**Synthesis of new carbocyclic C-nucleoside analogs**

Prashant Khirsariya\**1*, *2*, Lukáš Maier*1*, *2* and Kamil Paruch*1*, *2*

*1Masaryk University, Faculty of Science, Department of Chemistry, Kamenice 5/A8, 623 00 Brno, Czech Republic*

*2International Clinical Research Center, St. Anne’s University Hospital Brno, Pekarska 53, 656 91 Brno, Czech Republic*

*\*prashant@mail.muni.cz*

The chemical modification of nucleosides has been – and will continue to remain – a major research topic in medicinal chemistry. Classical nucleoside analogs (**A**) constitute an important class of biologically active compounds, which has promising antiviral and anticancer properties1. Since they possess labile hemiaminal motif, extensive effort has been invested into the identification of more stable substances while preserving the biological activity, e.g. C-nucleosides (**B**) or carbocyclic N-nucleosides (**C**).



It is conceivable that, at least in some cases, carbocyclic C-nucleosides (**D**) might be even more robust versions of nucleoside analogs **B** and **C.** In addition, installation of certain substituents (e.g. R1 = OH) is meaningful only in this class as this would lead to chemically unstable ketals and aminals in the series **A**, **B** and **C**. However, analogs **D** are quite rare and most published syntheses only produced single target compounds2.

Our recently developed flexible synthesis of compounds **D** enables selective manipulation of individual positions around the cyclopentane ring, including highly diastereoselective installation of carbo - and heterocyclic substituents at position 1´, orthogonal functionalization of position 5´, and efficient inversion of stereochemistry at position 2´, which are important for subsequent SAR development. Some of the newly prepared carbocyclic C-nucleosides inhibit human DNA glycosylases.

References:

1 a) *Modified Nucleosides in Biochemistry*,*Biotechnology and Medicine*; Ed.: P.     Herdewijn, Wiley-VCH, **2008**. (b) *Chemical Synthesis of Nucleoside Analogues*;     Ed.: P. Merino, Wiley, **2013**.

2 a) Just, G.; Reader, G. *Tetrahedron Lett.* **1973**, *14*, 1524. b) Just, G.; Kim, S.     *Tetrahedron Lett.* **1976**, *17*, 1063. c) Just, G.; Ouellet, R. *Can. J. Chem.* **1976**, *54*,     2925. d) Chun, B. K.; Song, G. Y.; Chu, Ch. K. *J. Org. Chem.* **2001**, *66*, 4852. e)     Rao, R. J.; Schinazi, R. F.; Chu, Ch. K. *Bioorg. Med. Chem.* **2007**, *15*, 839.f)     Maier, L.; Hylse, O.; Nečas, M.; Trbušek, M.; Arne, M. Y.; Dalhus, B.; Bjoras, M.;     Paruch, K. *Tetrahedron Lett*., **2014**, *55*, 3713.