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From Alcohols to Sugars—How Does the Reactivity of α-Hydroxyalkyl Radicals Change with Structure? A Quantitative Examination by Pulse Radiolysis

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Rate constants are reported for the 1-electron reduction of the azo dye Orange II in water (pH 7.0) by 10 different α-hydroxy radicals. The radicals were created by pulse radiolysis of aqueous solutions of the corresponding alcohol/sugar. The rate constants varied from 1×10^8 to 2.7×10^9 mol^{-1} dm^3 s^{-1} and radicals with β-hydroxy groups had the lowest rate constant. The reaction was found to be controlled by the reduction potentials of the radicals, with steric influences having little effects. Good fits of the data were obtained using the Marcus equation with λ =140 kJ/mol.

Introduction

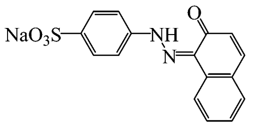
Primary and secondary alcohol moieties are frequently found in chemical and biological structures. For example, cellulose the world's most abundant polymer is composed of glucose monomers, which contain 4 HCOH groups.[1] Due to the relatively weak C−H bond in the alcohols (e.g., bond strength: $H{-}CH_2OH = 393$ kJ mol^{-1}) compared to alkanes (e.g., bond strength: $H{-}CH_3 = 438$ kJ mol^{-1}),[2] in the presence of hydrogen abstracting radicals and singlet/triplet excited states, α-hydroxyalkyl radicals are often preferentially formed. These abstraction reactions are important in the oxidation of materials and in synthetic procedures. Consequently, α-hydroxyalkyl radicals are significant reactive intermediates and in seeking to understand their behavior many investigators have used the 2-hydroxy-2-propyl radical as a model system.[3] Such endeavors have shown that the radical is extremely nucleophilic, rapidly adding to alkenes with electron withdrawing substituents:[4]

$$(CH_3)_2\dot{C}OH + CH_2{=}CHX \rightarrow (CH_3)_2C(OH)CH_2{-}\dot{C}HX \tag{1}$$

It also is an efficient 1-electron reductant of nearly all dyes[5]

$$(CH_3)_2\dot{C}OH + \text{dye} \rightarrow (CH_3)_2C{=}O + \text{dye}^{\bullet-} + H^+ \tag{2}$$

Little information is available on how the reactivity of α-hydroxyalkyl radicals changes with their structure, although a recent study showed little difference between 2-hydroxy-2-propyl and 1-hydroxyclohexyl.[5] To investigate this area further, a study of the reduction of the dye Orange II by 10 α-hydroxyalkyl radicals in water was conducted, the results of which are presented here. The radicals were chosen to have varying electrochemical potentials, steric hindrance, to be part of 5 and six-membered ring structures, and to be with and without β-hydroxy groups, thereby covering a broad range of commonly found structures. Dye reduction was chosen as an optically easy method to follow fundamental reaction of the radicals. By comparing to the relevant literature the effect of solvent is also discussed.



Orange II

Experimental Section

α-Hydroxyalkyl radicals were created at pH 7.0 in a nitrous oxide saturated aqueous solution of the corresponding alcohol by pulse radiolysis using a 4.3 MeV Millard Linear accelerator, which generates electron pulses of 1.6 μs.[6,7] The radiation pulse creates, through the radiolysis of water, hydroxyl radicals, that rapidly hydrogen abstract from the alcohols (0.1 mol dm^{-3}):

$$H\dot{O} + R{-}H \rightarrow H_2O + \dot{R} \tag{3}$$

For propan-2-ol, $k = 1.9 \times 10^9$ mol^{-1} dm^3 s^{-1} for this reaction.[8] At the dose/pulse used, approximately 1−2 μmol dm^{-3} hydroxyl

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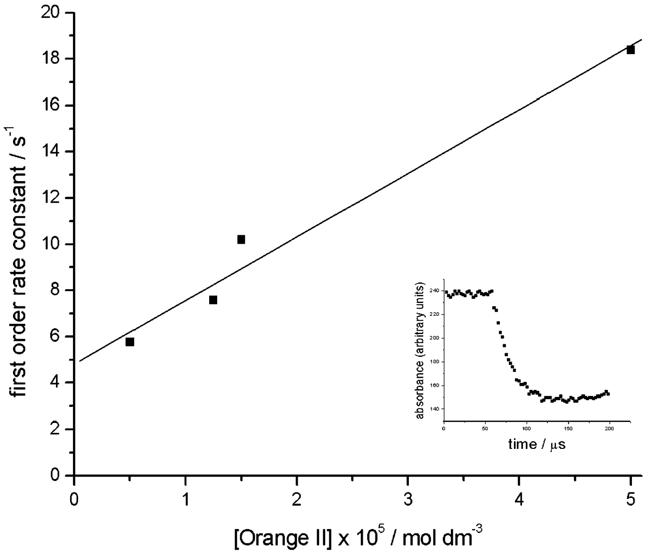


Figure 1. Dependence of the first-order rate constant on the concentration of Orange II for the reaction of the propan-2-ol radical with Orange II at pH 7. The inset shows the loss of optical absorbance of Orange II at 480 nm with time for a dose/pulse of 3 Gy and at pH 7.0.

radicals are produced. The hydroxyl radical predominately abstracts the HCOH hydrogen,[9] due to its lower bond energy in comparison with the other C−H bonds. For compounds with several HCOH groups abstraction occurs relatively nonselectively at each of these groups[10] to give a variety of α-hydroxy radicals. For sugar ring compounds there is a small preference to abstract the HCOH adjacent to the ring-oxygen.[11]

Reference $CO_2^{\bullet -}$ radicals were generated by irradiation of a 0.1 mol dm^{-3} formate solution saturated with N_2O. Azide radicals were generated by irradiation of N_2O saturated solution containing 0.1 mol dm^{-3} of NaN_3.

The reaction of Orange II with these radicals was followed kinetically by optically monitoring the dye bleaching at 480 nm, the λ_{max} of the optical density of the dye, as previously described.[6,7]

Analysis

A typical loss of optical absorbance with time for bleaching of Orange II with alcoholic radicals is shown in Figure 1. Second-order rate constants were extracted from the linear dependence of the pseudo-first-order rate constant for loss of transient optical absorption on the dye concentration, Figure 1b. To ensure dye reduction was the cause of the bleaching, the transient optical absorption spectrum of the dye radical formed by reaction with α-hydroxy radicals was recorded and compared to transient reference spectra for Orange II. In determination of these spectra, corrections for bleaching of Orange II were undertaken as described previously.[6,7] Reference spectra were recorded for dye bleaching by 1-electron oxidation, 1-electron reduction and hydroxyl radical addition, using azide radicals, $CO_2^{\bullet -}$ and $^{\bullet}OH$ as reagents, respectively.[6,7,8] The spectra are shown in Figure 2 and are quite distinct, confirming the chemistry occurring. Upon 1-electron reduction the spectrum shifts to lower wavelengths, whereas on oxidation an opposite shift to higher wavelength is observed. An electron paramagnetic resonance, EPR, and computational investigation of the reduced Orange II radical showed that the reduced dye rapidly picks up a proton to give a protonated hydrazyl radical, with electron density predominately on the naphthyl ring.[12] This loss in conjugation leads to a spectrum shifted to lower wavelength.

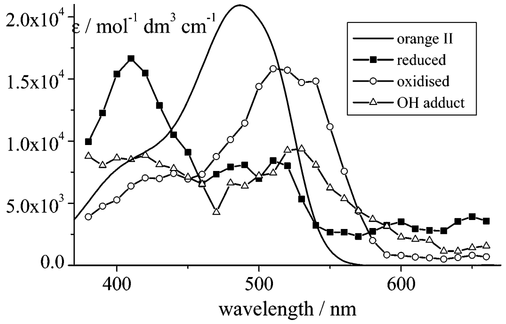
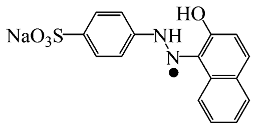
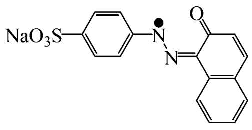


Figure 2. Optical absorption spectra recorded for radicals of Orange II produced by 1-electron reduction, 1-electron oxidation and hydroxyl radical addition, alongside the spectrum of the parent dye.

For the oxidized dye radical, the optical spectrum is very similar to that of the parent dye, indicating the conjugation is maintain and the radical is in the hydrazone form. The reduced and oxidized dye radicals may therefore most simply be represented as



reduced Orange II



oxidised Orange II

For the hydroxy adduct the spectrum becomes a more or less featureless broad band extending to 550 nm. These results agree with previous results for similar dyes,[6,7] and confirmed that the α-hydroxy radicals 1-electron reduce Orange II.

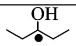
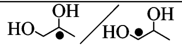
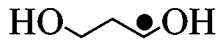
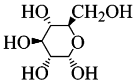
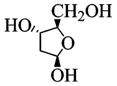
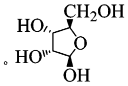
Although the hydroxyl radical predominately abstracts the HCOH hydrogen, [13] other hydrogen atoms in the molecule may also be abstracted creating further radicals, such as β-hydroxyalkyl radicals. To ensure these did not interfere with the kinetics, any bleaching of Orange II by $(CH_3)_2C(OH)^{\bullet}CH_2$ generated from *tert*-butyl alcohol was investigated. No bleaching was observed. An additional side reaction to consider is that the presence of adventitious oxygen leads to the formation of peroxy radicals and the superoxide/hydroperoxy radical. The direct creation of superoxide and hydroperoxy radicals from oxygen, showed that no reaction with the dye occurs.

Results and Discussion

The 10 radicals studied and the rate constants for the 1-electron reduction of Orange II are given in Table 1. For all the radicals studied, the rate constants are high, all greater than approximately 10^8 mol^{-1} dm^3 s^{-1}, although the rate constants vary over about 1 order of magnitude between some of the radicals. Most notably, all the radicals with β-OH groups, e.g., glucose, ribose, and glycol have much lower rate constants.

It is most likely that the key controlling factors for this reaction will be the reduction potential of the radical and/or steric effect. For the radical derived from methanol, ethanol and propan-2-ol, the reduction potentials (ketone, H$^+$/radical) are available[14] and given in the table. As would be expected for an electron-transfer reaction the bleach rate constant decreases with the reduction potential. To gain a better understanding, the data were analyzed in terms of the Marcus equation,[15] which allows the prediction of rate constants from knowledge of the reduction potentials and sizes of the reactants. In the current situation

TABLE 1: Second Order Rate Constants for the Reaction of Orange II with Various Radicals, Where Known the Reduction Potential (Ketone, H^+/Radical) Is Given in Paranthesis in V vs NHE[14]

Radical	k / 10^9 mol^{-1} dm^3 s^{-1}
$\overset{\bullet}{C}H_2OH$ (-1.18)	1.0
$CH_3\overset{\bullet}{C}HOH$ (-1.25)	2.3
 (-1.4)	2.7
	2.0
	0.15
	0.62
	1.5
Radicals from glucose 	~0.1
Radicals from deoxyribose 	0.89
Radicals from ribose 	~0.1

where there is no electrostatic work required to bring the 2 reactants together the equation may be expressed as[16]

$$k_{ET} = \frac{k_d}{1 + 0.25\left\{\frac{\lambda}{4RT}\left(1 + \frac{\Delta G}{\lambda}\right)^2\right\}} \tag{4}$$

where k_d is the diffusion limited rate constant, conveniently calculated via the Stokes- Einstein equation ($8RT/3\eta = 7 \times 10^9$ mol^{-1} s^{-1} for water); λ is the solvent reorganization energy and ΔG is the free energy of the reaction calculated from the reduction potentials of the dye and the ketone corresponding to the radical. Thus

$$\Delta G = -F\lfloor E(\text{dye/dye}^{\bullet -}) - E(\text{ketone,H}^+/\text{radical})\rfloor \tag{5}$$

where $E(\text{dye/dye}^{\bullet -}) = -0.43$V vs NHE for Orange II.[17] Previous work has measured the rate constants for reduction of Methyl Orange (−0.66 V) and Azo benzene (−0.76 V) by 2-hydroxy-2-propyl radicals as 7×10^8 and 4×10^8 mol^{-1} dm^3 s^{-1}, respectively, and to provide a wider range, these are also included in Figure 3. A good fit could be obtained, as shown in Figure 3, using a λ of 140 kJ/mol, which compares well to literature values of 100−180 kJ mol^{-1}.[5,15] The reactions are in the normal region, where increasing the magnitude of $-\Delta G$ leads to larger rate constants.

As may be expected, the bleaching of Orange II is dependent on the reduction potential of the α-hydroxy radical, which is in turn dependent on the substituents on the radical. It has been established that the reduction potential of these radicals vary with the solvent, in particular the reduction potential is known to be lower in organic solvents than in water.[14,18] Consequently, the rate constant for reduction of Orange II should be lower in organic solvents, as has indeed been found. For example the rate constant for 2-hydroxy-2-propyl bleaching of Orange II measured in methanol is 4.0×10^8 mol^{-1} dm^3 s^{-1},[5] compared to the value of 2.7×10^9 mol^{-1} dm^3 s^{-1} obtained here in water. From the Marcus plot this would correspond to a drop of approximately 0.3V in the reduction potential.

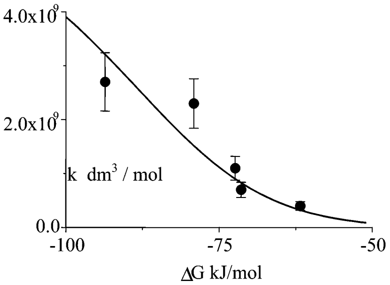


Figure 3. Fit of experimental data to the Marcus equation.

Aside from these reduction potential effects, steric constraints may be expected to alter the reaction rate.[4] The cleanest comparison for this is between 2-hydroxy-2-propyl and 3-hydroxy-3-pentyl radical, where the substituent methyl group of the former have a volume of 26.0 Å^3 compared with 42.5 Å^3 for the ethyl groups of the latter.[19] The change from methyl to ethyl would be expected to have a relatively small effect on the reduction potentials on the basis of their relative inductive effects. Only a small reduction in rate constant from 2.7×10^9 to 2.0×10^9 mol^{-1} dm^3 s^{-1} was observed, indicating that little steric effect is caused by the increased size of the ethyl substituent. A further comparison can be made between the 1-hydroxyethyl radical and the 1,3-dihydroxy propyl radical, again only a small change was observed. Hence steric effects, at least for the size of substituents considered here do not appear to play a key role.

From the analysis above, the reduction potential is the key controlling reaction factor in the reduction of Orange II by α-hydroxyl alkyl radicals. The order of magnitude lower rate constants for all the radicals with an OH on the carbon adjacent to the radical center, e.g., glucose, ribose and glycol, is consequently ascribed to a lowering of the reduction potential of these radicals. This may be due to internal H-bonding effects by the adjacent OH groups, or to significant overlap between the orbitals of the unpaired electron and the β-hydroxy group, stabilizing the radical. In agreement with the later suggestion, EPR work by Gilbert et al.[20−22] has shown that α-hydroxy alkyl radicals with β oxygen substituents are less electron-rich at the α-carbon and reduce Fe(III) more slowly than their unsubstituted counterparts. Comparing the ethanol and glycol radicals a decrease in the rate constant from 2.3×10^9 to 0.15×10^9 mol^{-1} dm^3 s^{-1} is observed. From the Marcus plot in Figure 3, this decrease would mean that for the glycol radicals, $E(\text{ketone, H}^+/\text{radical}) \sim -0.95$ V vs NHE compared to −1.25 V for the 1-hydroxyethyl radicals. The change in potential is reasonable when compared to the changes in reduction potential observed with different solvents, as a drop of 0.7V was observed on moving from water to acetonitrile.[14,18]

Contrasting to the β-OH effect, the presence of an OH on the γ carbon has little influence on the rate constant, as illustrated by comparing the ethanol and 1,3 propandiol radical. Similarly the rate constant for deoxyribose is also high at 0.89×10^9 mol^{-1} dm^3 s^{-1}, where all the OH groups are γ to each other. However, the value is still lower than those for ethanol or propan-2-ol. In deoxyribose it is predicted that the predominant radical formed will be from the HCOH adjacent to the ring oxygen.[11] A previous comparison has shown that the presence of a ring makes little difference to the dye bleaching rate constant,[5] therefore the lower rate constant for deoxyribose compared to propan-2-ol is probably also due to a lowering of the reduction potential, caused by the adjacent ring oxygen. This effect will of course also occur in the radicals formed in the analogous position on glucose and ribose, and combines with the β-OH effect to make these radicals the least chemically reducing.

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