reduction (THF, 25 °C) yielded a $C_{20}H_{36}O_2$ diol, characterized as a diacetate. In the customary assumption[4] that the structure and stereochemistry within the ABC framework correspond to those resulting from the normal biosynthetic pathway, structures **2**, **7**, and **8** may be allocated to the enzymatic product from oxide **1**, the cleavage product, and the derived diacetate, respectively. A mass spectral comparison substance was synthesized from a tricycle of secure structure, the keto acetate **9**,[5] in order to support these assignments. Initial reaction with ethoxyacetylide[5b] (Et_2O, −10 to −16 °C → room temperature), followed by 5% aqueous H_2SO_4 (MeOH, room temperature) produced the α,β-unsaturated ester **10**. Lithium aluminum hydride reduction (refluxing THF) generated (in addition to the allyl alcohol) the saturated diol **11**. The (GC facilitated) mass spectrum of its diacetate was *qualitatively* virtually indistinguishable (essential peak for peak matching, but differing intensities), from that of diacetate **8**, in keeping with the skeleton and functionality of **8** and therefore structures **7** and **2**. Buttressing of these assignments is embodied in the close similarity[6] of the NMR (100 MHz, benzene-d_6) C–Me signals of **7** (δ 0.76, 2 × 0.84, 1.04) and **11** (δ 0.77, 0.81, 0.82, 0.97), especially in regard to the ones at highest field (ring-C Me's), a particular comparison rendering unlikely a conceivable **7**/**2** alternative, viz., the isomeric perhydrocyclopenta[*a*]-naphthalene, for which a cyclopentanoid methyl peak at δ ~0.69 would be expected.[7]

Acknowledgment is given to the National Institutes of Health (Grant 5 R01 GM10421) and the Swiss NSF (fellowship, H. R.W.) for financial support, R. Hanzlik for preliminary enzyme experiments, Professor R. Clayton for counsel, and NIH (Grant RR00711) and NSF (Grant GP23633) for support of the Stanford HXS-360 NMR facility.

(4) E.g.: Corey, E. J.; Lin, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1969**, *91*, 2132.
(5) (a) Ireland, R. E.; Baldwin, S. W.; Dawson, D. J.; Dawson, M. I.; Dolfini, J. E.; Newbould, J.; Johnson, W. S.; Brown, M.; Crawford, R. J.; Hudrlik, P. F.; Rasmussen, G. H.; Schmiegel, K. K. *Ibid.* **1970**, *92*, 5743. (b) Baldwin, S. W. Ph.D. Dissertation, California Institute of Technology, 1969.
(6) In related cases, chemical shifts of angular Me's in tricyclic ABC systems are virtually independent of trans,anti,trans and trans,syn,trans relative stereochemistry: van Tamelen, E. E.; Sharpless, K. B.; Hanzlik, R.; Clayton, R. B.; Burlingame, A. L.; Wszolek, P. C. *J. Am. Chem. Soc.* **1967**, *89*, 7150. Sharpless, K. B. Ph.D. Dissertation, Stanford University, 1968.
(7) Zücher, R. F. *Helv. Chim. Acta* **1963**, *46*, 2054 and spectra of other cyclopentanes from this laboratory.

Bioorganic Characterization and Mechanism of the 2,3-Oxidosqualene → Lanosterol Conversion

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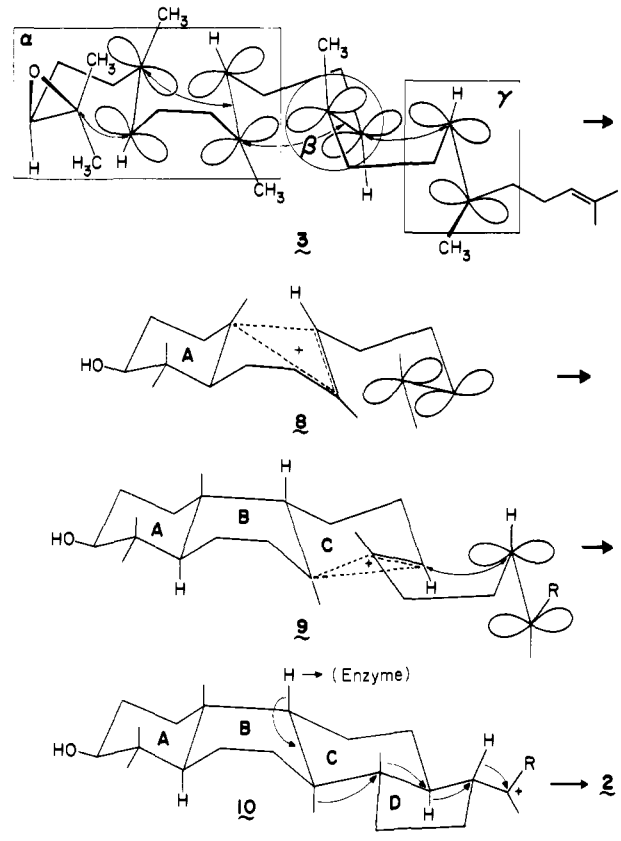
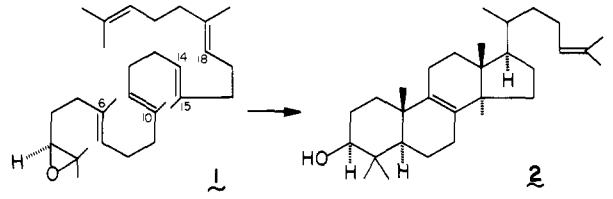
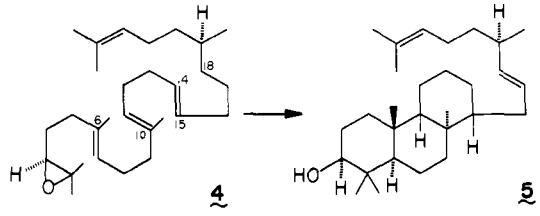
In regard to the biological conversion of 2,3-oxidosqualene (**1**) to lanosterol (**2**), previous study[1-7] of various enzymic and nonenzymic reactions of squalene oxide and its variants have led to inter alia the following observations and inferences regarding the cyclization process: (a) polycyclization involves A-ring formation with a high degree of S_N2-like participation of the neighboring, Δ^6 π bond[5] and an ensuing series of conformationally rigid, partially cyclized carbocationic intermediates;[4,5,7] (b) the oxide–tetra-π-bond sequence (α, β, γ) in **3** constitutes the essential substrate requirement for tetracyclization, the nonoxidic C-5 terminus and the methyls at C-6, -10, and -15 not being individually necessary;[1] (c) the chiral, trisubstituted oxide, Δ^6, Δ^{10} array (α) currently represents the minimum requirement for significant cyclase action;[1] (d) distances (↔, **3**) between, and required conformational orientations of, C-2 and C-7,[6] C-6 and Δ^{10} as well as C-10 and Δ^{14}, must be optimized;[1] (e) except for the terminating C-9 proton loss and for behavior in the Δ^{14} area, all chemical (including conformational) behavior can be qualitatively simulated in nonenzymic, related systems.[1-3] By contrast, illuminating biochemical information regarding relationships between the Δ^{10} and Δ^{18} sites and that at Δ^{14} (β) has been lacking, a shortcoming alleviated by the recent finding[8] that 15′-nor-18,19-dihydrosqualene 2,3-oxide (**4**) is transformed enzymically

Scheme I







(1) van Tamelen, E. E. *Int. Congr. Pure Appl. Chem., 23rd* **1971**, *5*, 85 and references cited therein.
(2) van Tamelen, E. E. *Acc. Chem. Res.* **1968**, *1*, 111; **1975**, *8*, 152.
(3) van Tamelen, E. E.; Anderson, R. J. *J. Am. Chem. Soc.* **1972**, *94*, 8225.
(4) van Tamelen, E. E.; Lees, R. G.; Grieder, A. *J. Chem. Soc.* **1974**, *96*, 2255.
(5) van Tamelen, E. E.; James, D. R. *J. Am. Chem. Soc.* **1977**, *99*, 950.
(6) van Tamelen, E. E.; Pedlar, A. D.; Li, E.; James, D. R. *J. Am. Chem. Soc.* **1977**, *99*, 6778.
(7) van Tamelen, E. E.; Hopla, R. E. *J. Am. Chem. Soc.* **1979**, *101*, 6112.
(8) van Tamelen, E. E.; Leopold, E.; Marson, S. A.; Waespe, H. R. *J. Am. Chem. Soc.*, preceding communication in this issue.

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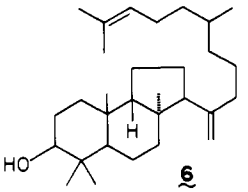
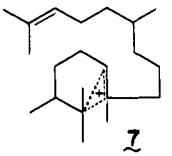
to the tricycle **5**, a reaction apparently involving hydrogen transfer from the side chain to the cationic C-ring intermediate. Since purely spontaneous hydrogen transfer between two distant carbons within a nonrigid acyclic framework, namely C-14 and (presumably) C-18 in **4**, is improbable, the two carbons involved must be held in close proximity by the enzyme; such constraints operating on the natural substrate require that C-14 and the Δ^{18} π bond be similarly juxtaposed (↔, **3**), thereby ensuring bond formation between these centers, *contrary to Markovnikov behavior*, as observed in the *nonenzymic* cyclization of squalene oxide.[9] With the enforcement of such behavior, bond formation between C-10 and C-15 must then necessarily occur, thus overriding, in effect, purely chemical behavior at the Δ^{14} site and providing the observed six- (rather than five-) membered C-ring. Moreover, in the biosynthesis of a host of other tetra- and pentacyclic triterpenoids, the generation of six-membered rings rather than the five-membered rings anticipated on a purely chemical basis may be ascribed to similar forces at work in related cyclase cases.

Indications of the transient involvement of a five-membered C ring in lanosterol biosynthesis have been presented,[10,11] in particular the enzymic formation of perhydrocyclopenta[*a*]-naphthalene **6** from 18,19-dihydro-2,3-oxidosqualene, a result also expected on purely chemical grounds. In the 15′-nor-18,19-dihydro (**4** → **5**) case production of a perhydrocyclopentanaphthalene is *not* chemically preferred, and the formation of **5** indicates that the enzyme does not compel generation of a bona fide, if tem-



6


7

porary, five-membered C ring. It appears that formation of **6** merely signifies that elimination of a proton from the parent carbocation, more stable than that from **4**, is a process of lower energy than some other reaction pathway (for example, hydrogen transfer of the type observed in the **4** → **5** conversion), not an uncommon result in organic chemistry. The tricyclic cations derived from these 18,19-dihydro epoxides are formulated as nonclassical species (e.g., **7**) because that structural type best explains the partitioning between five- and six-membered rings, is in keeping with the enzyme-enforced proximity of carbons involved in its genesis as well as the preservation of stereochemistry during cyclization, and most simply accommodates the closely linked chain of interactions C-10, C-14, C-15, and C-18. Accordingly, this interpretation has been extended to the squalene oxide cyclization itself (**9**, and for consistency, **8**; Scheme I).

The entirety of the above results thus permits for the first time a comprehensive view of substrate behavior during the bioconversion of oxidosqualene to lanosterol and presumably other polycyclic triterpenes. This view is shown, and the foregoing body of findings represented, in the sequence **3** → **8** → **9** → **10** → **2**.[12]

(9) van Tamelen, E. E.; Willett, J.; Schwartz, M.; Nadeau, R. *J. Am. Chem. Soc.* **1966**, *88*, 5937.
(10) van Tamelen, E. E.; Willett, J. D.; Clayton, R. B. *J. Am. Chem. Soc.* **1967**, *89*, 3371.
(11) van Tamelen, E. E.; Sharpless, K. B.; Hanzlik, R.; Clayton, R. B.; Burlingame, A. L.; Wszolek, P. *J. Am. Chem. Soc.* **1967**, *89*, 7150.
(12) For early stereochemical portrayals of a hypothetical hydroxonium ion induced oxidative cyclization of squalene see: (a) Eschenmoser, A.; Ruzicka, L.; Jeger, O.; Arigoni, D. *Helv. Chim. Acta* **1955**, *38*, 1890. (b) Stork, G.; Burgstahler, A. W. *J. Am. Chem. Soc.* **1955**, *77*, 5068.

Book Reviews

Quantum Chemistry Symposium No. 14. 1980. Proceedings of the International Symposium on Atomic, Molecular, and Solid-State Theory, Collision Phenomena, Quantum Statistics, and Computational Methods. Edited by P.-O. Löwdin and Y. Öhrn. John Wiley & Sons, New York. 1980. xix + 732 pp. $40.00.

For two decades the Quantum Chemistry Project at the University of Florida, led by the indefatigable Per-Olov Löwdin, has been conducting (among many other meetings) annual international symposia on quantum chemistry at Sanibel Island and more recently at Flagler Beach. The present volume contains the invited and contributed papers at the 20th Symposium, held March 9–15, 1980, in honor of E. Bright Wilson. Featured are Wilson's personal reminiscences of quantum chemistry and quantum chemists (13 pages). Otherwise, there is the usual mix for symposium volumes, from trivial outlines of published works to significant original research papers, with the latter in the majority in this case. Altogether there are 72 contributions having 132 authors. A bibliography of Wilson's papers is included, as is a fine picture of him.

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Organic Compounds of Sulfur, Selenium, and Tellurium. Volume 6. By D. R. Hogg (University of Aberdeen). Royal Society of Chemistry, London, England. 1981. xviii + 331 pp. $127.00.

This is in the series of review volumes published by the Royal Society called Specialist Periodical Reports, this one covering the literature from April 1978 to March 1980 (except the literature for compounds with S=N functional groups goes through February 1980). The chemistry of these elements is under very active study, as examination of the topics and literature citations in this volume attests. These Reports are like a very good encyclopedia: you start to look up a topic you are interested in and find yourself reading with fascination at other pages that you happen to open.

For workers in the field, reading this Report is a must; it, of course, mainly covers the organic chemistry of these elements, with biochemistry and biology covered only in passing. This volume includes chapters on aliphatic compounds (by G. C. Barrett), ylides and related structures (by E. Block, D. L. J. Clive, N. Furukawa, and S. Oae), thiocarbonyl and selenocarbonyl compounds (by D. R. Hogg, J. K. Landquist, and A. Ohno), small ring compounds of S and Se (by G. C. Venier), saturated cyclic compounds (by P. K. Claus), and heteroaromatic compounds (by M. Davis).

William A. Pryor, *Louisiana State University, Baton Rouge*

An Introduction to Inorganic Chemistry. By Keith F. Purcell (Kansas State University) and John C. Kotz (State University of New York, College at Oneonta). Saunders, Philadelphia. 1980. xv + 637 pp. $30.95.

Professors Purcell and Kotz have amended, rewritten, and omitted parts of their earlier book (*Inorganic Chemistry*, reviewed *J. Am. Chem. Soc.* **1977**, *100*, 6797) to eliminate 480 pages and create a text more suitable for an advanced inorganic course. The level of presentation in this "Introduction" has not been lowered, however, and a challenging text has resulted.

The initial section (120 pp) deals with atomic orbitals, molecular structures (including ionic lattices), and an unusual and effective approach to molecular orbital theory. The second section (175 pp) is a novel analysis of nonmetal chemistry. After a chapter on acid/base (Donor/Acceptor) concepts, nonmetal chemistry is presented through a study of nonmetal functional groups (i.e., the B–O function, the Al–C function). Functional group description, reaction mechanism, and a systematic analysis of various functional group transformations are given in subsequent chapters. This is an effective and refreshing approach when contrasted with the more traditional, element-by-element, march across the periodic table.

The rest of the text covers transition-metal chemistry, with subsections on classical coordination chemistry (about 235 pp of bonding, structures, and reaction mechanisms) and organometallic reactions and catalysis (65