General Experimental

Solvents and reagents were purified by standard methods[1] where required prior to use. 2-(Bromomethyl)acrylic acid was prepared as previously described[2] from 2,2-bis(hydroxylmethyl) diethyl malonate; itself prepared from formaldehyde and diethyl malonate as previously described.[3] Fosmidomycin (sodium salt) was purchased from Toronto Research Chemicals. All other reagents were obtained from commercial sources, and used as received.

TLC was carried out on Merck Silica Gel 60 F254 aluminum-backed sheets. Flash chromatography was carried out on silica gel, 230-400 mesh.

All reactions were carried out under an inert atmosphere of dry argon or nitrogen, unless otherwise stated. NMR spectroscopy was carried out on a Bruker Avance® 400 MHz or Bruker Avance® 500 MHz NMR spectrometer, utilising a quadnuclei $^{1}H/^{13}C/^{19}F/^{31}P$ or $^{1}H/^{13}C$ inverse detection probe respectively, or on a Varian UNITY 300 MHz or Varian INOVA 500 MHz NMR spectrometer, utilising a standard $^{1}H/^{13}C$ probe or inverse detection $^{1}H/^{13}C$ probe respectively. ^{1}H and ^{13}C spectra are referenced to external tetramethylsilane; ^{31}P NMR spectra are referenced to external 85% phosphoric acid.
^{31}P NMR concentration determinations were performed relative to a known approximately equimolar quantity of potassium dihydrogen phosphate. Effects arising from different relaxation times were checked for prior to determination; and ^{1}H-coupled spectra were collected to avoid signal artifacts arising from NOE from the ^{1}H decoupling pulse.

High-resolution mass spectroscopy was carried out on a Micromass LCT spectrometer. Unless otherwise noted, high resolution mass spectral data (HRMS) reported for compounds refers to positive ion electrospray ionisation data.

Enzyme assays

UV-Visible spectrophotometry was carried out on a Varian Cary® One UV-Visible spectrophotometer, in stoppered 1 mL quartz cells. The temperature was continuously controlled at 298 K by the use of a jacketed multicell holder, connected to an external Varian Peltier temperature controller.

Enzyme activity was monitored by UV-Visible spectrophotometry, following the decrease in absorbance at 232 nm as the enol alkene of PEP is consumed. DAHP synthase inhibitor assays were conducted with recombinant *E. coli* DAH7P synthase (phenylalanine-repressed isozyme), which was prepared as previously described,[4] diluted to ~2 mg mL^{-1} and stored at -80°C until required. Enzyme solutions were thawed and centrifuged (14 000 rpm/ 2 minutes) prior to use, and stored on ice during use.

The BTP buffer utilised for both activity measurements and stock solution preparation was prepared by dissolving sufficient bis-tris-propane free base in MilliQ water to give a 50 mM solution, then adjusting the pH to 6.8 with hydrochloric acid. The resulting mixture was treated with Chelex® resin for two hours, then filtered through a 0.2 μm membrane and stored at 4°C until required. Stock solutions of PEP and E4P were prepared from monopotassium-PEP (Sigma) and sodium-E4P (Sigma) respectively, in buffer. Solutions were treated with Chelex® resin for 2 hours, and filtered through a 0.2 μm filter and stored until further use. PEP solutions were stored frozen at -20°C. To avoid problems with concentration-dependent oligomerization, E4P solutions were stored at 4°C. Stock solutions of manganese(II) sulfate, cobalt(II) chloride and iron(II) sulfate were prepared in MilliQ water at 10 mM; and were filtered through a 0.2 μm membrane before use. Inhibitor solutions were prepared in BTP buffer, treated with Chelex® resin and filtered through a 0.2 μm filter before use.

Inhibition constants were measured by enzyme assay. Cuvettes containing PEP, E4P, manganese(II) sulfate and inhibitor in BTP buffer at 25°C were initiated by the addition of ~2 μg enzyme, the initial rate of reaction was determined by linear least-squares fitting

of the change in absorbance with time. Collected initial rate data at given inhibitor and substrate concentrations were converted to positive values, and globally fitted by multivariable non-linear least squares regression using Grafit® to the Michealis-Menten equation modified for competitive inhibition:

$$v = \frac{V_{max}[S]}{K_m\left(1 + \frac{[I]}{K_i}\right) + [S]}$$

where v = initial rate;

V_{max} = maximum rate

[S] = competitive substrate concentration;

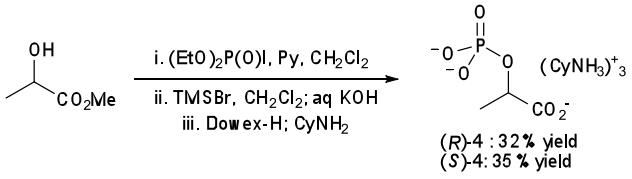
K_m = Michealis constant in the absence of inhibitor

[I] = inhibitor concentration

K_i = inhibition constant

Control experiments with possible contaminants in the inhibitor solutions, namely lactate, sodium bromide and cyclohexylamine showed no ability to inhibit *E. coli* DAH7P synthase up to concentrations of 1 mM.

Phospholactate 6



A solution of triethylphosphite (0.860 mL, 5.0 mmol) in dichloromethane (12 mL) under nitrogen was cooled to 0°C, and iodine (1.16 g, 4.57 mmol) was added. The solution was stirred until the characteristic brown iodine colour had been discharged (~ 5 minutes). The resulting solution of diethylphosphoryl iodide was added dropwise over 15 minutes

to (*S*)-methyl lactate (400 mg, 3.8 mmol) in pyridine (2.5 mL) and dichloromethane (60 mL) at 0°C under nitrogen. Once addition was complete the mixture was stirred for 1 hour, then quenched with saturated aqueous sodium bicarbonate (20 mL), and stirred vigorously for 5 minutes. The organic phase was separated, and washed with 1.2 M aqueous hydrochloric acid (2x 75 mL), saturated aqueous sodium bicarbonate (75 mL), and brine (75 mL), dried and evaporated. Flash chromatography (50% ethyl acetate/hexane) gave the desired phosphate ester (615.9 mg, 67%). Rf (50% ethyl acetate/hexane): 0.34; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 4.83 (qd, J = 14.1, 7.0 Hz, 1H, H2), 4.17-3.99 (m, 4H, POC$\underline{H_2}CH_3$), 3.70 (s, 3H, $CO_2\underline{Me}$), 1.48 (d, J = 6.9 Hz, 3H, H3), 1.27 (dt, J = 7.1, 3.3 Hz, 6H, POC$\underline{H_2}CH_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 171.0 (d, J = 5.2 Hz, C1), 71.6 (d, J = 5.2 Hz, C2), 64.2 (d, J = 6.0 Hz, PO$\underline{C}H_2CH_3$), 64.0 (d, J = 6.0 Hz, PO$\underline{C}H_2CH_3$), 52.4 ($CO_2\underline{Me}$), 19.2 (d, J = 5.4 Hz, C3), 16.0 (app dd, J = 6.9, 1.0 Hz, 2x PO$\underline{C}H_2CH_3$); ^{31}P NMR (162 MHz, $CDCl_3$) δ ppm -2.0 (C2O$\underline{P}$OEt).

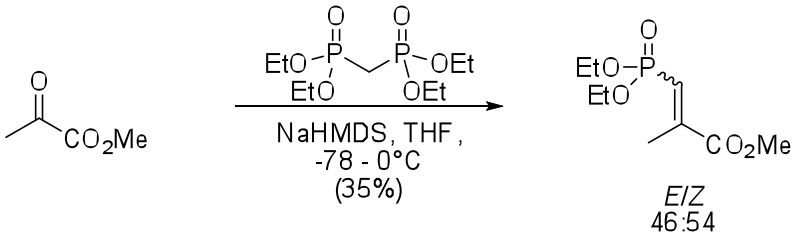
Treatment of (*R*)-methyl lactate (401 mg, 3.85 mmol) under the same conditions gave the corresponding (*R*)-phosphoester (476 mg, 51%), with identical spectral data.

To the (*R*)-phosphoester (471 mg, 1.96 mmol) in dichloromethane (15 mL) under nitrogen was added trimethylsilyl bromide (1.55 mL, 11.7 mmol), and the mixture was stirred overnight then evaporated. The residue was dissolved in 10% w/v aqueous potassium hydroxide, stirred for five minutes then extracted with dichloromethane (3x 2 mL) and the organic phases discarded. The aqueous phase was passed through a short column of Dowex-50X8 H^+-form, eluted with water (20 mL), neutralised with cyclohexylamine and lyophilised to give a white powder, (757 mg). Analysis of the solid (^{1}H NMR) showed the hydrolysis of the carboxylate ester was incomplete, so a portion of the solid (474 mg) was treated with 10% w/v aqueous potassium hydroxide (4 mL) for two hours, the mixture was extracted with dichloromethane (3x 2 mL) and the organic phases discarded. After treatment with Dowex-50X8 H^+-form and cyclohexylamine and lyophilisation, (*R*)-phospholactate cyclohexylammonium salt **6** was obtained as a white solid (361.7 mg, 63%), containing 23.7% lactate due to hydrolysis. ^{1}H NMR (500 MHz, D_2O) δ ppm 4.3-4.2 (app p, J = 7.3 Hz, 1H, H2-OP), 3.1-2.9 (q, J = 7.0 Hz, 0.25H, H2-OH), 1.9-1.7 (m, $CyNH_3^+$), 1.7-1.6 (m, $CyNH_3^+$), 1.6 (d, J = 6.9 Hz, 3H, C3), 1.5 (dm, J = 12.8 Hz, $CyNH_3^+$), 1.2-1.1 (m, $CyNH_3^+$), 1.0 (m, $CyNH_3^+$); ^{13}C NMR (75 MHz, D_2O) δ

ppm 181.5 (d, J = 6.4 Hz, C1), 71.9 (d, J = 5.0 Hz, C2), , 50.5 ($CyNH_3^+$), 30.5 ($CyNH_3^+$), 24.5 ($CyNH_3^+$), 24.0 ($CyNH_3^+$), 20.3 (d, J = 3.1 Hz, C3), lactate 182.6 (C1), 68.6 (C2), 20.2 (C3); ^{31}P NMR (121 MHz, D_2O) δ ppm 2.1 (C2O<u>P</u>); 2.0 (Pi). HRMS (ESI, negative ion, 20% AcOH matrix): required for $C_3H_6O_6P^-$: 168.9902, found 168.9904.

In a similar manner (*S*)-**6** was prepared, with the NMR spectral data in accordance with that above except the final product contained no unphosphorylated lactate by ^{1}H NMR. HRMS, (ESI, negative ion, 20% AcOH matrix): required for $C_3H_6O_6P^-$: 168.9902, found 168.9909.

Vinyl phosphonate 4

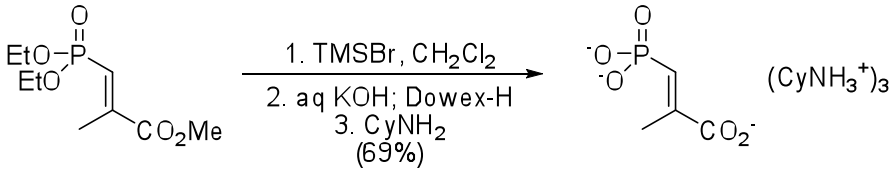


To a solution of tetraethyl methylene bisphosphonate (820 μL, 3.30 mmol) in tetrahydrofuran (4 mL) under nitrogen at -78°C was added a 0.846 M solution of sodium bis(trimethylsilyl)amide in tetrahydrofuran (3.6 mL, 3.05 mmol), and the mixture was stirred for 30 minutes, and allowed to come to -35°C over this time. The cold bath was replaced with an ice bath, and technical grade methyl pyruvate (96%, 290 μL, 3.08 mmol) was added dropwise. The mixture was stirred for 2.5 hours, and quenched with saturated potassium dihydrogen phosphate (5 mL). The tetrahydrofuran was removed on a rotary evaporator, and the residue extracted with ethyl acetate (5x 10 mL).The combined organic phases were washed with brine (50 mL), dried and evaporated. Flash chromatography (60% ethyl acetate/hexane) gave pure (*E*)-phosphonate (116 mg, 16%) and (*Z*)-phosphonate (137 mg, 24%), which contained ~10% (*E*)-isomer by NMR.

(*E*)-isomer: Rf (60% ethyl acetate/hexane): 0.25; ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 6.64 (dq, J = 16.0, 1.2 Hz, 1H, H3'), 4.11-4.04 (dq, J = 7.8, 7.1 Hz, 4H, C3'POC<u>H</u>$_2$CH$_3$), 3.76 (s, 3H, CO_2<u>Me</u>), 2.23 (dd, J = 3.6, 1.3 Hz, 3H, H3), 1.30 (t, J = 7.1, 6H,

C3'POCH$_2$C<u>H</u>$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 167.1 (d, J = 29.3 Hz, C1), 147.1 (d, J = 9.0 Hz, C2), 125.5 (d, J = 185.9 Hz, C3'), 62.2 (d, J = 5.6 Hz, C3'PO<u>C</u>H$_2$CH$_3$), 52.9 (s, CO$_2$<u>Me</u>), 16.6 (d, J = 6.4 Hz, C3'POCH$_2$<u>C</u>H$_3$), 16.0 (d, J = 6.3 Hz, C3); ^{31}P NMR (121 MHz, $CDCl_3$) δ ppm 13.0 (C3'<u>P</u>OCH$_2$CH$_3$). HRMS, required for $C_9H_{18}O_5P$ 237.0892, found 237.0885.

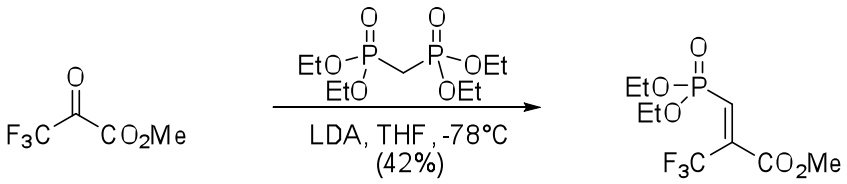
(*Z*)-isomer: Rf (60% ethyl acetate/hexane): 0.10; ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 5.72 (dq, J = 14.7, 1.4 Hz, 1H), 4.10-3.98 (m, 4H, C3'POC<u>H</u>$_2$CH$_3$), 3.76 (s, 3H, CO$_2$<u>Me</u>), 2.04 (app t, J = 1.4 Hz, 3H, H3), 1.26 (t, J = 7.1 Hz, 6H, C3'POCH$_2$C<u>H</u>$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 168.3 (d, J = 9.4 Hz, C1), 149.6 (d, J = 3.1 Hz, C2), 120.7 (d, J = 188.6 Hz, C3), 62.2 (d, J = 5.6 Hz, C3'PO<u>C</u>H$_2$CH$_3$), 52.6 (s, CO$_2$<u>Me</u>), 22.7 (d, J = 20.5 Hz, C3), 16.5 (d, J = 6.5 Hz, C3'POCH$_2$<u>C</u>H$_3$); ^{31}P NMR (121 MHz, $CDCl_3$) δ ppm 13.8 (C3'<u>P</u>OCH$_2$CH$_3$).



To a solution of (*E*)-vinylphosphonate (116 mg, 0.492 mmol) in dichloromethane (3.8 mL) under nitrogen was added trimethylsilyl bromide (390 μL, 2.95 mmol), and the mixture was stirred overnight then evaporated. The residue was dissolved in 10% w/v aqueous potassium hydroxide (2 mL), stirred for five minutes then extracted with dichloromethane (3x 2 mL) and the organic phases discarded. The aqueous phase was passed through a short column of Dowex-50X8 H^+-form (10 x 80 mm), eluted with water (30 mL), neutralised with cyclohexylamine and lyophilised to give a white powder (329 mg). Analysis of this powder by ^{1}H and ^{13}C NMR showed only the presence of the desired product **4**, and ^{31}P NMR quantitation (relative to an internal potassium dihydrogen phosphate standard) showed the powder was 48% pure (69% yield), the balance presumably being cyclohexylammonium salts (consistent with the ^{1}H NMR analysis) and/or waters of hydration.

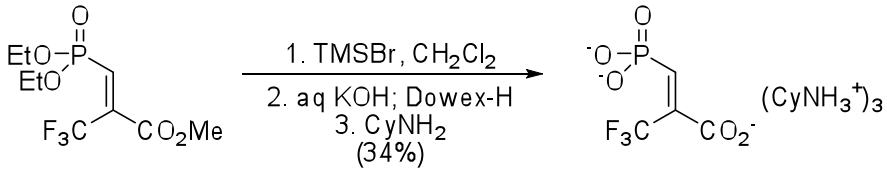
^{1}H NMR (500 MHz, D_2O) δ ppm 6.19 (dd, J = 14.6, 1.2 Hz, 1H, H3'), 3.10-2.88 ($CyNH_3^+$), 1.87 (dd, J = 2.9, 1.2 Hz, 3H, H3), 1.85-1.78 (m, $CyNH_3^+$), 1.67-1.59 (m, $CyNH_3^+$), 1.48 (dm, J = 12.8 Hz, $CyNH_3^+$), 1.24-1.09 (m, $CyNH_3^+$), 1.01 (ddm, J = 22.2, 10.1 Hz, $CyNH_3^+$); ^{13}C NMR (75 MHz, D_2O) δ ppm 178.4 (d, J = 22.5 Hz, C1), 144.7 (d, J = 4.2 Hz, C2), 131.2 (d, J = 165.9 Hz, C3'), 50.5 ($CyNH_3^+$), 30.5 ($CyNH_3^+$), 24.5 ($CyNH_3^+$), 24.0 ($CyNH_3^+$), 16.4 (d, J = 6.5 Hz, C3); ^{31}P NMR (121 MHz, D_2O, ^{1}H-decoupled) δ ppm 9.8 (C3'P); ^{31}P NMR (121 MHz, D_2O, ^{1}H-coupled) δ ppm 9.8 (d, J = 14.9 Hz, C3'PO_3^{2-}). HRMS (ESI, negative ion, 20% AcOH matrix) required for $C_4H_6O_5P^-$: 164.9953; found: 164.9948.

Vinyl phosphonate 5



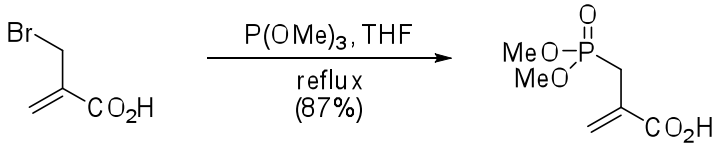
A stirred solution of diisopropylamine (340 μL, 2.41 mmol) in tetrahydrofuran (20 mL) was cooled to -78°C under nitrogen, and a 1.6 M solution of *n*-butyllithium in hexanes (1.38 mL, 2.21 mmol) was added. After 30 minutes, tetraethyl methylene bisphosphonate (620 μL, 2.49 mmol) was added, the mixture was stirred for 20 minutes before methyl 3,3,3-trifluoropyruvate (200 μL, 1.96 mmol) was added. The mixture was stirred for ten minutes, then brought to 0°C and stirred for 2.5 hours. The reaction was quenched with saturated aqueous potassium dihydrogen phosphate (5 mL), and the tetrahydrofuran removed on a rotary evaporator. The residue was partitioned between dichloromethane (20 mL) and water (10 mL), the aqueous phase was separated and extracted with further dichloromethane (10 mL). The combined organic phases were washed with 10% w/v sodium hydroxide (2x 10 mL), 1.2 M hydrochloric acid (10 mL) and brine (10 mL). The organic phase was dried and evaporated, flash chromatography (60 % ethyl acetate/hexane) gave the protected phosphonate as an oil (238.3 mg, 42%). Rf (60% ethyl acetate/hexane): 0.32; ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 6.47 (d, J = 9.3 Hz, 1H, H3'), 4.21-4.06 (m, 4H, POC$\underline{H_2}CH_3$), 3.82 (s, 3H, $CO_2\underline{Me}$), 1.28 (app dd, J = 14.9, 7.7 Hz, 6H,

$POCH_2C\underline{H}_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 170.9 (C1), 128.1 (dd, J = 185.0, 5.4 Hz, C3'), 62.9 (d, J = 5.8 Hz, $PO\underline{C}H_2CH_3$), 53.2 (d, J = 0.9 Hz, $CO_2\underline{Me}$), 16.1 (d, J = 6.0 Hz, $POCH_2\underline{C}H_3$); ^{31}P NMR (121 MHz, $CDCl_3$) δ ppm 9.8 (C3'$\underline{P}$).



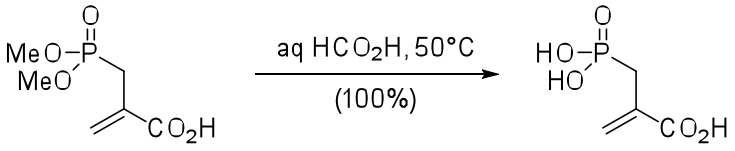
Deprotection of the protected vinyl phosphonate (283 mg, 0.821 mmol), by the method described for **3** gave free phosphonate **7** as a white powder (584 mg). The powder was near pure **7** by ^1H NMR, however the cyclohexylamine signals did not integrate correctly. Quantitation by ^{31}P NMR (relative to an internal potassium dihydrogen phosphate standard) showed the powder was 25% product **5** (34% yield), the balance presumably being cyclohexylammonium salts (consistent with the ^1H NMR analysis) and/or waters of hydration. ^1H NMR (300 MHz, D_2O) δ ppm 6.75 (d, J = 6.2 Hz, H3'), 3.21-2.89 (m, $CyNH_3^+$), 2.02-1.75 (m, $CyNH_3^+$), 1.75-1.59 (m, $CyNH_3^+$), 1.52 (dm, J = 12.2 Hz, $CyNH_3^+$), 1.21 (m, $CyNH_3^+$) ^{13}C NMR (75 MHz, D_2O) δ ppm 142.2 (dd, J = 153.1, 3.1 Hz, C3'), 50.6 ($CyNH_3^+$), 30.5 ($CyNH_3^+$), 24.5 ($CyNH_3^+$), 24.0 ($CyNH_3^+$); ^{31}P NMR (121 MHz, D_2O) δ ppm 4.6 (overlapping dq, J = 7.5, 2.4 Hz, $F_3CCC(H)\underline{P}$). HRMS (ESI, negative ion, 20% AcOH matrix): required for $C_4H_3O_5F_3P$: 218.9670, found 218.9670.

Allylic phosphonate 8



Trimethylphosphite (1.05 mL, 10.2 mmol) was added to a solution of 2-(bromomethyl)acrylic acid (1.60 g, 9.7 mmol) in THF (20 mL) and heated to reflux. After 40 hours, when no starting material was visible by TLC, the solvent was removed *in vacuo* to provide dimethyl 2-(phosphonomethyl)acrylic acid as a pale yellow oil (1.65 g,

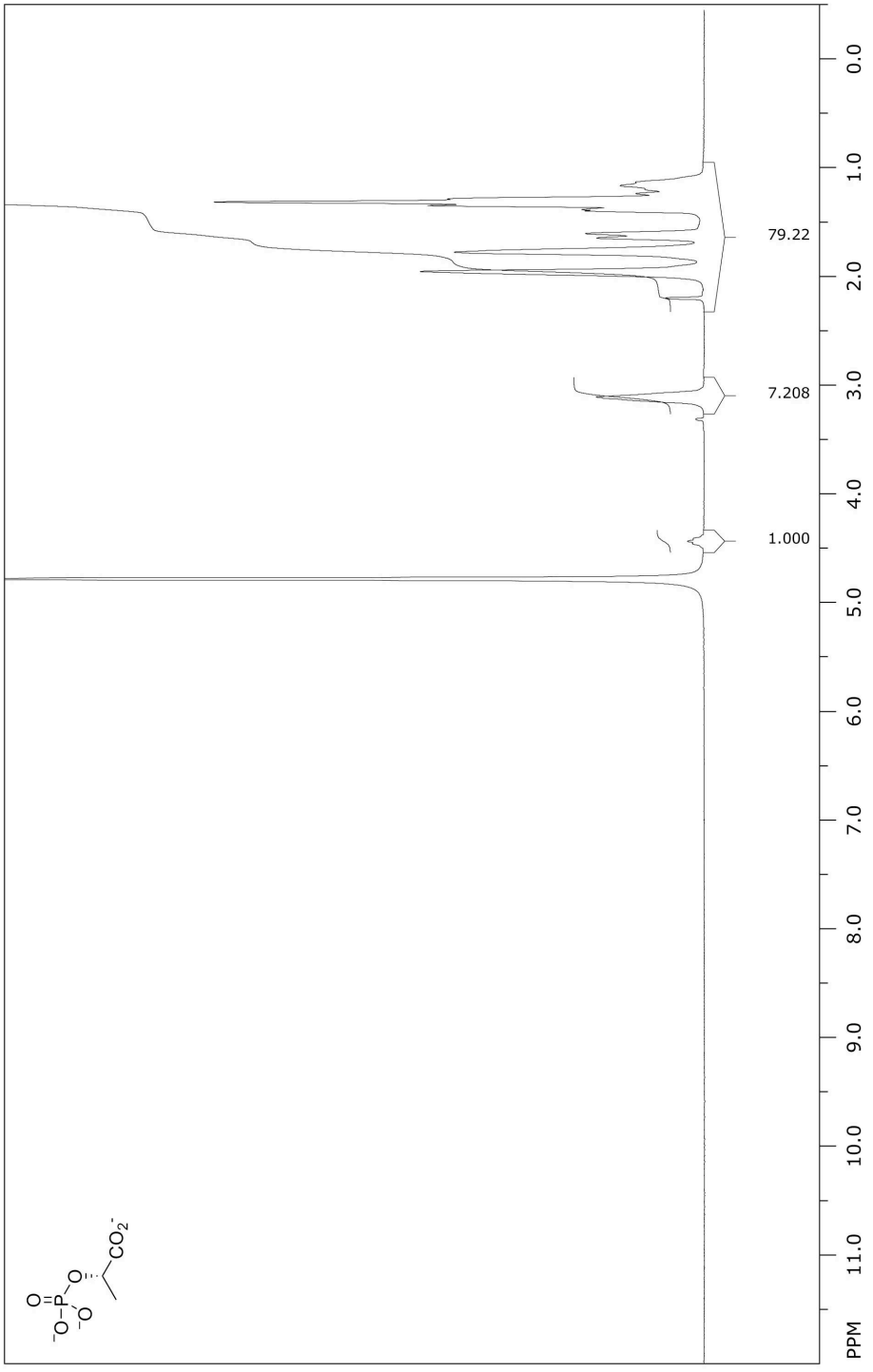
87%). ^{1}H NMR (500 MHz, $CDCl_3$): δ ppm 6.37 (1H, d, J = 6 Hz, H3), 5.83 (1H, d, J = 5.5 Hz, H3'), 3.70 (6H, d, J = 11 Hz, CH_3), 2.94 (2H, d, J = 22 Hz, C<u>H</u>2P).



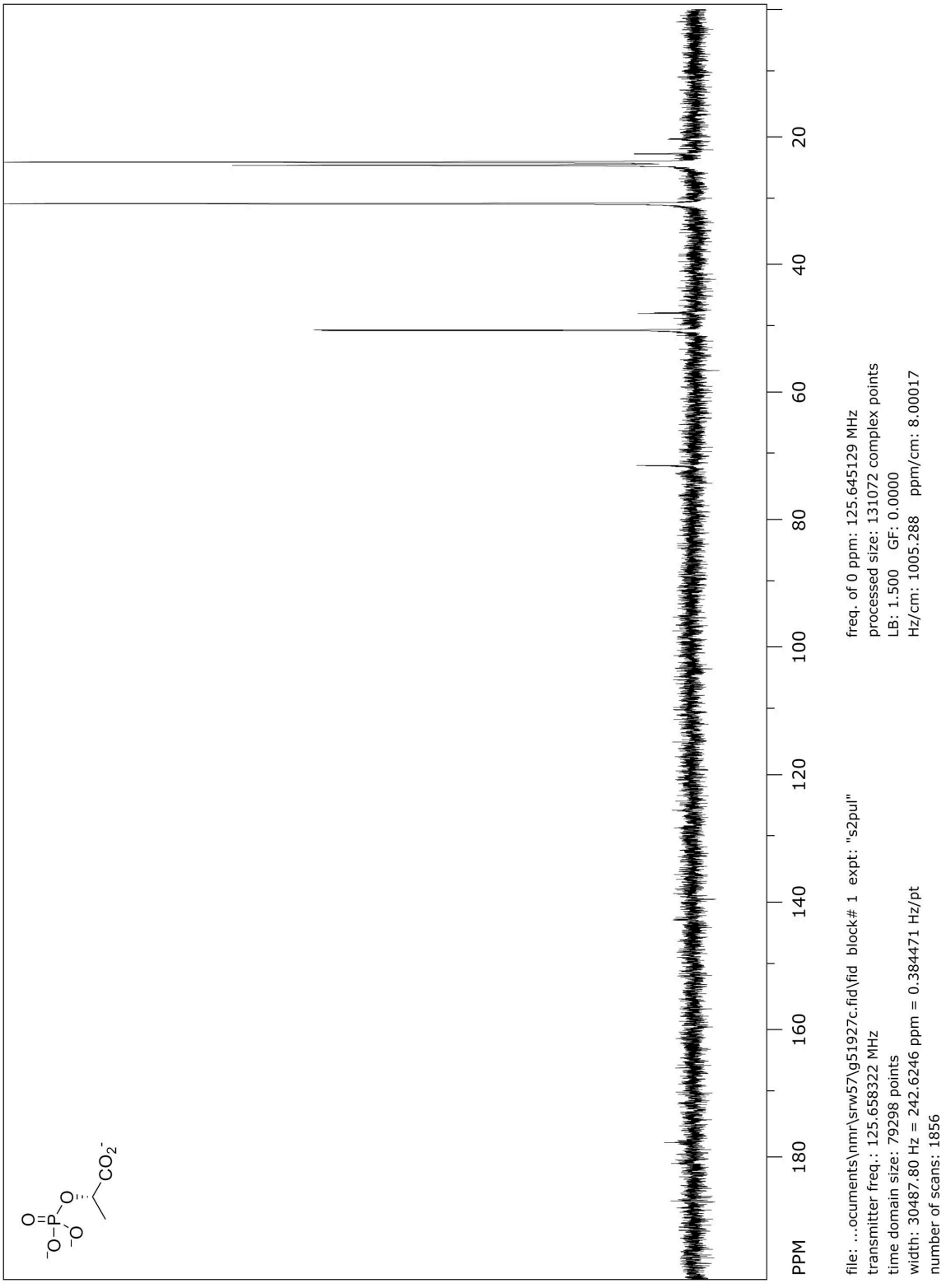
Dimethyl 2-(phosphonomethyl)acrylic acid (1.65 g, 8.5 mmol) was dissolved in 100 mM formic acid (20 mL) and heated at 50 °C for 72 hours. The solution was frozen with liquid nitrogen and lyophilised to provide the allylic phosphonate 8 as a white solid (1.41 g, 100%). ^{1}H NMR (500 MHz, D_2O): δ ppm 6.25 (1H, d, J = 6 Hz, CHH), 5.80 (1H, d, J = 6 Hz, CHH), 2.80 (2H, d, J = 21.5 Hz, CH_2). ^{13}C NMR (100 MHz, D_2O) δ ppm 172.5 (d, J = 3.7 Hz, C1), 134.5 (d, J = 10.8 Hz, C2), 132.6 (d, J = 10.2 Hz, C3), 32.5 (d, J = 133 Hz, <u>C</u>H_2P). ^{31}P{^{1}H} NMR (121 MHz, D_2O) δ ppm 23.3. HRMS (ESI, negative ion, 20% AcOH matrix) required for $C_4H_6O_5P^-$: 164.9953; found: 164.9957.

NMR spectra of final compounds

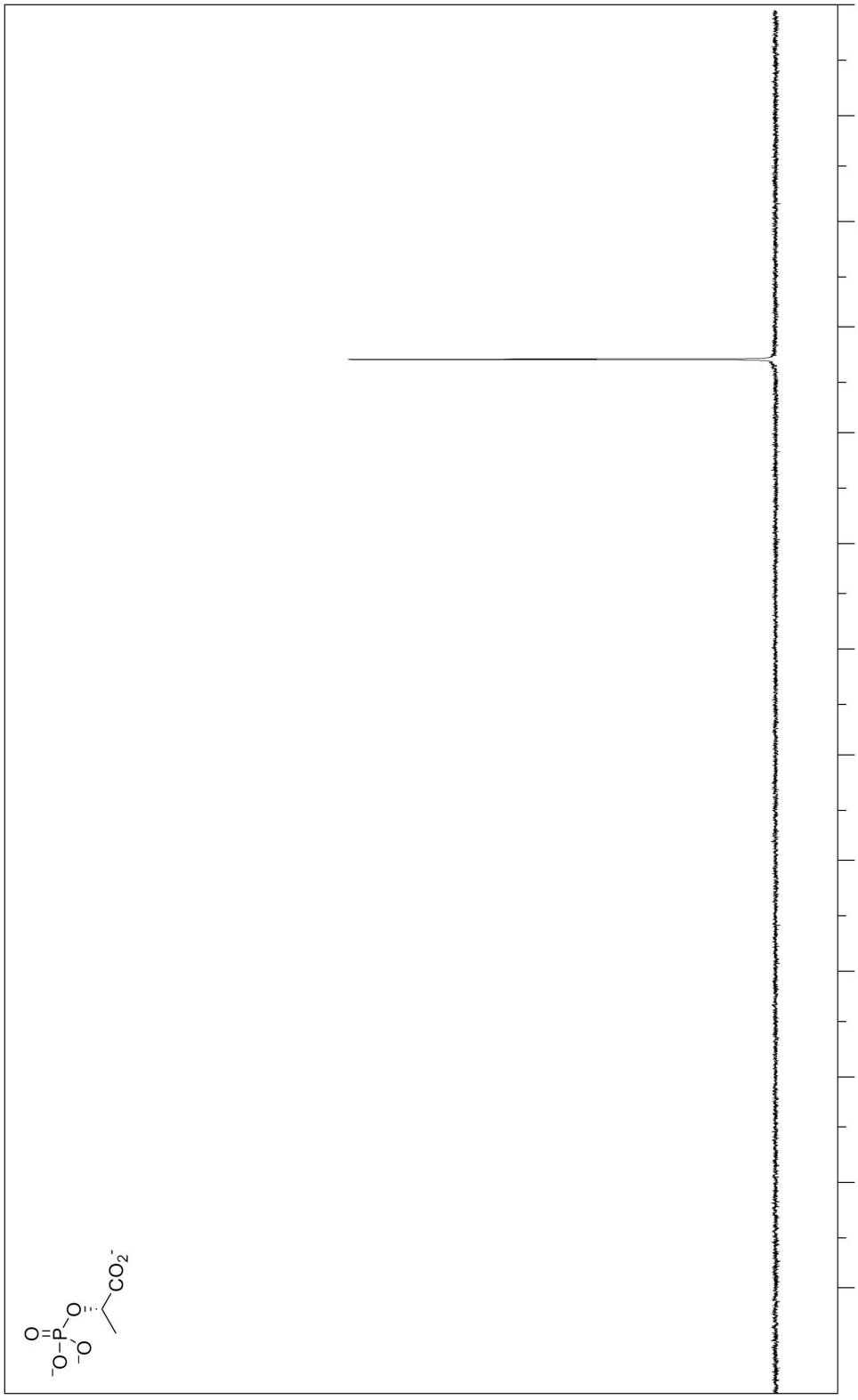
(*S*)-phospholactate **6**, cyclohexylammonium salt - ^{1}H NMR



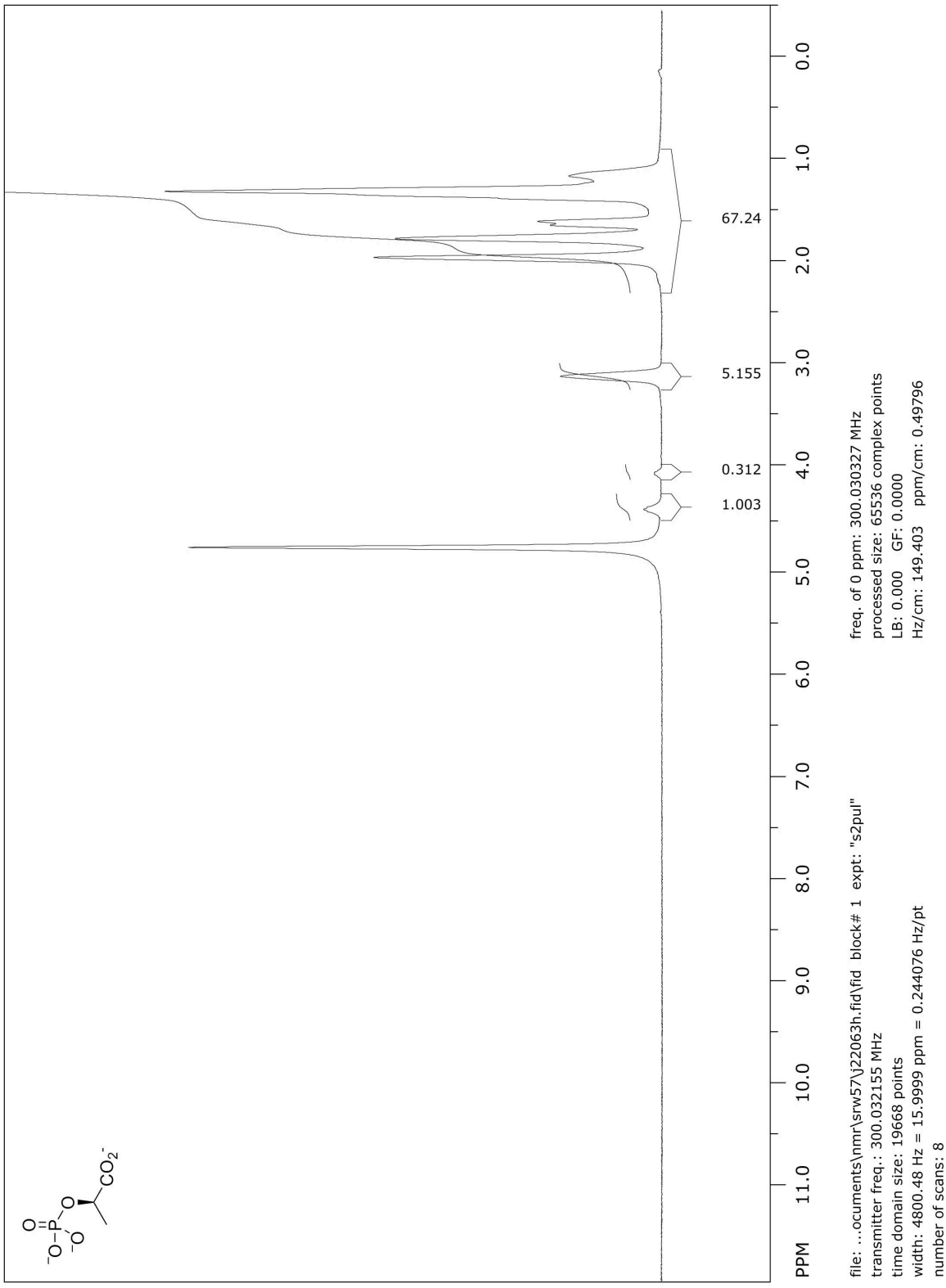
(*S*)-phospholactate **6**, cyclohexylammonium salt – ^{13}C NMR



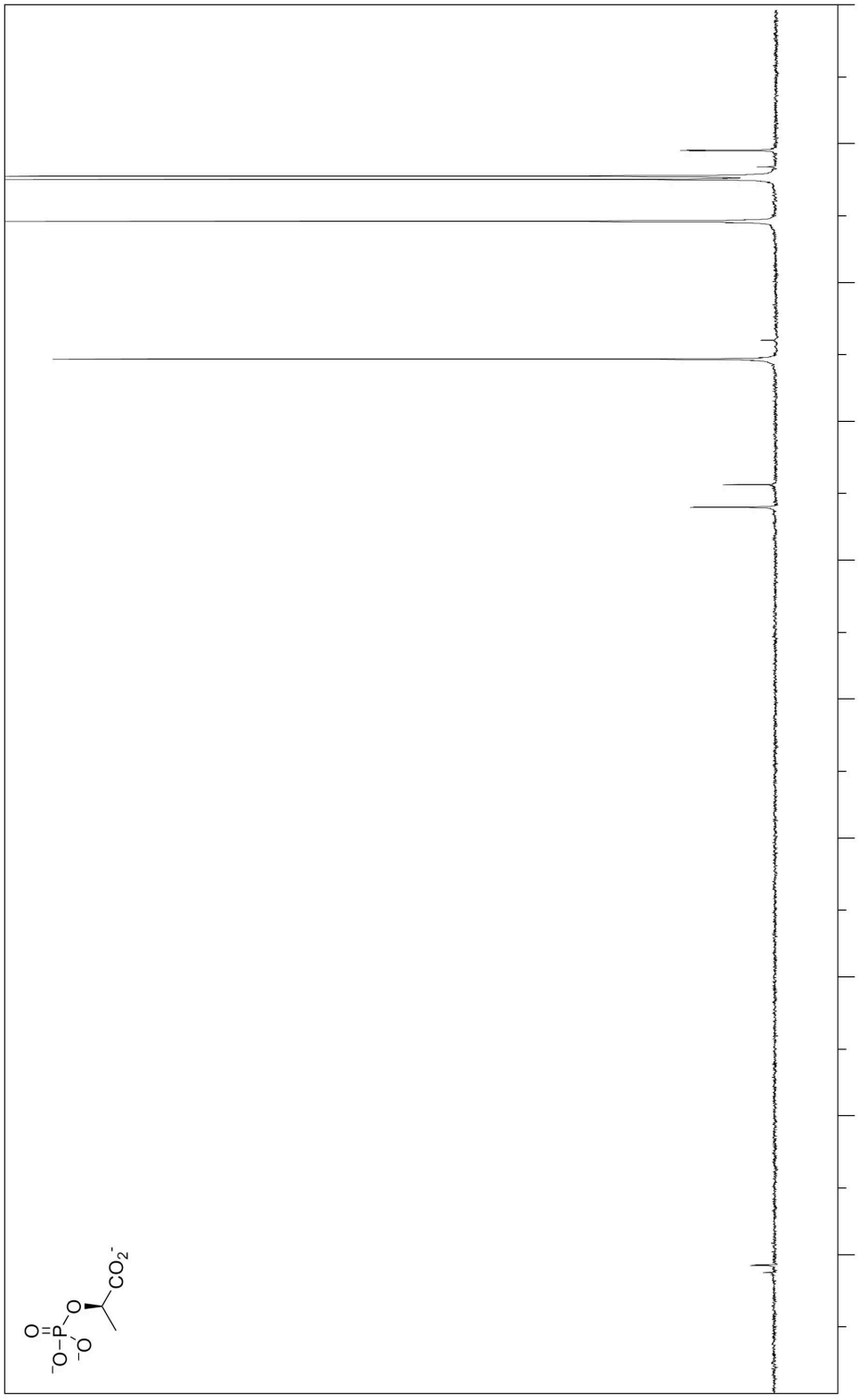
(*S*)-phospholactate **6**, cyclohexylammonium salt – $^{31}P\{^{1}H\}$ NMR



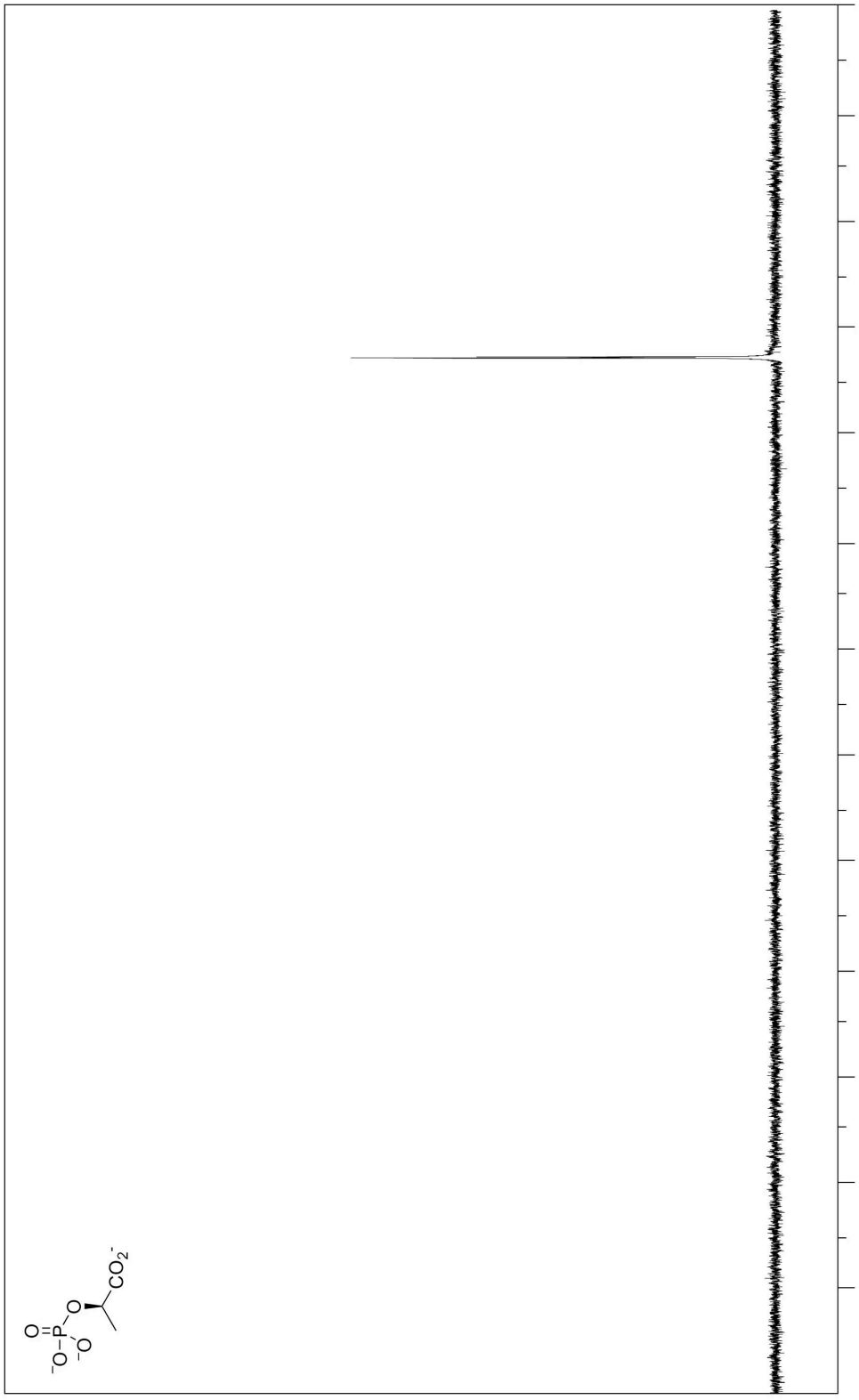
(*R*)-phospholactate **6**, cyclohexylammonium salt - ^{1}H NMR



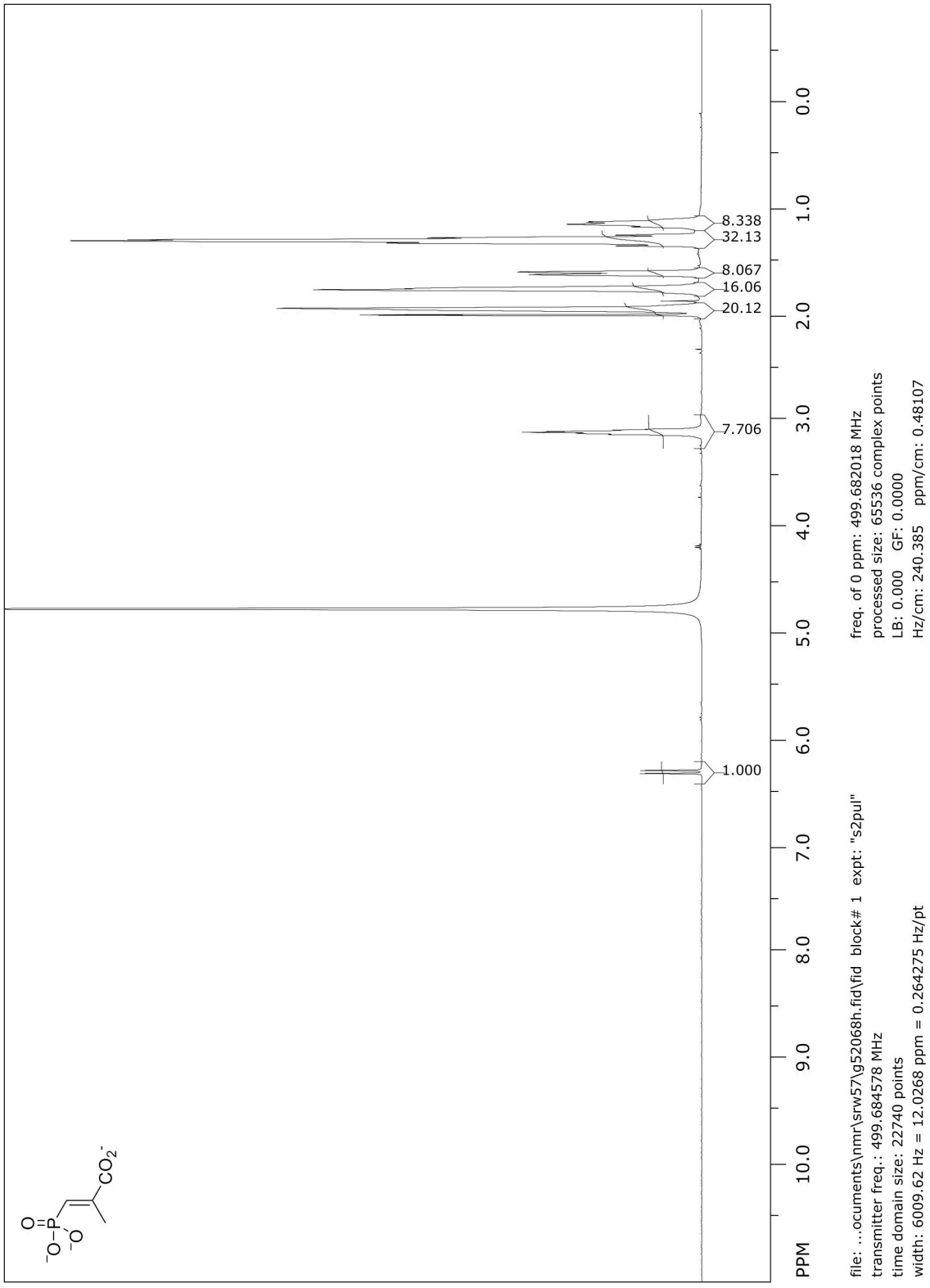
(*R*)-phospholactate **6**, cyclohexylammonium salt – ^{13}C NMR



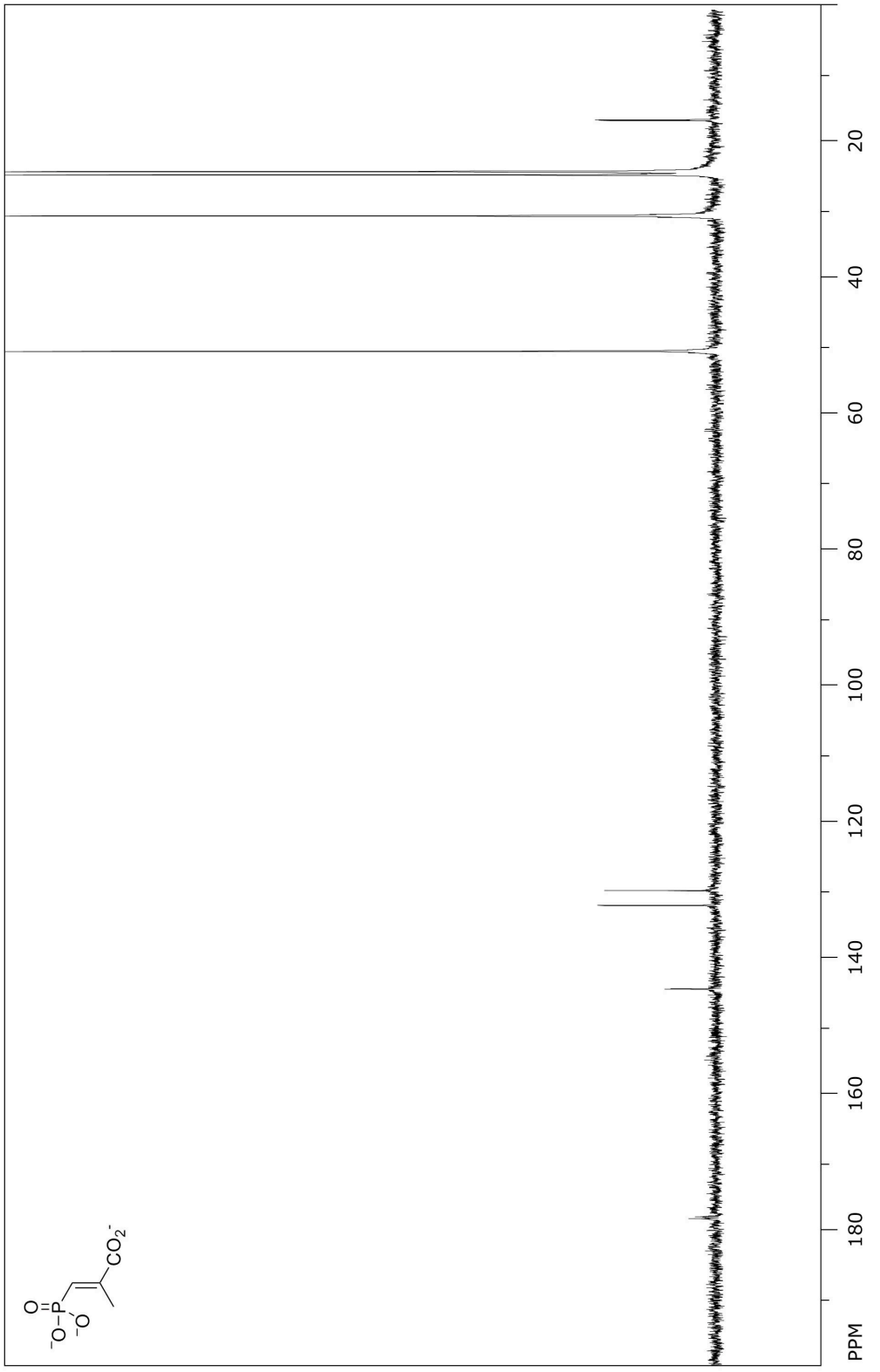
(*R*)-phospholactate **6**, cyclohexylammonium salt – $^{31}P\{^{1}H\}$ NMR



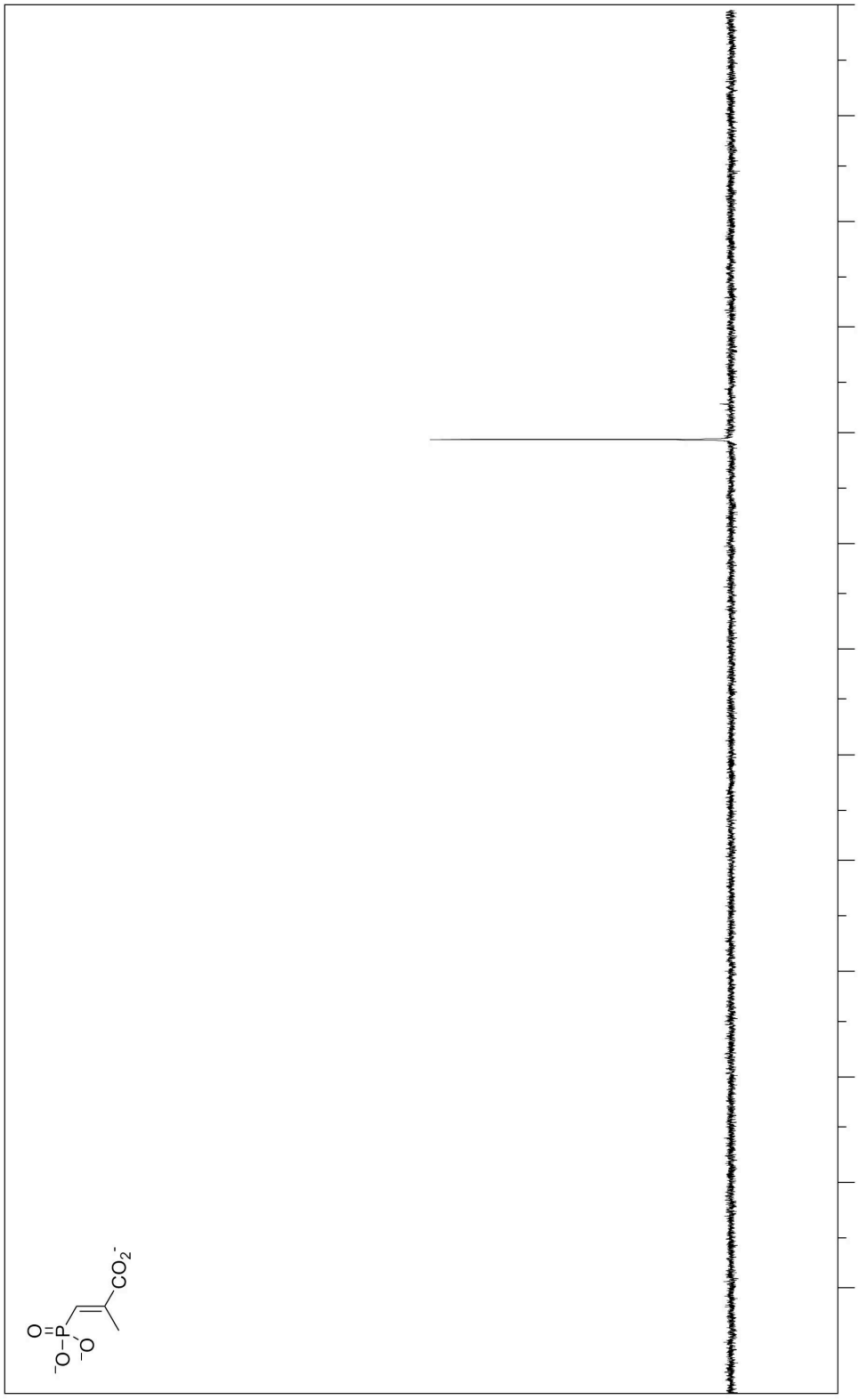
Vinyl phosphonate **4**, cyclohexylammonium salt - ^{1}H NMR



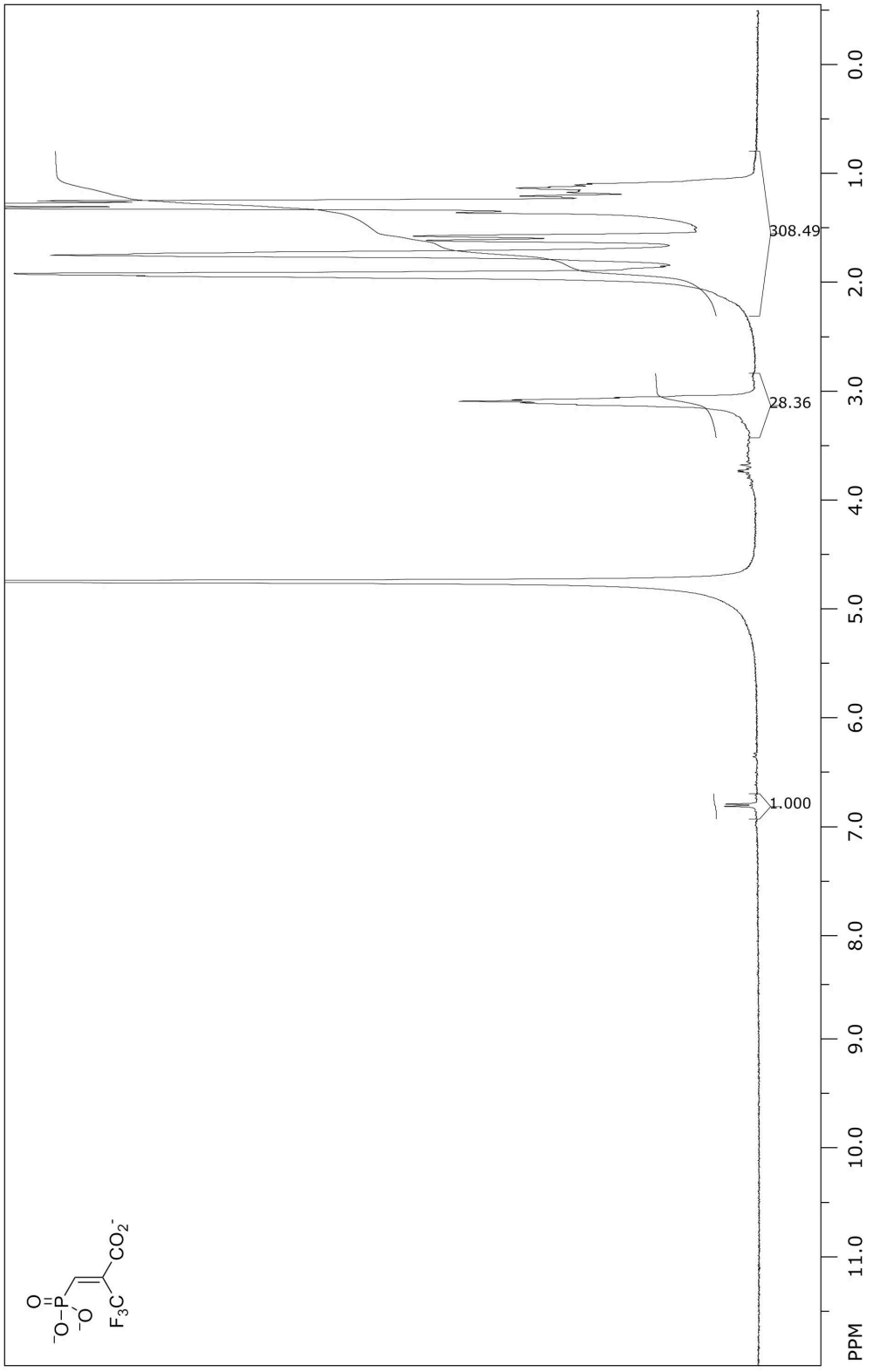
Vinyl phosphonate **4**, cyclohexylammonium salt – ^{13}C NMR



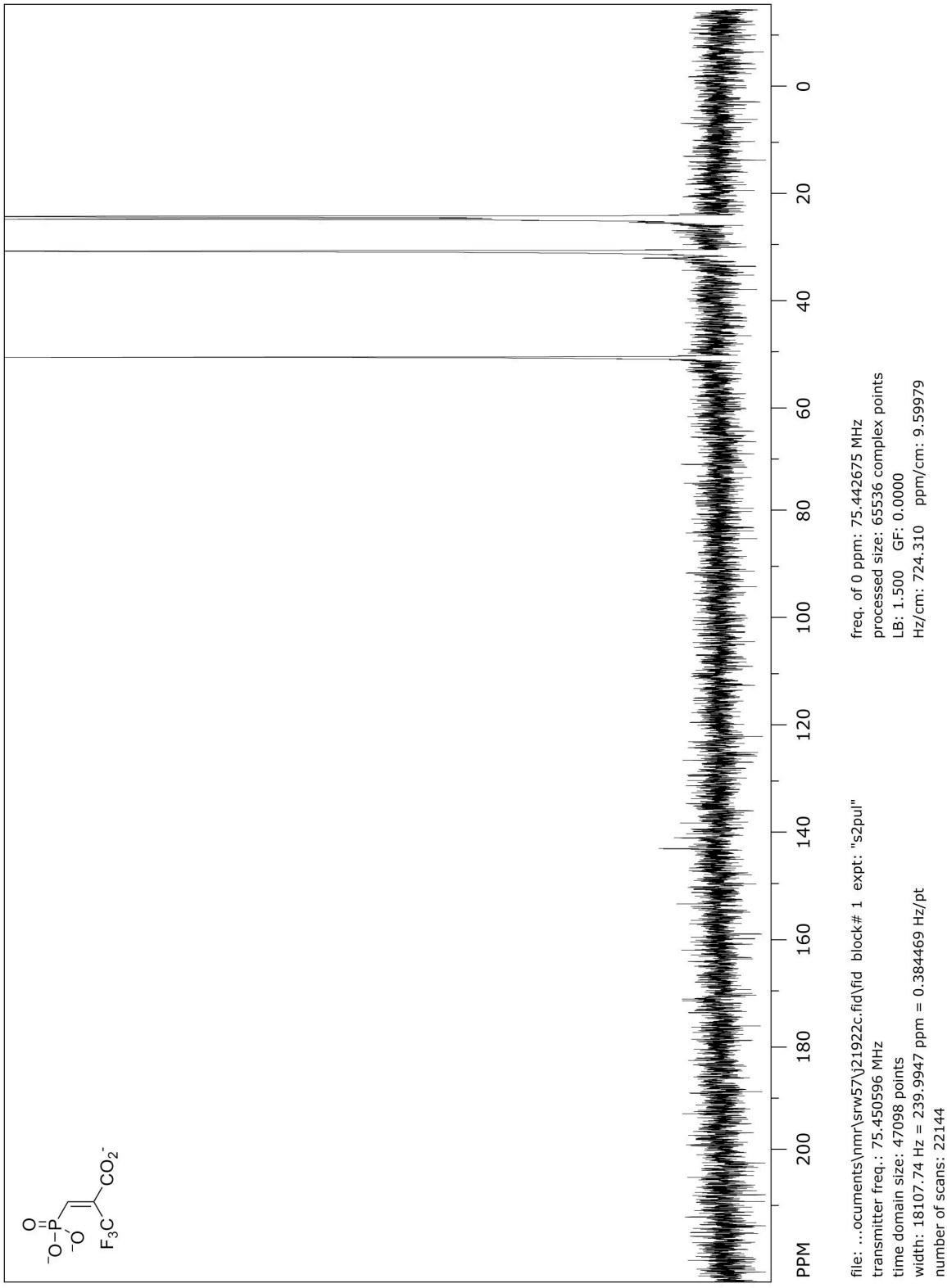
Vinyl phosphonate **4**, cyclohexylammonium salt – $^{31}P\{^{1}H\}$ NMR



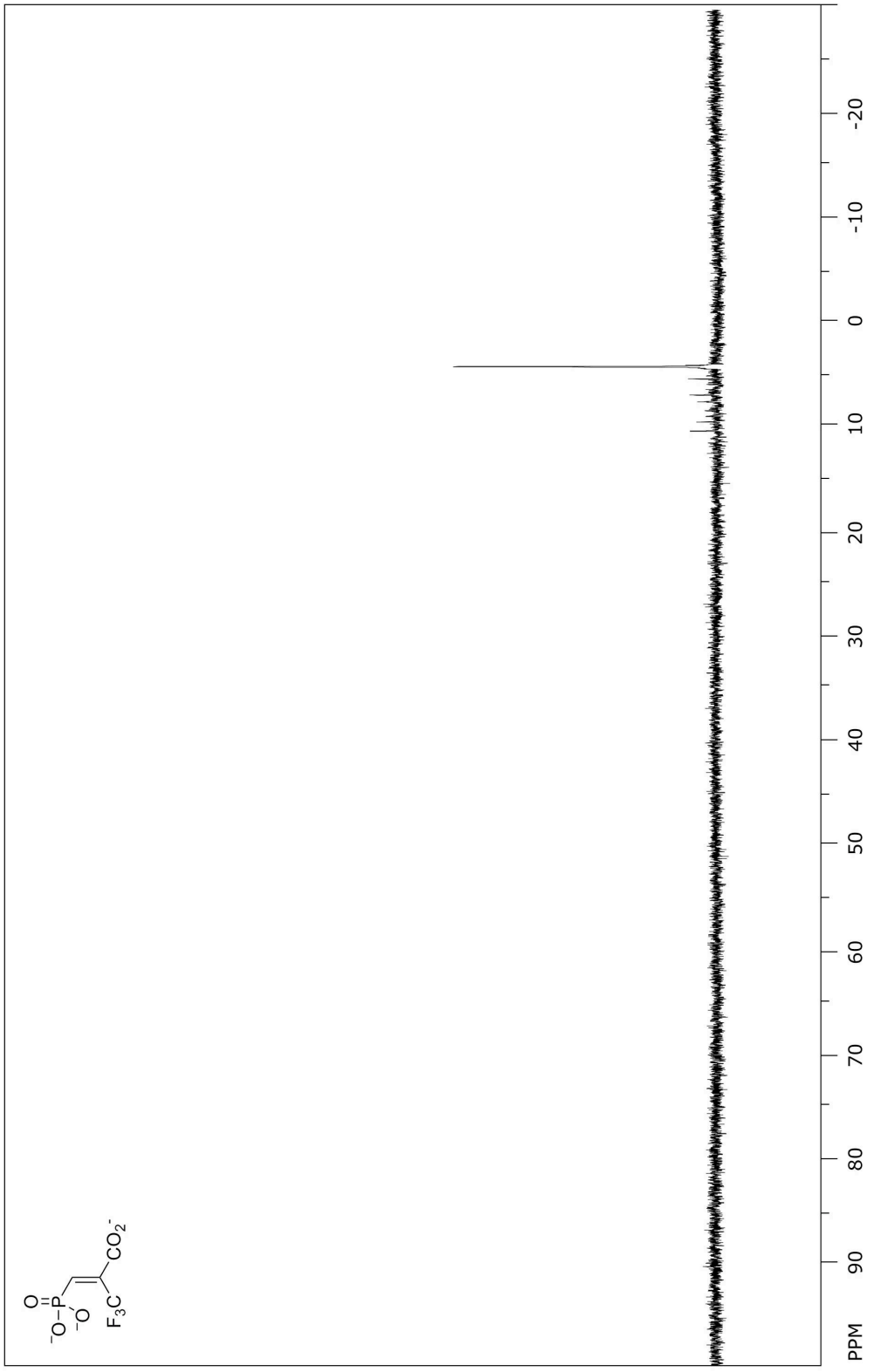
Trifluorovinyl phosphonate **5**, cyclohexylammonium salt - ^{1}H NMR



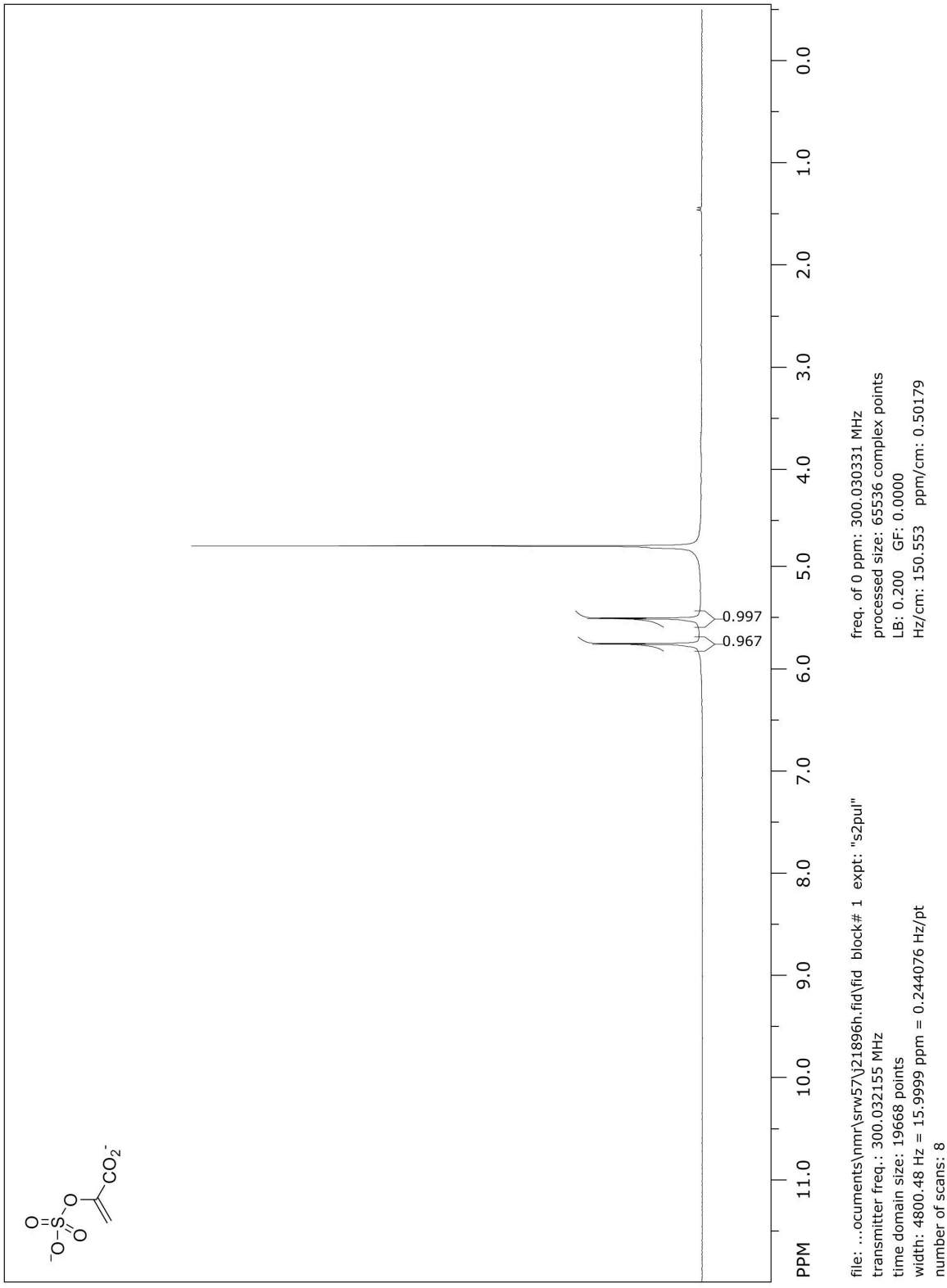
Trifluorovinyl phosphonate **5**, cyclohexylammonium salt – ^{13}C NMR



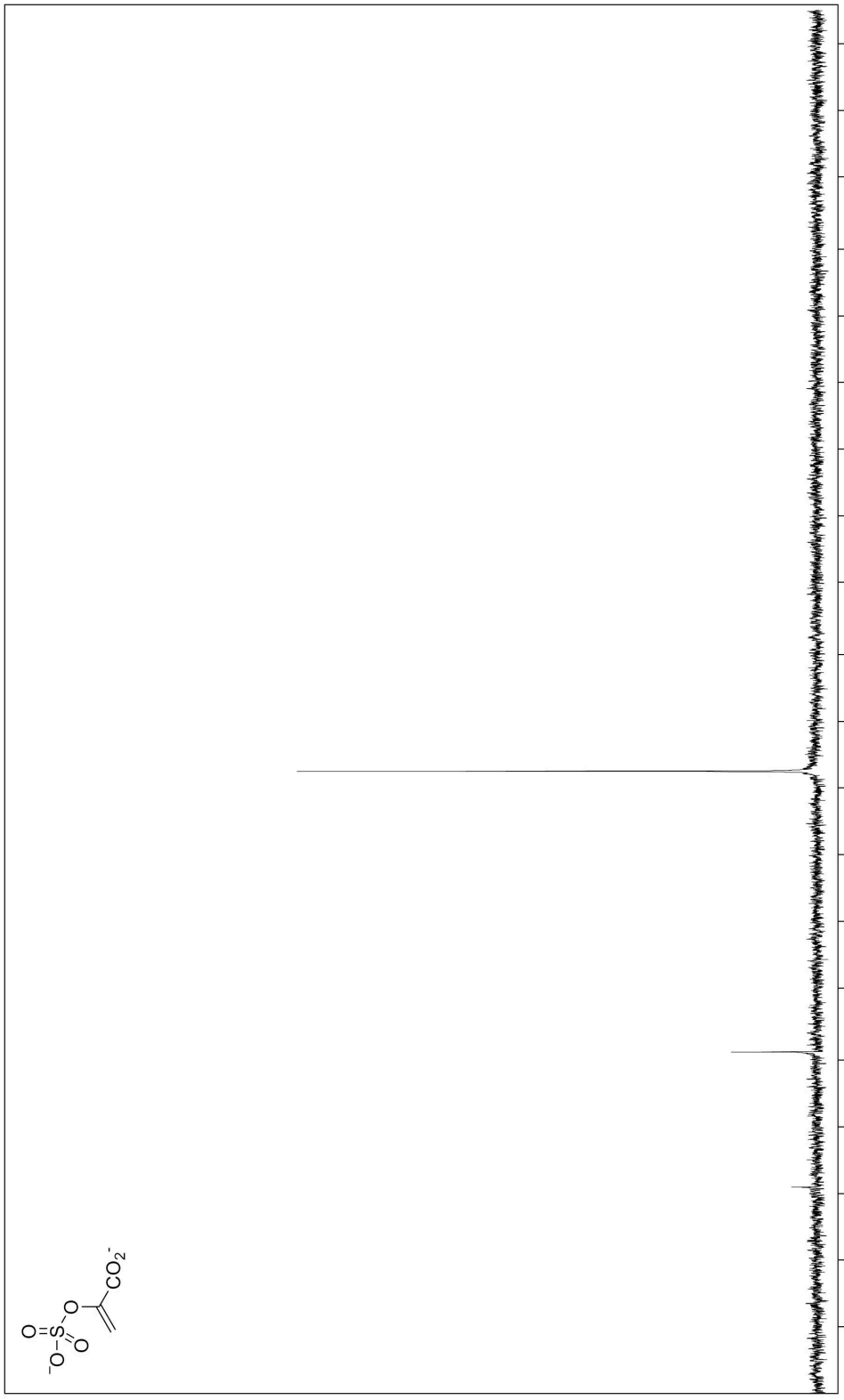
Trifluorovinyl phosphonate **5**, cyclohexylammonium salt – $^{31}P\{^{1}H\}$ NMR



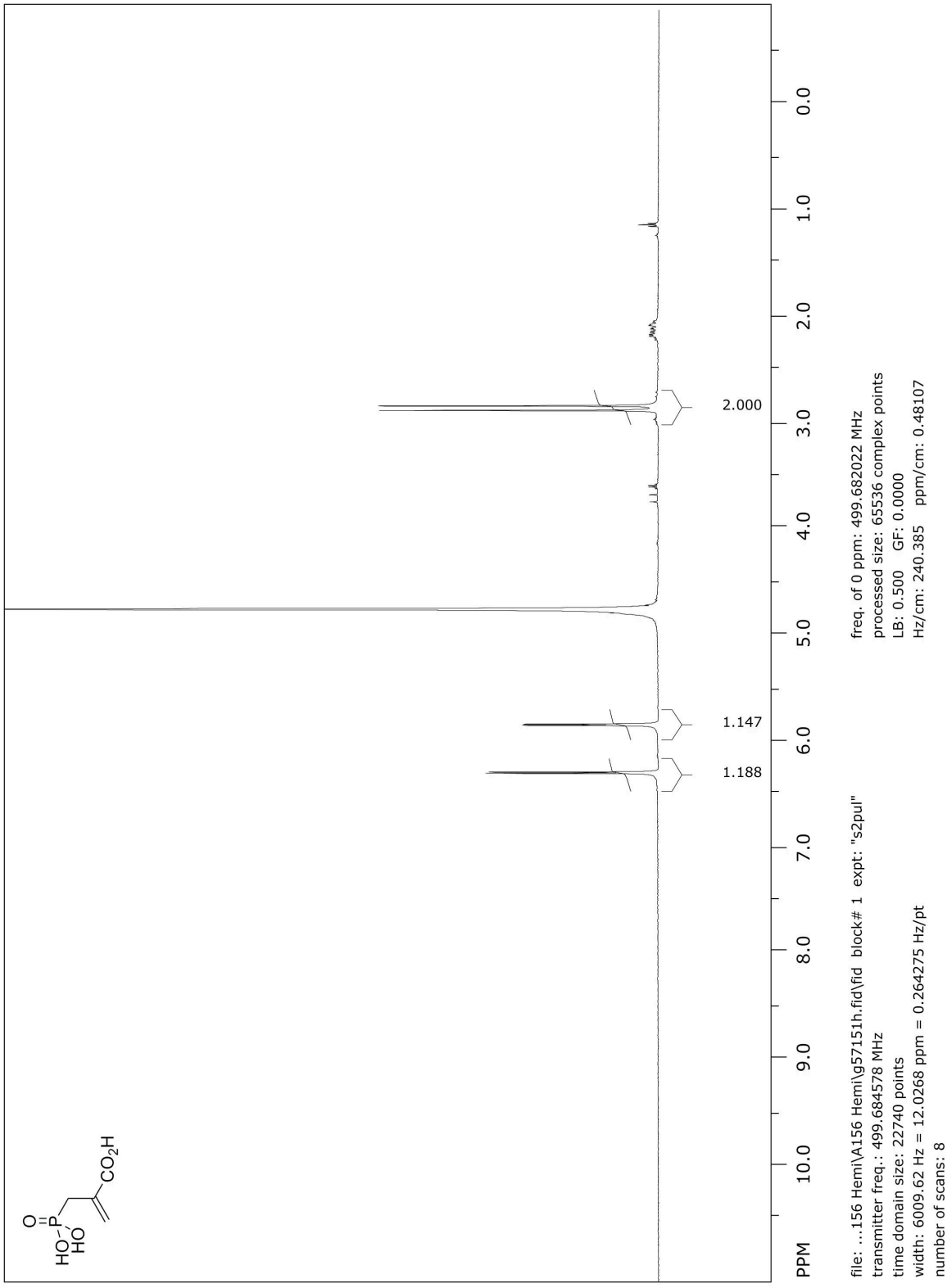
Sulfoenolpyruvate **7**, ^{1}H NMR



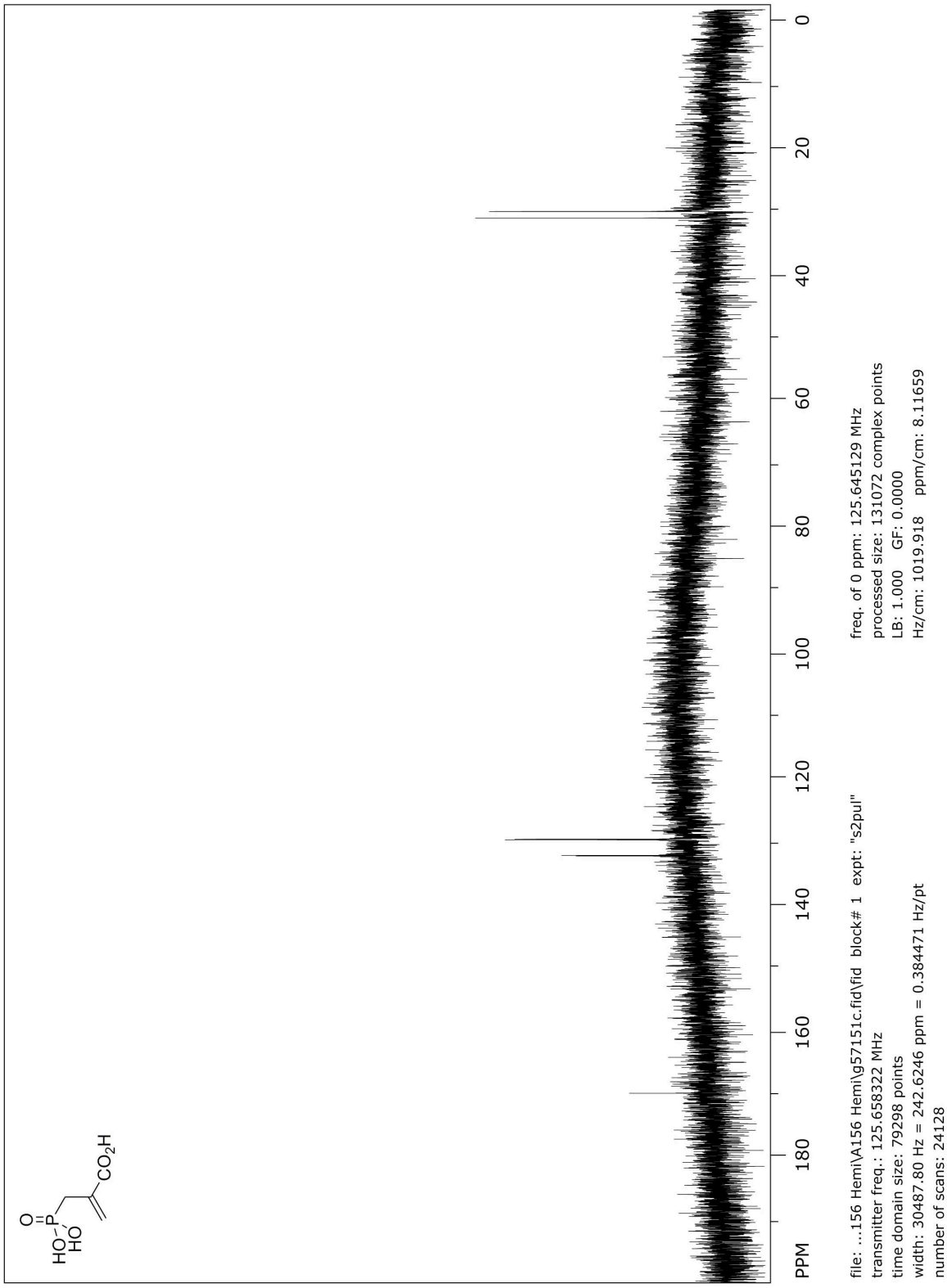
Sulfoenolpyruvate **7**, ^{13}C NMR



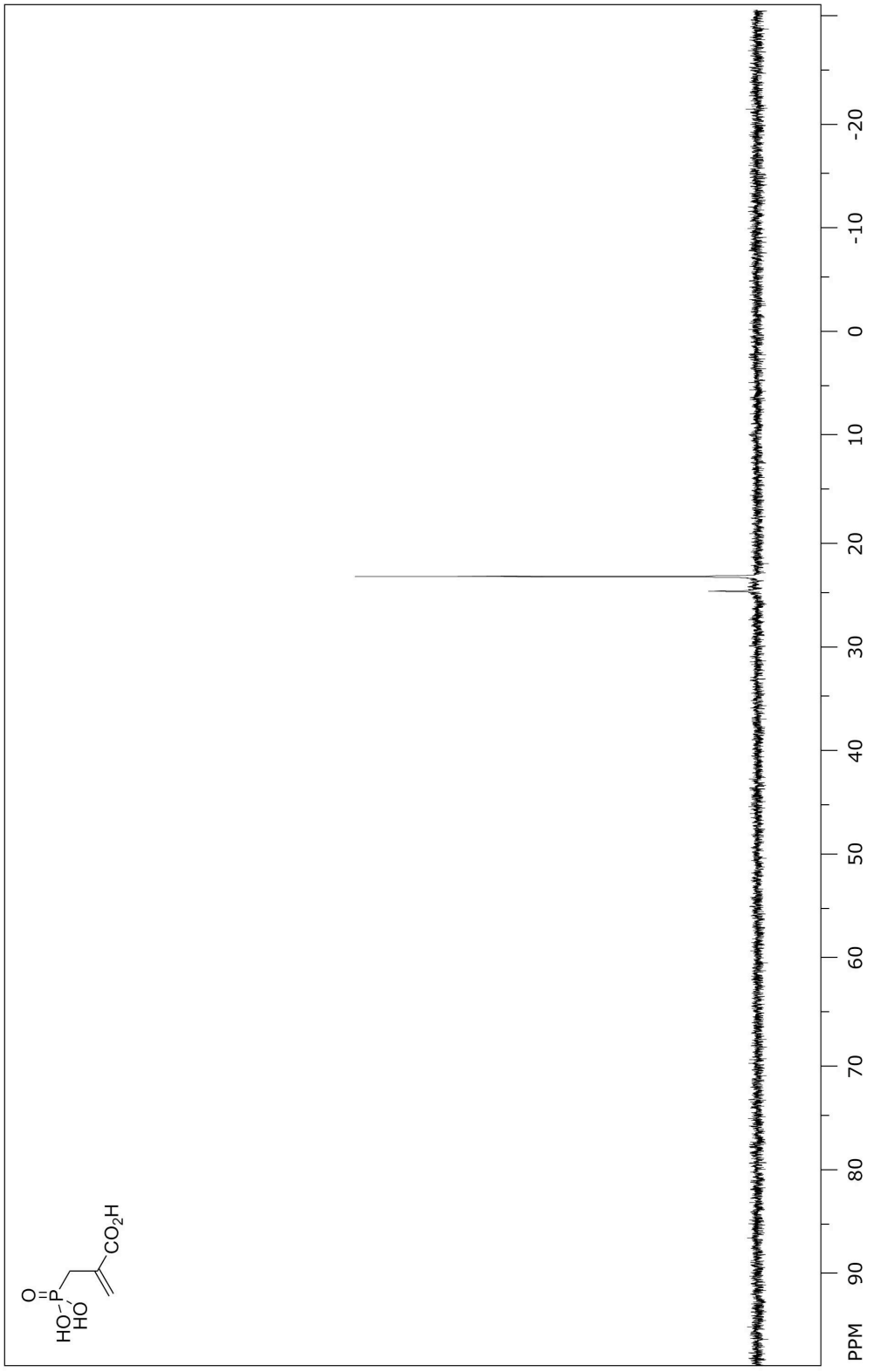
Allylic phosphonate **8** - ^{1}H NMR



Allylic phosphonate **8** – ^{13}C NMR

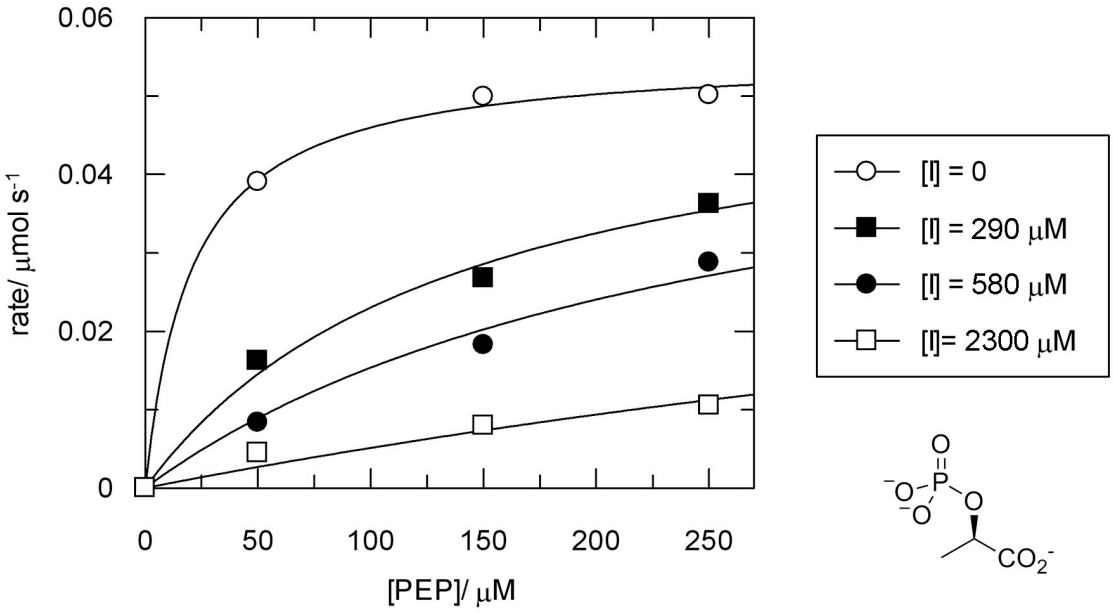


Allylic phosphonate **8** – $^{31}P\{^{1}H\}$ NMR

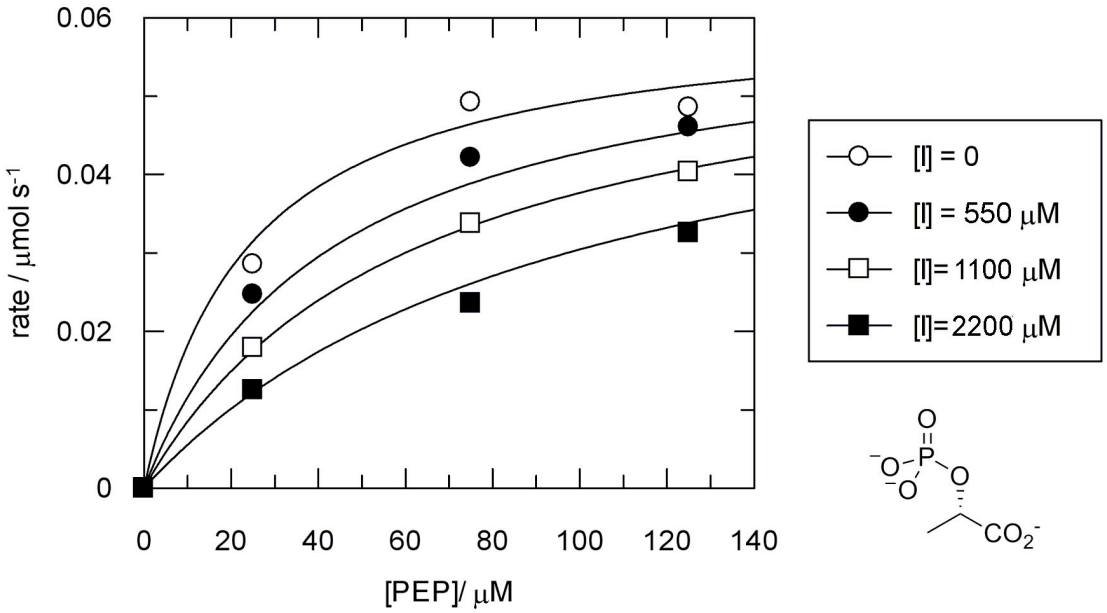


Inhibition data

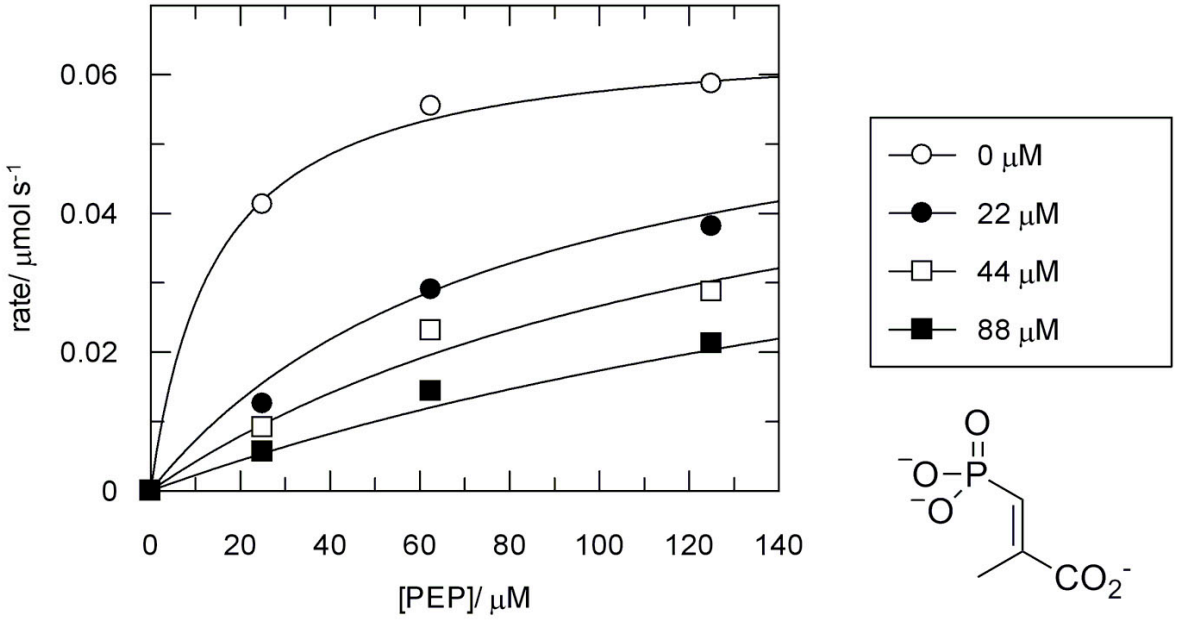
(*R*)-phospholactate 6



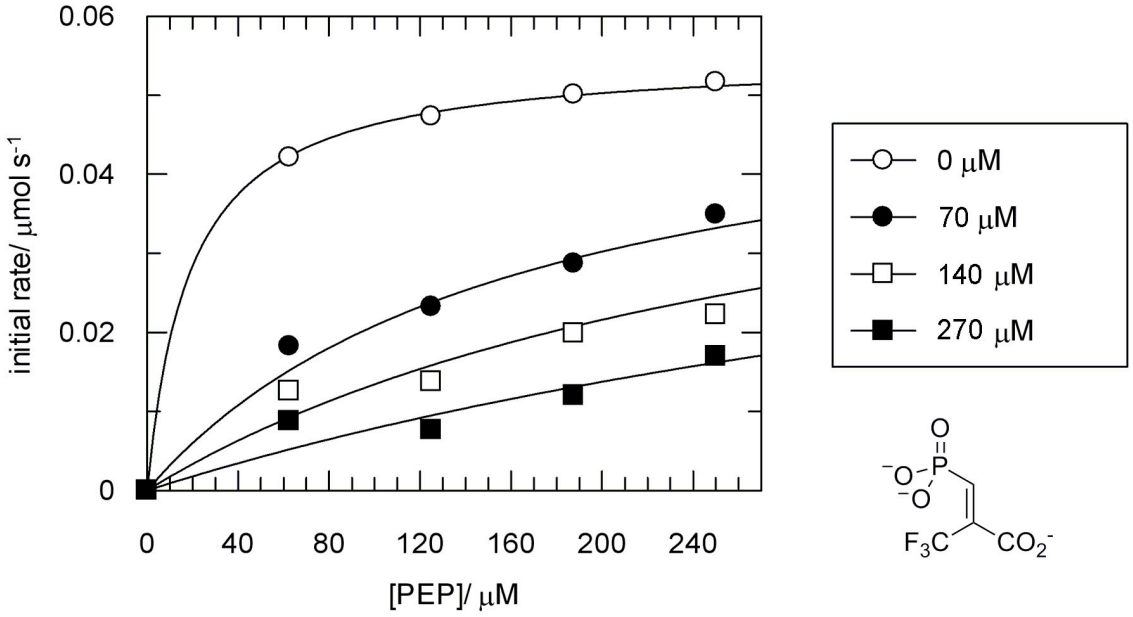
(*S*)-phospholactate 6



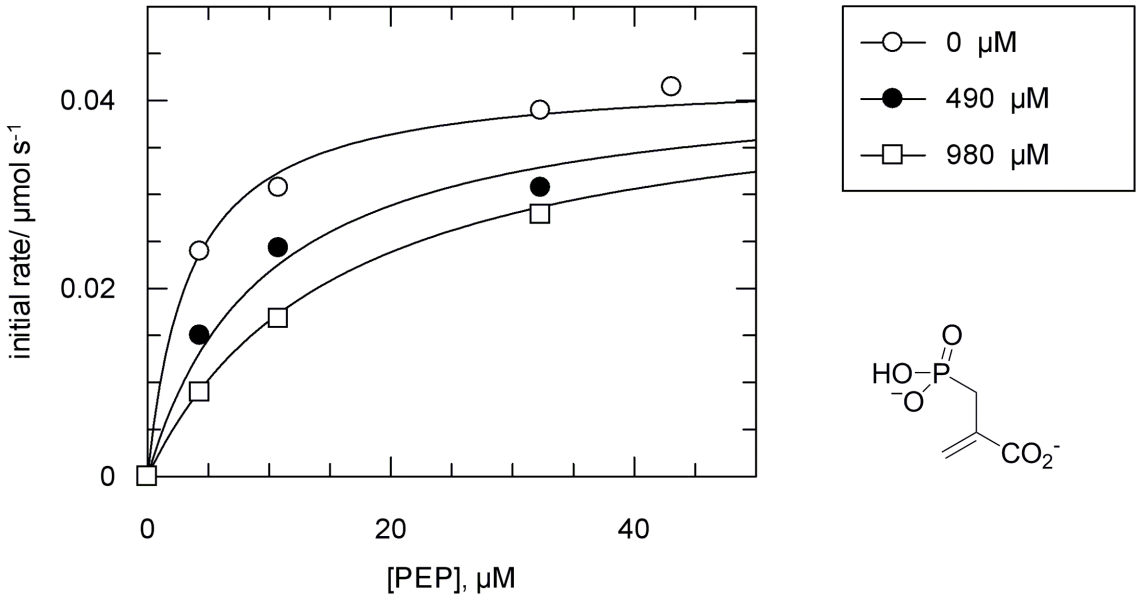
Vinyl phosphonate 4



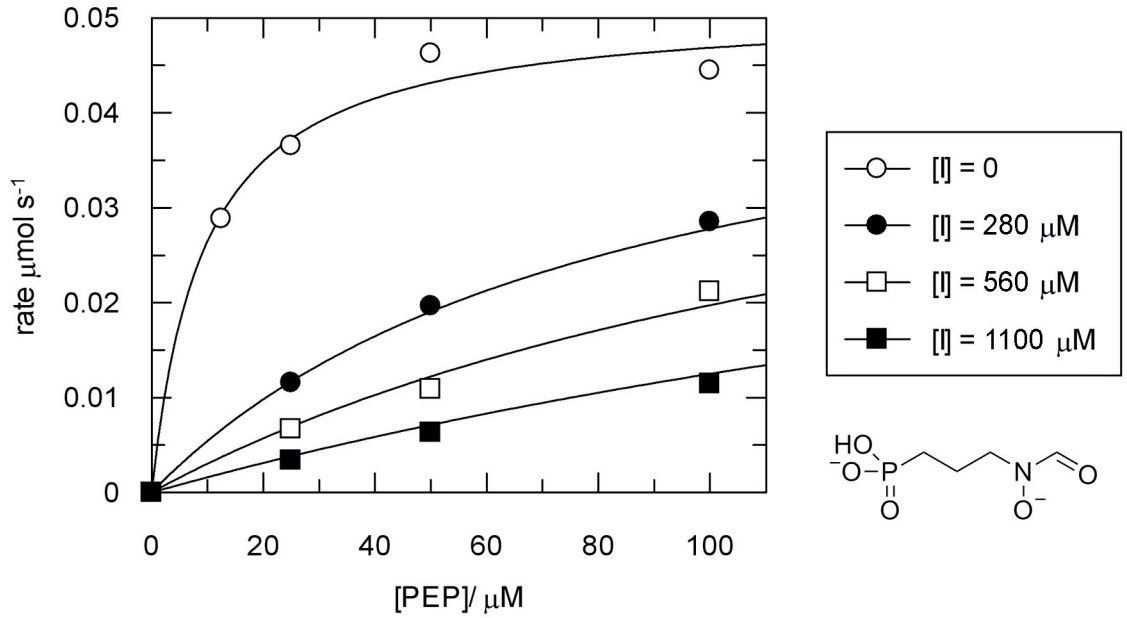
Trifluorovinyl phosphonate 5



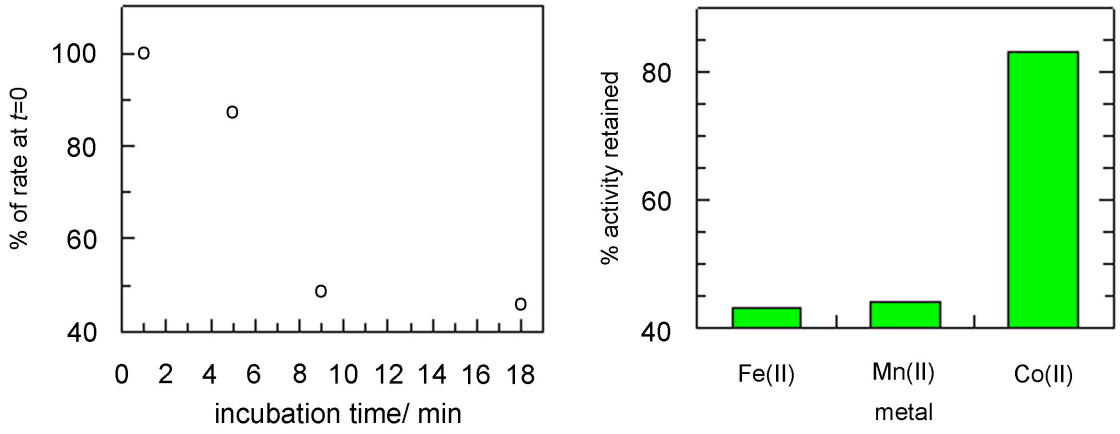
Allylic phosphonate 8



Fosmidomycin – with respect to [PEP]



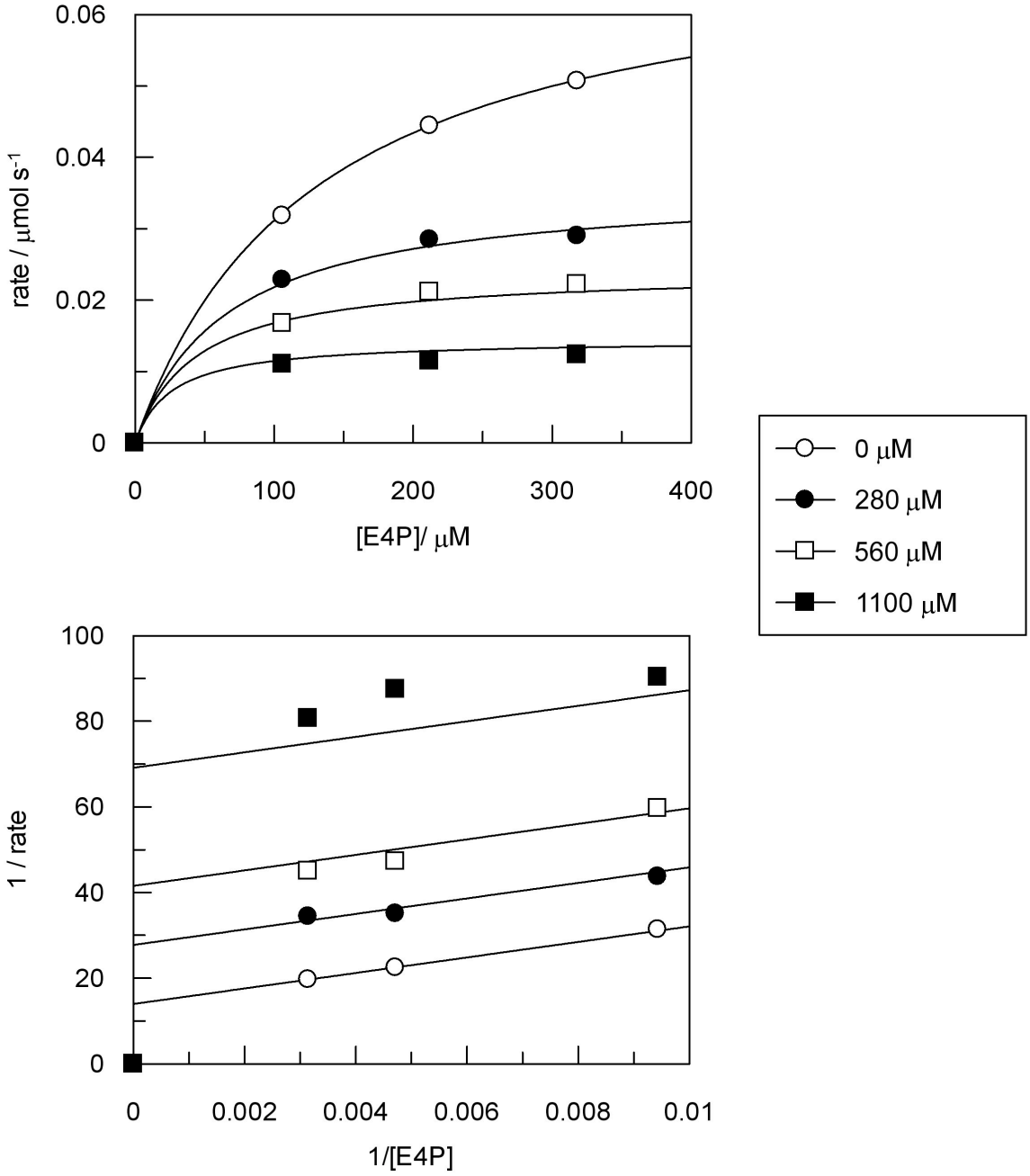
Fosmidomycin, time and metal dependence



Time dependence: Fosmidomycin (280 μmol) and *E. coli* DAH7P synthase (20 μg) were incubated at 0°C in 50 mM BTP, pH 6.8 (30 μL), and at the time indicated, a portion (2 μL) was removed and used to initiate a cuvette containing PEP (50 μM), E4P (200 μM) and manganese(II) sulfate (100 μM) in 1mL BTP buffer (50 mM, pH 6.8), and the initial rates taken.

Metal dependence: Cuvettes of PEP (50 μM), E4P (200 μM) and the appropriate metal salt ($FeSO_4$, $MnSO_4$, $CoCl_2$; 100 μM) in 50 mM BTP, pH 6.8 were initiated with *E. coli* DAH7P synthase (2 μg), and the initial rates taken. The measurement was repeated in the presence of 280 μM fosmidomycin. Reported values are the percentage of activity retained in the presence of fosmidomycin, and are the mean value of duplicate experiments.

Fosmidomycin – with respect to [E4P]



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1. C. Chai and W. L. F. Armarego, *Purification of Laboratory Chemicals. 5th Edition.*, Butterworth-Heinemann, 2003.
2. A. F. Ferris, *J. Org. Chem.*, 1955, **20**, 780-787.
3. K. N. Welch, *J. Chem. Soc.*, 1930, 257-261.
4. E. J. Parker, E. M. M. Bulloch, G. B. Jameson and C. Abell, *Biochemistry*, 2001, **40**, 14821-14828.