Tetrahedron Letters No. 1, pp. 18-22, 1960. Pergamon Press Ltd. Printed in Great Britain.

ALKALOIDS FROM ASPIDOSPERMA AUSTRALE MÜLL. ARGOV. (NOTE II). THE STRUCTURE OF OLIVACINE AND U-ALKALOID C (GUATAMBUINE)

Miguel A. Ondetti and Venancio Deulofeu

Laboratorios de Investigación, E. R. Squibb and Sons Argentina S.A.

Av. Sir Alexander Fleming 1653, Martínez, Buenos Aires, Argentina

(Received 7 December 1959)

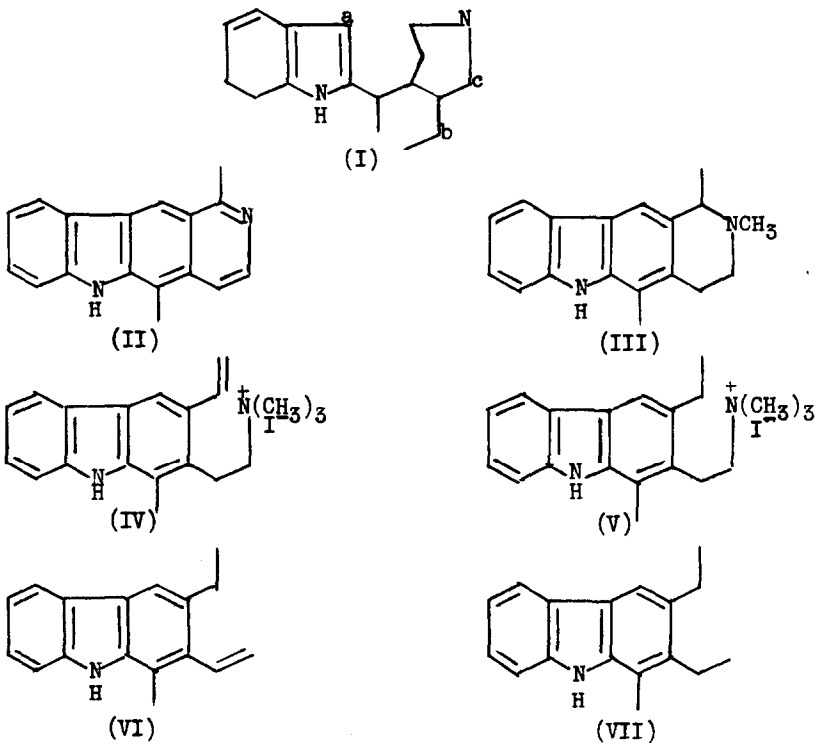
In our first note[1] we described some experiments with olivacine which lead to the conclusion that this base, isolated by Schmutz, Hunziker and Hirt[2] from A. ulei, and found by us in A. australe Müll. Argov., had a carbazol nucleus condensed with a pyridine ring; the indol-isoquinoline structure being preferred. Two methyls were also present in the alkaloid.

As N-methyl-tetrahydro olivacine was found to be identical with the racemic form of u-alkaloid C, a dextrorotatory base also present in both species of Aspidosperma, at least one of the methyls must be attached to the pyridine ring, as required by the existence of an asymmetric center in the last base; u-alkaloid C has also been

---

[1] M. A. Ondetti and V. Deulofeu, Tetrahedron Letters 7, 1 (1959).

[2] J. Schmutz, F. Hunziker and R. Hirt, Helv. chim. Acta 40, 1189 (1957).



found in A. longepetiolatum Kuhlm[3] and given the definitive name of guatambuine.

The recent clarification of the structure of uleine by

---

[3] P. Carvalho Ferreira and G. B. Marini-Bettolo, Ann. Chim. 49, 869 (1959). P. Carvalho Ferreira, G.B. Marini-Bettolo and J. Schmutz, Experientia 15, 179 (1959).

Büchi and Warnhoff[4] and of the structure and synthesis of ellipticine by Woodward, Iacobucci and Hochstein[5], showed a relationship between both alkaloids and the latter authors proposed a common genetic intermediate (I) for both bases. Woodward and Iacobucci[6] suggested also that the same entity could be an intermediate in the formation of olivacine, for which they proposed structure (II). (Bond c-N is broken; c joins a; b joins N). If this structure is accepted, some of the products obtained by Hofmann degradation from olivacine should be identical with those from uleine.

We wish to report some degradation work done with olivacine which agrees with this point of view. From N-methyl-tetrahydro-olivacine (III), $C_{18}H_{20}N_2$, a methiodide was obtained, m.p. 298-299°, that when submitted to a Hofmann degradation gave two products. One was an unsaturated tertiary base that without further purification was transformed into a new crystalline methiodide (IV), m.p. 284-285°, which analyzed well for $C_{20}H_{25}N_2I$. Its infrared spectrum showed the characteristic bands of the vinyl group and the UV spectrum had maxima at 241 and 280 mμ.

When the unsaturated tertiary base was first hydrogenated (Platinum oxide) and the crude reduced product treated with methyl

---

[4] G. Büchi and E. W. Warnhoff, J.Am.Chem.Soc. 81,4433(1959).

[5] R. B. Woodward, G. A. Iacobucci and F. A. Hochstein, J.Amer.Chem.Soc. 81, 4434 (1959).

[6] Private communication.

iodide, a different methiodide formed (V), m.p. 287-288°, which gave a typical carbazol spectrum ($\lambda_{max.}$ 240, 250, 262, 298 mμ). Although the m.p. of this methiodide could not be raised by further crystallization, it did not give any depression when mixed with a methiodide, m.p. 295-296° that was prepared by a Hofmann reaction from uleine methiodide. (Schmutz, Hunziker and Hirt[2] give m.p. 300-302°, correct.). IR-spectra of both compounds were identical.

When the above saturated methiodide derived from olivacine, m.p. 287-288°, was submitted to a second Hofmann degradation, it gave a new methine, m.p. 65-67° ($\lambda_{max.}$, 258 and 299 mμ) which gave no depression when mixed with the product, m.p. 69.5-70.5°, obtained from the similar methiodide prepared from uleine (Prof. Büchi). IR-spectra were superimposable.

By hydrogenation, this methine gave a compound (VII), m.p. 74.5-75.5°, with a carbazol spectrum ($\lambda_{max.}$: 240, 248, 261 and 298 mμ) and did not give any depression in the m.p. when mixed with a sample of the compound, m.p. 76.5-77.0° (Prof. Büchi) obtained from uleine, by a double Hofmann reaction and hydrogenation[2,4]. The IR-spectra were also identical.

(+) Guatambuine, which is N-methyltetrahydro olivacine, must then have structure (III). The fact that the methiodide of (+) guatambuine, when submitted to a Hofmann reaction gives an optically inactive methine, which methiodide is identical to that obtained from N-methyl tetrahydro olivacine (IV), is also in agreement with the proposed structure.

The second base obtained by Hofmann degradation of N-methyl-tetrahydro olivacine (III) did not change when submitted to hydrogenation. It gives a methiodide, m.p. 262-263°, with an IR-spectrum different from those recorded for the unsaturated methiodide (IV) and its reduction product (V). It has a UV-carbazol spectrum ($\lambda_{max.}$ 240, 250, 261 and 297 mμ).

Our m.p. were determined in a Kofler block and are uncorrected.

We thank Prof. R. B. Woodward for the information on the proposed structure of olivacine; Prof. B. Büchi for the generous gift of several compounds derived from uleine and for the control of some mixed m.p. and IR-spectra; Mr. J. F. Alicino and Dr. N. H. Coy, The Squibb Institute for Medical Research, New Brunswick, N.J., for the microanalysis and IR spectra.