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Properties and Structure Studies of New 2,6-Bis-(1,2,3-Triazolyl) Substituted Purine Arabinonucleosides

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Keywords **– Purine arabinonucleosides, 2,6-bistriazolyl derivatives, 1,3-dipolar cycloaddition, fluorescence.**

I. INTRODUCTION

Modified nucleosides are prominent anticancer and antiviral agents. Antimetabolic purine nucleosides used in anticancer therapy among others include fludarabine, clofarabine and cladribine [1]. Additionally, purine derivatives have found significant applications as agonists and antagonists of adenosine receptors [2]. Thus, the agonists of A1 receptor have provided clinical candidates for atrial arrythmias, type 2 diabetes and insulin-sensitizing agents, pain management, and angina [3].

II. RESULTS AND DISCUSSIONS

The aim of this study was to develop synthetic methodologies towards different types of novel (1,2,3-triazolyl)purine nucleosides, including those substituted with two triazolyl moieties (**1**) and to study chemical reactivity, fluorescence properties and biological activity of the title products (Fig. 1).

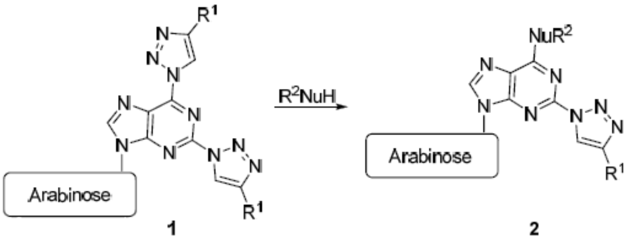

Fig.1. General synthesis of nucleophile substituted nucleoside triazole derivatives with main formula **2**.

2,6-Bis-(1,2,3-triazolyl)purine nucleosides (R^1 = phenyl, butyl, pentyl, hexyl, hydroxymethyl, acetoxymethyl, 1-hydroxycyclohexyl, 2-hydroxypropan-2-yl) **1** were obtained from diazido derivatives **3** via copper catalyzed azide-alkyne 1,3-dipolar cycloaddition reaction.

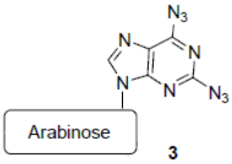

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Fig.2. The main structure of diazido derivatives **3**.

The diazido derivatives **3** can be obtained by linear or convergent synthesis methods. The first method consists from the reaction between protected monosaccharide and 2,6-dichloropurine in the presence of *N,O*-bis(trimethylsilyl)acetamide (BSA) and trimethylsilyltriflate (TMSOTf) and the following reaction with sodium diazide in ethanol. While the other method showed the reaction between sodium azide and 2,6-dichloropurine and later exposure with protected sugar by silylation conditions with BSA and TMSOTf.

We used D-arabinose as sugar in nucleosides synthesis both in pyranose and furanose form.

Then, nuclophile substituted nucleoside triazole derivatives **2** were synthesized exploring reactions with different *N*- and *S*-nucleophiles (R^2Nu = methylamine, dimethylamine, pirrolidine, piperidine, 1,1-dimethylhydrazine, undecane-1-thiol). The fluorescence properties of the nucleophilic substitution products were studied in THF, MeCN, DMSO and water. One example is given in Fig. 3.

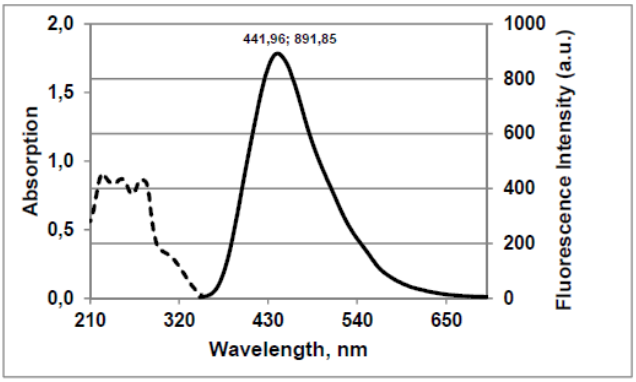

Fig.3. Absorption (dashed line) and emission (solid line) spectrum of 9-(α-D-arabinopyranosyl)-2-(4-(2-hydroxypropan-2-yl)-1*H*-1,2,3-triazol-1-yl)-6-(pyrrolidin-1-yl)-9*H*-purine ($7.7 \cdot 10^{-7}$ M) in water.

III. REFERENCES

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