$P_sAm(1)$, $\beta Ch(2)$, $\beta Ch(4)$, $\beta Ch(5)$, $\beta Ch(7)$, $\beta Tr(10)$, $\beta Tr(14)$, 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).

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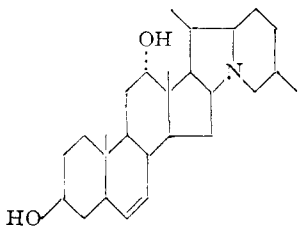
RECEIVED SEPTEMBER 20, 1954

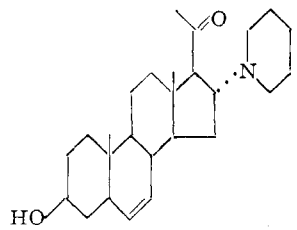
SYNTHETIC STEROIDAL CARDIOACTIVE AMINES

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
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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

equilibrium value throughout the resin which can, however, be different from the concentration c in the supernatant solution, as has been pointed out by Davies and .Thomas.[1] We define a distribution coefficient λ between pore liquid and supernatant solution

$$\lambda = \bar{c}/c \qquad (3)$$

which can be larger or smaller than unity, depending on the respective strength of the interactions reactant–resin and reactant–solvent. Substituting $\bar{c}$ by $c\lambda$, and considering that the reaction occurs in the pores only, we obtain for the over-all rate in the heterogeneous system consisting of pore liquid and supernatant solution

$$-\left(\frac{dn}{dt}\right)_{het} = -\frac{d\bar{n}}{dt} = -\bar{V}\bar{k}c\lambda \qquad (4)$$

where n is the number of moles and $\bar{V}$ is the pore volume. Evaluating this equation $\bar{k}$ can be calculated. (Equation (4) implies that $d\bar{V}/dt = 0$, *i.e.*, that no swelling or shrinking occurs with the reaction.)

Experimental results of other authors[1-6] show that the over-all rate in heterogeneous systems obeys first order kinetics

$$-\left(\frac{dc}{dt}\right)_{het} = \frac{1}{V}\left(\frac{dn}{dt}\right)_{het} = k^*c \qquad (5)$$

where the formal constant k^* does not depend on c. Comparison of (5) and (4) show that therefore $\bar{k}\lambda$, and very likely both $\bar{k}$ and λ, should be independent of c.

This approach can be extended to systems with reverse reactions and with other than first order kinetics.

The complex mathematics of diffusion controlled catalysis has been dealt with for spherical beads by Smith and Amundson.[7] Their concept can be extended by introducing the distribution coefficient λ which was not included in their treatment.

Other investigators[1-4] have compared homogeneous and heterogeneous systems containing equivalent amounts of catalyst (*i.e.*, $(\bar{V}\bar{c}_{cat})_{het} = (V c_{cat})_{hom}$), the homogeneous in a constant concentration throughout the system, the heterogeneous in a higher concentration in a part of the system. The efficiency q of a resin, as defined by Hammett,[2] is, in terms of this approach

$$q = \frac{k^*}{k} = \frac{\bar{k}\bar{V}}{kV}\lambda = \frac{\bar{k}'}{k'}\lambda \qquad (6)$$

when the relations $k = k'c_{cat}$ (2) are assumed to hold for both pore liquid and homogeneous solution. Hitherto published results of other authors[1-6,8] can be accounted for qualitatively in terms of λ, though, of course, $\bar{k}'/k'$ might differ from unity.

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RECEIVED AUGUST 26, 1954

(1) C. W. Davies and G. G. Thomas, *J. Chem. Soc. (London)*, 1607 (1952).

(2) S. A. Bernhard and L. P. Hammett, THIS JOURNAL, **75**, 1798 and 5834 (1953).

(3) V. C. Haskell and L. P. Hammett, *ibid.*, **71**, 1284 (1949).

(4) E. Mariani, *Annali chimica applicata*, **39**, 283 and 717 (1949); **40**, 500 (1950).

(5) L. Lawrence and W. J. Moore, THIS JOURNAL, **73**, 3973 (1951).

(6) W. Lautsch and W. Rothkegel, *Z. Naturforschung*, **6b**, 365 (1951).

(7) N. L. Smith and N. R. Amundson, *Ind. Eng. Chem.*, **43**, 2156 (1951).

(8) P. Mastagli, A. Floc'h and G. Durr, *Compt. rend.*, **235**, 1402 (1952).

LIGHT INDUCED PHOSPHORYLATION BY CELL-FREE PREPARATIONS OF PHOTOSYNTHETIC BACTERIA[1]

Sir:

In the course of a study of phosphorylation with cell-free preparations from *Rhodospirillum rubrum* (strain S-1)[2] it was observed that light induced anaerobically a pronounced disappearance of orthophosphate. This could be demonstrated with added yeast hexokinase, mannose[3] and catalytic amounts of adenosine polyphosphates, or with substrate amounts of ADP.[4] In the latter case the disappearance of orthophosphate could be stoichiometrically accounted for by the increase in P_7[4] (Table I).

TABLE I

Experimental conditions	Time of incubation in minutes	ΔP/reaction vessel in μM. ΔP_i	ΔP_7
Dark, + ADP	10	+ 1.6	− 1.6
(10.3 μM.)	35	+ 2.3	− 2.5
Light, alone	10	− 0.3	+ 0.7
	35	− 0.5	+ 0.7
Light, + ADP	10	− 4.7	+ 4.3
(10.3 μM.)	35	−10.9	+10.7

The above crude sonic preparation was obtained by disintegrating washed cells in a 10 KC. Raytheon magnetostrictive oscillator for 4 minutes at 5°. The resulting suspension was centrifuged for 5 minutes at 10,000 × gravity. The sediment was discarded and the supernatant filtered through a fine porous glass filter to remove large cell fragments. The filtrate was used as indicated. The experimental suspension contained 13.4 mg. of protein and the following additions: 35 μM. $MgCl_2$, 30 μM. KF, 20 μM. P_i, 10.3 μM. ADP, 1.5 μM. DPN; total volume, 3 ml.; suspending medium: 0.2 *M* potassium salt of glycylglycine, *p*H 7.4. All experiments performed at 25°, under anaerobic conditions (helium); illumination by incandescent lamps; intensity, 1200 foot candles.

The ATP formed by the light induced reaction was further identified through the hexokinase catalyzed phosphorylation of glucose.

On centrifuging the preparation at 135,000 × gravity for one hour (*cf.*[5]), all the phosphorylating activity was found in the sediment. Repeated washing of the sediment produced a slight increase in the specific activity. α-Ketoglutarate increased

(1) This investigation was carried out on sabbatical leave from the Department of Botany, University of Minnesota at Minneapolis, and was supported in part by grants from the Graduate School of the University of Minnesota and partly by a grant given to Dr. Lipmann by the Cancer Institute of the National Institutes of Health, Public Health Service.

(2) Cell-free suspensions prepared with modifications according to the method described by L. P. Vernon and M. D. Kamen, *Arch. Biochem. Biophys.*, **44**, 298 (1953).

(3) Mannose was employed because glucose-6-phosphate was rapidly metabolized by the preparation.

(4) Abbreviations used: P_i for orthophosphate, P_7 for orthophosphate liberated by 7 minute hydrolysis in *N* HCl at 100°, ADP for adenosinediphosphate, ATP for adenosinetriphosphate, DPN for diphosphopyridine nucleotide, cyt. c for cytochrome c, KGA for potassium salt of α-ketoglutaric acid, and mersalyl for sodium salt of *o*-[(3-hydroxymercuri-2-methoxypropyl)-carbamyl]-phenoxyacetic acid.

(5) H. K. Schachman, A. B. Pardee and R. Y. Stanier, *Arch. Biochem. Biophys.*, **38**, 245 (1952).