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Alkaloids of the Amaryllidaceae. IV. Crystalline Alkaloids of *Ammocharis coranica* (Ker-Gawl.) Herb., *Brunsvigia rosea* (Lam.) Hannibal and Two *Crinum* Species

BY L. H. MASON, E. R. PUSCHETT AND W. C. WILDMAN

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The bulbs of *Brunsvigia rosea* (Lam.) Hannibal (alternative name, *Amaryllis belladonna* L.) have been found to contain three new alkaloids of the Amaryllidaceae which have been named acetylcaranine, ambelline and caranine. Acetylcaranine and caranine also were isolated from the bulbs of *Ammocharis coranica* (Ker-Gawl.) Herb. A fourth new alkaloid designated as crinine was found in trace amounts in the two *Crinum* species studied. Lycorine was present in all bulbs tested. A sixth alkaloid, $C_{17}H_{19}NO_4$, m.p. 198–199°, isolated from *Ammocharis coranica* and the *Crinum* species, possessed physical and chemical properties which agree with those reported for crinamine. The molecular formulas and functional groups of acetylcaranine, ambelline, caranine, crinamine and crinine have been determined.

Extracts of the bulbs of various local Amaryllidaceae, notably *Crinum* species, have been used as medicinal preparations by natives of South Africa for at least two hundred years.[1,2] Although there are no reports of any drug use, crude material from *Brunsvigia rosea* (Lam.) Hannibal (alternative name, *Amaryllis belladonna* L.) was found by Kilmer[3] and Steyn[4] to be toxic to animals, killing them by respiratory paralysis. Neither the chemical constituents nor the physiological action of *Ammocharis* species has been investigated. This paper reports a study of the crystalline alkaloids present in these genera of the Amaryllidaceae.[5]

In addition to the known lycorine and a second alkaloid that we consider identical with crinamine, four new alkaloids of the Amaryllidaceae have been isolated and named acetylcaranine, ambelline, caranine and crinine. Table I records the percentages of these alkaloids (based on wet bulb weight) present in each of the samples investigated. The yields of crystalline alkaloids are low, but they are comparable with those from *Haemanthus*,[6] *Hymenocallis*[7] and other genera of the Amaryllidaceae.[5] Although the *B rosea* reported in this paper was grown domestically, we have found that samples of the same plant obtained from South Africa contain ambelline, caranine and lycorine in comparable amounts, but no acetylcaranine. The *Crinum* species N-40 and N-99 are of South African origin.

Isolation of crude basic material was achieved by a conventional extraction procedure using 1% ethanolic tartaric acid as the solvent. The crude extracts on trituration with ethanol usually deposited crystals of lycorine which were removed by filtration. The filtrate then was concentrated to constant weight, dissolved in benzene or ethyl acetate, and chromatographed on alumina. The crystalline alkaloids obtained by this technique are listed in Table II.

TABLE I

ALKALOIDAL CONTENT OF *Brunsvigia rosea*, *Ammocharis coranica* AND *Crinum* SPP.

Alkaloid	*Brunsvigia rosea* N-28[a]	*Ammocharis coranica* N-76	*Crinum* species N-40	*Crinum* species N-99
Acetylcaranine	0.002	0.010	...	...
Ambelline	.029	...	...	...
Caranine	.007	.008	...	...
Crinamine	...	.006	0.003	0.008
Crinine	...	...	.002	.002
Lycorine	.007	.101	.002	.033

[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.

TABLE II

Alkaloid	Formula	M.p., °C.	$[\alpha]^{\circ}$
Acetylcaranine	$C_{15}H_{14}N(OCOCH_3)(O_2CH_2)$	184–185	−177.5
Ambelline	$C_{15}H_{13}N(OH)(OCH_3)_2(O_2CH_2)$	260–261 dec.	+ 32.3
Caranine	$C_{15}H_{14}N(OH)(O_2CH_2)$	178–180	−196.6
Crinamine	$C_{15}H_{13}N(OH)(OCH_3)(O_2CH_2)$	198–199	+156.6
Crinine	$C_{15}H_{14}N(OH)(O_2CH_2)$	209–210	− 11.1
Lycorine	$C_{15}H_{13}N(OH)_2(O_2CH_2)$	250–255 dec.	− 75.1

Crinine and ambelline are distinctly different from any alkaloids of the Amaryllidaceae reported to date. The melting points of acetylcaranine and caranine are close to that reported by Fragner[8] for belamarine (m.p., *ca.* 181°) which he isolated from *B. rosea*. Unfortunately, he characterized belamarine only by melting point and several color reactions. When acetylcaranine and caranine were subjected to these color reactions, neither alkaloid gave results completely compatible with those described for belamarine.[9] Eliminating belamarine from consideration, caranine and acetylcaranine appear to be two new alkaloids. Crinamine, $C_{17}H_{19}$-

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

(2) T. S. Githens, "Drug Plants of Africa," The University of Pennsylvania Press, The University Museum, Philadelphia, Pennsylvania, 1949, pp. 33, 84.

(3) F. B. Kilmer, *J. Amer. Pharm. Ass.*, **5**, 1202 (1916).

(4) D. G. Steyn, *Rept. Director Vet. Services*, Anderstepoort, **17**, pt. 2, 707 (1931); *C. A.*, **27**, 5421 (1933).

(5) The alkaloids of the Amaryllidaceae have been reveiwed by J. W. Cook and J. D. Loudon in R. H. F. Manske, "The Alkaloids," Vol. II, Academic Press, Inc., New York, N. Y., 1952, p. 331, and by T. A. Henry, "The Plant Alkaloids," 4th ed., The Blakiston Co., Philadelphia, Pennsylvania, 1949, p. 406. For more recent work in this field, see ref. 6, footnote (10); E. Wenkert, Abstracts, Organic Division, National Meeting of the American Chemical Society, September 1954, p. 37-O; H.-G. Boit, *Chem. Ber.*, **87**, 624, 681, 724, 1339, 1448 (1954).

(6) W. C. Wildman and C. J. Kaufman, THIS JOURNAL, **77**, 1248 (1955).

(7) W. C. Wildman and C. J. Kaufman, *ibid.*, **76**, 5815 (1954).

(8) K. Fragner, *Ber.*, **24**, 1498 (1891).

(9) Both amarylline, m.p. 196°, isolated by Fragner[8] from *Amaryllis formosissima* and belamarine were considered by Gorter[10] to be impure lycorine. As suggested by Cook and Loudon,[5] this conclusion is not completely justified. We have isolated lycorine from ten different plant sources in varying states of purity. Our material never melted below 225° and was completely insoluble in ether. Since Fragner states that belamarine is ether soluble, it seems unlikely that it is identical with lycorine.

(10) K. Gorter, *Bull. Jard. Bot. Buitenzorg.*, [3] **2**, 331 (1920).

NO_4, m.p. 193–194°, was isolated by Tanaka[11] from *Crinum asiaticum* L. *var. japonicum*. It has not been isolated since that time although several *Crinum* species have been studied by other investigators.[12–14] Tanaka reported that crinamine contained one methoxyl group, was soluble in chloroform, and was not identical with lycorine or Base IX.[5] We propose that the material $C_{17}H_{19}NO_4$, m.p. 198–199°, which we isolated from *A. coranica* and the two *Crinum* species be considered identical with the material isolated by Tanaka. In addition to the similarity of melting points and identical molecular formula, our compound has one methoxyl group and is soluble in chloroform.[15]

Lycorine was identified by comparison with an authentic sample.[6] The molecular formulas of the new alkaloids were determined by the usual methods. Alcoholic hydroxyl groups were identified by infrared absorption spectra and the preparation of acetyl derivatives which showed absorption at 5.75–5.80 μ. Methoxyl groups were determined by analysis. In no case was the N-methyl group present. All of the new alkaloids possessed a methylenedioxyphenyl group as shown by a positive Labat[16] test for this functional group. Confirmation of this fact was found in the infrared spectrum of each alkaloid, since there was strong absorption at 9.6–9.8 μ and 10.6–10.7 μ.[6] The ultraviolet absorption spectra showed a maximum or shoulder near 240 mμ and a maximum near 295 mμ, both of which seem to be characteristic of all known alkaloids of the Amaryllidaceae containing the methylenedioxyphenyl chromophore. The ultraviolet absorption spectrum of ambelline was anomalous, showing only one maximum at 288 mμ. Each of the new alkaloids absorbed one mole of hydrogen when reduced catalytically.

The relationship of these alkaloids to each other as well as to the remaining alkaloids of the Amaryllidaceae is being investigated. One simple correlation was found when the alcohol group of caranine was acetylated. The product was identical with the pure alkaloid, m.p. 184–185°, which was isolated from *A. coranica* and *B. rosea*. This is the first alkaloid of the family to contain the ester function.

Of the alkaloids discussed in this paper, only crinamine shows hypotensive activity and the action is of short duration. Surprisingly, caranine, crinine and lycorine are not particularly toxic. Ambelline and crinamine are by far the most toxic of the drugs studied. Since ambelline caused death in dogs by respiratory paralysis, it appears likely that the toxicity of extracts of *B. rosea*[3,4] was due to the presence of ambelline.

TABLE III

ISOLATION OF CRUDE ALKALOID FRACTIONS

Species	Source	Stage collected	Wt. processed, g.	Crude alkaloids, %
B. rosea (N-28)	Los Angeles, Cal.	.....	4,512	0.18
A. coranica (N-76)	Natal, South Africa	1 mon. after blooming	318	.64
Crinum sp. (N-40)	Orange Free State, South Africa	After blooming	10,645	.18
Crinum sp. (N-99)	Transvaal, South Africa	Fruiting	2,480	.25

Experimental[17]

Isolation of Crude Alkaloid Fractions.—Since all of the isolation procedures were quite similar, the method for obtaining the crude alkaloid fraction from *B. rosea* (N-28) has been chosen as representative. The bulbs, 4.51 kg., were ground in a Ball and Jewell grinder and extracted twice at 55° with 10 l. of 1% ethanolic tartaric acid solution. The extract was concentrated to 1.8 l. and diluted with 3.4 l. of water. The aqueous solution was divided into two equal parts. Each part was washed five times with 200-ml. portions of chloroform. A test for the presence of alkaloids in this chloroform solution was negative. Each aqueous solution was made basic with solid sodium carbonate and extracted twelve times with 200-ml. portions of chloroform. Each chloroform solution was extracted seventeen times with 200-ml. portions of 2 *N* hydrochloric acid, and the combined aqueous solutions were made basic with solid sodium carbonate. The basic aqueous solution was divided into three parts, and each was extracted eight times with 200-ml. portions of chloroform. The chloroform solutions were combined, dried and concentrated to constant weight, 8.22 g. (0.18%). The same method of extraction was used for the other specimens. A summary of the isolation work is given in Table III.

Isolation of Alkaloids from *B. rosea* (N-28).—A Soxhlet cup was filled with 7.17 g. of the crude alkaloid fraction of *B. rosea* (N-28) and extracted with hot benzene for 36 hours. The cup residue of 33 mg. was discarded. The benzene solution had deposited 764 mg. of insoluble gum in the extraction flask. The solution was decanted from this gum, and the residue was triturated with ethanol to give crude brown solid which was removed by filtration. The crude material was dissolved in dilute hydrochloric acid, heated to boiling, treated with Darco and filtered. The colorless solution was made basic with 10% sodium hydroxide solution, and the precipitated lycorine, 173 mg., m.p. 240–243° dec., was removed by filtration. The benzene solution, containing 6.37 g. of soluble alkaloids, was chromatographed on 400 g. of aluminum oxide (Merck).

Fraction	Eluent	Wt. of concd. eluate, g.	Product
1–12	Benzene	0.345	Fluorescent wax and oil
13–20	10% Ethyl acetate in benzene	.108	94 mg. acetylcaranine, m.p. 180–185°
21–41	10% Ethyl acetate in benzene	.758	264 mg. caranine, m.p. 178–180°
42–49	25% Ethyl acetate in benzene	.110	Oil
50–68	50% Ethyl acetate in benzene	1.715	1.168 g. ambelline, m.p. 250–254° dec.
69–87	Ethyl acetate	0.656	
88–112	10% Ethanol in ethyl acetate	1.695	0.102 g. lycorine, m.p. 252–255° dec.
113–128	50% Ethanol in ethyl acetate	0.588	Oil

(11) K. Tanaka, *J. Pharm. Soc. Japan*, **57**, 139 (1937).

(12) N. Kutani and Y. Matsumoto, *ibid.*, **64**, 239 (1944).

(13) B. Reichert, *Arch. Pharm.*, **276**, 328 (1938).

(14) A. Hunger and T. Reichstein, *Helv. Chim. Acta*, **36**, 824 (1953).

(15) By courtesy of Prof. S. Uyeo, we have received an authentic specimen of crinamine as isolated by Dr. Tanaka. By comparison of infrared spectra and mixture melting point, it has been shown that our crinamine is identical with the authentic material.

(16) A. Labat, *Bull. soc. chim. Biol.*, **15**, 1344 (1932).

(17) All melting points were observed on a Kofler microscope hot-stage equipped with polarizer and are corrected. Analyses were performed by Dr. W. C. Alford and his staff and the Clark Microanalytical Laboratory, Urbana, Illinois. 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.

Isolation of Alkaloids from *A. coranica* (N-76).—Trituration of 1.81 g. of the crude alkaloid fraction with ethanol gave 0.351 g. of insoluble, crystalline material. This was dissolved in dilute hydrochloric acid, heated to boiling with Darco, and filtered. The colorless solution was made basic with 10% sodium hydroxide solution, and the precipitated lycorine was removed by filtration, 0.287 g., m.p. 240–245° dec. The basic material, which was soluble in ethanol, was concentrated to dryness under reduced pressure, dissolved in 100 ml. of dry, thiophene-free benzene, and chromatographed on 224 g. of alumina (Fisher).

Fraction	Eluent	Wt. of concn. eluate, g.	Product
1–5	Benzene	0.005	Oil
6–9	5% Ethyl acetate in benzene	.005	Oil
10–16	10% Ethyl acetate in benzene	.016	Oil
17–19	25% Ethyl acetate in benzene	.006	Oil
20–22	50% Ethyl acetate in benzene	.044	28 mg. acetylcaranine, m.p. 182–183°
23–27	50% Ethyl acetate in benzene	.009	Oil
28–39	Ethyl acetate	.069	23 mg. caranine, m.p. 178–180°
40–43	50% Ethyl acetate in chloroform	.017	Oil
44–53	1% Ethanol in chloroform	.091	17 mg. crinamine. m.p. 193–196°
54–64	5% Ethanol in chloroform	.340	Oil
65–69	50% Ethanol in chloroform	.484	Oil

Isolation of Alkaloids from *Crinum* species (N-99).—Trituration of 3.65 g. of the crude alkaloid fraction with ethanol gave 0.47 g. of crude lycorine. The infrared spectrum of this material was identical with that of an authentic specimen. The filtrate was concentrated to dryness and extracted with benzene for 48 hours in a Soxhlet extractor. The insoluble residue, 0.72 g., contained no lycorine. The benzene-soluble material was chromatographed on 150 g. of Merck aluminum oxide. Elution with ethyl acetate gave 182 mg. of oil which crystallized from ethyl acetate to yield 124 mg. of crinamine, m.p. 192–194°. Elution with 1% ethanol in ethyl acetate gave 146 mg. of oil which crystallized from ethyl acetate to yield 34 mg. of crinine, m.p. 205–210°. Increasing the concentration of ethanol in the eluent of ethanol–ethyl acetate gave oils and an additional 22 mg. of lycorine, m.p. 245–250° dec.

A similar technique was used for the *Crinum* species N-40.

Ambelline.—Crude ambelline was recrystallized from ethanol or ethyl acetate to give colorless plates, m.p. 260–261° dec; $[\alpha]^{26}D$ +32.3° (*c* 1.25, chloroform).

Anal. Calcd. for $C_{18}H_{21}NO_5$: C, 65.24; H, 6.39; N, 4.23; 2 CH_3O, 18.73; act. H, 0.30; mol. wt., 331; neut. equiv., 331. Found: C, 64.93; H, 6.42; N, 4.08; CH_3O 18.76; act. H, 0.34; Rast mol. wt., 332; neut. equiv.,[18] 328.

The ultraviolet absorption spectrum (ethanol) showed a maximum at 288 mμ (log ε 3.14).

Ambelline Hydrochloride.—Gaseous hydrogen chloride was passed into a suspension of 81 mg. of ambelline in 1 ml. of absolute ethanol. The solution was concentrated under reduced pressure to give an oil that was dissolved in acetone. The addition of ether caused the precipitation of 87 mg. of needles, m.p. 227–230° dec. The solid was recrystallized from acetone–ether containing three drops of water, m.p. 227–230° dec.

Anal. Calcd. for $C_{18}H_{21}NO_5 \cdot HCl \cdot H_2O$: C, 56.03; H, 6.27; N, 3.63. Found: C, 56.36; H, 5.92; N, 3.84.

Ambelline Methiodide.—A solution of 100 mg. of ambelline in 30 ml. of hot benzene was treated with 10 ml. of methyl iodide and refluxed for 3 hours. The benzene was removed, and the solid was recrystallized twice from absolute ethanol to give 80 mg. of colorless needles, m.p. 297–298° dec.; $[\alpha]^{26}D$ +14.6° (*c* 0.3, water).

Anal. Calcd. for $C_{18}H_{21}NO_5 \cdot CH_3I$: C, 48.21; H, 5.11; N, 2.96. Found: C, 48.04; H, 5.09; N, 3.06.

Ambelline Perchlorate.—A solution of 0.064 g. of ambelline in 2 ml. of glacial acetic acid was treated with 2.5 ml. of 0.1 *N* perchloric acid in glacial acetic acid. The precipitate, 0.077 g., m.p. 195–196° dec., was recrystallized from water to give 0.065 g. of colorless needles, m.p. 200° dec.

Anal. Calcd. for $C_{18}H_{21}NO_5 \cdot HClO_4$: C, 50.06; H, 5.13; N, 3.24. Found: C, 49.87; H, 5.14; N, 3.29.

Dihydroambelline.—A suspension of 283 mg. of ambelline and 123 mg. of 10% palladium-on-charcoal in 15 ml. of ethanol absorbed one mole of hydrogen at atmospheric pressure and room temperature. The catalyst was removed by filtration, and the residual oil was crystallized from ethyl acetate to give 239 mg. of colorless prisms, m.p. 196–198°. Two recrystallizations from ethyl acetate gave pure **dihydroambelline**, m.p. 198–199°; $[\alpha]^{22}D$ −13.0° (*c* 1.3, chloroform).

Anal. Calcd. for $C_{18}H_{23}NO_5$: C, 64.85; H, 6.95; N, 4.20. Found: C, 64.93; H, 7.04; N, 4.10.

The ultraviolet absorption spectrum (chloroform) showed maxima at 245 mμ (log ε 3.65) and 287 mμ (log ε 3.19).

Ambelline Acetate.—A solution of 267 mg. of ambelline in 5 ml. of pyridine and 4 ml. of acetic anhydride was refluxed for 2.5 hours. The solvent was removed in an air stream. The residue was dissolved in chloroform and washed with concentrated sodium carbonate solution. The solution was dried over anhydrous potassium carbonate and evaporated to dryness, yielding 230 mg. of brown oil which was chromatographed on 20 g. of alumina. None of the fractions could be induced to crystallize.

An **oxalate** of this oily acetate was prepared in dry ether and recrystallized from ethanol, m.p. 163–164°.

Anal. Calcd. for $C_{20}H_{23}NO_6 \cdot C_2H_2O_4 \cdot H_2O$: C, 54.88; H, 5.65; N, 2.91. Found: C, 54.62; H, 5.74; N, 2.73.

Caranine.—Crude caranine, 0.50 g., was dissolved in hot ethyl acetate and decolorized with Darco. On cooling, the solution deposited 0.40 g. of colorless prisms, m.p. 178–180°, which were recrystallized from ethyl acetate for analysis, m.p. 178–180°; $[\alpha]^{27}D$ −196.6° (*c* 2.0, chloroform).

Anal. Calcd. for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16; neut. equiv., 271. Found: C, 70.67; H, 6.29; N, 5.02; neut. equiv., 272.

The ultraviolet absorption spectrum (ethanol) showed a shoulder at 233–236 mμ (log ε 3.47) and a maximum at 292–296 mμ (log ε 3.68).

Caranine Methiodide.—A solution of 140 mg. of caranine in 10 ml. of hot benzene was treated with 5 ml. of methyl iodide. The solution was refluxed for 10 minutes and then concentrated in an air stream to a light tan powder which was recrystallized three times from methanol, m.p. 316–318° dec.

Anal. Calcd. for $C_{16}H_{17}NO_3 \cdot CH_3I$: C, 49.39; H, 4.88; N, 3.39. Found: C, 49.29; H, 4.91; N, 3.59.

Caranine Perchlorate.—A solution of 1.2 mmoles of caranine in glacial acetic acid was treated with 1.2 mmoles of 0.1 *N* perchloric acid in glacial acetic acid. The solution was concentrated to give 414 mg. of solid which was recrystallized twice from absolute ethanol to give 276 mg. of **caranine perchlorate**, changing crystalline form at 260° and gradually charring from 270° upward.

Anal. Calcd. for $C_{16}H_{17}NO_3 \cdot HClO_4$: C, 51.68; H, 4.88; N, 3.77. Found: C, 51.71; H, 4.98; N, 3.81.

Dihydrocaranine.—A solution of 108 mg. of caranine in ethanol absorbed 0.84 mole of hydrogen when reduced at atmospheric pressure and room temperature with 10% palladium-on-charcoal catalyst. The product was recrystallized twice from ether–hexane to give 17 mg. of needles, m.p. 162–163°.

Anal. Calcd. for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.13. Found: C, 70.14; H, 6.77; N, 5.18.

Acetylcaranine.—A solution of 150 mg. of caranine in 4 ml. of pyridine was treated with 3 ml. of acetic anhydride, allowed to stand 16 hours at 25°, and then refluxed for 2

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

hours. The solution was concentrated under reduced pressure to a yellow oil which partially solidified. The oil was dissolved in water and made basic with sodium carbonate. The tan precipitate was removed by filtration and dried (150 mg.). An additional 20 mg. of oily acetate was extracted from the basic solution with chloroform. Both precipitate and oil were crystallized from ether to give 95 mg. of colorless needles, m.p. 184–185°; $[\alpha]^{24}D$ −174.1° (*c* 1.19, chloroform).

Anal. Calcd. for $C_{18}H_{19}NO_4$: C, 68.99; H, 6.11; N, 4.47. Found: C, 68.65; H, 6.26; N, 4.55.

The acetylcaranine isolated from the bulbs by chromatography was recrystallized from ethyl acetate (Darco), m.p. 184–185°; $[\alpha]^{22.5}D$ −177.5° (*c* 0.76, chloroform). This material was identical with the acetylation product of caranine as shown by a comparison of infrared spectra and a mixture melting point determination.

Anal. Calcd. for $C_{18}H_{19}NO_4$: C, 68.99; H, 6.11; N, 4.47. Found: C, 69.24; H, 6.15; N, 4.38.

The ultraviolet absorption spectrum (ethanol) showed a shoulder at 235 mμ (log ε 3.66) and a maximum at 292 mμ (log ε 3.72).

Crinamine.—Crinamine was purified by repeated recrystallization from ethyl acetate to give colorless needles, m.p. 198–199°; $[\alpha]^{28}D$ +156.6° (*c* 1.65, chloroform).

Anal. Calcd. for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36; N, 4.65; CH_3O, 10.30; mol. wt., 301; neut. equiv., 301. Found: C, 67.76; H, 6.40; N, 4.41; CH_3O, 10.15; Rast mol. wt., 266; neut. equiv., 302.

The ultraviolet absorption spectrum (ethanol) showed a shoulder at 234–240 mμ (log ε 3.53) and a maximum at 297 mμ (log ε 3.71).

Crinamine Picrate.—A saturated aqueous solution of picric acid was added to a solution of 51 mg. of crinamine in 1 ml. of ethanol until no further precipitation occurred. The picrate was removed by centrifugation and recrystallized from aqueous ethanol, 73 mg., m.p. 271–272° dec. A second recrystallization gave the pure picrate, m.p. 273–274° dec.

Anal. Calcd. for $C_{17}H_{19}NO_4 \cdot C_6H_3N_3O_7$: C, 52.08; H, 4.18; N, 10.50. Found: C, 51.92; H, 4.31; N, 10.56.

Crinamine Perchlorate.—The solution from the determination of the neutral equivalent was concentrated to dryness in an air stream, and the solid was recrystallized twice from isopropyl alcohol–ethanol, m.p. 201–201.5° dec.

Anal. Calcd. for $C_{17}H_{19}NO_4 \cdot HClO_4$: C, 50.81; H, 5.02; N, 3.49. Found: C, 50.71; H, 5.16; N, 3.47.

Dihydrocrinamine.—A solution of 207 mg. of crinamine in 10 ml. of ethanol absorbed one mole of hydrogen when reduced at atmospheric pressure and room temperature with 60 mg. of prereduced platinum oxide in 5 ml. of ethanol. The catalyst was removed by filtration, and the solution was concentrated in an air stream. Trituration with ethyl acetate produced a colorless solid which was recrystallized from ethyl acetate to give 147 mg. of colorless plates, m.p. 228–230°. Several recrystallizations from ethyl acetate afforded pure dihydrocrinamine, m.p. 232–233°.

Anal. Calcd. for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98; N, 4.62. Found: C, 67.11; H, 6.75; N, 4.47.

Crinamine Acetate.—A solution of 154 mg. of crinamine in 4 ml. of pyridine and 3 ml. of acetic anhydride was allowed to stand for 16 hours at 25° and then was refluxed for 2 hours. The solution was concentrated in an air stream and dried under reduced pressure to yield 212 mg. of brown oil. The oil was partitioned between chloroform and aqueous sodium carbonate. The aqueous layer was extracted twice with chloroform. The combined chloroform extracts were dried over anhydrous potassium carbonate and concentrated in an air stream to 173 mg. of colorless oil. The oil was triturated with acetone to give colorless prisms, m.p. 158–160°, which were sublimed twice for analysis, m.p. 161.5–163°; $[\alpha]^{24}D$ +18.2° (*c* 0.55, chloroform).

Anal. Calcd. for $C_{19}H_{21}NO_5$: C, 66.46; H, 6.16; N, 4.08. Found: C, 66.48; H, 6.25; N, 3.96.

Crinine.—Crinine was recrystallized from acetone to give colorless needles, m.p. 209–210°; $[\alpha]^{28}D$ −11.1° (*c* 1.9, chloroform).

Anal. Calcd. for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16; neut. equiv., 271. Found: C, 70.82; H, 6.55; N, 5.28; neut. equiv., 272.

The ultraviolet absorption spectrum (ethanol) showed maxima at 240 mμ (log ε 3.52) and 296 mμ (log ε 3.72).

Crinine Perchlorate.—The solution from the determination of the neutral equivalent was concentrated in an air stream. The solid was removed by filtration and recrystallized from water to give colorless prisms, m.p. 135–137°.

Anal. Calcd. for $C_{16}H_{17}NO_3 \cdot HClO_4 \cdot {}^1/_2H_2O$: C, 50.46; H, 5.03; N, 3.68; Cl, 9.31. Found: C, 50.45; H, 5.33; N, 3.90; Cl, 9.14.

Dihydrocrinine.—A solution of 73 mg. of crinine in ethanol absorbed 90% of the theoretical amount of hydrogen when reduced with 10% palladium-on-charcoal catalyst at atmospheric pressure and room temperature. The catalyst was removed by filtration, and the solution was concentrated in an air stream. Trituration of the residual oil with ethyl acetate gave 35 mg. of dihydrocrinine, m.p. 212–214°. Two recrystallizations from benzene–cyclohexane did not change the melting point.

Anal. Calcd. for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.13. Found: C, 70.34; H, 7.07; N, 4.83.

Crinine Acetate.—A solution of 150 mg. of crinine in 3 ml. of acetic anhydride and 4 ml. of pyridine was allowed to stand at room temperature for 2 days and then was refluxed for 2 hours. The solvent was removed under reduced pressure. The residual oil was dissolved in chloroform and washed with 5% potassium carbonate solution. The chloroform solution was dried over anhydrous potassium carbonate and concentrated in an air stream to give 188 mg. of yellow oil which crystallized upon trituration with ether. Two recrystallizations from ether gave colorless, elongated prisms, m.p. 143–145°.

Anal. Calcd. for $C_{18}H_{19}NO_4$: C, 68.99; H, 6.11; N, 4.50. Found: C, 68.69; H, 6.08; N, 4.47.

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BETHESDA 14, MARYLAND