Hydroxyl Radical Adduct at Sulfur in Substituted Organic Sulfides stabilized by Internal Hydrogen Bond

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The stability of an OH radical adduct at sulfur atoms in substituted organic sulfides is greatly enhanced by the formation of an internal hydrogen bond between the hydroxyl hydrogen and an oxygen located either in an adjacent carbonyl or methoxy group; the first absolute rate constants of the reactions of such adducts with molecular oxygen are reported.

The initial step in the reaction of hydroxyl radicals with alkyl sulfides and their derivatives which carry additional functional groups (OH, CO_2H, NH_2) is the formation of an OH-adduct at the sulfur atom.[1–14] These adducts are generally very short-lived ($\tau_{\frac{1}{2}} < 1$ μs) and convert into sulfur-centred radical cations,[1,2,4,5,7–10,13] S.·.N,[3,8,12,13] S.·.O[3,5,7,9–13]-three-electron-bonded radicals, and/or α-thioalkyl radicals.[1–4,8,12–14] The nature and rates of the reactions of OH-adducts have so far not been investigated directly due to their short lifetime. Product studies indicate that they are influenced by neighbouring functional groups and their respective distance, and by the geometry of the molecule.[10,15–17] Since such hydroxyl adducts are possible intermediates in redox processes leading to sulfoxide formation,[18,19]† it is essential to provide model systems whose molecular architecture favours their stability, and thus enables investigation of their chemical reactions with other molecules, especially with oxygen. In this communication we provide evidence for stabilization of an OH-adduct at the sulfur atoms in substituted organic sulfides by the formation of an internal hydrogen bond[20,21] (*vide infra*) between the hydroxyl hydrogen and an oxygen located either in an adjacent carbonyl or methoxy group. We also report the first absolute rate constants of the reactions of the OH-adducts at the sulfur atoms with molecular oxygen.

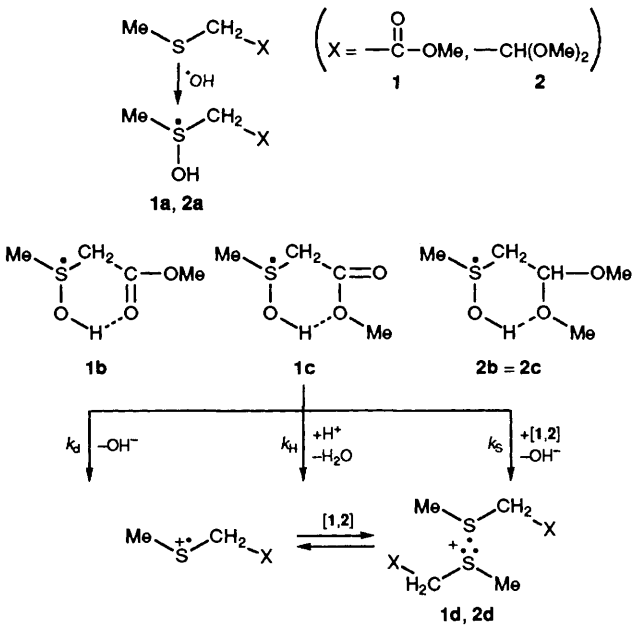
Nanosecond pulse radiolysis[22] of 10^{-2} mol dm^{-3} methylthiomethyl acetate, $MeSCH_2CO_2Me$ **1** in N_2O saturated aqueous solutions at pH 3.7 results in the formation of a transient absorption band with λ_{max} at 330 nm (see Fig. 1), [$k_{OH+1} = (6.7 \pm 0.2) \times 10^9$ dm^3 mol^{-1} s^{-1}]. On the basis of previous experimental observations[1,2,5] this absorption can unambiguously be assigned to the OH-adduct at the sulfur atom **1a**. Sterically, formation of an S.·.O-three-electron bond with either of the two ester oxygens in **1** would require an unfavourable four-membered ring structure and can thus be

† The photosensitized deactivation of several enzymes such as phosphoglucomutase and chymotrypsin has been correlated with photooxidation of methionine to the corresponding sulfoxide (C. S. Foote and J. W. Peters, *IUPAC Congr., 23rd, Spec. Lect.*, 1971, **4**, 129).

excluded. The hydroxyl adduct **1a** subsequently converts into the dimeric radical cation (> S.·.S <)$^+$ **1d** as indicated by formation of the characteristic 470 nm absorption band [see Fig. 1 and insert (*a*)]. This conversion is pseudo-first-order, dependent on the concentrations of both H^+ and **1**. This observed rate constant can be deconvoluted into three processes, namely uncatalysed *i.e.* spontaneous dissociation of **1a** (k_d), acid-catalysed elimination of the OH^- from **1a** (k_H), and displacement of the OH^- from **1a** involving a second molecule of **1** (k_s), (see Scheme 1) as shown in eqn. (1).

$$k_{exptl} = k_d + k_H[H^+] + k_s[\mathbf{1}] \quad (1)$$

Monitoring the pseudo-first-order decay rate of **1a** at various H^+ and **1** concentrations, respectively, then yields the individual rate constants k_d, k_H and k_s. The intercept of a plot of the first-order rate constant of the decay at 330 nm *vs.* H^+ concentration, at constant concentration of **1** [see Fig. 1, insert (b)] yields $k_d + k_s[\mathbf{1}] = (1.49 \pm 0.13) \times 10^5\ s^{-1}$, whereas the slope gives $k_H = (2.29 \pm 0.07) \times 10^{10}\ dm^3\ mol^{-1}\ s^{-1}$. A similar plot *vs.* concentration of [**1**] [see Fig. 1, insert (*c*)], at constant concentration of H^+, yields $k_d + k_H[H^+] = (1.23 \pm 0.01) \times 10^6\ s^{-1}$, and $k_s = (8.9 \pm 0.4) \times 10^6\ dm^3\ mol^{-1}\ s^{-1}$. Using eqn. (1) we then calculate the rate constant of the spontaneous dissociation of **1a**, $k_d = (6.5 \pm 0.5) \times 10^4\ s^{-1}$. This value ($k_d$) is in an excellent agreement with the observed first-order rate constant for the decay of **1a** ($k_{exptl} = 6.5 \times 10^4\ s^{-1}$) measured in 5×10^{-4} mol dm^{-3} of **1** in N_2O saturated solution at pH 7.7, *i.e.* under conditions where the contributions of $k_H[H^+]$ and $k_s[\mathbf{1}]$ can be neglected. The same approach is also applied to determine the rate of the spontaneous dissociation of the OH-adduct at the sulfur atom in dimethyl sulfide (Me_2S). It must be noted that the value determined $k_d = (1.6 \pm 0.2) \times 10^6\ s^{-1}$ is 25-fold higher than k_d for **1a**. The high stability of **1a** is likely due to the formation of the internal hydrogen bond (as shown in Scheme 1) between the hydroxyl hydrogen and the oxygen located either in the carbonyl group **1b** or the methoxy group **1c**. This hydrogen bonding seems to be particularly facilitated by the formation of a sterically favourable six-



Scheme 1

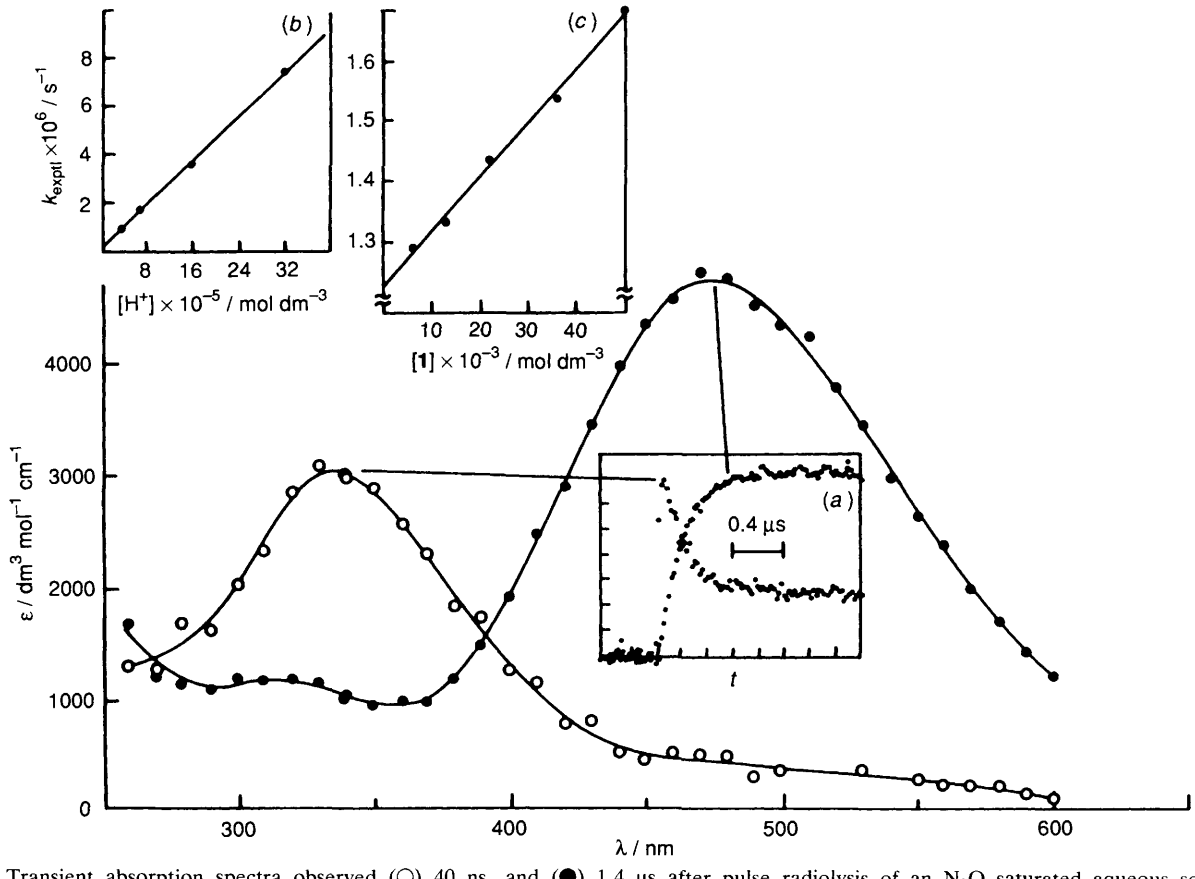


Fig. 1 Transient absorption spectra observed (○) 40 ns, and (●) 1.4 μs after pulse radiolysis of an N_2O saturated aqueous solution containing 10^{-2} mol dm^{-3} of **1**, at pH 3.7. Inserts: (*a*) the absorption time profiles of the decay of **1a** (330 nm), and the formation of **1d** (470 nm); plots of the observed first-order rate constant of the decay of the 330 nm absorption band of **1a** as a function of the H^+ (*b*) and **1** (*c*) concentrations.

membered ring configuration. A similar stabilization of the OH-adduct at sulfur **2a** (λ_{max} = 340 nm) is observed for 3-(methylthio)acetaldehyde dimethyl acetal $MeSCH_2$-$CH(OMe)_2$ **2**. Deconvolution of the observed k_{exptl} yields: k_d = (2.72 ± 0.22) × 10^5 s^{-1}, k_H = (2.61 ± 0.07) × 10^{10} dm^3 mol^{-1} s^{-1} and k_s = (1.41 ± 0.03) × 10^7 dm^3 mol^{-1} s^{-1}. The higher value of k_d for **2a** indicates less of a tendency for the hydroxyl hydrogen to form hydrogen bonds with the methoxy oxygens **2b, 2c**. Hence, the higher stability of **1a** is explained by a preferred hydrogen bond with the carbonyl oxygen adopting structure **1b**.

The reactions of **1a** and **2a** with molecular oxygen are measured by monitoring the pseudo-first-order decay of **1a** and **2a** as a function of oxygen concentration. From the slopes of the linear dependence of k_{exptl} on $[O_2]$, bimolecular rate constants k (**1a** + O_2) = (1.13 ± 0.07) × 10^8 dm^3 mol^{-1} s^{-1} and k (**2a** + O_2) = (1.28 ± 0.10) × 10^8 dm^3 mol^{-1} s^{-1} are derived. Although, these values do not allow for the moment to differentiate between possible mechanisms (addition *vs.* electron transfer), these results represent the first measurements of the rate constant of the OH-adducts at the sulfur atom with molecular oxygen.

In conclusion, our results also relate to redox processes initiated by hydroxyl radicals in peptides and proteins composed of some sulfur containing amino acids. Stabilization of the OH-adducts at the sulfur atom through hydrogen bond formation might obtain particular assistance from the carbonyl oxygen atoms located in a peptide linkage.

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