Tetrahedron, 1958, Vol. 2, pp. 173–182. Pergamon Press Ltd., London

ALKALOIDS FROM *STEMMADENIA* SPECIES—I*

THE ALKALOIDS OF *S. Donnell-Smithii* AND *S. Galeottiana* †

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(*Received* 29 *November* 1957)

Abstract—From *Stemmadenia Donnell-Smithii* and *S. Galeottiana*, the following new alkaloids were isolated: (+)-quebrachamine (IV), an optical isomer of the known (−)-quebrachamine; *iso*voacangine (IIIa), a position isomer of voacangine, and stemmadenine. In addition, the following known alkaloids were also found: voacangine (Ia), voacamine, tabernanthine (IIIb) and ibogamine.

IN view of the great current interest in alkaloids of the *Apocynaceae* family, we undertook a study of some species of the genus *Stemmadenia* belonging to the same family.

We wish to report here the results obtained with *Stemmadenia Donnell-Smithii* and *S. Galeottiana*, two species growing in the tropical jungle of Mexico. The two were collected by the authors§ in the State of Veracruz and represent trees 5–10 m high.

Stemmadenia Donnell-Smithii (Rose) Woodson

From this tree the following alkaloids were obtained:

Voacangine (Ia), described by Janot and Goutarel,[1] who first isolated it from *Voacanga africana;* its structure was established by Taylor.[2]

(+)-*Quebrachamine*, an optical isomer of the well-known quebrachamine, showing the same constants and empirical formula but with the opposite rotation. The proof that it is the mirror image was obtained by determination of the optical rotation dispersion, as shown in Fig. 1. By mixing equal amounts of the two isomers and crystallising them from alcohol, the pure racemate was obtained. We propose, therefore, the name (+)-*quebrachamine* for our isomer and the name (−)-*quebrachamine* for the previously known alkaloid.[3–6]

iso*Voacangine* IIIa proved to be a new isomer of voacangine with the difference that the methoxyl group, which in voacangine is attached to position 5 of the indole ring, is located at C-6 in the new isomer. By decarboxylation of it, tabernanthine[7] (IIIb) was obtained, whose structure was established by Taylor.[2]

Tabernanthine (IIIb), identical with the alkaloid described by Delourme-Houdé,[7] and *Voacamine*. The constants of our alkaloid seem to coincide with those reported

* This work was done with the financial help of the Rockefeller Foundation (Grant No. 56130).
† Taken from a D.Sc. thesis of F. Walls.
‡ Fellow of the Instituto Nacional de la Investigación Científica.
§ We wish to thank Dr. F. Miranda of the Instituto de Biología de la Universidad Nacional Autónoma de México, for his assistance in localisation and classification of the species.
|| We wish to thank Dr. J. S. E. Holker of Wayne State University, Detroit, Mich., who carried out these determinations.

[1] M. M. Janot and R. Goutarel *C. R. Acad. Sci., Paris* **240**, 1800 (1955).
[2] W. I. Taylor *J. Amer. Chem. Soc.* **79**, 3298 (1957).
[3] O. Hesse *Liebigs Ann.* **211**, 249 (1882).
[4] E. Field *J. Chem. Soc.* **125**, 1444 (1924).
[5] E. Schlittler and E. Gellért *Helv. Chim. Acta* **34**, 920 (1951); E. Gellért and B. Witkop *Helv. Chim. Acta* **35**, 114 (1952).
[6] O. O. Orazi, R. A. Corral, J. S. E. Holker and C. Djerassi *J. Org. Chem.* **21**, 979 (1956).
[7] J. Delourme-Houdé *Ann. Pharm. France* **4**, 30 (1946); *Chem. Abstr.* **41**, 1390^d (1947).

by Janot and Goutarel,[8] except that our analytical results correspond to $C_{34}H_{39}O_4N_3$ rather than $C_{42}H_{52}O_5N_4$[8] or $C_{45}H_{56}O_6N_4$[9].

Stemmadenine, a new alkaloid with an empirical formula $C_{21}H_{26-28}O_3N_2$, whose structure elucidation is currently in progress.

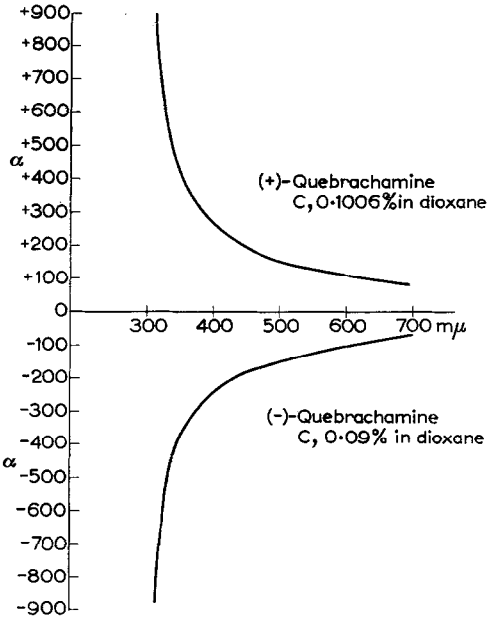


FIG. 1.

The only alkaloid isolated from *Stemmadenia Galeottiana* (*A. Rich.*) *Miers.* in appreciable amount was the known alkaloid *ibogamine* described by Janot *et al.*,[10] whose structure was also proved by Taylor.[2]

Before the structure of these alkaloids were announced by Taylor, several degradation experiments were carried out, and we wish to report here those which do not duplicate the already published ones.*

Voacangine (Ia). The selenium dehydrogenation produced ibogaine (Ib),[11] which had been obtained previously by saponification and decarboxylation of voacangine (Ia).

The ozonisation of voacangine (Ia) furnished a yellow compound —$C_{22}H_{28}O_5N_2$ (IIa)—, which is presumed to be the product of oxidative fission of the indole double-bond. It was not possible to decarboxylate this compound (IIa) as is the case with the parent alkaloid, since the acid (IIb) which could be isolated and which upon methylation with diazomethane regenerates compound (IIa), is completely destroyed when heated with aqueous hydrochloric acid. However, the ozonisation product (IIa) produced the 3-methyl-5-ethyl-pyridine, when dehydrogenated with palladium–charcoal.

* At the time this work was done, the structure of voacangine had not been established. We wish to thank Profs. V. Prelog, H. C. Brown, Takeo Ishiguro, E. R. Wallsgrove and H. L. Lochte, who supplied us with samples of substituted pyridines to compare with our degradation products.

[8] M. M. Janot and R. Goutarel *C. R. Acad. Sci., Paris* **240**, 1719 (1955).

[9] Physical Data of Indole and Dihydroindole Alkaloids. Lilly Research Laboratories, Indianapolis 6, Indiana, U.S.A.

[10] M. M. Janot, R. Goutarel and R. P. A. Sneeden *Helv. Chim. Acta* **34**, 1205 (1953).

[11] M. M. Janot and R. Goutarel *C.R. Acad. Sci., Paris* **241**, 986 (1955).

The reduction with lithium aluminium hydride of voacangine (Ia), produced the alcohol *voacanginol* (Ic) $C_{21}H_{28}O_2N_2$, which upon ozonisation led to a similar scission product corresponding to $C_{21}H_{28}O_4N_2$ (IIc).

TABLE 1. ABSORPTION SPECTRA OF SUBSTITUTED INDOLES DETERMINED IN A BECKMAN DK-2 SPECTROPHOTOMETER

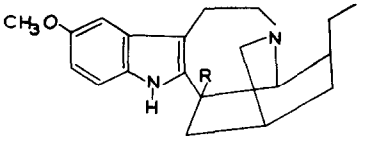
	mμ	ε
(+)-Quebrachamine	228, 284, 291	32,820; 7650; 7290
Indole	217, 263, 270, 279, 287	36,450; 4050; 4520; 4370; 3400
2-Methyl-indole[13]	220, 270, 288	32,400; 7770; 5030
3-Methyl-indole[14]	223, 281, 290	32,400; 6310; 5500
2,3-Dimethyl-indole[15]	227, 283, 290	36,400; 8130; 7250
2,3-*Cyclo*pentene-indole[16]	229, 280	26,750; 5070
1,2,3,4-Tetrahydrocarbazole[17]	227, 282, 290	53,100; 9500; 8460
2,3-*Cyclo*heptene-indole[18]	228, 284, 291	25,020; 7460; 6840
3-[N-piperidil-methyl]-indole[19]	215, 269–277, 279, 286	55,280; 8650; 8770; 7570
2-Methyl-3-[N-piperidil-methyl]-indole[20]	220, 270–280, 287	58,410; 9790; 8100

With cyanogen bromide, voacangine (Ia) gives three different products. Two of them were isomers with formulae $C_{23}H_{28}O_3N_3Br$, while the third had a formula $C_{23}H_{27}O_3N_3$. When one of the two isomers, obtained as main product, was treated with Raney nickel, it produced 2 new compounds: $C_{23}H_{30}O_4N_2$, which seems to be an aldehyde, and the other one $C_{23}H_{31}O_3N_3$, which seems to be an amine obtained by the reduction of the nitrile moiety, but their structures were not further investigated.

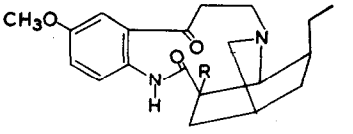
(+)-*Quebrachamine* (IV). By functional group analysis, evidence was obtained of the presence of one N-methyl grouping. By comparison (see Table 1) of its ultra-violet spectrum with those of different synthetic indoles, we have come to the conclusion that (+)-quebrachamine is an α,β-disubstituted indole. Although it was not possible to obtain recognisable degradation products, it has been reported by Witkop[12] that (−)-quebrachamine gives, by degradation, 3,5-diethylpyridine. Taking these facts into consideration, we are proposing the following partial structure (IV) for (+)-quebrachamine, which differs significantly from that proposed by Witkop[12] in that no free α-indole position is present.

(+)-Quebrachamine reacts with cyanogen bromide by addition of the CN grouping to the double bond of the indole, giving a compound $C_{20}H_{25}N_3$, whose ultra-violet absorption spectrum points to an indolenine. By hydrolysis of the latter with potassium hydroxide, the original (+)-quebrachamine was recovered. Therefore it is assumed that the addition compound has structure V.

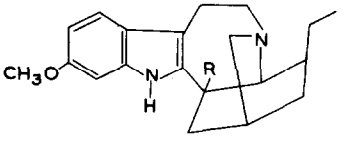
[12] B. Witkop *J. Amer. Chem. Soc.* **79**, 3193 (1957).
[13] *Beilstein* Vol. XX, p. 311.
[14] *Beilstein* Vol. XX, p. 315.
[15] *Beilstein* Vol. XX, p. 319.
[16] W. H. Perkin and P. Plant *J. Chem. Soc.* **123**, 3242 (1923).
[17] *Beilstein* Vol. XX, II, p. 257.
[18] W. H. Perkin, S. Glennand and P. Plant *J. Chem. Soc.* 2583 (1928).
[19] H. Kuhn and O. Stein *Ber. Dtsch. Chem. Ges.* **70**, 567 (1937).
[20] W. J. Brehn and H. G. Lindwall *J. Org. Chem.* **15**, 685 (1950).



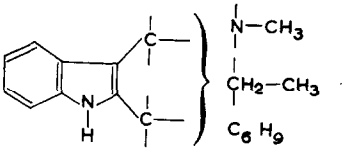
I a, R=$COOCH_3$
b, R=H
c, R=CH_2—OH



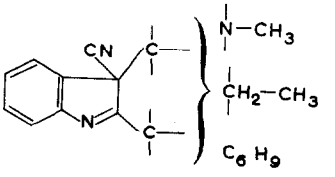
II a, R=$COOCH_3$
b, R=COOH
c, R=CH_2—OH



III a, R=$COOCH_3$
b, R=H



IV



V

EXPERIMENTAL*

Both *Stemmadenias* were collected in the tropical jungle of the State of Veracruz, near the road leading from Catemaco to Montepío.

Stemmadenia Donnell-Smithii

(*A*) *Wood*

A trunk of about 40 cm in diameter and weighing about 100 kg was cut into small pieces, ground to a powder in a Mikro-Pulverizer 1-W mill and dried at 37°. As a typical example, a 11·5 kg portion was continuously extracted with ethanol. The concentrated extract was evaporated to 1·5 l. and 2 l. of 5% HCl were added. The precipitate that formed was filtered off and the solution was extracted with ether. The aqueous acid phase was made alkaline with conc. NaOH, adding ice to avoid overheating, and then it was extracted with ether. The ethereal fraction was washed with water, dried and evaporated under vacuum. The residue (35 g) was dissolved in benzene and chromatographed on 1·5 kg of activated alumina, collecting fractions of 300 cc. In the first three fractions, eluted with benzene, 21 g of crude voacangine was obtained.

From fractions 7–8 (benzene–1% MeOH), 0·22 g was obtained of an alkaloid

* All melting points were determined with a Kofler block. Optical rotations were determined in chloroform unless otherwise stated. Ultra-violet spectra were measured in 96% ethanol in a Beckman DK-2 spectrophotometer and infra-red spectra, in chloroform solution, in a Perkin-Elmer Model 21 double-beam spectrophotometer. The microanalyses were carried out by Dr. F. Pascher, Bonn, Germany, and Mr. J. F. Alicino, Metuchen, N. J. As adsorbents, Harshaw Chemical Co. Activated alumina or Alcoa grade F-20 alumina were used.

which showed m.p. 233–235° (dec.) after three recrystallisations from ether–methanol. It has not been investigated further.

From fractions 11–13 (benzene–3% MeOH), 0·30 g of another alkaloid was obtained, which after recrystallisation from ether–methanol showed m.p. 135–139°. It similarly has not been investigated further.

Voacangine. The 21 g of crude voacangine were recrystallised from ether–methanol until a sharp melting point was reached, yielding 11·2 g, which showed m.p. 137–138°; $[\alpha]_D^{25}$ −28°; λ_{max} 224, 288 mμ; ε, 32,580; 10,220; λ_{max} 5·83 μ.

The comparison of this sample with one of authentic voacangine* did not show depression of the mixture melting point, and the infra-red curves were identical.

(Found: C, 71·60; H, 7·58; O, 13·39; N, 7·52. Calc. for $C_{22}H_{28}O_3N_2$: C, 71·71; H, 7·66; O, 13·03; N, 7·60%).

It gives a picrate which shows m.p. 148° (dec.) from methanol.

(Found: C, 56·42; H, 5·49; O, 26·74; N, 11·73. Calc. for $C_{28}H_{31}O_{10}N_5$: C, 56·27; H, 5·23; O, 26·78; N, 11·72%).

Degradation of voacangine. (a) With palladium: A mixture of 0·5 g of voacangine and 1·0 g of 5% palladium–charcoal was heated at 220° for 45 min. The volatile fraction was condensed and at the end of the reaction it was dissolved in methanol and treated with a methanolic solution of picric acid. The picrate was filtered and crystallised from acetone (0·09 g) and showed m.p. 181–182°. The m.p. was undepressed when mixed with the picrate of an authentic sample of 3-methyl-5-ethyl pyridine, (m.p. 181–182°).†

(Found: C, 48·63; H, 4·12; O, 31·50; N, 15·95. Calc. for $C_{14}H_{14}O_7N_4$: C, 48·00; H, 4·03; O, 31·97; N, 16·00%).

From the picrate, the free base was obtained, which was an oil with λ_{max} 262, 268, 274; ε, 2780; 3230; 2600.

The non-volatile fraction of the degradation was extracted with benzene, the palladium–charcoal was filtered off and the residue was chromatographed on 50 g of alumina F-20. From the fraction eluted with ether, a residue was obtained which was purified by sublimation at 90° and 0·01 mm, giving a crystalline sublimate with m.p. 80–81°; λ_{max} 228, 285; ε, 24,580; 7020.

(Found: C, 69·14; H, 7·50; O, 16·37; N, 7·03. Calc. for $C_{11}H_{13}O_2N$: C, 69·09; H, 6·85; O, 16·73; N, 7·33. Calc. for $C_{23}H_{30}O_4N_2$: C, 69·32; H, 7·59; O, 16·06; N, 7·03%).

It has not been possible to identify this compound until now. In the infra-red it does not show a carbonyl band and therefore there is no explanation as to why there are 2 or 4 oxygens in the molecule. The ultra-violet spectrum seems to correspond to a 5-methoxy-2,3-disubstituted indole (Table 2).

(b) With selenium: A mixture of 1 g of voacangine and 2·5 g of selenium was heated for 1 hr at 220°. The residue was extracted with benzene and the solution was chromatographed on 50 g of alumina F-20, collecting fractions of 50 cc. Fractions 12–15 (100 per cent ether) gave 0·12 g of a crystalline product, that, after recrystallisation from methanol, gave m.p. 150–151°; $[\alpha]_D^{25}$ −56° (alcohol); λ_{max} 227, 293 mμ; ε, 27,800; 7190.

* We wish to thank Prof. M. M. Janot from the Faculté de Pharmacie de Paris for supplying us with a sample of his voacangine.

† We wish to thank Prof. H. L. Lochte from the University of Texas for supplying us with this authentic sample.

TABLE 2

5-Methoxy-1,2,3,4-tetrahydrocarbazole[24]	λ_{max} 227, 273, 293 mμ; ε, 35,000; 7600; 7400
6-Methoxy-1,2,3,4-tetrahydrocarbazole[24]	λ_{max} 229, 270, 300 mμ; ε, 33,000; 4500; 5100
7-Methoxy-1,2,3,4-tetrahydrocarbazole[24]	λ_{max} 226, 271; ε, 42,000; 7050
2,3-Dimethyl-6-methoxyindole[25]	λ_{max} 228, 273, 298; ε, 32,400; 4790; 5500
*iso*Voacangine (6-methoxy)	λ_{max} 227, 278, 300; ε, 35,650; 4580; 6540
$C_{12}H_{15}ON$ (6-methoxy) (obtained by dehydrogenation of *iso*voacangine)	λ_{max} 228, 273, 298; ε, 35,830; 2360; 2720
Voacangine (5-methoxy)	λ_{max} 224, 288; ε, 32,580; 10,220
$C_{11}H_{13}O_2N$ (obtained by dehydrogenation of voacangine)	λ_{max} 228, 285; ε, 24,580; 7020

(Found: C, 77·01; H, 8·47; O, 5·40; N, 9·23. Calc. for $C_{20}H_{26}ON_2$: C, 77·30; H, 8·44; O, 5·31; N, 9·03%).

These constants coincide with those reported for ibogaine:[21,22] m.p. 150°; $[\alpha]_D^{25}$ −53° (alcohol); λ_{max} 226, 298 mμ; ε, 24,400; 8590 and a formula $C_{20}H_{26}ON_2$.

Ozonization of voacangine. Isolation of II(a). Following Karrer's directions,[23] the equivalent of 1·3 moles of ozone was bubbled through a solution of 3 g of voacangine in 60 ml of acetic acid and 22·5 ml of water, cooled externally with ice. The resulting solution, deep-red in colour, was basified with conc. NaOH and the precipitate was filtered off (3 g). This was dissolved in benzene and chromatographed on 150 g of alumina. From the benzene eluates, 1·08 g of yellow crystals were obtained, which exhibited m.p. 160–163°. By recrystallisation from chloroform–methanol, 0·96 g (30·1 per cent) of analytical sample (II) was obtained, m.p. 186–187°; $[\alpha]_D^{25}$ +136°; λ_{max} 270, 384 mμ; ε, 8640; 17,760; λ_{max} 5·83, 5·93, 6·0, 6·5 μ.

(Found: C, 65·75; H, 7·01; O, 20·34; N, 6·98. Calc. for $C_{22}H_{28}O_5N_2$: C, 65·98; H, 7·05; O, 19·98; N, 7·00%).

Compound (IIa) (0·3 g) was saponified with 0·6 g of potassium hydroxide in 60 ml of methanol by boiling for 8 hr. The alcohol was then evaporated, water was added and it was acidified with HCl to congo-red. The solution was extracted with chloroform. After the usual work-up, 0·18 g of a yellow solid acid was obtained which could not be crystallised. It was dissolved in methanol and esterified with diazomethane. After 30 min it was evaporated to dryness. The resulting crystalline residue showed the same m.p. as the original compound (IIa) and the mixture m.p. was not altered.

Compound IIa (0·5 g) was dehydrogenated with 1 g of 5% palladium–charcoal by heating the mixture for 1 hr at 250°. The volatile fraction was collected and a picrate (0·01 g m.p. 181–182°) was obtained from methanol. The mixture with an authentic picrate of 3-methyl-5-ethyl pyridine did not depress the melting point.

Compound IIa did not give any recognisable degradation products when it was treated with $LiAlH_4$; $NaBH_4$; KOH in ethylene–glycol, etc.

Voacanginol (Ic). To 1·0 g of voacangine (Ia) in 25 ml of anhydrous tetrahydrofuran,

[21] J. Dybowski and E. Landrin *C. R. Acad. Sci., Paris* **133,** 748 (1901).
[22] M. Raymond-Hamet *Bull. Soc. Chim. France* **9,** 620 (1942).
[23] P. Karrer and P. Enslin *Helv. Chim. Acta* **32,** 1390 (1949).
[24] J. R. Chalmers, H. T. Openshaw and G. F. Smith *J. Chem. Soc.* 1115, (1957).
[25] N. Neuss, H. E. Boaz and J. W. Forbes *J. Amer. Chem. Soc.* **76,** 2463 (1954).

1 g of $LiAlH_4$ in 25 ml of anhydrous tetrahydrofuran was added. It was boiled for 4 hr and then worked up in the usual way. From the chromatography of the residue, the fractions obtained with ether and ether–10% chloroform gave 0·570 g of crystals with m.p. 203–205°; λ_{max} 228, 292 mμ; ε, 20,300; 5660; λ_{max} 3·0 μ.

(Found: C, 74·27; H, 8·61; O, 9·27; N, 8·14. Calc. for $C_{21}H_{28}O_2N_2$: C, 74·08; H, 8·29; O, 9·40; N, 8·23%).

Voacanginol gives a hydrochloride that crystallises only if acetone is added, showing then, m.p. 202–204° (dec.); $[\alpha]_D^{25}$ ±0° (water); λ_{max} 211, 228, 292 mμ; ε, 27,360; 26,650; 9660; λ_{max} 3·2, 5·85 μ (Nujol).

(Found: C, 67·08; H, 8·09; O, 9·59; N, 6·66; Cl, 8·68. Calc. for $C_{21}H_{28}O_2N_2$—HCl—C_3H_6O: C, 66·26; H, 8·11; O, 11·03; N, 6·44; Cl, 8·15%).

When the crystals are boiled several times with methanol, and then evaporated to dryness, an oily residue is obtained that does not show the maximum at 5·85 μ due to the acetone.

Voacanginol (1·8 g) was ozonised in 40 ml of acetic acid and 20 ml of water with 1·3 moles of ozone. The reddish solution was alkalinised with NaOH, extracted with ether and the red residue was chromatographed on 50 g of alumina. The eluate of benzene–ether (9 : 1) afforded 0·4 g of crystals with m.p. 124–125°. After recrystallisation from acetone–hexane, the m.p. was 130–131°; $[\alpha]_D^{25}$ +72°; λ_{max} 275, 395 mμ; ε, 18,140; 22,920; λ_{max} 3·05, 5·9, 6·15 μ.

(Found: C, 67·88; H, 7·73; O, 16·68; N, 8·23. Calc. for $C_{21}H_{28}O_4N_2$: C, 67·72; H, 7·58; O, 17·18; N, 7·52%).

von Braun degradation of voacangine (Ia). A mixture of 10 g of voacangine (Ia), 20 g of freshly prepared cyanogen bromide and 150 ml of chloroform, was boiled for 9 hr, and let stand at room temperature overnight. The chloroform and the excess of BrCN were evaporated. The residue crystallised from ether, affording 9·45 g of a product with m.p. 198–200°. By recrystallisation from chloroform–methanol and acetone–methanol, 5.26 g of analytical sample of compound A were obtained which showed m.p. 203–204°; $[\alpha]_D^{18}$ −92°; λ_{max} 218, 285 mμ; ε, 29,140; 10,810; λ_{max} 3·13, 4·59, 5·82 μ.

(Found: C, 58·89; H, 5·98; O, 10·67; N, 8·95; Br, 16·71. Calc. for $C_{23}H_{28}O_3N_3Br$: C, 58·22; H, 5·96; O, 10·11; N, 8·85; Br, 16·84%).

By chromatography of the mother liquors, 3 g more of compound A were obtained plus very small amounts of 2 other crystalline compounds:

Compound B (370 mg) m.p. 238–240°; $[\alpha]_D^{25}$ +46°; λ_{max} 221, 284 mμ; ε, 28,200; 9470; λ_{max} 2·95, 4·58, 5·81 μ.

(Found: C, 58·59; H, 5·96; O, 10·41; N, 8·76; Br, 17·01. Calc. for $C_{23}H_{28}O_3N_3Br$: C, 58·21; H, 5·96; O, 10·11; N, 8·85; Br, 16·84%).

Compound C (100 mg) m.p. 175–176°; $[\alpha]_D^{25}$ −34°; λ_{max} 233, 284 mμ; ε, 12,800; 7300; λ_{max} 4·57, 5·81 μ.

(Found: C, 70·50; H, 6·84; O, 12·23; N, 10·65. Calc. for $C_{23}H_{27}O_3N_3$: C,70·20; H, 6·92; O, 12·20; N, 10·68%).

This compound seems to be an indolenine. The reduction of compound A (1·5 g) by boiling it for 3 hr with 3 g of Raney nickel in 100 ml of ethanol, produced 0·45 g of a compound with m.p. 230–233°. By recrystallisation, an analytical sample was obtained which showed m.p. 240–241°; $[\alpha]_D^{25}$ ±0°; λ_{max} 218, 284mμ; ε, 37,200; 20,000; λ_{max} 5·80 μ.

(Found: C, 69·51; H, 7·43; O, 15·94; N, 7·43. Calc. for $C_{23}H_{30}O_4N_2$: C, 69·32; H, 7·59; O, 16·06; N, 7·03%).

This compound is probably an aldehyde produced by the transformation of the nitrile group.

By chromatography of the mother liquors another compound (0·16 g) was obtained which showed m.p. 200°. The recrystallisation from chloroform–ethanol afforded an analytical sample with m.p. 212°; $[\alpha]_D^{25}$ −215°; λ_{max} 212, 285 mμ; ε, 38,750; 15,500; λ_{max} 3·2, 5·81, 6·2 μ.

(Found: C, 69·71; H, 7·92; O, 12·27; N, 10·27. Calc. for $C_{23}H_{31}O_3N_3$: C, 69·49; H, 7·86; O, 12·08; N, 10·57%).

This product is probably an amine produced by the reduction of the nitrile.

(B) Bark

50 kg of bark were pulverised in a Mikro-Pulverizer 1-W mill and the powder was dried at 30°; 35 kg of dried material were obtained, which were continuously extracted with alcohol in a pilot plant. The extract was concentrated to 4 l., and with continuous agitation 10 l. of 5% aqueous hydrochloric acid were added. The precipitate was filtered off and discarded. The filtrate was made alkaline with a solution of sodium–hydroxide, and the precipitate was filtered, washed, and dried, producing 240 g of solids. By extraction of this powder with benzene, 55 g of an oil was obtained and this was chromatographed on 2·5 kg of alumina. In the first 4 fractions (benzene–hexane 1 : 1), 6 g of crude (+)-quebrachamine m.p. 133–137° were obtained. From the rest of the fractions, 35 g of oil were isolated, which on rechromatography gave *tabernanthine*, iso*voacangine* and *voacamine*.

The recrystallisation from hexane and then from methanol of the crude (+)-quebrachamine, followed by sublimation at 130° and 0·001 mm, afforded 3 g of pure (+)-quebrachamine, m.p. 147–149°; $[\alpha]_D^{25}$ +111°; λ_{max} 228, 284, 291 mμ; ε, 32,820; 7650; 7290; λ_{max} 2·95 μ. The infra-red spectra of (+)- and (−)-quebrachamines were identical.

(Found: C, 81·01; H, 9·63; N, 9·81; Calc. for $C_{19}H_{26}N_2$: C, 80·80; H, 9·28; N, 9·92%). (Found: 1·4. Calc. for one C—CH_3, 5·3%). (Found: 2·73. Calc. for one N—CH_3, 5·3%*).

By mixing equal amounts of (+)- and (−)-quebrachamines and crystallising from aqueous methanol, the racemate was obtained, which showed m.p. 112–115°; $[\alpha]_D^{20}$ ±0·00°.†

(+)-quebrachamine (IV) gives a bright red picrate which shows m.p. 190–193°. By mixing equal amounts of it with (−)-quebrachamine picrate and recrystallising from methanol, a product with m.p. 176–179°; $[\alpha]_D^{20}$ ±0·00° was obtained.†

To 1·7 g of (+)-quebrachamine (IV) in 20 ml of chloroform, a solution of 5 g of cyanogen bromide in 60 ml of chloroform was added and the mixture was boiled for 4 hr. At this time the solution was deep-red. The solvent and the excess of BrCN were evaporated under vacuum and the residue, dissolved in chloroform, was chromatographed on 170 g of alumina F-20. From the chloroform–2% methanol fractions, 0·173 g of a product m.p. 105–110° was obtained. It was purified by

* A N—CH_3 determination on (−)-quebrachamine, kindly supplied by Dr. C. Djerassi, from Syntex, S.A., Mexico City, gave a value of 3·11.

† We wish to thank Dr. J. S. E. Holker from Wayne State University, Detroit, Michigan, for preparing these racemates.

sublimation at 95° and 0·001 mm showing m.p. 111–112°; λ_{max} 224, 286 mμ; ε, 18,000; 8460; λ_{max} 4·52 μ.

(Found: C, 78·27; H, 8·17; N, 13·66; MW, (Rast) 289. Calc. for $C_{20}H_{25}N_3$: C, 78·13; H, 8·20; N, 13·67%; MW, 307).

When 0·11 g of this compound was refluxed for 2 hr with 10 ml of 10% potassium hydroxide in ethanol, and then left standing at room temperature overnight, 0·075 g of crystals was obtained. By recrystallisation from chloroform–methanol they showed m.p. 143–144°, and after sublimation at 130° and 0·001 mm the m.p. was 147–149°; λ_{max} 226, 283, 290 mμ; ε, 37,860; 10,840; 10,270; λ_{max} 2·95 μ. The mixture melting point with (+)-quebrachamine was undepressed and the infra-red spectra were identical.

Rechromatography of the 35 g of oil on 1 kg of activated alumina gave, in the fractions eluted with benzene–hexane (50:50), 4·2 g of oil from which *tabernanthine* was crystallised out; from the fractions obtained by elution with benzene–hexane (80 : 20), 5·38 g of oil were obtained, from which iso*voacangine* was isolated; finally, from the fractions eluted with benzene–ether (1 : 1), 2·7 g of oil were obtained from which *voacamine* was isolated.

Tabernanthine. The 4·2 g of oil were crystallised from benzene–hexane, obtaining 400 mg of crude *tabernanthine*, m.p. 203–208°. By recrystallisation and sublimation at 160° and 0·005 mm, 204 mg of analytical sample were obtained which showed m.p. 211–212°; $[\alpha]_D^{25}$ −35°; λ_{max} 229, 271, 299 mμ; ε, 35,970; 4410; 5810.

(Found: C, 77·63; H, 8·57; O, 5·17; N, 9·18; O—CH_3, 10·35. Calc. for $C_{20}H_{26}ON_2$: C, 77·38; H, 8·44; O, 5·15; N, 9·03%; O—CH_3, 10·00).

The mixture melting point with an authentic sample of tabernanthine, obtained by decarboxylation of *iso*voacangine, was undepressed and the infra-red spectra were identical.

iso*Voacangine*. The oil (5·38 g) obtained from the chromatogram was crystallised from ether–methanol giving 1·45 g of crude *iso*voacangine, m.p. 148–149°, which after sublimation (140° and 0·01 mm) gave 1·2 g of pure *iso*voacangine m.p. 156–157°; $[\alpha]_D^{22}$ −52°; λ_{max} 227, 278, 300 mμ; ε, 35,650; 4580; 6540; λ_{max} 2·96, 5·8, 6·17 μ.

(Found: C, 71·24; H, 7·71; O, 13·56; N, 7·67; OCH_3, 16·96. Calc. for $C_{22}H_{28}O_3N_2$: C, 71·71; H, 7·66; O, 13·03; N, 7·60%; 2—OCH_3, 16·86).

*iso*Voacangine gives a crystalline hydrochloride, m.p. 225–228°, from methanol.

This compound is called *iso*voacangine because it was established that it was an isomer of voacangine in which the methoxyl grouping was attached to position 6 of the indole instead of at C-5 as in voacangine, by comparison of the ultra-violet spectra (Table 2) and by decarboxylation to tabernanthine.

When 0·5 g of *iso*voacangine was saponified with 20 ml of 15% potassium hydroxide in ethanol, by boiling for 12 hr and then the solution was acidified to pH3 with HCl, an acid was obtained which on heating for ½ hr on the steam bath, underwent decarboxylation. The solution was made alkaline and extracted with ether. From the ethereal fraction, after the usual work-up, 0·26 g of tabernanthine were obtained. [Reported constants[7] are m.p. 210°; $[\alpha]_D^{25}$ −40° (acetone); λ_{max} 228, 299 mμ; ε, 33,600; 5800]. Found: m.p. 211–212°; $[\alpha]_D^{25}$ −35°; λ_{max} 226, 295 mμ; ε, 37,160; 5760.

(Found: C, 77·43; H, 8·53; O, 5·20; N, 9·08; O—CH_3, 9·98. Calc. for $C_{20}H_{26}ON_2$: C, 77·38; H, 8·44; O, 5·15; N, 9·03%; O—CH_3, 9·91).

The dehydrogenation of 0·5 g of *iso*voacangine with 1 g of 5% palladium–charcoal, heating at 220–240° for 45 min, produced a volatile fraction which gave a picrate (0·042 g). By recrystallisation from methanol, the m.p. of the picrate was 179–182°, which was undepressed when mixed with an authentic sample of the picrate of 3-methyl 5-ethyl pyridine.

By extraction with benzene of the residue of the dehydrogenation, and chromatography on 25 g of alumina F-20, from the fractions eluted with ether, 135 mg of a semi-crystalline compound was obtained, which was sublimed three times at 65° and 0·005 mm, giving 22 mg of a crystalline product, m.p. 81–82°; λ_{max} 228, 273, 298 mμ; ε, 35,830; 2360; 2720.

(Found: C, 75·86; H, 7·95; O, 9·00; N, 7·18; O—CH_3, 16·87. Calc. for $C_{12}H_{15}ON$: C, 76·15; H, 7·99; O, 8·45; N, 7·40%; 1 O—CH_3, 16·39).

From the ultra-violet spectrum and the microanalysis, this compound seems to be a 6-methoxy-2 (or 3)-methyl-3 (or 2)-ethyl-indole.

Voacamine. From the fraction of 2·7 g of oil obtained in the chromatogram, 0·23 g crystallised out, and by further recrystallisation, there was isolated 0·14 g of pure *voacamine*, m.p. 223–224° (dec.); $[\alpha]_D^{26}$ −46°; λ_{max} 225, 286, 292; ε, 48,400; 14,860; 15,180.

(Found: C, 74·07; H, 7·58; O, 11·48; N, 7·54; O—CH_3, 12·73. Calc. for $C_{34}H_{39}O_4N_3$:* C, 73·75; H, 7·10; O, 11·56; N, 7·59%; 2 O—CH_3, 11·20).

This analysis does not check for the suggested formulae $C_{42}H_{52}O_5N_4$[8] or $C_{45}H_{56}O_6N_4$.[9]

The infra-red spectrum of our sample was identical with that reported for voacamine.[8]

(C) Fruits

1 kg of ground fruits of *S. Donnell-Smithii* was extracted with hot alcohol. The extract was concentrated, diluted with 1 l. of 5% acetic acid and extracted with hexane; the aqueous phase was made alkaline with NaOH and extracted with chloroform. This phase, after evaporation to dryness, left 2 g of residue, which was chromatographed on 200 g of alumina. From the fractions eluted with ether, 0·15 g of *stemmadenine* was obtained, showing m.p. 199–200° (dec.); $[\alpha]_D^{25}$ +324° (pyridine); λ_{max} 227, 284, 292 mμ; ε, 35,720; 7345; 7060; λ_{max} 3·05, 3·85 μ (nujol).

(Found: C, 70·80; H, 7·51; O, 14·09; N, 7·81. Calc. for $C_{21}H_{26}O_3N_2$: C, 71·16; H, 7·39; O, 13·54; N, 7·90%).

The structure of this alkaloid will be reported in a future paper.

Stemmadenia Galeottiana

Wood

Following the same procedure as in the case of the wood of *S. Donnell-Smithii*, from 16 kg of wood dust, 3·4 g of pure alkaloid was obtained, which showed m.p. 163–164°; $[\alpha]_D^{25}$ −60°; λ_{max} 225, 283, 291 mμ; ε, 36,180; 9130; 8710; λ_{max} 2·94 μ.

(Found: C, 81·33; H, 8·64; N, 9·91; C—CH_3, 4·34. Calc. for $C_{19}H_{24}N_2$: C, 81·38; H, 8·63; N, 9·99%; C—CH_3, 5·36).

The physical constants and the empirical formula coincide for those reported for *ibogamine*[10]: m.p. 163°; $[\alpha]_D$ −54° (ethanol).

* The calculated analysis was obtained following the method suggested by R. Krzikalla. Rechentafeln zur chemischen elementar-analyse. Verlag Chemie (1956.)