synthesized in 83% yield as described for the corresponding L-homolysine analog:[2] mp 229–231°; $R_f$(A) 0.60, $R_f$(B) 0.63; $[\alpha]^{25}D$ −45.3° (c 1, DMF).

**1-Deamino-8-L-homoarginine-vasopressin.** The protected nonapeptide (150 mg) was reduced with Na in liquid $NH_3$ and oxidized in dilute solution with 0.01 *M* $K_3Fe(CN)_6$ according to the procedure in ref 2. After passage through a short column (1 × 3.5 cm) of Dowex 1-X2 (200–400 mesh, acetate form), the solution was lyophilized; the residue (244 mg) was dissolved in 0.1 *M* AcOH (5 ml), applied to a column (1.4 × 86 cm) of Sephadex G-15, and eluted with the same solvent. The fractions corresponding to the main peak (104–153 ml) were freeze-dried to give 83 mg of impure product. After ion-exchange chromatography on SE-Sephadex C-25 using a linear gradient of 0.025–0.25 *M* $NH_4OAc$, pH 6.9, the main component, which was eluted at a concentration of 0.06 *M*, $R_f$(C) 0.51 (cellulose), was still accompanied by trace amounts of two impurities, $R_f$(C) 0.47 and 0.37. The lyophilized material (69 mg) was dissolved in 5 ml of the lower phase of the solvent system 0.2 *M* AcOH–pyridine–95% EtOH–*n*-BuOH (7:1:1:4)[20] and applied to a column (2.5 × 70 cm) of Sephadex G-25 (superfine) equilibrated with the lower phase. Elution was performed with the upper phase at a flow rate of 9.3 ml/hr. The fractions from 198 to 229 ml were combined, thus discarding a shoulder on the front edge of the main peak, and evaporated to dryness *in vacuo* at 25°. The evaporation was repeated twice after addition of absolute EtOH and the residue was dissolved in 0.2 *M* AcOH (3 ml) and chromatographed on Sephadex G-25 (superfine) (1.4 × 88 cm) in the same solvent. After lyophilization and drying *in vacuo*, the purified product weighed 22 mg. Rechromatography under the same conditions of the front part of the main peak in the partition purification and subsequent gel filtration on Sephadex G-25 afforded a further 19 mg of the same product. Single spots were obtained on thin-layer chromatograms on cellulose, $R_f$(C) 0.51, $R_f$(D) 0.68, and silica gel, $R_f$(D) 0.41. On paper electrophoresis at pH 6.46 (1.24 *M* pyridine–0.069 *M* AcOH) at 42 V/cm, 1-deamino-8-L-homoarginine-vasopressin moved toward the cathode as a single spot, 6.8 cm in 1.5 hr ($E_{arg}$ 0.32): $[\alpha]^{25}D$ −87.9° (*c* 0.5, 1 *M* AcOH); amino acid analysis, Tyr 0.96, Phe 1.01, Glu 1.00, Asp 0.99, Cys (as cysteic acid) 0.97, Pro 1.00, Har 1.01, Gly 0.99, $NH_3$ 3.05.

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# *Book Reviews*

**The Biological Role of the Clot Stabilizing Enzymes: Transglutaminase and Factor XIII. Volume 202.** Edited by K. Laki with 30 contributors. New York Academy of Sciences [*Ann. N. Y. Acad. Sci.*, **202**, 1 (1972)], New York, N. Y. 1972. 348 pp. 14.9 × 22.7 cm. $26.00.

The New York Academy of Sciences has published a monograph of the proceedings of a conference held by the Academy on November 18–19, 1971. The 30 papers presented cover the field of the clot-stabilizing enzymes as it stood at the end of 1971; both laboratory and clinical aspects have been considered. The term "transglutaminase" is used to describe all of the enzymes involved in clot stabilization. The 30 presentations are recorded under eight general headings. These include Part I, Clot-Stabilizing Enzymes and Their Precursors (fibrin-stabilizing factor system of blood plasma; synthesis site of factor XII); Part II, Mode of Transglutaminase Action (factor XIII biosynthesis and function; hepatic transglutaminase properties); Part III, Fibrin Cross-Linking Plasma Enzyme (fibrinogen molecular structure; structure in normal and factor XIII-deficient individuals; effects of stabilizing factor); Part IV, Structural Aspects of Fibrin Cross-Linking (factor XIII free human fibrinogen; acceptor cross-linking site titration; transglutaminase precursor structure; cross-links and heredity); Part V, Pathological Aspects of Cross-Link Enzymes (hereditary aspects of cross-linking and hemorrhagic disease; cross-link inhibitors); Part VI, Fibrin Cross-Linkage, Thrombosis and Atherosclerosis (effects of oral contraceptives, thrombosis, pregnancy and atherosclerosis on cross-linkage and stabilization); Part VII, Fibrin Cross-Linking Enzymes in Tissues (tissue comparisons of molecular properties and activities of enzymes from different sources); Part VIII, Tumor Growth, Fibrinolysis and Fibrin Stabilization (stabilizing factor inhibitors; evolutionary consideration of clotting factors; mammalian fibrin and fibrinogen carboxy terminal structure; clot degradation studies; polypeptide organization in cross-linking; inhibition of factor XIII: tumor growth/transglutaminase considerations). A short editor's introduction precedes the contents of the book.

All of the papers represent scholarly research presentations of clinical, chemical, and biochemical studies on the clot-stabilizing enzymes. The individual papers vary in length from 3 to 22 pages, are generally well documented, and contain graphic presentations of the current status of the knowledge of each enzyme or factor discussed. The papers have been written by researchers active in the particular field of review and contain considerable material of interest for those scientists concerned with specific biochemical or metabolic studies of these enzyme systems. Medicinal chemists intrigued with specific structural or biochemical considerations of the clot-stabilizing factors in normal and selected disease states should find many papers of interest in this monograph.

*College of Pharmacy*
*Division of Medicinal Chemistry*
*The Ohio State University*
*Columbus, Ohio 43210*
**Neil J. Lewis**

**Progress in Medicinal Chemistry. Volume 9.** Edited by G. P. Ellis and G. B. West with ten contributors. American Elsevier, New York, N. Y. 1973. 347 pp. 15.5 × 21.5 cm. $25.75.

This latest volume in the well-established series combines Parts I and II which were issued in limp covers during 1972; hence, the material in the combined volume reflects the state of the art some 3 or 4 years ago.

Chapter 1, "Naturally Occurring Antitumor Agents," is a compilation of chemical structures with a brief statement of antineoplastic test results and an occasional comment on some organic chemical aspect, not always obviously germane to the topic. While encyclopedic, the chapter does provide a brief overview of the topic. However, there is no discussion of the material nor is any attempt made to stimulate the reader's use of the textual material in design of new chemical entities.

Chapter 2, "Chromone-2- and -3-carboxylic Acids and Their Derivatives," seems to have been stimulated by the recent interest in cromoglycic acid. The authors' approach to the topic is reminiscent of Elderfield's "Heterocyclic Chemistry:" Nomenclature; Synthetic Methods; Spectral Properties; Chemical Reactions. However, the survey is well done and seems comprehensive and thorough. The final section on Biological Properties tends to brevity and almost seems an afterthought. Very little is presented in this section which would stimulate the medicinal chemist or pharmacologist with new ideas. The entire chapter is aimed at the "pure" organic chemist who has little interest in biologically active compounds, *per se*.

Chapter 3, "4-Oxopyranoazoles and 4-Oxopyranoazines," appears to be a brief extension of the previous chapter. The discussion, almost completely organic chemical, tends to be sketchy and incohesive. A few biological implications are suggested for selected compounds, but little of genuine value or utility is included.

Chapter 4, "Isotope Techniques in the Study of Drug Metabolism," provides a good general survey of the topic without any depth. It may be quite useful to the complete novice in the field, who wishes to gain a speaking knowledge. The chapter is short enough and is clearly enough written that it can be read in one evening.

Chapter 5, "The Pharmacotherapy of Parkinsonism," provides a survey of Parkinson's Disease: History; Etiology; Biochemistry; Clinical Aspects; Pharmacology; SAR; Drugs Used. An addendum reports some of the 1972 literature and, in general, the chapter is well documented. The author attempts to provide some food for thought for further research in drug design. This chapter seems to be among the more useful reviews on Parkinson's disease, among the many which have appeared in the recent past.

Chapter 6, "Adrenochrome and Related Compounds," provides a thorough chemical discussion of aminochromes in general and includes material on biosynthesis and metabolism and on physiological activity. The chapter is well written and well documented. The authors have attempted to relate chemistry to biological aspects, and the chapter should be useful to workers in this rather specialized, narrow field.

*College of Pharmacy*
*The University of Iowa*
*Iowa City, Iowa 52242*

**Joseph G. Cannon**

**Hormonal Proteins and Peptides. Volumes I and II.** Edited by Choh Hao Li with 13 contributors. Academic Press, New York, N. Y. 1973. Volume I, xi + 270 pp. $14.50. Volume II, xi + 292 pp. $17.50.

Detailed knowledge of the chemical nature of the protein and polypeptide hormones has grown at a rapid rate in recent years. Choh Hao Li, one of the major contributors to this development, has assembled a superb group of authors, each actively at the forefront of the field chosen for critical review. Their contributions provide an early glimpse of the common origins and structural and functional interrelationships presently emerging for these hormones, features which will be most likely completely defined during the coming decade.

Volume I focuses on a select group of the hormonal glycoproteins, noted for their difficulty of purification and characterization. Richard Winzler introduces the group with a brief, but admirably clear description of the known types of sugar–amino acid linkages, the nature of the biosynthesis of the oligosaccharide chain, and its role in the heterogeneity of the glycoproteins. Even this brief section defines challenging general problems, such as the need for a simple method for characterizing the N-glycosidic link between asparagine and *N*-acetylglucosamine. Chapters on the chemistry of thyrotropin (TSH) and human chorionic gonadotropin (HCG) and on the chemistry and biology of interstitial cell-stimulating hormone (ICSH or luteinizing hormone, LH) provide a valuable detailed comparison of these structurally interrelated hormones, including the intriguing problem of the biosynthetic origins of their biologically interchangable $\alpha$ subunits and the as yet undefined features of the structures of their $\beta$ subunits which impart biological specificity. These chapters by John Pierce, Harold Papkoff, Choh Hao Li, Om Bahl, and their collaborators contain details of isolation, purification, and characterization, which are not found elsewhere and which impress the reader with the rapidly changing level of understanding made possible by access to highly purified and characterized materials. Salvatore and Edelhoch provide an excellent review of the nature and biosynthesis of the thyroid iodoproteins. This chapter on thyroglobulin, as a glycoprotein composed of associated subunits, is a fitting companion to those on the gonadotropins and critically examines current knowledge and speculation of the reactions which lead to the formation of the thyroid hormones as components of the iodinated protein. The only major omission was a description of the probable nature of the reactions of the protein-bound iodotyrosines to form the iodothyronines.

In Volume II, J. Ramachandran presents a clear and detailed analysis of the structure–function relationships of adrenocorticotropin (ACTH). In addition to providing valuable insight into the nature of the active core sequence, this chapter points out the properties of the sequences which enhance or modify ACTH-like activity, particularly as these relate to an "anchoring sequence," to protection against enzymatic degradation, or to alteration of the steroidogenic properties, and enhancement of lipolytic or melanocyte stimulating effects. Recently revised sequences of human, porcine, ovine, and bovine ACTH also serve to demonstrate the ease of defining and maintaining erroneous peptide sequences and to further emphasize that full hormonal activity of synthetic peptides is not sufficient proof of a proposed structure.

Miklos Bodanszky presents a refreshing overall view of the history, progress, interrelationships, and future of the gastrointestinal peptide hormones, including speculations on possible roles for hydrophobic residues in the hormone–receptor interactions of secretin which will stimulate further physical, chemical, and synthetic studies. His analogy between the sequential appearance and function through a defined time period, of orchestral instruments and of the hormones of the gastrointestional tract, is representative of his entertaining, colorful, and imaginative style which added greatly to the pleasure of reading this volume.

The major work of Volume II is the definitive chapter on the solid-phase method of peptide synthesis by Johannes Meienhofer. This should be required reading for anyone who is planning to embark or who is well underway on a program of peptide hormone synthesis or for biologists who use synthetic peptides for their biological studies. It is a detailed, scholarly study which describes the strengths and weaknesses of both solid-phase and classical solution methods of peptide synthesis and which clearly defines the limitations of both methods at the current state of the art. This chapter is, without doubt, the best appraisal of the solid-phase method of peptide synthesis yet presented and one which will remain a model for those to come.

If the first two volumes are indicative of the future, this series belongs in the library of all those involved in peptide and protein chemistry, in endocrinology, and in anticipating a potential major new area of drug development in the control of hormone-related diseases.

*School of Pharmacy*
*University of California*
*San Francisco, California 94143*

**Eugene C. Jorgensen**