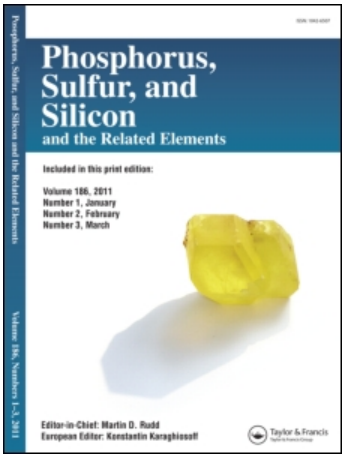

Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Penta-Coordinate Phosphorus Compounds and Biochemistry

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Online publication date: 27 October 2010

To cite this Article Zhao, Yu-Fen , Han, Bo , Chen, Jing and Jiang, Yang(2002) 'Penta-Coordinate Phosphorus Compounds and Biochemistry', Phosphorus, Sulfur, and Silicon and the Related Elements, 177: 6, 1391 — 1396
To link to this Article: DOI: 10.1080/10426500212228
URL: http://dx.doi.org/10.1080/10426500212228

Phosphorus, Sulfur and Silicon, 2002, Vol. 177:1391–1396

1042-6507/02 $12.00 + .00
DOI: 10.1080/10426500290093739

PENTA-COORDINATE PHOSPHORUS COMPOUNDS AND BIOCHEMISTRY

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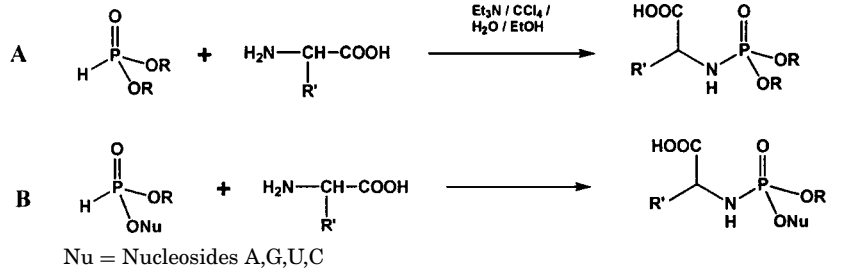
(Received July 29, 2001; accepted December 25, 2001)

In the human body, the phosphorus element amounts to only 1%, of body weight and most of it present in the bones and teeth. However, phosphorus plays very important role in biochemistry. With about 9% phosphorus by weight, DNA, the genetic information material is built up by phospho-diester bond as backbone. Some of the cell functions are regulated by phosphorylation and dephosphorylation of proteins. ATP is one of the most important molecules. Many biochemistry procedures such as necleotide transfer and protein synthesis are ATP dependent.

The clarification of the role of phosphorus chemistry in all these biological phenomenon is one of the most exciting field. Penta-coordinate phosphorus intermediates have been widely proposed. In this lab, some models have been synthesized to study the penta-coordinate phosphorus chemistry.[1–4]



SCHEME 1 Two model compounds used to study the penta-coordinated phosphorus. A. N-dialkyl-phosphoryl amino acids; B. conjugates of nucleosides and amino acids.

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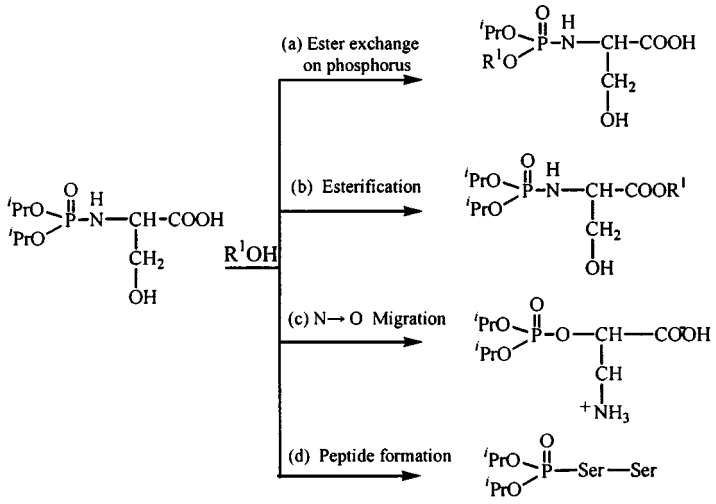
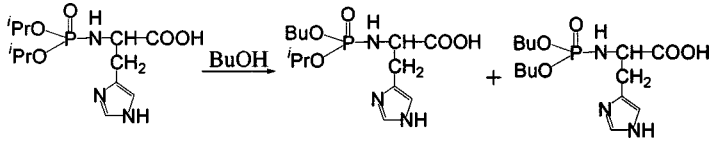
It has been found that N-dialkyl-phosphoryl amino acids have some special reaction activity, such as ester exchange, on phosphorus, esterification, N to O migration, and peptide formation[5–7] (Scheme 2).



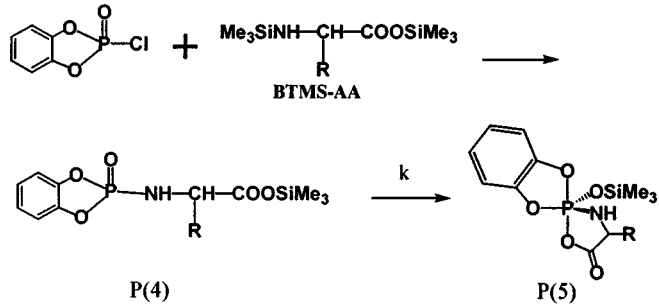
SCHEME 2 Reaction activity of N-diisopropylphosphoryl serine.

To further study these reactions, it was found that penta-coordinate phosphorus intermediate might play a very important role. For example, N-diisopropylphosphoryl histidine (DIPP-His) has been found to be reactive in the presence of butanol and formed mono- or di-ester exchange products (Scheme 3). While under the same reaction condition, N-diisopropylphosphoryl histidine methyl ester (DIPP-His-OMe) was inert. Therefore, a C-terminal carboxyl group assisting penta-coordinate phosphorus intermediate was proposed.



SCHEME 3 Ester exchange reaction of DIPP-His in presence of butanol.

To trap the penta-coordinate phosphorus intermediate, different silicon-protected penta-coordinate phosphorus amino acids were synthesized through the following procedures and studied by ^{31}P NMR (Scheme 4, Figure 1). It was found that histidine, serine thereonine,



SCHEME 4 Synthesis of silicon-protected penta-coordinate phosphorus amino acids.

and aspartic acid were the most reactive ones for the P(4) to P(5) transformation. In fact, within 10 min, at 25, P(4) histidine was completely transferred into P(5) histidine. P(4) α-alanine can be converted into P(5) α-alanine within 30 min, while the P(4) β-alanine stayed at P(4) forever.[8]

With the activation of amino acid by penta-coordinate phosphorus, peptide was formed, which has been supported by HPLC and FAB mass spectrometry (Figure 2).[9]

The activation of amino acids by penta-coordinate phosphorus provides some clue on the prebiotic evolution. During the study of peptide formation through phosphorus activation, we found that all of the reactions mentioned above for a amino acid did not occur to β-alanine[10] (Figure 3).

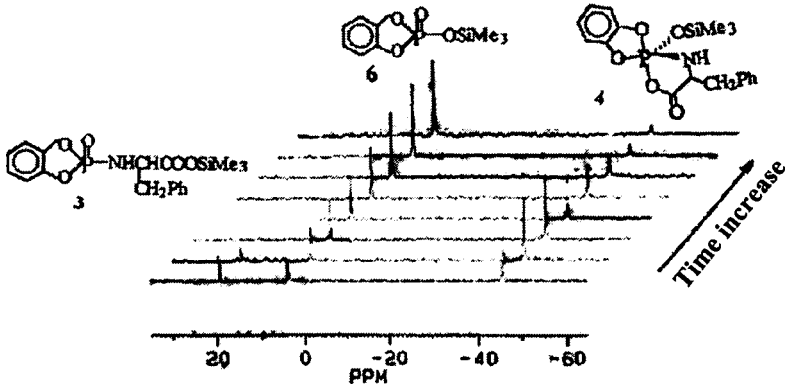


FIGURE 1 ^{31}P NMR stacked files of penta-coordinate phosphorus phenylalanine.

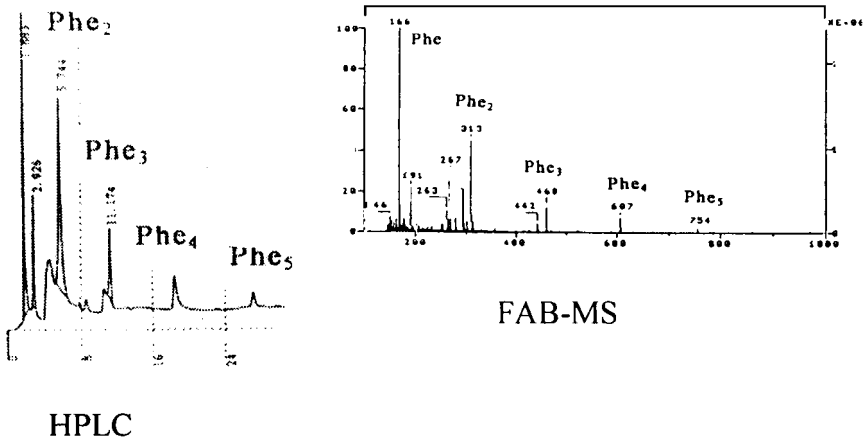


FIGURE 2 Peptide formation of penta-coordinate phosphorus-activated phenylalanine. HPLC (left) was operated on 254 nm.

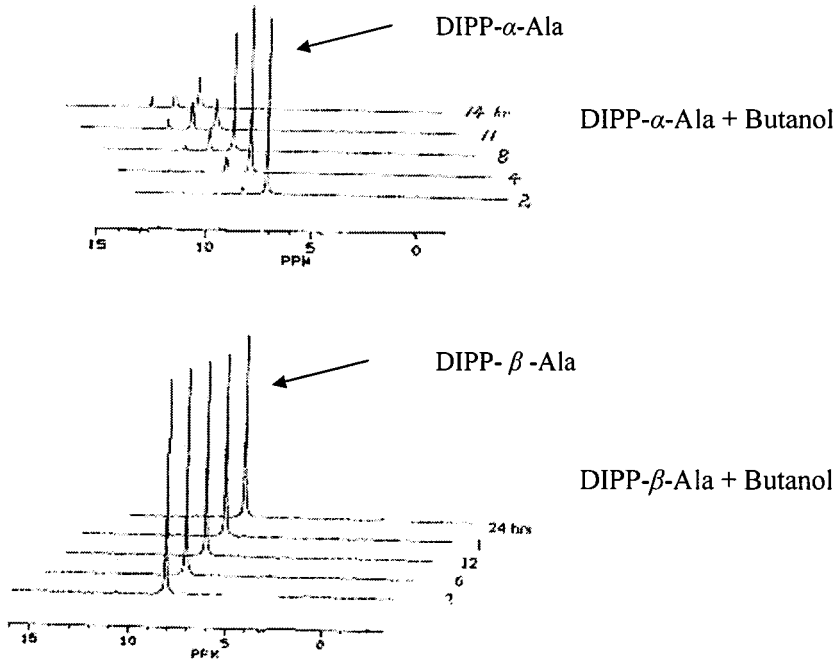
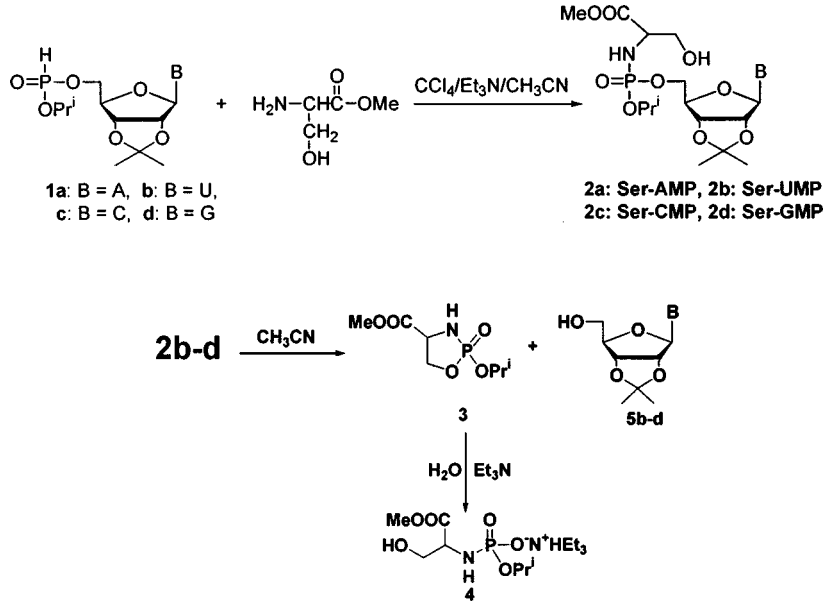


FIGURE 3 ^{31}P NMR stacked files of ester exchange reaction of DIPP-α-Ala and DIPP-β-Ala with butanol.

With the molecular modeling study of two series compounds of A and B (Figure 4), it was found that the reactivity difference resulted from the penta-coordinate phosphorus intermediate, in which a five-membered ring intermediate for a amino acid is energetically more favorable than a six-membered ring intermediate for β-alanine. The differentiation of α and β amino acid by N terminal phosphorylation might give us some clue on why the nature chooses α amino acid.

Some special phenomenon also presented in the conjugates of nucleosides and amino acids, which go through the penta-coordinate intermediate. Dephosphorylation could occur easily in the presence of base for the serine conjugation with UMP, CMP, and GMP but not for the serine conjugation with AMP.[11]



SCHEME 5 Recognition of UMP, CMP, and GMP from AMP by serine conjugation.

The recognition of UMP, CMP, and GMP from AMP by serine conjugation might explain some biological phenomenon, such as the nucleotide transfer and nucleic acid shuffling.

In conclusion, the participant of amino acids and/or nucleoside to the penta-coordinate phosphorus chemistry is highly chemical, stereo selective, and energetically favorable. The penta-coordinate phosphorus chemistry might play very important role in some biological phenomenon.

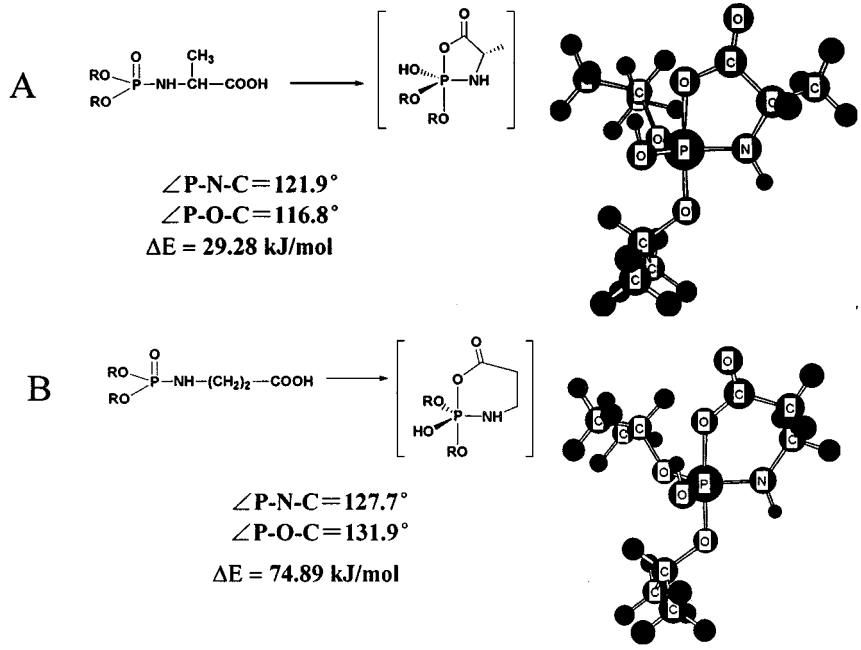


FIGURE 4 Molecular modeling of the penta-coordinate intermediate of DIPP-α-alanine and DIPP-β-alanine.

ACKNOWLEDGMENTS

The authors would like to thank the Chinese National Natural Science Foundation (No. 29632004, No. 39870415), the Ministry of Science and Technology, for their financial support.

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