Formation of Carbonium Ions from Dihydropyrimidyl Radicals in the γ-Radiolysis of Aqueous Solutions of Dihydropyrimidines

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Summary Dihydropyrimidyl radicals, formed in the γ-radiolysis of aqueous solutions of dihydropyrimidines, react with each other, or with cupric ions, by a charge-transfer mechanism; chemical products are accounted for by reactions of the carbonium ions thus produced.

In the γ-radiolysis of aqueous solutions of dihydropyrimidines ($pyrH_2$) it has been found that oxidation at the C(5)–C(6) bonds leads to the production of the parent pyrimidines.[1] The immediate precursors of the latter must be the dihydropyrimidine radicals, (pyrH·), formed from reaction with OH radicals and H atoms by the process:

$$pyrH_2 + OH\ (H) \longrightarrow pyrH\cdot + H_2O\ (H_2) \qquad (1)$$

According to conventional free-radical chemistry the pyrH· radicals may then either dimerise or dismutate, and it is by the latter process that pyrimidine (pyr) is presumed to be formed, [equatrial (2)].

$$2\text{pyrH}\cdot \longrightarrow \text{pyr} + \text{pyrH}_2 \qquad (2)$$

However, evidence is presented here indicating that the interaction between pyrH· radicals is one of charge transfer, the nature of the products being interpreted in terms of the intermediate production of carbonium ions.

Solutions of the dihydropyrimidines, saturated with N_2O to remove solvated electrons ($N_2O + e^-_{aq} \rightarrow N_2 + OH^- + OH$), were irradiated with ^{60}Co γ-rays, and the yields of pyr determined. Both dihydrouracil and dihydrothymine were investigated, but, since the results and conclusions were similar, the Figure presents only the data from dihydrouracil. In neutral solution, $G(\text{pyrH}\cdot) = G_{OH} + G_H + Ge^-_{aq} \simeq 6$; it is therefore clear from the observed uracil yield under these conditions ($G = 1{\cdot}6$) that only about 50% of the pyrH· radicals undergo dismutation. The dihydropyrimidine–N_2O system can be simplified somewhat if an oxidising agent is present which can convert all of the pyrH· radicals to pyr; cupric ion was selected for this purpose, the overall oxidation process being represented by the equation:

$$\text{pyrH}\cdot + Cu^{2+} \longrightarrow \text{pyr} + Cu^+ + H^+ \qquad (3)$$

The data from irradiated neutral dihydrouracil–N_2O–Cu^{2+} solutions (see Figure) can, in fact, be adequately interpreted in terms of the overall reactions (1) and (3), since, taking into consideration the known rate constants of reactions of the primary species with dihydrouracil, N_2O and Cu^{2+} ions, it can be shown that $G(\text{pyrH}\cdot)$ from reaction (1) should be $\simeq 5$.

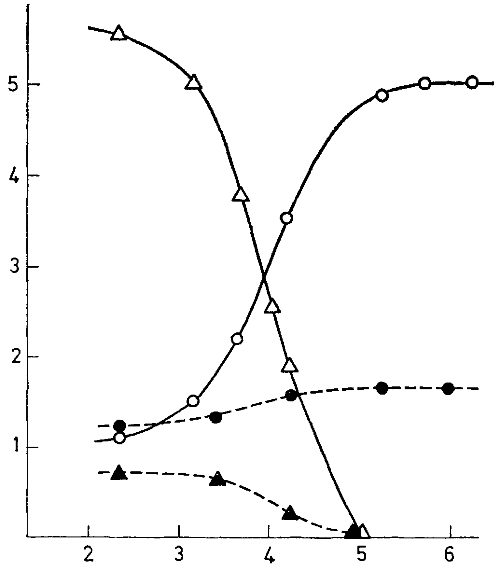

FIGURE. *pH-Dependence of the yields* (G) *of uracil and hydrohydroxyuracil in the γ-radiolysis of aqueous* N_2O*-saturated solutions of dihydrouracil.* 10^{-3} M *Dihydrouracil:* ---●--- *uracil;* ---▲--- *hydrohydroxyuracil.* 3×10^{-3} M *Dihydrouracil* + 10^{-3} M $CuSO_4$*:* ——○—— *uracil;* ——△—— *hydrohydroxyuracil.* Abs: pH. Ord: G.

It has been found, however, that lowering of the pH of the irradiated solutions leads to a drop in G(pyr)—quite markedly when Cu^{2+} is present—so that the above simple scheme cannot hold under these conditions. Although in acid solutions protons will compete with N_2O for the solvated electrons, ($e^-_{aq} + H_3O^+ \rightarrow H + H_2O$), this should not alter $G(\text{pyrH}\cdot)$. The effect of pH must therefore be associated with the radical processes (2) and (3), and this has been traced to a change in the reaction mechanism whereby, as the pH is lowered, pyrimidine hydrohydroxy compounds, [pyrH(OH)], rather than pyr, are progressively formed. The yields of hydrohydroxyuracil as a function of pH are given in the Figure. The observation of two products from both reactions (2) and (3) is consistent with the intermediate formation and reactions of a carbonium ion, pyrH^+, paralleling the well-known simultaneous solvolytic substitution and elimination reactions of alkyl and aryl carbonium ions.[2] Thus, from pyrH^+, solvolytic substitution (S_N1) or elimination ($E1$) processes will lead to pyrH(OH) and pyr, respectively, *viz*:

$$\text{pyrH}^+ \begin{array}{l} \xrightarrow{H_2O(S_N1)} \text{pyrH(OH)} + H_3O^+ \\ \xrightarrow[H_2O(E1)]{} \text{pyr} + H_3O^+ \end{array} \qquad (4)$$

It follows, therefore, that reactions (2) and (3) proceed by electron transfer, giving presumably, the ion-pairs (pyrH^+, Cu^+) and (pyrH^+, pyrH^-); although clearly anticipated for the reaction with Cu^{2+} ions this was not for the radical–radical reaction where hydrogen atom transfer seemed a likely alternative. The effect of pH in the radiolysis is essentially to change the $S_N1:E1$ ratio of reaction (4), and the precise mechanistic details of this are currently under investigation. The intermediate formation of carbonium ions from pyrimidine radicals accounts for the observation of both glycols and isobarbituric acid derivatives in the radiolysis of aqueous solutions of uracil and of cytosine containing Cu^{2+} ions.[3]

These findings have some significance in the wider field of organic radical interactions, where the factors controlling dimerisation and dismutation are relatively little understood; charge transfer in the transition state, with the alternatives of ion-pair recombination (dimerisation) or solvolysis (dismutation), clearly has an intimate bearing upon this.

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[1] W. Snipes and W. Bernhard, *Radiation Res.*, 1968, **33**, 162.
[2] *cf.* A. Liberles, 'Theoretical Organic Chemistry,' MacMillan, New York, 1968.
[3] J. Holian and W. M. Garrison, *Nature*, 1966, **212**, 394.