Vitamin E Synthesis of α-Tocopherol

THE recent announcement by Karrer, Fritzsche, Ringier and Salomon[1] makes it desirable for us to place on record the fact that we have also synthesized racemic α-tocopherol by a rather simpler method, namely, direct condensation of phytol with ψ-cumoquinol by heating a mixture of these two substances in presence of a little zinc chloride. This synthesis, like that of the Swiss workers, while it confirms the view originally expressed by ourselves[2] and by Fernholz[3] that the tocopherols are chroman or coumaran derivatives, nevertheless fails to distinguish between the two types of structure.

Karrer's arguments[4] in favour of a coumaran structure for the synthetic product rest on an assumption that phytyl bromide will condense with a phenol in exactly the same way as allyl bromide. This assumption seems to us unjustifiable, and it is indeed more probable that condensations of this type would lead to chroman structures when phytol derivatives are used. Recent degradative evidence, although inconclusive, is on the whole more indicative of a chroman structure for the tocopherols[3,5].

On the synthetic side we have found that 6-hydroxychromans, 5-hydroxycoumarans, and α- and β-tocopherol are nearly identical as regards absorption spectrum, reducing properties, and effect of esterification on absorption spectrum.

We are at present engaged on the synthesis of the tocopherols by unequivocal methods, since it seems that only in this way can a final decision be reached as to their structure.

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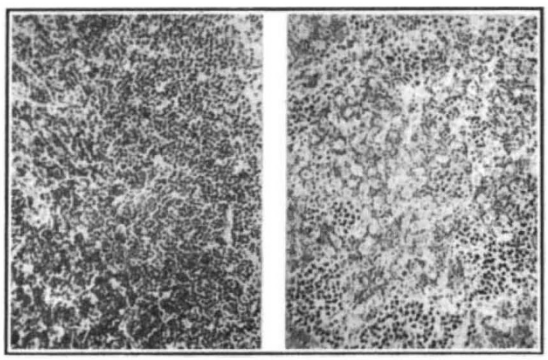
June 17.

[1] NATURE, **141**, 1057 (1938).
[2] Bergel, Todd and Work, *J. Chem. Soc.*, 253 (1938); Bergel Jacob, Todd and Work, NATURE, **141**, 646 (1938).
[3] Fernholz, *J. Amer. Chem. Soc.*, **60**, 700 (1938).
[4] Karrer, Fritzsche, Ringier and Salomon, *Helv. chim. Acta*, **21**, 520 (1938).
[5] Dietzel, Günther and Emte, *Naturwiss.*, 366 (1938).

Formation of Hæmolymph-Glands in Tumour-Bearing Rats

A CHANGE has been observed in the appearance of the lymph-glands of rats bearing a Jensen sarcoma, the animals being examined usually fifteen to eighteen days after the subcutaneous inoculation of the tumour. While the lymph-glands of normal rats were found to be almost entirely of a light yellowish colour, a more or less large number of the lymph-glands of the tumour-bearing rats showed, to a varying extent and degree, a red discoloration. The change occurred in glands of all regions, although unequally, and in an irregular manner in different animals. The size of the tumour and the age of the animal, within the given limits, appeared to have little influence.

Microscopical examination of these lymph-glands showed that a conversion into more or less pronounced hæmolymph-glands had taken place. The normal lymph-tissue had to a varying extent disappeared. Its place was, in the first instance, taken by red blood corpuscles, which were more or less densely aggregated. Among them could be observed, in most cases, a considerable number of particularly large, sometimes pigmented cells, probably the descendants of normal (non-lymphocytic) tissue cells. The whole of this structural change is evident from a comparison of the accompanying illustrations. In each is illustrated part of a section through a lymph-gland taken from the left axilla of a female rat, (*a*) referring to a normal animal (weight about 170 gm.) and (*b*) to an animal bearing, at the right side, a sarcoma of more than 50 gm. weight (animal weight, without tumour, about 160 gm.; inoculation fifteen days before examination).



(*a*) (*b*)

STRUCTURE OF A LYMPH-GLAND, (*a*) FROM A NORMAL RAT, (*b*) FROM A TUMOUR-BEARING RAT. HÆMATOXYLIN—EOSIN. (× 120).

The simplest explanation of the origin of this change appears to be that it is due to the action of a certain substance produced by the growing tumour cell. Investigations with the aim of finding out the chemical nature of this substance are now in progress. In this connexion it is of interest to note that a similar change was previously observed in the lymph-glands of rats which had received a series of subcutaneous injections of a preparation of carcinogenic tar[1]. Further, it is important that Clarkson, Mayneord and Parsons[2] have obtained a corresponding result with the lymph-glands of animals which had been irradiated with X-rays. In addition, the authors mentioned that a derivative of 1 : 2 : 5 : 6-dibenzanthracene was likewise capable of producing the change.

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[1] Lasnitzki, A., *J. Hygiene*, in the press.
[2] Clarkson, J. R., Mayneord, W. V., and Parsons, L. D., *J. Path. and Bact.*, **46**, 221 (1938).

Kallikrein as a Reynals Factor

THE spreading or diffusing factors, also termed Reynals factors or shortly *R.* factors, after F. Duran-Reynals[1], who found these factors in watery extracts of testicle of mammals, are endowed with the property of enhancing tissue permeability. When indicators, such as Indian ink, trypan blue or diphtheria toxin are added to such extracts and a certain amount of the mixture is injected intracutaneously in rabbits, an extensive spread of the particles of Indian ink, trypan blue or the toxin takes place, resulting in much larger coloured or inflamed areas than can be obtained by mixing other substances (excluding the few other *R.* factors) with the indicators. As a control in experiments with *R.* factors a mixture of 0·9 per cent sodium chloride with the indicator is generally used.