

ABSTRACT

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Title of diploma thesis: Synthesis of precursors of fluorescent polyene ceramide

Ceramides, a complex group of lipids belonging to sphingolipids, have significant functions in many processes in living systems. Their crucial importance consists in the cell signaling and co-creation of functional skin barrier.

Fluorescently labelled lipid analogues are often used in the lipid research. Polyene-lipids, in which the fluorophore is formed by five conjugated double bonds, represent an advanced way of fluorescent labelling of lipid molecules. Thanks to their structure, the polyene-lipids uniquely mimic their natural counterparts.

This thesis studies the possibilities of the synthesis of fluorescent polyene ceramide and describes the precursors, i.e. the key substances, suitable for the preparation of the target labelled ceramide. The fluorophore was planned to be situated in the sphingosine part of the molecule, so as the properties of analogues with variable acyl chain length could be studied in the future.

Three synthetic ways have been designed and investigated. The first way (Synthesis A) consists in the reaction of the terminal alkyne carrying polyene fluorophore with Garner aldehyde. The mentioned terminal alkyne was obtained from (2*E*,4*E*)-hexa-2,4-dienal as starting compound in several steps. Since the obtained polyene intermediates were relatively unstable, other approaches were designed, in which the polyene fluorophore, represented by unsaturated aldehyde, should be attached on a ceramide analogue carrying halogen in the sphingosine part in the latter stage of the synthesis. Thus the sequence of reactions was reversed in comparison to the first approach. The first step for the preparation of the chloro derivative of ceramide was alkynylation of Garner aldehyde (Synthesis B), the bromo derivative was obtained by Grubbs metathesis (Synthesis C).

The prepared precursors are (2*E*,4*E*,6*E*,8*E*)-deca-2,4,6,8-tetraenal and *N*-((2*S*,3*R*,*E*)-8-bromo-1,3-dihydroxyoct-4-en-2-yl)tetracosanamide. These substances will be used in further study for the synthesis of fluorescent polyene ceramides.