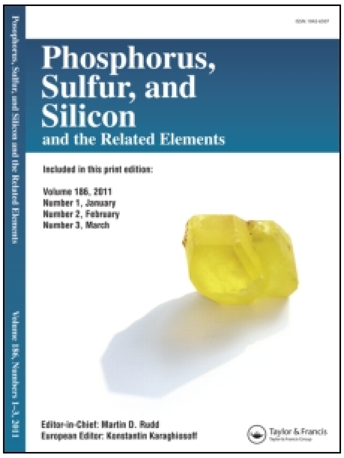

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Phosphoryl Group Participation Reaction is the Key to the Life Chemistry

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PHOSPHORYL GROUP PARTICIPATION REACTION IS THE KEY TO THE LIFE CHEMISTRY

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Abstract Novel chemical properties of the N–phosphoaminoacids were varied with their side chains′ functions. A hexa coordinate phosphorus intevmediate was proposed.

INTRODUCTION

It is known that DNA is the genetic storage system, in which the information of life has been passed from one generation to another. For the purpose of keeping stable species the DNA structurally must be very stable. On the other hand, the RNA plays the role of conducting the protein synthesis which delicately regulates the whole metabolic process. Due to this speculation, the daily ATP turnover amount is his or her body weight. It indicates that one extra hydroxyl group presence in RNA makes it much more reactive than the DNA. This reactivity enhancement must be originated from the participation of the phosphoryl group.

RESULTS

In addition, it has been confirmed that the activities of many enzymes are regulated through phosphorylation–dephosphorylation mechanism in which the phosphoryl group participation reaction executes the vital role.

In this paper, it is showed that when the stable amino acids were N–phosphorylated, they became reactive and derived into many types of products. Depending on the side chain′s difference, their chemical properties were varied as following:

(a). **For simple alkyl side chain amino acids,**such as alanine, proline, their N–phosphorylated derivatives′ reactivities are dependent on the size of the alkoxyl group substituted on the phosphorus. For example, there were elongation reaction to form the amide (1), ester exchange on the phosphorus (2) and the esterification (3) reactions happened for R = nButyl, but not for R = iPr

$$(RO)_2\text{–}P(O)\text{–}NH\text{–}CH(CH_3)\text{–}COOH \xrightarrow{R'OH}$$

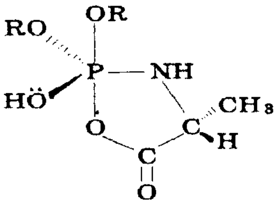
$$(RO)_2\text{–}P(O)\text{–}NH\text{–}CH(CH_3)\text{–}C(O)\text{–}NH\text{–}CH(CH_3)\text{–}COOH \qquad (1)$$

$R = nBu$

$$(RO)(R'O)\text{–}P(O)\text{–}NH\text{–}CH(CH_3)COOH \qquad (2)$$

$$(RO)_2\text{–}P(O)\text{–}NH\text{–}CH(CH_3)\text{–}C(O)OR' \qquad (3)$$

These reactions must pass through the intramolecular phosphoryl–carboxyl mixed anhydride intermediate in which the phosphoryl group participation is indispensable. Because the corresponding Cbz–, Boc– or the sulfonyl protected amino acids were inert under the same conditions.



(b). **For the hydroxyl amino acids,** such as the serine and threonine, except the (1–3) reactions, there were also the N O phosphoryl group migration, together with the ester exchange on the phosphorus atom (4) even for R = iPr.

$$(R^1O)_2P(O)\text{–}NH\text{–}CHR(CHOH)\text{–}COOH \;\; R^2OH$$

$$(R^1O)(R^2O)P(O)\text{–}O\text{–}CH(R)\text{–}CH(NH_2)\text{–}COOH \qquad (4)$$

When the serine methyl ester was N–phosphorylated, it became an inactive compound. Also, the N–phosphoryl–r–hydroxyl proline (Fig.1), although with the presence of three groups: phosphoryl, hydroxyl and carboxylic, is stable at 40 ° , and there were no reactions (1–4) occurred at all. It implys that the molecule has to be in a proper conformation for a ″THREE POINTS CONTACT″

which could be the plausible mechanism proceeded in the active sites of the enzymes.

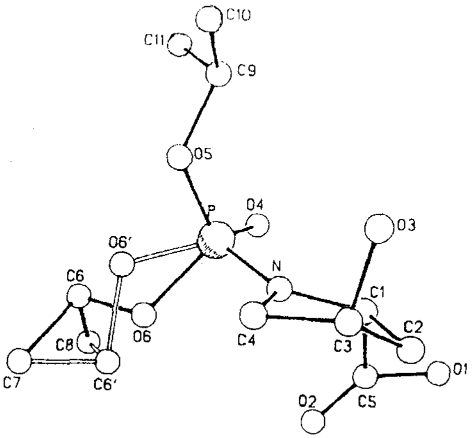
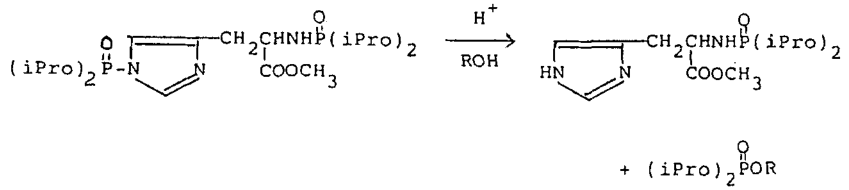


Fig.1 X–ray structure of N–DIPP–Hydroxyl–proline

(c). **For the basic amino acid histidine,** there was also reactions (1–3) happened. In addition, there was inter–molecular phosphoryl group migration reaction from the N, N–bis–phosphoryl histidine to the media alcohol (5). which is similar to the function of the phosphoryl histidine in the phosphoryl transferase enzyme.



(d). **For the acidic amino acid,** Aspartic acid, it was extremely reactive, that there were many further reactions followed the reactions (1–3). Through the model study, it showed that both free α– and β– COOH groups were necessary for the self–activation. However, its homologue Glutamic acid, after N–Phosphorylated gave a very stable compound which only proceeded very slightly ester exchange reaction (2) with no (1) nor (3) to take place. It is amazing that one methylene unite will make such tremendous difference.

$(iPrO)_2P(O)\text{–}NH\text{–}CH(CH_2COOH)\text{–}COOH$ very reactive
N–DIPP–Asp

$(iPrO)_2P(O)\text{–}NH\text{–}CH(CH_2CH_2COOH)\text{–}COOH$ very stable
N–DIPP–Glu

In conclusion, the three types amino acids, hydroxyl– basic– and acidic–amino acids are important for composing of the active site the enzyme. But they are not reactive themselves. The so called "PHOSPHORYLATED ENZYME IS ACTIVE" is due to the participation of the phosphoryl group to push the reactions (1–5) to happen in the "ACTIVE SITE". In other words, phosphoryl group participation reaction is the KEY to the life chemistry.

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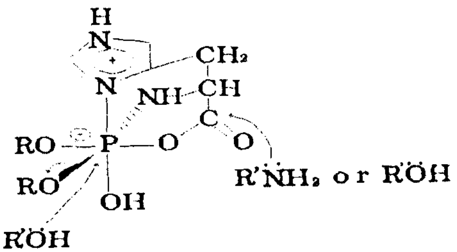

Dipp-His-His-OH

Dipp-His-His-His-OH