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## Synthesis and properties of new nucleobase containing amphiphiles and bola-amphiphiles

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**Abstract:** We present here synthesis and properties of new amphiphiles and homoditopical bolaamphiphiles, containing nucleobases. This amphiphilic and bolaamphiphilic compounds were prepared by the addition of the amino group to the isothiocyano group attached to a nucleobase. This compounds are capable of creating several non-covalent interactions, especially the hydrogen bonds resulting in formation of aggregates

**Keywords:** Nucleobases, Amphiphiles, Bolaamphiphiles, Thiourea

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### 1. Introduction

Molecular organization via the formation of complementary hydrogen bonds has become a powerful strategy for the construction of well-defined nanostructures. Typical self-assembly systems in line with this concept include lyotropic mesophases, supramolecular fibers and membranes, twodimensional (2-D) monolayers, and supramolecular polymers<sup>1</sup>. The five main natural nucleobases adenine, cytosine, guanine, thymine and uracil are involved in the self-assembly of one of nature's most interesting and intriguing class of biopolymers, the nucleic acids<sup>2</sup>. Those compounds are capable of forming many non-covalent interactions. Such non-covalent interactions range from purely electrostatic bonds to hydrophobic effects, from hydrogen bonding to phase segregation and from metal–ligand chemistry to  $\pi$ – $\pi$  interactions<sup>2</sup>.

Scientists have found an unprecedented hierarchical self-assembly of high-axial-ratio nanostructures utilizing internucleobase interactions. They was synthesized nucleobase-appended amphiphiles and bolaamphiphiles<sup>3</sup>. Conventional amphiphiles contain a head-polar group and one or two hydrophobic tails. The polar head can be represented by various functional groups, including carboxylic acid, amino acid, sugar, phosphate, or quaternary amine. Similarly, there is much variation in the number, length, and flexibility of the hydrophobic tails. Such molecules are prevalent in nature and are known to form a variety of aggregates in aqueous solutions, including hydrogels<sup>4</sup>. A bola-amphiphile is defined as a molecule in which two or more hydrophilic groups are connected through a hydrophobic bridging chain. Most of these compounds have been studied for their polymorphic behavior in water as a function of their structures. When dispersed in aqueous medium, upon sonication, these molecules often self-organize into monolayer vesicles (monolayer lipid membranes), which are stable over a long period of time to variations of temperature or to ionic strength changes and could be used as membrane models<sup>5</sup>. Those compounds present the intriguing group of organogelators and hydrogelators.

Isothiocyanates are versatile synthetic intermediates that have been widely used in the synthesis of thiocarbamoyl derivatives. The strong electrophilicity of the NCS group enables these heterocumulenes to take part in addition and cycloaddition reactions, making them extremely useful in the preparation of thioureas and heterocyclic compounds<sup>6</sup>. Thioureas groups readily create hydrogen bonds and compounds containing thioureas groups are good organogelators.

We now report very effective synthesis and properties of new amphiphiles and 1, $\omega$ -homoditopical bolaamphiphiles containing nucleobases.

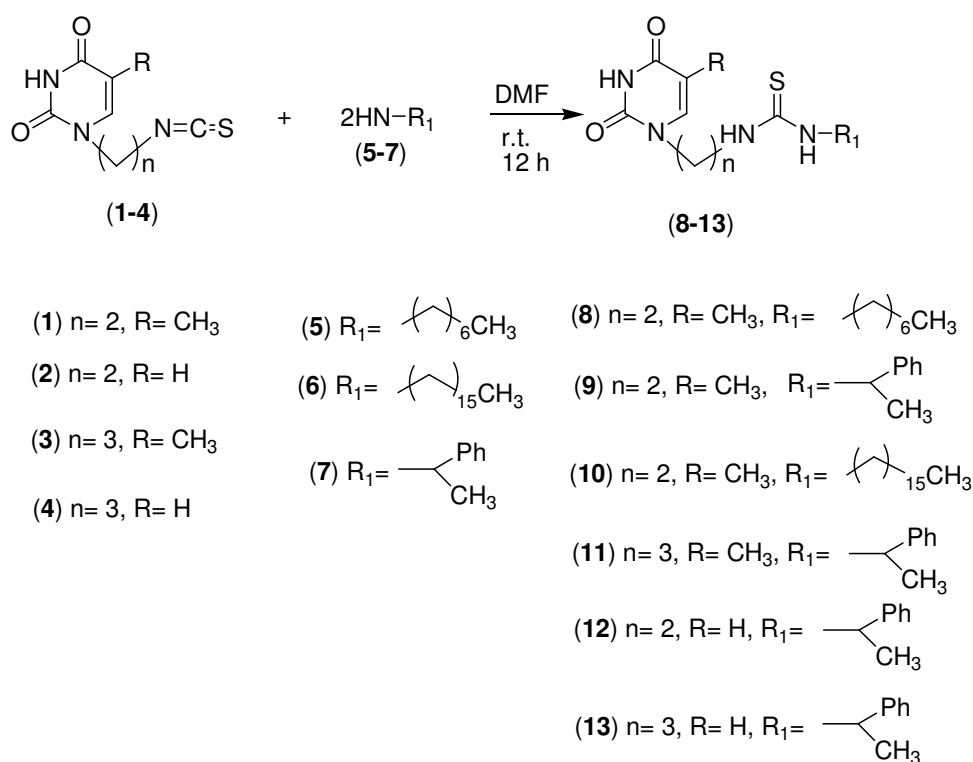
## 2. Results and discussion

### Synthesis of amphiphiles

The synthesis of the amphiphilic compounds is based on the reaction of the nucleobase containing an isothiocyano group (**1-4**) with various commercially available amines (**5-7**) (Scheme 1). Thymine (**1,3**) and uracil (**2,4**) derivatives with two (**1,2**) or three (**3,4**) carbon spacers between the nucleobase and the isothiocyano groups were used. Reactions were performed at room temperature in DMF. Products **8, 9, 10 and 12** with the shorter spacer are crystalline solids obtained in very good yields (>90%). Compounds **11** and **13** containing longer spacer are oils.

The behaviour of amphiphiles was studied in various solvents at room temperature and high temperature (5 mg compound and 1cm<sup>-3</sup> solvent).

**Scheme 1** Synthesis of the amphiphilic compounds



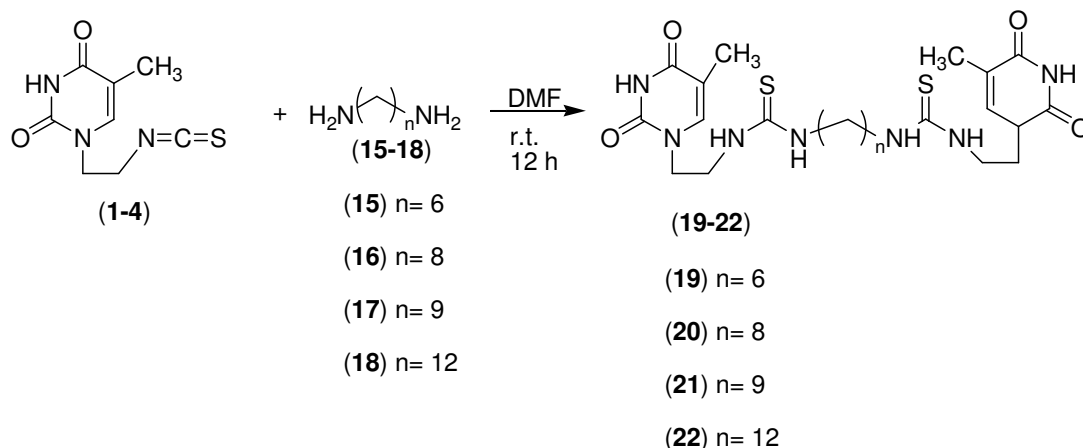
Products were insoluble in majority of solvents (ethanol, THF, acetonitrile, acetone, toluene) and soluble in aq.NaOH (2M) and in chloroform at high temperature. The aqueous solutions of compounds **8** and **10** after cooling had viscous consistence.

### Synthesis of 1, $\omega$ -homoditopical bolaamphiphiles

The bolaamphiphilic compounds were prepared by reaction of 1-(2-isothiocyanatoethyl)-thymine (**1**) with commercial diamines having various chain-lengths (**15-**

**18**) (Scheme 2). Reactions were performed at room temperature in DMF with good yields. All the products are crystalline solid. As for the amphiphiles, the solubility of bolaamphiphiles was studied in various solvents at room temperature and high temperature (5 mg compound and 1 cm<sup>-3</sup> solvent).

**Scheme 2.** Synthesis of the bolaamphiphilic compounds



The solubility of the bolaamphiphiles in majority of common solvents is very low similarly to the amphiphiles. They are soluble in aq. NaOH (2M) and in water at high temperature. The aqueous solutions of compounds **19** and **20** had viscous consistence after cooling to the room temperature. This compounds create intramolecular hydrogen bonds as expected, resulting in formation of aggregates

The structures created by the synthesized amphiphiles and bolaamphiphiles in the solution will be subject of the further study by the electron microscopy techniques.

### **3. Experimental**

#### **General procedure for the synthesis of amphiphiles**

Nucleobase containing an isothiocyano group (0,5 mmol) (**1-4**) was dissolved in 5 cm<sup>-3</sup> DMF and was added commercially amine (0,5mmol) (**5-7**). Reaction mixture was stirred overnight at room temperature. After the completion of the reaction, verified by TLC, the solvent was evaporated under reduced pressure. The product was washed with small quantity of methanol and dried. The yields is >90%. NMR spectra were consistent with structures.

#### **General procedure for the synthesis of bolaamphiphiles**

The 1-(2-isothiocyanatoethyl)-thymine (0,24 mmol) (**1**) was dissolved in 5 cm<sup>-3</sup> DMF and was added commercially diamine (0,12 mmol) (**15-17**). Reaction mixture was stirred overnight at room temperature. After the completion of the reaction, verified by TLC, the solvent was evaporated under reduced pressure. The product was washed with small quantity methanol and dried. The yields is >90%. NMR spectra were consistent with structures.

#### **4. Conclusion**

We have synthesized a new group of amphiphilic and 1, $\omega$ -bolaamphiphilic compounds containing nucleobases. Some of the compounds exhibit an aggregation in the solution as evidenced by the change in the viscosity. Further study is necessary to understand the nature of this phenomenon.

#### **5. References**

- 1.) Shimizu T., *J. Am. Chem. Soc.* 2001,123, 5947-5955
- 2.) Sivakova S., Rowan J. S., *Chem. Soc. Rev.*, 2005, 34, 9-21
- 3.) Shimizu, T., *Macromol. Rapid Commun.* 2002, 23, No. 5/6
- 4.) Estroff A. L., Hamilton D. A., *Chemical Reviews*, 2003, 104, No.3
- 5.) Prata C., Mora N., Polidori A., Lacombe M. J., Pucci B., *Carbohydrate Research*, 1999, 321, 15–23
- 6.) López Ó., Maja I., Fuentes J., Fernandez-Bolanos G.J., *Tetrahedron*, 2004, 60, 61-72

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