

Supporting Information

**Amino acid functionalisation using the 2-phosphaethynolate anion. A
facile route to (phosphanyl)carbonyl-amino acids.**

Érica N. Faria, Andrew R. Jupp, Jose M. Goicoechea*

Department of Chemistry, University of Oxford

Chemistry Research Laboratory, 12 Mansfield Road, OX1 3TA, Oxford, United

Kingdom

E-mail: jose.goicoechea@chem.ox.ac.uk

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1. Experimental details

1.1 General experimental details

All reactions and product manipulations, with the exception of manipulations involving amino acids (which were performed in air), were carried out under an inert atmosphere of argon using standard Schlenk-line or glovebox techniques (MBraun UNIlab glovebox maintained at < 0.1 ppm H_2O and < 0.1 ppm O_2). $[\text{K}(18\text{-crown-6})][\text{PCO}]$ and $[\text{Na}(\text{dioxane})_x][\text{PCO}]$ were synthesized according to literature procedures and stored at ambient temperature in an inert atmosphere glovebox.^[1,2] Pyridinium trifluoromethanesulfonate (pyridinium triflate; Alfa Aesar, 97%) was used as purchased. Tetrahydrofuran (THF; Sigma Aldrich, 99.9%) and pyridine (py; Alfa Aesar, 99+%) were distilled over a potassium metal/benzophenone mixture and CaH_2 , respectively. Toluene (tol; Sigma Aldrich, HPLC grade) and dichloromethane (DCM; Sigma-Aldrich, HPLC grade, $\geq 99.8\%$) were purified using an MBraun SPS-800 solvent system. d_5 -Pyridine (d_5 -py; Cambridge Isotope Laboratories Inc, 99.5%), was dried over CaH_2 and vacuum distilled before use. D_2O was used as purchased. All solvents were stored under argon in gas tight ampoules over activated 3 Å molecular sieves. Deionised water was obtained from a Millipore Milli-Q purification system and sparged overnight with nitrogen.

NMR spectroscopy. NMR samples were prepared inside an inert atmosphere glovebox in NMR tubes fitted with a gas-tight valve. ^1H NMR spectra were recorded at either 499.9 MHz or 400.1 MHz on a Bruker AVIII 500 or a Bruker AVIII 400 NMR spectrometer, respectively. $^{13}\text{C}\{^1\text{H}\}$ NMR spectra were recorded at either 125.8 MHz or 100.6 MHz on a Bruker AVII 500 fitted with a cryoprobe or a Bruker AVIII 400 NMR spectrometer, respectively. ^{31}P NMR spectra were recorded on 202.4 MHz or 162.0

MHz on a Bruker AVIII 500 or a Bruker AVIII 400 NMR spectrometer, respectively. ^1H and ^{13}C NMR spectra are reported relative to TMS and referenced to the most downfield residual solvent resonance where possible (*d*₅-py: $\delta_{\text{H}} = 8.74$ ppm, $\delta_{\text{C}} = 150.35$ ppm). ^{31}P NMR spectra were externally referenced to an 85% solution of H_3PO_4 in H_2O ($\delta = 0$ ppm). Data analysis was performed using Bruker TopSpin 3.5 software.

Mass spectrometry. Analyses were performed using a Thermo Exactive mass spectrometer equipped with Waters Acquity liquid chromatography system. Instrument control and data processing were performed using Thermo Xcalibur Software. The system was calibrated on the day of the analysis and its mass accuracy with external calibration (as used for these experiments) is better than 5 ppm for 24 hours following calibration. The mass spectrometer was operated using the heated electrospray (HESI-II) probe and resolution was set to 50,000. Electrospray source conditions were adjusted to maximise sensitivity. A mixture of 10% water, 89.9% methanol and 0.1% formic acid was used to transport samples to the mass spectrometer at a flow rate of 0.2 mL/min.

1.2. Synthesis of compounds

[K(18-crown-6)][H₂PC(O)NHCHMeCO₂] ([K(18-crown-6)][**1a**)

[K(18-crown-6)][PCO] (20 mg, 0.06 mmol) and L-alanine (5 mg, 0.06 mmol) were weighed into a gas-tight NMR tube and pyridine (0.4 mL) was added to give a pale yellow solution and undissolved white solid. To aid the dissolution of the amino acid, deionised water (0.4 mL) was added and the mixture was sonicated for 30 minutes. The reaction was monitored by ^{31}P NMR spectroscopy, and was shown to go to completion after 24 hours. The pale yellow solution was transferred to a small Schlenk tube, and the volatiles were removed *in vacuo* to afford a yellow oily solid. Single crystals of [K(18-

crown-6)][**1a**] suitable for single crystal X-ray diffraction were obtained by slow diffusion of hexane (20 mL) into a solution of the product in a 50/50 mixture of pyridine/THF (5 mL). The off-white microcrystalline solid was subsequently isolated (9 mg, 36% crystalline yield). The reaction could also be carried out only in deionised water.

¹H NMR (499.9 MHz, *d*₅-pyridine): δ (ppm) 8.68 (br s, 1H; *NH*), 4.79 (dq, virtual quint, ³*J*_{H-H} = 7 Hz, 1H; *NCH*(CH₃)), 3.72 (m, ¹*J*_{H-P} = 205 Hz, ²*J*_{H-H} = 11 Hz, 1H; *PHH*), 3.69 (m, ¹*J*_{H-P} = 205 Hz, ²*J*_{H-H} = 11 Hz, 1H; *PHH*), 3.50 (s, 24H; 18-crown-6), 1.87 (d, ³*J*_{H-H} = 7 Hz, 3H; *NCH*(CH₃)).

¹H{³¹P} NMR (499.9 MHz, *d*₅-pyridine): δ (ppm) 3.72 (m, ²*J*_{H-H} = 11 Hz), 3.69 (m, ²*J*_{H-H} = 11 Hz), other resonances unchanged.

³¹P NMR (162.0 MHz, *d*₅-pyridine): δ (ppm) -131.4 (dd, virtual triplet, ¹*J*_{P-H} = 205 Hz).

³¹P{¹H} NMR (162.0 MHz, *d*₅-pyridine): δ (ppm) -131.4 (s).

¹³C{¹H} NMR (100.6 MHz, *d*₅-pyridine): δ (ppm) 175.9 (s; CO₂⁻), 171.0 (d, ¹*J*_{C-P} = 5 Hz; PC(O)), 70.7 (s; 18-crown-6), 53.1 (s; *NCH*(CH₃)), 20.8 (s; *NCH*(CH₃)).

ESI-MS (-ve ion mode, DMF): *m/z* = 334.6 {K[H₂PC(O)NHCHMeCO₂]₂}⁻.

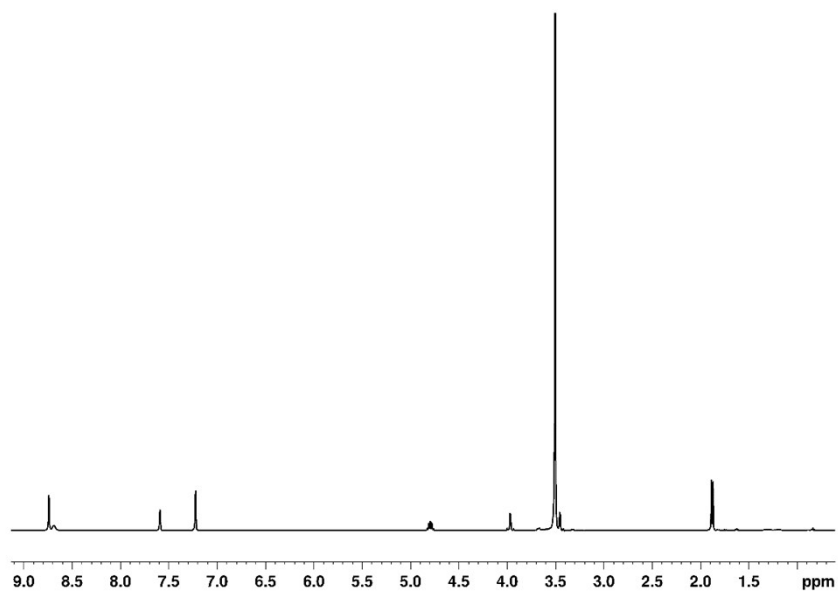


Figure S1. ^1H NMR spectrum of a d_5 -pyridine solution of $[\text{K}(18\text{-crown-6})][\mathbf{1a}]$.

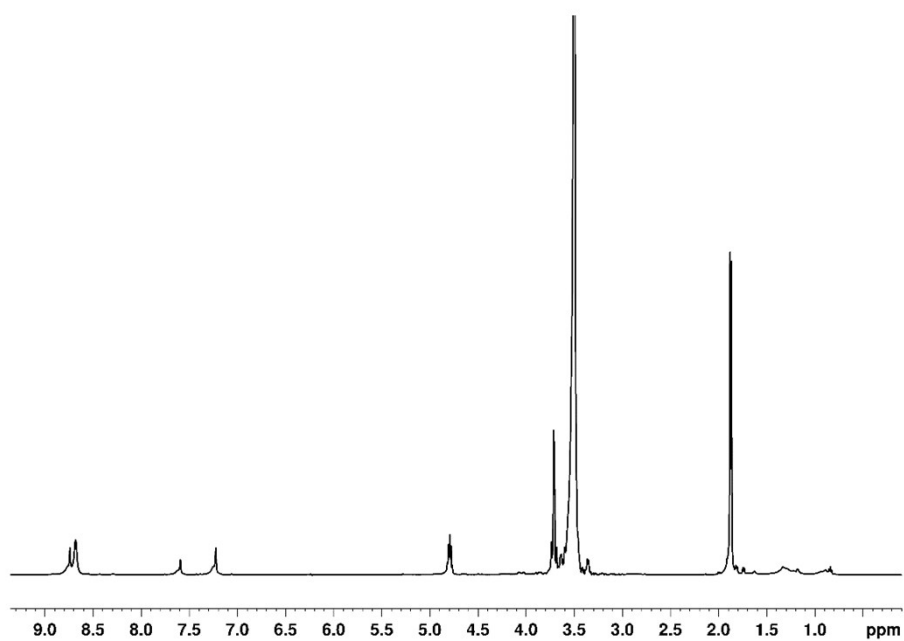


Figure S2. $^1\text{H}\{^{31}\text{P}\}$ NMR spectrum of a d_5 -pyridine solution of $[\text{K}(18\text{-crown-6})][\mathbf{1a}]$.

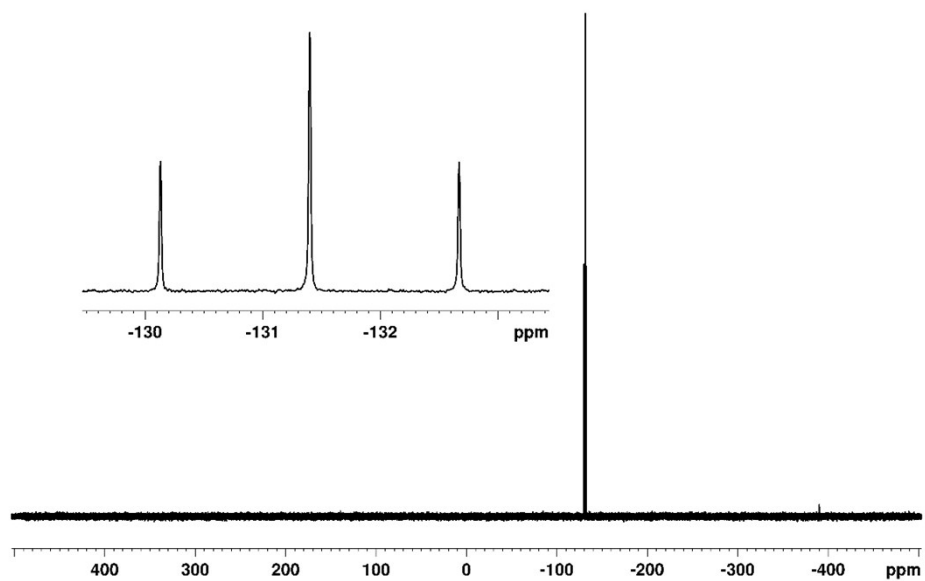


Figure S3. ^{31}P NMR spectrum of a d_5 -pyridine solution of $[\text{K}(18\text{-crown-}6)][\mathbf{1a}]$.

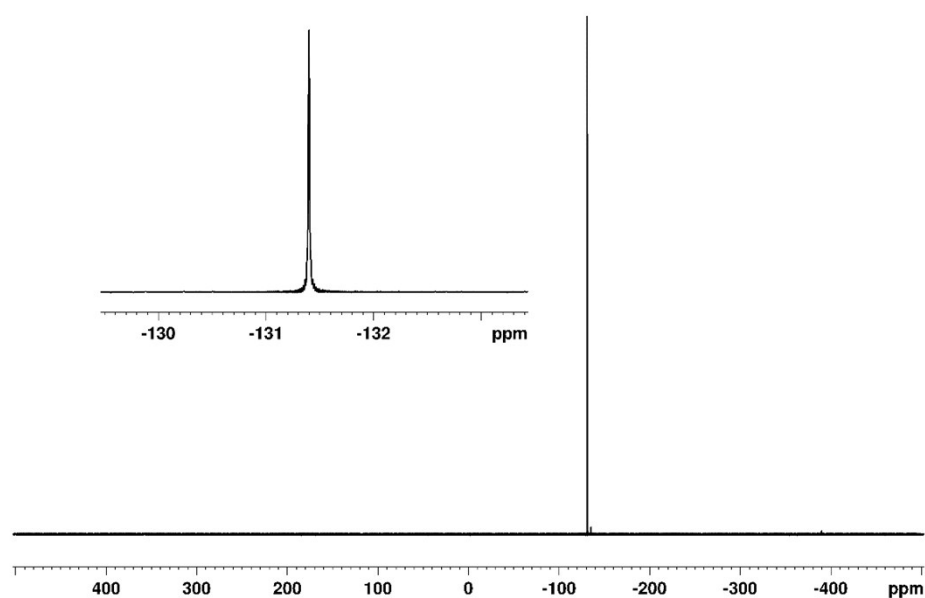


Figure S4. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution of $[\text{K}(18\text{-crown-}6)][\mathbf{1a}]$.

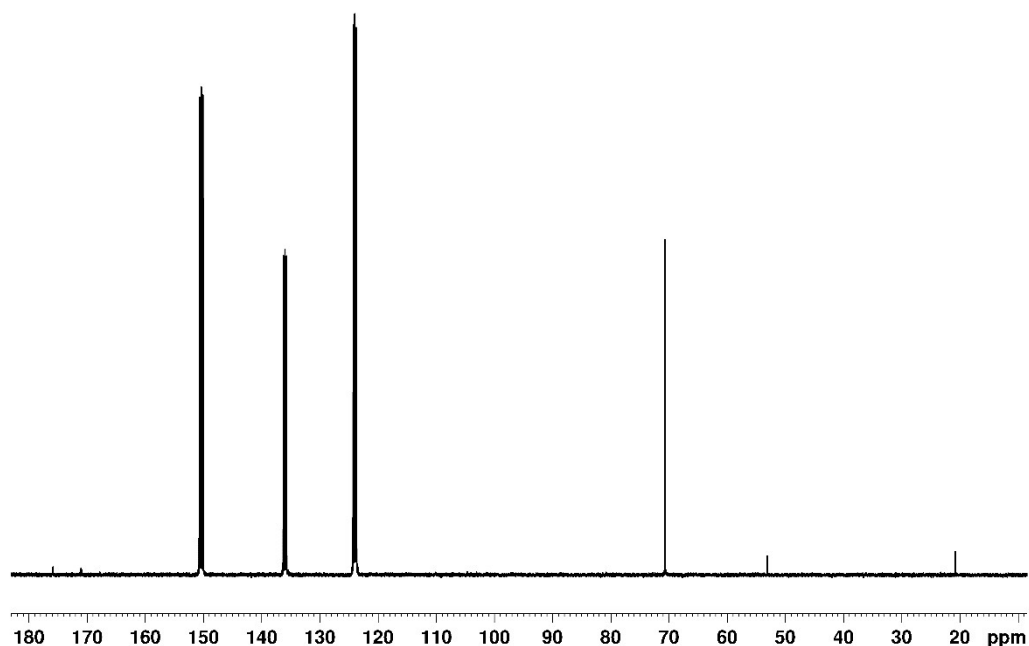


Figure S5. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution of $[\text{K}(18\text{-crown-6})][\mathbf{1a}]$.

$\text{Na}[\text{H}_2\text{PC}(\text{O})\text{NHCHMeCO}_2]$ ($\text{Na}[\mathbf{1a}]$)

$[\text{Na}(\text{dioxane})_{3.36}(\text{PCO})]$ (3.00 g, 8.88 mmol) and L-alanine (0.79 g, 8.88 mmol) were weighed out into a Schlenk tube, dissolved in a mixture of pyridine (40 mL) and distilled water (6 mL). The resulting pale orange solution was stirred overnight at room temperature. The solution was pale orange the following day. Filtration of the solution and removal of volatiles under dynamic vacuum yielded the product as a pale pink solid (1.49 g, 96% yield).

^1H NMR (400.2 MHz, d_5 -pyridine and a drop of H_2O , 298 K): δ (ppm) 8.89 (bs, 1H; NH), 4.93 (q, 1H; $\text{NCH}(\text{CH}_3)$), 3.93 (m, $^1J_{\text{H-P}} = 211$ Hz, $^2J_{\text{H-H}} = 12$ Hz, 1H; PHH), 3.90 (m, $^1J_{\text{H-P}} = 211$ Hz, $^2J_{\text{H-H}} = 12$ Hz, 1H; PHH), 1.76 (d, $^3J_{\text{H-H}} = 7$ Hz, 3H; $\text{NCH}(\text{CH}_3)$).

$^1\text{H}\{^{31}\text{P}\}$ NMR (400.2 MHz, d_5 -pyridine and a drop of H_2O , 298 K): δ (ppm) 3.93 (m, $^2J_{\text{H-H}} = 12$ Hz), 3.90 (m, $^2J_{\text{H-H}} = 12$ Hz), other resonances unchanged.

^{31}P NMR (162.0 MHz, d_5 -pyridine and a drop of H_2O , 298 K): δ (ppm) -131.0 (t, $^1J_{\text{P-H}}$ = 211 Hz).

$^{31}\text{P}\{^1\text{H}\}$ NMR (162.0 MHz, d_5 -pyridine and a drop of H_2O , 298 K): δ (ppm) -131.0 (s).

$^{13}\text{C}\{^1\text{H}\}$ NMR (125.8 MHz, d_5 -pyridine and a drop of H_2O , 298 K): δ (ppm) 179.7 (s; CO_2^-), 175.0 (d, $^1J_{\text{C-P}} = 8$ Hz; PC(O)), 53.6 (s; αC), 20.7 (s; βC).

ESI-MS (–ve ion mode, MeOH): $m/z = 148.0168$.

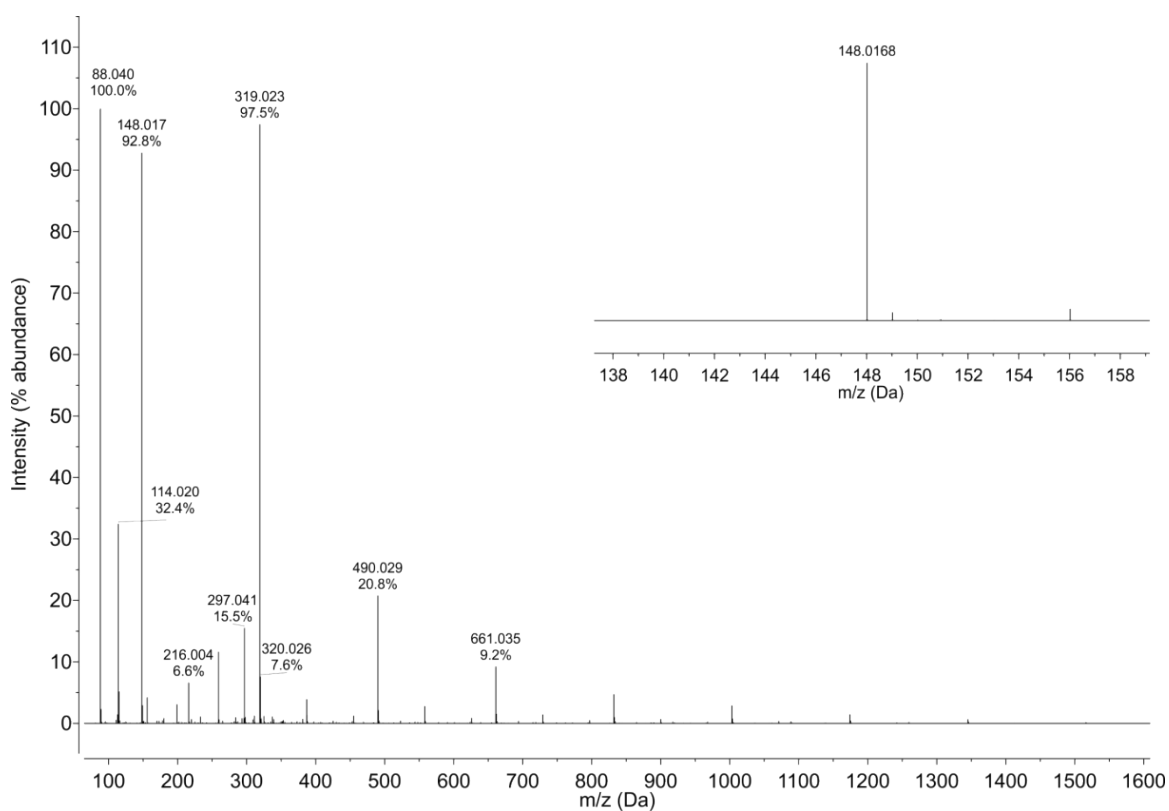


Figure S6. Negative ion mode ESI-MS spectrum of $\text{Na}[\mathbf{1a}]$. Inset: molecular ion peak

($\text{C}_4\text{H}_7\text{NO}_3\text{P}^-$: Calcd. 148.0164).

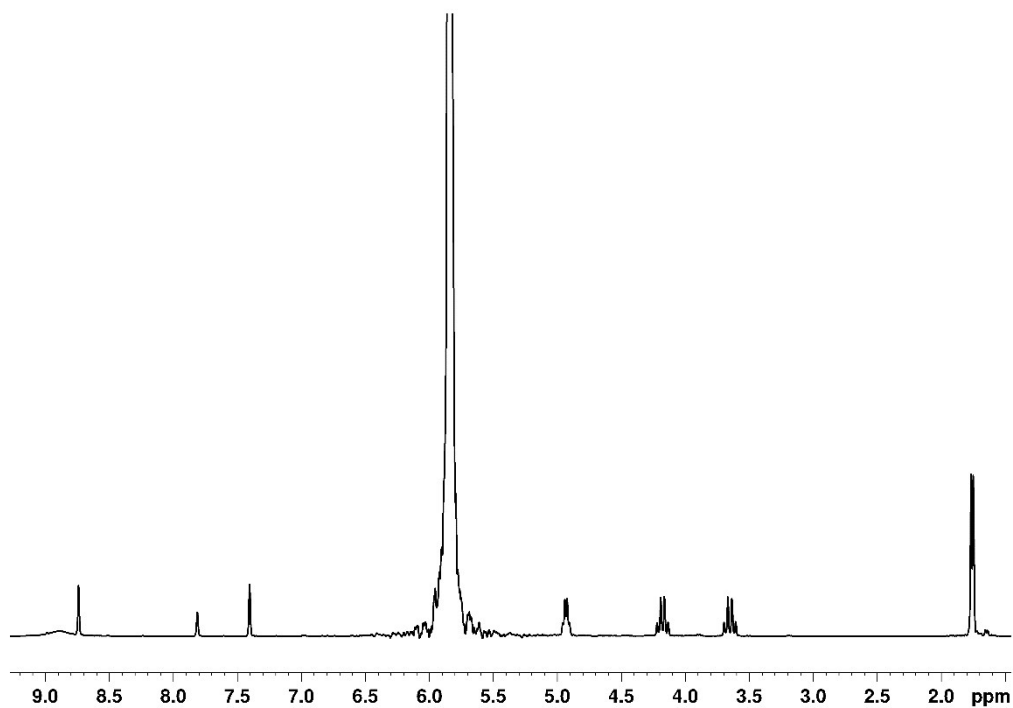


Figure S7. ^1H NMR spectrum of a d_5 -pyridine (w/ a drop of H_2O) solution of $\text{Na}[\mathbf{1a}]$.

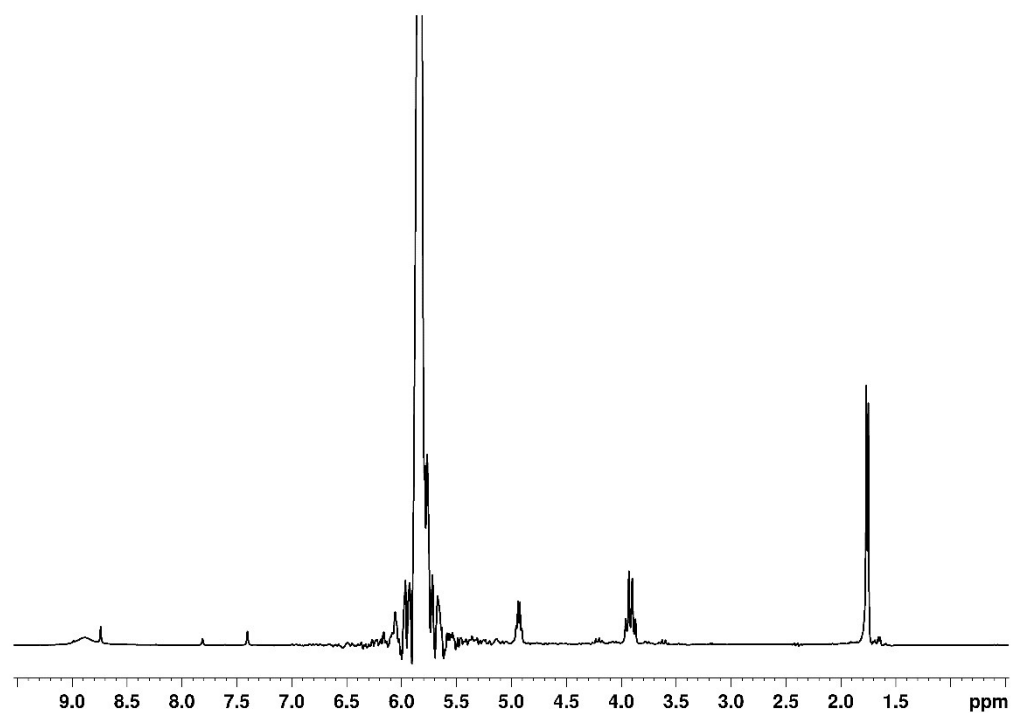


Figure S8. $^1\text{H}\{^{31}\text{P}\}$ NMR spectrum of a d_5 -pyridine (w/ a drop of H_2O) solution of $\text{Na}[\mathbf{1a}]$.

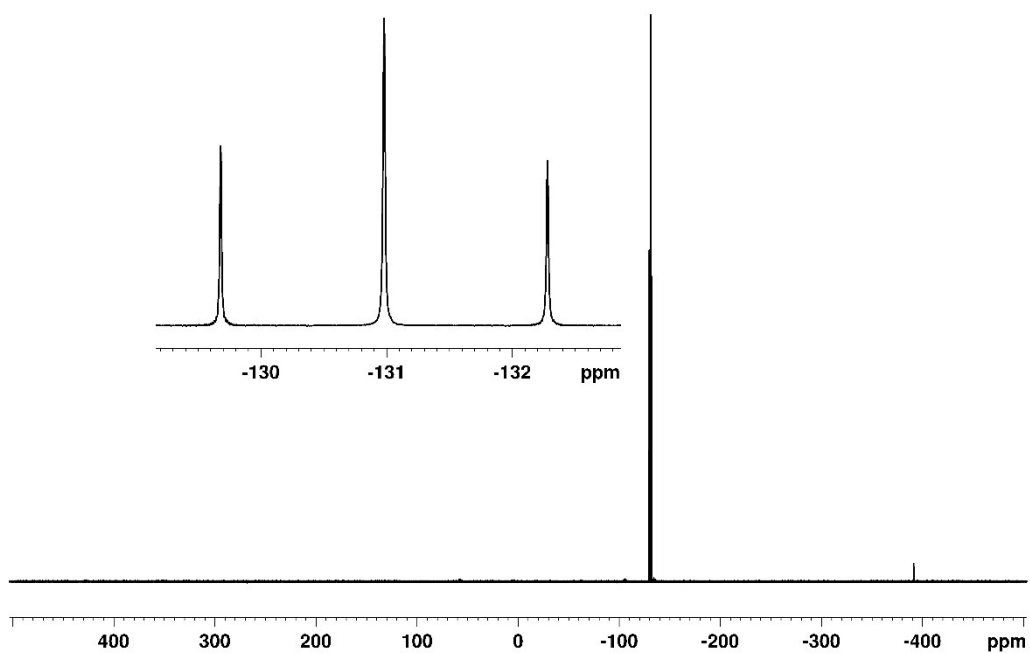


Figure S9. ^{31}P NMR spectrum of a d_5 -pyridine (w/ a drop of H_2O) solution of $\text{Na}[\mathbf{1a}]$.

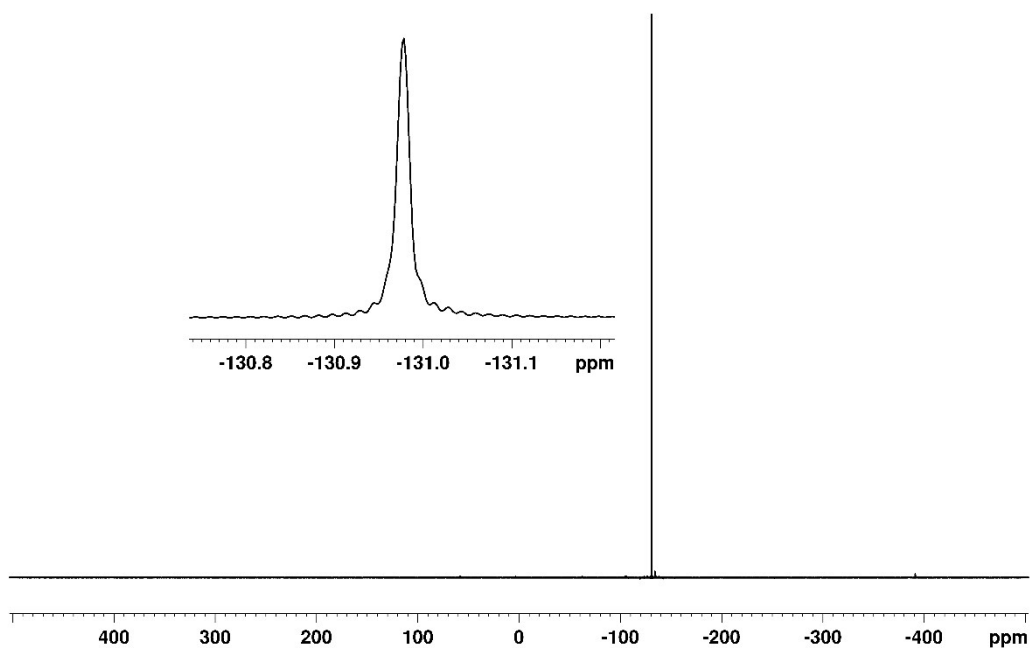


Figure S10. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine (w/ a drop of H_2O) solution of $\text{Na}[\mathbf{1a}]$.

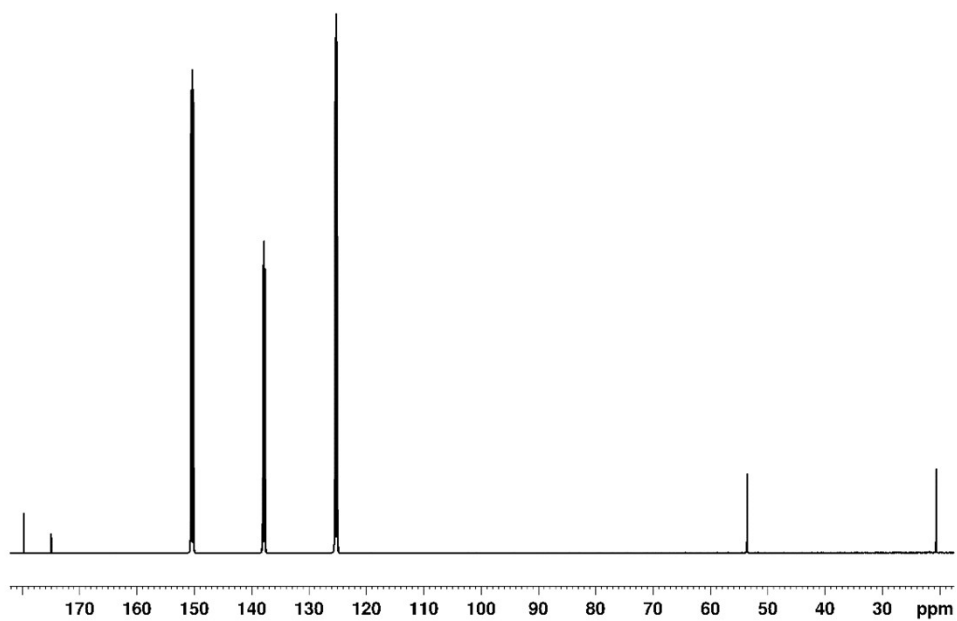


Figure S11. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine (w/ a drop of H_2O) solution of Na[**1a**].

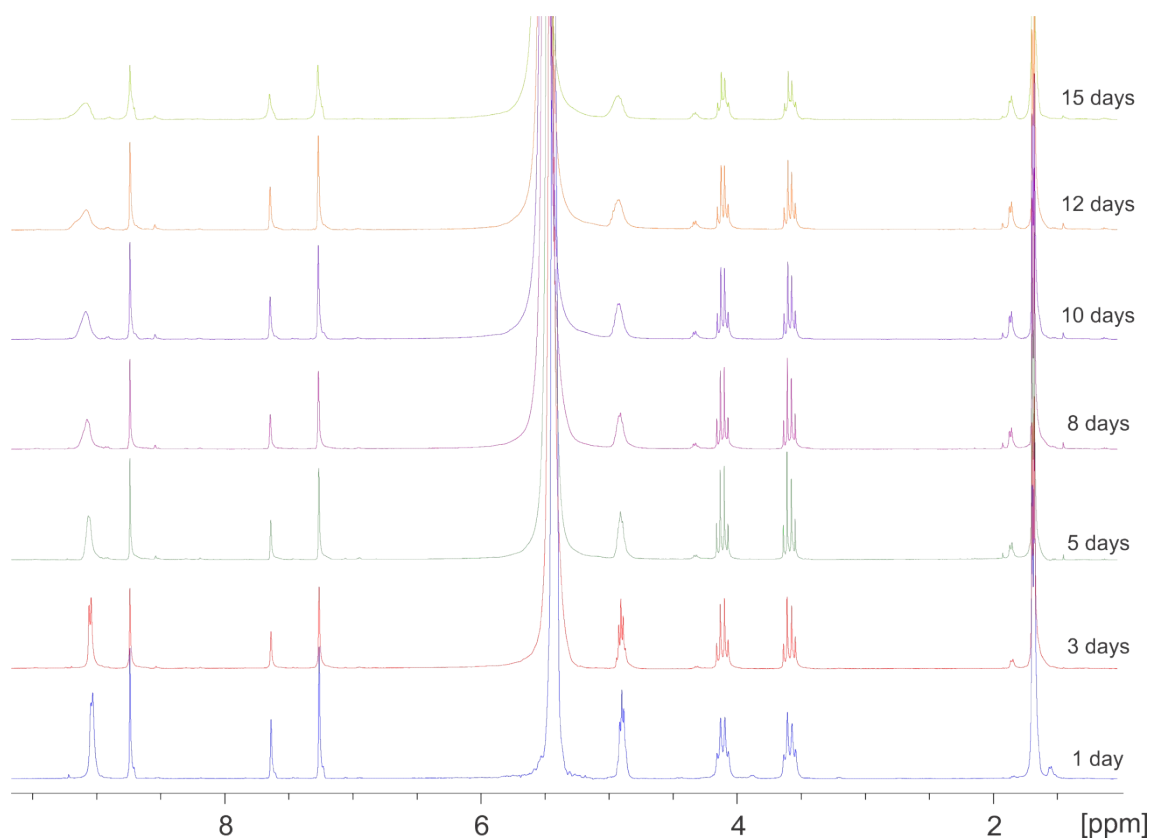


Figure S12. ^1H NMR spectra of a d_5 -pyridine (w/ a drop of H_2O) solution of Na[**1a**] that was exposed to air overnight on a daily basis.

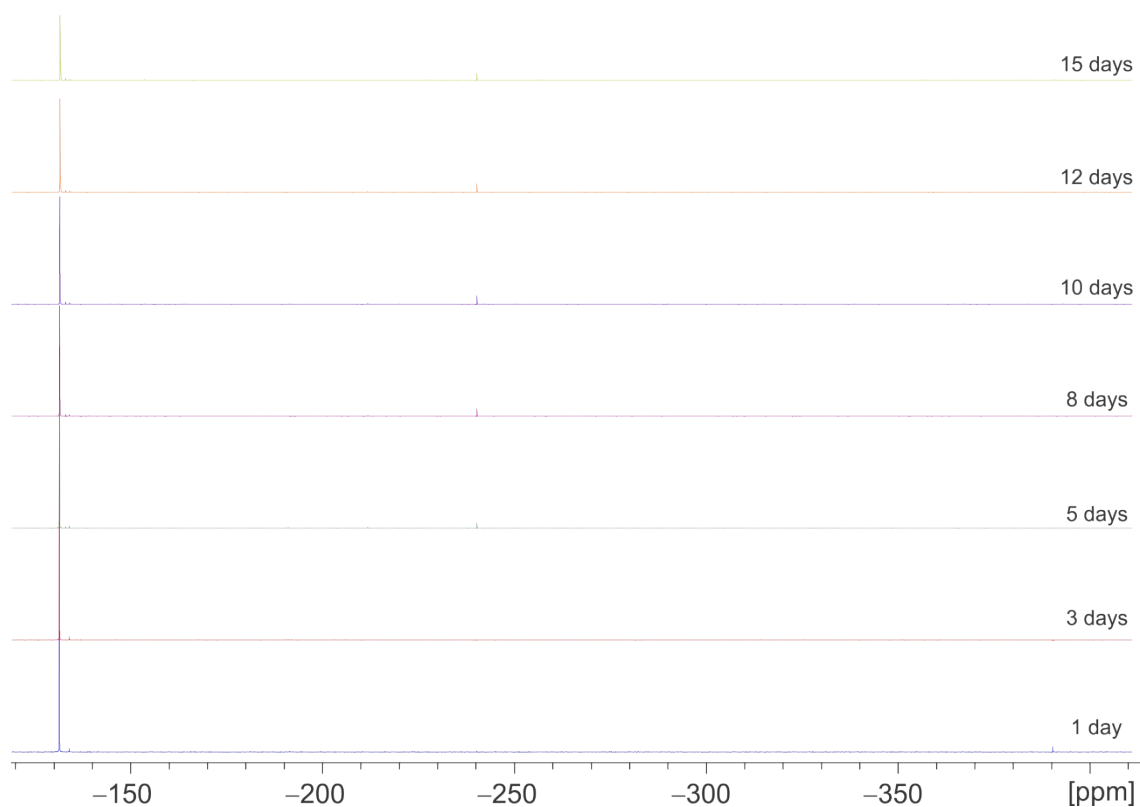


Figure S13. $^{31}\text{P}\{^1\text{H}\}$ NMR spectra of a d_5 -pyridine (w/ a drop of H_2O) solution of $\text{Na}[\mathbf{1a}]$ that was exposed to air overnight on a daily basis.

Deuterium exchange experiment with $\text{Na}[\mathbf{1a}]$

$\text{Na}[\mathbf{1a}]$ (16 mg, 0.09 mmol) was dissolved in D_2O . The resulting pale yellow solution was slightly cloudy. The ^{31}P NMR spectrum shows deuterium exchange with the phosphine protons. The ^1H NMR spectrum shows no evidence of the broad amide singlet or of the doublet corresponding to the PH_2 moiety.

^1H NMR (400.2 MHz, D_2O , 298 K): δ (ppm) 4.22 (q, 1H; $\text{NCH}(\text{CH}_3)$), 1.35 (d, $^3J_{\text{H-H}} = 7$ Hz, 3H; $\text{NCH}(\text{CH}_3)$).

^{31}P NMR (162.0 MHz, D_2O , 298 K): δ (ppm) -134.1 (q, $^1J_{\text{P-D}} = 33$ Hz).

$^{31}\text{P}\{^1\text{H}\}$ NMR (162.0 MHz, D_2O , 298 K): δ (ppm) -134.1 (q, $^1J_{\text{P-D}} = 33$ Hz).

$^{13}\text{C}\{^1\text{H}\}$ NMR (125.8 MHz, D_2O , 298 K): δ (ppm) 179.8 (s; CO_2^-), 176.9 (d, $^1J_{\text{C-P}} = 11.7$ Hz; $\text{PC}(\text{O})$), 51.6 (s; αC), 17.1 (s; βC).

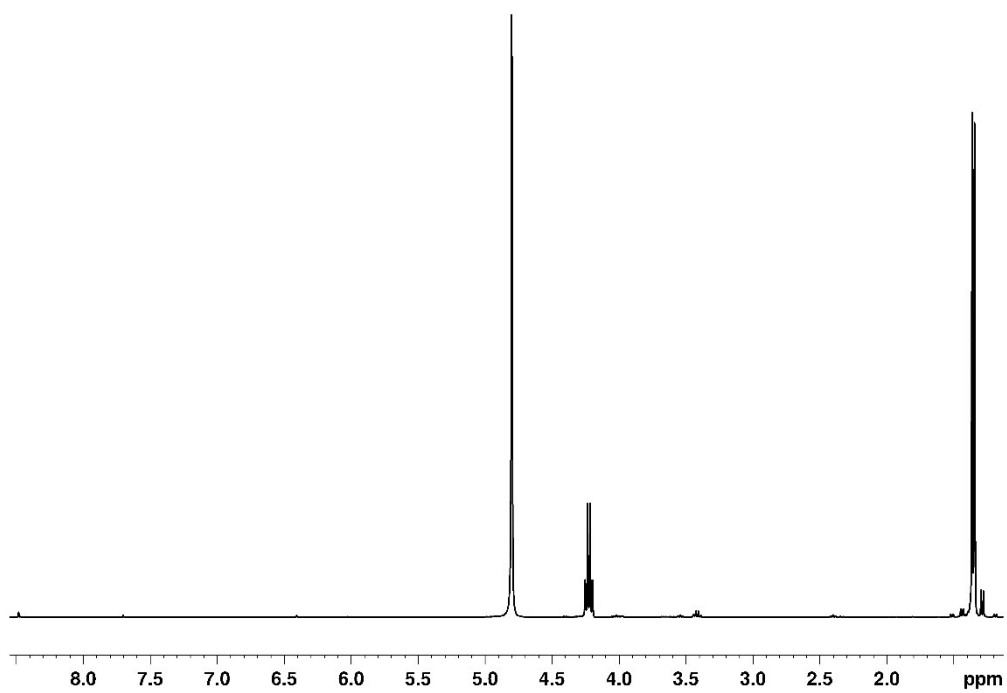


Figure S14. ^1H NMR spectrum of a D_2O solution of $\text{Na}[\mathbf{1a}]$.

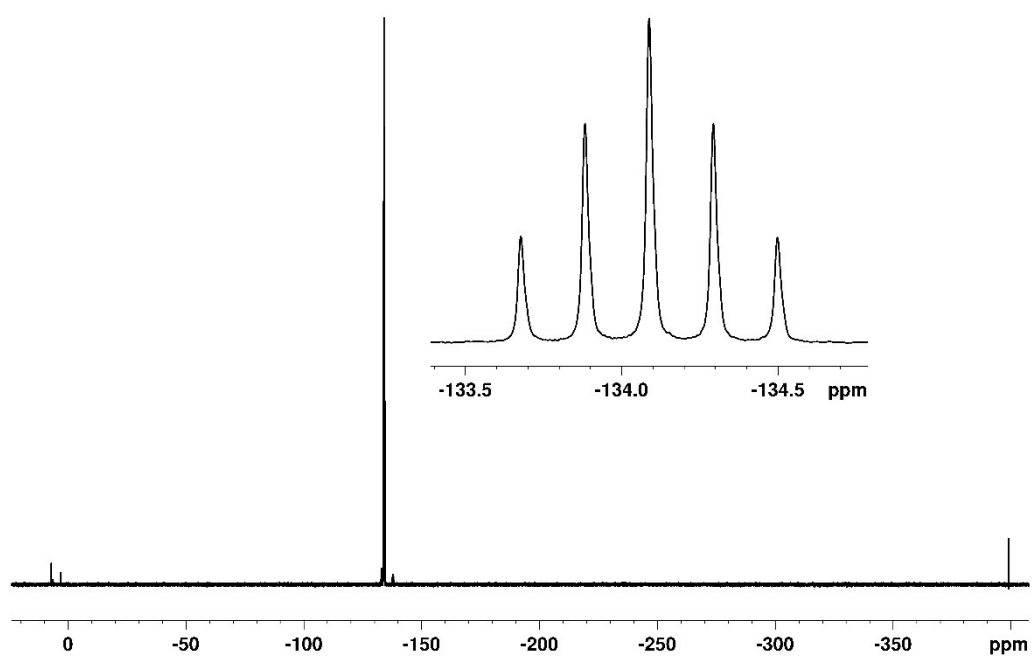


Figure S15. ^{31}P NMR spectrum of a D_2O solution of $\text{Na}[\mathbf{1a}]$.

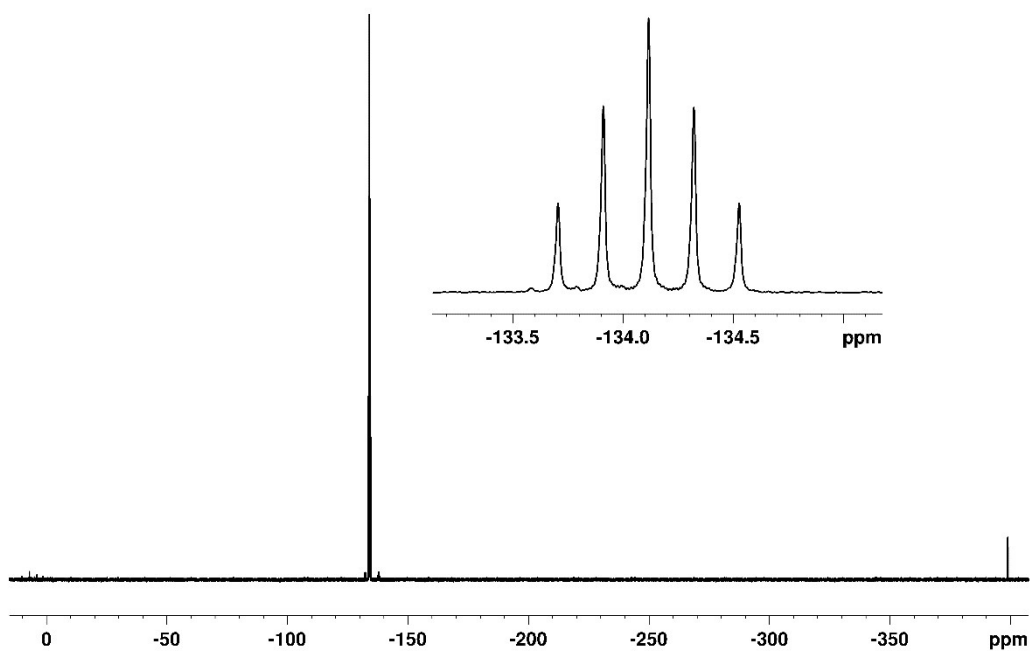


Figure S16. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of a D_2O solution of $\text{Na}[\mathbf{1a}]$.

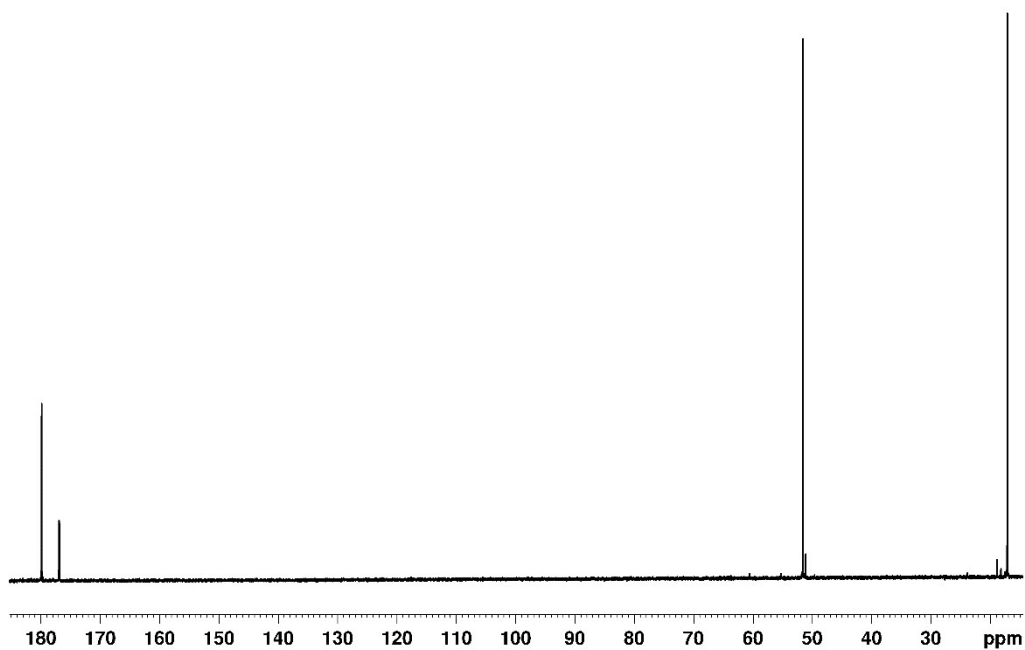


Figure S17. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of a D_2O solution of $\text{Na}[\mathbf{1a}]$.

Na[H₂PC(O)NH(CH₂OH)CO₂] (Na[**1b**])

[Na(dioxane)_{4.17}(PCO)] (4.00 g, 8.90 mmol) and L-serine (0.94 g, 8.90 mmol) were weighed out into a Schlenk tube, dissolved in a mixture of pyridine (50 mL) and distilled water (3 mL) and stirred overnight at room temperature. Addition of extra amino acid (0.14 mg, 0.001 mmol) was necessary for the reaction to reach completion. The mixture was stirred overnight at room temperature. Filtration of the solution and removal of volatiles under dynamic vacuum yielded the product as a pale pink solid (1.62 g, 96% yield).

¹H NMR (400.2 MHz, *d*₅-pyridine and a drop of H₂O, 298 K): δ (ppm) 9.02 (d, 1H; NH), 5.10 (s, 1H; αH), 4.46 (m, 2H; βH), 3.84 (m, ¹J_{H-P} = 210 Hz, ²J_{H-H} = 12 Hz, 1H; PHH), 3.83 (m, ¹J_{H-P} = 210 Hz, ²J_{H-H} = 12 Hz, 1H; PHH).

¹H{³¹P} NMR (400.2 MHz, *d*₅-pyridine and a drop of H₂O, 298 K): δ (ppm) 3.84 (m, ²J_{H-H} = 12 Hz, 1H; PHH), 3.83 (m, ²J_{H-H} = 12 Hz, 1H; PHH), other resonances unchanged from ¹H NMR spectrum.

³¹P NMR (161.9 MHz, *d*₅-pyridine and a drop of H₂O, 298 K): δ (ppm) -131.4 (t, ¹J_{P-H} = 210 Hz).

³¹P{¹H} NMR (161.9 MHz, *d*₅-pyridine and a drop of H₂O, 298 K): δ (ppm) -131.4 (s).

¹³C{¹H} NMR (100.6 MHz, *d*₅-pyridine and a drop of H₂O, 298 K): δ (ppm) 177.2 (s, CO₂⁻), 174.2 (d, ¹J_{C-P} = 8 Hz, PC(O)), 64.6 (s, αC), 59.1 (s, βC).

ESI-MS (-ve ion mode, MeOH): *m/z* = 164.0117.

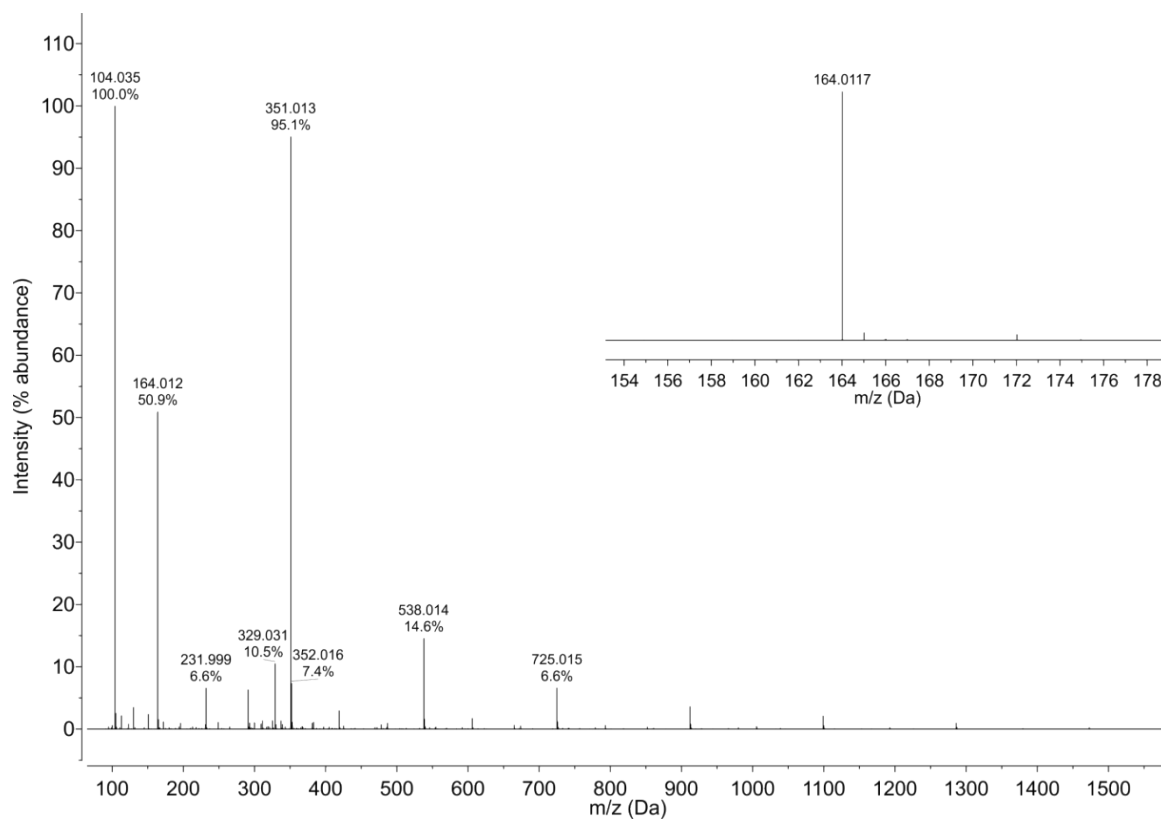


Figure S18. Negative ion mode ESI-MS spectrum of Na[**1b**]. Inset: molecular ion peak ($C_4H_7NO_4P^-$: Calcd. 164.0113).

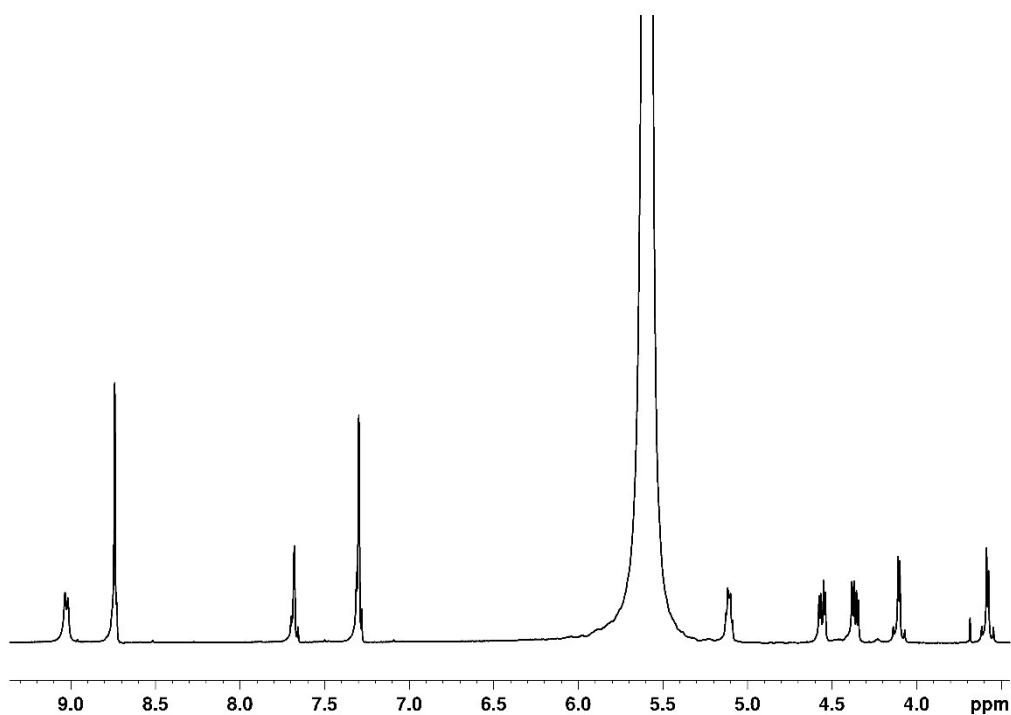


Figure S19. 1H NMR spectrum of a d_5 -pyridine solution (w/ a drop of H_2O) of Na[**1b**].

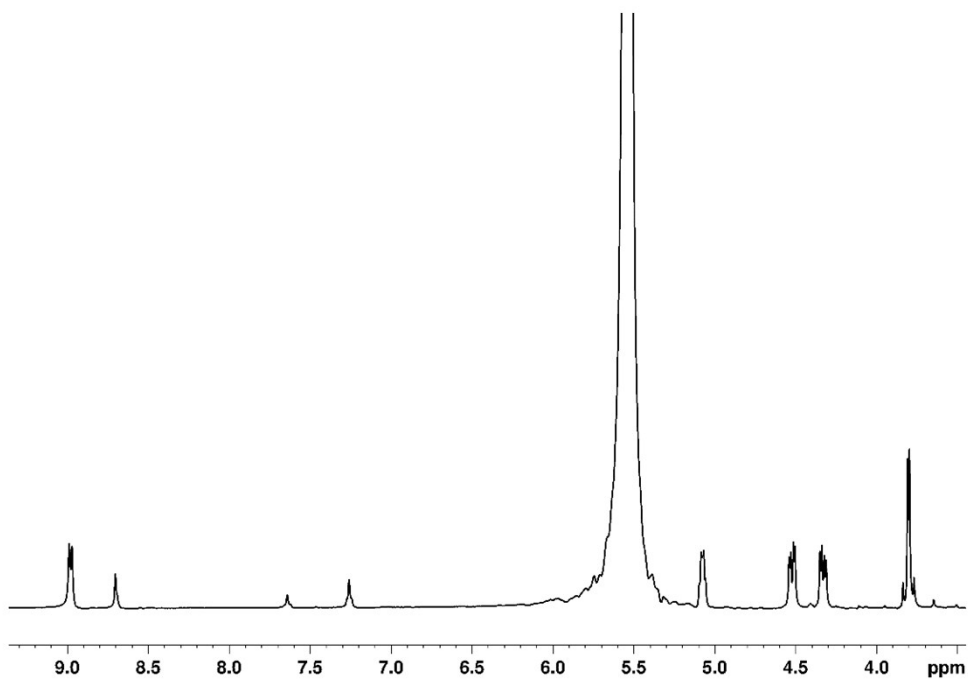


Figure S20. $^1\text{H}\{^{31}\text{P}\}$ NMR spectrum of a d_5 -pyridine solution (w/ a drop of H_2O) of **Na[1b]**.

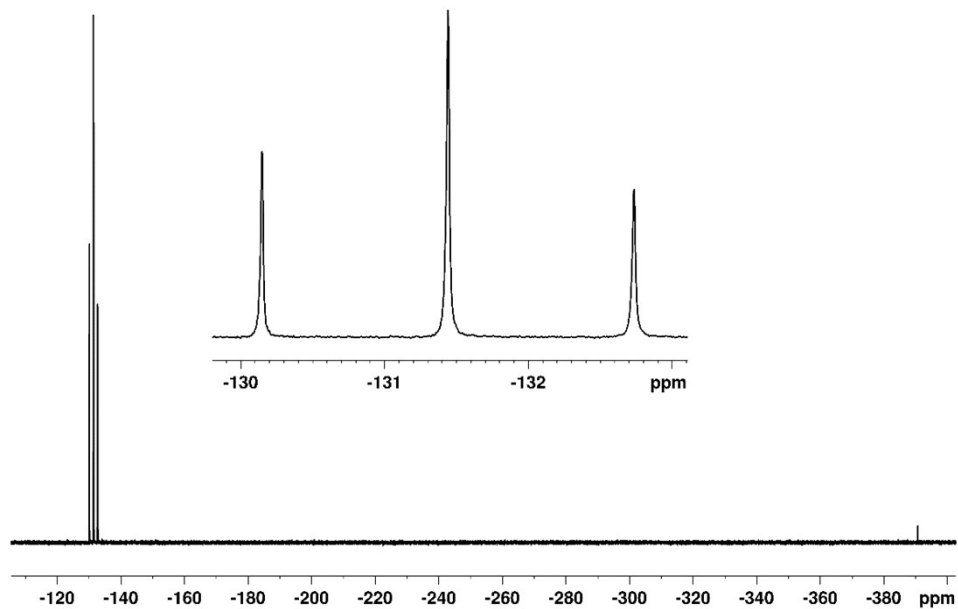


Figure S21. ^{31}P NMR spectrum of a d_5 -pyridine solution (w/ a drop of H_2O) of **Na[1b]**.

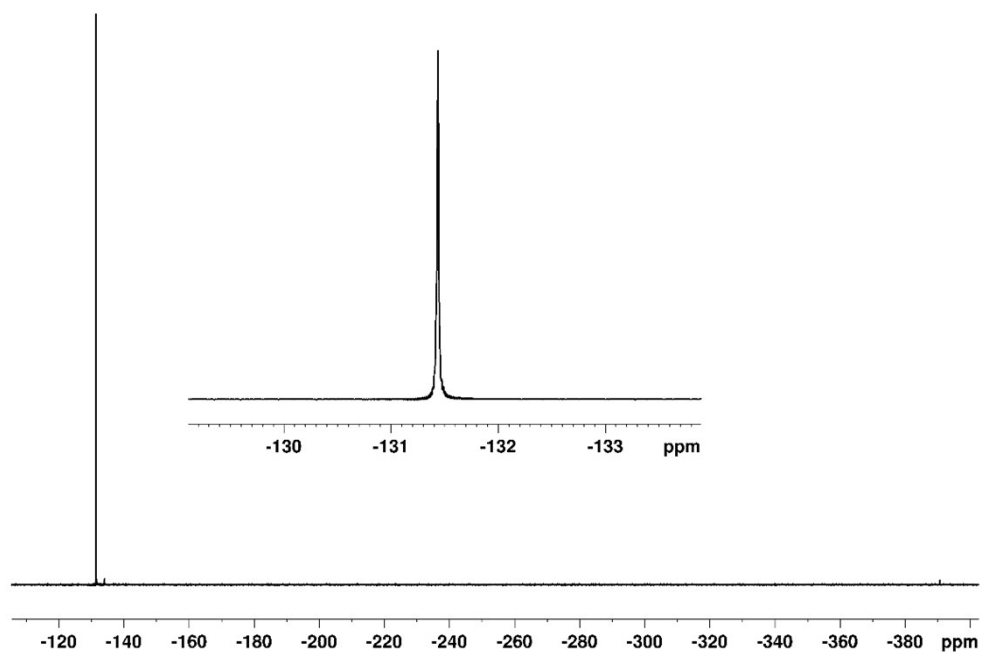


Figure S22. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution (w/ a drop of H_2O) of $\text{Na}[\mathbf{1b}]$.

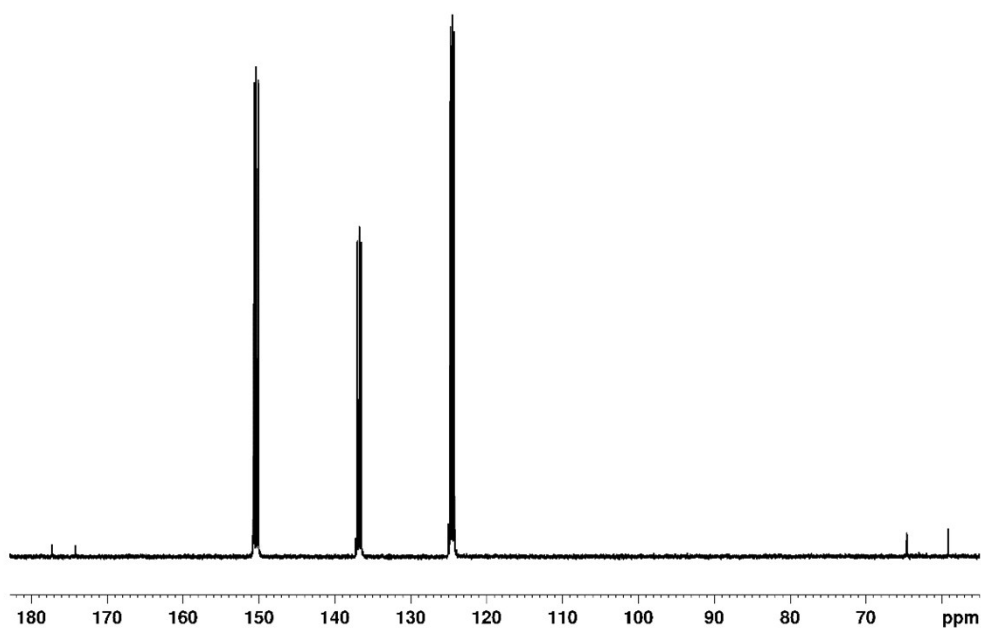


Figure S23. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution (w/ a drop of H_2O) of $\text{Na}[\mathbf{1b}]$.

Na[H₂PC(O)NH(CH₂SH)CO₂] (Na[**1c**])

[Na(dioxane)_{1.78}(PCO)] (4.00 g, 16.75 mmol) and L-cysteine (2.03 g, 16.75 mmol) were dissolved in pyridine (50 mL) at room temperature. Distilled water was added to the resulting pale orange solution, which contained some undissolved amino acid and the mixture was stirred overnight. After this time, the solution was almost clear. Filtration of the solution and removal the volatiles under dynamic vacuum yielded the product as a pale pink solid (3.19 g, 92% yield).

¹H NMR (400.2 MHz, *d*₅-pyridine, 298 K): δ (ppm) 9.25 (d, 1H; *NH*), 5.02 (q, 1H; *αH*), 3.86 (bd, ¹*J*_{H-P} = 210 Hz, 2H; *PH*₂), 3.38 (m, 2H; *βH*), 2.62 (bs, *SH*).

¹H{³¹P} NMR (400.2 MHz, *d*₅-pyridine, 298 K): δ (ppm) 3.86 (bs, 2H; *PH*₂), other resonances unchanged from ¹H NMR spectrum.

³¹P NMR (161.9 MHz, *d*₅-pyridine, 298 K): δ (ppm) -130.6 (t, ¹*J*_{P-H} = 210 Hz).

³¹P{¹H} NMR (161.9 MHz, *d*₅-pyridine, 298 K): δ (ppm) -130.6 (s).

¹³C{¹H} NMR (100.6 MHz, *d*₅-pyridine, 298 K): δ (ppm) 176.8 (s, CO₂⁻), 174.6 (d, ¹*J*_{C-P} = 8 Hz, PC(O)), 59.4 (s, *αC*), 28.2 (s, *βC*).

ESI-MS (-ve ion mode, MeOH): *m/z* = 179.9888.

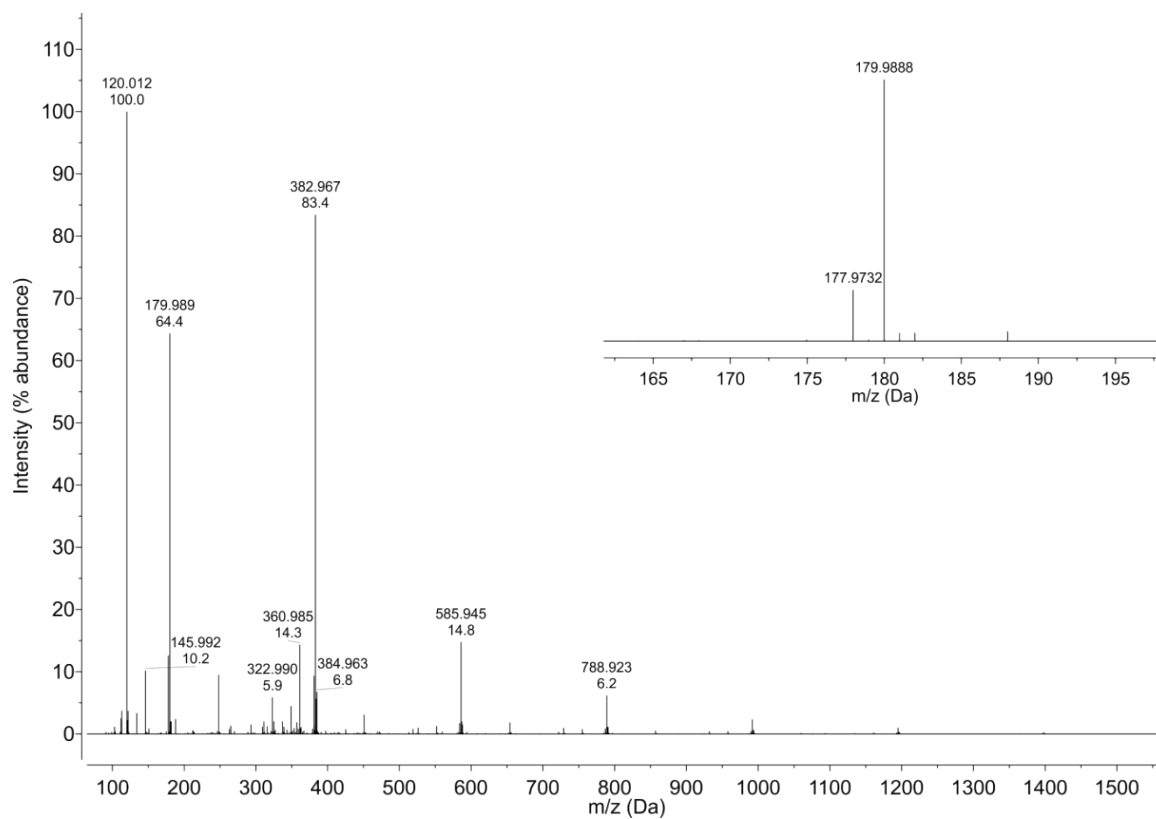


Figure S24. Negative ion mode ESI-MS spectrum of Na[**1c**]. Inset: molecular ion peak ($C_4H_7NO_3SP^-$: Calcd. 179.9884).

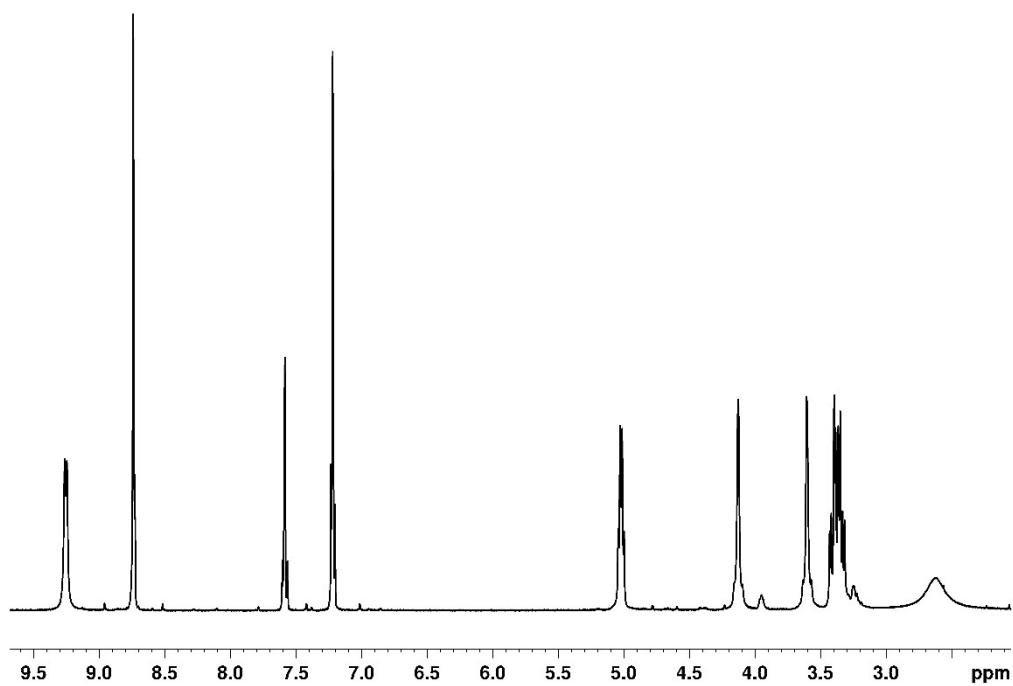


Figure S25. 1H NMR spectrum of a d_5 -pyridine solution of Na[**1c**].

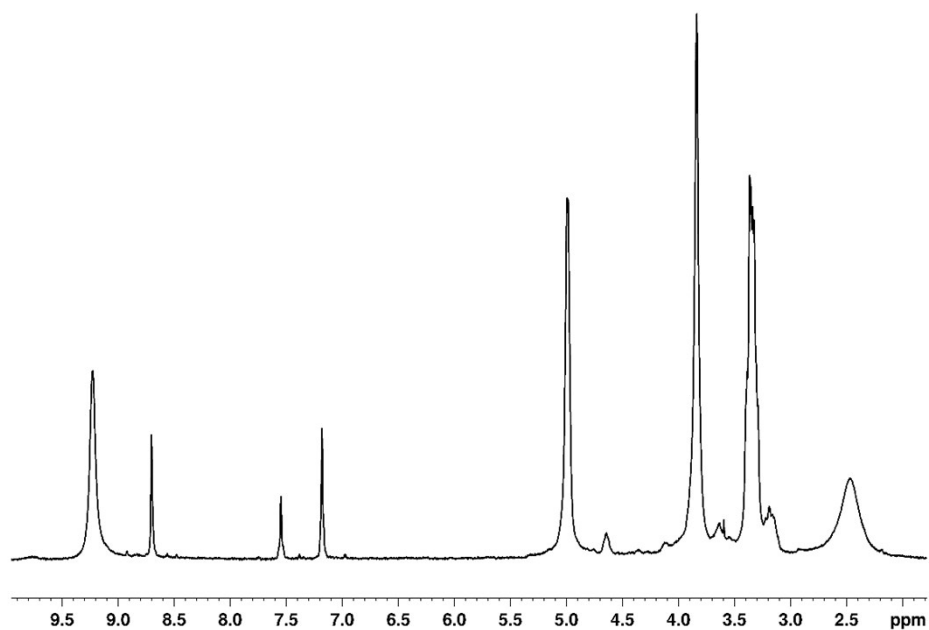


Figure S26. $^1\text{H}\{^{31}\text{P}\}$ NMR spectrum of a d_5 -pyridine solution of Na[**1c**].

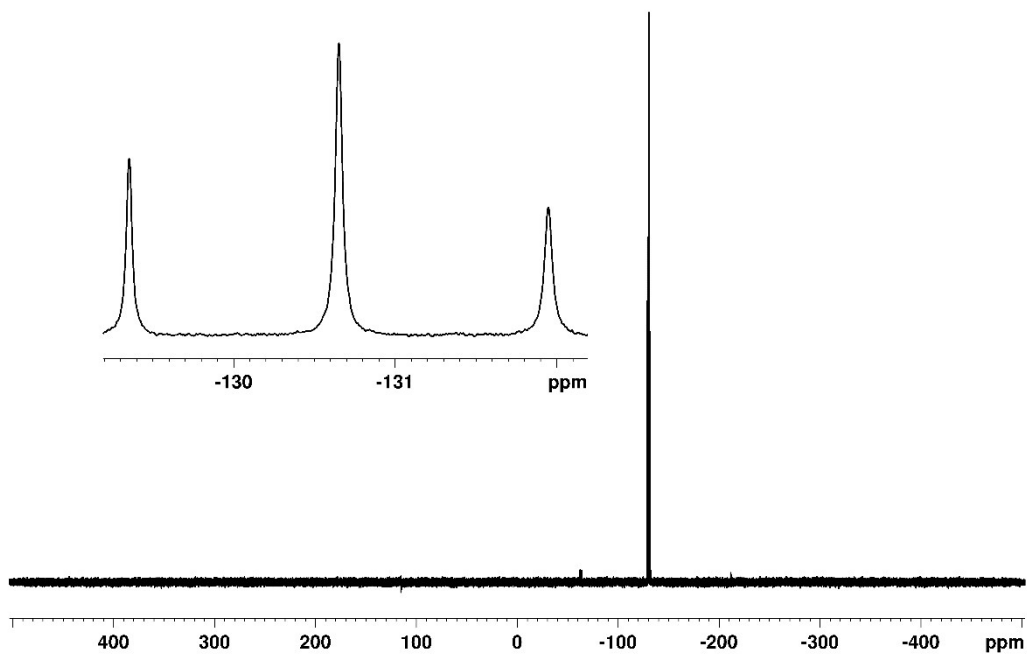


Figure S27. ^{31}P NMR spectrum of a d_5 -pyridine solution of Na[**1c**].

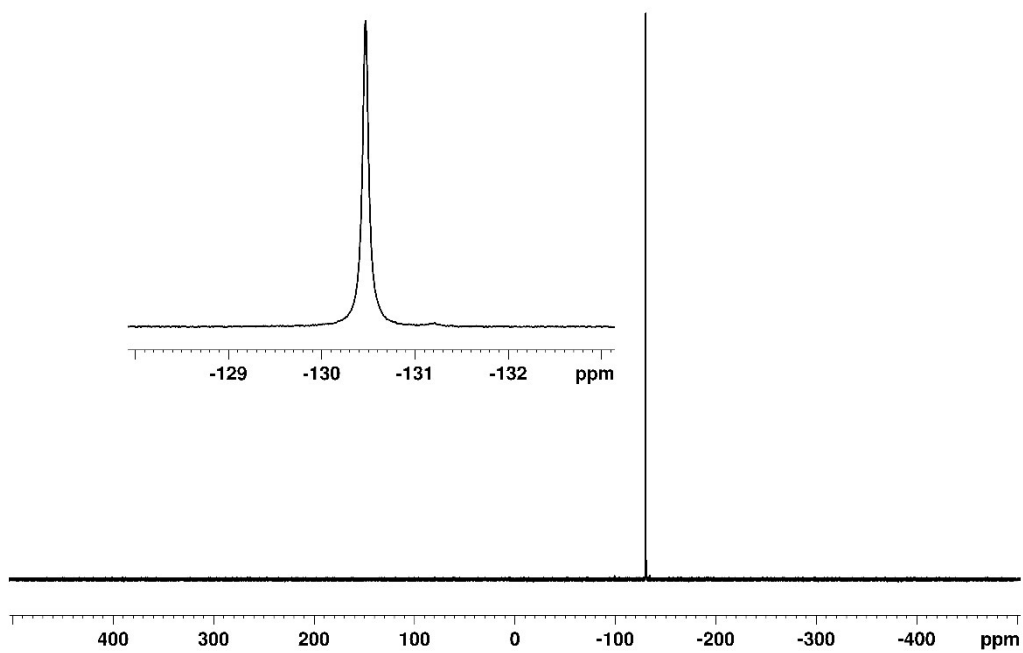


Figure S28. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution of Na[**1c**].

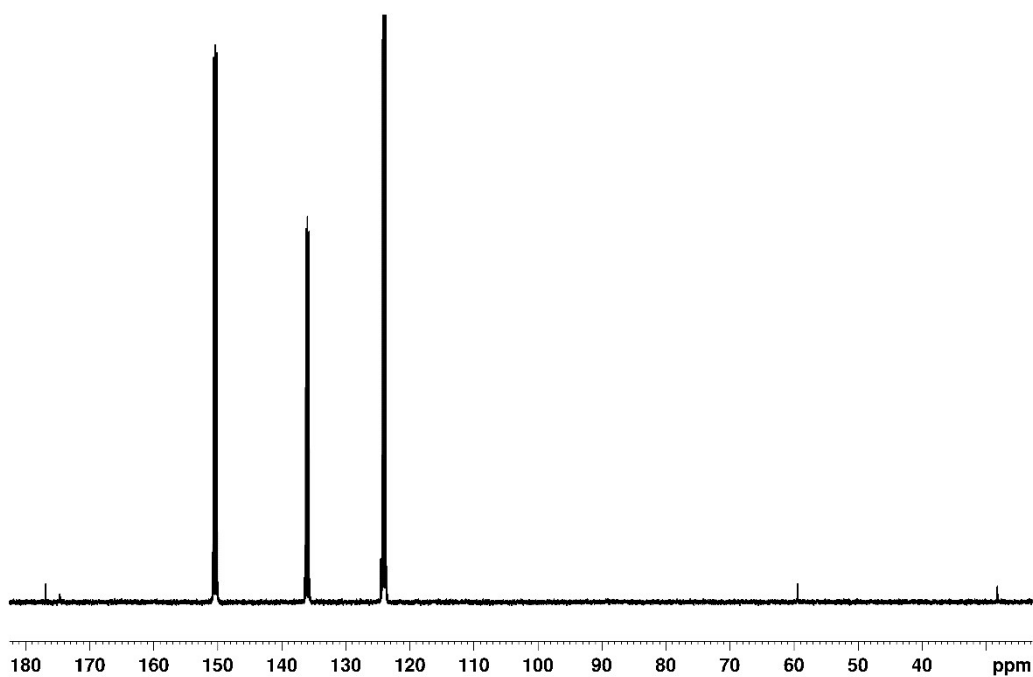


Figure S29. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution of Na[**1c**].

Na[H₂PC(O)NH(CH₂C(O)NH₂)CO₂] (Na[**1d**])

Pyridine (40 mL) and distilled water (40 mL) were added to a mixture of [Na(dioxane)_{4.17}(PCO)] (4.00 g, 8.90 mmol) and L-asparagine monohydrate (1.34 g, 8.90 mmol) at room temperature. The resulting pale yellow solution was stirred for 1h at which stage NMR spectroscopy revealed the presence of some PCO⁻. Addition of extra 0.001 mmol of the amino acid was necessary for the reaction to reach completion. Filtration of the solution and removal of volatiles under a dynamic vacuum yielded the product as a beige solid (1.89 g, 98% yield).

¹H NMR (400.2 MHz, *d*₅-pyridine and a drop of H₂O, 298 K): δ (ppm) 9.07 (d, 1H; *NH*), 8.54 (s, 1H; *NHH*), 7.59 (s, 1H; *NHH*), 5.38 (q, 1H; αH), 3.92 (m, ¹*J*_{H-P} = 211 Hz, ²*J*_{H-P} = 12 Hz 1H; *PHH*), 3.91 (m, ¹*J*_{H-P} = 211 Hz, ²*J*_{H-P} = 12 Hz 1H; *PHH*), 3.35 (m, 2H; βH).

¹H{³¹P} NMR (400.2 MHz, *d*₅-pyridine and a drop of H₂O, 298 K): δ (ppm) 3.92 (m, ²*J*_{H-P} = 12 Hz 1H; *PHH*), 3.91 (m, ²*J*_{H-P} = 12 Hz 1H; *PHH*), other resonances unchanged from ¹H NMR spectrum.

³¹P NMR (161.9 MHz, *d*₅-pyridine and a drop of H₂O, 298 K): δ (ppm) -131.0 (t, ¹*J*_{P-H} = 211 Hz).

³¹P{¹H} NMR (161.9 MHz, *d*₅-pyridine and a drop of H₂O, 298 K): δ (ppm) -131.0 (s)

¹³C{¹H} NMR (100.6 MHz, *d*₅-pyridine and a drop of H₂O, 298 K): δ (ppm) 177.7 (s, CO₂⁻), 177.0 (s, γC), 175.8 (d, ¹*J*_{C-P} = 9 Hz, PC(O)), 55.1 (s, αC), 41.0 (s, βC).

ESI-MS (-ve ion mode, MeOH): *m/z* = 191.0226.

CHN Calcd. (Found) for C₅H₈N₂NaO₄P: 28.05(28.07), 3.77(3.84), 13.08 (12.90).

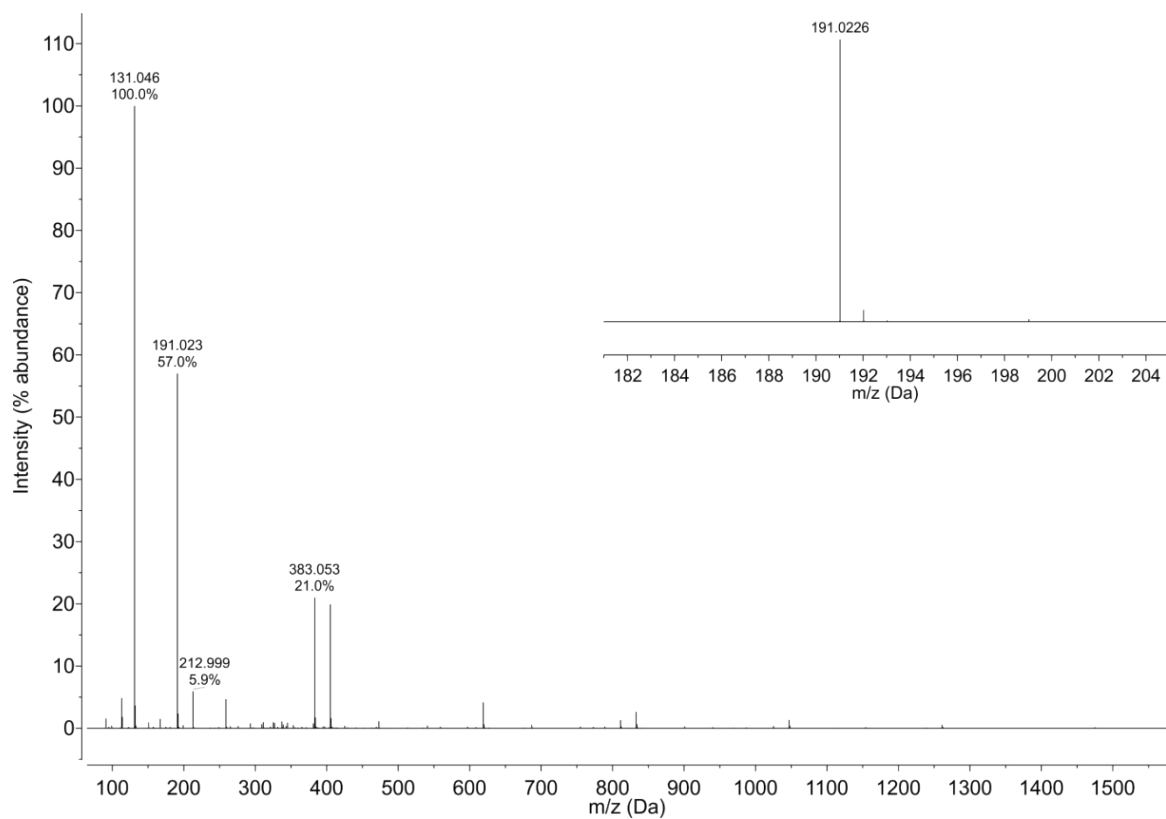


Figure S30. Negative ion mode ESI-MS spectrum of Na[**1d**]. Inset: molecular ion peak ($C_5H_8N_2O_4P^-$: Calcd. 191.0222).

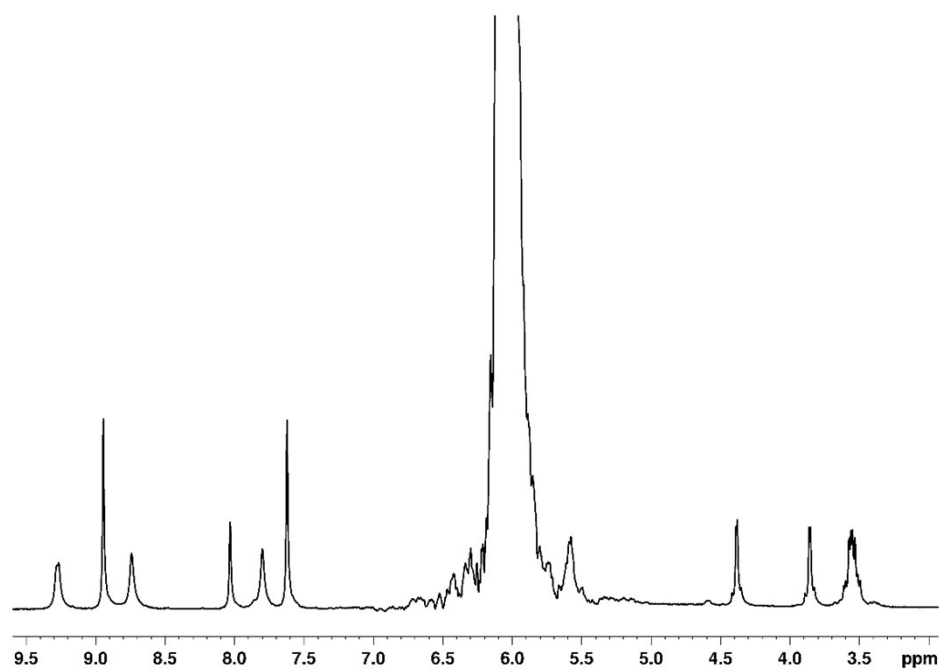


Figure S31. 1H NMR spectrum of a d_5 -pyridine solution (w/ a drop of H_2O) of Na[**1d**].

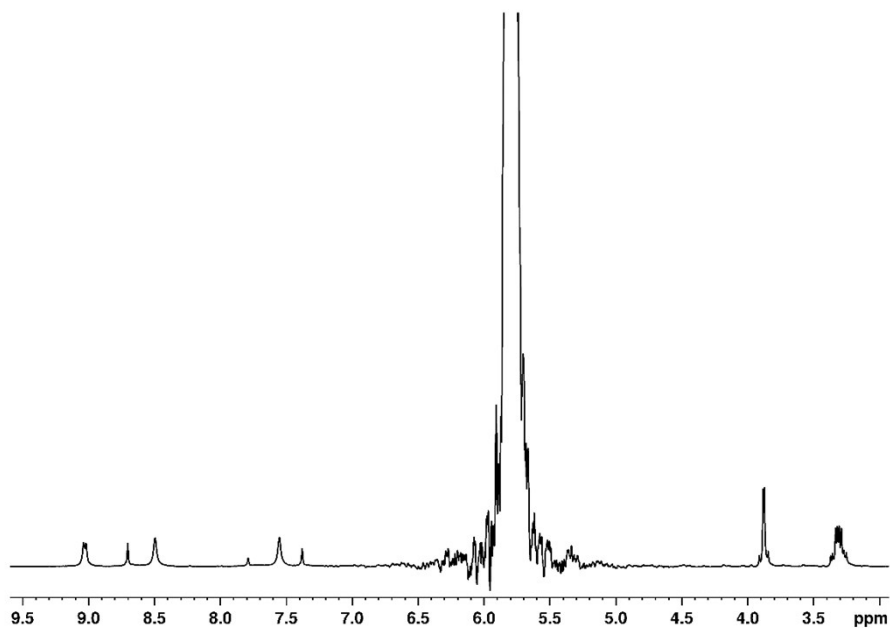


Figure S32. $^1\text{H}\{^{31}\text{P}\}$ NMR spectrum of a d_5 -pyridine solution (w/ a drop of H_2O) of $\text{Na}[\mathbf{1d}]$.

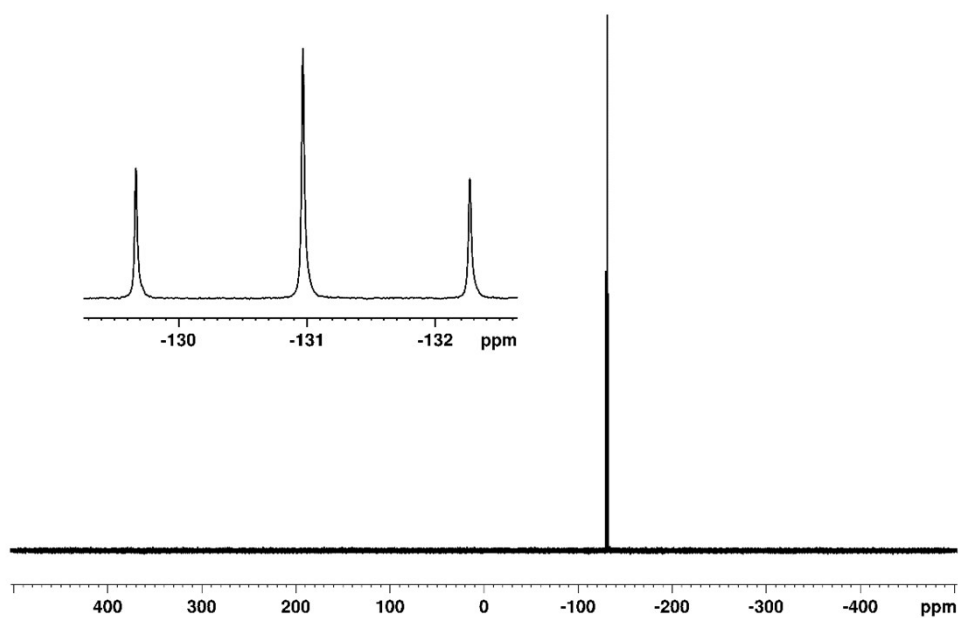


Figure S33. ^{31}P NMR spectrum of a d_5 -pyridine solution (w/ a drop of H_2O) of $\text{Na}[\mathbf{1d}]$.

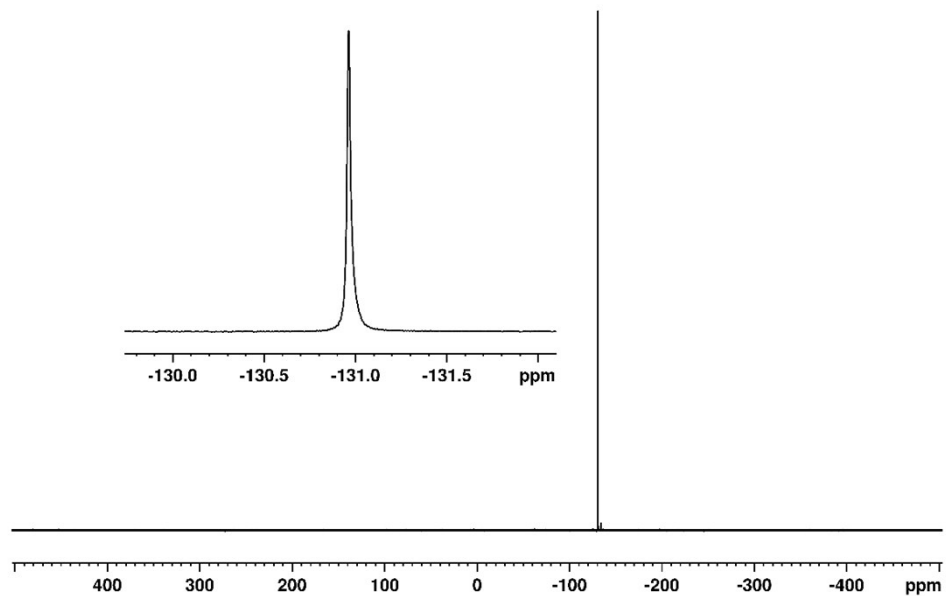


Figure S34. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution (w/ a drop of H_2O) of Na[**1d**].

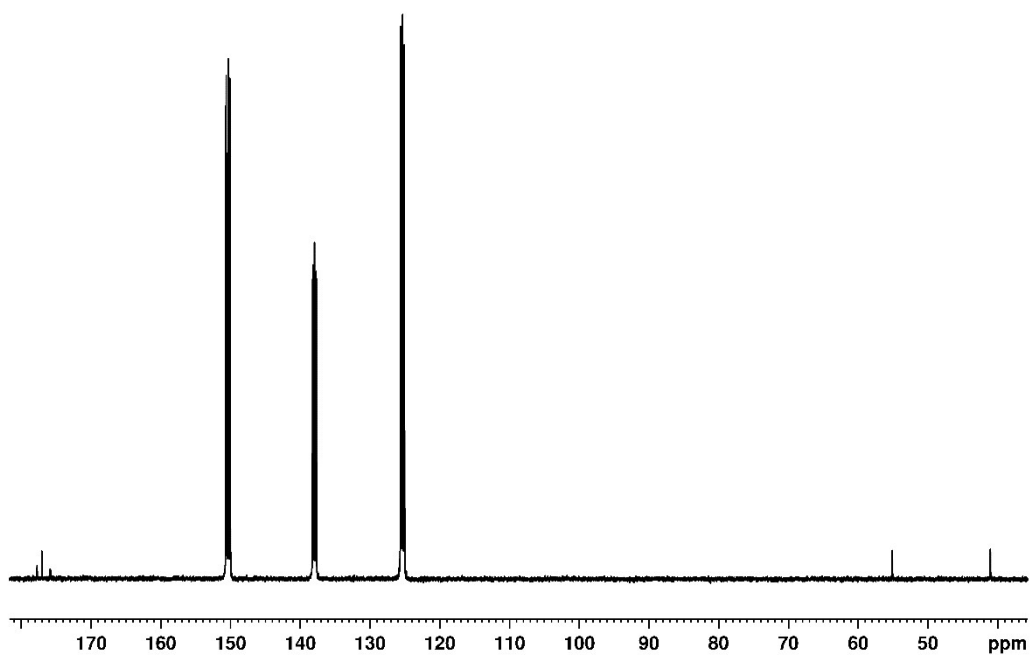


Figure S35. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution (w/ a drop of H_2O) of Na[**1d**].

Na[H₂PC(O)NH(CH₂)₂C(O)NH₂)CO₂] (Na[**1e**])

Pyridine (30 mL) and sparged water (30 mL) were added to a mixture of [Na(dioxane)_{3.36}(PCO)] (3.00 g, 8.88 mmol) and L-glutamine (1.30 g, 8.88 mmol) at room temperature. The resulting pale brown cloudy solution was stirred overnight. Filtration of the solution and removal of the volatiles under dynamic vacuum afforded the product as a beige solid (1.20 g, 59 % yield).

¹H NMR (400.2 MHz, *d*₅-pyridine and a drop of H₂O, 298 K): δ (ppm) 8.85 (d, 1H; *NH*), 8.49 (s, 1H; *NHH*), 7.55 (s, 1H; *NHH*), 5.07 (q, 1H; αH), 3.86 (m, ¹*J*_{H-P} = 210 Hz, ²*J*_{H-P} = 12 Hz 1H; *PHH*), 3.85 (m, ¹*J*_{H-P} = 210 Hz, ²*J*_{H-P} = 12 Hz 1H; *PHH*), 2.74 (m, 4H; β, γH).

¹H{³¹P} NMR (400.2 MHz, *d*₅-pyridine and a drop of H₂O, 298 K): δ (ppm) 3.86 (m, ²*J*_{H-P} = 12 Hz 1H; *PHH*), 3.85 (m, ²*J*_{H-P} = 12 Hz 1H; *PHH*), other resonances unchanged from ¹H NMR spectrum.

³¹P NMR (161.9 MHz, *d*₅-pyridine and a drop of H₂O, 298 K): δ (ppm) -131.3 (t, ¹*J*_{P-H} = 210 Hz).

³¹P{¹H} NMR (161.9 MHz, *d*₅-pyridine and a drop of H₂O, 298 K): δ (ppm) -131.3 (s).

¹³C{¹H} NMR (100.6 MHz, *d*₅-pyridine and a drop of H₂O, 298 K): δ (ppm) 178.6 (s, CO₂⁻), 177.7 (s, δC), 174.5 (d, ¹*J*_{C-P} = 8 Hz, PC(O)), 57.3 (s, αC), 34.0 (s, γC), 31.1 (s, βC).

ESI-MS (-ve ion mode, MeOH): *m/z* = 205.0381.

CHN Calcd. (Found) for C₆H₁₀N₂NaO₄P: 31.59(30.69), 4.42(4.37), 12.28 (11.67).

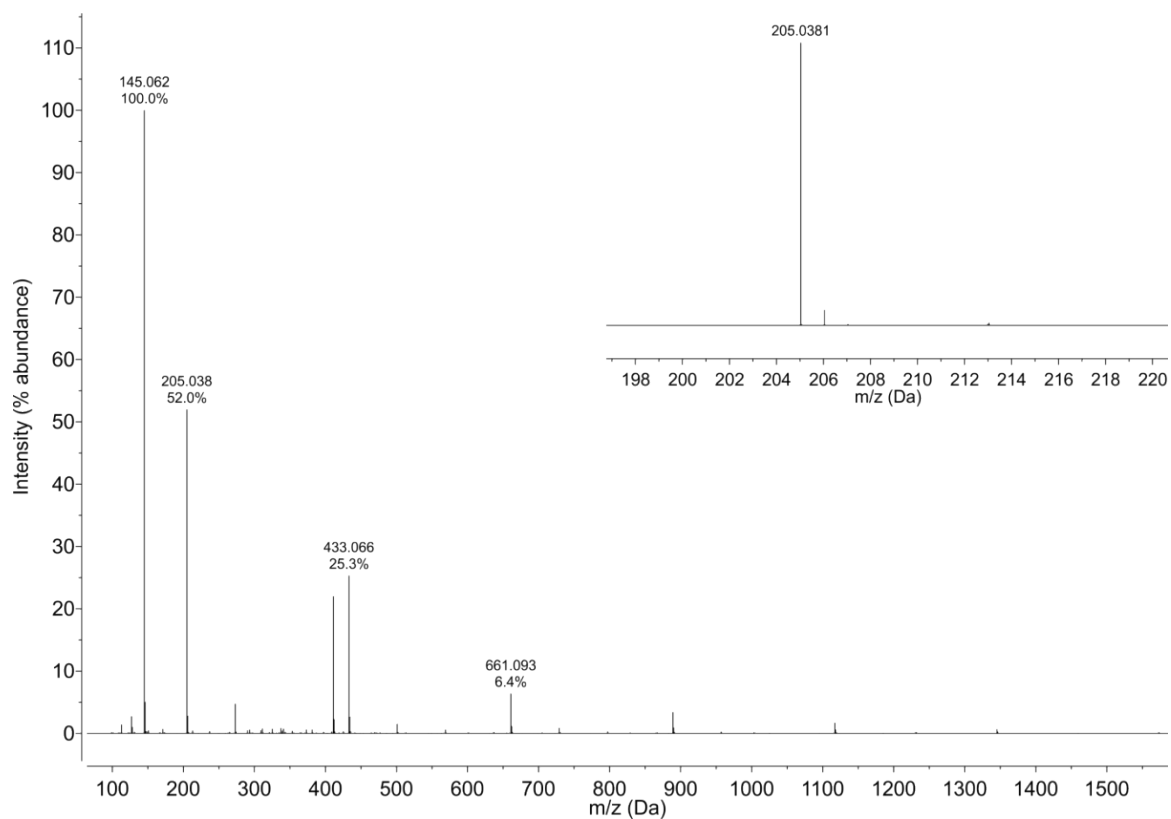


Figure S36. Negative ion mode ESI-MS spectrum of Na[**1e**]. Inset: molecular ion peak ($C_6H_{10}N_2O_4P^-$: Calcd. 205.0378).

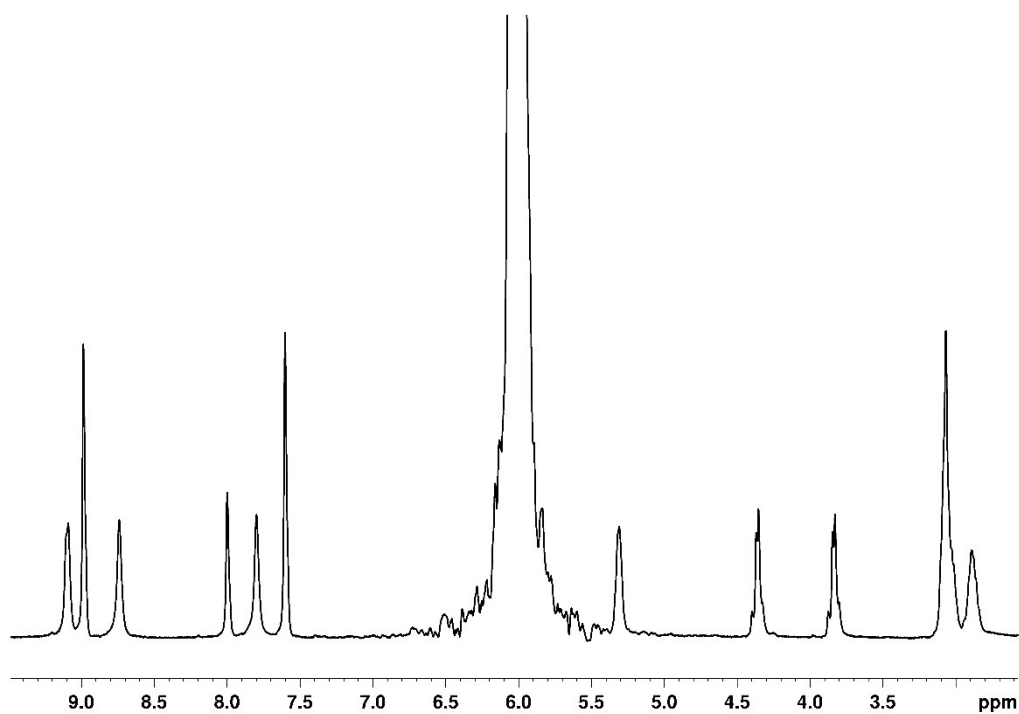


Figure S37. 1H NMR spectrum of a d_5 -pyridine solution (w/ a drop of H_2O) of Na[**1e**].

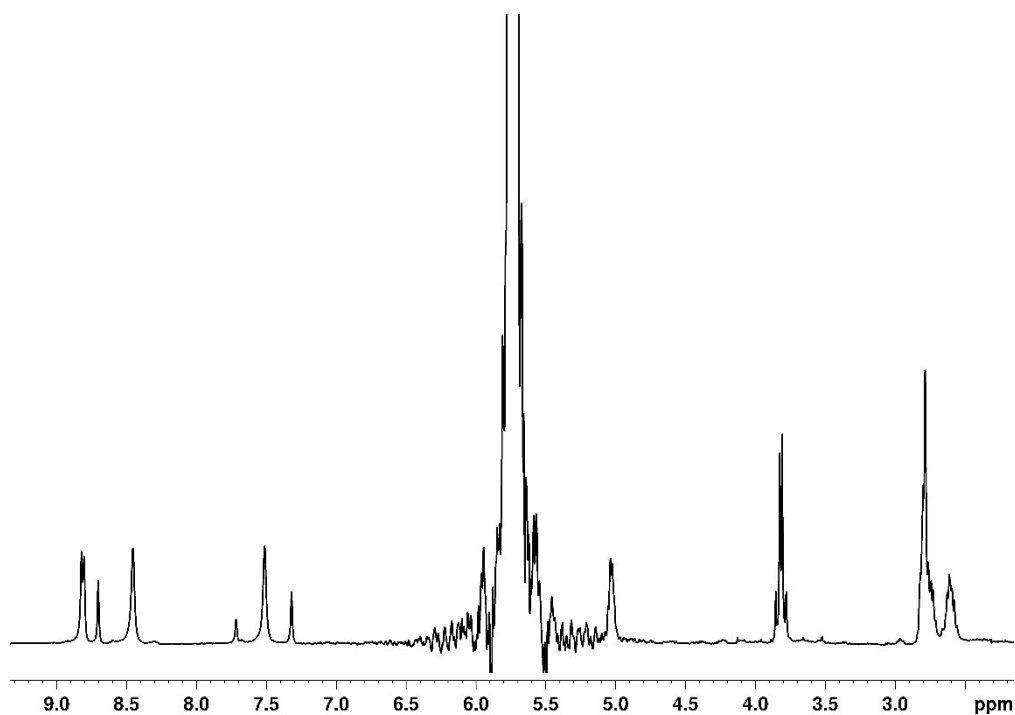


Figure S38. $^1\text{H}\{^{31}\text{P}\}$ NMR spectrum of a d_5 -pyridine solution (w/ a drop of H_2O) of $\text{Na}[\mathbf{1e}]$.

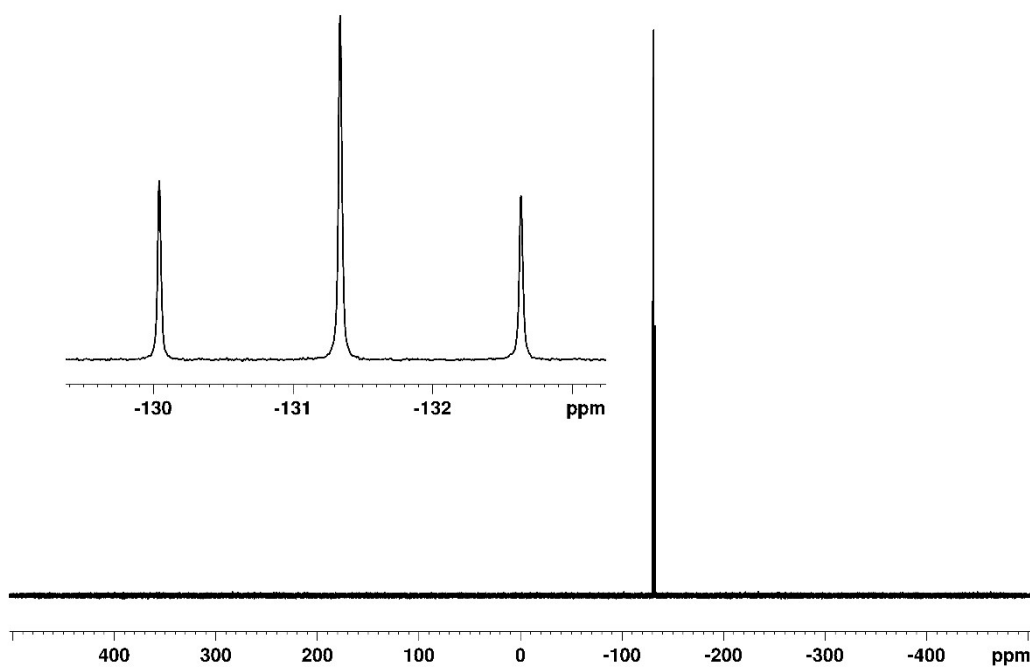


Figure S39. ^{31}P NMR spectrum of a d_5 -pyridine solution (w/ a drop of H_2O) of $\text{Na}[\mathbf{1e}]$.

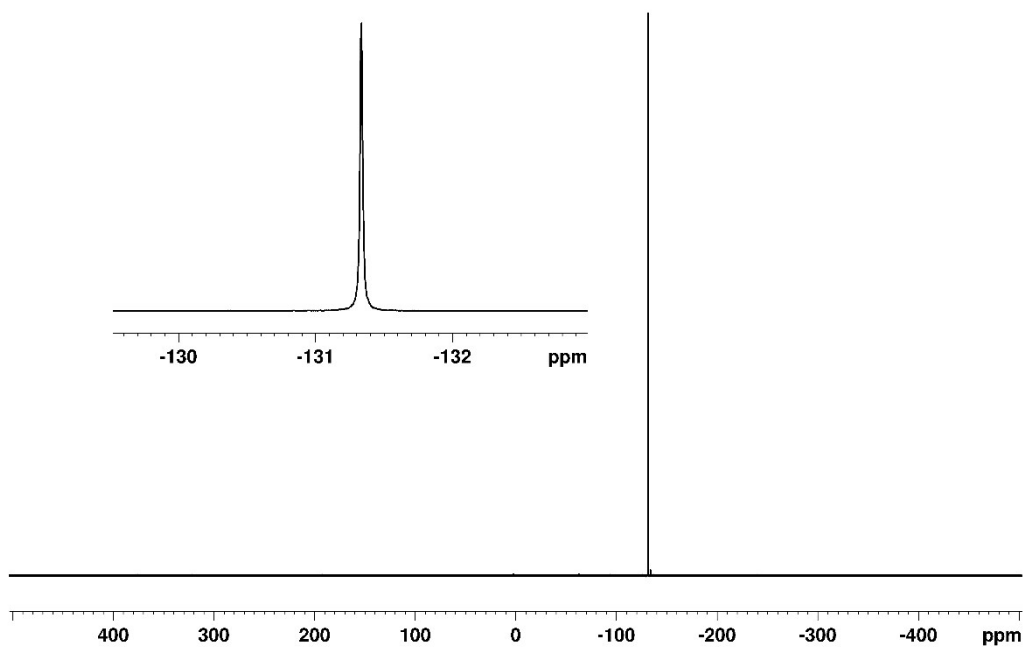


Figure S40. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution (w/ a drop of H_2O) of Na[**1e**].

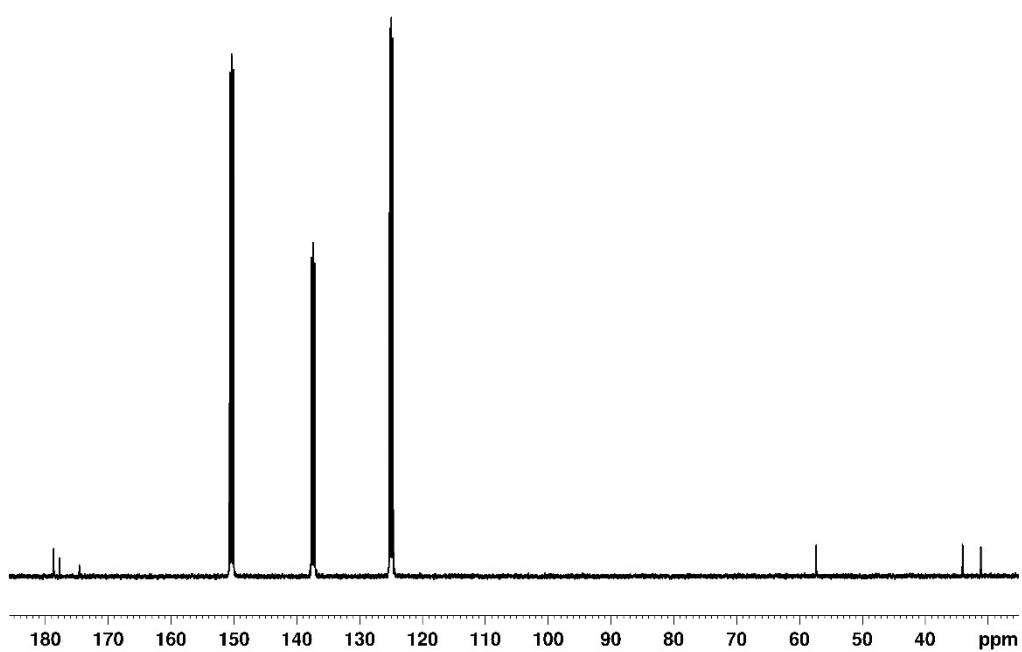


Figure S41. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution (w/ a drop of H_2O) of Na[**1e**].

Na[H₂PC(O)N(CH₂)₃CHCO₂] (Na[**1f**])

Pyridine (60 mL) and distilled water (2 mL) were added to a mixture of [Na(dioxane)_{3.36}(PCO)] (2.00 g, 5.91 mmol) and L-proline (0.68 g, 5.91 mmol) at room temperature. The resulting pale orange solution was stirred overnight. Volatiles were removed under dynamic vacuum to yield the product as a pale yellow solid (1.15 g, 97 % yield).

¹H NMR (499.9 MHz, *d*₅-pyridine, 298 K): δ (ppm) 4.70 (bs, 1H; αH (*cis*)), 4.51 (d, 1H; αH (*trans*)), 4.08 (dd, ¹J_{H-P} = 213 Hz, ²J_{H-H} = 11 Hz, 1H; PHH (*trans*)), 3.97 (dd, ¹J_{H-P} = 213 Hz, ²J_{H-H} = 11 Hz, 1H; PHH (*trans*)), 3.87 (m, 1H; δH (*trans*)), 3.85 (bd, ¹J_{H-P} = 217 Hz, 2H; PH₂ (*cis*)), 3.72 (m, 1H; δH (*trans*)), 3.59 (bs, 1H; δH(*cis*)), 3.33 (bs, 1H; δH (*cis*)), 2.50 (bs, 1H; βH (*trans*)), 2.34 (bs, 1H; βH (*cis*)), 2.15 (m, 1H; βH (*trans*)), 2.06 (bs, 1H; βH (*cis*)), 1.69 (s, 1H; γH (*cis*)), 1.69 (s, 1H; γH (*trans*)).

¹H{³¹P} NMR (499.9 MHz, *d*₅-pyridine, 298 K): δ (ppm) 4.08 (dd, ²J_{H-H} = 11 Hz, 1H; PHH (*trans*)), 3.97 (dd, ²J_{H-H} = 11 Hz, 1H; PHH (*trans*)), 3.85 (s, 2H; PH₂ (*cis*)); other resonances unchanged from ¹H NMR spectrum.

³¹P NMR (161.9 MHz, *d*₅-pyridine, 298 K): δ (ppm) -127.6 (t, ¹J_{P-H} = 217 Hz; *cis*), -131.2 (t, ¹J_{P-H} = 213 Hz; *trans*).

³¹P{¹H} NMR (161.9 MHz, *d*₅-pyridine, 298 K): δ (ppm) -127.6, -131.2.

¹³C{¹H} NMR (125.8 MHz, *d*₅-pyridine, 298 K): δ (ppm) 178.7 (s, CO₂⁻ (*cis*)), 178.2 (s, CO₂⁻ (*trans*)), 174.2 (d, ¹J_{C-P} = 7 Hz, PC(O) (*cis*)), 173.6 (d, ¹J_{C-P} = 6 Hz, PC(O) (*trans*)), 65.0 (d, ²J_{C-P} = 2 Hz, αC (*trans*)), 63.7 (s, αC (*cis*)), 49.7 (d, ²J_{C-P} = 5 Hz, δC (*cis*)), 47.5 (s, δC (*trans*)), 32.3 (s, βC (*trans*)), 30.6 (s, βC (*cis*)), 25.4 (s, γC (*trans*)), 23.8 (s, βC (*cis*)).

ESI-MS (-ve ion mode, MeOH): *m/z* = 174.0324.

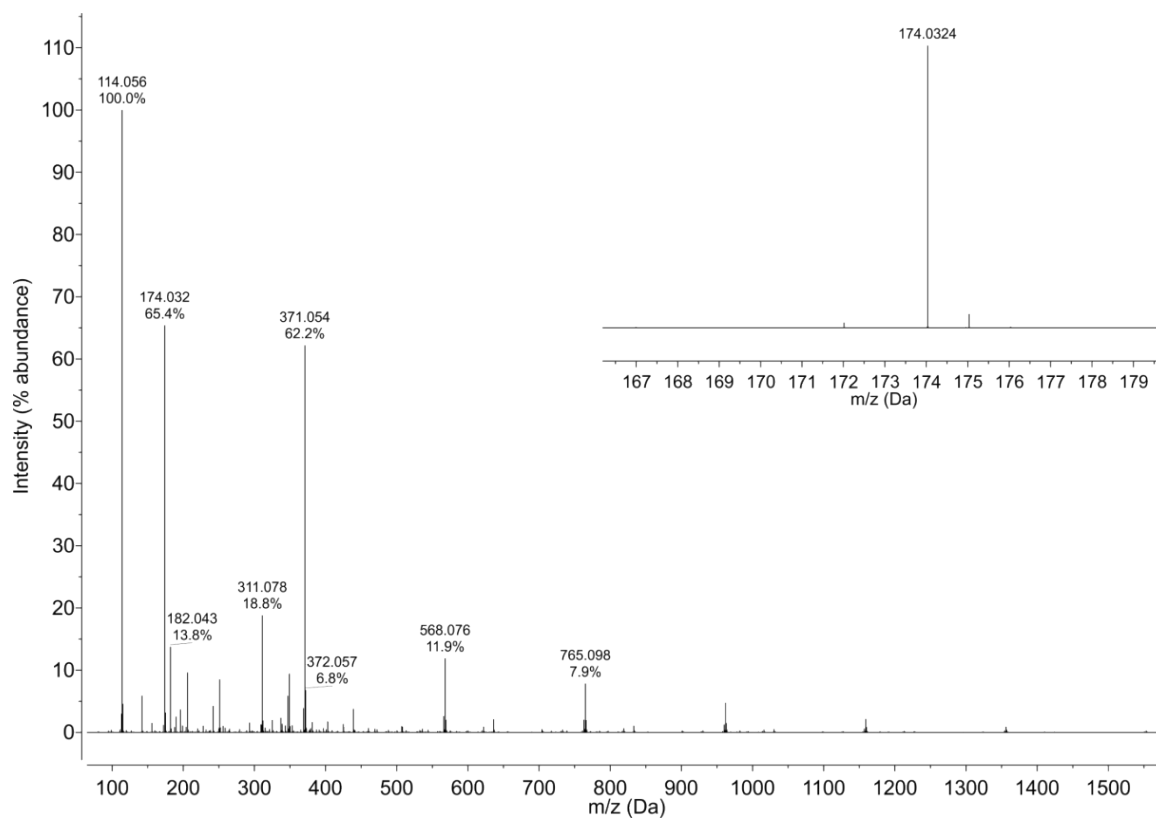


Figure S42. Negative ion mode ESI-MS spectrum of Na[**1f**]. Inset: molecular ion peak ($C_6H_7NO_3P^-$: Calcd. 174.0320).

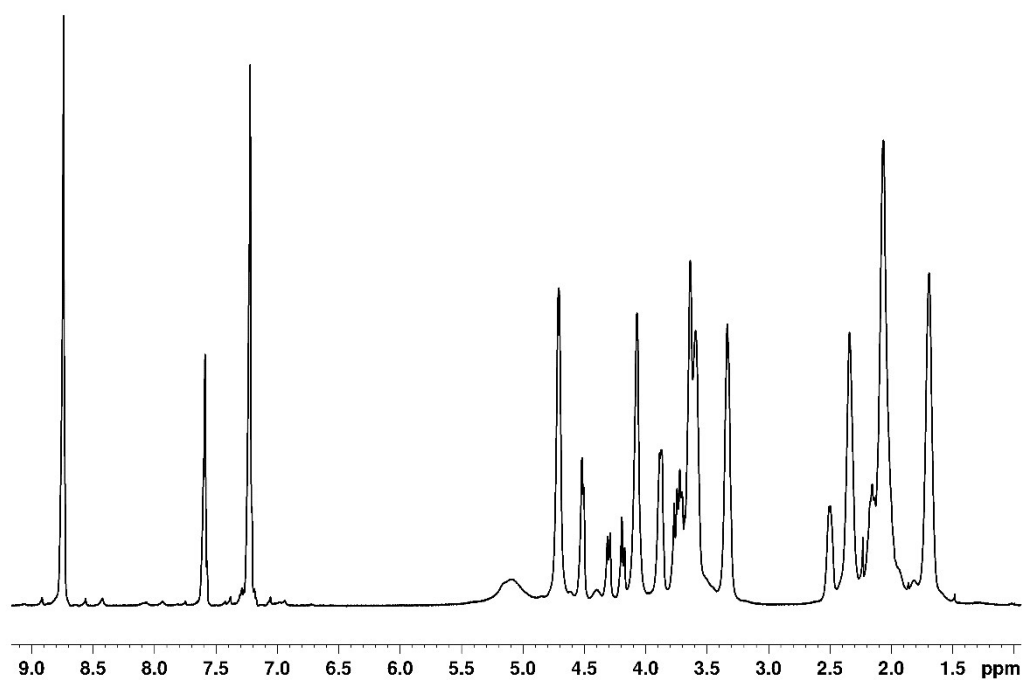


Figure S43. 1H NMR spectrum of a d_5 -pyridine solution of Na[**1f**].

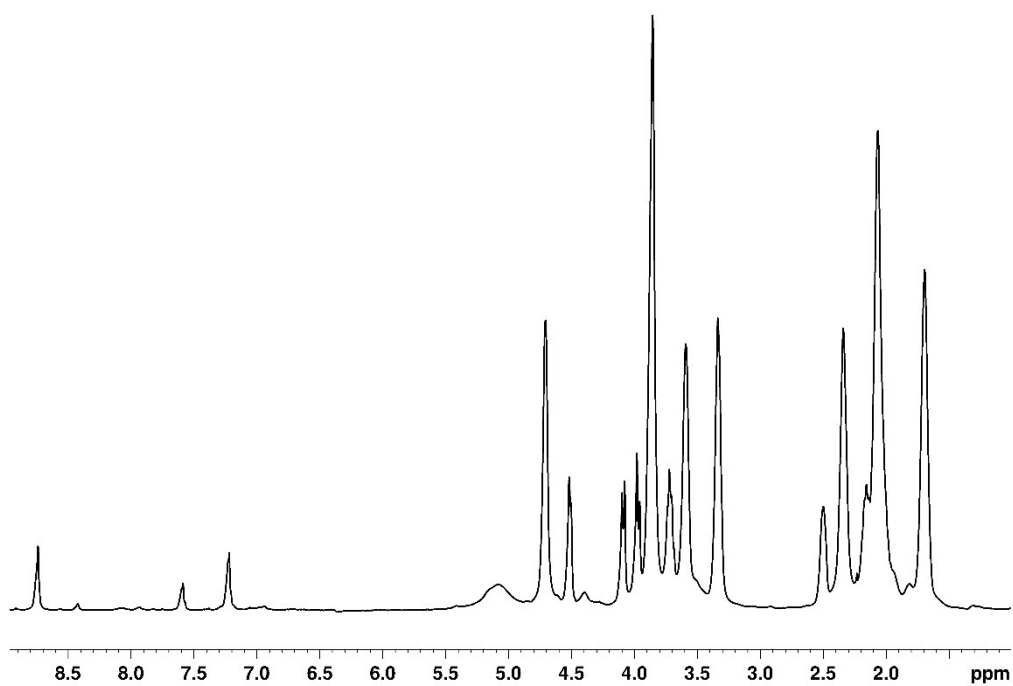


Figure S44. $^1\text{H}\{^{31}\text{P}\}$ NMR spectrum of a d_5 -pyridine solution of $\text{Na}[\mathbf{1f}]$.

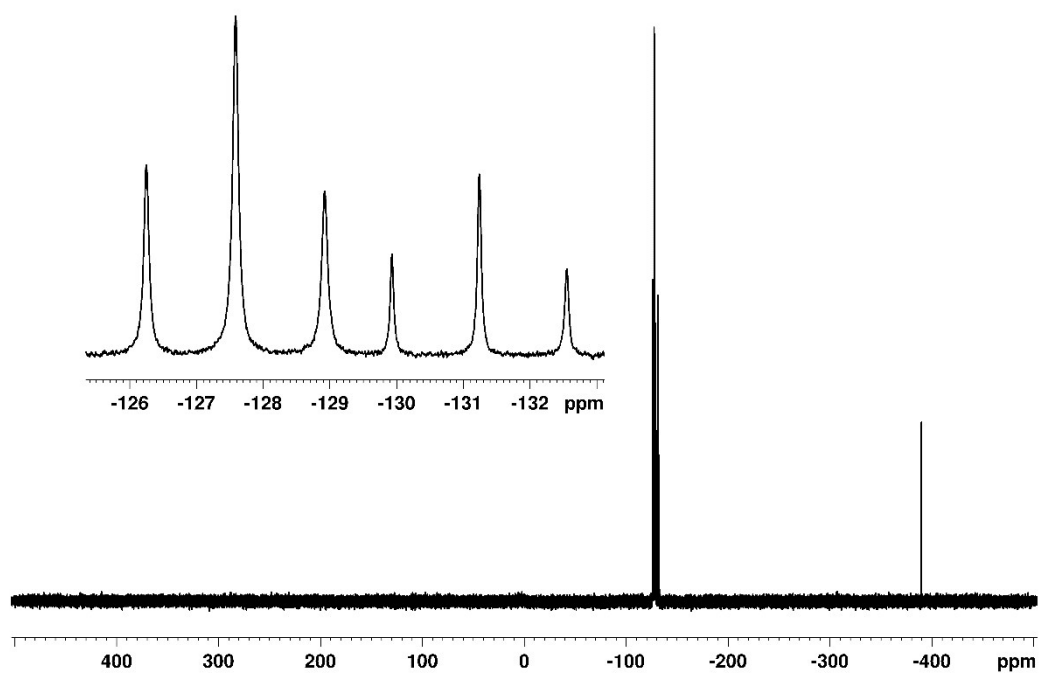


Figure S45. ^{31}P NMR spectrum of a d_5 -pyridine solution of $\text{Na}[\mathbf{1f}]$.

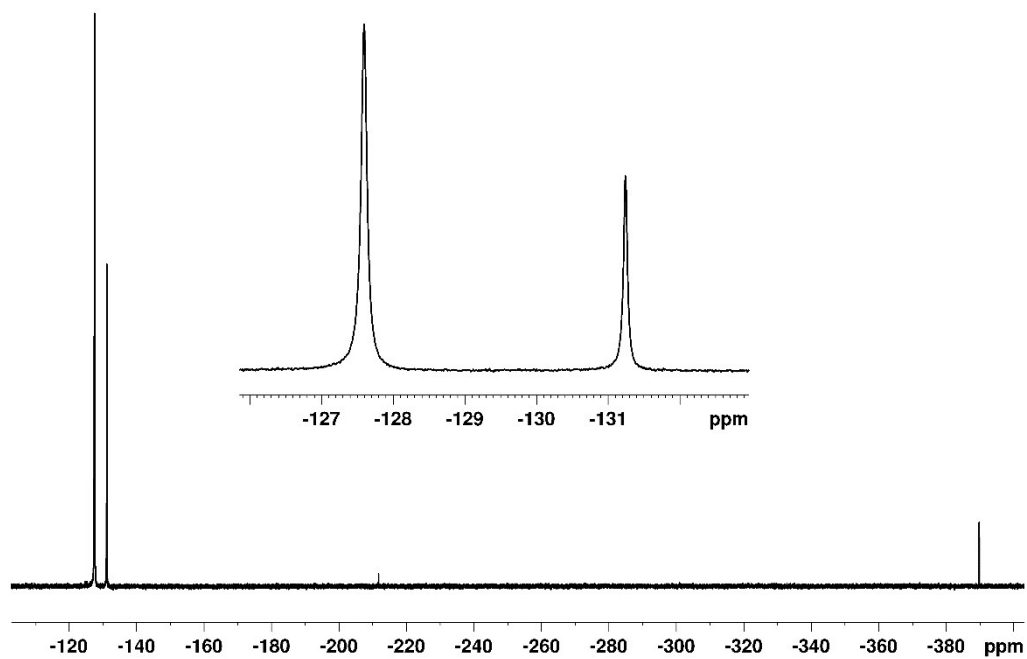


Figure S46. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution of Na[**1f**].

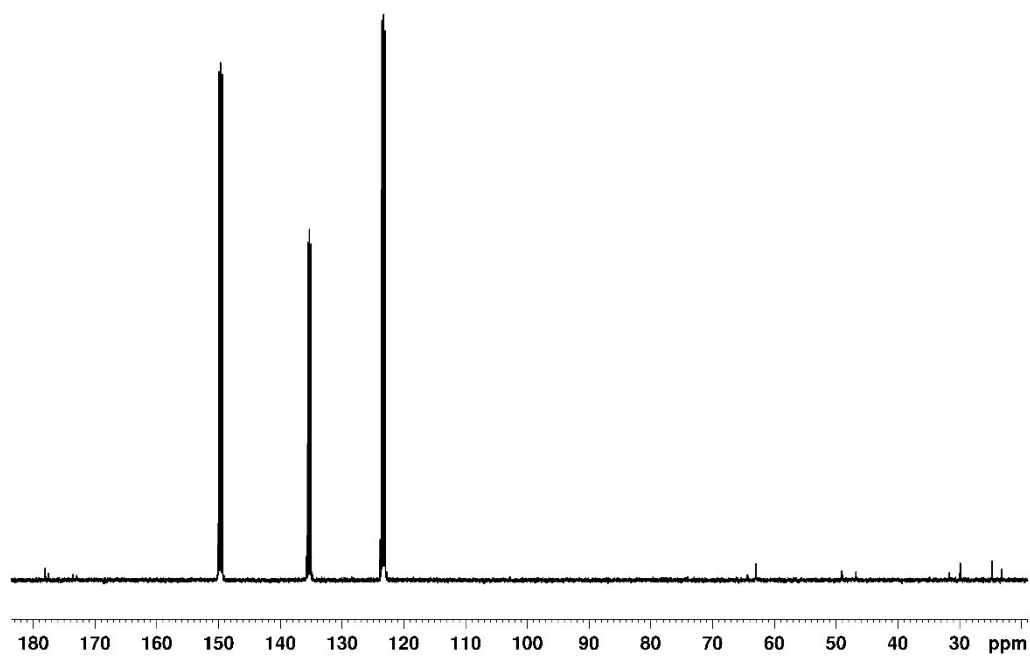


Figure S47. $^{13}\text{C}\{^{31}\text{P}\}$ NMR spectrum of a d_5 -pyridine solution of Na[**1f**].

H₂PC(O)NHCHMeCOOH (2a)

Pyridinium chloride (67.6 mg, 0.58 mmol) and Na[**1a**] (100 mg, 0.58 mmol) were weighed into a Schlenk tube and dissolved in DCM (3 mL). The mixture was stirred overnight. The colorless solution was then filtered to be separated from the pale yellow precipitate formed. Volatiles were removed under vacuum affording a colourless oil. Freezing with liquid nitrogen and treatment under a dynamic vacuum did not yield a solid. Addition of the minimum amount of DCM, just enough to dissolve the oil, and further addition of hexane (2 mL) precipitated the product as a white solid, which was dried under dynamic vacuum. (43.2 mg, 49.96% yield).

¹H NMR (400.2 MHz, *d*₅-pyridine, 298K): δ (ppm) 15.34 (bs, 1H; COOH), 9.80 (d, 1H; NH), 5.16 (q, ³*J*_{H-H} = 7 Hz, 1H; NCH(CH₃)), 3.86 (m, ¹*J*_{H-P} = 209 Hz, ²*J*_{H-H} = 11.6 Hz, 1H; PHH), 3.85 (m, ¹*J*_{H-P} = 209 Hz, ²*J*_{H-H} = 11.6 Hz, 1H; PHH), 1.60 (d, ³*J*_{H-H} = 7 Hz, 3H; NCH(CH₃)).

¹H{³¹P} NMR (400.2 MHz, *d*₅-pyridine, 298K): δ (ppm) 3.86 (m, ²*J*_{H-H} = 12 Hz, 1H; PHH), 3.85 (m, ²*J*_{H-H} = 12 Hz, 1H; PHH), other resonances unchanged.

³¹P NMR (162.0 MHz, *d*₅-pyridine, 298K): δ (ppm) -132.6 (t, ¹*J*_{P-H} = 209 Hz).

³¹P{¹H} NMR (162.0 MHz, *d*₅-pyridine, 298K): δ (ppm) -132.6 (s).

¹³C{¹H} NMR (125.8MHz, *d*₅-pyridine, 298K): δ (ppm) 175.9 (s; CO₂⁻), 173.2 (d, ¹*J*_{C-P} = 7.3 Hz; PC(O)), 49.9 (s; αC), 18.6 (s; βC).

ESI-MS (-ve ion mode, DCM): *m/z* = 148.0167.

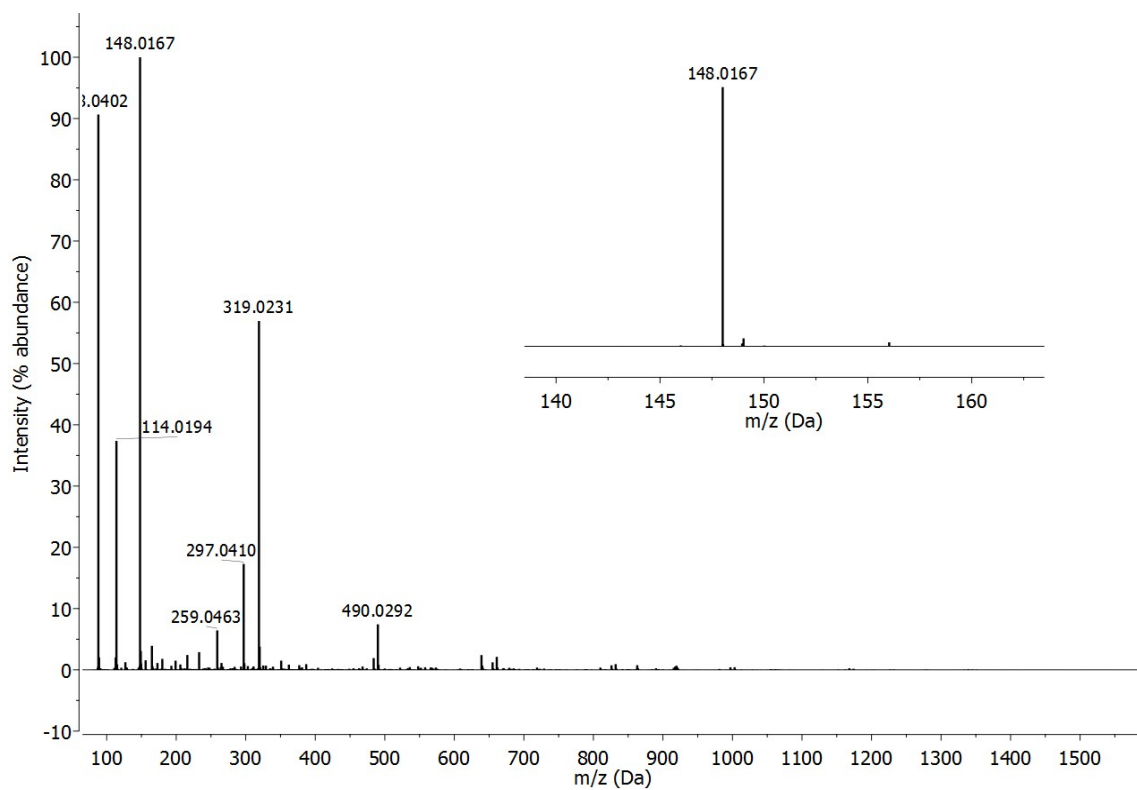


Figure S48. Negative ion mode ESI-MS spectrum of **2a**. Inset: molecular ion peak ($C_4H_7NO_3P^-$: Calcd. 148.0169)

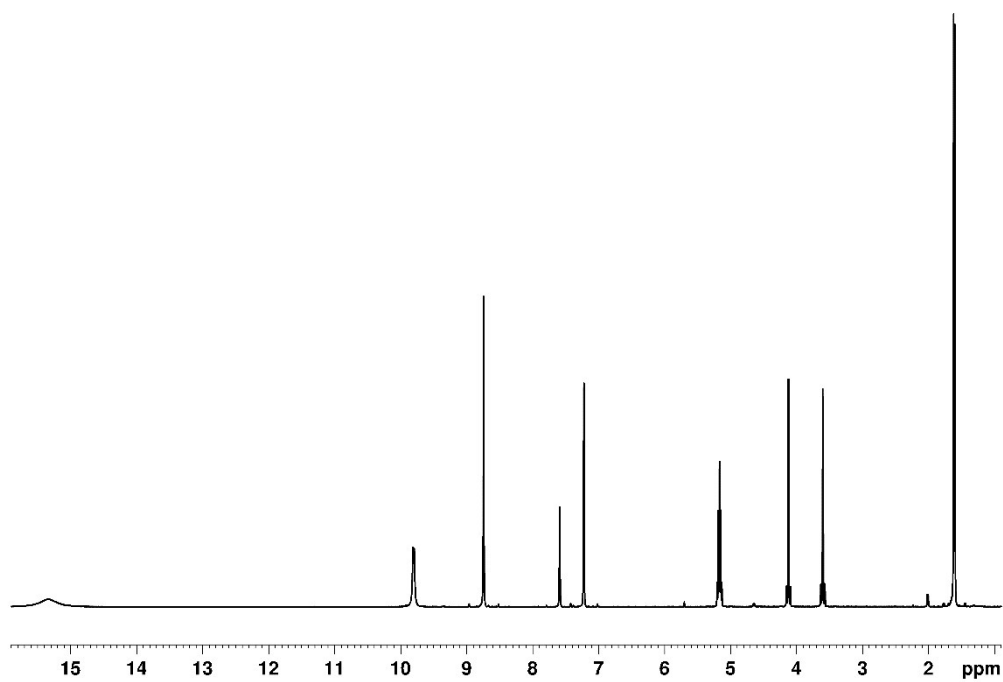


Figure S49. 1H NMR spectrum of a d_5 -pyridine solution of **2a**.

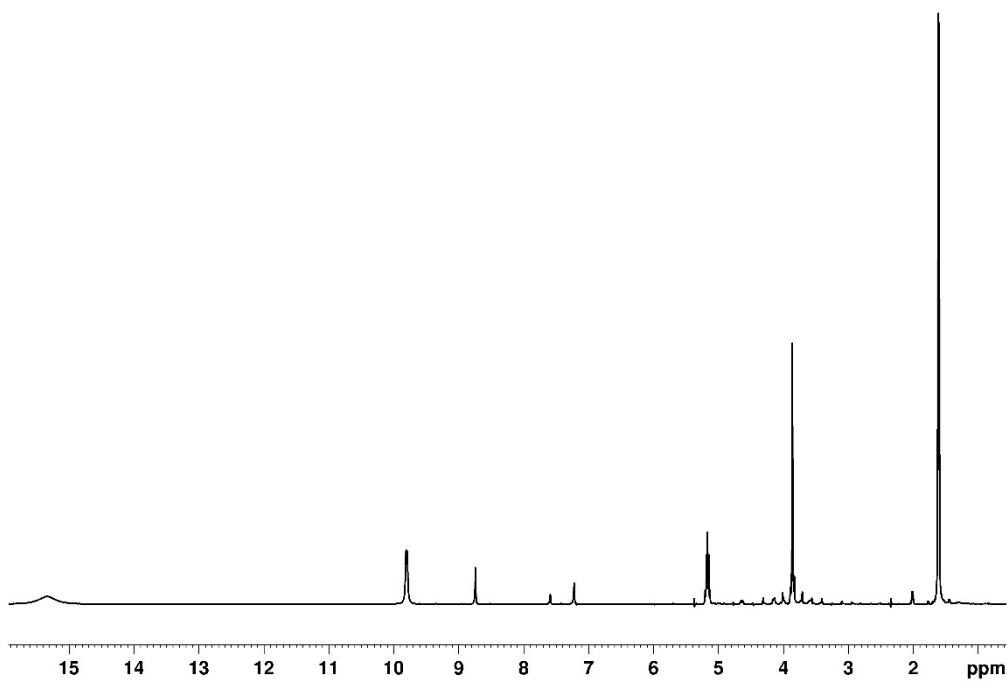


Figure S50. $^1\text{H}\{^{31}\text{P}\}$ NMR spectrum of a d_5 -pyridine solution of **2a**.

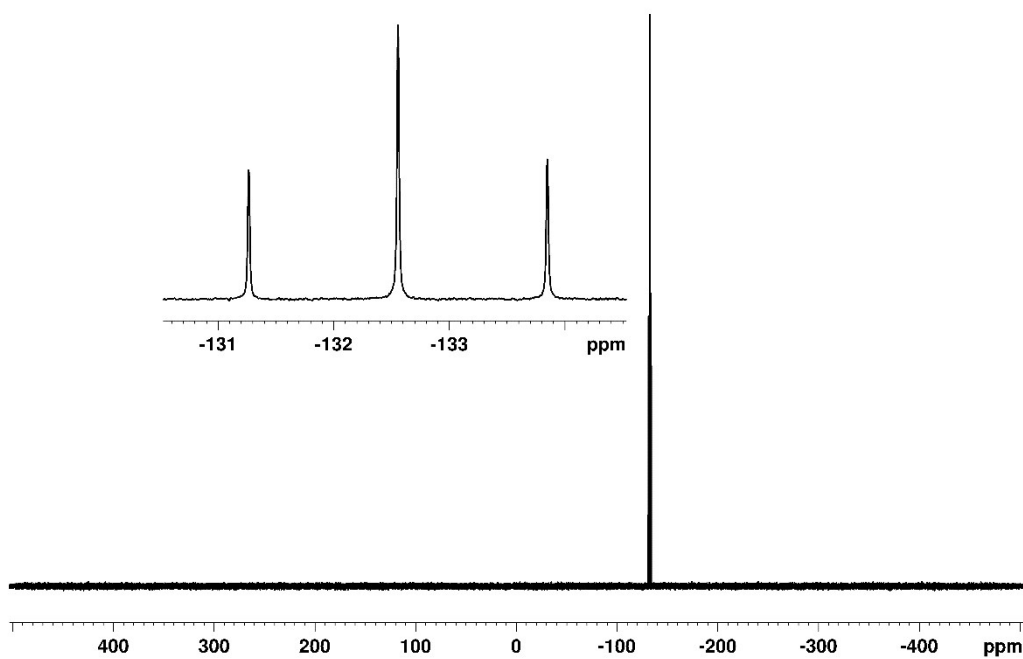


Figure S51. ^{31}P NMR spectrum of a d_5 -pyridine solution of **2a**.

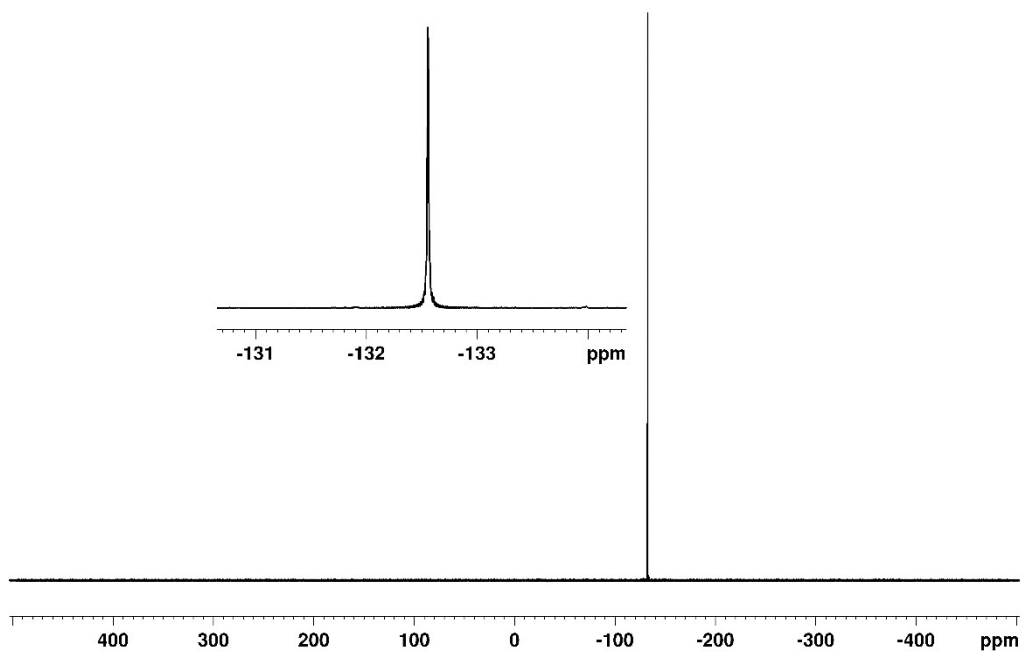


Figure S52. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution of **2a**.

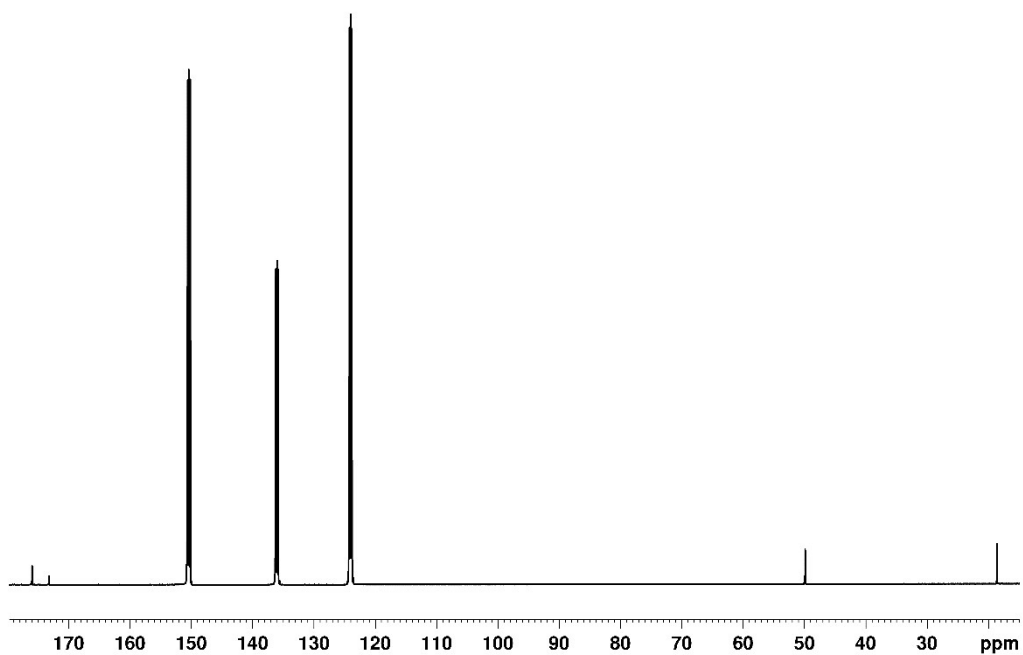


Figure S53. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution of **2a**.

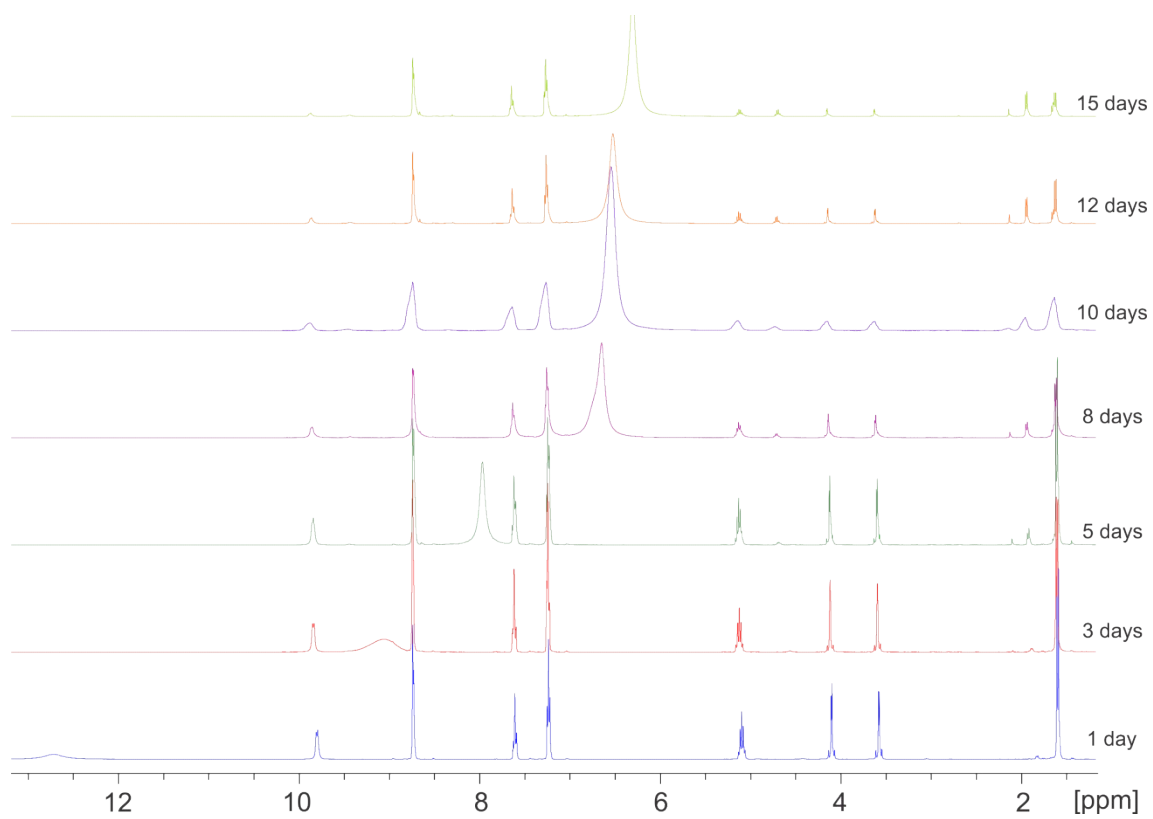


Figure S54. ¹H NMR spectra of a *d*₅-pyridine solution of **2a** that was exposed to air overnight on a daily basis.

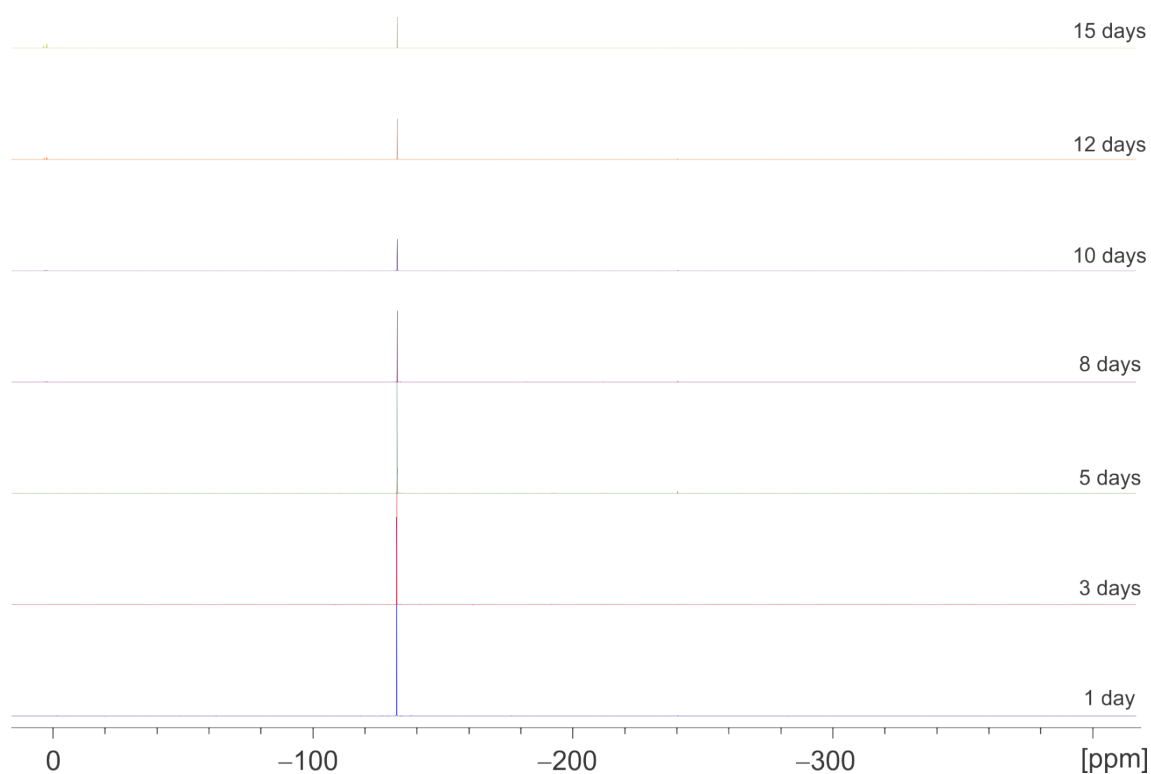


Figure S55. $^{31}\text{P}\{^1\text{H}\}$ NMR spectra of a d_5 -pyridine solution of **2a** that was exposed to air overnight on a daily basis.

$\text{H}_2\text{PC(O)NH(CH}_2\text{OH)COOH}$ (**2b**)

Pyridinium triflate (12 mg, 0.05 mmol) and the previously synthesized Na[**1b**] (10 mg, 0.05 mmol) were weighed into a gas-tight NMR tube and d_5 -pyridine (0.5 mL) was added to give a pale yellow solution where the product was formed. Attempts to scale up this reaction were made but the purification step was challenging due to solubility issues.

^1H NMR (400.2 MHz, d_5 -pyridine, 298 K): δ (ppm) 12.26 (bs, 2H; COOH), 9.84 (d, 1H; NH), 5.42 (m, 1H; αH), 4.49 (m, 2H; βH), 3.88 (bd, $^1J_{\text{H-P}} = 210$ Hz, 2H; PH_2).

$^1\text{H}\{^{31}\text{P}\}$ NMR (400.2 MHz, d_5 -pyridine, 298 K): δ (ppm) 3.88 (bs, 2H; PH_2), other resonances unchanged from ^1H NMR spectrum.

^{31}P NMR (161.9 MHz, d_5 -pyridine, 298 K): δ (ppm) -131.6 (t, $^1J_{\text{P-H}} = 210$ Hz).

$^{31}\text{P}\{^1\text{H}\}$ NMR (161.9 MHz, d_5 -pyridine, 298 K): δ (ppm) -131.6 (s)

$^{13}\text{C}\{^1\text{H}\}$ NMR (100.6 MHz, d_5 -pyridine, 298 K): δ (ppm) 174.3 (s, COOH), 174.0 (d, $^1J_{\text{C-P}} = 8$ Hz, PC(O)), 63.5 (s, αC), 57.3 (s, βC).

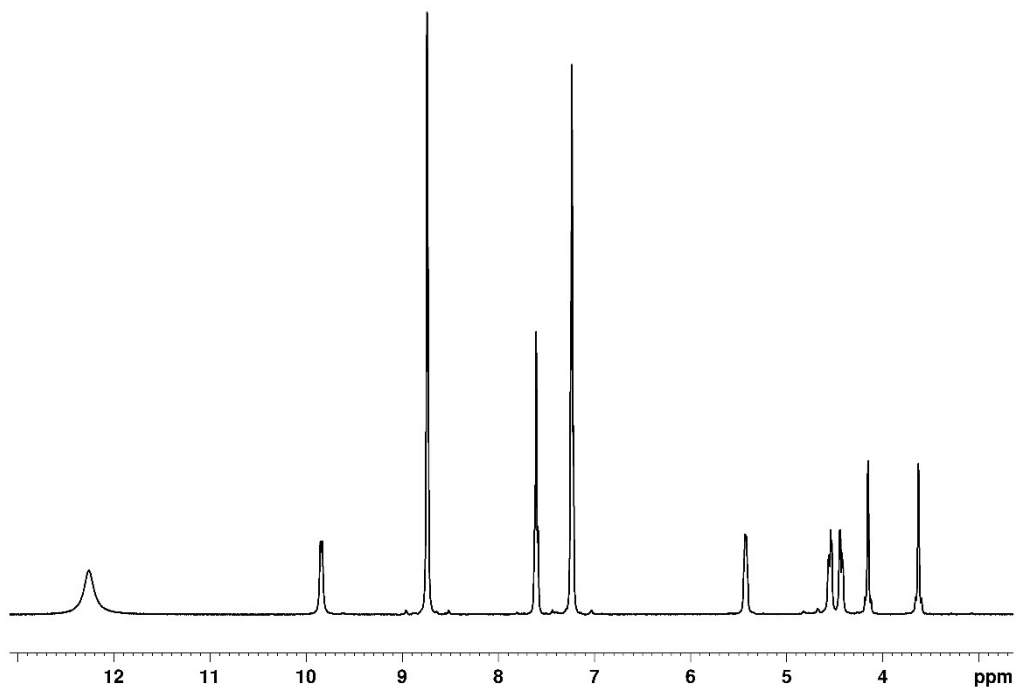


Figure S56. ^1H NMR spectrum of a d_5 -pyridine solution of **2b**.

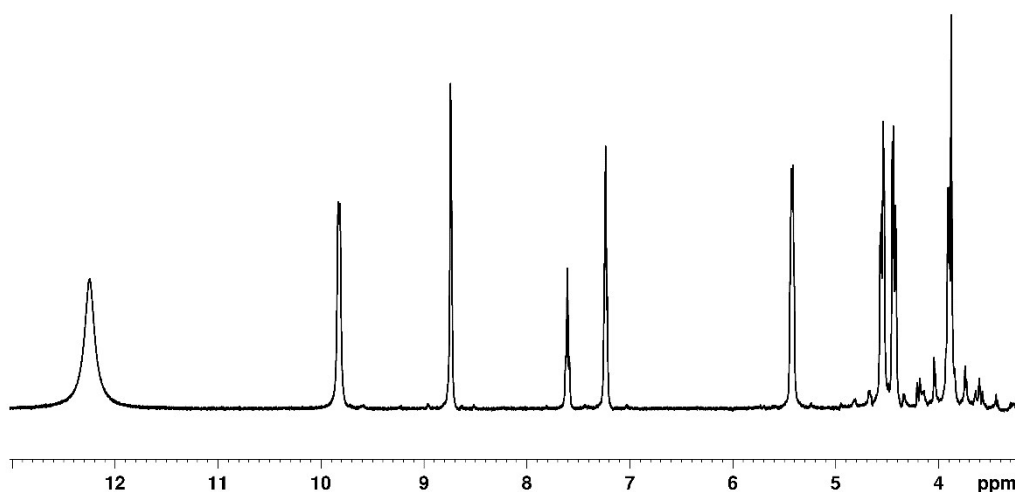


Figure S57. $^1\text{H}\{^{31}\text{P}\}$ NMR spectrum of a d_5 -pyridine solution of **2b**.

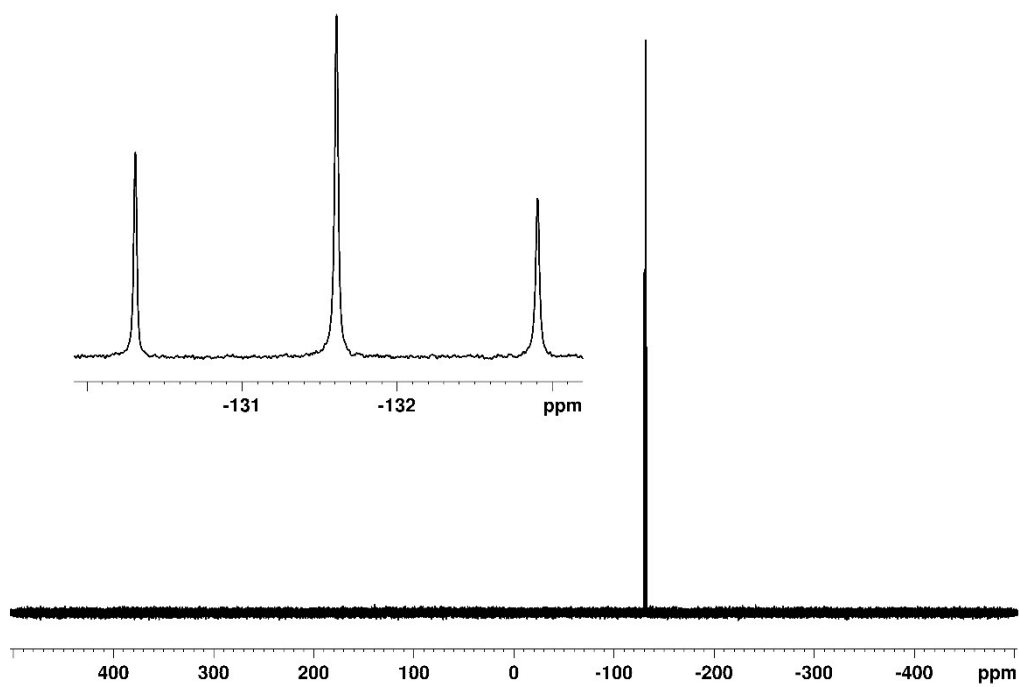


Figure S58. ^{31}P NMR spectrum of a d_5 -pyridine solution of **2b**.

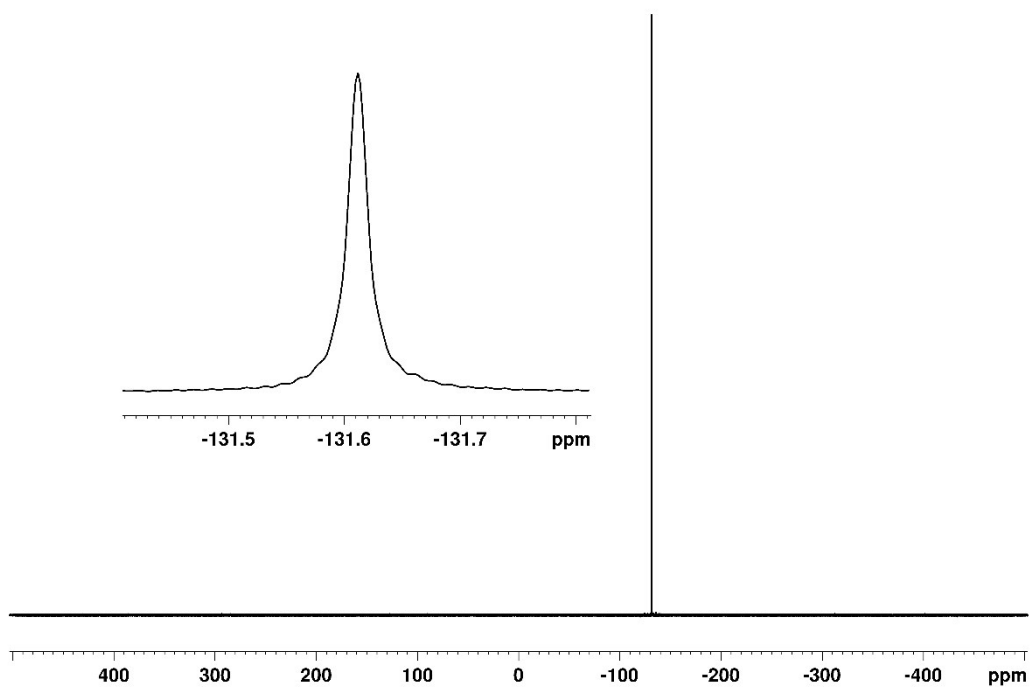


Figure S59. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution of **2b**.

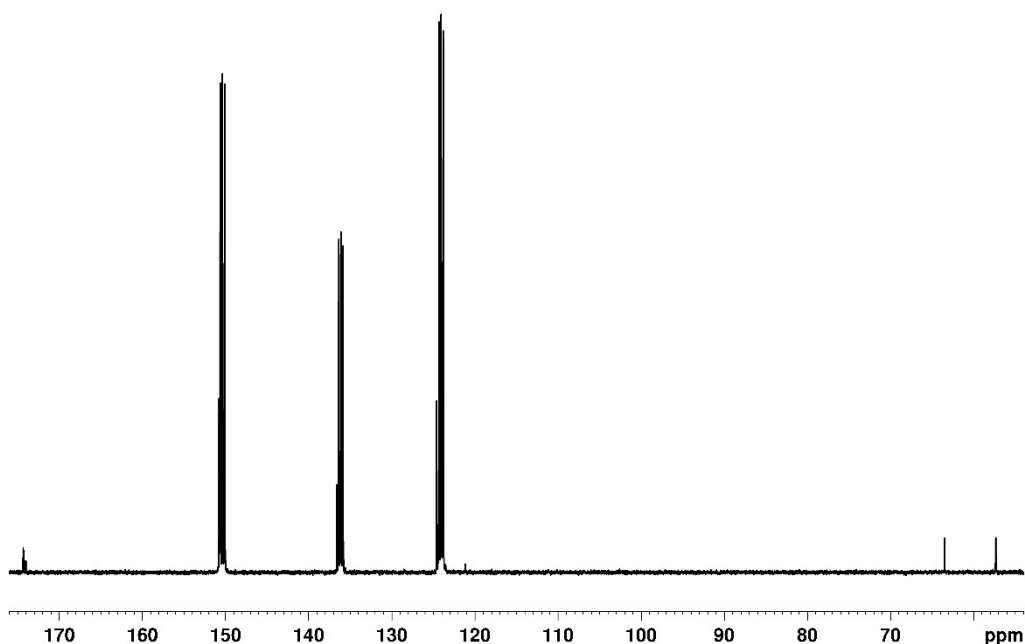


Figure S60. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution of **2b**.

$\text{H}_2\text{PC}(\text{O})\text{NH}(\text{CH}_2\text{SH})\text{COOH}$ (**2c**)

Pyridinium chloride (113.78 mg, 0.99 mmol) and Na[**1c**] (200 mg, 0.99 mmol) were weighed into a Schlenk tube and dissolved in DCM (5 mL). The mixture was stirred overnight. The colorless solution was then filtered to be separated from the white precipitate formed. Volatiles were removed under vacuum affording a colourless oil. Hexane (5 mL) was added to this oil and the mixture was stirred overnight. Removal of the volatiles under a dynamic vacuum yielded an oily white solid. Several cycles of freeze/pump/thaw degassing ultimately afforded the product as a pale yellow solid. (92.5 mg, 51.84% yield).

^1H NMR (500.3 MHz, d_5 -pyridine, 298 K): δ (ppm) 16.01 (bs, 1H; COOH), 9.95 (d, 1H; NH), 5.45 (m, 1H; αH), 3.89 (bd, $^1J_{\text{H-P}} = 210$ Hz, 2H; PH_2), 3.35 (m, 2H; βH), 2.58 (bs; SH).

$^1\text{H}\{^{31}\text{P}\}$ NMR (400.2 MHz, d_5 -pyridine, 298 K): δ (ppm) 3.89 (bs, 2H; PH_2), other resonances unchanged from ^1H NMR spectrum.

^{31}P NMR (161.9 MHz, d_5 -pyridine, 298 K): δ (ppm) -131.9 (t, $^1J_{\text{P-H}} = 210.2$ Hz).

$^{31}\text{P}\{^1\text{H}\}$ NMR (161.9 MHz, d_5 -pyridine, 298 K): δ (ppm) -131.9 (s).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100.6 MHz, d_5 -pyridine, 298 K): δ (ppm) 173.8 (d, $^1J_{\text{C-P}} = 8.2$ Hz, PC(O)), 173.5 (s, COOH), 56.5 (s, αC), 27.7 (s, βC).

ESI-MS (–ve ion mode, DCM): $m/z = 179.9888$.

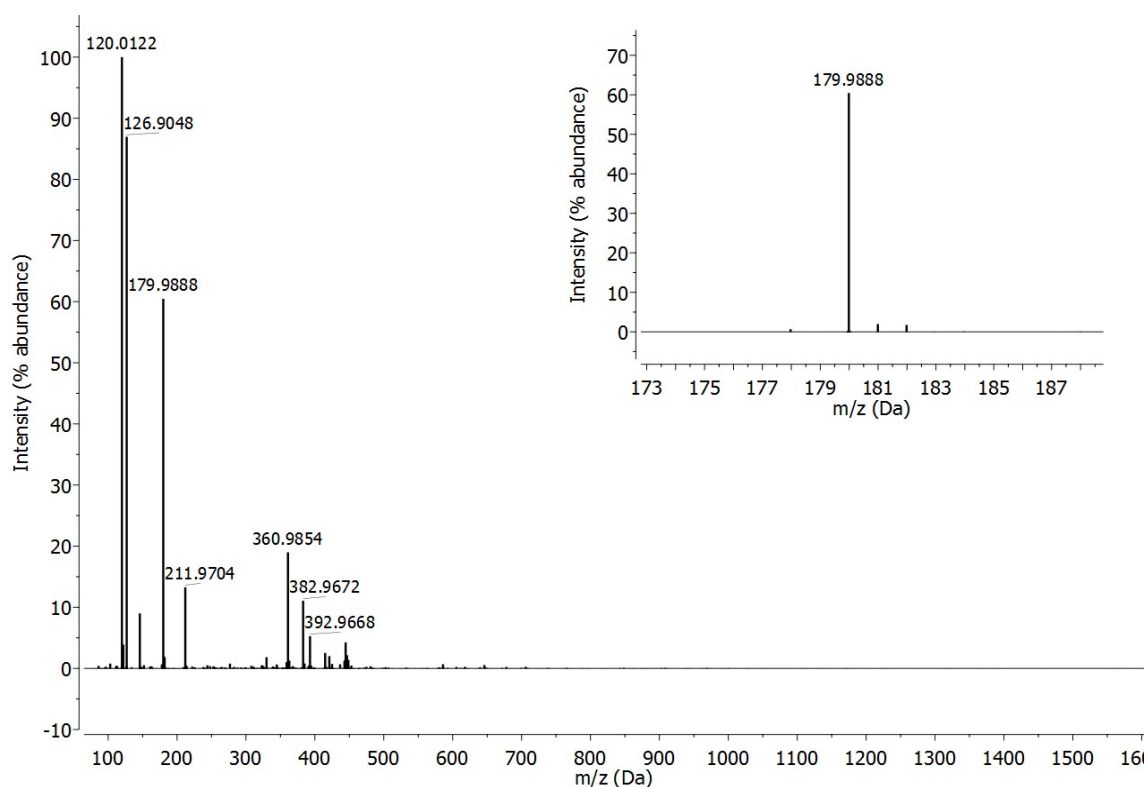


Figure S61. Negative ion mode ESI-MS spectrum of **2c**. Inset: molecular ion peak

($\text{C}_4\text{H}_7\text{NO}_3\text{PS}^-$: Calcd. 179.9889)

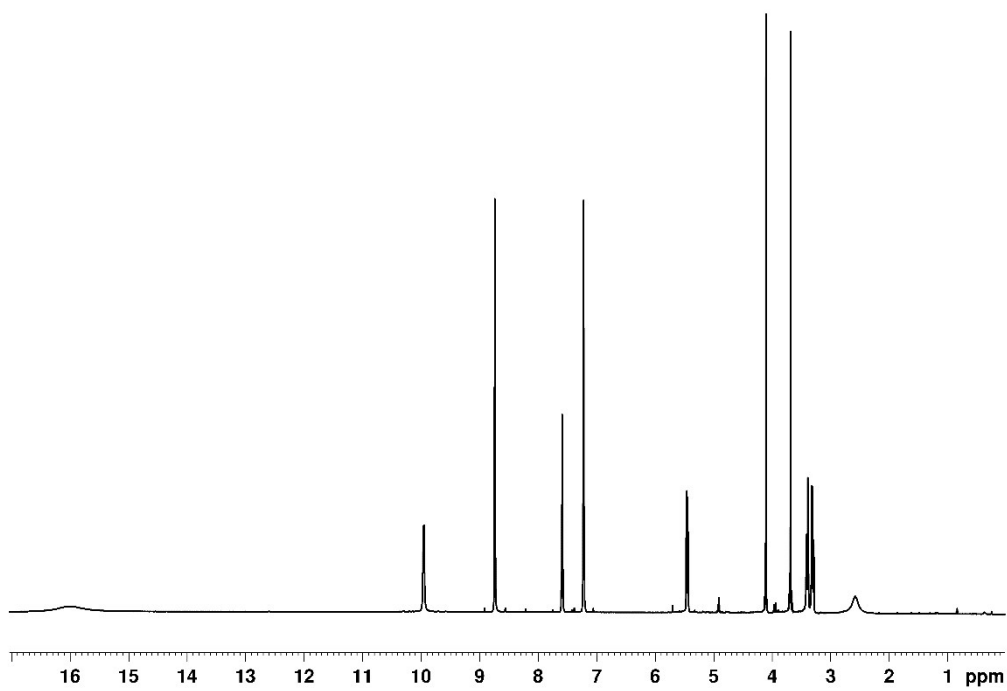


Figure S62. ^1H NMR spectrum of a d_5 -pyridine solution of **2c**.

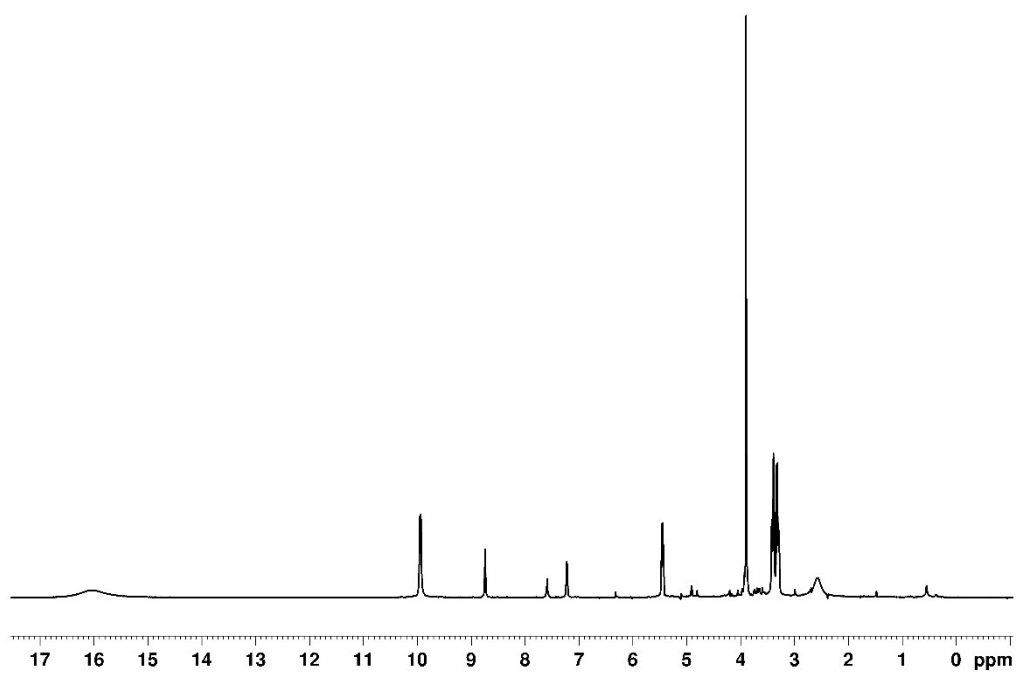


Figure S63. $^1\text{H}\{^{31}\text{P}\}$ NMR spectrum of a d_5 -pyridine solution of **2c**.

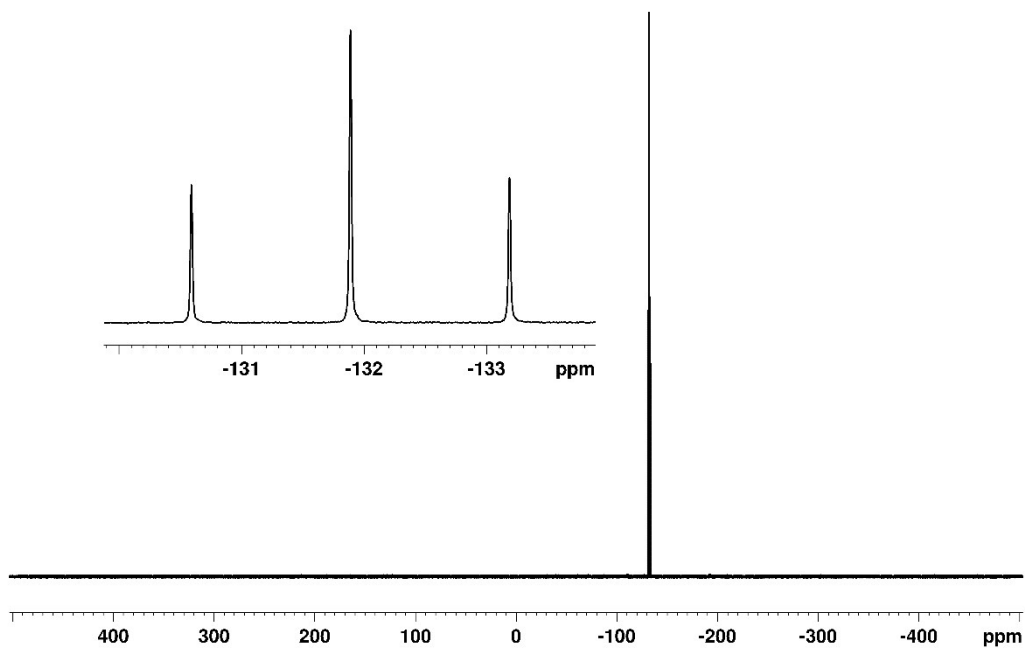


Figure S64. ^{31}P NMR spectrum of a d_5 -pyridine solution of **2c**.

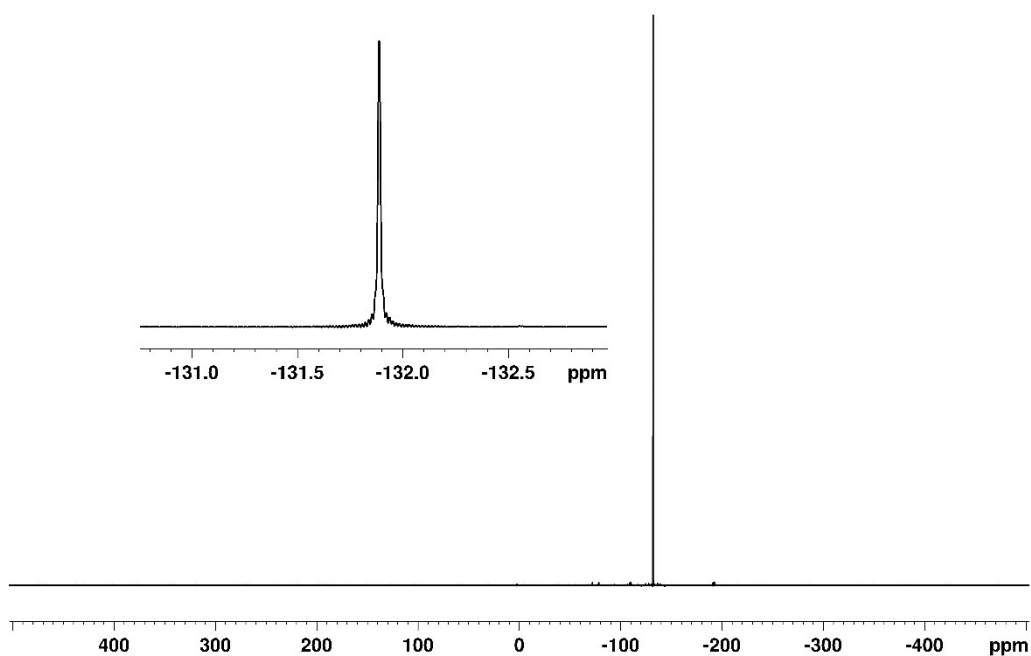


Figure S65. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution of **2c**.

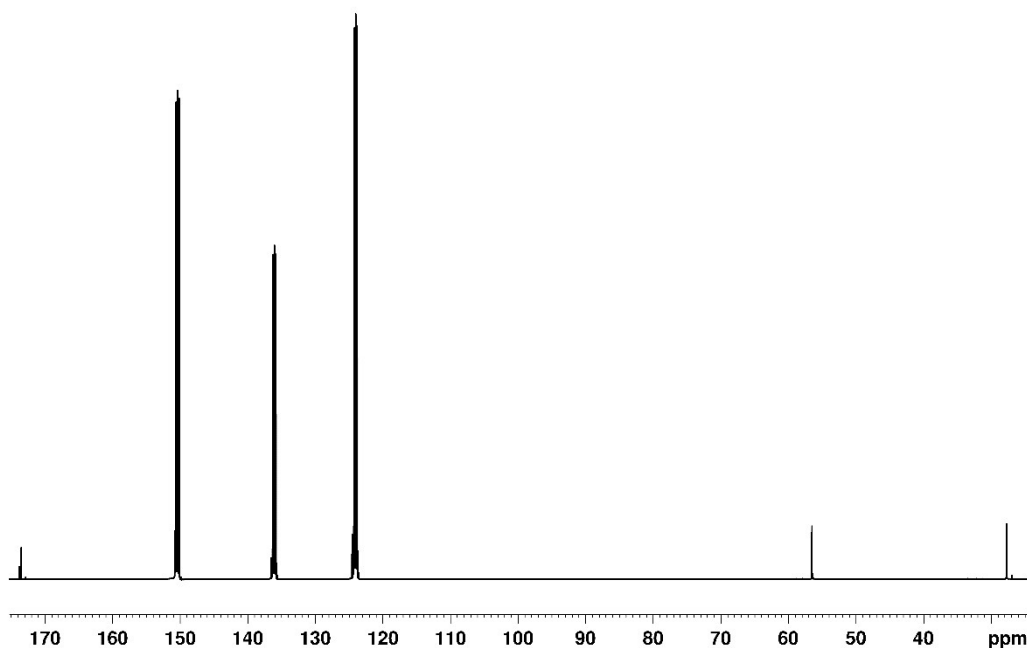


Figure S66. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution of **2c**.

$\text{H}_2\text{PC(O)NH(CH}_2\text{C(O)NH}_2\text{)COOH (2d)}$

Pyridinium chloride (57.8 mg, 0.50 mmol) and Na[**1c**] (107.2 mg, 0.50 mmol) were weighed into a Schlenk tube and dissolved in DCM (3 mL). The mixture was stirred overnight. The colorless solution was then filtered to be separated from the white precipitate formed. Volatiles were removed under vacuum affording a colourless oil. Extraction of the product into distilled water (0.5 mL), followed by filtration and treatment of the filtrate under a dynamic vacuum yielded the product as a colourless solid. (18.2 mg, 18.95% yield).

$^1\text{H NMR}$ (400.2 MHz, d_5 -pyridine, 298 K): δ (ppm) 15.95 (bs, 1H; COOH), 9.86 (d, 1H; NH), 8.56 (s, 1H; NHH), 7.98 (s, 1H; NHH), 5.72 (m, 1H; αH), 3.83 (d, $^1J_{\text{H-P}} = 209$ Hz, 2H; PH_2), 3.40 (d, 2H; βH).

$^1\text{H}\{^{31}\text{P}\}$ NMR (400.2 MHz, d_5 -pyridine, 298 K): δ (ppm) 3.83 (s, 1H; PH_2), other resonances unchanged from $^1\text{H NMR}$ spectrum.

^{31}P NMR (162.0 MHz, d_5 -pyridine, 298 K): δ (ppm) -131.9 (t, $^1J_{\text{P-H}} = 209$ Hz).

$^{31}\text{P}\{^1\text{H}\}$ NMR (162.0 MHz, d_5 -pyridine, 298 K): δ (ppm) -131.9 (s)

$^{13}\text{C}\{^1\text{H}\}$ NMR (100.6 MHz, d_5 -pyridine, 298 K): δ (ppm) 174.7 (s, COOH), 173.5 (d,

$^1J_{\text{C-P}} = 7.7$ Hz, PC(O)), 173.4 (s, γC), 51.5 (s, αC), 38.5 (s, βC).

ESI-MS (–ve ion mode, DCM): $m/z = 191.0224$

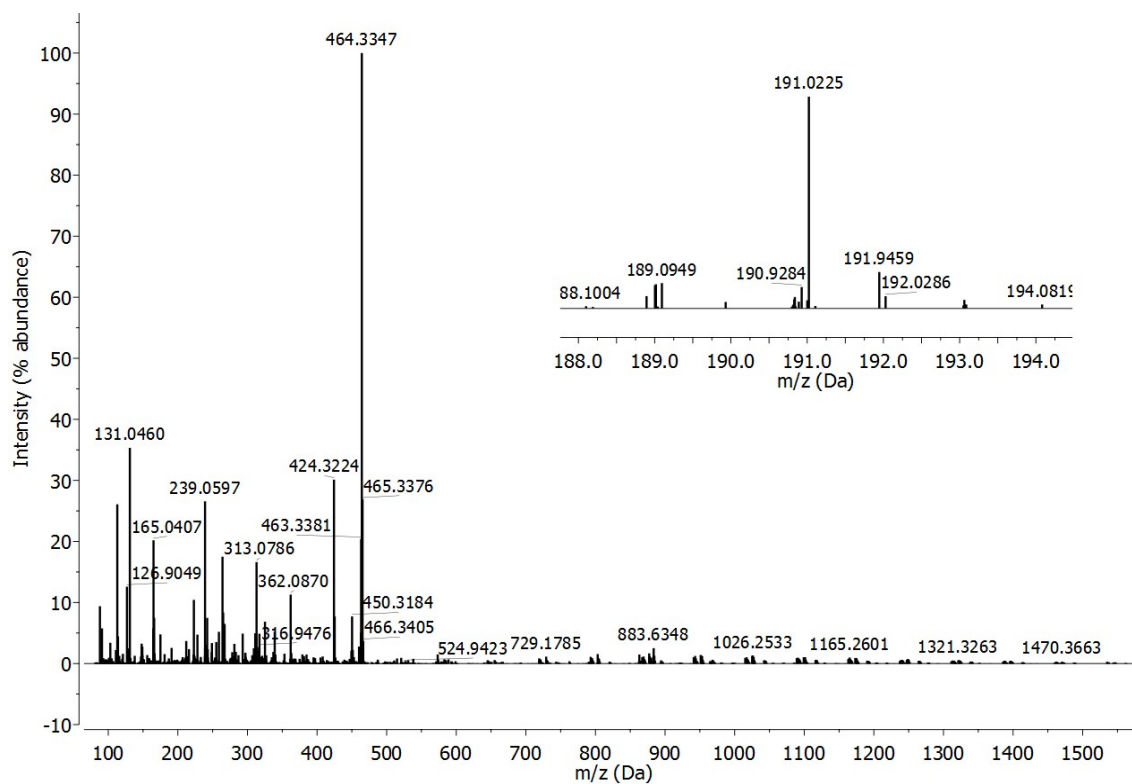


Figure S67. Negative ion mode ESI-MS spectrum of **2d**. Inset: molecular ion peak

($\text{C}_5\text{H}_8\text{N}_2\text{O}_4\text{P}^-$: Calcd. 191.0227)

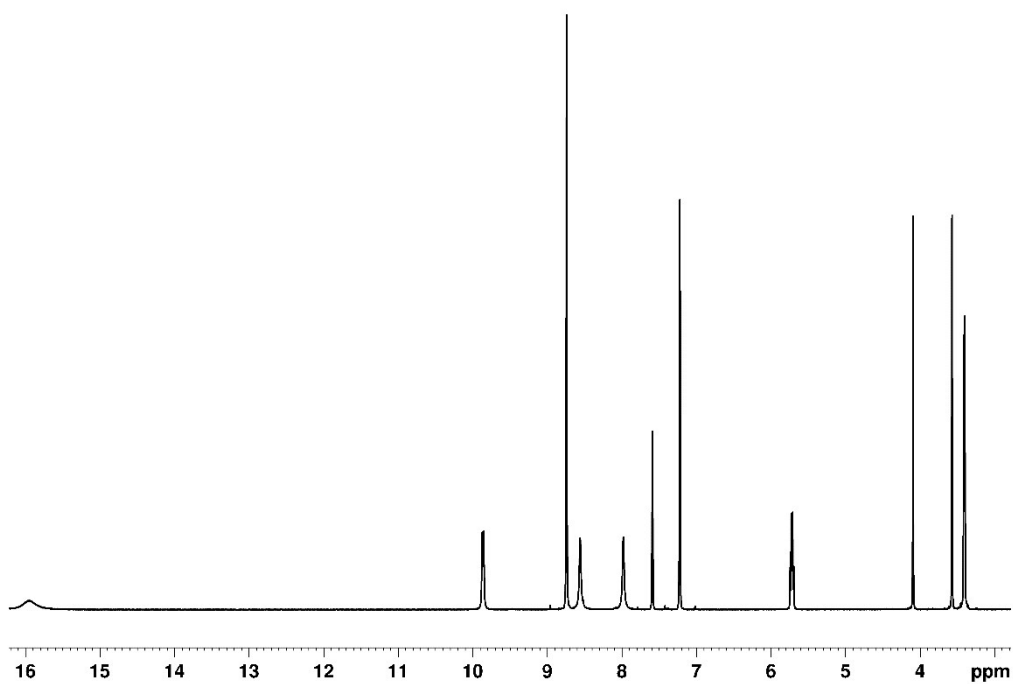


Figure S68. ^1H NMR spectrum of a d_5 -pyridine solution of **2d**.

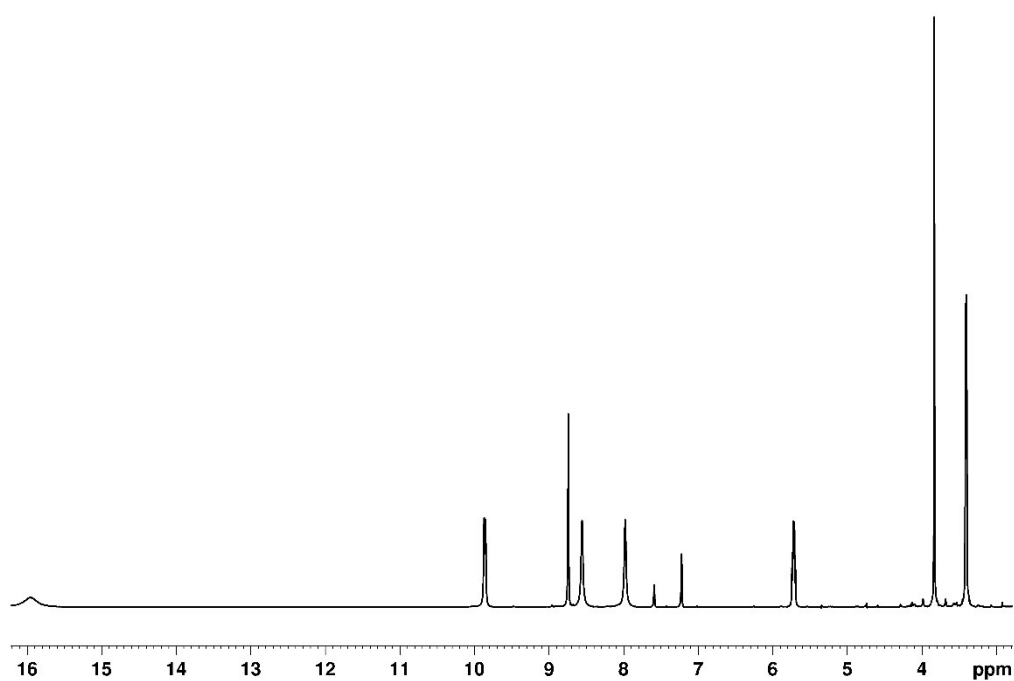


Figure S69. $^1\text{H}\{^{31}\text{P}\}$ NMR spectrum of a d_5 -pyridine solution of **2d**.

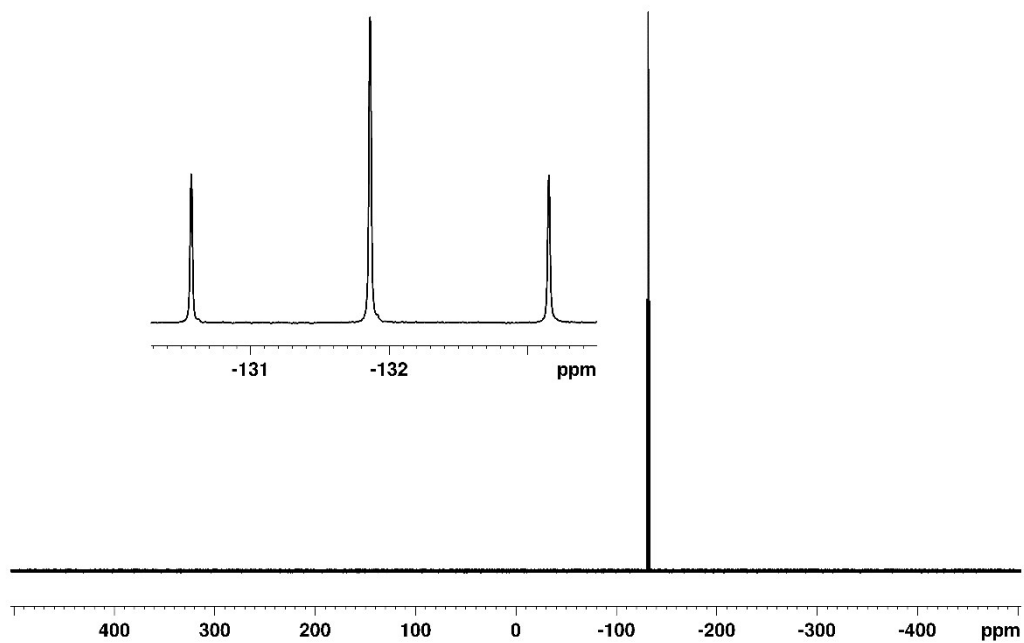


Figure S70. ^{31}P NMR spectrum of a d_5 -pyridine solution of **2d**.

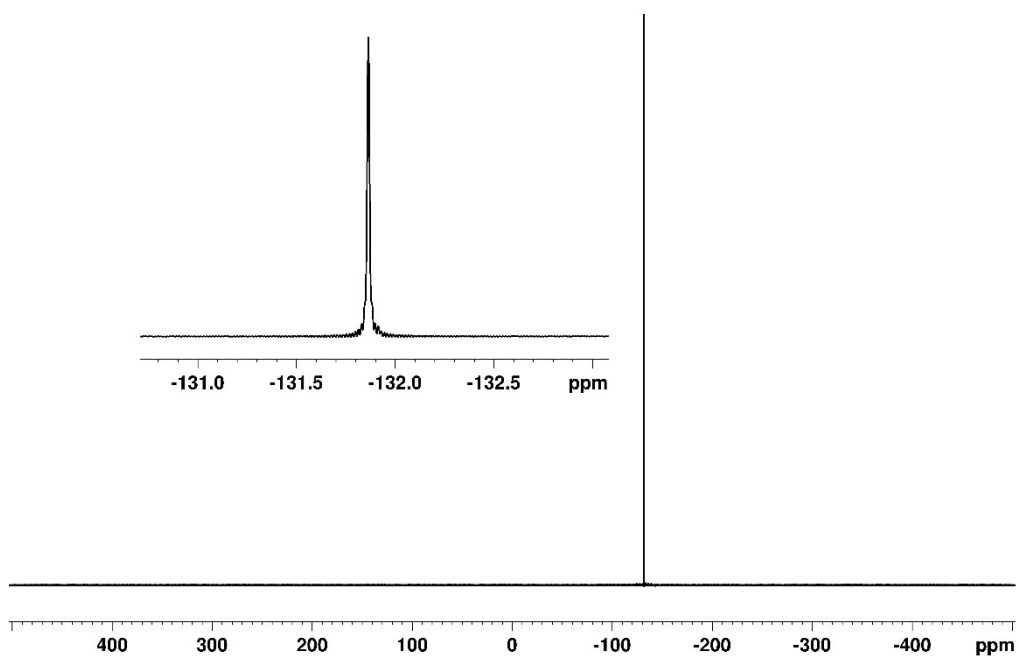


Figure S71. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution of **2d**.

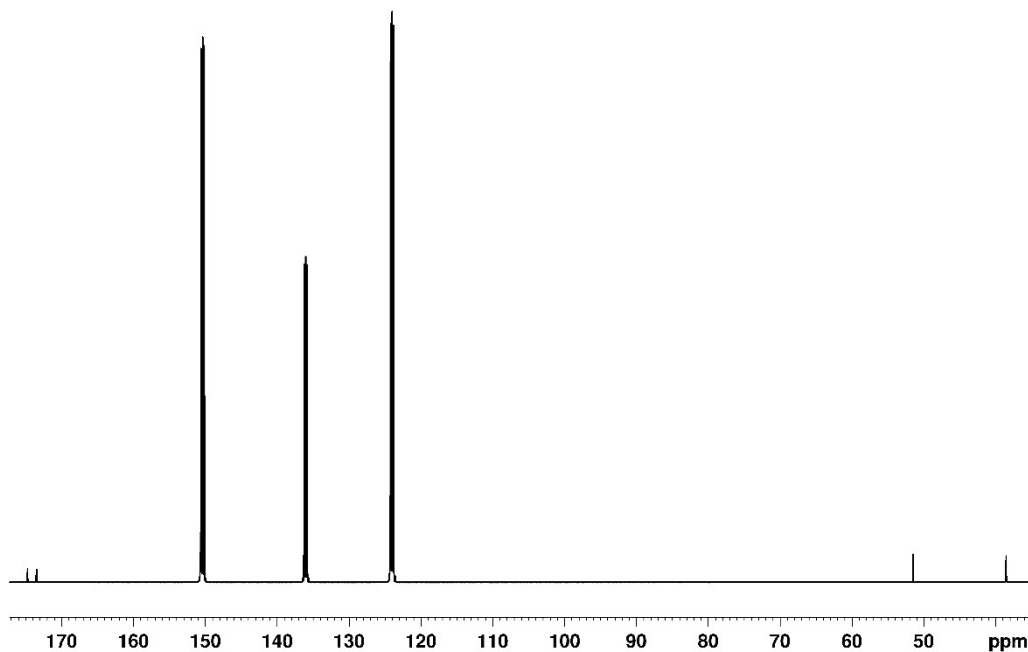


Figure S72. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution of **2d**.

$\text{H}_2\text{PC(O)NH(CH}_2)_2\text{C(O)NH}_2\text{COOH}$ (**2e**)

Pyridinium triflate (15 mg, 0.07 mmol) and Na[**1e**] (15 mg, 0.07 mmol) were weighed into a gas-tight NMR tube and d_5 -pyridine (0.5 mL) was added to give a pale yellow solution where the product was formed. Attempts to scale up this reaction up were made but the purification step was limiting due to solubility issues.

^1H NMR (400.2 MHz, d_5 -pyridine, 298 K): δ (ppm) 12.42 (bs, H; COOH), 9.95 (d, 1H; NH), 8.45 (s, 1H; NHH), 7.82 (s, 1H; NHH), 5.30 (m, 1H; αH), 3.84 (bd, $^1J_{\text{H-P}} = 210$ Hz 2H; PH_2), 2.66 (m, 4H; β , γH).

$^1\text{H}\{^{31}\text{P}\}$ NMR (400.2 MHz, d_5 -pyridine, 298 K): δ (ppm) 3.84 (m, 2H; PH_2), other resonances unchanged from ^1H NMR spectrum.

^{31}P NMR (162.0 MHz, d_5 -pyridine, 298 K): δ (ppm) -132.3 (t, $^1J_{\text{P-H}} = 210$ Hz).

$^{31}\text{P}\{^1\text{H}\}$ NMR (162.0 MHz, d_5 -pyridine, 298 K): δ (ppm) -132.3 (s)

$^{13}\text{C}\{^1\text{H}\}$ NMR (100.6 MHz, d_5 -pyridine, 298 K): δ (ppm) 175.9 (s, COOH), 175.3 (s, δC), 174.0 (d, $^1J_{\text{C-P}} = 8$ Hz, PC(O)), 54.1 (s, αC), 33.1 (s, γC), 29.1 (s, βC).

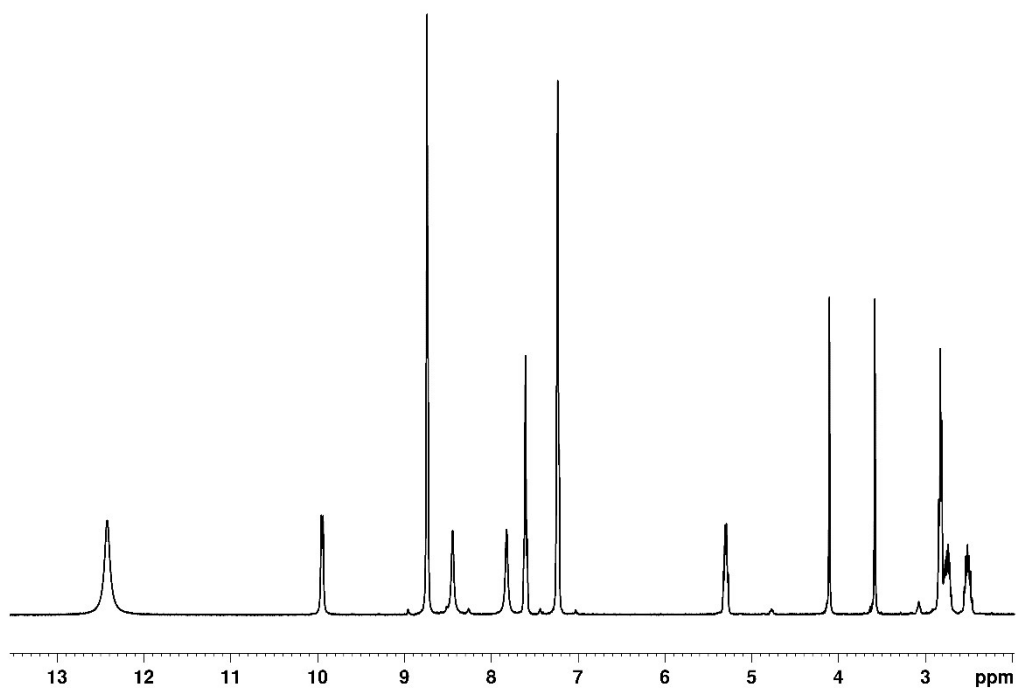


Figure S73. ^1H NMR spectrum of a d_5 -pyridine solution of **2e**.

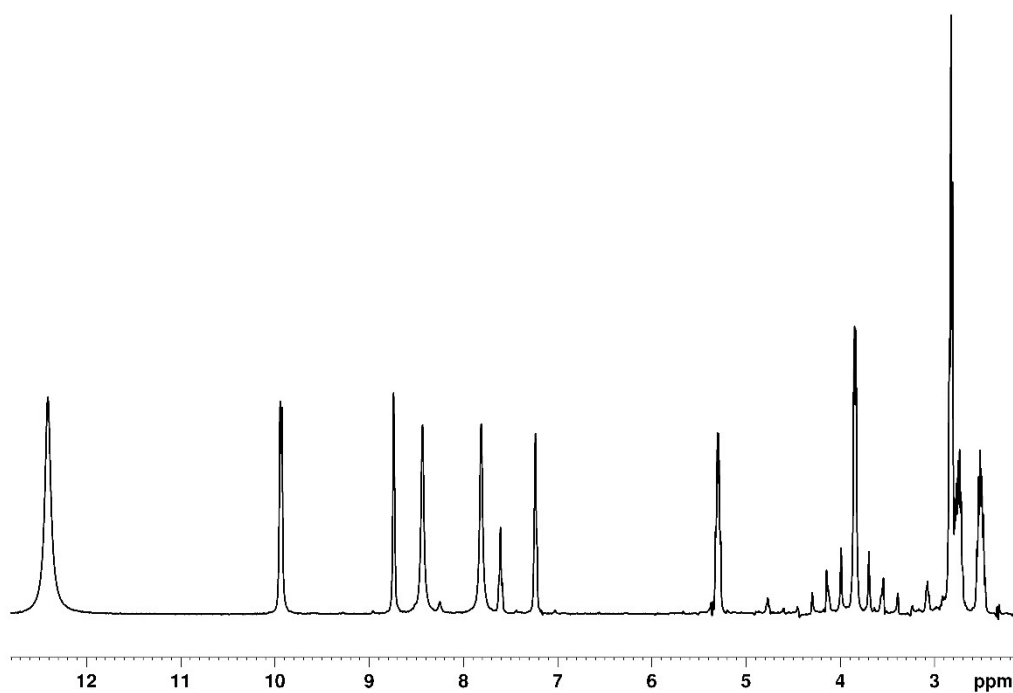


Figure S74. $^1\text{H}\{^{31}\text{P}\}$ NMR spectrum of a d_5 -pyridine solution of **2e**.

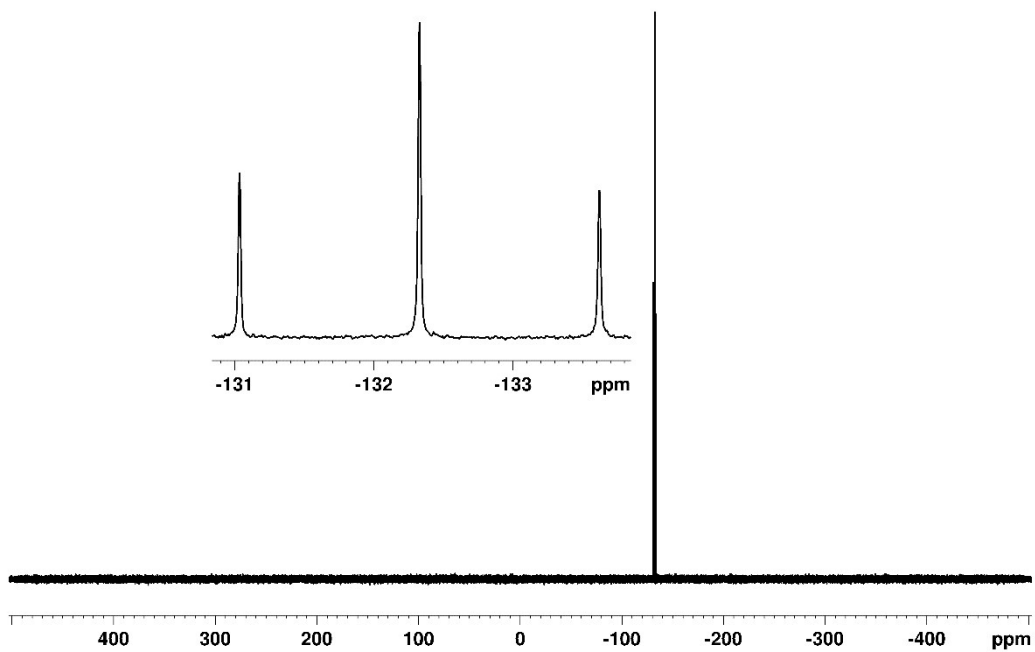


Figure S75. ^{31}P NMR spectrum of a d_5 -pyridine solution of **2e**.

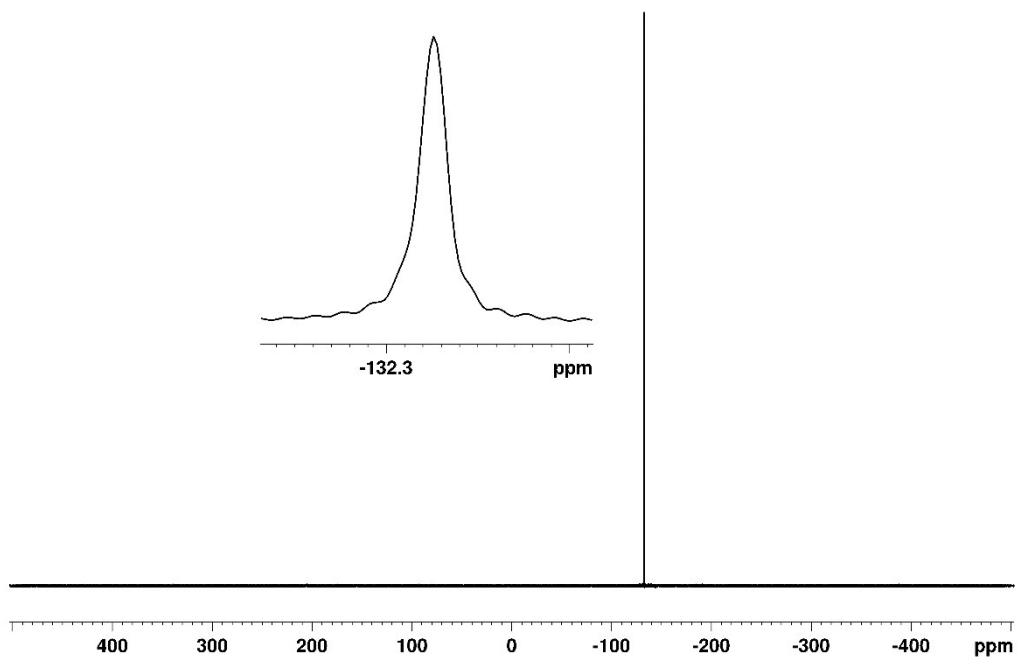


Figure S76. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution of **2e**.

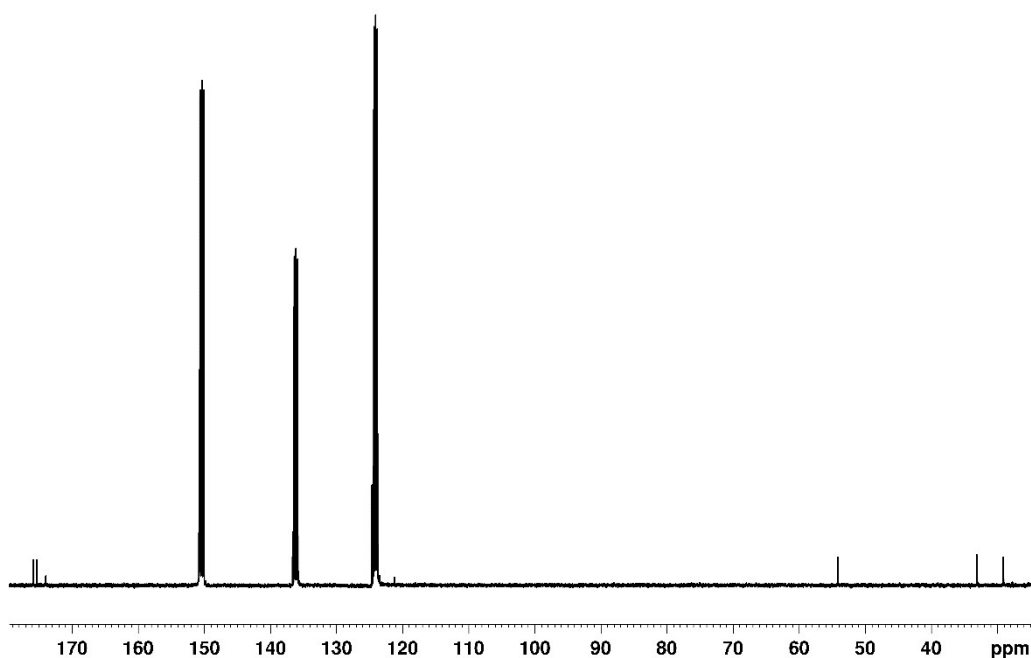


Figure S77. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution of **2e**.

$\text{H}_2\text{PC(O)N(CH}_2)_3\text{CHCOOH (2f)}$

Pyridinium chloride (58.7 mg, 0.51 mmol) and Na[**1f**] (100 mg, 0.51 mmol) were weighed into a Schlenk and dissolved in DCM (3 mL). The mixture was stirred for 5h. The colorless solution was then filtered to be separated from the white precipitate formed. Volatiles were removed under vacuum give a pale yellow oil. The oil was treated with hexane (3 mL) and stirred overnight. Removal of volatiles under vacuum yielded the product as a pale yellow solid (58.0 mg, 64.9% yield).

$^1\text{H NMR}$ (499.9 MHz, d_5 -pyridine, 298 K): δ (ppm) 15.85 (bs, 1H; COOH), 4.87 (t, 1H; αH (*cis*)), 4.72 (dd, 1H; αH (*trans*)), 3.96 (m, $^1J_{\text{H-P}} = 212$ Hz, $^2J_{\text{H-H}} = 12$ Hz, 1H; *PHH* (*trans*)), 3.85 (m, 1H; δH (*trans*)), 3.83 (m, $^1J_{\text{H-P}} = 216$ Hz, $^2J_{\text{H-H}} = 11$ Hz, 1H; *PHH* (*cis*)), 3.68 (m, 1H; δH (*trans*)), 3.62 (m, 1H; δH (*cis*)), 3.39 (q, 1H; δH (*cis*)), 2.31 ((m, 1H; βH (*trans*)), 2.23 (m, 1H; βH (*cis*)), 2.14 (m, 1H; βH (*trans*)), 2.02 (m, 1H; βH (*cis*)), 1.89 (m, 1H; γH (*cis*)), 1.77 (m, 1H; γH (*trans*)).

$^1\text{H}\{^{31}\text{P}\}$ NMR (499.9 MHz, d_5 -pyridine, 298 K): δ (ppm) 3.95 (d, $^2J_{\text{H-H}} = 14$ Hz, 2H; PH_2 (*trans*)), 3.82 (bs, 2H; PH_2 (*cis*)); other resonances unchanged from ^1H NMR spectrum.

^{31}P NMR (202.4 MHz, d_5 -pyridine, 298 K): δ (ppm) -129.4 (t, $^1J_{\text{P-H}} = 216$ Hz), -130.2 (t, $^1J_{\text{P-H}} = 212$ Hz).

$^{31}\text{P}\{^1\text{H}\}$ NMR (202.4 MHz, d_5 -pyridine, 298 K): δ (ppm) -129.4 (s), -130.2 (s)

$^{13}\text{C}\{^1\text{H}\}$ NMR (125.8 MHz, d_5 -pyridine, 298 K): δ (ppm) 175.4 (s, COOH (*trans*)), 174.9 (s, COOH (*cis*)), 173.5 (d, $^1J_{\text{C-P}} = 10.5$ Hz, PC(O) (*trans*)), 172.9 (d, $^1J_{\text{C-P}} = 9.8$ Hz, PC(O) (*cis*)), 62.4 (d, $^2J_{\text{C-P}} = 3.6$ Hz, αC (*trans*)), 60.2 (s, αC (*cis*)), 49.1 (d, $^2J_{\text{C-P}} = 5.8$ Hz δC (*cis*)), 47.5 (s, δC (*trans*)), 31.9 (s, βC (*trans*)), 30.3 (s, βC (*cis*)), 25.2 (s, γC (*cis*)), 23.5 (s, βC (*trans*)).

ESI-MS (–ve ion mode, DCM): $m/z = 174.0323$.

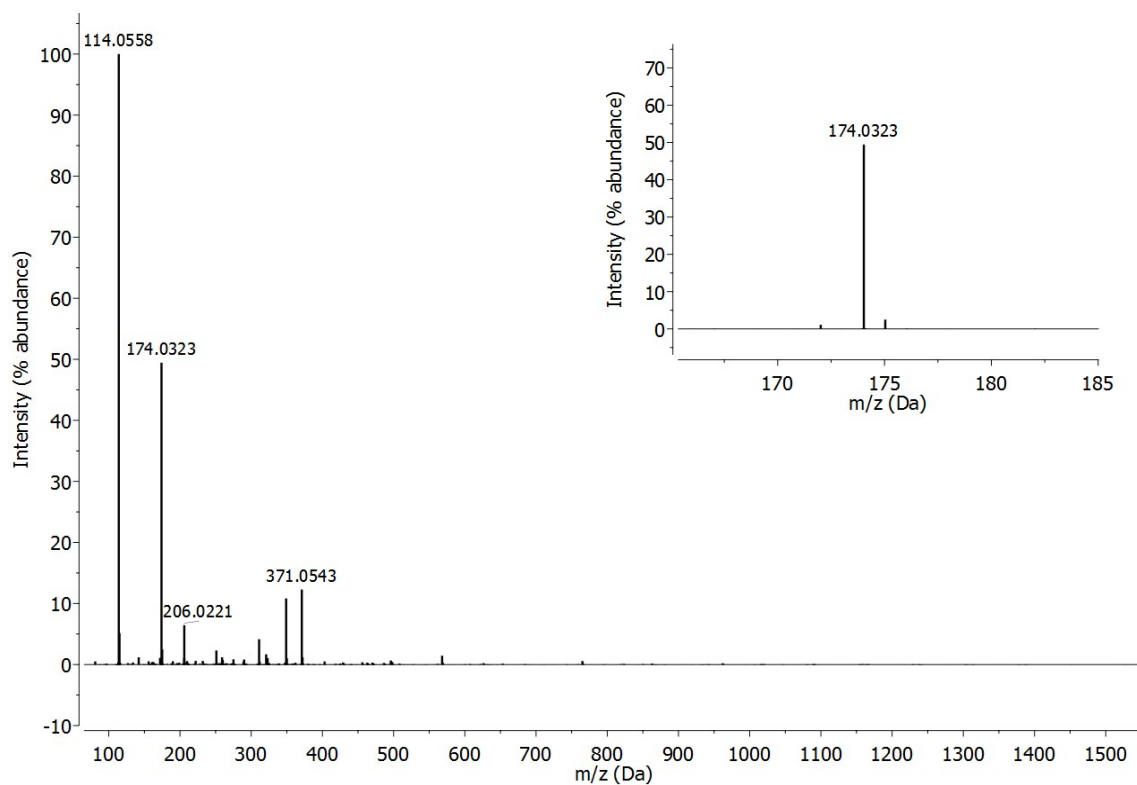


Figure S78. Negative ion mode ESI-MS spectrum of **2f**. Inset: molecular ion peak ($C_6H_9NO_3P^-$: Calcd. 174.0325)

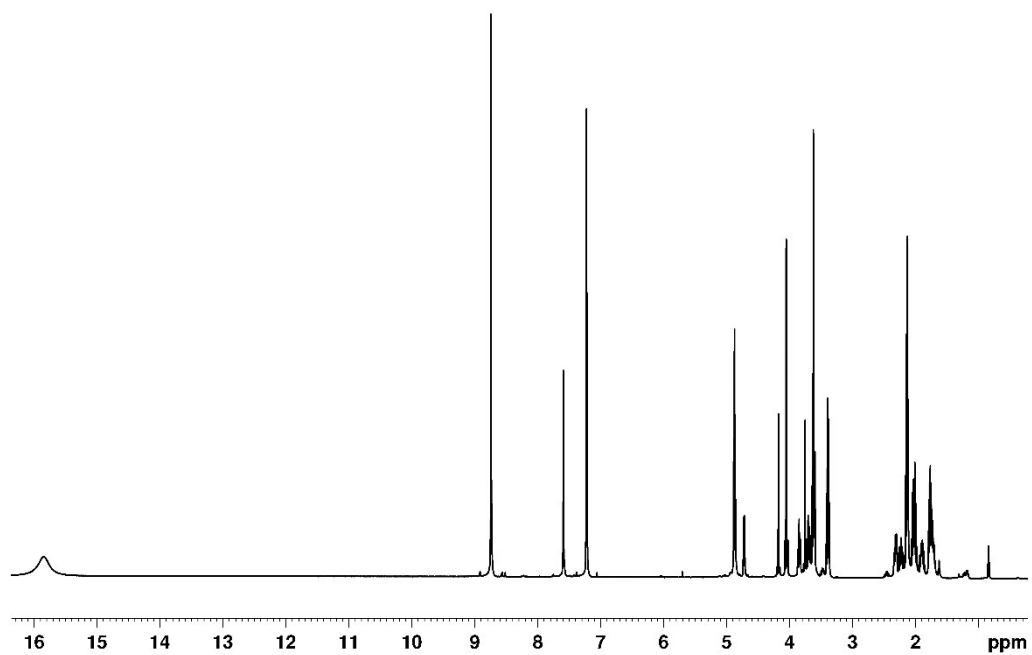


Figure S79. 1H NMR spectrum of a d_5 -pyridine solution of **2f**.

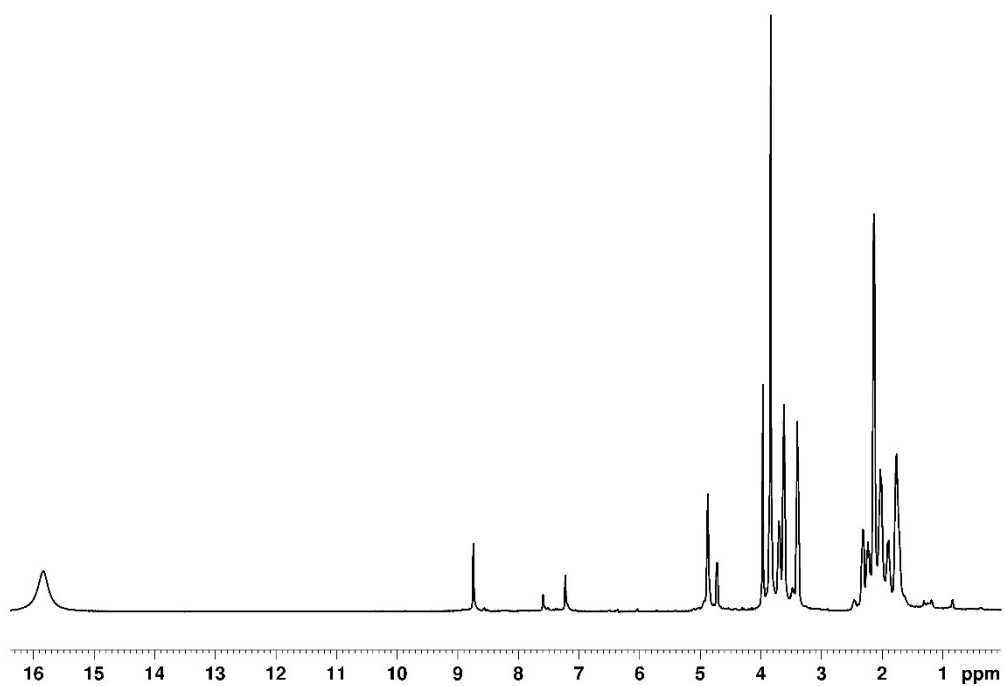


Figure S80. $^1\text{H}\{^{31}\text{P}\}$ NMR spectrum of a d_5 -pyridine solution of **2f**.

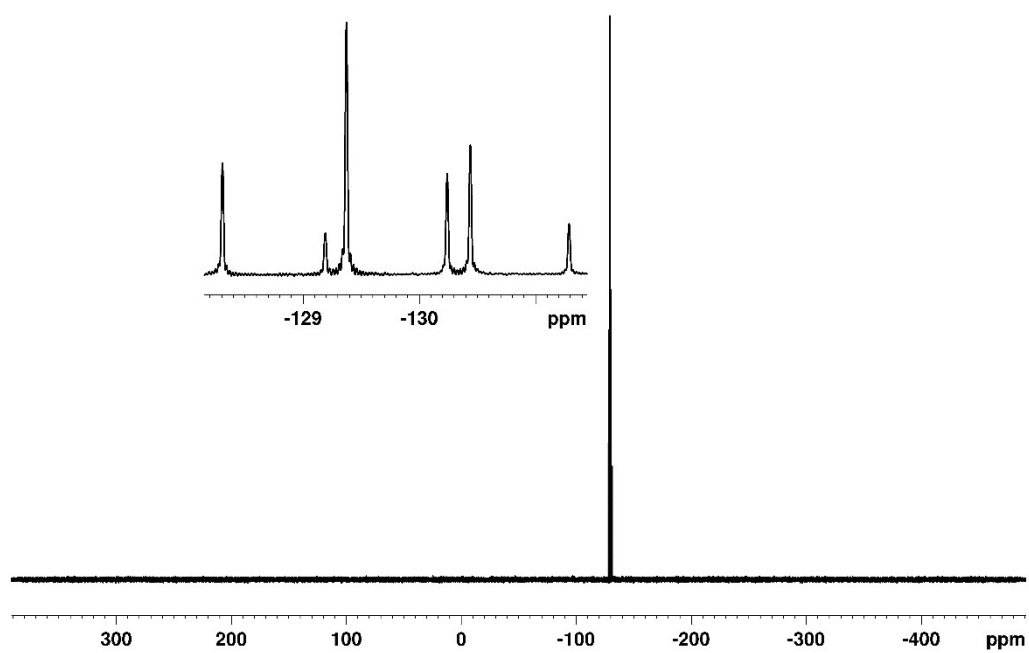


Figure S81. ^{31}P NMR spectrum of a d_5 -pyridine solution of **2f**.

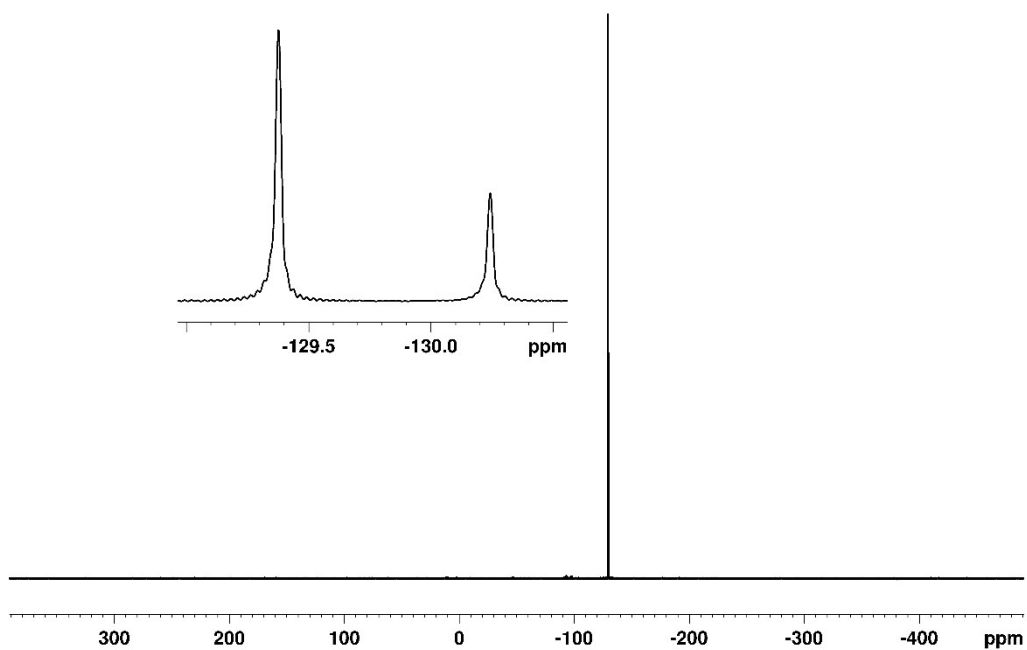


Figure S82. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution of **2f**.

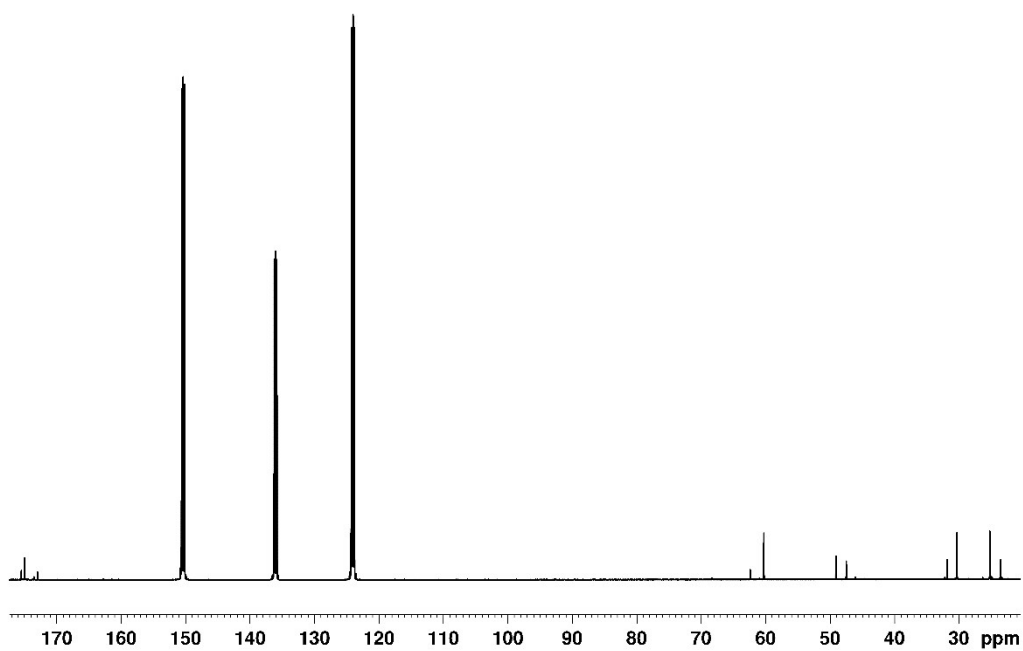


Figure S83. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of a d_5 -pyridine solution of **2f**.

2. Single crystal X-ray diffraction data

Table S1. Selected X-ray data collection and refinement parameters for [K(18-crown-6)][**1a**].

	[K(18-crown-6)][1a]
Formula	C ₁₆ H ₃₁ KNO ₉ P
CCDC depository number	1533100
Fw [g mol ⁻¹]	451.49
crystal system	monoclinic
space group	<i>P</i> 2 ₁
<i>a</i> (Å)	8.6146(2)
<i>b</i> (Å)	29.8779(5)
<i>c</i> (Å)	17.5654(3)
β (°)	99.466(2)
<i>V</i> (Å ³)	4459.53(15)
<i>Z</i>	8
radiation, λ (Å)	1.54178, Cu Kα
<i>T</i> (K)	150(2)
ρ _{calc} (g cm ⁻³)	1.345
μ (mm ⁻¹)	3.166
reflections collected	26764
independent reflections	13248
parameters	1036
R(int)	0.0463
R1/wR2, ^[a] I ≥ 2σI (%)	4.21/11.04
R1/wR2, ^[a] all data (%)	4.69/11.37
GOF	1.017

^[a] R1 = $[\sum(|F_o| - |F_c|)]/\sum|F_o|$; wR2 = $\{[\sum w[(F_o)^2 - (F_c)^2]^2]/[\sum w(F_o)^2]\}^{1/2}$; w = $[\sigma^2(F_o)^2 + (AP)^2]^{-1}$, where P = $[(F_o)^2 + 2(F_c)^2]/3$ and the A value is 0.0724 for [K(18-crown-6)][**1a**].

Table S2: Bond distances (Å) and angles (°) for the four distinct molecules of [K(18-crown-6)]**1a** in the asymmetric unit.

Bond distance (Å)	1a_1	1a_2	1a_3	1a_4	1a_DFT
P1–C1	1.846(5)	1.853(6)	1.872(5)	1.876(5)	1.893
C1–O1	1.205(7)	1.234(7)	1.225(6)	1.220(6)	1.246
C1–N1	1.349(7)	1.330(7)	1.335(6)	1.330(6)	1.344
N1–C2	1.452(6)	1.463(6)	1.456(5)	1.449(6)	1.464
C2–C3	1.527(7)	1.525(6)	1.524(6)	1.509(6)	1.536
C2–C4	1.536(6)	1.548(6)	1.543(6)	1.534(6)	1.559
C4–O2	1.270(6)	1.264(6)	1.258(5)	1.264(5)	1.271
C4–O3	1.238(5)	1.247(5)	1.248(6)	1.248(5)	1.264
K1–O2	2.628(4)	2.660(4)	2.725(4)	2.668(3)	N.A
K1–O3	2.909(3)	2.886(3)	2.790(4)	2.776(3)	N.A
Bond angle (°)					
P1–C1–O1	117.6(4)	117.9(4)	117.7(4)	118.0(4)	119.0
P1–C1–N1	117.5(4)	117.3(4)	116.5(4)	116.5(4)	116.6
N1–C1–O1	124.9(5)	124.9(5)	125.6(4)	125.4(5)	124.2
C2–C4–O2	117.2(4)	114.9(4)	118.6(4)	118.4(4)	117.4
C2–C4–O3	117.8(4)	119.9(4)	115.5(4)	116.6(4)	115.6
O2–C4–O3	125.0(4)	125.2(4)	126.0(4)	125.0(4)	127.0
K1–O2–C4	97.2(3)	97.0(3)	93.0(3)	93.6(3)	N.A.
K1–O3–C4	84.9(3)	86.9(3)	90.2(3)	89.0(2)	N.A.

3. Computational details

All geometry optimizations were performed using the Amsterdam Density Functional package (ADF2014).^[3] An TZ2P Slater-type basis set of triple- ζ quality, extended with two polarization functions, was used to describe all atoms. Geometry optimizations were performed using the Becke88 exchange functional with Perdew86 local correlation functional.^[4,5] Relativistic effects were incorporated using the Zeroth Order Relativistic Approximation (ZORA).^[6] The Grimme3 empirical dispersion correction was applied to all calculations.^[7] The presence of cations in the crystal lattice was modelled by surrounding the anions with a continuum dielectric model (COSMO).^[8] The chosen dielectric constant $\epsilon = 12.5$ corresponds to pyridine, although structural parameters are not strongly dependent on this choice. All structures were optimized using the gradient algorithm of Versluis and Ziegler.^[9]

Table S3. Computed total bonding energies (with solvation shell) for different isomers of phosphinecarboxamide-functionalised amino acids.

Amino acid	Product	<i>Trans</i> -	<i>Cis</i> -
L-alanine	1a	-9565.96	-9558.69
L-serine	1b	-10197.37	-10189.51
L-cysteine	1c	-9919.28	-9909.50
L-asparagine	1d	-12294.78	-12281.81
L-glutamine	1e	-13880.06	-13872.45
L-proline	1f	-11960.82	-11964.63

Cartesian coordinates [Å] for the optimized computed geometry of 1a.

Atom	x	y	z
1. P	-0.245988000	0.022305000	0.398572000
2. H	0.849032000	0.722108000	0.993164000
3. H	0.558781000	-0.610283000	-0.591915000
4. C	-0.846961000	1.385416000	-0.770177000
5. O	-1.493956000	1.067767000	-1.785982000
6. N	-0.625021000	2.652569000	-0.381395000
7. H	0.014624000	2.872619000	0.386410000
8. C	-1.049075000	3.837210000	-1.129245000
9. H	-0.852914000	3.664241000	-2.197534000
10. C	-2.544352000	4.123073000	-0.928121000
11. H	-3.140228000	3.258578000	-1.246770000
12. H	-2.837384000	4.998011000	-1.520616000
13. H	-2.754456000	4.325469000	0.131263000
14. C	-0.182442000	5.050487000	-0.672536000
15. O	0.572556000	4.882645000	0.335479000
16. O	-0.326935000	6.110138000	-1.347218000

Cartesian coordinates [Å] for the optimized computed geometry of 1b.

Atom	x	y	z
1. P	0.000000000	0.000000000	0.000000000
2. H	-1.378302000	-0.363277000	-0.095748000
3. H	-0.105829000	1.063588000	-0.941677000
4. C	0.684259000	-1.224085000	-1.271533000

5. O	1.688326000	-0.923721000	-1.940341000
6. N	0.085502000	-2.432590000	-1.311880000
7. H	-0.827536000	-2.587915000	-0.874211000
8. C	0.427329000	-3.485388000	-2.268402000
9. H	0.640407000	-3.031025000	-3.248131000
10. C	-0.800206000	-4.438570000	-2.426774000
11. O	-1.802649000	-4.218950000	-1.680632000
12. O	-0.670023000	-5.351126000	-3.289146000
13. C	1.680236000	-4.255132000	-1.832695000
14. H	1.922376000	-4.997643000	-2.600548000
15. H	2.520231000	-3.549506000	-1.733395000
16. O	1.485073000	-4.989072000	-0.606996000
17. H	1.238329000	-4.341043000	0.079364000

Cartesian coordinates [\AA] for the optimized computed geometry of 1c.

Atom	x	y	z
1. P	0.000000000	0.000000000	0.000000000
2. H	-1.368181000	-0.340081000	-0.219992000
3. H	-0.006693000	1.091770000	-0.913856000
4. C	0.773843000	-1.210373000	-1.231185000
5. O	1.844211000	-0.920304000	-1.797816000
6. N	0.159761000	-2.400966000	-1.342869000
7. H	-0.767268000	-2.567517000	-0.943469000
8. C	0.622433000	-3.502797000	-2.175155000
9. H	0.827965000	-3.124636000	-3.190284000

10. C	-0.528012000	-4.556337000	-2.302382000
11. O	-1.622796000	-4.286839000	-1.723795000
12. O	-0.247394000	-5.587129000	-2.975878000
13. C	1.926786000	-4.129209000	-1.664073000
14. H	2.267834000	-4.884530000	-2.379759000
15. H	2.695779000	-3.353212000	-1.570741000
16. S	1.818208000	-4.882298000	0.009295000
17. H	0.971000000	-5.882829000	-0.332434000

Cartesian coordinates [Å] for the optimized computed geometry of 1d.

Atom	x	y	z
1. P	0.000000000	0.000000000	0.000000000
2. H	-0.115800000	-0.671556000	-1.249768000
3. H	-0.768760000	-0.966518000	0.715455000
4. C	1.715972000	-0.703434000	0.369019000
5. O	2.647660000	-0.516900000	-0.434573000
6. N	1.866643000	-1.289490000	1.572084000
7. H	1.056039000	-1.568839000	2.128118000
8. C	3.124440000	-1.841310000	2.064354000
9. H	3.577577000	-2.456102000	1.270746000
10. C	2.815389000	-2.807782000	3.255883000
11. O	1.602253000	-3.093847000	3.467831000
12. O	3.823252000	-3.216312000	3.906414000
13. C	4.145749000	-0.734225000	2.414124000
14. H	4.332261000	-0.130534000	1.519955000

15. H	5.078448000	-1.227159000	2.715657000
16. C	3.671352000	0.203222000	3.517392000
17. O	3.301007000	1.368965000	3.284852000
18. N	3.684314000	-0.324617000	4.762984000
19. H	3.302141000	0.206514000	5.538967000
20. H	3.914700000	-1.308910000	4.897819000

Cartesian coordinates [Å] for the optimized computed geometry of 1e.

Atom	<i>x</i>	<i>y</i>	<i>z</i>
1. P	0.000000000	0.000000000	0.000000000
2. H	-1.075111000	-0.559936000	0.754553000
3. H	-0.833632000	0.438790000	-1.066825000
4. C	0.549647000	-1.575129000	-0.888639000
5. O	1.101029000	-1.495814000	-2.001296000
6. N	0.409925000	-2.720608000	-0.194702000
7. H	-0.129440000	-2.742733000	0.670249000
8. C	0.846163000	-4.034683000	-0.668885000
9. H	0.563247000	-4.129524000	-1.725710000
10. C	0.114369000	-5.144271000	0.139605000
11. O	0.112522000	-6.292724000	-0.377530000
12. O	-0.373526000	-4.815206000	1.270970000
13. C	2.379810000	-4.214732000	-0.567248000
14. H	2.650593000	-5.077469000	-1.189730000
15. H	2.861438000	-3.330110000	-1.005836000
16. C	2.923108000	-4.468152000	0.852962000

17. H	2.426886000	-5.347806000	1.286764000
18. H	3.994098000	-4.694585000	0.778695000
19. C	2.801445000	-3.277884000	1.797308000
20. O	3.652067000	-2.367015000	1.813569000
21. N	1.737135000	-3.301573000	2.635567000
22. H	0.943078000	-3.913877000	2.406807000
23. H	1.555445000	-2.474181000	3.197624000

Cartesian coordinates [Å] for the optimized computed geometry of *cis*-1f.

Atom	<i>x</i>	<i>y</i>	<i>z</i>
1. P	0.000000000	0.000000000	0.000000000
2. H	0.197291000	0.562121000	1.293555000
3. H	1.205620000	-0.752799000	0.013992000
4. C	-1.073996000	-1.481478000	0.469053000
5. O	-0.826815000	-2.590656000	-0.052991000
6. N	-2.155435000	-1.255670000	1.240091000
7. C	-2.516730000	0.023853000	1.883418000
8. H	-2.524573000	0.825734000	1.130079000
9. C	-1.596448000	0.460120000	3.062798000
10. O	-0.909636000	-0.425323000	3.643144000
11. O	-1.673512000	1.691574000	3.358782000
12. C	-3.950891000	-0.235538000	2.420755000
13. H	-4.583264000	0.652352000	2.319456000
14. H	-3.894519000	-0.491910000	3.488052000
15. C	-4.455910000	-1.447380000	1.624017000

16. H	-5.251518000	-1.995636000	2.142451000
17. H	-4.833697000	-1.134563000	0.640063000
18. C	-3.189109000	-2.286436000	1.445591000
19. H	-3.208435000	-2.965360000	0.586998000
20. H	-2.958885000	-2.870973000	2.350291000

Cartesian coordinates [Å] for the optimized computed geometry of *trans*-1f.

Atom	<i>x</i>	<i>y</i>	<i>z</i>
1. P	0.000000000	0.000000000	0.000000000
2. H	.280021000	-0.401646000	-0.473820000
3. H	-0.435158000	0.522109000	-1.256094000
4. C	-0.739544000	-1.734726000	-0.172629000
5. O	-0.039403000	-2.739654000	0.059494000
6. N	-2.054209000	-1.801704000	-0.454231000
7. C	-2.739207000	-3.101030000	-0.597959000
8. H	-2.628605000	-3.665461000	0.338285000
9. C	-2.203441000	-3.973658000	-1.768561000
10. O	-1.655539000	-3.386812000	-2.742153000
11. O	-2.437754000	-5.217419000	-1.655889000
12. C	-4.212854000	-2.698105000	-0.850654000
13. H	-4.909888000	-3.412897000	-0.400748000
14. H	-4.399932000	-2.671582000	-1.934079000
15. C	-4.329062000	-1.279509000	-0.272573000
16. H	-5.166588000	-0.709330000	-0.691615000
17. H	-4.444512000	-1.314450000	0.820128000

18. C	-2.971937000	-0.662815000	-0.626669000
19. H	-2.694317000	0.170949000	0.030896000
20. H	-2.953725000	-0.311806000	-1.671126000

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