by air oxidation of III and provides a clue to the nature of veranthridine itself (*vide infra*). Huang-Minlon reduction of V regenerated veranthridine, m.p. 228–230°; mixed m.p. undepressed; ultraviolet spectrum identical with that of authentic III.

The facile oxidation of both cevanthridine and veranthridine under mild conditions to colored ketobases and the smooth reduction of the latter to the parent bases by the very specific method employed indicates that these red ketones are fluorenones and hence that cevanthridine and veranthridine are fluorene derivatives.[5] These results support our earlier conclusion that the non-nitrogenous portion of cevine (and the related polyhydroxy tertiary bases) *does not possess a normal steroid skeleton, but rather has the C-nor/D homo-steroid type of structure* which has been adopted for jervine and veratramine by Wintersteiner, *et al.*[6]

[5] *Cf.* the ease of oxidizing fluorene to fluorenone and of regenerating fluorene by the Wolff–Kishner reduction.

[6] For leading references see O. Wintersteiner and M. Moore, This Journal, **75**, 4938 (1953).

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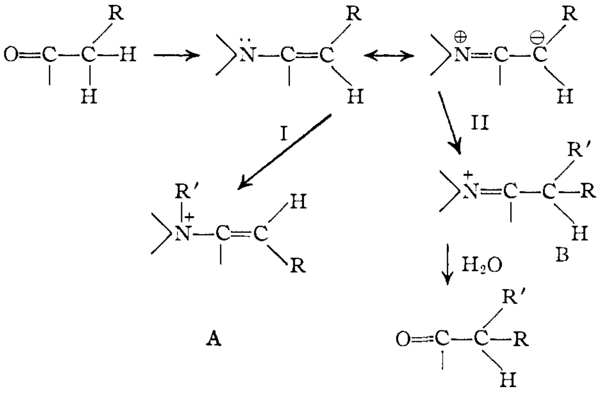
A NEW SYNTHESIS OF 2-ALKYL AND 2-ACYL KETONES

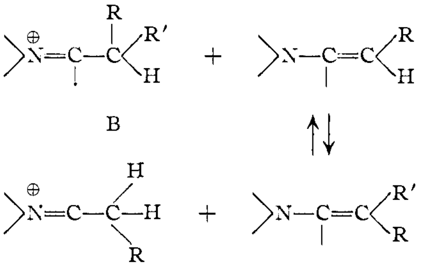
Sir:

We have discovered a new method for the alkylation and acylation of ketones. The condensation products of ketones and secondary amines are well known.[1,2] It is evident that these substances can undergo reaction with proper electron acceptors either at N or C according to path I or II:



We have found that the synthetically important path II is followed in a number of instances.[3] The pyrrolidine enamine from cyclohexanone reacts with methyl iodide in boiling methanol to yield a quaternary salt of type B, which is decomposed by water to produce about 70% of 2-methylcyclohexanone. Similar alkylation with benzyl chloride produces 2-benzylcyclohexanone. Functional groups may be present in the halide: *Ethyl bromoacetate leads to ethyl 2-oxo-cyclohexaneacetate in good yield.* It may be noted that the conventional synthesis of the latter compound requires five steps from cyclohexanone. The mildness of this new reaction lends itself to the alkylation of substances containing alkoxide labile groups: 4-hydroxycyclohexanone benzoate gives 2-methyl-4-hydroxycyclohexanone benzoate without loss of the benzoyl group in addition to the N-methiodide of the starting enamine (path I), isolated in 11% yield. The reaction may also be of interest, conversely, in cases where the halide contains base sensitive functions. The new reaction is not limited to alkyl halides: Acrylonitrile heated with the pyrrolidine enamine of cyclohexanone in dioxane solution *gives an 80% yield of 2-cyanoethylcyclohexanone,* a substance which is only obtained with difficulty by other methods. Methyl vinyl ketone gives directly, after treatment of the intermediate with water, $\Delta^{1,9}$-2-octalone in about 30–40% yield. Treatment of the enamine from cyclohexanone with benzoyl chloride gives 2-benzoylcyclohexanone and with ethyl chlorocarbonate in dioxane solution 2-carbethoxycyclohexanone is obtained.[4]

The monoalkylation obtained with alkyl halides is clearly the result of the much lower reactivity of the alkylated enamines since the salts of type B can produce alkylatable enamines by loss of a proton to the parent enamine



In agreement with this view, we have found that the pyrrolidine enamine from 2-methylcyclohexanone gives mostly recovered starting material under the conditions used with cyclohexanone itself.

This low reactivity of the fully substituted enamines is useful in certain cases, *e.g.*, the monomethylation of β-tetralones which is usually very difficult to achieve by direct methylation: Here again the reaction is easily applied in the presence of base sensitive groups: 5-phthalimido-2-tetralone produces the 1-methyl derivative in about 50–60% yield without interference from the imide function.[5]

The specially interesting case of the enamines

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(1) C. Mannich and H. Davidson, *Ber.*, **69**, 2106 (1936).

(2) An especially convenient synthetic method has recently been described by F. E. Heyl and M. E. Herr, This Journal, **75**, 1918 (1953).

(3) In a formal sense an electronic archetype for these reactions may well be the transformation of 1,3,3-trimethyl-2-methyleneindoline into 1,3,3-trimethyl-2-isopropylidene indoline on treatment with methyl iodide (C. Zatti and A. Ferratini, *Ber.*, **23**, 2302 (1890); G. Plancher, *ibid.*, **31**, 1488 (1898)).

(4) For a theoretically related reaction in the ketene acetal series see S. M. McElvain and R. V. Mullineaux, This Journal, **74**, 1811 (1952).

(5) In this special case, the reaction recalls the monoalkylation of acetoacetic ester which may be effected with sufficiently reactive alkyl halides *via* dialkylaminocrotonic ester: R. Robinson, *J. Chem. Soc.*, **109**, 1038 (1916); W. M. Lauer and G. W. Lones, This Journal, **59**, 232 (1937); G. Eglinton and M. C. Whiting, *J. Chem. Soc.*, 3052 (1953).

from aldehydes and the factors which determine the course of the reaction are being investigated, in particular the effect of structure on the extent to which paths I and II are followed. That there is a fine balance between these two possibilities is illustrated by the fact that the enamine of cycloheptanone gives no C-alkylation with methyl iodide, while on the other hand it gives 2-cyanoethylcycloheptanone with acrylonitrile. Dr. P. C. Mukharji in this Laboratory has also found that N-methylation is the principal result with the enamine of testosterone.[6]

[6] Prepared according to reference 2. A number of enamines are known which show simple N-methylation on treatment with methyliodide, *e.g.*, 1,6-dimethyl-1,2,3,4-tetrahydropyridine: A. Lipp, *Ann.*, **289**, 216 (1896); neostrychnine, O. Achmatowicz, G. R. Clemo, W. H. Perkin, Jr., and R. Robinson, *J. Chem. Soc.*, 787 (1932).

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BOOK REVIEWS

Low Temperature Physics. BY CHARLES F. SQUIRE, Professor of Physics, The Rice Institute, Houston, Texas. McGraw-Hill Book Company, Inc., 330 West 42nd Street, New York 18, New York, 1953. x + 244 pp. 16 × 23.5 cm. Price $6.50.

This is a very interesting and well-written book, and is recommended to those interested in learning more about the phenomena of very low temperatures—mostly below 4°K. Some of the phenomena discussed in the book are observable only below 50°K. which makes the book not only interesting but important for those inclined to physical theory. Those interested in the thermodynamics will find many interesting applications of theory to the unusual properties of liquid helium, superconductivity, para- and diamagnetism and the liquefaction of gases. There is a good balance between theory and experiment so that the interested non-mathematical reader will find the purchase of the book justified.

The book begins with a discussion of the liquefaction of gases. Only the liquefaction of helium with a S. C. Collins-type cryostat is discussed in much detail. This may disappoint some but the reviewer approves the author's choice. The book was written to cover low temperature physics not engineering and the Collins-cryostat has been by far the most used liquefier in the U.S.A. for the investigation of the phenomena discussed in this book. The inclusion of such topics as lubrication of the gas compressor, and the draining of oil and water traps will point up for the alert liquefier operator the kind of information needed for the operation of other kinds of liquefaction plants.

There follows a good theoretical discussion of the equation of state of real gases from the point of view of statistical mechanics. The quantum-statistical equations of state for ideal gases at low temperatures are included.

Three chapters on liquid helium follow—really on the strange phenomena of liquid helium below 2.2°K. characterizing a strange state of matter designated Liquid Helium(II). Two chapters are on experimental phenomena—one on thermal and the other on flow phenomena—and the third chapter is on the Theory of Liquid Helium(II). No theory yet proposed really "explains" the strange phenomena of helium(II) beyond showing that they are undoubtedly a consequence of a large accumulation of helium atoms in states of low translational energy.

Superconductivity follows; first there is a discussion of the experimental phenomena and then the pertinent theory. As the author points out there is as yet no adequate theory of superconductivity, though there are a number of equations, some empirical and some derived from classical thermodynamics and electrodynamics, tying together otherwise disjointed properties of superconductors.

There is a chapter on magnetic phenomena with pertinent classical and quantum theory. Besides the regularly included topics the authors discussed the newer phenomena of alignment of nuclear magnetic moments, nuclear magnetic resonance with r.f. fields, anti-ferromagnetism and the production of lowest attained temperatures (0.002°K.) by the adiabatic demagnetization of a paramagnetic salt.

In a chapter on thermal energy of solids at low temperatures, coöperative phenomena and rotation of molecules and radicals are discussed. These are of especial interest to physical chemists.

The final chapter of the book is on dielectric properties at low temperatures. The most interesting phenomena here result from the orientation in the solid state of electric-dipole molecules and radicals. This gives rise to phenomena of electrical polarization of a solid that are analogous to para- and ferromagnetism.

The mathematical parts of the book are at the level of the graduate physics student. A knowledge of elementary statistical mechanics and quantum theory is presupposed. The M.K.S. system of units has been used. This system is not uncommon among physicists, but newton as a unit of force, and $\epsilon_0 = 8.85 \times 10^{-12}$ coulomb^2/newton-m^2 and $\mu_0 = 12.57 \times 10^{-7}$ weber/amp-m for the dielectric constant and magnetic permeability of free space will seem strange to many chemists familiar with $\epsilon_0 = \mu_0 = 1$.

This book is pre-eminent among books covering the whole low temperature field. It is not to be expected however that a book of 250 pages covering so extensive a field could treat a subject like superconductivity in such detail as the specialized monographs on superconductivity by F. London and by D. Shoenberg.

The book is recommended to all who are interested in reading about a comparatively new field of physics that is not only stimulating but is challenging because more remains to be understood than we know about it today.

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Annual Review of Biochemistry. Volume 22. BY J. MURRAY LUCK, Stanford University (Editor); HUBERT S. LORING, Stanford University; and GORDON MACKINNEY, University of California (Associate Editors). annual Reviews, Inc., Stanford, California. 1953. ix + 729 pp. 16.5 × 23 cm. Price $6.00.

The Prefatory Chapter in this volume is an innovation in the series. In discussing his experiences in the study of foods and nutrition as a student, a teacher and an investigator, Professor E. V. McCollum presents a fascinating account of his early associations in New Haven and Madison with such eminent pioneers in biochemistry as Babcock, Chittenden, Hart, Osborne, Mendel and Underhill. Professor McCollum established (1907) the first rat colony in America for the study of nutrition, obtained (1913) the first evidence that fats contain an indispensable nutrient (vitamin A), and published (1918) the first edition of his outstanding book "The Newer Knowledge of Nutrition." In 1917 he was appointed to take charge of the department of chemistry in the newly established School of Hygiene and Public Health in Johns Hopkins University, a post which he fillled with distinction for more than three decades.

Half of the topics surveyed in volume 22—biological oxidations, proteolytic and non-proteolytic enzymes, amino