affect the P^{32} label. In the case of II, the C^{14} label is in the active alkylating portion of the molecule and only its position is of interest.

Conclusion. From the work relating to the penetration of the CNS by organic boron compounds, the human biopsy studies with P^{32}-triethylenethiophosphoramide and these data it would appear that lipid solubility is a good criterion in determining whether a compound will enter the brain readily. However, in using cancer chemotherapeutic agents, the primary factor is whether the compounds are able to interfere with the neoplastic process in brain tumors. If such active materials are highly lipid soluble, it may be possible to modify this property by the introduction of hydrophilic groups. An investigation is currently underway to screen agents against this malignant ependymoma in C3H mice. Preliminary results have been reported.[16]

(16) R. N. Kjellberg, V. H. Mark, G. A. Austin, G. A. Bendixen, R. B. Ojemann, A. H. Soloway, R. S. Shaw, J. W. Raker, and W. S. Sweet, Harvey Cushing Society Meeting, Mexico City, April 17, 1961.

Constituents of Cocculus Leaeba DC—Correction for Mistaken Botanical Identity

A. V. SUBBARATNAM* and WILLIAM B. COOK

Department of Chemistry, Montana State College, Bozeman, Montana and Organic Chemistry Division, National Chemical Laboratory of India, Poone-8, India

Received September 5, 1962

In a previous communcation[1] we reported the isolation and characterization of allantoin, m.p. 236–237°, a bitter yellow crystalline substance, m.p. 279–286° (dec.) identical with aristolochic acid present in the Austrian variety of *Aristolochia clematitis*[2] and *Aristolochia indica*[3] of Indian origin, a small quantity of another bitter yellow crystalline substance, m.p. 245–250° (dec.) and a green viscous essential oil consisting mainly of a hydrocarbon, $C_{15}H_{24}$, b.p. 85–87°

* The Wilson Laboratories, 4221 S. Western Blvd., Chicago 9, Illinois.

(1) Presented before the Chemistry Section, at the 44th Indian Science Congress, Calcutta, January, 1957 (Abstract No. 3, Part IV) and I.U.P.A.C. Symposium on the Chemistry of Natural Products, Australia, 1960 (Abstract 50).

(2) M. Pailer, L. Belohlav, and E. Simonitsch, *Monatsh.*, **87**, 249 (1956).

(3) P. R. Krishnaswami, B. L. Manjunath, and S. J. Venkata Rao, *J. Ind. Chem. Soc.*, **12**, 476 (1935). See also (a) *ibid.*, **12**, 494 (1935), (b) **15**, 646 (1938), and (c) A. Somasekar Rao and M. S. Muthana, *J. Ind. Inst. Sci.*, **37**(*A*), 266 (1955).

TABLE I
TESTS WITH ARISTOLOCHIC ACID

	ED_{50}, mg./kg.
Hyperreflexia	115
Hypermotility	229
Straub-tail	501
Ataxia of gait	263
Death (24 hr.)	126

(0.6 mm.), and a pale yellow ketone, $C_{15}H_{24}O$, b.p. 135–136° (2.5 mm.), from the roots of *Cocculus leaeba DC*.[4a–f]

Identity of the product, m.p. 279–286° (dec.) with artistolochic acid was effected through derivatives and also by direct comparison of melting point, ultraviolet and infared spectra with both a sample of aristolochic acid from *A. clematitis*, kindly supplied by Prof. Pailer,[2] and aristolochic acid isolated by us from a fresh supply of the roots of *A. indica* obtained from the Ayurvedia Aushadi Bhandar, Bombay, India. The lower melting yellow crystalline substance, m.p. 245–250° (dec.), was lost in transit and could not be compared with nor-aristolochic acid of Pailer, *et al.*[2]

Kupchan and Doskotch,[5] in the course of a screening program for tumor inhibitors from plant sources, recently isolated aristolochic acid from the roots of *A. indica* gathered from Madras, India, and found it to be a good tumor inhibitor. Aristolochic acid obtained by us from the so-called roots of *Cocculus leaeba DC*, on intraperitoneal administration to mice in a series of experiments, gave results shown in Table I.

The roots of the so-called *Cocculus leaeba DC* used in our investigation were collected by (the late) Dr. S. Rajagopalan of Mandapam Camp, South India, in November of 1951. In a private communication, Prof. S. Morris Kupchan informed us that a first shipment of similar roots obtained by him from India from a collection of the associates of Dr. Rajagopalan were initially mistaken for *Cocculus leaeba DC*, but subsequent checking indicated the error and confirmed identity with *Aristolochia indica*. On his timely advice, we submitted for botanical verification both our samples of the mistaken *Cocculus*

(4) (a) "The Wealth of India, Raw Materials," Vol. II, B. N. Sastri, Ed., C.S.I.R., Delhi, 1950, p. 258; (b) R. N. Chopra, S. L. Nayar, and I. C. Chopra, "Glossary of Indian Medicinal Plants," C.S.I.R., New Delhi, 1956, p. 72; (c) A. K. Nadkarni, "Indian Materia Medica," Vol. I (Third Revised Edition), Popular and Dhootapapeshwar, Bombay, 1954, p. 360; (d) K. R. Kirtikar and B. D. Basu, "Indian Medicinal Plants," Vol. I, E. Blatter, S.J., J. F. Cauis, S.J., and K S. Mhaskar, Ed. (Second Revised Edition), Lalit Mohan Basu, Allahabad, India, 1933, p. 88; (e) J. F. Caius, S.J., *J. Bombay Nat. Hist. Soc.*, **40**, 85 (1938); (f) L. Beauquesne, *Bull. Sci. Pharmacol.*, **45**, 7 (1938).

(5) S. M. Kupchan and R. W. Doskotch, *J. Med. Pharm. Chem.*, **5**, 657 (1962).

leaeba and roots of *A. indica* supplied to us by the Ayurvedia Aushadi Bhandar, Bombay, India. The Wisconsin school has since kindly identified our samples as *A. indica*. Dean Heber W. Youngken, Jr., of the College of Pharmacy, University of Rhode Island, also has confirmed the identity of our samples as *A. indica* by comparison with an authentic sample of *A. indica* from the Harvard University Botanical Museum. Microscopic studies of the two samples reveal that both are from the same plant and tissues including starch granules and cellular components in both dried root samples seem to be identical. Dean Youngken has informed us that comparative pharmacognostic studies have not been concluded due to the non-availability of an authentic specimen of *Cocculus leaeba DC* and lack of sufficient information about it in the literature.

Acknowledgments.—We are indebted to Prof. S. Morris Kupchan, Dean Heber W. Youngken, Jr., and Prof. M. Pailer. We also thank Dr. Edward Pelican for pharmacological screening of aristolochic acid.

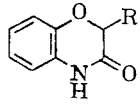
Some 2-Substituted 2H-1,4-Benzoxazin-3(4H)-ones

KEITH W. WHEELER

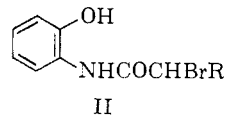
The Wm. S. Merrell Co. Division of Richardson-Merrell Inc., Cincinnati 15, Ohio

Received May 25, 1962

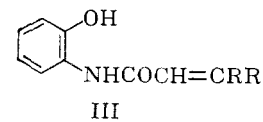
Although the heterocyclic system 2H-1,4-benzoxazin-3(4H)-one (I, R = H) has been known[1] since 1879, very few 2-substituted de-



I



II



III

rivatives of the ring system have been reported. The 2-methyl,[2] 2,2-dimethyl,[3] the 2-isopropyl and 2-isobutyl[4] and the 2-benzyl[5]

(1) P. Fritzche, *J. prakt. Chem.*, [2] **20**, 288 (1879).
(2) C. A. Bischoff, *Ber.*, **33**, 924 (1900).
(3) C. A. Bischoff, *ibid.*, **33**, 931 (1900).
(4) G. Sanna and A. Vacca, *Gazz. chim. ital.*, **62**, 555 (1932).
(5) J. D. Loudon and J. Ogg, *J. Chem. Soc.*, 739 (1955).