Effect of pH on One-Electron Oxidation Chemistry of Organoselenium Compounds in Aqueous Solutions

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Pulse radiolysis coupled with absorption detection has been employed to study one-electron oxidation of selenomethionine (SeM), selenocystine (SeCys), methyl selenocysteine (MeSeCys), and selenourea (SeU) in aqueous solutions. Hydroxyl radicals ($^{\bullet}$OH) in the pH range from 1 to 7 and specific one-electron oxidants $Cl_2^{\bullet-}$ (pH 1) and $Br_2^{\bullet-}$ (pH 7) have been used to carry out the oxidation reactions. The bimolecular rate constants for these reactions were reported to be in the range of 2×10^9 to 10×10^9 M^{-1} s^{-1}. Reactions of oxidizing radicals with all these compounds produced selenium-centered radical cations. The structure and stability of the radical cation were found to depend mainly on the substituent and pH. SeM, at pH 7, produced a monomer radical cation ($\lambda_{max} \sim 380$ nm), while at pH 1, a dimer radical cation was formed by the interaction between oxidized and parent SeM ($\lambda_{max} \sim 480$ nm). Similarly, SeCys, at pH 7, on one-electron oxidation, produced a monomer radical cation ($\lambda_{max} \sim 460$ nm), while at pH 1, the reaction produced a transient species with ($\lambda_{max} \sim 560$ nm), which is also a monomer radical cation. MeSeCys on one-electron oxidation in the pH range from 1 to 7 produced monomer radical cations ($\lambda_{max} \sim 350$ nm), while at pH < 0, the reaction produced dimer radical cations ($\lambda_{max} \sim 460$ nm). SeU at all the pH ranges produced dimer radical cations ($\lambda_{max} \sim 410$ nm). The association constants of the dimer radical cations of SeM, MeSeCys, and SeU were determined by following absorption changes at λ_{max} as a function of concentration. From these studies it is concluded that formation of monomer and dimer radical cations mainly depends on the substitution, pH, and the heteroatoms like N and O. The availability of a lone pair on an N or O atom at the β or γ position results in monomer radical cations having intramolecular stabilization. When such a lone pair is not available, the monomer radical cation is converted into a dimer radical cation which acquires intermolecular stabilization by the other selenium atom. The pH dependency confirms the role of protonation on stabilization. The oxidation chemistry of these selenium compounds is compared with that of their sulfur analogues.

1. Introduction

Selenium is an essential trace element that has provoked considerable interest because of the recent identification of the prokaryotic and eukaryotic enzymes containing the 21st amino acid, selenocysteine. Many of these compounds find applications as radioprotectors[1−9] and are important building blocks for the synthesis of biologically important sulfur/selenium compounds.[10,11] It has also been reported that some enzyme-catalyzed redox (reduction−oxidation) reactions, for example, glutathione peroxidase, require the participation of Se-containing proteins.[12−14] Organoselenium compounds have also been shown to possess an antioxidant property, which arises from its free-radical scavenging ability.[4,5,14−17]

One of the reasons for the widespread interest in selenium is its specific redox properties. During redox reactions, selenium compounds can exist in the different oxidation states of −2, 0, +4, and +6. Similarly, the radical species generated from organoselenium compounds play an important role in a number of chemical and biological processes and are considered to be the possible intermediates in redox reactions of biomolecules containing selenium.[13] Hence, characterization of the radicals formed on redox reactions of some important organoselenium compounds is necessary in understanding the role played by them in chemistry and biology.

Although some of the properties of organic selenium compounds are similar to those of their sulfur counterparts, due to their proximity in group 16 of the periodic table, the chemistry of selenium and tellurium compounds has been found to be different from the chemistry of their lighter analogues. This is mainly due to the difference in the electronegativity, polarizability, and availability of d-orbitals for bonding.[8,13] For example, selenol (−SeH) is known to be a more powerful nucleophile than thiol (−SH). The radiation-induced chemical changes in organic sulfur compounds has been reasonably well understood, and a large number of reports are available in the literature.[18−29] On the other hand, only a few reports have appeared in the literature on radiation-induced free-radical chemistry of organoselenium compounds.[4,30−34]

Pulse radiolysis is a clean method to generate the transients formed by redox reaction and to perform the time-resolved studies in short time scales ranging from nanoseconds to milliseconds. In this present paper, we have studied the one-electron oxidation reactions of organoselenium compounds such as two selenides (selenomethionine and methylselenocysteine), a diselenide (selenocystine), and a selenone (selenourea). Selenocystine and selenomethionine are important selenium containing amino acids, which are present in plants and animals and act as selenium reservoir in them. The one-electron oxidation chemistry of these compounds has been compared with their sulfur analogues.

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2. Experimental Section

Materials. Selenomethionine (SeM), selenocystine (SeCys), methyl selenocystine (MeSeCys), and selenourea (SeU) were obtained from Sigma/Aldrich Chemicals and used without any further purification. All the other chemicals and reagents were of “Analar” grade and used as such. Solutions were prepared in nanopure water with a conductivity of 0.1 μS cm^{-1}, obtained from a nanopure water purification system, and freshly prepared solutions were used for each experiment. The absorption spectra of the parent compounds were recorded on a Hitachi spectrometer, model 330. The pH of the solutions was adjusted using $HClO_4$, $Na_2HPO_4{\cdot}2H_2O$, and KH_2PO_4.

Pulse Radiolysis Studies. The pulse radiolysis experiments were carried out with high-energy electron pulses (7 MeV, 50 or 500 ns) obtained from a linear electron accelerator whose details are given elsewhere.[35] An aerated aqueous solution of KSCN (1×10^{-2} M) was used for determining the dose delivered per pulse, using $G\epsilon_{500} = 21\,520$ M^{-1} cm^{-1} per 100 eV for the transient $(SCN)_2^{\bullet-}$ species.[36] G denotes the number of species per 100 eV of absorbed energy ($G = 1$ corresponds to 0.1036 μmol J^{-1}), and ϵ is the molar absorptivity of the $(SCN)_2^{\bullet-}$ species at 500 nm. The dose per pulse was close to 8 Gy (1 Gy = 1 J kg^{-1}).

The transient species formed on pulse radiolysis were detected by an optical absorption method, and the details are reported elsewhere.[35] Radiolysis of an N_2-saturated neutral aqueous solution leads to the formation of three highly reactive species (${}^{\bullet}H$, ${}^{\bullet}OH$, and e_{aq}^{-}) in addition to the less reactive or inert molecular products (H_2, H_2O_2, and H_3O^+).[1,37]

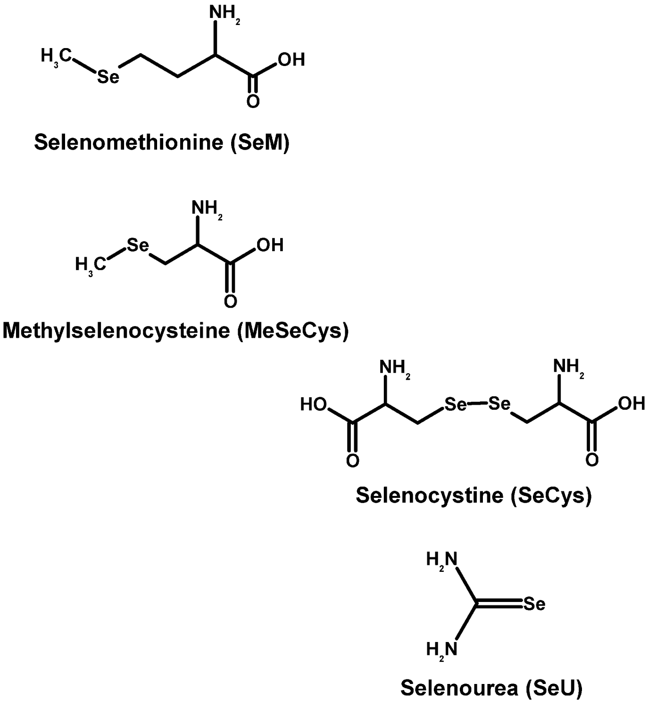
$$H_2O \rightarrow {}^{\bullet}H, {}^{\bullet}OH, e_{aq}^{-}, H_2, H_2O_2, H_3O^{+} \qquad (1)$$

The reaction with ${}^{\bullet}OH$ radicals was carried out in N_2O-saturated solutions, where e_{aq}^{-} is quantitatively converted to ${}^{\bullet}OH$ radicals with a G value of 0.56.

$$N_2O + e_{aq}^{-} \rightarrow {}^{\bullet}OH + OH^{-} + N_2 \qquad (2)$$

The reactions of specific one-electron oxidants were carried out under the condition such that ${}^{\bullet}OH$ radicals do not react with the solute and only the one-electron oxidants react with the solute. $Cl_2^{\bullet-}$ and $Br_2^{\bullet-}$ are the two specific one-electron oxidants employed at pH 1 and at pH 7, respectively, with their respective one-electron potentials of 2.3 and 1.7 V.[1,38] $Cl_2^{\bullet-}$ was generated by pulse-radiolysing an air-saturated aqueous solution of 0.1 M KCl at pH 1, whereas $Br_2^{\bullet-}$ was generated by pulse-radiolysing an N_2O saturated aqueous solution of 0.1 M KBr at pH 7.[1,38,39] To rule out the contribution of an H atom reaction at lower pH, its reaction was studied independently at pH 1 in N_2-saturated solutions containing *tert*-butyl alcohol (0.3 M), which is an efficient scavenger of ${}^{\bullet}H$ radicals and a weak $H^{\bullet}$ atom scavenger. For recording the transient spectrum of the selenium compounds, their concentration was kept at $\sim 3 \times 10^{-4}$ to 5×10^{-4} M, and the spectra were recorded 1.5−10 μs after the pulse. The chemical structures of these selenium compounds are given in Scheme 1, and their ground-state absorption spectra and pK_a values are listed in Table 1.

SCHEME 1: Chemical Structures of the Selenium Compounds



Selenomethionine (SeM)

Methylselenocysteine (MeSeCys)

Selenocystine (SeCys)

Selenourea (SeU)

TABLE 1: Absorption Maxima and pK_a of Selenium Compounds

compound	absorption maxima (nm)	pK_a	oxidation state of selenium
SeU	250		−2
SeM	220	2.2, 9.3	−2
MeSeCys	215	∼2, 8.8	−2
SeCys	300	1.7, 2.3, 7.9, 9.8	−2

3. Results

SeM and MeSeCys have two pK_a values at pH ∼ 2 and the other at pH ∼ 9 corresponding to COOH and NH_3^+ groups, respectively, and an isoelectric point at 5.75.[40−42] SeCys has four pK_a values, two at pH ∼ 2 and two at pH ∼ 8 (Table 1). Theses compounds are in the zwitterionic form, in the range of pH 2−10. In this form, both NH_3^+ and COO^- groups are exceptional proton-donor and proton-acceptor groups, respectively, and there is a fast proton transfer from the protonated amino group.[40] Therefore in this pH range, the three compounds provide enough concentration of an unprotonated amino group in the neutral solution. As SeU is not an amino acid, such prototropic equilibria and proton transfer are not observed.

Rate Constants with ${}^{\bullet}$OH, $Cl_2^{\bullet-}$, and $Br_2^{\bullet-}$. The rate constants for the reaction of ${}^{\bullet}OH$ radicals with the compounds were determined by competition kinetics using 2-propanol (IP) as the standard solute ($k_{OH+IP} = 1.9 \times 10^9$ M^{-1} s^{-1}).[29,43] $Cl_2^{\bullet-}$ and $Br_2^{\bullet-}$ absorb with maxima at 345 and 360 nm, respectively. The bimolecular rate constants of the selenium compounds with these oxidants were determined by following the decay at the respective λ_{max} of the oxidant in the absence and the presence of different concentration of the selenium compounds. Details about the transient spectra and decay kinetics in individual cases are given below. The bimolecular rate constants for the selenium compounds with these radicals are listed in Table 2.

Reactions with SeM. The reaction of SeM with ${}^{\bullet}OH$ radicals at pH 7 produced a transient showing a broad absorption band with λ_{max} at 380 nm and a shoulder at the 280−290 nm region (Figure 1a). The transient at 380 nm decayed by first-order kinetics with $k = (1.2 \pm 0.1) \times 10^4$ s^{-1} and remained unaffected in the presence of oxygen. The contribution of the $H^{\bullet}$ atom reaction with SeM was found to be negligible as confirmed by running independent experiments. On the basis of our previous experience with the reactions of organic and organosulfur compounds with ${}^{\bullet}OH$ radicals, we can attribute the transient

TABLE 2: Absorption Maxima, Equilibrium Constants, and Rate Constants for the Formation and Decay of the Radical Cation of Selenium Compounds at Different pH

			rate constant for the reaction of selenium compounds with $^\bullet$OH, $Cl_2^{\bullet-}$, and $Br_2^{\bullet-}$ (M^{-1} s^{-1})				
compound	pH	λ_{max} (nm)	$^\bullet$OH/10^9	$Cl_2^{\bullet-}/10^9$	$Br_2^{\bullet-}/10^9$	$k_{(decay)}$ (selenium radical cations)	equilibrium constant (M^{-1})
SeU	7	410	9.9		4.1	2.7×10^9 M^{-1} s^{-1} (2k)	7.9×10^4
SeU	1	410		3.6		1.2×10^9 M^{-1} s^{-1} (2k)	1.9×10^4
SeM	7	380	14		5.2	1.1×10^4 s^{-1}	
SeM	1	480	5.6	4.6	1.3	7.5×10^8 M^{-1} s^{-1} (2k)	9.2×10^3
MeSeCys	7	350			1.0	4.3×10^5 s^{-1}	
MeSeCys	1	350	6.1	2.8		1.1×10^4 s^{-1}	
MeSeCys	0	370				1.6×10^4 s^{-1}	
		460				1.5×10^4 s^{-1}	1.3×10^3
SeCys	7	460	8.1		3.4	2.4×10^3 s^{-1}	
SeCys	1	560		5.3		1.1×10^4 s^{-1}	

absorption band at 380 nm either to an OH-adduct, where the $^\bullet$OH radical is attached to the selenium atom, or to one-electron oxidized species with selenium-centered radical cations. To distinguish between these two, pulse radiolysis studies were carried out with the specific one-electron oxidant, $Br_2^{\bullet-}$. The transient spectrum obtained by the reaction of $Br_2^{\bullet-}$ with SeM was compared with that obtained on the reaction of $^\bullet$OH radicals and found to be similar (spectra not shown). From this, the transient absorption spectrum given in Figure 1a is assigned to the one-electron oxidized species. This could be due to either a monomeric radical cation or a dimeric radical cation as such compounds have been found to form both. For this, the absorbance at 380 nm was monitored as a function of concentration in the concentration range of 0.025−1.5 mM and was found to remain independent of SeM concentration. This confirmed that the 380 nm absorption is only due to the monomer radical cation centered on the selenium atom. The absorbance at 280−290 nm is due to a carbon-centered radical which is formed because of H-abstraction.

At pH 1, the reaction of $^\bullet$OH radicals with SeM showed formation of a transient having a strong and broad absorption band at 480 nm (Figure 1b). To identify the nature of the transient species, the transient spectrum was compared with that produced by the reaction of $Cl_2^{\bullet-}$ radicals with SeM. The similarity in the spectrum confirmed that the reaction of $^\bullet$OH radicals with SeM at pH 1 also produced one-electron oxidation only.

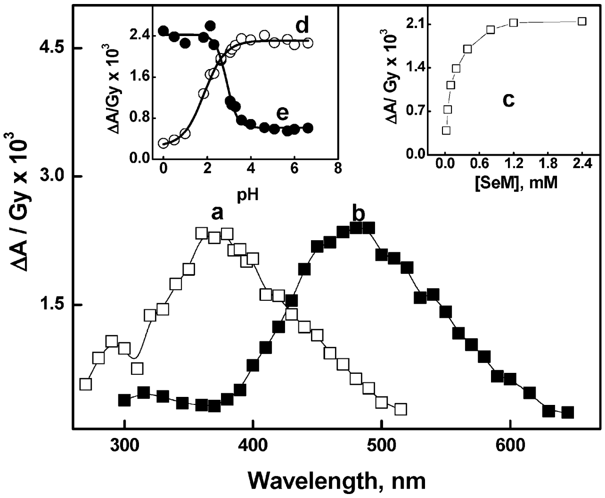


Figure 1. Difference absorption spectrum of the transient obtained on pulse radiolysis of (a) N_2O saturated solution of SeM (0.5 mM) at pH 7 and (b) N_2 saturated aqueous solution of SeM (1mM) at pH 1. Plot c of the inset shows the variation of absorbance at 480 nm as a function of the SeM concentration at pH 1, and plots d and e of the inset show the variation of absorbance at 380 and 480 nm, respectively, as a function of pH.

Unlike the results at pH 7, the absorbance at 480 nm was found to increase with increasing concentration of SeM in the range 0.025−2.4 mM and reach a saturation value for an SeM concentration of 1−2 mM (inset (plot c) of Figure 1). This increase in the absorbance cannot be due to the reaction of $^\bullet$OH radicals with increasing concentration of SeM but due to the reaction of initially formed transient species with SeM, indicating the formation of a dimeric species.

The transient absorption band at 480 nm decayed by second-order kinetics with a 2k value of $(7.5 \pm 0.2) \times 10^8$ M^{-1} s^{-1} and remained the same in N_2O/O_2 conditions. Since the kinetic and spectroscopic properties of the transient species formed on reaction of $^\bullet$OH radicals with SeM at pH 1 were different from those observed at pH 7, the absorption changes at 380 and 480 nm were followed as a function of pH in the range from pH 1 to 7.

As the pH of the solution is decreased, the transient absorbance at 380 nm decreases with the appearance of a new band at 480 nm. The variation in the absorbance at 380 and 480 nm, formed at a fixed SeM concentration of $\sim 5 \times 10^{-4}$ M, as a function of pH is given in the inset (plots e and d) of Figure 1, which shows an inflection point at 2.2 ± 0.3. This point corresponds to the pK_a of the carboxylic group, indicating the role of the functional group in the nature and formation of monomer and dimer radical cations. In addition to the increase in the absorbance of the 480 nm band with decrease in pH, the rate of formation was also observed to increase with a decrease in the pH. At pH 7, the 480 nm band is almost absent. The pseudo-first-order rate constant for the formation of the dimer, determined from the buildup kinetics at 480 nm, was found to increase from $(5.1 \pm 0.6) \times 10^4$ s^{-1} at pH 2.6 to $(1.1 \pm 0.1) \times 10^5$ s^{-1} at pH 1.8 and $(2.5 \pm 0.2) \times 10^5$ s^{-1} at pH 1.

Reactions with SeCys. The transient absorption spectrum obtained on reaction of $^\bullet$OH radicals with SeCys at pH 7 exhibits a broad absorption band with λ_{max} at 460 nm (Figure 2a), which decays by first-order kinetics with $k = (2.4 \pm 0.3) \times 10^3$ s^{-1}. Its decay remained unaffected in the presence of oxygen. On addition of *tert*-butyl alcohol (0.3 M), the transient absorption was completely quenched showing that the contribution of the $H^\bullet$ atom reaction with SeCys is negligible.

A reaction of SeCys with $Br_2^{\bullet-}$ at pH 7 was also studied, where a similar transient spectrum was observed (spectrum not shown). From the similarity, the transient absorption band at 460 nm is assigned to a selenium-centered radical cation. Also, the transient absorbance at 460 nm remained independent of

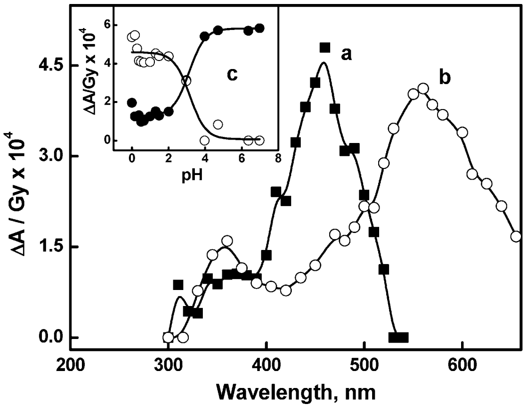


Figure 2. Difference absorption spectrum of the transient obtained on pulse radiolysis of N_2O saturated solution of SeCys (0.5 mM) at pH 7 (a) and pH 1 (b). The inset of Figure 2 shows variation of absorbance at 560 nm (○) and 460 nm (●) as a function of pH.

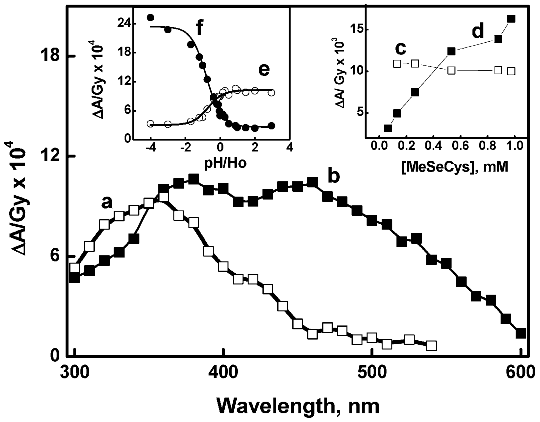


Figure 3. Difference absorption spectrum of the transient obtained on pulse radiolysis of (a) N_2O saturated solution of MeSeCys (0.5 mM) at pH 7 and (b) N_2 saturated aqueous solution of MeSeCys (1 mM at pH 0). Plots c and d of the inset show variation of absorbance at 350 and 460 nm, respectively, as a function of MeSeCys concentration at pH 0. Plots e and f of the inset show variation in the absorbance at 350 and 460 nm as a function of pH and Hammett acidity function scale Ho.

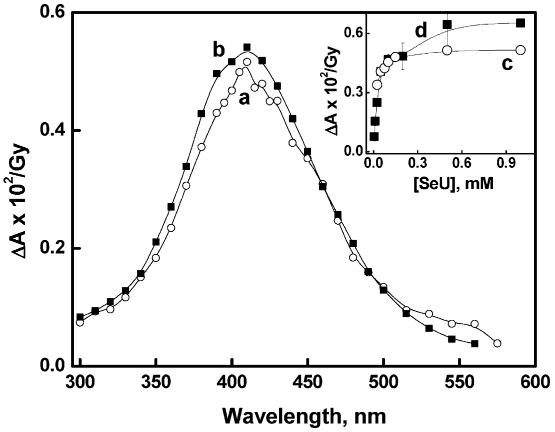


Figure 4. Difference absorption spectrum of the transient generated by pulse radiolysis of an N_2O saturated aqueous solution of selenourea at pH 7 (a) and pH 1 (b). The inset shows variation in absorbance at 410 nm as a function of selenourea concentration at pH 7 (c) and pH 1 (d).

the SeCys concentration in the 0.1−1 mM region, suggesting the nature of the transient to be of a monomeric species.

At pH 1, the reaction of SeCys with the $^{\bullet}$OH radical formed a transient absorbing at 560 nm (Figure 2b). This transient was found to decay by first-order kinetics with a rate constant of $(1.1 \pm 0.1) \times 10^4$ s^{-1}. The reaction with $Cl_2^{\bullet-}$ also gave the same transient absorbing at 560 nm, confirming that the transient formed with specific one-electron oxidation in the acidic medium is also a radical cation. This absorbance at 560 nm was found to be independent of the parent concentration, indicating the absence of any dimer radical cation formation. Although a monomeric radical cation is formed at pH 1 and at pH 7, there is a significant change in the absorption spectrum of the transient with pH, indicating the involvement of prototropic equilibrium. To understand the pH dependency, the variation of absorbance at 460 and 560 nm, formed on a pulse radiolysis of an N_2O-saturated aqueous solution of SeCys (5×10^{-4} M), as a function of pH was plotted as shown in the inset (plot c) of Figure 2, to get an inflection point at 3.13 ± 0.01. This point corresponds to the pK_a of the carboxylic group, indicating the role of the functional group in the nature and formation of the monomer radical cation.

Reactions with MeSeCys. The $^{\bullet}$OH radical reaction of MeSeCys at pH 7 produced a transient absorbing at 350 nm (Figure 3a). This transient is found to decay by first-order kinetics with a rate constant of $(4.3 \pm 0.4) \times 10^5$ s^{-1}. As noted in the case of other selenium-centered radical cations, no reaction with oxygen was observed. The reaction with the $^{\bullet}$OH radical at pH 1 also produced similar transient absorbing at 350 nm. Here, the reactions of $Cl_2^{\bullet-}$ and $Br_2^{\bullet-}$ with MeSeCys at pH 1 and pH 7 also produced similar transient absorbing at 350 nm. This 350 nm absorbing transient at all pHs from 1 to 7 was found to be independent of the parent concentration, indicating no contribution from the dimer radical cation, and is a monomer radical cation. At pH 1, this transient was found to decay by first-order kinetics with a rate constant of $(1.1 \pm 0.1) \times 10^4$ s^{-1}. When the pH was further decreased to 0 or less than that, a new transient absorption at 460 nm was observed (Figure 3b) in addition to a broad peak with the absorption maximum at 370 nm. While the transient absorbance in the 350−370 nm region was independent of the parent concentration (inset (plot c) of Figure 3), the transient absorbance at 460 nm was found to depend on the parent concentration in the range 0.06−1 mM, (inset (plot d) of Figure 3), indicating the formation of a dimer radical cation at high acidic conditions. At pH = 0, the band observed at 370 nm may be due to a monomeric species as its absorbance remained independent of solute concentration. With increasing acid concentration, the absorbance due to the dimer radical cation at 460 nm increased, while that at the 350−370 nm region decreased as seen in the inset of Figure 3 (e and f). A conversion of the monomer radical cation to the dimer radical cation is suggested by these absorbance changes.

Reactions with SeU. Some of earlier results on one-electron oxidation of SeU have been published in refs 33 and 34; however, for comparison they are briefly mentioned here. The reaction of $^{\bullet}$OH radicals and one-electron oxidants $Cl_2^{\bullet-}$ and $Br_2^{\bullet-}$ were studied with SeU at both acidic and neutral pH. The $^{\bullet}$OH radical reaction at both the pHs produced a similar transient showing an absorption maximum at 410 nm (Figure 4a and Figure 4b, at pH 1 and pH 7, respectively). Unlike the other compounds discussed above, the reaction of the H atom with SeU also produced a similar reaction. The absorbances at 410 nm increased with increasing concentration of SeU in the range 0.06−1.5 mM (inset (plots c and d) of Figure 4 at pH 1 and pH 7, respectively), suggesting dimer radical cation formation. The dimer radical cations of SeU react with oxygen with a rate constant of 8.6×10^7 M^{-1} s^{-1}. Similar transient spectra and kinetics was observed with one-electron specific oxidants, $Cl_2^{\bullet-}$

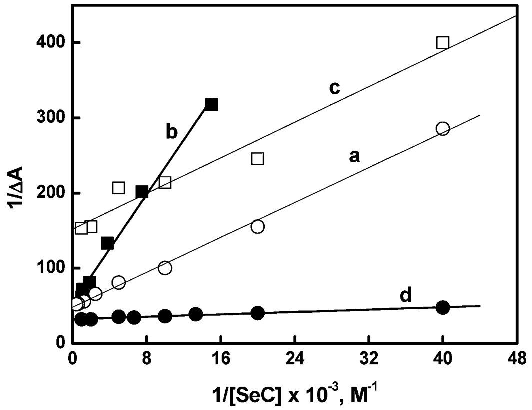
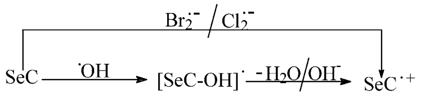


Figure 5. Double reciprocal plot showing the variation of absorbance at λ_{max} as a function of the concentration of the selenium compound according to eq 5. Here SeC represents a selenium compound: a = SeM (pH 1), b = MeSeCys (pH 0), c = SeU (pH 1), and d = SeU (pH 7).

at pH 1 and $Br_2^{\bullet-}$ at pH 7, confirming its radical cation nature. The 410 nm transient decayed by second-order kinetics with a $2k$ value of $(1.2 \pm 0.2) \times 10^9$ M^{-1} s^{-1}.

The overall reactions of all these selenium compounds (SeC) with $^{\bullet}OH$ radicals and $Cl_2^{\bullet-}$ and $Br_2^{\bullet-}$ radicals are given in eqs 3 and 4.



(3)

Under some favorable conditions, the monomer radical cation reacts with the parent molecule to form the dimer radical cation

$$(SeC)^{\bullet+} + SeC \rightleftharpoons (SeC)_2^{\bullet+} \quad (4)$$

Determination of Equilibrium Constant for the Formation of Dimer Radical Cations of Selenium Compounds (SeC). The dimer radical cations are formed in equilibrium with the monomer radical cations as per the equilibrium given in eq 4.

The equilibrium constant (K) for such dimer formation at a given pH is determined by following the absorbance changes at the absorption maximum of the transient at different concentrations of the parent and at a given dose, according to eq 5,

$$\frac{1}{\Delta A_{obs}} = \frac{1}{\Delta A_{max}} + \frac{1}{\Delta A_{max} K[SeC]} \quad (5)$$

where ΔA_{obs} and ΔA_{max} are the absorbance at a known wavelength and at any given concentration of selenium compound (0.025−2.4 mM) and the saturation absorbance of SeC (2.4 mM), respectively. The plot of $1/\Delta A_{obs}$ versus $[SeC]^{-1}$ gave a straight line with a slope of $1/K\Delta A_{max}$ and an intercept of $1/\Delta A_{max}$. Parts a−d of Figure 5 show linear plots for SeM at pH 1, MeSeCys at pH 0, and SeU at pH 1 and pH 7, respectively. From these data the equilibrium constants for the dimer radical cations of all these compounds were estimated and listed in Table 2.

4. Discussion

Structures of Monomer and Dimer Radical Cations. In the above compounds, since selenium has the high electron density and low ionization potential, the radical cations produced by the reaction of hydroxyl radicals and one-electron oxidants are mostly centered on the selenium atom. After oxidation, both monomer and dimer radical cations are observed in concentrations that are dependant on the pH and substitution. It is reported earlier that the seleniumcentered radical cation would be highly unstable and would have a high tendency to stabilize on coordination with another selenium or heteroatom. The monomer radical cation therefore has to attain stabilization through the intramolecular heteroatoms. Such stabilization is possible through the lone pair of electrons available on either the N or the O atom. The proposed structures of radical cations discussed below have been given in Scheme 2.

In the case of SeM, at pH 7, the radical cation on selenium can interact with the lone pair on either N atom of the amino group (**Ia**) or the O atom of the carboxylic group (**Ib**) forming a thermodynamically stable five-membered or six-membered ring, respectively. The six-membered ring is slightly less stable than the five-membered ring. At this pH, even though the amino group is in zwitterionic form, there will be a fast proton transfer from the NH_3^+ group to COO^- group thereby making the lone pair available. Both the structures are expected to show a similar optical absorption maximum.[18] However, because of a higher difference in the electronegativity between Se and O as compared to Se and N, the O atom can stabilize the radical cation more effectively than the N atom. Also **Ia** as observed in the case of methionine[18] is expected to be less stable and undergoes decarboxylation to produce a highly reducing α-amino selenyl radical. By an independent experiment, we have found no such reducing radical formation. These facts prompted us to suggest that the monomer radical cation of SeM is probably due to **Ib**. However, in the absence of conductivity studies and with this limited data, it is not possible to assign the exact nature of the monomer radical cation structure of SeM; probably both the structures may be considered.

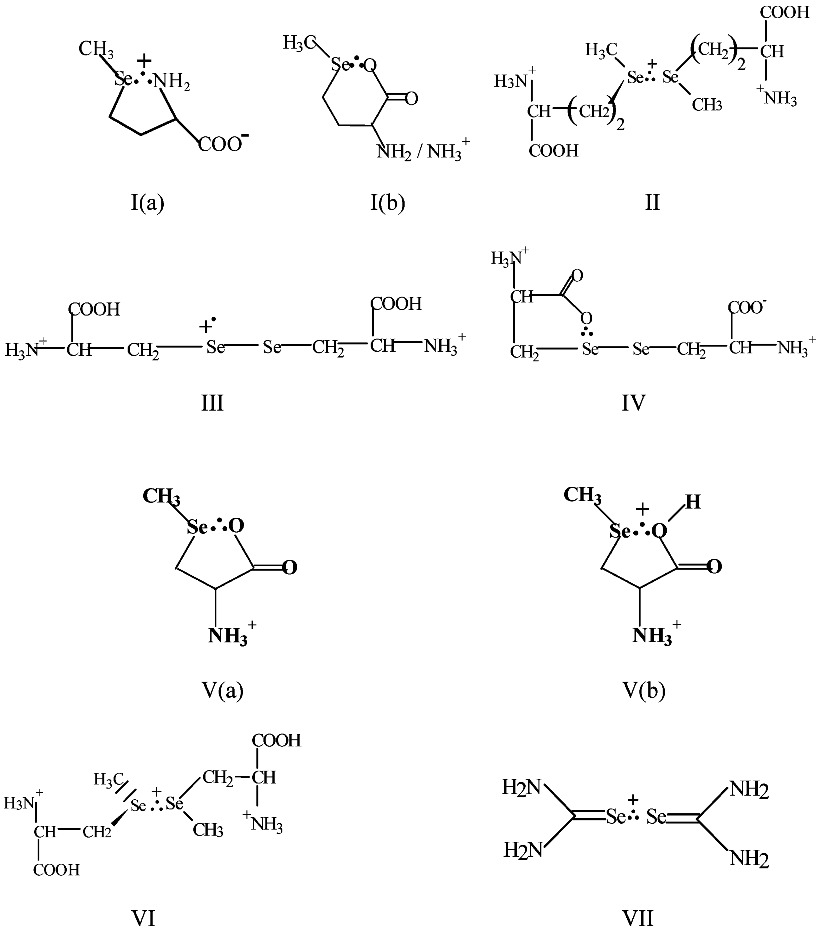
At pH 1, if the monomer radical cation of SeM is represented by **Ia**, because of the protonation of the amino group and the absence of a lone pair on the NH_3^+ group, intramolecular bonding between oxidized selenium and nitrogen is not expected. Similarly **Ib** also undergoes protonation at this pH and decreases the stability of the monomer. Therefore, at this pH, the stabilization can occur only intermolecularly through another selenium atom. Moreover, experimentally it is confirmed that the transient absorption band at 480 nm is due to a dimeric species. Thus the transient formed at pH 1 is assigned to a dimer radical cation (**II**) formed on the p orbital overlap of oxidized Se with the Se atom of another SeM molecule. The dimer radical cation is stabilized by the intermolecular two-center three-electron (2c−3e) bond between two Se atoms, where the two valance p-orbitals are mixed head-on, resulting in a hemibond of σ nature.[18,19,31−33]

As discussed above, this process of formation of either a monomer or a dimer radical cation is pH dependent with an inflection point at 2.1, which is similar to the pK_a of SeM. This indicates that these processes are controlled by the pK_a of the carboxylic acid group, which further facilitates the availability of the lone pair on either the O atom or the N atom.

Since SeCys is a diselenide, on oxidation by hydroxyl radicals and one-electron oxidants it produced a radical cation, which can be stabilized as a monomer radical cation due to the presence of an intramolecular Se−Se bond and its chemical structure, given in **III**.

If **III** represents the monomer radical cation, one would not expect any pH dependency on the transient absorption spectrum, as a similar radical cation should be formed at all the pHs. However, the radical cations of SeCys show significant spectral

SCHEME 2: Chemical Structures of the Monomer and Dimer Radical Cations of Selenium Compounds



shift, and by following the absorbance changes as a function of pH, an inflection point at 3.1 was observed. This indicates that the radical cation structure of such a diselenide is also influenced by the pK_a of the carboxylic acid group; therefore a different structure involving the participation of the O atom of the carboxylic acid group is possible. Accordingly, the species formed at pH 7, absorbing at 460 nm, is assigned to **IV**, which acquires stabilization through the carboxylic oxygen atom, while the transient species formed at pH 1 and absorbing at 560 nm is assigned to **III**.

MeSeCys is structurally similar to SeM; it is only a smaller analogue. Therefore, one would expect very similar oxidation chemistry. But its oxidation produced radical cations at all the pHs from 1 to 7 absorbing at 350 nm. The dimer radical cation formation was observed at pH < 0 only. Here the selenium-centered radical cations can be stabilized only by the carboxylic oxygen and not through the amino group, as it involves only four-membered ring formation, while the former gives a five-membered ring stabilization. However due to the pK_a of the carboxylic acid group, the nature of the radical will be different at a different pH, as seen by slightly different absorption spectra at pH 7 (350 nm) and pH 1 (350−370 nm). Accordingly, the possible structures are given by **Va** at pH 7 and **Vb** at pH 1. As observed in case of SeM, the proton transfer between the amino group and the carboxylic acid anion may not be significant in the formation of monomer radical cations, as the N atom is not involved in stabilization. The possible dimer observed at pH < 0 is given in **VI**.

SeU, at all pHs in the pH range of 1−7, showed only formation of dimer radical cations. Here the monomer radical cation could not be stabilized by any intramolecular heteroatoms such as N or O atoms, as such stabilization yields highly strained structures. Therefore the only possibility is the formation of a dimer radical cation absorbing at 410 nm (**VII**), which does not show any spectral shift with pH.

Comparison with Sulfur Analogues. It is interesting to compare the nature of oxidation chemistry of the above selenium compounds with that of their sulfur analogues. The one-electron oxidation chemistry using pulse radiolysis coupled with absorption and conductivity detection of most of the sulfur compounds has been well documented in the literature.[1−3,18−29] It is reported that the one-electron oxidized sulfur atoms in organic sulfides generally show a high tendency to be stabilized in S∴S or S∴X bonds by coordination with a second sulfur atom or heteroatom. To test whether such similarity in the nature of radical cation structure is seen between selenium and sulfur, comparisons were made between each individual pair as discussed below.

The nature and spectral behavior of one-electron oxidation of SeM are similar to those reported for methionine, that is, monomer radical cations at neutral pH and dimer radical cations at acidic pH, with their respective transient absorption maxima at 380 and 480 nm. The equilibrium constant for the formation of a dimer radical cation of SeM (9.2×10^3 M^{-1}) is higher as compared to that of methionine (1.9×10^3 M^{-1}). The decay of the dimer radical cation of SeM is slower (7.3×10^4 s^{-1}) as compared to that of the methionine dimer radical cation (1.5×10^5 s^{-1}). Unlike the monomer radical cations of methionine, the ones from SeM are much longer lived and easily detectable. The half-life of a monomer radical cation of methionine is reported to be 200 ns[18] whereas that of a SeM monomer radical cation is 6.4×10^3 μs. The monomer radical cations of methionine undergo fast decarboxylation to give highly reducing α-amino thiyl radicals, and no such reaction was observed with SeM.

SeCys being a diselenide forms a monomer radical cation at all the pHs both neutral and acidic. No dimer radical cation formation is observed at any of the pHs studied. Similarly, its sulfur analogue cystine also forms a monomer radical cation at all the pHs.[41] The radical cations of SeCys exhibit maximum absorption at 460 nm at pH 7, and at 560 nm at pH 1, with an inflection point of 3.2 ± 0.2. On the other hand, the radical cations of cystine do not show any detectable absorption spectrum in these wavelength regions under these conditions.[41] The radical cations of SeCys decay by first-order kinetics with an observed rate constant of 2.4×10^3 s^{-1}, while those of cystine are expected to be much shorter lived.

MeSeCys forms monomer radical cations in the pH range from 1 to 7, with absorption maximum at 350 to 370 nm. At pH 0, formation of a dimer radical cation is observed with absorption maximum at 460 nm. Methyl cystine under these conditions exhibits very similar pH dependent transient behavior, with the monomer radical cation absorbing at 385−400 nm in the pH range from 1 to 7 and the dimer radical cation at pH < 0 absorbing at 475 nm.[44] However, for methyl cystine, transient spectra could be observed only under highly acidic conditions,[44] whereas in the case of MeSeCys, it was possible to observe transient spectra at all the pH values from 1 to 7. The monomer radical cations of MeSeCys decay by first-order kinetics with rate constants of 4.3×10^5 and 1.1×10^4 s^{-1} at pH 7 and pH 1, respectively, and the dimer radical cations at pH 0 decay by first-order kinetics with a rate constant of 1.5×10^4 s^{-1}. The decay kinetics of the monomer radical cations of methylcysteine was reported to be 2.6×10^4 s^{-1} at pH 0.[43]

Since SeU is a selenone, it forms dimer radical cations only at all the pHs, with no detectable formation of monomer radical cations even under highly acidic conditions and low substrate concentrations, similar to that observed for thiourea. The corresponding absorption maxima for the dimer radical cations of SeU and thiourea are respectively 410 and 400 nm. The dimer radical cations in both the cases display similar kinetic behavior with the respective second-order rate constants of 1.2×10^9 and 9.0×10^8 M^{-1} s^{-1}. Earlier we reported that the dimer radical cations of SeU are more stable than those of thiourea.[33]

The above studies indicate that the oxidation chemistry of selenium compounds is comparable to that of their sulfur analogues. The nature of the transients is very similar. In both the cases, the radical cations are stabilized either by the lone pair available from intramolecular heteroatoms or by the intermolecular dimerization. However, the radical cations from selenium analogues show much longer lifetimes and the dimers are more stable. This similarity in the pH dependent transient behavior of selenium and sulfur compounds and the easier oxidation of selenium compounds make them better alternatives as antioxidants, radioprotectors, and GPx mimics.

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