

POSTER PRESENTATIONS

ENZYMATIC SYNTHESIS AND BIOLOGICAL EVALUATION OF NEW 3'-DEOXYRIBONUCLEOSIDE ANALOGUES OF RIBAVIRIN

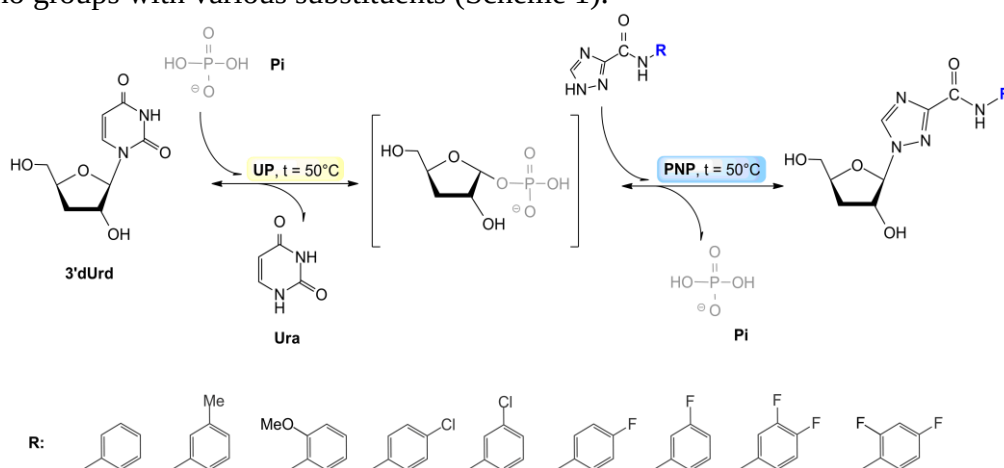
**E.A. Zorina¹, E.K. Kharlamova^{1,2}, A.O. Baculina^{1,2}, M.A. Simonova¹,
A.L. Kayushin¹, I.D. Konstantinova¹**

¹*Shemyakin and Ovchinnikov Institute of Bioorganic Chemistry RAS, Miklukho-Maklaya
16/10, 117997 GSP, B-437 Moscow, Russia*

²*MIREA – Russian Technological University, 86 Vernadsky Avenue, Moscow, 119571,
Russia*

3'-Deoxyribonucleosides are an important class of modified nucleosides. The key structural feature of which is the absence of a hydroxyl group in the third position of the ribose fragment. This modification causes increased resistance of compounds to the action of cellular enzymes, and also gives them new biological properties that differ from their natural counterparts. The most effective approach to obtaining such structures is enzymatic transglycosylation catalyzed by purine nucleoside phosphorylase (PNP) and uridine phosphorylase (UP).

These studies are particularly relevant in the context of the search for safe substitutes for ribavirin, a well-known antiviral drug whose use is associated with toxicity and side effects. In solving this problem, our attention was focused on the synthesis of 3'-deoxyribonucleosides containing 1,2,4-triazole-3-carboxamide fragments modified by amino groups with various substituents (Scheme 1).



Scheme 1.

To increase the yield of the target compounds, key parameters of enzymatic synthesis were optimized (molar ratio of substrates, concentrations of UP and PNP). Preparative syntheses were carried out on the basis of selected conditions. The total yield of purified compounds ranged from 20 to 73%, and the purity according to HPLC exceeded 97%. The structures of the substances obtained have been confirmed by mass spectrometry and NMR spectroscopy. Primary screening on a wide panel of tumor and normal cell lines (HEK293, HepG2, L929, MCF-7, Raji, THP-1, U937) revealed no pronounced cytotoxic or cytostatic effects of the synthesized analogues.

The study was supported by RSF grant (Project No. 24-14-00458).