SUPPORTING INFORMATION

Efficient microwave-assisted selective alkaline hydrolysis of diversely substituted phosphonate esters.

Lucas Mele,[a] Raphael El Bekri Saudain,[a] Jean-Luc Pirat,[a] Tahar Ayad[*a] and David Virieux[*a]

[a] ICGM Univ Montpellier, CNRS, ENSCM, Montpellier, France

[*] E-mail: david.virieux@enscm.fr, tahar.ayad@enscm.fr

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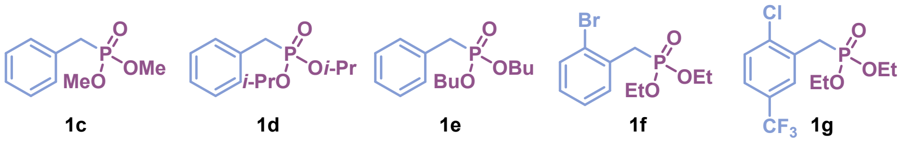
1. General Information

Unless specified, all of the reagents and starting materials were purchased from Fluorochem®, TCI®, Alfa Aesar® or Sigma-Aldrich® and used as received. All NMR spectroscopy measurements were performed with a Bruker AC 400 MHz spectrometer and are calibrated using the residual proton in the deuterated solvent ($CHCl_3$ at 7.26 ppm ^{1}H NMR, 77.16 ppm ^{13}C NMR; DMSO at 2.50 ppm ^{1}H NMR, 39.52 ppm ^{13}C NMR; MeOH at 3.31 ppm ^{1}H NMR, 49.00 ppm ^{13}C NMR). The chemical shifts are reported in ppm, and the coupling constant (*J*) are reported in Hz. The following abbreviations were used to explain multiplicities: s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, p = pentuplet and m = multiplet. For ^{13}C

NMR (101 MHz) and ^{31}P NMR (162 MHz) all spectra were decoupled from the proton unless stated otherwise. High-resolution mass spectra (HRMS) were recorded on an Agilent 6210 ESI (electrospray ionization) TOF (time of flight) mass spectrometer. Microwave reactions were performed using a CEM Discover SP® apparatus. The temperature of the mixture was determined using a volume-independent infrared (IR) temperature measurement.

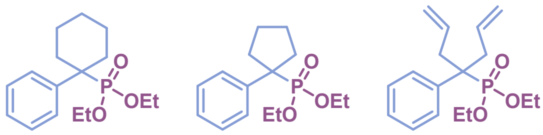
2. Procedures

Synthesis of starting materials



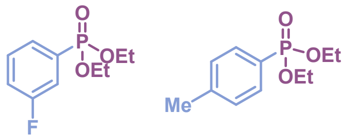
1c **1d** **1e** **1f** **1g**

Starting materials **1c-g** are known and they were synthesized by an Arbuzov reaction following the procedure reported by Kekeç and co-workers.[1]



1a **1i** **1j**

Starting materials **1a,i-j** are known and they were synthesized by an α,α'-dialkylation reaction following the procedure reported by Collignon and co-workers.[2]



1o **1p**

Starting materials **1o-p** are known and they were synthesized by Hirao coupling following the procedure reported by Stawinski and co-workers.[3]

General procedure for the microwave assisted selective hydrolysis of substituted phosphonates

Substituted phosphonate (1.0 mmol, 1.0 eq), sodium hydroxide (2.4 mmol, 2.4 eq) and the appropriate alcohol (EtOH, MeOH, *i*-PrOH or *n*-BuOH, 1 mL) were placed in a 10 mL microwave reaction vial equipped with a magnetic stirrer. The microwave reaction vial was sealed with a rubber cap and then placed in the microwave oven to be heated at 200 W to reach the appropriate temperature reported in Table 1 usually within 30 s to 1 min 30. Full conversion for each substrate (monitored by ^{31}P NMR analysis on the crude mixture with a DMSO-d_6

probe) were observed after the time described on Table 1. The reaction mixture was partitioned between EtOAc (5 mL) and 1N HCl (5 mL), decanted and the organic layer was washed with brine (5 mL). The combined aqueous layers were extracted with EtOAc (3 × 10 mL), then the combined organic layers were dried over $MgSO_4$ (1.5 g) and concentrated under reduced pressure to give the desired phosphonic acid monoester.

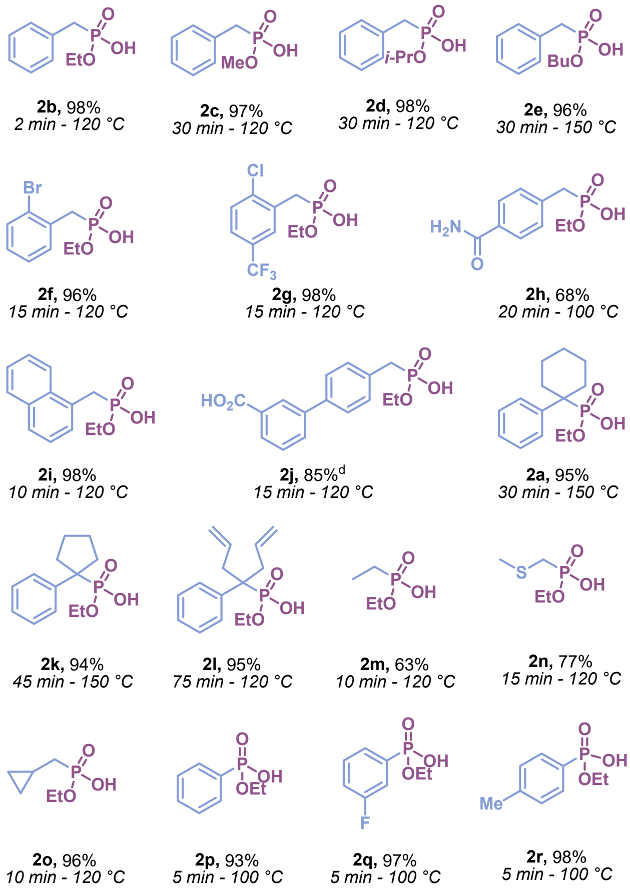
Greener procedure for the microwave assisted selective hydrolysis of substituted phosphonates

Substituted phosphonate (1.0 mmol, 1.0 eq), sodium hydroxide (2.4 mmol, 2.4 eq) and the appropriate alcohol (EtOH, MeOH, *i*-PrOH or *n*-BuOH, 1 mL) were placed in a 10 mL microwave reaction vial along with a magnetic stirrer. The microwave reaction vial was sealed with a rubber cap and then placed in the microwave oven to be heated at 200 W to reach the appropriate temperature reported in Table 1 usually within 30 s to 1 min 30. Full conversion for each substrate (monitored by ^{31}P NMR analysis on the crude mixture with a DMSO-d_6 probe) were observed after the time described on Table 1. The reaction mixture was partitioned between EtOAc (5 mL) and citric acid 10%wt (5 mL). The aqueous layers were extracted with EtOAc (2 × 5 mL), then the combined organic layers were dried over $MgSO_4$ (1.5 g) and concentrated under reduced pressure to give the desired phosphonic acid monoester.

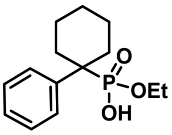
Grams scale procedure for the microwave assisted selective hydrolysis of 1b

Diethyl benzylphoshonate **1b** (3.60 g, 15.8 mmol, 1.0 eq), sodium hydroxide (1.51 g, 37.8 mmol, 2.4 eq) and EtOH (16 mL) were placed in a 35 mL microwave reaction vial along with a magnetic stirrer. The microwave reaction vial was sealed with a rubber cap and then placed in the microwave oven to be heated at 200 W to reach 130 °C within 1 min 30. After 10 minutes of heating, full conversion was observed (monitored by ^{31}P NMR analysis on the crude mixture with a DMSO-d_6 probe). The reaction mixture was partitioned between EtOAc (80 mL) and 1N HCl (80 mL), decanted and the organic layer was washed with brine (80 mL). The combined aqueous layers were extracted with EtOAc (3 × 150 mL), then the combined organic layers were dried over $MgSO_4$ (20 g) and concentrated under reduced pressure to give the desired ethyl hydrogen benzylphosphonate **2b** as a white solid (2.95 g, 94%).

Table 1: Substrate scope

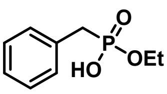


Cyclohexylbenzylphosphonic acid monoethyl ester (2a)



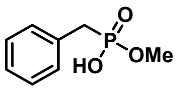
White solid (255 mg, 95%). ^{1}H NMR (400 MHz, MeOD) δ 7.53 – 7.44 (m, 2H, ArH), 7.40 – 7.31 (m, 2H, ArH), 7.30 – 7.18 (m, 1H, ArH), 3.88 – 3.75 (m, 2H, OCH_2), 2.64 – 2.55 (m, 2H, $CH_{2(Cy)}$), 2.05 – 1.94 (m, 2H, $CH_{2(Cy)}$), 1.57 (m, 3H, $CH_{2(Cy)}$), 1.41 – 1.22 (m, 3H, $CH_{2(Cy)}$) 1.17 (t, J = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, MeOD) δ 138.3 (d, J = 6.4 Hz), 130.6 (d, J = 5.4 Hz), 129.2 (d, J = 3.3 Hz), 127.4 (d, J = 3.7 Hz), 63.0 (d, J = 7.7 Hz), 45.1 (d, J = 136.7 Hz), 30.7 (d, J = 4.2 Hz), 27.3 (d, J = 1.4 Hz), 22.0 (d, J = 12.7 Hz), 16.7 (d, J = 5.9 Hz). ^{31}P NMR (162 MHz, MeOD) δ 29.3. HRMS (ESI-TOF): calc'd for $C_{14}H_{22}O_3P$ $[M+H]^+$: 269.1301, found: 269.1305.

Benzylphosphonic acid monoethyl ester (2b)



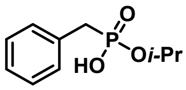
White solid (196 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.60 (br s, 1H, OH), 7.34 – 7.18 (m, 5H, ArH), 3.88 (dq, J = 8.1, 7.1 Hz, 2H, OCH_2), 3.03 (d, J = 22.1 Hz, 2H, CH_2P), 1.20 (t, J = 7.0 Hz, 3H, CH_3). ^{31}P NMR (162 MHz, $CDCl_3$) δ 29.4.

Benzylphosphonic acid monomethyl ester (2c)



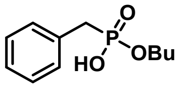
White solid (181 mg, 97%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.10 (br s, 1H, OH), 7.36 – 7.24 (m, 5H, ArH), 3.56 (d, *J* = 11.0 Hz, 3H, OCH_3), 3.11 (d, *J* = 22.2 Hz, 2H, CH_2P). ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.8 (d, *J* = 9.3 Hz), 129.9 (d, *J* = 6.5 Hz), 128.5 (d, *J* = 2.7 Hz), 126.8 (d, *J* = 3.4 Hz), 52.2 (d, *J* = 6.9 Hz), 33.4 (d, *J* = 140.2 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ 28.3. HRMS (ESI-TOF): calc'd for $C_8H_{12}O_3P$ $[M+H]^+$: 187.0519, found: 187.0521.

Benzylphosphonic acid monoisopropyl ester (2d)



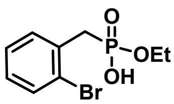
Light yellow solid (212 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.36 (br s, 1H, OH), 7.32 – 7.15 (m, 5H, ArH), 4.45 (dh, *J* = 7.8, 6.1 Hz, 1H, OCH), 3.01 (d, *J* = 22.1 Hz, 2H, CH_2P), 1.18 (d, *J* = 6.2 Hz, 6H, $(CH_3)_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 132.0 (d, *J* = 9.2 Hz), 129.9 (d, *J* = 6.6 Hz), 128.3 (d, *J* = 3.0 Hz), 126.6 (d, *J* = 3.6 Hz), 70.6 (d, *J* = 7.3 Hz), 34.3 (d, *J* = 140.8 Hz), 23.9 (d, *J* = 4.4 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ 27.3. HRMS (ESI-TOF): calc'd for $C_{10}H_{16}O_3P$ $[M+H]^+$: 215.0832, found: 215.0834.

Benzylphosphonic acid n-monobutyl ester (2e)



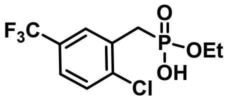
White solid (220 mg, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.85 (br s, 1H, OH), 7.31 .16 (m, 5H, ArH), 3.83 (dt, *J* = 6.7, 6.7 Hz, 2H, OCH_2), 3.05 (d, *J* = 22.3 Hz, 2H, CH_2P), 1.56 – 1.47 (m, 2H, CH_2), 1.34 – 1.24 (m, 2H, CH_2), 0.86 (t, *J* = 7.4 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.9 (d, *J* = 9.2 Hz), 129.9 (d, *J* = 6.6 Hz), 128.4 (d, *J* = 3.0 Hz), 126.7 (d, *J* = 3.5 Hz), 65.3 (d, *J* = 7.1 Hz), 33.8 (d, *J* = 140.1 Hz), 32.4 (d, *J* = 6.4 Hz), 18.6, 13.6. ^{31}P NMR (162 MHz, $CDCl_3$) δ 27.6. HRMS (ESI-TOF): calc'd for $C_{11}H_{18}O_3P$ $[M+H]^+$: 229.0988, found: 229.0991.

2-Bromobenzylphosphonic acid monoethyl ester (2f)



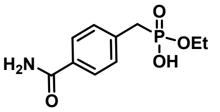
White solid (269 mg; 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.39 (br s, 1H, OH), 7.56 (d, *J* = 8.0 Hz, 1H, ArH), 7.46 (d, *J* = 7.6 Hz, 1H, ArH), 7.26 (t, *J* = 7.4 Hz, 1H, ArH), 7.10 (t, *J* = 7.7 Hz, 1H, ArH), 3.98 (dq, *J* = 7.2, 7.2 Hz, 2H, OCH_2), 3.37 (d, *J* = 22.0 Hz, 2H, CH_2P), 1.25 (t, *J* = 7.0 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 132.9 (d, *J* = 2.2 Hz), 132.0 (d, *J* = 8.7 Hz), 131.7 (d, *J* = 4.7 Hz), 128.4 (d, *J* = 2.9 Hz), 127.4 (d, *J* = 2.7 Hz), 125.1 (d, *J* = 8.6 Hz), 62.0 (d, *J* = 6.3 Hz), 33.6 (d, *J* = 141.1 Hz), 16.3 (d, *J* = 5.9 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ 26.7. HRMS (ESI-TOF): calc'd for $C_9H_{13}BrO_3P$ $[M+H]^+$: 278.9780, found: 278.9784.

2-Chloro-5-trifluoromethylbenzylphosphonic acid monoethyl ester (2g)



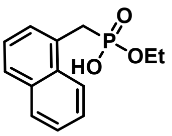
White solid (297 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.22 (br s, 1H, OH), 7.67 (s, 1H, ArH), 7.50 – 7.38 (m, 2H, ArH), 3.98 (dq, *J* = 7.2, 7.2 Hz, 2H, OCH_2), 3.35 (d, *J* = 23.1 Hz, 2H, CH_2P), 1.21 (t, *J* = 7.0 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.3 (d, *J* = 7.8 Hz), 131.7 (d, *J* = 9.1 Hz), 130.2 (d, *J* = 2.8 Hz), 129.3 (qd, *J* = 33.3, 3.7 Hz), 128. 6 (dq, *J* = 5.0, 3.7 Hz), 125.0 (q, J = 3.6 Hz), 123.7 (q, *J* = 271.8 Hz), 62.2 (d, *J* = 6.8 Hz), 31.1 (d, *J* = 141.4 Hz), 16.1 (d, *J* = 6.4 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ 24.8. HRMS (ESI-TOF): calc'd for $C_9H_{13}BrO_3P$ $[M+H]^+$: 303.0159, found: 303.0164.

4-Carbamoylbenzylphosphonic acid monoethyl ester (2h)



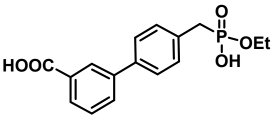
White solid (165 mg; 68%). ^{1}H NMR (400 MHz, MeOD) δ 7.85 – 7.80 (m, 2H, ArH), 7.46 – 7.37 (m, 2H, ArH), 4.02 (dq, *J* = 7.9, 7.1 Hz, 2H, $-OCH_2$), 3.25 (d, *J* = 22.1 Hz, 2H, CH_2-P), 1.26 (t, *J* = 7.1 Hz, 3H, $-CH_3$). ^{13}C NMR (101 MHz, MeOD) δ 172.06, 138.13 (d, *J* = 9.2 Hz), 133.33 (d, *J* = 3.7 Hz), 131.06 (d, *J* = 6.3 Hz), 128.78 (d, *J* = 3.1 Hz), 62.96 (d, *J* = 6.6 Hz), 34.62 (d, *J* = 136.2 Hz), 16.73 (d, *J* = 6.4 Hz). ^{31}P NMR (162 MHz, MeOD) δ 24,92. HRMS (ESI-TOF): calc'd for $C_{10}H_{15}NO_4P$ $[M+H]^+$: 244.0739, found: 244.0734.

Naphthalen-1-ylmethylphosphonic acid monoethyl ester (2i)



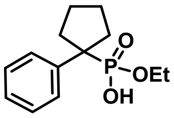
Light yellow solid (246 mg, 98%). 1H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.3 Hz, 1H, ArH), 7.84 – 7.68 (m, 2H, ArH), 7.47 (dddd, *J* = 17.7, 8.0, 6.7, 1.4 Hz, 2H, ArH), 7.43 – 7.30 (m, 2H, ArH), 3.69 (dq, *J* = 7.2, 7.2 Hz, 2H, OCH_2), 3.42 (d, *J* = 22.4 Hz, 2H, CH_2P), 1.06 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.8 (d, *J* = 2.9 Hz), 132.0 (d, *J* = 5.1 Hz), 128.7 (d, *J* = 7.6 Hz), 128.5, 127.9 (d, *J* = 9.9 Hz), 127.7 (d, *J* = 4.2 Hz), 126.1, 125.7, 125.4 (d, *J* = 4.2 Hz), 124.6 (d, *J* = 1.9 Hz), 61.6 (d, *J* = 7.2 Hz), 30.7 (d, *J* = 141.4 Hz), 16.1 (d, *J* = 6.5 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ 29.1. HRMS (ESI-TOF): calc'd for $C_{13}H_{16}O_3P$ $[M+H]^+$: 251.0832, found: 251.0835.

4'-((ethoxy(hydroxy)phosphoryl)methyl)-[1,1'-biphenyl]-3-carboxylic acid (2j)



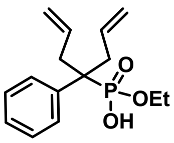
White solid (272 mg; 85%). ^{1}H NMR (400 MHz, MeOD) δ 8.24 (t, *J* = 1.8 Hz, 1H, ArH), 7.99 (dt, *J* = 7.8, 1.4 Hz, 1H, ArH), 7.82 (ddd, *J* = 7.8, 2.0, 1.1 Hz, 1H, ArH), 7.65 – 7.57 (m, 2H, ArH), 7.56 – 7.50 (m, 1H, ArH), 7.41 (dd, *J* = 8.3, 2.5 Hz, 2H, ArH), 4.03 (dq, *J* = 7.9, 7.1 Hz, 2H, $-OCH_2$), 3.21 (d, *J* = 21.4 Hz, 2H, CH_2-P), 1.27 (t, *J* = 7.1 Hz, 3H, $-CH_3$). ^{13}C NMR (101 MHz, MeOD) δ 169.70, 142.34, 139.87 (d, J = 3.9 Hz), 133.37 (d, J = 9.4 Hz), 132.52, 132.36, 131.61 (d, J = 6.5 Hz), 130.10, 129.48 (d, J = 6.7 Hz), 128.96, 128.03 (d, J = 3.2 Hz), 62.93 (d, J = 6.5 Hz), 34.30 (d, J = 136.5 Hz), 16.76 (d, J = 6.3 Hz). ^{31}P NMR (162 MHz, MeOD) δ 25.80. HRMS (ESI-TOF): calc'd for $C_{16}H_{18}O_5P$ $[M+H]^+$: 321.0892, found: 321.0891.

Cyclopentylbenzylphosphonic acid monoethyl ester (2k)



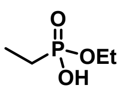
White solid (194 mg, 94%). ^{1}H NMR (400 MHz, MeOD) δ 7.46 (ddd, J = 8.3, 2.7, 1.2 Hz, 2H, ArH), 7.33 – 7.25 (m, 2H, ArH), 7.23 – 7.14 (m, 1H, ArH), 3.82 (dq, J = 7.2, 7.2 Hz, 2H, OCH_2), 2.49 – 2.13 (m, 4H, 2 CH_2), 1.89 – 1.75 (m, 2H, CH_2), 1.64 – 1.48 (m, 2H, CH_2), 1.15 (t, J = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, MeOD) δ 142.4 (d, J = 4.3 Hz), 129.7 (d, J = 5.1 Hz), 128.9 (d, J = 3.2 Hz), 127.5 (d, J = 3.4 Hz), 62.9 (d, J = 7.5 Hz), 52.2 (d, J = 139.6 Hz), 35.6 (d, J = 1.1 Hz), 25.2, 16.7 (d, J = 6.0 Hz). ^{31}P NMR (162 MHz, MeOD) δ 30.9. HRMS (ESI-TOF): calc'd for $C_{13}H_{20}O_3P$ $[M+H]^+$: 255.1145, found: 255.1148.

Diallylbenzylphosphonic acid monoethyl ester (2l)



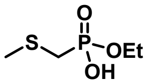
White solid (175 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.47 (br s, 1H, OH), 7.51 (ddd, J = 8.4, 2.6, 1.3 Hz, 2H, ArH), 7.32 (t, J = 7.6 Hz, 2H, ArH), 7.27 – 7.12 (m, 1H, ArH), 5.82 (ddt, J = 17.0, 10.1, 6.9 Hz, 2H, $CH_{C=C}$), 5.17 – 5.01 (m, 4H, $CH_{2(C=C)}$), 3.76 (dq, J = 7.2, 7.2 Hz, 2H, OCH_2), 3.03 – 2.79 (m, 4H, $CH_{2(allyl)}$), 1.16 (t, J = 7.0 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.4 (d, J = 6.1 Hz), 133.7 (d, J = 9.5 Hz), 129.1 (d, J = 5.4 Hz), 127.9 (d, J = 2.8 Hz), 126.7 (d, J = 3.0 Hz), 118.3, 61.8 (d, J = 7.9 Hz), 45.1 (d, J = 137.7 Hz), 37.0 (d, J = 2.8 Hz), 16.2 (d, J = 6.1 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ 32.2. HRMS (ESI-TOF): calc'd for $C_{15}H_{22}O_3P$ $[M+H]^+$: 281.1301, found: 281.1305.

Ethylphosphonic acid monoethyl ester (2m)



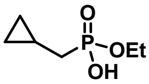
White solid (87 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.90 (br s, 1H, OH), 4.09 (dq, J = 7.3, 7.3 Hz, 2H, OCH_2), 1.74 (dq, J = 18.6, 7.5 Hz, 2H, CH_2P), 1.33 (t, J = 7.1 Hz, 3H, CH_3), 1.18 (dt, J = 20.1, 7.7 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 61.1 (d, J = 6.7 Hz), 19.1 (d, J = 145.0 Hz), 16.4 (d, J = 6.4 Hz), 6.4 (d, J = 6.6 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ 35.8. HRMS (ESI-TOF): calc'd for $C_4H_{12}O_3P$ $[M+H]^+$: 139.0519, found: 139.0520.

Methylthiomethylphosphonic acid monoethyl ester (2n)



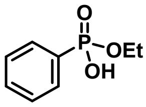
Colorless oil (131 mg, 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.03 (br s, 1H, OH), 4.23 – 4.14 (m, 2H, OCH_2), 2.72 (d, *J* = 13.0 Hz, 2H, CH_2P), 2.28 (d, *J* = 1.1 Hz, 3H, H_3CS), 1.36 (t, *J* = 7.0 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 62.4 (d, *J* = 7.2 Hz), 27.6 (d, *J* = 153.8 Hz), 17.4, 16.4 (d, *J* = 6.3 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ 27.7. HRMS (ESI-TOF): calc'd for $C_4H_{12}O_3PS$ $[M+H]^+$: 171.0239, found: 171.0246.

Cyclopropylmethylphosphonic acid monoethyl ester (2o)



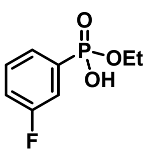
Colorless oil (157 mg, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (br s, 1H, OH), 4.11 (dq, *J* = 7.2, 7.2 Hz, 2H, OCH_2), 1.70 (dd, *J* = 17.9, 7.1 Hz, 2H, CH_2P), 1.33 (t, *J* = 7.0 Hz, 3H, CH_3), 1.05 – 0.86 (m, 1H, CH), 0.57 (tdd, *J* = 6.0, 4.5, 1.4 Hz, 2H, $CH_{2(c\text{-Pr})}$), 0.23 (dt, *J* = 6.2, 4.7 Hz, 2H, $CH_{2(c\text{-Pr})}$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 61.1 (d, *J* = 6.7 Hz), 31.0 (d, *J* = 143.4 Hz), 16.4 (d, *J* = 6.3 Hz), 5.1 (d, *J* = 10.1 Hz), 4.2 (d, *J* = 5.2 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ 33.8. HRMS (ESI-TOF): calc'd for $C_6H_{14}O_3P$ $[M+H]^+$: 165.0675, found: 165.0680.

Phenylphosphonic acid monoethyl ester (2p)



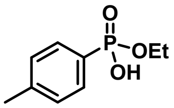
Brown oil (174 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.26 (br s, 1H, OH), 7.84 (dd, *J* = 13.7, 7.5 Hz, 2H, ArH), 7.54 (t, *J* = 7.6 Hz, 1H, ArH), 7.44 (dt, *J* = 11.2, 5.3 Hz, 2H, ArH), 4.07 (dq, *J* = 7.3, 7.3 Hz, 2H, OCH_2), 1.29 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 132.2 (d, *J* = 3.1 Hz), 131.5 (d, *J* = 10.1 Hz), 129.1 (d, *J* = 193.7 Hz), 128.4 (d, *J* = 15.3 Hz), 62.0 (d, *J* = 5.7 Hz), 16.3 (d, *J* = 6.8 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ 19.4. HRMS (ESI-TOF): calc'd for $C_8H_{12}O_3P$ $[M+H]^+$: 187.0519, found: 187.0523.

3-Fluorophenylphosphonic acid monoethyl ester (2q)



Brown oil (198 mg, 97%). ^{1}H NMR (400 MHz, DMSO) δ 7.61 – 7.50 (m, 2H, ArH), 7.48 – 7.38 (m, 2H, ArH), 3.95 – 3.85 (m, 2H, OCH_2), 1.18 (t, *J* = 7.0 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, DMSO) δ 162.2 (dd, *J* = 246.4, 20.4 Hz), 135.1 (dd, *J* = 182.2, 5.9 Hz), 131.4 (dd, *J* = 16.5, 7.7 Hz), 127.6 (dd, *J* = 8.9, 3.0 Hz), 119.1 (dd, *J* = 20.8, 3.0 Hz), 117.9 (dd, *J* = 21.7, 10.5 Hz), 61.4 (d, *J* = 5.3 Hz), 16.7 (d, *J* = 6.3 Hz). ^{31}P NMR (162 MHz, DMSO) δ 12.5 (d, *J* = 8.3 Hz). HRMS (ESI-TOF): calc'd for $C_8H_{11}FO_3P$ $[M+H]^+$: 205.0424, found: 205.0428.

4-Methylphenylphosphonic acid monoethyl ester (2r)



Brown oil (196 mg, 98%). ^{1}H NMR (400 MHz, DMSO) δ 7.59 (dd, *J* = 12.8, 8.1 Hz, 2H, ArH), 7.33 – 7.28 (m, 2H, ArH), 3.85 (dq, *J* = 7.9, 7.1 Hz, 2H, OCH_2), 2.36 (s, 3H, CH_3C_q), 1.17 (t, *J* = 7.0 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, DMSO) δ 142.0 (d, *J* = 3.1 Hz), 131.5 (d, *J* = 10.1 Hz), 129.4 (d, *J* = 14.7 Hz), 128.6 (d, *J* = 185.0 Hz), 60.9 (d, *J* = 5.1 Hz), 21.6 (d, *J* = 1.3 Hz), 16.7 (d, *J* = 6.4 Hz). ^{31}P NMR (162 MHz, DMSO) δ 15.4. HRMS (ESI-TOF): calc'd for $C_9H_{14}O_3P$ $[M+H]^+$: 201.0675, found: 201.0682.

3. Unsuccessful substrates

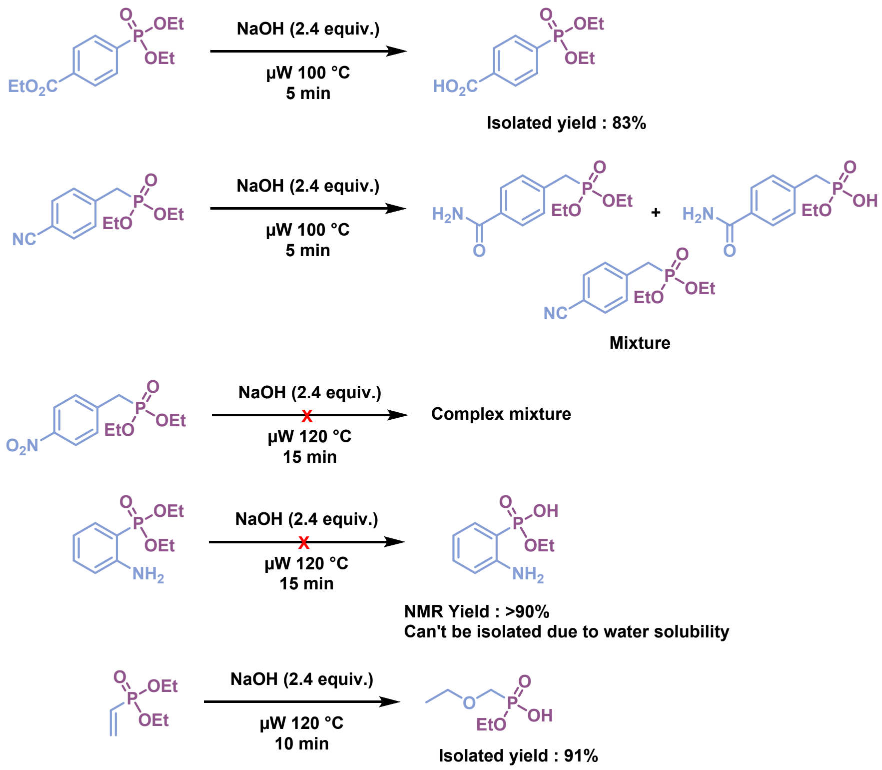


Figure 1: Unsuccessful substrates.

4. Thermal vs MW activation

General procedure for the microwave assisted selective hydrolysis of substituted phosphonates

Substituted phosphonate (1.0 mmol, 1.0 eq), sodium hydroxide (2.4 mmol, 2.4 eq) and ethanol (1 mL) were placed in a 10 mL Schott® sealed tube equipped with a magnetic stirrer. The reaction vessel was heated at the appropriate temperature with a heat-on. After the indicated time, the reaction mixture was cooled down in an ice bath, partitioned between EtOAc (5 mL) and 1N HCl (5 mL), decanted and the organic layer was washed with brine (5 mL). The combined aqueous layers were extracted with EtOAc (3 × 10 mL), then the combined organic layers were dried over $MgSO_4$ (1.5 g) and concentrated under reduced pressure to give the desired phosphonic acid monoester.

Comparison of kinetics

The selective hydrolysis kinetic of substrate **1b** was evaluated at 100 °C for a reaction time of 5, 10 and 15 minutes with a conventional heating in a sealed tube and 1, 5 and 10 minutes with MW irradiation (Figure 2). On the other hand, the selective hydrolysis kinetic of substrate **1a** was evaluated at 150 °C for a reaction time of 15 and 30 minutes with a conventional heating in a sealed tube and with MW irradiation (Figure 3). The data were modelized according to a 2nd order kinetic as suitable for a basic hydrolysis reaction without large excess of reagent. The reaction rate was manually optimized to fit as best as possible the experimental data hence the relative rate $\frac{v_{MW}}{v_{thermal}}$ was evaluated.

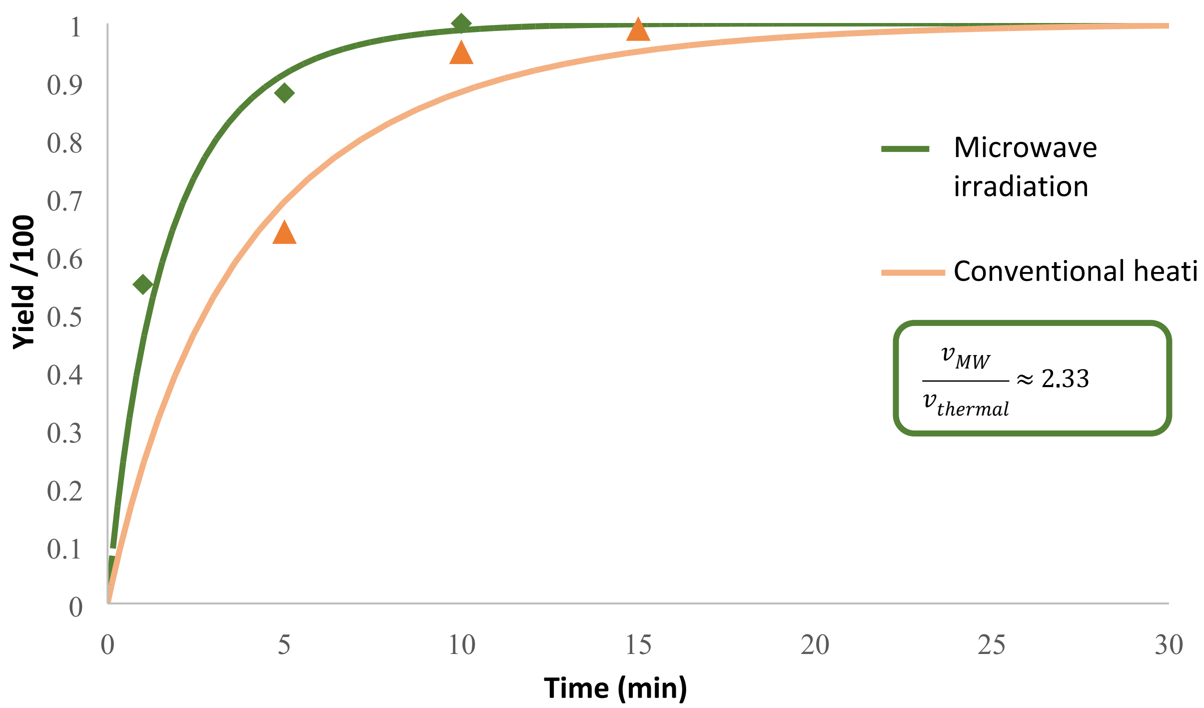


Figure 2: Kinetic monitoring by ^{31}P NMR for the formation of **2b**.

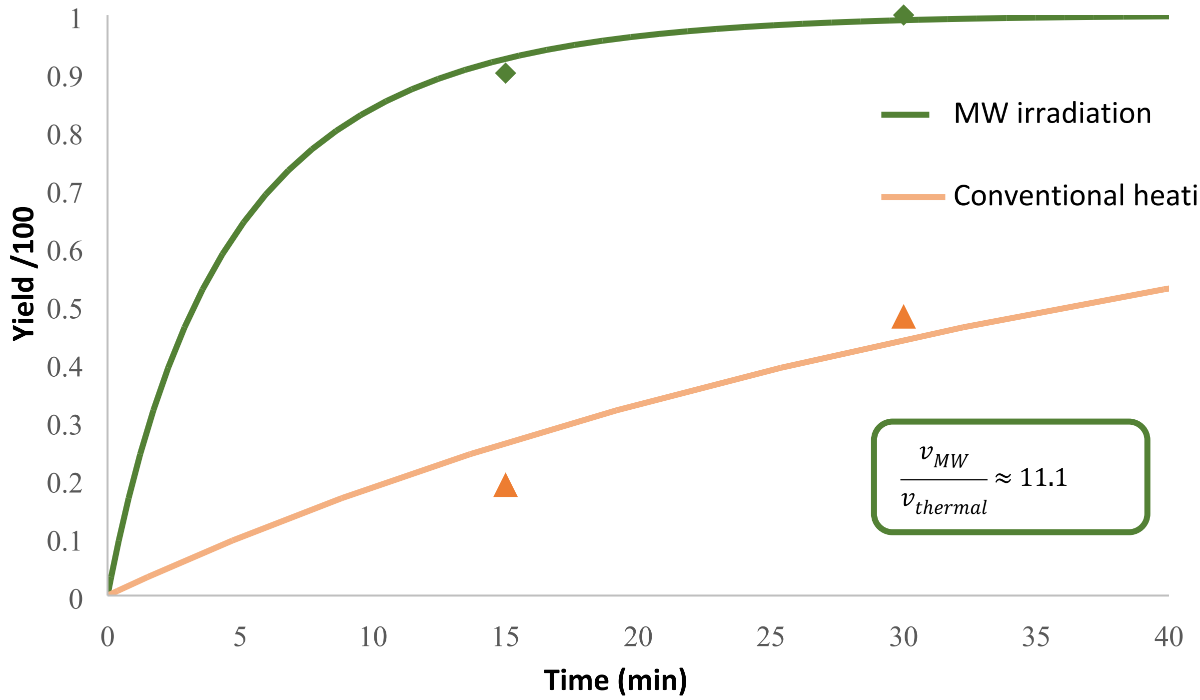
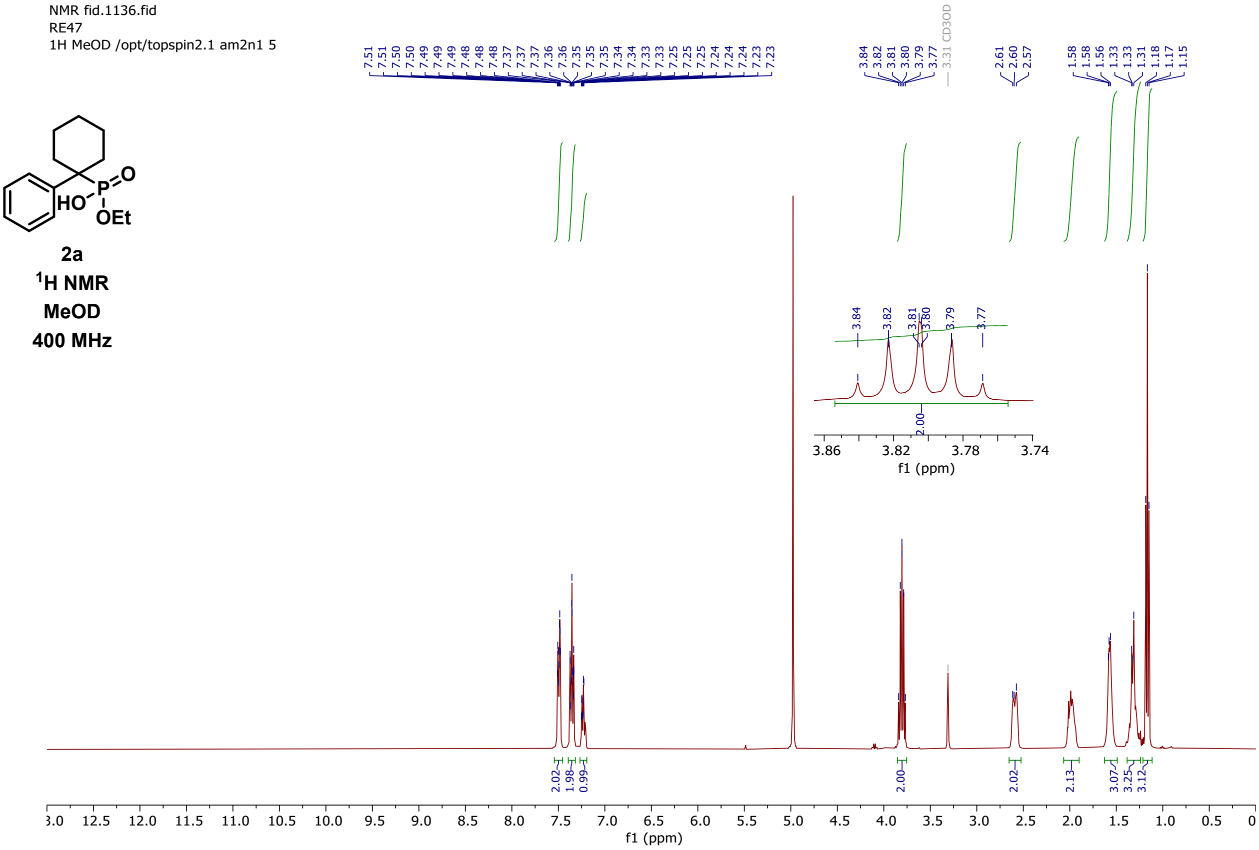
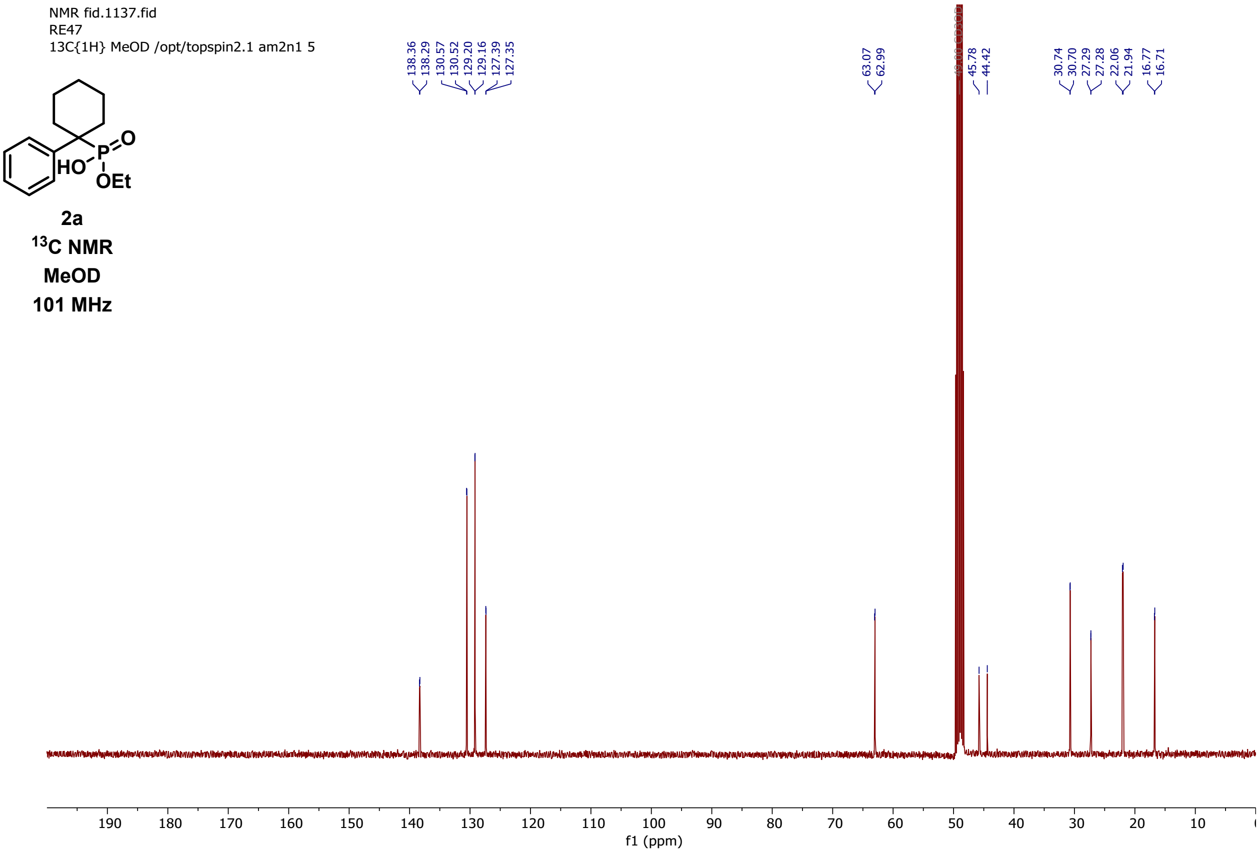


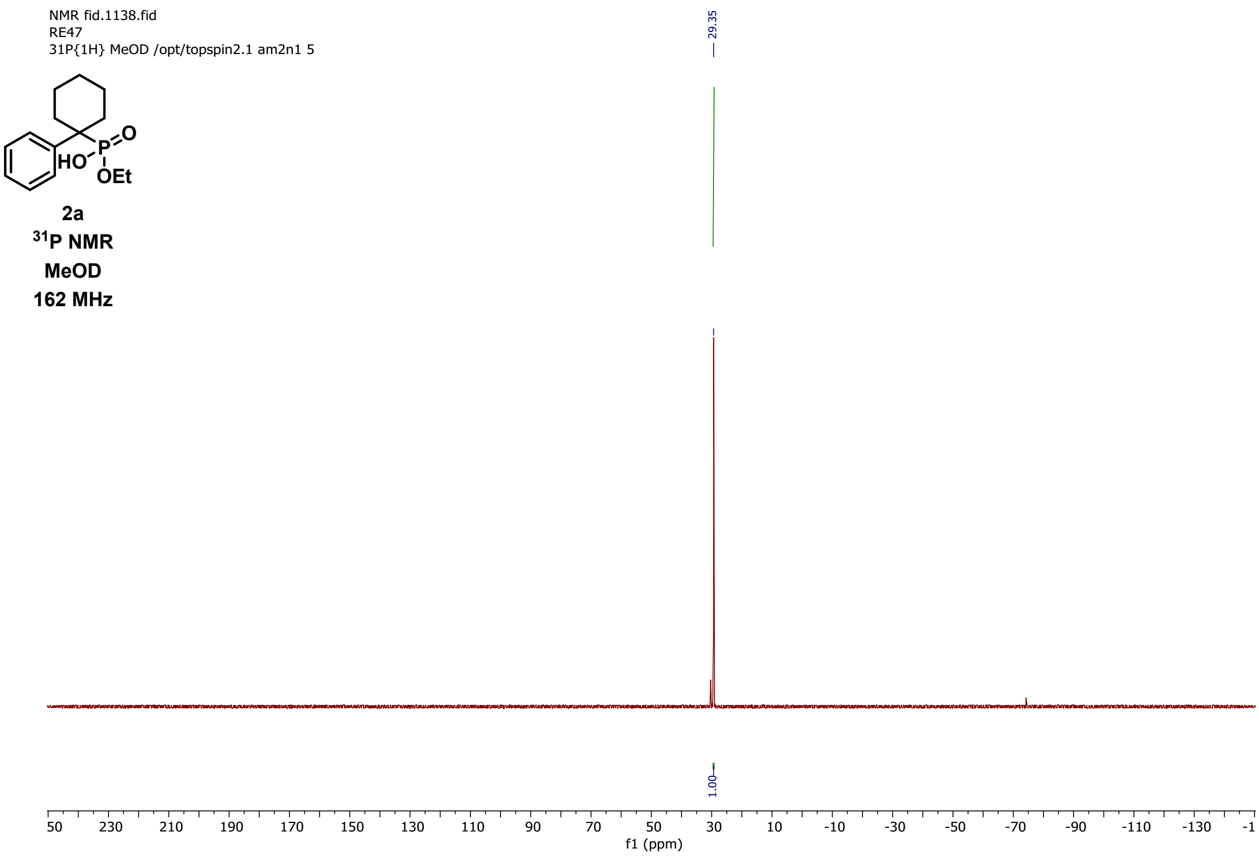
Figure 3: Kinetic monitoring by ^{31}P NMR for the formation of **2a**.

5. NMR data

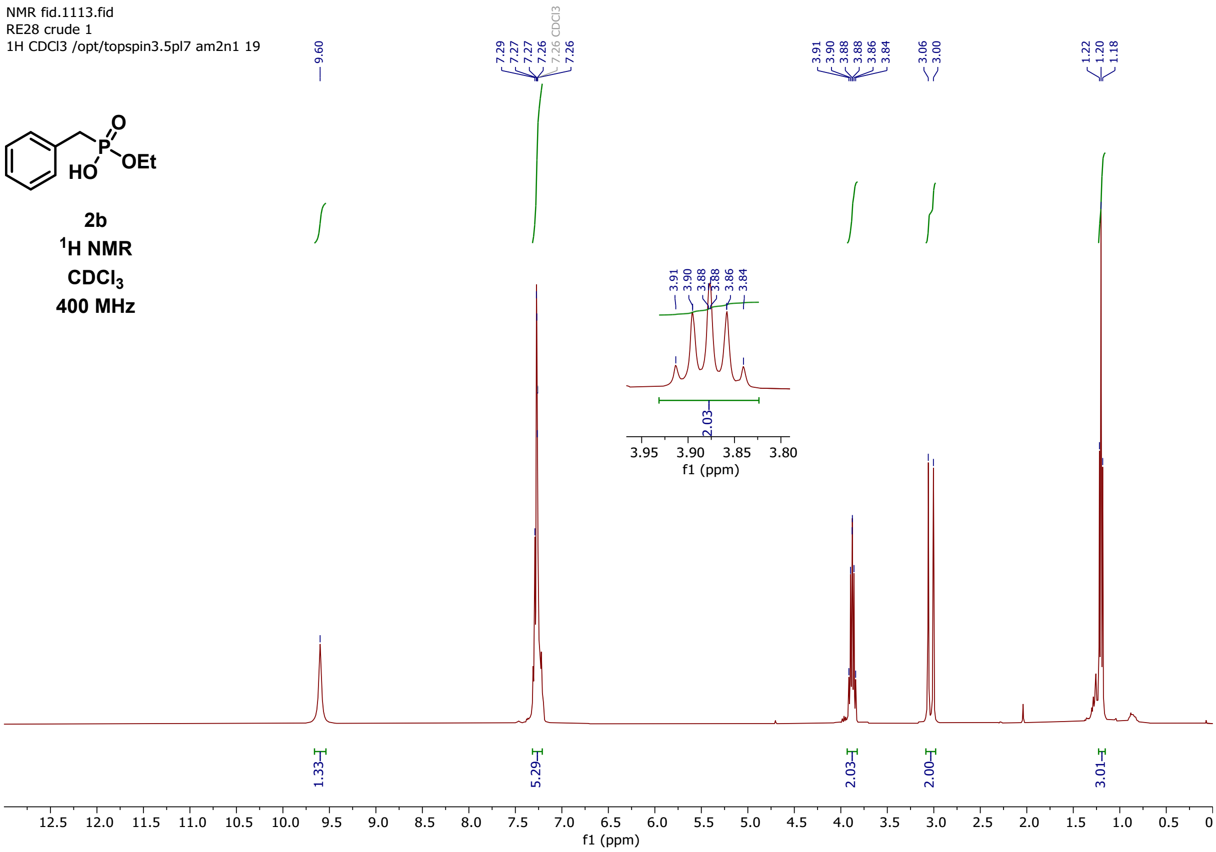
Cyclohexylbenzylphosphonic acid monoethyl ester (2a)

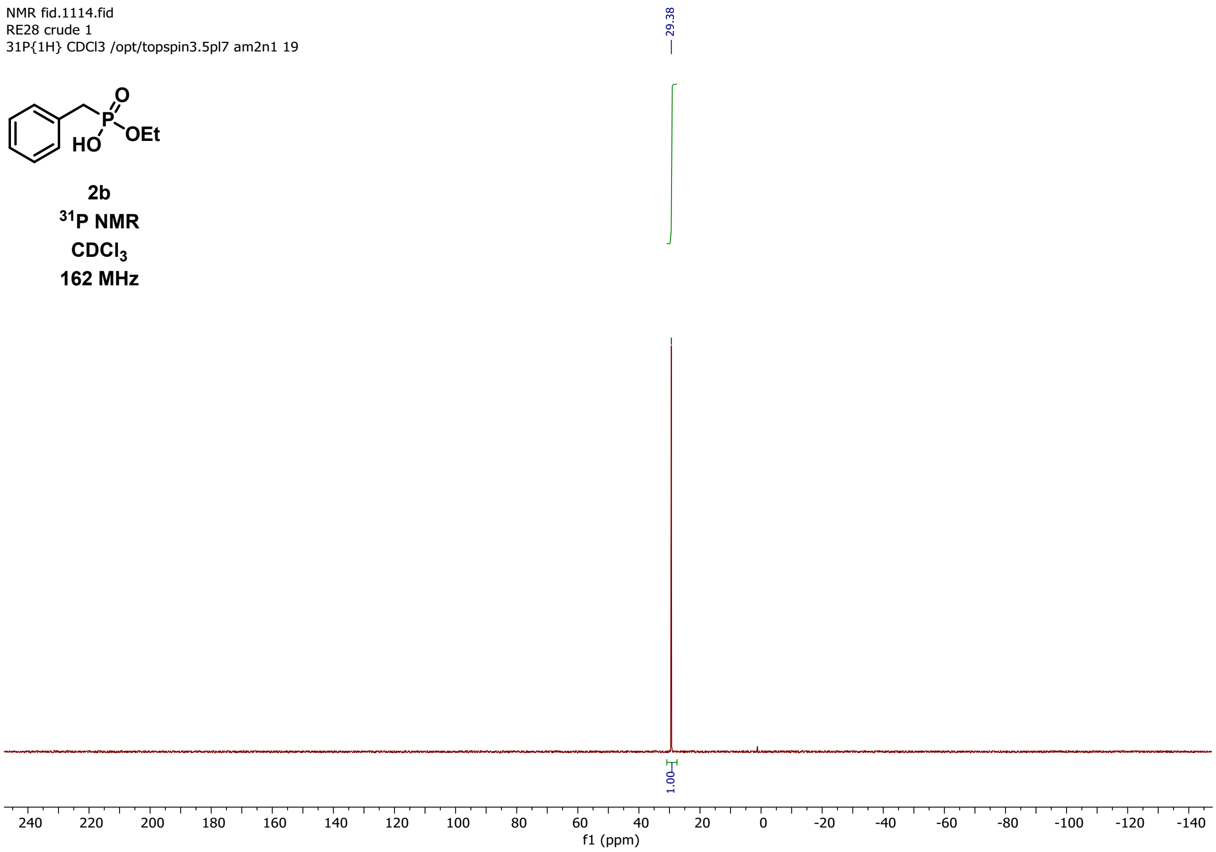




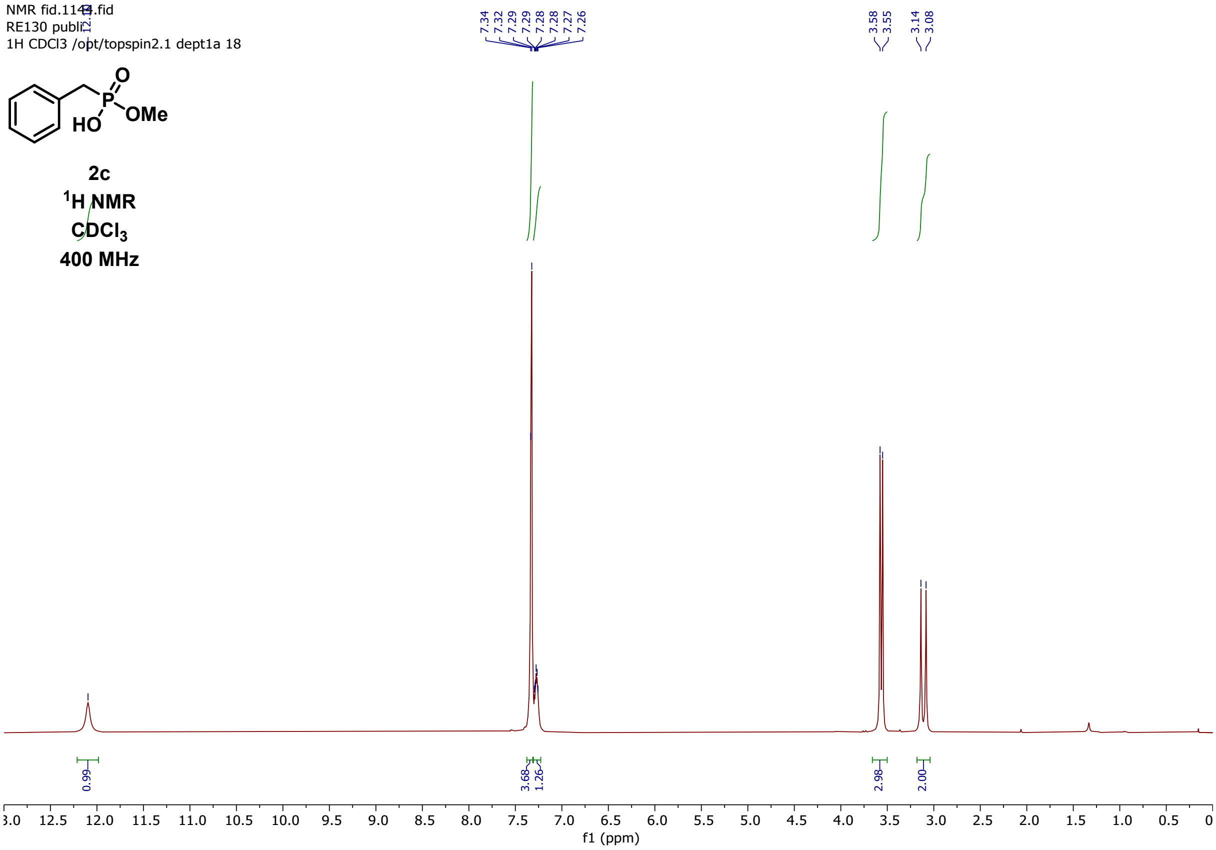


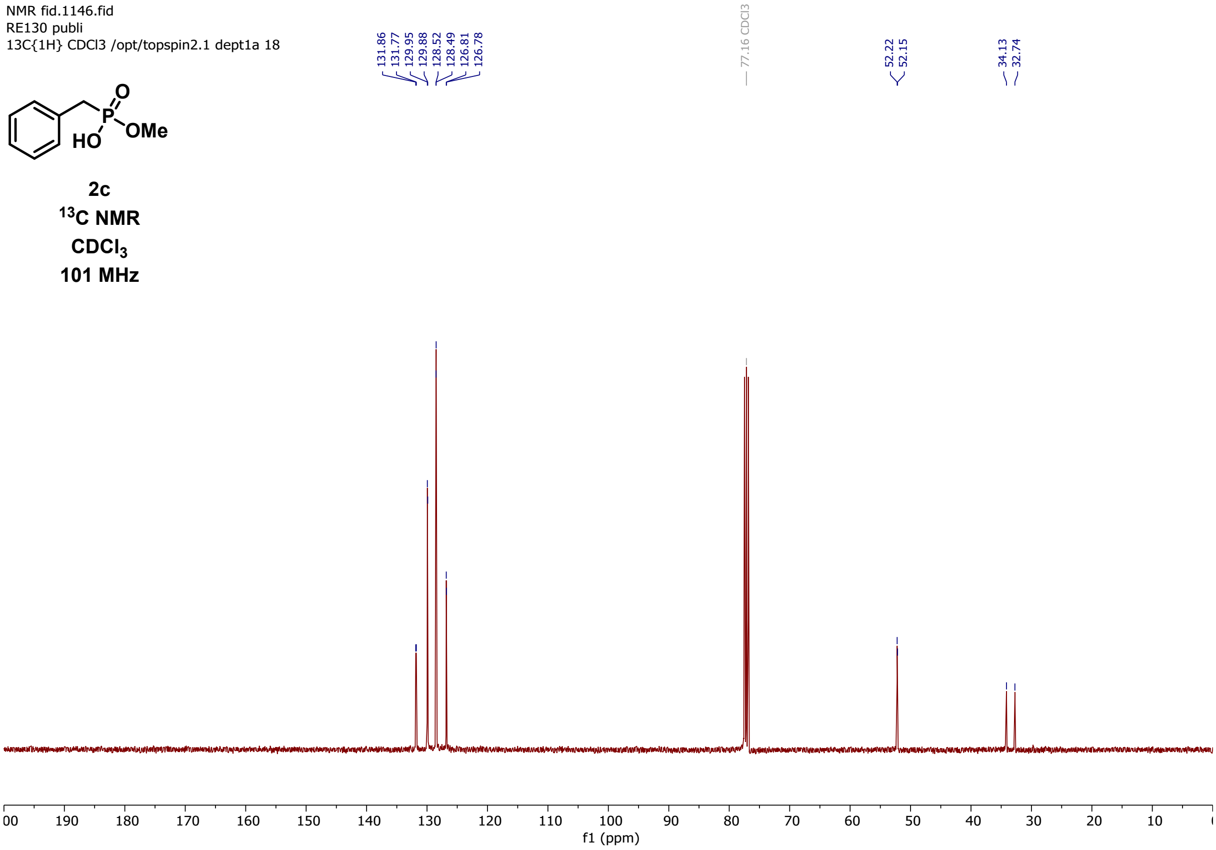
Benzylphosphonic acid monoethyl ester (2b)





Benzylphosphonic acid monomethyl ester (2c)


NMR fid.1144.fid
RE130 publi
1H CDCl3 /opt/topspin2.1 dept1a 18
2c
1H NMR
CDCl3
400 MHz
12.10
7.34 7.32 7.29 7.29 7.28 7.28 7.27 7.26
3.58 3.55
3.14 3.08
0.99
3.68 1.26
2.98
2.00
f1 (ppm)


NMR fid.1146.fid
RE130 publi
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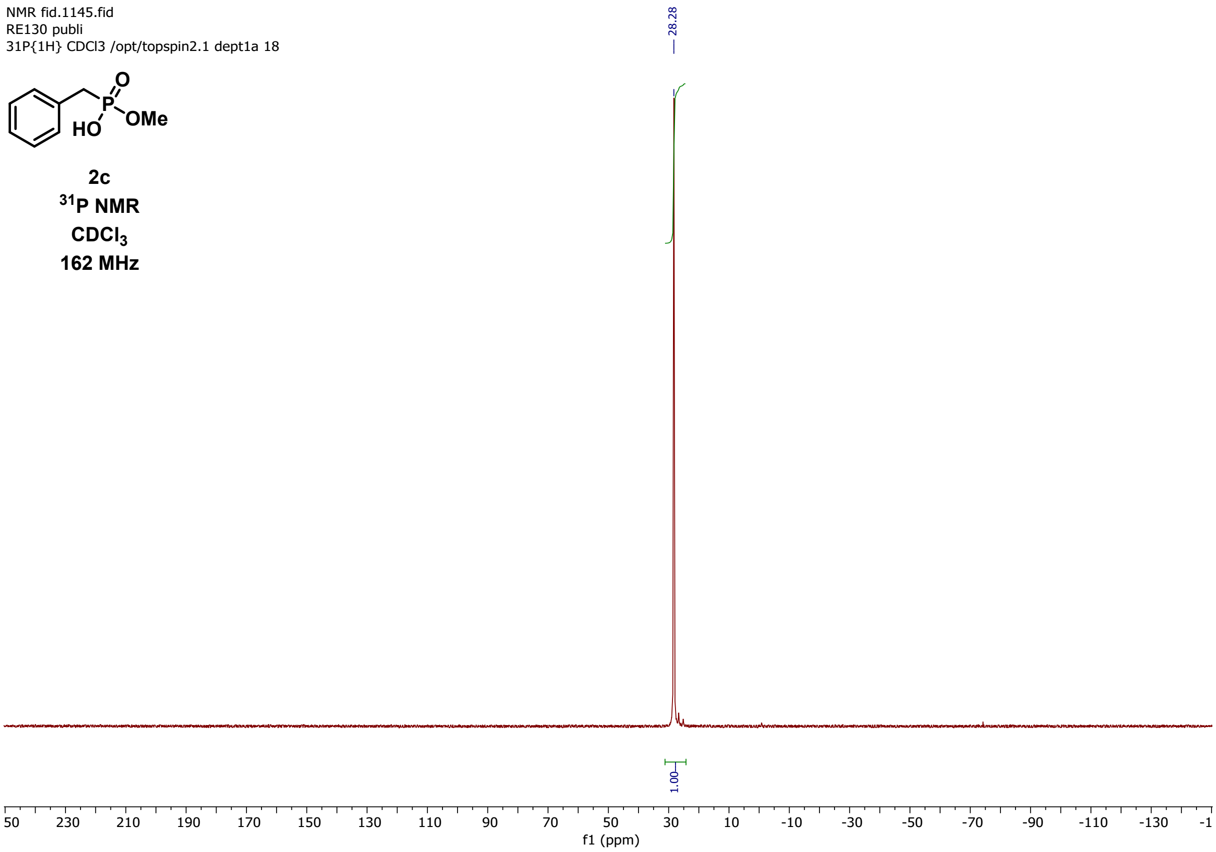
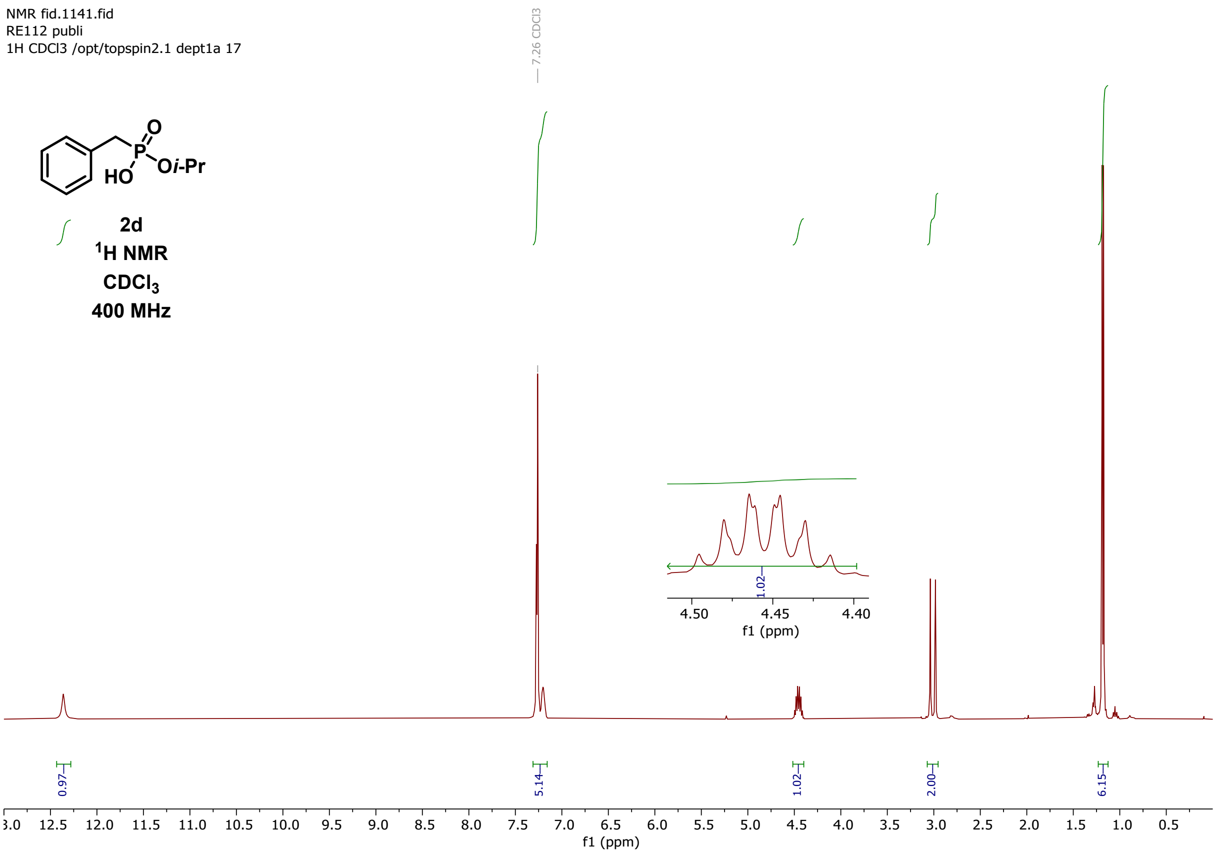
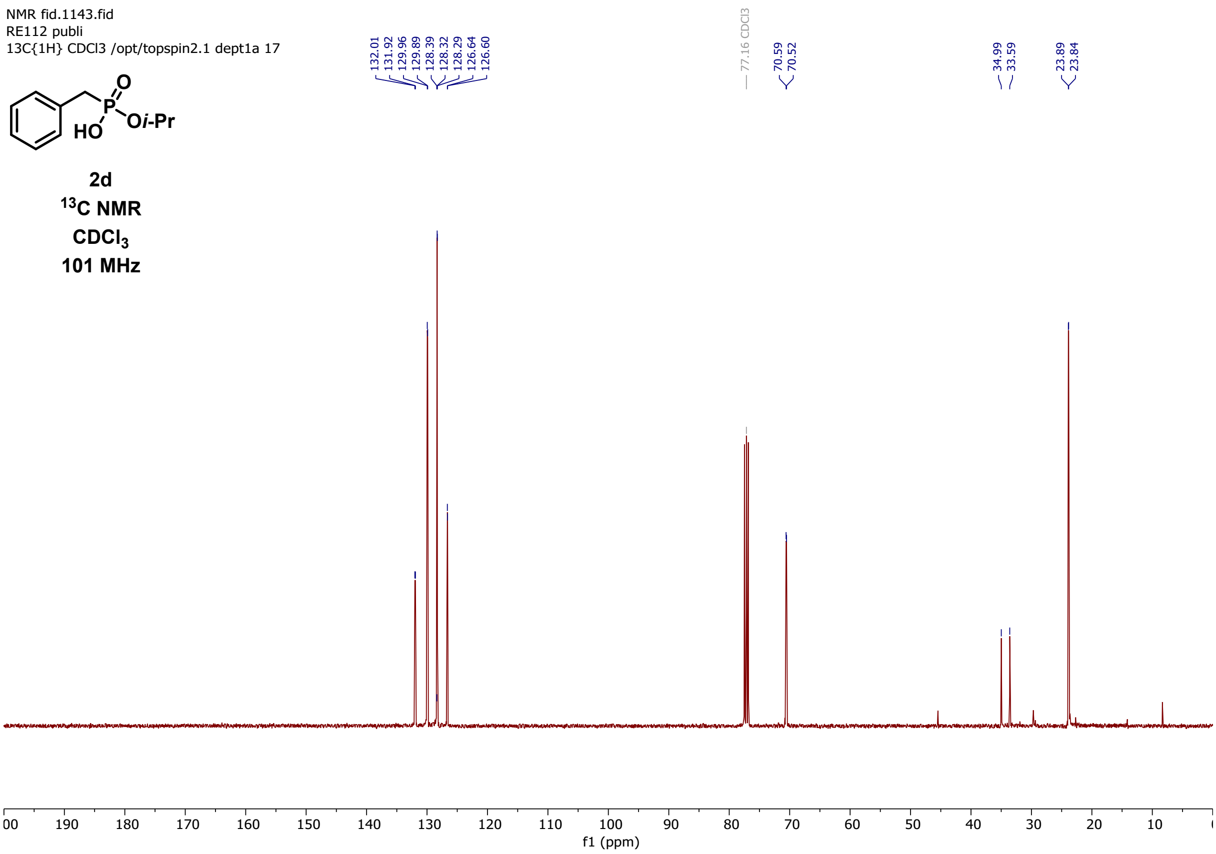
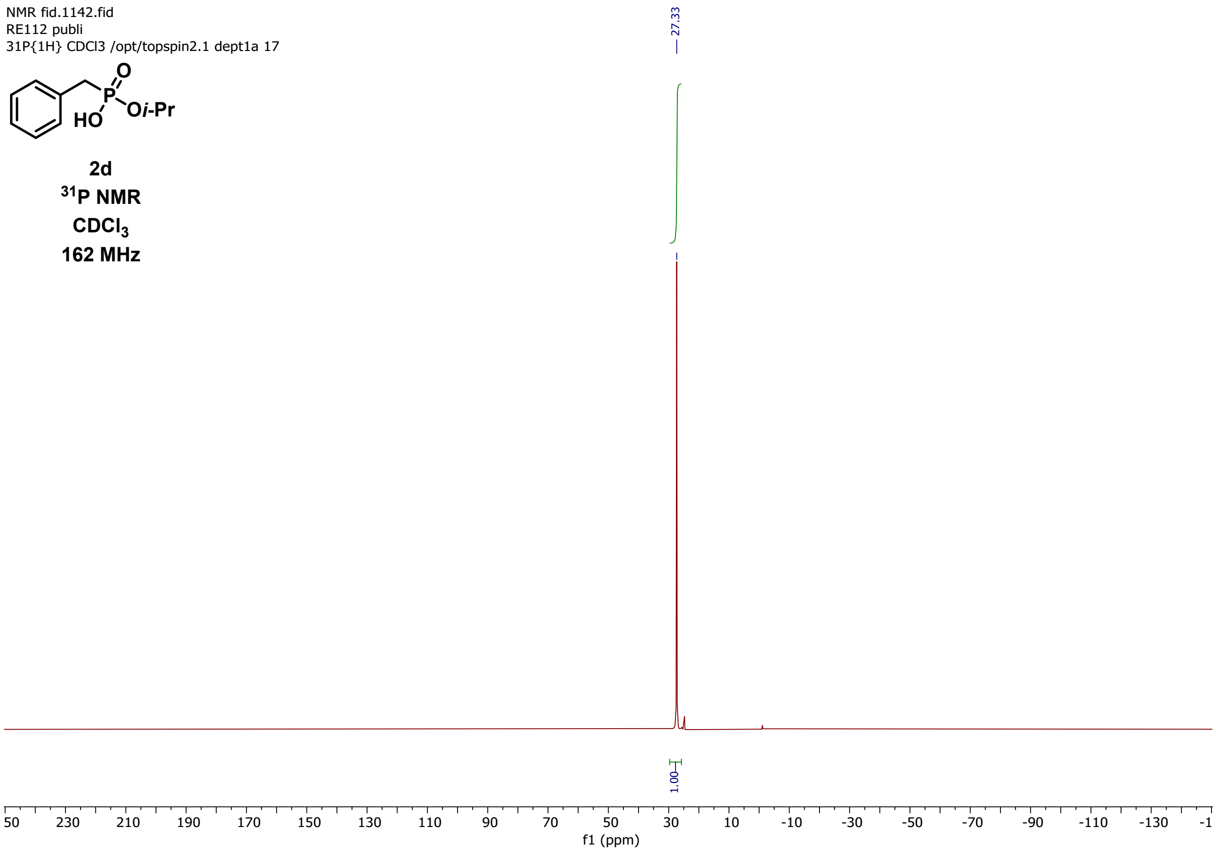
2c
13C NMR
CDCl3
101 MHz
131.86 131.77 129.95 129.88 128.52 128.49 126.81 126.78
77.16 CDCl3
52.22 52.15
34.13 32.74
f1 (ppm)


NMR fid.1145.fid
RE130 publi
31P{1H} CDCl3 /opt/topspin2.1 dept1a 18
HO
OMe
O
P
2c
31P NMR
CDCl3
162 MHz
28.28
1.00
50
230
210
190
170
150
130
110
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-1
f1 (ppm)

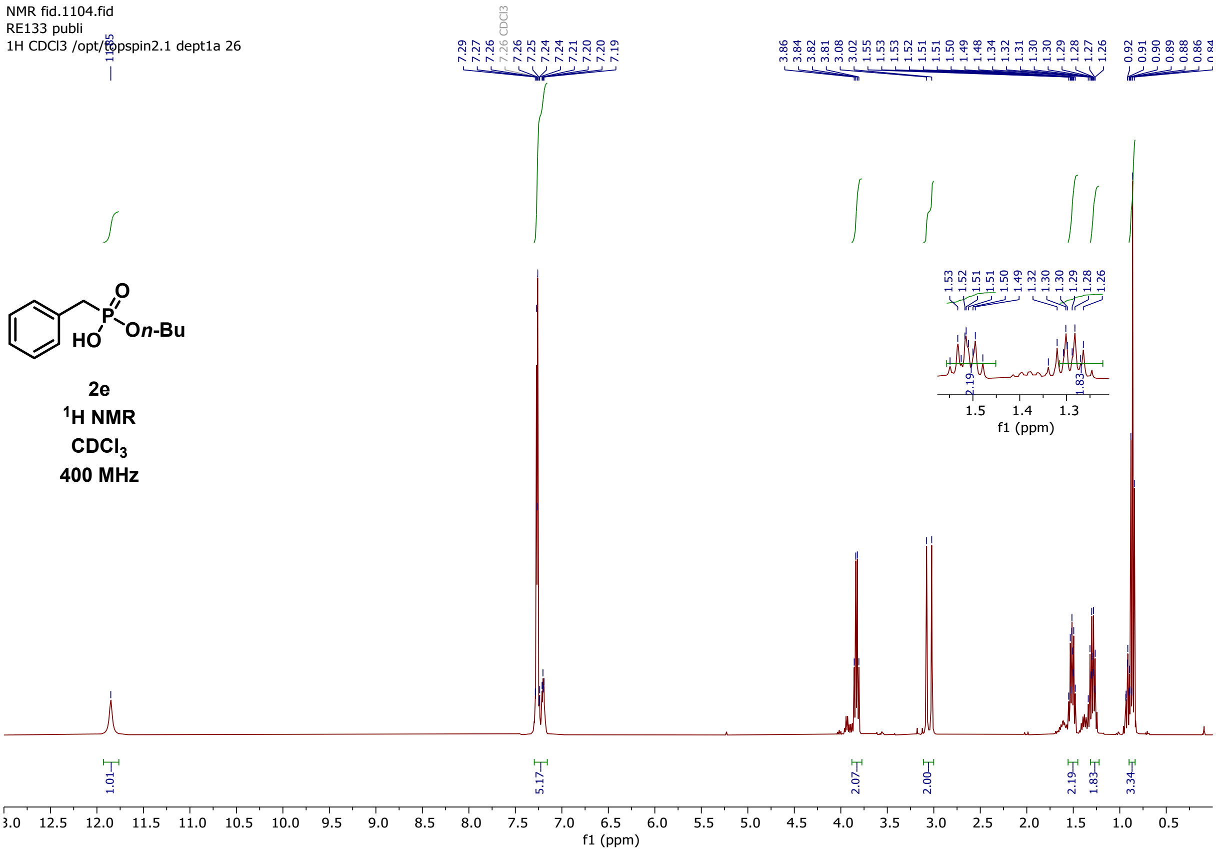
Benzylphosphonic acid monoisopropyl ester (2d)



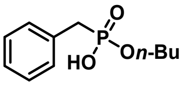




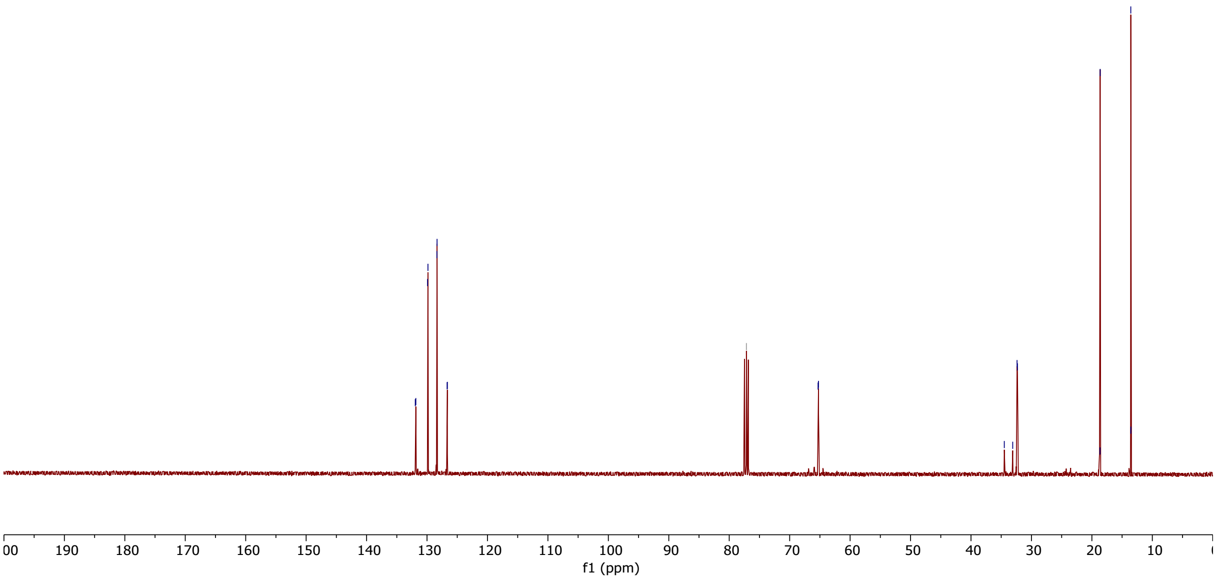
Benzylphosphonic acid n-monobutyl ester (2e)



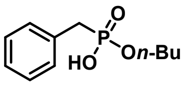
NMR fid.1106.fid
RE133 publi
13C{1H} CDCl3 /opt/topspin2.1 dept1a 26



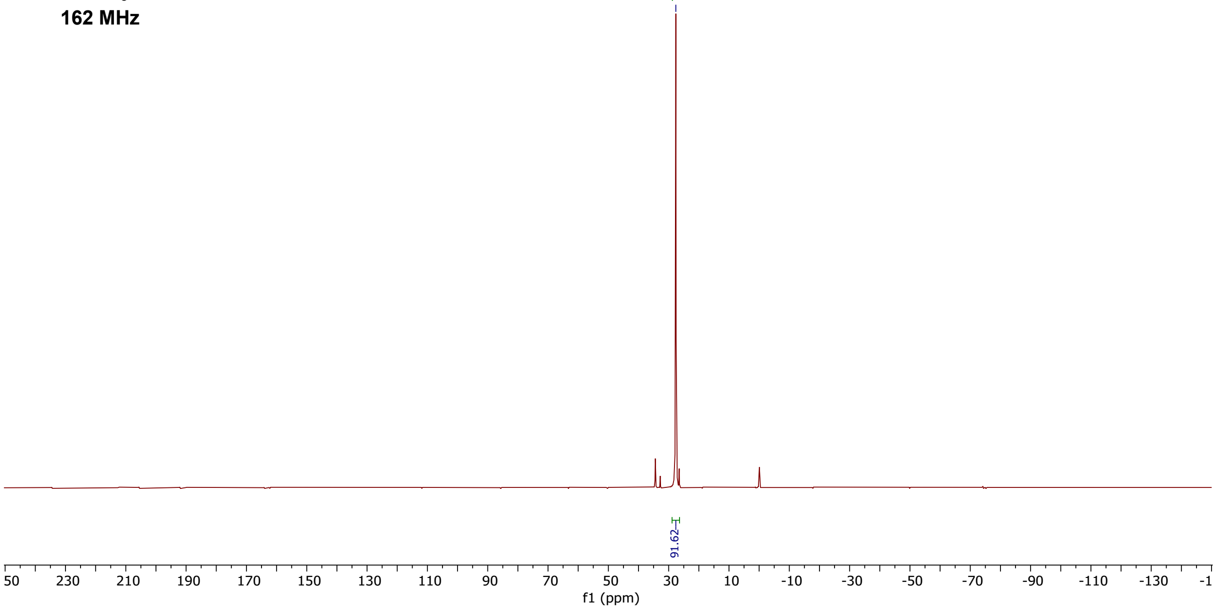
2e
^{13}C NMR
$CDCl_3$
101 MHz



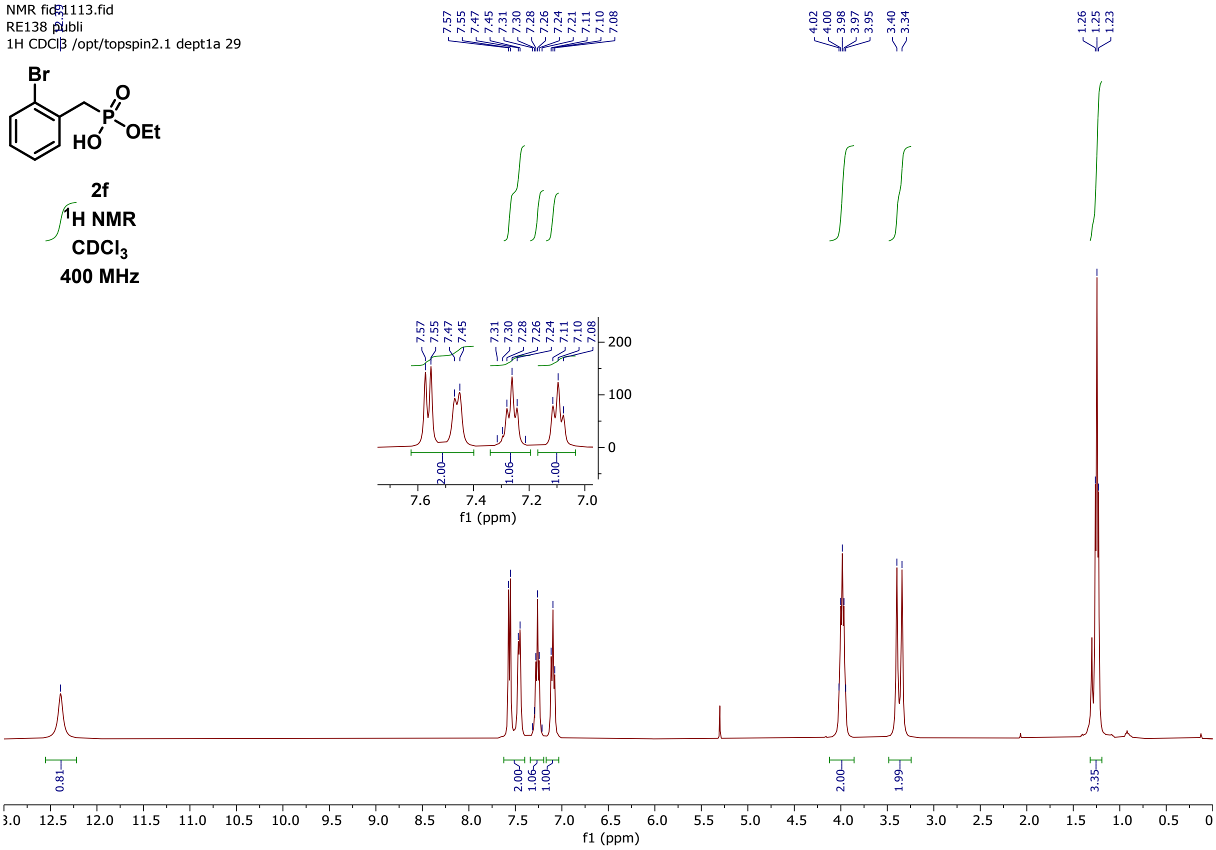
NMR fid.1105.fid
RE133 publi
31P{1H} CDCl3 /opt/topspin2.1 dept1a 26

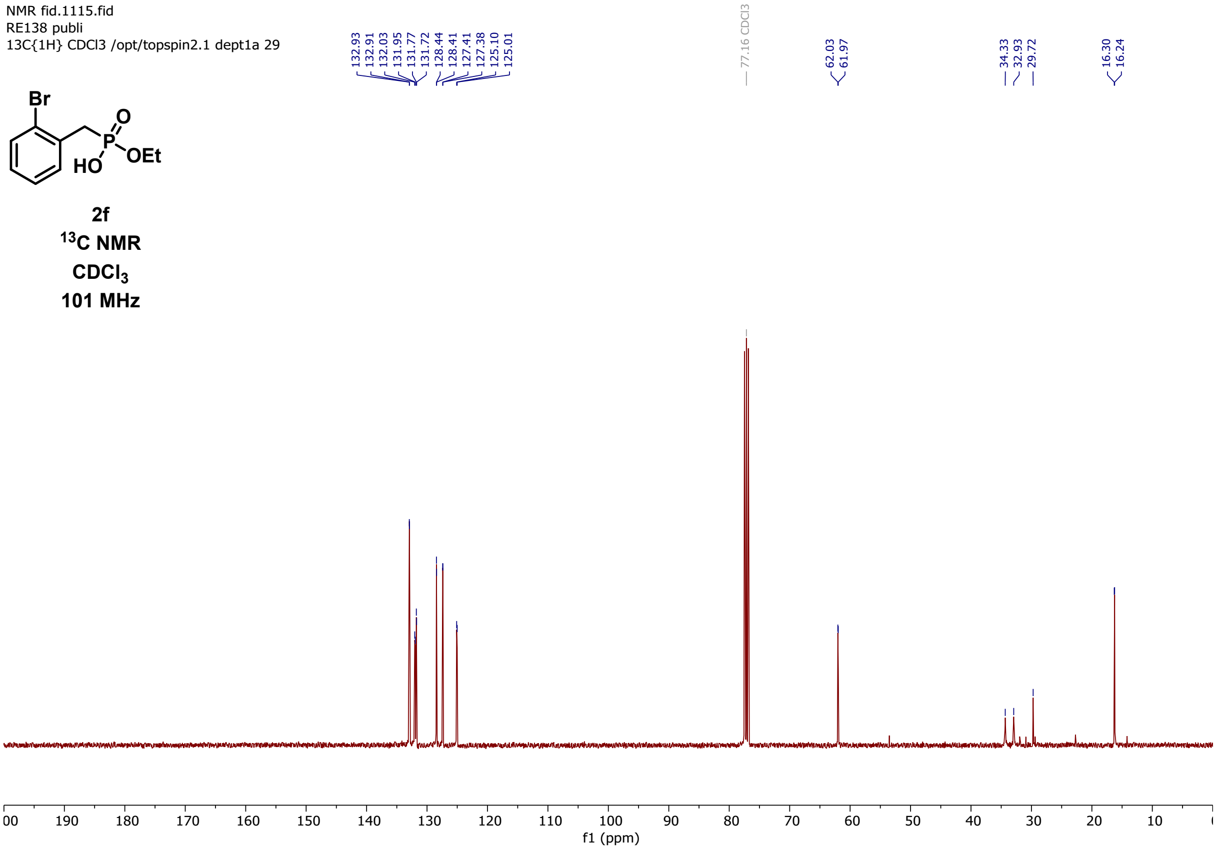


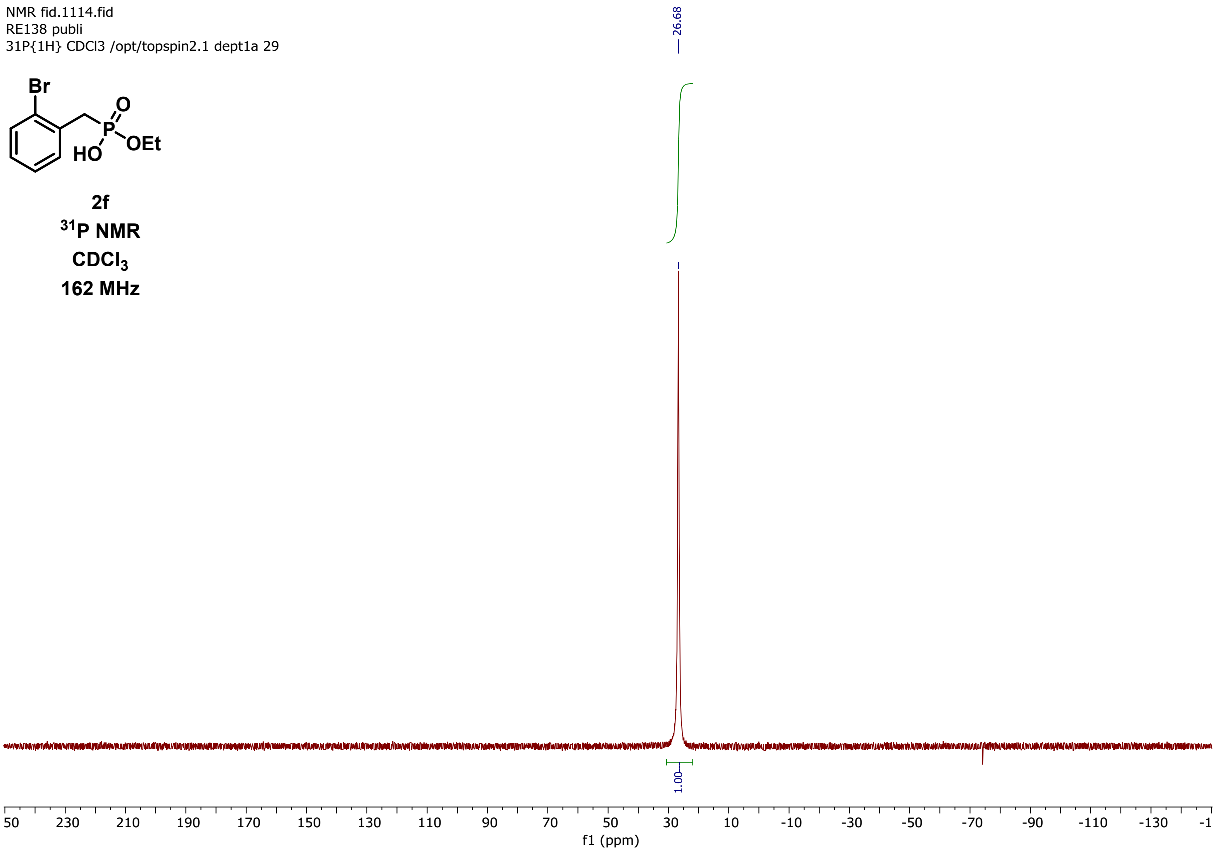
2e
^{31}P NMR
$CDCl_3$
162 MHz



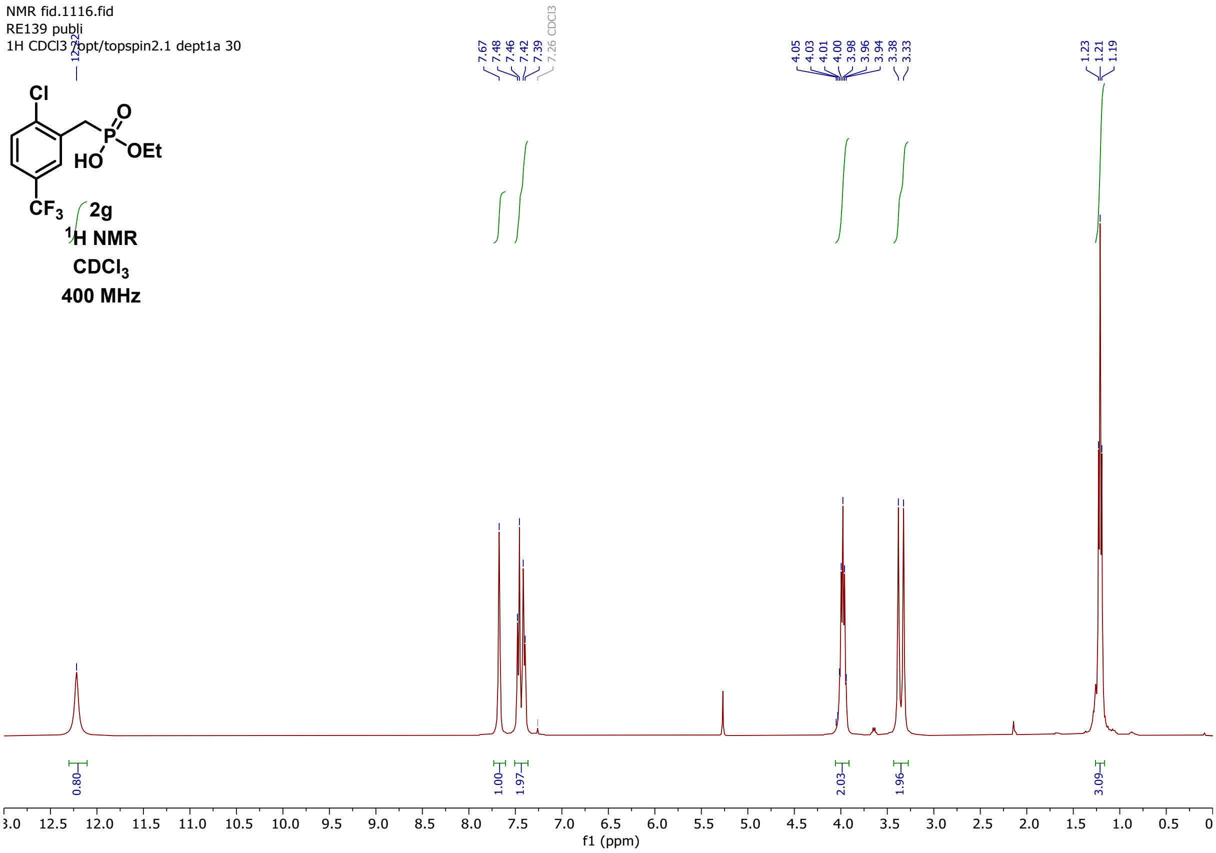
2-Bromobenzylphosphonic acid monoethyl ester (2f)

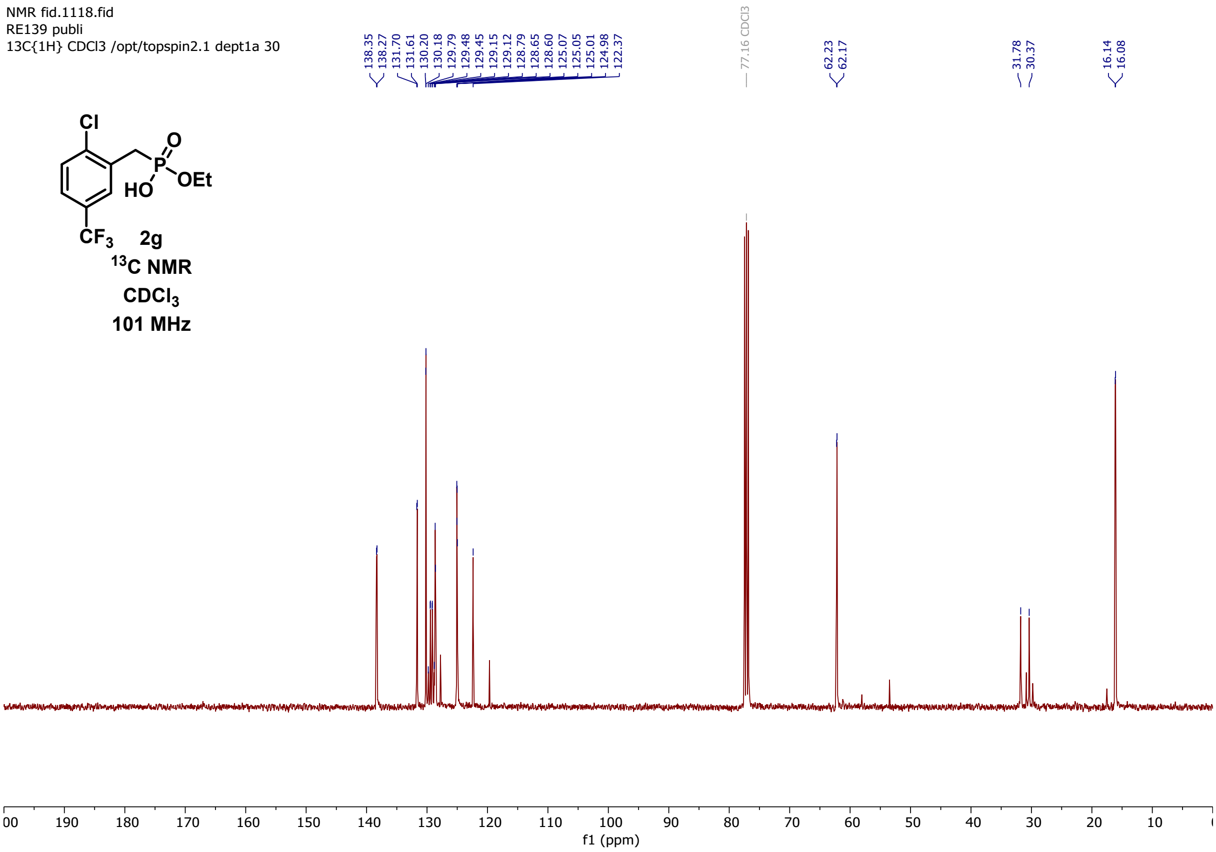


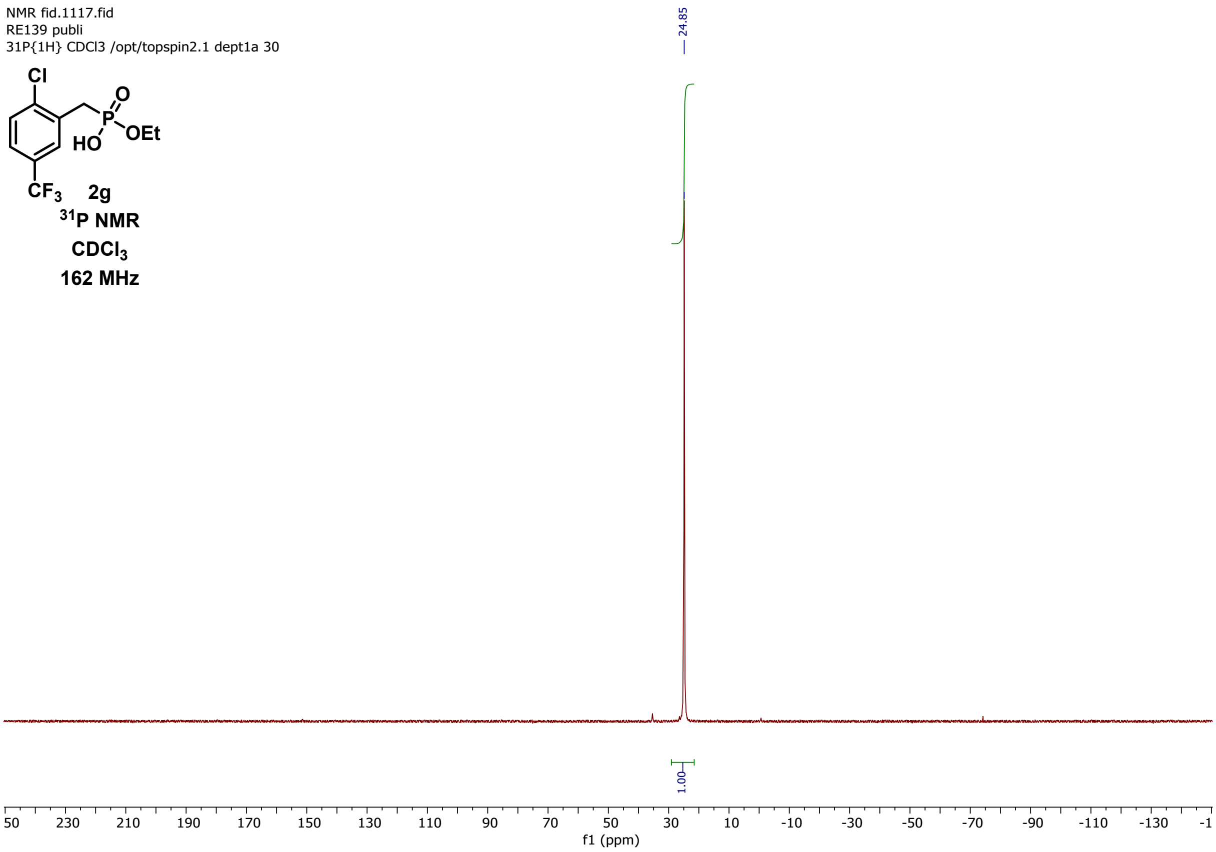




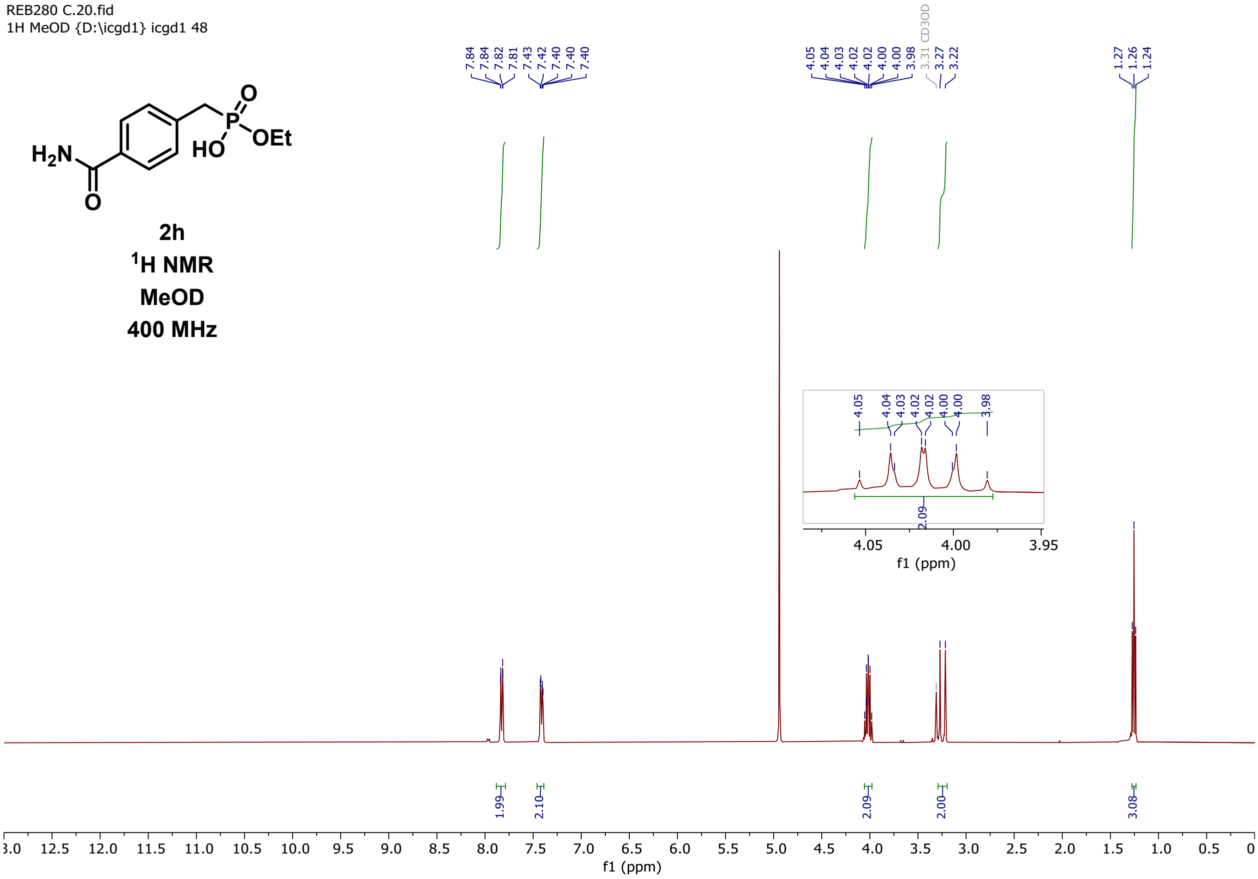
2-Chloro-5-trifluoromethylbenzylphosphonic acid monoethyl ester (2g)

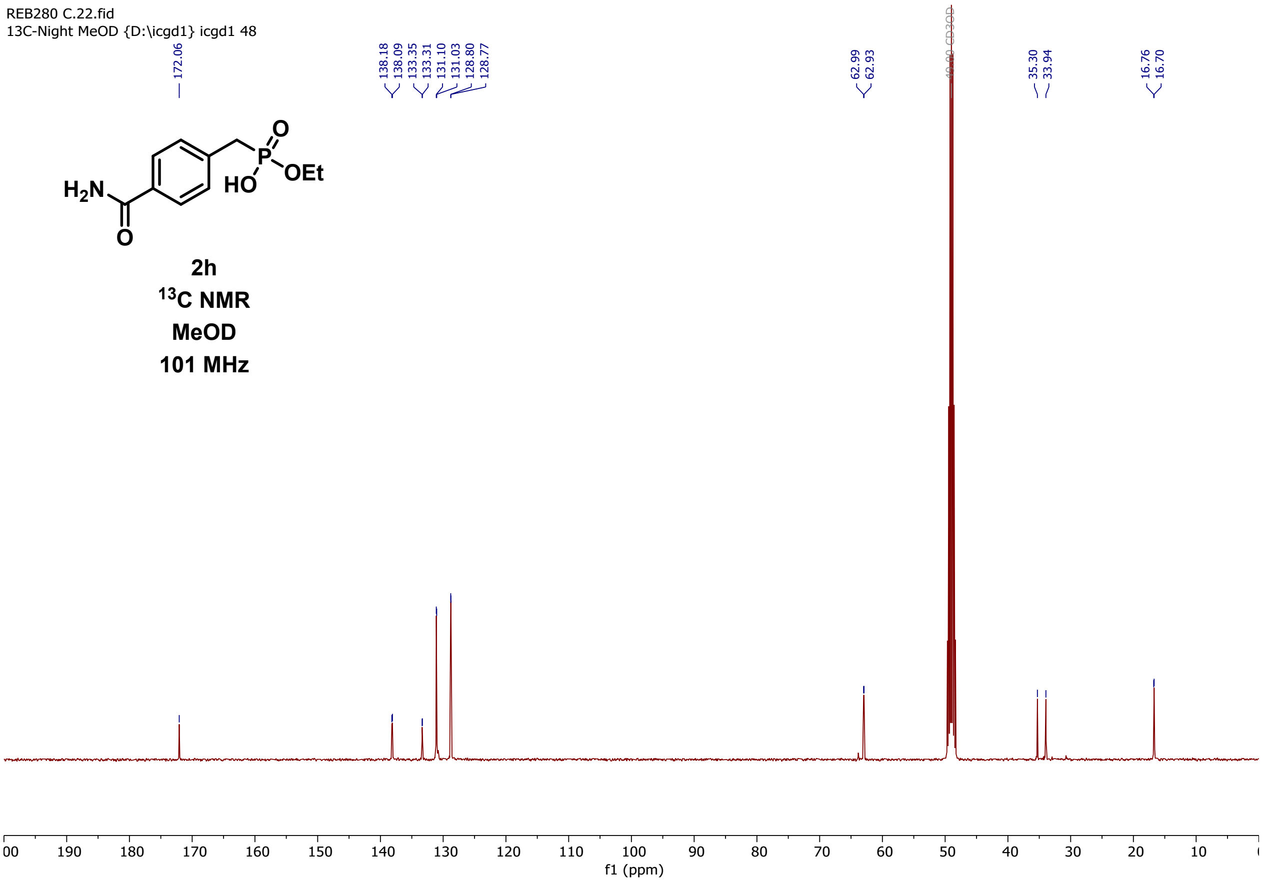


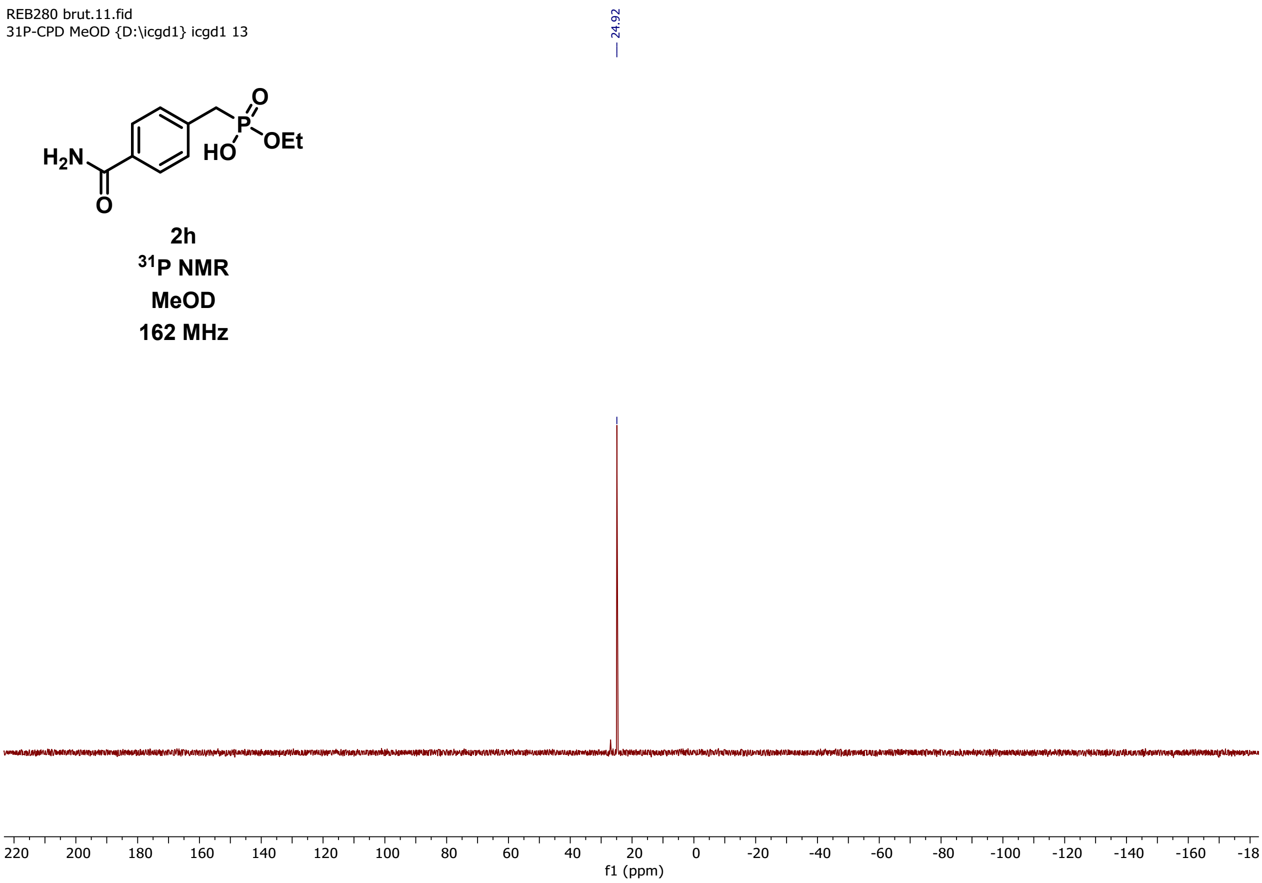

NMR fid.1118.fid
RE139 publi
13C{1H} CDCl3 /opt/topspin2.1 dept1a 30
2g
13C NMR
CDCl3
101 MHz
f1 (ppm)


NMR fid.1117.fid
RE139 publi
31P{1H} CDCl3 /opt/topspin2.1 dept1a 30
2g
31P NMR
CDCl3
162 MHz
24.85
f1 (ppm)

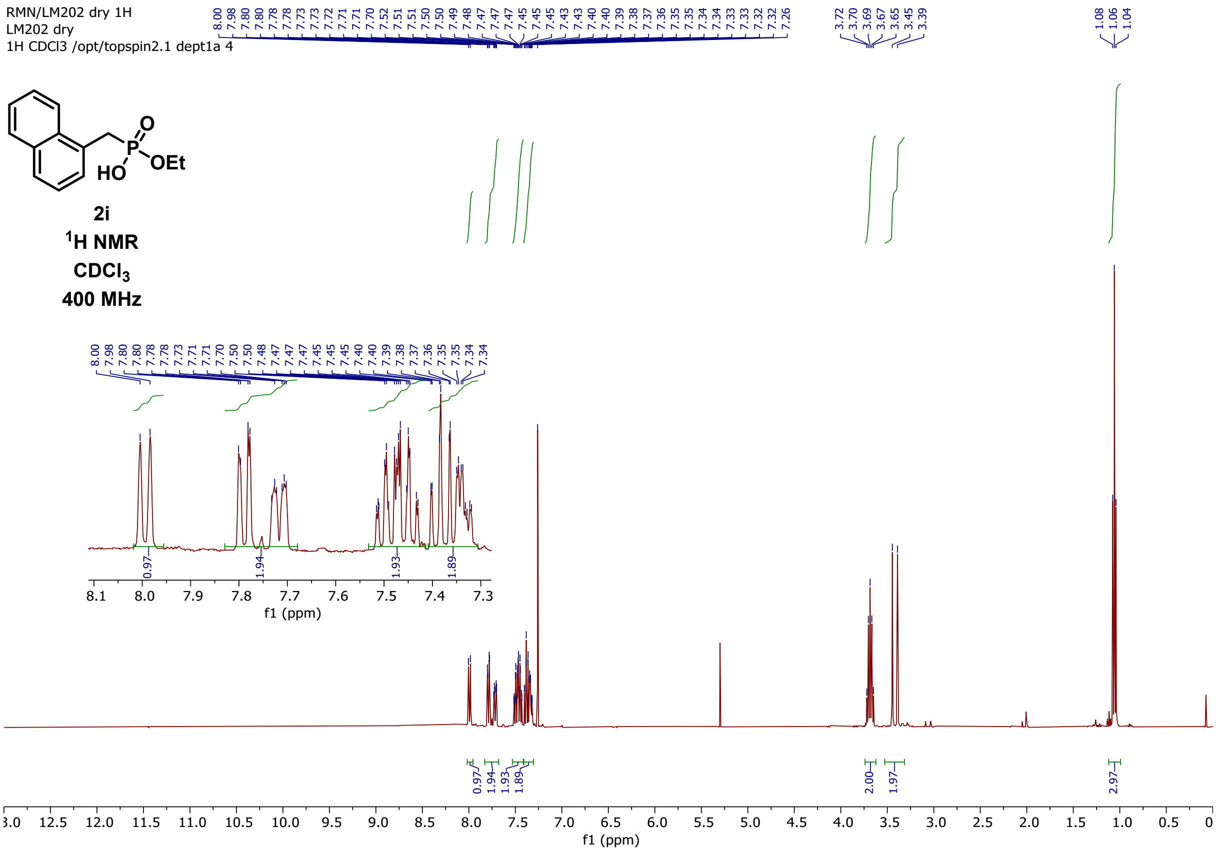
4-Carbamoylbenzylphosphonic acid monoethyl ester (2h)

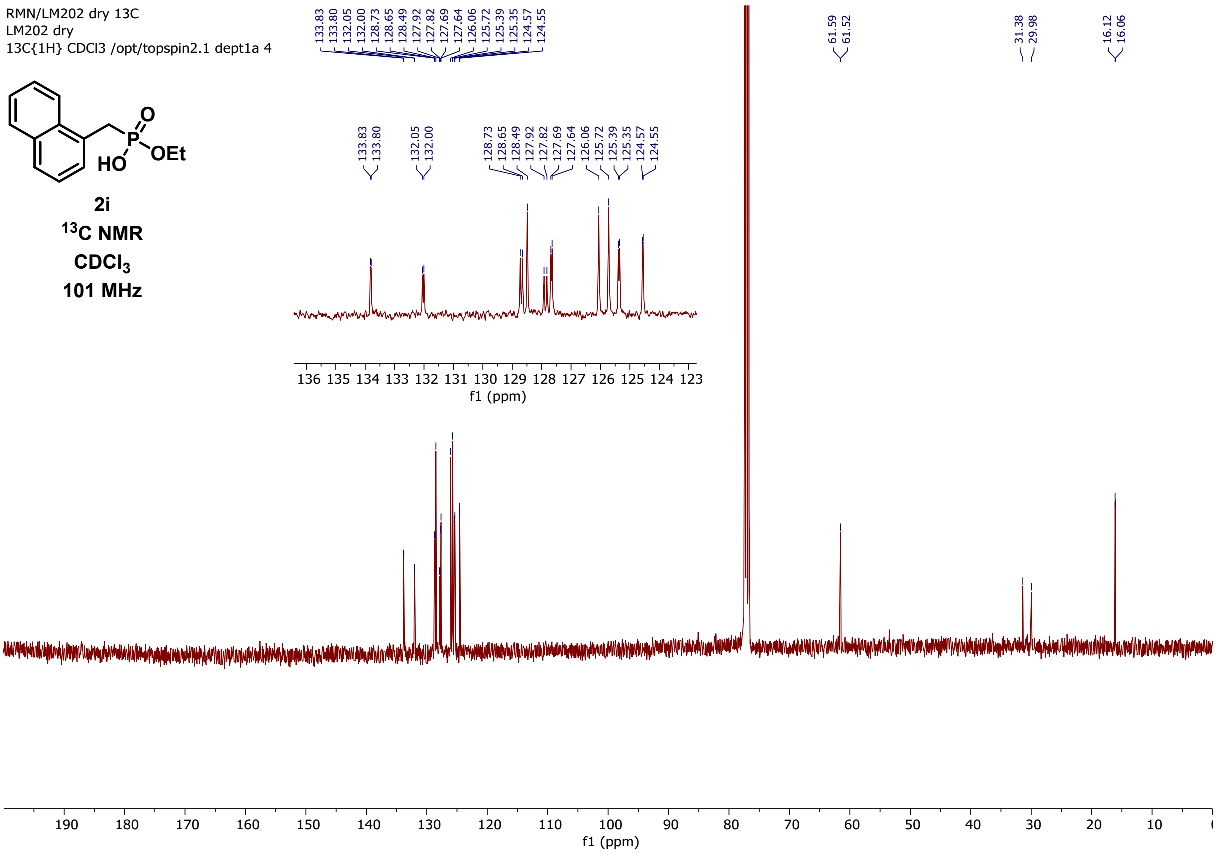




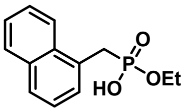


Naphthalen-1-ylmethylphosphonic acid monoethyl ester (2i)

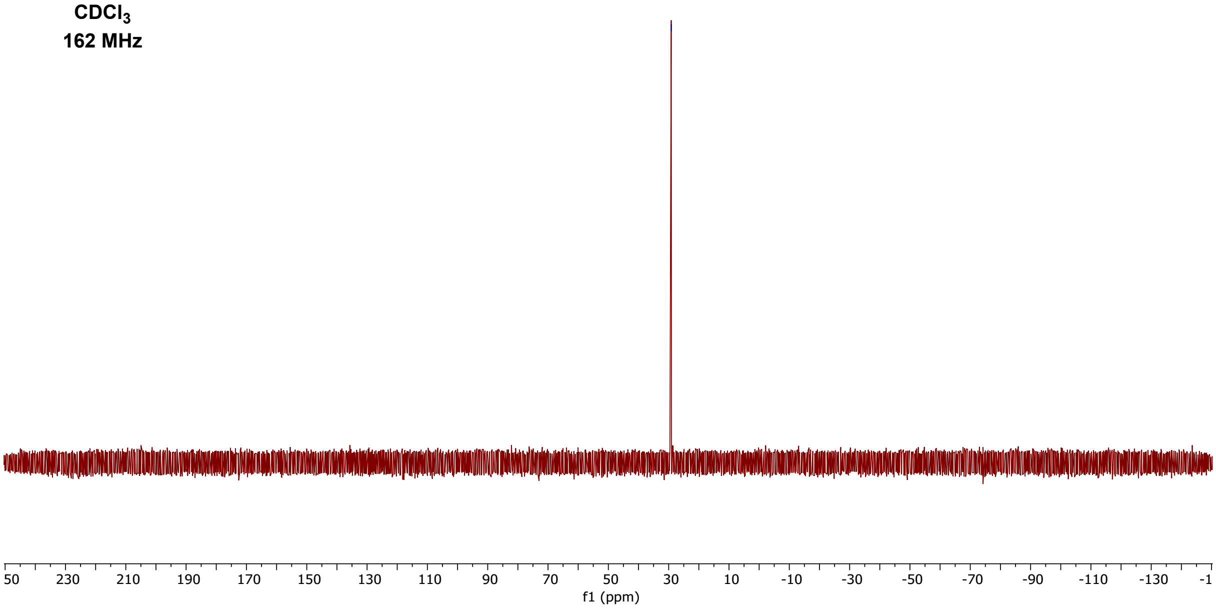

RMN/LM202 dry 1H
LM202 dry
1H CDCl3 /opt/topspin2.1 dept1a 4
2i
1H NMR
CDCl3
400 MHz
8.00 7.98 7.80 7.80 7.78 7.78 7.73 7.73 7.72 7.71 7.71 7.71 7.70 7.52 7.51 7.51 7.50 7.50 7.49 7.48 7.47 7.47 7.47 7.45 7.45 7.45 7.43 7.43 7.40 7.40 7.39 7.38 7.37 7.36 7.35 7.35 7.34 7.34 7.33 7.33 7.32 7.32 7.26
3.72 3.70 3.69 3.67 3.65 3.45 3.39
1.08 1.06 1.04
0.97 1.94 1.93 1.89 2.00 1.97 2.97
f1 (ppm)


RMN/LM202 dry 13C
LM202 dry
13C{1H} CDCl3 /opt/topspin2.1 dept1a 4
2i
13C NMR
CDCl3
101 MHz
133.83 133.80 132.05 132.00 128.73 128.65 128.49 127.92 127.82 127.69 127.64 126.06 125.72 125.39 125.35 124.57 124.55
61.59 61.52
31.38 29.98
16.12 16.06
f1 (ppm)

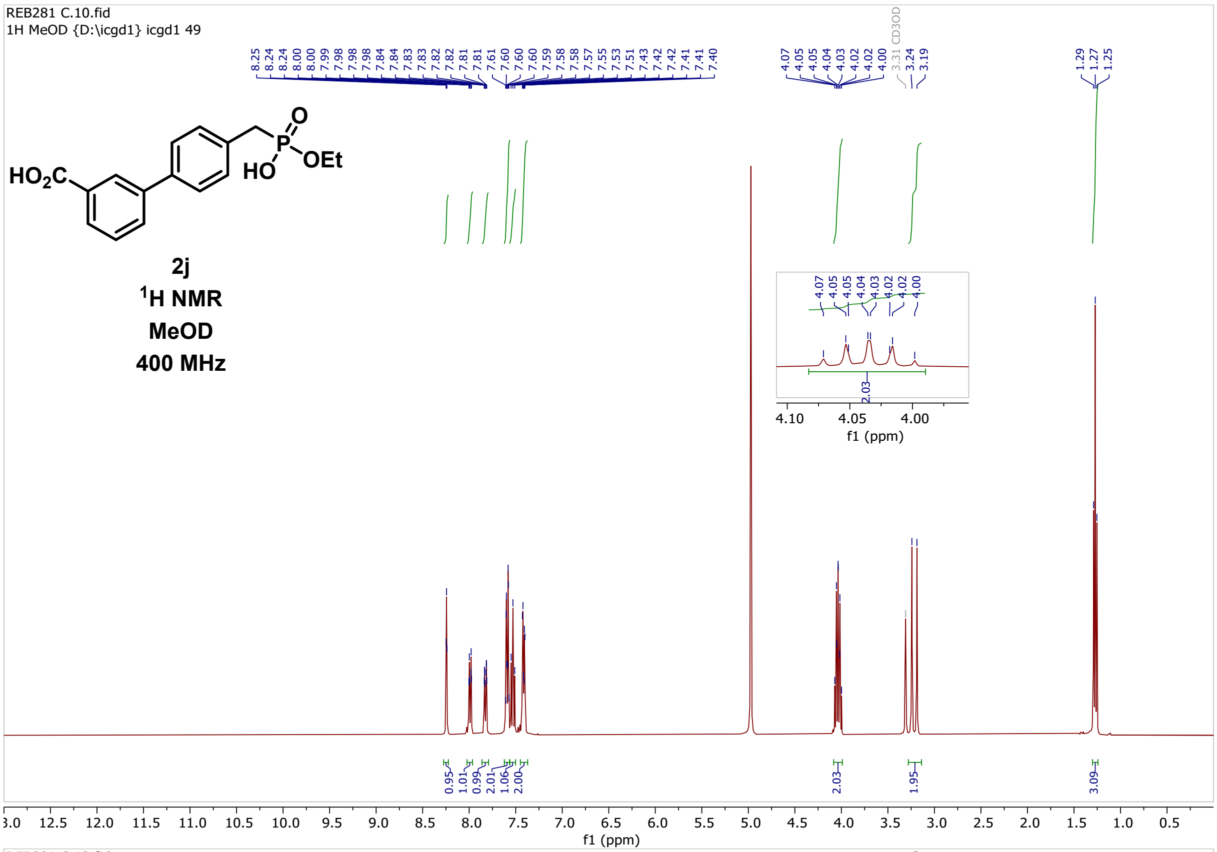
RMN/LM202 dry 31P
LM202 dry
31P{1H} CDCl3 /opt/topspin2.1 dept1a 4

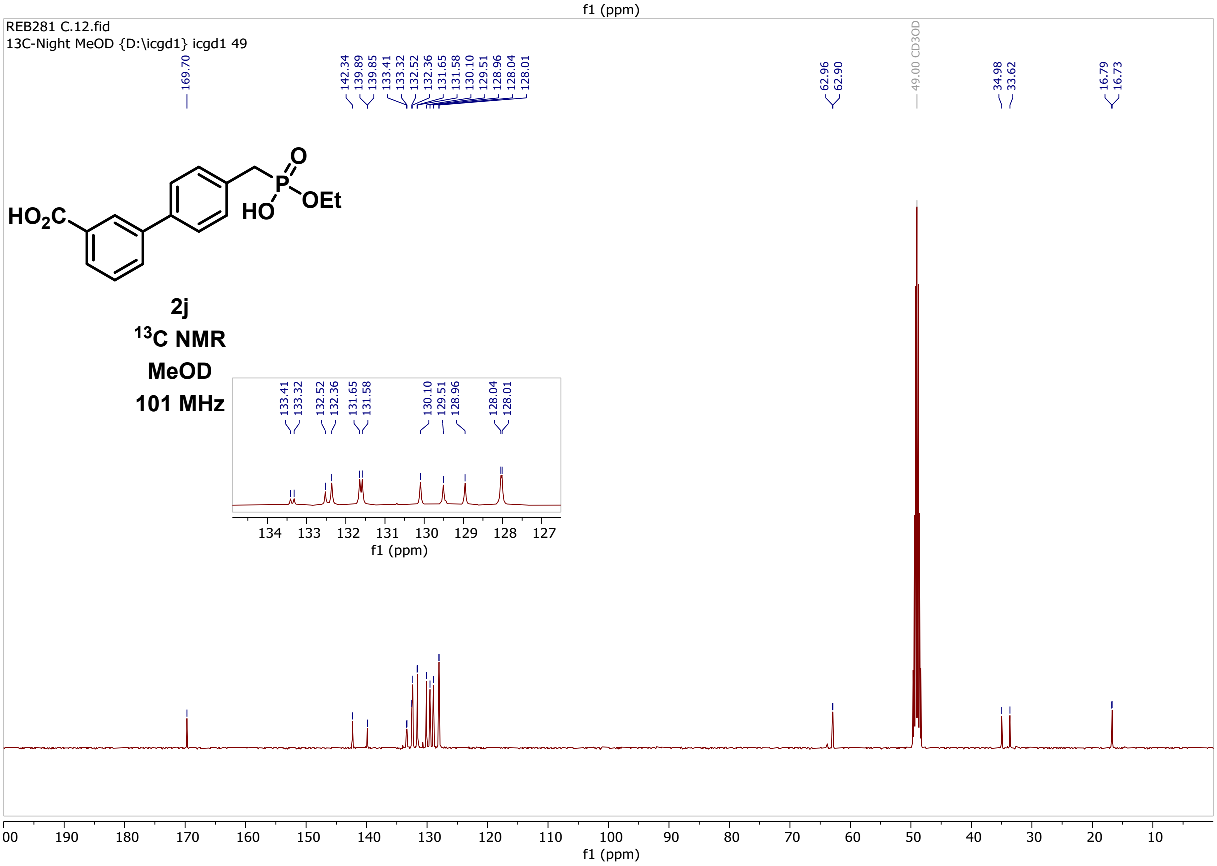


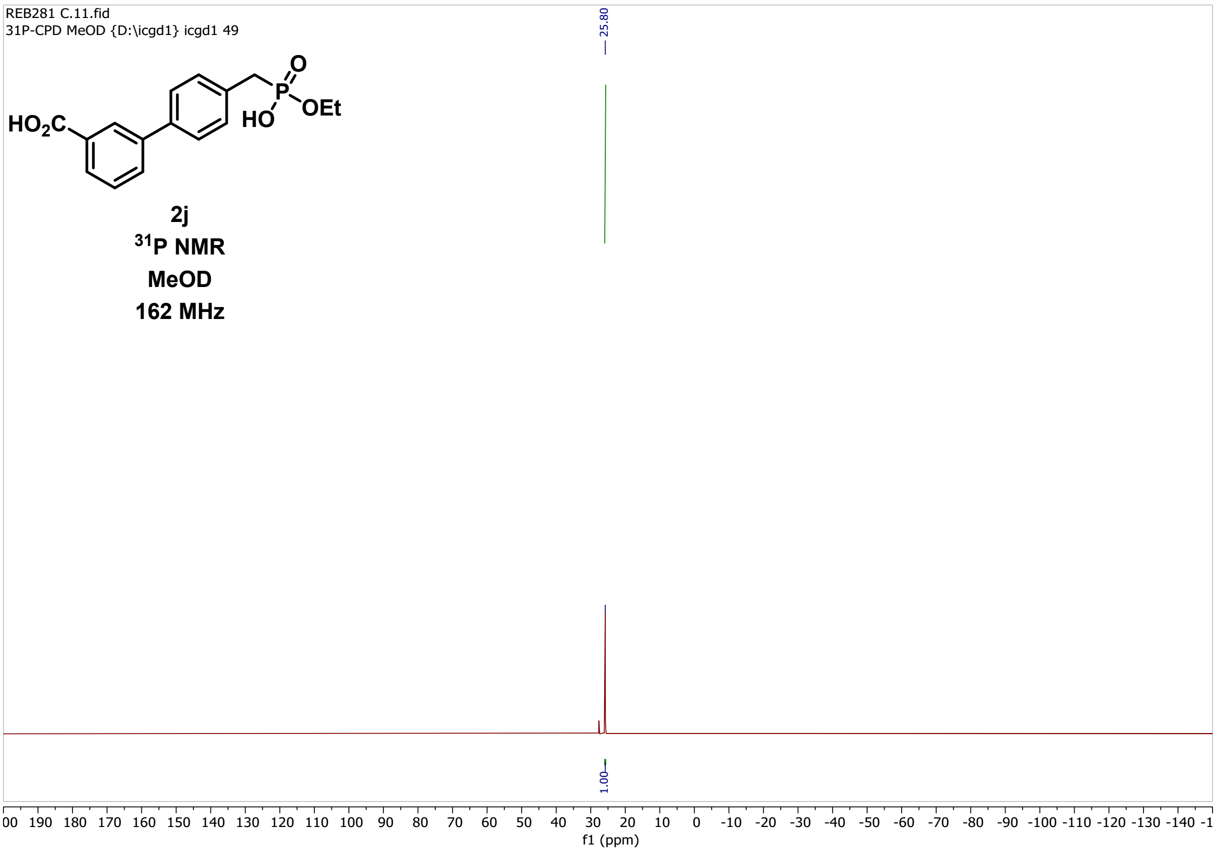
2i
^{31}P NMR
$CDCl_3$
162 MHz



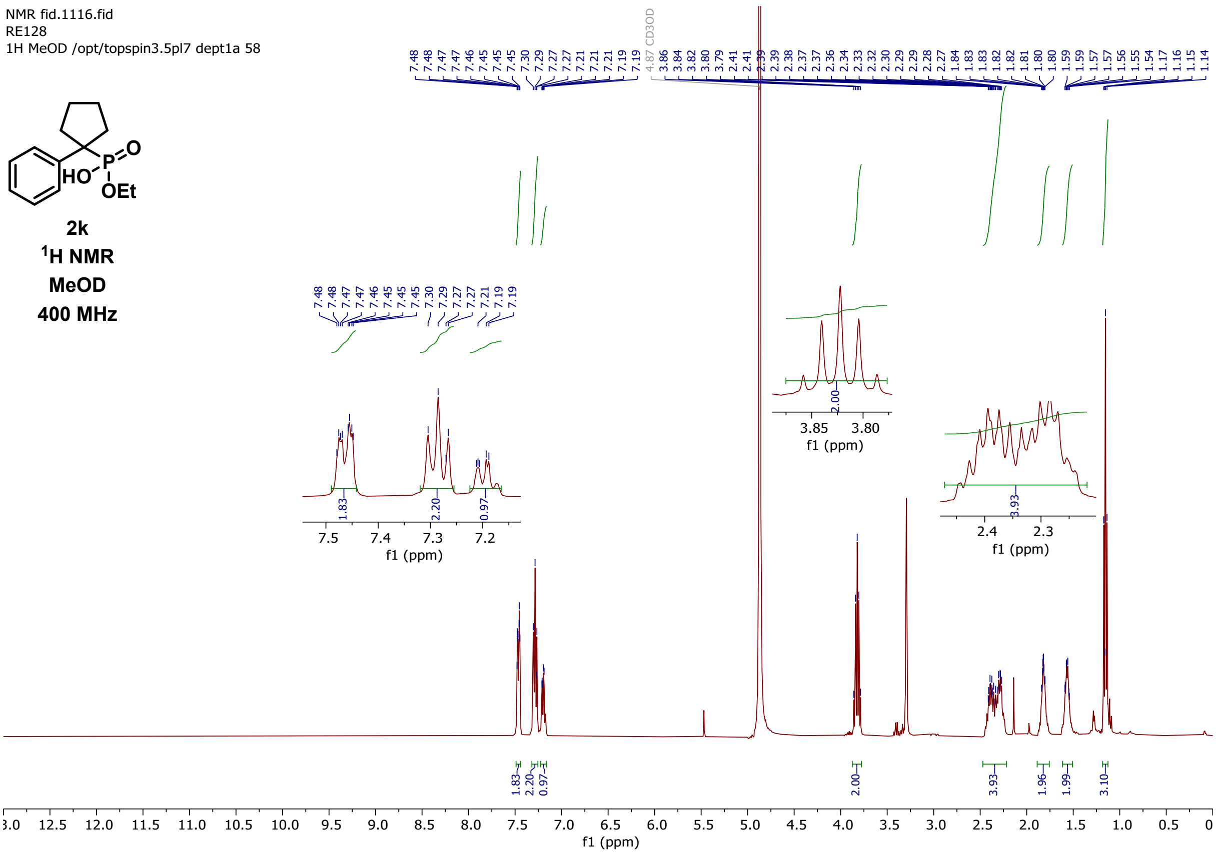
4'-((ethoxy(hydroxy)phosphoryl)methyl)-[1,1'-biphenyl]-3-carboxylic acid (2j)





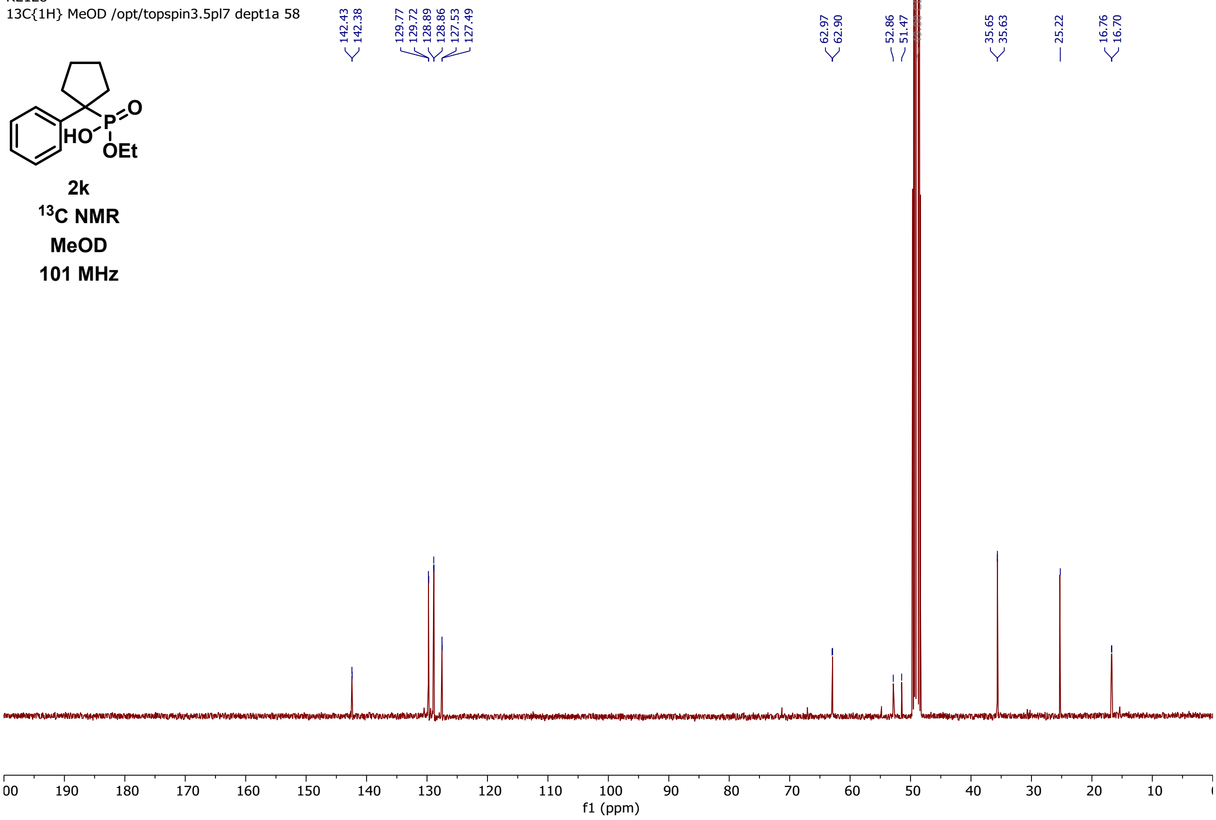


Cyclopentylbenzylphosphonic acid monoethyl ester (2k)



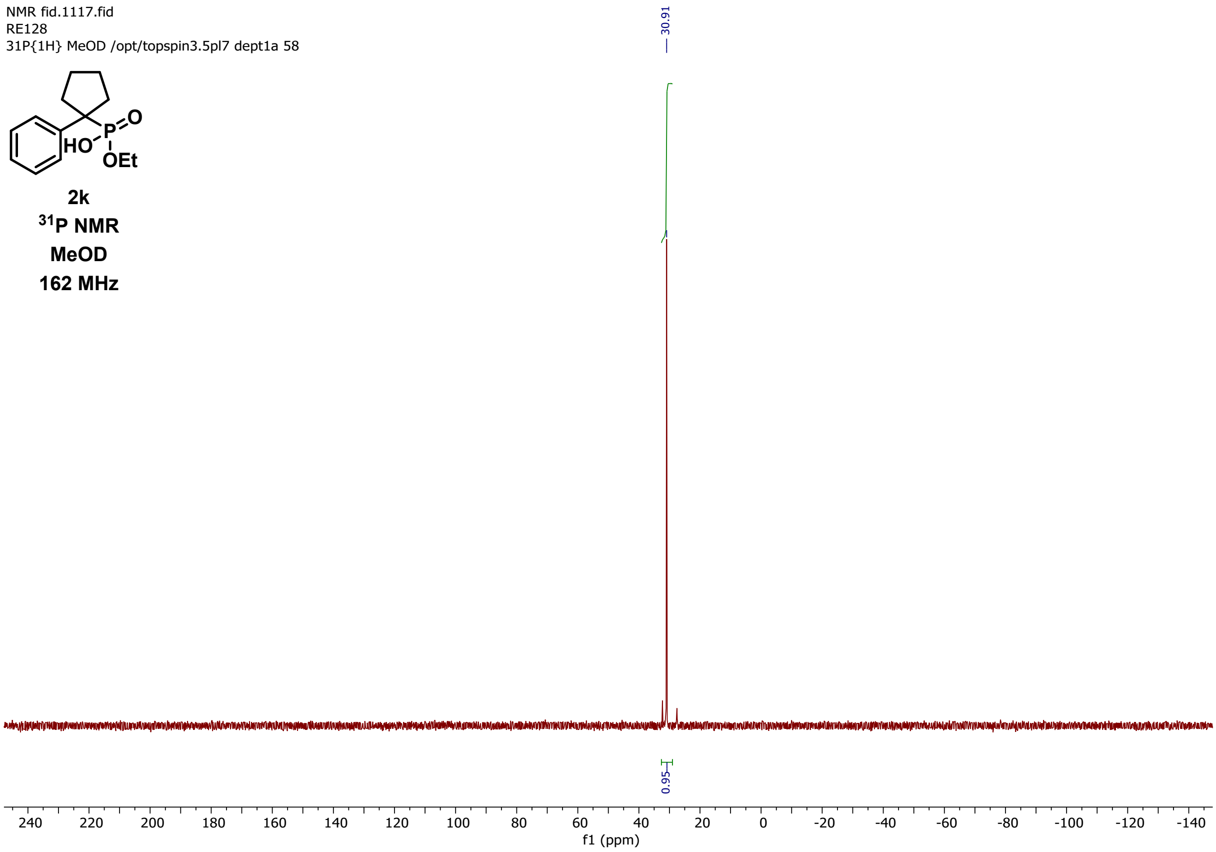
NMR fid.1118.fid
RE128
13C{1H} MeOD /opt/topspin3.5pl7 dept1a 58

2k
^{13}C NMR
MeOD
101 MHz

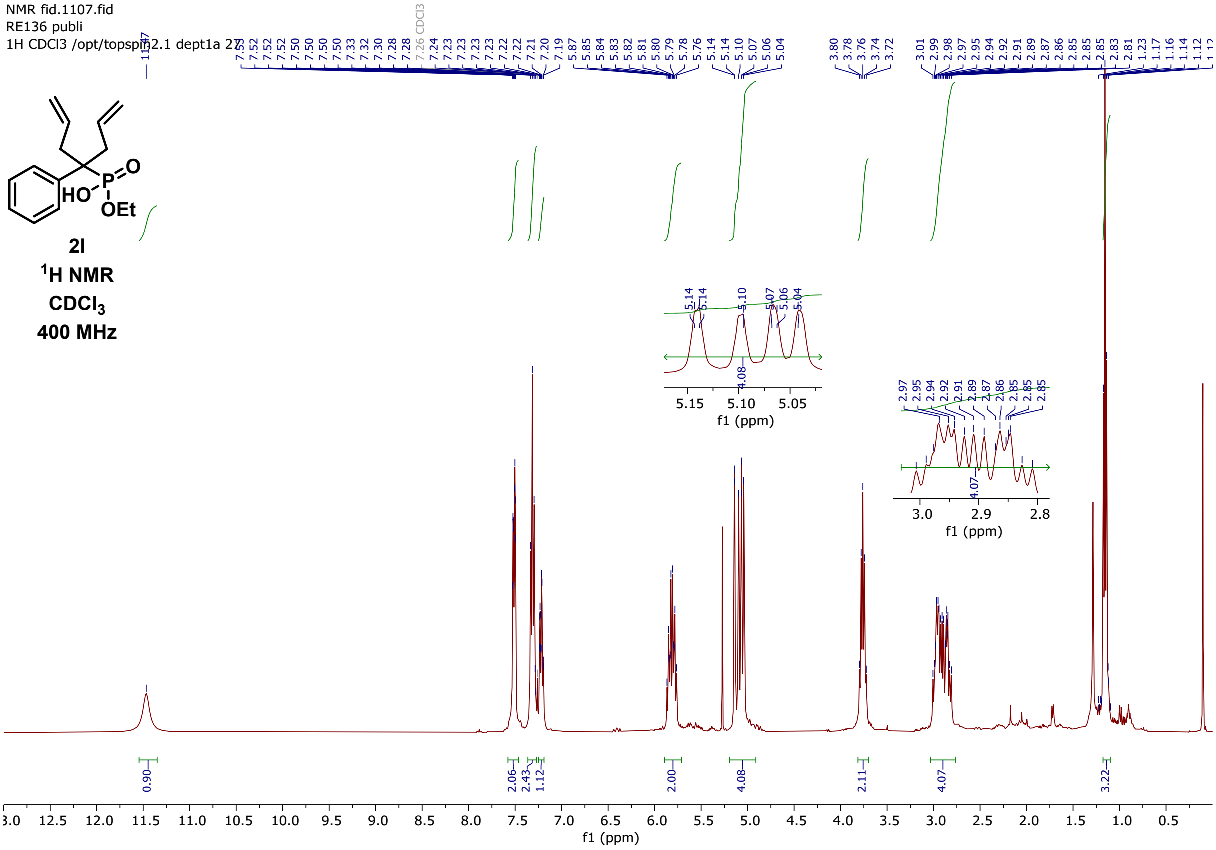


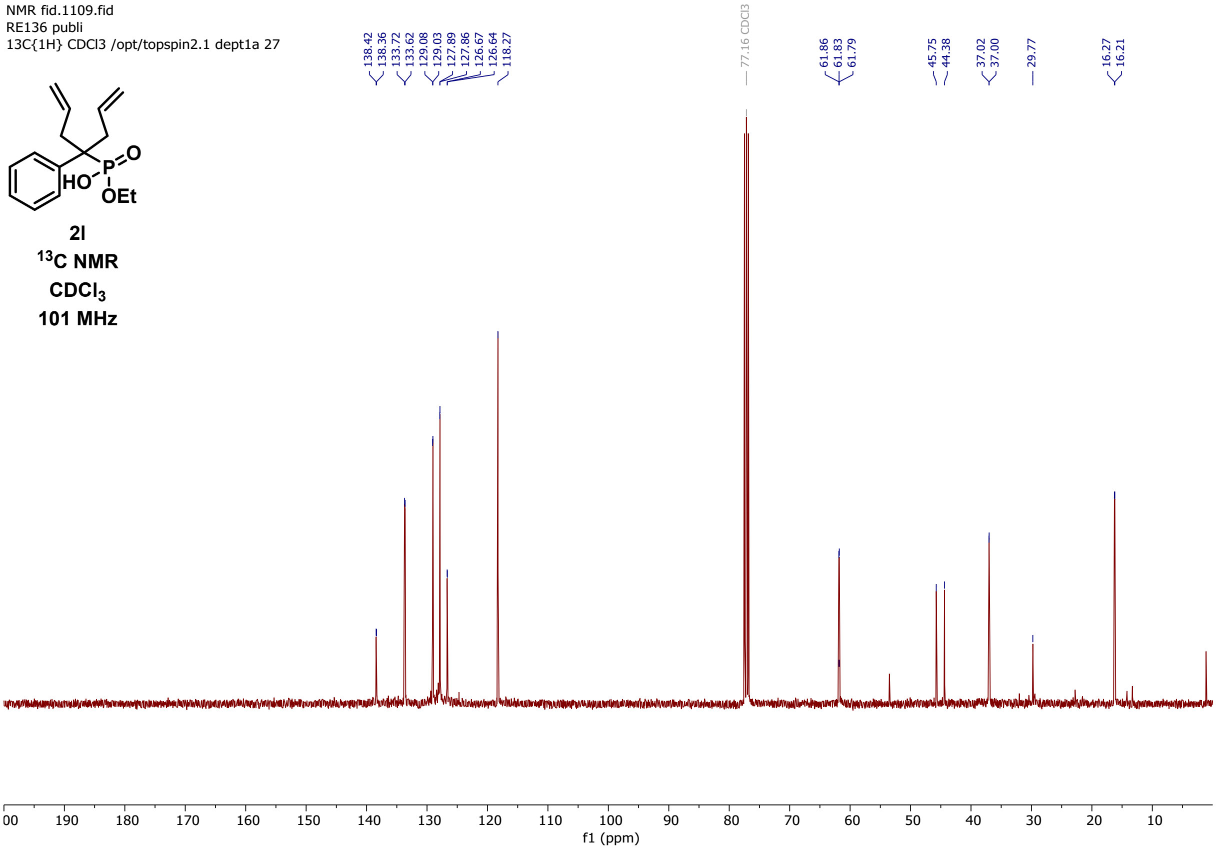
NMR fid.1117.fid
RE128
31P{1H} MeOD /opt/topspin3.5pl7 dept1a 58

2k
^{31}P NMR
MeOD
162 MHz

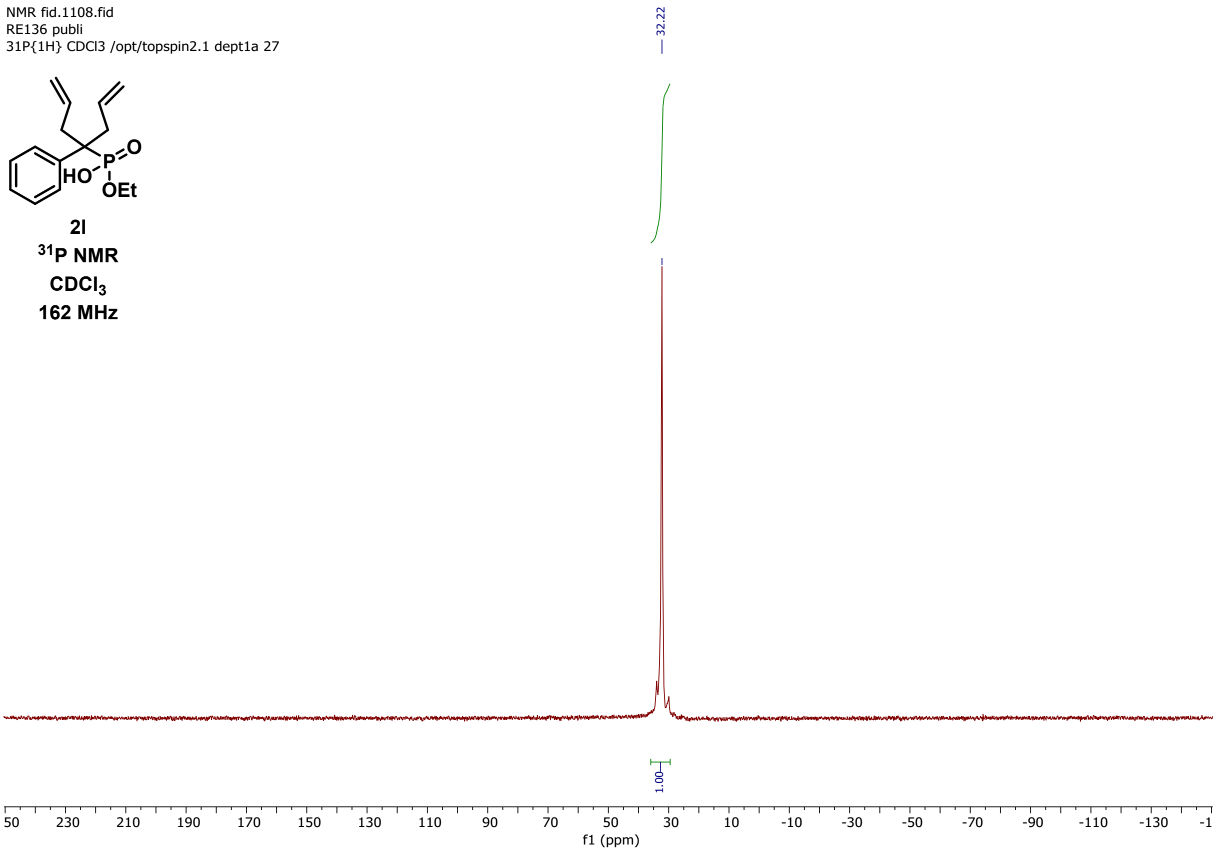


Diallylbenzylphosphonic acid monoethyl ester (2l)



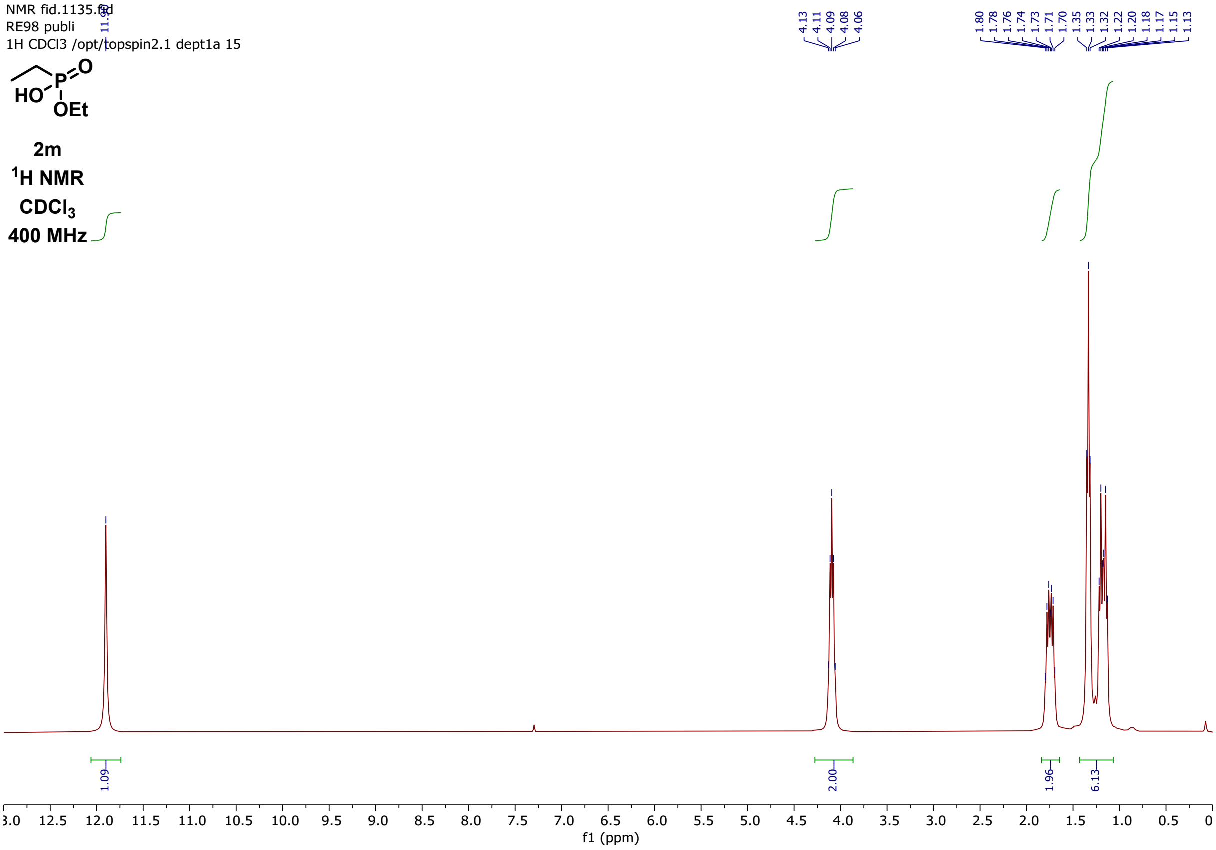


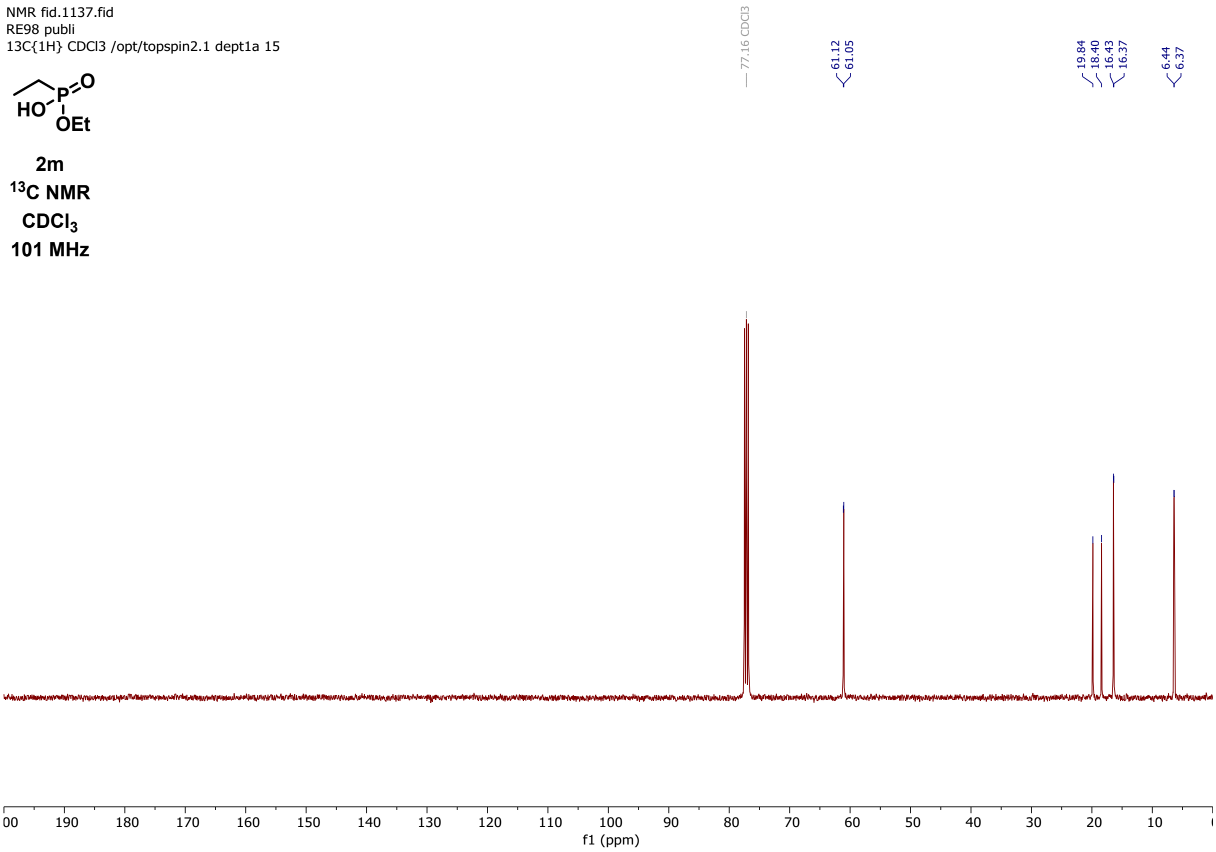
NMR fid.1108.fid
RE136 publi
31P{1H} CDCl3 /opt/topspin2.1 dept1a 27

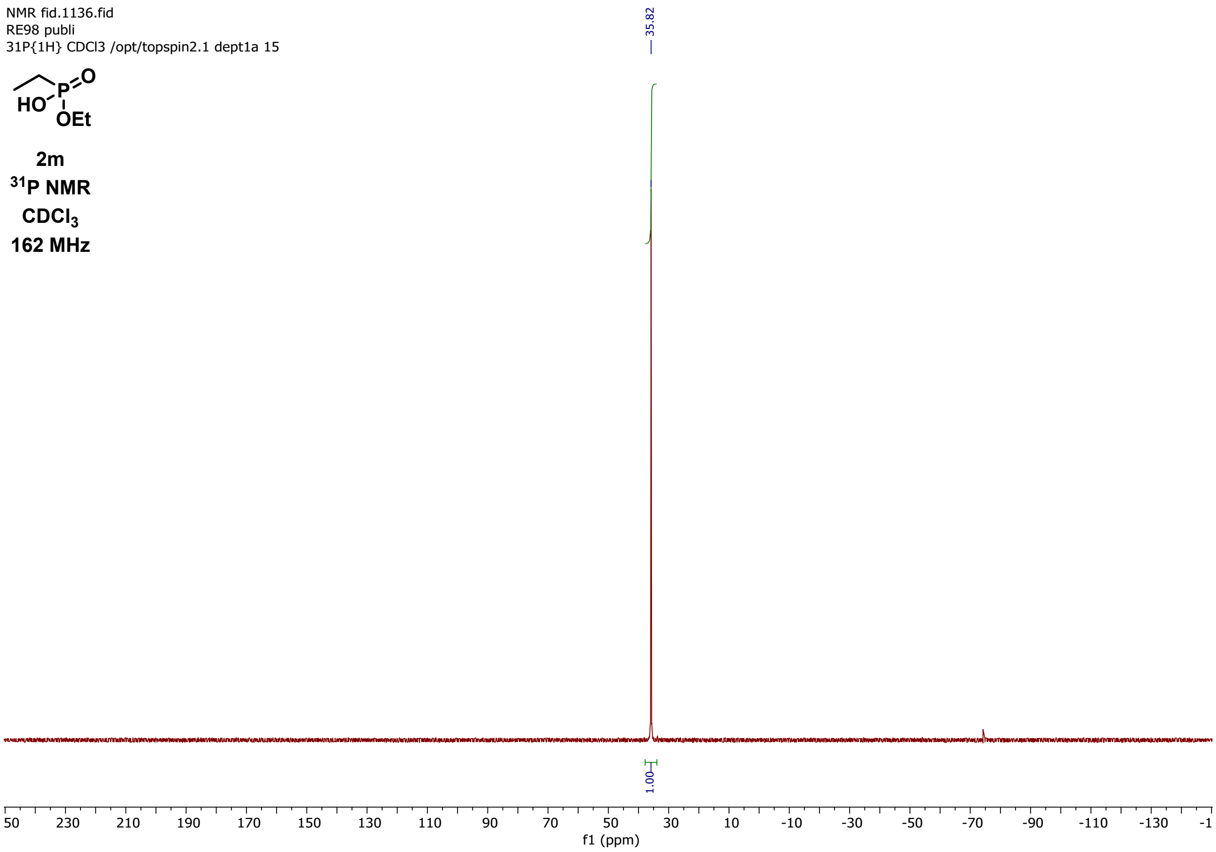


Ethylphosphonic acid monoethyl ester (2m)

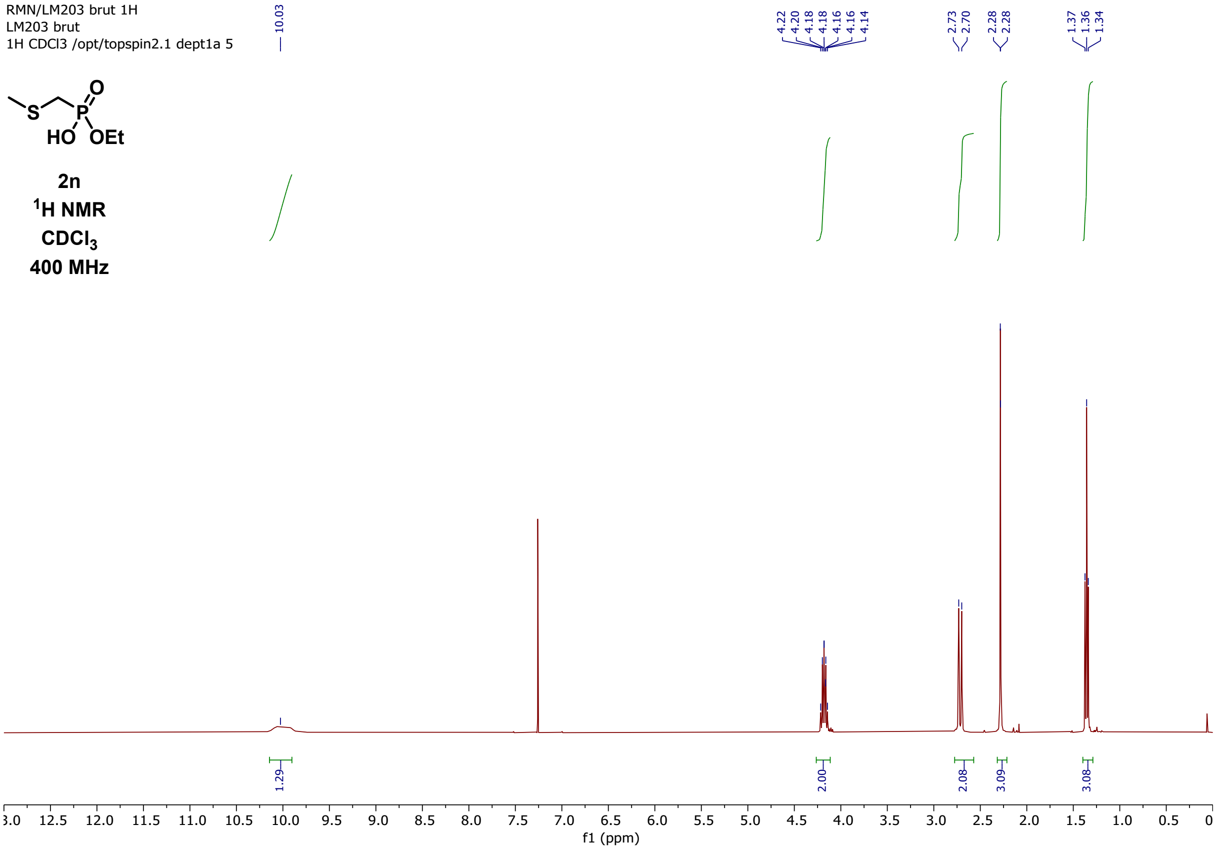
NMR fid.1135.fid
RE98 publi
1H CDCl3 /opt/topspin2.1 dept1a 15

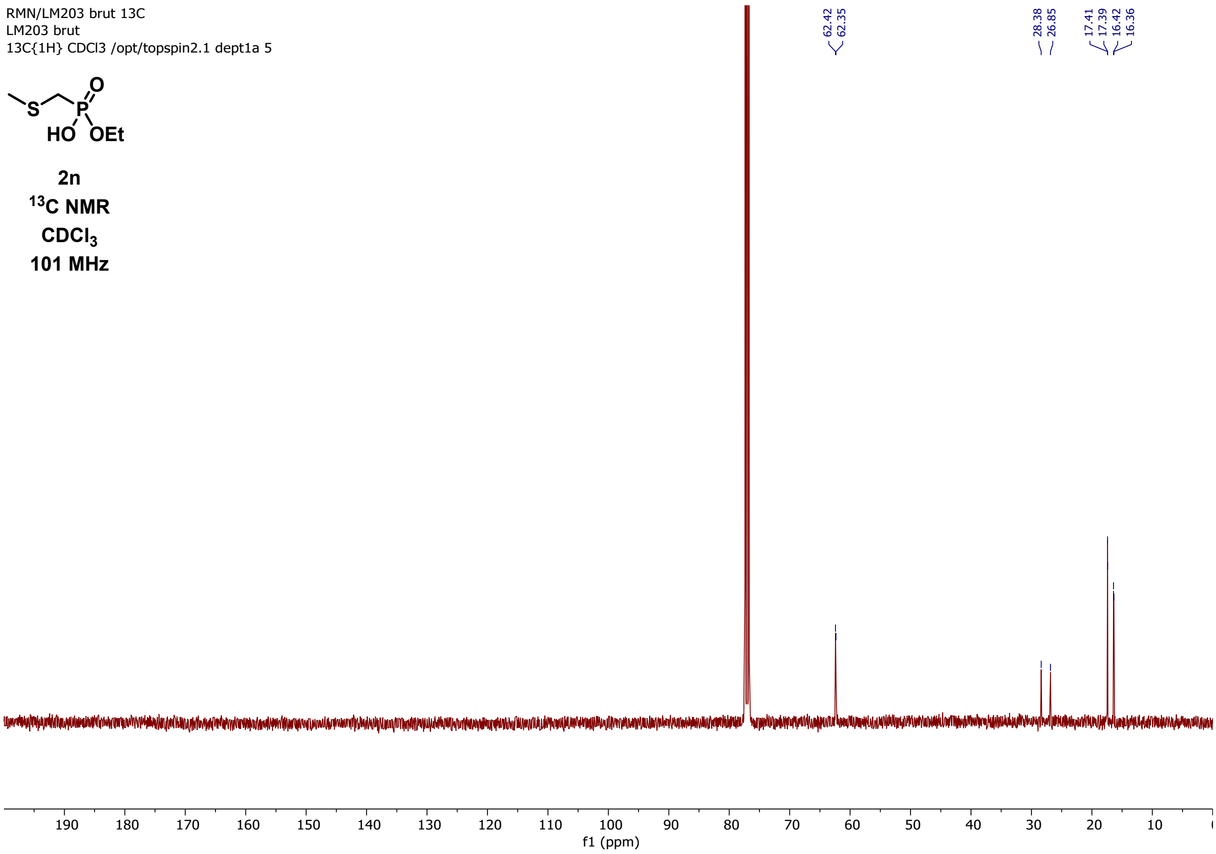


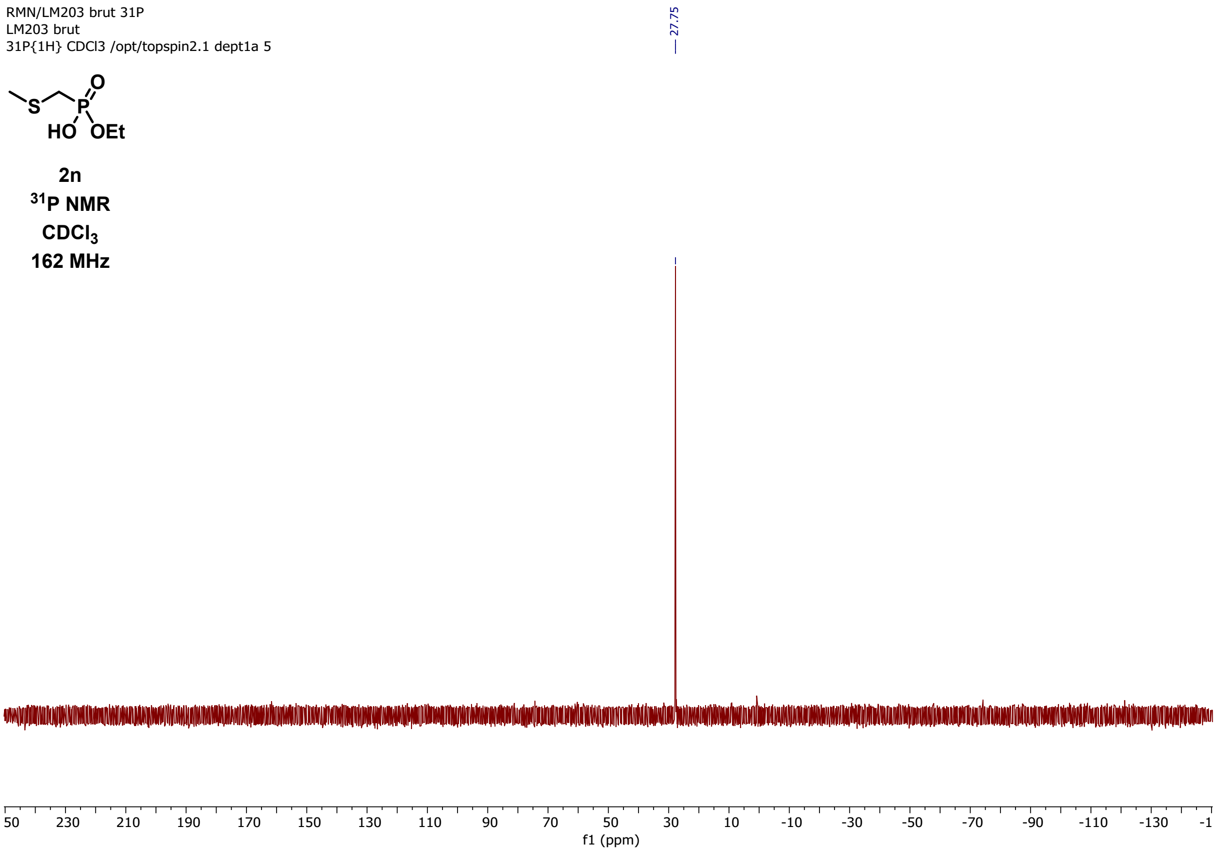

NMR fid.1137.fid
RE98 publi
13C{1H} CDCl3 /opt/topspin2.1 dept1a 15
HO
P
O
OEt
2m
13C NMR
CDCl3
101 MHz
77.16 CDCl3
61.12
61.05
19.84
18.40
16.43
16.37
6.44
6.37
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


NMR fid.1136.fid
RE98 publi
31P{1H} CDCl3 /opt/topspin2.1 dept1a 15
HO
P
O
OEt
2m
31P NMR
CDCl3
162 MHz
35.82
1.00
230
210
190
170
150
130
110
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
f1 (ppm)

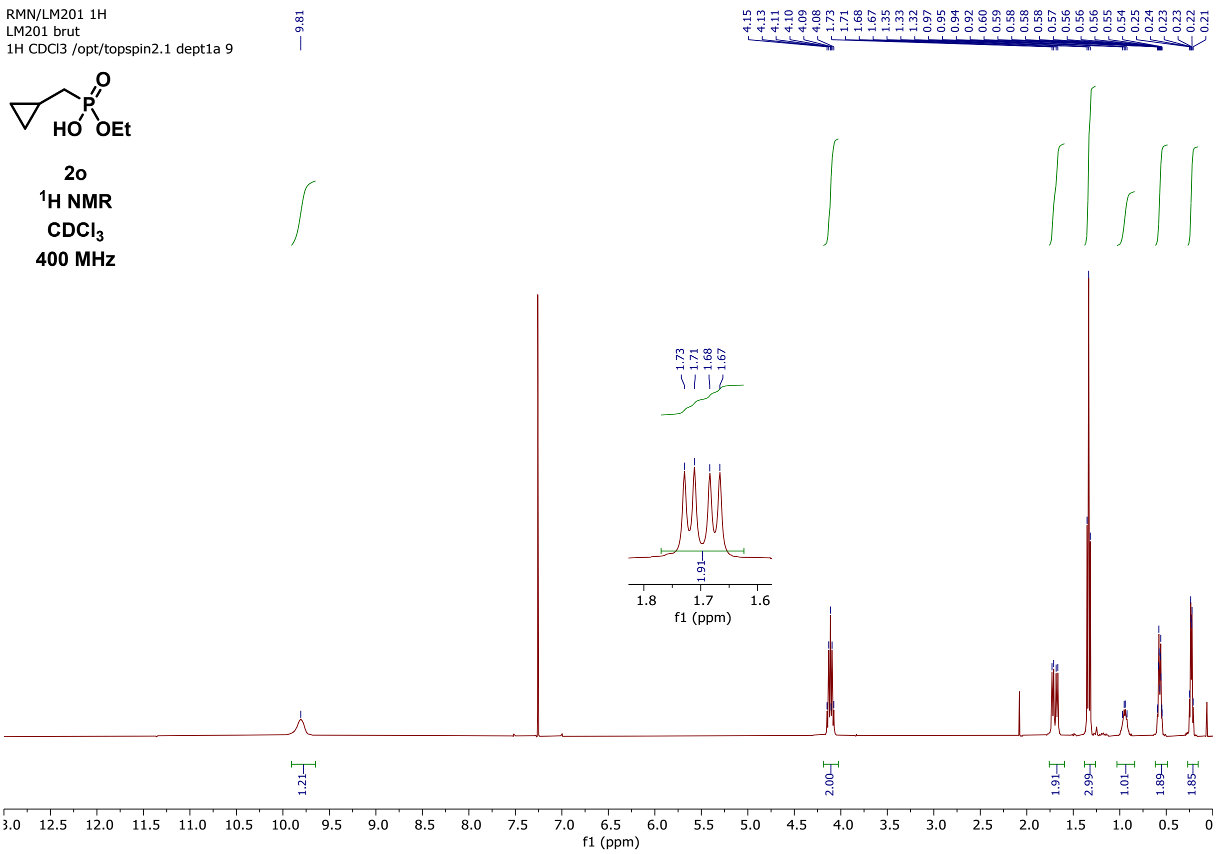
Methylthiomethylphosphonic acid monoethyl ester (2n)

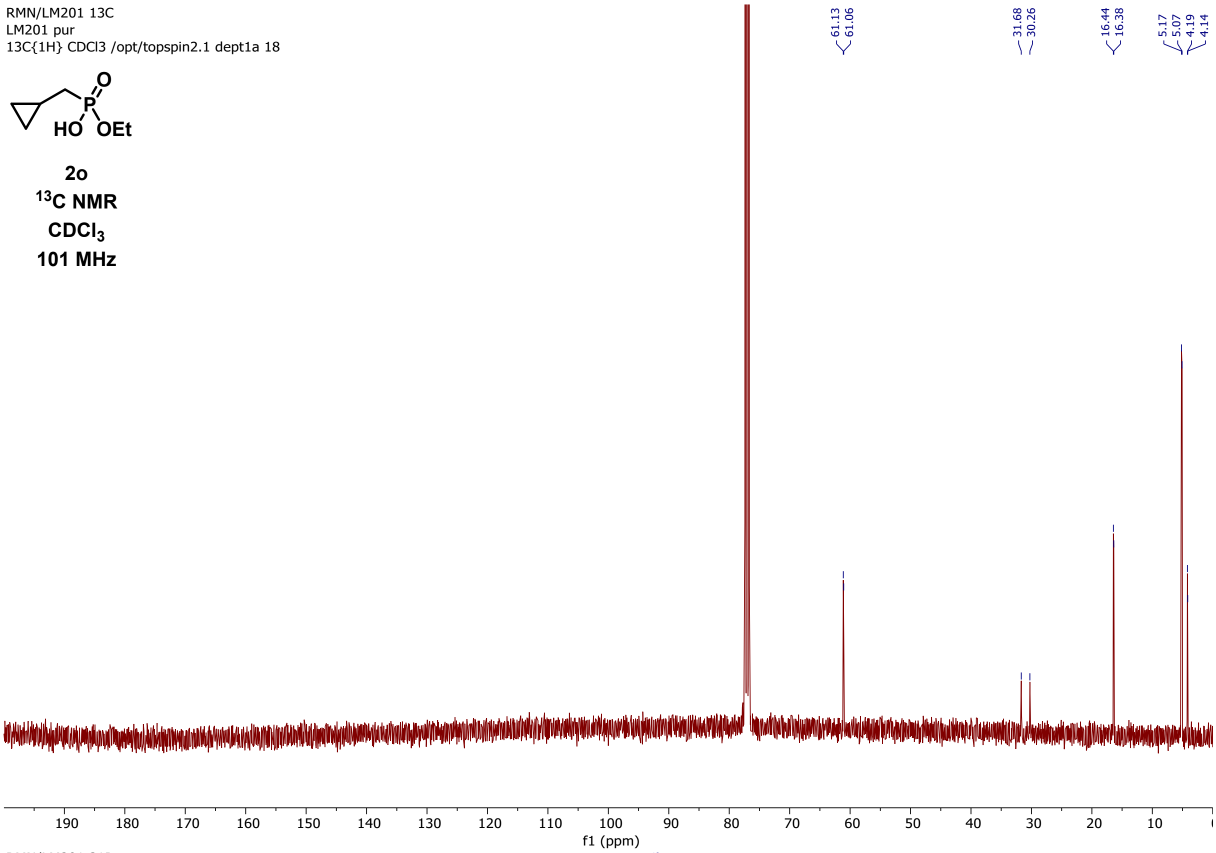


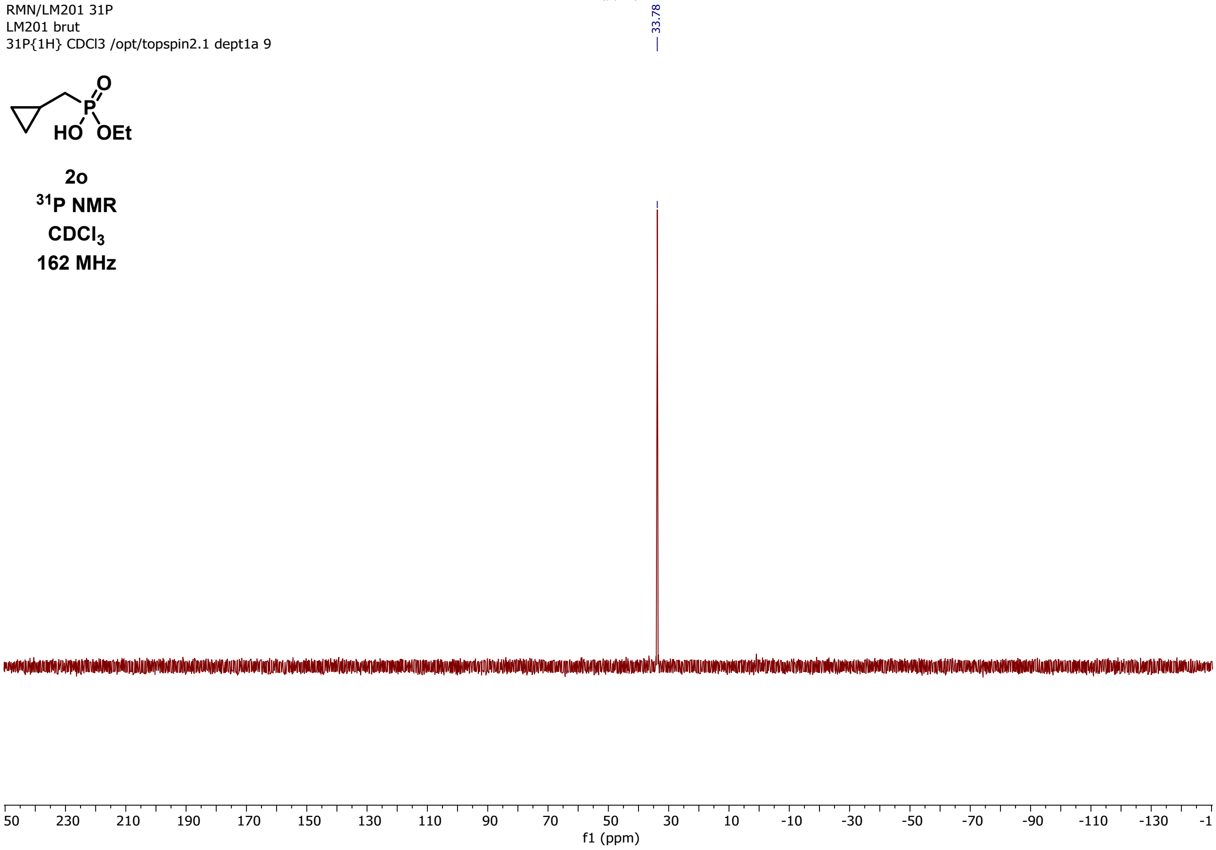




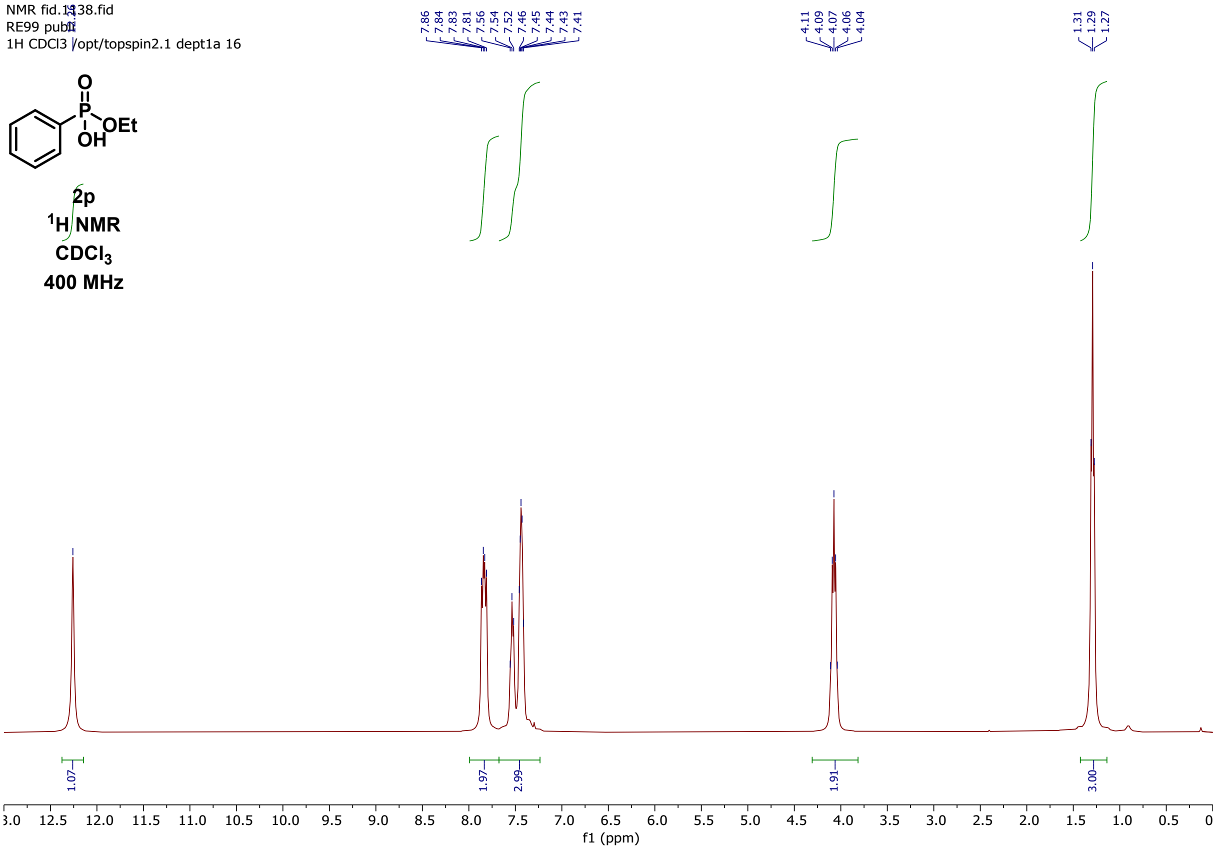
Cyclopropylmethylphosphonic acid monoethyl ester (2o)

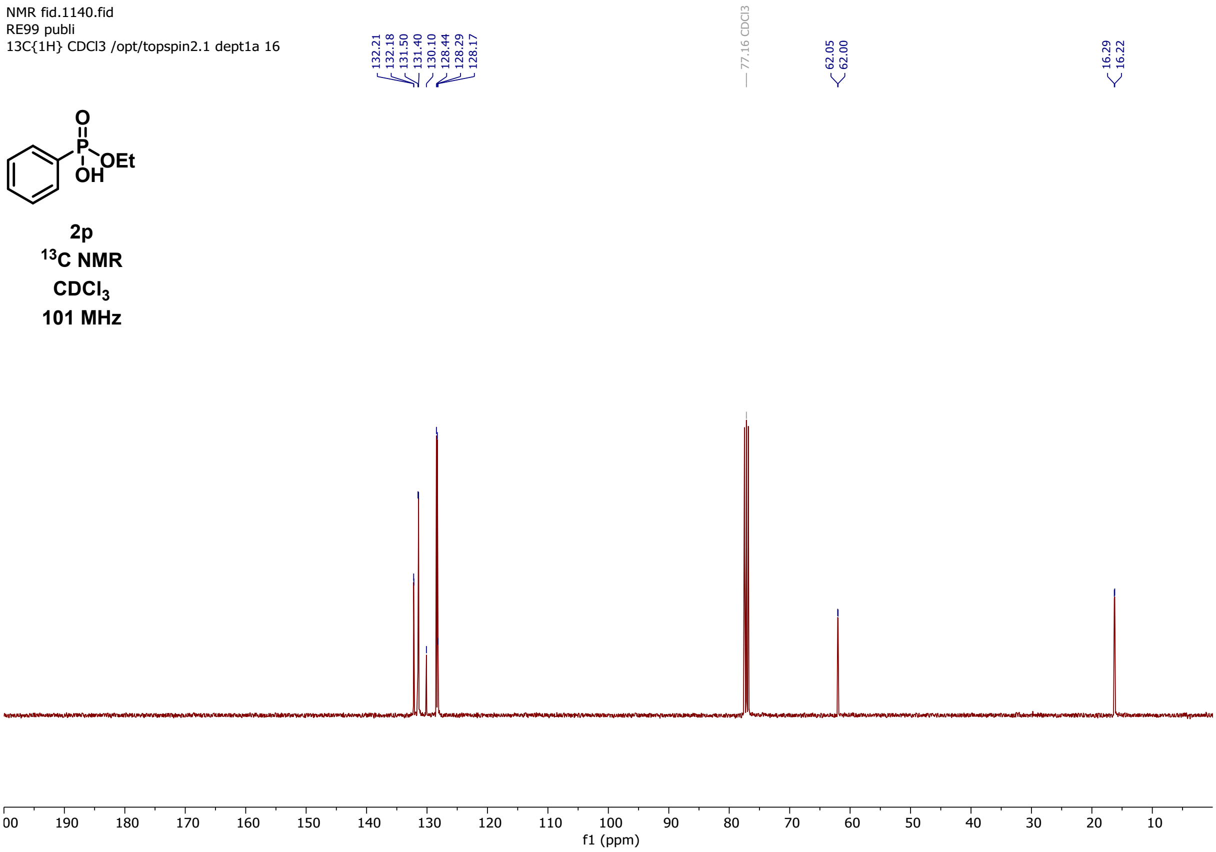


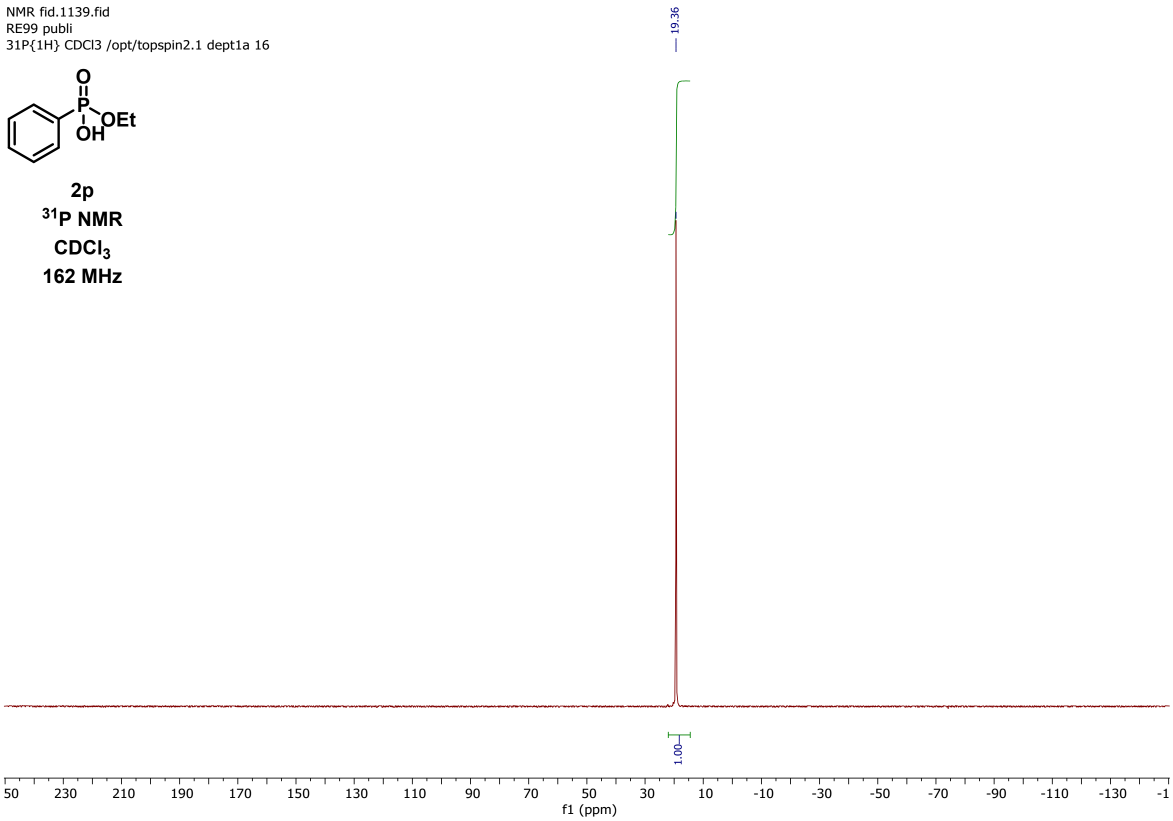

RMN/LM201 13C
LM201 pur
13C{1H} CDCl3 /opt/topspin2.1 dept1a 18
HO OEt
2o
13C NMR
CDCl3
101 MHz
61.13
61.06
31.68
30.26
16.44
16.38
5.17
5.07
4.19
4.14
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


RMN/LM201 31P
LM201 brut
31P{1H} CDCl3 /opt/topspin2.1 dept1a 9
HO OEt
2o
31P NMR
CDCl3
162 MHz
33.78
230 210 190 170 150 130 110 90 70 50 30 10 -10 -30 -50 -70 -90 -110 -130
f1 (ppm)

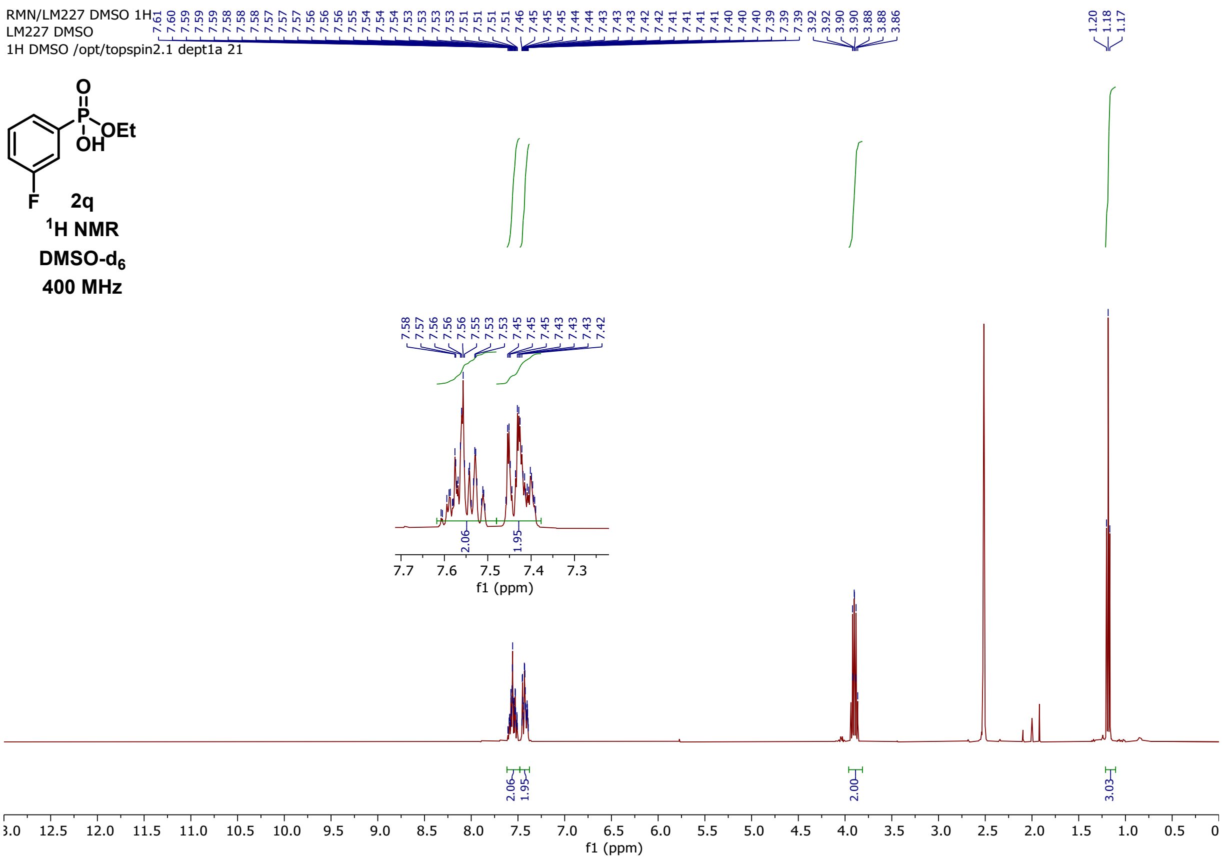
Phenylphosphonic acid monoethyl ester (2p)

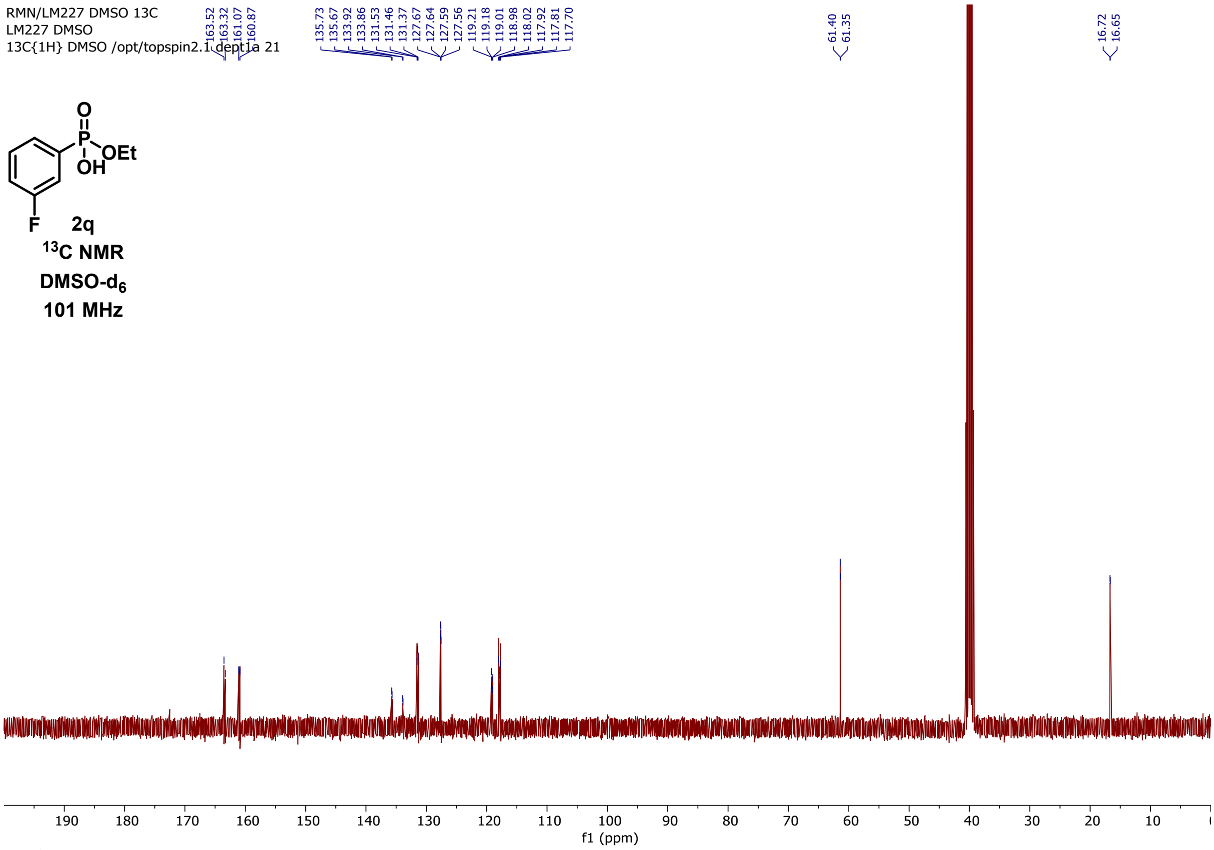


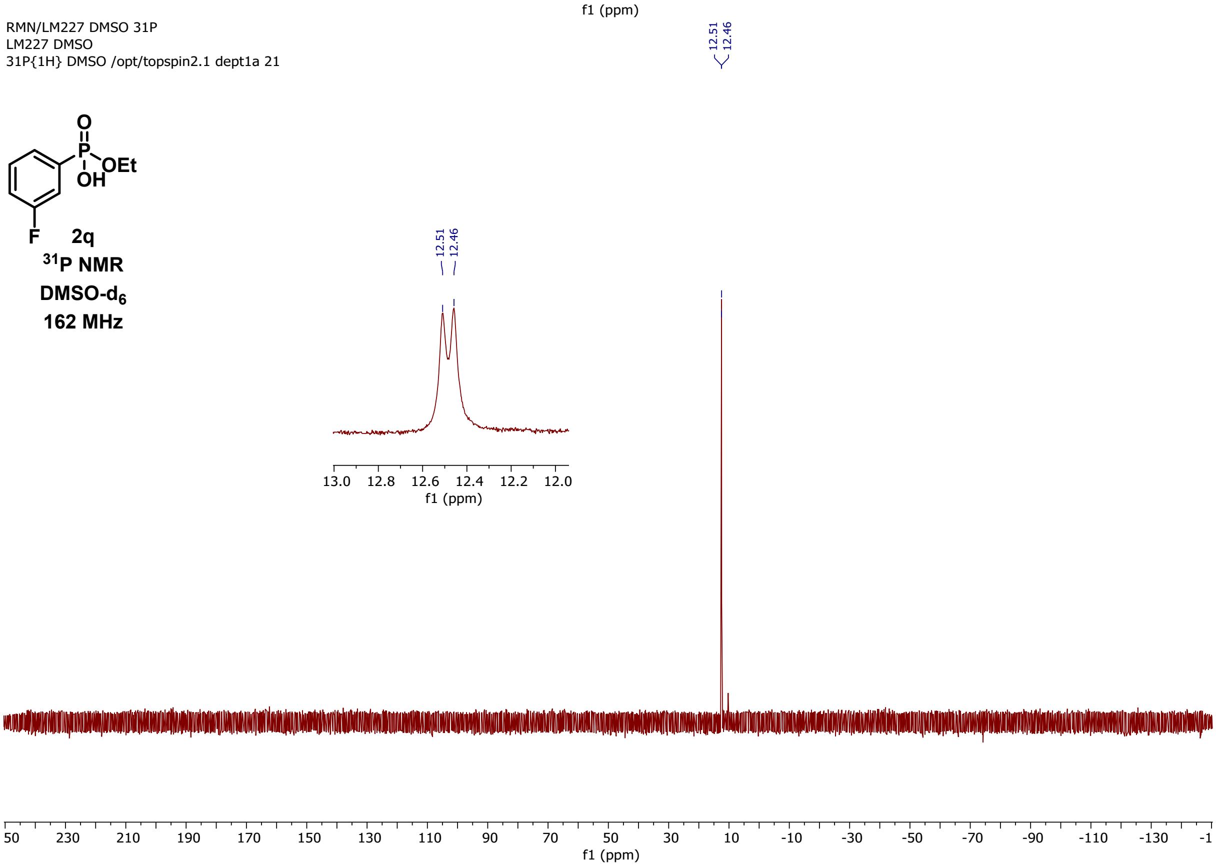




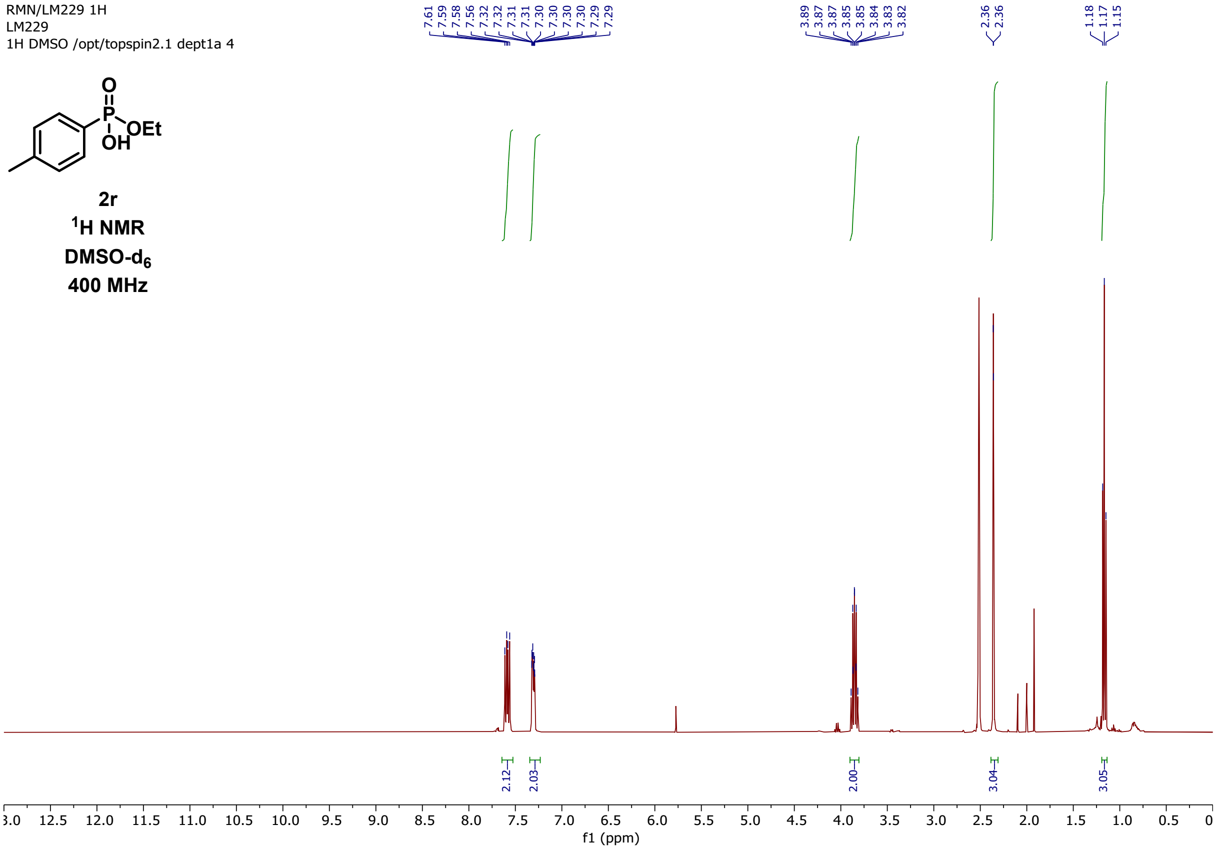
3-Fluorophenylphosphonic acid monoethyl ester (2q)

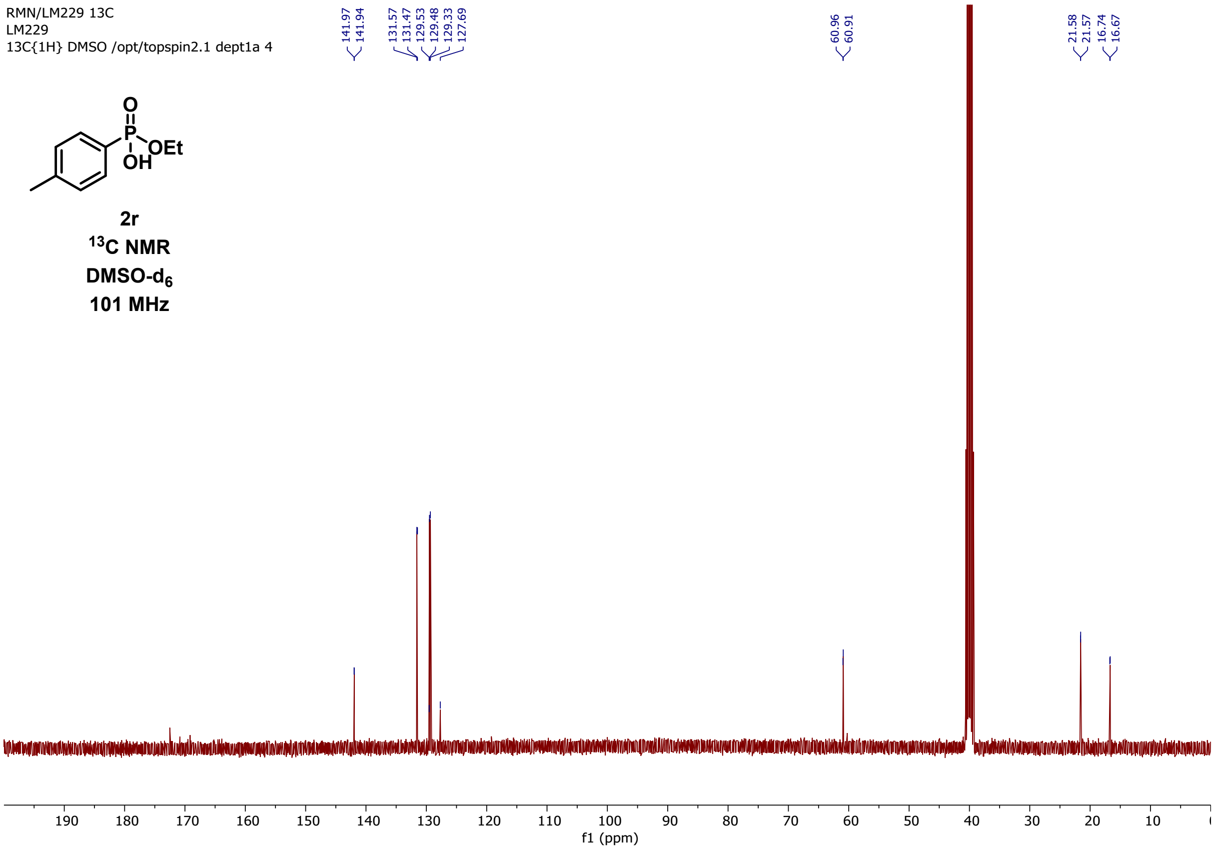


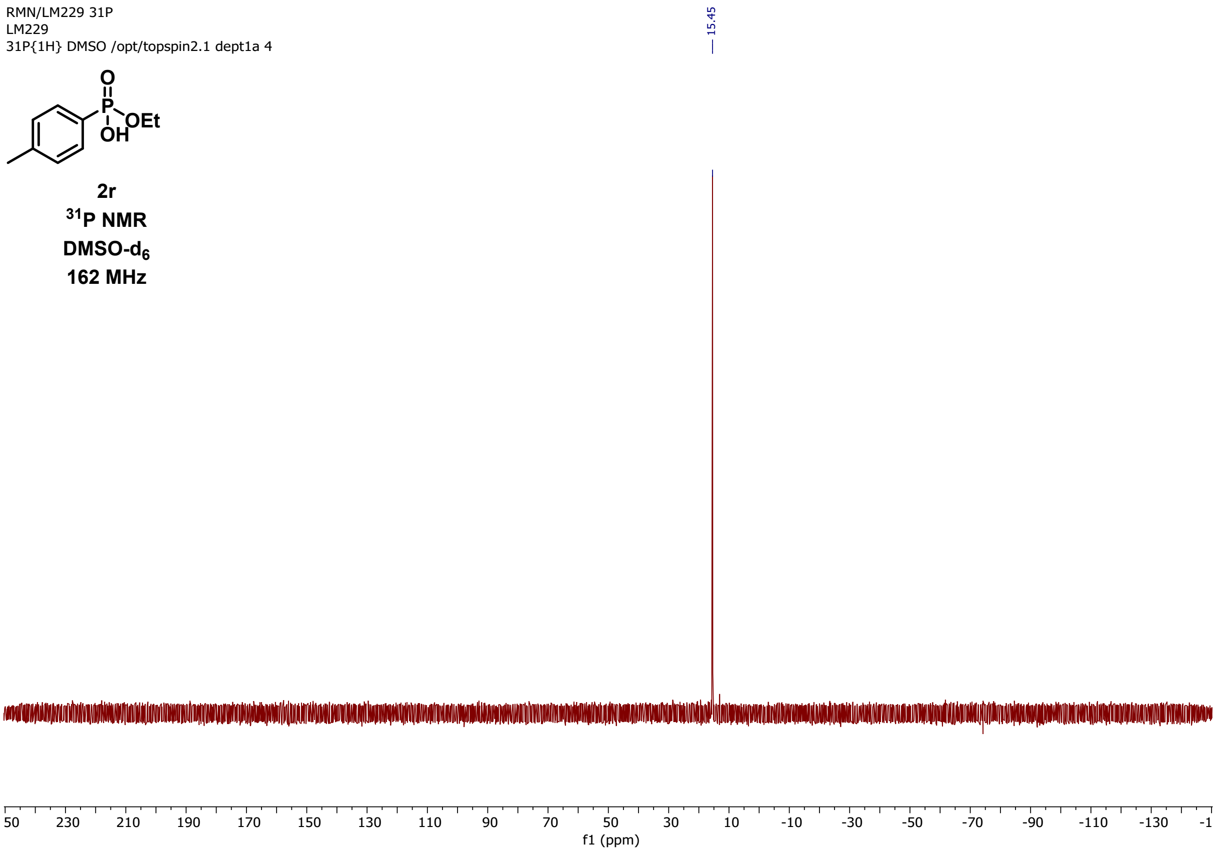

RMN/LM227 DMSO 13C
LM227 DMSO
13C{1H} DMSO /opt/topspin2.1 dept1a 21
163.52
163.32
161.07
160.87
135.73
135.67
133.92
133.86
131.53
131.46
131.37
127.67
127.64
127.59
127.56
119.21
119.18
119.01
118.98
118.02
117.92
117.81
117.70
61.40
61.35
16.72
16.65
2q
13C NMR
DMSO-d6
101 MHz
f1 (ppm)


RMN/LM227 DMSO 31P
LM227 DMSO
31P{1H} DMSO /opt/topspin2.1 dept1a 21
12.51
12.46
2q
31P NMR
DMSO-d6
162 MHz
f1 (ppm)

4-Methylphenylphosphonic acid monoethyl ester (2r)






RMN/LM229 31P
LM229
31P{1H} DMSO /opt/topspin2.1 dept1a 4
O
P
OEt
OH
2r
31P NMR
DMSO-d6
162 MHz
15.45
50
230
210
190
170
150
130
110
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-1
f1 (ppm)

6. Metrics

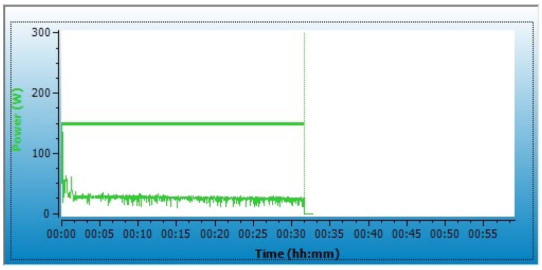


Figure 4: Power consumption for the synthesis of compound **2a** monitored by CEM Explorer software.

Reactant (Limiting reactant Firs	Mass (g)	MW	Mol	Catalyst	Mass (g)	Reagent	Mass (g)	Reaction Solven	Volume (cm3)	Density (g ml-1	Mass (g)	Work up chemical	Mass (g)	Work up solven	Volume (cm3	Density (g ml-1	Mass (g)		
Phosphonate	0,296	296,35	0,000999					EtOH	1	0,789	0,789	HCl	0,185	Water	10	1	10		
NaOH	0,096	40	0,0024								0	NaCl	1,5	EtOAc	35	0,89	31,15		
			#DIV/0!								0	MgSO4	1,5				0		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
Total	0,392	336,35			0		0				0,789		3,185				41,15	Total mass	45,516

$$RME = \frac{mass\ of\ isolated\ product}{total\ mass\ of\ reactants} \times 100$$

$$AE = \frac{molecular\ weight\ of\ product}{total\ molecualr\ weight\ of\ reactants} \times 100$$

$$mass\ intensity = \frac{total\ mass\ in\ a\ process\ or\ process\ step}{mass\ of\ product}$$

$$OE = \frac{RME}{AE} \times 100$$

Eco-Scale	85,5
Yield	95,2
Conversion	100,0
AE	79,8
RME	65,1
OE	81,6
PMI total	178,5
PMI reaction	4,6
reagent catalyst	1,5
solvent	3,1
PMI Workup	173,9
chemical	12,5
solvent	161,4

	Mass	MW	Mol
Product	0,255	268,29	0,0009505

	mass
Unreacted limited	0

Figure 5: Green Metrics for the general procedure applied on the synthesis of compound **2a**.

Reactant (Lin	Mass (g)	MW	Mol	Catalyst	Mass (g)	Reagent	Mass (g)	Reaction Solv	Volume (cm3	Density (g m	Mass (g)	Work up chei	Mass (g)	Work up solv	Volume (cm3	Density (g m	Mass (g)		
Phosphonat	0,296	296,35	0,00099882					EtOH	1	0,789	0,789	Citric acid	0,5	Water	5	1	5		
NaOH	0,096	40	0,0024								0	MgSO4	1,5	EtOAc	15	0,89	13,35		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
Total	0,392	336,35			0		0				0,789		2				18,35	Total mass	21,531

Yield	71,6
Conversion	100,0
AE	79,8
RME	49,0
OE	61,4
PMI total	112,1
PMI reaction	6,2
reagent catal	2,0
solvent	4,1
PMI Workup	106,0
chemical	10,4
solvent	95,6

	Mass	MW	Mol
Product	0,192	268,29	0,00071564

	mass
Unreacted li	0

Figure 6: Green Metrics for the greener procedure applied on the synthesis of compound **2a**.

Reactant (Lir	Mass (g)	MW	Mol	Catalyst	Mass (g)	Reagent	Mass (g)	Reaction Sol	Volume (cm	Density (g m	Mass (g)	Work up che	Mass (g)	Work up soh	Volume (cm	Density (g m	Mass (g)		
Phosphonat	0,296	296,35	0,00099882					EtOH	1	0,789	0,789	HCl	0,185	Water	10	1	10		
NaOH	0,096	40	0,0024								0	NaCl	1,5	EtOAc	35	0,89	31,15		
			#DIV/0!								0	MgSO4	1,5				0		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
Total	0,392	336,35			0		0				0,789		3,185				41,15	Total mass	45,516

$$RME = \frac{mass\ of\ isolated\ product}{total\ mass\ of\ reactants} \times 100$$

$$AE = \frac{molecular\ weight\ of\ product}{total\ molecualr\ weight\ of\ reactants} \times 100$$

$$mass\ intensity = \frac{total\ mass\ in\ a\ process\ or\ process\ step}{mass\ of\ product}$$

$$OE = \frac{RME}{AE} \times 100$$

Eco-Scale	73,5
Yield	69,0
Conversion	100,0
AE	79,8
RME	47,2
OE	59,2
PMI total	246,0
PMI reaction	6,4
reagent cata	2,1
solvent	4,3
PMI Workup	239,6
chemical	17,2
solvent	222,4

	Mass	MW	Mol
Product	0,185	268,29	0,0006896

	mass
Unreacted li	0

Figure 7: Green Metrics for the batch procedure applied on the synthesis of compound **2a**.

Our method

Reactant (Lir	Mass (g)	MW	Mol	Catalyst	Mass (g)	Reagent	Mass (g)	Reaction Solvent	Volume (cm	Density (g m	Mass (g)	Work up che	Mass (g)	Work up sol	Volume (cm3	Density (g m	Mass (g)		
Phosphonat	0,228	228,23	0,000998992					EtOH	1	0,789	0,789	HCl	0,185	Water	10	1	10		
NaOH	0,096	40	0,0024								0	NaCl	1,5	EtOAc	35	0,89	31,15		
			#DIV/0!								0	MgSO4	1,5				0		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
			#DIV/0!								0						0		
Total	0,324	268,23			0		0				0,789		3,185				41,15	Total mass	45,448

Eco-Scale	87	
Yield	98,0	
Conversion	100,0	
AE	74,6	
RME	60,5	
OE	81,1	
PMI total	231,9	
PMI reaction	5,7	94,3
reagent catalyst	1,7	
solvent	4,0	
PMI Workup	226,2	
chemical	16,3	
solvent	209,9	

	Mass	MW	Mol
Product	0,196	200,17	0,000979168

	mass
Unreacted li	0

Org. Biomol. Chem., 2021, 19, 6007-6014

Reactant (Lir	Mass (g)	MW	Mol	Catalyst	Mass (g)	Reagent	Mass (g)	Reaction Solvent	Volume (cm	Density (g m	Mass (g)	Work up che	Mass (g)	Work up sol	Volume (cm3	Density (g m	Mass (g)		
Phosphonat	0,045646	228,23	0,0002					DCM	1	1,33	1,33	HCl	0,25	Water	7	1	7		
Tf2O	0,085	282,13	0,000300011								0	NaOH	0,028	Et2O	2	0,713	1,426		
Pyridine	0,032	79,1	0,0004								0	Na2SO4	1,5	DCM	30	1,33	39,9		
H2O	0,072	18	0,004								0						0		
											0						0		
											0						0		
											0						0		
											0						0		
											0						0		
Total	0,233928	607,46			0		0				1,33		1,778				48,326	Total mass	51,667928

Eco-Scale	80	
Yield	93,7	
Conversion	100,0	
AE	33,0	
RME	16,0	
OE	48,6	
PMI total	1377,8	
PMI reaction	41,7	58,3
reagent catalyst	6,2	
solvent	35,5	
PMI Workup	1336,1	
chemical	47,4	
solvent	1288,7	

	Mass	MW	Mol
Product	0,0375	200,17	0,000187341

	mass
Unreacted li	0

Bioorg. Med. Chem. Lett., 2007, 17, 3745-3748 Work up not detailed

Reactant (Lir	Mass (g)	MW	Mol	Catalyst	Mass (g)	Reagent	Mass (g)	Reaction Solvent	Volume (cm	Density (g m	Mass (g)	Work up che	Mass (g)	Work up sol	Volume (cm3	Density (g m	Mass (g)		
Phosphonat	0,015	228,23	6,57232E-05					THF	0,579	0,89	0,51531						0		
LiHBEt3	0,008	105,95	7,89995E-05								0						0		
											0						0		
											0						0		
											0						0		
											0						0		
											0						0		
											0						0		
											0						0		
Total	0,02337	334,18			0		0				0,51531		0				0	Total mass	0,53868

Eco-Scale	73	
Yield	78,3	
Conversion	100,0	
AE	59,9	
RME	44,1	
OE	73,6	
PMI total	52,3	
PMI reaction	52,3	47,7
reagent catalyst	2,3	
solvent	50,0	
PMI Workup	0,0	
chemical	0,0	
solvent	0,0	

	Mass	MW	Mol
Product	0,0103	200,17	5,14563E-05

	mass
Unreacted li	0

Org. Biomol. Chem., 2014, 12, 2592-2595 ON DIBENZYLBENZYLPHOSPHONATE/ Work up not detailed

Reactant (Lir	Mass (g)	MW	Mol	Catalyst	Mass (g)	Reagent	Mass (g)	Reaction Solvent	Volume (cm	Density (g m	Mass (g)	Work up che	Mass (g)	Work up sol	Volume (cm3	Density (g m	Mass (g)		
Phosphonat	0,765	352,37	0,002171013					Acetonitrile	40	0,786	31,44			MeOH	15	0,792	11,88		
LiBr	0,377	86,845	0,004341067								0			Acetonitrile		0,786	0		
											0						0		
											0						0		
											0						0		
											0						0		
											0						0		
											0						0		
											0						0		
Total	1,142	439,215			0		0				31,44		0				11,88	Total mass	44,462

Eco-Scale	88,5	
Yield	95,0	
Conversion	100,0	
AE	59,7	
RME	47,4	
OE	79,3	
PMI total	82,2	
PMI reaction	60,2	39,8
reagent catalyst	2,1	
solvent	58,1	
PMI Workup	22,0	
chemical	0,0	
solvent	22,0	

	Mass	MW	Mol
Product	0,541	262,24	0,002062996

	mass
Unreacted li	0

Figure 8: Green Metrics comparison between reported procedure[4-6] and our applied on the synthesis of compound **2b**.

7. References

[1] Y. Gök, S. Küloğlu, H. Z. Gök and L. Kekeç, *Appl. Organometal. Chem.*, 2014, **28**, 835–838.

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[3] M. Kalek, M. Jezowska and J. Stawinski, *Adv.Synth. Catal.*, 2009, **351**, 3207–3216.

[4] J. Ash, H. Huang, P. Cordero and J. Y. Kang, *Org. Biomol. Chem.*, 2021, **19**, 6007–6014.

[5] S. Chowdhury, N. J. Muni, N. P. Greenwood, D. R. Pepperberg and R. F. Standaerdt, *Bioorg. Med. Chem. Lett.*, 2007, **17**, 3745–3748.

[6] B. P. Rempel and S.G. Withers, *Org. Biomol. Chem.*, 2014, **12**, 2592–2595.