

POSTER PRESENTATIONS

ENZYMATIC SYNTHESIS OF NOVEL 1,2,4-TRIAZOLE-3-CARBOXAMIDE NUCLEOSIDES: STUDY OF SUBSTRATE SPECIFICITY OF *E. coli* NUCLEOSIDE PHOSPHORYLASES

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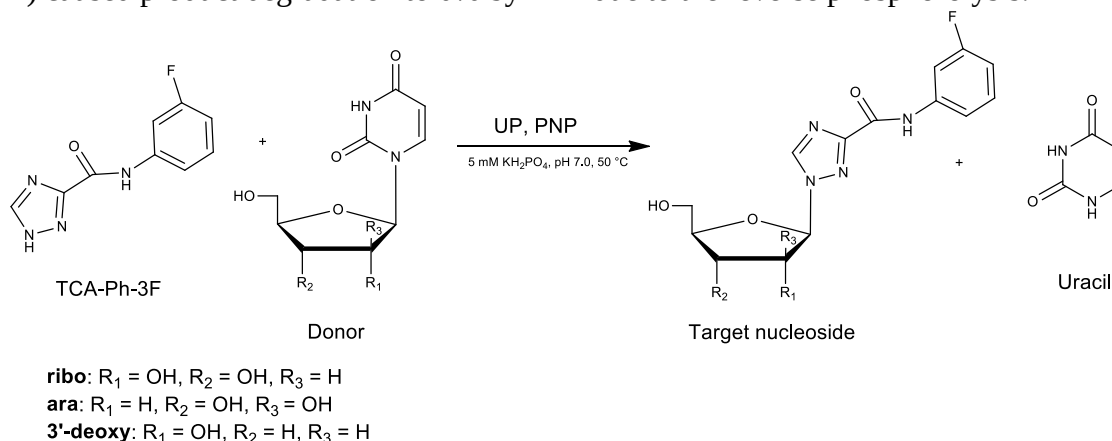
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Enzymatic synthesis of nucleosides using *E. coli* uridine (UP) and purine nucleoside (PNP) phosphorylases is an excellent alternative to chemical methods. We have investigated the substrate specificity of the UP/PNP cascade towards a novel acceptor, N-(3-fluorophenyl)-1H-1,2,4-triazole-3-carboxamide (TCA-Ph-3F), using natural and modified carbohydrate donors - uridine (Urd), arabinofuranosyluracil (Ara-U), and 3'-deoxyuridine (3'-dU) (see Scheme). The conditions of the transglycosylation reaction : 5 mM potassium phosphate, pH 7.0, 50 °C, donor:acceptor ratio 9:1. The reaction progress was monitored by RP-HPLC.

Ribosylation with Urd was highly efficient: 1.7 U/mL of UP and 1.4 U/mL of PNP yielded 100% conversion in 1 h, whereas an excess (51 U/mL of UP and 42 U/mL of PNP) caused product degradation to 0% by 41 h due to the reverse phosphorolysis.



In contrast, under common conditions (5.1 U/mL of UP and 4.2 U/mL of PNP, 24 h), transfer of modified sugars was slow due to strict enzyme specificity, yielding only 6% conversion for Ara-U and 14% for 3'-dU. Optimization (51 U/mL of UP and 42 U/mL of PNP, 72 h) overcame this kinetic barrier, raising conversions to 62% (Ara-U) and 82% (3'-dU). This should allow a successful synthesis of modified triazole nucleosides in high yields.