

Prebiotic Chemistry

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A Stark Contrast to Modern Earth: Phosphate Mineral Transformation and Nucleoside Phosphorylation in an Iron- and Cyanide-Rich Early Earth Scenario

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Abstract: Organophosphates were likely an important class of prebiotic molecules. However, their presence on the early Earth is strongly debated because the low availability of phosphate, which is generally assumed to have been sequestered in insoluble calcium and iron minerals, is widely viewed as a major barrier to organophosphate generation. Herein, we demonstrate that cyanide (an essential prebiotic precursor) and urea-based solvents could promote nucleoside phosphorylation by transforming insoluble phosphate minerals in a “warm little pond” scenario into more soluble and reactive species. Our results suggest that cyanide and its derivatives (metal cyanide complexes, urea, ammonium formate, and formamide) were key reagents for the participation of phosphorus in chemical evolution. These results allow us to propose a holistic scenario in which an evaporitic environment could concentrate abiotically formed organics and transform the underlying minerals, allowing significant organic phosphorylation under plausible prebiotic conditions.

Introduction

The environment of present-day Earth bears little resemblance to what it was like 3.8–4.2 billion years ago, the point in Earth’s history when life is thought to have first arisen.^[1] Among numerous differences, the early Earth environment has been speculated to have been highly reducing,^[2,3] with

similarities to Saturn’s moon Titan,^[4] or to be at least sufficiently reducing to allow for robust redox chemistry to take place.^[5] In either case, the majority of organisms living on the modern Earth would have found the prebiotic environment to be poisonous, having evolved along with the changing environment of the Earth.^[6,7] Experiments that simulate prebiotic chemical pathways must take into account the possible environmental conditions present on the early Earth. The work presented here utilizes previous mineral-based phosphorylation pathways^[8] while taking into account a significantly more robust prebiotic scenario in which cyanide and iron are key agents in the origin of organophosphates. We first examine the geochemical aspects by exploring phosphate mineral synthesis and evolution in iron- and cyanide-rich environments. Next, we study the reactivity of these iron phosphate minerals with organic molecules in a urea-rich solvent system. These investigations provide important insight into the general relevance of these environmental conditions while demonstrating the effectiveness of iron phosphates as a source of prebiotic phosphate. In addition, we highlight the vital role that cyanide and its complexes might have played in circumventing the prebiotic “phosphate problem” under reaction conditions that consider the influence of the prebiotic chemistry upon the geochemical and mineralogical setting.

The phosphate problem stems from the fact that organophosphates, major components of all biological systems, have been considered essential prebiotic molecules but integrating phosphate into prebiotic chemical reactions has proven to be problematic.^[9–11] This problem arises from challenges associated with prebiotic reactions for the phosphorylation of organic molecules, and the perception that phosphate was unavailable due to its sequestration in insoluble minerals.^[12] Historically, these issues have been addressed through urea-catalyzed phosphorylation with soluble phosphate salts and minerals.^[13–15] More recently, experimental studies have demonstrated that different pathways can be utilized to create organophosphate species under prebiotic conditions,^[16–21] while eutectic and alternative low-water solvents have been shown to liberate phosphate from insoluble minerals.^[8,22,23] While these results have gone a long way to address the problem of prebiotic phosphorylation, major questions remain regarding whether or not these, or similar, reactions would be compatible with the environments present on the prebiotic Earth. Would these reactions have been thermodynamically favored in certain environments? Can

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new doors to overlooked chemical dynamics in prebiotic environments be opened?

Results and Discussion

On the prebiotic Earth, crustal phosphate was likely more evenly distributed than it is currently found on modern Earth, where it is mostly found in biogenic deposits of apatite minerals. We previously observed that in a plausible prebiotic urea-rich medium containing Mg^{2+} and Ca^{2+} , the preferential phosphate mineral assemblages were not apatites, but instead more mobile phosphate minerals such as struvite ($\text{MgNH}_4\text{PO}_4 \cdot 6\text{H}_2\text{O}$), newberyite ($\text{MgHPO}_4 \cdot 3\text{H}_2\text{O}$), and brushite ($\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$).^[8] On a prebiotic Earth, the deposition of mafic and ultramafic (komatiite) lavas^[24] probably fed the ocean floor and shallow water ponds with magnesium and iron. Such environments, enriched in Mg^{2+} at elevated HCO_3^- concentration (expected in the CO_2 -enriched prebiotic atmosphere), would inhibit the nucleation of apatite,^[25] making it possible that newberyite and struvite were the main phosphate minerals in subaquatic environments.^[26,27] Given the availability of dissolved ferrous iron on the early Earth, it is also likely that iron phosphates were among the mineral assemblages. On modern Earth, iron is mostly fixed in the form of ferric or ferrous–ferric oxides and iron-bearing carbonates, with mobile ferrous iron being found only in trace amounts in anaerobic environments. In contrast, it is likely that iron phosphate minerals, particularly vivianite ($\text{Fe}^{2+}_3(\text{PO}_4)_2 \cdot 8\text{H}_2\text{O}$),^[28,29] were formed by the same processes that led to struvite/newberyite formation on the prebiotic Earth. In addition to these processes, localized environments enriched in phosphate minerals could also be formed as secondary mineral from volcanic phosphate tephra, similar to what is seen on present-day Earth,^[30] or by corrosion of meteoritic iron. Studies have shown that in the absence of Mg^{2+} , vivianite is the most likely mineral precipitate from phosphate even when Fe^{2+} is less abundant than Ca^{2+} .^[19] Due to the affinity of iron upon cyanide, the significant occurrence of vivianite opens up an interesting scenario for the mobilization of phosphate in HCN-rich prebiotic conditions.^[45]

Expanding upon this, we thermodynamically modeled mineral formation under a wide range of pH and redox conditions. We took particular interest in the region of moderate reduction potential in the pH range of 2–10—conditions currently thought to represent the predominant environmental conditions during the Hadean.^[24,31] These calculations show that under likely Hadean conditions, the minerals struvite, newberyite, and vivianite are the likely phosphate sinks in the presence of urea, Mg^{2+} , Fe^{2+} , and Ca^{2+} (Figure 1). Further modeling was done to simulate a wide range of prebiotic conditions exploring the interplay of Mg^{2+} , Fe^{2+} , Ca^{2+} , H^+ , PO_4^{3-} , and CN^- in mineral formation and phosphate availability, showing a pronounced preference for mobile phosphate phases at slightly acidic pH (see the Supporting Information, Figures S1–S4). These Eh–pH diagrams predict that dry–wet cycles and cyanide content could have been essential variables in the prebiotic geochemistry of phosphate. Ionic eutectic solvents, representing low water

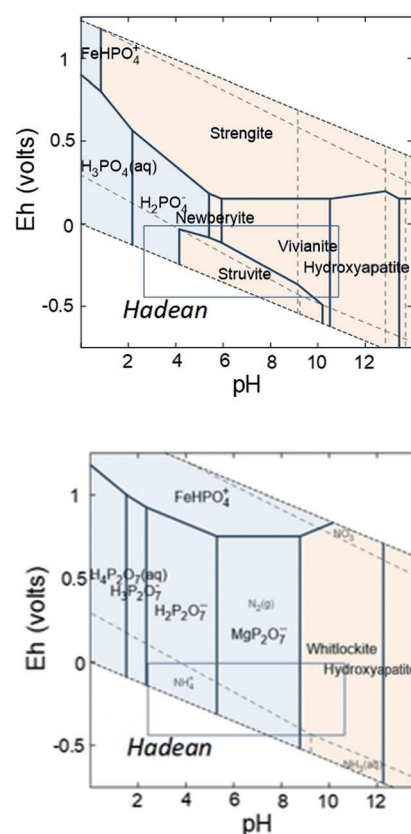


Figure 1. Top: Eh–pH diagram of the phosphate species in a system containing dissolved equimolar Mg^{2+} and Fe^{2+} , including Ca^{2+} $0.2 \times a(\text{Mg}^{2+})$ and NH_3 and CO_2 generated by decomposition of a 10 mM solution of urea in which the total $a(\text{HPO}_4^{2-})$ is 10^{-3} . The predominant mineral phase expected in the estimated redox conditions of a Mg–Fe rich Hadean Earth is vivianite, with struvite expected under reducing conditions and newberyite at $\text{pH} < 6$. An increase in the activity of iron with respect to magnesium leads to the dominance of vivianite. Bottom: A solvent based on ammonium formate and urea, with $a(\text{H}_2\text{O}) < 10^{-5}$, stabilizes the mobile phosphate species, especially pyrophosphate, and the precipitation of whitlockite at higher pH. Phases resulting from autooxidation of vivianite and cyanide incorporation have not been included in this calculation. Orange region: stability of solid phases; blue region: mobile/solution species.

activity environments, are shown to prevent the precipitation of vivianite by rendering it thermodynamically unstable, instead giving rise to more mobile iron phosphate complexes. Furthermore, the presence of cyanide is seen to prevent the precipitation, or corrode existing inventories, of vivianite and other ferrous phosphates through the stabilization of ferrocyanide complexes. The availability of cyanide and the formation of these ferrocyanide complexes is thought to be likely either through atmospheric production of cyanide^[32] directly leading to the formation of ferrocyanide complexes (Figure S4),^[33,34] or through binding with minerals such as phyllosilicates.^[35] These iron cyanide complexes also appear quite important in promoting the availability of phosphate from hydroxyapatites in a similar manner to those seen for vivianite or ferrous phosphates. These modeling studies help to paint a picture where fully sequestered phosphate is unlikely under prebiotic conditions and is instead readily



available for utilization. These thermodynamic predictions guided us to experimentally consider the behavior of iron phosphates and hydroxyapatite as a source of phosphate under prebiotic conditions and how the presence of cyanide could impact phosphorylation under our reaction conditions.

As mentioned above, struvite, newberyite, and hydroxyapatite are likely phosphate sinks on a prebiotic Earth,^[8,12] and have been shown to be effective phosphorylation sources when used with a urea-rich solvent. Along with Mg^{2+} and Ca^{2+} , Fe^{2+} was a major component of the prebiotic hydrosphere,^[36] making it likely that similar minerals would have been formed with Fe^{2+} as the major divalent cation. In order to investigate the formation of ferrous-iron-based minerals and their impact on prebiotic phosphorylation, we synthesized iron phosphate minerals under anaerobic conditions. This synthesis was conducted following protocols that had previously been used to synthesize hydroxyapatite and struvite, but with the divalent cation (Ca^{2+} or Mg^{2+}) replaced with Fe^{2+} . These protocols produced vivianite (Figure S5), and an amorphous iron phosphate mineral lacking any incorporated ammonium (Figure S6a,b). This lack of nitrogen was confirmed through Nessler's test and further supported through modeling, which showed the stability of iron phosphate and could explain the lack of an iron-based struvite analogue in nature (Figure S7).

The prebiotic hydrosphere was also significantly different from that of the modern Earth, free of abundant oxygen and enriched in reduced chemical species. Small lakes and ponds of water were likely enriched in urea, formed through multiple prebiotic reactions,^[37–39] along with formamide and ammonium formate, resulting from the hydrolysis of cyanide and cyanamide.^[40,41] These small bodies of water, through repeated heating and evaporation, could become enriched in these dissolved organics, which would oscillate in compositions and concentrations depending on changing levels of water activity. At some points this could create a viscous, multicomponent solvent during times of particularly low water activity.^[8,22] Thus, the components of this pond would be expected to exist in a dynamic equilibrium upon repeated drying and rewetting with their ratios depending, at any point in time, on the temperature, water activity, and the recent history of the pond. The formation of this low-water-activity solvent would inhibit further loss of some volatile components, including ammonium, formate, and formamide, but might protect some molecules that are labile in high-water-activity mediums.^[8,22,41] The interaction between this urea- and organic-enriched prebiotic milieu and the minerals from the local geosphere were likely a key step in the formation of secondary minerals that have proven to be more favorable for organic molecule phosphorylation.^[8]

When allowed to evolve anaerobically at ambient temperature and in the presence of indirect sunlight, this amorphous iron phosphate mineral phase was observed to crystallize into the mixed-iron-valence phosphate phase beraunite $[(Fe^{2+}Fe^{3+})_5(OH)_5(PO_4)_4 \cdot 4H_2O]$; Figure S6c,d]. The formation of beraunite and vivianite demonstrates that it is possible to create mixed-valence-iron minerals on a prebiotic Earth (without oxygen) through sunlight-driven oxidation in a Schickorr-like reaction, producing H_2 and OH^- from waters

of crystallization.^[42] Previously, a urea-rich solvent composed of urea, ammonium formate, and water initially in a 1:2:4 molar ratio (UAFW) has been shown to promote reactions between mineral phosphate sources and organic substrates, leading to the generation of organophosphates under dehydration conditions with moderate heating.^[8,22] Here, phosphorylation of adenosine in the UAFW solvent was tested under anaerobic, dehydrating conditions, with synthetic vivianite and iron phosphate as phosphate sources along with sodium phosphate monobasic, newberyite, and hydroxyapatite.

LC-MS and ^{31}P NMR analysis were used to distinguish between phosphorylated and non-phosphorylated products from these reactions, with total phosphorylation being quantified by LC-MS (Figures S8–S11). The detailed analysis by ^{31}P NMR spectroscopy shows that all studied phosphate sources produced a similar composition of phosphorylated products dominated by 5'-AMP, 2'-AMP and 3'-AMP, 2',3'-cAMP, phosphorylated adenosine esterified with additional phosphates, and carbamoylated adenosine phosphates expected from urea degradation and formation of isocyanate under our reaction conditions. In spite of the significant formation of pyrophosphate during the reaction, no evidence of formation of pyrophosphate esters (ADP or ATP) was found. These results also demonstrate that pyrophosphate could reach significant concentrations at moderate temperature in a prebiotic pond under dehydration and formation of urea-rich eutectic fluids. All five of our phosphate sources were found to be effective in producing adenosine phosphates, with the ferrous iron phosphate minerals showing reduced yields when compared to their non-ferrous counterparts (Figure 2). In the cyanide-rich environment that could have led to UAFW formation, it is also likely that small amounts of cyanide ions would exist in solution. Cyanide could reach high concentrations in these small pools through evaporation or complexation with metals such as iron. Metal complexation is particularly interesting as it would not only allow for the accumulation of cyanide, but also allow for its slow release from these organic "minerals" to be utilized for key prebiotic reactions.^[33,43,44] Thus, we decided to investigate the possibility that the presence of cyanide ions would further alter the availability of phosphate, perhaps by forming a complex with the iron of the iron phosphate minerals.

We observed that the addition of NaCN (600 mM, in excess to the phosphate sources) to the reactions containing ferrous iron phosphate minerals resulted in a marked improvement in phosphorylation (Figure 2). After 9 days, phosphorylation yields from the synthetic iron phosphate increased almost twofold when compared to the non-NaCN reaction, showing 14% more phosphorylated adenosine. Vivianite showed an even more remarkable change, exhibiting a sixfold increase (15% more phosphorylated adenosine) in phosphorylation yields when NaCN was added, making vivianite a significantly better phosphate source than hydroxyapatite. Sodium phosphate and newberyite showed lower phosphorylation yields when NaCN was added, likely because of the excess sodium present in solution (Figure S12). Intriguingly, phosphorylation using hydroxyapatite with

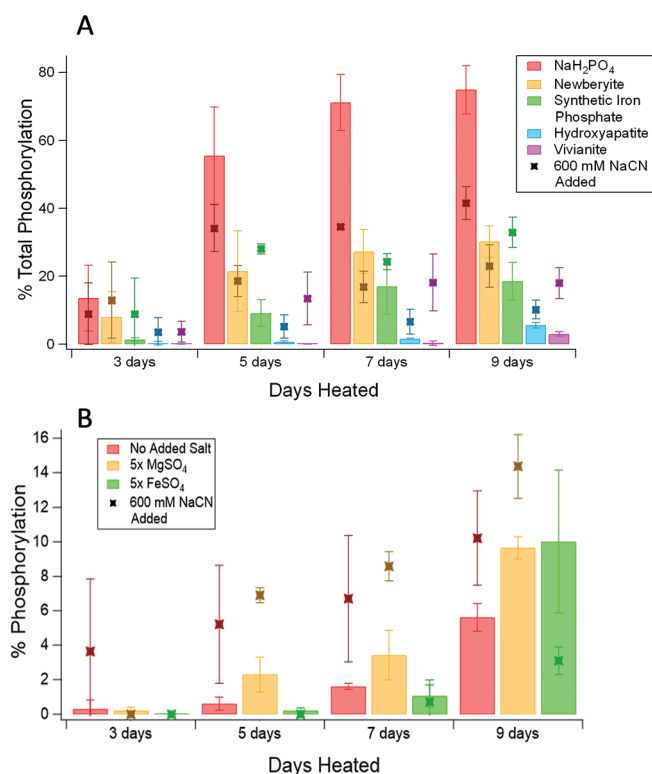


Figure 2. A) Total phosphorylation yields for adenosine reacting with different phosphate sources in a solution of urea, ammonium formate, and water (UAFW) at 85 °C. B) Total phosphorylation yields for adenosine reacting with hydroxyapatite in a solution of urea, ammonium formate, and water (UAFW) at 85 °C. All reactions were run under dark, anaerobic conditions. Samples were rehydrated after day 7.

NaCN increased phosphorylation by approximately twofold, resulting in 5% more phosphorylated adenosine.

Previously, we had demonstrated that the inclusion of MgSO₄ in the UAFW solvent increased phosphorylation from hydroxyapatite by mobilizing the phosphate, which involved the sequestration of some Ca²⁺ as gypsum (CaSO₄·2H₂O).^[8] This result motivated us to investigate if FeSO₄ would have a similar impact. After 9 days, comparable results were, indeed, obtained when hydroxyapatite was incubated in the UAFW solvent in the presence of FeSO₄ (Figure 2B). However, to achieve this level of phosphorylation, the samples containing FeSO₄ required rehydration after 7 days. At that point, these samples were no longer liquid and showed a decrease in phosphorylation compared to the salt-free sample. Following rehydration and two additional days of heating, the samples containing either MgSO₄ or FeSO₄ showed remarkable improvement compared to the 7 day reactions, ultimately showing an almost twofold improvement in phosphorylation of adenosine when compared to the salt-free hydroxyapatite reactions. In addition, increases in phosphorylation yields were observed with the addition of excess NaCN for the salt-free and MgSO₄ reactions, but, interestingly, not for the reactions containing FeSO₄ (Figure 2).

³¹P NMR analysis confirmed the stimulating effect that the addition of NaCN has upon phosphate release, pyrophos-

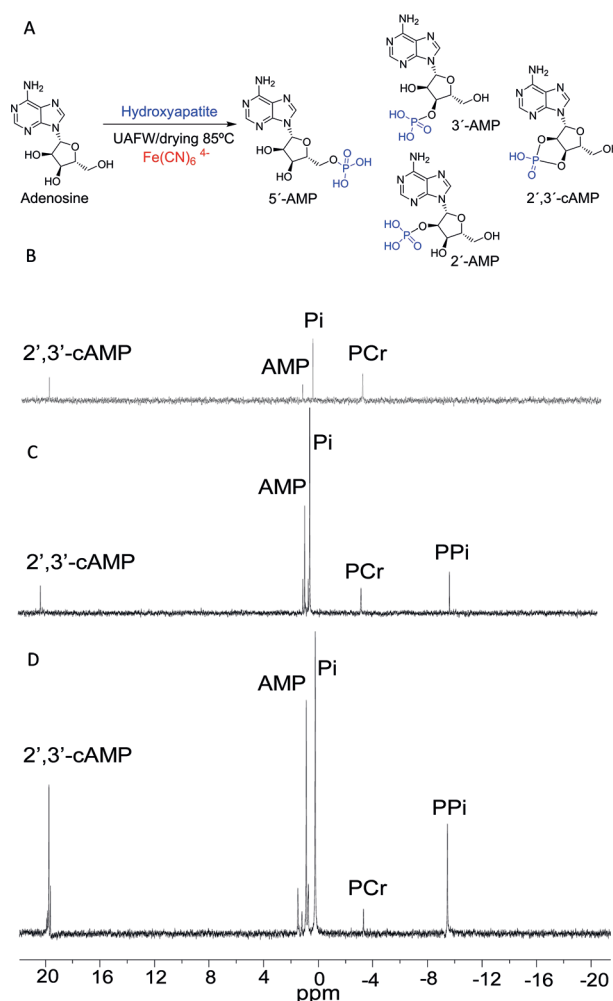


Figure 3. ³¹P NMR analysis of phosphate species for the phosphorylation of adenosine with hydroxyapatite in UAFW solution at 85 °C after 7 days. A) Reaction scheme showing the main phosphorylated species formed. Corresponding multi-phosphorylated and carbamoylated derivatives are also formed (Figure S8). B) Reaction without addition of cyanide species. The AMP label indicates the location of the ³¹P resonances of 2', 3', and 5'-AMP. C) In the presence of 600 mM NaCN. D) In the presence of 100 mM ammonium ferrocyanide. The addition of cyanides leads to increased phosphorylation, correlated with increases in free phosphate (Pi) and pyrophosphate (PPi). PCr: phosphocreatine (5 mM) added as internal standard.

phate accumulation, and adenosine phosphorylation using hydroxyapatite (Figure 3). This result further demonstrates that phosphate mineral corrosion by urea-based eutectics could be an efficient prebiotic source of pyrophosphate (Figure 3B,C) Also, we observed that addition of ferrocyanide salt (sodium, ammonium, or potassium) significantly increases both phosphate release and adenosine phosphorylation, especially when a K⁺ or NH₄⁺ salt was used, suggesting that excess sodium ions could have an inhibitory effect on phosphorylation balance. These adenosine phosphorylation results utilizing a range of phosphate minerals, sulfate salts, and cyanide help to create a picture of the complex factors in a prebiotic environment that could have



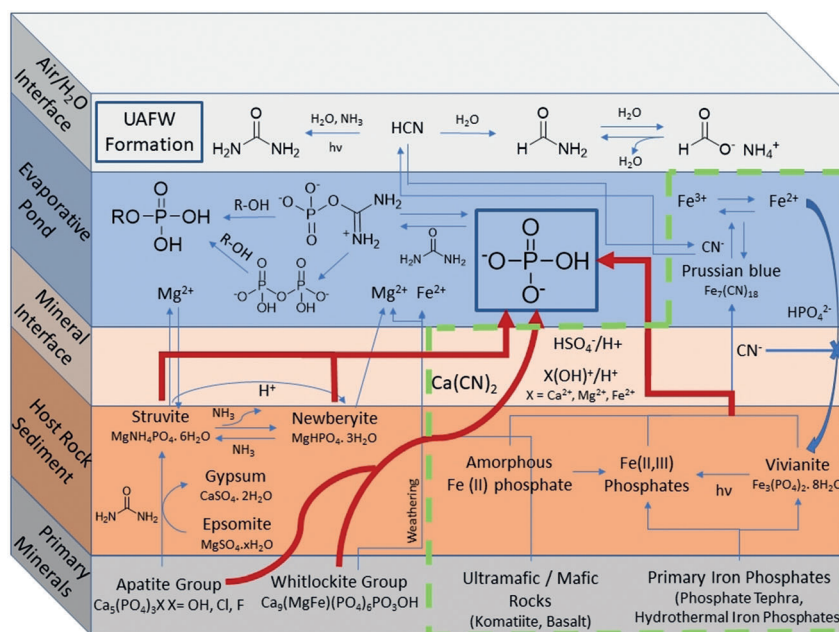
contributed to phosphate mineral formation, corrosion, and organic molecule phosphorylation.

Improved phosphorylation does not seem to be solely due to the presence of Fe^{2+} or the changes in pH of the diluted solution (Figure S13 and Table S1). The increased yields observed with the ferrous phosphate minerals in the presence of cyanide ions (Figure 2) are likely associated with the formation of stable ferrocyanide complexes, as evidenced by the blue color observed in these solutions at day 2 of the reactions (Figure S14). This iron cyanide complex (Figure S15) leads to increased phosphate availability in solution and a subsequent increase in phosphorylation yields. Cyanide is also seen to improve phosphorylation from hydroxyapatite (Figures 2 and 3), which may likewise be due to the formation of $\text{Ca}(\text{CN})_2$ —a complex known to be unstable in water but that we hypothesize to be stable under the low water activity of these reactions. Furthermore, the presence of CN^- stabilizes the eutectic, leading to a higher concentration of urea and formamide after 9 days, which would also favor phosphorylation. In addition, similar complexes are observed with hydroxyapatite when ferrocyanide salts are used as the CN^- source, forming stable calcium ferrocyanide complexes and demonstrating that both free and complexed CN^- can effectively lead to the release of phosphate from apatite minerals, in a system modulated by activities of metal ions and free CN^- (Figure S16).

Our results also point to the role that small amounts of water and divalent cations play in mobilizing phosphate from mineral sources. Fe^{2+} and Mg^{2+} can increase hydrogen ion (H^+) activity by forming $\text{X}(\text{OH})^+/\text{H}^+$ ions (along with $\text{HSO}_4^-/\text{H}^+$ in the presence of sulfate) in low-water-activity solutions.

This increased hydrogen ion activity, along with the formation of CaSO_4 ,^[8] likely leads to the localized corrosion of the hydroxyapatite and iron phosphate minerals, liberating the phosphate for reactivity, but also creating a less stable environment for organophosphates in the presence of sulfate. The results also suggest the ability of these corrosion mechanisms to work cooperatively, ultimately leading to the greatest amount of phosphorylation from hydroxyapatite when ferrocyanide salts or both MgSO_4 and NaCN are present.

By using Raman and ^1H NMR spectroscopy to track the evolution of the UAFW solution while heated at 85°C , we were able to observe the formation of formamide and formamide–urea interactions in solution in the presence of minerals and cyanide species (Figures S17–S19). By incorporating these results, we are able to provide a comprehensive “warm little pond” model for phosphate mineral evolution, UAFW formation, and activated phosphate mobility through a prebiotic geochemical environment (Scheme 1). This model demonstrates how organophosphates can be formed in the evaporative pond scenario through urea-catalyzed phosphorylation using solvents containing water and molecules derived from HCN and water, as well as Mg^{2+} , Ca^{2+} , and Fe^{2+} from both primary and secondary minerals. One fundamental issue addressed in this multilayer interface model is the inherent generation of a cyanide reservoir, which is necessary to form urea and formate.^[32,38] Free cyanide, according to simulations, reached atmospheric mixing ratios in the ppb range,^[32] making it difficult to utilize it as a prebiotic agent for robust chemical synthesis. However, on a prebiotic world with abundant mobile iron in the hydrosphere, the formation of



Scheme 1. Path of phosphate through the geosphere and hydrosphere. The input of HCN from atmospheric or extraterrestrial sources drives the formation of unique prebiotic mineral assemblages. Secondary amorphous iron phosphate and vivianite, formed by precipitation of mobile Fe^{2+} or by the alteration of primary phosphates in the host rock, release phosphate in the presence of cyanide-forming Prussian blue. In turn, this complex could act as a CN^- reservoir, leading to the localized concentration of CN^- and the formation of urea-based solvent components. This mixture helps to corrode apatite and modify the mineral assemblages by inhibiting the precipitation of iron phosphates or corrosion of previously formed phosphates. The area outlined in green is the focus of this study.

iron cyanide complexes, or iron cyanide containing organic “minerals”,^[43] could act to create a large cyanide reservoir. Furthermore, we demonstrate that ppb concentrations of CN⁻ are enough to stabilize iron cyanide complexes and destabilize the iron phosphate mineral phase (Figure S2). These cyanide reservoirs could slowly release cyanide to the environment through ion exchange, driving not only the production of urea, formamide, ammonium formate, and other organics, but also making phosphate available for the formation of organophosphates. We argue here that phosphate would have been highly mobile in a moderately reducing prebiotic environment and would have been readily available for incorporation into organic molecules.

Conclusion

Overall, these results demonstrate that iron phosphate minerals were likely significant components of the prebiotic mineral inventory, and that they could be readily utilized to generate organophosphates under evaporative conditions. What is particularly interesting is the role that cyanide is seen to play in promoting these reactions. Not only does the cyanide ion help to promote phosphorylation from iron phosphate minerals and iron-containing solutions, but it also promotes phosphorylation with hydroxyapatite—a mineral with no iron present. In fact, the presence of iron cyanide complexes, which is more likely in a prebiotic scenario than large cyanide concentrations, improves the overall yield of organophosphates when compared to FeSO₄-containing and salt-free reactions. These remarkable results expand the roles that cyanide and iron may have played on an early Earth from a simple source of vital organic molecules to a possible catalyst in mineral transformations and phosphate utilization. Finally, these results demonstrate that the “warm little pond” envisioned by Charles Darwin may have actually been a beautiful Prussian blue in color, rich with organics working together with the local minerals to generate organic “minerals”, organophosphates, and other essential components of the prebiotic soup.

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Conflict of interest

The authors declare no conflict of interest.

Keywords: cyanide · origins of life · phosphate minerals · phosphorylation · prebiotic chemistry

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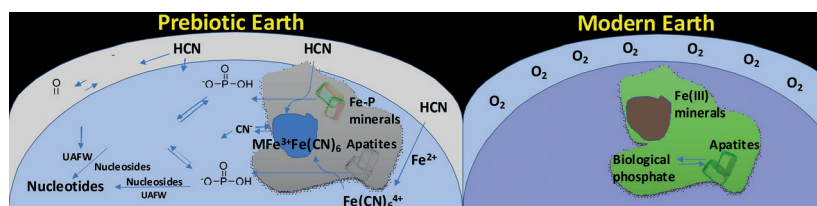
Research Articles



Prebiotic Chemistry

B. Burcar, A. Castañeda, J. Lago,
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A Stark Contrast to Modern Earth:
Phosphate Mineral Transformation and
Nucleoside Phosphorylation in an Iron-
and Cyanide-Rich Early Earth Scenario



Iron and cyanide: A new role is proposed for cyanide as a geochemical agent in promoting prebiotic phosphorylation. Cyanide and its metal complexes can transform and mobilize phosphate from

its insoluble iron and calcium minerals, suggesting that phosphate could have been more mobile and prebiotic phosphorylation not as challenging as previously believed on the early Earth.