Tetrahedron Letters No. 14, pp. 869-871, 1963. Pergamon Press Ltd.
Printed in Great Britain.

STEREOSPECIFIC TOTAL SYNTHESIS OF RACEMIC LATIFOLINE AND CONESSINE[*1]

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(Received 2 March 1963)

LATIFOLINE was first isolated from the plant, Funtumia latifolia STAPF, by the French workers (1) and proved to have the structure VI. Prior to its isolation, this substance had already been derived from conessine (2). Very recently, Marshall and Johnson (3) and Stork and co-workers (4) reported independently the total synthesis of rac. conessine. We wish to report on the synthesis of latifoline and conessine, which was carried out along lines similar to those of the former researching group, but quite independently.

Racemic 13β-cyano-18-nor-pregnane derivative II — the stereospecific total synthesis of this compound from 6-methoxy-1-tetralone (I) was reported in our preceding paper (5) — was transformed, in a single step,[*2] into the pyrrolidino derivative III,[*3] m.p. 200~201°,[*4] ν_{max}^{Nujol} 3473, 3258, 3123 cm^{-1}, by reduction with lithium aluminum hydride at 95~100°. The yield of III was 59 %. The latter compound was treated

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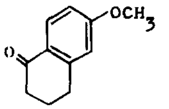
[*1] Studies on Total Syntheses of Steroids XIV

[*2] Marshall and Johnson reported a three-step synthesis of the corresponding pyrrolidino derivative (see ref. 3).

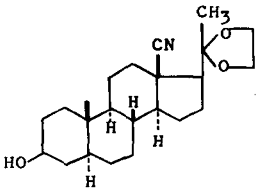
[*3] All compounds reported gave satisfactory analyses.

[*4] All melting points were measured on a Kofler block and corrected.

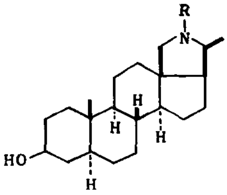
with formaldehyde and formic acid (6) to effect N-methylation and gave rac. dihydrolatifoline (IV) (1,7), m.p. 167~169°, $\nu_{max}^{CS_2}$ 3600, 2780, 2686, 2600 cm^{-1}. The identity of the infra-red spectrum of IV with that of an authentic sample[*5] of the natural steroid establishes that the above reductive cyclization proceeded in the desired stereochemical sense.



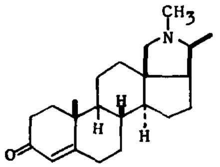
I

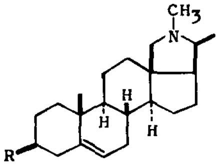


II



III R=H
IV R=CH_3





V

VI R=OH
VII R=$N(CH_3)_2$

Chromic acid oxidation of dihydrolatifoline (IV) in acetic acid gave the 3-ketone, m.p. 144~146°, $\nu_{max}^{CS_2}$ 2786, 2686, 2606, 1713 cm^{-1}. By applying the method of Rosenkranz et al. (8), this was converted into rac. conan-4-en-3-one (V); an oil, λ_{max}^{EtOH} 241 mμ (ε 16300), $\nu_{max}^{CS_2}$ 2780, 2680, 2600, 1675, 1617 cm^{-1}; the carbonate, m.p. 50~55°; the picrolonate, m.p. 155~165°. On enolacetylation and subsequent sodium borohydride reduction (9), compound V finally led to rac. latifoline

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[*5] We are very grateful to Dr. V. Černý and Dr. J. Hora for kindly supplying us with the samples of the alkaloids.

(VI), m.p. 170.5~171.5°, $\lambda_{max}^{CS_2}$ 3607, 3025, 2781, 2681, 2596, 1668 cm^{-1}. The infra-red spectrum of this compound is completely identical with that of the natural product[*5] (1,2). Since rac. conan-4-en-3-one (V) has been converted into rac. conessine (VII) by Marshall and Johnson (3), the synthesis of V constitutes a total synthesis of rac. conessine.

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