Tetrahedron Letters No.46, pp. 4035-4036, 1969. Pergamon Press. Printed in Great Britain.

SYNTHESIS OF SEPTICINE

Jeff H. Russel and H. Hunziker

Research Institute, DR. A. WANDER S.A., Berne, Switzerland

(Received in UK 14 August 1969; accepted for publication 5 September 1969)

The proposal that Septicine, an alkaloid isolated from Ficus septica, has the structure 6,7-Bis-(3,4-dimethoxyphenyl)-6,7-dehydroindolizidine(1) has been proven by synthesis. The synthetic route is shown in the diagram.

Homoveratric acid and veratrumaldehyde were condensed in the presence of acetic anhydride and potassium acetate to give the acid I, mp 215-217°. The ester II, mp 97-98°, was obtained by refluxing I in ethanol in the presence of HCl. Lithium aluminium hydride reduction of II in THF gave the alcohol III, mp 114-115°, which was converted to the chloro compound IV, mp 133-136°, by suspending in absolute ether and passing in HCl gas in the presence of anhydrous sodium sulphate. The chloro compound IV was reacted with L-prolinol (2) in DMF/pyridine to give the amino alcohol V, mp 43-44°/69-71°, $[\alpha]_D^{22}$ -81.4°(c=1 in MeOH). On treatment of the amino alcohol with methanesulphonyl chloride in pyridine at 0°, the mesylate VI, mp 96-97°,$[\alpha]_D^{22}$ + 9.2°(c=1 in MeOH), was obtained and was further reacted with sodium hydride in anhydrous DMF to give an oil from which, after chromatography on silica gel, Septicine VII, mp 135-136°,$[\alpha]_D^{22}$ - 16.2°(c=1 in MeOH), was isolated*. The synthetic product was identical in all respects to natural Septicine.

Attempts to carry out a ring closure of V or VI to give VII under Friedel-Craft conditions gave only small yields of the desired product. This has also been observed recently by another group (3).

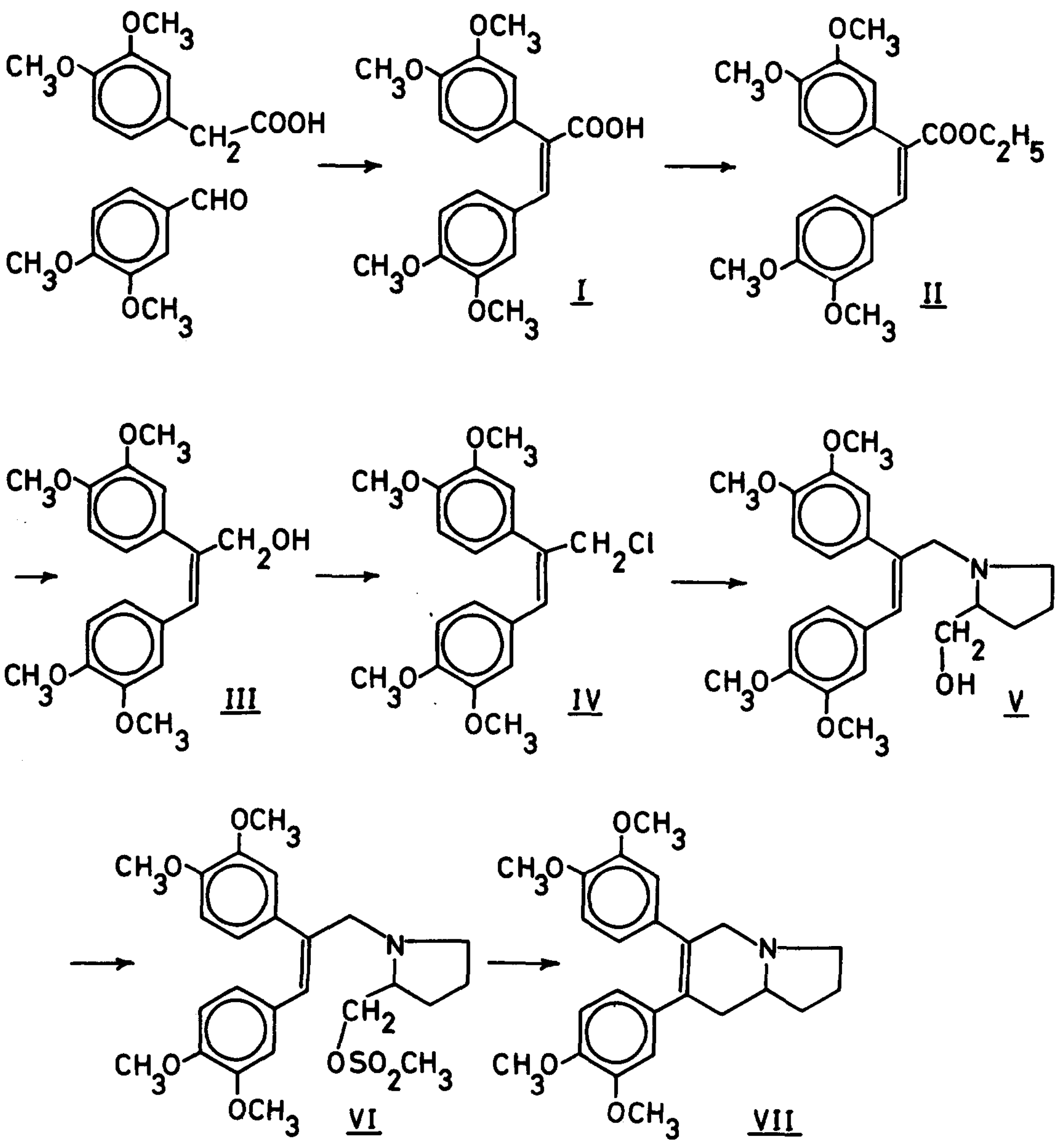
Septicine is a member of a class of compounds which most likely represent the biogenetic precursors** of the phenanthroindolizidine alkaloids as originally suggested by Wenkert (4). Racemic Septicine has been independently synthesised by T.R. Govindachari and N. Viswanathan using a different route. Their material shows identical mp and spectra to both our natural and synthetic compounds***.

---

[*] All synthesised compounds have been fully characterised by elemental analyses, UV and IR spectra.

[**] We thank Dr. R.B. Herbert, University of Leeds, England, for communicating his views on the subject. Dr. Herbert agrees with us on this point.

[***] We are grateful to Dr. N. Viswanathan, Ciba Research Centre, Bombay, India, for informing us of his synthetic work before publication.



References

(1) Jeff H. Russel: Naturwiss., 50, 443 (1963)
(2) P.G. Gassman and A. Fentiman: J. Org. Chem., 32, 2388 (1967)
(3) B. Chauncy, E. Gellert, and K.N. Trivedi: Australian J. Chem., 22, 427 (1969)
(4) E. Wenkert: Experientia, 15, 165 (1959)