

THE THREE-PHASE TEST: THE CONANT-SWAN REACTION

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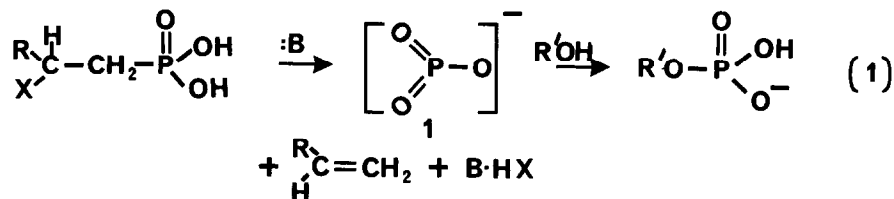
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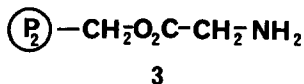
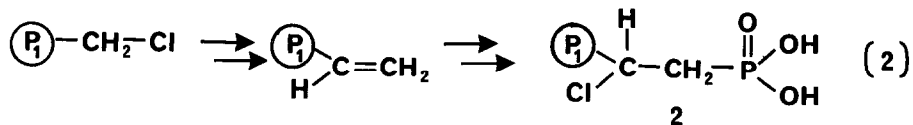
(Received in USA 29 June 1977; received in UK for publication 7 July 1977)

The phosphorylations observed during the base-induced decomposition of  $\beta$ -halo phosphonates (the Conant-Swan reaction<sup>1</sup>) may proceed by direct nucleophilic attack on the phosphorous or via the intermediacy of the monomeric metaphosphate ion, **1**. While reasonable arguments<sup>2</sup> and experimental data<sup>3</sup> are in accord with the indicated mechanism (eq. 1), detection of an intermediate would strengthen the postulate that these reactions generate **1**. Reactive intermediates

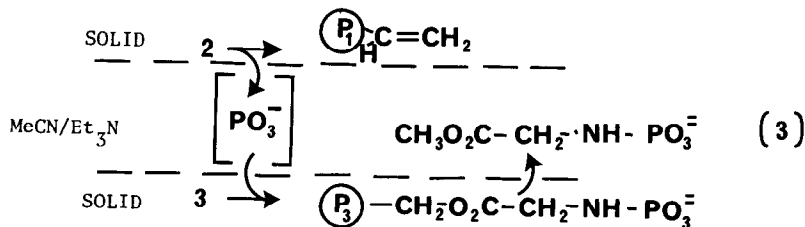


in other phosphate transfer reactions have been exposed using three-phase methods<sup>4</sup> and here we report application of this technique to the Conant-Swan reaction.

The polymer-bound phosphonate **2**, (eq. 2) was prepared by successive treatment of chloromethylated, 2% crosslinked polystyrene (Merrifield's resin) with  $\text{Ph}_3\text{P}$  and  $\text{H}_2\text{CO}/\text{NaOH}$ <sup>5</sup>, followed by  $\text{PCl}_5$  and then hydrolysis<sup>6(1d)</sup>. Merrifield resin beads of a different mesh were used to prepare the glycine derivative **3** following the established methods of solid phase peptide synthesis.



Suspension of the two solid phases in MeCN containing triethylamine resulted in phosphorylation (56% phosphate transfer in 4 hrs) of the polymer-bound amine. Separation (by screening) and transesterification (MeOH/Me<sub>2</sub>N-(CH<sub>2</sub>)<sub>2</sub>OH) liberated the methyl ester of glycine N-monophosphate, identical with an authentic sample (eq. 3).



The monophosphorylation of **3** requires an intermediate in solution since direct reaction of the two solid phases does not occur. The present experiment does not permit the assignment of a unique structure to the actual phosphorylating agent even though the intermediate exhibits the behavior expected for monomeric metaphosphate.<sup>7</sup> The recent isolation<sup>8</sup> and characterization<sup>9</sup> of a metaphosphate derivative underscores the importance of these species in phosphate transfer reactions.

**Acknowledgements** - Acknowledgements are made to the Petroleum Research Fund administered by the American Chemical Society and to the National Institutes of Health for support of this work.

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