Redox Dependence of the Rate of Interaction of Hydroxyl Radical Adducts of DNA Nucleobases with Oxidants: Consequences for DNA Strand Breakage

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Abstract: Oxidants and oxygen enhance the sensitivity of cells to radiation. To understand this effect at the mechanistic level, the kinetics of interaction of the OH adducts of pyrimidines and 2′-deoxynucleosides with oxidants (quinones, viologens, nitroarenes) of differing one-electron reduction potentials (−447 to 99 mV) have been determined in aqueous solution at pH 7.5−8 using the technique of pulse radiolysis. With quinones and viologens, this interaction produces the one-electron-reduced species of the oxidants, with rate constants (3.0×10^6 to 2.0×10^9 $dm^3\ mol^{-1}\ s^{-1}$), which depend significantly on the redox potential of the oxidant. This dependence is consistent with an outer-sphere electron-transfer mechanism. In contrast, an addition (nitroxyl) adduct is formed with nitroarenes with rate constants that are weakly if at all dependent on the one-electron redox potentials of the nitroarenes. Using poly C as a probe for strand breakage, the resulting nitroxyl adduct of the nucleobase radical species in the absence of oxygen leads to strand breakage involving a base to sugar transfer of the radical site with a rate constant of 2.7 s^{-1}. In contrast with benzoquinone, the resulting carbocation of the cytosine moiety of poly C does not result in strand breakage but leads to a decrease in the yield of ssb by ∼60%. Therefore nitroarenes mimic the effects of oxygen in leading to ssb on interaction with hydroxyl radical damage of nucleobases.

Introduction

Exposure of cells to ionizing radiation causes biologically deleterious effects such as inactivation, transformation, and mutagenesis. These various biological effects are generally thought to be a consequence of chemical modifications to DNA.[1] A significant contribution to DNA damage results from attack by radicals formed from ionization of the water molecules in the immediate environment of DNA. Of these radicals, the hydroxyl radical is thought to be the most damaging.[2,3] Further, the endogenous attack on DNA of this oxidative species generated at low steady-state levels leads to detected DNA damage.[4−7]

The interaction of the $OH^•$ radical with purines and pyrimidines has been widely studied and results in the formation of adducts with different redox properties, reflecting the site of addition of the $OH^•$ radical.[1,8,9] The situation is less clear-cut in the case of purines[1,9,10−15] although OH radicals add to purines with a pronounced preference for addition to C(4), C(5), and C(8) ring positions.[9,10,15]

Nitroarenes, developed as oxygen mimetics,[16] sensitize hypoxic cells to ionizing radiation, involving interactions at the free-radical stage in the development of DNA damage. The presence of low concentrations of nitroarenes dramatically enhances the yield of cellular DNA strand breaks[17,18] but not the yield of oxidative base damage.[19,20] The OH adducts of the nucleobases interact with oxygen by addition to form peroxyl radicals.[21] Significantly, substituted nitrobenzenes also interact with the "reducing" OH adducts of pyrimidine nucleosides by addition to form a nitroxyl-type radical,[22,23] which is stable to

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heterolysis at physiological pH. In contrast with thymine and cytosine, where N(1) is protonated, the adduct undergoes heterolysis to yield the corresponding radical anion of the nitrobenzenes and an oxidized pyrimidine.[22] With thymine, its glycol, an indicator of oxidative damage, is a major product of this interaction.[24] 1,4-Benzoquinone also produces a glycol on its interaction with the C(5)−hydroxyl adduct of thymine and uracil.[25]

Very little is known about the mechanism of interaction of other types of oxidants such as quinones and viologens with the "reducing" OH adducts of the DNA nucleobases; hence it is timely to determine whether this reaction occurs by an outer-sphere electron-transfer mechanism[26] or by adduct formation[27] by investigation of the redox dependence of the reactivity of the OH adducts of the DNA nucleobases with a series of oxidants (quinones, nitroaromatics, viologens) on their one-electron reduction potential. Since nitrobenzenes[22] form adducts on interaction with the OH adducts of pyrimidines, the question arises as to whether these nitroxyl adducts induce single-strand breakage (ssb) involving H-atom abstraction from the sugar moiety analogous to the formation of ssb by peroxyl radical adducts of the polynucleobases[5,6,28−30] using poly C as a probe for ssb formation. Therefore, consequences of an outer-sphere electron-transfer reaction in contrast to adduct formation leading to ssb induction have significant implications for modification of DNA damage by oxidants.

Experimental Section

All gases (BOC, zero grade) and chemicals used (Aldrich, Sigma, BDH, Pharmacia) were of highest purity (95−100%). The following oxidants together with their one-electron redox potentials (E_7^1 value[31] shown in parentheses) were used: benzoquinone (BQ) (99 mV), methyl-1,4-benzoquinone (23 mV), 1,4-naphthoquinone-2-sulfonate (−60 mV), 1,4-naphthoquinone (NQ, −140 mV), duroquinone (−240 mV), nifuroxime (−253 mV), nitrofurantoin (NFT, −264 mV), 3,4-dinitrobenzoic acid (PNBA, −271 mV), benzyl viologen (−350 mV), 4-nitroacetophenone (PNAP, −353 mV), 9,10-anthraquinone-2-sulfonate (−390 mV), 4-nitrobenzoic acid (−396 mV), and methyl viologen (−447 mV). BQ was recrystallized from absolute ethanol and NQ was purified by sublimation under reduced pressure. All the solutions were prepared using water that had been purified using a Milli-Q system (Millipore). The pyrimidines, purines, and their nucleosides (2×10^{-3} mol dm^{-3}) were prepared in 5 mmol dm^{-3} phosphate buffer (pH 7.4). The concentrations of the oxidants range from 0.25 to 1×10^{-4} mol dm^{-3} for the strong oxidants having redox potential up to −240 mV and from 0.25 to 1×10^{-3} mol dm^{-3} for weaker oxidants. The concentrations of the nucleobases were chosen so that the majority of the OH radicals interact with the nucleobase instead of the oxidants. Poly C (Pharmacia Biotech) (2×10^{-3} mol dm^{-3}) was used without further purification and prepared in 5 mmol dm^{-3} phosphate buffer at pH 7.8 containing 7×10^{-2} mol dm^{-3} $NaClO_4$ and allowed to dissolve at 277 K for ∼18 h. The pH values of the solutions were adjusted when necessary using either $HClO_4$ or NaOH. Solutions were generally saturated with N_2O to convert e^-_{aq} to OH radicals or with N_2 to remove O_2, for at least 30 min prior to irradiation using a syringe-bubbling technique which permits small amounts to be fully and rapidly saturated.

Pulse radiolysis experiments were performed using a 4.3-MeV linear accelerator with either optical detection system[11] or laser light-scattering detection[5,32] as previously described. The data-handling procedures have been described previously.[33] For optical studies, solutions were irradiated in a quartz cell of 0.2 dm path length at 296 ± 3 K with electron pulses of 1.6-μs duration. Due to their sensitivity to light, quinones were handled with care using glass filters and a shutter which was opened only a few seconds before irradiation. Dosimetry was carried out using KSCN as dosimeter at 480 nm and assuming $G = 0.3$ μmol dm^{-3} J^{-1} and $\epsilon = 710$ m^2 mol^{-1}. A dose/pulse of 11 Gy was used to determine the optical absorption spectra of the various species formed. A dose/pulse of ∼2 Gy was used for kinetic measurements. To determine the optical absorption spectra of the one-electron reduced oxidants sodium formate was used in excess (0.1 mol dm^{-3}) to convert H-atoms and OH radicals into the reducing $CO_2^{\bullet-}$ radical.

Time-resolved laser light-scattering (TRLS) measurements with aerated and N_2O-saturated, aqueous solutions of poly C (2×10^{-3} mol dm^{-3}) were monitored and recorded as indexes of strand break formation. For solutions containing BQ or NFT, a concentration of 5×10^{-5} mol dm^{-3} was used to ensure that the majority of the OH radicals interacted with poly C. Prior to irradiation, the poly C solutions were centrifuged at 9−10 krpm for 20 min. After saturation of the solutions with N_2O or aerating, the poly C solution was transferred to the cuvette by filtering through an "in-line" Durapore membrane filter (0.45 μm, Millipore). The method for ensuring that the enclosed system sustains anaerobic conditions has previously been described.[6] The radiation dose used was 21 Gy/pulse.

Results

Interaction of OH Adducts of Nucleosides with Quinones and Viologens. The interaction of the OH adducts of purines and pyrimidines with a series of quinones and viologens of different E_7^1 values[31] were carried out in aqueous solution at pH 7.5−8.0. From the optical absorption spectrum of the species produced on the interaction of BQ with the OH adduct of 2′-deoxycytidine, it is evident that the OH adduct of 2′-deoxycytidine reduces BQ to form its semiquinone radical anion.[34] With all the oxidants, the interaction of the OH adduct of thymine, cytosine, thymidine, 2′-deoxycytidine, 2′-deoxyguanosine, and 2′-deoxyadenosine produces the one-electron reduced species of the oxidant. The yields of benzosemiquinone radicals produced on reaction with the OH adducts are cytosine 83%, thymine 63%, 2′-deoxycytidine 75%, thymidine 47%, 2′-deoxyguanosine 44%, and 2′-deoxyadenosine 67% and are comparable with those of the OH adducts with reducing properties.[1,8,9,15,25,35]

The second-order rate constants for interaction of the OH adducts of the nucleobases with the oxidants were determined from the linear dependence of the first-order rate of formation of the one-electron reduced oxidant on the concentration of the oxidant. The dependences of these rate constants for reaction of the purine and pyrimidine OH adducts with the quinones and viologens on their E_7^1 values are shown in Figure 1. For cytosine, 2′-deoxycytidine, and thymine, the rate constants do not show a strong dependence on the redox potential of the oxidant for those with E_7^1 values more positive than −240 mV, whereas the rate constants show a linear dependence for oxidants with more negative redox potentials. With thymidine, the dependence on the one-electron redox potentials of the oxidants has been treated as linear, although there is some curvature.

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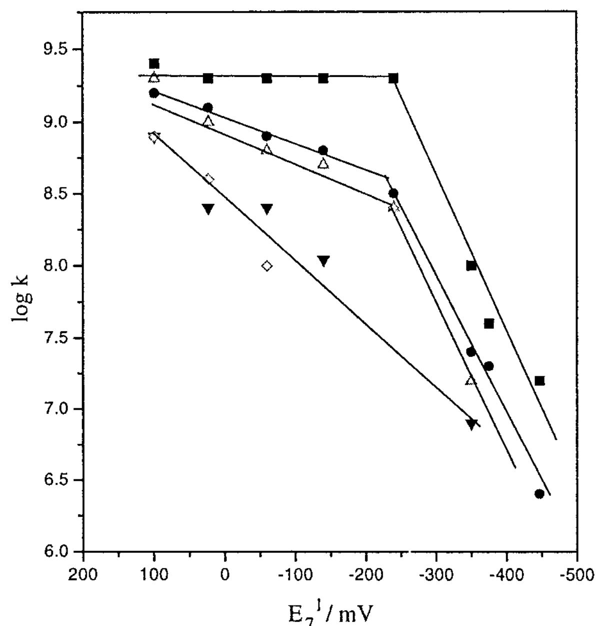

Figure 1. Redox dependence of the rate constants determined for the interaction of quinones and viologens with the OH adducts of the following purines and pyrimidines: cytosine (■), thymine (●), 2′-deoxycytidine (△), thymidine (▽), and 2′-deoxyguanosine (◇).

The slopes of the redox dependencies for cytosine, 2′-deoxycytidine, thymine, and thymidine are 11.7, 11.0, 10.9, and 8.5 V^{-1}, respectively, and are consistent with those of ~10 V^{-1} for processes that involve an outer-sphere electron-transfer process.[36]

With 2′-deoxyguanosine, the rate constants for the interaction of its OH adducts with oxidants depend on the E_7^1 value of the oxidant with a slope of ~8.5 V^{-1}. With 2′-deoxyadenosine, the rate of reaction of its OH adducts is too slow to observe with BV^{2+}, consistent with the lack of reaction also reported with MV^{2+}, a weaker oxidant.[14] An additional complication with 2′-deoxyadenosine is that the C(8)−OH adduct, which has reducing properties, undergoes a ring-opening process with a rate constant[14] of 3.3×10^4 s^{-1}. This ring opening will compete with the interaction of the C(8)−OH adduct with the oxidants and complicate the redox assessment of the interactions. Therefore, the rate constants for interactions with 2′-deoxyadenosine have not been included in Figure 1.

Redox Reactions of OH Adducts of Nucleosides with Nitroaromatics. The interactions of the nitroarenes with OH adducts of cytosine, thymine, and 2′-deoxycytidine were investigated. Figure 2 shows the time-resolved optical absorption spectrum of the transient species formed on interaction of the OH adduct of cytosine with PNBA. The λ_{max} of the transient optical absorption is 20 nm less than that for the one-electron reduced radical of PNBA. Similar spectral shifts of the optical absorption to the blue have been observed for the reaction of other nitroarenes with the OH adducts of nucleobases.[22] It is confirmed that these nitroarenes interact by formation of a nitroxyl radical adduct, as reported earlier where the yield of addition products is quantitative for thymine and cytosine.[22]

The rate constants for formation of the nitroxyl adduct were determined from the linear dependence of its first-order rate constant for formation on the concentration of the nitroarene. The dependence of the rate constants for interaction of the OH adducts of the pyrimidines and 2′-deoxycytidine with the

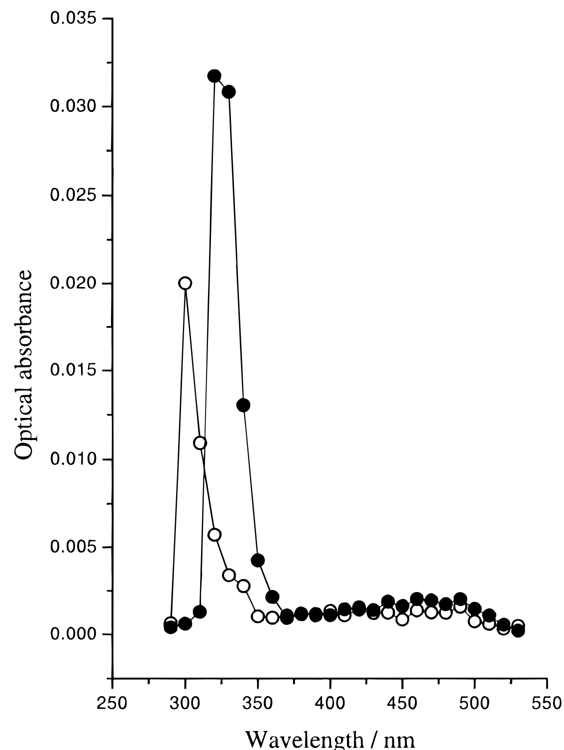

Figure 2. Optical absorption spectra of the one-electron reduced form of PNBA (●) and the nitroxyl adduct (○) formed on reaction of PNBA (5×10^{-5} mol dm^{-3}) with the OH adduct of cytosine (2×10^{-3} mol dm^{-3} cytosine).

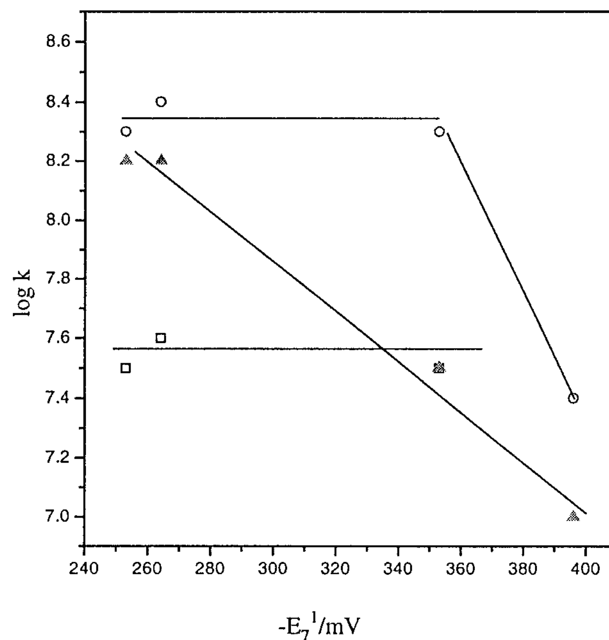

Figure 3. Redox dependence of the rate constant determined for the interaction of nitroarenes with the OH adducts of cytosine (○), thymine (□) and 2′-deoxycytidine (▲).

nitroarenes on their redox potentials is shown in Figure 3. With thymine and cytosine, the rate constants are essentially independent of the redox potential of the nitroarenes with the exception of PNBA, the weakest nitroarene oxidant used, where the rate constant is significantly lower. With 2′-deoxycytidine, the interaction of its OH adducts with the nitroarenes shows a redox dependence with a slope of ~6 V^{-1}.

Redox Reactions of OH Adducts of Polynucleotides with Oxidants. The rate constants for reaction of the OH adducts

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Table 1. *A*-Values and Rate Constants for Strand Breakage on Interaction of OH Adduct of Poly C with BQ or NFT

	air[a]		N_2O[a]	
	A-value	rate const/s^{-1}	*A*-value	rate const/s^{-1}
poly C	0.09[b]	1.4	0.07[b]	5.5 (7.9)[d]
	0.30[c]		0.34[c]	
poly C + BQ	0.04[b]	1.0	0.04[b]	7.3
	0.24[c]		0.10[c]	
poly C + NFT	0.05[b]	2.6	0.07[b]	2.7
	0.31[c]		0.33[c]	

[a] Irradiated in the presence of air or N_2O. [b] The *A*-value for the prompt change occurs within <0.2 s. [c] The *A*-value determined at 4 s. [d] Reference 6.

of the polynucleotides, poly A, C, and U with selected oxidants (BQ, NQ, NFT) were determined to be in the range $(1.2-6) \times 10^8$ dm^3 mol^{-1} s^{-1}. The respective semiquinone radicals of BQ and NQ are formed on interaction with the OH adducts of the nucleobase moiety. The yields of BQ semiquinone radical are consistent with the OH adducts with reducing properties being involved in the electron-transfer process.[37,38] With NFT, the λ_{max} of the resulting transient species is blue shifted after reaction with the OH adducts of the polynucleotides compared with that for the one-electron reduced species of NFT. From the similarity of these findings, it is inferred that NFT reacts with the OH adducts of the polynucleotides with reducing properties by addition to form a nitroxyl radical adduct as proposed with the nucleobases.[21]

Strand Breakage. The changes in light-scattering intensity (LSI) following pulse radiolysis of an aqueous solution of poly C at pH 7.8 under aerobic and N_2O-saturated conditions are used as benchmarks for the corresponding changes in the presence of oxidants. The changes in LSI, expressed as *A*-values, are shown in Table 1 and are similar to the yields of ssb determined previously.[5,6] In both aerobic and N_2O conditions, there is an initial fast change of LSI representing ~20-30% of the total change, followed by a slower one. The initial fast change in LSI is due to direct attack of OH radicals on the sugar moiety[5,6] whereas the slow process arises from hydrogen abstraction from an adjacent sugar[39] by a base peroxyl radical[5,40] under aerobic conditions or the reducing OH adduct under anaerobic conditions.

The time-dependent changes in LSI produced on interaction of BQ with the OH adducts of poly C at pH 7.8 under N_2O saturation conditions are shown in Figure 4. The *A*-value and the rate constant determined for the slow process are shown in Table 1. BQ has a small effect on the induction of ssb by the prompt process whereas the slow process, seen in the absence of BQ, is reduced dramatically with formation of the BQ semiquinone radical anion. Aeration of the samples results in similar changes in LSI in the absence and presence of BQ, since BQ does not compete efficiently with oxygen for the OH adducts of the cytosine moiety.

The changes in LSI on reaction of the OH adducts of poly C with NFT under N_2O-saturated conditions are shown in Figure 4. The *A*-values and rate constants for formation of ssb by the slow process are shown in Table 1. Under N_2O conditions, the yield of ssb (*A*-value) is the same in the presence and absence of NFT. However, the rate constant for formation of the ssb by the slower process is a factor of ~2 less than that in the absence of NFT. The yield of the prompt ssb is not significantly affected by the presence of NFT. The nitroxyl adduct of NFT observed optically decays, resulting in bleaching of absorption at 400 nm, presumably due to formation of a product that absorbs less than NFT. The decay as shown in Figure 4, consists of two components, the slower one of which represents

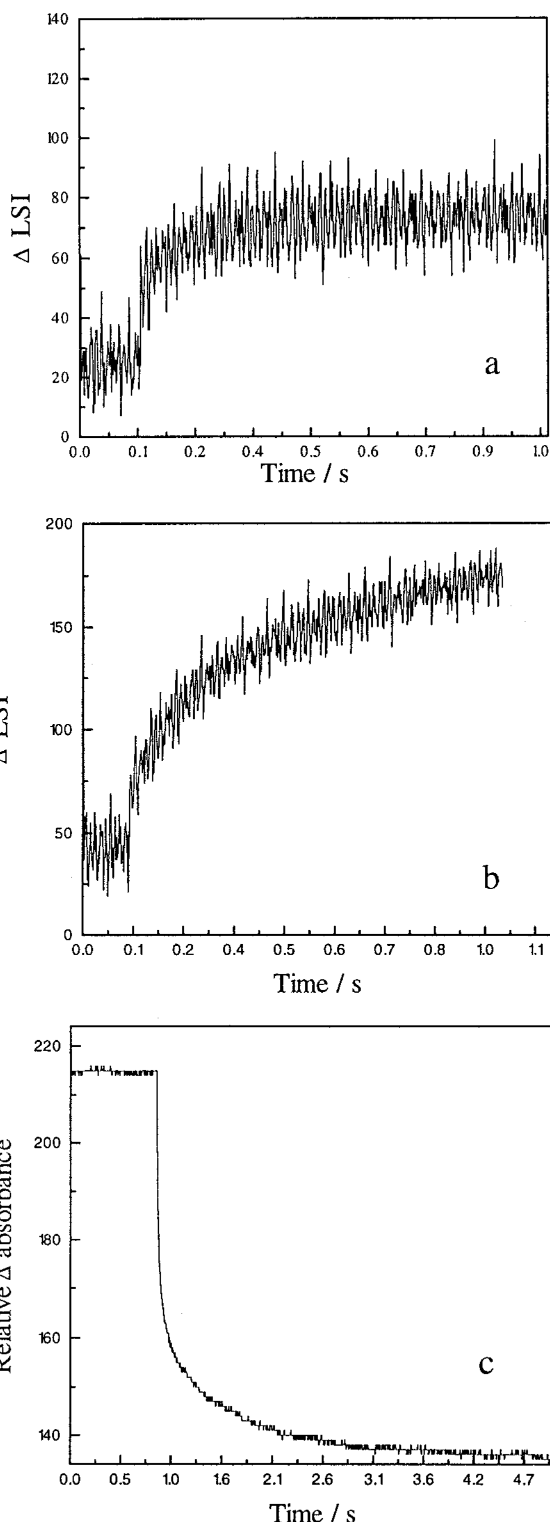

Figure 4. Time-resolved changes in light-scattering intensity (a) and (b) and optical absorption (c) on pulse irradiation of a N_2O-saturated, aqueous solution containing 2×10^{-3} mol dm^{-3} poly C and either (a) 5×10^{-5} mol dm^{-3} BQ or (b and c) 5×10^{-5} mol dm^{-3} NFT.

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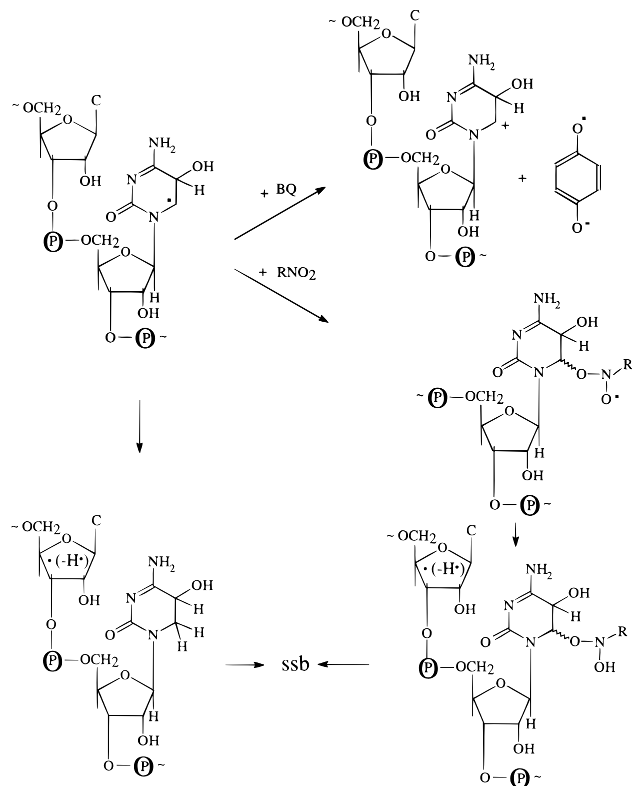
Scheme 1. Proposed Mechanism for the Interaction of the Various Oxidants with the OH Adducts of Nucleobases, Using Poly C as an Example[a]



[a] For clarity, H-atom abstraction from the 5′ neighboring sugar moiety is shown but abstraction from the 3′ neighboring sugar moiety may also occur.

~50% of the overall loss of absorbance and decays with a rate constant similar with that for ssb formation, determined by LSI. Decay of the one-electron reduced species of NFT does not lead to significant bleaching of absorbance at 400 nm. Therefore the faster component, although not leading to ssb, represents loss of the nitroxyl adduct resulting in significant bleaching. These findings reflect formation of two adducts, one of which is preferentially involved in ssb formation (see Discussion). Under aerobic conditions, the yields of ssb are similar in the absence and presence of NFT.

Discussion

It is evident that the mechanism for the interaction of the OH adduct of pyrimidines and deoxynucleosides depends on the type of oxidant used. It is proposed that the reaction involving quinones and viologens proceeds by an outer-sphere electron transfer in contrast to the formation of an adduct with nitroarenes.[22] The interaction of the OH adduct of the pyrimidines and deoxynucleosides with the quinones and viologens is shown in Scheme 1, using poly C and BQ as the example. It is proposed that the interaction of the OH adducts with the stronger oxidants is diffusion controlled. With the weaker oxidants, the interaction becomes activation controlled and proceeds by an outer-sphere electron transfer at pH 7−8. Oxidation of the C(5)−OH adduct of thymine and uracil by BQ gives their corresponding glycols of the pyrimidines in stoichiometric amounts.[25] From these yields of one-electron reduced quinones and viologens and glycols,[25] the OH adducts of the nucleobases, known to have reducing properties, are involved. Further support for this mechanism is obtained from the dependences in Figure 1, where the slopes correspond with those predicted for outer-sphere electron transfer.[16,26] An alternative reaction involving adduct formation followed by heterolysis could only account for the observations if heterolysis occurs with a rate constant of $\gg 2 \times 10^5\ s^{-1}$. An interaction to produce a radical adduct on reactions of methyl or OH radicals with BQ has been proposed occurring at carbon[41,42] followed by rapid tautomerization to give a semiquinone adduct. It is predicted though that the dependence for adduct formation from the Marcus relationship would be $\sim 3-6\ V^{-1}$ as determined for adduct formation between α-hydroxyalkyl radicals and nitroarenes.[43,44] Therefore, an outer-sphere electron transfer is the preferred interaction with quinones and viologens where the transition state must have significant ionic character, as discussed for the interaction of α-hydroxyalkyl radicals, known reducing radicals, with oxidants.[26,44] From the redox dependence in Figure 1, it is evident that the 5-hydroxycytosin-6-yl radical is a stronger reductant than the 5-hydroxythymin-6-yl radical.

Scheme 1 shows the proposed mechanism for interaction of the nitroarenes with OH adducts of pyrimidines involving an addition reaction, using poly C as an example. It has previously been shown[22,23] that the interaction of substituted nitrobenzenes involves those OH adducts of the pyrimidines with reducing properties and produces nitroxyl radical adducts. Using a series of nitroarenes, it is confirmed that nitroxyl adducts are formed at pH 7.4. The nitroxyl radical adducts are stable and do not decay by heterolysis to produce the radical anion of the nitroarene if N(1) is substituted. With several nitroarenes including misonidazole, elevated levels of glycolic products are formed following irradiation of thymine under anaerobic conditions.[24] Elevated levels of oxidative damage such as thymine glycols however were not observed in DNA or in cellular DNA on irradiation under anaerobic conditions in the presence of the nitroarene, misonidazole,[19,20] consistent with the stability of the nitroxyl adduct to hydrolysis. These observations are consistent with the reaction proceeding via an adduct which, depending on the nucleobases, may have some ionic character. From the redox dependence in Figure 3, the magnitude of the slopes is consistent with adduct formation[26] and not outer sphere electron transfer.

Since the reaction mechanisms discussed depend on the type of oxidant, poly C was used to investigate if the nitroxyl radical adduct and/or the carbocation, produced on one electron reduction of quinones, act as precursors to ssb. At the concentrations of BQ, NFT and poly C used, the majority of the OH radicals interact with poly C (> 85%).[45] Under anaerobic conditions but in the presence of BQ the yield of ssb induced in poly C is reduced so that the majority of the ssb are produced by the fast process, previously assigned to sugar radical precursors.[5] Since the 5-hydroxycytosin-6-yl radical interacts with BQ by outer-sphere electron transfer, it is inferred that the resulting carbocation is not a precursor to ssb. A possible hydration reaction of the carbocation may occur to produce glycolic products or deprotonation may also occur to yield a hydroxylated product at C(5). Under the conditions used,

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the interaction of BQ with the C(5)−OH adduct of cytosine ($k \sim 2.6 \times 10^4$ s^{-1}) will compete favorably with the radical-transfer process from the cytosine radical to give a ssb ($k = 5.5$ s^{-1}). The protection against ssb by BQ is not due to scavenging of OH radicals. With poly U, tetranitromethane, a powerful oxidant, was also shown to protect against ssb involving base to sugar radical transfer.[46] Irradiation under oxic conditions in the presence of BQ results in the formation of ssb. The yields and kinetics (Table 1) are consistent with involvement of peroxyl radicals, since oxygen competes favorably with BQ for the OH adduct of poly C at the concentrations used (<20% of the nucleobase OH adducts will interact with BQ). Further, the peroxyl radical resulting from oxygen addition to the OH adduct is expected to have oxidizing properties[47] and therefore should not be reactive with BQ, consistent with the formation of ssb.

In contrast, ssb are formed on irradiation of poly C under anaerobic conditions in the presence of NFT. The reaction mechanism proposed is shown in Scheme 1. The C(5)−OH adduct of poly C interacts preferentially with NFT under anaerobic conditions, resulting in the formation of an adduct.[22,23] From the lifetime of the nitroxyl adducts of poly C, it is inferred that two adducts are formed. These adducts are suggested to represent the two possible isomeric forms, e.g., the cis and trans isomers, which have slightly different stabilities. A factor of 2 difference in the stability of the isomeric forms of the adducts produced on reaction of 5-hydroxy-6-methylisocytosine with PNAP has been observed.[23] At pH 7.8, one of the adducts is proposed to abstract an H-atom from the sugar moiety, since the loss of the adduct is concomitant with the formation of ssb. If the H-atom is abstracted from C(2′) or C(4′) of the sugar moiety, a ssb is formed.[21,48] A similar mechanism occurs with peroxyl radical adducts of pyrimidines, produced on addition of oxygen to the C(5)−OH adducts of the pyrimidines[5,6] and analogous to the nitroxyl adducts, with a rate constant of 1.4 s^{-1}. The majority of the evidence to date indicates that the H-atom abstraction occurs from an adjacent sugar moiety.[39] With poly C, the 5-hydroxycytosin-6-yl radical is a precursor to ssb, even in the absence of oxygen, with ssb formation occurring with a rate constant of 5.5 s^{-1} (see Scheme 1).[6] Recent observations[49] that the 5-yl radical of uracil, which should have oxidizing properties, does not induce ssb via an interaction with the sugar moiety is additional confirmation that the C(5)−OH adduct of cytosine is involved. From the yield of ssb resulting from the NFT adduct, it is inferred that the probability of ssb formation is similar to that for formation of ssb in the absence of NFT but with a lower rate constant. That the rate-determining step is the base to sugar radical transfer arises from the expected fast process for ssb once the radical site is situated on the appropriate carbon of the sugar for ssb formation. It has been proposed that strand cleavage involving the C-4′ sugar radical in the presence of oxygen occurs prior to its interaction with oxygen.[50] Therefore, prompt ssb may occur prior to interaction with NFT, so that NFT may have little influence on the fast processes to strand breakage.

Conclusions

It is concluded that the mechanism by which nitroxyl radical adducts of the nucleobases induce ssb mimics that of the corresponding peroxyl radical adducts produced on addition of oxygen, whereas oxidants (e.g., quinones and viologens) that undergo outer-sphere electron-transfer reactions may inhibit ssb production involving a base to sugar radical transfer.

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Supporting Information Available: Figure of optical absorption spectrum of the semiquinone radical formed on interaction of the OH adduct of 2′-deoxycytidine with BQ at pH 7.4, table of rate constants for interaction of OH adducts of DNA nucleobases with the oxidants, and table of the rate constants for interaction of the OH adducts of polynucleotides with selected oxidants (3 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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