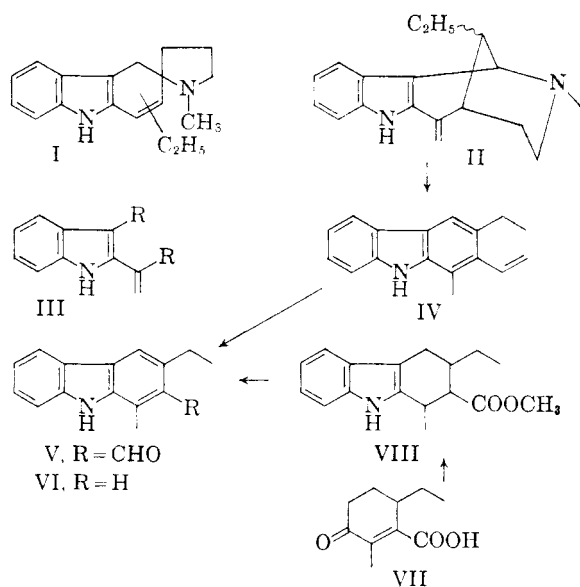


V, m.p. 152°, infrared bands at 2800, 1675 and 1625  $\text{cm}^{-1}$  (arom. aldehyde), n.m.r. peaks at  $-25\delta$  ( $-\text{CH}=\text{O}$ );  $-112$  to  $-42$  (carbazole NH, 5 arom. H); a quadruplet centered at 196 ( $\text{CH}_2$  of ethyl); 218 (arom. methyl) and a triplet centered at 304 c.p.s. ( $\text{CH}_3$  of ethyl);  $\lambda_{\text{max}}^{\text{EtOH}}$  255 (40700); 324 (25000) and 378  $\text{m}\mu$  ( $\epsilon$  4350). The ultraviolet spectrum of V was very similar to that of 2-formylcarbazole,  $\lambda_{\text{max}}^{\text{EtOH}}$  252 (34200), 321 (25300) and 372  $\text{m}\mu$  ( $\epsilon$  4350) but entirely different from the spectra of the three remaining formylcarbazoles<sup>2</sup> kindly provided by Mrs. Tomlinson, Oxford. It had been suggested previously<sup>1</sup> that uleine contains a N-methyl and a C-ethyl grouping and this was confirmed by its n.m.r. spectrum which contained the anticipated N-methyl peak at 249 and a multiplet corresponding to five hydrogens in the 300–350 c.p.s. region. Furthermore, a single hydrogen at 138 c.p.s. is split into two lines in the spectra of II and dihydrouleine indicating part structure  $\beta$ -indolyl- $\text{CH}-\text{NCH}_3$  which explains the

exceedingly facile first Hofmann degradation.



The facts presented are in agreement only with II which was confirmed by chemical evidence. Decarbonylation of V over Pd/C at 270° yielded VI, m.p. 101°, identical in m.p., mixed m.p., ultraviolet and infrared spectra with an authentic sample prepared as described. Ethyl  $\alpha$ -ethoxalylbutyrate<sup>3</sup> was converted to VII, m.p. 95° (after sublimation),  $\lambda_{\text{max}}^{\text{EtOH}}$  246  $\text{m}\mu$  ( $\epsilon$  9800) by a Robinson-Mannich synthesis.<sup>4</sup> Reduction with zinc and then treatment with phenylhydrazine, sulfuric acid and esterification gave VIII which was transformed to VI by dehydrogenation over Pd/C.

(2) P. H. Carter, S. G. C. Plant and M. Tomlinson, *J. Chem. Soc.*, 2210 (1957).

(3) F. Adickes and G. Andresen, *Ann.*, **555**, 41 (1943).

(4) V. Prelog, M. M. Wirth and L. Ruzicka, *Helv. Chim. Acta*, **29**, 1425 (1946).

Uleine (II) shows a clear structural relationship to U-alkaloid B (N-methyltetrahydroellipticine), a minor constituent of *A. ulei*,<sup>1</sup> whose structure and synthesis are outlined in an accompanying communication.<sup>5</sup> We are much indebted to Dr. J. Schmutz, Berne, for the uleine and friendly discussions and to Chas. Pfizer and Co., Inc., for financial aid.

(5) R. B. Woodward, G. A. Iacobucci and F. A. Hochstein, *THIS JOURNAL*, **81**, 4434 (1959).

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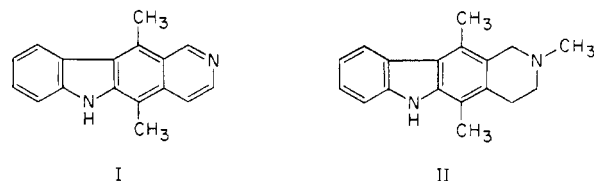
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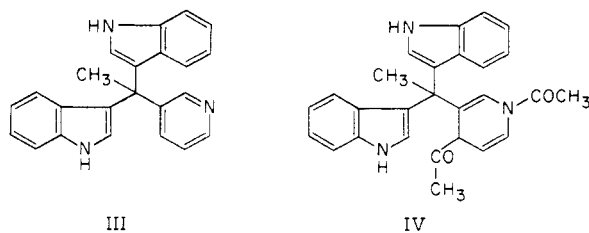
## THE SYNTHESIS OF ELLIPTICINE

Sir:

It has been reported recently that *Ochrosia elliptica* Labill. and *Ochrosia sandwicensis* A.DC. contain a novel alkaloid, ellipticine,<sup>1</sup> and that the N-methyltetrahydroellipticine derived from the base by reduction of its methiodide with sodium borohydride is identical with alkaloid B from *Aspidosperma ulei* Mgf.<sup>2</sup> We have isolated both of these alkaloids from a Peruvian plant which bears the common name *quillo bordon*, and is believed to be *Aspidosperma subincanum* Mart.<sup>3</sup>; our structural studies have led us to the conclusion that ellipticine and N-methyltetrahydroellipticine are represented by the structures I and II. We now wish to record the synthesis of ellipticine.



Condensation of indole with 3-acetylpyridine in acetic acid in the presence of zinc chloride gave 1,1-bis-(3-indolyl)-1-(3-pyridyl)-ethane (III), m.p. 253° [dec.] [calcd. for  $\text{C}_{23}\text{H}_{19}\text{N}_3$ : C, 81.87; H, 5.68; N, 12.45. Found: C, 81.50; H, 5.59; N, 12.98], which was reduced by zinc and acetic anhydride at reflux to the N,γ-diacetyldihydropyridine derivative<sup>4</sup> (IV), m.p. 220–225° [dec.] [infrared bands at 5.80  $\mu$  and 6.05  $\mu$ ]. Pyrolysis of



IV at 200° *in vacuo* [ $5 \times 10^{-4}$  mm.] gave a distillate from which ellipticine (I) was separated readily in ca. 2% yield, in part by direct crystallization and

(1) S. Goodwin, A. F. Smith and E. C. Horning, *THIS JOURNAL*, **81**, 1903 (1959).

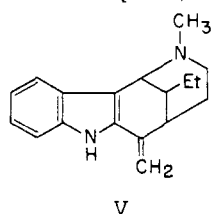
(2) J. Schmutz and F. Hunziker, *Helv. Chim. Acta*, **41**, 288 (1958).

(3) F. A. Hochstein, Anita M. Paradies and R. B. Woodward, paper in preparation.

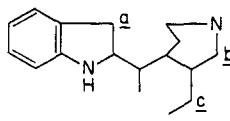
(4) Cf. J. P. Wibaut and J. F. Arens, *Rec. trav. chim.*, **60**, 120 (1941).

in part by chromatography on neutral alumina [activity I]. Recrystallized from methanol, the synthetic ellipticine separated in yellow prismatic needles, m.p. 312–314° [dec.] alone or in admixture with natural ellipticine. The chromatographic behavior, on neutral alumina or on paper,<sup>1</sup> and the infrared [KBr] and ultraviolet [MeOH] spectra [both unusually rich in detail] of the synthetic and natural bases were identical in all respects.

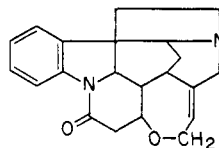
In an accompanying communication, Büchi and Warnhoff<sup>5</sup> present evidence which demonstrates that uleine, the major alkaloid of *Aspidosperma ulei* Mg.<sup>6</sup> possesses the structure V. In view of the elaboration of N-methyltetrahydro-ellipticine (II) by the same plant,<sup>1,2</sup> it is of much interest that the two alkaloids possess closely related structures. The expression VI suggests a simple biogenetic relationship<sup>7</sup> between the two alkaloids [ $a \rightarrow b$ , uleine;  $a \rightarrow c$ , ellipticine] as well as



V



VI



VII

a natural connection with earlier known types [cf. strychnine (VII)].

We wish to express our appreciation to Professor George Büchi, who has kept us informed of the progress of his investigation of uleine, and to Dr. Sidney Goodwin and Professor Harold Conroy for stimulating discussions and exchanges of information. Our work has been generously supported by the Guggenheim Foundation and the National Institutes of Health.

(5) G. Büchi and E. W. Warnhoff, *THIS JOURNAL*, **81**, 4434 (1959).

(6) J. Schmutz, F. Hunziker and R. Hirt, *Helv. Chim. Acta*, **40**, 1189 (1957).

(7) R. B. Woodward, *Nature*, **162**, 155 (1948); *Angew. Chem.*, **68**, 13 (1956).

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RECEIVED JULY 8, 1959

#### THE MOLECULAR STRUCTURE OF $(\text{Me}_2\text{N})_3(\text{BH}_2)_3$

Sir:

The compound previously reported<sup>1</sup> to be  $(\text{Me}_2\text{N})_3\text{B}_3\text{H}_4$  has been shown, by a three-dimensional X-ray diffraction study to be  $(\text{Me}_2\text{N})_3(\text{BH}_2)_3$ , a cyclic trimer of  $\text{Me}_2\text{NBH}_2$  with alternating B and N atoms in a chair configuration. Presumably this

(1) A. B. Burg, *THIS JOURNAL*, **79**, 2129 (1957).

compound is closely related to the trimer of N-methylaminoborane.<sup>2</sup>

The symmetry is orthorhombic in the space group  $\text{Pn}2_1\text{a}$ , with four molecules in a unit cell having dimensions  $a = 11.20$ ,  $b = 13.17$  and  $c = 8.07$  Å., in agreement with values obtained by J. Donohue.<sup>3</sup> Thus the symmetry is lower than that shown by the related compound<sup>4</sup>  $(\text{Me}_2\text{P})_3(\text{BH}_2)_3$ . Refinement of the structure, still in progress, has reached values<sup>5</sup> of  $R = 0.23$  and  $r = 0.16$ , with bonded distances of  $1.61 \pm 0.04$  Å. for B—N and  $1.55 \pm 0.07$  Å. for N—CH<sub>3</sub>. Methyl hydrogen atoms have not yet been included in the refinement. Values of  $R_{0kl} = 0.18$ ,  $R_{h0l} = 0.25$  and  $R_{hk0} = 0.16$  have been obtained for the three principal zones.

These results extend the inorganic-organic structural analogy of B—N compounds to include the cyclohexane type of ring, in the sense that  $\text{BH}_2\text{NH}_2$  and  $\text{C}_2\text{H}_6$ , and  $\text{B}_3\text{N}_3\text{H}_6$  and  $\text{C}_6\text{H}_6$  are pairs of analogs.

Our structure proof agrees with a concurrent, and independent study<sup>6</sup> of the hydrogen hyperfine splitting of the  $\text{B}^{11}$  n.m.r. resonance showing a single 1:3:1 triplet strongly suggesting three equivalent  $\text{BH}_2$  groups in the molecule.

We wish to thank the Office of Naval Research and the Office of Ordnance Research for support of this research. We are indebted to Professor A. B. Burg for the sample, and to Professor J. Donohue for his preliminary X-ray diffraction results.

(2) T. C. Bissot and R. W. Parry, *ibid.*, **77**, 3481 (1956).

(3) J. Donohue, private communication.

(4) W. C. Hamilton, *Acta Crystallographica*, **8**, 199 (1955).

(5) R. E. Dickerson, P. J. Wheatley, P. A. Howell and W. N. Lipscomb, *J. Chem. Phys.*, **27**, 200 (1957).

(6) G. W. Campbell and L. Johnson, *THIS JOURNAL*, to be published.

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RECEIVED JULY 6, 1959

#### 6-METHYL-17 $\alpha$ -ACETOXY-21-FLUORO-4,6-PREGNADIENE-3,20-DIONE. A NEW ORALLY ACTIVE PROGESTIN

Sir:

Our recent discovery of the high oral progestational activity of 21-fluoro-17 $\alpha$ -acyloxyprogesterones<sup>1</sup> coupled with the demonstrated utility of 6-methylated steroids<sup>2</sup> as progestational agents, led us to attempt the synthesis of a molecule containing both of these desirable features.

6 $\alpha$ -Methyl-17 $\alpha$ -hydroxyprogesterone (I)<sup>2b</sup> was iodinated according to the method of Ringold and Stork<sup>3</sup> using 2 moles of iodine and 9.2 moles of calcium oxide per mole of steroid. The resulting, crude iodo-compound [ $\lambda_{\text{max}}^{\text{methanol}}$  240 m $\mu$ , ( $\epsilon$  8,450), 291 m $\mu$ , ( $\epsilon$  10,500); I, 28.56%] was treated with silver fluoride<sup>4</sup> plus a small quantity of silver oxide in acetonitrile for 16 hours. The crude

(1) C. G. Bergstrom, P. B. Sollman, R. T. Nicholson and R. M. Dodson, unpublished data.

(2) (a) A. David, F. Hartley, D. R. Millson and V. Petrow, *J. Pharm. Pharmacol.*, **IX**, 929 (1957); (b) J. C. Babcock, E. S. Gutsell, M. E. Herr, J. A. Hogg, J. C. Stucki, L. E. Barnes and W. E. Dulin, *THIS JOURNAL*, **80**, 2904 (1958); (c) H. J. Ringold, E. Batres and G. Rosenkranz, *J. Org. Chem.*, **22**, 99 (1957).

(3) H. J. Ringold and G. Stork, *THIS JOURNAL*, **80**, 250 (1958).

(4) P. Tannhauser, R. J. Pratt, E. V. Jensen, *ibid.*, **78**, 2658 (1956).