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Application of Triazolyl Purine Derivatives to Nucleophilic Aromatic Substitution Reactions

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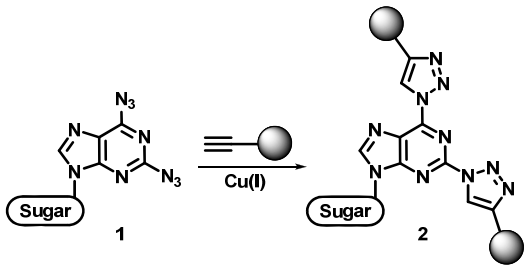
Purine derivatives are widely used in anticancer and antiviral therapy and as agonists and antagonists of adenosine receptors. Many modifications of the purine system have been developed to this day, but the attempt to find ever new drugs is in progress. Only a few scientific groups work with either 2- or 6-(1,2,3-triazolyl) purine nucleosides [1].

Recently, we have developed the synthesis of novel 2,6-bis-(1,2,3-triazol-1-yl)purine nucleosides **2** [2].

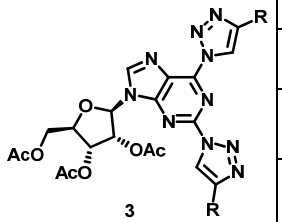
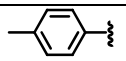
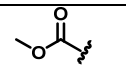
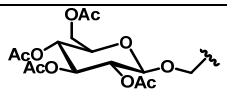


Scheme 1. Synthesis of 2,6-bis-(1,2,3-triazol-1-yl)purine nucleosides **2**

The bis-triazole formation was accomplished in Cu(I) catalyzed "click" reactions between diazido derivatives **1** and various terminal alkynes (Scheme 1). Some examples of obtained bis-triazolyl compounds are given in Table 1. Variously functionalized alkynes can be used for bis-triazole formation, for example, reaction with 1-*O*-propargyl-2,3,4,6-tetraacetyl-β-D-glucose gave the expected product **3c** in 42% isolated yield.

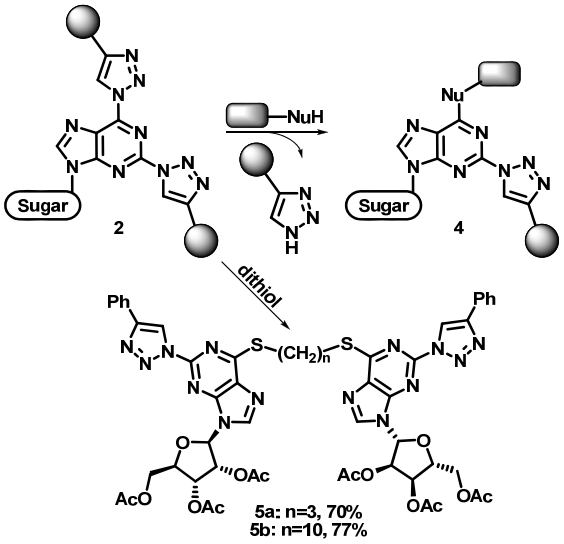
TABLE 1

EXAMPLES OF BIS-TRIAZOLYL DERIVATIVES **3**

	R	Yield %
	**3a:** 	67
	3b: 	51
	3c: 	42

Further, the 1,2,3-triazolyl group at C(6) position of purine was shown to be a good leaving group in nucleophilic aromatic substitution reactions (Scheme 2). *N*-Nucleophiles, such as methylamine, dimethylamine, pyrrolidine and piperidine, were successfully used in substitution reactions and gave products **4** in good to excellent yields. Either THF or THF/H_2O was used as a solvent system. Reaction temperatures varied from 20 till 40°C and time – from 30 min to 4 hours.

Bis-triazolyl purines also undergo aromatic nucleophilic substitution with thiols. In this way, various thioethers of 2-triazolylpurines can be generated. If dithiols (e.g.: propane-1,3-dithiol, decane-1,10-dithiol) are used, dimers **5** are isolated in good yields.



Scheme 2. Synthesis of purine C(6)-substituted analogues **4**

Additionally, we have discovered that products **4** exhibit interesting photophysical properties. The absorption and emission spectra ($\lambda_{emission}$ = 390-440 nm, quantum yields up to 53%) of products containing 6-amino-2-triazolylpurine group were studied in THF, MeCN, DMSO and water.

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Dr.chem. M.Turks.

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