for microanalyses. We are indebted to Mr. William H. Washburn and his associates for the recording and interpretation of the infrared spectra. We also thank Mr. Victor E. Papendick for the measurement of the ultraviolet spectrum. Our thanks are expressed to Dr. Richard W. Mattoon and Mr. Russell Kriese for the recording of the n.m.r. spectra and for their assistance in making certain frequency assignments.

The Alkaloids of *Cephalotaxus drupacea* and *Cephalotaxus fortunei*

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A new alkaloid, cephalotaxine, $C_{18}H_{21}NO_4$, has been isolated from *Cephalotaxus fortunei* and *Cephalotaxus drupacea*, and a partial structure VIII–IX has been proposed for it.

The presence of alkaloids in *Cephalotaxus drupacea*,[2] *C. henryi*,[3] *C. wilsonia*,[4] and *C. fortunei*[5] has been demonstrated, but these alkaloids have not been chemically investigated. We now wish to report on the separation and partial identification of the major alkaloid of *Cephalotaxus fortunei* and *drupacea*.

Although the botanical classification of these plants is not yet clear, *Cephalotaxus* generally is listed as a genus of the family *Taxaceae* and a member of the *Taxeae*.[6] The Taxaceae belong to the order *Coniferae*. Many species have been listed for *Cephalotaxus*,[6-8] but the genus is now considered to contain only four pure ones: *C. pedunculata*, a native of Japan; *C. oliveri*, a Native of China; *C. drupacea;* and *C. fortunei*.[9] *C. drupacea*, a small tree which is found predominantly in China and Japan, is commonly known as Cow's Tail Pine or Japanese plum-yew. *C. fortunei*, known as the Chinese plum-yew, is found in North China.

The powdered leaves and stems of *C. fortunei* and *C. drupacea*[10] yielded 0.39% and 0.35%, respectively, of crude alkaloidal material by a conventional acid–base extraction of the concentrated alcohol extracts. A comparison of paper chromatograms indicated the presence of at least four different alkaloids in *C. fortunei* and at least five different alkaloids in *C. drupacea*. Alumina-column chromatography yielded one crystalline alkaloid from each species. The identity of these two alkaloids was established by a comparison of their infrared, ultraviolet, and n.m.r. spectra, as well as by the nondepression of their melting points when mixed with each other. This alkaloid which was named cephalotaxine, was present to the extent of 50 and 54%, respectively, in the crude alkaloidal mixtures of *C. fortunei* and *C. drupacea*.

The molecular formula of cephalotaxine, $C_{18}H_{21}NO_4$, was determined by duplicate analysis of two different samples recrystallized from two different solvents, and by a molecular weight determination in benzene. Cephalotaxine is moderately basic (pK_a 8.95) and is optically active ($[\alpha]^{25}D$ −204°). It does not contain a C–CH_3 or N–CH_3 grouping. The presence of one methoxyl grouping was established by a Zeisel methoxyl determination. The existence of an absorption peak in the infrared spectrum of the alkaloid at 3500 cm.$^{-1}$ (in chloroform) indicates the presence of a –NH or hydrogen bonded –OH function.[11] The alkaloid does not give a ferric chloride test, suggesting the absence of a phenolic hydroxyl group. Cephalotaxine can be acetylated to a monoacetyl derivative ($C_{20}H_{23}NO_5$), which is still basic (pK_a 7.97) and whose infrared spectrum is transparent in the 3200–3600-cm.$^{-1}$ region, while showing the expected absorption peak (1735 cm.$^{-1}$) for the acetyl function. The 3500-cm.$^{-1}$ peak is consequently due to one –OH group. Since this peak does not shift upon dilution, the hydrogen bonding must be *intramolecular*. The possibility that the acetylcephalotaxine arises by a molecular rearrangement was eliminated by the isolation of cephalotaxine from a lithium aluminum hydride reduction of the acetyl compound. The absence of any absorption peaks between 3200–3600 cm.$^{-1}$ in acetylcephalotaxine also excludes the possibility that the nitrogen atom in cephalotaxine is either primary or secondary. That it is not a secondary amine is further established by the negative test obtained with the nickel chloride–carbon disulfide reagent for secondary amines.[12]

The presence of a strong infrared absorption peak at 1650 cm.$^{-1}$ could indicate the presence of a —C=N— linkage.[11] This peak should be altered upon protonation of the nitrogen atom. The observation that this peak is still present in the perchlorate and hydrochloride salt of cephalotaxine permits one to eliminate this possibility. The nitrogen atom in cephalotaxine is consequently tertiary.

Some insight into the relative steric relationships between the nitrogen atom and the hydroxyl group is gained by the observation (see previous discussion) that the hydroxyl group is strongly hydrogen bonded and

(1) Participant of an National Science Foundation Undergraduate Research Participation Program Fellowship, 1962.

(2) T. Kariyone, M. Takahashi, A. Nitta, and Yoshinao Tsunehisa, *J. Pharm. Soc. Japan*, **76**, 611 (1956).

(3) M. E. Wall, *J. Am. Pharm. Assoc.*, **43**, 505 (1954).

(4) I. H. Y. Hsu, *J. Taiwan Pharm. Assoc.*, **9**, 5 (1957).

(5) Smith, Kline and French Laboratories, private communication.

(6) W. Dallimore and A. B. Jackson, "Handbook of Coniferae," Longmans Green and Co., New York, N. Y., 1923, pp. 20–23.

(7) C. Coltman-Rogers, "Conifers and Their Characteristics," The MacMillan Co., New York, N. Y., 1920, p. 239.

(8) L. H. Bailey, "The Cultivated Conifers," The Macmillan Co., New York, N. Y., 1933, p. 33.

(9) P. Greguss, "Identification of Living Gynosperms on the Basis of Xylotomy," Akademiai Kiado, Budapest, 1955, p. 84.

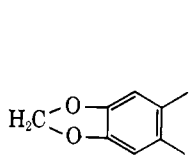
(10) We wish to express our gratitude to the Smith, Kline and French Laboratories of Philadelphia, Pa., for suggesting these plants to us as interesting, alkaloid-containing materials and for supplying us with the initial plant extracts and powdered plant materials.

(11) L. C. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1959.

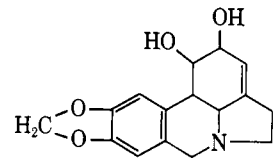
(12) W. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," Academic Press, Inc., New York, N. Y., 1955, p. 124.

by the substantial decrease in the basicity of the nitrogen atom (ΔpK_a 0.98) when the hydroxyl group is removed by acetylation. This suggests that the hydroxyl group might be located beta to the nitrogen or at least sterically close to it.[13]

Absorption peaks in the infrared region at 1037 cm.$^{-1}$ and at 934 cm.$^{-1}$ correspond to values reported[14] for the methylenedioxyphenyl grouping (1047–1034 and 939–930 cm.$^{-1}$). The presence of this functional grouping is further confirmed by a positive Labat[15] test. Wildman and Kaufman[16] have shown that alkaloids containing the 2,3-disubstituted methylenedioxyphenyl chromophore grouping (I) show very weak C=C stretching



I



II

absorption near 1600 cm.$^{-1}$. Cephalotaxine shows a weak band at 1625 cm.$^{-1}$ in agreement with the suggestion that it contains the chromophore grouping I. This further is confirmed by a comparison of the ultraviolet spectra of cephalotaxine and acetylcephalotaxine with the alkaloid lycorine (II) and its diacetylation product.[16]

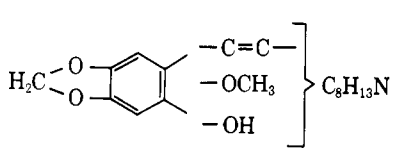
TABLE I

ULTRAVIOLET SPECTRA OF CEPHALOTAXINE AND LYCORINE AND SOME OF THEIR DERIVATIVES

Name	λ_{max} (log ϵ)	λ_{min} (log ϵ)	λ_{max} (log ϵ)
Lycorine	290 (3.65)	255 (2.52)	238 (3.55)
Cephalotaxine	290 (3.55)	260 (2.79)	238 (3.56)
Acetylcephalotaxine	290 (3.63)	260 (2.79)	238 (3.57)
Diacetylycorine	290 (3.66)	258 (2.52)	238 (3.52)

The table clearly shows that the spectra of all of these alkaloids are nearly superimposable. Unsaturation is indicated by the fact that cephalotaxine and acetylcephalotaxine add bromine in carbon tetrachloride and decolorize an aqueous potassium permanganate solution. The infrared spectrum of cephalotaxine also confirms the presence of a double bond by the presence of a strong peak at 1653 cm.$^{-1}$, indicative of the C=C stretching frequency of a modified (*vide infra*) double bond.[11]

The evidence described in the previous discussion permits the assignment of the following partial formula to cephalotaxine.



The n.m.r. spectra of cephalotaxine and of acetylcephalotaxine (Table II) in deuteriochloroform confirm and extend this partial formula.

(13) E. A. Braude and F. C. Nachod, Ed., "The Determination of Organic Structures by Physical Methods," Academic Press, Inc., New York, N. Y., 1955, p. 654.

(14) W. C. Wildman and C. J. Kaufman, *J. Am. Chem. Soc.*, **77**, 1248 (1955).

(15) J. A. Labat, *Bull. soc. chim. biol.*, **15**, 1344 (1932).

(16) W. C. Wildman and C. J. Kaufman, *J. Am. Chem. Soc.*, **77**, 4807 (1955).

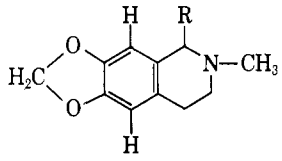
TABLE II

N.M.R. SPECTRA OF CEPHALOTAXINE AND OF ACETYLCEPHALOTAXINE

Cephalotaxine[a]				Acetylcephalotaxine			
δ (p.p.m.)	Multiplicity	J (c.p.s.)	No. of hydrogens	δ (p.p.m.)	Multiplicity	J (c.p.s.)	No. of hydrogens
6.63	1	..	1	6.56	1	..	1
6.60	1	..	1	6.53	1	..	1
5.90	1	..	2	5.82	1	..	2
4.85	1	..	1	5.76	2	9	1
4.71	2	9	1	5.02	1	..	1
3.67	1	..	3	3.75	2	9	1
3.62	2	9	1	3.68	1	..	3

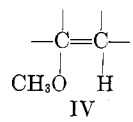
[a] The addition of deuterium oxide did not visibly alter the spectrum. This further shows the hydrogen-bonded nature of the hydroxyl group.

The two aromatic hydrogens in cephalotaxine appear as two one-proton singlets at 6.63 and 6.60 δ, respectively, while the two methylenedioxy protons are evident as a two-proton singlet at 5.90 δ. These assignments find confirmation by a comparison with the n.m.r. spectrum of the alkaloid hydrastine, whose partial structure is shown (III).



III

The methylenedioxy protons in hydrastine absorb at 5.88 δ while the two aromatic protons appear at 6.38 and at 6.57 δ, respectively. Cephalotaxine further shows a one-proton singlet at (4.85 δ), which is identified as an olefinic hydrogen, thus confirming the presence of a nonaromatic —C=C— linkage in the alkaloid. The three protons of the methoxyl group absorb at 3.67 δ. The position of these protons indicate a substantial amount of deshielding, as is observed in aromatic methoxyl groups (the methoxyl group of *p*-methyl anisole absorbs at 3.75 δ, for example). We have, however, demonstrated by ultraviolet, infrared, and n.m.r. spectra that the chromophore grouping I is present in cephalotaxine. The possibility that a second aromatic ring, totally substituted (since only two aromatic hydrogens are present in the molecule), is present in cephalotaxine is excluded not only by its ultraviolet spectrum, but also by the carbon to hydrogen ratio of the alkaloid. The methoxyl group, therefore, must be substituted on the double bond (IV). This structural feature is also consistent with the strong 1653-cm.$^{-1}$ peak in the infrared spectrum of cephalotaxine.

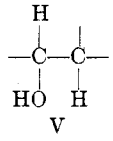


IV

That cephalotaxine indeed does contain a vinyl ether function is further demonstrated by the mild acid hydrolysis of the alkaloid. This reaction yields a compound which shows a strong infrared absorption peak at 1708 cm.$^{-1}$, typical of a carbonyl grouping. As expected, the 1653-cm.$^{-1}$ vinyl ether peak of cephalotaxine is no longer present in this compound. Un-

fortunately, we have not yet succeeded in obtaining this material in its crystalline state, even though it appears to be pure by paper chromatography. In this connection, it is of interest to note that this hydrolysis product gives a positive ferric chloride test. Until an elemental analysis of this compound becomes available, this test cannot be interpreted satisfactorily, since the methylenedioxy phenyl grouping appears to be intact (the infrared peaks ascribed to this group are still present).

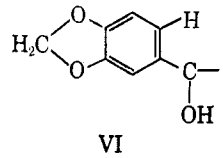
The n.m.r. spectrum of cephalotaxine also shows two one-proton doublets (J = 9 c.p.s.) centered at 4.71 and at 3.62 δ, respectively. These two coupled protons are assigned the structure V on the basis of the following results.



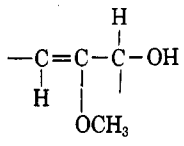
V

It is well established[17] that acetylation of a secondary hydroxyl group causes a paramagnetic shift of 1.0–1.5 p.p.m. of the proton alpha to the hydroxyl group. The n.m.r. spectrum of acetylcephalotaxine in deuteriochloroform reflects this shift. The low field doublet at 4.71 δ is shifted to 5.76 δ (J = 9 c.p.s.), for a paramagnetic shift of 1.05 p.p.m. This shift establishes that the hydroxyl group in cephalotaxine is secondary.

The 4.71-δ absorption peak in cephalotaxine assigned to the proton alpha to the hydroxyl group must be further deshielded. This deshielding could be due to either the adjacency of the phenyl ring (VI) [the hydrogen alpha to the hydroxyl group in α-(4-fluorophenyl)-ethanol absorbs at 4.75 δ] or due to the proximity of the olefin linkage (VII).



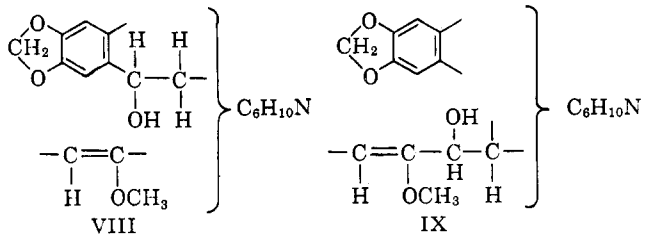
VI



VII

Experiments are under way to differentiate between these two possible allyl alcohols.

The partial structure of cephalotaxine can now be summarized by the expressions VIII or IX.



VIII IX

Experimental[18a]

R_f Values of Crude Alkaloidal Extracts.—Paper sheet chromatography of the concentrated alcoholic extracts of *C. fortunei* and *C. drupacea* gave the following values with a 50:50:20:80 *t*-amyl alcohol–isoamyl alcohol–88% formic acid–water solvent mixture: *C. fortunei*, 0.26, 0.35, 0.46, 0.55; *C. drupacea*, 0.16, 0.27, 0.39, 0.47, 0.57. The developing reagent was an aqueous potassium iodoplatinate solution.

Isolation of Crude Alkaloids from *C. drupacea*.—An 11.25-kg. portion of the powdered leaves and stems of *C. drupacea* was allowed to stand in 43 l. of absolute ethanol for 24 hr. The alcoholic extract was then flash evaporated to a volume of 2 l. and acidified with 2 l. of 6% aqueous tartaric acid. The acidic solution was filtered and the filtrate was extracted with three 1-l. portions of ether. The combined ether extracts were washed with 0.5 l. of 5% aqueous hydrochloric acid. The aqueous layer, combined with the hydrochloric acid extract, was made basic with concentrated ammonium hydroxide and extracted with three 1-l. portions of chloroform. The dried (over anhydrous sodium carbonate) chloroform extracts were evaporated to dryness *in vacuo* and yielded 10.70 g. of brown amorphous material. Two further extractions of the plant residue, using the same procedure, yielded an additional 18.66 and 9.72 g., respectively, of crude alkaloidal material. The total yield of crude alkaloid based on dried plant was 0.35%.

Isolation of Cephalotaxine from *C. drupacea*.—A solution of 10.708 g. of crude alkaloidal material in chloroform was chromatographed on 500 g. of grade III (Brockman scale) neutral alumina (Arthur H. Thomas C.). Elution with 100 ml. of hexane, followed by 300 ml. of 50% benzene–hexane, and 100 ml. of benzene, yielded no material. Elution with 100 ml. of 50% ether–benzene gave fractions containing a trace mixture of two alkaloids (R_f 0.45, 0.52). Elution with 800 ml. of ether yielded 5.793 g. of pure crystalline alkaloid, giving a single spot on paper chromatograms (R_f 0.35). The alkaloid, named cephalotaxine, was recrystallized from benzene, m.p. 131–132°. The melting point was not altered by further recrystallizations. Elution of the column consecutively with 250 ml. of a 50% mixture of ethyl–ethyl acetate, 800 ml. of ethyl acetate, 300 ml. of 50% ethyl acetate–ethanol, and 300 ml. of ethanol afforded two minor alkaloids (one of which had an R_f value of 0.42; the other, R_f 0.6, did not give a spot with potassium iodoplatinate). The total weight of all of the eluted material was 7.5339 g.

Cephalotaxine, m.p. 131–132°; pK_a (95% ethanol) 8.95; $[\alpha]^{25}D$ −204° (c 1.8, chloroform); ultraviolet spectrum (95% ethanol): λ_{max} 290 (log ϵ 3.55); λ_{min} 260 (log ϵ 2.79); λ_{max} 238 (log ϵ 3.56). The infrared spectrum of this alkaloid (chloroform solution) has the following major peaks (parenthesis indicates % transmission): 3500 cm.$^{-1}$ (25%), 1650 cm.$^{-1}$ (20%), 1520 cm.$^{-1}$ (24%), 1490 cm.$^{-1}$ (12%), 1360 cm.$^{-1}$ (23%), 1340 cm.$^{-1}$ (20%), 934 cm.$^{-1}$ (32%).

A sample was prepared for elemental analysis by recrystallizing a portion of cephalotaxine from ether to yield star-shaped crystals, m.p. 131–132°.

Anal. Calcd. for $C_{18}H_{21}NO_4$: C, 68.5; H, 6.72; N, 4.44; O 20.3; $-OCH_3$, 9.84; mol. wt., 315. Found: C, 68.5; H, 6.90; N, 4.34; O (by difference), 20.2; $-OCH_3$, 10.01; mol. wt. (camphor), 305; neut. equiv., 333.

A portion of the previous sample was recrystallized from benzene to yield cephalotaxine of the same melting point (131–132°).

Anal. Calcd. for $C_{18}H_{21}NO_4$: C, 68.5; H, 6.72; N, 4.44; O, 20.3. Found: C, 68.45; H, 6.85; N, 4.59; O (by difference), 20.11.

Cephalotaxine decolorized bromine in carbon tetrachloride and an aqueous solution of potassium permanganate, but it did not give a positive ferric chloride test. The alkaloid, when mulled with concentrated sulfuric acid, gave a red color which turned to deep purple. On dilution with water, the solution became green.[18b] A dilute solution of cephalotaxine in 2% hydrochloric acid did not give a precipitate with a nickel chloride–carbon disulfide solution.

Preparation of Cephalotaxine Hydrochloride and Cephalotaxine Perchlorate.—One drop of dilute hydrochloric acid was added to a solution of 45 mg. of cephalotaxine in 0.5 ml. of ethanol. The addition of 2 drops of ether to this solution precipitated 42 mg. of crystalline B·HCl (m.p. 174–177°, 188° dec.) from ethanol–ether. Cephalotaxine perchlorate was similarly prepared, m.p. 213–216° dec. The infrared spectra of these salts (potassium bromide mull) were compared with cephalotaxine and both showed the infrared peak at 1650 cm.$^{-1}$.

(17) L. M. Jackman, "Application of Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, New York, N. Y., 1959, p. 55.

(18) (a) Analyses were made by Galbraith Laboratories, Inc., Knoxville, Tenn., and by George I. Robertson, Jr., Florham Park, N. J. All infrared spectra were obtained using a Perkin-Elmer Model 21 infrared spectrophotometer. Ultraviolet spectra were recorded on a Cary Model 12 spectrophotometer. The n.m.r. spectra were recorded with a Varian A-60 proton resonance spectrometer. The paper chromatograms were obtained on Whatman no. 1 paper employing the descending technique. All melting points are uncorrected. (b) It is interesting to note that this behavior is typical of the amaryllidacea alkaloids.

Isolation of Cephalotaxine from *C. Fortunei*.—Following the procedure previously described for *C. drupacea*, an alcoholic extract of 0.342 kg. of the powdered leaves and stems of *C. fortunei* yielded 1.320 g., 0.39% of crude alkaloidal material. Chromatography of 1.25 g. of this material on alumina yielded 659 mg. of pure crystalline alkaloid (R_f 0.35, m.p. 130–132°). The infrared spectrum of this alkaloid was superimposable upon that of cephalotaxine. A mixture melting point of the two alkaloids was not depressed.

Acetylcephalotaxine.—A solution of 1.0432 g. of cephalotaxine in 8 ml. of acetic anhydride was heated under reflux for 1 hr. The resulting brown solution was evaporated to dryness, leaving the resulting brown oil which was dissolved in chloroform and chromatographed on 50 g. of grade II (Brockman scale) neutral alumina (Arthur H. Thomas Co.). Elution with 100 ml. of ether gave 0.9781 g. of crystalline material (R_f with respect to cephalotaxine, 2.1). The material was recrystallized from ether, m.p. 140–142°. This melting point was not altered by two subsequent recrystallizations. The infrared spectrum of this compond had new absorption peaks at 1735 cm.$^{-1}$ and 1240 cm.$^{-1}$, typical for an acetate, but lacked peaks in the region 3700–3500 cm.$^{-1}$ ascribable to hydroxyl groupings.[10] A portion of the alkaloidal material was prepared for elemental analysis by recrystallization from ether.

Anal. Calcd. for $C_{20}H_{23}NO_5$: C, 67.2; H, 6.45; N, 3.92; O, 22.4; mol. wt., 357. Found: C, 67.3; H, 6.65; N, 3.81; O (by difference), 21.7; mol. wt. in benzene, 356.

Acetylcephalotaxine, m.p. 140–142°; $[\alpha]^{25}D$ −97 (*c* 2.2, chloroform); pK_a 7.97 (95% ethanol). Acetylcephalotaxine decolorized an aqueous solution of potassium permanganate, as well as a solution of bromine in carbon tetrachloride.

Reduction of Acetylcephalotaxine with Lithium Aluminum Hydride.—A solution of 28.7 mg. (0.0804 mmole) of acetylcephalotaxine in 20 ml. of ether was refluxed in the presence of 82.2 mg. of lithium aluminum hydride, for 4 hr. The excess hydride was then decomposed by the slow addition of 1 ml. of water. The resulting emulsion was broken by the addition of 30 ml. of additional ether and the ether layer was collected. The dried ether extract (over anhydrous sodium carbonate) was then evaporated to dryness, leaving 21.8 mg. of a white crystalline solid, whose melting point (131–132°) was not depressed when mixed with cephalotaxine. The infrared spectrum of this compound was superimposable upon that of cephalotaxine.

Acid Hydrolysis of Cephalotaxine.—A solution of 70.3 mg. of cephalotaxine in 1.5 ml. of 1 *N* sulfuric acid was allowed to stand at room temperature for 18 hr. The yellow solution was then made basic by addition of 3.0 ml. of an aqueous sodium bicarbonate solution, and the basic solution was extracted with three 5-ml. portions of chloroform. The dried (over anhydrous sodium carbonate), combined extracts were evaporated to dryness under reduced pressure, leaving 61.0 mg. of white amorphous material. This compound gave a positive ferric chloride test. The infrared spectrum indicates the presence of a carbonyl function (1705 cm.$^{-1}$). A paper chromatogram showed the presence of a trace cephalotaxine (R_f 0.54) and of another alkaloidal constituent (R_f 0.37).

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The Alkaloids of *Hunteria eburnea* Pichon. III.[1] The Tertiary Bases

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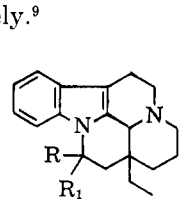
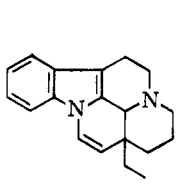
Received March 25, 1963

The isolation of nine tertiary bases from *Hunteria eburnea* Pichon is described. Eburnamine (I), isoeburnamine (II), eburnamonine (III), and eburnamenine (IV) are the first members of a new class of pentacyclic indole alkaloids. A new variant of the yohimbinoid ring skeleton is found in burnamicine (VI). Of the remaining alkaloids the indolines pleiocarpine (V) and pleiocarpamine are known compounds, while burnamine, an indoline with an echitamine type ultraviolet absorption spectrum, and neburnamine, an indole, are new compounds.

In the course of investigating extracts of *Hunteria eburnea* Pichon (Apocynaceae) for hypotensive principles,[2] a total of nine alkaloids were isolated from the tertiary base containing fraction.[3] The elucidation and synthesis of the structures of four of these, eburnamine (I),[4] isoeburnamine (II), eburnamonine (III), and eburnamenine (IV), a new class of pentacyclic indole alkaloids, were reported previously.[5] Two others, pleiocarpine (V, R_1 = $COOCH_3$, R_2 = H_2)[6,7] and pleiocarpamine,[6,8] also isolated from both *Pleiocarpa tubicina* and *Hunteria eburnea*[6] were readily recognized. The remaining three, burnamine, burnamicine, and neburnamine, were not available in sufficient amounts for complete structural determination by chemical methods, although preliminary investigation of the former alkaloid proved it to have very interesting properties (*vide infra*). A structure (VI) was proposed for burnamicine, mainly on the basis of its mass spectrogram, the details of which were published separately.[9]



I, R = H, R_1 = OH
II, R = OH, R_1 = H
III, R, R_1 = O



IV

(1) Previous paper, M. F. Bartlett, B. Korzun, R. Sklar, A. F. Smith, and W. I. Taylor, *J. Org. Chem.*, **28**, 1445 (1963).

(2)(a) Raymond-Hamet, *Compt. rend.*, **240**, 1470 (1955); (b) A. Engelhardt and H. Gelbrecht, *Naturwissenschaften*, **45**, 547 (1958); (c) A. Engelhardt and H. Gelbrecht, *Arzneimittel-Forsch.*, **11**, 414 (1961).

(3) A tenth tertiary base was isolated among the quaternary bases, ref. 1.

(4) Eburnamine and neburnamine were first isolated in trace amounts from a chromatogram of the total bases by D. F. Dickel.

(5) M. F. Bartlett, W. I. Taylor, and Raymond-Hamet, *Compt. rend.*, **249**, 1259 (1959); M. F. Bartlett and W. I. Taylor, *Tetrahedron Letters*, No. **20** 20, (1959); M. F. Bartlett and W. I. Taylor, *J. Am. Chem. Soc.*, **82**, 5941 (1960).

(6) W. G. Kump and H. Schmid, *Helv. Chim. Acta*, **44**, 1503 (1961). According to a paper chromatographic assay, our pleiocarpine contains a little pleiocarpinine (V, R_1 = CH_3, R_2 = H_2; W. G. Kump and H. Schmid, personal communication). These authors also isolated eburnamenine (IV) from *Pleiocarpa mutica*. Eburnamenine was found recently in two other plants, *Rhazya stricta* and *Aspidosperma quebracho*, eburnamonine also being recognized in the former [H. K. Schnoes, A. L. Burlingame, and K. Biemann, *Tetrahedron Letters*, 993 (1962)].

(7) W. G. Kump, D. J. Le Count, A. R. Battersby, and H. Schmid, *Helv. Chim. Acta*, **45**, 854 (1962).

(8) This compound has also been recognized as a product of the acid-catalyzed fission of villalstonine (B. S. Joshi and W. I. Taylor, unpublished observations).

(9) M. F. Bartlett and W. I. Taylor, *J. Am. Chem. Soc.*, **85**, 1203 (1963).