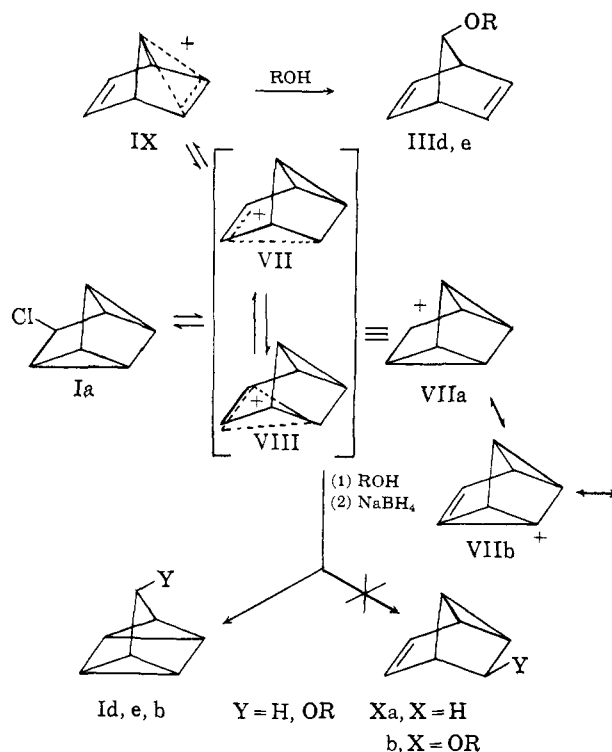


the quadricyclic (I) since Ib is converted essentially completely to norbornadiene (IIIa) at 200°. Furthermore, we find that quadricyclic derivatives (Ia,d,e) are converted rapidly and completely to their corresponding diene isomers (III) in dilute acid. Solvolysis of Ia in 50% aqueous ethanol without sodium bicarbonate yields only dienes (III d and III e, 41%) and what appear to be acid-catalyzed solvent addition products (55%).

Quite obviously, solvolysis of quadricyclic chloride (Ia) and diene chloride^{1,12} does not lead to a common carbonium ion intermediate. In like manner V and VI do not solvolyze to a common carbonium ion intermediate.^{13a} We suggest that by analogy to the tricyclic system (V)¹³ charge delocalization in the 7-quadricyclic carbonium ion could well be represented by the symmetrical homoallylic ion (VII) and/or by the unsymmetrical bicyclobutonium ion (VIII). These intermediate ions could easily leak over to the diene ion (IX) to give the observed diene products (III d,e). Under no circumstances, however, have we been able to observe the expected tricyclic olefin (X). Even sodium borohydride reduction of Ia failed to produce any of the known Xa¹⁴ which could have been detected in the hydrocarbon product in concentrations as low as 0.5%. It becomes necessary to argue, then, that resonance structure VIIb does not assume sufficient importance to cause accumulation of X as does the corresponding structure in the solvolysis of V.¹³ The absence of X does not appear to be simply a matter of ground state energies since Xa is formed from III b and appears to be unstable relative to both Ib and III a.

This interpretation of charge delocalization in I would explain the comparable reactivity of I and V and why the effect of the cyclopropyl groups is not linearly additive as noted by Richey and Buckley.³ This situation is highly reminiscent of the epimeric diene carbonium ions investigated by DePuy,¹⁵ which



were not interconvertible, nor was the effect of the double bonds additive. Consequently, by analogy to the 7-norbornadienyl carbonium ion^{1,12} and to DePuy's system¹⁵ it is perhaps not too surprising that the effect of the cyclopropyl groups is not additive. The quadricyclic system seems to offer another example of what we call "charge delocalization priority."

(15) C. H. DePuy, I. A. Ogawa, and J. C. McDaniels, *ibid.*, **82**, 2398 (1960).

BELL TELEPHONE LABORATORIES, INC.
MURRAY HILL
NEW JERSEY

PAUL R. STORY
SUSAN R. FAHRENHOLTZ

RECEIVED NOVEMBER 26, 1963

BOOK REVIEWS

Biochemical Frontiers in Medicine. HARRIS BUSCH, Ed., M.D., Ph.D., Professor of Pharmacology, Chairman, Dept. of Pharmacology, Baylor College of Medicine, Houston, Texas. Medical Book Department, Little, Brown and Co., Boston 6, Mass. 1963. 16 × 24 cm. 364 pp. Price, \$12.50.

At a time when knowledge in biochemistry is accumulating at so rapid a rate, the need for books that integrate the relationship of advances in biochemistry with medicine is great indeed. To accomplish this end, a book is needed which assists in the understanding of biochemical fundamentals and their pertinence to medicine rather than the collection of biochemical facts. In spite of its promising name, "Biochemical Frontiers in Medicine," edited by Harris Busch, fails to achieve this objective. It fails to communicate both the significant nature and the excitement of these frontiers to its medical audience. Thus it falls back to become just another catalog of biochemical phenomena in medicine, of which there is now quite a number.

In eight chapters by five authors, this book deals with selected topics in the biochemistry of genetics, metabolic diseases, cancer, chemotherapy, diagnostic methods, and pathology. As might be expected from a book by multiple authors, homogeneity is lacking and there is variation in style and quality. The chapter by O. Bodansky is superior and provides good reading. The biochemical bases of laboratory tests which aid the diagnosis and

management of pheochromocytoma, carcinoid, jaundice, and porphyria are summarized lucidly and succinctly.

In the chapter entitled "Biochemical Pathology," E. Farber demonstrates the impact of recent advances in biochemistry and electron microscopy upon current thinking and trends in research in pathology. Two of the most basic cellular pathologic alterations, necrosis and the accumulation of lipids by cells, are discussed in terms of the biochemical and metabolic responses to injury and alterations in the ultrastructure of the cell.

The action of selected purine analogs as therapeutic agents for cancer is discussed by R. Parks in terms of their chemistry and mechanisms of action. A report on these antimetabolites which have met with clinical success seems both pertinent and timely at a period when the state of knowledge in organic and biochemistry has made the design of more effective antitumor agents both feasible and practical. The synthesis of penicillin, its mechanism of action, and the problem of drug resistance are also reviewed.

In two chapters, genetically determined disorders of carbohydrate, amino acid, and protein metabolism are described in routine fashion. Clinical manifestations of the diseases, laboratory findings, metabolic defect, genetics of transmission, treatment, and prognosis are outlined.

The chapter on the biochemical basis of genetic aberrations discusses chromosomal structure, the chemistry of DNA and

RNA, and the current concepts of mechanisms whereby these macromolecules transmit information. The significance of the data cited is not always evident. In attempting to indicate some of the difficulties in technique and experimentation, clarity and the development of logical sequence are often sacrificed. The presentation unfortunately is further marred by errors due to oversight in editing (*e.g.*, p. 19).

The chapter "Biochemistry of Cancer Cells" describes some of the aberrations in metabolism and composition of proteins, DNA, and RNA of cancer cells, and serves to illustrate that knowledge and understanding about this disease are still lacking despite the large amount of research done. The hypothetical mechanism of carcinogenesis based on the removal of "suppressors" by carcinogens and other "promoting factors," is in need of experimental substantiation.

This book is compiled for medical students, general practitioners, and medical specialists. The starting level of proficiency in biochemistry and medicine that the reader is assumed to have varies from chapter to chapter. It is difficult to assess which group will find the book most useful. However, each chapter is followed by a fairly extensive bibliography.

HARVARD MEDICAL SCHOOL
PETER BENT BRIGHAM HOSPITAL
BOSTON 15, MASSACHUSETTS

T. K. LI

Technique of Organic Chemistry. Volume XI. Elucidation of Structures by Physical and Chemical Methods. Part One and Part Two. Edited by K. W. BENTLEY. Interscience Publishers, John Wiley and Sons, Inc., 605 Third Avenue, New York 16, N. Y. 1963. Part One, 642 pp. 16 × 23.5 cm. Price, \$19.50. Part Two, 535 pp. 16 × 23.5 cm. Price, \$16.50.

I, Isolation, Purification and Preliminary Observations, K. H. Overton; II, Applications of Ultraviolet Spectroscopy, J. C. D. Brand and A. I. Scott; III, Applications of Infrared Spectroscopy, A. R. H. Cole; IV, Applications of Nuclear Magnetic Resonance Spectroscopy, J. B. Stothers; V, Applications of Mass Spectrometry, K. Biemann; VI, Applications of Dissociation Constants, Optical Activity, and Other Physical Measurements, J. F. King; VII, Biogenetic Theory in Structural Elucidation, Edward Leete; VIII, Detection and Protection of Simple Functional Groups, G. A. Swan; IX, Reduction and Hydrogenation in Structural Elucidation, F. J. McQuillin; X, Dehydrogenation, Z. Valenta; XI, Zinc Dust Distillation, Z. Valenta; XII, Alkali Fusion and Some Related Processes, B. C. L. Weedon; XIII, Carbon-Oxygen Fission: Degradation of Polysaccharides, J. K. N. Jones and M. B. Perry; XIV, Carbon-Nitrogen and Carbon-Oxygen Fission, K. W. Bentley; XV, Hydrolytic Degradation of Polypeptides and Proteins, E. Y. Spencer; XVI, Carbon-Carbon Single Bond Fission, K. T. Potts; XVII, Carbon-Carbon Double Bond Fission, K. W. Bentley; XVIII, Degradation of Side Chains and Long Chain Compounds, N. Polgar; XIX, Determination of the Stereochemistry of Natural Products by Chemical Methods, B. Belleau and S. McLean; XX, Molecular Rearrangements, Paul DeMayo.

Natural products chemists will be delighted to find in these two volumes, at last, a comprehensive collection of all the diverse means used in structure determination, gathered together under one roof and treated at length. The teacher who, like this reviewer, has struggled to unfold the subject to students using only the traditional chemically-oriented qualitative analysis texts will be equally pleased to have available this balanced treatment of traditional chemical and modern physical methods, for, although the two volumes are too expensive to assign as a text, this important addition to the eminent Weissberger series must surely be incorporated into every academic library and so be available for reading assignments. Finally, with the trend of synthetic and mechanism studies to more subtle and complex reactions, the structure elucidation of unusual products is increasingly a separate and important phase of the work and chemists in such areas should also find the book valuable. Although the orientation throughout is strongly to natural product studies, the generalized nature of the exposition in most chapters renders it equally suitable for other chemists.

Before proceeding to a more detailed examination of the merits of individual chapters, we may consider several general comments on the treatise as a whole. It is increasingly and most deplorably true that multi-authored works of this kind are subject to intolerable delays between pen and print. Almost all of the chapters here contain no references later than 1960; some are even more outdated. Several authors, probably partly in pique, specifically state a cut-off date, one (Chapter II) as early as February, 1959, nearly five years ago! In view of the rapid pace of modern developments, not only should editors be urged to take drastic measures to avoid these lacunae, but potential authors may well be warned to exact meaningful assurances of publication time.

In general, the value of these books lies in bringing together a collection of previously widely scattered methods and in presenting them, together, as a unified armory for attacking unknown structures. In judging the books we may therefore ask not only for exposition of the methods but for specific attention, in dealing with their application, to the nature of the problem as it appears to an investigator with an unknown compound in hand. Exposition and breadth of applicability are easier and generally well done; applications are commonly approached with examples from the literature, often many and well-chosen, but these are outlined as *faits accomplis* with frequently not enough attention paid to the practical situations that must be faced by the investigator during the work, the pitfalls of interpretation, and the bases for experimental choice and sequence. Admittedly this cavil is somewhat vague, but should the authors one day revise the work, it could be valuable to others if they would apply this point of view more consistently. In this connection we may applaud the high incidence of attention to practical experimental detail in most chapters, however.

Finally, the chapters may be judged both on completeness and on the extent to which they duplicate other treatments. Much of Part One (primarily on physical methods) covers ground which has been extensively treated before. These chapters are generally admirable in their combination of adequacy and brevity with ample references to more exhaustive treatments of individual topics; the attention here to the point of view of the analyst's problem (*vide supra*) and to the breadth of applicability is commendable. Many of the chapters on chemical methods are not as good and we may observe that the good chapters often have previous models while the chapters with no previous models, although often not as good, may ironically be more useful by being unique of their kind! One very important deficiency in the chemical chapters is the failure to point up the value of combining physical techniques with the chemical procedures in order more fully to assess reaction course and to obtain the maximum amount of data. Examples are cited below.

The introductory chapter wisely refers the reader to other texts for the common techniques, although a somewhat more extensive treatment of practical pitfalls might have been in order. On molecular weights, the manuscript was too early to include the excellent thermistor osmometer, but should certainly have referred to the Signer-Clark method for isothermal distillation. The invaluable assemblage of important color test fills in an important gap and is generally excellent although the reviewer was distressed to note that the modern studies of the tetranitromethane and Gibbs tests were missing; they turned up however in Chapter II! The second chapter is generally admirable throughout. A somewhat more extensive commentary on how to approach interpretation of the spectrum of a completely new compound would enhance the value, however. The value of comparisons with actual curves of model compounds is not sufficiently emphasized, since often the particular shape of a curve is more revealing than a simple catalog of maxima. Also the value of spectral shifts in acid and base is hardly hinted at. Chapter III is concise, excellent in its treatment of experimental matters, and amply stocked with references to more exhaustive works, but it deals too exclusively with the author's chief interests in steroids and triterpenes (one eighth of the references are the author's work). The presentation of nuclear magnetic resonance is exemplary and includes an excellent compendium of structure with chemical shift, ample, clear, and useful. The exposition of mass spectrometry is also superb, a lucid introduction to the method and the extent or potential extent of its value; if this chapter seems now somewhat rudimentary or outdated, it is largely because of Prof. Biemann's own work since it was written! The application of acidity measurements is well handled and notable also for its useful and extensive tables of pK values. Prof. Leete's exposition of the important role biogenetic theory has played, and can increasingly play, in the unravelling of natural structures is very commendable in calling attention to this often overlooked or maligned theoretical tool.

Chapters VIII and IX contain serious deficiencies. Very little appreciation is given to the importance of mechanistic understanding of the reactions discussed to generalize and clarify their use. Is reduction with dissolving metals such a mystery, for example? Would the section on carbinolamines not be much more comprehensive and comprehensible if an appreciation of their ready formation of anhydro salts were included? The treatment of carbonyl reduction by hydrides is mechanistically inadequate and handled far better in Chapter XIX. Secondly, the value of instrumental techniques in conjunction with chemical reactions is not adequately treated, *e.g.*, recognition of -COOH by its infrared shift in -COO⁻, or of anilines by chromophoric destruction in acid, or the value of deuterium equilibration or introduction when used with n.m.r. studies. Chapter VIII is also deplorably weak on protecting groups (*e.g.*, no mention of the carbobenzoxy derivative of amines) as well as on quantitative determination of functional groups. The organization of Chapter