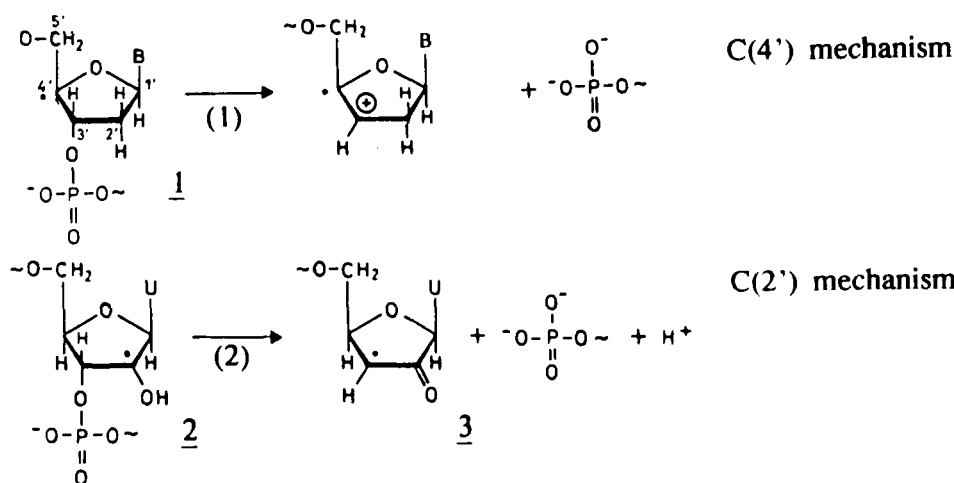


ESR STUDIES ON THE MECHANISM OF ·OH-INDUCED STRAND BREAKAGE OF POLY(U)

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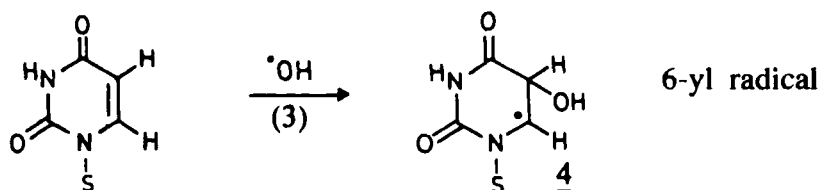
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The elementary step leading to strand break (sb) formation of DNA^{1,2} is known as C(4') mechanism [reaction (1)]. Upon reaction of OH radicals with ribose-poly-nucleotides heterolytic decay of the C(2') radical **2** may also contribute to sb formation³ [reaction (2); C(2') mechanism].

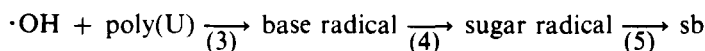


SCHEME 1

It is known that in the primary step OH radicals react mainly with the uracil moiety of poly(U) whereas H abstraction from the sugar is a side reaction.⁴



Therefore, in order to explain the high yields of sb formation of poly(U) [$G_{sb} = 0.24 \mu\text{mol J}^{-1}$] it has to be assumed that the radical site is transferred from the base to the sugar moieties within the macromolecule⁵ [reaction (4)].



Reaction of photolytically generated OH radicals with poly(U) in neutral aqueous solutions resulted in the esr spectrum of the 6-yl base radical, **4**, whereas at $\text{pH} \leq 4$ the spectrum of the C(2')-oxo-3'-yl sugar radical **3** was detected.⁶ The assignment was confirmed by model reactions with $\text{SO}_4^{\cdot-}$ as the radical-inducing agent.⁷ Time-resolved esr measurements showed that the rate of decay of the 6-yl base radical is very close to the rate of sb formation (see Table 1).⁶

TABLE I
Rates of decay of the 6-yl radical of poly(U), $k_{\text{esr}}^{\text{a}}$, and rates of $\cdot\text{OH}$ -induced sb formation of poly(U), k_{sb}^{b}

| Temp [°C] | $k_{\text{esr}}^{\text{a}} [\text{s}^{-1}]$ | $k_{\text{sb}}^{\text{b}} [\text{s}^{-1}]$ | |
|-----------|---|--|--------|
| | | pH 6.8 | pH 8.0 |
| 4 | 0.19 | 0.19 | 0.13 |
| 18 | 1.2 | 0.51 | 0.34 |
| 28 | 5.0 | 1.62 | 0.83 |

a) at pH 7.5; b) pulse conductivity measurements³

These results prove that i) the C(2') mechanism contributes to sb formation of poly(U) and ii) the decay of the 6-yl radical is the rate-determining step in the reaction sequence leading to strand breakage.

The pH dependence of the esr spectra and of the rate of sb formation is explained by proton-induced rearrangement of the 6-yl base radical **4** into the more reactive isomeric 5-yl radical, possibly via the base radical cation, and subsequent rapid H abstraction from neighbouring sugar moieties by either the radical cation and/or the 5-yl radical.

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