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Absolute Kinetics of Hydrogen Abstraction from α-Tocopherol by Several Reactive Species Including an Alkyl Radical[†]

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Abstract: Laser flash photolysis and competitive techniques have been employed to study the reactions of α-tocopherol with various radicals and ketone triplets in solution. For example benzophenone triplets abstract hydrogen with rate constants of 5.1×10^9 and 3.7×10^9 M^{-1} s^{-1} in benzene and benzene/1.3 M methanol. Similar near-diffusion-controlled values were obtained for several other ketone triplets, as well as *tert*-butoxyl and 4-methoxybenzoyloxyl radicals. Deuterium kinetic isotope effects are frequently very small, reflecting the expected lack of selectivity of fast reactions. The reactivity of the 5-hexenyl radical toward α-tocopherol was examined by studying the competition of this process with the radical cyclization to the cyclopentylmethyl radical. The value of $(1.7 \pm 0.2) \times 10^6$ M^{-1} s^{-1} (at 70 °C in benzene) for this hydrogen atom abstraction from α-tocopherol makes this process exceptionally fast in comparison with the limited available rate data for reactions of carbon-centered radicals with other phenols.

Introduction

It is now well established that α-tocopherol, the principal tocopherol constituting vitamin E, inhibits lipid peroxidation in vivo[1-6] as well as in vitro.[7,8] In fact α-tocopherol (αT) has been shown to be the major lipid-soluble chain-breaking antioxidant in human blood.[9-11] Chemical research into the reactions of vitamin E (EOH) continues to be simulated largely by this ability to protect living systems against free radical induced damage by inhibiting lipid peroxidation.[12-15] Much of this research has therefore been concerned with the reactivity of EOH toward peroxyl radicals.[7,8,13,14] A variety of studies have been carried out including EOH inhibition of autoxidation in model membrane systems such as micelles, multilamellar liposomes, and phosphatidylcholine bilayers.[16-19]

Ingold and co-workers have measured rate constants for the reaction of EOH and related phenols with poly(peroxystyryl) peroxyl radicals at 30 °C[7,8,20] in order to investigate factors which influence the antioxidant efficiency of this class of phenols. Typical values for these compounds fall in the range of 5×10^5 to 5×10^6 M^{-1} s^{-1} at this temperature. By contrast, phenols that lack the fused chromanol ring of the tocopherols react much more slowly with peroxyl radicals. For example, the rate constant for reaction of 2,6-di-*tert*-4-methylphenol with poly(peroxystyryl) peroxyl at 30 °C is only 2.4×10^4 M^{-1} s^{-1}.[20] The order of tocopherol reactivity toward peroxyl radicals was found to be the same as the order of their biological activity (i.e., $\alpha T > \beta T \sim \gamma T > \delta T$).[5,21] Ingold and co-workers attributed variations in antioxidant activity among these and related phenols to a stereoelectronic effect involving the p-type lone pair orbital of the oxygen atom which is para to the hydroxyl group.[7,8,13,14] The greater the overlap between this lone pair orbital and the phenoxyl radical orbital, the more efficient the phenol is as an antioxidant. In the better antioxidants such as EOH and 2,2,5,7,8-pentamethyl-6-hydroxychroman, the presence of the heterocyclic ring ensures that the dihedral angle between these two orbitals is relatively small.

Pulse radiolysis kinetic studies of the reaction of EOH with various peroxyl radicals in aqueous and alcoholic solvents have also been reported.[22-24] The rate constants determined by this technique were in the range 10^6–10^8 M^{-1} s^{-1}, with the largest value being that for the reaction of EOH with $Cl_3COO^{\bullet}$. It has been suggested that the rate-determining step for this particular reaction involved a electron-transfer oxidation rather than a hydrogen abstraction.

In contrast to the extensive body of kinetic data relating to reactions of EOH with peroxyls, much less is known about the reactivity of EOH toward other common classes of reactive species. For example, studies of the reactivity of EOH toward triplet ketones have relied on indirect methods,[25] while only approximate or relative rate data have been measured for the reaction of EOH with alkyl radicals. To the best of our knowledge no kinetic data have ever been reported for reactions of EOH with alkoxyl radicals. In addition, we also measured the rate constant for reaction of EOH with an aroyloxyl radical. This latter radical belongs to a class of oxyl radicals which has only recently become amenable to direct time-resolved kinetic studies,[26,27] despite its longtime use

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in the initiation of free radical polymerizations. In light of the fact that the absolute kinetics of reactions of EOH with many of these species has not been determined, we felt that it would be of value to make such measurements. Further, since the reactivity of EOH toward peroxyl radicals is so much greater than that of simple phenols (vide supra), we felt that it would be interesting to see if the same were true of the reactions of EOH with the classes of reaction intermediates mentioned above.

Experimental Section

Materials. Vitamin E, (2*R*,4′*R*,8′*R*)-α-tocopherol, was a high-purity product (>99%) from Eastman Kodak and was used as received. A slightly less pure vitamin E (Aldrich, about 98% pure) was used to determine the rate constant for reaction with the alkyl radical. Phenol (Aldrich) was recrystallized from cyclohexane.

Benzophenone and *p*-methoxyacetophenone were from Aldrich and were both recrystallized from ethanol. Di-*tert*-butyl peroxide (MCB Reagents) was treated in an alumina column immediately prior to use. Di-6-heptenoyl peroxide and bis(4-methoxybenzoyl) peroxide were both prepared according to literature procedures.[28,29]

Organic solvents were obtained from Aldrich, Fisher, or BDH and were of the highest quality commercially available. They were used as received. Water was of conductivity grade (resistance, >18 MΩ/cm^2) and was prepared by passing distilled water through a Sybron/Barnstead Nanopure II system. D_2O was purchased from MSD Isotopes.

Flash Photolysis Experiments. The details of the laser flash photolysis system have been provided elsewhere.[30,31] These experiments were carried out in cells made of 7 × 7 mm^2 Suprasil quartz tubing. The ketone concentrations used were typically on the order of 10^{-3} M, while the concentration of di-*tert*-butyl peroxide was at least 20% by volume. The concentration of bis(4-methoxybenzoyl) peroxide was such as to give an adequate absorbance at the laser wavelength (308 nm). Aliquots of EOH stock solutions were added via a microliter syringe, and the samples were rendered oxygen-free by bubbling with specially pure nitrogen for about 10 min.

Experiments designed to determine kinetic isotope effects on the reaction of EOH with radicals or excited states were carried out in benzene, CCl_4, or "wet" acetonitrile (acetonitrile + 10% water). In the nonpolar solvents, the exchange of the EOH hydrogen was facilitated by washing reagent stock solutions and the solvent of the reaction sample several times with D_2O.[32] In the wet acetonitrile experiments, 10% water was replaced with 10% D_2O.

Samples for laser flash photolysis were irradiated with the pulses from a Molectron UV-24 nitrogen laser (337 nm) or, less frequently, with the pulses from a Lumonics TE 860-2 excimer laser operating at 308 nm. Transient decay traces were averages of 10 laser shots with appropriate background or fluorescence corrections. The growth or decay traces were monitored at or near the λ_{max} of the species of interest.

The use of static samples (as opposed to a flow system) leads to only minor (<10%) overall substrate conversion during the course of the laser flash experiments. This was assured by comparison of the UV–vis spectra of the samples before and after the laser experiments. These spectra were obtained with a Hewlett-Packard 8451 diode array spectrometer.

5-Hexenyl Radical Clock. The rate constant for the reaction of EOH with the 5-hexenyl radical was determined using the 5-hexenyl radical "clock"[33,34] at 70 °C. At this temperature the rate constant for cyclization of the 5-hexenyl radical is 1.1×10^6 s^{-1}.[35] An aliquot of EOH stock solution at the desired concentration in benzene was placed in a quartz tube to which a ground glass vacuum joint had been attached. Next an aliquot of neat diheptenoyl peroxide was added to the EOH solution at a concentration about one-fifth that of the phenol. The samples prepared in this manner were then deoxygenated by several freeze–pump–thaw cycles on a vacuum line, following which the tubes were sealed and placed in an oil bath at 70 °C. The samples were allowed to react at 70 °C for 5 days to ensure complete decomposition of the peroxide. At the end of this time, the tubes were opened, and 2-μL aliquots were analyzed by gas chromatography. The products, 1-hexene and 1-methylcyclopentane, were quantified using authentic samples.

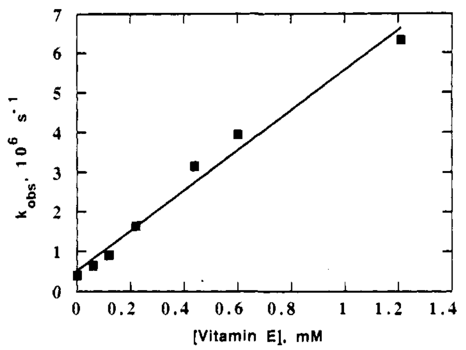

Figure 1. Quenching plot for the reaction of vitamin E with triplet benzophenone in benzene. Data recorded at 600 nm; [benzophenone] = 2 mM.

Table I. Rate Constants for the Reaction of α-Tocopherol with Various Reactive Species[a]

triplet state or radical	solvent	k, 10^9 M^{-1} s^{-1} [b]
benzophenone	C_6H_6	5.1 ± 0.6
	C_6H_6 + 1.3 M CH_3OH	3.7 ± 0.4
p-methoxyacetophenone	C_6H_6	5.9 ± 0.2
	C_6H_6 + 1.3 M CH_3OH	3.2 ± 0.4
xanthone	C_6H_6	5.7 ± 1.6
	C_6H_6 + 1.3 M CH_3OH	6.0 ± 0.8
butyrophenone	C_6H_6	3.3 ± 1.2[c]
tert-butoxyl	1:1 peroxide/C_6H_6	3.8 ± 0.5
	"wet" acetonitrile	0.66 ± 0.06
5-hexenyl	C_6H_6	0.0017 ± 0.0002[d]
4-methoxybenzoyloxyl	CCl_4	3.6 ± 0.6
	acetonitrile	8.6 ± 1.0
poly(peroxystyryl) peroxyl	styrene	0.0032[e]

[a] At 298 K except for the 5-hexenyl and poly(peroxystyryl) peroxyl radicals. [b] Random errors only are given as ±2σ. [c] Real errors may be significantly greater than indicated here. See text. [d] At 343 K. [e] At 303 K, from ref 20.

Results

Reaction of EOH with Ketone Triplets. (i) nπ* Triplets. The reactivity of EOH toward several aromatic ketones was examined. In each case laser excitation led to efficient formation of the triplet ketone, which was rapidly quenched by the phenol. Consider the case of benzophenone (K) as an example. The steps which may be involved in the quenching process are as follows:

$$\mathrm{K} \xrightarrow{h\nu,\ \mathrm{ISC}} {}^3\mathrm{K} \tag{1a}$$

$${}^3\mathrm{K} \rightarrow \mathrm{K} \tag{1b}$$

$${}^3\mathrm{K} + \mathrm{EOH} \rightarrow \mathrm{KH}^{\bullet} + \mathrm{EO}^{\bullet} \tag{1c}$$

$${}^3\mathrm{K} + \mathrm{EOH} \rightarrow \mathrm{K} + {}^3\mathrm{EOH} \tag{1d}$$

$${}^3\mathrm{K} + \mathrm{EOH} \rightarrow \mathrm{K} + \mathrm{EOH} \tag{1e}$$

where ^{3}EOH represents the triplet state of vitamin E. The last three reactions can potentially contribute to EOH quenching of triplet benzophenone, ^{3}K, and their individual rate constants can be summed to give an overall rate constant, k_q. The benzophenone triplet state has a λ_{max} at 525 nm but also absorbs weakly beyond 600 nm. The benzophenone ketyl radical, KH$^{\bullet}$, absorbs strongly at 545 nm. Thus, the absorptions of these two species can interfere with one another when both are present and the system is monitored at $\lambda < 600$ nm. We chose to study the EOH quenching of ^{3}K at 600 nm where the triplet absorbs weakly but the ketyl radical is essentially transparent.[36]

The decay of ^{3}K followed pseudo-first-order kinetics both in the absence and presence of EOH under our experimental con-

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Table II. Deuterium Isotope Effects on the Reactivity of α-Tocopherol at 298 K

triplet state or radical	solvent	k_H/k_D[a]
benzophenone	C_6H_6	1.09
p-methoxyacetophenone	C_6H_6	1.19
xanthone	C_6H_6	1.12
tert-butoxyl	1:1 peroxide/C_6H_6	1.31
	"wet" acetonitrile[b]	2.69
4-methoxybenzoyloxyl	CCl_4	0.95
poly(peroxylstyryl) peroxyl	styrene	5.4 ± 0.4[c]

[a] k_H values in Table I. [b] Containing H_2O or D_2O, as appropriate. [c] Reference 20.

ditions (3 mM ketone, partially attenuated laser beam). The experimentally observed pseudo-first-order rate constant, k_{obsd} is related to k_q according to eq 2

$$k_{obsd} = k_0 + k_q[\mathrm{EOH}] \tag{2}$$

where k_0 is the decay rate constant of ^{3}K in the absence of EOH (i.e., decay via reaction 1b or with the solvent). Plots based on this equation for triplet benzophenone quenching by EOH were found to be linear (Figure 1), permitting the value of k_q to be determined. The values of k_q for the reaction of EOH with triplet benzophenone in benzene and in benzene/methanol are presented in Table I. The Table also presents k_q values for the reaction of EOH with several other ketone triplets, which were determined in the same manner as those for benzophenone. Kinetic deuterium isotope effects for these reactions are given in Table II.

The data in Table I show that ketone triplets like benzophenone (^{3}nπ*), butyrophenone (^{3}nπ*), and xanthone (^{3}nπ* in nonpolar solvents and ^{3}π,π* in polar media)[30] are quenched by EOH at close to the diffusion-controlled limit. In the case of benzophenone, k_q is reduced slightly when a hydrogen-bonding co-solvent (methanol) is added to the reaction mixture. In addition, only minor deuterium isotope effects were observed for EOH quenching of nπ* triplets in benzene (benzophenone and xanthone).

The transient absorption spectrum observed following laser excitation of benzophenone in benzene corresponded to that of the benzophenone triplet.[37] When 1.25 mM EOH was added, the triplet spectrum was replaced by the transient spectra shown in Figure 2. The spectrum in Figure 2a was recorded 120 ns after the laser pulse. The band near 425 nm is characteristic of the vitamin E phenoxyl radical,[22] EO•, while that near 530 nm is due to triplet benzophenone. At 900 ns after the laser pulse (Figure 2b), the triplet has completely decayed, and its spectrum has been replaced by that of the benzophenone ketyl radical. In addition, the EO• absorbance has increased.

It should also be possible to measure k_q by monitoring the rate constant for growth of EO• in this system. If this value agrees with the value of k_q determined by monitoring the decay of triplet benzophenone, ^{3}K, it would be conclusive evidence that triplet benzophenone is a precursor for EO•. However, ^{3}K absorbs strongly enough in the 425-nm region to make accurate determination of the growth kinetics difficult. In effect the presence of ^{3}K causes an initial "jump" in the ΔOD to be superimposed on the EO• growth signal. In spite of this problem, it was clear that the formation of EO• was concurrent with the decay of the triplet that must therefore be its precursor.

Some light can be shed on the relative importance of the various quenching pathways (reactions 1c–e) contributing to the EOH-mediated deactivation of ^{3}K using a technique proposed by Das et al.[38,39] The maximum "end-of-pulse" optical density (top OD) of triplet benzophenone at 545 nm was measured for a sample containing 0.041 M benzophenone in benzene. This top OD value was compared to the top OD at 545 nm for an optically matched sample containing the same ketone concentration and sufficient EOH added to quench about 95% of the triplets. The transient absorption at 545 nm in the latter case would then be due primarily to the benzophenone ketyl radical. We found that at 545 nm the ratio top OD triplet/top OD ketyl was 2.69 ± 0.11 using 24% of the available nitrogen laser energy (attenuated to minimize any effect due to triplet–triplet annihilation). Using the literature value of 2.36 for the ratio of extinction coefficients for triplet benzophenone versus the benzophenone ketyl,[38,40,41] we concluded that 88 ± 4% of the quenching events led to ketyl radical formation. In view of the uncertainty in literature values of transient extinction coefficients, as well as the uncertainty in our measured top OD ratio, the efficiency of radical formation should not be considered different from 100%. Thus, there is no need to invoke any contribution from energy-transfer processes in the quenching of benzophenone triplets by EOH; in fact, we would not expect EOH to have a triplet state below that of benzophenone.

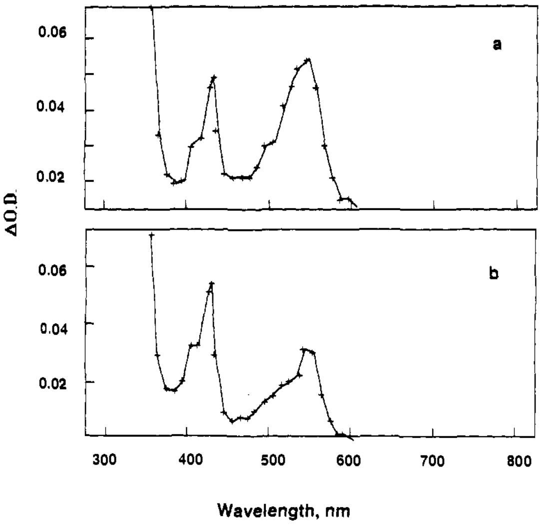

Figure 2. Transient absorption spectra recorded in nitrogen-saturated benzene in the presence of 3 mM benzophenone and 1.2 mM EOH 120 ns (a) and 900 ns (b) after the laser pulse.

Finally, a few words about the value of k_q found for triplet butyrophenone are in order. In the absence of EOH the triplet of butyrophenone was detected as a broad, weak absorption with λ_{max} near 360 nm. The lifetime of this triplet is limited by the Norrish Type II reaction and is measured to be 90 ns in deaerated benzene. When EOH was added to this system, the EO• spectrum was readily detected. However, because of the short triplet lifetime and because the strongly absorbing EO• radical interfered with the detection of the signal due to the triplet, it was not possible to measure k_q by monitoring triplet decay. However, it was possible to estimate k_q by monitoring the growth of the EO• signal at 425 nm. Because of the short lifetime of the butyrophenone triplet, rather large EOH concentrations were required in order for quenching by EOH to be the dominant mode of triplet decay. For this system, the plot based on eq 2 exhibited substantial scatter reflecting the short time scales involved. The error in the value of k_q for this reaction may therefore be even larger than that given in Table I.

(ii) ππ* Triplets. Values of k_q were determined for EOH quenching of the ππ* triplets of *p*-methoxyacetophenone and xanthone (in a polar solvent where its triplet has π,π* character).[30] The values of k_q are listed in Table I. As in the case of the nπ* triplets, only a minor deuterium isotope effect was observed (Table II). In analogy with the nπ* systems, we attribute k_q to the quenching of triplet ketone by EOH leading to, at least in part, formation of EO• and the corresponding ketyl radical.

We have also examined the influence of hydrogen bonding on the reactivity of EOH and phenol toward the triplet of *p*-methoxyacetophenone. These results are summarized in Table III.

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Table III. Effect of Hydrogen Bonding on the Reactivity of α-Tocopherol (EOH) and Phenol (PhOH) toward Triplet *p*-Methoxyacetophenone at 298 K

	k, 10^{-9} M^{-1} s^{-1} [a]	
solvent	EOH	PhOH
C_6H_6	5.9 ± 0.2	
H_2O-saturated C_6H_6		5.4 ± 0.3
acetonitrile	5.0 ± 0.3	0.41 ± 0.06
10% water in acetonitrile	4.8 ± 0.3	0.13 ± 0.01

[a] Random errors given as $\pm 2\sigma$.

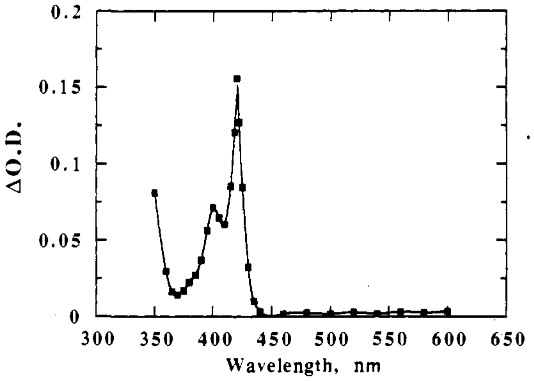


Figure 3. Absorption spectrum of the vitamin E phenoxyl radical in nitrogen-saturated 1:1 di-*tert*-butyl peroxide/benzene (v/v). Recorded 450 ns after laser excitation. [EOH] = 2.9 mM.

The value of k_q for EOH is subject to only a small decrease under conditions in which the phenoxyl hydrogen experiences hydrogen bonding. By contrast, k_q for phenol is highly sensitive to hydrogen bonding and changes by a factor of 42 on changing from benzene to 10% water in acetonitrile. The value of $(0.41 \pm 0.06) \times 10^9$ M^{-1} s^{-1} found in commercial acetonitrile may not be a limiting value, since spectrograde acetonitrile may contain traces of water.

Reaction of EOH with the 4-Methoxybenzoyloxyl Radical. The 4-methoxybenzoyloxyl radical was generated in CCl_4 and acetonitrile by 308-nm laser photolysis of bis(4-methoxybenzoyl) peroxide:[26,27]

$$ArC(O)OOC(O)Ar \rightarrow 2ArCO_2^{\bullet} \qquad (3)$$

where Ar = $4\text{-}CH_3OC_6H_4$. This radical has moderately strong absorptions at $\lambda > 500$ nm and has a lifetime of about 3 μs in CCl_4 and ≥ 50 μs in acetonitrile at 24 °C. Its decay was monitored at 720 nm in both solvents. In the presence of EOH, the lifetime of the 4-methoxybenzoyloxyl radical was reduced with a concurrent formation of the EO• signal (monitored at 425 nm). Values of the rate constant for the reaction

$$4\text{-}CH_3OC_6H_4CO_2^{\bullet} + EOH \xrightarrow{k_4} 4\text{-}CH_3OC_6H_4CO_2H + EO^{\bullet} \qquad (4)$$

were identical when measured from the decay of 4-methoxybenzoyloxyl or from the growth of EO•. These values are listed in Table I, while the isotope effect is given in Table II.

Reaction of EOH with the *tert*-Butoxyl Radical. Photodecomposition of di-*tert*-butyl peroxide by 337-nm nitrogen laser pulses yields *tert*-butoxyl radicals within the duration of the pulse. This radical is known to abstract the phenoxyl hydrogen from phenols very rapidly in comparison with its decay by β-scission or reaction with alkane solvents.[39]

Photolysis of solutions containing di-*tert*-butyl peroxide, an organic solvent, and EOH yields the 425-nm EO• absorption (Figure 3). The resolution of this EO• spectrum (±2 nm) is superior to those published previously.[22,42,43] Kinetic data for reaction 5 were obtained by monitoring the growth of the EO• absorption.

$$(CH_3)_3CO^{\bullet} + EOH \xrightarrow{k_5} (CH_3)_3COH + EO^{\bullet} \qquad (5)$$

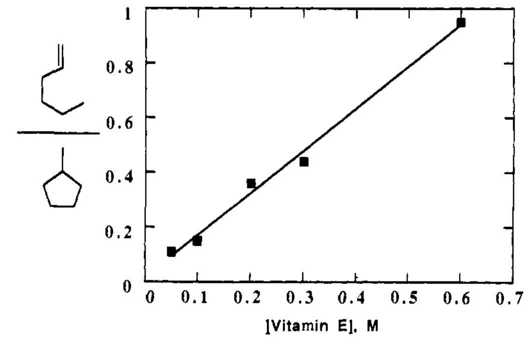
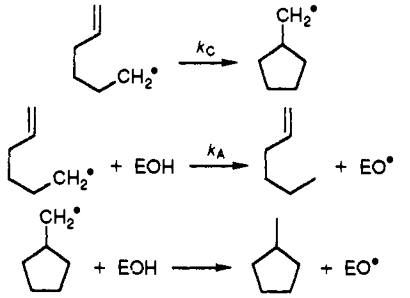


Figure 4. Plot of relative yields of unrearranged to rearranged product vs phenol concentration for hydrogen abstraction by 5-hexenyl in benzene at 70 °C (see eq 7).

The resulting rate constants are given in Table I, and the deuterium kinetic isotope effects are in Table II.

Reaction of EOH with the 5-Hexenyl Radical. The irreversible, unimolecular cyclization of the 5-hexenyl radical[33,34] can be used to determine the rate constant of a reaction that competes with the cyclization. In the present study, this method was used to determine the rate constant for hydrogen abstraction from EOH in benzene at 70 °C according to the following scheme.



(6)

The rate constant k_A can be calculated from a plot of the relative concentration of 1-hexene to methylcyclopentane vs the EOH concentration (see Figure 4), namely,

$$[\text{1-hexene}]/[\text{methylcyclopentane}] = (k_A/k_C)[EOH] \qquad (7)$$

At 70 °C, k_C is[35] 1.1×10^6 s^{-1} which, when combined with the slope of the line in Figure 4, yields $k_A = 1.7 \times 10^6$ M^{-1} s^{-1} (see Table I).

Discussion

Both n,π^* and π,π^* aromatic ketone triplets appear to react with EOH mainly by abstracting the phenolic hydrogen and forming the corresponding ketyl radical and the EO radical. These reactions occur at, or close to, the diffusion-controlled limit in benzene, benzene/1.3 M methanol (Table I), acetonitrile, and acetonitrile/10% water (Table III). The high rates of these reactions provide a ready explanation for the insignificant deuterium kinetic isotope effects that were observed (Table II), though other factors may play some role since Das et al.[38] found k_H/k_D = 1.2 for the benzophenone triplet/phenol reaction in a hydrogen-bonding solvent in which k_H was only 8×10^7 M^{-1} s^{-1}. In this connection, the strong retarding effect of hydrogen-bonding solvents on the rate of reaction of triplet *p*-methoxyacetophenone with phenol stands in dramatic contrast to their virtual lack of influence on the rate of reaction of this triplet with EOH (Table III). Presumably, the two "buttressed" ortho methyl groups in EOH sterically inhibit hydrogen bonding of the phenolic OH groups of α-tocopherol.

The 4-methoxybenzoyloxyl radical also reacts with EOH at, or close to, the diffusion-controlled limit (Table I) and without any deuterium kinetic isotope effect (Table II). Spectroscopic

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data (not shown) indicate that this reaction yields $EO^\bullet$. However, the fact that the quenching rate constant is about twice as large in acetonitrile as in CCl_4 suggests that this reaction does not necessarily involve a simple hydrogen atom abstraction but may, in polar solvents, involve an initial electron transfer followed by proton loss (reactions 8a and 8b). A similar suggestion has been made previously[27] for the reaction of this aroyloxyl radical with 2,4,6-tri-*tert*-butylphenol ($k = 1 \times 10^9$ M^{-1} s^{-1} in CCl_4).[27]

$$4\text{-}CH_3OC_6H_4CO_2^\bullet + EOH \rightarrow 4\text{-}CH_3OC_6H_4CO_2^- + (EOH)^{\bullet+} \tag{8a}$$

$$(EOH)^{\bullet+} \rightarrow EO^\bullet + H^+ \tag{8b}$$

The *tert*-butoxyl radical also reacts with EOH at close to the diffusion-controlled limit in 1:1 di-*tert*-butyl peroxide/benzene, and as expected therefore, the reaction shows only a trivial deuterium kinetic isotope effect (viz., 1.3; see Table II). This reaction is slower in acetonitrile where the isotope effect is 2.7. We tentatively attribute the differences in solvent effects on reaction rates with EOH between the aromatic ketone triplets and *tert*-butoxyl radicals to a greater contribution of charge-transfer interactions in the transition states for the reactions involving the triplets. These charge-transfer interactions counteract to some extent the rate-retarding effect of hydrogen bonding on hydrogen atom abstraction from EOH. We discount the possibility that hydrogen abstraction from EOH in wet acetonitrile involves the methyl radical formed by the β-scission reaction,

$$(CH_3)_3CO^\bullet \rightarrow CH_3^\bullet + (CH_3)_2CO \tag{9}$$

because the rate constant for the $CH_3^\bullet$ + EOH reaction is unlikely to be much in excess of about 10^6 M^{-1} s^{-1} at room temperature (vide infra).

There would appear to be very little kinetic data on hydrogen atom abstraction from phenols by nonpolymeric carbon-centered radicals, particularly in nonpolar and non-hydrogen-bonding media.[44,45] In fact, we uncovered only two separate studies of such reactions. Simic[23,46] has reported that the $EO^\bullet$ absorption spectrum was not detected upon the pulse radiolysis of deaerated cyclohexane solutions of EOH at room temperature, from which he concluded that $k_{10} \leq 10^5$ M^{-1} s^{-1}.

$$C_6H_{11}^\bullet + EOH \rightarrow C_6H_{12} + EO^\bullet \tag{10}$$

Rüegge and Fischer[47] have reported that in heptane the $HOCH_2^\bullet$ and *tert*-butyl radicals reacted with the sterically hindered 2,6-di-*tert*-butylphenol at room temperature with rate constants of 702 and 93 M^{-1} s^{-1}, respectively (and for *tert*-butyl + phenol in 1,2-epoxybutane, 14 M^{-1} s^{-1}). A relatively low rate constant might therefore have been anticipated for reaction of the primary 5-hexenyl radical with EOH. We were therefore somewhat surprised to obtain $k_A = (1.7 \pm 0.2) \times 10^6$ M^{-1} s^{-1} at 70 °C (see reaction 6). If we assume a normal Arrhenius preexponential factor of $10^{8.5}$ M^{-1} s^{-1} for this hydrogen atom abstraction,[48] we obtain an energy of activation of 3.6 kcal/mol and a value of $k_A \approx 8 \times 10^5$ M^{-1} s^{-1} at 25 °C. The large magnitude of this rate constant no doubt reflects the well-known high reactivity of α-tocopherol toward (peroxyl) radicals,[7,8,13,14,20] the presence of an (relatively) unhindered phenolic hydroxyl group, and the strong ($\Delta H \approx 22$ kcal/mol)[49-54] thermodynamic driving force for hydrogen atom abstraction from EOH by a primary alkyl radical. The greater rate constant (see Table I) found for the less exothermic hydrogen atom abstraction from EOH by peroxyl radicals ($\Delta H \approx 10$ kcal/mol)[49,53,54] can simply be attributed to the smaller "intrinsic" activation energy (i.e., activation energy for a thermoneutral reaction, E^*) for hydrogen atom transfer between two oxygen atoms ($E^* = 4.9$ kcal/mol) compared to its transfer between oxygen and carbon ($E^* = 10.0$ kcal/mol)[55] (there are many other examples of low activation energy, fast hydrogen atom transfer between two oxygen atoms).[56]

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Registry No. EOH, 59-02-9; $EO^\bullet$, 23531-69-3; di-*tert*-butyl peroxide, 110-05-4; di-6-heptenoyl peroxide, 26841-80-5; bis(4-methoxybenzoyl) peroxide, 849-83-2; 5-hexenyl radical, 16183-00-9; *tert*-butoxy radical, 3141-58-0; 4-methoxybenzoyloxy radical, 33574-06-0; styrene, 100-42-5; phenol, 108-95-2; cyclopentylmethyl radical, 23907-66-6; benzophenone ketyl, 16592-08-8; 1-hexene, 592-41-6; methylcyclopentane, 96-37-7.

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