The gel formed by thrombin dissolved readily in 6 *M* urea at *p*H 8.40 to give products of the same molecular weight as native fibrinogen under the same conditions. It was not however possible for the present to ascertain the absolute value of the molecular weight because of uncertainties as to the contribution of selective adsorption to the scattering of such a three component system.

Further work is in progress with the aim of ascertaining the nature of the sub-units involved in the actual formation of the three dimensional network and whether they correspond in size and shape to the aggregates found immediately prior to gelation.

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RECEIVED DECEMBER 16, 1950

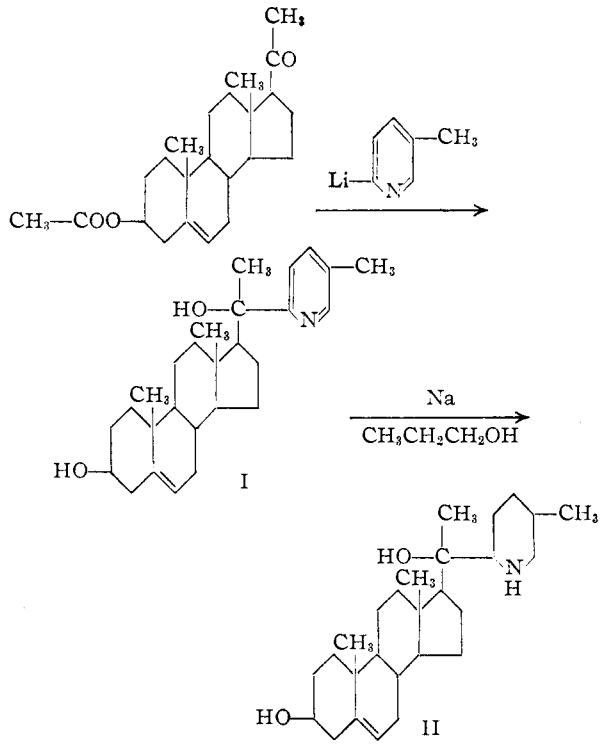
STEROID SECONDARY AMINES[1]

Sir:

The *veratrum*, and closely related *solanum*, alkaloids may be divided into two groups on the basis of the character of the nitrogen function, a separation reaffirmed in a parallel differentiation as a result of pharmacological studies. Because of the wide diversity of pharmacodynamic effects which they exhibit,[2] tertiary veratrum bases of the type of veratridine have been of interest to biologists for nearly a century, while protoveratrine and germitrine, powerful vasodepressor ester alkaloids derived from multiply oxygenated alkamines of this series, have been employed with a certain degree of success in the clinical management of hypertension.[3] The tertiary alkamines, which have been shown to be hexacyclic octahydropyrrocoline derivatives constructed from the perhydrocyclopentanophenanthrene ring system, have been obtained by partial synthesis as exemplified by the conversion of sarsasapogenin to 5-isosolanidane-3β-ol, one of the stereoisomeric dihydro derivatives of solanidine.[4]

The secondary alkamines of the class of veratramine and jervine, on the other hand, have only very recently been shown to exhibit an unprecedented type of remarkable specificity in their ability to annul the effects of accelerans stimulation, as well as to antagonize the positive chronotropic, or cardioaccelerator, properties of epinephrine and related sympathomimetic amines without disturbing the positive inotropic and vasopressor properties of these substances.[5] Steroid secondary amines characterized by the skeletal structure postulated for the naturally occurring secondary veratrum alkamines[6] and for the hydrogenation products of secondary solanum bases of the type of solasodine,[7] have now been obtained by partial synthesis.

2-Bromo-5-methylpyridine[8] has been converted to the 2-lithium derivative with *n*-butyllithium and allowed to react with Δ^5-pregnen-3β-ol-20-one 3-acetate[9] in ether solution to yield the pyridylcarbinol I, m.p. 281–282°; $[\alpha]^{25}D$ −76.8° ($CHCl_3$). *Anal.* Calcd. for $C_{27}H_{39}NO_2$: C, 79.17; H, 9.60; N, 3.42. Found: C, 79.39; H, 9.61; N, 3.42. 3-Acetate, m.p. 225–226°; $[\alpha]^{25}D$ −80.3° ($CHCl_3$); $\Delta^{Ac}_{MD} = -48°$. *Anal.* Calcd. for $C_{29}H_{41}NO_3$: C, 77.12; H, 9.15; N, 3.10. Found: C, 77.07; H, 9.11; N, 3.21. Reduction of I with sodium and *n*-propanol has afforded a fraction yielding an N-nitroso derivative and a slightly soluble picrate, m.p. 248–250°. *Anal.* Calcd. for $C_{33}H_{48}N_4O_9$: C, 61.47; H, 7.50; N, 8.69. Found: C, 61.38; H, 7.60; N, 8.82, which, on conversion to the base with dilute aqueous lithium hydroxide solution, has yielded 20-(5′-methyl-2′-piperidyl)-Δ^5-pregnen-3β,-20-diol (II) m.p. 207–208°; $[\alpha]^{25}D$ −54.8° ($CHCl_3$). *Anal.* Calcd. for $C_{27}H_{45}NO_2$: C, 78.02; H, 10.91; N, 3.37. Found: C, 78.15, H, 10.92; N, 3.64. Hydrochloride, m.p. 294–296°. *Anal.* Calcd. for $C_{27}H_{45}NO_2 \cdot HCl$: C, 71.72; H, 10.26; N, 3.10. Found: C, 71.28; H, 10.20; N, 3.04.



The synthetic alkaloid II, when examined by Dr. Otto Krayer, was found to display the antagonism to the cardioaccelerator properties of epinephrine characteristic of veratramine and jervine at a potency of the order of that exhibited by the latter naturally occurring substance.

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(2) Krayer and Acheson, *Physiol. Rev.*, **26**, 383 (1946).

(3) Meilman and Krayer, *Circulation*, **1**, 204 (1950); Fried, White and Wintersteiner, THIS JOURNAL, **72**, 4621 (1950).

(4) Uhle and Jacobs, *J. Biol. Chem.*, **160**, 243 (1945).

(5) Krayer, *J. Pharm. Ex. Therap.*, **96**, 422 (1949).

(6) Fieser and Fieser, "Natural Products Related to Phenanthrene," 3rd Ed., Reinhold Publishing Corp., New York, N. Y., p. 605.

(7) Briggs, Harvey, Locke, McGillivray and Seelye, *J. Chem. Soc.*, 3013, 3020 (1950).

(8) Case, THIS JOURNAL, **68**, 2574 (1946).

(9) The pregnenolone used in this work was supplied by the Schering Corporation, Bloomfield, New Jersey, and the Lederle Laboratories, Pearl River, New York.