was isolated with ether. The brown oily product was chromatographed on deactivated alumina. Elution with benzene–ether (1:1) gave 0.2 g of **38a**, which crystallized from aqueous methanol as colorless plates: mp 173–174°; infrared bands at 1695 (acid), 755 cm^{-1} (olefin), nmr signals at 10.0 br (COO*H*), 5.73, 5.51 (AB quartet, two protons, H-15, H-16, J_{AB} = 5.5 cps), 1.19, 1.00, 0.78 ppm (methyl singlets).

Anal. Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.55; H, 10.08.

Methyl Hibaate (38b).—The above experiment was repeated by refluxing 0.8 g. of **37**, 6 g of potassium hydroxide, and 2 ml of 95% hydrazine hydrate in 70 ml of diethylene glycol for 2.3 hr then concentrating to 200° (vapor) and refluxing for a further 3.5 hr under nitrogen. The product was methylated with excess ethereal diazomethane to give a brown oil which was chromatographed on a column of 30 g of alumina prepared in hexane. Elution with hexane–benzene (4:1 and 3:1) gave 0.65 g of **38b**, which crystallized from methanol as colorless needles: mp 85–86°; $[\alpha]D$ −25° (*c* 0.75); infrared bands at 1735, 1230 (ester), 755 cm^{-1} (olefin); nmr signals at 5.74, 5.49 (AB quartet, two protons, H-15, H-16, J_{AB} = 5.5 cps), 3.68 s (methoxyl), 1.18, 1.01, 0.78 ppm (methyl singlets).

Anal. Calcd for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 80.04; H, 10.29.

Hibaene (1).—Methyl hibaate, 0.6 g, was reduced with lithium aluminum hydride in refluxing anhydrous ether as described for methyl dihydrohibaate (**34a**) and the crude alcohol **38c** (0.6 g, infrared bands at 3400, 1060–1010, 750 cm^{-1}, no carbonyl) was oxidized to the corresponding aldehyde **38d** [infrared bands (CCl_4) at 2700, 1735 cm^{-1}, no hydroxyl] with Jones reagent in acetone at 0° as described for **34c** above. A mixture of the aldehyde, 6 g of potassium hydroxide, and 2 ml of 95% hydrazine hydrate in 70 ml of diethylene glycol was heated under reflux for 5 hr, cooled, and diluted with water; the product was isolated with ether. The pale yellow oil was taken up in hexane and filtered through a small column of alumina. The colorless oil thus obtained, $[\alpha]D$ −30°, showed two bands on vpc in the ratio of 2:1 approximately. The major and minor bands were found to represent hibaene and hibane, respectively, by enhancement of the corresponding peaks on addition of authentic material. Separation was effected by chromatography over silicic acid–silver nitrate.[33] Elution with hexane gave firstly (−)-hibane, identical with the previously prepared sample. Later fractions, monitored by vpc, contained (−)-hibaene: $[\alpha]D$ −47° (*c* 1.01); infrared bands (neat) at 1385, 1365 (*gem*-dimethyl), 755 cm^{-1} (olefin); nmr signals at 5.70 d, 5.44 d (AB quartet, two protons, H-15, H-16, J_{AB} = 6 cps), 0.99, 0.86, 0.83, 0.75 ppm (methyl singlets). The analytical sample, prepared by distillation at 200° (bath temperature, 2.0 mm), had mp and mmp 29°, and nmr and infrared spectra superimposable on the nmr and infrared spectra of authentic (−)-hibaene.

Anal. Calcd for $C_{20}H_{32}$: C, 88.16; H, 11.84. Found: C, 88.05; H, 11.91.

(33) H. L. Goering, W. D. Closson, and A. C. Olson, *J. Am. Chem. Soc.*, **83**, 3507 (1961).

The Isolation of Rupicoline and Montanine, Two Pseudoindoxyl Alkaloids of *Tabernaemontana Rupicola* Benth.[1a]

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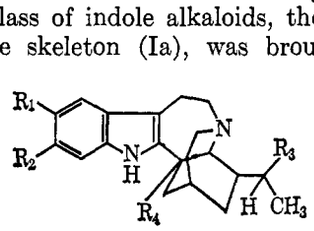
Two pseudoindoxyl alkaloids have been isolated from the South American shrub *Tabernaemontana rupicola* and, on the basis of spectral data, structures IVa and IVb were proposed for them. The structure of one of these alkaloids, called rupicoline (IVa), is confirmed by its partial synthesis from voacangine (Ib).

The investigation of alkaloids in plants of the tribe *Tabernaemontaneae*, family *Apocynaceae*, received a considerable stimulus from the structural elucidation of several alkaloids of *Tabernanthe iboga*.[3] At that time a new class of indole alkaloids, those possessing the ibogamine skeleton (Ia), was brought to light.



Ia, $R_1 = R_2 = R_3 = R_4 = H$
b, $R_1 = CH_3O$; $R_2 = R_3 = H$; $R_4 = CH_3OCO$
c, $R_1 = CH_3O$; $R_2 = H$; $R_3 = HO$; $R_4 = CH_3OCO$
d, $R_1 = R_2 = H$; $R_3 = HO$; $R_4 = CH_3OCO$

Subsequently the structures of several other alkaloids of this type have been deduced.[4] These have been isolated from species of several genera within the tribe *Tabernaemontaneae*.

Within the genus *Tabernaemontana*, alkaloids have been isolated from *Ervatamia coronaria* syn. *Tabernaemontana coronaria*,[5] *T. spharocarpa*,[6] *T. dichotoma*,[7] *T. undulata*,[5a] *T. oppositifolia*,[5a] *T. australis*,[5a] *T. crispa*,[8] *T. alba*,[9] *T. pachysiphon* var. *cumminsi*,[10] *T. affinis*,[11] *T. pandacaqui*,[12] and *T. mucronata*.[13]

T. rupicola, described by Bentham,[14] is a woody shrub 4–5 ft in height bearing white flowers. It is indiginous to the area of the Amazon and its subsidiaries in Brazil.

Two collections of this plant were studied. These varied greatly, both qualitatively and quantitatively, with respect to alkaloid content. The first, collected in October 1959 on the Rio Negro, contained 0.28% organic bases. Paper chromatography of the crude bases revealed a number of components. The second col-

(1) (a) From the Ph.D. Thesis of J. W. Kessel, California Institute of Technology, June 1963. (b) Author to whom inquiries should be directed at Distillation Products Industries, P. O. Box 1910, Rochester, N. Y. 14603. (c) National Institutes of Health Fellowship, 1960–1963.

(2) Deceased, April 29, 1964.

(3) (a) W. I. Taylor, *J. Am. Chem. Soc.*, **79**, 3298 (1957); (b) D. F. Dickel, C. L. Holden, R. C. Maxfield, L. E. Paszek, and W. I. Taylor, *J. Am. Chem. Soc.*, **80**, 123 (1958); (c) M. F. Bartlett, D. F. Dickel, and W. I. Taylor, *ibid.*, **80**, 126 (1958).

(4) *Cf.* W. I. Taylor, "The Alkaloids," Vol. VIII, R. H. F. Manske, Ed., Academic Press Inc., New York, N. Y., 1965, pp 203–235.

(5) (a) M. Gorman, N. Neuss, N. J. Cone, and J. A. Deyrup, *J. Am. Chem. Soc.*, **82**, 1142 (1960); (b) A. N. Ratnagiriswaran and K. Venkatachalam, *Quart. J. Pharm. Pharmacol.*, **12**, 174 (1939); (c) S. A. Warsi and B. Ahmad, *Pakistan J. Sci.*, **1**, 128 (1949).

(6) M. Greshoff, *Ber.*, **23**, 3537 (1890).

(7) A. V. Subbaratnam, *Current Sci.* (India), **23**, 66 (1954).

(8) A. R. S. Kartha and K. N. Menon, *ibid.*, **21**, 315 (1952).

(9) O. Collera, *et al.*, *Bol. Inst. Quim. Univ. Nacl. Auton. Mex.*, **14**, 3 (1962).

(10) J. Thomas and G. A. Starmer, *J. Pharm. Pharmacol.*, **15**, 487 (1963).

(11) M. P. Cava, *et al.*, *Chem. Ind.* (London), 1193 (1964).

(12) G. Aguilar-Santos, A. C. Santos, and L. M. Joson, *J. Philippine Pharm. Assoc.*, **50**, 321, 333 (1964).

(13) A. C. Santos, G. Aguilar-Santos, and L. L. Tibayan, *Anales Real Acad. Farm.*, **31**, 3 (1965).

(14) G. Bentham, *Hookers J. Botany*, **3**, 212 (1841).

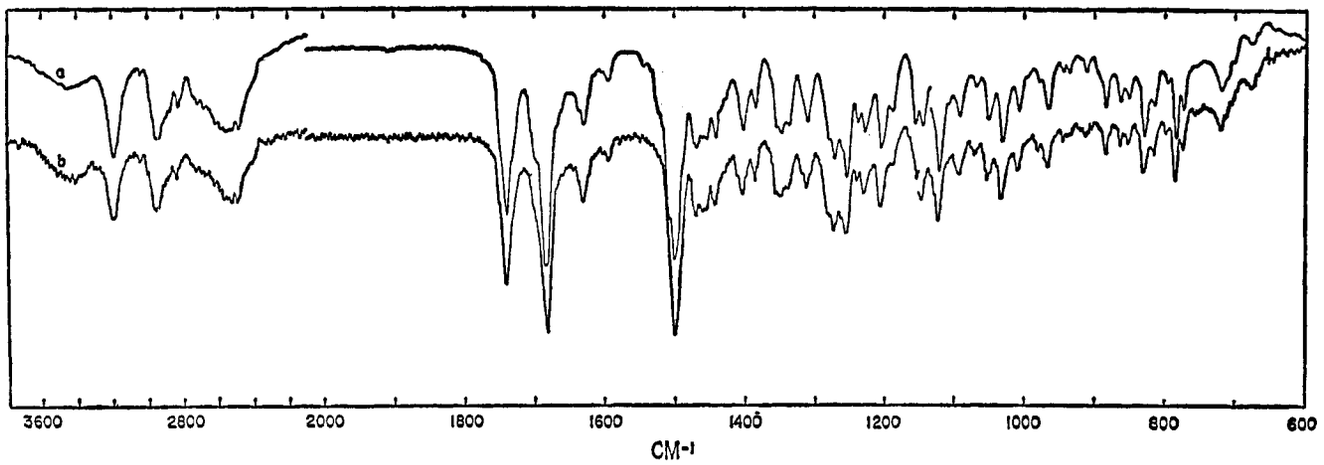


Figure 1.—The infrared spectra of rupicoline hydrochloride (a) and the pseudoindoxyl hydrochloride prepared from voacangine (b) (in potassium bromide).

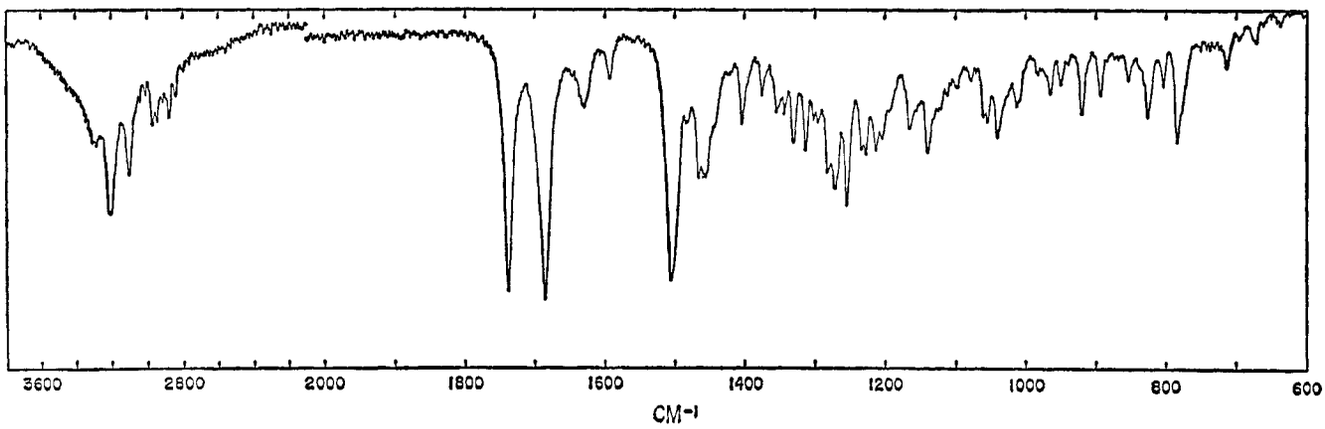


Figure 2.—The infrared spectrum of montanine hydrobromide (in potassium bromide).

lection, made in October 1961 on the grounds of the Instituto Agronomico do Norte at Belem, Brazil, contained only 0.007% organic bases. In addition, paper chromatography of the crude bases revealed only a few components and these differed in R_f value and fluorescence from the components of the chromatogram of the first collection. For this reason the second collection was not used.

The crude bases were isolated from the leaves and twigs of the first collection of *T. rupicola* by means of an alcohol extract. This extract was evaporated under reduced pressure and the residue was extracted with dilute hydrochloric acid. The acid extract was made basic and extracted with ether to yield the mixture of crude bases. Two alkaloids were separated from this alkaloid fraction chromatographically. These have been given the names rupicoline and montanine.

Rupicoline crystallized from methanol giving rupicoline methanolate which melted at 205–207° dec. Rupicoline formed a hydrochloride salt which could be recrystallized from isopropyl alcohol. Elemental analyses of this salt suggested the formula $C_{22}H_{28}N_2O_4 \cdot HCl$. This formula is supported by molecular weight studies on the base which gave an average of 380 for the molecular weight (calculated for $C_{22}H_{28}N_2O_4$, 384) and by means of the mass spectrum which has a peak for the molecular ion at m/e 384.

The second base, montanine, was not obtained crystalline. The amorphous base melted at 137–138° *in vacuo*. The alkaloid formed a hydrochloride salt melting at 258–259° dec *in vacuo*. Elemental analyses are consistant with the formula $C_{22}H_{28}N_2O_5 \cdot HBr$ for montanine hydrobromide.

Rupicoline and montanine have very similar ultraviolet and visible spectra. These spectra, which are not effected by acid, show absorption maxima at 228 and 410 and a shoulder at 260 mμ. They are quite similar to the spectra of ibolueine and desmethoxyiboluteine[15] and, like these compounds, rupicoline and montanine fluoresce a bright yellow-green.

The infrared spectra of rupicoline and montanine (Figures 1a and 2) each have a strong band at 1684 cm^{-1}. Iboluteine and demethoxyiboluteine have bands at 1675 and 1680 cm^{-1}, respectively. In addition, rupicoline and montanine each have a strong band in the infrared spectrum at 1737 cm^{-1} suggesting a nonconjugated ester function in each of these bases.

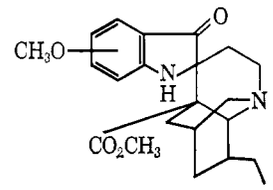
The nmr spectrum of rupicoline methanolate (Figure 3a) provides insight into its structure. The group of peaks at 390–434 cps[16] are in the region associated with aromatic hydrogen and have an integral equivalent to three protons. The absence of peaks in the region 270–390 cps suggests that olefinic protons are not present in rupicoline. The peaks at 224 and 197 cps fall in the region associated with O-methyl groups and each of these peaks has an integral equivalent to three protons.

(15) R. Goutarel, M. M. Janot, F. Mathys, and V. Prelog, *Helv. Chim. Acta*, **39**, 742 (1956).

(16) Given in cycles per second (cps) downfield from tetramethylsilane.

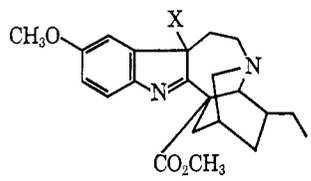
In addition there is a triplet centered at 53 cps (J = 6.5 cps) suggesting a C-methyl group.

These spectral properties and a consideration of the structural features found previously in alkaloids of this plant family suggested a tentative structure (II) for rupicoline. This structure is the pseudoindoxyl compound corresponding to either voacangine (Ib) or is ring-A methoxy isomers.



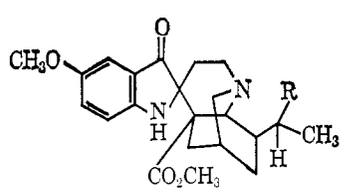
II

The catalytic oxidation of an iboga alkaloid to the corresponding pseudoindoxyl derivative has been carried out with ibogaine,[15] and a similar method was used to prepare the pseudoindoxyl compound corresponding to voacangine. Oxidation of voacangine with oxygen in the presence of platinum gave voacangine hydroperoxide (IIIa) which was not isolated but catalytically reduced to the alcohol (IIIb). Acid-catalyzed rearrangement of this alcohol gave a single pseudoindoxyl compound derived from voacangine. Sufficient material was not available for measurement of the optical rotation of this compound. The hydrochloride of this salt had an infrared spectrum and X-ray powder diagram identical with those of rupicoline hydrochloride. Rupicoline is therefore the pseudoindoxyl compound (IVa) corresponding to voacangine.



IIIa, X = HOO
b, X = HO

The nmr spectrum of montanine (Figure 3b) is quite similar to that of rupicoline. The triplet at 53 cps found in the spectrum of rupicoline is replaced by a doublet at 64 cps (J = 6.5 cps) suggesting that the



IVa, R = H
b, R = HO

hydroxyl group is located on the ethyl side chain as in voacangarine (Ic). The nmr spectra of heyneanine (Id) and voacangarine (Ic) each have doublets at 66 cps (J = 6.5 cps).[17] In addition a peak at 266 cps, having an integral of 1 hydrogen, appears in the spectrum of montanine. A structure accommodating this change in the nmr spectra is IVb. This structure is consistent with the spectra of montanine. An attempt

(17) T. R. Govindachari, *et al.*, *Tetrahedron Letters*, 3873 (1965).

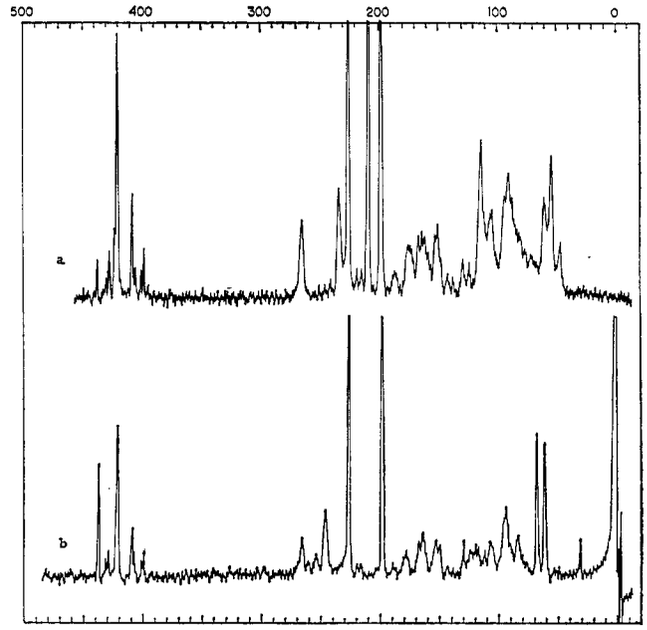


Figure 3.—The nmr spectra of rupicoline methanolate (a) and montanine (b) in deuteriochloroform

to correlate montanine chemically with voacangarine was unsuccessful and, since the limited amount of base available precluded an extensive chemical degradation, the structure of montanine is tentatively regarded as being IVb, by analogy to voacangarine (Ic).[18]

Prior investigators[3b,15] have suggested that the pseudoindoxyl iboga alkaloids may be attributed to a facile autoxidation of the parent alkaloids. If autoxidation were responsible for these bases, the parent indole alkaloids would be expected to be present in the plant. The initial chromatographic experiment revealed that the early fractions, in which the indole alkaloids would appear, if present, contained only a trace of material reacting with alkaloidal reagents. This fraction was not investigated. Paper chromatographic experiments revealed that voacangine was not present in the alkaloids of the second collection of *T. rupicola*.

Experiments were carried out with small samples of voacangine to determine whether or not the condition of isolation were such that the alkaloids would be oxidized to rupicoline. No rupicoline was observed, however. The possibility exists that such an oxidation would occur in the presence of other plant material or would be enzymatically catalyzed.

Experimental Section[19]

Plant Material.—Leaves and twigs (5.1 kg) of *T. rupicola* were collected by Dr. W. A. Rodriguez on the Rio Negro in October 1959. An ethanol extract of this material was prepared at Smith, Kline and French Laboratories. This solution (*ca.* 2 l.) was sent to us in January 1961.

A second collection of the plant was made by Dr. R. F. Raffauf and Sr. N. T. daSilva on the grounds of the Instituto Agronomico do Norte, Belem, Brazil, in October 1961. This

(18) D. Stauffacher and E. Seebeck, *Helv. Chim. Acta*, **41**, 169 (1958).

(19) Melting points were determined on a capillary apparatus calibrated with standards from a Kofler hot stage. Unless otherwise noted they were determined in evacuated capillaries. Elemental analyses were performed by Spang Microanalytical Laboratories, Ann Arbor, Mich. Nmr spectra were determined on a Varian A-60 spectrometer. Infrared spectra were recorded using a Beckman IR-7 spectrophotometer. Ultraviolet spectra were obtained using Cary Model 11M and 14 spectrophotometers.

plant material was examined at Smith, Kline and French Laboratories and then forwarded to us.

Extraction of Organic Bases.—A 500-ml portion of the ethanol extract of the first collection of *T. rupicola* was evaporated to a thick syrup under vacuum. This material was then extracted with 500 ml of 1 *N* HCl and the solution was filtered. The residue was extracted with sixteen successive 250-ml portion of 1 *N* HCl. The combined extracts were made basic by the addition of 1.2 equiv of NaOH. The solution was then shaken, in thirds, with 100-ml portions of chloroform until the extract no longer gave a precipitate with Wagner's or Mayer's reagents. The combined chloroform extracts were evaporated to dryness under vacuum. The residue from the evaporation of the chloroform extract was taken up in dilute acid, the pH was brought to below 2, and the solution was diluted to 500 ml. The solution was then extracted exhaustively with ether in a continuous liquid–liquid extractor. This was continued until extraction for 24 hr followed by evaporation of the solvent yielded less than 0.3 mg of material. The aqueous phase was then brought to pH 11.2 with dilute NaOH and extracted with ether. The ether extract was concentrated and treated with ferrous sulfate to reduce any peroxides formed and was then filtered. Evaporation of the ether yielded 1.28 g of organic bases. This method was repeated and, in all, a volume of the ethanol extract equivalent to 3.7 kg of the plant was extracted yielding 6.44 g of organic base.

Separation of Rupicoline and Montanine.—A portion (0.5 g) of the crude organic base was chromatographed on a 2 × 25 cm alumina (Merck acid-washed, activity II–III) column. The column was developed with benzene and then chloroform. A solvent gradient was then established by adding, with stirring, 500 ml of 1:1 methanol–pyridine to 2 l. of chloroform. The rate of this addition was one-fourth the rate at which the mixed solution was run onto the chromatographic column. The rate of flow of the chromatographic column was limited to approximately 4 ml/min. In this way a bright yellow band containing the alkaloids, rupicoline and montanine, was developed and eluted.

This fraction was evaporated to dryness under nitrogen. It was then taken up in benzene and chromatographed on a column of 200–300 mesh Florosil. The column was washed with chloroform followed by chloroform containing a few per cent methanol. The alkaloids rupicoline and montanine were developed in a single narrow band and eluted. This fraction was evaporated under nitrogen. The residue was taken up in benzene and chromatographed using preparative paper chromatography.[20] Whatman No. 1 paper soaked with 20% formamide in acetone was used.[21]

The solvent system was 9:1 cyclohexane–diethylamine. After development the sheets were allowed to dry somewhat and the spots corresponding to the alkaloids rupicoline and montanine were cut from the paper and separated. The alkaloids were then eluted from the paper with 9:1 chloroform–diethylamine. The alkaloidal solutions were diluted with ether and washed with several portions of dilute base and then with water. They were dried over potassium carbonate, filtered, and evaporated to dryness under vacuum.

The isolation procedure was repeated and from the 6.44 g of crude organic base there was obtained approximately 60 mg of crystalline rupicoline hydrochloride and 55 mg of crystalline montanine hydrochloride.

The free base rupicoline may be crystallized from cold methanol giving rupicoline methanolate. After three recrystallizations from methanol this material had a melting point (in air) of 205–207° dec. Rupicoline hydrochloride, recrystallized several times from isopropyl alcohol, had a melting point of 265° dec. The specific rotation of rupicoline hydrochloride was $[\alpha]^{25.2}D$ −228° (*c* 1.21, water).

Anal. Calcd for $C_{22}H_{20}ClN_2O_4$: C, 62.77; H, 6.94; Cl, 8.42; N, 6.66. Found: C, 62.44, 62.30; H, 7.11, 7.20; Cl, 8.08; N, 6.21, 6.35. Found for an earlier sample: C, 63.16; H, 6.67; N, 7.06.

The ultraviolet spectrum of rupicoline had peaks at 228 mμ (log ε 4.34) and 410 mμ (log ε 3.45) and a shoulder at approximately 260 mμ (log ε 3.42). This spectrum was unchanged by the addition of acid.

The free base montanine was not obtained in crystalline form. The amorphous base melted at 137–138°. The alkaloid formed a hydrochloride salt which crystallized from isopropyl alcohol very slowly and melted at 258–259° dec. Montanine formed a hydrobromide salt which could be recrystallized from isopropyl alcohol containing 2–3% water. The recrystallized compound melted at 273–274° dec, $[\alpha]^{26}D$ −206° (*c* 1.21, water).

Anal. Calcd for $C_{22}H_{29}BrN_2O_5$: C, 54.89, H, 6.07, Br, 16.60; N, 5.82. Found: C, 55.02, 54.80; H, 6.19, 6.06; Br, 16.72, 16.80; N, 5.84, 5.76.

The ultraviolet spectrum of montanine has peaks at 228 mμ (log ε 4.48) and 410 mμ (log ε 3.53) and a shoulder at approximately 260 mμ (log ε 3.75). The spectrum was unchanged by the addition of acid.

The infrared spectra of rupicoline hydrochloride and montanine hydrobromide were taken in potassium bromide pellets. These spectra are reproduced in Figures 1a and 2.

The nmr spectra of rupicoline methanolate and of amorphous montanine were taken in deuteriochloroform using a nylon microcell to limit the quantity of material required for the spectra. These spectra are reproduced in Figures 3a and b. Chemical shifts are given in cycles per second downfield from tetramethylsilane (0 cps). A trace of chloroform present in the deuteriochloroform causes the peak at 440.5 cps. (Tetramethylsilane was added for the calibration of the spectrum of montanine. The spectrum of rupicoline methanolate, Figure 3a, was calibrated by the chloroform peak.)

Separation of Organic Bases. Second Collection.—The second collection of *T. rupicola* was assayed as having alkaloids to the extent of 0.007%, a value much lower than that of the first collection. Dried leaves and twigs (560 g) of the second collection were extracted with ethanol and the organic bases of the extract were separated in the manner described for the first collection. A sample of the ether-extractable bases derived in this manner was paper chromatographed by the formamide–cyclohexane–diethylamine method. This chromatogram revealed only two fluorescent spots under the ultraviolet lamp. These had R_f values of 0.00 and 0.97. The later spot had a blue fluorescence. Rupicoline and montanine, which have R_f values of 0.59 and 0.06, respectively, were not present.

Molecular Weight Studies on Rupicoline.—The molecular weight was obtained using a thermistor bridge device based on the instrument of J. J. Newmayer.[22] By this method molecular weight values of 380, 382, 383, and 375 (average 380) were obtained for rupicoline. The mass spectrum of rupicoline has a peak for the molecular ion at *m/e* 384.

Catalytic Oxidation of Voacangine.—Voacangine was oxidized in a manner similar to that described by Goutarel, *et al.*,[15] for the conversion of ibogaine to iboluteine. The voacangine (0.040 g) was placed in a platinum boat in a microhydrogenation apparatus.[23] Platinum oxide (0.011 g) was then placed in the apparatus and 5 ml of ethyl acetate was added. The apparatus was then evacuated and filled with hydrogen. After the platinum oxide had been reduced the system was again evacuated and filled with oxygen. When the catalyst no longer absorbed oxygen, the voacangine was introduced into the solution. After approximately 30 hr at 25°, 0.97 equiv of oxygen had been taken up. The catalyst was then filtered off and the solvent was evaporated. The residue was an amorphous solid and all attempts to crystallize it were unsuccessful. The residue was placed in a platinum boat in the microhydrogenation apparatus. Platinum oxide (0.020 g) and 5 ml of ethanol were then added and the air in the system was displaced by hydrogen. After the catalyst had been reduced the material in the platinum boat was added and 0.75 equiv of hydrogen was added. At 25° the reaction was complete in 5–10 min. The catalyst was then removed by centrifugation and decantation. The solvent was evaporated and the residue was divided into two portions. To one portion 5 ml of 2 *N* methanolic NaOH was added. After 30 hr at room temperature, chromatography revealed that no spot corresponding to rupicoline was present in the solution. The solution was then refluxed for 2 hr and again tested with thin layer chromatography with the same results. The second portion of the reduced material was treated with 5 ml of 2 *N* methanolic HCl and the solution was allowed to stand for 30 hr at room temperature. Thin layer chromatography of this solution revealed a spot having an R_f value similar to that of rupicoline. The methanolic solution was then evaporated and the residue

(20) E. von Arx and R. Neher, *Helv. Chim. Acta*, **39**, 1664 (1956).
(21) D. Waldi, *Arch. Pharm.*, **292**, 206 (1959).
(22) J. J. Neumayer, *Anal. Chim. Acta*, **20**, 519 (1959).
(23) N. Clauson-Kaas and F. Limborg, *Acta Chem. Scand.*, **1**, 884 (1948).

was chromatographed preparatively on thin layer chromatographic plates (silica gel) using 9:1 cyclohexane–diethylamine as the solvent.

This method of oxidation and rearrangement of voacangine was repeated with an additional 0.040 g of voacangine. The bands on the thin layer chromatograms corresponding in R_f value to rupicoline were removed from the plates and eluted with methanol. The base derived in this manner was converted to a hydrochloride salt and recrystallized from isopropyl alcohol. The total yield was approximately 2 mg of fine yellow needles.

After a second recrystallization of the infrared spectrum of this material was taken in a potassium bromide pellet. This spectrum is reproduced in Figure 1b, superimposed on the spectrum of rupicoline.

The X-ray powder method was also used to prove the identity of this compound with rupicoline hydrochloride. A sample of each of the compounds was powdered and placed in a capillary tube. X-Ray exposures of 20 and 122 hr were then made using the Straumanis technique. Chromium radiation with a vanadic acid filter was used (the λ_{max} of Cr Kα = 2.2909 A). The camera used had a diameter of 99.812 mm. Arcs were measured on a comparator to ±0.02 mm. Relative intensities of the lines were estimated visually. The X-ray powder spectra were identical.

Further Oxidation of Voacangine.—A small sample of voacangine (0.010 g) was treated in the exact manner described earlier for the isolation of the ether extractable organic bases from the plant. The resulting fraction was thin layer chromatographed with rupicoline as a comparison. No spot corresponding to rupicoline could be detected in the material treated in this way.

A sample of voacangine (0.010 g) was refluxed in ether for approximately 1 month and the ether was evaporated to dryness. Thin layer chromatography of a sample of the residue did not reveal a spot of R_f value corresponding to rupicoline. The residue was then allowed to stand for 2 weeks in the sunlight and another sample was taken and chromatographed. A faint spot corresponding to rupicoline in R_f value and color could then be detected. Most of the material was unreacted voacangine.

Acknowledgments.—The authors wish to express their appreciation to Dr. R. F. Raffauf of Smith, Kline and French Laboratories for obtaining the plant materials studied, to Danual Kuwada of the Jet Propulsion Laboratory, and H. Budzikiewicz of Stanford University for obtaining the mass spectrum of rupicoline.

Chamissonin, a Germacranolide from an *Ambrosia* Species

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Chamissonin, a sesquiterpenoid lactone present in *Ambrosia chamissonis* (Less.) Greene, is shown to be a germacranolide, a structural type known in other tribes of the *Compositae* but hitherto unobserved in members of the subtribe *Ambrosiinae* of the tribe *Heliantheae*.

Ambrosia chamissonis (Less.) Greene (*Franseria chamissonis* ssp. *bipinnatisecta* Less.) (*Compositae*, tribe *Heliantheae*, subtribe *Ambrosiinae*)[1,2] is a perennial common to coastal Southern California. In view of the occurrence of sesquiterpenoid lactones in numerous other members of the *Ambrosiinae*,[3-5] an examination of *A. Chamissonis* was undertaken.

The plant is rich in sesquiterpenoid lactonic material, and the crude syrup that was obtained in *ca.* 1% yield (see Experimental Section) crystallized spontaneously to afford the compound chamissonin. Although crude chamissonin was obtained with ease, it proved to be unstable and appeared to polymerize when attempts were made to purify it. The pure compound was obtained by slow crystallization from benzene and, when free of contaminants, could be recrystallized from benzene. The mother liquors from which chamissonin separated, and which contained much of the compound, could be chromatographed on silica gel to yield eluate fractions that showed only a single (chamissonin) spot on thin layer chromatograms but which yielded the crystalline compound only reluctantly and in poor yield; yet these same syrupy materials gave high yields of the diacetate.

Chamissonin, mp 124–125°, has the composition $C_{15}H_{20}O_4$. It shows ultraviolet absorption at 200 mμ (ϵ 12,600), and its infrared spectrum contains the prominent peak at 1765 cm^{-1} and the less intense peak at 1650 cm^{-1} that are characteristic of the α-methylene γ-lactone, a structural feature common to many sesquiterpenoid lactones of the *Compositae* and especially prevalent in those of the *Ambrosiinae*. Except for an intense absorption in the hydroxyl region (3500 cm^{-1}), no other conspicuous structural features were obvious from the infrared spectrum. The nmr spectrum of chamissonin (in pyridine) showed two methyl groups (3 H singlets) at 1.67 and 2.26 ppm, but was not as clearly interpretable as the spectra of the derivatives to be discussed below.

Chamissonin readily formed a diacetate and a dibenzoate; both of these had compositions that agreed with the formulation of chamissonin as a dihydroxy lactone, $C_{15}H_{20}O_4$. The diacetate showed a Kuhn–Roth terminal methyl number of 3.3 and its infrared spectrum, which lacked absorption in the hydroxyl region, showed peaks at 1735 cm^{-1} (acetate) and 1755 and 1645 cm^{-1} (lactone). The nmr spectrum of the diacetate showed the acetyl methyl groups (as 3 H singlets) at 2.12 and 2.07 ppm, two methyl groups (3 H singlets) at 1.80 and 1.73 ppm, and the characteristic pair of doublets (J = 2 cps) for protons of the exocyclic methylene group at 6.27 and 5.94 ppm. The region of *ca.* 2–6 ppm is a complex grouping of signals which includes a 1 H multiplet centered at 4.3 ppm, assignable to the CH—O methine proton of the lactone grouping. The high-field position of this signal, and its multiplicity, indicate that it is nonallylic, and is in the structural grouping –CH–*CH*–CH–. The region between 2.1 and *ca.* 3.4 ppm integrates for five protons, and includes protons that are not adjacent to oxygenated functions. A group of four protons that give rise to a broad complex between 4.8 and 5.5 ppm includes the two methine

(1) The inclusion of the genus *Franseria* in *Ambrosia* is proposed by W. W. Payne [*J. Arnold Arboretum*, **45**, 401 (1964)].

(2) P. A. Munz and D. D. Keck, Ed., "A California Flora," University of California Press, Berkeley, Calif., 1959.

(3) W. Herz and Y. Sumi, *J. Org. Chem.*, **29**, 3438 (1964).

(4) W. Herz and G. Hogenauer, *ibid.*, **26**, 5011 (1961).

(5) T. A. Geissman and R. J. Turley, *ibid.*, **29**, 2553 (1964).