

A CONVENIENT SYNTHESIS OF PHOSPHOENOLPYRUVATE VIA SILYL-ESTER INTERMEDIATE¹⁾

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Summary: Phosphoenolpyruvate was synthesized in high yield by a simple procedure starting from pyruvic acid and dimethyl trimethylsilyl phosphite through trimethylsilylation, bromination, and the Perkow reaction.

The concept of "high energy phosphate bond" was originally proposed by Lipman in 1941.²⁾ Several types of high energy phosphates such as phosphoenolpyruvate (PEP), phosphocreatine, and acetyl phosphate were listed. They make a role of phosphate-transfer reaction involving ATP synthesis in biological systems Cramer³⁾ has studied 'Zur Chemie der energiereichen Phosphate' and proposed several types of compounds as phosphorylating agents. One of the interesting high energy phosphates is PEP since it has the highest free energy difference of hydrolysis ($\Delta G^\circ = -14.8$ Kcal/mole). While several synthetic routes to the esters of PEP have been developed,⁴⁾ the synthesis of naturally occurring unesterified PEP has not yet been achieved in satisfactory yields (< 50%).^{4,5)}

This paper describes a convenient synthesis of PEP by the Perkow reaction using silyl phosphites which are versatile agents in the synthesis of organophosphorus compounds.¹⁾ The most important subject of the synthesis of PEP by the Perkow reaction is the selection of the starting materials, both α -halopyruvic acid derivatives and phosphites, since the reaction is known to afford generally an enol-phosphate (the Perkow reaction product) and/or a phosphonate (the Arbuzov reaction product). Tris(trimethylsilyl) phosphite seems to be useful but it can not be employed in this reaction because it affords not only the desired PEP silyl esters but also 1,2-carbonyl addition products as described previously.⁶⁾ After several screenings, it was found that pyruvic acid and dimethyl trimethylsilyl phosphite were the most suitable starting materials for this purpose.

When pyruvic acid was allowed to react with trimethylsilyl chloride (TMSCl) (2.2 equiv.) and triethylamine (2.2 equiv.) in the presence of a catalytic amount (0.017 equiv.) of 4-dimethylaminopyridine⁷⁾ in dry benzene under reflux for 2 h, trimethylsilyl 2-trimethylsilyloxy-2-propenoate (1) (bp. 88-92°) was obtained and purified by distillation in 91% yield. Compound 1 was treated with one equiv. of bromine in methylene chloride at -78°.

