disulfide, m.p. 44–46°.[3] There was no depression in melting point when mixed with an authentic sample of di-*p*-tolyl disulfide.

A less soluble fraction, m.p. 132–134°, was also obtained. It weighed 0.250 g. Several recrystallizations from 2-propanol gave an analytical sample, m.p. 132–132.5°.

Anal. Calcd. for $C_{12}H_{11}Br_2NSO_2$: C, 38.45; H, 2.74; Br, 39.45; S, 7.91. Found: C, 38.89, 38.92; H, 2.92, 2.92; Br, 39.73, 39.46; S, 7.95, 8.02.

This compound gave no depression of melting point when mixed with N-tosyl-2,4-dibromoaniline prepared by the tosylation of the amine in pyridine.[12] The infrared absorption curves of the two compounds are identical.

In a similar experiment the ether precipitate of hydrobromides was benzoylated by the method of Schotten–Baumann to give, after recrystallization, 0.84 g. of N-benzoyl-*p*-bromoaniline, m.p. 200–201.5°. This material gave no depression of melting point when mixed with an authentic sample. Infrared data confirmed the identity of this derivative. There was also isolated 0.13 g. of N-benzoyl-2,4-dibromoaniline, m.p. 135–136°,[11] which gave no depression of melting point when mixed with an authentic sample of the benzoyl derivative of 2,4-dibromoaniline.[12] Infrared data confirmed the identity of this compound.

Detosylation of *p*-Toluenesulfonanilide in the Presence of Phenol.—A solution of 0.01 mole (2.5 g.) of *p*-toluenesulfonanilide and 0.02 mole (2.0 g.) of phenol in 23 g. of 30% hydrogen bromide in acetic acid was permitted to stand at 26° for 16 hours. The reaction mixture was poured into 150 ml. of anhydrous ether. The precipitate was filtered, washed with 100 ml. of ether and dried. It weighed 1.48 g. (86% yield), m.p. 283° (dec.).

Acetylation of the hydrobromide by the method of Schotten–Baumann gave 85% yield of acetanilide, m.p. 112.5–113.5°. There was no depression of melting point when this material was mixed with an authentic sample of acetanilide.

(12) We are indebted to Prof. H. R. Snyder, of the University of Illinois, for a sample of 2,4-dibromoaniline.

Detosylation of the other sulfonamides described in Table I was done in identical fashion.

Ethyl N-Carboxymethyl-*p*-aminobenzoate.—A solution of 8.25 g. (0.05 mole) of ethyl *p*-aminobenzoate, 7.45 g. (0.05 mole) of bromoacetic acid and 8.4 g. (0.10 mole) of sodium bicarbonate in 75 ml. of water and 25 ml. of ethanol was warmed on a steam-bath for 90 minutes. The mixture was cooled, filtered and the alcohol removed under reduced pressure. The *p*H of the aqueous solution was adjusted to 5.0 and the solution filtered to give 6.5 g. of product, m.p. 138–149°. An additional 1.5 g. of crystals, m.p. 136–147°, was collected when the *p*H was lowered to 2.0. The total yield was 72%. Two recrystallizations from dilute ethanol raised the melting point to 160–162°.

Anal. Calcd. for $C_{11}H_{13}NO$: C, 59.2; H, 5.9; N, 6.3; neut. equiv., 223.2. Found: C, 59.6, 59.7; H, 6.2, 6.2; N, 5.7, 6.0; neut. equiv., 225.2.

Detosylation of 3-(N-γ-Diethylaminopropyl-*p*-toluenesulfonamido)-4-(N-*n*-propyl-*p*-toluenesulfonamido)-anisole. (a).—A solution of 1.0 g. of 3-(N-γ-diethylaminopropyl-*p*-toluenesulfonamido)-4-(N-*n*-propyl-*p*-toluenesulfonamido)-anisole[9] and 0.9 g. of phenol in 7 ml. of 30% hydrogen bromide in acetic acid after 5.5 hours at 26° was poured into 250 ml. of anhydrous ether. The precipitate which formed was dried under vacuum and then dissolved by stirring with two 35-ml. portions of 0.05% hydrochloric acid. Neutralization, followed by extraction, gave a yellow oil, a portion of which rapidly darkened when exposed to the air. After drying at 0.1 mm. for 2 hours at 60° it weighed 0.58 g.

Anal. Calcd. for $C_{24}H_{27}N_3O_3S$: C, 64.39; H, 8.33; S, 7.16. Found: C, 64.70, 64.03; H, 8.03, 8.21; S, 7.23.

(b).—A similar experiment was permitted to stand at 26° for 3.5 days. When worked up as described above there was isolated 0.44 g. of a brown oil. Distillation of this material gave 0.21 g., b.p. 170–176° (0.7 mm.).

Anal. Calcd. for $C_{17}H_{31}N_3O$: C, 69.58; H, 10.65. Found: C, 70.27; H, 10.60; S, 0.

KALAMAZOO, MICHIGAN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE UNIVERSITY]

Alkaloid Studies. I. The Isolation of Pilocereine from the Cactus *Lophocereus schottii*[1]

BY CARL DJERASSI, N. FRICK[2] AND L. E. GELLER[3]

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The isolation of a crystalline alkaloid $C_{30}H_{42}O_4N_2$, termed pilocereine, from the cactus *Lophocereus Schottii* and its occurrence in the plant tissues is described. The alkaloid has been characterized by a number of derivatives and the nature of the functional groups has been investigated. Both nitrogen atoms are tertiary, one forming part of a heterocyclic ring, while of the four oxygen atoms, two are present as methoxyl groups, one as a phenolic hydroxyl group and the fourth appears to be present in an ether linkage.

The hallucinatory principle (mescaline) present in certain *Lophophora* species first stimulated research on cactus alkaloids[4] and a whole series of closely related alkaloids has subsequently been isolated and identified, all of them possessing a rather simple structure based on a single phenylethylamine or tetrahydroisoquinoline nucleus. According to Britton and Rose's classification,[5] the genus *Lophophora* (also referred to as *Anhalonium*) belongs to the subtribe *Echinocactanae* of the *Cactaceae* family and with few exceptions, it has only been this particular genus which has occupied the attention of alkaloid chemists. The giant cacti, which occur so widely in the southwestern United States and particularly in the semi-arid regions of Mexico, Central and South America, are encompassed in 38 genera[5] of the subtribe *Cerenae*. With one exception (*vide infra*), the few chemical studies of this subtribe have been limited to one species each of the genera *Pachycereus*[6] and *Carnegiea*[7] and to Reti's[4,8] investigations of Argentinian *Trichocereus* species; in all instances, the alkaloids isolated were found to belong to the β-phenylethylamine or isoquinoline group.

In view of the fact that the giant cacti of the subtribe *Cereanae* are comparatively readily accessible since many of them are indigenous to Mexico, a

(1) This work has been supported by a grant from the American Heart Association, Inc., to which we are greatly indebted.

(2) Postdoctorate Fellow, 1952–1953.

(3) Predoctorate Fellow, 1952.

(4) An excellent review on cactus alkaloids has been published by L. Reti in L. Zechmeister's "Progress in the Chemistry of Organic Natural Products," Vol. VI, Springer, Vienna, 1950, pp. 242–289.

(5) N. L. Britton and J. N. Rose, "The Cactaceae," Vols. I–IV, Carnegie Institution of Washington, Washington, D. C., 1919–1923.

(6) G. Heyl, *Arch. Pharm.*, **239**, 451 (1901).

(7) G. Heyl, *ibid.*, **266**, 668 (1928).

(8) L. Reti and J. A. Castrillon, THIS JOURNAL, **73**, 1767 (1951).

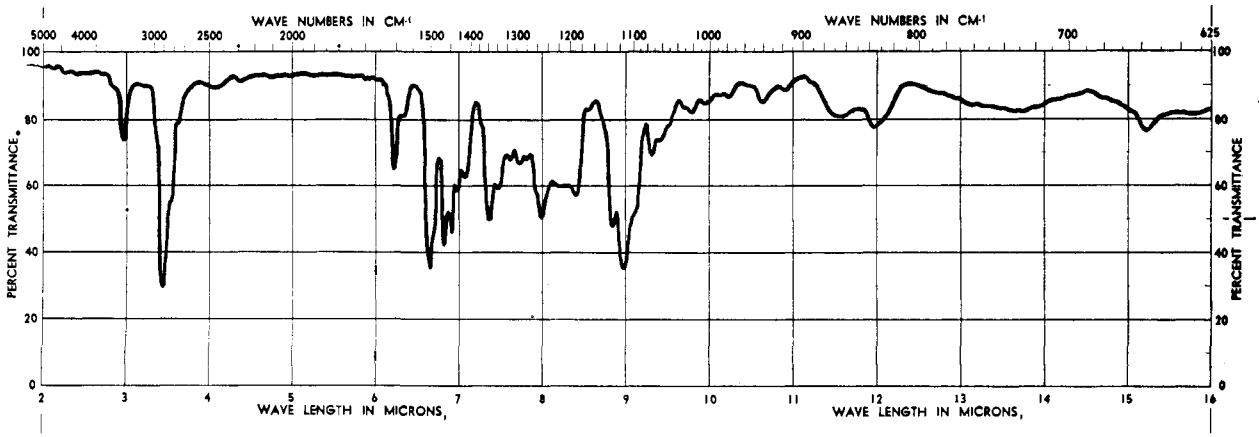

Fig. 1.—Infrared absorption spectrum of pilocereine in chloroform solution (0.1 mm. cell.)

study has been undertaken in this Laboratory of some of the natural products occurring in such plants. Particular emphasis has been placed on triterpenes[9] and alkaloids and the present paper deals with the isolation of an alkaloid of unknown constitution from the cactus *Lophocereus schottii*. Our attention was first directed at this plant when it was noted that Heyl[6] in an investigation of this cactus[10] reported the presence of 5.8% of an amorphous alkaloid, m.p. 82–86°, which he called pilocereine. The alkaloid could not be crystallized nor could crystalline derivatives be obtained, but according to Heyl it possessed the empirical formula $C_{30}H_{44}O_4N_2$. The significance of this observation was not apparent at that time, since the structures of the various cactus alkaloids had not yet been elucidated, and in fact it seems to have escaped general notice. However, if correct, this would indicate that a new type of alkaloid is present in cacti since none of the known cactus alkaloids[4] contains more than thirteen carbon atoms.

Lophocereus schottii occurs in southern Arizona, chiefly in the Organ Pipe Cactus National Monument, but efforts to obtain specimens from that locality have been unsuccessful since the plant is rigidly protected in this country. However, it is very abundant in northern Mexico,[11] especially in the states of Sonora (where it is known as "sinita"), Baja California and Sinaloa and it has been possible to secure considerable amounts of this plant from two localities in Sonora through the kind coöperation of Dr. R. R. Humphrey of the University of Arizona.

Only three studies[4] appear to have been made of the location of alkaloids in cactus tissue and these have indicated that the major portion exists in the cortex. It is of considerable interest to note, therefore, that a similar examination of *Lophocereus Schottii* stems has shown that the major part of the alkaloids resides in the skin (green epidermis), a minor part in the cortex and practically no alkaloids in the central core (vascular cylinder and pith). From a practical standpoint, it was not feasible to remove the skin from the plants and in larger scale experiments, the complete stems were reduced in size, dried and extracted exhaustively with ethanol. The crude alkaloid fraction (*ca.* 3.7%) obtained in the conventional manner as described in the experimental section, was difficult to crystallize and closely followed the description given by Heyl[6] for his amorphous alkaloid. That this fraction was not homogeneous was demonstrated readily by chromatography whereupon it was possible to separate in approximately 0.5% over-all yield (based on dry plant) a crystalline optically inactive alkaloid with m.p. 177°. Since it is obvious that Heyl's "pilocereine"[6] represents a mixture, we have retained this name for the pure alkaloid which by analysis was found to possess the empirical formula $C_{30}H_{42}O_4N_2$. Titration and preparation of a series of crystalline derivatives (hydrochloride, perchlorate, oxalate, methiodide) demonstrated the presence of two basic nitrogen atoms, which is in marked contrast to the presently known cactus alkaloids[4] which possess only one nitrogen atom. Pilocereine hydrochloride exhibits an interesting hypotensive action in cats[12] and a report of the pharmacological results will be published elsewhere.

The infrared spectrum (Fig. 1) of pilocereine shows the presence of a hydroxyl function and an aromatic or heterocyclic nucleus.[13] Of the four oxygen atoms, two were shown by analysis to be present as methoxyl groups, while the formation of a mono-acetate, which does not exhibit any more a free hydroxyl band in the infrared, proved the presence of a hydroxyl group. The infrared carbonyl band of this acetate is found at 5.68 μ, characteristic of phenolic acetates[14] while alcoholic acetates absorb near 5.80 μ.[14] The hydroxyl group, therefore, is clearly attached to an aromatic ring which may be kryptophenolic in character since it gave no color with ferric chloride, did not react with diazomethane and gave only a weak red color with Millon's reagent. Methylation of pilocereine with dimethyl sulfate was unsuccessful since only water-soluble material was obtained, apparently due to

(9) For the first paper see C. Djerassi, L. E. Geller and A. J. Lemin, THIS JOURNAL, **75**, 2254 (1953).

(10) Referred to at that time as *Pilocereus Sargentianus Orcutt.*

(11) H. Bravo, "Las Cactaceas de Mexico," Mexico, D. F., 1937, p. 303.

(12) We are indebted to Dr. K. K. Chen of the Lilly Research Laboratories for this information.

(13) L. Marion, D. A. Ramsey and R. N. Jones, THIS JOURNAL, **73**, 305 (1951).

(14) R. N. Jones, P. Humphries and K. Dobriner, *ibid.*, **72**, 956 (1950).

quaternary salt formation. However, the presence of the phenolic group was established by methylation with phenyltrimethylammonium hydroxide,[15] a method which has proved very useful in the conversion of morphine to codeine, since this yielded a nicely crystalline methyl ether. The fourth, inert oxygen is probably present in an ether linkage, and this is supported by the observation that pilocereine is unaffected by boiling alkali or lithium aluminum hydride.

The absence of an NH group, indicated by the various infrared spectra, was confirmed by the formation of a dimethiodide and the detection of one N-methyl group. Pilocereine is thus a ditertiary base with one of the nitrogen atoms forming part of a heterocyclic ring, while the other tertiary amine bearing the N-methyl group may conceivably be part of a tetrahydroisoquinoline nucleus so common among the simpler cactus alkaloids.[4] The nature of the heterocyclic ring has not been established yet, although the yellow color of the methiodide would point toward a quinoline nucleus. The ultraviolet absorption spectrum of pilocereine and its derivatives (Fig. 2) does not settle this point, probably because of the overlapping effects of the heterocyclic and phenolic nuclei. The maximum of pilocereine at 284 mμ is compatible with both a phenolic (free or methylated) and a quinoline system, but the latter's second maximum near 310 mμ[16] is not noticeable nor is there observed any appreciable change when the spectrum is measured in basic or acidic solution.[16] A maximum near 315 mμ is, however, apparent in the spectra of the acetate and methiodide (in alkaline solution).

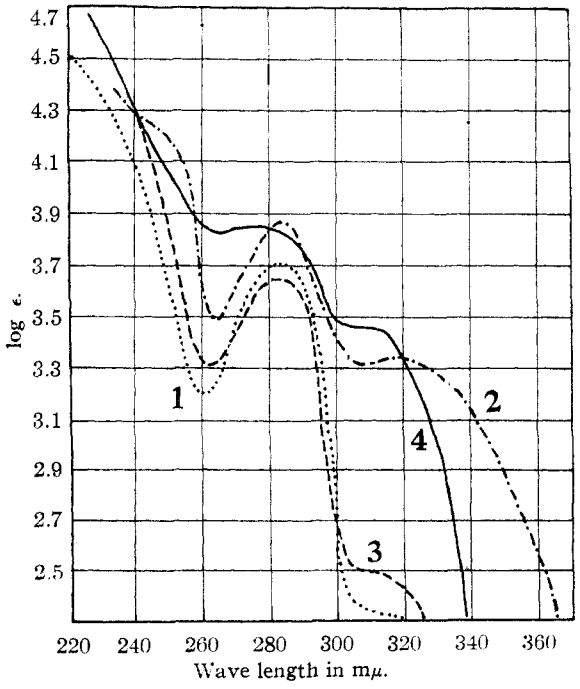

Fig. 2.—Ultraviolet absorption spectra in absolute ethanol of: 1, pilocereine; 2, pilocereine acetate; 3, pilocereine methiodide; 4, pilocereine methiodide in alkaline solution.

A more precise description of the basic skeleton present in pilocereine must await the results of degradation experiments which are now in progress.

(15) W. Rodionow, *Bull. soc. chim.*, [4] **39**, 305 (1926).

(16) G. W. Ewing and E. A. Steck, THIS JOURNAL, **68**, 2181 (1948).

Experimental[17]

Location of Alkaloids in Plant Tissues.—These experiments were carried out with a specimen of *Lophocereus schottii*, which was collected in April, 1952, by Dr. R. R. Humphrey (University of Arizona) approximately 15 miles southwest of Pitiquito, Sonora, along the road to Puerto Libertad. The stem was cut into smaller pieces which were dried for 4 weeks in the sun in Arizona before being shipped to Detroit. The spines were removed and the stem cuttings were separated into three parts: (a) skin (green epidermis), (b) cortex and (c) central core (vascular cylinder and pith), all of which were worked up separately in an identical fashion, the details of which follow.

The plant material was put through a manually operated kitchen meat grinder and then dried to constant weight at 80° which usually required 24 hours. The dried pieces were reduced further in size in a Waring blendor and then extracted continuously in a Soxhlet extractor with 95% ethanol for 20 hours. The alcoholic extract was evaporated to dryness and partitioned between ether and 5% hydrochloric acid. The ether layer was extracted repeatedly with 5% hydrochloric acid, the pooled extracts were washed once with ether and then made alkaline with ammonium hydroxide. The crude alkaloids were removed by extraction with ether, which was washed until neutral, dried and evaporated. The following results were obtained (all weights in grams).

	Sun-dried plant	Dry plant	Alcoholic ex. tract	Crude alkaloids
Skin	586	165	39	11 (6.7%)
Cortex	1106	279	30	3 (1.1%)
Vascular cylinder and pith	270	112	7	0.2 (0.2%)

Chromatographic purification (*vide infra*) of the crude alkaloids from the skin and cortex furnished crystalline pilocereine in each instance.

Isolation of Pilocereine from *Lophocereus schottii*.—Small scale experiments on a sample of *Lophocereus schottii* obtained from Sr. Lauro Paredes of Hermosillo, Sonora, indicated that the alkaloid content did not differ appreciably from that of the above described material collected near Pitiquito. As a result, a 50-kg. quantity of this cactus was collected by Dr. R. R. Humphrey in August, 1952, about 10 miles north of Hermosillo, Sonora, on the road to Nogales and the stems reached Detroit approximately 3 weeks later. Through the kindness of Dr. J. Controulis of Parke, Davis & Co., this material was ground and dried to constant weight in their pilot plant and the dried plant has been stored in the cold room without any apparent deterioration.

One kilogram of this dried plant material was extracted continuously with alcohol, the latter was evaporated and the residue was distributed between ether and 5% hydrochloric acid, a small amount of insoluble resinous material having been filtered and discarded. The ether solution was extracted several times with dilute acid and the combined acid extracts were made alkaline with ammonium hydroxide which caused the separation of nearly black, gummy material. Thorough extraction with ether did not dissolve all of this material and any insoluble material was discarded together with the dark aqueous layer. The ether extract was washed well with water, dried and evaporated, yielding 37.2 g. of crude alkaloid fraction. This material dissolved in 1 l. of benzene, was chromatographed on 1.06 kg. of alumina (activity III)[18] and all of the benzene–ether (1:1) eluates which were semi-crystalline were combined (15.6 g.) and crystallized from ethyl acetate yielding 5.0 g. (0.5% based on dry cactus) of crystalline pilocereine with m.p. 168–170°. The analytical sample was obtained as colorless needles after two recrystallizations from ethyl

(17) Melting points are corrected. Infrared spectra were obtained on a Baird Associates double beam recording spectrophotometer. We are indebted to Mr. Joseph F. Alicino, Metuchen, N. J., for the microanalyses.

(18) H. Brockmann and H. Schodder, *Ber.*, **74**, 73 (1941).

acetate and two from ethanol; m.p. 176.5–177°, no optical rotation, infrared spectrum (chloroform solution)—Fig. 1, ultraviolet absorption spectrum (absolute ethanol solution)—Figure 2 (maximum at 284 mμ, log ε 3.72). Millon's reaction gave a light red color which became somewhat more intense on warming and eventually turned to yellow.

Anal. Calcd. for $C_{30}H_{42}O_4N_2$: C, 72.84; H, 8.56; N, 5.66; 2-CH_3O, 12.56; (N)CH_3, 3.04; mol. wt., 494. Found: C, 73.06; H, 8.77; N, 5.82; CH_3O, 13.00; (N)-CH_3, 2.80; Rast, mol. wt., 532.

The neutral equivalent was determined by the perchloric acid[19] procedure in acetic acid solution and demonstrated the presence of two basic functions: 8.9 mg. of alkaloid required 2.46 cc. of 0.0146 *N* perchloric acid. 19.0 mg. of alkaloid required 5.26 mg. of 0.0146 *N* perchloric acid. Neutral equivalent, calcd. 247.3; found: 247.9, 247.4.

Pilocereine Dihydrochloride.—A solution of 110 mg. of pilocereine in 10 cc. of ether was treated with 10 cc. of ether saturated with hydrogen chloride, which resulted in the immediate precipitation of colorless crystals. Filtration and recrystallization[20] from methanol–ethyl acetate yielded 80 mg. of the **dihydrochloride dihydrate** with m.p. 228–232° (dec.), which was dried for 24 hours at 85° and 2 mm. An aqueous solution gave no color with ferric chloride.

Anal. Calcd. for $C_{30}H_{42}O_4N_2 \cdot 2HCl \cdot 2H_2O$: C, 59.65; H, 8.02; N, 4.64; Cl, 11.75. Found: C, 59.35; H, 8.06; N, 4.76; Cl, 12.26.

The water of crystallization was lost on drying the sample at 137° over phosphorus pentoxide.

Anal. Calcd. for $C_{30}H_{42}O_4N_2 \cdot 2HCl$: C, 63.48; H, 7.82; loss of $2H_2O$, 5.97. Found: C, 63.52; H, 7.79; $2H_2O$, 6.16.

Pilocereine Diperchlorate.—To an acetic acid solution of 100 mg. of pilocereine was added 27.7 cc. of 0.0146 *N* perchloric acid in acetic acid and the solution was evaporated to dryness *in vacuo*. Two recrystallizations from methanol–ethyl acetate furnished 0.13 g. of crystals with m.p. 214–217° (dec.), which were dried over phosphorus pentoxide for 4 hours at 137° before analysis.

Anal. Calcd. for $C_{30}H_{42}O_4N_2 \cdot 2HClO_4$: C, 51.79; H, 6.37; N, 4.03. Found: C, 51.49; H, 6.30; N, 4.09.

Pilocereine Dioxalate.—An ethereal solution of 120 mg. of pilocereine upon treatment with a similar solution of 100 mg. of oxalic acid furnished 140 mg. of the **oxalate dihydrate** which decomposed at 154–163° on quick heating. A sample was recrystallized three times from ethanol for analysis and dried 24 hours at 85° and 1 mm.; the decomposition point depended markedly upon the rate of heating: 158–163° (rapid heating), 198–200° (slow heating).

Anal. Calcd. for $C_{30}H_{42}N_2O_4 \cdot 2C_2H_2O_4 \cdot 2H_2O$: C, 57.44; H, 7.09; N, 3.94. Found: C, 57.51; H, 6.74; N, 3.86.

Pilocereine Dimethiodide.—A mixture of 100 mg. of pilocereine, 2 cc. of methyl iodide and 5 cc. of benzene was kept for 5 hours at room temperature and filtered. After one low-temperature crystallization from methanol–ethyl acetate, there was obtained 150 mg. of the yellowish *dimethiodide dihydrate* which decomposed at 230–240°. The substance was quite sensitive to heat and the analytical sample was twice recrystallized from the above solvent pair below 25° and dried at 25° and 1 mm. for 24 hours over phosphorus pentoxide; yellowish needles, decomposing at 233–244°.

Anal. Calcd. for $C_{30}H_{42}O_4N_2 \cdot 2CH_3I \cdot 2H_2O$: C, 47.18; H, 6.44; I, 31.16. Found: C, 47.43, 46.98; H, 6.45, 6.49; I, 31.01.

A methanol solution of the methiodide is nearly colorless but turns bright yellow on addition of one drop of sodium hydroxide solution; the color is discharged on acidification. The ultraviolet absorption spectrum of the methiodide, shown in Fig. 2, exhibits a single maximum at 284 mμ, log ε 3.65 and a plateau at 305–320 mμ (log ε *ca.* 2.5). A much higher extinction value (log ε 3.45) for the plateau was observed in ethanolic sodium hydroxide solution; on long standing (2–3 weeks) marked changes in the spectrum are observed which point toward the formation of a pseudo-base structure and chemical confirmation for this supposition is now under way.

Pilocereine Acetate.—A mixture of 200 mg. of pilocereine, 2 cc. of pyridine and 1 cc. of acetic anhydride was allowed to stand at room temperature overnight and then evaporated to dryness *in vacuo*. Crystallization of the light brownish, oily residue from ether–acetone furnished 100 mg. of colorless crystals with m.p. 181–182°. The analytical sample was twice recrystallized from ether–acetone and dried at 80° and 2 mm. for 24 hours; m.p. 186–186.5°, no optical rotation, $\lambda_{max}^{CS_2}$ 5.68 μ, but no free hydroxyl band, λ_{max}^{EtOH} 284 mμ, log ε 3.84 and plateau at 310–330 mμ, log ε 3.3 (Fig. 2). The spectrum was not changed in acid solution.

Anal. Calcd. for $C_{32}H_{44}O_5N_2$: C, 71.61; H, 8.26; N, 5.22; acetyl, 8.02; neut. equiv., 268. Found: C, 71.91; H, 8.14; N, 5.35; acetyl, 7.82; neut. equiv.,[19] 262.

The acetate was saponified by refluxing for 1 hour with 2% methanolic potassium hydroxide, whereupon pilocereine, m.p. 172–174°, was isolated.

Pilocereine Methyl Ether.—A mixture of 25 g. of methyl benzenesulfonate and 18 g. of dimethylaniline was warmed on the steam-bath until it solidified to a crystalline mass. One recrystallization from ethanol furnished 36 g. of the salt with m.p. 191° and this material was used in the methylation which was carried out essentially according to the method of Rodionow.[15]

A solution of 50 mg. of sodium in 1 cc. of absolute ethanol was treated with 550 mg. of the above salt in 1.5 cc. of absolute ethanol. The precipitated sodium benzenesulfonate was filtered, washed with a small amount of absolute ethanol and to the filtrate was added 420 mg. of pilocereine. The mixture was heated to 110° in an oil-bath until all the alcohol had distilled and was then maintained at that temperature for an additional hour. After cooling, the residue was taken up in ether, washed well with water, dried and evaporated. The crystalline mixture thus obtained was chromatographed on 15 g. of alumina (activity III[18]) and first developed with hexane–benzene (1:1) and benzene. Evaporation of these eluates to dryness and recrystallization from hexane furnished 230 mg. of the methyl ether with m.p. 103–105°, resolidifying and then melting at 150.5–151°. The analytical sample was recrystallized three times from hexane whereupon it showed the double melting point 103–105° and 153.5–154.5°. The first melting point appears to involve the loss of solvent of crystallization. The infrared spectrum showed the complete absence of free hydroxyl absorption while the ultraviolet absorption spectrum was quite similar to that of pilocereine; maxima at 282 and 320 mμ, log ε 3.68, 2.05 and minima at 248 and 310 mμ, log ε 3.16, 2.0.

From the benzene–ether eluates there was recovered 90 mg. of unreacted pilocereine, m.p. 171–173°.

Anal. Calcd. for $C_{31}H_{44}O_4N_2$: C, 73.19; H, 8.72; 3 CH_3O, 18.31. Found: C, 73.58; H, 8.65; CH_3O, 18.03.

Miscellaneous Experiments with Pilocereine.—The alkaloid was recovered unchanged in over 85% yield after (a) refluxing with excess lithium aluminum hydride in ether solution for 5 hours; (b) treatment with excess diazomethane at 20° for 24 hours; (c) refluxing for 24 hours under nitrogen with 10% ethanolic sodium hydroxide solution.

Pilocereine gave a negative test for the methylenedioxy group,[21] did not form a crystalline picrate and was converted into completely water-soluble material when it was treated with dimethyl sulfate in alkaline solution. Refluxing with hydriodic acid under nitrogen for 2.5 hours led to dark colored resinous material, which could not be purified even after chromatography.

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

(20) The hydrochloride decomposed slowly on warming and it was necessary, therefore, to recrystallize the substance by dissolving at room temperature and cooling to 0°.

(21) G. O. Gaebel, *Arch. Pharm.*, **248**, 225 (1910).