flaked ice (the beaker was immersed in a Dry Ice–acetone bath). White solid separated on scratching of the beaker. The product was immediately filtered through a medium-coarse sintered-glass funnel and washed twice with ice water. It was then dried overnight *in vacuo* (P_2O_5) to give 10.5 g (70% yield) of II: mp 244–246° (lit.[10] 220–222°); $\lambda_{max}^{pH\ 1}$ 276 mμ (ε 6600); $\lambda_{max}^{pH\ 1}$ 226 mμ (ε 11,800), 331 mμ (ε 6300). *Anal.* Calcd for $C_4H_2ClN_3O_4$: C, 25.08; H, 1.05; N, 21.93. Found: C, 24.80; H, 1.20; N, 21.60.

5-Acetamido-4-chlorouracil (III).—A solution of freshly prepared II (8.0 g, 0.04 mole) in 200 ml of AcOH and 30 ml of Ac_2O was hydrogenated at 4.2 kg/cm² in the presence of 5% Pt–C at room temperature. Theoretical amount of H_2 was absorbed in 3 hr. The catalyst was removed by filtration; the filtrate was heated on a steam bath for 30 min and evaporated *in vacuo* to dryness. To the cool syrup was added EtOH (20 ml). The product slowly solidified on standing. It was isolated by filtration giving 5.29 g (61% yield) of III, mp 238–242°. Recrystallization from AcOH–EtOAc gave an analytically pure sample as a white solid: mp 241–242°; $\lambda_{max}^{pH\ 1}$ 267 mμ (ε 12,200); $\lambda_{max}^{pH\ 11}$ 228 mμ (ε 7200), 286 mμ (ε 16,300). *Anal.* Calcd for $C_6H_6ClN_3O_3$: C, 35.40; H, 2.97; N, 20.64. Found: C, 35.67; H, 3.10; N, 20.60.

5-Acetamido-4-hydrazinouracil (IV).—A mixture of 2.0 g (0.01 mole) of III, 0.32 g of hydrazine, and 1.0 g of Et_3N in 120 ml of EtOH was refluxed on a steam bath for 3 hr. After the mixture was cooled, the solid product was collected by filtration and washed (EtOH, Et_2O) to give 2.2 g of IV, mp 230–232°. The product was identified as its acetone derivative (prepared from 0.2 g of IV, 2 ml of acetone, 20 ml of H_2O, and 5 drops of AcOH), white crystals (0.15 g), mp 324–325°. *Anal.* Calcd for $C_9H_{13}N_5O_3$: C, 45.18; H, 5.47; N, 29.28. Found: C, 44.80; H, 5.50; N, 29.10.

5,7-Dioxo-3-methyl-5,6,7,8-tetrahydropyrimido[5,4-*e*]-*as*-triazine (V).—A suspension of 500 mg (2.5 mmoles) of IV in 50 ml of Ph_2O was heated at 220–230° with stirring for 30 min. The hot reaction mixture was filtered and to the cold filtrate was added 20 ml of Et_2O. There was obtained a bright yellow solid, which was collected by filtration and washed [twice with 10 ml of petroleum ether (bp 35–60°), Et_2O (20 ml)] to give 100 mg (22% yield) of V, mp 281–282°. Recrystallization from PrOH yielded an analytical sample, mp 281–282°. The product was soluble in H_2O and MeOH. The nmr spectrum (D_2O) showed one singlet at τ 7.18 (CH_3); $\lambda_{max}^{pH\ 1}$ 231 mμ (ε 17,200); $\lambda_{max}^{pH\ 1}$ 270 mμ (ε 3100); $\lambda_{max}^{pH\ 11}$ 338 mμ (ε 4900); $\lambda_{max}^{pH\ 11}$ 252 mμ (ε 17,400), 390 mμ (ε 4100). *Anal.* Calcd for $C_6H_5N_5O_2$: C, 40.23; H, 2.81; N, 39.10. Found: C, 40.00; H, 2.65; N, 38.90.

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Book Reviews

Mechanisms of Reactions of Sulfur Compounds. Volume 1. 1966. By N. KHARASCH, B. S. THYAGARAJAN, and A. I. KHODAIR. Intra-Science Research Foundation, Santa Monica, Calif. 1967. 286 pp. 17.5 × 25.5 cm. $12.00.

This book surveys the literature for the period 1965–1966 of reactions of organic sulfur compounds which are interesting in respect to reaction mechanisms although many of the reactions reported are of more synthetic than theoretical interest. In many cases the reaction mechanisms proposed are speculative with little or no experimental tests of their validity. The book is extremely interesting, however, in that it brings together a great variety of much stimulating chemistry and can serve two distinct purposes, generating research ideas in the mind of the reader or as a convenient source of abstracts and references for the person planning or already carrying out work in a particular area. I enjoyed the book very much.

The references cited are treated in either of two ways, as a simple literature citation with no details, or as a summary describing the work in detail. The authors state in the introduction that "the importance of a paper should by no means be judged by whether or not a summary has been included in the report." This is the weakest aspect of the book. I have found that generally the papers abstracted were those which appeared in English in readily available journals, mainly the *Journal of the American Chemical Society* and the *Journal of Organic Chemistry*, while the papers cited but not summarized were those written in foreign languages and/or in journals less accessible. For example, a rough count gave the following: out of *ca.* 34 references to papers in Russian journals only one was summarized, none out of 14 in French, two out of 30 in German, and one out of 13 in Italian. Further, some of the papers which appeared in the *Journal of the American Chemical Society* were summarized twice. The value of this annual report could be increased many times if a greater effort were made to summarize the important papers in the foreign (non-English) literature.

The coverage is also spotty. None of Middleton's work on thiocarbonyl compounds (*J. Org. Chem.*, 1956) is even cited while every paper dealing with thiocarbonyl S-oxides is summarized. Only one of Cram's papers dealing with stereochemistry of sulfonyl-stabilized carbanions and none of Corey's is summarized even though this is one of the most important areas of current research and one which is subject to different interpretations.

I am confident that the editors will take measures to correct the weaknesses in a generally well-conceived and well-executed book and that future volumes will become increasingly valuable to those doing research in sulfur chemistry and organic chemists generally.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF VIRGINIA
CHARLOTTESVILLE, VIRGINIA

FRANCIS A. CAREY

Reviews of Pharmacological Topics. I. **Advances in Pharmacology. Volume 5.** Edited by SILVIO GARATTINI and PARKHURST A. SHORE. Academic Press Inc., New York and London. 1967. ix + 318 pp. 23.5 × 16 cm. $15.00.

The seven reviews of Volume 5 are as follows: Molecular forces in anesthesia (B. P. Schoenborn and R. M. Featherstone), The effect of endotoxin on resistance to infection and disease (F. M. Berger), Effect of drugs on mast cells (A. Goth), Drugs and aggressiveness (L. Valzelli), Pharmacologic and endocrine aspects of carcinoid syndrome (J. A. Oates and T. C. Butler), Drug actions on thermoregulatory mechanisms (H. L. Borison and W. G. Clark), and Pharmacology of benzodiazepines: laboratory and clinical correlations (G. Zbinden and L. O. Randall). One can see readily that with the exceptions of the first and last of the chapters which have been reviewed well in similar volumes under different sponsorship, the topics are of considerable timeliness and reviews of them are welcome. One is impressed with the versatility of one contributor (F. M. Berger) who after much notable work on muscle relaxants and antianxiety agents has now turned to endotoxin and resistance to disease. The chapter on drugs and aggressiveness (in animals) will provide much correlation of hitherto separated observations in the psychopharmacological laboratory.

All reviews are written well and lucidly, and the book is printed with unusual clarity and pictorial pleasantness. It will be received as one of the better educational efforts and surveys in contemporary professional pharmacology.

II. **Annual Review of Pharmacology. Volume 8.** Edited by H. W. ELLIOTT, W. C. CUTTING, and R. H. DREISBACH. Annual Reviews, Inc., Palo Alto, Calif. 1968. vii + 594 pp. 23 × 16.5 cm. $8.50.

This annual volume contains thirty reviews, some of them on repeatedly presented topics (SAR, metabolic fate of drugs, review

of reviews), the others on subjects of considerable experimental activity during the last few years. The majority of the contributors are well-known authorities in their respective fields, and their chapters reflect their proficiency and experience in their areas, and in writing.

It is not the purpose of this report to list the Table of Contents of this diversified book. Among the chapters are some which have been reviewed widely elsewhere, but some other topics are newcomers. Among the latter are Genetic factors in relation to drugs, Fluorides in man, Snake venoms, Marine toxins, Pharmacology of smog, Invertebrate pharmacology, and Paracalcitonin.

Some of the chapters have been written by foreign authors whose attempts to write in English are to be commended and whose linguistic troubles are to be excused. It is the duty of the editors to smooth out textual expressions and problems of nomenclature in such cases. At least in one instance, Highlights of Soviety Pharmacology, by S. W. Anichkov, the editors have fallen down badly on their job. It is to be hoped that the translating and chemical transliteration efforts will be more successful in future volumes.

UNIVERSITY OF VIRGINIA ALFRED BURGER
CHARLOTTESVILLE, VIRGINIA

Progress in Medicinal Chemistry. Volume 5. Edited by G. P. ELLIS and G. B. WEST. Plenum Press, New York, N. Y. 1967. xi + 391 pp. 25.5 × 16.5 cm. $22.00.

The fifth volume of this now well-recognized series of consecutive monographs presents six reviews: Polypeptide antibiotics of medicinal interest (R. O. Studer), Nonsteroidal antiinflammatory drugs (S. S. Adams), Heparin and heparinoids (L. B. Jaques), the Histidine decarboxylases (D. M. Shepherd and D. Mackay), Psychotropic drugs and neurohumoral substances in the CNS (J. Crossland), and the Nitrofurans (K. Miura and H. K. Reckendorf). Each review is documented extensively, with 250–550 references on the average, unfortunately without the initials of the authors. The subject index is minimal.

As with most medicinal reviews nowadays, emphasis is placed on biochemical causation of the disease entities, tests in experimental situations, the biological performance of enzymes and metabolites involved, and drugs used in the respective therapy. Structure–activity relationships are dealt with adequately in some chapters (*e.g.*, nitrofurans), and quite inadequately in others (*e.g.*, psychotropic agents). Similar statements could be made about the adequacy of biological areas in some of the other reviews.

As much as one welcomes high experimental and literary activity in interdisciplinary fields, and wants to be exposed to diverse viewpoints, one may well raise a question about the need for the many overlapping series of review monographs in medicinal chemistry. The same historical introductions, the same descriptions of early errors and trials, the same joyous recognition of underlying biochemical mechanisms, and often the same lists of drugs and references are to be found in parallel contemporary series. Competition between publishers and editors is a good thing and tends to keep the quality of reviews at a high level. What is needed are new thoughts on established facts and novel interpretations of debatable data. Or else, reviews ought to be beamed at different levels of understanding, expose novices to the facts of the field, and suggest to scientists in ancillary areas how they could use their experience and talents to fill unexplained gaps of knowledge in medicinal researches. It would be gratifying if these remarks would orient the present series of monographs, or others, in the direction suggested.

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CHARLOTTESVILLE, VIRGINIA

Advances in Drug Research. Volume 4. Edited by N. J. HARPER and ALMA B. SIMMONDS. Academic Press Inc., New York and London. 1967. vi + 274 pp. 23.5 × 16 cm. $12.50.

Seven contributors have united to present reviews on some chemical classes of drugs of established or potential interest. Cephalosporins, now fairly well worked over, are surveyed by an author of considerable experience in this field, E. Van Heyningen of the Lilly Research Laboratories. C. A. Stone and C. C. Porter of the Merck Institute for Therapeutic Research write authoritatively about methyldopa and related structures. Ralph J. and Joan S. Fessenden, formerly of San Jose State College, review the biological properties of silicon compounds, a subject to which they virtually gave birth some years ago. C. I. Furst of Ciba reports on the biochemistry of guanethidine, and C. R. Ganelin of the British branch of Smith Kline and French Laboratories, on indanes and indenes in a comprehensive review. Thus, specialized topics which are not readily found elsewhere are dealt with by experts, many of whom have been deeply involved in creating or developing their subject. The treatment accorded the various topics is modern, interdisciplinary, and up-to-date. References and indexes are adequate. The editors are to be commended for their careful attention to uniformity.

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Chemical Psychoses: LSD and Related Drugs. By LEO E. HOLLISTER. Charles C Thomas, Publisher, Springfield, Ill. 1967. xi + 190 pp. 23.5 × 16 cm. $8.00.

The impact of the wide-spread use and abuse of psychotomimetics and hallucinants has opened questions about these drugs in the minds of physicians, psychiatrists, medical scientists, politicians, the lay public, the youthful abusers of the drugs, and those charged with the legal regulation of the agents concerned. A good, compact, readable, and authoritatively documented book on the subject that can be read profitably by critical and uncritical groups as well seems almost too much to ask for. However, Dr. Hollister's present volume has achieved this almost ideal combination. All of the major psychotomimetic drugs are treated well and comprehensively. The medicinal chemist will find enough structures (there is a double-bonded OH on p 97) and their relations to activity to satisfy his curiosity; psychopharmacologists and psychiatrists will be interested in the considerable differences between the manifestations of endogenous hallucinations and those evoked by the drugs. There are detailed chapters on EEG and neuropharmacological studies in man and animals, biochemical and metabolic data, and the controversial chemical theories of psychoses. Among the suggestions for much-needed research is that for pharmacological work on *Cannabis* which is virtually nonexistent.

The unsettled questions concerning the use of psychotomimetics in therapy are discussed critically in a good chapter. This section should be of special value to psychiatrists and physicians. They will learn from it about the apparent advantages and adverse reactions, a subject so widely held against these drugs. The concluding chapter is entitled "Drugs in Our Culture" and deals with the search for altered consciousness, adverse reactions following nonmedical use of hallucinogens, and legal and social implications arising from their possession and use.

This reviewer has read many chapters on the subject and has written some himself. However, the present book represents the most readable and credible source of information and will be read with pleasure by laymen and scientists alike. A few proofreading errors will not detract from this enjoyable volume.

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Topics in Pharmaceutical Sciences. Volume 1. Edited by D. PERLMAN. Interscience Publishers, Inc., New York, N. Y. 1968. ix + 136 pp. 23.5 × 15.5 cm. $7.95.

This slim booklet is the print-out of two symposia held in Las Vegas, Nevada, in April 1967. Its title is perhaps a misnomen, since one of the symposia deals with the chemistry, biosynthesis, allergenicity, and enzymatic destruction of the penicillins and cephalosporins, and the other one with pharmacological effects of steroids on cellular processes. Both of these broad topics transcend what one usually classifies as pharmaceutical sciences, unless these symposia constitute an interdisciplinary raid on the premises of medicinal chemistry, immunology, and clinical pharmacology. Be that as it may (the editors of future volumes of this series might consider staying closer to their traditional spheres of interest) a star cast was assembled for the occasion. E. P. Abraham unrolls the history of the penicillins and cephalosporins, their molecular modifications, and behavior toward lactamases. Karl Heusler relates the total synthesis of

β-lactam antibiotics including that of cephalosporin C, which had been published only 1 year ago in detail after R. B. Woodward had presented it in his Nobel lecture. J. L. Strominger then surveys authoritatively the effect of the β-lactam antibiotics on cell wall synthesis.

The second symposium also contains three presentations: Control of steroid hormone biosynthesis in the testis (R. I. Dorfman), Effects of corticosteroids on fibroblast functions (D. L. Berliner), and Effect of steroids on lysosomes and artificial lipid structures (Gerald Weissmann). The last two of these articles add to and modify prevailing views of the therapeutic role of antiinflammatory corticosteroids.

Those interested in these topics will find the little book a well-illustrated, well-documented, and carefully edited review and preview of timely medicinal problems of acknowledged theoretical difficulty and high practical priority.

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CHARLOTTESVILLE, VIRGINIA

An Introduction to the Alkaloids. By G. A. SWAN. John Wiley and Sons, Inc., New York, N. Y. 1967. viii + 326 pp. 24.5 × 17 cm. $10.50.

The preface and the dust jacket announce that this book wishes to provide an up-to-date introduction to the alkaloids in a small volume for students at a reasonable price. The student can get a first glimpse at structural and synthetic work on alkaloids as done by modern methods and in recent years, with natural emphasis on those groups of alkaloids which have received most attention in the last 15 years. This leaves much of the classical work in the field in jeopardy, especially the structure elucidation done "by a comedy of errors" as by older deductive methods. Since much of the earlier work on natural products concentrated on alkaloids, the student loses the benefit of reading about those older but instructive chemical methods. On the other hand, their inclusion would have defeated the purpose of this introductory survey which should serve well as a companion to a one-semester course on the alkaloids. The book is recommended for such courses.

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Les méthods statistiques en pharmacie et en chimie (Applications à la recherche, à la production et au contrôle). By JEAN PHILIPPE. Masson et Cie, Paris. 1967. x + 377 pp. 24 × 16.5 cm. 82 Francs (paperback).

This text book is addressed to chemists in the health sciences, and to pharmacists who would like to apply statistical analysis to their experimental data but hesitate to get involved in mathematical speculations. Among the chapter headings are several which ought to aid in evaluating decision making and taking risks in selecting variable manufacturing methods. They are Characteristics of the sample, Normal distribution, Tests for significance, Control charts (including automated equipment), Variance analysis, Experiment planning and improvement of assaying precision, Regression analysis, Statistical interpretation of dosages by quantitative measurements, Optimal improvements in industrial processes, etc.

The mathematics is not as harmless as the stated purpose of the book wishes to convey. However, anyone interested in statistical methods and able to read about them in French will find this volume quite profitable.

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CHARLOTTESVILLE, VIRGINIA

Die Klinische Bedeutung der Pantothensäure unter besonderer Berücksichtigung der Kinderheilkunde. By ISTVÁN SZÓRÁDY. Studia Medica, Szeged. 1967. 104 pp. 24 × 17 cm. Paperback (in German).

This booklet details the history, occurrence, properties, requirements, metabolism, and clinical applications of pantothenic acid and its commercially available derivatives. There is virtually no chemistry, and not many of the important American investigators in this area are listed in the author index; the subject index is 3 pages long, but there are 672 references.

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CHARLOTTESVILLE, VIRGINIA

Fluorine Chemistry Reviews. Volume 1. Edited by PAUL TARRANT. Marcel Dekker, Inc., New York, N. Y. 1967. vi + 424 pp. $18.50.

Since World War II the literature of fluorine chemistry has been expanding at a phenomenal rate. Two or more national and international fluorine symposia are being held each year, chapters on fluorine are found in many new chemical treatises, books on specialized areas of fluorine chemistry are appearing more frequently, and reviews and research papers on fluorine are quite evident in journals. Also, there are several well-known review series on fluorine chemistry which publish additional volumes at intervals. In 1967 the first fluorine chemistry journal, *Fluorine Chemistry Reviews*, appeared under the able editorship of Paul Tarrant assisted by an international advisory board.

The present book, also edited by Paul Tarrant, is simply a bound volume of the papers that appeared in the initial volume of the above journal. Both the subject matter and paging are identical. Author and subject indices were added to this hard-cover volume. Presumably this procedure will be followed with subsequent volumes of the journal.

This book consists of a series of eight articles on the synthesis, properties, and toxicity of organic fluorine compounds, principally aliphatic and alicyclic systems. Each article except the one on toxicity contains a brief historical background, methods of synthesis, chemical and physical properties with tables, recent developments, some unpublished results of the authors, and an excellent bibliography. The toxicity article is essentially a discussion of the toxicity of fluoroalkanes, fluoroalkenes, and fluoropolymers. The topics covered and their authors are Synthesis, Compounding, and Properties of Nitroso Rubbers (M. C. Henry, C. G. Griffis, and E. C. Stump), Electrochemical Fluorination (S. Nagase), The Fluoroketenes (Y. A. Cheburkov and I. L. Knunyants), Hexafluoroacetone (C. G. Krespan and W. J. Middleton), Fluorocarbon Toxicity and Biological Action (J. W. Clayton, Jr.), Diels–Alder Reactions of Organic Fluorine Compounds (D. R. A. Perry), Methods for the Introduction of Hydrogen into Fluorinated Compounds (F. J. Metville and D. J. Burton), and Reactions Involving Fluoride Ion and Polyfluoroalkyl Anions (J. A. Young).

The articles are well written, and the reader will appreciate the completeness of the subject matter covered by the authorities in each field. With the present-day interest in health hazard control, the chapter on fluorocarbon toxicity and biological activity is especially timely. The book has very few of the usual inconsistencies of multiauthors. Additional yield data in some of the chapters would have been desirable. A few authors thoughtfully provided *Chemical Abstracts* citations in their bibliographies where the journal references might not be readily available. The book will be a useful purchase to research libraries, specialists in fluorine chemistry, and especially to the non-subscribers of the parent journal.

ILLINOIS STATE GEOLOGICAL SURVEY G. C. FINGER
URBANA, ILLINOIS