On the prebiotic potential of reduced oxidation state phosphorus. The H-phosphinate-pyruvate system.

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Electronic Supplementary Information

ESI.1 General.

All reactions were performed in de-ionised water (Purite Select Purewater 300 system) unless otherwise stated. NMR spectroscopy was carried out using a Bruker Avance DPX300 or DPX500 spectrometer, all NMR spectra were recorded at probe temperature of 27°C (300K) unless noted otherwise. X-Ray crystallography was performed on a Bruker Apex 8 diffractometer, IR spectra obtained using a Nicolet 6700 FTIR or a Perkin Elmer Spectrum One FTIR, microanalyses (C,H and N) obtained using a Thermo Electron Flash EA 1112 series analyzer, sodium determined using a Perkin Elmer Aanalyst 100 AA spectrometer in emission mode and mass spectrometry using a Bruker Daltronics microTOF electrospray mass spectrometer. pH Measurements made on a pre-calibrated Schochem pH meter. All chemical yields reported are un-optimised.

ESI.2 Reaction of Sodium Phosphinate with Pyruvic acid. *Synthesis of 2-hydroxyphosphinoylpropionic acid, sodium salt* ***1****. (mono-insertion pyruvate* $C_3H_6O_5PNa$*)*

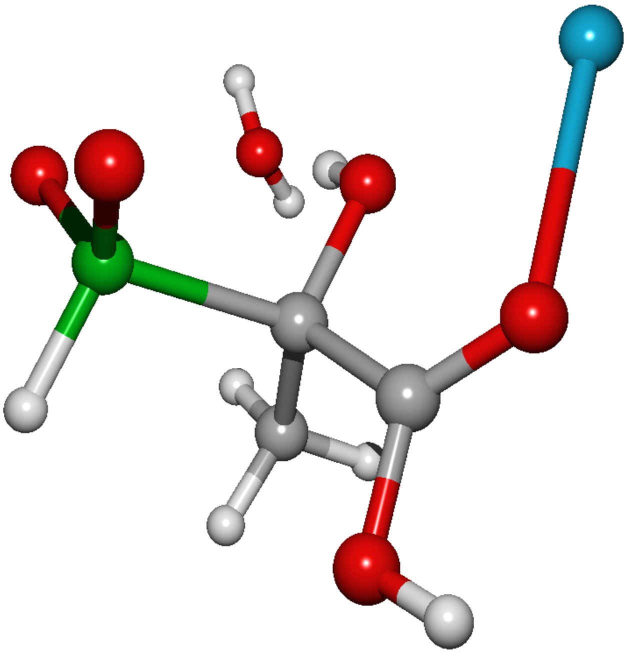
In a round bottomed flask fitted with a reflux condenser a solution of pyruvic acid (3.1 g, 35 mmol) in water (50 cm^3) was heated with NaH_2PO_2 (3.1 g, 35 mmol) for 24 hrs at 70°C under a dinitrogen atmosphere. ^{31}P-NMR spectroscopy shows the reaction mixture to contain 55% (**1**) with the remainder mostly starting material. The water is removed on a rotary evaporator to leave a gum which was dissolved in methanol (50 cm^3). On standing a white solid precipitates and attaches to the flask. This was washed with diethylether (3 x 25 cm^3) and recrystallised from water (5 cm^3) to afford **1-Na** (yield 0.62 g, 9%) ^{1}H-NMR (300 MHz, D_2O) δ (ppm) 6.72 (d, J = 540 Hz, 1H, PH), 1.43 (d, J = 15 Hz, 3H, CH_3). ^{13}C{^{1}H}-NMR (75MHz, D_2O) δ (ppm) 176.5 (C=O), 75.68 (d, J = 96 Hz, C_q), 19.68 (d, J = 4 Hz, CH_3). ^{31}P-NMR (121 MHz, D_2O) δ 27.65 (dq, ^1J = 535 Hz, ^3J = 15 Hz). HRMS (ES, negative ion) calculated for $C_3H_6O_5P$ 152.9958, found 152.9962. IR (KBr, cm^{-1}) 1720 (C=O), 2357 (P-H), 1178 (P=O). Found: C, 18.57; H, 4.16; Na, 11.85. $C_3H_6O_5PNa.H_2O$ requires C, 18.75; H, 4.05; Na, 12.10.

Crystallographic data (excluding structure factors) for (**1**) have been deposited with the *Cambridge Crystallographic Data Centre* as deposition No. CCDC760816. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 (1223) 336033; email: deposit@ccdc.cam.ac.uk

Single crystal X-ray diffraction analysis of $C_3H_8NaO_6P$ (1)

Formula weight	194.05	
Size	0.5 x 0.07 x 0.07 mm	
Crystal morphology	Colourless flat plate	
Temperature	123(2) K	
Wavelength	0.71073 Å [Mo-K_α]	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 6.0112(12) Å	α = 90°
	b = 9.5047(19) Å	β = 93.49(3)°
	c = 12.665(3) Å	γ = 90°
Volume	722.2(2) Å^3	
Z	4	

Density (calculated)	1.785 Mg/m^3
Absorption coefficient	0.421 mm^{-1}
F(000)	400
Data collection range	$2.68 \leq \theta \leq 27.45°$
Index ranges	$-7 \leq h \leq 7$, $-12 \leq k \leq 12$, $-16 \leq l \leq 16$
Reflections collected	10809
Independent reflections	1653 [R(int) = 0.1109]
Observed reflections	1282 [$I > 2\sigma(I)$]
Absorption correction	multi-scan
Max. and min. transmission	0.9711 and 0.817
Refinement method	Full
Data / restraints / parameters	1653 / 0 / 132
Goodness of fit	1.105
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0397$, $wR_2 = 0.0906$
R indices (all data)	$R_1 = 0.0576$, $wR_2 = 0.0998$
Largest diff. peak and hole	0.411 and -0.605e.Å^{-3}



ESI.3 Reaction of H_3PO_2 with pyruvic acid under conditions of varying pH

Five solutions of H-phosphinic acid (50wt% H_2O, 0.38 g, 2.9 mmol of H_3PO_2) and pyruvic acid (0.52 g, 5.9 mmol) in water (7 cm^3) were made up. Solid sodium hydroxide was added in varying quantities to produce solutions differing in pH between pH 2.1 and pH 10.5. The solutions were heated at 70°C under dynamic dinitrogen atmosphere for 48 h. An aliquot (1 cm^3) of each solution was removed and NMR analysis was carried out using a D_2O capillary insert in the NMR tube. The yield of each product was calculated by integration of the signal for that specific product relative to other signals (Table ESI1). The right hand peak of H-phosphinic acid was referenced to δ 4.2 ppm so shifts in signals could be compared (Figure ESI1). A closer look at the region between δ 23 – 35 ppm shows a small quantity of **1** was synthesised, with the observation of a doublet of quartets around δ 28.5 ppm (Figure ESI2) due to the P coupling with the methyl hydrogen nuclei on the adjacent carbon atom.

Sample	pH	Percentage					
		2	**3**	**1**	**Quartets**	H_3PO_2	H_3PO_3
a	2.7	50	5	35	2	0	8
b	4.1	0	0	3	0	95	1
c	6.4	0	0	1	0	98	1
d	9.4	0	0	1	0	98	2
e	10	0	0	1	0	98	1

TableESI1. Percentages of the products formed when H-phosphinic acid and pyruvic acid were reacted in solutions of differing pH.

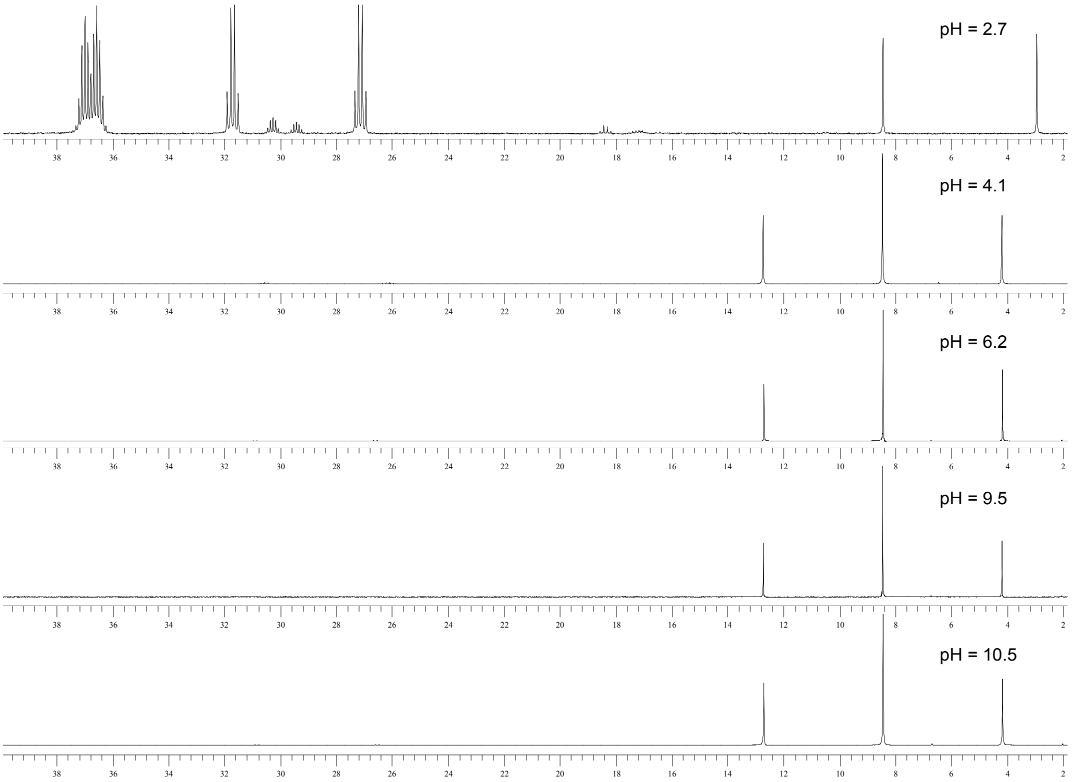


Figure ESI1. ^{31}P NMR (D_2O, 300 K, 121.49 MHz) analysis of the H-phosphinic acid: pyruvic acid system synthesised under different pH concentrations.

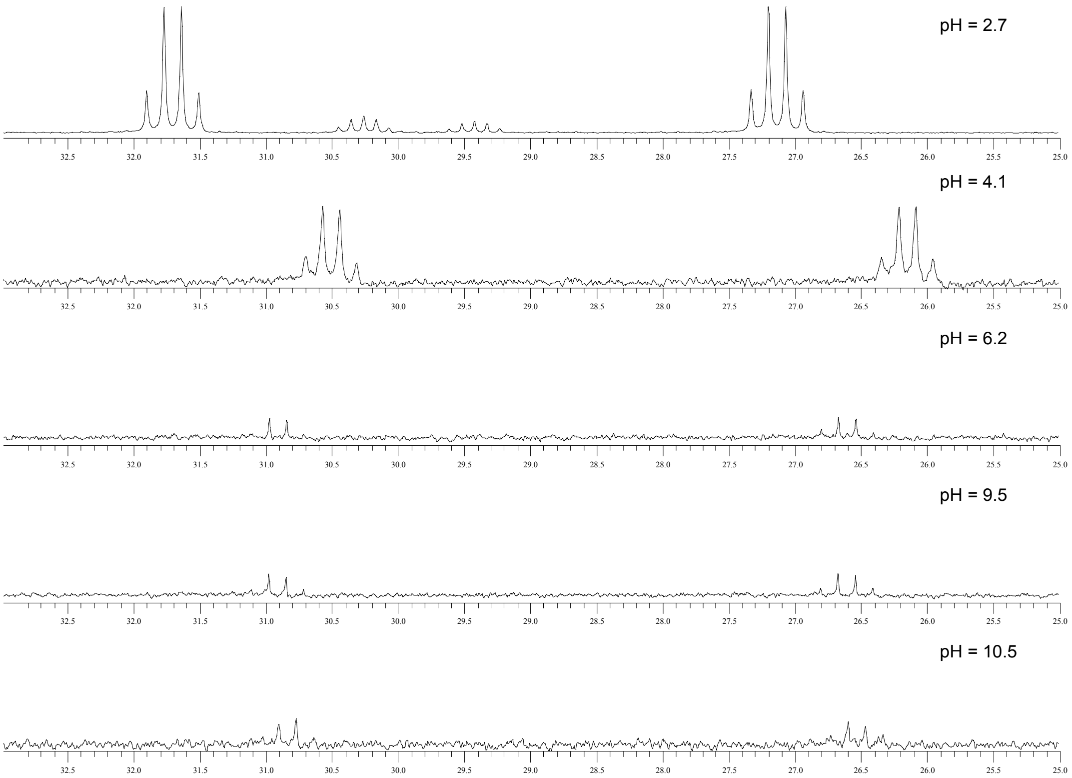


Figure ESI2. Expansion of the region between δ 23 – 35 ppm of the ^{31}P NMR (D_2O, 300 K, 121.49 MHz) analysis of the H-phosphinic acid: pyruvic acid system synthesised under different pH concentrations. The spectrum shows a small quantity of 1 was synthesised but di-insertion inhibited.

ESI.4 Reaction of Sodium Phosphinate with Pyruvic acid. *Synthesis of 2-[(1-carboxy-1-hydroxyethyl)-hydroxy-phosphinoyl]-2-hydroxypropionic acid, di-sodium salt* ***2.*** *(di-insertion pyruvate sodium salt),* $C_6H_9O_8PNa_2$.

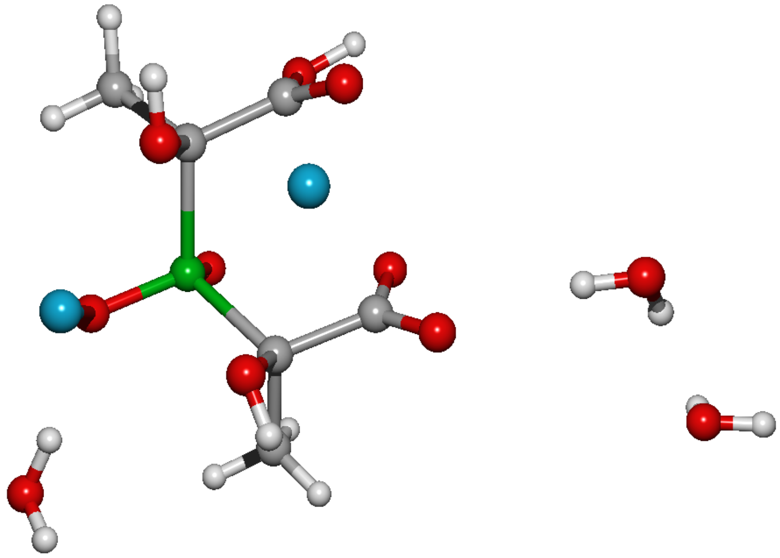
NaH_2PO_2 (4.4 g, 50 mmol) was heated in water (50 cm^3) with pyruvic acid (9.2 g, 105 mmol) for 124 h at 70°C under a dinitrogen atmosphere. The resulting solution was then reduced on a rotary evaporator to a gum, washed with methanol (3 x 25 cm^3) and a crude product precipitated by adding a concentrated aqueous solution drop-wise into a large excess of methanol. Filtration followed by drying under reduced pressure afforded a free flowing white powder. This powder was shown by ^{31}P-NMR spectroscopy to be composed of H_3PO_3 (2%), **1** (6%) and **2** (92%) where **2** was present as a *ca.* 1:1 mixture of diastereoisomers. This material formed crystals from concentrated aqueous solution by slow evaporation (yield 1.93 g, 12%). The same result can be obtained by reacting pyruvic acid with phosphinic acid and on completion of reaction, forming the sodium salt by addition of NaOH. The reaction goes to completion after approximately 24 h at 70°C and reaches >85% (**2** + **3**) after 20 weeks at ambient temperature. Compound **2** analysed as a mixture of diastereoisomers. NMR spectroscopy performed on a sample at pH 11 to better distinguish the isomers. ^{1}H-NMR (300 MHz, D_2O) δ (ppm) 1.43 (d, ^{3}J = 13 Hz, 3H, C*H*$_3$ *meso*), 1.42 (d, ^{3}J = 13 Hz, 3H, C*H*$_3$, *R,R/S,S*). ^{13}C{^{1}H}-NMR (75 MHz, D_2O) δ (ppm) 180.9 (d, $^{2}J_{C\text{-}P}$ 6 Hz *C*=O, *meso*), 180.8 (d, $^{2}J_{C\text{-}P}$ 5 Hz *C*=O, *R,R/S,S*),78.3 (d, $^{1}J_{C\text{-}P}$ 97 Hz, C_q *meso*), 77.8 (d, $^{1}J_{C\text{-}P}$ 98 Hz, C_q *R,R/S,S*), 22.3 (s,*C*H$_3$, *R,R/S,S*), 23.0 (s,*C*H$_3$, *meso*) . ^{31}P-NMR (121 MHz, D_2O) δ (ppm) 35.6 (sept., ^{3}J = 13 Hz, *R,R/S,S*), 34.4 (sept., ^{3}J = 13 Hz, *meso*). Melting point 175°C (decomposed). IR (KBr disc, cm^{-1}) 1715 (C=O), 1147 (P=O). HRMS (ES, negative ion) calculated for $C_6H_{10}O_8P$ 241.0119, found 241.0116. Found: C, 22.37; H, 4.07; Na, 14.3. $C_6H_9O_8PNa_2.2H_2O$ requires C, 22.65; H, 4.35; Na, 14.4.

Crystallographic data (excluding structure factors) for (**2**) have been deposited with the *Cambridge Crystallographic Data Centre* as deposition No. CCDC 740974. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 (1223) 336033; email: deposit@ccdc.cam.ac.uk

Single crystal X-ray diffraction analysis of $C_6H_9O_8PNa_2.3H_2O$ (2)

Formula weight	340.13	
Size	0.295 x 0.212 x 0.148 mm	
Crystal morphology	Colourless rhombohedral	
Temperature	150(2) K	
Wavelength	0.71073 Å [Mo-K_α]	
Crystal system	Triclinic	
Space group	$P\,\bar{1}$	
Unit cell dimensions	a = 6.2983(9) Å	α = 91.799(5)°
	b = 9.0885(12) Å	β = 92.303(6)°
	c = 11.6210(14) Å	γ = 95.488(6)°
Volume	661.21(15) Å^3	

Z	2
Density (calculated)	1.708 $\mathrm{Mg/m^3}$
Absorption coefficient	0.326 $\mathrm{mm^{-1}}$
F(000)	352
Data collection range	$1.75 \leq \theta \leq 30.26°$
Index ranges	$-8 \leq h \leq 8$, $-12 \leq k \leq 12$, $-16 \leq l \leq 16$
Reflections collected	60539
Independent reflections	3880 [R(int) = 0.03]
Observed reflections	3688 [$I > 2\sigma(I)$]
Absorption correction	none
Max. and min. transmission	
Refinement method	Full
Data / restraints / parameters	3880 / 0 / 241
Goodness of fit	1.077
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0198$, $wR_2 = 0.0566$
R indices (all data)	$R_1 = 0.021$, $wR_2 = 0.0573$
Largest diff. peak and hole	0.45 and -0.254e.$\mathrm{Å^{-3}}$



ESI.5. Reaction of Phosphinic acid with Pyruvic acid and benzylamine. *Synthesis of 2[(1-benzylcarbamoyl-1-hydroxyethyl)-hydroxy-phosphinoyl]-2-hydroxypropionic acid, di-benzylammonium salt. (4) (di-insertion pyruvate benzylamide, di-benzylammonium salt),* $2[C_7H_{10}N]^+ [C_{13}H_{16}NO_7P]^{2-}.H_2O$.

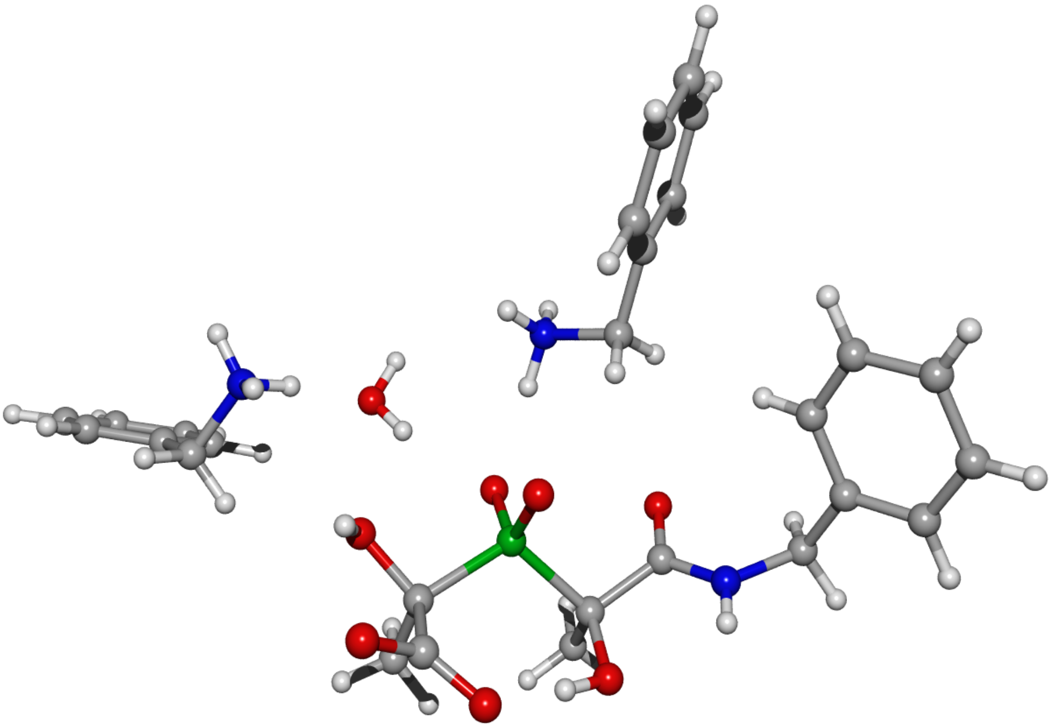
A solution generated from pyruvic acid (2.0 g, 22 mmol) and phosphinic acid (0.8 g, 6 mmol) in water (75 cm^3) was heated in the presence of benzylamine (0.32 g, 3 mmol) at 75°C for 7 h under the influence of a dynamic atmosphere of dinitrogen to ensure evaporative condition. Upon cooling the aqueous solution which had condensed to *ca.* half the original volume, **4** crystallises directly from solution. The product is filtered and washed with ethanol and recrystallised from hot water to afford pure **4** (0.27 g; 14 %). ^{1}H-NMR (300MHz, D_2O) δ (ppm) 7.2-7.7 (m, Ph*H*), 4.36 (d, ^2J = 15 Hz, 1H, CH_2), 4.28 (d, ^2J = 15 Hz, 1H, CH_2), 4.12 (s, 2H ,CH_2NH_3^+), 1.50 (d, ^3J = 12Hz, 3H, CH_3), 1.43 (d, ^3J = 13 Hz, 3H, CH_3). ^{13}C{^{1}H}-NMR (75 MHz, D_2O) δ (ppm) 182.6 (s, *C*=O), 179.2 (s, *C*=O), 141.07 (s, Ar), 135.52 (s, Ar), 132.08 (s, Ar), 132.06 (s, Ar), 131.67 (s, Ar), 131.62 (s, Ar), 130.21 (s, Ar), 130.12 (s, Ar), 80.81 (d, ^1J = 100Hz, C_q), 80.04 (d, ^1J = 96 Hz ,C_q), 45.82, (Ph*C*H_2NX where X = HR or H_3^+), 45.96 (Ph*C*H_2NX where X = HR or H_3^+), 25.21 (d, ^2J = 38 Hz, *C*H_3). ^{31}P- NMR (121 MHz, D_2O) δ (ppm) 33.16 (sept., ^3J = 13 Hz, *R,R/S,S* isomers), 32.34 (sept., ^3J = 12 Hz, *S,R/R,S* isomers). IR (KBr disc, cm^{-1}) 1635, 1500 (C=O), 1161 (P=O). HRMS (ES, negative ion) calculated for $C_{13}H_{17}NO_7P$ 330.0748, found 330.0737. Found: C, 57.54; H, 6.80; N, 7.46. $C_{27}H_{36}N_3O_7P.H_2O$ requires C, 57.45; H, 6.80; N 7.45.

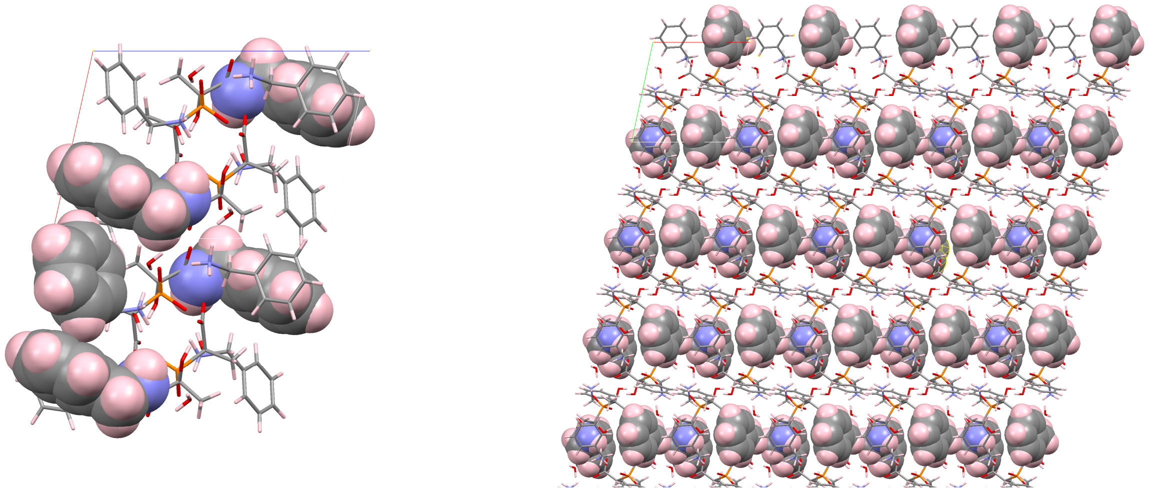
Crystallographic data (excluding structure factors) for **(4)** have been deposited with the *Cambridge Crystallographic Data Centre* as deposition No. CCDC 740973. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 (1223) 336033; email deposit@ccdc.cam.ac.uk

Single crystal X-ray diffraction analysis of $C_{27}H_{36}N_3O_7P.H_2O$ (4)

Formula weight	563.57	
Size	0.26 x 0.09 x 0.05 mm	
Crystal morphology	Colourless fragment	
Temperature	150(2) K	
Wavelength	0.7107 Å [Mo-K_α]	
Crystal system	Triclinic	
Space group	$P\bar{1}$	
Unit cell dimensions	*a* = 10.1313(13) Å	α = 99.470(7)°
	b = 10.6117(15) Å	β = 100.513(7)°
	c = 14.621(2) Å	γ = 99.949(7)°
Volume	1490.7(4) Å^3	
Z	2	
Density (calculated)	1.256 Mg/m^3	
Absorption coefficient	0.143 mm^{-1}	
F(000)	600	
Data collection range	$1.99 \le \theta \le 26.87°$	
Index ranges	$-12 \le h \le 12$, $-13 \le k \le 13$, $-18 \le l \le 18$	
Reflections collected	32061	

Independent reflections	6339 [R(int) = 0.0449]
Observed reflections	5087 [$I > 2\sigma(I)$]
Absorption correction	multi-scan
Max. and min. transmission	0.9925 and 0.964
Refinement method	Full
Data / restraints / parameters	6339 / 0 / 504
Goodness of fit	1.042
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0349$, $wR_2 = 0.0852$
R indices (all data)	$R_1 = 0.0495$, $wR_2 = 0.0929$
Largest diff. peak and hole	0.437 and -0.366e.Å^{-3}





(*Above left*) Structure of **4** expanded along the crystallographic b axis emphasising stacked arrangement of amide benzyl functions and intercalating benzylammonium phenyl groups (space-filling). (*Above right*) A 5 x 5 unit cell array in the ab plane of **4** emphasising lamellar arrangements of hydrophilic (capped sticks) and amide functionality (space-filling).

ESI.6. A study of the dehydration of (2) by ^{31}P-NMR and negative ion electrospray mass spectrometry.

Pyruvic acid (10 g, 0.11 mol) was reacted with phosphinic acid (4 g, 0.03 mol) for 24 hrs at 70^{o}C after which time the reaction mixture contained 78% of the di-insertion product **2** by ^{31}P-NMR This solution was then dehydrated at 70^{o}C for 3 hours *in vacuo* and one portion of the dried residue dissolved in D_2O (0.5 cm^3) for ^{31}P-NMR spectroscopy with a second portion dissolved in acetonitrile for mass spectrometry. The remainder was re-dissolved in water (20 cm^3) and heated to 70^{o}C for a further 3 hours under static nitrogen. This was also then subsequently submitted for MS and ^{31}P-NMR analysis. The integrals for the “start”, “dehydrated” and “rehydrated” samples are as follows, as percentage of total solution P.

Compound	**"start" composition (%)**	**"dehydrated" composition (%)**	**"rehydrated" composition (%)**
2	78	26	61
1	1	Not seen	Not seen
3	9	60	22
1-oxidised	5	8	9
H_3PO_3	7	6	7

Table ESI2. Percentage compositions of HPP system under dehydration and rehydration conditions. Analysis by ^{31}P NMR (121.49 MHz, D_2O)

High resolution mass spectroscopic data were obtained for samples which were in the "dehydrated" and "rehydrated" states respectively. These MS results agree with the previously reported ^{31}P-NMR results. Firstly, compound **3** is confirmed as mass 223 and compound **2** as mass 241. In the dehydrated state the ratio of 241/223 is 0.27 (NMR peak integral ratio 0.43) and in the hydrated state the 241/223 peak ratio is 1.64 (NMR peak integral ratio 2.73). Of course the two techniques cannot exactly agree on the ratios for many reasons but the trend is clear.

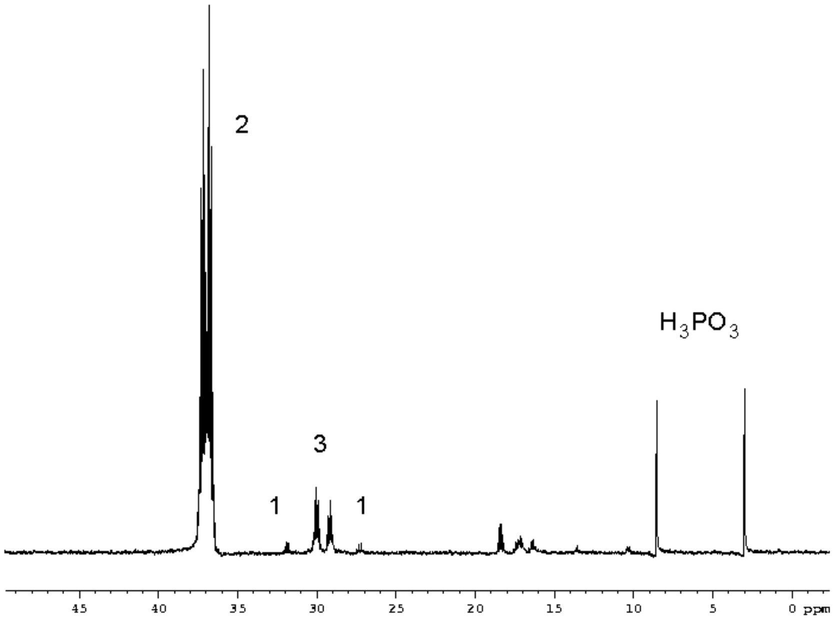
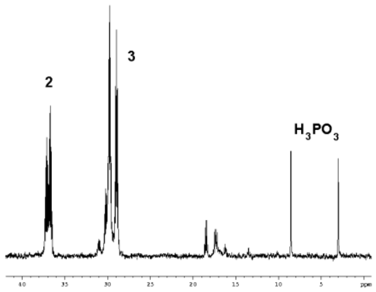
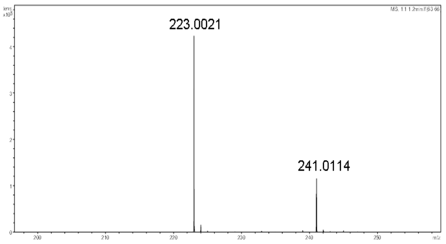
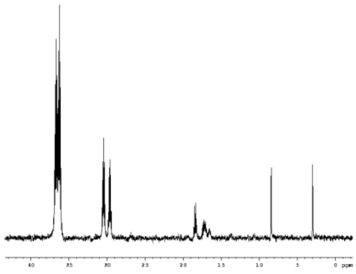
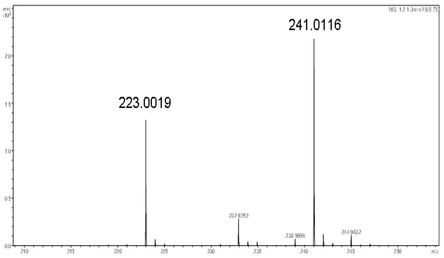


Figure ESI3. ^{31}P NMR spectrum of starting reaction mixture (121.49 MHz, D_2O, 293K, pH 2, column 1 in Table SI2)

 **Figure ESI4.** ^{31}P NMR spectrum of dehydrated reaction mixture (column 2 in Table ESI2)	 **Figure ESI5.** Image of HRMS (-ve) of dehydrated reaction mixture
 **Figure ESI6.** ^{31}P NMR spectrum of rehydrated mixture (column 3 in Table ESI2) similar to starting point figure SI3	 **Figure ESI7.** Image of HRMS (-ve) of rehydrated reaction mixture.

ESI.7. pH Dependence of 2-3 equilibrium. A ^{31}P-NMR study

A solution of the H-phosphinic acid:pyruvic acid system (5.1 g, 21.2 mmol of DIP) in D_2O (15 cm^3) was studied. An aliquot of the sample was taken for ^{31}P NMR analysis. A half molar equivalent (0.43 g, 10.0 mmol) of sodium hydroxide was added to the solution, an aliquot was removed for ^{31}P NMR analysis before another half molar equivalent of sodium hydroxide was added. This was repeated for nine (9) consecutive concentrations of sodium hydroxide. The pH of each sample was measured and ^{31}P NMR analysis was conducted. The yield of each product was calculated by integration of the signal for that specific product relative to other signals (Table ESI3). The right hand side H_3PO_3 (5) peak was referenced to δ 2.96 ppm so shifts in peaks could be compared.

Sample	**pH**	**Percentage**				
		2	**3**	**1-oxidised**	**Unknown**	**H_3PO_3**
a	2.1	71	17	5	3	5
b	2.3	78	10	5	3	4
c	3.2	75	11	6	2	5
d	4.2	68	19	6	2	5
e	5.4	71	17	5	2	5
f	8.2	87	0	5	2	5
g	11.9	87	0	7	2	5

Table ESI3. Percentage compositions of each product was calculated by integration of the ^{31}P NMR signals (D_2O, 300 K, 121.49 MHz)

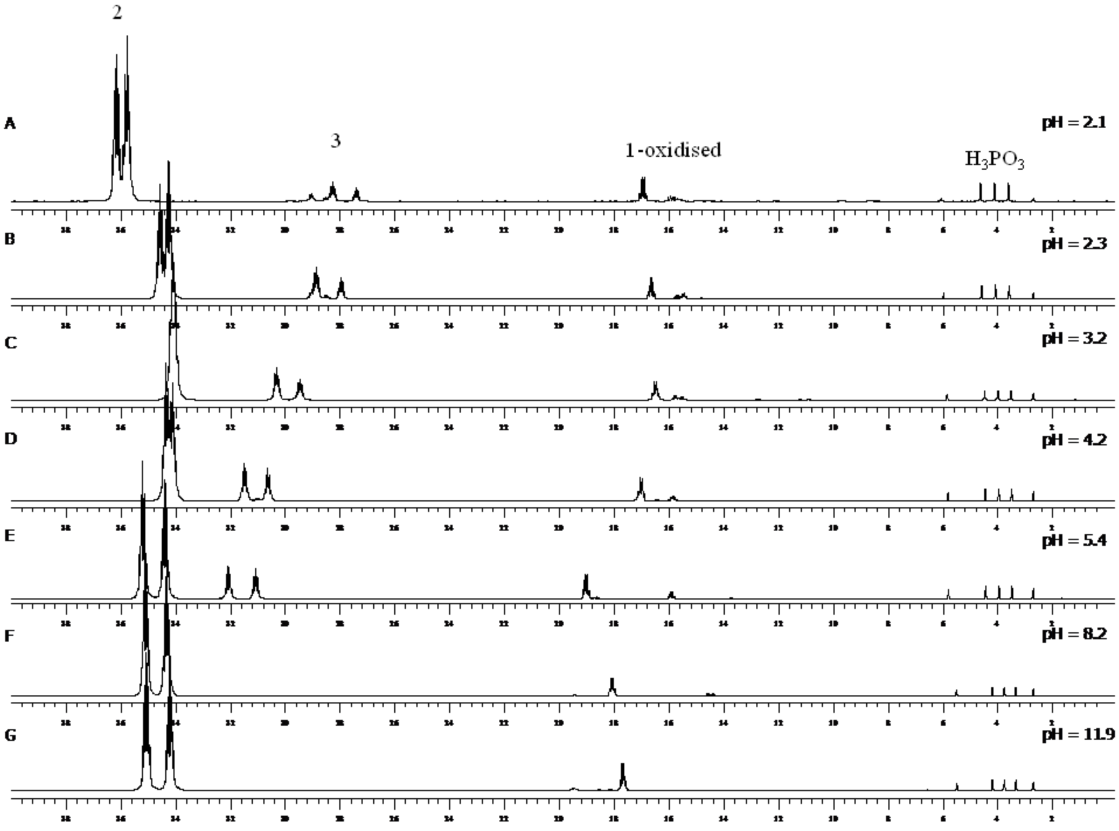


Figure ESI8. ^{31}P NMR (D_2O, 300 K, 121.49 MHz) analysis of the H-phosphinic acid: pyruvic acid system at different pH values.

ESI.8. Synthesis of lactone 3. *Synthesis of 2-carboxy-4-hydroxy-2,4-dimethyl-3,5-dioxo-3λ^5-[1,3]oxaphospholan-3-olate triethylammonium salt.*

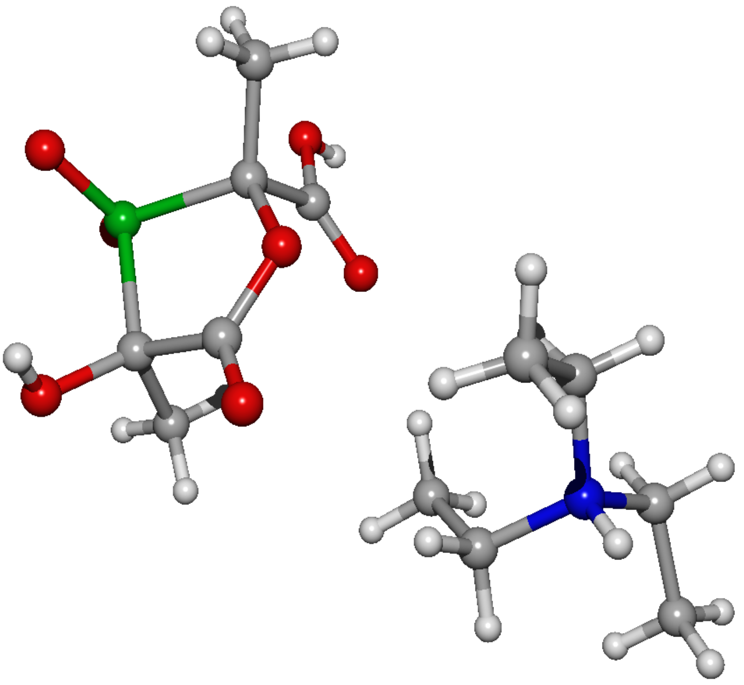
H-Phosphinic acid (0.77 g, 11.6 mmol) and pyruvic acid (2.0 g, 232.7 mmol) were dissolved in distilled water (7 cm^3) and the solution heated at 70°C for 48 h under an atmosphere of dinitrogen gas. An aliquot was removed, evaporated to dryness and analysed by ^{31}P-NMR spectroscopy which confirmed that **2** was the dominant component (*ca.* 85% of total phosphorus) with trace amounts of **1**, oxidised **1** and H_3PO_3. Triethylamine (6.6 g, 65.3 mmol) was added to the remaining solution which was then heated again to 70°C for 16 h but now under conditions where the water solvent was allowed to evaporate under flowing dinitrogen gas. The residue was dissolved in the minimal volume of methanol (*ca.* 6 cm^3) and the solution washed with diethylether (*ca.* 5 cm^3) to remove excess triethylamine. Once the volume had been reduced by 50%, the methanol solution was allowed to cool slowly producing **3** small colourless needle like crystal (yield 0.96 g, 16%). ^{1}H-NMR (300MHz, D_2O) δ (ppm) 3.15 (q, ^3J = 7 Hz, 6H, $NHCH_2CH_3$), 1.71 (d, ^3J = 11 Hz, 3H, C(OH)CH_3), 1.48 (d, ^3J =11 Hz, 3H, C(COOH)CH_3), 1.23 (t, ^3J =7 Hz, 6H, $NHCH_2CH_3$). ^{13}C{^{1}H}-NMR (300 MHz, D_2O) δ (ppm) 178.02 (s, C(CH_3)CO_2H), 174.09 (s, *C*=O ring), 84.23 (d, ^1J = 74 Hz, *C*(CH_3)OH) δ 67.56 (d, ^1J = 113 Hz, *C*(CH_3)CO_2H), 21.61 (s, C(CH_3)CO_2H), 19.78 (s, C(CH_3)OH). ^{31}P-NMR (300 MHz, D_2O) δ (ppm) 30.08 (sept, ^3J = 11 Hz). HRMS (ES, negative ion) calculated for $C_6H_8O_7P_1$ 223.0013, found 223.0012. Found: C, 44.31; H, 7.44; N, 4.31. $C_6H_8O_7P.C_6H_{16}N$ requires: C, 44.35; H, 7.50; N, 4.30.

Crystallographic data (excluding structure factors) for **3** have been deposited with the *Cambridge Crystallographic Data Centre* as deposition No. CCDC740975. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 (1223) 336033; email: mail to deposit@ccdc.cam.ac.uk

Single crystal X-ray diffraction analysis of $C_{12}H_{24}NO_7P$ (3)

Formula weight	325.29
Size	0.42 x 0.13 x 0.07 mm
Crystal morphology	Colourless needle
Temperature	150(2)K

Wavelength	0.71073 Å [Mo-K_α]	
Crystal system	Triclinic	
Space group	$P\bar{1}$	
Unit cell dimensions	a = 6.8028(8) Å	α = 81.041(6)°
	b = 10.2088(13) Å	β = 86.642(6)°
	c = 12.2089(16) Å	γ = 87.114(6)°
Volume	835.38(18) Å^3	
Z	2	
Density (calculated)	1.293 Mg/m^3	
Absorption coefficient	0.194 mm^{-1}	
F(000)	348	
Data collection range	$1.69 \leq \theta \leq 27.9°$	
Index ranges	$-8 \leq h \leq 8$, $-13 \leq k \leq 13$, $-15 \leq l \leq 15$	
Reflections collected	37192	
Independent reflections	3940 [R(int) = 0.0405]	
Observed reflections	3221 [$I > 2\sigma(I)$]	
Absorption correction	multi-scan	
Max. and min. transmission	0.9866 and 0.897	
Refinement method	Full	
Data / restraints / parameters	3940 / 0 / 197	
Goodness of fit	1.052	
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0405, wR_2 = 0.1066	
R indices (all data)	R_1 = 0.0532, wR_2 = 0.1169	
Largest diff. peak and hole	0.531 and -0.297e.Å^{-3}	



ESI.9. Time evolution analysis of the HPP system

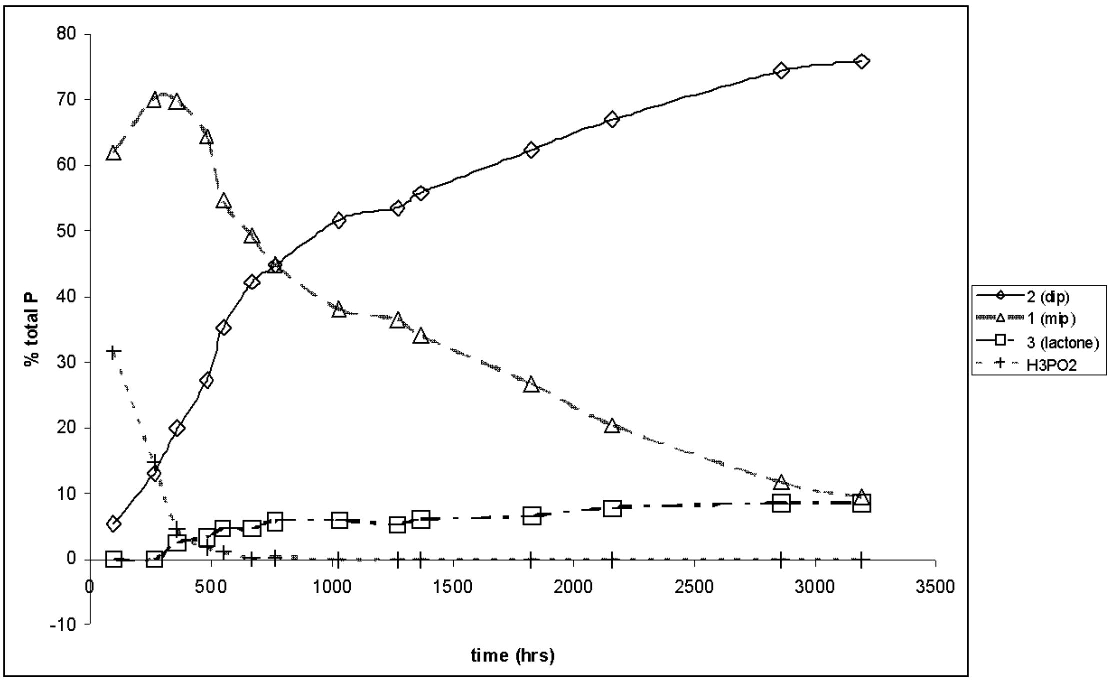


Figure ESI9. Time evolution of the H-phosphinate-pyruvate system

Time evolution of the H-phosphinate-pyruvate system (25°C; pH 1.3; H_2O; N_2 atmosphere) with H_3PO_2 (75 mM) and pyruvic acid (2.8 M). Percentage (%) total phosphorus determined from integration of ^{31}P-NMR spectra. The data indicate that **1** builds up initially to a maximum of *ca*. 70% of the total solution phosphorus and then, in the presence of excess pyruvic acid reacts further yet slower to afford **2**. The [**2**]/[**3**] ratio remains relatively constant throughout as expected of a process under thermodynamic control.

ESI.10 Reactions of lactone 3 with benzylamine.

Compound **2** was made in the acid form as above. Pyruvic acid (7.0 g; 0.08 mol) was reacted with phosphinic acid (4.0 g; 0.03 mol) for 24 hrs at 70°C in water (40 cm^3) at which point the reaction mixture contained 78% of the di-insertion product **2** by ^{31}P-NMR. This solution was reacted with aqueous ammonia (0.03 mol; 1 cm^3; 88%) and reduced in volume to a gum which was washed with methanol (25 cm^3) and dissolved in minimal water (*ca*. 10 cm^3). This solution was added slowly to a large excess of methanol (500 cm^3) causing a white precipitate. The precipitate is free of pyruvic acid and contains a higher proportion of (**2**) typically > 95% by ^{31}PNMR and can be crystallised from water. The crystals were re-dissolved in water and the pH adjusted with HCl to pH 3. The water was removed and the resulting precipitate heated in vacuum at 140°C for 16 hrs forming the ammonium salt of the lactone.

A portion of lactone (50 mg, 0.22 mmol) was added in a glovebox to a Schlenk containing benzylamine (3 cm^3; 28 mmol) dried over molecular sieves. The Schlenk tube was kept under nitrogen and on gentle warming the lactone dissolved. After a few (how many days?) days standing a gelatinous precipitate formed which was washed with diethyl ether. The precipitate was examined by ESI HRMS and found to contain the benzylamide (**4**). In addition analysis by ^{1}HNMR showed the typical amide CH_2 protons δ 4.25, 4.30, 4.35, 4.40 (AA',1H, CH_2) and crystals of (**4**) were grown from the precipitate and analysed by single crystal X-ray diffraction.

In a separate experiment, NaH_2PO_2 (0.05 mol, 4.4 g) and pyruvic acid (0.05 mol, 4 g) were heated in water (25 cm^3) for 16 hrs at 75°C leading to a reaction mixture containing (**1**) (79%) and (**2**) (7%). To this mixture was added an excess of benzylamine (3.0 g, 28 mol) and heating continued for 4 days. Analysis of the resulting solution by HRMS (ES; negative ion) found a small peak at *m/z* 330 corresponding to (**4**) but no peak at *m/z* 242, the mass that would result from the formation of an amide from (**1**). Thus the di-substituted (**2**) reacts in preference to the mono-substituted (**1**) even when present at only a tenth of the concentration and with both compounds presenting an identical carboxylic acid moiety. We interpret these findings as the ability of (**2**) to form the lactone (**3)** which is considerably more reactive and that reaction proceeds *via* the lactone. This hypothesis is further supported by the observation that (**5**) which resembles (**2**) in structure (CH_3 is replaced by H) does not appear to form a lactone and will only form an amide with benzylamine at temperatures above 130°C. We see no evidence for the formation of a cyclic anhydride from compound 2 but equally, we cannot yet discount such a highly reactive compound being present at low levels and acting as an intermediate.

ESI.11 Thermal decomposition of 1

1-Na (1.29 g, 7.3 mmol) was heated as a dry powder under vacuum in a 100 cm^3 round bottomed flask at 140°C for 16 hrs. Analysis of the flask contents by $^{31}P\{^1H\}$-NMR spectroscopy (D_2O) showed there to be 71% by integration of pyrophosphite (remainder starting materials and phosphonic acid). Analysis of the flask contents by ES HRMS also showed two series of oligomers, each oligomers of lactic acid, one hydroxyl terminated, one H-phosphonate terminated (see Figure ESI10). The tap leading to the vacuum pump was found to have material condensed in it. Analysis by ^{31}P-NMR spectroscopy (D_2O) showed a pentet due to D_3PO_2 from exchange with D_2O. In addition crystals were found in the tap which were confirmed as being lactic acid dimer by single crystal X-ray diffraction. No thermal decomposition reaction was observed at 120°C.

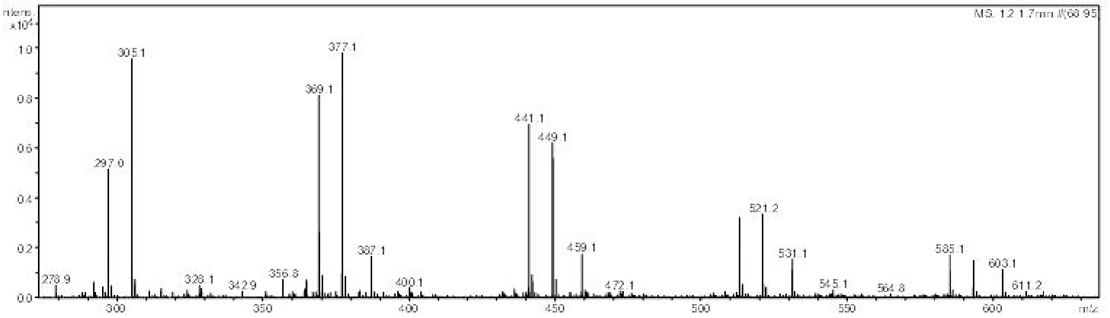
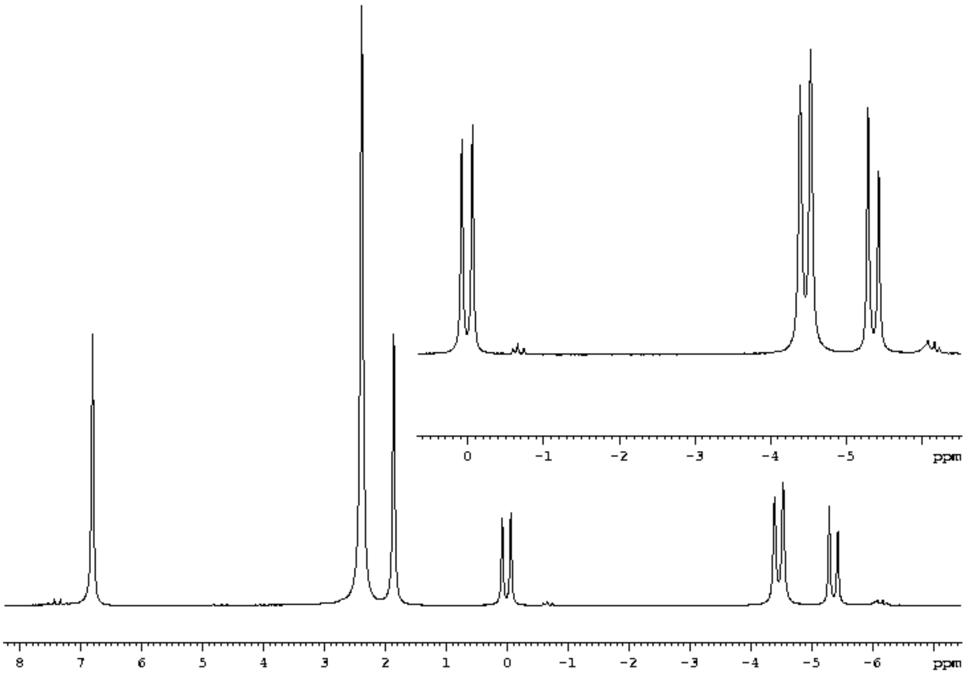


Figure ESI10. Electrospray mass spectrometric analysis (negative ion; H_2O) of the organic components from experiment ESI11. Mass fragments 297, 369, 441, 513 and 585 represent oligomers of the form $H(^{-}O)P(O)[OCHMeC(O)]_nOH$ where n = 3-7 respectively and mass fragments 305, 377, 449, 521 represent oligomers of the form $H[OCHMeC(O)]_nOH$ where n = 4-7 respectively.

ESI.12 Preliminary investigations on the phosphorylating potential of pyrophosphite

Solutions containing (i) $Na_2HPO_4.2H_2O$ (14 mM) $Na_2H_2P_2O_5$, (20 mM) in H_2O (20 cm^3) at pH 6 and (ii) $Na_4P_2O_7$ (19 mM), $Na_2H_2P_2O_5$ (20 mM) in H_2O (20 cm^3) at pH 6.8, pH 6, 70^{o}C, were heated to 70^{o}C under an atmosphere of dinitrogen for 16 hrs. After this time, each solution was analysed by ^{31}P-NMR spectroscopy using a D_2O insert which revealed *ca*. 30% conversion to **6** in system (i) and 9% conversion to **7** within system (ii). Longer reaction times do lead to increased conversion but as yet these have not been optimised. In each case the majority P-containing product was observed to be phosphite ($H_2PO_3^-$) identified by comparison to an authentic sample. Repeating the experiment of system (i) in the presence of $MgCl_2$ (14 mM) led to reduction of the amount of **6** observed after 16hrs to 14% total solution P. Within system (ii) $H_2PO_3^-$ was observed at 43% (total solution P), and isohypophosphate, **6** at 11%, the latter presumably formed by reaction of pyrophosphite **5** with phosphate produced by hydrolysis of pyrophosphate under the reaction conditions.


0
-1
-2
-3
-4
-5
ppm
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
-5
-6
ppm

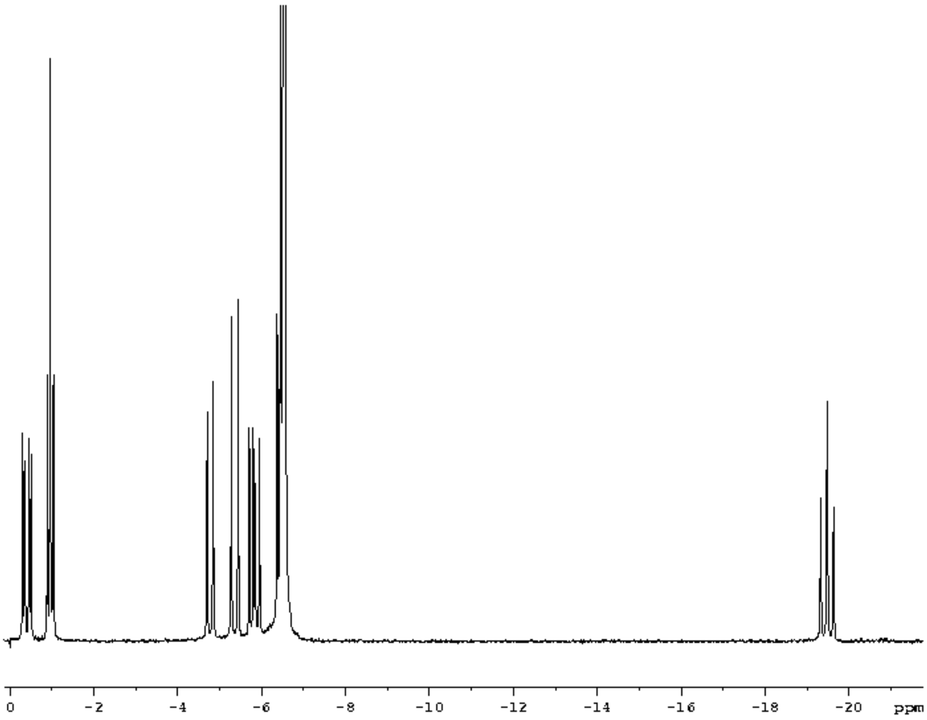

0
-2
-4
-6
-8
-10
-12
-14
-16
-18
-20
ppm

Figure ESI11 (*top*) and ESI12(*bottom*). (*top*) ^{31}P-NMR spectrum (H_2O; 298K) of a reaction system comprising $Na_2HPO_4.2H_2O$ and $Na_2H_2P_2O_5$. Reaction products are $H_2PO_3^-$ δ 4.13 (d, $^1J_{PH}$ 598Hz), $H_2PO_4^-$ δ 2.21 (s) and isohypophosphate **6**: δ -2.68 (dd, $^1J_{PH}$ 650Hz, $^2J_{PP}$ 17Hz), δ -4.46 (d, $^2J_{PP}$ 17Hz). (***bottom***) ^{31}P-NMR spectrum (H_2O; 298K) of a reaction system comprising $Na_4P_2O_7$ (19 mM), $Na_2H_2P_2O_5$ (20 mM), H_2O (20 cm^3), pH 6.8, 70°C: 9% conversion to **7** after 16h. Compound **7** has: δ -2.9 (dd, $^1J_{PH}$ 650Hz, $^2J_{PP}$ 18Hz), δ -5.3 (d, $^2J_{PP}$ 18Hz), δ -19.46 (t, $^2J_{PP}$ 18Hz) ppm. Signals for **5** & **6** are also present.

ESI.13 Reaction between NaH_2PO_3 and $[(MeO)HP(O)O]^-[^tBuNH_3]^+$. Synthesis of pyrophosphite

Dimethylphosphite (5.0 g, 0.045 mol) was heated for 16 hrs in neat *tert*-butylamine (50 cm^3, 0.48 mol) at 60°C and subsequently allowed to cool. A crystalline precipitate of $[(MeO)HP(O)O]^-[^tBuNH_3]^+$ (4.5g, 59% yield) is filtered off, washed with ethanol and dried under vacuum. In a 100 cm^3 round bottomed flask (3.68 g, 0.025 mol) $[(MeO)HP(O)O]^-[^tBuNH_3]^+$ and Na_2HPO_3 (2.60 g, 0.022 mol) were heated as intimately mixed dry powders for 50 hrs at 150°C under reduced pressure. The resultant mixture was analysed by ^{31}P-NMR spectroscopy (D_2O) and found to be 88% pyrophosphite by integration (remainder being starting materials).

ESI.13 On the Prebiotic Plausibility of the HPP System.

We have outlined aspects of the prebiotic plausibility of both pyruvic acid and H-phosphinic acid in the main body of the paper. It is perhaps worth emphasising the case for reduced P with as much as 10% of the total crustal P originating from extraterrestrial material (Pasek and Lauretta, *OLEB*, 2008, **38**, 5), and well over half of this forming reduced P compounds like phosphonate and phosphinate (references 4-7 in manuscript), reduced P compounds will likely dominate in solution due to differences in solubility between phosphates and reduced P species (the latter of which are 10^3-10^6 times more soluble than orthophosphate salts).

In addition, it is worth considering the prebiotic feasibility for the whole HPP system within an early earth geochemical context. In essence an environment is required which combines moderate-high temperatures (60-100^{o}C), low pH (<3) and the potential for evaporative-rehydration cycles. Such conditions may be found within acidic hot springs, volcanic fumarole environments such as those in California (Bumpass Hell in the Lassen National Park) or Russia (Kamchatka Peninsula). Indeed, the Bumpass Hell site has been used by scientists conducting experiments into the condensation of oligonucleotides under putative prebiotic conditions: http://www.newscientist.com/article/mg20126911.400-did-life-begin-in-a-pool-of-acidic-gloop.html

ESI.14 DFT Calculations. Computed Cartesian coordinates (Å), SCF energies and enthalpies (0 K and 298.15 K) and free energies (298.15 K) in atomic units for all stationary points. Solvent-corrected (water, PCM method) SCF Energies are also indicated. Species are numbered according to the scheme in the main text and **1-4** are computed in the monoanionic protonation state.

Computed Structures and Energies

$[H_2PO_2]^-$

BP86 Energy = -493.087970636
Enthalpy 0K= -493.063931
Enthalpy 298K= -493.060573
Free Energy 298K= -493.089294
PCM(H_2O)= -493.193405537

O	1.34999	-0.42800	-0.00001
P	-0.00005	0.28737	-0.00001
O	-1.34987	-0.42809	-0.00001
H	-0.00014	1.26926	-1.10098
H	-0.00014	1.26887	1.10130

Pyruvic acid

BP86 Energy = -342.410823428
Enthalpy 0K= -342.341947
Enthalpy 298K= -342.335412
Free Energy 298K= -342.372904
PCM(H_2O)= -342.42254082

O	-0.95770	-1.49802	-0.00011
C	-0.71729	-0.30016	-0.00002
C	-1.76078	0.79353	0.00008
C	0.74968	0.21701	-0.00001
O	1.04465	1.40478	-0.00012
O	1.64579	-0.79857	0.00011
H	-1.62796	1.44491	0.88105
H	-2.76416	0.34708	-0.00012
H	-1.62777	1.44540	-0.88047
H	2.52825	-0.36518	0.00010

1

BP86 Energy = -835.554456500
Enthalpy 0K= -835.455511
Enthalpy 298K= -835.445651
Free Energy 298K= -835.491280
PCM(H_2O)= -835.649069801

O	-2.16268	1.05135	-0.62470
P	-1.25153	-0.16576	-0.54522
C	0.33186	0.23061	0.57560
C	1.54005	0.03948	-0.30610
O	2.03181	0.87989	-1.06577
O	2.03538	-1.24716	-0.28694
O	-1.67660	-1.51274	0.07837
O	0.25788	-0.70978	1.63559
C	0.23979	1.67230	1.08980
H	-0.66736	-0.41998	-1.84347
H	2.72731	-1.20857	-0.98340
H	-0.48838	-1.30971	1.31342
H	0.95455	1.82414	1.91984

H	0.47400	2.38235	0.28234
H	-0.78380	1.87145	1.44133

2 (meso)

BP86 Energy = -1177.99790500
Enthalpy 0K= -1177.825036
Enthalpy 298K= -1177.808368
Free Energy 298K= -1177.868610
PCM(H_2O) = -1178.08521948

C	-2.81121	-0.39599	0.91505
H	-2.44201	-0.26554	1.94195
H	-3.05302	-1.45861	0.76719
H	-3.72698	0.20707	0.77516
C	-1.75812	0.03791	-0.11983
C	-1.22511	1.43552	0.14286
O	-0.98922	2.29268	-0.70185
O	-0.91263	1.61392	1.47450
H	-0.21377	2.30851	1.46350
O	-2.27800	-0.06669	-1.43131
H	-1.59455	-0.63439	-1.89074
P	-0.24936	-1.22967	-0.04129
O	-0.48527	-2.22354	1.08649
O	-0.17249	-1.65000	-1.53886
C	1.57959	-0.48401	0.18768
C	2.07602	-0.78008	1.60313
H	1.83977	-1.82301	1.85704
H	3.16663	-0.61229	1.66163
H	1.57907	-0.11552	2.32561
O	2.31843	-1.24654	-0.76670
H	1.61617	-1.50578	-1.43098
C	1.69764	1.00283	-0.11946
O	1.73549	1.92003	0.71050
O	1.73666	1.26206	-1.45776
H	1.59229	2.23236	-1.50777

2(rac)

BP86 Energy = -1178.00006790
Enthalpy 0K= -1177.827176
Enthalpy 298K= -1177.810518
Free Energy 298K= -1177.871181
PCM(H_2O) = -1178.08662033

C	2.07742	-0.64659	1.59564
H	3.15072	-0.39714	1.67656
H	1.51329	-0.00195	2.28591
H	1.91406	-1.69580	1.87890
C	1.60021	-0.43197	0.15840
C	1.65594	1.04608	-0.20894
O	1.72894	1.99346	0.58038
O	1.59314	1.25321	-1.55758
H	1.43908	2.22034	-1.63217
O	2.38921	-1.19212	-0.75392
H	1.69583	-1.57341	-1.37325
P	-0.19617	-1.23568	-0.08075

O	-0.49942	-2.09440	1.16332
O	-0.04351	-1.83806	-1.48843
C	-1.75478	-0.01927	-0.04390
C	-2.50496	-0.12621	-1.37628
H	-1.90049	0.28046	-2.19945
H	-3.45136	0.44075	-1.31325
H	-2.72845	-1.18114	-1.59215
C	-1.26868	1.39610	0.20202
O	-1.11342	2.26223	-0.66085
O	-0.91639	1.60405	1.50921
H	-0.31670	2.38315	1.46580
O	-2.54322	-0.49156	1.03717
H	-1.96687	-1.22337	1.41852

3 (meso)

BP86 Energy =-1101.56537668
Enthalpy 0K= -1101.417782
Enthalpy 298K= -1101.403314
Free Energy 298K=-1101.458499
PCM(H_2O) = -1101.65485699

C	-2.73332	-0.02173	-1.13845
H	-3.17081	-1.03070	-1.21616
H	-2.29472	0.24444	-2.11434
H	-3.52662	0.70346	-0.88863
C	-1.66507	-0.01673	-0.04850
O	-2.18416	-0.49882	1.21244
H	-1.73480	-1.39327	1.27011
P	-0.15170	-1.09169	-0.40975
O	-0.36377	-2.33217	0.47629
O	0.25741	-1.12626	-1.87079
C	0.95391	0.19482	0.57231
C	1.17110	-0.24186	2.02105
H	0.19029	-0.38822	2.49691
H	1.71919	-1.19448	2.03682
H	1.74324	0.51917	2.58179
C	2.25351	0.36656	-0.17297
O	3.24211	-0.34553	-0.00672
O	2.22930	1.36216	-1.10907
H	3.08497	1.24466	-1.57627
O	0.21193	1.45274	0.54845
C	-1.11973	1.39672	0.19509
O	-1.75501	2.43834	0.12252

3 (rac)

BP86 Energy = -1101.56478799
Enthalpy 0K= -1101.417265
Enthalpy 298K= -1101.402763
Free Energy 298K= -1101.458127
PCM(H_2O) = -1101.65432309

C	2.94273	0.42823	0.00332
H	3.23122	1.22903	-0.69710
H	2.98125	0.83125	1.02877
H	3.65545	-0.40957	-0.08525

C	1.53513	-0.05759	-0.34138
O	1.45416	-0.46778	-1.71929
H	0.80847	0.20027	-2.08713
P	0.17881	1.23051	-0.07662
O	-0.27076	1.61334	-1.49522
O	0.49520	2.21642	1.03756
C	-1.01295	-0.13591	0.66133
C	-1.66922	0.34158	1.95453
H	-0.91474	0.82889	2.58914
H	-2.45072	1.07559	1.70790
H	-2.13410	-0.50458	2.49135
C	-2.04404	-0.52269	-0.37543
O	-3.14781	0.00286	-0.49796
O	-1.61816	-1.51209	-1.21968
H	-2.34013	-1.56707	-1.88251
O	-0.15982	-1.27985	0.97689
C	1.14690	-1.26273	0.53236
O	1.88342	-2.18378	0.85217

4 (S,R/R,S)

BP86 Energy = -1428.50659103
Enthalpy 0K= -1428.214517
Enthalpy 298K= -1428.192185
Free Energy 298K= -1428.265396
PCM(H_2O)= -1428.59432839

C	2.72732	2.69555	-0.38894
H	2.82337	3.55545	0.29742
H	3.72481	2.34398	-0.69004
H	2.16209	3.01257	-1.27798
C	2.00311	1.55311	0.32832
C	0.54357	1.92354	0.57807
O	-0.09495	2.82092	0.03173
O	-0.03904	1.08190	1.49406
H	-0.99618	1.30372	1.46319
O	2.69295	1.28462	1.54943
H	2.49476	0.33658	1.77570
P	2.03925	0.01720	-0.85543
O	3.46766	-0.14792	-1.35250
O	0.84316	0.12922	-1.84070
C	1.63819	-1.51347	0.27052
C	2.33523	-2.72372	-0.38829
H	3.40851	-2.50313	-0.48589
H	2.18225	-3.62135	0.23795
H	1.92716	-2.91277	-1.39507
O	2.14549	-1.36302	1.61665
H	1.35396	-1.66999	2.14433
C	0.13384	-1.83659	0.43252
O	-0.28011	-2.21482	1.55470
N	-0.61877	-1.76885	-0.69587
H	-0.18533	-1.12558	-1.42034
C	-2.05227	-2.00346	-0.64386
H	-2.36317	-2.47834	-1.59584
H	-2.23797	-2.73216	0.16459
C	-2.91119	-0.76123	-0.40371
C	-2.42661	0.53313	-0.67588

C	-3.23796	1.65800	-0.44413
C	-4.54663	1.50352	0.04075
C	-5.04126	0.21412	0.29970
C	-4.22542	-0.90681	0.08404
H	-1.41008	0.66894	-1.06635
H	-2.81944	2.65192	-0.63013
H	-5.17628	2.38182	0.22334
H	-6.05849	0.08155	0.68677
H	-4.60832	-1.91045	0.30932

4 (S,S/R,R)

BP86 Energy = -1428.50563773
Enthalpy 0K= -1428.213584
Enthalpy 298K= -1428.191082
Free Energy 298K= -1428.265723
PCM(H_2O) = -1428.59226942

C	2.86599	0.28507	1.94460
H	1.86963	0.59293	2.30045
H	3.40603	-0.20463	2.77445
H	3.43059	1.17487	1.63035
C	2.74575	-0.73682	0.79791
C	4.02923	-0.78900	-0.01667
O	4.73895	0.18390	-0.27542
O	4.33719	-2.03646	-0.47843
H	5.10864	-1.86522	-1.06204
O	2.39848	-2.01670	1.31236
H	1.41941	-2.07063	1.10439
P	1.30733	-0.36117	-0.46518
O	0.18172	-1.21799	0.15231
O	1.77580	-0.56665	-1.91927
C	0.76555	1.50292	-0.54983
C	1.87590	2.52653	-0.26880
H	1.98608	2.69193	0.81273
H	2.83918	2.19712	-0.69028
H	1.58848	3.48048	-0.74639
O	0.33762	1.60351	-1.92218
H	0.84802	0.84071	-2.34464
C	-0.42716	1.70611	0.39272
O	-0.29806	1.91508	1.61236
N	-1.64000	1.62461	-0.23869
H	-1.58039	1.42152	-1.24008
C	-2.88872	1.56237	0.49332
H	-3.51946	2.45122	0.28320
H	-2.59340	1.62245	1.55956
C	-3.69815	0.30120	0.22367
C	-3.06219	-0.95037	0.07687
C	-3.83423	-2.10233	-0.14176
C	-5.23572	-2.02838	-0.21515
C	-5.87070	-0.78462	-0.07229
C	-5.10262	0.37098	0.14090
H	-1.96411	-1.02022	0.12252
H	-3.32907	-3.06768	-0.25801
H	-5.82940	-2.93329	-0.38940
H	-6.96276	-0.71087	-0.13709
H	-5.59845	1.34523	0.24207

PhNH$_2$

BP86 Energy = -326.911743950
Enthalpy 0K= -326.769791
Enthalpy 298K= -326.762471
Free Energy 298K= -326.801551
PCM(H_2O) = -326.919066986

N	-2.75699	-0.48971	-0.29873
H	-2.64804	-0.48148	-1.31961
H	-3.74363	-0.27865	-0.11435
C	-1.91476	0.56974	0.28315
H	-2.10359	1.59193	-0.11857
H	-2.16104	0.62052	1.36261
C	-0.43272	0.25919	0.12906
C	0.50309	1.30017	-0.02298
C	1.87544	1.02380	-0.12423
C	2.32966	-0.30381	-0.08504
C	1.40244	-1.34922	0.05687
C	0.03173	-1.07033	0.16457
H	0.15106	2.33834	-0.06455
H	2.58928	1.84599	-0.24338
H	3.39934	-0.52257	-0.17012
H	1.74919	-2.38807	0.08415
H	-0.70293	-1.87520	0.26651

H_2O

BP86 Energy = -76.4195806439
Enthalpy 0K= -76.398806
Enthalpy 298K= -76.395971
Free Energy 298K=-76.417147
PCM(H_2O) = -76.4287380583

H	0.76177	-0.48619	0.00000
O	0.00000	0.12149	0.00000
H	-0.76177	-0.48571	0.00000