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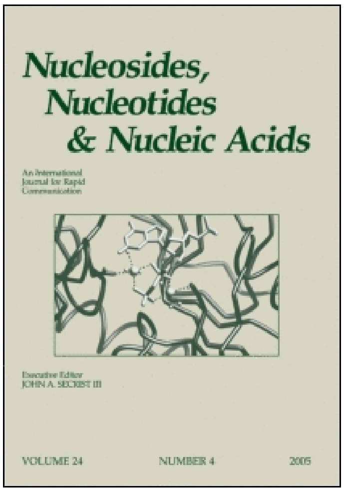

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Mechanism of pH-independent Cleavage and Isomerization of 3'-Ribonucleotide Phosphodiesters

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MECHANISM OF pH-INDEPENDENT CLEAVAGE AND ISOMERIZATION OF 3'-RIBONUCLEOTIDE PHOSPHODIESTERS

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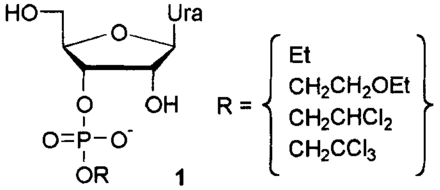
ABSTRACT: The detailed mechanisms of pH-independent cleavage and isomerization reactions of the phosphodiester bond are evaluated by examining kinetics of hydrolytic reactions of selected mono- and dialkyl esters of 3'-uridylic acid. The mechanistic choices are made by comparing LFER's between reaction rates and acidity of the alkyl group of phosphodi- and triesters.

The pH- and buffer-independent reaction rates of alkyl esters of 3'-uridylic acid (1) are determinated, and correlations between logaritmic reaction rate constants and pK_a's of alcohols corresponding to alkyl groups are calculated. The β values obtained are compared to the ones of spesific base- and specific acid-catalyzed reactions,[1] and to those of the reactions of phosphotriester analogues (**2**).[2]



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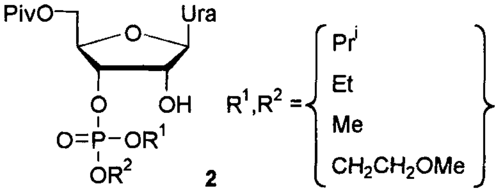
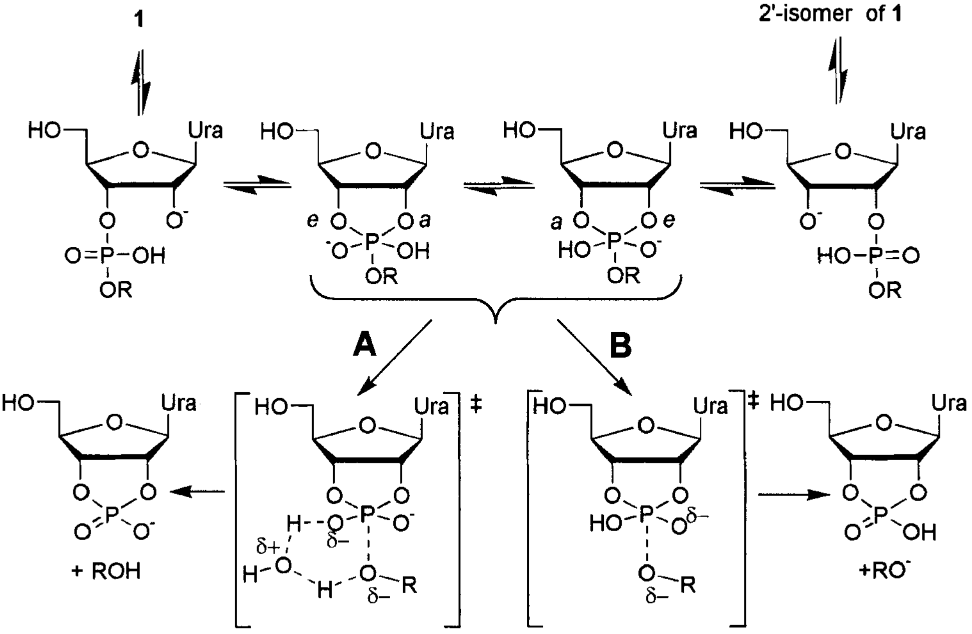


2

On the basis of our triester studies[2] we assume, that the pH-independent reactions of **1** are initiated from the minor tautomer where the phosphate moiety is protonated and 2'-hydroxy group is deprotonated. Accordingly, the reactions are formally equivalent to the hydroxide-ion-catalyzed reactions of triesters (**2**).

The β_{lg} value of the pH-independent cleavage of **1** to uridine 2',3'-cyclic phosphate and appropriate alcohol is -0.59 ∓ 0.12, while the β_{lg} of the hydroxide-ion-catalyzed cleavage of **2** is -1.26 ∓ 0.07[2]. Moreover, the $k_{isomerization}/k_{clevage}$ ratio is 70 or less in the former and in the order of 10^5 in the later reaction. These differences indicate that the reaction pathways are not equivalent. Moreover, the moderate β_{lg} value of the former reaction might well refer to partial protonation of the leaving group in the transition state. We suggest, that in the pH-independent cleavage of **1** proceeds by route **A** rather than route **B** in (route **B** is equivalent to OH$^-$-catalyzed cleavage of **2**). The first formed monoanionic intermediate breaks down to cleavage products *via* a water-mediated proton transfer from hydroxy ligand to the leaving group and a more or less developed dianionic phosphorane. A full version of this paper is published in *J.C.S. Perkin 2*[3].



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