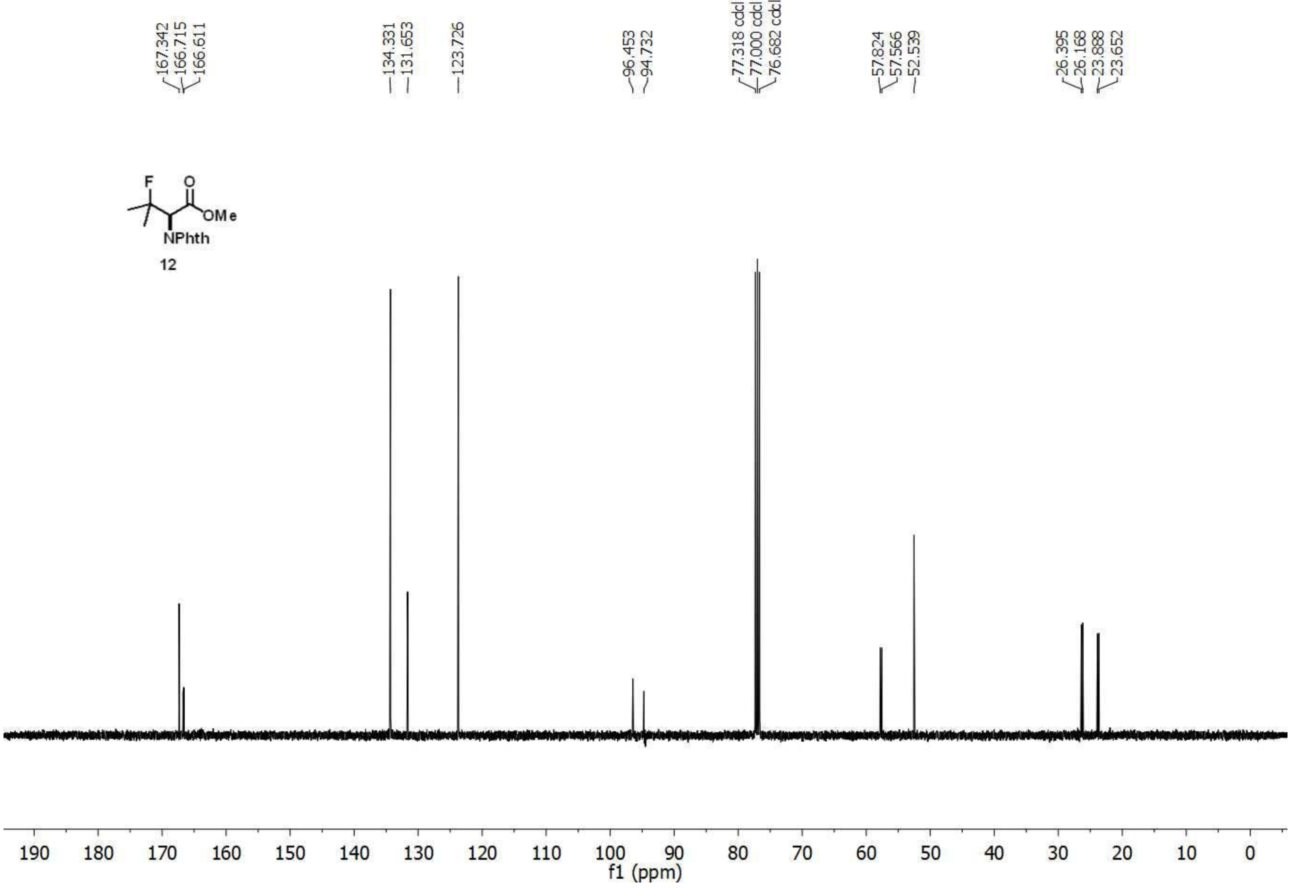

176.034
175.932
128.241 c6d6
127.759 c6d6
93.262
91.569
45.708
45.447
26.764
26.525
F
O
OH
9
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

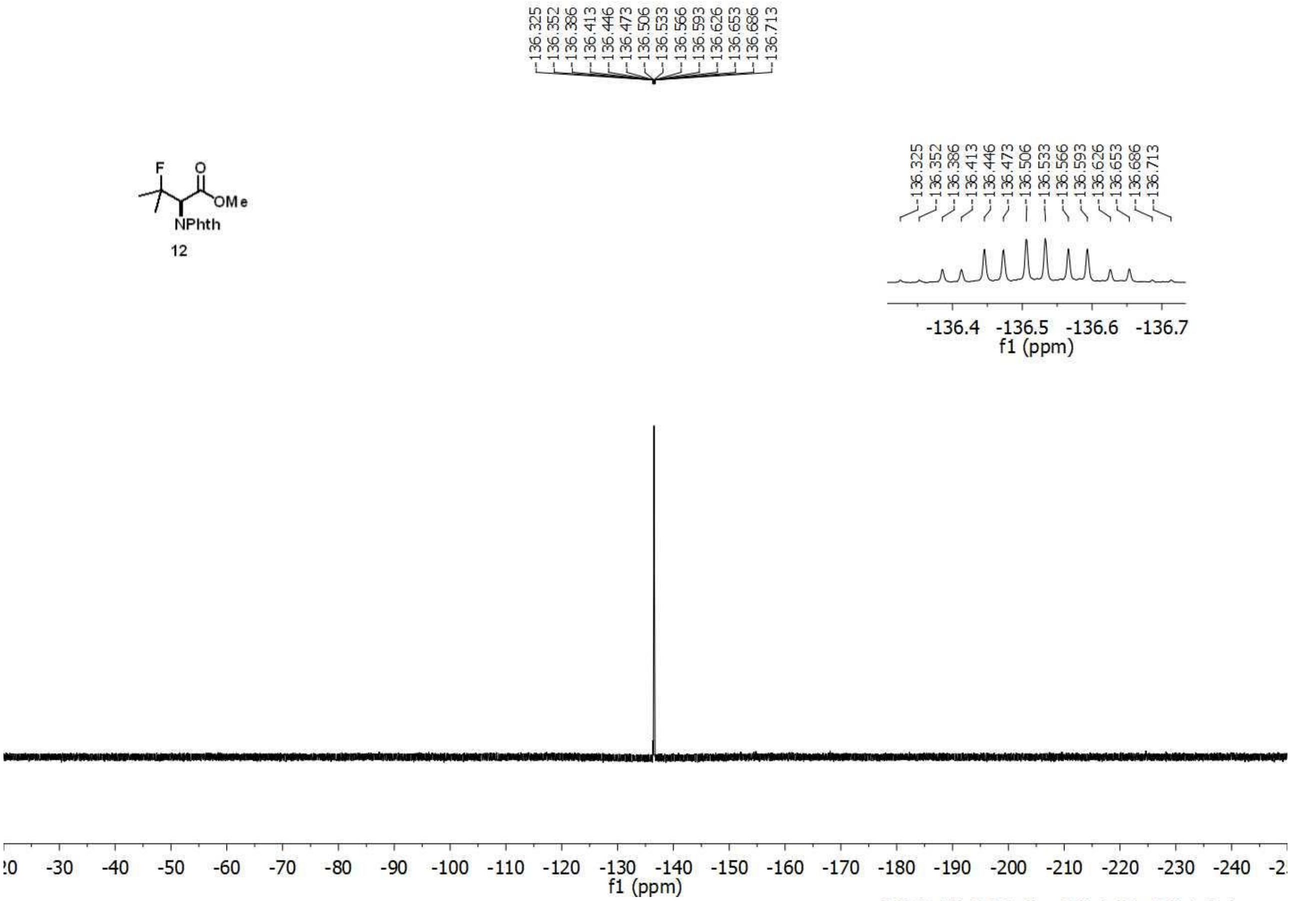

134.230
134.244
134.287
134.302
134.330
134.345
134.360
134.388
134.403
134.417
134.446
134.460
134.475
134.504
134.518
134.561
134.576
F
O
OH
9
-134.3 -134.4 -134.5
f1 (ppm)
-30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230
f1 (ppm)

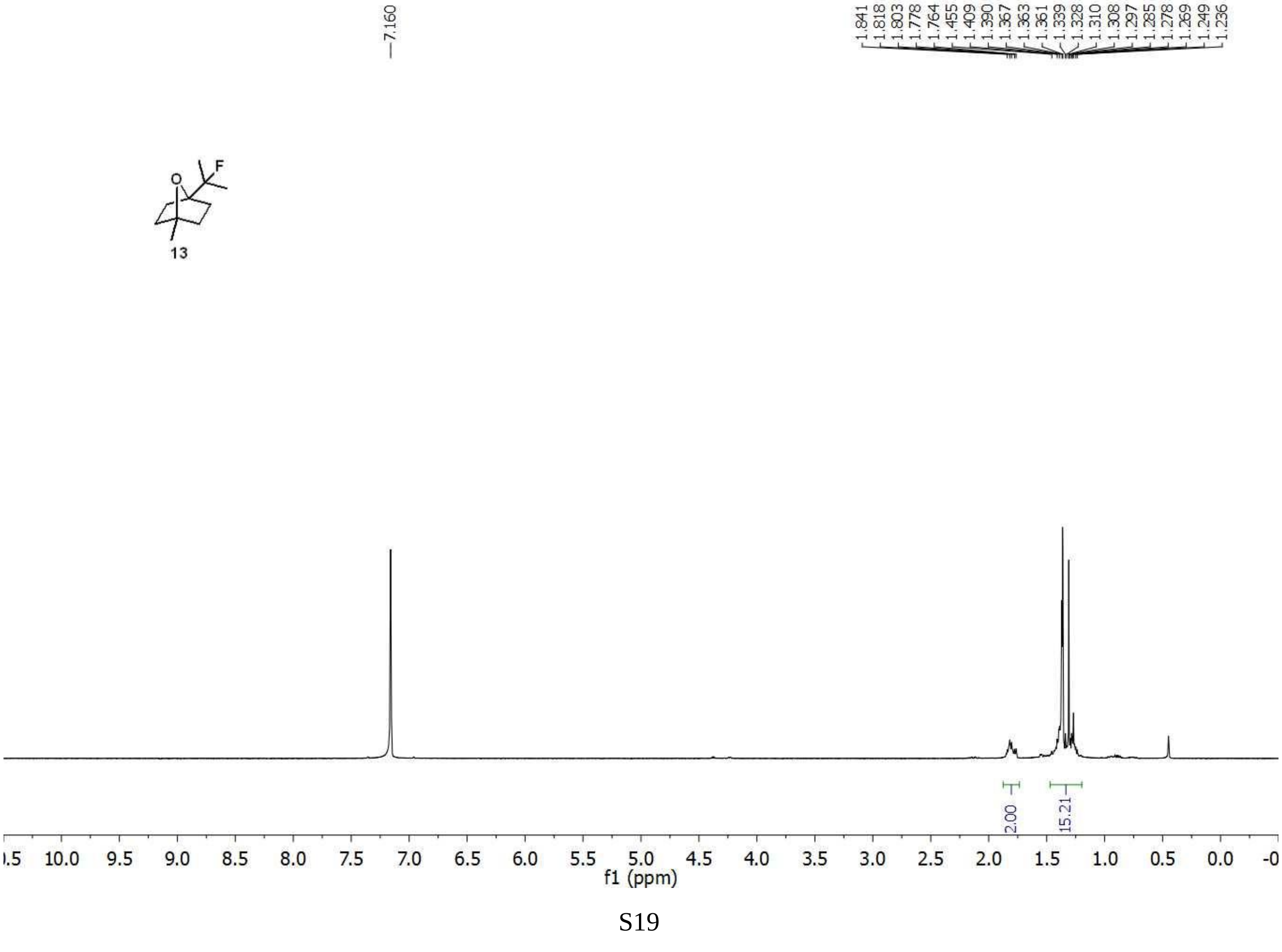

3.610
2.656
2.612
1.940
1.442
1.388
F
O
OMe
10
crude ^{1}H NMR
3.06
1.89
6.03
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

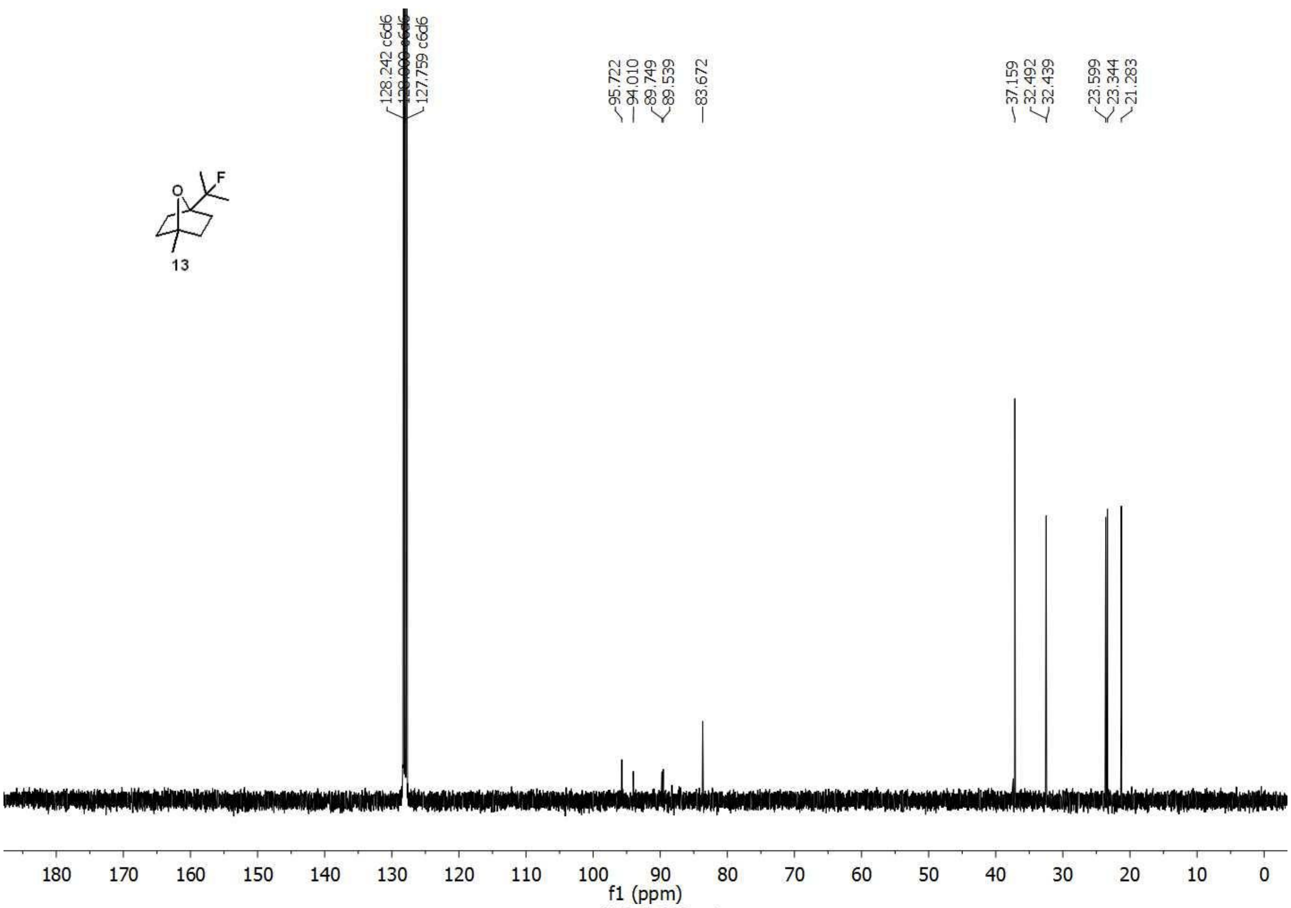

-114.889
-114.904
-114.914
-114.930
-114.945
-114.954
-114.970
-134.739
-134.749
-134.796
-134.807
-134.843
-134.854
-134.864
-134.901
-134.912
-134.922
-134.958
-134.969
-134.979
-135.016
-135.027
-135.074
-135.085
F
O
OMe
10
crude ^{19}F NMR
-134.739
-134.749
-134.796
-134.807
-134.843
-134.854
-134.864
-134.901
-134.912
-134.922
-134.958
-134.969
-134.979
-135.016
-135.027
-135.074
-134.7
-134.9
-135.1
f1 (ppm)
C_6H_5F
BF_4^-
-40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

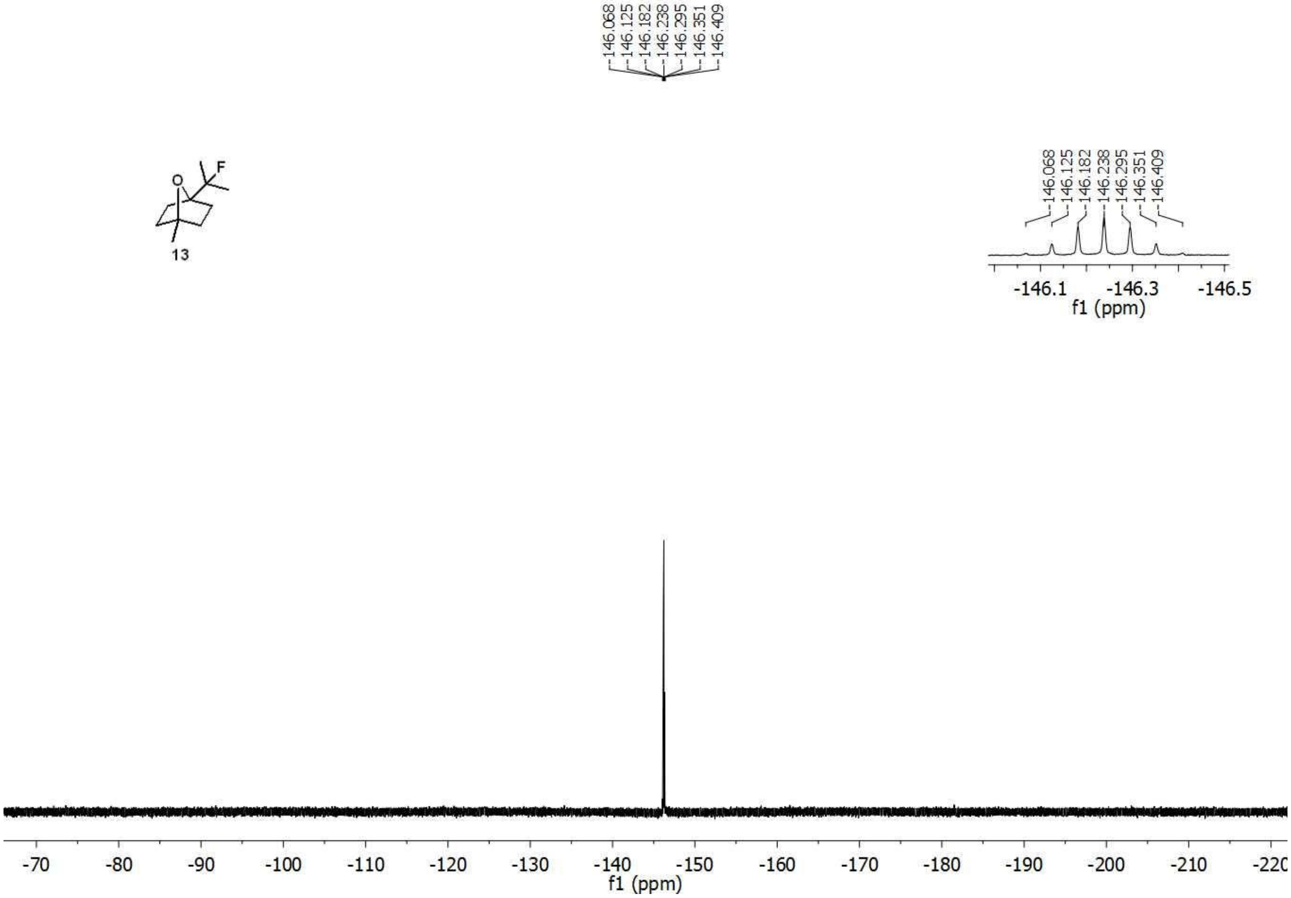

7.904
7.896
7.890
7.882
7.775
7.767
7.761
7.754
7.260
4.998
4.973
3.721
1.722
1.665
1.578
1.522
F
O
OMe
NPhth
12
1.95
2.03
0.94
3.00
2.94
2.91
.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

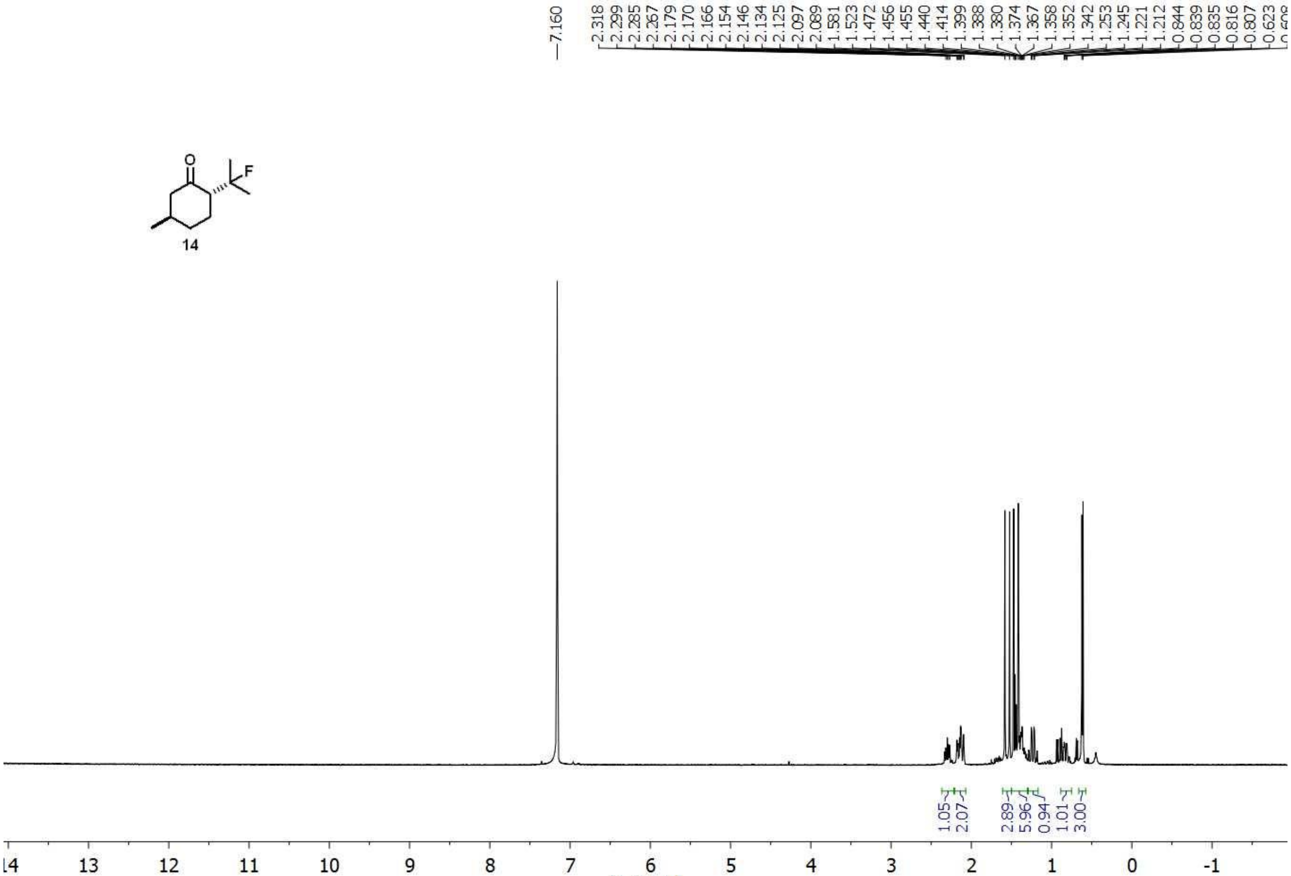

167.342
166.715
166.611
134.331
131.653
123.726
96.453
94.732
77.318 cdcl3
77.000 cdcl3
76.682 cdcl3
57.824
57.566
52.539
26.395
26.168
23.888
23.652
F
O
OMe
NPhth
12
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

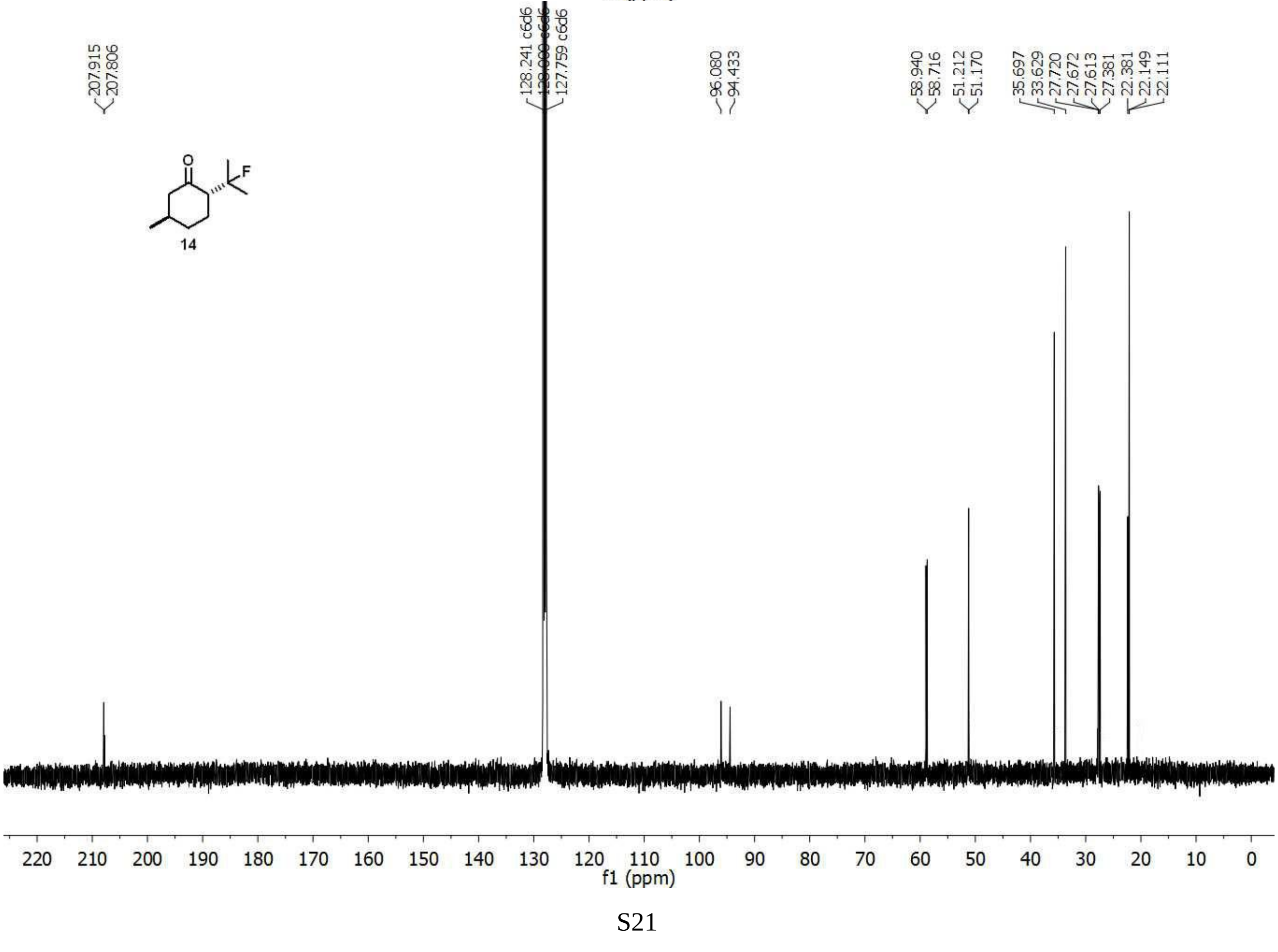

-136.325
-136.352
-136.386
-136.413
-136.446
-136.473
-136.506
-136.533
-136.566
-136.593
-136.626
-136.653
-136.686
-136.713
F
O
OMe
NPhth
12
-136.4
-136.5
-136.6
-136.7
f1 (ppm)
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220
-230
-240
f1 (ppm)

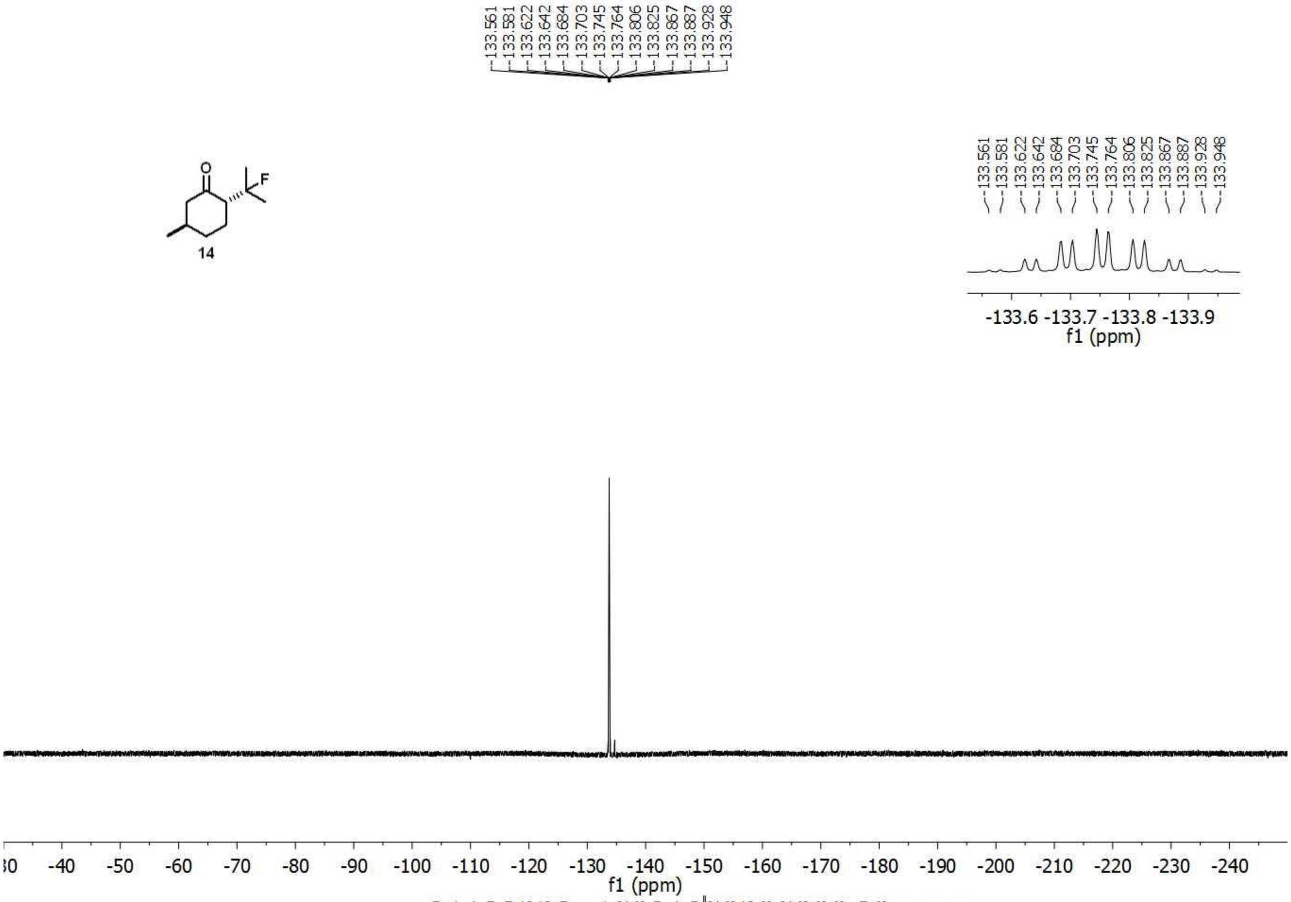

7.160
1.841
1.818
1.803
1.778
1.764
1.455
1.409
1.390
1.367
1.363
1.361
1.339
1.328
1.310
1.308
1.297
1.285
1.278
1.269
1.249
1.236
O
F
13
2.00
15.21
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


128.242 c6d6
128.000 c6d6
127.759 c6d6
95.722
94.010
89.749
89.539
83.672
37.159
32.492
32.439
23.599
23.344
21.283
O
F
13
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

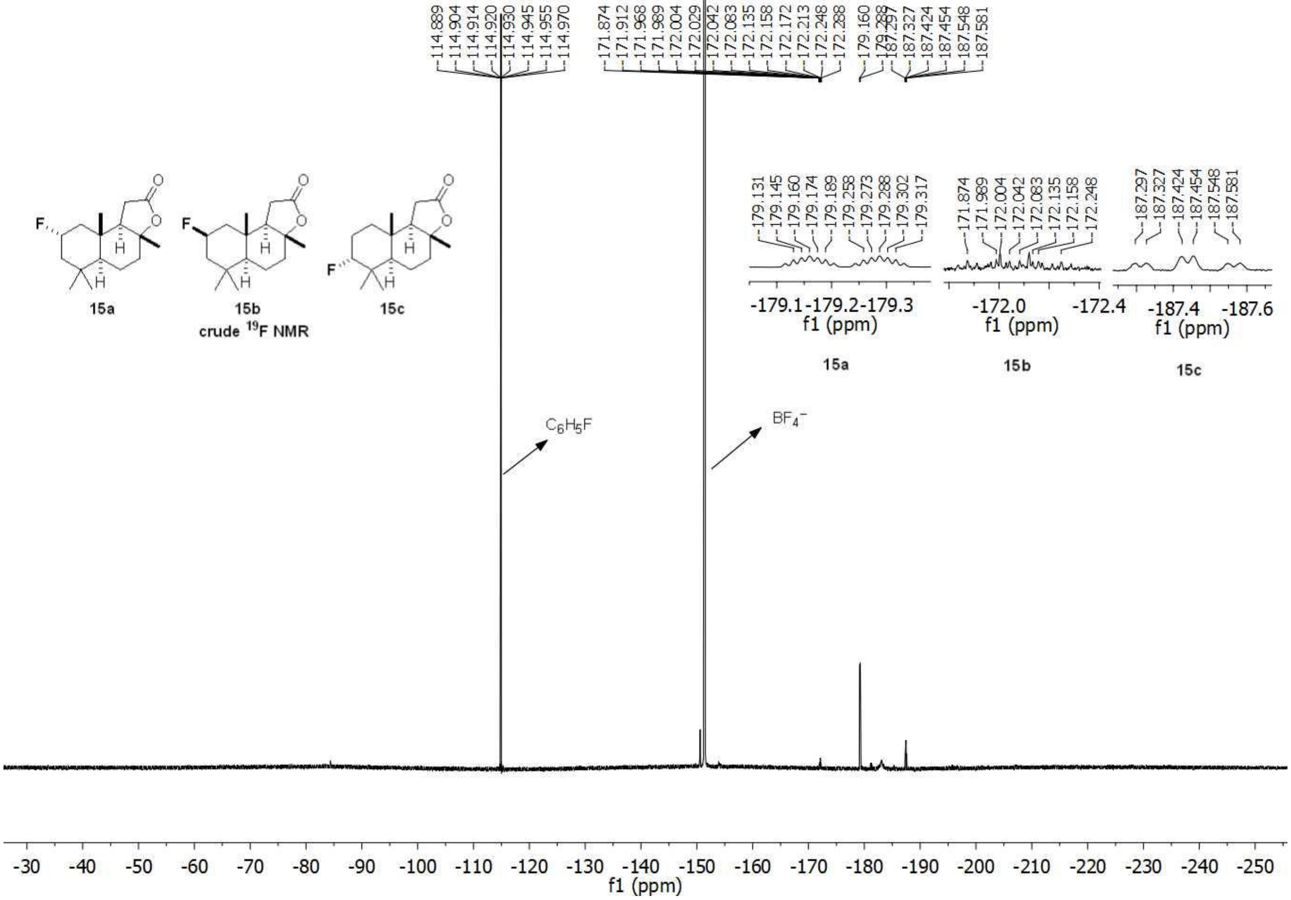

-146.068
-146.125
-146.182
-146.238
-146.295
-146.351
-146.409
O
F
13
-146.1 -146.3 -146.5
f1 (ppm)
-70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)


7.160
2.318
2.299
2.285
2.267
2.179
2.170
2.166
2.154
2.146
2.134
2.125
2.097
2.089
1.581
1.523
1.472
1.456
1.455
1.440
1.414
1.399
1.388
1.380
1.374
1.367
1.358
1.352
1.342
1.253
1.245
1.221
1.212
0.844
0.839
0.835
0.816
0.807
0.623
O
F
14
1.05
2.07
2.89
5.96
0.94
1.01
3.00
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

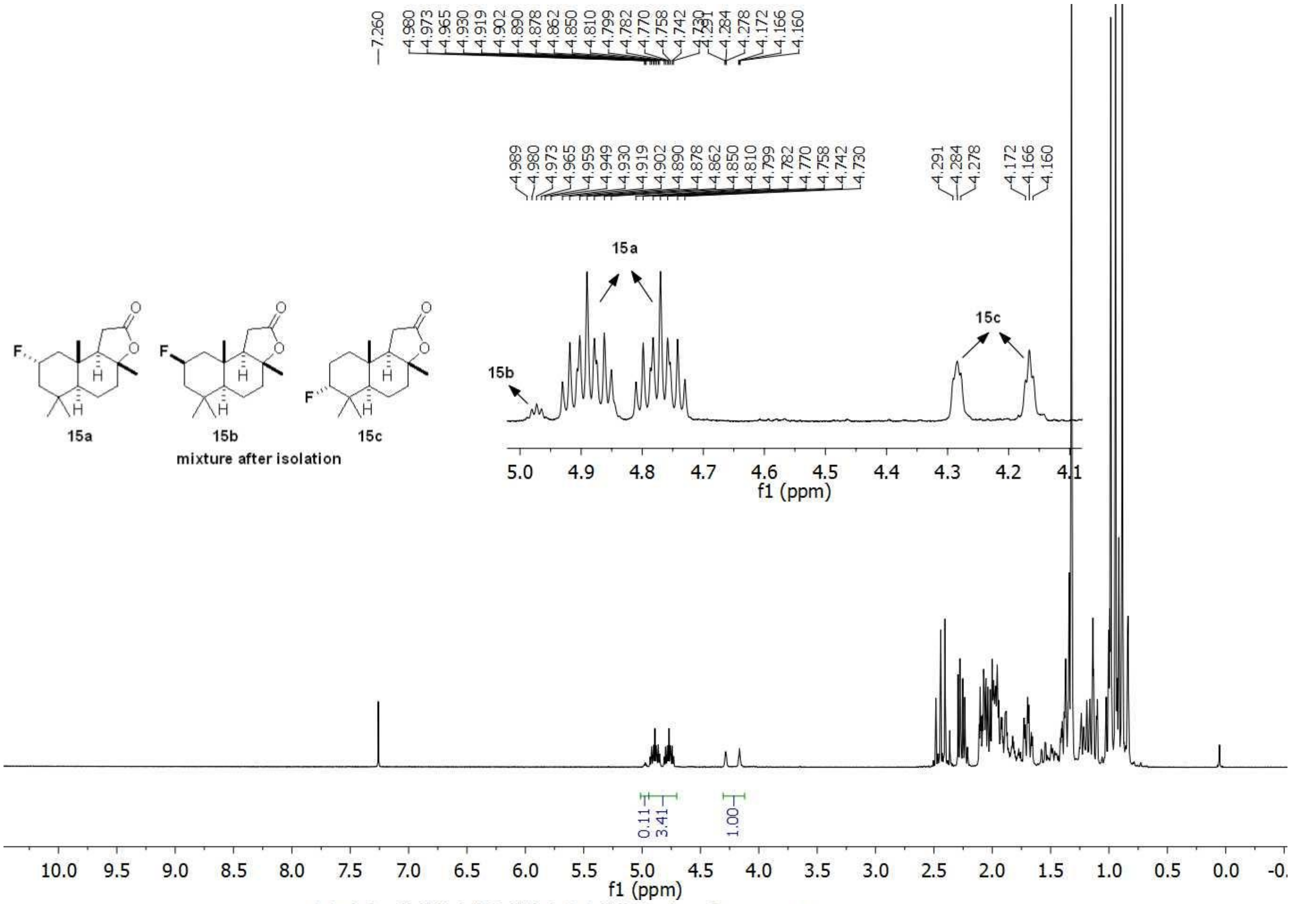

207.915
207.806
128.241 c6d6
128.000 c6d6
127.759 c6d6
96.080
94.433
58.940
58.716
51.212
51.170
35.697
33.629
27.720
27.672
27.613
27.381
22.381
22.149
22.111
O
F
14
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

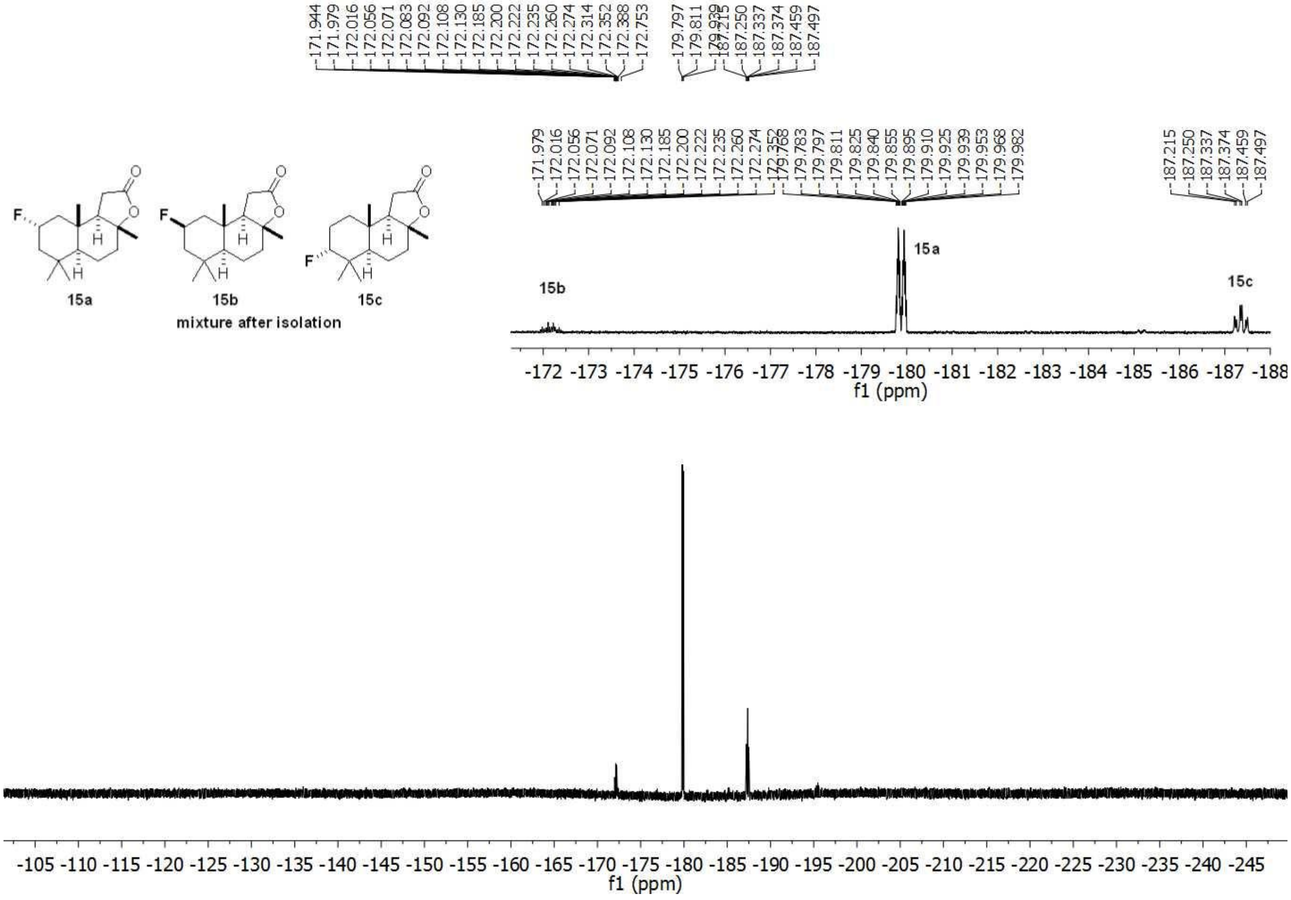


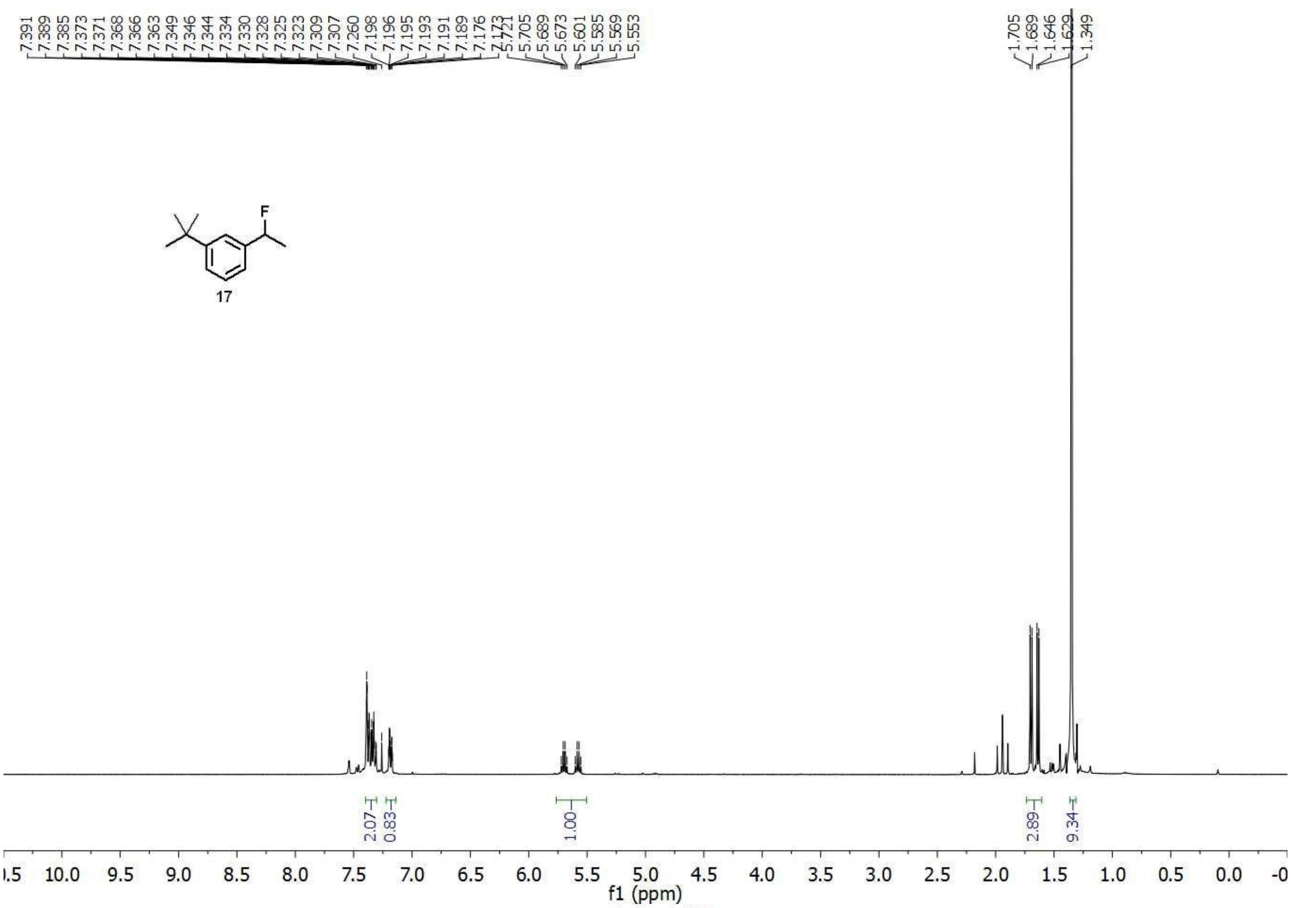
-133.561
-133.581
-133.622
-133.642
-133.684
-133.703
-133.745
-133.764
-133.806
-133.825
-133.867
-133.887
-133.928
-133.948
F
O
14
-133.6 -133.7 -133.8 -133.9
f1 (ppm)
-40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

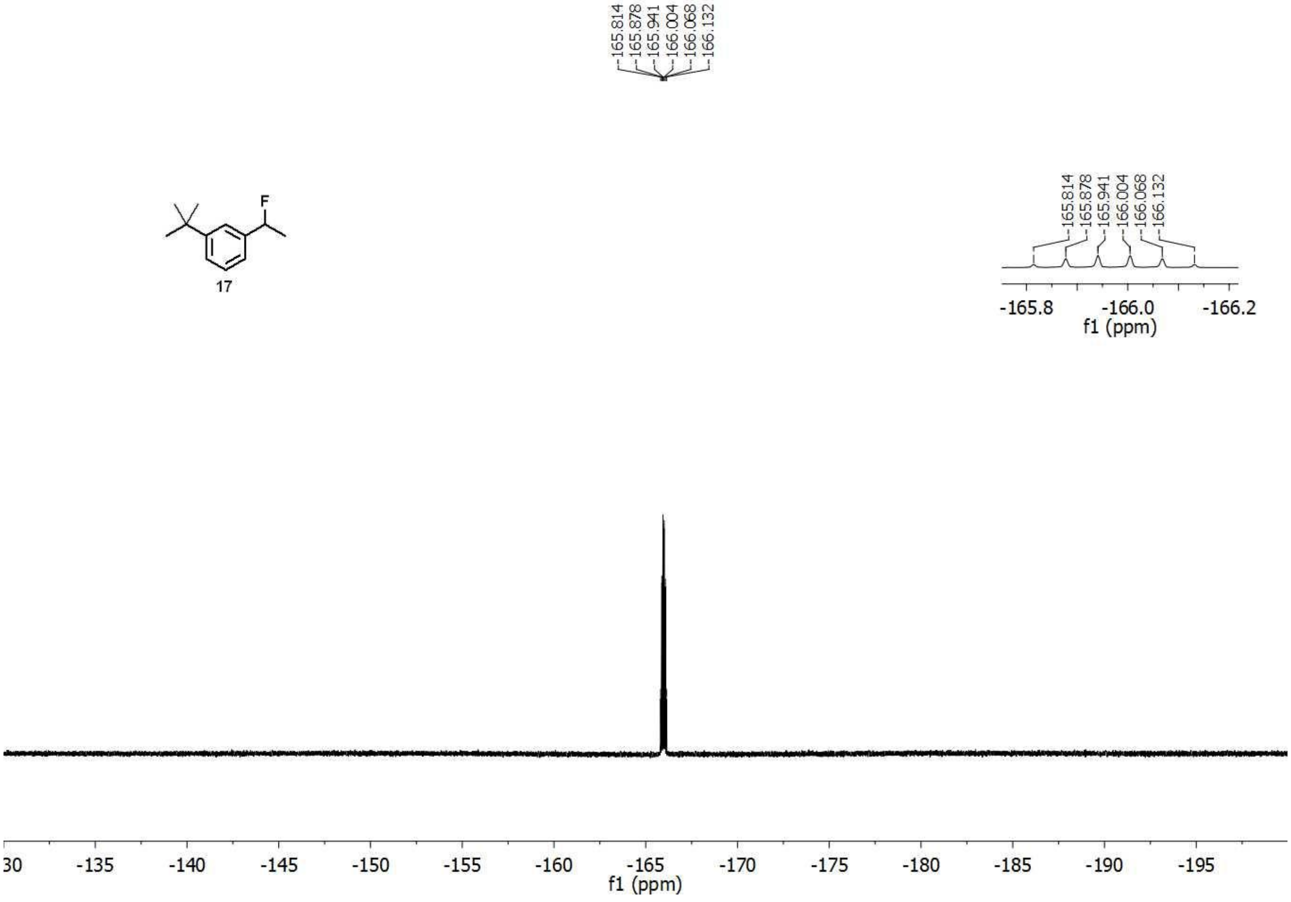


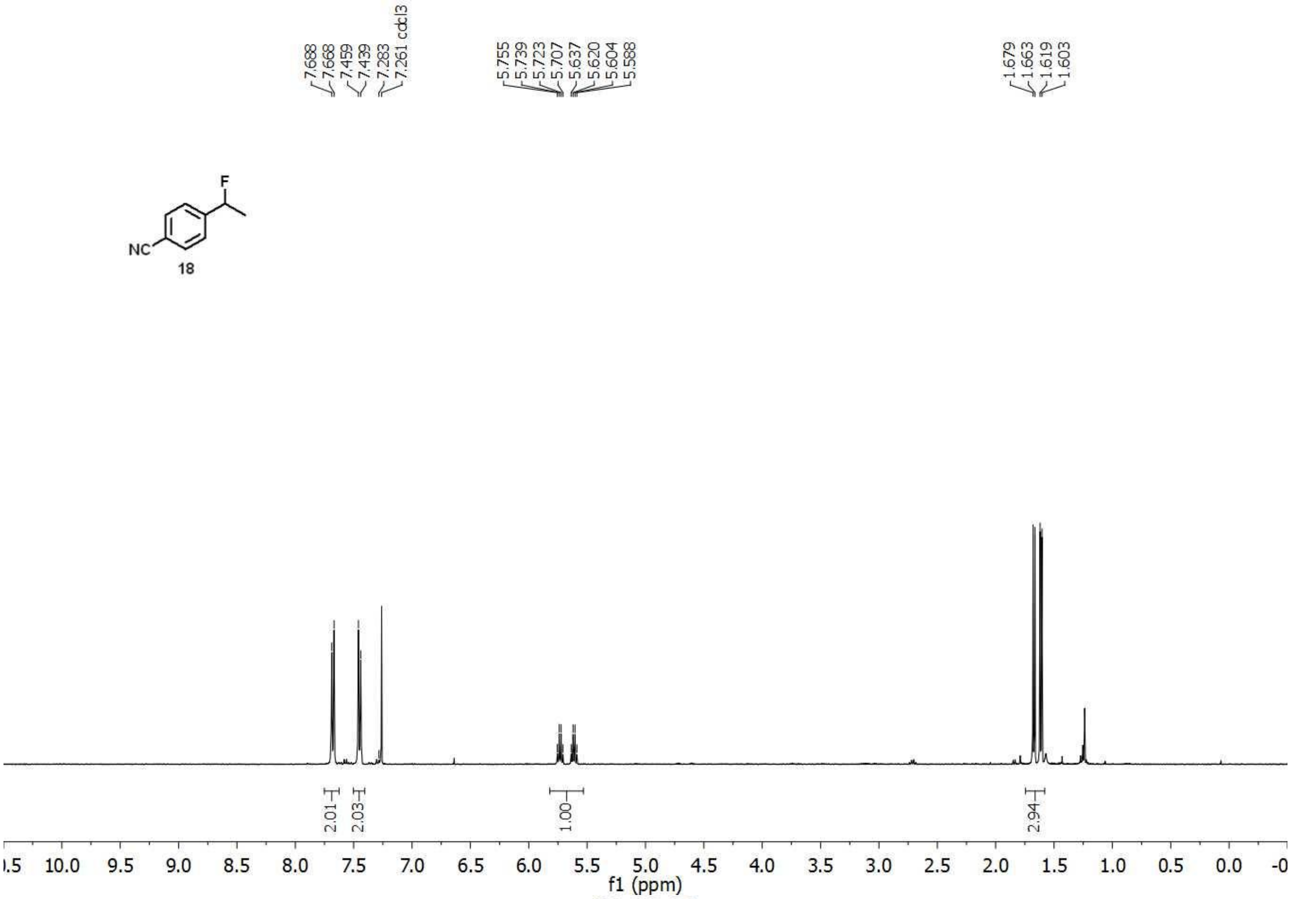
-114.889
-114.904
-114.914
-114.920
-114.930
-114.945
-114.955
-114.970
-171.874
-171.912
-171.968
-171.989
-172.004
-172.029
-172.042
-172.083
-172.135
-172.158
-172.172
-172.213
-172.248
-172.288
-179.160
-179.288
-187.297
-187.327
-187.424
-187.454
-187.548
-187.581
F
H
15a
15b
crude 19F NMR
15c
-179.131
-179.145
-179.160
-179.174
-179.189
-179.258
-179.273
-179.288
-179.302
-179.317
-179.1-179.2-179.3
f1 (ppm)
15a
-171.874
-171.989
-172.004
-172.042
-172.083
-172.135
-172.158
-172.248
-172.0
-172.4
f1 (ppm)
15b
-187.297
-187.327
-187.424
-187.454
-187.548
-187.581
-187.4
-187.6
f1 (ppm)
15c
C6H5F
BF4−
-30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240 -250
f1 (ppm)

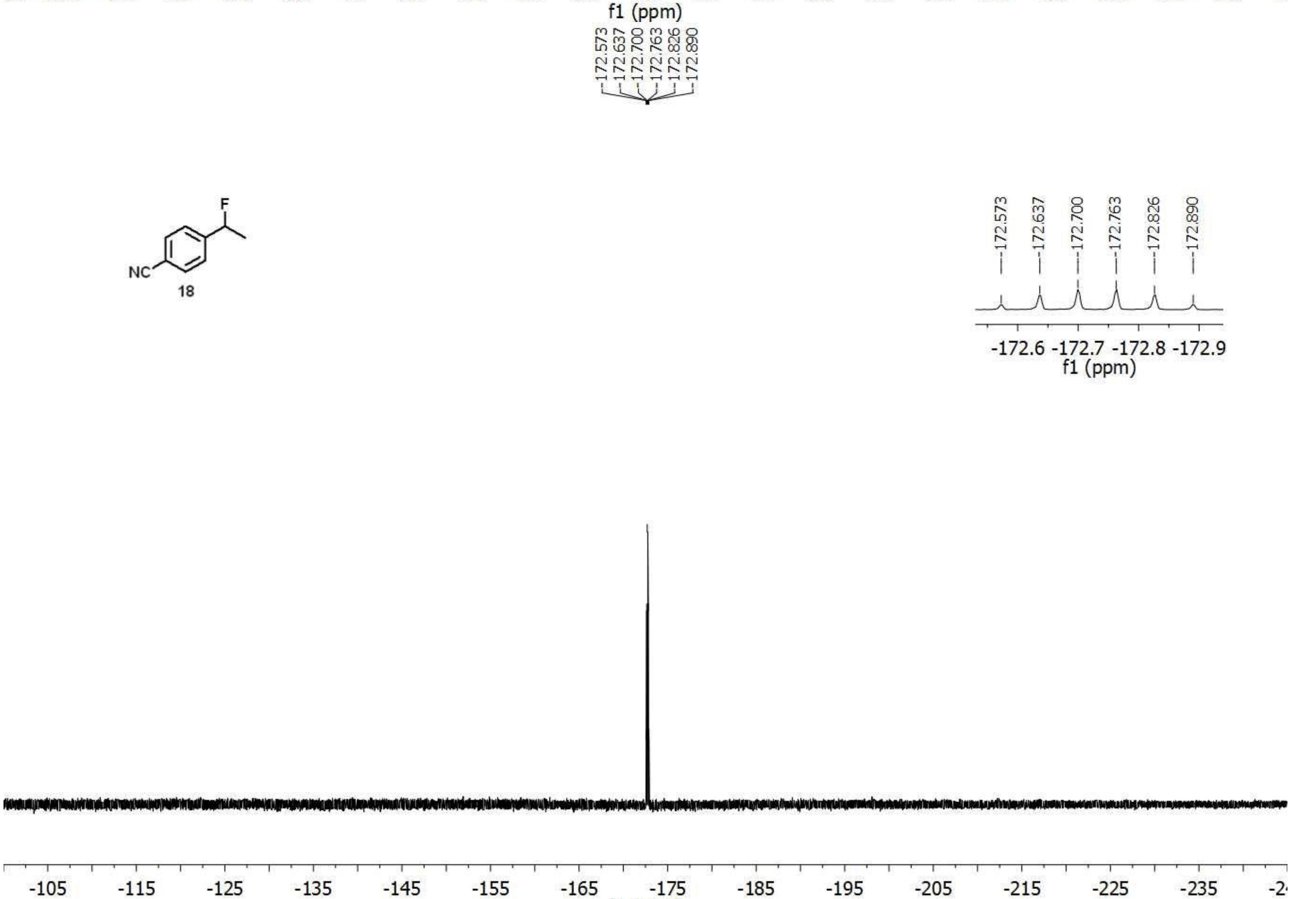

7.260
4.980 4.973 4.965 4.930 4.919 4.902 4.890 4.878 4.862 4.850 4.810 4.799 4.782 4.770 4.758 4.742 4.730 4.291 4.284 4.278 4.172 4.166 4.160
4.989 4.980 4.973 4.965 4.959 4.949 4.930 4.919 4.902 4.890 4.878 4.862 4.850 4.810 4.799 4.782 4.770 4.758 4.742 4.730
4.291 4.284 4.278
4.172 4.166 4.160
15a
15b
15c
F
H
O
15a
15b
15c
mixture after isolation
5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1
f1 (ppm)
0.11
3.41
1.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

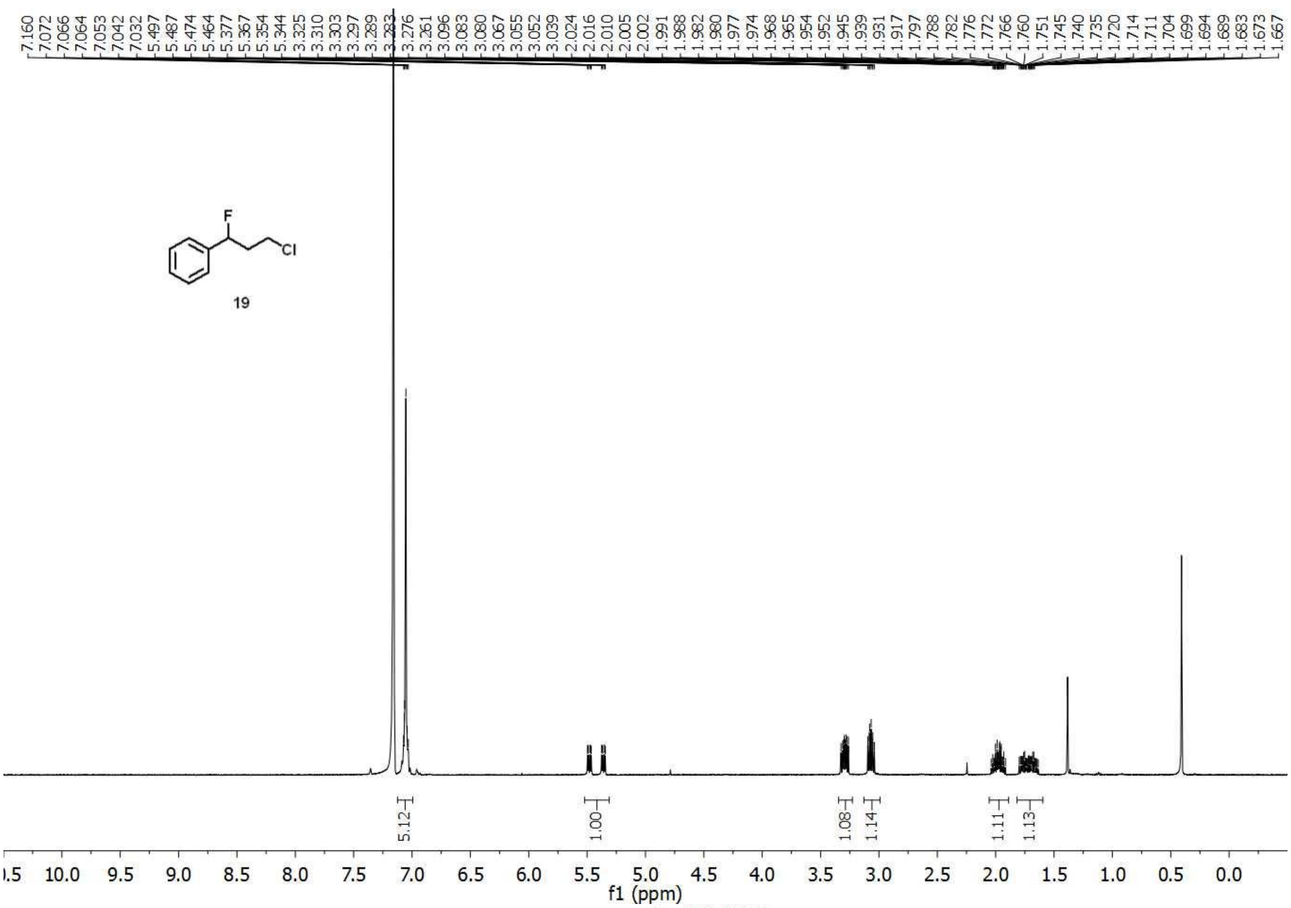

-171.944 -171.979 -172.016 -172.056 -172.071 -172.083 -172.092 -172.108 -172.130 -172.185 -172.200 -172.222 -172.235 -172.260 -172.274 -172.314 -172.352 -172.388 -172.753
-179.797 -179.811 -179.939 -187.215 -187.250 -187.337 -187.374 -187.459 -187.497
-171.979 -172.016 -172.056 -172.071 -172.092 -172.108 -172.130 -172.185 -172.200 -172.222 -172.235 -172.260 -172.274 -172.352 -179.768 -179.783 -179.797 -179.811 -179.825 -179.840 -179.855 -179.895 -179.910 -179.925 -179.939 -179.953 -179.968 -179.982
-187.215 -187.250 -187.337 -187.374 -187.459 -187.497
F
H
O
15a
15b
15c
mixture after isolation
15b
15a
15c
-172 -173 -174 -175 -176 -177 -178 -179 -180 -181 -182 -183 -184 -185 -186 -187 -188
f1 (ppm)
-105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180 -185 -190 -195 -200 -205 -210 -215 -220 -225 -230 -235 -240 -245
f1 (ppm)

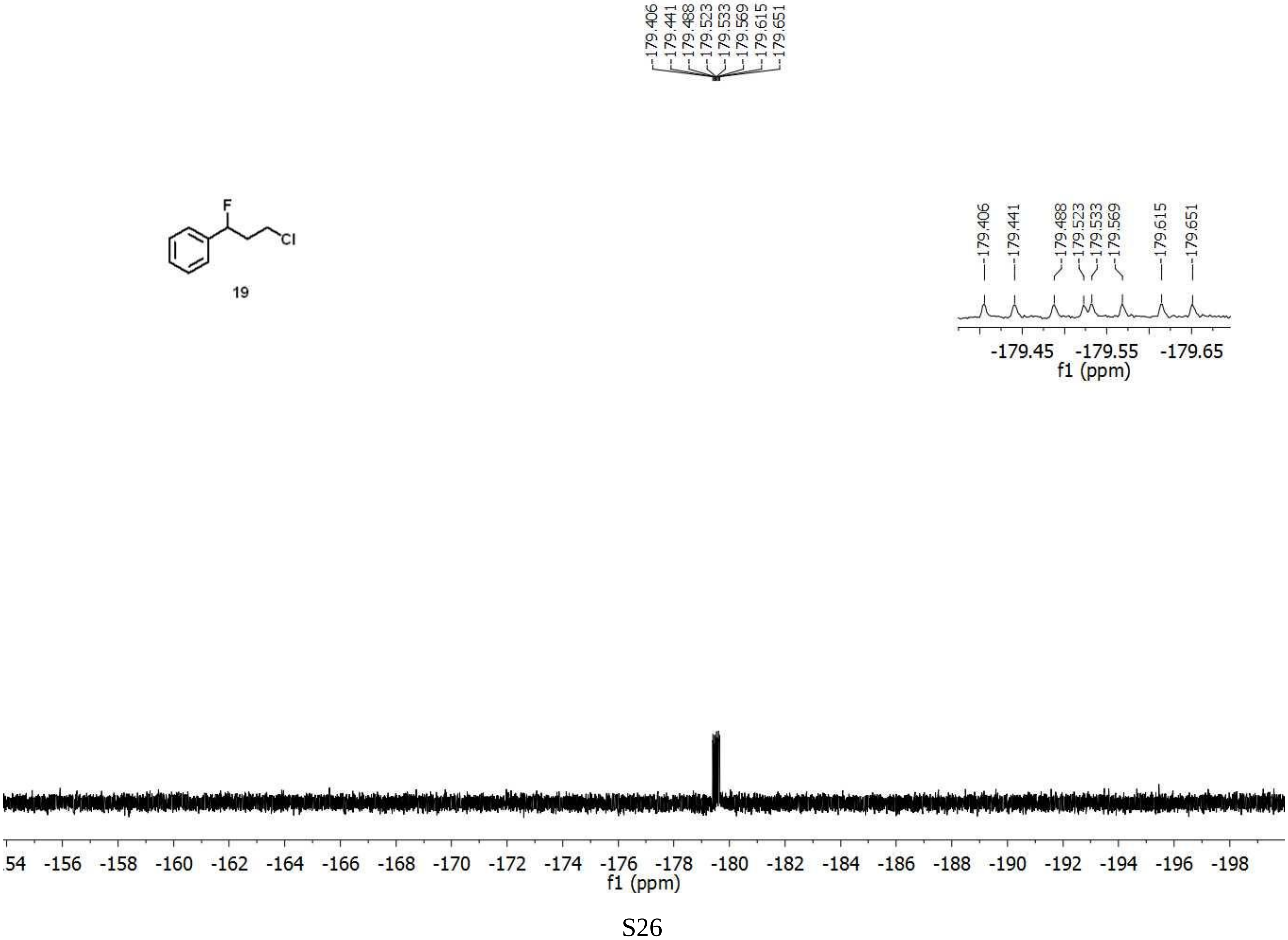

7.391
7.389
7.385
7.373
7.371
7.368
7.366
7.363
7.349
7.346
7.344
7.334
7.330
7.328
7.325
7.323
7.309
7.307
7.260
7.198
7.196
7.195
7.193
7.191
7.189
7.176
7.173
5.721
5.705
5.689
5.673
5.601
5.585
5.569
5.553
1.705
1.689
1.646
1.629
1.349
F
17
2.07
0.83
1.00
2.89
9.34
.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

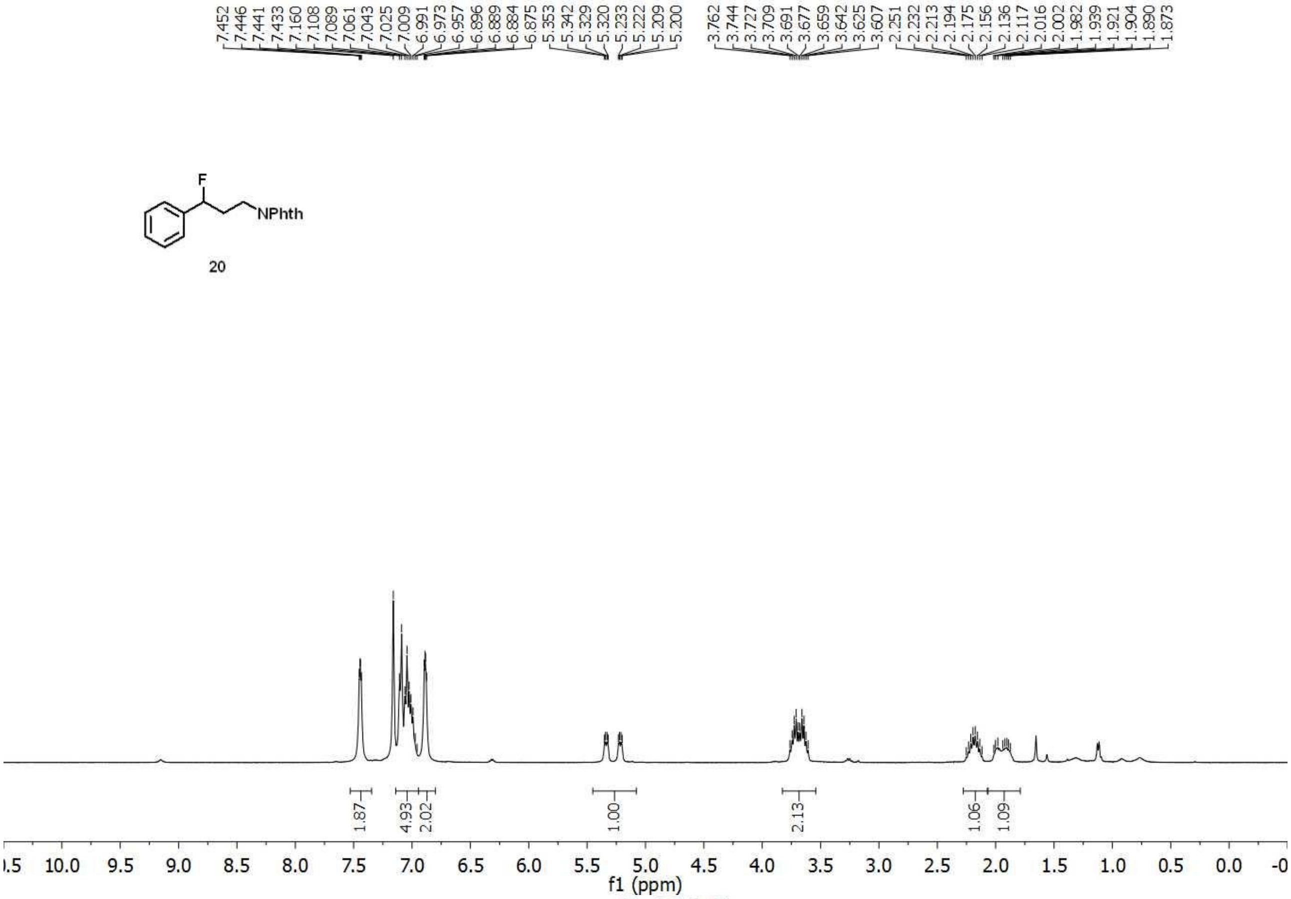

165.814
165.878
165.941
166.004
166.068
166.132
F
17
165.814
165.878
165.941
166.004
166.068
166.132
-165.8
-166.0
-166.2
f1 (ppm)
30
-135
-140
-145
-150
-155
-160
-165
-170
-175
-180
-185
-190
-195
f1 (ppm)

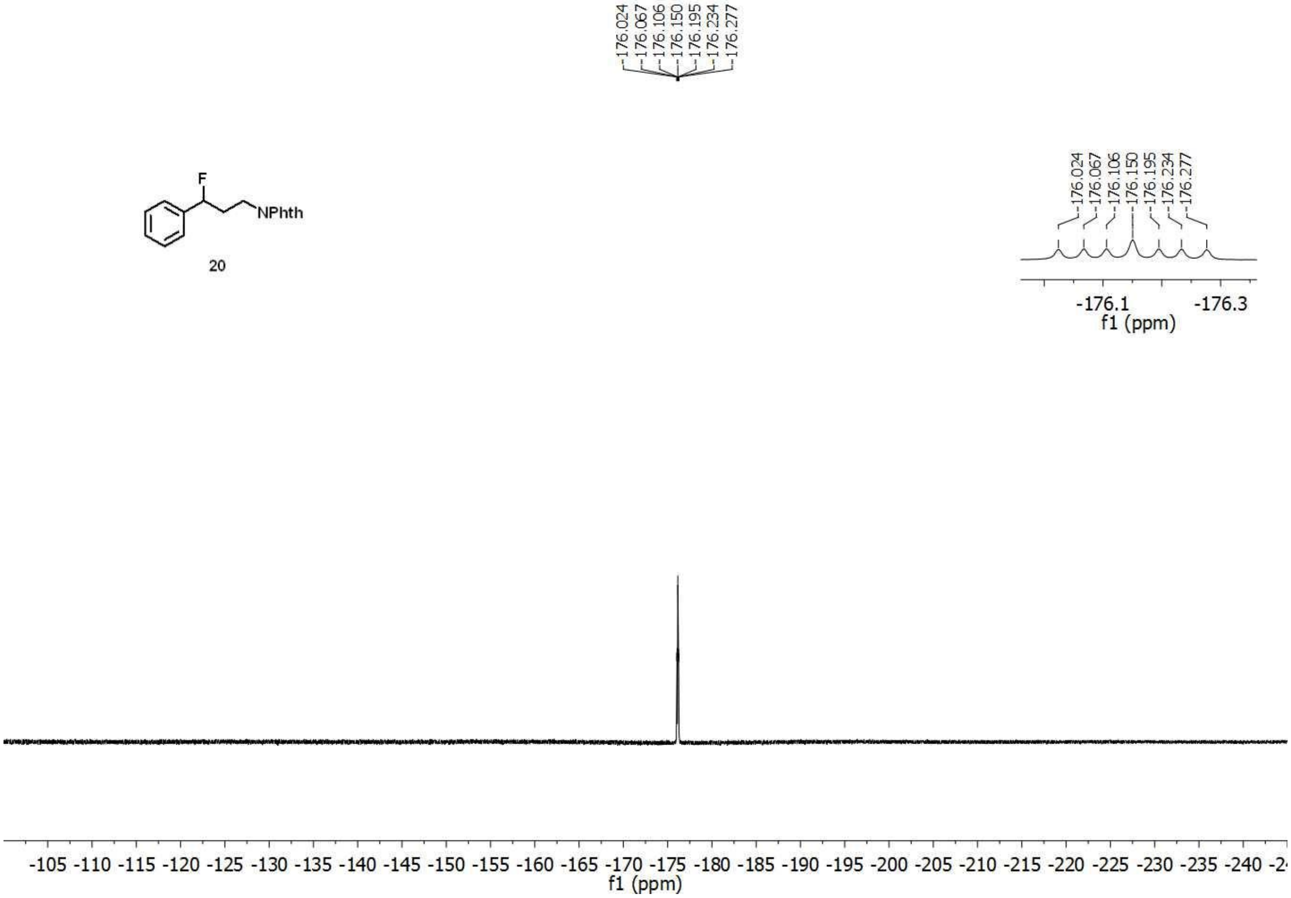

7.688
7.668
7.459
7.439
7.283
7.261 cdcl3
5.755
5.739
5.723
5.707
5.637
5.620
5.604
5.588
1.679
1.663
1.619
1.603
F
NC
18
2.01
2.03
1.00
2.94
.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)


-172.573
-172.637
-172.700
-172.763
-172.826
-172.890
F
NC
18
-172.6 -172.7 -172.8 -172.9
f1 (ppm)
-105 -115 -125 -135 -145 -155 -165 -175 -185 -195 -205 -215 -225 -235 -2
f1 (ppm)


7.160
7.072
7.066
7.064
7.053
7.042
7.032
5.497
5.487
5.474
5.464
5.377
5.367
5.354
5.344
3.325
3.310
3.303
3.297
3.289
3.283
3.276
3.261
3.096
3.083
3.080
3.067
3.055
3.052
3.039
2.024
2.016
2.010
2.005
2.002
1.991
1.988
1.982
1.980
1.977
1.974
1.968
1.965
1.954
1.952
1.945
1.939
1.931
1.917
1.797
1.788
1.782
1.776
1.772
1.766
1.760
1.751
1.745
1.740
1.735
1.720
1.714
1.711
1.704
1.699
1.694
1.689
1.683
1.673
1.667
F
Cl
19
5.12
1.00
1.08
1.14
1.11
1.13
.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


-179.406
-179.441
-179.488
-179.523
-179.533
-179.569
-179.615
-179.651
F
Cl
19
-179.406
-179.441
-179.488
-179.523
-179.533
-179.569
-179.615
-179.651
-179.45 -179.55 -179.65
f1 (ppm)
54 -156 -158 -160 -162 -164 -166 -168 -170 -172 -174 -176 -178 -180 -182 -184 -186 -188 -190 -192 -194 -196 -198
f1 (ppm)


7.452
7.446
7.441
7.433
7.160
7.108
7.089
7.061
7.043
7.025
7.009
6.991
6.973
6.957
6.896
6.889
6.884
6.875
5.353
5.342
5.329
5.320
5.233
5.222
5.209
5.200
3.762
3.744
3.727
3.709
3.691
3.677
3.659
3.642
3.625
3.607
2.251
2.232
2.213
2.194
2.175
2.156
2.136
2.117
2.016
2.002
1.982
1.939
1.921
1.904
1.890
1.873
F
NPhth
20
1.87
4.93
2.02
1.00
2.13
1.06
1.09
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


-176.024
-176.067
-176.106
-176.150
-176.195
-176.234
-176.277
F
NPhth
20
-176.024
-176.067
-176.106
-176.150
-176.195
-176.234
-176.277
-176.1
-176.3
f1 (ppm)
-105
-110
-115
-120
-125
-130
-135
-140
-145
-150
-155
-160
-165
-170
-175
-180
-185
-190
-195
-200
-205
-210
-215
-220
-225
-230
-235
-240
f1 (ppm)