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A Novel Method for the Synthesis of Acetyl Phosphate

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A facile method for the synthesis of acetyl phosphate by a reaction of 2-hydroxypropylphosphate with acetic acid is described.

Keywords Acetyl phosphate; 2-hydroxypropyl phosphate; propylene oxide

INTRODUCTION

Many enzyme-catalyzed reactions consume adenosine triphosphate, which is regenerated by Acetyl Phosphate (AcP).^{1,2} Various methods for the synthesis of AcP are known.^{3–11} To obtain AcP, the acetylation of phosphoric acid or its potassium salts with acetic anhydride is most frequently used.

RESULTS

Now, I would like to report the preparation of AcP by the use of 2-Hydroxypropyl Phosphate (2-HPP) as the starting reagent. The vicinal hydroxy esters of phosphoric acid are known to hydrolyze in an acid medium with phosphoryl group migration.¹² A mechanism characterized by the release of the respective diol has been proposed.¹³ 2-hydroxy esters of oxophosphoric acid have been used in the phosphorylation of glucose, deoxynucleosides,^{14,15} and glycine.¹⁶

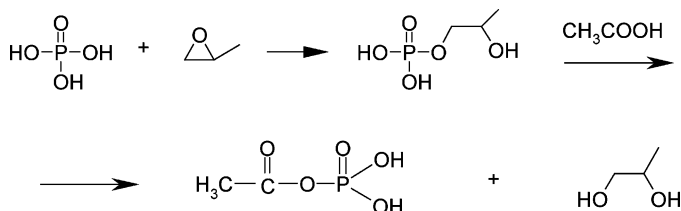
The reported preparation of AcP is performed without the use of any solvent and proceeds in two stages—the formation of 2-HPP and the reaction of the latter with acetic acid, according to Scheme 1.

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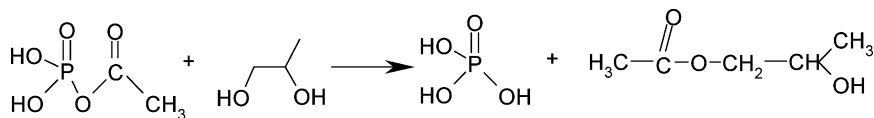
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SCHEME 1

The removal of excess propylene glycol is necessary to avoid a further reaction with AcP, leading to the formation of 2-hydroxypropyl acetate, according to Scheme 2, which has been proved by gas-chromatography with a standard compound. The acetyl phosphate thus produced may be directly used or stored by a transformation into its dilithium salt.



SCHEME 2

EXPERIMENTAL

Acetyl Phosphate

One mole of H_3PO_4 (anhydrous) was treated with 1.3 mol of 1,2-propylene oxide. As the reaction was exothermic, a temperature of 20°C was maintained by the use of a water bath. To the resulting oily product one mole of AcOH was added. The characteristic smell of AcOH disappeared in about 15–20 min. The formation of AcP in the reaction mixture was monitored by ^1H NMR spectroscopy in DMSO. Immediately after the addition of acetic acid to 2-HPP, the NMR spectrum of the reaction mixture exhibited the signal at 1.91 for the CH_3 group of AcOH. This signal disappeared, and a dublet at 1.94 with $J_{\text{H,P}}$ 1.7 Hz was observed instead 20 min after mixing. The latter signal was assigned to the methyl protons in AcP. The transformation was quantitative. The oily product thus obtained was washed with diethyl ether to eliminate propylene glycol and was stored in the presence of P_2O_5 under reduced pressure. Gas-chromatography: Carlo Erba 4100, HP-5 column, $25\text{ m} \times 0.32\text{ mm} \times 0.52\text{ }\mu\text{m}$ film thickness.

^1H -NMR (DMSO, Bruker DRX-250): δ 1.84 d, 3H, $J_{\text{H,P}}$ 1.7 Hz, $\text{CH}_3\text{C}(\text{O})$; ^{13}C -HMR: δ 172.7 $\text{CH}_3\text{C}(\text{O})$; ^{31}P -NMR (101.26 MHz): δ 7.2; IR (Bruker IFS 113v, in layer) ($\text{P}=\text{O}$) 1271 cm^{-1} , ($\text{C}=\text{O}$) 1754 cm^{-1} .

Dilithium Acetyl Phosphate

The AcP was dissolved in a 1:1 ice:water medium and was potentiometrically titrated with 1N LiOH. Intensive hydrolysis with pH 2.6 was observed. Titration went up to pH 8.6. About 25% of the AcP was lost in hydrolysis, as calculated by comparing the amount of phosphoric acid used in the reaction and the equivalents of LiOH used in titration. The deposit formed during titration were discarded, and the filtrate was added to an equal volume of EtOH. After cooling, dilithium acetyl phosphate crystallized. It was separated by filtration, washed with ethanol and diethyl ether, and vacuum-dried. An enzyme analysis of the dilithium salt thus prepared showed the presence of 60% pure acetyl phosphate.

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