

University of Groningen

## The enzymic cyclization of 6'-norsqualene-2,3-oxide

Smaal, Jan Auke

**IMPORTANT NOTE:** You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

*Document Version*

Publisher's PDF, also known as Version of record

*Publication date:*

1971

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

Smaal, J. A. (1971). *The enzymic cyclization of 6'-norsqualene-2,3-oxide*. [s.n.].

### Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

### Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

## SUMMARY

The present study is a part of an effort to determine the mechanism of action of squalene oxide-lanosterol cyclase. A brief introduction to the biosynthesis of lanosterol is given, together with a survey on the *in vitro* enzymic cyclizations of modified squalene-2,3-oxides. From this introduction the objective of this study becomes clear, this being the determination of the role of the 6'-methyl group in the enzymic cyclization of squalene-2,3-oxide. The approach to this problem is the replacement of the 6'-methyl group by hydrogen and feeding this modified squalene-2,3-oxide to a solubilized and partially purified squalene oxide-lanosterol cyclase from rat liver. The synthesis of radio-labeled racemic 6'-norsqualene-2,3-oxide\* is described.

The results from the incubations (*in vitro*) are divided into two categories: (1) small scale incubations with 5 ml of the cyclase solution, (2) large scale incubations with about 100 ml of the cyclase solution. This division was necessitated by the occurrence of two enzymic products. Spectral measurements of the enzymic products, and some chemical transformations from the steroid field together with pertinent spectral data of the derived products, provided evidence for the structure of each of the enzymic products. The product from the large scale incubation proved to be 19-nor-5 $\alpha$ -lanosterol, while the product from the small scale incubations was the C10 epimer, *i. e.* 19-nor-5 $\alpha$ ,10 $\alpha$ -lanosterol. A mechanism leading to the product with the unusual A:B-*cis* fused (5 $\alpha$ ,10 $\alpha$ ) ring system is proposed.

The conversion efficiency of the substrate to product is shown also to be related to the severity of the non-bonding interaction relieved by removal of a specific methyl group in the unrearranged "C20 carbonium ion".

The occurrence of 19-nor-5 $\alpha$ ,10 $\alpha$ -lanosterol sheds light on some of the characteristics of the cyclizing enzyme. It is concluded that (i) the participation of the enzyme in the termination step cannot be denied, (ii) the removal of the 6'-methyl group might be detrimental to the *in vivo* biosynthesis of lanosterol in rat liver.

\* 21-<sup>3</sup>H-22,23-epoxy-2,6,10,15,23-pentamethyl-2,6,10,14,18-tetracosapentaene