Synthesis of α,α-Difluoro-β-amino Amides using Aldimines and Bromodifluoroacetamides via Reformatsky Reaction

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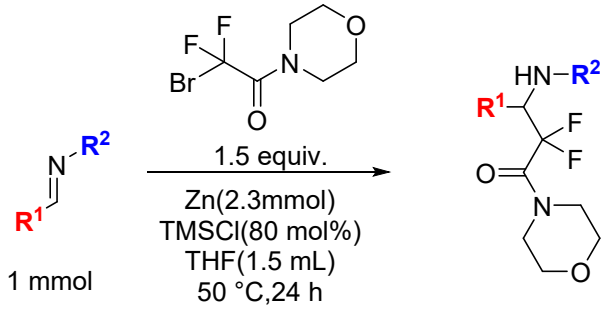
General Remarks

All reactions were carried out under an argon atmosphere. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a Brucker AVANCE III 400 spectrometer (400.15 MHz) at ambient temperature. High-resolution mass spectra were taken with a JEOL AccuTOF LC-plus 4G. Commercially available organic and inorganic compounds were used without purification. Compound **1** was prepared by adding MS4A, based on the report of L. Silverberg *et al*. [SI 1] Compounds **2** was prepared according to the literature procedures.[SI 2,3]

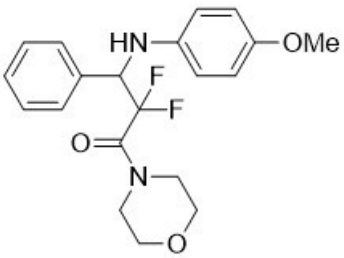
General Procedure of α,α-Difluoro-β-amino Amides



Imine **1** (1 mmol) and Zn (2.3 mmol) were charged in a 10 mL test tube sealed with a rubber septum. The test tube was evacuated and backfilled with argon. This sequence was repeated three times. Then, THF(1.5 mL), Bromoacetamide **2** (1.5 mmol) and TMSCl (150 µL, 1.19 mmol) was added via the rubber septum with syringe. In an argon flow, the rubber septum was replaced with a Teflon liner screw cap. The test tube was placed into an oil bath preheated at 50 °C. After the reaction mixtures stirred for 24 h. The reaction was carefully quenched by NH_4Cl aq. Then the mixture was extracted with AcOEt and the extract was washed with $NaHCO_3$, brine and dried over Na_2SO4. Then the extract was concentrated in vaquo, and the residue was purified by column chromatography on silica gel with a AcOEt/hexane/toluene eluent.

Characterization Data of Amides 3

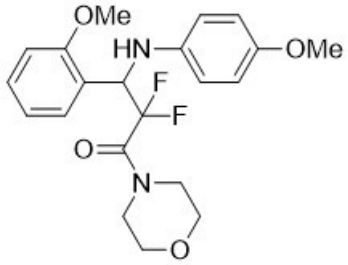
2,2-Difluoro-3-((4-methoxyphenyl)amino)-1-morpholino-3-phenylpropan-1-one **3a**



Using Zn (0.154 g, 2.35 mmol), (*E*)-*N*-(4-methoxyphenyl)-1-phenylmethanimine **1a** (0.212 g, 1.00 mmol), 2-bromo-2,2-difluoro-1-morpholinoethan-1-one **2a** (0.362 g, 1.48 mmol) and TMSCl (150 µL, 1.19 mmol), the product was obtained in 95 % yield (0.356 g, 0.95 mmol) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.46 (d, 1H, *J* = 7.2 Hz), 7.35–7.29 (3H, m), 6.70–6.67 (2H, m), 5.04 (1H, dd, *J* = 9.8, *J* = 9.9 Hz), 4.64 (1H, bs), 3.66 (3H, s), 3.59–3.46 (8H, m); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 161.6 (t, *J* = 28.1 Hz), 152.9, 140.1, 135.3, 128.8, 128.6, 128.6, 117.1(t, *J* =257.9 Hz), 115.6, 114.8, 66.5, 62.6(t, *J* = 24.4 Hz), 55.6, 46.5,43.5; ^{19}F NMR (376 MHz, $CDCl_3$, ppm): δ -100.9(d, *J* = 270.9 Hz), -105.9(d, *J* =270.8 Hz); HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{20}H_{22}F_2N_2O_3$: 377.1671. Found: 377.1646.

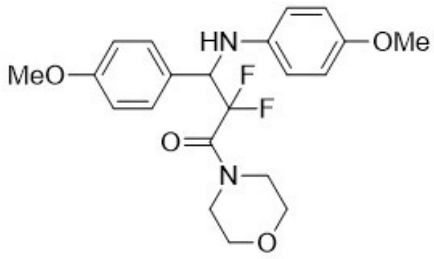
2,2-Difluoro-3-(2-methoxyphenyl)-3-((4-methoxyphenyl)amino)-1-morpholinopropan-1-one **3b**



Using Zn (0.153 g, 2.35 mmol), (*E*)-1-(2-methoxyphenyl)-*N*-(4-methoxyphenyl)methanimine **1b** (0.214 g, 0.887 mmol), 2-bromo-2,2-difluoro-1-morpholinoethan-1-one **2a** (0.3661 g, 1.50 mmol) and TMSCl (150 µL, 1.19 mmol), the product was obtained in 70 % yield (0.2829 g, 0.70 mmol) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.43 (d, 1H, *J* = 7.6 Hz), 7.28–7.23 (1H, m), 6.95–6.88 (2H, m), 6.70–6.67 (2H, m), 6.60–6.56 (2H, m), 5.60 (d, 2H, *J* = 19.0 Hz), 4.60 (1H, bs), 3.86 (3H, s), 3.68–3.58 (11H, m); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 161.9 (t, *J* = 28.2 Hz), 157.9 ,152.8 ,140.1 , 129.7 , 129.0 , 123.3 , 121.0 , 116.8 (t, *J* = 256.2 Hz) , 115.3 , 114.8, 114.2 , 110.8, 66.6, 55.8, 55.6, 55.1 (dd, *J* = 23.2 Hz, *J* = 23.2 Hz), 46.7, 43.6; ^{19}F NMR (376 MHz, $CDCl_3$, ppm): δ -102.0 (d, *J* = 266.7 Hz), -110.0 (d, *J* =266.6 Hz); HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{21}H_{24}F_2N_2O_4$: 407.1777. Found: 407.1757.

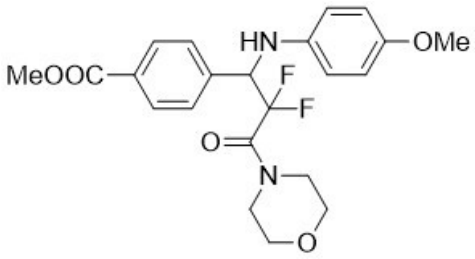
2,2-Difluoro-3-(4-methoxyphenyl)-3-((4-methoxyphenyl)amino)-1-morpholinopropan-1-one **3c**



Using Zn (0.151 g, 2.31 mmol), (*E*)-*N*,1-bis(4-methoxyphenyl)methanimine **1c** (0.241 g, 1.0 mmol), 2-bromo-2,2-difluoro-1-morpholinoethan-1-one **2a** (0.367 g, 1.50 mmol) and TMSCl (150 µL, 1.19 mmol), the product was obtained in 85 % yield (0.344 g, 0.85 mmol) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.37 (d, 2H, *J* = 8.6 Hz), 6.86 (d, 2H, *J* = 8.7 Hz), 6.72–6.68 (2H, m), 6.60–6.57 (2H, m), 4.97 (1H, dd, *J* = 10.0 Hz, *J* = 10.0 Hz), 4.59 (1H, bs), 3.76 (3H, s), 3.67 (3H, s), 3.62–3.51 (8H, m); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 161.7 (t, *J* = 28.2 Hz), 159.7, 152.9, 140.1, 129.9, 127.0, 117.0 (t, *J* = 258.3 Hz), 115.7, 114.8, 114.0, 66.5, 62.0(t, *J* = 24.5 Hz), 55.6, 55.2, 46.5, 43.5; ^{19}F NMR (376 MHz, $CDCl_3$, ppm): δ -101.1 (d, *J* = 270.2 Hz), -105.9 (d, *J* =269.9 Hz); HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{21}H_{24}F_2N_2O_4$: 407.1777. Found: 407.1764.

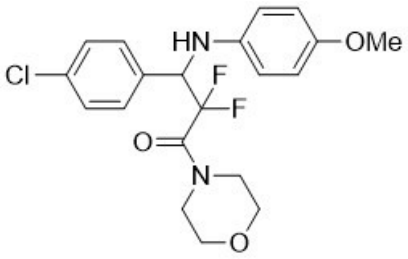
Methyl 4-(2,2-difluoro-1-((4-methoxyphenyl)amino)-3-morpholino-3-oxopropyl)benzoate **3d**



Using Zn (0.153 g, 2.35 mmol), (*E*)-4-(((4-methoxyphenyl)imino)methyl)phenyl acetate **1d** (0.296 g, 1.10 mmol), 2-bromo-2,2-difluoro-1-morpholinoethan-1-one **2a** (0.366 g, 1.50 mmol) and TMSCl (150 µL, 1.19 mmol), the product was obtained in 74 % yield (0.355 g,0.82 mmol) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.01 (d, 2H, *J* = 8.3 Hz), 7.57 (d, 2H, *J* = 8.1 Hz), 6.70 (d, 2H, *J* = 8.9 Hz), 6.59 (d, 2H, *J* = 8.9 Hz), 5.12 (dd, 1H, *J* = 9.6 Hz, *J* = 9.8 Hz), 4.70 (1H, bs), 3.88 (3H, s), 3.67–3.56 (11H, m); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 166.6 , 161.2 (t, *J* = 28.2 Hz), 153.1, 140.5, 139.7, 130.3, 129.7, 129.0, 116.8 (t, *J* = 259.6 Hz), 115.7, 114.8, 66.5, 62.4 (t, *J* =24.6 Hz), 55.6, 52.2, 46.5, 43.5; ^{19}F NMR (376 MHz, $CDCl_3$, ppm): δ -100.0 (d, *J* = 277.1 Hz), -105.4 (d, *J* =276.8 Hz); HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{22}H_{24}F_2N_2O_5$: 435.1727. Found: 435.1732.

3-(4-Chlorophenyl)-2,2-difluoro-3-((4-methoxyphenyl)amino)-1-morpholinopropan-1-one **3e**

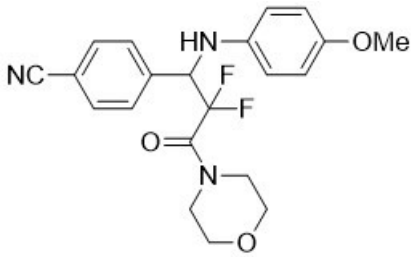


Using Zn (0.153 g,2.35 mmol), (*E*)-1-(4-chlorophenyl)-*N*-(4-methoxyphenyl)methanimine **1e** (0.246 g, 1 mmol), 2-bromo-2,2-difluoro-1-morpholinoethan-1-one **2a** (0.367 g, 1.50 mmol) and TMSCl (150 µL, 1.19 mmol), the product was obtained in 87 % yield (0.359 g, 0.87 mmol) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.42 (d, 2H, *J* = 8.4 Hz), 7.31–7.29(2H, m), 6.72–6.68 (2H, m), 6.60–6.56 (2H, m) 5.03 (1H, dd, *J* = 9.9, *J* = 10.0 Hz), 4.67 (1H, bs), 3.67-3.56 (11H, m); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 161.2 (t, *J* = 28.2 Hz), 153.1, 139.7, 134.4, 133.9, 133.9, 130.3, 128.7, 116.8 (t, *J* =259.4

Hz), 115.7, 114.9, 66.6, 62.0 (t, J = 24.7 Hz), 55.6, 46.5 ,43.5; ^{19}F NMR (376 MHz, $CDCl_3$, ppm): δ -100.1 (d, J = 277.2 Hz), -105.4 (d, J =277.3 Hz); HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{20}H_{21}ClF_2N_2O_3$: 411.1282. Found: 411.1284.

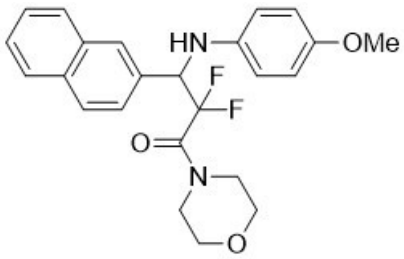
4-(2,2-Difluoro-1-((4-methoxyphenyl)amino)-3-morpholino-3-oxopropyl)benzonitrile **3f**



Using Zn (0.152 g, 2.33 mmol), (*E*)-4-(((4-methoxyphenyl)imino)methyl)benzonitrile **1f** (0.236 g, 1.00 mmol), 2-bromo-2,2-difluoro-1-morpholinoethan-1-one **2a** (0.365 g, 1.50 mmol) and TMSCl (150 µL, 1.19 mmol), the product was obtained in 78 % yield (0.315 g,0.78 mmol) as a yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.61 (s, 4H), 6.73–6.69 (2H, m), 6.60–6.56 (2H, m), 5.12 (1H, bs), 4.76 (1H, bs), 3.68–3.63 (11H, m); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 160.8 (t, J = 28.2 Hz), 153.2, 140.9, 140.9, 139.4, 132.1, 129.8, 118.6, 116.6 (t, J = 260.4 Hz), 115.7, 114.9, 112.3, 66.6, 62.3 (t, J = 24.8 Hz), 55.6, 46.5, 43.5 ; ^{19}F NMR (376 MHz, $CDCl_3$, ppm): δ -99.3 (d, J = 281.9 Hz), -104.7 (d, J = 281.8 Hz); HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{21}H_{21}ClF_2N_3O_3$: 402.1624. Found: 402.1620.

2,2-Difluoro-3-((4-methoxyphenyl)amino)-1-morpholino-3-(naphthalen-2-yl)propan-1-one **3g**

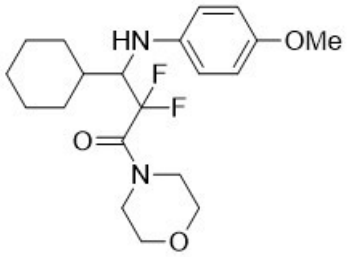


Using Zn (0.153 g, 2.35 mmol), (*E*)-*N*-(4-methoxyphenyl)-1-(naphthalen-2-yl)methanimine **1g** (0.261 g, 1.00 mmol), 2-bromo-2,2-difluoro-1-morpholinoethan-1-one **2a** (0.367 g, 1.50 mmol) and TMSCl (150 µL, 1.19 mmol), the product was obtained in 63 % yield (0.267 g,0. 63mmol) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.94 (s, 1H), 7.80–7.77 (3H, m), 7.59 (d, 1H, J = 8.6 Hz), 7.45–7.43 (2H, m), 6.69–6.62 (4H, m) , 5.21 (dd, 1H, J = 9.8 Hz, J = 9.9 Hz), 4.76 (1H, bs), 3.63 (3H, s), 3.55–3.39 (8H, m); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 161.6 (t, J = 28.1 Hz), 153.0, 140.1, 133.4, 133.2, 132.7, 128.1, 127.7, 126.5, 126.4 , 126.1, 117.2 (t, J = 258.7 Hz), 115.8, 114.9, 66.5, 62.8 (t, J = 24.4 Hz), 55.6,

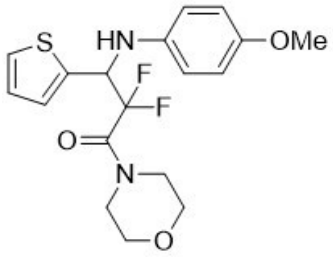
46.5, 43.5; ^{19}F NMR (376 MHz, $CDCl_3$, ppm): δ -100.6 (d, *J* = 271.7 Hz), -105.4 (d, *J* = 271.7 Hz); HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{24}H_{24}F_2N_2O_3$: 427.1828. Found: 427.1846.

3-Cyclohexyl-2,2-difluoro-3-((4-methoxyphenyl)amino)-1-morpholinopropan-1-one **3h**



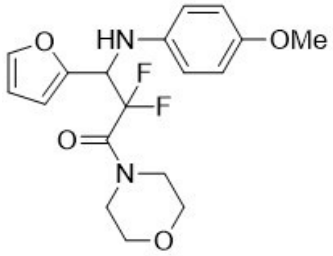
Using Zn (0.151 g, 2.31 mmol), (*E*)-1-cyclohexyl-*N*-(4-methoxyphenyl)methanimine **1h** (0.217 g, 1.00 mmol), 2-bromo-2,2-difluoro-1-morpholinoethan-1-one **2a** (0.367 g, 1.50 mmol) and TMSCl (150 µL, 1.19 mmol), the product was obtained in 25 % yield (0. 094 g, 0.25 mmol) as a white solid.
^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 6.76 (d, 2H, *J* = 8.8 Hz), 6.63 (d, 2H, *J* = 8.8 Hz), 3.84–3.47 (13H, m), 1.95–1.63 (6H, m), 1.28–1.08 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 162.3 (t, *J* = 28.6 Hz), 152.4, 142.0, 118.8 (t, *J* = 258.8 Hz), 114.9, 114.7, 66.6, 62.2 (t, *J* = 23.0 Hz), 55.7, 46.7, 43.4, 39.2, 31.5, 28.3, 26.4, 26.1, 26.1; ^{19}F NMR (376 MHz, $CDCl_3$, ppm): δ -100.4 (d, *J* = 270.0 Hz), -106.1 (d, *J* = 269.9 Hz); HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{20}H_{28}F_2N_2O_4$: 383.2141. Found: 383.2128.

2,2-Difluoro-3-((4-methoxyphenyl)amino)-1-morpholino-3-(thiophen-2-yl)propan-1-one **3i**



Using Zn (0.153 g, 2.35 mmol), (*E*)-*N*-(4-methoxyphenyl)-1-(thiophen-2-yl)methanimine **1i** (0.218 g, 1.00 mmol), 2-bromo-2,2-difluoro-1-morpholinoethan-1-one **2a** (0.367 g, 1.50 mmol) and TMSCl (150 µL, 1.19 mmol), the product was obtained in 66 % yield (0.252 g,0.65 mmol) as a yellow solid.
^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.24 (dd, 1H, *J* = 1.2 Hz, *J* = 1.2 Hz), 7.11 (d, 1H, *J* = 3.4 Hz), 6.95 (dd, 1H, *J* = 3.6 Hz, *J* = 3.6 Hz), 6.75–5.65 (4H, m), 5.31 (dd, 1H, *J* = 10.5 Hz, *J* = 10.1 Hz), 4.52 (1H, bs) , 3.68–3.58 (11H, m); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 161.2 (t, *J* = 27.9 Hz), 153.3, 139.9, 139.1, 139.1, 127.3, 127.0, 126.1, 116.5 (t, *J* = 259.6 Hz), 116.0, 114.8, 66.6, 59.3 (t, *J* = 26.1 Hz), 55.6, 46.5, 43.5; ^{19}F NMR (376 MHz, $CDCl_3$, ppm): δ -100.4 (d, *J* = 270.0 Hz), -106.1 (d, *J* = 269.9 Hz); HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{18}H_{20}F_2N_2O_3S$: 383.1236. Found: 383.1194.

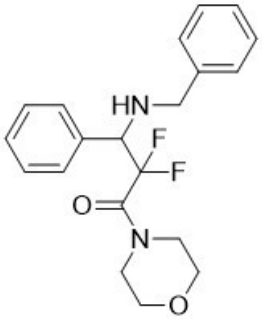
2,2-Difluoro-3-(furan-2-yl)-3-((4-methoxyphenyl)amino)-1-morpholinopropan-1-one **3j**



Using Zn (0.152 g, 2.31 mmol), (*E*)-1-(furan-2-yl)-*N*-(4-methoxyphenyl)methanimine **1j** (0.201 g, 1.00 mmol), 2-bromo-2,2-difluoro-1-morpholinoethan-1-one **2a** (0.367 g, 1.51 mmol) and TMSCl (150 µL, 1.19 mmol), the product was obtained in 64 % yield (0.236 g,0.64 mmol) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.61 (s, 4H), 6.73–6.69 (2H, m), 6.60–6.56 (2H, m), 5.12 (1H, bs), 4.76 (1H, bs), 3.68–3.63 (11H, m); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 161.3 (t, *J* = 27.9 Hz), 153.4, 149.1, 149.1, 142.7, 139.9, 116.6 (t, *J* = 259.6 Hz), 116.2, 114.8, 110.7, 109.6, 66.6, 57.4 (t, *J* = 26.1 Hz), 55.6 , 46.5 ,43.5; ^{19}F NMR (376 MHz, $CDCl_3$, ppm): δ -101.5 (d, *J* = 275.6 Hz), -106.6 (d, *J* = 275.6 Hz); HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{18}H_{20}F_2N_2O_4$: 367.1464. Found: 367.1486.

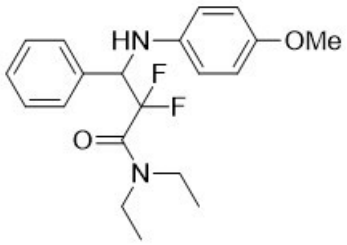
3-(Benzylamino)-2,2-difluoro-1-morpholino-3-phenylpropan-1-one **3k**



Using Zn (0.155 g, 2.36 mmol), (*E*)-*N*-benzyl-1-phenylmethanimine **1k** (0.227 g, 1.16 mmol) and 2-bromo-2,2-difluoro-1-morpholinoethan-1-one **2a** (0.3665 g, 1.74 mmol), TMSCl(175 µL, 1.38mmol) and THF(1.75 mL), the product was obtained in 37 % yield (0.156 g, 0.43 mmol) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.43–7.20 (10H, m), 4.29 (dd, 1H, *J* = 8.4 Hz, *J* = 8.4 Hz), 3.77 (d, 1H, *J* = 13.3 Hz), 3.61–3.38 (9H, m); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 162.0 (t, *J* = 28.3 Hz), 139.4, 134.7, 129.6, 128.7, 128.5, 128.4, 127.2, 117.2 (dd, *J* = 255.5 Hz, *J* = 255.3 Hz), 66.6, 66.5, 64.2 (dd, *J* = 22.1 Hz, *J* = 21.7 Hz), 51.0, 46.5, 43.5; ^{19}F NMR (376 MHz, $CDCl_3$, ppm): δ -101.5 (d, *J* = 272.8 Hz), -109.0 (d, *J* = 272.8 Hz); HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{20}H_{22}F_2N_2O_2$: 361.1723. Found: 361.1726.

N,*N*-Diethyl-2,2-difluoro-3-((4-methoxyphenyl)amino)-3-phenylpropanamide **3l**

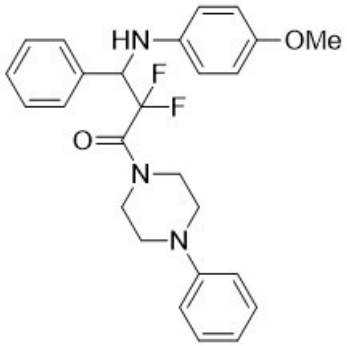


Using Zn (0.153 g,2.34 mmol), (*E*)-*N*-(4-methoxyphenyl)-1-phenylmethanimine **1a** (0.211 g, 1.0 mmol), 2-bromo-*N*,*N*-diethyl-2,2-difluoroacetamide**2b** (0.345 g, 1.50 mmol) and TMSCl (150 μL, 1.19 mmol), the product was obtained in 77 % yield (0.277 g,0.77 mmol) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.46 (d, 2H, *J* = 7.1 Hz) , 7.34–7.28 (3H, m) , 6.70–6.66 (2H, m), 6.61–6.57 (2H, m), 5.06 (1H, dd, *J* = 10.0, *J* = 10.0 Hz), 4.74 (1H, bs), 3.66 (s, 3H), 3.38–3.12 (4H, m), 1.08 (3H, t, *J* = 7.0 Hz), 1.07 (3H, t, *J* = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 162.3 (t, *J* = 27.8 Hz), 152.7, 140.3, 135.5, 128.8, 128.4, 117.0 (t, *J* = 258.9 Hz), 115.5, 114.8, 62.7 (t, *J* = 24.7 Hz), 55.7, 42.2, 41.9 (t, *J* = 6.7 Hz), 14.4, 12.1; ^{19}F NMR (376 MHz, $CDCl_3$, ppm): δ -102.4 (d, *J* = 267.5 Hz), -106.8 (d, *J* =267.3 Hz) ; HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{20}H_{24}F_2N_2O_2$: 363.1879. Found: 363.1897.

2,2-Difluoro-3-((4-methoxyphenyl)amino)-3-phenyl-1-(4-phenylpiperazin-1-yl)propan-1-one

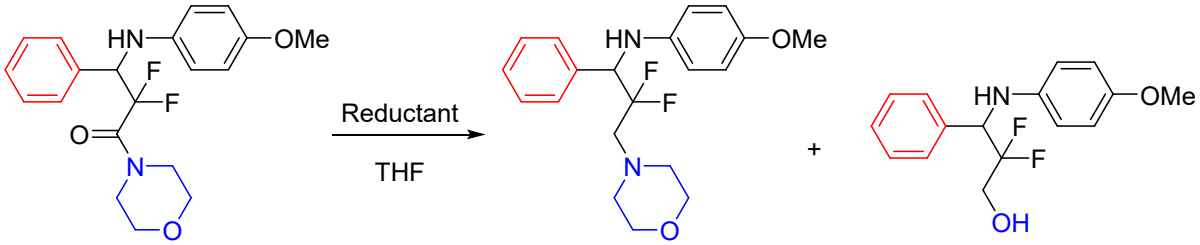
3m



Using Zn (0.153 g, 2.33 mmol), (*E*)-*N*-(4-methoxyphenyl)-1-phenylmethanimine **1a**(0.211 g, 1.0 mmol), 2-bromo-2,2-difluoro-1-(4-phenylpiperazin-1-yl)ethan-1-one **2c** (0.479 g, 1.50 mmol) and TMSCl (150 μL, 1.19 mmol), the product was obtained in 74 % yield (0.335 g,0.74 mmol) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.49 (d, 2H, *J* = 7.3 Hz), 7.35–7.22 (5H, m), 6.90–6.84 (3H, m), 6.69 (d, 2H, *J* = 8.9 Hz), 6.60 (d, 2H, *J* = 8.9 Hz), 5.06 (1H, dd, *J* = 9.8, *J* = 9.8 Hz), 4.65 (1H, bs), 3.75–3.66 (7H, m), 3.10–3.00 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 161.5 (t, *J* = 28.1 Hz), 152.9, 140.1, 135.3, 128.8, 128.6, 128.6, 120.7, 117.8 (t, *J* =259.1 Hz), 116.6, 115.7, 114.8, 62.7 (t, *J* = 24.5 Hz), 55.7, 49.5, 49.2, 45.7, 43.3; ^{19}F NMR (376 MHz, $CDCl_3$, ppm): δ -100.7 (d, *J* = 271.5 Hz), -105.6 (d, *J* = 271.5 Hz); HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{26}H_{27}F_2N_3O_2$: 452.2145. Found: 452.2114.

General Procedure of 1,3-diamines 4 or *γ*-amino alcohol 5



3a **4a** **5**

Use of solid-reductant such as $LiAlH_4$ or $NaBH_4$

β-amino-α,α-difluoroacetamide **3a** (1 mmol) and $LiAlH_4$ or $NaBH_4$ (6 mmol,) added in 50 mL Two-necked Nass flask. The flask was evacuated and backfilled with argon. This sequence was repeated three times. Then, THF (10 mL) was added via the rubber septum with syringe. After the reaction mixtures stirred at r.t. for 2 h, the mixture was cooled to 0 °C. Following the solution was filtrated through Celite with diethyl ether, the filtrate was extracted with AcOEt and the organic layer was washed with brine, dried with Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography on silica gel with AcOEt/hexane eluent.

Use of liquid-reductant such as $BH_3{\cdot}Me_2S$

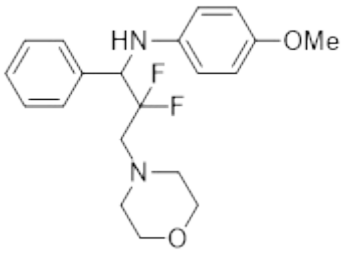
β-amino-α,α-difluoroacetamide **3a** (1 mmol)was added in 50 mL Two-necked Nass flask. The flask was evacuated and backfilled with argon. This sequence was repeated three times. Then, THF (10 mL) and $BH_3{\cdot}Me_2S$ (6 mmol) were added via the rubber septum with syringe. After the reaction mixtures stirred at r.t. for 2 h, the mixture was cooled to 0 °C. Following the solution was filtrated through Celite with diethyl ether, the filtrate was extracted with AcOEt and the organic layer was washed with brine, dried with Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography on silica gel with AcOEt/hexane eluent.

Use of $NaBH_4$ and $BF_3{\cdot}Et_2O$ as a reductant

β-amino-α,α-difluoroacetamide **3** (1 mmol) and $NaBH_4$ (6 mmol,) added in 50 mL Two-necked Nass flask. The flask was evacuated and backfilled with argon. This sequence was repeated three times. Then, THF (10 mL) and $BF_3{\cdot}Et_2O$ (6 mmol) were added via the rubber septum with syringe. The reaction mixture was stirred at r.t. for 1 h, and then at 75 °C for 2 h. After the mixture was cooled to 0 °C. the solution was filtrated through Celite with diethyl ether. The filtrate was extracted with AcOEt and the organic layer was washed with brine, dried with Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography on silica gel with AcOEt/hexane eluent.

Characterization Data of 1,3-Diamine 4

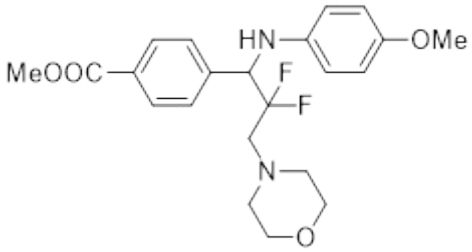
N-(2,2-Difluoro-3-morpholino-1-phenylpropyl)-4-methoxyaniline 4a



Using 2,2-difluoro-3-((4-methoxyphenyl)amino)-1-morpholino-3-phenylpropan-1-one **3a** (0.376 g,1.00 mmol), $NaBH_4$ (0.228 g,6.02 mmol) and $BF_3{\cdot}Et_2O$ (0.605 g,4.26 mmol), the product was obtained in 94 % yield (0.3397 g,0.94 mmol) as clear oil.

^{1}H NMR (400 MHz, CD_3OD, ppm): δ 7.44 (2H, d, *J* = 7.4 Hz), 7.30–7.22 (3H, m), 6.67 (4H, m), 4.99 (1H, dd, *J* = 7.9 Hz, *J* = 7.9 Hz), 4.83 (1H, s), 3.66 (4H,t, *J* = 4.6 Hz), 3.59 (3H, s), 2.99–2.88 (1H, m), 2.69–2.58 (1H, m), 2.57–2.46 (4H, m); ^{13}C NMR (100 MHz, CD_3OD, ppm): δ 152.3, 141.0, 137.0, 128.6, 127.8, 127.6, 123.4 (t, *J* = 246.3 Hz), 114.9, 114.4, 66.8, 60.5 (dd, *J* = 22.7 Hz, *J* = 22.7 Hz), 59.6 (dd, *J* = 25.2 Hz, *J* = 25.2 Hz), 54.8, 54.3; ^{19}F NMR (376 MHz, CD_3OD, ppm): δ -114.8 (d, *J* = 254.4 Hz), -119.9 (d, *J* =254.4 Hz); HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{20}H_{24}F_2N_2O_2$: 363.1879. Found: 363.1868.

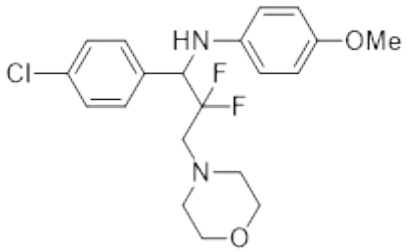
Methyl 4-(2,2-difluoro-1-((4-methoxyphenyl)amino)-3-morpholinopropyl)benzoate **4b**



Using methyl 4-(2,2-difluoro-1-((4-methoxyphenyl)amino)-3-morpholino-3-oxopropyl)benzoate **3d** (0.434 g,1.00 mmol), $NaBH_4$ (0.227 g, 6.00 mmol) and $BF_3{\cdot}Et_2O$ (0.565 g, 3.98 mmol) and the reaction was carried out at room temperature for 2 h, the product was obtained in 63 % yield (0.263 g,0.63 mmol) as clear oil.

^{1}H NMR (400 MHz, CD_3OD, ppm): δ7.95–7.92 (2H, m), 7.56 (d, *J* =8.2 Hz), 6.67–6.61 (4H, m), 5.10 (1H, dd, *J* = 6.5 Hz, *J* = 6.5 Hz), 4.83 (1H, s) , 3.83 (3H, s), 3.66 (t, 4H, *J* =4.7 Hz), 3.60 (3H, s), 3.06–2.94 (1H, m), 2.73–2.64 (1H, m), 2.61–2.47 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ166.9, 152.5, 142.8, 140.6, 129.4, 128.9, 123.4 (t, *J* =4.7 Hz), 114.8, 114.4, 66.7, 60.0 (dd, *J* = 22.5 Hz, *J* = 22.5 Hz), 59.4 (dd, *J* = 24.5 Hz, *J* = 24.6 Hz), 54.7, 54.3, 51.2; ^{19}F NMR (376 MHz, CD_3OD, ppm) δ -100.6 (d, *J* = 256.8 Hz), -107.6 (d, *J* =256.6 Hz); HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{22}H_{26}F_2N_2O_4$: 421.1934. Found: 421.1970.

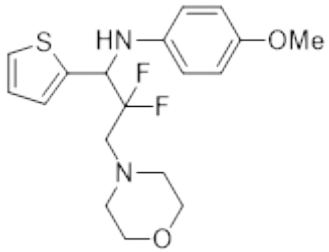
N-(1-(4-Chlorophenyl)-2,2-difluoro-3-morpholinopropyl)-4-methoxyaniline **4c**



Using 3-(4-chlorophenyl)-2,2-difluoro-3-((4-methoxyphenyl)amino)-1-morpholinopropan-1-one **3e** (0.411 g, 1.00 mmol), $NaBH_4$ (0.227 g, 6.00 mmol) and $BF_3{\cdot}Et_2O$ (0.569 g, 4.01 mmol),the product was obtained in 93 % yield (0.370 g,0.93 mmol) as clear oil.

^{1}H NMR (400 MHz, CD_3OD, ppm): δ7.42 (2H, d, *J* = 8.4 Hz), 7.29–7.26 (2H, m), 6.68–6.60 (4H, m), 5.00 (1H, dd, *J* = 7.0 Hz, *J* = 7.0 Hz), 4.83 (1H, s), 3.65 (4H, t, *J* = 4.6 Hz), 3.61 (3H, s), 3.02–2.91 (1H, m), 2.71–2.62 (1H, m), 2.59–2.46 (4H, m) ; ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ152.4, 140.7, 135.9, 133.3, 130.2, 127.9, 123.3 (t, *J* = 246.5 Hz), 114.9, 114.4, 66.7, 59.7 (dd, *J* = 27.8 Hz, *J* = 29.3 Hz), 59.5 (dd, *J* = 29.1 Hz, *J* = 30.5 Hz), 54.7, 54.3; ^{19}F NMR (376 MHz, CD_3OD, ppm) δ -104.7 (d, *J* = 256.2 Hz), -111.2 (d, *J* =256.3 Hz) ; HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{20}H_{23}ClF_2N_2O_2$: 397.1489. Found: 397.1509.

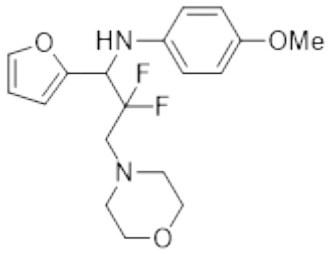
N-(2,2-Difluoro-3-morpholino-1-(thiophen-2-yl)propyl)-4-methoxyaniline **4d**



Using 2,2-difluoro-3-((4-methoxyphenyl)amino)-1-morpholino-3-(thiophen-2-yl)propan-1-one **3i** (0.517 g, 1.35 mmol), $NaBH_4$ (0.306 g,8.10 mmol) and $BF_3{\cdot}Et_2O$ (0.738 g,5.20 mmol), the product was obtained in 88 % yield (0.436 g,1.18 mmol) as clear oil.

^{1}H NMR (400 MHz, CD_3OD, ppm): δ7.24 (1H, dd , *J* = 1.2 Hz, *J* = 1.2 Hz), 7.10 (1H, d, *J* = 3.4 Hz), 6.92 (1H, dd , *J* = 3.6 Hz, *J* = 3.6 Hz), 6.71–6.65 (4H, m), 5.28 (1H, dd, *J* = 7.4 Hz, *J* = 7.5 Hz), 4.81 (1H, s) , 3.65–3.61 (m, 7H), 3.03–2.92 (1H, m), 2.74–2.65 (1H, m), 2.59–2.46 (4H, m); ^{13}C NMR (100 MHz, CD_3OD, ppm): δ152.7, 140.8, 140.5, 126.7, 126.4, 125.1, 123.0 (t, *J* = 246.7 Hz), 115.0, 114.5, 66.8, 59.3 (dd , *J* = 24.9 Hz, *J* = 24.9 Hz), 57.0 (dd , *J* = 24.4 Hz, *J* = 24.3 Hz), 54.8, 54.3; ^{19}F NMR (376 MHz, CD_3OD, ppm): δ -105.1 (d, *J* = 254.6 Hz), -110.3 (d, *J* =254.6 Hz) ; HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{18}H_{22}F_2N_2O_2S$: 369.1443. Found: 369.1432.

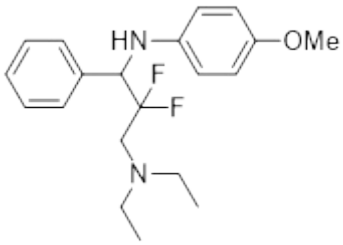
N-(2,2-Difluoro-1-(furan-2-yl)-3-morpholinopropyl)-4-methoxyaniline **4e**



Using 2,2-difluoro-3-(furan-2-yl)-3-((4-methoxyphenyl)amino)-1-morpholinopropan-1-one **3j** (0.387 g, 1.06 mmol), $NaBH_4$ (0.240 g,6.33 mmol) and $BF_3{\cdot}Et_2O$ (0.604 g, 4.25 mmol), the product was obtained in 76 % yield (0.284 g,0.81 mmol) as clear oil.

^{1}H NMR (400 MHz, CD_3OD, ppm): δ7.41 (1H, dd „*J* = 7.9 Hz, *J* = 7.9 Hz), 6.71–6.71 (4H, m), 6.37 (1H, d, *J* = 3.2 Hz), 6.32–6.31 (1H, m), 5.14 (1H, dd, *J* = 6.8 Hz, *J* = 6.8 Hz), 4.81 (1H, s), 3.66–3.64 (7H, m), 3.05–2.94 (1H, m), 2.73–2.64 (1H, m) , 2.62–2.45(4H, m); ^{13}C NMR (100 MHz, CD_3OD, ppm): δ152.8, 150.7, 142.2, 140.8, 123.1 (t, *J* = 246.6 Hz), 115.2, 114.4, 110.1, 108.7, 66.8, 59.3 (dd „*J* = 24.3 Hz, *J* = 24.2 Hz), 55.1 (dd „*J* = 24.1 Hz, *J* = 24.2 Hz), 54.8, 54.3; ^{19}F NMR (376 MHz, CD_3OD, ppm) δ -106.0 (d, *J* = 255.0 Hz), -111.1 (d, *J* =254.9 Hz) ; HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{18}H_{22}F_2N_2O_3$: 353.1672. Found: 353.1650.

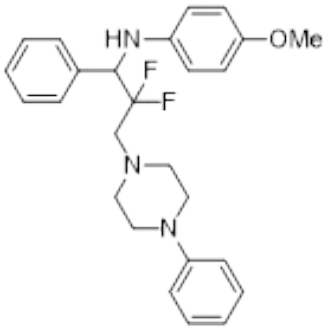
N^3,*N*^{3}-Diethyl-2,2-difluoro-*N*^{1}-(4-methoxyphenyl)-1-phenylpropane-1,3-diamine **4f**



Using *N*,*N*-diethyl-2,2-difluoro-3-((4-methoxyphenyl)amino)-3-phenylpropanamide **3l** (0.362 g,1.00 mmol), $NaBH_4$ (0.227 g, 6.00 mmol) and $BF_3{\cdot}Et_2O$ (0.559 g, 3.93 mmol), the product was obtained in 95 % yield (0.3154 g,0.905 mmol) as clear oil.

^{1}H NMR (400 MHz, CD_3OD, ppm): δ 7.43 (2H, d, *J* = 7.4 Hz), 7.27–7.18 (3H, m), 6.64–6.57 (4H, m) , 4.91 (1H, dd, *J* = 5.60 Hz, *J* = 5.68 Hz), 4.85 (1H, s) , 3.56 (3H, s), 3.15–3.03 (1H, m), 2.88–2.79 (1H, m), 2.68–2.58 (4H, m), 0.98 (4H, t, *J* = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 152.4 , 140.7 , 137.0 , 128.7 , 128.4 , 128.1 , 123.0 (t, *J* = 246.6 Hz) , 115.0 , 114.9 , 61.6 (dd, *J* = 23.4 Hz, *J* = 23.5 Hz) , 56.0 (dd, *J* = 25.5 Hz, *J* = 25.3 Hz) , 55.6 , 47.8 , 11.6; ^{19}F NMR (376 MHz, CD_3OD, ppm) δ -105.4 (d, *J* = 253.5 Hz), -113.0 (d, *J* =253.6 Hz) ; HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{20}H_{26}F_2N_2O$: 349.2086. Found: 349.2099.

N-(2,2-Difluoro-1-phenyl-3-(4-phenylpiperazin-1-yl)propyl)-4-methoxyaniline **4g**

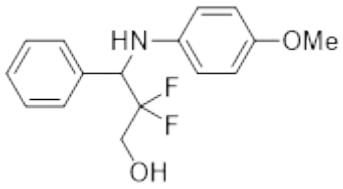


Using 2,2-difluoro-3-((4-methoxyphenyl)amino)-3-phenyl-1-(4-phenylpiperazin-1-yl)propan-1-one **3m** (0.452 g, 1.00 mmol), $NaBH_4$ (0.2258 g, 5.97 mmol) and $BF_3{\cdot}Et_2O$ (0.5677 g, 4.00 mmol), the product was obtained in 90 % yield (0.394 g,0.90 mmol) as clear oil.

^{1}H NMR (400 MHz, CD_3OD, ppm): δ 7.46 (2H, d, *J* = 7.4 Hz), 7.32–7.21 (5H, m), 6.96–6.94 (2H, m), 6.83 (1H, t, *J* = 7.3 Hz), 6.67–6.61 (4H, m) , 5.02 (1H, dd, *J* = 7.8 Hz, *J* = 7.8 Hz), 4.86 (1H, s) , 3.62 (3H, s) , 3.16 (4H,t, *J* = 4.9 Hz) , 3.08–2.96 (1H, m) , 2.79–2.67 (5H, m) ; ^{13}C NMR (100 MHz, CD_3OD, ppm): δ 152.3, 151.3, 141.0 , 137.1, 128.7, 128.6, 127.8, 127.5, 123.4 (t, *J* = 246.3 Hz), 119.7, 116.1, 114.9, 114.4, 60.6 (dd, *J* = 23.2 Hz, *J* = 23.1 Hz), 59.1 (dd, *J* = 25.2 Hz, *J* = 25.4 Hz), 54.7, 53.9, 49.4; ^{19}F NMR (376 MHz, CD_3OD, ppm): δ -105.6 (d, *J* = 255.7 Hz),

-110.8 (d, *J* =255.7 Hz); HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{26}H_{29}F_2N_3O$: 438.2351. Found: 438.2335.

2,2-Difluoro-3-((4-methoxyphenyl)amino)-3-phenylpropan-1-ol **5**



Using 2,2-difluoro-3-((4-methoxyphenyl)amino)-1-morpholino-3-phenylpropan-1-one **3a** (0.376 g,1.00 mmol) and $NaBH_4$ (0.2278 g, 6.02 mmol), the product was obtained in 49 % yield (0.145 g,0. 56mmol) as clear oil.

^{1}H NMR (400 MHz, CD_3OD, ppm): δ 7.45 (2H,d, *J* = 7.4 Hz) , 7.30–7.20 (3H,m) , 6.63 (3H,s) , 4.94–4.85 (2H,m) , 3.98–3.88 (1H,m) 3.76–3.67 (1H,m) , 3.58 (3H,s) ; ^{13}C NMR (100 MHz, CD_3OD, ppm): δ 152.4, 140.9, 136.7, 128.5, 127.9, 127.6, 122.0 (t, *J* = 246.0 Hz), 115.2, 114.3, 61.3 (dd, *J* = 28.6Hz, *J* = 28.3 Hz), 59.6 (dd, *J* = 22.4 Hz, *J* = 22.4 Hz), 54.7; ^{19}F NMR (376 MHz, CD_3OD, ppm) δ -114.6 (d, *J* = 254.3 Hz), -119.7 (d, *J* =254.0 Hz); HRMS (DART) m/z: $[M+H]^+$ calcd. For $C_{16}H_{17}F_2NO_2$: 294.1301. Found: 294.1297.

References

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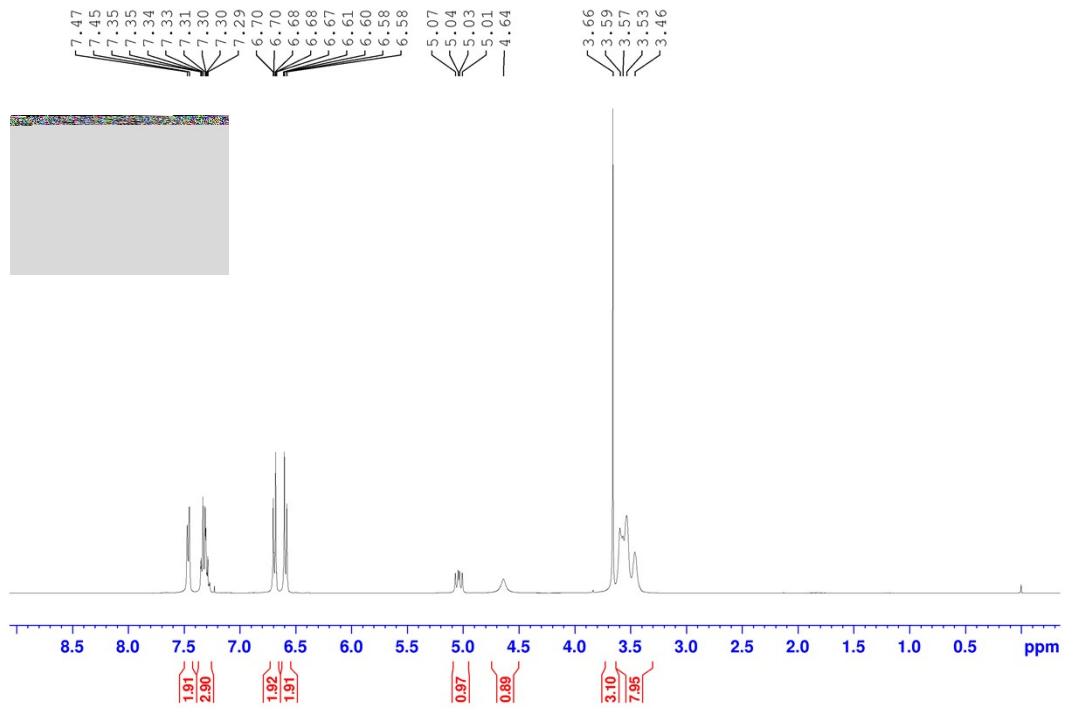
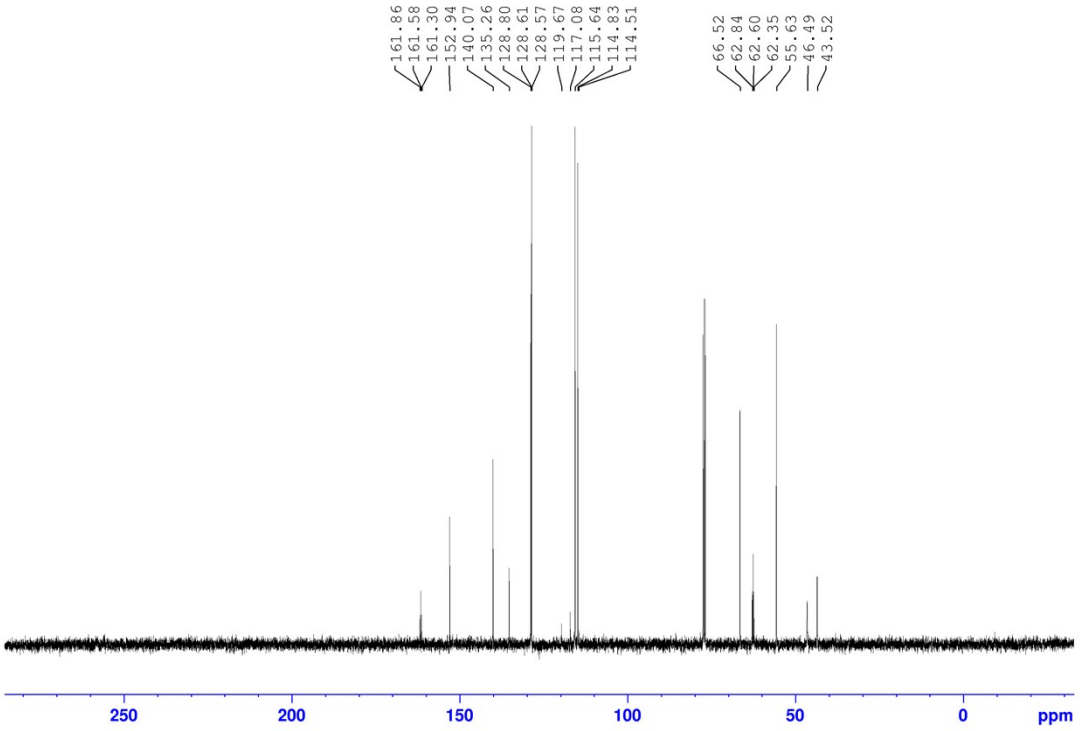
SI-2) S. Ge, S.Arlow, M. Mormino and J. Hartwig, *J. Am. Chem. Soc.,* 2014, **136***,* 14401–14404.

SI-3) A. Tarui, S. Shinohara, K. Sato, M. Omote, and A. Ando , *Org. Lett*., 2016, **18**, 1128–1131.

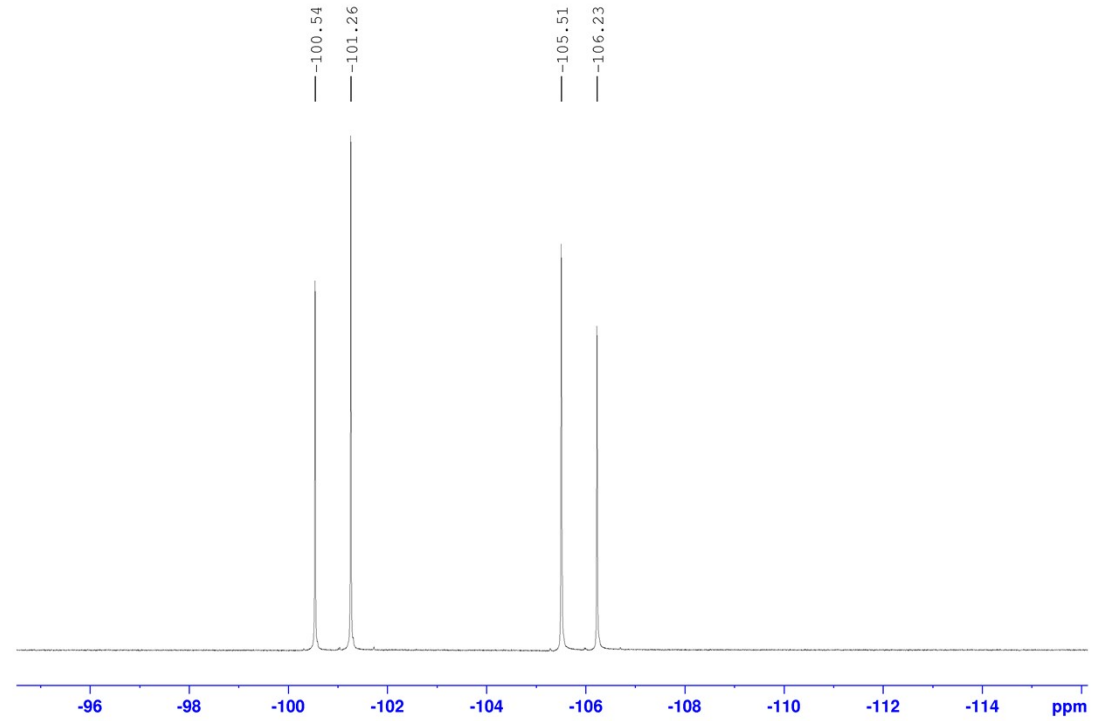
1D-1H zg30



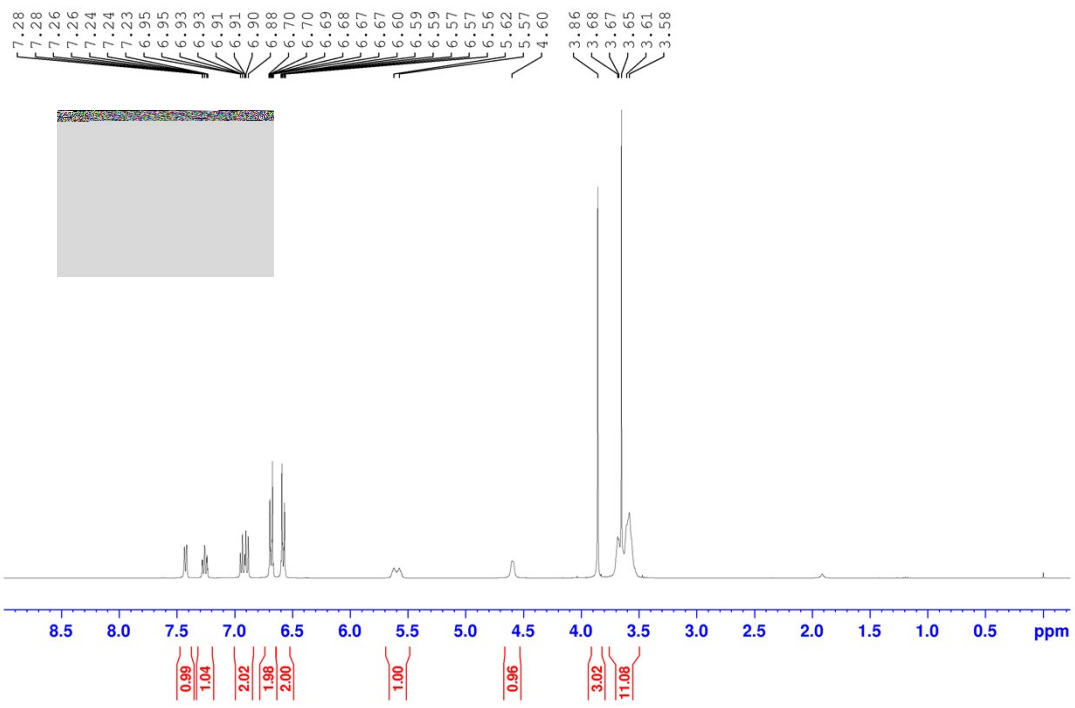
13C



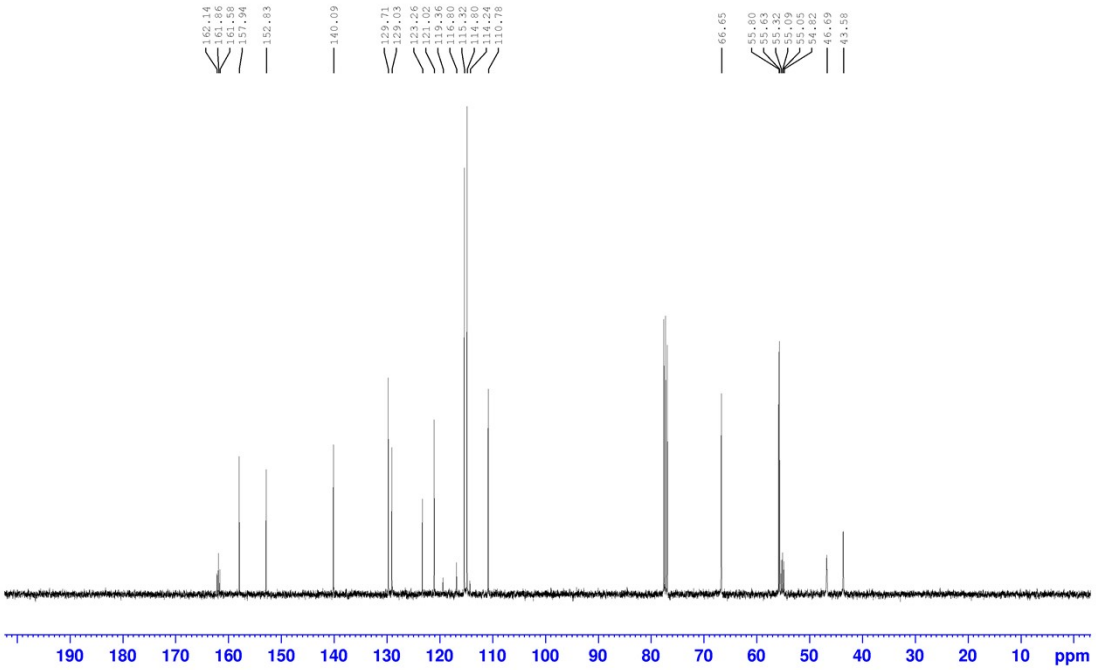
F19CPD



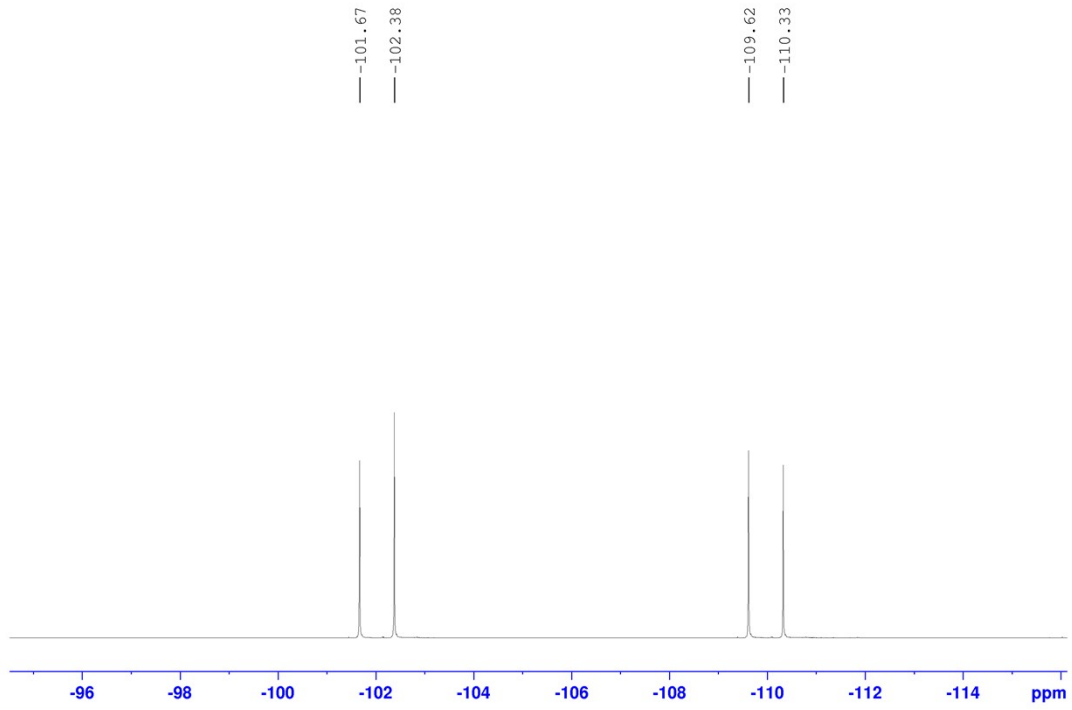
1D-1H zg30



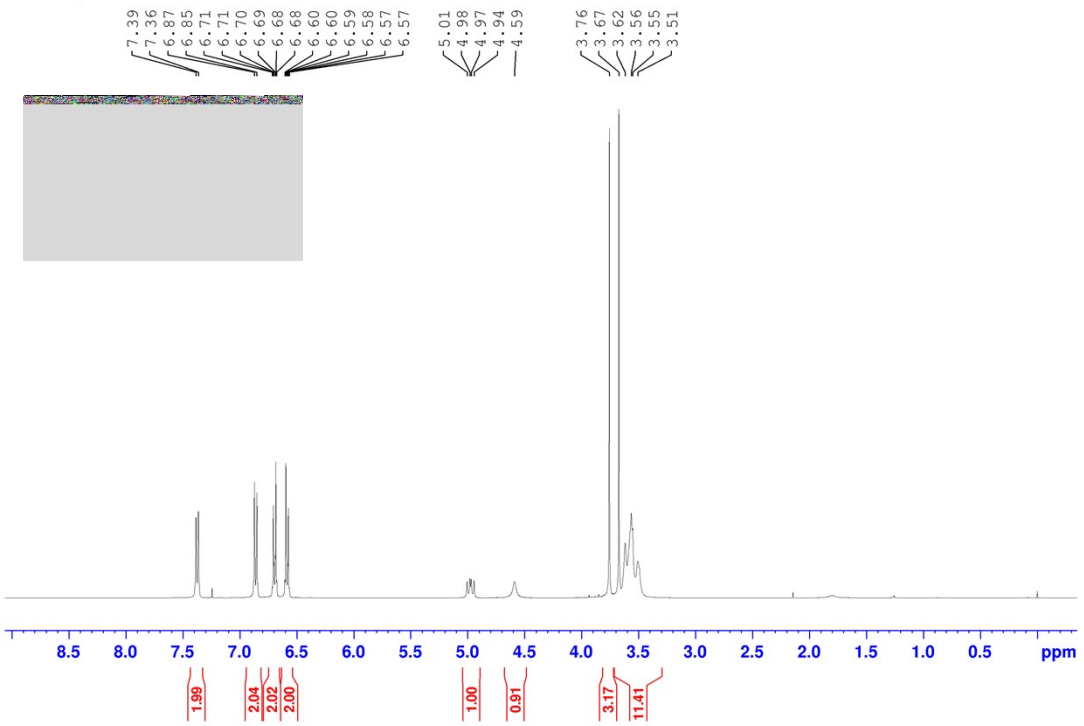
13C


162.14
161.86
161.58
157.94
152.83
140.09
129.71
129.03
123.26
121.02
119.36
116.60
115.32
114.80
114.24
110.78
66.65
55.80
55.63
55.32
55.09
55.05
54.82
46.69
43.58
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

F19CPD


-101.67
-102.38
-109.62
-110.33
-96 -98 -100 -102 -104 -106 -108 -110 -112 -114 ppm

1D-1H zg30



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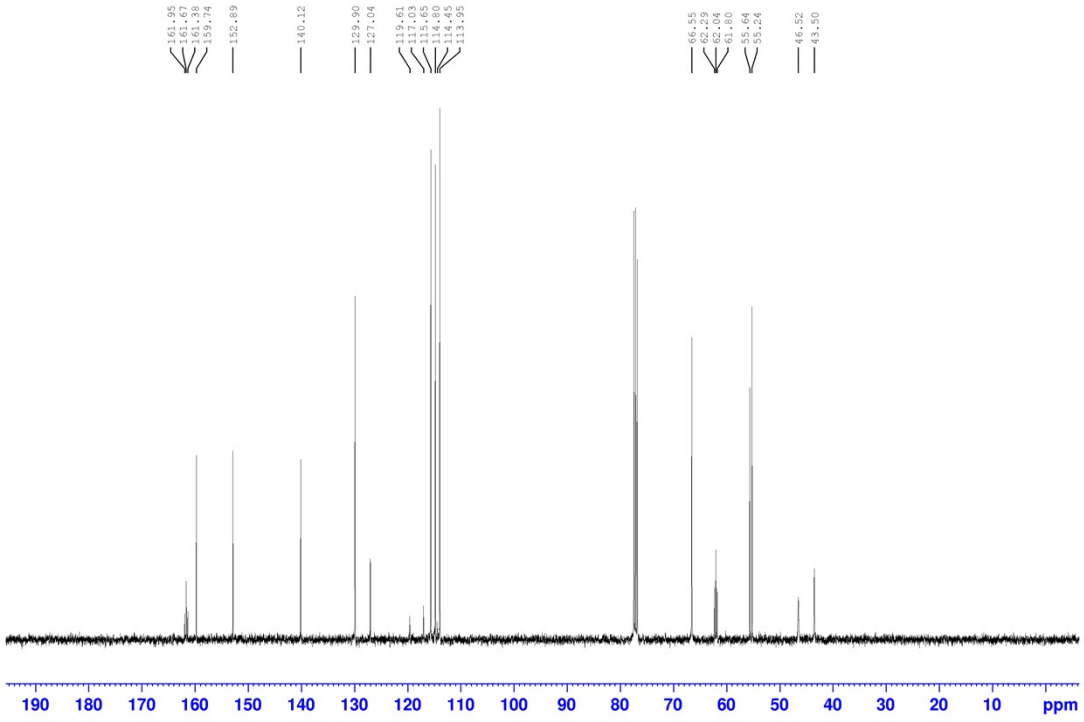

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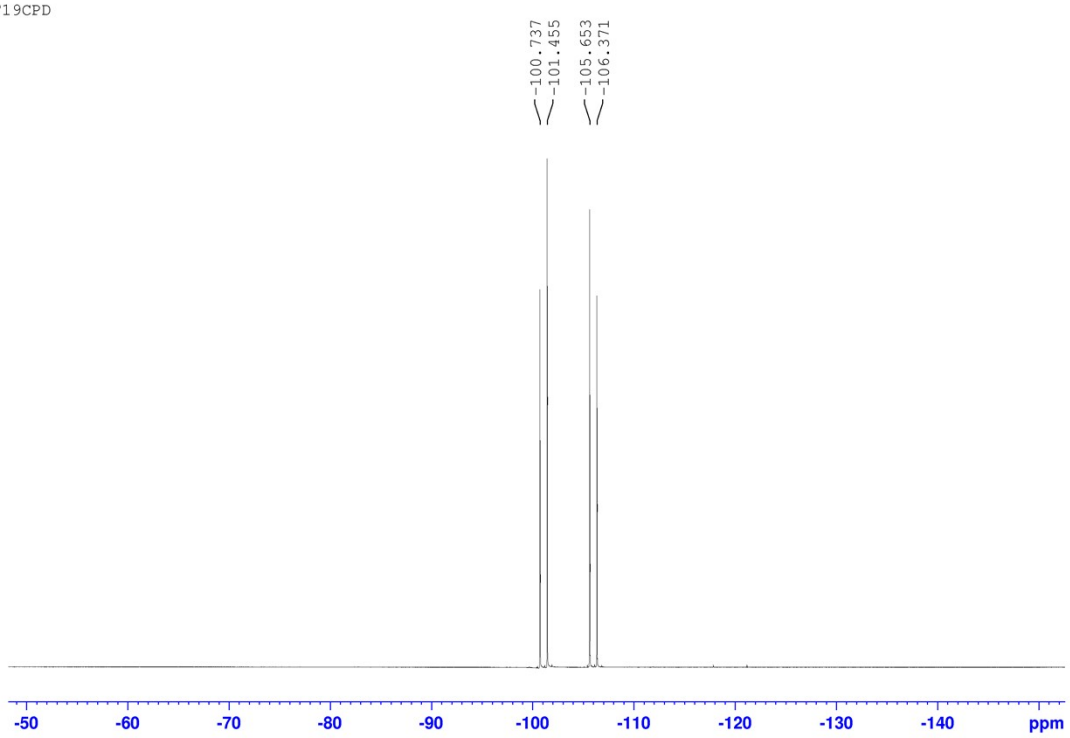
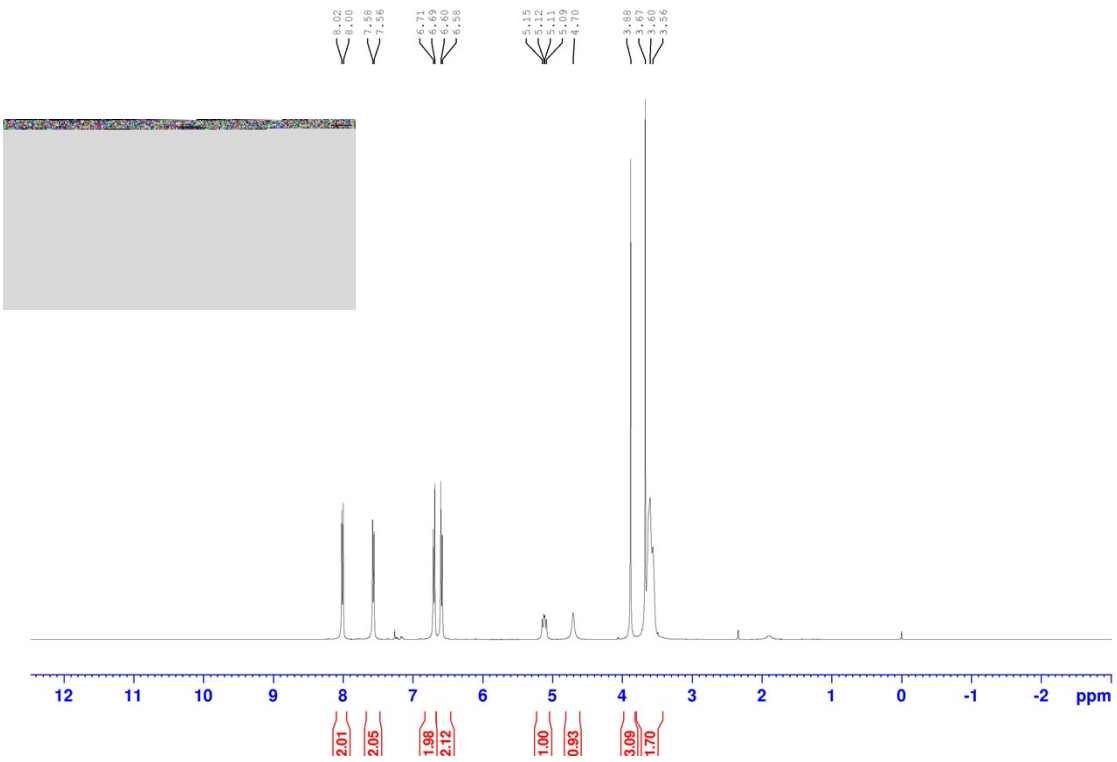


1D-1H zg30



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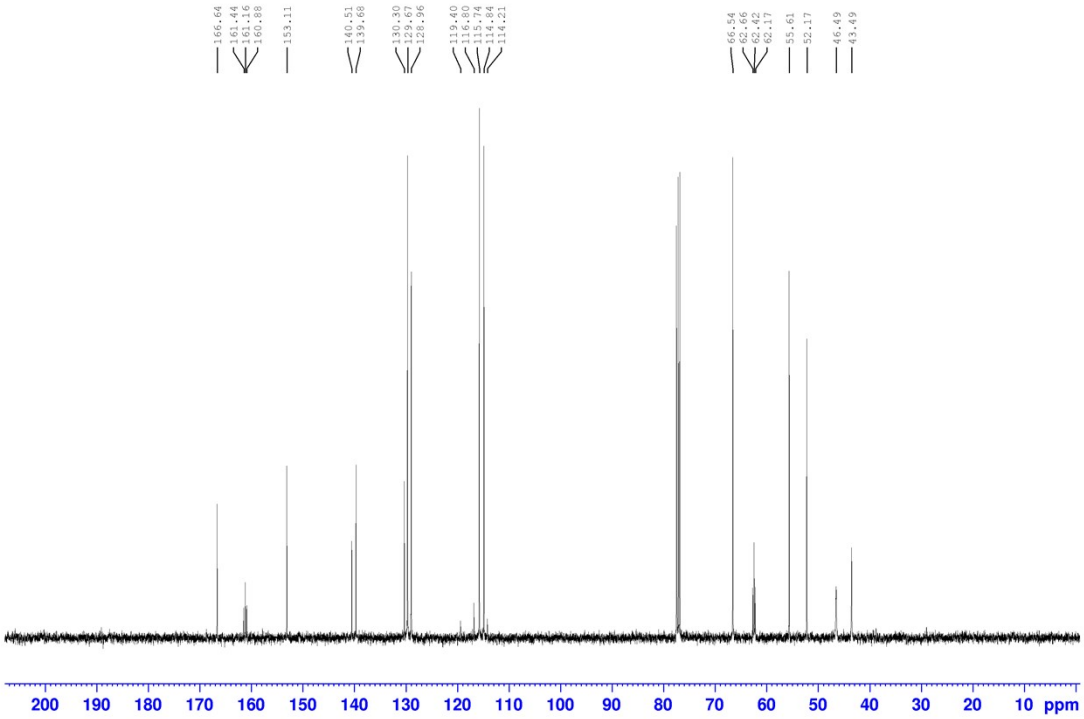
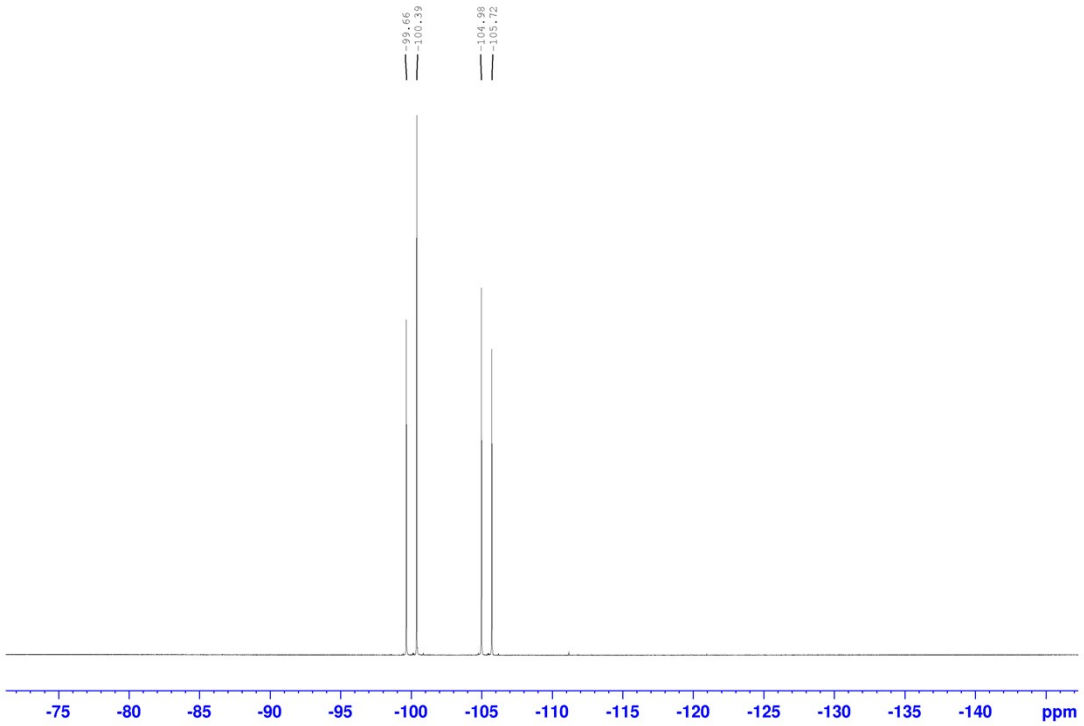
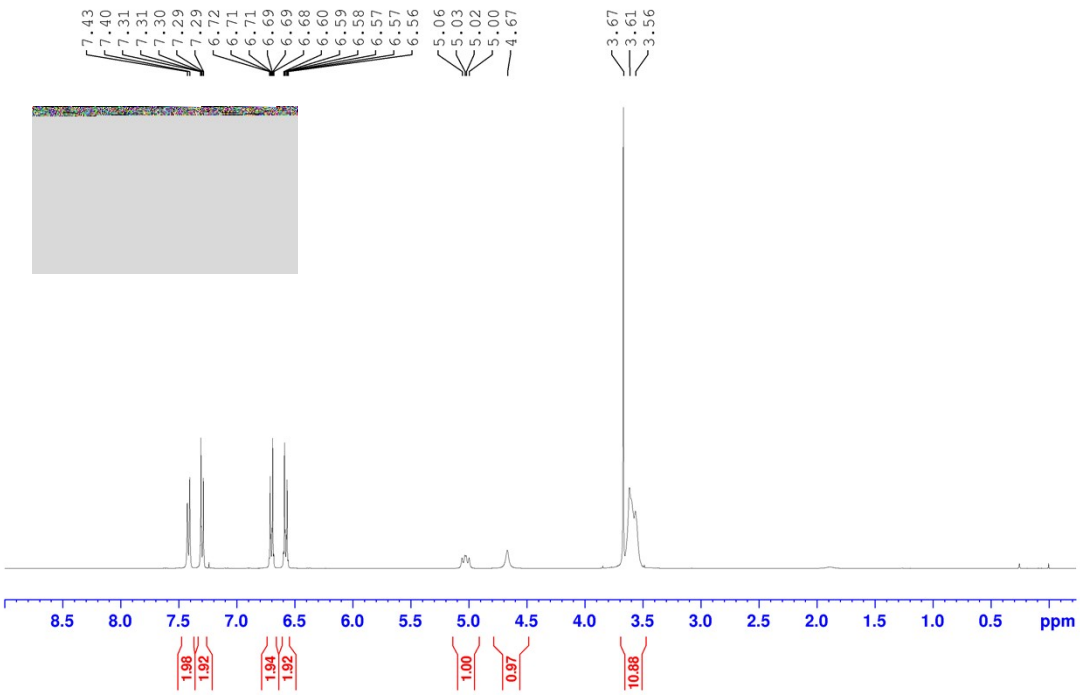

166.64
161.44
161.16
160.88
153.11
140.51
139.68
130.30
129.67
128.96
119.40
116.80
115.74
114.84
114.21
66.54
62.66
62.42
62.17
55.61
52.17
46.49
43.49
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

F19CPD


-99.66
-100.39
-104.98
-105.72
-75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 ppm

1D-1H zg30



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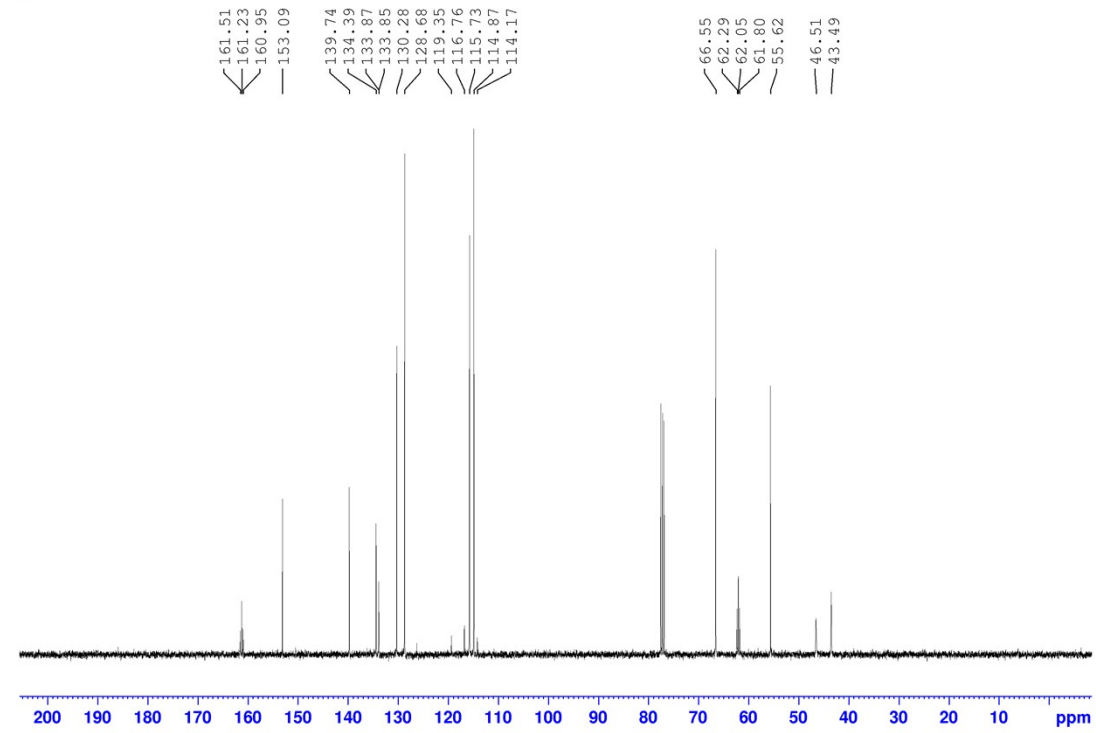

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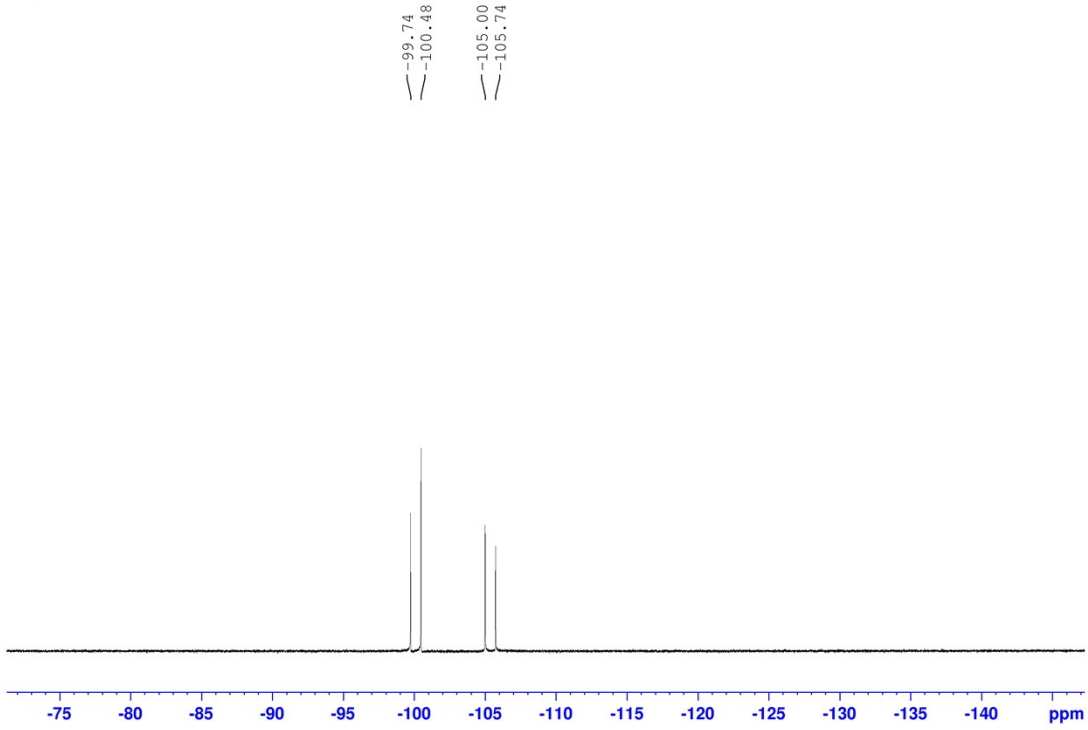
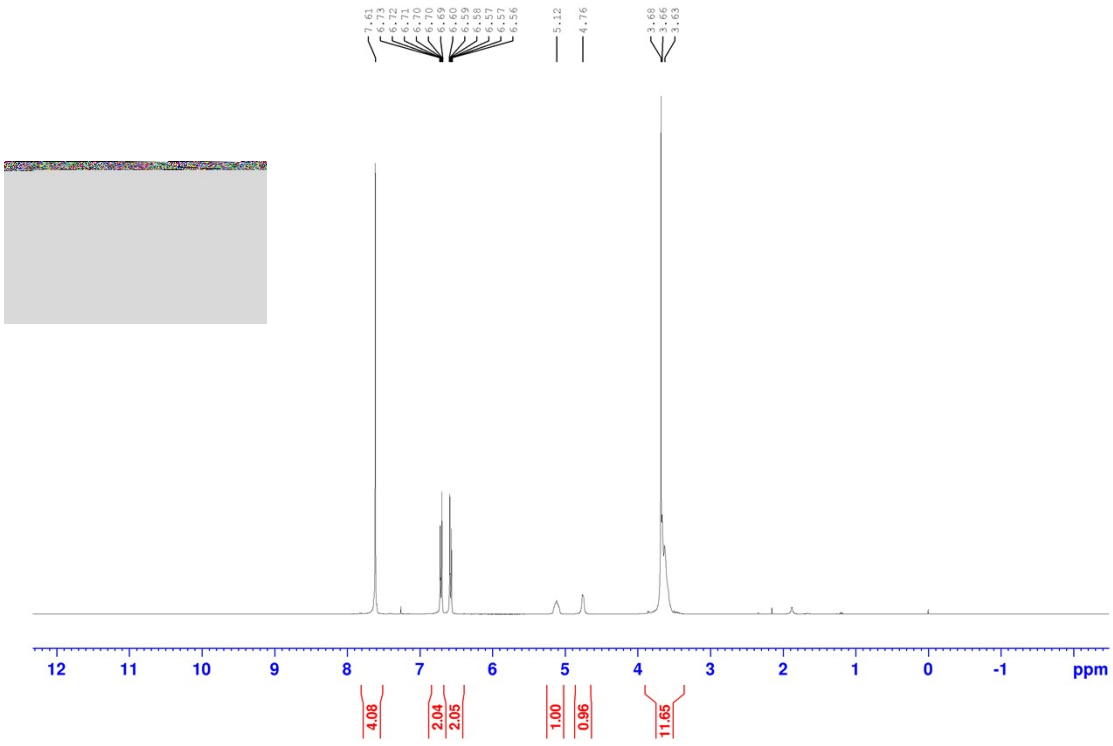


1D-1H zg30



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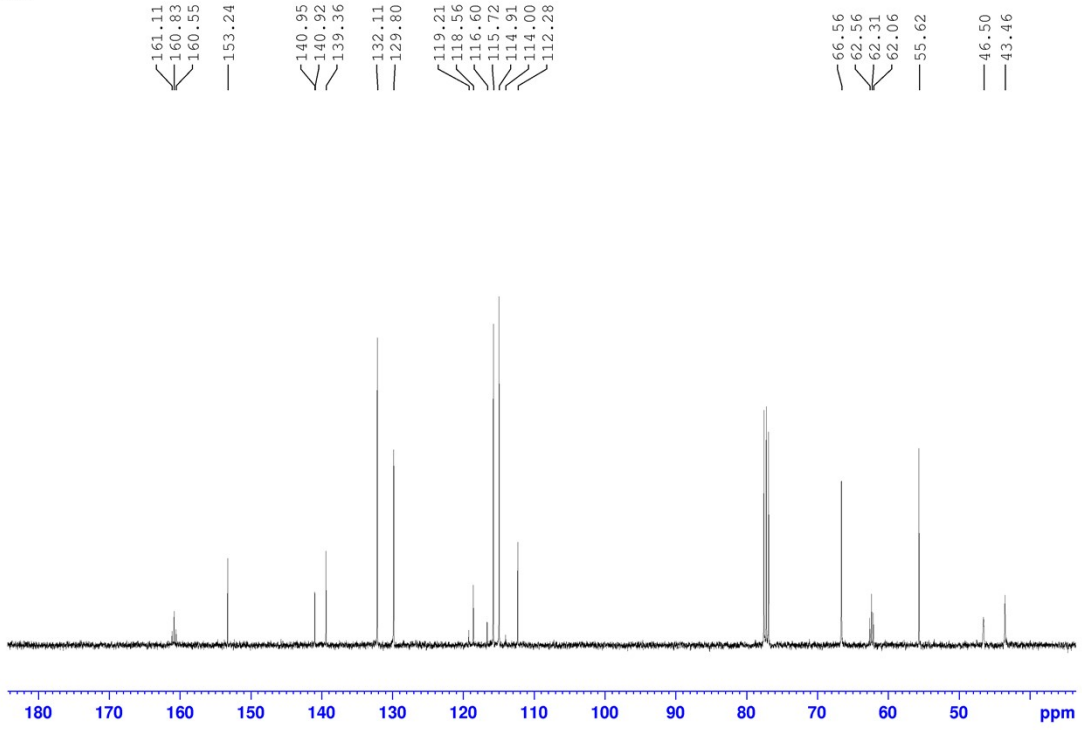
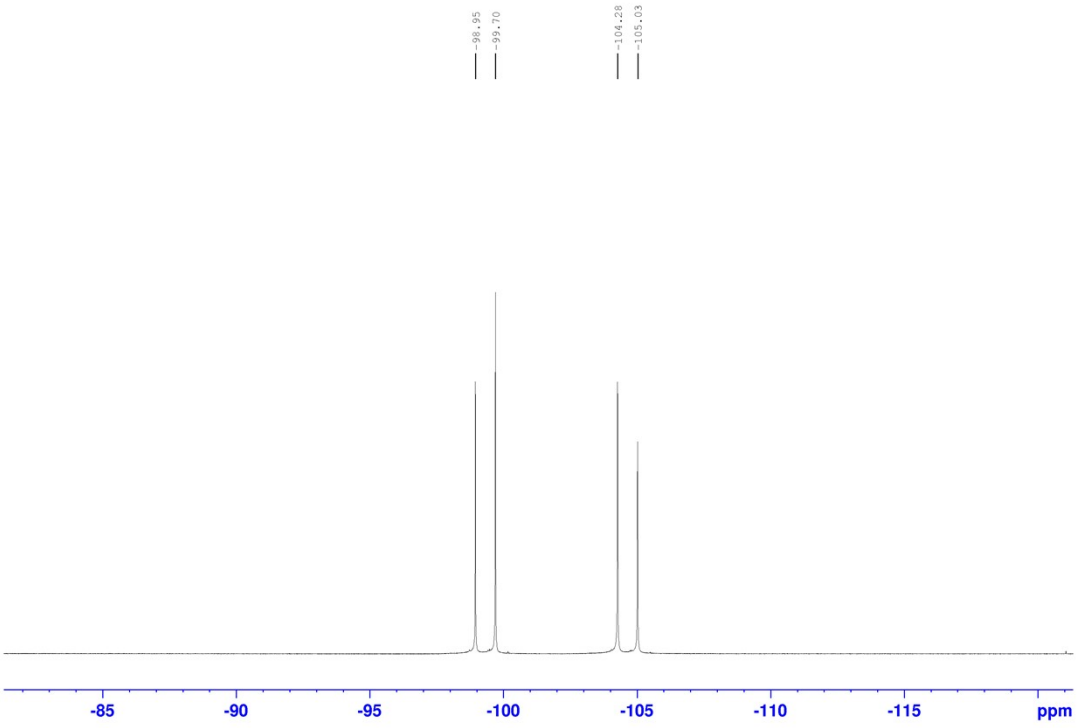
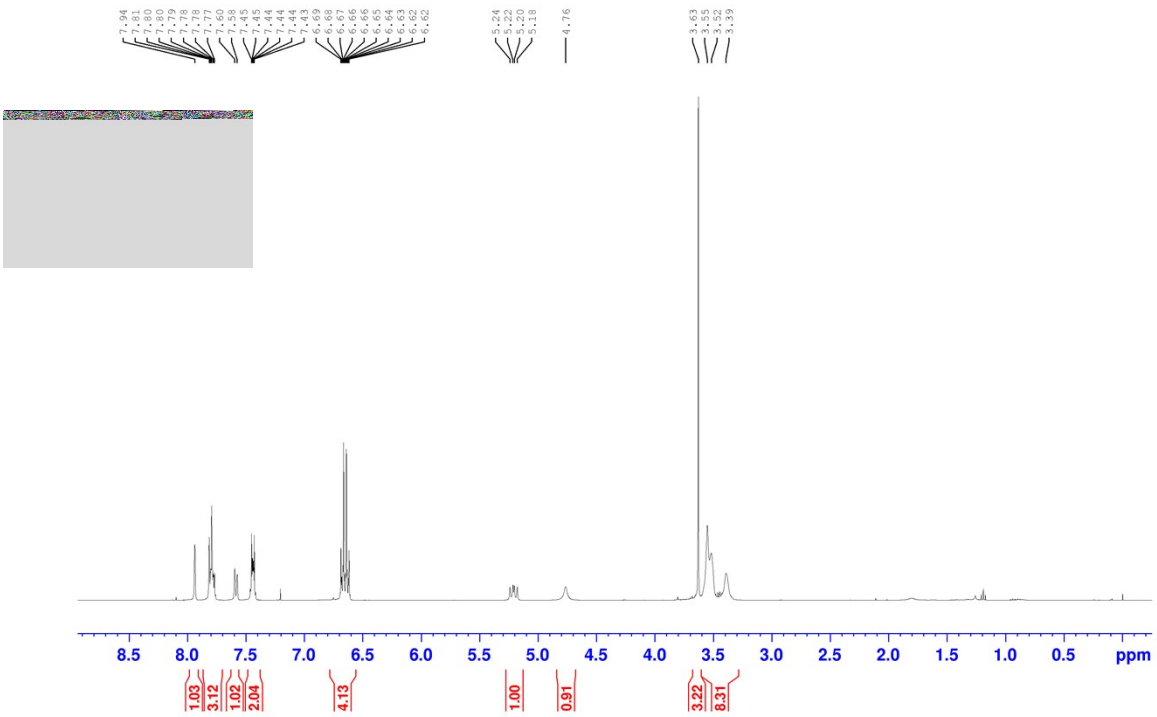

161.11
160.83
160.55
153.24
140.95
140.92
139.36
132.11
129.80
119.21
118.56
116.60
115.72
114.91
114.00
112.28
66.56
62.56
62.31
62.06
55.62
46.50
43.46
180
170
160
150
140
130
120
110
100
90
80
70
60
50
ppm

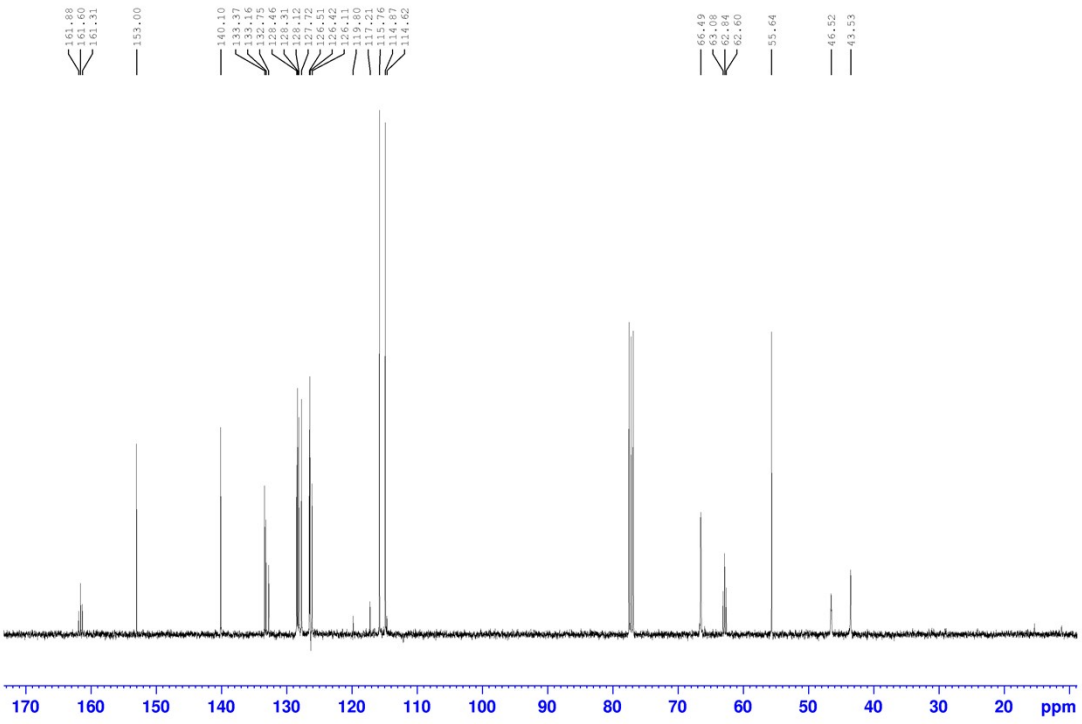
F19CPD


-98.95
-99.70
-104.28
-105.03
-85
-90
-95
-100
-105
-110
-115
ppm

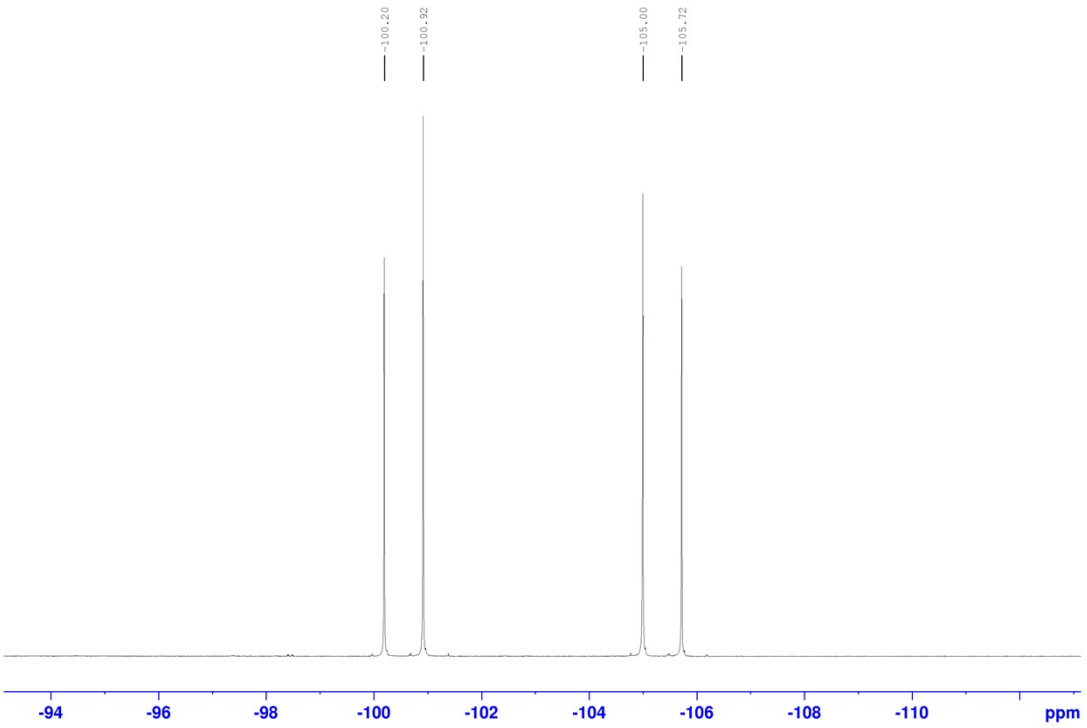
1D-1H zg30



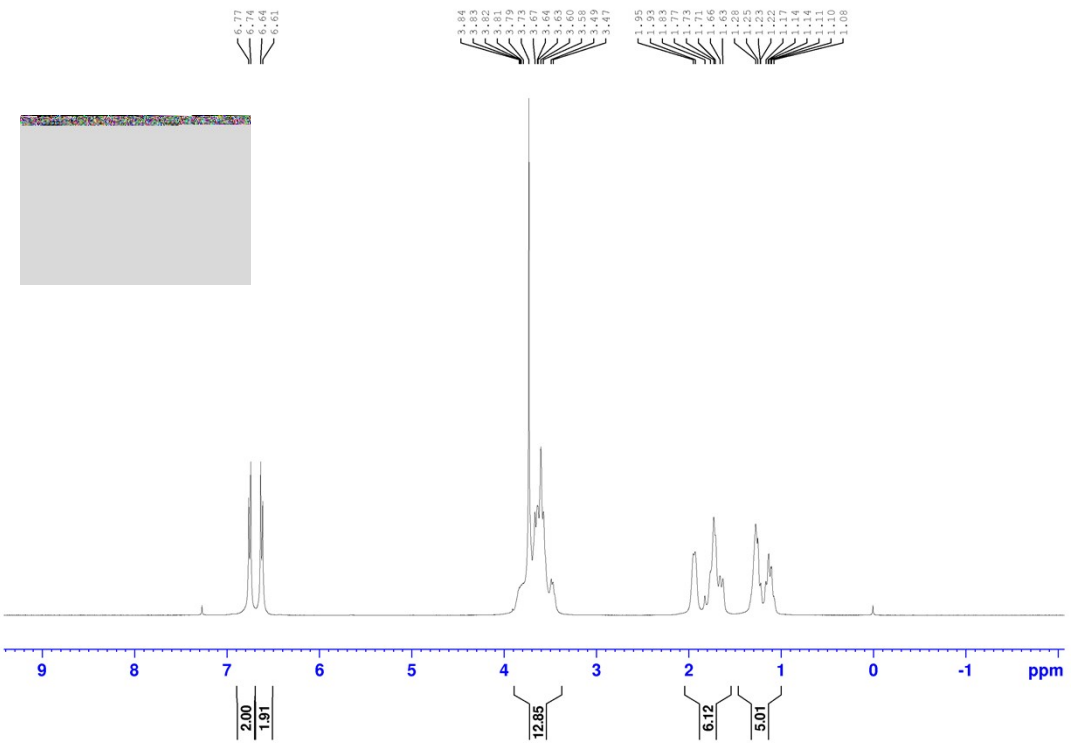
13C



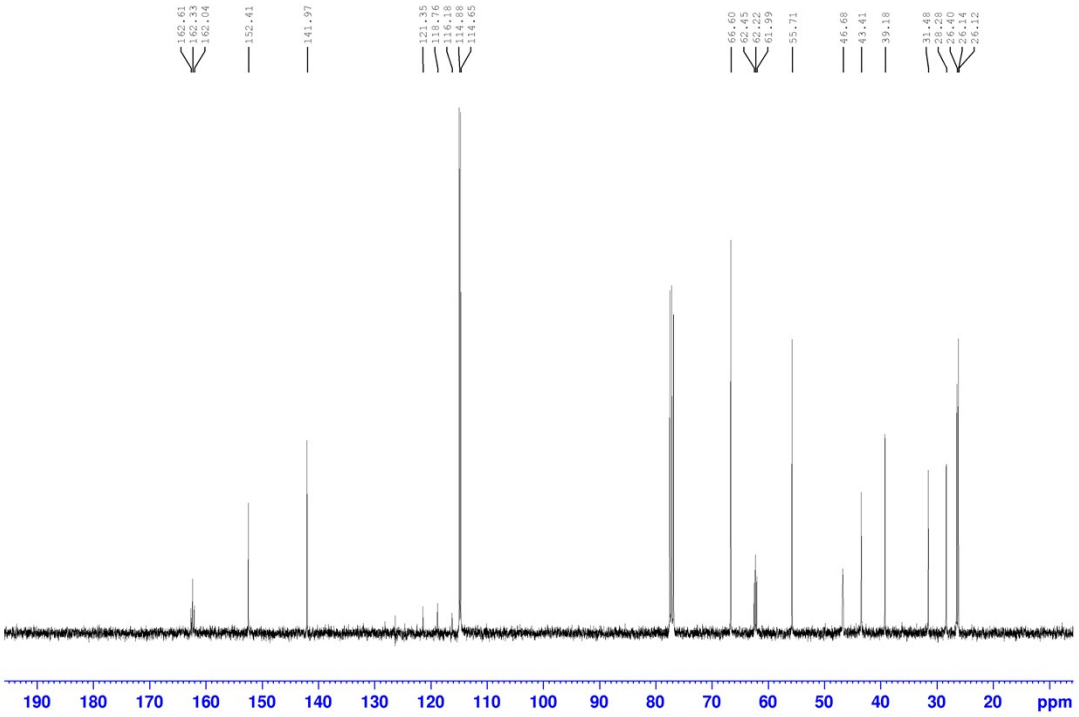
F19CPD



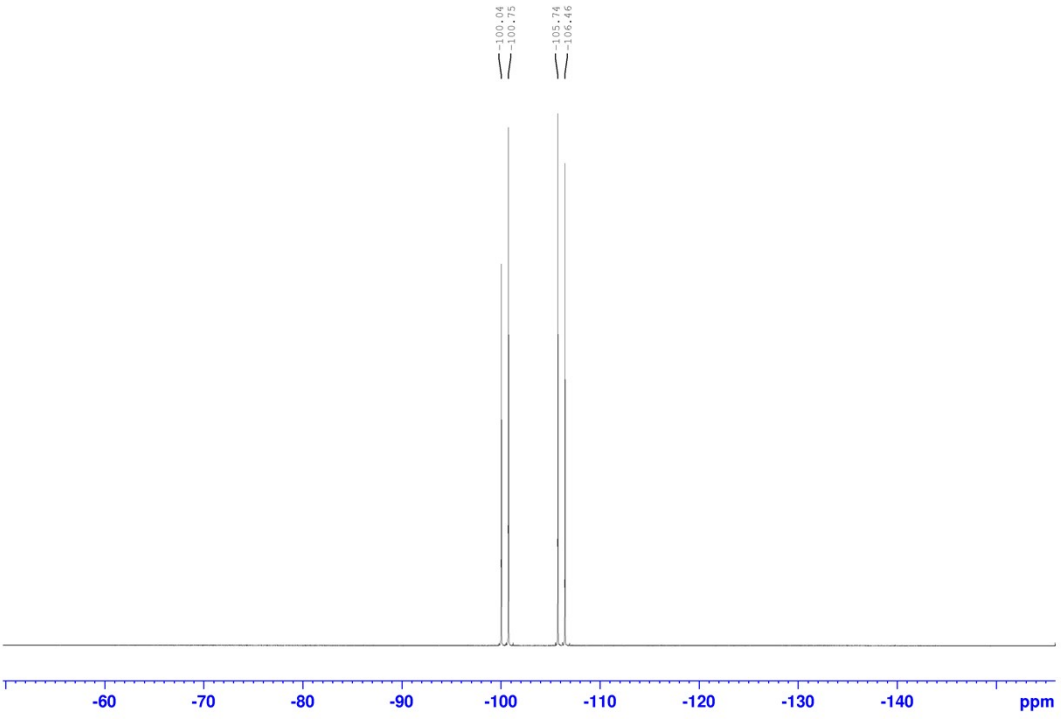
1D-1H zg30



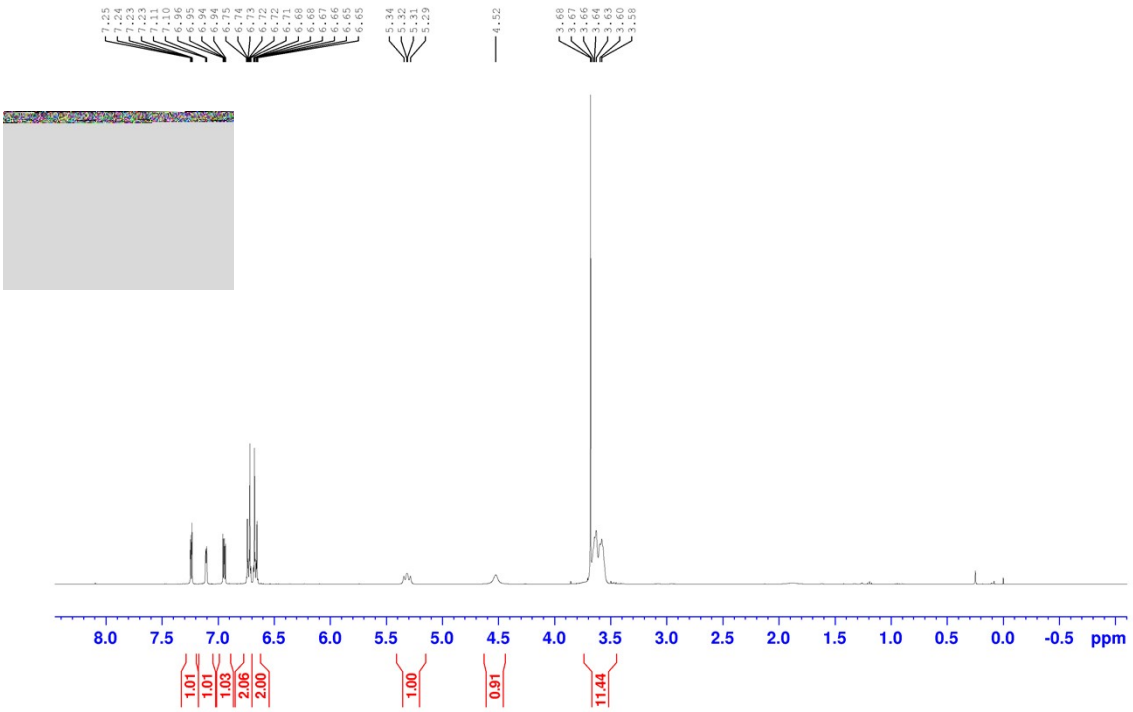
13C


162.61
162.33
162.04
152.41
141.97
121.35
118.76
116.18
114.88
114.65
66.60
66.45
62.22
61.99
55.71
46.68
43.41
39.18
31.48
28.28
26.40
26.14
26.12
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

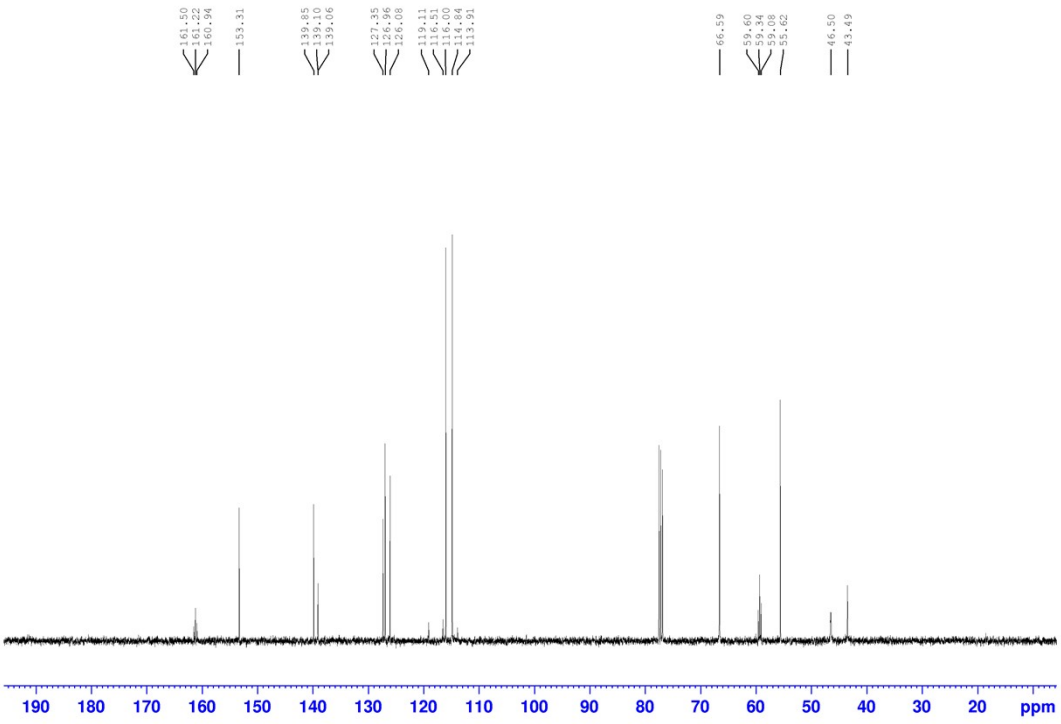
F19CPD


-100.04
-100.75
-105.74
-106.46
-60 -70 -80 -90 -100 -110 -120 -130 -140 ppm

1D-1H zg30



13C



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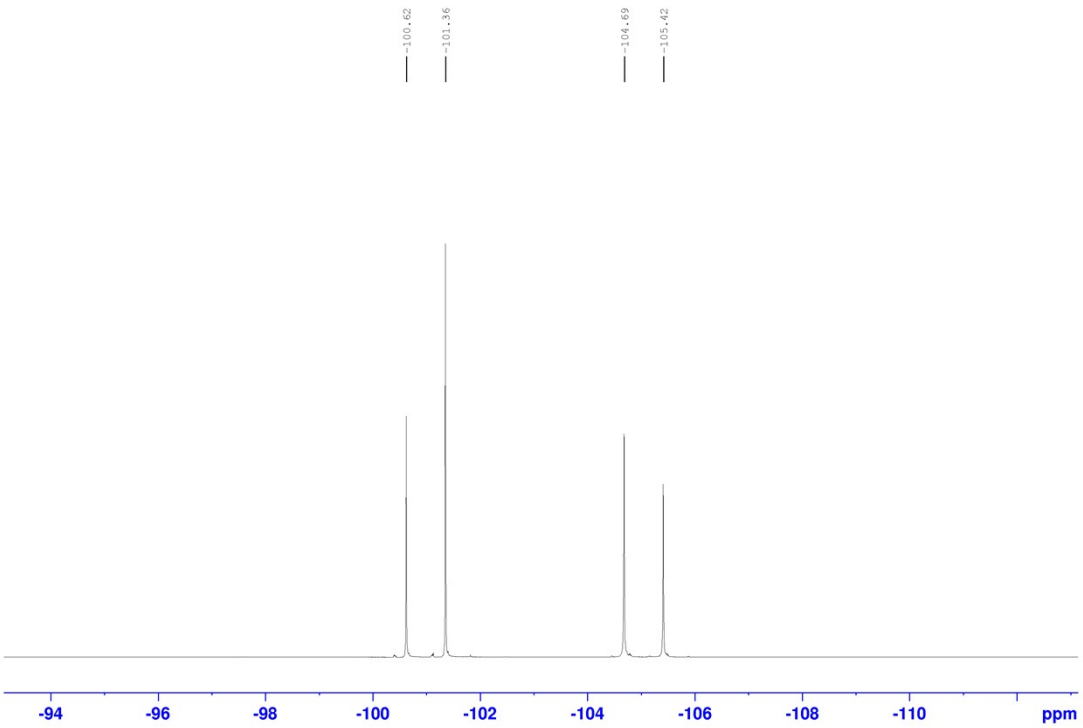
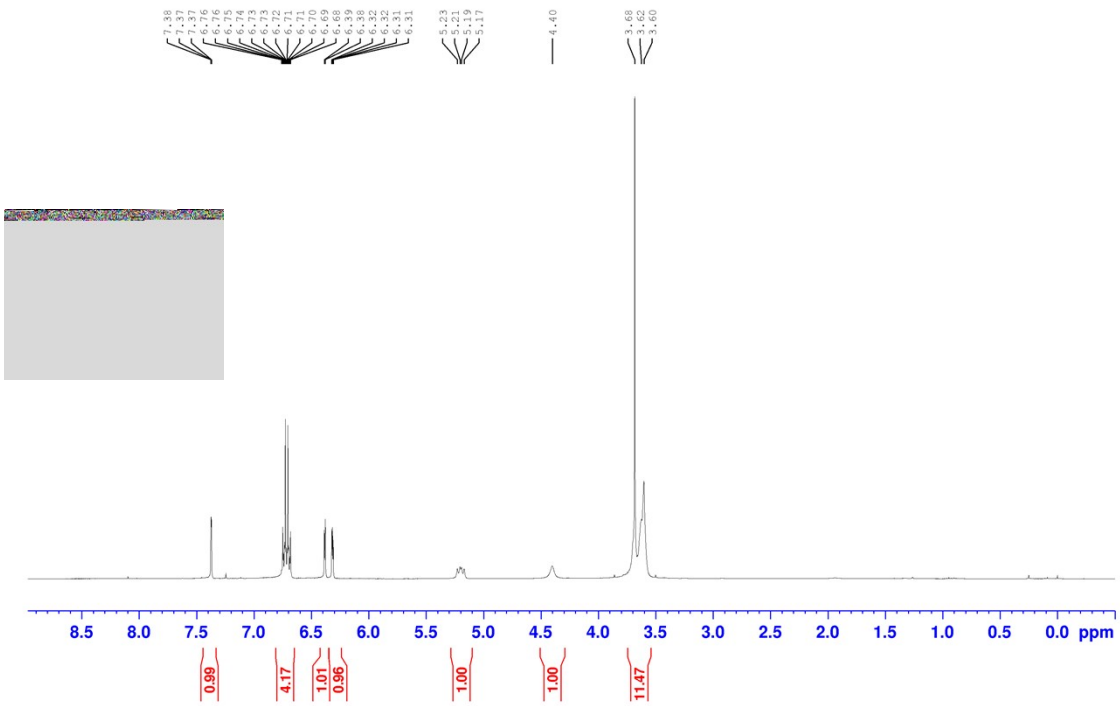
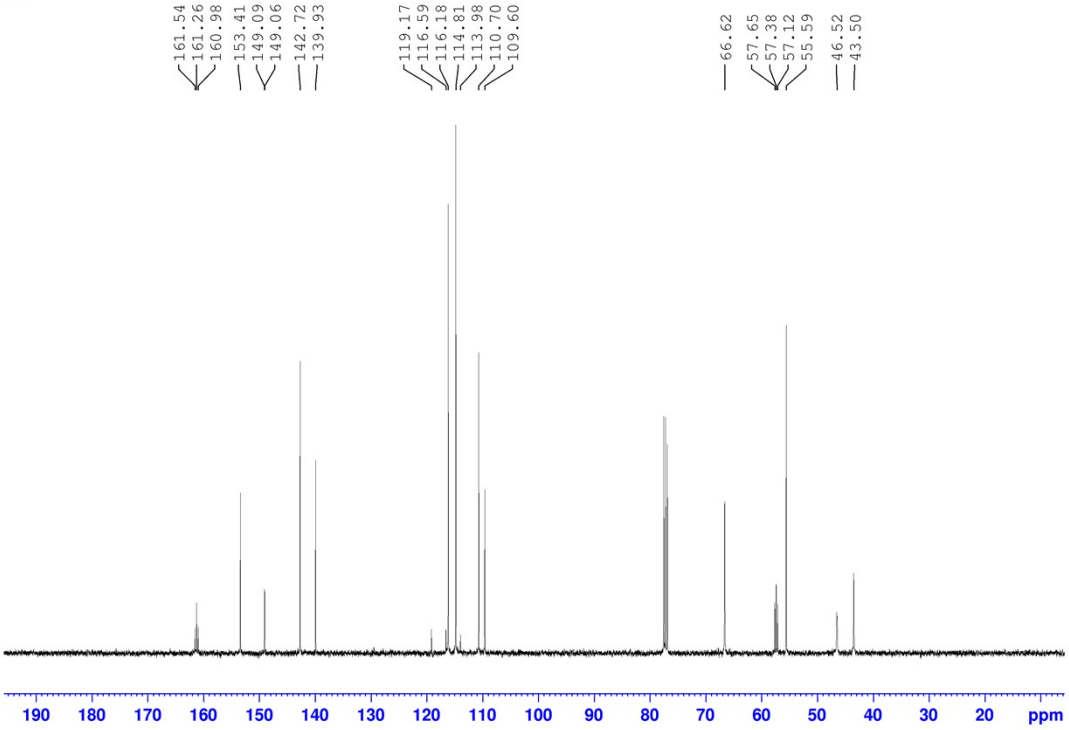


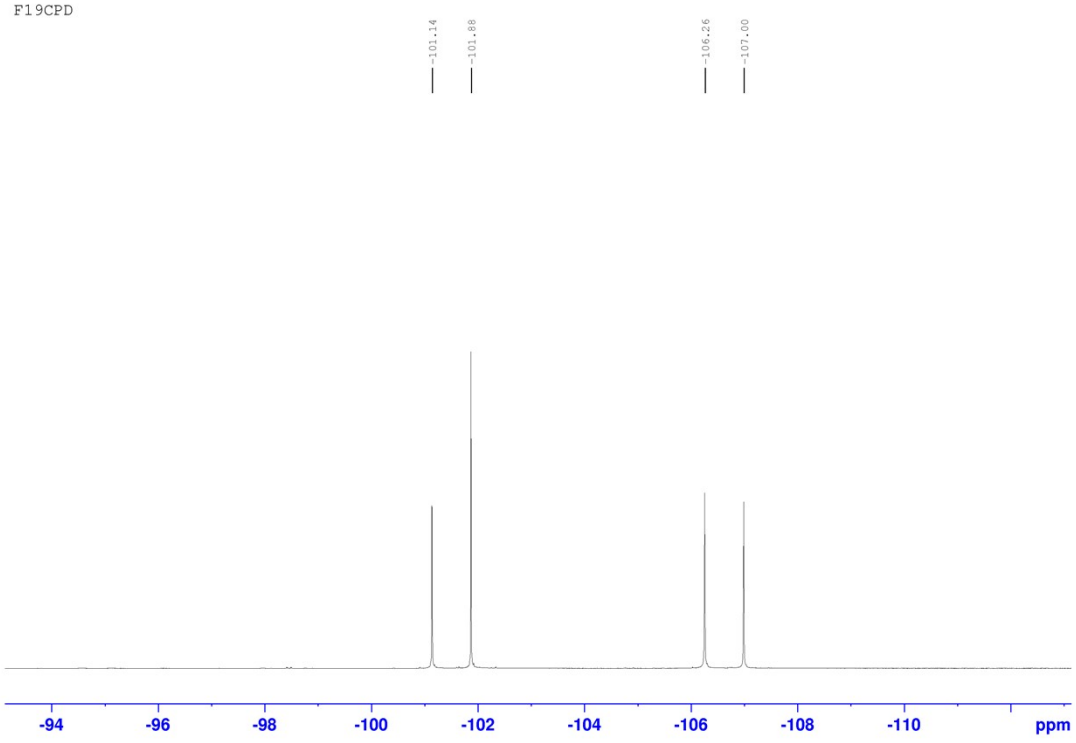
1D-1H zg30

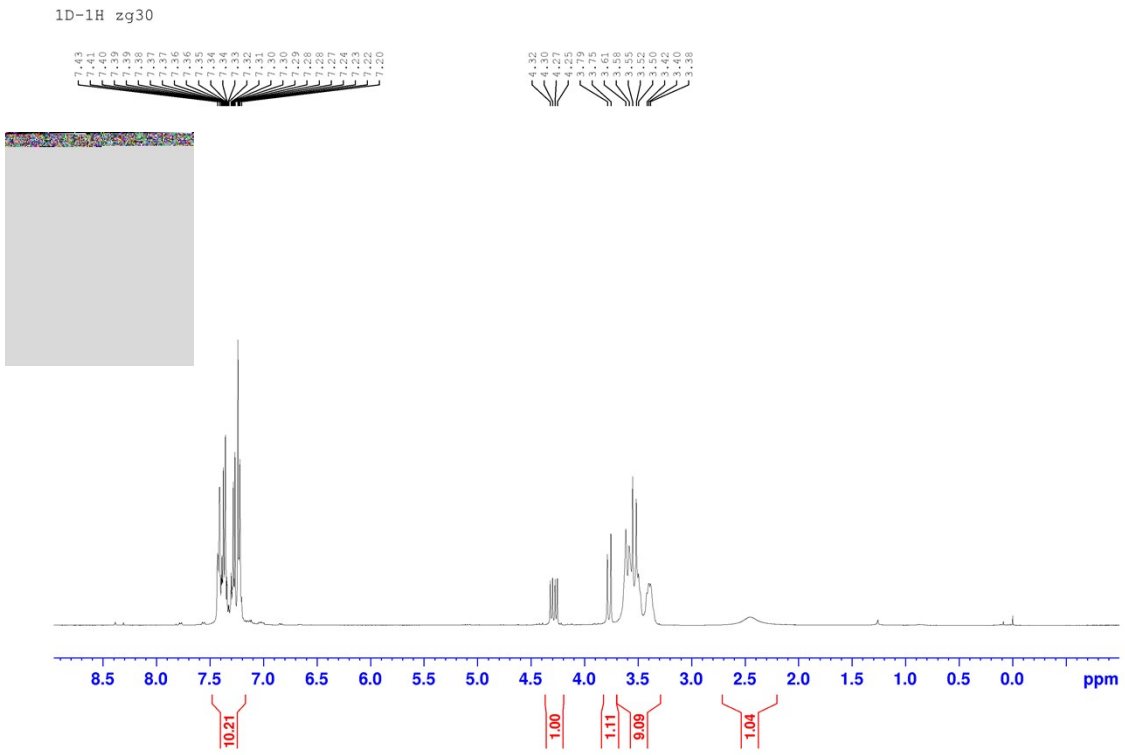


13C

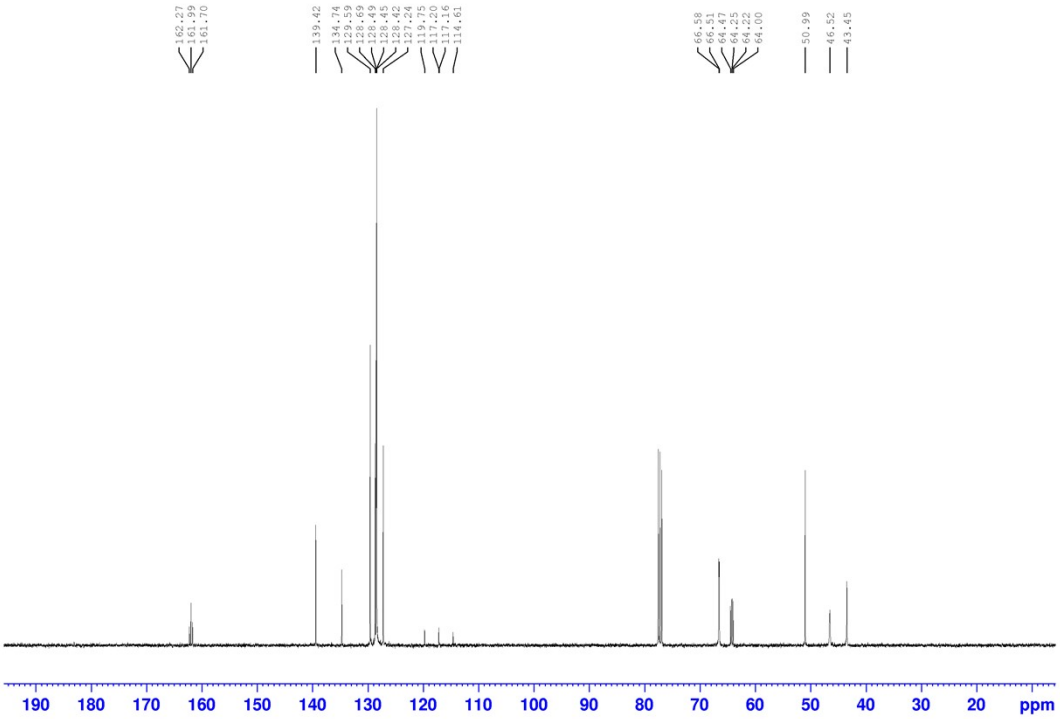

161.54
161.26
160.98
153.41
149.09
149.06
142.72
139.93
119.17
116.59
116.18
114.81
113.98
110.70
109.60
66.62
57.65
57.38
57.12
55.59
46.52
43.50
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

F19CPD

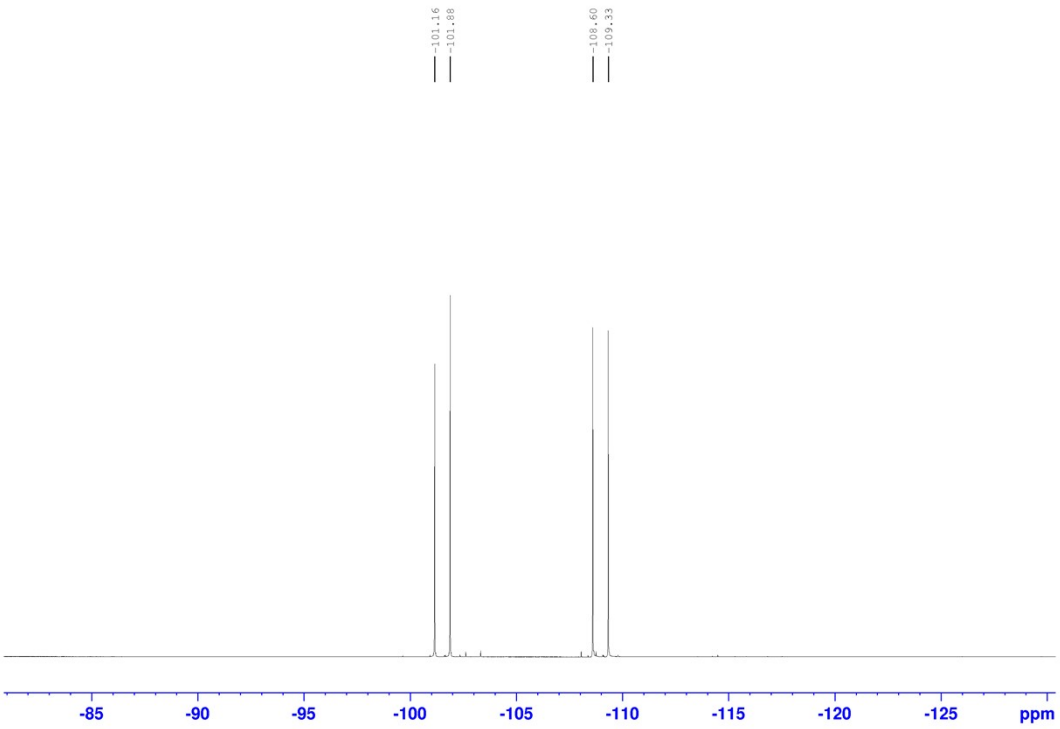

-101.14
-101.88
-106.26
-107.00
-94 -96 -98 -100 -102 -104 -106 -108 -110 ppm


1D-1H zg30
7.43
7.41
7.40
7.39
7.39
7.38
7.37
7.37
7.36
7.36
7.35
7.34
7.34
7.33
7.32
7.31
7.30
7.30
7.29
7.28
7.28
7.27
7.24
7.23
7.22
7.20
4.32
4.30
4.27
4.25
3.79
3.75
3.61
3.58
3.55
3.52
3.50
3.42
3.40
3.38
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
10.21
1.00
1.11
9.09
1.04

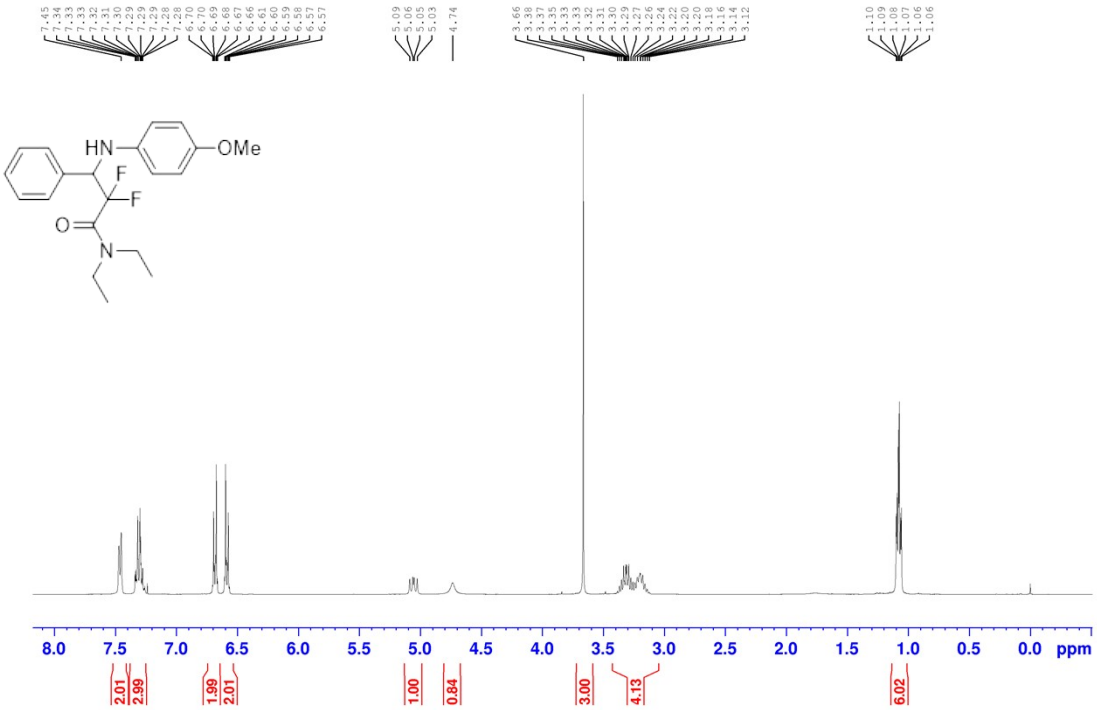
13C


162.27
161.99
161.70
139.42
134.74
129.59
128.69
128.49
128.45
128.42
128.24
119.75
117.20
117.16
114.61
66.58
66.51
64.47
64.25
64.22
64.00
50.99
46.52
43.45
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

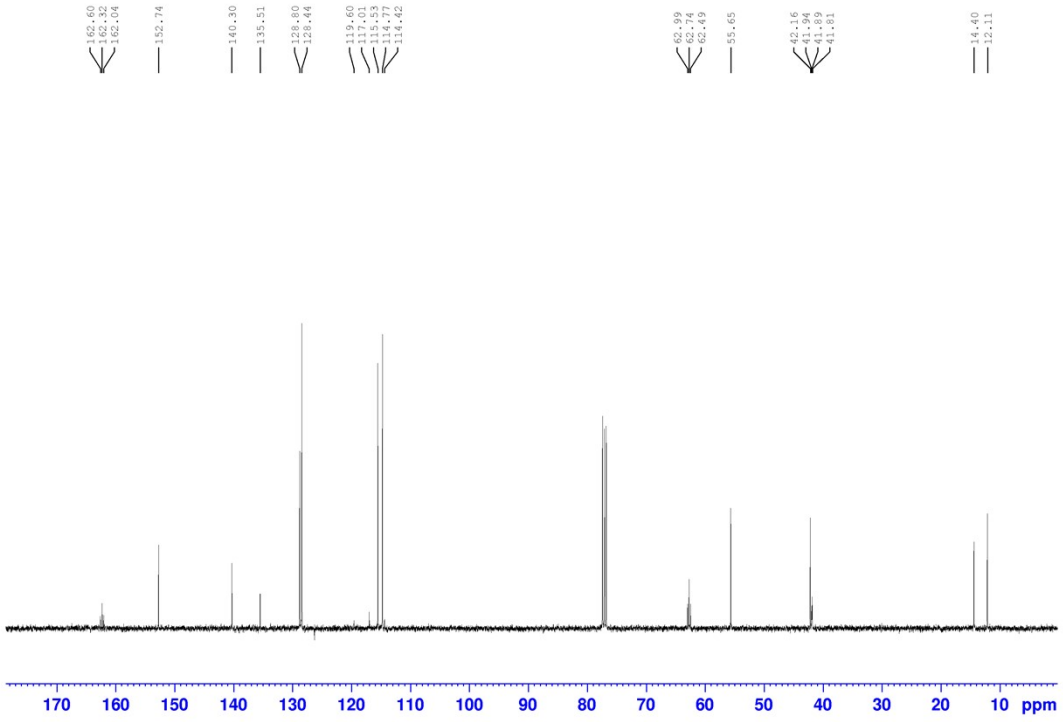
F19CPD


-101.16
-101.88
-108.60
-109.33
-85 -90 -95 -100 -105 -110 -115 -120 -125 ppm

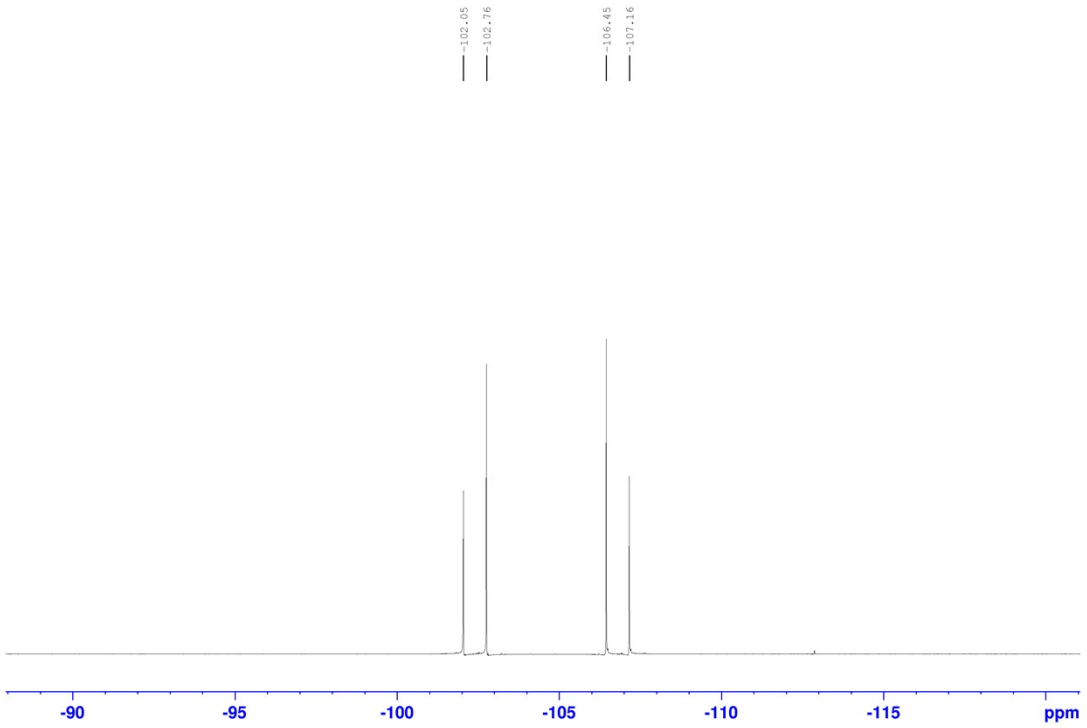
1D-1H zg30



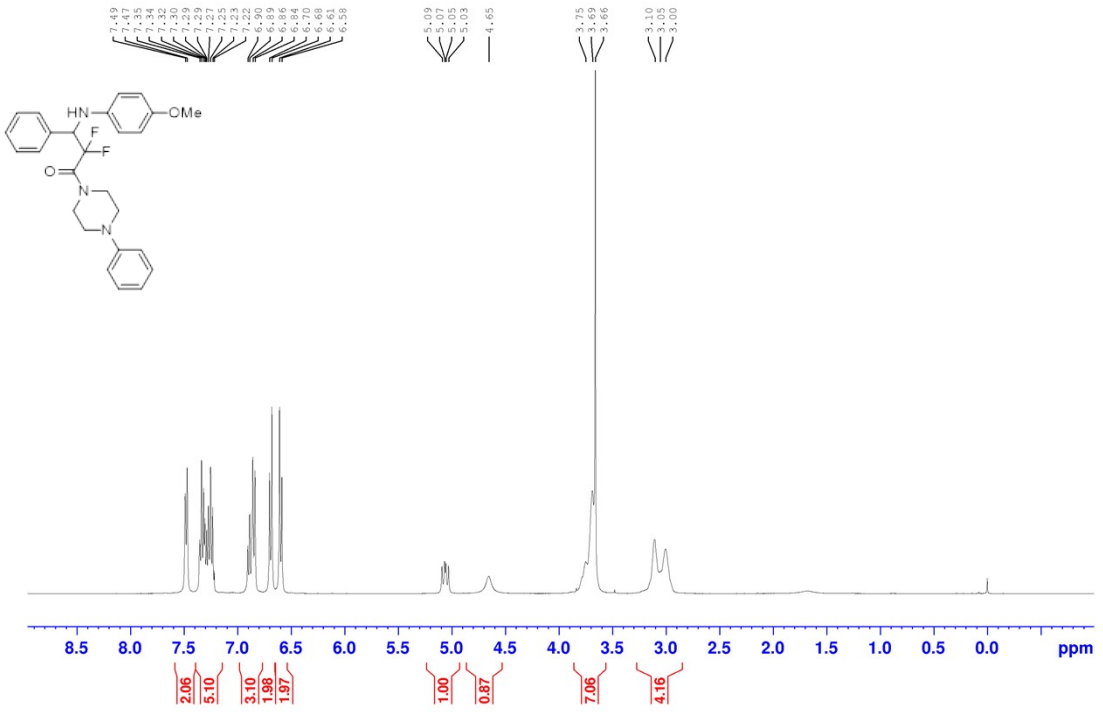
13C



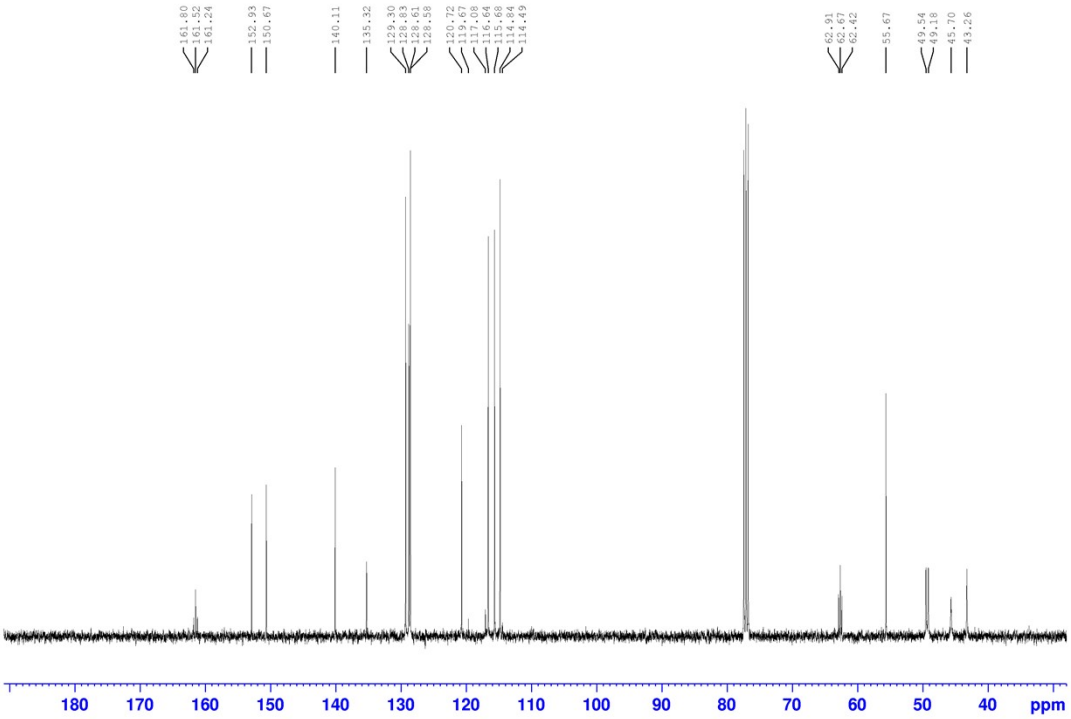
F19CPD



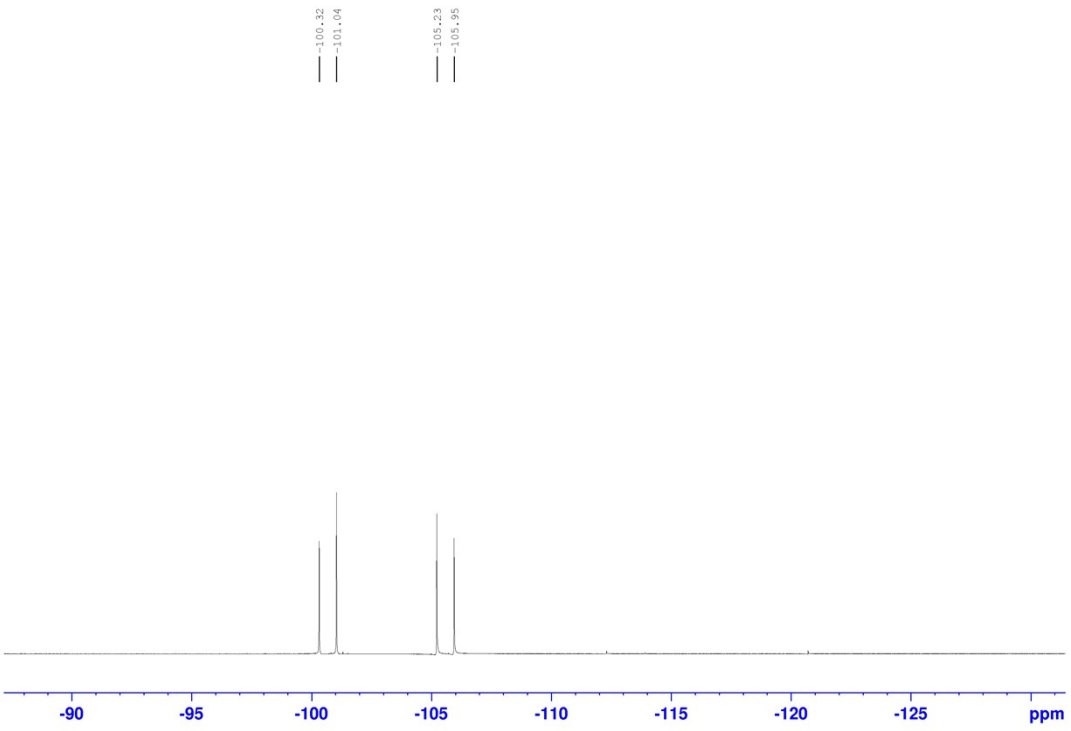
1D-1H zg30



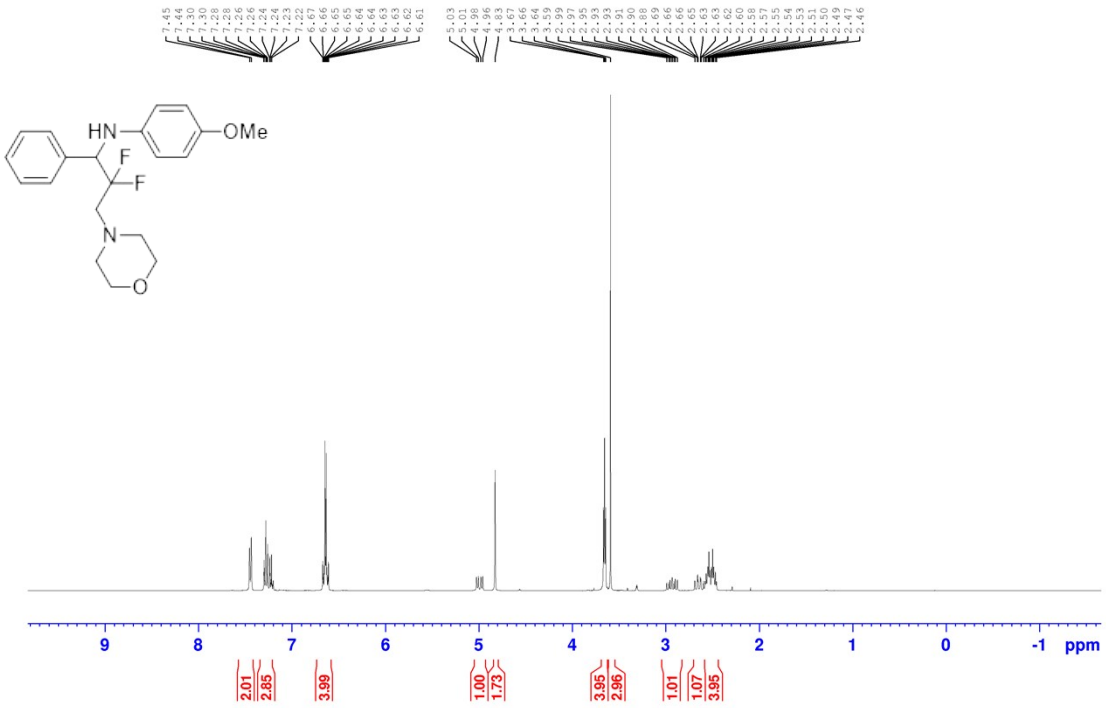
13C


161.80
161.52
161.24
152.93
150.67
140.11
135.32
129.30
128.83
128.61
128.58
120.72
119.67
117.08
116.64
115.68
114.84
114.49
62.91
62.67
62.42
55.67
49.54
49.18
45.70
43.26
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
ppm

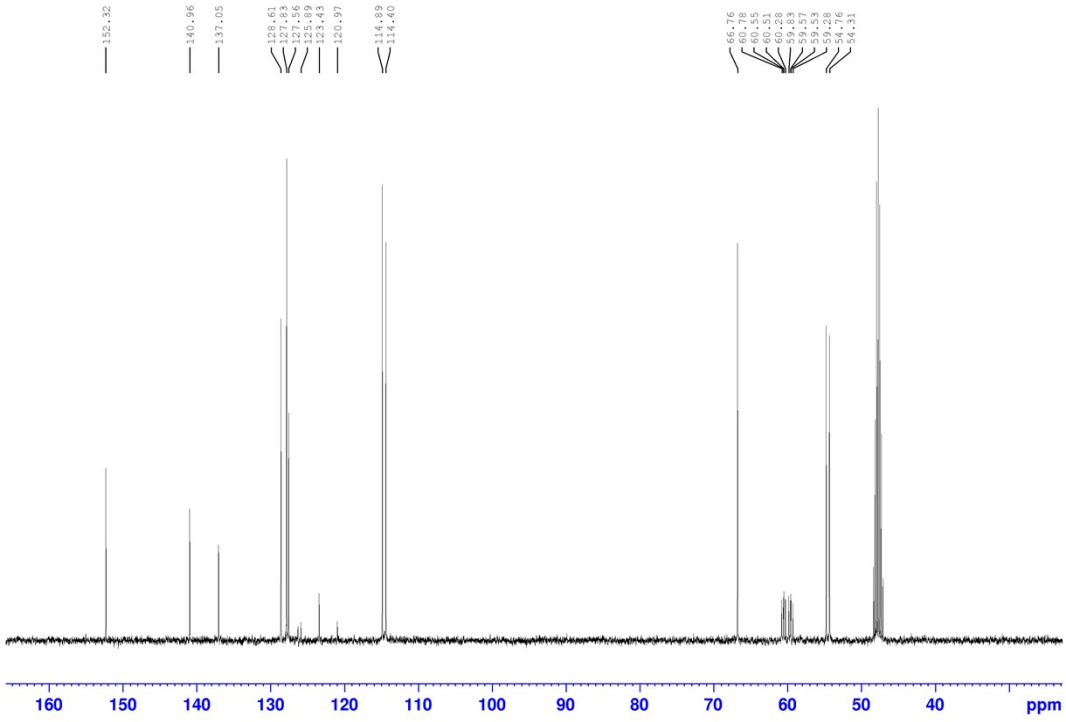
F19CPD


-100.32
-101.04
-105.23
-105.95
-90
-95
-100
-105
-110
-115
-120
-125
ppm

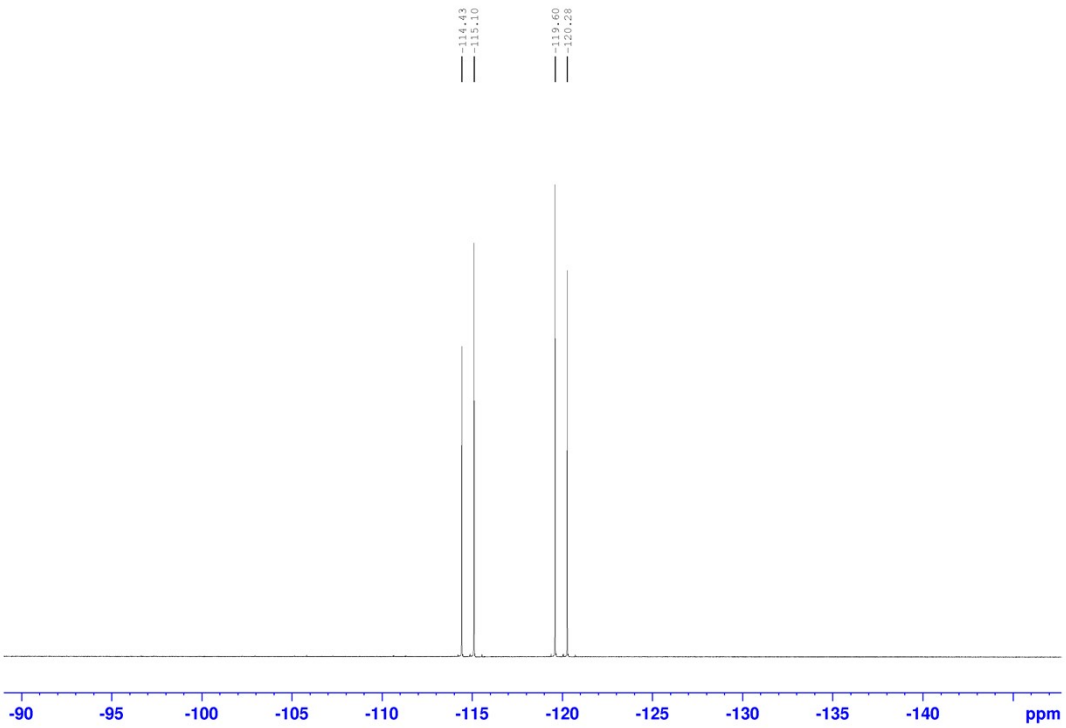
1D-1H zg30



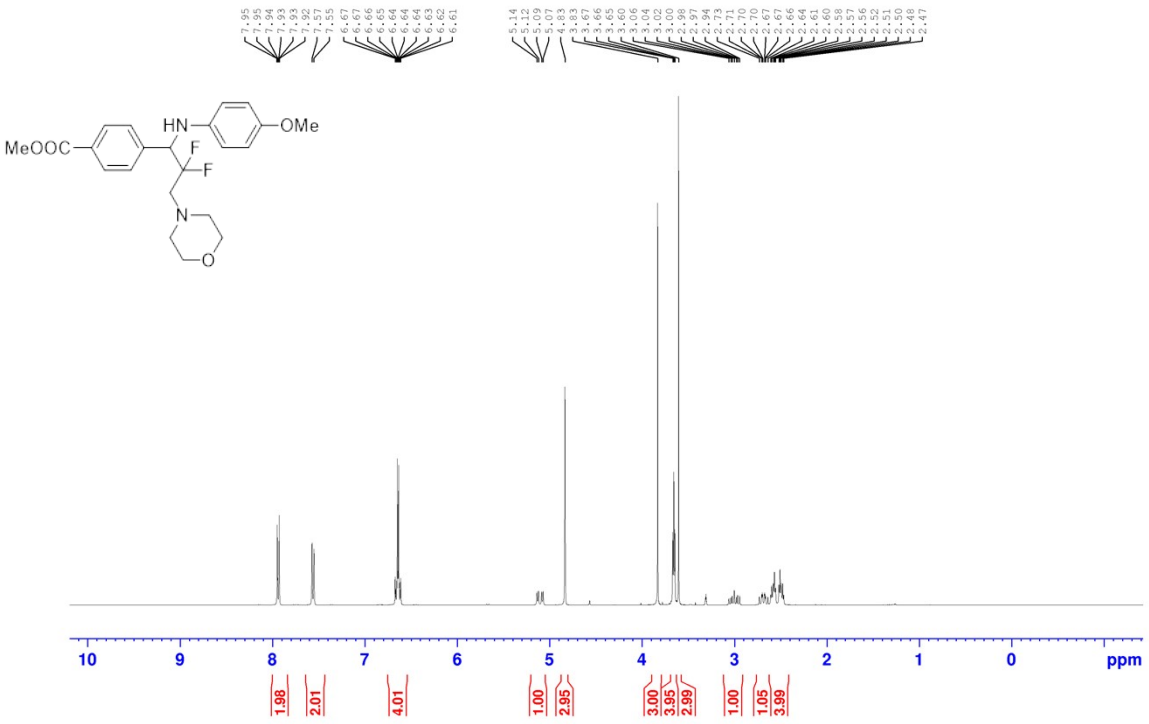
13C



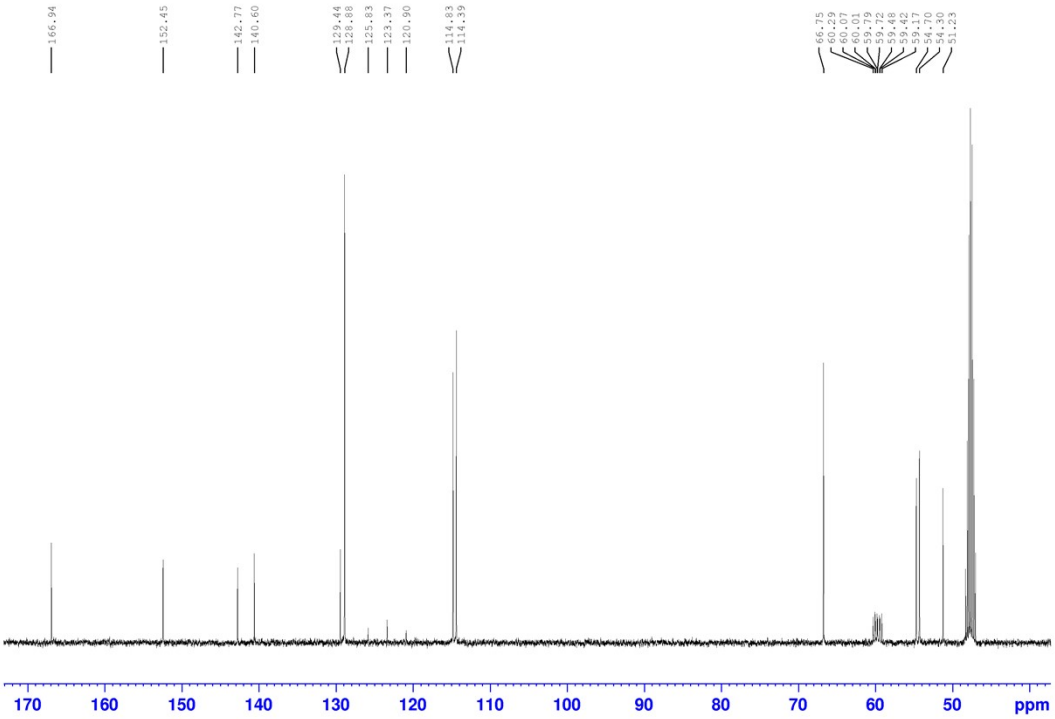
F19CPD



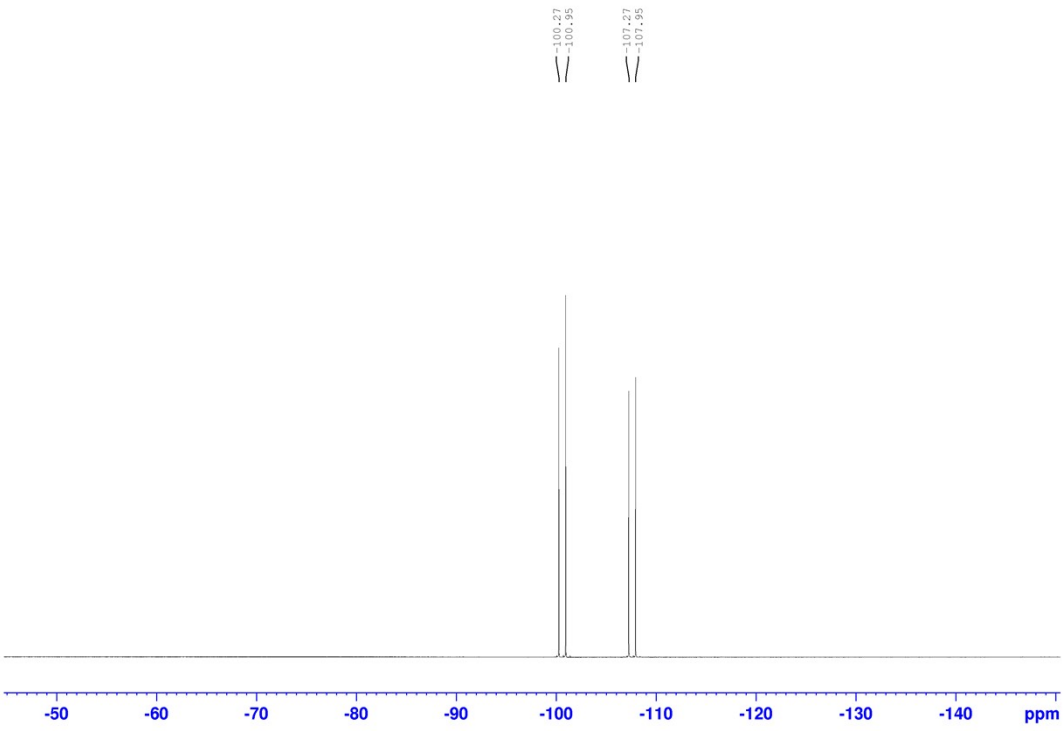
1D-1H zg30



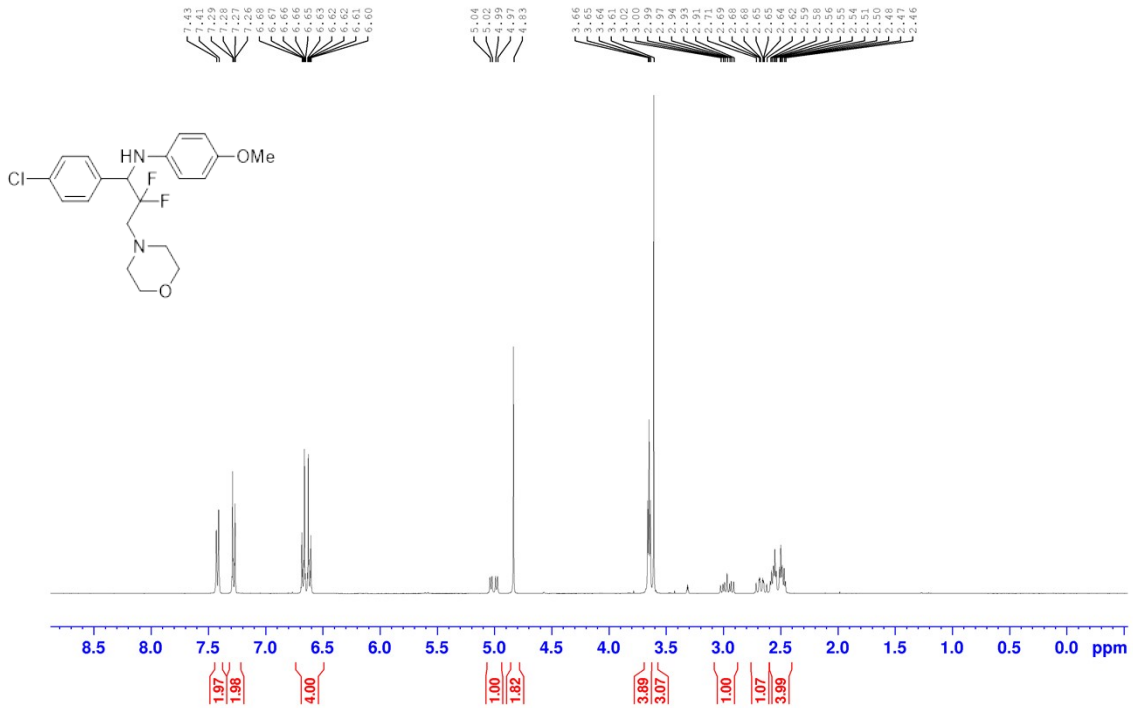
13C


166.94
152.45
142.77
140.60
129.44
128.88
125.83
123.37
120.90
114.83
114.39
66.75
60.29
60.07
60.01
59.79
59.72
59.48
59.42
59.17
54.30
54.00
51.23
170
160
150
140
130
120
110
100
90
80
70
60
50
ppm

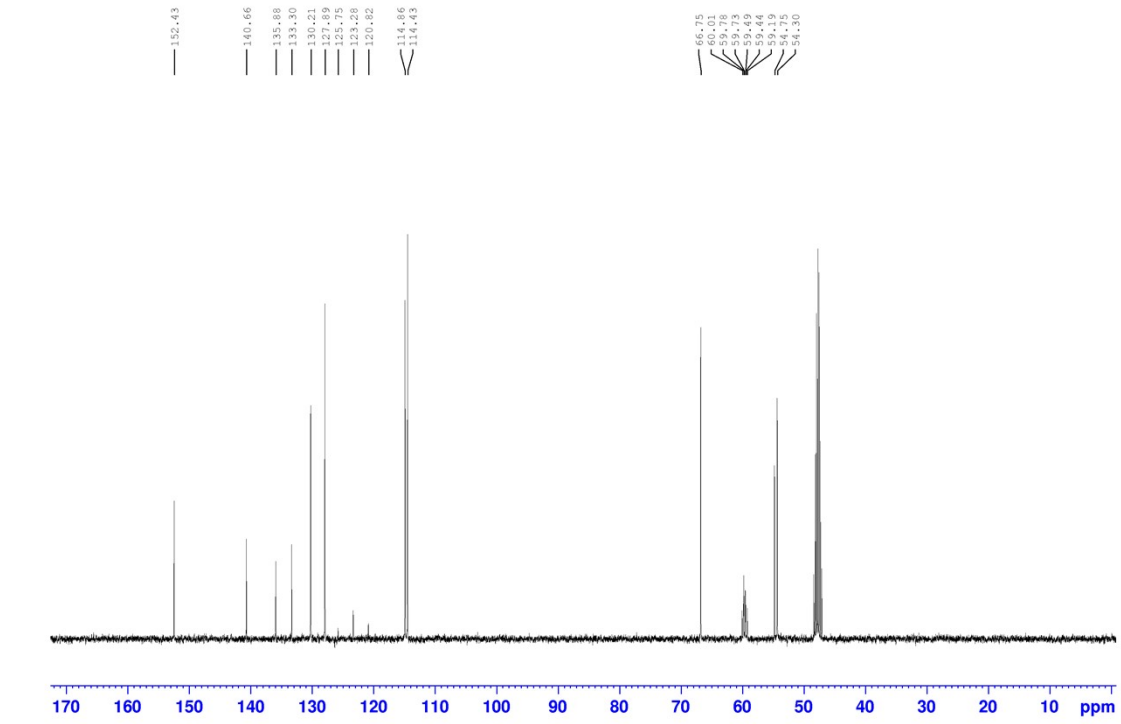
F19CPD


-100.27
-100.95
-107.27
-107.95
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
ppm

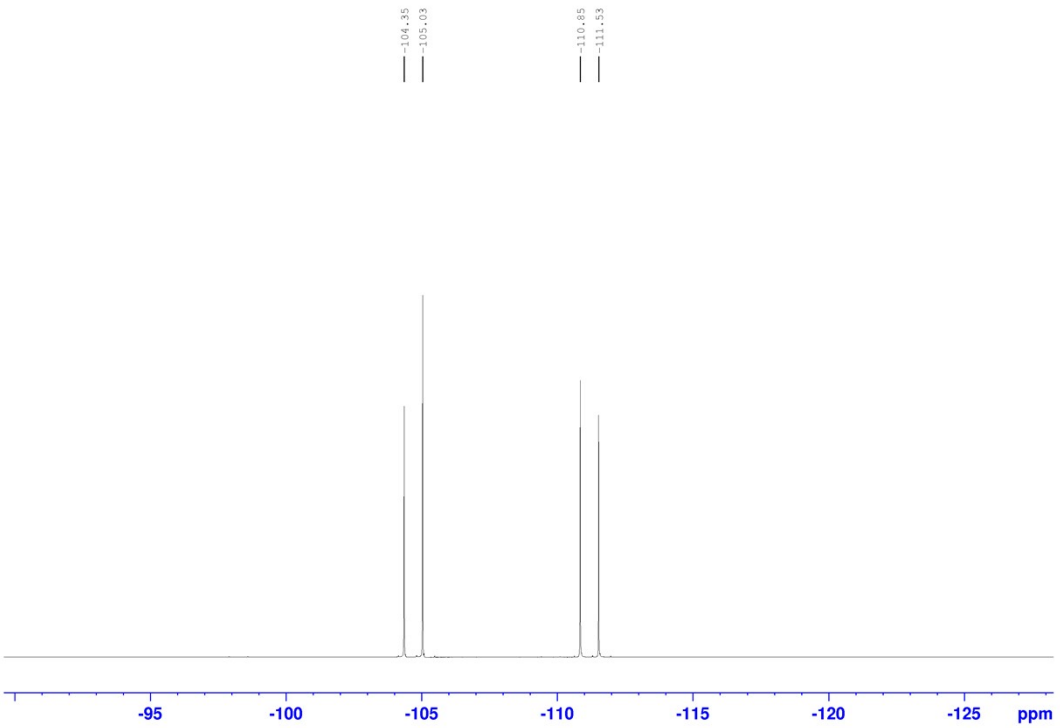
1D-1H zg30



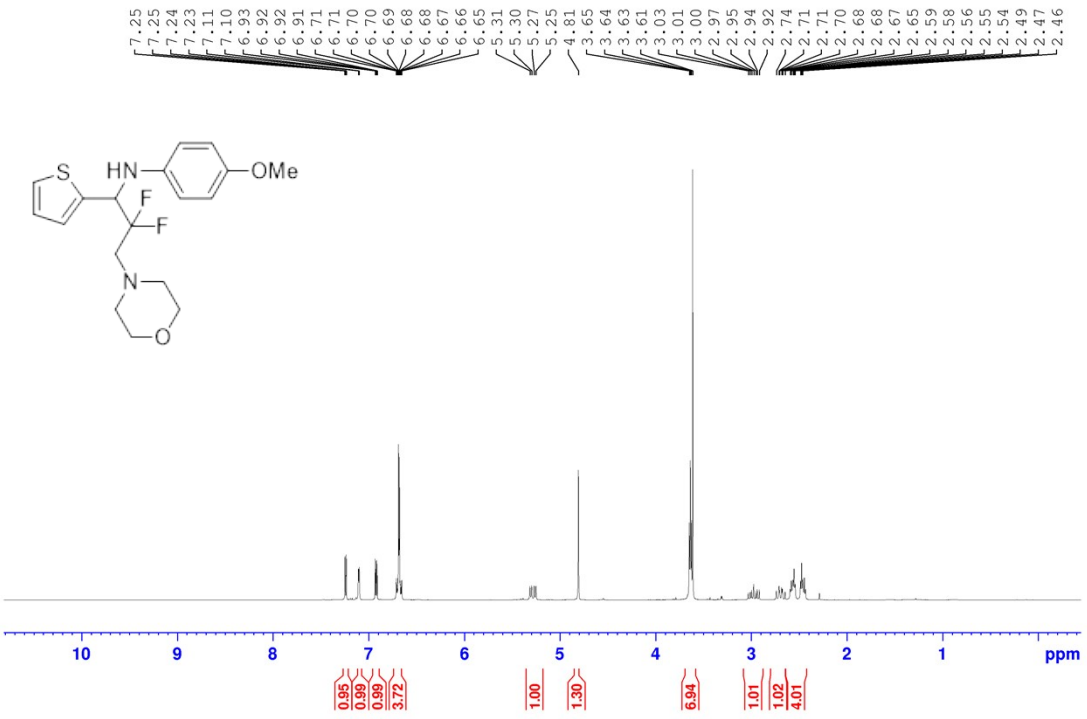
13C

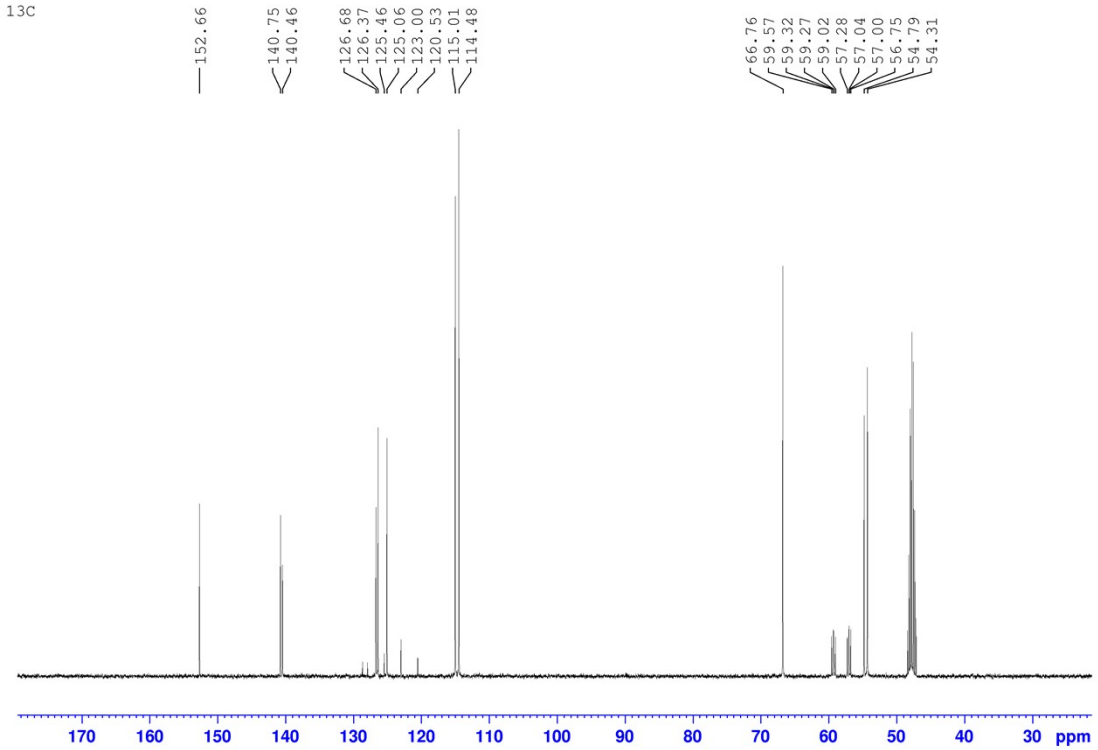


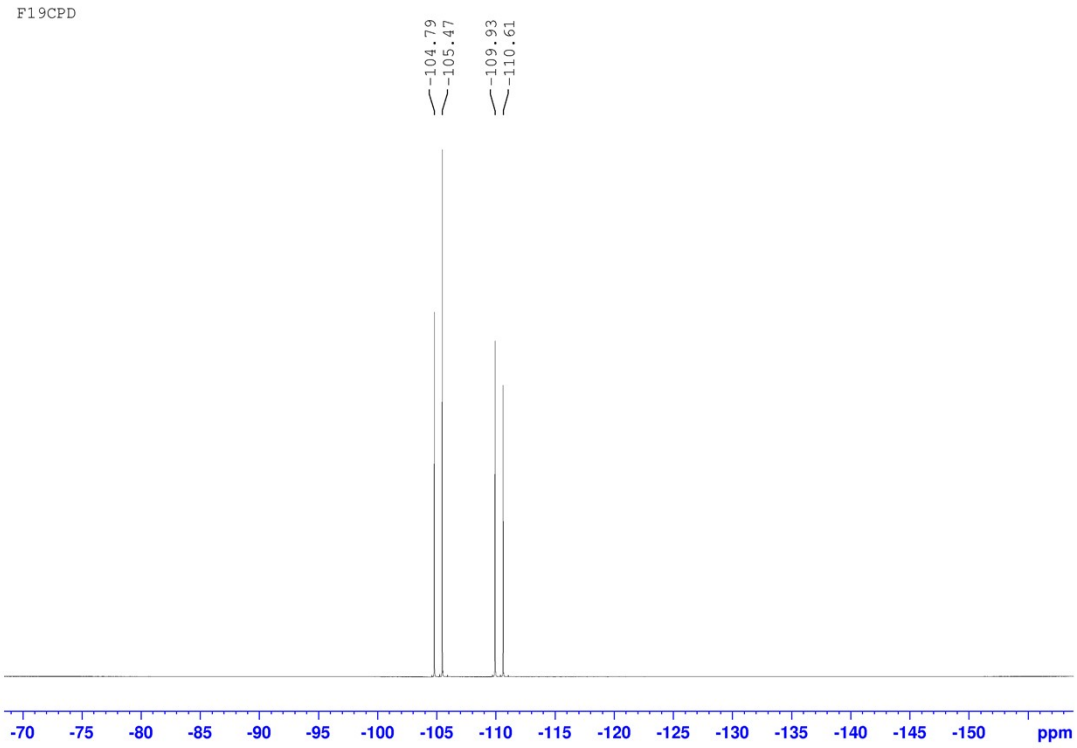
F19CPD



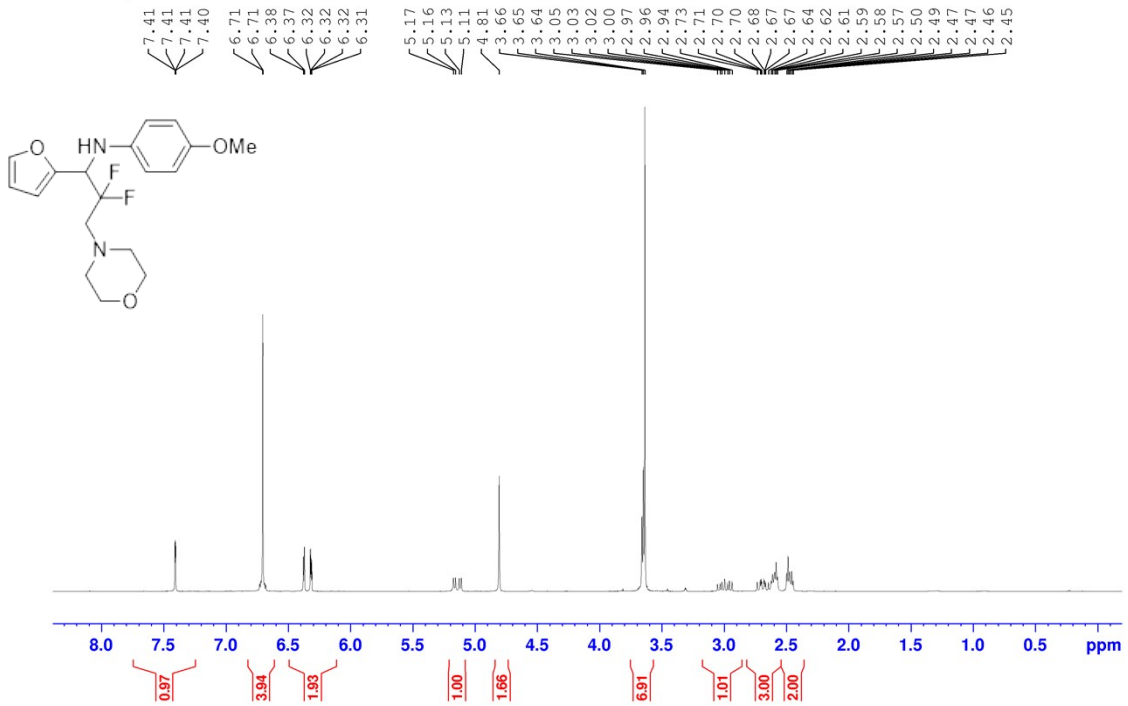
1D-1H zg30



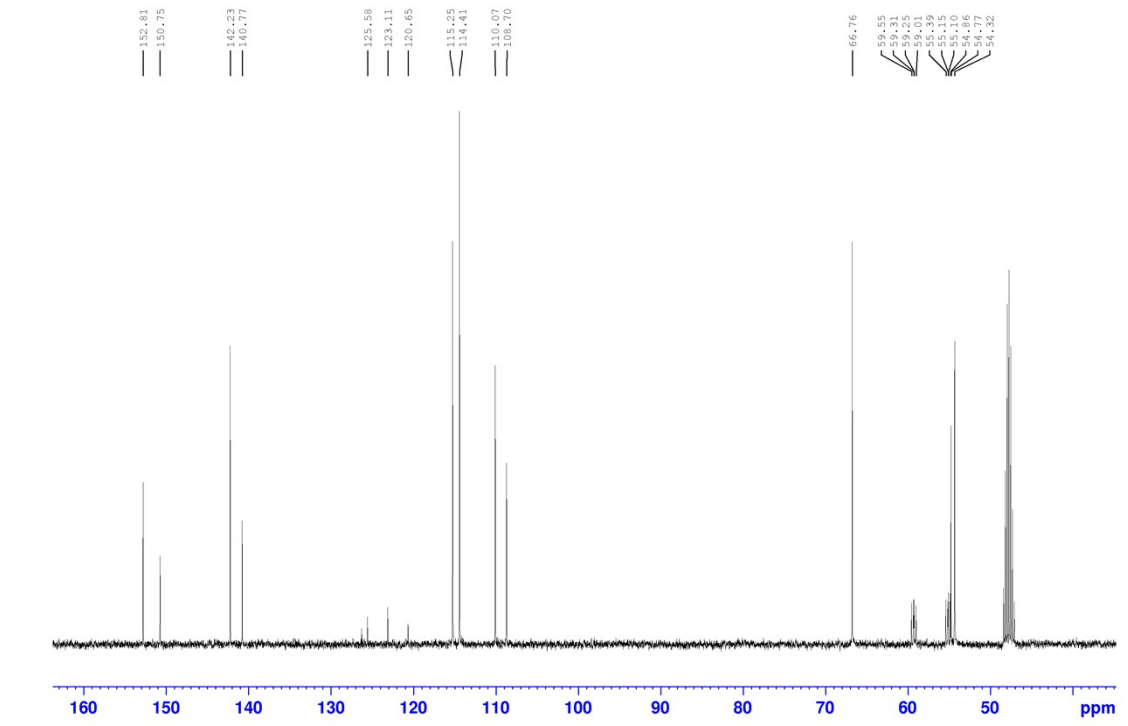

13C
152.66
140.75
140.46
126.68
126.37
125.46
125.06
123.00
120.53
115.01
114.48
66.76
59.57
59.32
59.27
59.02
57.28
57.04
57.00
56.75
54.79
54.31
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 ppm


F19CPD
-104.79
-105.47
-109.93
-110.61
-70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 ppm

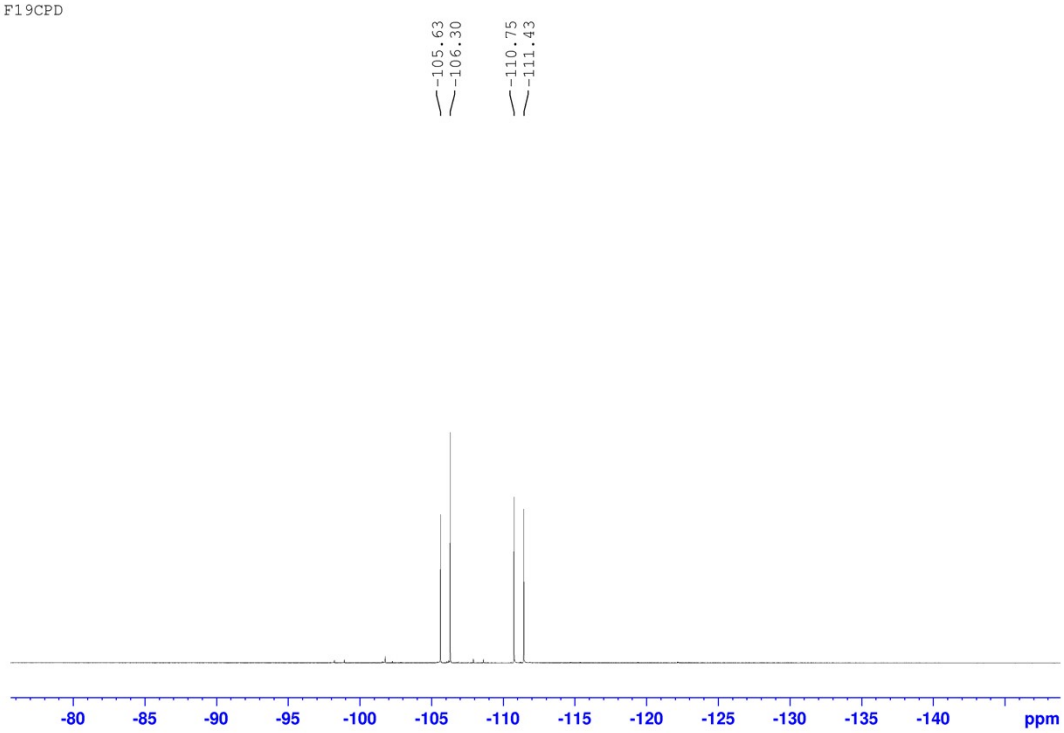
1D-1H zg30



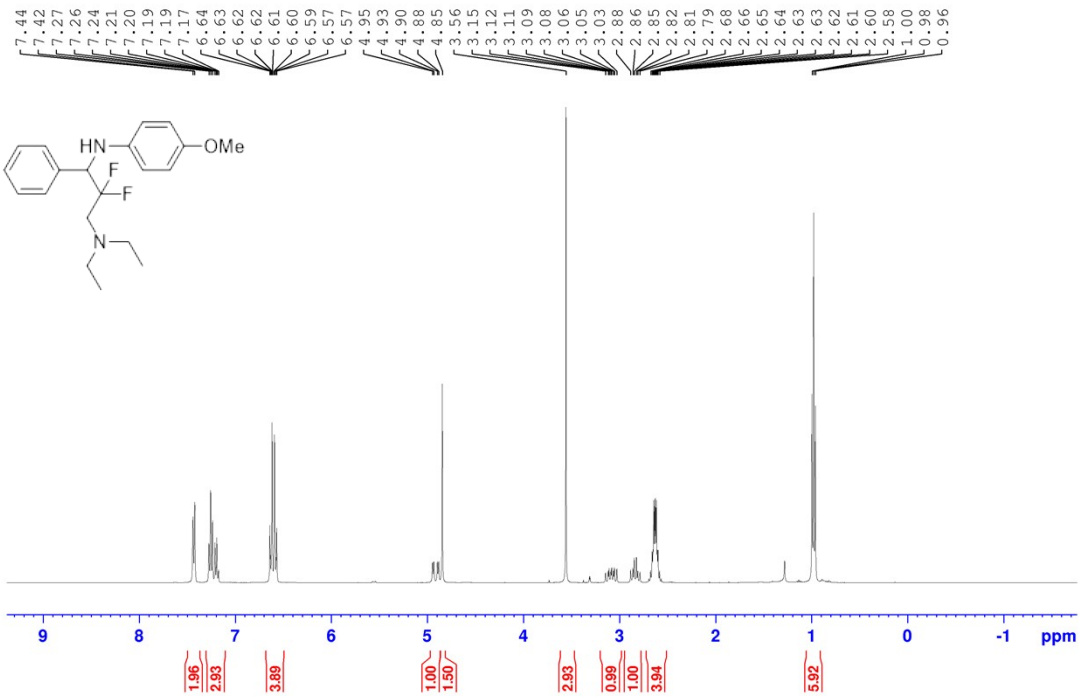
13C



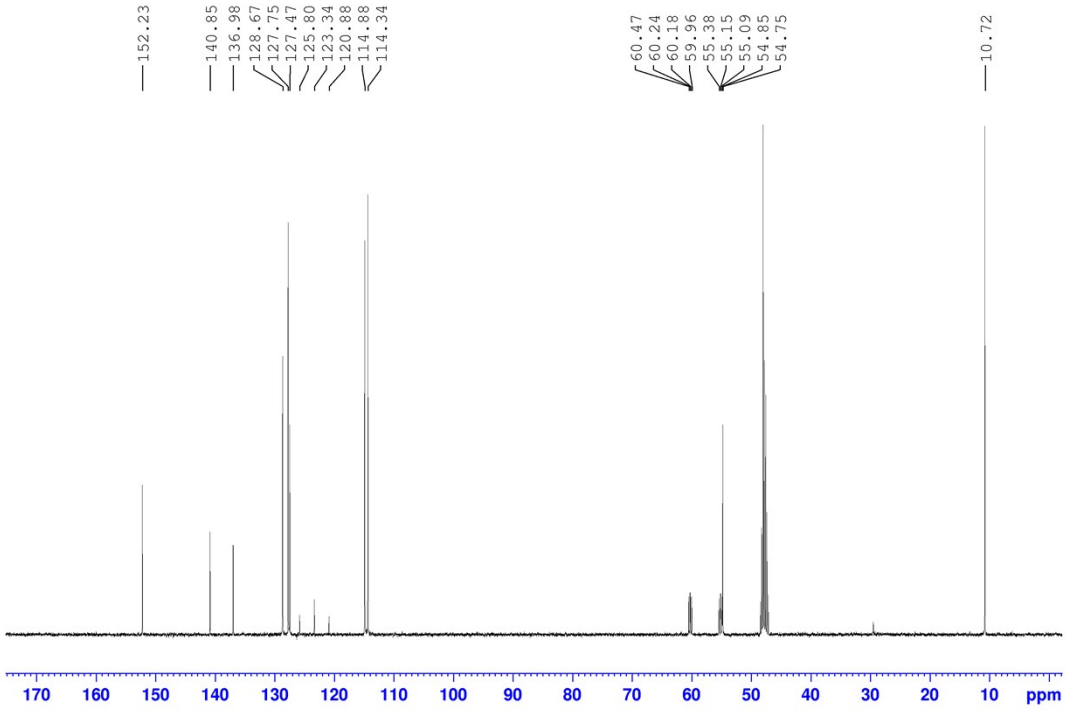
F19CPD



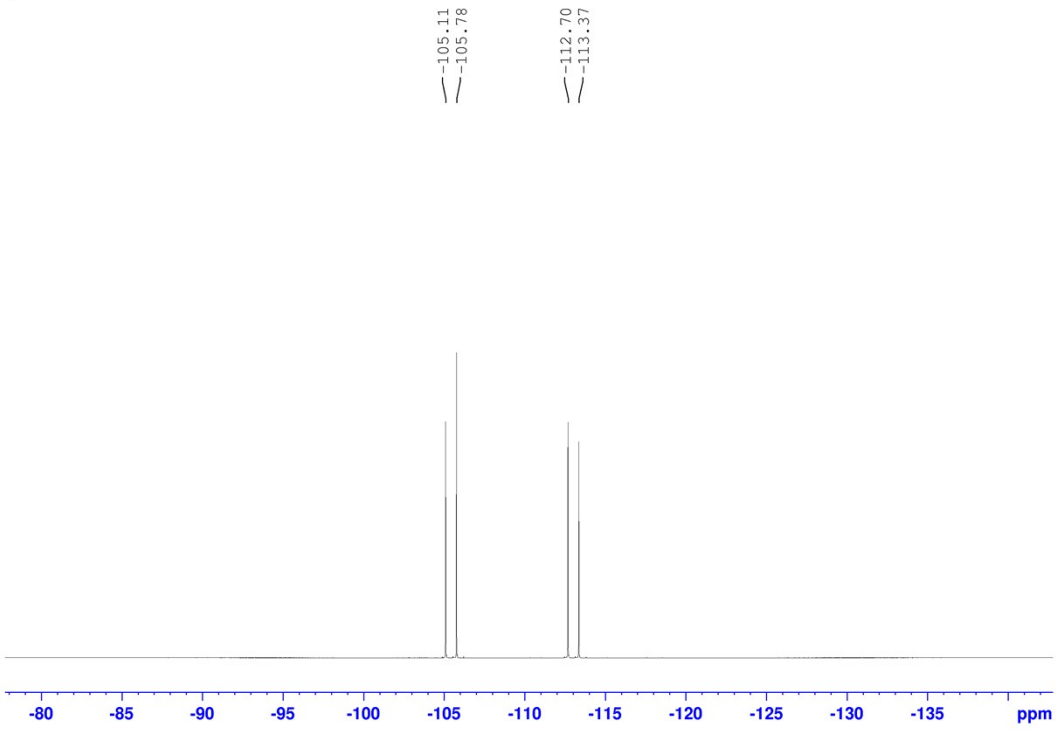
1D-1H zg30

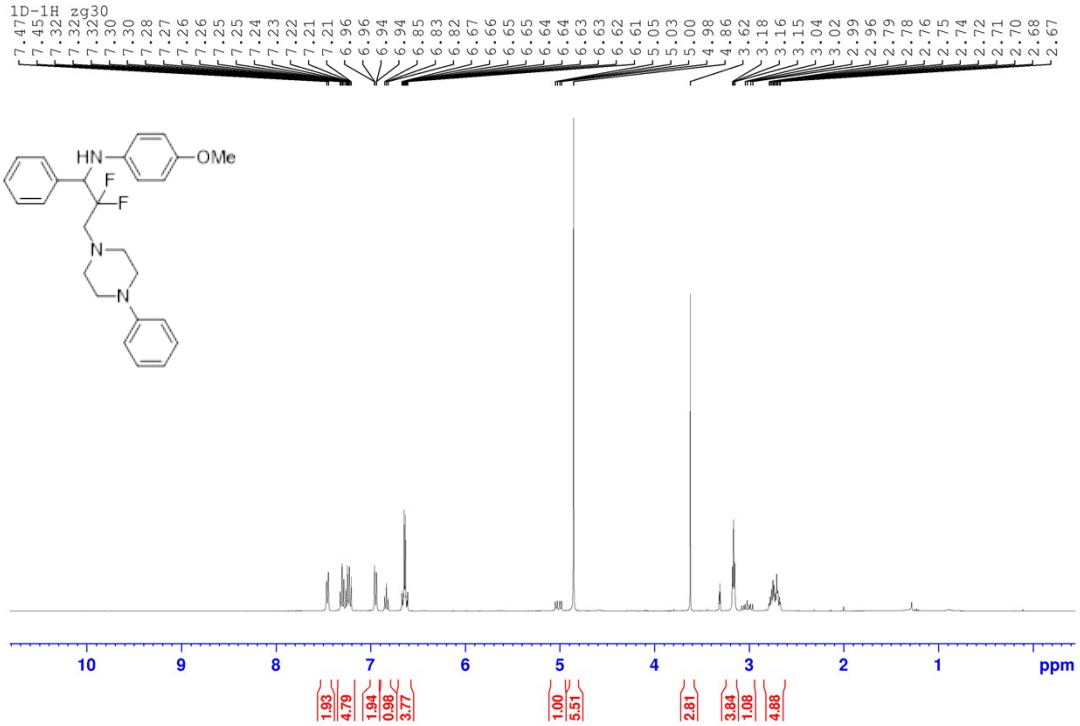


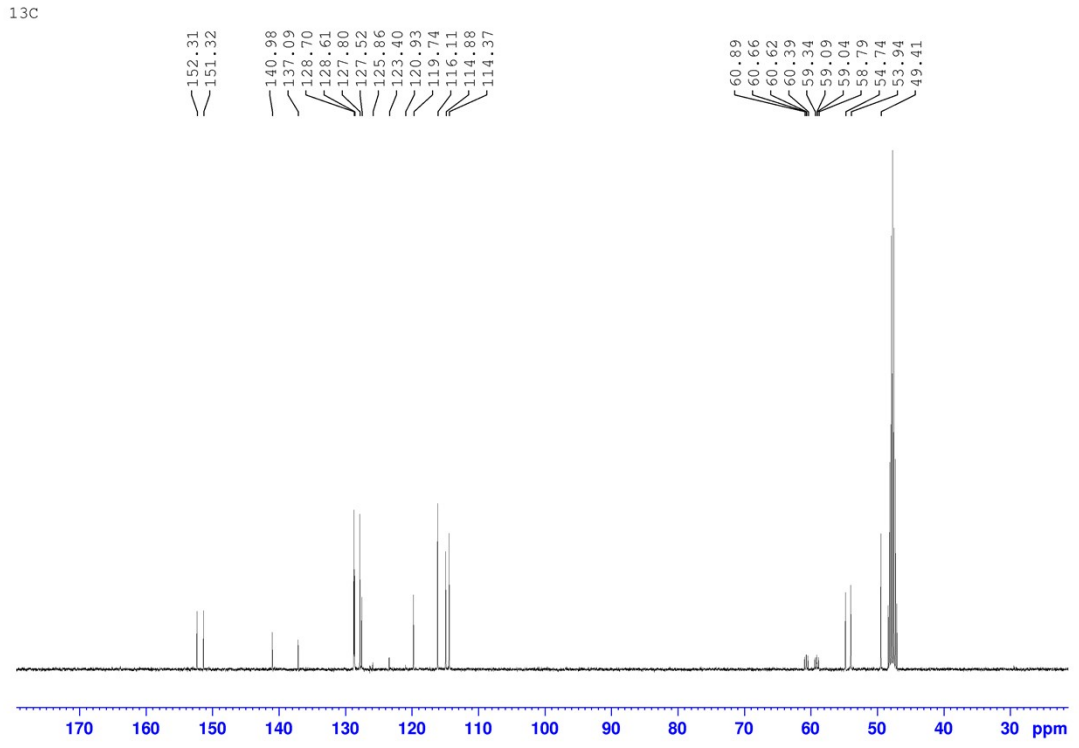
13C


152.23
140.85
136.98
128.67
127.75
127.47
125.80
123.34
120.88
114.88
114.34
60.47
60.24
60.18
59.96
55.38
55.15
55.09
54.85
54.75
10.72
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

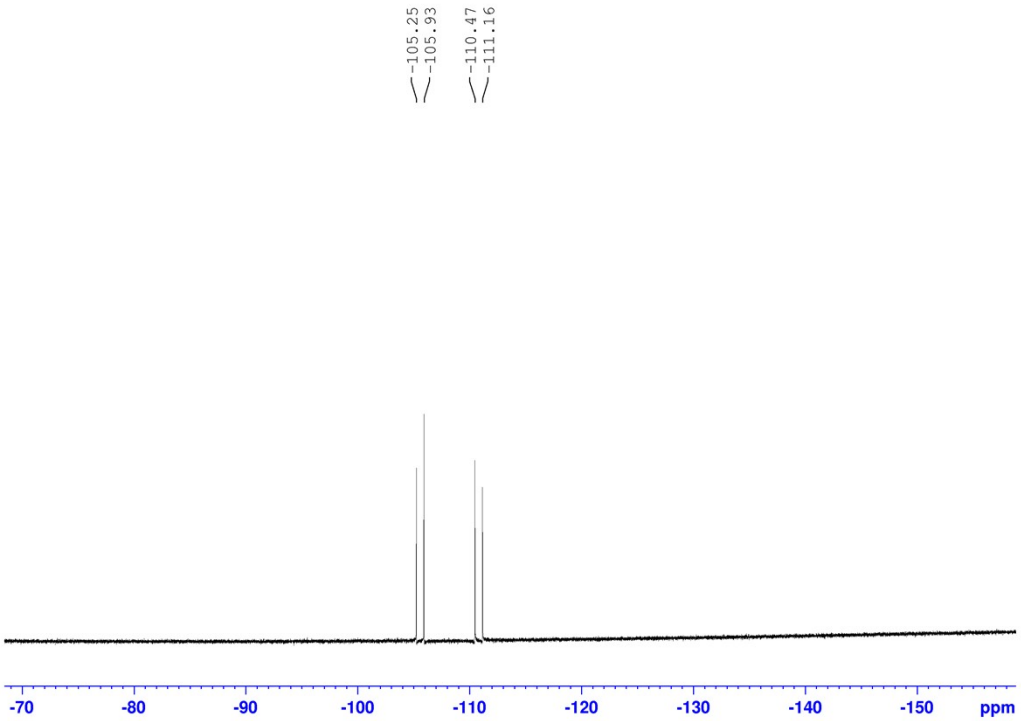
F19CPD


-105.11
-105.78
-112.70
-113.37
-80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 ppm

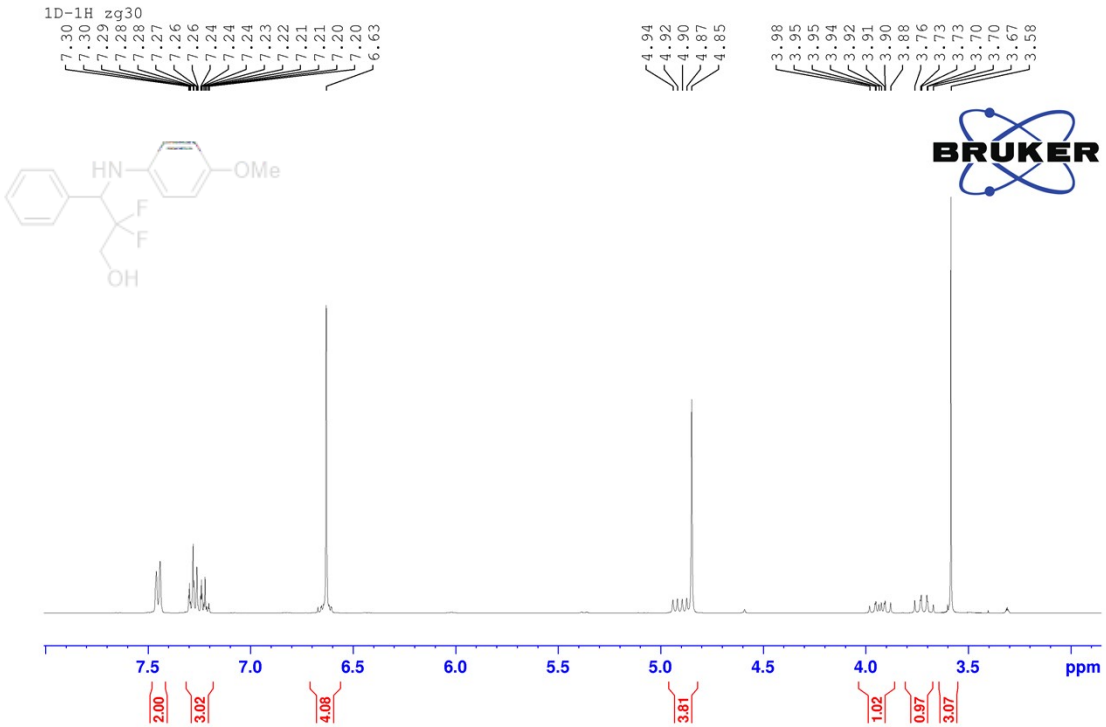

1D-1H zg30
7.47 7.45 7.32 7.32 7.32 7.30 7.30 7.28 7.27 7.26 7.26 7.25 7.24 7.23 7.22 7.21 7.21 6.96 6.96 6.94 6.94 6.85 6.83 6.82 6.67 6.66 6.65 6.65 6.64 6.64 6.63 6.63 6.62 6.61 5.05 5.03 5.00 4.98 4.86 3.62 3.18 3.16 3.15 3.04 3.02 2.99 2.96 2.79 2.78 2.76 2.75 2.74 2.72 2.71 2.70 2.68 2.67
HN
OMe
F
F
N
N
10 9 8 7 6 5 4 3 2 1 ppm
1.93 4.79 1.94 0.98 3.77 1.00 5.51 2.81 3.84 1.08 4.88


13C
152.31 151.32 140.98 137.09 128.70 128.61 127.80 127.52 125.86 123.40 120.93 119.74 116.11 114.88 114.37
60.89 60.66 60.62 60.39 59.34 59.09 59.04 58.79 54.74 53.94 49.41
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 ppm

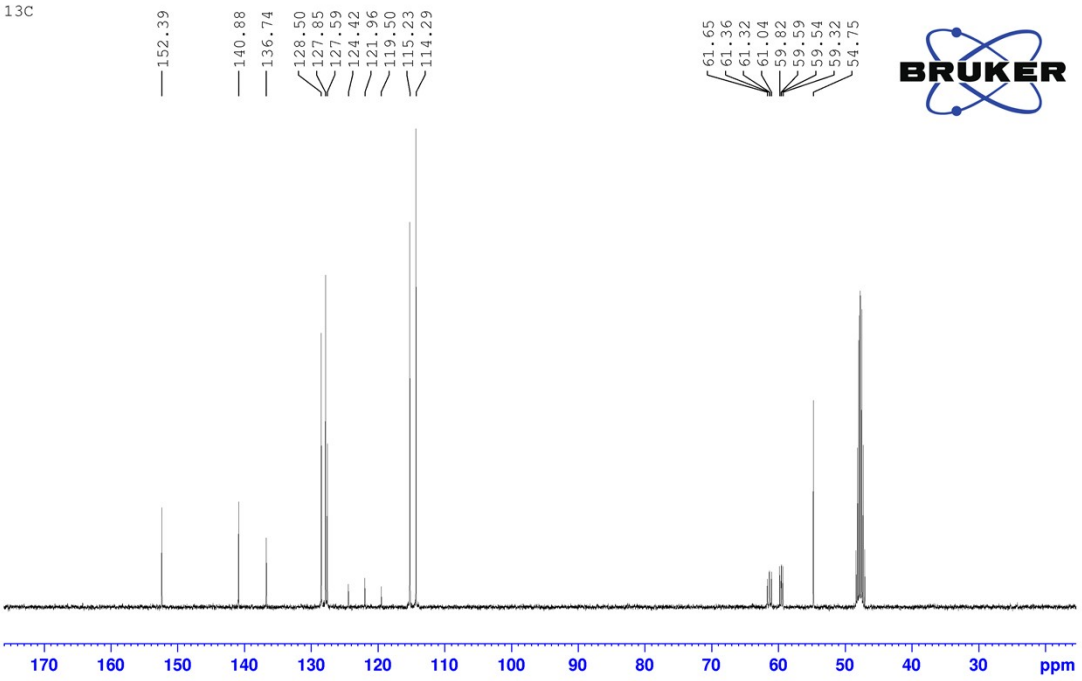
F19CPD



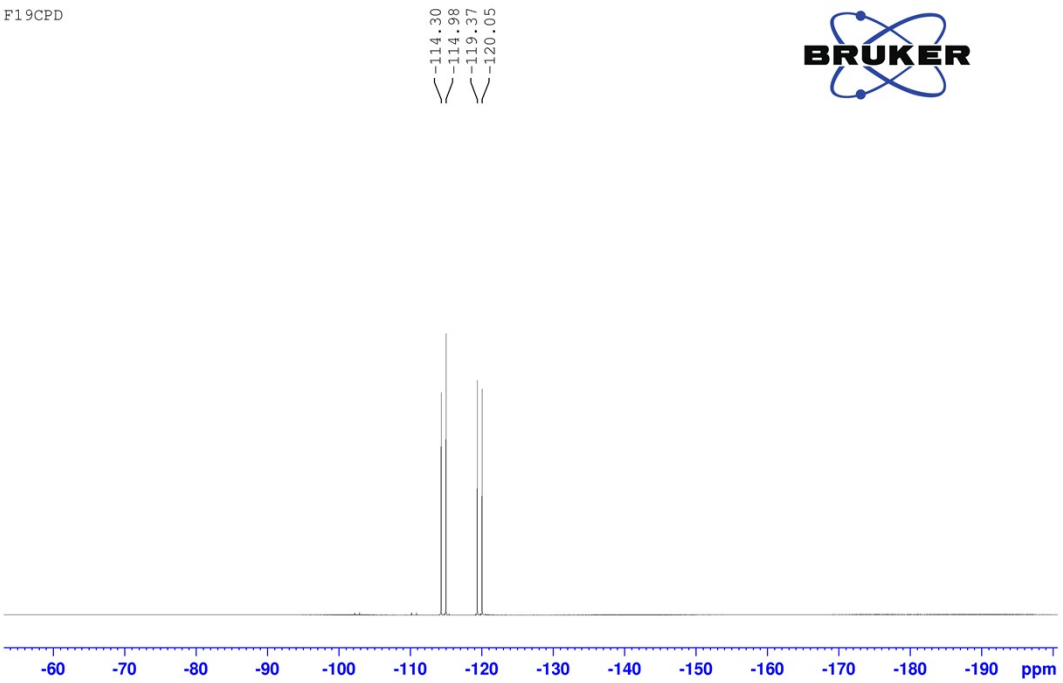
1D-1H zg30



13C


152.39
140.88
136.74
128.50
127.85
127.59
124.42
121.96
119.50
115.23
114.29
61.65
61.36
61.32
61.04
59.82
59.59
59.54
59.32
54.75
BRUKER
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
ppm

F19CPD


-114.30
-114.98
-119.37
-120.05
BRUKER
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
ppm