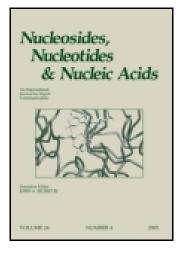
This article was downloaded by: [University of Newcastle (Australia)] On: 05 October 2014, At: 15:00 Publisher: Taylor & Francis Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Nucleosides, Nucleotides and Nucleic Acids

Publication details, including instructions for authors and subscription information: http://www.tandfonline.com/loi/lncn20

Rearrangement Reactions of Guanosine Cyclonucleosides and Their Analogs

Jerzy Boryski^{a b} & Tomasz Zandecki^a

^a Institute of Bioorganic Chemistry, Polish Academy of Sciences, Poznan, Poland

^b Institute of Bioorganic Chemistry, Polish Academy of Sciences, Noskowskiego 12/14, PL-61704, Poznan, Poland Published online: 31 Aug 2006.

To cite this article: Jerzy Boryski & Tomasz Zandecki (2003) Rearrangement Reactions of Guanosine Cyclonucleosides and Their Analogs, Nucleosides, Nucleotides and Nucleic Acids, 22:5-8, 735-737, DOI: 10.1081/NCN-120022622

To link to this article: <u>http://dx.doi.org/10.1081/NCN-120022622</u>

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at http://www.tandfonline.com/page/terms-and-conditions

Rearrangement Reactions of Guanosine Cyclonucleosides and Their Analogs

Jerzy Boryski* and Tomasz Zandecki

Institute of Bioorganic Chemistry, Polish Academy of Sciences, Poznan, Poland

ABSTRACT

Under acid-catalyzed transglycosylation conditions 5',8-cyclo-8-oxoguanine nucleosides undergo a ring-opening reaction to 8-oxoguanine derivatives, instead of the 7–9 isomerization.

Key Words: Guanine cyclonucleosides; 8-Oxoguanine nucleosides; Transglyco-sylation.

It has been shown that fully protected 6-oxopurine nucleosides (e.g., guanosine, inosine) readily undergo a reversible $7 \rightleftharpoons 9$ transglycosylation in the presence of acidic catalysts, and only N7 and N9 of the imidazole ring may act as donors or acceptors of a glycosyl cation.^[1-3] The glycosyl migration process is an intermolecular reaction and therefore, the 6-oxopurine nucleosides may serve as versatile substrates in the synthesis of new nucleoside analogs by applying the exchange methods.^[1,4-6] The transglycosylation reactions have never been studied in the case of purine cyclonucleosides, i.e., in situation, where the sugar portion and the purine part are linked together with an additional chemical bond, besides the N-glycosylic one. In the

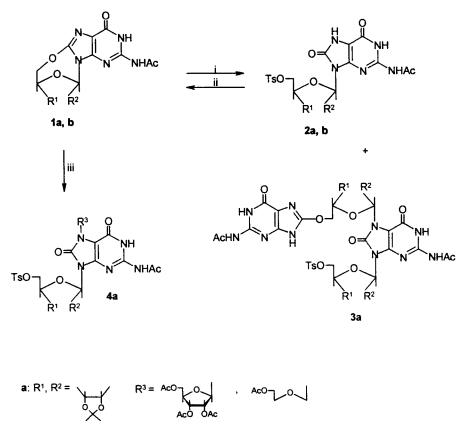
735

DOI: 10.1081/NCN-120022622 Copyright © 2003 by Marcel Dekker, Inc.

Downloaded by [University of Newcastle (Australia)] at 15:00 05 October 2014

1525-7770 (Print); 1532-2335 (Online) www.dekker.com

^{*}Correspondence: Jerzy Boryski, Institute of Bioorganic Chemistry, Polish Academy of Sciences, Noskowskiego 12/14, PL-61704 Poznan, Poland; Fax: +48 61 852 0532; E-mail: jboryski@ibch.poznan.pl.



b: R¹ = R² = H

Scheme 1. *i*, *p*-TsOH (1 eq.), C₆H₅Cl, reflux, 2.5 h; *ii*, Et₃N, CH₃Cl, 48°C, 22 h, or DBU, DMF, 65°C, 30 min; *iii*, 1,2,3,5-tetra-O-acetyl- β -D-ribofuranose or AcOCH₂OCH₂CH₂OAc, *p*-TsOH, C₆H₅Cl, reflux, 30 min.

present study, the model compounds (1a, b) of structure of 5',8-cyclo-8-oxonucleosides were prepared from guanosine.

A preliminary study of transglycosylation reactions (refluxing in chlorobenzene in the presence of *p*-toluenesulfonic acid) of 5',8-cyclo-8-oxo-2',3'-O-isopropylidene-N²-guanosine (**1a**)^[7] gave quite unexpected results (Sch. 1). The cyclonucleoside did not undergo the $7 \rightleftharpoons 9$ isomerization, which could be anticipated by comparison with 'regular' 6-oxopurine nucleosides.^[2] Instead of the N-glycosylic bond, the 5',8-oxygen bridge was cleaved, resulting in the formation of 5'-tosyl-8-oxoguanine derivative (**2a**; 77%). In addition, a dimer **3a** was isolated from the reaction mixture as a side-product (7%). In a similar manner, the pseudosugar analog **1b**^[8] was transformed to compound **2b** (66%). The reaction mechanism can be explained in the following way. After protonation of N7, a nucleophilic attack of tosyl anion at C5' results in the ring opening and the formation of 8-oxoguanine derivatives. The transformation is reversible: treatment of **2a** with bases (triethylamine, DBU) gave the

736

Reactions of Guanosine Cyclonucleosides

Downloaded by [University of Newcastle (Australia)] at 15:00 05 October 2014

starting cyclonucleoside **1a**. Recyclization of the pseudosugar analog **2b** was considerably slower.

In turn, reactions of **1** with 1,2,3,5-tetra-O-acetyl- β -D-ribofuranose or with 2-acetoxyethyl acetoxymethyl ether (an acyclic analog of peracylated sugar) gave 7,9-diglycosyl-8-oxoguanine compounds of the type **4a**. Interestingly, compound **1** did not undergo isomerization when subjected to action of sodium O,O-diethyl phosphate, an effective catalyst in the $1 \rightarrow 3$ transglycosylation of O²,3'-cycloanhydro-thymidine.^[9]

Structure of all obtained products were confirmed by ¹H and ¹³C NMR spectroscopy, mass spectrometry and UV analysis.

REFERENCES

- 1. Boryski, J.; Golankiewicz, B. Application of the transpurination reaction to synthesis of acyclic guanosine analogues. Nucleosides Nucleotides **1989**, *8*, 529.
- Boryski, J. Transglycosylation of purine nucleosides. A review. Nucleosides Nucleotides 1996, 15, 771; and references cited therein.
- 3. Boryski, J. Regioselectivity and mechanism of transpurination reactions in the guanine nucleosides series. J. Chem. Soc., Perkin Trans. 2 **1997**, 649.
- Boryski, J.; Golankiewicz, B. A facile synthesis of 9-(1,3-dihydroxy-2-propoxymethyl)guanine (ganciclovir) from guanosine. Synthesis 1999, 625.
- Boryski, J. A novel approach to synthesis of 2'-deoxy-β-D-ribofuranosides via transglycosylation of 6-oxopurine ribonucleosides. Nucleosides Nucleotides 1998, 17, 1547.
- Shiragami, H.; Koguchi, Y.; Tanaka, Y.; Takamatsu, S.; Uchida, Y.; Ineyama, T.; Izawa, K. Synthesis of 9-(2-hydroxyethoxymethyl)guanine (acyclovir) from guanosine. Nucleosides Nucleotides 1995, 14, 337.
- Srivastava, P.C.; Nagpal, K.L.; Dhar, M.M. Synthesis of purine cyclonucleosides. Indian J. Chem. 1969, 7, 1.
- Madre, M.; Geita, L.; Zhuk, R.; Koomen, G.J. Purine nucleoside analogues. 7. 9-[2-(alkylthio)ethoxymethyl) derivatives of adenine, hypoxanthine and guanine. Chinese Pharm. J. 1995, 47, 469.
- Yang, X.B.; Misiura, K.; Stec, W.J.; Potrzebowski, M.J.; Kazmierski, S.; Wieczorek, M.; Majzner, W.R.; Bujacz, G.D. Nucleophilic N1–N3 rearrangement of 5'-O-trityl-O2,3'-cycloanhydrothymidine. Nucleosides, Nucleotides & Nucleic Acids 2000, 19, 1657.

737



Copyright © 2003 by Marcel Dekker, Inc. Marcel Dekker, Inc. 270 Madison Avenue, New York, New York 10016