

Abstract

Ceramides are group of lipids which belong to sphingolipids. Skin ceramides have several functions in the organisms. They are important part of the lipid matrix of the *stratum corneum*, the outermost layer of the epidermis, where they participate in the barrier function of the skin. Furthermore, ceramides are secondary messengers in cell apoptosis and participate in many metabolic processes. Ceramides are composed of sphingoid base, which is *N*-acylated by fatty acid. Sphingoid base can be sphingosine, phytosphingosine, dihydrosphingosine or 6-hydroxysphingosine.

Lower level of ceramides in the *stratum corneum* is associated with various skin diseases especially atopic dermatitis and psoriasis. Manifestations of these diseases is significantly improved by topical administration of ceramide. Exogenously administered ceramides help regenerate damaged skin and improve hydration of the skin. However, it is not fully known, in which way topically administered ceramides improve the progress of diseases.

The aim of this work is synthesize physiological ceramide NS by using Grubbs metathesis reactions and optimize the conditions for achieving the highest yields.

Synthesis of ceramide NS was based on pentadecan-1-ol, which was eliminated to terminal alkene. The elimination was carried out in three different ways. The second part of the synthesis was the preparation of sphingosine analog for Grubbs metathesis with terminal alkene. The sphingosine analogue was prepared from Garner's aldehyde. The critical step was the Grubbs metathesis of alkene with the sphingosine analogue, for which 4 procedures were examined. This was followed by the removal of the protecting groups to afford sphingosine and acylation of sphingosine with lignoceric acid to afford ceramide NS.

This method of synthesis should be used as a model for the preparation of ceramides based on deuterated alcohol. Ceramides with deuterated chain can be used for further studies on lipid membranes. Study of deuterium-labeled ceramides finds its application in the evaluation ceramides. Methods that use deuterated molecules include e.g. infrared spectroscopy or nuclear magnetic resonance in solid phase. This could explain the behavior of ceramides in the *stratum corneum*.