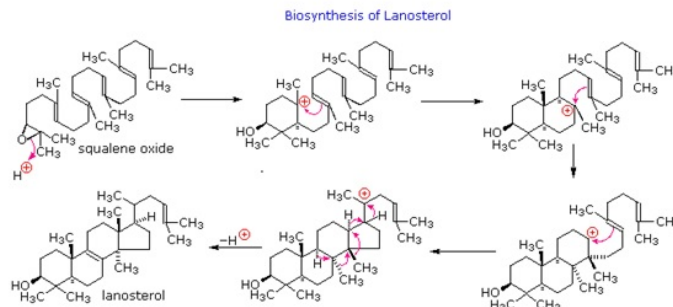
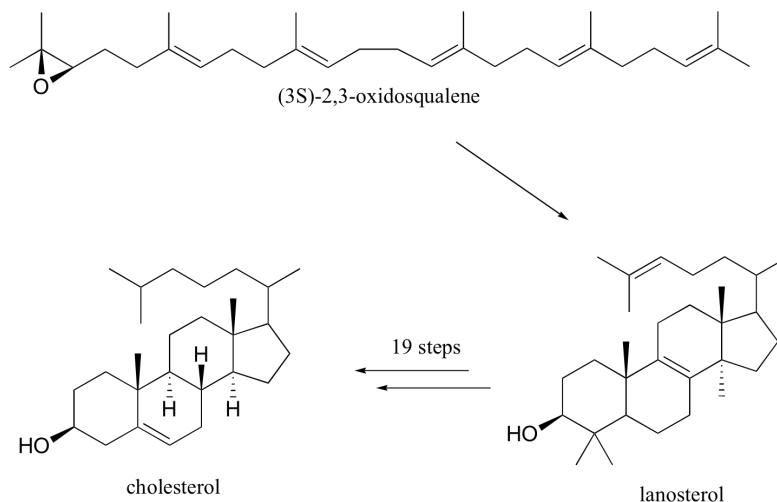


26.8: BIOSYNTHESIS OF STEROIDS

On the diagram below, the series of cation-like cyclizations and rearrangements, known as the Stork-Eschenmoser hypothesis, is shown, which were identified in the biosynthesis of the triterpene lanosterol. Lanosterol is a precursor in the biosynthesis of steroids. This takes place by metabolic removal of three methyl groups and degradation of the side chain.

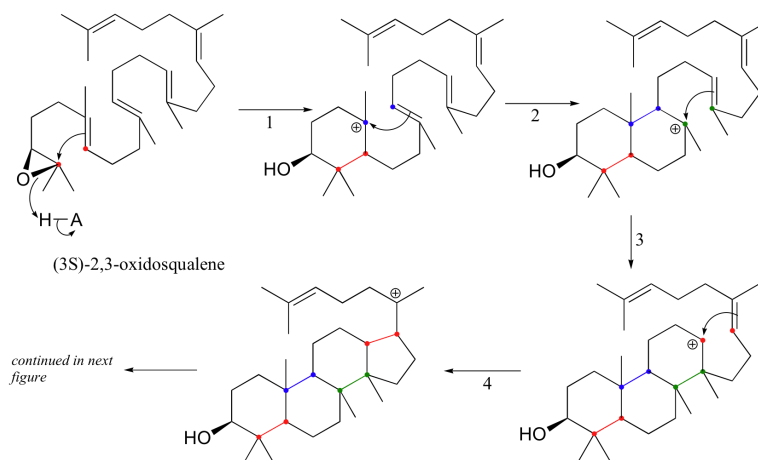


Rearrangements are particularly important in carbocation-intermediate reactions in which isoprenoid molecules cyclize to form complex multi-ring structures. One of the key steps in the biosynthesis of cholesterol is the electrophilic cyclization of oxidosqualene to form a steroid called lanosterol.

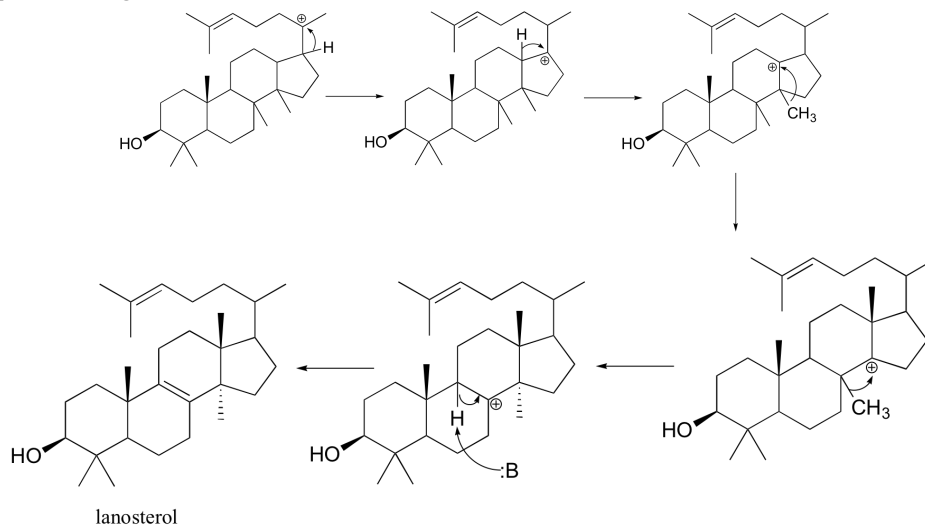


This fascinating reaction has two phases. The first phase, in which the actual cyclization takes place, is a series of electrophilic addition steps. The second phase is a series of hydride and methyl shifts. There is some argument about whether these processes occur in a stepwise fashion (with discrete carbocation intermediates) or in a concerted manner. For the sake of clarity, we will show the reaction proceeding stepwise.

The cyclization phase begins with attack by pi electrons on an epoxide electrophile (step 1 - review epoxide ring-opening reactions in [section 8.6B](#)).



Steps 2, 3, and 4 are simply successive attacks by pi electrons on the carbocation generated by the previous attack. The overall result of this electrophilic cascade is the opening of the epoxide ring, and closure of three six-membered and one five-membered ring. Next comes the rearrangement phase of the reaction, which is a series of two hydride shifts and two methyl shifts, followed by a proton abstraction which finally quenches the positive charge to form lanosterol.



CONTRIBUTORS AND ATTRIBUTIONS

- Dr. Dietmar Kennepohl FCIC (Professor of Chemistry, [Athabasca University](#))
- Prof. Steven Farmer ([Sonoma State University](#))
- William Reusch, Professor Emeritus ([Michigan State U.](#)), [Virtual Textbook of Organic Chemistry](#)
- [Organic Chemistry With a Biological Emphasis](#) by Tim Soderberg (University of Minnesota, Morris)

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