

# Lythraceae Alkaloids. IX. The Isolation and Structure Elucidation of the Alkaloids of *Lagerstroemia indica* L.<sup>1,2</sup>

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**Abstract:** Six alkaloids have been isolated from the Lythraceae plant *Lagerstroemia indica* L. and structures have been assigned to all of them on the basis of spectroscopic and degradative studies. Three of the alkaloids—decamine, decinine, and decodine—were isolated previously from *Decodon*. Dihydroverticillatine had not been isolated previously; it had been prepared by the catalytic hydrogenation of verticillatine. Lagerstroemine (I, R = H) is a new methoxylation pattern in the verticillatine series of alkaloids. Lagerine (V, R = H) has a biphenyl ether quinolizidine skeleton which differs from that of any known Lythraceae alkaloid; however, this structure is consistent with current biogenetic theory.

Since the initial report<sup>4</sup> of crystalline alkaloids from *Decodon verticillatus* over a dozen bases have been isolated from this and other members of the Lythraceae family of plants. Structures have been assigned to almost every one of these alkaloids by a combination of X-ray crystallographic, chemical, and spectroscopic studies. During the course of these investigations a number of physical and chemical methods were devised for the structure elucidation of these novel quinolizidine bases.<sup>2,5</sup> Furthermore the structural relationships that were observed suggested a biosynthesis for these alkaloids.<sup>6</sup> With the work on *Decodon* completed we then turned to an investigation of *Lagerstroemia indica* L. to see if the same chemical and biogenetic criteria could be applied to the alkaloids present in other members of the Lythraceae plant family.

*Lagerstroemia indica* is a decorative shrub common in the southern United States and is commonly called "crape myrtle." It flowers early in the summer and produces seed pods which mature in the early fall. Preliminary studies showed that the alkaloids are concentrated in the seed pods with only trace amounts in the leaves and stems.<sup>7</sup> The mature seeds were collected near Tallahassee, Fla., and the crude alkaloid was fractionated by a procedure devised in our studies of *Decodon*.<sup>2</sup> Extraction of a strongly basic solution of the alkaloids gave an organic extract containing the monophenolic bases. When the pH was adjusted to

10 the bases with two phenolic hydroxyl groups were obtained. These two fractions were further purified by column chromatography to yield the alkaloids listed in Table I.

Table I. Alkaloids from *Lagerstroemia indica* L.

Alkaloids	Mp, °C	Formula	OCH <sub>3</sub>	OH	Yield, % <sup>a</sup>
Decinine	222	C <sub>26</sub> H <sub>31</sub> NO <sub>5</sub>	2	1	2.8
Decamine	222	C <sub>26</sub> H <sub>31</sub> NO <sub>5</sub>	2	1	0.8
Lagerstroemine	230	C <sub>26</sub> H <sub>31</sub> NO <sub>5</sub>	2	1	16.0
Lagerine	210	C <sub>25</sub> H <sub>29</sub> NO <sub>5</sub>	1	1	10.0
Dihydroverticillatine	263	C <sub>25</sub> H <sub>29</sub> NO <sub>5</sub>	1	2	0.5
Decodine	193	C <sub>25</sub> H <sub>29</sub> NO <sub>5</sub>	1	2	Trace

<sup>a</sup> Based on crystalline alkaloid isolated from the crude alkaloid extract.

Decinine, decamine, and decodine have been isolated previously from *Decodon* and were identified by direct comparison with authentic samples.<sup>4</sup> Dihydroverticillatine had not been observed previously as a naturally occurring alkaloid but had been prepared by catalytic hydrogenation of verticillatine.<sup>8</sup> The sample from *Lagerstroemia* was identified by direct comparison with a sample prepared in this way.

Lagerstroemine<sup>9</sup> was shown to be a new member in the verticillatine (D) series of biphenylquinolizidine alkaloids<sup>5</sup> since treatment with diazomethane converted it to the known verticillatine derivative dihydrodimethylverticillatine (Chart I).<sup>8</sup> This interconversion established structure I (R = CH<sub>3</sub>) for methylagerstroemine. The structure of lagerstroemine was ascertained by reduction to diol II and the subsequent conversion of the diol methiodide to the benzopyran III on treatment with base. The pyran structure was assigned on the basis of nuclear magnetic resonance

(8) J. P. Ferris, *J. Org. Chem.*, **28**, 817 (1963).

(9) This alkaloid was given the name indicamine in our preliminary communication.<sup>10</sup> However, Dr. Bryce Douglas of Smith, Kline and French advised me that this name had already been assigned to a *Plantaginaceae* alkaloid.<sup>11</sup>

(10) J. P. Ferris, C. B. Boyce, R. C. Briner, B. Douglas, J. L. Kirkpatrick, and J. A. Weisbach, *Tetrahedron Lett.*, 3641 (1966).

(11) H. G. Boit, "Ergebnisse der Alkaloid-Chemie Bis 1960," Academic-Verlag, Berlin, 1961, p 949.

(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, R. C. Briner, and C. B. Boyce, *J. Amer. Chem. Soc.*, **93**, 2953 (1971).

(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) J. P. Ferris, C. B. Boyce, and R. C. Briner, *J. Amer. Chem. Soc.*, **93**, 2942 (1971).

(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) Private communication from Dr. I. Pachter, Smith, Kline and French Laboratories.

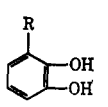
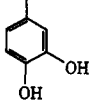
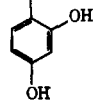


a combination of chemical and spectral methods. The basic product (VIIIa) exhibited *O*-methyl and *N*-methyl resonances in the nmr. Reaction with diazomethane yielded a dimethoxy derivative (VIIIb) which could be acetylated to an aliphatic monoacetate (VIIIc). Direct acetylation of VIIIa yielded a diacetate (VIId) in which one of the acetate groupings is phenolic (1770  $\text{cm}^{-1}$ ) and the other aliphatic (1740  $\text{cm}^{-1}$ ). The mass spectrum of the diacetate exhibited a molecular ion at 377 consistent with the proposed structure and peaks at  $m/e$  98 and 84 characteristic of the piperidine ring.<sup>2</sup> These results are in agreement with the functionality shown in VIII and confirm the previous conclusion that there is one methoxyl group attached to each of the aromatic rings in methyllagerine.

The substitution pattern of ring C of methyllagerine remained to be elucidated. The absence of substitution in the 3'' and 4'' positions was established by the observation of a one proton low-field doublet (1.84  $\tau$ ,  $J = 9$  Hz) in the nmr spectrum of methyllagerine *N*-oxide (V-*N*-oxide,  $R = \text{CH}_3$ ). A similar low-field proton has been observed in every Lythraceae alkaloid *N*-oxide studied to date and has been assigned to H-3''. Therefore this low-field signal can be assigned to H-3'' in methyllagerine *N*-oxide as well. From these data it can be concluded that there is a proton at the 3'' position and from the splitting pattern of this proton it can be concluded that there is also a proton at the 4'' position.

The ring C methoxyl group of methyllagerine was shown to be at the 6'' position by comparison of the uv spectrum of VIIIb *N*-oxide with that of the alkylpyrocatechol and alkylresorcinol derivatives (Table II).<sup>14</sup> Clearly the ultraviolet spectrum of the cleavage

Table II. Uv Spectra of Dihydroxybenzene Derivatives<sup>a</sup>

R						
	$\lambda_{\text{max}}$ , nm	Log $\epsilon$	$\lambda_{\text{max}}$ , nm	Log $\epsilon$	$\lambda_{\text{max}}$ , nm	Log $\epsilon$
Me	275	3.26	283	3.44	282	3.45
Et	276.5	3.27	283	3.48	281	3.46
VIIIb <i>N</i> -oxide	273	3.27				

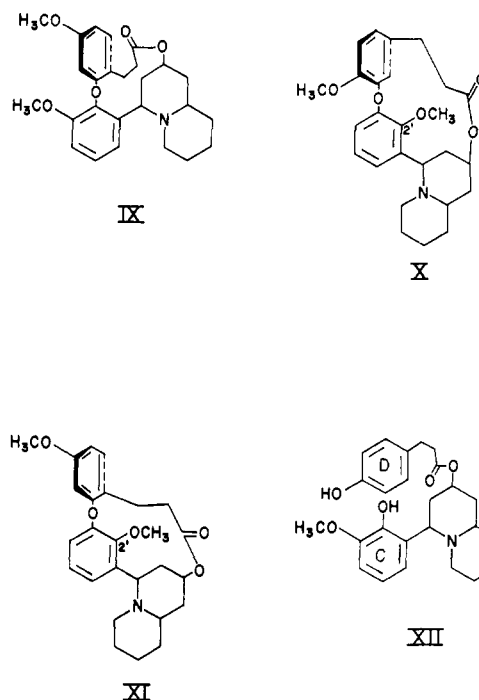
<sup>a</sup> See ref 14.

product is only consistent with spectra of the 3-alkylpyrocatechols. In addition the nmr chemical shift of the aromatic protons in VIII was compared with chemical shifts for simple methoxybenzenes. The aromatic protons of VIIIb come as a single peak at  $\tau$  3.25 in good agreement with the nmr spectrum of *o*-dimethoxybenzene where a single peak at  $\tau$  3.30 is reported.<sup>15</sup> By comparison *m*-dimethoxybenzene exhibits multiplets in the range 3.05–3.75.<sup>16</sup> Furthermore using the empirical constants of Ballantine and Pillinger<sup>17</sup> a 3- or 4-alkylpyrocatechol is predicted to have two resonances at 3.35 and 3.30. A 4-alkyl-

resorcinol is predicted to have three peaks at 3.70, 3.65, and 3.00. The observed and calculated chemical shifts of VIIIb are well within the errors of the empirical constants for the pyrocatechol derivatives but are not for the resorcinol derivatives.

Finally we observed that sodium-ammonia cleavage of acetylagerine methiodide (V-methiodide,  $R = \text{COCH}_3$ ) yielded VIIIa. Since VIIIa contains one aromatic methoxyl the methoxyl group of lagerine must be attached to ring C and the phenolic hydroxyl group to ring D.

There are four possible structures for methyllagerine consistent with the structures of the sodium-ammonia cleavage products (V ( $R = \text{H}$ ), IX, X, XI). Structures



X and XI were eliminated from further consideration by the observation that the *O*-methyl resonances of methyllagerine are at 6.00 and 6.05. In structures X and XI the 2''-methoxyl is shielded by the adjacent phenyl ring and would be observed at 6.2–6.3. Furthermore the Dreiding model of XI shows considerable strain and nonbonded repulsions which suggest that it is an unlikely possibility.

Structure IX may be eliminated from further consideration since the highest field aromatic proton in the nmr of methyllagerine is a doublet at 3.4. Models show that the biphenyl ether is in the "skewed" conformation in IX in which 6'-H would be observed at 3.8–4.0.<sup>18</sup> Structure V ( $R = \text{CH}_3$ ) remains for methyllagerine. Models show that the biphenyl ether is present in the "butterfly" conformation in this structure in which there is a minimum of shielding of the substituents in one ring by the other phenyl ring.<sup>18</sup>

In addition to the above arguments it should be noted that the mechanism proposed for the sodium-ammonia cleavage reaction is not consistent with X and XI.<sup>2</sup> It was observed that the reaction takes place only on the quaternary salt and not on the tertiary amine; therefore, the initial step probably involves

(14) L. Barker and N. W. Hollingworth, *J. Appl. Chem.*, **9**, 16 (1959).

(15) J. Martin and B. P. Darley, *J. Chem. Phys.*, **37**, 2594 (1962).

(16) C. Heathcock, *Can. J. Chem.*, **40**, 1866 (1962).

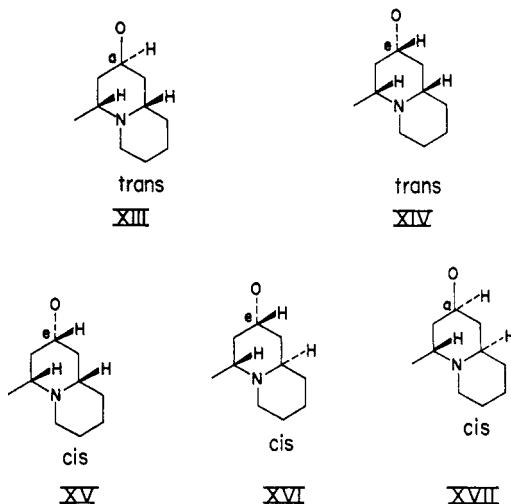
(17) J. A. Ballantine and C. T. Pillinger, *Tetrahedron*, **23**, 1691 (1967).

(18) P. A. Lehman and E. C. Jorgensen, *Tetrahedron*, **21**, 363 (1965); W. D. Chandler, W. MacFarlane Smith, and R. Y. Moir, *Can. J. Chem.*, **42**, 2549 (1964).

benzylic cleavage with VII as the most likely reaction intermediate. The electron shift shown in VII is not likely when the biphenyl ether group is meta to the ring C benzylic anion.

Finally it should be noted that the ring D resorcinol substitution pattern of structures IX and XI is not likely on biogenetic grounds. The final stage in the lagerine biosynthesis probably involves the oxidative coupling of XII.<sup>6</sup> Coupling to a position which is meta to the ring D hydroxyl group is highly unlikely.

The stereochemistry of the quinolizidine ring in lagerine remained to be established. The previously mentioned low field shift of H-3'' in methylagerine *N*-oxide limits the number of possible lagerine structures to XIII–XVII.<sup>2</sup> The trans-fused quinolizidines XIII



and XIV can be eliminated as possibilities by the absence of "Bohlmann bands" in the ir characteristic of such structures.<sup>19</sup> Furthermore the chemical shifts of H-4, the *N*-methyl (in the methiodide), and H-3'' (in the *N*-oxide) correspond closely to that which was observed for the cis-fused quinolizidine vertaline and not with the corresponding trans-fused isomer (decaline) (Table III).<sup>2</sup> From these data it was concluded that a cis juncture is present in lagerine.

Table III. Lagerine, Vertaline, and Decaline Chemical Shifts

	H-4 <i>N</i> - oxide	H-4 meth- iodide	<i>N</i> -Methyl meth- iodide	H-3'' <i>N</i> - oxide
Methylagerine	6.14	5.79	6.49	1.84
Acetylagerine	6.02	5.80	6.51	1.90
Vertaline	5.97	5.79	6.41	2.08
Decaline	6.50	6.65	6.79	2.37

The *cis*-quinolizines XV and XVI were eliminated from further consideration by the observation that the half-height width of H-2 in the nmr is the same in lagerine derivatives as it is in vertaline and decaline derivatives.<sup>2</sup> This is consistent only with structure XVII in which H-2 is equatorial in a gauche relationship with the protons on the adjacent carbon atoms.

As was anticipated on the basis of our experience with other Lythraceae alkaloids the relative stereochemistry of lagerine is the same as that of vertaline.

(19) F. Bohlmann, *Chem. Ber.*, **91**, 2137 (1958).

Presumably the main biosynthetic difference in the two alkaloids is that ring C of lagerine originates from 2,3-dihydroxybenzaldehyde or its equivalent and C of vertaline and decaline originates from 3,4-dihydroxybenzaldehyde.<sup>6</sup>

The proposed lagerine structure is consistent with the optical rotation of the cleavage product VIIIb. A rotation of +26° was observed in the lagerine series as compared with +59° for the comparable derivative from vertaline.<sup>2</sup> The corresponding product from decaline with the opposite configuration at C-10 has a rotation of -36°. These data suggest that both lagerine and vertaline have the same configuration at C-10 in agreement with structure V (R = H) for lagerine.

## Experimental Section

The general experimental procedures used in this study are given in ref 2 and 5.

**Isolation of the Lagerstroemia Alkaloids.** Essentially the same procedure used with the *Decodon* alkaloids was applied in this work.<sup>2</sup> The total alkaloid yield varied from 0.03 to 0.3% with an average value of 0.1%. The crude alkaloid was suspended in a small volume of methanol and sufficient 0.3 *N* NaOH was added until solution was complete. Extraction of this solution with CHCl<sub>3</sub> yielded the "pH 14" alkaloids. The pH of the aqueous solution was adjusted to 10 and the solution was extracted with CHCl<sub>3</sub> to yield the "pH 10" alkaloids.

The "pH 14" alkaloids were dissolved in a small volume of benzene and chromatographed on Woelm grade III neutral alumina and the separation was monitored by tlc.<sup>2</sup> Decinine, lagerstroemine, decamine, and lagerine were eluted in that order using benzene, 1:1 ether-benzene, and ether as eluents.

**Decinine** was purified by preparation of the hydrochloride from dilute HCl. The decinine recovered from the salt was identical (melting point, mixture melting point, and ir) with an authentic sample from *Decodon*.<sup>4</sup>

**Lagerstroemine** was isolated by crystallization from ethyl acetate. An analytical sample was prepared by recrystallization from ethanol: mp 240°; ir (KBr) 3000 cm<sup>-1</sup> (OH), 1720 cm<sup>-1</sup> (C=O); uv max (CH<sub>3</sub>OH) 294 nm (ε 4750), 220 (28,200); base 323 nm (ε 1280), 294 (3890); nmr (CDCl<sub>3</sub>) τ 6.30 (s, 3, PhOCH<sub>3</sub>), 6.12 (s, 3, PhOCH<sub>3</sub>), 5.05 (m, 1, -CO<sub>2</sub>CH-); pK<sub>a</sub> (CH<sub>3</sub>CH<sub>2</sub>OH) 7.7; [α]<sub>D</sub><sup>25</sup> -137°.

*Anal.* Calcd for C<sub>26</sub>H<sub>31</sub>NO<sub>5</sub>: C, 71.37; H, 7.14; N, 3.20; 2OCH<sub>3</sub>, 14.19; mol wt, 437. Found: C, 70.60; H, 7.05; N, 3.20; OCH<sub>3</sub>, 14.22; mol wt (by titration), 435.

The **methyl ether** was prepared using CH<sub>2</sub>N<sub>2</sub> and recrystallized from acetone-ether, mp 187–188°. The preparation was identical (melting point, mixture melting point, ir, uv, and nmr) with dimethyldihydroverticillatine.<sup>8</sup>

The filtrates from the crystallization of lagerstroemine were concentrated and the residue was crystallized from 95% ethanol to give **lagerine** as flat plates: mp 203–204°; ir (KBr) 2600 cm<sup>-1</sup> broad (OH), 1725 cm<sup>-1</sup> (C=O); uv max (CH<sub>3</sub>OH) 275 nm (ε 3100), 232.5 (20,200) (base), 290 (5130), 240 (16,300), [α]<sub>D</sub><sup>25</sup> -184°; pK<sub>a</sub> 7.3 (ethanol).

*Anal.* Calcd for C<sub>25</sub>H<sub>29</sub>NO<sub>5</sub>: C, 70.90; H, 6.90; N, 3.31; O, 18.89; OCH<sub>3</sub>, 7.33. Found: C, 71.21; H, 6.69; N, 3.37; O, 18.73; OCH<sub>3</sub>, 7.33.

The **methiodide** was crystallized from ethanol, mp 266°.

*Anal.* Calcd for C<sub>26</sub>H<sub>32</sub>INO<sub>5</sub>: C, 55.22; H, 5.66; I, 23.47. Found: C, 55.31; H, 5.77; I, 24.11.

The **methyl ether** was prepared with CH<sub>2</sub>N<sub>2</sub> and crystallized from ethyl acetate, mp 230°. An analytical sample was purified by vacuum sublimation: mp 240°; uv max (CH<sub>3</sub>OH) 282.5 nm (ε 2030), no change in base; nmr (CDCl<sub>3</sub>) τ 5.99 (s, 3, PhOCH<sub>3</sub>), 6.02 (s, 3, PhOCH<sub>3</sub>), 5.05 (m, 1, -CO<sub>2</sub>CH-); [α]<sub>D</sub><sup>25</sup> -178°.

*Anal.* Calcd for C<sub>26</sub>H<sub>31</sub>NO<sub>5</sub>: C, 71.40; H, 7.14; N, 3.20; O, 18.26. Found: C, 71.30; H, 7.17; N, 3.20; O, 18.28.

**Methiodide of the methyl ether** was recrystallized from tetrahydrofuran-methylene chloride, mp 212–213°.

***N*-Oxide of methyl ether** was recrystallized from ethyl acetate, mp 204–206°.

**Acetylagerine** was recrystallized from ether: mp 217°; ir (KBr) 1770 cm<sup>-1</sup> (PhOCOCH<sub>3</sub>) 1740 (C=O); uv max (CH<sub>3</sub>OH)

282.5 nm ( $\epsilon$  2340), 235 (24,500); nmr ( $\text{CDCl}_3$ )  $\tau$  7.7 (s, 3,  $\text{CH}_3\text{CO}_2$ ) 6.12 (s, 3,  $\text{PhOCH}_3$ ).

**Acetylagerine methiodide** was recrystallized from tetrahydrofuran, mp 247°.

Chromatography of the filtrates from the crystallization of lagerine on Woelm grade III neutral alumina yielded decamine, mp 221°. This material was identical (melting point, mixture melting point, and ir) with an authentic sample.<sup>4</sup>

The "pH 10" alkaloids were chromatographed on grade IV neutral Woelm alumina. The fraction eluted with ethyl acetate was recrystallized from methanol, mp 258–259°; mixture melting point with an authentic sample of dihydroverticillatine<sup>4</sup> was not depressed.

The nmr and ir spectra, melting point, and mixture melting point of the **dimethyl ether**<sup>4</sup> and **diacetate**<sup>4</sup> were identical with those of authentic samples.

The filtrates from the crystallization of dihydroverticillatine were combined and acetylated. The acetyl derivatives were chromatographed on grade IV Woelm neutral alumina. Elution with benzene yielded mainly **diacetyldecodine** which was recrystallized from ether-petroleum ether, mp 202°. This compound was identified by comparison of its ir spectrum with that of an authentic sample.<sup>4</sup>

**LAH Reduction of Lagerstroemine (I, R = H).** The same procedure used for the LAH reduction of dihydroverticillatine was applied here.<sup>5</sup> The amorphous diol product was converted to the methiodide and used directly in the next reaction.

**Preparation of Dibenzopyran III.** The methiodide of II (1 g) was dissolved in 2 ml of 95% ethanol and the solution was added to 75 ml of aqueous  $\text{Na}_2\text{CO}_3$ . The mixture was heated at reflux for 3 days and then extracted with ethyl acetate. Concentration of the extracts yielded 0.5 g of an amorphous solid.

The **methiodide** derivative of III (mp 193°) was identical (melting point, mixture melting point, and nmr) with the corresponding pyran prepared from dihydroverticillatine.<sup>5</sup>

**Preparation of Tetrahydromethylagerine (VI).** LAH (50 mg) was added to a solution of 100 mg of methylagerine in anhydrous tetrahydrofuran and the mixture was allowed to stand at room temperature overnight.  $\text{H}_2\text{O}$  was added and the solution was

filtered and concentrated to yield 90 mg of amorphous solid, ir ( $\text{CHCl}_3$ ) no absorption at  $1726\text{ cm}^{-1}$ .

The **methiodide** was recrystallized from ethanol, mp 150–151°.

**Emde Reduction of Methylagerine Methiodide (V-Methiodide, R =  $\text{CH}_3$ ).** Small pieces of Na were added to a solution of 2.5 g of the title compound in 100 ml of liquid ammonia until blue color remained for 10 min.  $\text{NH}_4\text{Cl}$  was added to discharge the blue color and the ammonia was allowed to evaporate. The residue was taken up in dilute HCl and extracted with ether. Concentration of the ether solution yielded an oil with an infrared spectrum that was identical with that of 3-(*p*-methoxyphenyl)propanol.<sup>13</sup>

The acidic solution was made basic with  $\text{Na}_2\text{CO}_3$  and extracted with  $\text{CHCl}_3$ . Concentration of the  $\text{CHCl}_3$  extract yielded 1.1 g (75%) of basic material (VIIIa): nmr ( $\text{CDCl}_3$ )  $\tau$  7.45 (s, 3,  $\text{NCH}_3$ ), 6.25 (s, 3,  $\text{OCH}_3$ ), 3.28 (s, 3,  $\text{PhH}$ ).

The **diacetate** (VIIId) was eluted with ether from Woelm grade II neutral alumina: mp 215°; ir (KBr)  $1770\text{ cm}^{-1}$  ( $\text{PhOCOCH}_3$ ),  $1740\text{ cm}^{-1}$  ( $>\text{CHOCOCH}_3$ ); mass spectrum (70 eV)  $m/e$  (relative intensity) 377 (1), 362 (8), 301 (11), 260 (20), 259 (19), 177 (47), 115 (40), 98 (43), 84 (100), 72 (51), 60 (75), 55 (30), 42–46 (50–100). Molecular weight calculated from  $\text{C}_{21}\text{H}_{31}\text{NO}_5$  is 377.

The **methyl ether** (VIIIb) was prepared using  $\text{CH}_2\text{N}_2$  and was an oil,  $[\alpha]_{\text{CH}_2\text{OH}_D}^{25} +26^\circ$ .

The **N-oxide of the methyl ether** was an amorphous solid: nmr ( $\text{CDCl}_3$ )  $\tau$  6.70 (s, 3,  $\text{NCH}_3$ ), 6.18 (s, 6,  $2\text{PhOCH}_3$ ), 3.25 (s, 3,  $\text{PhH}$ ); uv max ( $\text{CH}_3\text{OH}$ ) 275 nm ( $\epsilon$  2170).

**Emde Reduction of Acetylagerine Methiodide (V-Methiodide, R =  $\text{COCH}_3$ ).** A 75% yield of basic material was obtained when 1 g of the title compound was allowed to react in the usual manner with Na in ammonia. The diacetate was identical (ir, nmr, tlc) with VIIId prepared from methylagerine methiodide.

**Emde Reduction of Tetrahydromethylagerine Methiodide (VI-Methiodide).** The title compound was allowed to react in the usual manner with Na in ammonia. Extraction of the acidified reaction mixture with ether yielded a yellow gum which on vacuum sublimation, 60° (2 mm), yielded a solid: mp 51° (lit.<sup>13</sup> mp 52°); ir identical with that reported for 3-(*p*-hydroxyphenyl)propanol.<sup>13</sup>

The material obtained from the basic extract (VIIIa) was identical with that obtained from methylagerine methiodide.