Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

2-Oxo Promoted Hydrophosphonylation & Aerobic Intramolecular Nucleophilic Displacement Reaction

Satyanarayana Battula,[§,†] Narsaiah Battini, [§,†] Deepika Singh[¤] and Qazi Naveed Ahmed[§,†*]

[§]Medicinal Chemistry Division, Indian Institute of Integrative Medicine (IIIM), Jammu, India-180001.
[†]Academey of Scientific and Innovative Research (AcSIR Fax: +91-1912569333), 2-Rafi Marg, New Delhi, India.
[¤]Quality Control and Quality Assurance (QC & QA), IIIM, Jammu, India.

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(A) General Information.

^{1}H and ^{13}C NMR spectra were recorded on DPX FT-NMR 500 and 400 MHz instruments. Chemical shifts of protons reported in parts per million (ppm) downfield from tetramethylsilane and are referenced to the residual proton in the NMR solvents ($CDCl_3$: 7.26 ppm). ^{13}C-NMR spectra were recorded at 125 MHz or 100 MHz: chemical data for carbons are reported in parts per million (ppm, δ scale) down field from tetra methyl silane and are referenced to the carbon resonance of the solvent ($CDCl_3$:77.0 ppm). Mass spectra of compounds were recorded with ESI-MS and HRMS spectra were recorded on 1100 LC-Q-TOF and HRMS-6540-UHD machines. IR spectra were recorded on IR spectrophotometer. Melting points of compounds were recorded with B-545 instrument.

(B) Synthetic procedures.

General procedure for the synthesis of *α*-Hydroxy-*β*-oxo phosphonate (HOP).

A reaction vessel charged with a stir bar and it was added 2-oxoaldehyde[1] (0.460 mmol) and dialkyl phosphite (0.506 mmol). The reaction was allowed to stir at 80 ^{o}C for about 20 min. After completion of reaction, reaction mixture was cooled to room temperature. Volatiles were removed under reduced pressure, and products were obtained by washing the crude product with n-hexane. The product was with enough purity and yields were in the range of 92-99 %.

General procedure for the synthesis of α-oxoester (OE)

Reaction vessel equipped with a stir bar, it was added 2-oxoaldehyde[1] (0.460 mmol), dialkyl phosphite (0.506 mmol), and toluene (1 mL). The reaction mixture was subjected to stirring (40 rpm) at 80 °C for 9 h. After completion of reaction, reaction mixture allowed to cool at room temperature and extracted with ethyl acetate. The crude product was purified by column chromatography using ethyl acetate and hexane (2:98) producing desired product in good yields (65-87 %).

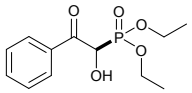
General procedure to the synthesis of α-oxoester (OE) directly from HOP

Reaction vessel equipped with a stir bar and was added HOP (0.183 mmol), toluene (1 mL). This reaction mixture was allowed to stir at 80 °C for 9 h. After completion of the reaction, reaction mixture allowed to cool at room temperature and extracted with ethyl acetate. Crude product was purified by column chromatography using ethyl acetate and hexane (2:98) to produce OE.

*** Note:** Since DOP is not so stable it was not possible to take all spectral data.

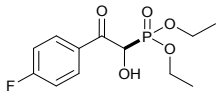
(C) Spectral Data of HOP (3) Compounds

Diethyl (1-hydroxy-2-oxo-2-phenylethyl)phosphonate (**3a**).



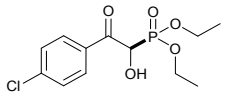
White solid; yield 98% (122 mg); m.p. 111-113 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.4 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 2H), 5.54 (d, *J* = 16.2 Hz, 1H), 4.23-4.02 (m, 4H), 1.23 (dt, *J* = 17.7, 7.0 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.26, 134.56, 133.78, 130.08, 129.52, 128.54, 128.35, 73.46, 71.96, 63.89, 63.82, 63.73, 63.66, 16.25, 16.22, 16.19, 16.16; ^{31}P NMR (162 MHz, $CDCl_3$) δ 14.49; IR ($CHCl_3$, cm^{-1}) ν 3416 (OH), 1692 (C=O), 1224 (P=O), 1025 (P-O-C); ESI-MS: 273.2 m/z $(M + H)^+$; HRMS: 273.0878 m/z calcd for $C_{12}H_{17}O_5P + H^+$ (273.0892).

Diethyl (2-(4-fluorophenyl)-1-hydroxy-2-oxoethyl)phosphonate (**3b**).



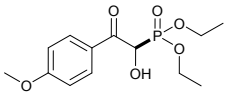
White solid; yield 99% (118 mg); m.p. 92-94 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15-8.09 (m, 2H), 7.18 (t, *J* = 8.6 Hz, 2H), 5.52 (d, *J* = 16.1 Hz, 1H), 5.15 (s, 1H), 4.26-4.06 (m, 4H), 1.25 (dt, *J* = 23.1, 7.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.59, 193.57, 167.90, 165.34, 132.70, 132.61, 132.46, 132.37, 130.16, 130.13, 115.93, 115.71, 115.62, 115.40, 73.39, 71.90, 64.02, 63.94, 63.87, 63.80, 16.28, 16.22, 16.17; ^{31}P NMR (162 MHz, $CDCl_3$) δ 14.44; IR ($CHCl_3$, cm^{-1}) ν 3361 (OH), 1682 (C=O), 1234 (P=O), 1025 (P-O-C); ESI-MS: 291.3 m/z $(M + 1)^+$; HRMS: 291.0791 m/z calcd for $C_{12}H_{16}FO_5P + H^+$ (291.0798).

Diethyl (2-(4-chlorophenyl)-1-hydroxy-2-oxoethyl)phosphonate (**3c**).



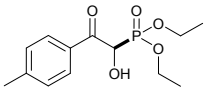
White solid; yield 98% (112 mg); m.p. 98-100 °C. ^{1}H NMR (400 MHz, CDCl3) δ 8.01 (d, J = 8.6 Hz, 2H), 7.48 (d, J = 8.6 Hz, 2H), 5.50 (d, J = 16.3 Hz, 1H), 4.43-4.26 (m, 1H), 4.23-4.05 (m, 4H), 1.25 (dt, J = 24.4, 7.0 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.09, 141.25, 132.01, 131.88, 131.47, 130.94, 129.24, 128.93, 128.72, 73.51, 72.02, 64.03, 63.96, 63.90, 63.83, 16.29, 16.24, 16.19; ^{31}P NMR (162 MHz, $CDCl_3$) δ 14.19; IR ($CHCl_3$, cm^{-1}) ν 3417 (OH), 1691 (C=O), 1232 (P=O), 1033 (P-O-C); ESI-MS: 307.1 m/z $(M + 1)^+$; HRMS: 307.0492 m/z calcd for $C_{12}H_{16}ClO_5P + H^+$ (307.0502).

Diethyl (1-hydroxy-2-(3-methoxyphenyl)-2-oxoethyl)phosphonate (**3d**).



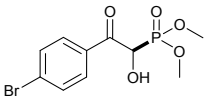
White solid; yield 93% (108 mg); m.p. 125-127 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.6 Hz, 1H), 7.57 (s, 1H), 7.41 (t, *J* = 8.0 Hz, 1H), 7.18 (dd, *J* = 8.1, 2.1 Hz, 1H), 5.52 (d, *J* = 16.2 Hz, 1H), 4.21-4.04 (m, 4H), 3.87 (s, 3H), 3.86 (s, 1H), 1.24 (dt, *J* = 12.2, 7.0 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.12, 159.69, 135.00, 129.50, 122.31, 121.23, 113.41, 73.59, 72.09, 63.88, 63.81, 63.69, 63.62, 55.52, 16.25, 16.20, 16.19; ^{31}P NMR (162 MHz, $CDCl_3$) δ 14.50; IR ($CHCl_3$, cm^{-1}) ν 3408 (OH), 1687 (C=O), 1257 (P=O), 1043 (P-O-C); ESI-MS: 303.5 m/z $(M + 1)^+$; HRMS: 303.0991 m/z calcd for $C_{13}H_{19}O_6P$ + H^+ (303.0997).

Diethyl (R)-(1-hydroxy-2-oxo-2-(p-tolyl)ethyl)phosphonate (**3e**).



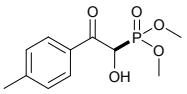
White solid; yield 95% (114 mg); m.p. 102-104 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 5.51 (d, *J* = 15.8 Hz, 1H), 4.22 – 4.02 (m, 6H), 2.43 (s, 3H), 1.24 (dt, *J* = 27.3, 7.1 Hz, 7H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.61, 145.80, 131.19, 129.69, 129.24, 73.28, 71.79, 63.78, 63.69, 63.61, 21.82, 16.22, 16.16; ^{31}P NMR (162 MHz, $CDCl_3$) δ 14.64; IR ($CHCl_3$, cm^{-1}) ν 3405 (OH), 1679 (C=O), 1242 (P=O), 1021 (P-O-C); ESI-MS: 287.0 m/z $(M + 1)^+$; HRMS: 287.1051 m/z calcd for $C_{13}H_{19}O_5P + H^+$ (287.1048).

Dimethyl (2-(4-bromophenyl)-1-hydroxy-2-oxoethyl)phosphonate (**3f**).



White solid; yield 97% (107 mg); m.p. 113-115 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.5 Hz, 2H), 7.66 (d, *J* = 8.5 Hz, 2H), 5.52 (d, *J* = 16.3 Hz, 1H), 4.20 (s, 1H), 3.78 (dd, *J* = 25.0, 10.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.02, 132.13, 132.06, 131.79, 131.62, 130.93, 130.33, 73.35, 71.85, 54.43, 54.36, 54.26, 54.19; ^{31}P NMR (162 MHz, $CDCl_3$) δ 16.53; IR ($CHCl_3$, cm^{-1}) ν 3361 (OH), 1682 (C=O), 1234 (P=O), 1025 (P-O-C); ESI-MS: 323.1 m/z $(M + 1)^+$; HRMS: 322. 9679 m/z calcd for $C_{10}H_{12}BrO_5P + H^+$ (322.9684).

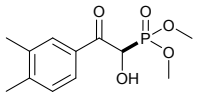
Dimethyl (1-hydroxy-2-oxo-2-(p-tolyl)ethyl)phosphonate (**3g**).



White solid; yield 95% (103 mg); m.p. 85-87 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 5.55 (d, J = 15.8 Hz, 1H), 3.75 (dd, J = 20.8, 10.8 Hz, 6H), 2.43 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.30, 146.04, 130.90, 129.65, 129.37, 73.10, 71.61, 54.26, 54.19, 54.10,

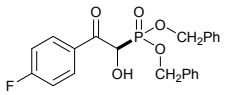
54.03, 21.86; ^{31}P NMR (162 MHz, $CDCl_3$) δ 17.08; IR ($CHCl_3$, cm^{-1}) ν 3405 (OH), 1681 (C=O), 1240 (P=O), 1038 (P-O-C); ESI-MS: 259.5 m/z $(M + 1)^+$; HRMS: 259.0722 m/z calcd for $C_{11}H_{15}O_5P + H^+$ (259.0735).

Dimethyl (2-(3,4-dimethylphenyl)-1-hydroxy-2-oxoethyl)phosphonate (**3h**).



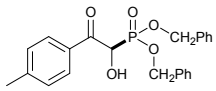
White solid; yield 92% (97 mg); m.p. 92-94 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.79 (d, *J* = 7.9 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 5.55 (d, *J* = 15.7 Hz, 1H), 3.97 (s, br, 1H), 3.75 (dd, *J* = 17.4, 10.8 Hz, 6H), 2.33 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.47, 194.45, 144.83, 137.18, 131.26, 130.41, 129.84, 127.39, 73.05, 71.55, 54.27, 54.20, 54.09, 54.02, 20.23, 19.72; ^{31}P NMR (162 MHz, $CDCl_3$) δ 17.20; IR ($CHCl_3$, cm^{-1}) ν 3416 (OH), 1681 (C=O), 1250 (P=O), 1035 (P-O-C); ESI-MS: 273.2 m/z $(M + 1)^+$; HRMS: 273.0881 m/z calcd for $C_{12}H_{17}O_5P + H^+$ (273.0892).

Dibenzyl (2-(4-fluorophenyl)-1-hydroxy-2-oxoethyl)phosphonate (**3i**).



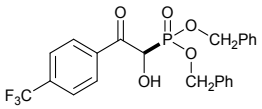
White solid; yield 98% (167 mg); m.p. 104-106 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (dd, J = 8.5, 5.4 Hz, 2H), 7.36-7.17 (m, 10H), 7.02 (t, J = 8.5 Hz, 2H), 5.50 (d, J = 16.0 Hz, 1H), 5.09-4.92 (m, 4H), 4.83 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.29, 167.81, 165.25, 135.60, 135.54, 135.51, 135.45, 132.39, 132.30, 129.99, 129.97, 128.70, 128.60, 128.56, 128.26, 128.05, 127.82, 115.88, 115.66, 73.62, 72.12, 69.19, 69.14, 69.12, 69.07; ^{31}P NMR (162 MHz, $CDCl_3$) δ 15.05; IR ($CHCl_3$, cm^{-1}) ν 3259 (OH), 1692 (C=O), 1230 (P=O), 1039 (P-O-C); ESI-MS: 415.3 m/z $(M + 1)^+$; HRMS: 415.1099 m/z calcd for $C_{22}H_{20}FO_5P + H^+$ (415.1111).

dibenzyl (1-hydroxy-2-oxo-2-(p-tolyl)ethyl)phosphonate (**3j**).



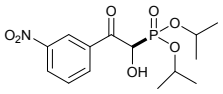
White solid; yield 96% (165 mg); m.p. 113-115 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.2 Hz, 2H), 7.33-7.21 (m, 10H), 7.16 (d, *J* = 7.8 Hz, 2H), 6.34 (s, 1H), 5.55 (d, *J* = 15.8 Hz, 1H), 5.07-4.93 (m, *J* = 18.6, 4H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.28, 145.74, 135.67, 131.13, 129.65, 129.27, 128.73, 128.53, 128.51, 128.18, 128.07, 127.99, 127.84, 73.43, 71.93, 69.10, 69.03, 21.86; ^{31}P NMR (162 MHz, $CDCl_3$) δ 15.51; IR ($CHCl_3$, cm^{-1}) ν 3355 (OH), 1679 (C=O), 1245 (P=O), 1011 (P-O-C); ESI-MS: 411.2 m/z $(M + 1)^+$; HRMS: 411.1345 m/z calcd for $C_{23}H_{23}O_5P + H^+$ (411.1361).

Dibenzyl (R)-(1-hydroxy-2-oxo-2-(4-(trifluoromethyl)phenyl)ethyl)phosphonate



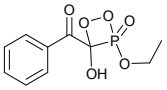
White solid; yield 97% (143 mg); m.p. 121-123 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.1 Hz, 2H), 7.58 (d, *J* = 8.1 Hz, 2H), 7.34 – 7.27 (m, 6H), 7.24 – 7.15 (m, 2H), 5.54 (d, *J* = 16.9 Hz, 1H), 5.09 – 4.91 (m, 4H), 4.88 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.40, 136.31, 135.50, 135.40, 135.35, 135.28, 135.23, 134.98, 129.76, 128.84, 128.73, 128.64, 128.61, 128.53, 128.31, 128.13, 128.06, 127.84, 125.49, 125.46, 125.43, 124.43, 122.26, 73.92, 72.72, 69.34, 69.28, 69.25, 69.19; ^{31}P NMR (162 MHz, $CDCl_3$) δ 14.62; IR ($CHCl_3$, cm^{-1}) ν 3342 (OH), 1685 (C=O), 1234 (P=O), 1001 (P-O-C); ESI-MS: 465.2 m/z $(M + 1)^+$; HRMS: 465.1081 m/z calcd for $C_{23}H_{21}F_3O_5P + H^+$ (465.1079).

Diisopropyl (R)-(1-hydroxy-2-(3-nitrophenyl)-2-oxoethyl)phosphonate (**3k**).



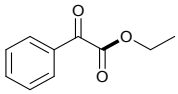
Pale yellow semi solid; yield 92% (112 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.37 (dd, *J* = 27.5, 7.3 Hz, 2H), 7.72 – 7.61 (m, 1H), 5.72 (s, 1H), 5.50 (d, *J* = 17.5 Hz, 1H), 4.79 – 4.56 (m, 2H), 1.19 (m, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.06, 148.06, 135.54, 135.08, 129.71, 128.13, 124.32, 77.44, 77.12, 76.80, 74.24, 73.44, 73.37, 73.26, 73.19, 72.73, 23.86, 23.56, 23.52, 23.48; ^{31}P NMR (162 MHz, $CDCl_3$) δ 12.21; IR ($CHCl_3$, cm^{-1}) ν 3417 (OH), 1693 (C=O), 1229 (P=O), 1008 (P-O-C); ESI-MS: 346.0 m/z $(M + 1)^+$; HRMS: 346.1051 m/z calcd for $C_{14}H_{20}NO_7P + H^+$ (346.1056).

(3-Ethoxy-4-hydroxy-3-oxido-1,2,3-dioxaphosphetan-4-yl)(phenyl)methanone (DOP).



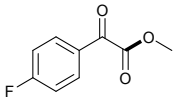
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 7.4 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 4.22-4.10 (m, 2H), 1.35-1.17 (m, 3H); ESI-MS: 259.2 m/z $(M + 1)^+$.

Ethyl-2-oxo-2-phenylacetate (**4a**).[2a]



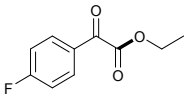
Yield: 73%, 59 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98-7.91 (m, 2H), 7.63-7.56 (m, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 4.39 (q, *J* = 7.1 Hz, 2H), 1.36 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.39, 163.83, 134.84, 132.56, 130.02, 128.87, 62.30, 14.10; IR ($CHCl_3$, cm^{-1}) ν 2986, 1732, 1683, 1300, 1177, 1016, 675.

Methyl 2-(4-fluorophenyl)-2-oxoacetate (**4b**). [2a]



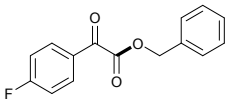
Yield: 77%, 58 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 8.4, 5.4 Hz, 2H), 7.12 (t, *J* = 8.4 Hz, 2H), 3.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.14, 168.17, 165.60, 163.63, 133.10, 133.01, 129.02, 116.41, 116.19, 52.91; IR ($CHCl_3$, cm^{-1}) ν 2924, 2852, 1737, 1690, 1454, 1265, 1134, 1024, 692.

Ethyl-2-(4-fluorophenyl)-2-oxoacetate (**4c**). [2a]



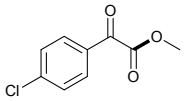
Yield: 80%, 64 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11-8.05 (m, 2H), 7.19 (t, *J* = 8.6 Hz, 2H), 4.45 (q, *J* = 7.1 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.54, 168.09, 165.53, 163.41, 133.01, 132.91, 129.05, 116.36, 116.14, 62.48, 14.08; IR ($CHCl_3$, cm^{-1}) ν 2923, 2854, 1736, 1687, 1240, 1155, 1018, 681.

Benzyl-2-(4-fluorophenyl)-2-oxoacetate (**4d**). [2b]



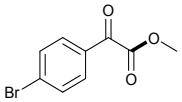
Yield: 87%, 92 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 7.9, 5.7 Hz, 2H), 7.50-7.33 (m, 5H), 7.16 (t, *J* = 8.4 Hz, 2H), 5.41 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.18, 168.12, 165.55, 163.23, 134.47, 132.99, 132.90, 128.89, 128.78, 128.63, 116.39, 116.17, 67.90; IR ($CHCl_3$, cm^{-1}) ν 2921, 2851, 1738, 1688, 1415, 1191, 998, 697.

Methyl 2-(4-chlorophenyl)-2-oxoacetate (**4e**). [2a]



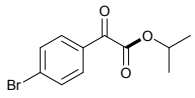
Yield: 76%, 56 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.6 Hz, 2H), 7.50 (d, *J* = 8.6 Hz, 2H), 3.99 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.48, 163.43, 141.75, 131.49, 130.90, 129.32, 52.93; IR ($CHCl_3$, cm^{-1}) ν 2923, 2851, 1729, 1681, 1403, 1209, 1004, 671.

Methyl 2-(4-bromoophenyl)-2-oxoacetate (**4f**). [2a]



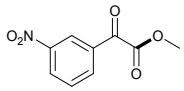
Yield: 78%, 57 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.6 Hz, 2H), 7.67 (d, J = 8.6 Hz, 2H), 3.99 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.71, 163.39, 132.34, 131.51, 131.30, 130.66, 52.96; IR ($CHCl_3$, cm^{-1}) ν 2923, 2852, 1729, 1688, 1440, 1326, 1170, 1003, 669.

Isopropyl-2-(4-bromophenyl)-2-oxoacetate (**4g**). [2c]



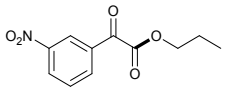
Yield: 80%, 77 mg; ^{1}H NMR (400 MHz, CDCl3) δ 7.88 (d, *J* = 8.6 Hz, 2H), 7.66 (d, *J* = 8.6 Hz, 2H), 5.36 – 5.27 (m, 1H), 1.41 (d, *J* = 6.3 Hz, 6H); IR ($CHCl_3$, cm^{-1}) ν 2921, 2852, 1730, 1695, 1209, 1171, 989, 669.

Methyl-2-(3-nitrophenyl)-2-oxoacetate (**4h**). [2d]



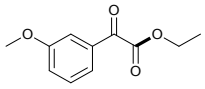
Yield: 71%, 52 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (s, 1H), 8.52 (d, *J* = 8.3 Hz, 1H), 8.42 (d, *J* = 7.5 Hz, 1H), 7.75 (t, *J* = 8.0 Hz, 1H), 4.04 (s, 3H); IR ($CHCl_3$, cm^{-1}) ν 2943, 2854, 1739, 1690, 1464, 1342, 1153, 1027, 699.

propyl 2-(3-nitrophenyl)-2-oxoacetate (**4i**). [2d]



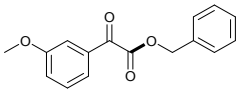
Yield: 78%, 66 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 – 8.88 (m, 1H), 8.52 (ddd, *J* = 8.2, 2.1, 1.0 Hz, 1H), 8.42 – 8.38 (m, 1H), 7.76 (t, *J* = 8.0 Hz, 1H), 4.41 (t, *J* = 6.7 Hz, 2H), 1.92 – 1.79 (m, 2H), 1.04 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.04, 163.77, 149.87, 136.87, 135.40, 131.66, 130.28, 126.42, 69.89, 23.26, 11.69; IR ($CHCl_3$, cm^{-1}) ν 2932, 2850, 1728, 1687, 1415, 1135, 998, 697.

Ethyl-2-(3-methoxyphenyl)-2-oxoacetate (**4j**). [2e]



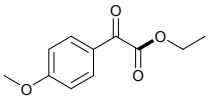
Yield: 69%, 55 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.5 Hz, 1H), 7.53 (s, 1H), 7.45-7.39 (m, 1H), 7.21 (d, *J* = 7.8 Hz, 1H), 4.45 (q, *J* = 7.0 Hz, 2H), 3.87 (s, 3H), 1.43 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.33, 163.86, 159.97, 133.73, 129.91, 128.76, 128.67, 123.14, 121.87, 113.27, 62.34, 55.53, 14.12; IR ($CHCl_3$, cm^{-1}) ν 2924, 2852, 1737, 1688, 1464, 1251, 1155, 1021, 679.

Benzyl-2-(3-methoxyphenyl)-2-oxoacetate (**4k**).[2e]



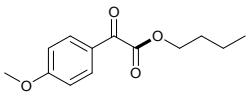
Yield: 72%, 74 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.6 Hz, 1H), 7.45 (d, *J* = 6.6 Hz, 3H), 7.43-7.34 (m, 4H), 7.19 (dd, *J* = 8.0, 2.2 Hz, 1H), 5.41 (s, 2H), 3.81 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.02, 163.72, 159.92, 134.54, 133.60, 129.96, 128.87, 128.79, 128.72, 123.15, 122.17, 113.04, 67.81, 55.50; IR ($CHCl_3$, cm^{-1}) ν 2924, 2853, 1731, 1643, 1431, 1154, 1041, 696.

Ethyl-2-(4-methoxyphenyl)-2-oxoacetate (**4l**).[2f]



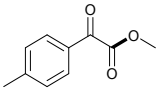
Yield: 68%, 54 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.9 Hz, 2H), 6.98 (d, *J* = 8.9 Hz, 2H), 4.44 (q, *J* = 7.1 Hz, 2H), 3.90 (s, 3H), 1.42 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.87, 165.02, 164.16, 132.60, 125.57, 114.25, 62.16, 55.65, 14.13; IR ($CHCl_3$, cm^{-1}) ν 2983, 1732, 1672, 1310, 1163, 1019, 617.

Butyl 2-(4-methoxyphenyl)-2-oxoacetate (**4m**).[2c]



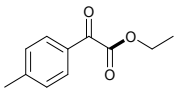
Yield: 74%, 76 mg; ^{1}H NMR (400 MHz, CDCl3) δ 7.99 (d, *J* = 8.9 Hz, 2H), 6.98 (d, *J* = 8.9 Hz, 2H), 4.38 (t, *J* = 6.7 Hz, 2H), 3.89 (s, 3H), 1.82 – 1.70 (m, 2H), 1.49 – 1.39 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H); IR ($CHCl_3$, cm^{-1}) ν 2933, 1737, 1677, 1267, 1164, 1026, 617.

Methyl 2-oxo-2-(p-tolyl)acetate (**4n**). [2a]



Yield: 65%, 49 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 7.9 Hz, 2H), 3.91 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.69, 164.24, 146.34, 130.23, 130.02, 129.64, 52.69, 21.92; IR ($CHCl_3$, cm^{-1}) ν 2922, 2851, 1739, 1671, 1463, 1378, 1168, 1024, 594.

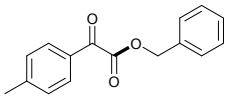
Ethyl-2-oxo-2-(p-tolyl)acetate (**4o**).[2g]



Yield: 70%, 56 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 7.9 Hz, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 2.37 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.14, 164.06,

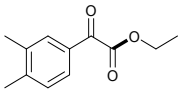
146.29, 130.20, 130.01, 129.65, 62.28, 21.97, 14.15; IR ($CHCl_3$, cm^{-1}) ν 2923, 2852, 1738, 1682, 1383, 1175, 1016, 618.

Benzyl-2-oxo-2-(p-tolyl) acetate (**4p**).[2b]



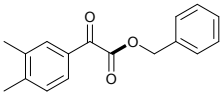
Yield: 75%, 80 mg; ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.9 Hz, 2H), 7.41-7.26 (m, 5H), 7.20 (d, *J* = 7.9 Hz, 2H), 5.33 (s, 2H), 2.35 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.77, 163.88, 146.39, 134.61, 130.21, 129.96, 129.68, 128.93, 128.82, 128.77, 128.64, 67.71, 21.98; IR ($CHCl_3$, cm^{-1}) ν 2922, 2852, 1737, 1681, 1303, 1169, 999, 696.

Ethyl 2-(3,4-dimethylphenyl)-2-oxoacetate (**4q**).[2h]



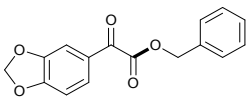
Yield: 67%, 53 mg; ^1H NMR (400 MHz, $CDCl_3$) δ 7.80-7.71 (m, 2H), 7.27 (s, 1H), 4.44 (q, *J* = 7.1 Hz, 2H), 2.35 (s, 3H), 2.33 (s, 3H), 1.42 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.45, 164.21, 145.13, 137.51, 130.88, 130.33, 130.17, 128.75, 127.97, 62.23, 20.36, 19.79, 14.16; IR ($CHCl_3$, cm^{-1}) ν 2923, 2852, 1738, 1682, 1454, 1204, 1036, 668.

Benzyl-2-(3,4-dimethylphenyl)-2-oxoacetate (**4r**).[2h]



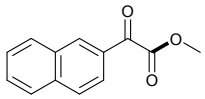
Yield: 69%, 71 mg; ^1H NMR (400 MHz, $CDCl_3$) δ 7.61 (s, 2H), 7.33 (dt, *J* = 13.5, 6.4 Hz, 5H), 7.20-7.12 (m, 1H), 5.33 (s, 2H), 2.25 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.05, 164.06, 145.13, 137.47, 134.72, 130.95, 130.34, 130.18, 128.77, 128.73, 128.63, 127.84, 67.58, 20.29, 19.68; IR ($CHCl_3$, cm^{-1}) ν 2923, 2853, 1738, 1680, 1455, 1313, 1163, 1053, 697.

Benzyl 2-(benzo[d][1,3]dioxol-5-yl)-2-oxoacetate (**4s**).[2i]



Yield: 70%, 71 mg; ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.2 Hz, 1H), 7.47-7.30 (m, 6H), 6.86 (d, *J* = 8.2 Hz, 1H), 6.08 (s, 2H), 5.39 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.20, 163.82, 153.60, 148.53, 134.59, 128.81, 128.79, 128.76, 128.61, 128.58, 127.95, 127.91, 127.21, 108.70, 108.34, 102.27, 102.25, 67.72; IR ($CHCl_3$, cm^{-1}) ν 2923, 2852, 1737, 1674, 1449, 1243, 1037, 698.

Methyl 2-(naphthalen-2-yl)-2-oxoacetate (**4t**).[2j]



Yield: 75%, 55 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (d, *J* = 8.6 Hz, 1H), 8.13 (d, *J* = 8.2 Hz, 1H), 7.98 (dd, *J* = 7.3, 0.9 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.70 (t, *J* = 7.1 Hz, 1H), 7.63 – 7.54 (m, 2H), 4.02 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.46, 164.90, 135.90, 134.00, 133.95, 130.97, 129.33, 128.78, 128.21, 127.08, 125.59, 124.30, 52.87; IR ($CHCl_3$, cm^{-1}) ν 2952, 2853, 1725, 1681, 1451, 1382, 1158, 1034, 611.

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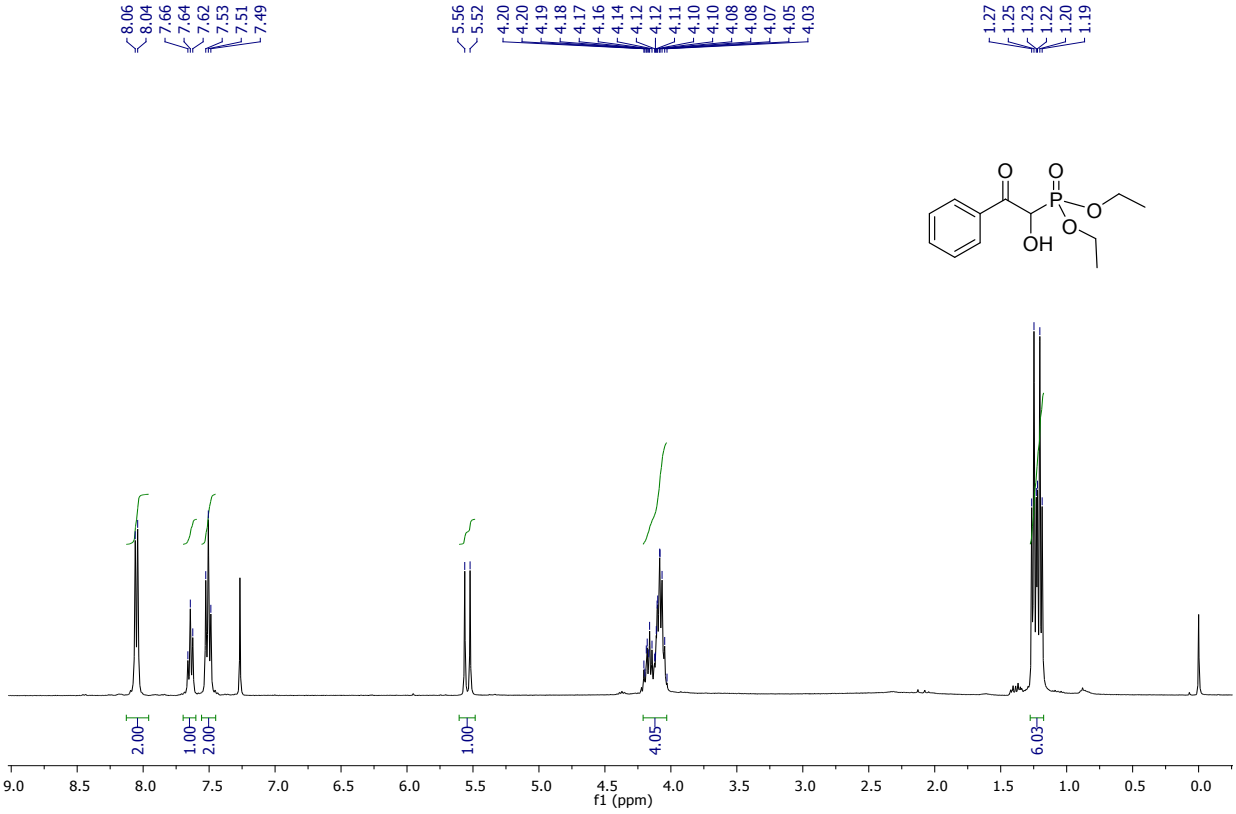
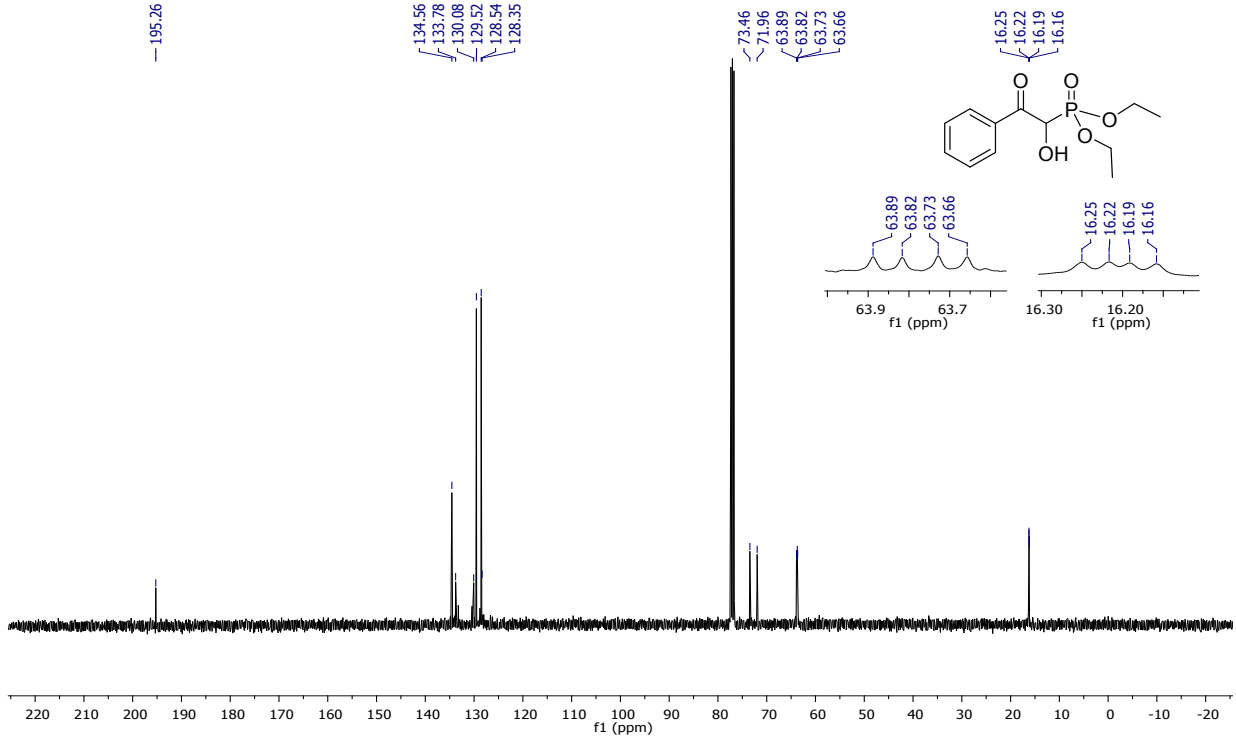
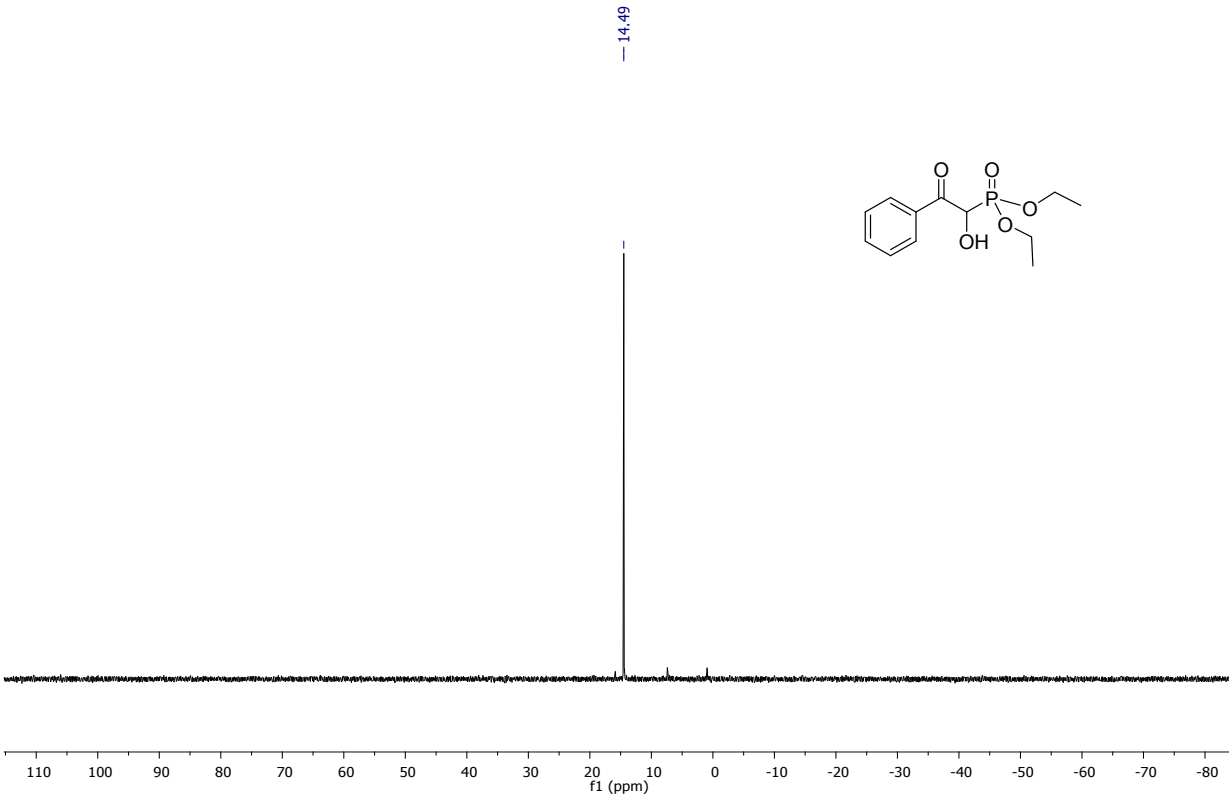
(E) NMR Spectra of all compounds

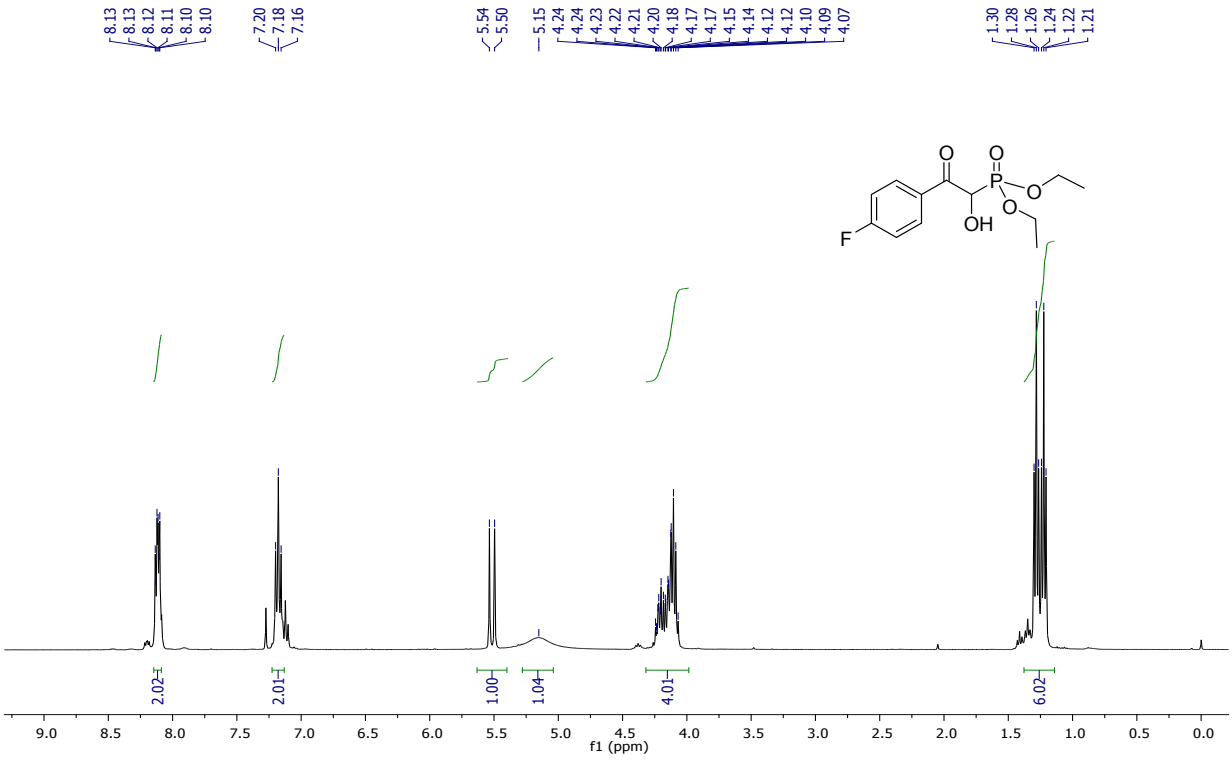
3a. Diethyl (1-hydroxy-2-oxo-2-phenylethyl)phosphonate

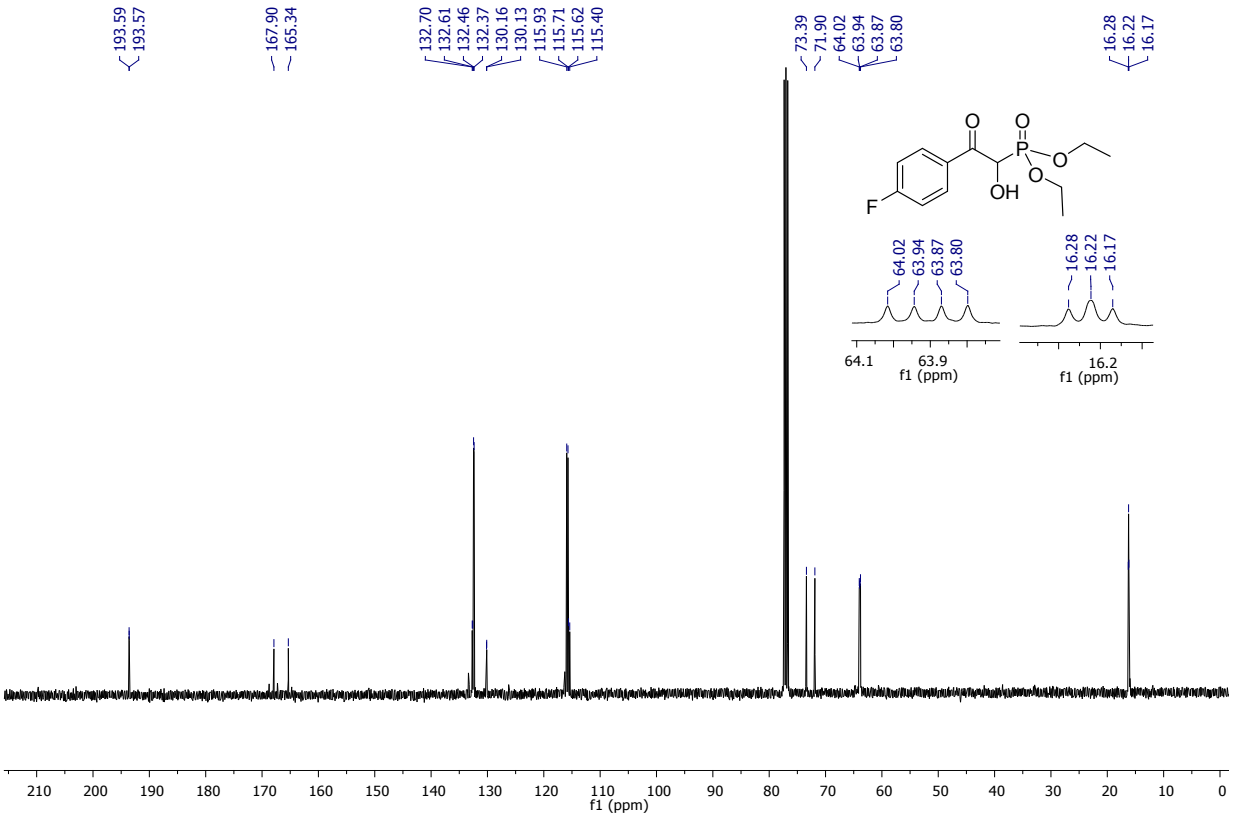


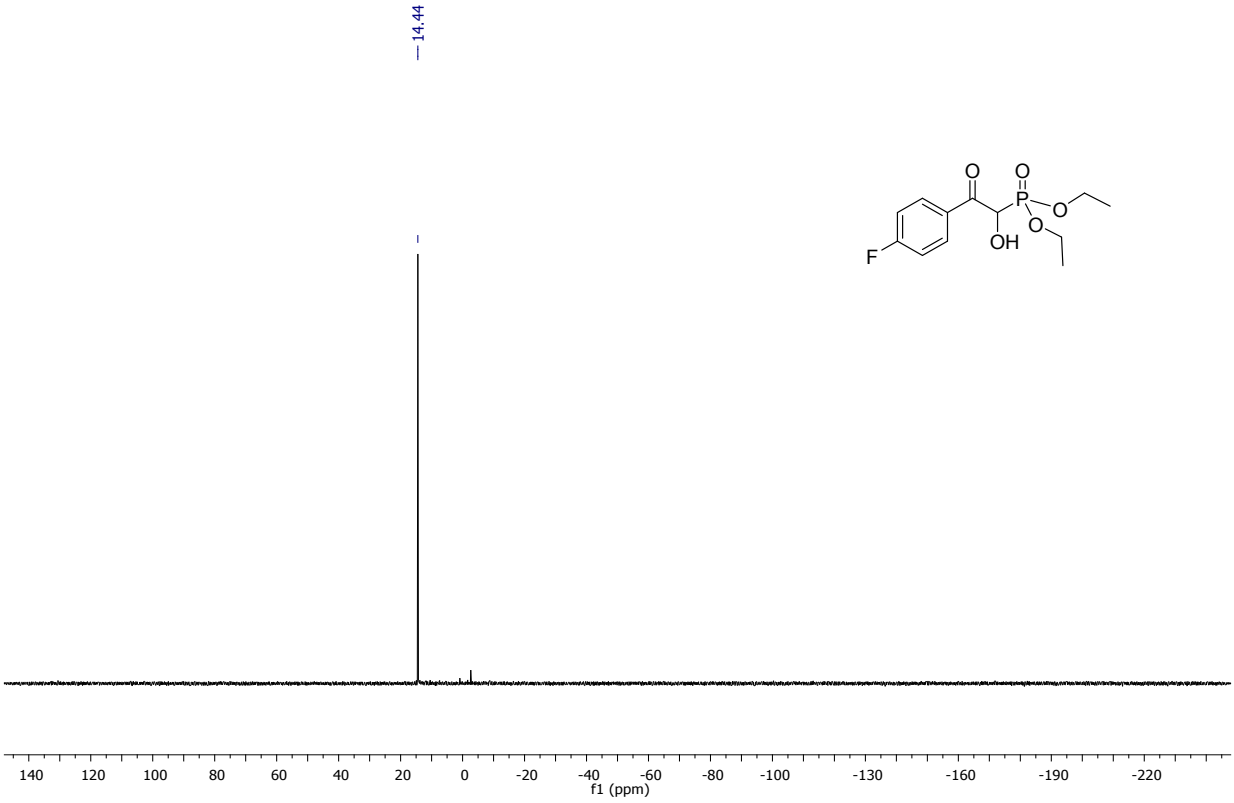




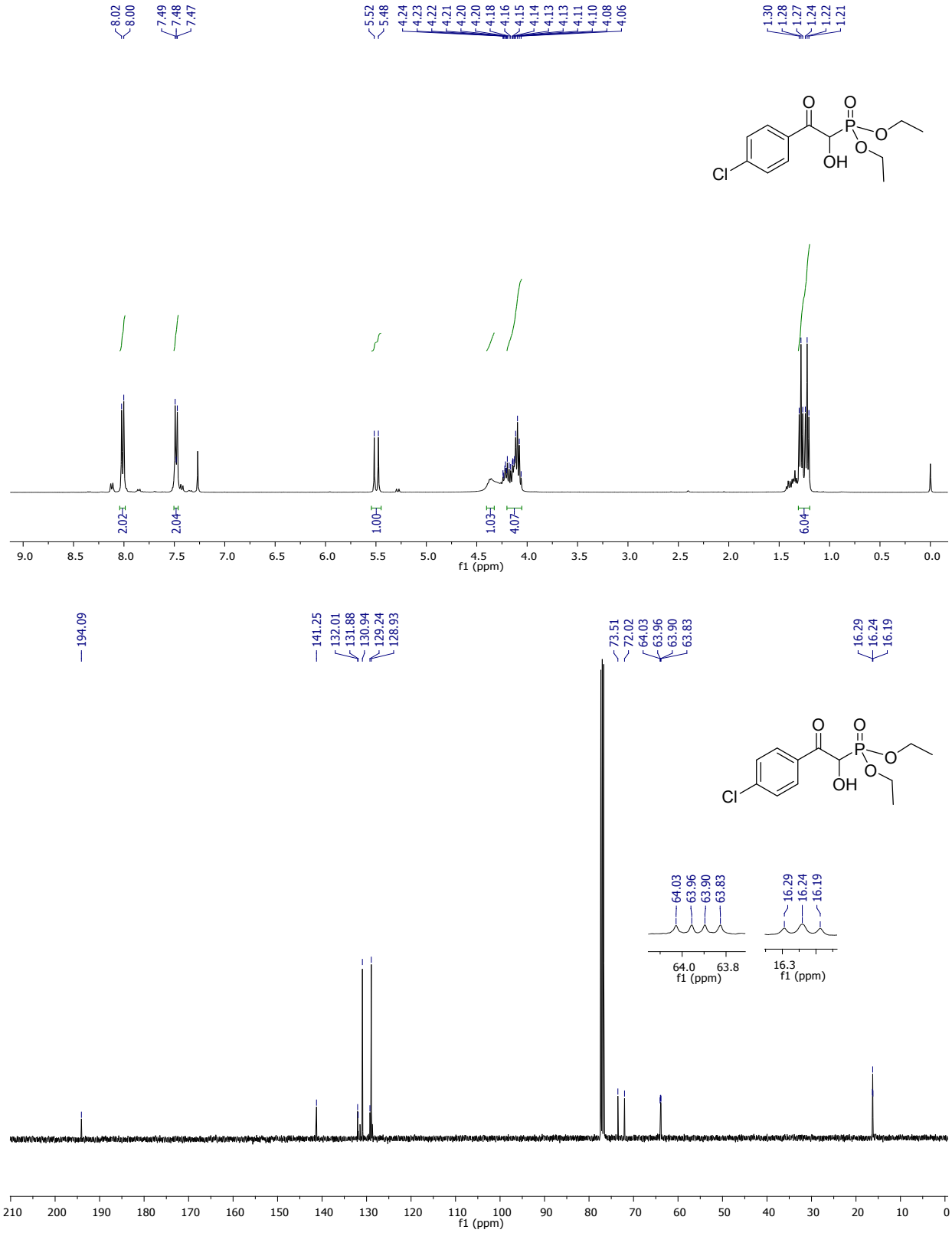
3b. Diethyl (2-(4-fluorophenyl)-1-hydroxy-2-oxoethyl)phosphonate

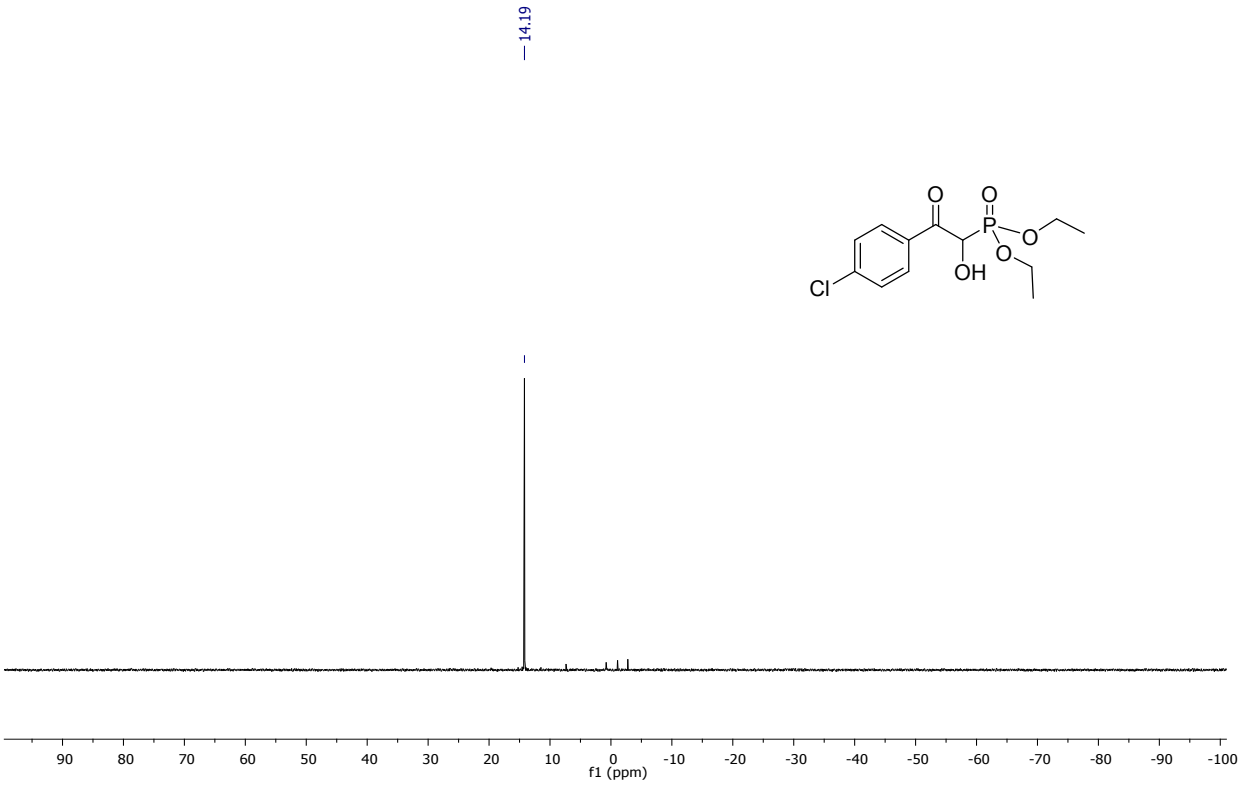



193.59
193.57
167.90
165.34
132.70
132.61
132.46
132.37
130.16
130.13
115.93
115.71
115.62
115.40
73.39
71.90
64.02
63.94
63.87
63.80
16.28
16.22
16.17
O
O
P
O
O
OH
F
64.02
63.94
63.87
63.80
64.1
63.9
f1 (ppm)
16.28
16.22
16.17
16.2
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

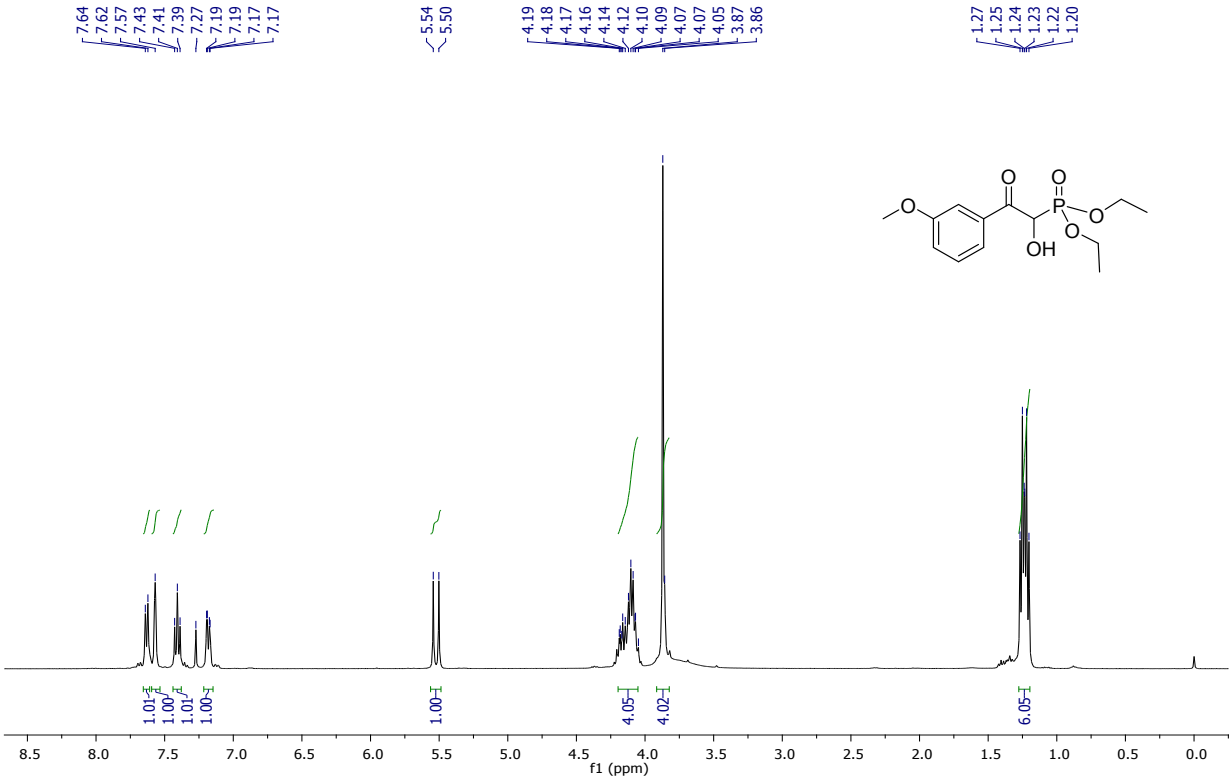

14.44
O
O
P
O
O
OH
F
140
120
100
80
60
40
20
0
-20
-40
-60
-80
-100
-130
-160
-190
-220
f1 (ppm)

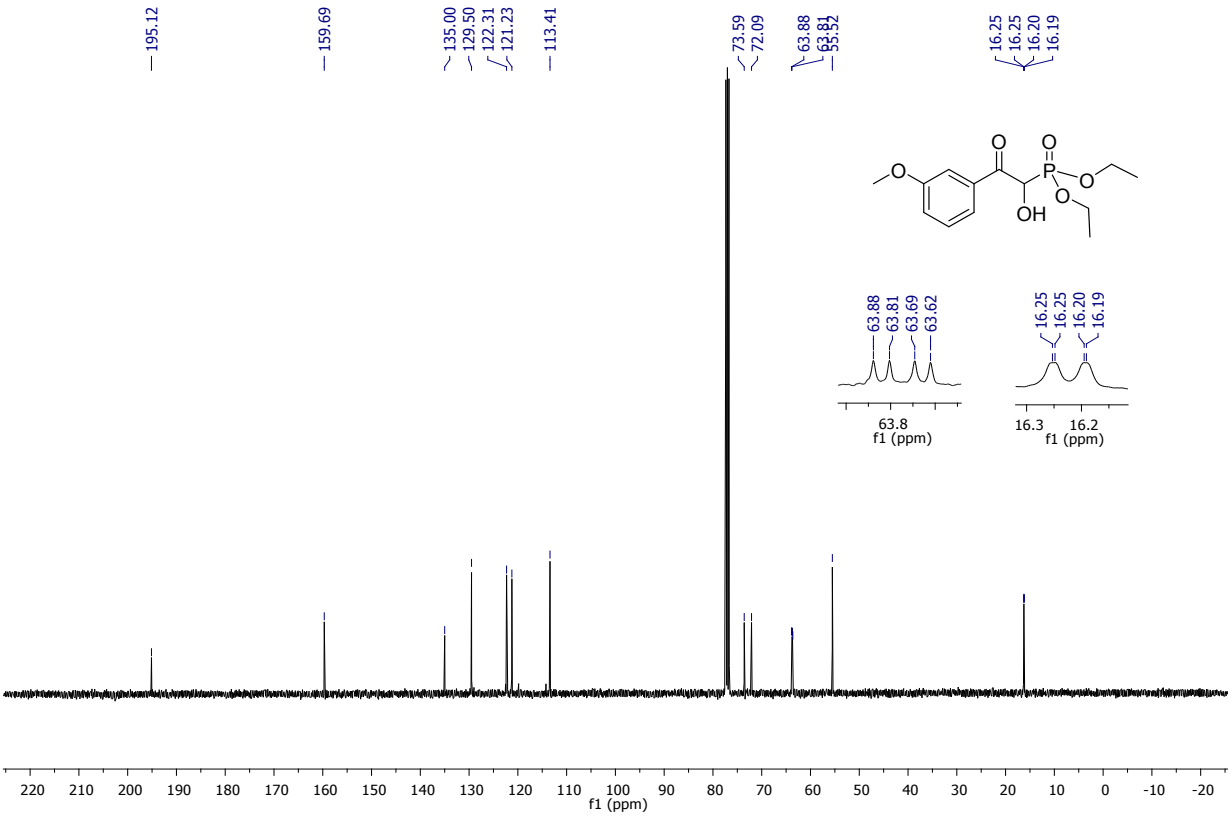
3c. Diethyl (2-(4-chlorophenyl)-1-hydroxy-2-oxoethyl)phosphonate

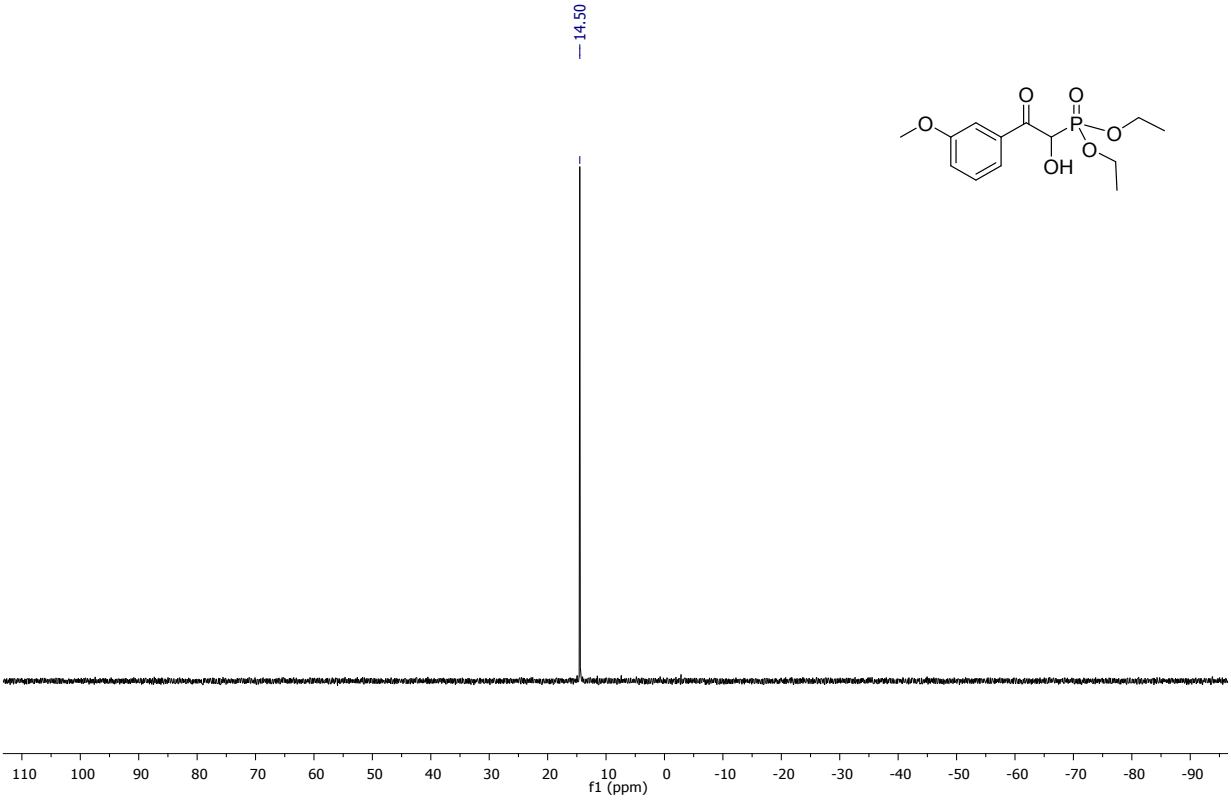




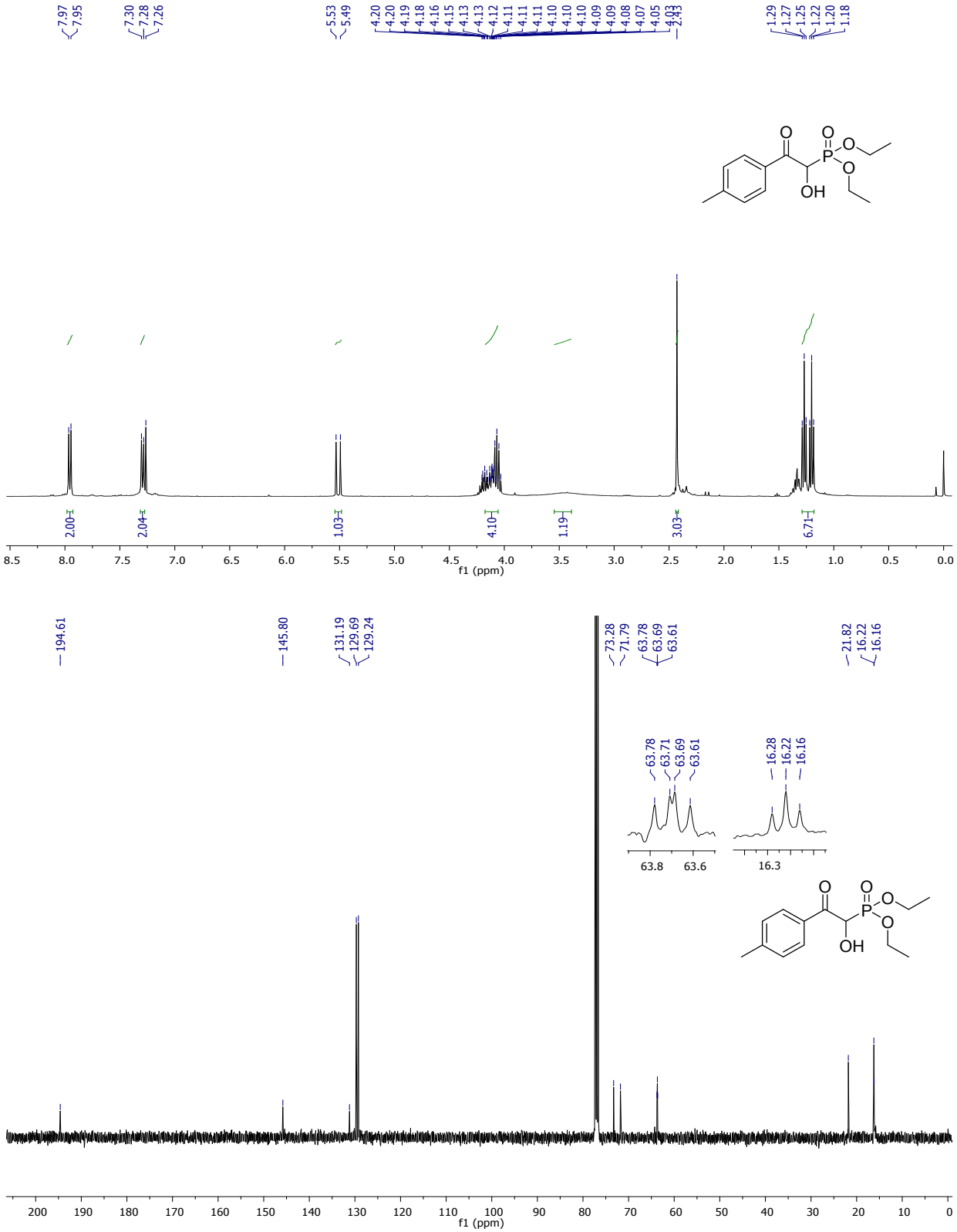
3d. Diethyl (1-hydroxy-2-(3-methoxyphenyl)-2-oxoethyl)phosphonate

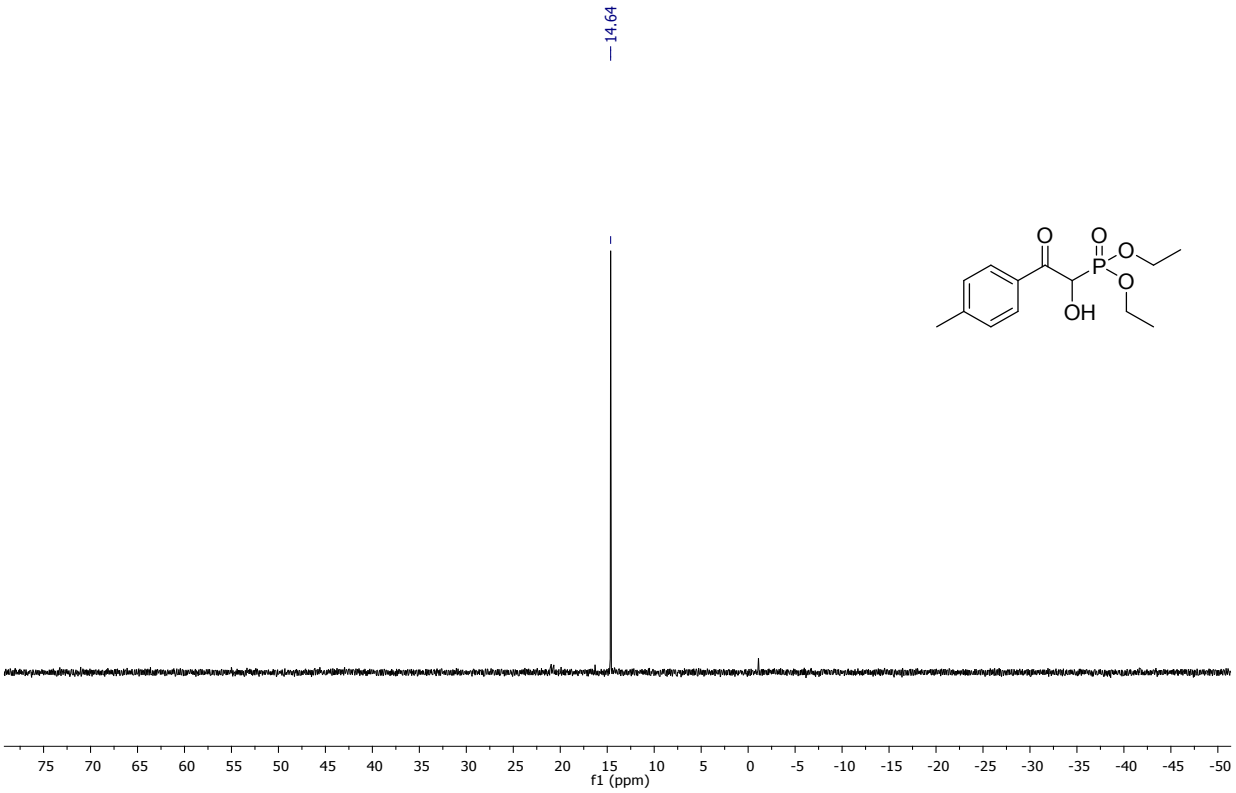



195.12
159.69
135.00
129.50
122.31
121.23
113.41
73.59
72.09
63.88
63.81
63.69
63.62
16.25
16.25
16.20
16.19
O
O
P
O
O
OH
63.8
f1 (ppm)
16.3
16.2
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

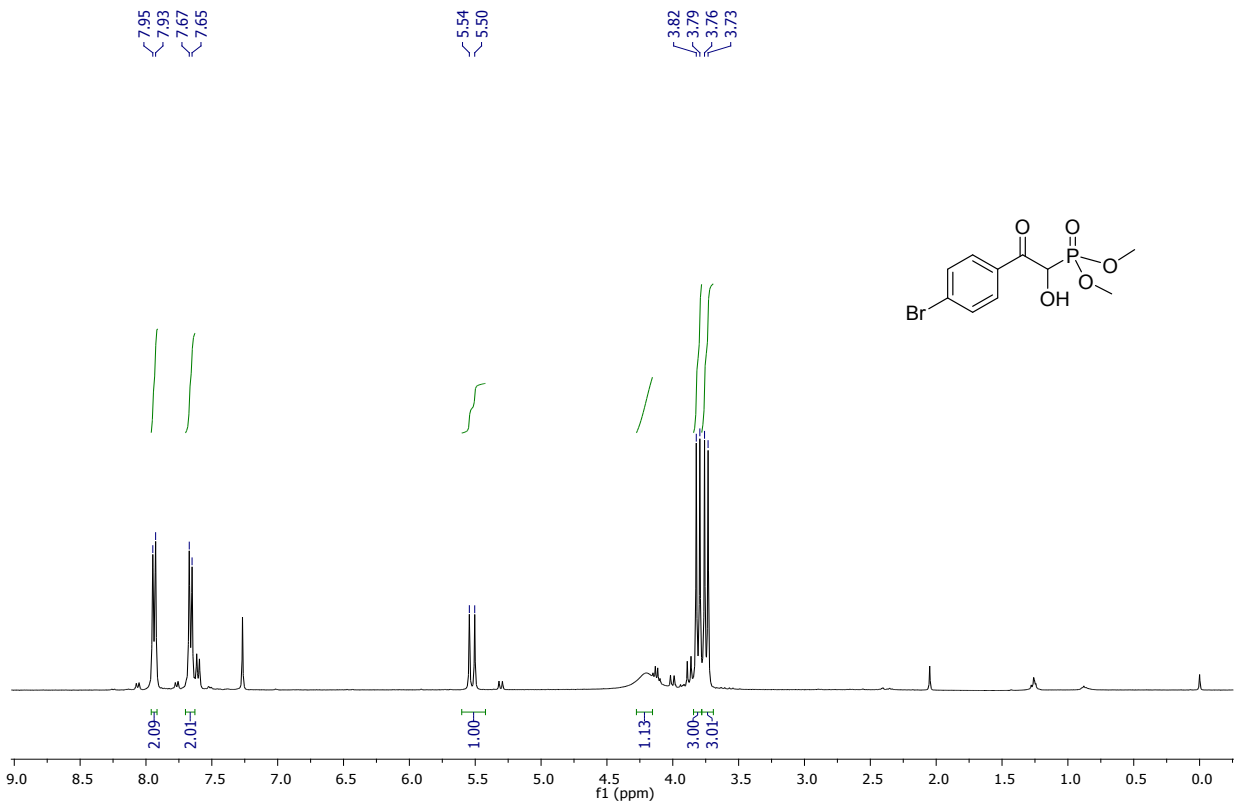

14.50
O
O
P
O
O
OH
110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90
f1 (ppm)

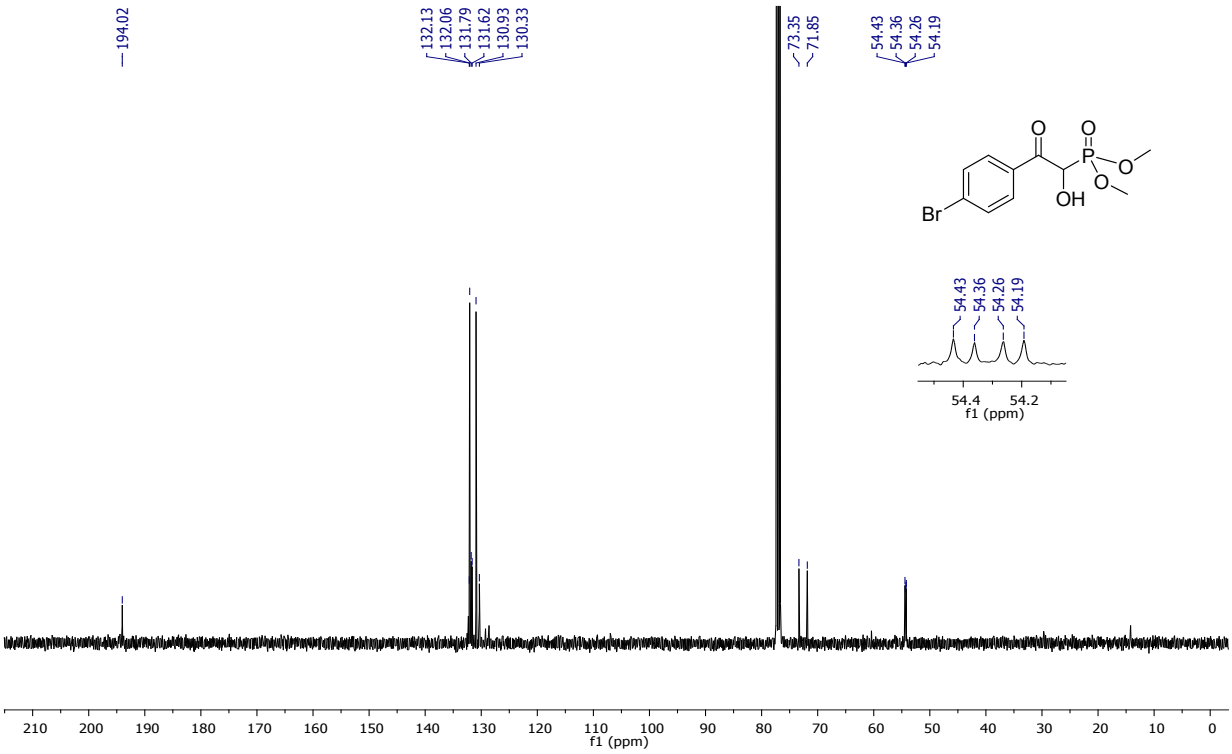
3e. Diethyl (1-hydroxy-2-oxo-2-(p-tolyl)ethyl)phosphonate

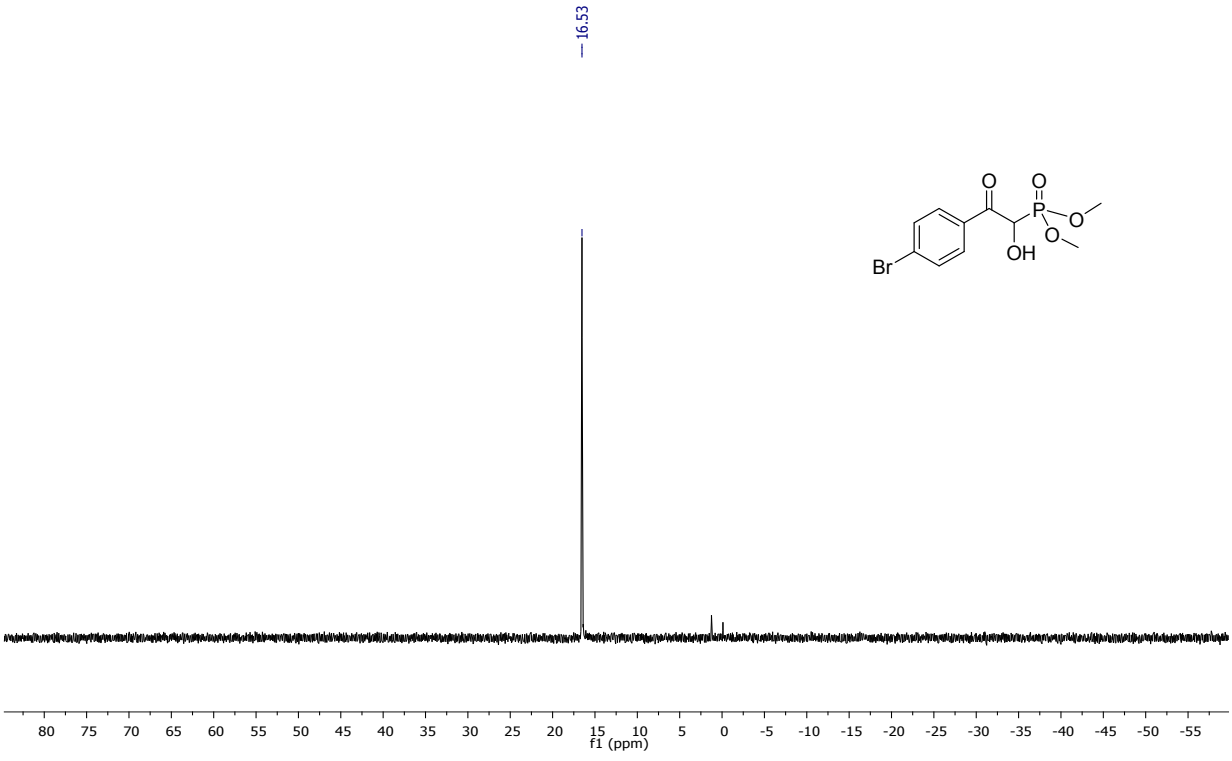




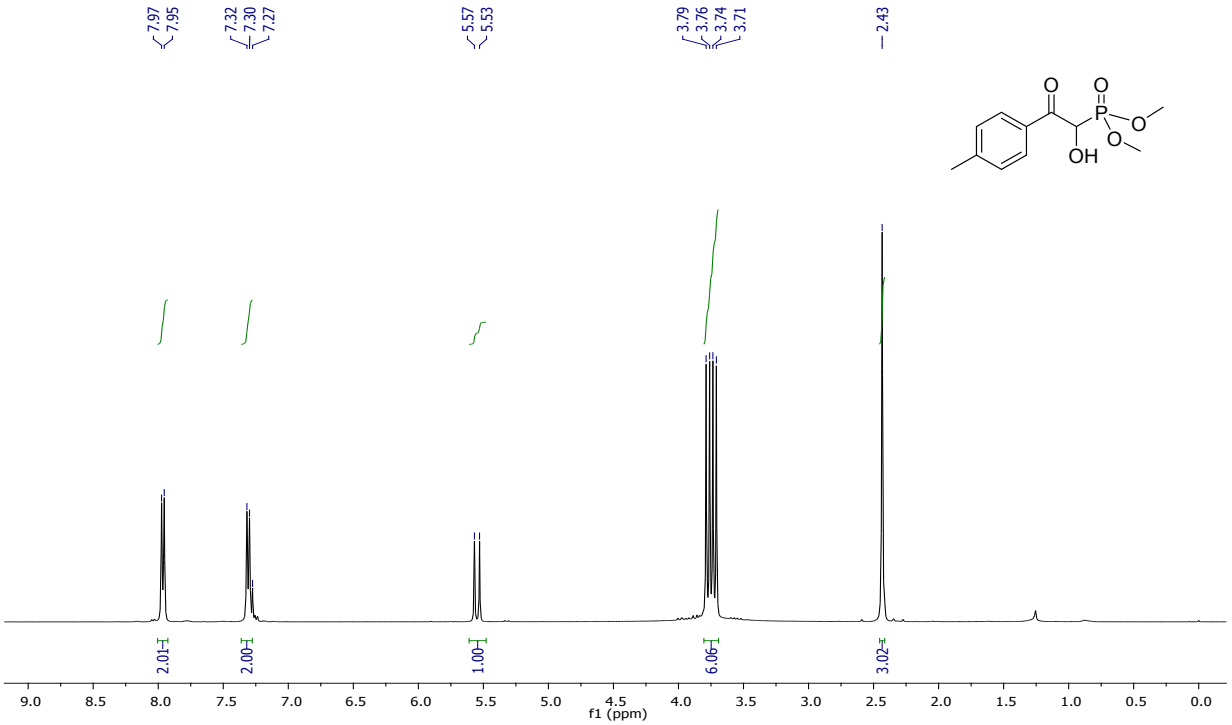
3f. Dimethyl (2-(4-bromophenyl)-1-hydroxy-2-oxoethyl)phosphonate

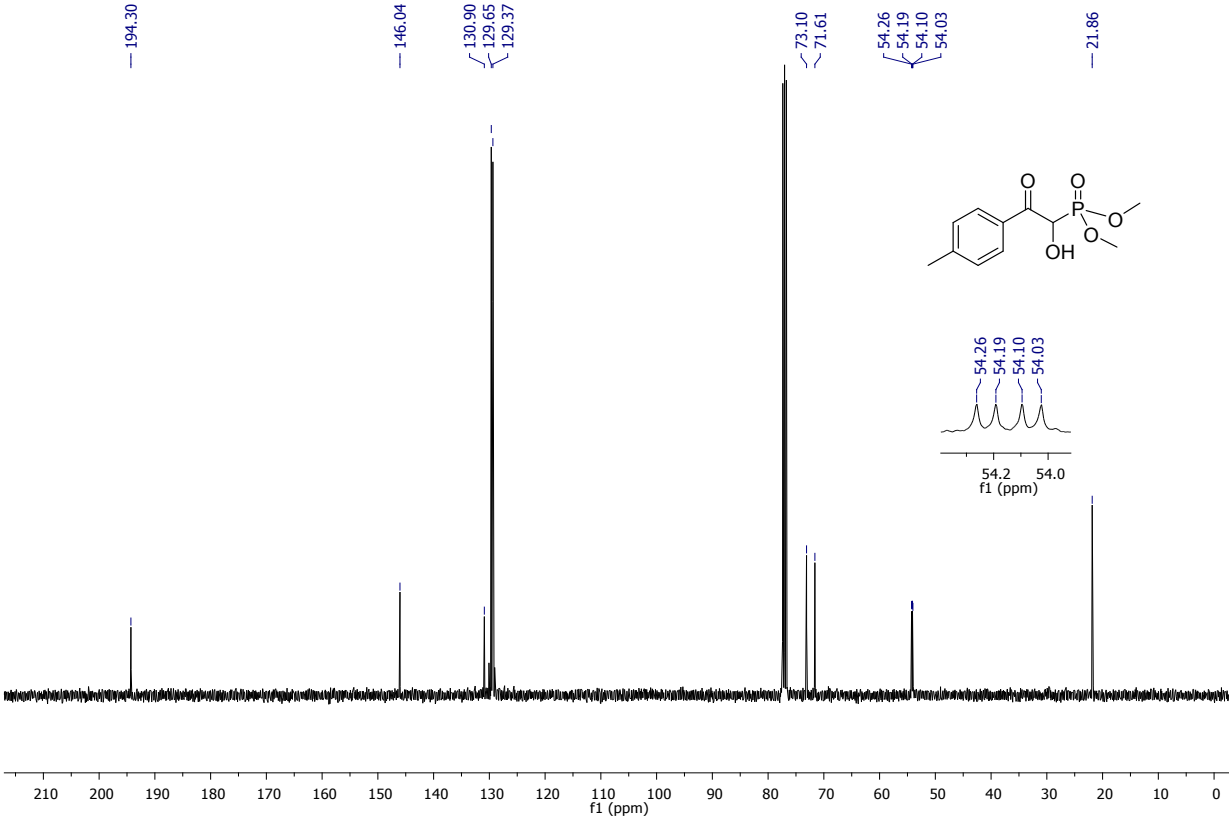


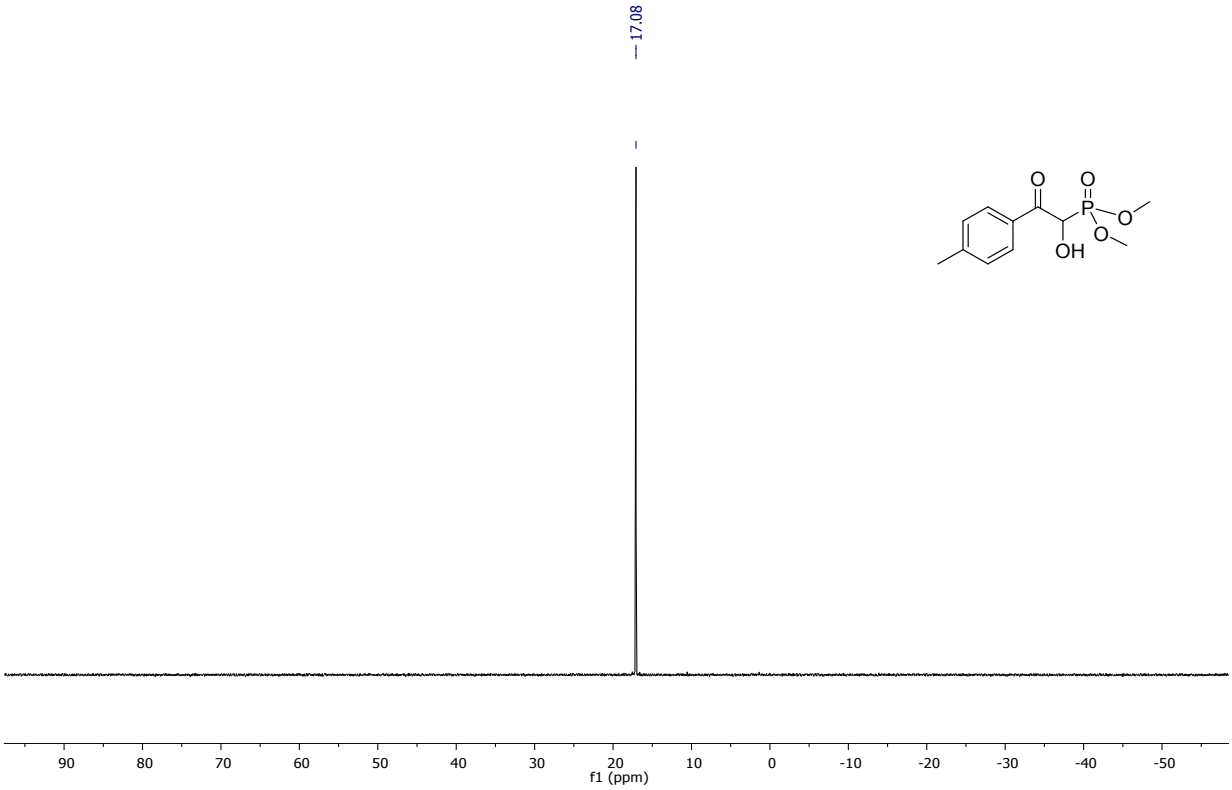

194.02
132.13
132.06
131.79
131.62
130.93
130.33
73.35
71.85
54.43
54.36
54.26
54.19
O
O
P
O
O
OH
Br
54.43
54.36
54.26
54.19
54.4
54.2
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


16.53
O
O
P
O
O
OH
Br
80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55
f1 (ppm)

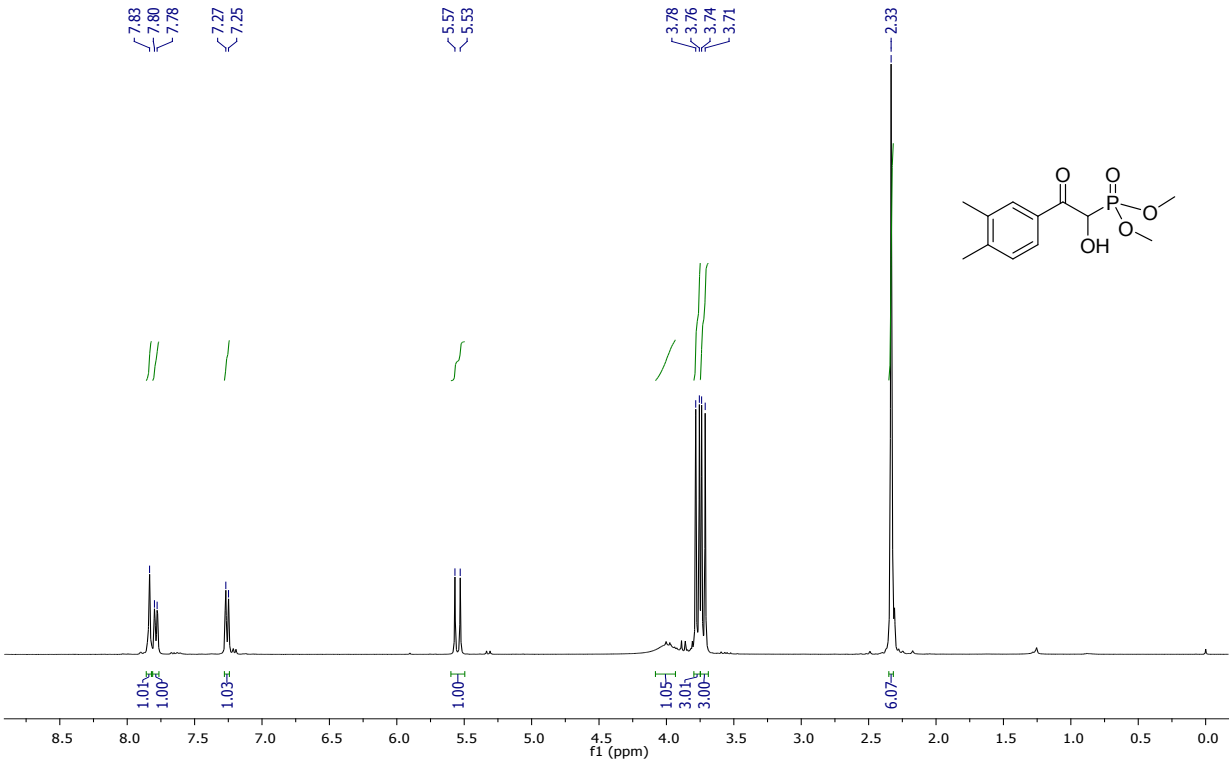
3g. Dimethyl (1-hydroxy-2-oxo-2-(p-tolyl)ethyl)phosphonate

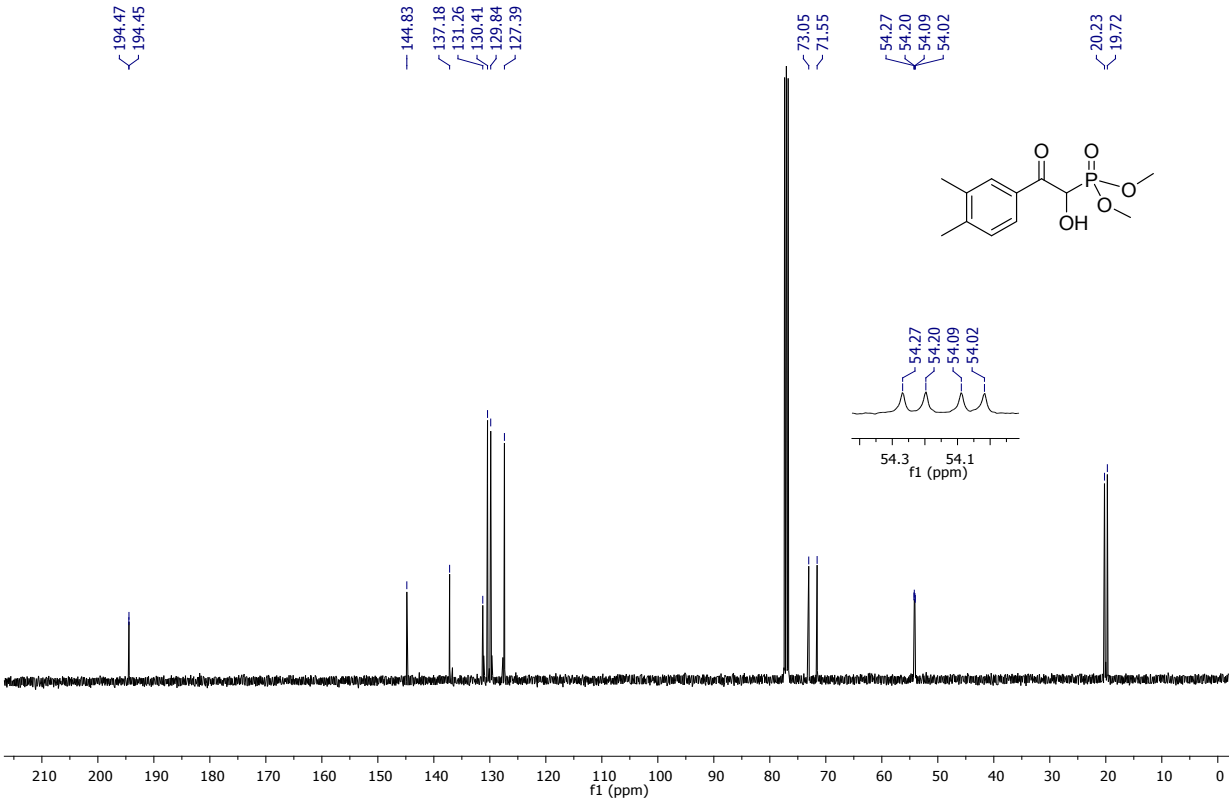


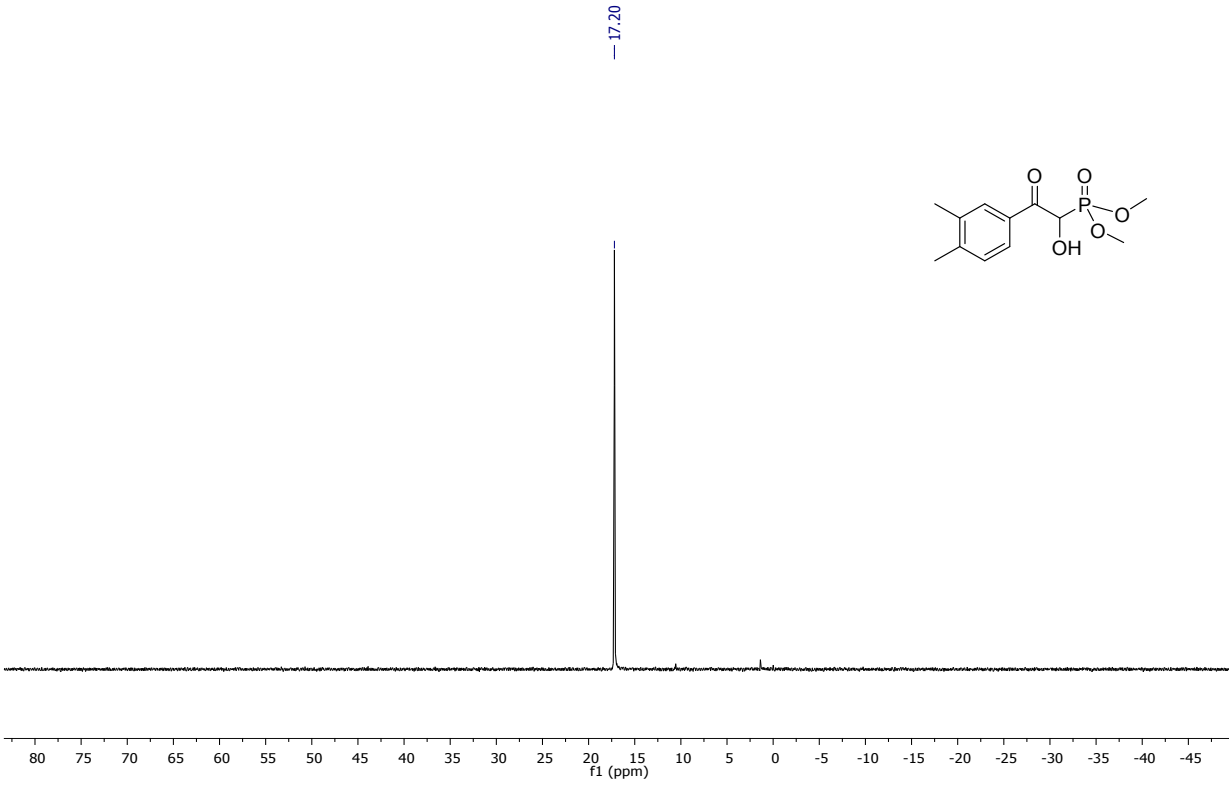




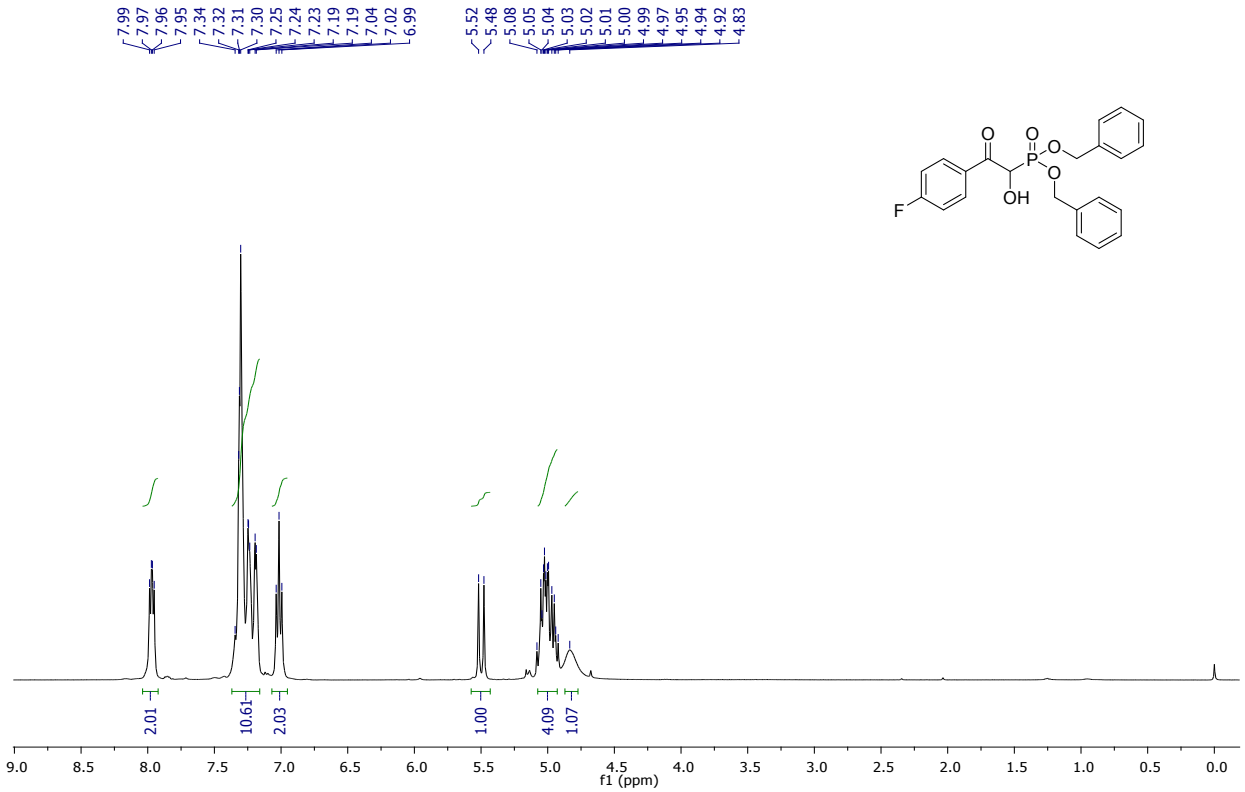
3h. Dimethyl (2-(3,4-dimethylphenyl)-1-hydroxy-2-oxoethyl)phosphonate

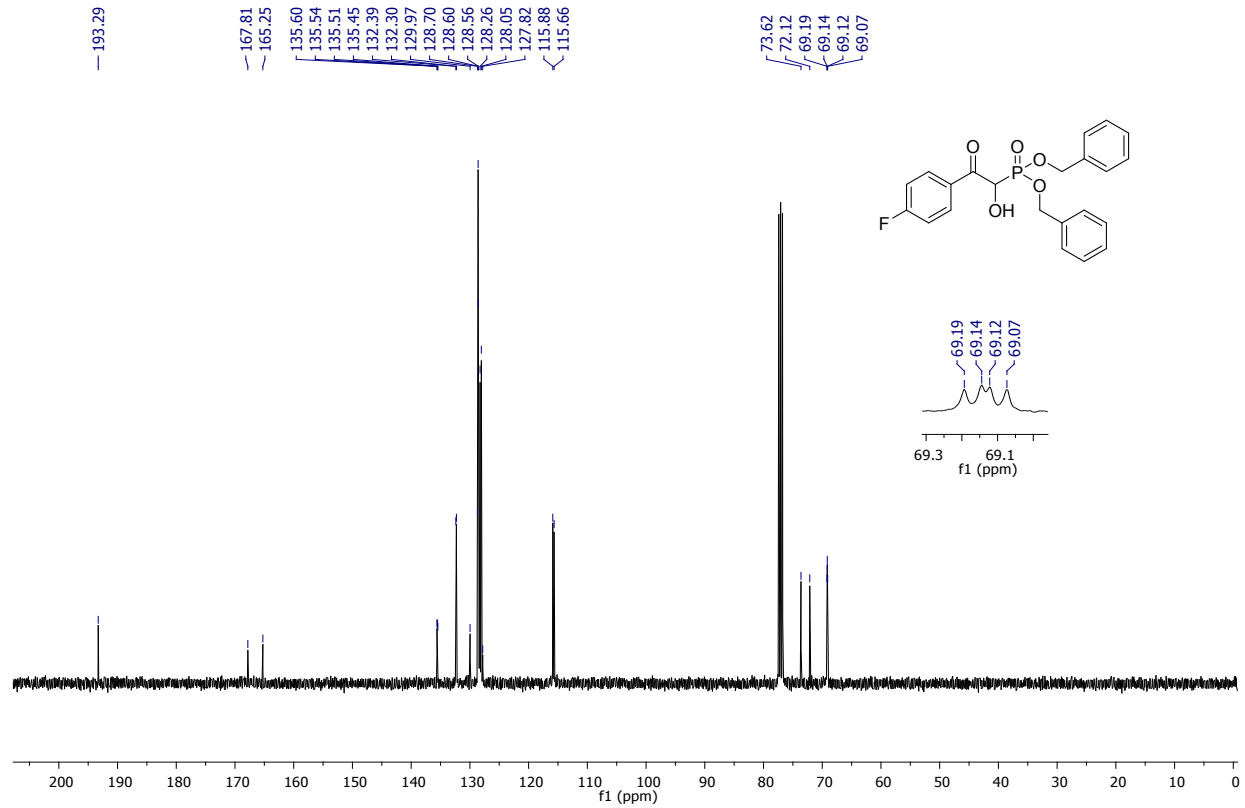


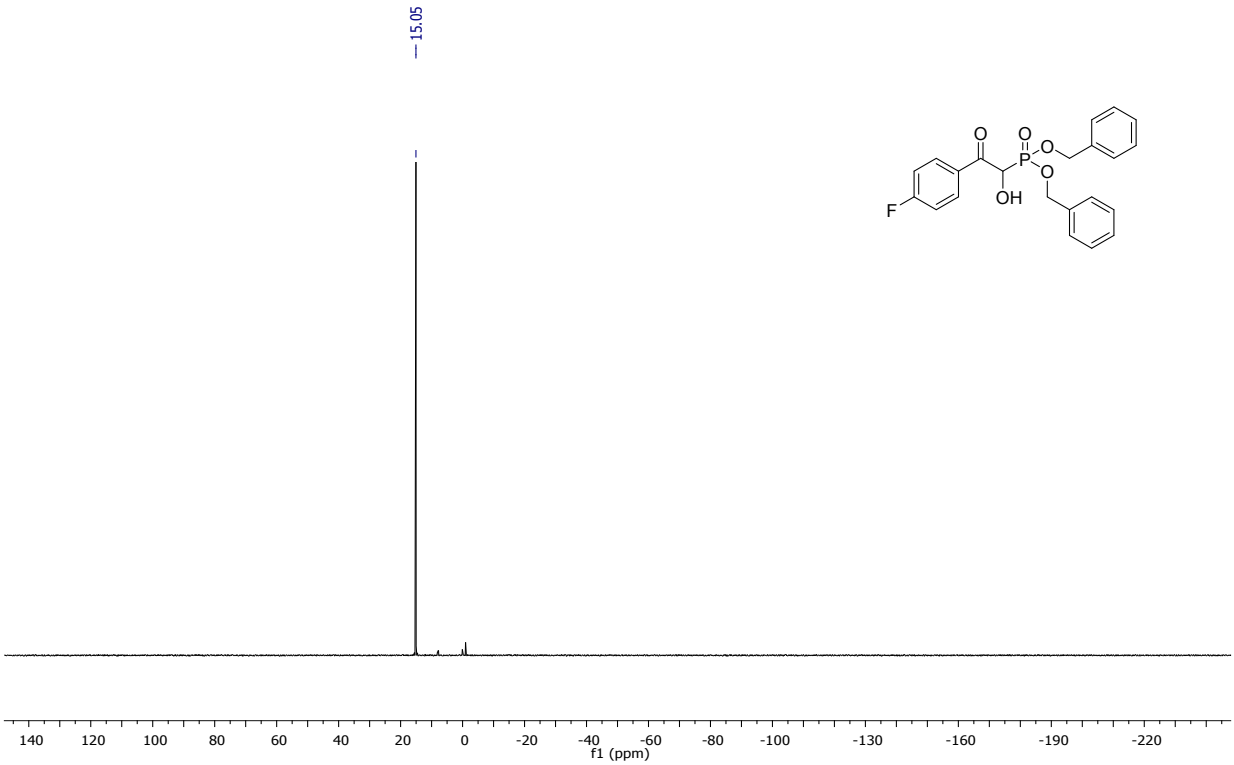

194.47
194.45
144.83
137.18
131.26
130.41
129.84
127.39
73.05
71.55
54.27
54.20
54.09
54.02
20.23
19.72
O
O
P
O
O
OH
54.27
54.20
54.09
54.02
54.3
54.1
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


17.20
O
O
P
O
O
OH
80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 -5 -10 -15 -20 -25 -30 -35 -40 -45
f1 (ppm)

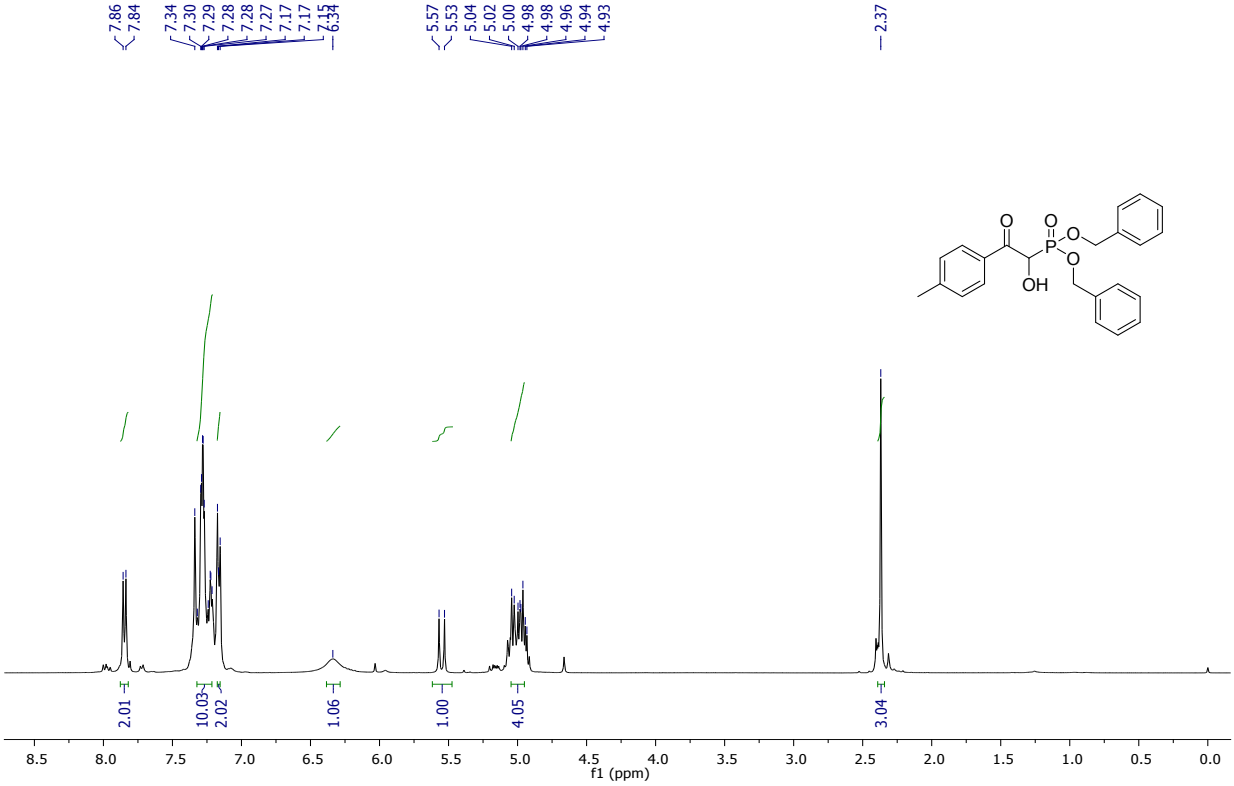
3i. Dibenzyl (2-(4-fluorophenyl)-1-hydroxy-2-oxoethyl)phosphonate

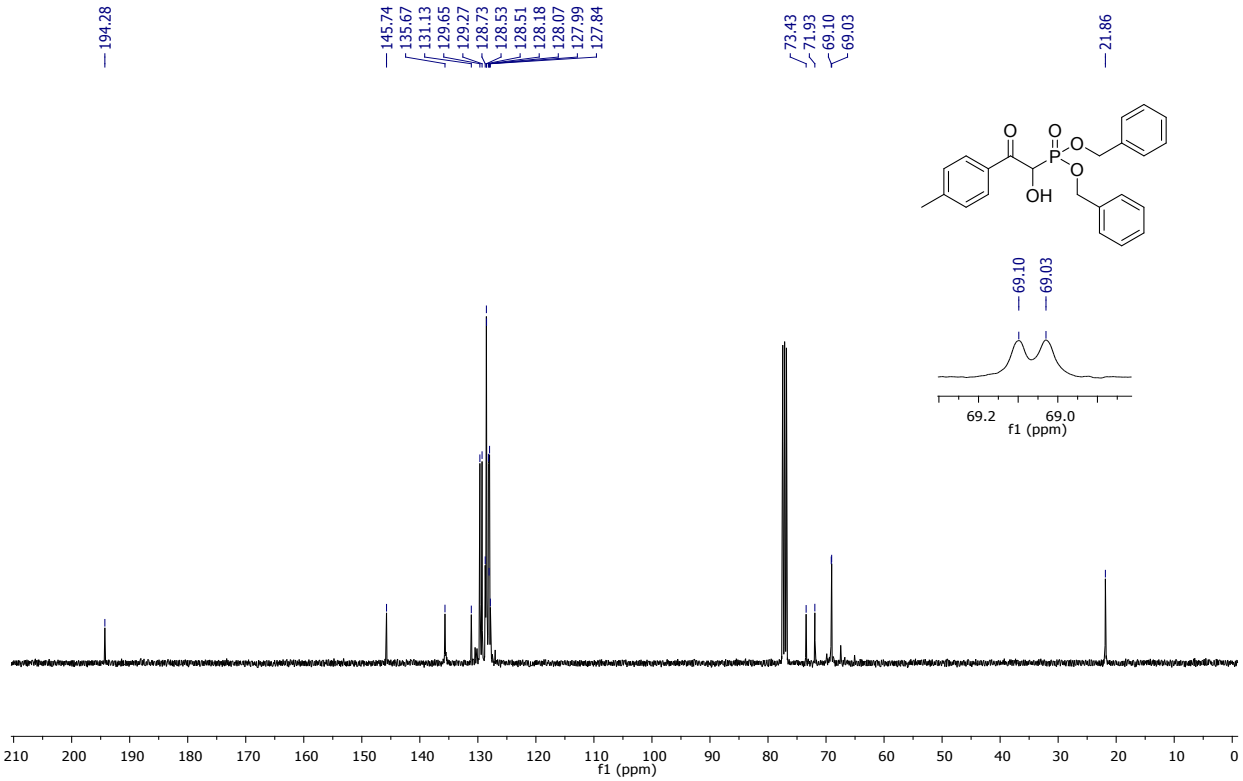


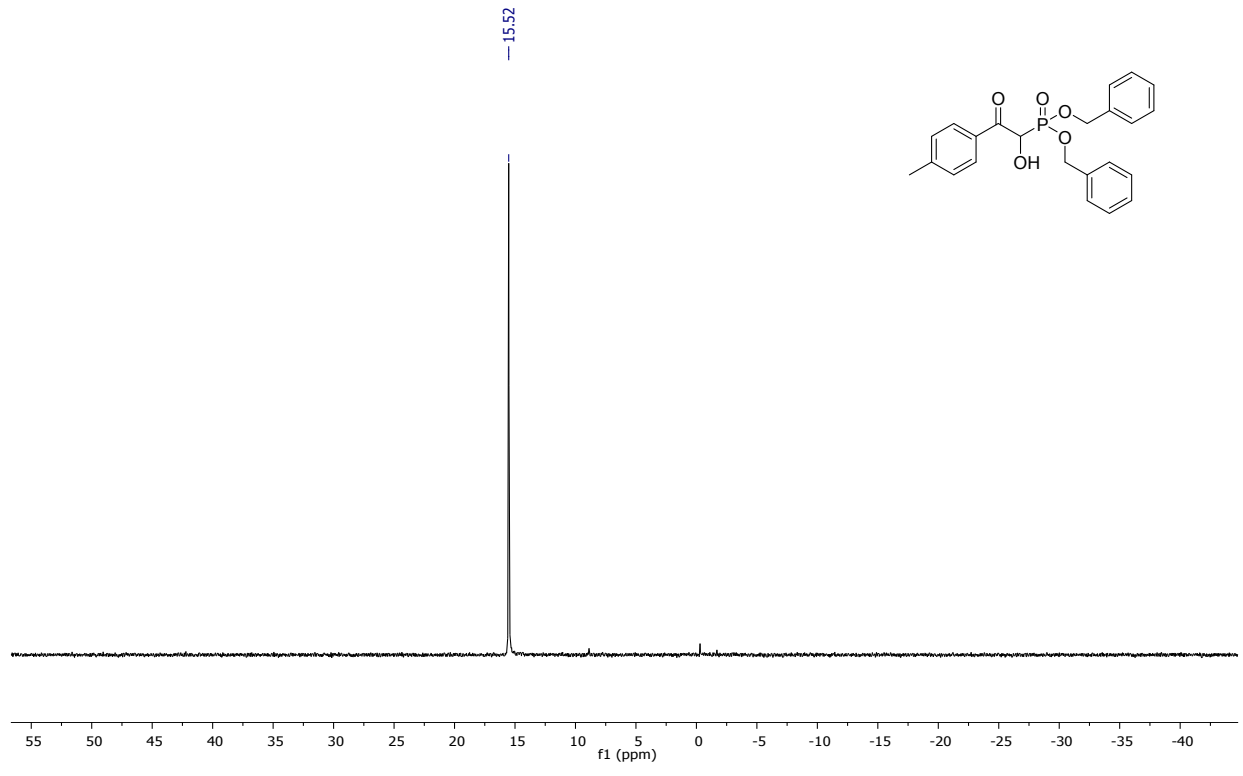




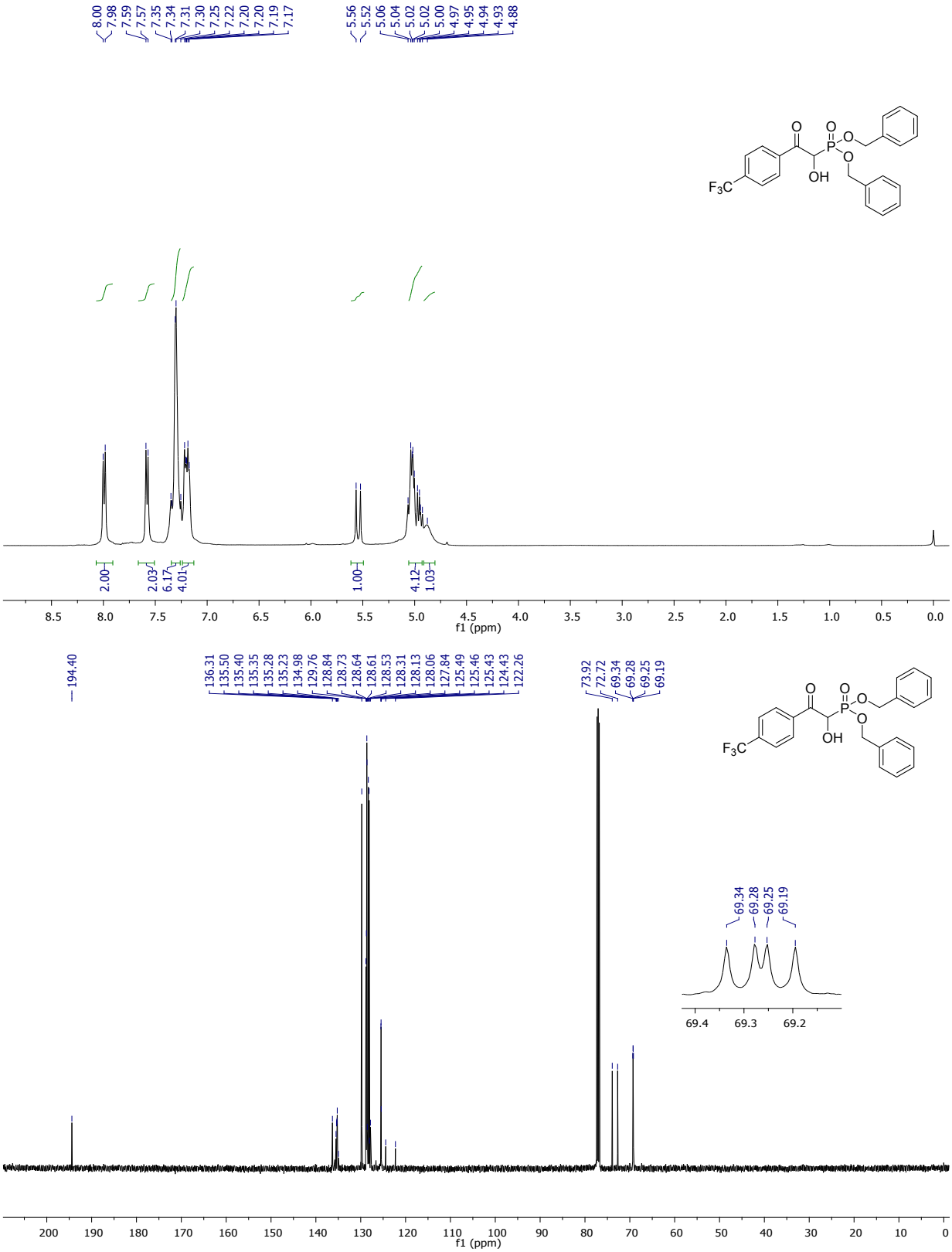
3j. Dibenzyl (1-hydroxy-2-oxo-2-(p-tolyl)ethyl)phosphonate

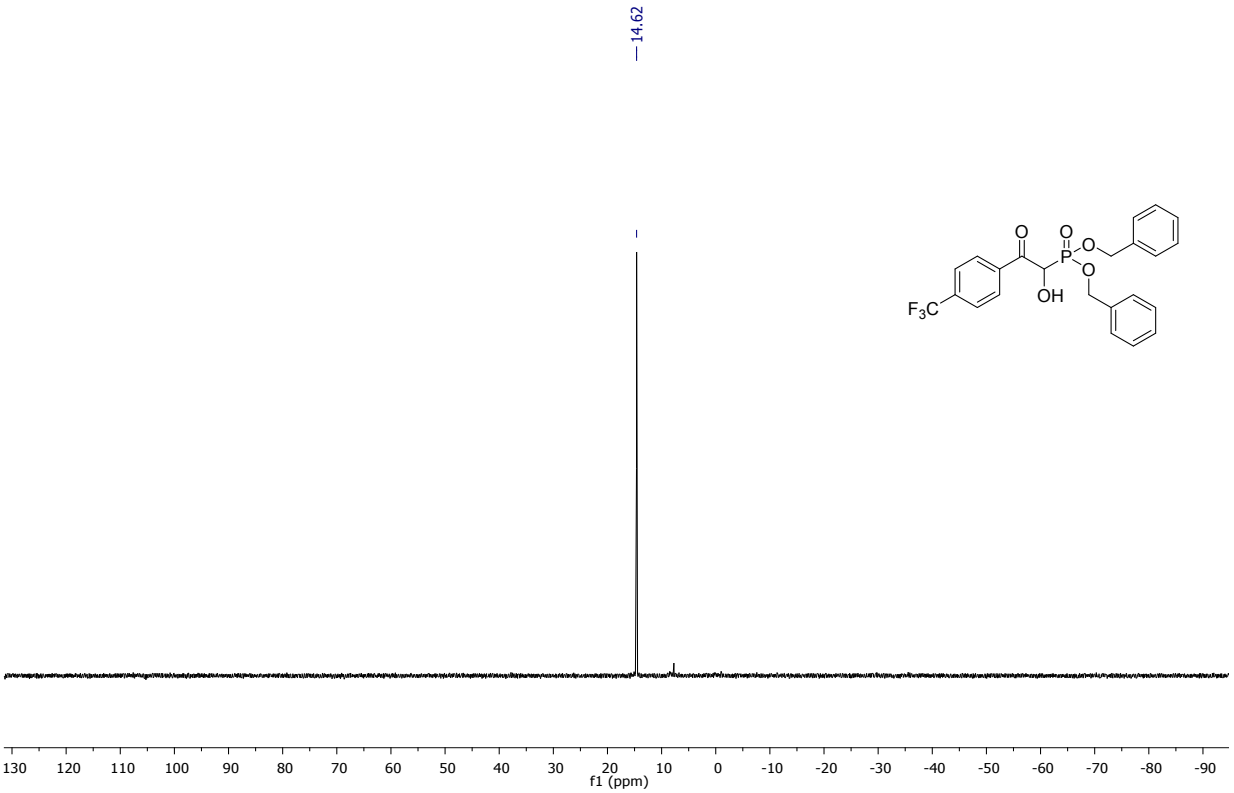



194.28
145.74
135.67
131.13
129.65
129.27
128.73
128.53
128.51
128.18
128.07
127.99
127.84
73.43
71.93
69.10
69.03
21.86
O
O
P
O
O
OH
69.10
69.03
69.2
69.0
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

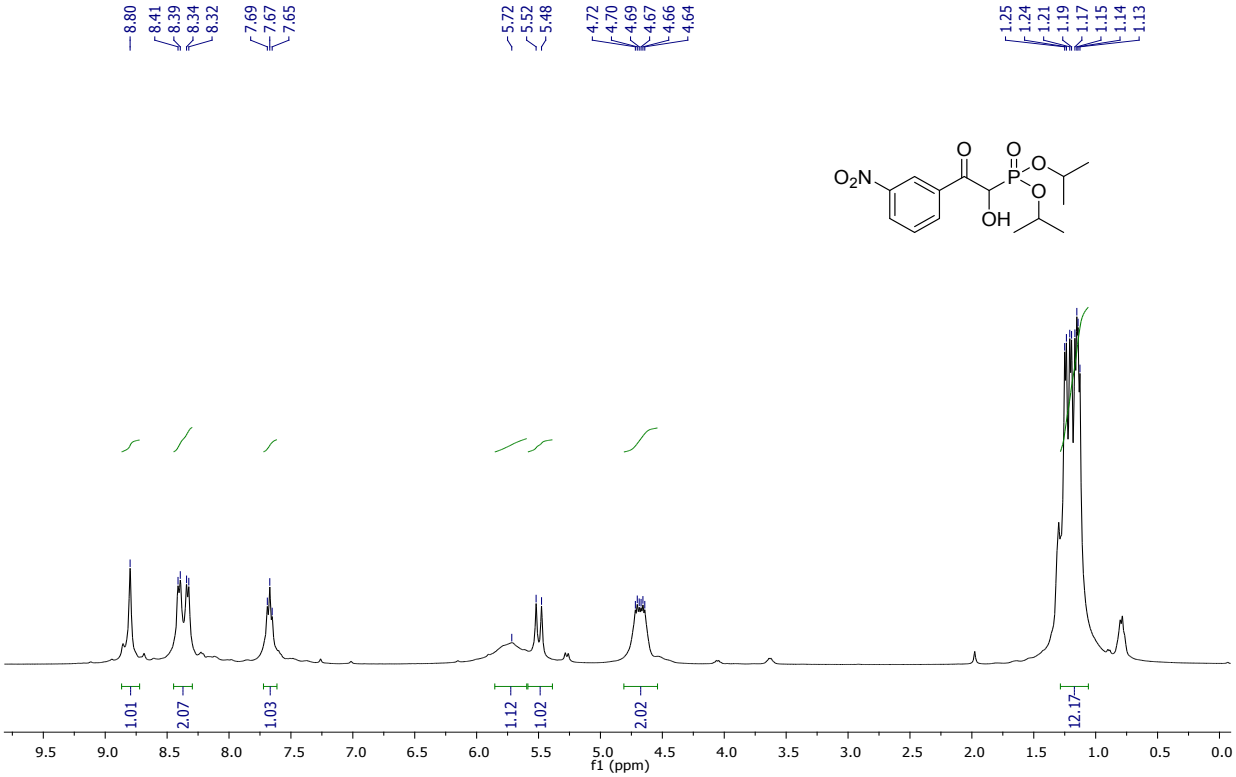

15.52
O
O
P
O
O
OH
55
50
45
40
35
30
25
20
15
10
5
0
-5
-10
-15
-20
-25
-30
-35
-40
f1 (ppm)

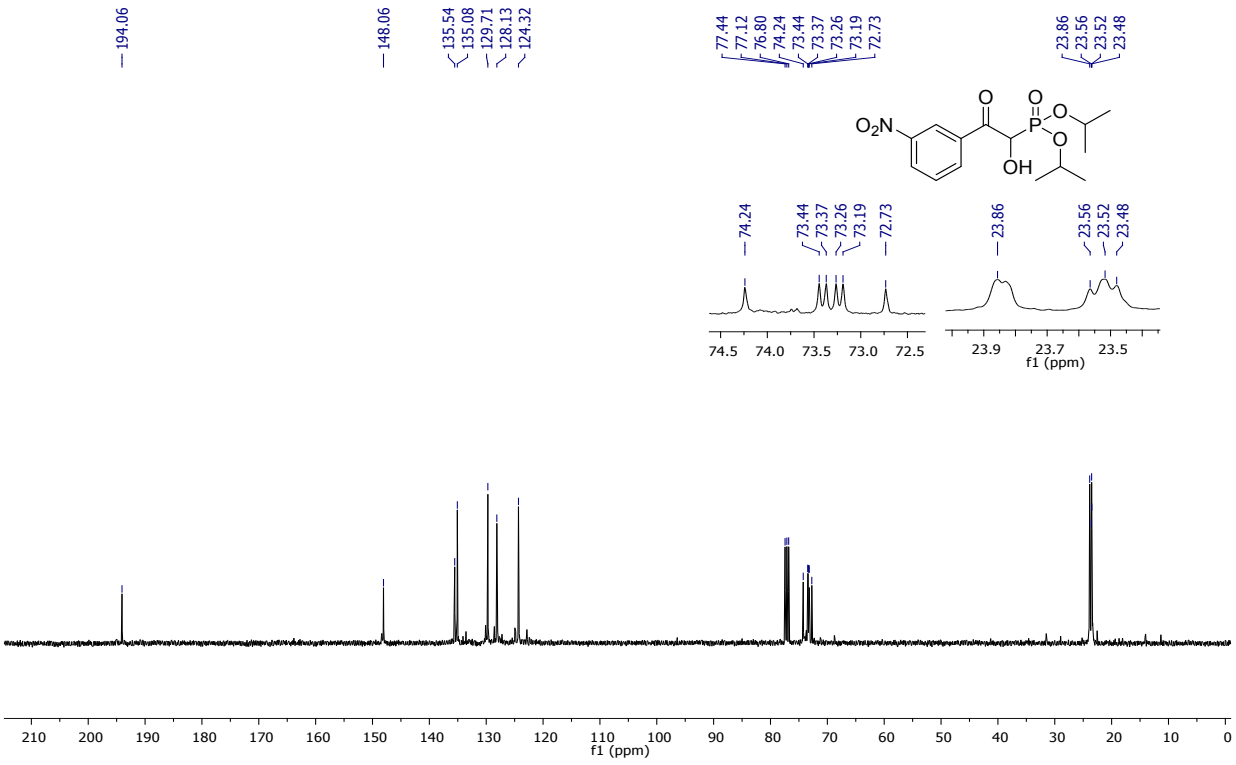
3k. Dibenzyl (R)-(1-hydroxy-2-oxo-2-(4-(trifluoromethyl)phenyl)ethyl)phosphonate

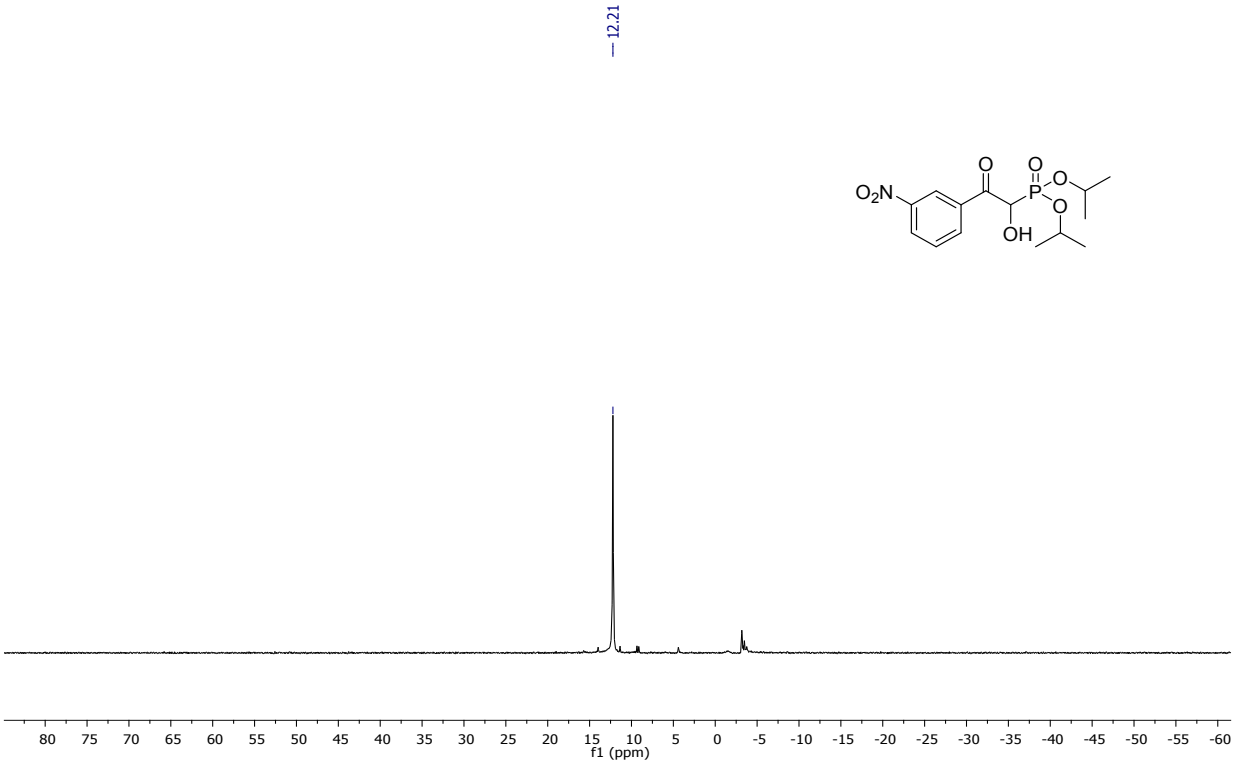




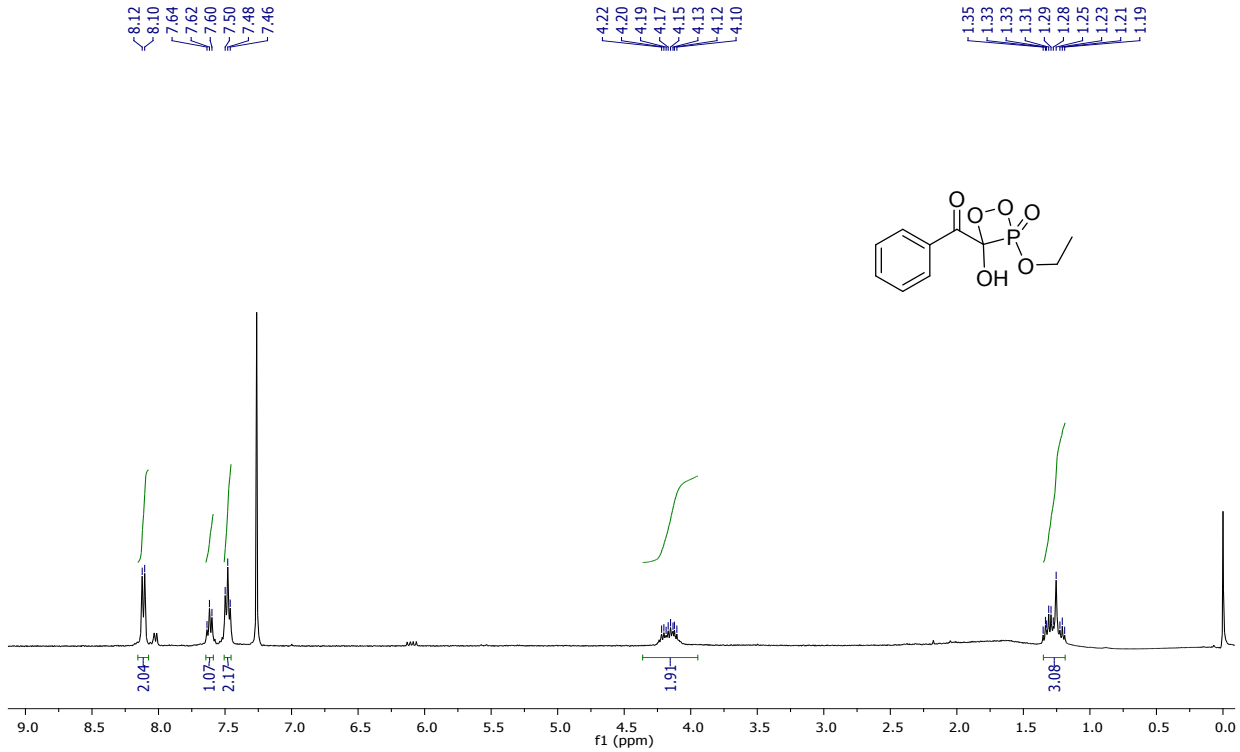
3l. Diisopropyl (1-hydroxy-2-(3-nitrophenyl)-2-oxoethyl)phosphonate



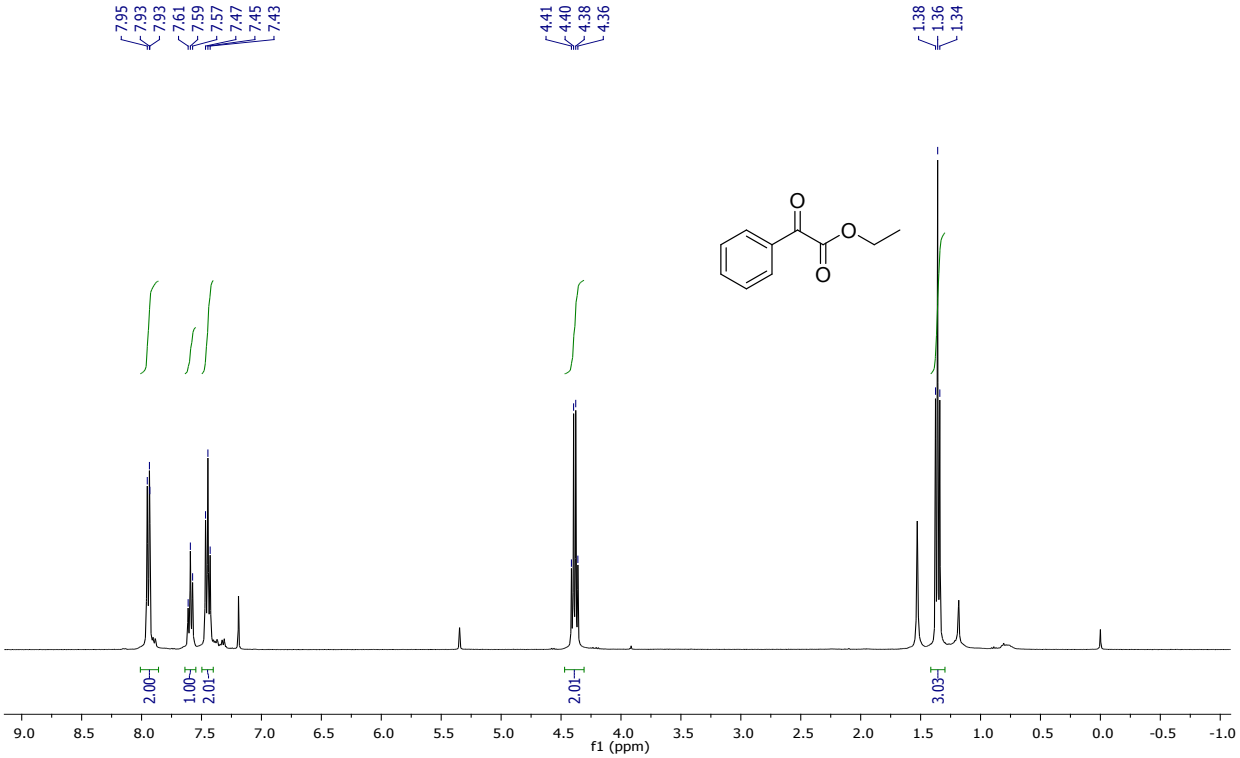

194.06
148.06
135.54
135.08
129.71
128.13
124.32
77.44
77.12
76.80
74.24
73.44
73.37
73.26
73.19
72.73
23.86
23.56
23.52
23.48
O2N
O
O
P
O
O
OH
74.24
73.44
73.37
73.26
73.19
72.73
23.86
23.56
23.52
23.48
74.5 74.0 73.5 73.0 72.5
23.9 23.7 23.5
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

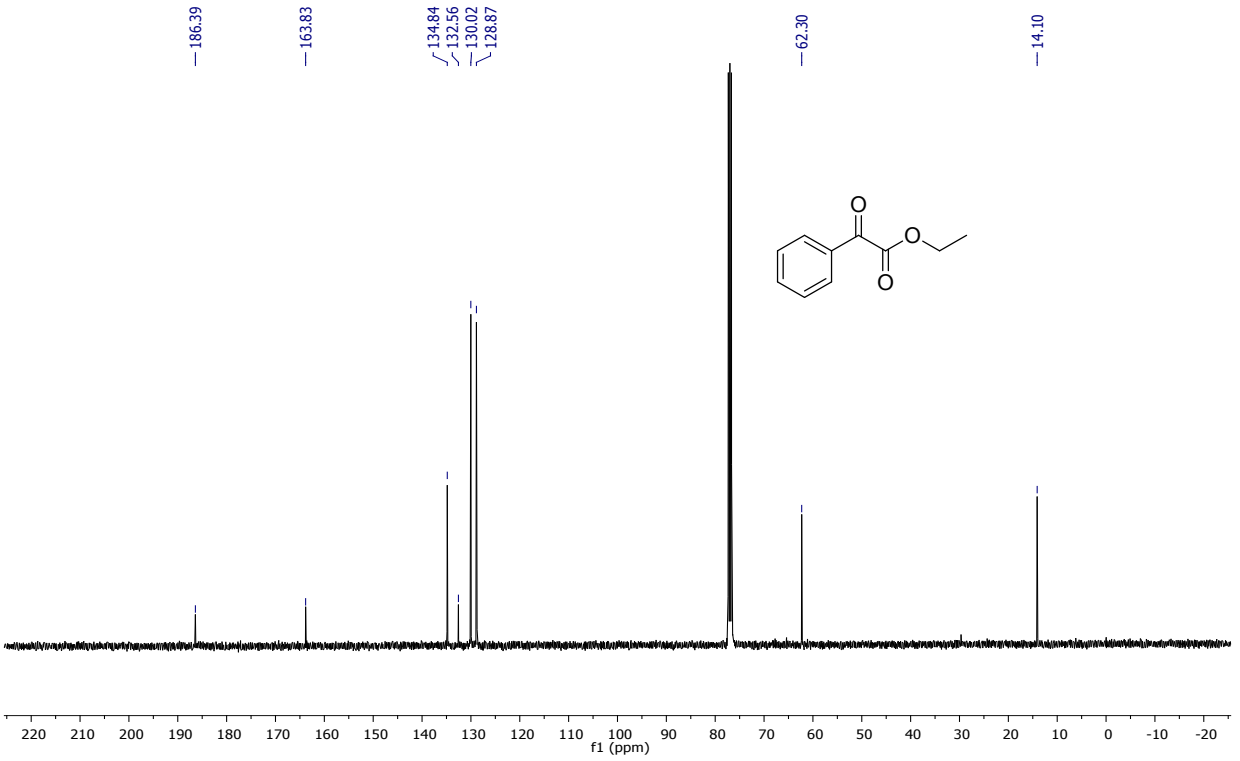

12.21
O2N
O
O
P
O
O
OH
80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60
f1 (ppm)

[1]H-NMR Spectra of DOP intermediate

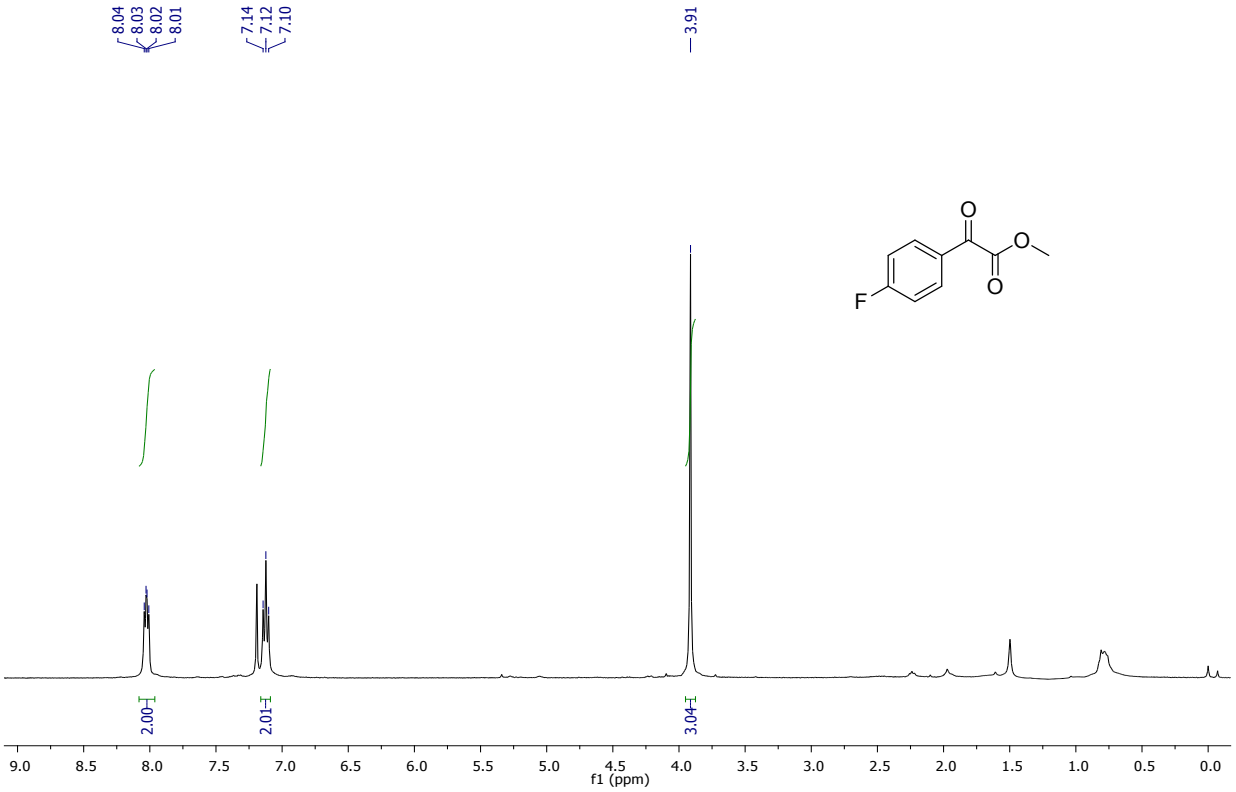


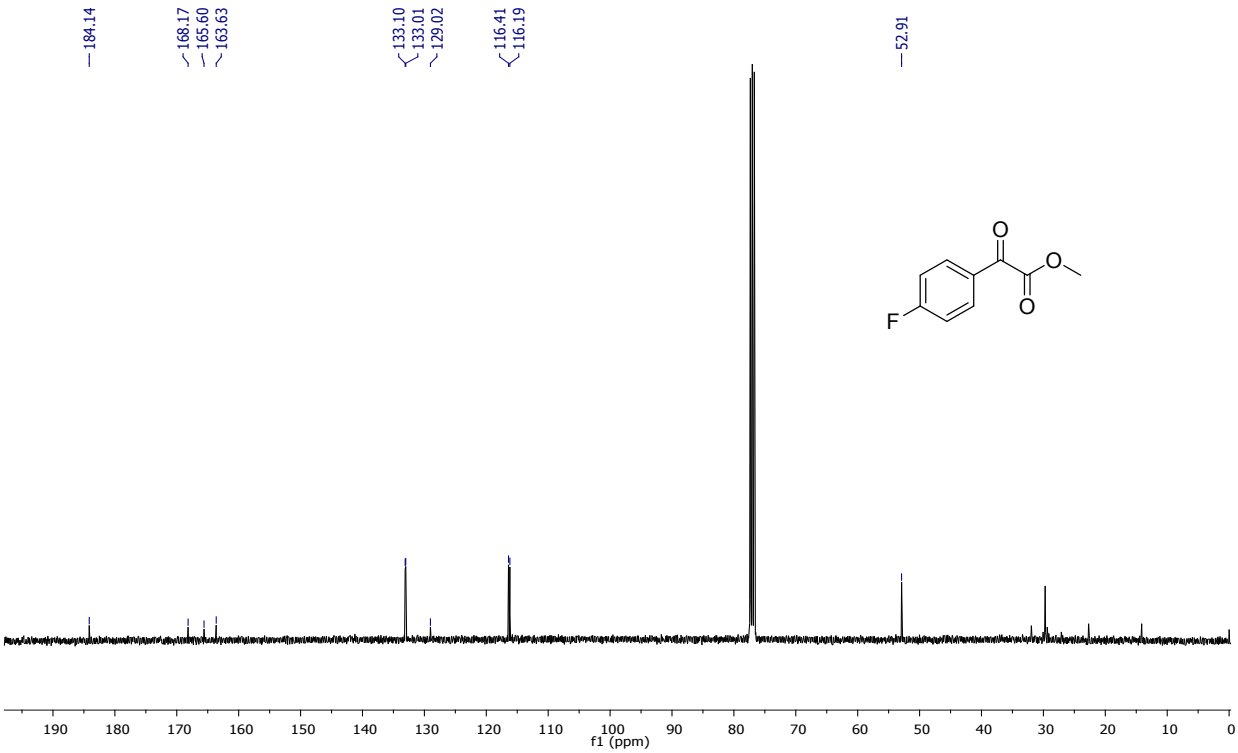
4a. Ethyl-2-oxo-2-phenylacetate



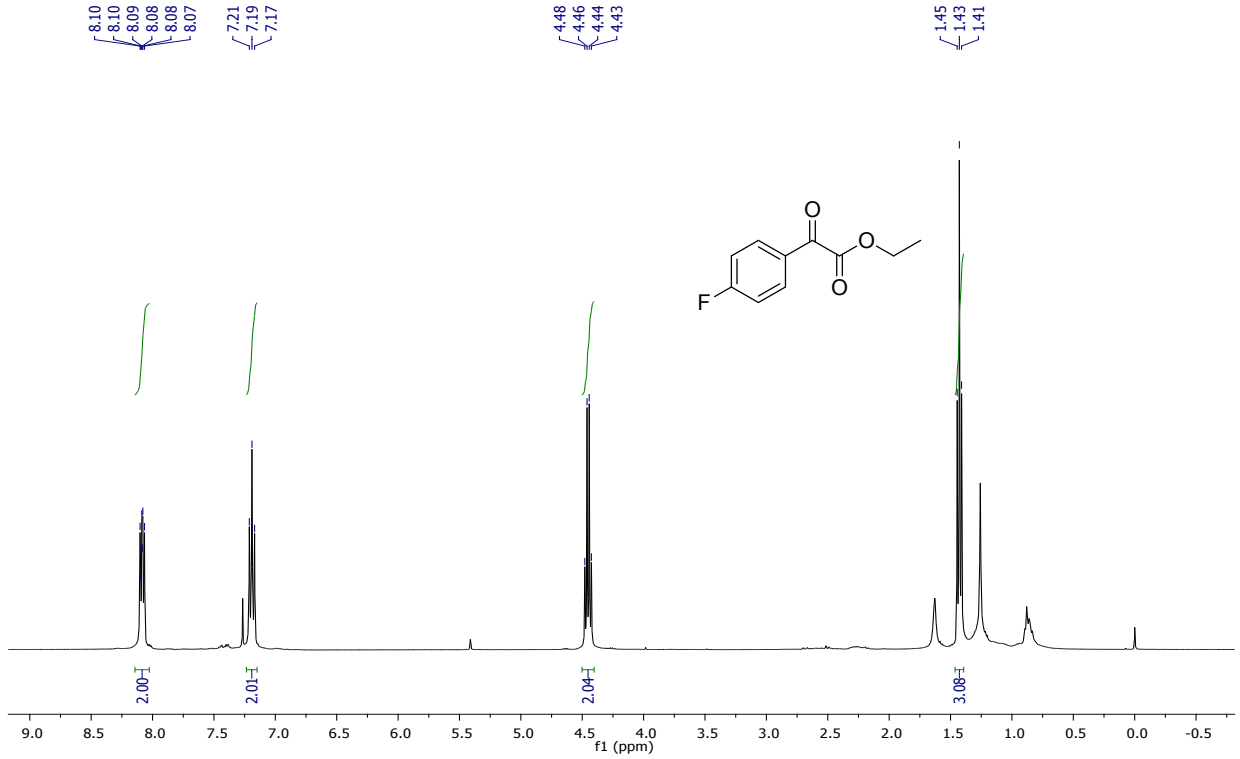


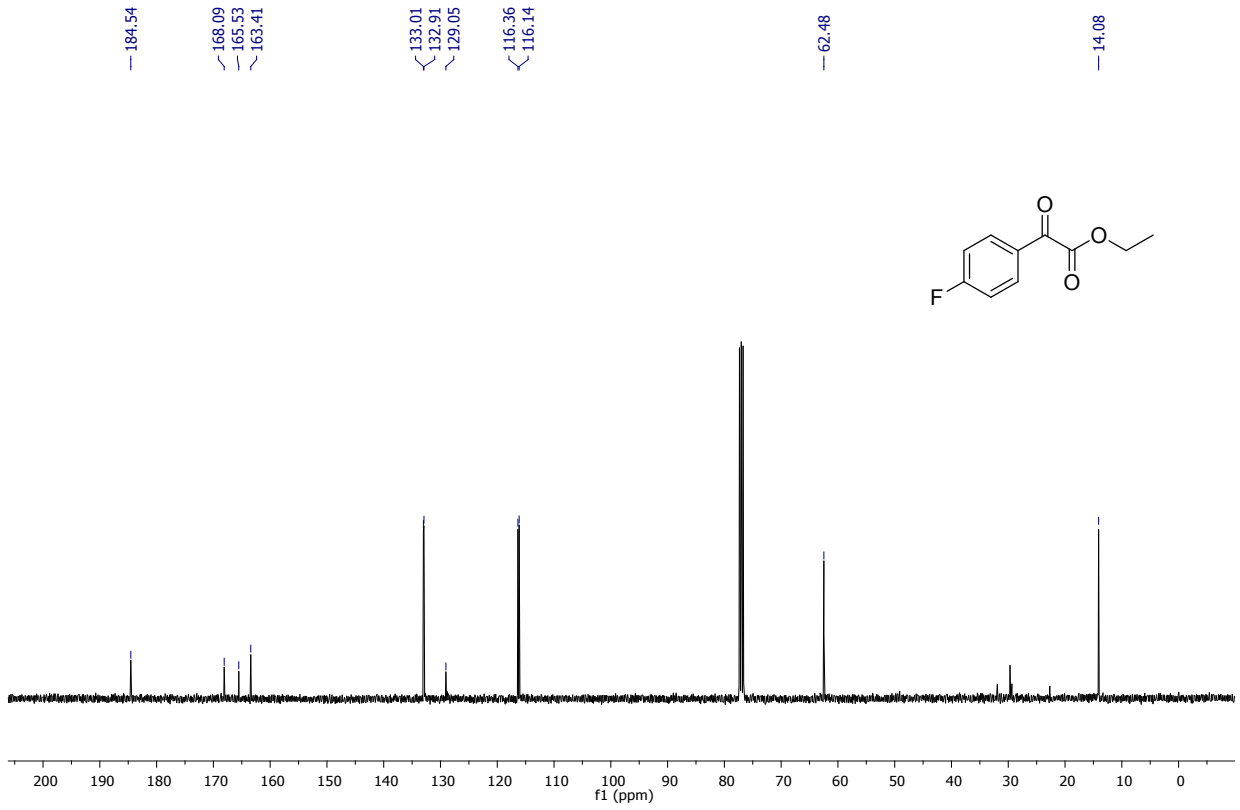
4b. Methyl-2-oxo-2-phenylacetate.



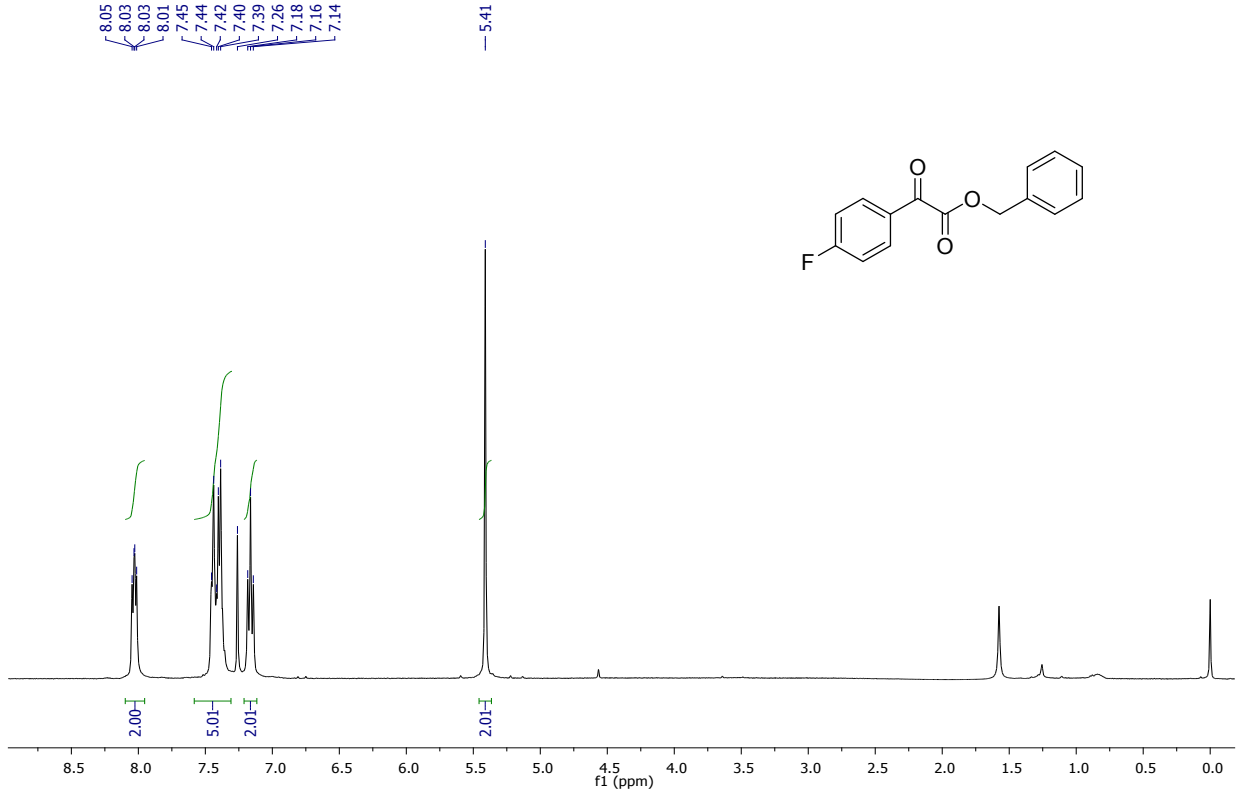


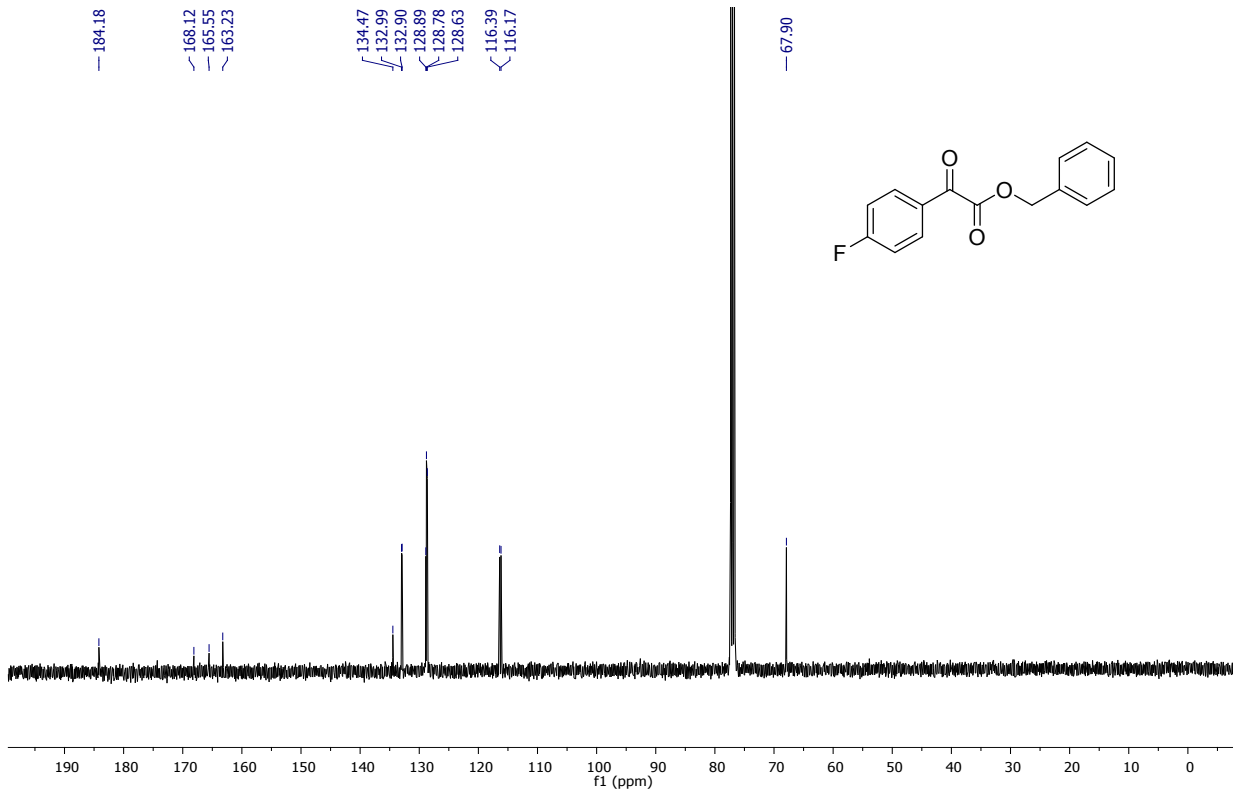
4c. Ethyl-2-(4-fluorophenyl)-2-oxoacetate



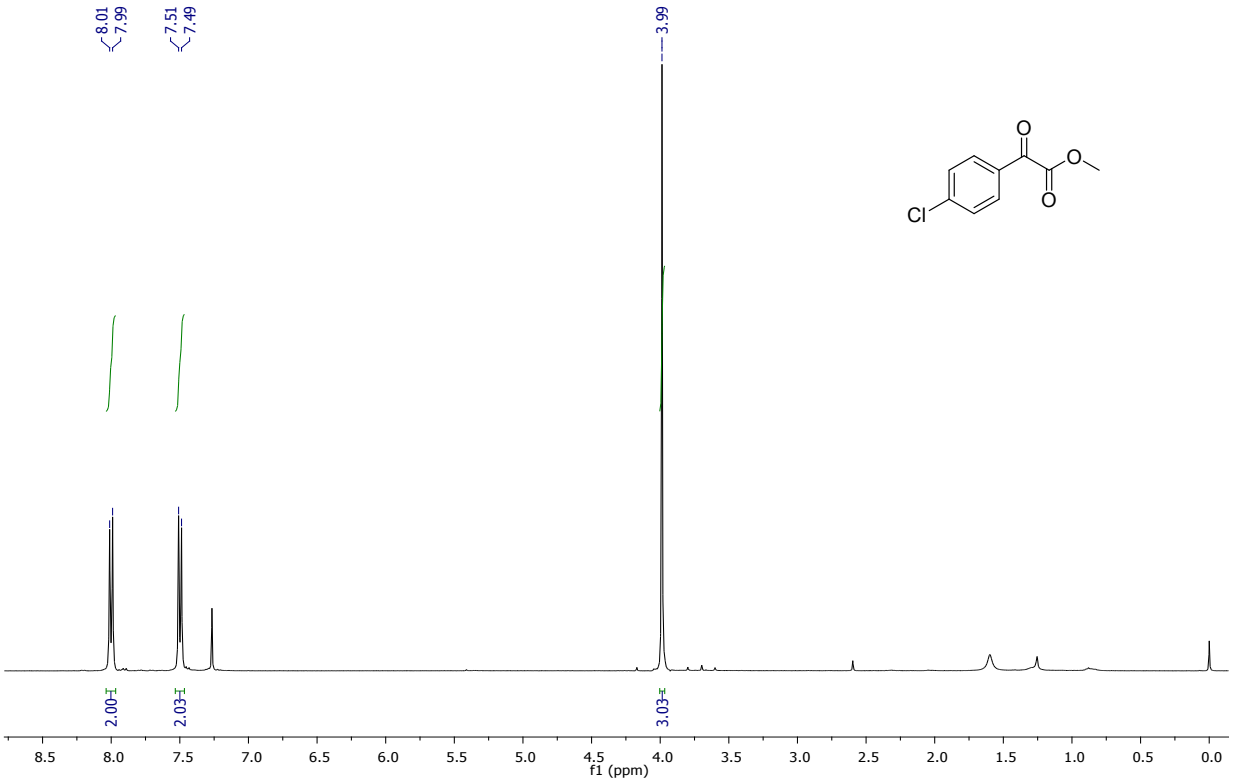


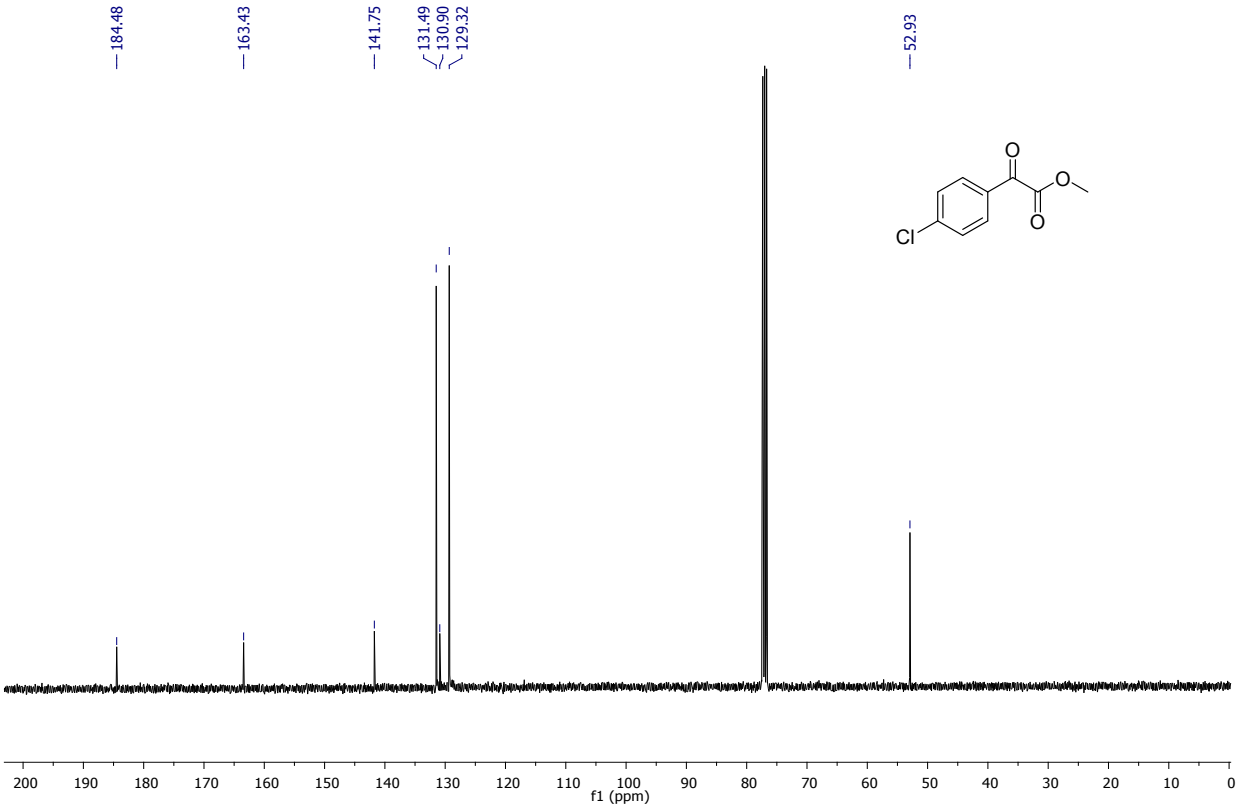
4d. Benzyl-2-(4-fluorophenyl)-2-oxoacetate



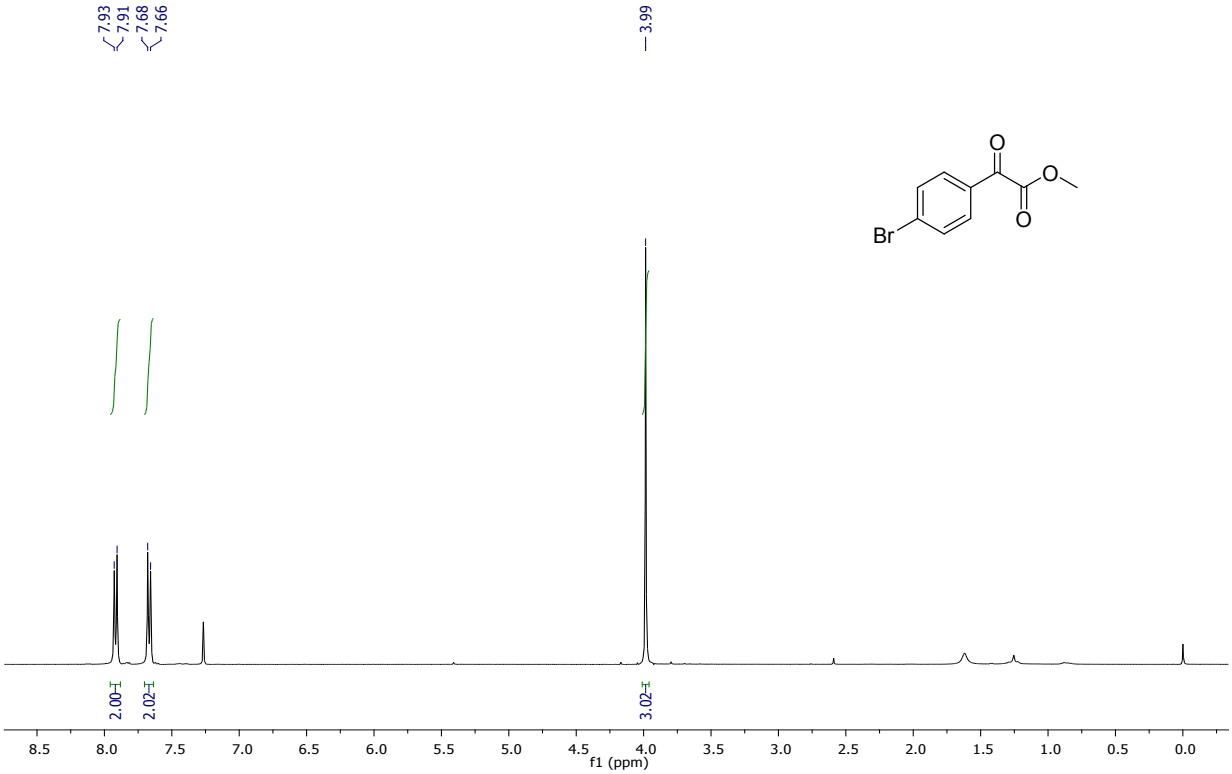


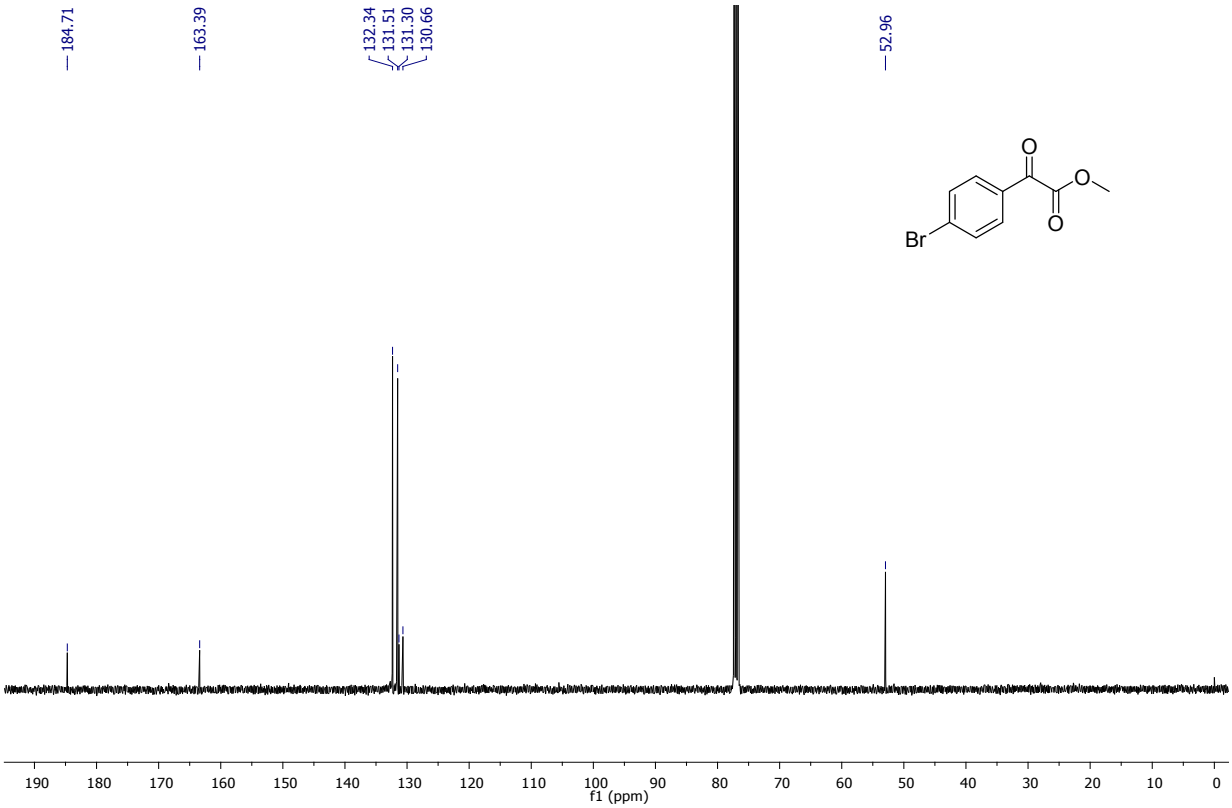
4e. Methyl 2-(4-chlorophenyl)-2-oxoacetate



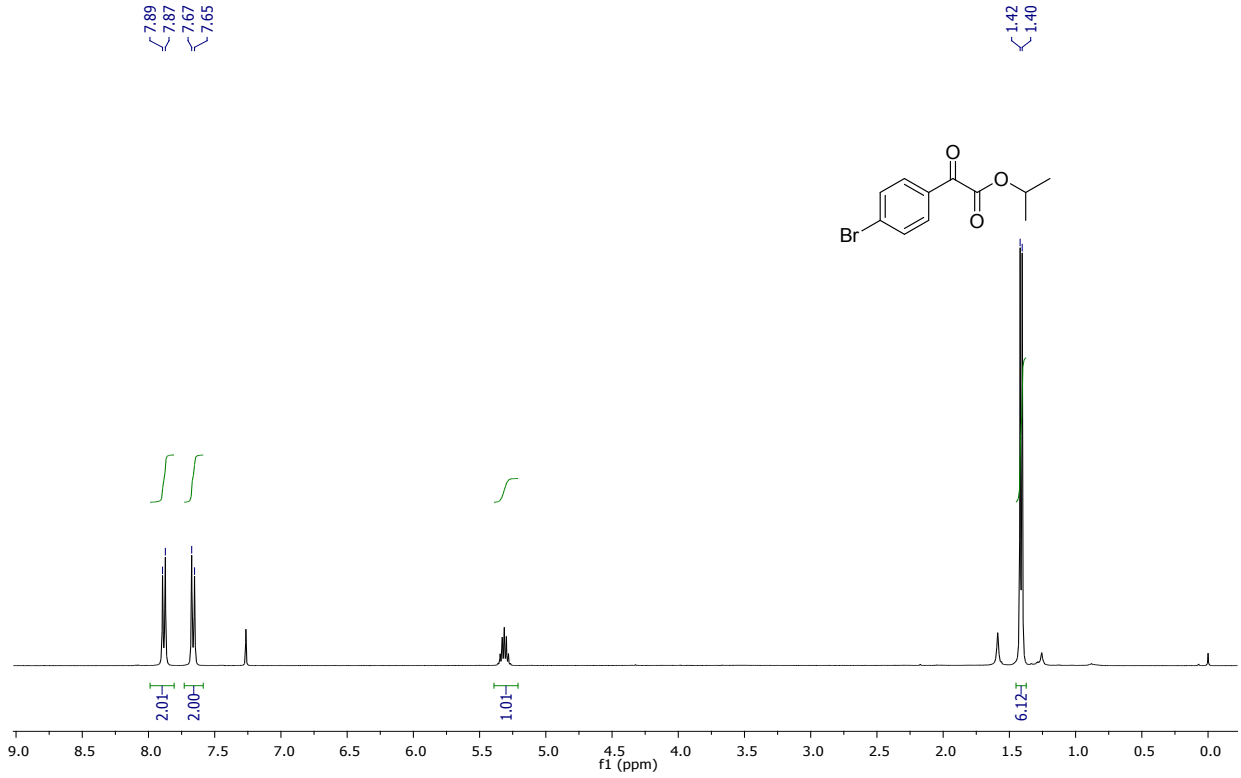


4f. Methyl 2-(4-bromophenyl)-2-oxoacetate

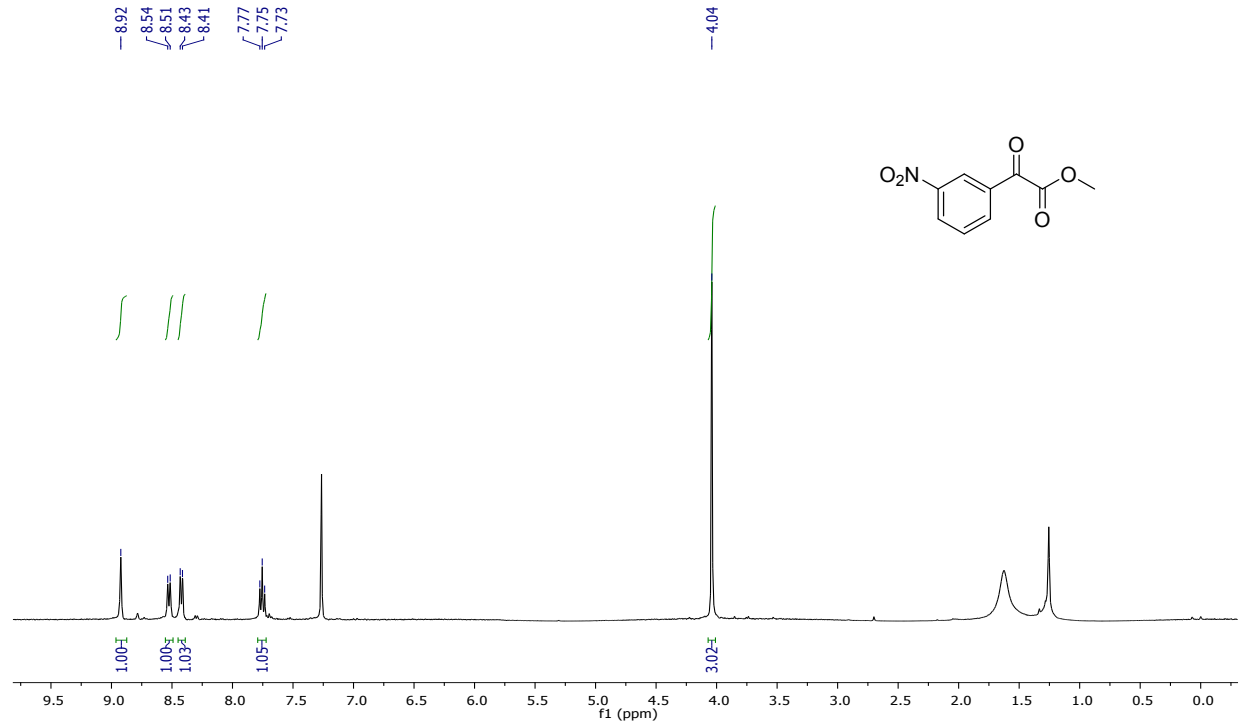




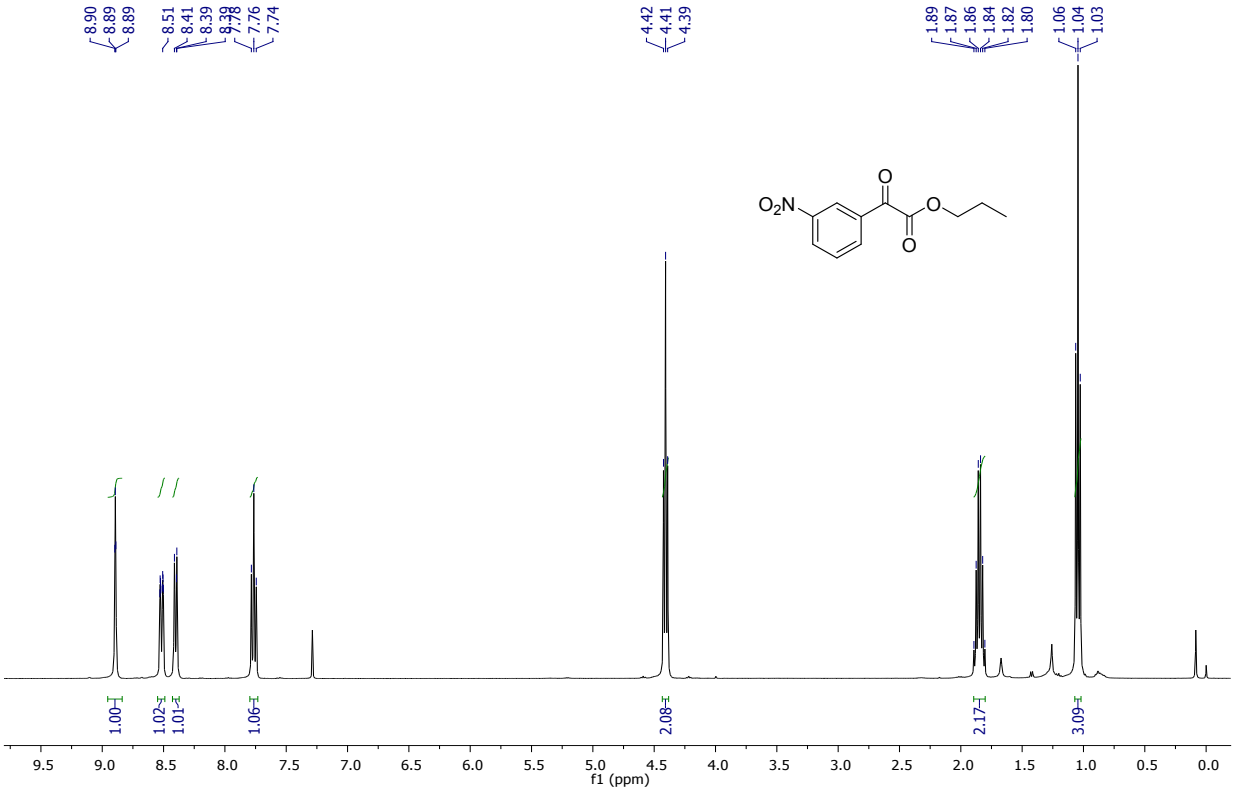
4g. Isopropyl 2-(4-bromophenyl)-2-oxoacetate

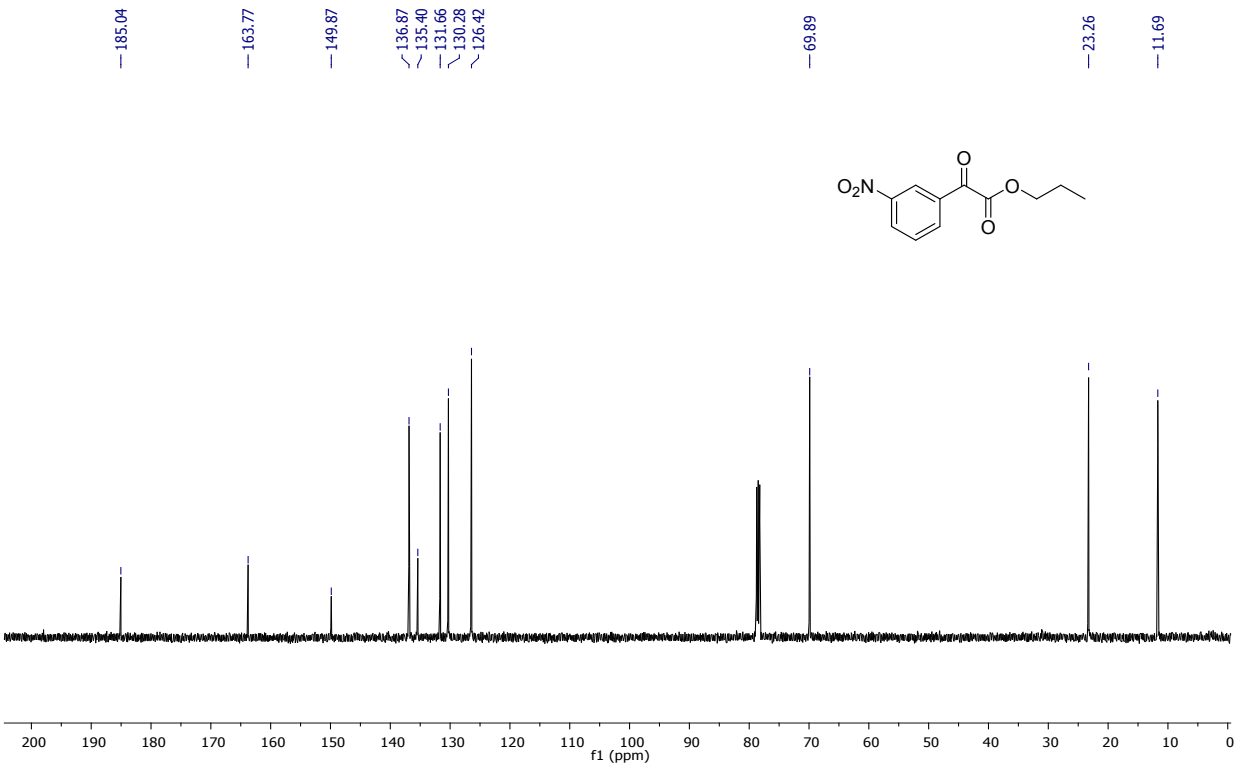


4h. Methyl-2-(3-nitrophenyl)-2-oxoacetate

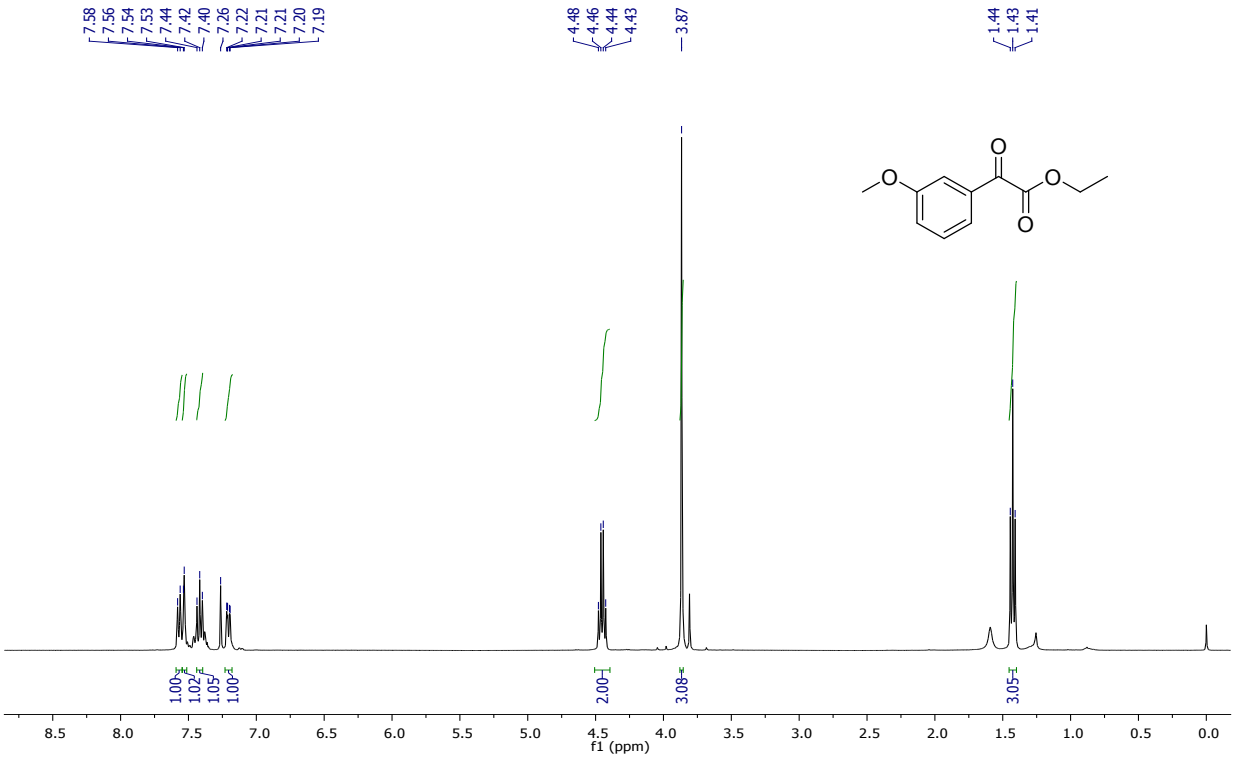


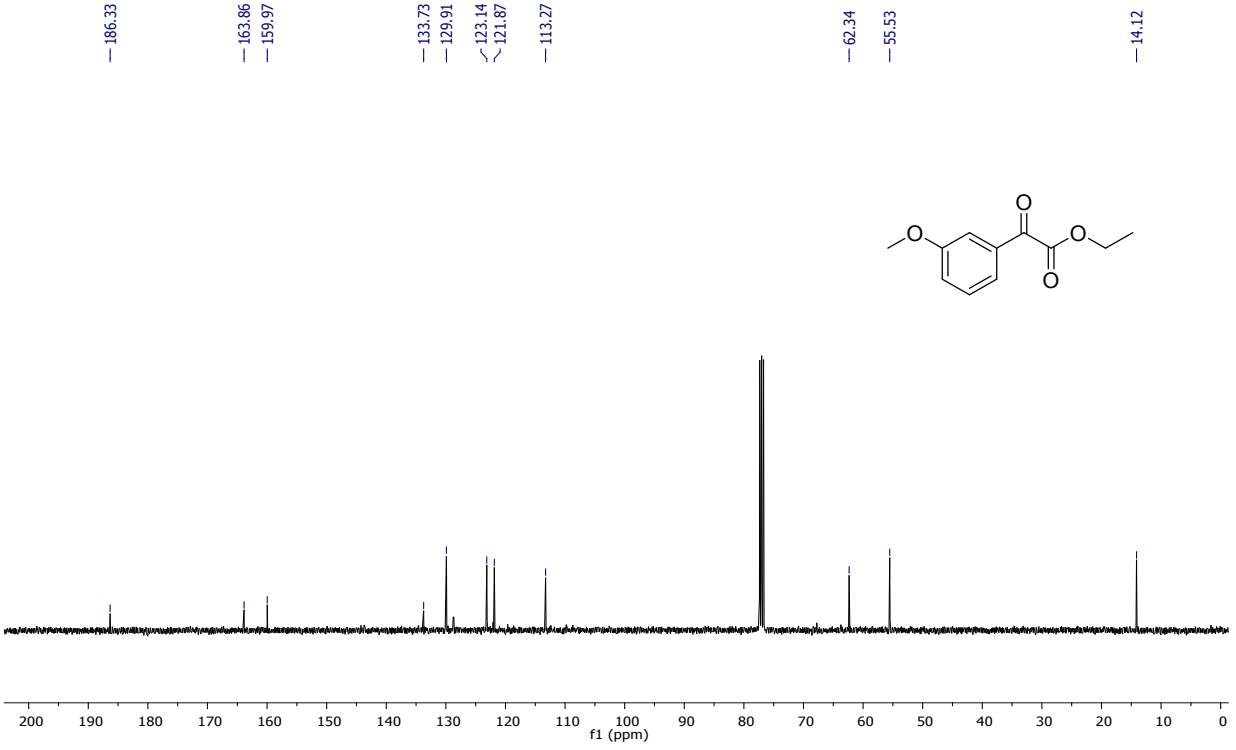
4i. Dipropyl (1-hydroxy-2-(3-nitrophenyl)-2-oxoethyl)phosphonate



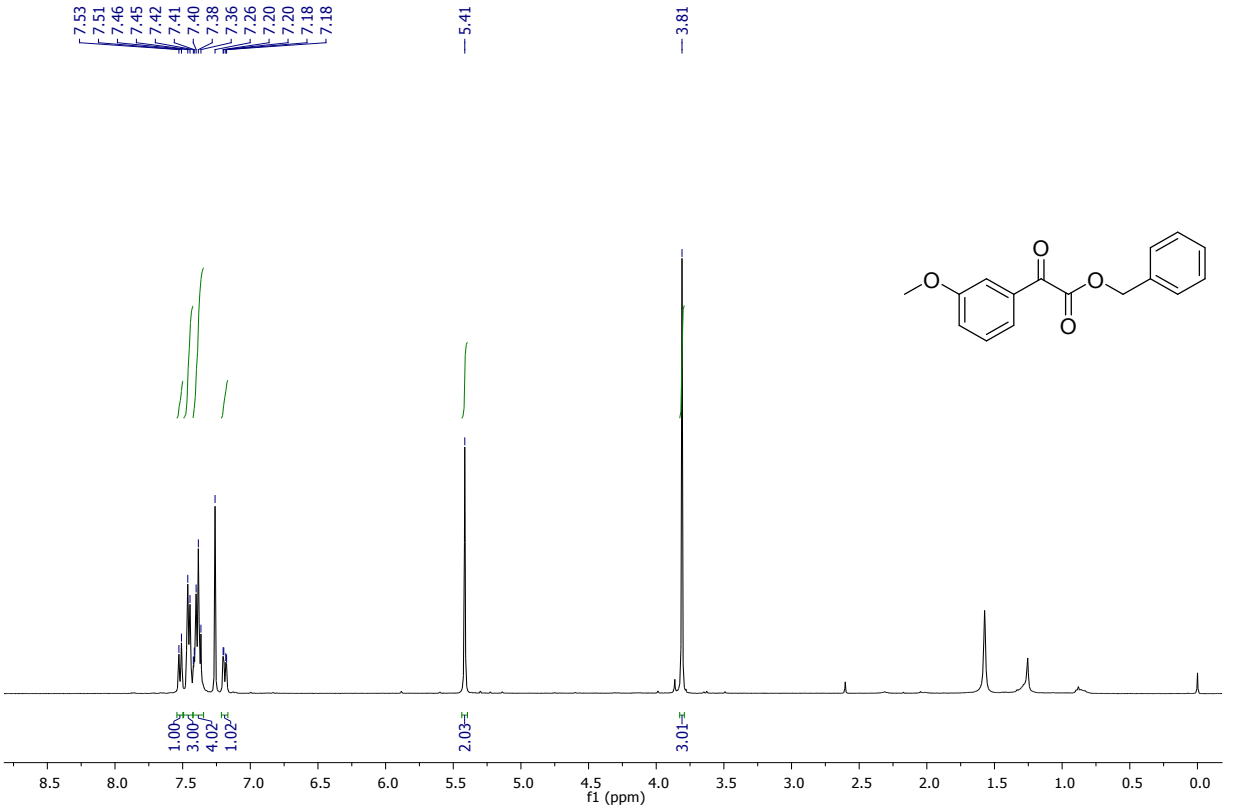


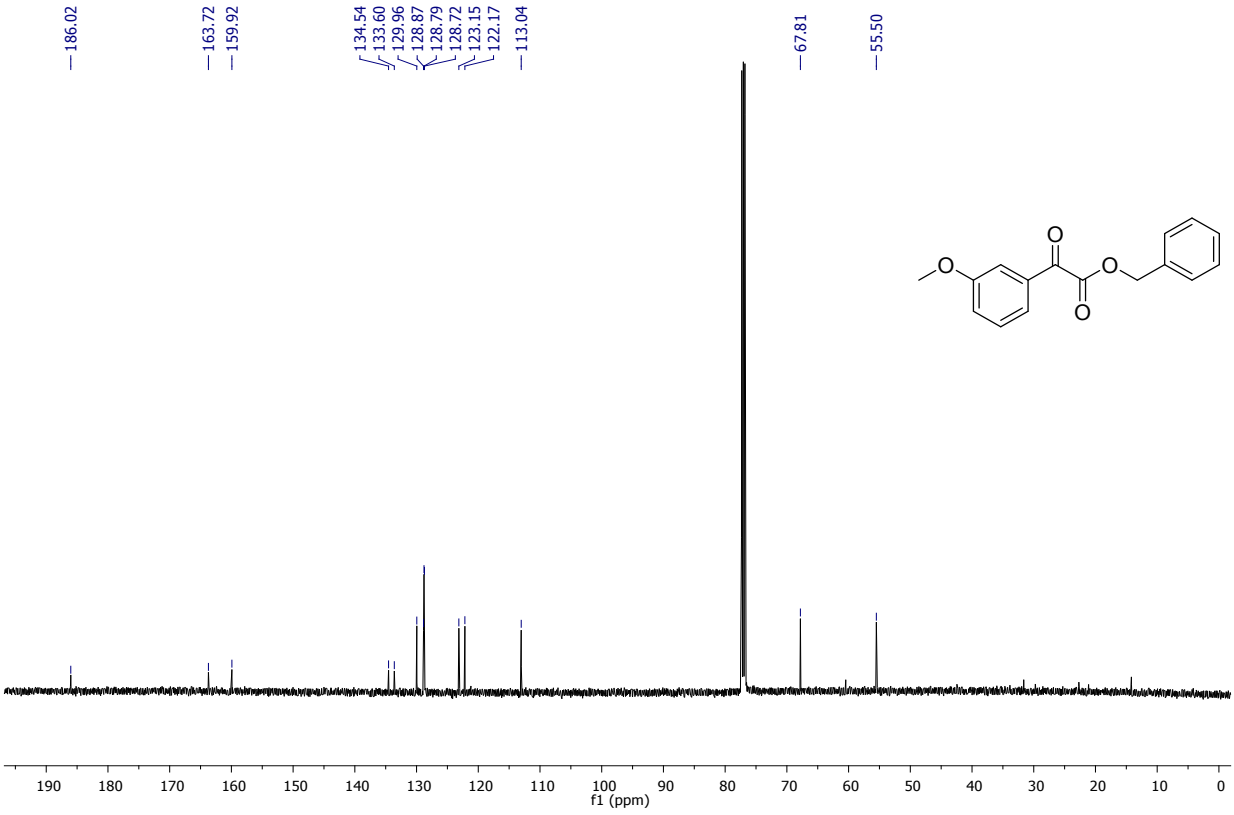
4j. Ethyl 2-(3-methoxyphenyl)-2-oxoacetate



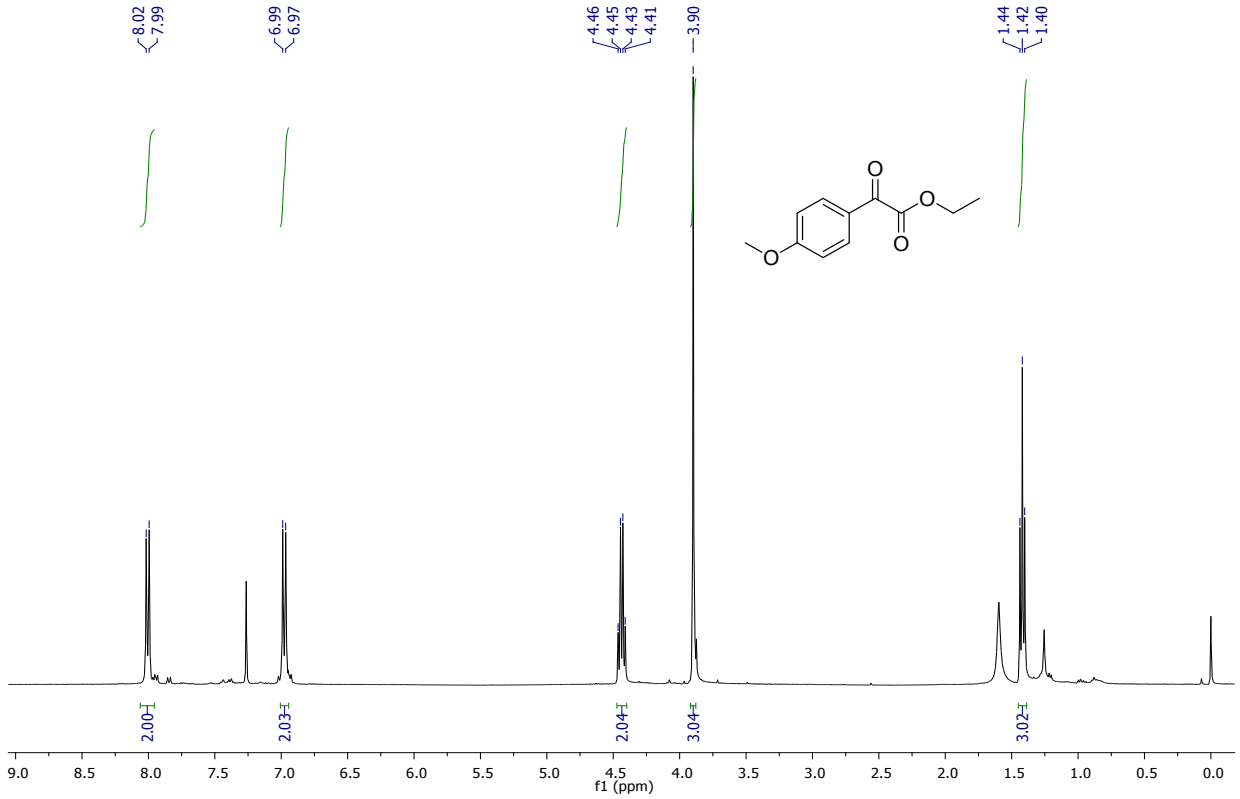


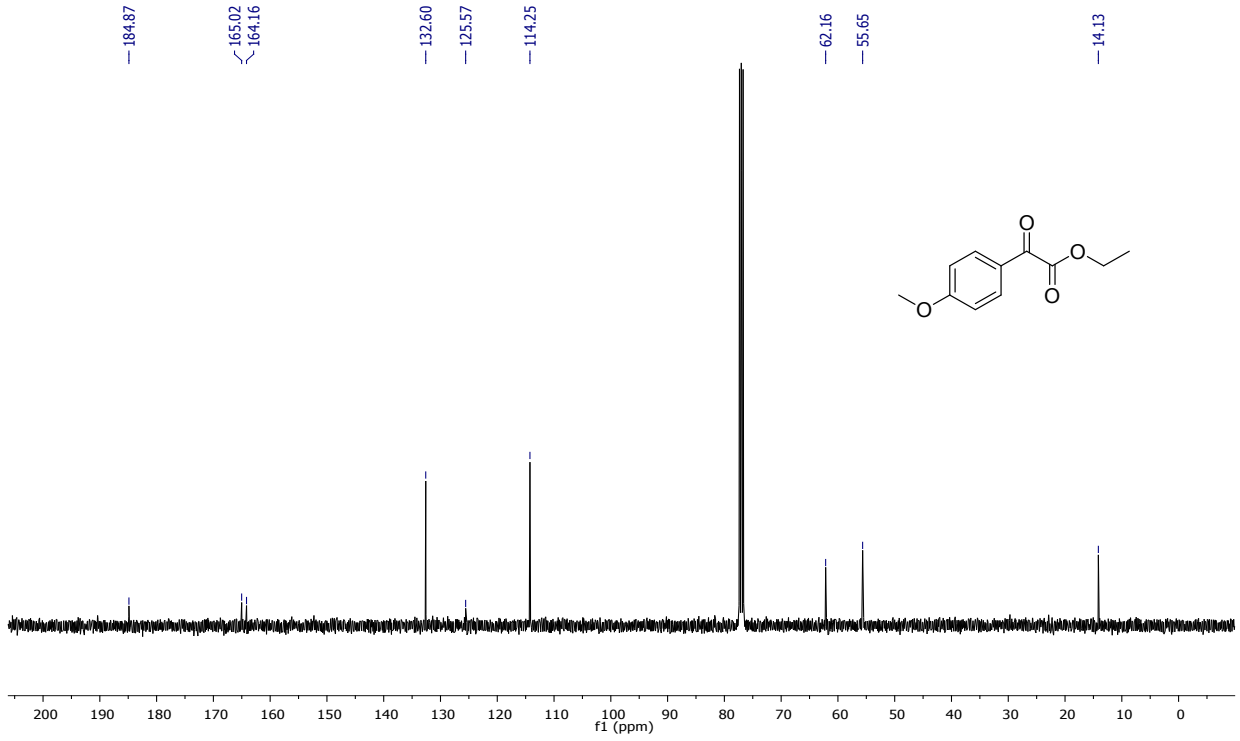
4k. Benzyl 2-(3-methoxyphenyl)-2-oxoacetate



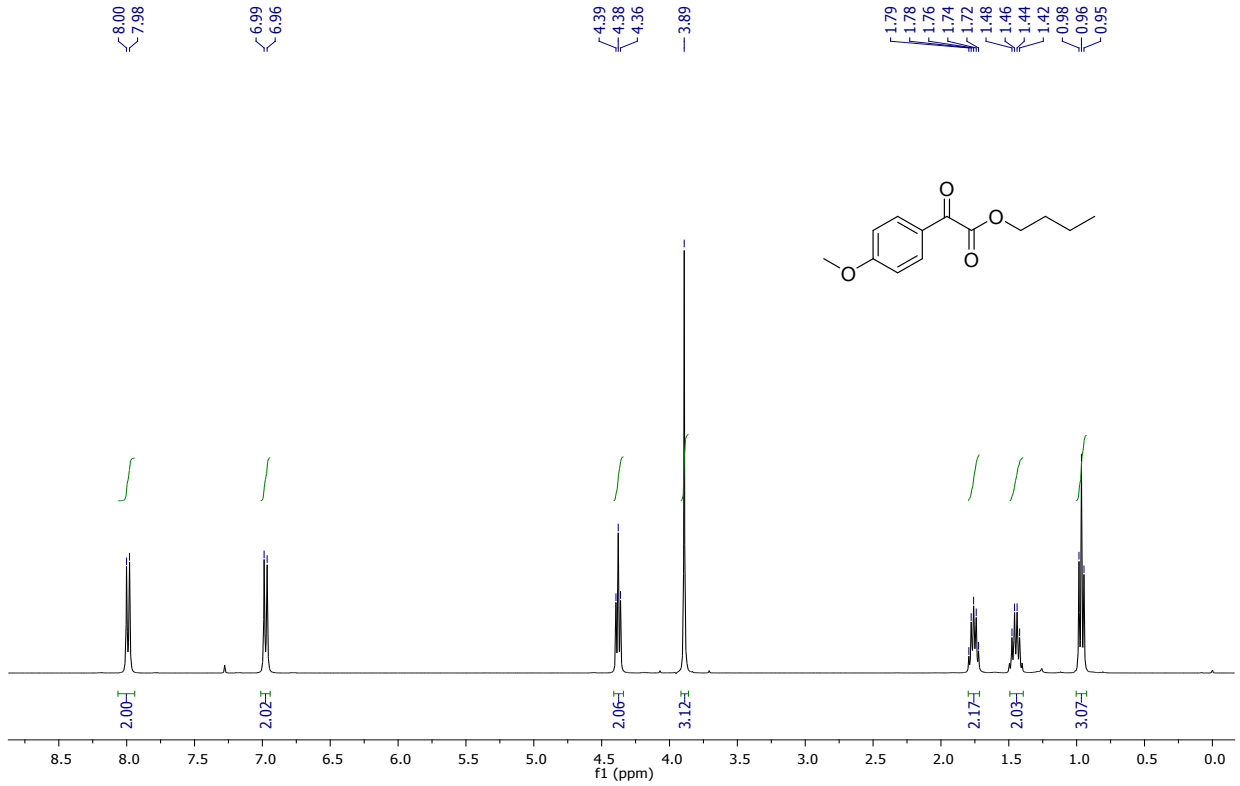


4l. Ethyl-2-(4-methoxyphenyl)-2-oxoacetate

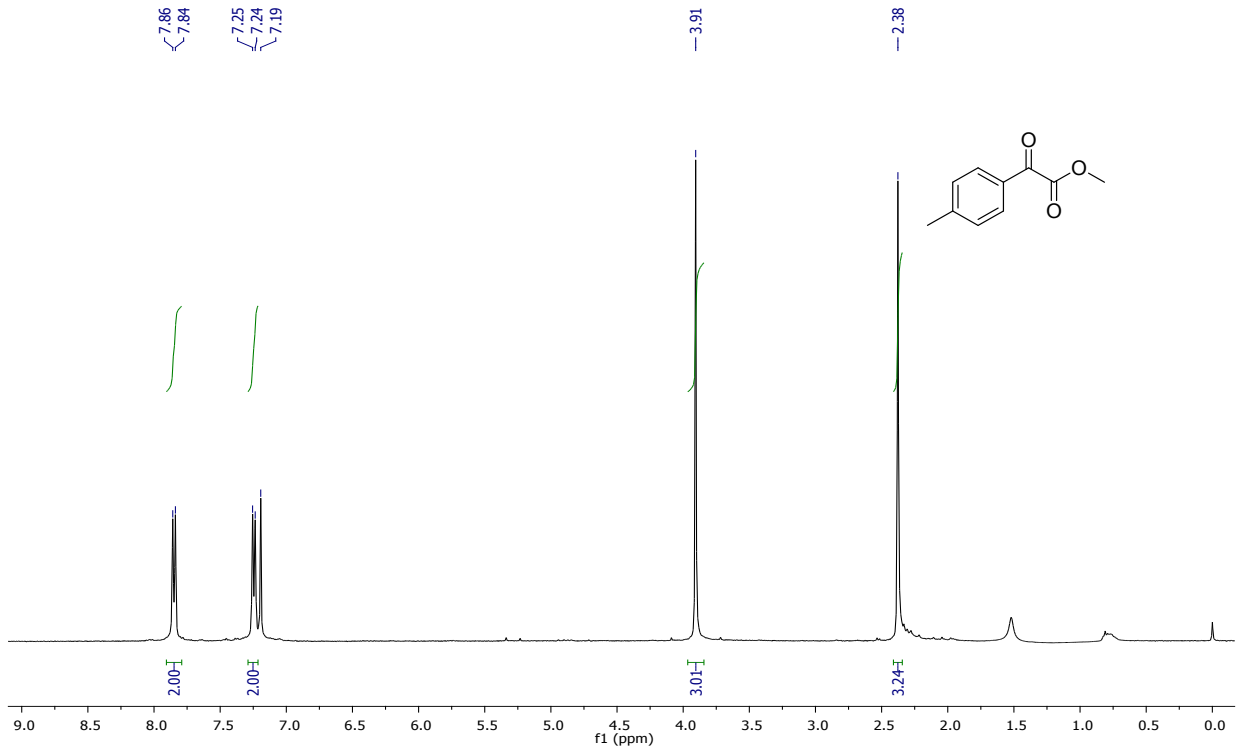


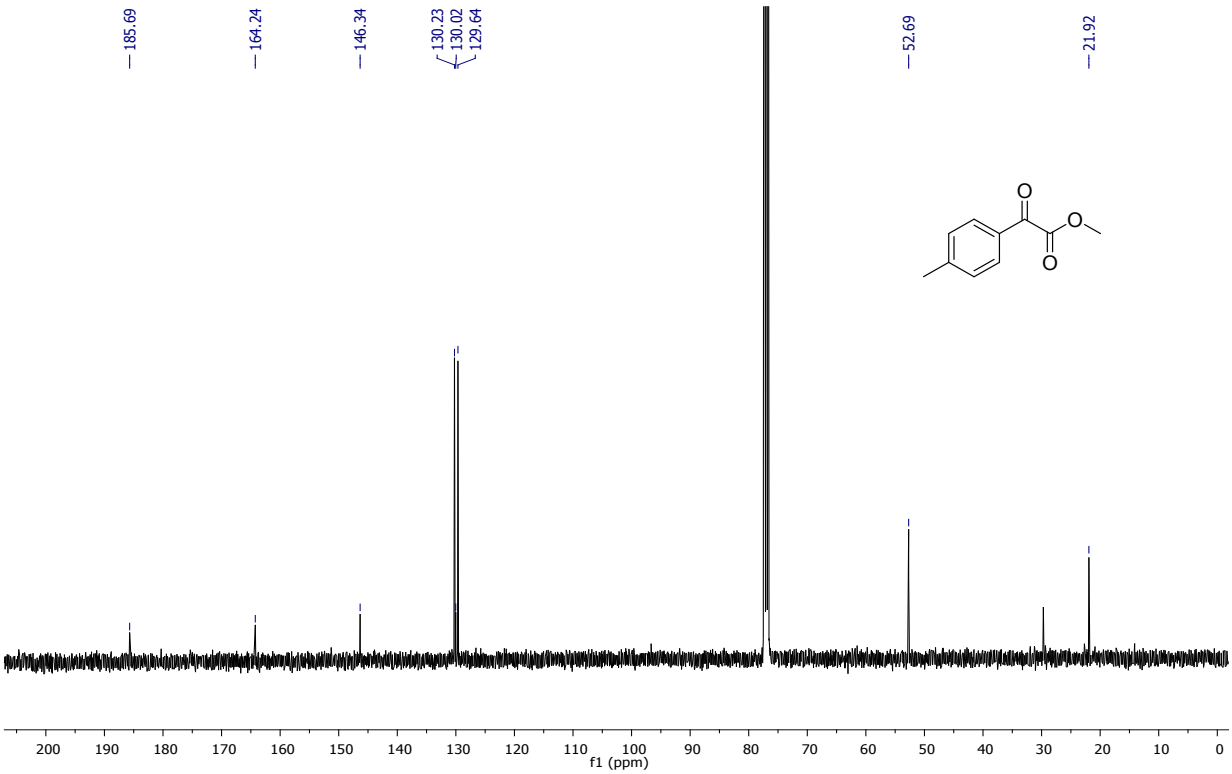


4m. Butyl 2-(4-methoxyphenyl)-2-oxoacetate

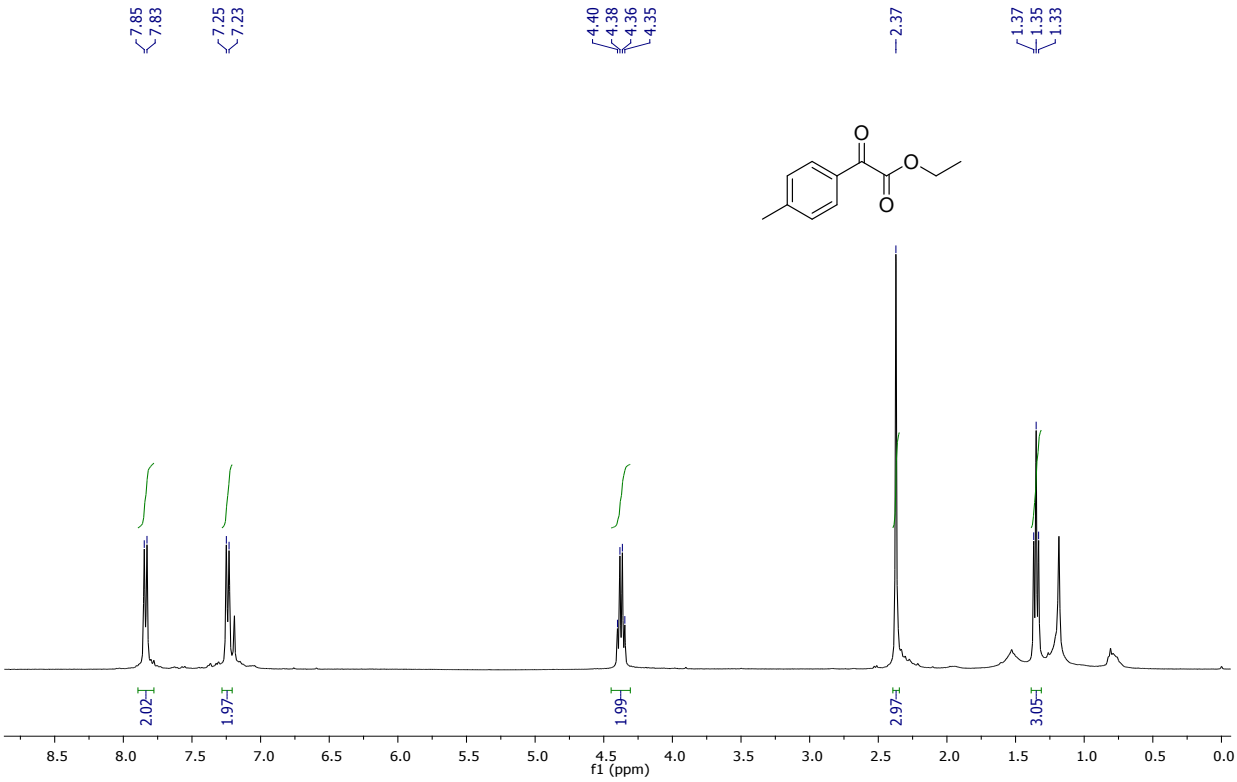


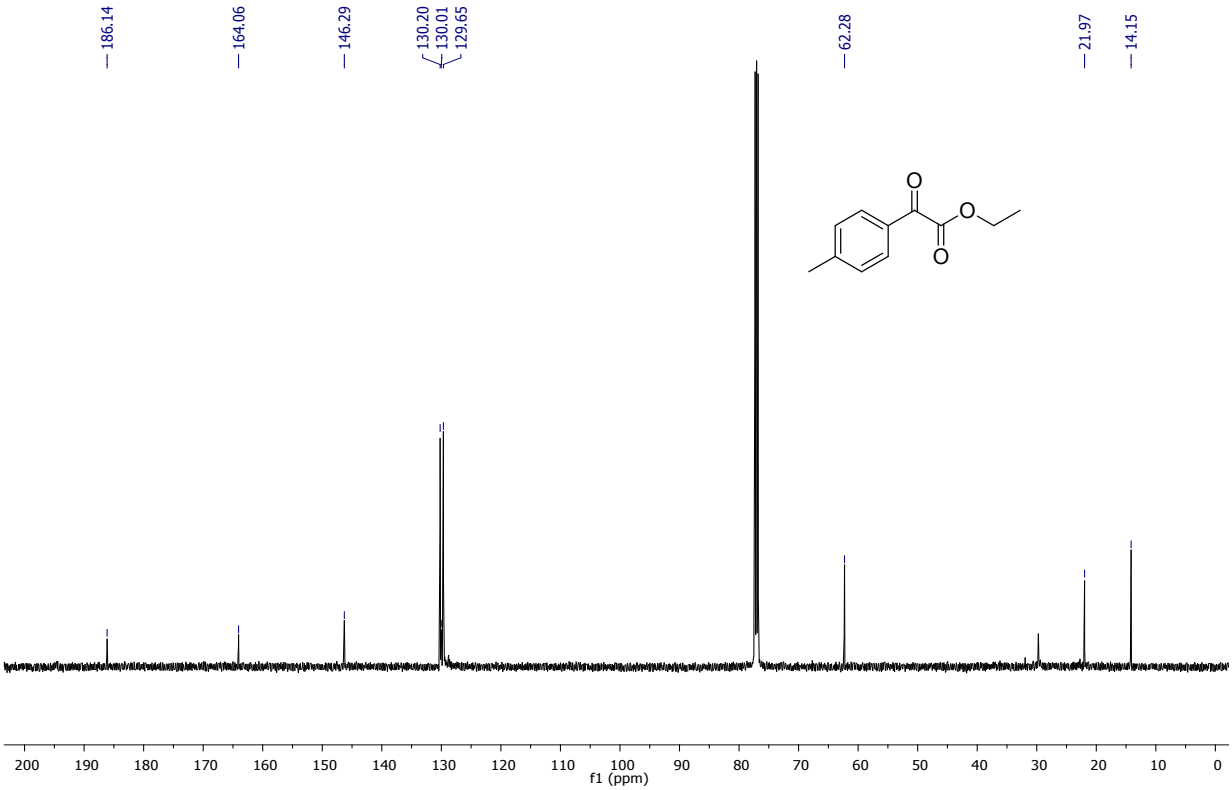
4n. Methyl 2-oxo-2-(p-tolyl)acetate



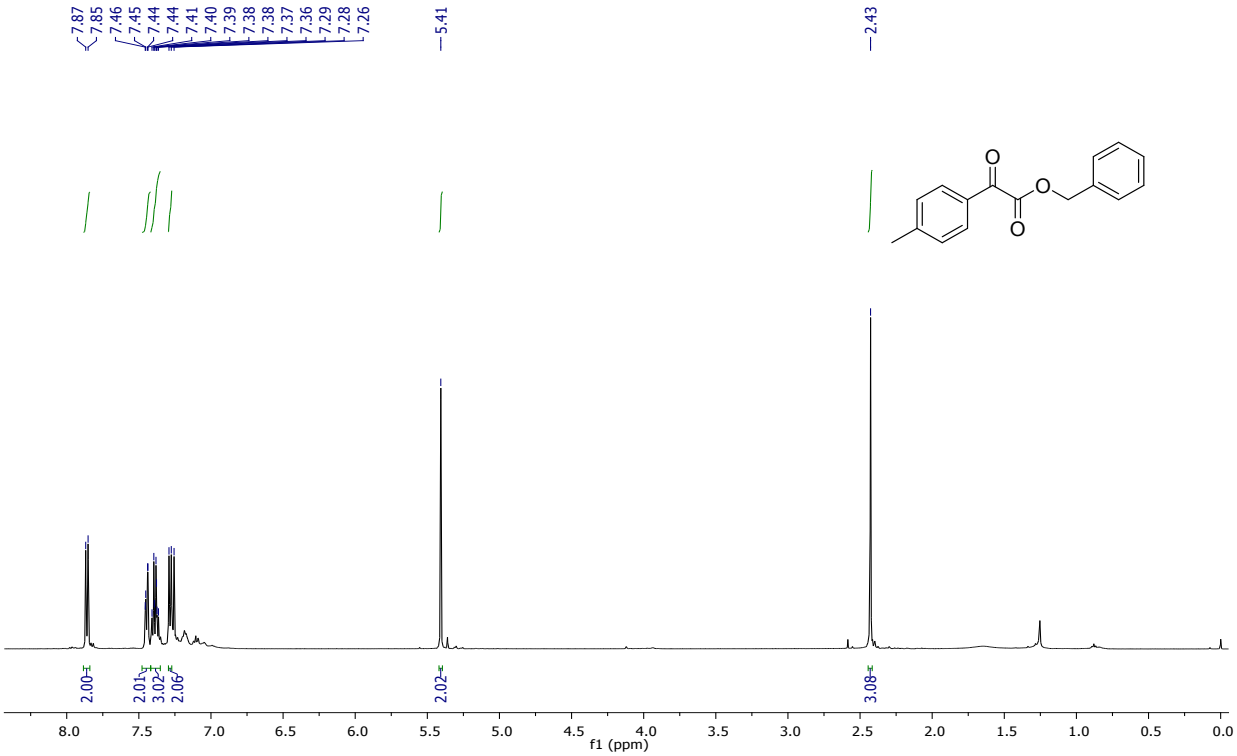


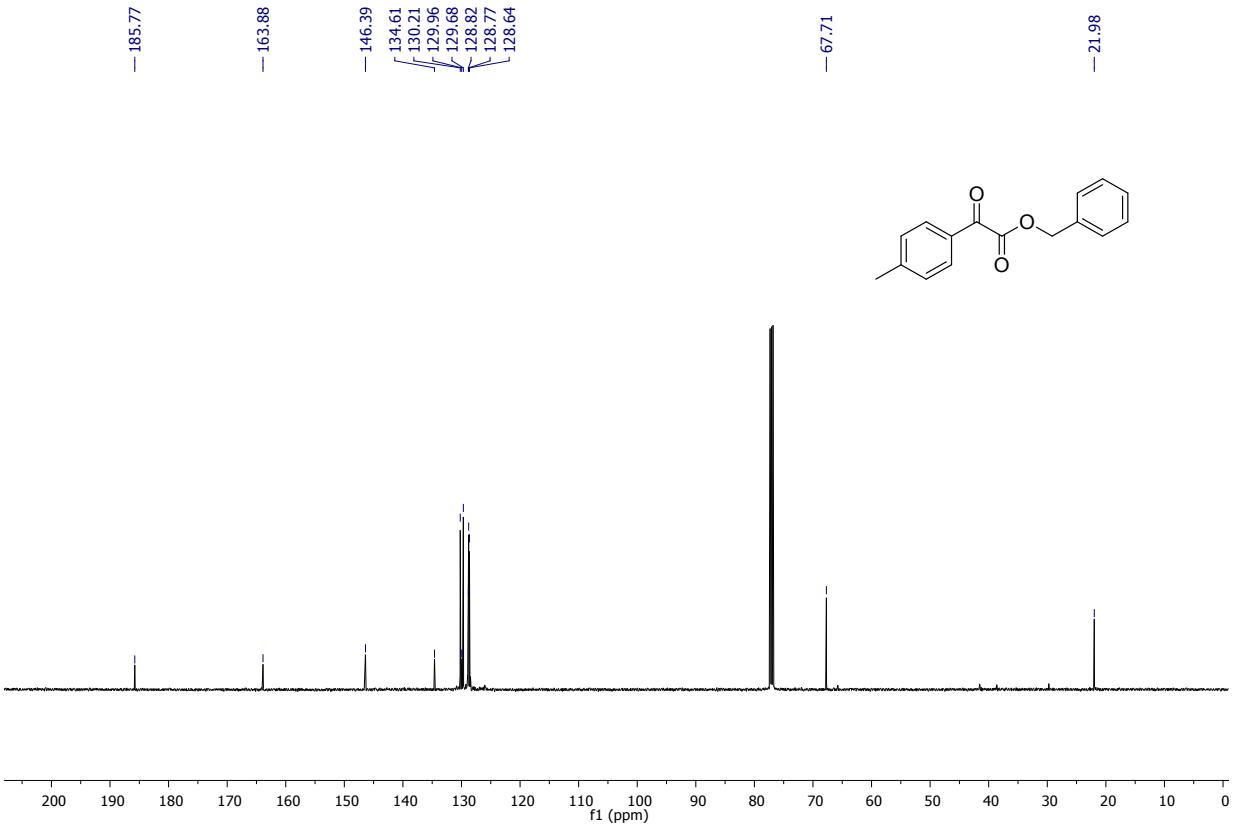
4o. Ethyl-2-oxo-2-(p-tolyl)acetate



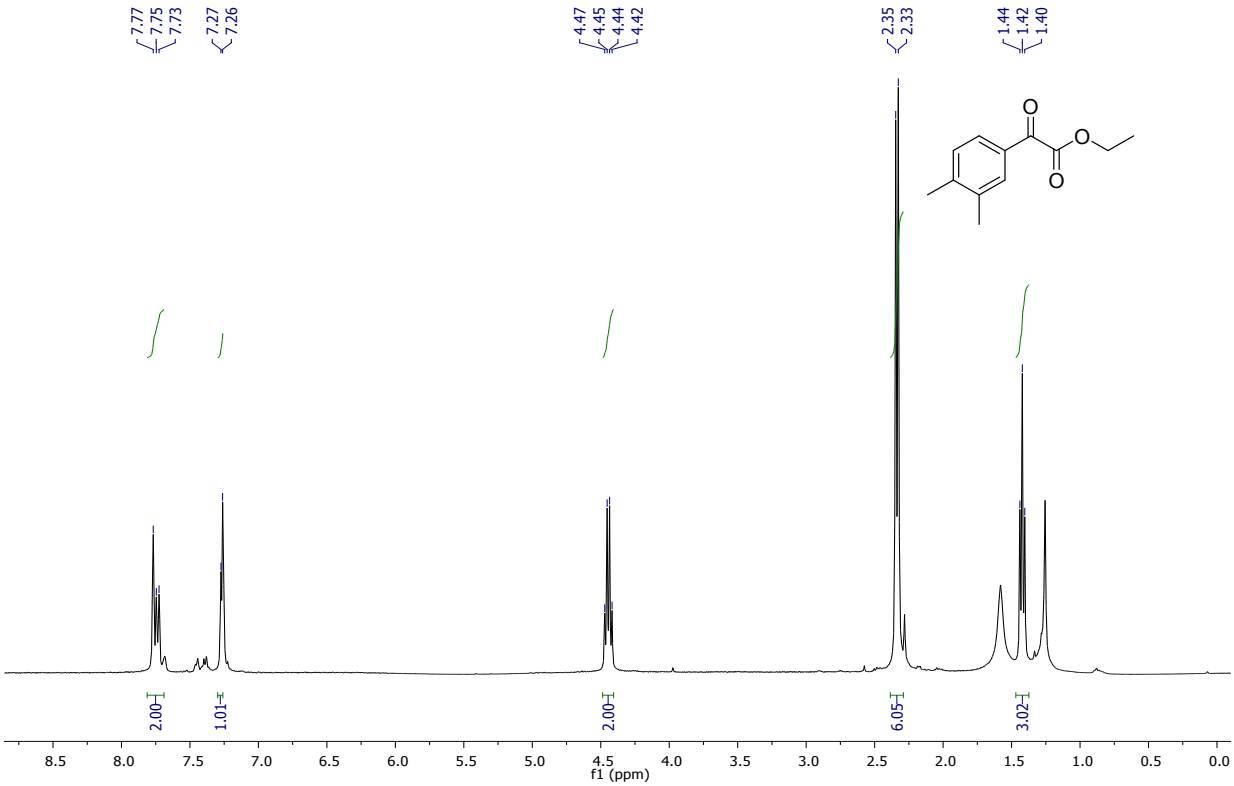


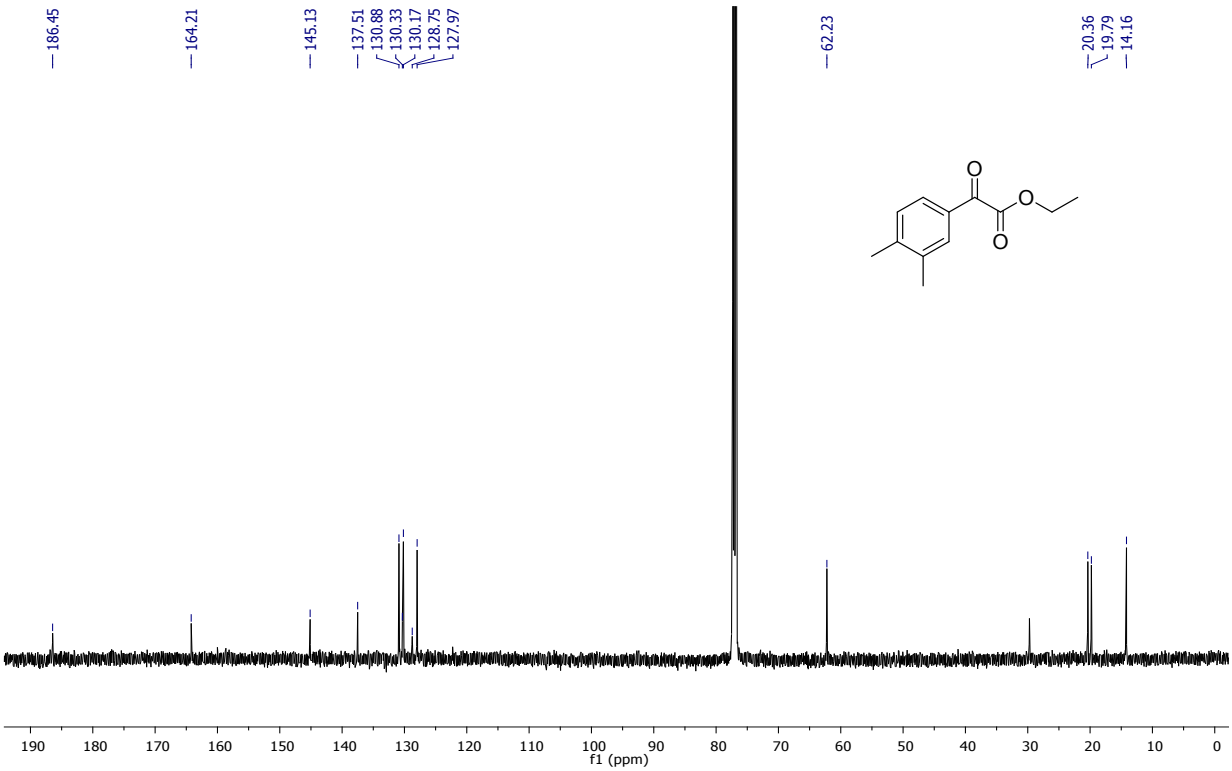
4p. Benzyl-2-oxo-2-(p-tolyl) acetate



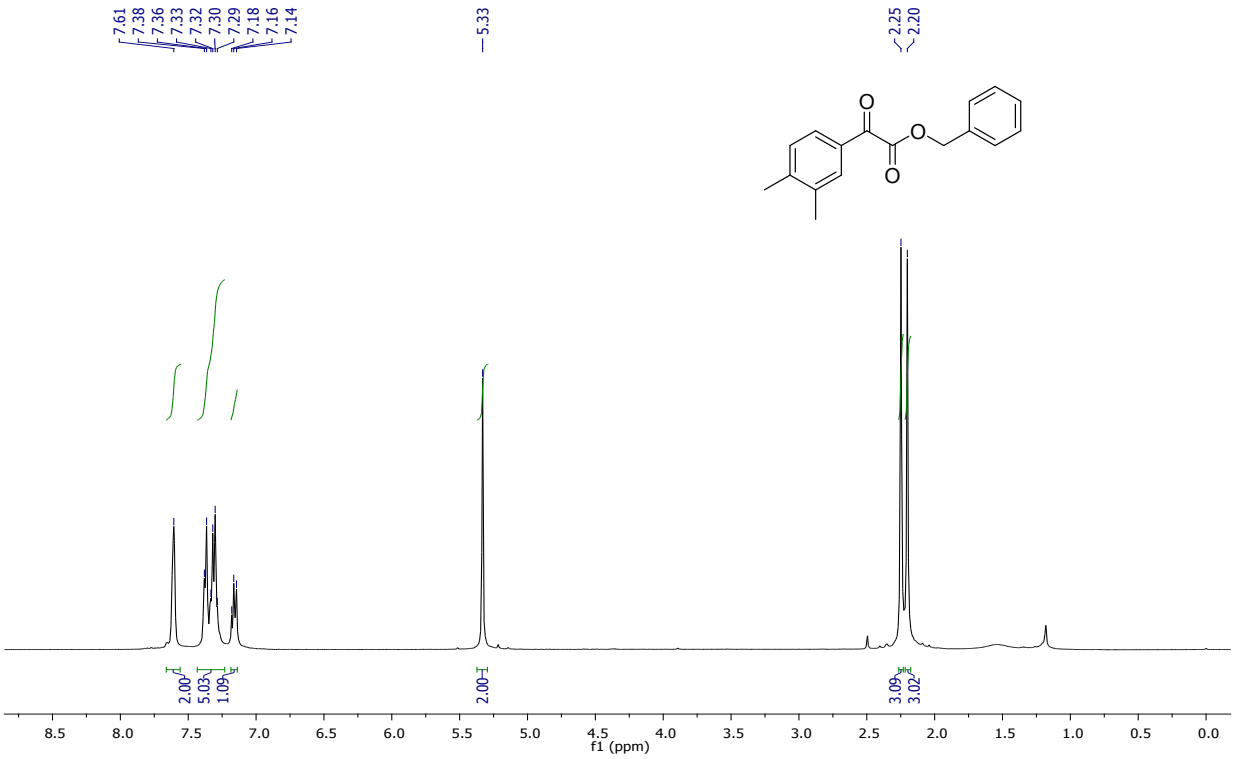


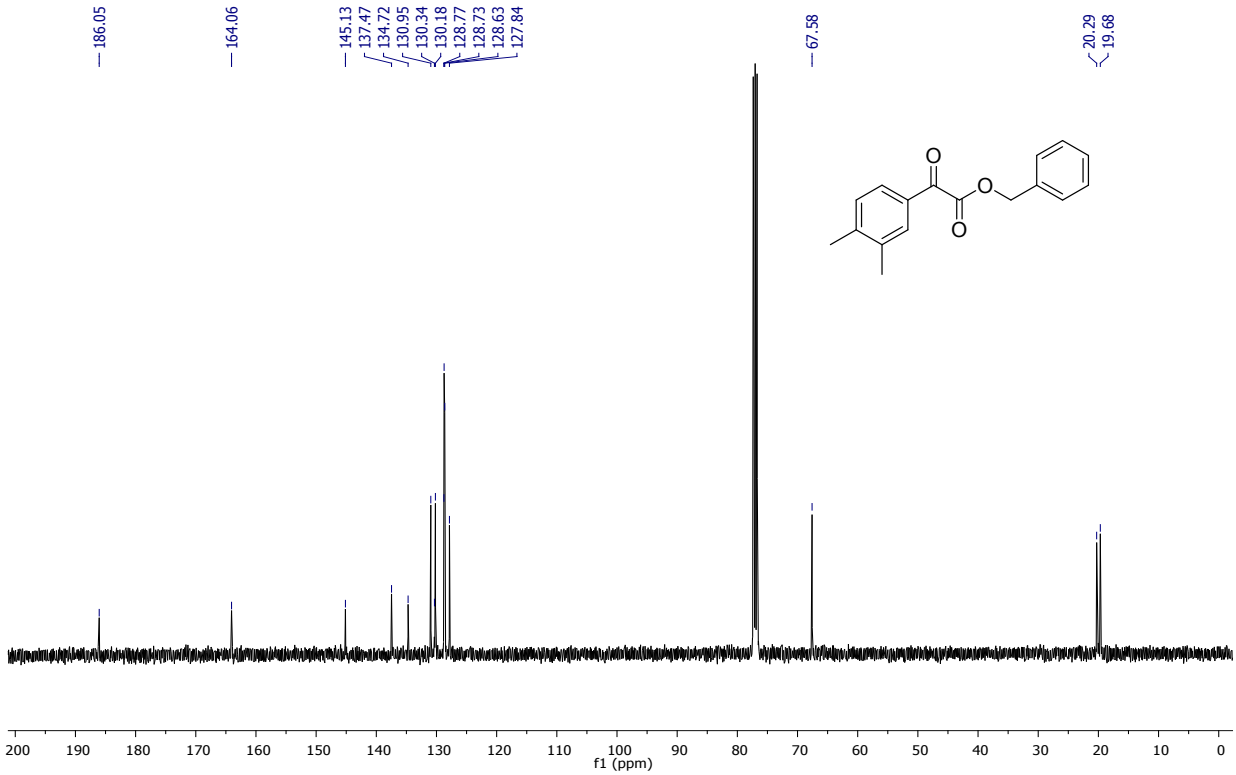
4q. Ethyl 2-(3,4-dimethylphenyl)-2-oxoacetate



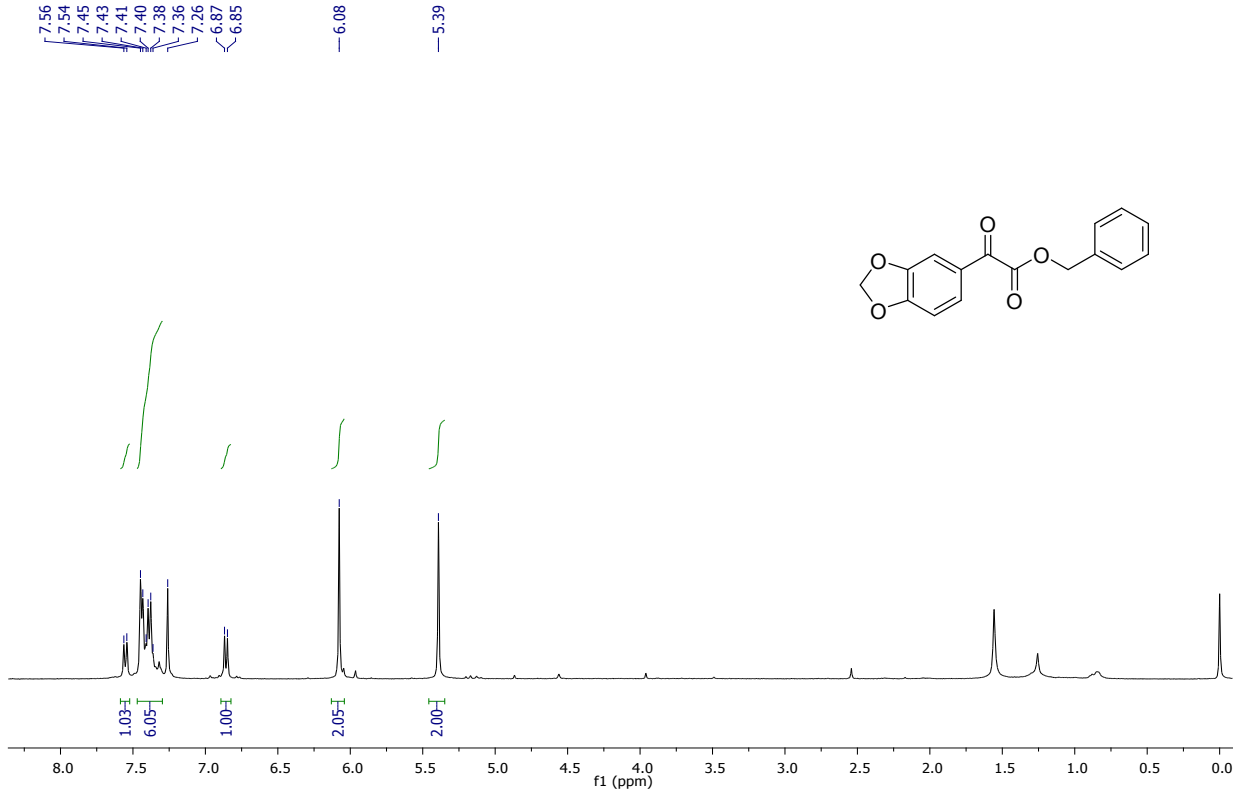


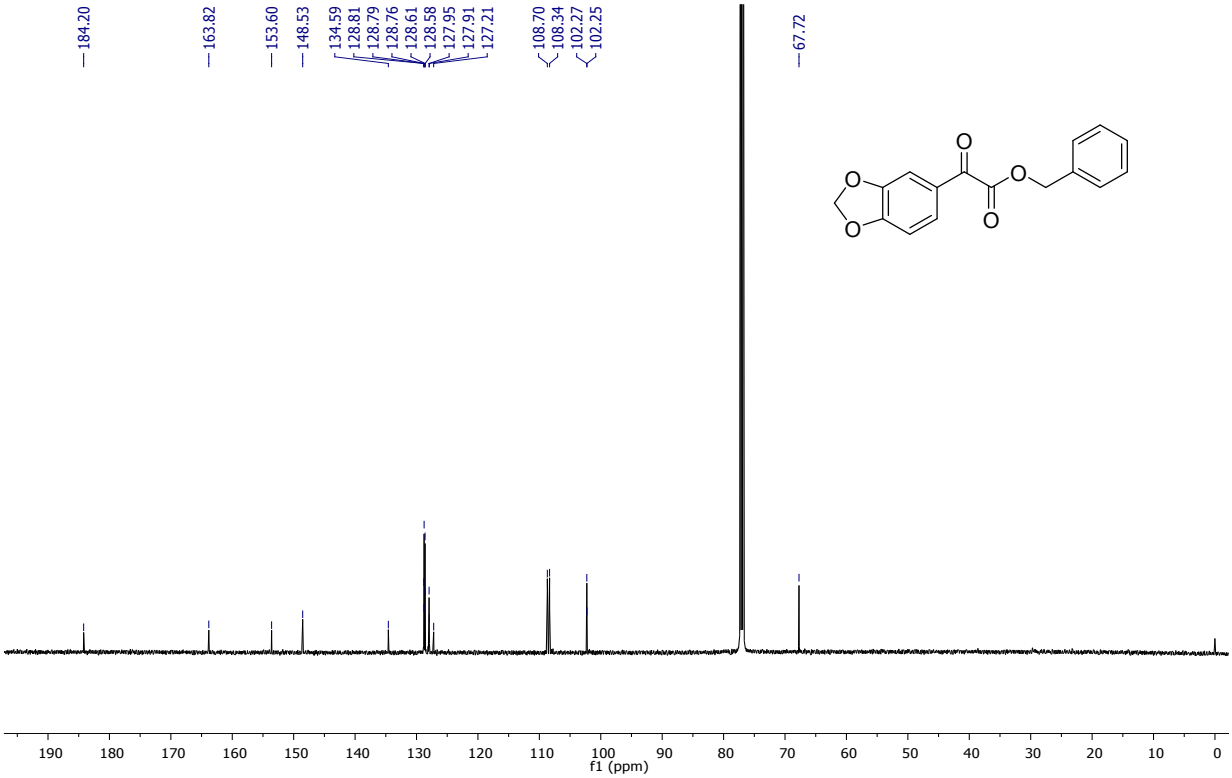
4r. Benzyl-2-(3,4-dimethylphenyl)-2-oxoacetate



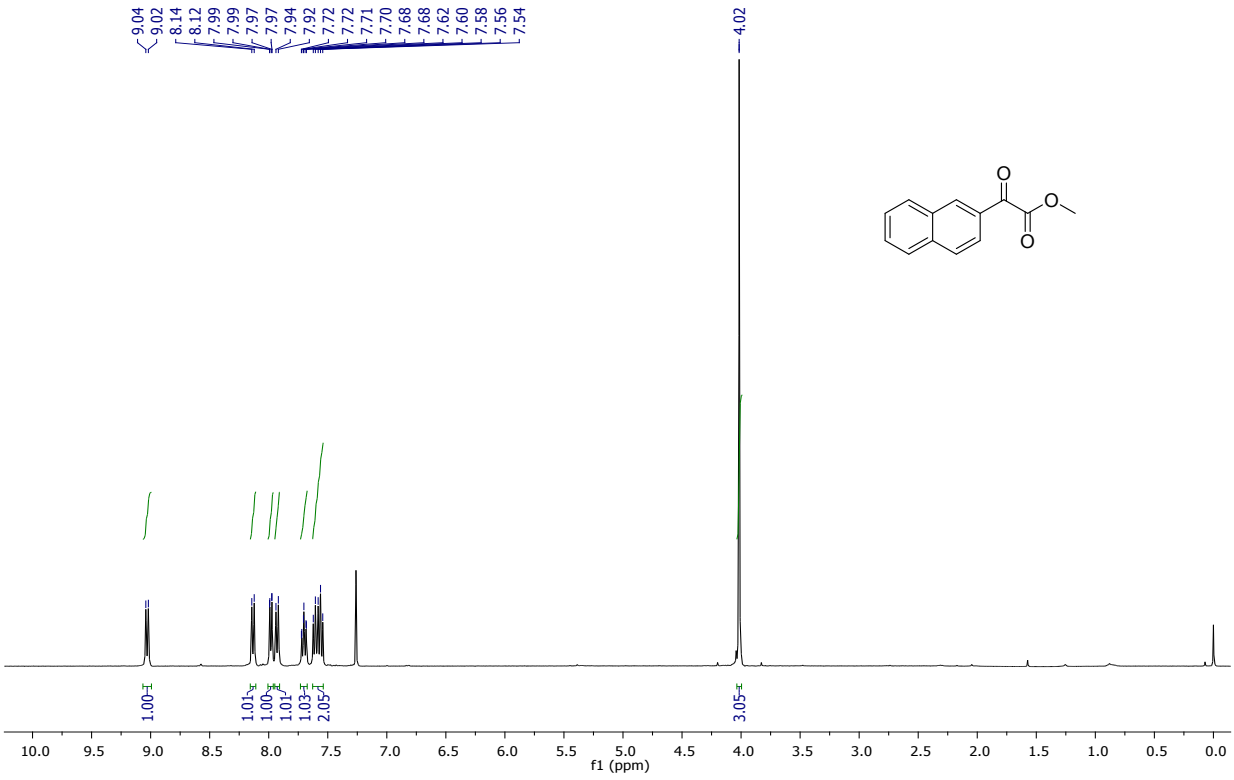


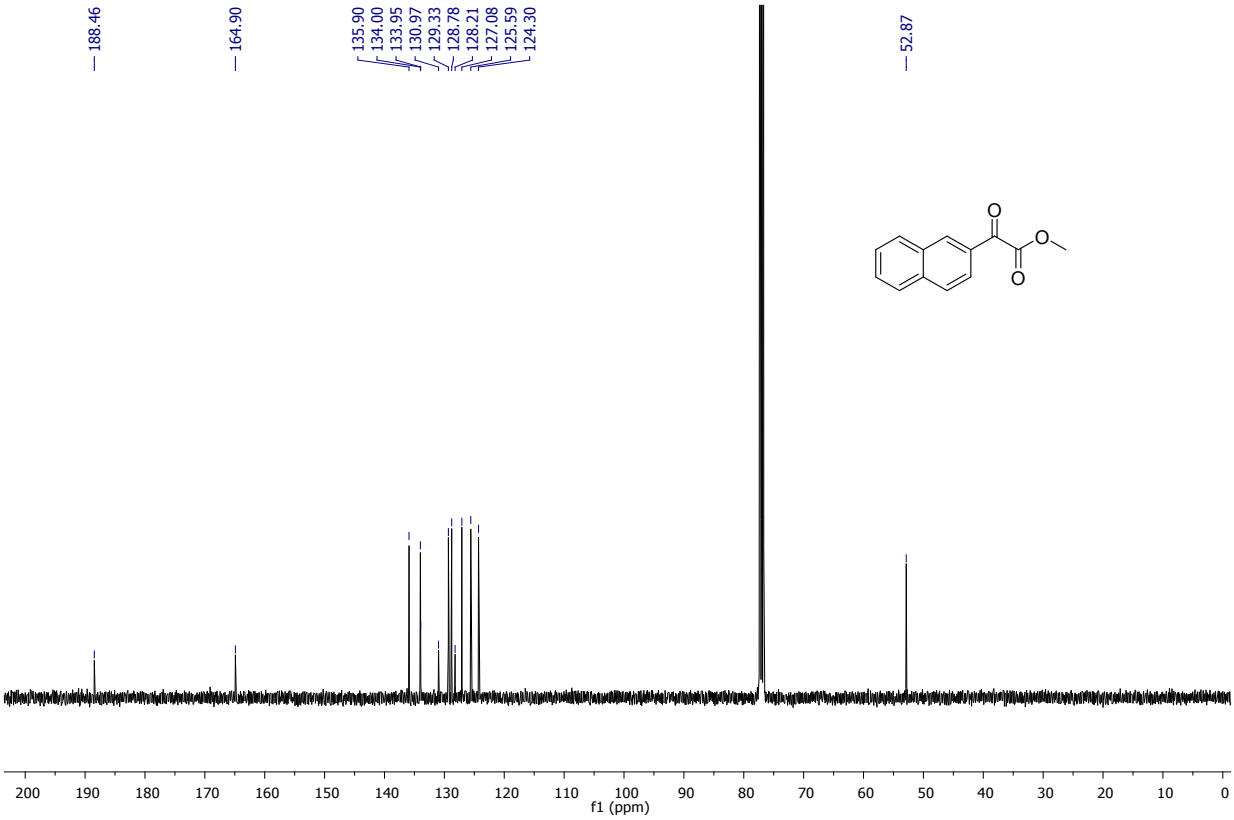
4s. Benzyl 2-(benzo[d][1,3]dioxol-5-yl)-2-oxoacetate





4t. Methyl 2-(naphthalen-2-yl)-2-oxoacetate

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