

# Synthesis of Phosphoanhydrides by Selective Reaction of Phosphoramidites with Phosphates

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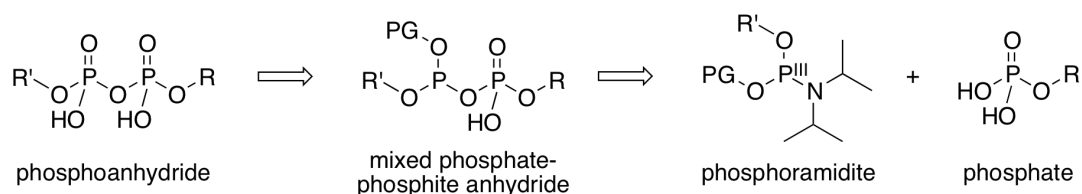
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Due to their high importance in biology, phosphoanhydrides and their preparation have thoroughly been investigated in organic chemistry<sup>1</sup>. The synthesis of an important range of compounds containing such functions however remains challenging, and despite the development of a multitude of procedures for their preparation, the quest for fast and high-yielding methods of universal applicability is still going on.



One of the several methods to build up such bonds is the use of P<sup>III</sup> chemistry as it is commonly in practice for the synthesis of nucleic acids<sup>2</sup>. It was found recently in our group that phosphoramidites react selectively with phosphates in appropriate conditions. Thus, other nucleophilic functional groups do not necessarily need to be protected as it was generally presumed. This finding was adapted for a straightforward preparation of ATP from ADP and adenosine tetraphosphate from ATP in a one-pot procedure.

The synthetic pathway using P<sup>III</sup> chemistry is interesting since it allows the preparation of ATP analogs from the protected mixed phosphite-phosphate anhydride intermediate. Instead of being oxidized, this compound can be treated in situ with sulfurizing reagents to yield  $\gamma$ -thiophosphate ATP whereas direct deprotection leads to an H-phosphonate analog of ATP. Both these compounds are of interest in chemical biology, for example to introduce modifications of phosphate groups on proteins<sup>3</sup>.

The reaction sequence will possibly allow the synthesis of longer phosphate chains that play an interesting role in biology<sup>4</sup>. Another planned step will be the adaption of this procedure for the preparation of still difficultly accessible sugar nucleosides or of dinucleotides with polyphosphate linkers of various length.

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