

Errata

Dear Sir,

As a reader of *Synthesis* I would like to comment on the publication entitled: „Synthesis of Acyclovir, Ganciclovir and Their Prodrugs: A Review”, written by Hongwu Gao and Ashim K. Mitra. The paper appeared in *Synthesis* **2000**, 329-351. This is perhaps an interesting review, which covers many synthetic routes towards guanine acyclonucleosides. However, one important method seems to have slipped the author’s attention.

To my best knowledge, a direct synthesis of acyclovir and ganciclovir from guanosine *via* exchange of glycosyl substituents is the simplest and highly efficient method. Thus, the ribofuranosyl portion of naturally occurring nucleoside may be replaced by other glycosyl substituents in the acid-catalyzed reaction with acyclosugar analogs, *e.g.* 2-oxobutane-1,4-diol diacetate for synthesis of acyclovir. This transpurination approach was reported for the first time in 1987,¹ then full papers on synthesis of acyclovir² and ganciclovir^{2,3} were published. Mechanism of the conversion of guanosine to acyclovir has been studied in detail.^{4,5} The exchange reaction proceeds via unstable 7,9-diglycosylguanine intermediates,⁶ and the regioselectivity of glycosylation is related to the tautomerism of guanine.⁷ As a result of these studies, a new and well-documented mechanism of glycosylation of guanine has been proposed.⁸ Some other aspects of regioselectivity and the role of acidic catalysts in the formation of acyclovir have been discussed recently.⁹

Furthermore, side-products in the synthesis of guanine acyclonucleosides, the 7-substituted isomers of acyclovir and ganciclovir, can be easily transformed to the desired 9-isomers in the thermal 7-9 transglycosylation reaction.^{1-6,10} This important, fully reversible isomerization of 6-oxopurine nucleosides,⁸ crucial for the final distribution of acyclonucleoside 7- and 9-regioisomers, has hardly been mentioned in the review.

More recently, the transpurination approach in the acyclovir synthesis² has been modified for industrial purposes by applying unprotected guanosine and 1,3-dioxolane in a one-pot procedure.^{11,12} This simplified method offers an excellent yield of acyclovir (78% from guanosine) and high regioselectivity (only traces of the 7-isomer). Therefore, I may recommend the method as the best and the most economic synthetic route to acyclovir.

To my surprise, none of the papers listed below – so important as far as mechanism and efficiency of the synthesis of guanine acyclonucleosides are concerned – has been cited in the discussed review.

Prof. Jerzy Boryski, Ph.D.
Institute of Bioorganic Chemistry
Polish Academy of Sciences
Noskowskiego 12/14
PL-61704 Poznan, Poland
Phone: (+48 61) 852 85 03
Fax: (+48 61) 852 05 32
E-mail: jboryski@ibch.poznan.pl

References

- (1) Boryski, J.; Golankiewicz, B. *Nucleosides Nucleotides* **1987**, *6*, 385.
- (2) Boryski, J.; Golankiewicz, B. *Nucleosides Nucleotides* **1989**, *8*, 529.
- (3) Boryski, J.; Golankiewicz, B. *Synthesis* **1999**, 625.
- (4) Boryski, J. *Collect. Czech. Chem. Commun.* **1993**, *58*, 5.
- (5) Boryski, J. *J. Chem. Soc., Perkin Trans. 2* **1997**, 649.
- (6) Boryski, J.; Manikowski, A. *Nucleosides Nucleotides* **1999**, *18*, 1057.
- (7) Boryski, J.; Manikowski, A. *Nucleosides Nucleotides* **1995**, *14*, 287.
- (8) Boryski, J. *Nucleosides Nucleotides* **1996**, *15*, 771 (invited author).
- (9) Singh, D.; Wani, M.J.; Kumar, A. *J. Org. Chem.* **1999**, *64*, 4665.
- (10) Boryski, J.; Golankiewicz, B. *Nucleic Acids Res., Symp. Ser.* **1987** No 18, 45.
- (11) Shiragami, H.; Koguchi, Y.; Tanaka, Y.; Takamatsu, S.; Uchida, Y.; Ineyama, T.; Izawa, K. *Nucleosides Nucleotides* **1995**, *14*, 337.
- (12) Izawa, K.; Shiragami, H. *Pure Appl. Chem.* **1998**, *70*, 313.