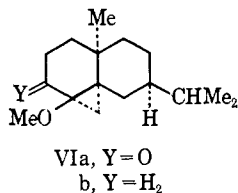


Wolff-Kishner reduction yielded the tricyclic ether VIb [80%;  $[\alpha]_D^{25} -55.6^\circ$  ( $c$  0.8,  $\text{CHCl}_3$ ); infrared (neat):  $3.30 \mu$  (probably cyclopropyl H, w); pmr ( $\text{CDCl}_3$ ): three-proton singlet at  $\delta$  3.25 (methoxyl), 0.91 (angular Me), six-proton doublet at 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.<sup>13</sup>



(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-.

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### Biosynthesis of Mesembrine. The Incorporation of One-Carbon Units and the Origin of the C<sub>6</sub> Unit<sup>1</sup>

Sir:

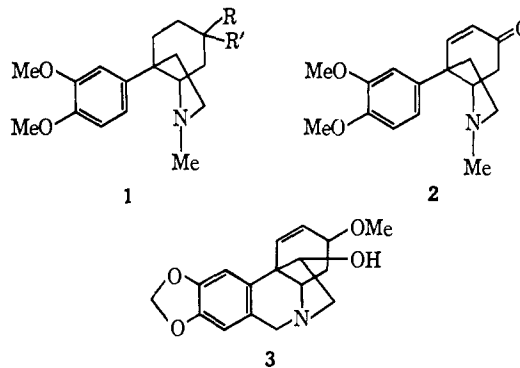
The alkaloid mesembrine (1, R = R' = O) along with several congeners, mesembrinol (1, R = OH; R' = H) and mesembrinine (2), occur in several plants of the *Aizoacea* family.<sup>2</sup> The biosynthesis of these alkaloids is of interest since the skeletal framework would appear to contain a C<sub>6</sub>-C<sub>2</sub>-N unit, which in the case of mesembrine is comprised of the cyclohexanone ring and the attached C<sub>2</sub>-N bridge, and a C<sub>6</sub> unit represented by the aromatic ring. The presence of an isolated C<sub>6</sub> 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<sup>14</sup> into mesembrine.

The labeled compounds were fed to *Sceletium strictum* L. Bol.,<sup>3</sup> 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) 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,



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

Table I. Incorporation of Radioactive Compounds into Mesembrine<sup>a</sup>

Precursor	In-jected, $\mu$ curies	Isolation, days	Incor-poration, % <sup>b</sup>
Methionine S-methyl-C <sup>14</sup>	50	3	0.75
Tyrosine-3-C <sup>14</sup>	50	10	0.051
Phenylalanine-2-C <sup>14</sup>	50	10	<0.001
Phenylalanine [uniformly labeled in the ring with C <sup>14</sup> ]	50	22	0.059
	50	10	0.053

<sup>a</sup> Samples were counted on a Nuclear Chicago Unilux scintillation counter in toluene or dioxane-methanol-water scintillator solutions. <sup>b</sup> 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.

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.<sup>4</sup>

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<sup>14</sup>-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<sup>14</sup> and the lack of activity in the mesem-

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 <sup>14</sup>	Phenylalanine (C <sup>14</sup> -ring labeled)
Mesembrine	1.00	1.00
Veratric acid	0.64	1.00
Protocatechuic acid	<0.01	1.01
Methoxyls <sup>a</sup>	0.58	...
	0.64 <sup>b</sup>	...
N-Methyl <sup>a</sup>	0.36	...

<sup>a</sup> 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<sub>3</sub>)<sub>4</sub>NI and converted to the chloride on Dowex AG 1-X8 before counting.

<sup>b</sup> Figure obtained from demethylation of veratric acid.

brine derived from phenylalanine-2-C<sup>14</sup>, indicate (1) that phenylalanine is not converted to tyrosine before incorporation into mesembrine, (2) phenylalanine can serve as the precursor of the aromatic C<sub>6</sub> unit of the alkaloid, and (3) further suggest but do not prove that

tyrosine may serve as a precursor of the C<sub>6</sub>-C<sub>2</sub>-N unit.<sup>5</sup>

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

(5) Degradation studies designed to determine the position of the label in the mesembrine derived from tyrosine-3-C<sup>14</sup> 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.

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## 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 chem-

istry, 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.

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**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—