Title

PRODUCTION OF PYRAZINE DERIVATIVES IN THE RADIOLYSIS OF AQUEOUS SOLUTIONS OF THE CYCLIC DIPEPTIDES

Authors

Kland-English, Mathilde
Garrison, Warren M.

Publication Date

1960-11-01

UCRL-9490

UNIVERSITY OF
CALIFORNIA

Ernest O. Lawrence
Radiation
Laboratory

BERKELEY, CALIFORNIA

DISCLAIMER

UCRL-9490

UNIVERSITY OF CALIFORNIA

Lawrence Radiation Laboratory
Berkeley, California

Contract No. W-7405-eng-48

PRODUCTION OF PYRAZINE DERIVATIVES IN THE RADIOLYSIS OF AQUEOUS SOLUTIONS OF THE CYCLIC DIPEPTIDES

Mathilde Kland-English and Warren M. Garrison

November 1960

UCRL-9490
mabel

PRODUCTION OF PYRAZINE DERIVATIVES IN THE RADIOLYSIS OF AQUEOUS SOLUTIONS OF THE CYCLIC DIPEPTIDES

By

Mathilde Kland-English and Warren M. Garrison

Crocker Laboratory, Lawrence Radiation Laboratory, University of California
Berkeley, California

Radiation-induced reactions in aqueous solutions of amino acids, peptides, and related compounds have been treated in a number of reports from this laboratory.[1] In connection with these studies, we have had occasion to examine the effects of γ-irradiation on the ultraviolet absorption spectra of solutions of various simple peptides. The measurements reveal that solutions of the cyclic dipeptides under specific conditions exhibit pronounced and characteristic postirradiation changes. If, for example, an oxygen-free solution of alanine anhydride is irradiated and examined spectrophotometrically, the differential spectrum (read against unirradiated solution) shows negligible absorption above 2600 Å as long as the solution is not exposed to the atmosphere. However, if oxygen is introduced, an absorption maximum in the longer wave length region slowly appears. This postirradiation change is accelerated by addition of either acid or base. In neutral and basic solution the absorption maximum is at about 320 mμ; in acid solution the maximum shifts to 340 mμ. This shift is reversible, and the evidence is that the final yield of the absorbing species is essentially independent of the pH of the solution during the postirradiation oxidation. Solutions of glycine anhydride exhibit quite similar properties except that the wave length of maximum absorption (320 mμ) is independent of pH. It is also to be noted that these postirradiation changes are not observed if oxygen is present during irradiation.

We believe the phenomenon involves the radiation-induced reduction (and subsequent dehydration) of the diketopiperazine molecule (I) to the corresponding

1:2-dihydropyrazine derivative (II) which is of a class of compounds known[2] to be readily oxidized (i.e., in air) to the corresponding pyrazine structure (III)

Isolation of 2-hydroxy-3:6-dimethylpyrazine (III) from an irradiated solution of alanine anhydride (Nutritional Biochemicals Corporation, Lot 2104, recrystallized 3X from water) has been effected. The irradiated solution was lyophilized, and an appropriate aliquot of a methanolic solution of the residue was transferred to a filter-paper strip, and then chromatographed in a butanol-ammonia solvent system.[3] At low radiation dosages a single fluorescent compound ($R_f \sim 0.7$) was observed. This was eluted and compared spectrophotometrically with authentic material prepared according to the method of Baxter and Spring.[4] Figure 1 shows a normalized plot of the data. Co-chromatographic studies of the authentic material and the isolated irradiation product fully support the identification. The initial yield of 2-hydroxy-3:6-dimethylpyrazine in 0.1 *M* alanine anhydride corresponds to a G-value of ~ 0.4 (Co^{60} γ-rays; 7×10^{19} ev/ml).

This work was performed under the auspices of the U. S. Atomic Energy Commission.

REFERENCES

[1] A review of earlier work has been given. Garrison, W. M., Mechanisms of Radiation-Chemical Reaction in Biochemical Systems, Lawrence Radiation Laboratory Report, UCRL-9218, September 1960

[2] Rodd, E. H., Chemistry of Carbon Compounds, Elsevier Publishing Co., 1959, Vol. IVB, p. 1333

[3] Cavallini, D., Frontali, N., and Toschi, D., Nature 163, 568 (1949).

[4] Baxter, R. A., and Spring, F. S., J. Chem. Soc., 1179 (1947).

FIGURE LEGENDS

Figure 1. Absorption spectra of authentic 2-hydroxy-3:6-dimethylpyrazine [-O-] and of product isolated from irradiated solutions of alanine anhydride [-(i)-]. — MU 22047

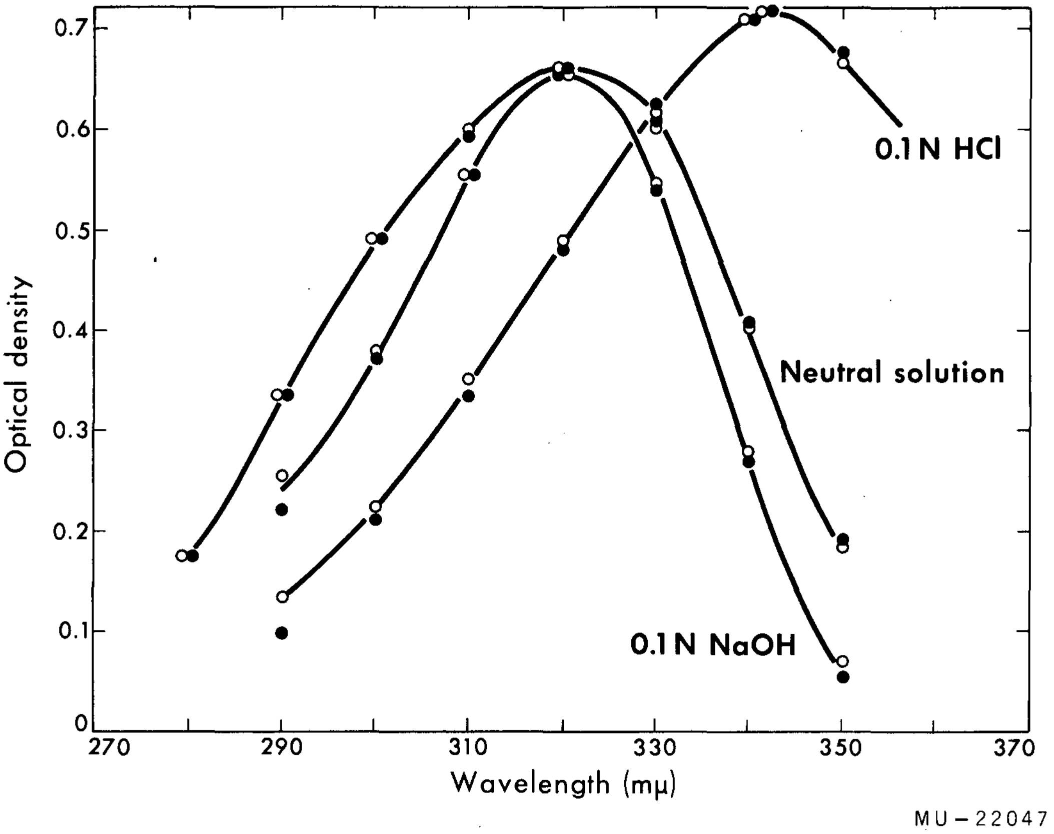
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Optical density
270
290
310
330
350
370
Wavelength (mμ)
0.1 N HCl
Neutral solution
0.1 N NaOH
MU-22047

Fig. 1