Supporting Information

Direct C−H Difluoromethylenephosphonation of Arenes and Heteroarenes with Bromodifluoromethyl phosphonate *via* Visible-Light Photocatalysis

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1. General Information

1.1 Solvents and Reagents

Materials were obtained from commercial suppliers and used without further purification. Solvents were dried using standard methods and distilled before use. *fac*-Ir(ppy)$_3$, CH_2Cl_2 and K_3PO_4 were purchased from Nichem, J&K and Acros Co. Ltd., Diethyl (bromodifluoromethyl) phosphonate **2** was purchased from Matrix Scientific.

1.2 NMR and Mass Spectrometry & Chromatography

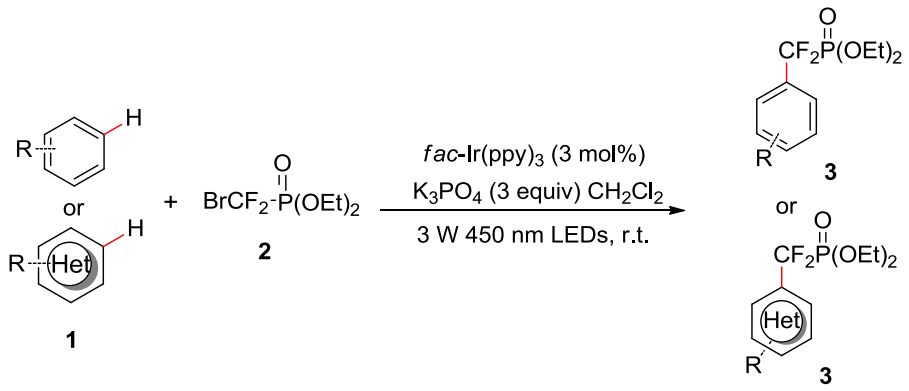
The ^{1}H NMR, ^{13}C NMR spectra, ^{19}F NMR spectra and ^{31}P NMR were recorded on Bruker AM-400 MHz instruments in $CDCl_3$ with TMS as internal standard. The chemical shifts (δ) are reported in ppm and coupling constants (*J*) in Hz. The abbreviations are used: s = singlet, d = doublet, t = triplet, q = quart et, dd = double doublet, m = multiplet, ddd = triple doublet. Chemical shifts are reported in parts per million (δ) relative to $CDCl_3$ (7.27 ppm) for ^{1}H NMR data and $CDCl_3$ (77.0 ppm) for ^{13}C NMR data. Mass spectra were obtained on Bruker ESQ6K4. The IR spectra were measured on NEXUS 670 spectrometers. High resolution mass spectra and were performed on Bruker Daltonics APEXII 47e Specifications. Column chromatography was performed with silica gel (200-300 meshes).

1.3 Electrochemistry

Electrochemical investigation was studied on a RST 5000 electrochemical workstation. Voltammograms were obtained using a standard three electrode cell under argon at room temperature with a glassy carbon working electrode and a platinum wire auxiliary electrode. A $Ag/AgNO_3$ (0.01 mmol.L^{-1}) reference electrode was used and the supporting electrolyte solution was 0.1 M $(nBu)_4NPF_6$, and potentials are reported relative to the Fc/Fc^+couple as 0.00 V. Between each scan the glassy carbon electrode was removed and polished using a 0.05 μm polycrystalline diamond suspension and rinsed with both acetone and deionized water to remove any adsorbed material.

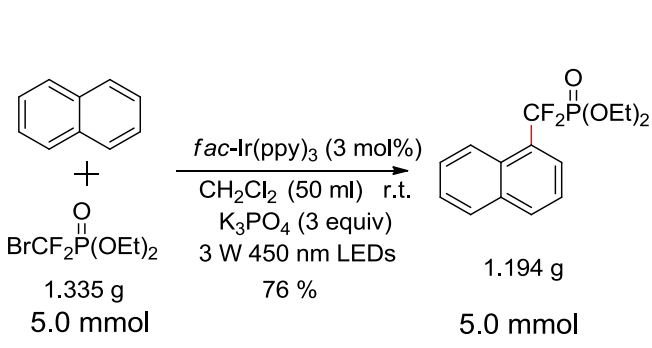
Measurement conditions: solvent, CH_3CN; concentration, 1×10^{-4} mol L^{-1}; supporting electrolyte, $(nBu)_4NPF_6$; work electrode, Pt/C; counter electrode, Pt; reference electrode, Ag/AgCl; scan speed, 0.1 V s^{-1}; temperature, room temperature.

2. General experimental procedure for visible-light-driven difluoromethylene phosphonation of arenes and heteroarenes.



In a 10 mL snap cap vial equipped with a magnetic stirring bar and fitted with a septum, the K_3PO_4 (59 mg, 0.6 mmol, 3.0 equiv), *fac*-Ir(ppy)$_3$ (3 mol %), arene and heteroarenes (2 mmol) were dissolved in dry CH_2Cl_2. The mixture was bubbled with a stream of argon for 20 min via a syringe needle. The vial was then irradiated using a 3W 450 nm LED. The process of the reaction was monitored by thin-layer chromatography at regular intervals. After 36 hours the mixture was removed to a round-bottom flask, then the solvent was removed under reduced pressure and the residue was purified by column chromatography using petroleum ether/ethyl acetate to give the desired product **3**

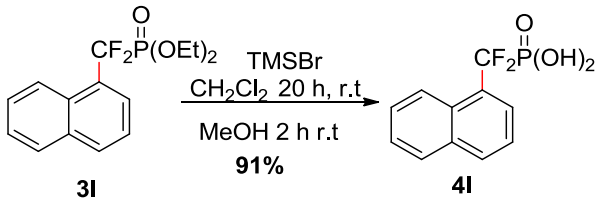
3. Gram-scale synthesis of difluoromethylphosphonate 3l.



In a 100 mL flame dried round-bottom flask equipped with a magnetic stirring bar and fitted with a septum, the K_3PO_4 (3.2 g, 15.0 mmol, 3.0 equiv), *fac*-Ir(ppy)$_3$ (3 mol %) and naphthalene (6.4 g, 50 mmol) was dissolved in dry CH_2Cl_2 (50 ml). Subsequently, (bromodifluoromethyl)phosphonate **2** (888 µl, 5.0 mmol, 1.0 equiv) was added. The mixture was bubbled with a stream of argon for 30 min via a syringe needle. The vial was then irradiated by three 3W blue LEDs. The process of the reaction was monitored by thin-layer chromatography at regular intervals. After 36 hours, the

solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography using petroleum ether/ethyl acetate (5:1) to give the desired product **3l** in 76% yield, the excessive naphthalene was recycled.

4. Synthesis of protein tyrosine phosphatase 1B (PTP-1B) (difluoro(naphthalen-1-yl)methyl)phosphonic acid 4l. [1]

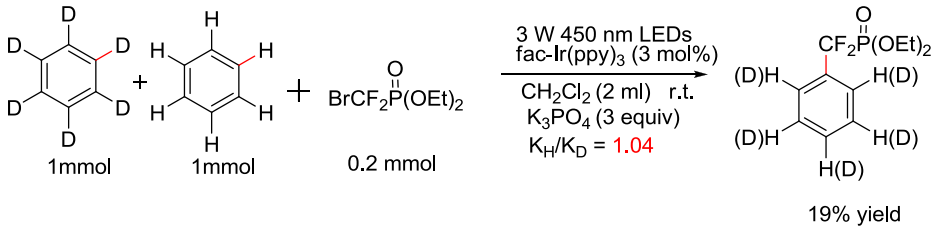


In a flame dried round-bottom flask, (difluoro(naphthalen-1-yl)methyl)phosphonate **3l** (0.942 g, 3.0 mmol), bromotrimethylsilane (0.918 g, 792 μL, 6.0 mmol) were dissolved in dichloromethane (20.0 mL) in argon atmosphere, the mixture was stirred at RT for 20 h. After consumption of starting materials (monitored by TLC), the solvent was evaporated, MeOH (15.0 mL) and water mixture (1.20 mL) were added, after being stirred for 2 h, the solvent was removed in vacuo. A crystalline solid was collected by washing with cold $CHCl_3$ to give **4l** (0.705 g, 91%). This compound is known and results were in accordance with the data reported in the literature.[1]

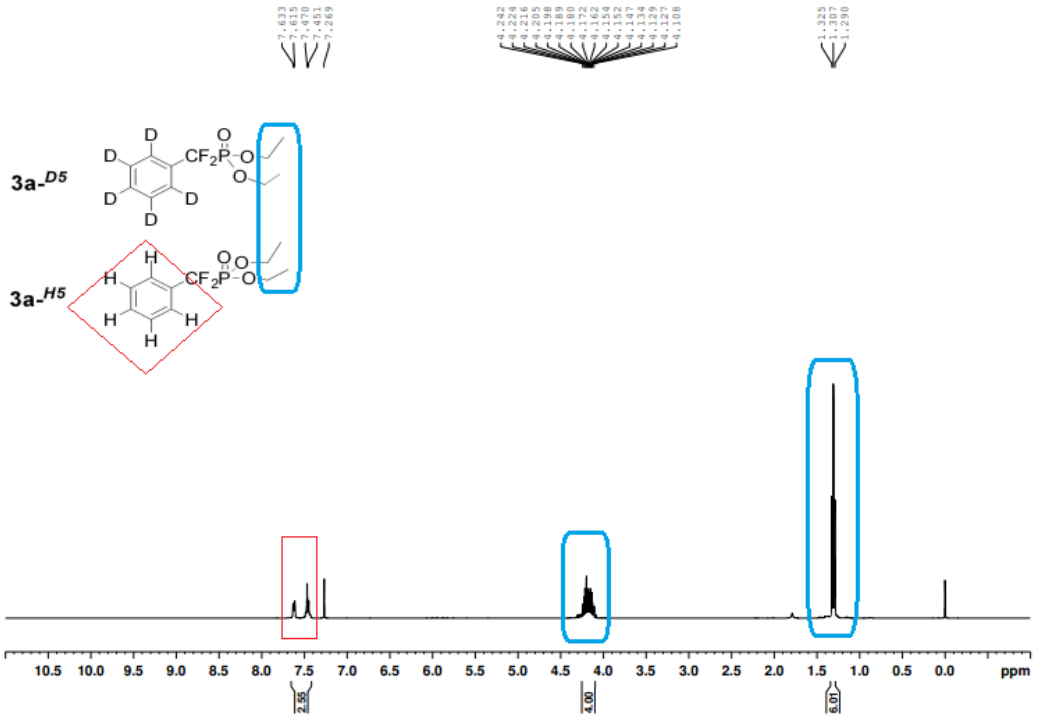
^{1}H NMR (400 MHz, DMSO-d_6) δ 8.60 (d, *J* = 8.0 Hz，1H) , 7.95-7.88 (m, 3H), 7.53-7.49 (m, 3H). **^{13}C NMR (100 MHz, DMSO-d_6)** δ 134.2, 132.6, 131.9 (d, *J* = 12.0 Hz), 130.4, 128.2, 127.9, 127.3 (d, *J* = 9.0 Hz), 126.8 (dt, *J* = 11.0 Hz, *J* = 6.0 Hz), 126.6, 125.9 (t, *J* = 10.0 Hz), 125.6 (dt, *J* = 260.0 Hz, *J* = 214.0 Hz), 124.0, 123.3. **^{19}F NMR (376 MHz, DMSO-d_6)** δ –103.5 (d, *J* = 110.3 Hz). **^{31}P NMR (162 MHz, DMSO-d_6)** δ 4.91(t, *J* = 119.1 Hz). **MS** (+ESI) Calculated m/z for $[M+H]^+$ = 259.0. Experimental m/z for $[M+H]^+$= 259.1.

1. T. Murano, H. Takechi, Y. Yuasa, T. Yokomatsu, I. Umesue, S. Soeda, H. Shimeno, S.Shibuya, *ARKIVOC* 2003, **8,** 256-266.

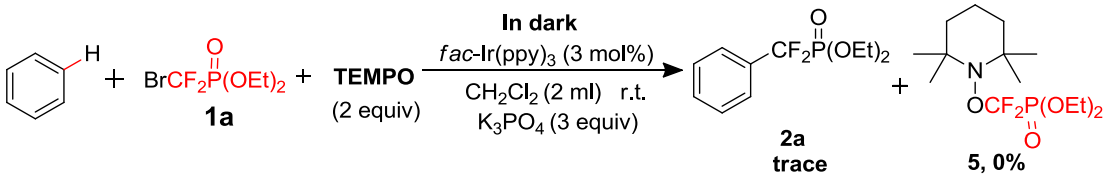
4. Kinetic isotope effect experiments.



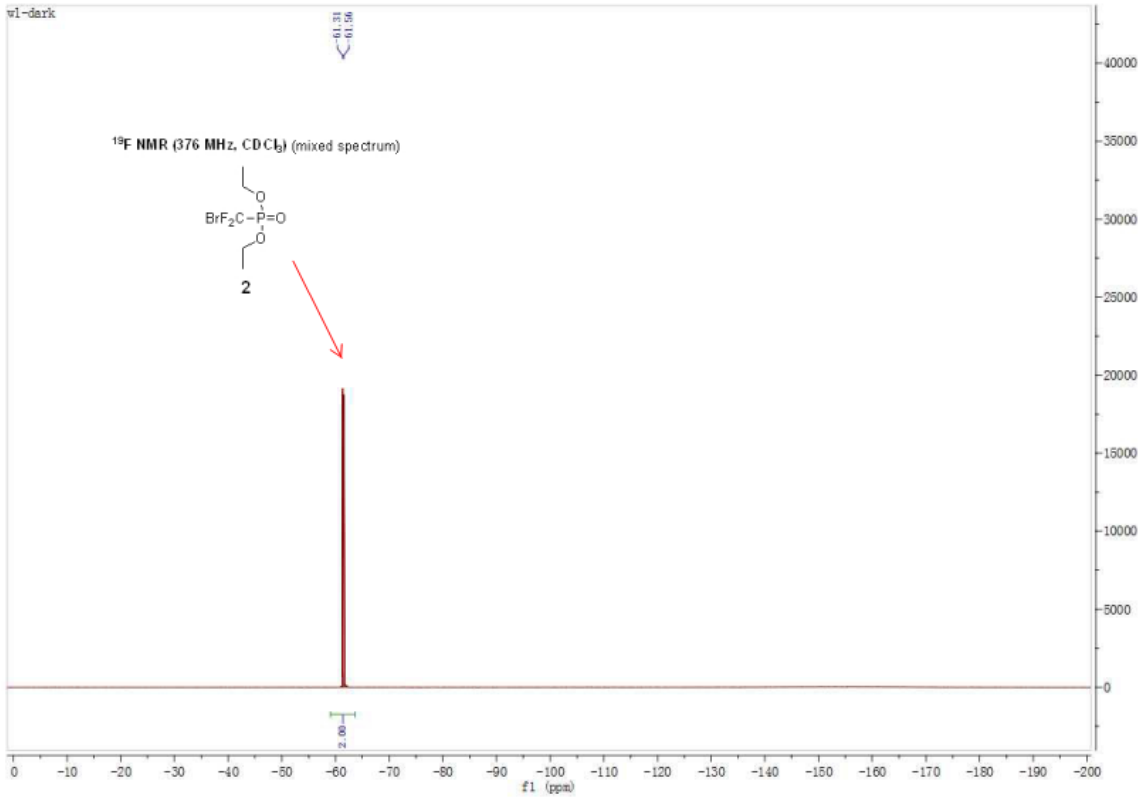
In a 10 mL tube equipped with a rubber septum and magnetic stirring bar, K_3PO_4 (59 mg, 0.6 mmol, 3.0 eq), *fac*-Ir(ppy)$_3$ (3 mol %) and (bromodifluoromethyl)phosphonate **1a** (48.6 mg, 0.2 mmol, 1.0 eq) were dissolved in the dry CH_2Cl_2. Then the benzene (1.0 mmol) and benzene-d_6 (1.0 mmol) was added. The mixture was bubbled with a stream of argon for 20 min via a syringe needle. The vial was then irradiated under two 3W blue LED. The process of the reaction was monitored by thin-layer chromatography at regular intervals. After 3 hours the mixture was removed to a round-bottom flask, and the solvent was removed under reduced pressure. Then the residue was purified by silica gel column chromatography using petroleum ether/ethyl acetate. The isolated difluoroacetamidated benzene and benzene-d_5 was investigated by proton NMR spectrum. The KIE value was determined by the ratios of the proton integral of the product obtained by two parallel experiments. A representative proton NMR spectrum was provided as below.

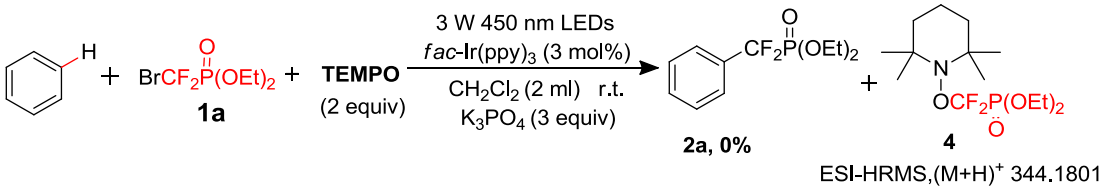


5. The radical trapping experiments.



A 10 mL round bottom flask equipped with a rubber septum and magnetic stir bar, K_3PO_4 (59 mg, 0.6 mmol, 3.0 equiv), *fac*-Ir(ppy)$_3$ (3 mol %), TEMPO (0.40 mmol, 2.0 equiv) and diethyl (bromodifluoromethyl)phosphonate **2** (48.6 mg, 0.2 mmol, 1.0 equiv) were dissolved in CH_2Cl_2, Then benzene (2.0 mmol) was added. The mixture was bubbled with a stream of argon for 20 min via a syringe needle. The mixture was stirred under dark for 36 hours and then be characterized by crude ^{19}F NMR spectroscopy.

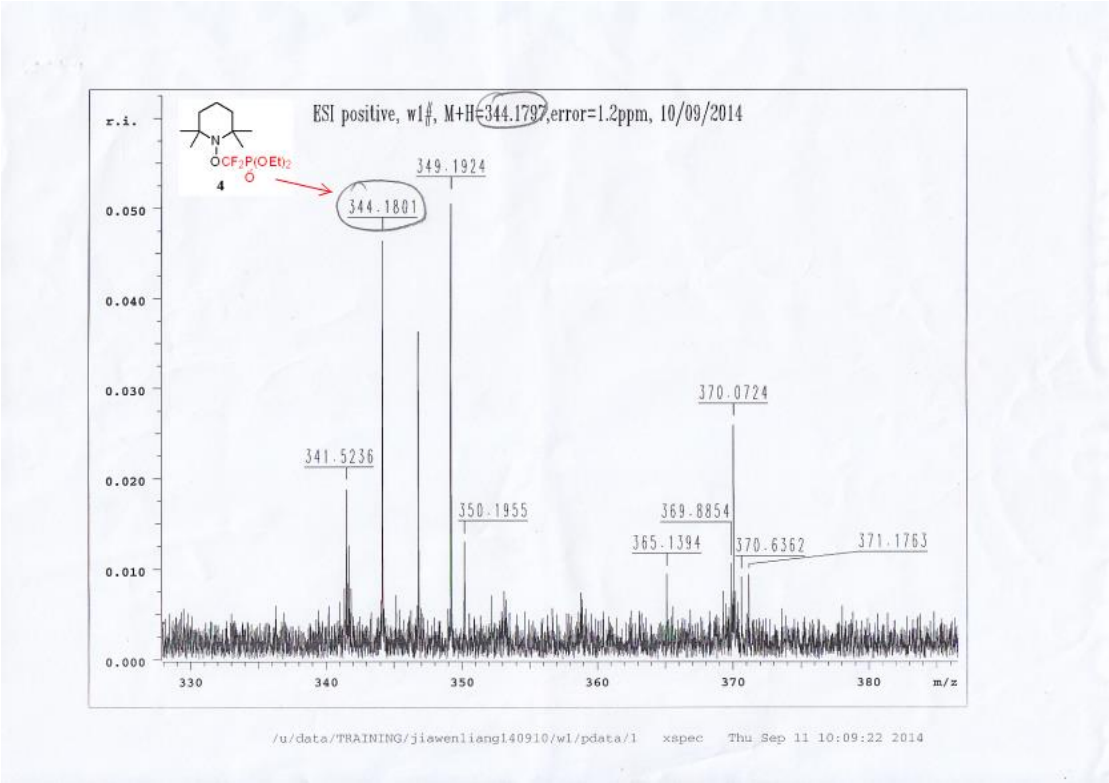


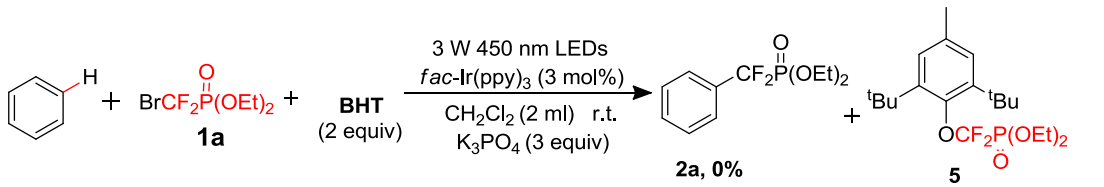


ESI-HRMS,$(M+H)^+$ 344.1801

In a 10 mL round bottom flask equipped with a rubber septum and magnetic stir bar, K_3PO_4 (59 mg, 0.6 mmol, 3.0 equiv), *fac*-Ir(ppy)$_3$ (3 mol %), TEMPO (0.40 mmol, 2.0 equiv) and diethyl (bromodifluoromethyl)phosphonate **2** (48.6 mg, 0.2 mmol, 1.0 equiv) was dissolved in CH_2Cl_2,

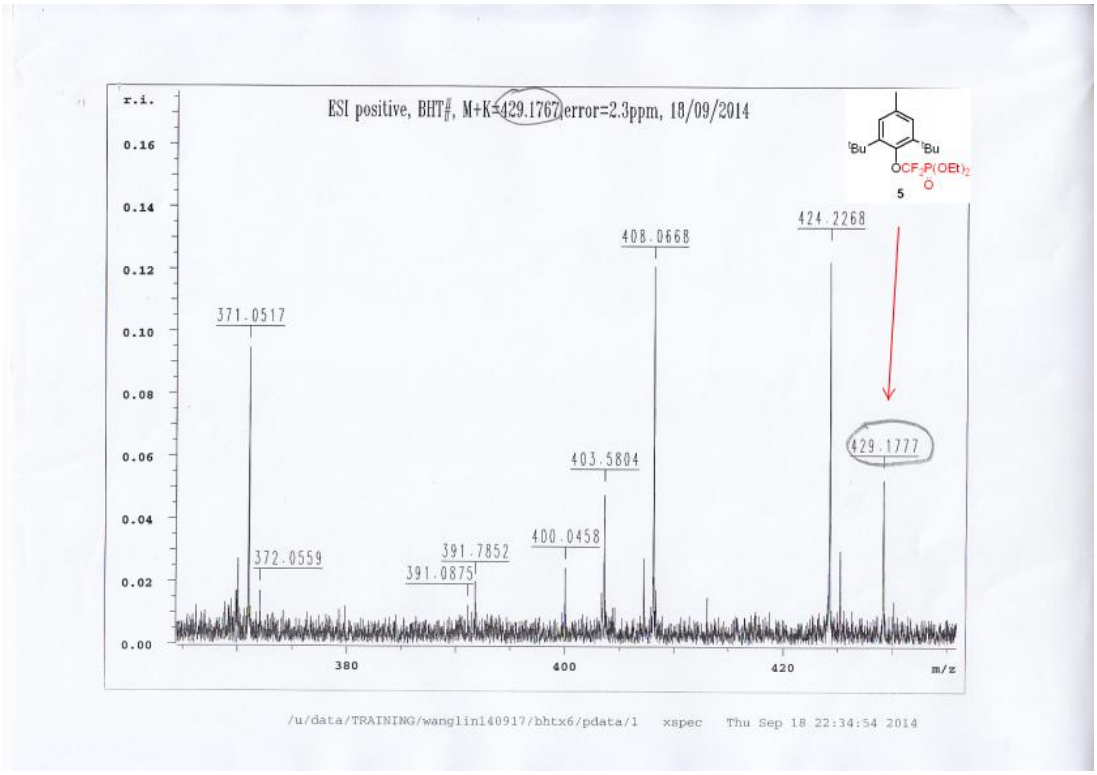
Then benzene (2.0 mmol) was added. The mixture was bubbled with a stream of argon for 20 min via a syringe needle. The vial was irradiated under two 3W blue LED for 36 hours and then be characterized by high resolution mass spectra.

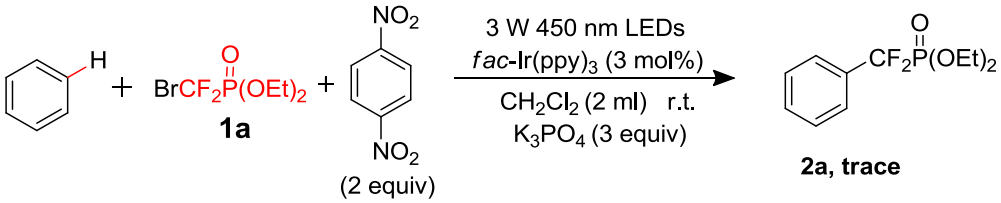




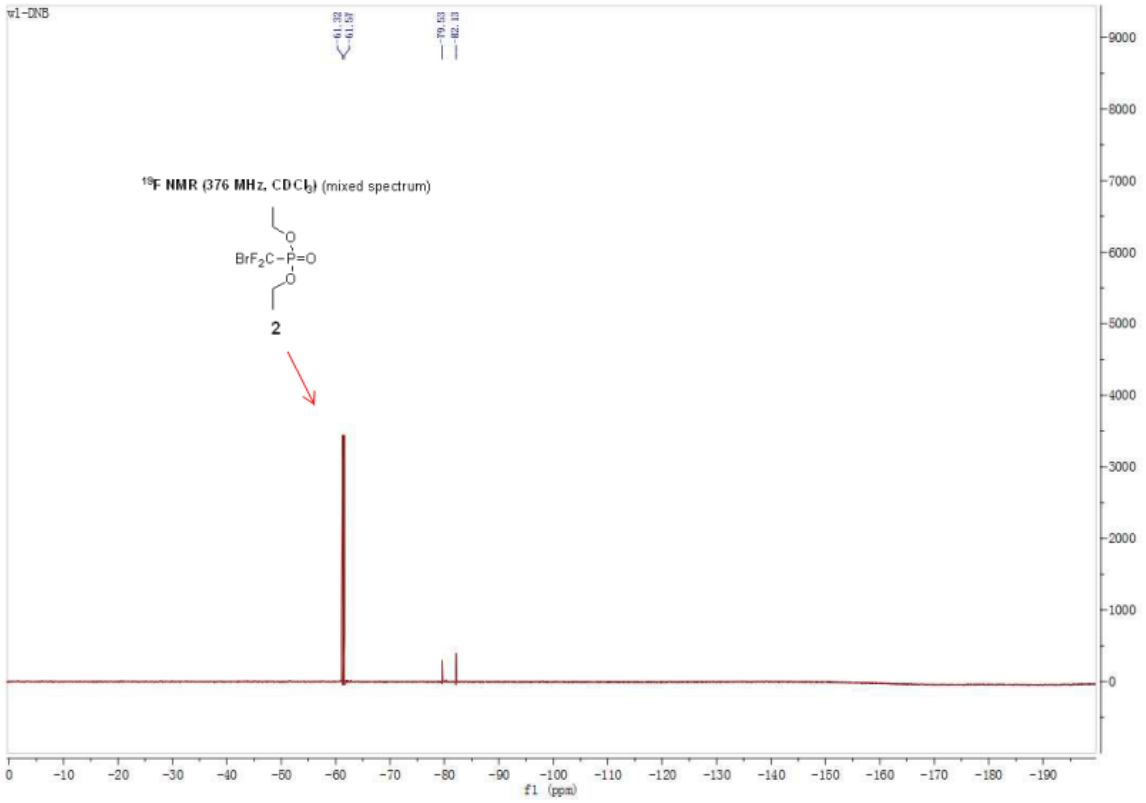
ESI-HRMS,$(M+K)^+$ 429.1777

In a 10 mL round bottom flask equipped with a rubber septum and magnetic stir bar, K_3PO_4 (59 mg, 0.6 mmol, 3.0 equiv), *fac*-Ir(ppy)$_3$ (3 mol %), BHT (0.40 mmol, 2.0 equiv) and diethyl (bromodifluoromethyl)phosphonate **2** (48.6 mg, 0.2 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 , then benzene (2.0 mmol) was added. The mixture was bubbled with a stream of argon for 20 min via a syringe needle. The vial was irradiated under two 3W blue LED for 36 hours and then be characterized by high resolution mass spectra.

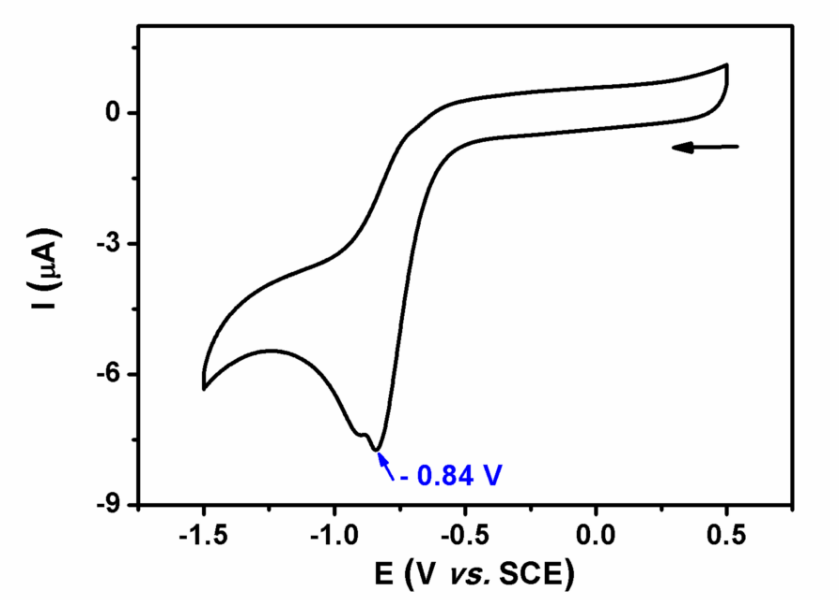




In a 10 mL round bottom flask equipped with a rubber septum and magnetic stir bar, K_3PO_4 (59 mg, 0.6 mmol, 3.0 equiv), *fac*-Ir(ppy)$_3$ (3 mol %), 1,4-dinitrobenzene (0.40 mmol, 2.0 equiv) and diethyl (bromodifluoromethyl)phosphonate **2** (48.6 mg, 0.2 mmol, 1.0 equiv) was dissolved in CH_2Cl_2, then benzene (2.0 mmol) was added. The mixture was bubbled with a stream of argon for 20 min via a syringe needle. The vial was then irradiated under two 3W blue LED for 36 hours and then be characterized by crude ^{19}F NMR spectroscopy.

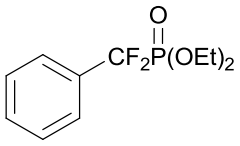


6. The electrochemistry of 2.



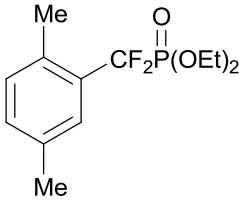
The potential of diethyl bromodifluoromethylphosphonate **2** was investigated by cyclic voltammograms. Compound **2** shows an irreversible reduction event at -0.84 V (vs. SCE) in acetonitrile containing 0.1 mol.L^{-1} tetrabutylammonium hexafluorophosphate.

7. Analytical data of products



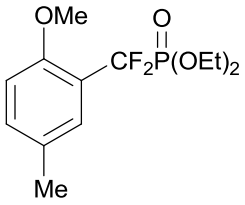
3a

Diethyl (difluoro(phenyl)methyl)phosphonate (3a). The general procedure was followed using dry benzene **1a** (178 µl, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 12:1→PE/EtOAc = 5:1) yielded **3a** (40.1 mg, 76%) as a pale yellow oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.63 (m, 2 H), 7.47 (m, 3 H), 4.25-4.11 (m, 4 H), 1.31 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 132.7 (td, *J* = 22.0 Hz, *J* = 14.0 Hz), 130.7, 128.4, 126.2 (td, *J* = 5.0 Hz, *J* = 2.0 Hz), 119.3 (d, *J* = 45.0 Hz),116.9, 64.73, 64.66, 16.3, 16.2. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -108.5 (d, *J* = 116.6 Hz, 2F). **^{31}P NMR (162 MHz, $CDCl_3$):** 6.38 (t, *J* = 116.6 Hz). **IR (thin film) ν_{max}** 3070, 2986, 1546, 1451, 1272,1126, 1045 cm^{-1}. **HRMS (ESI, m/z):** Calculated for $[C_{11}H_{16}F_2O_3P]$ $(M+H)^+$ 265.0800, found 265.0807.



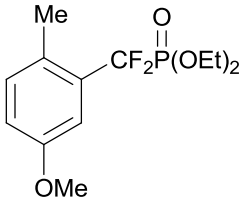
3b

Diethyl ((2,5-dimethylphenyl)difluoromethyl)phosphonate (3b). The general procedure was followed using 99% pure, p-xylene **1b** (247 µl, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 12:1→PE/EtOAc = 6:1) yielded **3b** (45.5 mg, 78%) as a pale yellow oil and the excess **1b** can be recycled and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** 7.32 (s, 1 H), 7.14 (dd, *J* = 8.0 Hz, 2 H),4.26-4.07 (m, 4 H), 2.51 (s, 3H), 2.34 (s, 3H), 1.32 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 135.2 (d, *J* = 1.0 Hz), 134.37, 134.34, 131.34 (d, *J* = 2.0 Hz), 130.4 (td, *J* = 13.0 Hz, J = 7.0 Hz),130.12(128.1 (td, *J* = 6.0 Hz, *J* = 4.0 Hz), 128.0 (m), 123.4, 121.3, 120.8, 118.0, 116.0, 64.61, 64.54, 20.9, 20.1 (t, *J* = 4.0 Hz), 16.31, 16.25. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -104.1 (d, *J* = 117.7 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 7.08 (t, *J* = 117.9 Hz). **IR (thin film) ν_{max}** 2985, 2929, 1736, 1271, 1178, 1112, 1022, 588, 582 cm^{-1}. **HRMS (ESI, m/z):** Calculated for $[C_{13}H_{19}F_2O_3PNa]$ $(M+Na)^+$ 315.0932, found 315.0936.



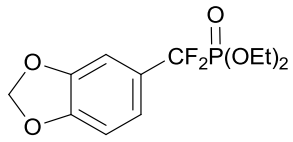
3c-A

Diethyl (difluoro(2-methoxy-5-methylphenyl)methyl)phosphonate (3c-A). The general procedure was followed using 4-methylanisole **1c** (252 µl, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 10:1→PE/EtOAc = 3:1) yielded **3c-A** (34.3 mg, 55.6%) as a pale yellow oil and the excess **1c** can be recycled and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** 7.31 (s, 1 H), 7.21 (d, *J* = 8.4 Hz, 1 H), 6.86 (d, *J* = 8.4 Hz, 1 H), 4.29-4.13 (m, 4 H), 3.83 (s, 3H), 2.30 (s, 3H), 1.32 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 155.65 (d, *J* = 2.0 Hz), 132.66 (d, *J* = 2.0 Hz),129.7, 128.5 (td, *J* = 6.0 Hz, J = 3.0 Hz), 122.2, 120.6 (m), 120.1, 119.6, 117.4, 117.0,114.8, 112.3, 64.47, 64.41, 56.0, 20.4, 16.26 (d, *J* = 6.0 Hz). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -104.5 (d, *J* = 114.6 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 6.73 (t, *J* = 116.6 Hz). **IR (thin film) ν_{max}** 2985, 2933, 1615, 1506, 1266, 1181, 1031, 980, 580, 536 cm^{-1}. **HRMS (ESI, m/z):** Calculated for $[C_{13}H_{20}F_2O_4P]$ $(M+H)^+$ 309.1062, found 309.1067.



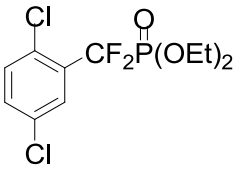
3c-B

Diethyl (difluoro(5-methoxy-2-methylphenyl)methyl)phosphonate (3c-B). The general procedure was followed using 4-methylanisole **1c** (252 µl, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 10:1→PE/EtOAc = 3:1) yielded **3c-B** (13.1 mg, 21.4%) as a pale yellow oil and the excess **1c** can be recycled and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** 7.12 (d, *J* = 8.4 Hz, 1 H), 7.04 (s,1H), 6.88 (d, *J* = 8.4 Hz, 1 H), 4.30-4.09 (m, 4 H), 3.79 (s, 3H), 2.47 (s, 3H), 1.31 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 157.4, 133.2, 131.3 (d, *J* = 13.0 Hz), 129.3, 128.5, 123.1, 120.6, 118.1 116.3, 115.6, 115.0, 113.8, 112.9 (m), 110.2 (d, *J* = 45 Hz), 107.8, 64.58, 64.40, 55.3, 19.59 (t, *J* = 4.0 Hz), 16.28 (t, *J* = 6.0 Hz). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -104.5 (d, *J* = 116.9 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 6.88 (t, *J* = 116.6 Hz). **IR (thin film) ν_{max}** 2985, 2936, 1729, 1615, 1269, 1111, 1036, 981, 542 cm^{-1}. **HRMS (ESI, m/z):** Calculated for $[C_{13}H_{23}F_2O_4NP]$ $(M+NH_4)^+$ 326.1327, found 326.1324.



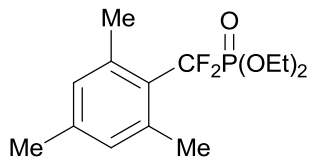
3d

Diethyl (benzo[d][1,3]dioxol-5-yldifluoromethyl)phosphonate (3d). The general procedure was followed using 1,3-benzodioxole **1d** (230 μl, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 9:1→PE/EtOAc = 2:1) yielded **3d** (49.9 mg, 81%) as a pale yellow oil and the excess **1d** can be recycled and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** 7.11 (d, *J* = 8.4 Hz, 1 H), 7.04 (s,1H), 6.84 (d, *J* = 8.0 Hz, 1 H), 5.99 (s, 2H), 4.24-4.11 (m, 4 H), 1.31 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 149.6, 147.7, 126.1 (td, *J* = 14.0 Hz, J = 8.0 Hz), 121.6, 120.6 (td, *J* = 5.0 Hz, *J* = 2.0 Hz), 117.8 (td, *J* = 262.0 Hz, *J* = 220.0 Hz), 114.1, 108.1, 106.8 (td, *J* = 7.0 Hz, *J* = 2.0 Hz), 64.69, 64.62, 16.28, 16.22. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -106.5 (d, *J* = 118.8 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 6.32 (t, *J* = 118.8 Hz). **IR (thin film) ν_{max}** 2987, 2914, 1508, 1493, 1446, 1256, 1121, 1039, 814, 607, 545 cm^{-1}. **HRMS (ESI, m/z):** Calculated for $[C_{12}H_{16}F_2O_5P]$ $(M+H)^+$ 309.0698, found 309.0700.



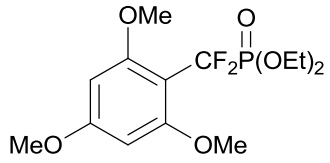
3e

Diethyl ((2,5-dichlorophenyl)difluoromethyl)phosphonate (3e). The general procedure was followed using 4-dichlorobenzene **1e** (294.0 mg, 2.0 mmol). Purified by column chromateraphy (PE/EtOAc = 12:1→PE/EtOAc = 7:1) yielded **3e** (33.2 mg, 41%) as a pale yellow oil containing some unreacted **2** as polarity is same and the excess **1e** can be recycled and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** 7.59 (s, 2 H), 7.40-7.35 (m,2 H), 4.41-4.21 (m, 4 H), 1.35 (t, *J* = 6.8 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 132.9, 131.7 (td, *J* = 21.0 Hz, *J* = 7.0 Hz), 130.9, 129.4 (td, *J* = 11.0 Hz, *J* = 9.0 Hz), 117.1 (td, *J* = 217.0 Hz, *J* = 172.0 Hz), 66.24, 65.06, 16.31, 16.25. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -105.58 (d, *J* = 111.3 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 5.14 (t, *J* = 111.5 Hz). **IR (thin film) ν_{max}** 2987, 2933, 1466, 1387, 1279, 1219, 1022, 586, 530 cm^{-1}. **HRMS (ESI, m/z):** Calculated for $[C_{11}H_{13}Cl_2F_2O_3PNa]$ $(M+Na)^+$ 354.9839, found 354.9840.



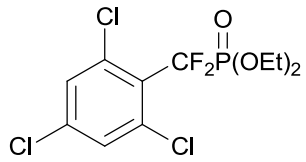
3f

Diethyl (difluoro(mesityl)methyl)phosphonate (3f). The general procedure was followed using extra pure mesitylene **1f** (277 µl, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 12:1→PE/EtOAc = 6:1) yielded **3f** (48.3 mg, 79%) as a pale yellow oil and the excess **1f** can be recycled and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** 6.87 (s, 2 H), 4.24-4.08 (m, 4 H), 2.50 (t, *J* = 4.8 Hz, 6H), 2.26 (s, 3H), 1.32 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 139.9, 138.5 (td, *J* = 7.0 Hz, *J* = 4.0 Hz), 138.1, 131.3, 129.2, 126.2 (td, *J* = 33.0 Hz, *J* = 19.0 Hz), 125.2, 124.8, 122.3 (td, *J* = 264.0 Hz, *J* = 216.0 Hz), 117.8, 64.41, 64.34, 22.2 (t, *J* = 7.0 Hz), 20.7, 16.32, 16.26. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -97.46 (d, *J* = 115.1 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 8.11 (t, *J* = 118.7 Hz). **IR (thin film) ν_{max}** 2985, 2931, 1611, 1458, 1269, 1167, 1027, 585 cm^{-1}. **HRMS (ESI, m/z):** Calculated for $[C_{14}H_{25}F_2O_3PN]$ $(M+NH_4)^+$ 324.1535, found 324.1537.



3g

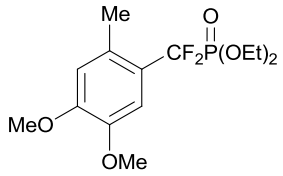
Diethyl (difluoro(2,4,6-trimethoxyphenyl)methyl)phosphonate (3g). The general procedure was followed using 1,3,5-trimethoxybenzene **1g** (336.38 mg, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 7:1→PE/EtOAc = 2:1) yielded **3g** (60.1 mg, 85%) as a pale yellow oil and the excess **1g** can be recycled and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** 6.09 (s, 2 H), 4.22-4.13 (m, 4 H), 3.82 (t, *J* = 6.4 Hz, 9H), 1.31 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 164.9, 160.6, 111.4, 90.8, 63.52, 63.45, 56.0, 55.5, 16.38, 16.32. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -98.39 (d, *J* = 115.4 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 7.40 (t, *J* = 119.1 Hz). **IR (thin film) ν_{max}** 2981, 2929, 1604, 1461, 1230, 1157, 1131, 1026 cm^{-1}. **HRMS (ESI, m/z):** Calculated for $[C_{14}H_{22}F_2O_6P]$ $(M+H)^+$ 355.1117, found 355.1121.



3h

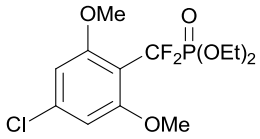
Diethyl (difluoro(2,4,6-trichlorophenyl)methyl)phosphonate (3h). The general procedure was followed using 1,3,5-trichlorobenzene **1h** (363 mg, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 12:1→PE/EtOAc = 7:1) yielded **3h** (32.8 mg, 35%) as a pale yellow oil containing some unreacted **2** as polarity is same and the excess **1h** can be recycled

and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** 7.41 (s, 2 H), 4.40-4.25 (m, 4 H), 1.37 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 136.8, 135.9 (d, *J* = 3.0 Hz), 130.8, 127.1 (d, *J* = 14.0 Hz), 125.5, 125.0, 121.1, 119.5, 118.9 (d, *J* = 22.0 Hz), 116.2 (td, *J* = 261.0 Hz, *J* = 237.0 Hz), 66.3, 65.14, 65.07, 16.28 (t, *J* = 5.0 Hz). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.78 (d, *J* = 109.1 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 5.01 (t, *J* = 108.7 Hz). **IR (thin film) ν_{max}** 2986, 2927, 1574, 1545, 1370, 1279, 1217, 1021 cm^{-1}. **HRMS (ESI, m/z):** Calculated for $[C_{11}H_{12}C_{l3}F_2O_3PNa]$ $(M+Na)^+$ 388.9449, found 388.9451.



3i

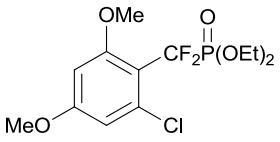
Diethyl ((4,5-dimethoxy-2-methylphenyl)difluoromethyl)phosphonate (3i). The general procedure was followed using 3,4-dimethoxytoluene **1i** (287 μl, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 6:1→PE/EtOAc = 2:1) yielded **3i** (55.6 mg, 81%) as a pale yellow oil and the excess **1i** can be recycled and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** 6.99 (s, 1 H), 6.68 (s, 1 H), 4.24-4.06 (m, 4 H), 3.87 (d, *J* = 7.2 Hz, 6 H), 1.31 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 150.2, 146.5, 133.5, 130.6 (d, *J* = 3.0 Hz), 121.9 (td, *J* = 21.0 Hz, *J* = 13.0 Hz), 120.1 (td, *J* = 263.0 Hz, *J* = 220.0 Hz), 115.8 (d, *J* = 15.0 Hz), 114.8, 113.5, 110.6 (t, *J* = 11.0 Hz), 64.49, 64.42, 56.0, 55.8, 20.1 (t, *J* = 4.0 Hz), 16.32, 16.26. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -103.17 (d, *J* = 119.9 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 7.15 (t, *J* = 117.2 Hz). **IR (thin film) ν_{max}** 2983, 2939, 1605, 1581,1467, 1328, 1268, 1204, 1162, 1045, 549 cm^{-1}. **HRMS (ESI, m/z):** Calculated for $[C_{14}H_{22}F_2O_5P]$ $(M+H)^+$ 339.1177, found 339.1178.



3j-A

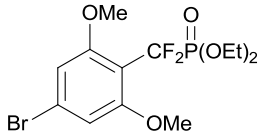
Diethyl ((4-chloro-2,6-dimethoxyphenyl)difluoromethyl)phosphonate (3j-A). The general procedure was followed using 5-chloro-1,3-dimethoxybenzene **1j** (345 mg, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 6:1→PE/EtOAc = 1:1) yielded **3j-A** (35.9 mg, 50 %) as a pale yellow oil and the excess **1j** can be recycled and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** 6.58 (s, 2 H), 4.29-4.17 (m, 4 H), 3.81 (s, 6 H), 1.32 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.0, 138.2, 122.54 (d, *J* = 20.0 Hz), 118.9 (td, *J* = 265.0 Hz, *J* = 221.0 Hz), 115.2, 112.3, 108.6 (d, *J* = 20.0 Hz), 106.1, 64.40, 64.34, 56.5, 16.34, 16.28. **^{19}F NMR (376 MHz,**

$CDCl_3$) δ -99.95 (d, *J* = 118.4 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 6.76 (t, *J* = 115.5 Hz). **IR (thin film) ν_{max}** 2984, 2942, 1582, 1461, 1270, 1230, 1137, 1052, 937, 592, 555 cm^{-1}. **HRMS (ESI, m/z):** Calculated for $[C_{13}H_{19}ClF_2O_5P]$ $(M+H)^+$ 359.0621, found 359.0625.



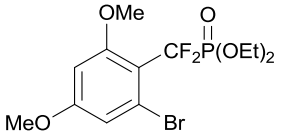
3j-B

Diethyl ((2-chloro-4,6-dimethoxyphenyl)difluoromethyl)phosphonate (3j-B). The general procedure was followed using 5-chloro-1,3-dimethoxybenzene **1j** (345 mg, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 6:1→PE/EtOAc = 1:1) yielded **3j-B** (19.9 mg, 28 %) as a pale yellow oil and the excess **1j** can be recycled and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** 6.56 (s, 1 H), 6.40 (s, 1 H), 4.29-4.18 (m, 4 H), 3.81 (s, 3 H), 3.79 (s, 3 H), 1.32 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 161.8, 160.9, 135.1, 123.9, 122.4, 118.7 (td, *J* = 266.0 Hz, *J* = 222.0 Hz), 114.9, 112.0 (m), 110.2, 109.0, 64.40, 98.7, 64.51, 64.44, 56.4, 55.5, 16.33, 16.27. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -98.48 (d, *J* = 115.4 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 6.54 (t, *J* = 115.7 Hz). **IR (thin film) ν_{max}** 2984, 2940, 1603, 1569, 1460, 1412, 1271, 1226, 1160, 1039, 835, 753, 555 cm^{-1}. **HRMS (ESI, m/z):** Calculated for $[C_{13}H_{19}ClF_2O_5P]$ $(M+H)^+$ 359.0621, found 359.0625.



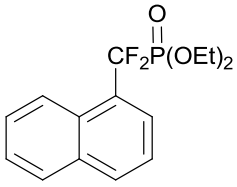
3k-A

Diethyl ((4-bromo-2,6-dimethoxyphenyl)difluoromethyl)phosphonate (3k-A). The general procedure was followed using 1-bromo-3,5-dimethoxybenzene **1k** (434 mg, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 6:1→PE/EtOAc = 1:1) yielded **3k-A** (34.2 mg, 43 %) as a pale yellow oil and the excess **1k** can be recycled and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** 6.76 (s, 2 H), 4.31-4.19 (m, 4 H), 3.84 (s, 6 H), 1.34 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.0, 126.1, 122.7, 118.9 (td, *J* = 264.0 Hz, *J* = 220.0 Hz), 115.2, 114.0, 109.0 (t, *J* = 14.0 Hz), 64.39, 64.32, 56.6, 16.34, 16.28. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -100.05 (d, *J* = 115.4 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 7.59 (t, *J* = 115.1 Hz). **IR (thin film) ν_{max}** 2983, 2931, 1579, 1460, 1406, 1269, 1230, 1136, 1052, 935, 834, 733, 583 cm^{-1}. **HRMS (ESI, m/z):** Calculated for $[C_{13}H_{19}BrF_2O_5P]$ $(M+H)^+$ 403.0116, found 403.0121.



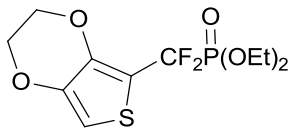
3k-B

Diethyl ((2-bromo-4,6-dimethoxyphenyl)difluoromethyl)phosphonate (3k-B). The general procedure was followed using 1-bromo-3,5-dimethoxybenzene **1k** (434 mg, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 6:1→PE/EtOAc = 1:1) yielded **3k-B** (17.7 mg, 22 %) as a pale yellow oil and the excess **1k** can be recycled and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** 6.83 (s, 1 H), 6.46 (s, 1 H), 4.31-4.20 (m, 4 H), 3.84 (s, 3 H), 3.82 (s, 3 H), 1.35 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 161.9, 161.0, 135.1, 123.9, 122.4, 118.7 (td, *J* = 266.0 Hz, *J* = 222.0 Hz), 114.9, 112.7, 99.4, 64.53, 64.46, 56.5, 55.6, 16.40, 16.34. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -97.65 (d, *J* = 115.4 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 7.45 (t, *J* = 118.5 Hz). **IR (thin film) ν_{max}** 2982, 2926, 1601, 1563, 1459, 1409, 1269, 1227, 1159, 1031, 570, 548 cm^{-1}. **HRMS (ESI, m/z):** $[C_{13}H_{19}BrF_2O_5P]$ $(M+H)^+$ 403.0116, found 403.0120.



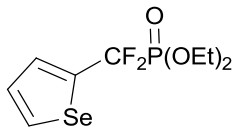
3l

Diethyl (difluoro(naphthalen-1-yl)methyl)phosphonate (3l). The general procedure was followed using naphthalene **1l** (256 mg, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 12:1→PE/EtOAc = 6:1) yielded **3l** (51.5 mg, 82%) as a pale yellow oil and the excess **1l** can be recycled and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** 8.47 (d, *J* = 8.4 Hz, 1 H), 7.97 (d, *J* = 8.0 Hz, 1 H), 7.88 (d, *J* = 8.0 Hz, 1 H), 7.83 (d, *J* = 7.2 Hz, 1 H), 7.60-7.50 (m, 3H), 4.23-4.06 (m, 4 H), 1.27 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 134.08 (d, *J* = 12.0 Hz), 131.2 (d, *J* = 39.0 Hz), 129.9, 128.44 (td, *J* = 20.0 Hz, *J* = 17.0 Hz), 127.61 (d, *J* = 18.0 Hz), 126.7, 126.3 (m), 124.3, 123.6, 122.7, 119.9 (td, *J* = 263.0 Hz, *J* = 215.0 Hz), 116.2, 64.70, 64.64, 16.25, 16.19. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -101.79 (d, *J* = 110.1 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 6.72 (t, *J* = 113.4 Hz). **IR (thin film) ν_{max}** 2986, 2933, 1513, 1273, 1123, 1022, 801, 776, 601, 575, 525 cm^{-1}. **HRMS (ESI, m/z):** $[C_{15}H_{18}F_2O_3P]$ $(M+H)^+$ 315.0956, found 315.0959.



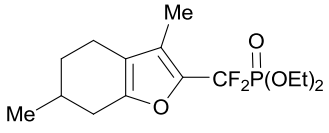
3m

Diethyl ((2,3-dihydrothieno[3,4-b][1,4]dioxin-5-yl)difluoromethyl)phosphonate (3m). The general procedure was followed using 3,4-ethylenedioxythiophene **1m** (214 µl, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 6:1→PE/EtOAc = 1:1) yielded **3m** (59 mg, 90 %) as a pale yellow oil and the excess **1m** can be recycled and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** 6.50 (s, 1 H), 4.33-4.27 (m, 4 H), 4.26-4.21 (m, 4 H), 1.36 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.9, 141.6 (td, *J* = 9.0 Hz, *J* = 4.0 Hz), 141.3, 120.3, 116.6 (td, *J* = 262.0 Hz, *J* = 229.0 Hz), 112.8, 106.7 (m), 102.3 (td, *J* = 6.0 Hz, *J* = 3.0 Hz), 64.7 (t, *J* = 8.0 Hz), 64.0, 60.2, 20.8, 16.19, 16.14. 14.0. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.53 (d, *J* = 119.6 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 4.89 (t, *J* = 119.4 Hz). **IR (thin film) ν_{max}** 2986, 2926, 1501, 1436, 1368, 1271, 1173, 1050, 915, 886, 735, 572 cm^{-1}. **HRMS (ESI, m/z):** $[C_{11}H_{16}F_2O_5PS]$ $(M+H)^+$ 329.0419, found 329.0417.



3n

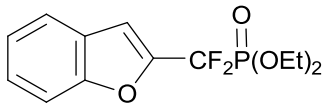
Diethyl (difluoro(selenophen-2-yl)methyl)phosphonate (3n). The general procedure was followed using selenophene **1n** (182 µl, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 8:1→PE/EtOAc = 2:1) yielded **3n** (40 mg, 63 %) as a pale yellow oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.21 (d, *J* = 6.8 Hz, 1 H), 7.71-7.69 (m, 1 H), 7.35-7.32 (m, 1 H), 4.30-4.21 (m, 4 H), 1.35 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 147.1, 134.82 (d, *J* = 3.0 Hz), 131.3 (t, *J* = 4.0 Hz), 129.5, 123.8, 119.7, 65.1, 65.0, 16.33, 16.27. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -93.74 (d, *J* = 115.4 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 5.12 (t, *J* = 115.3 Hz). **IR (thin film) ν_{max}** 2925, 1725, 1443, 1241, 1117, 1030, 798, 705, 580 cm^{-1}. **HRMS (ESI, m/z):** $[C_9H_{14}F_2O_3PSe]$ $(M+H)^+$ 318.9809, found 318.9818.



3o

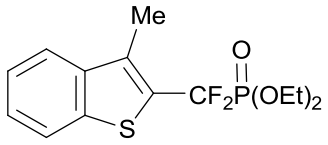
Diethyl ((3,6-dimethyl-4,5,6,7-tetrahydrobenzofuran-2-yl)difluoromethyl)phosp- honate (3o). The general procedure was followed using menthofuran **1o** (310 µl, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 6:1→PE/EtOAc = 1:1) yielded **3o** (55 mg, 82 %) as a

pale yellow oil and the excess **1o** can be recycled and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.29-4.18 (m, 4 H), 2.64 (d, *J* = 16.0 Hz, 1 H), 2.34-2.23 (m, 2 H), 2.18-2.12 (m, 1 H), 2.03 (s, 3 H), 1.89-1.79 (m, 2H), 1.33 (t, *J* = 7.2 Hz, 7 H), 1.04 (d, *J* = 7.2 Hz, 3 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 152.3, 136.9 (m), 122.94 (t, *J* = 3.0 Hz), 119.4, 115.2 (td, *J* = 259.0 Hz, *J* = 225.0 Hz), 111.5, 64.65, 64.58, 31.2, 21.2, 19.5, 16.26, 16.20, 7.98. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -106.95 (d, *J* = 120.3 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 5.45 (t, *J* = 118.6 Hz). **IR (thin film) ν_{max}** 2927, 1702, 1619, 1528, 1458, 1380, 1298, 1253, 1027, 762 cm^{-1}. **HRMS (ESI, m/z):** $[C_{15}H_{27}F_2O_4PN]$ $(M+NH_4)^+$ 354.1641, found 354.1643.



3p

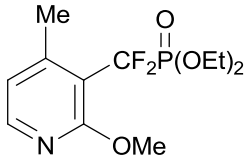
Diethyl (benzofuran-2-yldifluoromethyl)phosphonate (3p). The general procedure was followed using benzofuran **1p** (215 µl, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 7:1→PE/EtOAc = 2:1) yielded **3p** (51.5 mg, 85 %) as a pale yellow oil and the excess **1p** can be recycled and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.66 (d, *J* = 8.0 Hz, 1 H), 7.57 (d, *J* = 8.4 Hz, 1 H), 7.40 (t, *J* = 7.6 Hz, 1 H), 7.31 (t, *J* = 7.6 Hz, 1 H), 7.21 (s, 1H), 4.38-4.28 (m, 4 H), 1.39 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 155.5, 146.8 (t, *J* = 18.0 Hz), 128.19, 126.5 (d, *J* = 48.0 Hz), 123.8 (d, *J* = 24.0 Hz), 122.2, 121.3, 113.8 (td, *J* = 259.0 Hz, *J* = 219.0 Hz), 109.7 (d, *J* = 37.0 Hz), 108.7 (d, *J* = 8.0 Hz, *J* = 5.0 Hz), 65.25, 65.18, 16.36, 16.30. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -108.80 (d, *J* = 102.8 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 4.11 (t, *J* = 107.6 Hz). **IR (thin film) ν_{max}** 2987, 2922, 1598, 1452, 1276, 1164, 1039, 752, 560 cm^{-1}. **HRMS (ESI, m/z):** $[C_{13}H_{16}F_2O_4P]$ $(M+H)^+$ 305.0749, found 305.0754.



3q

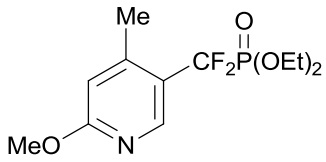
Diethyl (difluoro(3-methylbenzo[b]thiophen-2-yl)methyl)phosphonate (3q). The general procedure was followed using 3-methylthioindene **1q** (262 µl, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 7:1→PE/EtOAc = 2:1) yielded **3q** (59.1 mg, 89 %) as a pale yellow oil and the excess **1q** can be recycled and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.82-7.79 (m, 1 H), 7.77 -7.74 (m, 1 H), 7.42-7.27 (m, 2 H), 4.31-4.15 (m, 4 H), 2.59 (s, 3H), 1.34 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 143.5, 140.1, 139.0, 134.5 (td, *J* = 9.0 Hz, *J* = 4.0 Hz), 133.2, 127.5 (m), 126.2, 125.8 (d, *J* = 18.0 Hz), 124.6 (d, *J* = 59.0 Hz), 122.3 (td, *J* = 42.0 Hz, *J* = 20.0

Hz), 121.4, 117.6 (td, *J* = 262.0 Hz, *J* = 224.0 Hz), 113.9, 64.82, 64.76, 16.19, 16.14,12.3. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -97.78 (d, *J* = 116.9 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 5.53 (t, *J* = 116.8 Hz). **IR (thin film) ν_{max}** 2987, 2930, 1439, 1272, 1214, 1021, 757, 731, 615, 562 cm^{-1}. **HRMS (ESI, m/z):** $[C_{14}H_{21}F_2O_3PSN]$ $(M+NH_4)^+$ 352.0942, found 352.0943.



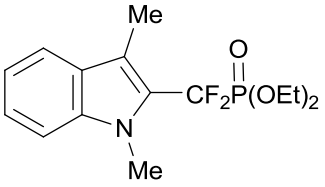
3r-A

Diethyl (difluoro(2-methoxy-4-methylpyridin-3-yl)methyl)phosphonate (3r-A). The general procedure was followed using 2-methoxy-4-methylpyridine **1r** (246 mg, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 9:1→PE/EtOAc = 2:1) yielded **3r-A** (40 mg, 65 %) as a pale yellow oil and the excess **1r** can be recycled and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.03 (d, *J* = 5.2 Hz, 1 H), 6.72 (d, *J* = 5.2 Hz, 1 H), 4.29-4.17 (m, 4 H), 3.94 (s, 3H), 2.50 (t, *J* = 4.0 Hz, 3H), 1.32 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 161.9, 150.8 (d, *J* = 2.0 Hz), 147.9, 123.2, 121.1, 118.4, 117.9, 115.8, 114.1 (m), 109.8, 64.60, 64.53, 53.75, 21.38 (t, *J* = 6.0 Hz), 16.32, 16.27. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -100.77 (d, *J* = 111.2 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 6.59 (t, *J* = 114.5 Hz). **IR (thin film) ν_{max}** 2985, 2951, 1591, 1565, 1471, 1386, 1310, 1273, 1127, 1047, 938, 581, 506 cm^{-1}. **HRMS (ESI, m/z):** $[C_{12}H_{19}F_2NO_4P]$ $(M+H)^+$ 310.1014, found 310.1015.



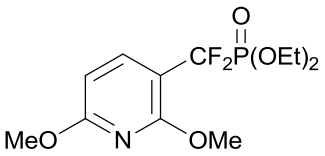
3r-B

Diethyl (difluoro(6-methoxy-4-methylpyridin-3-yl)methyl)phosphonate (3r-B). The general procedure was followed using 2-methoxy-4-methylpyridine **1r** (246 mg, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 9:1→PE/EtOAc = 2:1) yielded **3r-B** (9.3 mg, 15 %) as a pale yellow oil and the excess **1r** can be recycled and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.27 (s, 1 H), 6.61 (s, 1 H), 4.32-4.17 (m, 4 H), 3.96 (s, 3H), 2.52 (s, 3H), 1.35 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.6, 149.6, 146.6, 113.0, 109.1, 64.81, 64.74, 53.63, 20.30, 16.37, 16.32. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -104.19 (d, *J* = 116.9 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 6.40 (t, *J* = 117.3 Hz). **IR (thin film) ν_{max}** 2986, 2928, 1688, 1610, 1553, 1496, 1450, 1378, 1268, 1155, 1048, 563 cm^{-1}. **HRMS (ESI, m/z):** $[C_{12}H_{19}F_2NO_4P]$ $(M+H)^+$ 310.1014, found 310.1017.



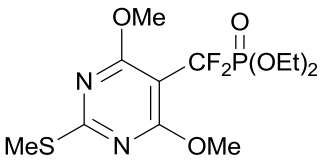
3s

Diethyl ((1,3-dimethyl-1H-indol-2-yl)difluoromethyl)phosphonate (3s). The general procedure was followed using 1,3-dimethyl-1H-indole **1s** (290 mg, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 5:1→PE/EtOAc = 1:1) yielded **3s** (63.1 mg, 95 %) as a pale yellow oil and the excess **1s** can be recycled and reused. **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.66 (d, *J* = 8.0 Hz, 1 H), 7.38 -7.32 (m, 2 H), 7.21-7.17 (m, 1 H), 4.31-4.12 (m, 4 H), 3.93 (s, 3H), 2.51 (s, 3H), 1.36 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 138.1, 130.5, 127.5, 124.5 (m), 123.5 (d, *J* = 29.0 Hz), 121.0, 119.4 (d, *J* = 15.0 Hz), 117.3 (td, *J* = 263.0 Hz, *J* = 225.0 Hz), 114.5 (td, *J* = 8.0 Hz, *J* = 4.0 Hz), 113.5, 109.7 (d, *J* = 53.0 Hz), 64.66, 64.59, 31.6 (t, *J* = 5.0 Hz), 16.20, 16.15, 9.0 (t, *J* = 3.0 Hz). **^{19}F NMR (376 MHz, CDCl$_3$)** δ -102.56 (d, *J* = 118.8 Hz, 2 F). **^{31}P NMR (162 MHz, CDCl$_3$):** 6.24 (t, *J* = 118.6 Hz). **IR (thin film) ν_{max}** 2984, 2934, 1553, 1470, 1403, 1360, 1270, 1220, 1162, 1042, 794, 742, 553 cm^{-1}. **HRMS (ESI, m/z):** [$C_{15}H_{21}F_2NO_3P$] $(M+H)^+$ 332.1222, found 332.1219.



3t

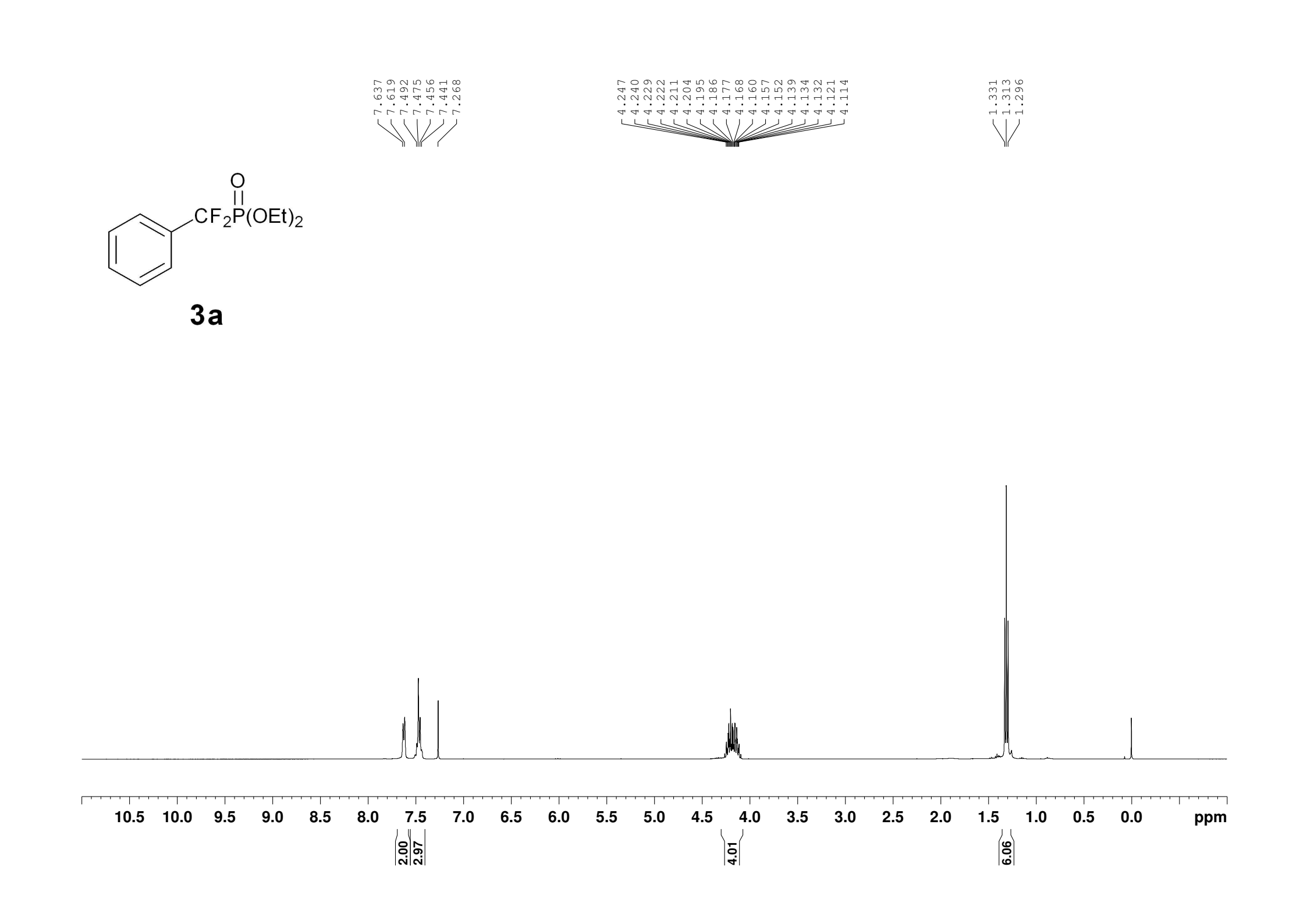
Diethyl ((2,6-dimethoxypyridin-3-yl)difluoromethyl)phosphonate (3t). The general procedure was followed using 2,6-dimethoxypyridine **1t** (264 μl, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 5:1→PE/EtOAc = 1:1) yielded **3s** (53.7 mg, 83 %) as a pale yellow oil and the excess **1s** can be recycled and reused. **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.68 (d, *J* = 8.4 Hz, 1 H), 6.33 (d, *J* = 8.4 Hz, 1 H), 4.30-4.16 (m, 4 H), 3.98 (s, 3H), 3.93 (s, 3H), 1.32 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 164.5, 160.3 (d, *J* = 2.0 Hz), 140.1 (m), 121.7, 118.0 (td, *J* = 262.0 Hz, *J* = 222.0 Hz), 114.3, 114.0, 106.3 (d, *J* = 11.0 Hz), 106.0 (d, *J* = 11.0 Hz), 101.2, 64.54, 64.48, 53.65, 53.52, 16.30, 16.24. **^{19}F NMR (376 MHz, CDCl$_3$)** δ -105.30 (d, *J* = 119.9 Hz, 2 F). **^{31}P NMR (162 MHz, CDCl$_3$):** 6.31 (t, *J* = 120.2 Hz). **IR (thin film) ν_{max}** 2986, 2951, 1603, 1486, 1467, 1387, 1327, 1272, 1236, 1122, 1045, 814, 571cm^{-1}. **HRMS (ESI, m/z):** [$C_{12}H_{19}F_2NO_5P$] $(M+H)^+$ 326.0963, found 326.0959.



3u

Diethyl ((4,6-dimethoxy-2-(methylthio)pyrimidin-5-yl)difluoromethyl)phosphonate (3u). The general procedure was followed using 4,6-dimethoxy-2-methylthiopyrimidine **1u** (372 mg, 2.0 mmol). Purification by column chromateraphy (PE/EtOAc = 6:1→PE/EtOAc = 1:1) yielded **3u** (61.6 mg, 83 %) as a pale yellow oil and the excess **1u** can be recycled and reused. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.29-4.18 (m, 4 H), 3.97 (s, 6H), 2.52 (s, 3H), 1.32 (t, *J* = 7.2 Hz, 6 H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 172.8, 167.5 (d, *J* = 1.0 Hz), 121.5, 117.7 (td, *J* = 264.0 Hz, *J* = 224.0 Hz), 114.0 92.3 (m), 64.53, 64.46, 54.61, 16.34, 16.29, 13.99. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -102.98 (d, *J* = 119.2 Hz, 2 F). **^{31}P NMR (162 MHz, $CDCl_3$):** 6.30 (t, *J* = 119.1 Hz). **IR (thin film) ν_{max}** 2990, 1568, 1545, 1462, 1365, 1272, 1204, 1175, 1137, 1052, 943, 795, 568 cm^{-1}. **HRMS (ESI, m/z):** $[C_{12}H_{20}F_2N_2O_5PS]$ $(M+H)^+$ 373.0793, found 373.0801.

8. Copies of NMR spectra of compounds.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4.177
4.168
4.160
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4.152
4.139
4.134
4.132
4.121
4.114
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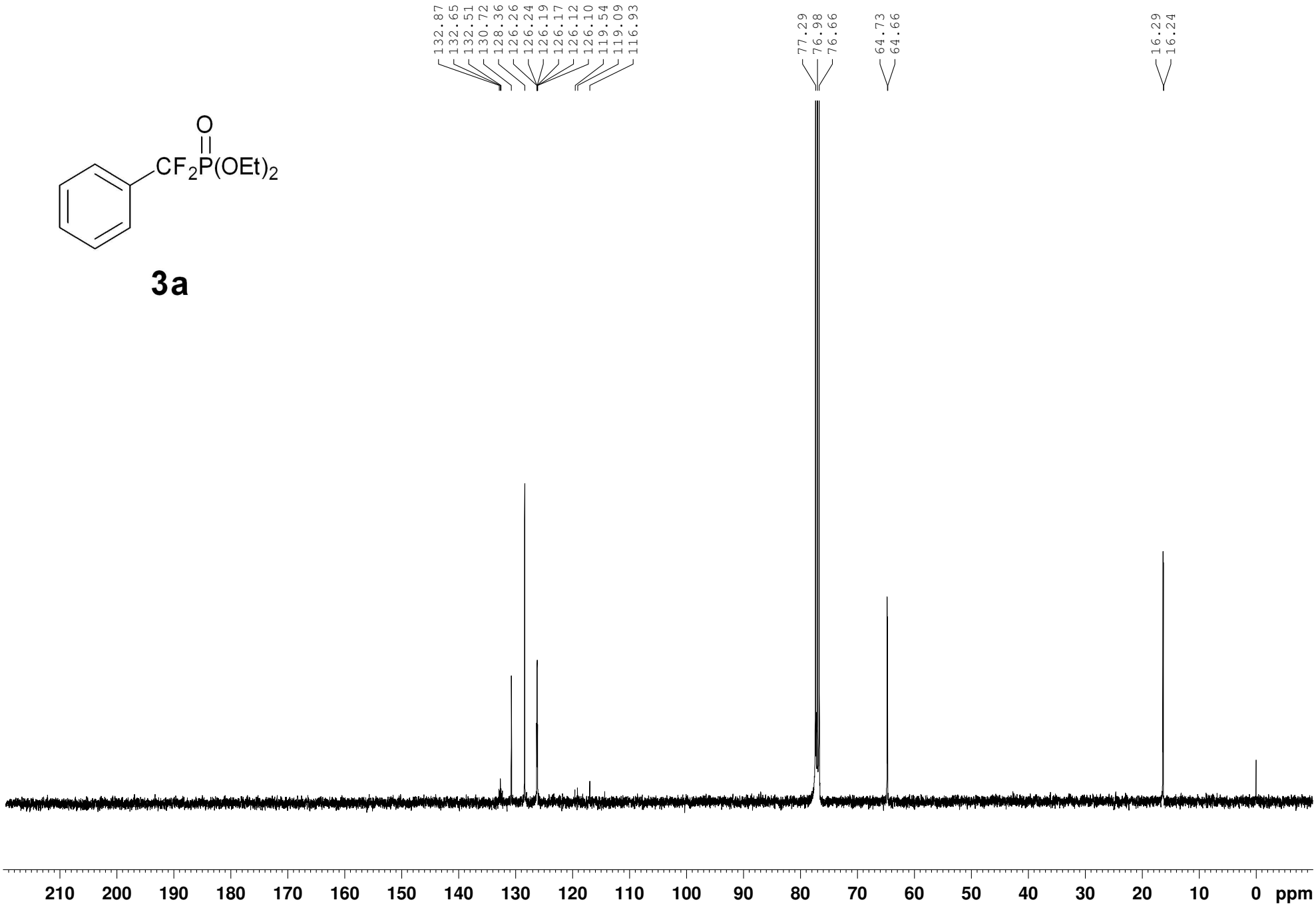
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126.19
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126.12
126.10
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116.93
77.29
76.98
76.66
64.73
64.66
16.29
16.24
O
CF2P(OEt)2
3a
210
200
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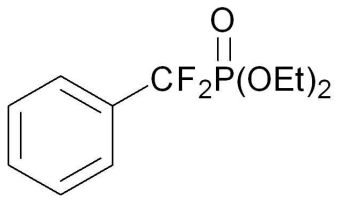
O
CF2P(OEt)2

3a

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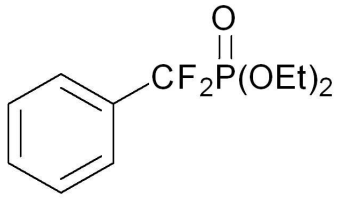
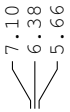
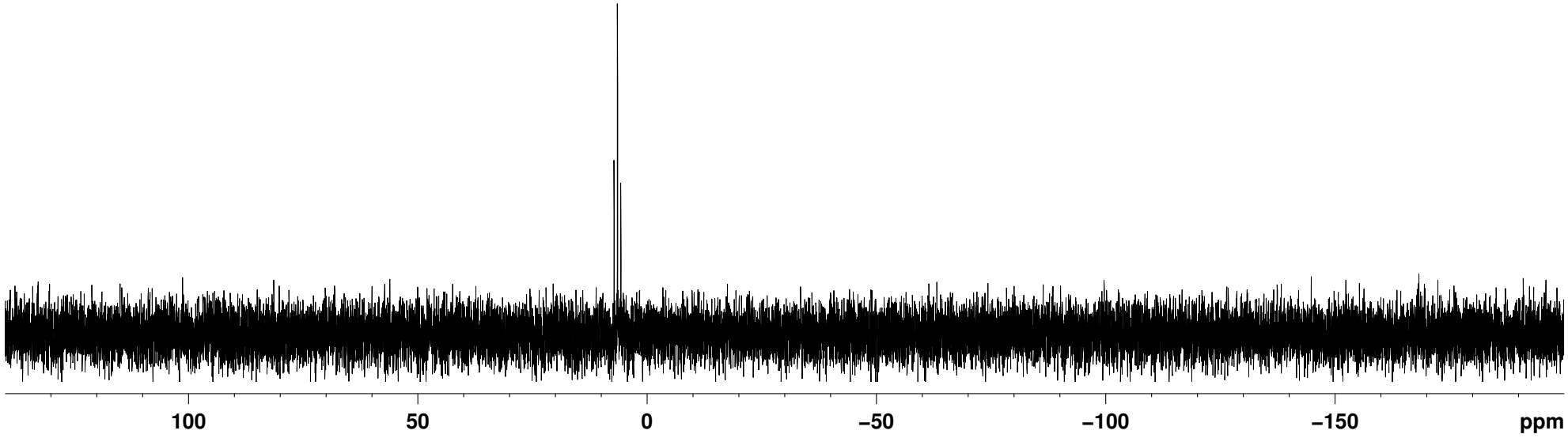
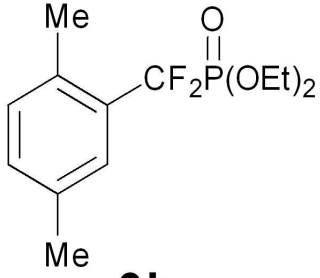


3a






Me
O
CF2P(OEt)2
Me

3b

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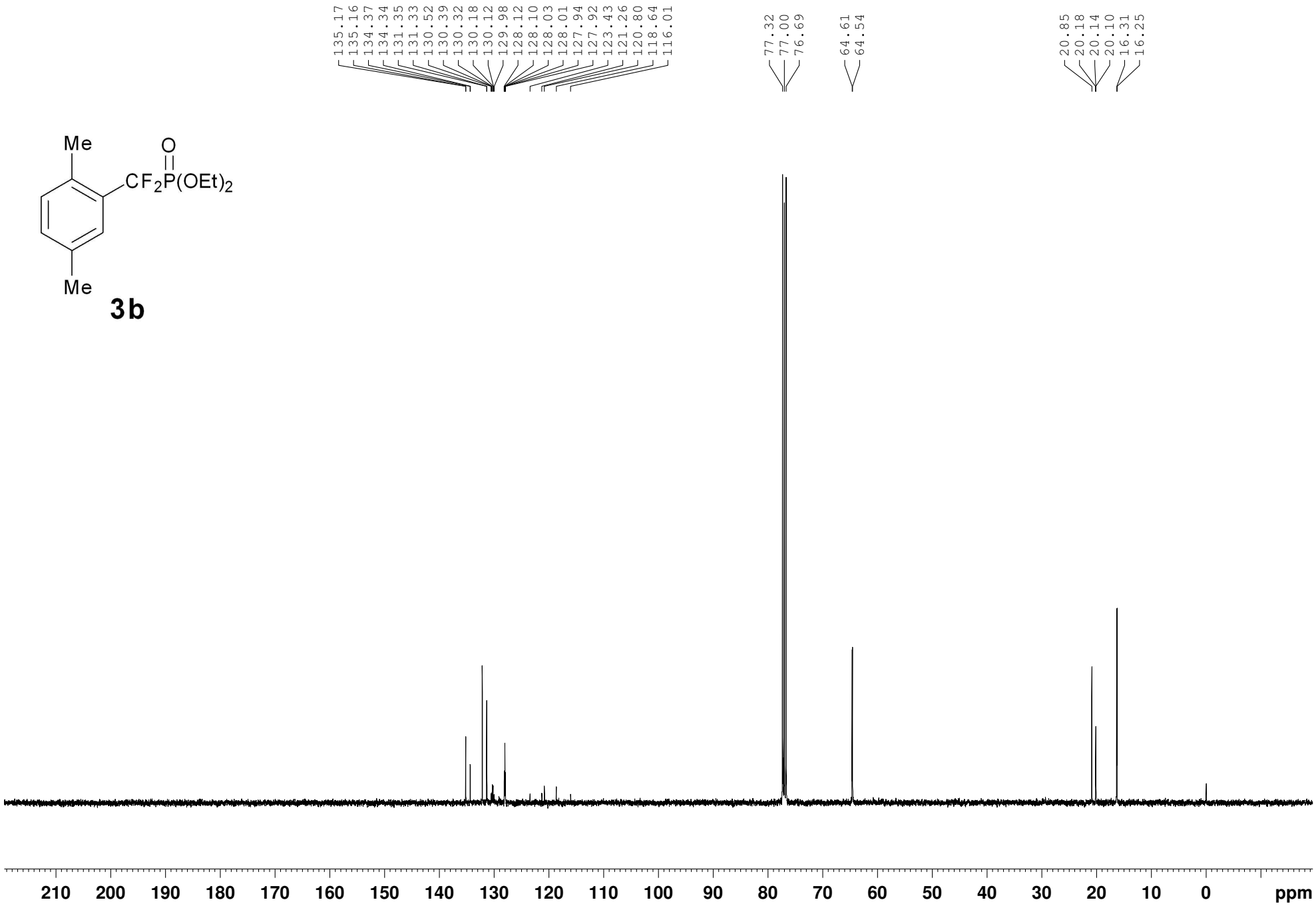
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64.54
20.85
20.18
20.14
20.10
16.31
16.25
Me
O
CF2P(OEt)2
Me
3b
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200
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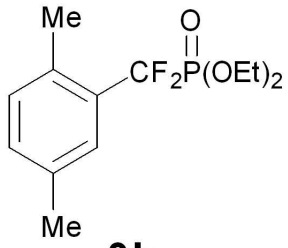
ppm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Me

3b

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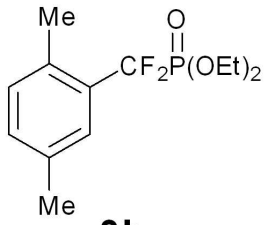
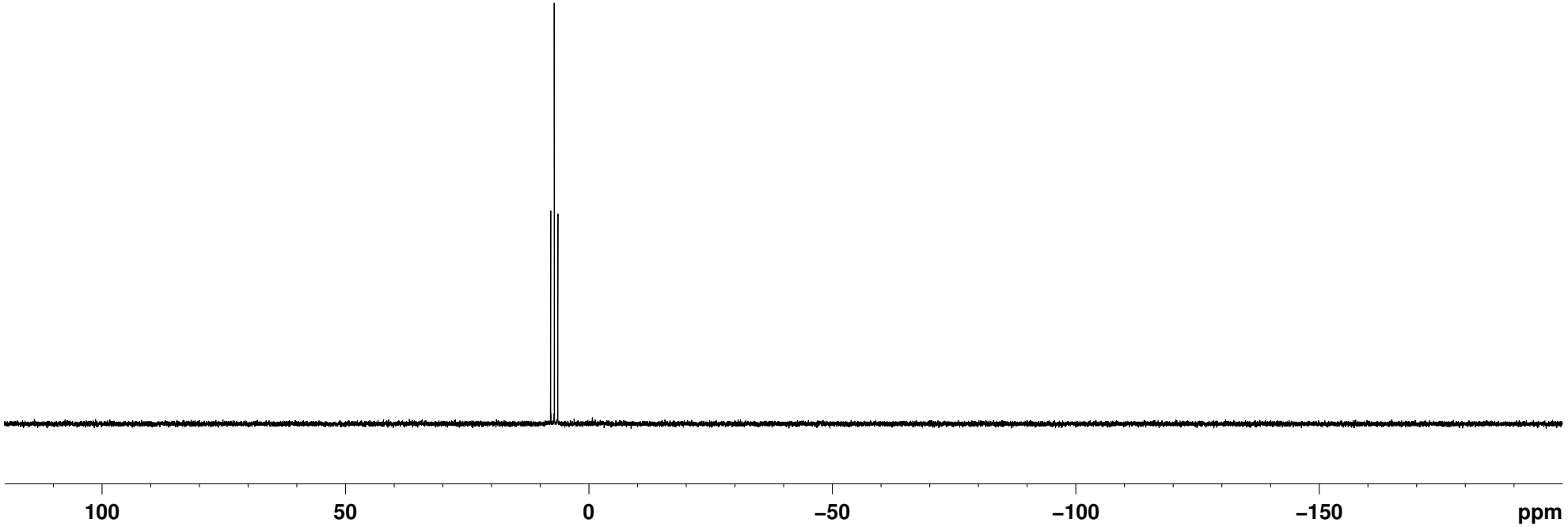
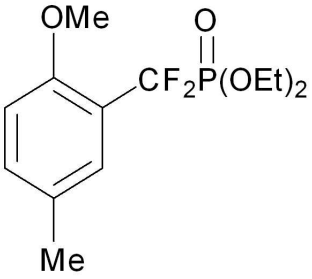


3b

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Me

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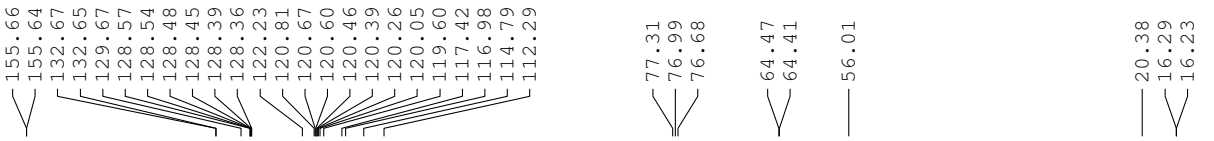
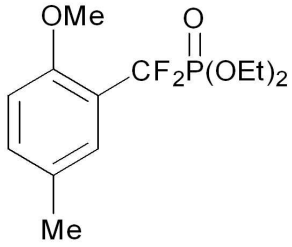
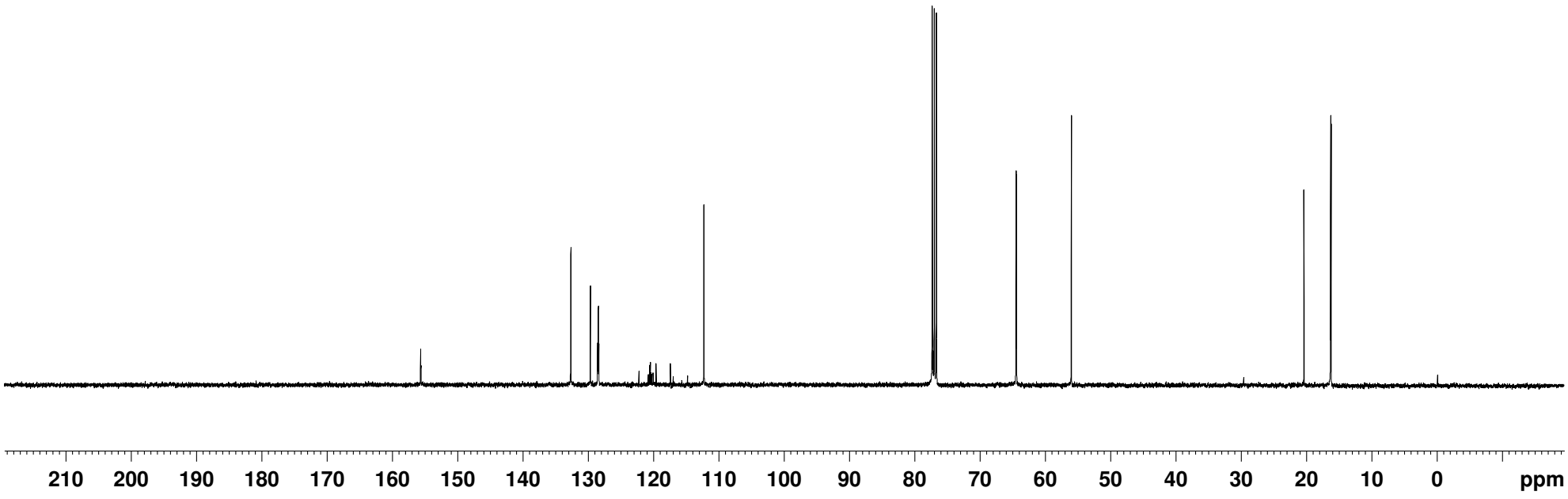
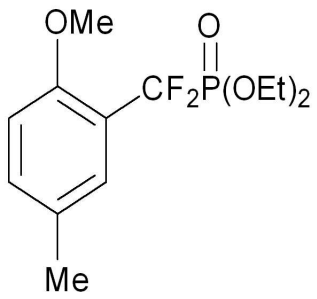
4.211
4.193
4.186
4.174
4.168
4.156
4.149
4.131
3.833
2.299
1.335
1.317
1.299
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00
0.97
1.02
4.10
3.06
3.05
6.05


155.66
155.64
132.67
132.65
129.67
128.57
128.54
128.48
128.45
128.39
128.36
122.23
120.81
120.67
120.60
120.46
120.39
120.26
120.05
119.60
117.42
116.98
114.79
112.29
77.31
76.99
76.68
64.47
64.41
56.01
20.38
16.29
16.23

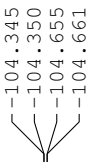

OMe
O
CF2P(OEt)2
Me

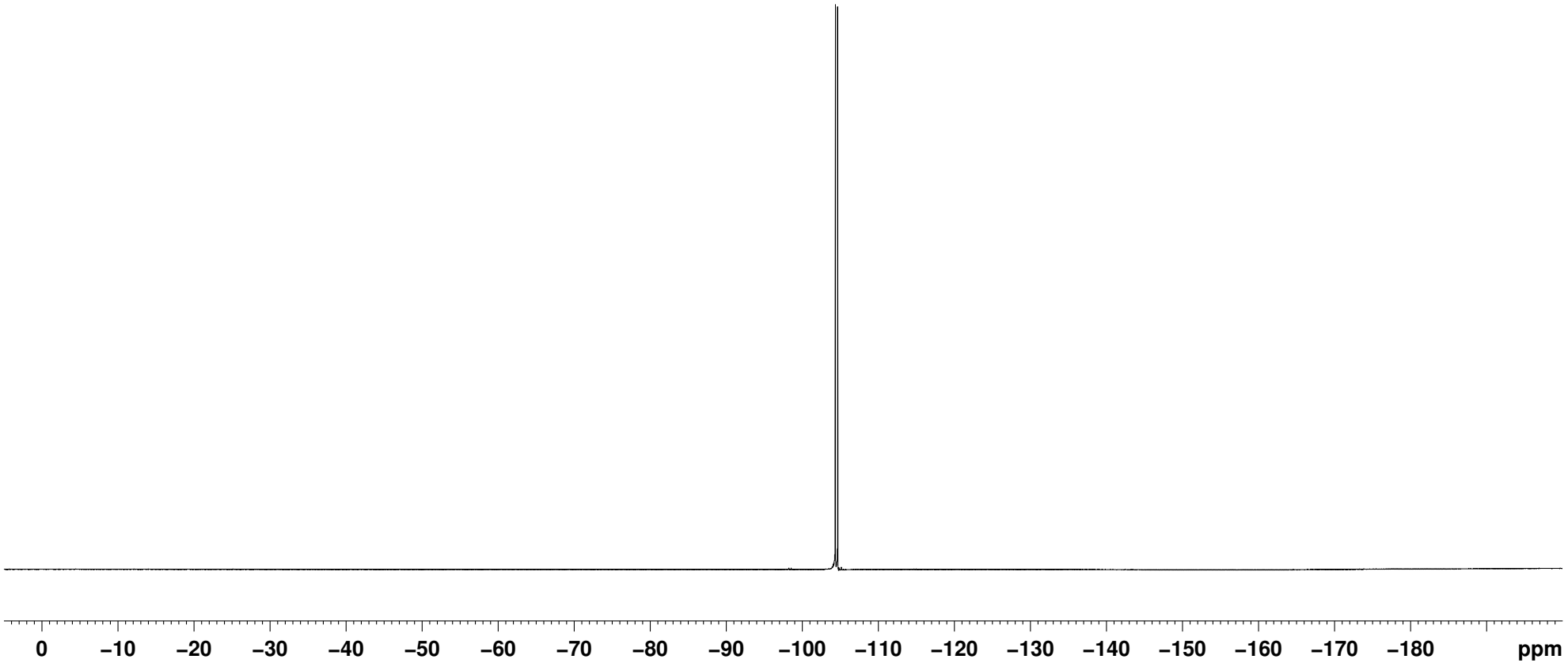
3c-A

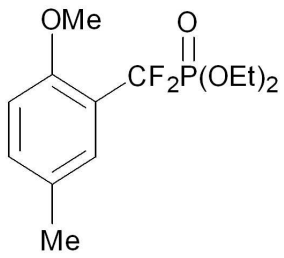

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


OMe
O
CF2P(OEt)2
Me

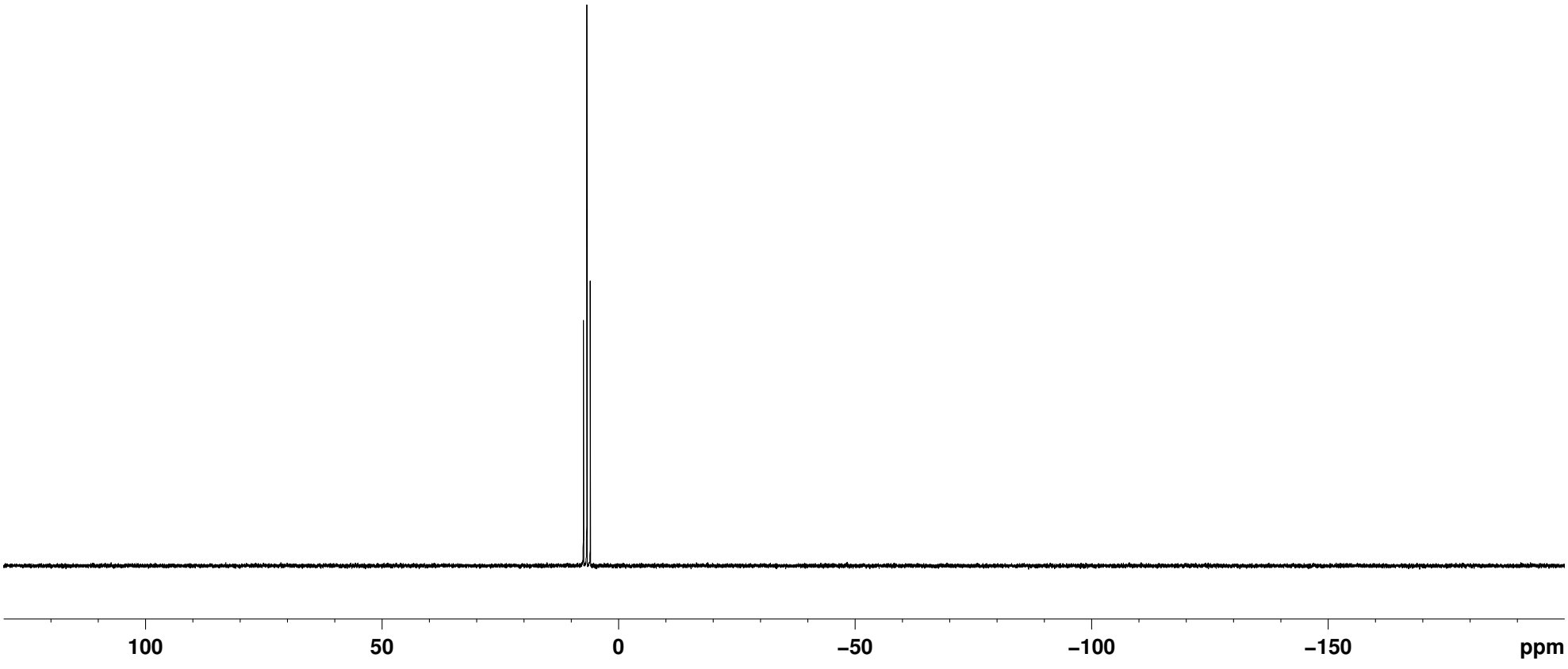
3c-A

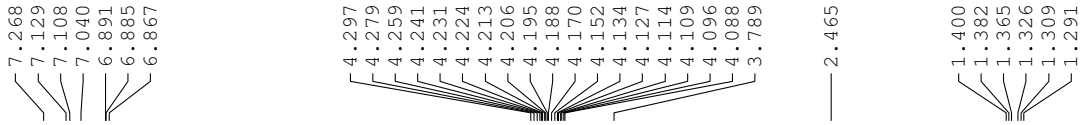

-104.345
-104.350
-104.655
-104.661

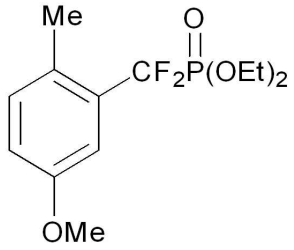

0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
ppm



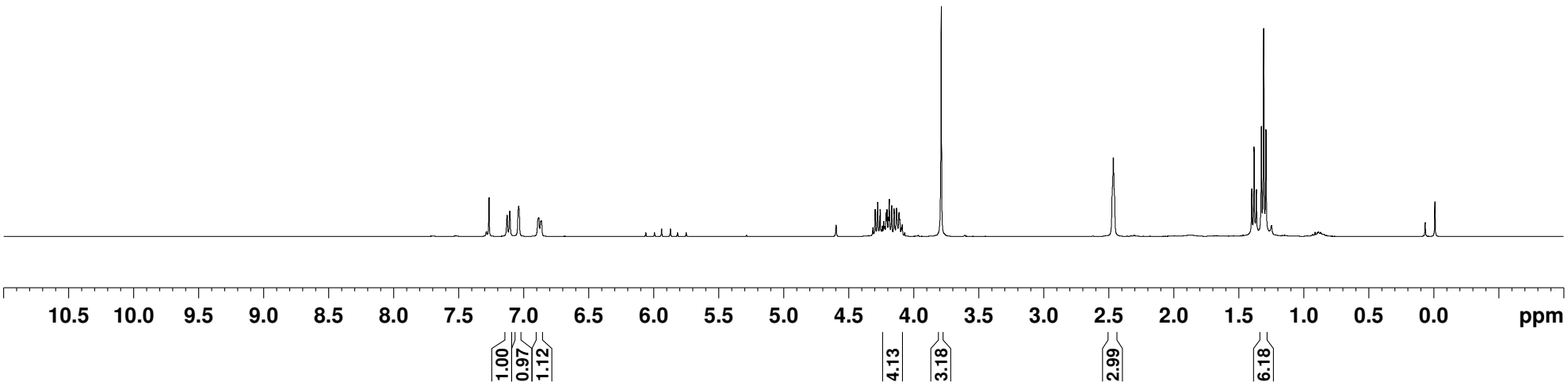
3c-A

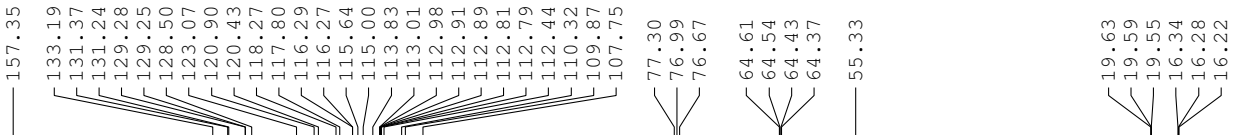



7.268
7.129
7.108
7.040
6.891
6.885
6.867
4.297
4.279
4.259
4.241
4.231
4.224
4.213
4.206
4.195
4.188
4.170
4.152
4.134
4.127
4.114
4.109
4.096
4.088
3.789
2.465
1.400
1.382
1.365
1.326
1.309
1.291


Me
O
CF2P(OEt)2
OMe

3c-B


10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
0.97
1.12
4.13
3.18
2.99
6.18


157.35
133.19
131.37
131.24
129.28
129.25
128.50
123.07
120.90
120.43
118.27
117.80
116.29
116.27
115.64
115.00
113.83
113.01
112.98
112.91
112.89
112.81
112.79
112.44
110.32
109.87
107.75
77.30
76.99
76.67
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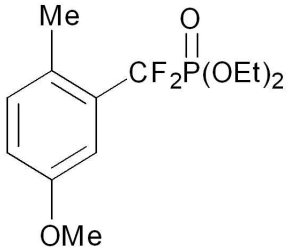
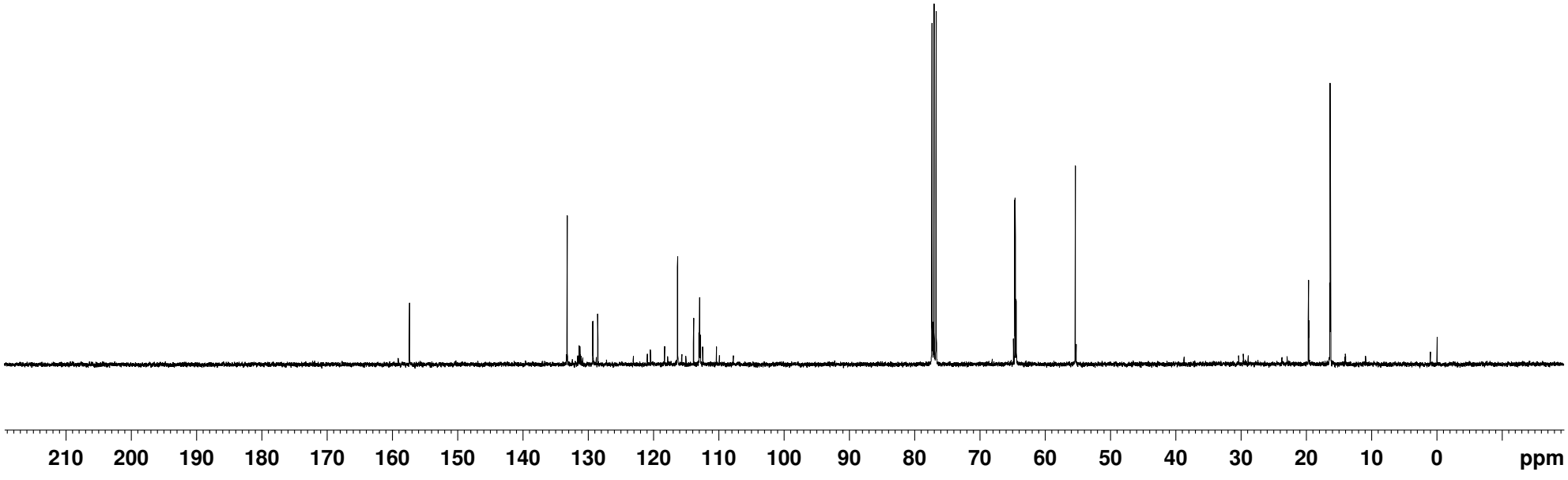
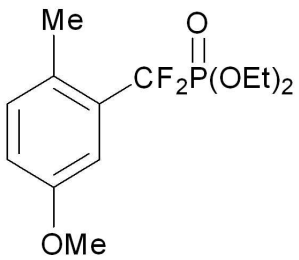
19.63
19.59
19.55
16.34
16.28
16.22


Me
O
CF2P(OEt)2
OMe

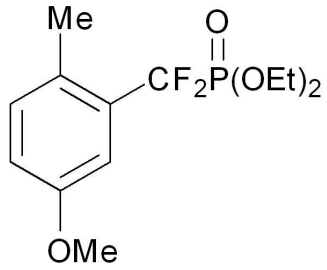
3c-B


210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

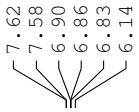

Me
O
CF2P(OEt)2
OMe

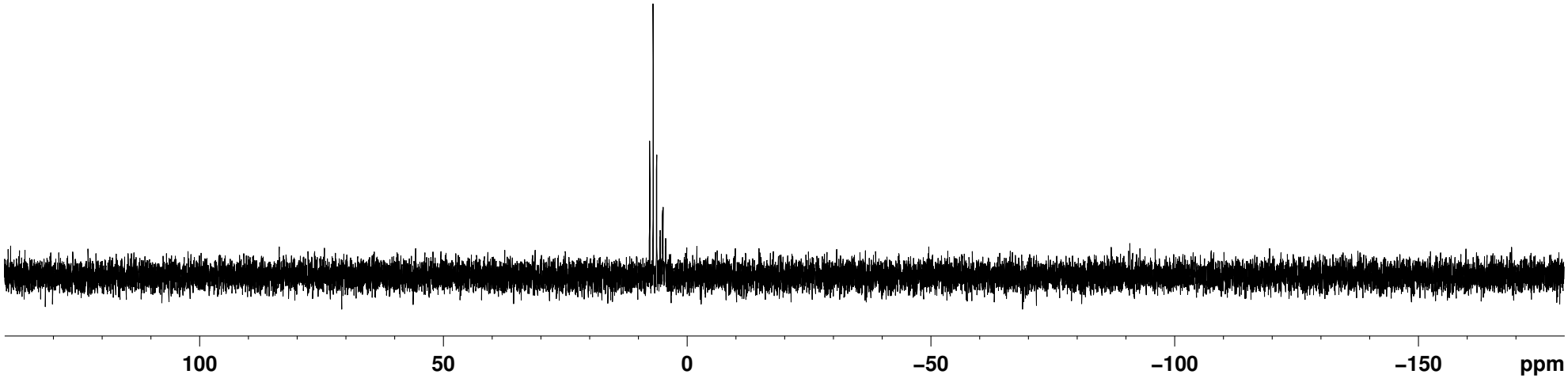
3c-B

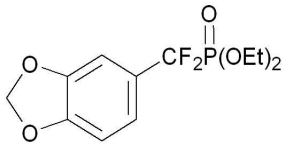
-104.340
-104.651
-135.113
-135.356
–10
–20
–30
–40
–50
–60
–70
–80
–90
–100
–110
–120
–130
–140
–150
–160
–170
–180
ppm



3c-B

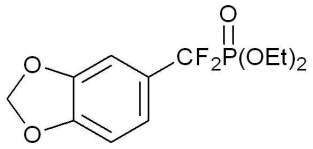





O
CF2P(OEt)2
O
O

3d

7.270
7.122
7.101
7.052
6.851
6.831
5.994
4.241
4.233
4.223
4.215
4.204
4.197
4.186
4.179
4.171
4.160
4.157
4.153
4.140
4.135
4.132
4.122
4.114
1.329
1.311
1.293
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
0.97
0.99
2.02
4.05
6.06



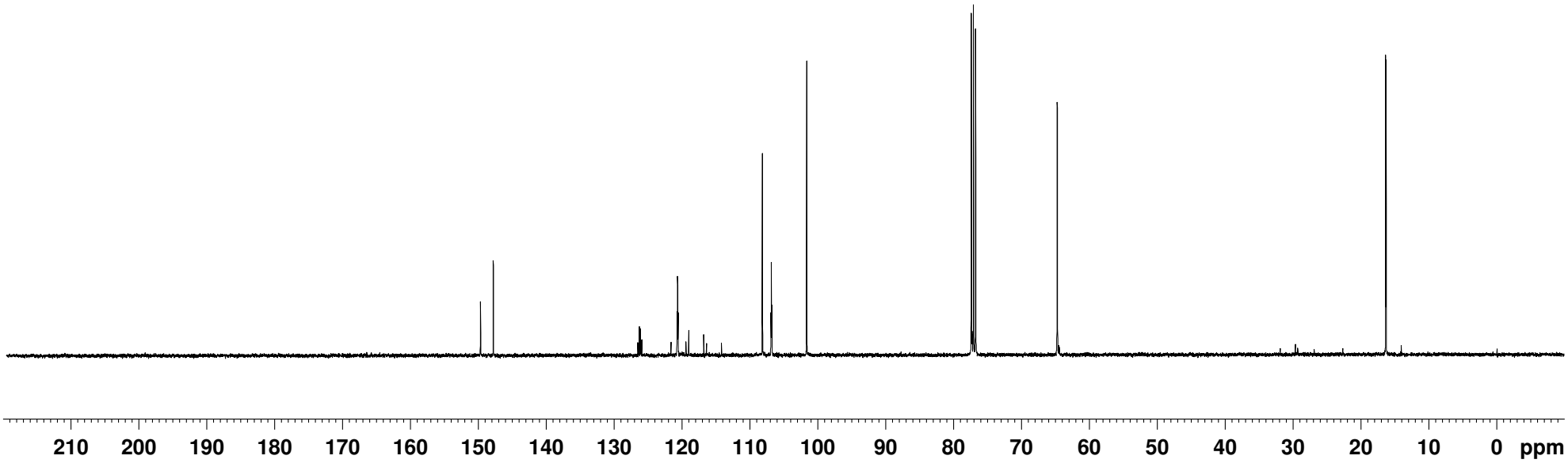
3d

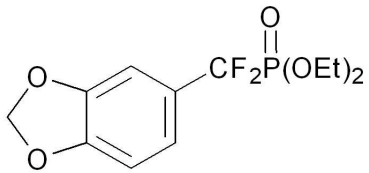
149.63
149.61
147.73
126.45
126.30
126.22
126.08
126.00
125.86
121.56
120.68
120.65
120.60
120.58
120.53
120.50
119.36
118.94
116.74
116.31
114.12
108.09
106.85
106.83
106.78
106.76
106.71
106.69

77.32
77.00
76.68

64.69
64.62

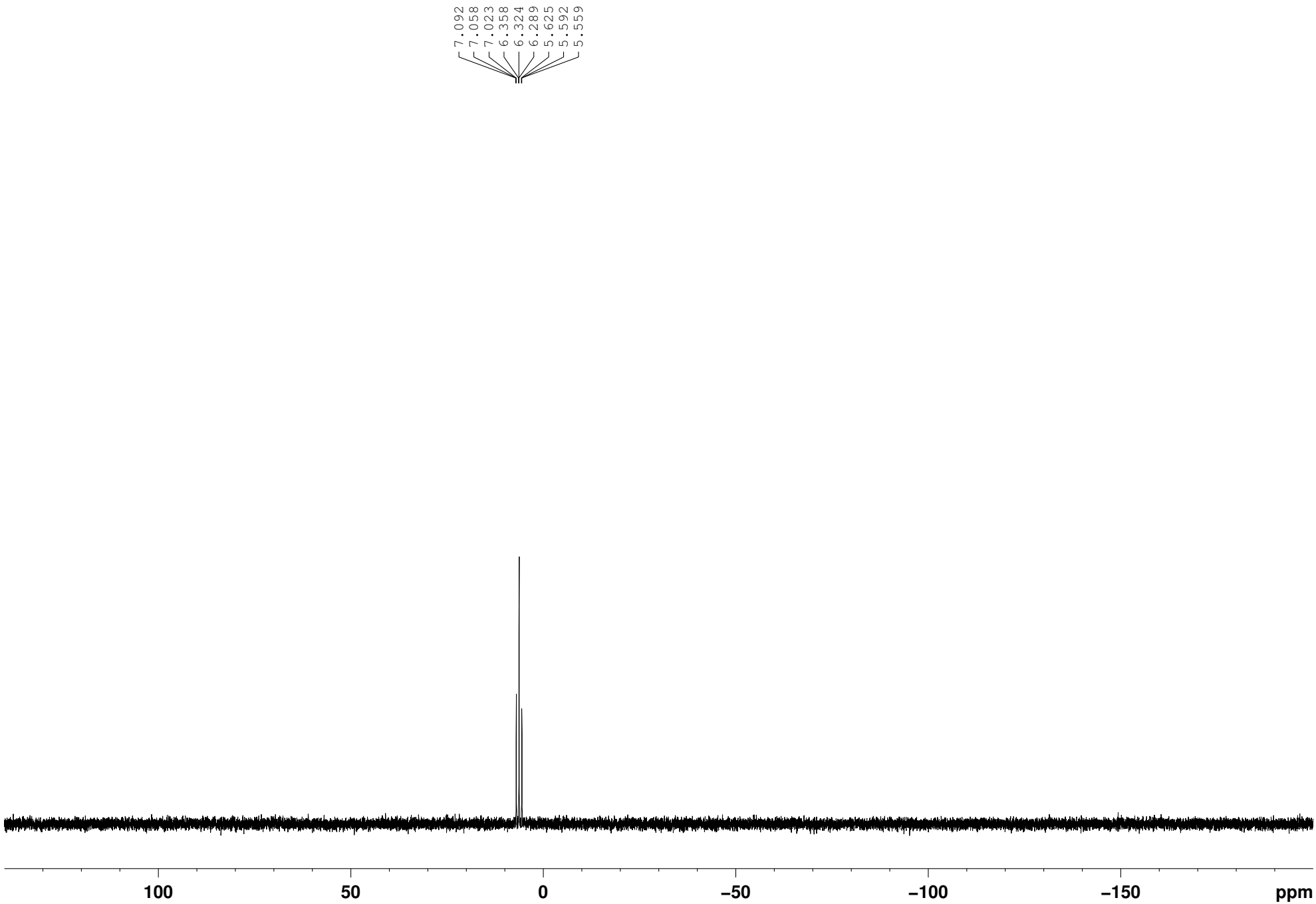
16.28
16.22

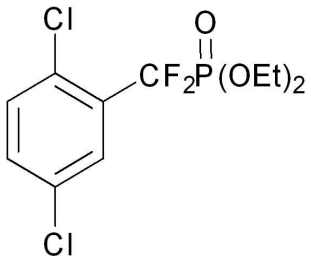



O
CF2P(OEt)2
O
O

3d

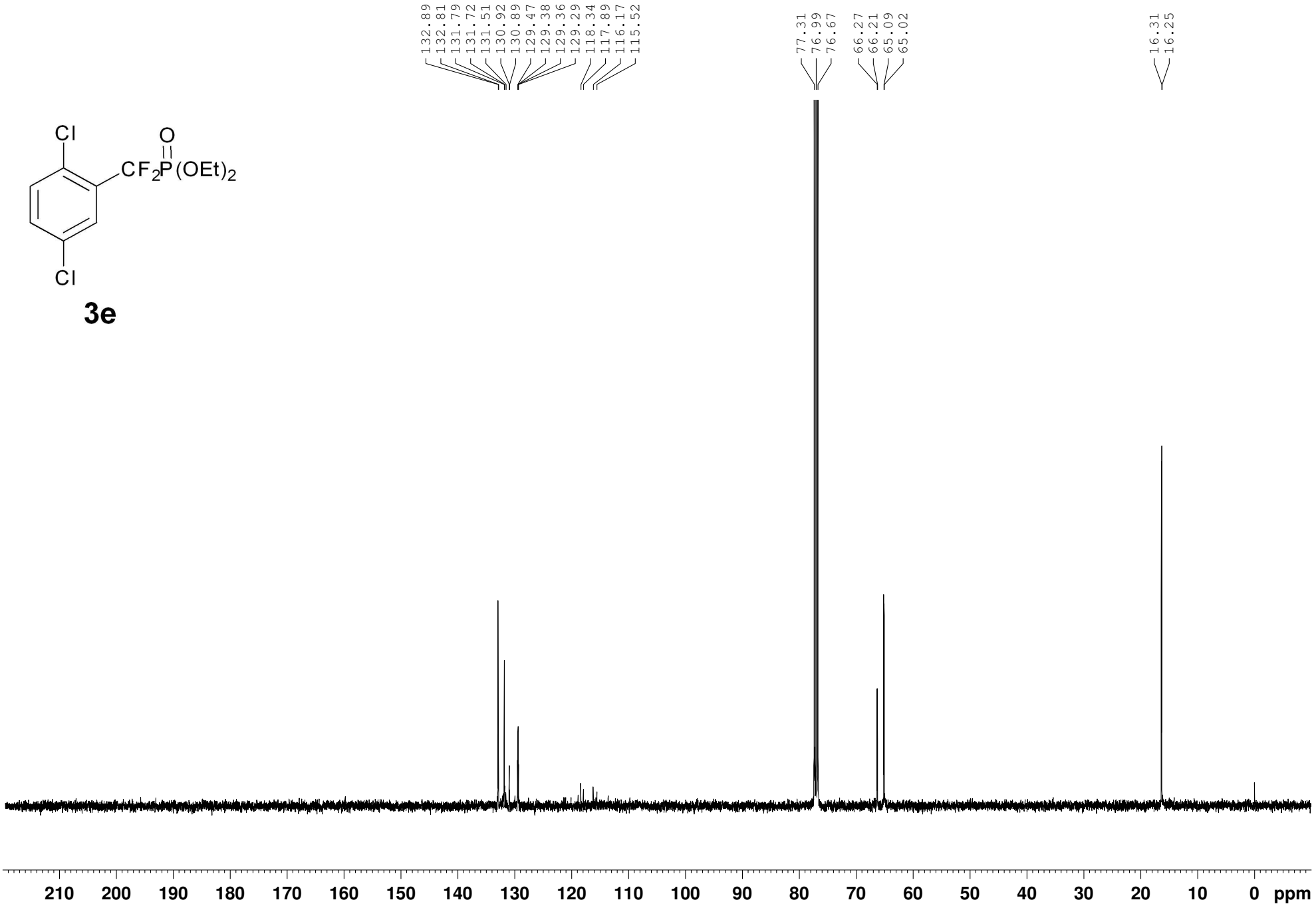
-106.306
-106.622
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
ppm

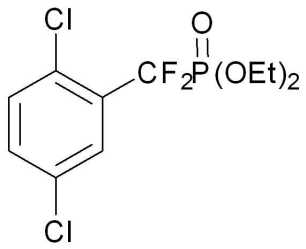

7.092
7.058
7.023
6.358
6.324
6.289
5.625
5.592
5.559
100
50
0
−50
−100
−150
ppm


Cl
O
CF2P(OEt)2
Cl

3e

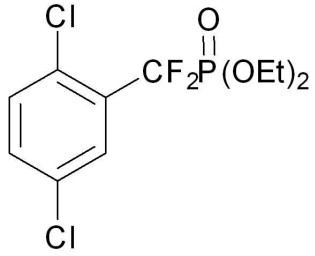
7.592
7.400
7.378
7.371
7.345
7.270
4.408
4.397
4.390
4.379
4.372
4.361
4.358
4.354
4.340
4.336
4.322
4.315
4.308
4.297
4.289
4.278
4.271
4.253
4.231
4.213
4.206
1.433
1.415
1.397
1.369
1.352
1.334
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
2.02
4.13
6.28


132.89
132.81
131.79
131.72
131.51
130.92
130.89
129.47
129.38
129.36
129.29
118.34
117.89
116.17
115.52
77.31
76.99
76.67
66.27
66.21
65.09
65.02
16.31
16.25
Cl
O
CF2P(OEt)2
Cl
3e
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

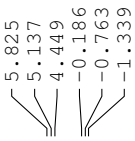

Cl
O
CF2P(OEt)2
Cl

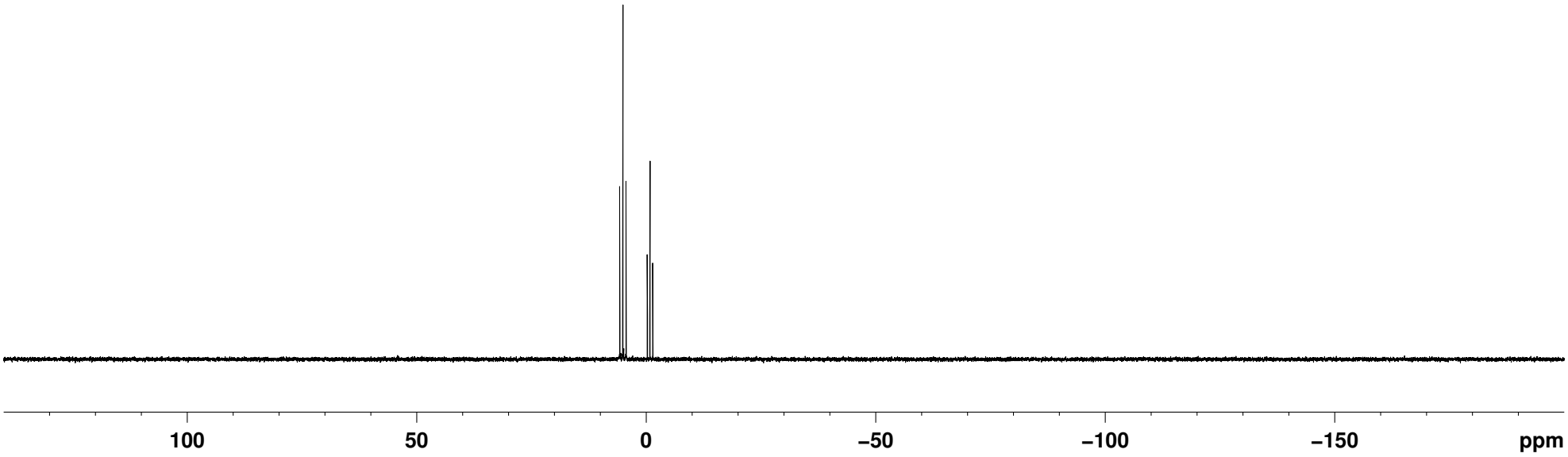
3e

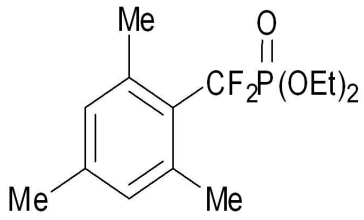
-61.304
-61.553
-105.429
-105.725
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
ppm


Cl
O
CF2P(OEt)2
Cl

3e

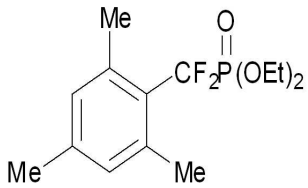

5.825
5.137
4.449
-0.186
-0.763
-1.339


100
50
0
−50
−100
−150
ppm


Me
O
CF2P(OEt)2
Me
Me

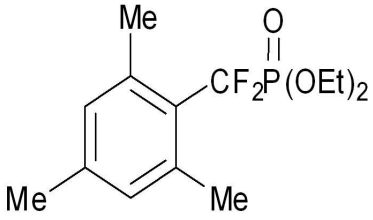
3f

7.265
6.867
4.242
4.224
4.217
4.206
4.199
4.181
4.162
4.143
4.123
4.119
4.105
4.101
4.098
4.080
2.513
2.501
2.489
2.260
1.336
1.318
1.301
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
2.00
4.02
6.08
3.04
6.02


Me
O
CF2P(OEt)2
Me
Me

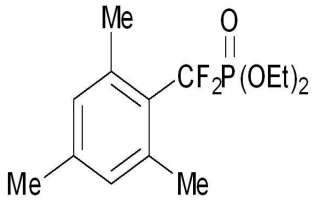
3f

139.87
138.53
138.50
138.47
138.43
138.08
131.29
129.14
126.40
126.21
126.07
125.87
125.21
124.78
123.06
122.58
120.42
119.94
117.78
77.32
77.00
76.68
64.41
64.34
22.23
22.16
22.10
20.73
16.32
16.26
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

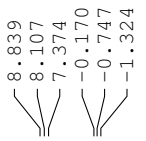

Me
O
CF2P(OEt)2
Me
Me

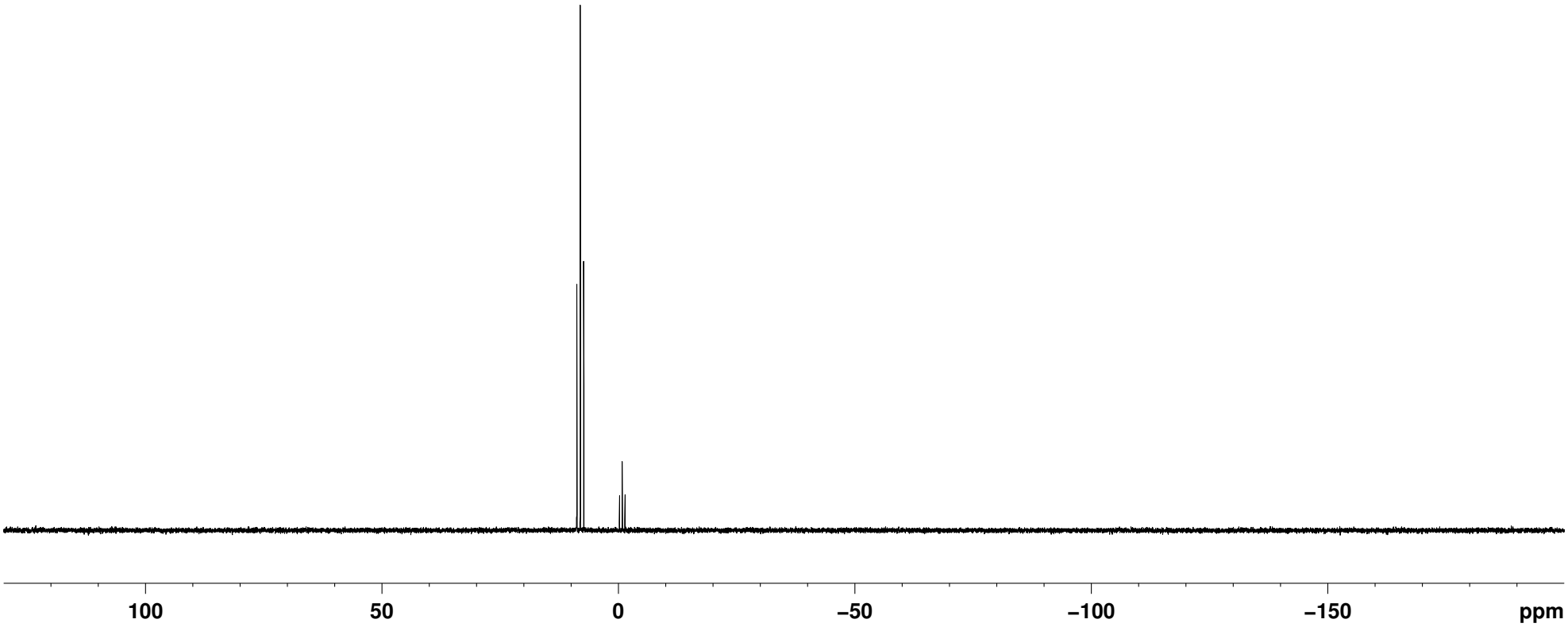
3f

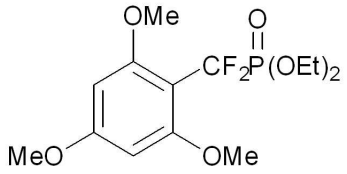
-61.287
-61.535
-97.302
-97.311
-97.617
-97.626
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
ppm


Me
O
CF2P(OEt)2
Me
Me

3f

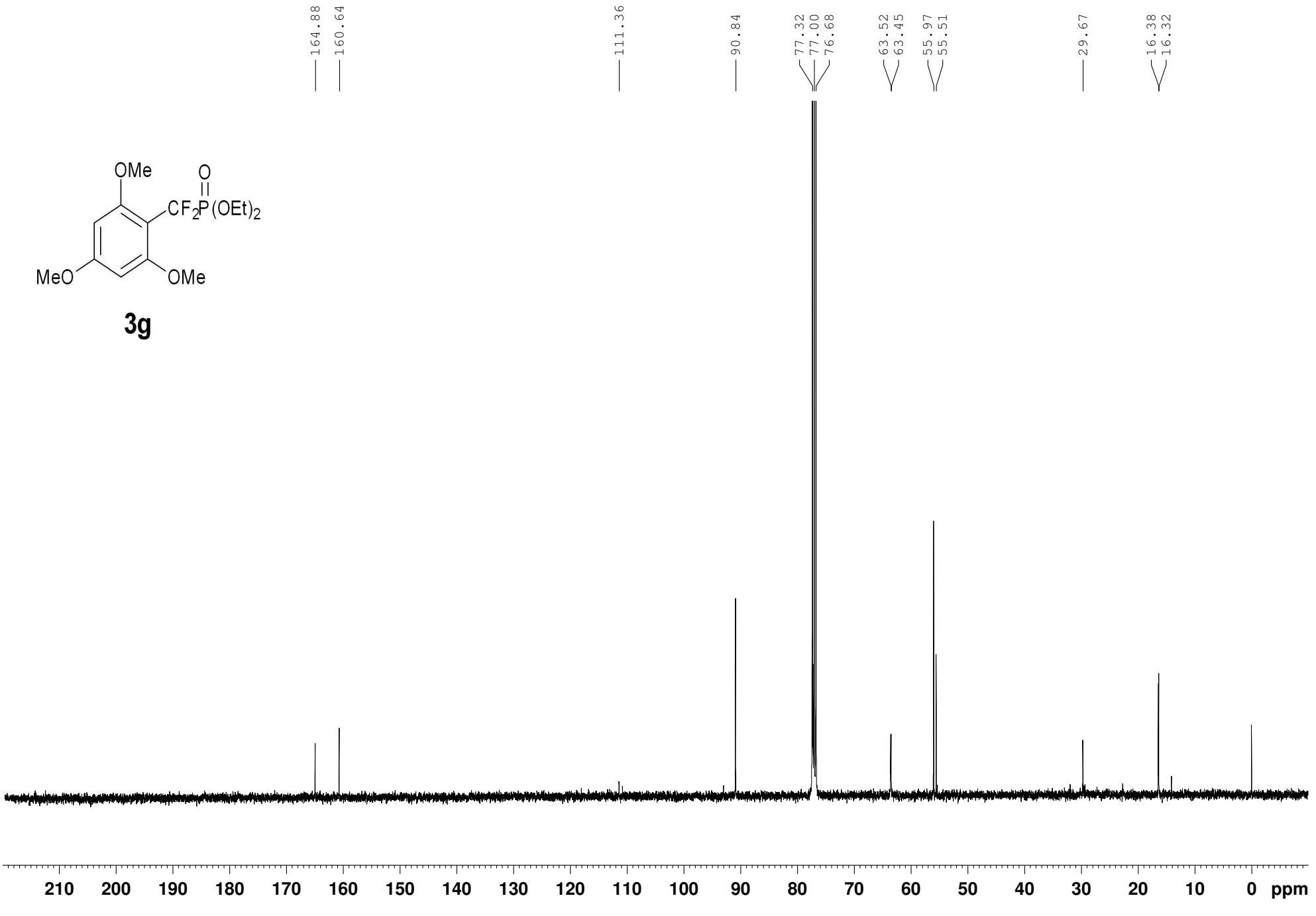

8.839
8.107
7.374
-0.170
-0.747
-1.324

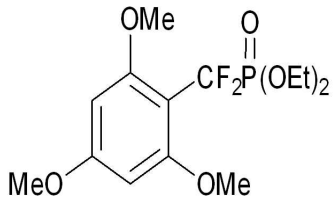

100
50
0
−50
−100
−150
ppm


OMe
O
CF2P(OEt)2
MeO
OMe

3g

7.253
6.089
6.087
4.221
4.214
4.206
4.204
4.196
4.189
4.177
4.171
4.169
4.159
4.151
4.146
4.141
4.133
4.125
3.833
3.817
1.331
1.314
1.296
1.245
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
2.00
4.03
9.04
6.30

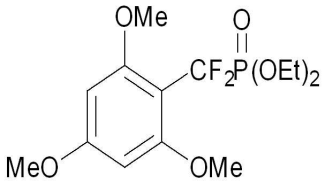

164.88
160.64
111.36
90.84
77.32
77.00
76.68
63.52
63.45
55.97
55.51
29.67
16.38
16.32
OMe
O
CF2P(OEt)2
MeO
OMe
3g
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


OMe
O
CF2P(OEt)2
MeO
OMe

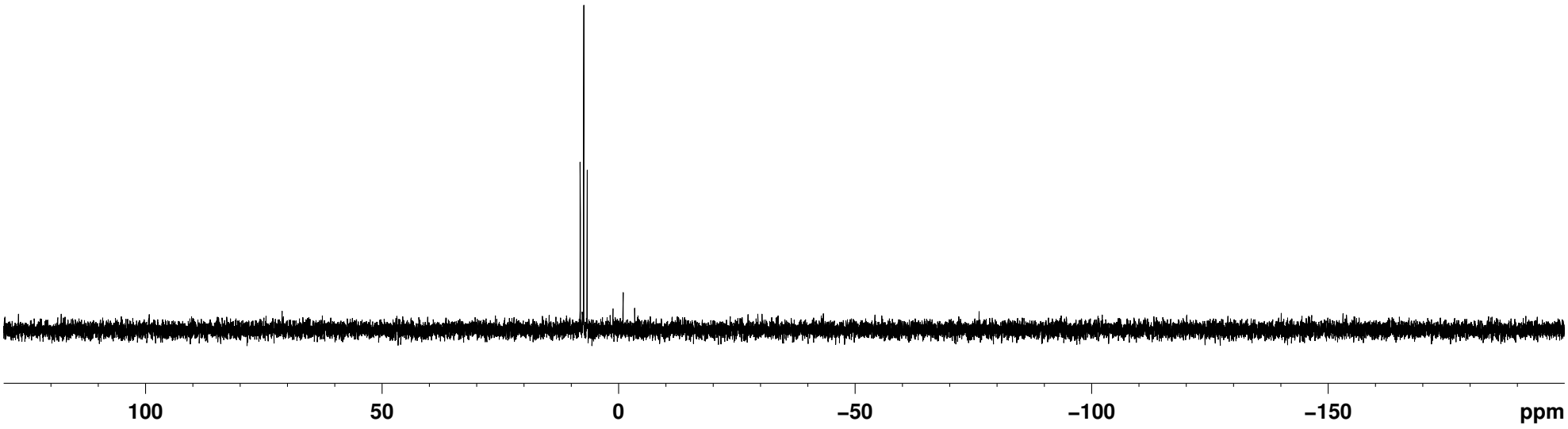
3g

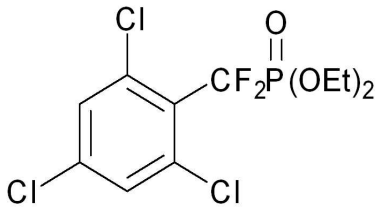
-98.226
-98.234
-98.541
-98.549
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
ppm

8.135
7.399
6.664



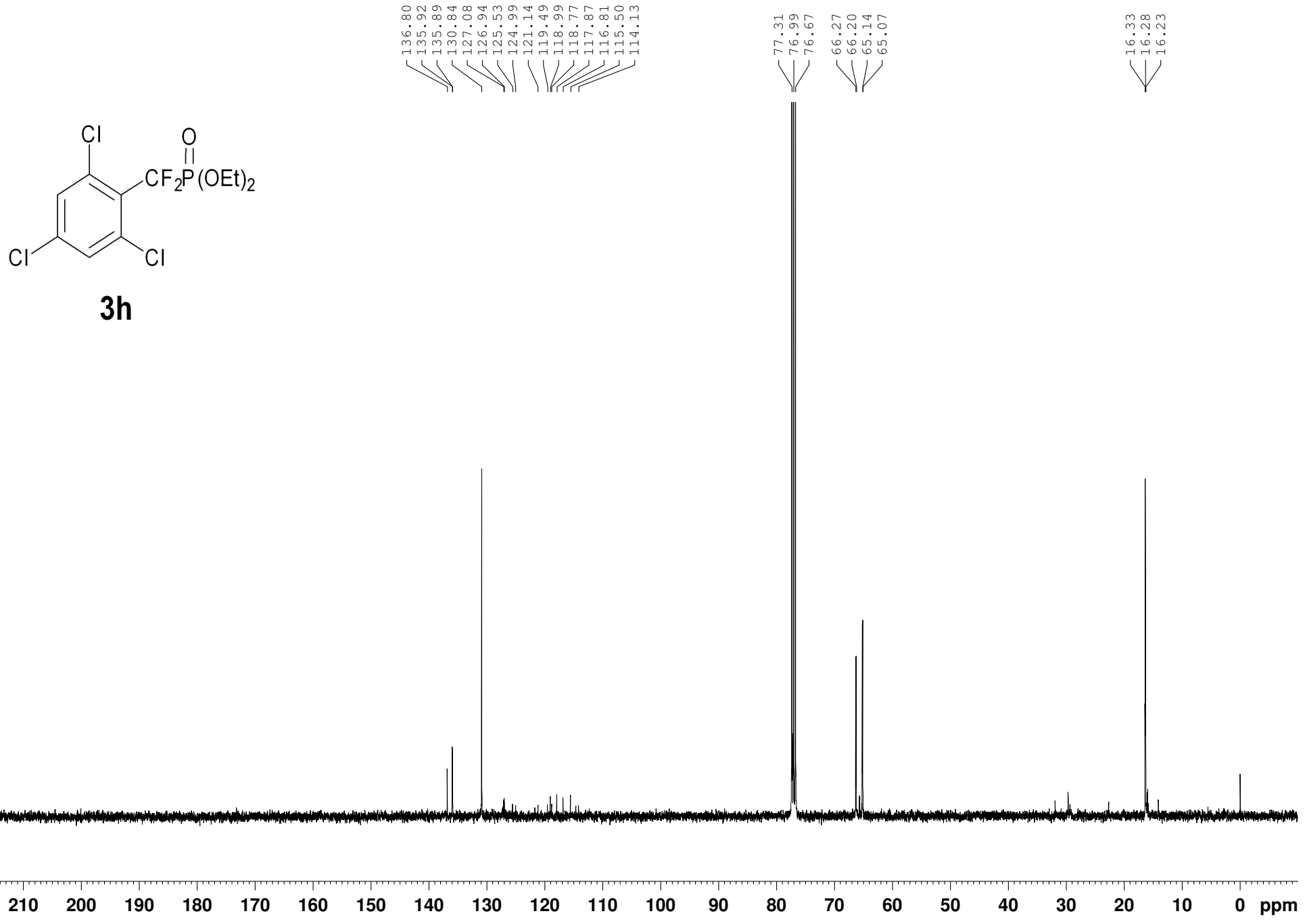
3g

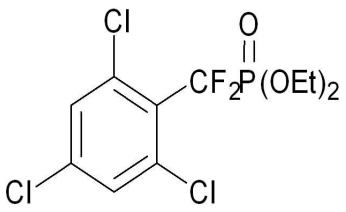



Cl
O
CF2P(OEt)2
Cl
Cl

3h

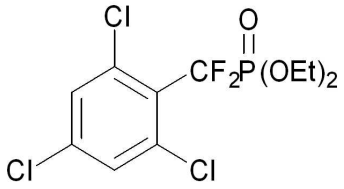
7.414
7.272
4.396
4.390
4.378
4.372
4.354
4.340
4.335
4.327
4.309
4.290
4.267
4.250
1.432
1.415
1.397
1.384
1.366
1.349
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.00
4.02
6.08


136.80
135.92
135.89
130.84
127.08
126.94
125.53
124.99
121.14
119.49
118.99
118.77
117.87
116.81
115.50
114.13
77.31
76.99
76.67
66.27
66.20
65.14
65.07
16.33
16.28
16.23
Cl
O
CF2P(OEt)2
Cl
Cl
3h
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

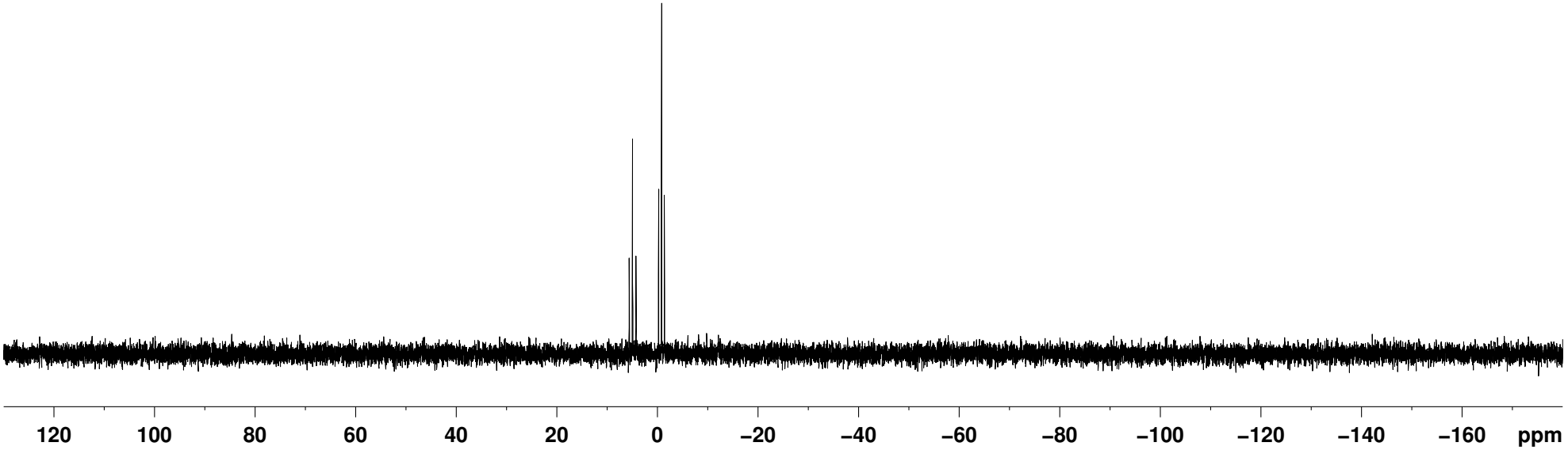

Cl
O
CF2P(OEt)2
Cl
Cl

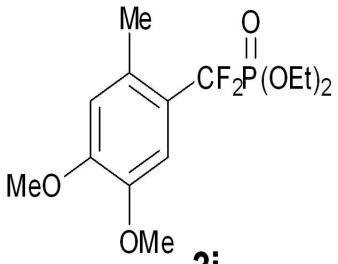
3h

-99.63
-99.92
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
ppm


Cl
O
CF2P(OEt)2
Cl
Cl

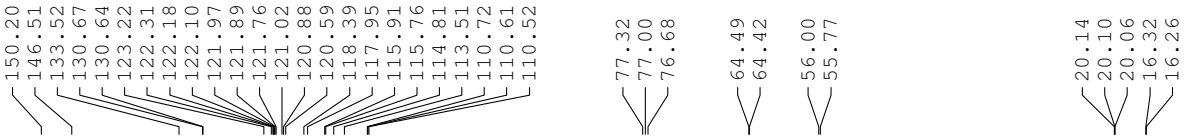
3h

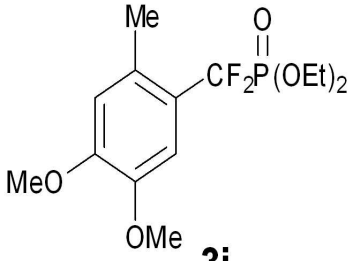

5.665
4.995
4.324
-0.187
-0.766
-1.344
120
100
80
60
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
ppm


Me
O
CF2P(OEt)2
MeO
OMe

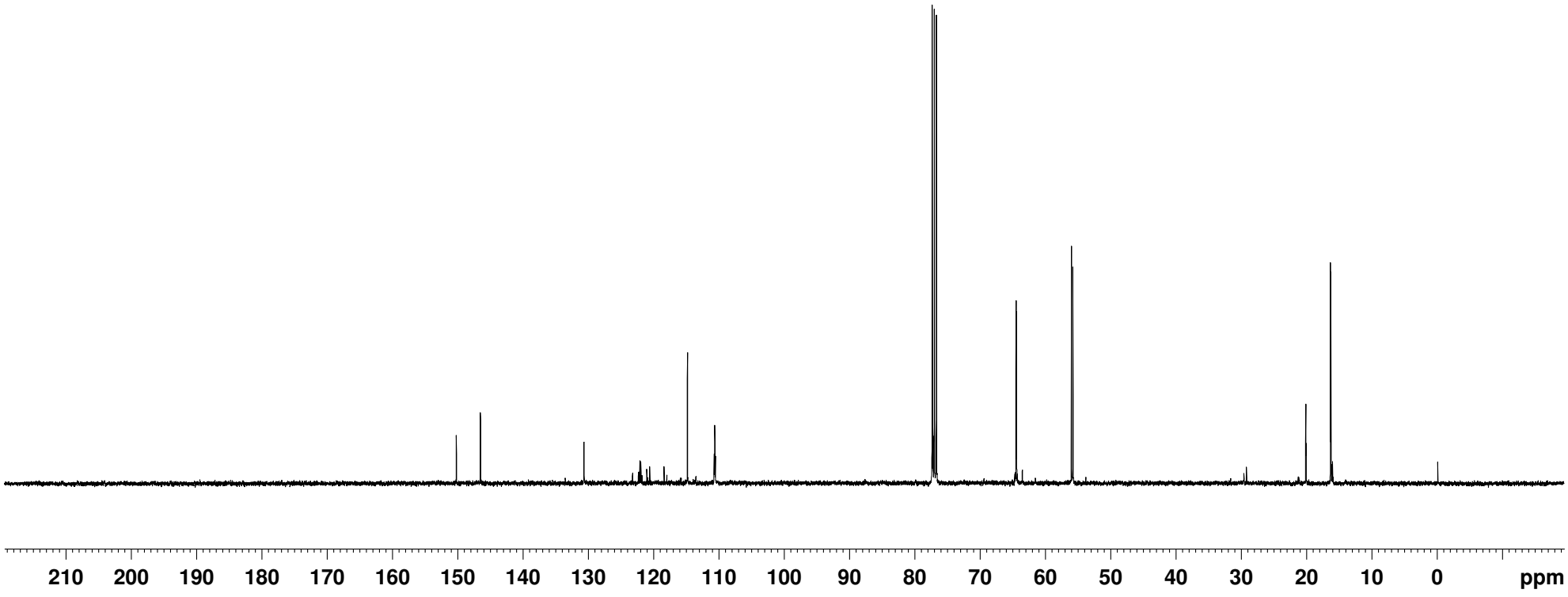
3i

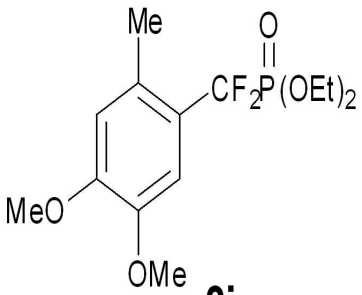
7.275
6.987
6.684
4.244
4.233
4.226
4.218
4.208
4.200
4.190
4.182
4.172
4.164
4.143
4.137
4.125
4.122
4.118
4.105
4.100
4.087
4.082
4.080
4.062
3.880
3.862
2.479
2.476
1.327
1.310
1.292
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.06
4.36
6.01
3.00
6.42


150.20
146.51
133.52
130.67
130.64
123.22
122.31
122.18
122.10
121.97
121.89
121.76
121.02
120.88
120.59
118.39
117.95
115.91
115.76
114.81
113.51
110.72
110.61
110.52
77.32
77.00
76.68
64.49
64.42
56.00
55.77
20.14
20.10
20.06
16.32
16.26


Me
O
CF2P(OEt)2
MeO
OMe

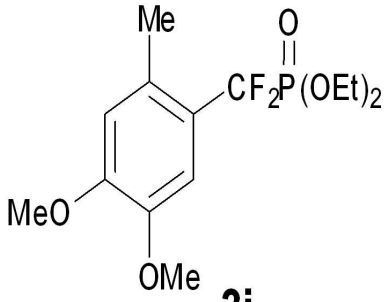
3i


210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

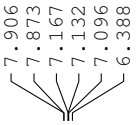

Me
O
CF2P(OEt)2
MeO
OMe

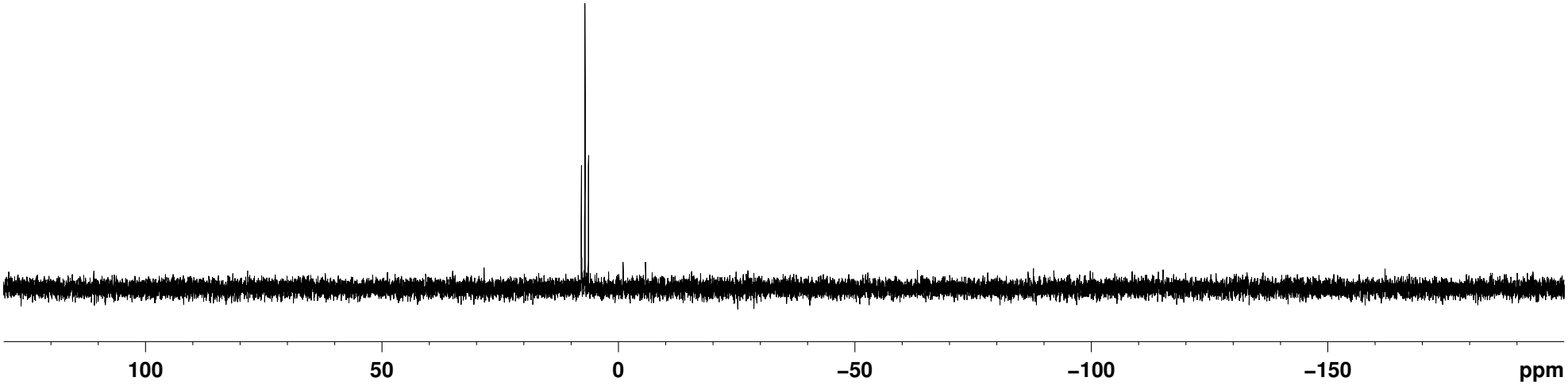
3i

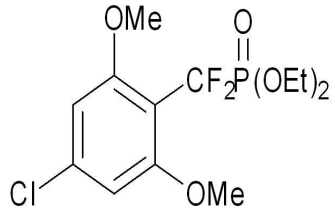
-103.007
-103.326
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
ppm


Me
O
CF2P(OEt)2
MeO
OMe

3i

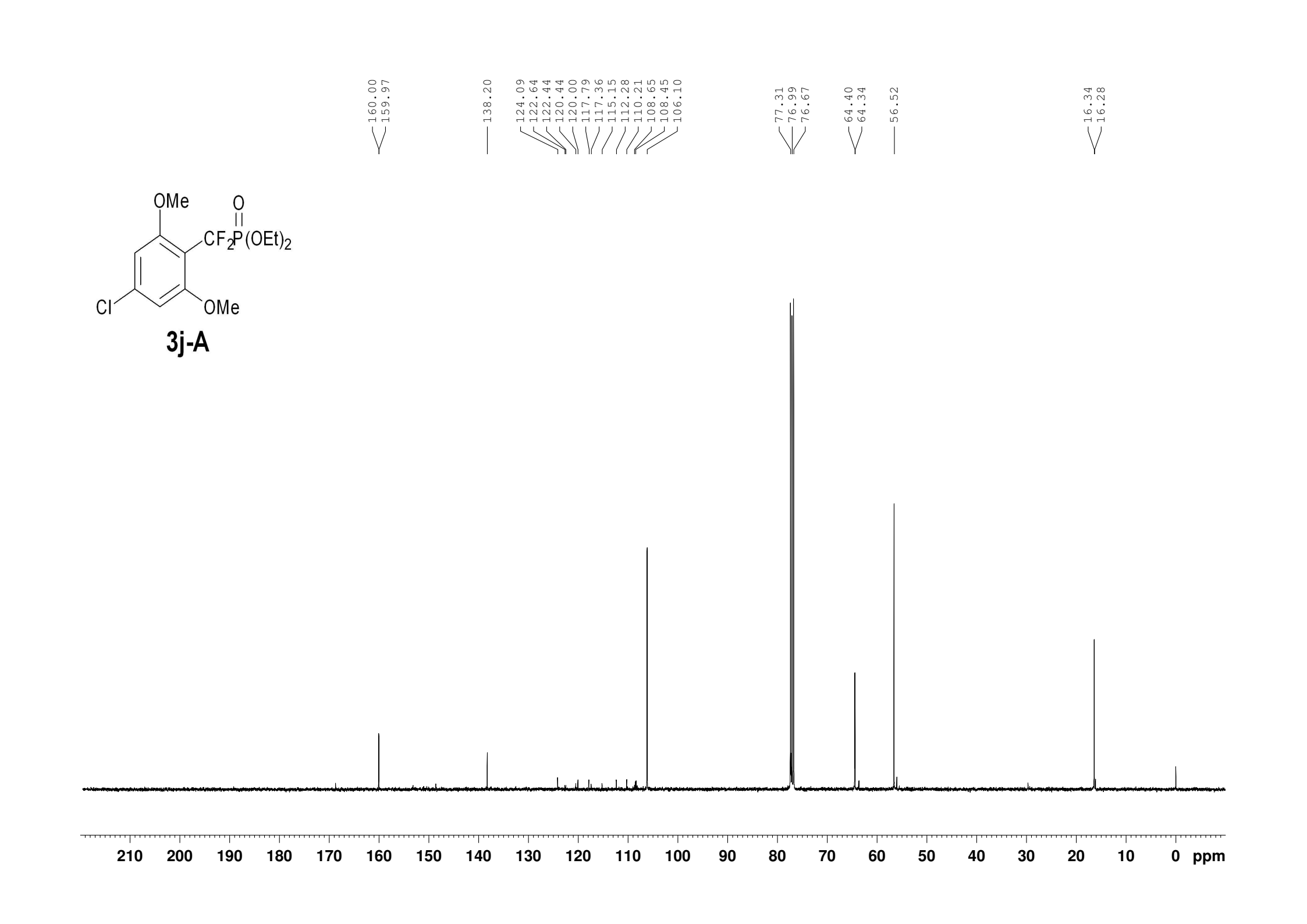

7.906
7.873
7.167
7.132
7.096
6.388

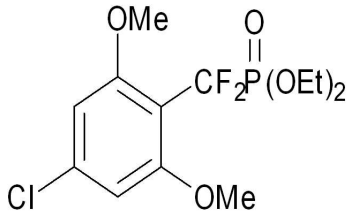

100
50
0
−50
−100
−150
ppm


OMe
O
CF2P(OEt)2
Cl
OMe

3j-A

7.266
6.582
4.289
4.281
4.271
4.263
4.246
4.232
4.229
4.214
4.196
4.189
4.178
4.171
3.813
1.336
1.319
1.301
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.00
4.12
6.08
6.33

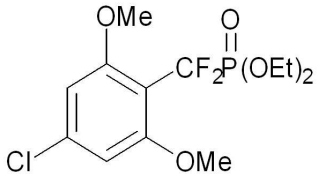

160.00
159.97
138.20
124.09
122.64
122.44
120.44
120.00
117.79
117.36
115.15
112.28
110.21
108.65
108.45
106.10
77.31
76.99
76.67
64.40
64.34
56.52
16.34
16.28
OMe
O
CF2P(OEt)2
Cl
OMe
3j-A
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


OMe
O
CF2P(OEt)2
Cl
OMe

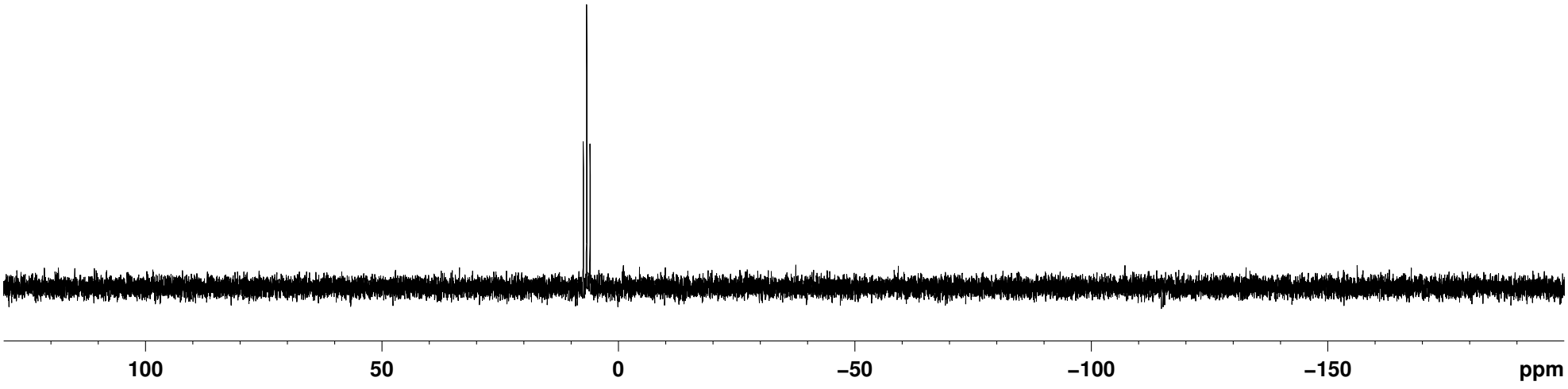
3j-A

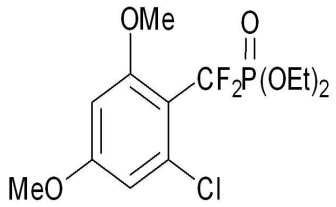
-99.798
-100.104
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
ppm

7.471
6.760
6.047



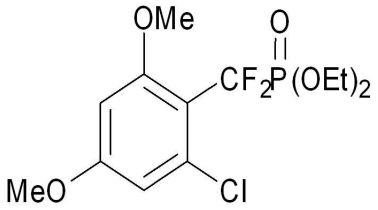
3j-A




OMe
O
CF2P(OEt)2
MeO
Cl

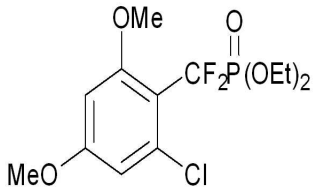
3j-B

7.265
6.563
6.558
6.397
6.395
4.289
4.282
4.271
4.264
4.254
4.246
4.237
4.228
4.219
4.218
4.211
4.200
4.194
4.193
4.182
4.175
3.812
3.789
1.342
1.324
1.306
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
0.96
4.01
5.98
6.04


OMe
O
CF2P(OEt)2
MeO
Cl

3j-B

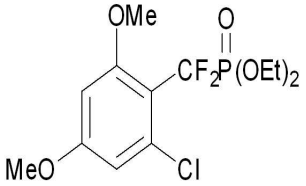
161.77
160.86
135.08
135.05
123.94
122.42
120.21
119.77
117.55
117.12
114.90
112.26
112.17
112.03
111.97
111.82
111.61
110.16
108.99
98.71
77.32
77.00
76.68
64.51
64.44
56.43
55.52
16.33
16.27
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


OMe
O
CF2P(OEt)2
MeO
Cl

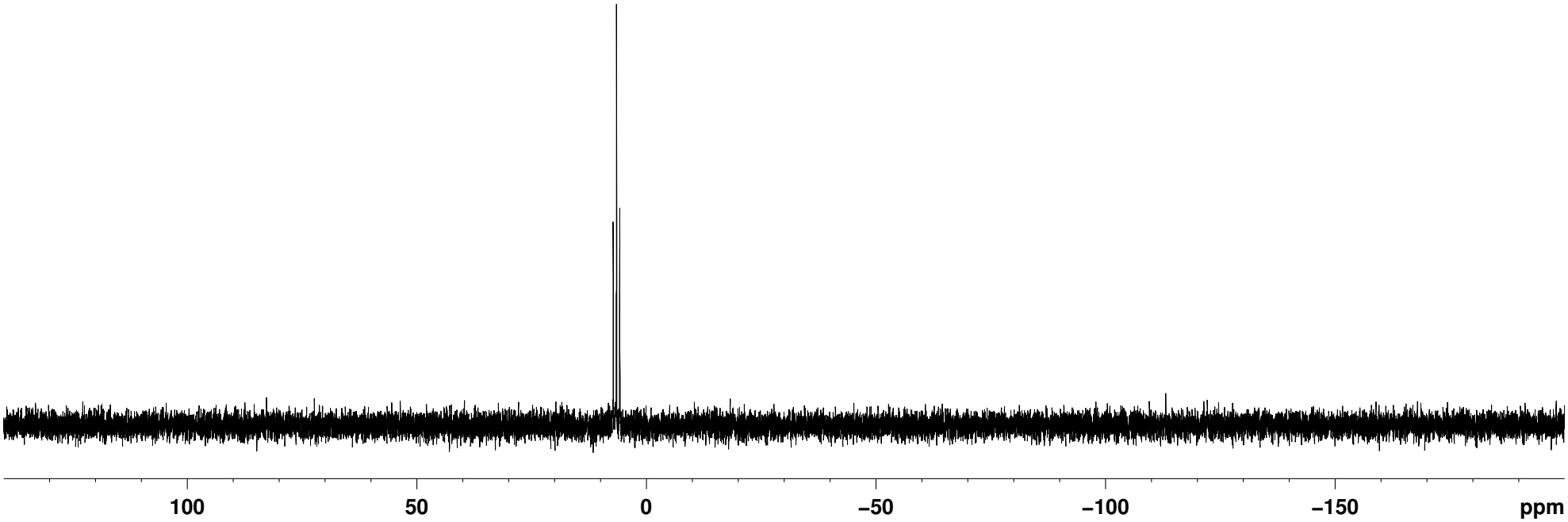
3j-B

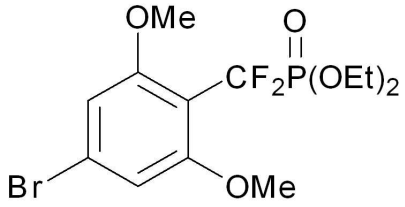
-98.326
-98.633
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
ppm

7.256
6.542
5.828



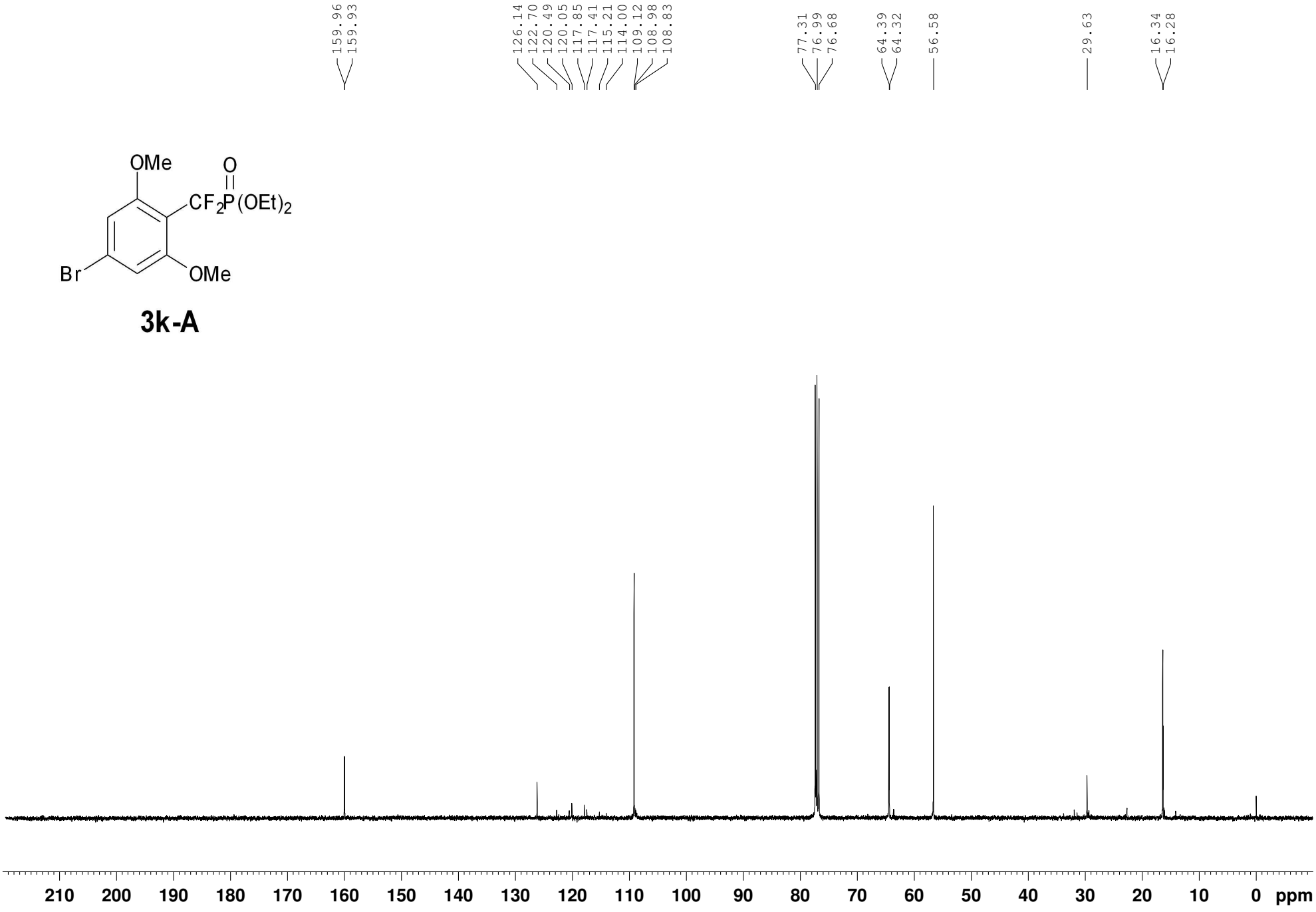
3j-B

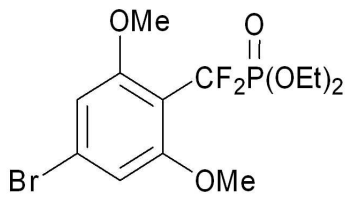



OMe
O
CF2P(OEt)2
Br
OMe

3k-A

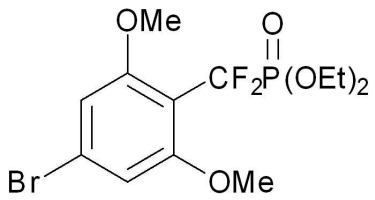
7.284
6.757
4.307
4.299
4.289
4.282
4.264
4.250
4.246
4.233
4.214
4.208
4.196
4.189
3.837
1.358
1.340
1.323
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.00
4.03
6.03
6.39


159.96
159.93
126.14
122.70
120.49
120.05
117.85
117.41
115.21
114.00
109.12
108.98
108.83
77.31
76.99
76.68
64.39
64.32
56.58
29.63
16.34
16.28
OMe
O
CF2P(OEt)2
Br
OMe
3k-A
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


OMe
O
CF2P(OEt)2
Br
OMe

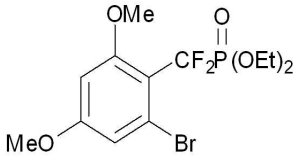
3k-A

-99.898
-100.205
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
ppm


OMe
O
CF2P(OEt)2
Br
OMe

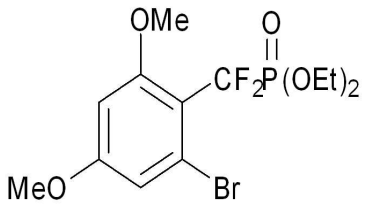
3k-A

8.305
7.594
6.884
120
100
80
60
40
20
0
−20
−40
−60
−80
−100
−120
−140
−160
ppm


OMe
O
CF2P(OEt)2
MeO
Br

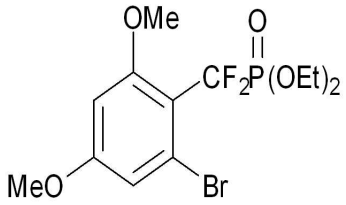
3k-B

7.269
6.829
6.824
6.463
4.314
4.307
4.296
4.289
4.279
4.271
4.264
4.253
4.245
4.227
4.221
4.209
4.202
3.836
3.817
1.372
1.354
1.336
1.261
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
0.99
4.00
6.17
6.14


OMe
O
CF2P(OEt)2
MeO
Br

3k-B

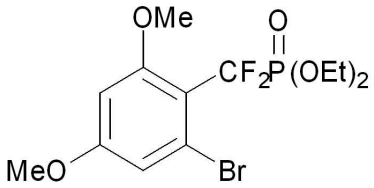
161.85
160.97
122.11
122.07
112.71
99.40
77.29
76.98
76.66
64.53
64.46
56.48
55.58
29.24
16.40
16.34
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


OMe
O
CF2P(OEt)2
MeO
Br

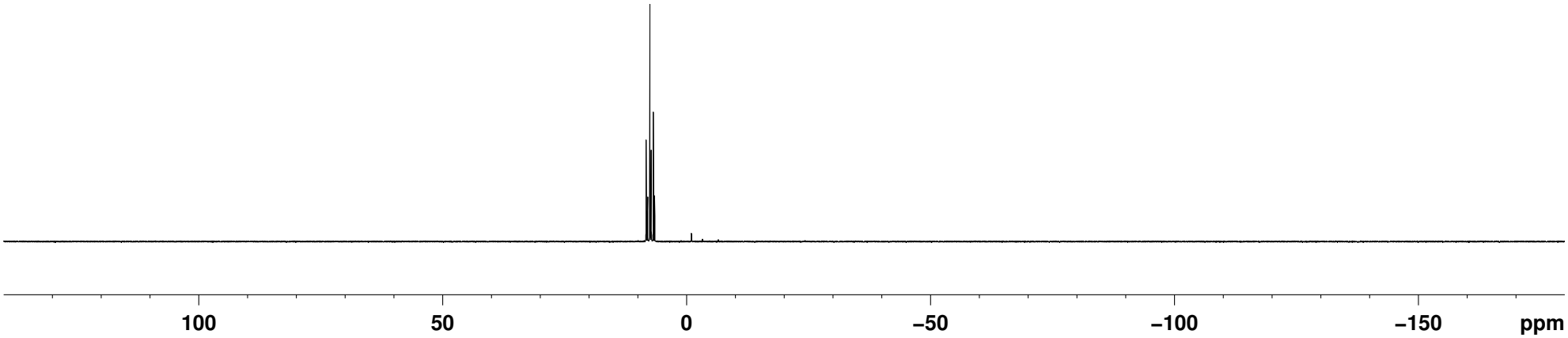
3k-B

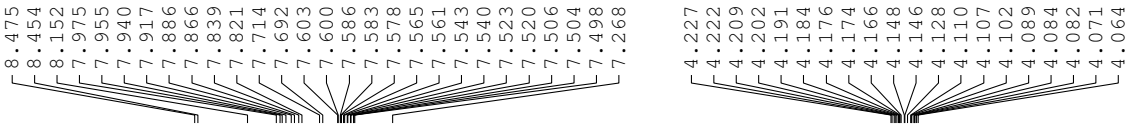
-97.501
-97.808
0
−20
−40
−60
−80
−100
−120
−140
−160
−180
−200
ppm

8.335
8.026
7.593
7.301
6.855
6.576



3k-B




8.475
8.454
8.152
7.975
7.955
7.940
7.917
7.886
7.866
7.839
7.821
7.714
7.692
7.603
7.600
7.586
7.583
7.578
7.565
7.561
7.543
7.540
7.523
7.520
7.506
7.504
7.498
7.268
4.227
4.222
4.209
4.202
4.191
4.184
4.176
4.174
4.166
4.148
4.146
4.128
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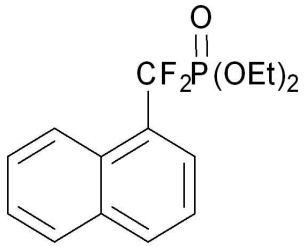
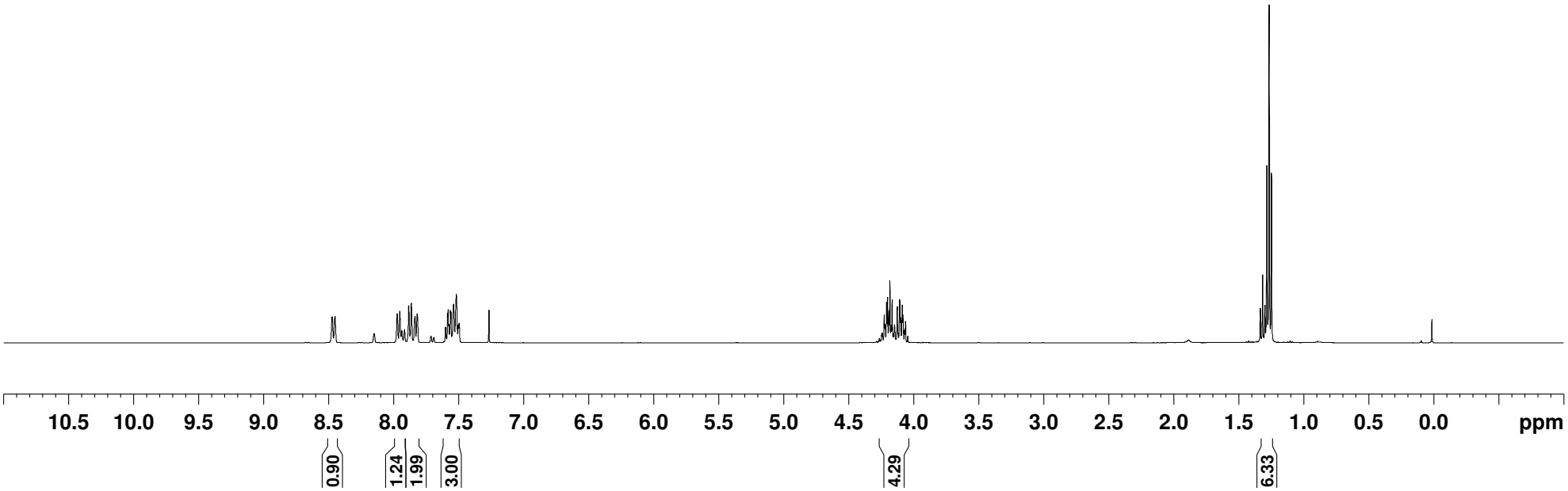
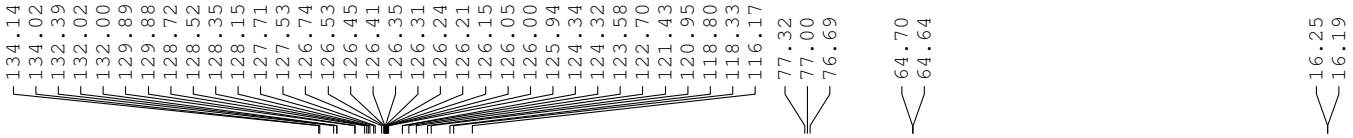
4.102
4.089
4.084
4.082
4.071
4.064
1.284
1.267
1.249


O
CF2P(OEt)2

3l


10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.90
1.24
1.99
3.00
4.29
6.33


134.14
134.02
132.39
132.02
132.00
129.89
129.88
128.72
128.52
128.35
128.15
127.71
127.53
126.74
126.53
126.45
126.41
126.35
126.31
126.24
126.21
126.15
126.05
126.00
125.94
124.34
124.32
123.58
122.70
121.43
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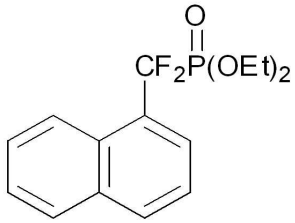
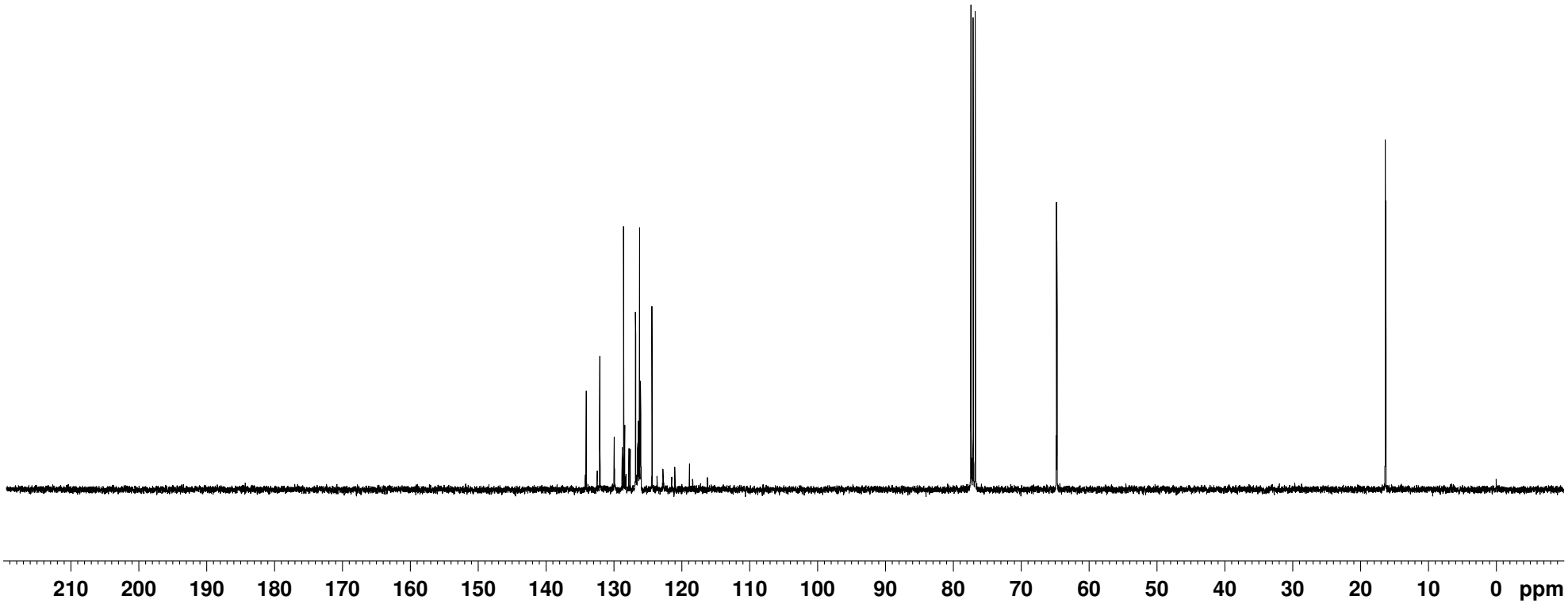
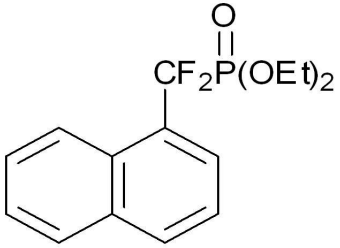
77.00
76.69
64.70
64.64
16.25
16.19


O
CF2P(OEt)2

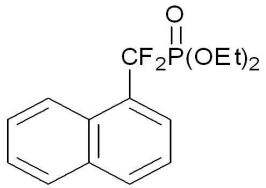
3l


210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

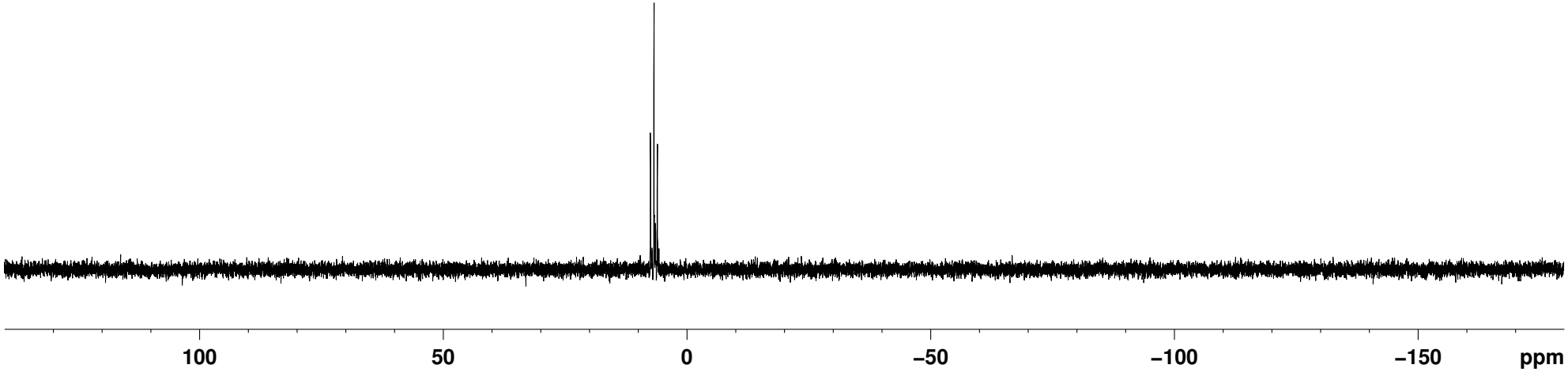

O
CF2P(OEt)2

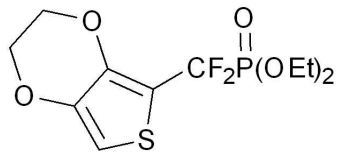
3l

-101.64
-101.94
-107.64
-107.95
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
ppm



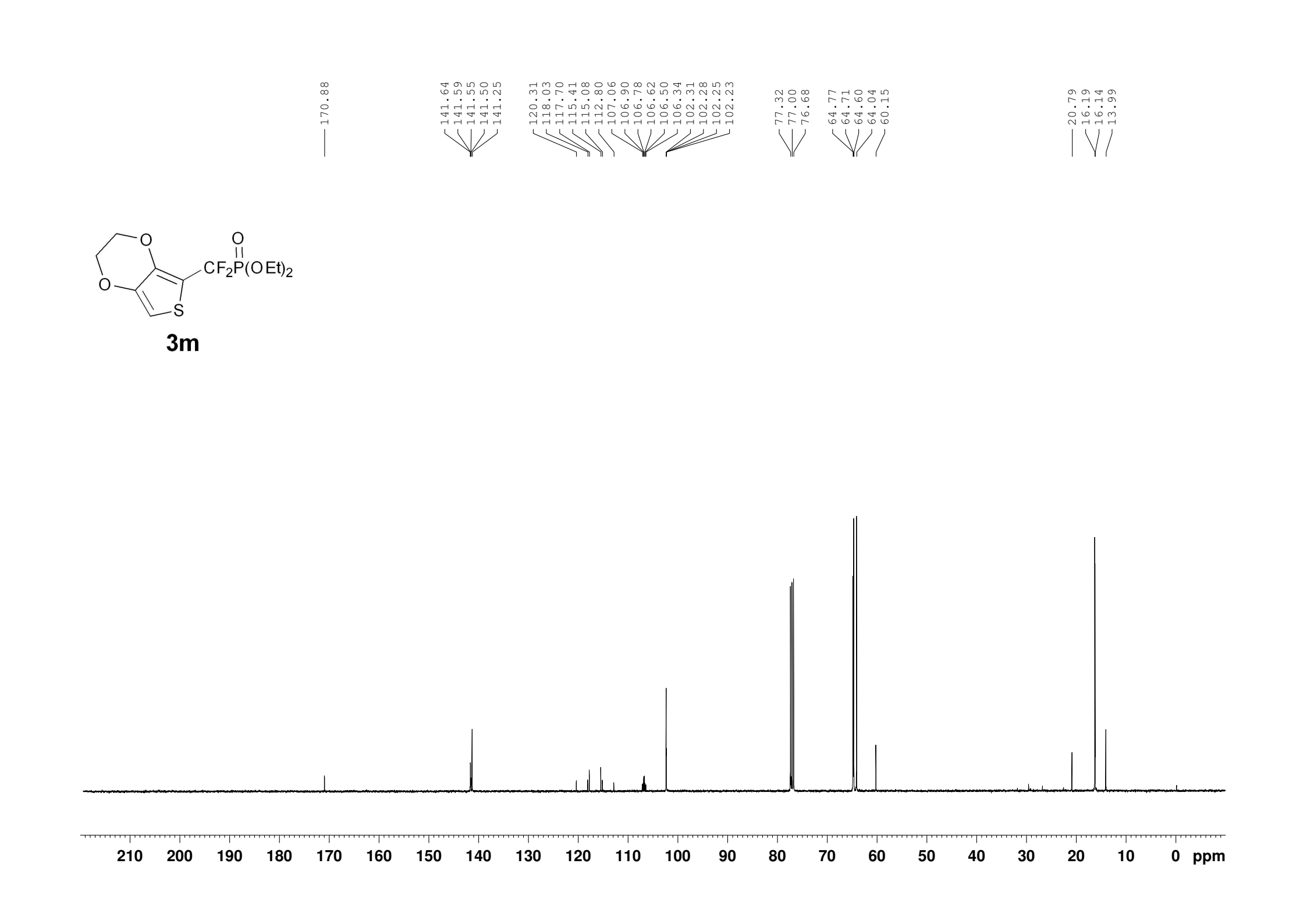
3l

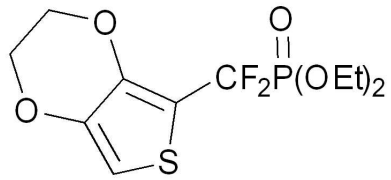



O
O
O
CF2P(OEt)2
S

3m

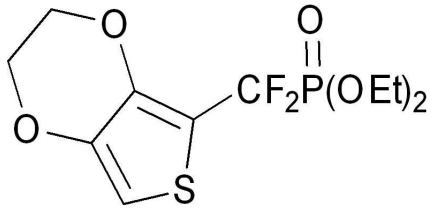
7.270
6.503
4.326
4.318
4.308
4.301
4.291
4.283
4.276
4.273
4.265
4.258
4.252
4.247
4.239
4.230
4.228
4.222
4.216
4.207
1.381
1.363
1.346
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
4.30
4.10
6.16


170.88
141.64
141.59
141.55
141.50
141.25
120.31
118.03
117.70
115.41
115.08
112.80
107.06
106.90
106.78
106.62
106.50
106.34
102.31
102.28
102.25
102.23
77.32
77.00
76.68
64.77
64.71
64.60
64.04
60.15
20.79
16.19
16.14
13.99
O
O
O
CF2P(OEt)2
S
3m
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

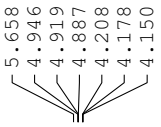

O
O
O
CF2P(OEt)2
S

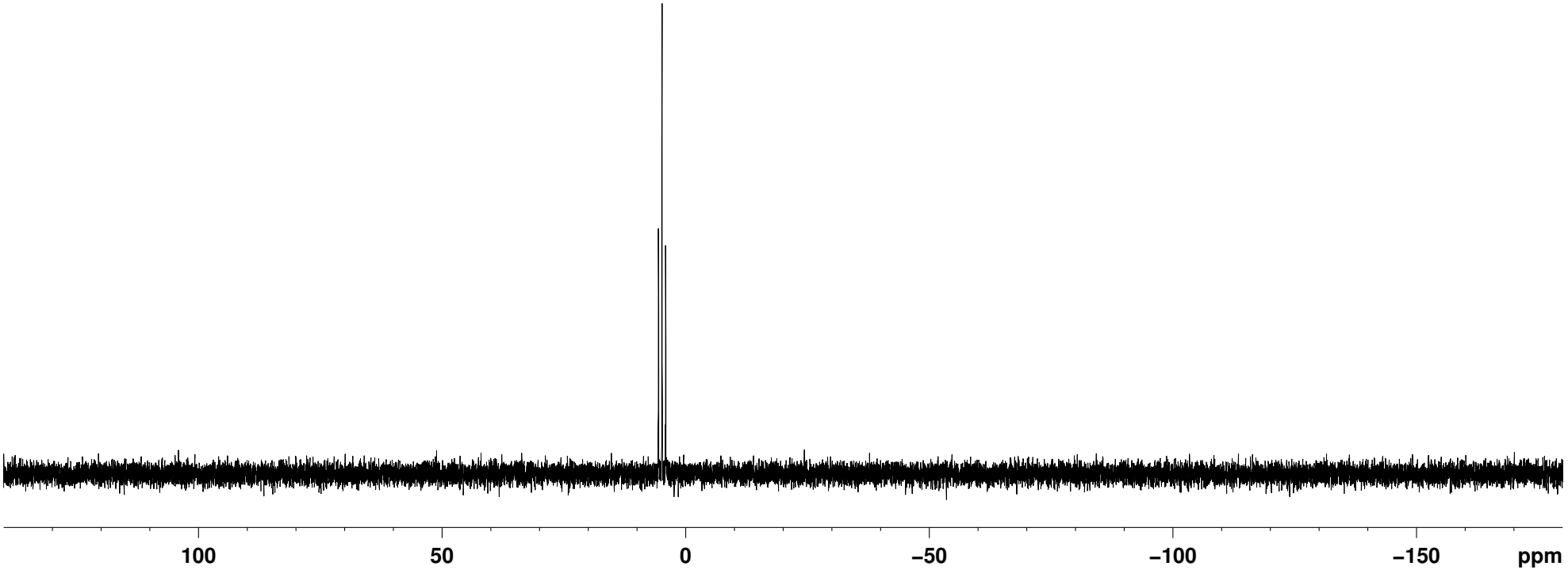
3m

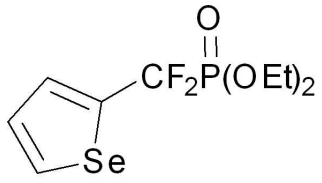
-99.370
-99.688
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
ppm


O
O
O
CF2P(OEt)2
S

3m

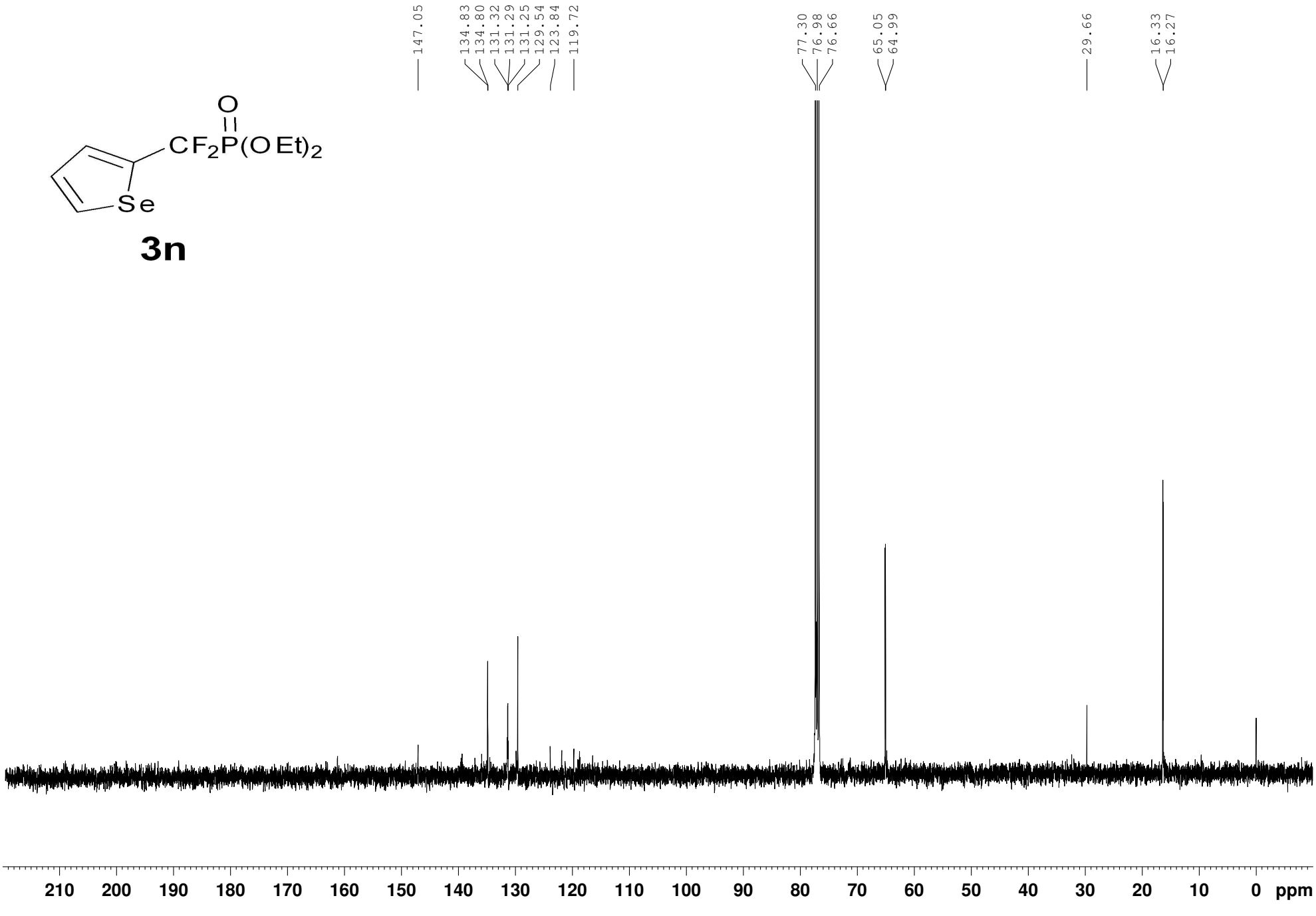

5.658
4.946
4.919
4.887
4.208
4.178
4.150

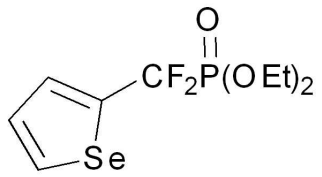

100
50
0
−50
−100
−150
ppm


O
CF2P(OEt)2
Se

3n

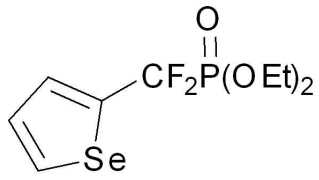
8.218
8.204
7.707
7.702
7.699
7.694
7.689
7.347
7.342
7.337
7.333
7.328
7.324
7.270
4.295
4.288
4.277
4.270
4.251
4.233
4.230
4.225
4.212
4.208
1.368
1.350
1.332
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.70
1.00
0.86
4.04
6.33


147.05
134.83
134.80
131.32
131.29
131.25
129.54
123.84
119.72
77.30
76.98
76.66
65.05
64.99
29.66
16.33
16.27
O
CF2P(OEt)2
Se
3n
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

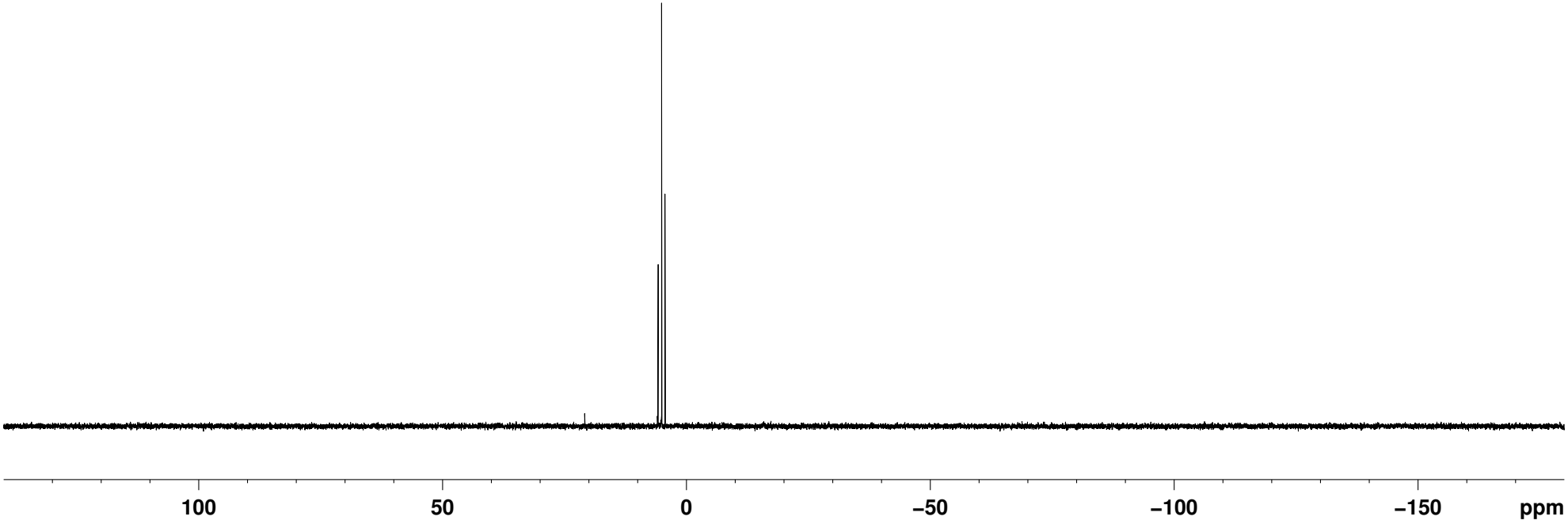

O
CF2P(OEt)2
Se

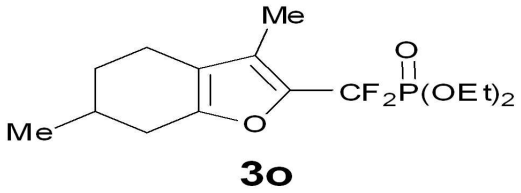
3n

-93.589
-93.896
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
ppm



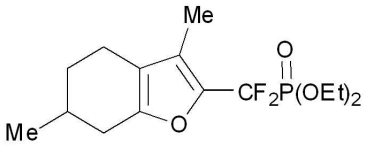
3n




Me
O
CF2P(OEt)2
Me
O

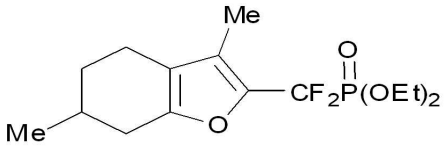
3o

7.268
4.285
4.278
4.261
4.242
4.224
4.205
4.183
2.659
2.619
2.368
2.329
2.307
2.300
2.288
2.276
2.269
2.248
2.229
2.180
2.152
2.116
2.028
2.022
1.888
1.878
1.872
1.830
1.825
1.807
1.792
1.352
1.334
1.317
1.053
1.036
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
4.00
1.05
2.17
1.10
3.07
2.15
7.08
3.09


Me
O
CF2P(OEt)2
Me
O

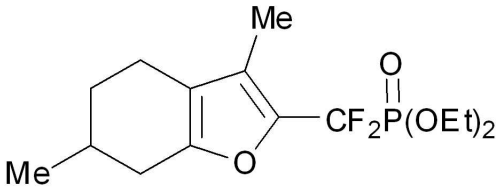
3o

152.32
152.30
137.25
137.12
136.95
136.82
136.65
136.52
122.97
122.94
122.92
119.37
118.98
116.73
116.39
114.14
113.80
111.54
77.32
77.00
76.68
64.65
64.58
31.15
30.81
29.32
21.18
19.54
16.26
16.20
7.98
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

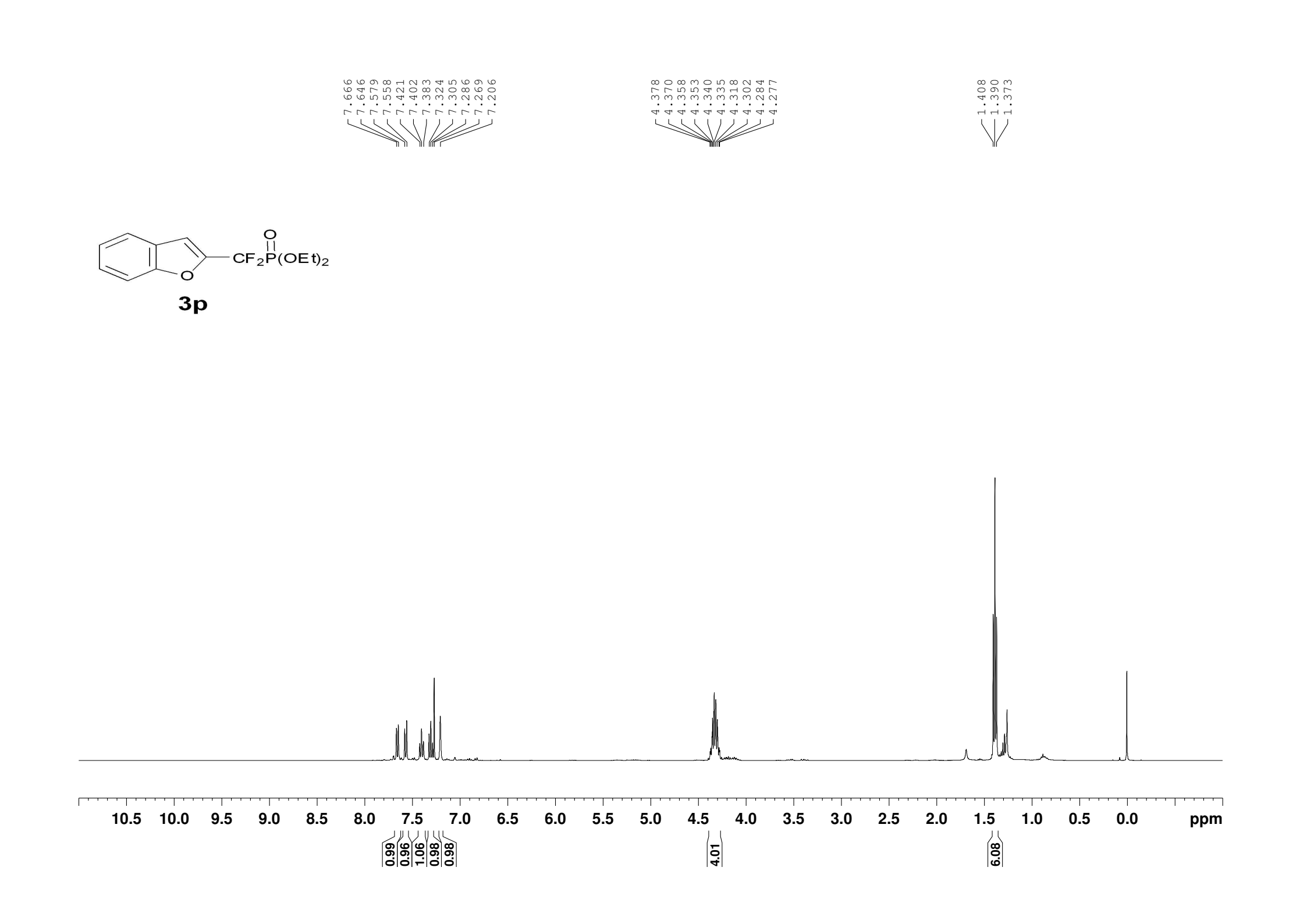

Me
O
CF2P(OEt)2
Me
O

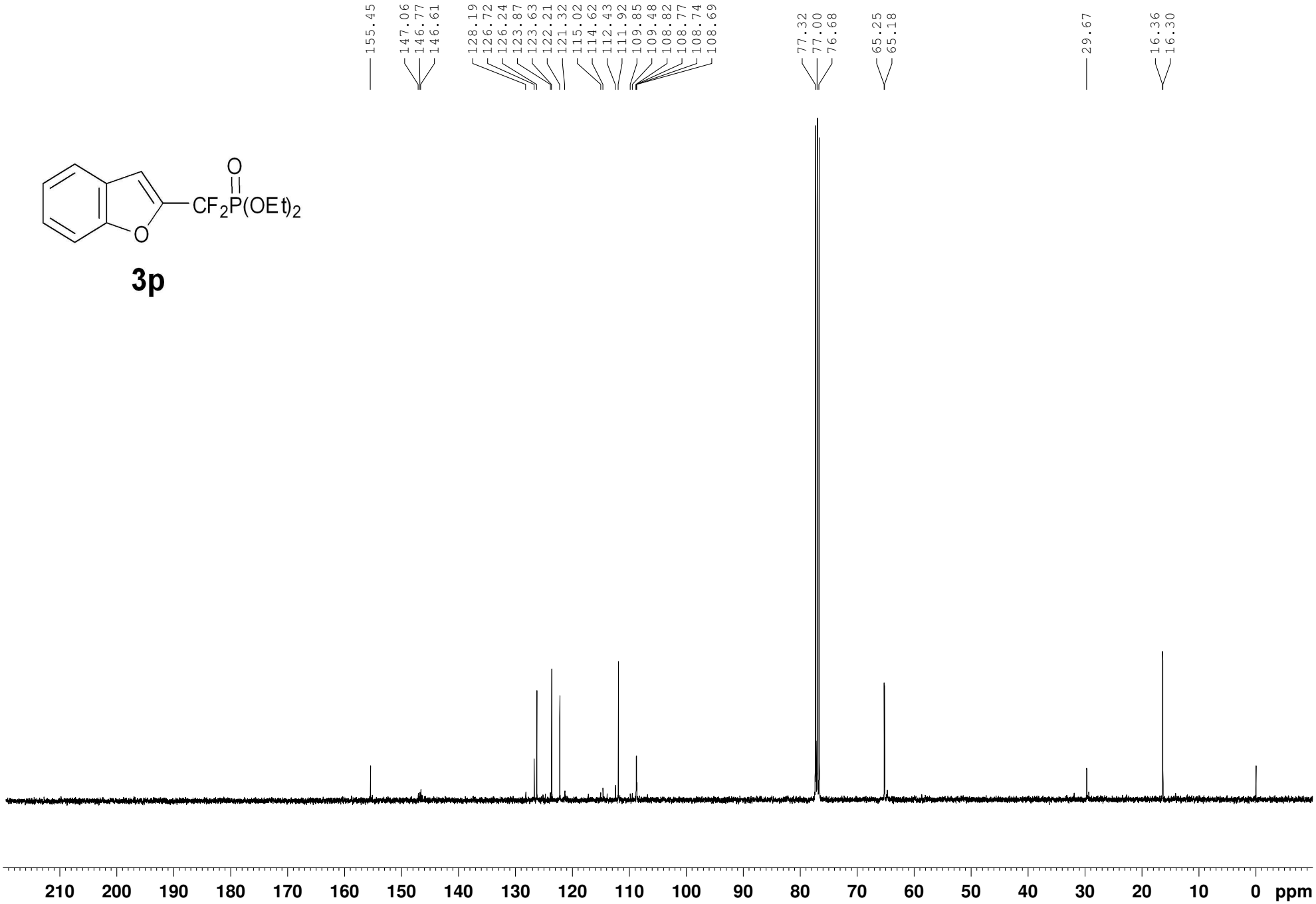
3o

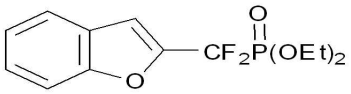
-106.77
-106.80
-107.09
-107.12
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
ppm



3o

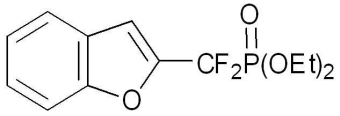

7.666
7.646
7.579
7.558
7.421
7.402
7.383
7.324
7.305
7.286
7.269
7.206
4.378
4.370
4.358
4.353
4.340
4.335
4.318
4.302
4.284
4.277
1.408
1.390
1.373
O
CF2P(OEt)2
O
3p
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.99
0.96
1.06
0.98
0.98
4.01
6.08


155.45
147.06
146.77
146.61
128.19
126.72
126.24
123.87
123.63
122.21
121.32
115.02
114.62
112.43
111.92
109.85
109.48
108.82
108.77
108.74
108.69
77.32
77.00
76.68
65.25
65.18
29.67
16.36
16.30
O
CF2P(OEt)2
O
3p
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

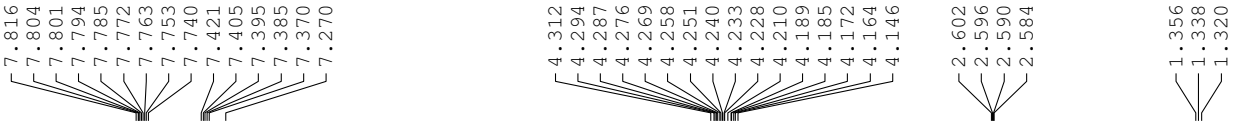

O
CF2P(OEt)2
O

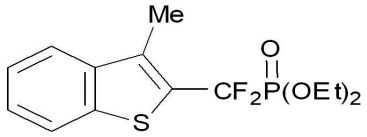
3p

-108.653
-108.937
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
ppm

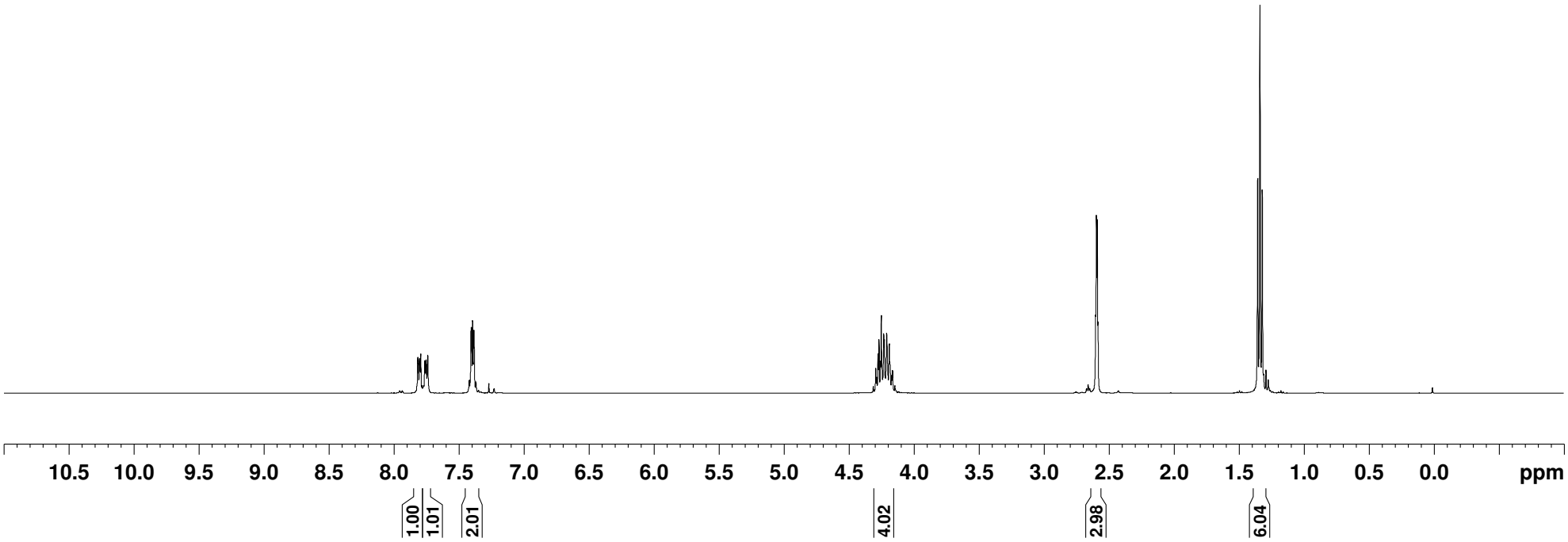


3p


7.816
7.804
7.801
7.794
7.785
7.772
7.763
7.753
7.740
7.421
7.405
7.395
7.385
7.370
7.270
4.312
4.294
4.287
4.276
4.269
4.258
4.251
4.240
4.233
4.228
4.210
4.189
4.185
4.172
4.164
4.146
2.602
2.596
2.590
2.584
1.356
1.338
1.320


Me
O
CF2P(OEt)2
S

3q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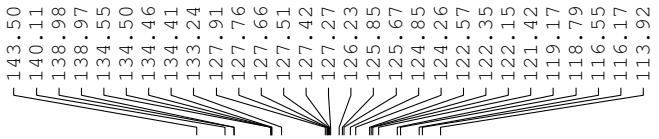
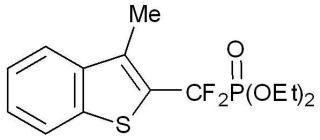
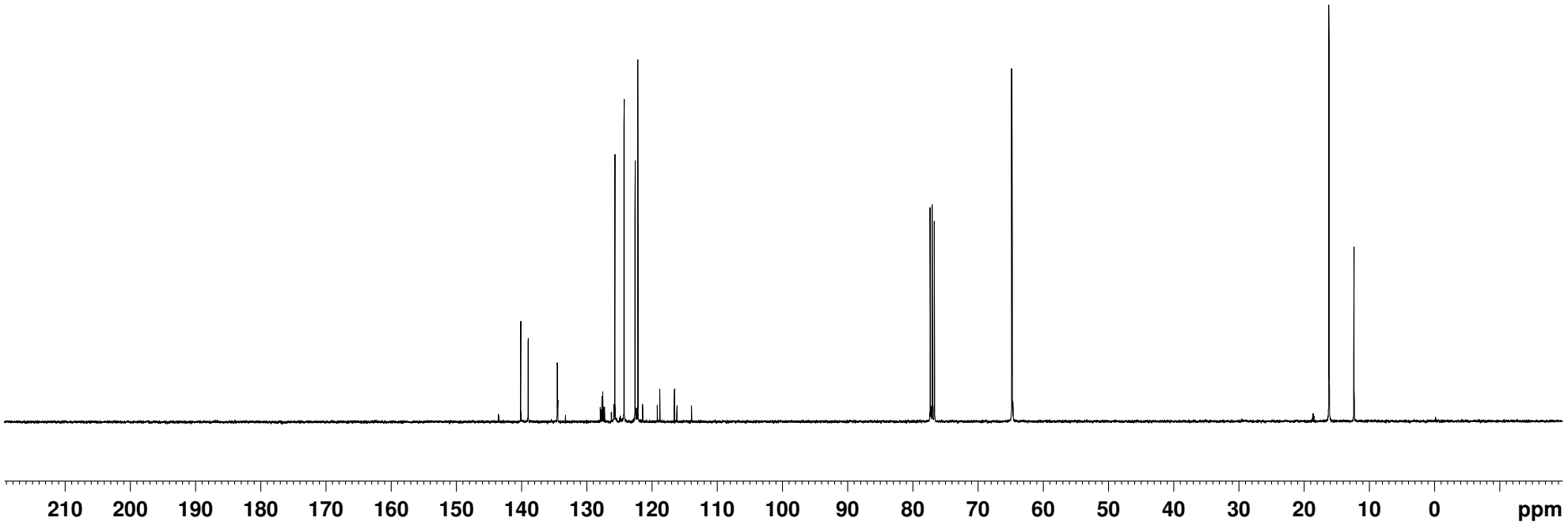
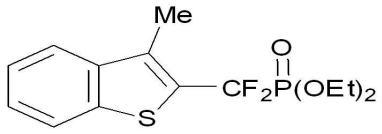
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.01
2.01
4.02
2.98
6.04


143.50
140.11
138.98
138.97
134.55
134.50
134.46
134.41
133.24
127.91
127.76
127.66
127.51
127.42
127.27
126.23
125.85
125.67
124.85
124.26
122.57
122.35
122.15
121.42
119.17
118.79
116.55
116.17
113.92
77.32
77.00
76.68
64.82
64.76
16.19
16.14
12.33
12.32


Me
O
CF2P(OEt)2
S

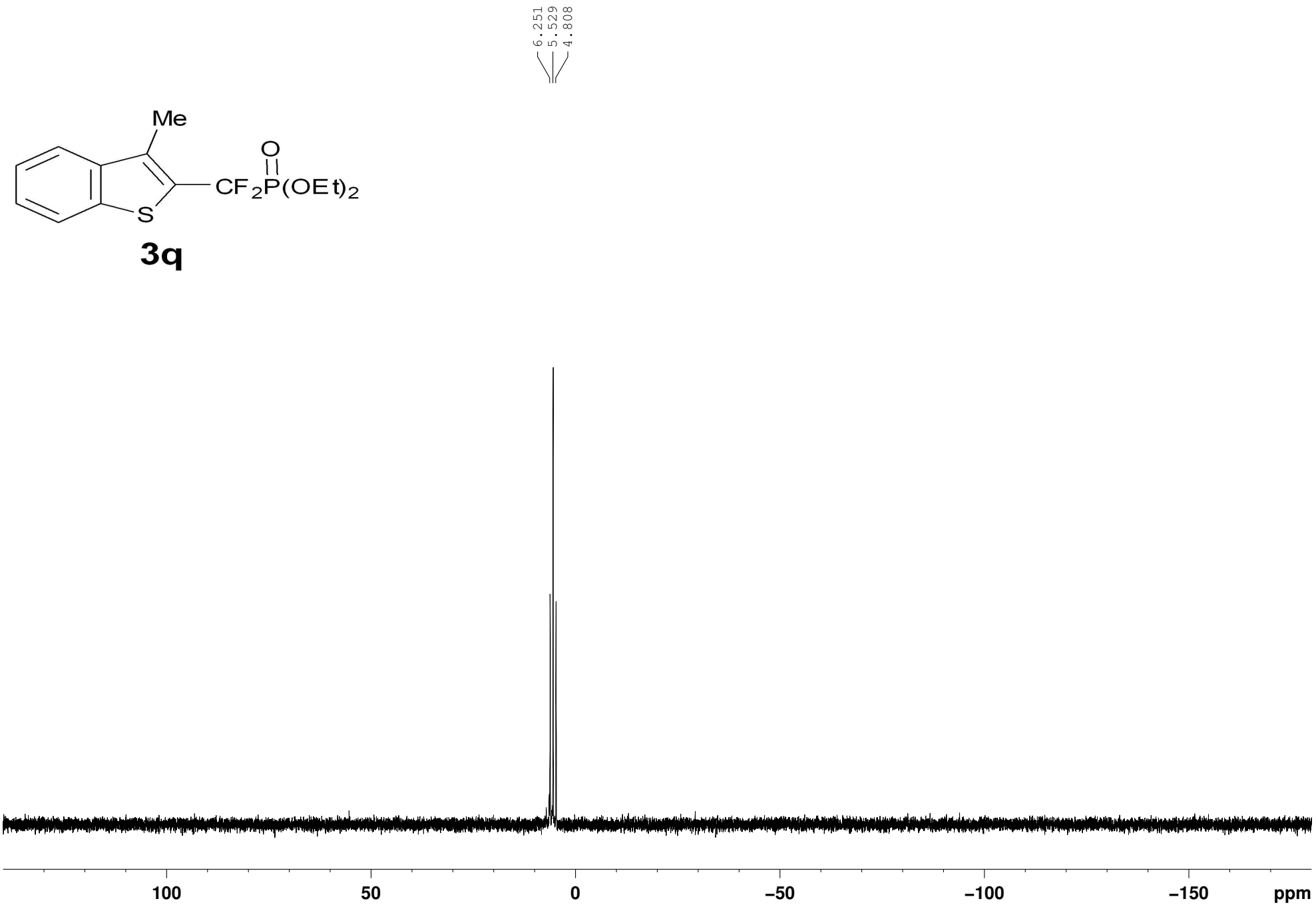
3q

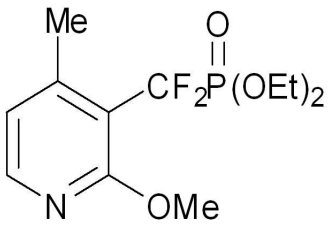

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


Me
O
CF2P(OEt)2
S

3q

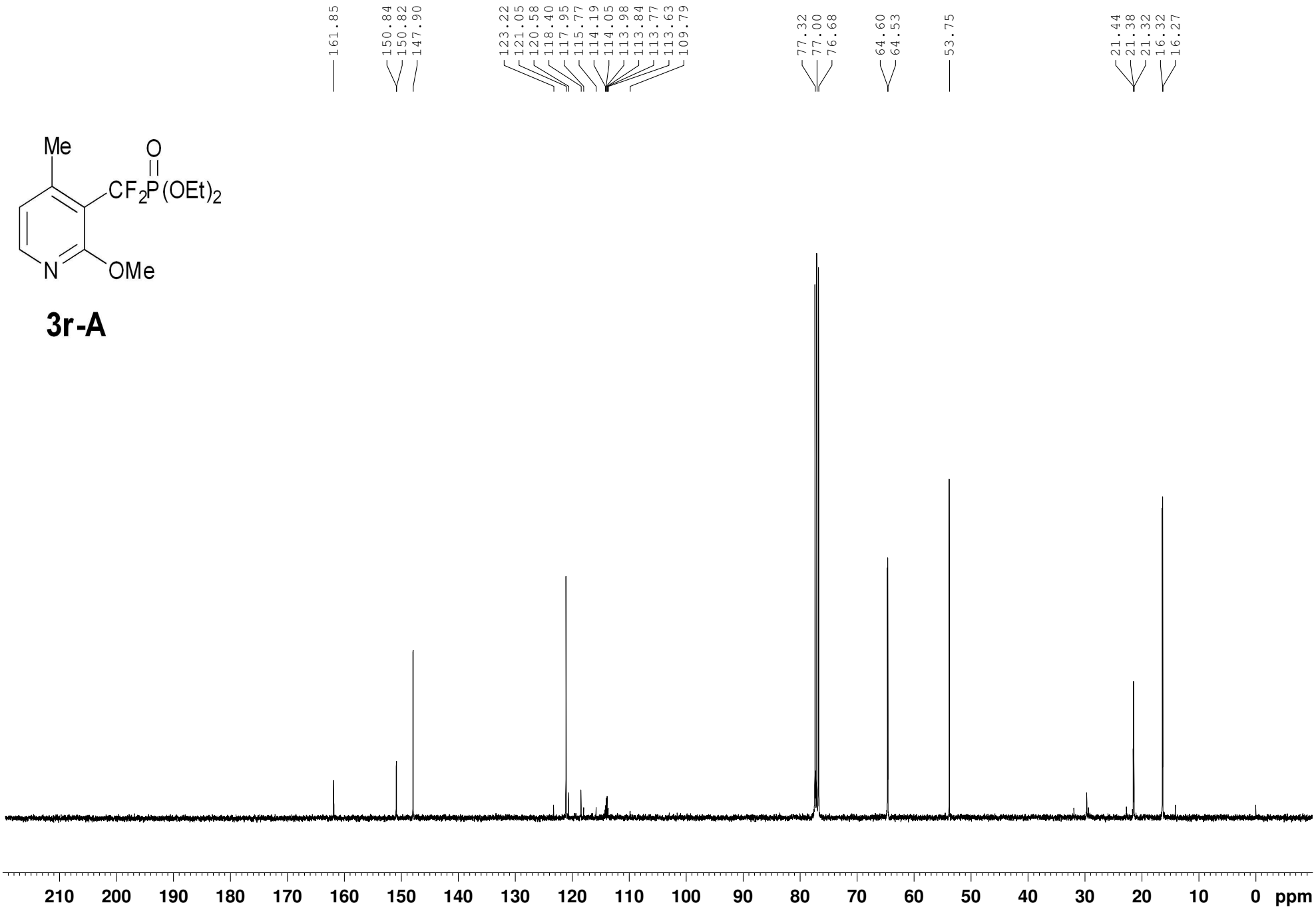
-97.629
-97.940
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
ppm

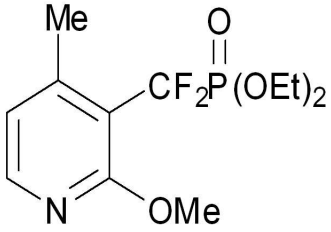

6.251
5.529
4.808
Me
O
CF2P(OEt)2
S
3q
100
50
0
−50
−100
−150
ppm


Me
O
CF2P(OEt)2
N
OMe

3r-A

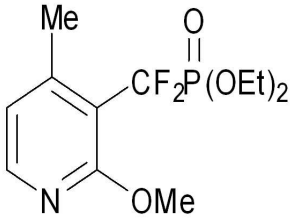
8.036
8.023
7.261
6.727
6.714
4.286
4.279
4.268
4.261
4.250
4.243
4.226
4.208
4.203
4.191
4.184
4.173
4.165
3.940
2.508
2.498
2.487
1.339
1.322
1.304
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
–1
–2
ppm
1.00
1.00
4.13
3.08
3.11
6.35


161.85
150.84
150.82
147.90
123.22
121.05
120.58
118.40
117.95
115.77
114.19
114.05
113.98
113.84
113.77
113.63
109.79
77.32
77.00
76.68
64.60
64.53
53.75
21.44
21.38
21.32
16.32
16.27
Me
O
CF2P(OEt)2
N
OMe
3r-A
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

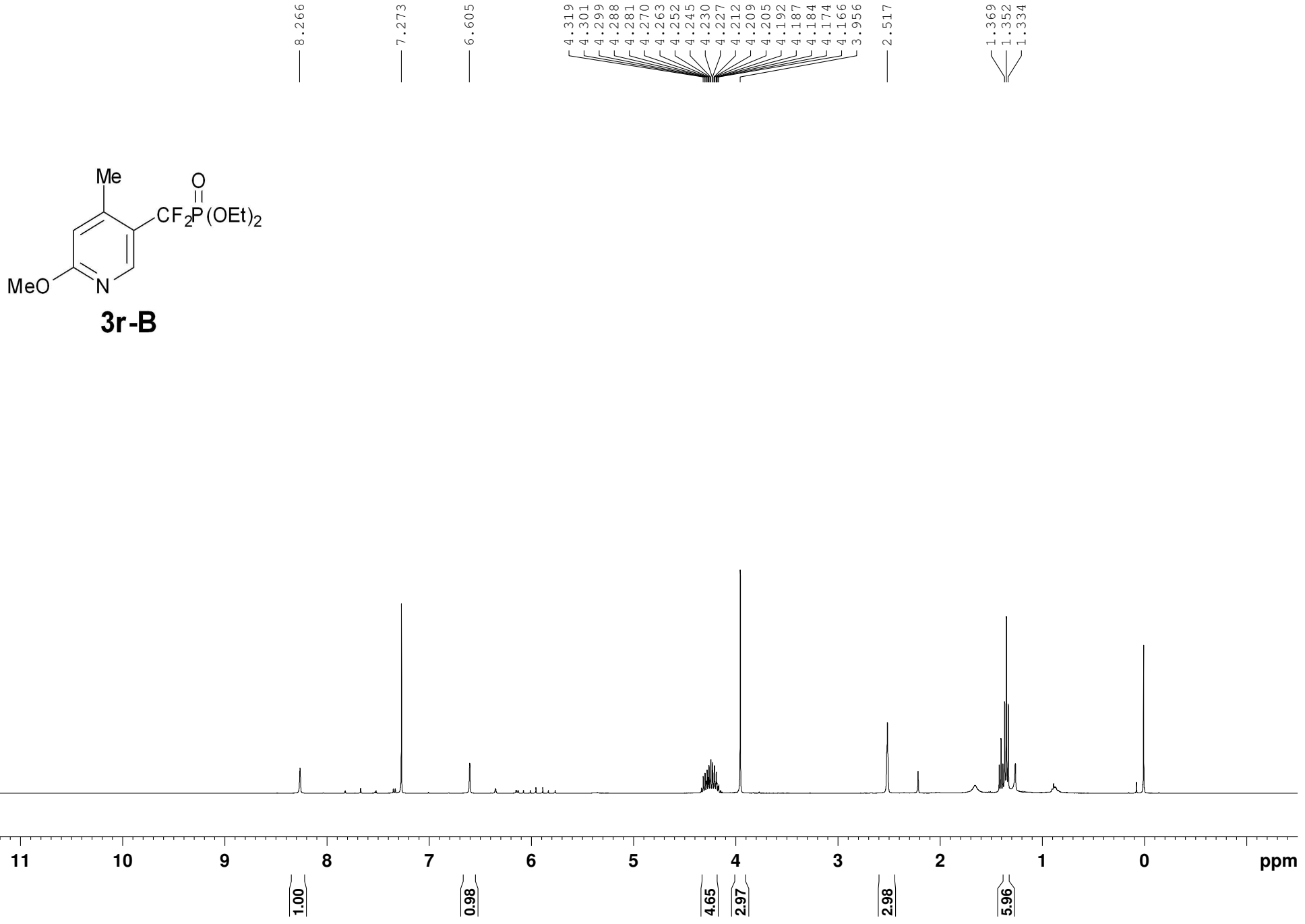

Me
O
CF2P(OEt)2
N
OMe

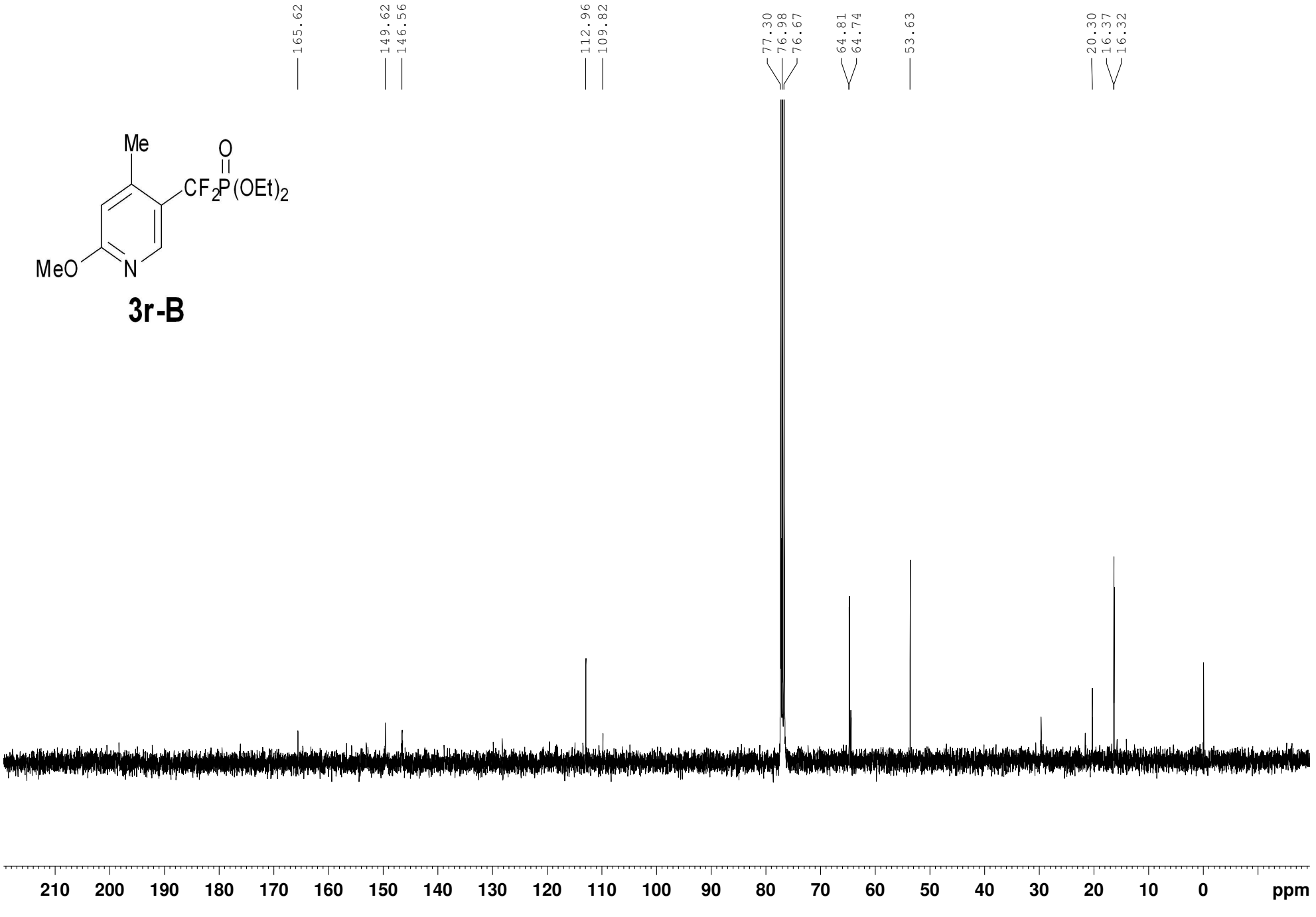
3r-A

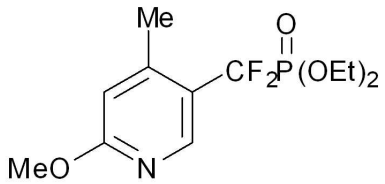
-100.609
-100.619
-100.916
-100.922
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
ppm



3r-A

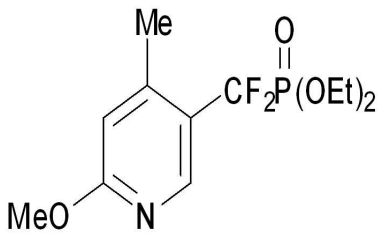

8.266
7.273
6.605
4.319
4.301
4.299
4.288
4.281
4.270
4.263
4.252
4.245
4.230
4.227
4.212
4.209
4.205
4.192
4.187
4.184
4.174
4.166
3.956
2.517
1.369
1.352
1.334
Me
O
CF2P(OEt)2
MeO
N
3r-B
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
0.98
4.65
2.97
2.98
5.96


165.62
149.62
146.56
112.96
109.82
77.30
76.98
76.67
64.81
64.74
53.63
20.30
16.37
16.32
Me
O
CF2P(OEt)2
MeO
N
3r-B
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

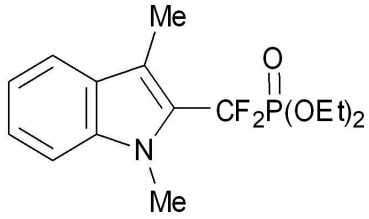

Me
O
CF2P(OEt)2
MeO
N

3r-B

-104.036
-104.347
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm

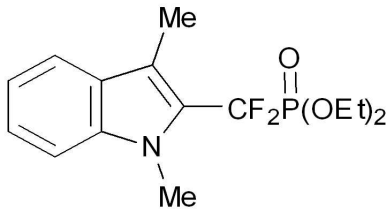


3r-B

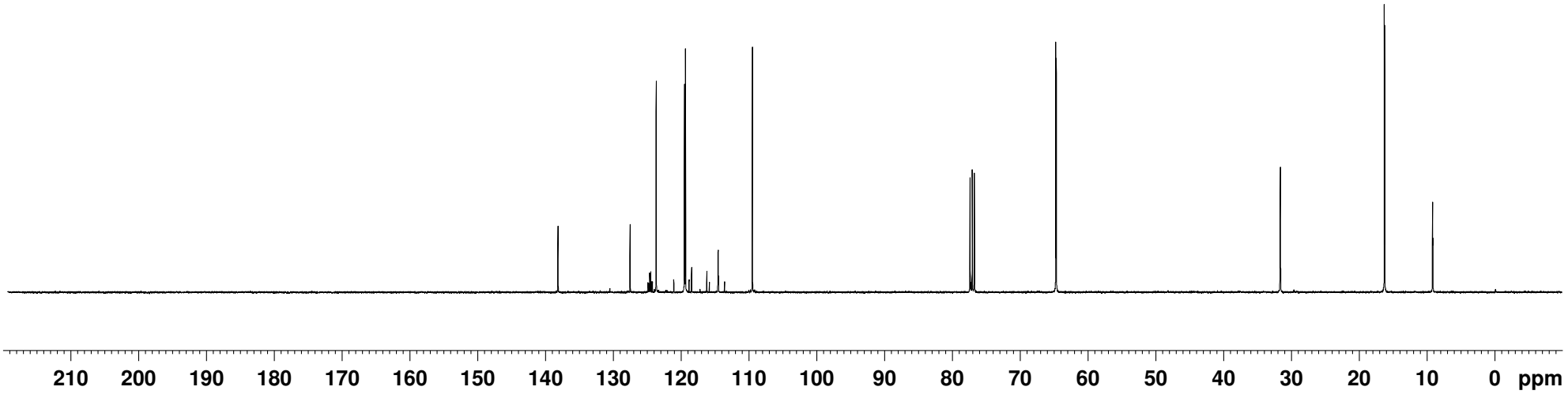

Me
O
CF2P(OEt)2
N
Me

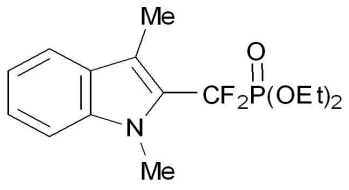
3s

7.669
7.649
7.375
7.359
7.344
7.323
7.269
7.205
7.200
7.191
7.185
7.180
7.170
7.165
4.306
4.288
4.280
4.270
4.263
4.252
4.245
4.234
4.226
4.216
4.209
4.198
4.191
4.180
4.177
4.173
4.159
4.155
4.152
4.142
4.134
4.116
3.927
2.523
2.515
2.508
2.500
1.377
1.360
1.342
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
2.03
1.01
4.16
3.03
3.05
6.11


Me
O
CF2P(OEt)2
N
Me

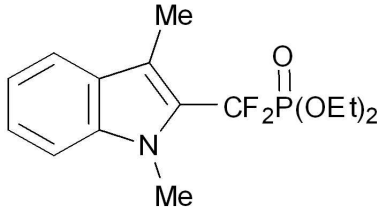
3s


138.11
130.46
127.47
124.82
124.69
124.57
124.43
124.31
124.18
123.91
123.62
121.02
119.44
119.29
118.78
118.40
117.16
116.15
115.77
114.53
114.49
114.45
114.41
113.53
109.96
109.43
77.31
77.00
76.68
64.66
64.59
31.59
31.55
31.50
16.20
16.15
9.06
9.03
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


Me
O
CF2P(OEt)2
N
Me

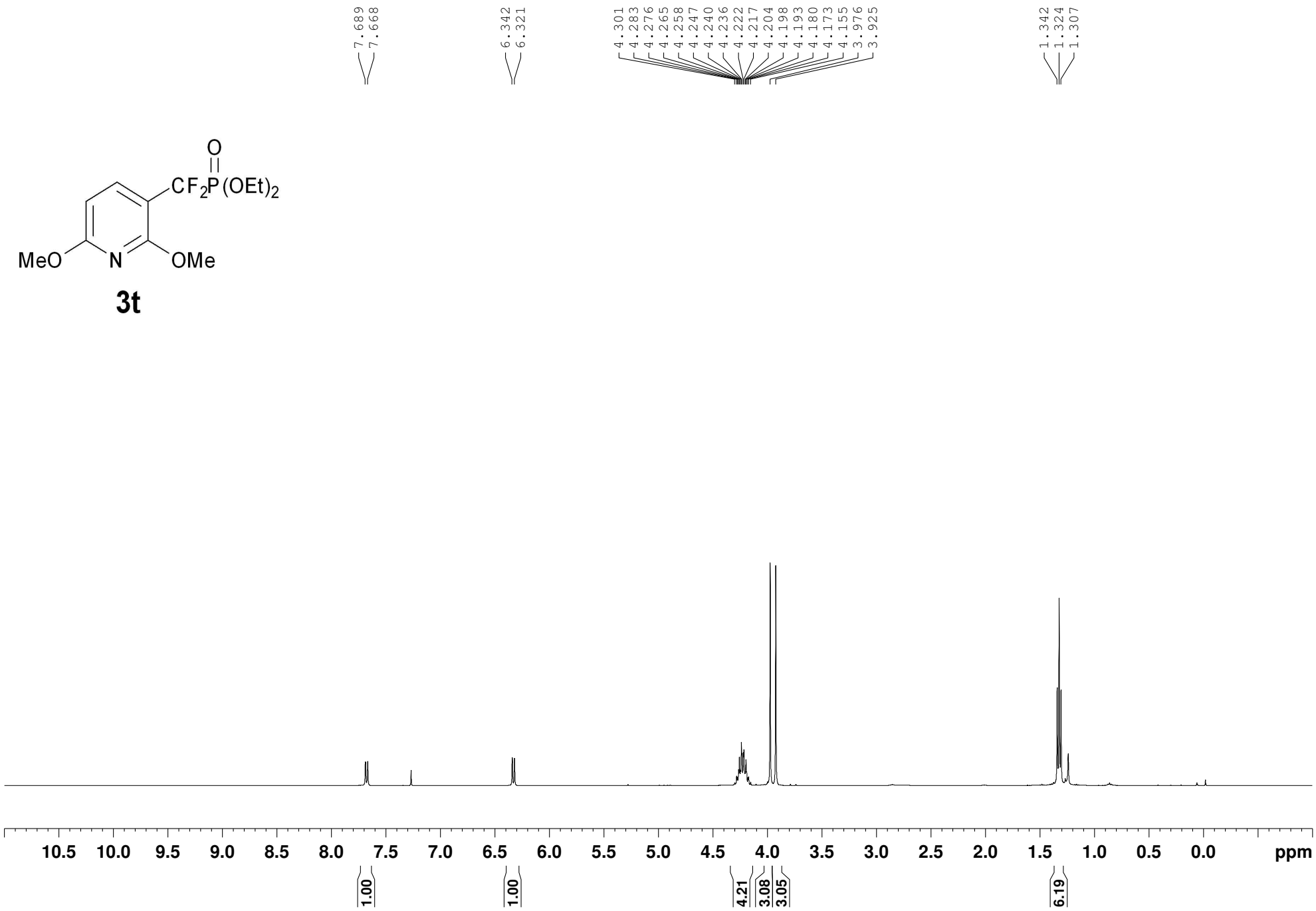
3s

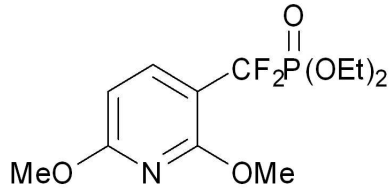
-102.399
-102.715
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
ppm


Me
O
CF2P(OEt)2
N
Me

3s

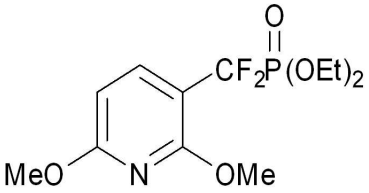
6.976
6.271
6.241
5.536
5.509
5.481
100
50
0
−50
−100
−150
ppm


7.689
7.668
6.342
6.321
4.301
4.283
4.276
4.265
4.258
4.247
4.240
4.236
4.222
4.217
4.204
4.198
4.193
4.180
4.173
4.155
3.976
3.925
1.342
1.324
1.307
O
CF2P(OEt)2
MeO
N
OMe
3t
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.00
4.21
3.08
3.05
6.19


O
CF2P(OEt)2
MeO
N
OMe

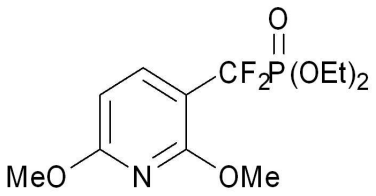
3t

164.49
160.26
160.24
140.16
140.14
140.08
140.07
140.01
139.99
121.72
119.49
119.09
116.87
116.47
114.25
113.97
106.40
106.25
106.17
106.02
105.93
105.79
101.16
77.32
77.00
76.68
64.54
64.48
53.65
53.52
29.60
16.30
16.24
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

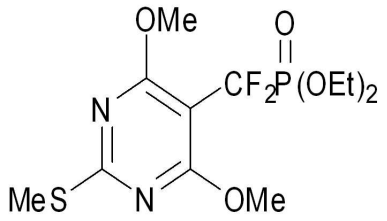

O
CF2P(OEt)2
MeO
N
OMe

3t

-105.137
-105.143
-105.456
-105.462
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
ppm

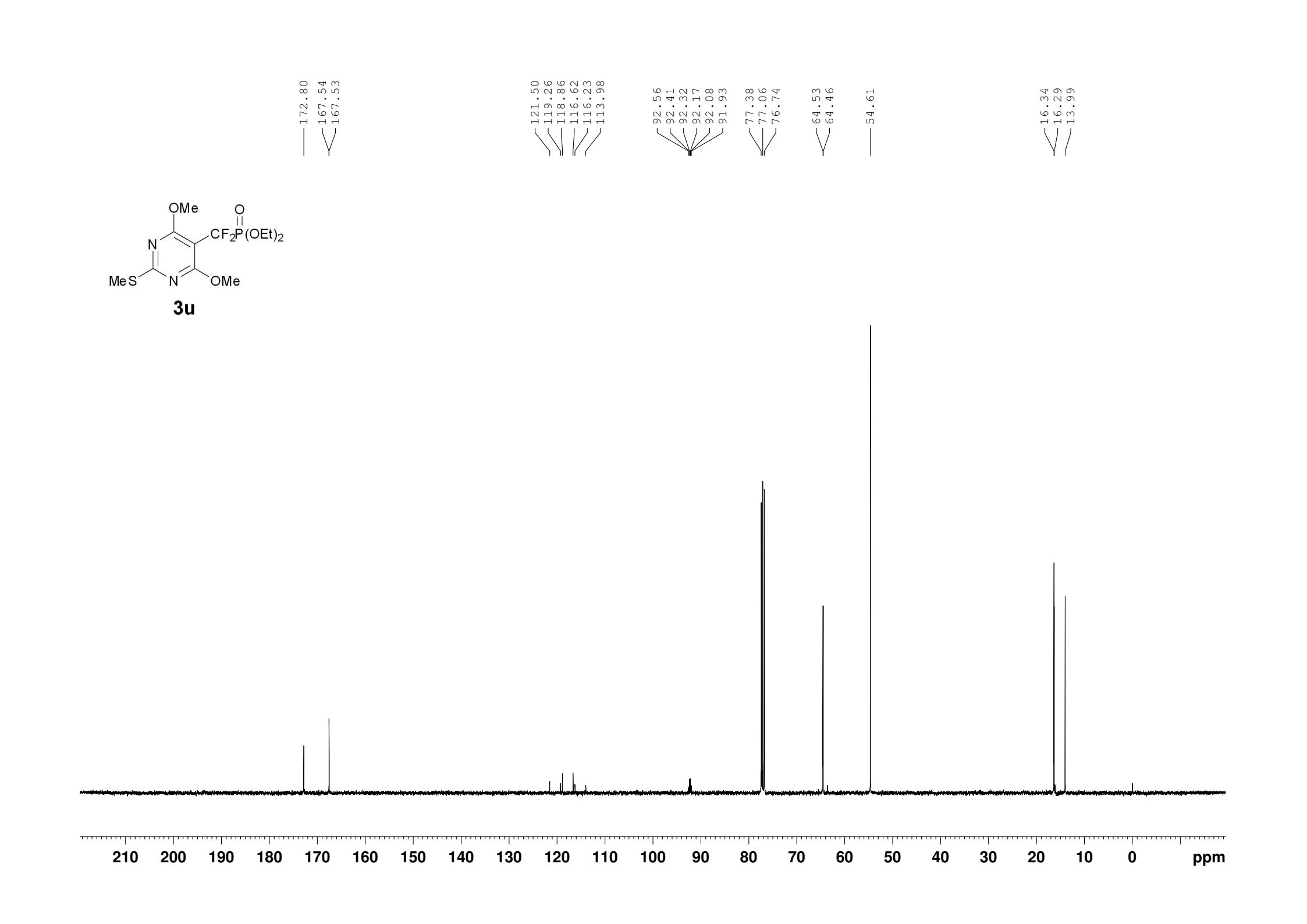


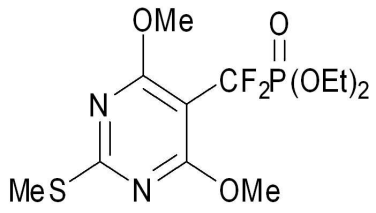
3t


OMe
O
CF2P(OEt)2
N
MeS
N
OMe

3u

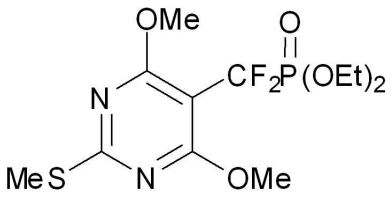
7.267
4.288
4.281
4.271
4.263
4.256
4.253
4.245
4.239
4.228
4.220
4.213
4.210
4.202
4.195
4.184
4.177
3.965
2.515
1.335
1.317
1.299
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
4.00
6.01
3.04
6.15


172.80
167.54
167.53
121.50
119.26
118.86
116.62
116.23
113.98
92.56
92.41
92.32
92.17
92.08
91.93
77.38
77.06
76.74
64.53
64.46
54.61
16.34
16.29
13.99
OMe
O
N
CF2P(OEt)2
MeS
N
OMe
3u
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


OMe
O
CF2P(OEt)2
N
MeS
N
OMe

3u

-102.825
-103.142
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
ppm


OMe
O
CF2P(OEt)2
N
MeS
N
OMe

3u

7.036
7.014
6.300
6.277
5.565
100
50
0
−50
−100
−150
ppm