

## Abstract

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Title of thesis                Preparation of fluorescent azaphthalocyanines for labeling of oligonucleotide probes I.

Azaphthalocyanines (AzaPc) are macrocyclic compounds with large system of conjugated bonds and are therefore used as dyes and pigments. Their potential as diagnostic and therapeutic means is also under intensive examination. The aim of this thesis is a synthesis of precursors for cyclotetramerization of asymmetric fluorescent tetrapyrazinoporphyrazines (TPyzPz) via solid phase method bearing two various moieties, one suitable for binding to solid phase and the other intended for binding of the final TPyzPz to oligonucleotides. At the beginning of the thesis, basic terms related to AzaPc are defined. Also the main principles of synthesis of TPyzPz as well as possible modifications of their final structure are discussed. An important part of the thesis is the description of the typical properties of TPyzPz, the influence of the structure on the individual parameters and the fields of their use. Afterwards the preparation of each precursor with two different substituents for cyclotetramerization is described. Procedure was started by preparation of the essential intermediate 4-hydroxy-3,5-diisopropylbenzoic acid, a bulky compound preventing aggregation of macrocycles when used as a peripheral substituent. Various methods for the synthesis were used, their efficiency was evaluated and the most yielding one was selected. After 4-hydroxy-3,5-diisopropylbenzoic acid was prepared, it was functionalized to amides using variety of amines bearing an azido moiety or primary alcoholic group. Several methods of amidation were tested and optimized to obtain high yield and purity of the product. Prepared precursors were used for replacement of chlorines in 5,6-dichloro-2,3-dicyanopyrazine to first or second degree. Due to cyanogroups sensitivity to basic environment, the substitution conditions were optimized to obtain pure product and high-yielding reaction. Potassium carbonate or sodium hydrogen carbonate were found the most suitable to run these reactions. The synthesized compounds were characterized by NMR and in majority of cases also by IR spectroscopy. Prepared monomers were bound to the solid phase activated by either trichloroacetimidate group or propynyl moiety. The solid phase method of cyclotetramerization could enable assembly of the ABBB macrocycle with B bearing highly polar peripherally substituted structure.