

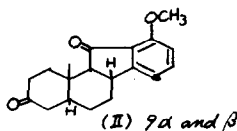
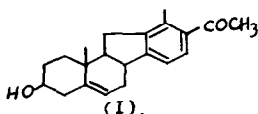
SYNTHESIS OF A NITROGEN-FREE DERIVATIVE OF VERATRAMINE
STUDIES ON C-NOR-D-HOMOSTEROIDS. III

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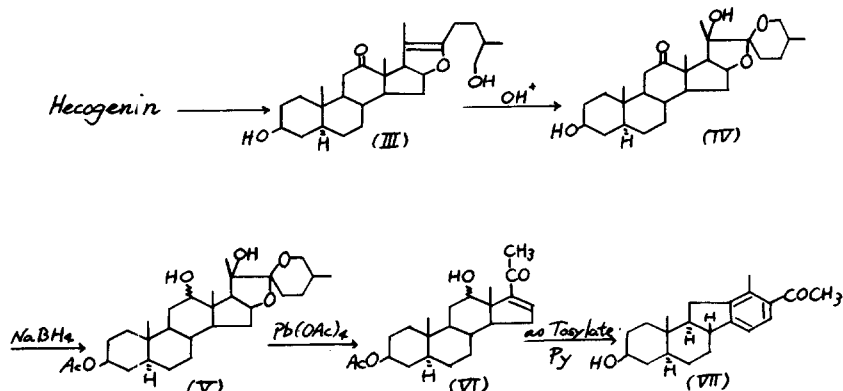
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(Received 23 June 1964)

For the purpose of the synthesis of steroidal alkaloid possessing unusual C-nor-D-homo ring system, we have synthesized, as an intermediate for the synthesis, a large number of C-nor-D-homosteroids from 12-oxygenated ones.¹ Recently, Johnson and Franck² have degraded the heterocyclic ring E of veratramine to give I as a relay substance for comparison with totally synthetic material. In 1961, Mitsuhashi and Shimizu³ have shown that the E/C configuration of jervine is trans, but in respect to C-9 configuration of veratramine, there was a possibility that it has E/C (9B) configuration, since 11-ketoveratramine derived from jervine⁴ would render C-9 readily epimerizable and the cis-benzindanone is considerably more stable than the trans-epimer.^{4,5} Johnson and his co-worker have determined that the E/C configuration of veratramine is trans on the basis of NMR spectrometric comparison with a derivative of 11-ketoveratramine and II.⁵

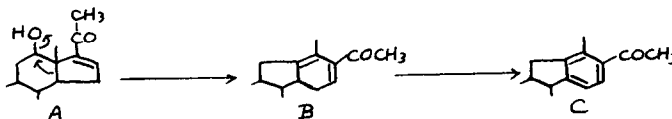


In this paper, we wish to report the final determination for C-9 configuration of veratramine by means of the synthesis of VII from hecogenin. Substance VII was recently synthesized from 5,6-dihydroveratramine by Masamune and Takasugi⁷ in the same manner as Johnson's fragmentation reaction.



20 ξ -Hydroxyhecogenin (IV) was prepared by pseudomerization of hecogenin and subsequent peracid oxidation.⁸ Acetylation and sodium borohydride reduction of IV yielded 3 β ,12 ξ ,20 ξ -trihydroxy-spirostane-3-monoacetate (V), m.p. 226-228°, $\nu_{\text{max}}^{\text{Nujol}}$ 3400 (OH), 1740, 1240 cm^{-1} (acetate), no carbonyl absorption, (Found: C, 71.04; H, 9.55), which was oxidized to 3 β ,12 ξ -dihydroxypregn-16-en-20-one-3-monoacetate (VI), m.p. 220-224.5°, $\lambda_{\text{max}}^{\text{EtOH}}$ 243 μ ($\epsilon=8,900$), $\nu_{\text{max}}^{\text{Nujol}}$ 3400 (OH), 1740, 1245 (acetate), 1640 (conjugated C=O), 1585 cm^{-1} (conjugated C=C), (Found: C, 73.59; H, 8.9), by lead tetraacetate in 90% AcOH .⁹ The tosylate of VI, which was obtained on treatment of VI with tosylchloride in pyridine, was refluxed in pyridine for 4 hrs.¹ The product purified by column chromatography has m.p. 170-175.5°, $\lambda_{\text{max}}^{\text{EtOH}}$ 259 μ ($\epsilon=13,600$), $\nu_{\text{max}}^{\text{Nujol}}$ 1670 (aromatic ketone C=O), 1600 (aromatic) cm^{-1} , (Found: C, 80.78; H, 9.09).

Initially, it was expected that the dienone B might be obtained by a rearrangement of A, however the reaction proceeded to C with aromatization.



This compound was completely identical with the degradation product (VII)⁷ prepared from veratramine by mixed melting point and comparison of IR spectra. It was conclusively confirmed that veratramine, therefore, has the B/C trans configuration.

Acknowledgement: We thank Dr. N.Masamune, Hokkaido University, for kind donation of VII, and Dr. K. Takeda, Director of Shionogi Laboratory for the starting materials.

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