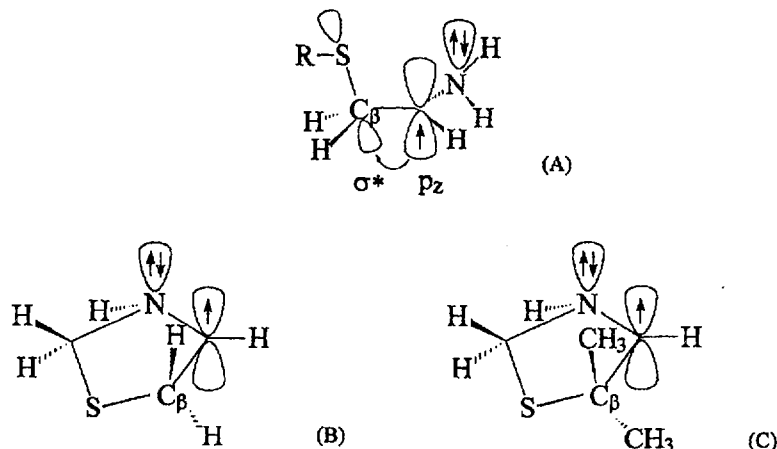


Scheme 2.

Decarboxylation of thiaproline derivatives containing the carboxylic group in the position - (2) the C_α bond undergoing cleavage) readily achieved in the flexible Cys(Me)-like systems (Scheme 3A) do



Scheme 3.

leads to the formation of α -aminoalkyl- α -alkyl-thioalkyl radicals in the position - (2). These radicals do not undergo β -cleavage (Scheme 2B).

The β -cleavage in thiaproline derivatives is less effective than in linear (open chain) amino acids due to:

- (i) the lack of driving force from the entropy increase, resulting from the formation of two entities from one,
- (ii) the transition complex for the β -cleavage process involving a triangular grouping of reactive centres (generated by interaction of the semi-occupied orbital p_z on C_α with the σ^* antibonding orbital of

not be attained when the radical centre is located within the thiaproline ring (Scheme 3B). The effective formation of the transition complex is additionally made hard by methylation in the position - (5), (Scheme 3C).

References

- [1]. Pogocki D., Bobrowski K., Asmus K.-D.: INCT Annual Report 1993, p. 21.

* Part of this work was presented at the conference "Pulse Investigation in Chemistry, Physics and Biology, PULS'97", 13-19 September 1997, Szczyrk, Poland.

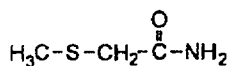


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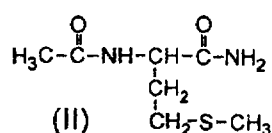
REACTIONS OF HYDROXYL RADICAL WITH THIOAMIDES

P. Wiśniowski, K. Bobrowski

Nanosecond pulse radiolysis of nitrogen saturated aqueous solutions of α -(methylthio)-acetamide (I) and N-acetylo-L-metionine amide (II) over the pH range 1-12 has been used to generate hydroxysulfuranyl radicals.



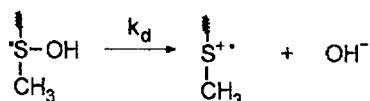
(I)



(II)

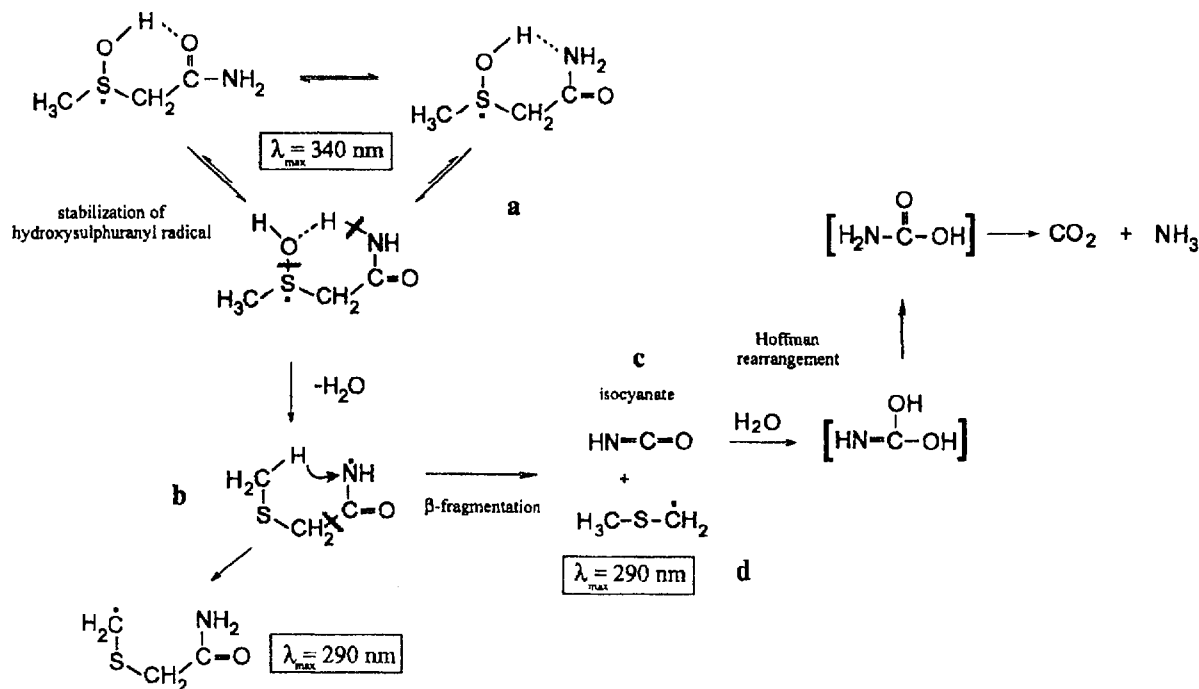
A transient absorption band with $\lambda_{\text{max}}=340$ nm (assigned to the hydroxysulfuranyl radicals) was observed immediately after the pulse which was subsequently converted to an absorption band with $\lambda_{\text{max}}=480$ nm (assigned to the S·S⁺-three-electron-bonded radical cations) and/or absorption band $\lambda_{\text{max}}=290$ nm (assigned to the α -thioalkyl radical). Monitoring the pseudo-first-order decay rate of the hydroxysulfuranyl radicals at various H⁺ and (I) and (II) concentrations, respectively, one

can extract the individual rate constant (k_d) of their spontaneous dissociation



which are one-order of magnitude lower than the k_d for dimethyl thioether. The high stability of the hydroxysulfuranyl radicals formed in thioamides is likely due to the formation of the internal hydrogen bond between the hydroxyl hydrogen and either the oxygen or the nitrogen located in the adjacent amide group.

Any discussion of the oxidation mechanism of α -MTA and AMA must take into account the following observations:



Scheme 1. $\cdot\text{OH}$ -induced oxidation of α -(methylthio)acetamide in neutral solution.

(i) for both compounds hydroxyl radicals ($\cdot\text{OH}$) act primarily with the sulfur of the thioether group forming hydroxysulfuranyl radical (Scheme 1a);
 (ii) the $\cdot\text{OH}$ -induced oxidation in α -MTA does not lead at a neutral pH to a stable sulfur-centred radical cation ($\text{S}^{+\cdot}$), indicated through the lack of formation of the intermolecularly three-electron-bonded ($\text{S}\cdot\cdot\text{S}$) $^+$ radical cations even at high concentrations of the solute ($\sim 10^{-2}$ M) (Fig.1). On the other hand, $\cdot\text{OH}$ -induced oxidation in AMA leads to the absorption bands similar as in the aliphatic thioether $(\text{CH}_3)_2\text{S}$;
 (iii) carbon dioxide is a stable product of γ -radiolysis of neutral solutions containing α -MTA and the decrease in radiation chemical yields of the intermolecularly three-electron-bonded ($\text{S}\cdot\cdot\text{S}$) $^+$ radical cations correlates with the parallel increase in radiation chemical yields of CO_2 .

The key to understanding the differences between radiation chemical yields of stable sulfur-centred radical cation ($\text{S}^{+\cdot}$) and formation of car-

bon dioxide at low and neutral pH lies in the structures of α -MTA and AMA.

In aqueous neutral solution of α -MTA the stabilised hydroxysulfuranyl radical subsequently undergoes water elimination by intramolecular hydrogen transfer via six-membered transition state leading to the formation of imine radicals (Scheme 1b). Intramolecular hydrogen transfer competes with spontaneous dissociation of hydroxysulfuranyl radical. Imine radicals are expected to undergo β -fragmentation of carbon-carbon bond leading to α -(alkyl)thioalkyl radicals 1d and isocyanate 1c. In aqueous solution isocyanates undergo well-known Hoffman rearrangement which produces ammonia and carbon dioxide as shown (Scheme 1). It rationalises the formation of carbon dioxide as a stable

product of γ -radiolysis of neutral solutions containing α -MTA.

In α -MTA specific location of the methylene group between the electron-donor sulfur and the electron-acceptor amide group facilitates hydrogen abstraction from the methylene group. The radical

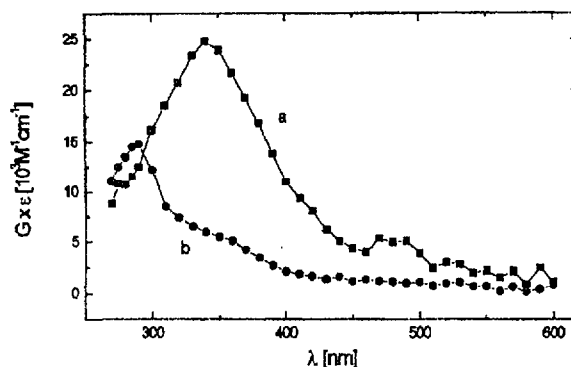
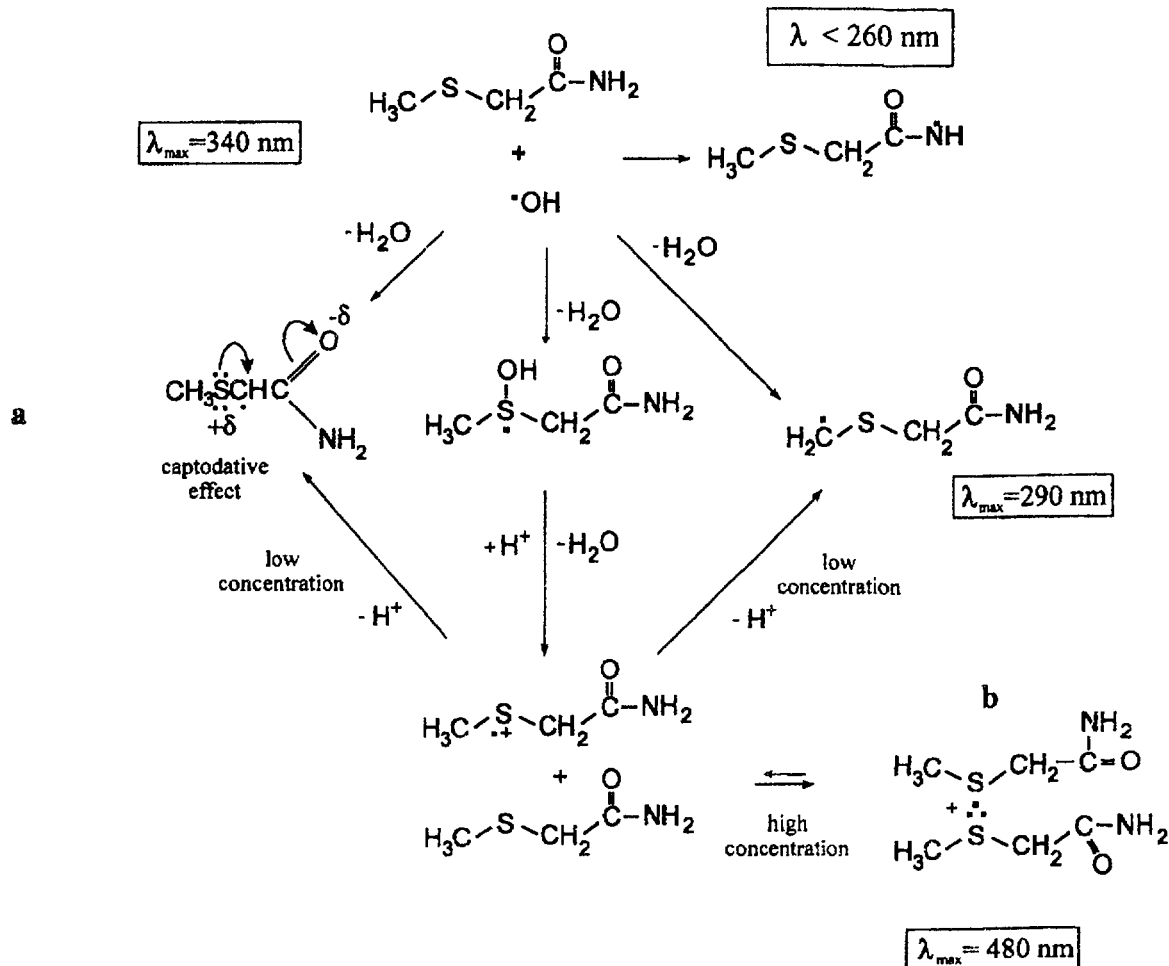


Fig.1. Transient absorption spectra observed (a) 500 ns and (b) 7 μs after pulse irradiation of an N_2O -saturated solution containing 10^{-2} M α -MTA at pH 6.45.

formed is stabilised by the captodative effect (Scheme 2a). At high concentration of α -MTA 1a subsequently converts into the dimeric radical cation ($>S \cdot S<$)⁺ (Scheme 2b) as indicated by the formation of the characteristic 480 nm absorption band.

pathways of α -MTA and AMA originates from the initial interaction of the oxidising species and the thioether group that leads to the formation of hydroxysulfuranyl radical and sulfur radical cation and the subsequent interaction of these intermediates with the neighbouring groups. The key step is



Scheme 2. $\cdot\text{OH}$ -induced oxidation of α -(methylthio)acetamide in acid solution.

In conclusion, the geometric structure of species during oxidation of organic sulfides is of great importance. The difference between the oxidation

the intramolecular hydrogen transfer in a six-membered cyclic transition state during decomposition of the hydroxysulfuranyl radical.

DIRECT EFFECT OF IONISING RADIATION ON DNA, INFLUENCE OF COPPER IONS



PL9801982

H.B. Ambroź, E. Kornacka, G. Przybytniak

The presence of additives modifies the yield of particular intermediates to a great extent. This effect for Cu(II) ions is discussed below. Copper ions exhibit the effect of a decrease of the $\cdot\text{TH}$ population in DNA, but to a minor degree than Fe(III) (Fig.1). Even addition of Cu(II) at 5 mM concentration still leads to the detection of above 7% of remaining population of the protonated thymine base (the $\cdot\text{TH}$ concentration in samples without added metal ions equals to 22%). This is presumed to be the consequence of the lower electron-scavenging ability exhibited by Cu(II) in comparison to Fe(III).

Careful analysis of the EPR spectra recorded pre- and post-irradiation at 77 K and upon annealing enables one to conclude that copper ions participate not only in primary but also in secondary processes. The Cu(II)-DNA complexes have well-defined EPR spectral parameters and almost the same signal is obtained under various conditions [1]. The parallel component of the spectrum undergoes transformation after exposure to 10 kGy (Fig.2). The additional lines marked (\downarrow) ($A_{||} = 15.2 \text{ mT}$, $g_{||} = 2.28$) for the 2-5 mM concentrations of Cu(II) have been detected in the range of 77-220 K. We