acid, the dihydrovellosiminol obtained melted from 150–160° and had $[\alpha]^{28}\mathrm{D}$ +60°.

B. **From Vellosiminol.**—A solution of 25 mg. of vellosiminol in 5 ml. of glacial acetic acid was hydrogenated at atmospheric pressure using 10 mg. of platinum oxide catalyst. The product was recrystallized twice from absolute ethanol and dried at 100° (0.1 mm.; 17 hr.), m.p. 154–163°, $[\alpha]^{21}\mathrm{D}$ +64°.

O-Acetyldihydrovellosiminol.—A solution of 120 mg. of dihydrovellosiminol, $[\alpha]^{24}\mathrm{D}$ +48°, in 2 ml. of acetic anhydride and 2 ml. of pyridine, was allowed to stand at room temperature for 6 hr. The slightly brown solution was made alkaline with cold, dilute ammonium hydroxide and extracted with chloroform which gave an oil on evaporation. The oil was dissolved in a small amount of ethanol and the solution was diluted with water, giving a precipitate which was crystallized from carbon disulfide. Two recrystallizations from methanol gave prisms, m.p. 238–240°[13] after drying at 105° (0.1 mm.; 20 hr.).

Anal. Calcd. for $C_{21}H_{26}N_2O_2$: C, 74.5; H, 7.7. Found: C, 74.3; H, 7.4.

Geissolosimine (VII).—The alkaloid previously designated as D_2[2] was recrystallized several times from 4:1 methanol-water and dried at 125° (0.1 mm.; 24 hr.), m.p. 140°; $[\alpha]^{22}\mathrm{D}$ +70.4°; ultraviolet absorption: $\lambda_{\max}^{\text{ethanol}}$ 250 mμ (ϵ 13,600), 284 (6700), 292 (7000); in 1.0 *N* ethanolic hydrochloric acid, $\lambda_{\max}$ 268 mμ (ϵ 6300), 289 (4700).

Anal. Calcd. for $C_{38}H_{44}N_4O \cdot {}^1/_2H_2O$: C, 78.7; H, 7.8; N, 9.7; O, 3.8. Found: C, 78.6; H, 8.1; N, 9.7; O, 3.9.

The previous values reported[2] for alkaloid D_2 were m.p. 133–135°, $[\alpha]^{25}\mathrm{D}$ +74°, and the molecular formula $C_{39}H_{46}N_4O \cdot {}^1/_2H_2O$.

Acid Cleavage of Geissolosimine.—A solution of 600 mg. of geissolosimine in 5 ml. of concentrated hydrochloric acid was allowed to stand at room temperature for 15 min. and then was poured into a mixture of 40 ml. of concentrated ammonium hydroxide and ice. Extraction with chloroform and evaporation of the chloroform gave 600 mg. of a gum which was dissolved in 100 ml. of 0.5 *M* sodium dihydrogenphosphate. The solution was adjusted to pH 6 with sodium hydroxide and extracted continuously with ether to give 500 mg. of a mixture of vellosimine and unchanged geissolosimine on evaporation of the ether. The pH was changed to 10, and continuous extraction with ether gave 100 mg. of crude geissoschizoline. Chromatography on 3 g. of neutral alumina and elution with 100 ml. of 1:1 chloroform–benzene gave 70 mg. of crystalline **geissoschizoline (VIII)**, identical in all respects with an authentic sample.[2]

Chromatography of the vellosimine–geissolosimine fraction on neutral alumina and elution with 100 ml. of 1:1 chloroform–benzene gave 50 mg. of crystalline **vellosimine,** identical with the vellosimine described above.

Preparation of Geissolosimine (VII) from Vellosimine (I) and Geissoschizoline (VIII).—A solution of 65 mg. of vellosimine and 100 mg. of geissoschizoline chloroformate in 10 ml. of 1.5 *N* acetic acid was allowed to stand at room temperature for 2 days. The solution was made alkaline with ammonium hydroxide, the resulting precipitate was dissolved in 4:1 methanol–water, and the solution was seeded with geissolosimine. After standing for 1 day, 20 mg. of crude geissolosimine crystallized and was recrystallized from 4:1 methanol–water, m.p. 140°. This material was identical with the geissolosimine described above.

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[13] O-Acetyldeoxydihydrosarpagine has been reported to melt at 253–254° [M. F. Bartlett, R. Sklar, and W. I. Taylor, *J. Am. Chem. Soc.*, **82**, 3790 (1960)] and O-acetylnormacusine-B at 192° and 219–220°.[4] Our material is undoubtedly a mixture of these C_{20} epimers.

Lythraceae Alkaloids. I. Isolation and Structural Studies of the Alkaloids of *Decodon verticillatus* (*L.*) *Ell.*[1]

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Seven alkaloids have been isolated from *Decodon verticillatus* (*L.*) *Ell.* All are pentacyclic and contain the following structural features: a six-membered or greater lactone ring, the ether oxygen of which is derived from a secondary alcohol; a tertiary nitrogen atom; and two nonconjugated aromatic rings substituted with methoxyl and/or hydroxyl groups. Two of the alkaloids, vertine and verticillatine, have an additional olefinic bond located between one of the aromatic rings and the lactone carbonyl. This suggests that the lactone carbonyl group is gamma with respect to an aromatic ring in all *Decodon* alkaloids. The data are consistent with II as the part structure for vertine and verticillatine. The other alkaloids, with the possible exception of decaline and vertaline, may be represented by II also except that the cinnamic ester double bond is saturated.

Although some *Lythraceae* species have been investigated for alkaloidal content,[2] no structural investigation has been carried out on this plant family. We have undertaken an investigation of *Lythraceae* in hopes of finding alkaloids with unique structures and physiological activity. In this paper we wish to report structure studies on the alkaloids of *Decodon verticillatus* (*L.*) *Ell.* ("water oleander" or "swamp loosestrife"), a plant which occurs in moderate amounts in some swampy areas near Tallahassee.

The isolation of the alkaloid fraction was carried out in the usual way by extraction with methanol or chloroform followed by acid and base fractionation. Chloroform was found to be a more satisfactory extraction solvent because the alkaloids, extracted in equally good yield, were not accompanied by large quantities of nonbasic substances which tend to form very stable emulsions at later stages of the fractionation.

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[1] Supported by a Frederick Gardner Cottrell grant from the Research Corporation and by a grant (MY-4748) from the U.S. Public Health Service. Presented in part at the 141st National American Chemical Society Meeting, Washington, D. C., p. 13-O of the abstracts.

[2] Technical Bulletin 1234, U.S. Department of Agriculture, Washington, D. C., p. 143.

TABLE I

YIELD OF ALKALOIDS FROM *Decodon verticillatus* AT VARIOUS TIMES OF THE YEAR

Date collected	Dried plant (g.)	Alkaloid (g.)	Yield (%)
5-8-60	4090	4.48	0.09
6-20-60	5000	3.20	.06
7-25-60	5000	20.99	.42
8-27-60^a	5230	20.93	.40
9-18-60^a	5000	17.0	.34
10-8-60^b	6360	14.2	.22
10-26-60^b	5000	3.8	.08

^{a} In flower. ^{b} In fruit.

Table I shows that the yield of basic extract varies during the growing season and reaches a maximum during the flowering period. Collections made late in the year were not only low in alkaloid content, but also exhibited some variation in the relative amounts of the alkaloids. It is of interest that a sample of the total alkaloid[3] extracted from *Decodon verticillatus* collected in the fall of 1958 in New Jersey consisted of the same alkaloids as were isolated from Florida collections. Thus it appears that climate has little effect on the alkaloids produced in the plant.

TABLE II

PHYSICAL CONSTANTS FOR THE DECODON ALKALOIDS (IN ORDER OF ELUTION)

Alkaloid	Formula	Melting point	Specific rotation^a	Percent of total alkaloids
Decaline	$C_{26}H_{31}NO_5$	80–81°^{b} 102–118°	−136°	0.7
Vertaline	$C_{26}H_{31}NO_5$	194°	−170°	0.5
Decinine	$C_{26}H_{31}NO_5$	222°	−142°	7.0
Decamine	$C_{26}H_{31}NO_5$	222°	−145°	0.5
Vertine	$C_{26}H_{29}NO_5$	245°	+ 39°	0.5
Decodine	$C_{25}H_{29}NO_5$	193°	− 97°	6.4
Verticillatine	$C_{25}H_{27}NO_5$	312°	+119°^{c}	10.2

^{a} In chloroform. ^{b} Solvated. ^{c} As hydrochloride salt in methanol.

Isolation of the seven alkaloids listed in Table II was effected by chromatography and fractional crystallization. It was possible to separate the alkaloids with no hydroxyl groups or one hydroxyl group from those with two hydroxyl groups using alumina neutralized with ethyl acetate. There was some fractionation within each of these main groups making it possible to isolate some pure compounds by fractional crystallization. The filtrates from each of these main groups were combined and rechromatographed separately on Woelm neutral alumina[4], an alumina which was effective in separating the very closely related alkaloids in each of these two groups and the pure alkaloids were obtained by fractional crystallization.

The presence of a tertiary nitrogen atom in all these alkaloids was shown by the isolation of basic compounds on treatment with acetic anhydride. N-Methyl analyses were somewhat ambiguous as close to 50% of theoretical for one N-methyl was obtained in some cases.[5] N.m.r. resolved this difficulty in that none of the compounds had the strong signal at 7.8 τ expected for methyl-on-nitrogen.[6a] The base strengths of decodine and decinine were determined in 50% aqueous methanol and were found to be 7.6 and 7.4, respectively. These bases are therefore not derivatives of aniline[7] but are aliphatic amines, containing perhaps electron attracting groups beta and/or gamma with respect to the nitrogen atom.[8] The fact that the ultraviolet spectra of all the bases did not change appreciably in going from neutral to acid solution confirmed the conclusion that the alkaloids were not aniline derivatives.[9]

The n.m.r. spectra of the bases also eliminated the possibility of the presence of C-methyl groups since the aliphatic proton region of the spectrum (at 9.1 τ^{6c}) exhibited no sharp peaks but only a broad signal. Analysis of decinine by the Kuhn-Roth procedure confirmed the absence of C-methyl groups in this alkaloid.

The presence of a carbonyl group was indicated by an intense band at about 1725 cm.$^{-1}$ in the infrared spectra of all bases except in those of vertine and verticillatine which exhibit maxima at about 1700 cm.$^{-1}$. The usual tests for ketone and aldehyde groups were negative suggesting that an ester or lactone grouping was present. Evidence for these groups was found in the n.m.r. spectra which show a broad, one-hydrogen signal at 5.10 τ characteristic of a hydrogen atom alpha to the ether oxygen of a lactone or ester.[6b] Chemical evidence which supports the presence of a lactone group will be presented in a subsequent paper. It is therefore concluded that all of these alkaloids have as part of their structure a six-membered or greater lactone ring,[10a] the ether oxygen of which is derived from a secondary alcohol. The absence of a well defined splitting pattern for this lactone hydrogen in the n.m.r. suggests that there are several hydrogen atoms on the carbon atoms flanking it which split its signal into the observed broad envelope.

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(3) Kindly supplied by Dr. I. J. Pachter.

(4) Alupharm Chemicals, New Orleans, Louisiana.

(5) Aspidosine gives 94% of theory for one N—CH_3, yet has none. H. Conroy, P. R. Brook, M. K. Rout, and N. Silverman, *J. Am. Chem. Soc.*, **80**, 5178 (1958).

(6) (a) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy to Organic Chemistry," Pergamon Press, New York, 1959, p. 56. (b) *Ibid.*, p. 55. (c) *Ibid.*, p. 52.

(7) The pK_a, of *N*,*N*-dimethylaniline in 50% ethanol is 4.09; H. C. Brown, D. H. McDaniel, and O. Hafliger in E. A. Braude and F. C. Nachod, "Determination of Organic Structures by Physical Methods," Academic Press, 1955, New York, p. 610.

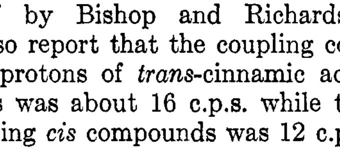
(8) Voacangine, a compound with an indole nucleus and a carbomethoxy group beta to the nitrogen, has a pK_a' of 7.4 in 40% methanol; D. F. Dickel, C. L. Holden, R. C. Maxfield, L. E. Paszek, and W. I. Taylor, *J. Am. Chem. Soc.*, **80**, 123 (1958).

(9) (a) A. E. Gillam and E. S. Stern, "Electronic Absorption Spectroscopy," Edward Arnold, London, 1958, p. 140. (b) *N*-Methylemitine dimethiodide has λ_{max} 284 mμ (log ϵ 3.8); *Ibid.*, p. 172. (c) *Ibid.*, p. 112. (d) 3,3′-Dimethoxydiphenyl has λ_{max} 274 and 256 mμ (ϵ 6000 and 12,000, respectively); *Ibid.*, p. 275.

(10) (a) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley, New York, 1958, p. 185. (b) *Ibid.*, p. 182. (c) *Ibid.*, p. 179. (d) *Ibid.*, p. 97.

A carbonyl band at 1700 cm.$^{-1}$ in the infrared spectra of vertine and verticillatine suggested the presence of an α,β-unsaturated lactone grouping in these alkaloids. This band shifted to 1725 cm.$^{-1}$ upon the uptake of one molar equivalent of hydrogen by these based to yield dihydro derivatives. The dihydro derivative from vertine was decamine, an alkaloid which occurs naturally in *Decodon*, while dihydroverticillatine yielded an isomer of decodine. The ultraviolet maxima of vertine and verticillatine were much more intense in the 290-mμ region than were the corresponding maxima in the dihydro compounds. α,β-Unsaturated lactones are known to absorb at 220 mμ[9c] so that the enhanced absorption in the 290-mμ region cannot be due to this chromophore alone. The n.m.r. spectra of the diacetate of verticillatine (Fig. 1) and the monoacetate of vertine are consistent with a *cis*-cinnamic lactone unit in these alkaloids, a structural feature which is consistent with the ultraviolet spectra of vertine and verticillatine.[11] A pair of doublets with the AB splitting pattern expected for the vinyl hydrogens of the double bond of cinnamic acid are centered at 4.03 and 3.13 τ (J 12.8 c.p.s.). Very similar results have been reported for *cis*-cinnamic acid itself by Bishop and Richards.[12] These authors also report that the coupling constant for the vinyl protons of *trans*-cinnamic acid and its derivatives was about 16 c.p.s. while that of the corresponding *cis* compounds was 12 c.p.s., an observation consistant with the assignment of the *cis* structure to the cinnamic acid system in vertine and verticillatine.

The n.m.r. spectra of the acetates of vertine and verticillatine show other differences from the spectra of corresponding dihydro derivatives. Diacetylverticillatine has a doublet centered at 5.71 τ (J 10.8 c.p.s.) and acetylvertine has a doublet centered at 5.48 τ (J 9.2 c.p.s.) which are not present in the n.m.r. spectra of diacetyldihydroverticillatine (Fig. 1) and acetyldecamine. These doublets appear to be equivalent in area to one hydrogen. These chemical shifts correspond to the chemical shift observed for a proton in the three position of the reserpine skeleton—e.g. the equatorial C-3 proton of methyl reserpate (I) is reported to absorb at 5.57 τ.[13] If such a structural unit (a carbon atom bearing one equatorial proton flanked by an aromatic nucleus and a nitrogen atom) were present in vertine and verticillatine, then this proton must change to the axial conformation[13] upon hydrogenation of the cinnamic double bond because this signal is not present in n.m.r. spectra of the dihydro derivatives. The steric requirements of the double bond could force these molecules into a conformation which is not favored in the dihydro derivatives so that such a conformational change is possible. A weak signal at 6.30 τ in diacetyldihydroverticillatine (Fig. 1), partially concealed by the O-methyl peak, could be assigned to the same proton in the axial conformation. The splitting pattern for the equatorial proton in the vinyl compounds requires the presence of one axial proton on the adjacent carbon atom.[13] Further chemical evidence is necessary to confirm these assignments.



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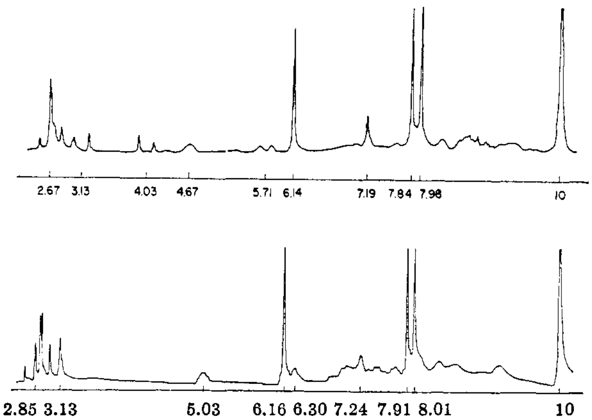

Fig. 1.—N.m.r. spectra of diacetylverticillatine (top) and diacetyldihydroverticillatine (bottom). Peak at 10 τ due to tetramethylsilane reference.

Elemental analysis requires the presence of five oxygen atoms in all the bases listed in Table II. Two of these oxygens are accounted for by the lactone ring. In all these alkaloids except decaline and vertaline, the other three oxygens can be ascribed to hydroxyl or methoxyl groups by Zeisel analysis and acetylation experiments. In each case the number of acetoxy or methoxy groups was confirmed by an appropriately located unsplit methyl signal in the n.m.r. The infrared spectra of the acetyl derivatives identified them as phenolic acetates with the characteristic absorption maximum at 1760 cm.$^{-1}$.[10b] Acetyl derivatives of aliphatic alcohols have maxima[10c] at about 1740 cm.$^{-1}$ The shift of ultraviolet maxima to longer wave lengths in basic solution is further evidence for the presence of phenolic hydroxyl groups.[9c] Decaline and vertaline are exceptions and do not exhibit this shift (see Table III). That all the methoxyl groups were attached to an aromatic nucleus was shown by a signal at 6.1 τ in the n.m.r.

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(11) There are no literature reports on the ultraviolet spectra of substituted *cis*-cinnamic acid derivatives which would correspond to the chromophore present in vertine and verticillatine. However, 2-hydroxy-3-methoxy-*trans*-cinnamic acid has its principal maximum at 282 mμ [I. A. Pearl and D. L. Meyer, *J. Org. Chem.*, **16**, 216 (1951)].

(12) E. O. Bishop and R. E. Richards, *Mol. Phys.*, **3**, 114 (1960).

(13) An axial proton in this position absorbs above 6.1 τ. W. E. Rosen and J. N. Shoolery, *J. Am. Chem. Soc.*, **83**, 4816 (1961).

TABLE III

Alkaloid	Oxygen substituents[a] OH	Oxygen substituents[a] OCH$_3$	Ultraviolet maxima in methanol[b] (mμ) Neutral solution	Ultraviolet maxima in methanol[b] (mμ) Basic solution	Ultraviolet maxima in methanol[b] (mμ) Acetate neutral solution
Decaline	. . .	2	293, 280[c]	293, 280[c]	. . .
Vertaline	. . .	2	293, 280[c]	293, 280[c]	. . .
Decinine	1	2	294	293, 313	287
Decamine[e]	1	2	294	293, 313	287
Decodine	2	1	287, 312[c,d]	310	281
Dihydroverticillatine	2	1	289, 311[c,d]	308	280
Vertine	1	2	285, 260, 308[c]	318, 298[c]	258, 282[c]
Verticillatine	2	1	293	300	261[c]

[a] Excluding lactone. [b] No major changes where observed in acid solution. [c] Inflection. [d] Inflection disappears in acid solution. [e] Dihydrovertine.

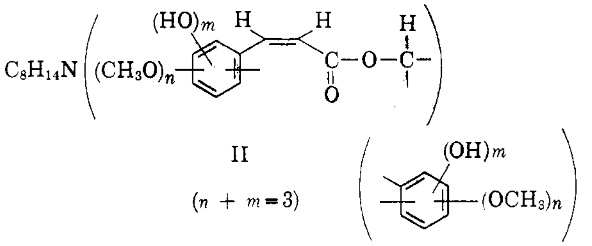
Aliphatic methoxyl groupings generally absorb at 6.7 τ.[6b] The above evidence requres that all the hydroxyl and methoxyl groups be attached to an aromatic ring, a structural feature consistent with the ultraviolet spectra of these bases.[9b]

It has not been possible so far to account for all five of the oxygen atoms of decaline and vertaline. Two of the oxygens are present in the lactone ring and two as methoxyl groups, but the fifth oxygen has not been identified. There is no infrared band in the 3500-cm.$^{-1}$ region indicating the absence of any hydroxyl groups.[10d] The possibility that strong hydrogen bonding might be responsible for the absence of a hydroxyl band in the infrared was eliminated because the ultraviolet spectra of these compounds did not change on addition of base and starting material was recovered on treatment with acetic anhydride. It must be concluded that the fifth oxygen atom is present as an internal ether linkage.

It was not clear from the ultraviolet spectra whether one or two aromatic rings were present in the alkaloids. Conclusive evidence for the presence of two aromatic nuclei was obtained from the n.m.r. spectra of decodine and decinine. Integration of the area under the aromatic proton region at 3.1 τ indicated the presence of 5 ± 1 aromatic hydrogens. Five hydrogens attached to an aromatic ring along with the other oxygen substituents would require two aromatic nuclei. For all the alkaloids except decaline and vertaline one can account for eight of the twelve positions on the aromatic rings by oxygen or hydrogens. This requires that the remaining four positions be substituted by carbon atoms. It is clear from the ultraviolet spectra that the two aromatic rings are not conjugated with each other.[9d]

From the above information and the empirical formulas, these alkaloids must be pentacyclic with at least one of the rings being greater than six-membered. The present knowledge of the structures of the olefinic alkaloids verticine and verticillatine may be summarized by formula II. The other alkaloids (except possibly decaline and vertaline) have the same structural unit except that the cinnamic ester double bond is saturated.

The chemical and physical evidence obtained so far allows one to classify these seven alkaloids into three main groups which become apparent if one considers the data listed in Table III. One group consists of decaline and vertaline which have identical ultraviolet spectra and very similar infrared spectra. These two bases are eluted together from a chromatography column and have the same functional groups. Another pair consists of decinine and decamine which have very similar infrared spectra and the same ultraviolet spectra. Vertine is included in this group because on hydrogenation it yields decamine. A third such group includes decodine and verticillatine, the properties of dihydroverticillatine being very close to those of decodine. As these compounds seem to exist in pairs, one might suspect that they differ in stereochemistry at a secondary carbon atom. The most obvious possibility is the carbon atom bearing the ether-type oxygen of the lactone ring. This is now being investigated.



II

(n + m = 3)

Experimental[14]

Isolation of the Alkaloids.—Eleven pounds (5230 g.) of finely ground and dried aerial portions of *Decodon verticillatus*, collected near Tallahassee, Florida, August 27, 1960, was mixed with a solution of 150 ml. of 30% ammonia and was extracted continuously with chloroform for 2 days. The extract was filtered, concentrated to near dryness, and taken up in 2 l. of ether. The ether solution was extracted with two 1-l. portions of dilute hydrochloric acid and the

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[14] Ultraviolet spectra were run on a Cary Model 14 spectrophotometer in methanol and infrared spectra were run on a Perkin-Elmer Model 221 spectrophotometer in chloroform by Mrs. M. Osmond and Mrs. D. DeTar. Rotations were determined at the sodium D line at 26 + 2° in chloroform solution except when noted otherwise; potentiometric titrations were carried out in 50% methanol; n.m.r. spectra were run in deuterochloroform on a Varian HR60 spectrometer. Melting points were determined in open capillaries and are uncorrected. Analyses were carried out by Messers. Weiler and Strauss, Oxford, England; Midwest Microlab, Indianapolis, Indiana; and F. Pascher, Bonn, West Germany. Water was added to the neutral activity alumina according to a procedure provided by M. Woelm Eschwage Co. to give the activities citied.[4]

acid extracts were washed with ether, made basic with sodium carbonate, and extracted into chloroform. The chloroform extract was washed with water, dried with sodium sulfate, and concentrated to dryness to yield 20.93 g. (0.4% yield) of tan, amorphous solid. The yield of bases over the course of one year is summarized in Table I.

Separation of the Alkaloids.—The mixture of bases was dissolved in 1:1 chloroform–benzene and was chromatographed on 370 g. of neutralized "Alcoa" alumina.[15] Elution with benzene and 20% ether–benzene yielded a fraction which when crystallized from methanol gave 1.69 g. of crystalline material, m.p. 202–208°. Treatment of this with 4 ml. of hot methanol and filtration yielded 0.496 g. of methanol-insoluble material, m.p. 183–204°. Repetition of the hot methanol extraction on this material yielded 100 mg. of decamine, m.p. 219–221°, as the methanol insoluble fraction. An analytical sample was prepared by recrystallization from a large volume of methanol, m.p. 223–224°, $[\alpha]$ − 145° (c 1.0), $\lambda_{\max}$ 294 mμ (ϵ 7370), $\lambda_{\min}$. 268 mμ (ϵ 3220), λ(inflection) 253 mμ (ϵ 6320), $\nu_{\max}$ 3480, 1728 cm.$^{-1}$.

Anal. Calcd. for $C_{26}H_{31}NO_5$: C, 71.37; H, 7.14; N, 3.20; O, 18.29; 2-OCH_3 14.18; 1-NCH_3 6.63. Found: (after drying to constant weight at 100°) C, 71.10; H, 6.97; N, 3.27; O, 18.21; OCH_3, 12.20; NCH_3, 2.67.

Concentration of the filtrates from the decamine yielded two crops of decinine; 0.983 g., m.p. 211–215° and 0.400 g., m.p. 216–219°. An analytical sample was prepared by recrystallization from methanol and drying for 24 hr. at 77° *in vacuo*, m.p. 222–224°, $[\alpha]$ −142° (c 1.37), $\lambda_{\max}$ 294 mμ (ϵ 7180), $\lambda_{\min}$ 269 mμ (ϵ 2870), λ(inflection) 251 mμ (ϵ 6380), $\nu_{\max}$ 3500, 1724 cm.$^{-1}$, pK_a 7.4.

Anal. Calcd. for $C_{26}H_{31}NO_5$: C, 71.37; H, 7.14; N, 3.20; 2-OCH_3, 14.18; 1-NCH_3, 6.63; 1-CH_3 (on carbon), 3.43; molecular weight 437.52. Found: C, 71.24; H, 7.23; N, 3.58; OCH_3, 14.22; NCH_3, 0; CH_3 (on carbon), 0; molecular weight (by titration), 436.

Further elution of the column with ethyl acetate yielded 7.14 g. which crystallized from methanol to give 2.23 g. of a mixture of large octahedra imbedded in a matrix of cubes. The two types of crystals were separated mechanically and the octahedra were recrystallized from methanol to yield 1.338 g. of decodine, m.p. 193–197°, $[\alpha]$ −97° (c 1.78); $\lambda_{\max}$ 287 mμ (ϵ 6510); $\lambda_{\min}$ 261 mμ (ϵ 1960), λ(inflection) 312 mμ (ϵ 610); $\nu_{\max}$ 3500, 1723 cm.$^{-1}$, pK_a 7.6.

Anal. Calcd. for $C_{25}H_{29}NO_5$: C, 70.90; H, 6.90; N, 3.31; O, 18.89; 1-OCH_3, 7.32; 1-NCH_3, 6.84; mol. wt. 423.49. Found; C, 70.22; H, 6.99; N, 3.52; O, 19.07; OCH_3, 7.10; NCH_3 2.77; mol. wt. (by titration) 430.

The above-mentioned matrix of cubes was also recrystallized from methanol to yield 0.426 g., m.p. 193–195° with frothing, which appeared to be a homogenous compound as further recrystallization did not change the melting point or the infrared spectrum. However, this was shown to be a mixture of decodine and vertine as on treatment with acetic anhydride it yielded two different acetates (see below).

Elution of the column with methanol yielded 10.44 g. of material which when crystallized from methanol gave 3.3 g. of yellow crystals, m.p. 280° dec. This was dissolved as completely as possible in hot methanol and the yellow insoluble precipitate was filtered to yield 2.146 g. of verticillatine, m.p. 312 dec., $\lambda_{\max}$ 293 mμ (ϵ 11,950), $\lambda_{\min}$ 267 mμ (ϵ 8150). The hydrochloride salt of verticillatine was prepared by dissolution of the alkaloid in methanolic hydrogen chloride and addition of ether. The compound was recrystallized from methanol–ether, m.p. 240° dec., $[\alpha]$ + 119° (c 1.93 in methanol), $\lambda_{\max}$ 292 mμ (ϵ 11,750), $\lambda_{\min}$ 260 mμ (ϵ 8050).

Anal. Calcd. for $C_{25}H_{27}NO_5 \cdot HCl \cdot {}^1/_2\, CH_3OH$: C, 64.62; H, 6.38; O, 18.57; N, 2.96; Cl, 7.48; 1.5 OCH_3, 9.80. Found: C, 64.75; H, 5.99; O, 18.32; N, 3.03; Cl, 7.27; OCH_3, 9.42.

In more recent studies it was found that if the chloroform extract of the total alkaloids were dried briefly with sodium sulfate and then concentrated to about 500 ml., 2 g. of compound precipitated, m.p. 312° dec., which had an infrared spectrum that was quite different from that of verticillatine. However, attempts to dissolve this compound in methanol for crystallization resulted in the conversion of the off-white crystals to the yellow ones of verticillatine.[16] The lability and insolubility of this compound has made it difficult to study further.

The filtrates from the crystallization of decamine and decinine (material eluted with benzene and 20% ether–benzene) were dissolved in benzene and chromatographed on 255 g. of Woelm neutral alumina, Grade 3.[3] Elution of the column with benzene yielded 150 mg. of material which when crystallized from methanol and dried at 77° *in vacuo* melted at 102–121°. Recrystallization from methanol yielded long needles of decaline which melted with frothing at 81–82°. These were dried for analysis at 77° *in vacuo*, m.p. 102.5–118°, $[\alpha]$ −136° (c 1.06); $\lambda_{\max}$ 293 mμ (ϵ 6220); $\lambda_{\min}$ 264 mμ (ϵ 1900); λ(inflection) 280, 241, 223 mμ (ϵ 4175, 9780, 16,200), $\nu_{\max}$ 1720 cm.$^{-1}$.

Anal. Calcd. for $C_{26}H_{31}NO_5$: C, 71.37; H, 7.14; N, 3.20; 2—OCH_3, 14.18; 1—NCH_3, 6.63. Found: C, 71.39; H, 7.13; N, 3.02; —OCH_3, 14.65; —NCH_3, 1.60.

Further elution with 10% ether in benzene yielded a second band consisting of 460 mg. of material. Two crystallizations from methanol and drying at 77° *in vacuo* yielded 97 mg. of vertaline, m.p. 194–196°, $[\alpha]$ −170° (c 1.25), $\lambda_{\max}$ 293 mμ (ϵ 6400); $\lambda_{\min}$ 264 mμ (ϵ 1960), λ(inflection) 280, 241, 223 mμ (ϵ 4340, 9940, 17,050), $\nu_{\max}$ 1720 cm.$^{-1}$.

Anal. Calcd. for $C_{26}H_{31}NO_5$: C, 71.37; H, 7.14; N, 3.20; O, 18.28; 2-OCH_3, 14.18; NCH_3, 6.63. Found: C, 70.93; H, 7.41; N, 3.19; O, 18.43; OCH_3, 14.42; NCH_3, 1.30.

An additional 80 mg. of decinine were eluted with 10% and 20% ether in benzene to make a total yield of 1.46 g. of this alkaloid.

The filtrates from the crystallization of decodine and verticillatine were dissolved in 1:1 chloroform–benzene and chromatographed on 150 g. of Woelm Grade 4 neutral alumina. Benzene eluted 2.19 g. of material from which approximately 100 mg. of the alkaloid vertine were isolated by crystallization from methanol. Recrystallization from methanol–chloroform yielded an analytical sample, m.p. 245–247°, $[\alpha]$ +39° (c 0.95), $\lambda_{\max}$ 285, 260 mμ (ϵ 13,500, 12,250), $\lambda_{\min}$ 266, 248 mμ (ϵ 12,150, 11,650), λ(inflection) 308 mμ (ϵ 7650), $\nu_{\max}$ 3530, 1700 cm.$^{-1}$.

Anal. Calcd. for $C_{26}H_{29}NO_5$: C, 71.70; H, 6.71; N, 3.22; O, 18.37; 2-OCH_3, 14.25. Found C, 71.26; H, 6.59; N, 3.45; O, 18.86; OCH_3, 14.19.

Further washing of the column with benzene and 20% ether in benzene eluted 3.88 g. of material which when crystallized from methanol yielded 1.346 g. of decodine, m.p. 193–194°. The total yield of decodine from both chromatograms was 2.68 g.

An additional 1.50 g. of material was eluted with 20% ether in benzene and with ether which when crystallized from methanol yielded 195 mg. of the decodine–vertine complex, m.p. 193–194° with frothing.

It was found that the composition of the alkaloid mixture obtained from the plant closely approximated the amounts indicated above from July through the middle of September. The basic fraction isolated from the plant material collected in October, however, was more difficult to purify and yielded

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[15] Neutralized by standing 2 days with ethyl acetate and then washing with distilled water and methanol. It was reactivated by drying at room temperature *in vacuo* for about 18 hr. (1.5 mm. pressure at the end of drying period).

[16] The procedure for the isolation of this alkaloid and of its subsequent transformation into verticillatine was devised by M. Barerra.

only a much smaller proportion of crystalline bases with decamine being the predominent one, along with smaller amounts of vertine and decodine–vertine complex, decinine, and vertaline.

Dihydroverticillatine.—Verticillatine (79.3 mg.), dissolved in ethanol acidified with hydrochloric acid, was hydrogenated using 56 mg. of platinum oxide. At the end of 25 min. 4.10 ml. of hydrogen was absorbed (theory for 1 mole equivalent, 4.22 ml.). The catalyst was then removed by centrifugation and the ethanol removed by warming at the water pump. The residue was taken up in water, made basic with sodium carbonate, and extracted into chloroform. Crystallization from methanol yielded 74 mg. of dihydroverticillatine, m.p. 260–265° dec. An analytical sample was prepared by dissolving in 1:1 methanol–chloroform and then repeated concentration of the solution and addition of methanol until the product began to crystallize as rhombs. A sample dried at 154° for 24 hr. *in vacuo* had the following constants: m.p. 260–263° dec. λ_{max} 288 mμ (ϵ 6780), λ_{min} 266 mμ (ϵ 3680), λ(inflection) 311 mμ (ϵ 2900), ν_{max} 1725 cm.$^{-1}$ (KBr). The sample for analysis was dried to constant weight at 150°.

Anal. Calcd. for $C_{25}H_{29}NO_5$: C, 70.90; H, 6.90; Found: C, 69.99; H, 6.60.

Dihydrovertine (decamine).—Vertine (53.7 mg.), was hydrogenated under the same conditions as verticillatine using 37 mg. of platinum oxide. After 18 hr. 2.63 ml. of hydrogen were absorbed (theoretical 2.77 ml.). The same workup procedure yielded 48 mg. of decamine after crystallization from methanol, m.p. 221–222°. The mixed melting point and infrared spectrum of this sample were identical with that of a sample of decamine isolated directly from the plant.

Acetylation Experiments.—The procedure described for the preparation of acetylvertine was followed for all the alkaloids.

Acetylvertine.—To 100 mg. of vertine was added 1 ml. of acetic anhydride and 1 ml. of pyridine and the mixture was allowed to stand overnight at room temperature. The solution was then concentrated to near dryness with warming under water pump vacuum and the residue was taken up in ether. The ether solution was extracted with three 10-ml. portions of dilute hydrochloric acid, the combined acid extracts were washed with ether, made basic with sodium carbonate and the bases extracted into ether. The ether extract was washed with water, dried over sodium sulfate, and concentrated to yield 106 mg. of product. Crystallization from ether afforded 84 mg., m.p. 177–180°. It was found that recrystallization from warm methanol resulted in deacetylation of the compound to yield vertine as the product. An analytical sample was prepared by recrystallization from ether, m.p. 183–185°, [α] −92.7° (*c* 0.96), λ_{max} 258 mμ (ϵ 15,410), λ_{min} 244 mμ (ϵ 13,820), λ(inflection) 282 mμ (ϵ 10,000), ν_{max} 1760, 1712 cm.$^{-1}$.

Anal. Calcd. for $C_{28}H_{31}NO_6$: C, 70.42; H, 6.54; N, 2.93; O, 20.10. Found: C, 70.34; H, 6.49; N, 2.91; O, 20.34.

Acetyldecamine.—Decamine (371 mg.) yielded 304 mg. of acetyldecamine after crystallization from methanol, m.p. 195–197°. Heating a solution of acetyldecamine in methanol resulted in deacetylating but an analytical sample could be prepared by recrystallization from cold methanol and drying at 77° *in vacuo*, m.p. 197–198°, [α] − 188°, (*c* 1.16), λ_{max} 287 mμ (ϵ 2300), λ_{min} 274 mμ (ϵ 1830), λ(inflection) 253 mμ (ϵ 3360), ν_{max} 1764, 1726 cm.$^{-1}$.

Anal. Calcd. for $C_{20}H_{33}O_6N$: C, 70.12; H, 6.94; N, 2.92; O, 20.02. Found (after drying to constant weight at 100°): C, 69.98; H, 7.07; N, 2.87; O, 20.50.

Diacetyldecodine.—Decodine (130 mg.) yielded 124 mg. of diacetyldecodine when crystallized from ether, m.p. 202–203. An analytical sample was prepared by recrystallization from ether, m.p. 202–203°, [α] −66° (*c* 1.18), λ_{max} 281m μ (ϵ 2560), λ_{min} 258 mμ (ϵ 1025), ν_{max} 1768, 1726 cm.$^{-1}$.

Anal. Calcd. for $C_{29}H_{33}NO_7$: C, 68.62; H, 6.55; N, 2.76. Found: C, 68.42; H, 6.23; N, 2.75.

Acetyldecinine.—Decinine (52 mg.) yielded 38 mg. of acetyldecinine, m.p. 195–197°, when crystallized from ether. An analytical sample was prepared by recrystallization from ether, m.p. 197–198°, [α] −139° (*c* 1.59), λ_{max} 287 mμ (ϵ 2610). λ_{min} 274 mμ (ϵ 2090), λ(inflection) 252 mμ (ϵ 3700), ν_{max} 1764, 1729 cm.$^{-1}$.

Anal. Calcd. for $C_{28}H_{33}NO_6$: C, 70.12; H, 6.94. Found: C, 69.98; H, 7.05.

Diacetylverticillatine.—From 100 mg. of verticillatine was obtained 74 mg. of diacetylverticillatine after crystallization from ether, m.p. 172–175°. An analytical sample was prepared by recrystallization from cold methanol (warm methanol causes hydrolysis), m.p. 176–178°, [α] + 36° (*c* 2.41), λ inflection 262 mμ (ϵ 11,600), ν_{max} 1761, 1702 cm.$^{-1}$.

Anal. Calcd. for $C_{29}H_{31}NO_7$: C, 68.91; H, 6.18; N, 2.77; O, 22.15. Found: (after drying to constant weight at 100° C) C, 68.47; H, 6.43; N, 2.74; O, 22.23.

Acetylvertine and Diacetyldecodine from the Decodine–Vertine Complex.—From 100 mg. of the complex was obtained 43 mg. of diacetyldecodine, m.p. 194–197°, after recrystallization from ether. This did not depress the melting point of an authentic sample of diacetyldecodine. Chromatography of the filtrate of 5 g. of Woelm Grade 3 alumina and elution with bezene yielded an additional 22 mg. of diacetyldecodine. Acetylvertine (29 mg.) was eluted after the diacetyldecodine using benzene and ether. The infrared spectrum of this product was identical with that of acetylvertine.

Attempted Acetylation of Decaline.—From 40 mg. of decaline was recovered 37 mg. of starting material when crystallized from methanol. The melting point (102–123°), mixed melting point, and infrared spectrum of the product were identical with decaline.

Attempted Acetylation of Vertaline.—From 88 mg. of vertaline was obtained 69 mg. of starting material when crystallized from ether. The melting point (194–195°), mixed melting point and infrared spectrum of the product were identical with vertaline.

Diacetyldihydroverticillatine.—From 54 mg. of dihydroverticillatine was obtained 45 mg. of diacetyldihydroverticillatine after crystallization from ether, m.p. 194–195°. An analytical sample was prepared by recrystallization from acetone, m.p. 198–199°, [α] −99° (*c* 1.15) λ_{max} 280 mμ (ϵ 2280), λ_{min} 258 mμ (ϵ 1080), ν_{max} 1764, 1721 cm.$^{-1}$.

Anal. Calcd. for $C_{29}H_{33}NO_7$: C, 68.62; H, 6.55. Found: (after drying to constant weight at 100° C, 68.49; H, 6.40.

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