REACTIVITY STUDIES OF 2,6-BIS-(1,2,3-TRIAZOLYL)PURINE NUCLEOSIDES WITH HYDRAZINES AND AMINO ACIDS

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ABSTRACT

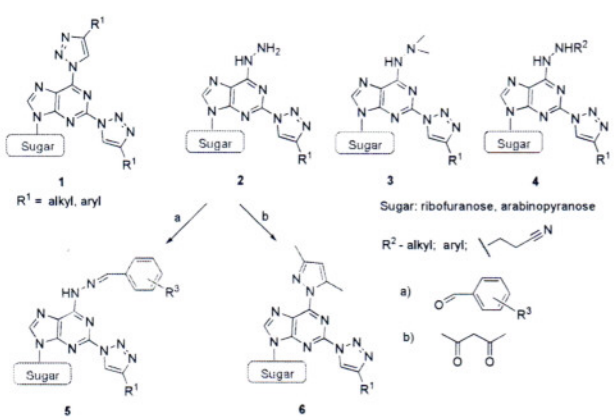
Reactions of 2,6-bis-(1,2,3-triazolyl)purine nucleosides with nucleophiles is efficient route to C(6)-derivatization of purine base. To extend the field of application of the method, we studied reactivity of bis-(1,2,3-triazolyl)purine derivatives toward hydrazines and amino acids and obtained nucleosides substituted at C(6) with hydrazine and amino acid moieties.

INTRODUCTION

Purine derivatives have found significant applications as agonists and antagonists of adenosine receptors. In recent years the series of 2-hydrazinyl and 2-pyrazolyl adenosine derivatives were synthesized and investigated as adenosine receptor ligands [1]. The published synthetic routes to *N*-(purin-6-yl) substituted amino acids are based on the reactions of protected amino acids with 6-chloropurines [2].

RESULTS AND DISCUSSION

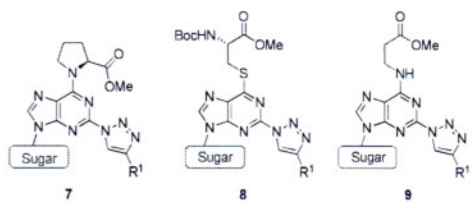
Recently, we have reported the synthesis and applications of 2,6-bis-(1,2,3-triazol-1-yl)purine nucleosides **1.** The 1,2,3-triazolyl moiety at C(6) position of purine has been shown as a good leaving group in S_NAr reactions with amines and thiols [3]. In this study, we extended the range of nucleophiles with hydrazines and amino acid esters to obtain products with general formulas **2-4** and **7-9**.



6-Hydrazinopurine derivative **2** was reacted with aromatic aldehydes to obtain hydrazones **5** and with diketones, such as acetylacetone to give 6-pyrazolyl derivatives **6**. Therefore, **2** is valuable intermediate allowing various modifications.

Further, we extended investigations to the reactions of amino acid esters as nucleophiles. Reaction of **1** with L-proline methyl ester proceeds under mild conditions to give **7**, however other natural α-amino acids failed to react. β-Alanine gave **9** with good yield. We were especially interested in reaction of **1** with L-cysteine as *S*-nucleophile. *N-Boc* protected cysteine methyl ester appeared to react with **1** at ambient or slightly elevated temperature to give **8**.

This might initiate the new program towards attachment of purine derivatives to oligopeptides via cysteine residues.



CONCLUSION

We have demonstrated the versatility of 2,6-bis-(1,2,3-triazol-1-yl)purine nucleosides **1** as reactive intermediates suitable for derivatization of purine nucleosides at C(6) with hydrazino and amino acid moieties.

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