

Supporting Information

Instrumentation

General procedure A: synthesis of dialkyl *P*-alkylphosphonates 1a – 1b, 1d – 1g

Synthesis of diethyl benzylphosphonate 1d

Synthesis of sarcosine methyl ester hydrochloride

Synthesis of homoserine lactone hydrobromide

General procedure B: Synthesis of phosphorus-containing products 2, 3, 4, 6 and 7

Synthesis of dimethyl alkylphosphonates 11a – 11b

Synthesis of methyl *P*-alkyl-*N*-((*S*)-2-oxotetrahydrofuran-3-yl) phosphonamidates 8a – 8b

Synthesis of phenyl *P*-alkyl-*N*-((*S*)-2-oxotetrahydrofuran-3-yl) phosphonamidates 9a – 9b

General procedure C: synthesis of phosphoramidates 15a – 15d

Bibliography

NMR spectra

Instrumentation

Commercially available starting materials, reagents and solvents were purchased from common chemical suppliers and used without further purification. Dry solvents were obtained via the MBraun SPS-800 solvent purification system. Under pressure of N₂ gas the solvents flow through two filter/dry columns. The columns are made of stainless steel (1.4301/US 304) with an internal volume of 4.8 L. The molecular sieves, as packing material, varies in accordance to the desired solvent. Methanol was dried over activated molecular sieves and the absence of water was confirmed by ¹H NMR analysis.

GC-MS analysis was performed on an Agilent 8890 GC System equipped with an Agilent J&W HP-5ms (30 m x 0.25 mm x 0.25 µm) column and an Agilent 5977B mass spectrometer with quadrupole mass analyser and Extractor EI source (Electron Ionization, 70 eV). HRMS analysis was conducted on an Agilent 1100 high-performance liquid chromatograph (HPLC) coupled to an Agilent 6220A TOF MS (Time of Flight Mass Spectrometer) equipped with an ESI/APCI (Electrospray Ionisation/ Atmospheric Pressure Chemical Ionization) multimode ionisation source. IR spectra with a S/N-ratio of 30,000:1 were obtained from samples in neat form with a Quest ATR (Attenuated Total Reflectance) accessory with diamond crystal puck using a Shimadzu IRAFFINITY-1S Fourier Transform Infrared Spectrophotometer (FTIR). LC-MS analyses were conducted with an Agilent 1200 Series High performance liquid chromatograph equipped with a Supelco Ascentic Express C18 column (3 cm x 4.6 mm, 2.7 µm fused-core particles, 90 Å), Phenomenex Guard column (SecurityGuard Standard). The mobile phase was a mixture of acetonitrile (ACN), methanol and/or water, depending on the selected program. The HPLC was coupled to an UV-DAD (Ultra-Violet Diode Array Detector) and an Agilent 1100 Series MS with Electrospray Ionisation (ESI, 4000 V) with a single quadrupole detector. Melting points of solid compounds were determined using a Kofler Bench, type WME Heizbank of Wagner & Munz or a Büchi M-560 melting point system. Automatic flash chromatography was performed on a Büchi Reveleris X2 flash chromatography system or a Büchi C815 Pure Chromatography System. Reusable columns (SiO₂, particle size of 0.040-0.063 mm) were used for the purification of the crude products. The effluent was analysed by an Evaporative Light Scattering Detector (ELSD) and three ultraviolet detectors of which the wavelengths were adjusted depending on the mixture to be purified. ¹H, ¹³C and ³¹P NMR spectra, as well as the 2D NMR spectra, were recorded at 400, 100.6 or 161.9 MHz respectively, on a Bruker Avance III, equipped with 1H/BB z-gradient probe (BBO, 5 mm). Before analysis, samples were dissolved in deuterated solvents (CDCl₃ and [D₆]DMSO) and tetramethylsilane (TMS) was added as internal chemical shift standard. All spectra were processed using TOPSPIN 3.6.2. The chemical shift as δ-value was reported in ppm. TLC was used to determine a suitable mobile phase for the automated flash chromatography via determination of the R_f-value. Compound mixtures were spotted on silica plates (Merck Silicagel 60 F254, precoated, thickness 0.25 mm). Detection of the compounds was done using a UV detector and iodine crystals in an enclosed recipient.

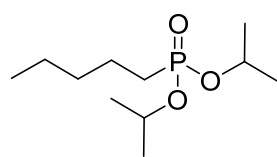
General procedure A: synthesis of dialkyl *P*-alkylphosphonates **1a** – **1b**, **1d** – **1g**

For the synthesis of these products, the same procedure was used as in our previous paper, the procedure and spectral data for diethyl pentylphosphonate **1a**, diethyl undecylphosphonate **1b** and diisopropyl undecylphosphonate **1g** can also be found there.⁵

The corresponding alkyl bromides (1 equiv.) and trialkyl phosphite (2.8 equiv.) are added to a 250 mL flask containing an Allihn condenser. The mixture was left for 16 hours while stirring at a temperature of 150 °C or 160 °C (for triethyl and triisopropyl phosphite respectively). The title compound was purified using vacuum distillation and the purity was determined using ³¹P NMR. The resulting product was used without further purification.

Diisopropyl pentylphosphonate **1c**

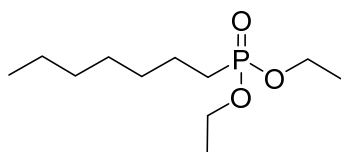
Following general procedure A, 1-bromopentane (70 mmol) and freshly distilled triisopropyl phosphite (196 mmol) were used as starting products. Finally, 16.06 g diisopropyl pentylphosphonate **1c** was collected as a transparent oil with a yield of 97%.



¹H NMR (400 MHz, CDCl₃): δ = 0.89 (t, *J* = 7.1 Hz, 3H, CH₃CH₂CH₂), 1.28 – 1.40 (m, 16H, CH₃(CH₂)₂ and 2 x (CH₃)₂CHO), 1.53 – 1.72 (m, 4H, CH₂CH₂P and CH₂P), 4.62 – 4.75 (m, 2H, 2 x (CH₃)₂CHO) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 13.9 (s, CH₃CH₂CH₂), 22.2 (d, *J* = 1.5 Hz, CH₃CH₂CH₂), 22.3 (d, *J* = 5.1 Hz, CH₂CH₂P), 24.2 (d, *J* = 3.7 Hz, 2 x (CH₃)₂CHO), 27.0 (d, *J* = 142.3 Hz, CH₂P), 32.9 (d, *J* = 16.9 Hz, CH₂(CH₂)₂P), 69.7 (d, *J* = 6.6 Hz, 2 x (CH₃)₂CHO) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 30.58 (P) ppm; **IR** (ATR, cm⁻¹): ν = 2976 (C-H), 2932 (C-H), 1466, 1385, 1240, 1109, 978 (ν_{max}), 893; **MS** (ES⁺): *m/z* (%): 237 (M+H⁺, 42), 473 (2M+H⁺, 100); **EI-MS** *m/z* (rel. int.): 236 [M] (1), 221 (6), 195 (11), 179 (29), 152 (100), 135 (14), 123 (14), 109 (7), 96 (26), 43 (10); **HRMS** (ESI⁺): *m/z* calculated: C₁₁H₂₆O₃P⁺ [M+H⁺] 237.1614, found: 237.1622.

Diethyl heptylphosphonate **1e**

Following general procedure A, 1-bromoheptane (45 mmol) and triethyl phosphite (126 mmol) were used as starting products. Finally, 8.97 g diethyl heptylphosphonate **1e** was collected as a transparent oil with a yield of 84%.

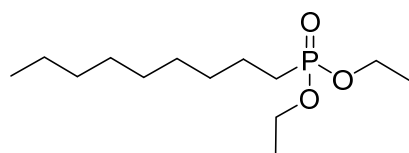


¹H NMR (400 MHz, CDCl₃): δ = 0.81 (3H, t, *J* = 6.4 Hz, CH₃CH₂CH₂), 1.15-1.35 (14H, m, CH₃(CH₂)₄ and 2 x CH₃CH₂O), 1.46-1.59 (2H, m, CH₂CH₂P), 1.59-1.71 (2H, m, CH₂P), 3.94-4.09 (4H, m, 2 x CH₃CH₂O) ppm; **¹³C NMR** (100.5 MHz, CDCl₃): δ = 13.9 (s, CH₃CH₂CH₂), 16.4 (d, *J* = 5.9 Hz, CH₃CH₂O), 23.0 (d, *J* = 5.1 Hz, CH₂CH₂P), 22.5 (s, CH₃CH₂CH₂), 25.6 (d, *J* = 140.5 Hz, CH₂P), 28.6 (s, CH₃(CH₂)₂CH₂), 30.5 (d, *J* = 16.7, CH₂(CH₂)₂P), 31.5 (s, CH₃CH₂CH₂), 61.2 (d, *J* = 6.6 Hz, CH₃CH₂O) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 32.48 (P) ppm; **IR** (ATR, cm⁻¹): ν = 2930 (C-H), 2857 (C-H), 1456, 1390, 1242, 1026 (ν_{max}), 953, 785; **MS** (ES⁺): *m/z* (%): 237 (M+H⁺, 100), 473 (2M+H⁺, 100); **EI-MS** *m/z* (rel. int.):

236 [M] (4), 207 (14), 193 (13), 179 (27), 165 (48), 152 (100), 138 (32), 125 (62), 111 (21), 97 (19); **HRMS** (ESI⁺): *m/z* calculated: C₁₁H₂₆O₃P⁺ [M+H⁺] 237.1614, found: 237.1616.

Diethyl nonylphosphonate **1f**

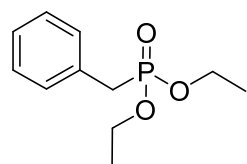
Following general procedure A, 1-bromononane (35 mmol) and triethyl phosphite (98 mmol) were used as starting products. Finally, 7.85 g diethyl nonylphosphonate **1f** was collected as a transparent oil with a yield of 85%.



¹H NMR (400 MHz, CDCl₃): δ = 0.88 (3H, *J* = 6.8 Hz, CH₃CH₂CH₂), 1.22-1.40 (18H, m, CH₃(CH₂)₆ and 2 x CH₃CH₂O), 1.54-1.66 (2H, m, CH₂CH₂P), 1.67-1.76 (2H, m, CH₂P), 4.02-4.16 (4H, m, 2 x CH₃CH₂O) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 14.1 (s, CH₃CH₂CH₂), 16.5 (app. t, *J* = 5.9 Hz, 2 x CH₃CH₂O), 22.5 (d, *J* = 5.1 Hz, CH₂CH₂P), 22.7 (s, CH₃CH₂CH₂), 25.8 (d, *J* = 140 Hz, CH₂P), 29.2 (s, CH₃(CH₂)₂CH₂), 29.3 (s, CH₃(CH₂)₃CH₂), 29.4 (s, CH₃(CH₂)₄CH₂), 30.7 (d, *J* = 16.9 Hz, CH₂(CH₂)₂P), 31.9 (s, CH₃CH₂CH₂), 61.4 (d, *J* = 6.6 Hz, 2 x CH₃CH₂O) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 32.61 (P) ppm; **IR** (ATR, cm⁻¹): ν = 2924 (C-H), 2853 (C-H), 1458, 1391, 1244, 1030 (ν_{max}), 959, 787; **MS** (ESI⁺): *m/z* (%): 265 (M+H⁺, 20), 529 (2M+H⁺, 100), 551 (2M+Na⁺, 100); **EI-MS** *m/z* (rel. int.): 264 [M] (3), 193 (13), 179 (24), 166 (17), 164 (47), 152 (100), 137 (17), 125 (48), 111 (15), 108 (13); **HRMS** (ESI⁺): *m/z* calculated: C₁₃H₃₀O₃P⁺ [M+H⁺] 265.1927, found: 265.1931.

Synthesis of diethyl benzylphosphonate **1d**

The title compound was synthesized according to Koehne et al., with benzyl bromide (42.1 mol) and triethyl phosphite (46.3 mmol) used as starting products. Finally, 8.7 g diethyl benzylphosphonate **1d** was collected as a transparent oil with a yield of 90%. The physical data, ¹H, ¹³C and ³¹P NMR data were in agreement with those reported by Koehne and Pietschnig.⁶



¹H NMR (400 MHz, CDCl₃): δ = 1.23 (t, *J* = 7.1 Hz, 6H, 2 x CH₃CH₂O), 3.14 (d, *J* = 21.5 Hz, 2H, CH₂P), 3.93–4.07 (m, 4H, 2 x CH₃CH₂O), 7.18–7.35 (m, 5H, 5 x CH_{arom}) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 16.3 (d, *J* = 5.9 Hz, 2 x CH₃CH₂O), 33.8 (d, *J* = 138.1 Hz, CH₂P), 62.1 (d, *J* = 6.6 Hz, 2 x CH₃CH₂O), 126.8 (d, *J* = 3.7 Hz, CH_{arom,para}), 128.5 (d, *J* = 3.0 Hz, 2 x CH_{arom,meta}), 129.8 (d, *J* = 6.6 Hz, 2 x CH_{arom,ortho}), 131.6 (d, *J* = 9.5 Hz, CH_{arom,quat}) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 26.36 (P) ppm; **EI-MS** *m/z* (rel. int.): 228 [M] (50), 200 (17), 172 (36), 124 (30), 118 (42), 109 (28), 91 (100), 65 (19).

Synthesis of sarcosine methyl ester hydrochloride

Dry methanol (60 equiv., 230 mL) was added to a flame dried flask under nitrogen atmosphere and cooled down to 0 °C. Acetyl chloride (6 equiv., 41 mL) is subsequently added via a dropping funnel and stirred for 20 minutes at 0 °C. Subsequently the corresponding sarcosine (5.12 g, 57.5 mmol, 1 equiv.) is added and

the mixture is stirred for 18 hours under nitrogen atmosphere at room temperature. The solvent was removed *in vacuo* to obtain the target product as a white powder in a yield of 93%. Spectral data were in accordance with literature.⁷

Synthesis of homoserine lactone hydrobromide

The synthesis of homoserine lactone hydrobromide proceeded similarly as already described in our group by Syrpas et al.^{8,9} In a 500 mL flask, (S)-methionine (15.2 g; 0.10 mol) and bromoacetic acid (1.1 equiv.; 15.4 g; 0.11 mol) were added to a 150 mL solvent mixture of H₂O-iPrOH-AcOH (5:5:2 v:v:v). The solution was left stirring overnight under reflux. After solvent removal under reduced pressure, the orange sticky oil was dissolved in 50 mL of a 4:1 mixture (v:v) of iPrOH – HBr (33% in AcOH) and crystallisation of the title compound set in. The first batch of homoserine lactone hydrobromide was collected by filtration and the purification procedure was repeated starting by evaporation of the filtrate to dryness. Additionally, both batches underwent a washing step with iPrOH, followed by evaporation under reduced pressure to obtain the pure, crystallized homoserine lactone hydrobromide salt (yield: 58-69%). All physical data, the LC-MS analyses and ¹H and ¹³C NMR data were in agreement with those previously reported.^{10,11}

General procedure B: Synthesis of phosphorus-containing products 2, 3, 4, 6 and 7

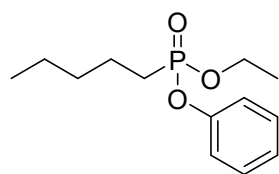
Under nitrogen atmosphere, oxalyl chloride (1.32 – 2.64 equiv., 4.9 - 9.7 mmol) is added dropwise to a stirred solution of the corresponding phosphonate **1** (1 equiv., 3.7 mmol) in 20 mL dry DCM. This solution is stirred for 16 hours at room temperature and the conversion is monitored via ³¹P NMR. After completion of the reaction, solvent is evaporated under reduced pressure to yield a crude mixture of phosphonochloridate. Due to the instability of the compound, the crude compound is immediately used in subsequent reactions.

The corresponding phosphonochloridate and triethylamine (1.1 equiv., 4.0 mmol) were dissolved in 30 mL dry THF under nitrogen atmosphere and left stirring for 30 min at room temperature, after which the reaction mixture was analysed using ³¹P NMR. The desired phenol (1.1 equiv., 4.0 mmol), alcohol (5.5 equiv., 20.2 mmol), amine (1.5 equiv., 5.5 mmol) or amino acid hydrochloride (1.5 equiv., 5.5 mmol and 1.6 equiv., 5.9 mmol extra Et₃N) was dissolved in 30 mL dry ACN under nitrogen atmosphere, while stirring at room temperature. The solution containing the phosphonochloridate was added dropwise to the solution of nucleophile at room temperature and stirred for 1 hour or until completion (monitored with ³¹P NMR). Subsequently, the solids were removed via filtration, after addition of 60 mL diethyl ether and the solvent was evaporated under reduced pressure. The remaining mixture was purified via normal phase automatic flash chromatography.

Ethyl phenyl *P*-pentylphosphonate **2a**

Diethyl pentylphosphonate **1a** (3.7 mmol, 1 equiv.), oxalyl chloride (1.98 equiv.) and 1.1 equivalents of phenol (4.0 mmol) were used as starting products for general procedure B. After completion of the phosphoramidate coupling, the reaction mixture was extracted twice with 40 mL 1N NaOH, dried over MgSO₄ and the solvent was evaporated under reduced pressure. The crude product was purified using normal phase automatic flash chromatography (SiO₂, 30% ethyl acetate in hexane, 5% Et₃N) after which 700 mg of product **2a** was obtained as a pale yellow oil in a yield of 74%.

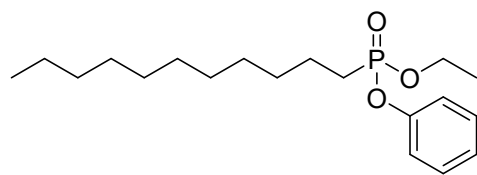
For the large scale synthesis of this product, general procedure B was followed on a scale of 36.8 mmol, with the modifications described above. Finally, 5207 mg product **2a** was obtained as a pale yellow oil in a yield of 55 %.



¹H NMR (400 MHz, CDCl₃): δ = 0.90 (t, J = 7.1 Hz, 3H, CH₃CH₂CH₂), 1.20 – 1.45 (m, 7H, CH₃(CH₂)₂ and CH₃CH₂O), 1.62 – 1.77 (m, 2H, CH₂CH₂P), 1.81 – 1.96 (m, 2H, CH₂P), 4.05 – 4.28 (m, 2H, CH₃CH₂O), 7.11 – 7.18 (m, 1H, CH_{arom,para}), 7.18 – 7.25 (m, 2H, 2 x CH_{arom,ortho}), 7.29 – 7.35 (m, 2H, 2 x CH_{arom,meta}) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 13.9 (s, CH₃CH₂CH₂), 16.5 (d, J = 6.0 Hz, CH₃CH₂O), 22.1 (d, J = 5.3 Hz, CH₂CH₂P), 22.2 (d, J = 1.4 Hz, CH₃CH₂CH₂), 25.8 (d, J = 140.4 Hz, CH₂P), 32.7 (d, J = 17.0 Hz, CH₂CH₂CH₂P), 62.4 (d, J = 7.0 Hz, CH₃CH₂O), 120.6 (d, J = 4.2 Hz, 2 x CH_{arom,ortho}), 124.8 (s, CH_{arom,para}), 129.8 (s, 2 x CH_{arom,meta}), 150.8 (d, J = 8.4 Hz, C_{arom,quat}) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 29.64 (P) ppm; **IR** (ATR, cm⁻¹): ν = 2957 (C-H), 2932 (C-H), 2872 (C-H), 1593, 1489, 1246, 1204, 1036, 916 (ν_{\max}), 760, 690; **MS** (ES⁺): m/z (%): 257 (M+H⁺, 95), 513 (2M+H⁺, 100), 535 (2M+Na⁺, 45); **EI-MS** m/z (rel. int.): 256 [M] (45), 227 (15), 213 (48), 200 (18), 185 (35), 172 (100), 135 (53), 118 (18), 104 (45), 94 (94), 77 (25), 65 (13), 43 (13); **HRMS** (ESI⁺): m/z calculated: C₁₃H₂₂O₃P⁺ [M+H⁺] 257.1301, found: 257.1306.

Ethyl phenyl *P*-undecylphosphonate **2b**

Diethyl undecylphosphonate **1b** (3.7 mmol, 1 equiv.), oxalyl chloride (1.98 equiv.) and 1.1 equivalents of phenol (4.0 mmol) were used as starting products for general procedure B. After completion of the phosphoramidate coupling, the reaction mixture was extracted twice with 40 mL 1N NaOH, dried over MgSO₄ and the solvent was evaporated under reduced pressure. The crude product was purified using normal phase automatic flash chromatography (SiO₂, 30% ethyl acetate in hexane, 5% Et₃N) after which 920 mg of product **2b** was obtained as a pale yellow oil in a yield of 74%.

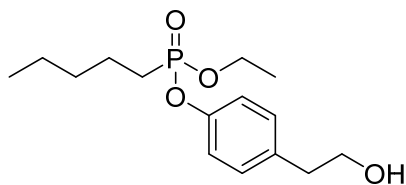


¹H NMR (400 MHz, CDCl₃): δ = 0.86 (t, J = 7.0 Hz, 3H, CH₃CH₂CH₂), 1.16 – 1.46 (m, 19H, CH₃(CH₂)₈ and CH₃CH₂O), 1.61 – 1.76 (m, 2H, CH₂CH₂P), 1.81 – 1.94 (m, 2H, CH₂P), 4.01 – 4.37 (m, 2H, CH₃CH₂O), 7.12 – 7.18 (m, 1H, CH_{arom,para}), 7.18 – 7.23 (m, 2H, 2 x CH_{arom,ortho}), 7.28 – 7.35 (m, 2H, 2 x CH_{arom,meta}) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 14.2 (s, CH₃CH₂CH₂), 16.5 (d, J = 6.0 Hz, CH₃CH₂O), 22.4 (d, J = 5.3 Hz, CH₂CH₂P), 22.8 (s, CH₃CH₂CH₂), 25.9 (d, J = 140.3 Hz, CH₂P), 29.1, 29.1, 29.4, 29.4, 29.7 (s, CH₃CH₂CH₂(CH₂)₅), 30.6 (d, J = 17.1 Hz, CH₂(CH₂)₂P), 32.0 (s, CH₃CH₂CH₂), 62.3 (d, J = 7.0 Hz, CH₃CH₂O), 120.6 (d, J = 4.3 Hz, 2 x CH_{arom,ortho}), 124.8 (s, CH_{arom,para}), 129.8 (s, 2 x CH_{arom,meta}), 150.8 (d, J = 8.4 Hz,

$\underline{C}_{arom,quat}$ ppm; ^{31}P NMR (161.9 MHz, CDCl_3): δ = 29.65 (P) ppm; IR (ATR, cm^{-1}): ν = 2924 (C-H), 2853 (C-H), 1595, 1491, 1258, 1206, 1036, 918 (ν_{max}), 760, 691; MS (ES^+): m/z (%): 341 ($\text{M}+\text{H}^+$, 100), 681 ($2\text{M}+\text{H}^+$, 90), 703 ($2\text{M}+\text{Na}^+$, 30); EI-MS m/z (rel. int.): 340 [M] (24), 311 (10), 283 (10), 269 (12), 255 (20), 241 (16), 227 (32), 213 (64), 200 (24), 185 (20), 172 (100), 118 (18), 104 (36), 94 (56), 77 (10), 55 (12), 41 (8); HRMS (ESI^+): m/z calculated: $\text{C}_{19}\text{H}_{34}\text{O}_3\text{P}^+$ [$\text{M}+\text{H}^+$] 341.2240, found: 341.2246.

Ethyl 4-(2-hydroxyethyl)phenyl *P*-pentylphosphonate **2c**

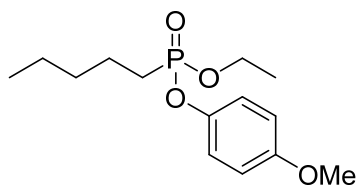
Diethyl pentylphosphonate **1a** (3.9 mmol, 1 equiv.), oxalyl chloride (1.98 equiv.) and 1.1 equivalents of tyrosol (4.3 mmol) were used as starting products for general procedure B. After completion of the phosphoramidate coupling, the reaction mixture was extracted twice with 40 mL 1N NaOH, dried over MgSO_4 and the solvent was evaporated under reduced pressure. The crude product was purified using normal phase automatic flash chromatography (SiO_2 , 0% – 40% (EtOAc:iPA, 3:1 v:v) in hexane), after which 842 mg of product **2c** was obtained as an orange oil in a yield of 72%.



^1H NMR (400 MHz, CDCl_3): δ = 0.90 (t, J = 7.1 Hz, 3H, $\text{CH}_3\text{CH}_2\text{CH}_2$), 1.28 – 1.40 (m, 7H, $\text{CH}_3(\text{CH}_2)_2$ and $\text{CH}_3\text{CH}_2\text{O}$), 1.57 – 1.79 (m, 2H, $\text{CH}_2\text{CH}_2\text{P}$), 1.80 – 1.95 (m, 2H, CH_2P), 2.22 (br s, 1H, OH), 2.82 (t, J = 6.7 Hz, 2H, $\text{CH}_2\text{CH}_2\text{OH}$), 3.80 (t, J = 6.7 Hz, 2H, $\text{CH}_2\text{CH}_2\text{OH}$), 4.11 – 4.23 (m, 2H, $\text{CH}_3\text{CH}_2\text{O}$), 7.08 – 7.22 (m, 4H, 4 x CH_{arom}) ppm; ^{13}C NMR (100.6 MHz, CDCl_3): δ = 13.9 (s, $\text{CH}_3\text{CH}_2\text{CH}_2$), 16.5 (d, J = 6.0 Hz, $\text{CH}_3\text{CH}_2\text{O}$), 22.1 (d, J = 5.5 Hz, $\text{CH}_2\text{CH}_2\text{P}$), 22.2 (d, J = 1.4 Hz, $\text{CH}_3\text{CH}_2\text{CH}_2$), 25.8 (d, J = 140.3 Hz, CH_2P), 32.7 (d, J = 17.0 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{P}$), 38.6 (s, $\text{CH}_2\text{CH}_2\text{OH}$), 62.4 (d, J = 7.0 Hz, $\text{CH}_3\text{CH}_2\text{O}$), 63.6 (s, $\text{CH}_2\text{CH}_2\text{OH}$), 120.6 (d, J = 4.3 Hz, 2 x POC_qCH), 130.3 (s, 2 x $\text{CH}_2\text{C}_q\text{CH}$), 135.3 (s, CH_2C_q), 149.3 (d, J = 8.5 Hz, POC_q) ppm; ^{31}P NMR (161.9 MHz, CDCl_3): δ = 29.81 (P) ppm; IR (ATR, cm^{-1}): ν = 3414 (O-H), 2932 (C-H), 2875 (C-H), 1713, 1506, 1209, 1036, 916 (ν_{max}), 827, 528; MS (ES^+): m/z (%): 301 ($\text{M}+\text{H}^+$, 100), 323 ($\text{M}+\text{Na}^+$, 20), 601 ($2\text{M}+\text{H}^+$, 14); EI-MS m/z (rel. int.): 300 [M] (6), 270 (100), 242 (31), 214 (6), 186 (8), 163 (18), 135 (31), 107 (38), 77 (6), 43 (6); HRMS (ESI^+): m/z calculated: $\text{C}_{15}\text{H}_{26}\text{O}_4\text{P}^+$ [$\text{M}+\text{H}^+$] 301.1563, found: 301.1554.

Ethyl 4-methoxyphenyl *P*-pentylphosphonate **2d**

Diethyl pentylphosphonate **1a** (3.7 mmol, 1 equiv.), oxalyl chloride (1.98 equiv.) and 1.1 equivalents of 4-methoxyphenol (4.0 mmol) were used as starting products for general procedure B. After completion of the phosphoramidate coupling, the reaction mixture was extracted twice with 40 mL 1N NaOH, dried over MgSO_4 and the solvent was evaporated under reduced pressure. The crude product was purified using normal phase automatic flash chromatography (SiO_2 , 30% ethyl acetate in hexane, 5% Et_3N), after which 687 mg of product **2d** was obtained as a pale yellow oil in a yield of 65%.

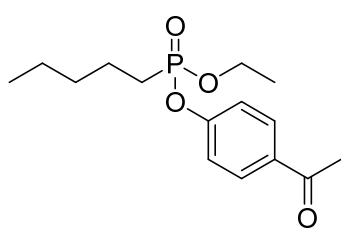


^1H NMR (400 MHz, CDCl_3): δ = 0.90 (t, J = 7.1 Hz, 3H, $\text{CH}_3\text{CH}_2\text{CH}_2$), 1.22 – 1.46 (m, 7H, $\text{CH}_3(\text{CH}_2)_2$ and $\text{CH}_3\text{CH}_2\text{O}$), 1.57 – 1.75 (m, 2H, $\text{CH}_2\text{CH}_2\text{P}$), 1.79 – 1.93 (m, 2H, CH_2P), 3.78 (s, 3H, OCH_3), 4.03 – 4.26 (m, 2H, $\text{CH}_3\text{CH}_2\text{O}$), 6.81 – 6.87 (m, 2H, 2 x $\text{CH}_3\text{OC}_q\text{CH}$), 7.09 – 7.16 (m, 2H, 2 x POC_qCH) ppm;

¹³C NMR (100.6 MHz, CDCl₃): δ = 13.8 (s, CH₃CH₂CH₂), 16.4 (d, *J* = 6.0 Hz, CH₃CH₂O), 22.0 (d, *J* = 5.4 Hz, CH₂CH₂P), 22.1 (d, *J* = 1.3 Hz, CH₃CH₂CH₂), 25.6 (d, *J* = 140.4 Hz, CH₂P), 32.7 (d, *J* = 17.1 Hz, CH₂CH₂CH₂P), 55.6 (s, OCH₃), 62.3 (d, *J* = 6.9 Hz, CH₃CH₂O), 114.7 (s, 2 x CH₃OC_qCH), 121.4 (d, *J* = 4.1 Hz, 2 x POC_qCH), 144.2 (d, *J* = 8.5 Hz, POC_q), 156.6 (s, CH₃OC_q) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 29.95 (P) ppm; **IR** (ATR, cm⁻¹): ν = 2932 (C-H), 2872 (C-H), 1504 (ν_{max}), 1248, 1200, 1032, 912; **MS** (ES⁺): *m/z* (%): 287 (M+H⁺, 84), 573 (2M+H⁺, 100), 595 (2M+Na⁺, 40); **EI-MS** *m/z* (rel. int.): 286 [M] (100), 243 (29), 215 (23), 202 (19), 138 (42), 124 (94), 121 (87), 109 (26); **HRMS** (ESI⁺): *m/z* calculated: C₁₄H₂₄O₄P⁺ [M+H⁺] 287.1407, found: 287.1411.

4-Acetylphenyl ethyl *P*-pentylphosphonate **2e**

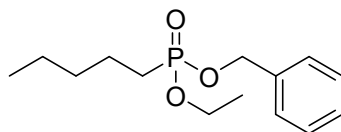
Diethyl pentylphosphonate **1a** (3.7 mmol, 1 equiv.), oxalyl chloride (1.98 equiv.) and 1.1 equivalents of 4-acetylphenol (4.0 mmol) were used as starting products for general procedure B. After completion of the phosphoramidate coupling, the reaction mixture was extracted twice with 40 mL 1N NaOH, dried over MgSO₄ and the solvent was evaporated under reduced pressure. The crude product was purified using normal phase automatic flash chromatography SiO₂, 30% ethyl acetate in hexane, 5% Et₃N, after which 670 mg of product **2e** was obtained as a yellow oil in a yield of 61%.



¹H NMR (400 MHz, CDCl₃): δ = 0.90 (t, *J* = 7.0 Hz, 3H, CH₃CH₂CH₂), 1.27 – 1.44 (m, 7H, CH₃(CH₂)₂ and CH₃CH₂O), 1.62 – 1.75 (m, 2H, CH₂CH₂P), 1.84 – 1.98 (m, 2H, CH₂P), 2.59 (s, 3H, CH₃C=O), 4.06 – 4.28 (m, 2H, CH₃CH₂O), 7.28 – 7.33 (m, 2H, 2 x POC_qCH), 7.91 – 8.02 (m, 2H, 2 x O=CC_qCH) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 13.8 (s, CH₃CH₂CH₂), 16.4 (d, *J* = 6.0 Hz, CH₃CH₂O), 22.0 (d, *J* = 5.5 Hz, CH₂CH₂P), 22.1 (d, *J* = 1.3 Hz, CH₃CH₂CH₂), 25.9 (d, *J* = 140.2 Hz, CH₂P), 26.5 (s, CH₃C=O), 32.6 (d, *J* = 17.0 Hz, CH₂CH₂CH₂P), 62.6 (d, *J* = 7.0 Hz, CH₃CH₂O), 120.4 (d, *J* = 4.5 Hz, 2 x POC_qCH), 130.4 (s, 2 x O=CC_qCH), 133.8 (s, 2 x O=CC_q), 154.7 (d, *J* = 8.3 Hz, POC_q), 196.8 (s, C=O) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 29.99 (P) ppm; **IR** (ATR, cm⁻¹): ν = 2932 (C-H), 2872 (C-H), 1682, 1597, 1504, 1263, 1217, 1034, 912 (ν_{max}); **MS** (ES⁺): *m/z* (%): 299 (M+H⁺, 100), 597 (2M+H⁺, 25), 619 (2M+Na⁺, 20); **EI-MS** *m/z* (rel. int.): 298 [M] (35), 283 (100), 255 (35), 227 (53), 214 (23), 199 (31), 146 (17), 135 (16), 121 (50), 43 (13); **HRMS** (ESI⁺): *m/z* calculated: C₁₅H₂₄O₄P [M+H⁺] 299.1407, found: 299.1408.

Benzyl ethyl *P*-pentylphosphonate **2f**

Diethyl pentylphosphonate **1a** (3.7 mmol, 1 equiv.), oxalyl chloride (1.98 equiv.) and 5.5 equivalents of benzyl alcohol (20.21 mmol) were used as starting products for general procedure B. The crude product was purified using reversed-phase automatic flash chromatography (C18, 5 CV at 1/1 ACN/H₂O, then in 10 CV to 100% ACN), after which 680 mg of product **2f** was obtained as a yellow oil in a yield of 68%.

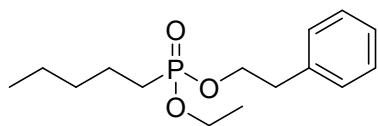


¹H NMR (400 MHz, CDCl₃): δ = 0.88 (t, *J* = 7.2 Hz, 3H, CH₃CH₂CH₂), 1.23 – 1.38 (m, 7H, CH₃(CH₂)₂ and CH₃CH₂O), 1.52 – 1.64 (m, 2H, CH₂CH₂P), 1.67 – 1.78 (m, 2H, CH₂P), 3.94 – 4.16 (m, 2H, CH₃CH₂O), 5.00 – 5.13 (m, 2H,

$C_{arom,quat}CH_2O$), 7.28 – 7.43 (m, 5H, 5 x CH_{arom}) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 13.9 (s, $CH_3CH_2CH_2$), 16.5 (d, J = 6.0 Hz, CH_3CH_2O), 22.1 (d, J = 5.2 Hz, CH_2CH_2P), 22.2 (d, J = 1.4 Hz, $CH_3CH_2CH_2$), 25.9 (d, J = 140.1 Hz, CH_2P), 32.8 (d, J = 16.9 Hz, $CH_2CH_2CH_2P$), 61.6 (d, J = 6.6 Hz, CH_3CH_2O), 67.0 (d, J = 6.5 Hz, $C_{arom,quat}CH_2O$), 127.9 (s, 2 x $CH_{arom,ortho}$), 128.4 (s, $CH_{arom,para}$), 128.7 (s, 2 x $CH_{arom,meta}$), 136.8 (d, J = 5.9 Hz, $C_{arom,quat}$) ppm; ^{31}P NMR (161.9 MHz, $CDCl_3$): δ = 33.20 (P) ppm; IR (ATR, cm^{-1}): ν = 2955 (C-H), 2932 (C-H), 2872 (C-H), 1456, 1238, 1005, 1001 (ν_{max}), 959, 696; MS (ES⁺): m/z (%): 271 (M+H⁺, 52), 541 (2M+H⁺, 100); EI-MS m/z (rel. int.): 270 [M] (23), 214 (8), 179 (54), 151 (58), 124 (19), 108 (35), 91 (100), 65 (19); HRMS (ESI⁺): m/z calculated: $C_{14}H_{24}O_3P^+$ [M+H⁺] 271.1458, found: 271.1463.

Ethyl phenethyl *P*-pentylphosphonate **2g**

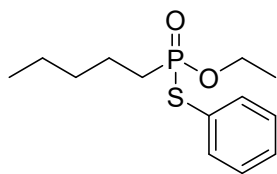
Diethyl pentylphosphonate **1a** (3.7 mmol, 1 equiv.), oxalyl chloride (1.98 equiv.) and 5.5 equivalents of phenethyl alcohol (20.21 mmol) were used as starting products for general procedure B. The crude product was purified using reversed-phase automatic flash chromatography (C18, 5 CV at 1/1 ACN/ H_2O , then in 10 CV to 100% ACN) and normal phase automatic flash chromatography (SiO_2 , 0% - 100% ethyl acetate in hexane), after which 350 mg of product **2g** was obtained as a pale oil in a yield of 34%.



1H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, J = 6.9 Hz, 3H, $CH_3CH_2CH_2$), 1.20 – 1.38 (m, 7H, $CH_3(CH_2)_2$ and CH_3CH_2O), 1.46 – 1.58 (m, 2H, CH_2CH_2P), 1.58 – 1.75 (m, 2H, CH_2P), 2.97 (t, J = 6.3 Hz, 2H, $C_{arom,quat}CH_2CH_2O$), 3.83 – 4.10 (m, 2H, CH_3CH_2O), 4.13 – 4.36 (m, 2H, $C_{arom,quat}CH_2CH_2O$), 7.12 – 7.44 (m, 5H, 5 x CH_{arom}) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 14.0 (s, $CH_3CH_2CH_2$), 16.6 (d, J = 6.1 Hz, CH_3CH_2O), 22.1 (d, J = 5.4 Hz, CH_2CH_2P), 22.3 (d, J = 1.4 Hz, $CH_3CH_2CH_2$), 25.7 (d, J = 140.3 Hz, CH_2P), 32.9 (d, J = 16.9 Hz, $CH_2CH_2CH_2P$), 37.2 (d, J = 6.2 Hz, $C_{arom,quat}CH_2CH_2O$), 61.5 (d, J = 6.6 Hz, CH_3CH_2O), 65.9 (d, J = 6.7 Hz, $C_{arom,quat}CH_2CH_2O$), 126.8 (s, $CH_{arom,para}$), 128.6 (s, 2 x $CH_{arom,meta}$), 129.2 (s, 2 x $CH_{arom,ortho}$), 137.6 (s, $C_{arom,quat}CH_2CH_2O$) ppm; ^{31}P NMR (161.9 MHz, $CDCl_3$): δ = 32.79 (P) ppm; IR (ATR, cm^{-1}): ν = 2955 (C-H), 2930 (C-H), 2872 (C-H), 1454, 1391, 1236, 1011 (ν_{max}), 959; MS (ES⁺): m/z (%): 285 (M+H⁺, 100), 569 (2M+H⁺, 83), 591 (2M+Na⁺, 36); EI-MS m/z (rel. int.): 284 [M] (1), 104 (100), 91 (5), 78 (5); HRMS (ESI⁺): m/z calculated: $C_{15}H_{26}O_3P^+$ [M+H⁺] 285.1614, found: 285.1618.

O-Ethyl *S*-phenyl *P*-pentylphosphonothioate **3**

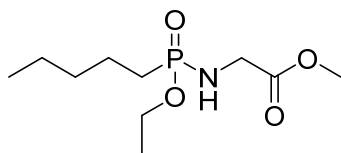
Diethyl pentylphosphonate **1a** (3.7 mmol, 1 equiv.), oxalyl chloride (2.64 equiv.) and 1.1 equivalents of thiophenol (4.0 mmol) were used as starting products for general procedure B. After completion of the phosphoramidate coupling, the reaction mixture was extracted twice with 40 mL 1N NaOH, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The crude product was purified using normal phase automatic flash chromatography (SiO_2 , 30% ethyl acetate in hexane, 5% Et_3N), after which 630 mg of product **3** was obtained as a clear oil in a yield of 63%.



¹H NMR (400 MHz, CDCl₃): δ = 0.87 (t, *J* = 7.2 Hz, 3H, CH₃CH₂CH₂), 1.21 – 1.40 (m, 7H, CH₃(CH₂)₂ and CH₃CH₂O), 1.53 – 1.77 (m, 2H, CH₂CH₂P), 1.81 – 1.91 (m, 2H, CH₂P), 4.09 – 4.38 (m, 2H, CH₃CH₂O), 7.31 – 7.39 (m, 3H, 2 x CH_{arom,ortho} and CH_{arom,para}), 7.50 – 7.59 (m, 2H, 2 x CH_{arom,meta}) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 13.8 (s, CH₃CH₂CH₂), 16.2 (d, *J* = 6.7 Hz, CH₃CH₂O), 21.7 (d, *J* = 5.0 Hz, CH₂CH₂P), 22.1 (d, *J* = 1.4 Hz, CH₃CH₂CH₂), 31.4 (d, *J* = 104.6 Hz, CH₂P), 32.5 (d, *J* = 17.4 Hz, CH₂CH₂CH₂P), 61.6 (d, *J* = 7.5 Hz, CH₃CH₂O), 127.5 (d, *J* = 5.2 Hz, C_{arom,quat}), 129.0 (d, *J* = 2.5 Hz, CH_{arom,para}), 129.4 (d, *J* = 1.9 Hz, 2 x CH_{arom,ortho}), 135.0 (d, *J* = 4.1 Hz, 2 x CH_{arom,meta}) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 55.91 (P) ppm; **IR** (ATR, cm⁻¹): ν = 2930 (C-H), 2870 (C-H), 1440, 1231, 1020 (ν_{max}), 953, 744, 691; **MS** (ES⁺): *m/z* (%): 273 (M+H⁺, 100), 545 (2M+H⁺, 60), 567 (2M+Na⁺, 40); **EI-MS** *m/z* (rel. int.): 272 [M] (38), 230 (14), 216 (28), 188 (34), 163 (40), 135 (100), 110 (66), 71 (22), 69 (28), 65 (22), 43 (20); **HRMS** (ESI⁺): *m/z* calculated: C₁₃H₂₂O₂PS⁺ [M+H⁺] 273.1073, found: 273.1076.

Methyl *N*-(ethoxy(pentyl)phosphoryl)glycinate **4a**

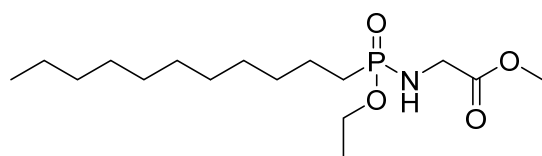
Diethyl pentylphosphonate **1a** (3.7 mmol, 1 equiv.), oxalyl chloride (1.98 equiv.) and glycine methyl ester hydrochloride (5.5 mmol, 1.5 equiv.) were used as starting products for general procedure B. Together with the amino acid, 1.6 equiv. of triethylamine (5.9 mmol) was added to neutralize the hydrochloride salt. The crude mixture was purified via normal phase automatic flash chromatography (SiO₂, 20% (EtOAc:iPA, 3:1 v:v) in hexane), after which 690 mg of product **4a** was obtained as a yellow oil in a yield of 75%.



¹H NMR (400 MHz, CDCl₃): δ = 0.89 (t, *J* = 6.9 Hz, 3H, CH₃CH₂CH₂), 1.22 – 1.43 (m, 7H, CH₃(CH₂)₂ and CH₃CH₂O), 1.48 – 1.87 (m, 4H, CH₂CH₂P and CH₂P), 2.93 – 3.17 (m, 1H, NHCH₂), 3.63 – 3.87 (m, 5H, COOCH₃ and NHCH₂), 3.95 – 4.24 (m, 2H, CH₃CH₂O) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 13.9 (s, CH₃CH₂CH₂), 16.5 (d, *J* = 6.5 Hz, CH₃CH₂O), 22.1 (d, *J* = 5.2 Hz, CH₂CH₂P), 22.3 (s, CH₃CH₂CH₂), 27.8 (d, *J* = 131.0 Hz, CH₂P), 32.9 (d, *J* = 17.1 Hz, CH₃CH₂CH₂), 42.6 (s, NHCH₂), 52.3 (s, COOCH₃), 59.8 (d, *J* = 6.9 Hz, CH₃CH₂O), 172.1 (d, *J* = 5.4 Hz, COO) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 34.94 (P) ppm; **IR** (ATR, cm⁻¹): ν = 3199 (N-H), 2931 (C-H), 1753 (C=O), 1454, 1436, 1195 (C-O), 1147 (ν_{max}), 1035, 950, 856; **MS** (ES⁺): *m/z* (%): 252 (M+H⁺, 100), 503 (2M+H⁺, 80), 525 (2M+Na⁺, 18); **EI-MS** *m/z* (rel. int.): 251 [M] (8), 219 (8), 208 (8), 192 (100), 163 (37), 148 (15), 135 (43), 122 (7), 108 (15), 71 (7), 43 (7); **HRMS** (ESI⁺): *m/z* calculated: C₁₀H₂₃NO₄P⁺ [M+H⁺] 252.1359, found: 252.1365.

Methyl *N*-(ethoxy(undecyl)phosphoryl)glycinate **4b**

Diethyl undecylphosphonate **1b** (3.7 mmol, 1 equiv.), oxalyl chloride (1.32 equiv.) and glycine methyl ester hydrochloride (5.5 mmol, 1.5 equiv.) were used as starting products for general procedure B. Together with the amino acid, 1.6 equiv. of triethylamine (5.9 mmol) was added to neutralize the hydrochloride salt. The crude product was purified using normal phase automatic flash chromatography (SiO₂, EtOAc:hexane 3:1 v:v, gradient MeOH 0-7 v%), after which 940 mg of product **4b** was obtained as a white powder in a yield of 76%.



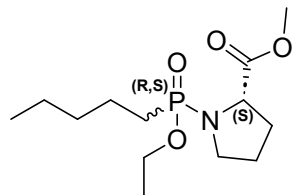
Melting point: 60 °C; **¹H NMR** (400 MHz, CDCl₃): δ = 0.88 (t, *J* = 6.8 Hz, 3H, CH₃CH₂CH₂), 1.23 – 1.42 (m, 19H, CH₃(CH₂)₈ and CH₃CH₂O), 1.51 – 1.79 (m, 4H, CH₂CH₂P and CH₂P), 2.84-2.94 (m, 1H, NHCH₂), 3.72-3.80 (m, 5H, COOCH₃ and NHCH₂), 3.93 – 4.17 (m, 2H, CH₃CH₂O) ppm;

¹³C NMR (100.6 MHz, CDCl₃): δ = 14.1 (s, CH₃CH₂CH₂), 16.4 (d, *J* = 6.6 Hz, CH₃CH₂O), 22.4 (d, *J* = 4.8 Hz, CH₂CH₂P), 22.7 (s, CH₃CH₂CH₂), 27.8 (d, *J* = 130.5 Hz, CH₂P), 29.2, 29.3, 29.4, 29.6 (s, CH₃CH₂CH₂(CH₂)₅), 30.7 (d, *J* = 17.1 Hz, CH₂(CH₂)₂P), 31.9 (s, CH₃CH₂CH₂), 42.5 (s, NHCH₂), 52.3 (s, COOCH₃), 59.8 (d, *J* = 6.9 Hz, CH₃CH₂O), 172.0 (d, *J* = 5.7 Hz, COO) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 34.86 (P) ppm; **IR** (ATR, cm⁻¹): ν = 3197 (N-H), 2914 (C-H), 2848 (C-H), 1749 (C=O), 1463, 1197 (ν_{max}), 1159 (C-O), 1041, 945, 866, 802, 769; **MS** (ES⁺): *m/z* (%): 336 (M+H⁺, 100), 671 (2M+H⁺, 75), 693 (2M+Na⁺, 35); **EI-MS** *m/z* (rel. int.): 335 [M] (16), 276 (100), 248 (25), 208 (23), 195 (27), 163 (61), 135 (25), 108 (30), 90 (9), 65 (8), 43 (10); **HRMS** (ESI⁺): *m/z* calculated: C₁₆H₃₅NO₄P⁺ [M+H⁺] 336.2298, found: 336.2300.

Methyl *N*-(ethoxy(pentyl)phosphoryl)-L-prolinate **4c**

Diethyl pentylphosphonate **1a** (3.7 mmol, 1 equiv.), oxalyl chloride (1.98 equiv.) and L-proline methyl ester hydrochloride (5.5 mmol, 1.5 equiv.) were used as starting products for general procedure B. Together with the amino acid, 1.6 equiv. of triethylamine (5.9 mmol) was added to neutralize the hydrochloride salt. The crude mixture was purified via normal phase automatic flash chromatography (SiO₂, EtOAc:hexane 3:1 v/v, gradient MeOH 0-7 v%), after which 800 mg of product **4c** was obtained as a yellow oil in a yield of 75%.

Spectral data derived from the mixture of diastereomers (dr= 47/53).

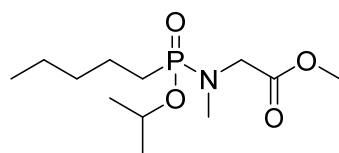


¹H NMR (400 MHz, CDCl₃): δ = 0.86 – 0.93 (m, 6H, 2 x CH₃CH₂CH₂), 1.25 – 1.41 (m, 14H, 2 x CH₃(CH₂)₂ and 2 x CH₃CH₂O), 1.43 – 2.07 (m, 14H, 2 x CH₂CH₂P, 2 x CH₂P, 2 x CH₂CH₂CHN and 2 x CH_aH_bCHN), 2.09 – 2.24 (m, 2H, 2 x CH_aH_bCHN), 3.14 – 3.31 (m, 4H, 2 x CH₂N), 3.69 – 3.73 (m, 6H, 2 x COOCH₃), 3.79 – 3.87 (m, 1H, CH₃CH₂O), 4.02 – 4.20 (m, 3H, CH₃CH₂O), 4.25 – 4.30 (m, 1H, CHN), 4.35 –

4.42 (m, 1H, CHN) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 14.0 (s, CH₃CH₂CH₂), 14.0 (s, CH₃CH₂CH₂), 16.4 (d, *J* = 4.3 Hz, CH₃CH₂O), 16.5 (d, *J* = 5.1 Hz, CH₃CH₂O), 21.8 (d, *J* = 5.0 Hz, CH₂CH₂P), 21.8 (d, *J* = 5.0 Hz, CH₂CH₂P), 22.3 (s, CH₃CH₂CH₂), 25.4 (d, *J* = 2.9 Hz, CH₂CH₂CHN), 25.4 (d, *J* = 3.7 Hz, CH₂CH₂CHN), 25.9 (d, *J* = 131.3 Hz, CH₂P), 26.7 (d, *J* = 130.6 Hz, CH₂P), 31.2 (d, *J* = 6.6 Hz, CH₂CHN), 31.4 (d, *J* = 7.3 Hz, CH₂CHN), 33.0 (d, *J* = 16.9 Hz, CH₃CH₂CH₂), 33.1 (d, *J* = 17.6 Hz, CH₃CH₂CH₂), 46.4 (d, *J* = 5.1 Hz, CH₂N), 46.6 (d, *J* = 5.1 Hz, CH₂N), 52.1 (s, COOCH₃), 52.1 (s, COOCH₃), 59.2 (d, *J* = 6.7 Hz, CH₃CH₂O), 59.7 (d, *J* = 4.4 Hz, CHN), 59.8 (d, *J* = 5.1 Hz, CHN), 59.8 (d, *J* = 7.3 Hz, CH₃CH₂O), 174.8 (s, COO), 175.1 (s, COO) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 33.06 (P), 33.82 (P) ppm; **IR** (ATR, cm⁻¹): ν = 2953 (C-H), 1745 (C=O), 1444, 1205, 1147 (C-O), 1087, 1031, 1020 (ν_{max}), 947, 761; **MS** (ES⁺): *m/z* (%): 292 (M+H⁺, 100), 583 (2M+H⁺, 16), 605 (2M+Na⁺, 11); **EI-MS** *m/z* (rel. int.): 291 [M] (1), 232 (100), 204 (30), 135 (7), 70 (2); **HRMS** (ESI⁺): *m/z* calculated: C₁₃H₂₇NO₄P⁺ [M+H⁺] 292.1672, found: 292.1676.

Methyl *N*-(isopropoxy(pentyl)phosphoryl)sarcosinate **4d**

Diisopropyl pentylphosphonate **1c** (3.9 mmol, 1 equiv.), oxalyl chloride (1.32 equiv.) and sarcosine methyl ester hydrochloride (5.9 mmol, 1.5 equiv.) were used as starting products for general procedure B. Together with the amino acid, 1.6 equiv. of triethylamine (6.2 mmol) was added to neutralize the hydrochloride salt. The crude mixture was purified via normal phase automatic flash chromatography (SiO₂, 0-75 v% (EtOAc + 5v% Et₃N) in hexane), after which 600 mg of product **4d** was obtained as a pale yellow oil in a yield of 55%.



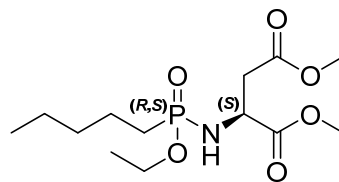
¹H NMR (400 MHz, CDCl₃): δ = 0.90 (t, *J* = 7.1 Hz, 3H, CH₃CH₂CH₂), 1.22 – 1.41 (m, 10H, CH₃(CH₂)₂ and (CH₃)₂CHO), 1.49 – 1.64 (m, 2H, CH₂CH₂P), 1.64 – 1.82 (m, 2H, CH₂P), 2.66 (d, *J* = 8.4 Hz, 3H, NCH₃), 3.72 (s, 3H, COOCH₃), 3.89 (d, *J* = 9.9 Hz, 2H, NCH₂), 4.72 (dxhept, *J* = 8.8, 6.2 Hz, 1H, CHO) ppm;

¹³C NMR (100.6 MHz, CDCl₃): δ = 14.0 (s, CH₃CH₂CH₂), 21.9 (d, *J* = 4.6 Hz, CH₂CH₂P), 22.4 (d, *J* = 1.3 Hz, CH₃CH₂CH₂), 23.6 (d, *J* = 5.9 Hz, CH₃CHO), 24.4 (d, *J* = 3.7 Hz, CH₃CHO), 26.2 (d, *J* = 132.7 Hz, CH₂P), 33.0 (d, *J* = 17.0 Hz, CH₃CH₂CH₂), 34.2 (d, *J* = 4.8 Hz, NCH₃), 50.3 (d, *J* = 4.4 Hz, NCH₂), 51.9 (s, COOCH₃), 68.2 (d, *J* = 7.1 Hz, CH₃CHO), 171.7 (d, *J* = 1.9 Hz, C=O) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 35.19 (P) ppm; **IR** (ATR, cm⁻¹): ν = 2955 (C-H), 1755 (C=O), 1665, 1206, 983, 950, 727 (ν_{max}); **MS** (ES⁺): *m/z* (%): 280 (M+H⁺, 100), 581 (2M+Na⁺, 15); **EI-MS** *m/z* (rel. int.): 279 [M] (11), 220 (32), 178 (100), 44 (21); **HRMS** (ESI⁺): *m/z* calculated: C₁₂H₂₇NO₄P⁺ [M+H⁺] 280.1672, found: 280.1672.

Dimethyl *N*-(ethoxy(pentyl)phosphoryl)-L-aspartate **4e**

Diethyl pentylphosphonate **1a** (3.7 mmol, 1 equiv.), oxalyl chloride (1.98 equiv.) and dimethyl L-aspartate hydrochloride (5.5 mmol, 1.5 equiv.) were used as starting products for general procedure B. Together with the amino acid, 1.6 equiv. of triethylamine (5.9 mmol) was added to neutralize the hydrochloride salt. The crude product was purified using normal phase automated column chromatography (SiO₂, 55% - 75% ethyl acetate in hexane), after which, 520 mg of product **4e** was obtained as an orange oil with a yield of 44%.

Spectral data derived from the mixture of diastereomers (dr = 51/49).



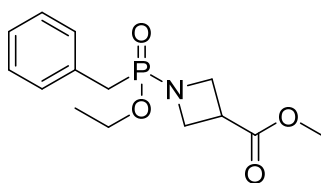
¹H NMR (400 MHz, CDCl₃): δ = 0.89, 0.90 (2 x t, *J* = 7.0, 3H, CH₃CH₂CH₂), 1.23 – 1.45 (m, 7H, CH₃(CH₂)₂ and CH₃CH₂O), 1.49 – 1.85 (m, 4H, CH₂CH₂P and CH₂P), 2.73 – 2.83 (m, 1H, CH_aH_bCHNH), 2.92 – 3.02 (m, 1H, CH_aH_bCHNH), 3.45 (t, *J* = 10.6 Hz, 1H, CHNH), 3.70 (2 x s, 3H, CH₂COOCH₃), 3.75, 3.76 (2 x s, 3H, CHCOOCH₃), 3.87 – 4.17 (m, 2H, CH₃CH₂O), 4.22 – 4.38 (m, 1H, CHNH) ppm;

¹³C NMR (100.6 MHz, CDCl₃): δ = 13.9 (s, 2 x CH₃CH₂CH₂), 16.4 (app t, *J* = 6.7 Hz, 2 x CH₃CH₂O), 22.0 (d, *J* = 5.1 Hz, CH₂CH₂P), 22.2 (d, *J* = 5.1 Hz, CH₂CH₂P), 22.3 (s, 2 x CH₃CH₂CH₂), 28.3 (d, *J* = 129.1 Hz, CH₂P), 28.4 (d, *J* = 132.0 Hz, CH₂P), 32.9 (d, *J* = 17.3 Hz, CH₃CH₂CH₂), 33.0 (d, *J* = 17.6 Hz, CH₃CH₂CH₂), 39.1 (d, *J* = 4.0 Hz, CH₂CHNH), 39.1 (d, *J* = 3.6 Hz, CH₂CHNH), 50.3 (s, CHNH), 50.6 (s, CHNH), 52.0 (s, 2 x CH₂COOCH₃), 52.8 (s, 2 x CHCOOCH₃), 59.8 (d, *J* = 7.0 Hz, CH₃CH₂O), 60.2 (d, *J* = 6.8 Hz, CH₃CH₂O), 171.4 (s, CH₂COOCH₃), 171.6 (s, CH₂COOCH₃), 172.8 (2 x d, *J* = 4.2 Hz, 2 x CHCOOCH₃) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 33.76 (P), 34.68 (P) ppm; **IR** (ATR, cm⁻¹): ν = 2955 (C-H), 2932 (C-H), 2873 (C-H), 1736 (C=O), 1732 (C=O), 1437,

1275, 1198, 1167 (C-O, ν_{\max}), 1036, 962; **MS** (ES^+): m/z (%): 324 ($\text{M}+\text{H}^+$, 100), 669 ($2\text{M}+\text{Na}^+$, 17); **EI-MS** m/z (rel. int.): 323 [M] (4), 292 (4), 264 (100), 232 (35), 204 (50), 164 (8), 135 (18), 104 (10), 70 (5), 43 (8); **HRMS** (ESI^+): m/z calculated: $\text{C}_{13}\text{H}_{27}\text{NO}_6\text{P}^+$ [$\text{M}+\text{H}^+$] 324.1571, found: 324.1574.

Methyl *N*-(benzyl(ethoxy)phosphoryl)azetidine-3-carboxylate **4f**

Diethyl benzylphosphonate **1d** (3.9 mmol, 1 equiv.) and methyl azetidine-3-carboxylate hydrochloride (5.9 mmol, 1.5 equiv.) were used as starting products for general procedure B. The chlorination step was executed with 1.32 equiv. of oxalyl chloride and a catalytic amount of DMF (5 drops). Together with the amino acid, 1.6 equiv. of triethylamine (6.2 mmol) was added to neutralize the hydrochloride salt. The crude product was purified using normal phase automated column chromatography (SiO_2 , 0% – 40% ($\text{EtOAc}:\text{iPA}$, 3:1 v:v) in hexane), after which, 790 mg of product **4f** was obtained as an orange oil with a yield of 68%.

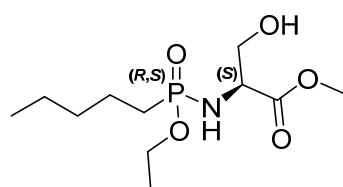


^1H NMR (400 MHz, CDCl_3): δ = 1.30 (t, J = 7.0 Hz, 3H, $\text{CH}_3\text{CH}_2\text{O}$), 3.14 (d, J = 20.2 Hz, 2H, CH_2P), 3.35 (ttd, J = 8.8, 6.5, 2.3 Hz, 1H, CHCOO), 3.71 (s, 3H, COOCH_3), 3.77 – 3.98 (m, 4H, CH_2NCH_2), 3.99 – 4.15 (m, 2H, $\text{CH}_3\text{CH}_2\text{O}$), 7.19 – 7.38 (m, 5H, 5 x CH_{arom}) ppm; **^{13}C NMR** (100.6 MHz, CDCl_3): δ = 16.4 (d, J = 6.1 Hz, $\text{CH}_3\text{CH}_2\text{O}$), 33.7 (d, J = 124.1 Hz, CH_2P), 34.1 (d, J = 16.8 Hz, CHCOO), 51.2 (2 x d, J = 7.0 Hz, CH_2NCH_2), 52.1 (s, COOCH_3), 60.7 (d, J = 7.0 Hz, $\text{CH}_3\text{CH}_2\text{O}$), 126.8 (d, J = 3.4 Hz, $\text{CH}_{\text{arom,para}}$), 128.5 (d, J = 3.0 Hz, 2 x $\text{CH}_{\text{arom,meta}}$), 129.8 (d, J = 6.2 Hz, 2 x $\text{CH}_{\text{arom,ortho}}$), 131.9 (d, J = 8.5 Hz, $\text{C}_{\text{arom,quat}}$), 172.9 (d, J = 2.9 Hz, COO) ppm; **^{31}P NMR** (161.9 MHz, CDCl_3): δ = 27.33 (P) ppm; **IR** (ATR, cm^{-1}): ν = 2980 (C-H), 2889 (C-H), 1732 (C=O), 1437, 1200 (C-O), 1026 (ν_{\max}), 945, 698, 519; **MS** (ES^+): m/z (%): 298 ($\text{M}+\text{H}^+$, 100), 595 ($2\text{M}+\text{H}^+$, 55), 617 ($2\text{M}+\text{Na}^+$, 35); **EI-MS** m/z (rel. int.): 297 [M] (50), 266 (11), 206 (36), 182 (18), 152 (68), 124 (21), 114 (57), 91 (100), 55 (29); **HRMS** (ESI^+): m/z calculated: $\text{C}_{14}\text{H}_{21}\text{NO}_4\text{P}^+$ [$\text{M}+\text{H}^+$] 298.1203, found: 298.1206.

Methyl *N*-(ethoxy(pentyl)phosphoryl)-L-serinate **4g**

Diethyl pentylphosphonate **1a** (3.9 mmol, 1 equiv.), oxalyl chloride (1.32 equiv.) and L-serine methyl ester hydrochloride (5.9 mmol, 1.5 equiv.) were used as starting products for general procedure B. Together with the amino acid, 1.6 equiv. of triethylamine (6.2 mmol) was added to neutralize the hydrochloride salt. The crude product was purified using normal phase automated column chromatography (SiO_2 , 0% – 40% ($\text{EtOAc}:\text{iPA}$, 3:1 v:v) in hexane), after which, 650 mg of product **4g** was obtained as a yellowish oil with a yield of 59%.

Spectral data derived from the mixture of diastereomers (dr = 52/48).



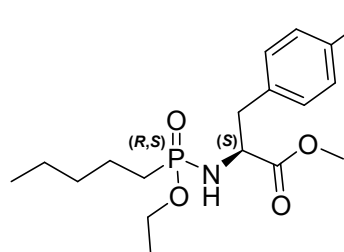
^1H NMR (400 MHz, CDCl_3): δ = 0.89 (t, J = 6.3 Hz, 3H, $\text{CH}_3\text{CH}_2\text{CH}_2$), 1.25 – 1.38 (m, 7H, $\text{CH}_3(\text{CH}_2)_2$ and $\text{CH}_3\text{CH}_2\text{O}$), 1.52 – 1.64 (m, 2H, $\text{CH}_2\text{CH}_2\text{P}$), 1.67 – 1.81 (m, 2H, CH_2P), 3.77 (s, 3H, COOCH_3), 3.80 – 3.90 (m, 3H, CH_2OH and NHCH), 3.95 – 4.17 (m, 3H, NHCH and $\text{CH}_3\text{CH}_2\text{O}$) ppm; **^{13}C NMR** (100.6 MHz, CDCl_3): δ = 13.9 (s, 2 x $\text{CH}_3\text{CH}_2\text{CH}_2$), 16.4 (d, J = 6.9 Hz, $\text{CH}_3\text{CH}_2\text{O}$), 16.4 (d, J

= 6.7 Hz, CH₃CH₂O), 22.0 (d, *J* = 5.1 Hz, CH₂CH₂P), 22.1 (d, *J* = 5.1 Hz, CH₂CH₂P), 22.3 (s, CH₃CH₂CH₂), 27.8 (d, *J* = 131.0 Hz, CH₂P), 27.8 (d, *J* = 131.0 Hz, CH₂P), 32.9 (d, *J* = 17.6 Hz, CH₃CH₂CH₂), 32.9 (d, *J* = 17.6 Hz, CH₃CH₂CH₂), 52.6 (s, COOCH₃), 56.4 (s, CHNH), 56.5 (s, CHNH), 60.2 (d, *J* = 6.9 Hz, CH₃CH₂O), 65.1 (app t, *J* = 3.3 Hz, CH₂OH), 65.3 (app t, *J* = 4.4 Hz, CH₂OH), 172.5 (s, COO) ppm; ³¹P NMR (161.9 MHz, CDCl₃): δ = 35.55 (P), 35.59 (P) ppm; IR (ATR, cm⁻¹): ν = 3289 (N-H & O-H), 2955 (C-H), 1746 (C=O), 1439, 1194 (C-O), 1032 (ν_{max}), 955; MS (ES⁺): *m/z* (%): 282 (M+H⁺, 100), 585 (2M+Na⁺, 18); EI-MS *m/z* (rel. int.): 281 [M] (1), 176 (100), 106 (11); HRMS (ESI⁺): *m/z* calculated: C₁₁H₂₅NO₅P⁺ [M+H⁺] 282.1465, found: 282.1468.

Methyl *N*-(ethoxy(pentyl)phosphoryl)-L-tyrosinate **4h**

Diethyl pentylphosphonate **1a** (3.7 mmol, 1 equiv.), oxalyl chloride (1.98 equiv.) and L-tyrosine methyl ester hydrochloride (5.5 mmol, 1.5 equiv.) were used as starting products for general procedure B. Together with the amino acid, 1.6 equiv. of triethylamine (5.9 mmol) was added to neutralize the hydrochloride salt. The crude product was purified using normal phase automated column chromatography (SiO₂, 50% - 75% ethyl acetate in hexane) after which, 805 mg of product **4h** was obtained as a viscous orange oil with a yield of 61%.

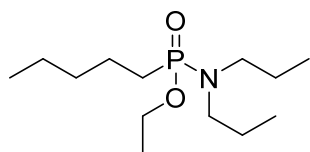
Spectral data derived from the mixture of diastereomers (dr = 54/46).



¹H NMR (400 MHz, CDCl₃): δ = 0.85, 0.86 (2 x t, *J* = 6.9 Hz, 3H, CH₃CH₂CH₂), 1.13, 1.19 (2 x t, *J* = 7.1 Hz, 3H, CH₃CH₂O), 1.22 – 1.80 (m, 8H, CH₃(CH₂)₄P), 2.65 – 2.92 (m, 2H, CH₂H_bCHN and NHCH), 2.97 – 3.19 (m, 1H, CH₂H_bCHN), 3.53 – 3.97 (m, 5H, CH₃CH₂O and COOCH₃), 4.04 – 4.28 (m, 1H, CHNH), 6.72 – 6.82 (m, 2H, 2 x HOC_qCH), 6.99 – 7.04 (m, 2H, 2 x CH₂C_qCH), 8.15 (br s, 1H, OH) ppm; ¹³C NMR (100.6 MHz, CDCl₃): δ = 14.0 (s, 2 x CH₃CH₂CH₂), 16.4, 16.5 (2 x d, *J* = 6.8 Hz, 2 x CH₃CH₂O), 22.0 (app t, *J* = 4.7 Hz, 2 x CH₂CH₂P), 22.3 (d, *J* = 3.7 Hz, 2 x CH₃CH₂CH₂), 27.6 (d, *J* = 130.6, CH₂P), 28.0 (d, *J* = 131.3, CH₂P), 32.9 (d, *J* = 17.6 Hz, CH₂CH₂CH₂P), 32.9 (d, *J* = 17.4 Hz, CH₂CH₂CH₂P), 40.3, 40.4 (2 x d, *J* = 5.1 Hz, 2 x CH₂CHNH), 52.4 (2 x s, 2 x COOCH₃), 55.5 (s, CHNH), 55.7 (s, CHNH), 59.9, 60.0 (2 x d, *J* = 11.8, 2 x CH₃CH₂O), 115.7 (s, 4 x HOC_qCH), 127.0, 127.1 (s, 2 x CH₂C_qCH), 130.5 (s, 4 x CH₂C_qCH), 156.4, 156.5 (s, 2 x HOC_q), 174.0 (d, *J* = 2.9 Hz, COO), 174.2 (d, *J* = 2.2 Hz, COO) ppm; ³¹P NMR (161.9 MHz, CDCl₃): δ = 34.51 (P), 34.89 (P) ppm; IR (ATR, cm⁻¹): ν = 3150 (N-H), 2953 (C-H), 2918 (C-H), 2851 (C-H), 1772 (C=O), 1518, 1454, 1375, 1169, 1028 (C-O, ν_{max}), 951; MS (ES⁺): *m/z* (%): 358 (M+H⁺, 100), 715 (2M+H⁺, 19), 737 (2M+Na⁺, 25); HRMS (ESI⁺): *m/z* calculated: C₁₇H₂₉NO₅P⁺ [M+H⁺] 358.1778, found: 358.1782.

Ethyl *N,N*-dipropyl-*P*-pentylphosphonamidate **4j**

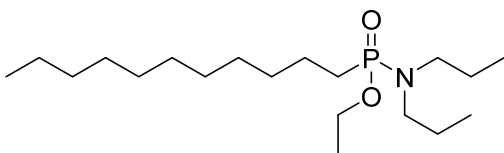
Diethyl pentylphosphonate **1a** (3.7 mmol, 1 equiv.), oxalyl chloride (2.64 equiv.) and distilled di-*n*-propylamine (5.5 mmol, 1.5 equiv.) were used as starting products for general procedure B. The crude product was purified using normal phase automatic flash chromatography (SiO₂, EtOAc:hexane 3:1 v:v, 5% Et₃N, gradient MeOH 0-7 v%) after which 600 mg of product **4j** was obtained as a pale yellow oil in a yield of 62%.



¹H NMR (400 MHz, CDCl₃): δ = 0.78 – 0.92 (m, 9H, CH₃CH₂CH₂CH₂ and 2 x CH₃CH₂CH₂N), 1.14 – 1.37 (m, 7H, CH₃(CH₂)₂CH₂ and CH₃CH₂O), 1.40 – 1.75 (m, 8H, CH₂CH₂P, CH₂P and 2 x CH₃CH₂CH₂N), 2.84 – 2.95 (m, 4H, 2 x CH₃CH₂CH₂N), 3.71 – 4.08 (m, 2H, CH₃CH₂O) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 11.4 (s, 2 x CH₃CH₂CH₂N), 14.0 (s, 2 x CH₃CH₂CH₂CH₂), 16.4 (d, *J* = 6.9 Hz, CH₃CH₂O), 22.1 – 22.5 (m, CH₂CH₂P, CH₃CH₂CH₂ and 2 x CH₃CH₂CH₂N), 26.9 (d, *J* = 131.2 Hz, CH₂P), 33.1 (d, *J* = 17.2 Hz, CH₃CH₂CH₂), 46.9 (d, *J* = 4.2 Hz, 2 x CH₃CH₂CH₂N), 58.9 (d, *J* = 6.7 Hz, CH₃CH₂O) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 36.38 (P) ppm; **IR** (ATR, cm⁻¹): ν = 2960 (C-H), 2873 (C-H), 1460, 1381, 1226, 1209, 1035 (ν_{max}), 947, 821, 729; **MS** (ES⁺): *m/z* (%): 264 (M+H⁺, 32), 527 (2M+H⁺, 100); **EI-MS** *m/z* (rel. int.): 263 [M] (3), 234 (100), 206 (16), 190 (9), 164 (11), 135 (22), 100 (9), 72 (7); **HRMS** (ESI⁺): *m/z* calculated: C₁₃H₃₁NO₂P⁺ [M+H⁺] 264.2087, found: 264.2093.

Ethyl *N,N*-dipropyl-*P*-undecylphosphonamidate **4k**

Diethyl undecylphosphonate **1b** (3.7 mmol, 1 equiv.), oxalyl chloride (2.64 equiv.) and distilled di-*n*-propylamine (5.5 mmol, 1.5 equiv.) were used as starting products for general procedure B. The crude product was purified using normal phase automatic flash chromatography (SiO₂, EtOAc:hexane 3:1 v:v, 5% Et₃N, gradient MeOH 0-7 v%) after which 650 mg of product **4k** was obtained as a pale yellow oil in a yield of 51 %.

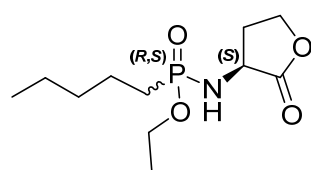


¹H NMR (400 MHz, CDCl₃): δ = 0.84 (t, *J* = 7.3 Hz, 9H, CH₃CH₂CH₂ and 2 x CH₃CH₂CH₂N), 1.15 – 1.39 (m, 19H, CH₃(CH₂)₈ and CH₃CH₂O), 1.40 – 1.74 (m, 8H, CH₂CH₂P, CH₂P and 2 x CH₃CH₂CH₂N), 2.82 – 2.96 (m, 4H, 2 x CH₃CH₂CH₂N), 3.68 – 4.14 (m, 2H, CH₃CH₂O) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 11.4 (s, 2 x CH₃CH₂CH₂N), 14.2 (s, CH₃CH₂CH₂), 16.4 (d, *J* = 6.9 Hz, CH₃CH₂O), 22.2 (d, *J* = 1.8 Hz, 2 x CH₃CH₂CH₂N), 22.5 (d, *J* = 4.3 Hz, CH₂CH₂P), 22.8 (s, CH₃CH₂CH₂), 26.9 (d, *J* = 131.3 Hz, CH₂P), 29.3, 29.4, 29.5, 29.7 (s, CH₃CH₂CH₂(CH₂)₅), 31.0 (d, *J* = 17.2 Hz, CH₂(CH₂)₂P), 32.0 (s, CH₃CH₂CH₂), 46.9 (d, *J* = 4.1 Hz, 2 x CH₃CH₂CH₂N), 58.9 (d, *J* = 6.7 Hz, CH₃CH₂O) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 36.34 (P) ppm; **IR** (ATR, cm⁻¹): ν = 2959 (C-H), 2924 (C-H), 2855 (C-H), 1458, 1227, 1036 (ν_{max}), 1016, 947, 729; **MS** (ES⁺): *m/z* (%): 348 (M+H⁺, 20), 695 (2M+H⁺, 100); **EI-MS** *m/z* (rel. int.): 347 [M] (2), 318 (100), 290 (10), 274 (7), 247 (9), 219 (5), 164 (7), 136 (9), 100 (11), 72 (5); **HRMS** (ESI⁺): *m/z* calculated: C₁₉H₄₃NO₂P⁺ [M+H⁺] 348.3026, found: 348.3032.

Ethyl *P*-pentyl-*N*-((*S*)-2-oxotetrahydrofuran-3-yl)phosphonamidate **6a**

Diethyl pentylphosphonate **1a** (3.7 mmol, 1 equiv.), oxalyl chloride (1.32 equiv.) and L-homoserine lactone hydrobromide (5.5 mmol, 1.5 equiv.) were used as starting products for general procedure B. Together with the amino acid, 1.6 equiv. of triethylamine (5.9 mmol) was added to neutralize the hydrobromide salt. The crude product was purified using normal phase automated column chromatography (SiO₂, EtOAc:hexane 3:1 v:v, gradient MeOH 0-7 v%) after which, 830 mg of product **6a** was obtained as a yellowish oil with a yield of 81%.

Spectral data derived from the mixture of diastereomers (dr = 50/50).

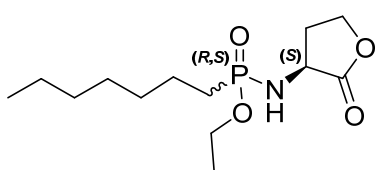


¹H NMR (400 MHz, CDCl₃): δ = 0.88 (t, *J* = 6.5 Hz, 3H, CH₃CH₂CH₂), 1.22 - 1.41 (m, 7H, CH₃(CH₂)₂ and CH₃CH₂O), 1.52 - 1.66 (m, 2H, CH₂CH₂P), 1.68 - 1.85 (m, 2H, CH₂P), 2.04 - 2.21 (m, 1H, CH_aH_bCHN), 2.64 - 2.75 (m, 1H, CH_aH_bCHN), 2.96 - 3.05 (m, 1H, CHNH), 3.98 - 4.29 (m, 4H, CHN, CH₃CH₂O and CH_aH_bOC=O), 4.39 (t, *J* = 8.9 Hz, 1H, CH_aH_bOC=O) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 14.0 (s, CH₃CH₂CH₂), 16.4 (app. t, *J* = 5.8 Hz, CH₃CH₂O), 22.1 (d, *J* = 10.3 Hz, CH₂CH₂P), 22.1 (d, *J* = 10.3 Hz, CH₂CH₂P), 22.2 (s, CH₃CH₂CH₂), 28.3 (d, *J* = 131 Hz, CH₂P), 28.4 (d, *J* = 128 Hz, CH₂P), 32.6 (s, CH₂CHN), 32.8 (s, CH₂CHN), 32.8 (d, *J* = 16.9 Hz, CH₃CH₂CH₂), 32.9 (d, *J* = 16.9 Hz, CH₃CH₂CH₂), 50.3 (s, CHNH), 50.6 (s, CHNH), 60.0 (d, *J* = 6.6 Hz, CH₃CH₂O), 60.1 (d, *J* = 6.6 Hz, CH₃CH₂O), 65.2 (s, CH₂OC=O), 65.3 (s, CH₂OC=O), 176.6 (app. t, *J* = 7 Hz, C=O) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 34.59 (P), 35.01 (P) ppm; **IR** (ATR, cm⁻¹): ν = 3180 (N-H), 2929 (C-H), 1776 (C=O), 1452, 1375, 1199, 1149 (C-O, ν_{max}), 1022, 948, 758; **MS** (ES⁺): *m/z* (%): 264 (M+H⁺, 100), 527 (2M+H⁺, 17), 549 (2M+Na⁺, 15); **EI-MS** *m/z* (rel. int.): 263 [M] (53), 190 (99), 181 (40), 164 (25), 162 (30), 135 (38), 108 (25), 57 (26), 56 (10); **HRMS** (ESI⁺): *m/z* calculated: C₁₁H₂₃NO₄P⁺ [M+H⁺] 264.1359, found: 264.1351.

Ethyl *P*-heptyl-*N*-((*S*)-2-oxotetrahydrofuran-3-yl)phosphonamidate **6b**

Diethyl heptylphosphonate **1e** (8.8 mmol, 1 equiv.), oxalyl chloride (1.32 equiv.) and L-homoserine lactone hydrobromide (13.0 mmol, 1.5 equiv.) were used as starting products for general procedure B. Together with the amino acid, 1.6 equiv. of triethylamine (13.9 mmol) was added to neutralize the hydrobromide salt. The crude product was purified using normal phase automated column chromatography (SiO₂, EtOAc:hexane 3:1 v:v, gradient MeOH 0-7 v%) after which, 880 mg of product **6b** was obtained as a yellowish oil with a yield of 35%.

Spectral data derived from the mixture of diastereomers (dr = 41/59).

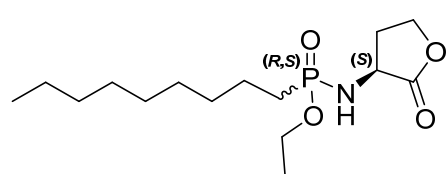


¹H NMR (400 MHz, CDCl₃): δ = 0.88 (t, *J* = 6.5 Hz, 3H, CH₃CH₂CH₂), 1.22 - 1.41 (m, 11H, CH₃(CH₂)₄ and CH₃CH₂O), 1.52 - 1.66 (m, 2H, CH₂CH₂P), 1.68 - 1.85 (m, 2H, CH₂P), 2.04 - 2.21 (m, 1H, CH_aH_bCHN), 2.64 - 2.75 (m, 1H, CH_aH_bCHN), 2.89 - 2.97 (m, 1H, CHNH), 3.98 - 4.29 (m, 4H, CHN, CH₃CH₂O and CH_aH_bOC=O), 4.39 (t, *J* = 8.9 Hz, 1H, CH_aH_bOC=O) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 14.0 (s, CH₃CH₂CH₂), 16.4 (app. t, *J* = 5.8 Hz, CH₃CH₂O), 22.4 (d, *J* = 9.7 Hz, CH₂CH₂P), 22.4 (d, *J* = 9.7 Hz, CH₂CH₂P), 22.6 (s, CH₃CH₂CH₂), 28.4 (d, *J* = 131 Hz, CH₂P), 28.4 (d, *J* = 128 Hz, CH₂P), 28.8 (s, CH₃(CH₂)₂CH₂), 30.6 (d, *J* = 17.6 Hz, CH₂(CH₂)₂P), 30.7 (d, *J* = 17.6 Hz, CH₂(CH₂)₂P), 31.6 (s, CH₃CH₂CH₂), 32.6 (s, CH₂CHN), 32.9 (s, CH₂CHN), 50.3 (s, CHN), 50.6 (s, CHN), 59.9 (d, *J* = 6.6 Hz, CH₃CH₂O), 60.1 (d, *J* = 6.6 Hz, CH₃CH₂O), 65.2 (s, CH₂OC=O), 65.3 (s, CH₂OC=O), 176.6 (app. t, *J* = 7.2 Hz, C=O) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 34.64 (P), 35.04 (P) ppm; **IR** (ATR, cm⁻¹): ν = 3184 (N-H), 2932 (C-H), 2858 (C-H), 1778 (C=O), 1454, 1371, 1199, 1149 (C-O, ν_{max}), 1037, 1001, 948, 816; **MS** (ES⁺): *m/z* (%): 292 (M+H⁺, 100), 583 (2M+H⁺, 17), 605 (2M+Na⁺, 15); **EI-MS** *m/z* (rel. int.): 291 [M] (59), 218 (89), 209 (43), 207 (31), 176 (31), 163 (22), 125 (24), 108 (24), 57 (38), 56 (100); **HRMS** (ESI⁺): *m/z* calculated: C₁₃H₂₇NO₄P⁺ [M+H⁺] 292.1672, found: 292.1683.

Ethyl *P*-nonyl-*N*-((*S*)-2-oxotetrahydrofuran-3-yl)phosphonamidate **6c**

Diethyl nonylphosphonate **1f** (8.8 mmol, 1 equiv.), oxalyl chloride (1.32 equiv.) and L-homoserine lactone hydrobromide (13.0 mmol, 1.5 equiv.) were used as starting products for general procedure B. Together with the amino acid, 1.6 equiv. of triethylamine (13.9 mmol) was added to neutralize the hydrobromide salt. The crude product was purified using normal phase automated column chromatography (SiO₂, EtOAc:hexane 3:1 v:v, gradient MeOH 0-7 v%) after which, 680 mg of product **6c** was obtained as a yellowish oil with a yield of 24%.

Spectral data derived from the mixture of diastereomers (dr= 48/52).

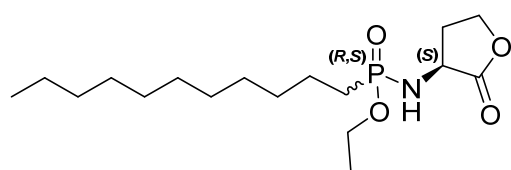


¹H NMR (400 MHz, CDCl₃): δ = 0.88 (t, *J* = 6.7 Hz, 3H, CH₃CH₂CH₂), 1.22 - 1.42 (m, 15H, CH₃(CH₂)₆ and CH₃CH₂O), 1.54 - 1.68 (m, 2H, CH₂CH₂P), 1.70 - 1.85 (m, 2H, CH₂P), 2.05 - 2.22 (m, 1H, CH_aH_bCHN), 2.66 - 2.76 (m, 1H, CH_aH_bCHN), 2.78 - 2.83 (m, 1H, CHNH), 3.99 - 4.29 (m, 4H, CHN, CH₃CH₂O and CH_aH_bOC=O), 4.40 (t, *J* = 9 Hz, 1H, CH_aH_bOC=O) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): 14.1 (s, CH₃CH₂CH₂), 16.4 (app. t, *J* = 5.8 Hz, CH₃CH₂O), 22.4 (d, *J* = 9.5 Hz, CH₂CH₂P), 22.4 (d, *J* = 10 Hz, CH₂CH₂P), 22.7 (s, CH₃CH₂CH₂), 28.4 (d, *J* = 131 Hz, CH₂P), 28.4 (d, *J* = 128 Hz, CH₂P), 29.2, 29.3, 29.4 (s, CH₃CH₂CH₂(CH₂)₃), 30.7 (d, *J* = 17.6 Hz, CH₂(CH₂)₂P), 30.7 (d, *J* = 17.6 Hz, CH₂(CH₂)₂P), 31.9 (s, CH₃CH₂CH₂), 32.6 (s, CH₂CHN), 32.9 (s, CH₂CHN), 50.3 (s, CHN), 50.6 (s, CHN), 59.9 (d, *J* = 6.6 Hz, CH₃CH₂O), 60.1 (d, *J* = 7.0 Hz, CH₃CH₂O), 65.2 (s, CH₂OC=O), 65.3 (s, CH₂OC=O), 176.6 (app. t, *J* = 6.2 Hz, C=O); **³¹P NMR** (161.9 MHz, CDCl₃): δ = 34.65 (P), 35.10 (P) ppm; **IR** (ATR, cm⁻¹): ν = 3201 (N-H), 2926 (C-H), 1780 (C=O), 1600, 1448, 1219, 1151 (C-O), 1026 (ν_{max}), 947, 692; **MS** (ES⁺): *m/z* (%): 320 (M+H⁺, 100), 639 (2M+H⁺, 12), 661 (2M+Na⁺, 12); **EI-MS** *m/z* (rel. int.): 319 [M] (68), 246 (81), 237 (39), 220 (26), 207 (37), 176 (30), 125 (27), 108 (23), 57 (31), 56 (100); **HRMS** (ESI⁺): *m/z* calculated: C₁₅H₃₁NO₄P⁺ [M+H⁺] 320.1985, found: 320.1983.

Ethyl *P*-undecyl-*N*-((*S*)-2-oxotetrahydrofuran-3-yl)phosphonamidate **6d**

Diethyl undecylphosphonate **1b** (8.8 mmol, 1 equiv.), oxalyl chloride (1.32 equiv.) and L-homoserine lactone hydrobromide (13.0 mmol, 1.5 equiv.) were used as starting products for general procedure B. Together with the amino acid, 1.6 equiv. of triethylamine (13.9 mmol) was added to neutralize the hydrobromide salt. The crude product was purified using normal phase automated column chromatography (SiO₂, EtOAc:hexane 3:1 v:v, gradient MeOH 0-7 v%) after which, 890 mg of product **6d** was obtained as a yellowish oil with a yield of 29%.

Spectral data derived from the mixture of diastereomers (dr = 50/50).



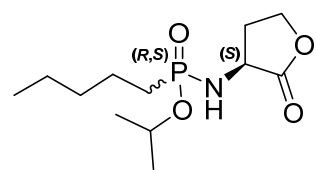
¹H NMR (400 MHz, CDCl₃): δ = 0.88 (t, *J* = 6.8 Hz, 3H, CH₃CH₂CH₂), 1.21 - 1.40 (m, 19H, CH₃(CH₂)₈ and CH₃CH₂O), 1.55 - 1.65 (m, 2H, CH₂CH₂P), 1.70 - 1.83 (m, 2H, CH₂P), 2.04 - 2.21 (m, 1H, CH_aH_bCHN), 2.66 - 2.75 (m, 1H, CH_aH_bCHN), 2.83 - 2.88 (m, 1H, CHNH), 4.00 - 4.29 (m, 4H, CHN, CH₃CH₂O and CH_aH_bOC=O), 4.40 (t, *J* = 8.8 Hz, 1H, CH_aH_bOC=O) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 14.1 (s,

$\underline{\text{CH}_3\text{CH}_2\text{CH}_2}$), 16.4 (app. t, $J = 6.2$ Hz, $\underline{\text{CH}_3\text{CH}_2\text{O}}$), 22.5 (d, $J = 9.5$ Hz, $\underline{\text{CH}_2\text{CH}_2\text{P}}$), 22.5 (d, $J = 9.5$ Hz, $\underline{\text{CH}_2\text{CH}_2\text{P}}$), 22.7 (s, $\text{CH}_3\underline{\text{CH}_2\text{CH}_2}$), 28.5 (d, $J = 131$ Hz, $\underline{\text{CH}_2\text{P}}$), 28.5 (d, $J = 128$ Hz, $\underline{\text{CH}_2\text{P}}$), 29.2, 29.3, 29.4, 29.6 (s, $\text{CH}_3\text{CH}_2\text{CH}_2(\underline{\text{CH}_2})_5$), 30.7 (d, $J = 16.8$ Hz, $\underline{\text{CH}_2(\text{CH}_2)_2\text{P}}$), 30.7 (d, $J = 16.8$ Hz, $\underline{\text{CH}_2(\text{CH}_2)_2\text{P}}$), 31.9 (s, $\text{CH}_3\text{CH}_2\underline{\text{CH}_2}$), 32.7 (s, $\underline{\text{CH}_2\text{CHN}}$), 32.9 (s, $\underline{\text{CH}_2\text{CHN}}$), 50.3 (s, $\underline{\text{CHN}}$), 50.6 (s, $\underline{\text{CHN}}$), 60.0 (d, $J = 18$ Hz, $\text{CH}_3\underline{\text{CH}_2\text{O}}$), 60.0 (d, $J = 18$ Hz, $\text{CH}_3\underline{\text{CH}_2\text{O}}$), 65.2 (s, $\underline{\text{CH}_2\text{OC=O}}$), 65.3 (s, $\underline{\text{CH}_2\text{OC=O}}$), 176.7 (app. t, $J = 6.0$ Hz, $\underline{\text{C=O}}$) ppm; ^{31}P NMR (161.9 MHz, CDCl_3): $\delta = 34.61$ (P), 35.07 (P) ppm; IR (ATR, cm^{-1}): $\nu = 3142$ (N-H), 2916 (C-H), 1848 (C-H), 1778 (C=O), 1465, 1381, 1163, 1031 (ν_{max}), 954; MS (ES $^+$): m/z (%): 348 ($\text{M}+\text{H}^+$, 100), 695 ($2\text{M}+\text{H}^+$, 10), 717 ($2\text{M}+\text{Na}^+$, 15); EI-MS m/z (rel. int.): 347 [M] (100), 274 (82), 265 (36), 220 (26), 207 (50), 176 (29), 125 (26), 57 (29), 56 (83); HRMS (ESI $^+$): m/z calculated: $\text{C}_{17}\text{H}_{35}\text{NO}_4\text{P}^+$ [$\text{M}+\text{H}^+$] 348.2298, found: 348.2291.

Isopropyl *P*-pentyl-*N*-((*S*)-2-oxotetrahydrofuran-3-yl)phosphonamidate **7a**

Diisopropyl pentylphosphonate **1c** (3.9 mmol, 1 equiv.), oxalyl chloride (1.32 equiv.) and L-homoserine lactone hydrobromide (5.9 mmol, 1.5 equiv.) were used as starting products for general procedure B. Together with the amino acid, 1.6 equiv. of triethylamine (6.2 mmol) was added to neutralize the hydrobromide salt. The crude product was purified using normal phase automated column chromatography (SiO_2 , 0-75 v% (EtOAc + 5v% Et_3N) in hexane), after which, 750 mg of product **7a** was obtained as an orange oil with a yield of 69%.

Spectral data derived from the mixture of diastereomers (dr = 52/48).



^1H NMR (400 MHz, CDCl_3): $\delta = 0.90$ (t, $J = 6.9$ Hz, 3H, $\underline{\text{CH}_3\text{CH}_2\text{CH}_2}$), 1.20 – 1.43 (m, 10H, $\text{CH}_3(\underline{\text{CH}_2})_2$ and $(\underline{\text{CH}_2})_2\text{CHO}$), 1.51 – 1.85 (m, 4H, $\underline{\text{CH}_2\text{CH}_2\text{P}}$ and $\underline{\text{CH}_2\text{P}}$), 2.08 – 2.23 (m, 1H, $\underline{\text{CH}_a\text{H}_b\text{CHN}}$), 2.64 – 2.78 (m, 1H, $\underline{\text{CH}_a\text{H}_b\text{CHN}}$), 2.89 (t, $J = 8.8$ Hz, 1H, $\underline{\text{CHNH}}$), 4.07 – 4.33 (m, 2H, $\underline{\text{CHN}}$ and $\underline{\text{CH}_a\text{H}_b\text{OC=O}}$), 4.39 (t, $J = 8.9$ Hz, 1H, $\underline{\text{CH}_a\text{H}_b\text{OC=O}}$), 4.65 – 4.86 (m, 1H, $\underline{\text{CHO}}$) ppm; ^{13}C NMR (100.6 MHz, CDCl_3):

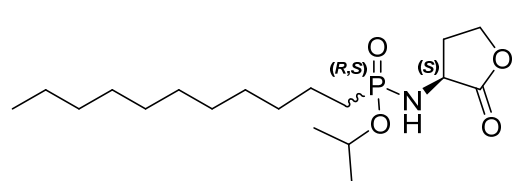
$\delta = 14.0$ (s, $\underline{\text{CH}_3\text{CH}_2\text{CH}_2}$), 22.2 (d, $J = 4.4$ Hz, $\underline{\text{CH}_2\text{CH}_2\text{P}}$), 22.3 (d, $J = 4.4$ Hz, $\underline{\text{CH}_2\text{CH}_2\text{P}}$), 22.3 (s, $\text{CH}_3\underline{\text{CH}_2\text{CH}_2}$), 24.3 (d, $J = 4.8$ Hz, $2 \times \underline{\text{CH}_3\text{CHO}}$), 24.5 (d, $J = 3.7$ Hz, $2 \times \underline{\text{CH}_3\text{CHO}}$), 29.0 (d, $J = 129.1$ Hz, $\underline{\text{CH}_2\text{P}}$), 29.1 (d, $J = 132.1$ Hz, $\underline{\text{CH}_2\text{P}}$), 32.8 (d, $J = 2.2$ Hz, $\underline{\text{CH}_2\text{CHN}}$), 32.9 (d, $J = 16.9$ Hz, $\text{CH}_3\text{CH}_2\underline{\text{CH}_2}$), 33.0 (d, $J = 16.9$ Hz, $\text{CH}_3\text{CH}_2\underline{\text{CH}_2}$), 33.1 (d, $J = 1.5$ Hz, $\underline{\text{CH}_2\text{CHN}}$), 50.5 (s, $\underline{\text{CHN}}$), 50.8 (s, $\underline{\text{CHN}}$), 65.2 (s, $\underline{\text{CH}_2\text{OC=O}}$), 65.4 (s, $\underline{\text{CH}_2\text{OC=O}}$), 69.0 (d, $J = 14.7$ Hz, $\text{CH}_3\underline{\text{CH}_2\text{O}}$), 69.0 (d, $J = 14.7$ Hz, $\text{CH}_3\underline{\text{CH}_2\text{O}}$), 176.8 (d, $J = 7.0$ Hz, $\underline{\text{C=O}}$) ppm; ^{31}P NMR (161.9 MHz, CDCl_3): $\delta = 33.46$ (P), 33.99 (P) ppm; IR (ATR, cm^{-1}): $\nu = 3173$ (N-H), 2932 (C-H), 1775 (C=O), 1466, 1373, 1199, 1149 (C-O), 980 (ν_{max}); MS (ES $^+$): m/z (%): 278 ($\text{M}+\text{H}^+$, 100), 555 ($2\text{M}+\text{H}^+$, 5), 577 ($2\text{M}+\text{Na}^+$, 20); EI-MS m/z (rel. int.): 277 [M] (2), 235 (72), 218 (16), 191 (29), 176 (9), 160 (100), 135 (26), 121 (14), 101 (12), 71 (14), 56 (33), 41 (33); HRMS (ESI $^+$): m/z calculated: $\text{C}_{12}\text{H}_{25}\text{NO}_4\text{P}^+$ [$\text{M}+\text{H}^+$] 278.1516, found: 278.1520.

Isopropyl *P*-undecyl-*N*-((*S*)-2-oxotetrahydrofuran-3-yl)phosphonamidate **7b**

Diisopropyl undecylphosphonate **1g** (8.8 mmol, 1 equiv.), oxalyl chloride (1.32 equiv.) and L-homoserine lactone hydrobromide (13.0 mmol, 1.5 equiv.) were used as starting products for general procedure B. Together with the amino acid, 1.6 equiv. of triethylamine (13.9 mmol) was added to neutralize the

hydrobromide salt. The crude product was purified using normal phase automated column chromatography (SiO₂, EtOAc:hexane 3:1 v:v, gradient MeOH 0-7 v%) after which, 810 mg of product **7b** was obtained as a yellowish oil with a yield of 25%.

Spectral data derived from the mixture of diastereomers (dr = 45/55).



¹H NMR (400 MHz, CDCl₃): δ = 0.88 (t, *J* = 6.8 Hz, 3H, CH₃CH₂CH₂), 1.19 - 1.41 (m, 22H, CH₃(CH₂)₈ and CH(CH₃)₂), 1.53 - 1.65 (m, 2H, CH₂CH₂P), 1.66 - 1.82 (m, 2H, CH₂P), 2.07 - 2.21 (m, 1H, CH_aH_bCHN), 2.67 - 2.76 (m, 1H, CH_aH_bCHN), 2.79 - 2.84 (m, 1H, CHNH), 4.14 - 4.31 (m, 2H, CH₂OC=O),

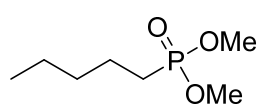
4.39 (t, *J* = 9.0 Hz, 1H, CHN), 4.68 - 4.84 (m, 1H, CH(CH₃)₂) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 14.2 (s, CH₃CH₂CH₂), 22.5 (d, *J* = 8.8 Hz, CH₂CH₂P), 22.5 (d, *J* = 8.8 Hz, CH₂CH₂P), 22.8 (s, CH₃CH₂CH₂), 24.2 (d, *J* = 9.5 Hz, 2 x CH₃CH), 24.3 (d, *J* = 9.5 Hz, 2 x CH₃CH), 29.0 (d, *J* = 132.0 Hz, CH₂P), 29.0 (d, *J* = 132.0 Hz, CH₂P), 29.2, 29.3, 29.4, 29.6 (s, CH₃CH₂CH₂(CH₂)₅), 30.7 (d, *J* = 16.9 Hz, CH₂(CH₂)₂P), 30.7 (d, *J* = 17.6 Hz, CH₂(CH₂)₂P), 32.0 (s, CH₃CH₂CH₂), 32.7 (s, CH₂CHN), 33.0 (s, CH₂CHN), 50.4 (s, CHN), 50.7 (s, CHN), 65.2 (s, CH₂OC=O), 65.3 (s, CH₂OC=O), 68.9 (d, *J* = 14.7 Hz, (CH₃)₂CH), 68.9 (d, *J* = 14.7 Hz, (CH₃)₂CH), 176.6 (d, *J* = 7.6 Hz, C=O), 176.6 (d, *J* = 8.1 Hz, C=O) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 33.47 (P), 34.0 (P) ppm; **IR** (ATR, cm⁻¹): ν = 3149 (N-H), 2916 (C-H), 2848 (C-H), 1780 (C=O), 1475, 1182 (C-O), 1031 (ν_{max}), 991, 962, 794, 767; **MS** (ES⁺): *m/z* (%): 362 (M+H⁺, 100), 723 (2M+H⁺, 20), 745 (2M+Na⁺, 10); **EI-MS** *m/z* (rel. int.): 361 [M] (6), 319 (100), 246 (67), 180 (24), 102 (24), 56 (74), 41 (60); **HRMS** (ESI⁺): *m/z* calculated: C₁₈H₃₇NO₄P⁺ [M+H⁺] 362.2455, found: 362.2454.

Synthesis of dimethyl alkylphosphonates **11a** – **11b**

The synthesis of dimethyl alkylphosphonates **11** was adapted from Delorme et al.¹² To a suspension of washed sodium hydride (60 % suspension in mineral oil, 1079.6 mg, 45 mmol, 1.8 equiv.) in dry THF (100 mL), dimethyl phosphite **10** (4814.7 mg, 4012 μL, 43.8 mmol, 1.75 equiv.) was added dropwise over a period of 10 min at room temperature under a nitrogen atmosphere. After the addition was complete, the reaction mixture was stirred at 0 °C for 1 additional hour. The corresponding alkyl bromide (25 mmol, 1 equiv.) was then added and the reaction mixture was refluxed overnight. The solvent was removed and 100 mL diethyl ether was added. The solution was filtered to remove the salts, washed 3 times with water, dried over MgSO₄ and solvent was evaporated. The resulting product **11** was used without further purification.

Dimethyl pentylphosphonate **11a**

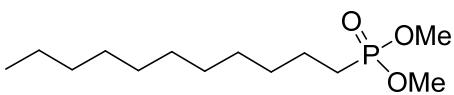
For this product, 1-bromopentane (25 mmol) was used as starting product. Finally, 1230 mg dimethyl pentylphosphonate **11a** was collected as a transparent oil with a yield of 27%. The ¹H, ¹³C and ³¹P NMR data were in agreement with those reported by Antczak and Montchamp.¹³



¹H NMR (400 MHz, CDCl₃): δ = 0.90 (t, J = 7.0 Hz, 3H, CH₃CH₂CH₂), 1.23 – 1.42 (m, 4H, CH₃(CH₂)₂), 1.53 – 1.80 (m, 4H, CH₂CH₂P and CH₂P), 3.74 (d, J = 10.7 Hz, 6H, 2 x OCH₃) ppm; **¹³C NMR** (100.5 MHz, CDCl₃): δ = 13.8 (s, CH₃CH₂CH₂), 22.0 (d, J = 5.4 Hz, CH₂CH₂P), 22.2 (s, CH₃CH₂CH₂), 24.7 (d, J = 140.1 Hz, CH₂P), 32.8 (d, J = 16.9 Hz, CH₂(CH₂)₂P), 52.3 (d, J = 6.6 Hz, 2 x OCH₃) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 35.21 (P) ppm; **IR** (ATR, cm⁻¹): ν = 2953 (C-H), 2927 (C-H), 2853 (C-H), 1468, 1348, 1240, 1055, 1024 (ν_{\max}), 837; **MS** (ES⁺): m/z (%): 181 (M+H⁺, 100), 361 (2M+H⁺, 59); **EI-MS** m/z (rel. int.): 180 [M] (1), 179 (2), 165 (6), 152 (37), 137 (20), 124 (100), 110 (18), 94 (15), 79 (9).

Dimethyl undecylphosphonate **11b**

For this product, 1-bromoundecane was used as starting product. Finally, 2.1 g dimethyl undecylphosphonate **11b** was collected as a transparent oil with a yield of 40%. The ¹H, ¹³C and ³¹P NMR data were in agreement with those reported by Li and coworkers.¹⁴



¹H NMR (400 MHz, CDCl₃): δ = 0.88 (t, J = 7.5 Hz, 3H, CH₃CH₂CH₂), 1.21 - 1.41 (m, 16H, CH₃(CH₂)₈), 1.52 – 1.66 (m, 2H, CH₂CH₂P), 1.66 – 1.80 (m, 2H, CH₂P), 3.73 (d, J = 10.7 Hz, 6H, 2 x OCH₃) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 14.2 (s, CH₃CH₂CH₂), 22.4 (d, J = 5.3 Hz, CH₂CH₂P), 22.8 (s, CH₃CH₂CH₂), 24.8 (d, J = 140.3 Hz, CH₂P), 29.2, 29.2, 29.5, 29.5, 29.7 (s, CH₃CH₂CH₂(CH₂)₅), 30.7 (d, J = 16.8 Hz, CH₂(CH₂)₂P), 32.0 (s, CH₃CH₂CH₂), 52.4 (d, J = 6.6 Hz, 2 x OCH₃) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 35.25 (P) ppm; **IR** (ATR, cm⁻¹): ν = 2922 (C-H), 2853 (C-H), 1460, 1244, 1057, 1026 (ν_{\max}), 810; **MS** (ES⁺): m/z (%): 265 (M+H⁺, 100), 529 (2M+H⁺, 99); **EI-MS** m/z (rel. int.): 264 [M] (2), 235 (5), 221 (6), 207 (8), 193 (9), 179 (15), 165 (15), 152 (18), 137 (33), 124 (100), 110 (43), 94 (39), 79 (22).

Synthesis of methyl *P*-alkyl-*N*-((*S*)-2-oxotetrahydrofuran-3-yl) phosphonamidates **8a** – **8b**

Under nitrogen atmosphere, oxalyl chloride (2.64 equiv., 9.7 mmol) is added dropwise to a cooled solution (0 °C) of the corresponding dimethyl *P*-alkylphosphonate **11** (1 equiv., 3.7 mmol) and 3 drops of DMF in 20 mL dry DCM. This solution is stirred for 16 hours and allowed to warm to room temperature and the conversion is monitored via ³¹P NMR. After completion of the reaction, solvent is evaporated under reduced pressure to yield a crude mixture of phosphonochloridate. Due to the instability of the compound, the crude compound is immediately used in subsequent reactions.

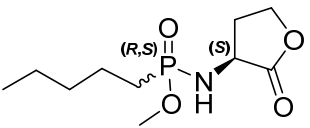
The corresponding phosphonochloridate and triethylamine (1.1 equiv., 4.0 mmol) were dissolved in 30 mL dry THF under nitrogen atmosphere and left stirring for 30 min at room temperature, after which the reaction mixture was analysed using ³¹P NMR. Triethylamine (1.6 equiv., 5.9 mmol) and L-homoserine lactone hydrobromide (1.5 equiv., 5.5 mmol) was dissolved in 30 mL dry ACN under nitrogen atmosphere, while stirring at room temperature. The solution containing the phosphonochloridate was added dropwise to the amine solution at room temperature and stirred for 1 hour (monitored with ³¹P NMR).

Subsequently, the solids were removed via filtration, after addition of 60 mL diethyl ether and the solvent was evaporated under reduced pressure. The remaining mixture was purified via normal phase automatic flash chromatography.

Methyl *P*-pentyl-*N*-((*S*)-2-oxotetrahydrofuran-3-yl)phosphonamidate **8a**

Dimethyl pentylphosphonate **11a** was used as starting product on a scale of 2.1 mmol. The crude product was purified using normal phase automated column chromatography (SiO₂, EtOAc:hexane 3:1 v:v, gradient MeOH 0-10 v%) after which, 75 mg of product **8a** was obtained as an orange oil with a yield of 15%.

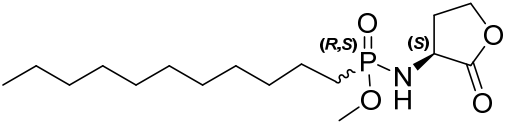
Spectral data derived from the mixture of diastereomers (dr = 50/50).

 **¹H NMR** (400 MHz, CDCl₃): δ = 0.90 (t, *J* = 7.2 Hz, 3H, CH₃CH₂CH₂), 1.30 – 1.40 (m, 4H, CH₃(CH₂)₂), 1.55 – 1.70 (m, 2H, CH₂CH₂P), 1.70 – 1.93 (m, 2H, CH₂P), 2.09 – 2.28 (m, 1H, CH_aH_bCHN), 2.65 – 2.78 (m, 1H, CH_aH_bCHN), 2.79 – 2.89 (m, 1H, CHNH), 3.69, 3.74 (2 x d, *J* = 11.1 Hz, 3H, CH₃O), 4.08 – 4.34 (m, 2H, CHN and CH_aH_bOC=O), 4.40 (t, *J* = 9.0 Hz, 1H, CH_aH_bOC=O) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 14.0 (s, CH₃CH₂CH₂), 22.1 (d, *J* = 5.0 Hz, CH₂CH₂P), 22.2 (d, *J* = 5.0 Hz, CH₂CH₂P), 22.3 (s, CH₃CH₂CH₂), 28.1 (d, *J* = 132.1 Hz, CH₂P), 28.2 (d, *J* = 128.5 Hz, CH₂P), 32.7 (s, 2 x CH₂CHN), 32.9 (d, *J* = 17.2 Hz, CH₃CH₂CH₂), 33.0 (d, *J* = 17.0 Hz, CH₃CH₂CH₂), 50.4 (s, CHNH), 50.6 (d, *J* = 7.3 Hz, CH₃O), 50.8 (s, CHNH), 50.8 (d, *J* = 7.3 Hz, CH₃O), 65.3 (s, CH₂OC=O), 65.4 (s, CH₂OC=O), 176.7 (s, C=O) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 34.51 (P), 34.89 (P) ppm; **IR** (ATR, cm⁻¹): ν = 3169 (N-H), 2953 (C-H), 2930 (C-H), 2872 (C-H), 1776 (C=O), 1452, 1377, 1152 (C-O, ν_{max}), 1024, 949; **MS** (ES⁺, 70 eV): *m/z* (%): 250 (M+H⁺, 100), 521 (2M+Na⁺, 22); **EI-MS** *m/z* (rel. int.): 249 [M] (31), 207 (22), 193 (13), 176 (76), 167 (38), 149 (33), 135 (22), 121 (13), 109 (27), 94 (31), 79 (56), 56 (100), 44 (51); **HRMS** (ESI⁺): *m/z* calculated: C₁₀H₂₀NO₄P⁺ [M+H⁺] 250.1203, found: 250.1206.

Methyl *P*-undecyl-*N*-((*S*)-2-oxotetrahydrofuran-3-yl)phosphonamidate **8b**

Dimethyl undecylphosphonate **11b** was used as starting product on a scale of 3.7 mmol. The crude product was purified using normal phase automated column chromatography (SiO₂, EtOAc:hexane 3:1 v:v, gradient MeOH 0-10 v%) after which, 500 mg of product **8b** was obtained as a yellow solid with a yield of 41%.

Spectral data derived from the mixture of diastereomers (dr = 51/49).

 **¹H NMR** (400 MHz, CDCl₃): δ = 0.88 (t, *J* = 6.9 Hz, 3H, CH₃CH₂CH₂), 1.18 – 1.46 (m, 16H, CH₃(CH₂)₈), 1.50 – 1.68 (m, 2H, CH₂CH₂P), 1.69 – 1.88 (m, 2H, CH₂P), 2.15 (app pd, *J* = 11.9, 8.6 Hz, 1H, CH_aH_bCHN), 2.65 – 2.78 (m, 1H, CH_aH_bCHN), 2.81 – 2.90 (m, 1H, CHNH), 3.69, 3.74 (2 x d, *J* = 11.1 Hz, 3H, CH₃O), 4.10 – 4.32 (m, 2H, CHN and CH_aH_bOC=O), 4.40 (t, *J* = 9.1 Hz, 1H, CH_aH_bOC=O) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 14.1 (s, CH₃CH₂CH₂), 22.5 (d, *J* = 9.5 Hz, CH₂CH₂P), 22.5 (d, *J* = 9.5 Hz, CH₂CH₂P), 22.7 (s, CH₃CH₂CH₂), 28.1 (d, *J* =

131.6 Hz, $\underline{\text{CH}_2\text{P}}$), 28.5 (d, $J = 128$ Hz, $\underline{\text{CH}_2\text{P}}$), 29.3, 29.4, 29.5, 29.7 (s, $\text{CH}_3\text{CH}_2\text{CH}_2(\underline{\text{CH}_2})_5$), 30.8 (d, $J = 16.9$ Hz, $\underline{\text{CH}_2(\text{CH}_2)_2\text{P}}$), 30.9 (d, $J = 17.6$ Hz, $\underline{\text{CH}_2(\text{CH}_2)_2\text{P}}$), 31.9 (s, $\text{CH}_3\text{CH}_2\underline{\text{CH}_2}$), 32.7 (s, $\underline{\text{CH}_2\text{CHN}}$), 33.0 (s, $\underline{\text{CH}_2\text{CHN}}$), 50.4 (s, $\underline{\text{CHNH}}$), 50.6 (d, $J = 7.3$ Hz, $\underline{\text{CH}_3\text{O}}$), 50.8 (s, $\underline{\text{CHNH}}$), 50.8 (d, $J = 6.9$ Hz, $\underline{\text{CH}_3\text{O}}$), 65.3 (s, $\underline{\text{CH}_2\text{OC=O}}$), 65.4 (s, $\underline{\text{CH}_2\text{OC=O}}$), 176.43 (d, $J = 7.7$ Hz, $\underline{\text{C=O}}$) ppm; ^{31}P NMR (161.9 MHz, CDCl_3): $\delta = 35.69$ ($\underline{\text{P}}$), 36.44 ($\underline{\text{P}}$) ppm; IR (ATR, cm^{-1}): $\nu = 3150$ (N-H), 2918 (C-H), 2851 (C-H), 1788 (C=O), 1773 (C=O), 1466, 1377, 1165 (ν_{max}), 1034, 951, 795; MS (ES^+): m/z (%): 334 ($\text{M}+\text{H}^+$, 100), 667 ($2\text{M}+\text{H}^+$, 11), 689 ($2\text{M}+\text{Na}^+$, 21); EI-MS m/z (rel. int.): 333 [M] (22), 281 (40), 260 (24), 251 (15), 207 (100), 193 (13), 162 (11), 134 (10), 109 (11), 79 (13), 56 (26), 44 (40); HRMS (ESI^+): m/z calculated: $\text{C}_{16}\text{H}_{33}\text{NO}_4\text{P}^+$ [$\text{M}+\text{H}^+$] 334.2142, found: 334.2153.

Synthesis of phenyl *P*-alkyl-*N*-((*S*)-2-oxotetrahydrofuran-3-yl) phosphoramidates **9a** – **9b**

The procedure for the McKenna dealkylation was adapted from Dash et al.¹⁵ Ethyl phenyl *P*-alkylphosphonate **2a** or **2b** (2 mmol, 1 equiv.) was dissolved in anhydrous acetonitrile (25 mL) and the reaction mixture was cooled to 0 °C. Trimethylsilyl bromide (16 mmol, 8 equiv.) was added portionwise and the resulting mixture was allowed to come to room temperature overnight. The solvent was evaporated and residue re-evaporated with acetonitrile (25 mL) and subsequently dissolved in dioxane (25 mL). After addition of water (8 mmol, 4 equiv.), the solution was stirred for 30 min at room temperature followed by evaporation of the solvents. Afterwards, the residue was redissolved in 30 mL diethyl ether, extracted with 30 mL 3N HCl, dried and evaporated under reduced pressure to yield product **13**. This product is used in the coupling step without further purification.

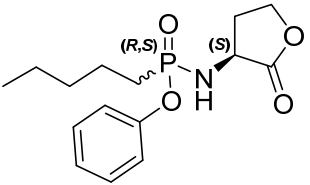
Under nitrogen atmosphere, oxalyl chloride (1.32 equiv., 2.64 mmol) is added dropwise to a solution of the corresponding hydrogen phenyl *P*-alkylphosphonate **13** (2 mmol, 1 equiv.) and 3 drops of DMF in 15 mL dry DCM. This solution is stirred for 3 hours at room temperature and the conversion is monitored via ^{31}P NMR. After completion of the reaction, solvent is evaporated under reduced pressure to yield a crude mixture of phosphonochloridate. Due to the instability of the compound, the crude compound is immediately used in subsequent reactions.

The corresponding phosphonochloridate and triethylamine (1.1 equiv., 2.2 mmol) were dissolved in 30 mL dry THF under nitrogen atmosphere and left stirring for 30 min at room temperature, after which the reaction mixture was analysed using ^{31}P NMR. Triethylamine (1.6 equiv., 3.2 mmol) and L-homoserine lactone hydrobromide (1.5 equiv., 3 mmol) was dissolved in 15 mL dry ACN under nitrogen atmosphere, while stirring at room temperature. The solution containing the phosphonochloridate was added dropwise to the amine solution at room temperature and stirred for 1 hour (monitored with ^{31}P NMR). After completion of the reaction the organic layer was diluted with 60 mL diethyl ether, washed with 50 mL water, 50 mL bicarbonate and 50 mL brine and dried with MgSO_4 . The solvent was evaporated under reduced pressure and the remaining mixture was purified via normal phase automatic flash chromatography.

Phenyl *P*-pentyl-*N*-((*S*)-2-oxotetrahydrofuran-3-yl)phosphonamidate **9a**

Ethyl phenyl *P*-pentylphosphonate **2a** was used as starting product. The crude product was purified using normal phase automated column chromatography (SiO₂, EtOAc:hexane 1:1 v:v, 10 CV gradient to EtOAc:hexane 3:1 v:v) after which, 150 mg of product **9a** was obtained as an orange oil with a yield of 24%.

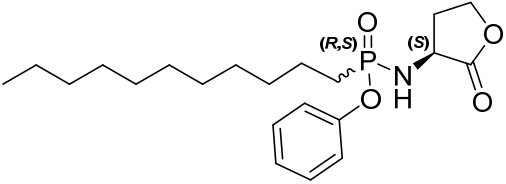
Spectral data derived from the mixture of diastereomers (dr = 53/47).

 **¹H NMR** (400 MHz, CDCl₃): δ = 0.91 (td, *J* = 7.1, 1.9 Hz, 3H, CH₃CH₂CH₂), 1.28 – 1.48 (m, 4H, CH₃(CH₂)₂), 1.62 – 2.19 (m, 5H, CH₂P, CH₂CH₂P and CH_aH_bCHN), 2.45 (ddd, *J* = 12.7, 8.1, 5.1 Hz, 0.5H, CH_aH_bCHN), 2.45 (ddd, *J* = 12.8, 8.2, 5.0 Hz, 0.5H, CH_aH_bCHN), 3.10 (dd, *J* = 11.8, 8.0 Hz, 0.5H, CHNH), 3.37 (dd, *J* = 9.5, 6.9 Hz, 0.5H, CHNH), 4.02 – 4.39 (m, 3H, CHNH and CH₂OC=O), 7.13 – 7.36 (m, 5H, 5 x CH_{arom}) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 14.0 (s, CH₃CH₂CH₂), 22.0 (d, *J* = 5.0 Hz, CH₂CH₂P), 22.2 (d, *J* = 5.1 Hz, CH₂CH₂P), 22.3 (s, CH₃CH₂CH₂), 28.4 (d, *J* = 130.6 Hz, CH₂P), 28.9 (d, *J* = 129.8 Hz, CH₂P), 32.6 (s, CH₂CHN), 32.8 (s, CH₂CHN), 32.9 (d, *J* = 16.9 Hz, CH₃CH₂CH₂), 32.9 (d, *J* = 16.9 Hz, CH₃CH₂CH₂), 50.6 (s, CHNH), 50.7 (s, CHNH), 65.4 (s, CH₂OC=O), 65.6 (s, CH₂OC=O), 120.7 (d, *J* = 4.4 Hz, 2 x CH_{arom,ortho}), 121.0 (d, *J* = 4.4 Hz, 2 x CH_{arom,ortho}), 125.0 (s, CH_{arom,para}), 125.0 (s, CH_{arom,para}), 129.8 (s, 2 x CH_{arom,meta}), 129.9 (s, 2 x CH_{arom,meta}), 150.4 (d, *J* = 9.4 Hz, C_{arom,quat}), 150.6 (d, *J* = 8.8 Hz, C_{arom,quat}), 176.2 (d, *J* = 8.8 Hz, C=O), 176.5 (d, *J* = 9.5 Hz, C=O) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 33.22 (P), 33.38 (P) ppm; **IR** (ATR, cm⁻¹): ν = 3177 (N-H), 2955 (C-H), 2930 (C-H), 2872 (C-H), 1778 (C=O), 1591, 1489, 1375, 1201, 1150 (C-O, ν_{max}), 1003, 914, 897; **MS** (ES⁺): *m/z* (%): 312 (M+H⁺, 100), 645 (2M+Na⁺, 23); **EI-MS** *m/z* (rel. int.): 311 [M] (10), 281 (5), 238 (5), 218 (100), 190 (32), 162 (10), 135 (7), 94 (71), 77 (12), 66 (16), 56 (19); **HRMS** (ES⁺): *m/z* calculated: C₁₅H₂₃NO₄P⁺ [M+H⁺] 312.1359, found: 312.1360.

Phenyl *P*-undecyl-*N*-((*S*)-2-oxotetrahydrofuran-3-yl)phosphonamidate **9b**

Ethyl phenyl *P*-undecylphosphonate **2b** was used as starting product. The crude product was purified using normal phase automated column chromatography (SiO₂, EtOAc:hexane 1:1 v:v, 10 CV gradient to EtOAc:hexane 3:1 v:v) after which, 260 mg of product **9b** was obtained as a yellow solid with a yield of 33%.

Spectral data derived from the mixture of diastereomers (dr = 54/46).

 **¹H NMR** (400 MHz, CDCl₃): δ = 0.88 (t, *J* = 6.9 Hz, 3H, CH₃CH₂CH₂), 1.22 - 1.36 (m, 14H, CH₃(CH₂)₇), 1.37 - 1.45 (m, 2H, CH₂CH₂CH₂P), 1.64 – 2.19 (m, 5H, CH₂P, CH₂CH₂P and CH_aH_bCHN), 2.46 (ddd, *J* = 12.7, 8.2, 5.0 Hz, 0.5H, CH_aH_bCHN), 2.61 (ddd, *J* = 12.5, 8.2, 5.4 Hz, 0.5H, CH_aH_bCHN), 3.08 (dd, *J* = 12.0, 8.0 Hz, 0.5H, CHNH), 3.34 (dd, *J* = 9.2, 7.0 Hz, 0.5H, CHNH), 4.00 – 4.41 (m, 3H, CHNH and CH₂OC=O), 7.13 – 7.35 (m, 5H, 5 x CH_{arom}) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 14.3 (s, CH₃CH₂CH₂), 22.4 (d, *J* = 5.1 Hz, CH₂CH₂P), 22.5 (d, *J* = 5.1 Hz, CH₂CH₂P), 22.8 (s, CH₃CH₂CH₂), 28.5 (d, *J* = 130.6 Hz, CH₂P), 28.9 (d, *J* = 128.9 Hz, CH₂P), 29.3, 29.5, 29.5, 29.7 (s, CH₃CH₂CH₂(CH₂)₅), 30.8 (d, *J* = 17.6

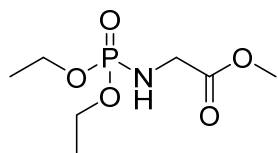
Hz, $\underline{\text{CH}_2(\text{CH}_2)_2\text{P}}$, 30.8 (d, $J = 17.6$ Hz, $\underline{\text{CH}_2(\text{CH}_2)_2\text{P}}$), 32.0 (s, $\text{CH}_3\text{CH}_2\underline{\text{CH}_2}$), 32.6 (s, $\underline{\text{CH}_2\text{CHN}}$), 32.8 (s, $\underline{\text{CH}_2\text{CHN}}$), 50.6 (s, $\underline{\text{CHNH}}$), 50.7 (s, $\underline{\text{CHNH}}$), 65.4 (s, $\underline{\text{CH}_2\text{OC=O}}$), 65.6 (s, $\underline{\text{CH}_2\text{OC=O}}$), 120.7 (d, $J = 5.1$ Hz, 2 x $\underline{\text{CH}_{\text{arom,ortho}}}$), 121.03 (d, $J = 4.6$ Hz, 2 x $\underline{\text{CH}_{\text{arom,ortho}}}$), 125.0 (s, $\underline{\text{CH}_{\text{arom,para}}}$), 125.0 (s, $\underline{\text{CH}_{\text{arom,para}}}$), 129.8 (s, 2 x $\underline{\text{CH}_{\text{arom,meta}}}$), 129.9 (s, 2 x $\underline{\text{CH}_{\text{arom,meta}}}$), 150.4 (d, $J = 9.5$ Hz, $\underline{\text{C}_{\text{arom,quat}}}$), 150.6 (d, $J = 9.3$ Hz, $\underline{\text{C}_{\text{arom,quat}}}$), 176.2 (d, $J = 8.8$ Hz, $\underline{\text{C=O}}$), 176.4 (d, $J = 9.6$ Hz, $\underline{\text{C=O}}$) ppm; ^{31}P NMR (161.9 MHz, CDCl_3): $\delta = 33.24$ (P), 33.39 (P) ppm; IR (ATR, cm^{-1}): $\nu = 3164$ (N-H), 2916 (C-H), 2851 (C-H), 1775 (C=O), 1591, 1489, 1204, 1159, 1001, 891 (ν_{max}), 773; MS (ESI^+): m/z (%): 396 ($\text{M}+\text{H}^+$, 100), 813 ($2\text{M}+\text{Na}^+$, 14); HRMS (ESI^+): m/z calculated: $\text{C}_{21}\text{H}_{35}\text{NO}_4\text{P}^+$ [$\text{M}+\text{H}^+$] 396.2298, found: 396.2302.

General procedure C: synthesis of phosphoramidates 15a – 15d

The corresponding dialkyl chlorophosphate **14** (3.7 mmol) and triethylamine (1.1 equiv.; 567 μL ; 4.0 mmol) were dissolved in 25 mL dry THF under nitrogen atmosphere and left stirring for 30 min at room temperature, after which the reaction mixture was analysed using ^{31}P NMR. The amino acid ester salt (1.5 equiv.; 5.5 mmol) and triethylamine (1.6 equiv.; 825 μL ; 5.9 mmol) were dissolved in 25 mL dry ACN under nitrogen atmosphere, while stirring at room temperature. The solution containing the phosphorochloridate was added dropwise to the amino acid solution at room temperature and stirred for 1 hour. Subsequently, the excess salts were removed via filtration, upon addition of 60 mL diethyl ether and the solvent was evaporated under reduced pressure. The remaining mixture was purified via normal phase automatic flash chromatography.

Methyl *N*-(diethoxyphosphoryl)-glycinate **15a**

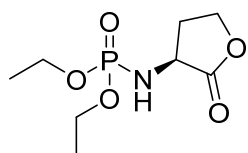
Glycine methyl ester hydrochloride and diethyl chlorophosphate **14a** were used as starting product for general procedure C. The crude product was purified using normal phase automatic flash chromatography (SiO_2 , 40% (EtOAc:iPA) 3:1 v:v in hexane), after which 760 mg of product **15a** was obtained as a pale yellow oil in a yield of 95%.



^1H NMR (400 MHz, CDCl_3): $\delta = 1.31$ (td, $J = 7.1, 0.9$ Hz, 6H, 2 x $\underline{\text{CH}_3\text{CH}_2\text{O}}$), 3.21 – 3.38 (m, 1H, $\underline{\text{NHCH}_2}$), 3.64 – 3.82 (m, 5H, COOCH_3 and $\underline{\text{NHCH}_2}$), 3.99 – 4.19 (m, 4H, 2 x $\text{CH}_3\text{CH}_2\text{O}$) ppm; ^{13}C NMR (100.6 MHz, CDCl_3): $\delta = 16.1$ (d, $J = 7.0$ Hz, 2 x $\underline{\text{CH}_3\text{CH}_2\text{O}}$), 42.8 (d, $J = 1.4$ Hz, $\underline{\text{NHCH}_2}$), 52.2 (s, $\underline{\text{OCH}_3}$), 62.5 (d, $J = 5.2$ Hz, 2 x $\underline{\text{CH}_3\text{CH}_2\text{O}}$), 171.4 (d, $J = 7.5$ Hz, $\underline{\text{COO}}$) ppm; ^{31}P NMR (161.9 MHz, CDCl_3): $\delta = 7.63$ (P) ppm; IR (ATR, cm^{-1}): $\nu = 3240$ (N-H), 2983 (C-H), 1753 (C=O), 1436, 1205, 1151, 1020 (ν_{max}), 960, 869, 794, 731; MS (ESI^+): m/z (%): 226 ($\text{M}+\text{H}^+$, 100), 451 ($2\text{M}+\text{H}^+$, 21), 473 ($2\text{M}+\text{Na}^+$, 23); EI-MS m/z (rel. int.): 225 [M] (2), 166 (100), 152 (4), 138 (27), 122 (8), 110 (54), 94 (6), 81 (4); HRMS (ESI^+): m/z calculated: $\text{C}_7\text{H}_{16}\text{NO}_5\text{P}^+$ [$\text{M}+\text{H}^+$] 226.0839, found: 226.0841.

Diethyl (S)-(2-oxotetrahydrofuran-3-yl)phosphoramidate **15b**

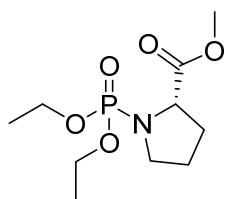
L-homoserine lactone hydrobromide and diethyl chlorophosphate **14a** were used as starting product for general procedure C. The crude product was purified using normal phase automatic flash chromatography (SiO₂, 40% (EtOAc:iPA) 3:1 v:v in hexane), after which 860 mg of product **15b** was obtained as a yellow oil in a yield of 89%.



¹H NMR (400 MHz, CDCl₃): δ = 1.34 (2 x td, J = 7.1, 0.8 Hz, 6H, 2 x CH₃CH₂O), 2.13 – 2.26 (m, 1H, NHCHCH_aH_b), 2.65 – 2.73 (m, 1H, NHCHCH_aH_b), 3.44 (t, J = 8.2, 1H, NHCH), 3.98 – 4.25 (m, 6H, 2 x CH₃CH₂O, NHCH and CH_aH_bOCO), 4.41 (t, J = 8.9 Hz, 1H, CH_aH_bOCO) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 16.2 (d, J = 4.4 Hz, CH₃CH₂O), 16.3 (d, J = 5.1 Hz, CH₃CH₂O), 32.1 (d, J = 1.5 Hz, NHCHCH₂), 50.8 (s, NHCH), 62.9, 63.0 (2 x d, J = 5.2 Hz, 2 x CH₃CH₂O), 65.4 (s, CH₂OCO), 176.0 (d, J = 11.0 Hz, COO) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 7.20 (P) ppm; **IR** (ATR, cm⁻¹): ν = 3196 (N-H), 2982 (C-H), 2911 (C-H), 1778 (C=O), 1452, 1229, 1155, 1055, 1022 (ν_{\max}), 972, 732; **MS** (ES⁺): m/z (%): 238 (M+H⁺, 100), 475 (2M+H⁺, 5), 497 (2M+Na⁺, 25); **EI-MS** m/z (rel. int.): 237 [M] (17), 193 (98), 179 (26), 164 (100), 152 (7), 136 (98), 124 (11), 109 (13), 81 (22), 56 (78); **HRMS** (ESI⁺): m/z calculated: C₈H₁₆NO₅P⁺ [M+H⁺] 238.0839, found: 238.0841.

Methyl N-(diethoxyphosphoryl)-L-prolinate **15c**

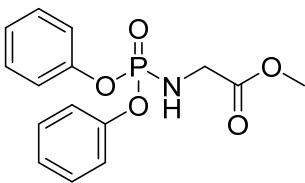
L-proline methyl ester hydrochloride and diethyl chlorophosphate **14a** were used as starting product for general procedure C. The crude product was purified using normal phase automatic flash chromatography (SiO₂, 40% (EtOAc:iPA) 3:1 v:v in hexane), after which 865 mg of product **15c** was obtained as an orange oil in a yield of 88%.



¹H NMR (400 MHz, CDCl₃): δ = 1.22 – 1.39 (m, 6H, 2 x CH₃CH₂O), 1.83 – 2.07 (m, 3H, CHCH_aH_b and CHCH₂CH₂), 2.11 – 2.24 (m, 1H, CHCH_aH_b), 3.22 – 3.36 (m, 2H, NCH₂), 3.72 (s, 3H, COOCH₃), 3.93 – 4.22 (m, 4H, 2 x CH₃CH₂O), 4.23 – 4.31 (m, 1H, CHN) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 16.1, 16.2 (2 x d, J = 7.1 Hz, 2 x CH₃CH₂O), 25.2 (d, J = 8.4 Hz, CHCH₂CH₂), 31.3 (d, J = 8.4 Hz, CHCH₂), 47.0 (d, J = 4.7 Hz, NCH₂), 52.0 (s, OCH₃), 60.0 (d, J = 6.6 Hz, NCH), 62.2, 62.3 (2 x d, J = 5.2 Hz, 2 x CH₃CH₂O), 174.5 (s, COO) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = 6.03 (P) ppm; **IR** (ATR, cm⁻¹): ν = 2981 (C-H), 1747 (C=O), 1444, 1253, 1209, 1151 (C-O), 1020 (ν_{\max}), 962, 794, 727; **MS** (ES⁺): m/z (%): 266 (M+H⁺, 100), 553 (2M+Na⁺, 25); **EI-MS** m/z (rel. int.): 265 [M] (2), 206 (100), 178 (33), 150 (85), 132 (11), 70 (7); **HRMS** (ESI⁺): m/z calculated: C₁₀H₂₀NO₅P⁺ [M+H⁺] 266.1152, found: 266.1154.

Methyl N-(diphenoxyphosphoryl)-glycinate **15d**

Glycine methyl ester hydrochloride and diphenyl chlorophosphate **14b** were used as starting product for general procedure C. The crude product was dissolved in 10 mL methanol, diluted with water and filtered off to yield the desired product, after which 1068 mg of product **15d** was obtained as a white powder in a yield of 91%.



Melting point: 87 °C; **¹H NMR** (400 MHz, CDCl₃): δ = 3.67 – 3.76 (m, 4H, NHCH₂ and COOCH₃), 3.87 (dd, *J* = 9.3, 6.0 Hz, 2H, NHCH₂), 7.17 (t, *J* = 7.2 Hz, 2H, 2 x CH_{arom,para}), 7.22 - 7.26 (m, 4H, 4 x CH_{arom,ortho}), 7.30 - 7.36 (m, 4H, 4 x CH_{arom,meta}) ppm; **¹³C NMR** (100.6 MHz, CDCl₃): δ = 43.2 (s, NHCH₂), 52.6 (s, OCH₃), 120.3 (d, *J* = 5.2 Hz, 4 x CH_{arom,ortho}), 125.3 (s, 2 x CH_{arom,para}), 129.9 (s, 4 x CH_{arom,meta}), 150.7 (d, *J* = 6.6 Hz, 2 x CH_{arom,quat}), 170.7 (d, *J* = 9.5 Hz, C=O) ppm; **³¹P NMR** (161.9 MHz, CDCl₃): δ = -2.27 (P) ppm; **IR** (ATR, cm⁻¹): ν = 3231 (N-H), 1740 (C=O), 1587, 1485, 1240, 1180, 1147, 927 (ν_{max}), 772, 692; **MS** (ES⁺): *m/z* (%): 322 (M+H⁺, 100), 643 (2M+H⁺, 5), 665 (2M+Na⁺, 25); **EI-MS** *m/z* (rel. int.): 321 [M] (11), 262 (29), 228 (100), 200 (89), 168 (23), 94 (69), 77 (31), 65 (17); **HRMS** (ESI⁺): *m/z* calculated: C₁₅H₁₆NO₅P⁺ [M+H⁺] 322.0839, found: 322.0839.

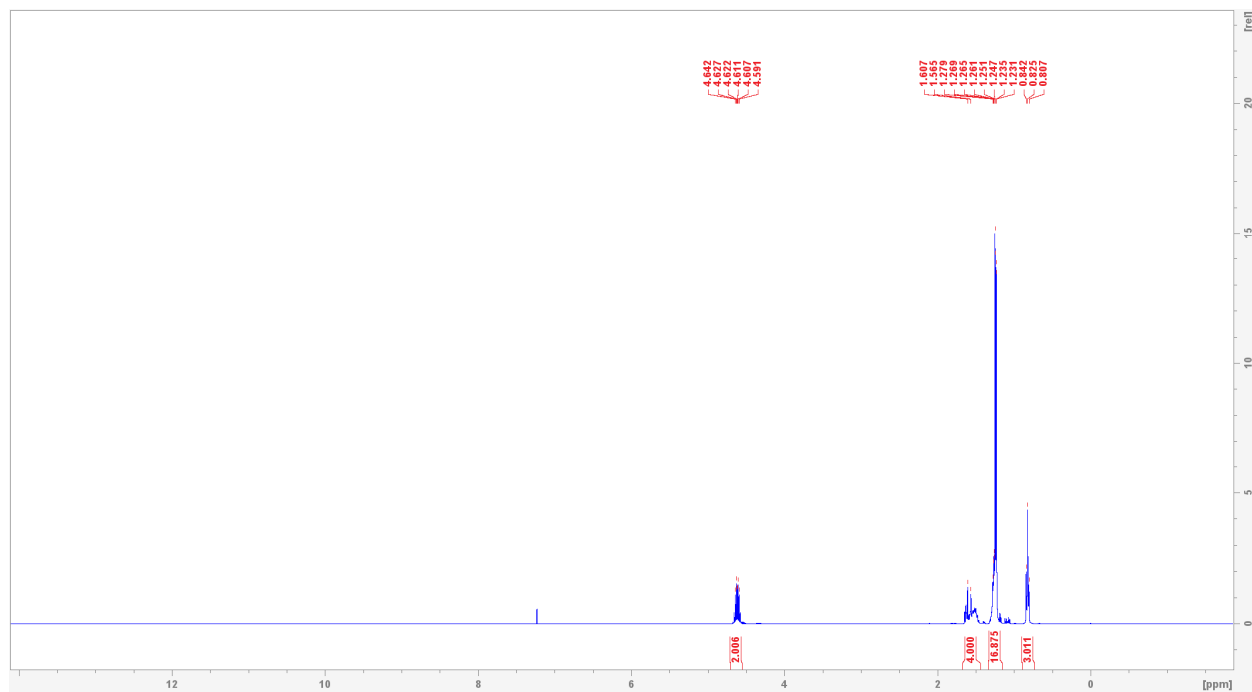
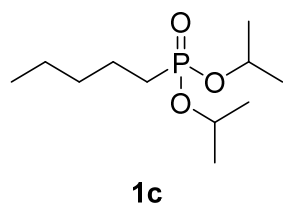
References

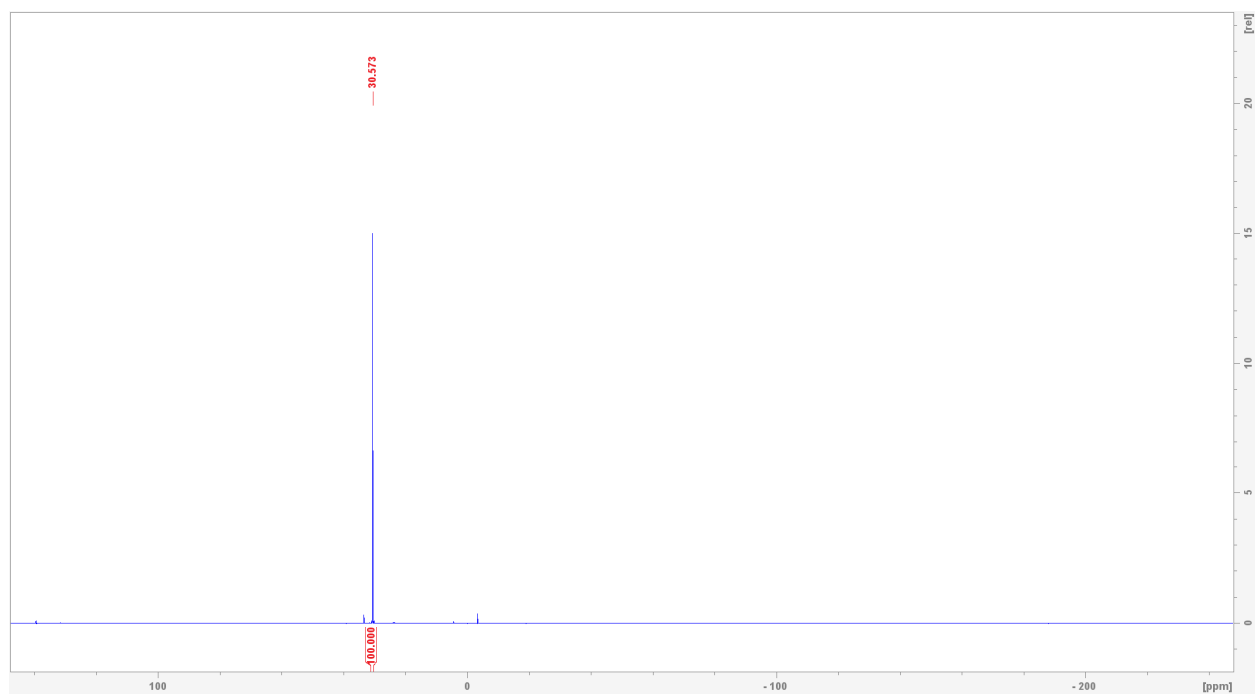
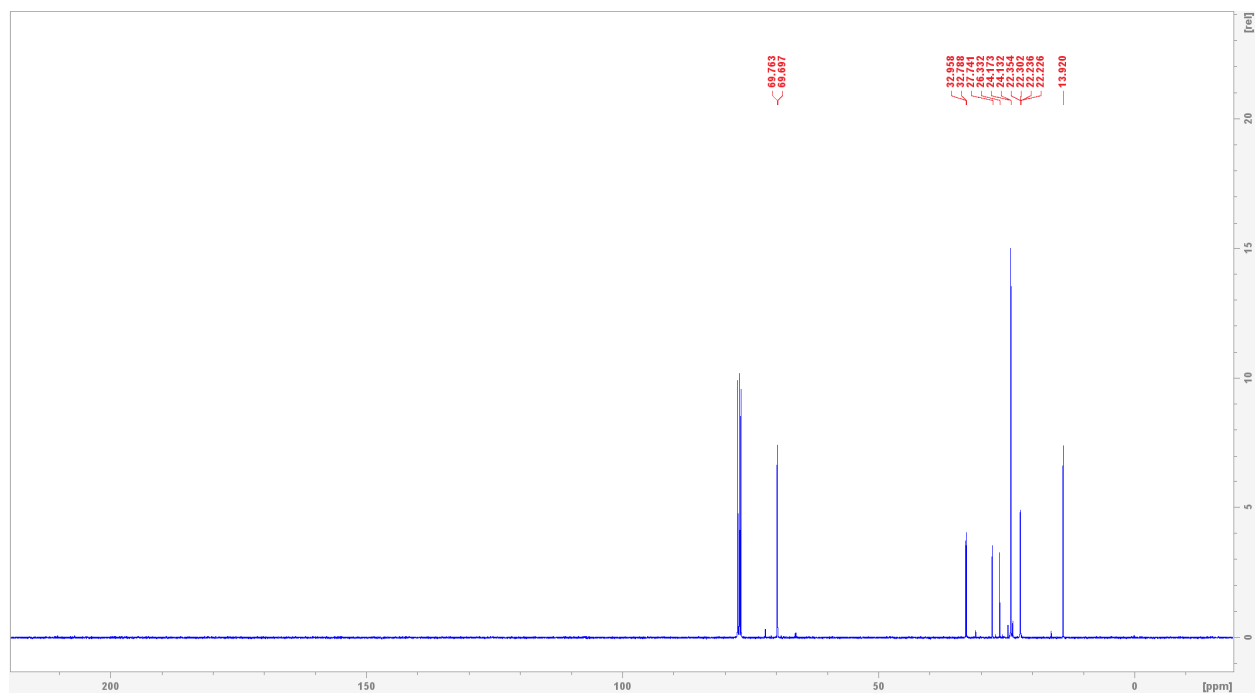
- (1) Desmedt, W.; Ameye, M.; Filipe, O.; De Waele, E.; Van Nieuwerburgh, F.; Deforce, D.; Van Meulebroek, L.; Vanhaecke, L.; Kyndt, T.; Höfte, M.; Audenaert, K. Molecular Analysis of Broad-Spectrum Induced Resistance in Rice by the Green Leaf Volatile Z-3-Hexenyl Acetate. *J Exp Bot* **2023**, *74* (21), 6804–6819.
- (2) De Zutter, N.; Ameye, M.; Debode, J.; De Tender, C.; Ommeslag, S.; Verwaeren, J.; Vermeir, P.; Audenaert, K.; De Gelder, L. Shifts in the Rhizobiome during Consecutive in Planta Enrichment for Phosphate-Solubilizing Bacteria Differentially Affect Maize P Status. *Microb Biotechnol* **2021**, *14* (4), 1594–1612.
- (3) Baker, N. R. Chlorophyll Fluorescence: A Probe of Photosynthesis In Vivo. *Annu Rev Plant Biol* **2008**, *59*, 89–113.
- (4) Wu, C.; Varanasi, V.; Perez-Jones, A. A Nondestructive Leaf-Disk Assay for Rapid Diagnosis of Weed Resistance to Multiple Herbicides. *Weed Sci* **2021**, *69* (3), 274–283.
- (5) Backx, S.; Dejaegere, A.; Simoens, A.; Van de Poel, J.; Krasowska, D.; Stevens, C. V.; Mangelinckx, S. Triethylamine-Mediated Transformation of Phosphonates into Phosphoramidates. *European J Org Chem* **2023**, *26* (26), e202300172.
- (6) Koehne, I.; Pietschnig, R. Synthesis of Geminal Bis- and Tetrakisphosphonate Ester Derivatives and Their Coordination Behavior Towards Ca(II) Ions. *Eur J Inorg Chem* **2022**, *2022* (17), e202200194.
- (7) Nathanael, J. G.; White, J. M.; Richter, A.; Nuske, M. R.; Wille, U. Oxidative Damage of Proline Residues by Nitrate Radicals (NO₃[•]): A Kinetic and Product Study. *Org Biomol Chem* **2020**, *18* (35), 6949–6957.
- (8) Syrpas, M.; Ruysbergh, E.; Stevens, C. V.; De Kimpe, N.; Mangelinckx, S. Synthesis and Biological Evaluation of Novel N- α -Haloacylated Homoserine Lactones as Quorum Sensing Modulators. *Beilstein Journal of Organic Chemistry* **2014**, *10* (1), 2539–2549.
- (9) Syrpas, M.; Ruysbergh, E.; Blommaert, L.; Vanellander, B.; Sabbe, K.; Vyverman, W.; De Kimpe, N.; Mangelinckx, S. Haloperoxidase Mediated Quorum Quenching by *Nitzschia Cf Pellucida*: Study of the Metabolization of N-Acyl Homoserine Lactones by a Benthic Diatom. *Mar Drugs* **2014**, *12* (1), 352–367.
- (10) Persson, T.; Hansen, T. H.; Rasmussen, T. B.; Skindersø, M. E.; Givskov, M.; Nielsen, J. Rational Design and Synthesis of New Quorum-Sensing Inhibitors Derived from Acylated Homoserine Lactones and Natural Products from Garlic. *Org. Biomol. Chem.* **2005**, *3* (2), 253–262.
- (11) Angle, S. R.; Henry, R. M. Studies toward the Synthesis of (+)-Palustrine: The First Asymmetric Synthesis of (–)-Methyl Palustramate. *Journal of Organic Chemistry* **1998**, *63* (21), 7490–7497.
- (12) Delorme, V.; Raux, B.; Puppo, R.; Leclaire, J.; Cavalier, J. F.; Marc, S.; Kamarajugadda, P. K.; Buono, G.; Fotiadu, F.; Canaan, S.; Carrière, F. Supported Inhibitor for Fishing Lipases in Complex Biological Media and Mass Spectrometry Identification. *Biochimie* **2014**, *107* (Part A), 124–134.

- (13) Antczak, M. I.; Montchamp, J.-L. Mild Synthesis of Organophosphorus Compounds: Reaction of Phosphorus-Containing Carbenoids with Organoboranes. *Org Lett* **2008**, *10* (5), 977–980.
- (14) Li, C. K.; Tao, Z. K.; Shoberu, A.; Zhang, W.; Zou, J. P. Copper-Catalyzed Cross-Coupling of Alkyl and Phosphorus Radicals for C(Sp³)-P Bond Formation. *Org Lett* **2022**, *24* (32), 6083–6087.
- (15) Dash, R. P.; Tichý, T.; Veeravalli, V.; Lam, J.; Alt, J.; Wu, Y.; Tenora, L.; Majer, P.; Slusher, B. S.; Rais, R. Enhanced Oral Bioavailability of 2-(Phosphonomethyl)-Pentanedioic Acid (2-PMPA) from Its (5-Methyl-2-Oxo-1,3-Dioxol-4-yl)Methyl (ODOL)-Based Prodrugs. *Mol Pharm* **2019**, *16* (10), 4292–4301.

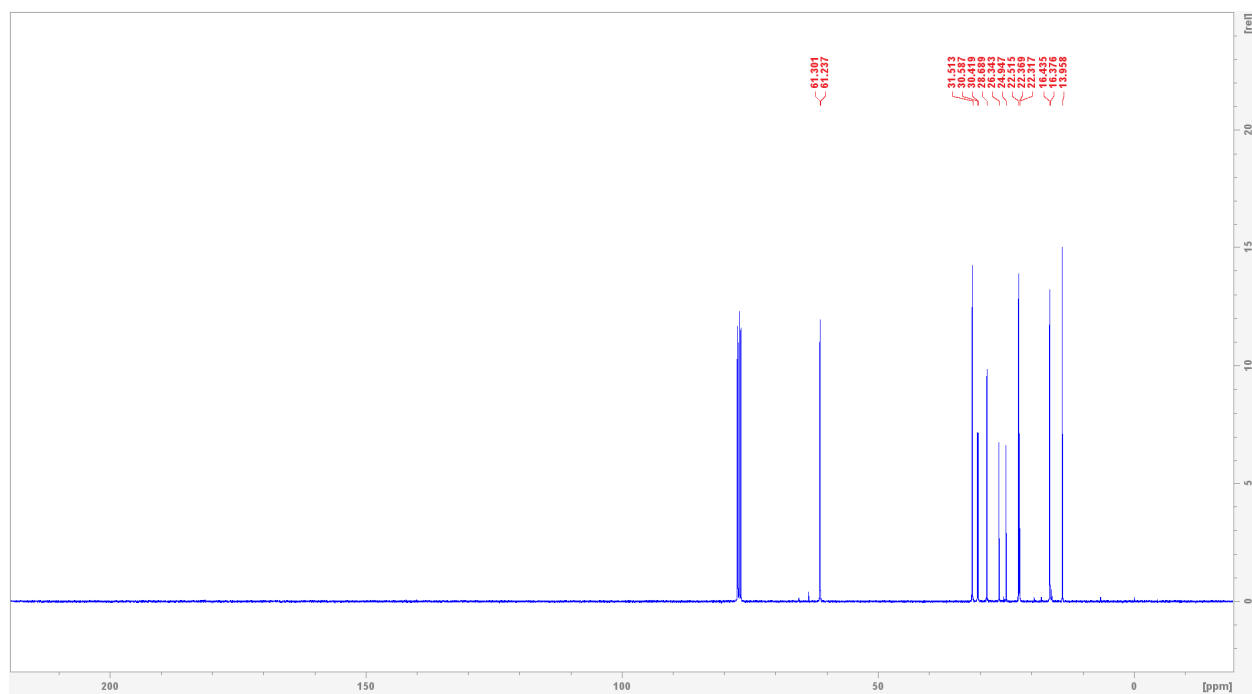
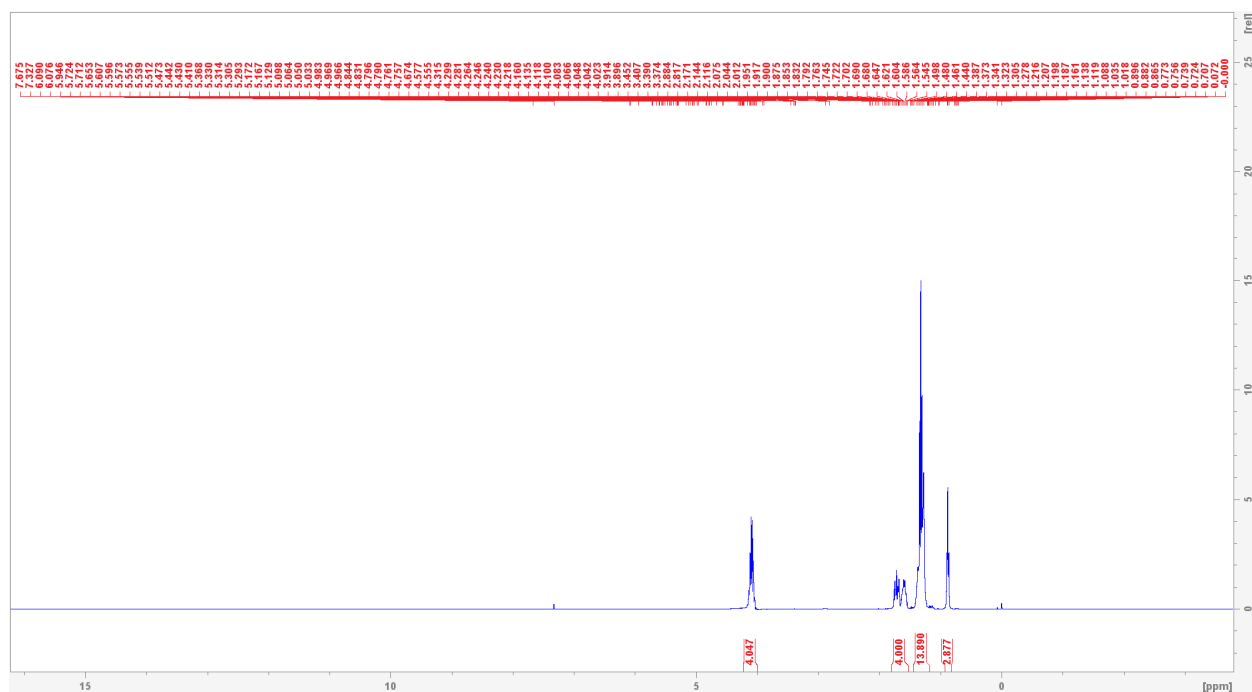
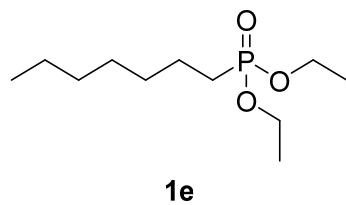
NMR spectra

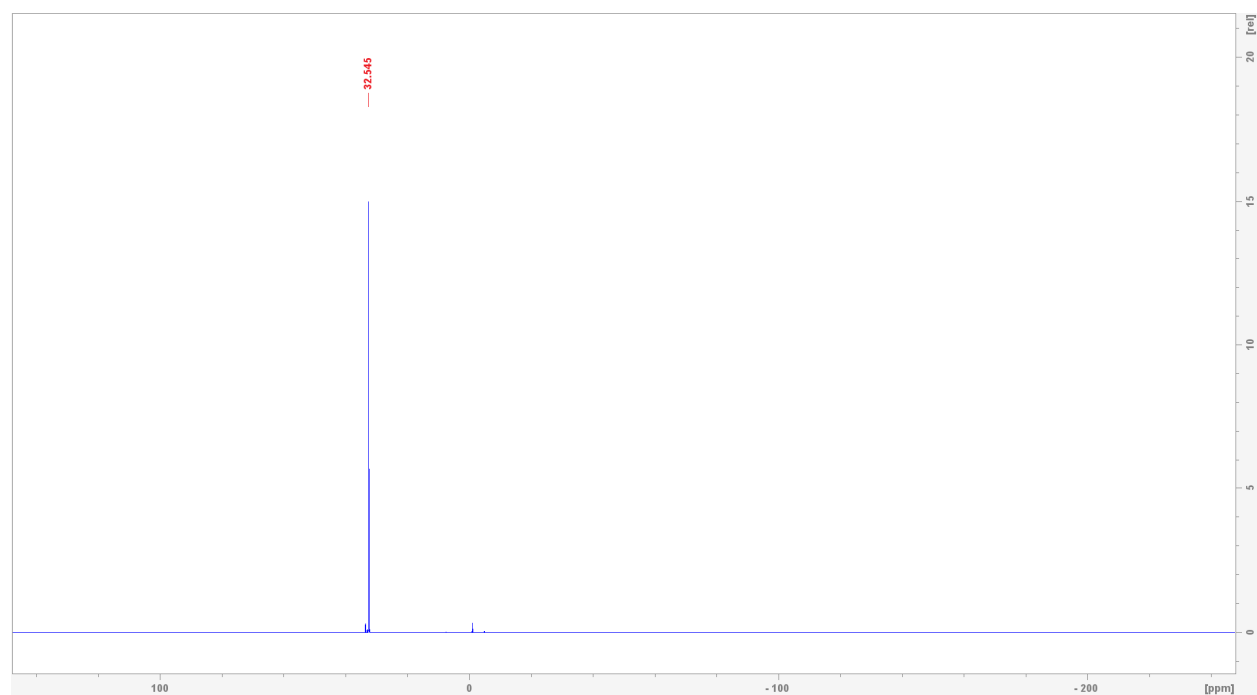
Compound **1c**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).



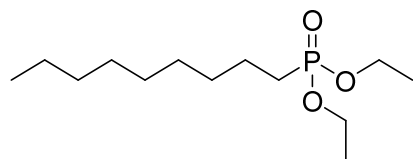


Compound **1e**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

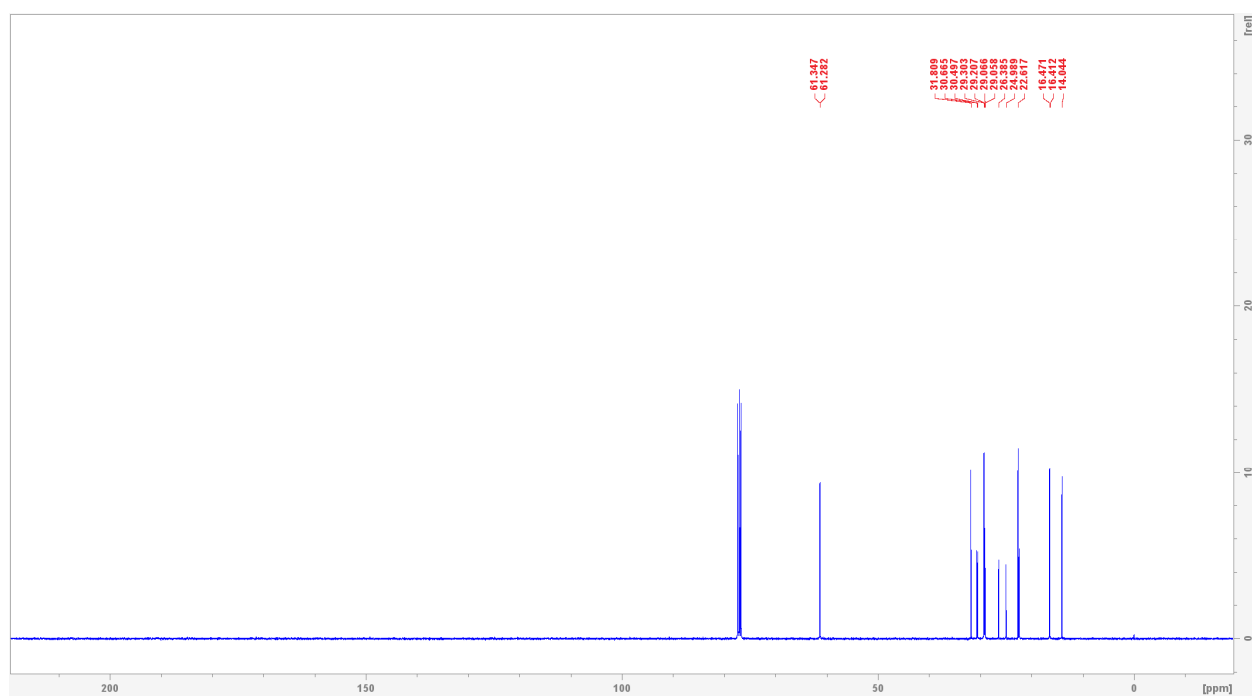
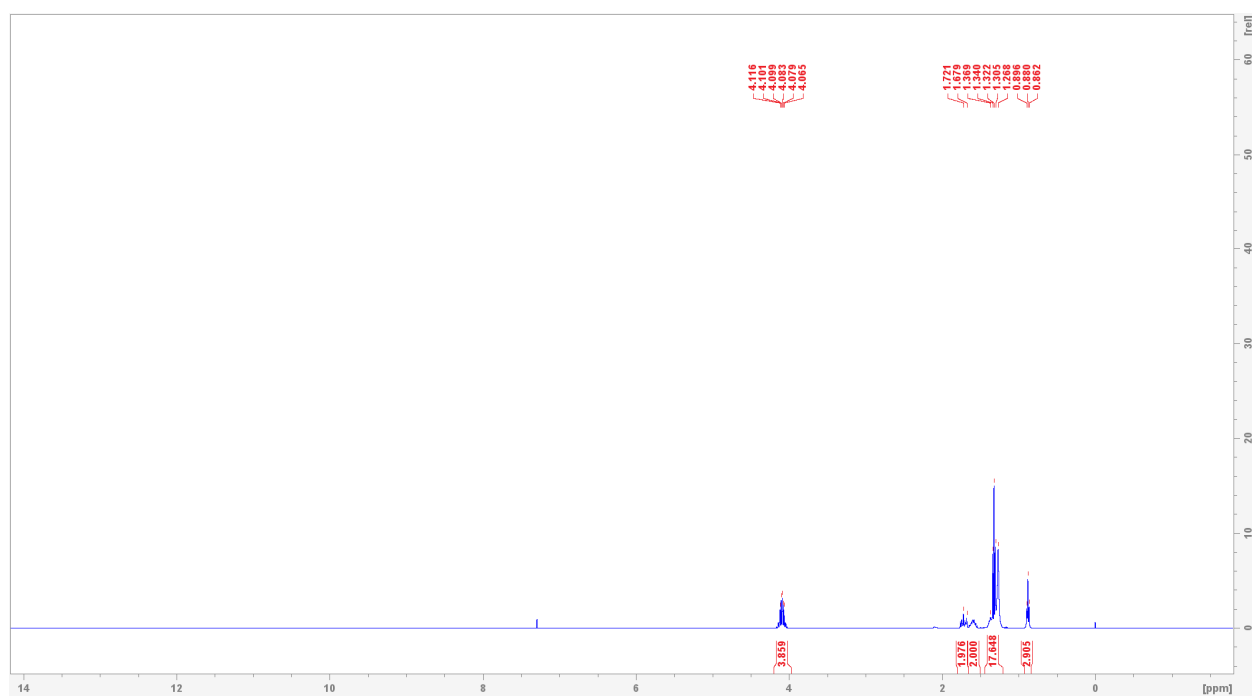


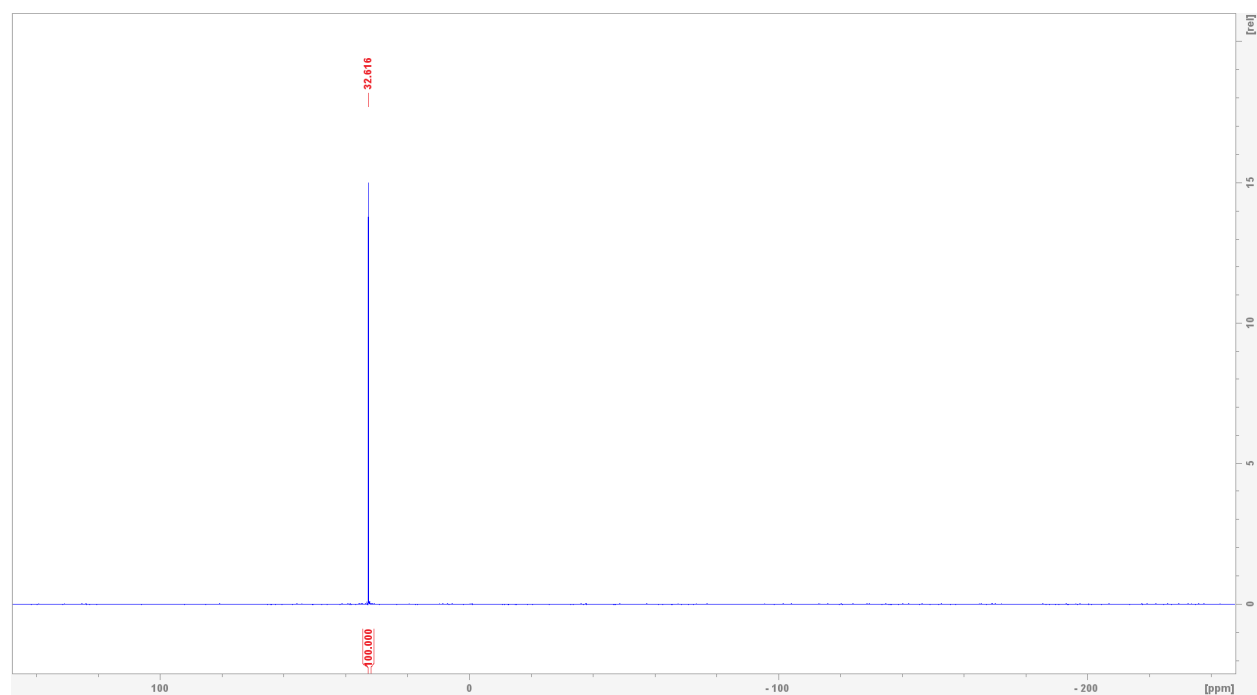


Compound **1f**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

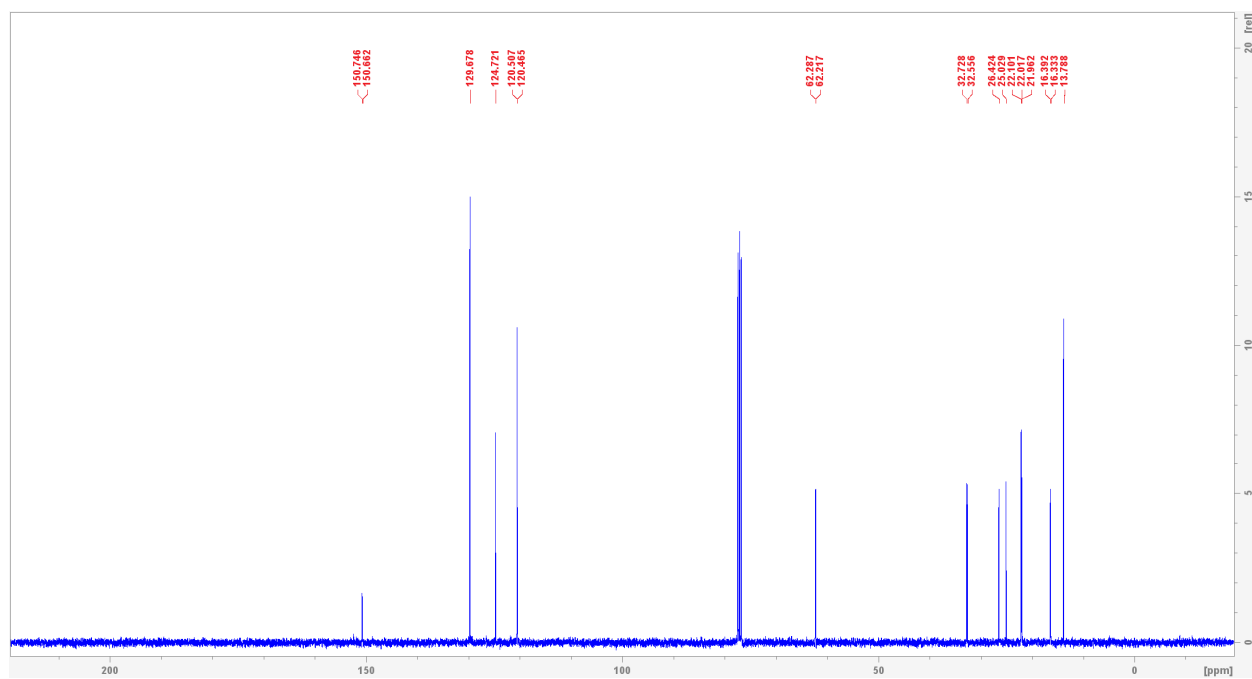
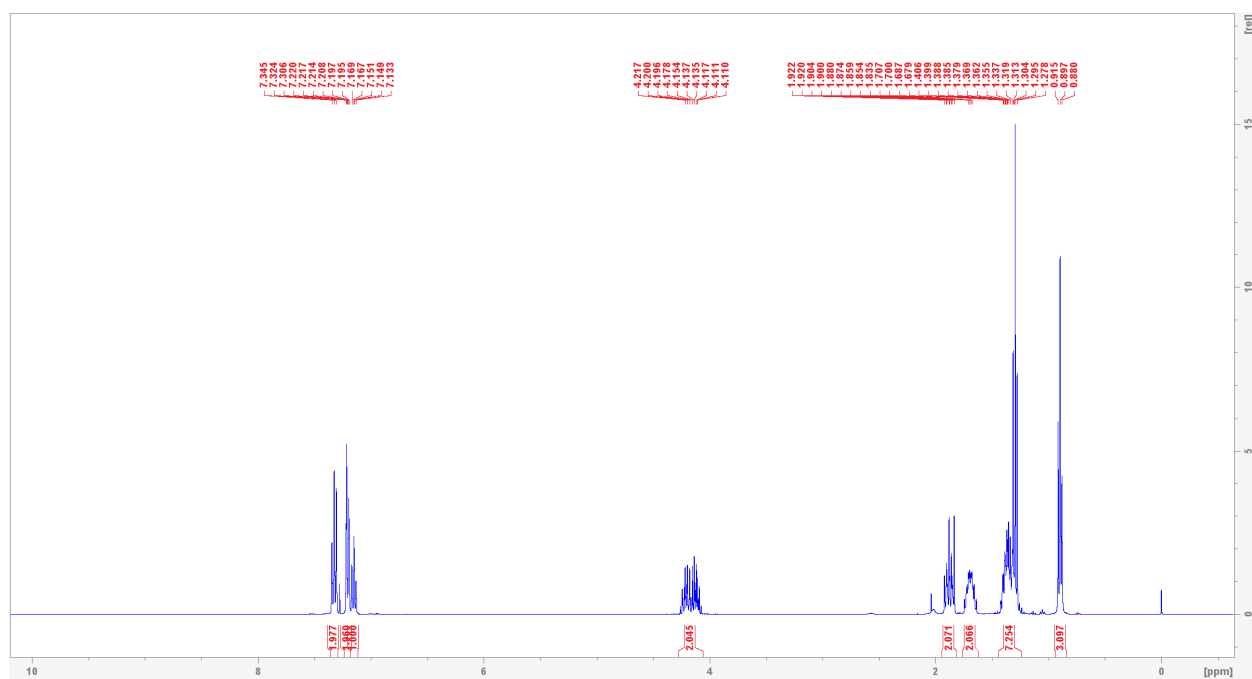
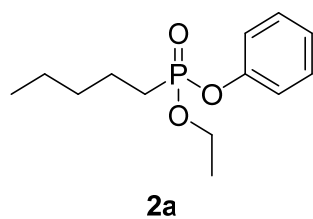


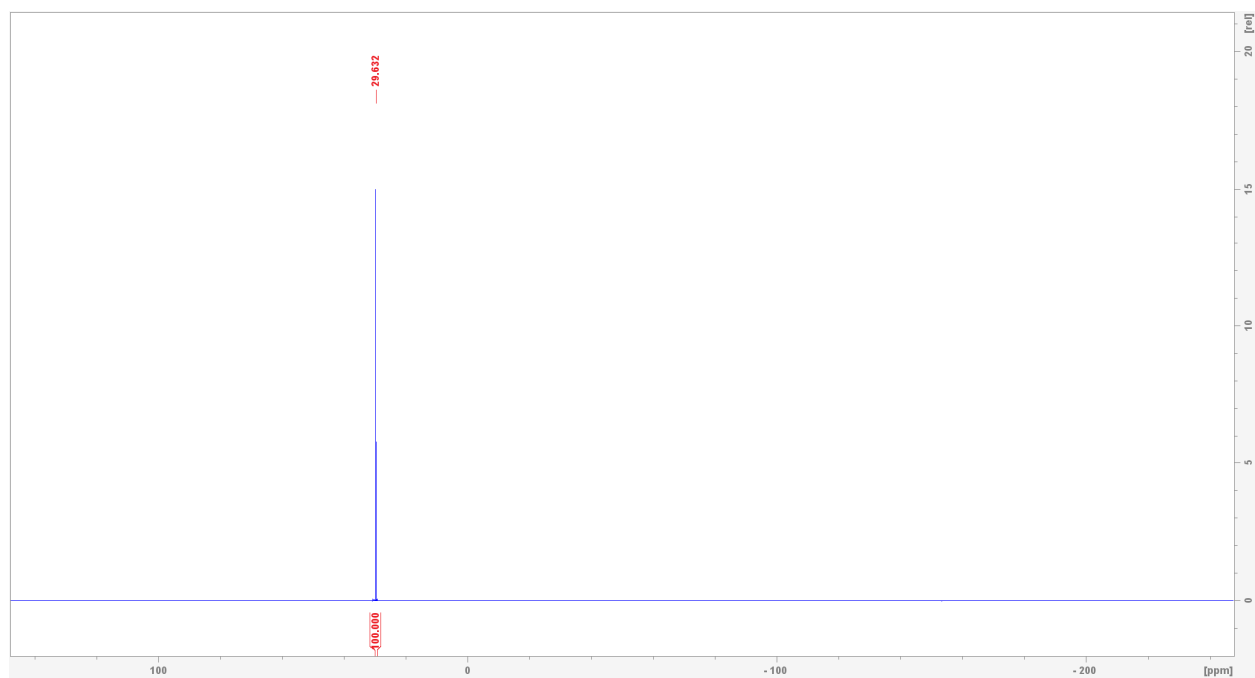
1f



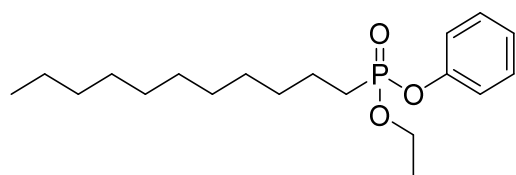


Compound **2a**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

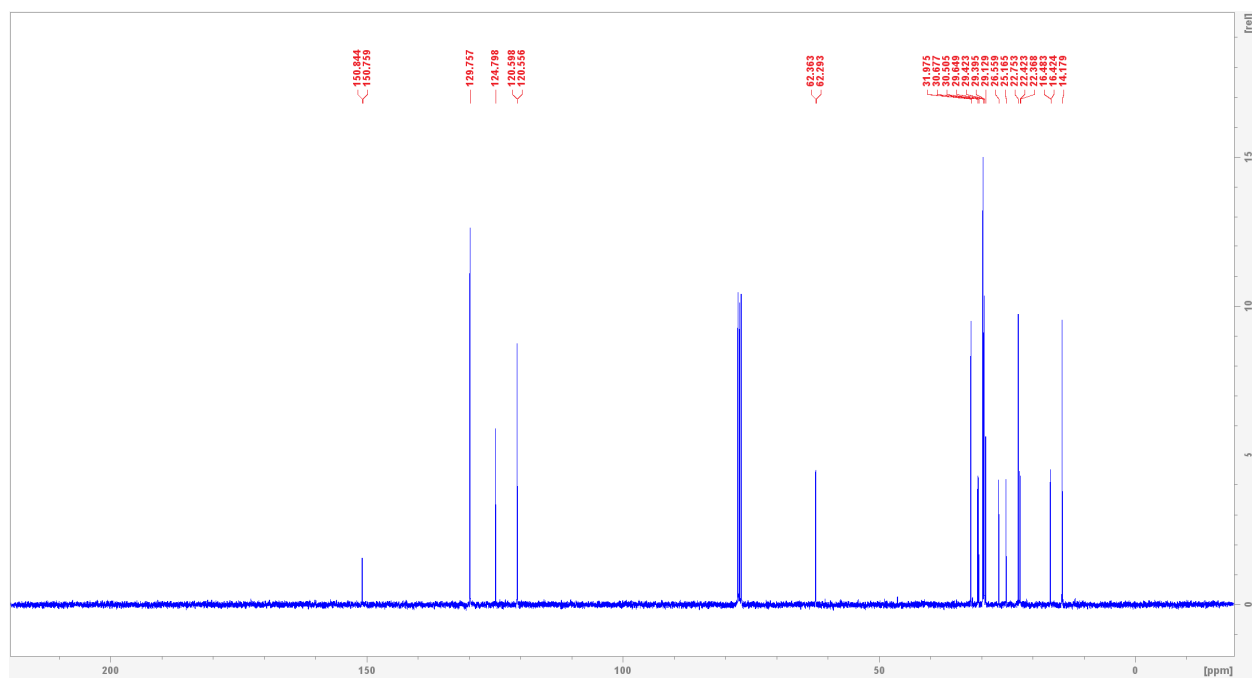
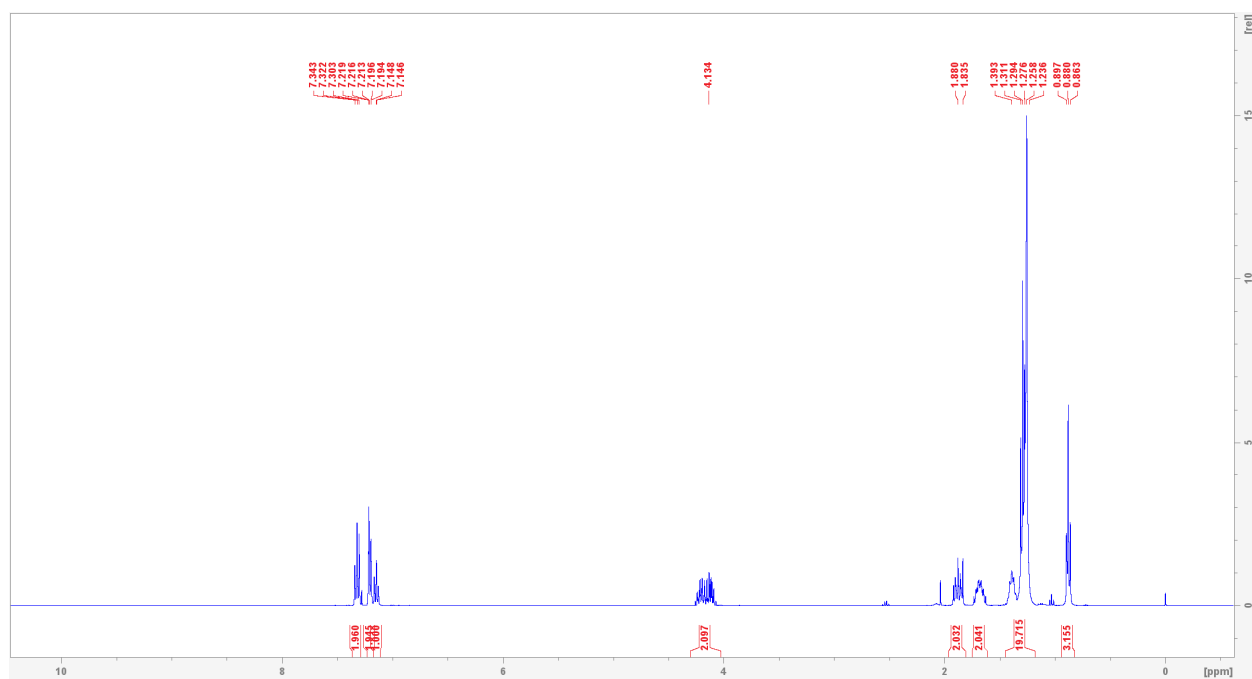


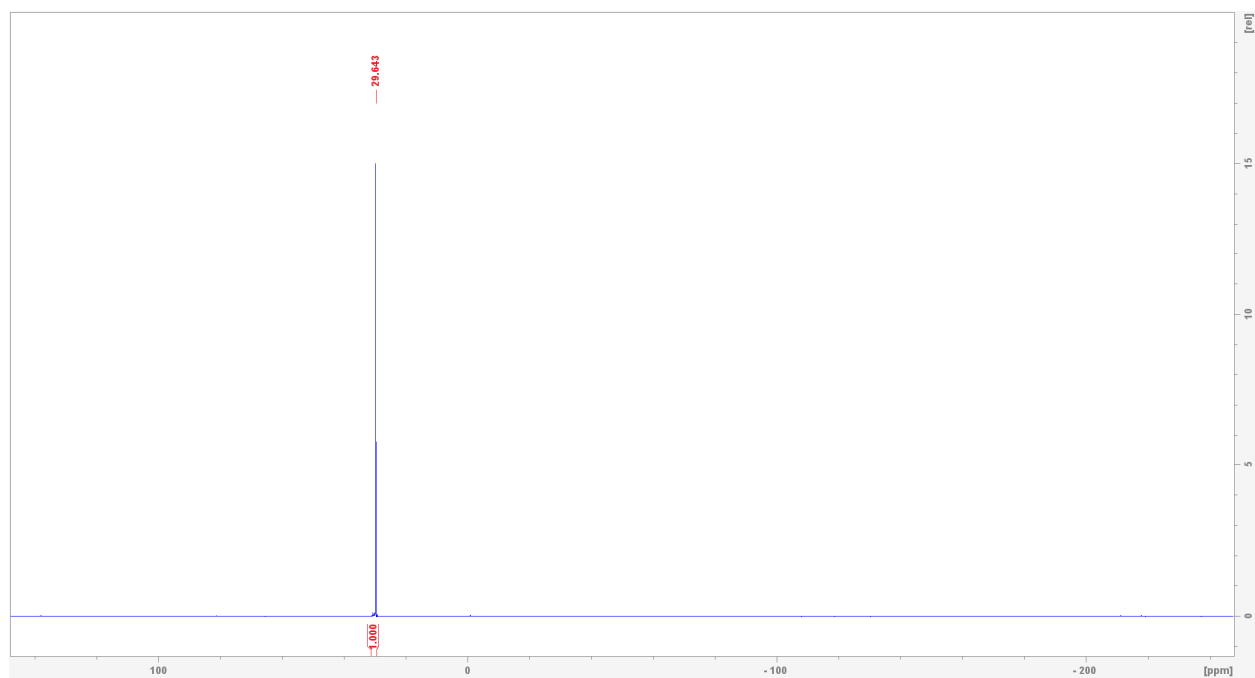


Compound **2b**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

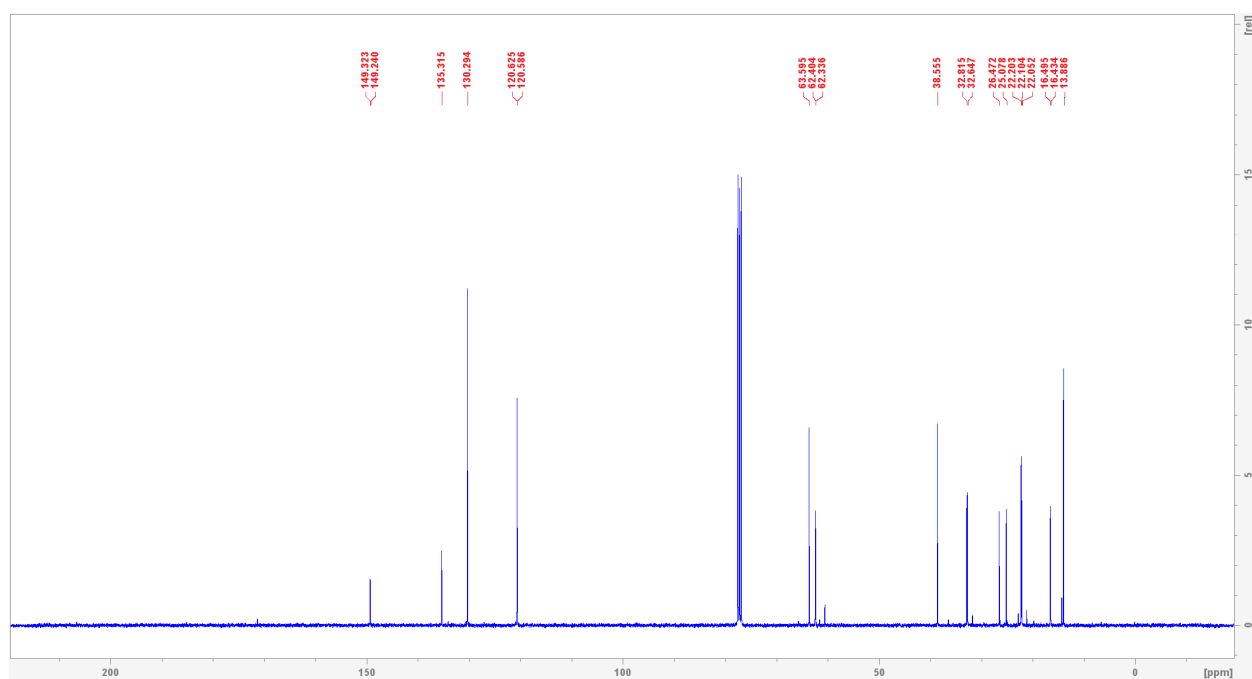
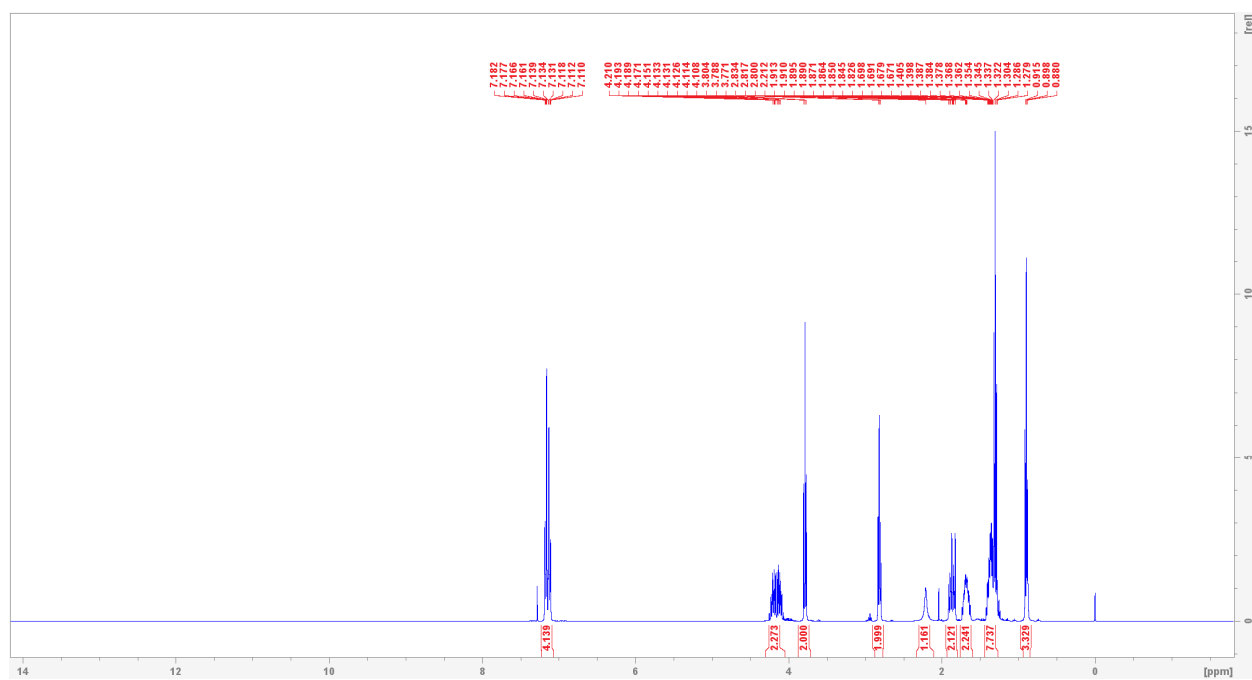
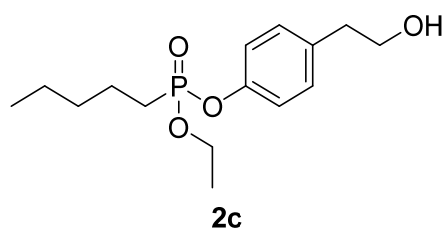


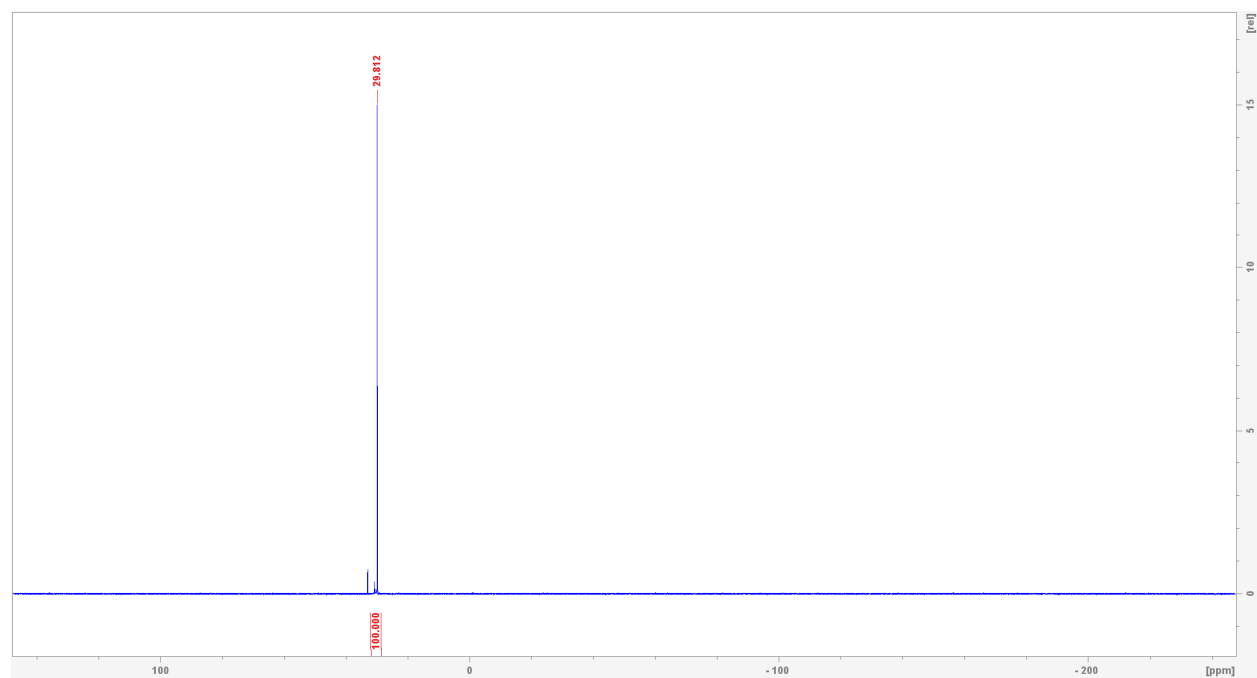
2b



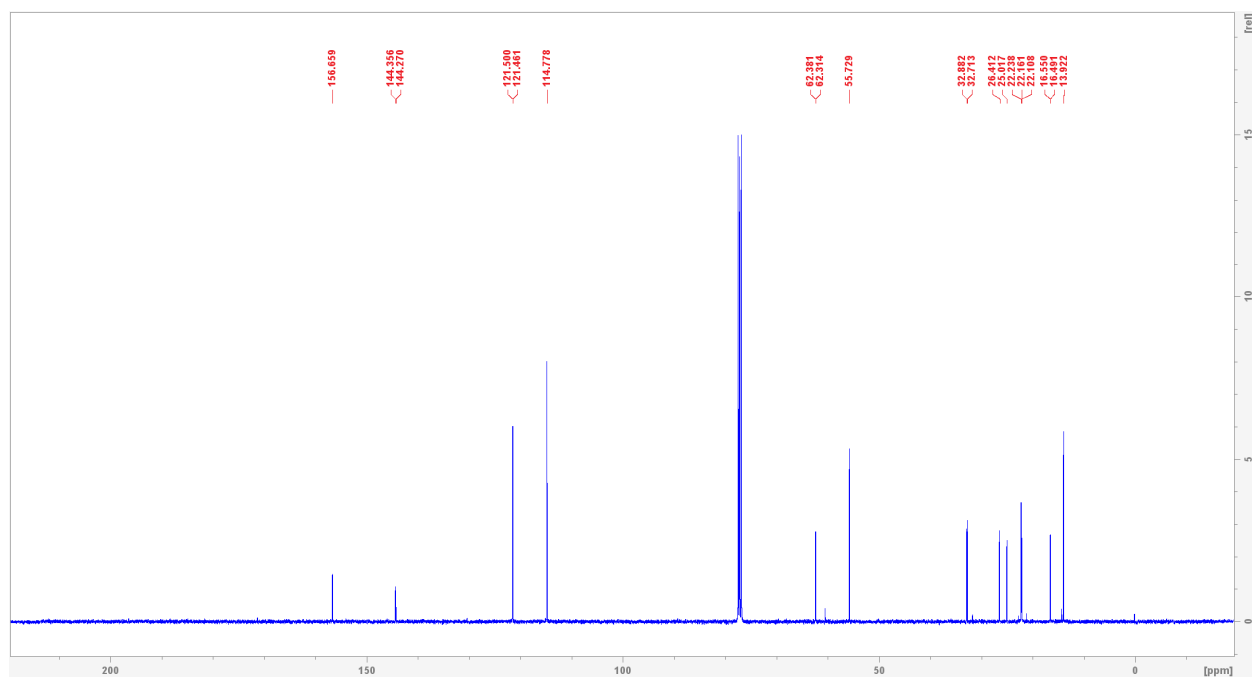
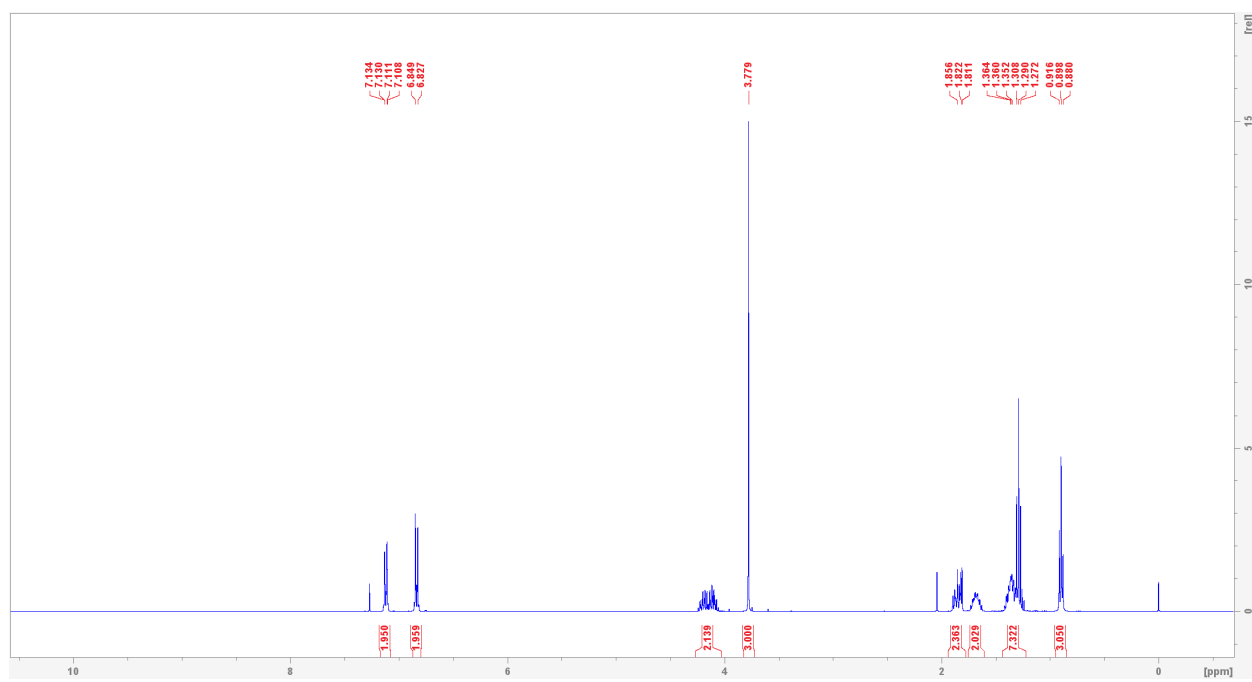
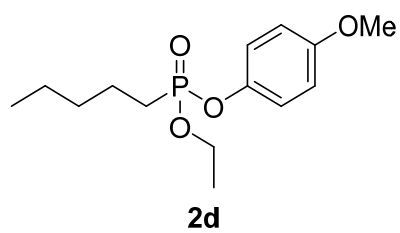


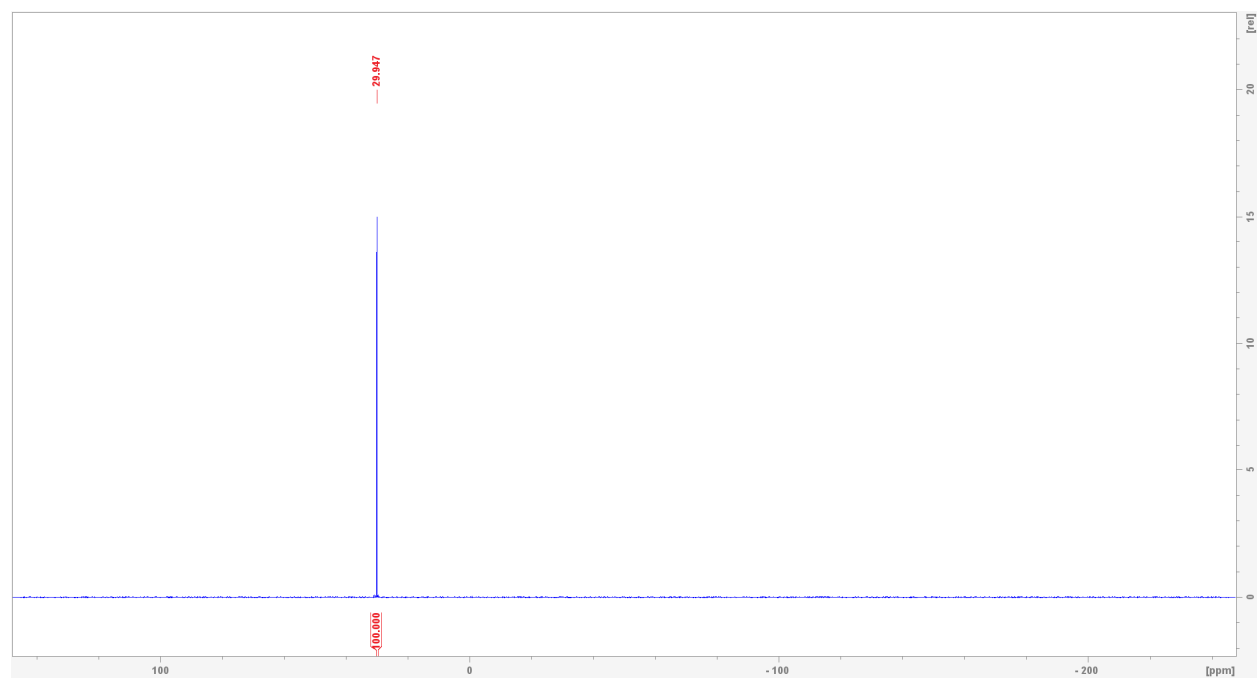
Compound **2c**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

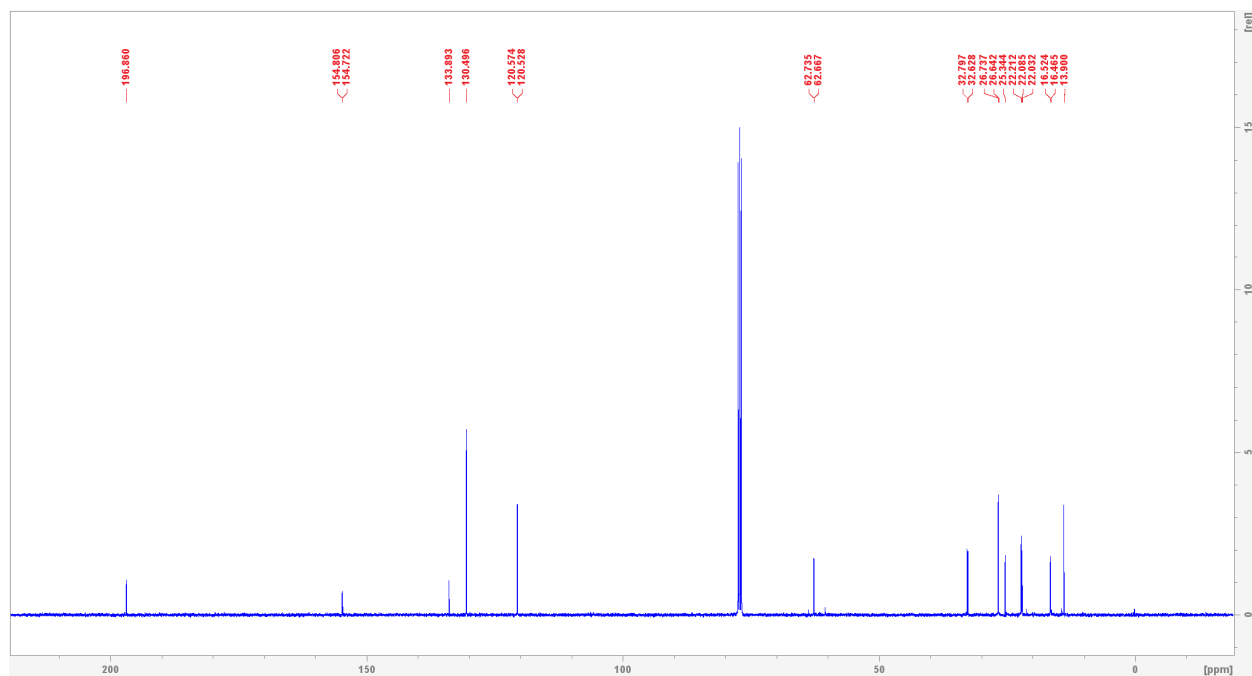
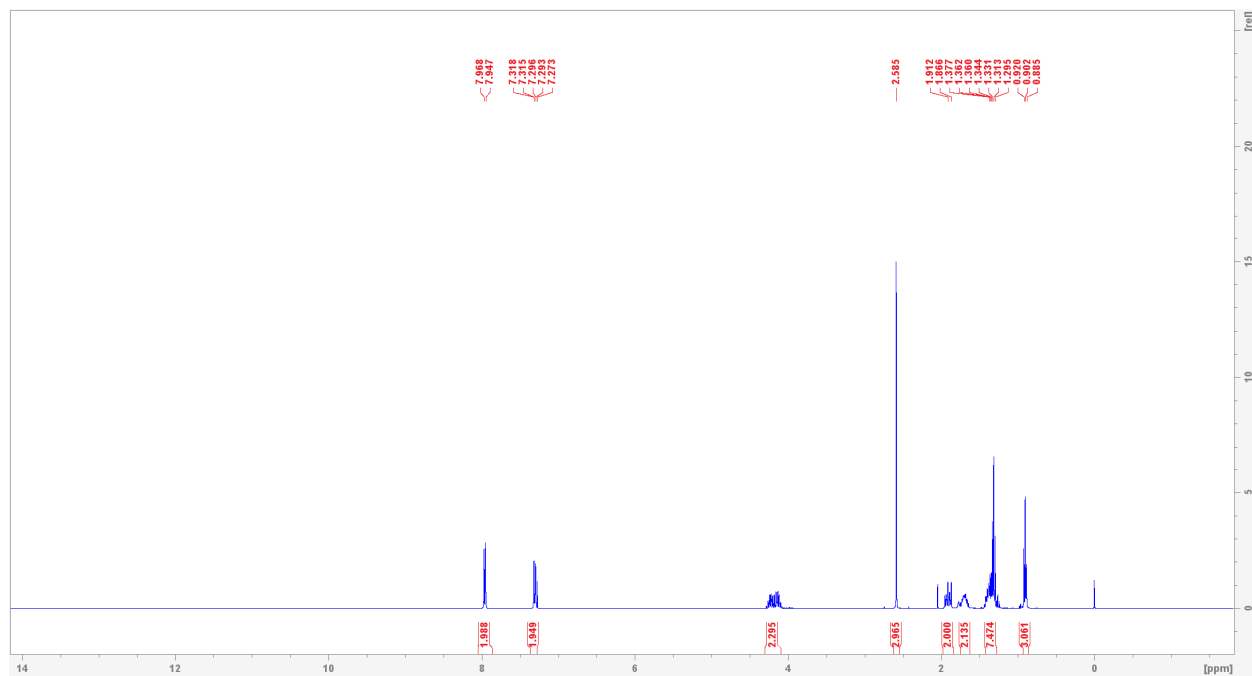


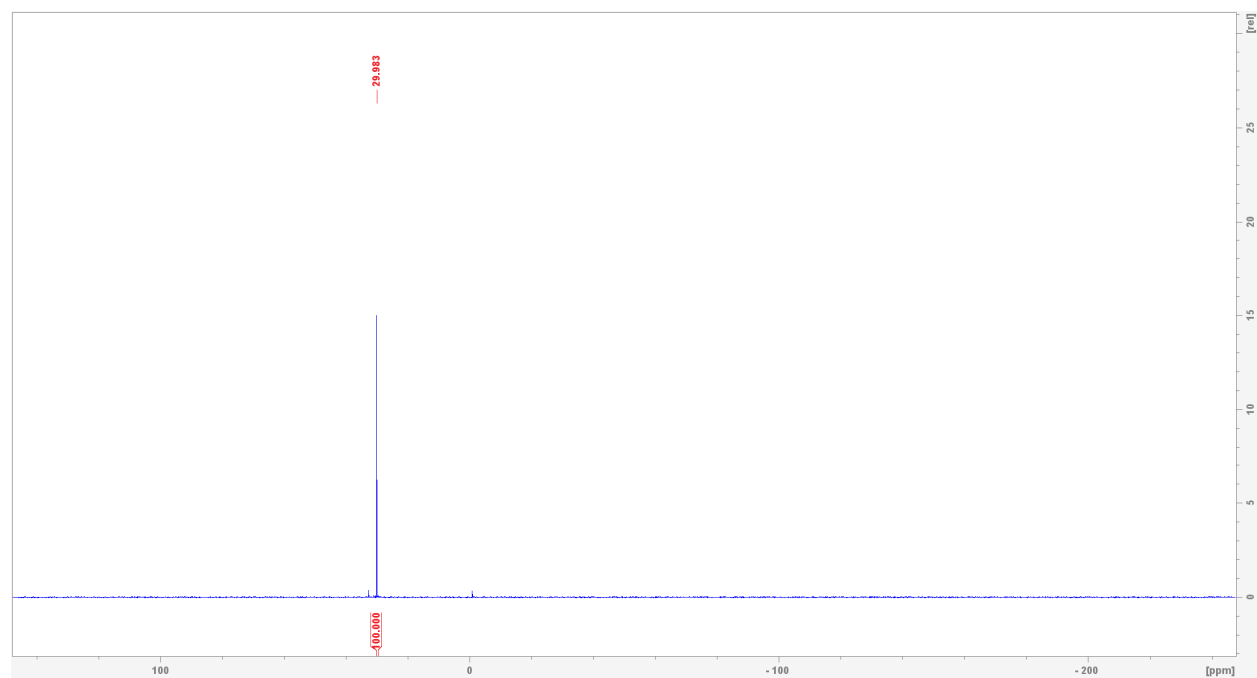


Compound **2d**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

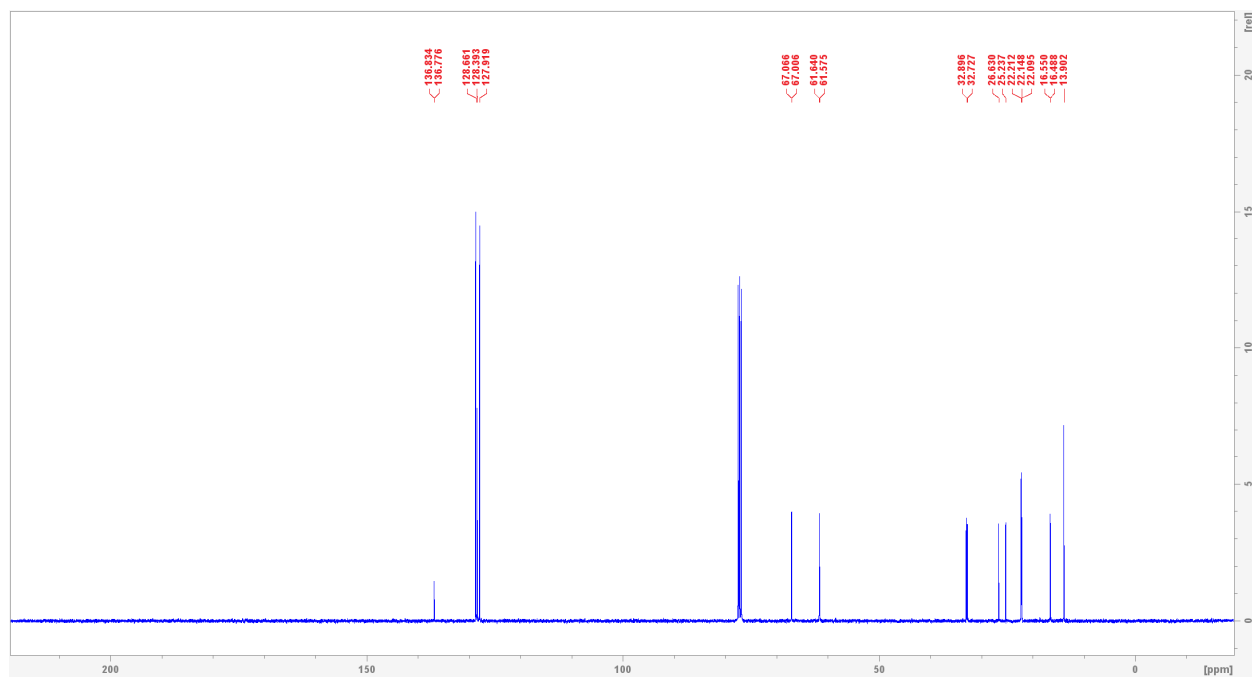
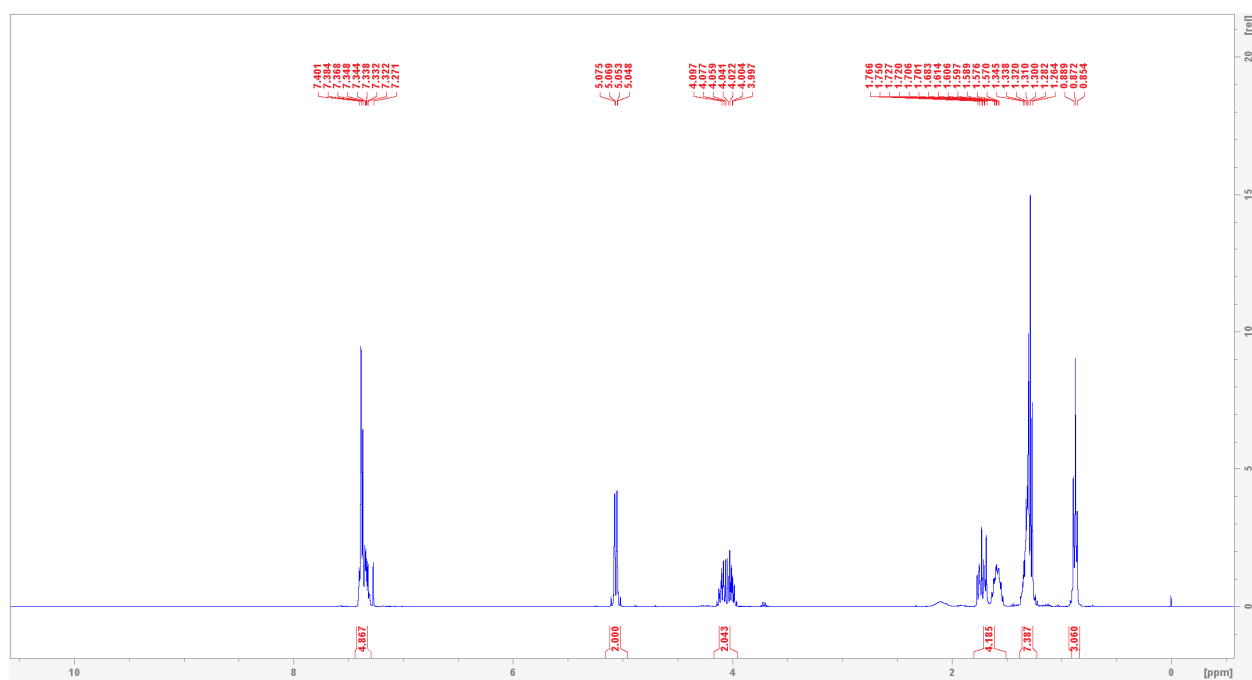
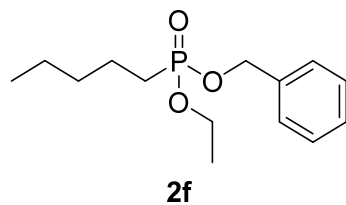


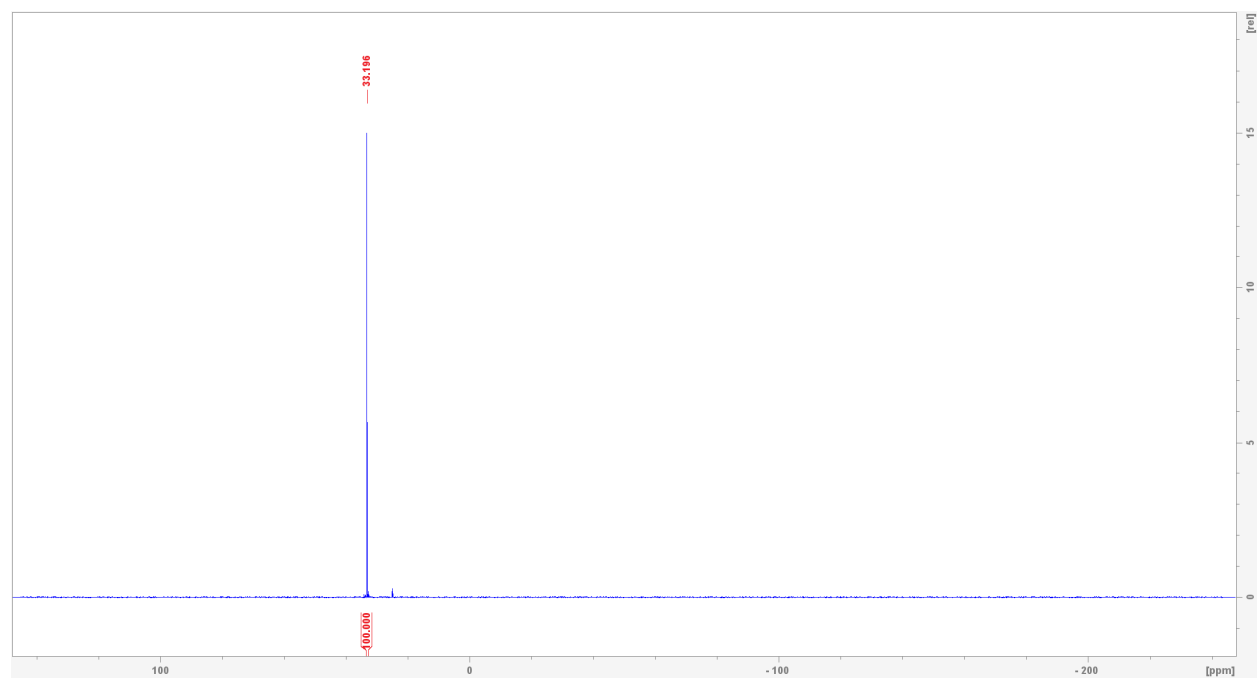


CCCCCP(=O)(OCC)Oc1ccc(cc1)C(=O)C

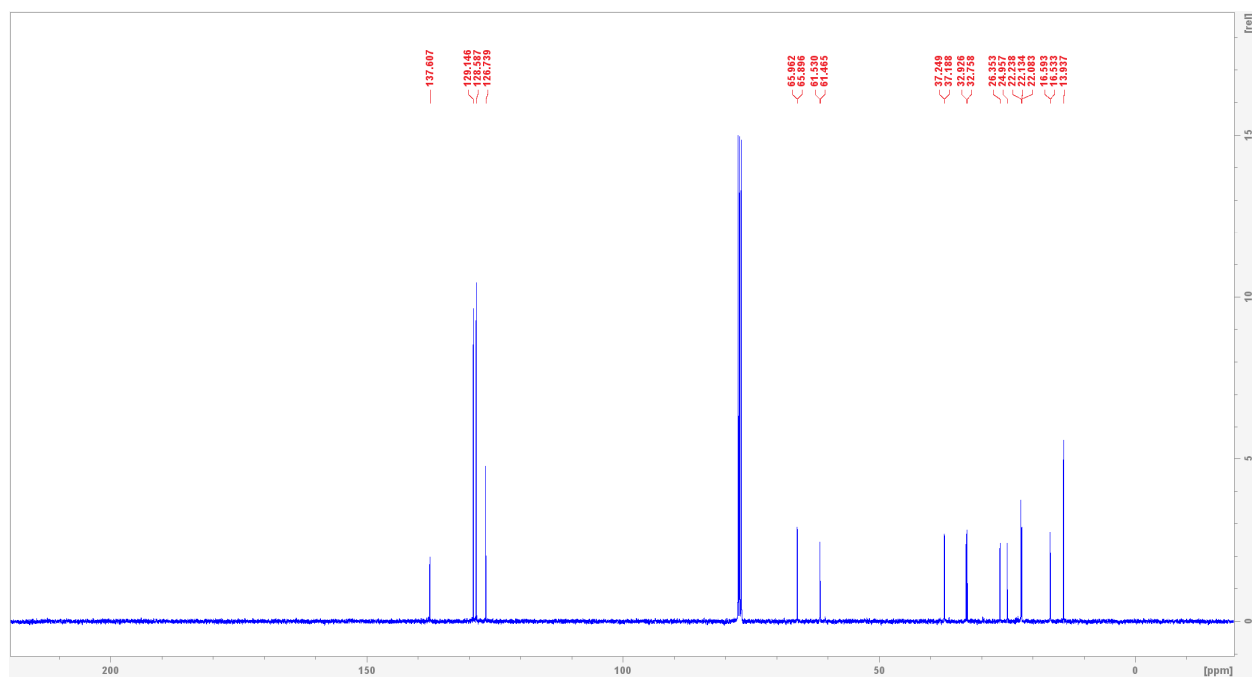
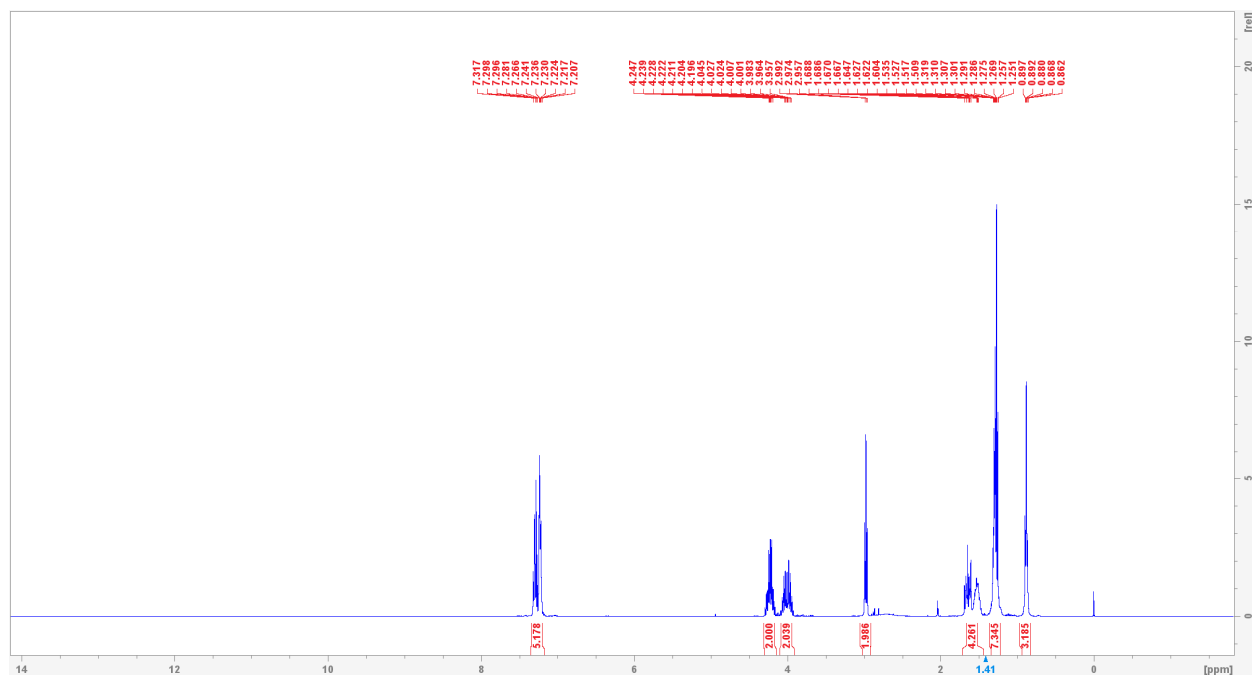
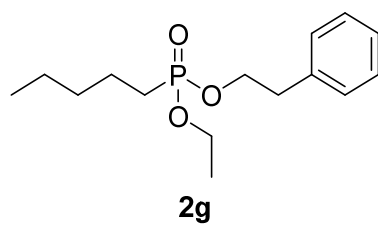


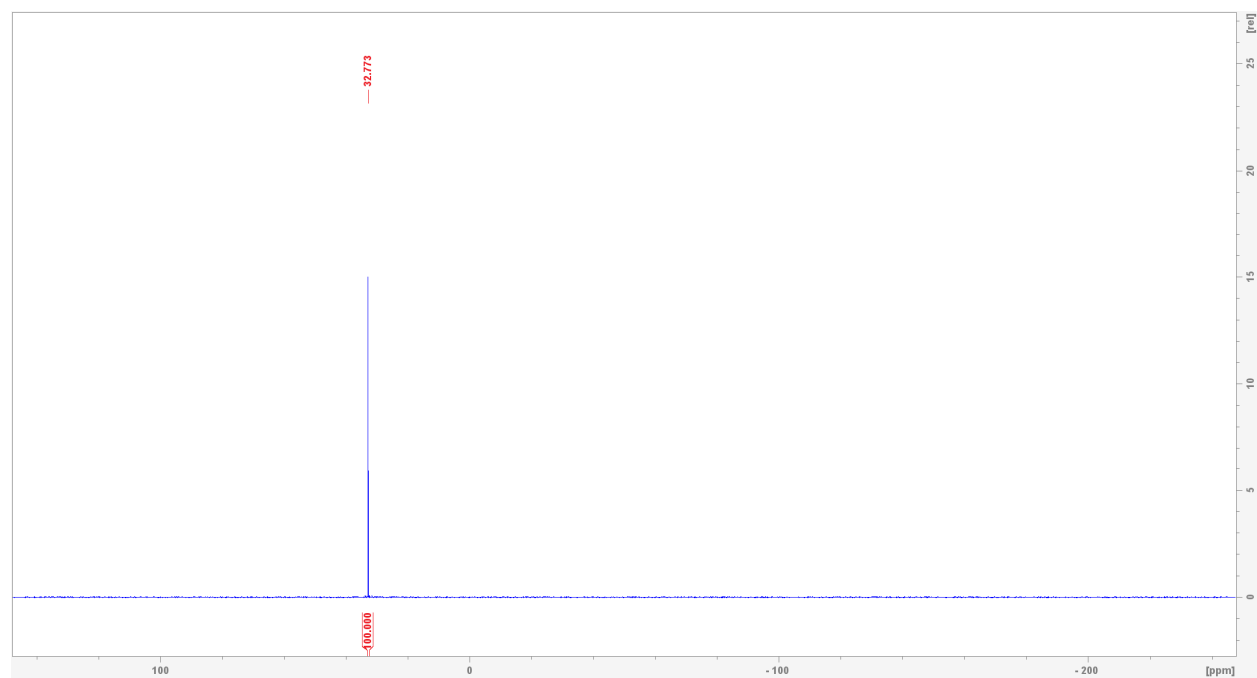
Compound **2f**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).



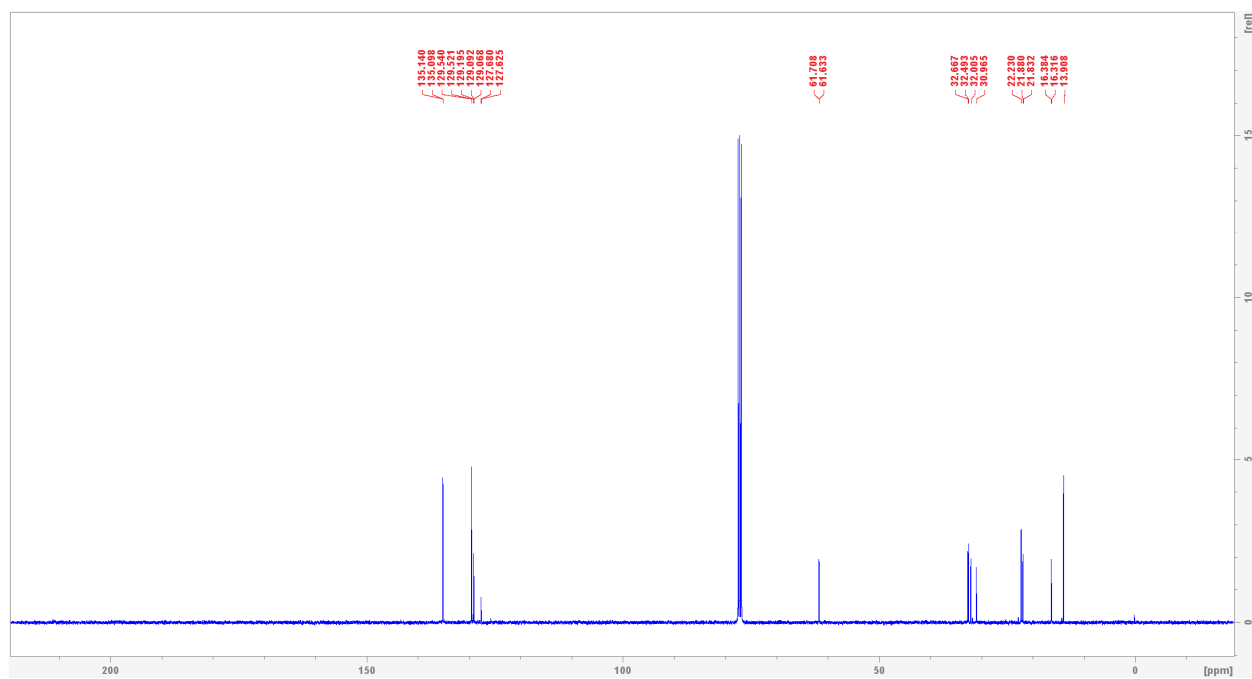
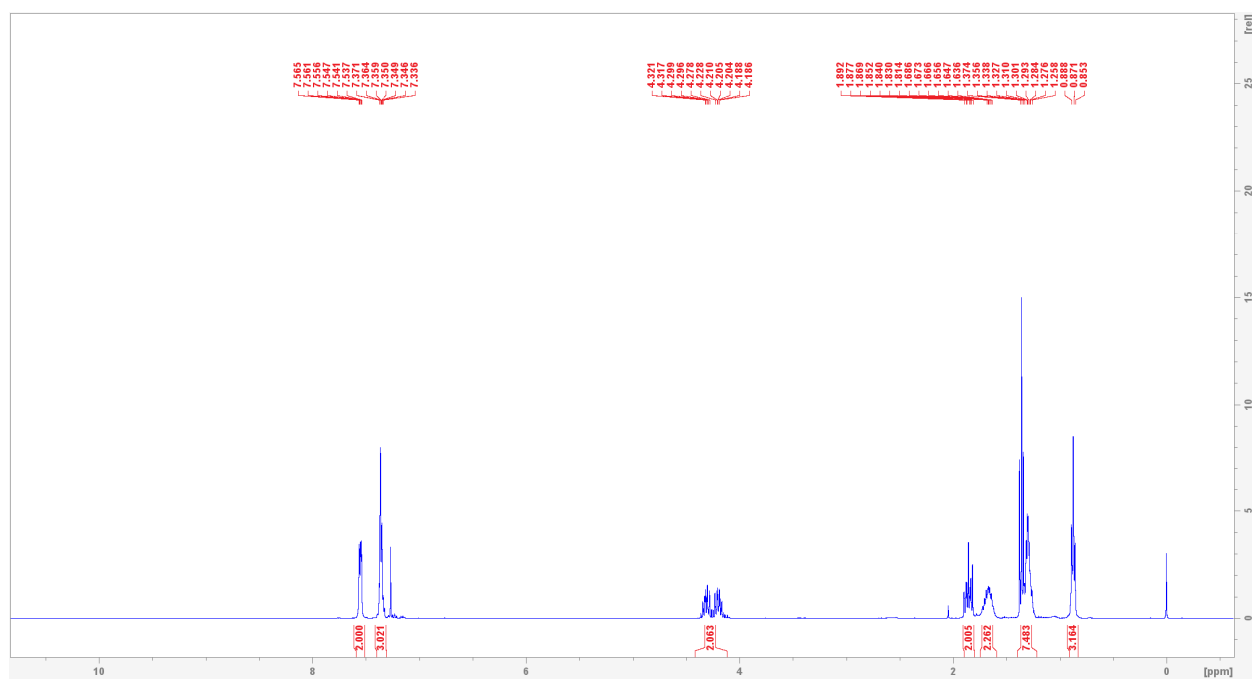
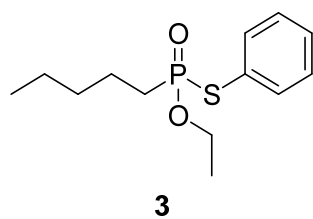


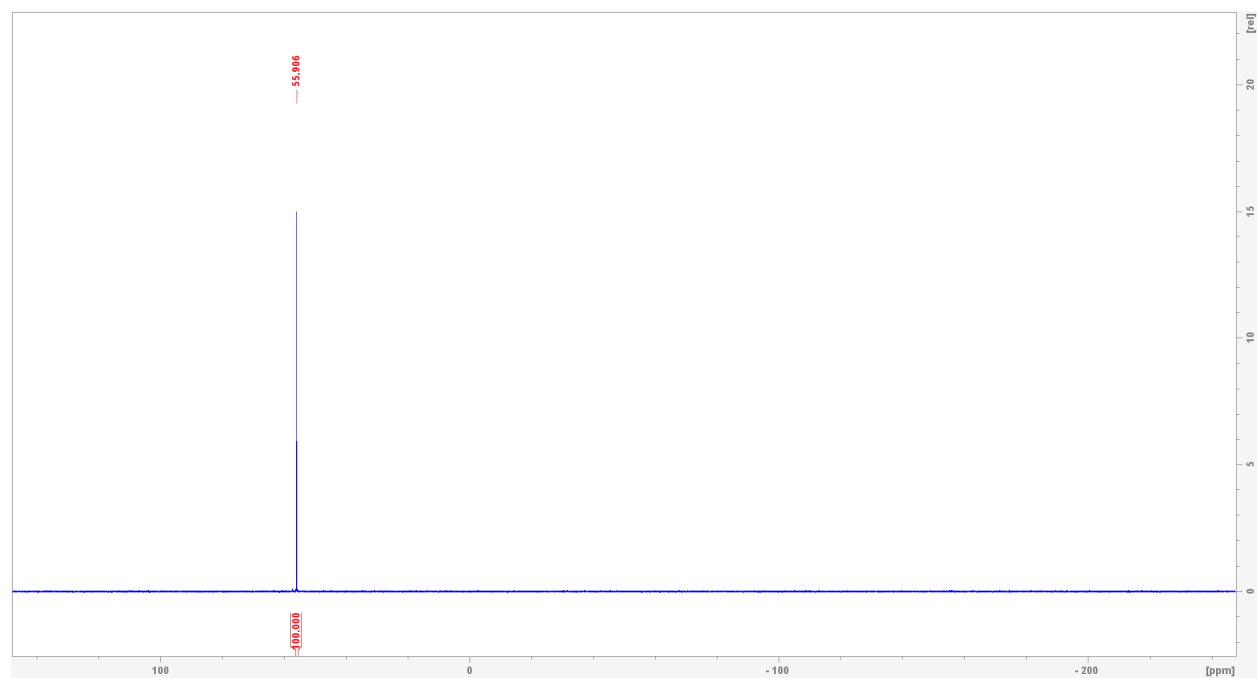
Compound **2g**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).





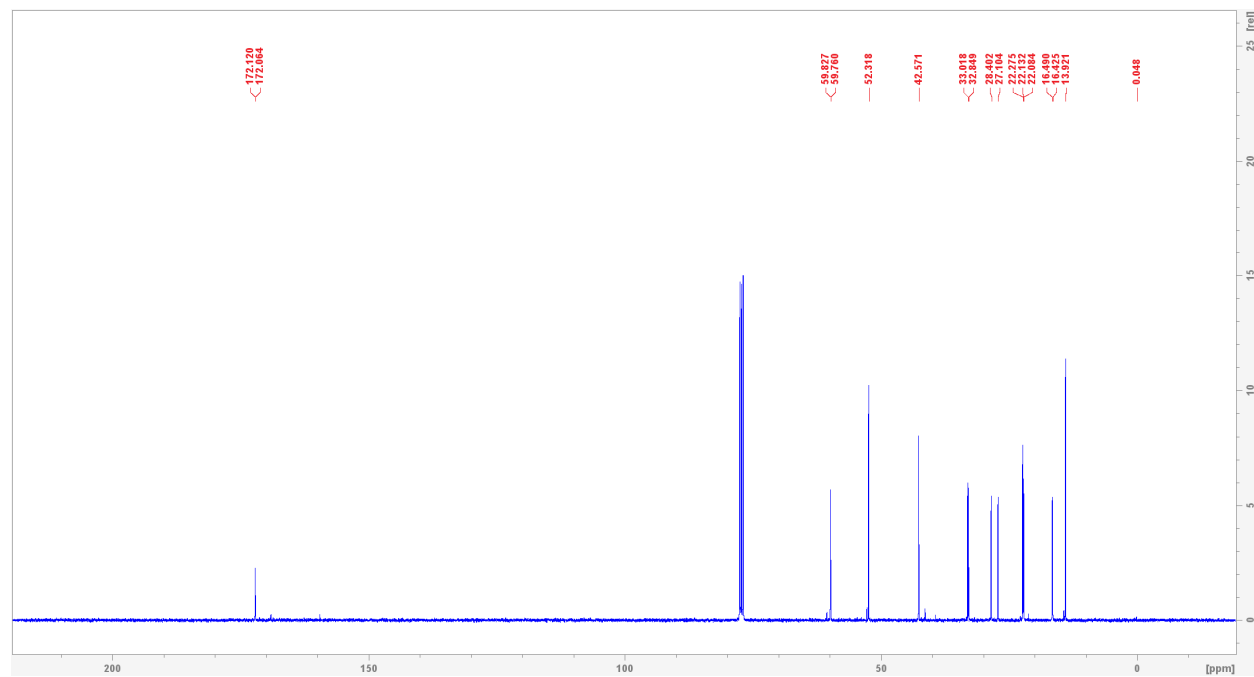
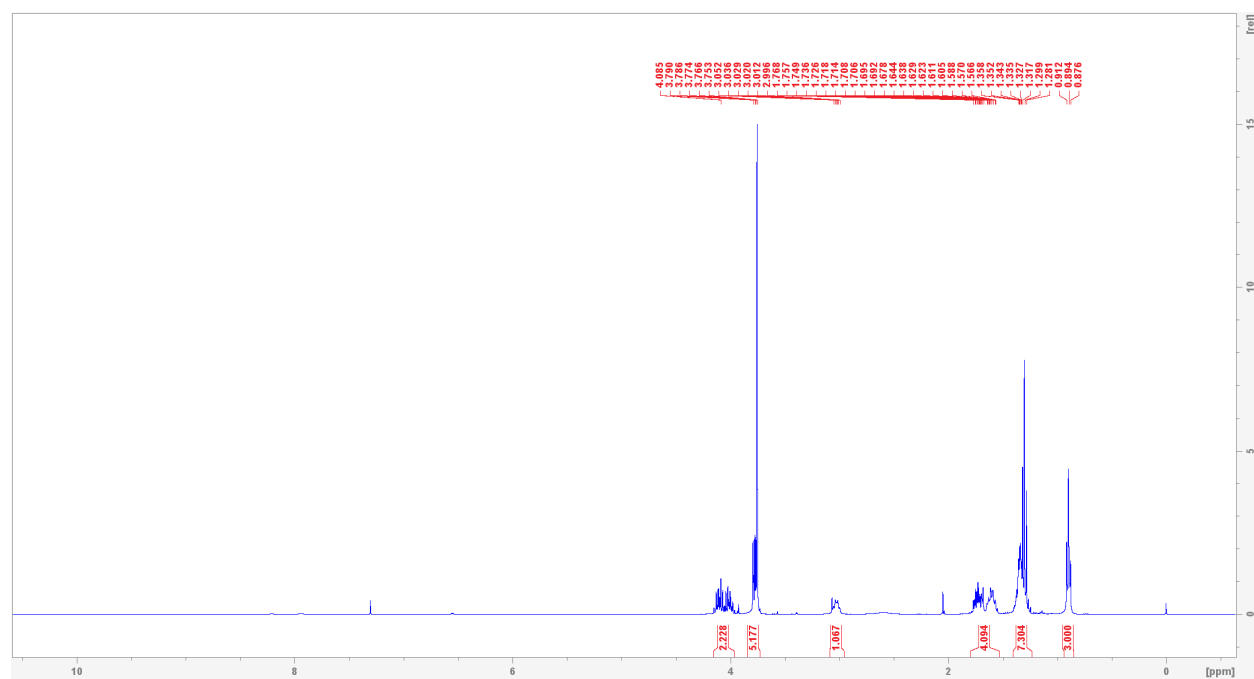
Compound **3**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

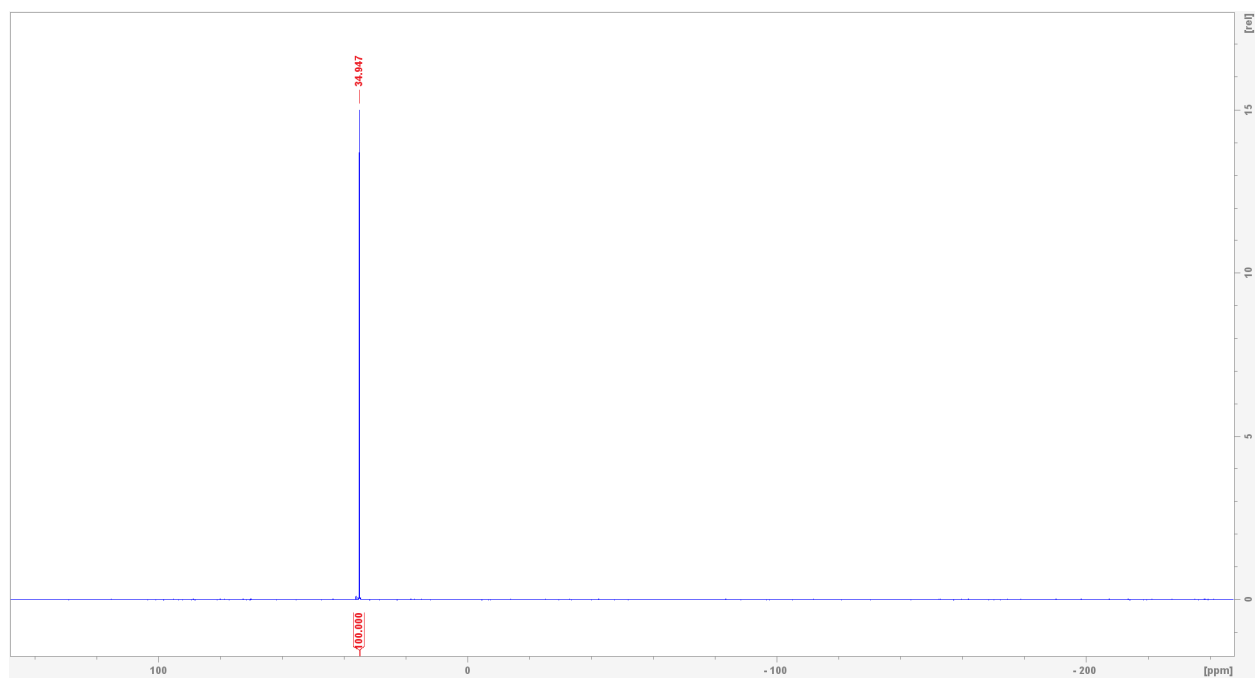




CCCCCP(=O)(OCC)NC(=O)OC

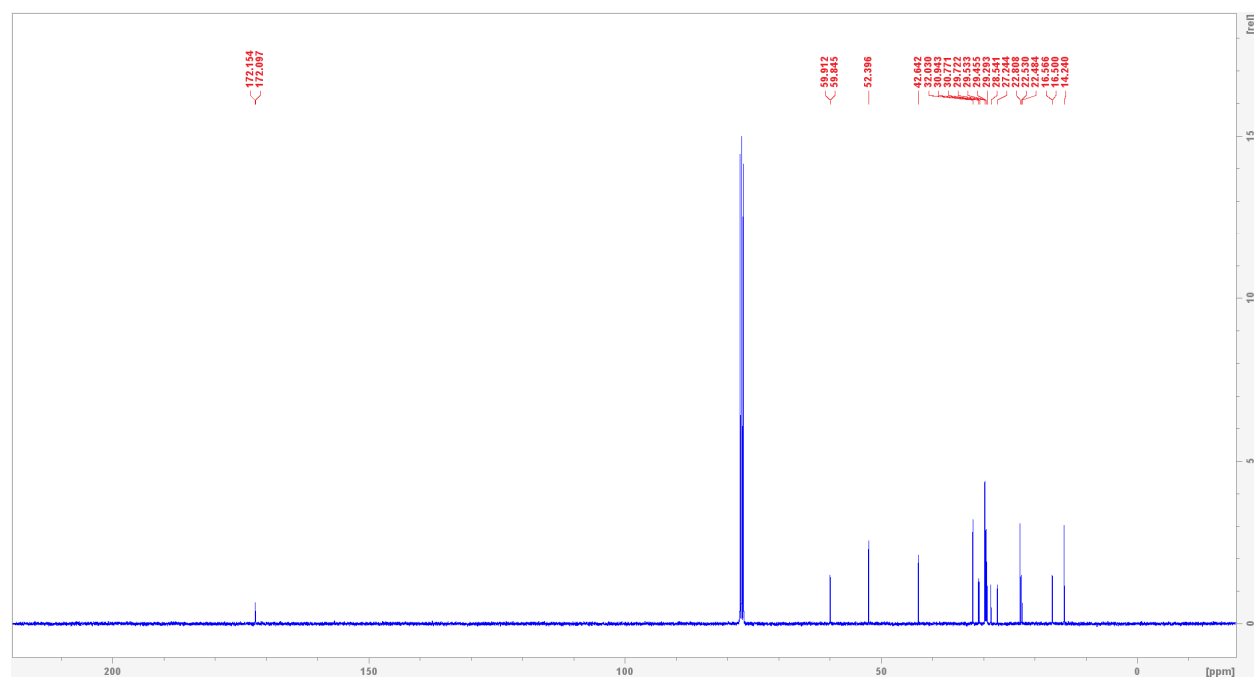
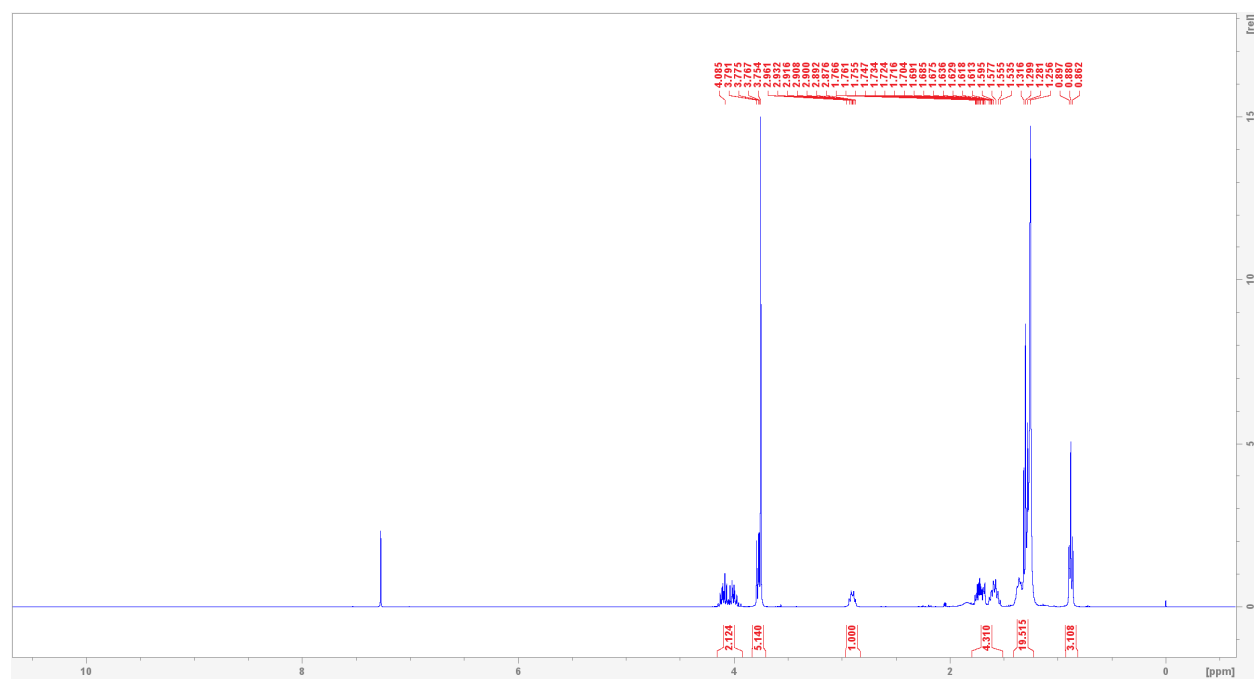
4a

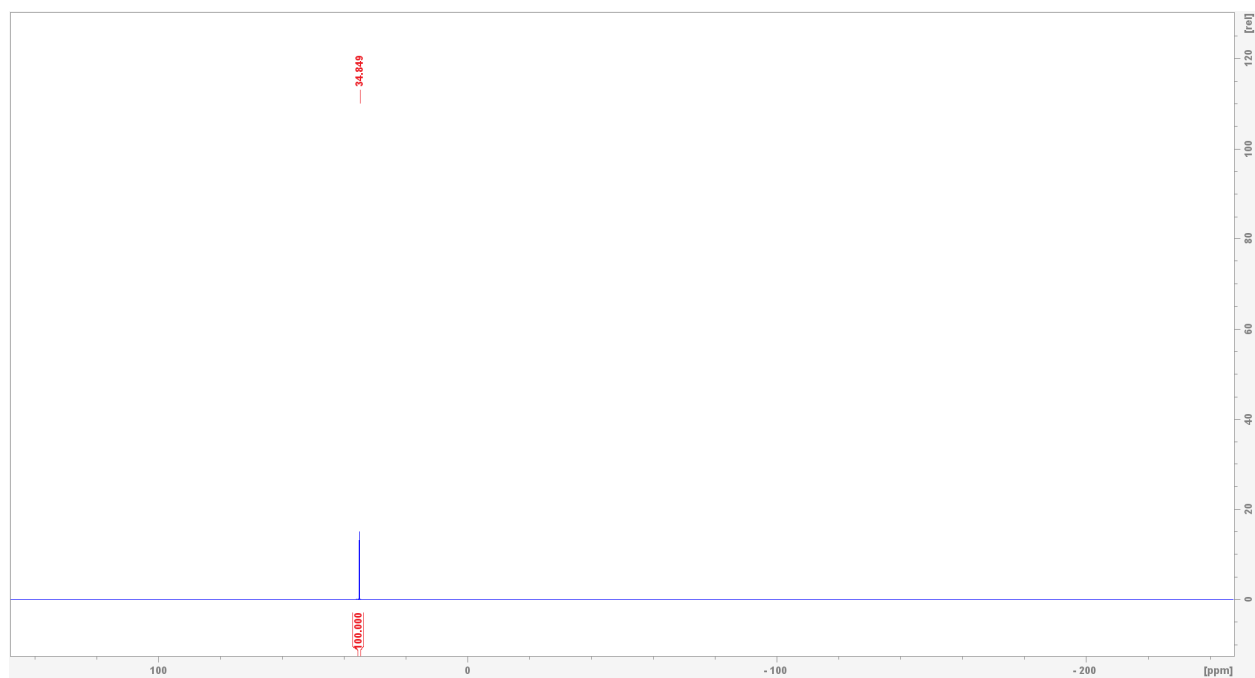




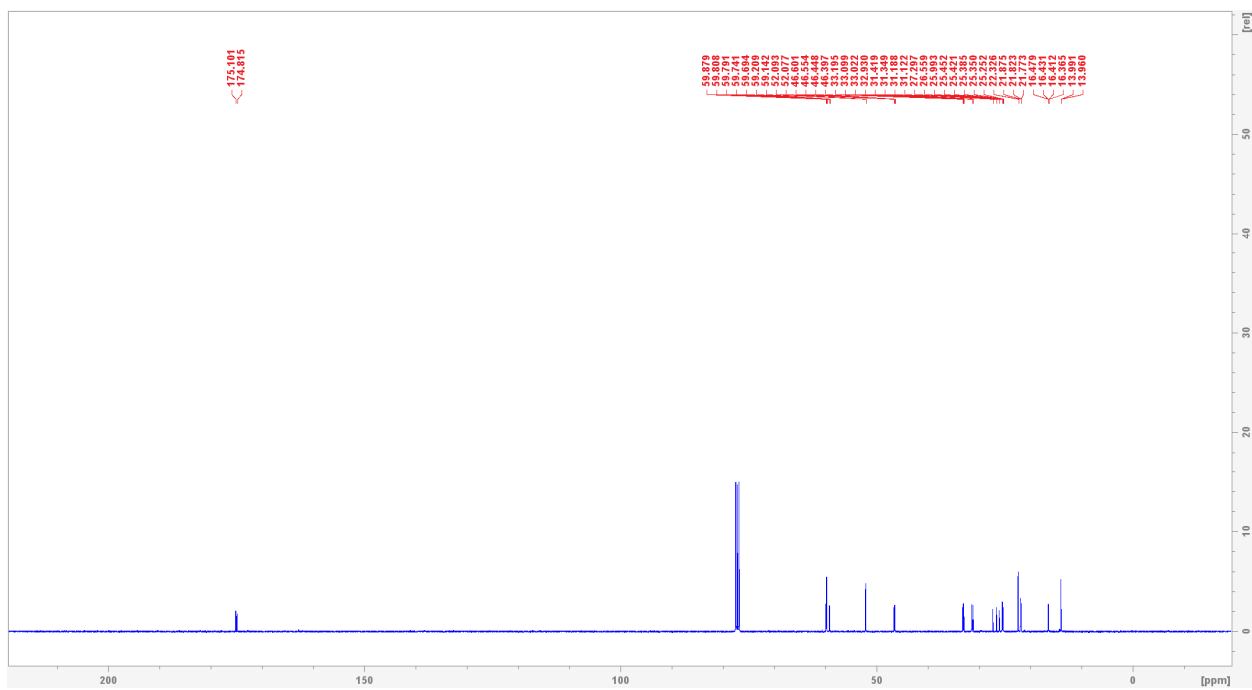
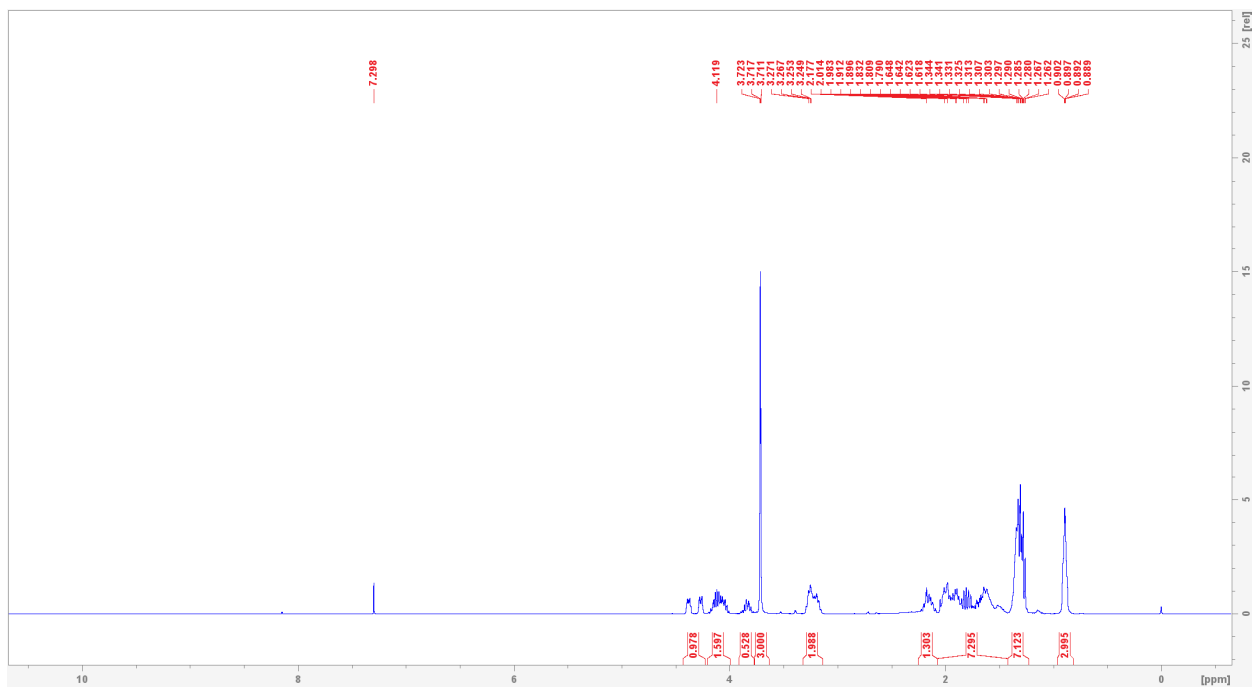
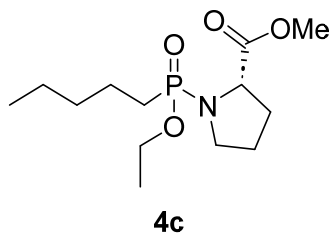
CCCCCCCCCCCCCP(=O)(OCC)NC(=O)OC

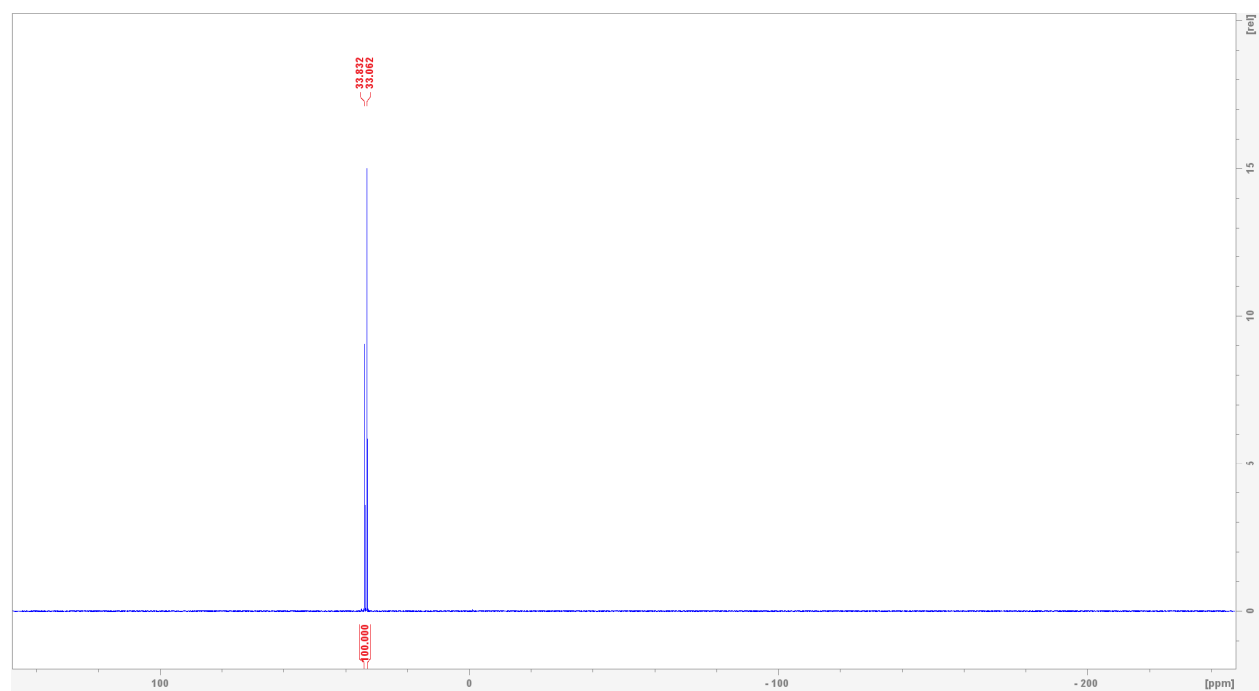
4b



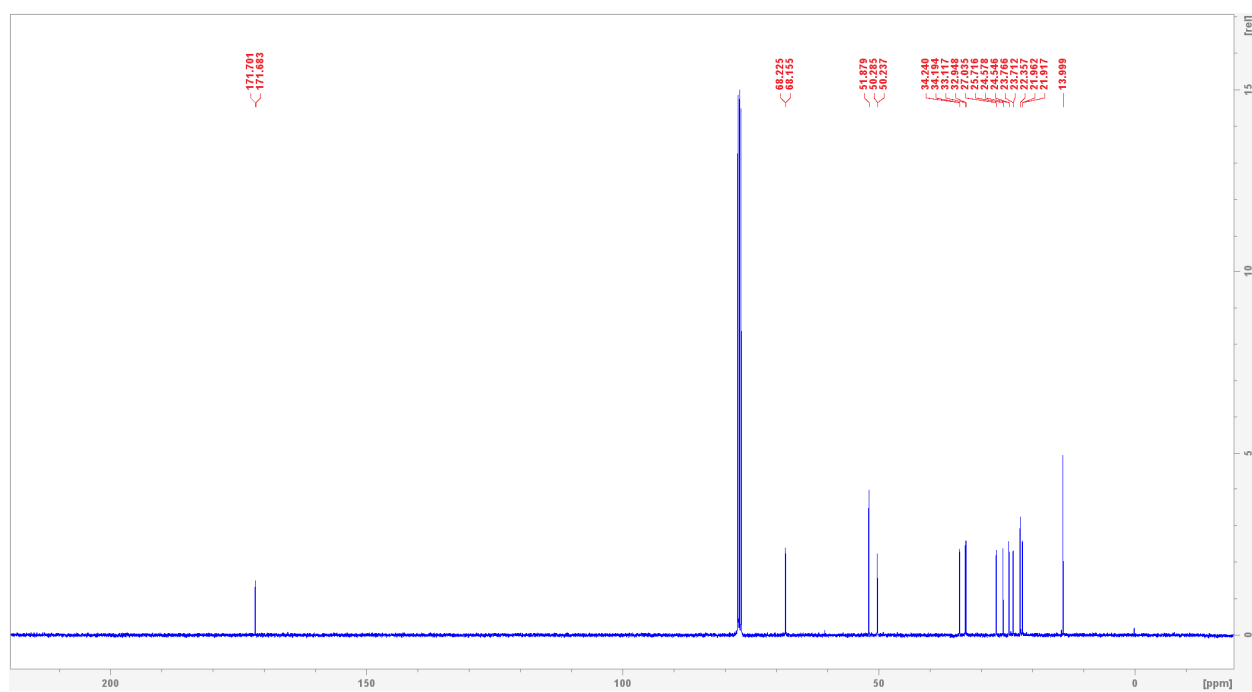
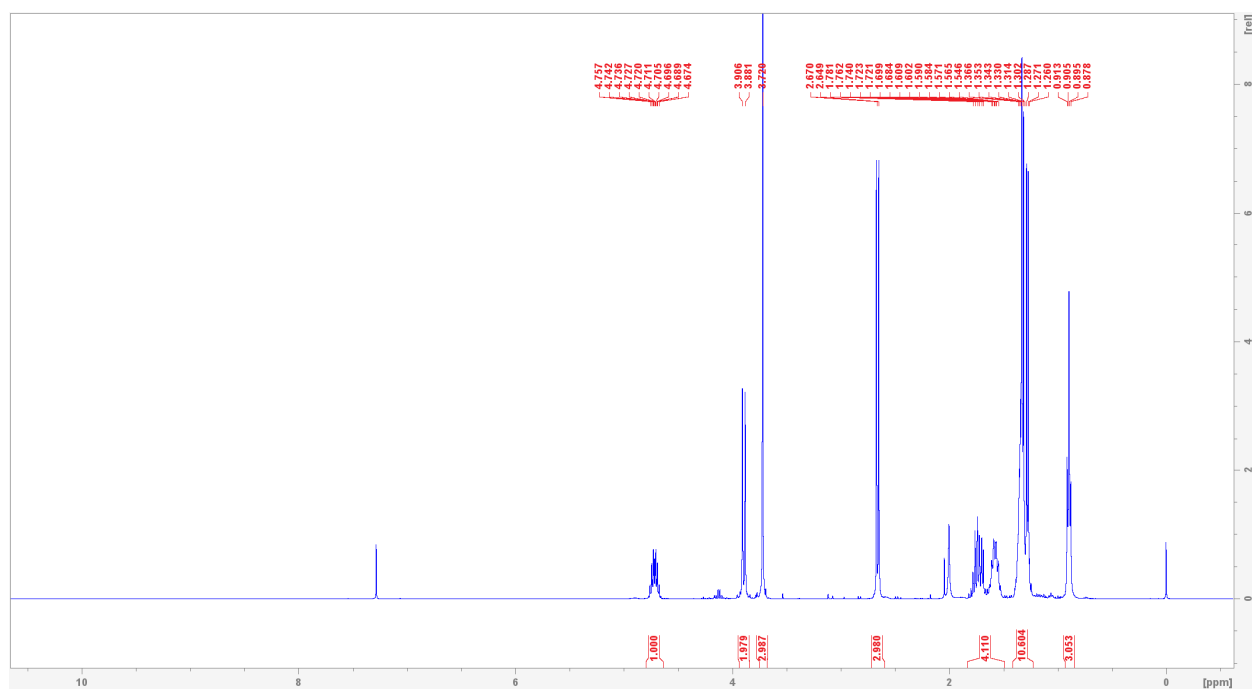
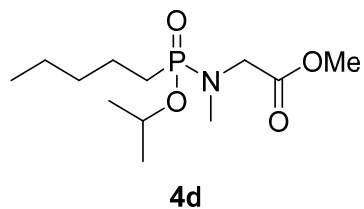


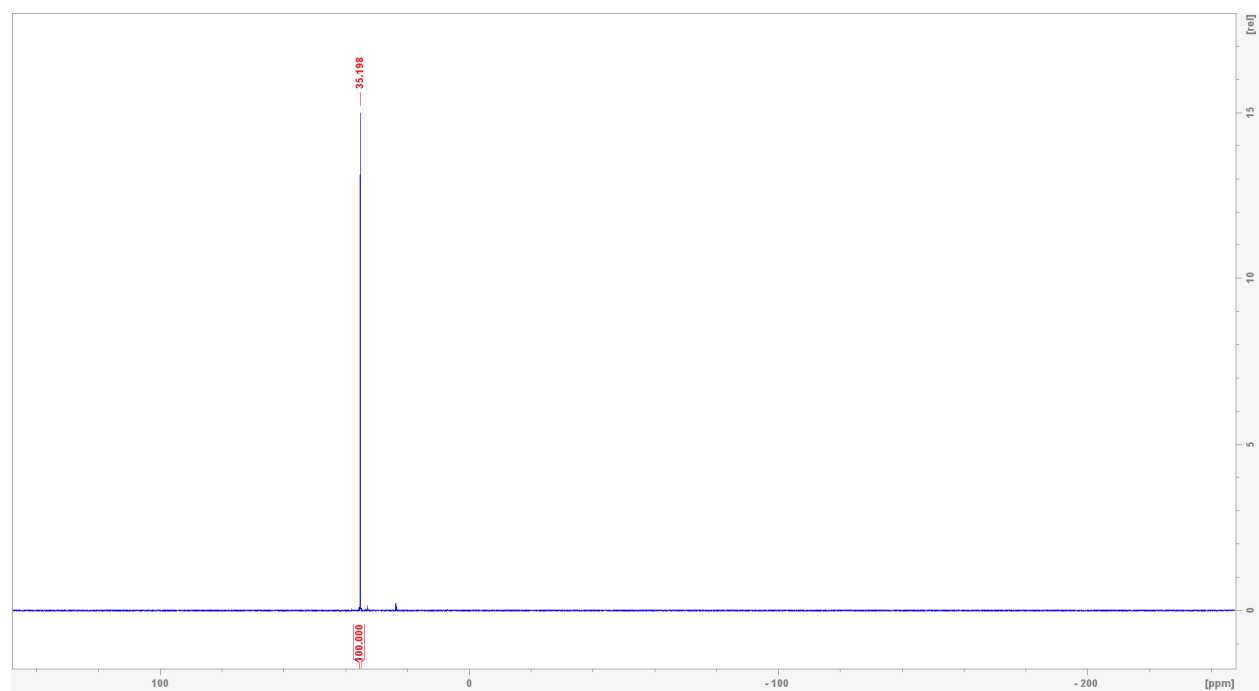
Compound **4c**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).



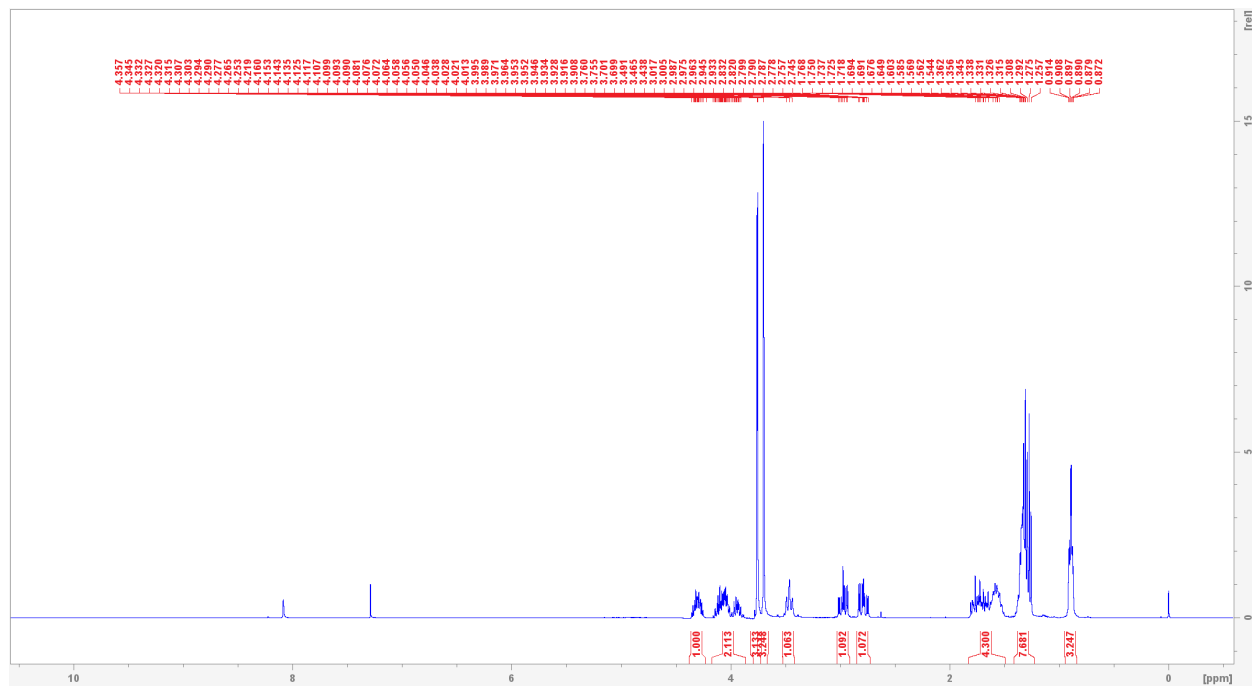
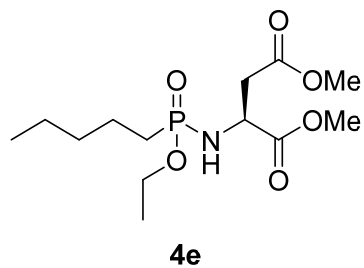


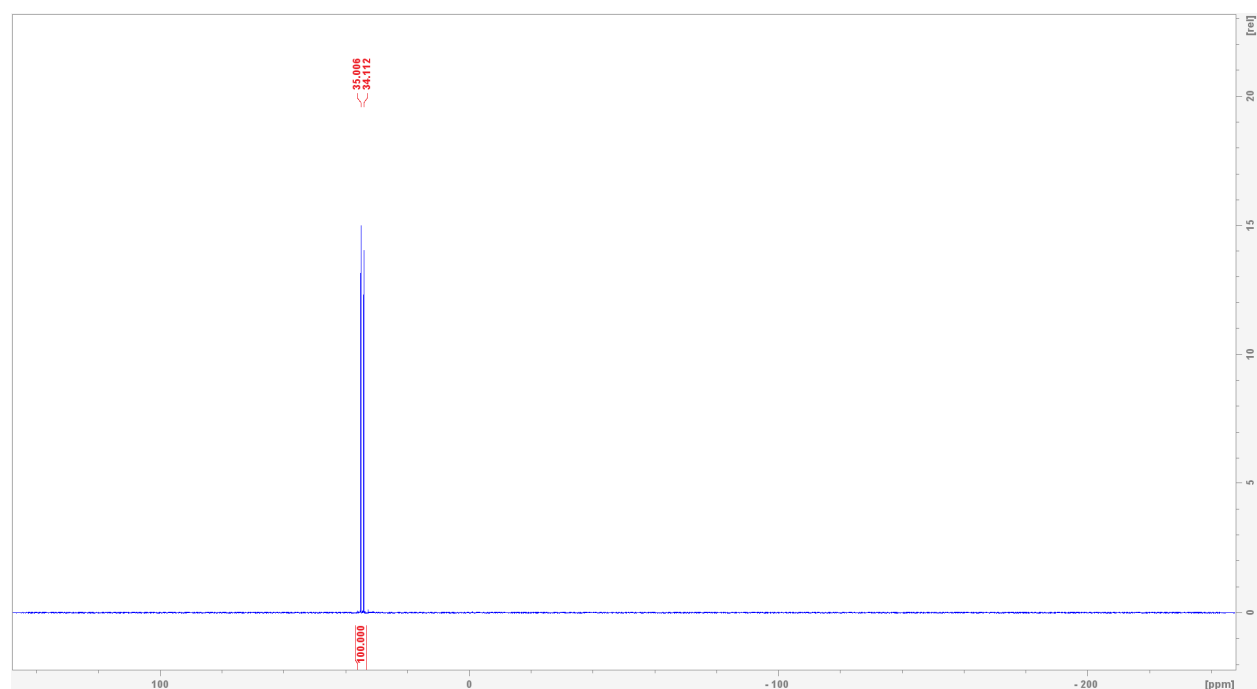
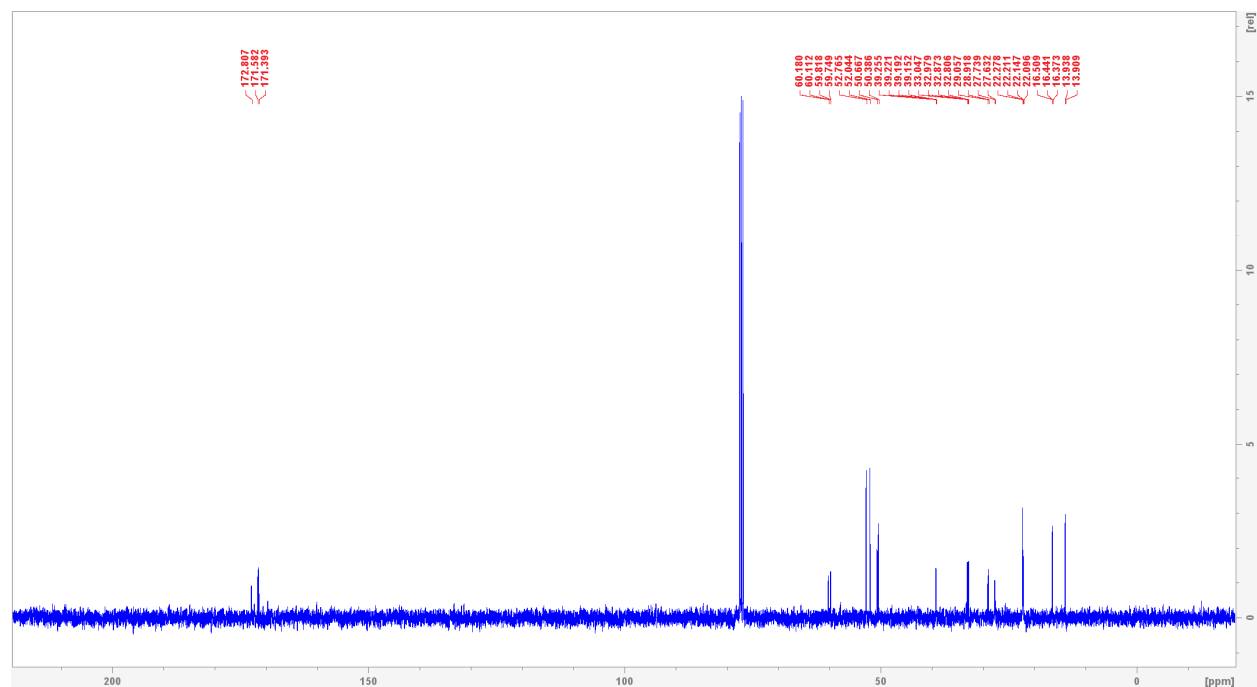
Compound **4d**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).



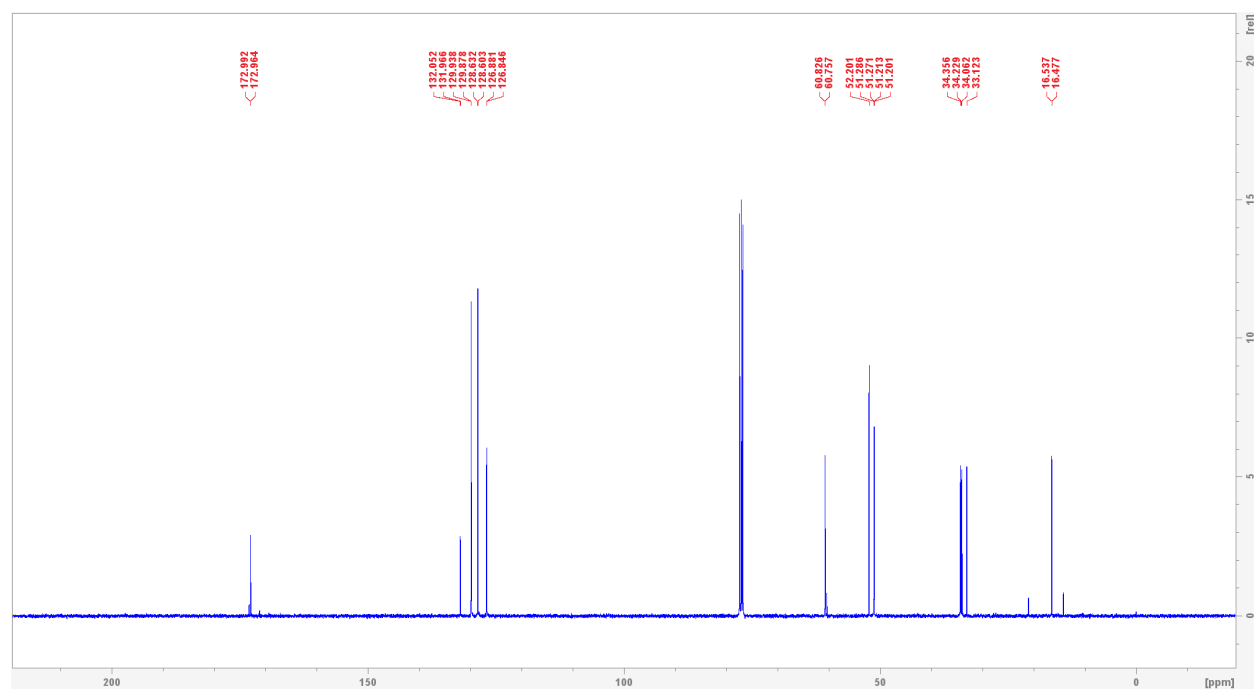
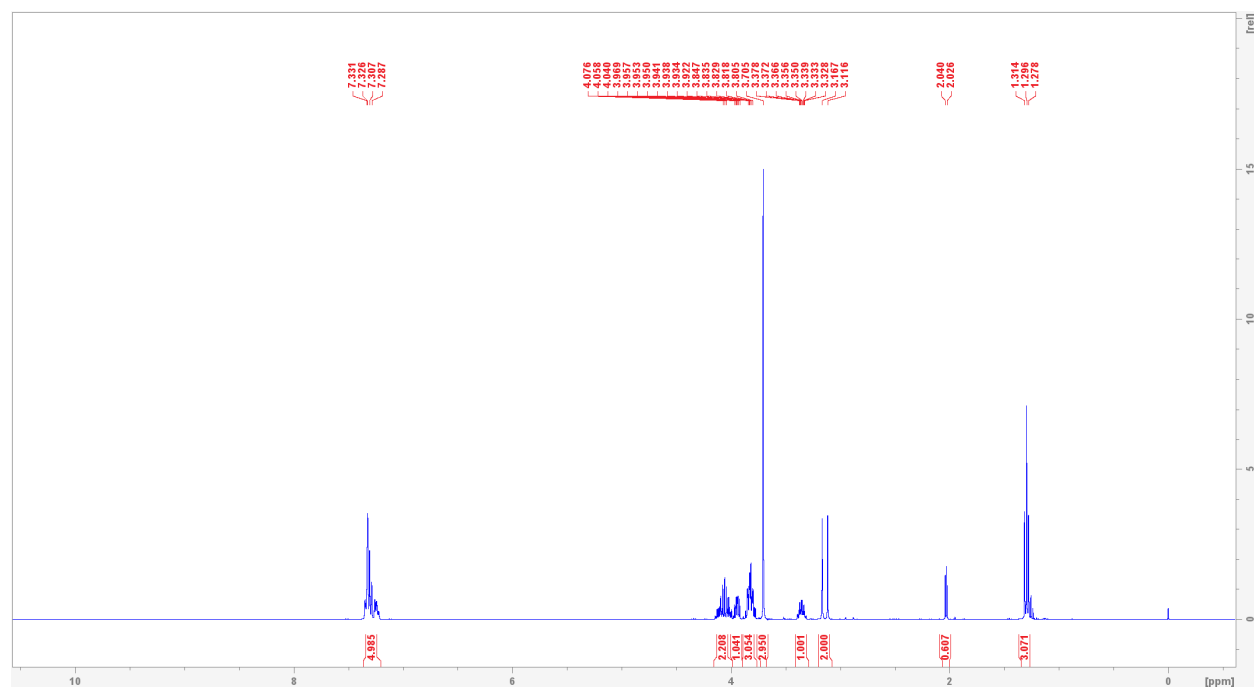


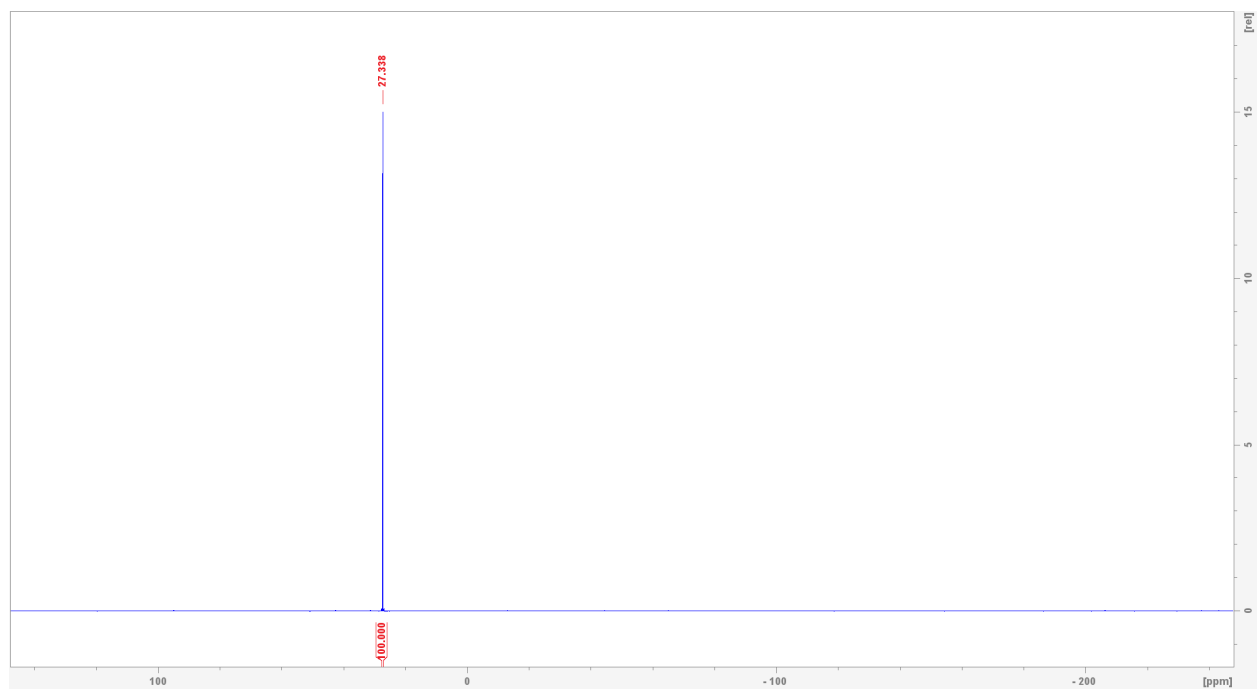
Compound **4e**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).



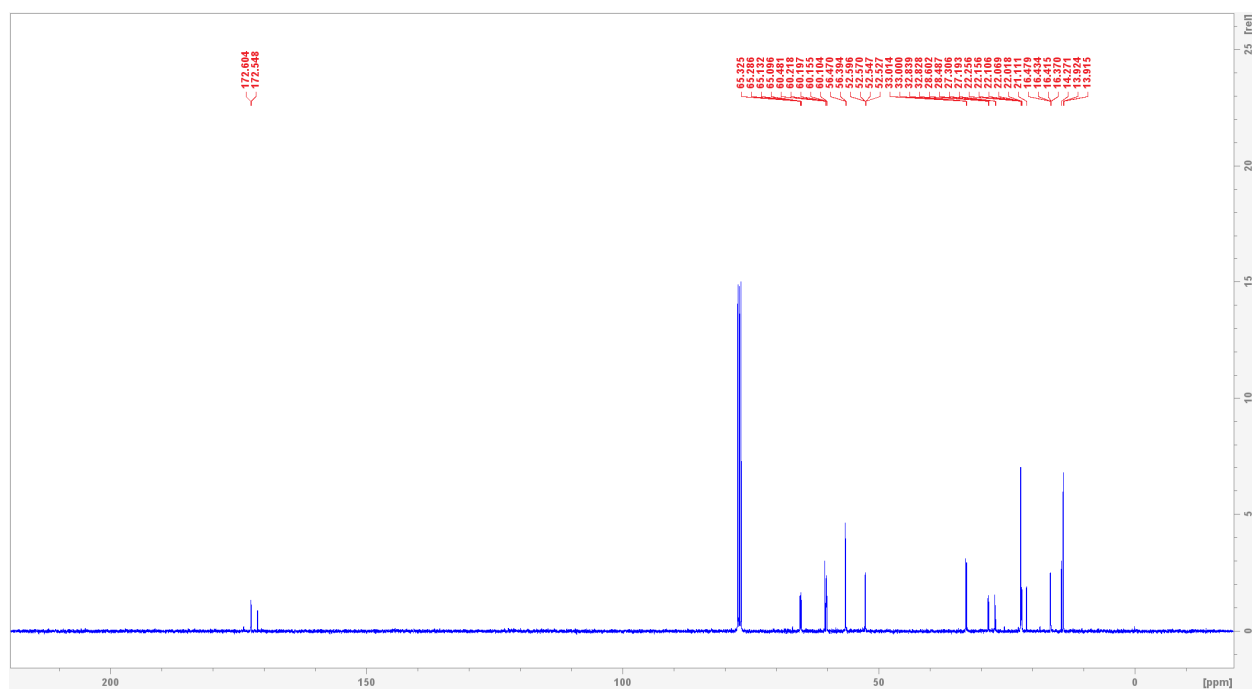
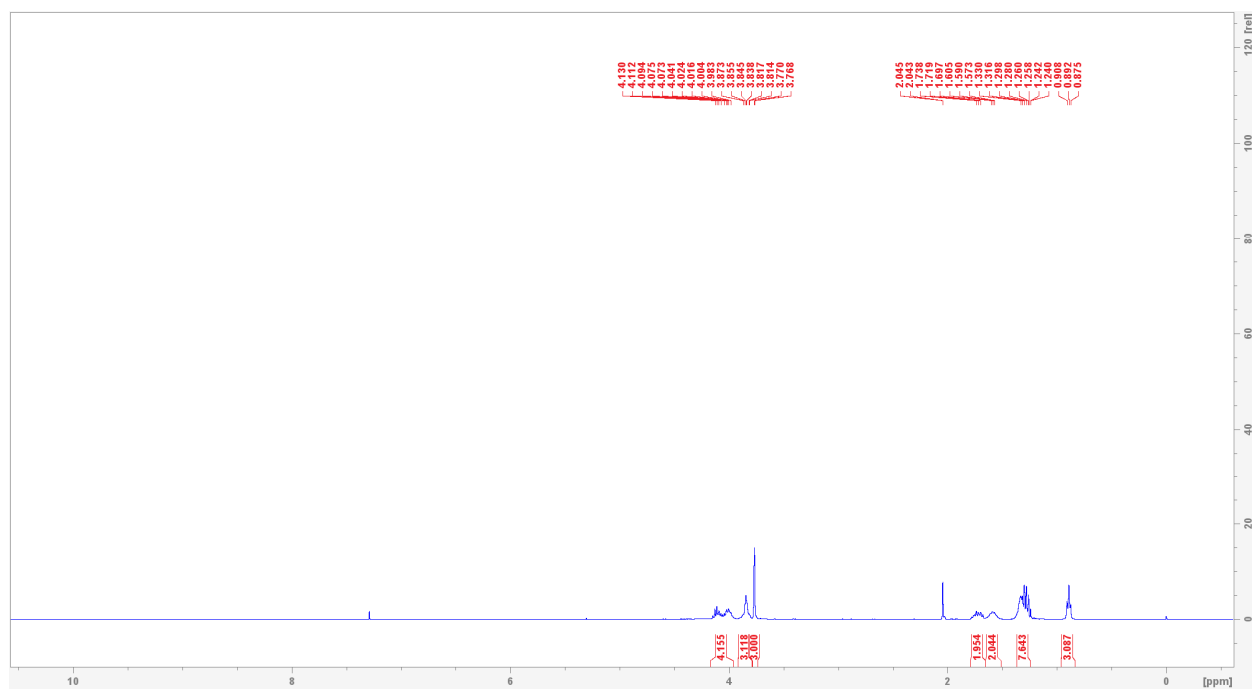
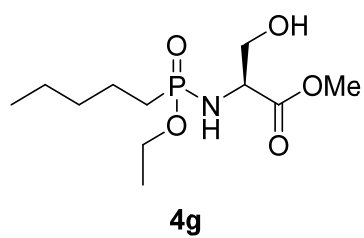


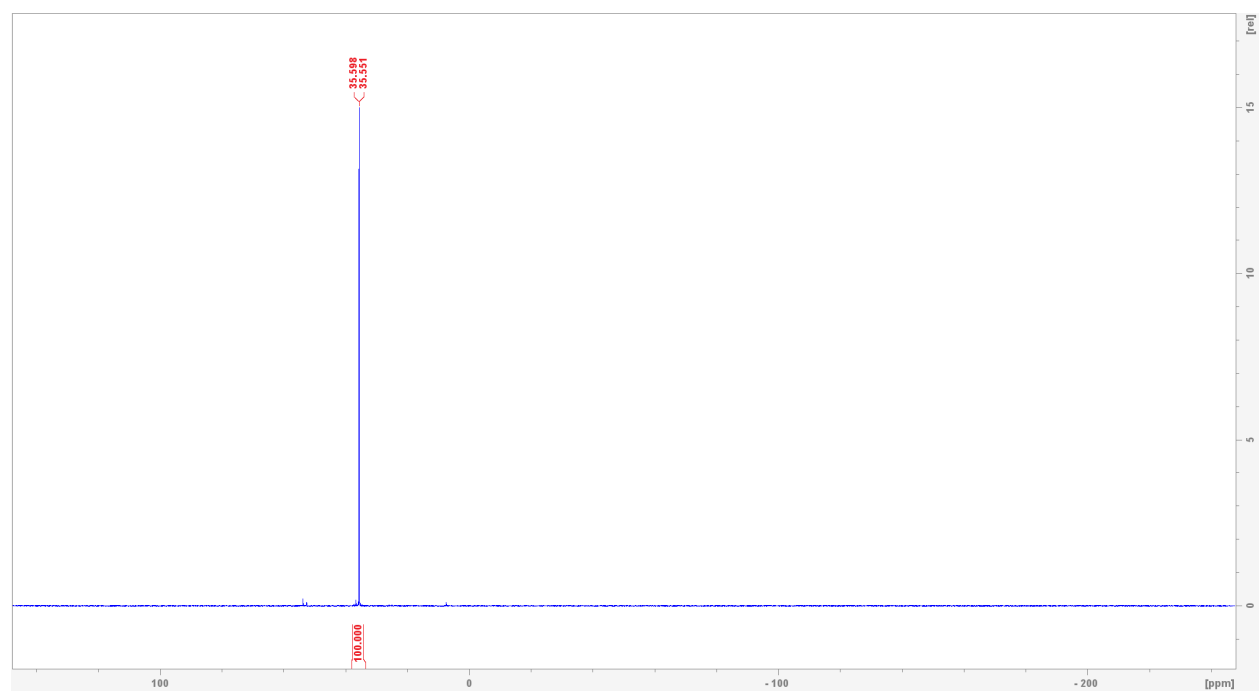
4f



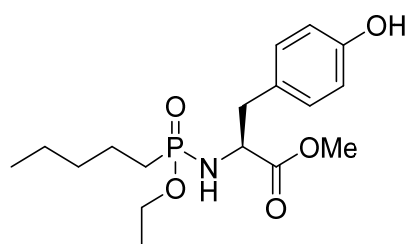


Compound **4g**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

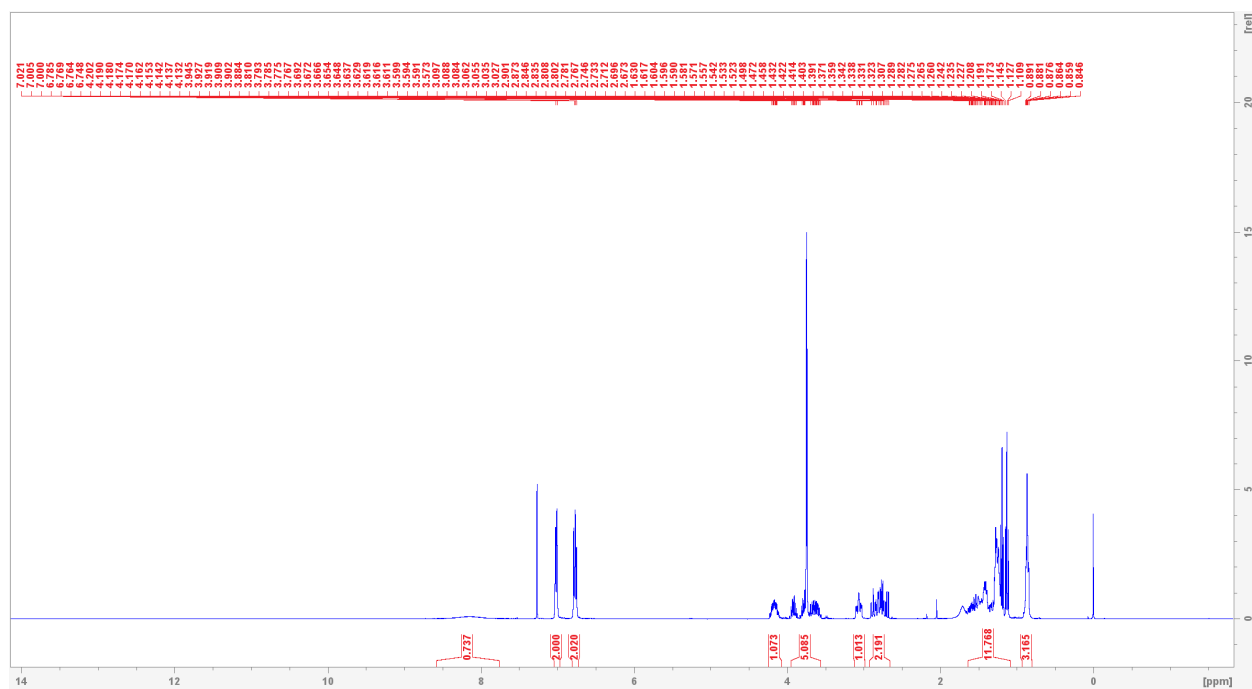


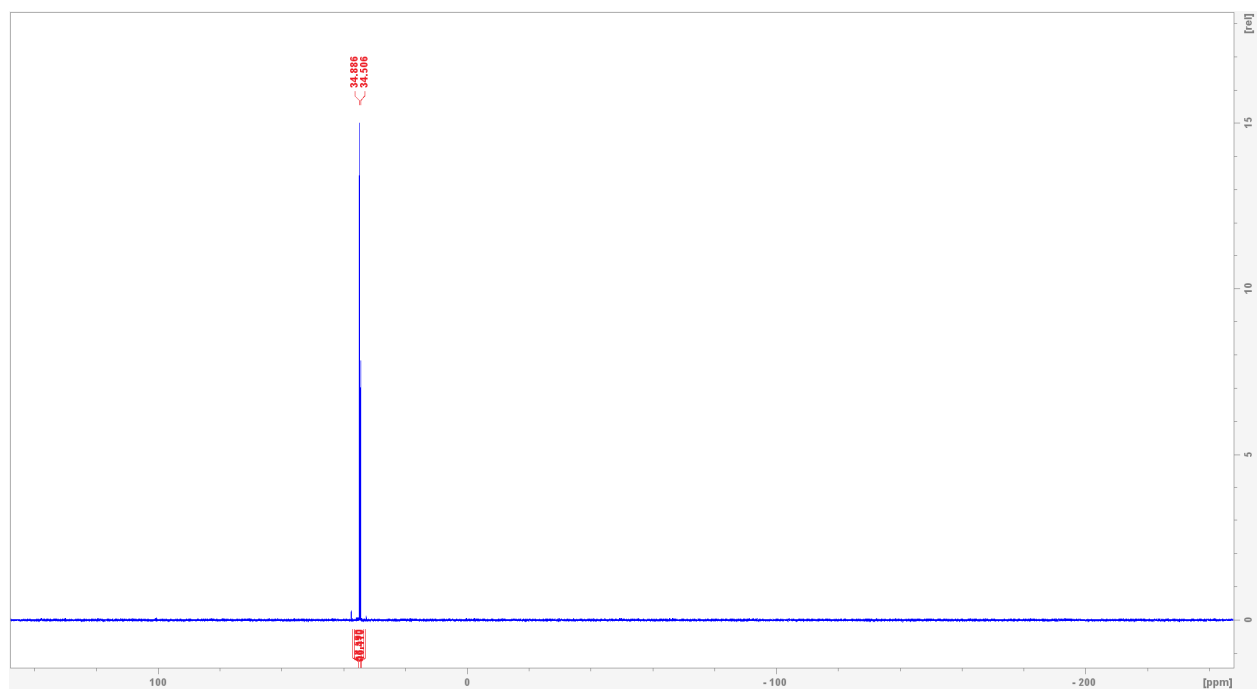
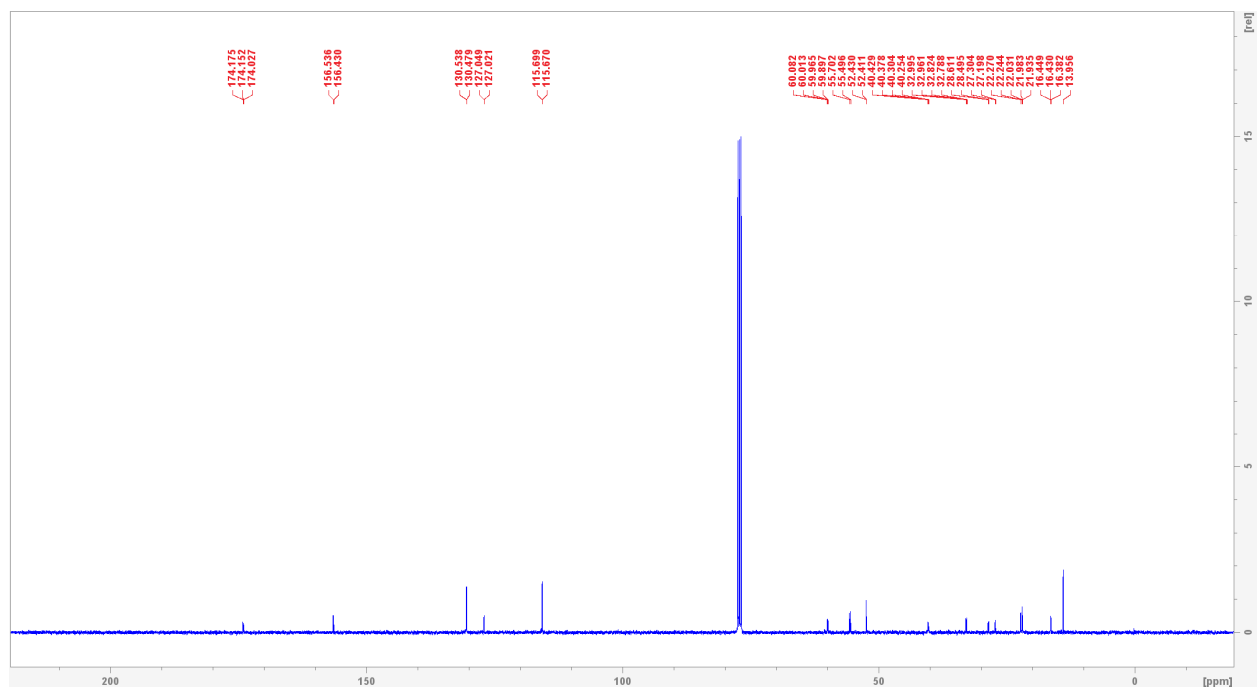


Compound **4h**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

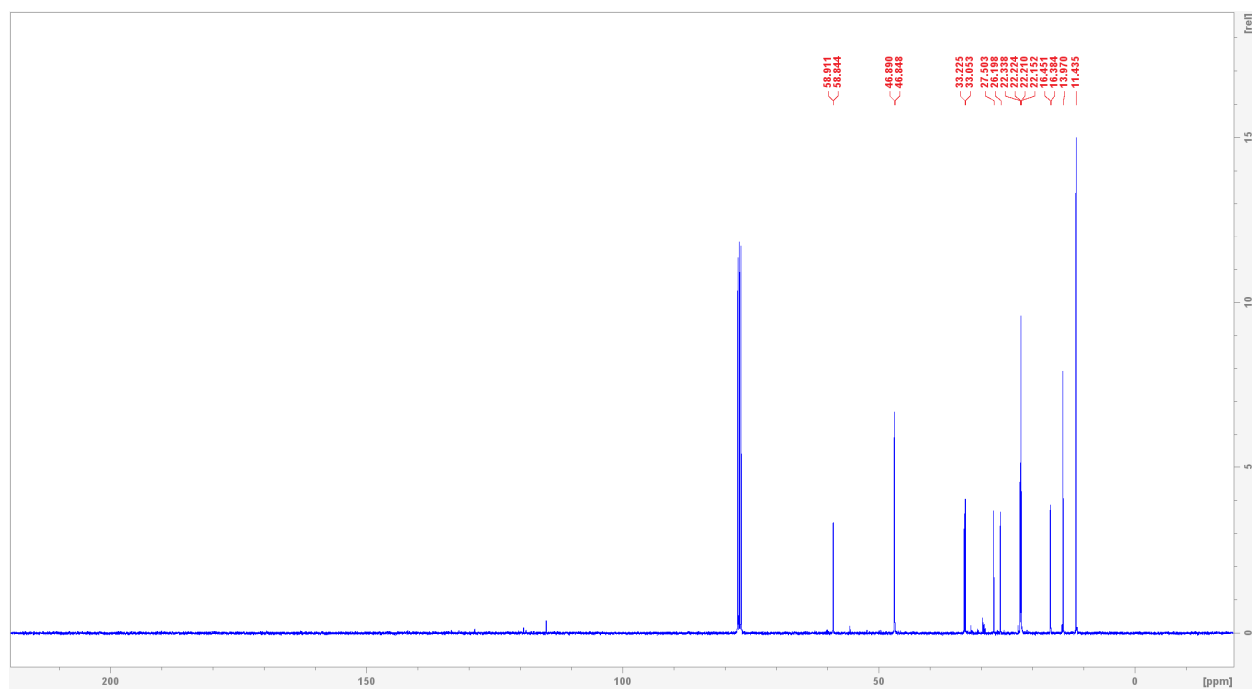
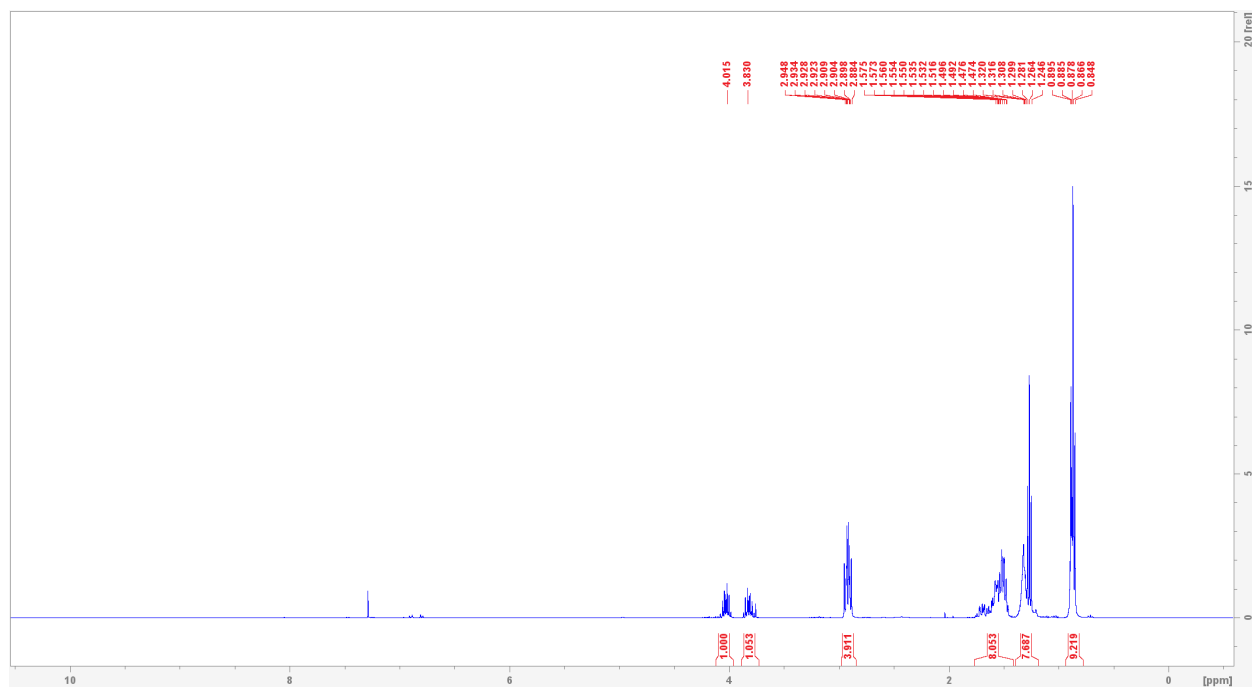
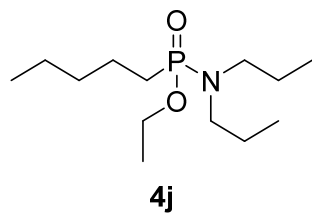


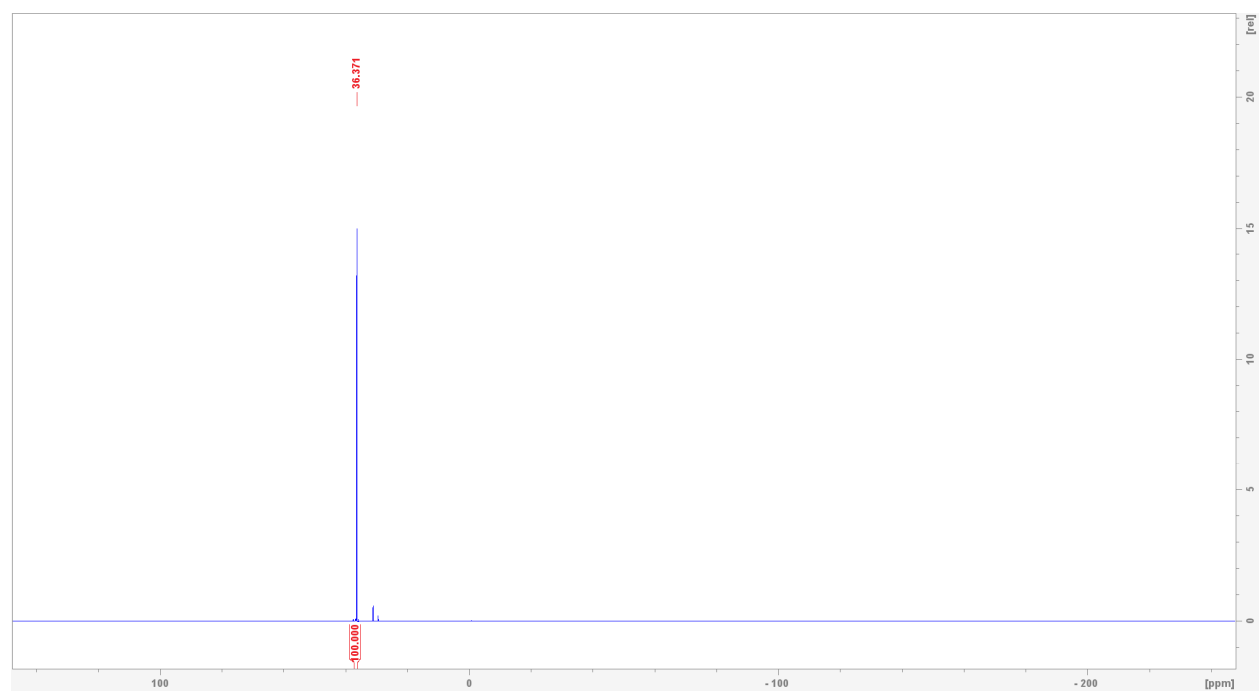
4h



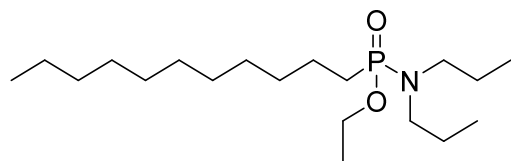


Compound **4j**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

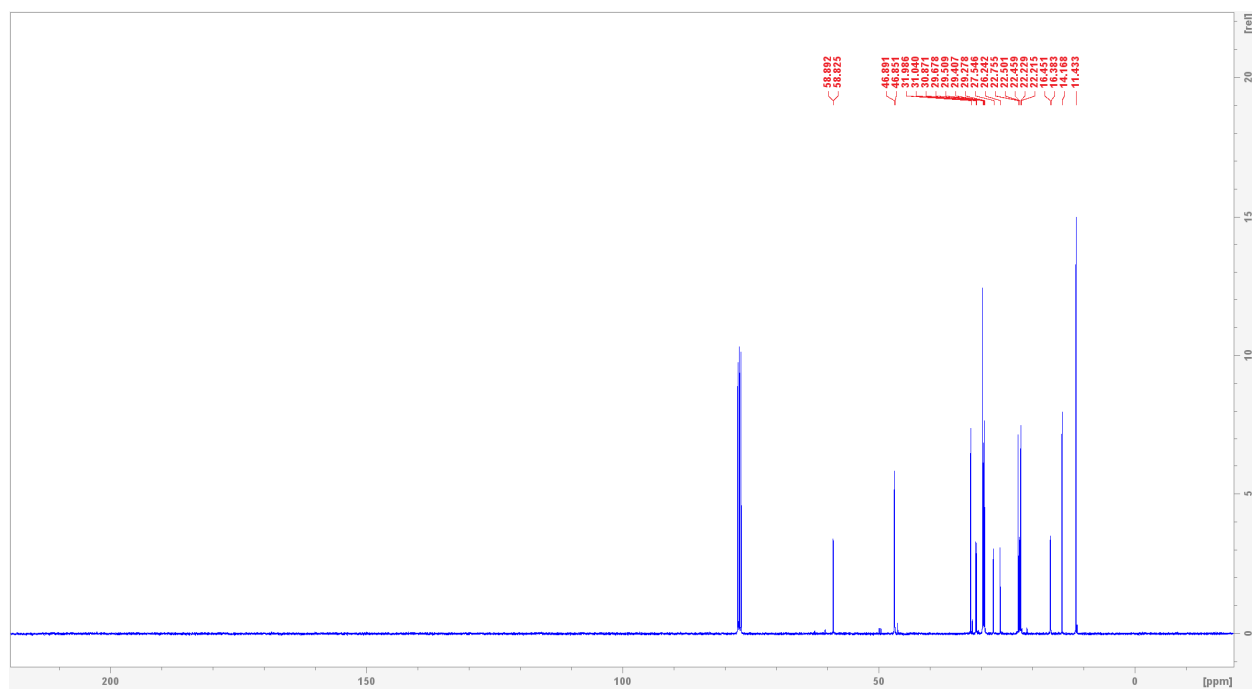


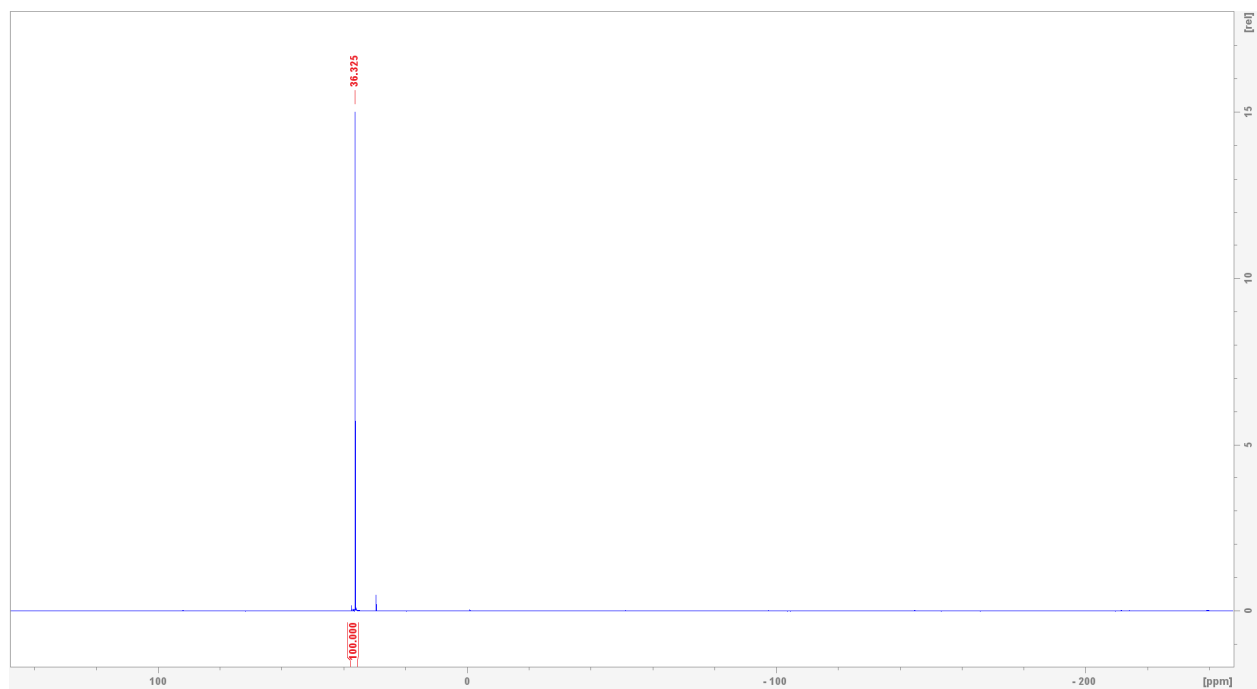


Compound **4k**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

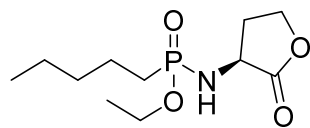


4k

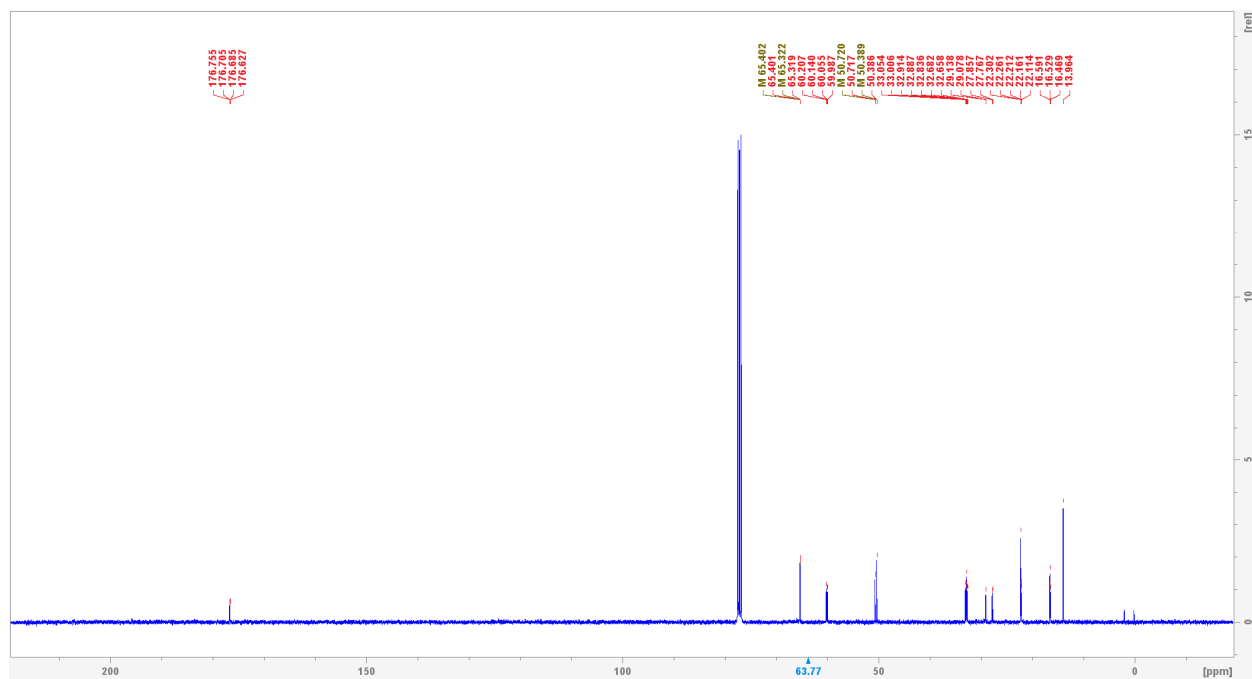
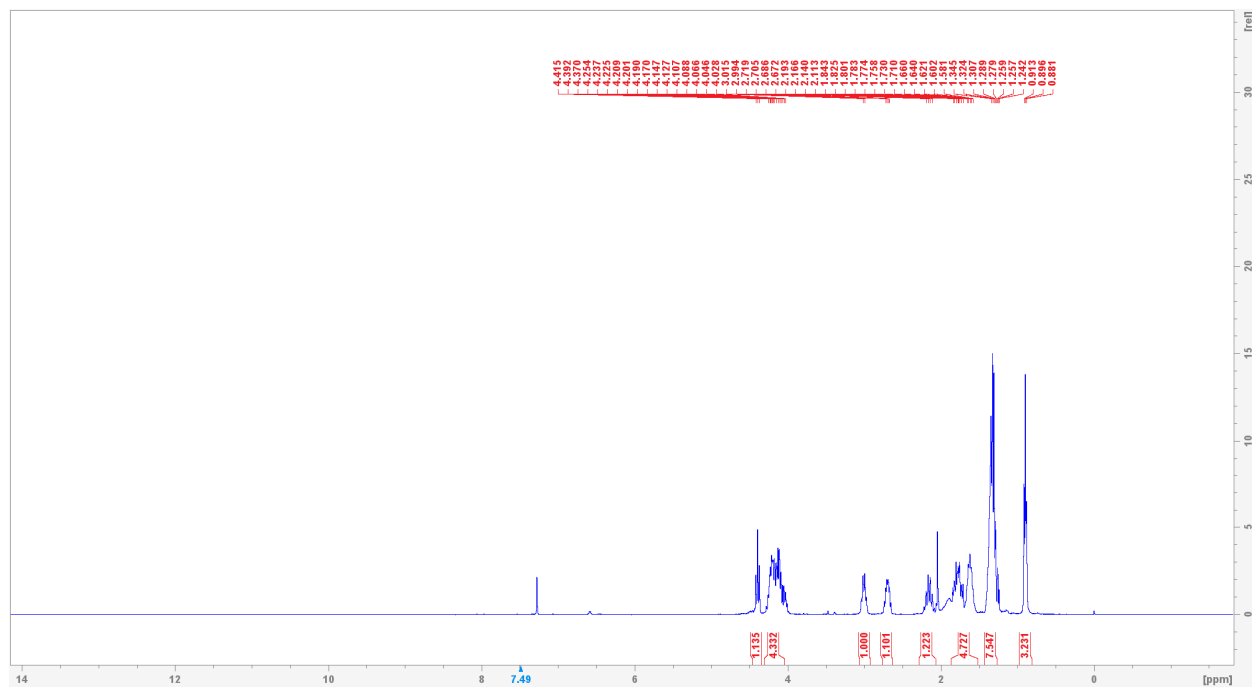


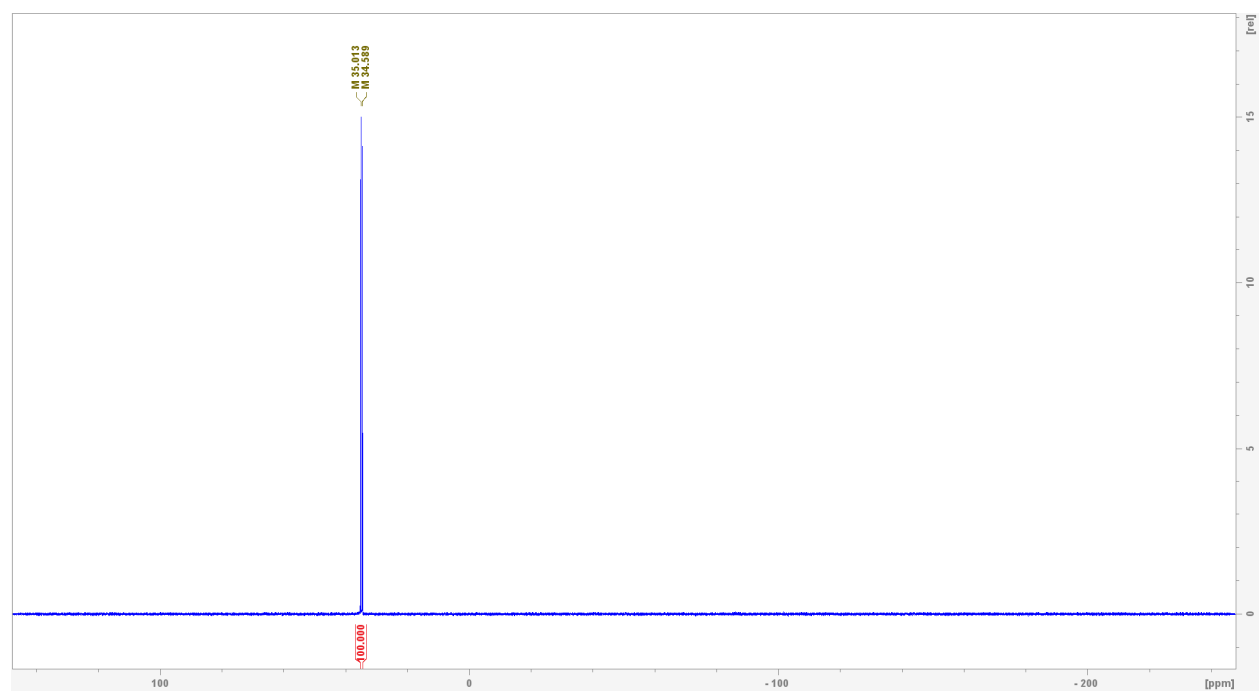


Compound **6a**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

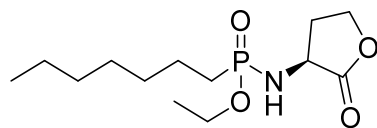


6a

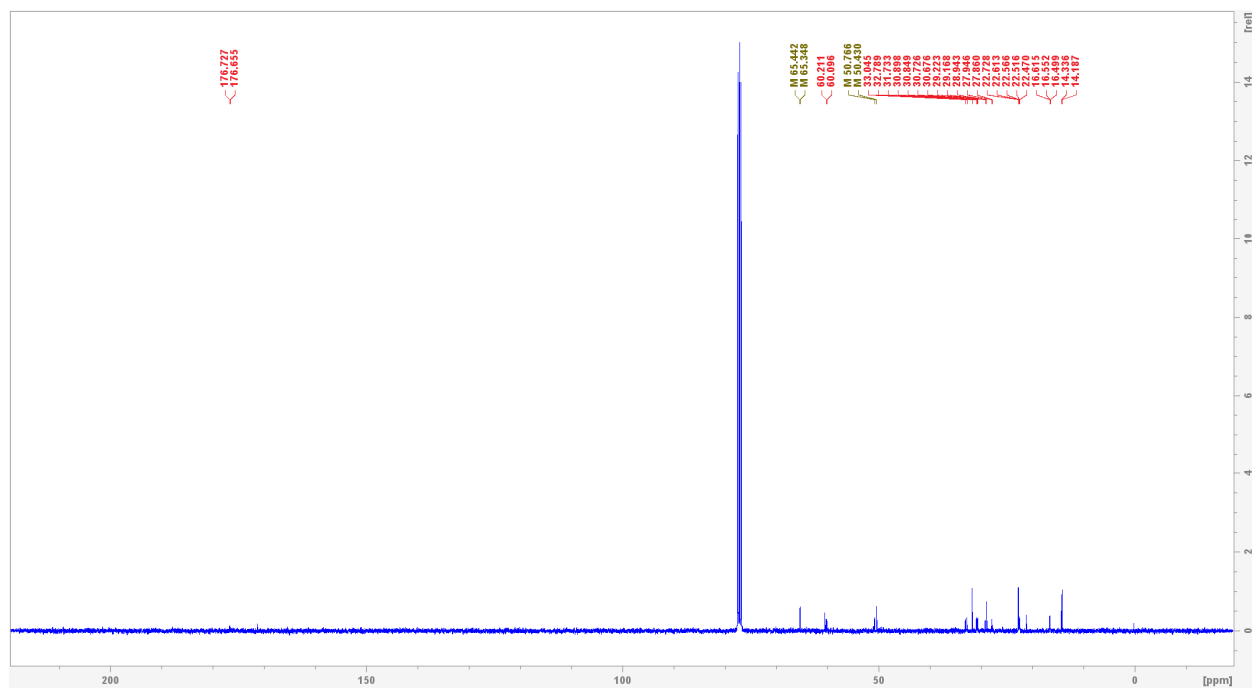
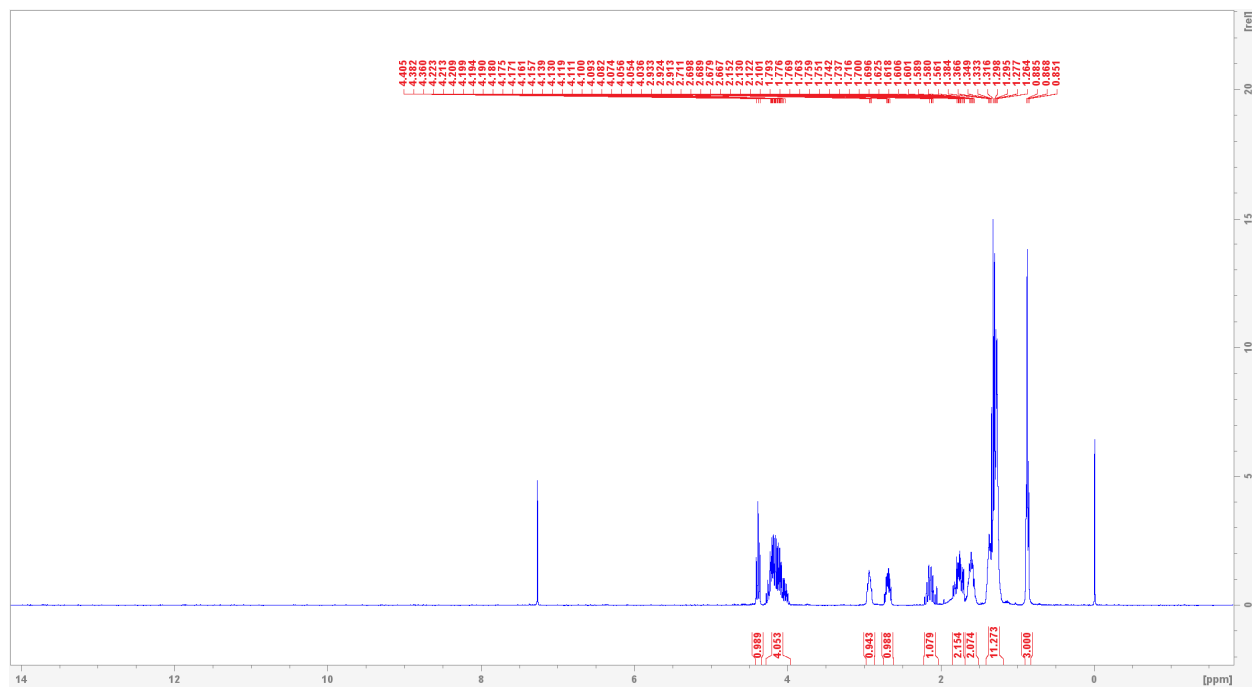


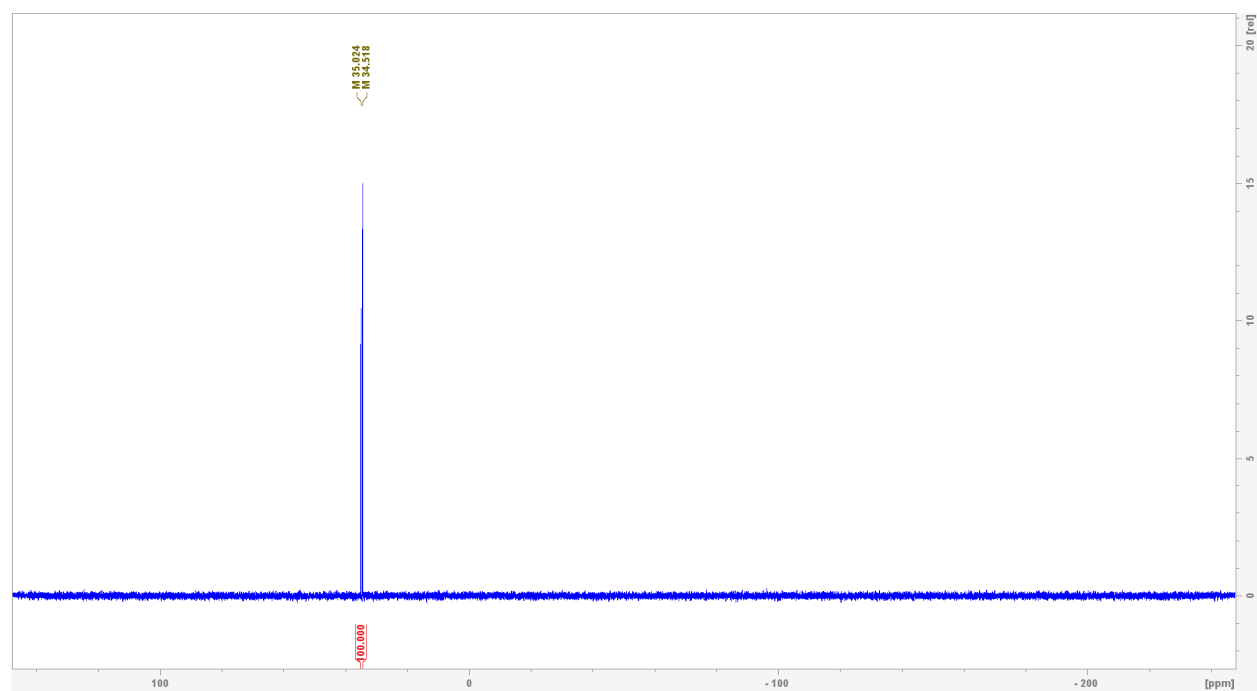


Compound **6b**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

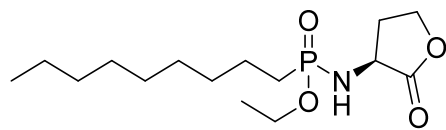


6b

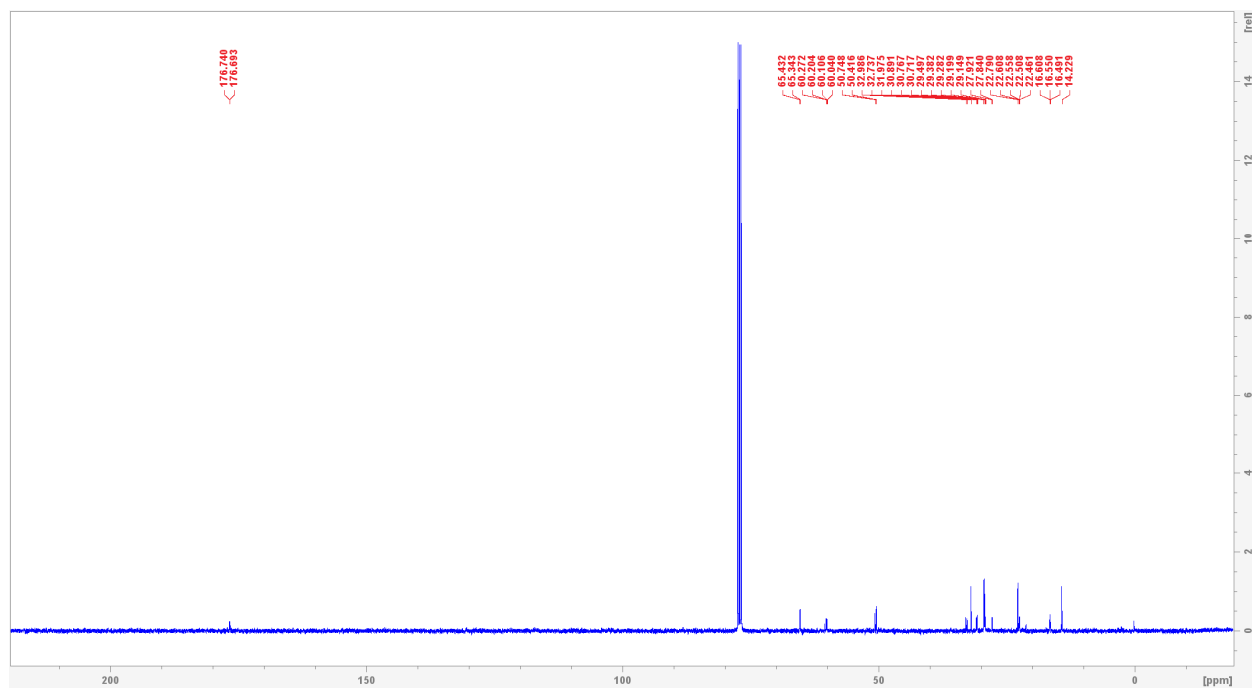
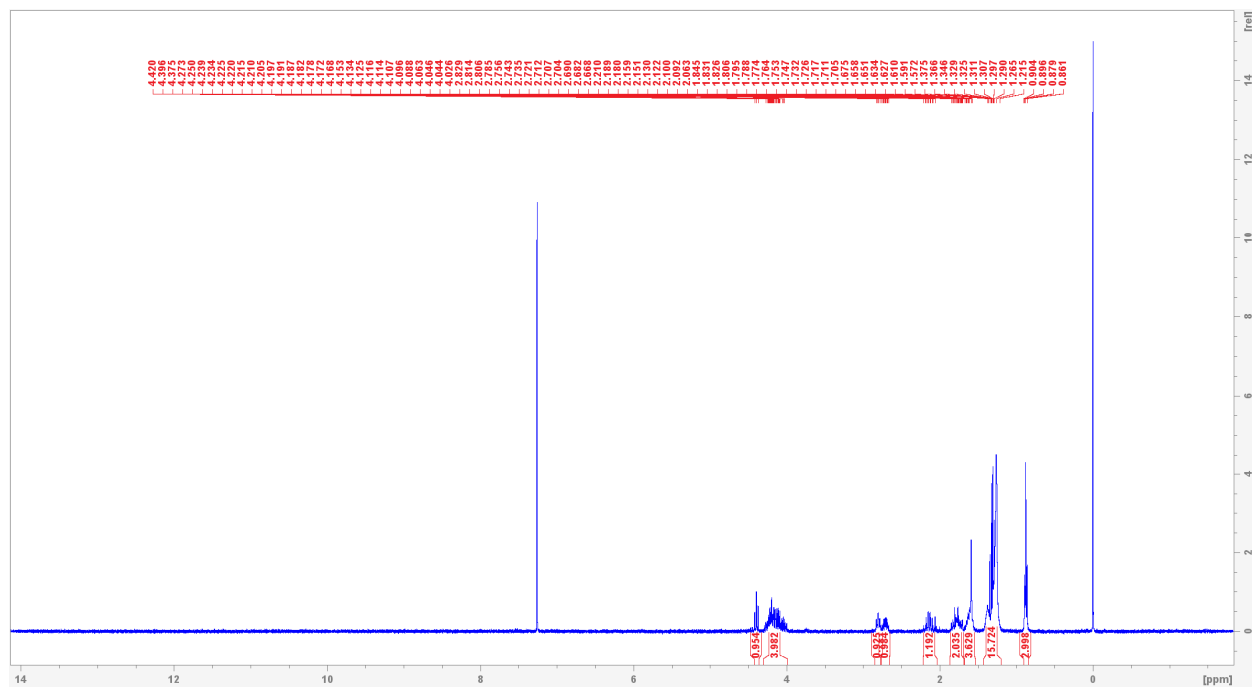


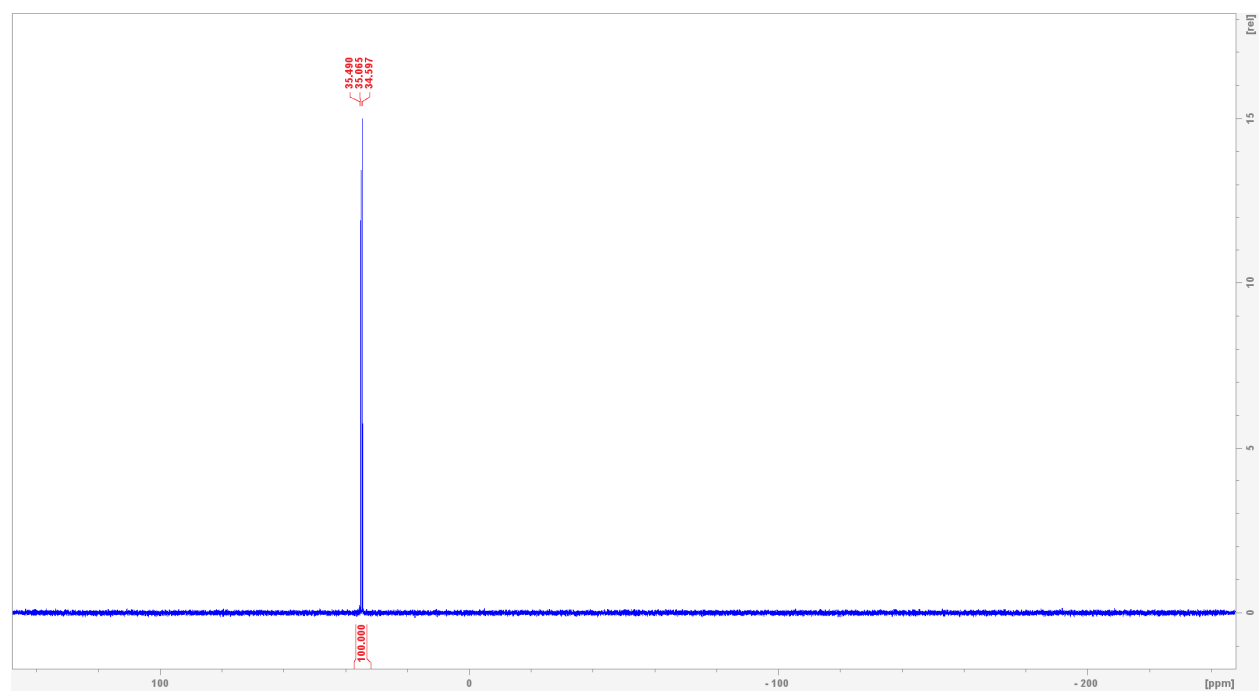


Compound **6c**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).



6c



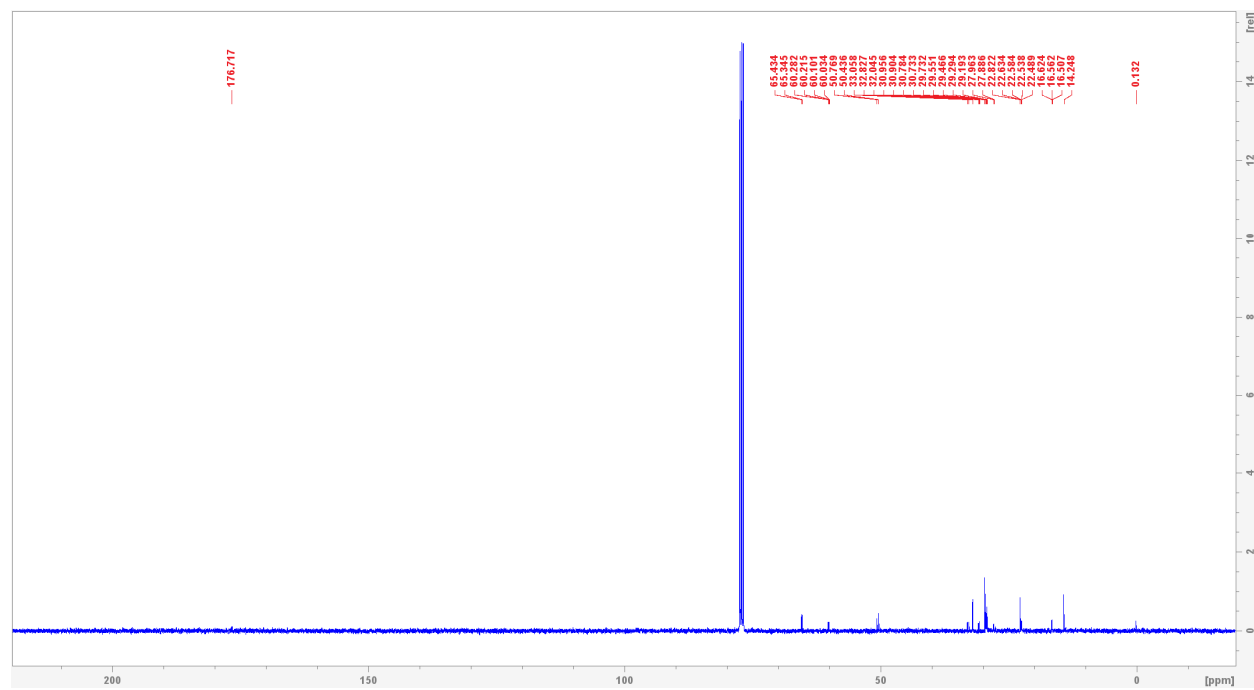


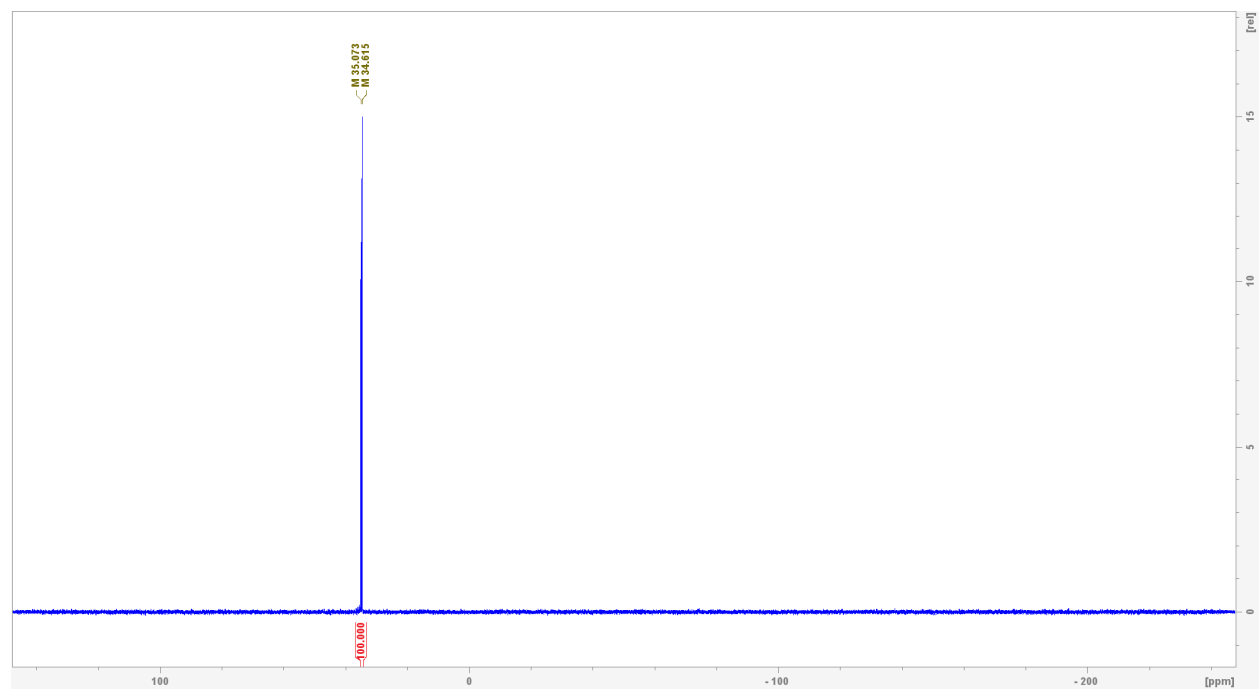
CCCCCCCCCCCCOP(=O)(OCC)N[C@H]1CCOC(=O)1

¹H NMR spectrum of compound 10 in CDCl₃. The x-axis represents the chemical shift in ppm, ranging from 0 to 14. The spectrum shows several peaks, with integration values indicated below the baseline. A list of chemical shifts (δ) is provided on the right side of the spectrum.

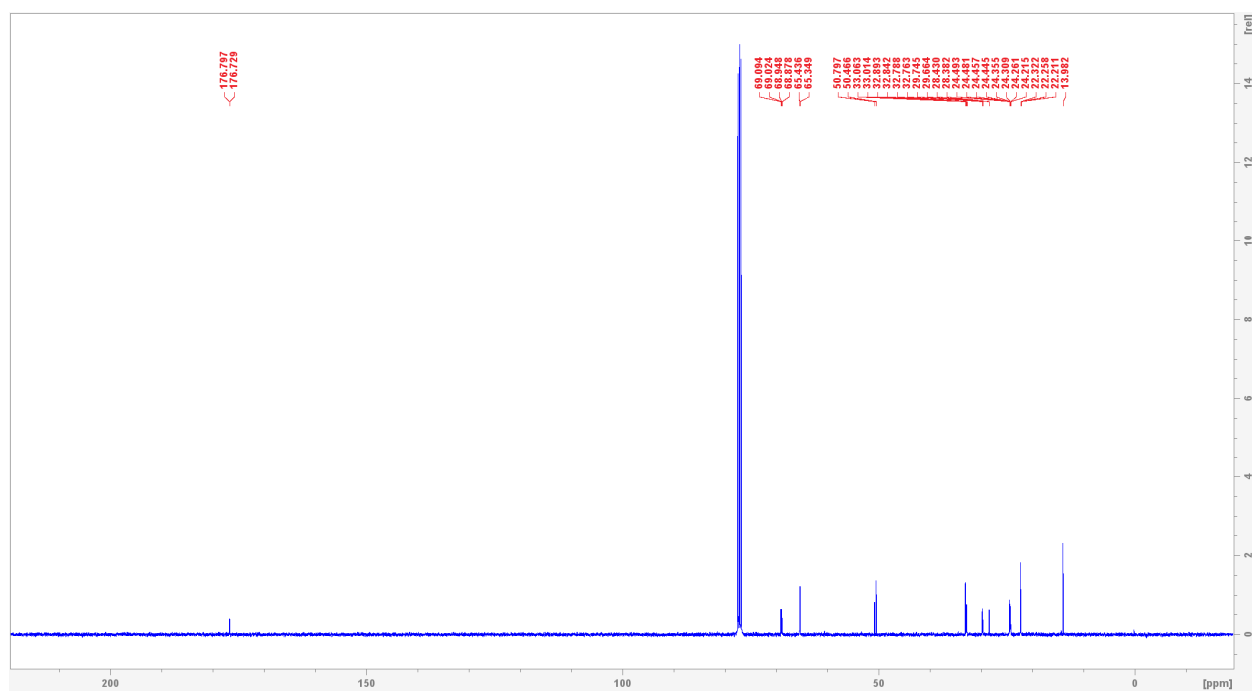
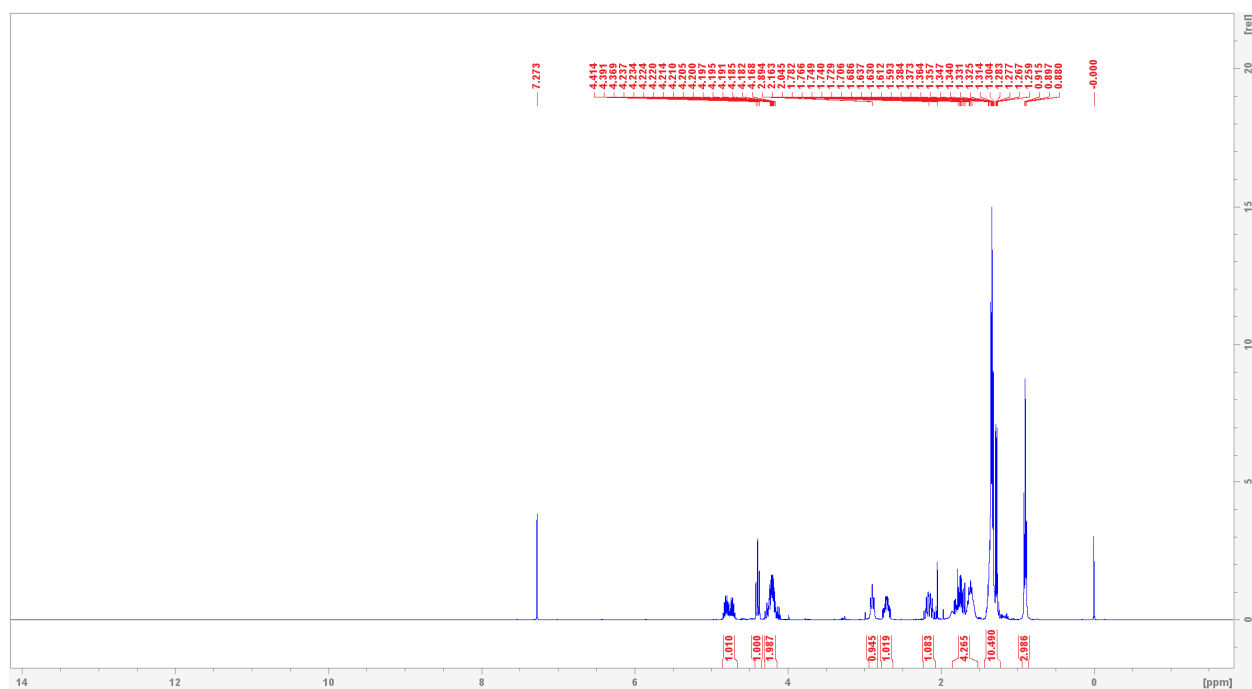
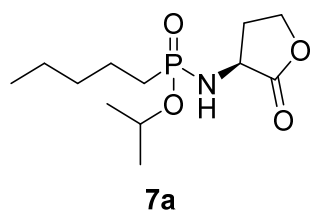
Chemical shifts (ppm): 4.418, 4.396, 4.390, 4.290, 4.270, 4.246, 4.235, 4.226, 4.216, 4.206, 4.202, 4.187, 4.173, 4.170, 4.152, 4.133, 4.124, 4.106, 4.088, 4.070, 4.046, 4.027, 4.021, 2.877, 2.855, 2.835, 2.752, 2.730, 2.710, 2.708, 2.689, 2.678, 2.666, 2.194, 2.183, 2.154, 2.144, 2.128, 2.104, 2.093, 2.082, 1.870, 1.850, 1.825, 1.796, 1.780, 1.775, 1.763, 1.747, 1.723, 1.711, 1.699, 1.659, 1.633, 1.613, 1.597, 1.588, 1.346, 1.325, 1.322, 1.307, 1.289, 1.255, 0.897, 0.880.

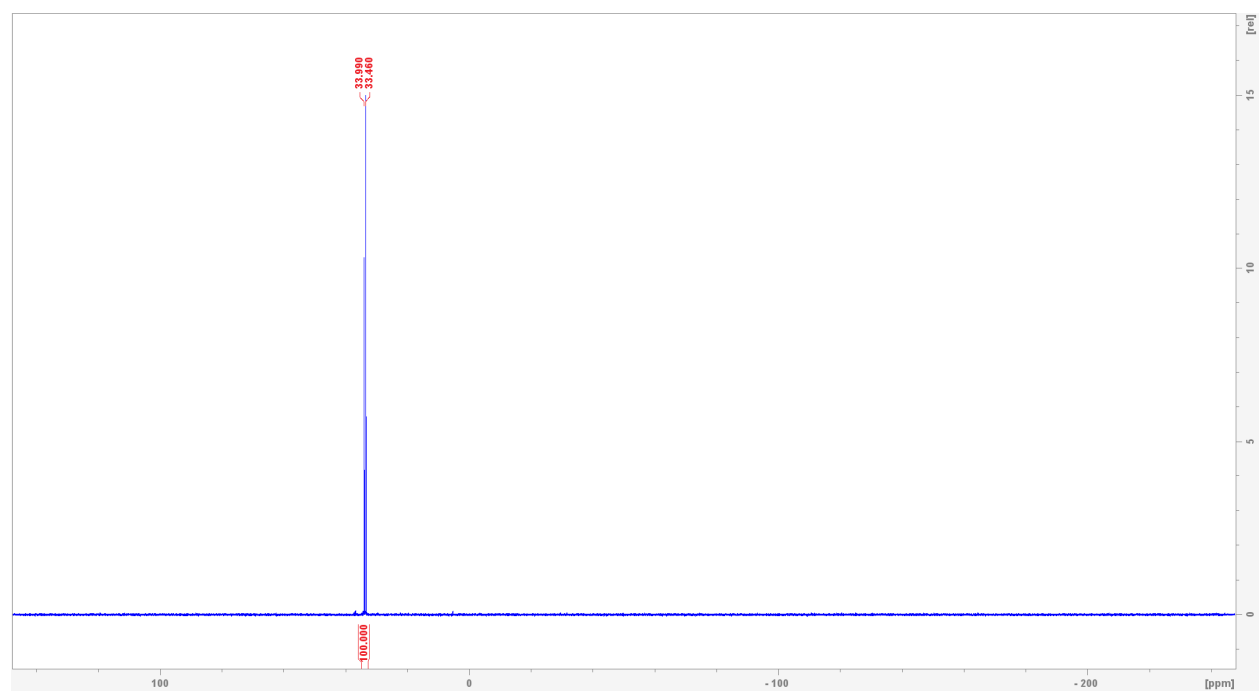
Integration values (from left to right): 0.068, 2.937, 0.959, 0.995, 1.098, 1.939, 2.827, 9.000, 3.016.



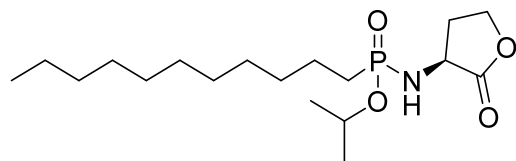


Compound **7a**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

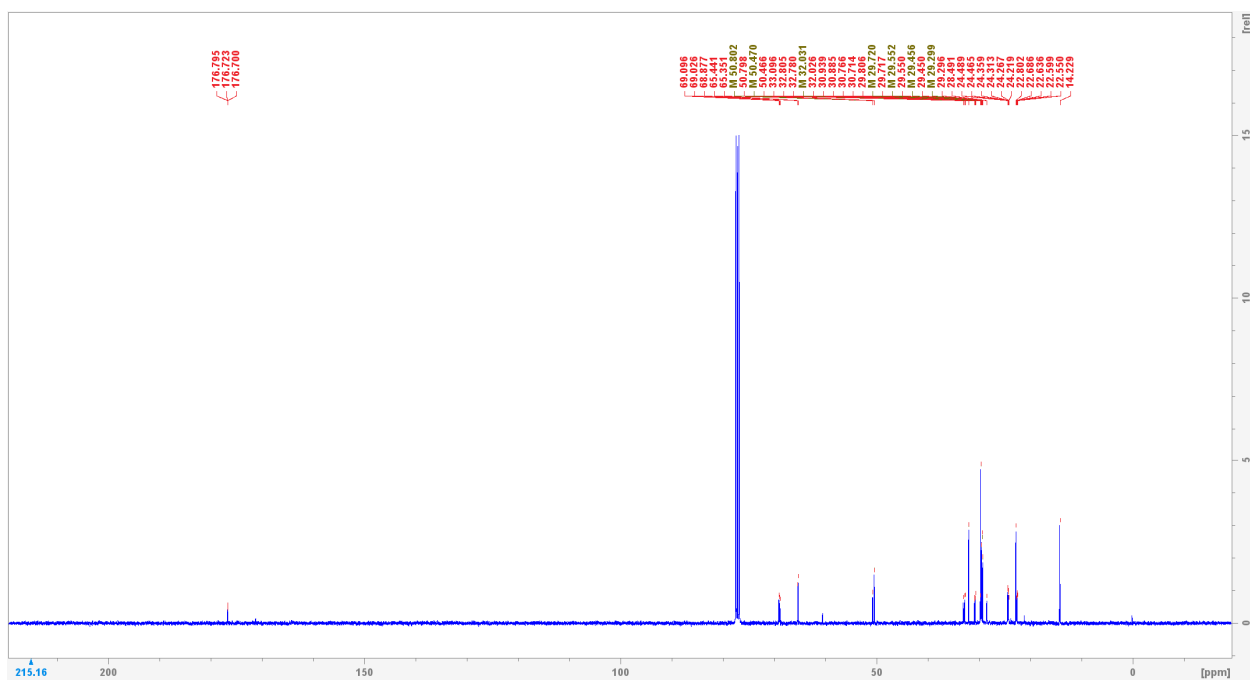
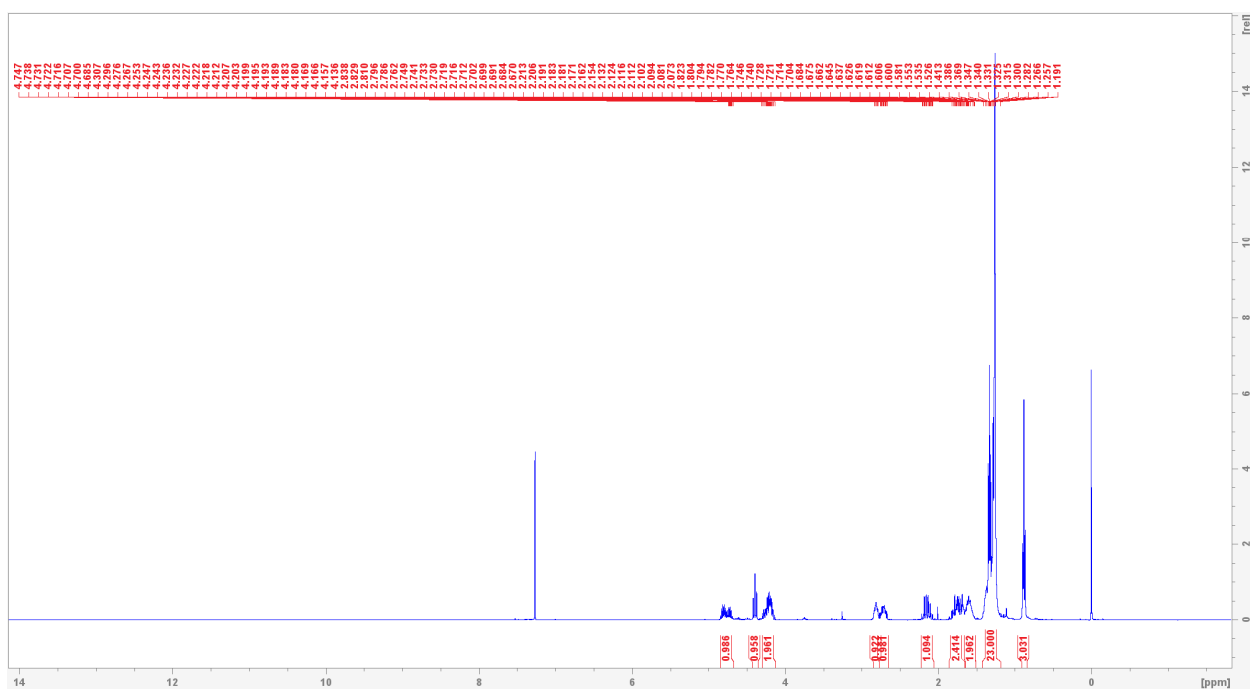


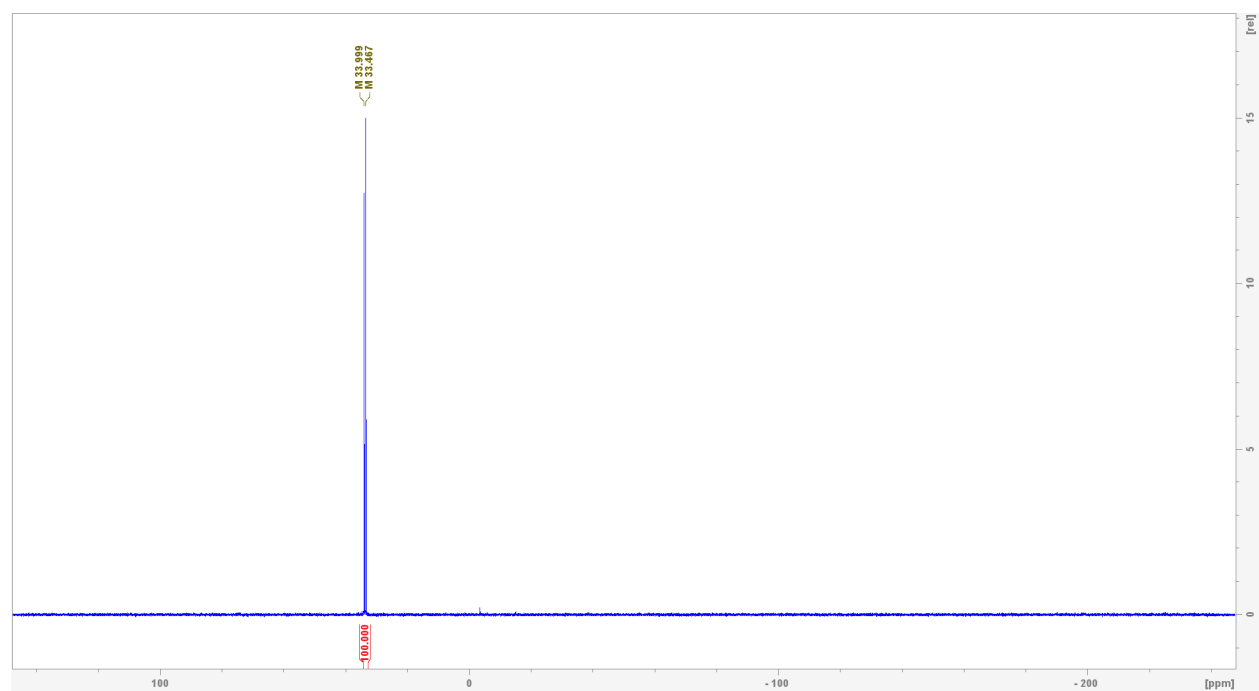


Compound **7b**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

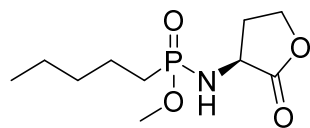


7b

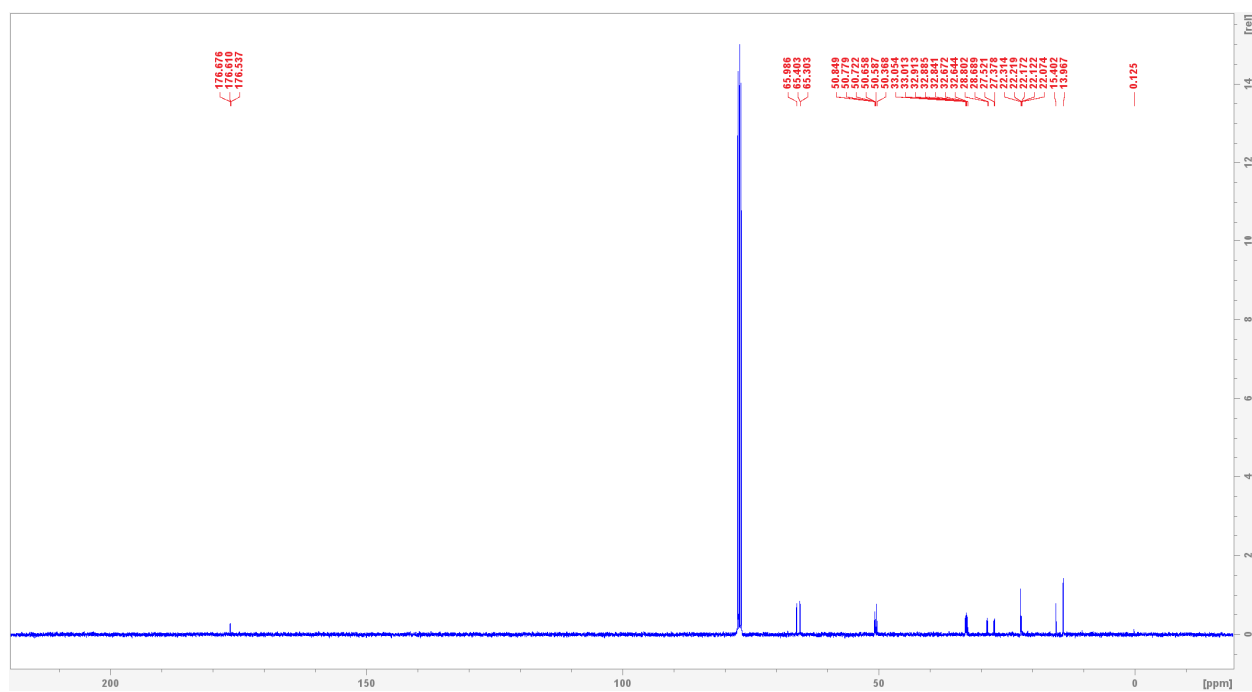
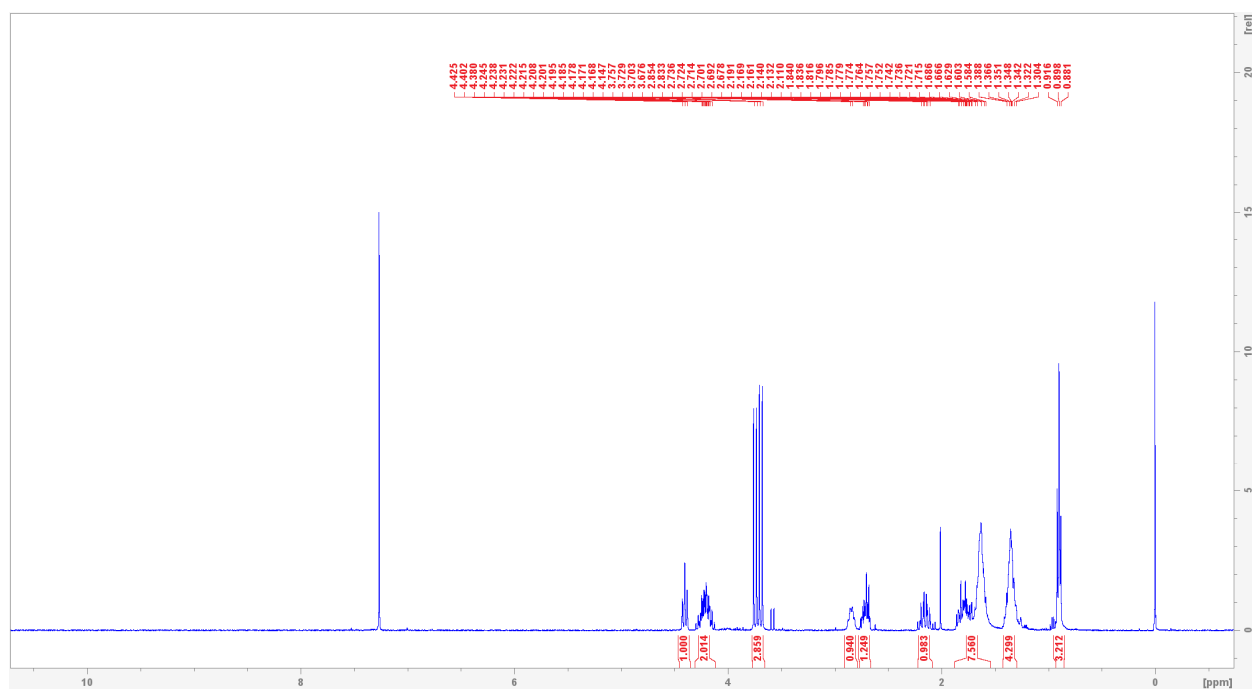


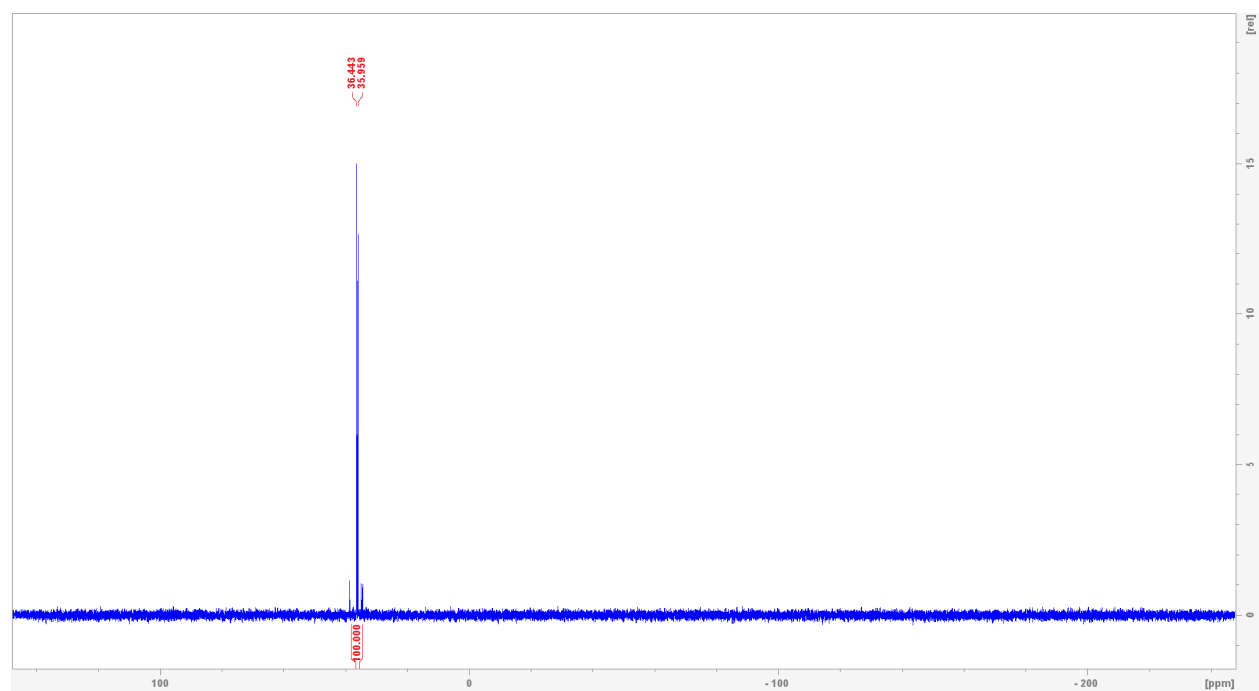


Compound **8a**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

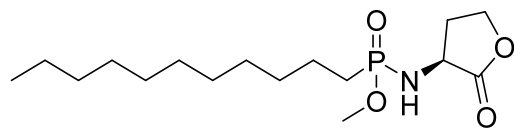


8a

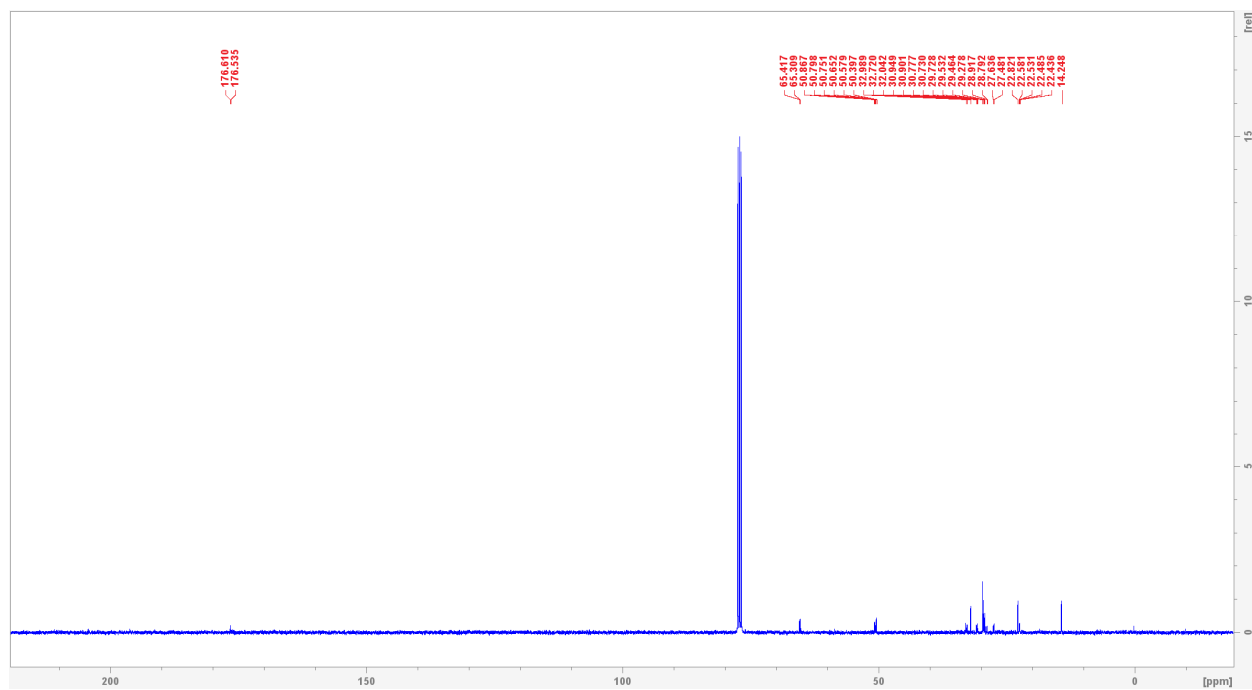
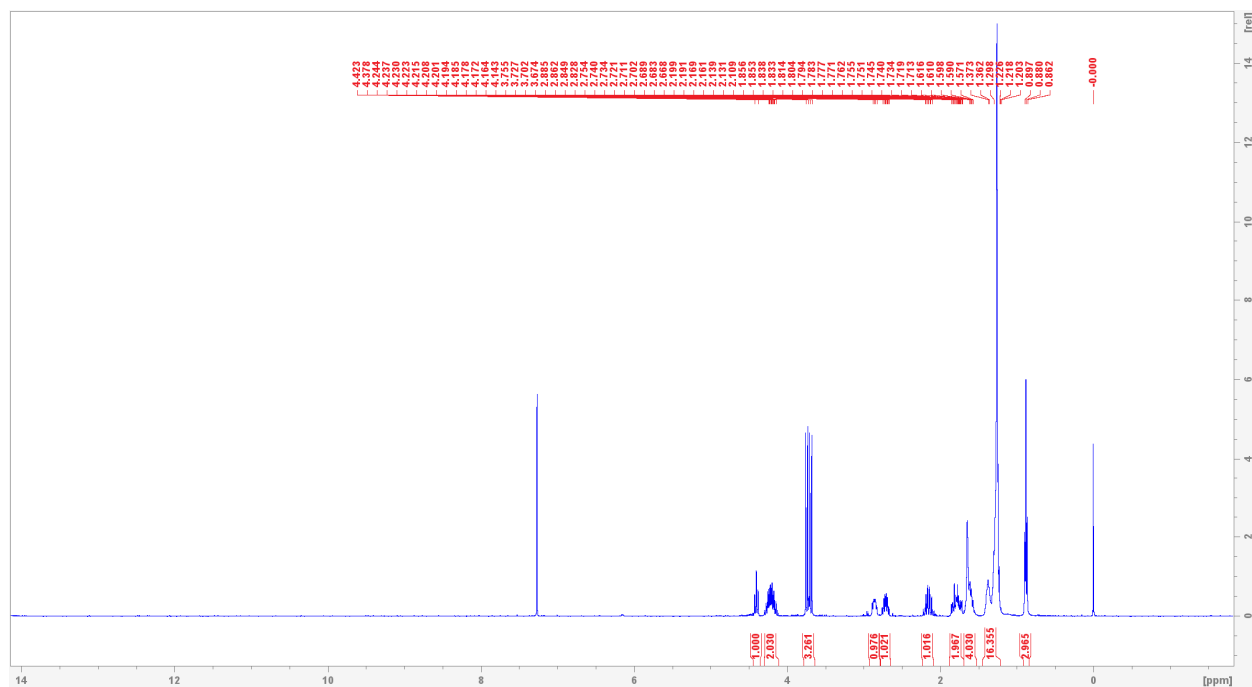


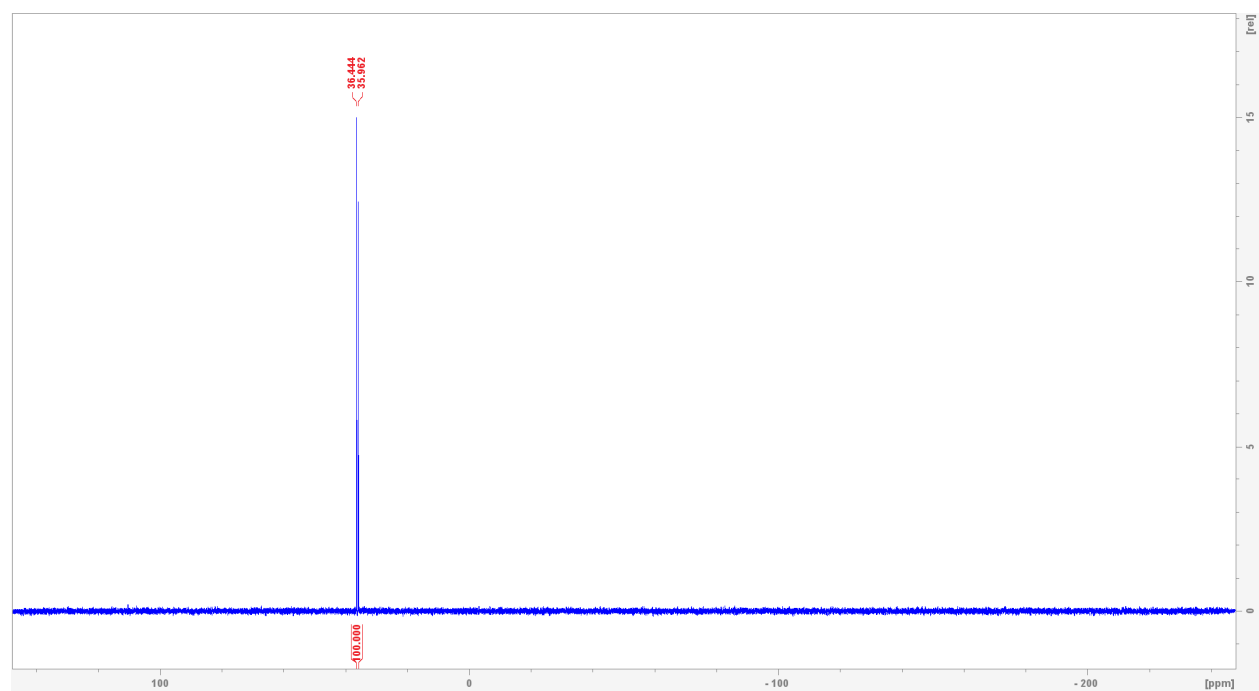


Compound **8b**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

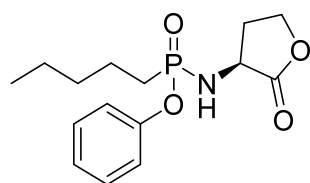


8b

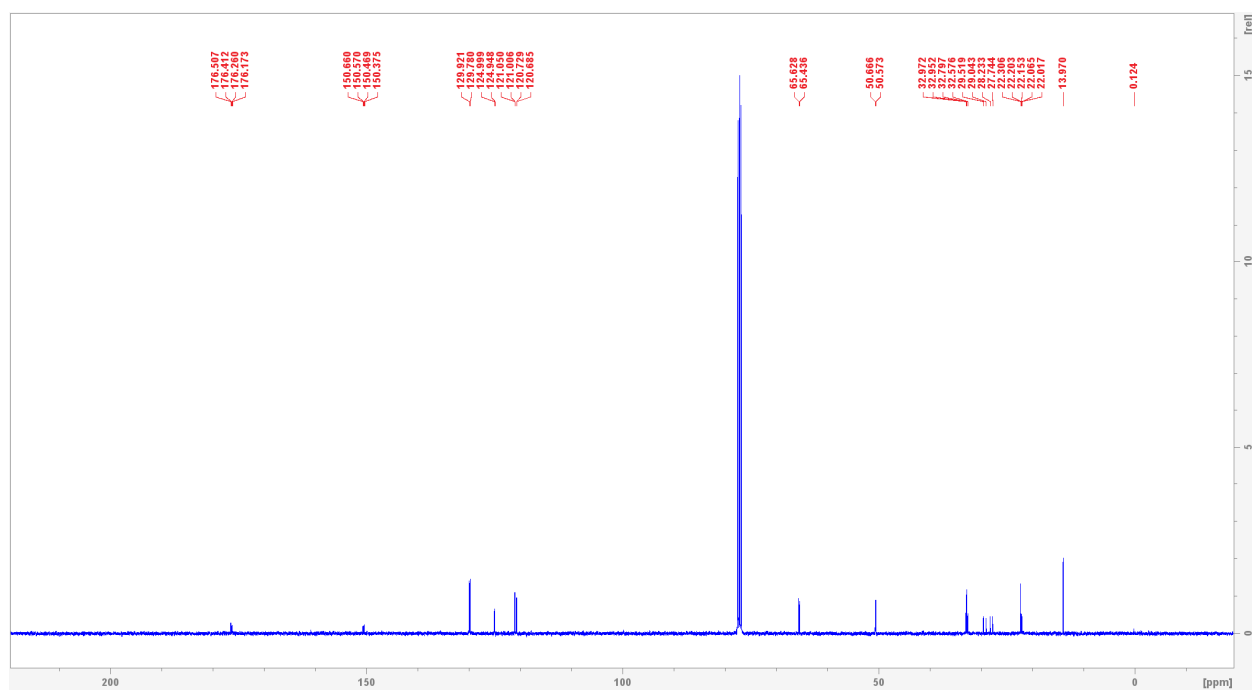
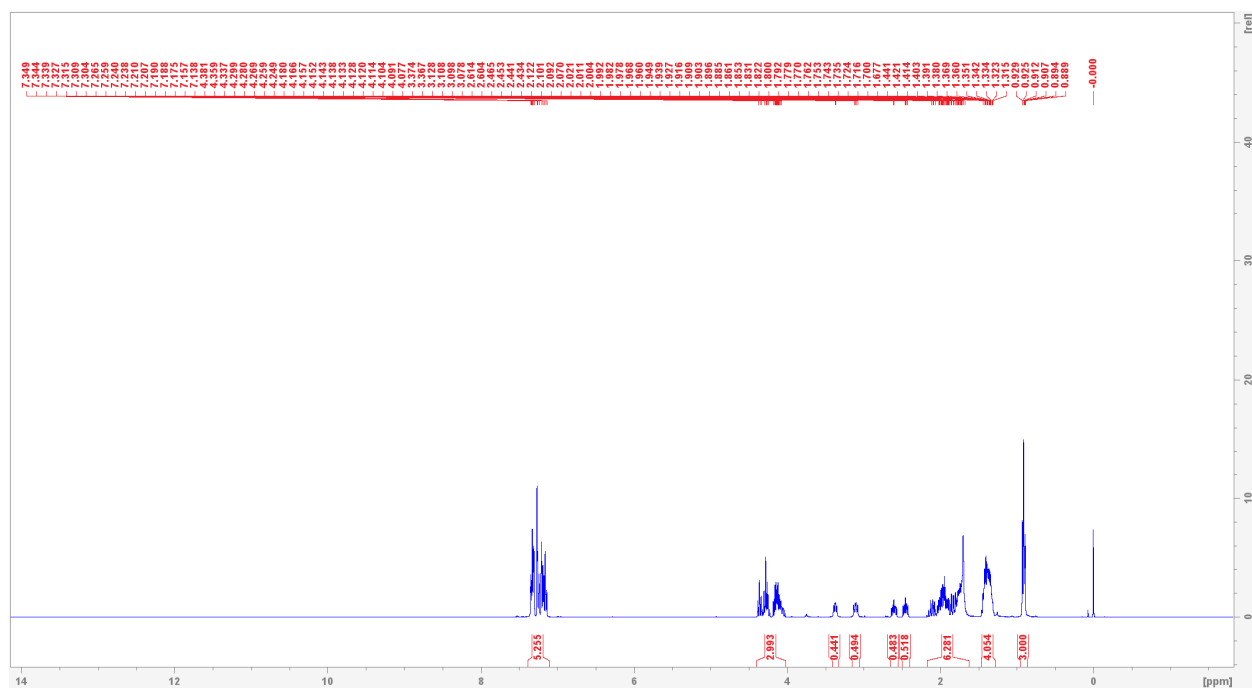


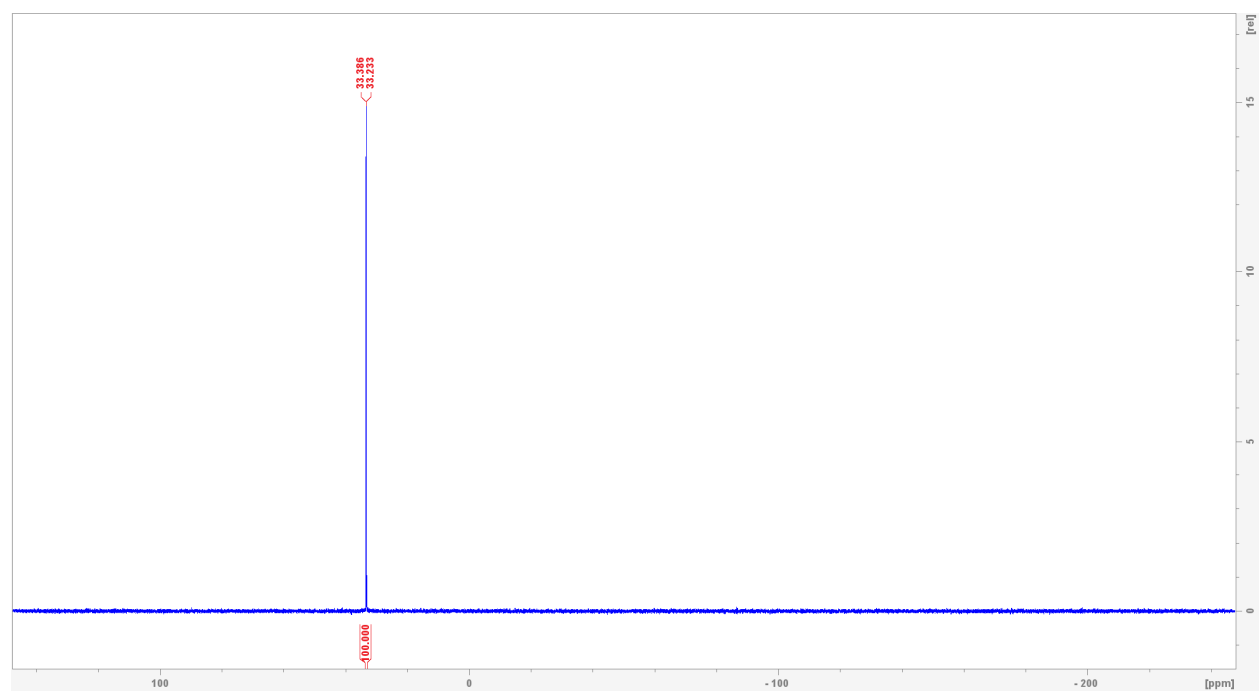


Compound **9a**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

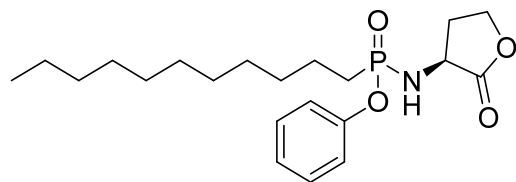


9a

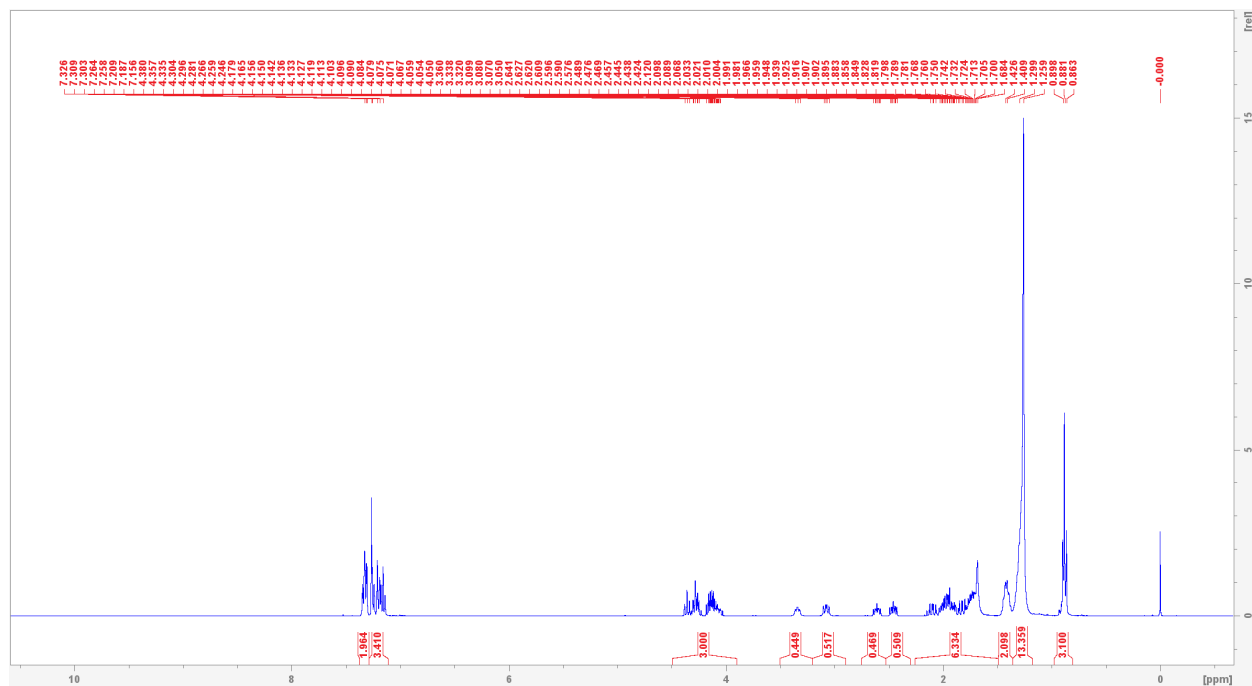


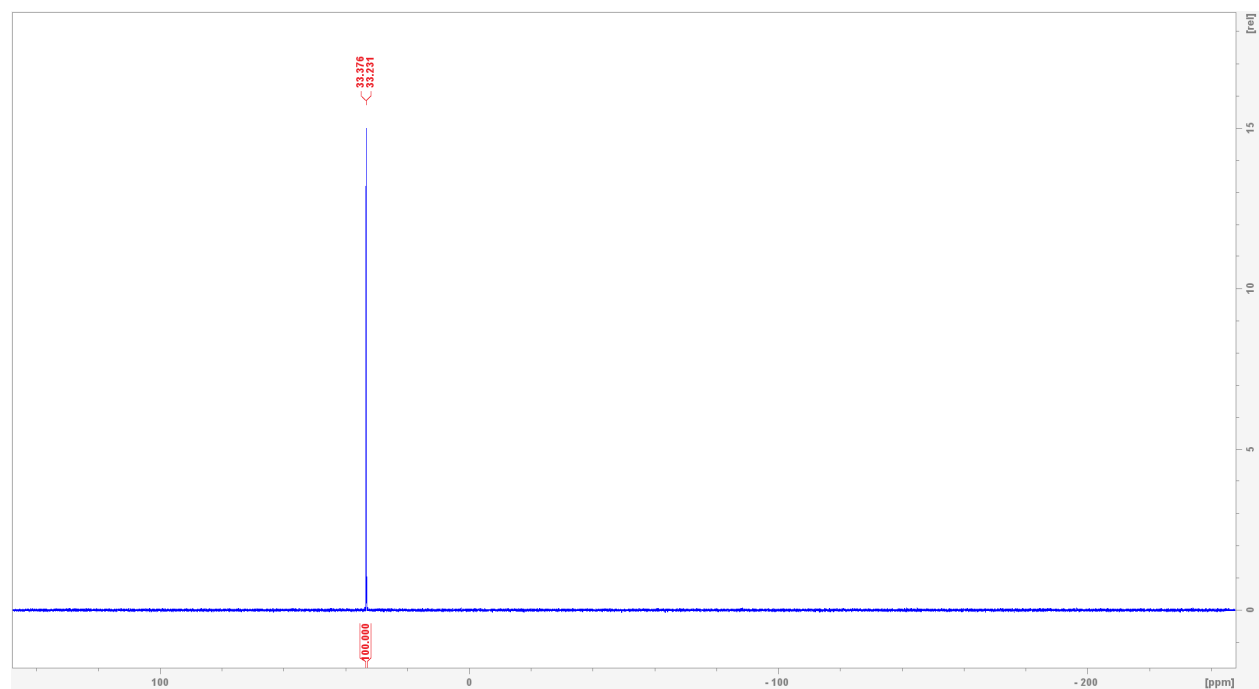
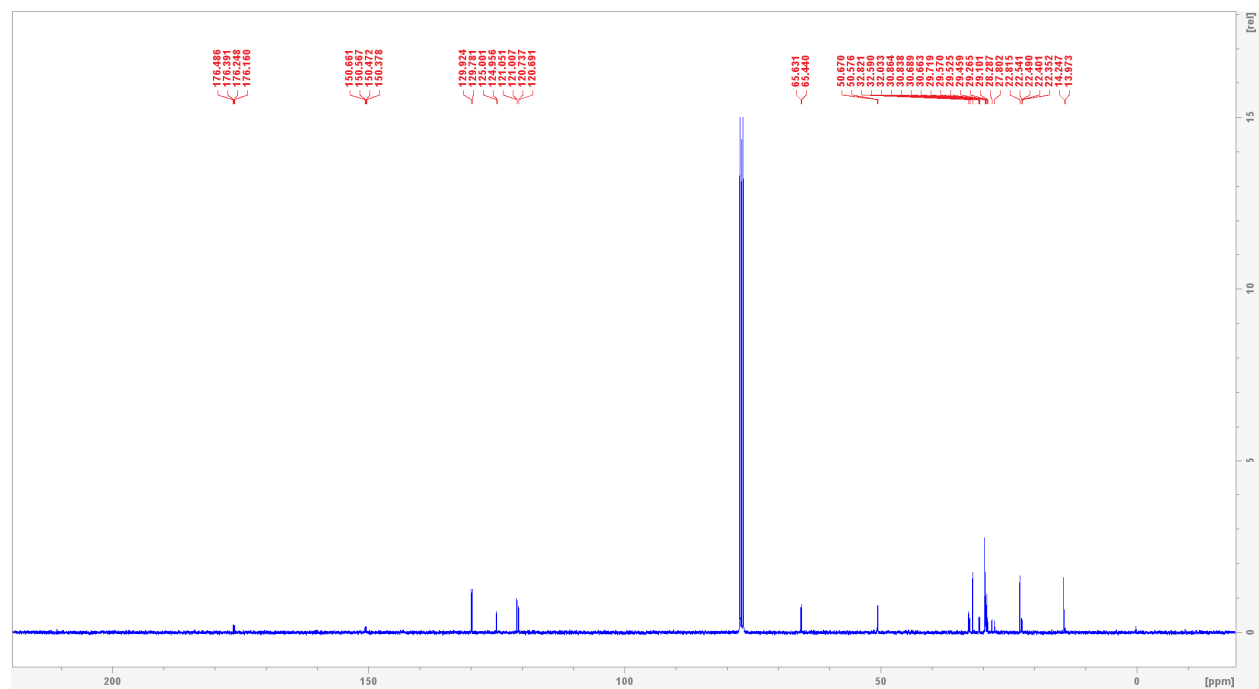


Compound **9b** ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

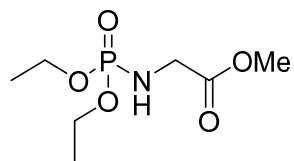


9b

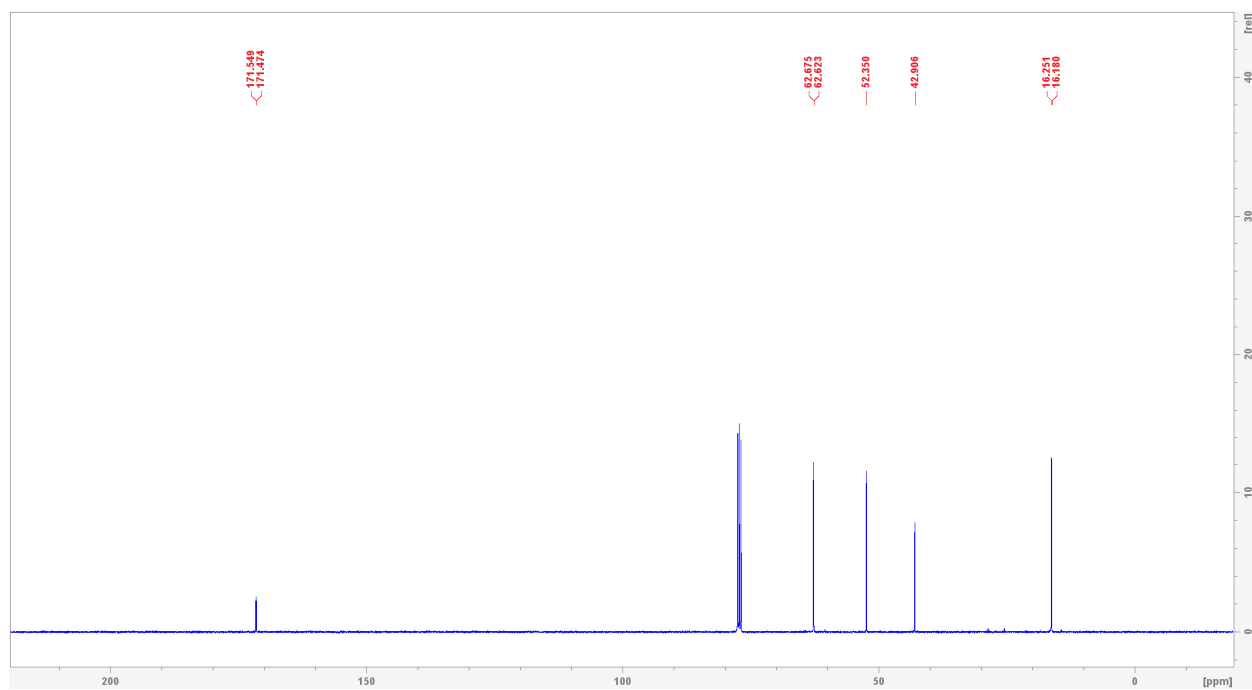
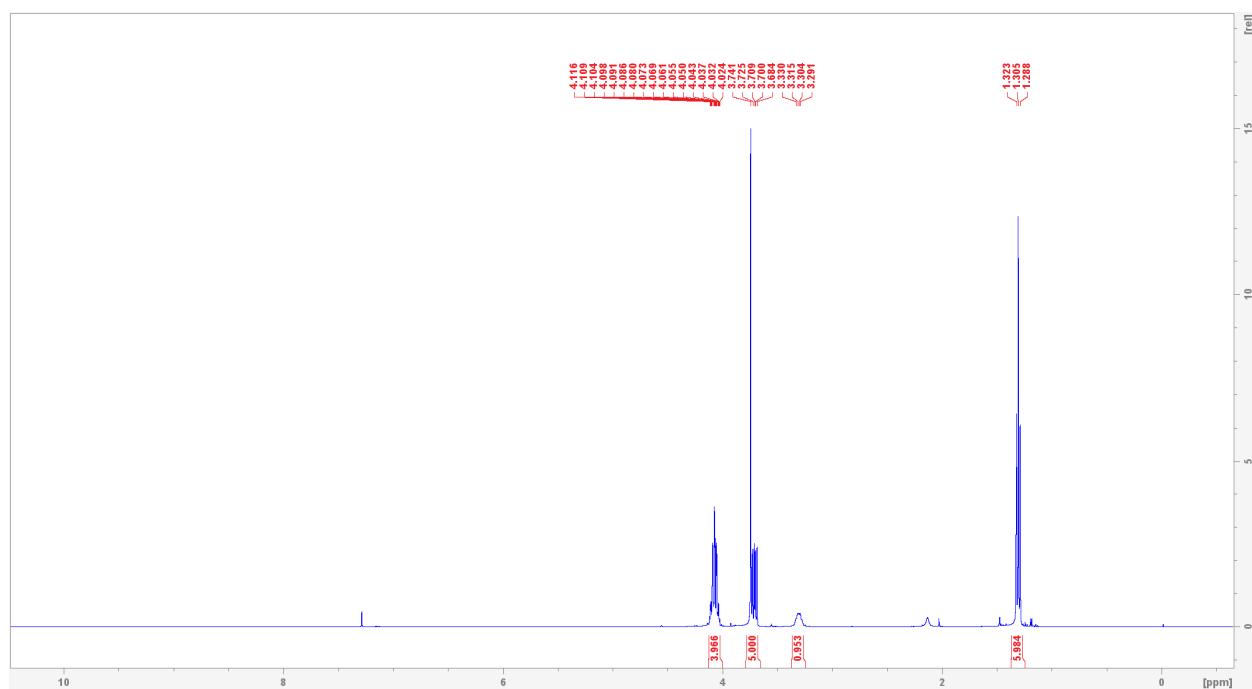


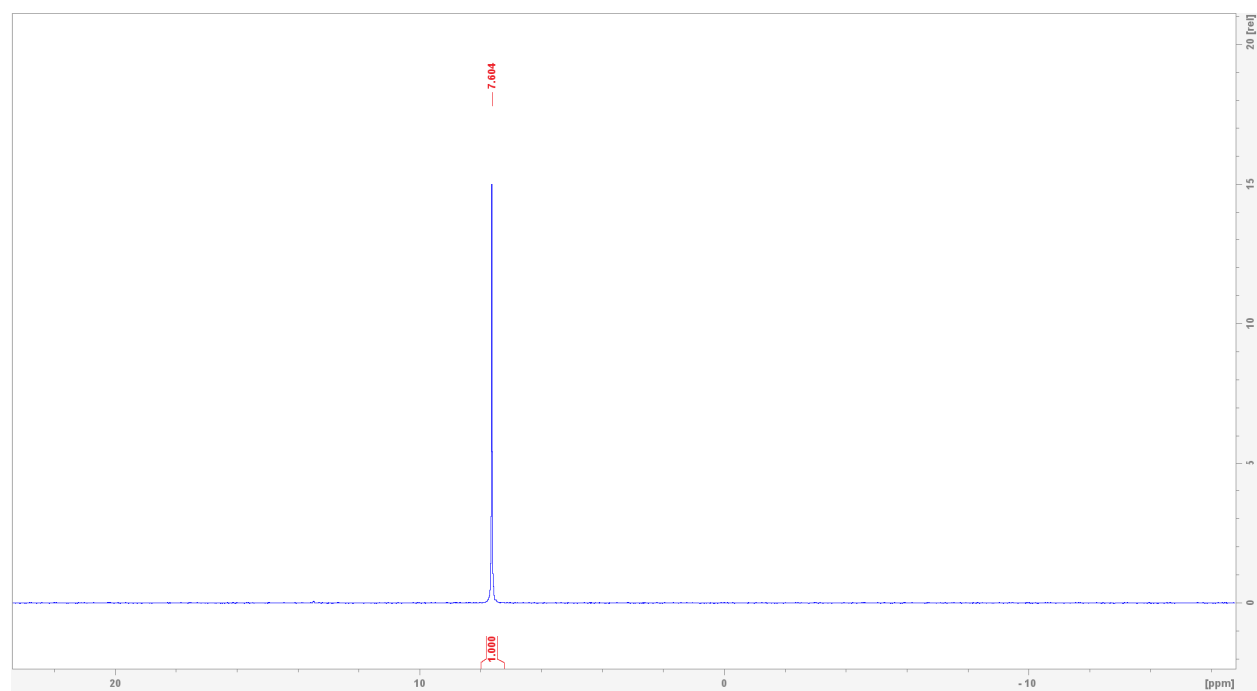


Compound **15a**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

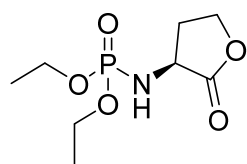


15a

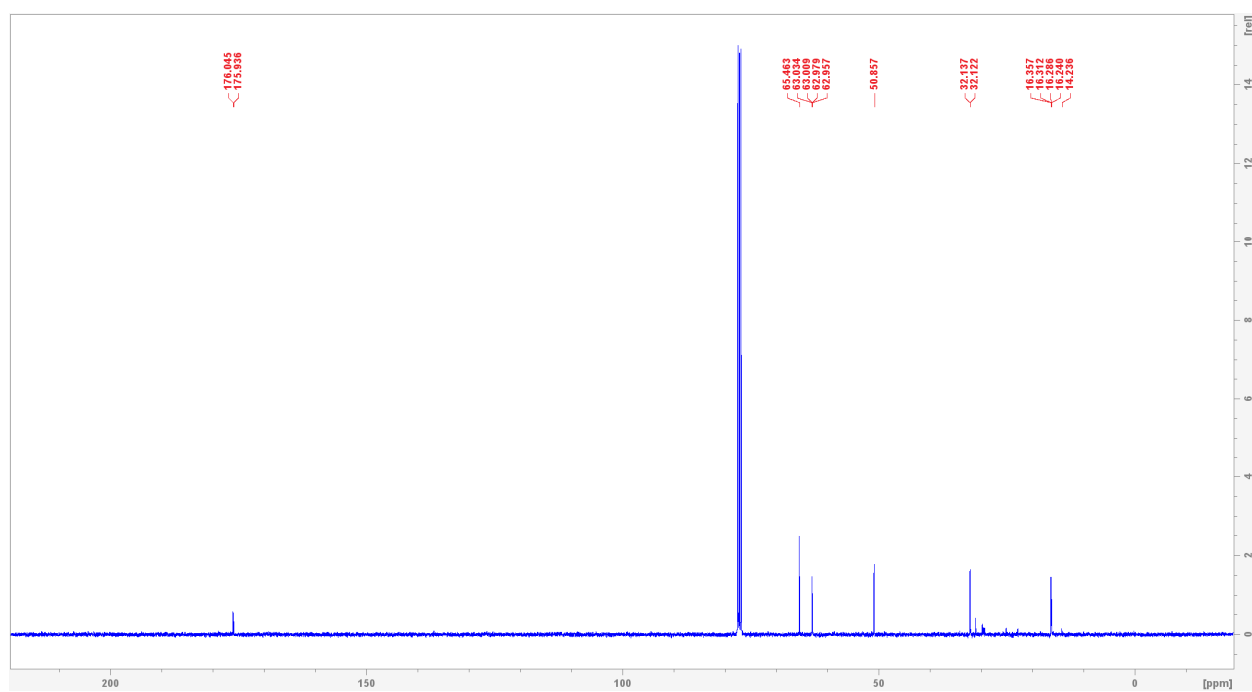
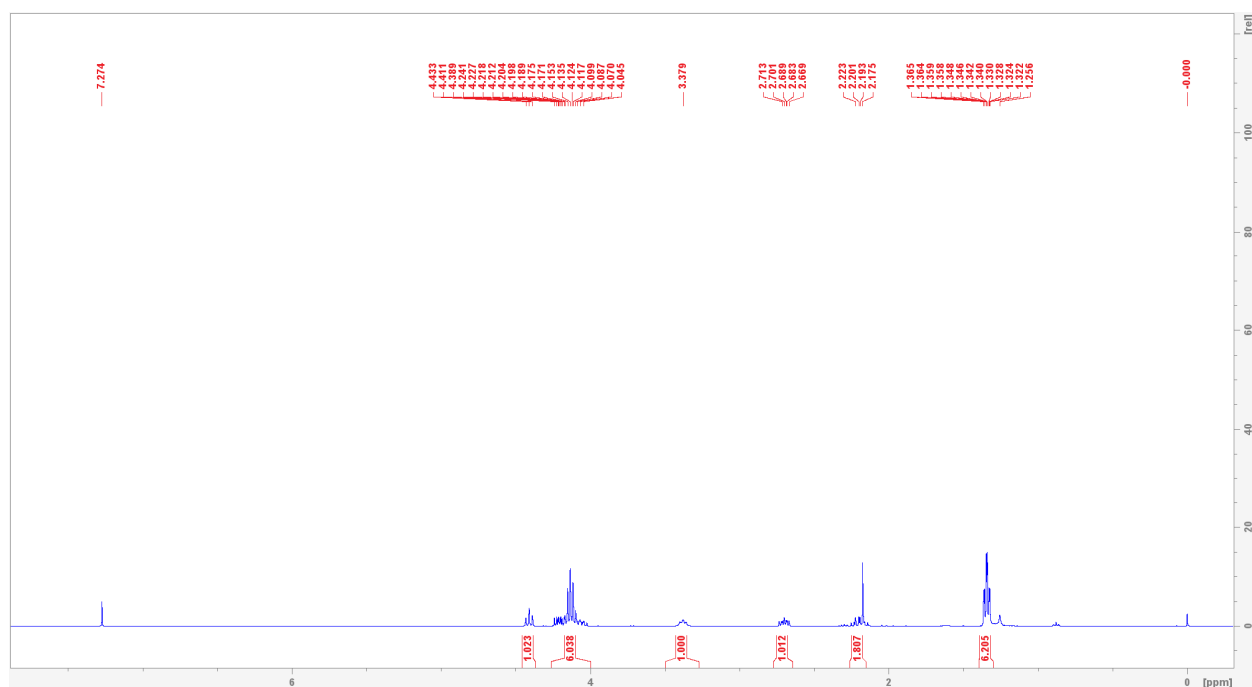


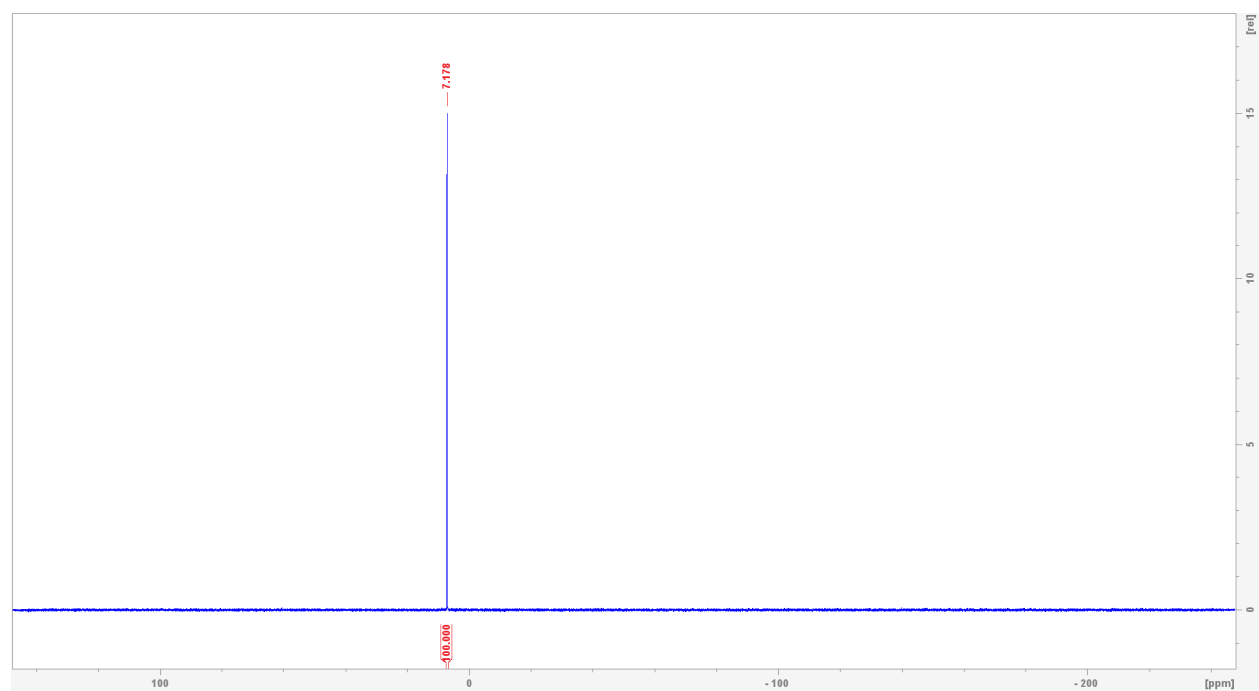


Compound **15b**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

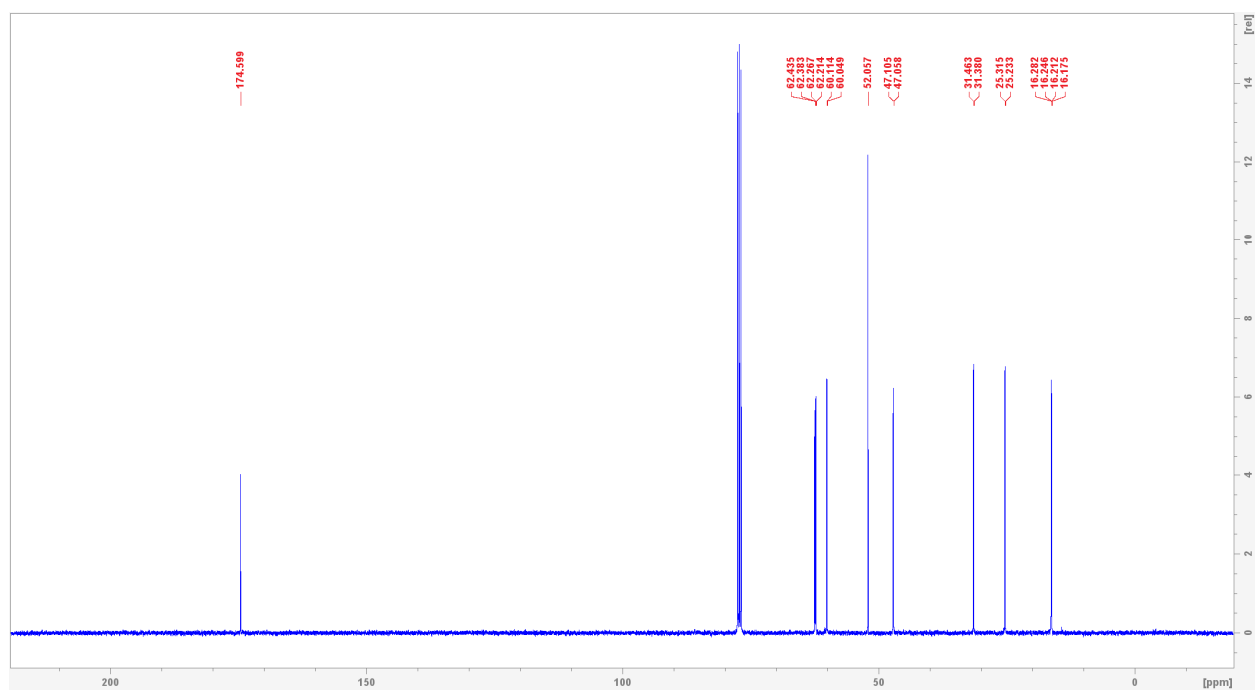
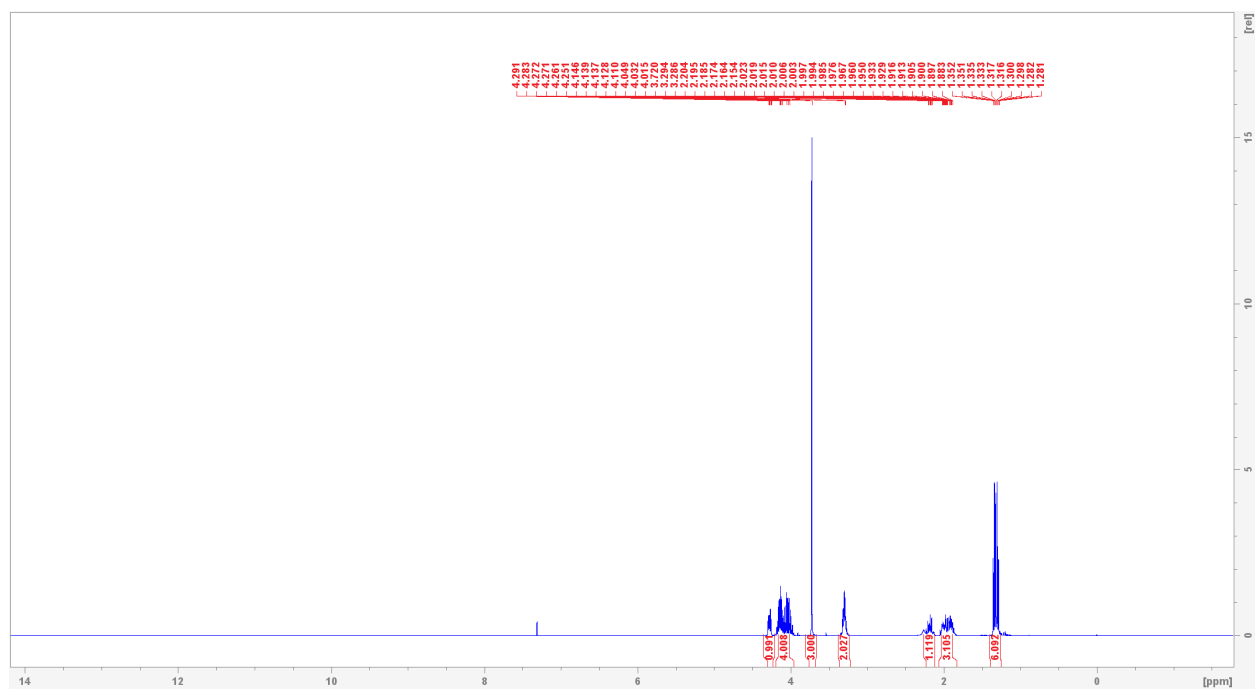
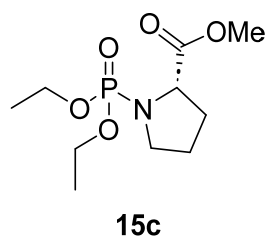


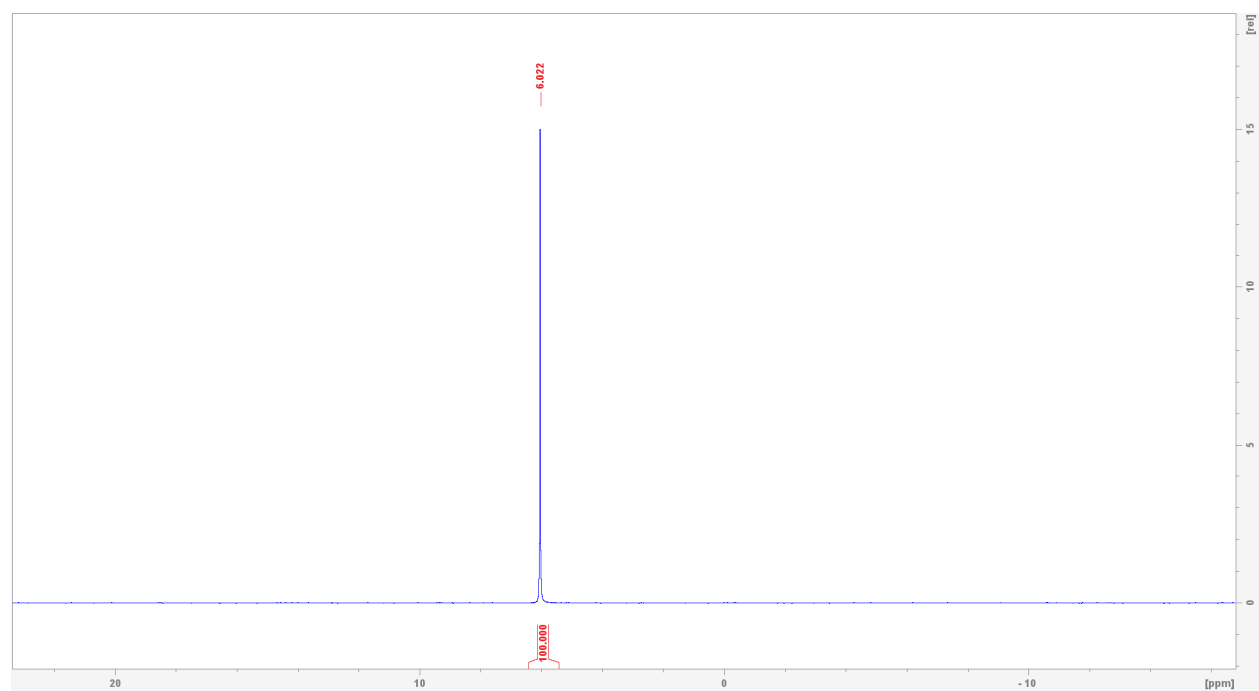
15b





Compound **15c**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).





Compound **15d**: ^1H NMR (400 MHz, CDCl_3), ^{13}C NMR (100.6 MHz, CDCl_3) and ^{31}P NMR (161.9 MHz, CDCl_3).

