ABSTRACT

Charles University, Faculty of Pharmacy in Hradec Králové

Department	Department of Pharmaceutical Chemistry and Pharmaceutical Analysis
Candidate	Daniel Mikula
Supervisor	doc. PharmDr. Miroslav Miletín, Ph.D.
Consultant	Mgr. Michaela Kolářová
Title of thesis	Preparation of fluorescent phthalocyanines for labeling of oligonucleotide probes IV.

Phthalocyanines (Pcs) are macrocyclic compounds with a conjugated system of double bonds. Thanks to this, they have interesting photophysical and photochemical properties that enable their practical use in pharmacy and medicine in the field of diagnostics or treatment of cancer diseases. This work deals with the preparation of axially disubstituted silicon complexes of phthalocyanines (SiPcs), which would have suitable properties for subsequent use in the labeling of oligonucleotide probes. The theoretical part is primarily devoted to the methods of Pcs preparation, from the choice of precursors, through the formation of the macrocycle and insertion of the central atom, to the modifications of the resulting molecule, including the specifics related to SiPcs. The basic properties of Pcs and the degree of influence of different changes of the molecule on these properties are also described. The basic areas of use of Pcs are also mentioned. The experimental part begins with an attempt of *de novo* synthesis of SiPc. This is followed by the preparation of various types of precursors, intended for subsequent substitution on SiPc in axial positions. Precursors bearing an adamantane-1-amine (A1A) fragment (for its possibility of non-covalent binding into the hydrophobic cavity of cucurbituril) or an azide moiety were prepared, through which the resulting molecules can be used in click chemistry. Substituents with different lengths of the connecting carbon chain between the mentioned functional groups and the SiPc macrocycle were compared. It was possible to prepare a compound with A1A attached to SiPc through a six-carbon connecting chain and a compound with an azide group attached to SiPc through an eleven-carbon chain. With SiPc containing azide groups in axial substituents, click reactions were performed by Huisgen cycloaddition to the oligonucleotide and to *N*-substituted A1A with a propargyl group. However, these reactions were unsuccessful. The possibility of connecting an axial substituent to SiPc through a nitrogen connecting atom was also verified, with a negative result.