

α -Tocopheroxyl Decay: Lack of Effect of Oxygen

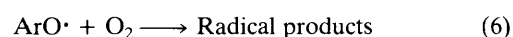
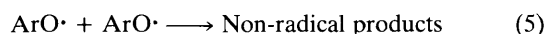
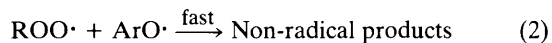
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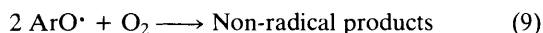
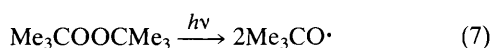
α -Tocopherol appears to have been selected as nature's major lipid-soluble, chain-breaking antioxidant because it has a number of superior properties when compared with most synthetic phenolic antioxidants: one of these properties is shown to be very low reactivity of α -tocopheroxyl towards oxygen.

Extensive studies of the inhibited autoxidation of organic compounds, RH, have shown that the more effective phenolic antioxidants react rapidly, and essentially irreversibly, with peroxy radicals,¹ reaction (1). The resultant phenoxyl radical should be relatively unreactive except towards a second peroxy radical,¹ reaction (2), and, in certain biological (model) systems, towards a suitable reducing agent such as ascorbate, AscH⁻,²⁻⁶ reaction (3). This means that chain transfer by reaction with RH, reaction (4), as well as by reaction (-1) should be slow.^{1,7} It further implies that both the bimolecular self-reaction of ArO[•] radicals, reaction (5), and their reaction with O₂, reaction (6), should also be slow.



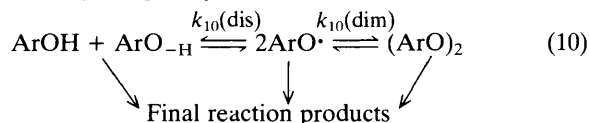
Living organisms, including man, utilize vitamin E as their major, and possibly only, lipid-soluble, phenolic antioxidant.^{8,9} We have shown that α -tocopherol, α -T (the most important of the 4 tocopherols constituting vitamin E) and a number of structurally related phenols react extremely rapidly with ROO \cdot radicals.^{10,11} That chain transfer can occur between the α -T radical α -T \cdot , and the methyl esters of unsaturated fatty acids [reaction (4)] appears to have been demonstrated,¹² but it seems probable that this is not a particularly fast (and, hence, important) reaction under physiological conditions. There have previously been some room temperature kinetic studies involving α -T \cdot in reaction (3) (fast, $k_3^{\alpha-T} = 1.55 \times 10^6 \text{ mol}^{-1} \text{ dm}^3 \text{ s}^{-1}$)³ and reaction (5) (slow, $2k_5^{\alpha-T} = 180 \text{ mol}^{-1} \text{ dm}^3 \text{ s}^{-1}$ in CHCl_3 ,¹³ $350 \text{ mol}^{-1} \text{ dm}^3 \text{ s}^{-1}$ in cyclohexane,¹⁴ and $0.061 \text{ mol}^{-1} \text{ dm}^3 \text{ s}^{-1}$ in benzene¹⁵) but there do not appear to have been any kinetic studies involving α -T \cdot in reactions (-1), (2), and (6), though reactions (-1)¹⁵ and (2)^{10,11} appear to be fairly rapid. As we report herein, reaction (6) is too slow to compete with reaction (5) at the highest oxygen concentrations that are experimentally convenient.

Benzene-di-*t*-butyl peroxide (10:1, v/v) solutions of α -T were subject to a *single*, brief pulse of u.v. light while held in the cavity of an e.s.r. spectrometer. Generation of α -T \cdot was essentially instantaneous [reactions (7) and (8)]. Decay of α -T \cdot was monitored at 23°C using various initial concentrations of α -T (1, 5, and $50 \times 10^{-3} \text{ M}$) and with samples that had either been degassed and sealed under high vacuum or were continuously saturated with O₂ at 760 Torr. With initial $[\alpha\text{-T}\cdot] = \text{ca. } 2 \times 10^{-5} \text{ M}$, decay followed 'clean' second order kinetics down to $[\alpha\text{-T}\cdot] \leq 4 \times 10^{-6} \text{ M}$ in all cases with $2k_5^{\alpha-T} = 3 \times 10^3 \text{ mol}^{-1} \text{ dm}^3 \text{ s}^{-1}$ both in the absence and in the presence of oxygen. Since the O₂ concentration is *ca.* $9.2 \times 10^{-3} \text{ M}$,¹⁶ we estimate that k_6 must be $\ll 2k_5^{\alpha-T} [\alpha\text{-T}\cdot]/[\text{O}_2] = 6.5 \text{ mol}^{-1} \text{ dm}^3 \text{ s}^{-1}$. The PhO \cdot radical is also known to be unreactive towards O₂ on the time scale of its bimolecular self-reaction,¹⁷ which is, however, diffusion-controlled.¹⁸ The only ArO \cdot /O₂ reaction to have been subject to kinetic study involved the extremely persistent tri-*t*-butyl phenoxyl radical;¹⁹ decay followed termolecular kinetics [reaction (9)] and k_9 can be calculated to be *ca.* $3 \times 10^5 \text{ mol}^{-2} \text{ dm}^6 \text{ s}^{-1}$ at 25°C.¹⁹ If α -T \cdot reacts in this way, $k_9^{\alpha-T} \ll 2k_5^{\alpha-T} [\alpha\text{-T}\cdot]^2 [\text{O}_2] = 3 \times 10^5 \text{ mol}^{-2} \text{ dm}^6 \text{ s}^{-1}$. We conclude that the slowness of the reaction between α -T \cdot and O₂ provides yet one more reason why α -T appears to have been selected as nature's major lipid soluble, chain-breaking antioxidant.



The larger value found for $2k_5^{\alpha-T}$ in this work, compared with previous studies,¹³⁻¹⁵ is readily explained. The kinetics of the decay of a great many ArO \cdot are complicated by the reversible formation of diamagnetic dimer and/or disproportionation products [reaction (10)].²⁰⁻²² If ArO \cdot decay is monitored under anything other than 'initial' conditions, *i.e.*, in a completely 'fresh' solution of ArO \cdot , there is a high probability that the reversible and irreversible decay processes will become mixed in varying proportions. The measured value for $2k_5$ will be less than the true value for the *initial* dimerization and/or disproportionation, *i.e.*, it will be $< 2[k_{10}(\text{dim}) + k_{10}(\text{dis})]$, and the measured decay may even

follow first order kinetics.²² At low temperatures α -T \cdot has been reported to dimerize.²³ In our experiments with 'fresh' α -T \cdot decay followed clean second order kinetics for more than 80% of the reaction, but a small 'residual' signal took a long time to decay completely.



Kinetic studies on other T \cdot and related ArO \cdot serve to confirm the conclusion drawn from α -T \cdot . For example, with β -T \cdot the apparent value of $2k_5^{\beta-T}$ decreased drastically with repeated measurements on the same sample, while with γ -T \cdot the decay rapidly switched to first order kinetics. Initial values of $2k_5$ for β -, γ -, δ -, and 5,7-dimethyl-T \cdot are *ca.* 4×10^4 , 4.5×10^4 , 1.5×10^5 , and $4.5 \times 10^3 \text{ mol}^{-1} \text{ dm}^3 \text{ s}^{-1}$, respectively. For β - and δ -T \cdot it was shown that O₂ had no significant effect on these rate constants.

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