Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Supporting Information

Desymmetrization-like Catalytic Enantioselective Fluorination of Malonates and Its Application to Pharmaceutically Attractive Molecules

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General Methods:
All reactions were performed in oven-dried under positive of nitrogen. Solvents were transferred *via* syringe and were introduced into the reaction vessels though a rubber septum. All of the reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica gel (60-F254). The TLC plates were visualized with UV light and 7% phosphomolybdic acid or *p*-anisaldehyde in ethanol/heat. Column chromatography was carried out on a column packed with silica gel 60N spherical neutral size10-63 μm. The ^{1}H NMR (200, 300 MHz), ^{19}F NMR (188 MHz), and ^{13}C NMR (50.3 MHz, 100.6 MHz, 150.9 MHz) spectra for solution in $CDCl_3$ and CD_3OD were recorded on a Varian Gemini-200, XL-200, Unity-400plus, Bruker 600, chemical shifts (δ) are expressed in ppm downfield from internal TMS or $CHCl_3$ or CH_3OH. HPLC analyses were performed on a JASCO PU-2080 plus using 4.6 x 250 mm CHIRALCEL OJ-H or CHIRALCEL OD-H column. GC analyses were performed on a SHIMADZU GC 14B using a CP-CHIRASIL-DEX CB and HYDRODEX-β-TBDAc. Mass spectra were recorded on a SHIMADZU DCMS-QP5050A. Optical rotations were measured on a HORIBA SEPA-300. Infrared spectra were recorded on a JASCO FT/IR-200 spectrometer.

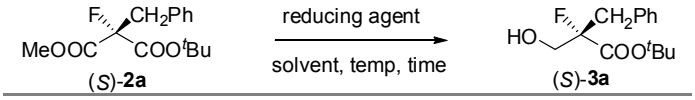
Materials
CH_2Cl_2 was distilled from CaH_2 prior to use. All commercially available reagents were used as received. Malonic esters were prepared according to literature.[1] (*R,R*)-4,6-Dibenzofurandiyl-2,2'-bis(4-phenyloxazoline) (DBFOX-Ph) was prepared following a literature procedure.[2]

Optimization of Chemoselective Reduction of 2a
Chemoselective reduction of **2a** was initially examined using the DIBAL-H conditions described for the chemoselective reduction of *tert*-butyl methyl diesters of asparagine and glutamine,[3a,b] however, attempts with our *tert*-butyl methyl malonate **2a** failed to occur (Table 3, runs 1—4). Attempted selective reduction of **2a** using $LiAlH_4$ at –78 °C according to the reported procedure[3c] gave the corresponding the 2-

[1] R. Shelkov, M. Nahmany, A. Melman, *J. Org. Chem.* **2002**, *67*, 8975-8982.
[2] U. Iserloh, D. P. Curran, S. Kanemasa, *Tetrahedron: Asymmetry* **1999**, *10*, 2417-2428.
[3] a) M. E. Swabrick, F. Gosselin, W. D. Lubell, *J. Org. Chem*. **1999**, *64*, 1993–2002; b) F. Gosselin, W. D. Lubell, *J. Org. Chem*. **1998**, *63*, 7463–7471; c) S. Yamazaki, T. Inoue, T. Hamada, T. Takada, K. Yamamoto, *J. Org. Chem*. **1999**, *64*, 282–286; d) T. A. Ayers, *Tetrahedron Lett.* **1999**, *40*, 5467–5470.

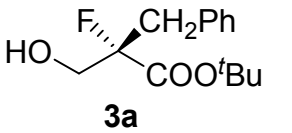
fluorinated hydroxyester **3a** in low yields (runs 5 and 6). The yield of **3a** was improved to 45% when the reduction was performed with $LiAl(O^tBu)_3H$[3d] in THF at –78 °C to rt (run 7). The best results were achieved with 5 equiv of $LiAl(O^tBu)_3H$ in THF at –78 °C to rt to give **3a** in 89% yield after optimization of the conditions (runs 7—10). Optimization of the chemoselective reduction of **2c** was also shown in Table S2.

Table S1: Optimization of Chemoselective Reduction of Chiral Fluorinated Malonate 2a

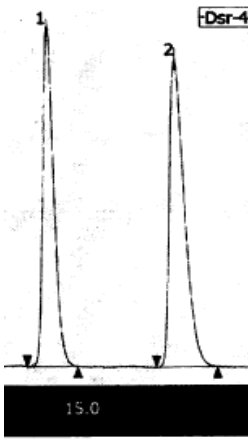


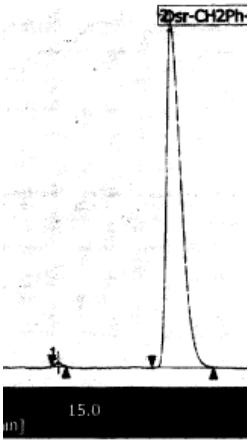
run	Reducing reagent	equiv	solvent	temp (°C)	time (h)	yield (%)[a]
1	DIBAL-H	1.0	CH_2Cl_2	–78	0.5	trace
2	DIBAL-H	2.0	CH_2Cl_2	–78	0.5	trace
3	DIBAL-H	3.0	CH_2Cl_2	–78	0.5	trace
4	DIBAL-H	2.0	THF	–78	0.5	trace
5	$LiAlH_4$	2.0	THF	–78	1.0	35
6	$LiAlH_4$	3.0	THF	–78	2.0	30
7	$LiAl(O^tBu)_3H$	1.1	THF	–78 to rt	24	45
8	$LiAl(O^tBu)_3H$	3.0	THF	–78 to rt	2.0	76
9	$LiAl(O^tBu)_3H$	4.0	THF	–78 to rt	1.0	86
10	$LiAl(O^tBu)_3H$	5.0	THF	–78 to rt	1.0	89

[a] Isolated yield.



HPLC: (CHIRALCEL OJ-H hexane/*i*-PrOH = 90/10, 0.5 mL/min)



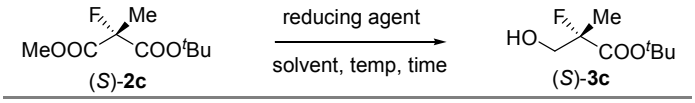


Racemic compound of **3a**

CH	PKNO	TIME	AREA%	HEIGHT%
9	1	14.26	50.16	57.36
9	2	17.52	49.83	42.63

CH	PKNO	TIME	AREA%	HEIGHT%
9	1	14.29	0.51	1.19
9	2	17.42	99.48	98.81

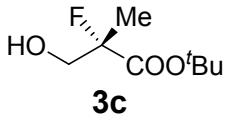
Table S2: Optimization of Chemoselective Reduction of Chiral Fluorinated Malonate 2c



(*S*)-**2c** (*S*)-**3c**

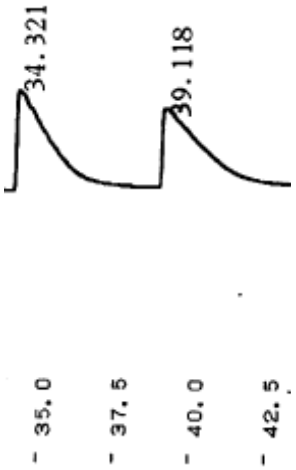
run	Reducing reagent	equiv	solvent	temp (°C)	time (h)	yield (%)[a]
1	DIBAL-H	1.0	CH_2Cl_2	–78	0.5	trace
2	DIBAL-H	2.0	CH_2Cl_2	–78	0.5	trace
3	DIBAL-H	3.0	CH_2Cl_2	–78	0.5	trace
4	DIBAL-H	2.0	THF	–78	0.5	trace
5	$LiAlH_4$	2.0	THF	–78	1.0	31
6	$LiAlH_4$	3.0	THF	–78	1.0	34
7	$LiAl(O^tBu)_3H$	1.0	THF	–78 to rt	24	37
8	$LiAl(O^tBu)_3H$	3.0	THF	–78 to rt	1.0	74
9	$LiAl(O^tBu)_3H$	4.0	THF	–78 to rt	1.0	79
10	$LiAl(O^tBu)_3H$	5.0	THF	–78 to rt	1.0	85

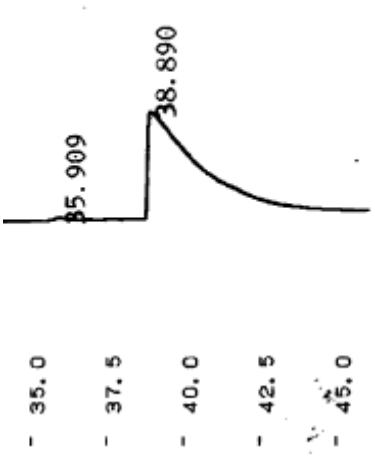
[a] Isolated yield.



3c

GC (CP–CHIRASIL–DEX CB, 90 °C isothermal)

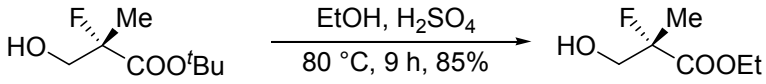




Racemic compound of **3c**

CH	PKNO	TIME	AREA%	HEIGHT	CH	PKNO	TIME	AREA%	HEIGHT
1	1	34.32	51.13	1483	1	1	35.90	0.592	44
1	2	39.11	48.86	1183	1	2	38.89	99.40	1602

Determination of the absolute configuration of 2c



3c **21**

$[\alpha]_D^{25}$ −13.1 (*c*=0.24, CH_3OH)
lit.[4] $[\alpha]_D$ −8.87 (*c*=1.81, CH_3OH)

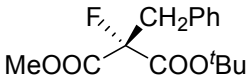
(*S*)-Ethyl- 2-fluoro-3-hydroxy-2-methyl propionate (21)

H_2SO_4 (2 drops) was added into a solution of **3c** (21.9 mg, 0.114 mmol) in ethanol (2.0 mL) at room temperature and the resulting mixture was stirred for 9 h at 80 °C. The reaction mixture was concentrated in vacuo to about 1/6 of its original volume, and then ether was added. The ether solution was washed with saturated sodium bicarbonate solution, brine, and dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with hexane/AcOEt = 70/30 to give **21** (85%) as a colourless oil.
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.32 (t, *J*=7.2 Hz, 3H); 1.54 (d, *J*=21.6 Hz, 3H); 2.20 (s, 1H); 3.73-4.01 (m, 2H); 4.28 (q, *J*=7.2 Hz, 2H); ^{19}F NMR (188 MHz, $CDCl_3$): δ −164.2- −163.6 (m); ^{13}C NMR (150.9 MHz, $CDCl_3$): δ 14.1, 19.7 (d, *J*=23.5 Hz), 61.9, 67.0 (d, *J*=23.4 Hz), 95.4 (d, *J*=184 Hz), 170.6 (d, *J*=25.5 Hz); MS (EI): m/z 120 (M^+–Et); IR (neat): 3443, 2987, 2939, 1740, 1665, 1454, 1384, 1308, 1228, 1136, 1067, 1019, 901 cm^{-1}.

General procedure for the Catalytic Enantioselective Fluorination of Malonic esters (1):

$Zn(OAc)_2$ (10 mol%) and the (*R,R*)-4,6-dibenzofurandiyl-2,2'-bis(4-phenyloxazoline) (11 mol%) were stirred under vacuum for 2 h at room temperature. Dry CH_2Cl_2 (0.3 mL) and MS 4A (substrate/MS 4A=1:500 mol/g) were added under nitrogen atmosphere and stirred for 1 h. Then a solution of malonic esters (0.10-0.25 mmol) in dry CH_2Cl_2 (0.2 mL) was added to catalyst solution. After stirring for another 30 min, *N*-fluorobenzenesulfonimide (1.2 equiv) was added directly to the reaction mixture. The reaction was stirred under reflux for 15-48 h with monitoring by TLC, it was stopped by the addition of water. The reaction mixture was then diluted with CH_2Cl_2, washed with saturated aqueous sodium bicarbonate solution, washed with brine, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. Crude product was purified by column chromatography on silica gel eluting with hexane/AcOEt to give compound **2**. The ee of the product **2** was determined by chiral HPLC on CHIRALCEL OJ-H or CHIRALCEL OD-H column and GC.

(*S*)-1-*tert*-Butyl 3-methyl 2-benzyl-2-fluoromalonate (2a)



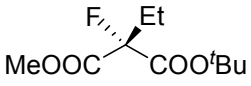
2a

The reaction of **1a** (40.0 mg, 0.151 mmol) with DBFOX-Ph (7.5 mg, 0.016 mmol), $Zn(OAc)_2$ (2.4 mg, 0.015 mmol) and NFSI (57.2 mg, 0.186 mmol) in CH_2Cl_2 (0.5 mL) at reflux for 15 h, gave **2a** (38.0 mg, 90%) as a colourless oil.

[4] T. Kitazume, T. Yamamoto, *J. Fluorine Chem.* **1987**, *35*, 467-476.

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.41 (s, 9H), 3.42 (d, *J*=25.8 Hz, 2H), 3.76 (s, 3H), 7.16-7.25 (m, 5H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –163.4 (t, *J*=26.3 Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 27.9, 40.2 (d, *J*=20.8 Hz), 53.1, 84.1, 95.1 (d, *J*=200 Hz), 127.2, 128.1, 130.1, 133.0, 164.1 (d, *J*=26.4 Hz), 166.3 (d, *J*=25.5 Hz); MS (EI): m/z 263 (M^+); IR (neat): 2980, 1753, 1604, 1497, 1455, 1437, 1395, 1371, 1307, 1254, 1157, 1085, 1056, 841, 744, 700 cm^{-1}; HPLC: (CHIRALCEL OJ-H hexane/*i*-PrOH = 90/10, 1.0 mL/min, 254 nm) t_R (major) = 13.6 min, t_R (minor) = 11.4 min; $[\alpha]_D^{25}$ +13.92 (*c*=1.0, MeOH), 98% ee.

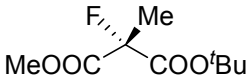
(*S*)-1-*tert*-Butyl 3-methyl 2-ethyl-2-fluoromalonate (2b)



2b

The reaction of **1b** (50.0 mg, 0.247 mmol) with DBFOX-Ph (12.3 mg, 0.027 mmol), $Zn(OAc)_2$ (4.0 mg, 0.024 mmol) and NFSI (93.0 mg, 0.296 mmol) in CH_2Cl_2 (0.5 mL) at reflux for 24 h, gave **2b**(51.0 mg, 94%) as a colourless oil.
^{1}H NMR (200 MHz, $CDCl_3$): δ 0.99 (t, *J*=7.6 Hz, 3H), 1.49 (s, 9H), 1.85-1.92 (m, 2H), 3.82 (s, 3H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –167.24 (t, *J*=23.7 Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 7.14 (d, *J*=4.4 Hz), 27.4, 27.8, 52.9, 83.6, 95.0 (d, *J*=197 Hz), 164.6 (d, *J*=25.2 Hz), 166.6 (d, *J*=25.6 Hz); MS (EI): m/z 220 (M^+); IR (neat): 2981,1752, 1458, 1371, 1315, 1243, 1139, 1101, 1022, 842, 805 cm^{-1}; GC: (CHIRALDEX G-TA, 100 °C) t_R (major) = 20.6 min, t_R (minor) = 22.7 min; $[\alpha]_D^{25}$ +15.5 (*c*=1.0, $CHCl_3$), 96% ee.

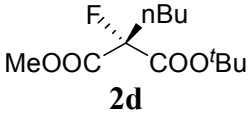
(*S*)-1-*tert*-Butyl 3-methyl-2-fluoro-2-methylmalonate (2c)



2c

The reaction of **1c** (40.0 mg, 0.212 mmol) with DBFOX-Ph (10.6 mg, 0.023 mmol), $Zn(OAc)_2$ (3.3 mg, 0.021 mmol) and NFSI (80.0 mg, 0.255 mmol) in CH_2Cl_2 (0.5 mL) at reflux for 24 h, gave **2c** (39.0 mg, 90%) as a colourless oil.
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.49 (s, 9H), 1.74 (d, *J*=22.0 Hz, 3H), 3.82 (s, 3H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –155.8 (q, *J*=22.3 Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 20.6 (d, *J*=23.1 Hz), 27.7, 52.9, 83.6, 92.3 (d, *J*=194 Hz), 165.1 (d, *J*=24.7 Hz), 167.1 (d, *J*=25.2 Hz); MS (EI): m/z 206 (M^+); IR (neat): 2982, 1753, 1448, 1396, 1372, 1305, 1257, 1124, 982, 944, 841, 794 cm^{-1}; GC: (HYDRODEX- β-TBDAc, 65 °C) t_R (major) = 60.5 min, t_R (minor) = 58.6 min; $[\alpha]_D^{23}$ +11.4 (*c*=1.0, $CHCl_3$), 99% ee.

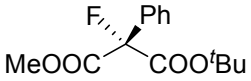
(*S*)-1-*tert*-Butyl 3-methyl 2-butyl-2-fluoromalonate (2d)



2d

The reaction of **1d** (40.0 mg, 0.173 mmol) with DBFOX-Ph (8.6 mg, 0.019 mmol), $Zn(OAc)_2$ (2.7 mg, 0.017 mmol) and NFSI (65.7 mg, 0.208 mmol) in CH_2Cl_2 (0.5 mL) at reflux for 36 h, gave **2d** (40.0 mg, 93%) as a colourless oil.
^{1}H NMR (200 MHz, $CDCl_3$): δ 0.91 (t, *J*=6.6 Hz, 3H), 1.33-1.46 (m, 4H), 1.49 (s, 9H), 2.01-2.20 (m, 2H), 3.82 (s, 3H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –165.4 (t, *J*=22.3 Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 14.0, 22.7, 25.0 (d, *J*=2.8 Hz), 28.0, 34.0 (d, *J*=21.6 Hz), 53.1, 83.8, 95.0 (d, *J*=197 Hz), 164.8 (d, *J*=25.1 Hz), 166.9 (d, *J*=25.9 Hz); MS (EI): m/z 248 (M^+); IR (neat): 2960, 2874, 1753, 1457, 1370, 1287, 1248, 1142, 1047, 842 cm^{-1}; GC: (CP CHIRASIL-DEX CB, 85 °C) t_R (major) = 118.1 min, t_R (minor) = 122.7 min; $[\alpha]_D^{25}$ +5.7 (*c*=0.5, $CHCl_3$), 99% ee.

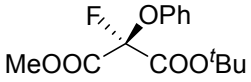
(*S*)-1- *tert*-Butyl 3-methyl 2-fluoro-2-phenylmalonate (2e)



2e

The reaction of **1e** (40.0 mg, 0.15 mmol) with DBFOX-Ph (8.0 mg, 0.017 mmol), $Zn(OAc)_2$ (2.5 mg, 0.015 mmol) and NFSI (56.3 mg, 0.178 mmol) in CH_2Cl_2 (0.5 mL) at reflux for 24 h, gave **2e** (40.0 mg, 95%) as a colorless oil.
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.49 (s, 9H), 3.84 (s, 3H), 7.38-7.43 (m, 3H), 7.55-7.60 (m, 2H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –159.2 (s); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 27.9, 53.5, 84.5, 94.2 (d, *J*=200 Hz), 125.5, 128.0, 129.0, 133.7 (d, *J*=21.9 Hz), 163.9 (d, *J*=25.6 Hz), 166.1 (d, *J*=26.0 Hz); MS (EI): m/z 268 (M^+); IR (neat): 2981, 1754, 1451, 1395, 1371, 1281, 1157, 1120, 1071, 1050, 840, 737 cm^{-1}; HPLC: (CHIRALCEL OJ-H, hexane/*i*-PrOH = 95/5, 0.5 mL/min, 254 nm) t_R (major) = 24.0 min, t_R (minor) = 22.9 min; $[\alpha]_D^{25}$ +5.7 (*c* =1.0, MeOH), 99% ee.

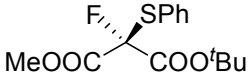
(*S*)-1-*tert*-Butyl 3-methyl-2-fluoro-2-(phenoxy)malonate (2f)



2f

The reaction of **1f** (40.0 mg, 0.132 mmol) with DBFOX-Ph (6.0 mg, 0.014 mmol), $Zn(OAc)_2$ (2.2 mg, 0.013 mmol) and NFSI (52.0 mg, 0.159 mmol) in CH_2Cl_2 (0.5 mL) at reflux for 15 h, gave **2f** (36.0 mg, 85%) as a colourless oil.
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.37 (s, 9H), 3.87 (s, 3H), 7.15-7.31 (m, 5H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –110.8 (s); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 27.7, 53.6, 85.0, 104.1 (d, *J*=243 Hz), 119.9, 124.9, 129.2, 153.0 (d, *J*=2.4 Hz), 160.6 (d, *J*=34.3 Hz), 162.8 (d, *J*=33.6 Hz); MS (EI): m/z 284 (M^+); IR (neat): 2981, 1767, 1591, 1491, 1457, 1396, 1372, 1321, 1259, 1210, 1144, 1082, 949, 863, 837, 758, 692, 642 cm^{-1}; HPLC: (CHIRALCEL OD-H, hexane/*i*-PrOH = 98/2, 0.5 mL/min, 254 nm) t_R (major) = 14.4 min, t_R (minor) = 16.2 min; $[\alpha]_D^{25}$ +6.44 (*c*=0.5, MeOH), 98% ee.

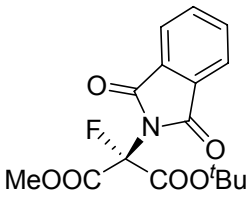
(*S*)-1-*tert*-Butyl 3-methyl-2-fluoro-2-(phenylthio)malonate (2g)



2g

The reaction of **1g** (40.0 mg, 0.126 mmol) with DBFOX-Ph (6.3 mg, 0.013 mmol), $Zn(OAc)_2$ (2.0 mg, 0.012 mmol) and NFSI (47.7 mg, 0.151 mmol) in CH_2Cl_2 (0.5 mL) at reflux for 24 h, gave **2g** (35.0 mg, 81%, 90% ee) as a colourless oil.
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.39 (s, 9H), 3.75 (s, 3H), 7.33-7.41 (m, 3H), 7.54-7.59 (m, 2H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –130.7 (s); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 27.7, 53.7, 85.2, 101.0 (d, *J*=242 Hz), 127.3, 128.8, 129.9, 135.6, 161.5 (d, *J*=28.0 Hz), 163.7 (d, *J*=29.1 Hz); MS (EI): m/z 300 (M^+); IR (neat): 2980, 1752, 1439, 1371, 1288, 1154, 1048, 837, 792, 749, 691 cm^{-1}; MS (EI): m/z 300 (M^+); HPLC: (CHIRALCEL OJ-H hexane/*i*-PrOH = 90/10, 0.5 mL/min, 254 nm) t_R (major) = 44.2 min, t_R (minor) = 41.3 min; $[\alpha]_D^{25}$ +13.39 (*c*=0.5, MeOH), 90% ee.

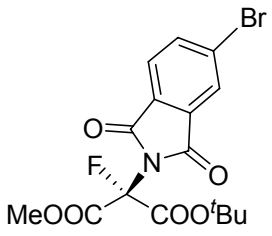
(*S*)-1- *tert*-Butyl 3-methyl 2-fluoro-2-(*N*-phthalimido)malonate (2h)



2h

The reaction of **1h** (50.0 mg, 0.15 mmol) with DBFOX-Ph (7.5 mg, 0.016 mmol), $Zn(OAc)_2$ (2.4 mg, 0.015 mmol) and NFSI (56.0 mg, 0.18 mmol) in CH_2Cl_2 (0.5 mL) at reflux for 18 h, gave **2h** (47.5 mg, 91%) as a white solid.
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.56 (s, 9H), 3.95 (s, 3H), 7.80-7.91 (m, 4H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –127.4 (s); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 27.7, 54.2, 85.8, 89.2 (d, *J*=229 Hz), 124.0, 130.9, 134.90, 159.5 (d, *J*=30.7 Hz), 162.2 (d, *J*=31.3 Hz), 164.8 (d, *J*=2.0 Hz); MS (EI): m/z 337 (M^+); IR (KBr): 2982, 1776, 1742, 1582, 1450, 1400, 1371, 1295, 1188, 1141, 1113, 1082, 948, 794, 754, 724, 682, 625 cm^{-1}; HPLC: (CHIRALCEL OJ-H hexane/*i*-PrOH = 90/10, 0.5 mL/min, 254 nm) t_R (major) = 48.1 min, t_R (minor) = 42.5 min; $[\alpha]_D^{25}$ +4.5 (*c*=0.5, MeOH), 93% ee.

(*S*)-1- *tert*-Butyl 3-methyl 2-fluoro-2-(*N*-(4-bromophthalimido))malonate (2i)

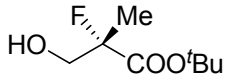


2i

The reaction of **1i** (40.0 mg, 0.096 mmol) with DBFOX-Ph (4.5 mg, 0.010 mmol), $Zn(OAc)_2$ (1.7 mg, 0.009 mmol) and NFSI (36.4 mg, 0.115mmol) in CH_2Cl_2 (0.5 mL) at reflux for 24 h, gave **2i** (39.0 mg, 93%) as a white solid.
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.55 (s, 9H), 3.94 (s, 3H), 7.79 (t, *J*=7.4 Hz, 1H), 7.96 (dd, *J*=8.0, 1.6 Hz, 1H), 8.04 (d, *J*=1.2 Hz, 1H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –127.8 (s); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 27.7, 54.3, 86.1, 89.2 (d, *J*=230 Hz), 125.4, 127.4, 129.4, 130.1, 132.4, 138.0, 159.3, (d, *J*=30.3 Hz), 161.9 (d, *J*=31.1 Hz), 163.5, 164.1; MS (EI): m/z 416 (M^+); IR (KBr): 2981, 1740, 1604, 1420, 1359, 1296, 1143, 946, 838, 745, 647 cm^{-1}; HPLC: (CHIRALCEL OJ-H hexane/*i*-PrOH = 95/5, 1.0

mL/min, 254 nm) t_R (major) = 43.8 min, t_R (minor) = 34.8 min; $[\alpha]_D^{24}$ +15.38 (*c*=1.0, MeOH), 97% ee.

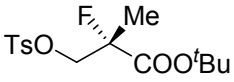
(*S*)-*tert*-Butyl 2-fluoro-2-(hydroxymethyl)propionate (3c)



3c

To a solution of **2c** (200 mg, 0.970 mmol) in dry THF (5.0 mL) was added a solution of $LiAl(O^tBu)_3H$[5] (1.0 M in THF, 3.8 mL, 3.81 mmol) at –78 °C by syringe over 20 min. The solution was allowed to warm to room temperature, which was stirred for 1 h at that temperature. After addition of a saturated solution of potassium sodium tartrate, the organic materials were extracted with ethyl acetate three times and the combined organic phase was washed with brine three times and dried over Na_2SO_4, and concentrated, the crude materials were purified by column chromatography using (hexane/AcOEt = 5/1) to afford alcohol **3c** quantitatively in 85% yield.
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.50 (d, *J*=20.2 Hz, 3H), 1.51 (s, 9H), 2.07-2.13 (m, 1H), 3.70-3.94 (m, 2H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –163.4- –162.9 (m); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 19.7 (d, *J*=23.6 Hz), 27.9, 66.8 (d, *J*=23.5 Hz), 82.7, 95.0 (d, *J*=184 Hz), 169.3 (d, *J*=25.6 Hz); MS (EI); m/z 178 (M^+); IR (neat): 3450, 2981, 2938, 2293, 1735, 1476, 1457, 1395, 1370, 1318, 1251, 1139, 1065, 955, 928, 901, 843, 748, 701 cm^{-1}; GC: (CP CHIRASIL-DEX CB, 90 °C) t_R (major) = 38.89 min, t_R (minor) = 35.90 min; $[\alpha]_D^{22}$ –12.48 (*c*=1.0, $CHCl_3$), 99% ee.

(*S*)-2-(*tert*-Butoxycarbonyl)-2-fluoropropyl-4-methylbenzenesulfonate (12)

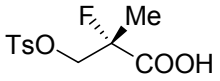


12

To a solution of alcohol **3c** (250 mg 1.302 mmol) in dry $CHCl_3$ (3.0 mL) and pyridine (0.20 mL, 2.604 mmol) was added. The solution was cooled to 0 ºC, and *p*-tosyl chloride[6] (290 mg, 1.56 mmol) was added directly. After stirring for 10 min at 0 °C, the cooling bath was removed, and the solution was stirred at room temperature for 12 h. 1N HCl was added, and the product was extracted three times with CH_2Cl_2, the combined organic layers were washed with water and brine. The organic solution was dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuum. The product was purified by column chromatography on silica gel (hexane/AcOEt = 10/1) to give a colourless gummy syrup compound **12** in 81% yield.
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.44 (s, 9H), 1.49 (d, *J*=20.8 Hz, 3H), 2.45 (s, 3H), 4.06-4.38 (m, 2H), 7.34 (d, *J*=8.6 Hz, 2H), 7.78 (d, *J*=8.6 Hz, 2H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –160.3- –159.7 (m); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 20.0 (d, *J*=23.5 Hz), 21.7, 27.8, 71.5 (d, *J*=23.1 Hz), 83.5, 91.9 (d, *J*=187 Hz), 127.6, 129.6, 132.1, 144.8, 167.0 (d, *J*=25.5 Hz); MS (EI): m/z 332 (M^+); IR (neat): 2982, 1758, 1597, 1455, 1369, 1249, 1190, 178, 1141, 1097, 1005, 939, 910, 826, 760 cm^{-1}; $[\alpha]_D^{23}$ –6.50 (*c*=1.0, $CHCl_3$).

[5] T. A. Ayers, *Tetrahedron Lett.* **1999**, *40*, 5467-5470.
[6] P. Schwerdtfeger, G. A. Heath, M. Dolg, M. A. Bennett, *J. Am. Chem. Soc.* **1992**, *118*, 7517-7528.

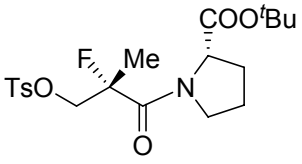
(*S*)-3-(4-Methylbenzenesulfonyl)-2-fluoro-2-methylpropionic acid (13).



13

To a 30 ml round-bottomed flask charged with *tert*-butyl compound **12** (100 mg, 0.300 mmol) was added CH_2Cl_2 (1.0 mL) and TFA (0.17 mL, 1.504 mmol), and the mixture was stirred at room temperature for 3 h, reaction progress was assessed by TLC, since the starting material had been consumed. The mixture was concentrated in vacuum and subsequently co-evaporated with toluene (2 x 10 mL) to afforded carboxylic compound, which was purified on column chromatography on silica gel eluted (hexane/AcOEt = 1/1), in 90% yield as a white solid.
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.60 (d, *J*=21.0 Hz, 3H), 2.45 (s, 3H), 4.19-4.35 (m, 2H), 7.35 (d, *J*=8.0 Hz, 2H), 7.78 (d, *J*=8.2 Hz, 2H), 8.15 (bs, 1H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –161.2- –160.8 (m); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 19.9 (d, *J*=23.1 Hz), 21.6, 71.4 (d, *J*=22.3 Hz), 92.5 (d, *J*=190 Hz), 127.6, 129.6, 131.7, 145.0, 170.3 (d, *J*=24.7 Hz); MS (EI): m/z 276 (M^+); IR (KBr): 3340, 3070, 1931, 1776, 1733, 1592, 1491, 1453, 1372, 1304, 1290, 1271, 1188, 1121, 1011, 940, 892, 826 cm^{-1}; $[\alpha]_D^{24}$ +6.55 (*c*=1.0, EtOH).

***(S)-tert*-Butyl 3-(4-methylbenzenesulfonyl)-2-fluoro-2-(methylpropanoyl)-1-pyrrolidine-2-carboxylate (14)**



14

To a 10 mL round-bottomed flask equipped with a nitrogen balloon and charged with carboxylic compound **13** (120 mg, 0.508 mmol) in CH_2Cl_2 (1.0 mL) was added a solution of L-proline *tert*-butyl ester[7] (83.8 mg, 0.508 mmol) in CH_2Cl_2 (0.5 mL) at room temperature, then EDC·HCl (116 mg, 0.609 mmol) was added and HOBt (83 mg, 0.609 mmol) added at under nitrogen atmosphere. The solution was cooled to 0 ºC, then DIPEA (0.17 mL, 1.016 mmol) was added dropwise, the reaction was stirred at room temperature for 24 h. This solution was diluted with CH_2Cl_2, washed with 1N HCl and water, the organic layer was dried over Na_2SO_4, filtered and concentrated in vacuum. The crude product was purified by column chromatography on silica gel eluted (hexane/AcOEt = 2/1) in 67% yield as colourless syrup.
^{1}H NMR (200 MHz $CDCl_3$): δ 1.43 (s, 9H), 1.57 (d, *J*=21.2 Hz, 3H), 1.87-2.04 (m, 4H), 2.44 (s, 3H), 3.74-3.76 (m, 2H), 4.18-4.44 (m, 2H), 4.57 (t, *J*=7.8 Hz, 1H), 7.32 (d, *J*=8.2 Hz, 2H), 7.76 (d, *J*=8.4 Hz, 2H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –160.5 (q, *J*=21.1 Hz, major), –158.3 (q, *J*=20.5 Hz, minor); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 20.3 (d, *J*=23.2 Hz), 21.7, 25.3 (d, *J*=4.8 Hz), 28.0, 47.6 (d, *J*=15.5 Hz), 61.2, 72.3 (d, *J*=21.2 Hz), 81.1, 95.1 (d, *J*=194 Hz), 127.7, 129.6, 132.3, 144.7, 166.6 (d, *J*=22.3 Hz), 170.3; MS (EI): m/z 429 (M^+); IR (neat): 3648, 2978, 2255, 1736, 1641, 1597, 1455, 1429, 1367, 1290, 1225, 1178, 1153, 1096, 1004, 916, 884, 833, 732, 680 cm^{-1}; $[\alpha]_D^{25}$ –39.44 (*c*=1.0, EtOH).

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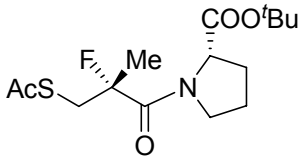
[7] (a) A. J. Vernall, A. D. Abell, *Org. Biomol. Chem.* **2004**, *2*, 2555-2557; (b) V. D. Bock, R. Perciaccante, T. P. Jansen, H. Hiemstra, J. H. van Maarseveen, *Org. Lett.* **2006**, *8*, 919-922.

***(S)-tert*-Butyl 3-(acetylthio)-2-fluoro-2-(methylpropanoyl)-1-pyrrolidine-2-carboxylate (15)**

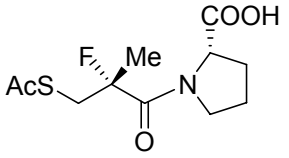


15

Sodium hydride[8] (13.0 mg, 0.325 mmol) was placed into a 20 mL flask and added dry hexane (1.0 mL), stirred for 10 min, then hexane was removed by syringe under nitrogen condition, then DMF (0.5 mL) was added. The solution was cooled to 0 °C, thioacetic acid (8.2 mg, 0.108 mmol) was added drop wise with syringe at 0 ºC, which was stirred for 30 min at room temperature, then tosyl compound **14** (42 mg, 0.108 mmol) in DMF (0.5 mL) was added to the above mixture, raised the temperature up to 70 °C for 4 h. The reaction mixture cooled to room temperature, added water and ethyl acetate, extracted organic layer, washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuum. The crude product was purified by column chromatography on silica gel eluted (hexane/AcOEt = 2/1) in 77% yield as light yellow syrup.

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.45 (s, 9H), 1.66 (d, *J*=21.4 Hz, 3H), 2.02-2.13 (m, 4H), 2.35 (s, 3H), 3.39-3.80 (m, 4H), 4.53-4.58 (m, 1H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –154.8 (q, *J*=21.1 Hz, major), –151.6 (q, *J*=21.1 Hz, minor); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 23.0 (d, *J*=23.1 Hz), 25.4, 28.0, 30.5, 47.8 (d, *J*=15.1 Hz), 61.2, 81.0, 96.5 (d, *J*=190 Hz), 168.6 (d, *J*=23.5 Hz), 170.5, 193.7; MS (EI): m/z 334 (M^+); IR (neat): 2978, 2936, 1737, 1698, 1639, 1455, 1425, 1368, 1289, 1222, 1155, 1093, 845, 919, 846, 761, 731, 652 cm^{-1}; $[\alpha]_D^{25}$ –84.5 (c = 1.0, EtOH).

***(S)*-3-(Acetylthio)-2-fluoro-2-(methylpropanoyl)-1-pyrrolidine -2-carboxylic acid (16)**



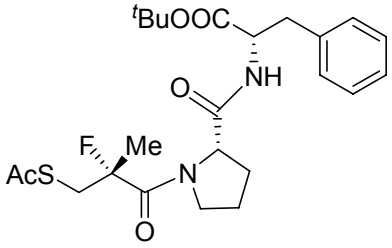
16

Under the similar procedure described for the synthesis of **13**, the reaction of **15** (100.0 mg, 0.299 mmol) with TFA (0.113 ml, 1.495 mmol) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h, gave **16** (78.0 mg, 95%) as a brown solid.

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.65 (d, *J*=21.4 Hz, 3H), 2.01-2.15 (m, 4H), 2.36 (s, 3H), 3.49 (d, *J*=20.6 Hz, 2H), 3.76-3.85 (m, 2H), 4.54-4.59 (m, 1H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –154.3 (q, *J*=19.7 Hz, major), –151.4 (q, *J*=21.8 Hz, minor); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 23.0 (d, *J*=23.2 Hz), 25.6, 27.8, 30.4, 48.0 (d, *J*=15.7 Hz), 59.6 (d, *J*=14.7 Hz), 60.7, 96.6 (d, *J*=190 Hz), 169.5 (d, *J*=23.1 Hz), 175.6, 193.8; MS (EI), m/z 277 (M^+); IR (KBr): 2985, 1698, 1634, 1428, 1374, 1354, 1180, 1132, 958, 916, 731, 650, 624 cm^{-1}; $[\alpha]_D^{25}$ –77.3 (*c*=1.0, EtOH).

[8] M. Chmielewski, R. L. Whistler, *J. Org. Chem.* **1975**, *40*, 639-643.

1-[(*S*)-3-(Acetylthio)-2-fluoro-2-methylpropanoyl]-L-prolyl-L-phenylalanine *tert*-butyl ester (17)

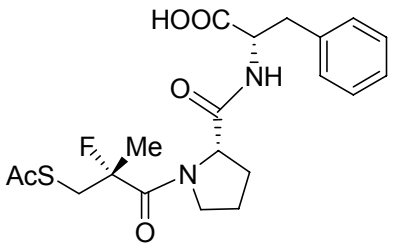


17

A solution of **16** (48.2 mg, 0.174 mmol) in CH_2Cl_2 (2.0 mL) was added L-phenylalanine *tert*-butyl ester hydrochloride (44.9 mg, 0.174 mmol), HOBt (30.5 mg, 0.226 mmol), TEA (0.061 mL, 0.435 mmol), and EDC·HCl (43.3 mg, 0.226 mmol) at 0 °C and stirred for 5 h at room temperature. The reaction mixture was diluted with CH_2Cl_2, washed with saturated sodium bicarbonate solution, brine, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The purified by column chromatography on silica gel eluting with CH_2Cl_2/MeOH = 95/5 to give **17** (82%) as brown oil.

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.55 (d, *J*=21.6 Hz, 3H); 1.87-1.98 (m, 4H); 2.35 (s, 3H); 3.06-3.10 (m, 2H); 3.46 (d, *J*=20.4 Hz, 2H); 3.67-3.79 (m, 2H); 4.54-4.70 (m, 2H); 6.82 (d, *J*=7.4 Hz, 1H); 7.12-7.26 (m, 5H); ^{19}F NMR (188 MHz, $CDCl_3$): δ −153.7 (q, *J*=19.7 Hz, major), −150.5 (q, *J*=21.1 Hz, minor); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 23.2 (d, *J*=23.6 Hz), 25.4 (d, *J*=4.6 Hz), 27.0, 27.9, 30.4, 36.0 (d, *J*=24.0 Hz), 37.9, 47.9 (d, *J*=15.6 Hz), 53.7, 61.6, 82.2, 96.8 (d, *J*=191 Hz), 126.8, 128.2, 129.5, 136.3, 169.9 (d, *J*=23.0 Hz), 170.4, 170.5, 194.1; MS (EI): m/z 480 (M^+), 424 (M^+–^{t}Bu), 381 (M^+–COO^{t}Bu); IR (neat): 3323, 3062, 2978, 2934, 1730, 1695, 1633, 1519, 1455, 1427, 1369, 1253, 1156, 957, 845, 741, 702 cm^{-1}; $[\alpha]_D^{25}$ −59.9 (*c*=0.82, EtOH).

1-[(*S*)-3-(Acetylthio)-2-fluoro-2-methylpropanoyl]-L-prolyl-L-phenylalanine (6)



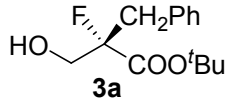
6

To CH_2Cl_2 (1.0 mL) solution of **17** (68.4 mg, 0.142 mmol) was added TFA (0.1 mL) at room temperature, and stirred for 16 h. The solvent was removed under reduced pressure. The purified by column chromatography on silica gel eluting with CH_2Cl_2/MeOH = 90/ 10 to give **6** (73%) as yellow oil.

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.50 (d, *J*=21.8 Hz, 3H); 1.91-2.17 (m, 4H), 3.01-3.27 (m, 2H); 3.44 (d, *J*=20.8 Hz, 2H); 3.65-3.74 (m, 2H); 4.52-4.76 (m, 2H); 6.92 (d, *J*=7.4 Hz, 1H); 7.14-7.25 (m,5H); ^{19}F NMR (188 MHz, $CDCl_3$): δ −153.6 (q, *J*=21.1 Hz, major), −150.5 (q, *J*=19.7 Hz, minor); ^{13}C NMR (150.9 MHz, $CDCl_3$): δ 23.1 (d, *J*=23.4 Hz), 25.3 (d, *J*=4.7 Hz), 27.1, 30.4, 35.9 (d, *J*=24.3 Hz), 37.2, 48.1 (d, *J*=15.7 Hz), 53.4, 61.8, 96.8 (d, *J*=191 Hz), 126.9, 128.4, 129.4, 136.1, 170.2 (d, *J*=23.4 Hz),

171.2, 174.3, 194.2; MS (EI): m/z 424 (M^+); IR (neat): 3325, 2981, 2933, 1738, 1636, 1524, 1456, 1422, 1192, 1131, 958, 702 cm^{-1}; $[\alpha]_D^{25}$ −22.8 (*c*=0.88, EtOH).

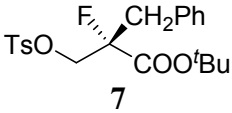
(*S*)-*tert*-Butyl 2-fluoro-2-(hydroxymethyl)-3-phenylpropionate (3a)



3a

To a solution of **2a** (50.0 mg, 0.177 mmol) in dry THF (1.0 mL) was added a solution of $LiAl(O^tBu)_3H$ (1.0 M in THF, 0.88 mL, 0.885 mmol) at −78 °C by syringe over 10 min. The solution was allowed to warm to room temperature, which was stirred for 1 h at that temperature, gave **3a** (40.0 mg, 89%) as a colourless oil.
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.38 (s, 9H), 2.02-2.10 (m, 1H), 3.13 (d, *J*=24.0 Hz, 2H), 3.74-3.99 (m, 2H), 7.24-7.27 (m,5H); ^{19}F NMR (188 MHz, $CDCl_3$): δ −169.2- −168.9 (m); ^{13}C NMR (150.9 MHz, $CDCl_3$): δ 27.8, 39.4 (d, *J*=21.3 Hz), 66.2 (d, *J*=24.0 Hz), 83.1, 97.2 (d, *J*=190 Hz), 127.2, 128.3, 130.2 (d, *J*=0.9 Hz), 134.0, 168.6 (d, *J*=25.2 Hz); MS (EI): m/z 254 (M^+); IR (neat): 3455, 2979, 2932, 1732, 1496, 1456, 1370, 1252, 1161, 1093, 1044, 842, 742, 701 cm^{-1}; HPLC: (CHIRALCEL OJ-H hexane/*i*-PrOH = 90/10, 0.5 mL/min, 210 nm) t_R (major) = 17.42 min, t_R (minor) = 14.29 min; $[\alpha]_D^{25}$ +9.05 (*c*=0.35, $CHCl_3$).

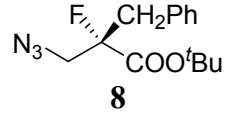
(*S*)-2-(*tert*-Butoxycarbonyl)-2-fluoro-3-phenylpropyl 4-methylbenzenesulfonate (7)



7

To a solution of alcohol **3a** (390.0 mg 1.624 mmol) in dry pyridine (1.0 mL) and dry $CHCl_3$ (2.0 mL) was cooled to 0 ºC, and *p*-tosyl chloride (371.0 mg, 1.948 mmol) was added directly. After stirring for 10 min at 0 °C, the solution was stirred at room temperature for 12 h. 1N HCl was added, and the product was extracted three times with CH_2Cl_2, the combined organic layers were washed with water and brine. The organic solution was dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuum. The product was purified by column chromatography on silica gel (hexane/AcOEt = 10/1) to give compound **7** in (590.0 mg, 90%) as a white solid.
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.34 (s, 9H); 2.45 (s, 3H), 3.04 (d, *J*=3.0 Hz, 1H); 3.16 (s, 1H); 4.16-4.39 (m, 2H); 7.17-7.35 (m, 5H); ^{19}F NMR (188 MHz, $CDCl_3$): δ −167.5- −167.0 (m); ^{13}C NMR (150.9 MHz, $CDCl_3$): δ 21.6, 27.7, 70.9 (d, *J*=23.1 Hz), 83.8, 94.3 (d, *J*=197 Hz), 127.4, 128.0, 128.4, 130.0, 130.2, 132.5, 132.9, 145.1, 166.4 (d, *J*=25.0 Hz); MS (EI): m/z 408 (M^+), 352 (M^+–^{t}Bu); IR (KBr): 3060, 3032, 2979, 2928, 1760, 1596, 1496, 1445, 1371, 1246, 1193, 987, 943, 861, 818, 764, 697, 666 cm^{-1}; $[\alpha]_D^{24}$ −1.08 (*c*=0.23, $CHCl_3$).

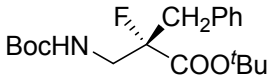
(*S*)-*tert*-Butyl 3-azido-2-benzyl-2-fluoro propionate (8)



8

To a solution of **7** (48.2 mg, 0.118 mmol) in DMF (2.0 mL) was added NaN_3 (23.0 mg, 0.354 mmol) and resulting mixture was stirred at 80 °C for 24 h. The reaction mixture was diluted with CH_2Cl_2, washed with water, brine, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The purified by column chromatography on silica gel eluting with hexane/AcOEt = 90/10 to give **8** in 95% as colourless syrup.
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.39 (s, 9H); 3.08 (d, *J*=2.2 Hz, 1H), 3.20 (s, 1H); 3.50-3.70 (m, 2H); 7.20-7.30 (m, 5H); ^{19}F NMR (188 MHz, $CDCl_3$): δ −164.1- −163.6 (m); ^{13}C NMR (150.9 MHz, $CDCl_3$): δ 27.8, 40.6 (d, *J*=21.1 Hz), 55.6 (d, *J*=22.1 Hz), 83.5, 95.8, 96.4 (d, *J*=195 Hz), 127.4, 128.4, 130.2 (d, *J*=0.9 Hz), 133.4, 167.6 (d, *J*=24.9 Hz); MS (EI): m/z 279 (M^+) ; IR (neat): 2981, 2932, 2107, 1758, 1731, 1496, 1456, 1095, 950, 843, 700 cm^{-1}; $[\alpha]_D^{24}$ −40.5 (*c*=0.31, $CHCl_3$).

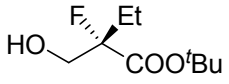
tert-Butyl (*S*)-2-(_tert_-butoxycarbonyl)-2-fluoro-3-phenylpropylcarbamate (4)



4

To a solution of **8** (47.7 mg, 0.171 mmol) in ethyl acetate (2.5 mL), $(Boc)_2O$ (56.1 mg, 0.257 mmol), Pd-C (5.0 mg) were added and resulting mixture was stirred under hydrogen atmosphere for 2 h at room temperature. This reaction mixture was filtered through celite to remove Pd-C. After removal of the solvent, the crude product was purified by column chromatography on silica gel eluting with hexane/AcOEt = 80/20 to give 4 (95%) as colourless oil.
^{1}H NMR (200 MHz, $CDCl_3$): δ 1.36 (s, 9H); 1.43 (s, 9H); 3.07 (s, 1H); 3.19 (d, *J*=2.2 Hz, 1H); 3.41 (td, *J*=14.8, 4.8 Hz, 1H), 3.70-3.79 (m, 1H); 4.84 (s, 1H); 7.24-7.25 (m, 5H); ^{19}F NMR (188 MHz, $CDCl_3$): δ −165.0- −164.5 (m); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 27.7, 28.3, 40.5 (d, *J*=21.3 Hz), 46.1 (d, *J*=21.7 Hz), 79.7, 83.0, 96.5 (d, *J*=189 Hz), 127.1, 128.2, 130.2, 134.0, 155.4, 167.9 (d, *J*=25.7 Hz); MS (EI): m/z 353 (M^+), 277 (M^+–^{t}Bu); IR (neat): 3383, 3033, 2979, 2932, 1722, 1514, 1456, 1393, 1368, 1250, 1166, 1108, 1037, 999, 913, 843, 741, 700 cm^{-1}; $[\alpha]_D^{24}$ +23.6 (*c*=0.35, $CHCl_3$).

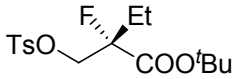
(*S*)-_tert_-Butyl 2-fluoro-2-(hydroxymethyl)butanoate (3b)



3b

To a solution of **2b** (180.0 mg, 0.818 mmol) in dry THF (2.0 mL) was added a solution of $LiAl(O^tBu)_3H$ (1.0 M in THF, 4.0 mL, 4.09 mmol) at −78 °C by syringe over 10 min. The solution was allowed to warm to room temperature, which was stirred for 1 h at that temperature, gave **3b** (126.0 mg, 80%) as a colorless oil.
^{1}H NMR (200 MHz, $CDCl_3$): δ 0.98 (t, *J*=7.4 Hz, 3H); 1.52 (s, 9H); 1.72-1.97 (m, 2H), 2.02-2.04 (m, 1H), 3.75-3.92 (m, 2H); ^{19}F NMR (188 MHz, $CDCl_3$): δ −173.9- −173.4 (m); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 7.22 (d, *J*=4.4 Hz), 26.5 (d, *J*=22.3 Hz), 28.0, 66.2 (d, *J*=23.1 Hz), 82.6, 98.0 (d, *J*=186 Hz), 168.8 (d, *J*=26.0 Hz); MS (EI), m/z 192 (M^+); IR(neat): 3441, 2978, 2938, 2284, 1732, 1459, 1394, 1370, 1323, 1254, 1139, 1072, 1010, 963, 909, 841, 746 cm^{-1}; $[\alpha]_D^{25}$ −5.42 (*c*=1.0, $CHCl_3$).

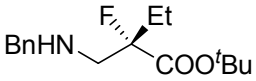
(*S*)-2-(*tert*-Butoxycarbonyl)-2-fluorobutyl 4-methylbenzenesulfonate (9)



9

To a solution of alcohol **3b** (120.0 mg 0.625 mmol) in dry pyridine (2.0 mL) and dry $CHCl_3$ (2.0 mL) was cooled to 0 ºC, and *p*-tosyl chloride (142.0 mg, 0.75 mmol) was added directly. After stirring for 10 min at 0 °C, the solution was stirred at room temperature for 12 h. 1N HCl was added, and the product was extracted three times with CH_2Cl_2, the combined organic layers were washed with water and brine. The organic solution was dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuum. The product was purified by column chromatography on silica gel (hexane/AcOEt = 10/1) to give compound **9** in (185.0 mg, 85%) as a white solid.
^{1}H NMR (200 MHz, $CDCl_3$): δ 0.93 (t, *J*=7.4 Hz, 3H), 1.47 (s, 9H), 1.74-1.87 (m, 2H), 2.44 (s, 3H), 4.15-4.34 (m, 2H), 7.33 (d, *J*=8.2 Hz, 2H), 7.77 (d, *J*=8.4 Hz, 2H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –171.1- –170.6 (m); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 7.03 (d, *J*=4.4 Hz), 21.7, 26.8 (d, *J*=22.3 Hz), 27.9, 71.1 (d, *J*=22.7 Hz), 83.4, 94.6 (d, *J*=193 Hz), 127.6, 129.6, 132.1, 144.8, 166.3 (d, *J*=26.0 Hz); MS (EI), m/z 346 (M^+); IR (KBr): 2982, 1758, 1597, 1455, 1369, 1249, 1190, 178, 1141, 1097, 1005, 939, 910, 826, 760 cm^{-1}; $[\alpha]_D^{24}$ +0.63 (*c*=1.0, $CHCl_3$).

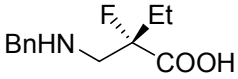
(*S*)-*tert*-Butyl 2-((benzylamino)methyl)-2-fluorobutanoate (10)



10

Tosyl derivative[9] **9** (180 mg, 0.520 mmol) was dissolved in toluene (0.5 mL) and sodium bicarbonate (131 mg, 1.56 mmol) was added. To the resulting suspension benzyl amine (0.28 mL, 2.601 mmol) was added, and the mixture was left stirring at 80 ºC for 48 h. More toluene (0.4 mL) was added and also benzyl amine (0.28 mL, 2.601 mmol) and the mixture was stirred at 80 °C another 24 h. The reaction mixture was then cooled to room temperature, filtered, and evaporated. The crude product was purified by column chromatography on silica gel eluted (hexane/AcOEt = 10/1) in 72% yield as a light yellow syrup.
^{1}H NMR (200 MHz, $CDCl_3$): δ 0.94 (t, *J*=7.6 Hz, 3H), 1.49 (s, 9H), 1.74-1.91 (m, 2H), 2.87 (s, 1H), 2.93 (d, *J*=14.8 Hz, 1H), 3.04 (d, *J*=14.8 Hz, 1H), 3.74 (d, *J*=13.4 Hz, 1H), 3.87 (d, *J*=13.4 Hz, 1H), 7.24-7.31 (m, 5H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –170.54- –170.1 (m); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 7.45 (d, *J*=4.4 Hz), 28.1, 53.7, 54.4 (d, *J*=21.2 Hz), 81.9, 98.2 (d, *J*=186 Hz), 126.6, 127.7, 128.0, 139.8, 169.3 (d, *J*=26.3 Hz); MS (EI): m/z 281 (M^+); IR(neat): 3344, 3063, 3027, 2952, 2929, 1735, 1495, 1461, 1368, 1250, 1168, 1136, 1028, 914, 843, 737, 638 cm^{-1}; $[\alpha]_D^{24}$ = –12.1 (*c*=1.0, EtOH).

(*S*)-2-((Benzylamino)methyl)-2-fluorobutanoic acid (11)

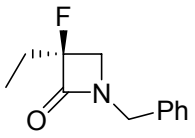


11

[9] M. T. Barros, A. M. F. Phillips, *Molecules* **2006**, *11*, 177-196.

Under the similar procedure described for the synthesis of **13**, the reaction of **10** (100.0 mg, 0.355 mmol) with TFA (0.27 ml, 3.554 mmol) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h, gave **11** (70.2 mg, 87%) as a solid.
^{1}H NMR (200 MHz, $CDCl_3$): δ 0.78 (t, *J*=7.2 Hz, 3H), 1.55-1.85 (m, 2H), 3.10-3.46 (m, 2H), 4.19 (d, *J*=12.8 Hz, 1H), 4.33 (d, *J*=12.6 Hz, 1H), 7.25-7.44 (m, 5H), 9.00 (bs, 1H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –167.8 (br); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 6.85 (d, *J*=3.7 Hz), 27.7, 28.7 (d, *J*=21.7 Hz), 51.7 (d, *J*=21.7 Hz), 52.4, 85.0, 94.7 (d, *J*=193 Hz),128.7, 129.4, 129.9, 130.8, 172.4 (d, *J*=21.7 Hz); MS (EI): m/z 225 (M^+); IR(neat): 3362, 2974, 1723, 1606, 1499, 1455, 1212, 1133, 1090, 912, 733, 700 cm^{-1}; $[\alpha]_D^{23}$ –1.72 (*c*=1.0, MeOH).

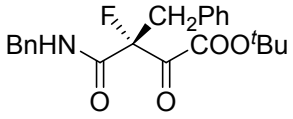
(*S*)-1-Benzyl-3-ethyl-3-fluoroazetidin-2-one (5)



5

To a 20 mL round-bottomed flask charged with carboxylic compound[10] **11** (50.0 mg, 0.222 mmol) was added CH_2Cl_2 (10.0 mL) and 2-chloro-1-methylpyridinium iodide (62.4 mg, 0.244 mmol) in CH_2Cl_2 under high-dilution conditions and the mixture was stirred at room temperature for 15 min, then added TEA (0.09 mL, 0.666 mmol). The reaction mixture was stirred at room temperature for 6 h. The reaction progress was assessed by TLC, the mixture was concentrated in vacuum and which was purified on column chromatography on silica gel eluted (hexane/AcOEt = 15/1), in 70% yield as colourless syrup.
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.05 (t, *J*=7.5 Hz, 3H), 1.87-2.04 (m, 2H), 3.28 (dddd, *J*=37.5, 6.3, 8.4, 11.1 Hz, 2H), 4.39 (d, *J*=17.7 Hz, 1H), 4.46 (d, *J*=11.4 Hz, 1H), 7.22-7.25 (m, 2H), 7.32-7.40 (m, 3H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –165.0- –164.7 (m); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 7.35 (d, *J*=6.4 Hz), 25.0 (d, *J*=23.6 Hz), 45.6 (d, *J*=1.9 Hz), 51.5 (d, *J*=26.4 Hz), 102.7 (d, *J*=216 Hz), 128.0, 128.2, 128.9, 134.6, 165.8 (d, *J*=24.4 Hz); MS (EI): m/z 207 (M^+); IR (neat): 2975, 1766, 1455, 1406, 1309, 1196, 1076, 970, 910, 852, 725, 700 cm^{-1}; $[\alpha]_D^{24}$ –70.1 (*c*=1.0, MeOH).

(*S*)-*tert*-Butyl 2-fluoro-2-bezylamide-3-phenylpropanate (18)



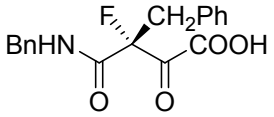
18

To a solution of benzyl ester **2a** (100 mg, 0.354 mmol) and benzylamine (36.0 mg, 0.337 mmol) in 1.0 mL (1.00 M in ester substrate) of toluene was added HOAt (24.0 mg, 0.177 mmol) followed by $Zr(O^tBu)_4$ (67.0 mg, 0.177 mmol). The reaction was stirred at the 60 ºC for 24 h and quenched by addition of MeOH (2 mL) and CH_2Cl_2 (2 mL). The reaction mixture was filtered through a silica gel pad and concentrated in *vacuo*. Amide products were isolated by column chromatography using silica gel, eluted in hexane/AcOEt = 85/15 in 55% yield of compound **18** as a white solid.

[10] (a) H. Huang, N. Iwasawa, T. Mukaiyama, *Chem. Lett.* **1984**, *13*, 1465-1466; (b) N. Iwasawa, H. Huang, T. Mukaiyama, *Chem. Lett.* **1985**, *14*, 1045-1048.

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.46 (s, 9H), 3.48 (dd, *J*=10.0, 20.4 Hz, 2H), 4.36 (d, *J*=5.8 Hz, 2H), 6.48 (s, 1H), 6.96-7.01 (m, 2H), 7.20-7.25 (m, 8H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –163.17 (ddd, *J*=22.2, 11.0, 3.9 Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 27.9, 39.8 (d, *J*=19.9 Hz), 43.3, 84.0, 96.8 (d, *J*=200 Hz), 127.0, 127.2, 127.3, 128.1, 128.4, 130.3, 133.4, 164.7 (d, *J*=24.7 Hz), 165.4 (d, *J*=21.5 Hz); MS (EI): m/z 357 (M^+); IR (KBr): 3374, 2979, 1743, 1677, 1533, 1455, 1370, 1258, 1158, 1085, 841, 737, 699 cm^{-1}.

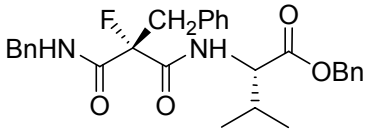
(*S*)-2-Fluoro-2-bezylamide-3-phenylpropanoic acid (19)



19

The reaction of **18** (28.0 mg, 0.072 mmol) with TFA (0.054 ml, 0.727 mmol) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h, reaction progress was assessed by TLC. The reaction mixture was concentrated in vacuum and subsequently co-evaporated with toluene (2 x 10 mL) to afforded carboxylic compound, which was purified on column chromatography on silica gel eluted (CH_2Cl_2 /MeOH = 9/1), in 74% yield **19** as a white solid; ^{1}H NMR (200 MHz, CD_3OD): δ 3.13-3.57 (m, 2H), 4.11 (d, *J*=16.6 Hz, 1H), 4.31 (d, *J*=15.4 Hz, 1H), 6.89 (s, 2H), 7.08-7.21 (m, 8H), 8.53 (bs, 1H); ^{19}F NMR (188 MHz, $CDCl_3$): δ –163.17 (ddd, *J*=22.2, 11.0, 3.9 Hz); MS (EI): m/z 301 (M^+); IR (KBr): 3280, 3029, 2965, 1758, 1671, 1530, 1495, 1454, 1383, 1358, 1299 cm^{-1}; $[\alpha]_D^{25}$ +20.11 (*c*=0.5, CH_2Cl_2) [lit.[11] $[\alpha]_D$ –24 (*c*=0.5, CH_2Cl_2)].

(*S*)-2-Fluoro-2-(bezyloxy-L-valylcarbonyl)-3-phenylpropanoic acid benzylamide (20)



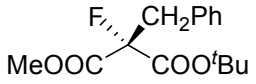
20

A solution of acid **19** (16.0 mg, 0.053mmol), L-valine benzyl ester *p*-toluenesulfonate (15.3 mg, 0.053 mmol), HOBt (7.3 mg, 0.053 mmol) and *N*-methylmorpholine (0.05 mg, 0.053 mmol) in dry THF (2 mL) was stirred and cooled in an ice-water bath while DCC (10.9 mg, 0.053 mmol) was added. Stirring was continued for 2 h at 0 °C and additional 20 h at room temperature. The *N*,*N*′-dicyclohexylurea formed during the reaction was removed by filtration and the filtrate was poured in to a mixture of AcOEt (10 mL) and an aqueous saturated solution of $NaHCO_3$ (5 mL). The organic phase was extracted with 10% solution citric acid in water (5 mL), then washed with saturated $NaHCO_3$ and water. The solution was dried over Na_2SO_4 and concentrated. The resulting residue was chromatographed (hexane/AcOEt) to afford 20.5 mg of compound **20** (77% yield) as a white solid.

^{1}H NMR (200 MHz, $CDCl_3$): δ 0.87 (d, *J*=6.8 Hz, 3H), 0.92 (d, *J*=6.8 Hz, 3H), 2.13-2.29 (m, 1H), 3.37 (d, *J*=4.4 Hz, 1H), 3.49 (d, *J*=15.2 Hz, 1H), 4.24 (dd, *J*=14.8, 5.2 Hz, 1H), 4.44 (dd, *J*=14.9, 6.4 Hz, 1H), 4.53 (dd, *J*=8.8, 5.0 Hz, 1H), 5.12 (s, 2H), 6.82 (bs, 1H), 6.93-6.98 (m, 2H), 7.23-7.36 (m, 12H), 7.55 (d, *J*=8.6 Hz, 1H); ^{19}F

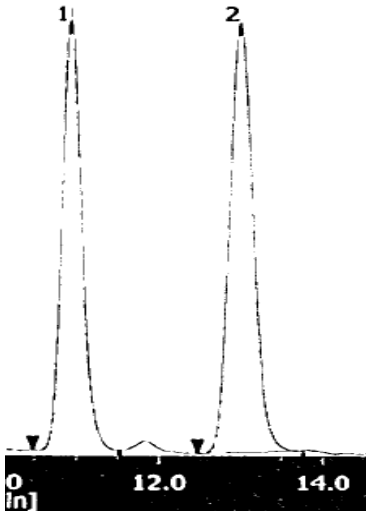
[11] A. abouabdellah, J. T. Welch, *Tetrahedron: Asymmetry* **1994**, *5*, 1005-1013.

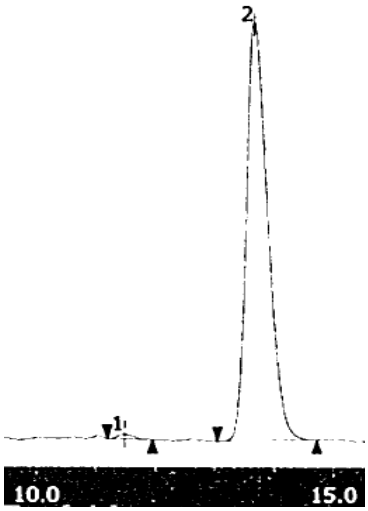
NMR (188 MHz, $CDCl_3$): δ –168.20 (dd, *J*=30.9, 21.1 Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 17.6, 19.2, 31.4, 43.4 (d, *J*=21.2 Hz), 43.5, 57.3, 67.1, 96.2 (d, *J*=199 Hz), 127.3, 127.4, 128.11, 128.17, 128.24, 128.36, 128.42, 130.1, 132.6, 135.0, 136.6, 166.4 (d, *J*=23.1 Hz), 166.5 (d, *J*=22.3 Hz), 170.2; MS (EI): m/z 357 (M^+); IR (KBr): 3341, 3032, 2965, 1740, 1687, 1539, 1455, 1216, 1148, 1086, 1050, 746, 698 cm^{-1}; $[\alpha]_D^{22}$ –4.82 (*c*=1.5, CH_2Cl_2) [lit.[11] $[\alpha]_D$ +7.3 (*c*=1.5, CH_2Cl_2)].



2a

HPLC using an OJ-H column
(*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm)

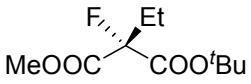




Racemic compound of **2a**

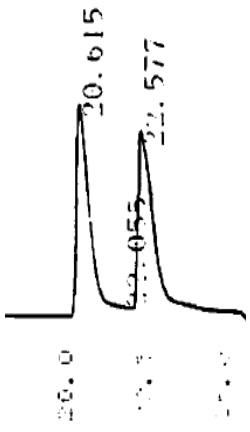
CH	PKNO	TIME	AREA%	HEIGHT%
1	1	10.908	45.494	50.010
1	2	12.967	54.506	49.990

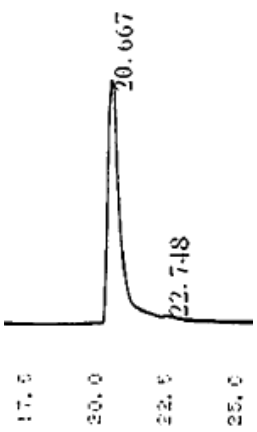
CH	PKNO	TIME	AREA%	HEIGHT%
1	1	11.492	0.743	1.052
1	2	13.658	99.257	98.948



2b

GC analysis (CP–CHIRALDEX G-TA, 100 °C isothermal)

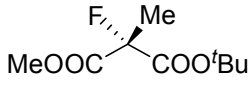




Racemic compound of **2b**

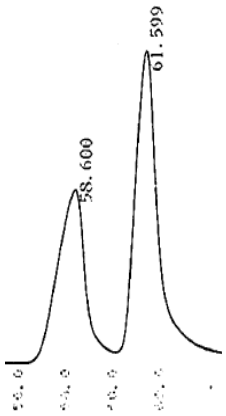
CH	PKNO	TIME	AREA%	HEIGHT
1	1	20.615	47.162	2553
1	2	22.577	49.430	2203

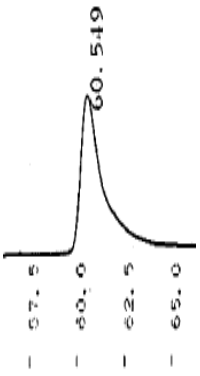
CH	PKNO	TIME	AREA%	HEIGHT
1	1	20.667	98.015	4083
1	2	22.748	1.984	84



2c

GC analysis (HYDRODEX-β-TBDAc, 65 °C isothermal)



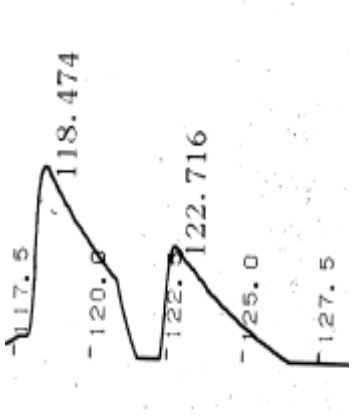


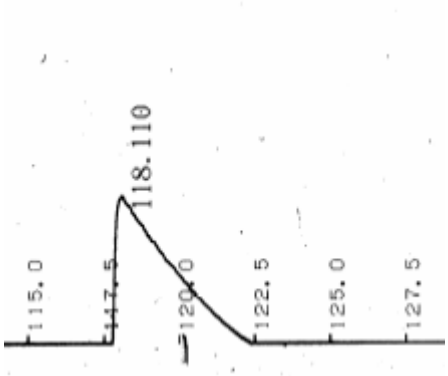
Racemic compound of **2c**

CH	PKNO	TIME	AREA%	HEIGHT	CH	PKNO	TIME	AREA%	HEIGHT
1	1	58.600	45.860	7237	1	1	58.600	0.010	0.001
1	2	61.599	54.139	12944	1	2	60.549	99.990	2056

GC analysis (CP–CHIRASIL–DEX CB, 85 °C isothermal)

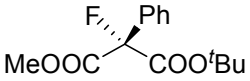
2d





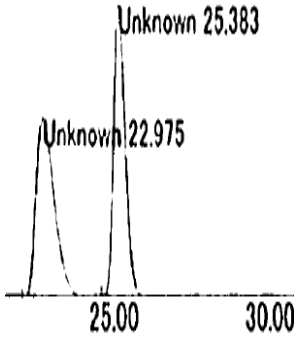
Racemic compound of **2d**

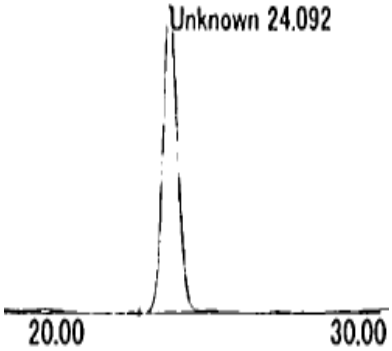
CH	PKNO	TIME	AREA%	HEIGHT	CH	PKNO	TIME	AREA%	HEIGHT
1	1	118.47	57.357	1175	1	1	118.11	99.990	1455
1	2	122.71	40.928	758	1	2	122.71	0.010	0.001



2e

HPLC using an OJ-H column
(*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 254 nm)

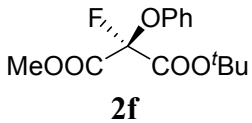




Racemic compound of **2e**

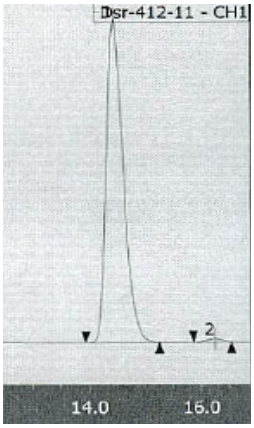
CH	PKNO	TIME	AREA%	HEIGHT%
1	1	22.975	50.04	38.285
1	2	25.383	49.96	61.714

CH	PKNO	TIME	AREA%	HEIGHT%
1	1	22.975	0.010	0.001
1	2	24.092	99.990	99.999



2f

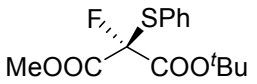
HPLC using an OD-H column
(*n*-hexane/*i*-PrOH = 98/2, flow rate 0.5 mL/min, λ =254 nm)



Racemic compound of **2f**

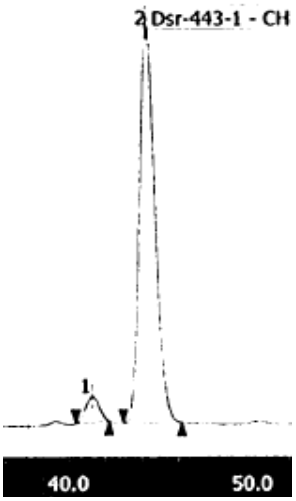
CH	PKNO	TIME	AREA%	HEIGHT%
1	1	14.187	45.644	50.264
1	2	17.187	54.356	49.736

CH	PKNO	TIME	AREA%	HEIGHT%
1	1	14.442	99.031	98.966
1	2	16.250	0.969	1.034



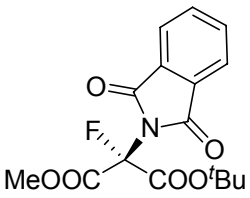
HPLC using an OJ-H column

2g (*n*-hexane/*i*-PrOH = 90/10, flow rate 0.5 mL/min, λ = 254 nm)



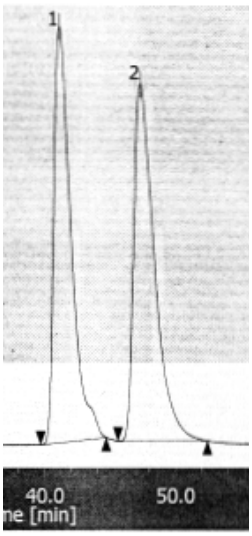
Racemic compound of **2g**

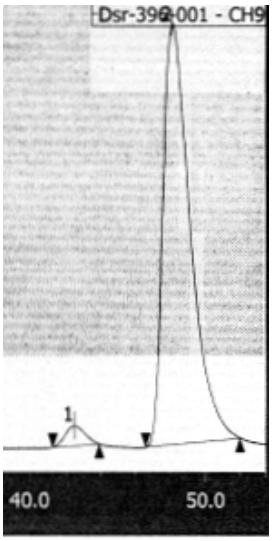
CH	PKNO	TIME	AREA%	HEIGHT%	CH	PKNO	TIME	AREA%	HEIGHT%
1	1	41.117	49.814	51.588	1	1	41.300	5.311	6.014
1	2	44.342	50.186	48.412	1	2	44.283	94.689	93.986



HPLC using an OJ-H column

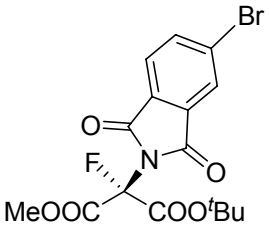
2h (*n*-hexane/*i*-PrOH = 90/10, flow rate 0.5 mL/min, λ = 254 nm)





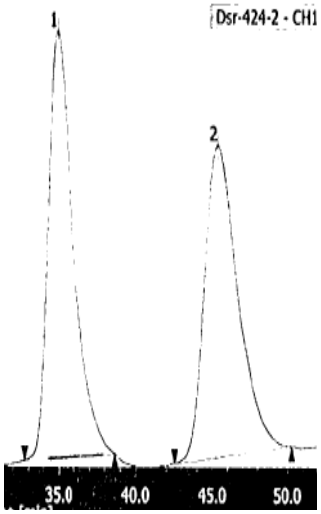
Racemic compound of **2h**

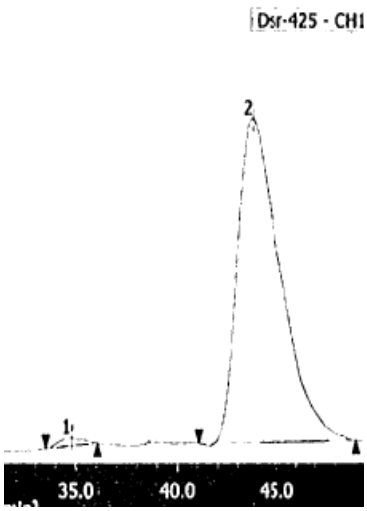
CH	PKNO	TIME	AREA%	HEIGHT%	CH	PKNO	TIME	AREA%	HEIGHT%
9	1	41.120	49.739	53.889	9	1	42.507	3.317	4.638
9	2	47.347	50.261	46.111	9	2	48.120	96.683	95.362



2i

HPLC using an OJ-H column
(*n*-hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm)

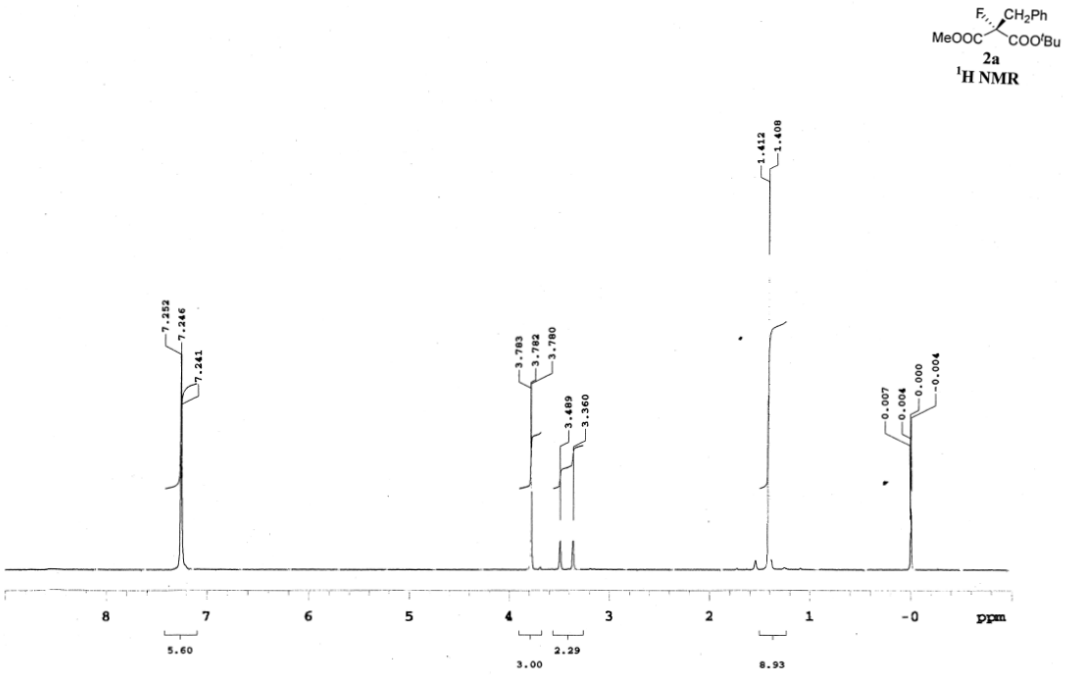


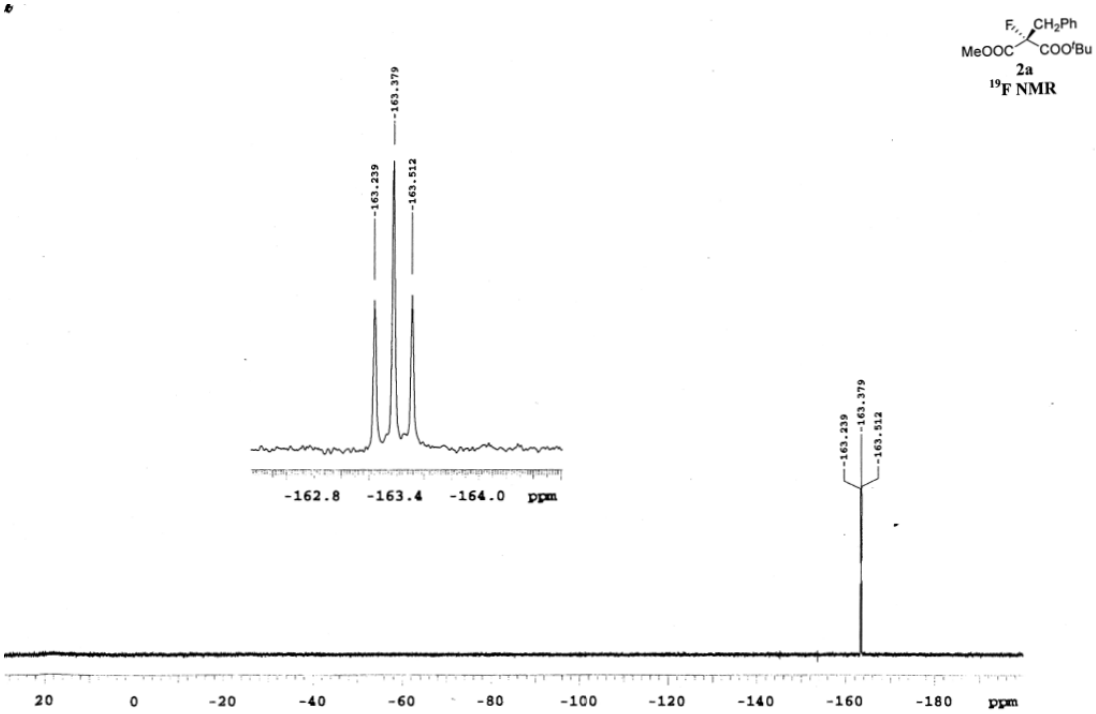


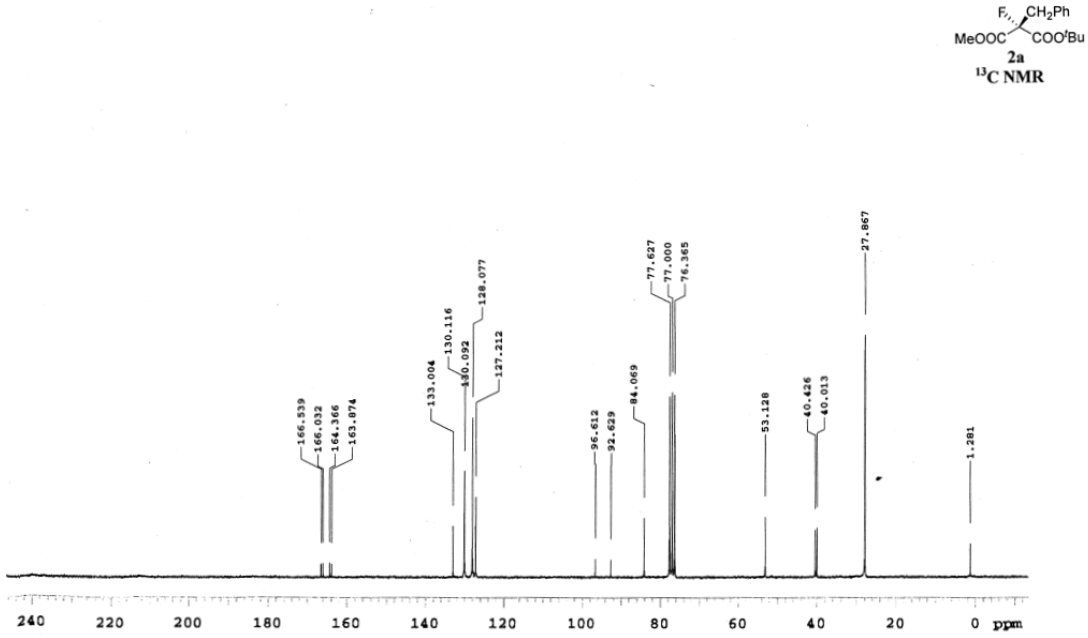
Racemic compound of **2i**

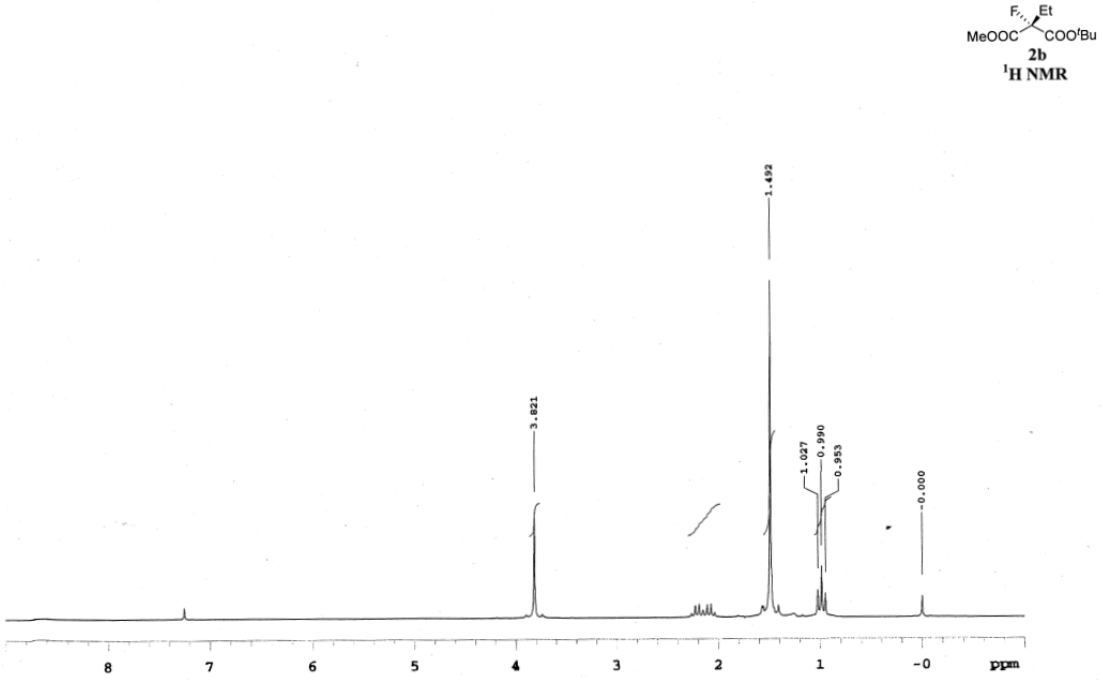
CH	PKNO	TIME	AREA%	HEIGHT%
1	1	34.908	50.743	57.826
1	2	45.342	49.257	42.174

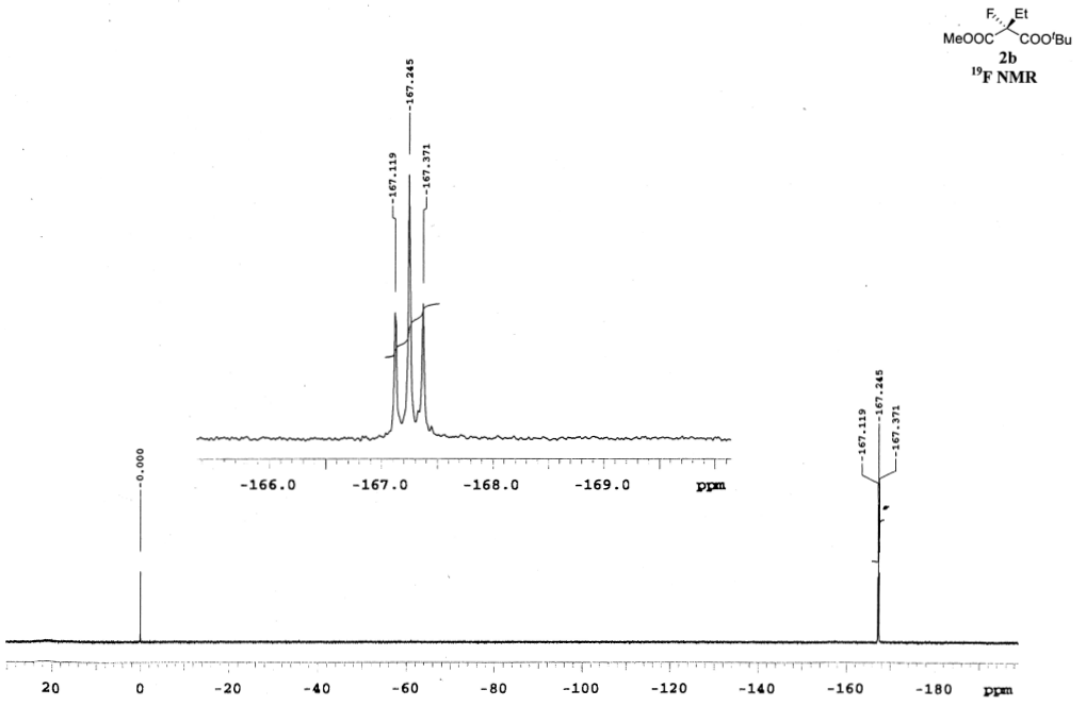
CH	PKNO	TIME	AREA%	HEIGHT%
1	1	34.808	1.325	2.403
1	2	43.817	98.675	97.597

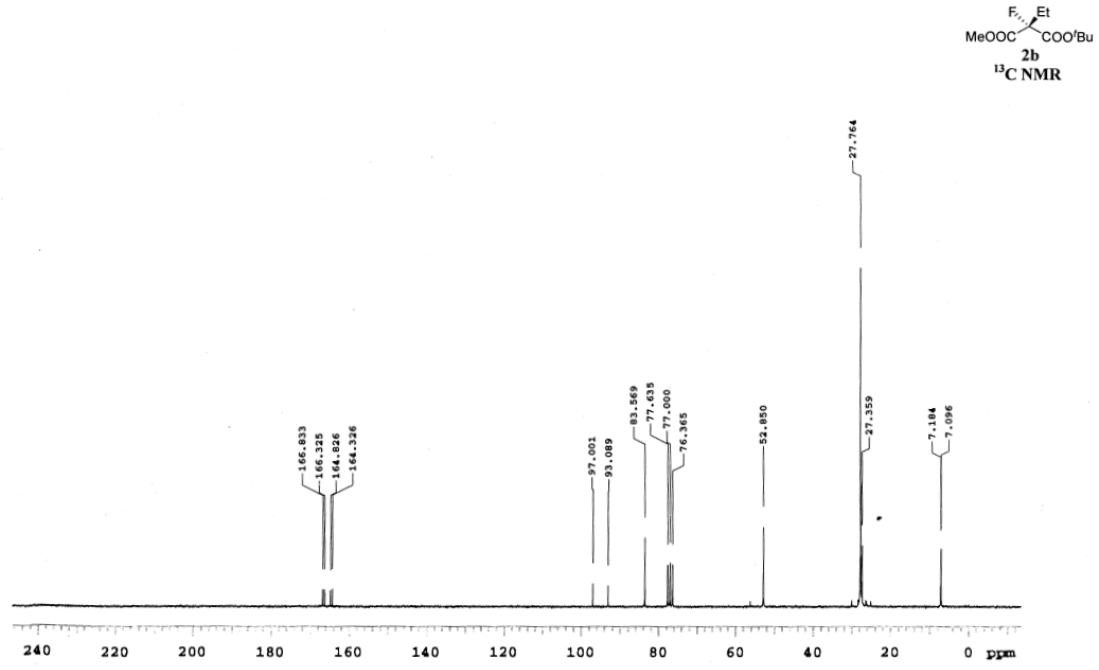

F, CH2Ph
MeOOC COO'Bu
2a
1H NMR
7.252
7.246
7.241
3.783
3.782
3.780
3.489
3.360
1.412
1.408
0.007
0.004
0.000
-0.004
8 7 6 5 4 3 2 1 -0 ppm
5.60
3.00
2.29
8.93

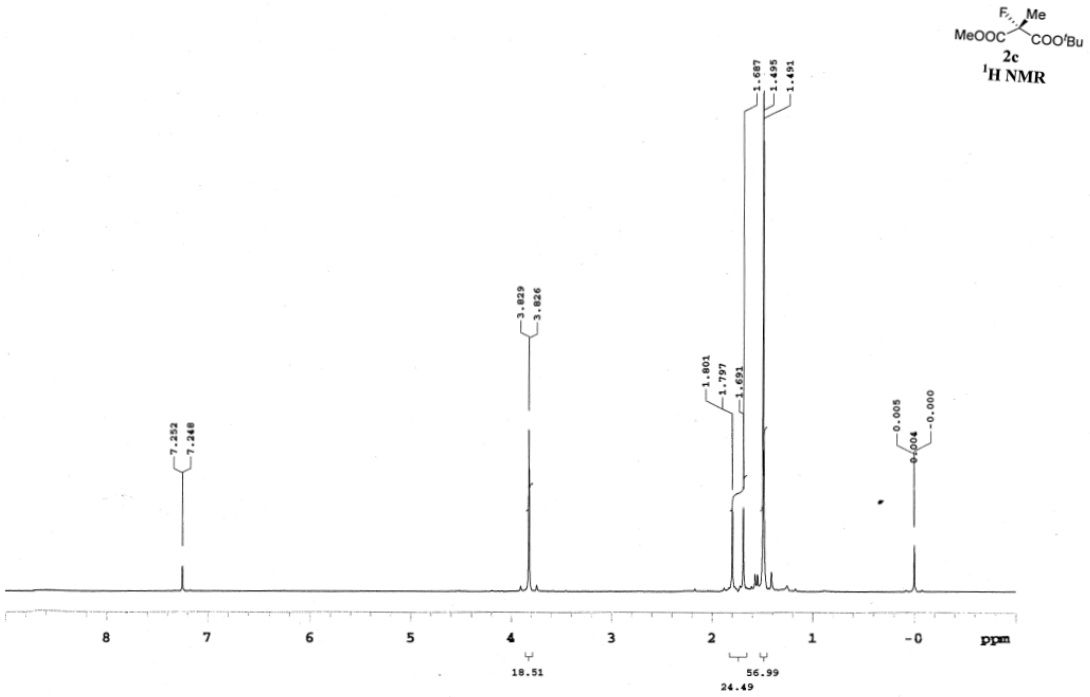

F, CH2Ph
MeOOC COO'Bu
2a
19F NMR
-163.379
-163.239
-163.512
-162.8 -163.4 -164.0 ppm
20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 ppm

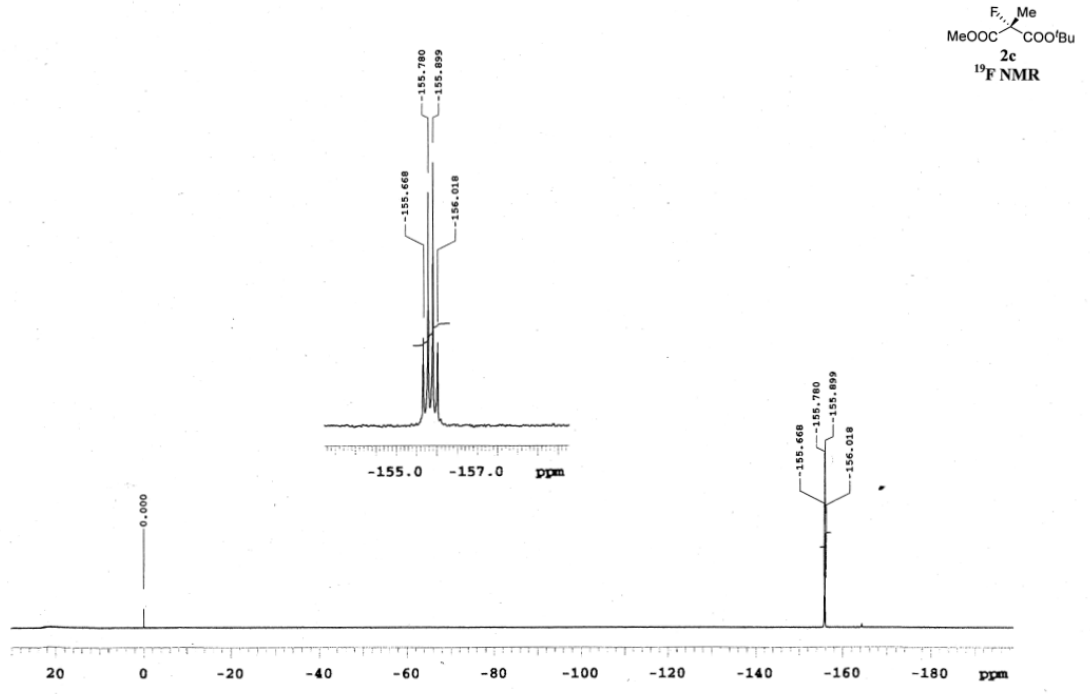

F, CH2Ph
MeOOC COO'Bu
2a
13C NMR
166.539
166.032
164.366
163.074
133.004
130.116
130.092
128.077
127.212
96.612
92.629
84.069
77.627
77.000
76.365
53.128
40.426
40.013
27.867
1.281
240
220
200
180
160
140
120
100
80
60
40
20
0 ppm

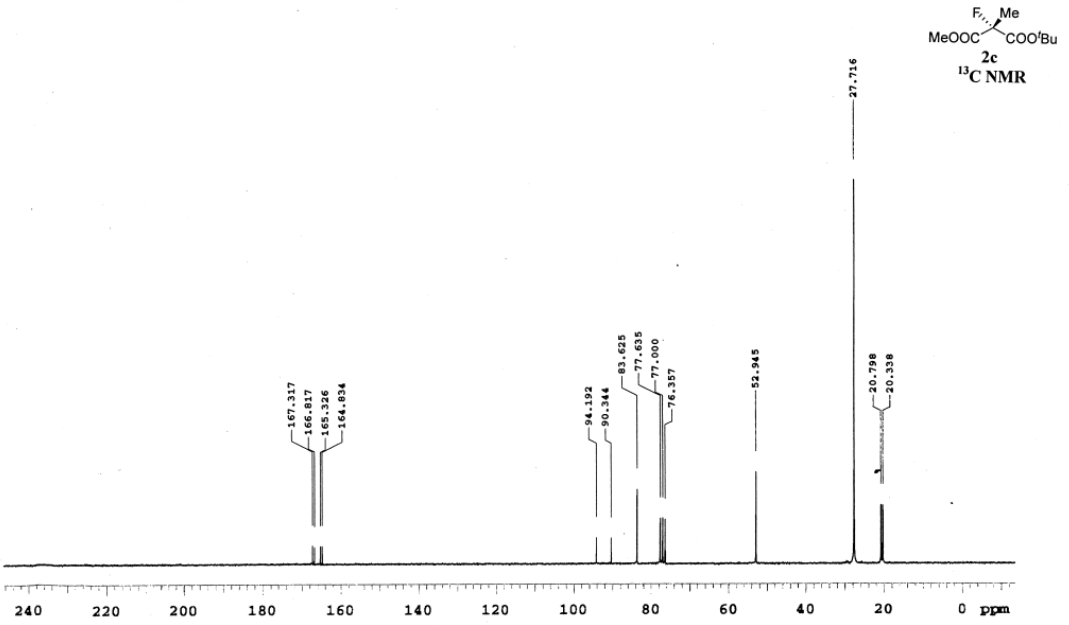

F, Et
MeOOC COO'Bu
2b
1H NMR
3.821
1.492
1.027
0.990
0.953
0.000
8
7
6
5
4
3
2
1
-0
ppm

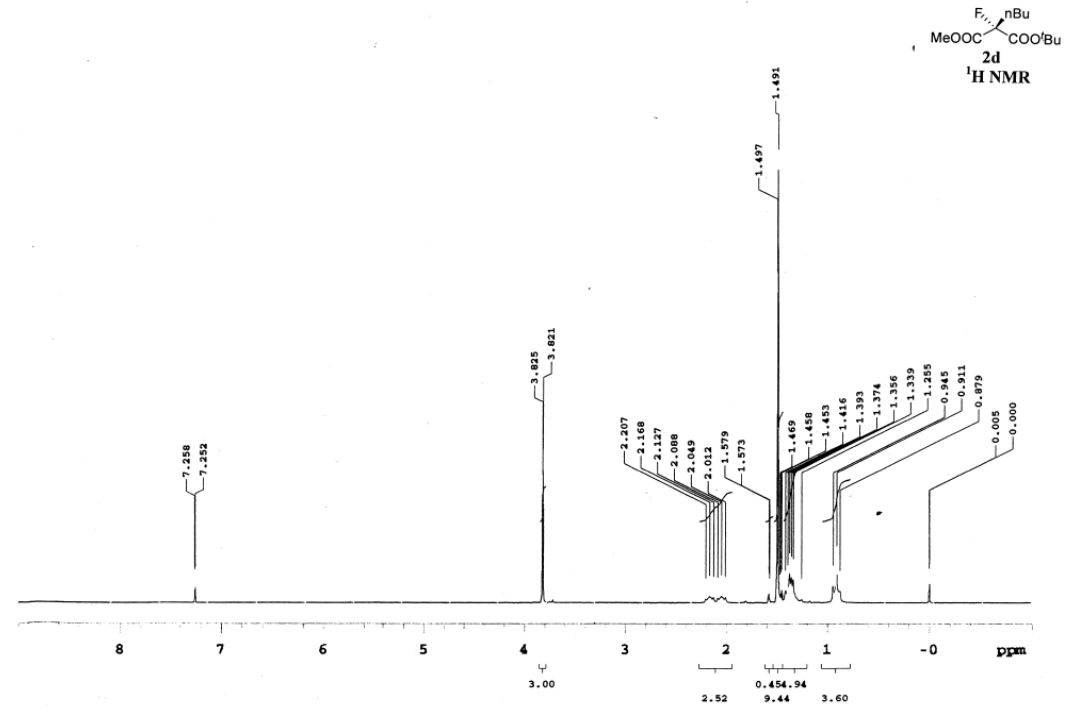

F Et
MeOOC COO^{t}Bu
2b
^{19}F NMR
-167.245
-167.119
-167.371
-0.000
-166.0
-167.0
-168.0
-169.0
ppm
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

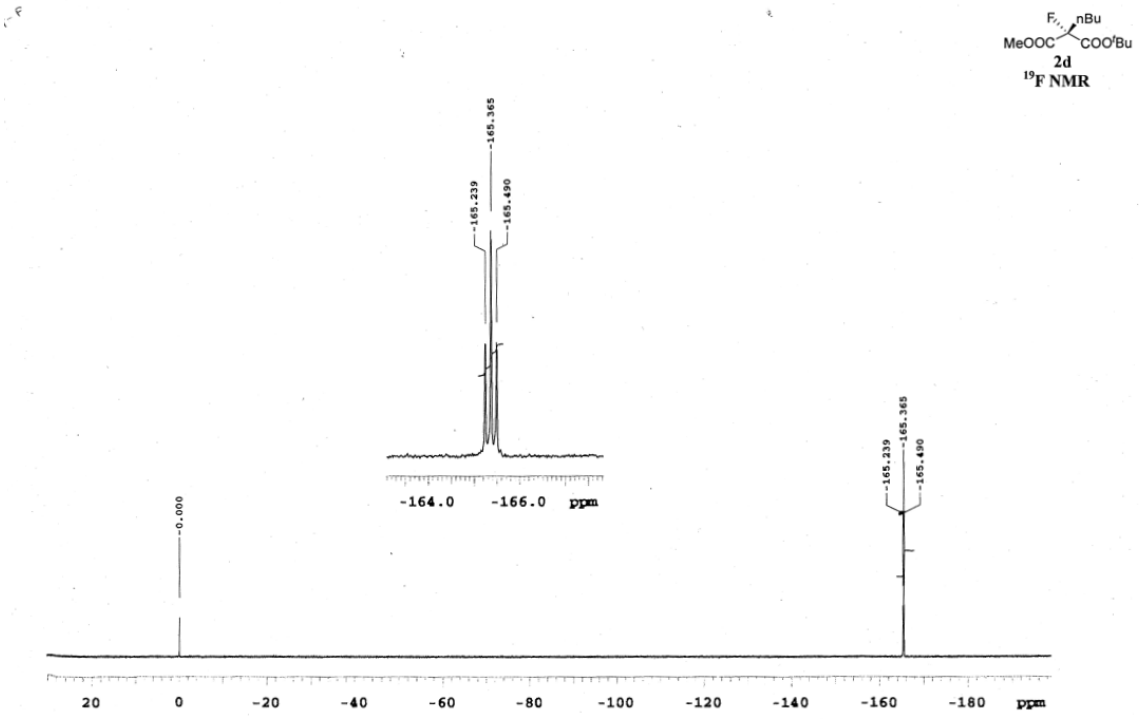

F Et
MeOOC COO^{t}Bu
2b
^{13}C NMR
166.833
166.325
164.826
164.326
97.001
93.089
83.569
77.635
77.000
76.365
52.850
27.764
27.359
7.184
7.096
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

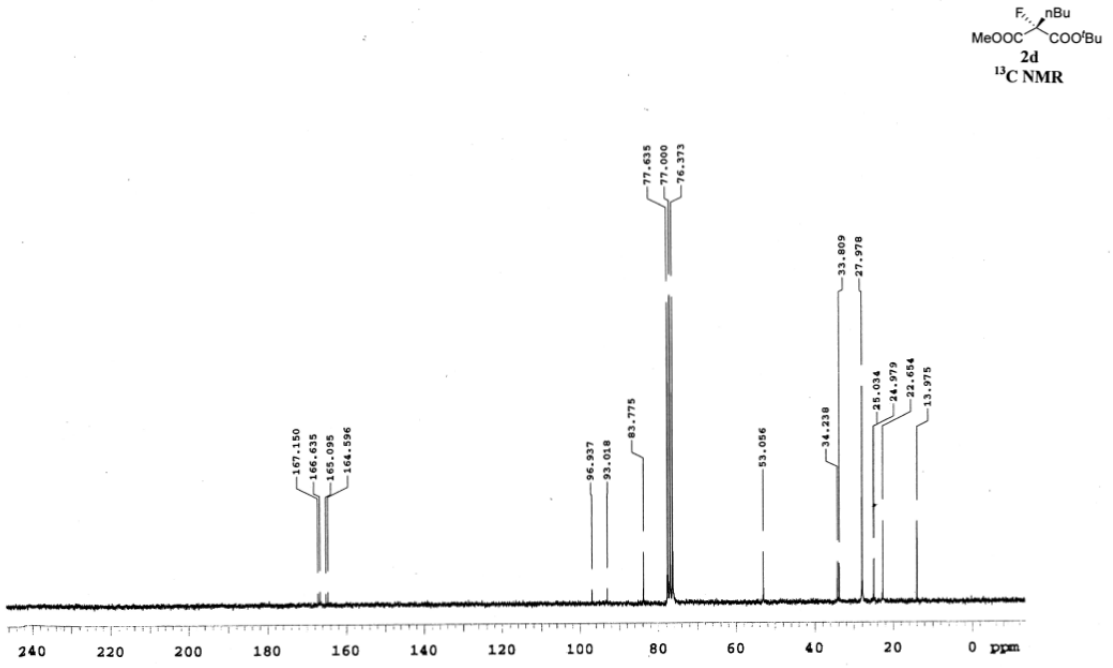

F
Me
MeOOC
COO^{t}Bu
2c
^{1}H NMR
7.252
7.248
3.829
3.826
1.801
1.797
1.691
1.687
1.495
1.491
0.005
0.004
0.000
8
7
6
5
4
3
2
1
-0
ppm
18.51
24.49
56.99

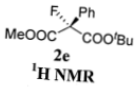

F
Me
MeOOC
COO^{t}Bu
2c
^{19}F NMR
-155.780
-155.899
-155.668
-156.018
-155.0
-157.0
ppm
0.000
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm


F, Me
MeOOC COO^{t}Bu
2c
^{13}C NMR
167.317
166.817
165.326
164.834
94.192
90.344
83.625
77.635
77.000
76.357
52.945
27.716
20.798
20.338
240 220 200 180 160 140 120 100 80 60 40 20 0 ppm


F, nBu
MeOOC COO^{t}Bu
2d
^{1}H NMR
7.258
7.252
3.825
3.821
2.207
2.168
2.127
2.088
2.049
2.012
1.579
1.573
1.497
1.491
1.469
1.458
1.453
1.416
1.393
1.374
1.356
1.339
1.255
0.945
0.911
0.879
0.005
0.000
8 7 6 5 4 3 2 1 -0 ppm
3.00
2.52
0.45
4.94
9.44
3.60

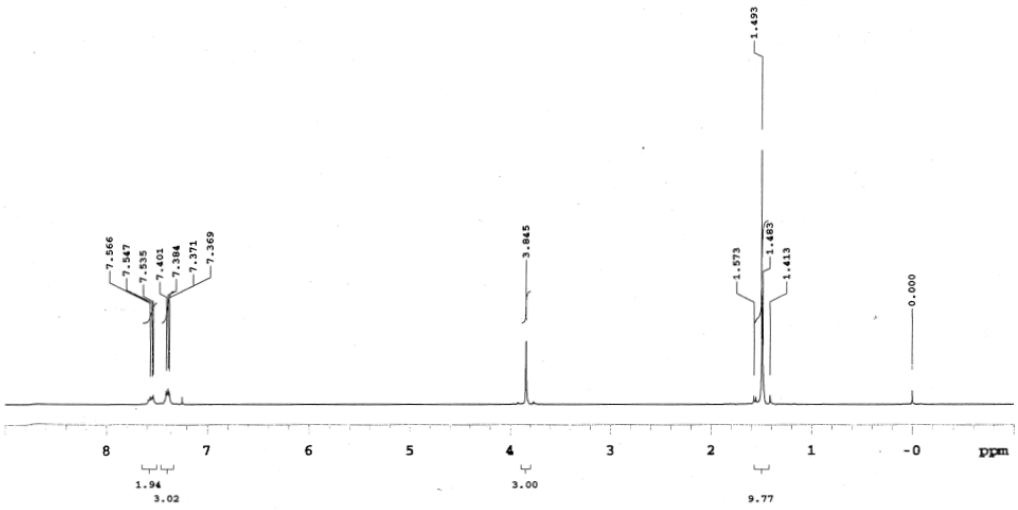

F, nBu
MeOOC COO'Bu
2d
19F NMR
-165.365
-165.239
-165.490
-0.000
-164.0
-166.0
ppm
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

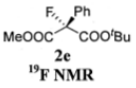

F, nBu
MeOOC COO'Bu
2d
13C NMR
77.635
77.000
76.373
33.809
27.978
26.034
24.979
22.654
13.975
167.150
166.635
165.095
164.596
96.937
93.018
83.775
53.056
34.238
240
220
200
180
160
140
120
100
80
60
40
20
0 ppm



2e

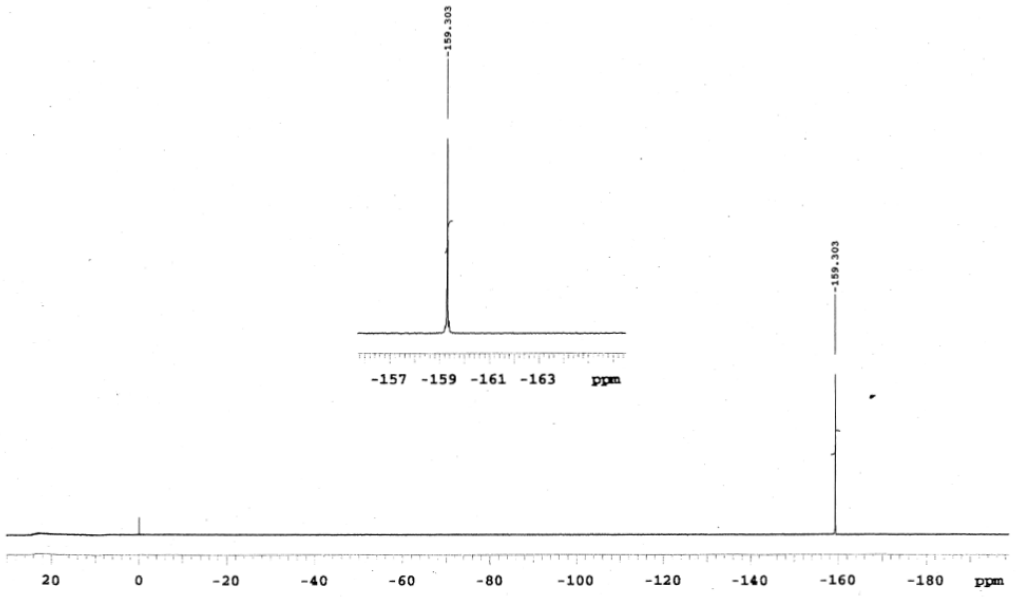
^{1}H NMR

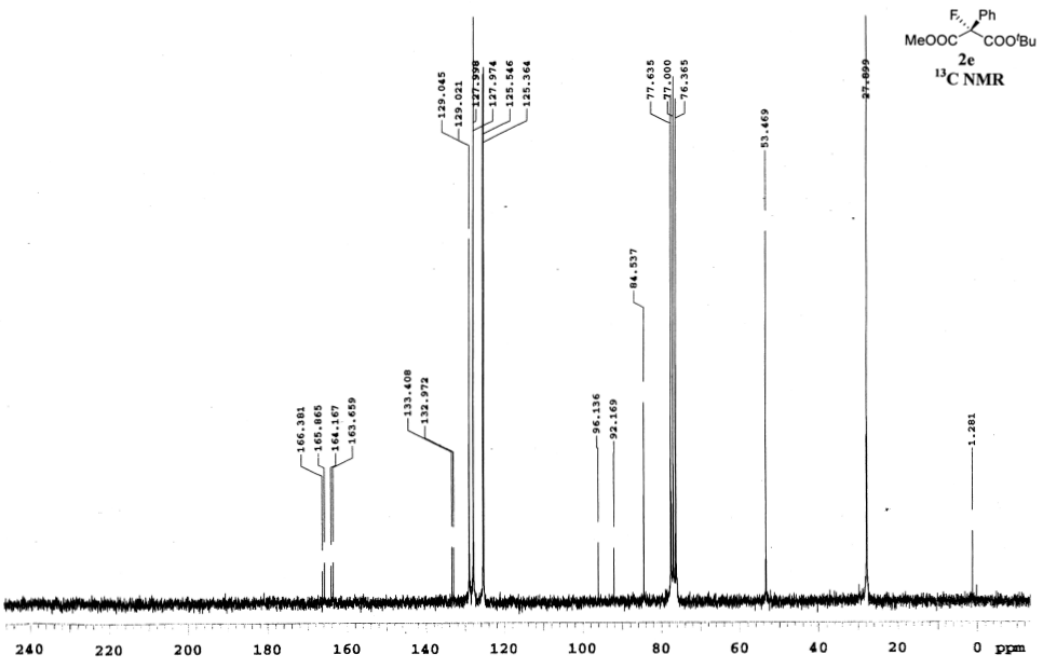


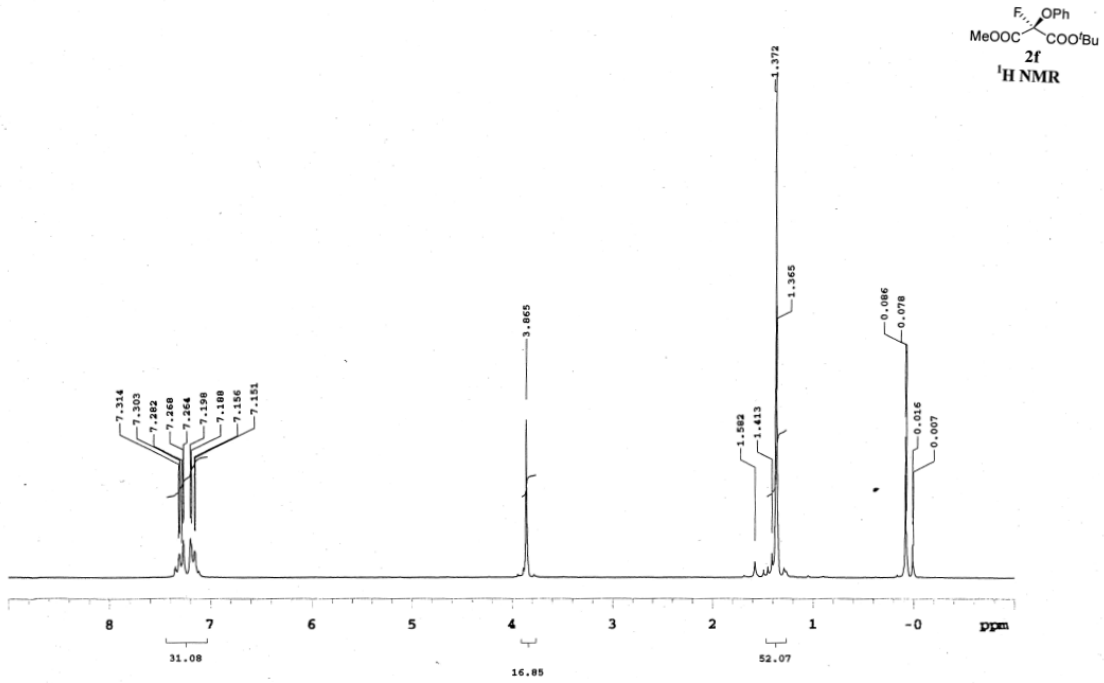


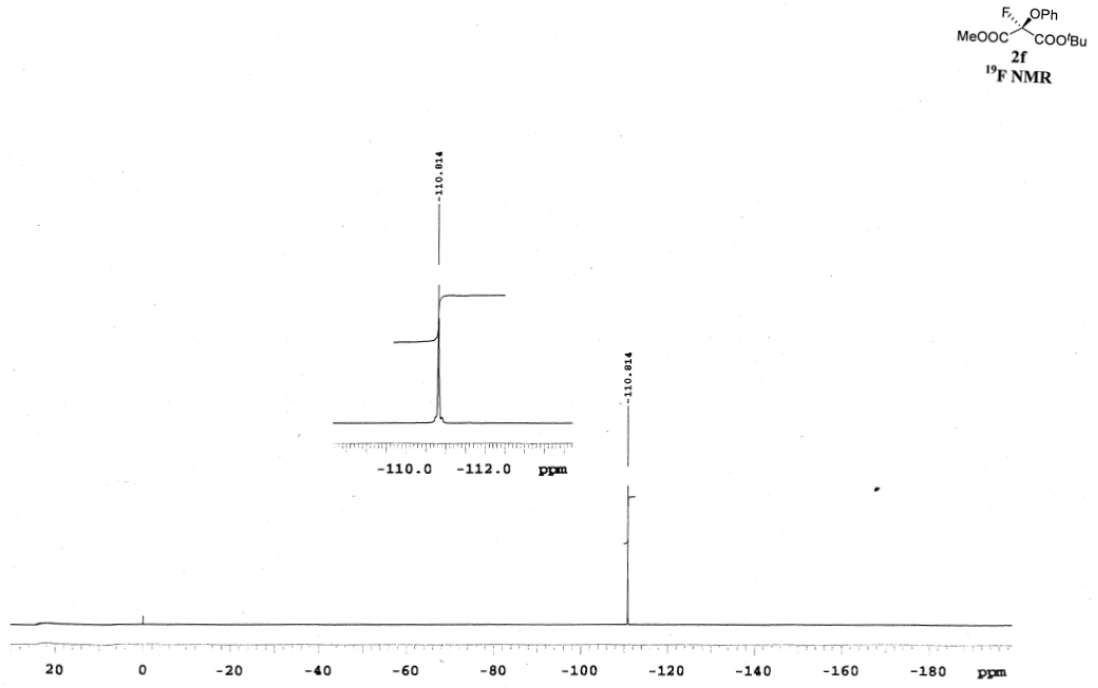
2e

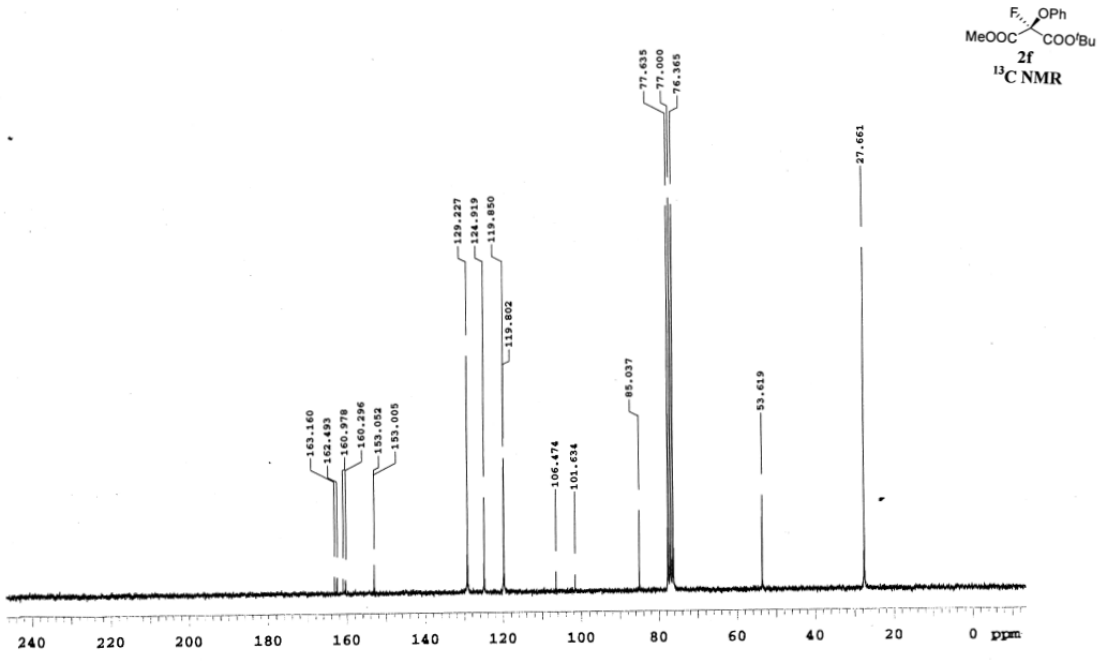
^{19}F NMR

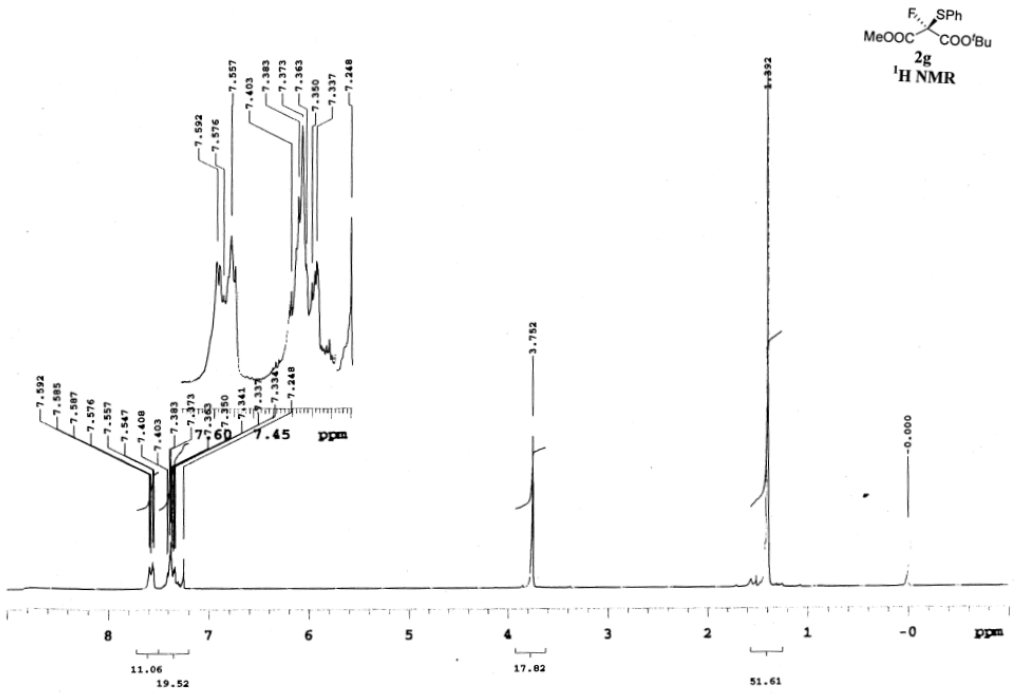


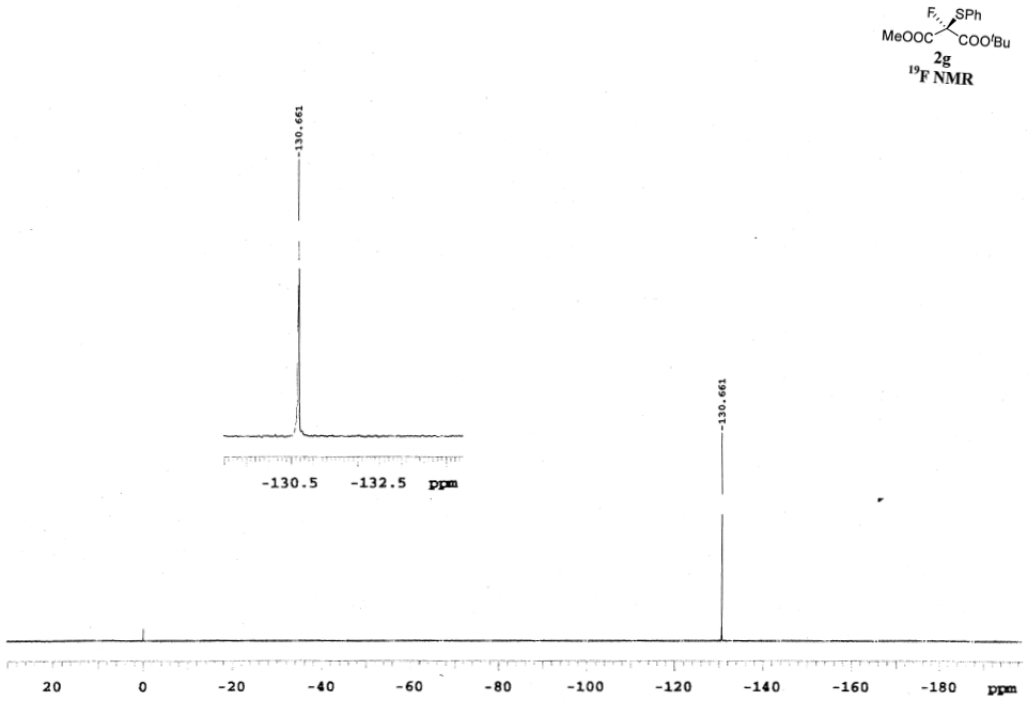

F, Ph
MeOOC COO^{t}Bu
2e
^{13}C NMR
166.301
165.065
164.167
163.659
133.408
132.972
129.045
129.021
127.998
127.974
125.546
125.364
96.136
92.169
84.537
77.635
77.000
76.365
53.469
27.699
1.281
240 220 200 180 160 140 120 100 80 60 40 20 0 ppm

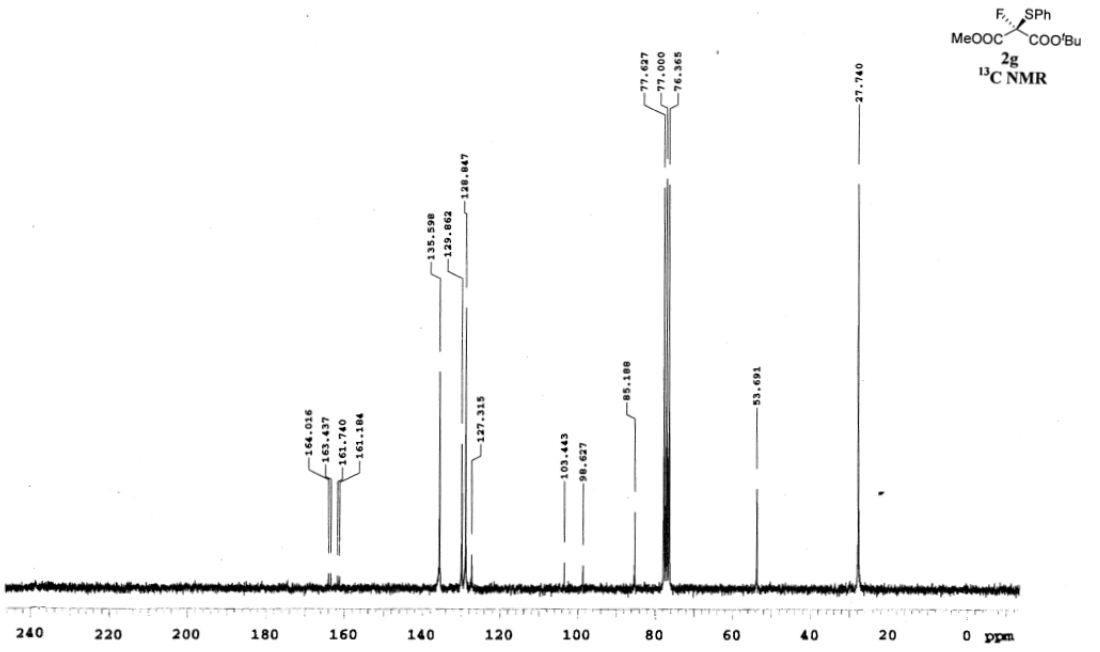

F, OPh
MeOOC COO^{t}Bu
2f
^{1}H NMR
7.314
7.303
7.282
7.269
7.264
7.198
7.188
7.156
7.151
3.865
1.582
1.413
1.372
1.365
0.086
0.078
0.016
0.007
8 7 6 5 4 3 2 1 -0 ppm
31.08
16.85
52.07

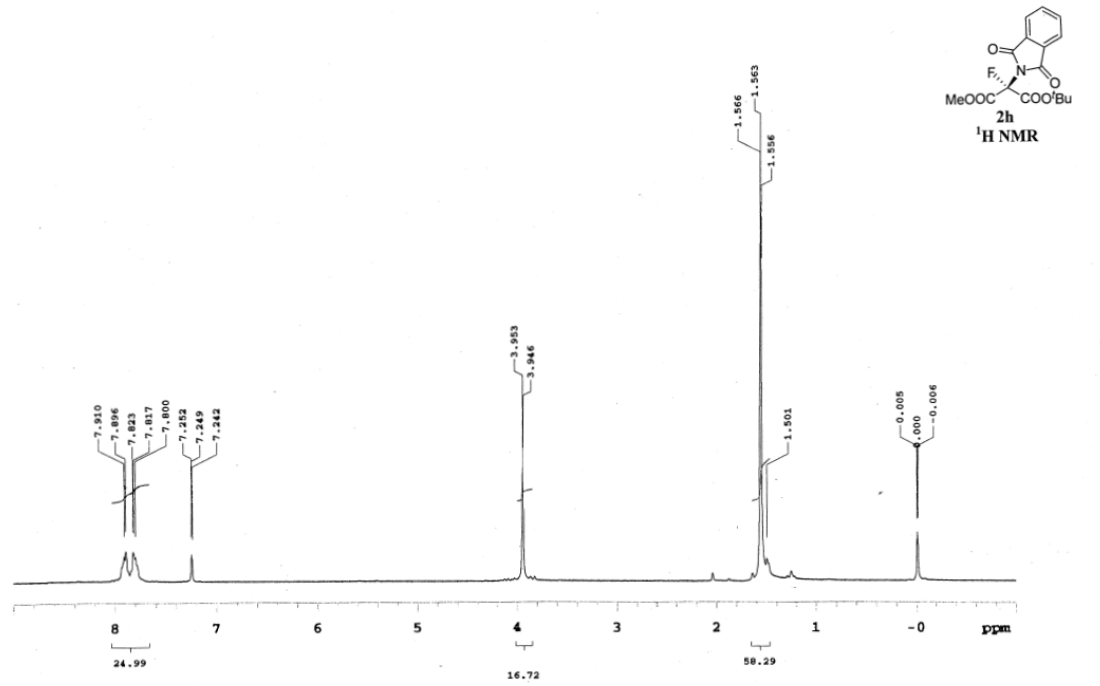

F, OPh
MeOOC COO^{t}Bu
2f
^{19}F NMR
-110.814
-110.814
-110.0 -112.0 ppm
20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 ppm

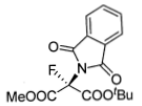

F, OPh
MeOOC COO^{t}Bu
2f
^{13}C NMR
77.635
77.000
76.365
27.661
139.227
124.919
119.850
119.802
85.037
53.619
163.160
162.493
160.978
160.296
153.052
153.005
106.474
101.634
240 220 200 180 160 140 120 100 80 60 40 20 0 ppm


F
SPh
MeOOC
COO^{t}Bu
2g
^{1}H NMR
7.592
7.585
7.587
7.576
7.557
7.547
7.408
7.403
7.383
7.373
7.350
7.341
7.337
7.324
7.248
7.60
7.45
ppm
3.752
1.892
0.000
8
7
6
5
4
3
2
1
-0
ppm
11.06
19.52
17.82
51.61


F
SPh
MeOOC
COO^{t}Bu
2g
^{19}F NMR
-130.661
-130.5
-132.5
ppm
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

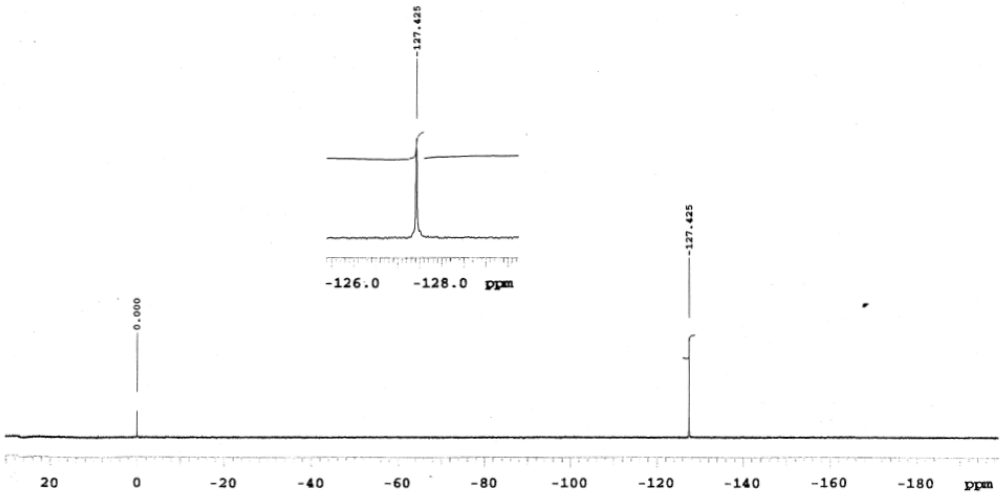

F, SPh
MeOOC COO^{t}Bu
2g
^{13}C NMR
164.016
163.437
161.740
161.184
135.598
129.862
126.847
127.315
103.443
98.627
85.188
77.627
77.000
76.365
53.691
27.740
240 220 200 180 160 140 120 100 80 60 40 20 0 ppm

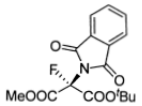

O
N
F,
O
MeOOC COO^{t}Bu
2h
^{1}H NMR
7.910
7.896
7.823
7.817
7.800
7.252
7.249
7.242
3.953
3.946
1.566
1.563
1.556
1.501
0.005
0.000
-0.006
8 7 6 5 4 3 2 1 -0 ppm
24.99
16.72
58.29



2h

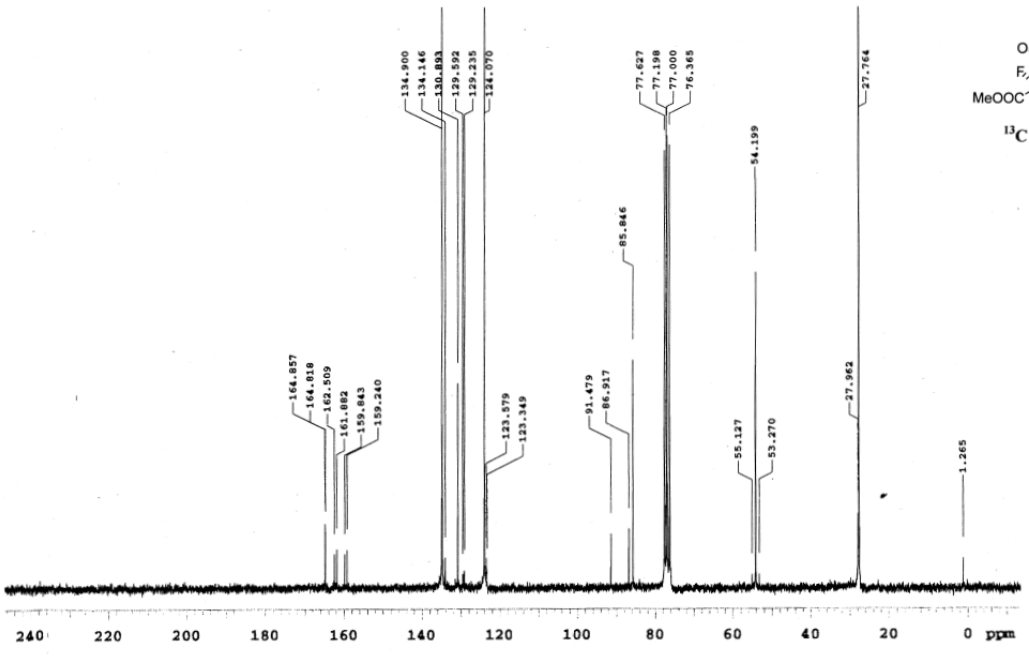
^{19}F NMR

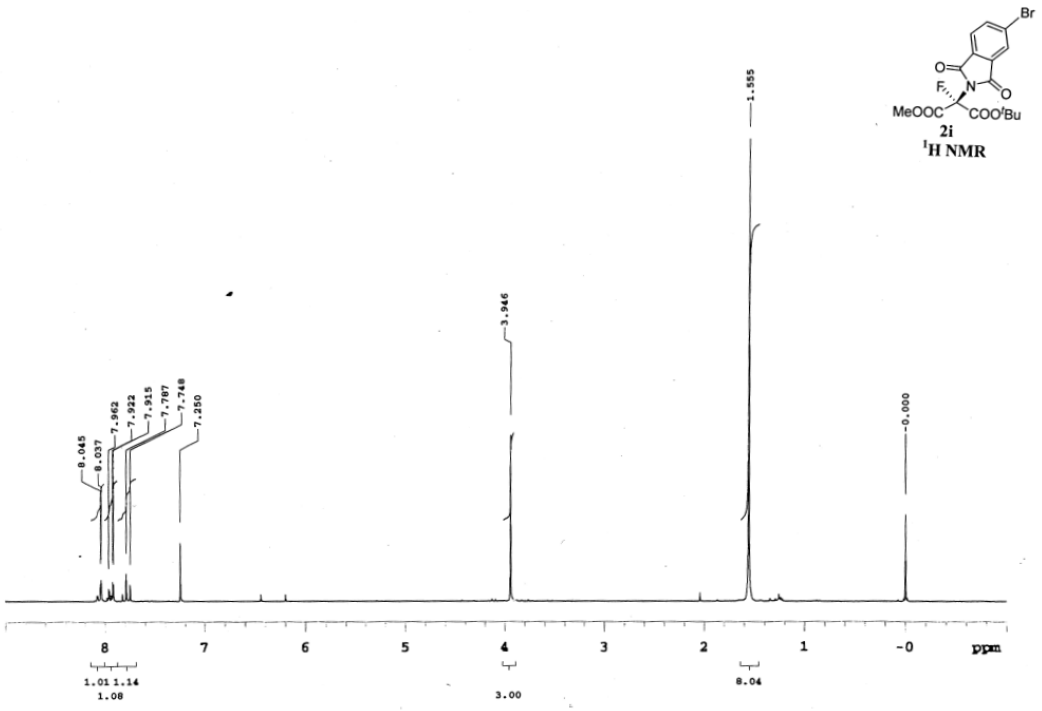


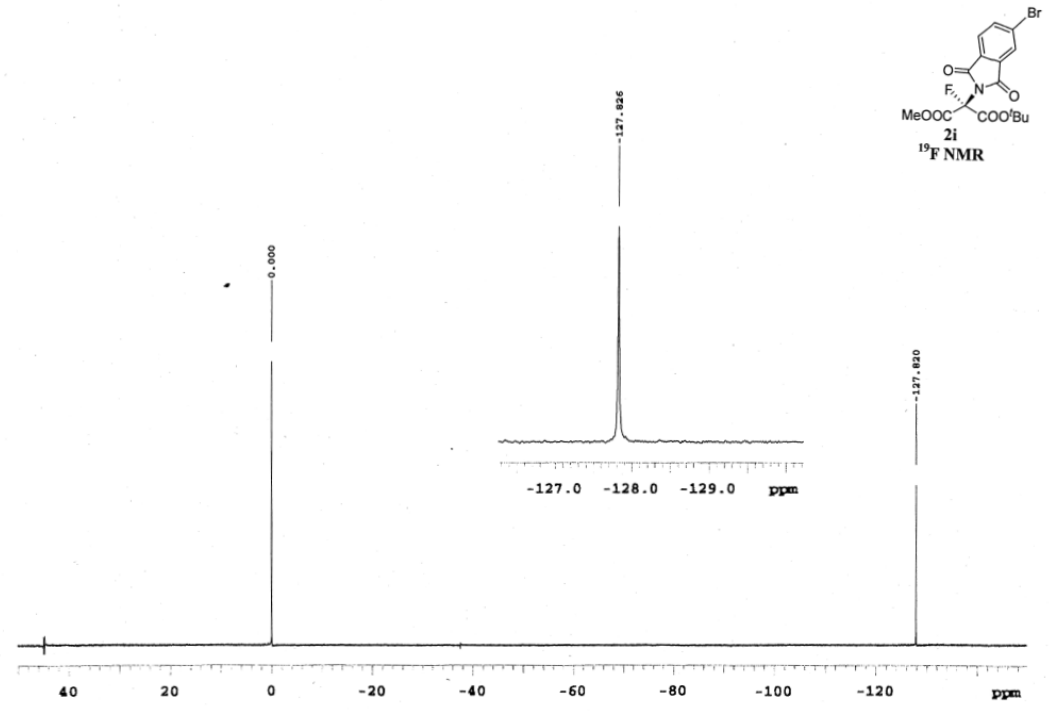


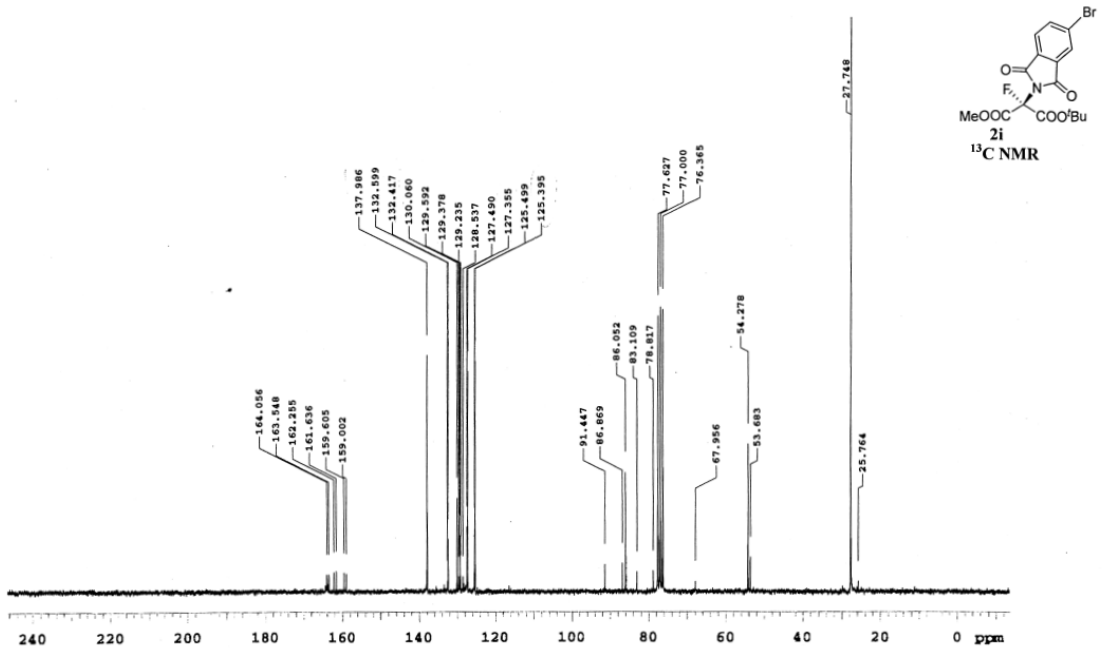
2h

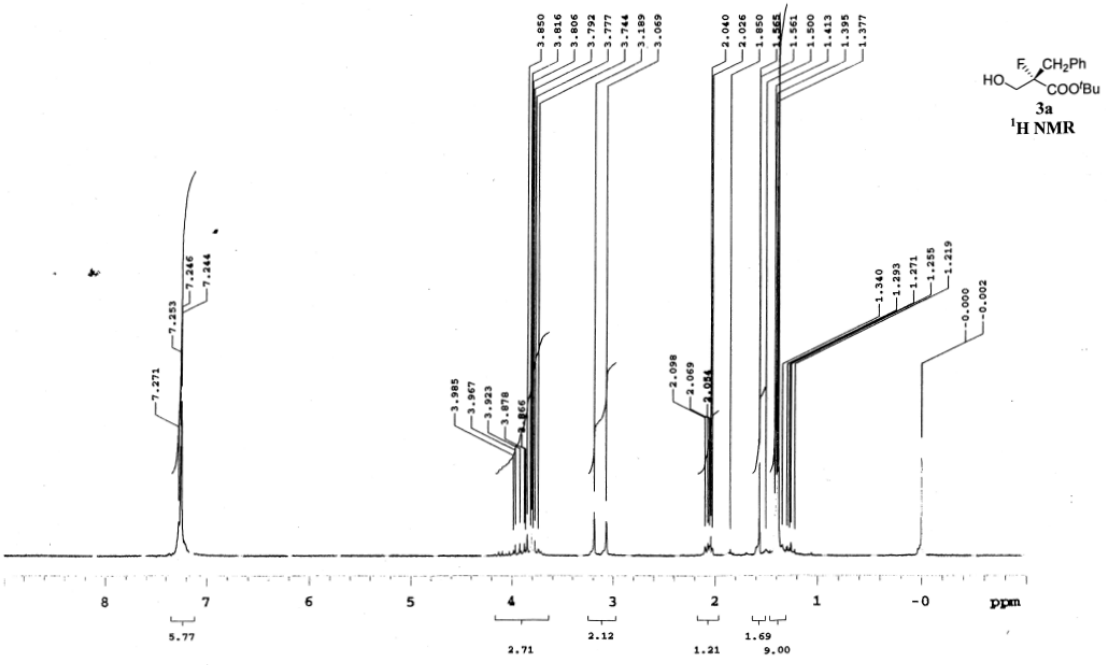
^{13}C NMR

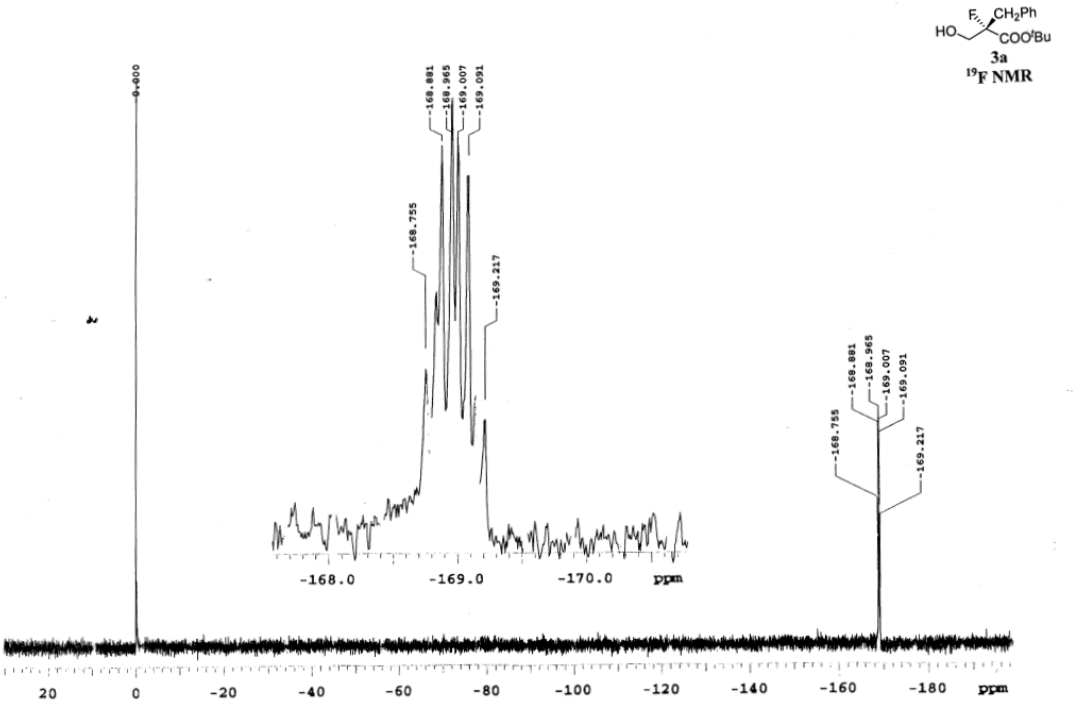


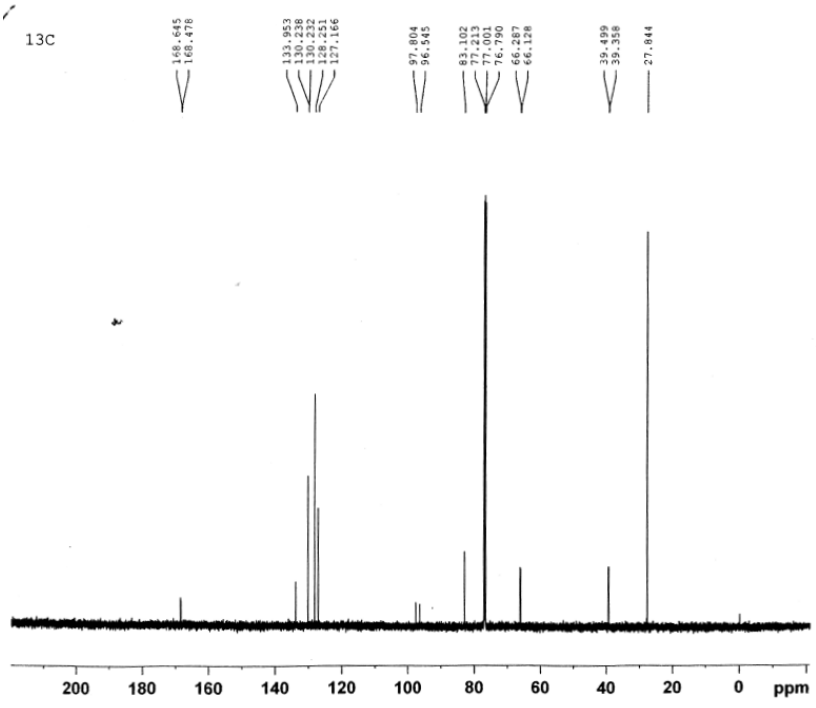

Br
O
F
N
O
MeOOC
COO^{t}Bu
2i
^{1}H NMR
8.045
8.037
7.962
7.922
7.915
7.787
7.748
7.250
3.946
1.555
0.000
8
7
6
5
4
3
2
1
-0
ppm
1.01 1.14
1.08
3.00
8.04

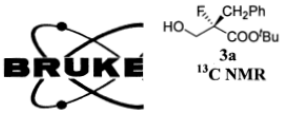

Br
O
F
N
O
MeOOC
COO^{t}Bu
2i
^{19}F NMR
-127.826
0.000
-127.820
-127.0
-128.0
-129.0
ppm
40
20
0
-20
-40
-60
-80
-100
-120
ppm


Br
O
N
O
F
MeOOC
COO^{t}Bu
2i
^{13}C NMR
164.056
163.548
162.255
161.636
159.605
159.002
137.986
132.599
132.417
130.060
129.592
129.378
129.235
128.537
127.490
127.355
125.499
125.395
91.447
86.669
86.052
83.109
78.817
77.627
77.000
76.365
67.956
54.278
53.683
27.748
25.764
240
220
200
180
160
140
120
100
80
60
40
20
0 ppm


F
CH$_2$Ph
HO
COO^{t}Bu
3a
^{1}H NMR
7.271
7.253
7.246
7.244
3.985
3.967
3.923
3.878
3.866
3.850
3.816
3.806
3.792
3.777
3.744
3.189
3.069
2.098
2.069
2.054
2.040
2.026
1.850
1.565
1.561
1.500
1.413
1.395
1.377
1.340
1.293
1.271
1.255
1.219
-0.000
-0.002
8
7
6
5
4
3
2
1
-0
ppm
5.77
2.71
2.12
1.21
1.69
9.00







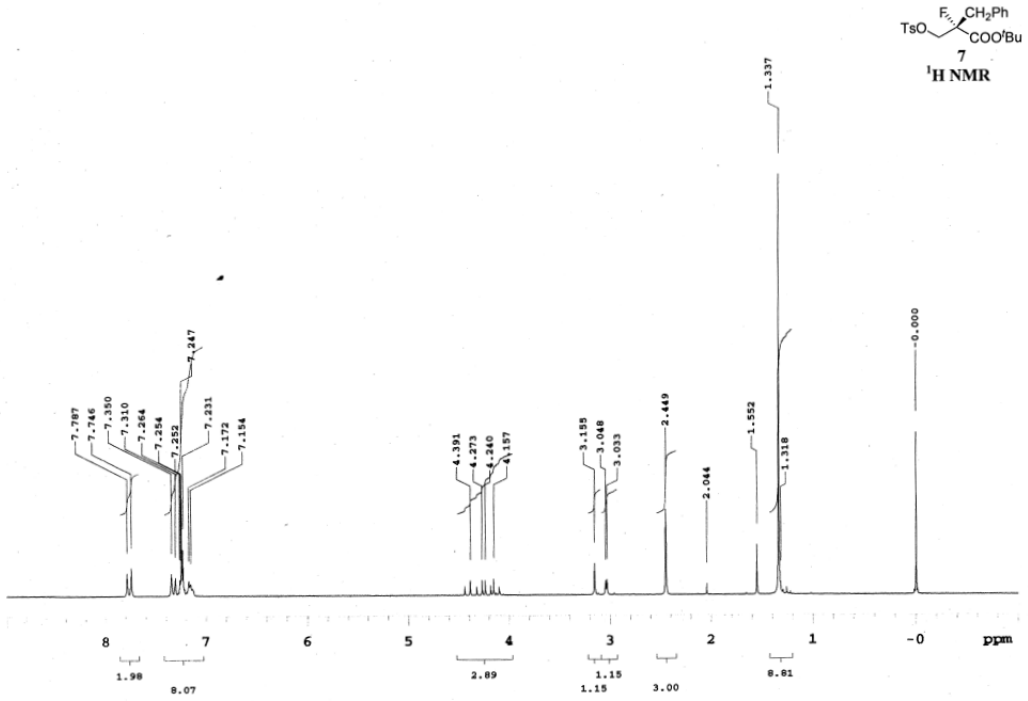

```
Current Data Parameters
NAME                  NJy-473C
EXPNO                       10
PROCNO                       1

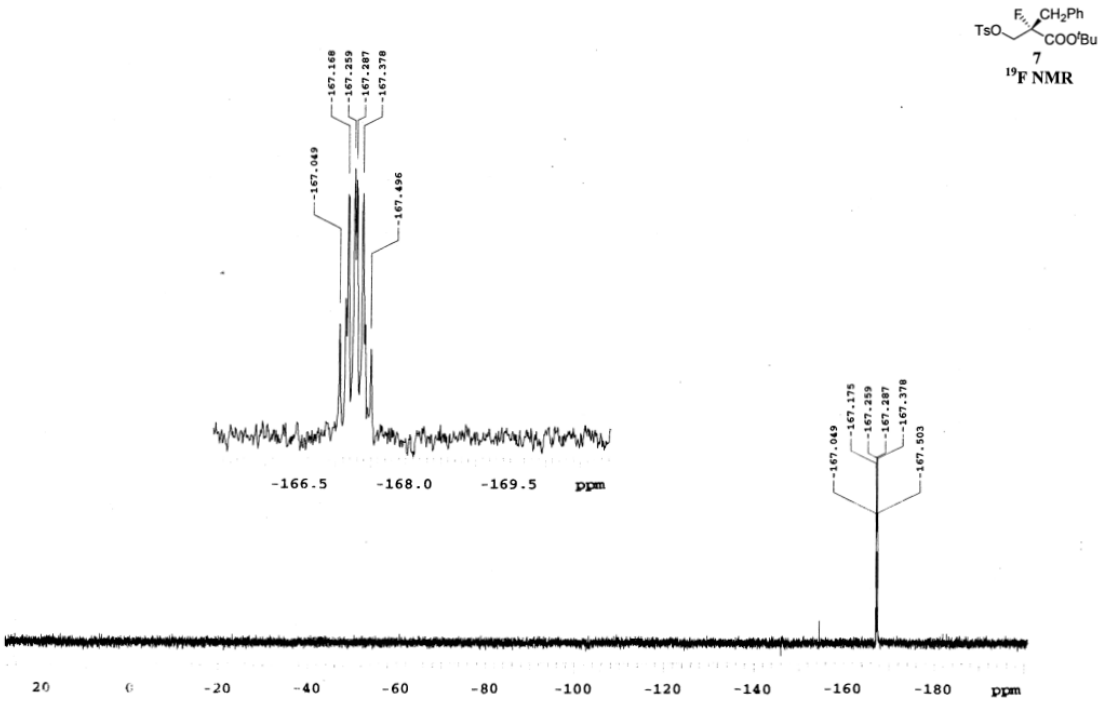
F2 - Acquisition Parameters
Date_                 20070726
Time                     17.39
INSTRUM                  drx600
PROBHD   5 mm BBO BB-1H
PULPROG                 zgpg30
TD                      131072
SOLVENT                  CDCl3
NS                         303
DS                           4
SWH                 45454.547 Hz
FIDRES               0.346791 Hz
AQ                   1.4418530 sec
RG                        8192
DW                      11.000 usec
DE                       6.00 usec
TE                      298.5 K
D1                0.60000002 sec
d11               0.03000000 sec
DELTA             0.50000000 sec
TD0                          1

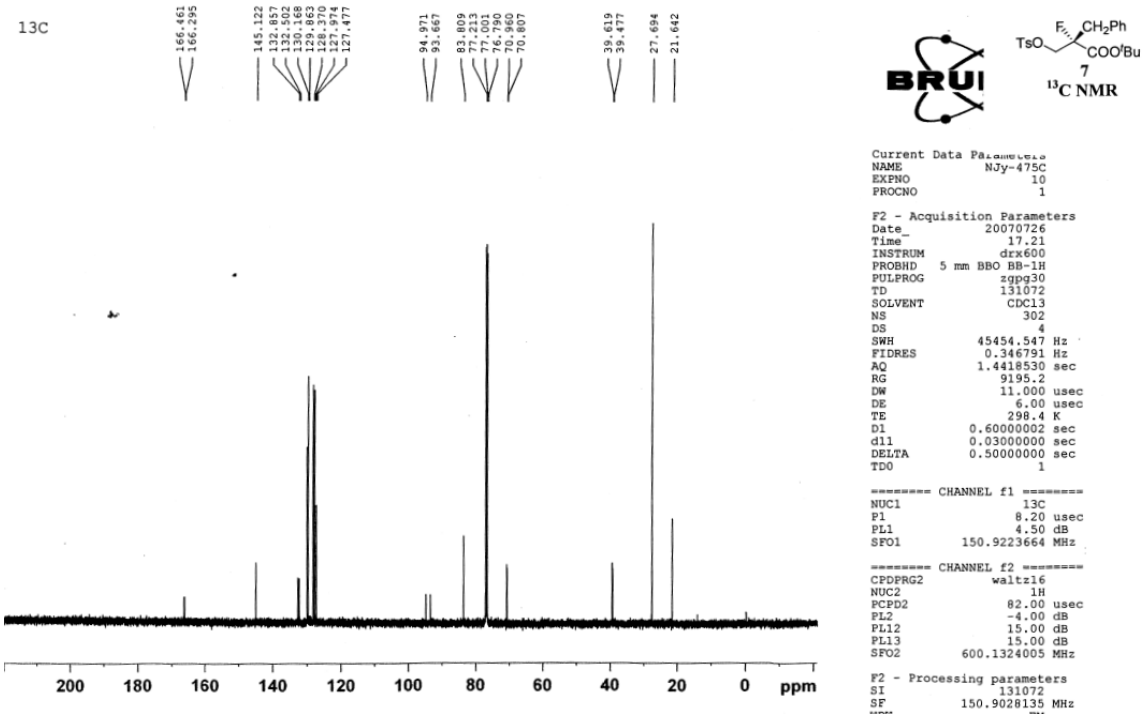
======== CHANNEL f1 ========
NUC1                       13C
P1                        8.20 usec
PL1                       4.50 dB
SFO1              150.9223664 MHz

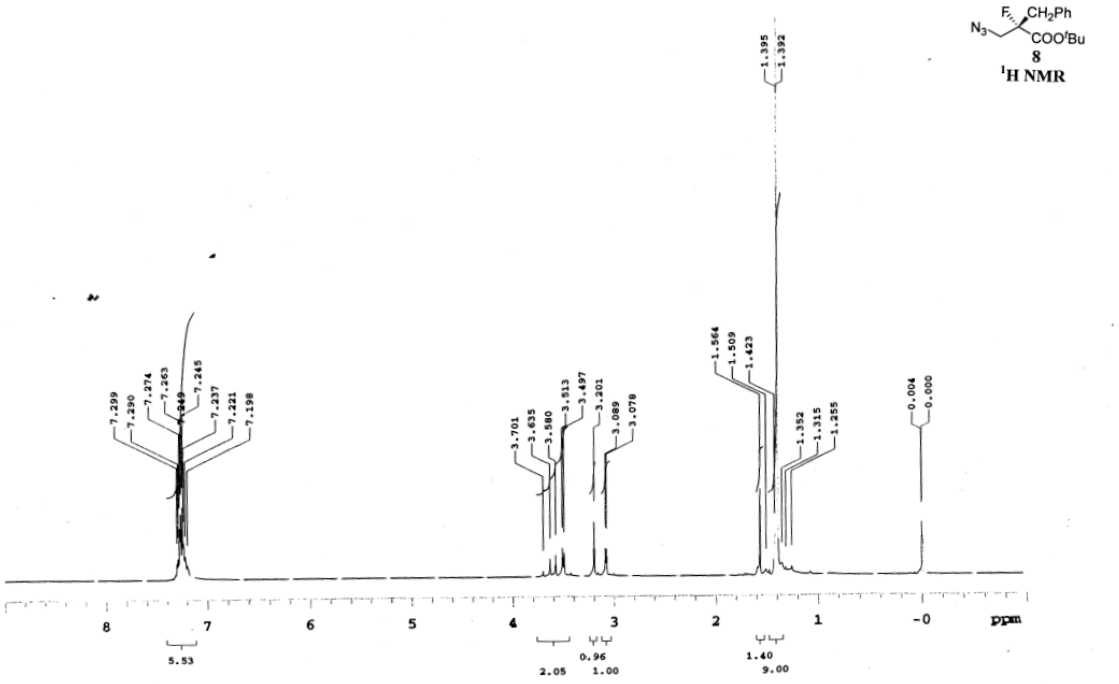
======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                        1H
PCPD2                    82.00 usec
PL2                      -4.00 dB
PL12                     15.00 dB
PL13                     15.00 dB
SFO2              600.1324005 MHz

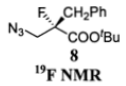
F2 - Processing parameters
SI                       131072
SF                150.9028118 MHz
```


TsO
F
CH2Ph
COO'Bu
7
1H NMR
7.787
7.746
7.350
7.310
7.264
7.254
7.252
7.247
7.231
7.172
7.154
4.391
4.273
4.240
4.157
3.155
3.048
3.033
2.449
2.044
1.552
1.337
1.318
0.000
8
7
6
5
4
3
2
1
0
ppm
1.98
8.07
2.89
1.15
1.15
3.00
8.61


TsO
F
CH2Ph
COO'Bu
7
19F NMR
-167.168
-167.259
-167.287
-167.378
-167.049
-167.496
-166.5
-168.0
-169.5
ppm
-167.049
-167.175
-167.259
-167.287
-167.378
-167.503
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

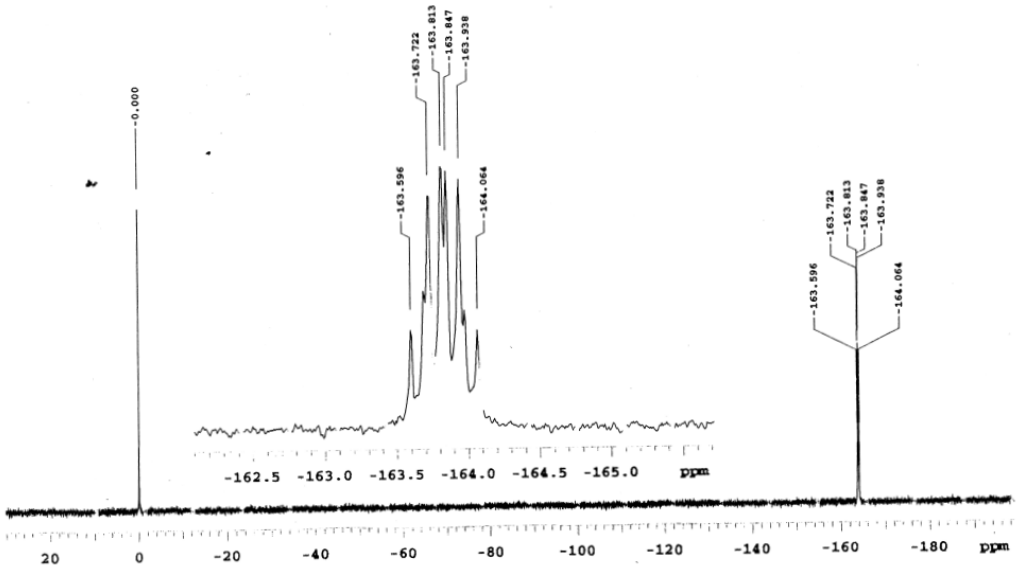

13C
166.461
166.295
145.122
132.857
132.502
130.168
128.853
128.370
127.974
127.477
94.971
93.667
83.809
77.213
77.001
76.790
70.960
70.807
39.619
39.477
27.694
21.642
200 180 160 140 120 100 80 60 40 20 0 ppm
BRUKER
TsO F CH2Ph COO^{t}Bu
7
^{13}C NMR
Current Data Parameters
NAME NJy-475C
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20070726
Time 17.21
INSTRUM drx600
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 131072
SOLVENT CDCl3
NS 302
DS 4
SWH 45454.547 Hz
FIDRES 0.346791 Hz
AQ 1.4418530 sec
RG 9195.2
DW 11.000 usec
DE 6.00 usec
TE 298.4 K
D1 0.60000002 sec
d11 0.03000000 sec
DELTA 0.50000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.20 usec
PL1 4.50 dB
SFO1 150.9223664 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 82.00 usec
PL2 -4.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 600.1324005 MHz
F2 - Processing parameters
SI 131072
SF 150.9028135 MHz

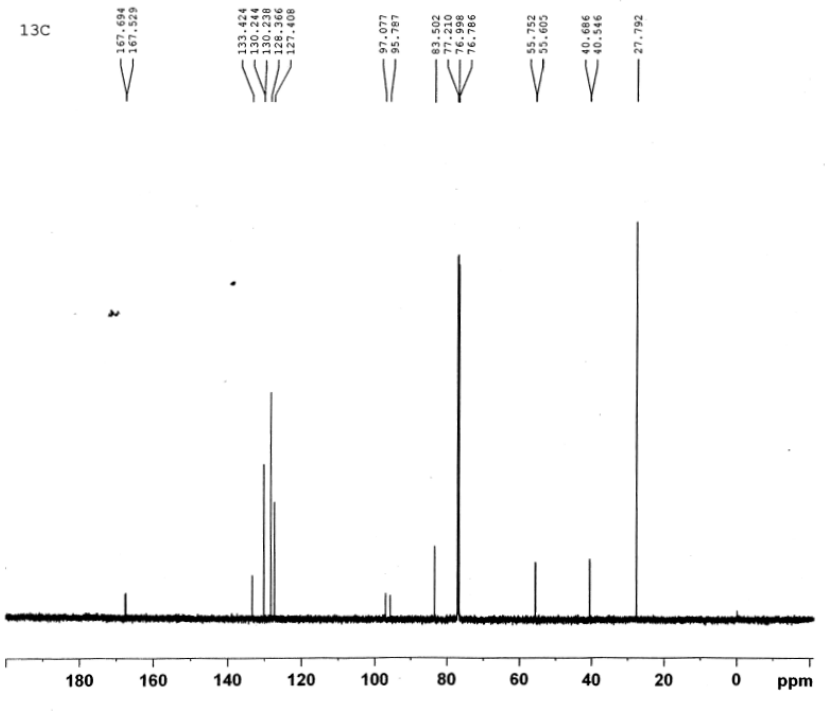

N3 F CH2Ph COO^{t}Bu
8
^{1}H NMR
1.395
1.392
7.299
7.290
7.274
7.263
7.245
7.237
7.221
7.198
3.701
3.635
3.580
3.513
3.497
3.201
3.089
3.078
1.564
1.509
1.423
1.352
1.315
1.255
0.004
0.000
8 7 6 5 4 3 2 1 -0 ppm
5.53
2.05
0.96
1.00
1.40
9.00



8

^{19}F NMR





8

^{13}C NMR

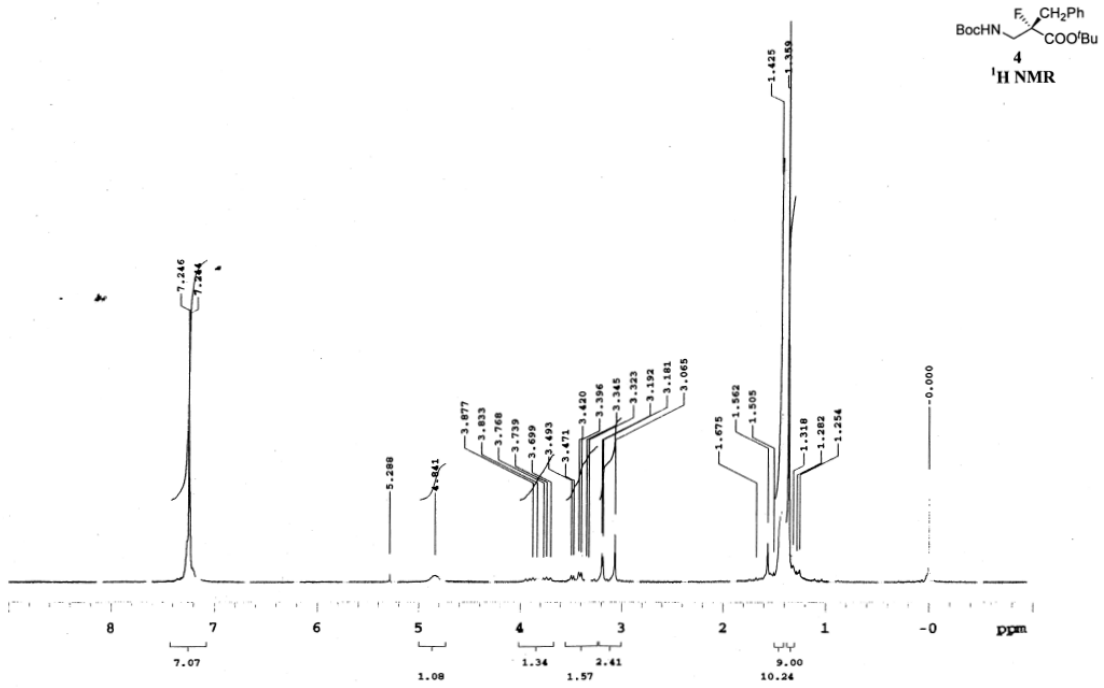
```
Current Data Parameters
NAME                  NJy-478C
EXPNO                       10
PROCNO                       1

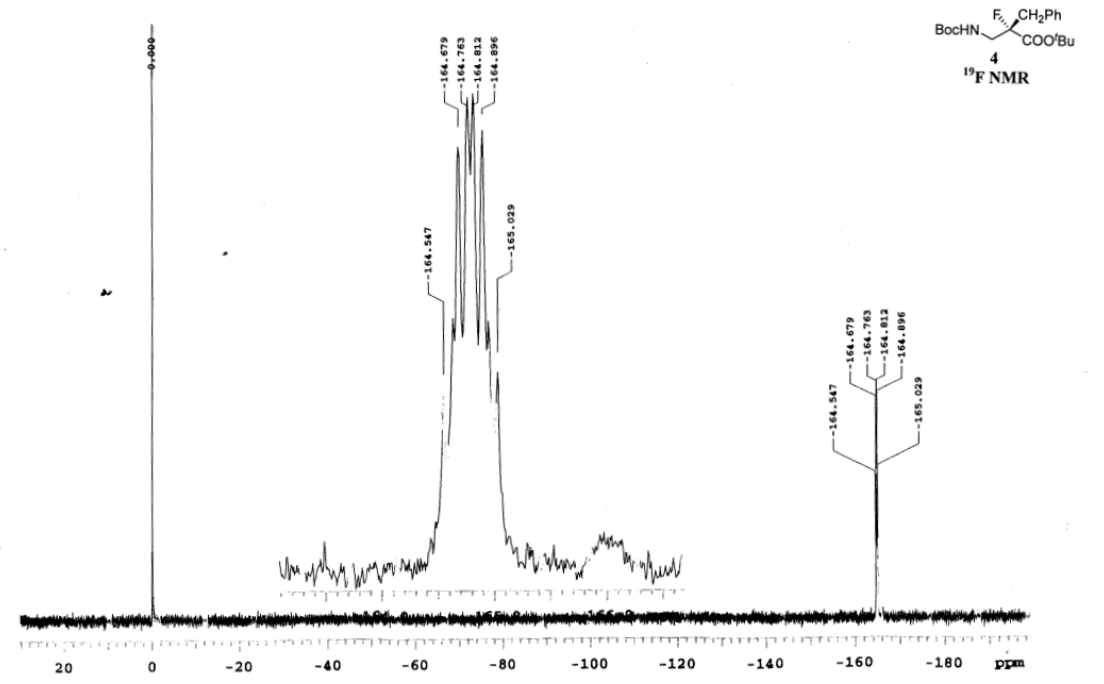
F2 - Acquisition Parameters
Date_                 20070726
Time                     11.35
INSTRUM                drx600
PROBHD     5 mm BBO BB-1H
PULPROG                zgpg30
TD                     131072
SOLVENT                CDCl3
NS                        305
DS                          4
SWH                45454.547 Hz
FIDRES             0.346791 Hz
AQ                 1.4418530 sec
RG                    1824.6
DW                    11.000 usec
DE                     6.00 usec
TE                    298.6 K
D1                 0.60000002 sec
d11                0.03000000 sec
DELTA              0.50000000 sec
TD0                          1

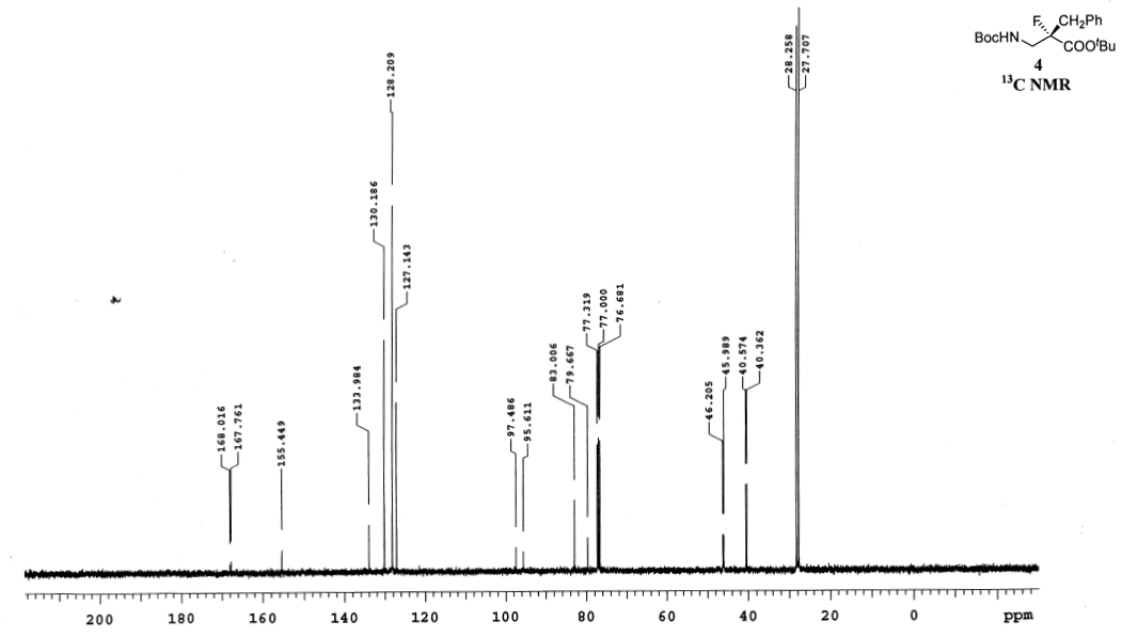
======== CHANNEL f1 ========
NUC1                      13C
P1                       8.20 usec
PL1                      4.50 dB
SFO1             150.9223664 MHz

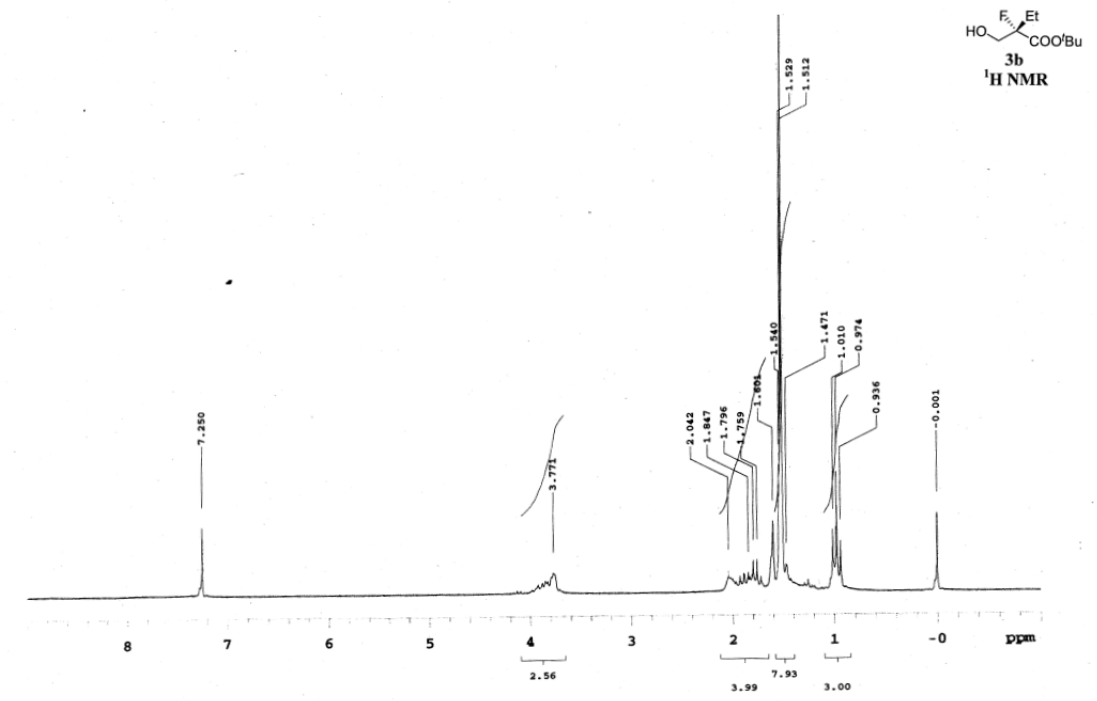
======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                   82.00 usec
PL2                     -4.00 dB
PL12                    15.00 dB
PL13                    15.00 dB
SFO2             600.1324005 MHz

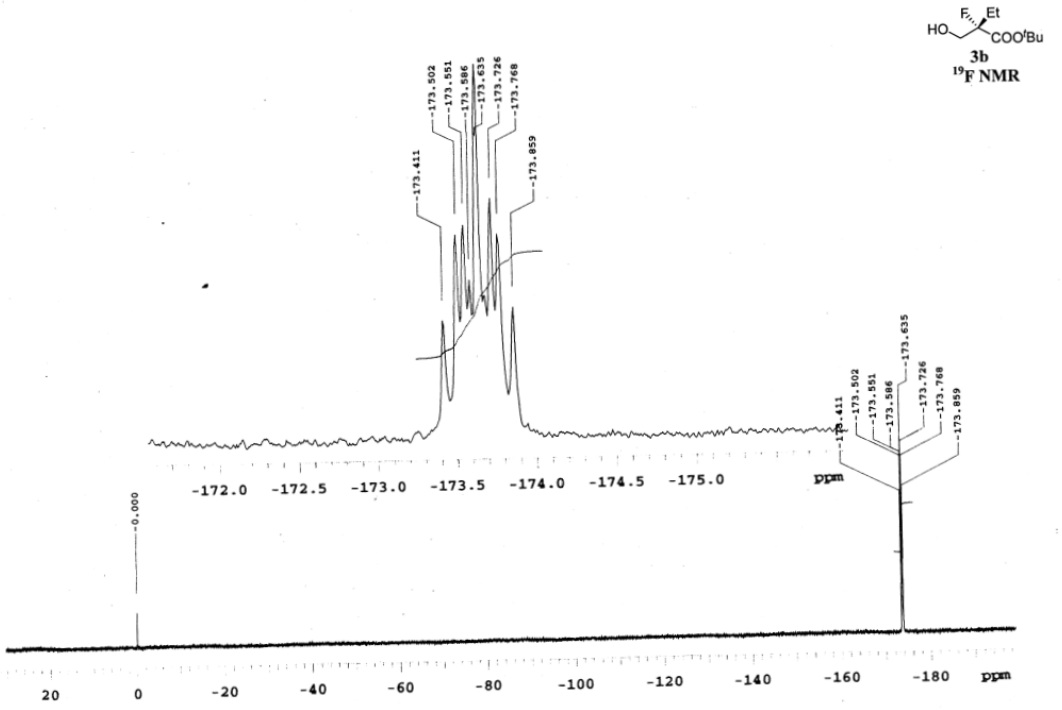
F2 - Processing parameters
SI                       131072
SF               150.9028117 MHz
WDW                          EM
```

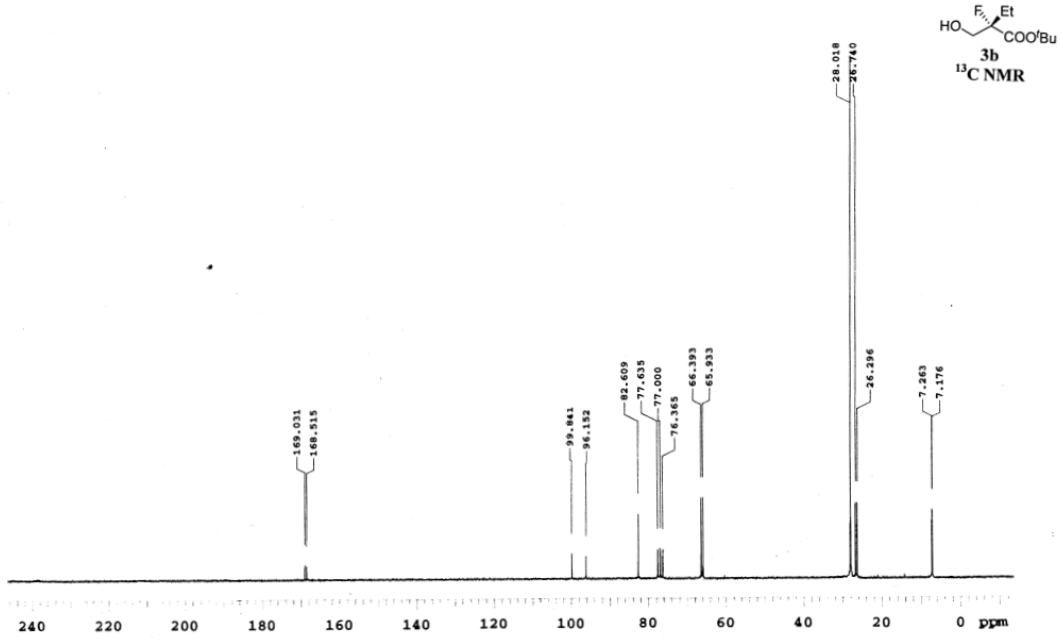

BocHN
F
CH2Ph
COO'Bu
4
1H NMR
7.246
7.244
5.288
4.841
3.877
3.833
3.768
3.739
3.699
3.493
3.471
3.420
3.396
3.345
3.323
3.192
3.181
3.065
1.675
1.562
1.505
1.425
1.359
1.318
1.282
1.254
0.000
8
7
6
5
4
3
2
1
-0
ppm
7.07
1.08
1.34
2.41
1.57
9.00
10.24

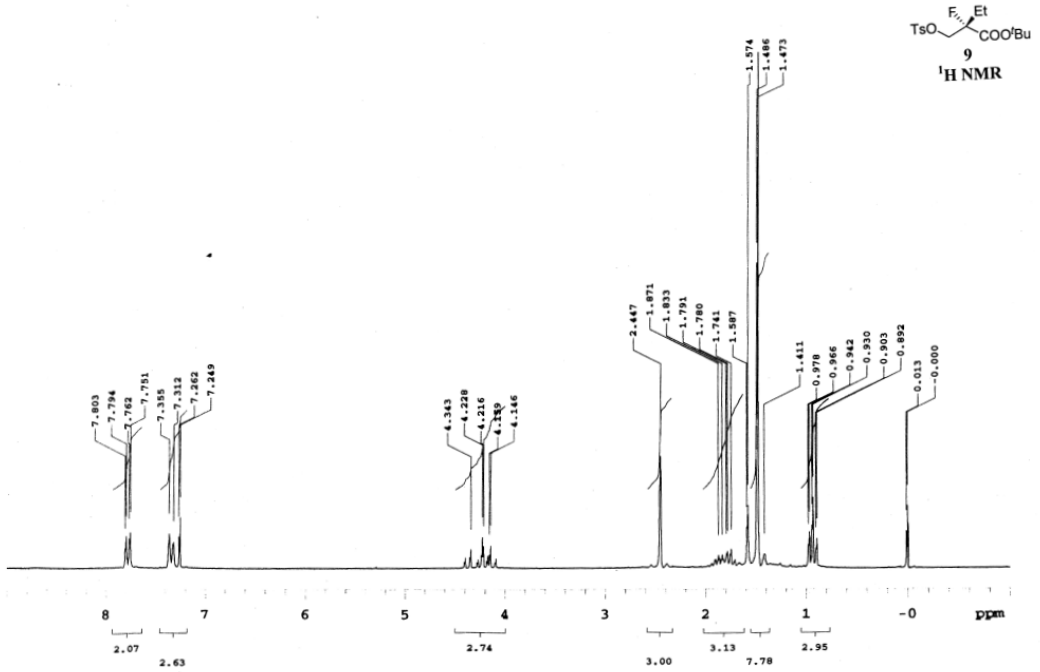

BocHN
F
CH2Ph
COO'Bu
4
19F NMR
0.000
-164.679
-164.763
-164.812
-164.896
-164.547
-165.029
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

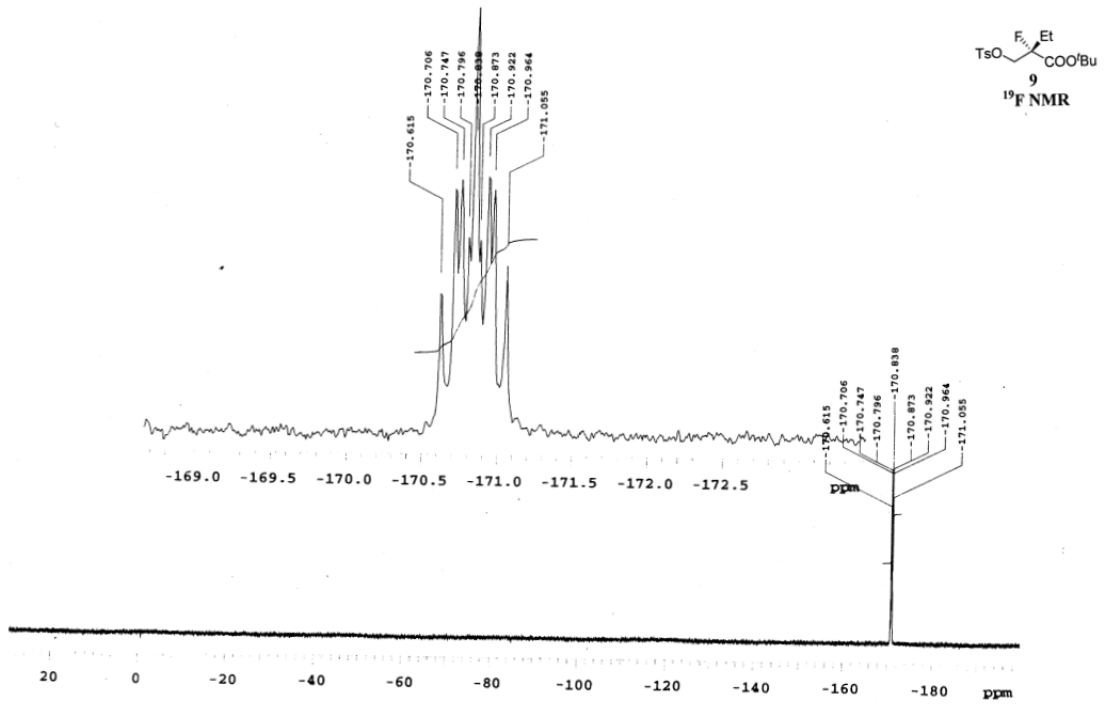

BocHN
F
CH2Ph
COO'Bu
4
13C NMR
168.016
167.761
155.449
133.984
130.186
128.209
127.143
97.486
95.611
83.006
79.667
77.319
77.000
76.681
46.205
45.989
40.574
40.362
28.258
27.707
200
180
160
140
120
100
80
60
40
20
0
ppm

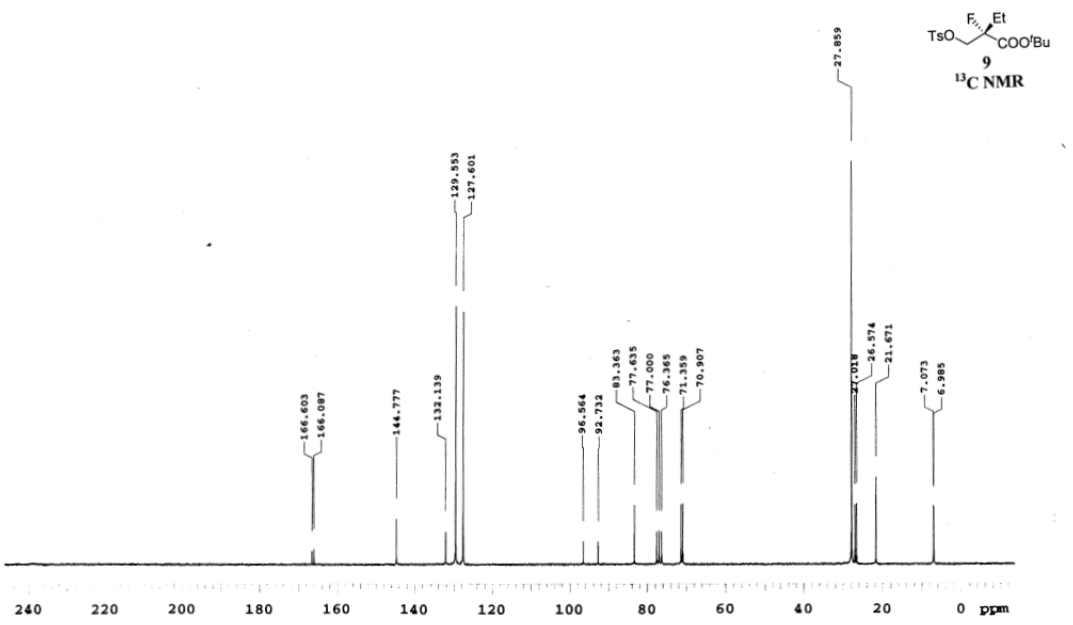

HO
F
Et
COO'Bu
3b
1H NMR
7.250
3.771
2.042
1.847
1.796
1.759
1.695
1.540
1.529
1.512
1.471
1.010
0.974
0.936
0.001
8
7
6
5
4
3
2
1
-0
ppm
2.56
3.99
7.93
3.00

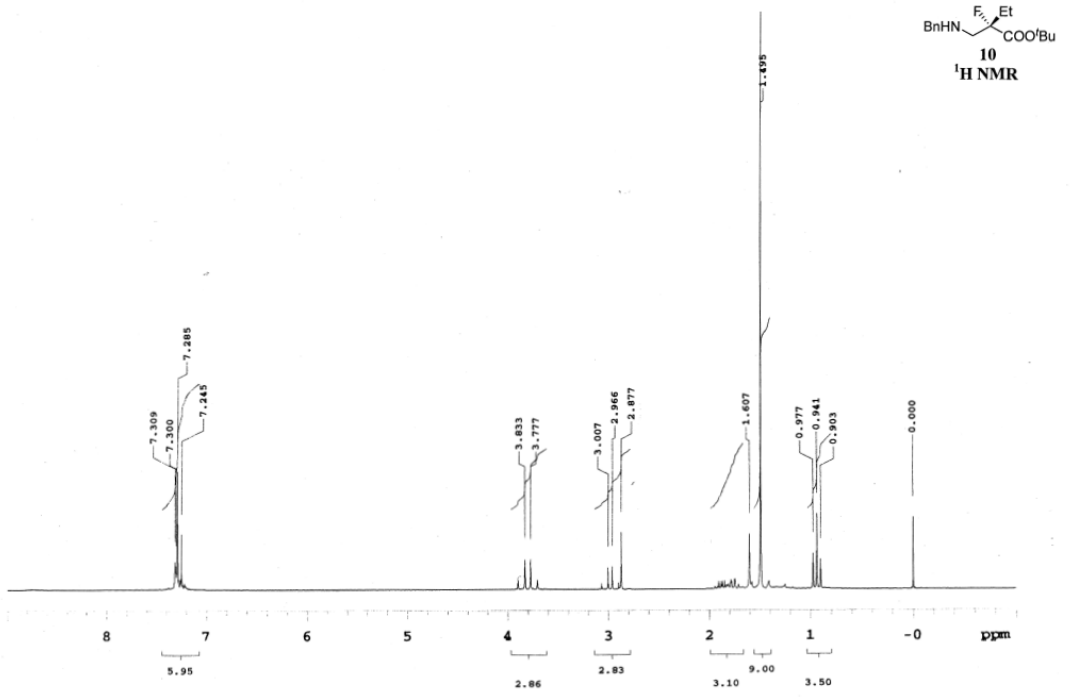

3b
^{19}F NMR
-173.411
-173.502
-173.551
-173.586
-173.635
-173.726
-173.768
-173.859
-172.0
-172.5
-173.0
-173.5
-174.0
-174.5
-175.0
ppm
-0.000
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

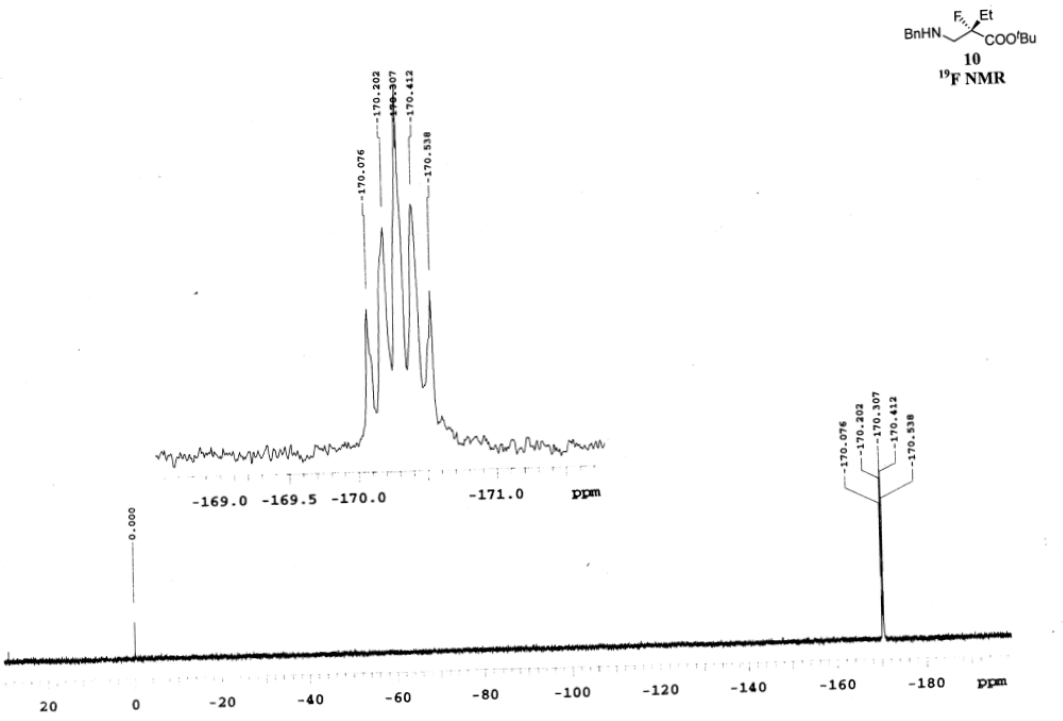

3b
^{13}C NMR
169.031
168.515
99.841
96.152
82.609
77.635
77.000
76.365
66.393
65.933
28.018
26.740
26.296
7.263
7.176
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

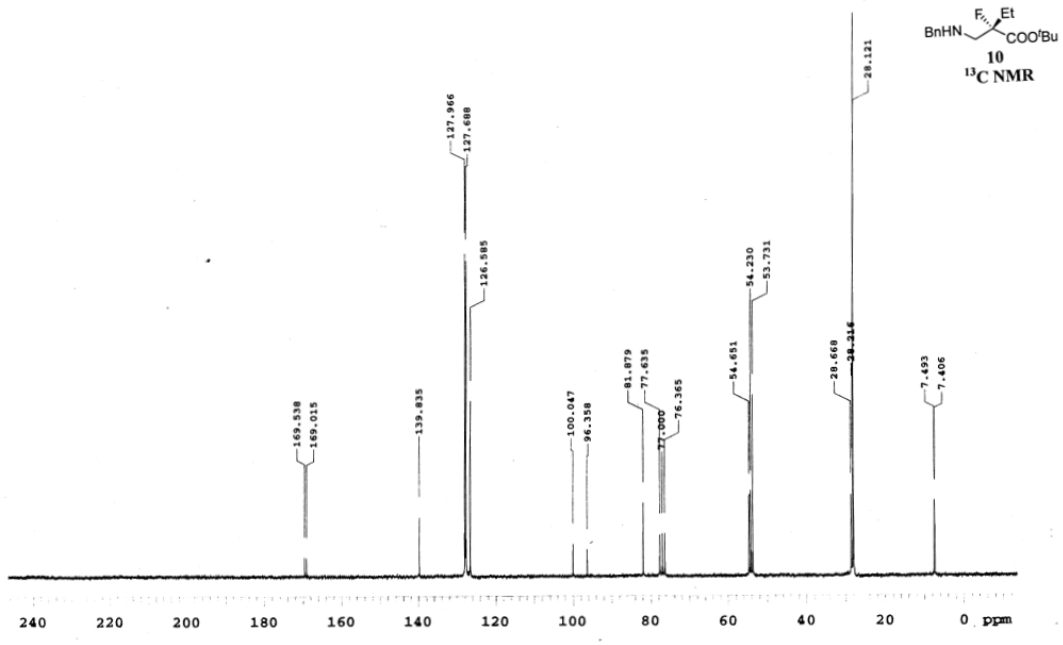

TsO
F
Et
COO^{t}Bu
9
^{1}H NMR
7.803
7.794
7.762
7.751
7.355
7.312
7.262
7.249
4.343
4.228
4.216
4.189
4.166
2.447
1.871
1.833
1.791
1.780
1.741
1.587
1.574
1.486
1.473
1.411
0.978
0.966
0.942
0.930
0.903
0.892
0.013
0.000
8
7
6
5
4
3
2
1
-0
ppm
2.07
2.63
2.74
3.00
3.13
7.78
2.95

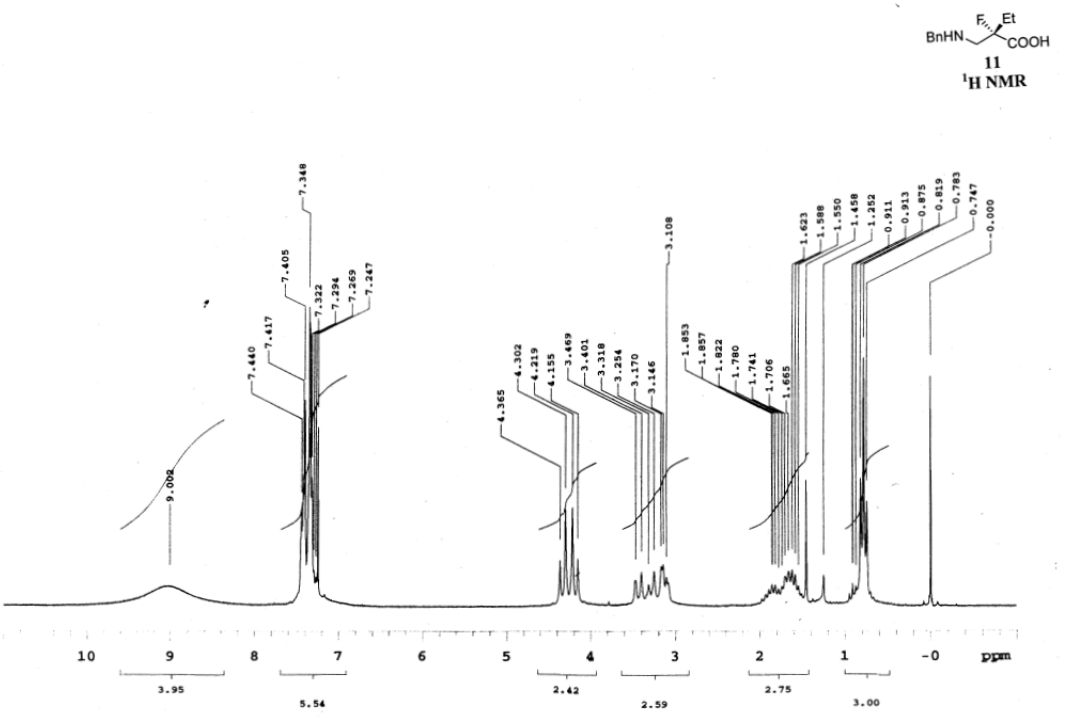

TsO
F
Et
COO^{t}Bu
9
^{19}F NMR
-170.615
-170.706
-170.747
-170.796
-170.838
-170.873
-170.922
-170.964
-171.055
-169.0
-169.5
-170.0
-170.5
-171.0
-171.5
-172.0
-172.5
ppm
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

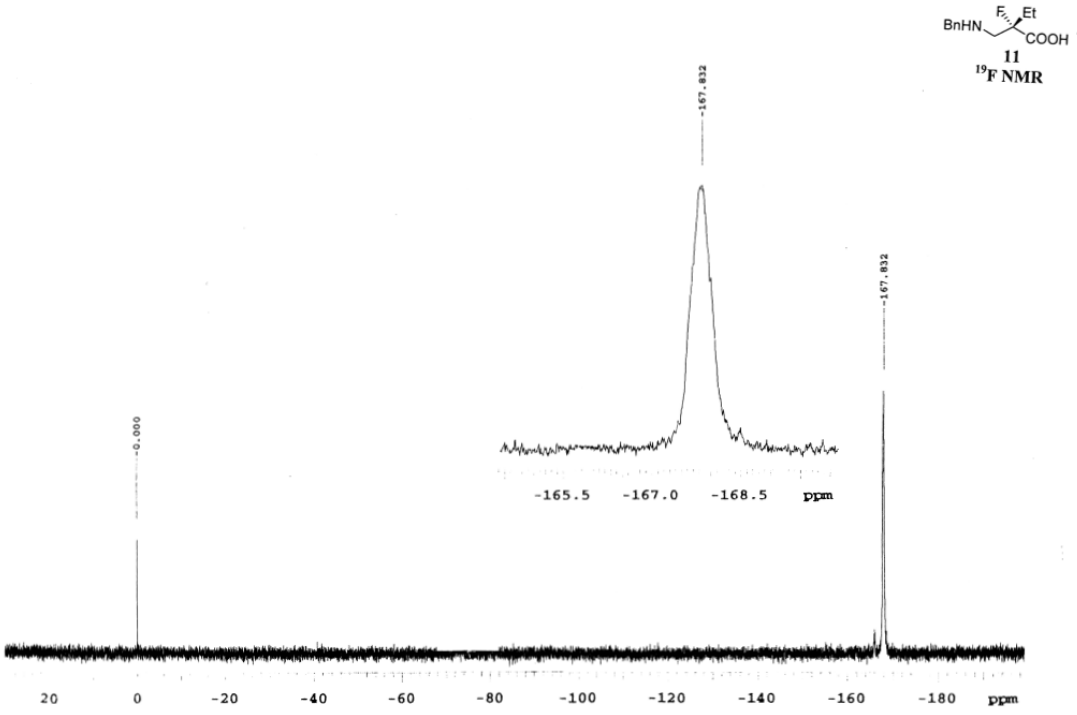

TsO
F
Et
COO^{t}Bu
9
^{13}C NMR
166.603
166.087
144.777
132.139
129.553
127.601
96.564
92.732
83.363
77.635
77.000
76.365
71.359
70.907
27.859
27.018
26.574
21.671
7.073
6.985
240
220
200
180
160
140
120
100
80
60
40
20
0 ppm

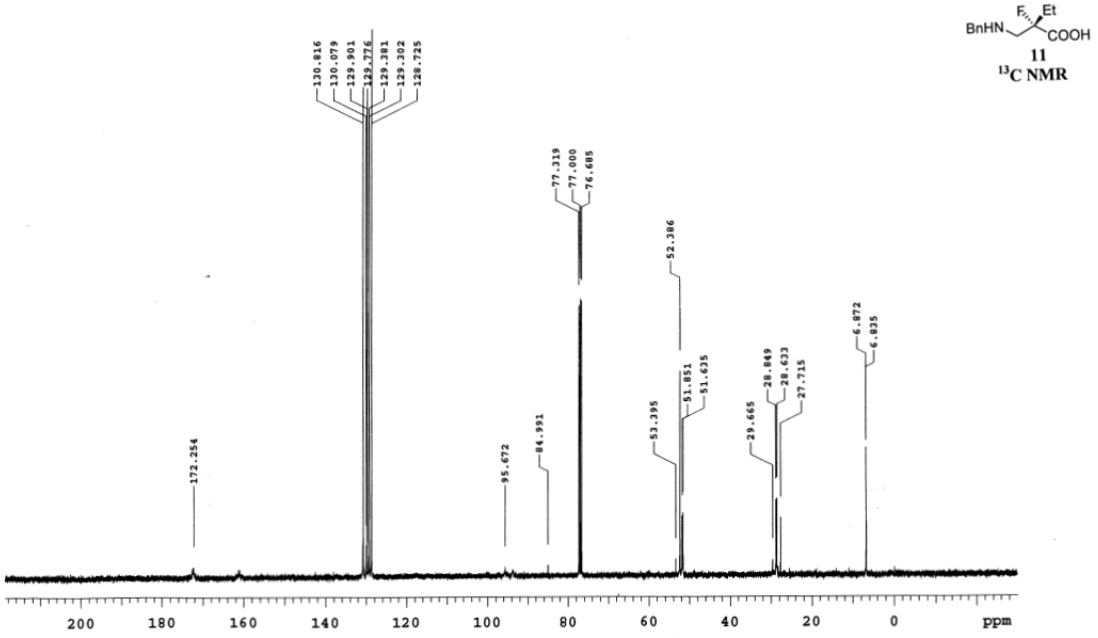

BnHN
F
Et
COO^{t}Bu
10
^{1}H NMR
7.309
7.300
7.285
7.245
3.833
3.777
3.007
2.966
2.877
1.607
1.495
0.977
0.941
0.903
0.000
8
7
6
5
4
3
2
1
-0
ppm
5.95
2.86
2.83
3.10
9.00
3.50

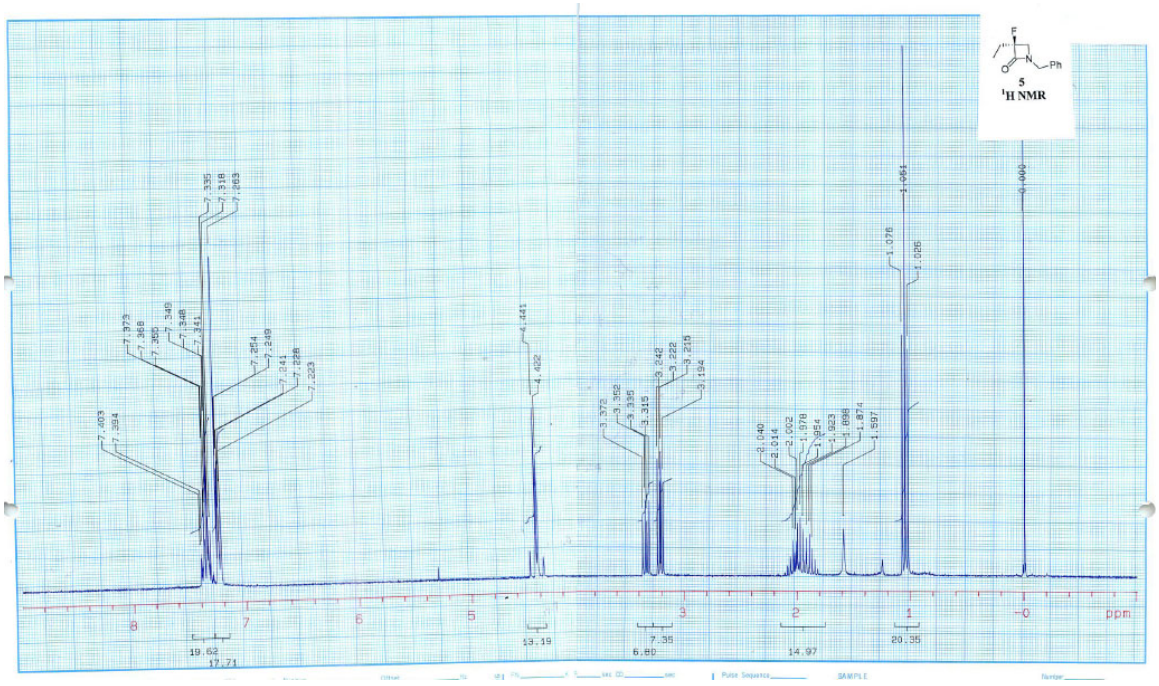

BnHN
F
Et
COO^{t}Bu
10
^{19}F NMR
-170.076
-170.202
-170.307
-170.412
-170.538
0.000
-169.0 -169.5 -170.0 -171.0 ppm
20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 ppm

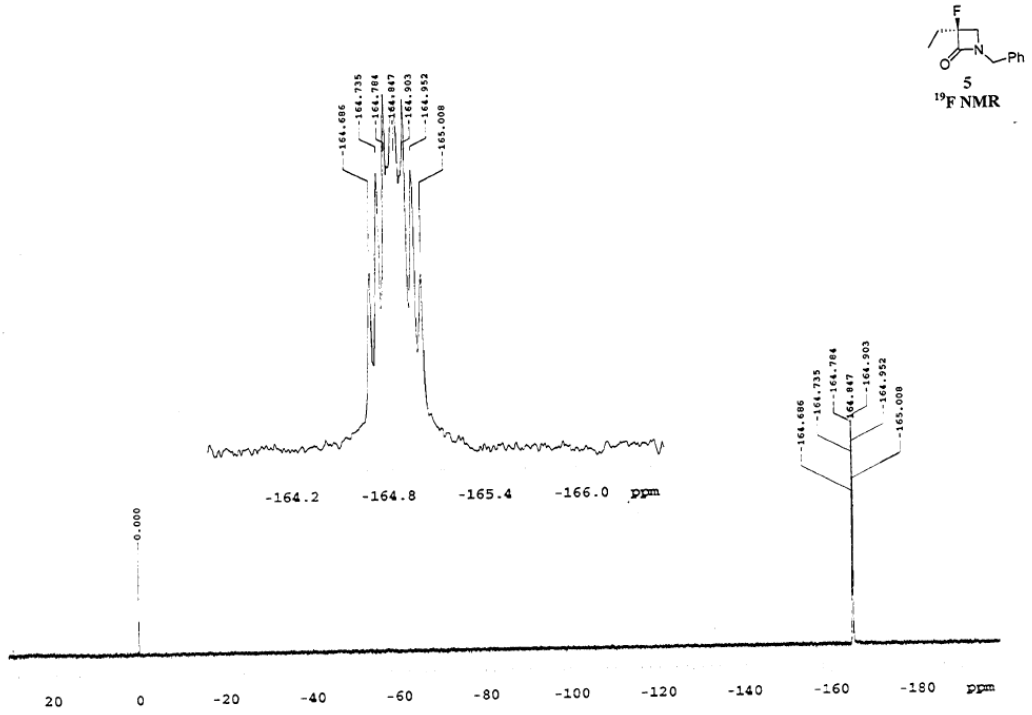

BnHN
F
Et
COO^{t}Bu
10
^{13}C NMR
169.538
169.015
139.835
127.966
127.688
126.585
100.047
96.358
81.879
77.635
77.000
76.365
54.651
54.230
53.731
28.668
28.316
28.121
7.493
7.406
240 220 200 180 160 140 120 100 80 60 40 20 0 ppm

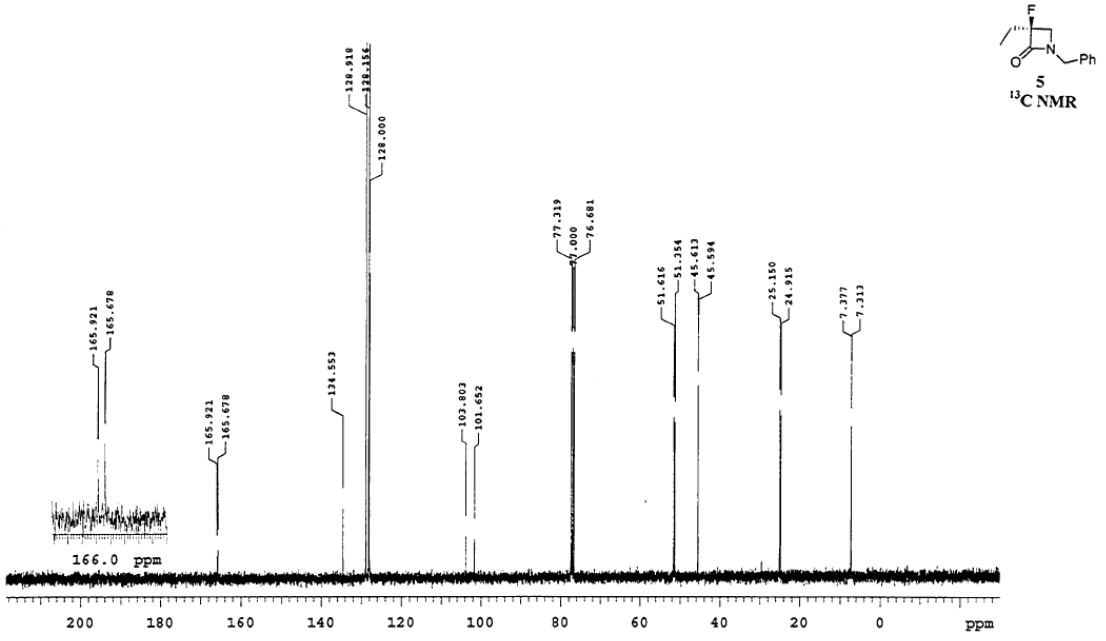

BnHN
F
Et
COOH
11
1H NMR
9.002
7.440
7.417
7.405
7.348
7.322
7.294
7.269
7.247
4.365
4.302
4.219
4.155
3.469
3.401
3.318
3.254
3.170
3.146
3.108
1.853
1.857
1.822
1.780
1.741
1.706
1.665
1.623
1.588
1.550
1.458
1.252
0.911
0.913
0.875
0.819
0.783
0.747
-0.000
10
9
8
7
6
5
4
3
2
1
-0
ppm
3.95
5.54
2.42
2.59
2.75
3.00

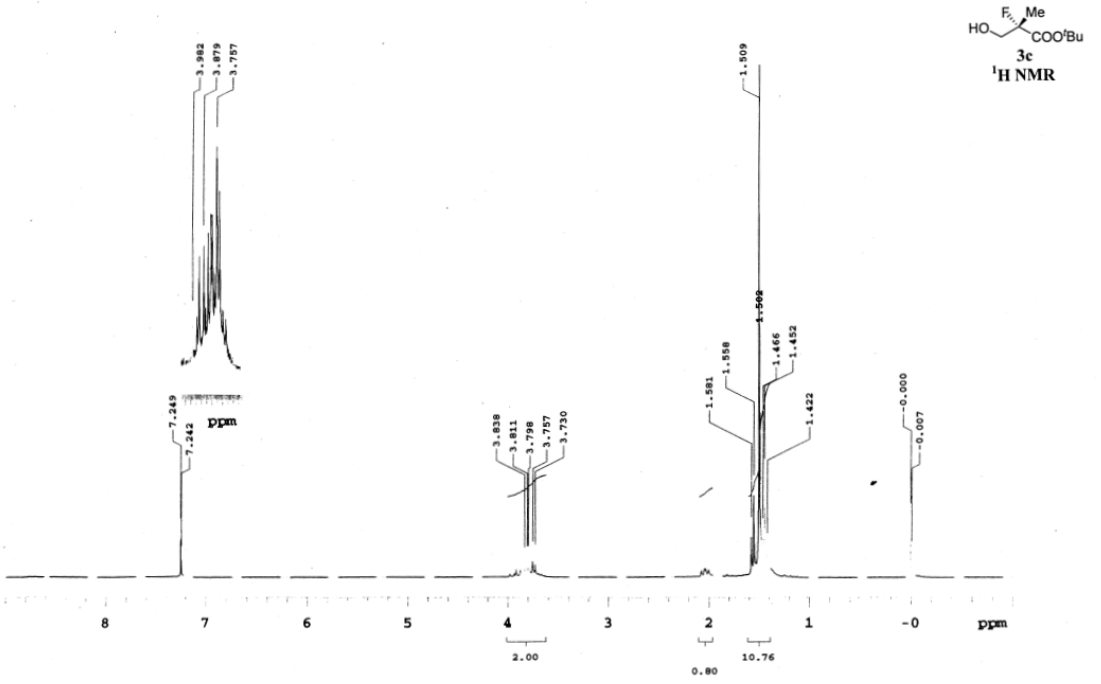

BnHN
F
Et
COOH
11
19F NMR
-167.832
-167.832
-0.000
-165.5
-167.0
-168.5
ppm
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

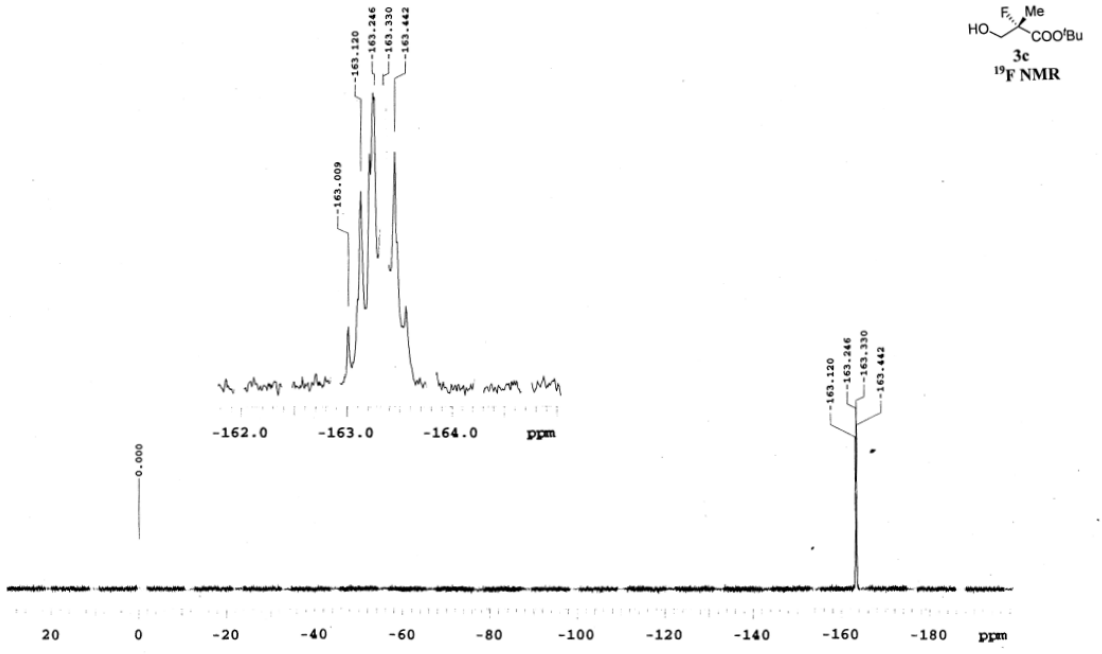

F
Et
BnHN
COOH
11
13C NMR
130.816
130.079
129.901
129.776
129.381
129.302
128.725
77.319
77.000
76.685
52.386
51.851
51.635
53.395
29.665
28.849
28.623
27.715
6.872
6.835
95.672
84.991
172.254
200
180
160
140
120
100
80
60
40
20
0
ppm

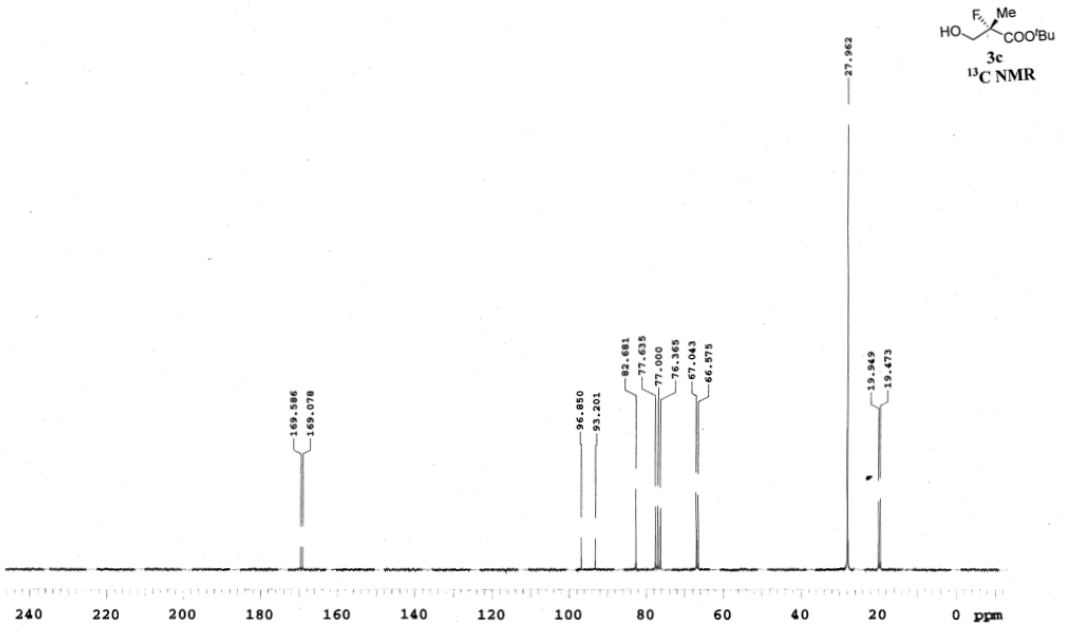

F
N
O
Ph
5
1H NMR
7.335
7.318
7.269
7.373
7.366
7.305
7.349
7.348
7.341
7.264
7.249
7.241
7.228
7.223
7.403
7.394
4.441
4.402
3.372
3.362
3.335
3.315
3.242
3.222
3.205
3.184
2.040
2.014
2.002
1.978
1.954
1.923
1.898
1.874
1.597
1.061
1.026
0.000
8
7
6
5
4
3
2
1
0
ppm
19.62
17.71
13.19
7.38
6.80
14.97
20.35

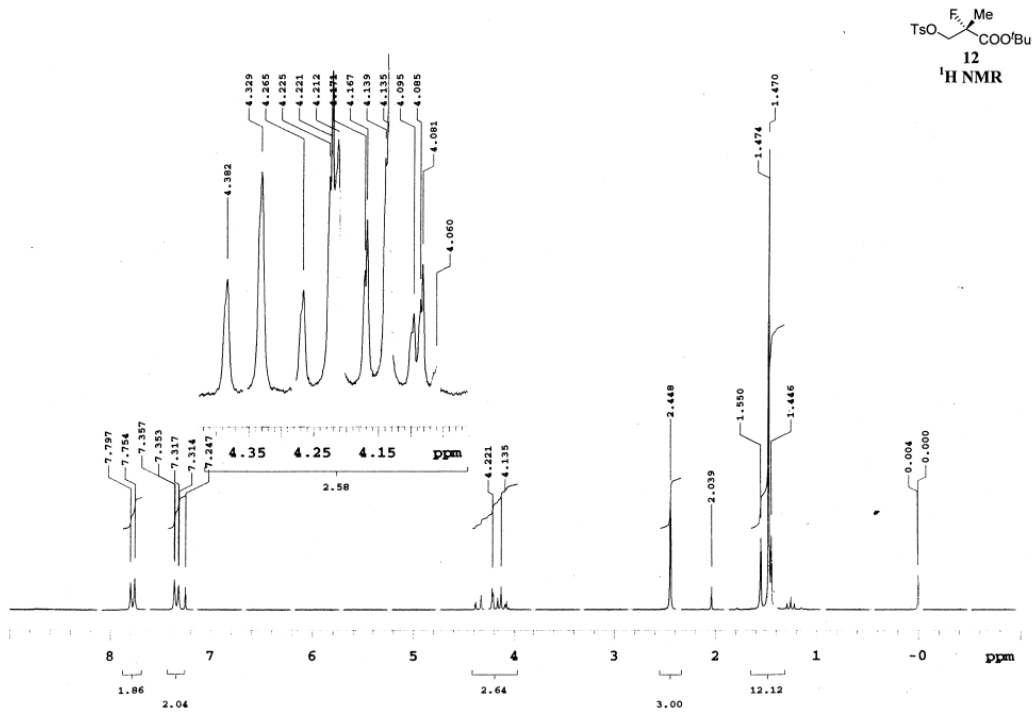

F
N
Ph
O
5
19F NMR
-164.686
-164.735
-164.784
-164.847
-164.903
-164.952
-165.000
-164.2
-164.8
-165.4
-166.0
ppm
-0.000
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

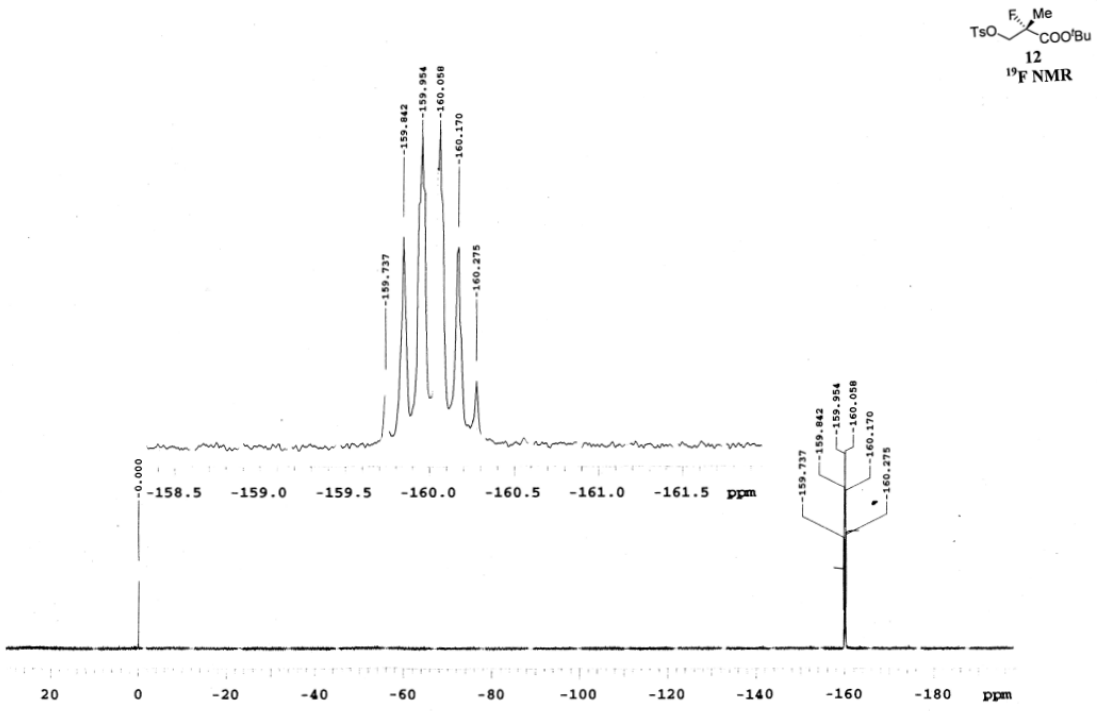

F
N
Ph
O
5
13C NMR
128.918
128.351
128.000
165.921
165.678
134.553
103.803
101.652
77.319
77.000
76.681
51.616
51.354
45.613
45.594
25.150
24.915
7.377
7.313
166.0 ppm
200
180
160
140
120
100
80
60
40
20
0
ppm

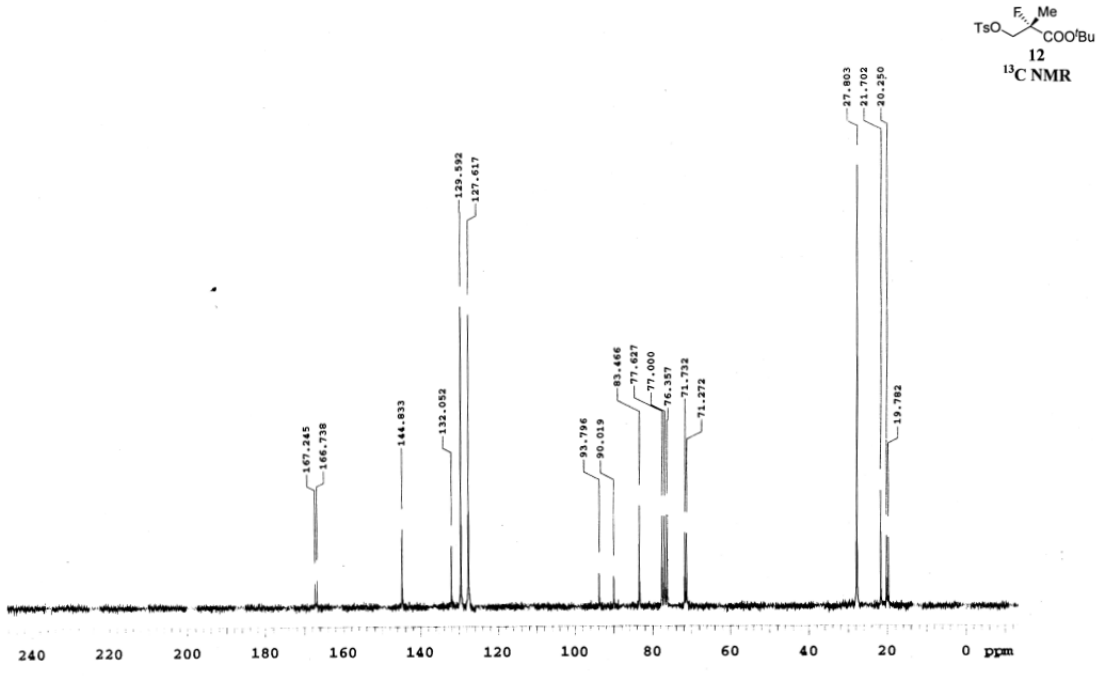

3c
1H NMR
3.982
3.879
3.757
7.249
7.242
ppm
3.838
3.811
3.798
3.757
3.730
1.581
1.558
1.509
1.466
1.452
1.422
0.000
-0.007
8
7
6
5
4
3
2
1
-0
ppm
2.00
0.80
10.76

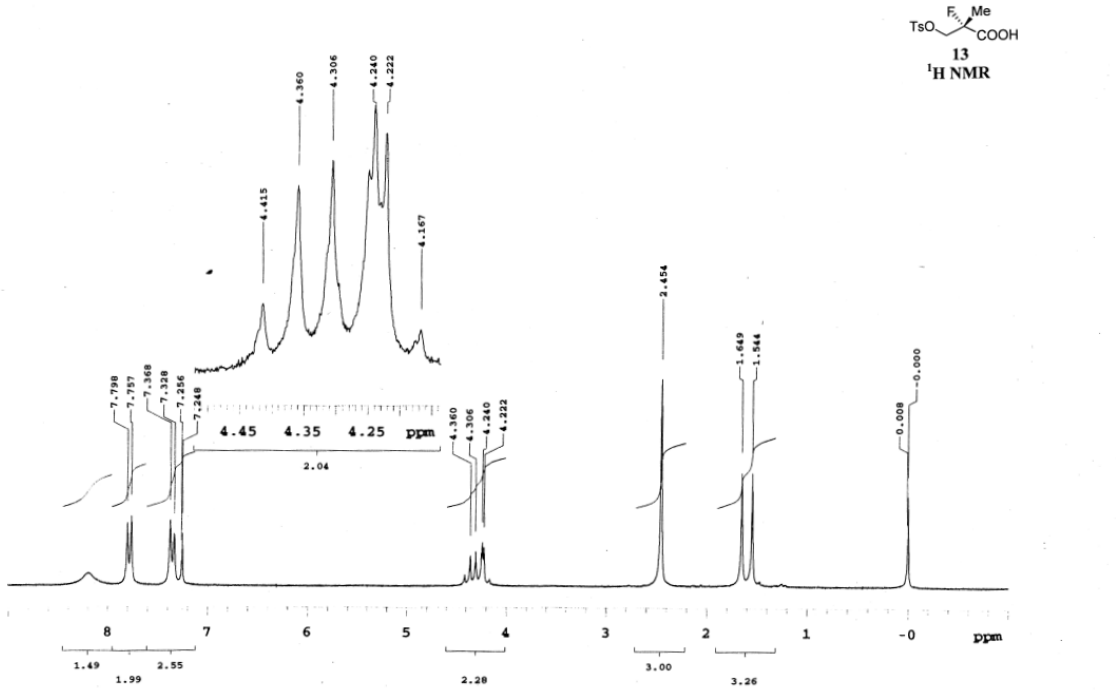

3c
19F NMR
-163.120
-163.246
-163.330
-163.442
-163.009
-162.0
-163.0
-164.0
ppm
0.000
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

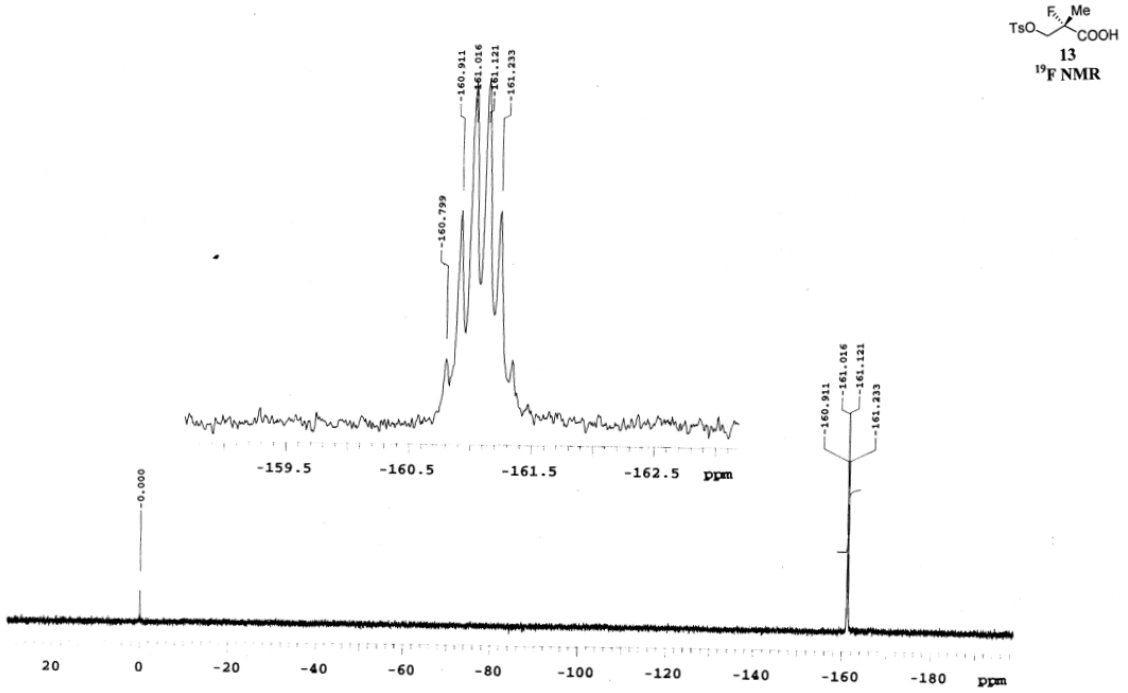

3c
^{13}C NMR
169.586
169.078
96.850
93.201
82.681
77.635
77.000
76.365
67.043
66.575
27.962
19.849
19.473
240 220 200 180 160 140 120 100 80 60 40 20 0 ppm

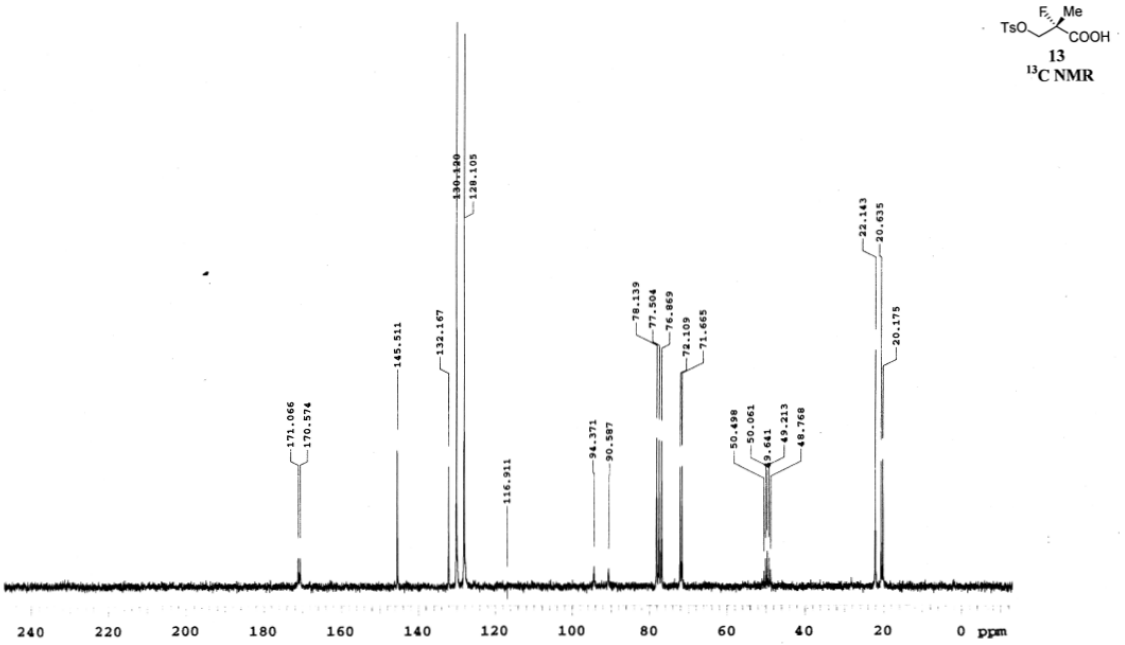

12
^{1}H NMR
4.382
4.329
4.265
4.225
4.221
4.212
4.171
4.167
4.139
4.135
4.095
4.085
4.081
4.060
4.35 4.25 4.15 ppm
2.58
7.797
7.754
7.357
7.353
7.317
7.314
7.247
4.221
4.135
2.448
2.039
1.550
1.474
1.470
1.446
0.004
0.000
8 7 6 5 4 3 2 1 -0 ppm
1.86
2.04
2.64
3.00
12.12

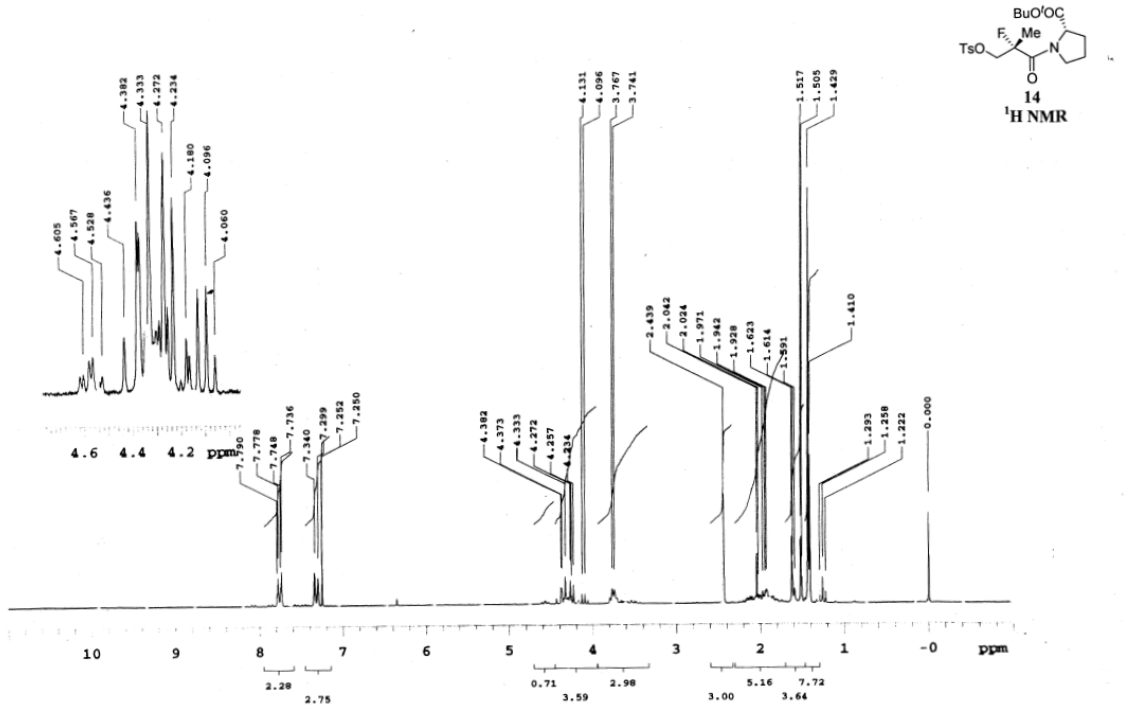

F
Me
TsO
COO^{t}Bu
12
^{19}F NMR
-159.737
-159.842
-159.954
-160.058
-160.170
-160.275
-0.000
-158.5
-159.0
-159.5
-160.0
-160.5
-161.0
-161.5
ppm
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

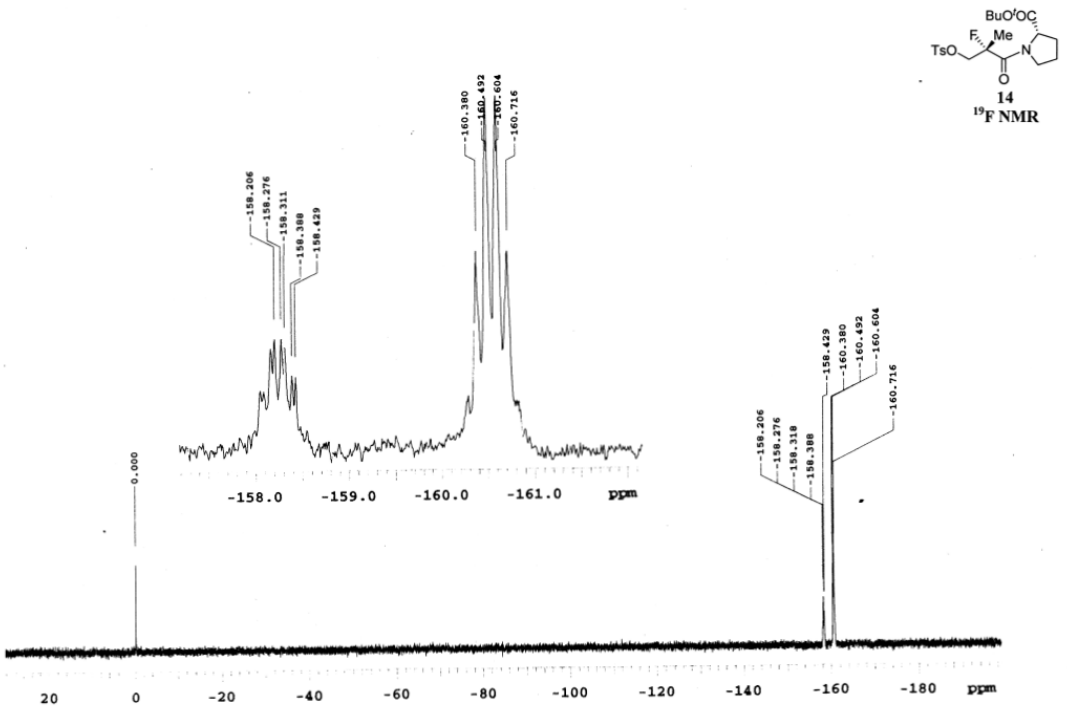

F
Me
TsO
COO^{t}Bu
12
^{13}C NMR
167.245
166.738
144.833
132.052
129.592
127.617
93.796
90.019
83.466
77.627
77.000
76.357
71.732
71.272
27.803
21.702
20.250
19.782
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm

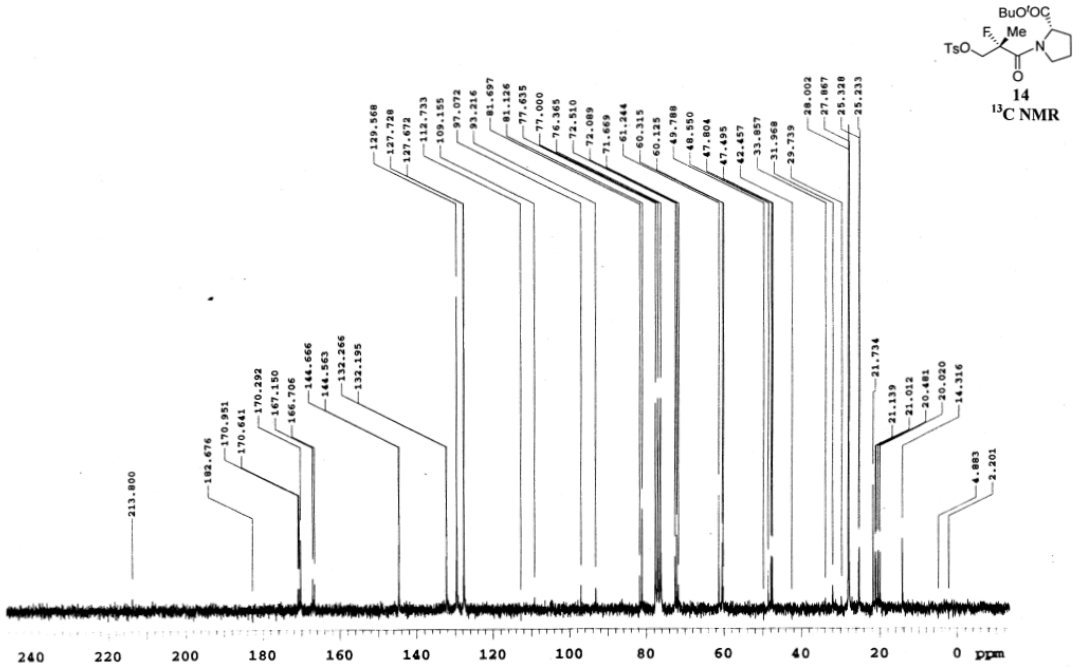

TsO
F
Me
COOH
13
1H NMR
4.415
4.360
4.306
4.240
4.222
4.167
2.454
1.649
1.544
0.008
0.000
7.798
7.757
7.368
7.328
7.256
7.248
4.45 4.35 4.25 ppm
2.04
8 7 6 5 4 3 2 1 -0 ppm
1.49
2.55
1.99
2.28
3.00
3.26

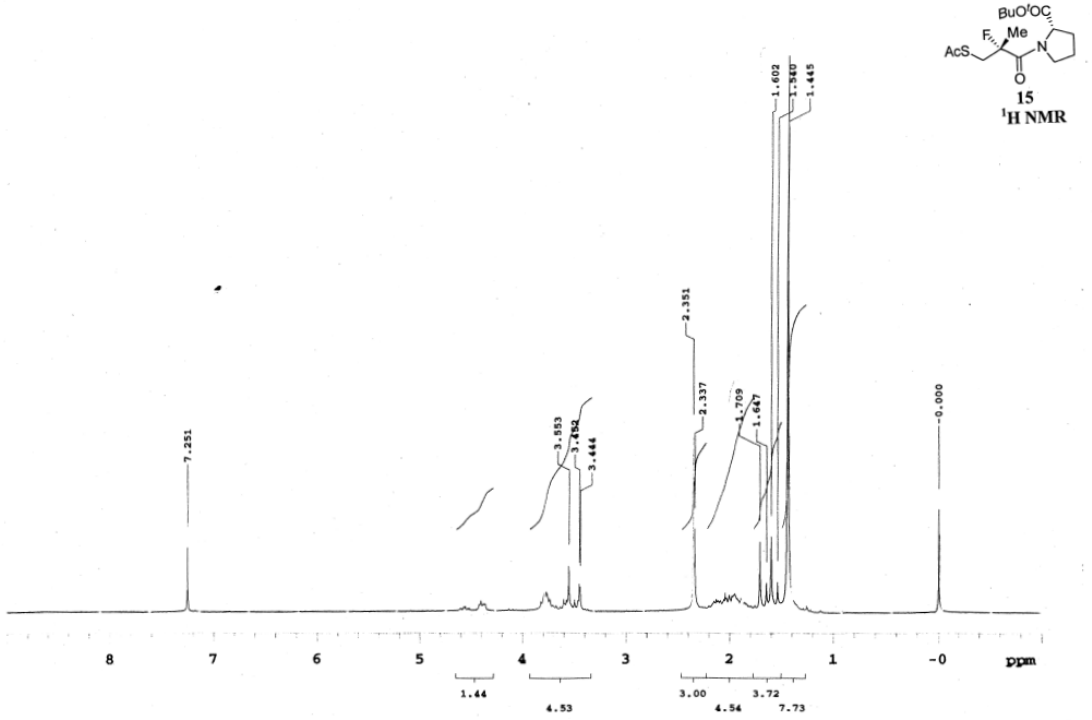

TsO
F
Me
COOH
13
19F NMR
-160.911
-161.016
-161.121
-161.233
-160.799
-159.5 -160.5 -161.5 -162.5 ppm
-0.000
20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 ppm

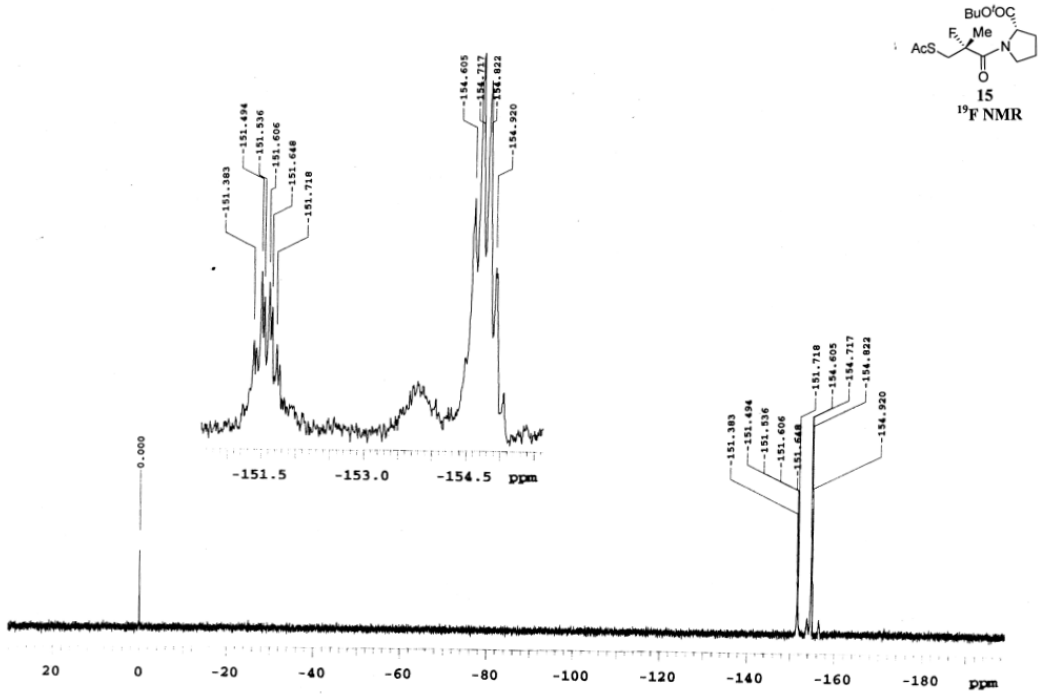

13
^{13}C NMR
171.066
170.574
145.511
132.167
130.490
130.105
116.911
94.371
90.587
78.139
77.504
76.869
72.109
71.665
50.498
50.061
49.641
49.213
48.768
22.143
20.635
20.175
240 220 200 180 160 140 120 100 80 60 40 20 0 ppm

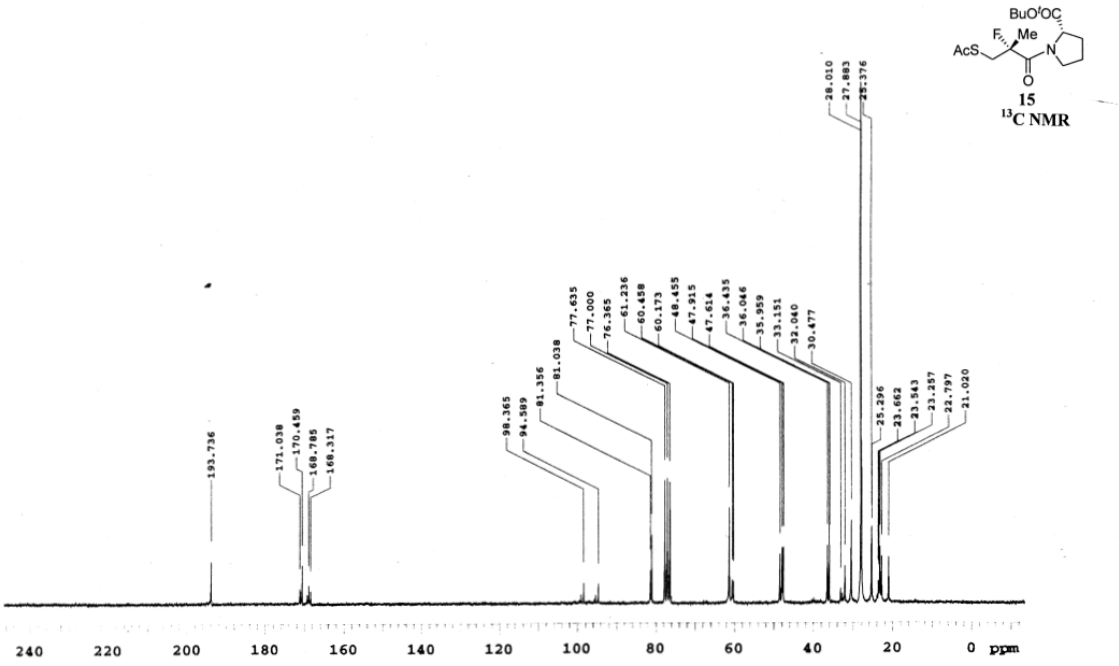

14
^{1}H NMR
4.605
4.567
4.528
4.436
4.382
4.333
4.272
4.234
4.180
4.096
4.060
4.6 4.4 4.2 ppm
7.790
7.778
7.748
7.736
7.340
7.299
7.252
7.250
4.382
4.373
4.333
4.272
4.257
4.234
4.131
4.096
3.767
3.741
2.439
2.042
2.024
1.971
1.942
1.928
1.623
1.614
1.591
1.517
1.505
1.429
1.410
1.293
1.258
1.222
0.000
10 9 8 7 6 5 4 3 2 1 -0 ppm
2.28
2.75
0.71
3.59
2.98
3.00
5.16
3.64
7.72

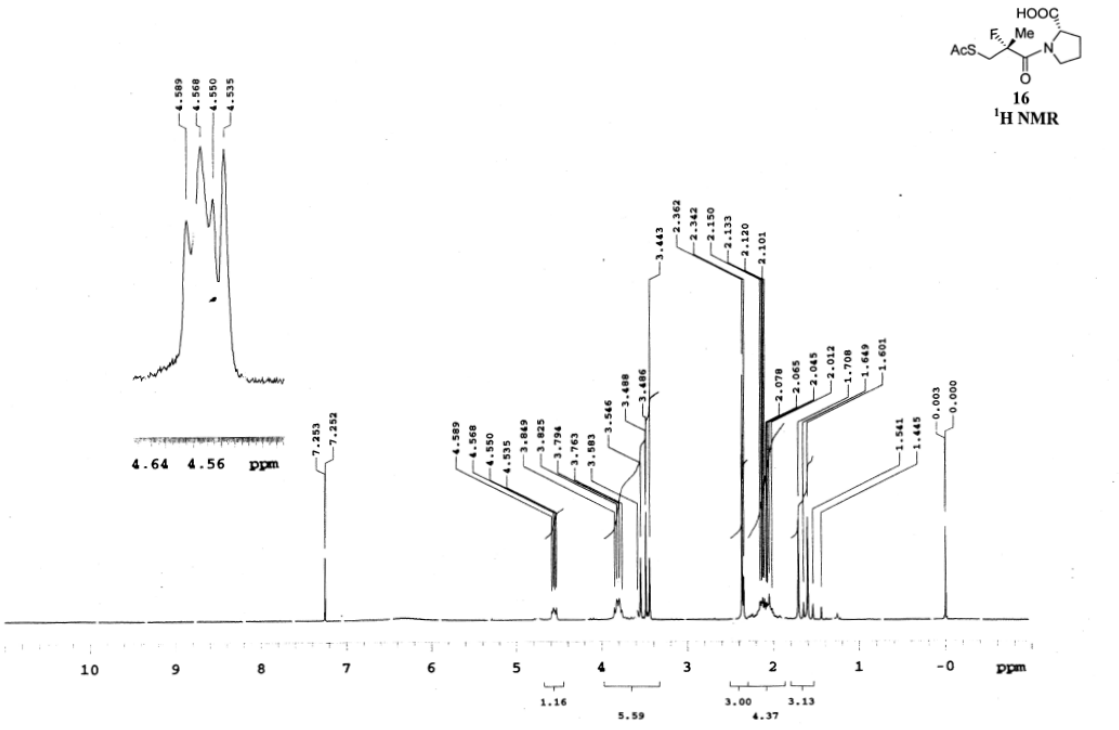

BuO^{t}OC
F
Me
TsO
N
O
14
^{19}F NMR
-158.206
-158.276
-158.311
-158.388
-158.429
-160.380
-160.492
-160.604
-160.716
0.000
-158.0
-159.0
-160.0
-161.0
ppm
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

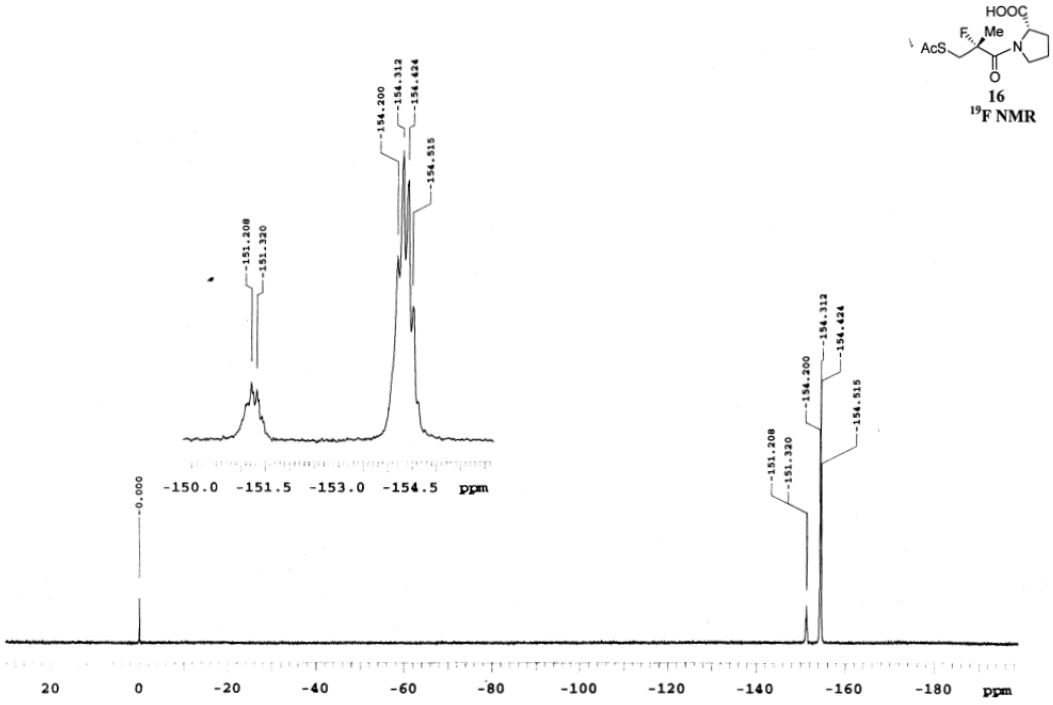

BuO^{t}OC
F
Me
TsO
N
O
14
^{13}C NMR
213.800
182.676
170.951
170.641
170.292
167.150
166.706
144.666
144.563
132.266
132.195
129.568
127.728
127.672
112.733
109.155
97.072
93.216
81.697
81.126
77.635
77.000
76.365
72.510
72.089
71.669
61.244
60.315
60.125
49.788
49.550
47.804
47.495
42.457
33.857
31.968
29.739
28.002
27.867
25.328
25.233
21.734
21.139
21.012
20.481
20.020
14.316
4.883
2.201
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm


BuO^{t}OC
F
Me
AcS
N
O
15
^{1}H NMR
7.251
3.553
3.482
3.444
2.351
2.337
1.709
1.647
1.602
1.540
1.445
0.000
8
7
6
5
4
3
2
1
-0
ppm
1.44
4.53
3.00
4.54
3.72
7.73

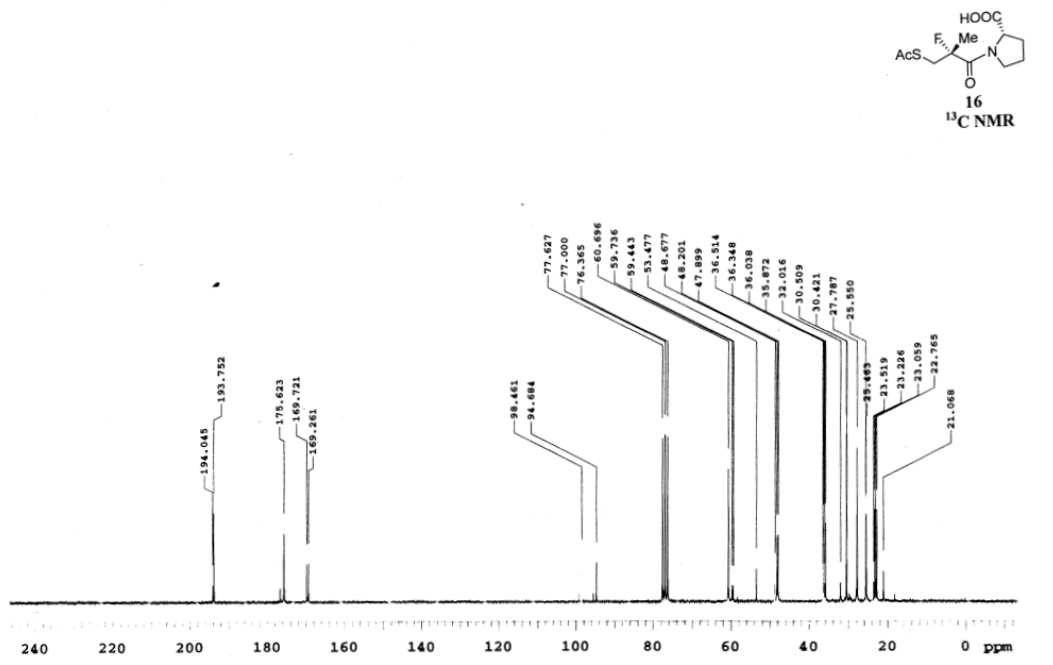

BuO^{t}OC
F
Me
AcS
N
O
15
^{19}F NMR
-151.383
-151.494
-151.536
-151.606
-151.648
-151.718
-154.605
-154.717
-154.822
-154.920
0.000
-151.5
-153.0
-154.5
ppm
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm


BuO'OC
F
Me
AcS
N
O
15
13C NMR
193.736
171.038
170.459
169.785
168.317
98.365
94.589
81.356
81.038
77.635
77.000
76.365
61.236
60.458
60.173
48.455
47.915
47.614
36.435
36.046
35.959
33.151
32.040
30.477
28.010
27.883
25.376
25.296
23.662
23.543
23.257
22.797
21.020
240 220 200 180 160 140 120 100 80 60 40 20 0 ppm

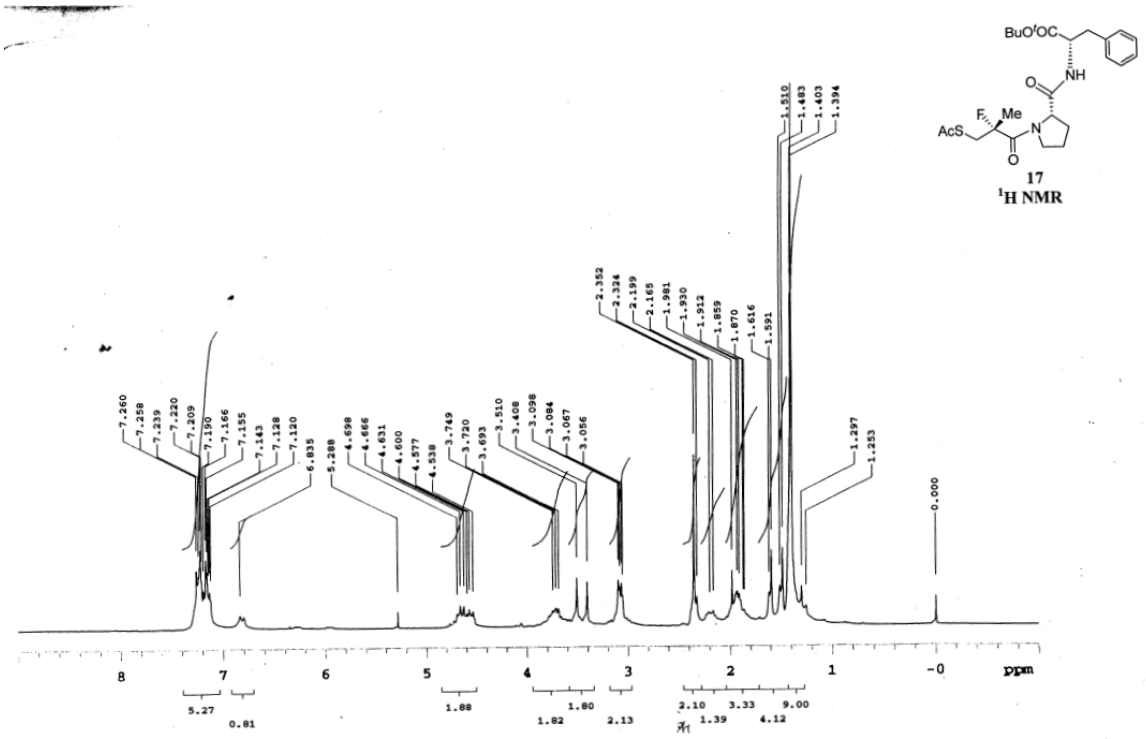

HOOC
F
Me
AcS
N
O
16
1H NMR
4.589
4.568
4.550
4.535
4.64 4.56 ppm
7.253
7.252
4.589
4.568
4.550
4.535
3.849
3.825
3.794
3.763
3.583
3.546
3.488
3.486
3.443
2.362
2.342
2.150
2.133
2.120
2.101
2.078
2.065
2.045
2.012
1.708
1.649
1.601
1.541
1.445
0.003
0.000
10 9 8 7 6 5 4 3 2 1 -0 ppm
1.16
5.59
3.00
3.13
4.37



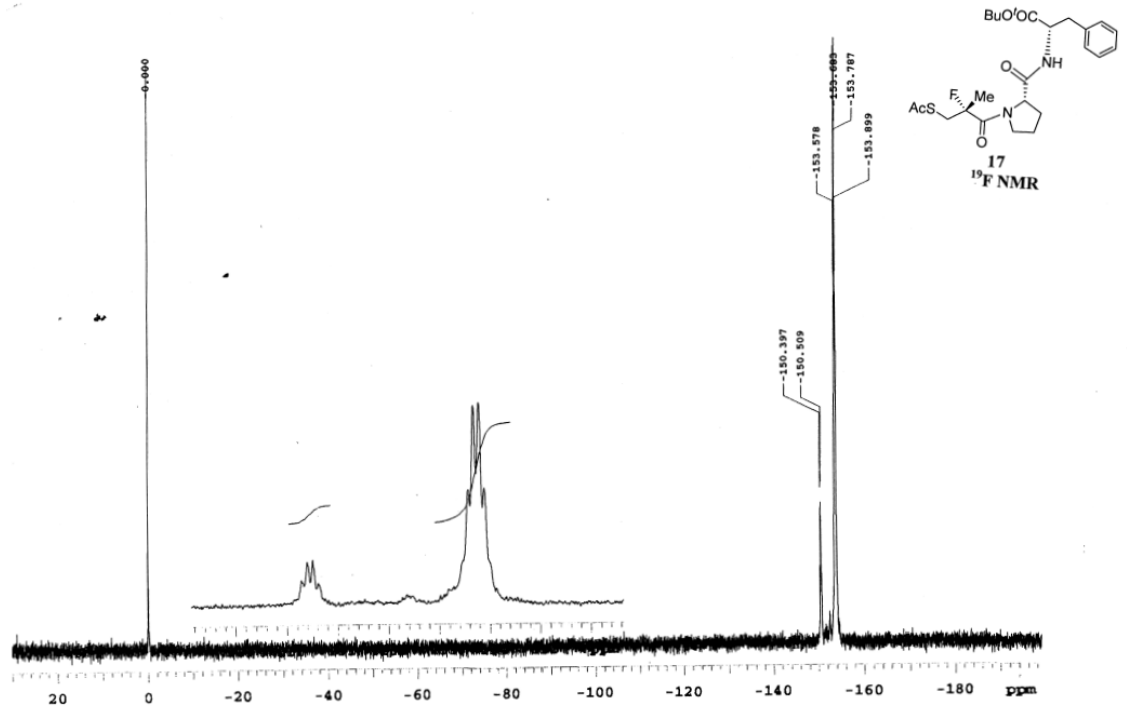
16
^{19}F NMR



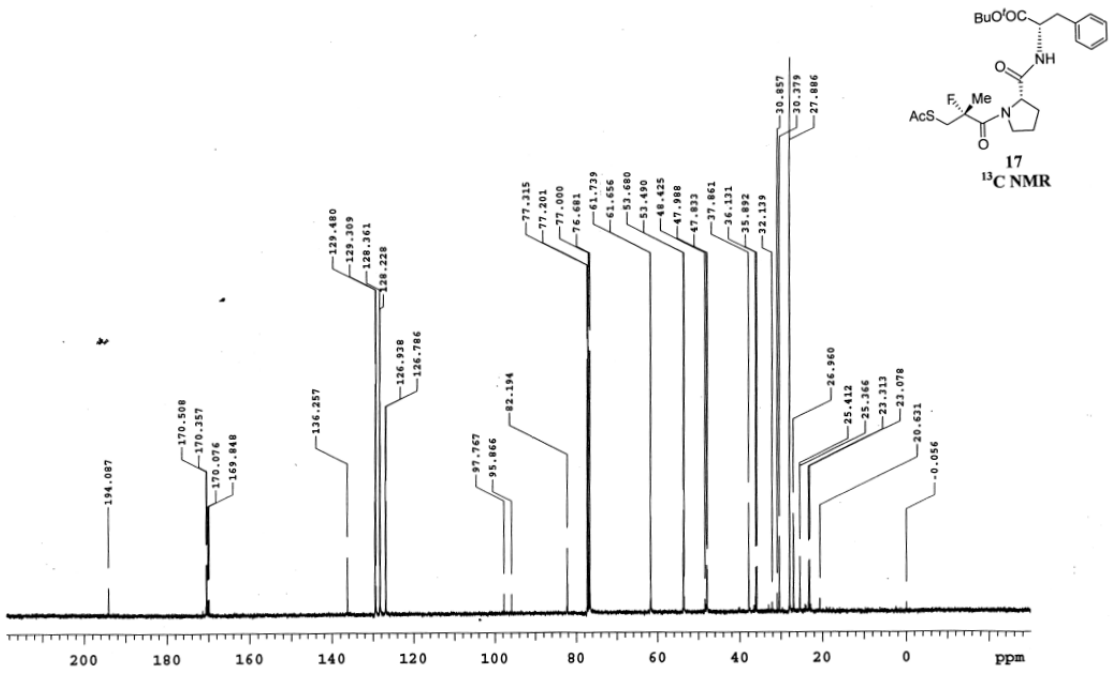
16
^{13}C NMR

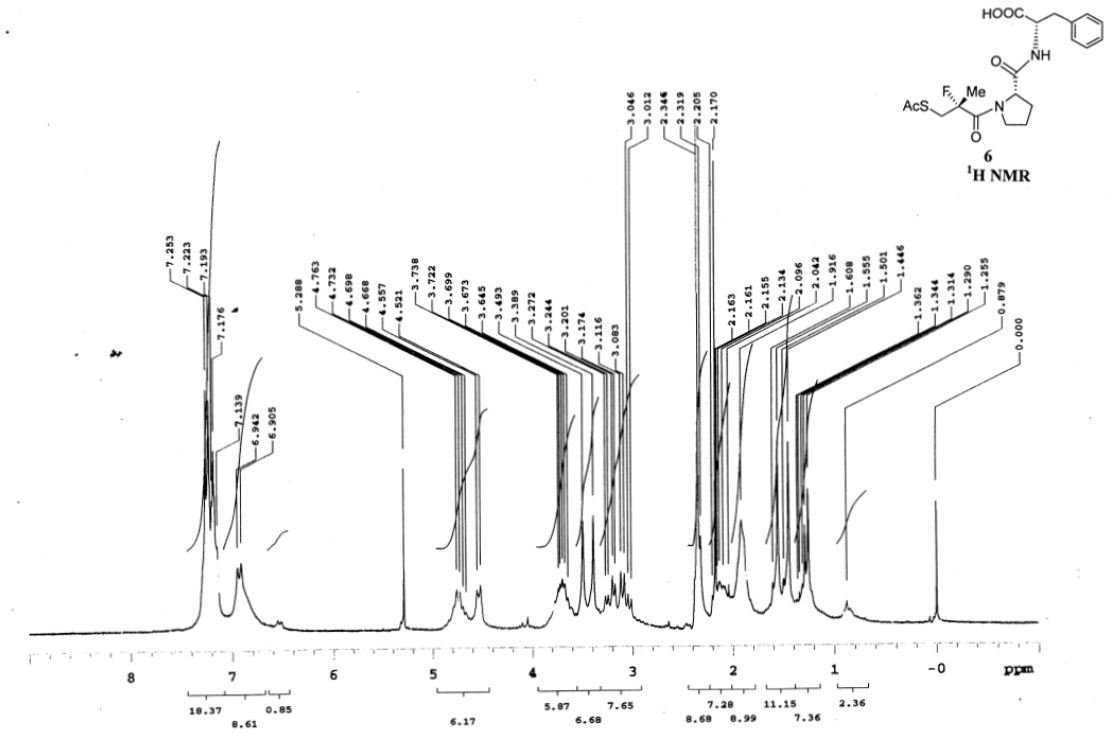


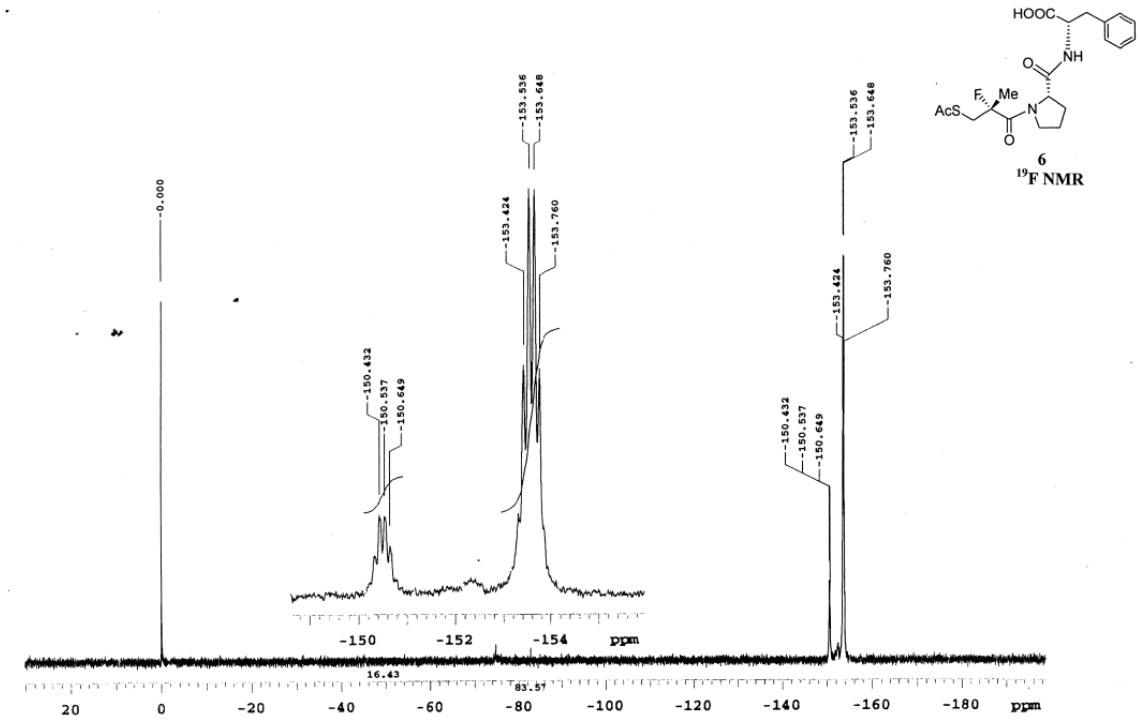
17
^{1}H NMR



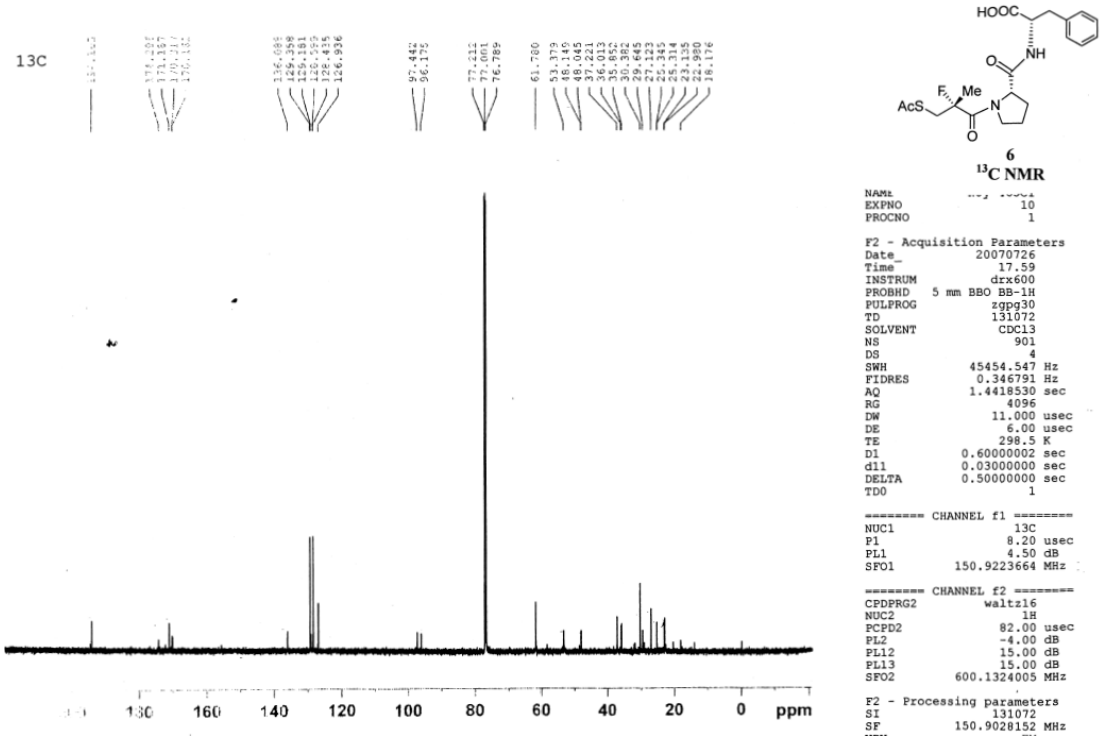
17
^{19}F NMR


BuO^{t}OC
NH
O
F
Me
AcS
N
O
17
^{13}C NMR
194.087
170.508
170.357
170.076
169.848
136.257
129.480
129.309
128.361
128.228
126.938
126.786
97.767
95.866
82.194
77.315
77.201
77.000
76.681
61.739
61.656
53.680
53.490
48.425
47.988
47.833
37.861
36.131
35.892
32.139
30.857
30.379
27.886
26.960
25.412
25.366
23.313
23.078
20.631
-0.056
200
180
160
140
120
100
80
60
40
20
0
ppm


HOOC
NH
O
F
Me
AcS
N
O
6
^{1}H NMR
7.253
7.223
7.193
7.176
7.139
6.942
6.905
5.288
4.763
4.732
4.698
4.668
4.557
4.521
3.738
3.722
3.699
3.673
3.645
3.493
3.389
3.272
3.244
3.201
3.174
3.116
3.083
3.046
3.012
2.346
2.319
2.205
2.170
2.163
2.161
2.155
2.134
2.096
2.042
1.916
1.608
1.555
1.501
1.446
1.362
1.344
1.314
1.290
1.255
0.879
0.000
8
7
6
5
4
3
2
1
-0
ppm
10.37
0.85
8.61
6.17
5.87
7.65
6.68
7.28
8.68
8.99
11.15
7.36
2.36



6
^{19}F NMR



6
^{13}C NMR

```
NAME                 ----- -----
EXPNO                   10
PROCNO                   1

F2 - Acquisition Parameters
Date_                20070726
Time                    17.59
INSTRUM                drx600
PROBHD    5 mm BBO BB-1H
PULPROG                zgpg30
TD                     131072
SOLVENT                 CDCl3
NS                        901
DS                          4
SWH                 45454.547 Hz
FIDRES                0.346791 Hz
AQ                  1.4418530 sec
RG                       4096
DW                     11.000 usec
DE                      6.00 usec
TE                     298.5 K
D1                 0.60000002 sec
d11                0.03000000 sec
DELTA              0.50000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                      8.20 usec
PL1                     4.50 dB
SFO1               150.9223664 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                  82.00 usec
PL2                    -4.00 dB
PL12                   15.00 dB
PL13                   15.00 dB
SFO2               600.1324005 MHz

F2 - Processing parameters
SI                      131072
SF                 150.9028152 MHz
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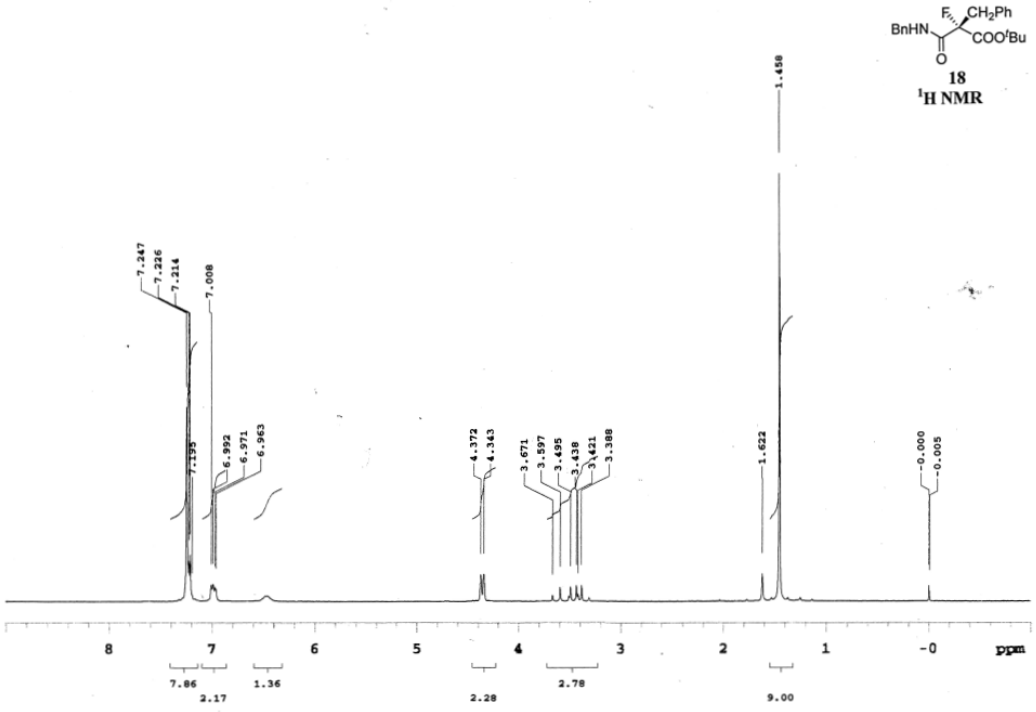
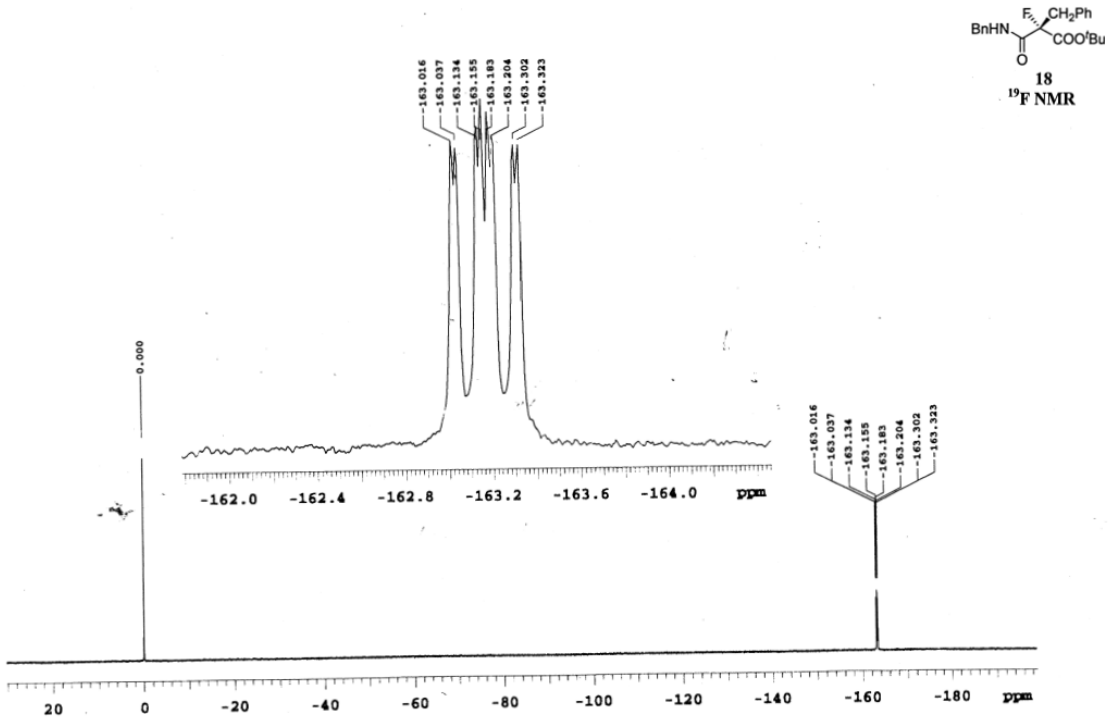
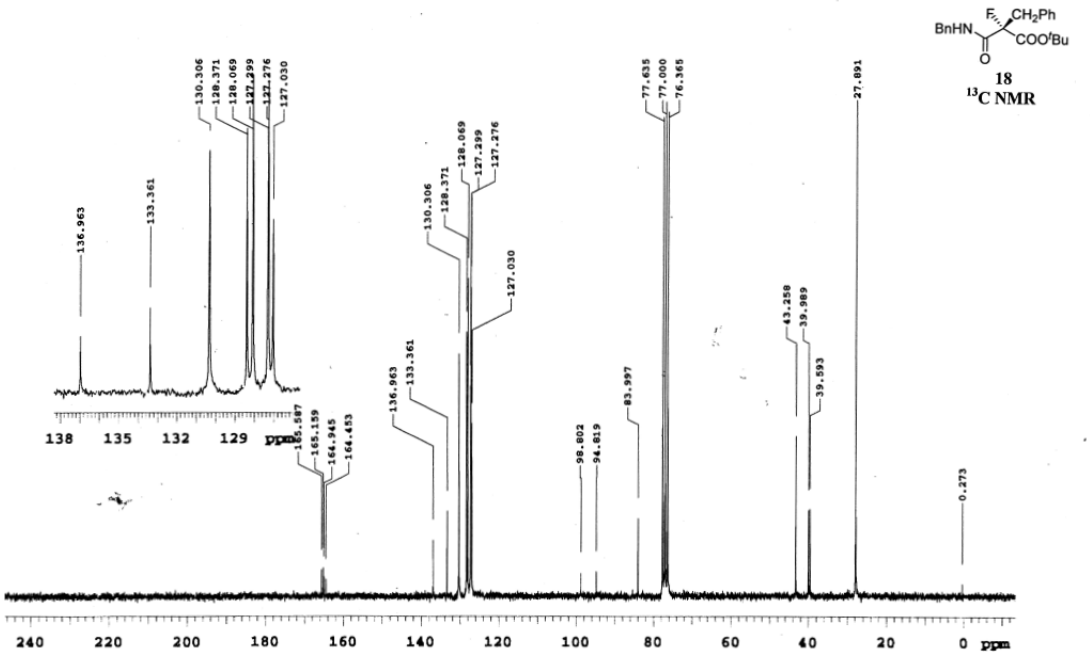
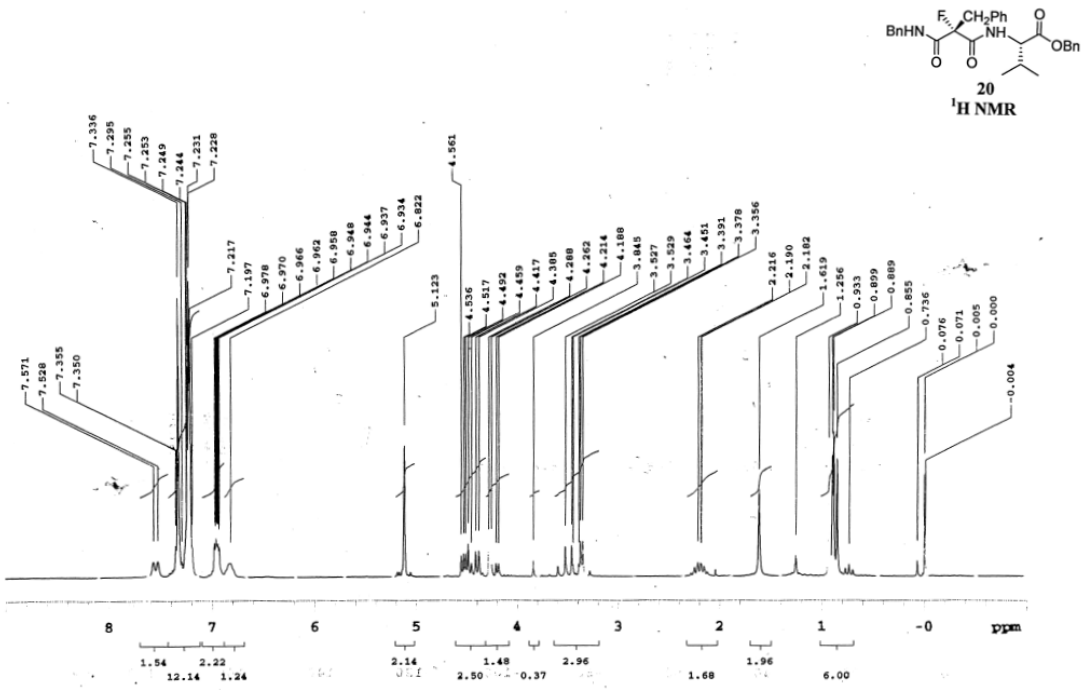
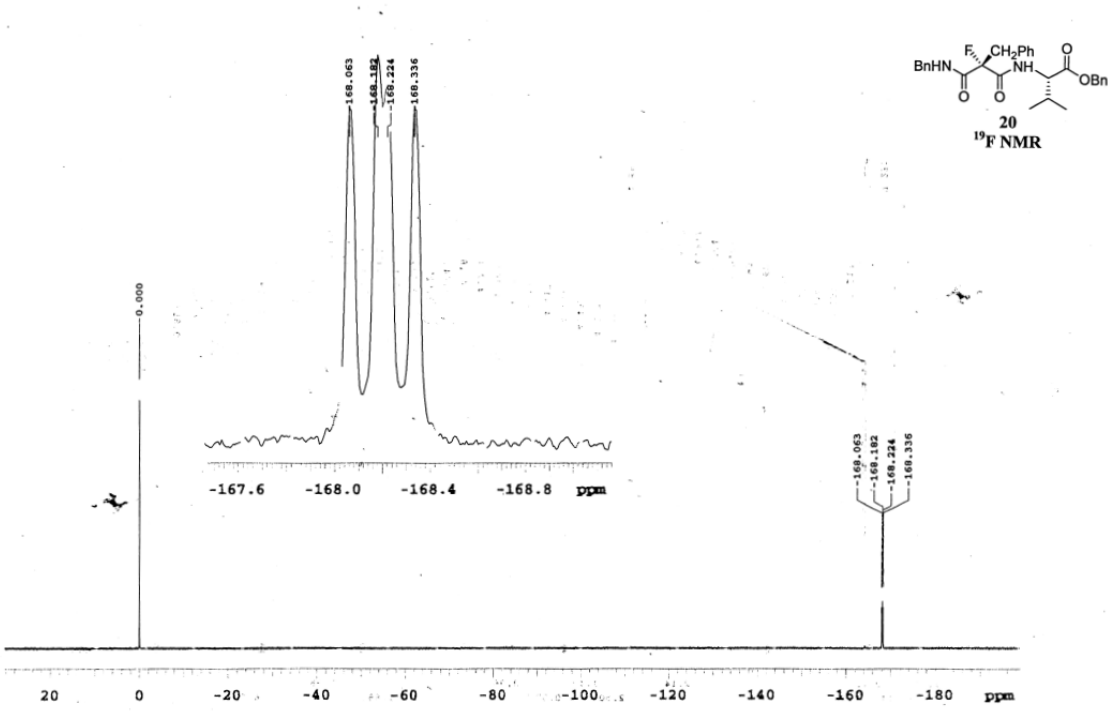
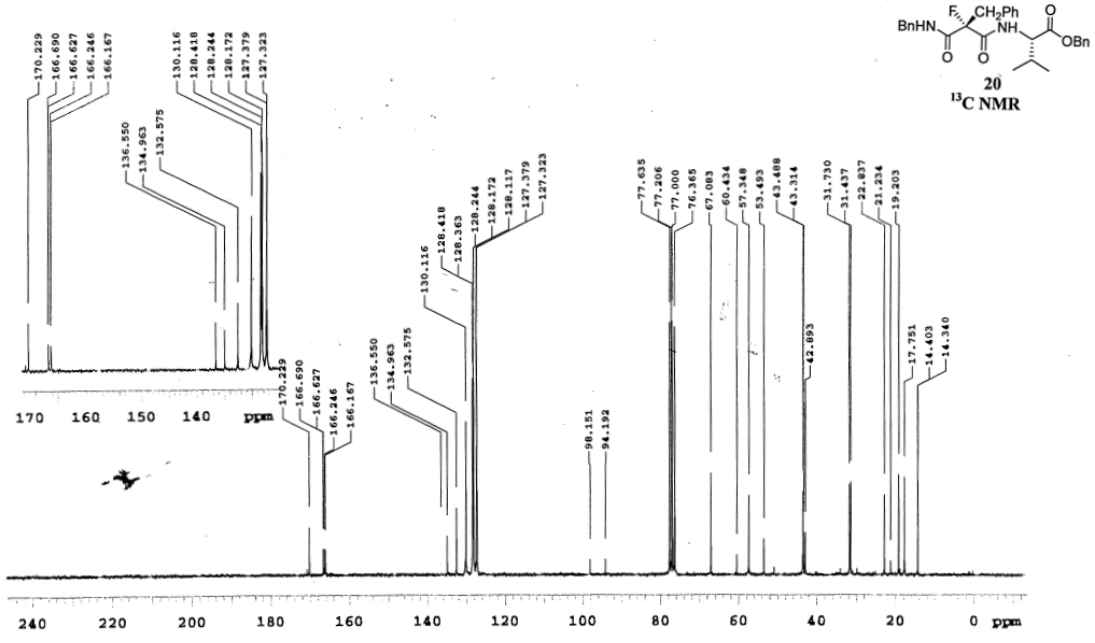

18
^{1}H NMR
7.247
7.226
7.214
7.008
7.195
6.992
6.971
6.963
4.372
4.343
3.671
3.597
3.495
3.438
3.421
3.388
1.622
1.458
0.000
-0.005
8
7
6
5
4
3
2
1
-0
ppm
7.86
2.17
1.36
2.28
2.78
9.00

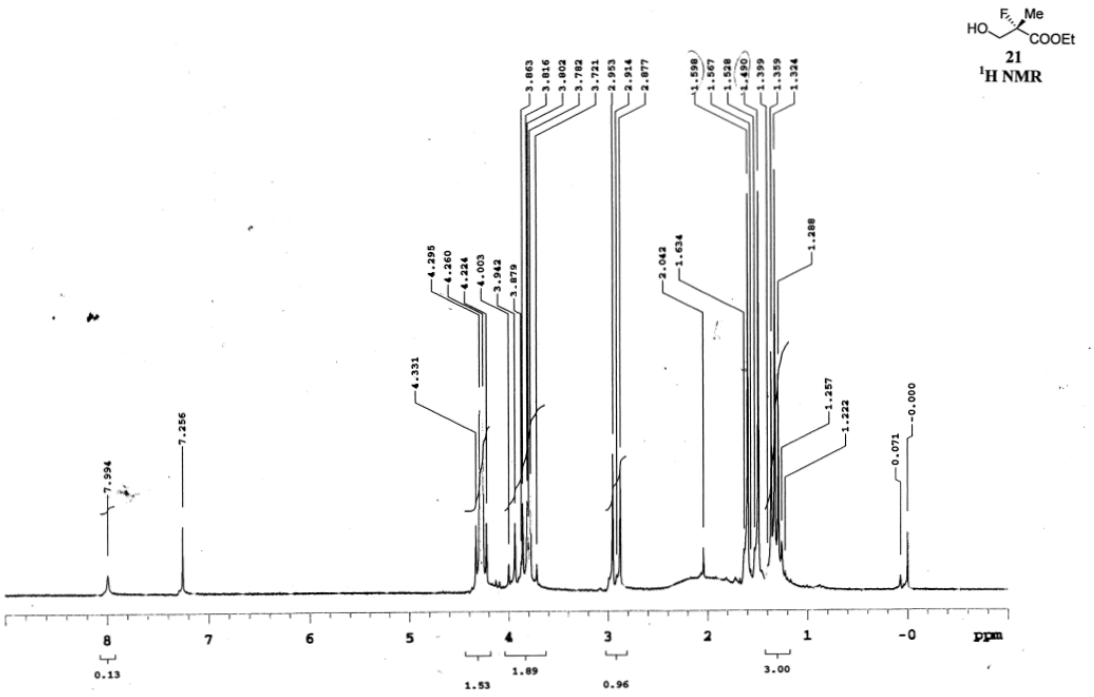

18
^{19}F NMR
-163.016
-163.037
-163.134
-163.155
-163.183
-163.204
-163.302
-163.323
0.000
-162.0
-162.4
-162.8
-163.2
-163.6
-164.0
ppm
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

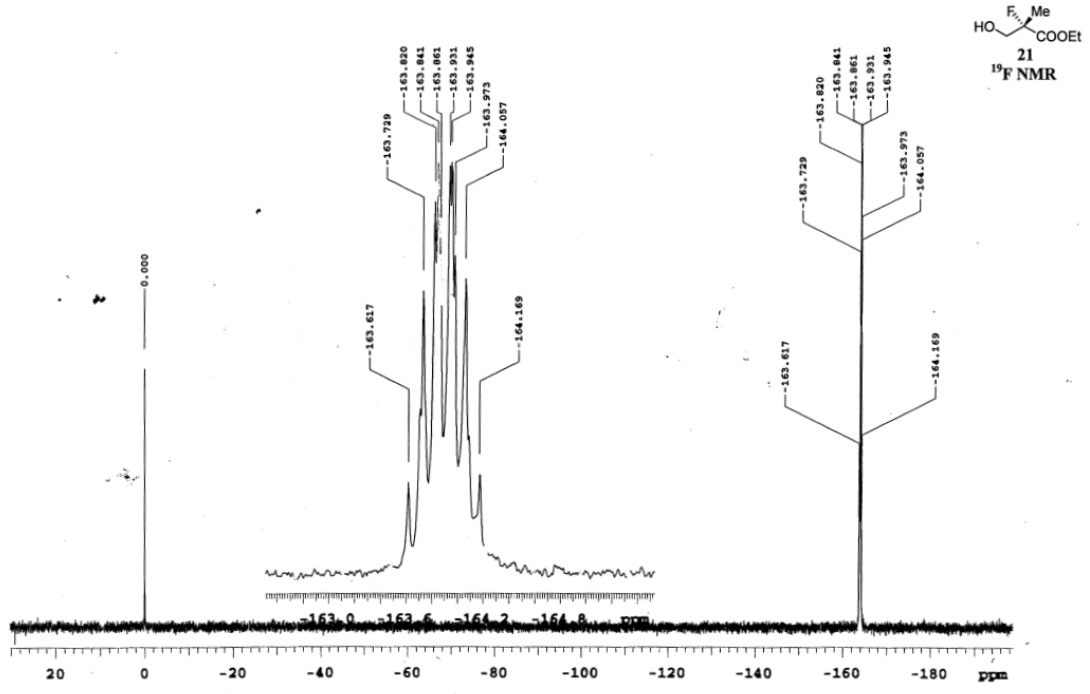

BnHN
F
CH2Ph
COO'Bu
18
13C NMR
240 220 200 180 160 140 120 100 80 60 40 20 0 ppm

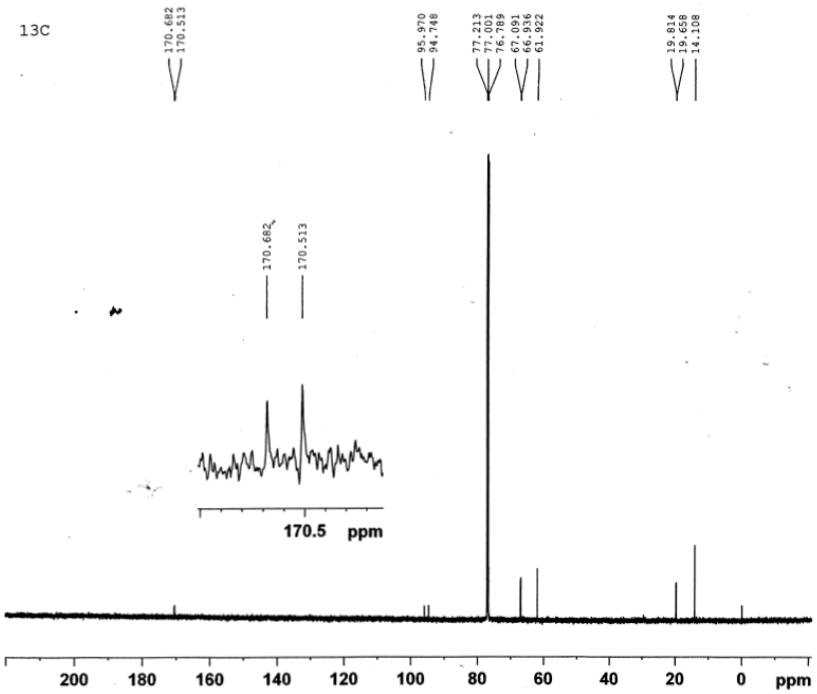

BnHN
F
CH2Ph
NH
OBn
20
1H NMR
8 7 6 5 4 3 2 1 -0 ppm

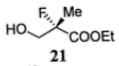

BnHN
F
CH2Ph
NH
OBn
20
19F NMR
168.063
168.182
168.224
168.336
0.000
-167.6
-168.0
-168.4
-168.8
ppm
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm


BnHN
F
CH2Ph
NH
OBn
20
13C NMR
170.229
166.690
166.627
166.246
166.167
136.550
134.963
132.575
130.116
128.418
128.244
128.172
127.379
127.323
77.635
77.206
77.000
76.365
67.083
60.434
57.348
53.493
43.488
43.314
42.893
31.730
31.437
22.837
21.234
19.203
17.751
14.403
14.340
98.151
94.192
170
160
150
140
ppm
240
220
200
180
160
140
120
100
80
60
40
20
0
ppm


21
^{1}H NMR
7.994
7.256
4.331
4.295
4.260
4.224
4.003
3.942
3.879
3.863
3.816
3.802
3.782
3.721
2.953
2.914
2.877
2.042
1.634
1.598
1.567
1.528
1.488
1.399
1.359
1.324
1.288
1.257
1.222
0.071
-0.000
ppm
0.13
1.53
1.89
0.96
3.00


21
^{19}F NMR
0.000
-163.617
-163.729
-163.820
-163.841
-163.861
-163.931
-163.945
-163.973
-164.057
-164.169
ppm





21
^{13}C NMR

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Current Data Parameters
NAME                  NJy-477C
EXPNO                       10
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20070726
Time                     18.48
INSTRUM                  drx600
PROBHD   5 mm BBO BB-1H
PULPROG                 zgpg30
TD                      131072
SOLVENT                    CDC13
NS                          1001
DS                             4
SWH                  45454.547 Hz
FIDRES                0.346791 Hz
AQ                    1.4418530 sec
RG                        16384
DW                       11.000 usec
DE                        6.00 usec
TE                       298.5 K
D1                    0.60000002 sec
d11                   0.03000000 sec
DELTA                 0.50000000 sec
TD0                            1

======== CHANNEL f1 ========
NUC1                         13C
P1                          8.20 usec
PL1                         4.50 dB
SFO1                150.9223664 MHz

======== CHANNEL f2 ========
CPDPRG2                  waltz16
NUC2                          1H
PCPD2                      82.00 usec
PL2                        -4.00 dB
PL12                       15.00 dB
PL13                       15.00 dB
SFO2                600.1324005 MHz

F2 - Processing parameters
SI                          131072
SF                  150.9028103 MHz
WDW                             EM
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