Photodecarboxylation and Photohydration of Substituted Pyrimidines

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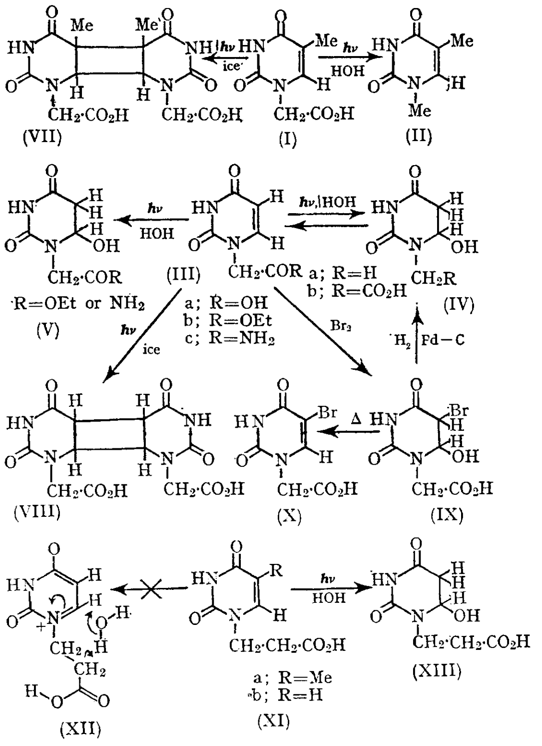
ULTRAVIOLET irradiation of thymine-1-acetic acid (I) in aqueous solution resulted in quantitative decarboxylation, forming 1-methylthymine (II), while uracil-1-acetic acid (IIIa) gave 5,6-dihydro-6-hydroxy-1-methyluracil (IVa) through decarboxylation and hydration. It is known that thymine derivatives form photohydration products but they are too unstable for isolation.[1] Thus, it is of interest to investigate whether processes of hydration and decarboxylation are inter-related.

When (I) and (IIIa) were irradiated as dry, solid films,[2] no detectable change was observed and the original compounds were recovered. These results suggest that the absorption of photic energy alone was not responsible for decarboxylation. Furthermore, the lactone formation, which may occur in the solid state, is unlikely in these photoreactions. The latter aspect was further shown by quantitative isolation of the corresponding photohydration products (V) from ethyl uracil-1-acetate (IIIb) and uracil-1-acetamide (IIIc) irradiated in aqueous solutions. In no instance was the formation of lactone or azalactone detected. Irradiation of (I) and (IIIa) in frozen aqueous solutions[3] resulted in the formation of cyclobutyl dimer [(VII) and (VIII)] as the major product with no decarboxylation. Thus, it is unlikely that photochemical saturation of the 5,6-double bond or the absorption of photic energy after such a process caused decarboxylation.



Ground-state decarboxylation after saturation of the 5,6-double bond by the formation of the bromohydrin (IX)[4] is unlikely since, on heating, (IX) gave 5-bromouracil-1-acetic acid (X) without decarboxylation. Hydrogenolysis of (IX)[5] resulted in the formation of an unstable water addition-product (IVb) which was isolated as (IIIa). Therefore, decarboxylation does not depend on the presence of the 6-OH group in the saturated molecules. In addition, thermal decarboxylation of (I) and (IIIa) occurs only at temperatures >280°. When (IIIa) was irradiated in aqueous acetonitrile, the decarboxylation, or the amount of (IVa) formed, was found to be directly related to the percentage of reaction proceeding *via* hydration.

The above indicate that decarboxylation and hydration processes are interdependent. They must occur either simultaneously or decarboxylation must occur immediately after hydration. If decarboxylation should precede the hydration step, 1-methyluracil should be the intermediate for (IIIa) and the rates of hydration of 1-methyluracil and (IIIa) should be the same. However, the hydration rate of (IIIa) was shown to be faster than that of 1-methyluracil,[6] suggesting that decarboxylation did not occur before hydration.

Any mechanism that assumes that a certain electronic configuration favours the stabilization of a carbanion or a free-radical intermediate for decarboxylation would require the decarboxylation to precede the hydration process, which is inconsistent with the observations. Likewise, several conceivable "concerted" processes (XII) would suggest that thymine-1-propionic acid (XIa) and uracil-1-propionic acid (XIb) should decarboxylate in a manner similar to (I) and (IIIa). However, (XIa) was isolated without change after irradiation, and (XIb) was converted into 5,6-dihydro-6-hydroxyuracil-1-propionic acid (XIII). It is interesting to note that with an additional CH_2 group in (XI) decarboxylation no longer occurred.

For both the decarboxylation and hydration processes to occur, the intermediate species must possess energy of *ca.* 40 kcal/mole.[7] The possibility of reaction occurring from upper vibrational levels[8] may be favoured by the large "energy drop" between this and the lowest lying singlet state,[9] the energy of which is about 90 kcal./mole.[10]

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[1] S. Y. Wang, *Nature*, 1959, **184**, 59.
[2] S. Y. Wang, *Nature*, 1963, **200**, 879.
[3] S. Y. Wang, *Nature*, 1961, **190**, 690; *Fed. Proc.*, 1965, **24**, S-71.
[4] S. Y. Wang, *J. Org. Chem.*, 1959, **24**, 11.
[5] S. Y. Wang, *J. Amer. Chem., Soc.*, 1959, **80**, 6196.
[6] S. Y. Wang and J. C. Nnadi, preceding Communication.
[7] The energy of activation for dehydration of these hydrates was found to be *ca.* 20 kcal./mole [J. C. Nnadi, Ph.D. Thesis (1968)], and that for decarboxylation is also in this range (B. R. Brown, *Quart. Rev.*, 1951, **5**, 131).
[8] J. C. Nnadi and S. Y. Wang, submitted for publication.
[9] N. J. Turro, "Molecular Photochemistry," W. A. Benjamin, New York: 1965, p. 186.
[10] From luminescence data, M. Grierson, J. Eisinger, and R. G. Shulman, *J. Chem. Phys.*, 1967, **47**, 4077, 90 kcal./mole may be obtained as energy of the lowest lying S_1 state of derivatives of uracil. These results also show that internal conversion processes are important for both S_1 and T_1 states of pyrimidines.