

pounds (0.2 mol) were added. The suspension was heated to 80° and a stream of nitrogen was passed into the solution. In portions 0.4 mol of iron powder was added and the mixture was heated at reflux for 2 hr. The clear solution was poured into H₂O and the oil extracted twice with CH₂Cl₂. The combined organic layers were washed with a NaHCO₃ solution and dried (MgSO₄). The solvent was evaporated and the residue was distilled in vacuo.

Amidophenylthienyl Sulfides 20–27 (Table II). The amines 11–18 (0.1 mol) were dissolved in 300 ml of benzene and 0.15 mol of formic acid was added. The mixture was refluxed for 3 hr and poured into H₂O; the benzene layer was separated, washed with a NaHCO₃ solution, and dried (MgSO₄). The solvent was evaporated and the remaining solids were recrystallized.

The amide 19 was made in the same way with Ac₂O (0.1 mol) and pyridine (0.1 mol) in benzene.

Amido-3'-(2'-bromo)phenylthienyl Sulfides 28–30 (Table II). The amides 19–21 (0.05 mol) were dissolved in a mixture of HOAc–CHCl₃ (1:1). To the stirred solution NBS (0.05 mol) was added in portions. After this addition the yellow solution was stirred for 2 hr and poured into H₂O. The CHCl₃ layer was washed with H₂O, a 10% KOH solution, and H₂O. The solution was dried (MgSO₄) and concentrated. The solid residue was recrystallized from the appropriate solvents.

Amidothieno[1,4]benzothiazines 31–39 (Table III). The bromamides (10 mmol) were dissolved in 200 ml of diphenyl ether. To this solution a mixture of 2 g of KOAc and 1 g of activated copper bronze was added. The reaction mixture was stirred vigorously under nitrogen and heated to 190–200°. The reaction was followed with TLC and heating was continued until 80–90% of the starting material was converted into the thiazine. The reaction mixture was cooled and chromatographed over a silica gel column with *n*-hexane to remove the diphenyl ether and further eluted with CHCl₃. The CHCl₃ fractions were collected and concentrated leaving light-green to light-purple substances which were recrystallized.

Thieno[1,4]benzothiazines 40–47 (Table III). **Procedure A.** The formylthiazine (5 mmol) was dissolved in 60 ml of EtOH. In a nitrogen atmosphere a solution of 8 mmol of KOH in 10 ml of H₂O was added. Stirring was continued until the reaction was complete, which could be followed on TLC. The colored solution was poured into a saturated NaCl solution and the precipitate was taken up in ether. The ether was washed (H₂O), dried (MgSO₄) under stirring with decolorizing carbon, and then removed, leaving a solid compound which was recrystallized.

Procedure B. To a solution of 6.6 mmol of the thiazine in 200

ml of ether a solution of 1.6 g of KOH in 10 ml of H₂O was added under vigorous stirring. A stream of nitrogen was passed into the heterogeneous mixture and sufficient EtOH was added to obtain a reasonable reaction rate (10–20 ml). After the reaction was complete, the reaction mixture was poured into a saturated NaCl solution. The ethereal layer was washed (NaCl) and dried on MgSO₄ under stirring with decolorizing carbon and the ether was evaporated. The isolated thiazines were then recrystallized.

N,N-Dimethylaminopropylthieno[1,4]benzothiazines 48–55 (Table IV). The thiazine (4.7 mmol) was dissolved in 30 ml of dry xylene. Under nitrogen and with stirring 200 mg (5 mmol) of powdered NaNH₂ was added and the reaction mixture was heated for 2 hr. Then 730 mg (6 mmol) of 3-(dimethylamino)propyl chloride was added and the red-colored reaction mixture was refluxed (1–4 hr). The disappearance of the starting thiazine was followed on TLC. When the reaction was complete, the mixture was cooled and washed several times with H₂O. The organic layer was extracted with 15% tartaric acid and the acid layer was washed with toluene. The tartaric acid solution was rendered alkaline with a 15% NaOH solution and the oil was extracted into toluene. The organic layer was dried (CaCl₂) and concentrated leaving a dark-colored oil. This oil was distilled in vacuo and dissolved in absolute ether. A solution of ether saturated with dry HCl gas was added and the precipitate was collected and dried in vacuo. The HCl salts were recrystallized twice from absolute EtOH–ether.

Acknowledgments. The authors wish to thank Mrs. A. Westerbrink and Mr. D. Dijkstra for their valuable technical assistance. We also are indebted to the Pharmacological Department of Janssen Pharmaceutica, Beerse, Belgium, for carrying out the pharmacological tests.

References and Notes

- (1) (a) C. J. Grol and J. S. Faber, *Recl. Trav. Chim. Pays-Bas*, **89**, 68 (1970). (b) C. J. Grol, *J. Heterocycl. Chem.*, **11**, 953 (1974).
- (2) H. Fenner, *Arch. Pharm. (Weinheim, Ger.)*, **304**, 36 (1972).
- (3) A. Fehlmeister, R. Schoubman, and H. Home, *J. Pharm. Sci.*, **54**, 1589 (1965).
- (4) L. Levy, T. N. Tozer, L. O. Tuck, and D. B. Loveland, *J. Med. Chem.*, **15**, 898 (1972).
- (5) P. A. J. Janssen, C. J. E. Niemegeers, K. H. L. Schellekens, and F. M. Lenaerts, *Arzneim.-Forsch.*, **17**, 841 (1967).

Book Reviews

The Theory of Rate Processes in Biology and Medicine. By Frank H. Johnson, Henry Eyring, and Betsy J. Stover. Wiley, New York, N.Y. 1974. 703 pp. \$27.50.

The theory that any process, chemical or biological, which involves an orderly progressive change at some characteristic or definable rate follows the same fundamental laws was first proposed in 1935. During the intervening years a number of investigators have shown the application of the theory to processes ranging from simple chemical reactions to complex biological processes. According to the authors, "the purpose of this volume is to outline the conceptual basis of modern rate theory and to apply the net results of this rational quantitative theory to representative rate processes in biology and medicine in an effort to achieve a better understanding of the phenomena involved".

The book includes six chapters, a bibliography, an author index, a list of sources for the 257 illustrations presented in the text, an index to the genera and species mentioned in the book, and a concise subject index. The first chapter introduces the theory of rate processes and the application of this theory in biology and medicine. Chapter two discusses the application of the theory of rate processes to the phenomena of bioluminescence and chemilumi-

nescence. In Chapter three, the role of temperature as an agent affecting rate processes is discussed. The next chapter discusses the influence of hydrostatic pressure and molecular volume changes on the rate process theory. Chapter five evaluates the action of inhibitors in relation to concentration, temperature, and hydrostatic pressure on rate processes. The final chapter is a highly interesting application of the theory of absolute rate processes to the complex dynamics of mammalian life. The bibliography contains 76 pages of references, providing a highly useful source of additional information. The book's value is greatly enhanced by the numerous useful illustrations provided throughout the book.

This book should prove highly interesting to biologists wishing to understand the theoretical basis of rate processes, to chemists wishing to know more about biological processes, and to physicians attempting to understand the fundamental, molecular basis of medical problems.

Department of Life and Behavioral
Sciences
U.S. Air Force Academy
Colorado 80840

Donald F. Logsdon, Jr.

Bilayer Lipid Membranes (BLM). Theory and Practice. By H. Ti Tien. Marcel Dekker, New York, N.Y. 1974. ix + 655 pp. \$39.50.

The preface of the book may provide some insight into the overall objective of the author. Bilayer lipid membranes (BLM) were developed by the author in collaboration with others. He states that BLM "... constitute one of the most realistic and useful models for biological membranes". Thus, the book emerges as a historical perspective of their research and as a promoter of their concept.

The author describes the format and chemical composition of several model bilayer lipid membranes and details their physical and chemical properties, such as, interfacial chemistry, optical and electron properties, and quantum phenomenon. Several chapters relate normal biological properties of membranes to those of BLM: water and solute permeability, antibiotic and ion permeability, and the concept of electron conduction. These chapters are organized well and the author provides sufficient background information and details for relatively easy comprehension. One chapter, or approximately one-fourth of the book, reviews bilayer lipid membranes as models for several biological membranes: plasma, mitochondria, nerve, photo receptor, and chloroplasts. As is so often the case, the author has simplified very complex biological membranes and their functions in order to accommodate the BLM model. The lipid composition of the BLM models utilized ill-defined or nonbiological lipids such as "oxidized" cholesterol, egg lecithin, and extracts of brain, bacteria, and chloroplasts, etc. Most biological membranes carry out multiple functions and, consequently, the BLM model, in order to be useful, has to differentiate effectively among these multiple functions. The author has given this aspect minimum attention but alludes to them in this "... chop suey or Smorgasbord model" biological membranes.

At the end of the book, one finds a selected bibliography of bilayer lipid membranes containing authors, titles, and references. This selected bibliography of 625, together with additional references cited in the author's index, will cover the subject adequately prior to 1973; thereafter, only a few references have been cited.

The reviewer recommends it as a source of information on bilayer lipid membranes as models for examining biological membrane phenomena.

Life Sciences Section
Author D. Little, Inc.
Cambridge, Massachusetts 02140

David W. Yesair

Chemical Induction of Cancer. Volumes IIA and IIB. By Joseph C. Arcos and Mary F. Argus. Academic Press, New York, N.Y. 1974. Volume IIA, xv + 385 pp. \$34.50. Volume IIB, xv + 379 pp. \$33.50.

The first edition of "Chemical Induction of Cancer" by George Wolf was published in 1952 by the Harvard University Press. The second edition of this work was planned for three volumes to be coauthored by Arcos, Argus, and Wolf, and Volume I, which appeared in 1968, was written under this arrangement, but, after its completion, Dr. Wolf was forced to withdraw. For this and other reasons, the appearance of Volume II was delayed until 1974 and was updated by "notes added after completion". The organization of the series is somewhat confusing since Part I, "Molecular Architecture and the Physical Bases of Molecular Forces", and Part II, "The Nature of Tumors. Concepts and Techniques of Testing Chemical Agents for Carcinogenic Activity", appear in Volume I, whereas Part III, "Structure-Activity Relationships of Chemical Carcinogens. Effect of Chemical Reactivity, Molecular Geometry and Metabolism on Carcinogenic Activity", is contained in Volume IIA, IIB, and IIC and Part IV, "Cross-Reactions between Carcinogens: Anti- and Cocarcinogenesis. Influence of Exogenous Factors and Biological Parameters on Carcinogenic Activity", is in Volume IID. The final part, Part V, "Cell Structure and Function. Effect of Carcinogens on Living Tissues. Mechanisms of Biological Action", is the entire subject of Volume III (Volumes IIC, IID, and III have not appeared at this writing). Cross-indexing thus becomes unclear and is repeatedly explained by the same footnote, which appears on so many pages that it is a little distracting.

Volume IIA is devoted to the condensed polycyclic compounds,

with emphasis on the aromatic hydrocarbons, and IIB to aromatic amines. For such a complex review, both volumes are well written and easy to read. The authors show their command of the subject, which should allow these volumes to serve as basic references in the field of oncogenesis. Nevertheless, some deficiencies can be detected. It is a bit disconcerting to shift from numbered sections to "notes" to "notes added after completion...". Although the authors point out that the addition of supplementary notes was necessary, this organization detracts from the high quality otherwise evident.

Even though it is probably unavoidable for such comprehensive works, the most recent references in IIA are nearly 3 years old. In this period of time, knowledge of the biotransformation of polycyclic hydrocarbons has rapidly expanded, with a wave of interest in epoxides as metabolic intermediates. In 1972, this surge was just beginning. For complex molecules, nomenclature is always a problem. The numbering system selected by the authors for rings of polycyclic hydrocarbons is not that which is most widely accepted. For instance, 3-hydroxybenzo[*a*]pyrene is, according to their system, 8-hydroxy-3,4-benzopyrene. In reading this volume, one must translate the names applied. Fortunately, the numerous structures provided facilitate this process. In view of present information, the sections on the K-L region theory of oncogenesis and that on non-covalent interactions are overemphasized.

Most of these comments are less applicable to Volume IIB. The references are more up to date; the metabolic activation, and deactivation, of the aromatic amines had been more clearly defined at the time this volume was written than had the metabolic activation of the polycyclic hydrocarbons, and numbering of the ring systems is no problem. At the same time, the tendency noted in Volume IIA to devote too much attention to outmoded ideas is still in evidence here.

These are minor criticisms, however, and both Volumes IIA and IIB represent high-quality work by competent authors.

Southern Research Institute
Birmingham, Alabama 35205

John A. Montgomery

Chemistry and Biochemistry of Amino Acids, Peptides and Proteins. Volumes 2 and 3. Edited by Boris Weinstein. Marcel Dekker, New York, N.Y. 1974. Volume 2, 380 pp, 15 × 23 cm, \$27.50. Volume 3, 324 pp, 15 × 23 cm, \$27.50.

Following the format of Volume 1 (1971), Volumes 2 and 3 of this series present a collection of informative reviews which serve to summarize and update the current state of the respective topics.

All five chapters of Volume 2 concern themselves with various aspects of amino acid and peptide synthesis. Chapter I (Chemistry and Biochemistry of Gramicidin S and Related Compounds) by T. Kato and N. Izumiya explores the functional-structural relationships of the class of gramicidin antibiotics. After a brief history, the biological and chemical synthesis of gramicidin is followed by a detailed summary of the effects of chemical alterations on its antibiotic activity. A short discussion of possible modes of action terminates the chapter. In a similar approach, Chapter 2 (Synthesis of ACTH-Active Peptides and Analogs) by H. Yajima and H. Kawatani outlines the extensive synthetic achievements on adrenocorticotropic hormone and its analogs. The authors lead with a cursory section covering the biochemistry, assay, isolation, and structure determination of ACTH. Synthetic methodologies are classified, interestingly, by the deblocking procedures employed (HBr, sodium in liquid NH₃, HCl, trifluoroacetic acid, HF, and solid phase). The elucidation of those portions of the molecule responsible for physiologic response through the use of various derivatives of ACTH is summarized. In Chapter 3 (Reaction of Small Heterocyclic Compounds with Amino Acids), K. Jankowski presents studies on the mechanisms and products of the reactions of three- and four-membered heterocyclic ring systems (epoxides, epulfides, aziridines, seleniranes, lactones, and lactams) with amino acids. Detailed examples of nine simple synthetic procedures, extracted directly from the literature followed by a tabular survey of the many reactions considered in the article, complete the chapter. In a complete, clear, and concise expose, D. J. Woodman (The Isoxazolium Salt Method of Peptide Synthesis) recounts the synthesis, chemistry, and use of isoxazolium salts for peptide synthe-

sis. The mechanistic features of carboxyl group activation to the enol-ester acylating agents are presented forming the basis for discussion of racemization and other side-product reactions. Applications, primarily with *N*-ethyl-5-phenylisoxazolium-3'-sulfonate, are presented with an extensive tabulation of peptides synthesized and their yields. The final chapter (Synthesis of Amino Acids and Peptides Under Possible Prebiotic Conditions) by K. Harada presents the recent results obtained in studies attempting to mimic conditions for amino acid and peptide formation on primordial earth. Reports are presented in capsular form of the various amino acids and peptides formed when electric discharges, heat, light, and ionizing radiation are used to initiate reactions of various gases and small molecules.

Volume 3 of the series consists of three chapters, the first of which (Conformations of Peptides in Solution as Determined by NMR Spectroscopy and Other Physical Methods) by V. J. Hruby is an extensive review (188 pp, 678 ref) of results and conclusions obtained, chiefly through NMR techniques, regarding peptide and polypeptide conformations in solution. Progressing from short linear and cyclic peptides to longer polymers and cyclic tri- to hexapeptides, and finally to biologically active peptides, the author critically assesses information obtained from NMR, ORD, CD, ir, deuterium exchange, and thin-film dialysis studies regarding cis-trans peptides, hydrogen bonding, α -helical structure, and other factors contributing to peptide conformation. Considerable attention is directed toward the biologically active peptides such as angiotensin, oxytocin, and vasopressin, various antibodies such as the enniatins and valinomycin, the gramicidins, and the mushroom toxins including phalloidin and α -amanitin. J. P. Scannell and D. L. Pruess (Naturally Occurring Amino Acid and Oligopeptide Antimetabolites) have prepared, in Chapter 2, a brief account defining, outlining detection methods for, and mechanism of action of antimetabolites. A tabulation of natural antimetabolites (source, structure, mechanism, and reversant) is included. The final chapter (The Chemistry of the Dioxygenases) by D. G. Brown presents a survey of the number of these interesting metalloenzymes which can oxidatively cleave aromatic rings. Some physical-chemical studies of various properties such as absorption, ESR, magnetic susceptibility, and Mössbauer spectroscopy are briefly presented.

Department of Biological Chemistry
Harvard Medical School
Boston, Massachusetts 02115

Barton Holmquist

Psychopharmacology, Sexual Disorders and Drug Abuse. Proceedings of the Symposia held at the VIIIth Congress of the Collegium Internationale Neuro-Psychopharmacologicum, Copenhagen. North-Holland Publishing Co., Amsterdam. 727 pp. \$38.00.

This volume represents a compilation of papers presented in the plenary sessions and symposia held at the VIIIth Congress of the Collegium Internationale Neuro-Psychopharmacologicum in Copenhagen (1972). It is organized into 12 sections, each section containing between 5 and 12 papers. Approximately 20% of the reports are written in French or German.

Although provocative, the title of this book is deceptive. Of the 12 sections in it, one is concerned with sexual disorders and one (on the psychopharmacology of Cannabis) with drug abuse. The remaining sections cover many less sensational topics ranging from "Metabolism of CNS Stimulating Drugs" to "Training Models in Psychopharmacology". Indeed, one of the features of this book is the diversity of topics covered. One can only wonder as to the significance of the title.

Again, within the section on sexual disorders, reality is something other than what the section title suggests (Drugs for Treatment of Sexual Disorders). The drug treatment of impotency is the concern of a single paper, while one other paper discusses the use of the androgen antagonist, cyproterone, in various hypersexual disorders. The remainder of this section deals primarily with the effects of manipulating various biogenic amines on the sexual behavior of rats and rabbits!

Implicit in the section on Cannabis is the concept of drug-induced behavioral toxicity. This is the "Catch-22" of behavioral pharmacology. In order for a drug to be nontoxic, it must not pro-

duce any behavioral effect. Since the drugs that are studied are known to be psychoactive, that is, they have effects on behavior, they must be toxic. So it is with marihuana. Reports in the literature on the adverse effects of marihuana abound. Four accounts of its "behavioral toxicity" are included in this section. Only one small paragraph is devoted to possible beneficial effects (e.g., in glaucoma, anorexia nervosa). Whether it is the availability of government funds, the general tendency of scientists to conform to social norms, or other factors that account for the preponderance of negative research with this and similar "drugs of abuse", this situation is damaging not only to the integrity of scientists but to the welfare of those who might benefit from the therapeutic effects of these drugs.

The strength of this book resides in the four sections dealing with schizophrenia and antipsychotic drugs. Two papers on tryptophan and *N*-methylation and their possible relationship to the etiology of this mental disorder are especially worthwhile. They do not, however, compensate for the generally uneven quality of the remaining papers.

Behavioral Pharmacology Laboratory
The Squibb Institute for Medical
Research
Princeton, New Jersey 08540

R. I. Schoenfeld

Advances in Neurology. Volume 9. Dopaminergic Mechanisms. Edited by D. Calne, T. N. Chase, and A. Barbeau. Raven Press, New York, N.Y. 1975. xvii + 427 pp. 15.5 × 24.5 cm. \$26.50.

A symposium was held in Neuilly, France, in May 1974, sponsored by the Institut de Recherches Servier to review recent progress in the study of dopaminergic mechanisms. This area of neuropharmacology is of significance in our understanding of parkinsonism where the dopamine receptors play an important part. It is becoming increasingly apparent that dopamine receptors in the CNS will also prove to be a valuable way of studying schizophrenia. The dopamine antagonist effect of neuroleptic drugs presents a hypothesis that serves to stimulate a considerable amount of interest. There are dopamine receptors far from the brain, in the kidney, which are of clinical significance for the treatment of certain forms of hypertension. This symposium explicitly excludes the topic of L-Dopa since it has been covered in a previous symposium (Volume 3 of this series) although reference is frequently made by several of the authors to the dopaminergic and clinical effects of this drug.

This monograph serves as a progress report by many of the same distinguished participants as in the previous symposium and is a collection of the 41 papers presented by morphologists, biochemists (including one medicinal chemist), pharmacologists, physiologists, and neurologists.

The first section of this volume considers the dopamine receptors—their morphology, biochemistry, and pharmacology. The discovery of dopamine-sensitive adenylate cyclase activity in regions of the CNS containing dopamine has stimulated a considerable amount of activity and has proved to be a valuable *in vitro* model for looking at the drug specificity of dopamine receptor sites in the CNS. The present state of morphologic knowledge of the nigrostriatal pathway is reviewed and it was pointed out that at least one of the postsynaptic striatal cells innervated by the nigrostriatal pathway may be a cholinergic interneuron. It also pointed out that the dopamine-containing neurons in the substantia nigra receive a massive GABA inhibitory input. It was suggested that the main transmitter function of dopamine in the striatum is probably inhibitory.

The second section of this volume is concerned with changes in dopaminergic sensitivity induced by denervation and drug administration. From many different lines of evidence it is pointed out that CNS dopamine-receptor mechanisms can show a phenomenon similar to the supersensitivity seen in peripheral autonomic or neuromuscular synapses on disuse. The third section discusses the dopamine antagonists, particularly the neuroleptics and antimuscarinic drugs. Chemically the DA receptor-blocking agents can be divided into three distinct groups: phenothiazine derivatives, butyrophenone derivatives, bulbocapnine, and a new drug butaclamol. Animals administered these agents as models of drug-induced parkinsonism in man are discussed.

The final section reviews the properties of dopamine agonists, stressing their effects on experimental systems and their current status as potential therapeutic agents in extrapyramidal disorders. There is currently available a range of animal models that are valid for the evaluation of anti-Parkinson drugs, particularly the behavioral model of rotational behavior in animals after unilateral lesions of the nigrostriatal pathway, the induction of stereotyped behavior in animals, and the reduction of tremor in monkeys with ventromedial tegmental lesions. Another possible model is based on the fact that dopaminergic pathways play a crucial role in the control of neuroendocrine functions in the basal hypothalamus which may offer in animal systems another useful model for investigating dopaminergic drugs. The clinical application of dopamine agonists is reviewed in this volume. The current emphasis appears to be limited to two specific chemical classes: apomorphine and the *N*-propyl derivative of apomorphine, and piribedil and combinations of these agonists with L-Dopa. The dopamine agonist activity of piribedil is an enigma in that according to what is known about dopamine receptors, this compound should not be an agonist even if one considers the possibility of the conversion of piribedil to its catechol metabolite S-584.

This monograph points out that current drugs that are being evaluated as dopamine receptor agonists are insufficiently specific to interact uniquely with the dopamine receptors. These highly specific sites recognize only those chemical moieties closely related to dopamine. The design and synthesis of novel and therapeutically beneficial dopamine agonists and antagonists that can surpass current drugs in their anti-parkinsonian effects is a clear challenge to the skill and ingenuity of medicinal chemists.

This volume suffers from a number of more or less serious errors which could have been avoided by more careful proofreading. An inadequate index is provided which is of little value in the location of specific information. Reference is made on p 368 to *N*-propylapomorphine (sic) conceivably referring to *N*-*n*-propylnorapomorphine. No literature citation could be found nor does this compound appear in the index. Although this collection of papers has its weak points, it presents reviews and current research on virtually all aspects of dopaminergic mechanisms. The fact that the material that appears in this volume is normally scattered through a variety of sources argues persuasively for the value of the book. There is ample food for thought for those chemists, pharmacologists, and clinicians actively engaged in this exciting area of research.

Department of Medicinal Chemistry and Pharmacology
College of Pharmacy and Allied Health Professions
Northeastern University
Boston, Massachusetts 02115

John L. Neumeayer

Basic Principles in Nucleic Acid Chemistry. Volume 2. Edited by Paul O. P. T'so with six contributors. Academic Press, New York, N.Y. 1974. xi + 519 pp. 15 × 23 cm.

This is Volume 2 of a comprehensive three-part treatise under the editorial leadership of Paul O. P. T'so, who once again contrib-

utes a major chapter of his own. Volume 1 was reviewed earlier [A. Rosowsky, *J. Med. Chem.*, 17, 1129 (1974)], and the present opus continues to uphold, and in some respects surpass, the excellent standard set by its predecessor.

The introductory chapter, and the one from which medicinal chemists are most likely to gain direct benefit, is entitled "Chemical Reactions of Polynucleotides and Nucleic Acids". In this chapter D. M. Brown provides a thorough and extremely lucid account of various electrophilic and nucleophilic substitution reactions to which the purine and pyrimidine bases of RNA and DNA may be subjected if one wishes to modify the structure of these polynucleotides, especially for conformational or other studies. Included are important reactions of DNA with assorted mutagenic and/or carcinogenic agents such as nitrosamines, polycyclic aromatic hydrocarbons, *N*-acetyl-2-acetamidofluorene (AAF), and alkylating agents. Chemical reactions that affect the internucleotide phosphate linkages are also considered, and there is an especially illuminating discussion of reactive small molecules (e.g., nitrous acid, acrylonitrile, nitrogen mustard, etc.) as tools for the elucidation of the tertiary structure in tRNA.

Chapter 2, by C. Allen Bush, will be of interest primarily to physical biochemists since it deals in a very technical way with the uv, CD, and ORD spectra of nucleosides, nucleotides, oligonucleotides, and polynucleotides. Even more difficult from a medicinal chemist's perspective is Chapter 3 by H. Eisenberg, entitled "Hydrodynamic and Thermodynamic Studies", which covers among other topics the influence of various cations on the stability of DNA and the effect of interaction with polycyclic aromatic hydrocarbons and heterocyclic dyes (including the antibiotic actinomycin D) on intrinsic viscosity. Chapter 4 by W. Bauer and J. Vinograd is devoted to circular DNA, a fascinating molecule whose novel properties have come to be recognized largely through the studies of the senior author and his associates during the past decade. A very welcome part of this chapter is a glossary of the arcane terminology used by workers in the circular DNA field to mystify the general reader ("closed duplex DNA," "open circular DNA," "singly open dimeric catenane", and many other marvelous beasts!).

The closing chapter by P. O. P. T'so, entitled "Dinucleoside Monophosphates, Dinucleosides, and Oligonucleotides", is the longest in the book, a panoramic survey of the structure and physical biochemistry of these compounds. Included is a wealth of material on stereochemical conformation from X-ray diffraction, nuclear magnetic resonance, and uv, ORD/CD, and fluorescence studies. Once again, as in T'so's chapter in Volume 1, there is likely to be some duplication of data presented elsewhere in the treatise, but the overlap is probably unavoidable and easily forgiven.

The overall quality of production is excellent, the figures and structures are clearly drawn, and there appear to be fewer errors than in Volume 1. A minor blemish which caught the Reviewer's eye is the equation at the bottom of page 46 which should give DMSO-Ac₂O rather than DMF-Ac₂O as the oxidant. On page 48, the species derived from compound 174 by breakage of the glycosidic bond is lacking a negative charge on N-1.

As the editor so enthusiastically proclaims in his Preface, "Onward to Volume 3"!

Sidney Farber Cancer Center
Boston, Massachusetts 02115

Andre Rosowsky