

Synthesis of pyrimidine nucleosides by method of enzymatic transglycosylation

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Abstract

Nucleosides represent one of the most important classes of natural compounds consisting of carbohydrate residue and heterocyclic base. Nucleosides are components of nucleic acids. More than 100 minor nucleosides were isolated from tRNA. About 100 drugs were developed on the basis of nucleosides, half of them being antiviral drugs and a quarter being anticancer drugs. Nucleosides can be synthesized by chemical or enzymatic methods. Chemical methods are based on the modification of natural compounds or on chemical synthesis of heterocyclic bases and monosaccharides with their subsequent condensation. To date, convenient and effective methods for producing of ribonucleosides based on trimethylsilyl derivatives of heterocyclic bases and fully acylated ribofuranose in the presence of Lewis acids have been developed. Enzymatic methods of synthesis significantly complement chemical ones and, in some cases, have undoubted advantages, such as high region- and stereoselectivity, the possibility to perform reactions in aqueous media, the use of environmentally friendly reagents. To obtain practically important nucleosides, a method based on the enzymatic transglycosylation reaction – the transfer of carbohydrate residue from one heterocyclic base to another – is actively elaborated and used.

In the course of the work, the method for nucleoside synthesis by the reaction of the enzymatic transglycosylation from 7-methyl-2'-deoxyguanosine and 7-methylguanosine as donors of carbohydrate residue in the presence of purine and various pyrimidine nucleoside phosphorylases has been optimized and the possibility of its application for the synthesis of various pyrimidine ribo- and 2'-deoxyribonucleosides has been shown. The optimal conditions for the enzymatic transglycosylation reaction leading to the production of practically important 5-substituted pyrimidine nucleosides in the presence of purine nucleoside phosphorylase and thymidine phosphorylase or uridine phosphorylase have been proposed.

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