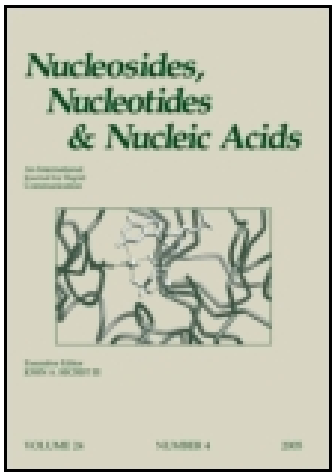

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Rearrangement Reactions of Guanosine Cyclonucleosides and Their Analogs

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Rearrangement Reactions of Guanosine Cyclonucleosides and Their Analogs

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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; Transglycosylation.

It has been shown that fully protected 6-oxopurine nucleosides (e.g., guanosine, inosine) readily undergo a reversible 7⇄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

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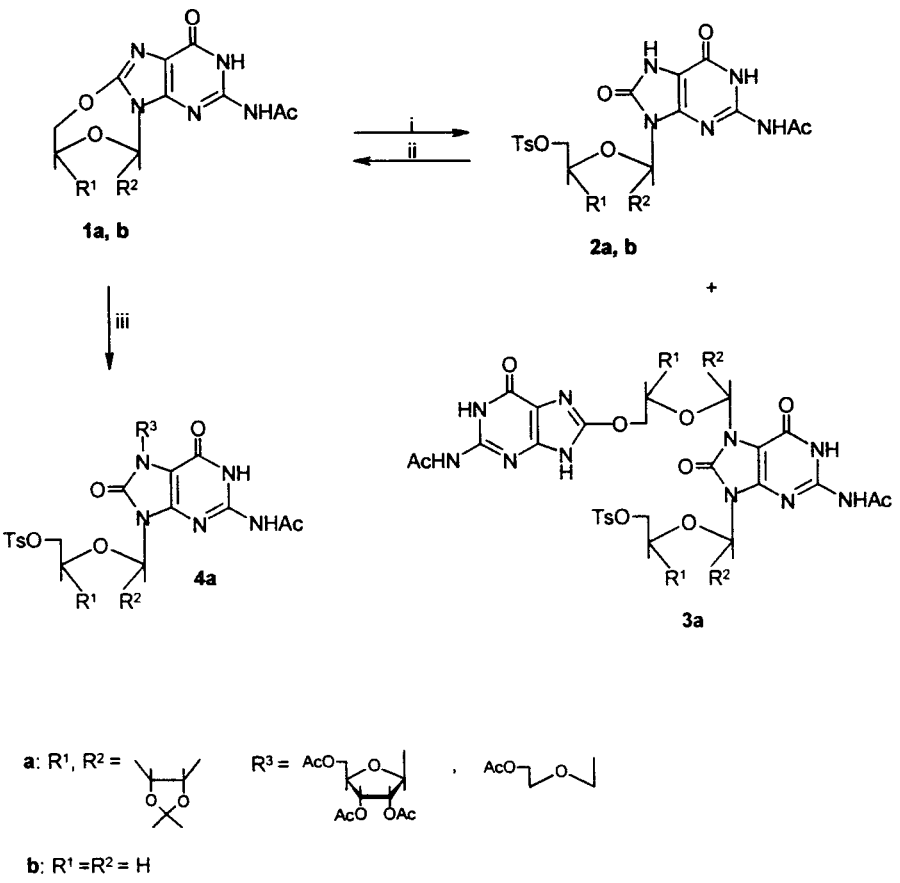

Scheme 1. *i*, *p*-TsOH (1 eq.), C_6H_5Cl, reflux, 2.5 h; *ii*, Et_3N, CH_3Cl, 48°C, 22 h, or DBU, DMF, 65°C, 30 min; *iii*, 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose or $AcOCH_2OCH_2CH_2OAc$, *p*-TsOH, C_6H_5Cl, reflux, 30 min.

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-N^2-guanosine (**1a**)[7] gave quite unexpected results (Sch. 1). The cyclonucleoside did not undergo the 7⇄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

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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 O^2,3′-cycloanhydrothymidine.[9]

Structure of all obtained products were confirmed by ^1H and ^{13}C 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.
2. 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.
4. Boryski, J.; Golankiewicz, B. A facile synthesis of 9-(1,3-dihydroxy-2-propoxymethyl)guanine (ganciclovir) from guanosine. Synthesis **1999**, 625.
5. Boryski, J. A novel approach to synthesis of 2′-deoxy-β-D-ribofuranosides via transglycosylation of 6-oxopurine ribonucleosides. Nucleosides Nucleotides **1998**, *17*, 1547.
6. 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.
7. Srivastava, P.C.; Nagpal, K.L.; Dhar, M.M. Synthesis of purine cyclonucleosides. Indian J. Chem. **1969**, *7*, 1.
8. 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.
9. 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.

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