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Received January 24, 1974.
Accepted for publication March 26, 1974.
Supported in part by research grants from Smith Kline and French Laboratories, Philadelphia, PA 19101, and by Sandoz-Wander, Inc., East Hanover, NJ 07936
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Alkaloids of *Lindera benzoin* (L.) Blume (Lauraceae) I: Isolation and Identification of Laurotetanine

Keyphrases □ Laurotetanine—isolation and identification from *L. benzoin* □ *Lindera benzoin* (L.) Blume (Lauraceae)—isolation and identification of laurotetanine

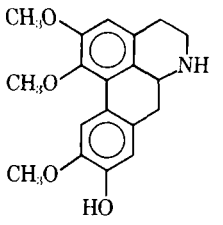
To the Editor:

The isolation of aporphine alkaloids from other *Lindera* species (1, 2) and the reported cytotoxic activity of certain aporphines (3, 4) led to this investigation of the native *Lindera benzoin* (L.) Blume (Lauraceae), known commonly as spicebush.

L. benzoin plants were collected locally[1]. The stems were separated from the leaves and roots, air dried, and ground for extraction. Preliminary TLC examination indicated one major and at least five minor nonquaternary alkaloids.

The stem material (36.3 kg) was defatted with *n*-hexane[2], and this alkaloid-free extract was reserved for further study. The defatted material was macerated and exhaustively extracted with methanol by percolation. The viscous residue (1.6 kg) remaining after removal of the methanol *in vacuo* at 40° was stirred with 0.1 *M* citric acid, vacuum distilled to remove the remaining traces of methanol, and filtered. The acid solution was alkalinized with ammonium hydroxide solution and extracted with chloroform. A phenolic fraction (38.5 g) and a nonphenolic fraction (4.0 g) were prepared from the chloroform solution by the method of Johns and Lamberton (5).

The dark-brown phenolic fraction was extracted with benzene to yield an orange benzene-soluble residue (23.5 g) which was found to contain the major alkaloid (I) by TLC [silica gel G, chloroform–methanol (9:1)]. A total of 0.4 g of I was separated from 0.6 g of the benzene-soluble phenolic residue by preparative



I

TLC [silica gel[3], chloroform–methanol (9:1)] and was further purified by precipitation from hot cyclohexane to yield a cream-colored amorphous precipitate (II) which failed to crystallize from the usual solvents. Compound II gave a single spot with several TLC solvent systems and $[\alpha]D^{25}$ + 94.6° (c 0.38 in ethanol). The mass spectrum showed the apparent molecular ion at *m/e* 327 (72%) followed by other prominent peaks at *m/e* 326 (100%), 312 (23), 310 (10), and 296 (16). The UV absorption spectrum showed λ_{max} (C_2H_5OH) 219 (log ε 4.51), 282 (4.2), and 304 (4.19) nm; λ_{max} (C_2H_5OH–NaOH) 232 and 329 nm; and λ_{min} (C_2H_5OH–NaOH) 270 nm.

The NMR spectrum run in deuterated chloroform, with tetramethylsilane as the internal standard, showed one aromatic proton at δ8.08, 6.61, and 6.08, three methoxyl protons at δ3.70, six methoxyl protons at δ3.91, and no *N*-methyl protons as shown by the absence of a signal at the δ2.5 region. The specific rotation (6), mass spectroscopy (7, 8), UV (9), and NMR (10) data suggested that II could be identified as the noraporphine alkaloid laurotetanine. The identification of II as laurotetanine was confirmed by co-TLC and by comparison of the IR, UV, and mass spectroscopy data with those derived from authentic laurotetanine. Furthermore, preparation of the *N*-methyl hydrobromide derivative of II furnished a crystalline product that gave melting points and IR, UV, and mass spectroscopy data in good agreement with those derived from authentic *N*-methyllaurotetanine hydrobromide.

This is the first report in the literature of the occurrence of laurotetanine in *L. benzoin*. The isolation and identification of other alkaloids from *L. benzoin* will be reported later.

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[1] The plants were collected in September 1972 at Oldwick, N.J., and a voucher specimen was deposited at the College of Pharmacy, Rutgers University.
[2] Skelly-B (bp 60–68°), Skelly Oil Co.
[3] PF-254, Brinkmann Instruments Inc., Westbury, N.Y.

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Received April 24, 1974.
Accepted for publication June 20, 1974.
The authors are grateful to Dr. M. Tomita of Kyoto College of Pharmacy, Kyoto, Japan, and to Dr. A. Rüegger of Sandoz Ltd., Basle, Switzerland, for generously supplying reference samples of laurotetanine and *N*-methyllaurotetanine hydrobromide, respectively.
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BOOKS

REVIEWS

A Guide to Molecular Pharmacology-Toxicology, Parts I and II. Edited by R. M. FEATHERSTONE. Dekker, 95 Madison Ave., New York, NY 10016, 1973. Part I, pp. 1-425; Part II, pp. 427-811. 16 × 24 cm. Price: Part I, $29.50; Part II, $27.75.

These two volumes consist of twenty-one chapters concerning a number of areas of what may be defined as molecular pharmacology-toxicology. Certainly, the emphasis in every chapter but one is quite heavily molecular. There is no apparent theme or continuity among the chapters which cover a number of topics including cell membranes, sugar transport, receptor isolation, analgesic and curare receptors, general anesthetics, conformational change, spectroscopic tools, quantum pharmacology, *etc.* Indeed the editor states that the book is intended as a guide, rather than a comprehensive map, to some areas of molecular pharmacology where the authors are actively working and to demonstrate to the reader how the systems discussed can generate information of general significance about big molecule-little molecule interactions. It would be generally agreed that it is a capital mistake for any scientist to confine his or her attention and reading to too narrow a span and there is a necessary role for essays and reviews that indicate the approaches and problems in near and distant fields.

The volumes in question contain a rather heterogeneous selection of essays with considerable variations in length, depth of treatment, and quality. Some chapters take the broad view and others are narrowly confining. Among the best chapters are those by Miller and Smith which present an admirably clear discussion of intermolecular forces and general anesthesia and by Shirachi, Chan, and Trevor on the isolation of pharmacological receptors both of which are very clear expositions taking care to outline the basic problems and the necessary background. More specialized chapters include that by Casy which is a most interesting review of analgesic structure-activity relationships and by Taylor and Kitz on the curare receptor and acetylcholinesterase, respectively, and by Martin, Rousseau, and Baxter on steroid hormones. Other chapters present fairly cursory surveys of NMR, ESR, ORD, and CD spectra and it is not apparent that they are likely to give much insight into the physical and intellectual power of these approaches. There is a certain amount of unnecessary overlap among the chapters—general anesthetic action is covered twice, curare receptors in three places, *etc.*

On the whole I think that the book is only partially successful in meeting its objectives. However, it is certainly worthy of general perusal and close reading of some chapters, but it is doubtful that many individuals will feel driven to purchase these volumes, the combination of uneven quality and high price likely proving an effective deterrent.

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Reference Values in Human Chemistry. Edited by N. G. SIEST. S. Karger AG, Medical and Scientific Publishers, Arnol-Bocklin-Strasse 25, CH-4011 Basel, Switzerland. 347 pp. 17 × 24.5 cm. Price $46.90. (Distributed in United States by Albert J. Phiebig, Inc., P. O. Box 352, White Plains, NY 10602).

This publication contains material presented at the Second International Conference on Automatization and Prospective Biology in October 1972. Information on usual values in clinical biochemistry and reference values in human physiological and pathological biochemistry is presented.

The general theme of two of the seven sessions was a detailed study of analytical, physiological intraindividual and interindividual variations of reference values, followed by a study of variations due to age, sex, tobacco, and climatic factors. Chemical parameters, *e.g.*, urea, glucose, and electrolytes, steroids, and plasmatic enzymes are discussed.

The effects of food intake and standard and particular diets are described in both healthy and hyperlipemic subjects.

An examination of drug interferences both from an analytical point of view as well as from physiological and pharmacological points of view is of particular interest.

Staff Review

Alcohol Intoxication and Withdrawal: Advances in Experimental Medicine and Biology, vol. 35. Edited by M. M. GROSS, Plenum, 227 West 17th St., New York, NY 10011, 1973. 422 pp. 17 × 25.5 cm. Price $24.00.

This volume is based upon the symposium entitled "Experimental Studies of Acute Alcohol Intoxication and Withdrawal," a part of the Proceedings of the 30th International Congress on Alcoholism and Addiction, held in Amsterdam, The Netherlands, in September 1972.

Alcoholism is a worldwide social and medical problem. Experimental research on alcoholic intoxication and withdrawal is presented in this publication, including investigations on the metabolic, psychological, and neurological impact of alcohol and alcoholism. Human and animal research into such areas as mechanisms of alcohol, tolerance and physical dependence, biochemical changes in response to alcohol, and disruption of sleep, memory, and psychological equilibrium caused by alcohol intake and withdrawal is covered.

Staff Review