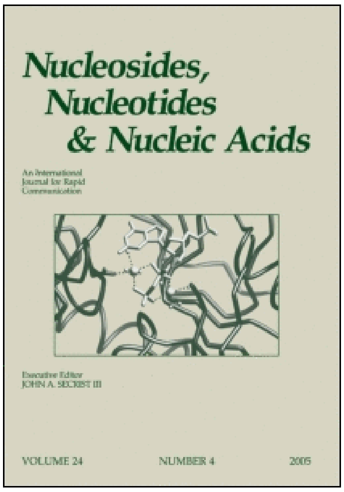

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Interconversion and Hydrolysis of Monoalkyl Esters of Adenosine 2'- and 3'-Monophosphates: Kinetics and Mechanisms

Mikko Oivanen[a]; Ralf Schnell[b]; Wolfang Pfleiderer[b]; Harri Lönnberg[a]
[a] Department of Chemistry, University of Turku, Turku, Finland [b] Faculty for Chemistry, University of Konstanz, Konstanz, FRG

To cite this Article Oivanen, Mikko , Schnell, Ralf , Pfleiderer, Wolfang and Lönnberg, Harri(1991) 'Interconversion and Hydrolysis of Monoalkyl Esters of Adenosine 2'- and 3'-Monophosphates: Kinetics and Mechanisms', Nucleosides, Nucleotides and Nucleic Acids, 10: 1, 569 — 570

To link to this Article: DOI: 10.1080/07328319108046530

URL: http://dx.doi.org/10.1080/07328319108046530

NUCLEOSIDES & NUCLEOTIDES, 10(1-3), 569-570 (1991)

INTERCONVERSION AND HYDROLYSIS OF MONOALKYL ESTERS OF ADENOSINE 2'- AND 3'-MONOPHOSPHATES: KINETICS AND MECHANISMS

Mikko Oivanen,[a] Ralf Schnell,[b] Wolfgang Pfleiderer[b]
and Harri Lönnberg[a]

[a]Department of Chemistry, University of Turku, SF-20500
Turku, Finland, and [b]Faculty for Chemistry, University of
Konstanz, D-7750 Konstanz, FRG

Abstract. Kinetics for the reactions that monomethyl and monoisopropyl esters of adenosine 2'- and 3'-monophosphates undergo in aqueous solution have been studied by HPLC over an acidity range from $\underline{H}_o$ -0.20 to pH 12.

Migration of a phosphate group between the 2'- and 3'-positions of a ribofuranose residue is a reaction frequently encountered, when oligoribonucleotides are treated with aqueous acids or incubated in buffer solutions at elevated temperatures. The present study is aimed to clarify quantitatively competition between the phosphate migration and hydrolysis of the phosphodiester bond over a wide pH range, using the monomethyl and monoisopropyl esters of 2'- and 3'-AMP as model compounds.

The only reaction that takes place under neutral conditions ($3 < pH < 8$) is a pH-independent interconversion of the 2'- and 3'-esters, resulting in an almost equimolar mixture of both isomers ($\underline{x}_{2'} = 0.6$). The reaction most likely proceeds by an intramolecular nucleophilic attack of neighboring hydroxyl group on the 2'- or 3'-alkylphosphate monoanion, followed by pseudorotation and subsequent cleavage of the pentavalent intermediate to isomeric phosphodiesters. The methyl esters are isomerized 4 times as fast as the isopropyl derivatives.

At pH < 3 the phosphate migration becomes acid-catalyzed, exhibiting a second-order dependence of rate on hydronium ion concentration at pH > pK_a of the phosphate group and first-order dependence in more acidic solutions. However, the equilibrium composition is not attained, since hydrolysis of the phosphodiester bond competes efficiently with the migration. Obviously both reactions proceed via the same pentavalent intermediate, which is formed by a nucleophilic attack of neighboring hydroxyl group on protonated alkylphosphate group. This intermediate may undergo a breakdown to either a 2'- or 3'-alkylphosphate, or to a cyclic-2',3'-monophosphate, depending on which one of the alkoxy functions becomes protonated. The cyclic monophosphate undergoes a fast subsequent hydrolysis to a mixture of 2'- and 3'-AMP. The isomerization, as well as the hydrolysis of phosphodiester bond, is considerably faster with the methyl than with the isopropyl esters. Depurination, which is a first-order reaction with respect to hydronium ion, competes with the migration and phosphodiester hydrolysis at 1 < pH < 2, but plays a minor role at higher acidities.

Under alkaline conditions (pH > 9) the methyl esters of 2'- and 3'-AMP are hydrolyzed to a mixture of the free monophosphates, most likely via an attack of ionized hydroxyl group on alkylphosphate monoanion giving a cyclic-2',3'-mono phosphate. No sign of mutual isomerization was detected. With the isopropyl esters, hydrolysis of the phosphodiester bond is too slow to compete with alkaline degradation of the base moiety.