

theoretical information which a medical student in this country is required to assimilate. Efficient use of the limited space would necessitate extremely careful selection of material, and there is no evidence of this. A student for whom it is deemed necessary, for example, to outline the elementary organic chemistry of esters and ethers (p. 22) is unlikely to be able to grasp the implications of the information summarized (pp. 25-27) concerning polysaccharides. He could, presumably, also make little out of the statement (p. 70) that "proteins can be made to sediment in very high speed centrifuges" unless it were at least hinted that the proteins were in solution.

Misstatements also abound. It is, for example, incorrect to assert that casein is a globulin (p. 69), that "all mono-saccharides can be converted into furfural if they are boiled long enough with strong acid" (p. 23) and that phenylalanine gives a positive xanthoproteic test. The validity is questionable of the general statement (p. 35) that "saturated fatty acids can be oxidized with difficulty to acids with two atoms less in the carbon chain, together with 2CO_2 ." There is also occasional evidence of lack of care in proof-reading: "toluidine" for "tolidine" (p. 91), "a copious excreta" (p. 200), the omission of an oxygen atom in the formula for cerebrosides (p. 44), the faulty ring structure for cholesterol (p. 48).

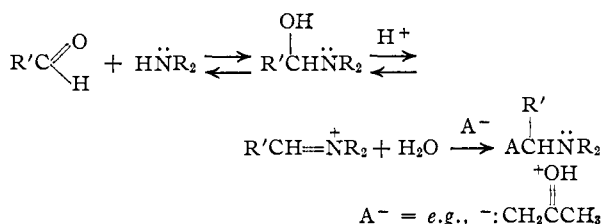
In textbooks intended for the instruction of unsophisticated beginners and other uncritical readers, errors of any kind may lead to misunderstandings and other difficulties.

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Die Mannich-Reaktion. BY BENNO REICHERT, Dr. Phil., Apl. Professor and der Universität München. Springer Verlag, Heidelberger Platz 3, Berlin-Wilmersdorf, Germany. 1959. viii + 195 pp. 16 X 23.5 cm. Price, DM. 36.—

Dr. Reichert, a student of Mannich, has written an authoritative, well-documented, though not entirely complete account of the development and the synthetic applications of the Mannich reaction, covering the period up to and including 1957. The Mannich reaction is, as shown, the condensation of an aldehyde with ammonia, or a primary or a secondary amine, and a compound containing reactive hydrogen atoms (a CH- or NH- acidic reagent), to form what came to be called a C- or N-Mannich base.



The exploration of the general synthetic potentialities of this reaction, from 1917 on, was Mannich's life work, explained in some 70 articles published before his death in 1947.

Previous reviews of the reaction were published in *Archiv. der Pharmazie* by Karbe, in 1950, with emphasis on compounds of pharmacological interest, and in "Organic Reactions, Vol. I" by Blicke, in 1942, in more general terms. However, while Dr. Blicke's article cited 74 references, Dr. Reichert now cites over 1000. Of these approximately 700 cover the years 1942-1957, the period since the last review; six citations are included for the year 1958. Consequently Dr. Reichert's book is the best available record to date on the Mannich reaction.

Dr. Reichert divides his book into seven sections. After a brief historical survey he presents a section on the scope and the mechanism of the reaction. In it he credits Hellmann and Opitz with the clarification of the mechanism of the Mannich reaction, although in fact the late Eliot R. Alexander and E. J. Underhill carried out the quantitative kinetic study of it before the appearance of "Die Mannich-Reaktion." The book mentions their study very briefly, but does not discuss their data and conclusions; because of this omission the mechanism on p. 6 is not entirely satisfactory

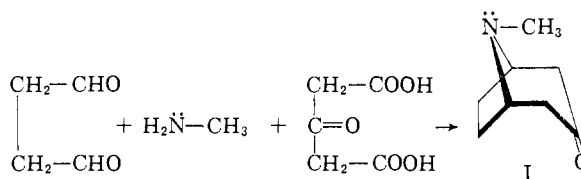
in all detail for the general case of the acid-catalyzed Mannich reaction. It should be mentioned here that in a very recent kinetic study Cummings and Shelton (*J. Org. Chem.*, **25**, 419 (1960)) have borne out Alexander and Underhill's findings, with only minor modifications. The chapter does not indicate specifically, either, that basic catalysis of the Mannich reaction is possible, nor does it cite evidence for the formation of aminomethyl ethers, $\text{R}_2\text{NCH}_2\text{OR}'$, as intermediates in alcoholic media, though such evidence was available.

The next section explains experimental procedures and conditions; it is not as well organized as similar chapters in "Organic Reactions." However, Dr. Reichert compensates for this by including in the rest of the text about 70 individual procedures for the preparation of particular compounds.

The bulk of this volume, 104 pages, deals in two sections with the various CH-acidic and NH-acidic components used in the Mannich reaction. Separate chapters cover ketones, aldehydes, acetylenes, carboxylic acids, di-, tri- and tetracarboxylic acids and their esters, β -keto-diesters, phenols, nitro compounds, heterocyclic compounds, and aliphatic and heterocyclic amides as NH-acidic components. Thirty pages are devoted to ketones alone, five pages to Mannich bases with nitro compounds, a relatively recent field; eighteen pages cover Mannich bases derived from indene. As might be expected in a volume covering over 1000 separate sources, referencing and cross-referencing is not always complete; for instance, several articles on nitro compounds are not mentioned in the appropriate chapter. However, there is wealth of material in these two major sections, and Dr. Reichert has gone to great trouble to present it in digestible form. Some of the highlights from these pages are the formation of 2-methylenecyclohexanone, its dimerization and subsequent ring-contraction to a spirane (no mechanism given); the failure of dihydrocodeinone to undergo aminomethylation; the preparation of *d,l*-cytisine, a vegetable alkaloid; the successful aminomethylation of various tetracyclines; and the syntheses of the plant growth factor heteroauxin and of tryptophan by way of Mannich reactions.

Two concluding sections give applications of the Mannich reaction in synthesis, and a list of C- and N-Mannich bases (with references). Both parts are very useful, but neither section is entirely complete. The section on synthetic applications omits a good example, with experimental procedure, for the formation of olefins from Mannich bases, and it omits also the preparation of pyrazolines, which is dealt with only briefly elsewhere. The reverse Mannich reaction is particularly interesting in these final chapters. At the end of the volume an author index is missing.

I should like to make one more point in connection with the coverage of the book. In 1917, the same year in which Mannich started his intensive work in Germany, Robert Robinson in England prepared tropanone (I) and thence atropine, from acetonedicarboxylic acid (or its dimethyl ester, or even acetone), succindialdehyde and methylamine hydrochloride, in a reaction that was clearly a double Mannich condensation.



He reasoned that tropanone, a precursor of atropine, could arise phytochemically in a similar non-enzymatic reaction. Clemens Schöpf investigated the Robinson condensation in Germany; his and Robinson's work had tremendous influence on biogenetic theory in the field of alkaloids. Not only were a host of tropanone and atropine derivatives, and other tropanone-like compounds obtained by this method for the first time, but the principle of the condensation was also applied to the synthesis of a large number of other alkaloids, or precursors. Furthermore, practically all contemporary workers in the biogenetic field postulate the Mannich-Robinson condensation as a fundamental reaction in the phytochemical formation of alkaloids.

Last year then, after the appearance of Dr. Reichert's monograph, Edward Leete demonstrated in isotopic tracer feeding experiments (*J. Am. Chem. Soc.*, **81**, 3948 (1959))

that in the case of norlaudanosine and morphine at least, Robinson's biogenetic theory is correct, and that the plant actually synthesizes both compounds in a manner analogous to a Mannich reaction from 3,4-dihydroxyphenylalanine and 3,4-dihydroxyphenylacetaldehyde. More recently still, the syntheses of 1-hydroxymethylpyrrolizidine, *d,l*-epilupinine, *d,l*-lupinine and *d,l*-sparteine have been accomplished through Robinson-type condensations (Leonard, Bloom, *J. Am. Chem. Soc.*, **82**, 504 (1960); van Tamelen, Foltz, *ibid.*, **82**, 502, 2400 (1960)). Some of the alkaloids and related compounds that chemists have prepared in the laboratory by similar condensations during the 40 years prior to the appearance of "Die Mannich-Reaktion" include hygrine, cuskhygrine, lobelanine, arecaidine aldehyde, isopelletierine, *N*-methyl-isopelletierine, pseudopelletierine, the numerous natural and synthetic tropanone derivatives (e.g., cocaine, meteloidine), salsoline, nor-salsoline, tetrahydroharmane, hexahydrovohimbol and desoxyvasicine.

Yet Dr. Reichert's book hardly even hints at all in this active field of biogenetic theory and alkaloid synthesis, though his preface acknowledges its importance from the point of view of the Mannich reaction. The book deals with Robinson's original work shortly on p. 51, but it does not mention the syntheses of tropanone from acetone or from free acetonedicarboxylic acid at all. And among other alkaloids or related compounds this reader found only lobelanine and arecaidine aldehyde cited as having been prepared through Mannich condensations. The Pictet-Spengler synthesis of tetrahydroisoquinolines, "Organic Reactions, Vol. VI," which is germane to the Mannich reaction is also omitted in this book.

In summary then, the major drawbacks of this work are the consideration of the Mannich reaction as a *specific* rather than as a *general* condensation reaction, and the slighting of physical-organic considerations and reaction mechanisms with regard to it. But it represents a great deal of work, and extensive assimilation of the subject matter; it also successfully synthesizes most of the widely scattered primary literature sources. Dr. Reichert's monograph is encyclopedic in nature, rather than a critical account. As such it is a worthwhile addition to chemical literature, and as a specialized reference work a recommended acquisition for well-equipped chemical libraries.

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Advances in Inorganic Chemistry and Radiochemistry.

Vol. 2. Editors, H. J. EMELÉUS and A. G. SHARPE, University Chemical Laboratory, Cambridge, England. Academic Press Inc., 111 Fifth Avenue, New York 3, N. Y. 1960. viii + 392 pp. 16.5 × 23.5 cm. Price, \$12.00.

The remarkable resurgence of interest in Inorganic Chemistry and the rapid parallel development of Radiochemistry within the past 20 years have made it increasingly apparent to every research worker or teacher in these areas that he can hope to keep abreast of publication only through reference to carefully prepared, critical reviews covering rather specific topics. In establishing the current series, the editors dedicated themselves to the task of providing such reviews while stressing the application of physical and physicochemical principles to inorganic problems and integrating these with descriptive chemistry. That they have been eminently successful in achieving their goals is attested by the excellence and breadth of coverage of both the current volume and its predecessor. No person interested in modern Inorganic Chemistry can afford to be without access to these summaries.

The present volume presents in order "Stereochemistry of Ionic Solids" by J. D. Dunitz and L. E. Orgel; "Organometallic Compounds" by J. Eisch and H. Gilman; "Fluorine-Containing Compounds of Sulfur" by G. H. Cady; "Amides and Imides of the Oxyacids of Sulfur" by M. Becke-Goehring; "Halides of the Actinide Elements" by J. J. Katz and I. Sheft; "Structures of Compounds Containing Chains of Sulfur Atoms" by O. Foss; "Chemical Reactivity of the Boron Hydrides and Related Compounds" by F. G. A. Stone, and "Mass Spectrometry in Nuclear Chemistry" by H. G. Thode, C. C. McMullen and K. Fritze.

Each summary follows a general organizational pattern but retains its own individuality. Each is particularly well documented, and the majority of the references are to the newer literature. In general, balance between theory and description is excellent. This alone adds much to the desirability of the volume, for it points up very well what many believe to be overwhelmingly important in Inorganic Chemistry and Radiochemistry.

In the opinion of the reviewer, this second volume in the series fixes the pattern set by the first and indicates clearly that future volumes will be welcomed with real enthusiasm.

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Polysaccharides of Micro-organisms. By M. STACEY, F.R.S., Mason Professor and Head of the Department of Chemistry, University of Birmingham, and S. A. BARKER, Lecturer in Organic Chemistry, University of Birmingham. Oxford University Press, 417 Fifth Avenue, New York 16, N. Y. 1960. ix + 228 pp. 14.5 × 22 cm. Price, \$4.80.

It was over forty years ago when two distinguished American bacteriologists, Alfonse Dochez and Oswald Avery, published a paper which was destined to open a new era in the field of microbiology. The so-called "soluble specific substances" of pneumococcus which they first described were later shown by Avery and Heidelberger to be polysaccharides. To be sure, bacteria were known to elaborate carbohydrates, but these new substances were unique. Not only did they prove to be polysaccharides, but they endowed the microorganism from which they were obtained with type specificity and the ability to incite specific immunity in experimental animals. Now, some forty years later, there has appeared a book by two chemists, M. Stacey and S. A. Barker, entitled "Polysaccharides of Micro-organisms." This is a timely book for it has been ten years since a similar volume made its appearance in the English language, Burger's "Bacterial Polysaccharides."

As one peruses the pages of this new volume he can't help but be impressed by how vast our knowledge has become regarding these biologically important substances. The structure of this new book is conventional enough. It begins with a short chapter on carbohydrate nomenclature which embraces a description of the monosaccharides, the conformation of sugars, and a paragraph on oligo- and polysaccharides. This in turn is followed by a second chapter on the monosaccharide components of polysaccharides and antibiotics, and a word regarding their biosynthesis. In so far as it goes this is first rate, but this reviewer regards the introduction as rather thin fare.

After these brief remarks we come to the meat of the book. Three successive accounts, the function of polysaccharides, their isolation and the criteria of their homogeneity, and the determination of their structure, prepare the reader for that which is to follow—a description of the polysaccharides derived from a variety of microorganisms. These accounts, which constitute the remaining two-thirds of the book, form a good compilation of our newer knowledge concerning the polysaccharides of viruses, bacteria, molds, yeasts and protozoa. Their discourse on the structural determination of polysaccharides is very informative, for here the writers, both chemists, are treading on firm and familiar ground. They present an excellent review of the modern techniques employed in the study of the structure of carbohydrates. When we come to that portion of the book which is devoted to a description of microbial polysaccharides themselves, it is puzzling for the uninitiated to understand the rationale of the authors, for there is no chronological sequence. Certainly one cannot deny that the classical work in the whole field is that on the pneumococcus, yet the whole section begins with an account of the polysaccharides of rickettsiae and viruses—a newcomer to the field if ever there was one.

The book itself is well put together; the typography is excellent and each chapter ends with a bibliography. The subject index is good, but it is unfortunate that the references at the end of each chapter have not been further classified to form a cumulative author index.

Perhaps the most serious criticism which can be leveled at the book is the dearth of discussion pertaining to the immunological role of microbial polysaccharides and the