ammoniate." The solid splits out hydrogen slowly at room temperature. Only slight evolution of hydrogen occurs upon solution of the solid in distilled water; in the presence of aqueous acid, hydrogen is evolved rapidly. It has a negative temperature coefficient of solubility in ether. At room temperature a white solid, believed to be the "diammoniate of diborane" and perhaps some $(H_2NBH_2)_x$, is slowly deposited from ether solution. A trace quantity of hydrogen is liberated also.

The relative intensities and interplanar spacings, which were obtained from the X-ray powder pattern of the crystalline material, are tabulated below.

Intensity	d, Å.	Intensity	d, Å.	Intensity	d, Å.
VVS	3.72	S	2.13	MW	1.66
VS	3.65	MS	2.09	MS	1.60
S	2.63	W	1.86	VW	1.40
MS	2.52	W	1.82	W	1.37

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IN VITRO CONVERSION OF SQUALENE TO LANOSTEROL AND CHOLESTEROL[1]

Sir:

According to a scheme of sterol biogenesis proposed in 1953,[2] squalene cyclizes to an intermediate having the structure of a 4,4′,14-trimethylcholestane derivative while the formation of cholesterol occurs subsequently by removal of the three methyl substituents. As proposed, the scheme also provided an explanation for the origin of lanosterol from a triterpenoid precursor. Recently the synthesis of lanosterol from acetic acid and the conversion of this sterol to cholesterol have been shown to occur in homogenates of rat liver.[3] These findings have furnished strong support for the view that C_{30} sterols are intermediates in the biosynthesis of cholesterol from squalene. During the present study of squalene metabolism we have found that in one type of liver preparation squalene is converted to a mixture of sterols with cholesterol predominating while in another preparation lanosterol accumulates.

TABLE I

	Microsomes + Supernatant, (Prep. A)[a]		Microsome Extract + Supernatant, (Prep. B)[b]	
	+ DPN (6.5 mg.) c.p.m.	... c.p.m.	+ DPN (6.5 mg.) c.p.m.	... c.p.m.
C^{14} squalene added	5700	5700	11400	11400
C^{14} squalene recovered	2400	2380	2200	3040
Lanosterol	62	72	145[d]	133
Cholesterol	789[c]	566	<10	<10

[a] 14.5 ml. of preparation A per experiment. [b] 22.5 ml. of preparation B per experiment. [c] Specific activities 17.7, 18.2; 23.0 and 18.0 c.p.m./mg. on successive crystallizations. [d] Specific activities 8.7, 10.7; 9.5 and 11.5 c.p.m./m.g. on successive crystallizations.

The enzyme systems for the over-all synthesis of cholesterol from acetic acid, as shown by Bucher and McGarrahan,[4] are constituents of the microsome and supernatant fraction of rat liver homogenates. A conversion of squalene to digitonin precipitable steroids by liver extracts has been reported by Dituri, *et al.*[5] In the present experiments with C^{14} squalene, two liver preparations were used. Rat liver was homogenized[6] and centrifuged for 40 minutes at 100,000 × g and the microsomes from 40 ml. of homogenate were combined with 10 ml. of supernatant (Preparation A). The microsomes from another 95 ml. of homogenate were suspended in 20 ml. of supernatant, subjected to sonic oscillation (9 Kc.) for 15 seconds and, after addition of another 20 ml. of supernatant, centrifuged at 100,000 × g for 40 minutes. The resulting particle-free supernatant is designated Preparation B. The source of C^{14} squalene was liver and intestinal tissue of rats which had received 1-C^{14} acetate by injection, and were killed 10 minutes later. The radioactive hydrocarbon was characterized as squalene as described previously.[7] It was suspended in supernatant and incubated with the two liver preparations for three hours at 37°. The petroleum ether extracts containing the unsaponifiable material were first chromatographed on active alumina and the sterol fraction rechromatographed on partially deactivated alumina after the addition of non-isotopic lanosterol and cholesterol as carrier. Lanosterol and cholesterol thus separated were recrystallized three times without loss of radioactivity. Also, the specific activity of one sample of cholesterol was not diminished by purification through the dibromide. DPN[8] which is essential for the incorporation of acetate into cholesterol in homogenates[9] had no marked effect on the yields of sterols formed from squalene in these preparations, nor did its presence significantly alter the ratio of C^{14} recovered in the two sterols. As shown in Table I about ten times as much C^{14} is found in cholesterol as in lanosterol when the enzyme preparation contains intact microsomes, while in the particle-free preparation the C^{14} content of cholesterol is insignificant compared to that of lanosterol. Thus, both the cyclization of squalene to lanosterol and demethylation to cholesterol take place when the

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[1] Supported by grants-in-aid from the National Science Foundation and the Life Insurance Medical Research Fund.

[2] R. B. Woodward and K. Bloch, THIS JOURNAL, **75**, 2023 (1953); W. G. Dauben, *et al.*, *ibid.*, **75**, 3038 (1953).

[3] R. B. Clayton and K. Bloch, *Fed. Proc.*, **14**, 194 (1955).

[4] N. L. R. Bucher and K. McGarrahan, *ibid.*, **14**, 187 (1955).

[5] F. Dituri, F. Cobey, J. V. B. Warms and S. Gurin, *ibid.*, **14**, 203 (1955).

[6] N. L. R. Bucher, THIS JOURNAL, **75**, 498 (1953).

[7] R. G. Langdon and K. Bloch, *J. Biol. Chem.*, **200**, 129 (1953).

[8] DPN is diphosphopyridine nucleotide.

[9] I. D. Frantz and N. L. R. Bucher, *J. Biol. Chem.*, **206**, 471 (1954).

microsomes are intact. The particle-free preparation retains the ability to cyclize squalene but is no longer efficient in catalyzing the demethylation reactions leading to cholesterol. The present findings in conjunction with earlier ones establish the sequence squalene-lanosterol-cholesterol as a major pathway in sterol biogenesis.

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BOOK REVIEWS

Electrolyte Solutions. The Measurement and Interpretation of Conductance, Chemical Potential and Diffusion in Solutions of Simple Electrolytes. By R. A. ROBINSON, D.Sc., Ph.D., F.R.I.C., Professor of Chemistry, University of Malaya, Singapore, and R. H. STOKES, Ph.D., D.Sc., F.R.A.C.I., A.R.I.C., Reader in Physical Chemistry, University of Western Australia. Academic Press Inc., Publishers, 125 East 23rd Street, New York 10, N. Y. 1955. xiii + 512 pp. 15 × 22.5 cm. Price, $9.50.

To all who are interested in the properties of electrolytic solutions, the appearance of this authoritative volume should be a welcome event. The substantial contributions of both authors to this field qualify them admirably to write on the subject, and they have produced a book that has much to offer to specialist and student alike.

Robinson and Stokes have restricted themselves to three fundamental properties of electrolytes–conductance, chemical potential and diffusion—and their penetrating analysis of the experimental and theoretical studies in these fields has produced interpretations and generalizations that are both new and important. The discussions, based upon the interionic attraction theory of Debye and Hückel and especially upon the later contributions of Falkenhagen and of Onsager and Fuoss, demonstrate a surprising adequacy of modern theory when allowance is made for the dimensions of the ions. The reader will be impressed with the progress that has been made in the past two decades, developments that have fashioned equations valid for solutions of moderate and even high concentrations from limiting laws applicable only to "slightly polluted water."

During the first major period in the development of solution theory, exact thermodynamics was applied extensively to the study of electrolytic solutions, and the Debye–Hückel theory was used to extrapolate to the experimentally inaccessible region of extreme dilution. From reading the present volume one may conclude that the investigation of ionic solutions has entered a new phase in which the kinetic approach will take its place beside the thermodynamic. The submicroscopic view is introduced in chapter 1—"Properties of Ionizing Solvents." In subsequent chapters the reader comes to regard ions not as the time-honored point charges but as kinetic units with several relatively firmly attached water molecules migrating at a rate of perhaps 1 cm./hr. in a field of 1 v./cm. while subject to instantaneous Brownian velocities of 200 miles/hr. In the reviewer's opinion, the thermodynamic approach is never outmoded and rarely overemphasized, yet the complexity of the problem justifies a twofold attack. For this reason, the present book is complementary to such valuable existing treatises as that of Harned and Owen. The fruitfulness of the coordinated assault is particularly evident in the section on ion-solvent interactions and the chapter on ion-pair formation.

The key to a quantitative theory of electrolyte solutions is an ionic distribution function that gives the probability of finding one ion in a certain position relative to another and permits a distribution of electric potential to be calculated. In pure water, thermal motion overcomes the short-range order near the central molecule, and random distribution obtains at distances greater than a few ångströms. However, the distribution is more complicated in an electrolytic solution, where competition between long-range coulomb forces and thermal motion maintains non-random distribution even at considerable distances. Unfortunately, an inconsistency between the Boltzmann distribution and the principle of linear superposition of fields adds materially to the difficulty; the most expedient escape from this dilemma leaves the theory really adequate only for symmetrical electrolytes. In one of the best sections of their book, Robinson and Stokes gave a critical evaluation of the Bagchi treatment, the Eigen–Wicke modifications, and other distribution functions and justify in a convincing way their selection of the modified Debye–Hückel treatment of the interionic forces.

Although the chemical potential is known to be strongly influenced in concentrated solutions by interactions of the ion-solvent and non-electrolyte types, many complicating factors not fully understood still bar the way to a satisfactory theory. On the other hand, "we are now in the unexpected position that, at least for uni-univalent electrolytes, the theory of conductivity is more exact and successful than the theory of chemical potential." Thus by introducing the factor $1 + ka$ (where a is the ion-size parameter) into both the electrophoretic and relaxation terms, an equation representing the conductance of hydrochloric acid up to 0.09 M and at temperatures from 5 to 65° is obtained. The value of a (4.3 Å.) is the same as is found from measurements of electromotive force and does not vary with temperature. Furthermore, the introduction of a relative fluidity into these formulas yields calculated conductivities for lithium chloride solutions that agree approximately with the measured values up to 9 M. The equations for transport numbers involve only electrophoretic terms, the relaxation factors having cancelled out, and the computation is again very successful up to a concentration of 3 M for hydrochloric acid and to 1 M for lithium and potassium chlorides. Although the migration of ions in electric fields has been studied very extensively, it is only recently that diffusion, one of the simplest of irreversible processes, has been given the attention it deserves. The chapters devoted to this topic summarize the remarkable progress that has already been made.

The first three of the 15 chapters concern themselves with basic concepts and a discussion of the state of the solute and solvent in electrolye solutions. Chapter 4 deals with ionic distribution functions, and chapters 5, 6 and 7 present both the theoretical and experimental aspects of electrolytic conductance. Chapters 8 and 9 treat the measurement and interpretation of chemical potentials, whereas chapters 10 and 11 are devoted to a similar discussion of diffusion. The last four chapters are entitled, respectively, "Weak Electrolytes," "The 'Strong' Acids," "Ion Association," and "The Thermodynamics of Mixed Electrolytes." The list of symbols and the table of important constants will be of much help to the reader, and the 62-page appendix is an admirable and most welcome feature of the book. The extensive tables of activity and osmotic coefficients and water activities included therein will be particularly useful. Likewise, the data on ionization constants of weak electrolytes in water and in mixed solvents and the variation of these constants with temperature can be found in such a complete and convenient form in no other source known to the reviewer.