INVESTIGATION OF HYDROGEN EXCHANGE IN URACIL
AND ITS DERIVATIVES LABELLED WITH TRITIUM

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Acid-catalyzed hydrogen exchange of uracil derivatives labelled with tritium at position 6 and substituted at position 5 has been investigated. The mechanism of the reaction is discussed and the exchange curves are shown.

Урцил derivatives are compounds of considerable interest in the field of molecular biology because they are components of nucleic acids. Labelled with tritium, they are important radiotracers for studying physiological effects and investigating problems of structure. Information on the stability of the carbon-tritium bond under the experimental conditions is important for estimating the practical use of such radioactive tracers.

We have studied the acid-catalyzed hydrogen exchange at position 6 of uracil (2,4-dioxotetrahydropyrimidine) and of some derivatives substituted at position 5 (R = OH, CH₃, F, Br, NO₂). These compounds have been tritiated at position 6 to follow the exchange of tritium between uracil derivatives and solvent /1-3/. Aromatic hydrogen-tritium exchange has low steric requirements and can be measured with high accuracy even at positions of low reactivity.

The results indicate that a tritium atom at position 6 of uracil is extraordinarily stable. This stability may be influenced by substituents at position 5. Therefore, chemical reactions with these tritium-labelled uracil derivatives occur without considerable loss of radioactivity.
Acid-catalyzed tritium-hydrogen exchange of these specifically labelled uracil derivatives in 50% trifluoroacetic acid at a temperature of 70±1 °C was investigated for 1000 h. We postulate the following mechanism:

\[
\begin{align*}
\text{R} & \quad \text{N} \quad \text{H} \\
\text{N} & \quad \text{CF}_3\text{COOH} \\
\text{R} & \quad \text{NH} \\
\text{C} & \quad \text{CF}_3\text{COOH} \\
\text{H} & \quad \text{T} \quad \text{O} \\
\text{R} & \quad \text{NT} \\
\text{H} & \quad \text{T} \quad \text{O} \\
\text{R} & \quad \text{NT} \quad \text{CF}_3\text{COOH}
\end{align*}
\]

Fig. 1. Mechanism of the exchange reaction

It is a complicated isotope exchange reaction, because there are hydrogen atoms of different stability in the uracil derivatives. In the presence of excess trifluoroacetic acid the reaction follows first-order kinetics and a simple isotope exchange reaction occurs. We assume an associative mechanism corresponding to general acid catalysis and the formation of a cyclic intermediate of the following structure:

\[
\begin{align*}
\delta^- & \quad \delta^+ \\
\delta^- & \quad \delta^- \\
\text{C} & \quad \text{CF}_3
\end{align*}
\]

The uracil derivatives had a specific radioactivity of $3.7 \times 10^9$ Bq/mmol and a chemical and radiochemical purity of > 98%. The amount of tritium that has exchanged was measured in trifluoroacetic acid by the liquid-scintillation counting method. The following figure shows the exchange curves of 5-nitouracil,