Radiation Chemistry of DNA-Model Compounds, VII*
On the Formation of 5-Deoxy-D-erythro-pentos-4-ulose and the Identification of Twelve Further Products from γ-Irradiated Aqueous Solutions of Ribose-5-phosphate

LOTHAR STELTER, CLEMENS VON SONNTAG, and DIETRICH SCHULTE-FROHLINDE

Institut für Strahlenchemie im Max-Planck-Institut für Kohlenforschung, Mülheim a.d. Ruhr

(Z. Naturforsch. **30b**, 656–657 [1975]; received February 19, 1975)

γ-Radiolysis, Ribose-5-phosphate, Carbohydrates, Radical Reactions, Radical Cations.

Different mechanisms are considered to explain the formation of 5-deoxy-D-erythro-pentos-4-ulose in the γ-radiolysis of ribose-5-phosphate in aqueous solution. On the basis of deuterium labelling experiments one mechanism involving an enol as an intermediate could be excluded.

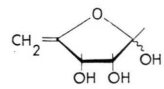
The identification of twelve further radiolysis products from ribose-5-phosphate is reported.

Radiation induced strand breaks of nucleic acids in aqueous solution may be caused by reactions of radicals which abstract a hydrogen atom from the sugar moiety of the nucleic acid. A possible reaction of the DNA radical formed is the scission of the sugar-phosphate linkage. To study the chemical steps involved in such a scission ribose-5-phosphate (**2**) has been used as a model compound. In the γ-radiolysis of deoxygenated N_2O saturated aqueous solutions of ribose-5-phosphate release of inorganic phosphate and the formation of 5-deoxy-D-erythro-pentos-4-ulose (**7**) as one of the phosphate free products has been observed by STELTER *et al.*[1] as well as by KOCHETKOV *et al.*[2]. However, quite different reaction schemes have been proposed. In reference[1] the reaction is believed to start with an attack of an OH radical (from the radiolysis of the solvent water) at C–4 of the ribose-5-phosphate (reaction(1)). In reference[2] the position of OH attack is proposed to be at C–5 of ribose-5-phosphate.

The knowledge of the correct mechanism is of importance since it has recently been shown that irradiation of deoxygenated aqueous solutions of DNA yields the analogous product 2,5-dideoxy-pentos-4-ulose[3].

Arguments for the feasibility of every step described in reference[1] have already been given[1] and will not be repeated here.

In reference[2] **1** has been postulated as an intermediate which will yield



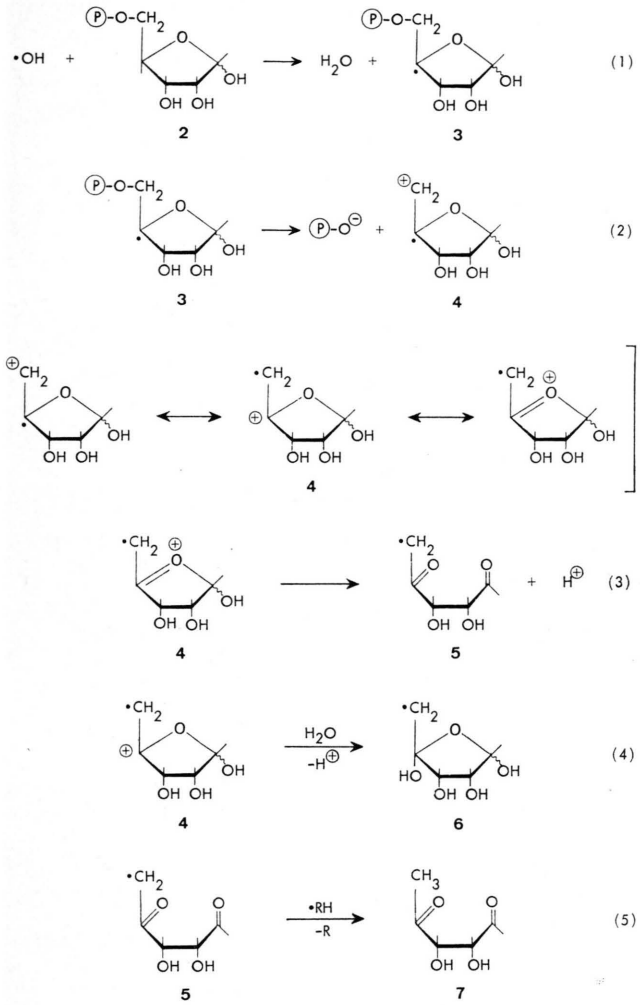
1

product **7** *via* an enol. In D_2O the protons of the hydroxyl groups of **1** are expected to be exchanged against deuterium which ultimately will be located at C–5 in the product molecule **7** if the latter is formed *via* the enol. However, on γ-irradiation of ribose-5-phosphate in 99.8% D_2O no deuterium was incorporated in **7**. This was shown by mass spectrometry. On reduction of **7** (from 10^{-2}M N_2O saturated, deoxygenated solutions of **2**, γ-irradiated in D_2O at room temperature, dose $3.5 \cdot 10^{19}$ eV/g, dose rate $2.8 \cdot 10^{17}$ eV/g · min) with $NaBH_4$ two stereoisomeric 1-deoxy pentitols were obtained which, after trimethylsilylation, were analyzed by GC–MS. The prominent fragment at *m/e* 117 contains the methyl and the adjacent CHOTMS group[1,4]. The mass spectra of the samples irradiated in H_2O and D_2O were identical and no shift to *m/e* 118 was observed in the D_2O case. This excludes an enol as an intermediate and indicates that the product **7** is not formed according to the mechanism proposed by KOCHETKOV *et al*[2].

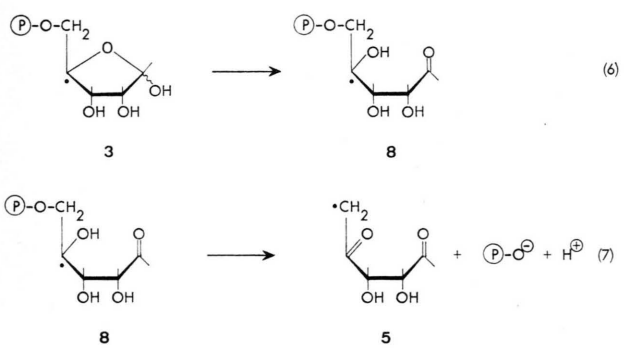
ESR[5,6] and radiation chemical kinetic and product studies[6] on the fragmentation reactions of the radicals obtained by OH attack on 2-chloro and 2-acetoxy ethyl methyl ether permitted to conclude that in these cases radical cations are formed as intermediates in the elimination of chloride and acetate. It is very likely that a similar mechanism as in the chloride and acetate is followed by the phosphates. Then the formation of **7** occurs as follows. The primary event is expected to be hydrogen atom abstraction from C–4 by an OH radical to give radical **3** (reaction (1)). Elimination of phosphate from **3** leads to the radical cation **4** (reaction (2)). Ringopening of **4** and loss of a proton may immediately lead to **5** (reaction (3)), or **4** is converted into **6** by addition of water and loss of a proton (reaction (4)). Radical **6** is the hydrated, cyclic form of radical **5**. In a disproportionation reaction with other radicals (·RH) present **5** (or **6**) gives the end product **7** (reaction (5)).

* Part VI: J. M. CAMPBELL, C. VON SONNTAG, and D. SCHULTE-FROHLINDE, Z. Naturforsch. **29b**, 750 [1974].

Requests for reprints should be sent to Priv.-Doz. Dr. C. VON SONNTAG, Institut für Strahlenchemie im Max-Planck-Institut für Kohlenforschung, *D–4330 Mülheim a.d. Ruhr*, Stiftstraße 34–36.



As a modification[1] of the mechanism proposed above reaction (1) is followed by ringopening to give radical 8 (reaction (6)) which eliminates phosphate and a proton (reaction (7)). Model studies[7,8] indicate that reaction (7) should be fast.



Therefore, we conclude that the relative rates of reaction (2) and of the ring-opening process (reaction (6)) determine whether phosphate is released *via* reaction (2) or reaction (7).

OH-attack at C–4 of ribose-5-phosphate is certainly not the only route leading to a phosphate ester cleavage in ribose-5-phosphate. This is strongly suggested by the appearance of a number of further phosphate free products in γ-irradiated N_2O saturated deoxygenated aqueous solutions of ribose-5-phosphate (10^{-2}M, room temperature, dose $3.85 \cdot 10^{18}$ eV/g, dose rate $2.8 \cdot 10^{17}$ eV/g · min). In addition to ribodialdose which has also been described by KOCHETKOV *et al.*[2] the following products have been identified:

CH_2OH–CO–CH_2OH, CH_3–CO–CHOH–CH_2OH,
CHO–CH_2–CHOH–CH_2OH, CHO–CH_2–CO–CH_2OH,
CH_2OH–CO–CHOH–CH_2OH,
CHO–CHOH–CHOH–CHO,
CHO–CH_2–CO–CH_2–CHO,
CHO–CH_2–CO–CHOH–CHO,
CHO–CH_2–CHOH–CHOH–CHO,
CH_2OH–CHOH–CHOH–CH_2–COOH,
CHO–CHOH–CH_2–CO–CHO,
CHO–CHOH–CHOH–CHOH–CHO (arabo-form)
or/and CH_2OH–CO–CHOH–CHOH–CHO.

The mechanisms of formation of these products are presently under investigation[9]. In connection with the deuterium labelling experiments, described above, it may be noted that deuterium incorporation has been observed for 3-deoxy-pentodialdos-2-ulose (CHO–CHOH–CH_2–CO–CHO). Therefore, in this case an enol is most likely to be an intermediate.

[1] L. STELTER, C. VON SONNTAG, and D. SCHULTE-FROHLINDE, Int. J. Radiat. Biol. **25,** 515 [1974].
[2] N. K. KOCHETKOV, L. I. KUDRJASHOV, M. A. CHLENOV, and L. P. GRINEVA, Carbohydrate Res. **35,** 235 [1974].
[3] M. DIZDAROGLU, C. VON SONNTAG, and D. SCHULTE-FROHLINDE, J. Amer. Chem. Soc. **97,** 2277 1975].
[4] M. DIZDAROGLU, D. HENNEBERG, and C. VON SONNTAG, Org. Mass. Spetr. **8,** 335 [1974].
[5] B. C. GILBERT, J. P. LARKIN, and R. O. C. NORMAN, J. Chem. Soc. Perkin II **1972,** 794.
[6] G. KOLTZENBURG, G. BEHRENS, D. SCHULTE-FROHLINDE, to be published.
[7] A. SAMUNI and P. NETA, J. Phys. Chem. **77,** 2425 [1973].
[8] S. STEENKEN, G. BEHRENS, and D. SCHULTE-FROHLINDE, Int. J. Radiat. Biol. **25,** 205 [1974].
[9] L. STELTER, C. VON SONNTAG, and D. SCHULTE-FROHLINDE, to be published.