

Modifications at the C(5) position of pyrimidine nucleosides

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This review summarizes the state of knowledge on the chemical methods of C(5)-modifications of uridine and cytidine derivatives and may serve as a useful tool for synthetic chemists to choose an appropriate reaction protocol. The synthesis of 5-substituted uracil derivatives is gaining an increasing interest because of their possible applications in medicine and pharmacy. Modifications at the C(5) position of pyrimidine nucleosides can enhance their biostability, bioavailability or (and) biological activity. Among the C(5)-modified nucleosides, 5-halopyrimidines exhibit anticancer, antiviral, radio- and photosensitizing properties. Besides 5-halo-substituted derivatives, there are other examples of nucleosides with confirmed biological activity containing a C–C bond at the C(5) position in the pyrimidine ring. In recent decades, scientists have achieved great progress in the field of cross-coupling reactions. Among them, nickel-catalyzed processes provide a broad spectrum of synthetic methods that are based on less toxic and cheaper starting materials. This review summarizes the synthetic approaches based on the coupling or halogenation reactions, which enable 5-substituted pyrimidine nucleosides to be obtained. Moreover, the importance of the systems considered for medicine and pharmacy is briefly discussed. The bibliography includes 197 references.

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1. Introduction

The synthesis of 5-substituted uracil derivatives is gaining increasing interest because of their biological activities.^{1–3} Chemical modification at the C(5) position of pyrimidine nucleosides can enhance their biostability and bioavailability or change their effect on an organism.^{4,5} Among the

C(5)-modified nucleosides, 5-halopyrimidines exhibit anticancer, antiviral, radio- and photosensitizing properties. Research carried out with these compounds, revealed an important information regarding their cellular biochemistry and affinity towards transporter proteins; moreover, enzyme–substrate specific interactions have been elucidated with their help.^{6,7}