showed that they were different, giving bands at 3180, 1106, 1032, 988, 950, 925, 888 and 865 cm.$^{-1}$.

Anal. Calcd. for $C_9H_{16}BrNO_2$: C, 43.21; H, 6.45; Br, 31.95; N, 5.60. Found: C, 43.41; H, 6.53; Br, 31.86; N, 5.42.

Scopoline Methyl Bromide (III) by Rearrangement of the Scopolamine Hydrolysis Product.—A 0.1-g. sample of crystalline scopine methyl bromide was heated under nitrogen in an oil-bath at 225–244° for one hour. The slightly darkened crystalline residue was recrystallized from 5 ml. of absolute ethanol giving typical cubic shaped crystals, m.p. 297–299° dec.[11] The infrared spectrum[8] showed this to be identical with scopoline methyl bromide (III).

This ability to rearrange without melting doubtless explains the lack of depression in the mixed melting point between scopoline methyl bromide and scopine methyl bromide.

Scopine Methyl Bromide (IV) from Scopine.—Scopine was prepared by the hydrolysis of scopolamine with an ammonium chloride–ammonium hydroxide buffered solution as described by Willstätter and Berner.[7] Nicely crystalline material was obtained, m.p. 75.5–77° in a capillary tube heated in a liquid bath; and m.p. 82–82.5° on a Fisher–Johns melting point block.[14]

A solution of 0.5 g. (0.0032 mole) of this scopine in 5 ml., of absolute ethanol was cooled to 0° and about 2 ml. of cold methyl bromide was added. The stopper was clamped in the flask and it was allowed to stand at room temperature. Within a half-hour crystals had started to separate and after 22 hours the product was collected, washed with absolute ethanol and absolute ether and dried giving 0.73 g. (90%) of nicely crystalline needles, m.p. 295–295.5° dec. (with darkening from about 230°).[11] The infrared spectrum[8] was identical with that of the above scopolamine methyl bromide hydrolysis product.

(14) Willstätter and Berner[7] report a m.p. 79° (cor.).

KALAMAZOO, MICHIGAN

[CONTRIBUTION FROM THE LABORATORY OF CHEMISTRY OF NATURAL PRODUCTS, NATIONAL HEART INSTITUTE]

Alkaloids of the Amaryllidaceae. III. Isolation of Five New Alkaloids from *Haemanthus* Species[1]

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The alkaloid content of ten identified and three unidentified species of *Haemanthus* has been investigated. Five new alkaloids named coccinine, manthidine, manthine, montanine and natalensine have been isolated and characterized. Tazettine was the major alkaloid found in *H. albiflos* and lycorine was isolated in trace amount from *H. coccineus*.

The plant genus *Haemanthus*, which is native to South Africa, has been known for many years to possess physiological activity. Nearly fifty years ago, Juritz[2] reported on the toxicity of several *Haemanthus* species. The native Africans have employed extracts of *Haemanthus* and the closely related *Boophone* (earlier spelling *Buphane*) as topical treatment of such diverse afflictions as leprosy, ulcers, febrile colds, asthma, coughs and wounds.[3,4]

While no work has been reported[4a] since that of Juritz on the alkaloids of *Haemanthus*, the alkaloids of *Boophone disticha* Herb. (*Haemanthus toxicarius* Herb.) have been investigated more completely. Tutin[5] isolated buphanine, lycorine and two amorphous bases from this source. Lewin[6] found the amorphous base haemanthine in the same plant. This early work has been extended and strengthened by Cooke and Warren[7] who have verified the existence of haemanthine and revised its molecular formula to $C_{18}H_{23}NO_6$.[8] Recently a new amorphous alkaloid, distichine, $C_{19}H_{23}NO_4$, has been isolated from *B. disticha*.[8]

This paper reports a study of the crystalline alkaloids found in nine species of *Haemanthus*. *H. puniceus* (N-951) was received in this country in 1951 and cultivated at the U. S. Plant Introduction Garden, Glenn Dale, Maryland, until April, 1954, when it was sent to this Laboratory for processing. The bulbs of *H. albiflos* were of South African origin, purchased in 1938 from nurseries in Haarlem, Netherlands, and propagated in Maryland until April, 1954. The remaining specimens were gathered in South Africa during the period from December, 1952, through February, 1953, and processed shortly after arrival in this country. Approximately thirty grams of each species was examined first for the presence of alkaloids by precipitation tests with silicotungstic acid and Mayer reagent. Those bulbs which gave negative or very weakly positive tests were not studied further. The bulbs which gave positive reactions were processed according to a standard procedure outlined in the previous paper.[1b]

With the exception of *H. natalensis*, which was much richer in alkaloidal material, the alkaloid fractions appear to represent between 0.1 and 0.6% of the total bulb weight. The absence of alkaloids in the sample of *H. magnificus* was surprising since all other species of *Haemanthus* contained alkaloidal material. It is of interest to note that *H. amarylloides*, *H. coccineus* and the unidentified species N-47 and N-50, all of which possessed nearly the same amount of basic material, contained the same major alkaloids.

(1) Papers I and II of this series: (a) W. C. Wildman and W. T. Norton, THIS JOURNAL, **76**, 152 (1954); (b) W. C. Wildman and C. J. Kaufman, *ibid.*, **76**, 5815 (1954).

(2) C. F. Juritz, *S. African J. Sci.*, **8**, 98 (1911); *ibid.*, **11**, 116 (1921); *Rept. Senior Analyst*, Cape of Good Hope, **G-43**, 40 (1906).

(3) T. S. Githens, "Drug Plants of Africa," The University of Pennsylvania Press, The University Museum, Philadelphia, Penna., 1949, pp. 33, 91.

(4) J. M. Watt and M. G. Breyer-Brandwijk, "The Medicinal and Poisonous Plants of Southern Africa," E. and S. Livingston, Edinburgh, 1932, p. 25.

(4a) Since this paper was submitted, papers by H.-G. Boit [*Chem. Ber.*, **87**, 1339, 1448 (1954)] have appeared on alkaloids of the *Haemanthus* genus. From the *Haemanthus* hybrid "King Albert," he obtained lycorine, "haemanthamine," and "haemanthidine." Actual comparison has not been effected, but it is obvious that "haemanthamine" and "haemanthidine" are identical with our natalensine and the alkaloid of m.p. 190–192° from *H. puniceus*, respectively. We have found that the alkaloid of m.p. 188–194° from *H. albiflos* is impure lycorenine which is identical in its infrared spectrum with an authentic sample of lycorenine kindly furnished by Prof. S. Uyeo. Lycorenine and tazettine were isolated by Boit from *H. albiflos*.

(5) F. Tutin, *J. Chem. Soc.*, **99**, 1240 (1911).

(6) L. Lewin, *Arch. exptl. Path. Pharmakol.*, **68**, 333 (1912).

(7) J. Cooke and F. Warren, *J. S. African Chem. Inst.*, **6**, 2 (1953).

(8) F. L. Warren, *J. Chem. Soc.*, submitted for publication.

TABLE I

YIELD OF AMORPHOUS ALKALOID FRACTION BASED ON WET BULB WEIGHT

Species	Source	Wt. processed, g.	Yield of amorphous alkaloids, %
H. albiflos Jacq.	South Africa	7,590	0.18
H. albomaculatus Baker	Durban, Natal	3,480	.33
H. amarylloides Jacq.	Brandfort, Orange Free State	504	.18
H. coccineus L.	Cape Peninsula, Cape Province	11,890	.16
H. hirsutus Baker	Koppie, Natal	1,090	.32
H. magnificus Herb.	Johannesburg, Transvaal	....	No alk.
H. montanus Baker	Johannesburg, Transvaal	1,207	0.57
H. natalensis Hook.	Durban, Natal	2,482	1.08
H. nelsonii Baker	Johannesburg, Transvaal	295	0.21
H. puniceus L. (N-192)[a]	Durban, Natal	....	Weakly pos. qual. test
H. puniceus L. (N-951)	Braeside, Cape Province	905	0.18
Unidentified (N-47)	Piquetberg, Cape Province	5,150	.15
Unidentified (N-50)	Dutoitskloof Pass, Cape Province	2,540	.16
Unidentified (N-121)	Kreuger National Park, Transvaal	2,003	.50

[a] N-numbers are assigned by this Laboratory to plant materials as they are received; they serve as identification when different samples of the same genus and species are processed.

Isolation of the pure alkaloids from the benzene- or benzene–ethyl acetate-soluble portions of the crude amorphous fractions was achieved by chromatography on alumina. Elution of the columns gave oily fractions which often were induced to crystallize upon trituration. A small amount of lycorine was isolated from the benzene-insoluble material of *H. coccineus* when the latter was triturated with a few milliliters of ethanol. Since no crystalline material was produced from the other species by this procedure, the gums were not investigated further.

In Table II are listed those species of *Haemanthus* which gave crystalline alkaloids and the yields based on the original wet bulb weight. The alkaloids of *H. albomaculatus* and *H. nelsonii* are not included since our current information indicates the presence of two additional new alkaloids which were found only in these species. The characterization of these two alkaloids is not sufficiently complete for publication. No crystalline alkaloids could be isolated from *H. hirsutus*. In no case have the known alkaloids of *Boophone*—buphanine, haemanthine and distichine—been isolated. It is quite possible that these alkaloids are not present in the species investigated or that they may be found in some of the oils which were obtained in our work but not studied further.

TABLE II

CRYSTALLINE ALKALOIDS OF *Haemanthus* SPECIES

Species	Alkaloid(s) present	Yield, %
H. albiflos Jacq.	Tazettine	0.077
H. amarylloides Jacq.	Coccinine	.007
	Manthine	.044
	Montanine	.060
H. coccineus L.	Coccinine	.024
	Lycorine	.013
	Manthidine	.001
	Montanine	.018
H. montanus Baker	Montanine	.510
H. natalensis Hook.	Natalensine[a]	.274
H. puniceus L. (N-951)	Natalensine	.025
Unidentified (N-47)	Coccinine	.040
	Manthidine	.008
	Manthine	.001
	Montanine	.050
Unidentified (N-50)	Coccinine	.016
	Manthidine	.0007
	Manthine	.006
	Montanine	.050
Unidentified (N-121)	Natalensine	.009

[a] Named in consultation with Professor F. L. Warren.

All of the alkaloids that we have isolated are optically active. Each alkaloid possesses a methylenedioxy group attached to an aromatic ring as shown by a positive Labat[9] test. We have accumulated additional evidence for the presence of this functional group from the infrared spectra of the alkaloids. Two strong absorption bands, one at 9.55–9.67 μ and the second at 10.63–10.75 μ, appear to be indicative of this functional group when the infrared absorption spectra are run in chloroform solution. These bands are present in the new alkaloids and in the known compounds: bicuculline, hydrastine, hydrohydrastinine, myristicin, *nor*hydrohydrastinine, picropodophyllin, piperine, piperonal, piperonylamine, podophyllotoxin and tazettine. The band at 10.7 μ is absent in N-acetylhomoveratrylamine, 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline and its N-methyl derivative, *d*-glaucine, papaverine and *l*-tetrahydropalmatine hydrochloride. The ultraviolet spectra of the alkaloids are strikingly uniform and show in general two maxima, one in the 240–244 mμ region and the second from 294–297 mμ. The spectrum of tazettine, an alkaloid that is known to contain a methylenedioxyphenyl group,[10] is very similar to those of the new alkaloids. Simplified synthetic compounds[11] modelled upon the phenanthridine structure for lycorine and tazettine show these two maxima, but there is a definite hypsochromic shift of the first maximum to the region of 236 mμ. 1,4,5,6,13,14-Hexahydro-5-methyl-8,9-methylenedioxyphenanthridine, hydrohydrastinine and N-methylpiperonylamine exhibit this behavior. It is hoped that work in prog-

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

(10) J. W. Cook and J. D. Loudon in R. H. F. Manske and H. L. Holmes, "The Alkaloids," Vol. II, Academic Press, Inc., New York, N. Y., 1952, p. 331.

(11) L. H. Mason and W. C. Wildman, THIS JOURNAL, **76**, 6194 (1954).

ress will determine the significance of this shift.

Coccinine, montanine and natalensine are isomeric and possess the molecular formula $C_{17}H_{19}NO_4$. In each alkaloid, the oxygen atoms are associated with a methylenedioxy group, one hydroxyl and one methoxyl function. A crystalline *m*-nitrobenzoate was obtained from natalensine, but the alcoholic derivatives of montanine and coccinine were non-crystalline. Evidence for the hydroxyl group in these two alkaloids is based on infrared absorption at 2.85 μ and compatible spectra for the amorphous alcoholic derivatives. Each of the three alkaloids absorbed one mole of hydrogen when reduced with platinum in acetic acid. These alkaloids are tertiary bases; an aqueous solution of the methiodide of each was soluble in dilute sodium hydroxide. Herzig–Meyer determinations showed the absence of an N-methyl group in these bases, and Kuhn–Roth oxidations showed the absence of C-methyl groups in coccinine, montanine and dihydronatalensine. All of the facts outlined above suggest that coccinine, montanine and natalensine are methoxy derivatives related to lycorine, but conclusive proof is lacking.

The minor alkaloids manthine and manthidine are isomeric and possess the molecular formula $C_{18}H_{21}NO_4$. The extreme paucity of these alkaloids in the species under investigation has limited their characterization to the following information. Analysis has shown that, in addition to the methylenedioxy function, the two remaining oxygen atoms of manthine are present in methoxyl groups. Except for the absence of a hydroxyl-stretching band in manthine, the infrared spectra of montanine and manthine are almost identical. It then seems probable that manthine is methoxymontanine. Manthidine possesses one methoxyl group, as shown by analysis, and a hydroxyl group is indicated by absorptino at 2.82 μ.

Although natalensine could be isolated with ease from *Haemanthus* species (N-121), *H. natalensis* and *H. puniceus*, the major crystalline fraction from these bulbs was a hygroscopic solid that has proven difficult to characterize. Analysis of the purest material, m.p. 190–192°, which was obtained from *H. puniceus*, as well as of its picrate and methopicrate has not permitted the determination of a molecular formula.

Of the abundant alkaloids—natalensine, montanine, tazettine and coccinine—montanine and natalensine have slight hypotensive activity. Detailed pharmacology of these alkaloids will be reported. Further investigation of the structures of these new alkaloids will be conducted if additional supplies of the bulbs can be obtained.

Experimental[12]

Qualitative Test for Alkaloids.—Approximately 20 g. of each species was ground in a mortar with sea sand and enough 1% hydrochloric acid solution to make a paste. The paste was filtered through a mat of Super-cel, and the filtrate was made basic with solid sodium carbonate. This solution was extracted with 10 ml. of chloroform, and the chloroform solution was extracted with 5–10 drops of 0.5% hydrochloric acid solution. The acid solution was divided into two parts, one of which was tested with Mayer reagent and the other with 12% silicotungstic acid solution. A turbid solution or a precipitate indicated a positive test for alkaloids.

Isolation of the Crude Alkaloid Fraction.—The procedure essentially followed that reported in a previous paper,[1b] but was scaled up or down depending upon the quantity of bulbs to be processed.

Isolation of Alkaloids from *H. amarylloides*, *H. coccineus* and *H.* spp. (N-47 and N-50).—The procedures used for the isolation of alkaloids from these species were very similar, and the isolation of pure alkaloids from N-50 is representative. A solution of 4.6 g. of the crude alkaloid fraction of *Haemanthus* sp. (N-50) in benzene was chromatographed on 120 g. of aluminum oxide (Merck, Suitable for Chromatography). About 30 mg. of waxy, non-basic material was eluted with 500 ml. of dry thiophene-free benzene. Elution with 2.5 l. of benzene–ethyl acetate (3:1) gave two major fractions; the first, 270 mg. of colorless oil, when triturated with ethyl acetate afforded crystalline manthine, m.p. 109–114°. One recrystallization of this material from ethyl acetate–cyclohexane gave the pure base, m.p. 114–116°. The second fraction, 1.23 g., when triturated with ethyl acetate gave a crystalline mixture of crude coccinine and manthidine. The mixture was heated to boiling with 5 ml. of ethyl acetate, and the insoluble manthidine was removed by filtration, 20 mg., m.p. 269–270°. Colorless plates of nearly pure coccinine formed when the ethyl acetate solution was cooled, 474 mg., m.p. 157–161°. Elution with 2.5 l. of ethyl acetate followed by 1 l. of ethyl acetate–chloroform (2:1) gave 1.42 g. of montanine which crystallized on trituration with water, acetone or chloroform. Elution with 1.5 l. of chloroform–ethanol (3:1) gave 600 mg. of brown oil that could not be induced to crystallize.

In the case of *H. coccineus*, isolation of the alkaloids followed the pattern above except that about 15% of the crude alkaloid fraction was insoluble in benzene. Trituration with ethanol gave 640 mg. of crude lycorine, m.p. 228–240° dec. Ethanol trituration of the oil eluted with chloroform–ethanol gave 43 mg. of solid material, m.p. 232–240° dec., which was identified as crude lycorine. In each case the identification of lycorine was based upon its infrared absorption spectrum.

Isolation of Montanine from *H. montanus*.—A solution of 5.36 g. of crude alkaloid fraction in benzene was chromatographed on 143 g. of alumina. Elution with 250 ml. of ethyl acetate–chloroform (4:1) followed by 750 ml. of ethyl acetate–chloroform (1:1) and 2 l. of chloroform gave 4.774 g. of oily montanine which crystallized on trituration with acetone, water, or chloroform. Elution with 500 ml. of chloroform–ethanol (1:1) gave 450 mg. of brown oil that could not be induced to crystallize.

Isolation of Natalensine from *H. natalensis*, *H. puniceus* and *H.* sp. (N-121).—The crude alkaloid fraction, 5.04 g., of *H. natalensis* was dissolved in 150 ml. of boiling benzene containing the minimum amount of ethyl acetate to effect complete solution. The mixture was chromatographed on 140 g. of alumina (Fisher, No. A-540). Elution with 500 ml. of chloroform–ethyl acetate (1:1) followed by 750 ml. of chloroform gave 1.434 g. of natalensine which crystallized on trituration with acetone. One recrystallization from acetone gave 1.277 g. of nearly pure natalensine as colorless prisms, m.p. 202–203.5°. Elution with 500 ml. of chloroform–ethanol (1:1) gave 3.02 g. of yellow oil which partially crystallized on trituration with acetone. Recrystallization of the solid gave 1.87 g. of a mixture of alkaloids, m.p. 168–172°. The mixture defied all attempts at further purification.

A solution of 1.64 g. of the crude alkaloid fraction of *H. puniceus* in 100 ml. of dry, thiophene-free benzene containing enough ethyl acetate to effect complete solution was chromatographed on 150 g. of aluminum oxide (Merck). Elution with 500 ml. of ethyl acetate–chloroform (1:1) followed by 1250 ml. of chloroform gave 0.337 g. of crude natalensine. Recrystallization from acetone afforded 0.225 g. of natalensine, m.p. 202–203.5°. Elution with 500 ml. of

(12) All melting points are corrected and were observed on a Kofler microscope hot-stage equipped with polarizer. Analyses were performed by Dr. W. C. Alford and his staff and the Clark Microanalytical Laboratory, Urbana, Ill. Infrared spectra were recorded with a Perkin–Elmer model 21 double-beam spectrophotometer; ultraviolet spectra were recorded with a Cary model 11MS spectrophotometer. Unless otherwise noted, the ultraviolet spectra were run in Pharmco absolute ethanol. The spectral work was performed by Mrs. I. J. Siewers and Miss F. C. Bateman.

chloroform–ethanol (6:1) and 500 ml. of chloroform–ethanol (3:1) gave 1.203 g. of yellow oil that crystallized upon the addition of ethyl acetate. The crude solid was recrystallized twice from acetone to yield 0.477 g. of colorless prisms, m.p. 190–192° dec. The infrared spectrum (Nujol) of this material was identical with that of the crude alkaloids, m.p. *ca.* 170°, from *H. natalensis* and *H.* sp. (N-121). Analytical data on this material, its picrate and methopicrate have not been sufficient to construct a molecular formula.

Chromatography of 4.75 g. of the crude alkaloid fraction from *H.* sp. (N-121) followed the same pattern as that of *H. natalensis*, but only traces of natalensine were present. Elution with chloroform–ethanol (4:1) gave 3.11 g. of oil which afforded 1.10 g. of a crystalline mixture of alkaloids, m.p. 150–162°. The mixture could not be purified further by chromatography, countercurrent distribution or fractional crystallization.

Isolation of Tazettine from *H. albiflos*.—A solution of 5.82 g. of the crude alkaloid fraction of *H. albiflos* in 50 ml. of benzene was chromatographed on 335 g. of aluminum oxide (Merck, Suitable for Chromatography). Elution with 500 ml. of benzene–ethyl acetate (3:1) gave 1.82 g. of crude tazettine which was recrystallized from ethanol to give 1.25 g. of pure tazettine, m.p. 210–211°. Its identity was proven by comparison of the infrared spectrum with that of an authentic sample.[1b] A mixed melting point with authentic tazettine was not depressed. The mother liquors of this crystallization and subsequent fractions from the column (eluted with 1500 ml. of benzene–ethyl acetate (1:1) and 1500 ml. of ethyl acetate) were crystallized from ethanol to yield an additional 0.820 g. of tazettine, m.p. 208–210°. Elution with chloroform–ethanol (4:1) gave 0.572 g. of oil from which 50 mg. of solid, m.p. 228–231°, was obtained upon trituration with acetone. When the tazettine filtrates were rechromatographed, an additional 464 mg. of tazettine, m.p. 208–210°, was obtained upon elution with benzene–ethyl acetate (3:1). Elution with more polar solvents gave 696 mg. of an oil. The oil crystallized upon trituration with acetone to give 368 mg. of a crude solid, m.p. 188–194°. Neither this material nor that melting at 228° was investigated further.

Coccinine: m.p. 162–163°, $[\alpha]^{27}D$ −188.8° (*c* 1.89, ethanol). For analysis, a sample was dried at 1.0 mm. for 18 hours at room temperature and 4 hours at 110°. The ultraviolet absorption spectrum showed maxima at 213 mμ (log ε 4.25), 244 mμ (log ε 3.58) and 296 mμ (log ε 3.64).

Anal. Calcd. for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36; N, 4.65; CH_3O, 10.30; neut. equiv., 301.3. Found: C, 67.91; H, 6.29; N, 4.54; CH_3O, 10.27; neut. equiv.,[13] 299.5.

Coccinine Picrate.—Seventy milligrams of coccinine in ethyl acetate gave 89 mg. of coccinine picrate, m.p. 155–160° dec. Two recrystallizations from ethyl acetate did not improve the melting point. The derivative was solvated with ethyl acetate as shown by analysis and infrared absorption at 5.76 μ. For analysis, a sample was dried at room temperature, and 1.0 mm. for 18 hours.

Anal. Calcd. for $C_{17}H_{19}NO_4 \cdot C_6H_3N_3O_7 \cdot {}^1/_2C_4H_8O_2$: C, 52.26; H, 4.56; N, 9.75. Found: C, 52.15; H, 4.68; N, 9.77.

The unsolvated picrate, m.p. 154–161° dec., was obtained by drying the above sample at 110° and 1.0 mm. for 17 hours.

Anal. Calcd. for $C_{17}H_{19}NO_4 \cdot C_6H_3N_3O_7$: C, 52.07; H, 4.18; N, 10.56. Found: C, 51.77; H, 4.05; N, 10.42.

Coccinine Perchlorate.—The solution of coccinine perchlorate in acetic acid prepared during the determination of the neutral equivalent of coccinine was concentrated to give a solid. Four recrystallizations from methanol gave colorless prisms, m.p. 254–255° dec. For analysis, a sample was dried at 1.0 mm. for 18 hours at 25° and 4 hours at 110°.

Anal. Calcd. for $C_{17}H_{19}NO_4 \cdot HClO_4$: C, 50.81; H, 5.02; N, 3.49. Found: C, 50.77; H, 4.97; N, 3.76.

Coccinine Methiodide.—Prepared in acetone and recrystallized twice from water, the methiodide formed colorless prisms, m.p. 219–220°, $[\alpha]^{26}D$ −60.5° (*c* 1.41, water). For analysis, a sample was dried at 1.0 mm. for 18 hours at room temperature and 4 hours at 110°.

(13) J. S. Fritz, *Anal. Chem.*, **22**, 1028 (1950).

Anal. Calcd. for $C_{17}H_{19}NO_4 \cdot CH_3I$: C, 48.76; H, 5.00; N, 3.16. Found: C, 48.73; H, 5.02; N, 3.15.

Dihydrococcinine.—A solution of 432 mg. of coccinine in 15 ml. of glacial acetic acid was hydrogenated at atmospheric pressure and room temperature with platinum oxide catalyst. The reduction ceased when 104% of the theoretical amount of hydrogen had been absorbed. The catalyst was removed by filtration, and the filtrate was concentrated in an air jet. The solution was made basic with 10% sodium carbonate solution and the base was extracted with chloroform. The chloroform solution was dried and concentrated to a pale yellow oil that resisted all attempts at crystallization.

Manthine: recrystallized from ether for analysis, m.p. 114–116°, $[\alpha]^{26}D$ −71.3° (*c* 0.47, chloroform).

Anal. Calcd. for $C_{18}H_{21}NO_4$: C, 68.55; H, 6.71; N, 4.44; 2 CH_3O, 19.68. Found: C, 68.26; H, 6.22; N, 4.32; CH_3O, 19.69.

The ultraviolet absorption spectrum showed maxima at 243 mμ (log ε 3.64) and 294 mμ (log ε 3.71).

Manthidine.—For analysis, a sample was sublimed at 250° and 0.1 mm., m.p. 269–270°, $[\alpha]^{21.5}D$ −26.6° (*c* 0.6, chloroform).

Anal. Calcd. for $C_{18}H_{21}NO_4$: C, 68.55; H, 6.71; N, 4.44; CH_3O, 9.84. Found: C, 68.71; H, 6.44; N, 4.34; CH_3O, 9.79.

The ultraviolet absorption spectrum showed maxima at 240 mμ (log ε 3.63) and 294 mμ (log ε 3.72).

Montanine.—The unsolvated base was an oil which when triturated with acetone, chloroform or water formed a crystalline solvate. From acetone, montanine formed colorless prisms, m.p. 57–60°, $[\alpha]^{26}D$ −87.6 (*c* 0.57, chloroform). For analysis, a sample was dried at 25° and 0.1 mm. for 20 hours.

Anal. Calcd. for $C_{17}H_{19}NO_4 \cdot C_3H_6O$: C, 66.83; H, 7.01; N, 3.90. Found: C, 67.13; H, 6.91; N, 3.78.

When crystallized from chloroform, montanine formed colorless prisms, m.p. 59–65°; $[\alpha]^{26}D$ −70.2° (*c* 1.03, chloroform). For analysis, a sample was dried at 26° and 0.1 mm. for 20 hours.

Anal. Calcd. for $C_{17}H_{19}NO_4 \cdot 4/5\ CHCl_3$: C, 53.87; H, 5.02; N, 3.53; Cl, 21.44. Found: C, 53.88; H, 5.03; N, 3.65; Cl, 21.61.

From water, montanine formed microscopic needles, m.p. 88–89°. For analysis, a sample was dried at 56° and 1.0 mm. for 13 hours.

Anal. Calcd. for $C_{17}H_{19}NO_4 \cdot H_2O$: C, 63.93; H, 6.63; N, 4.39; CH_3O, 9.72. Found: C, 63.63; H, 6.34; N, 4.19; CH_3O, 9.71.

When this compound was dried over phosphorus pentoxide at 110° and 1.0 mm. for 5 hours, the base lost the water of hydration to give a gum, $[\alpha]^{26}D$ −97.9° (*c* 1.60, chloroform).

Anal. Calcd. for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36; N, 4.65; CH_3O, 10.30. Found: C, 67.56; H, 6.25; N, 4.55; CH_3O, 10.06.

The ultraviolet absorption spectrum showed maxima at 244 mμ (log ε 3.65) and 297 mμ (log ε 3.71).

Montanine Oxalate.—A solution of 289 mg. of montanine (chloroform solvate) in 15 ml. of dry ether was treated with an equal weight of anhydrous oxalic acid in 10 ml. of dry ether. The precipitate was recrystallized three times from 95% ethanol to give 159 mg. of colorless needle clusters, m.p. 227–229° dec. For analysis, a sample was dried at room temperature and 1.0 mm. for 24 hours.

Anal. Calcd. for $C_{19}H_{21}NO_8 \cdot {}^1/_2H_2O$: C, 56.99; H, 5.54; N, 3.50. Found: C, 56.99; H, 5.63; N, 3.52.

Montanine Perchlorate.—By the procedure outlined for coccinine perchlorate, 96 mg. of base gave 52 mg. of colorless prisms, m.p. 249–250° dec., $[\alpha]^{26}D$ −18.17° (*c* 1.23, methanol). For analysis, a sample was dried at 1.0 mm. for 18 hours at room temperature and 3 hours at 100°.

Anal. Calcd. for $C_{17}H_{19}NO_4 \cdot HClO_4$: C, 50.81; H, 5.02; N, 3.49. Found: C, 50.86; H, 5.02; N, 3.20.

Montanine Picrate.—An ethanolic solution of 200 mg. of montanine (acetone solvate) was treated with 4 ml. of a saturated aqueous solution of picric acid. The gummy precipitate was recrystallized three times from water to give 214 mg. of yellow needles, m.p. 225–226° dec. For analysis, a

sample was dried over phosphorus pentoxide at 110° and 1.0 mm. for 3 hours.

Anal. Calcd. for $C_{17}H_{19}NO_4 \cdot C_6H_3N_3O_7$: C, 52.07; H, 4.16; N, 10.56. Found: C, 52.03; H, 4.01; N, 10.53.

Montanine Methiodide.—A solution of 100 mg. of montanine (hydrate) in 5 ml. of acetone was treated with 4 ml. of methyl iodide and allowed to stand overnight. The acetone and excess methyl iodide were removed by evaporation, and the solid was recrystallized three times from water to give 118 mg. of colorless needles, m.p. 252–254° dec., $[\alpha]^{26}D$ + 118.45° (*c* 2.01, water). For analysis, a sample was dried at 1.0 mm. for 18 hours at 25° and 4 hours at 110°.

Anal. Calcd. for $C_{17}H_{19}NO_4 \cdot CH_3I$: C, 48.77; H, 5.00; N, 3.16. Found: C, 48.73; H, 5.00; N, 3.08.

Montanine Chloroplatinate.—To a solution of 50 mg. of montanine in 15 ml. of hot water was added 0.5 g. of chloroplatinic acid. The resultant precipitate was recrystallized from water to give 56 mg. of orange prisms, m.p. 220–221° dec.

Anal. Calcd. for $(C_{17}H_{19}NO_4)_2 \cdot H_2PtCl_6 \cdot H_2O$: C, 39.62; H, 4.11; N, 2.71; Pt, 18.94. Found: C, 39.61; H, 4.40; N, 2.66; Pt, 18.72.

Dihydromontanine.—Platinum prepared by the reduction of 52.3 mg. of platinum oxide suspended in 10 ml. of glacial acetic acid was employed as the catalyst for the hydrogenation at room temperature and atmospheric pressure of 303 mg. of montanine. The reaction stopped when the sample had absorbed 109% of the theoretical amount of hydrogen. The filtered solution was concentrated to a pale yellow oil which was made basic with 5% sodium hydroxide solution and extracted three times with chloroform. The chloroform extracts were washed with water, dried over anhydrous potassium carbonate and concentrated to 247 mg. of oil which could not be induced to crystallize.

This oil was converted to the **oxalate**, 120 mg., m.p. 198–213° dec., by the procedure used for montanine oxalate. Six recrystallizations from 95% ethanol failed to improve the melting point beyond 203–219° dec. For analysis, a sample was dried at 1.0 mm. for 18 hours at 25° and 4 hours at 110°.

Anal. Calcd. for $C_{19}H_{23}NO_8$: C, 58.01; H, 5.89; N, 3.56. Found: C, 58.16; H, 5.82; N, 3.31.

Natalensine: m.p. 203–203.5°, $[\alpha]^{25}D$ +19.66° (*c* 3.77, methanol).

Anal. Calcd. for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36; N, 4.65; active H, 0.34; CH_3O, 10.30; neut. equiv., 301.3. Found: C, 67.82; H, 6.18; N, 4.51; active H, 0.40; CH_3O, 10.16; neut. equiv., 302.4.

The ultraviolet absorption spectrum showed maxima at 240 mμ (log ε 3.51) and 297 mμ (log ε 3.71).

Natalensine Picrate.—Prepared in aqueous ethanol and recrystallized from aqueous ethanol, the picrate formed yellow plates, m.p. 224–226° dec.

Anal. Calcd. for $C_{17}H_{19}NO_4 \cdot C_6H_3N_3O_7$: C, 52.07; H, 4.18; N, 10.56. Found: C, 51.97; H, 4.24; N, 10.44.

Natalensine Methiodide.—A solution of 163 mg. of natalensine in 5 ml. of acetone was treated with 5 ml. of methyl iodide and allowed to stand at 30° for 2 hours. The crystalline methiodide was obtained on concentration of the reaction mixture and was removed by filtration, 157 mg., m.p. 186–191°. Two recrystallizations from water gave colorless, elongated prisms, m.p. 190–192°.

Anal. Calcd. for $C_{17}H_{19}NO_4 \cdot CH_3I \cdot {}^1/_2H_2O$: C, 47.80; H, 5.13; N, 3.10; I, 28.06; H_2O, 1.99. Found: C, 47.72; H, 5.19; N, 2.89; I, 27.84; H_2O, 1.58.

Dihydronatalensine.—Platinum prepared by the reduction of 101.5 mg. of platinum oxide suspended in 10 ml. of glacial acetic acid was employed as the catalyst for the hydrogenation at atmospheric pressure and room temperature of 224.0 mg. of natalensine. The reduction stopped when the sample had absorbed 103% of the theoretical amount of hydrogen. The filtered solution was concentrated to an oil which was made basic with 5% sodium hydroxide solution and extracted three times with chloroform. The chloroform extracts were washed with water, dried over anhydrous potassium carbonate and concentrated to an oil which was triturated with ethyl acetate to form needles, m.p. 228–228.5°. Recrystallization from ethyl acetate gave colorless needles, m.p. 229–230°.

Anal. Calcd. for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98; N, 4.62. Found: C, 67.33; H, 6.91; N, 4.48.

The ultraviolet absorption spectrum showed a shoulder at 233 mμ (log ε 3.54) and a maximum at 295 mμ (log ε 3.68).

Natalensine *m*-Nitrobenzoate.—A solution of 205.3 mg. of natalensine in 3 ml. of pyridine was refluxed with 250 mg. of *m*-nitrobenzoyl chloride. The reaction mixture was cooled and poured into water. The crystalline precipitate was removed by filtration, washed with 5% sodium carbonate solution and then with water and dissolved in benzene. After the water had been removed by distillation, the remaining benzene solution was passed through a column of 35.0 g. of alumina. Elution with benzene–ethyl acetate (3:1) gave 256.0 mg. of pale yellow oil which crystallized upon trituration with ethanol, m.p. 150–152°. Recrystallization from ethanol gave clusters of fine needles, m.p. 153–154°.

Anal. Calcd. for $C_{24}H_{22}N_2O_7$: C, 63.99; H, 4.92; N, 6.22. Found: C, 64.03; H, 5.02; N, 5.91.

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