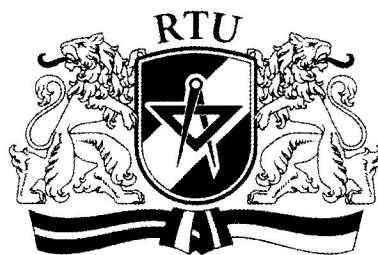


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Synthesis of New Fluorescent 9-Alkyl-2-(1,2,3-triazol-1-yl) Adenine Analogs

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INTRODUCTION

Fluorescent purine derivatives are useful as sensors and reporters for biological applications. In recent years new purine derivatives with improved photophysical properties have been synthesized and investigated [1]–[2]. On the other hand, acyclic nucleoside phosphonates represent catabolically stable nucleoside analogs with a variety of antiviral properties [3]. The synthesis of fluorescent 6-amino 2-triazolyl derivatives of purine nucleosides was reported by our group earlier [4].

RESULTS AND DISCUSSIONS

In this research a new synthetic strategy towards fluorescent purine derivatives was developed. As the starting material we used commercially available 2,6-dichloro-9H-purine (**1**). Alkylation of **1** at N(9) with different alkyl halides or alcohols, such as triethylene glycol C-phosphonate (Mitsunobu reaction) gave 9-alkylated purines **2**. In reaction of **2** with sodium azide 2,6-diazidopurines **3** were obtained. Further, two different routes towards **6** were possible. In the first method azido group at C(6) was replaced by different amines. The second step was copper (I) catalyzed azide-alkyne 1,3-dipolar cycloaddition (CuAAC) with different terminal alkynes using sodium ascorbate and copper (II) sulfate as catalyst generating system. In the second method amination and CuAAC were made *vice versa*. Triazole formations proceeded at 65 °C – 90 °C in DMF. Overall yield (**1**→**6**) was 20 % – 35 %.

Derivatives **6** exhibit strong fluorescence with emission maxima around 430 nm and quantum yields up to 50 % (reference: quinine sulfate in 0.1 M H₂SO₄).

In conclusion, two new synthetic routes towards **6** were developed. A novel acyclic nucleoside C-phosphonate ester **6f** was obtained. The properties of compounds **6a-f** and synthesis

of the related compounds are under investigation and will be discussed.

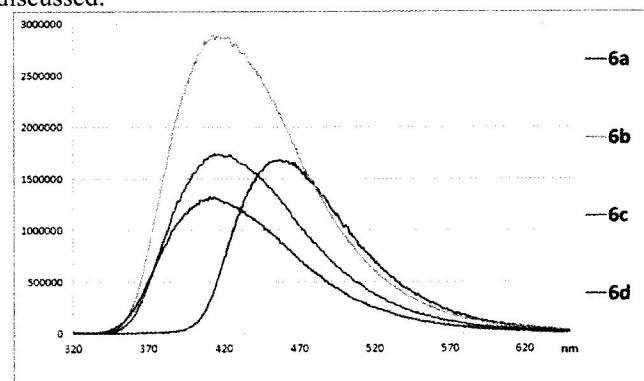


Fig. 1. Emission spectra for selected 9-alkyl-6-amino-2-triazolylpurines **6** (for **6a-d** NR³R⁴=piperidin-1-yl).

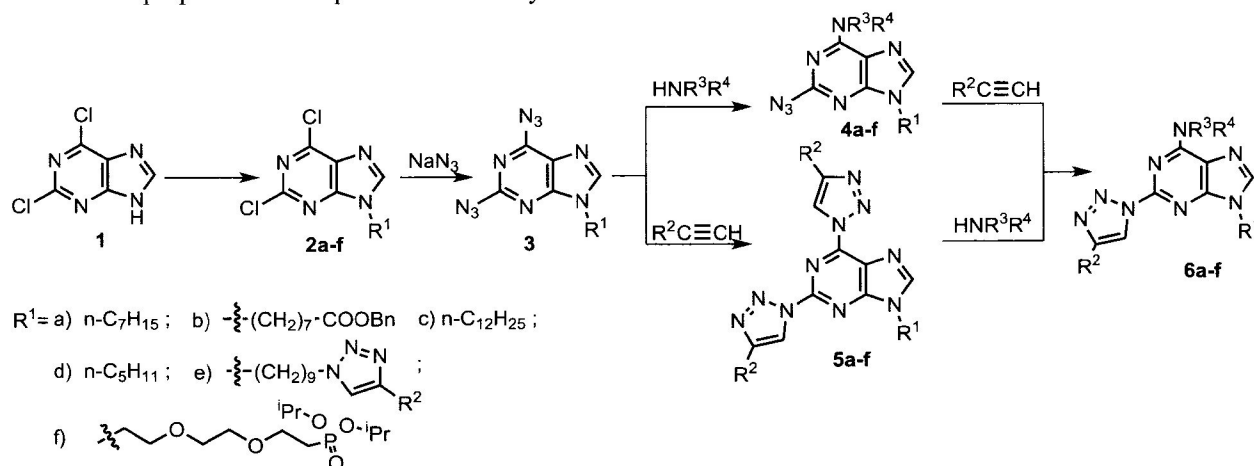
Supervisor: Dr. chem. Ērika Bizdēna

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Scheme 1. Synthesis of 9-alkyl-2-(1,2,3-triazol-yl) adenine analogs