Also, we wish to thank Dr. Bryce Douglas and Dr. J. A. Weissbach of Smith, Kline and French Laboratories for providing some of the vertine and all of the lythrine that was used in these studies. Finally we wish to acknowledge all those noted in the Experimental Section for spectral data.

Lythraceae Alkaloids. VIII. The Structure and Stereochemistry of the Biphenyl Ether Alkaloids from *Decodon verticillatus*[1,2]

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Abstract: Two new alkaloids have been isolated from *Decodon verticillatus* by an improved procedure for fractionation of the crude alkaloids. The new alkaloids have been converted to the known alkaloids vertaline and decaline by methylation of a phenolic hydroxyl group in each. Vertaline had been assigned structure II previously on the basis of X-ray data and decaline is assigned structure V on the basis of a series of degradative and spectral studies of both alkaloids. A key degradation was the conversion of VI to X and XI by sodium–ammonia. The new des-*O*-methyl alkaloids were assigned structures V and V-B (4″-OH, 5″-OCH_3) on biogenetic grounds.

The Lythraceae plant family elaborates a number of crystalline alkaloids, some of which have been assigned the biphenylquinolizidine skeleton I (R = H and CH_3). The alkaloids differ in three ways: (1) the nature of the substituents and the pattern of substitution on the biphenyl ring system, (2) the presence of a cinnamic or dihydrocinnamic lactone, (3) the stereochemistry at C-10.[2]

Our initial investigations of the Lythraceae plant *Decodon verticillatus* indicated that two of the alkaloids,[4] decaline and vertaline, differed structurally from those to which the biphenyl structure (I) has recently been assigned.[2] The structures of these two minor alkaloids became of increased interest with the isolation of relatively large amounts of their des-O-methyl derivatives from *Decodon* by an improved procedure for the fractionation of the crude alkaloid (see Experimental Section). The presence of a lactone ring and two methoxyl groups was evident in decaline and vertaline from spectral studies and by the lithium aluminum hydride (LAH) reduction of the lactone grouping in vertaline to a diol (tetrahydrovertaline). However, analytical data suggested the presence of another oxygen function which did not manifest itself chemically or spectroscopically and therefore was assumed to be present as an ether.

Once the structure of the biphenyl alkaloid lythrine was determined,[5] the biphenyl ether structure was considered to be a likely possibility for decaline and vertaline. This was suggested by the presence of six aromatic protons in the nuclear magnetic resonance (nmr) spectra of these bases and by the absence of any nmr signals that might be attributed to the protons of an aliphatic ether (other than methoxyl groups). The mass spectra of these bases showed fragments that could be assigned to a biphenyl ether grouping. Finally, the presence of both biphenyl and biphenyl ether alkaloids in the same plant is consistent with current biogenetic theory.[6]

These postulates were confirmed with the assignment of II to vertaline by an X-ray crystallographic study.[7] The biphenyl ether grouping is present in II together with a cis-fused quinolizidine ring containing an axial lactone grouping.

With the structure of vertaline in hand we set out to establish the structure of decaline. It was immediately apparent that decaline has the same skeleton and methoxylation pattern as vertaline as shown by the identity of the ultraviolet (uv) and mass spectra and the close similarity of the nmr and infrared (ir) spectra. Consequently, the differences in the two bases must be stereochemical. Since we already observed that the biphenyl alkaloids occur in pairs which differ stereochemically at C-10, structure V, which only differs from II by the configuration at C-10, seemed the most likely structure for decaline. This assignment was verified by a detailed structure analysis.

Decaline was shown to have the same configuration as vertaline at the biphenyl ether link since the optical rotatory dispersion (ORD) and circular dichroism

(1) Direct correspondence to J. P. F. at RPI. Supported by grants from Smith, Kline and French Laboratories and the U. S. Public Health Service (MY-4748).

(2) The previous paper in this series: J. P. Ferris, C. B. Boyce, and R. C. Briner, *J. Amer. Chem. Soc.*, 93, 2942 (1971). Some of this work was presented in preliminary form: J. P. Ferris, R. C. Briner, and C. B. Boyce, *Tetrahedron Lett.*, 5125 (1966).

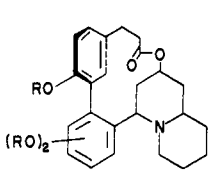
(3) (a) USPHS Career Awardee (GM 6380) of the National Institute of General Medical Sciences. (b) Abstracted from the doctoral dissertations of C. B. Boyce [*Diss. Abstr. B*, 27 (12), 4301 (1967); *Chem. Abstr.*, 67, 117015 (1967)] and R. C. Briner [*Diss. Abstr. B*, 27 (11), 3845 (1967); *Chem. Abstr.*, 67, 100290 (1967)] submitted to Florida State University, Dec 1966. R. C. B. was an NSF Summer Fellow (1962) and a USPHS Predoctoral Fellow (1962–1965).

(4) J. P. Ferris, *J. Org. Chem.*, 27, 2985 (1962).

(5) D. E. Zacharias, G. B. Jeffery, B. Douglas, J. A. Weisbach, J. L. Kirkpatrick, J. P. Ferris, C. B. Boyce, and R. C. Briner, *Experientia*, 21, 247 (1965).

(6) J. P. Ferris, C. B. Boyce, and R. C. Briner, *Tetrahedron Lett.*, 5129 (1966). Tracer experiments consistent with this proposal have been reported by A. Rother and A. E. Schwarting, *Chem. Commun.*, 1411 (1969), and S. H. Koo, R. N. Gupta, I. D. Spenser, and J. T. Wrobel, *ibid.*, 396 (1970).

(7) J. A. Hamilton and L. K. Steinrauf, *Tetrahedron Lett.*, 5121 (1966); *J. Amer. Chem. Soc.*, 93, 2939 (1971).



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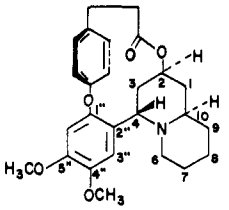

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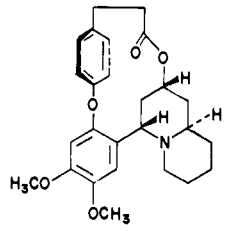

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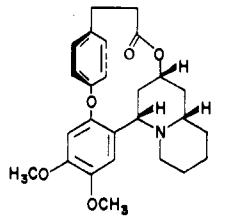
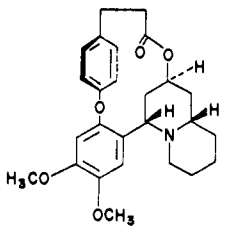


IV



V

curves of the two bases were identical. Furthermore since the curves are virtually superimposable, the alkaloids probably have the same configuration at C-4 as well.

The number of structures isomeric with II to be considered for decaline was reduced to three (III-V) by the observation of a low field shift of an aromatic proton in the nmr spectra of the *N*-oxides of decaline and vertaline (Table I). This shift had been noted

Table I. Proton Chemical Shifts for Decaline and Vertaline Derivatives (τ)

Alkaloid	H-3″ Free base	H-3″ *N*-Oxide	H-4 Free base	H-4 *N*-Oxide	NCH_3 Methiodide
Decaline	2.78	2.37	7.05	6.50	6.79
Vertaline	2.85	2.08	6.68	5.97	6.41
Acetyldesmethyl-vertaline	2.70	2.11	6.62	5.95	6.51

previously in the *N*-oxides of the biphenyl alkaloids and was attributed to the shielding of H-3″ by the *N*-oxide oxygen.[2] Inspection of a Dreiding model of vertaline revealed that this low field singlet is due to the shielding of H-3″ by the *N*-oxide oxygen in the biphenyl ether alkaloids as well. Decaline *N*-oxide also exhibits a low field singlet which we then assigned to an interaction of H-3″ and the *N*-oxide group. Inspection of Dreiding models revealed that the only structures in which such an interaction is possible are the cis-fused quinolizidine III and the trans-fused quinolizidines IV and V.

It is of interest that the magnitude of the H-3″ chemical shift is much less in the biphenyl ether alkaloids (τ 2.1–2.4) than in the biphenyl bases (1.5–1.9).[2] Comparison of models reveals that H-3″ is not held in as close proximity to the *N*-oxide in the biphenyl ether alkaloids because of the greater flexibility of this system. Also we noted that the chemical shift of H-3″ is greater for vertaline *N*-oxide than for decaline *N*-oxide (Table I). The *cis*-quinolizidine juncture in vertaline results in a repulsion between the quinolizidine ring and the biphenyl ether forcing H-3″ and the *N*-oxide oxygen into close proximity. Since the deshielding of H-3″ is not as great in decaline, the interaction between the quinolizidine ring and the biphenyl ether system must be much less, a result consistent with the presence of a trans-fused quinolizidine ring in decaline.

The following observations confirmed the presence of the trans juncture in decaline. "Bohlmann bands" are present in the ir spectrum of decaline at 2800–2700 cm^{-1} and are absent in vertaline.[8] Vertaline is converted to the methiodide more rapidly than decaline.[8] The nmr *N*-methyl resonance of the methiodide of vertaline is at lower field than the methiodide of decaline (Table I).[8] The chemical shift of H-4 is greater in vertaline derivatives than in the corresponding decaline compounds (Table I).[8] The coupling constants (doublet of a doublet, J = 10, 2 Hz) observed in the *N*-oxide derivatives are consistent with an axial orientation of H-4 in decaline and vertaline. All these data demonstrate that decaline does not contain a cis-ring juncture and eliminate the cis-fused form of III from further consideration as the structure of decaline.

Of the two structures remaining for decaline (IV and V) structure V may be assigned on the basis of the coupling observed for H-2 in the nmr.[8] In IV H-2 is axial while in V and vertaline H-2 is equatorial. If decaline were IV the base width and half-height width of the signal for H-2 should be much broader than that of vertaline due to the axial–axial coupling. If V is the structure of decaline then the H-2 signal should be the same in both alkaloids, which is what was observed.

Although the evidence for eliminating IV from further consideration seemed compelling, we felt that it was desirable to verify this conclusion by degradation studies. Since vertaline, IV, and V have the same configuration at both the biphenyl ether link and C-4 the plan was to remove both these centers of asymmetry and then to compare the degradation products. If IV is the correct structure of decaline then the resulting products would be mirror images. If V is correct the resulting products would be diastereomers.

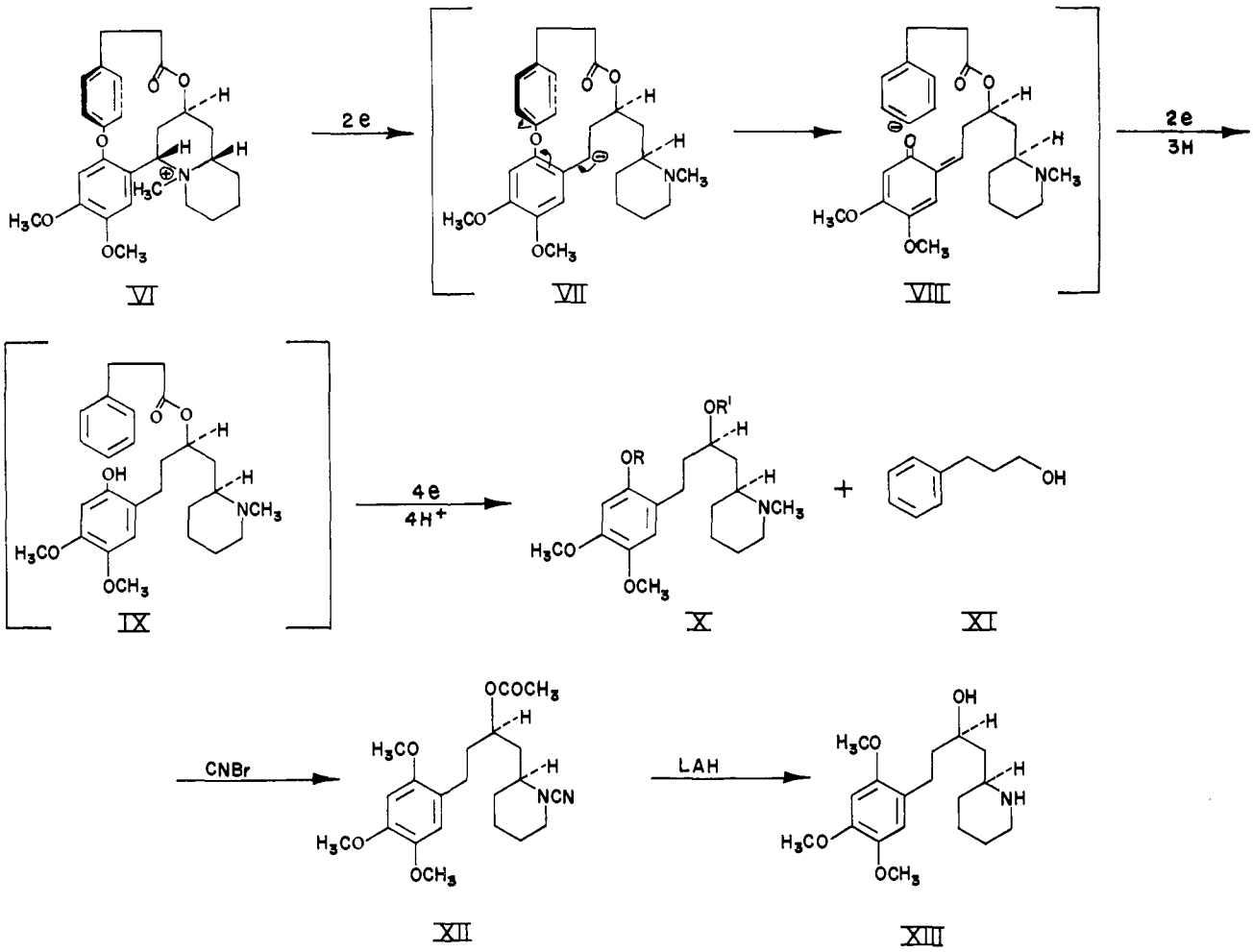
It was possible to remove these two centers of asymmetry and cleave three bonds at one time by the sodium–ammonia reduction of the methiodides of decaline and vertaline.[9] The reaction products from vertaline methiodide are shown in Chart I for the decaline series.[10] The 3-phenylpropanol (XI) was characterized by an ir spectrum which was identical with that of an authentic sample It was not possible to crystallize X and X-B (R = R′ = H); however these compounds were shown to be homogeneous by thin layer chro-

(8) See ref 2 for a detailed discussion of the use of this method for the determination of the stereochemistry of substituted quinolizidines.

(9) J. Clayson, *J. Chem. Soc.*, 2016 (1949). For recent references, see K. W. Bentley and A. W. Murray, *ibid.*, 2501 (1963).

(10) The compound numbers for the vertaline series are designated by "B"; *e.g.*, vertaline methiodide is VI-B.

Chart I



matography (tlc). Treatment with diazomethane produced the trimethoxy derivative X (R = CH_3; R′ = H) which on reaction with acetic anhydride yielded a monoacetate (X, R = CH_3; R′ = $COCH_3$). Direct reaction of the sodium–ammonia cleavage product with acetic anhydride produced the diacetate X (R = R′ = $COCH_3$). It was not possible to obtain a crystalline derivative of X (R = CH_3; R′ = H) by reaction with methyl iodide or conversion to the cyanamide XII or the secondary amine XIII.

Combustion analyses on X, XII, and XIII were precluded by the absence of crystalline compounds. However, each derivative of X, XII, and XIII exhibited nmr and ir spectra in agreement with the assigned structures (see Experimental Section). In addition the mass spectra of X (R = R′ = $COCH_3$), XII-B, and XIII-B each exhibited a molecular ion in agreement with the assigned formula. The mass spectrum of XII was troublesome in that it contained a fragment at *m/e* 420 while the assigned structure has a molecular weight of 390. We believe the 420 peak to be due to an impurity since the remainder of the spectrum of XII is very similar to that of XII-B including a peak at 390.

The mass spectral fragmentation pattern of these degradation products was also in agreement with the proposed structures. Of particular value is the piperidine ring fragment which was usually the most intense peak. In X this peak was at 98 (*N*-methylpiperidine ion) in XII and XIII-B at 109 (*N*-cyanopiperidine ion) and in XIII at 84 (piperidine ion). In addition mass spectra of these derivatives exhibit fragments at 56 and 43 characteristic of piperidine derivatives.[11]

The course of this novel sodium–ammonia cleavage reaction was investigated briefly. We observed that decaline and vertaline were not degraded under the conditions in which the methiodides were cleaved. Consequently the cleavage of the C_4–N bond (VI → X) must trigger the scission of the biphenyl ether and the ester bonds. A mechanism consistent with these data and what is known about phenyl ether cleavages[12] is shown in Chart I. (Only two-electron transfers are shown although it is recognized that one-electron transfers are possible.) In this scheme the subsequent biphenyl ether cleavage (VII → VIII) is more rapid than the rate at which VII abstracts a solvent proton. Reductive cleavage of the ester (IX → X) is probably the slowest step in the reaction. In some reactions ammonolysis of the ester competed with the reduction of the ester group as evidenced by the presence of amide bands at 1680 cm^{-1} in the ir spectrum of the neutral extract of the reaction.

With the structures of the degradation products established we then measured the rotations of X (R = CH_3; R′ = H) from decaline and vertaline. The observed rotations were −36 and +59°, respec-

(11) H. Budzidiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day Inc., San Francisco, Calif., 1964, pp 100–102.
(12) D. H. Eargle, Jr., *J. Org. Chem.*, **28**, 1703 (1963).

tively, showing that the products were diastereomers. Consequently these data confirm the assignment of V to decaline.

We have not determined whether the desmethyl derivatives of decaline and vertaline have 4''-OH, 5''-OCH_3 substituents or 4''-OCH_3, 5''-OH. However, if the assumption is made that the desmethyl alkaloids are a direct result of the biphenyl ether coupling reaction[6] and are not formed by demethylation of decaline and vertaline then the most likely substitution pattern is 4''-OH, 5''-OCH_3 with the hydroxyl group para to the biphenyl ether link.

Experimental Section

The general experimental techniques are outlined in ref 2.

Isolation of the Alkaloids from *Decodon*. The plant is dried and ground to a fine powder. For every 12 lb of ground plant 150 ml of 30% aqueous ammonia is added. This mixture is then extracted continuously with $CHCl_3$ for 2 days. The extract is concentrated nearly to dryness. To the residue is added 250 ml of CH_3OH and enough 20% H_2SO_4 to make the mixture strongly acidic. The mixture is heated for 10–15 min, diluted with water, and boiled to remove the residual $CHCl_3$ and CH_3OH. Boiling is continued until the insolubles coagulate into granules. The mixture is filtered, the precipitate washed with water, and the filtrate washed with ether. The aqueous acidic solution is made basic with Na_2CO_3 and extracted with $CHCl_3$ and the $CHCl_3$ extracts were concentrated to yield the crude mixture of *Decodon* alkaloids.

The remainder of the separation is outlined below. All of the steps must be monitored by tlc since it is occasionally necessary to repeat specific steps in order to obtain maximum separation. The order of elution of the alkaloids on tlc on neutral alumina in 5% methanol–benzene is decaline, vertaline, decinine, decamine, desmethyldecaline, vertine, desmethylvertaline, decodine, and verticillatine (near the origin).

The crude alkaloid extract (as a viscous gum containing some $CHCl_3$) is dissolved in about ten times its weight of acetone and refluxed 1–2 hr. All the alkaloid usually goes into solution and then precipitation usually occurs within a few minutes at reflux. At the end of the reflux period the *hot* acetone mixture is filtered and the precipitate (IA) washed with acetone. The filtrates (IB) are saved.

The precipitate (IA) is refluxed with ten times its weight of $CHCl_3$ for 2 hr and allowed to cool. The insoluble material is filtered and washed with $CHCl_3$ to yield crude *verticillatine*. The chloroform solution contains a mixture of at least three alkaloids which have not as yet been separated or identified. Verticillatine may be purified by conversion to the diacetyl derivative with acetic anhydride and triethylamine. When the crude diacetate is refluxed in CH_3OH pure *verticillatine* is slowly deposited as bright yellow crystals.

The acetone filtrates (IB) are allowed to stand for about 1 week and the crystals (2A) which form are collected and washed with acetone.

The crystals (2A) consist mainly of *vertine* and *decodine*. The vertine is separated by dissolving the crystals in 0.3 *N* NaOH and extracting the solution three times with $CHCl_3$. The $CHCl_3$ extracts are dried *briefly* over anhydrous Na_2SO_4 and the solution is concentrated until crystallization ensues. The crystals are recrystallized from 95% ethanol to give pure vertine. The decodine is recovered from the aqueous extract by lowering the pH to 10 and extracting with $CHCl_3$. The $CHCl_3$ extracts are evaporated to dryness. The residue is crystallized from CH_3OH to yield pure decodine.

The acetone filtrates (2B) from the crystallization of the vertine–decodine mixture are evaporated to dryness and taken up in a small volume of CH_3OH. The resulting solution should be a viscous oil. This oil is added to a rapidly stirred solution of 0.3 *N* NaOH (about 600 ml of solution/50 g of dry alkaloid). To this mixture is added 70 ml of saturated salt solution/600 ml of NaOH solution. If at the end of 1 or 2 hr of stirring a clear solution or a well-distributed emulsion is not obtained, the mixture is stirred 1 additional hr with 100–200 ml of ether. If there is still a significant amount of solid material present, the mixture must be filtered through a coarse sintered glass funnel. The ether layer is separated and the aqueous layer is extracted with two or three 100-ml portions of ether. The ether extracts (3A) are combined and back-washed with two 110-ml portions of a mixture of 100 ml of 0.3 *N* NaOH with 10 ml of saturated salt solution. The aqueous extracts are combined and saved (3B). The ether extracts (3A) contain *decaline*, *vertaline*, and traces of decinine. These may be separated by chromatography on Woelm activity IV acid washed alumina.

The aqueous basic extracts (3B) are extracted with four 200-ml portions of a mixture of 25% ether, 25% CCl_4, and 50% $CHCl_3$ (the use of $CHCl_3$ alone results in stable emulsions). The aqueous extracts (4B) are saved. The organic extracts (4A) are dried *briefly* over anhydrous Na_2SO_4 and reduced to dryness. A mixture of alkaloids tends to crystallize so the alkaloid extract is immediately concentrated. The residue is redissolved in about an equal volume (equal to the amount of residue) of acetone. Hot benzene is added to this solution and the acetone is boiled out. The benzene solution is reduced to a volume of about 2–2.5 times the weight of the dry alkaloidal mixture, then set aside to crystallize. After several days the crystals (5A) are collected and washed with benzene. The filtrates are combined and saved (5B).

The crystals (5A) are a mixture of *decinine* and *decamine*. Very little of these alkaloids remain dissolved in the benzene filtrate. The decamine may be obtained by stirring the crystals with about five times their weight of hot methanol and filtering. The residue is then dissolved in 95% ethanol and set aside to crystallize, yielding decamine.

Pure decinine is obtained by combining the ethanol and methanol filtrates from the isolation of decamine, concentrating to a small volume, and adding the hot alcoholic solution to boiling 1% HCl (about 50 ml/g of alkaloid). The mixture is stirred rapidly as the alcohol is boiled out. Decinine hydrochloride precipitates rapidly from the boiling solution. The mixture is boiled and stirred for about 30 min after precipitation to remove the alcohol and to prevent *severe bumping*. The *hot* mixture is filtered giving decinine hydrochloride. The hydrochloride is dissolved in aqueous dilute NaOH, extracted with $CHCl_3$, and recrystallized from methanol to give pure *decinine*.

The benzene filtrate (5B) from the crystallization of the decinine–decamine mixture contains primarily desmethylvertaline and desmethyldecaline. These may be separated by column chromatography on activity IV Woelm acid alumina. The only successful solvent for the crystallization of *desmethylvertaline* is CH_3OH with which it forms a strong complex. A 1-l. sample crystallized with difficulty without a seed and has a broad melting point (120–160°) even when pure. *Desmethyldecaline* has not been obtained crystalline.

The aqueous NaOH extract (4B), from the $CHCl_3$ extraction of the decinine, decamine, desmethyldecaline, and desmethylvertaline alkaloids, is reduced to a pH of about 10 and extracted with $CHCl_3$. This extract contains decodine and other unknown alkaloids. Two methods have been found to separate decodine in a crude form from most of the impurities. (a) The mixture of alkaloids is dissolved in approximately 20 ml of CH_3OH and 5 ml of concentrated HCl/20 g of crude alkaloidal mixture. To the mixture is added twice its volume of H_2O and the mixture is refluxed on a steam bath until crystallization takes place. The crystals are washed with a little hot water, yielding crude *decodine hydrochloride*. (b) The mixture of alkaloids is dissolved in about ten times its weight of acetone and set aside to crystallize. After about 1 week of standing the crystals are filtered, yielding crude *decodine*.

Preparation of Acetyldesmethylvertaline. Desmethylvertaline (200 mg) was dissolved in 2 ml of triethylamine and 2 ml of acetic anhydride. The reaction mixture was allowed to stand overnight and was then concentrated to a small volume under vacuum. The residue was taken up in dilute HCl and washed with ether. The acid–water layer was made basic with Na_2CO_3 and extracted with ether to yield 150 mg of basic material. The material would not crystallize but was purified by chromatography on neutral Woelm alumina, activity III (elution with ether): ir ($CHCl_3$) 1770 cm^{-1} (PhOCOCH_3); nmr ($CDCl_3$) τ 7.70 (s, 3, PhOCOCH_3), 6.12 (s, 3, PhOCOH_3). Acetyldesmethyldecaline was prepared in a similar manner.

Preparation of Vertaline (II) from Desmethylvertaline. To an acetone solution containing 3 g of NaOH 300 mg of desmethylvertaline was added. Two 0.1-ml portions of $(CH_3)_2SO_4$ were added at 2-hr intervals. The mixture was extracted with ether which was dried and concentrated to dryness. The residue was crystallized from CH_3OH, yielding 150 mg of vertaline (II), mp and mmp[4] 194–196°. The nmr and ir were identical with an authentic sample.[4]

The **hydrobromide** was prepared in tetrahydrofuran by reaction with hydrobromic acid. Recrystallization from methanol afforded an analytical sample, mp 275–278°.

Anal. Calcd for $C_{26}H_{31}NO_5 \cdot HBr$: C, 60.23; H, 6.18; Br, 15.44. Found: C, 60.29; H, 6.18; Br, 15.42.

The **methiodide** was recrystallized from tetrahydrofuran–methylene chloride, mp 221°.

Anal. Calcd for $C_{26}H_{34}INO_5 \cdot H_2O$: C, 53.50; H, 6.45. Found: C, 53.75; H, 6.01.

Preparation of Decaline (V) from Desmethyldecaline. Excess ethereal diazomethane was distilled into a CH_3OH–tetrahydrofuran solution containing 2 g of desmethyldecaline. The reaction was allowed to proceed for 12 hr and then the mixture was concentrated to a small volume and diluted with dilute HCl after which crystals of decaline hydrochloride (1.4 g) (V–HCl) were collected, mp 280°; the mixture melting point with authentic decaline hydrochloride was not depressed. The infrared and nmr spectra of the free bases were identical.[4]

The **methiodide** was recrystallized from tetrahydrofuran–methylene chloride, mp 215°.

Anal. Calcd for $C_{26}H_{74}INO_5$: C, 55.02; H, 6.32. Found: C, 55.02; H, 5.82.

Tetrahydrovertaline. Vertaline (153 mg) was added to a solution of 100 mg of LAH in 25 ml of tetrahydrofuran and the mixture was brought to reflux for 7 hr and then allowed to stand for 12 hr at room temperature. Water was added to destroy the excess LAH and the mixture was filtered, dried, and concentrated to yield 140 mg of a white frothy solid: nmr ($CDCl_3$) τ 6.45 (t, 2, CH_2CH_2OH), 5.4 (m, 1, $>CHOH$).

The **methiodide** was crystallized from acetone–ether: mp 191–194°.

Anal. Calcd for $C_{26}H_{38}INO_5$; C, 54.64; H, 6.66; O, 14.01. Found: C, 54.56; H, 6.76; O, 14.01.

Emde Reduction of Vertaline Methiodide (VI-B). Vertaline methiodide (600 mg) (VI-B) was dissolved in 100 ml of liquid ammonia and small pieces of sodium were added until the solution remained blue 10 min. Solid ammonium chloride was then added to discharge the blue color and then the ammonia was allowed to evaporate. The residue was dissolved in dilute HCl, extracted with ether, dried, and concentrated to dryness to yield a yellow oil which was shown by ir to be identical with 3-phenylpropanol (XI). The acidic water solution was made basic with Na_2CO_3 and extracted with $CHCl_3$. The organic layers were combined, dried, and concentrated to yield 200 mg (75%) of X-B (R = R′ = H): nmr ($CDCl_3$) τ 7.70 (s, 3, NCH_3), 6.21 (s, 6, 2-$PhOCH_3$), 3.57 (s, 1, Ph*H*), 3.45 (s, 1, Ph*H*).

The **diacetate** X-B (R = R′ = $COCH_3$) showed nmr ($CDCl_3$) τ 8.00 (s, 3, $PhOCOCH_3$), 7.80 (s, 3, NCH_3), 7.68 (s, 3, $ROCOCH_3$), 6.20 (s, 3, $PhOCH_3$), 6.15 (s, 3, $PhOCH_3$), 3.45 (s, 1, Ph*H*), 3.30 (s, 1, Ph*H*). The methiodide of the diacetate precipitated from ether as an amorphous solid.

Anal. Calcd for $C_{23}H_{36}INO_6$: C, 50.27; H, 6.82. Found: C, 50.89; H, 6.82.

The **methyl ether** X-B (R = CH_3, R′ = H) (CH_2N_2) was not crystalline: nmr ($CDCl_3$) τ 7.68 (s, 3, NCH_3), 6.25 (s, 3, $PhOCH_3$), 6.20 (s, 3, $PhOCH_3$), 6.18 (s, 3, $PhOCH_3$), 3.49 (s, 1, Ph*H*), 3.25 (s, 1, Ph*H*), $[\alpha]^{CH_3OH}D$ +59°.

Emde Reduction of Decaline Methiodide (VI). The same procedure was used as in the Emde reduction of vertaline methiodide. The 3-phenylpropanol was isolated in the neutral fraction and identified by comparison (ir) with an authentic sample. An 85% yield of basic product (X) was isolated: nmr ($CDCl_3$) τ 7.60 (s, 3, NCH_3), 6.20 (s, 6, 2$PhOCH_3$), 3.55 (s, 1, Ph*H*), 3.40 (s, 1, Ph*H*).

The **diacetate** X (R = R′ = $COCH_3$) could not be obtained crystalline. An analytical sample was purified by chromatography on Woelm neutral alumina, grade II: nmr ($CDCl_3$) τ 8.00 (s, 3, $ROCOCH_3$), 7.75 (s, 3, NCH_3), 7.70 (s, 3, $PhOCOCH_3$), 6.23 (s, 3, $PhOCH_3$), 6.18 (s, 3, $PhOCH_3$); mass spectrum (70 eV) *m/e* (relative intensity) 407 (5), 344 (10), 129 (17), 119 (17), 103 (11), 98 (100), 91 (29), 86 (72), 70 (92), 56 (55), 43 (65), 41 (99). Molecular weight calculated for $C_{22}H_{33}NO_6$, 407.

The **methyl ether** X (R = CH_3; R′ = H) was amorphous: nmr ($CDCl_3$) τ 7.60 (s, 3, NCH_3), 6.21 (s, 3, $PhOCH_3$), 6.19 (s, 3, $PhOCH_3$), 6.14 (s, 3, $PhOCH_3$), 3.50 (s, 1, Ph*H*), 3.25 (s, 1, Ph*H*), $[\alpha]^{CH_3OH}D$ −36°.

The **acetyl derivative** of the *methyl ether* X (R = CH_3; R′ = $COCH_3$) was not crystalline: ir ($CHCl_3$) 1740 cm^{-1} ($ROCOCH_3$).

Preparation of Cyanamide XII-B. Compound X-B (R = CH_3; R′ = $COCH_3$) (1.4 g) was dissolved in 70 ml of anhydrous ether, 700 mg of CNBr was added, and the mixture was allowed to stand at room temperature 4 hr. The solution was extracted twice with dilute HCl, dried, and concentrated to yield 1.3 g of an amorphous product (XI-B). An analytical sample was prepared by chromatography on Woelm activity II neutral alumina: ir ($CHCl_3$) 2200 cm^{-1} (C≡N); mass spectrum (70 eV) *m/e* (relative intensity) 390 (32), 359 (25), 332 (15), 300 (10), 182 (75), 168 (18), 152 (65), 138 (50), 125 (22), 109 (100), 84 (57), 55 (85), 43 (82). Molecular weight calculated for $C_{21}H_{30}N_2O_5$, 390.

Preparation of Des-*N*-methyl Compound XIII-B. Cyanamide XII-B (1 g) was dissolved in 100 ml of tetrahydrofuran (freshly distilled from LAH), 500 mg of LAH was added, and the mixture allowed to stand at room temperature overnight. Water was added and the solution was filtered, dried, and concentrated to an oil (XIII-B): mass spectrum (70 eV) *m/e* 322 (5), 283 (5), 184 (6), 159 (15), 129 (20), 107 (17), 84 (12), 70 (100), 55 (9), 43 (15). Molecular weight calculated for $C_{19}H_{29}NO_4$, 322.

Preparation of Cyanamide XII. The same procedure was used as in the synthesis of XII: ir ($CHCl_3$) 2200 cm^{-1} (C≡N); mass spectrum (420 (10) (impurity?), 390 (48), 375 (23), 359 (32), 323 (19), 300 (20), 182 (71), 168 (41), 152 (63), 138 (68), 125 (20), 109 (100), 84 (32), 55 (81), 43 (71). Molecular weight calculated for $C_{21}H_{30}N_2O_5$, 390.

Acknowledgment. We thank Professor Robert Godfrey for assistance locating and collecting the plant material, Mr. Alan Potter and Mr. Mark Wolf for technical assistance, and those individuals listed in the Experimental Section of ref 2 for spectral data.