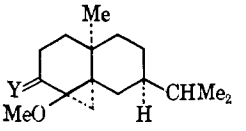
Wolff–Kishner reduction yielded the tricyclic ether VIb [80%; $[\alpha]^{21}D$ −55.6° (*c* 0.8, $CHCl_3$); infrared (neat): 3.30 μ (probably cyclopropyl H, w); pmr ($CDCl_3$): three-proton singlet at δ 3.25 (methoxyl), 0.91 (angular Me), six-proton doublet at 0.86 (J = 6.0 cps, isopropyl methyls), one-proton doublets at 0.30 and 0.16 (J = 5.0 cps, cyclopropyl methylene). *Anal.* Found: C, 81.49; H, 11.94]. Exposure of the latter to aqueous, methanolic hydrochloric acid afforded a quantitative yield of *l*-valeranone (I), identical in all respects with the natural plant product.[13]



VIa, Y = O
b, Y = H_2

(13) The authors are indebted to Dr. T. Takemoto (Tohoku University) for a gift of natural *l*-valeranone and to the National Science Foundation for partial support of this work.

(14) Public Health Service predoctoral fellow, 1965–.

Ernest Wenkert, David A. Berges[14]

Department of Chemistry, Indiana University
Bloomington, Indiana 47401

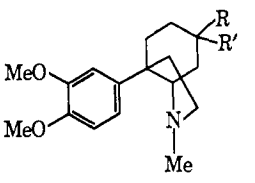
Received February 24, 1967

Biosynthesis of Mesembrine. The Incorporation of One-Carbon Units and the Origin of the C_6 Unit[1]

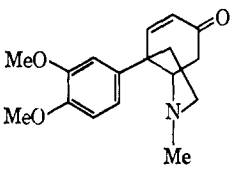
Sir:

The alkaloid mesembrine (**1**, R = R′ = O) along with several cogeners, mesembrinol (**1**, R = OH; R′ = H) and mesembrinine (**2**), occur in several plants of the *Aizoacea* family.[2] The biosynthesis of these alkaloids is of interest since the skeletal framework would appear to contain a C_6–C_2–N unit, which in the case of mesembrine is comprised of the cyclohexanone ring and the attached C_2–N bridge, and a C_6 unit represented by the aromatic ring. The presence of an isolated C_6 unit is an unusual structural feature, and its biosynthetic origin is therefore of interest. We report the results obtained which provide information on a precursor to this unit and also the results obtained from the incorporation of the label from methionine-S-methyl-C^{14} into mesembrine.

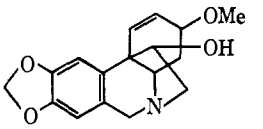
The labeled compounds were fed to *Sceletium strictum* L. Bol.,[3] and after periods ranging from 3 to 22 days the plants were harvested and the mesembrine isolated by using inactive mesembrine as a carrier. The results are summarized in Table I and are for mesembrine of constant activity. When the mesembrine derived



1



2



3

from the methionine feeding experiment was demethylated to give the activities for the O-methyl and N-methyl groups separately, the total activity was, within the limits of experimental error, the same as in the alkaloid. Furthermore, the ratio of the activities for the two methoxyls and the N-methyl group was 2:1. This suggests that each of these one-carbon sites makes an equal contribution to the total activity, in accordance with expectation for the result of a transmethylation process involving the S-methyl group of methionine.[4]

Table I. Incorporation of Radioactive Compounds into Mesembrine[a]

Precursor	Injected, μcuries	Isolation, days	Incorporation, %[b]
Methionine S-methyl-C^{14}	50	3	0.75
Tyrosine-3-C^{14}	50	10	0.051
Phenylalanine-2-C^{14}	50	10	<0.001
Phenylalanine [uniformly labeled in the ring with C^{14}]	50	22	0.059
	50	10	0.053

[a] Samples were counted on a Nuclear Chicago Unilux scintillation counter in toluene or dioxane–methanol–water scintillator solutions. [b] This figure may be regarded as a minimum since it was calculated on the basis of the weight of inactive mesembrine added to the plant extract.

These results were independently confirmed by the degradation of radioactive mesembrine to veratric acid and demethylation of the latter to protocatechuic acid. The relative activities of the products of the degradation sequence are shown in Table II.

Radioactive mesembrine derived from phenylalanine [C^{14}-ring labeled] was converted to veratric acid which was degraded further to protocatechuic acid. The relative activities of the degradation products indicate that the aromatic ring of phenylalanine is incorporated intact into the aromatic ring of mesembrine and that the label is restricted to this portion of the molecule. These results, when considered in conjunction with the results of the incorporation of radioactivity from tyrosine-3-C^{14} and the lack of activity in the mesem-

(1) Supported by National Science Foundation Grant GB-4361 and a grant-in-aid from Eli Lilly Co.

(2) A. Popelak, E. Haak, G. Lettenbauer, and H. Spengler, *Naturwissenschaften*, **47**, 150, 231 (1960); E. Smith, N. Hosansky, M. Shamma, and J. B. Moss, *Chem. Ind.* (London), 402 (1961); M. Shamma and H. Rodriguez, *Tetrahedron Letters*, 4847 (1965).

(3) We are indebted to Mr. H. Herre, Stellenbosch, South Africa, for supplying these rare botanicals, and to Mr. J. N. McQuay, Botany Department, Duke University, for invaluable help with their cultivation.

(4) See R. N. Gupta and I. D. Spenser, *Can. J. Chem.*, **43**, 133 (1965).

Table II. Relative Activities of Mesembrine and Its Degradation Products

	Methionine-S-methyl-C^{14}	Phenylalanine (C^{14}-ring labeled)
Mesembrine	1.00	1.00
Veratric acid	0.64	1.00
Protocatechuic acid	<0.01	1.01
Methoxyls[a]	0.58	...
	0.64[b]	
N-Methyl[a]	0.36	...

[a] The activity on the carbons of the methoxyls and the N-methyl group in mesembrine was determined by the Zeisel method in which the liberated methyl iodide was trapped as $(CH_3)_4NI$ and converted to the chloride on Dowex AG 1-X8 before counting. [b] Figure obtained from demethylation of veratric acid.

brine derived from phenylalanine-2-C^{14}, indicate (1) that phenylalanine is not converted to tyrosine before incorporation into mesembrine, (2) phenylalanine can serve as the precursor of the aromatic C_6 unit of the alkaloid, and (3) further suggest but do not prove that tyrosine may serve as a precursor of the C_6–C_2–N unit.[5]

The results on the incorporation of these precursors into mesembrine are reminiscent of those obtained for the *Amaryllidaceae* alkaloids of the structurally related crinane series; *cf.* haemanthamine (**3**).[6] Experiments to test the possibility that mesembrine is biosynthesized by a route which may be considered as an extension of that known to occur[7] in the crinane series are in hand.

(5) Degradation studies designed to determine the position of the label in the mesembrine derived from tyrosine-3-C^{14} which would establish this are in progress.

(6) A. R. Battersby, H. M. Fales, and W. C. Wildman, *J. Am. Chem. Soc.*, **83**, 4098 (1961); P. W. Jeffs, *Proc. Chem. Soc.*, 80 (1962); W. C. Wildman, H. M. Fales, and A. R. Battersby, *J. Am. Chem. Soc.*, **84**, 681 (1962); D. H. R. Barton, G. W. Kirby, J. B. Taylor, and G. M. Thomas, *J. Chem. Soc.*, 4545 (1963); R. J. Suhadolnik and J. Zulalian, *Proc. Chem. Soc.*, 216 (1963).

(7) For a summary, see A. R. Battersby, *ibid.*, 189 (1963); D. H. R. Barton, *ibid.*, 293 (1963).

(8) NSF Undergraduate Research Participant, 1964–1965.

(9) NASA Fellow, 1965 to present.

P. W. Jeffs, W. C. Archie,[8] D. S. Farrier[9]

Department of Chemistry, Duke University
Durham, North Carolina 27706

Received March 17, 1967

Book Reviews

Electrophilic Additions to Unsaturated Systems. By P. B. D. DE LA MARE, M.Sc. (New Zealand), D.Sc. (London), F.R.I.C. Professor of Chemistry, Bedford College, University of London, Regent's Park, London N.W.1, and R. BOLTON, B.Sc. (W. Australia), Ph.D. (Hull), Lecturer in Chemistry, Bedford College, University of London, Regent's Park, London, N.W.1. American Elsevier Publishing Co., 52 Vanderbilt Ave., New York, N. Y. 1966. x + 284 pp. 14.5 × 21.5 cm. $14.50.

There is a tremendous amount of useful information in this relatively small book, which is primarily concerned with acid-catalyzed additions to olefinic double bonds. The additions of electrophilic hydrogen (water, weak and strong acids), halogens, oxygen, sulfur, nitrogen, phosphorus, arsenic, and the elements of groups I–IV are covered in Chapters 3–10. In the last three chapters one finds a treatment of electrophilic additions to acetylenes and allenes (Chapter 11), conjugated double bonds and aromatic hydrocarbons (Chapter 12), multiple bonds between carbon and other atoms, and also the N=N and S=O double bonds (Chapter 13). The text is well written in a clear, uncomplicated manner. Although there is too much material covered to expect all of it to be presented critically, the authors do a good job of analyzing the validity of the results they review.

Books which contain discussions of so many isolated experiments often lack continuity, but Drs. de la Mare and Bolton somehow manage to avoid that pitfall. The only criticism I have to make is that Chapter 2, titled "The Chemistry of Carbonium Ions" (despite the claim on the dust jacket that it is an important chapter), could better have been omitted, for it is an attempt in 19 pages to review all other carbonium ion processes not included in electrophilic additions to unsaturated molecules. Such material has been so well covered elsewhere that it is unnecessary here, and, further, it cannot be adequately treated in so brief a manner.

The authors, however, have provided a gold mine of information for professors who give graduate courses in physical organic chemistry, because their effort has produced a competent and critical survey of a field which has not previously been well reviewed. This last fact alone is enough to make "Electrophilic Additions to Unsaturated Systems" a popular monograph, for it fills a glaring gap in the literature of carbonium ions.

Although the subject matter is probably too specialized to be of much use to the average undergraduate, most practicing organic chemists can profit by reading this book.

(1) Operated by the U. S. Atomic Energy Commission under contract with the Union Carbide Corp.

Clair J. Collins

Oak Ridge National Laboratory[1]
Oak Ridge, Tennessee
and University of Tennessee
Knoxville, Tennessee

The Peptides. Volume II. Synthesis, Occurrence, and Action of Biologically Active Polypeptides. By EBERHARD SCHRÖDER and KLAUS LÜBKE, Hauptlaboratorium der Schering AG, West Berlin, Germany. Translated by ERHARD GROSS, National Institutes of Health, Bethesda, Maryland. Academic Press Inc., 111 Fifth Ave., New York, N. Y. 1966. xxvii + 632 pp. 16 × 23 cm. $30.00.

This admirable book is a thorough, well-written compilation of information on biologically active peptides as it existed at the end of 1964. Together with the companion volume on synthesis, it will undoubtedly become the standard reference on peptides.

In common with most books designed to give a large amount of information in concise form, this book will not be exciting reading—

at least to the nonexpert. Its presentation is well organized, direct, and clear. The translation from the original German by Dr. E. Gross is excellent, and typographical errors are almost nonexistent.

The authors indicate in the Introduction that the book is written for the peptide chemist. Therefore, a critical comparison of different syntheses for a naturally occurring peptide could be expected, and indeed could be the most valuable contribution. Although some criticism is made, it is not enough. Take the example of oxytocin. The synthesis of this hormone by du Vigneaud and associates in 1953 is generally regarded as the first milestone in modern peptide synthesis. The importance of this synthesis is mentioned only in the Introduction. Reading on to the synthesis of oxytocin by Boissonnas and associates, we find a statement that their approach is more rational, but no reason is given why. Then, further on, the stepwise *p*-nitrophenyl ester synthesis by Bodanszky and du Vigneaud is given without any indication of its importance as the first significant synthesis by the now very popular active-ester approach.

There are many other places where the authors, who are well qualified by their own important contributions, could have given valuable critical appraisal as to the possibility of racemization, superiority of one synthesis over another in yields, etc. Generally speaking, the peptide chemist must still go back to the original literature for these comparisons, but Schröder and Lübke have given him a fine starting point.

This book will be useful to anyone interested in structure-activity relationships of peptides. Excellent tables for comparison are given; for instance, the table for oxytocin derivatives and analogs summarizes testing results on 67 compounds. The authors, of course, could only give results as reported in the literature, and, since biological testing results vary from one laboratory to another, absolute comparisons are not possible.

Since the peptide field is a broad one, including hormones, pressor and depressor substances, antibiotics, and even enzymes by an extension of the definition, it is unquestionably important. A few synthetic peptides are becoming available as drugs (oxytocin, angiotensin, ACTH derivatives), and undoubtedly there will be more. The work reported by Schröder and Lübke was mostly done in the past ten years, a testimony to improved methodology and increased interest. The next few years should bring even greater advances.

George W. Anderson

Organic Chemical Research Section, Lederle Laboratories
American Cyanamid Company, Pearl River, New York

Molecular Biology of Human Proteins with Special Reference to Plasma Proteins. Volume 1. Nature and Metabolism of Extracellular Proteins. By H. E. SCHULTZE, Formerly Scientific Director of the Behringwerke AG, Marburg/Lahn, Germany, and J. F. HEREMANS, Professor of Internal Medicine, University of Louvain, Belgium. American Elsevier Publishing Co., Inc., 52 Vanderbilt Ave., New York, N. Y. 1966. xii + 904 pp. 18 × 25 cm. $52.50.

The first of two volumes on "Molecular Biology of Human Proteins" is a veritable encyclopedia. It is extremely heavily documented, having over 5500 references, and will serve as an excellent starting point for becoming familiar with almost any aspect of the subject. A unique feature is a comprehensive large chart relating the sedimentation coefficients of the various serum proteins with their behavior on paper and starch gel electrophoresis and on immunoelectrophoresis, followed by a table listing 93 different proteins found in serum and 43 tables giving additional data on those which have been obtained in purified form. A general introduction to structure and molecular and genetic variation in proteins is followed by sections on analytical methods in protein chemistry, the data on the various serum proteins mentioned above, methods of fractionation, synthesis and turnover of plasma proteins, and exchange between mother and child. The final section contains 10 chapters on proteins of extravascular fluids including intestinal fluids, urine, cerebrospinal fluid, saliva, milk, and colostrum, etc.

Both authors have had extensive experience in working with serum proteins, and one finds useful critical comments in their presentation of the subject matter. As with all encyclopedic works it tends to be sketchy in some areas; for example, it is doubtful that one can learn much about the principle of electron spin resonance from the little more than a page devoted to it without consulting the references. A most objectionable feature is not the fault of the authors but of the publisher who used a very glossy paper so that one is constantly disturbed by reflection and glare while reading by artificial light. All in all the book is of great value and should be widely consulted.

Elvin A. Kabat

Department of Microbiology, Columbia University
New York, New York 10032

BOOKS RECEIVED, *March 1967*

U. W. ARNDT and B. T. M. WILLIS. "Single Crystal Diffractometry." Cambridge University Press, Cambridge, England. 1966. 331 pp. $15.00.

T. M. BIRSHTEIN and O. B. PTITSYN. "Conformations of Macromolecules." Interscience Publishers, John Wiley and Sons, Inc., 605 Third Ave., New York, N. Y. 1966. 350 pp. $14.50

MIKLOS BODANSZKY and MIGUEL A. ONDETTI. "Peptide Synthesis." Interscience Publishers, John Wiley and Sons, Inc., 605 Third Ave., New York, N. Y. 1966. 294 pp. $9.50.

RICHARD L. CARLIN, Editor. "Transition Metal Chemistry, A Series of Advances." Volume 2. Marcel Dekker, Inc., 95 Madison Ave., New York, N. Y. 1966. 350 pp. $14.75.

CHARLES B. COLBURN, Editor. "Developments in Inorganic Nitrogen Chemistry." Volume I. American Elsevier Publishing Co., Inc., 52 Vanderbilt Ave., New York, N. Y. 1966. 583 pp. $32.50.

RAOUL FELD and PETER L. COWE. "The Organic Chemistry of Titanium." Butterworth Inc., 7300 Pearl St., Washington, D. C. 1965. 213 pp. $9.95.

STANLEY K. FREEMAN, Editor. "Interpretive Spectroscopy." Reinhold Publishing Corp., 430 Park Ave., New York, N. Y. 1965. 295 pp. $17.50.

DAVID N. KENDALL, Editor. "Applied Infrared Spectroscopy." Reinhold Publishing Corp., 430 Park Ave., New York, N. Y. 1966. 560 pp. $23.00.

EDMUND YANOVICH LUKEVITS and MIKHAIL GRIGOR'EVICH VORONKOV. "Organic Insertion Reactions of Group IV Elements." Plenum Publishing Corp., 227 West 17th St., New York, N. Y. 1966. 413 pp. $25.00.

HENRY MCILWAIN. "Biochemistry and the Central Nervous System." Third Edition. Little, Brown and Co., 34 Beacon St., Boston, Mass. 1966. 412 pp. $18.00.

ROBERT L. MCINTOSH. "Dielectric Behavior of Physically Adsorbed Gases." Marcel Dekker, Inc., 95 Madison Ave., New York, N. Y. 1966. 160 pp. $9.75.

F. W. MCLAFFERTY. "Interpretation of Mass Spectra, An Introduction." W. A. Benjamin, Inc., 1 Park Ave., New York, N. Y. 1966. 229 pp. $9.00.

GEORGE H. NANCOLLAS. "Interactions in Electrolyte Solutions (Metal Complex and Ion-Pair Formation in Solution)." American Elsevier Publishing Co., Inc., 52 Vanderbilt Ave., New York, N. Y. 1966. 214 pp. $14.50.

HANS NEURATH, Editor. "The Proteins. Composition, Structure, and Function." Second Edition. Volume IV. Academic Press Inc., 111 Fifth Ave., New York, N. Y. 1966. 508 pp. $20.00.

WILLIAM A. PRYOR. "Free Radicals." McGraw-Hill Book Co., 330 West 42nd St., New York, N. Y. 1966. 354 pp. $12.00.

LEO REICH and A. SCHINDLER. "Polymerization by Organometallic Compounds." Interscience Publishers, John Wiley and Sons, Inc., 605 Third Ave., New York, N. Y. 1966. 740 pp. $25.00.

WARREN L. REYNOLDS and RUFUS W. LUMRY. "Mechanisms of Electron Transfer." The Ronald Press Co., 15 East 26th St., New York, N. Y. 1966. 175 pp. $9.00.

D. TER HAAR and H. WERGELAND. "Elements of Thermodynamics." Addison-Wesley Publishing Co., Inc., Reading, Mass. 1966. 160 pp. $9.75.

RICHARD H. TOURIN. "Spectroscopic Gas Temperature Measurement. Pyrometry of Hot Gases and Plasmas." American Elsevier Publishing Co., Inc., 52 Vanderbilt Ave., New York, N. Y. 1966. 139 pp. $10.75.

CHARLES WALTER. "Enzyme Kinetics. Open and Closed Systems." The Ronald Press Co., 15 East 26th St., New York, N. Y. 1966. 102 pp. $7.00.

D. H. WHIFFEN. "Spectroscopy." John Wiley and Sons, Inc., 605 Third Ave., New York, N. Y. 1966. 205 pp. $4.25.

A. H. WILSON. "Thermodynamics and Statistical Mechanics." Cambridge University Press, 32 East 57th St., New York, N. Y. 1966. 495 pp. $2.95.

H. ZEISS, P. J. WHEATLEY, and H. J. S. WINKLER. "Benzenoid-Metal Complexes. Structural Determinations and Chemistry." The Ronald Press Co., 15 East 26th St., New York, N. Y. 1966. 101 pp. $7.00.