OH Radical-Induced Charge Migration in Oligodeoxynucleotides

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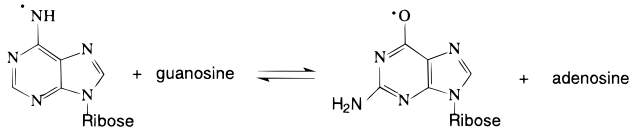
Using the technique of pulse radiolysis with spectrophotometric detection, OH radical (•OH)-induced electron transfer by intramolecular processes was studied in aqueous solutions containing either equimolar binary mixtures of deoxynucleosides or di- and oligodeoxynucleotides at pH 7.4. The time-resolved optical absorbance changes in mixtures of monodeoxynucleosides did not reveal significant electron transfer, indicating the lack of intermolecular electron transfer induced by •OH. Of the dinucleotides studied, only 2′-deoxyadenylyl-(3′→5′)-2′-deoxyguanosine (dApdG) shows •OH-induced intramolecular electron transfer. This reaction involves electron transfer from guanine to the adenine radical, which results from dehydration of its C(4)−•OH adduct and was monitored at 400 nm. The rate-determining step of electron transfer is the dehydration of the C(4)−•OH adduct of adenine. With the single-stranded oligodeoxynucleotides, dAGA, dAAGAA, and dAAGTA, the spectral changes with time are consistent with electron transfer occurring from guanine, but to only one of the possible neighboring adenine radicals produced by dehydration of the adenine C(4)−•OH adduct. In contrast, •OH interactions with dATGAA and dATGTA do not induce electron transfer from guanine to the adenine radical produced by dehydration of the C(4)−•OH adduct. These results indicate that the dehydrated adenine radical 5′ to the guanine is preferentially involved in the electron-transfer process.

Introduction

The reactions of primary radicals of water radiolysis (•OH, e^-_{aq}, •H) with DNA nucleobases and their nucleosides have been the subject of several investigations (see refs 1−4 for recent reviews). Of particular mention is the work on the reactions of the •OH with the nucleobases due to their importance in contributing to radiation-induced DNA damage, which is thought to lead to the various biological effects of ionizing radiation. The interaction of the •OH with pyrimidine[5−9] and purine[10−16] bases and their nucleosides has been quantified through identification of the different sites of •OH addition to the base moieties. Since the •OH is electrophilic in nature, it adds preferentially to unsaturated positions which are electron-rich. With the purines, •OH adds with a pronounced preference for the C(4), C(5), and C(8) ring positions.[10−16] Depending on the site of addition, the redox properties of the resulting adducts are different.[2,10] With 2′-deoxyadenosine and 2′-deoxyguanosine, the yields of the C(4) adducts, expressed as a percentage of the •OH yield, are ∼30%[2,12] and ∼50%,[10,15] respectively, whereas the yield of the reducing C(8) adduct is 37% for 2′-deoxyadenosine[15] and ∼16% with deoxyguanosine.[2,15] The C(4) adducts dehydrate to give radicals with oxidizing properties[11,14,15] (reaction 1). Since dehydration of the C(4)−•OH-adduct of adenine results in the same radical as that formed on one-electron oxidation/ionization of adenine,[2,3] the question arises as to whether the •OH in specific circumstances can initiate intramolecular transfer of oxidative damage through the bases to guanine in DNA.



For instance, one-electron oxidation of DNA results in migration and localization of the electron loss center (hole) to guanine.[17−20] The lifetime of the guanine radical cation in DNA was estimated[17] to be ∼0.05 s, reflecting the contribution from the hydration reaction to yield ultimately 8-oxo-7,8-dihydroguanine, a major product of oxidative damage to DNA. At present, the distance of this transfer of the radical site through the π-stacked base pairs involving charge-hopping and/or a superexchange mechanism[21,22] is under debate.

To date, there is little or no evidence for intramolecular transfer of •OH-induced damage involving electron-loss centers, in contrast to the evidence[18−20,23−28] for transfer of electron-loss centers in both single- and double-stranded DNA. Intermolecular electron transfer from guanosine to the one-electron oxidized radical of adenosine occurs with a rate constant[29] of 2.9×10^7 dm^3 mol^{-1} s^{-1}. The present study was undertaken to address the question of •OH-induced charge transfer/migration in binary mixtures of nucleosides and di- and polydeoxynucleotides.

Experimental Section

All nucleosides, nucleotides, and other chemicals used (Sigma, BDH) were of highest purity (>98%). The oligodeoxynucleotides (dAGA, dAAGAA, dATGAA, dAAGTA, and dATGTA) were synthesized, HPLC purified, and supplied by Cruachem. N_2O gas (BOC special gases, zero-grade) was used. Equimolar, binary mixtures of 2′-deoxynucleosides (0.1 mmol

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dm^{-3}) in aqueous solution were buffered to pH 7.4 using phosphate buffer (5.0 mmol dm^{-3}) or adjusted to pH ~4 using $HClO_4$. In experiments at pH ~4, the concentration of dideoxynucleotides was 0.2 mmol dm^{-3} and that of the oligodeoxynucleotides, 6×10^{-5} mol dm^{-3} (concentration based upon monomer units). Because of the high cost of these oligodeoxynucleotides, only time-resolved optical absorption changes at 310, 330, and 400 nm, at either pH 7.4 or 4.1, were determined.

All solutions were prepared in water purified by a Milli-Q system (Millipore). The aqueous solutions were saturated with N_2O for at least 30 min to convert e_{aq}^- into •OH. A dose/pulse of 11 Gy was used for spectral measurements, whereas a lower dose/pulse of 2 Gy was used to determine the kinetics with di- and oligodeoxynucleotides to minimize the loss of radicals in radical−radical interactions.

Pulse radiolysis experiments were performed using a 4.3 MeV linear accelerator with spectrophotometric detection as described previously.[11] The data handling procedures have been described previously.[30] The 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. To reduce the effects of photolysis, glass filters and a shutter, which was opened only a few seconds before irradiation, were used. 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}.

Results

(i) Absorption Spectra of OH Adducts of Deoxynucleosides. Optical absorption spectra of the transients formed on reaction of •OH with the deoxynucleosides, 2′-deoxyguanosine (dG) (Figure 1S), 2′-deoxycytidine (dC), 2′-deoxyadenosine (dA) (Figure 1S), and thymidine (T) were obtained as benchmark spectra to assess •OH-induced intra(inter)molecular charge transfer in mixtures of nucleosides and di- and oligonucleotides. The optical absorption spectra of the •OH adducts are similar to those previously reported.[31−33] With T and dC, the •OH adducts decay by second-order processes and there are no obvious spectral changes, reflecting first-order processes.

With dG, a fast increase of optical absorbance in the region 260−490 nm was observed. The rate constant for formation of the absorbance at 300 nm is 9.5×10^5 s^{-1}, whereas at 400 nm the rate constant determined is 2.0×10^4 s^{-1}. These rapid transformations still remain open to question. With dA, an increase of optical absorbance at 330 nm was observed with a rate constant of 4.4×10^4 s^{-1} at pH 7.4. This value is in reasonable agreement with the reported[2,14] value of 3.3×10^4 s^{-1}. At 400 nm, the rate constant for decay of optical density was determined to be 2.6×10^4 s^{-1}, consistent with the reported rate constant[34] of 2.9×10^4 s^1. This latter absorption change represents dehydration of the C(4)−•OH adduct to yield the same radical as that produced upon one-electron oxidation of the adenine moiety.[2,34]

(ii) Interaction of •OH in Mixtures of Deoxynucleosides. The optical absorption spectra of the •OH adduct of deoxynucleosides in equimolar (0.1 mmol dm^{-3}) mixtures were determined and compared with those of the individual deoxynucleosides. The mixtures investigated were dG + dC, dG + T, dA + T, and dA + dG.

For example, the time-resolved optical absorption spectrum of the transients obtained for the •OH interaction with a mixture of dG and dC is shown in Figure 1a. The spectrum is interpreted to be a composite of the •OH adducts of dG and dC. This is apparent from the reduction of the absorbance by ~ 60% in the wavelength region <350 nm in the presence of dC.

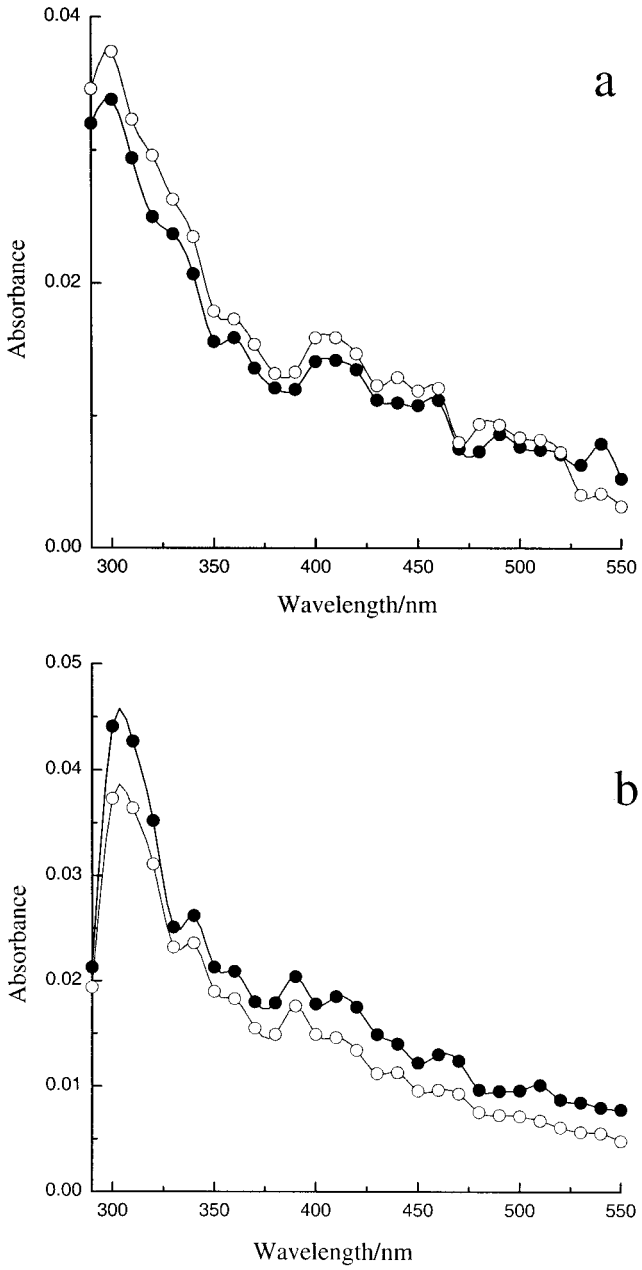


Figure 1. Optical absorption spectra determined after pulse irradiation of a N_2O-saturated, aqueous solution containing either (a) a mixture of 0.1 mmol dm^{-3} dC and dG (2 μs (●) and 15 μs (○)), or (b) 0.1 mmol dm^{-3} dCpdG (2 μs (●) and 160 μs (○)) at pH 7.4.

Furthermore, from the shoulder at 330−350 nm, it is apparent that the weaker absorbing •OH adducts of the cytosine moiety also contribute to the optical absorption spectrum in Figure 1a. The time-dependent loss of optical absorbance at 310 and 330 nm does not show contributions from first-order reactions involving possible radical transfer processes. The rates of decay were found to be dose-rate dependent, reflecting second-order processes. If significant transfer of the radical site from the •OH adducts of dC to guanine had occurred, the optical absorbance at 310 nm should have been significantly greater than that observed. It is thus inferred that insignificant radical transfer occurs. With all the other mixtures, the optical absorption spectra are consistent with the respective contributions of the individual •OH adducts based on their benchmark spectra.

With an equimolar mixture of dA and dG, the buildup at 310 nm with a rate constant of 6.8×10^5 s^{-1} is consistent with that determined in the reaction of the •OH with dG. The loss of

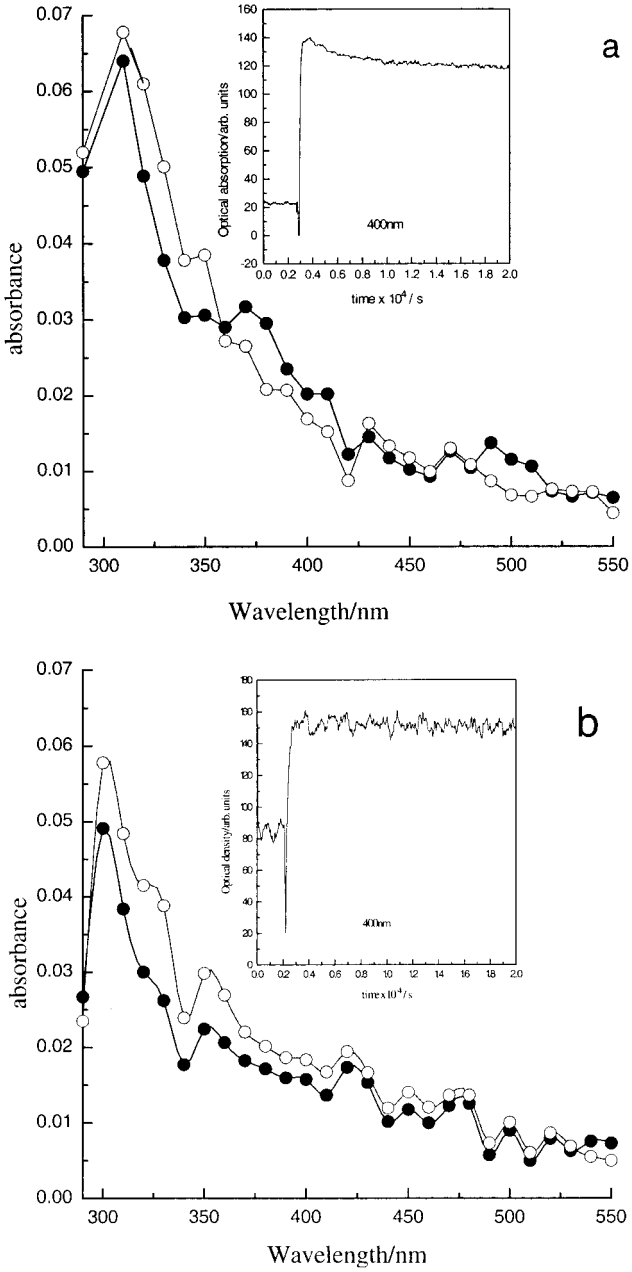


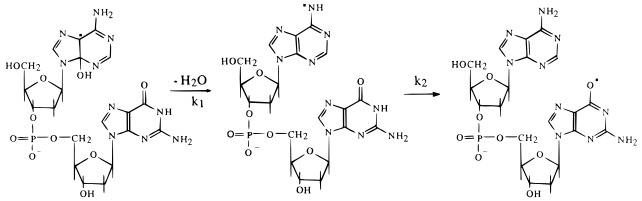
Figure 2. Optical absorption spectra determined 1 μs (●) and 15 μs (○) after pulse irradiation of a N_2O-saturated, aqueous solution containing either (a) a mixture of 0.1 mmol dm^{-3} dG and dA, or (b) 0.1 mmol dm^{-3} dApdG at pH 7.4. Insets show the respective changes of optical absorption at 400 nm with time.

absorption at 400 nm due to dehydration of the C(4)−•OH adduct of dA (Figure 2a, inset) still occurs. These changes are consistent with the absence of electron transfer on this time-scale. The slower intermolecular electron transfer reported previously[29] would occur at longer times.

(iii) Interaction of •OH with Deoxydinucleotides. The interaction of •OH with deoxydinucleotides, namely 2′-deoxycytidylyl-(3′→5′)-2′-deoxyguanosine (dCpdG), 2′-thymidylyl-(3′→5′)-2′-deoxyguanosine (TpdG), and 2′-deoxyadenylyl-(3′→5′)-thymidine (dApT) were investigated to obtain information on intramolecular electron transfer.

With dCpdG, TpdG, and dApT, the time-resolved optical absorption spectra of the transients obtained on interaction of the •OH with these dinucleotides are very similar to the optical

SCHEME 1: Mechanism for Oxidation of Guanine by the C(4)−•OH Adduct of Adenine



spectra obtained with the corresponding equimolar mixtures. The optical absorption spectra of the •OH adducts of dCpdG is shown in Figure 1b as an example. The rate of decay at 310 and 330 nm is dependent on the dose/pulse, indicating second-order and not first-order processes. With dApT, the rate constant of 3.5×10^4 s^{-1} for loss of absorption at 400 nm is similar to that determined for dehydration of the C(4)−•OH adduct of adenine in the mixture. From these spectral similarities and the decay kinetics, it is inferred that insignificant intramolecular radical transfer occurs between the •OH adducts of the respective nucleobases in these dinucleotides.

With 2′-deoxyadenylyl-(3′→5′)-2′-deoxyguanosine (dApdG), the time-resolved optical absorption spectrum of the transient formed on reaction of dApdG with •OH is shown in Figure 2b. This spectrum at longer times shows dominance of a contribution from the •OH adducts of guanine, even though ∼40% of the •OH react with the adenine moiety, based upon the respective rate constants for interaction of •OH with the nucleobases.[35] A contribution of the •OH adducts of adenine is apparent from the significantly reduced absorption intensity in the 300−320 nm region compared with that determined for the •OH adducts of guanine only. Further, the increase in absorption at 330 nm represents ring-opening of one of the adenine radicals. The loss of absorption at 400 nm, indicative of dehydration of the C(4)−•OH adduct of adenine, was not apparent (Figure 2b, inset) (taken separately at a low dose of ∼2 Gy to minimize radical−radical reactions), in contrast to the observed dehydration of the C(4)−•OH adduct of adenine in the corresponding nucleobase mixture (Figure 2a, inset). It is, therefore, proposed that radical transfer does occur intramolecularly from the dehydrated adenine radical to guanine in a non-rate-determining process as shown in Scheme 1. The optical absorbance changes with time at 310, 330, and 400 nm were observed to be independent of the concentration of dApdG in the range $0.8-2.3 \times 10^{-4}$ mol dm^{-3}, consistent with the proposed intramolecular electron transfer.

(iv) Interaction of •OH with Oligodeoxynucleotides. Because electron transfer from guanine to the radical resulting from dehydration of the C(4)−•OH adduct of adenine is proposed to occur with the dinucleotide dApdG, we also investigated the possibility of •OH-induced electron transfer in two specifically synthesized oligodeoxynucleotides, namely dAGA and dAAGAA.

These two oligodeoxynucleotides were designed to enhance the percentage of •OH that interact with adenine compared with guanine. Assuming the rate constants for interaction of the •OH with the nucleobases in these oligodeoxynucleotides are the same as those for the individual deoxynucleotides, the percentage of •OH that interact at the adenine moieties is calculated to be 60% and 75% with dAGA and dAAGAA, respectively. The optical absorbance changes with time determined at 400 nm are shown in Figure 3 for reaction of the •OH with dAGA and dAAGAA at pH 7.4 and with dA for comparison. With dAGA, the changes in optical absorbance with

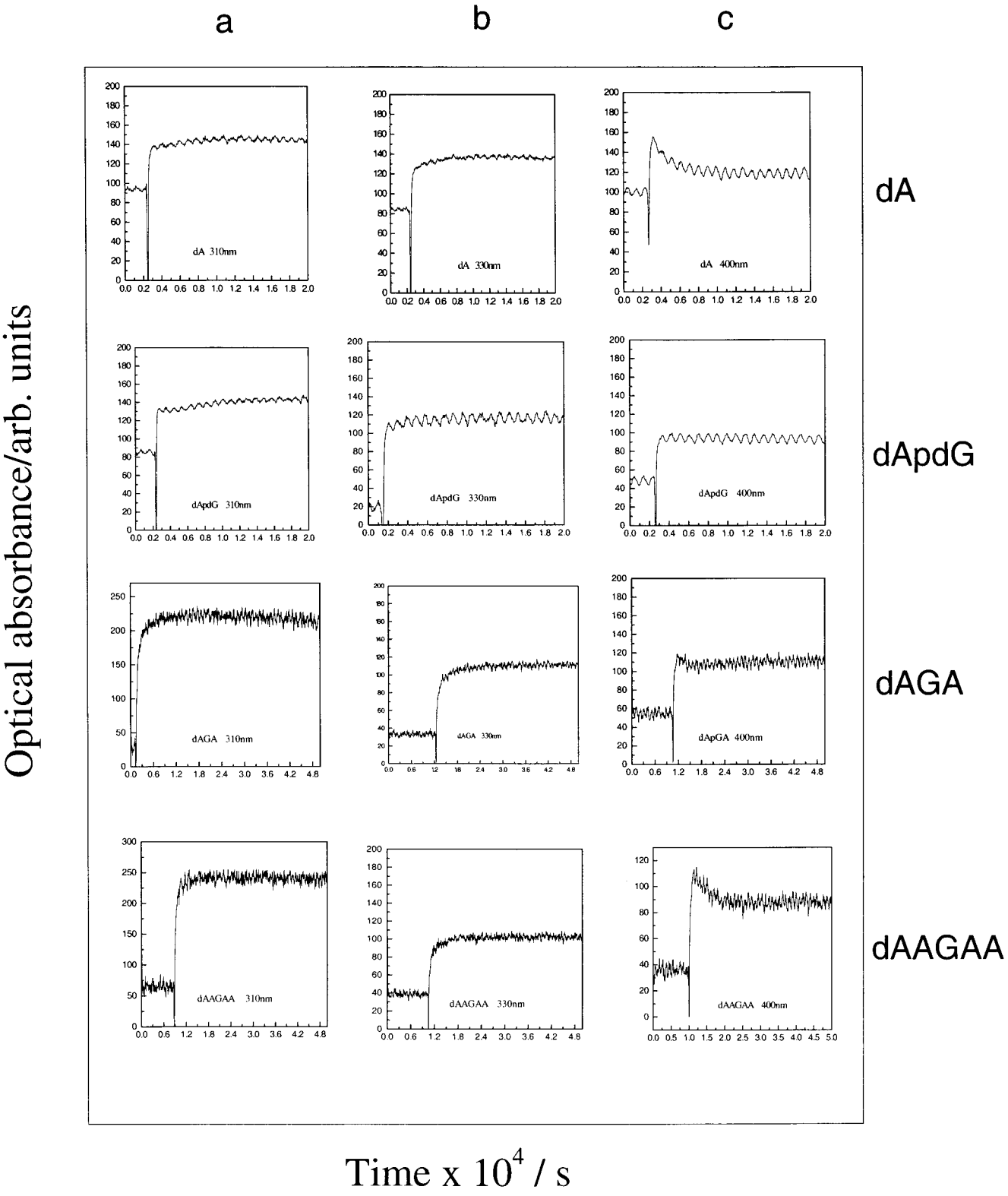


Figure 3. Optical absorption changes at (a) 310 nm, (b) 330 nm, and (c) 400 nm with time for the •OH adducts of dA, dApdG, dAGA, and dAAGAA at pH 7.4. Dose/pulse of 2.2 Gy.

time at 400 nm are not significant, whereas with dAAGAA a loss of optical absorption with time was observed at 400 nm, reflecting dehydration of the C(4)−•OH adduct of adenine. With both oligonucleotides, an increase in optical absorption with time occurs at both 310 and 330 nm. In Table 1, the percentage increase or loss of optical absorption at 400 nm over the initial 180 μs after the pulse has been determined and compared with the calculated values, assuming varying extents of electron transfer to the adenine radicals from guanine. The experimentally determined absorbance changes at 400 nm are consistent with electron transfer. With dAGA, a decrease of optical absorption of 2% was observed, consistent with the calculated change if only one of the possible two adenine radicals, on average, interacts with guanine. With dAAGAA, a measured value of 22% loss of optical absorption at 400 nm corresponds to electron transfer from guanine to only one of the possible adenine radical

TABLE 1: Absorbance at 400 nm Determined 5 μs (A_1) and 180 μs (A_2) after the Pulse Irradiation of N_2O-Saturated, Aqueous Solutions Containing dA, dG, Their Mixtures, and the Oligonucleotides at pH 7.4[a]

	experimental values			calculated values[b]					
				no ET			ET		
	OD × 10^3		% buildup (b)/	OD × 10^3		% build-up(b)/	OD × 10^3 [b]		% build-up (b)
species	A_1	A_2	decay (d)	A_1	A_2	decay (d)	A_1	A_2	/decay (d)
dA	4.59	1.79	61 (d)	–	–	–	–	–	–
dG	4.22	5.53	31 (b)	–	–	–	–	–	–
dA + dG	4.83	4.07	16 (d)	4.37	3.9	11 (d)	4.41	5.53	25 (b)
dApdG	4.30	5.26	22 (b)	4.37	3.9	11 (d)	4.41	5.53	25 (b)
dAGA	1.92	1.96	2 (b)	4.44	3.28	26 (d)	4.44	4.44	2(d) (e)
							4.52	5.53	25(b) (g)
dAAGAA	2.31	1.81	22 (d)	4.50	2.72	40 (d)	4.5	4.29	20(d) (e)
							3.6	4.5	5(d) (f)
							4.5	5.53	23(b) (g)

[a] Dose per pulse of 2 Gy. The calculated value of absorbance has been determined for various degrees of electron transfer to the adenine radical from guanine. [b] Absorbance calculated assuming the rate constants for interaction of •OH with dG and dA of 7.8×10^9 and 5.8×10^9 dm^3 mol^{-1} s^{-1}, respectively, and assuming the absorbance values obtained with these monomers. The percentage buildup or decay at 400 nm is $(A_2-A_1)/A_1$. Charge transfer from one of the adenines to guanine (e), from two of the adenines to guanine (f), and from any of the adenines to guanine (g), when the initial C(4)−•OH adduct resides at one of the adenines.

sites as shown in Table 1. In these calculations, it was assumed that the •OH interacts with equal probability at all the adenine sites.

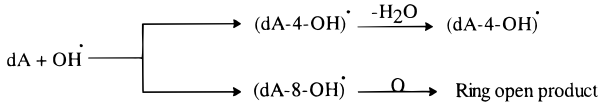
Because electron transfer was observed from the adenine radical in dApdG, it is tempting to speculate that the dehydrated adenine radical 5′ to the guanine in dA*GA and dAA*GAA (A marked with an asterisk) is involved in the electron-transfer process. To investigate a directional effect on electron transfer, the change in optical absorption at 400 nm was determined on reaction of the •OH with dATGTA, dATGAA, and dAAGTA. It was assumed that the thymine moieties may inhibit electron transfer from the dehydrated adenine radical to guanine. From the buildup and decay of optical density at 400 nm (see Table 1), •OH-induced electron transfer was detected only with dAAGTA, because the experimentally determined decrease in optical absorbance of 11% is comparable with the calculated value of 5% for electron transfer from, on average, one adenine. The calculated decrease of optical absorbance for no electron transfer is considerably greater, at 27%. In contrast, dATGAA and dATGTA did not show any significant electron-transfer induced by •OH. The decreases in optical absorbance at 400 nm of 38% and 29%, respectively, are similar to the calculated values of 27% and 20% (see Table 1 for calculation and using a rate constant[35] for reaction of •OH with thymidine of 4.6×10^9 dm^3 mol^{-1} s^{-1}), if electron transfer does not occur.

It is assumed that, in part, the changes observed at 310 nm reflect formation of the oxidized guanine radical resulting from electron transfer from guanine to the adenine radical, whereas the changes at 330 nm are due to the ring opening[15] reaction of the C(8)−•OH adduct of adenine. Rate constants were determined from the subsequent changes in optical absorption at 310, 330, and 400 nm following reaction of •OH with dA, dApdG, dAGA, and dAAGAA at pH 4.1 and 7.4 (Table 1S). From the data at 330 nm, the rates of ring opening of the C(8)−OH· adduct of adenine at both pH values are similar, consistent with previous observations.[14] In contrast, the rate constants determined at 310 nm decrease with a decrease of pH from 7.4 to 4.1. The pH dependence of the rate constants for dehydration of the adenine radical at 400 nm is similar to that for changes at 310 nm. From the differences in the effect of pH on these rate constants (Table 1S), the processes responsible for the changes at 330 nm are distinctly different from those resulting in the changes at 310 and 400 nm.

Discussion

Intermolecular Processes. For all the deoxydinucleotides studied except dApdG, there is no significant evidence for charge transfer between the •OH adducts of the nucleobases and the other nucleotide at times <200 μs. For those mixtures containing adenine, the dehydration reaction (monitored at 400 nm) and the ring-opening reaction (monitored at 330 nm) of the •OH adducts of adenine occurs. With the purine/pyrimidine mixtures, the majority of the •OH adducts of the pyrimidines have reducing properties, so they would not be predicted to reduce adenine or guanine. For instance, reasonably powerful oxidizing agents interact only very slowly with those pyrimidine •OH adducts with reducing properties.[9] The pyrimidine •OH adducts with oxidizing properties would not be expected to oxidize guanine, the DNA nucleobase where oxidation is expected to occur more readily. For instance, guanine is oxidized readily[11,36] by powerful oxidizing radicals such as $SO_4^{\bullet-}$ or $Br_2^{\bullet-}$, whereas $Br_2^{\bullet-}$ does not readily oxidize adenine. It is predicted that the •OH adducts of the pyrimidine bases with oxidizing properties are not sufficiently strong oxidizing agents to oxidize adenine.

Using the rate constants[35] for reaction of dG and dA with •OH and taking the benchmark optical absorbance spectra of the •OH adducts of the bases, we have listed the calculated optical changes for electron transfer and no electron transfer in Table 1. If electron transfer occurs with an equimolar mixture of dG/dA, a 25% buildup of absorbance at 400 nm over the time scale for dehydration of the adenine radical is predicted on reaction with the •OH. Experimentally, a 16% loss of optical absorption was observed, consistent with the calculated change (Table 1) if electron transfer does not occur. Based upon the redox potentials of one-electron oxidized guanosine and adenosine of 1.20 and 1.42 V, respectively,[37] electron transfer is thermodynamically favored and may have occurred as shown below. However, the rate constant[29] for intermolecular oxidation of guanine at pH 7 is 2.9×10^7 dm^3 mol^{-1} s^{-1}.



(1)

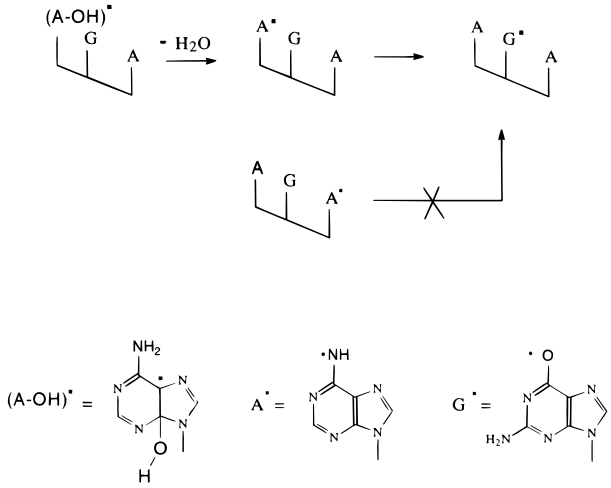
Intramolecular Processes. With the exception of dApdG, there is no evidence for •OH-induced intramolecular electron

transfer with dCpdG, TpdG, and dApT. In the case of dApdG, dehydration of the C(4)−•OH adduct of adenine is not apparent (Figure 2b). From Table 1, it is calculated that a 25% increase of optical absorbance at 400 nm following interaction of the •OH with dApdG should be observed, if electron transfer occurs from guanine to the radical resulting from dehydration of C(4)−•OH adduct of adenine. The experimentally measured increase in optical absorbance of 22% is consistent with that calculated for electron transfer. If electron transfer does not occur, a decrease in optical absorption should occur similar to that in the mixture of dA and dG. It is proposed that the oxidation of guanine by the radical resulting from dehydration of the C(4)−•OH adduct of adenine occurs by an intramolecular electron-transfer process as shown in Scheme 1. Consistent with electron transfer, as shown in Scheme 1, is the growth of optical absorption at 310 nm, a wavelength where the one-electron oxidized guanine radical absorbs (not shown). From the rate constant determined for the buildup of optical absorption with time at 310 nm, it is inferred that the rate-determining step for the intramolecular electron transfer in Scheme 1 is dehydration of the C(4)−•OH adduct of adenine. At 400 nm, the loss of absorption due to the dehydration reaction was not observed because the guanine radical, produced by electron transfer, absorbs more strongly at this wavelength than the adenine radical. The electron-transfer process must be fast, and an estimate for the time scale of electron transfer between-one electron oxidized adenine and guanine is <50 ns ($k > 2 \times 10^7$ s^{-1}), determined in the interaction[29] of $SO_4^{\bullet -}$ with GpA. On reaction of •OH with GpA, the dehydration reaction of the adenine radicals was observed[29] in contrast to our findings in this study at 400 nm with dApdG. From these differences, it remains open to question whether electron transfer occurs with GpA, if the electron transfer occurs preferentially in a 3′→5′ direction (see later). An alternative reaction could involve addition of the adenine radical to guanine to produce a covalently linked radical product, which has optical absorption characteristics similar to those of one-electron oxidized guanine. "Tandem" radical products have been detected[38] on interaction of •OH with various oligonucleotides. These products are produced in very low yields and involve mainly pyrimidine radicals. Therefore, a "tandem" radical product seems less likely than the thermodynamically favored electron-transfer process.

•OH-induced electron transfer as shown in Scheme 1 was also observed with dAGA and dAAGAA, where the rate-determining step is dehydration of the C(4)−•OH adduct of adenine. The concentration of •OH is at least an order of magnitude less than that of the oligodeoxynucleotides, and it is assumed that the •OH interacts with equal efficiency at any of the adenine moieties. However, on average, only one of the resulting adenine radical sites with dAGA and dAAGAA accounts for the intramolecular electron transfer with guanine (Table 1). It is proposed that electron transfer occurs from guanine to the adenine radical 5′ of the guanine as shown in Scheme 2. This directional electron transfer is consistent with the observed electron transfer with dAAGTA and the lack of transfer with dATGAA and dATGTA. It is assumed that the thymine between the purines inhibits electron transfer. Indeed, pyrimidines inhibit charge migration from adenine to guanine induced by 193-nm light in similar oligonucleotides,[19] and several AT bases inhibit electron migration in DNA.[39] The observation with GpA[29] would be consistent with a lack of transfer when the adenine radical is 3′ of the guanine.

From the similarity of the effect of pH change on the rate constants determined at 310 and 400 nm, it is inferred that the adenine radical formed on dehydration of its C(4)−•OH adduct undergoes electron transfer to produce the guanine radical which absorbs at 310 nm. That the optical absorption changes are slightly different at pH 4.1 than at pH 7.4 reflects the fact that the guanine radical is partially protonated[2] at pH 4.1 and absorbs less strongly at 400 nm in its protonated form.

SCHEME 2: Oxidation of Guanine by the •OH Adduct of Adenine, 5′ of the Guanine



From the evidence presented, it is concluded that following dehydration of the the C(4)−•OH adduct of adenine 5′ to the guanine, intramolecular electron transfer occurs in oligodeoxynucleotides to yield one-electron oxidized guanine. Dehydration of the C(4)−•OH adduct of adenine is rate-determining. Therefore, •OH-mediated electron transfer in DNA may contribute to enhance radiation-induced and oxidatively induced damage at guanine in DNA.

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Supporting Information Available: Figure 1S shows optical absorption spectra of the •OH adducts of dG and dA. Table 1S shows pH-dependent rate constants for optical absorption changes at various wavelengths on reaction of the •OH with the oligonucleotides. This material is available free of charge via the Internet at http://pubs.acs.org.

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