temperature. Material so purified melted at about $-2°$. It has been stored under nitrogen at $-195°$ for several months without apparent change, but a sample stored at $-40°$ contained some insoluble material when opened.

The infrared spectrum (CCl_4) of III: 3.27 μ (m), 3.41 (s), 6.13 (s), 6.41 (w), 6.88 (s), 6.95 (m), 7.30 (s), 7.40 (m), 8.05 (w), 9.12 (m), 9.27 (m), 10.12 (m), 10.58 (w), 10.89 (m), 11.11 (w), 11.47 (s), is consistent with its formulation as a fulvene,[5] first inferred from the red color. Its n.m.r. spectrum (neat) possesses a single sharp line at 3.73 τ assigned to the four protons of the cyclopentadiene ring, a pair of poorly resolved complex multiplets at 7.2 and 7.55 τ assigned to the methylene groups, and a quartet of triplets centered at 3.5 τ and assigned to the protons of C-3 and C-4.

For the ultraviolet spectrum of III—$\lambda\lambda_{max}^{isoctane}$ mμ (ϵ) 290 (sh.), 303 (sh.), 313 (22,000), 322 (sh.), 337 (sh.), 383 (260), $\epsilon_{200m\mu}$ 3000; $\lambda_{max}^{dimethylsulfoxide}$ 316 (28,000)[6]—no appropriate model could be located, but it is noteworthy that it differs from the spectrum—$\lambda\lambda_{max}^{pentane}$ 240 (4900), 335 (12,000)—of the hydrocarbon prepared by Doering and Matzner by oxidative coupling of sodium cyclopentadienide and assigned by them the 1,5-dihydrofulvalene structure on the basis of spectra and formation of a 1:2 adduct with tetracyanoethylene.[7] Šorm has reported the isolation of a dihydroazulene with an orange color and a spectrum—$\lambda\lambda_{max}$ 220 (14,000), 291 (3670), 432 (49)—suggesting that an additional double bond is in conjugation with a fulvene chromophore[8]; his substance is now best formulated as a 1-vinyl rather than a 6-vinyl fulvene (*i.e.*, as a 5,6-dihydroazulene rather than a 4,5-).

III forms a mono-adduct with N-phenylmaleimide[9] (IV), m.p. 143–145.5 dec., $\lambda\lambda_{max}^{EtOH}$ 242 (26,200), 287 (sh., 1000), (Calcd. for $C_{20}H_{17}NO_2$: C, 79.18; H, 5.65; N, 4.62; O, 10.55. Found: C, 79.09; H, 5.72; N, 4.64) which slowly dissociates in solution[10] (as evidenced by gradual appearance of a red-orange color) and which absorbs 3.0 molecules of hydrogen on reduction in absolute ethanol over reduced platinum oxide at atmospheric pressure.

Further evidence for the structure of III is adduced from its ready oxidation to fulvalene, identified by its characteristic ultraviolet spectrum.[7,11] When a dilute (*ca.* 10^{-5} *M*) solution of III in methanol is passed through a 4 × 10-mm. column of freshly-prepared anhydrous silver oxide,[12] the relatively featureless spectrum of III is replaced by the strikingly sharp maxima of fulvalene: $\lambda\lambda_{max}$ 313 (37,500), 299 (30,000), 289 (15,200), 278 (7,000) 265 (3,500), the last two being rather indistinct. The extinction coefficients are based on an $\epsilon_{316\ m\mu}$ of 28,000 for III, and are somewhat lower than the values of Doering and Matzner.[7] Probably, dissolved molecular oxygen is responsible for the oxidation of III, with the silver oxide functioning only as a base, since attempts to reproduce the oxidation in degassed dimethyl sulfoxide were unsuccessful.

(5) J. Thiec and J. Wiemann, *Bull. soc. chim. France*, 207 (1958).

(6) The different extinction coefficients may reflect differing degrees of purity in the two samples.

(7) W. von E. Doering in "Theoretical Organic Chemistry—The Kekulé Symposium," Butterworths, London, 1959, p. 45; E. A. Matzner, "Fulvalene," dissertation, Yale University, 1958.

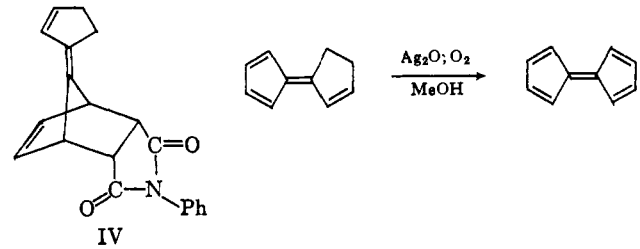
(8) F. Šorm, F. Vonašek and V. Herout, *Collection Czech. Chem. Commun.*, **14**, 91 (1949); Z. Čekan, V. Herout and F. Šorm, *Chem. Ind.* (London), 604 (1954).

(9) M. P. Cava, A. A. Deana, K. Muth and M. J. Mitchell, *Org. Syn.*, **41**, 93 (1961).

(10) R. B. Woodward and H. Baer, *J. Am. Chem. Soc.*, **66**, 645 (1944), and references cited therein.

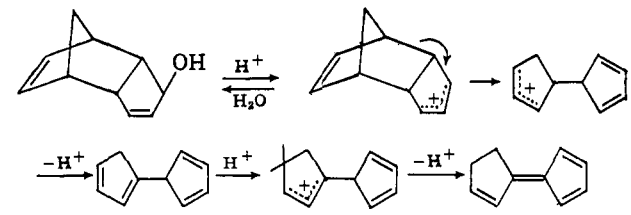
(11) W. B. DeMore, H. O. Pritchard and N. Davidson, *ibid.*, **81**, 5874 (1959).

(12) R. Willstatter and A. Pfannenstiel, *Ber.*, **37**, 4744 (1904).



IV

A reasonable mechanism for the formation of III is presented below.



Formation of the initial allylic carbonium ion presumably is reversible, since Woodward and Katz have effected acid-catalyzed epimerization of a dicyclopentadien-1-ol under conditions in which no fragmentation is observed.[3] The second step is merely the reverse of the solvolytic ring closure reaction recently reviewed by Bartlett.[13]

Acknowledgment.—The author is indebted to Professor R. B. Woodward and Dr. Tadamichi Fukunaga for valuable discussions, and to the National Science Foundation for a fellowship.

(13) P. D. Bartlett, *Ann.*, **653**, 45 (1962).

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THE STRUCTURE OF ARGEMONINE. A NEW NATURALLY-OCCURRING ALKALOID RING SYSTEM

Sir:

The alkaloid argemonine is present in *Argemone munita* Dur. & Hilg. subsp. *rotundata* (Rybd.) G. B. Ownb. along with norargemonine and bisnorargemonine, which are related to argemonine as mono- and bis-O-demethyl derivatives.[1a-c] As a result of a number of degradative experiments, it was suggested[1d,e] that argemonine was 2,3,9,10-tetramethoxyaporphine, although a 10,11 or 8,9 placement of the two methoxyl groups in ring D was not eliminated. (Such structures were disputed on the basis of optical and spectral data.[1f])

It did not seem to us that the ultraviolet spectra of the above alkaloids (λ_{max} 287 mμ) were consistent with an aporphine structure and, indeed, we found that the spectrum of bisnorargemonine shows a large enhancement of absorption and bathochromic shift in the presence of base. This indicates that the observed absorption is due to the phenol or methylated phenol chromophore and not a biphenyl system such as is present in the aporphine alkaloids.[2]

(1) (a) T. O. Soine and O. Gisvold, *J. Pharm. Sci.*, **33**, 185 (1944); (b) T. O. Soine and J. W. Schermerhorn, *ibid.*, **40**, 19 (1951); (c) T. O. Soine and L. B. Kier, *ibid.*, **49**, 187 (1960); (d) L. B. Kier and T. O. Soine, *ibid.*, **50**, 321 (1961); (e) T. O. Soine and L. B. Kier, *ibid.*, **51**, 1196 (1962); (f) M. Shamma, *Experientia*, **18**, 64 (1962).

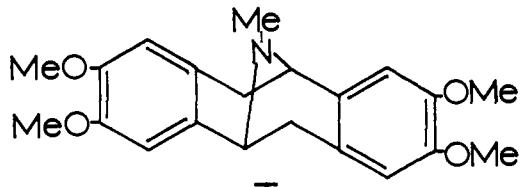
(2) The 2,3,9,10- and 2,3,10,11-tetramethoxyaporphine structures suggested by Soine and Kier are in any case not valid since both are known compounds (ref. 3) whose physical characteristics do not match those of argemonine.

(3) R. K. Callow, J. M. Gulland and R. D. Haworth, *J. Chem. Soc.*, **132**, 658 (1929).

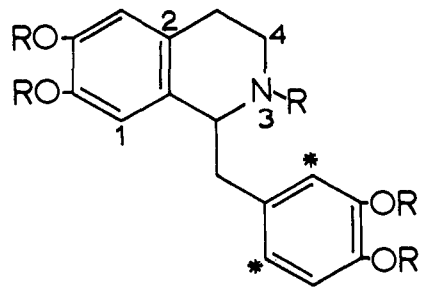
A search of the literature showed that the physical characteristics of argemonine matched fairly closely with those of the N-methyl derivative of pavine, an optically inactive base obtained by the reduction of papaverine with tin and hydrochloric acid.[4a-c] Extensive chemical characterization[5a,b] had showed that N-methylpavine has the structure I. The degradative work on argemonine[1a-e] parallels that on N-methylpavine[5b] step for step and, in particular, both series lead, by the same processes, to a nitrogen-free compound of m.p. 156°, identified[5b] as 2,3,8,9-tetramethoxy-5,6-dihydrodibenzo[*a*,*e*]cycloöctene.

We have prepared N-methylpavine using the procedure of Pyman[4c] and have compared it with (−)-argemonine from *A. munita*.[6] The ultraviolet and solution infrared spectra of the two are identical and the structural identity of these bases is thereby confirmed.

This is the first report of the nitrogen-bridged tetrahydrodibenzocycloöctene system in a natural product and the structure presents a novel problem in alkaloid biosynthesis. Most current biogenetic hypotheses for Papaveraceous alkaloids depict a benzyltetrahydroisoquinoline (II) as a key intermediate which can couple from the asterisked positions to positions 1, 2, or 3 to furnish the aporphine, morphine, or cyptaustoline series of alkaloids. Argemonine coud fit into this scheme if a coupling occurred to position 4. If the precursor is



I



II

similar to laudanosine (II, R = CH_3), then argemonine would be the primary alkaloid in this series and successive O-demethylations would lead to nor- and bisnorargemonine. This would be in keeping with the demethylation series (thebaine to codeine to morphine) shown to occur in the opium poppy.[7] Biosynthetic studies are currently underway to test these and other possible pathways of metabolism in this new series of plant alkaloids.[8]

Acknowledgment.—This investigation was supported by Public Health Service Research Grant RG-9300, Division of General Medical Sciences. We also wish to acknowledge the helpful suggestions of the students in Chem. 227 at Utah State University in 1962 who struggled with the structure of argemonine as a literature and term paper assignment.

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(4) (a) G. Goldschmiedt, *Monatsh.*, **7**, 485 (1886); (b) W. J. Pope and S. J. Peachy, *J. Chem. Soc.*, **73**, 893 (1898); (c) F. L. Pyman, *ibid.*, **107**, 176 (1915).

(5) (a) C. Schöpf, *Experientia*, **5**, 201 (1949); (b) A. R. Battersby and R. Binks, *J. Chem. Soc.*, 2888 (1955).

(6) A voucher sample of this species, collected near Brigham City, Utah, has been deposited in the Intermountain Herbarium, Utah State University, under No. 102032.

(7) F. R. Stermitz and H. Rapoport, *Nature*, **189**, 310 (1961); F. R. Stermitz and H. Rapoport, *J. Am. Chem. Soc.*, **83**, 4045 (1961).

(8) NOTE ADDED IN PROOF.—The correct structure of argemonine recently was established independently by M. J. Martell, T. O. Soine and L. B. Kier, *ibid.*, **85**, 1022 (1963).

STEREOCHEMISTRY AND SYNTHESIS OF AMOSAMINE: 4,6-DIDEOXY-4-DIMETHYLAMINO-D-GLUCOSE

Sir:

This communication reports the complete identification and synthesis of the first 4-aminosugar isolated from natural sources. 3-Aminosugars such as mycaminose,[1,2] mycosamine[3] and desosamine[4-6] have been investigated as important moieties of certain antibiotics. Amosamine,[7,8] the aminosugar moiety of the antibiotic amicetin,[9,10] is shown by synthesis in this investigation to be 4,6-dideoxy-4-dimethylamino-D-glucose.

One of the most significant properties of amosamine is its basicity. The free sugar, the α and the β methyl glycoside, the disaccharide amicetamine and the antibiotic amicetin have pK'_a values close to 7, which represent a tenfold decrease in basicity when compared with the 3-dimethylaminosugars mycaminose[11] and desosamine.[12] These data and the degradation studies reported earlier required the consideration of a 4-amino structure and an examination of the molecular rotation values of amosamine and the α and β methyl glycosides indicated the stereochemistry of the glucose series as a likely possibility. Synthesis of the crystalline methyl 4,6-dideoxy-4-dimethylamino-α,D-glucopyranoside (VI), the free sugar and the crystalline itol hydrochloride, identical with the natural material, confirmed these considerations.

The starting material for the synthesis was I, a known 4,6-ditosylate derivative of D-galactose.[13] Selective displacement of the 6-tosyl group with sodium iodide to give the 6-iodo derivative II, m.p. 131.5–133°, was accomplished in acetone solvent at 105–110°. II was separated from unreacted I and diiodo by-product by column chromatography over alumina. The 6-iodo derivative II was reduced to the 6-deoxy derivative III, m.p. 157–158.5°, using Raney nickel catalyst in the presence of a few drops of sodium hydroxide solution. The 4-tosyl group of III was displaced with azide ion in refluxing dimethylformamide to give the glucose derivative IV, which was not isolated but converted by successive treatment with hydrogen in the presence of plati-

(1) A. C. Richardson, *Proc. Chem. Soc.*, 430 (1961); *J. Chem. Soc.*, 2758 (1962).

(2) A. B. Foster, T. D. Inch, J. Lehmann, M. Stacey and J. M. Webber, *ibid.*, 2116 (1962).

(3) M. H. von Saltza, J. Reid, J. D. Dutcher and O. Wintersteiner, *J. Am. Chem. Soc.*, **83**, 2785 (1961).

(4) C. H. Bolton, A. B. Foster, M. Stacey and J. M. Webber, *Chem. Ind.* (London), 1945 (1962).

(5) W. Hofheinz and H. Grisebach, *Tetrahedron Letters*, **No. 9**, 377 (1962).

(6) P. W. K. Woo, H. W. Dion, L. Durham and H. S. Mosher, *ibid.*, **No. 17**, 735 (1962).

(7) C. L. Stevens, K. Nagarajan and T. H. Haskell, *J. Org. Chem.*, **27**, 2991 (1962).

(8) C. L. Stevens, R. J. Gasser, T. K. Mukherjee and T. H. Haskell, *J. Am. Chem. Soc.*, **78**, 6212 (1956).

(9) E. H. Flynn, J. W. Hinman, E. L. Caron and D. O. Woolf, Jr., *ibid.*, **75**, 5867 (1953).

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(11) F. A. Hochstein and K Murai, *ibid.*, **76**, 5080 (1954).

(12) E. H. Flynn, M. V. Sigal, Jr., P. F. Wiley and K. Gerzon, *ibid.*, **76**, 3121 (1954).

(13) *Cf.* E. J. Reist, R. R. Spencer and B. R. Baker, *J. Org. Chem.*, **24**, 1618 (1959), who show that the 4-tosyl group in I is successfully displaced with inversion by benzoate ion. Inversion of the 4-mesyl group in the galacto-series by azide ion is reported by E. J. Reist, R. R. Spencer, B. R. Baker and L. Goodman, *Chem. Ind.* (London), 1794 (1962).