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Synthesis of Analogs of Phosphoamino Acids and their Biomimic Reactions

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Abstract: In order to further confirm the biomimic properties of N-phosphoamino acids. A series of model compounds, analogue of phosphoryl amino acids, were synthesized and their biomimic mechanism was also investigated by NMR and MS methods. The results indicated that the reactivity of phosphoryl biological small molecules was depended on the configuration, function groups and positions.

Keywords: Synthesis, analogs of phosphoamino acid, biomimic reaction.

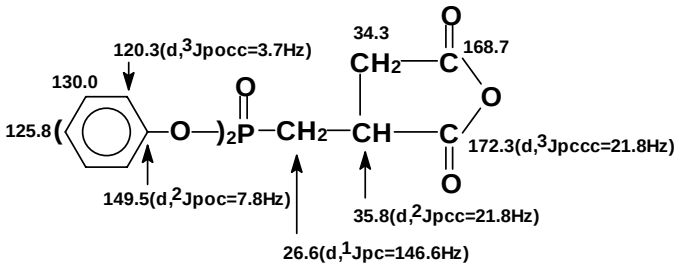
Previously it was found that phosphoamino acids could stimulate many interesting bioorganic reactions[1-3]. In order further to confirm the significance of phosphorus in biochemistry, two model compounds, analogue of phosphoryl amino acids containing P-C bond and phosphoryl glucoamino acids, were synthesized. Their reactions with alcohol and amino acid were also investigated by NMR and MS methods. The results indicated that the reaction characteristics of phosphoryl biological small molecules were dependent on the configuration, function groups and positions.

(O, O-biphenyl phosphinyl-methylene)-butanedioic anhydride **1** was synthesized by the reaction of itaconic acid and triphenyl phosphite [4, 5].

N- (O, O-diisopropyl) phosphoryl glucoamino acid **2** was synthesized *via* the reaction of 2-amino-2-deoxy-glucoamino acid with diisopropyl chlorophosphite [1, 6-7].

The structure of **1** was established as (O, O-diphenyl phosphinyl methylene) butanedioic anhydride (**Figure 1**). ^{13}CNMR data were showed in **Fig**.1. In our knowledge, both **1** and **2** are new compounds.

Figure 1. The structure of **1** and its ^{13}CNMR spectral data (coupling constants, Hz)



Chemical Properties: Exchange reaction with n-BuOH: Compound **1** or **2** were added into n-BuOH and kept for one day as the literature [2], and then the reaction mixtures were detected for the exchange products by using ^{31}PNMR spectrum and FAB-MS. The result showed that exchange products were only found in the reaction of compound **2**.

Reaction with amino acid: **1** reacted with amino acids or amino acid esters under the same conditions[2-4]. The reaction mixture was detected by FAB mass spectrum and indicated no peptide formation.

Conclusion

The investigation showed that the chemical properties of analogs of phosphoamino acid with P-C and P-N bonds are very different. The results indicated that the reaction characteristics of phosphoryl biological small molecules not only depended on the configuration, function groups and positions, but also depended on the kind of linked atoms. Further investigations are in progress.

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References and notes

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5. **1**: m.p. 107-108°C. EI-MS (m/z): 346 [M^+]. Element analysis: Found C 58.93, 58.84, H 4.44, 4.49% (Calculated for $C_{17}H_{15}O_6P$, C 58.93%, H 4.34%). IR ν^{KBr}: 1843, 1787 cm^{-1} (anhydride bond). ^{1}HNMR ($CDCl_3$, TMS as internal standard.): δ ppm: 3.59 (m, 1H, CH), 3.31 (dd, 1H, Jgem = -19.0, J=9.8Hz), 3.10 (dd, 1H, Jgem=-19.0, J=7.9Hz, CH_2CO), 2.83 (ddd, 1H, $^2J_{P-H}$ =19.0, Jgem = -5.6, J=3.0Hz), 2.38 (ddd, 1H, $^2J_{P-H}$=17.0, Jgem=-5.6, J=10.9Hz, CH_2PO), 7.12 (m, 10H, ArH). ^{31}PNMR (decoupling) δ ppm: 22.10.
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7. **2**: HRMS: $[M-H]^-$ m/z: 358.1264 ($C_{12}H_{26}O_9NP$-H, calculated value: 358.1267). FAB-MS m/z: 358 $[M-H]^-$, 316 [M-iso-Pr-H]$^-$, 273 [M-2 x iso-Pr-H]$^-$, 194 $[C_6H_{13}O_6N-H]^-$, 181 $[(iso\text{-}Pro)_2PONH]^-$. ^{31}PNMR (decoupling) δ ppm : 7.36
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