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Reactivity and Selectivity of Reactions of Small Radicals with a Multifunctional Heterocyclic Molecule: 3-(Mercaptoethyl)chinazoline-2,4-(1H,3H)dione

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Using pulse radiolysis, we studied the reactions of small radicals (e^-_{aq}, $OH^•$, $N_3^•$, and $^•CH_2OH$) with 3-(mercaptoethyl)chinazoline-2,4-(1H,3H)dione in aqueous solution. Whereas the solvated electron adds selectively to the carbonyl group near the aromatic moiety, the hydroxyl radical reacts by addition to the aromatic ring as well as by H abstraction at $>N_{(1)}H$ and −SH groups. Also, azide radicals nonspecifically oxidize the aromatic ring, the thiol group, or the thiolate anion and the amine group at $N_{(1)}$, as identified by subsequent radical products. In contrast, hydroxymethyl radicals (derived from methanol) abstract hydrogen selectively at the thiol group. The thiyl radical formed was used to study the kinetics of H abstraction in the bisallylic positions of linolenic acid. Product transient identification was performed by kinetic analysis as well as by comparison with reactions of molecules with structures less complex than that of the title compound, exhibiting relevant functional groups.

Introduction

3-(Mercaptoethyl)chinazoline-2,4-(1H,3H)dione (**I**), a recently synthesized quinazoline derivative with a thiol function,[1] exhibits immunostimulating activity and immunorestorative efficiency.[2] With respect to its potential involvement in radical reactions in organisms, we investigated the radiolytic and thermal formation of thiyl radicals of **I** and its effects on unsaturated fatty acids in the sense of oxidative damage[3] and the isomerization of double bonds.[4,5] Studying radiation-induced radical processes involving **I** and taking into account the multifunctionality of this molecule, we found the reactions of small radicals such as e^-_{aq} and $OH^•$, the main species of water radiolysis,[6] and some radicals derived from the radiolysis, such as $N_3^•$ and $^•CH_2OH$, with high and low oxidation power to be of interest—especially because in the case of the highly reactive radicals, a higher variety of products is expected, formed by reactions with more than one of the functional groups of **I**. The molecule structure of **I** consists of an aromatic ring connected in neighboring positions with the heterocyclic ring. One of the carbonyl and one of the (secondary) amine groups stand in anα-position to the aromatic ring, whereas $N_{(3)}$ is β-substituted with an ethylmercaptane group and is closer to a cyclic lactame structure. The heterocyclic molecule part is also reminiscent of the structure of a substituted pyrimidine.

In this paper, we report a detailed pulse radiolysis study in which radical reactions involving **I** and a few small radicals were analyzed in terms of reactivity and selectivity. For product transient identification, we used radical reactions with model compounds such as other quinazoline structures, a pyrimidine, α-tetralone, and cysteamine.

Experimental Section

Pulse radiolysis experiments were performed with high-energy electrons pulses (1 MeV, 15 ns duration) generated by a pulse-transformer-type electron accelerator ELIT (Institute of Nuclear Physics, Novosibirsk, Russia). The absorbed dose per pulse measured with an electron dosemeter was usually between 50 and 100 Gy. Irradiation of the samples was carried out in a on-line flow system having an optical path length of 1 cm quartz cell. The optical detection system consists of a pulsed Xenon lamp (XBO 900, Osram), a SpectraPro-500 monochromator (Acton Research Corporation), a R4220 photomultiplier (Hamamatsu Photonics) or a FND-100Q silicon photodiode (Laser Components), and a TDS 640 digitizing oscilloscope (Tektronix). More details about the pulse radiolysis setup are reported elsewhere.[7] High-purity gases such as N_2, O_2, and N_2O were used for purging the solutions.

As mentioned above, for the pulse radiolysis studies, 3-(mercaptoethyl)chinazoline-2,4-(1H,3H)dione (**I**) and some other model quinazolinediones (structures **II**−**V**) as well as α-tetralone (**VI**), 3,5,6-trimethyluracil (**VII**), and cysteamine (**VIII**) were used. The structures are shown in the scheme below (structure formulas of **I**−**VIII**). The quinazolinedione derivatives were synthesized by Leistner et al.[1,8] The other chemicals were used in analytical reagent grade. Water from the Millipore milli-Q plus system was used for the study in aqueous solutions.

Results and Discussion

Before studying the radical reactions of the quinazoline (**I**), we first defined the hitherto unknown pH-dependent acid−base behavior of the different functional groups. This was done by customary stationary spectroscopic measurements.

pK_a Values of Quinoxalinediones in Aqueous Solution. The pK_a values of 3-(mercaptoethyl)-chinazoline-2,4-(1H,3H)dione (**I**) and unsubstituted quinazolinedione-2,4 (**V**) were determined from UV−vis spectra taken in aqueous solutions at different pH values. Two values were obtained for **I**: pK_a = 9.8 for the thiol group and pK_a = 11.6 for $>N_{(1)}H$, which seem to be reasonable in comparison with that of ethanethiol (pK_a = 10.6, Schwetlick[9]) and considering that the conjugation states of

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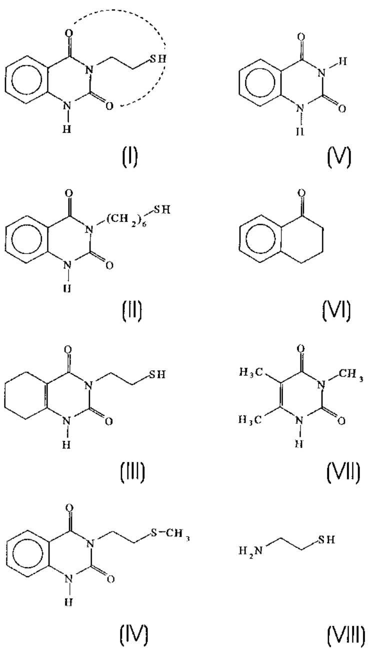
SCHEME 1



deprotonated $>N_{(1)}^-$ are in mesometry with the neighboring carbonyl group. In contrast, **V** has two different pK_a's for the >NH groups in position 3 (pK_a = 9.8) and position 1 (pK_a > 13), which can be explained by conjugation considerations and also agrees qualitatively with those of uracil (pK_a = 9.5, >13, Lide[10]). Hence, it can be stated that at a pH of around 7 and in pulse radiolysis under normal conditions (pH 5.5, caused by dissolved CO_2), the molecules exist in their undissociated ground state. More details of the pK_a value determination are given by Schwinn.[11]

Reactions of the Solvated Electron. The primary products of water radiolysis which emerge are solvated electrons, hydroxyl radicals, and hydrogen atoms (eq 1) in a yield characterized by the G value (radiolysis yield, μM J^{-1})

$$\mathrm{H_2O} \xrightarrow{\mathrm{vvv}} \mathrm{e^-_{aq}}\ (G = 0.27\ \mu\mathrm{M\ J^{-1}}),\ \mathrm{OH^\bullet}\ (G = 0.26\ \mu\mathrm{M\ J^{-1}}),\ \text{and H}\ (G = 0.05\ \mu\mathrm{M\ J^{-1}}) \quad (1)$$

$$\mathrm{H, OH^\bullet} + t\text{-}\mathrm{BuOH} \rightarrow {}^\bullet\mathrm{CH_2(CH_3)COH} + \mathrm{H_2, H_2O} \quad (2)$$

To selectively study reactions of e^-_{aq}, we avoided the potential interference from OH$^\bullet$ groups by converting them into much less reactive alkyl radicals in the presence of alcohols, as shown in reaction 2. Figure 1 shows optical absorption spectra obtained in the pulse radiolysis of a 10^{-4} M solution of **I** in water at pH 11 in the presence of 0.1 mol dm^{-3} t-butanol. The decay of e^-_{aq} and the formation of the ketyl radical anion located at $C_{(4)}$ can be clearly seen from the spectra and also from the time profiles (cf. reaction 3). Apart from the main band absorbing at λ_{max}= 300 nm, the transient shows two additional absorptions around 380 and 550 nm. At a lower pH, the anion disappears, according to equilibrium 4, as is observable at around 300 nm (not shown here)

$$\mathrm{e^-_{aq}} + >\mathrm{C_{(4)}{=}O} \rightarrow >\mathrm{C^\bullet{-}O^-} \qquad k_3 = 8.3 \times 10^9\ \mathrm{dm^3\,mol^{-1}\,s^{-1}} \quad (3)$$

$$>\mathrm{C^\bullet{-}O^-} + \mathrm{H_3O^+} \rightleftharpoons >\mathrm{C^\bullet{-}OH} + \mathrm{H_2O} \qquad \mathrm{p}K_a = 8.9 \quad (4)$$

Analogous experiments with α-tetralone (**VI**) resulted in absorption spectra similar to those observed for **I**, with a radical anion band at λ_{max} = 325 nm (satellite band at 450 nm), and for the corresponding ketyl radical at λ = 280 nm, p$K_{a(4)}$ = 10.2, and $k_3 = 2.6 \times 10^{10}$ dm^3 mol^{-1} s^{-1}.

The pK_a values measured are comparable to those found for other aromatic ketones such as benzophenone[12] and acetophenone.[13] The other functional groups of **I** were found to be inactive in the electron reaction.

Reaction of Hydroxyl Radicals. OH$^\bullet$ has oxidizing properties and chiefly reacts in addition and abstraction reactions and

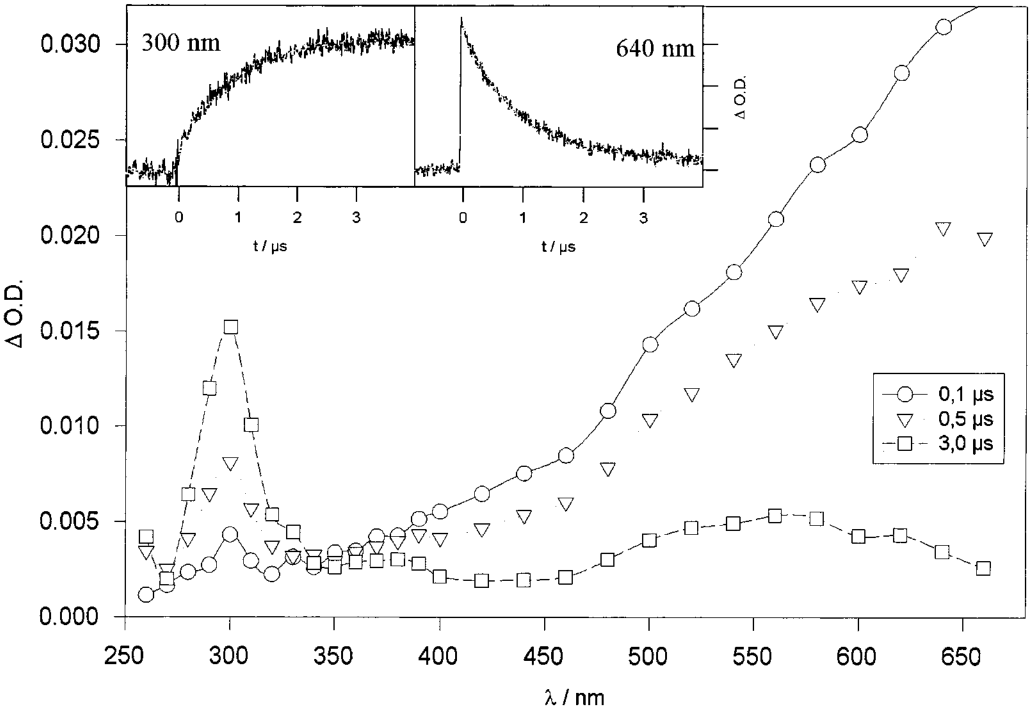


Figure 1. Transient optical absorption spectra taken in the pulse radiolysis of a solution of 10^{-4} mol dm^{-3} **I** in water at pH 11 (NaOH) containing 0.1 mol dm^{-3} t-butanol for OH scavenging. The insets show the decay of e_{aq}^- (640 nm) and the formation of the radical anion of **I**.

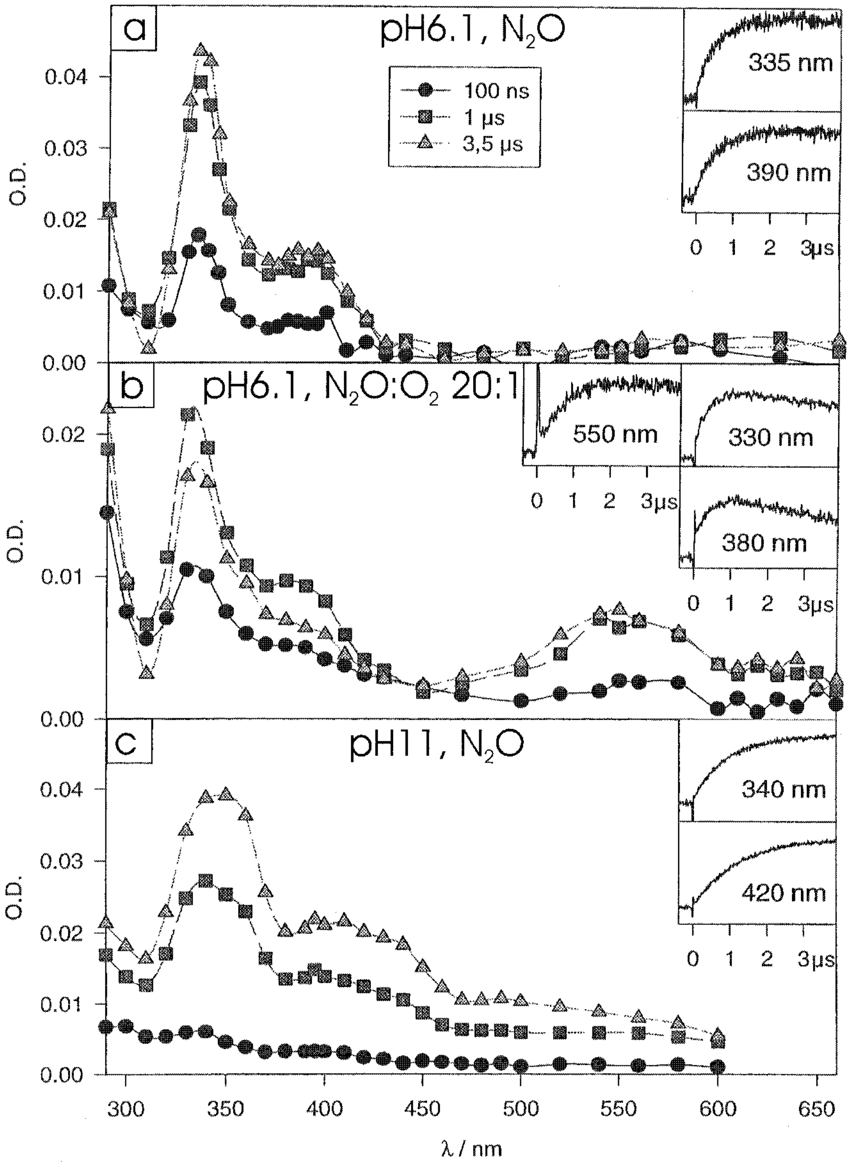


Figure 2. Transient optical absorption spectra of the products of the reaction of OH with **I** (10^{-4} mol dm^{-3}) at different pH values (a and c) and in the presence of oxygen traces (b). The insets give time profiles at characteristic wavelengths.

relatively seldomly in electron transfer. For its reactions to be selectively studied, the solvated electron should be converted according to reaction 5, which results in the doubling of the $G(OH^\bullet)$ value. The low amount of H ($G = 0.05$ μM J^{-1}) must be tolerated

$$e^-_{aq} + N_2O + H_2O \rightarrow OH^\bullet + OH^- + N_2 \qquad (5)$$

Figure 2 shows spectra of the products of the reaction of OH$^\bullet$ with **I** under different conditions. In aqueous solution at natural pH (Figure 2a), two bands are observable with maxima at $\lambda =$ 340 [strong] and 390 nm, which appear to be very similar to those obtained in the analogous reaction with α-tetralone (**VI**) as the scavenger ($\lambda_{max} = 320$ and 370 [strong] nm). Also, in analogy with benzophenone,[12] these absorptions are assigned mainly to be caused by cyclohexadienyl-type radicals formed by OH$^\bullet$ addition at different positions of the aromatic ring. In view of the molecular structure of **I**, we may also expect other transients of OH$^\bullet$ attack. For example, in the presence of traces of oxygen (Figure 2b), another species appears with a band at around 550 nm. This is assumed to be a thioperoxyl radical,[15] formed by the addition of oxygen to the thiyl radical,which does not itself have marked absorption in the visible range.[14]

In alkaline solution at pH 11, other absorptions appear, indicating OH$^\bullet$ attack at the other functional groups of **I**. Around $\lambda = 500$ nm, the absorption of disulfide radical anion (see later) is observed, while around $\lambda = 430$ nm, the absorption of an aminyl radical is to be seen. This very speculative and tentative assignment is based on both comparative experiments with model compounds (**II**−**VIII**) and other transient reactions such as one-electron oxidation with azide radicals. Those experiments supporting the identification of the transients are described below.

At first, a reaction scheme is given which elucidates the OH$^\bullet$ reaction paths (Scheme 2, reactions 6−12). All transients were directly observed, with the exception of the thiyl radical which, however, was derived from observing its following transients such as the thiylperoxyl radical and the dithioether radical anion.

When the thiol group of **I** is blocked by a methyl group, transient formation at the sulfur is nearly excluded in the resulting thioether. Hence, the product transient spectrum of the OH reaction with thioether **IV** shows only absorptions of cyclohexadienyl-type radicals ($\lambda_{max} = 340$ and 370 nm) and the aminyl radical bands at $\lambda_{max} = 440$ and probably at 280 nm. The latter ones appear more pronounced in alkaline solution

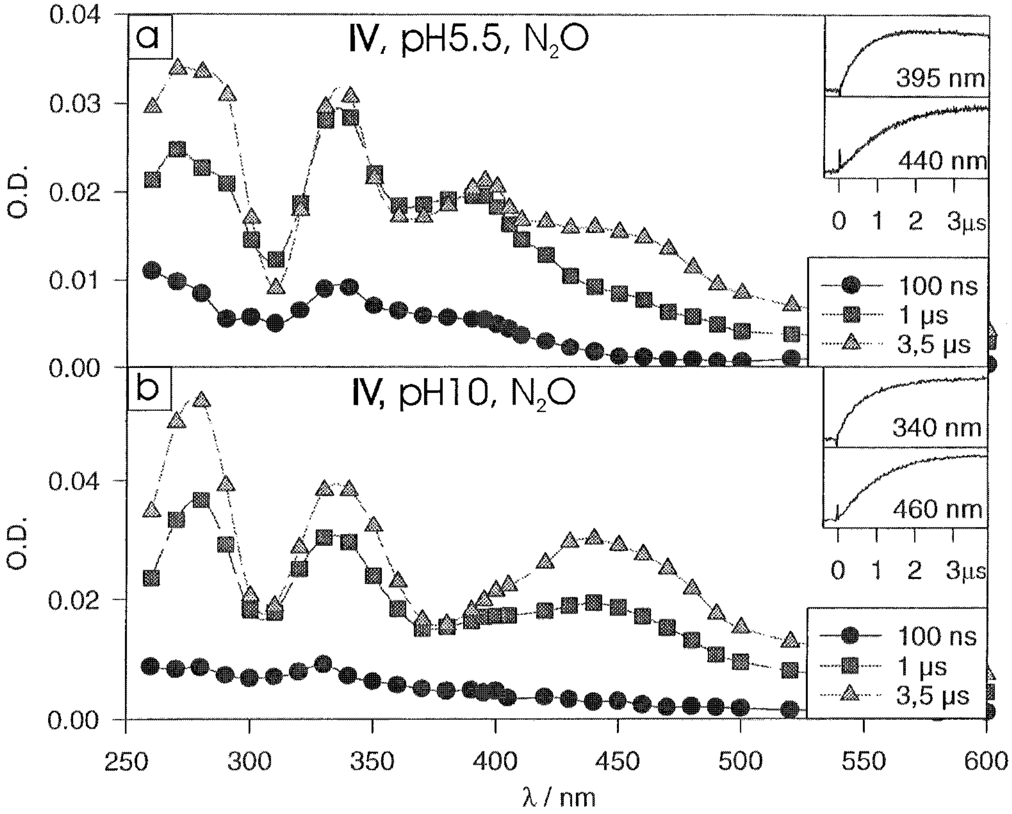
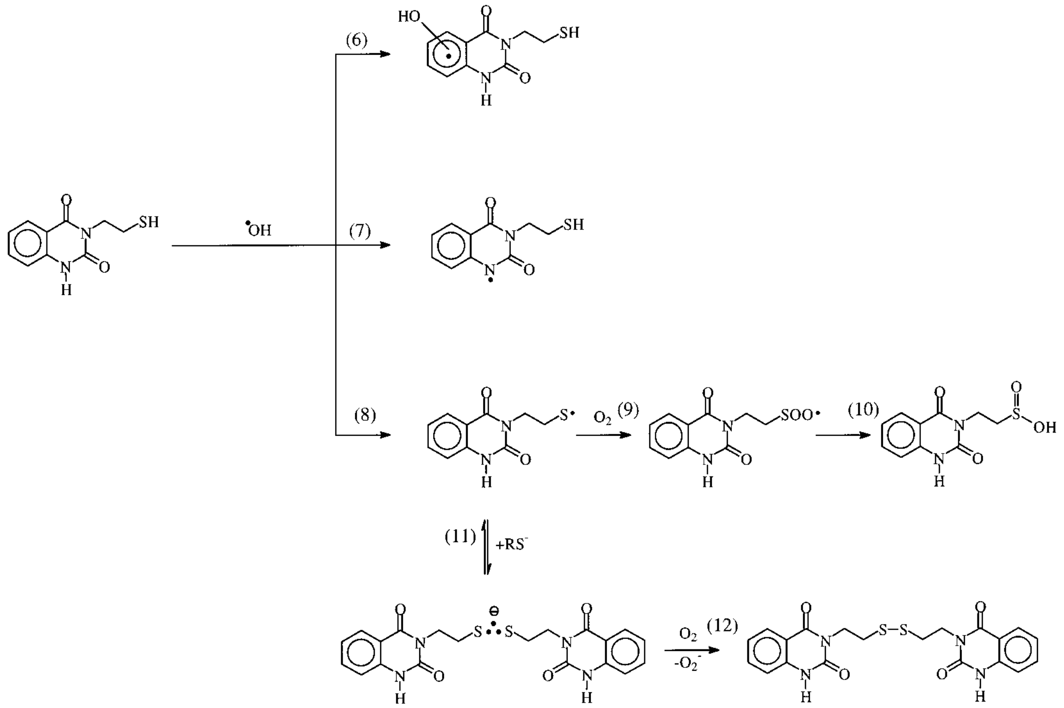


Figure 3. Transient optical absorption spectra of the products of the reaction of OH with the thioether **IV** (10^{-4} mol dm^{-3}) at different pH values, taken in N$_2$O-bubbled solution. The insets give corresponding time profiles.

SCHEME 2



at pH 10 (see Figure 3a,b). Therefore, an imaginable oxidation of the sulfide group is ignored.

Although at the N$_{(1)}$ position the amid group is derived from an aromatic amine, we compared the formation of N radicals of compound **I** with those of 3,5,6-trimethyluracil (**VII**), where instead of the aromatic ring a double bond exists substituted with two methyl groups. This molecule should represent the heterocyclic ring part of **I**, also excluding sulfur function. Figure 4a shows the transient spectrum of the reaction of OH$^•$ with **VII** with a dominating absorption at around 425 nm, which is understood to be caused by the aminyl radical,[16,17] reaction 13 corresponding with eq 7 for **I**

$$\mathrm{OH^\bullet + {>}NH \rightarrow H_2O + {>}N^\bullet} \qquad (13)$$

For further support the assignment of the sulfur-centered species

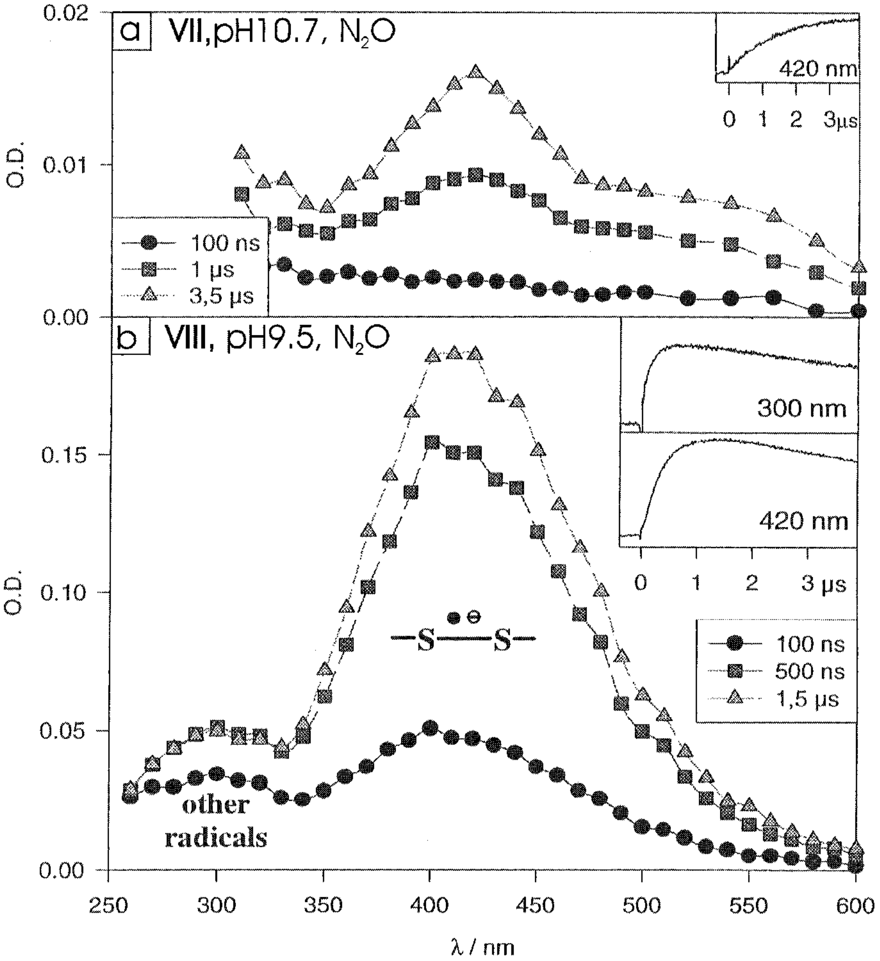


Figure 4. Transient optical absorption spectra of the products of the reaction of OH with the model compounds **VII** (10^{-4} mol dm^{-3}, a) and **VIII** (10^{-3} mol dm^{-3}, b) in alkaline aqueous solution bubbled with N_2O. Characteristic time profiles are given as insets.

derived from the hidden thiyl radical, we studied the $OH^•$ reaction with cysteamine (**VIII**; see Figure 4b). In this case, at pH values around the pK_a of the thiol group, H abstraction (eq 14a) with a subsequent dimerization-like reaction involving the thiolate[18,19] (eq 14b) could represent the anion formation presumed to happen also with **I** (reactions 8 and 11)

$$H_2N-CH_2-CH_2-SH + OH^• \rightarrow H_2O + H_2N-CH_2-CH_2-S^• \quad (14a)$$

$$H_2N-CH_2-CH_2-S^• + H_2N-CH_2-CH_2-S^- \rightarrow H_2N-CH_2-CH_2-S-^{•-}-S-CH_2-CH_2-NH_2 \quad (14b)$$

The dimer anions of **VIII** and **I** absorb at around 420 nm, which can be presumed from Figure 2c and seen even better in Figure 6a.

This argument indicates that $OH^•$ reacts with compound **I** in practically all positions of the molecule, even though at first sight the cyclohexadienyl type radicals seem to dominate by far as addition products to the aromatic ring.

One-Electron Oxidation with Azide Radicals. $N_3^•$ can be generated by $OH^•$ reaction (15) with the corresponding azide anion.[20] It is known to be a selective oxidant which mainly produces one-electron oxidation via primary formation of radical cations.[20,21] Concerning 3-(mercaptoethyl)-chinazoline-2,4-(1H,-3H)dione (**I**), three hypothetically possible groups exist for oxidation: the aromatic moiety, the thiol group, and the amid function at $N_{(1)}$. In fact, all these options are used.

$$N_3^- + OH^• \rightarrow N_3^• + OH^- \quad (15)$$

Figure 5a shows the results of the pulse radiolysis of an N_2O saturated aqueous solution of 0.1 mmol dm^{-3} of **I** at pH 11 containing 2×10^{-2} mol dm^{-3} sodium azide. In the spectra, four absorption peaks are observed, which are assigned to $N_3^•$ (280 nm), the cyclohexadienyl type radical (340 nm), the aminyl radical (450 nm), and the dithioether radical anion (420 nm). Although no radical cations are observed as direct products of the electron transfer, the species mentioned may clearly be derived from these intermediates (Scheme 3, reactions 16−18).

Hence, reaction of the intermediate aromatic radical cation with the nucleophile OH^- results in cyclohexadienyl radicals (eq 16), and deprotonation of $>N_{(1)}H$ group yields aminyl radicals (eq 17), whereas the thiyl radical and its successor are formed mainly by oxidation of the thiolate (eq 18).

For comparison, these paths were confirmed by pulsing solutions of the quinazoline derivatives **III** (without aromatic ring, Figure 5b) and **IV** (blocked −SH group, Figure 5c). As expected, in these cases for **III**, a superposition of aminyl radicals and dithioether radical anion between 360 and 500 nm is observed, and the peak at 300 nm is caused by $N_3^•$ decay and aminyl radical formation (see also the time profiles). For compound **IV** with decaying $N_3^•$ (280 nm), both the aminyl-type (near 300 nm, 460 nm) and cyclohexadienyl-type (340 nm)

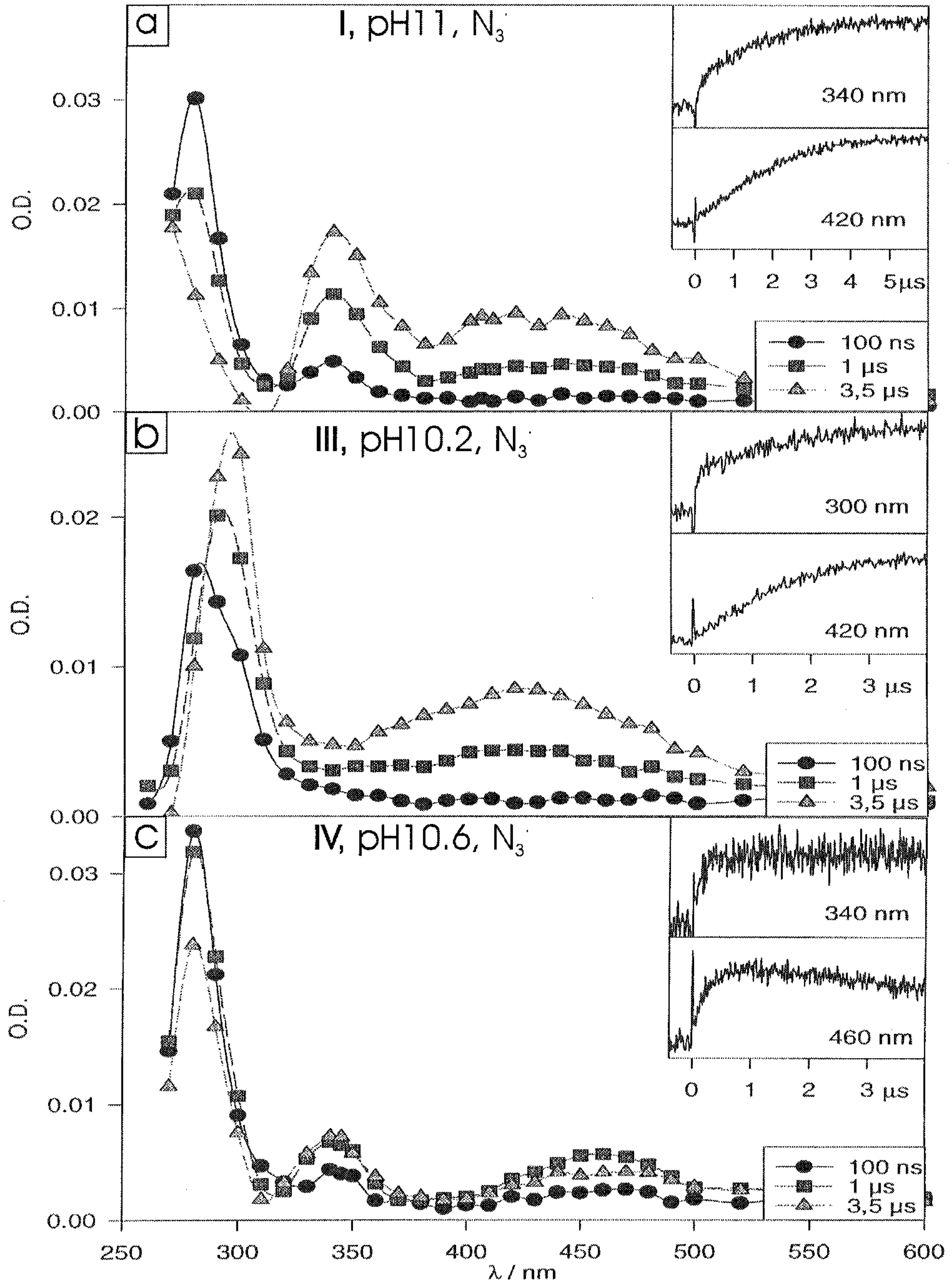


Figure 5. Transient optical absorption spectra of the reaction of azide radicals with compounds **I**, **III**, and **IV** (each 10^{-4} mol dm^{-3}) in alkaline aqueous solutions containing 0.02 mol dm^{-3} sodium azide, bubbled with N_2O. Insets give characteristic time profiles.

radicals appear. This also confirms the interpretation of the generation of three oxidation products of our basic compound **I** in the reaction with azide radicals, as described above.

Selective Formation of Thiyls by Reaction with Alkyl Radicals. Having found the multilateral reaction of **I** in radical and one-electron oxidation reactions, we beg the question concerning the possibility of the selective formation of thiyl radicals. This was of particular interest because we intended to use these types in model reactions with biological relevance.[3,4,22] Hence, in methanolic solution we converted OH$^•$ into α-hydroxyalkyl radicals (eq 19) and studied their reaction with **I**. Under these conditions at a slightly alkaline pH of 11 for monitoring thiyls by reaction 11, it was shown that in fact only thiyl radicals are formed, as is demonstrated by the transient absorption spectra given in Figure 6a. The hydroxyalkyl radicals decay (320−340 nm) and the disulfide radical anions grow in (around 420 nm). It cannot be completely excluded that the hidden thiyl radicals contribute to the 320−340 nm absorption. Indeed, reaction 20 is known to proceed also for other thiols[23]

$$OH^• + CH_3OH \rightarrow {}^•CH_2OH + H_2O \qquad (19)$$

$${}^•CH_2OH + RSH \rightarrow CH_3OH + RS^• \qquad \text{where RSH} = \mathbf{I} \qquad (20)$$

$$RS^• + RS^- \rightleftharpoons RS{-}^{•-}{-}SR \qquad (11)$$

Figure 6b shows the transient absorption spectra of the disulfide radical anions obtained in the analogous experiment with cysteamine. Hence, we found a method for the selective generation of thiyl radicals of the quinazoline derivative **I** and

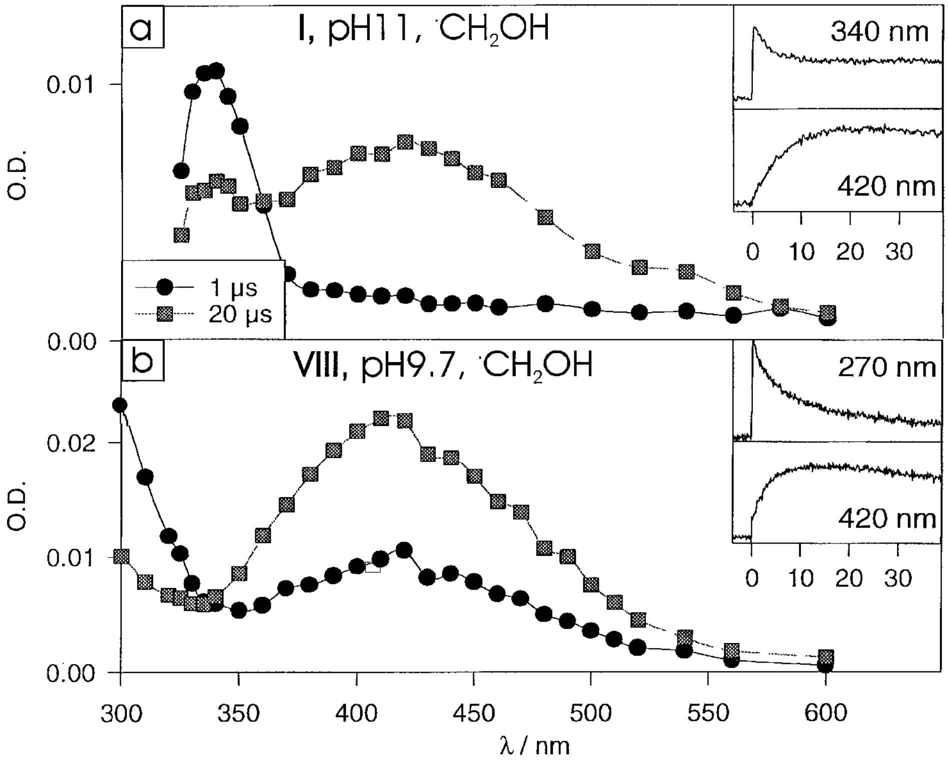
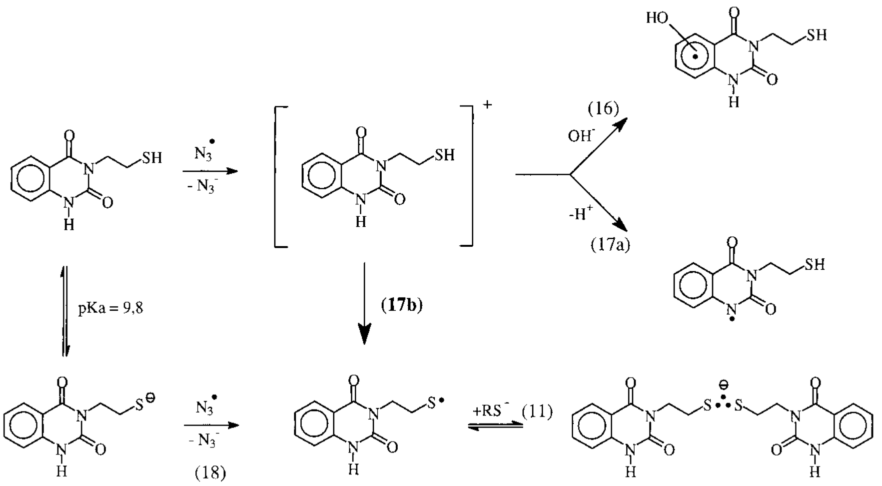


Figure 6. Transient absorption spectra of the reaction products of α-hydroxymethyl radicals with the compounds **I** or **VIII** (each 10^{-3} mol dm^{-3}) solved in a mixture of water and methanol (1:1 v/v) under alkaline conditions, bubbled with N_2O. Insets show characteristic time profiles.

SCHEME 3



also of cysteamine (**VIII**) and for monitoring them by a subsequent reaction equilibrium (eq 11).

Reaction of Thiyl Radicals with Linolenic Acid. Aliphatic thiol structures are commonly considered to be antioxidants, which are also active under biological conditions, i.e., within living cells. Gluthathione, for example, is well-known as a regulating and repairing antioxidant.[24] In the course of the reaction cycle of gluthathione with ascorbate, the intermediate thiyl radicals are considered to be harmless in that they do not undergo further transformations or induce any damage. However, recent experiments with unsaturated fatty acids revealed two modes of interaction between thiyl radicals and the bisallylic structures in the linolenic acid.[4,5,25] One mode is the cis–trans isomerization of olefinic (eq 21) and cummulated unsaturated groups by a catalytic reaction proceeding through unstable thiyl adducts, characterized by steady-state radiolysis, thermolysis,[5,22] and pulse radiolysis[4,5] experiments. The other channel[25] consists of the abstraction of the weakly bonded bisallylic hydrogen (eq 22) demonstrated below:

$$\mathrm{RS^\bullet} + cis\text{-}\mathrm{CH{=}CH{-}} \rightleftharpoons \mathrm{-CH(RS)\text{-}C^\bullet H-} \rightleftharpoons \mathrm{RS^\bullet} + trans\text{-}\mathrm{CH{=}CH{-}} \quad (21)$$

$$\mathrm{RS^\bullet} + \mathrm{{>}C{=}CH{-}CH_2{-}CH{=}C{<}} \rightarrow \mathrm{{>}C{=}CH{-}C^\bullet H{-}CH{=}C{<}} + \mathrm{RSH} \quad (22)$$

First of all, transient absorption spectra were taken in the maximum extinction in solutions of either **I** or its derivatives **II**, **III**, and **IV** in a water-ethanol mixture (1:1 v/v) containing 1 mmol dm^{-3} linolenic acid and saturated with N_2O. This is shown in Figure 7a, where for those compounds containing a thiol group, the product transient maxima at $\lambda = 280$ nm of the bisallylic linolenic acid radicals appear, which are also known otherwise.[25] Because of the absence of a thiol group, it was

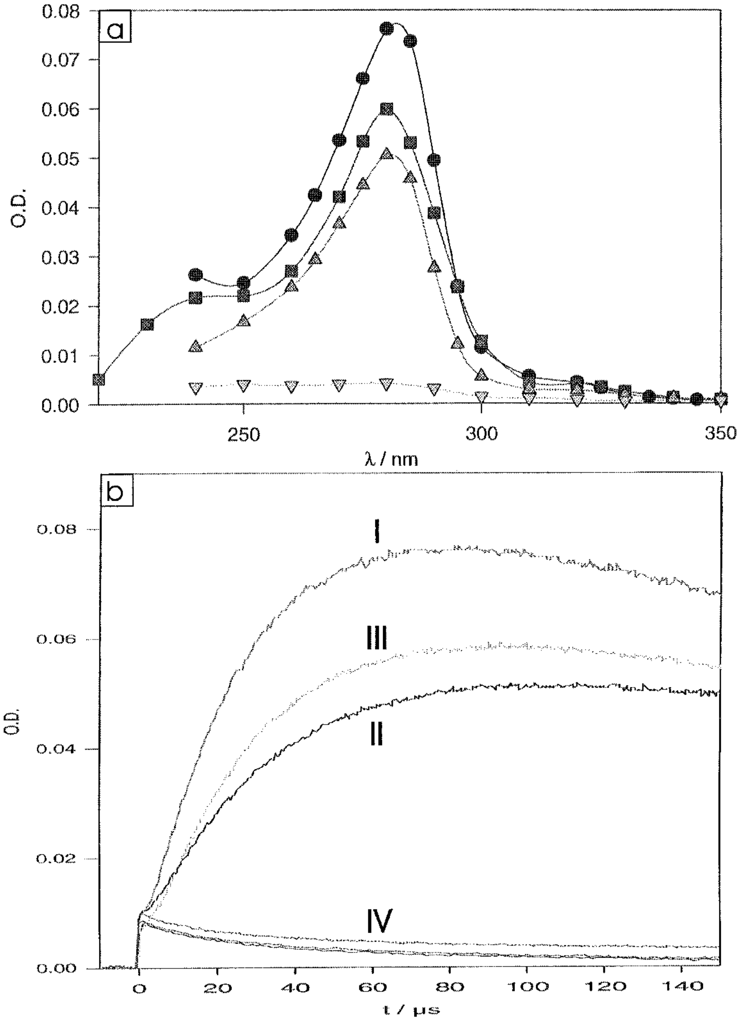


Figure 7. Maximum transient optical absorption spectra (a) and time profiles (b) taken from solutions of compounds **I** (●), **II** (▲), **III** (■), and **IV** (▼) (each 10^{-4} mol dm^{-3}) in a mixture of ethanol and water (1:1 v/v) containing 10^{-3} mol dm^{-3} linolenic acid, bubbled with N_2O. In (b), the lowest lines show time profiles only of the solvent background.

only for thioether **IV** that no bisallylic radical signal could be obtained. The time profiles of radical formation at $\lambda = 280$ nm in the presence of **I** to **III** show well-resolved growths, which can be described by a rate constant of $k_{22} = 2.5 \times 10^7$ dm^3 mol^{-1} s^{-1}.

In the presence of oxygen, H abstraction (eq 22) induces oxidative damage, which, under biological conditions, may play a role in the structural modification of cell membranes in the sense of aging. Furthermore, the cis–trans isomerization mentioned seems to also be important for the denaturation of the naturally occurring cis olefin structures of fatty acids. Although isomerization is known to be a property of thiyl radicals in general, because of their lipophilic behavior, the studied sulfur-containing quinazoline derivatives (**I**–**IV**) are of special interest for experiments concerning biologically relevant membrane systems. Hence, the study of details of those processes is currently underway.

Reactivity and Selectivity in the Studied Elementary Reactions. The main aim of this paper was the idea of testing quinazolinedione **I** in regard to selective transient generation, preferably of selective thiyl radical formation.

As expected, the hydroxyl radical, as an extremely reactive and, therefore, nonselective reagent, undergoes addition (to the aromatic ring) as well as hydrogen atom abstraction reactions at all energetically possible positions, i.e., at the secondary amine and at the thiol group. Alkyl radicals formed from the ethylthiyl group were not spectroscopically observed but cannot be excluded. All these reactions take place in a diffusion-controlled manner. Although located on one (multifunctional) molecule, the product radicals are stable and do not isomerize or rearrange.

Azide radicals are known to be selective oxidants. Because of the different groups of **I** available for oxidation, primarily the corresponding product radical cations located at the aromatic ring, the amine and the thiol groups should be formed, controlled by the encounter situation of the reactants, as indicated in Scheme 3. In such a conjugated molecule such as quinazolinedione **I**, subsequent charge migration to the energetically deepest trap or charge equilibration over the whole molecule could happen. But this does not hold in this case. In aqueous solution, rapid decay reactions of the radical cation intermediates take place, such as reaction with the nucleophile OH^- (eq 16) and deprotonation (eqs 17a and 17b). Those rapid reactions fix the position of oxidation by transforming the radical cation intermediates into stable radicals. Hence, we get a product spectrum similar to that observed for the reactions of $OH^•$. Additionally, in alkaline solution above the pK_a of the thiol group, oxidation of the thiolate anion to thiyl radicals occurs (eq 18).

Quantum–chemical analysis of **I** showed that it is an extremely polarized molecule which consists practically of two parts, the aromatic moiety, including the polar amine neighbor group, and the ethylthiol unit. From density functional theory

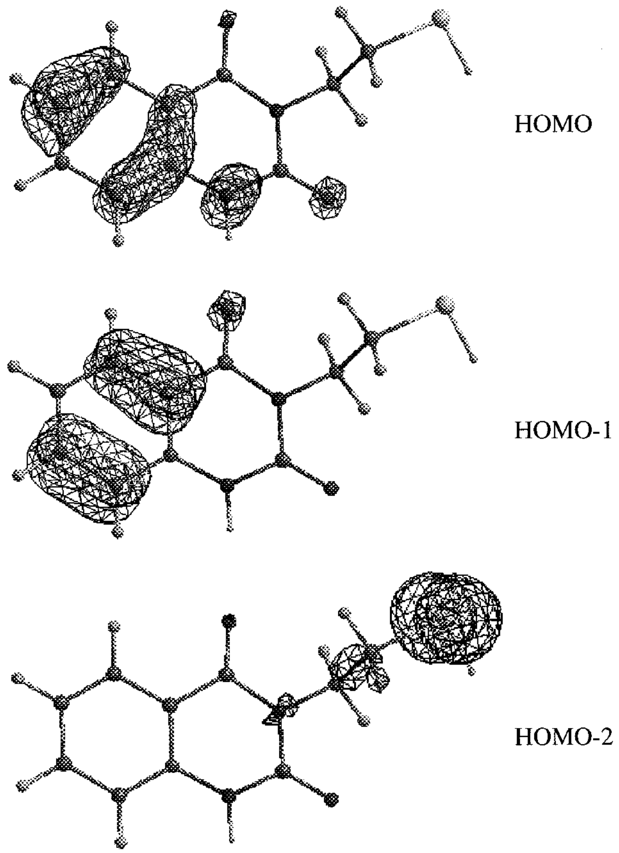


Figure 8. DFT B3LYP/6-31G(d) and SCRF−dipole calculated molecular orbitals of the singlet ground state of the quinazoline **I** (in aqueous solution).

and ab initio Hartree−Fock calculations (both with 6-31G(d) basis set) and taking into account aqueous surroundings (the molecular geometry was optimized using the Onsager self-consistent reaction field model), we find that the singlet ground-state HOMO of **I** shows electron distribution only involving the aromatic ring and the neighbored amine group. The next lower orbital HOMO-1 involves the aromatic ring and the carbonyl unit, whereas HOMO-2 showed an extreme electron localization at the thiol unit. This is demonstrated in Figure 8. It implies that the ethyl side group represents a real barrier for electron exchange between the two moieties.

Considering the charge situation in the radical cation of **I** on the basis of an open-shell calculation, we found extreme behavior in that the charge at the aromatic amine bond N_1−H is highly polarized, much more than those of the aromatic ring C−H and S−H bonds. The calculation of the bond dissociation energy of the $N_1^{\bullet +}$−H and $S^{\bullet +}$−H bonds showed that the deprotonation of the thiol radical cation group is favored by 20 kcal. Nevertheless, in the experiments we observed the formation of aminyl as well as of thiyl radicals to a similar extent. This confirms the above-mentioned electron exchance barrier in the form of the ethyl group.

Competing with amine deprotonation, the reaction of the nucleophile OH^- at the aromatic ring takes place, resulting in hydroxycyclohexadienyl radicals. Hence, the experimentally found product radicals can be derived from two separated charge centers, the aromatic amine unit and the thiol group.

The less reactive hydroxyalkyl radicals, however, were found to be selective reactants for H abstraction at the thiol group. By first transforming the hydroxyl radicals into alkyl radicals (eq 19), we can selectively generate thiyl radicals in a subsequent step (eq 20). Then these thiyls could be used to study reactions with membrane constituents (eqs 21 and 22). This is documented in the preceding paragraph and applied to studying thiyl-radical-induced transformations in lipid systems.[4,5]

Finally, it should be stated that in the reaction of solvated electrons with **I**, only reduction of the carbonyl group to form the ketyl radical anion occurs, and this is in protolytic equilibrium (eq 4) with the corresponding ketyl radical form.

Conclusions

Multifunctional compounds such as the studied 3-(mercaptoethyl)chinazoline-2,4-(1H,3H)dione (**I**) molecule are often found to be of pharmaceutical interest. If they are expected to be involved in radical reaction mechanisms, their reactivity in those processes needs to be ascertained. In this pulse radiolysis study under comparative identification with model compounds, we demonstrated the manifold of reaction possibilities of **I** with hydroxyl radicals and, more surprisingly, of one-electron oxidation with azide radicals. In the case of alkyl radicals, we found a selective reactant which abstracts hydrogen from the thiol group of **I**. Using this selective reaction pathway provides a way of studying subsequent processes of thiyl radicals with unsaturated carbon systems, as has been demonstrated for the thiyl-caused H abstraction at the bisallylic positions of linolenic acid.

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