

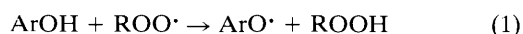
Phenol–Phenoxy Radical Equilibria by Electron Spin Resonance: are Radicals derived from Tocopherol and Analogues Exceptionally Stabilized?

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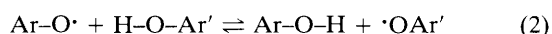
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The extra 'stabilization' of the 2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-oxyl radical compared with the 2,6-di-*tert*-butyl-4-methoxyphenoxy radical is attributed to entropy differences between the parent phenols.

A large number of kinetic studies^{1,2} has established the superiority of tocopherols such as α -tocopherol **1a**, and analogues such as **1b** and **2** over simple phenols such as **3g** as antioxidants. These phenols remove peroxy radicals by reaction (1).



Doba *et al.*³ have drawn attention to the maximization of overlap of a p orbital on the 4-oxygen substituent if the attached group is coplanar with the aromatic ring. In compounds such as **2**, near-coplanarity is enforced whereas in **1**, the puckering of the six-membered ring significantly increases the dihedral angle and reduces stabilization. However, effects other than radical stabilization may be important in a kinetic process. To isolate the thermodynamic factors, we have undertaken an equilibrium study of nine phenols of types **1**–**3** with phenoxy radicals [reaction (2)].



Mixtures of two phenols in benzene were degassed and treated with a deficiency of diphenylpicrylhydrazyl. Relative radical concentrations were found from the electron spin resonance (ESR) spectrum by FTMATCH—a development from our previous correlation program MATCH.⁴ The simulation of each radical is optimized independently, the proportions are optimized to give the best fit (cross-correlation) with the experimental spectrum, and the simulations are

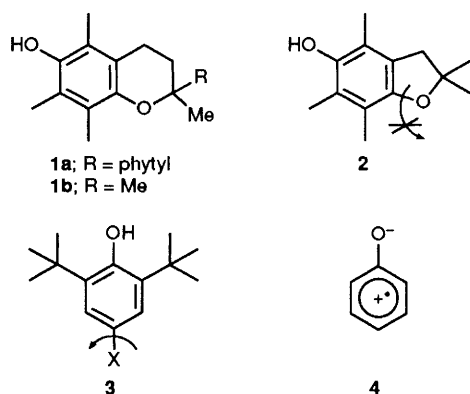
double-integrated to give the relative radical concentrations. Relative concentrations of the phenols were varied by factors of up to 16 without producing significant changes in the derived equilibrium constant. Twelve different pairs of phenols were studied, each phenol being used at least twice. The results, shown in Table 1, cover a range of 400 000, corresponding to a difference in ΔH of 32 kJ mol⁻¹ if entropy effects are unimportant. Individual values are consistent within a factor of 1.3.

The results are consistent with an early colorimetric result⁵ which gives K_2 (ArOH = **3e**, Ar'OH = **3g**) = 210, compared

Table 1 Derived values of equilibrium constants for reaction (2) (ArOH = **3a**) at room temperature (21 ± 2 °C)

Phenol Ar'OH	<i>K</i>	σ^+ (ref. 11)
3a , X = NO ₂	1.0 ^a	0.81
3b , X = CHO	9.3	0.47
3c , X = CH ₂ NMe ₂	430	
3d , X = Me	510	-0.31
3e , X = CMe ₃	580	-0.26
3f , X = CH=NOH	4 100	
1a	51 000	
3g , X = OMe	140 000	-0.78
2	400 000	

^a Defined.



with our value of 240, but agreement is not so good with a more recent ESR determination⁶ of $K_2(\text{ArOH} = \mathbf{3d}, \text{Ar}'\text{OH} = \mathbf{1a}) = 749$ and $K_2(\text{ArOH} = \mathbf{3e}, \text{Ar}'\text{OH} = \mathbf{3d}) = 11.0$, where we find values of 100 and 0.9, respectively. Our last value receives some support from the literature. There have been a number of recent indirect determinations of the bond dissociation energies of *para*-substituted phenols. Three groups have obtained values for both *p*-methylphenol and *p*-*tert*-butylphenol. Two of these groups^{7,8} find virtually identical ArO-H bond dissociation energies for these two compounds, in support of our result, while the third group⁹ find that the phenoxyl radical is stabilized to a greater extent by a *p*-methyl group than by a *p*-*tert*-butyl group, which would support a higher value of the equilibrium constant.

The results in Table 1 show that electron-releasing substituents in the 4-position stabilize the monocyclic radicals derived from the phenols **3**. There is a reasonably good correlation with σ^+ [$\log K = (2.27 \pm 0.21) - (3.00 \pm 0.36)\sigma^+$; $r = -0.98$], indicating the probable importance of contributions from structures such as **4** to the structure of the radical; stabilization of this type is not available to the parent phenol. Polar effects of this type have been observed in photoacoustic¹⁰ and redox⁷ studies of bond dissociation energies in phenols.

We have investigated the temperature variation of the equilibrium constant for two examples of reaction (2), involving ArOH = **3g** or **3d** and Ar'OH = **2** or **3g** in reactions (2a) and (2b), respectively. The first of these reactions (2a) shows no significant temperature variation from 3 to 39 °C ($\Delta H = 3 \pm 3 \text{ kJ mol}^{-1}$ from a $\log K$ vs. $1/T$ plot). This implies that ΔH is effectively zero for this reaction, corresponding to full conjugation of the oxygen substituent in both phenoxyl radicals. The difference of the equilibrium constant from 1.0 can therefore be attributed to an entropy effect, giving $\Delta S = 20 \pm 11 \text{ J mol}^{-1} \text{ K}^{-1}$. The methoxy group in the monocyclic phenol is capable of free rotation; this is effectively stopped in the radical if maximum overlap and stabilization is to be maintained. On the other hand, the bicyclic phenol **2** has no possibility of rotation round the O-C bond either in the molecule or in the derived radical; thus no entropy is lost on going from the phenol to the radical. Thus the equilibrium in (2a) lies to the right mainly due to this entropy effect. The analogous equilibrium in (2b) involves only monocyclic phenols. From equilibrium constant data at three temperatures, $\Delta H = -26 \pm 3 \text{ kJ mol}^{-1}$ and $\Delta S = -42 \pm 11 \text{ J mol}^{-1} \text{ K}^{-1}$. Stabilization of the phenoxyl radical by the *p*-methyl group does not depend on the orientation of the methyl group, so entropy is not lost on going to the radical. Thus the expected extra stabilization of the phenoxyl radical by the methoxy group should be offset to some extent by the ΔS term, as observed.

The greater stabilization of the radicals from **2** and **3g** over that for **1a** is seen as being due to the non-planarity of the oxygen-containing six-membered ring.

Comparison of our equilibrium results with earlier kinetic data is illuminating. Burton *et al.*² found that **2** was 1.8 times more effective than α -tocopherol in inhibiting the autoxidation of styrene and attributed this to the non-planarity of the six-membered oxygen-containing ring in α -tocopherol. Our equilibrium constant for reaction (2) involving these two phenols is 8.0, which indicates that if the relative rates and equilibrium constant values are determined only by energy effects, the resonance stabilization due to the incipient aroxyl radical is only about 28% developed in the transition state for the autoxidation reaction.

There is a striking difference between the equilibrium data and the kinetic behaviour of the bicyclic phenol **2** and the 2,6-di-*tert*-butylphenol **3g**. The equilibrium data shows a comparable degree of stabilization in the radicals derived from these two phenols, but the kinetic data² shows that **2** is approximately fifty times as efficient in reacting with peroxy radicals. Since this difference cannot be due to stabilization energy differences in the derived radicals, it is likely to be caused by the two bulky *tert*-butyl groups hindering the approach of the ROO \cdot radical to the phenol **3g**.

Thus our equilibrium studies provide further insight into the effectiveness of α -tocopherol **1a** and analogues in the inhibition of peroxidation. From the equilibrium point of view, the special effectiveness of **2** over **3g** is seen as an entropy effect: the five-membered ring cannot rotate freely either in the phenol or in the phenoxyl radical, whereas entropy is lost when 2,6-di-*tert*-butyl-4-methoxyphenol **3g** is converted into the corresponding phenoxyl radical. The greater kinetic effectiveness of **2** and **1a** over **3g** is due to steric hindrance to approach of the peroxy radical in **3g** by the two *ortho tert*-butyl groups; in **2** and **1a**, the hydroxy group is flanked only by methyl groups.

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