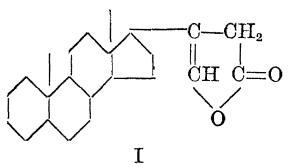
P. Debye, "Theory of X-Ray and Electron Diffraction"; J. Y. Beach, "Electron Diffraction Studies of Gaseous Molecules"; H. R. Nelson, "Electron Diffraction Studies of Solids and Solid Surfaces"; L. H. Germer, "Electron Diffraction Studies of Thin Films."

Since the accommodations on Gibson Island are very limited, it is advisable to make registration and reservations in advance. The registration fee is $3.00 per week per person, payable to Section C, A. A. A. S. On receipt of check, a registration card will be sent which will admit one to the island and entitle him to all the guest privileges of the island, including a reservation for a room. Rooms are $2.00 per day per person and board is *a la carte*. It is possible to make a few week-end reservations if made in advance. Any person making advance registration and reservations and finding later he is not able to attend may have his registration fee returned and his reservations cancelled, providing that a notice is received at least one week in advance of the date of the conference. The registration fee, request for room reservation or request for any additional information should be addressed to the Director of the Conferences, Neil E. Gordon, Central College, Fayette, Missouri.

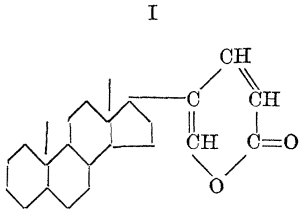
# SPECIAL ARTICLES

## SYNTHESES OF MODEL UNSATURATED LACTONES RELATED TO THE CARDIAC AGLYCONES

THE structures of the cardiac aglycones rest on a reasonably complete foundation as a result of the investigations of Jacobs, Windaus, Tschesche, Stoll and their collaborators.[1] For purposes of chemical classification the aglycones may be conveniently divided into two groups, *viz.*, those of the digitalis-strophanthus group the members of which are characterized by the presence of a side-chain consisting of the lactone of an enolized β-aldehydo-acid carrying the cyclopentanophenanthrene ring system on the β-carbon atom (type formula I), and those of the squill-toad venom group in which the cyclopentanophenanthrene ring system is present as a substituent in the 5-position of an α-pyrone ring (type formula II).



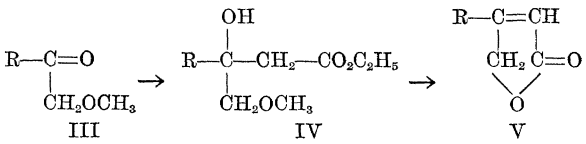
I



II

We have succeeded in synthesizing simple 5-substituted α-pyrones to serve as models for further work. Ethyl hexene-2-oate on condensation with ethyl oxalate in the presence of potassium ethylate gives diethyl 4-ethylhexene-2-on-5-dioate-1,6. This, after hydrolysis of the ester groups, on heating with hydrogen bromide in acetic acid yields 5-ethyl-6-carboxy-α-pyrone (calculated for $C_8H_8O_4$: C, 57.2; H, 4.8; found: C, 57.6; H, 4.9) which on distillation with copper powder yields 5-ethyl-α-pyrone.

At the same time we have been engaged in the synthesis of unsaturated γ-lactones related to the digitalis-strophanthus type, and have succeeded in preparing β-substituted $\Delta^{\alpha,\beta}$-unsaturated γ-lactones containing phenyl, cyclohexyl and *n*-butyl groups as representative substituents. ω-methoxy-methylketones (III) are readily prepared by the action of an appropriate Grignard reagent on methoxyacetonitrile.[2] These on condensation with ethyl bromoacetate in the presence of zinc give glycol-ether-esters (IV) which, after saponification of the ester, give unsaturated lactones (V) when heated with hydrogen bromide in acetic acid.[3]



III IV V

For the typical case where R is cyclohexyl: Calculated for $C_{10}H_{14}O_2$: C, 72.3; H, 8.5; found: C, 72.5; H, 8.8.

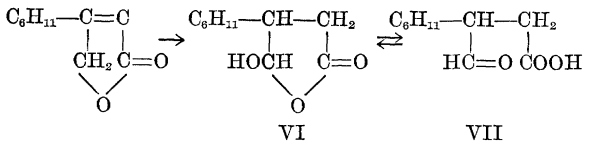
The properties of the latter lactones are not without interest. Thus the cyclohexyl lactone on treatment with a solution of potassium hydroxide in absolute methanol apparently undergoes irreversible isomerization to the $\Delta^{\beta,\gamma}$-lactone which adds the elements of water either during the reaction or during the subsequent working up to yield the hydroxylactone (VI). (Calculated for $C_{10}H_{16}O_3$: C, 65.2; H, 8.9; found: C, 65.7; H, 8.8.) Substances of the latter type have been shown to exist in equilibrium with the corresponding aldehyde-acid (VII).[4] The presence of both an aldehyde group and a carboxyl group in VI

[1] Elderfield, *Chem. Rev.*, 17: 187, 1935; Tschesche, *Ergeb. d. Physiol.*, 38: 31, 1936.

[2] Henze and Rigler, *Jour. Am. Chem. Soc.*, 56: 1350, 1934.

[3] Stoermer, *Ber.*, 39: 2297, 1906.

[4] Perkin, Jr., and Sprankling, *Jour. Chem. Soc.*, 75: 11, 1899; Harries and Alefeld, *Ber.*, 42: 159, 1909.



VI VII

or VII was shown by the preparation of the semicarbazone of the methyl ester. (Calculated for $C_{12}H_{21}O_3N_3$: C, 56.4; H, 8.3; found: C, 56.5; H, 8.5.)

The possible bearing of these observations on the structure of the cardiac aglycones and on the transformation of the aglycones into the iso-aglycones will be discussed in detail in a forthcoming communication.

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## NATURE OF THE PASTEUR ENZYME[1]

WHEN fermenting cells are brought in contact with oxygen, normally less carbohydrate is broken down and less fission products are formed. This phenomenon was discovered by Pasteur in 1861 and is to-day known as the Pasteur reaction. This effect has been interpreted in terms of an oxidative resynthesis of carbohydrate from the end products of fermentation (Meyerhof) of a suppression of fermentation by respiration (Warburg), and of an inhibition of fermentation dependent on the oxygen tension (Lipmann, Kempner, Laser). The selective inhibition of the Pasteur reaction by ethyl isocyanide,[2] by a lowering of the oxygen tension[3] and by suitable concentrations of carbon monoxide[4] indicates that a catalyst distinct from the respiratory enzyme is involved and that this agent contains heavy metal. The name *Pasteur enzyme* appears to be appropriate for this thermolabile catalyst.

The reversal of the carbon monoxide inhibition of the Pasteur effect by white light[4] has enabled us to apply the classical photochemical technique of Warburg to the study of the spectrum of the Pasteur enzyme. Rat retina was chosen for these experiments because its respiration remains unaffected by carbon monoxide at concentrations sufficient to inhibit the Pasteur enzyme.[4] The photochemical effect of monochromatic light of three different wave-lengths on the glycolysis in this system has been attributed by Warburg and Negelein[5] to the action of carbon monoxide and light on the respiratory enzyme causing a secondary effect on glycolysis. This view is no longer tenable in the light of Laser's observations,[4] which we have been able to confirm.

In the present work sixteen different wave-lengths of monochromatic light of high intensity have thus far been used for the charting of the relative photochemical absorption spectrum of the Pasteur enzyme in the visible region. The pattern obtained is that of an iron-porphyrin-protein, showing a high γ- or Soret band at 440–455 mμ, and lower β- and α-bands at 500–520 mμ and 570–590 mμ, respectively. The position of the maxima of these bands is indicated in the diagram (Fig. 1) together with the corresponding maxima of the bands of carbon monoxide hemoglobin and the carbon monoxide complex of the respiratory enzyme.

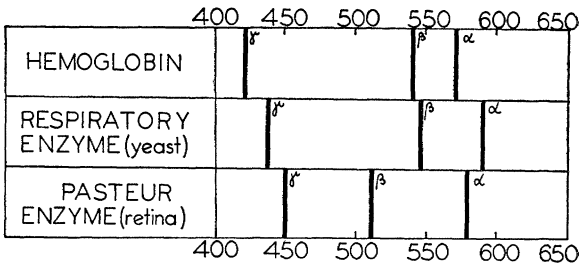


FIG. 1. Diagram showing the position of the absorption maxima of the carbon monoxide compounds of hemoglobin, the respiratory enzyme in yeast (Warburg) and the Pasteur enzyme in retina (present work) in the visible region of the spectrum.

A well-defined band at 450 mμ has also been recorded by direct spectrography of carbon monoxide-treated rat retinas. This band coincides in position with the main or γ-band of the Pasteur enzyme as revealed by the photochemical experiments.

The Pasteur enzyme in retina appears to be a pheohemin protein like the respiratory enzyme in yeast and in Acetobacter. It differs from them with regard to its affinity for carbon monoxide and oxygen as well as the position of the absorption bands of the carbon monoxide compound.

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## PROLIFICACY OF RATS TREATED WITH MARE GONADOTROPIC HORMONE

As an earlier paper[1] has demonstrated, adequate amounts of mare gonadotropic hormone will produce superovulation and estrus in immature rats. Mating of these rats[2] resulted in the implantation of as many

[1] This work was aided by a grant from the Jane Coffin Childs Memorial Fund for Medical Research.
[2] O. Warburg, *Biochem. Zeitschr.*, 172: 432, 1926.
[3] H. Laser, *Biochem. Jour.*, 31: 1671, 1937.
[4] *Ibid.*, 31: 1677, 1937.
[5] O. Warburg and E. Negelein, *Biochem. Zeitschr.*, 214: 101, 1929.
[6] Finney-Howell Research Foundation fellow, 1939–40.
[1] H. H. Cole, *Amer. Jour. Anat.*, 59: 299–331, 1936.
[2] H. H. Cole, *Am. Jour. Physiol.*, 119: 704–712, 1937.