siderable quantities of citrate, tartrate, etc., could be decomposed under physiological conditions.

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Effects of Massive Iron Overload in the Rat

THE low toxicity of iron–dextran complex ('Imferon') has made it possible to follow for the past eighteen months the effects of administering intramuscularly a total dose of 1,650 mgm. iron per kgm. to rats. Control animals on the same diet (M.R.C. diet 41 containing 1 per cent of cod liver oil) over the same time were treated with equivalent amounts of dextran, without iron.

The iron-loaded rats have remained in good health, though the growth-rate of male animals in particular has been below that of the dextran controls. At intervals, groups of rats have been killed: the dextran-treated controls showed no abnormality; in the others there was organ siderosis but nothing to suggest the development of hæmochromatosis[1]. On the contrary, the only changes noted to date in the iron-treated animals are effects which form part of the characteristic picture of vitamin E deficiency in the rat: rapid post-mortem renal autolysis[2][3] (from 9 weeks onward), brown uterus[4] (from 50 weeks onwards) and testicular atrophy[5] (only in two instances, at 47 and 52 weeks). The most striking feature in all the animals was the massive accumulation of ceroid-like pigments, particularly in the kidney (Fig. 1). A direct comparison with the organs of a rat deprived of vitamin E for 651 days was made possible through the kindness of Dr. T. Moore. A close similarity exists, with minor differences in the staining reactions and distribution of the ceroid pigments. It should be emphasized that none of these changes was present in control rats treated with dextran only.

In the vitamin E-deficient rat, renal autolysis is accompanied by an increase in tissue non-protein nitrogen[2]. This observation could not be repeated in the iron-loaded rats, where no significantly greater increase was observed than that obtained for normal rat kidneys under the same conditions; nor did the iron-loaded rat kidneys have a higher Q_{O_2}. Despite careful and repeated examination, no evidence has been found of the existence of some of the most important characteristics of vitamin E deficiency in the rat: muscles, nervous and adipose tissues, as well as incisor teeth were all normal; the dialuric acid hæmolysis test was negative and no excessive creatinuria, phosphaturia or amino-aciduria could be detected. The absence of these manifestations of vitamin E deficiency suggests that, if such a state of deprivation is present in the iron-loaded rats, it is localized in susceptible tissues.

Tappel[6] has given quantitative expression to the catalytic function of hæmoglobin, hæmin and cytochrome *c* in copolymer formation from unsaturated fats and proteins. We have produced a similar
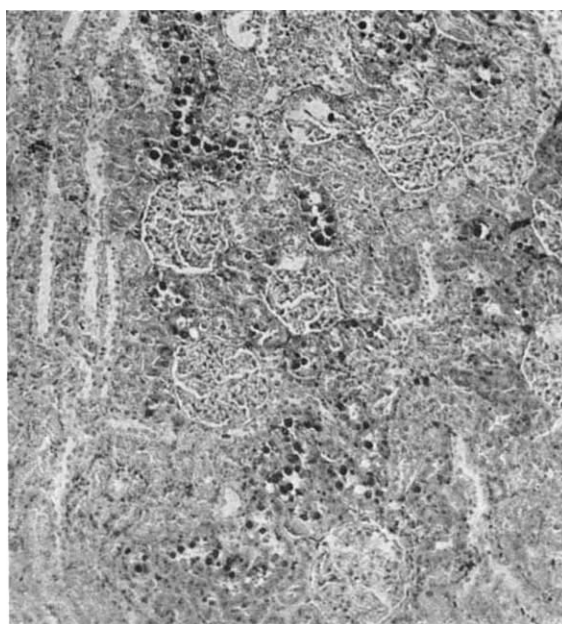

Fig. 1

ceroid-like polymer *in vitro* by using ferritin. In many of its characteristics it resembles the ceroid present in the iron-loaded rats, and differs distinctly from the ceroid which can be made *in vitro* by the catalytic action of hæmoglobin. It would appear likely that high concentrations of intracellular iron, either as ferritin or hæmosiderin, are capable of exercising hitherto unsuspected effects. These may perhaps provide an explanation for some of the pathological concomitants of Bantu siderosis.

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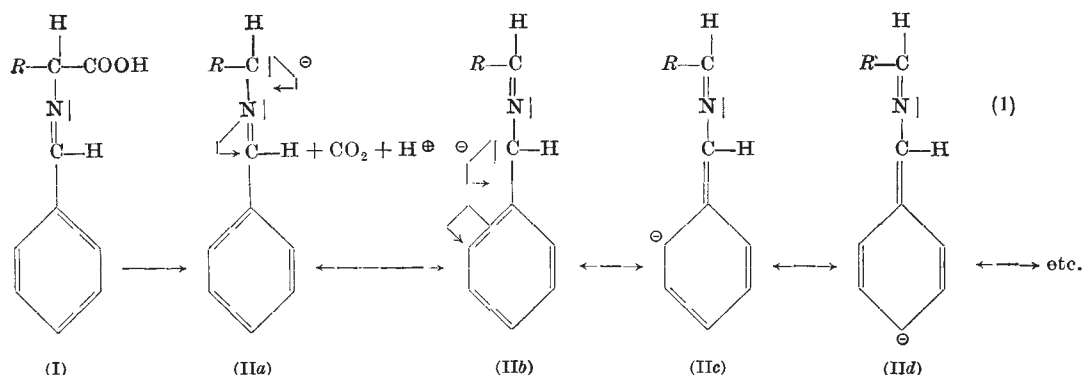[3] Moore, T., Sharman, I. M., and Ward, R. J., *Biochem. J.*, **64**, 13P (1956).
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[6] Tappel, A. L., *Arch. Biochem. Biophys.*, **54**, 266 (1955).

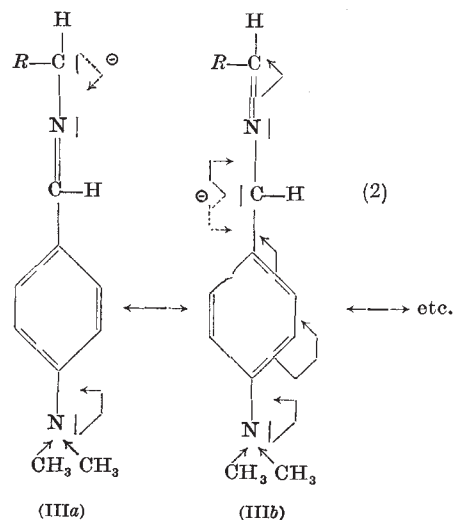## Catalytic Decarboxylation of α-Amino-Acids

NON-enzymatic decarboxylation of α-amino-acids was tried many years ago by heating them above 200° C., often dissolved or dispersed in an inert solvent too. As the reactions are always exothermic, heating is only required to reach the rather high energies of activation. The way in which Nature lowers these energies by enzymatic reactions has been frequently discussed. The formation of a Schiff's base between an α-amino-acid and pyridoxalphosphate as the proved prosthetic group of most of the decarboxylases is postulated by many authors, and the easiness of their decarboxylation may be understood with the help of the electronic theory of valence.

(1)

(I)   (IIa)   (IIb)   (IIc)   (IId)

Also in non-enzymatic decarboxylation of α-amino-acids aromatic aldehydes can act as catalysts. In 1886, Curtius and Lederer[1] obtained decarboxylation by heating a mixture of glycine and benzaldehyde up to 130° C. But the end-product of this reaction was not methylamine but benzylamine, which could not be understood by the authors.

I tried to modify the aromatic aldehyde component in several systematic experiments and found that in the o- or p-position to the aldehyde group there must be a group with free electrons significant enough to reduce fully the tendency of transamination in the Schiff's base.

An example is shown in the paper electropherogram given in Fig. 1. Using a mixture of valine and benzaldehyde the relation between formed benzyl-amine and isobutylamine was about 2 : 1 ; in the case of anisaldehyde it was about 1 : 1 (p-oxybenzylamine-methyl ether : isobutylamine) and finally, using p-di-methylaminobenzaldehyde, isobutylamine was the single product isolated after a method similar to that suggested by Curtius and Lederer[1]. The temperatures of decarboxylation increased for each amino-acid using p-dimethylaminobenzaldehyde instead of benz-

(2)

(IIIa)   (IIIb)

aldehyde as the catalytic aldehyde, but they never reached 200° C. (average value, 150° C.).

The yields for the formation of amines from most of the natural amino-acids are between 25 and 70 per cent of theory. But by this method it was not possible to get the corresponding amines of cystine, cysteine and tryptophan.

The mechanism of splitting the carbon dioxide from the Schiff's base and the significant reduction of the tendency of transamination using p-dimethyl-aminobenzaldehyde as aldehyde component may be understood from the accompanying formulæ.

In (1) the mesomeric states (IIb), (IIc), (IId), etc., are more probable than state (IIa). By the influence of the free electrons in the dimethylamino-group of p-dimethylaminobenzaldehyde the analogous states (IIIb), etc., are suppressed (see ref. 2). Here state (IIIa) is more probable. This demonstrates the signifi-cantly lowered tendency towards transamination in this reaction.

Detailed results on this reaction will be published elsewhere.

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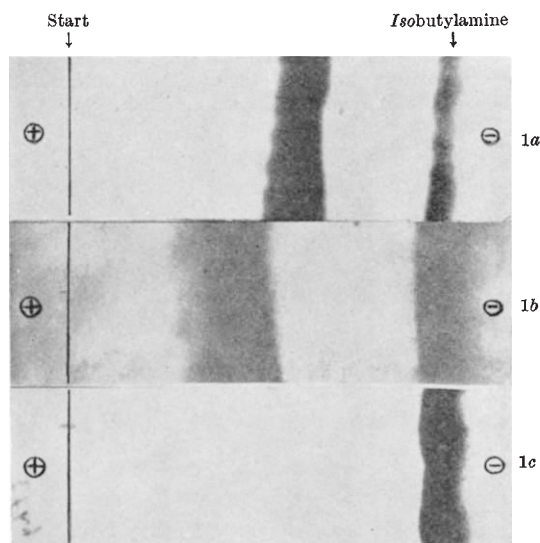[2] Wieland, T., et al., Angew. Chem., 67, 257 (1955).