

Development of a method of synthesis of trimethyl ester of phosphonacetic acid

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Abstract

In the recent years the methods of synthesis and biological activity of phosphorus-containing analogues of biogenic carboxylic acids that are potential anti-metabolites of corresponding endogenous ligands in metabolic processes have been intensively studied.

Phosphonacetic (PAA) and phosphonformic acids are the most important biological active phosphorus-containing carboxylic acids. Antiviral activity of phosphonacetic acid and some of its derivatives via inhibition of replication of viral DNA is proven by a number of studies, but searching of efficient and economical method of synthesis of PAA for industrial manufacturing still going on.

In this paper, development of the method of synthesis of trimethyl ester of PAA that is the most convenient initial compound for further PAA synthesis is considered. The basis of this development was taken the reaction of interphase alkylation of dimethylphosphite by methylchloroacetate without any solvents. Potassium carbonate or sodium carbonate in presence of appropriate phase transfer catalyst was used as a base in this reaction. In the course of the work, the kinetics and selectivity of this reaction were investigated using different bases and the corresponding kinetic curves were obtained. In case of sodium carbonate as a base the effect of using different phase transfer catalysts on yield and selectivity of this reaction was shown. As part of the study, a series of experiments were carried out and optimal process conditions were determined that allow it to be scaled using commercially available substrates and without the use of labor-intensive and high-cost technological methods.

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