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Faculty of Material Science and Applied Chemistry

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2,6-Diazidopurine Nucleosides as Useful Intermediates for the Synthesis of Novel Triazolyl Purine Analogs

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Keywords – Purine nucleosides, 2,6-diazidopurine nucleosides, 2,6-bis-triazolyl purine derivatives, 1,3-dipolar cycloaddition, nucleophilic aromatic substitution.

I. INTRODUCTION

Over the years a plethora of modifications in the structure of purine nucleosides has been made. Nevertheless, only few research groups have introduced 1,2,3-triazolyl moiety in the purine ring. Merely some of them developed synthesis of 2- or 6-(1,2,3-triazol-1-yl)-purine nucleosides [1].

In 2013, we described approach for the synthesis of novel 2,6-bis-triazolyl purine nucleosides **2** via 1,3-dipolar cycloaddition reaction and studied reactivity of obtained compounds to different nucleophiles (**Figure 1**) [2].

II. RESULTS AND DISCUSSIONS

Here we report the novel approach for the synthesis of modified triazolyl purine derivatives. We have subjected 2,6-diazidopurine nucleoside **1** to the nucleophilic aromatic substitution reactions with different alkyl- and arylthiols. The nature of the nucleophile affected the regioselectivity. When the S_NAr reaction between the diazide **1** and different alkylthiols was made, the C(2)-substituted products **4** were obtained. Contrary, when arylthiols were exploited, the C(6)-substituted products **6** were obtained (**Figure 1**, **Table I**).

The reactions were carried out in DMF in the presence of K_2CO_3 . Obtained products **4** and **6** exist as a mixture of two tautomeric forms – azide and tetrazole.

Further, 1,3-dipolar cycloaddition reaction between compounds **4** and **6** and different acetylenes were performed and triazolyl purine analogs **5** and **7** were obtained in good yields (**Table I**).

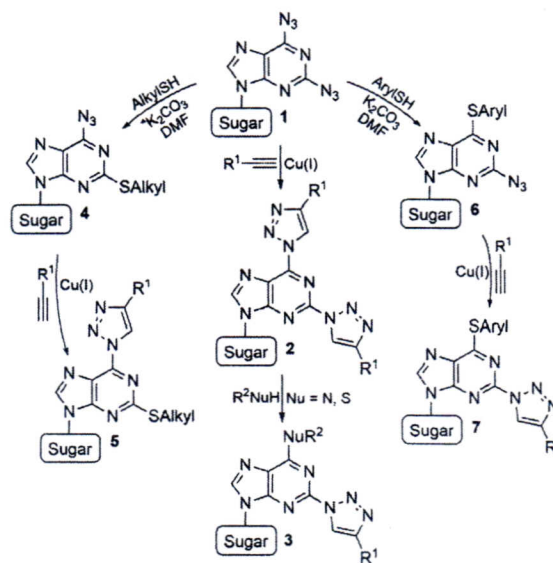


Figure 1. General synthesis of triazolyl purine nucleosides **2**, **3**, **5**, **7**

TABLE I
OBTAINED RESULTS OF TRIAZOLYL PURINE DERIVATIVES

Compound	R ¹	R ² Nu-	Alkyl/ Aryl	Yield, %
2a	C ₆ H ₅ -	-	-	83
3a	HOCH ₂ -		-	89
3b	C ₆ H ₅ C ₆ H ₄ -	C ₆ H ₅ CH ₂ -	-	89
4a	-	-	<i>n</i> -C ₄ H ₉ -	74
5a	C ₆ H ₅ -	-	<i>n</i> -C ₄ H ₉ -	89
6a	-	-	4-Br-C ₆ H ₄ -	31
7a	C ₆ H ₅ -	-	4-Cl-C ₆ H ₄ -	91

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