

Abstract

Acylceramides belong to the subgroup of ultralong chain ceramides. They are essential components of the extracellular lipid matrix of *stratum corneum*, where they play a crucial role in proper function of skin barrier (they help preventing the excessive water loss and penetration of exogenous substances and pathogens to the organism).

The 32-hydroxydotriacontanoic acid is one of the fatty acids forming the backbone of all the acylceramides. In the molecule of acylceramide, the carboxyl group of this acid is bound to a primary amino group of the sphingoid base and the ω -hydroxy group is esterified with linoleic acid. In the *stratum corneum*, 32-hydroxydotriacontanoic acid may remain as a part of free acylceramides or it can be covalently linked to the surface of corneocytes and form the “first lamella”, which then serves as a basis for the orientation of other lipids in the matrix.

The recent literature describes the synthesis of 32-hydroxydotriacontanoic acid but only with relatively small overall yields. The most problematic part of the synthesis seems to be the connection of two shorter fragments leading to the ultralong chain. The main aim of this research project was to optimise the reaction conditions to increase the yield of formation of the ultralong acid, focusing on the most complicated step. First possibility to increase the yield was by modifying the reaction conditions in the previously described Wittig reaction. In the literature, the Wittig reaction was described with a yield around only 38%. We expected that a change in the reaction time or temperature during the ylide formation might lead to an improvement. Unfortunately, we were not able to increase the yields significantly.

Since Wittig reaction belongs to a group of olefination reactions, the next aim was to examine additional olefination reactions to possibly increase the yield of this step. In this thesis, we mainly focused on Julia and Julia-Kocienski reactions and their modifications. For this purpose, a series of hitherto unpublished heterocyclic

derivates of hexadecanoic acid was prepared as starting materials for this type of reaction. The highest yields were obtained by the modified Julia-Kocienski reaction with (1-cyclohexyl-1*H*-tetrazole-5-yl)sulfonyl derivative of hexadecanoic acid as a starting material. In this case, we were able to increase the yields even over 70% which is approximately double compared to a previous procedure meaning a great improvement in the described reaction pathway.