

Progress Report

NUTRITIONAL AND BIOCHEMICAL EFFECTS OF RADIATION

By

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## ABSTRACT

The experiments involving the feeding of irradiated butterfat are being carried out as outlined in the last progress report.

Preliminary studies of the radiation-induced oxidation of N'-n-propyl-dihydro nicotinamide have been carried out. The rate of oxidation is similar to that of ascorbic acid. However, the dihydro compound is oxidized by hydrogen peroxide, and its rate of oxidation is concentration dependent. No evidence for the formation of the 2 or 6 pyridone derivatives has been obtained. Measurements of the stoichiometry of the reaction are being carried out.

## PROGRESS

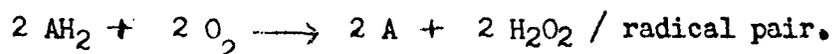
### I - Feeding Experiments:

This experiment was outlined in the last report. To date, only 14 litters have been born to the three groups of animals, and no data are reported here.

### II - Radiation-induced oxidation of N'-n-propyl-dihydro-nicotinamide:

#### Introduction

Barr and King have recently completed a study of the irradiation-induced oxidation of ascorbic acid (submitted for publication in the J. Am. Chem. Soc.). The experimental approach involved precise determinations of the rate of oxidation of ascorbic acid and that of ferrous ion, as well as polarographic determinations of the oxygen consumption in each case. The stoichiometry of the reaction using initial rate data was such that the following reaction took place:



A reaction mechanism similar to that for ferrous ion oxidation involving hydroxyl and HO<sub>2</sub> radicals was deduced. Clearly no chain utilization of oxygen occurred. It has been our purpose to extend this type of study to other compounds that are quite labile to oxidation, and of obvious importance in biological reactions.

The compound currently under study is N'-n-propyl-dihydro nicotinamide, an analogue of diphosphopyridine nucleotide (DPN). Karrer (1) demonstrated in 1936 that the oxidation rate of the reduced form of DPN was the same as that of a series of model compounds. More recently, Colowick (2)

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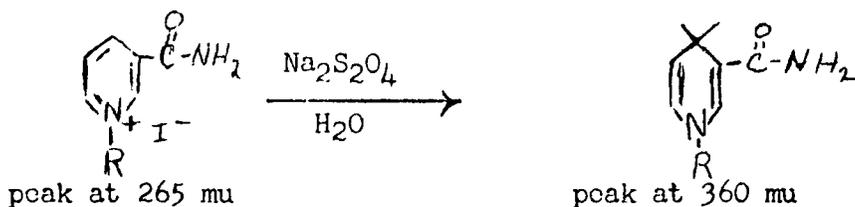
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has shown that the reversible oxidation-reduction in the pyridine ring of nicotinamide occurs in the 4 position, while oxidation leads to the 2 and 6 pyridones. Fortunately, these and related compounds have typical absorption spectra, and the analytical methods used are spectrophotometric. To date, the observations indicate that in the early stages of irradiation-induced oxidation in 0.1 N sodium hydroxide, no compounds corresponding to the 2 or 6 pyridones occur, the aerobic oxidation rate is concentration dependent, and the compound is oxidized by hydrogen peroxide. It appears then that the oxidation of the dihydro-nicotinamide derivative follows a course different from that of ascorbic acid.

### Experimental

Three compounds have been synthesized, essentially by the method of Karrer (3). N'-methyl-nicotinamide iodide, N'-ethyl-nicotinamide iodide, and N'-n-propyl-nicotinamide iodide. Reduction of the first two leads to products difficultly purified. Therefore the N'-n-propyl derivative has been used in this work. Reduction with  $\text{Na}_2\text{S}_2\text{O}_4$  yields crystalline N'-n-propyl-dihydro-nicotinamide, m.p.  $495-96^\circ\text{C}$  (uncorr.):



N'-n-propyl-dihydro-nicotinamide is unstable at acid pH's. Below pH 5, the 360 mu peak disappears rapidly, with a rise at 295 mu which then disappears also. Since stability improves with increasing pH, the studies are being carried out in 0.1 N sodium hydroxide. Addition of hydrogen peroxide to a solution of the dihydro compound brings about a disappearance of the 360 mu peak and the appearance of a 265 mu peak. It appears then that the compound reacts spontaneously with hydrogen peroxide.

Irradiation studies are being carried out in the 1 KC  $\text{Co}^{60}$  unit in pre-irradiated, sealed pyrex tubes, using the ferrous-ferric system as the dosimeter. Since the critical experiments have not been carried out, no rate data are included in this report.

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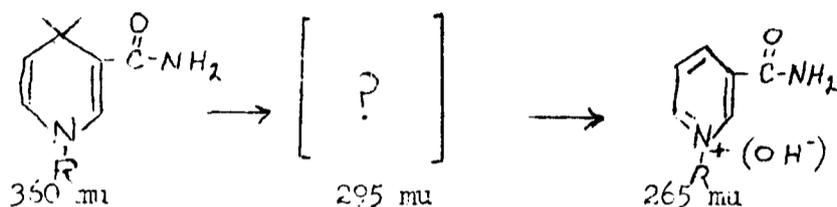
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The absorption spectra of the irradiated samples show a decrease at 360 mu, and increases at 295 mu and 265 mu, with the 295 peak later diminishing. At this point, we are concentrating on the rate of disappearance of the 360 peak, that is, the disappearance of the dihydro compound. It is hoped that the data for the other peaks can be quantitized so that a complete balance may be obtained. No evidence for further oxidation to the pyridones in the irradiated samples has been obtained. (The 6 pyridone has a peak at 260 mu and the 2 pyridone at 320 mu.)

With the data now in hand, the oxidation apparently follows this general course:



Before any mechanism can be proposed for the oxidation, it will be necessary to obtain the oxygen consumption data, the data for ferrous ion oxidation, a further check on the concentration dependence of the rate, as well as more clearly defining the products of the oxidation. These experiments are in progress.

#### REFERENCES

- (1) P. Karrer, G. Schwarzenbach, F. Benz, and U. Solmessen, *Helv. Chim. Acta* 19, 811 (1936).
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- (3) P. Karrer, and F. Blumer, *Helv. Chim. Acta* 30, 1157 (1947).

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