# Application of Photoacoustic Calorimetry to the Measurement of the O−H Bond Strength in Vitamin E (α- and δ-Tocopherol) and Related Phenolic Antioxidants[1]

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We recently demonstrated that photoacoustic calorimetry (PAC) can yield accurate enthalpies for the reaction of *tert*-butoxyl radicals (generated by 337 nm laser flash photolysis of di-*tert*-butyl peroxide) with phenol (reaction 1, Ar = Ph) both in hydrogen-bond accepting (HBA)

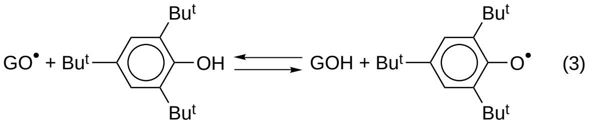
$$t\text{-BuO}^\bullet + \text{ArOH} \rightarrow t\text{-BuOH} + \text{ArO}^\bullet \qquad (1)$$

solvents and in non-HBA solvents.[2,3] Furthermore, we demonstrated that when due care is taken regarding the heats of solvation of the reactants and products,[2] these enthalpies could be converted into O−H bond dissociation enthalpies (BDE's) for phenol in each solvent, BDE(PhO−H)$^{\text{sol}}$, and that these quantities could be converted into gas-phase BDE's, BDE(PhO−H)$^{\text{gas}}$.[4] The mean value calculated for BDE(PhO−H)$^{\text{gas}}$ in five solvents[4] was 87.4 kcal/mol, in excellent agreement with the recommended value derived from measurements in the gas phase of 87.0 kcal/mol.

One of the most important uses for phenols is as radical-trapping antioxidants to protect organic materials from oxidative degradation. It can be argued that α-tocopherol (α-**T**OH) is *the* most important phenolic antioxidant because it is the major and most bioactive component of vitamin E.[5] It is also the most reactive of the fat-soluble biological antioxidants.[5] The high reactivity of α-**T**OH toward peroxyl radicals[5,6] necessarily implies that the O−H bond in this compound is considerably weaker than that in phenol. A very careful measurement of BDE(α-**T**O−H)$^{\text{PhH}}$ by Lucarini, Pedulli, and Cipolone (LPC)[9] supports this conclusion. LPC determined the equilibrium constant for the reaction between galvinoxyl (GO$^\bullet$, a very persistent phenoxyl radical commercially available as the pure compound) and α-**T**OH by EPR spectroscopy in benzene. The total radical

$$\text{GO}^\bullet + \alpha\text{-TOH} \rightleftarrows \text{GOH} + \alpha\text{-}\mathbf{TO}^\bullet \qquad (2)$$

concentration decreased during each experiment because α-**T**O$^\bullet$ radicals are not completely persistent.[9,10] In their calculations of $K_2$, LPC took this decrease carefully into account.[11] The absolute magnitude of BDE(α-**T**O−H)$^{\text{PhH}}$ was obtained by also measuring the equilibrium constant between GO$^\bullet$/GOH and 2,4,6-tri-*tert*-butylphenol and its persistent radical. The value of $\Delta H_f°(\text{Bu}^t{}_3\text{C}_6\text{H}_2\text{O}^\bullet)^{\text{PhH}} - \Delta H_f°(\text{Bu}^t{}_3\text{C}_6\text{H}_2\text{OH})^{\text{PhH}}$ is known to be 29.14 ± 0.08 kcal/mol from the calorimetric work of Mahoney *et al.*[12] LPC used their equilibrium data ($K_2$ and $K_3$) and Mahoney's calorimetric data to obtain a ΔBDE value for reaction 2. This was then converted to an absolute value of BDE(α-**T**O−H)$^{\text{PhH}}$ = 78.9 ± 0.4 kcal/mol by assuming that the heat of formation of the hydrogen atom in benzene was the same as that in the gas phase (52.1 kcal/mol).[16]



(3)

We decided to employ the PAC technique to measure BDE(α-**T**O−H)$^{\text{PhH}}$ in order to provide a value which did not depend on Mahoney's[12] calorimetry. Close agreement between our PAC BDE and LPC's BDE would also serve

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[2] Wayner, D. D. M.; Lusztyk, E.; Pagé, D.; Ingold, K. U.; Mulder, P.; Laarhoven, L. J. J.; Aldrich, H. S. *J. Am. Chem. Soc.* **1995**, *117*, 8737−8744.

[3] Details of the PAC technique and the experimental procedures can be found in ref 2.

[4] BDE(PhO−H)$^{\text{sol}}$ and BDE(PhO−H)$^{\text{gas}}$ in kcal/mol: isooctane, 88.2 and 86.2; CCl$_4$, 90.0 and 88.0; benzene, 89.3 and 86.3; CH$_3$CN, 95.0 and 88.3; ethyl acetate, 95.0 and 88.3.

[5] Burton, G. W.; Ingold, K. U. *Acc. Chem. Res.* **1986**, *19*, 194−201.

[6] $k^{303\text{K}} = 3.8 \times 10^6$ M$^{-1}$ s$^{-1}$;[7] from this rate constant and an empirical equation due to Mahoney and DaRooge[8] a value of 80.4 kcal/mol was estimated for BDE(α-**T**O−H).[7]

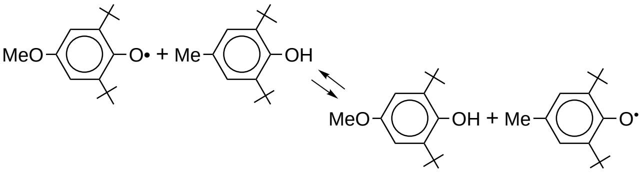
[7] Burton, G. W.; Doba, T.; Gabe, E. J.; Hughes, L.; Lee, F. L.; Prasad, L.; Ingold, K. U. *J. Am. Chem. Soc.* **1985**, *107*, 7053−7065.

[8] Mahoney, L. R.; DaRooge, M. A. *J. Am. Chem. Soc.* **1975**, *97*, 4722−4731.

[9] Lucarini, M.; Pedulli, G. F.; Cipollone, M. *J. Org. Chem.* **1994**, *59*, 5063−5070.

[10] Bowry, V. W.; Ingold, K. U. *J. Org. Chem.* **1995**, *60*, 5456−5467 and references cited.

[11] There had been two previous EPR equilibrium studies involving α-**T**OH and hindered phenols and their respective radicals in benzene. In both studies the general procedure of LPC was employed and (as with LPC) the results rest on Mahoney *et al.*'s[12] calorimetric determination of $\Delta H_f°(\text{Bu}^t{}_3\text{C}_6\text{H}_2\text{O}^\bullet) - \Delta H_f°(\text{Bu}^t{}_3\text{C}_6\text{H}_2\text{OH})$ and the assumption that $\Delta H_f°(\text{H}^\bullet)^{\text{benzene}} = \Delta H_f°(\text{H}^\bullet)^{\text{gas}}$ = 52.1 kcal/mol. In the first, 2,6-di-*tert*-butyl-4-methylphenol, BHT, was used; it yielded BDE(α-**T**O−H)$^{\text{PhH}}$ = 76.0 kcal/mol.[13] There can be little doubt that this value is too low. The error in this determination seems likely to lie in an insufficient correction for the decay of the aryloxyl radicals[9] since neither α-**T**O$^\bullet$ nor the aryloxyl from BHT are truly persistent. In the second study,[14] 2,6-di-*tert*-butyl-4-nitrophenol was employed as the reference phenol. From the measured equilibrium constants at 294 K (there would appear to have been errors in the entropy measurements)[9] with tri-*tert*-butylphenol (viz., 580) and α-**T**OH (viz., 51,000), we calculate a BDE(α-**T**O−H)$^{\text{PhH}}$ = 78.6 kcal/mol (which is in excellent agreement with the LPC value of 78.9 kcal/mol). The difficulties involved in these EPR equilibrium studies using phenoxyl radicals which are not truly persistent is readily apparent if we compare two studies of the "simple" equilibrium:



For this equilibrium, Jackson and Hosseini[14] give $K^{294\text{K}}$ = 140 000/510 = 275, Δ*H* = −6.2 kcal/mol, and Δ*S* = −10 cal/(mol K) in benzene whereas Coronel and Colussi[15] give ln $K^{294\text{K}}$ = 2.88, i.e., $K^{294\text{K}}$ = 18, Δ*H* = 3.0 kcal/mol, and Δ*S* = −4.4 cal/(mol K) in a benzene/toluene solvent mixture. Only LPC[9] would appear to have fully appreciated and then overcome the difficulties in such measurements.

[12] Mahoney, L. R.; Ferris, F. C.; DaRooge, M. A. *J. Am. Chem. Soc.* **1969**, *91*, 3883−3889.

[13] Coronel, M. E. J.; Colussi, A. J. *Int. J. Chem. Kinet.* **1988**, *20*, 749−752.

[14] Jackson, R. A.; Hosseini, K. M. *J. Chem. Soc., Chem. Commun.* **1992**, 967−968.

[15] Coronel, M. E. J.; Colussi, A. J. *J. Chem. Soc., Perkin Trans. 2* **1994**, 785−787.

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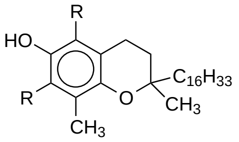
to "close the circle" and provide an independent verification of the reliability and accuracy of the PAC method. We have also made a measurement of BDE($\delta$-**T**O−H)$^{PhH}$, chosen because $\delta$-tocopherol is a minor component of vitamin E and is the least reactive and least biologically active of the four tocopherols which together constitute vitamin E.[5] In addition, we have applied the PAC technique to measure the O−H BDE's for five other phenolic antioxidants of commercial or specific scientific interest. For two of these phenols, viz., 2,6-di-*tert*-butyl-4-methylphenol (BHT) and 2,6-dimethyl-4-methoxyphenol, the PAC results can be compared with the BDE's obtained by LPC[9] using the EPR equilibrium method. In both of these cases, the agreement in O−H BDE's obtained by the two techniques are in satisfactory agreement (≤±l/mol ).



α-**T**OH (R = CH$_3$)
δ- **T**OH (R = H)

## Results and Discussion

The PAC technique measures the apparent enthalpy for the reaction of di-*tert*-butyl peroxide with the phenol to give *tert*-butyl alcohol and the phenoxyl radical, $(\Delta H_4^{PhH})_{app}$. Since very full details of the technique, experimental procedures, quantum yields for di-*tert*-butyl

$$t\text{-BuOOBu-}t + 2\text{ArOH} \rightarrow 2t\text{-BuOH} + 2\text{ArO}^{\bullet} \quad (4)$$

peroxide photolysis at 337 nm (0.83 for benzene), discussion of potential sources of experimental error, etc., are now available,[2] we will simply summarize our present results.

In two separate experiments with α-tocopherol,[19] the values found for $(\Delta H_4^{PhH})_{app}$ were −27.1 and −25.6 kcal/mol, which lead[2,20] to BDE(α-**T**O−H)$^{PhH}$ = 78.9 and 79.7 kcal/mol, respectively. The mean value for BDE(α-**T**O−H)$^{PhH}$ is 79.3 kcal/mol and should be accurate to better than ±2.0 kcal/mol.[2] A single experiment with $\delta$-tocopherol yielded $(\Delta H_4^{PhH})_{app} = -20.6$ kcal/mol and hence[2,20] BDE($\delta$-**T**O−H)$^{PhH}$ = 82.2 kcal/mol. These data, along with some relevant data from the literature for comparison, are shown in Table 1. Also listed in this table are the BDE(ArO−H) values previously measured by PAC for phenol[2] (now reduced by 0.1 kcal/mol)[20] and measured in this work for five other phenols together with relevant EPR equilibrium data and Mahoney *et al.*'s[12] calorimetric result. In all cases where comparison is possible, there is good agreement among the various methods used for the BDE determinations.

We estimate that in the gas phase BDE(α-**T**O−H)$^{gas}$ = 77.3 kcal/mol and BDE($\delta$-**T**O−H)$^{gas}$ = 80.2 kcal/mol.[22] Since the mean PAC value of BDE(PhO−H)$^{gas}$ = 87.3 kcal/mol,[2] the "extra" stabilization energies associated with homolysis of the O−H bonds of α-tocopherol and $\delta$-tocopherol are ∼10 kcal/mol and ∼7 kcal/mol, respectively, relative to phenol.

The differences in the bond dissociation energies of α- and $\delta$-tocopherol relative to phenol can be dissected into contributions from the various groups attached to the aromatic ring. Thus, the contribution from the (almost coplanar)[7] *p*-alkoxyl group amounts to ca. 5.6 kcal/mol (Table 1),[24] that from two *m*-methyl groups[30] amounts to ca. 0.8 kcal/mol,[31] and that from two *o*-methyl groups

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(16) There have also been two estimate of BDE(α-**T**O−H) based on kinetic measurements and assumed linear relations between the measured rate constants and the overall enthalpy of reaction, i.e., between *k* and the "known" BDE's of the phenols employed in these studies. Since the assumptions cannot be confirmed, such values are not comparable in reliability to those carefully measured by EPR[9] or by PAC. Nevertheless, and for the sake of completeness, these values of BDE(α-**T**OH) are 80.4 kcal/mol in aromatic solvents[6] and 78 kcal/mol in heptanol.[17] There is also an EPR equilibrium study involving BHT and a synthetic analog of α-**T**OH in which the phytyl tail was replaced by a methyl group and their respective radicals in benzene which gave an O−H BDE of 77.9 kcal/mol for the α-**T**OH analog.[18]

(17) Rousseau-Richard, C.; Richard, C.; Martin, R. *J. Chim. Phys. Phys-Chim. Biol.* **1989**, *86*, 2057−2066.

(18) Roginskii, V. A.; Krasheninnikova, G. A. *Kinet. Catal.* **1987**, *28*, 271−277.

(19) The photoacoustic signal generated in the reaction vessel, $S_{obs}$, was recorded as a function of the number of 337-nm photons absorbed by the sample ($1-10^{-OD}$), and this signal was normalized by dividing by the average laser energy.[2] A plot of $S_{obs}$ vs $1-10^{-OD}$ then yields an excellent straight line. However, any set of experiments for which $r <$ 0.9996 was discarded. Under the same experimental conditions the microphone response was calibrated against *o*-hydroxybenzophenone which absorbs at 337 nm and converts all the absorbed energy to heat.[2]

(20) According to ref 2: BDE(ArO−H)$^{PhH}$ = $^1/_2[(\Delta H_4^{PhH})_{app} + 9] + 2 + 86.1$ kcal/mol, where the 9 corresponds to an empirical solvent correction associated with the conversion of *t*-BuOOBu-*t* into two *t*-BuOH in benzene, the 2 to the enthalpy of solvation of the hydrogen atom in benzene, and the 86.1 comes from the relevant gas phase heats of formation of *t*-BuOH = −74.7, H$^{\bullet}$ = 52.1, and *t*-BuOOBu-*t* = 81.2 kcal/mol. According to these heats of formation, the constant should have been 86.2 kcal/mol. However, the value of $\Delta H_f°$(*t*-BuOOBu-*t*) has recently been very carefully measured and found to be −81.6 kcal/mol,[21] which would reduce the constant to 86.0 kcal/mol. Although a change of 0.1 kcal/mol in the calculated BDE values is trivial in view of our claimed accuracy of ca. 2.0 kcal/mol, all the data given in Table 1 and discussed below have been computed using 86.0 kcal/mol as the constant.

(21) Diogo, H. P.; Minas, M. E.; da Piedade, M.; Martinho Simoes, J. A.; Nagano, Y. *J. Chem. Thermodyn.* **1995**, *27*, 597−604.

(22) The benzene BDE's need to be corrected for the heat of solvation of the H$^{\bullet}$ atom in benzene (≈2.0 kcal/mol) and for the enthalpy of hydrogen bond formation between the tocopherols and benzene (relative to CCl$_4$).[2] For phenol the enthalpy for H-bond formation to benzene in CCl$_4$ is ca. 1.3 kcal/mol[23] and the equilibrium constant for H-bond formation at 25 °C is ca. 0.28 M$^{-1}$.[23a] It can therefore be calculated that about 75% of the phenol is H-bonded in neat benzene (11.2 M) and, hence, the effective correction, $\Delta H$(PhOH- - -PhH)$^{PhH}$ ≈ 0.75 × 1.3 ≈ 1.0 kcal/mol. Since all the phenols examined in the present work are much weaker acids than phenol itself and since most of them contain one or two *o*-alkyl groups which sterically protect the hydroxyl moiety and hence reduce its ability to act as a hydrogen-bond donor, it is clear that this correction must be <1.0, and generally ≪1.0 kcal/mol, for these phenols. We therefore contented ourselves by measuring *K* at 25 °C for the equilibrium:

$$\text{MeOC}_6\text{H}_4\text{OH/CCl}_4 + \text{PhH} \rightleftarrows \text{4-MeOC}_6\text{H}_4\text{OH- - -PhH/CCl}_4$$

using infrared spectroscopy and monitoring the change in the intensity of the O−H fundamental stretching band in CCl$_4$ in the presence of known concentrations of benzene. The value found for *K* at 25 °C was 0.07 M$^{-1}$ from which we concluded that any correction for hydrogen bonding to benzene, $\Delta H$(4-MeOC$_6$H$_4$OH- - -PhH)$^{PhH}$, is negligible for this phenol. It is probable, therefore, that no correction for hydrogen bonding is needed to obtain BDE(ArO−H)$^{gas}$ for any of the phenols listed in Table 1 *except* for phenol itself, *vide supra*.

(23) (a) Powell, D. L.; West, R. *Spectrochim. Acta* **1964**, *20*, 983−991. (b) Arnett, E. M.; Joris, L.; Mitchell, E.; Murty, T. S. S. R.; Gorrie, T. M.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1970**, *92*, 2365−2377.

(24) The following values have been reported for BDE(PhO−H) − BDE(4-CH$_3$OC$_6$H$_4$O−H) in various solvents using various experimental techniques: 5.9,[25] 5.6,[26] 5.3,[27] 5.7,[28] and 5.3[29] kcal/mol; mean 5.6 kcal/mol.

(25) Mulder, P.; Saastad, O., W.; Griller, D. *J. Am. Chem. Soc.* **1988**, *110*, 4090−4092.

(26) Lind, J.; Shen, X.; Ericksen, T. E.; Merenyi, G. *J. Am. Chem. Soc.* **1990**, *112*, 479−482.

(27) Bordwell, F. G.; Cheng, J.-P. *J. Am. Chem. Soc.* **1991**, *113*, 1736−1743.

(28) Parker, V. D. *J. Am. Chem. Soc.* **1992**, *114*, 7458−7462.

(29) Arnett, E. M.; Amarnath, K.; Harvey, N. G.; Venimadhavan, S. *J. Am. Chem. Soc.* **1990**, *112*, 7346−7353.

(30) We assume that the 4-CH$_2$ groups in the heterocyclic ring behaves much like a *m*-methyl group.

**Table 1. Thermochemical Data for α- and δ-Tocopherol and Some Other 2R, 4R′, 6R″ Phenolic Antioxidants in Benzene**[a]

| antioxidant | method[b] | $(\Delta H_4^{\mathrm{PhH}})_{\mathrm{app}}$ | $\Delta H_f°(\mathrm{ArO^•})^{\mathrm{PhH}} - \Delta H_f°(\mathrm{ArOH})^{\mathrm{PhH}}$ | BDE(ArO−H)$^{\mathrm{PhH}}$ [c] | BDE(ArO−H)$^{\mathrm{gas}}$ [d] | ref |
|---|---|---|---|---|---|---|
| α-**T**OH | PAC | −26.4 | 25.3 | 79.3 | 77.3 | e |
| | EPR | | 26.8 | 80.9 | 78.9 | 9 |
| | EPR | | 26.5 | 80.6 | 78.6 | 14 |
| δ-**T**OH | PAC | −20.6 | 28.2 | 82.2 | 80.2 | e |
| R R′ R″ | | | | | | |
| H H H | PAC | −6.5 | 35.2 | 89.2 | 87.3[f] | 2 |
| Bu$^t$ Bu$^t$ Bu$^t$ | CAL | | 29.1 | 83.2 | 81.2 | 12 |
| Bu$^t$ Me Bu$^t$ | PAC | −21.8 | 27.6 | 81.6 | 79.6 | e |
| | EPR | | 28.6 | 82.7 | 80.7 | 9 |
| Me Me Me | PAC | −17.4 | 29.8 | 83.8 | 81.8 | e |
| Me MeO Me | PAC | −26.5 | 25.2 | 79.2 | 77.2 | e |
| | EPR | | 25.5 | 79.6 | 77.6 | 9 |
| H MeO H | PAC | −18.4 | 29.3 | 83.3 | 81.3 | 24 |
| Bu$^t$ Bu$^t$ H | PAC | −16.8 | 30.1 | 84.1 | 82.1 | e |

[a] All thermochemical data are in kcal/mol. [b] PAC = photoacoustic calorimetry; EPR = equilibrium measurements on pairs of phenol/phenoxyl radicals using EPR spectroscopy; CAL = solution calorimetry. [c] BDE(ArO−H)$^{\mathrm{PhH}} = \Delta H_f°(\mathrm{ArO^•})^{\mathrm{PhH}} - \Delta H_f°(\mathrm{ArO{-}H})^{\mathrm{PhH}} + \Delta H_f(\mathrm{H^•})^{\mathrm{gas}} + (\Delta H(\mathrm{H^•}))_{\mathrm{solvation}}$. The enthalpy of solvation of H$^•$ in benzene has been estimated to be ca. 2 kcal/mol (see ref 2). The constant derived from the heats of formation of *t*-BuOH, H$^•$, and *t*-BuOOBu-*t* has been taken to be 86.0 kcal/mol, see footnote 20. [d] BDE(ArO−H)$^{\mathrm{gas}}$ = BDE(ArO−H)$^{\mathrm{PhH}} - (\Delta H(\mathrm{H^•}))_{\mathrm{solvation}} - \Delta H(\mathrm{ArOH{-}{-}{-}PhH})^{\mathrm{PhH}}$. In this equation, the last term corresponds to the enthalpy of the hydrogen bond between the phenol and benzene which is 1.0 kcal/mol for phenol and would appear to be negligible for all the other phenols listed in this table (see ref 2, footnote 22 and text). [e] This work. [f] "Best" gas phase value = 87 kcal/mol, see ref 2.

amounts to 4.3 kcal/mol (Table 1).[27] Thus, assuming simple additivity of the substituent effects on phenol O−H bond dissociation energies we can calculate that BDE(δ-**T**O−H)$^{\mathrm{gas}}_{\mathrm{calc}}$ = BDE(PhO−H)$^{\mathrm{gas}}$ − (5.6 + 0.8) = 87.3 − 6.4 = 80.9 kcal/mol (vs 80.2 kcal/mol, Table 1, *vide supra*) and BDE(α-**T**O−H)$^{\mathrm{gas}}_{\mathrm{calc}}$ = 87.3 − (5.6 + 0.8 + 4.3) = 76.6 kcal/mol (vs ca. 77.3 kcal/mol, Table 1, *vide supra*).[32]

An alternative approach to BDE(α-**T**O−H)$^{\mathrm{gas}}_{\mathrm{calc}}$ makes use of Jonsson et al.'s[33] empirical equation which relates differences in phenolic O−H bond strengths to the sum of the $\sigma^+$ constants for all the ring substituents.[34] This equation, viz.,[33]

$$\Delta\mathrm{BDE(O{-}H)/kcal/mol} = 7.14[\Sigma(\sigma_o^{\ +} + \sigma_m^{\ +} + \sigma_p^{\ +})] - 0.47 \qquad r^2 = 0.96 \quad \mathrm{(I)}$$

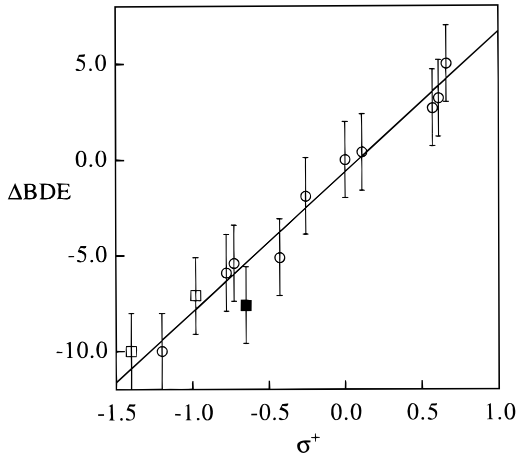

**Figure 1.** Plot of ΔBDE[(PhO−H)$^{\mathrm{PhH}}$ − (ArO−H)$^{\mathrm{PhH}}$] with error limits of ±2.0 kcal/mol vs the sum of the $\sigma^+$ constants of the substituents on the aromatic ring. The correlation equation II was obtained using only the open circles which correspond from the left to 2,6-dimethyl-4-methoxyphenol; 2,4,6-trimethylphenol; 2,4-di-*tert*-butylphenol; 4-*tert*-butylphenol; phenol; 4-chlorophenol; 3-(trifluoromethyl)phenol; 4-(trifluoromethyl)phenol; and 4-cyanophenol. The open squares represent α- and δ-tocopherol and the filled square, 2,6-di-*tert*-butyl-4-methylphenol (none of which were used in deriving equation II).

is based on BDE(O−H) values obtained by a variety of experimental techniques and is conditional upon the relationship $\sigma_o^{\ +} = 0.66\ \sigma_p^{\ +}$. A very similar equation can be obtained using only the BDE(O−H) values measured by PAC for the monosubstituted phenols, for the two 2,6-dimethyl-substituted phenols, and for 2,4-di-*tert*-butylphenol, viz.,[35]

$$\Delta\mathrm{BDE(O{-}H)/kcal/mol} = 7.32[\Sigma\,(\sigma_o^{\ +} + \sigma_m^{\ +} + \sigma_p^{\ +})] - 0.64 \qquad r^2 = 0.97 \quad \mathrm{(II)}$$

again with the proviso that $\sigma_o^{\ +} = 0.66\sigma_p^{\ +}$ (see Figure 1). The sterically hindered compound 2,6-di-*tert*-butyl-4-methylphenol has been excluded from this correlation but is represented in Figure 1 by the filled square. It is clear that the O−H BDE for this phenol is significantly lower than would have been expected on the basis of the electronic effect of the ring substituents. The presence of two *o*-*tert*-butyl groups destabilizes this phenol with respect to its phenoxyl radical because of steric repulsion of the phenolic hydrogen atom, *vide infra*.

The ΔBDE(O−H) values for α- and δ-tocopherol were not used to construct Figure 1 but are shown as open

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(31) BDE(PhO−H) − BDE(3-$CH_3C_6H_4O$−H) = 0.44 kcal/mol[25] and BDE(PhO−H) − BDE(3,5-$(CH_3)_2C_6H_3O$−H) = 0.74 kcal/mol: mean of 0.88 and 0.74 ≈ 0.8 kcal/mol.

(32) The assumption regarding additivity receives strong support from the fact that BDE(PhO−H)$^{\mathrm{PhH}}$ − BDE(2,6$(CH_3)_2$-4-$CH_3OC_6H_2O$−H)$^{\mathrm{PhH}}$ = 89.2 − ½(79.2 + 79.6) = 9.8 kcal/mol (see Table 1) while the calculated value would be 5.6[24] + 4.3[27] = 9.9 kcal/mol. Additional support comes from the fact that BDE(4-$CH_3OC_6H_5O$−H)$^{\mathrm{PhH}}$ − BDE(δ-**T**O−H)$^{\mathrm{PhH}}$ = 1.1 kcal/mol (Table 1) vs a calculated difference of 0.8 kcal/mol.[31]

(33) Jonsson, M.; Lind, J.; Ericksen, T. E.; Merényi, G. *J. Chem. Soc., Perkin Trans. 2* **1993**, 1567−1568.

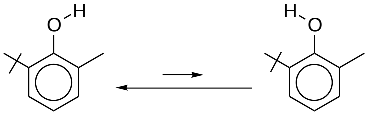
(34) Rate constants for hydrogen atom abstraction from ring-substituted phenols by peroxyl radicals have also been correlated with the $\sigma^+$ constants of the substituents: Howard, J. A.; Ingold, K. U. *Can. J. Chem.* **1963**, *41*, 1744−1751. Howard, J. A.; Ingold, K. U. *Can. J. Chem.* **1963**, *41*, 2800−2806.

(35) The data are from ref 25 and from Table 1 in the present paper together with two new measurements, viz., ΔBDE[(PhO−H)$^{\mathrm{PhH}}$ − (3-$CF_3C_6H_4O$−H)$^{\mathrm{PhH}}$] = −2.7 kcal/mol and ΔBDE[(PhO−H)$^{\mathrm{PhH}}$ − (4-N≡$CC_6H_4O$−H)$^{\mathrm{PhH}}$] = −5.0 kcal/mol. Since these two phenols are considerabley stronger acids than phenol, the correction for hydrogen-bond formation with the benzene solvent is expected to be larger than the estimated[2] 1.0 kcal/mol for phenol. That is, ΔBDE[(3-$CF_3C_6H_4O$−H)$^{\mathrm{gas}}$ − (PhO−H)$^{\mathrm{gas}}$] < 2.7 kcal/mol and ΔBDE[(4-N≡$CC_6H_4O$−H)$^{\mathrm{gas}}$ − (PhO−H)$^{\mathrm{gas}}$] < 5.0 kcal/mol.

squares in Figure 1 at the appropriate ΔBDE(O−H) (−10.0 and −7.1 kcal/mol, respectively) and $\Sigma\sigma^+$ (−1.40 and −0.98, respectively). It is clear that the measured BDE(O−H) values for the two tocopherols fall close to the correlation line given by eq II. A direct use of this correlation would yield a decrease in the BDE for α-**T**O−H of 10.1 kcal/mol (i.e., BDE(α-**T**O−H)$^{\text{gas}}_{\text{calc}}$ = 87.3 − 10.1 = 77.2 kcal/mol) and for $\delta$-**T**O−H of 7.8 kcal/mol (i.e., BDE($\delta$-**T**O−H)$^{\text{gas}}_{\text{calc}}$ = 87.3 − 7.8 = 79.3 kcal/mol) both values being in very satisfactory agreement with the PAC-measured values.

The excellent agreement between the PAC-measured value for BDE(α-**T**O−H)$^{\text{gas}}$ and the two independently calculated values of BDE(α-**T**O−H)$^{\text{gas}}_{\text{calc}}$ shows that there is nothing “magic” about the exceptional antioxidant activity of vitamin E. As we have pointed out previously,[5,7,36] α-tocopherol has almost the optimum structure for a simple phenolic antioxidant, that is the pattern of substitution around the aromatic ring minimizes the O−H bond strength and thus maximizes the rate at which it reacts with peroxyl radicals.

Finally, it is interesting to note that, although the O−H BDE for a phenol possessing two *ortho*-*tert*-butyl groups does not conform to empirical equation II (see Figure 1), the reduction in the O−H BDE for 2,6-di-*tert*-butyl-4-methylphenol relative to that of 2,4,6-trimethylphenol is equal (within experimental error) to the enthalpic difference between the two rotational isomers of 2-*tert*-butyl-6-methylphenol which one of us measured in the vapor phase by infrared spectroscopy over 30 years ago.[37] For



(5)

example, taking the difference between the PAC value for the BDE of (2,4,6-Me$_3$C$_6$H$_2$O−H)$^{\text{PhH}}$ and the mean of LPC’s EPR equilibrium value and the PAC value for the BDE of (2,6-Bu$^t_2$-4-MeC$_6$H$_2$O-H)$^{\text{PhH}}$, we have 83.8 − 82.15 = 1.65 kcal/mol, which is in rather satisfying agreement with the value reported for $\Delta H_5^{\text{gas}}$ of 1.2$_6$ kcal/mol.[37] Thus, the O−H bond weakening in 2,6-di-*tert*-butyl-4-methylphenol relative to 2,4,6-trimethylphenol is simply due to the steric destabilizing effect which arises from interaction of the relevant *o*-*tert*-butyl group with the phenolic O−H group.[38]

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(37) Ingold, K. U. *Can. J. Chem.* **1962**, *40*, 111−121. For earlier work in solution, see: Ingold, K. U.; Taylor, D. R. *Can. J. Chem.* **1961**, *39*, 471−480. Ingold, K. U.; Taylor, D. R. *Can. J. Chem.* **1961**, *39*, 481−487.

(38) The infrared-derived Δ*H* values for the two rotational isomers of other unsymmetrically *ortho*-alkylated phenols allow predictions to be made regarding ArOH BDE’s for several families of symmetrically *ortho*-substituted phenols. However, the IR data only take steric effects into account, not electronic effects.