

This article was downloaded by:

On: 27 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Nucleosides, Nucleotides and Nucleic Acids

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597286>

Kinetics and Mechanism for Acid-Catalyzed Hydrolysis of Regioisomeric 2'-Deoxyribonucleosides of 8-Azaadenine and Substituted Benzotriazoles

Rainer Käppi^a; Zygmunt Kazimierczuk^a; Frank Seela^b; Harri Lönnberg^a

^a Department of Chemistry, University of Turku, Turku, Finland ^b Department of Organic and Bioorganic Chemistry, University of Osnabrück, Osnabrück, FRG

To cite this Article Käppi, Rainer , Kazimierczuk, Zygmunt , Seela, Frank and Lönnberg, Harri(1991) 'Kinetics and Mechanism for Acid-Catalyzed Hydrolysis of Regioisomeric 2'-Deoxyribonucleosides of 8-Azaadenine and Substituted Benzotriazoles', *Nucleosides, Nucleotides and Nucleic Acids*, 10: 1, 571 – 572

To link to this Article: DOI: 10.1080/07328319108046531

URL: <http://dx.doi.org/10.1080/07328319108046531>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

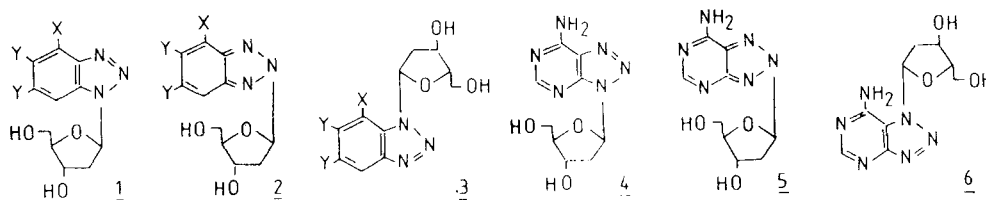
KINETICS AND MECHANISM FOR ACID-CATALYZED HYDROLYSIS OF
REGIOISOMERIC 2'-DEOXYRIBONUCLEOSIDES OF 8-AZAADENINE AND
SUBSTITUTED BENZOTRIAZOLES

Rainer Käppi,^a Zygmunt Kazimierczuk,^b Frank Seela^b
and Harri Lönnberg^a

^aDepartment of Chemistry, University of Turku, SF-20500
Turku, Finland, and ^bDepartment of Organic and Bioorganic
Chemistry, University of Osnabrück, D-4500 Osnabrück, FRG.

Abstract: Kinetics for the acid-catalyzed hydrolysis of regioisomeric 2'-deoxyribonucleosides of 8-azaadenine and various substituted benzotriazoles have been studied.

Regioisomeric 2'-deoxyribonucleosides of benzotriazole (1-3) and 8-azaadenine (4-6) constitute two sets of isosteric analogs of purine nucleosides, both of which exhibit significant biological activity. These nucleoside analogs all undergo acid-catalyzed hydrolysis to free base and sugar at a rate comparable to that of purine 2'-deoxyribosides.



X = H, NH₂, CH₃, NO₂; Y = H
X = H; Y = CH₃, Cl

The following observations suggest that 1-3 are hydrolyzed via rate-limiting formation of a cyclic glycosyl oxocarbenium ion, i. e. analogously to purine nucleosides. (i) The hydrolysis rate depends on acidity in a manner con-

sistent with rate-limiting departure of the mono- and/or diprotonated base moiety. (ii) Polar substituents on the base moiety exert opposite effects on protonation and heterolysis steps. (iii) The starting materials do not undergo anomerization concurrent with hydrolysis.

N2-Glycosylated benzotriazoles (2) are hydrolyzed considerably faster than their N1 counterparts (1). Their rate profiles remain linear on passing the pK_a value of substrate monocation, indicating that hydrolysis via the dicationic species predominates at $pH < pK_a$. By contrast, this reaction appears to be impeded with N1 nucleosides, since the hydrolysis rates of these compounds (except that of 1b) become pH-independent at $pH < pK_a$.

N3-Glycosylated benzotriazoles (3) are less stable than the N1 nucleosides, as well. For example, the 4-methyl derivative of 3 decomposes 11 times as fast as that of 1. This relatively modest rate-enhancement argues against steric acceleration as the main reason for the well known hydrolytic instability of N3-alkylated purine nucleosides.

The pH-rate profile obtained with 8-aza-2'-deoxyadenosine (4) passes through an inflection point at $pH < pK_a$. The reaction via substrate monocation is approximately as rapid as that of 2'-deoxyadenosine, whereas the reaction via dicationic species is more than one order of magnitude slower than with the adenine derivative. The N8-glycosylated 8-azaadenine (5) is hydrolyzed 8 times and the corresponding N7-glycosylated derivative (6) 75 times as fast as 4 under conditions where hydrolysis via the substrate monocation prevails.