at 2.90 and 5.78 μ). Conversion to the α-hydroxymethylene-δ-lactone Vb (not purified) was managed by treatment of Va with methyl formate in the presence of excess sodium triphenylmethyl in dioxane. Upon being heated in refluxing methanolic hydrogen chloride,[6] the hydroxymethylene lactone was transformed readily to the dihydropyran carboxylic ester (m.p. 222–225°). Infrared spectral comparison (chloroform solution) of authentic ajmalicine with the base thus produced demonstrated the latter to be *dl*-ajmalicine.[7]

Proper utilization of certain intermediates described above should permit establishment of the complete stereochemistry of ajmalicine and other hetero-ring E indole alkaloids, and such studies are now under way in this Laboratory.

Acknowledgment.—The authors are grateful to the National Institutes of Health (RG3892) and to the Wisconsin Alumni Research Foundation for financial support; to Mr. Ian G. Wright for the preparation of starting materials; and to Dr. Thomas A. Spencer, Jr., who first isolated intermediate IVb.

(6) F. Korte and K. H. Büchel, *Angew. Chem.*, **71**, 709 (1959).

(7) Complete spectral, physical, and analytical data will be recorded in the full paper to be published.

(8) Allied Chemical Corporation (Plastics Division) Fellow, 1959–1960.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF WISCONSIN
MADISON, WISCONSIN

E. E. VAN TAMELEN
C. PLACEWAY[8]

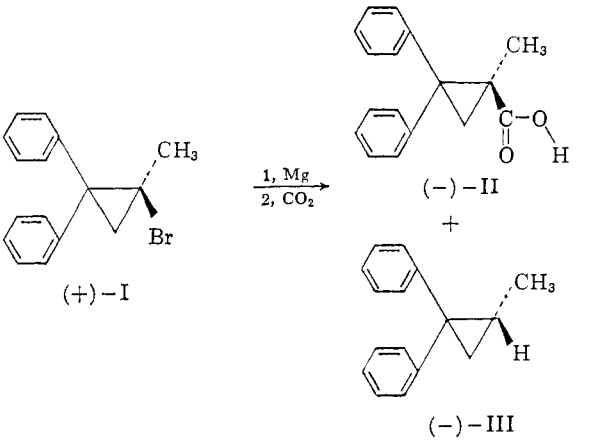
RECEIVED APRIL 19, 1961

CYCLOPROPANES. X. AN OPTICALLY ACTIVE GRIGNARD REAGENT[1]

Sir:

To date, all previous attempts to prepare optically active Grignard reagents from optically active halides have been unsuccessful[2]. We wish at this time to report that optically active (+)-1-bromo-1-methyl-2,2-diphenylcyclopropane[3] reacts with magnesium to form a Grignard reagent which on carbonation followed by hydrolysis produces optically active (−)-1-methyl-2,2-diphenylcyclopropanecarboxylic acid (II)[5] and (−)-1-methyl-2,2-diphenylcyclopropane. This result represents the first example of an optically active Grignard reagent.[5]

Magnesium powder (0.5 g.) and 2.30 g. of I, $[\alpha]^{28}D$ +106 ± 1° (*c*, 2.229)[6], were placed in 12 ml. of tetrahydrofuran and a solution of 0.5 ml. of ethylene dibromide[7] in 2.5 ml. of tetrahydrofuran was added over a period of ten minutes. The exothermic reaction brought the solution to reflux temperature (65°) and this temperature was maintained for an additional ten minutes. The reaction mixture was poured into Dry Ice and worked up in the usual manner to yield the optically active acid II (0.766 g., 38%), $[\alpha]^{23}D$ 5.3 ± 1.2° (*c*, 2.173). The infrared spectrum of the acid was identical in all respects with that of an authentic sample[4] and its rotation represents an optical purity of 14 ± 2%. A neutral fraction (0.624 g., 38%) was obtained and shown to be 1-methyl-2,2-diphenylcyclopropane (III)[3] by its b.p., infrared spectrum and retention time on vapor phase chromatography. The hydrocarbon III, $[\alpha]^{23}D$ −13.6 ± 1.2°, was 11 ± 2% optically pure.



In another experiment an excess of magnesium powder was treated with a solution of ethylene dibromide in tetrahydrofuran until gas evolution ceased and then a solution of I in tetrahydrofuran was added slowly, over a period of 40 minutes, in order to maintain the temperature between 25–27°. Carbonation of the reaction mixture gave these results: Acid II was isolated in 45% yield and was 12 ± 2% optically pure: Hydrocarbon III was obtained in 36% yield with an optical purity of 10 ± 2%.

Since (+)-I has been related to (−)-II and (−)-III the stereochemistry of the over-all reaction is that of retention of configuration.[3,8] A similar stereochemical result is obtained when 1-methyl-2,2-diphenylcyclopropyllithium[3] (by reaction of butyllithium with (+)-I) is carbonated to yield (−)-II and (−)-III.[9] There is, however, an important difference in these two reactions. Whereas carbonation of the lithium reagent gives 100% retention of configuration and activity, the Grignard reagent yields only *ca.* 12% retention of activity and 56% retention of configuration. Since a carbon–magnesium bond has less ionic character associated with it than does the carbon–lithium bond,[10] one might have expected a high retention

(1) This work was supported in part by a grant from the National Science Foundation and in part by a grant from the U. S. Army Research Office (Durham).

(2) R. H. Pickard and J. Kenyon, *J. Chem. Soc.*, **99**, 45 (1911); A. M. Schwartz and J. R. Johnson, *J. Am. Chem. Soc.*, **53**, 1063 (1931); C. W. Porter, *ibid.*, **57**, 1436 (1935); H. L. Goering and F. H. McCarron, *ibid.*, **80**, 2287 (1958).

(3) H. M. Walborsky and F. J. Impastato, *ibid.*, **81**, 5835 (1959).

(4) F. J. Impastato, L. Barash and H. M. Walborsky, *ibid.*, **81**, 1514 (1959).

(5) For the constitution of Grignard Reagents see, R. E. Dessy and G. S. Handler, *ibid.*, **80**, 5824 (1958).

(6) All rotations were taken in chloroform solution.

(7) D. E. Pearson, D. Cowan and J. D. Beckler, *J. Org. Chem.*, **24**, 504, (1958).

(8) H. M. Walborsky, L. Barash, A. E. Young and F. J. Impastato, *J. Am. Chem. Soc.*, **83**, 2517 (1961).

(9) It has been demonstrated that (−)-III is formed by reaction of 2,2-diphenylcyclopropyllithium with the solvent (unpublished results).

(10) L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1960.

of activity for the Grignard reagent. The fact that a large amount of racemization was obtained suggests that racemization is occurring in the Grignard formation step.

Further work pertaining to the mechanism of Grignard formation as well as to the optical stability of organometallics is now in progress.

DEPARTMENT OF CHEMISTRY
FLORIDA STATE UNIVERSITY H. M. WALBORSKY
TALLAHASSEE, FLORIDA A. E. YOUNG

RECEIVED APRIL 7, 1961

BOOK REVIEWS

Modern Probability Theory and its Applications. By EMANUEL PARZEN, Associate Professor of Statistics, Stanford University. John Wiley and Sons, Inc., 440 Fourth Avenue, New York 16, N. Y. 1960. xv + 464 pp. 15.5 × 23.5 cm. Price, $10.75.

The title of this book should perhaps be: Introduction to Probability Theory, since by mathematical standards it is a first undergraduate textbook. Content: Chapter I, Probability Theory as the Study of Mathematical Models of Random Phenomena; Chapter II, Basic Probability Theory; Chapter III, Independence and Dependence; Chapter IV, Numerical-Valued Random Phenomena; Chapter V, Mean and Variance of a Probability Law; Chapter VI, Normal, Poisson, and Related Probability Laws; Chapter VII, Random Variables, Chapter VIII, Expectation of a Random Variable; Chapter IX, Sums of Independent Random Variables; and Chapter X, Sequences of Random Variables.

The knowledge of Lebesgue integration is not assumed. Some theorems are stated without proof, the author usually pointing out this fact carefully. The book is written vividly, contains interesting bibliographical and historical remarks. Some points worth mentioning: Detailed treatment of elements of combinatorics in Chapters I–II; definition of conditional probability of an event given a random variable, without use of the Radon–Nikodym theorem, Chapter VII; an article on the measurement of the signal-to-noise ratio of a random variable, Chapter VIII; treatment of convergence in distribution by the method of characteristic functions, including in Chapter IX the proof of the inversion formulas for characteristic functions, in Chapter X the proof of the "continuity theorem of Probability Theory." A trivial flaw: the definition of a function, p. 269, is not correct.

In conclusion, it may be appropriate to compare this work with the classic treatise in the field, Feller's "Introduction to Probability Theory and Its Applications." At the price of limiting himself to the discrete case Feller achieves a mathematically admirable and completely self-contained treatment. The reviewer feels, however, that Parzen's book is to be preferred as an undergraduate textbook: it is considerably easier to understand and also treats the continuous case.

DEPARTMENT OF MATHEMATICS
UNIVERSITY OF ROCHESTER LOUIS SUCHESTON
ROCHESTER, NEW YORK

British Medical Bulletin. Volume 16. Number 3. Insulin. F. G. YOUNG, Scientific Editor. Medical Department, The British Council, 65 Davies Street, London, W. 1, England. 1960. pp. 175–264. 22 × 28.5 cm. Price, $3.25.

The issue "Insulin" of the British Medical Bulletin series is a worthy companion of its forerunners. In a group of 17 titles, the subject ranges from the chemical structure of insulin, its measurement in pancreatic extracts and in blood, the role of insulin (and hence the metabolic defects in diabetes) in carbohydrate, fat and protein metabolism, to more clinically oriented subjects including the chemistry and uses of synthetic hypoglycemic agents.

After a historical perspective and preview of the subject matter by the scientific editor, Charles H. Best describes in fine historical perspective his pioneer work with Banting on active insulin preparations, and his efforts to get on with studies of the physiological effects of insulin in the face of pressing problems in the commercial production of the life-saving hormone. Supplementing a never-tiring description of his classical work on insulin structure, the article by F. Sanger is followed by an excellent treatment by Ieuan Harris on the structures of oxytocin, vasopressin, corticotropin and MSH with emphasis on the relation of structure and amino acid replacements to biological activity. Of theoretical interest but also of great practical import are the articles dealing with the measurement of insulin concentrations, the metabolic fate of insulin and the presence of insulin antagonists and antibodies in blood. These subjects comprise five articles by G. A. Stewart, A. J. Kenney, P. J. Randle and K. W. Taylor, J. Vallance-Owen, and P. H. Wright.

There follows a group of four articles concerned with the action of insulin on metabolism, particularly at the tissue and enzyme levels. In weighing many reports, R. B. Fisher is led toward the conclusion that the stimulation of carbohydrate metabolism is through the increased transport of glucose into the cell, while S. J. Folley and A. L. Greenbaum present the case for a possible primary role of insulin in the synthesis of fatty acids, and A. Korner and K. L. Manchester gather information which indicates a direct effect of insulin on the biosynthesis of protein. Finally P. J. Randle and F. G. Young provide a critical and provocative paper with a unifying concept of insulin action based on its effect on cell permeability, which may account in ways not entirely clear at the present time, for the apparent diversity of actions of insulin on metabolism.

The issue is concluded with articles by R. Fraser on the interplay of insulin with other hormones, by W. Oakley on the types of insulin available for clinical practice, and finally articles on the chemistry of the newer hypoglycemic agents (R. F. Mahler) and their clinical use (J. D. N. Nabarro).

In summary, "Insulin" provides a useful collection of concise, factual and well-documented articles of diverse nature, making it valuable for medical scientists as well as physicians.

UNIVERSITY OF ROCHESTER SCHOOL
OF MEDICINE AND DENTISTRY ELMER H. STOTZ
ROCHESTER, NEW YORK

The Biosynthesis and Secretion of Adrenocortical Steroids. Biochemical Society Symposium No. 18 held at Senate House, University of London on 14 February, 1959. Organized by J. K. GRANT. Edited by F. CLARK and J. K. GRANT. Cambridge University Press, 32 East 75th Street, New York 22, N. Y. 1960. vii + 111 pp. 16 × 25.5 cm. Price, $5.00.

An excellent section on laboratory technology as applied to the elucidation of new structures of adrenal and other steroids opens this symposium. The usefulness of micro techniques using several paper chromatographic systems in conjunction with the preparation of derivatives to eliminate "mimics" is stressed and practical examples of these are given.

Most significant findings (up to 1959) concerned with the biogenesis and control of secretion of adrenocortical steroids are reported. In conjunction with these subjects the symposium authors have given liberal play to their ideas and the possible without unbridling fancy at the expense of facts. Most importantly, attention is drawn to areas requiring re-