

(c 2.5, H<sub>2</sub>O). A mixed melting point determination with the same salt prepared by the first method showed no depression of melting point.

*Anal.*—Calcd. for C<sub>25</sub>H<sub>31</sub>NO<sub>10</sub>: C, 59.40; H, 6.18. Found: C, 59.26; H, 6.28.

(-)-*N*-Methylpavine—The preparation of this base was carried out in exactly the same manner as for (+)-*N*-methylpavine from its bitartrate salt. The product, after recrystallization from aqueous ethanol, possessed a melting point of 130–140° (with effervescence);  $[\alpha]_D^{25} -209^\circ$  (c 1.0, C<sub>2</sub>H<sub>5</sub>OH). On drying the crystals in the same way as for the (+)-rotatory base, the white powder melted at 152–153°. A mixed melting point determination as well as infrared comparison with authentic dried argemonine base showed them to be completely identical.

### Spectra

**Nuclear Magnetic Resonance**—Spectra were obtained in CDCl<sub>3</sub> on a Varian A-60 spectrometer using tetramethylsilane as the internal standard.

**Mass**—Spectra were obtained on a C.E.C.-103-C instrument at 200° using a metal inlet at 70 e.v.

**Ultraviolet**—*N*-Methyl-1,2-dihydropapaverine (100 mg.) was dissolved in 100 ml. of 10% (w/v) aqueous tartaric acid. At various time intervals over a 72-hr. period the spectrum of the solution was examined over the wavelength range of 220–370 mμ to determine whether the characteristic absorption bands for argemonine were appearing in the 275–295-mμ region. The analysis was carried

out by diluting 1 ml. of the sample solution to 100 ml. with water and placing this solution in the sample cell. The reference cell was filled with a solution obtained by diluting 1 ml. of the 10% aqueous tartaric acid solution (without sample) to 100 ml. The measurements were carried out on a Bausch & Lomb model 505 recording spectrophotometer and showed no absorption in the region mentioned although maxima developed at 250 and 312 mμ.

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## Structures of Some Degradation Products of (±)-*N*-Methylpavine

By MAHMOUD M. ABDEL-MONEM\* and TAITO O. SOINE

The structures of three products encountered during structural studies on argemonine and (±)-*N*-methylpavine (I) have been determined. The first of these, obtained by hydrochloric acid treatment of 3-hydroxy-2':3':2'':3''-tetramethoxy-1:2-5:6-dibenzoöcta-1:5:7-triene (II), has been determined to be 3-chloromethyl-2':3':2'':3''-tetramethoxy-1:2-4:5-dibenzocyclohepta-1:4:6-triene. The second, known as argemoninic acid and resulting from permanganate oxidation of II, has been shown to be 2:2'-dicarboxy-4:5:4':5''-tetramethoxybenzil. The third product, resulting from alkaline ethyl chloroformate treatment of I, has been shown to be the corresponding *N*-carbethoxy derivative of pavine.

THE ISOLATION of three new alkaloids from *Argemone* species was accomplished in these laboratories (1–3), these alkaloids being named argemonine, norargemonine, and bisnorargemonine. Diazomethylation of the latter two showed them to be the mono- and diphenolic precursors, respectively, of argemonine. After initial studies

which led to an erroneous tentative structural postulation for argemonine as an aporphine (3, 4), the correct structure was reported by Martell, Soine, and Kier (5) as being (-)-*N*-methylpavine. The structure of synthetic (±)-*N*-methylpavine (I) had been elucidated in 1955 by Battersby and Binks (6) and the natural product proved to be identical to the synthetic product except for rotatory differences and melting point.

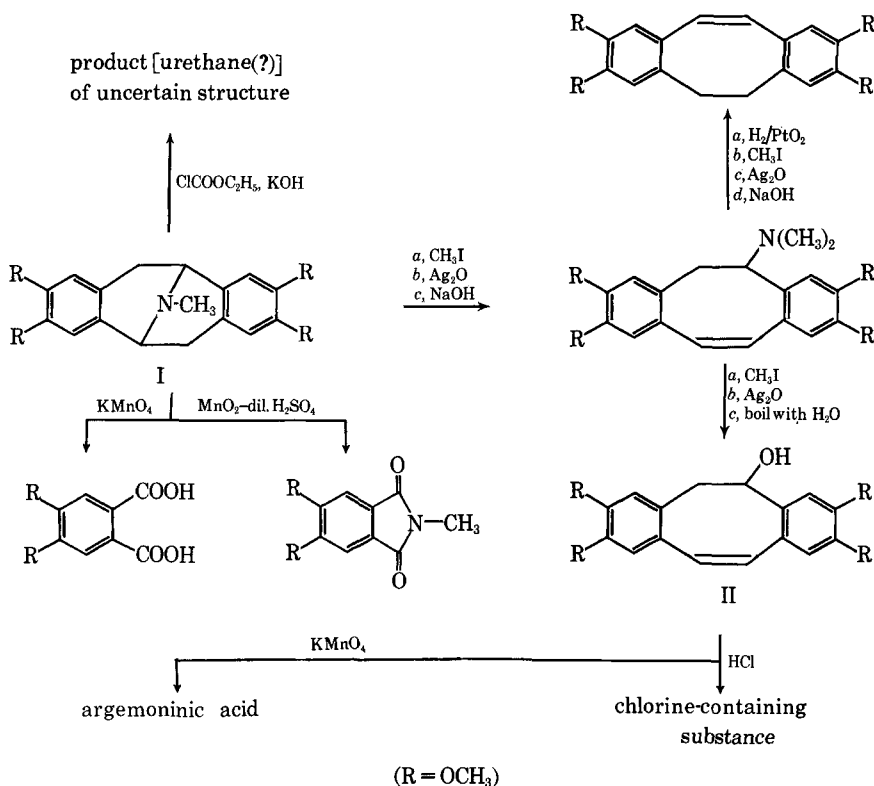
In the course of the early structural work on argemonine a number of degradation products were obtained as shown in Scheme I.

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\* Present address: Research Department, The Nile Company for Pharmaceuticals and Chemicals Industries, Cairo, Egypt, U.A.R.



Scheme I

Some of these had been reported earlier by Pyman (7) as well as by Battersby and Binks from their somewhat parallel studies on racemic *N*-methylpavine. In considering the possible structural assignments to the degradation products it appeared that some of them needed additional structural definition. The present work describes the structural elucidation of the three principal degradation products: (a) the chlorine-containing substance, (b) argemoninic acid, and (c) the ethyl chloroformate reaction product.

## DISCUSSION

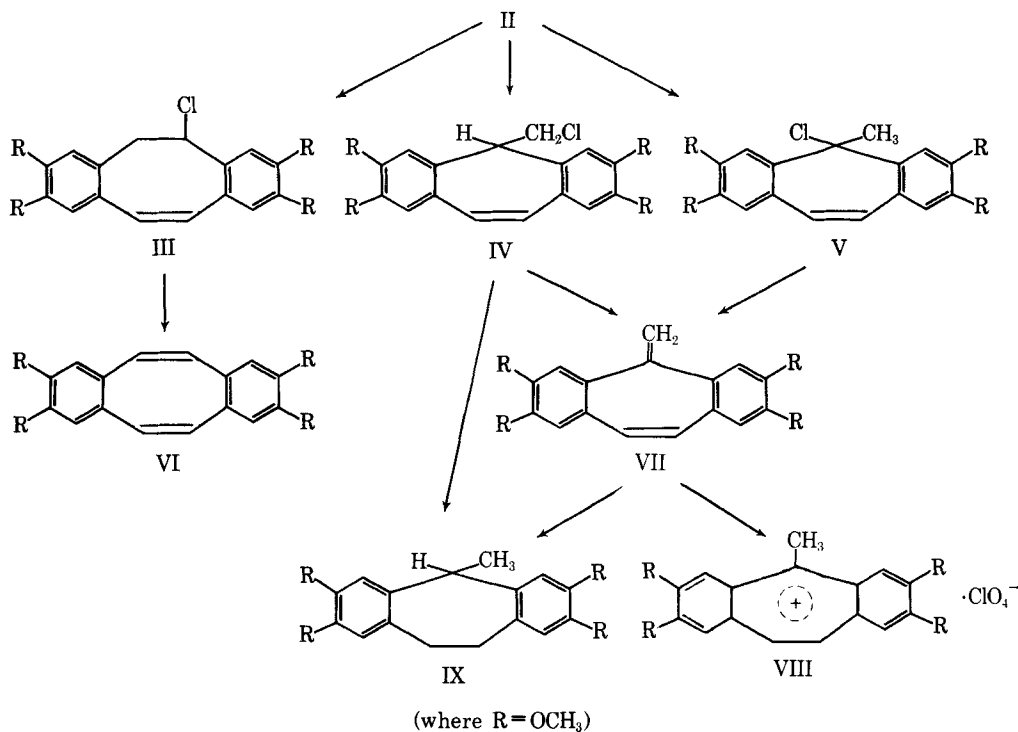
**The Chlorine-Containing Substance**—(±)-*N*-Methylpavine (I), when subjected to two steps of the Hofmann exhaustive methylation procedure, produced a nitrogen-free alcohol (II). The structure of II had been determined unambiguously (6) by Battersby and Binks as 3-hydroxy-2':3':-2''-3''-tetramethoxy-1:2-5:6-dibenzocycloocta-1:5:7-triene. When II was treated with acetyl chloride by Pyman (7) a chlorine-containing compound, C<sub>20</sub>H<sub>21</sub>ClO<sub>4</sub>, was produced which was assigned the structure III by Battersby and Binks. (Scheme II.)

(-)-*N*-Methylpavine (*i.e.*, argemonine), when subjected to a similar degradation, produced trimethylamine and a dextrorotatory nitrogen-free substance which was evidently an optically-active isomer of II (4). Treatment of an ethanolic solution of the latter with concentrated hydrochloric acid produced

a chlorine-containing substance which had identical properties with the chlorine-containing substance reported by Pyman and to which Battersby and Binks had assigned structure III.

In considering the possible reactions of hydrochloric acid with II there appeared to be three possible structures (III, IV, and V) for the chlorine-containing compound. From a comparison of the ultraviolet spectra of the two compounds, *i.e.*, the alcohol (II) and the chloro-compound, it was obvious that there had been a bathochromic shift in the maxima of the latter compared to II, a shift that suggested a more significant change in the nature of the chromophore than would be expected in passing from II to III. In contrast, structures IV and V were both more reasonable on the basis of the ultraviolet data because the rearrangement of the middle ring from a cyclooctatriene to a cycloheptatriene system would be expected to cause the two aromatic rings to become more coplanar.

The chloro-compound, when refluxed in 2-picoline or alcoholic sodium hydroxide, provided a halogen-free substance analyzing for C<sub>20</sub>H<sub>20</sub>O<sub>4</sub>, indicating that dehydrohalogenation had taken place. Structure III, on dehydrohalogenation, could be expected to produce a tetramethoxy-dibenzocyclooctatetraene (VI). The latter, however, is a known compound (7) and was not the product of the reaction. On the other hand, structures IV and V under the conditions of the reaction would give the same product, namely VII. In order to gain more information about the dehydrohalogenated product, it was subjected to nuclear magnetic resonance (NMR) study.



Scheme II

The NMR spectrum of this compound showed six distinct singlets integrating for a total of 20 protons. Aromatic protons with an intensity of two each were found as singlets at 3.26 and 3.32  $\tau$ . The singlets for the methoxyl protons integrating for six each were found at 6.06 and 6.10  $\tau$ . A singlet at 3.06  $\tau$ , integrating for two protons, was assigned to a pair of olefinic protons conjugated to aromatic rings. The difference in the chemical shift of this pair of protons, compared to the almost equivalent pair of olefinic protons in *cis*-stilbene (3.45  $\tau$ ), was attributed to the greater coplanarity of the benzene rings and the consequent deshielding effect. A singlet at 4.47  $\tau$  integrated for two protons and was assigned to a pair of terminal methylene protons. The NMR data, therefore, excluded structure VI but was compatible with structure VII.

Structure VII would be expected to form a tropylium salt on treatment with acids and it was found that the dehydrohalogenation product did, indeed, form a stable perchlorate with the correct analysis (VIII).

Hydrogenation of the dehydrohalogenation product provided a tetrahydro derivative, C<sub>20</sub>H<sub>24</sub>O<sub>4</sub>, a product that would be expected from VII and which would be represented by structure IX. This derivative, on C-methyl analysis, showed one terminal methyl group as expected. The NMR spectrum showed the aromatic protons as singlets integrating for two each at 3.23 and 3.36  $\tau$ . The methoxyl protons gave singlets integrating for six each at 6.13 and 6.17  $\tau$ . A singlet at 6.90  $\tau$ , integrating for four protons, was assigned to the four equivalent benzylic protons of the ethylene bridge. The protons of the terminal methyl group

appeared as a doublet centered at 8.32  $\tau$  with an integration of three protons ( $J = 7.5$  c.p.s.). A quartet centered at 5.80  $\tau$ , integrating for one proton, was assigned to the benzylic proton ( $J = 7.5$  c.p.s.) adjacent to the methyl group.

Compound IX had been synthesized unequivocally by Battersby and Binks (8) and the reported melting point coincided with that of the substance obtained in the present study by hydrogenation of VII. From the above data it appears that the dehydrohalogenation product can be assigned structure VII and its hydrogenation product, structure IX.

Although the structures of VII and IX appear unequivocal at this point, the structure of the chlorine-containing substance had not necessarily been proven since the possibility of rearrangement of III during dehydrohalogenation, although seemingly remote, could not be ignored. This possibility was dismissed by hydrogenolysis of the chloro-compound to yield IX. Since no rearrangement would be anticipated under these conditions, the chloro-compound would of necessity have structure IV or V. Because it was sparingly soluble in virtually all solvents which could be used for NMR analysis except pyridine, it was studied in the latter solvent. The methoxyl protons appeared as singlets at 6.15 and 6.17  $\tau$ . The chloromethyl group appeared as a doublet centered at 5.96  $\tau$  ( $J = 8$  c.p.s.). A triplet centered at 5.40  $\tau$  ( $J = 8$  c.p.s.) was assigned for the benzylic proton coupled to the protons of the chloromethyl group. The spectrum, in general, was not very clear and integration was not possible. Nevertheless, it appeared certain that the chloro-compound did not have structure V since its NMR spectrum should have

shown a singlet corresponding to the terminal methyl, this singlet together with the methoxyl proton peaks being the only ones expected in the region of 4.00 to 10.00  $\tau$ . Such absorption was not observed and, coupled with the observation (4) that C-methyl was not found by analysis, the evidence appears conclusive that the chlorine-containing substance may be represented by structure IV rather than III as suggested earlier by Battersby and Binks.

**Argemoninic Acid**—When II was oxidized with potassium permanganate, an optically inactive acid was obtained which was named argemoninic acid. The acid was tentatively identified in the earlier studies as a tetramethoxybiphenyltricarboxylic acid, based on an erroneous aporphine formulation of argemonine (4). Following elucidation of the correct structure (5), it became obvious that the proposed structure for the acid was incorrect. Furthermore, additional analyses suggested  $C_{20}H_{18-20}O_{10}$  as a more reasonable empirical formula, in keeping with neutral equivalent determinations which gave values of 215 and 219 (theory, 209 and 210).

Likely structures for argemoninic acid, based on the known structure of II, would be X and XI with the structure XII, which conceivably could arise from X by benzylic acid rearrangement, being untenable on the basis of analytical and neutral equivalent data. The indophenine test for 1,2-diketones (9) proved to be positive and was substantiated by hydrogen peroxide oxidation of argemoninic acid to yield the expected *m*-hemipinic acid (XIV) isolated as its *N*-methylimide (XV). These results suggested X as the most likely structural possibility.

To further eliminate the possibility of a benzoin structure such as in XI, the infrared spectra of the acid and its triethylamine salt were examined. In the case of the acid, a broad band due to carboxylic group hydroxyl at about 3400  $cm^{-1}$  precluded making a decision, but the triethylamine salt, on the other hand, while showing carbonyl absorption at 1690  $cm^{-1}$  ( $\alpha$ -diketone) and 1750  $cm^{-1}$  (carboxylate) failed to show absorption in the hydroxyl region.

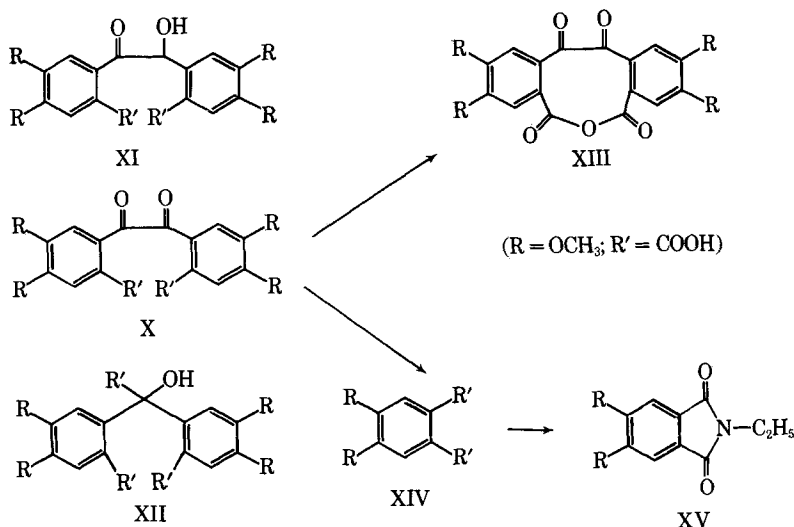
The NMR spectrum of argemoninic acid was determined in two solvent systems: (a) sodium bicarbonate in deuterium oxide and (b) sodium methoxide in dimethylsulfoxide. The spectrum of the acid in the first system was quite simple, showing only three distinct peaks corresponding to aromatic protons, methoxyl protons, and water. The aromatic protons appeared as a singlet at 2.90 $\tau$  with an intensity of four protons, whereas the methoxyl protons were singlets at 6.04 and 6.18  $\tau$  with an intensity of six protons each. A large peak at 5.3 $\tau$  was attributed to water. However, the possibility that the acid had still other spectral features that were masked by the water peak could not be ruled out. Inspection of the NMR spectrum in the second system showed the aromatic protons as a pair of singlets at 2.75 and 2.90 $\tau$ . The methoxyl peaks at 6.13 $\tau$  were complex due to interference of the methoxyl peak from sodium methoxide but, nevertheless, the spectrum failed to show peaks in the 3.0 to 6.0 $\tau$  region and, therefore, strongly pointed to structure X.

An interesting confirmation of structure X was

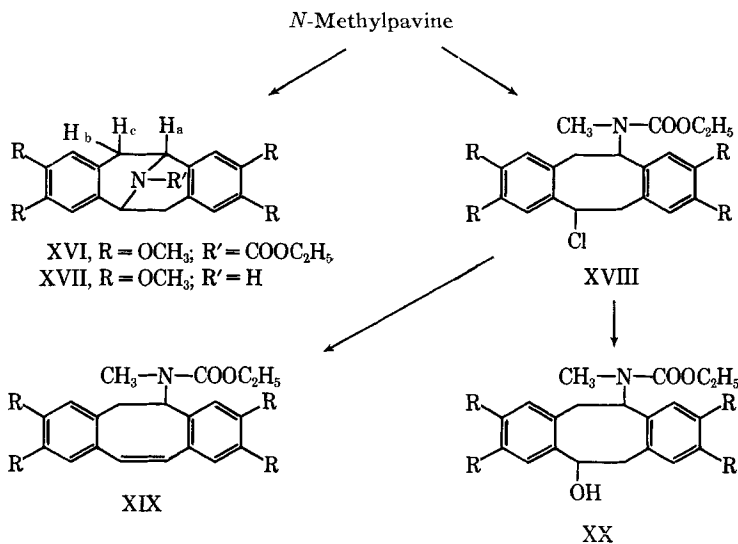
also achieved by taking advantage of the fact that Kier and Soine (4) had previously shown that the acid, at its melting point, effervesced and liberated a mole of water. The most likely possibilities would have been formation of an anhydride from X or an anhydride or lactone from XI. The solid residue from such a melt analyzed for  $C_{20}H_{16}O_9$ . Its infrared spectrum showed no hydroxyl absorption but did show carbonyl absorptions at 1690  $cm^{-1}$  ( $\alpha$ -diketone) and at 1750 and 1790  $cm^{-1}$  (anhydride). If argemoninic acid had structure XI it would have been impossible for it to form an anhydride or a lactone without leaving one hydroxyl group. The structure of the compound resulting from the melting of argemoninic acid can, therefore, be assigned as XIII and the structure of argemoninic acid is X. (Scheme III.)

**The Ethyl Chloroformate Reaction Product**—Subjectation of *N*-methylpavine to the action of ethyl chloroformate in the presence of alkali according to the method of Gadamer and Knoch (10) yielded a neutral product (11). This reaction, which specifically cleaves benzylic carbon-to-nitrogen bonds (12), ordinarily provides a urethane as the end product and the reaction has been used to some extent in alkaloidal structural work. It fails occasionally, as in the case of tetrahydroberberine (12) but with aporphines, for example, the reaction proceeds with facility. Since earlier tentative conclusions as to the structure of argemonine indicated that it might be an aporphine (4) this reaction was employed during the structural studies. In light of the now known structure of argemonine as (–)-*N*-methylpavine, it is apparent that there are *two* benzylic carbon-to-nitrogen bonds in the molecule, and therefore the fact that a neutral product was obtained was of considerable interest from the standpoint of its structure.

Analysis of the product, resulting in a probable formula of  $C_{23}H_{27}NO_6$ , rendered untenable the product that might have resulted from a simple cleavage of a benzylic carbon-to-nitrogen bond such as XVIII or structures XIX and XX which could result from XVIII. The ultraviolet spectrum of the compound further supported the assumption that no cleavage had occurred, since the spectrum was virtually identical with that of *N*-methylpavine and unlike that of II, and further, the infrared spectrum failed to show hydroxyl absorption. The loss of  $-CH_3$  during the reaction together with gain of  $-COOC_2H_5$  appeared compatible with the analytical data and the neutral character of the product and thus suggested structure XVI as the most likely possibility. On this basis, the compound was subjected to lithium aluminum hydride reduction, since such reductions of urethanes have been reported by Knabe (13) and others (14) to yield an *N*-methyl group. The reduction process yielded a basic compound which was isolated as the methiodide and which proved to be identical in melting point and mixed melting point with *N*-methylpavine methiodide. Unfortunately, the methiodide melts with decomposition, and therefore further evidence of the identity of the two products seemed desirable. The infrared spectrum of the methiodide of reduced XVI was found to be identical with the spectrum of *N*-methylpavine methiodide, as were the X-ray powder diffraction patterns. In addition, alkaline hydrolysis of the suspected



Scheme III



Scheme IV

urethane yielded a new basic substance which was identical in all respects to ( $\pm$ )-pavine. The NMR spectrum of this new basic substance was also identical in all respects to that of ( $\pm$ )-pavine (5). (Scheme IV.)

Examination of the NMR spectrum of the ethyl chloroformate reaction product was entirely compatible with structure XVI. The aromatic protons were singlets at 3.28 and 3.47 $\tau$  with an intensity of two each, whereas the methoxyl protons were singlets at 6.12 and 6.20 $\tau$  with an intensity of six each. The protons of the methyl group of the ethoxy moiety appeared as a triplet centering at 8.72 $\tau$  ( $J = 7$  c.p.s.) with an intensity of three protons and the methylene protons of this group were found as a quartet centering at 5.79 $\tau$  ( $J = 7$  c.p.s.) with an intensity of two protons. The bridgehead protons appeared as a broad peak at 4.47 $\tau$  with an intensity of two protons. As in the

case of ( $-$ )-*N*-methylpavine (5), protons H<sub>c</sub> coupled only with protons H<sub>b</sub> and were seen as a doublet centering at 7.24 $\tau$  ( $J_{bc} = 17$  c.p.s.). Protons H<sub>b</sub> were split by H<sub>a</sub> and H<sub>c</sub> and were observed as a pair of doublets at 6.41 and 6.68 $\tau$ .

On the basis of the above evidence, structure XVI can be assigned to the product of the ethyl chloroformate reaction.

#### EXPERIMENTAL

Melting points were determined on a Thomas-Hoover capillary melting point apparatus. Microanalyses were determined by the Microanalytical Laboratory, School of Chemistry, University of Minnesota, or by the Schwarzkopf Microanalytical Laboratory, Woodside, N. Y. The infrared spectra were determined as Nujol and halocarbon mulls by the Infrared Laboratory, School of Chemistry,

University of Minnesota, using a Perkin-Elmer 521 grating infrared spectrophotometer. Ultra-violet spectra were determined in ethanolic solution using a Bausch & Lomb Spectronic 505 recording spectrophotometer. Nuclear magnetic resonance spectra were determined through the courtesy of Dr. William Schwabacher, School of Chemistry, University of Minnesota, using a Varian Associates A-60 instrument.

**N-Methylpavine (I)**—This substance was prepared essentially following the method of Battersby and Binks (6), m.p. 139–140°. [Lit. m.p. 135–140° (6).]

**N-Methylpavinemethine Methiodide**—This derivative of I was prepared according to the procedure of Kier and Soine (4) and was used without further purification.

**3-Hydroxy-2':3':2'':3'''-tetramethoxy-1:2-5:6-dibenzocyclohepta-1:5:7-triene (II)**—A suspension of *N*-methylpavinemethine methiodide (10 Gm.) in water (200 ml.) was treated with freshly prepared silver oxide (from 5 Gm. of silver nitrate). The reaction mixture was kept in an ice bath and stirred until a filtered portion failed to give a test for iodide ion with silver nitrate T.S. The precipitated silver iodide and excess silver oxide were removed by filtration and the filtrate was then boiled for 30 min., during which time a white crystalline precipitate formed. This precipitate was separated by filtration and recrystallized from a methanol-water mixture. The dried crystals (4.97 Gm.) melted at 142–147°. [Lit. (5) m.p. 145–146°.]  $\lambda_{\min}$ , 267.5  $\mu$  ( $\log \epsilon$  3.97);  $\lambda_{\max}$ , 220 (4.49), 292  $\mu$  (4.05) in ethanol.

**3-Chloromethyl-2':3':2'':3'''-tetramethoxy-1:2-4:5-dibenzocyclohepta-1:4:6-triene (IV)**—A solution of II (300 mg.) in ethanol (30 ml.) was cooled in an ice bath and then concentrated hydrochloric acid (15 ml.) was added dropwise. The solution acquired a transient pink to violet color which disappeared on shaking. The solution was then refluxed for 20 min. on a steam bath. On cooling, a white crystalline material separated which was removed by filtration (270 mg.) and recrystallized from hot glacial acetic acid. The dried crystals melted at 219–220°. [Lit. (4) m.p. 219–220°.]  $\lambda_{\min}$ , 265  $\mu$  ( $\log \epsilon$  4.54);  $\lambda_{\max}$ , 238 (4.54), 316  $\mu$  (4.15) in ethanol.

*Anal.*—Calcd. for  $C_{20}H_{21}ClO_4$ : C, 66.57; H, 5.87; Cl, 9.83. Found: C, 66.65; H, 5.77; Cl, 9.55.

**3-Methylene-2':3':2'':3'''-tetramethoxy-1:2-4:5-dibenzocyclohepta-1:4:6-triene (VIII)**—This substance was obtained from IV by two different methods.

**Dehydrohalogenation Using 2-Picoline**—A solution of IV (250 mg.) in 2-picoline (25 ml.) was refluxed under a nitrogen atmosphere for 7 days. The solution was then treated with 1% hydrochloric acid (80 ml.) and extracted with three successive portions (50 ml.) of ether. The combined ethereal extracts were washed successively with 1% hydrochloric acid (20 ml.) and distilled water (20 ml.). The ether extract was then dried with anhydrous sodium sulfate and, following removal of the drying agent by filtration, was evaporated to dryness to yield a crystalline residue. Recrystallization from ethanol yielded 126 mg. of yellowish plates, m.p. 226–229°. Further recrystallization

from the same solvent provided faintly yellow crystals, m.p. 233.5–234.5°, which gave a negative halogen test.

*Anal.*—Calcd. for  $C_{20}H_{20}O_4$ : C, 74.06; H, 6.35. Found: C, 73.81; H, 6.34.

**Dehydrohalogenation with Alcoholic Sodium Hydroxide**—A solution of IV (300 mg.) in ethanol (300 ml.) was treated with sodium hydroxide pellets (3 Gm.) and refluxed for 24 hr. The ethanol was evaporated and the residue was treated with 100 ml. of boiling water, allowed to cool, and then filtered. The precipitate was then recrystallized from the least amount of boiling ethanol and colorless platelets (258 mg.), m.p. 234–236°, were obtained. The product gave no depression in melting point with the material obtained through the use of 2-picoline.

**3-Methyl-2':3':2'':3'''-tetramethoxy-1:2-4:5-dibenzocyclohepta-1:4-diene (IX)** from VII—Palladium-on-carbon catalyst (10%, 400 mg.) was added to a solution of VII (200 mg.) in ethanol (200 ml.), and the mixture was then shaken with hydrogen under atmospheric pressure until the uptake of hydrogen stopped. The hydrogenated mixture was then heated to boiling and filtered to remove the catalyst. The filtrate was evaporated to dryness under reduced pressure and the residue recrystallized from the least amount of hot ethanol to obtain a crystalline precipitate (82.5 mg.), m.p. 128–129°. [Lit. (6) m.p. 126–128°.]

*Anal.*—Calcd. for  $C_{20}H_{24}O_4$ : C, 73.14; H, 7.36; C-methyl, 4.37. Found: C, 73.37; H, 7.13; C-methyl, 5.34.

**3-Methyl-2':3':2'':3'''-tetramethoxy-1:2-4:5-dibenzocyclohepta-1:4-diene (IX)** from IV—Palladium-on-carbon catalyst (10%, 1.0 Gm.) was added to a solution of IV (400 mg.) in ethanol (300 ml.) and the mixture was then shaken with hydrogen under atmospheric pressure until the uptake of hydrogen stopped. The hydrogenated mixture was heated to boiling and filtered to remove the catalyst. The filtrate was evaporated to dryness and the residue recrystallized from the least amount of ethanol to yield a crystalline precipitate (79 mg.), m.p. 128–129°, which gave no depression of melting point with the product from the previous experiment.

**3-Methylene-2':3':2'':3'''-tetramethoxy-1:2-4:5-dibenzocyclohepta-1:4:6-triene Perchlorate (VIII)**—Perchloric acid (60%, 2 ml.) was added dropwise to a hot solution of VII (100 mg.) in glacial acetic acid (200 ml.). The solution was boiled, filtered, and allowed to stand overnight in the refrigerator to yield a brown crystalline precipitate (75 mg.). This material was recrystallized from glacial acetic acid to yield 10 mg. of product, m.p. 350°.

*Anal.*—Calcd. for  $C_{20}H_{21}ClO_8$ : C, 56.54; H, 4.98. Found: C, 56.47; H, 4.96.

**Argemoninic Acid (X)**—A suspension of II (1.0 Gm.) in distilled water (75 ml.) was warmed and potassium permanganate solution (5%, 75 ml.) was added slowly. The mixture was heated on a steam bath with occasional stirring for 1 hr., cooled, and the excess permanganate reduced with methanol. The suspension was cooled, acidified with 30 ml. of 50% sulfuric acid, and the dark color of manganese dioxide discharged by the careful addition of solid sodium bisulfite. A fine white

precipitate remained which was removed by filtration (899 mg.). The precipitate was recrystallized from methanol to give white crystals, m.p. 254–255.5°, with effervescence.  $\lambda_{\min}$ . 246  $m\mu$  ( $\log \epsilon$  4.03), 281 (3.91);  $\lambda_{\max}$ . 229 (4.71), 264 (4.21), and 295 (4.06).

*Anal.*—Calcd. for  $C_{20}H_{18}O_{10}$ : C, 57.41; H, 4.33; neut. equiv. (for 2 COOH), 209.18. Found: C, 57.12; H, 4.51; neut. equiv. 215, 219.

**Argemonic Acid Anhydride (XIII)**—X (300 mg.) was heated under a nitrogen atmosphere to the melting point, when effervescence was observed followed by solidification of the melt. The residue was cooled and recrystallized from ethyl acetate several times to obtain white needles, m.p. 280–281°.

*Anal.*—Calcd. for  $C_{20}H_{16}O_8$ : C, 60.00; H, 4.02. Found: C, 59.76; H, 4.00.

**N-Ethyl-*m*-hemipinimide (XV)**—A solution of X (100 mg.) in glacial acetic acid (20 ml.) was treated with 30% hydrogen peroxide (10 ml.) and refluxed for 4 hr. The cooled solution was finally evaporated to dryness. The residue was treated with ethylamine solution (33%, 4 ml.) and again taken to dryness, heated at 180° for 10 min., and then sublimed at 180°/5 mm. The white sublimate was recrystallized from ethanol to yield 10 mg. of white needles, m.p. 227–229°, which failed to depress the melting point of an authentic sample of *N*-ethyl-*m*-hemipinimide.

**N-Carboxypavine (XVI)**—A solution of I (1.5 Gm.) in chloroform (30 ml.) was treated at room temperature with ethyl chloroformate (4 ml.) and aqueous potassium hydroxide solution (15%, 40 ml.). The reaction mixture was shaken for 10 min., additional ethyl chloroformate (5 ml.) added, and shaking continued for 30 min. The addition of ethyl chloroformate (5 ml.) and aqueous potassium hydroxide (40 ml.) was repeated three times at 30-min. intervals, after which the reaction mixture was allowed to stand overnight. The chloroformic layer was separated, the aqueous layer was washed with a little chloroform, and the washing added to the original chloroformic solution. On shaking the chloroformic solution with 20 ml. of dilute (3.7%) hydrochloric acid, the acid extract was found to be positive to Valser's reagent. The chloroform layer, therefore, was extracted with successive portions of hydrochloric acid until the acid extract failed to give a turbidity with the reagent. The chloroform solution was then washed with distilled water dried over anhydrous sodium sulfate, and evaporated to dryness. Crystallization was effected from ethanol to obtain large cubical crystals which were recrystallized from the same solvent, m.p. 191–192°. The yield was 1.18 Gm. (68% of theory).

*Anal.*—Calcd. for  $C_{23}H_{27}NO_6$ : C, 66.81; H, 6.58; N, 3.38. Found: C, 66.92; H, 6.41; N, 3.61.

**Pavine (XVII)**—A solution of XVI (400 mg.) in ethanol (100 ml.) was treated with potassium hydroxide pellets (10 Gm.) and the solution then refluxed for 48 hr. The mixture was then concentrated and, finally, evaporated to dryness following which water (10 ml.) was added and distilled off to

remove any residual ethanol. The residue was suspended in water and extracted with three successive portions (50 ml.) of chloroform. The combined chloroformic extract was washed with water and then extracted with successive 50-ml. portions of 3.7% hydrochloric acid until the acid extracts gave a negative test with Valser's reagent. The combined acid extracts were washed with chloroform (20 ml.) and rendered alkaline by the careful addition of 20% sodium hydroxide solution following which the alkaline solution was extracted with successive 50-ml. portions of chloroform until the chloroform extracts gave a negative test with Valser's reagent. The combined chloroformic extracts were washed with water, filtered, and dried over anhydrous sodium sulfate. The dried extract was evaporated to dryness and the residue treated with absolute ethanol (10 ml.) and the ethanol then evaporated to remove traces of moisture. The dry residue was crystallized from xylene and then recrystallized from ethanol to provide 20 mg. of product, m.p. 198–199°. [Lit. (6) m.p. 199–200°.]

**N-Methylpavine Methiodide from XVI**—A solution of XVI (232 mg.) in dry tetrahydrofuran (40 ml.) was added dropwise to a suspension of lithium aluminum hydride (290 mg.) in dry tetrahydrofuran (50 ml.). After the addition was complete, the reaction mixture was refluxed for 10 hr., following which the excess lithium aluminum hydride was decomposed by the careful addition of moist ether. After filtering the reaction mixture, the precipitate was washed with tetrahydrofuran and the washings added to the filtrate. The filtrate was treated with enough ether (50 ml.) to complete the separation of an aqueous layer which was removed, washed with ether, and the ether washings added to the original ether layer. The ethereal solution was dried with anhydrous sodium sulfate, the drying agent removed by filtration, and the solvent removed by distillation. The dry residue was then dissolved in ethyl acetate, filtered, and treated with methyl iodide (1 ml.). The methiodide salt which separated was filtered off and recrystallized from ethanol, m.p. 265–266°. The yield of product was 214 mg. (61.4% of theory) and failed to depress the melting point of authentic *N*-methylpavine methiodide.

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