$P_sAm(1)$, $\beta Ch(2)$, $\beta Ch(4)$, $\beta Ch(5)$, $\beta Ch(7)$, $\beta Tr(10)$, $\beta Tr(14)$, and $\beta Tr(17)$. Sufficient data on the remaining peptides were obtained to show their compatibility with the assigned structures.[16]

The data on peptides $\beta Tr(1)$ and $\beta P_s(4)Tr(1)$ suggest the structure indicated in the parentheses of the structure. Research designed to remove this uncertainty is underway and will be reported along with the experimental details of this work in publications now in preparation.

(16) The N-terminal sequence H·Ser-Tyr-Ser-Met-Glu-His-Phe- has been shown to occur in *sheep* corticotropin [J. Harris and C. H. Li, THIS JOURNAL, **76**, 3607 (1954)]. The H·Ser-Tyr- N-terminal and Pro-Leu-Glu-Phe·OH C-terminal orders for corticotropin A from hog pituitaries were reported by W. A. Landmann, *et al.*, *ibid.*, **75**, 4370 (1953), and W. F. White, *ibid.*, **75**, 4877 (1953).

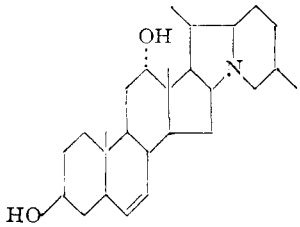
CHEMOTHERAPY DEPARTMENT
STAMFORD LABORATORIES
RESEARCH DIVISION PAUL H. BELL
AMERICAN CYANAMID COMPANY
STAMFORD, CONNECTICUT

RECEIVED SEPTEMBER 20, 1954

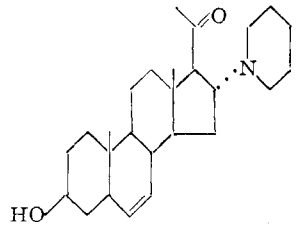
SYNTHETIC STEROIDAL CARDIOACTIVE AMINES

Sir:

In synthetic approaches to the structure of steroidal alkaloids such as rubijervine,[1] I, we have prepared various 16-aminopregnenolones, among them 16α-piperidino-5-pregnen-3β-ol-20-one, II.



I



II

5,16-Pregnadien-3β-ol-20-one was treated with excess piperidine and aqueous potassium hydroxide to give II, which was isolated in two crystalline forms, m.p. 149–151° and 160–162°; $[\alpha]^{25}D$ −23.5°, −24.7° (dioxane). *Anal.* Calcd. for $C_{26}H_{41}O_2N$: C, 78.14; H, 10.34; N, 3.51. Found: C, 78.28, 78.17; H, 10.22, 10.14; N, 3.60, 3.51, respectively. Both forms showed the same infrared spectrum and gave the same hydrochloride, m.p. 240–242° (dec.), $[\alpha]^{25}D$ +8.7° (95% EtOH). *Anal.* Calcd. for $C_{26}H_{41}O_2N\cdot HCl$: N, 3.21; Cl, 8.13. Found: N, 3.21; Cl, 8.06.

Although II only superficially resembles I, it shows some hypotensive action in dogs at a dose of 1–2 mg./kg.,[2] which is the order of activity of I.[3] In contrast to earlier experience,[4] however, II, although it contains a tertiary nitrogen similar to the known hypotensive veratrum ester alkaloids, also exhibits the bradycrotic and specific contra-accelerator action previously found only with the secondary steroidal alkamines such as jervine.[2,4]

Similarly, addition of cyclohexylamine to 5,16-pregnadienolone gave 16α-cyclohexylamino-5-pregnen-3β-ol-20-one, III, m.p. 151–152°, $[\alpha]^{25}D$ −29.8° (dioxane). *Anal.* Calcd. for $C_{27}H_{43}O_2N$: C, 78.40; H, 10.48; N, 3.39. Found: C, 78.35; H, 10.46; N, 3.53. Catalytic hydrogenation of III using platinum in acetic acid gave 16α-cyclohexylamino-allopregnane-3β,20ζ-diol (IV), m.p. 179–180.5°, $[\alpha]^{25}D$ −58.1° (dioxane). *Anal.* Calcd. for $C_{27}H_{47}O_2N$: C, 77.64; H, 11.34; N, 3.35. Found: C, 77.57; H, 11.30; N, 3.05.

These secondary amines, III and IV, show the contraaccelerator effect typical of secondary alkamines, but in addition have activity against arrhythmias of the heart. Thus IV shows a potency about five times that of jervine[5] against the chromotropic effect of epinephrine in the isolated heart, and also in intact animals; and a potency about four times that of quinidine against methacholine induced auricular arrhythmias in dogs.[2]

Further investigations of pharmacologically active synthetic steroidal amines are continuing and will be reported in detail at a later date.

(1) Y. Sato and W. A. Jacobs, *J. Biol. Chem.*, **179**, 623 (1949).

(2) We are indebted to Dr. O. Krayer, Department of Pharmacology, Harvard Medical School, for his continued interest and advice, and to Drs. S. Margolin and G. Lu, Pharmacology Department, Schering Corporation, for the pharmacological results which will be published elsewhere.

(3) G. L. Maison, E. Gotz and J. W. Stutzman, *J. Pharmacol. and Exper. Therap.*, **103**, 74 (1951).

(4) O. Krayer and L. H. Briggs, *Brit. J. of Pharmac. and Chemo.*, **5**, 118, 517 (1950); F. C. Uhle, THIS JOURNAL, **73**, 883 (1951).

(5) O. Krayer, F. C. Uhle and P. Ourisson, *J. Pharmacol. and Exper. Therap.*, **102**, 261 (1951).

CHEMICAL RESEARCH DIVISION DAVID GOULD
SCHERING CORPORATION ELLIOT L. SHAPIRO
BLOOMFIELD, NEW JERSEY E. B. HERSHBERG

RECEIVED OCTOBER 7, 1954

A QUANTITATIVE APPROACH TO ION EXCHANGE CATALYSIS

Sir:

The quantitative interpretation of ion exchange catalysis is simplified by treating the pore liquid of the resin, in which the reaction occurs, as a homogeneous system, and comparing it with a homogeneous solution containing dissolved electrolyte as catalyst, both at equal concentration of the catalyst ion, the supernatant solution in case of ion exchange catalysis being used merely as a means for determining the necessary quantities. Comparison of the rate constants and activation energies in both systems will then reveal special influences of the resin other than adsorption phenomena which can be accounted for separately.

The rate determining step in ion exchange catalysis can be the velocity of the reaction, or the diffusion within the resin. We deal first with reaction controlled catalysis.

For the simple case of a first order reaction without reverse reaction

$$AB \longrightarrow A + B \qquad (1)$$

(for instance sucrose inversion) the reaction rate in a homogeneous solution is given by

$$-dc/dt = kc \qquad (k = f(c_{cat.}) \approx k'c_{cat.}) \qquad (2)$$

where c is the concentration of the reactant AB. The rate constant k is a function of the catalyst concentration c_{cat} and approximately proportional to c_{cat}. An analogous equation may be written for the pore liquid, denoting all quantities referring to pore liquid with bars. The assumption of reaction controlled catalysis implies that $\bar{c}$ has its