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Kinetic Solvent Effects on Hydrogen-Atom Abstractions: Reliable, Quantitative Predictions via a Single Empirical Equation[1]

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Abstract: The rate of hydrogen-atom abstraction from XH by a radical, $Y^\bullet$, can be solvent-dependent. In many cases, the kinetic solvent effect (KSE) is directly related to hydrogen-bonding interactions between XH and the solvent. The relative hydrogen-bond acceptor (HBA) properties of solvents are given by β_2^H constants of Abraham et al. (Abraham, M. H.; Grellier, P. L.; Prior, D. V.; Morris, J. J.; Taylor, P. J. *J. Chem. Soc. Perkin Trans. 2* **1990**, 521−529). Room-temperature rate constants for hydrogen-atom abstraction, $k^S_{XH/Y^\bullet}$, have been determined in a number of solvents, S, where XH refers to several substituted phenols, *tert*-butyl hydroperoxide or aniline and $Y^\bullet$ is a *tert*-alkoxyl radical. In all cases, plots of $\log(k^S_{XH/Y^\bullet}/M^{-1}\ s^{-1})$ versus β_2^H gave excellent linear correlations, the slopes of which, M_{XH}, were found to be proportional to the hydrogen-bond-donating (HBD) ability of XH, as scaled with α_2^H parameters of Abraham et al. (Abraham, M. H.; Grellier, P. L.; Prior, D. V.; Duce, P. P.; Morris, J. J.; Taylor, P. J. *J. Chem. Soc., Perkin Trans. 2* **1989**, 699−711), with $M_{XH} = -8.3\alpha_2^H$. This leads to a general empirical equation which quantifies KSEs at room temperature: $\log k^S_{XH/Y^\bullet} = \log k^O_{XH/Y^\bullet} - 8.3\alpha_2^H\beta_2^H$, where $k^O_{XH/Y^\bullet}$ refers to the rate constant in a non-HBA solvent for which $\beta_2^H = 0$, generally a saturated hydrocarbon. Since M_{XH} depends only on XH, rate constants for hydrogen-atom abstraction from XH by any $Y^\bullet$ can be accurately predicted in any of the several hundred solvents for which β_2^H is known on the basis of one single measured rate constant, provided α_2^H for XH is known or measured. HBA solvents can have profound effects on some of the reactions and thermodynamic properties of hydroxylic substrates including: (i) reaction product profiles (ii) antioxidant activities, (iii) Hammett-type correlations, and (iv) O−H bond dissociation enthalpies. Finally, literature data (Nielsen, M. F.; Hammerich, O. *Acta Chem. Scand*, **1992**, *46*, 883−896) on KSEs for two proton-transfer reactions are shown to be correlated by the same equation which correlates KSEs for hydrogen-atom transfers.

There are immense compilations of rate constants for elementary reactions of organic free radicals in homogeneous solution[3] and perhaps as much as half of these data refers to hydrogen-atom abstraction reactions:

$$Y^\bullet + XH \xrightarrow{k} YH + X^\bullet \tag{i}$$

Although this huge body of information is neatly tabulated by attacking radical, $Y^\bullet$, there is no all-encompassing (or even partly encompassing) rationalization of the data. Thus, it is not obvious why H-atom abstractions from some substrates are subject to kinetic solvent effects (KSEs) while abstractions from other substrates are not.

Our interest in this area was sparked when we demonstrated that there was no KSE for $Y^\bullet$ = cumyloxyl ($CumO^\bullet$, $PhCMe_2O^\bullet$) and XH = cyclohexane[4,5] and that there were dramatic KSEs for $Y^\bullet = CumO^\bullet$ and XH = *tert*-butyl hydroperoxide or phenol.[7] The absence of a KSE on the cyclohexane reaction[4] necessarily implied that these KSEs were not due to solvent effects on the $CumO^\bullet$ radical.[8] The observed KSEs for the $Me_3COOH/CumO^\bullet$ and $PhOH/CumO^\bullet$ reactions were accounted for in a roughly quantitative manner by making three assumptions:[7,10]

Each substrate molecule, XH, can act as a hydrogen-bond donor (HBD) to only a single hydrogen-bond acceptor (HBA) solvent molecule, S, at any one time.

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[3] See, e.g.: *Radical Reaction Rates in Solution*; Fischer, H., Ed.; Landolt-Börnstein, New Series; Springer-Verlag: Berlin; 1984; Vol. 13, subvolumes 13a−e (∼2000 pages); 1994; Vol. 18, subvolumes 18a−e2 (∼3000 pages).

[4] Avila, D. V.; Brown, C. E.; Ingold, K. U.; Lusztyk, J. *J. Am. Chem. Soc.* **1993**, *115*, 466−470.

[5] We have also demonstrated[6] that there is no KSE for H-atom abstraction from 1,4-cyclohexadiene by cumyloxyl radicals. Furthermore, there can be no KSE for H-atom abstraction from a carbon atom by $HO^\bullet$ radicals, see: Kanabus-Kaminska, J. M.; Gilbert, B. C.; Griller, D. *J. Am. Chem. Soc.* **1989**, *111*, 3311−3314.

[6] 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.

[7] Avila, D. V.; Ingold, K. U.; Lusztyk, J.; Green, W. H.; Procopio, D. R. *J. Am. Chem. Soc.* **1995**, *117*, 2929−2930.

[8] Occasional suggestions[9] that solvents influence the *reactivity* of *tert*-alkoxyl radicals in H-atom abstractions are obviously incorrect.

[9] See e.g., Kim, S. S.; Kim, S. Y.; Ryou, S. S.; Lee, C. S.; Yoo, K. H. *J. Org. Chem.* **1993**, *58*, 192−196. Dokolas, P.; Loffler, S. M.; Solomon, D. H. *Aust. J. Chem.* **1998**, *51*, 1, 1119−1120.

[10] Assumptions adumbrated earlier by Nielsen[11] for phenols acting as *proton donors* to an aromatic anion radical, vide infra.

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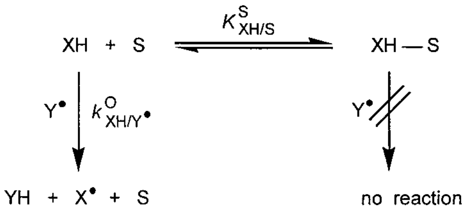
Scheme 1



The magnitude of the equilibrium constant, $K^{S}_{XH/S^\bullet}$, for the formation of an XH−S hydrogen-bonded complex is essentially independent of surrounding medium.

For steric reasons, the H-atom in the XH−S complex cannot be directly abstracted by $Y^\bullet$. The solvent molecule in the XH−S complex must first be replaced by $Y^\bullet$. A simple predissociation model is illustrated in Scheme 1. The experimentally measured rate constant for the XH/$Y^\bullet$ reaction in solvent, S, that is, $k^{S}_{XH/Y^\bullet}$, is given by:[7]

$$k^{S}_{XH/Y^\bullet} = \frac{k^{O}_{XH/Y^\bullet}}{1 + K^{S}{}_{XH/Y}\,[S]} \qquad \text{(ii)}$$

where $k^{O}_{XH/Y^\bullet}$ is the rate constant for reaction of $Y^\bullet$ with non-H-bonded XH.

It was recognized[7] that the magnitude of the KSE (e.g., $k^{CCl_4}_{XH/Y^\bullet}/k^{Me_3COH}_{XH/Y^\bullet}$) would generally be independent of $Y^\bullet$, because the KSE is determined by the strength of the interaction between XH and the HBA solvent. This was confirmed[12] by demonstrating that the magnitude of the KSE for H-atom abstraction from phenol by $CumO^\bullet$ was essentially identical[13] to that for H-atom abstraction by 2,2-diphenyl-1-picrylhydrazyl radicals, $DPPH^\bullet$, that is, $k^{S_1}_{PhOH/CumO^\bullet}/k^{S_2}_{PhOH/CumO^\bullet} = k^{S_1}_{PhOH/DPPH^\bullet}/k^{S_2}_{PhOH/DPPH^\bullet}$, although in any particular solvent, the former reaction is faster than the latter by the enormous factor of 10^{10}, that is, $k^{S_1}_{PhOH/CumO^\bullet} = 10^{10}k^{S_1}_{PhOH/DPPH^\bullet}$. The KSEs for H-atom abstraction from α-tocopherol (TocH, vitamin E) have also been shown to be essentially identical[13,19] for $Y^\bullet = Me_3CO^\bullet$ and $DPPH^\bullet$,[12] peroxyl radicals[14] and a primary alkyl radical.[18]

In any analysis of solvent effects on chemical reactions, it is customary to seek a linear relationship between some empirical solvent parameter and the logarithm of the rate constant for reaction, i.e., a linear free energy relationship.[20] The most reliable scales of relative HBA activities of common organic solvents would appear to be the 1983 β-constants of Taft and co-workers[21] and their subsequent expansion and refinement by Abraham and co-workers.[22] We have chosen to use β_2^{H} values of Abraham et al.,[23] which represent a general, thermodynamically related scale of solute hydrogen-bond basicities in CCl_4 and range in magnitude from 0.00 for a non-HBA solvent such as an alkane[24] to 1.00 for hexamethylphosphorustriamide (HMPA), the strongest organic base. We chose the β_2^{H} scale on the pragmatic grounds that it is the most extensive of all β scales with values tabulated for at least 400 organic compounds.[27] Values of $\log(k^{s}{}_{XH/RO^\bullet}/M^{-1}\,s^{-1})$, where $RO^\bullet$ = *tert*-alkoxyl, in various sterically nondemanding[17] HBA solvents have been plotted in Figure 1 for Me_3COOH[7] (10 solvents, $r^2 = 0.97$), phenol[7,12,17](11 solvents, $r^2 = 0.98$), and α-tocopherol[12,14] (11 solvents, $r^2 = 0.87$, the lowest linear coefficient of determination obtained with any substrate, vide infra). Obviously these KSE

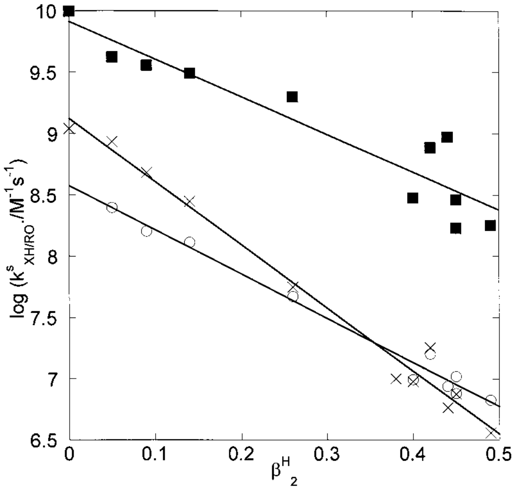


Figure 1. Plots of $\log(k^{S}_{XH/RO^\bullet}/M^{-1}\ s^{-1})$ vs the β_2^{H} value for the solvent, S, for XH = α-tocopherol (■), phenol (×), and *tert*-butyl hydroperoxide (○).

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(11) Nielsen, M. F. *Acta Chem. Scand.* **1992**, *46*, 533−548. (b) Nielsen, M. F.; Hammerich, O. *Acta Chem. Scand*, **1992**, *46*, 883−896.

(12) Valgimigli, L.; Banks, J. T.; Ingold, K. U.; Lusztyk, J. *J. Am. Chem. Soc.* **1995**, *117*, 9966−9971.

(13) Rate constants for some, but not all, H-atom abstractions are about 3−5 times faster in *tert*-butyl alcohol (but not in methanol or ethanol) than would be expected from *tert*-butyl alcohol's HBA ability. Specifically, this rate "acceleration" (actually, a less than expected rate reduction) has been found in O−H bond-breaking by $DPPH^\bullet$[12] and $ROO^\bullet$[14] and in C−H bond-breaking by $DPPH^\bullet$,[15] but not for C−H bond-breaking by $RO^\bullet$[4] or $ROO^\bullet$,[16] or O−H bond breaking by $RO^\bullet$[12, 17], or $PhCMe_2CH_2^\bullet$.[18] The reason(s) for the occasional anomalous behavior of *tert*-butyl alcohol are not currently understood.

(14) Valgimigli, L.; Banks, J. T.; Lusztyk, J.; Ingold, K. U. *J. Org. Chem.* **1999**, *64*, 3381−3383.

(15) Valgimigli, L.; Ingold, K. U.; Lusztyk, J. *J. Org. Chem.* **1996**, *61*, 7947−7950.

(16) Lucarini, M.; Pedulli, G. F.; Valgimigli, L. *J. Org. Chem.* **1998**, *63*, 4497−4499.

(17) MacFaul, P. A.; Ingold, K. U.; Lusztyk, J. *J. Org. Chem.* **1996**, *61*, 1316−1321.

(18) Franchi, P.; Lucarini, M.; Pedulli, G. F.; Valgimigli, L.; Lunelli, B. *J. Am. Chem. Soc.* **1999**, *121*, 507−514.

(19) The rate of the TocH/$Me_3CO^\bullet$ reaction reaches the diffusion-controlled limit in *n*-octane, *n*-hexadecane and CCl_4.[12]

(20) Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*; Verlag Chemie: Weinheim, Germany, 1990.

(21) Kamlet, M. J.; Abboud, J.-L. M.; Abraham, M. H.; Taft, R. W. *J. Org. Chem.* **1983**, *48*, 2877−2887 and references therein. See also: Marcus, Y.; Kamlet, M. J.; Taft, R. W. *J. Phys. Chem.* **1988**, *92*, 3613−3622.

(22) For a brief summary of, and references to, the various β-scales, see ref 17. For more detailed reviews of these scales, see: Abraham, M. H. *Port. Electrochim. Acta* **1992**, *10*, 121−134. Abraham, M. H. *Chem. Soc. Rev.* **1993**, 73−83. Abraham, M. H. NATO Advanced Study Institute Series C426; Plenum: New York, 1994, pp 63−78.

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(24) In most of Abraham's β_2^{H} compilations, $\beta_2^{H}(CCl_4)$ is given as 0.00, since CCl_4 is the solvent in which the strengths of the interactions between HBA's and HBD's are normally evaluated using infrared spectroscopy. However, it is known from infrared studies on phenols that CCl_4 is an HBA solvent relative to alkanes.[25] We have found that β_2^{H} $(CCl_4) = 0.05$ gives a much better fit for all our kinetic data than 0.00 and use 0.05 in this paper. It should also be noted that when cyclohexane was used as the reference, Abraham et al. reported β_2^{H} $(CCl_4) = 0.04$.[26]

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Table 1. Rate Constants ($10^{-7}\ k^{S}_{XH/RO^{\bullet}}/M^{-1}\ s^{-1}$) for H−Atom Abstraction from Seven Phenols by *tert*-Alkoxyl Radicals in Various Solvents at 23 ± 2 °C[a]

	substituents solvent	β_2^{H} [b]	TocH[c] (1)	2,4,6 Me$_3$ (2)	Me$_3$C (4)	none[d] (5)	4Cl (6)	4CF$_3$ (7)	3,5Cl$_2$ (8)
I	alkane[e]	0.00	990	210	−	110[f]	230	85[g]	94
II	CCl$_4$	0.05[h]	420	160	190	86	110	71	87
III	PhCI	0.09	360	−	130	48	−	17	29
IV	PhH	0.14	310	−	87	28	40	13	16
V	PhOMe	0.26	200	49	23	5.6	6.9	2.1	3.5
VI	HCO$_2$Me	0.38	−	12	4.6	1.0	1.9	0.39	0.59
VII	MeCO$_2$Me	0.40	30	−	−	0.95	−	−	−
VIII	MeCO$_2$H	0.42	77	−	6.0	1.8	−	0.54	−
IX	MeCN	0.44	94	8.3	4.1	0.58	0.79	0.21	−
X	MeCO$_2$Et	0.45	29	−	−	0.75	−	−	−
XI	Val-lact[i]	0.45	17	−	−	−	−	−	−
XII	Me$_3$COH	0.49	18	−	1.9	0.36	−	0.10	−

[a] RO$^{\bullet}$= Me$_3$CO$^{\bullet}$ for phenols 1 and 4; = CumO$^{\bullet}$ for phenols 2, 5, 6, 7 and 8. Estimated errors in $k = \pm 20\%$. Solvents are identified by Roman numbers and substrates by Arabic numbers in all Tables and Figures. [b] Values are from ref 23a except for CCl$_4$. [c] α-Tocopherol. Data are from refs 12 and 14. [d] Data are from refs 7, 12, and 17. [e] *n*-Pentane unless otherwise noted. [f] In *n*-octane. [g] In *n*-hexane. [h] See ref 24. [i] γ-Valerolactone.

data can be correlated by the equation:

$$\log(k^{S}_{XH/Y^{\bullet}}/M^{-1}\ s^{-1}) = \log(k^{O}_{XH/Y^{\bullet}}/M^{-1}\ s^{-1}) + M_{XH}\beta_2^{H} \qquad \text{(iii)}$$

where M_{XH} represents the magnitude of the KSE for the particular XH *and for any* Y$^{\bullet}$, and is the slope of the log $k^{S}_{XH/Y^{\bullet}}$ versus β_2^{H} line in Figure 1.

The magnitude of M_{XH} must depend on the ability of XH to form a hydrogen bond to a solvent molecule. This raises the exciting possibility that, if M_{XH} could be predicted from some easily measured physical property of XH, then a single kinetic measurement on an XH/Y$^{\bullet}$ reaction *in any solvent* would allow reliable rate constants to be calculated in *any* of the 400+ other solvents for which β_2^{H} values are known (and for any mixture of these solvents). This goal has been achieved by rate constant measurements for H-atom abstractions by *tert*-alkoxyl radicals from a series of phenols. A simple, empirical equation describes the observed KSEs (M_{XH} values) and this equation has been confirmed by extending our analyses to substrates which are not HBAs (cyclohexane) or are only weak HBAs, for example, *tert*-butyl hydroperoxide, 2-methoxyphenol (with its intramolecular H-bond) and aniline.

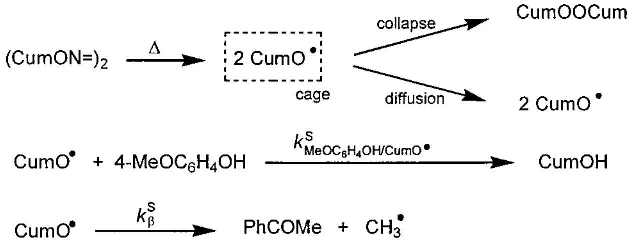
Results

We chose Y$^{\bullet}$ = Me$_3$CO$^{\bullet}$ or CumO$^{\bullet}$ because some data were already available (vide supra) and because of the simplicity and reliability of kinetic studies with these radicals using laser flash photolysis (LFP). These radicals were generated at room temperature by 308 nm LFP of either 0.22 M di-*tert*-butyl peroxide or 0.13 M dicumyl peroxide, concentrations which give an optical density (OD) of 0.3 at 308 nm in the 7 mm laser cell. Phenoxyl radicals usually have absorption bands in the 370−505 nm range.[28,29] The phenol was used in large excess relative to the *tert*-butoxyl radicals so that the signal at the phenoxyl radical's band maximum builds-up with pseudo-first-order kinetics:

$$k^{S}_{exptl} = k^{S}_{O} + k^{S}_{XH/Me_3CO^{\bullet}}[XH] \qquad \text{(iv)}$$

where k^{S}_{O} corresponds to the combined first-order and pseudo-first-order reactions of Me$_3$CO$^{\bullet}$ (i.e., to all reactions of Me$_3$CO$^{\bullet}$ other than its H-atom abstraction from XH).[30] In each solvent, at least five (often more) concentrations of XH were employed, and $k^{S}_{XH/Me_3CO^{\bullet}}$ was calculated via least-squares from the plot of k^{S}_{exptl} versus [XH]. All of these plots gave excellent straight lines ($r^2 \geq 0.98$).

Scheme 2



Extinction coefficients for some phenoxyl radicals were too weak to yield reliable kinetic data. In most such cases, LFP with dicumyl peroxide was employed and cumyloxyl radical decay at ~485 nm[31] was monitored using five or more phenol concentrations. Again the plots of k_{exptl} versus [XH] gave excellent straight lines ($r^2 \geq 0.98$).

The LFP measured bimolecular rate constants for H-atom abstraction by Me$_3$CO$^{\bullet}$ or CumO$^{\bullet}$ from the phenols in various solvents at room temperature are given in Table 1. These phenols exhibit a wide range of acidities (pK_a's) and hence were expected to exhibit a wide range of HBD activities.

The LFP technique could not be used with 4-methoxyphenol because this compound absorbs at the 308 nm laser wavelength. Rate constants were therefore obtained by competition kinetics/product analyses[32] using CumO$^{\bullet}$ radicals generated by thermal decomposition of dicumyl hyponitrite. Reactions were carried out at 25 °C in the dark in argon-purged, sealed Pyrex reaction vessels. Products were analyzed after 10 days which was sufficient time for >99% of the hyponitrite to decompose.[34] The products of principle interest are those derived from CumO$^{\bullet}$ radicals which escape the solvent cage and react either by H-atom abstraction to form cumyl alcohol or by β-scission to give acetophenone (see Scheme 2). To treat the H-atom abstraction as a pseudo-first-order process, the hyponitrite:4-methoxyphenol concentration ratio was 1:(≥40) in all experi-

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(28) (a) Land, E. J.; Porter, G.; Strachan, E. *Trans. Faraday Soc.* **1961**, *57*, 1885−1893. (b) Land, E. J.; Porter, G. *Trans. Faraday Soc.* **1963**, *59*, 2016−2026. (c) Das, P. K.; Encinas, M. V.; Steenken, S.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 4162−4166.

(29) For 2-methoxyphenoxyl, λ_{max} = 650−660 nm, see: Shukla, D.; Schepp, N. P.; Mathivanan, N.; Johnston, L. J.; *Can. J. Chem.* **1997**, *75*, 1820−1829.

(30) Radical/radical reactions are unimportant under the conditions employed.

(31) Avila, D. V.; Lusztyk, J.; Ingold, K. U.;. *J. Am. Chem. Soc.* **1992**, *114*, 6576−6577. Avila, D. V.; Ingold, K. U.; Di Nardo, A. A.; Zerbetto, F.; Zgierski, M. Z.; Lusztyk, J. *J. Am. Chem. Soc.* **1995**, *117*, 2711−2718.

Table 2. Kinetic Data Derived from Cumyl Alcohol/Acetophenone Product Ratios for the 4-Methoxyphenol (3)/ CumO$^•$ Reaction in Five Solvents at 25 °C

	solvent	$k^S_{3/CumO^•}/k^S_\beta$ (M^{-1})	$10^{-5}\ k^S_\beta$ (s^{-1})	$10^{-7}\ k^S_{3/CumO^•}$ ($M^{-1}\ s^{-1}$)
III	PhCl	7850	4.60[a]	361
IV	PhH	9710	3.11[a]	302
V	PhOMe	5134	2.95[b]	153
VIII	$MeCO_2H$	121	16.3[a]	19.6
IX	MeCN	211	5.25[a]	11.1

[a] Rate constants from ref 4 have been multiplied by 0.83 to correct for the 5 °C temperature difference. [b] This work, see text.

Table 3. Rate Constants ($M^{-1}\ s^{-1}$) for H−Atom Abstraction from Nine Phenols by DPPH$^•$ Radicals in *n*-Heptane at 23 ± 2 °C

	phenol	$\Sigma\sigma^+$ [a]	$k^O_{ArOH/DPPH^•}$ [b]
1	TocH[c]	−1.40[d]	7400[e]
2	2,4,6-$Me_3C_6H_2OH$	−0.72[d]	42
3	4-$MeOC_6H_4OH$	−0.78	240[f]
4	4-$Me_3CC_6H_4OH$	−0.26	3.1
5	C_6H_5OH	0.00	0.16[e,g]
6	4-ClC_6H_4OH	0.11	1.1
7	4-$CF_3C_6H_4OH$	0.61	0.044
8	3,5-$Cl_2C_6H_3OH$	0.80	0.037
12	3-ClC_6H_4OH	0.40	0.15

[a] From ref 37 assuming, when necessary, that multiple substituents have additive electronic effects. [b] These rate constants were measured using one concentration of DPPH and five or more concentrations of the phenols in *n*-heptane. The phenol, its maximum concentration (M) and in parentheses, 10^5 [DPPH] (M) were as follows: [2] $\leq 8.5 \times 10^{-4}$ (3.4); [3] $\leq 9.2 \times 10^{-4}$ (1.2); [4] $\leq 2.0 \times 10^{-2}$ (2.2); [6] $\leq 7.0 \times 10^{-2}$ (2.5); [7] ≤ 0.2 (2.6); [8] ≤ 0.14 (46); [12] ≤ 0.18 (1.8). [c] α-Tocopherol. [d] Calculated using $\sigma^+_0(\mathrm{Me}) = 0.66\ \sigma^+_p(\mathrm{Me})$, see ref 55b. [e] In *n*-octane, data from ref 12. [f] Measured value. The value calculated from a kinetic measurement in DMSO was 174 $M^{-1}\ s^{-1}$, see ref 57. [g] Because this rate constant makes phenol an outlier in Figure S1 (Supporting Information), it was remeasured in the present work, and a value of 0.22 $M^{-1}\ s^{-1}$ was obtained (see Table S7).

ments which assured that no more than 5% of the phenol could react with the CumO$^•$ radicals. At least six (often more) different phenol concentrations were used. Plots of the GC/FID-determined ratios of cumyl alcohol/acetophenone versus 4-methoxyphenol concentration gave excellent straight lines ($r^2 \geq 0.97$, see Supporting Information). The slopes of these lines correspond to the ratio of the rate constants for H-atom abstraction from the phenol to β-scission, that is, slope = $k^S_{MeOC_6H_4OH/CumO^•}/k^S_\beta$ (M^{-1}). The results of these experiments are summarized in Table 2. Mass balances were excellent in all solvents (see Experimental Section and Supporting Information). Values of k^S_β at 30 °C were available for four of the five solvents[4] and were corrected to 25 °C by multiplying by 0.83. For anisole, k^{PhOMe}_β was not available. It was measured at 30 °C by competition kinetics using cyclohexane (five concentrations) as the H-atom donor. The rate constant ratio: $k^{PhOMe}_{C_6H_{12}/CumO^•}/k^{PhOMe}_\beta$ was found to be 3.34 M^{-1} and, since $k^{PhOMe}_{C_6H_{12}/CumO^•} = 1.2 \times 10^6$ $M^{-1}\ s^{-1}$ at 30 °C in all solvents,[4] $k^{PhOMe}_\beta = 3.6 \times 10^5 s^{-1}$ at 30 °C and $3.0 \times 10^5 s^{-1}$ at 25 °C.

Rate constants, $k^O_{ArOH/DPPH^•}$, for H-atom abstraction by the 2,2-diphenyl-1-picrylhydrazyl radical, DPPH$^•$, from a number of phenols in a non-hydrogen-bonding solvent (*n*-heptane) were also determined and are given in Table 3.

Discussion

Deriving an Empirical Equation to Describe H−Atom Abstraction KSEs Quantitatively. Rate constants for H-atom abstraction by *tert*-alkoxyl radicals from the eight phenols studied decreased very substantially as the HBA abilities of the solvent increased (see Tables 1 and 2). Plots of log($k^S_{XH/RO^•}$/$M^{-1}\ s^{-1}$) versus β^H_2 gave excellent straight lines ($r^2 \geq 0.98$) for all phenols except α-tocopherol (for which some *k*'s approach the diffusion-controlled limit)[19] and 4-methoxyphenol (for which *k*'s were determined indirectly)[32] see Supporting Information and Table 3. The slopes of these lines, M_{XH}, give the magnitude of the KSE for XH, see eq iii. Values of M_{XH} and of the intercept, log($k^O_{XH/Y^•}$/$M^{-1}\ s^{-1}$), are collected in Table 4. It should be realized that an M_{XH} value of −1.0 means that the rate constant for H-atom abstraction will decrease by a factor of 10 on changing the solvent from an alkane to HMPA, that is, for α-tocopherol this change in solvents would reduce the rate constant by a factor of 1000 and for 3,5-dichlorophenol by 1,000,000. These KSEs are not small![35]

There is only a poor correlation between M_{XH} and pK_a (see Figure 2), the two 2,6-dimethyl-substituted phenols (1 and 2) having significantly smaller M_{XH} values than might have been expected from their pK_a's, probably for steric reasons. Any steric problems were overcome by using α^H_2 parameters of Abraham et al.,[38] which provide a direct measure of the relative ability of a solute to act as a HBD. Values of α^H_2 range from 0.00 (e.g., alkanes) to nearly 1.0 for strong acids, for example, α^H_2 (CF_3CO_2H) = 0.951 and have been tabulated for hundreds of substrates,[27,38] but not for α-tocopherol. We therefore redetermined α^H_2 for five phenols and obtained values in good agreement with the literature,[27,38] following which we determined α^H_2 for α-tocopherol (Table 4). The M_{XH} values are plotted against α^H_2 for the eight phenols (filled circles in Figure 3). There is no KSE for H-atom abstraction from alkanes[4] since the α^H_2 values for alkanes are 0.00.[27,38] This boundary condition is included in the data series (shown by a filled square). An excellent least-squares fitting is obtained:

$$M_{XH} = -8.3_1\alpha^H_2 + 0.005 \quad (r^2 = 0.99) \tag{v}$$

which, for practical purposes, can be written as:

$$M_{XH} = -8.3\alpha^H_2 \tag{vi}$$

Equation vi is also applicable to H-atom abstractions by *tert*-alkoxyl radicals from *tert*-butyl hydroperoxide,[7] aniline,[17] and 2-methoxyphenol[33] with its intramolecular hydrogen bond which reduces but does not eliminate intermolecular hydrogen bond-

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(32) KSE's for the $Me_3CO^•$/4-$MeOC_6H_4OH$ reaction were also investigated by 337 nm LFP of 30:70 (v/v) $Me_3COOCMe_3$/solvent mixtures.[33] The bimolecular rate constants were then recalculated for the pure solvents and, when plotted against β^H_2, gave a slope (M_{XH}) = -4.2_1 ($r^2 = 0.98$)[33] in excellent agreement with the product derived slope of -4.3_2, vide infra.

(33) de Heer, M. I.; Mulder, P.; Korth, H.-G.; Ingold, K. U.; Lusztyk, J. *J. Am. Chem. Soc.* **2000**, *122*, 2355−2360.

(34) The Arrhenius parameters for decomposition of this hyponitrite are: log(A/s^{-1}) = 14.97 and E_a = 27.3 kcal mol^{-1}, (see: Mendenhall, G. D.; Chen, H.-T. E. *J. Phys. Chem.* **1985**, *89*, 2849−2851) from which the half-life at room temperature is 16 h.

(35) Large KSEs have also been observed in solvent mixtures.[28c,32,33] For example, a plot of Das et al.'s[28c] log($k/M^{-1}\ s^{-1}$) for the PhOH/$Me_3CO^•$ reaction in 1:1 (v/v) mixtures of di-*tert*-butyl peroxide with benzene, methanol, *tert*-butyl alcohol and pyridine against β^H_2 for these last four compounds gives a good straight line with a slope of −3.9.

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

(37) Hansch, C.; Leo, A. *Substituent Constants for Correlation Analysis in Chemistry and Biology*; Wiley-Interscience: New York, 1979. See also: Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165−195.

(38) Abraham, M. H.; Grellier, P. L.; Prior, D. V.; Duce, P. P.; Morris, J. J.; Taylor, P. J. *J. Chem. Soc., Perkin Trans. 2* **1989**, 699−711.

Table 4. Slopes, M_{XH}, and Intercepts, $\log(k^{O}_{XH/t-RO^{\bullet}}/M^{-1}\ s^{-1})$, for Plots of $\log(k^{S}_{XH/t-RO^{\bullet}}/M^{-1}\ s^{-1})$ versus β_2^H for Various Substrates and Some Relevant Substrate Parameters

				α_2^H				
		pK_a[a]	$\Sigma\sigma^{+}$[b]	lit[c]	this work	intercept	slope M_{XH}	r^2
1	TocH[d]	20.0[e]	−1.40[f]	–	0.370	9.9_1	-3.0_6	0.87
2	2,4,6-$Me_3C_6H_2OH$	19.4[e]	−0.72[f]	0.374	–	9.3_7	-3.2_2	0.98
3	4-$MeOC_6H_4OH$	19.1	−0.78	0.573	0.550	$10._1$	-4.3_2[g]	0.95
4	4-$Me_3CC_6H_4OH$	19.05	−0.26	0.558	0.571	9.5_3	-4.4_8	0.98
5	C_6H_5OH	18.0	0.00	0.596	0.590	9.1_2	-5.1_5	0.98
6	4-ClC_6H_4OH	16.75	0.11	0.670	–	9.3_4	-5.5_4	0.99
7	4-$CF_3C_6H_4OH$	15.2	0.61	0.724	0.680	8.9_4	-5.8_8	0.98
8	3,5-$Cl_2C_6H_3OH$	13.56	0.80[h]	0.774	0.728	9.0_7	-5.9_9	0.98
9	Me_3COOH	–	–	–	0.442	8.57	-3.5_2	0.97
10	$C_6H_5NH_2$	–	–	0.264	–	8.76	-2.2_2	0.97
11	2-$MeOC_6H_4OH$	–	–	0.261	–	8.09	-2.0_0	0.98

[a] From ref 36. [b] From ref 37. [c] From ref 38.. [d] α-Tocopherol. [e] Values estimated by additivity principles; substituents (pK_a): 2,6-Me_2 (18.5); 3,5-Me_2 (18.4); 4-MeO (19.1); 4-Me (18.9), and none (18.0). [f] Calculated using $\sigma_0^+(\mathrm{Me}) = 0.66\ \sigma_p^+(\mathrm{Me})$, see ref 55b. [g] See also footnote 32. [h] $2 \times \sigma^{+}_{meta}(\mathrm{Cl})$.

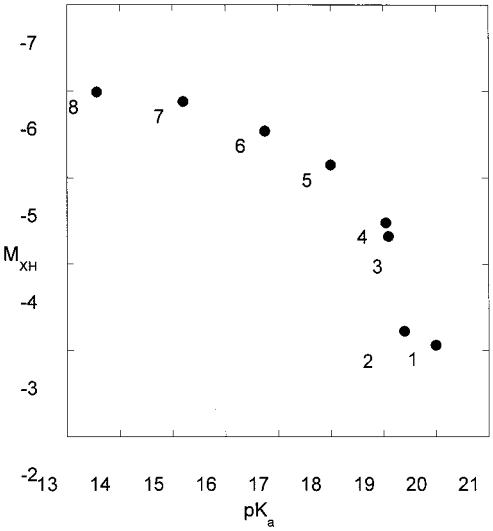

Figure 2. Values of M_{XH} plotted against pK_a for phenols 1−8. The data are from Table 4, and the phenols are identified by number.

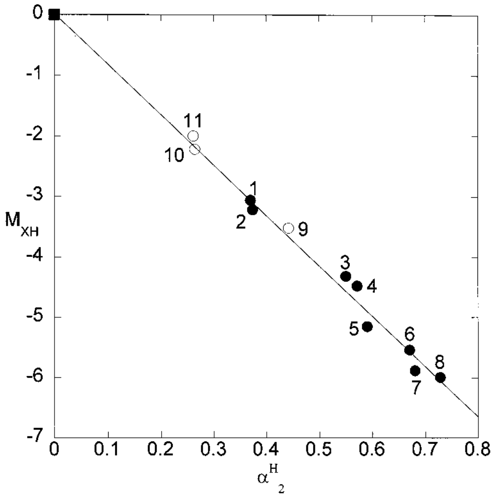

Figure 3. Values of M_{XH} plotted against α_2^H (using values measured in this work) for phenols 1−8 (●), cyclohexane (■), *tert*-butyl hydroperoxide, aniline, and 2-methoxy-phenol (○, numbers 9, 10, and 11, respectively). The data are from Table 4.

ing[33,49] (kinetic data are given in Table S6). These three substrates have been included in Table 4 and their M_{XH} values plotted against α_2^H as open circles in Figure 3.

The combination of eqs iii and vi yields a general, empirical equation which reliably describes and predicts KSEs for H-atom donors at ambient temperatures:

$$\log(k^{S}_{XH/Y^{\bullet}}/M^{-1}\ s^{-1}) = \log(k^{O}_{XH/Y^{\bullet}}/\ M^{-1}\ s^{-1}) - 8.3\alpha_2^H\beta_2^H \quad \text{(vii)}$$

Interestingly, a very similar equation can, be derived without using any experimental kinetic data by combining the three assumptions associated with Scheme 1 and Abraham's thermodynamic parameters for hydrogen bonding (see Supporting Information), viz.,

$$\log(\ k^{S}_{XH/Y^{\bullet}}/M^{-1}\ s^{-1}) = \log(k^{O}_{XH/Y^{\bullet}}/\ M^{-1}\ s^{-1}) - 7.8\ \alpha_2^H\beta_2^H \quad \text{(viii)}$$

The strengths and weaknesses of eq vii are adumbrated below:

Strengths. (i) This is a general equation for hydrogen-atom abstractions (and proton transfers, vide infra) in solution at room temperature for C−H, O−H, and N−H hydrogen-atom donors.

(ii) Many α_2^H and β_2^H values are available[22,23,26,27,38] or can be readily determined.

(iii) A single measured rate constant for the XH/Y• reaction in any solvent permits the calculation of the rate constant in any other solvent (or solvent mixture).

Weaknesses. These can only manifest themselves with XH having small α_2^H values (<0.2). For such substrates, the

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(39) de Heer, M. I.; Korth, H.-G.; Mulder, P. *J. Org. Chem.* **1999**, *64*, 6969−6975.

(40) Tronche, C.; Martinez, F. N.; Horner, J. H.; Newcomb, M.; Senn, M.; Giese, B. *Tetrahedron Lett.* **1996**, *37*, 5845−5848.

(41) Salikhov, A.; Fischer, H. *Appl. Magn. Reson.* **1993**, *5*, 445−455.

(42) For an overview of this work, see: Minisci, F.; Fontana, F. *Chim. Ind.* **1998**, *80*, 1309−1316.

(43) Bravo, A.; Bjorsvik, H.-R.; Fontana, F.; Ligouri, L.; Minisci, F. *J. Org. Chem.* **1997**, *62*, 3849−3857.

(44) Minisci, F.; Fontana, F.; Araneo, S.; Recupero, F.; Banfi, S.; Quici, S. *J. Am. Chem. Soc.* **1995**, *117*, 226−232.

(45) Bravo, A.; Bjorsvik, H.-R.; Fontana, F.; Minisci, F.; Serri, A. *J. Org. Chem.* **1996**, *61*, 9409−9416.

(46) We also have exploited this phenomenon by demonstrating that 4-$HOC_6H_4CH{=}CH_2$ can be converted in a free-radical chain reaction to a high molecular weight polymer in good HBA solvents such as HMPA.

(47) Howard, J. A.; Ingold, K. U. *Can. J. Chem.* **1964**, *42*, 1044−1056.

(48) Later, direct measurements of $k^{S}_{PhOH/Me_3COO^{\bullet}}$ at −32 °C by ESR in 11 solvents yielded rate constants which ranged from $5 \times 10^2\ M^{-1}\ s^{-1}$ in hexane to $\sim 6\ M^{-1}\ s^{-1}$ in an alcohol, an ether and two ketones. [49] These data correlate only roughly with β_2^H (slope = −4.2). Values of $k^{S}_{PhCHO/Me_3COO^{\bullet}}$ were about $0.4\ M^{-1}\ s^{-1}$ in all 11 solvents, as would be expected for a C−H bond-breaking reaction.

(49) Tavadyan, L. A.; Mardoyan, V. A.; Nalbandyan, A. B. *Sov. J. Chem. Phys.* **1990**, *5*, 2537−2556.

H-bonding contribution to an observed KSE will be small which allows other types of solvent effects to be observed. An interesting example is the reaction:[40]

$$H_2C{=}CH(CH_2)_3\dot{C}(CH_3)_2 + GSH \xrightarrow{k^S_{GSH/R^\bullet}} H_2C{=}CH(CH_2)_3CH(CH_3)_2 + GS^\bullet$$

where GSH represents glutathione diethylester. In solvents of increasing β_2^H (CH_2Cl_2 to CH_3CN) $k^S_{GSH/R^\bullet}$ slightly increases, whereas no change should have been expected since the substrate is an alkylthiol for which $\alpha_2^H = 0.00$.[27,38] Another type of solvent effect manifests itself, an increase in the stabilization of a highly polarized transition state as the polarity of the solvent is increased.

Similarly, the rate constants for *tert*-butyl radical addition to acrylonitrile increase slightly with solvent polarity because hydrogen bonding is unimportant and the highly polarized transition state is stabilized by more polar solvents. [41]

Effects of HBA Solvents on Some Important Properties of Hydroxylic Substrates. (i) Modulations of Reaction Products. Minisci and co-workers[42−45] have exploited KSEs to direct certain reactions down chosen pathways.[46] For example,[43] *tert*-butoxyl radicals generated in the presence of cyclohexene/*tert*-butyl hydroperoxide (5:1 to 20:1) in benzene yield *tert*-butylperoxyl and cyclohexenyl radicals in roughly equal amounts. Since this peroxyl radical is persistent, the persistent radical effect (PRE) ensures that only the cross radical coupling product is formed, *tert*-butyl cyclohexenyl peroxide. However, in the strong HBA solvent, pyridine, H-atom abstraction from the hydroperoxide is suppressed, and the major product then becomes dicyclohexenyl formed by cyclohexenyl/cyclohexenyl radical coupling. Similarly, in the Fe(III)-catalyzed reaction of Me_3COOH with α-methylstyrene the main product in benzene is epoxide:[44]

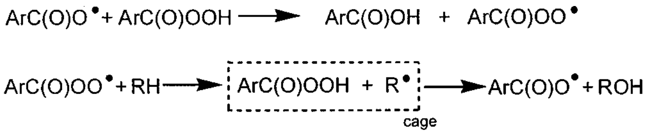
$$Me_3COOH \xrightarrow{Fe} Me_3CO^\bullet \xrightarrow{Me_3COOH} Me_3COO^\bullet$$

$$Me_3COO^\bullet + CH_2{=}C(Me)Ph \rightarrow Me_3COOCH_2C^\bullet(Me)Ph \rightarrow Me_3CO^\bullet + \overline{OCH_2C}(Me)Ph$$

However, in the presence of pyridine the main reaction takes a different course thanks to retardation of the $Me_3CO^\bullet/Me_3COOH$ reaction and the PRE:

$$Me_3CO^\bullet + CH_2{=}C(Me)Ph \rightarrow Me_3COCH_2C^\bullet(Me)Ph \xrightarrow{Me_3COO^\bullet} Me_3COCH_2C(OOCMe_3)MePh$$

Oxidation of alkanes by aromatic peracids occurs with high regio-, chemo-, and stereoselectivity, probably via the following radical chain reaction.[45] However, primary and secondary



alcohols are not oxidized by aromatic peracids when the alcohols are used as solvent despite their relatively weak H−COH bonds because the alcohols form HB complexes with the peracid and protect its labile hydrogen atom from abstraction by $ArCO_2\bullet$ radicals. Alcohols are actually more reactive toward peracid oxidation than alkanes, but this only becomes apparent if the reactions are carried out in a poor HBA solvent.[45]

(ii) Phenolic Antioxidant Activity. Phenols are chain-breaking antioxidants which retard the autoxidation of organic materials. They trap the chain-carrying peroxyl radicals in competition with the chain-propagating attack on the organic, that is,

$$ROO^\bullet + RH \xrightarrow{k^s_{RH/ROO^\bullet}} ROOH + R^\bullet \quad \text{or } ROO\dot{R}H$$

$$ROO^\bullet + ArOH \xrightarrow{k^s_{ArOH/ROO^\bullet}} ROOH + ArO^\bullet$$

The magnitude of $k^s_{ArOH/ROO^\bullet}$ decreases in HBA solvents, as was first recognized in 1964 on the basis of solvent-induced changes in the rate constant ratio, $k^s_{RH/ROO^\bullet}/k^s_{ArOH/ROO^\bullet}$ (RH = styrene), which were "determined by the strength of the hydrogen bond between the phenol and the solvent".[47,48] Steric protection of the phenol's hydroxylic group reduced the KSE, for example, 2,6-di-*tert*-butyl-4-methylphenol was a "much more efficient (antioxidant) than 4-methylphenol" in *tert*-butyl alcohol and acetic acid, but it was less efficient in *n*-decane and chlorobenzene.[47] These observations, which have been confirmed for several phenols[50] help provide a rationale for why nature "chose" α-tocopherol as the major lipid-soluble, radical-trapping antioxidant in mammals.[51,52] This phenol resides in phosphatidylcholine bilayers with its phenolic hydroxyl group close to the model membrane/water interface[52] where H-bonding would reduce the antioxidant activity of a less sterically hindered phenol.

(iii) Hammett Correlations for Substituted Phenols. Rate constants for H-atom abstraction from substituted phenols by, for example, peroxyl radicals are well correlated via the Hammett equation using Brown and Okamoto's σ^+ substituent constants,[37,53] that is,[54]

$$\log\left(\frac{k^S_{ArOH/Y^\bullet}}{k^S_{PhOH/Y^\bullet}}\right) = \rho^+_{kinet}\sum\sigma^+ \quad (Y^\bullet = ROO^\bullet) \tag{ix}$$

Recent experimental and theoretical studies of the gas-phase O−H bond dissociation enthalpies (BDEs) of substituted phenols have demonstrated that phenolic O−H BDEs can also be correlated by $\Sigma\sigma^+$.[55] In a non-HBA solvent the relative rates of H-atom abstraction from a series of sterically nonhindered phenols by a particular radical, $Y^\bullet$, will be determined solely by differences in the activation enthalpies, which must be proportional to the differences in reaction enthalpies (Evans−Polanyi principle),[56] and these must be proportional to the differences in phenolic O−H BDEs. The generality of eq ix was confirmed for $Y^\bullet$ = $DPPH^\bullet$ and a fairly good Hammett

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(50) Barclay, L. R. C.; Edwards, C. E.; Vinqvist, M. R. *J. Am. Chem. Soc.* **1999**, *121*, 6226−6231. See also: Barclay, L. R. C.; Vinqvist, M. R.; Antunes, F.; Pinto, R. E. *J. Am. Chem. Soc.* **1997**, *119*, 5764−5765. Iwatsuki, M.; Tsuchiya, J.; Komuro, E.; Yamamoto, Y.; Niki, E. *Biochim. Biophys. Acta* **1994**, *1200*, 19−26.

(51) Burton, G. W.; Joyce, A.; Ingold, K. U. *Lancet* **1982**, *2*, 327. Burton, G. W.; Joyce, A.; Ingold, K. U. *Arch. Biochem. Biophys.* **1983**, *221*, 281−290. Ingold, K. U.; Webb, A. C.; Witter, D.; Burton, G. W.; Metcalfe, T. A.; Muller, D. P. R. *Arch. Biochem. Biophys.* **1987**, *259*, 224−225.

(52) Burton, G. W.; Ingold, K. U. *Acc. Chem. Res.* **1986**, *19*, 194−201.

(53) Brown, H. C.; Okamoto, Y. *J. Am. Chem. Soc.* **1958**, *80*, 4979−4987.

(54) (a) Howard, J. A.; Ingold, K. U. *Can. J. Chem.* **1963**, *41*, 1744−1751. (b) Howard, J. A.; Ingold, K. U. *Can. J. Chem.* **1963**, *41*, 2800−2806.

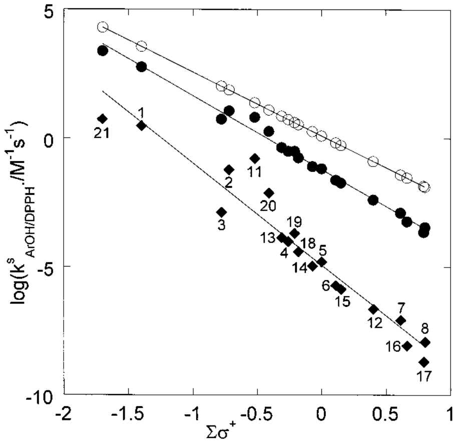


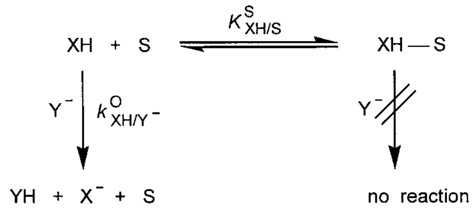
Figure 4. Plots of calculated $\log(k^{S}_{ArOH/DPPH^\bullet}/M^{-1}\ s^{-1})$ values vs $\Sigma\sigma^+$ for 19 phenols in an alkane (○, $\beta_2^H = 0.00$), anisole (●, $\beta_2^H = 0.26$), and HMPA (◆, $\beta_2^H = 1.00$). Phenols 1−8 and 11 are identified in Table 4. The substituent(s) and number for the remainder are 3-Cl (12), 4-Me (13), 4-F (14), 4-Br (15), 4-CN (16), 4-NO_2 (17), 4-Ph (18), 2-Me (19), 2,6-Me_2 (20), 4-Me_2N (21).

type correlation was obtained (see Table 3 and Figure S1).[57]

$$\log(k^{O}_{ArOH/DPPH^\bullet}/M^{-1}\ s^{-1}) = 0.10_3 - 2.4_7\sum\sigma^+ \quad (r^2 = 0.95) \tag{x}$$

If the kinetic data had been obtained in an HBA solvent, the rate constants for phenols, having relatively high and relatively low α_2^H values, would be affected to different extents by H-bonding, and this would change ρ^+. As far as we are aware, this point has not been previously addressed. We have therefore used eqs vii and x to calculate rate constants for H-atom abstraction by DPPH$^\bullet$ from 19 phenols having $\Sigma\sigma^+$ ranging from −1.70 to 0.80 and α_2^H values ranging from 0.26_1 (2-$MeOC_6H_4$-OH)[58] to 0.82_4 (4-$NO_2C_6H_4OH$) in five different solvents: an alkane ($\beta_2^H = 0.00$), benzene ($\beta_2^H = 0.14$), anisole ($\beta_2^H = 0.26$), pyridine ($\beta_2^H = 0.62$) and HMPA ($\beta_2^H = 1.00$) (see Table S8).Three sets of these data have been used to construct $\Sigma\sigma^+$ Hammett plots which in the alkane solvent necessarily give a perfect correlation ($\rho^+ = -2.4_7$, $r^2 = 1.00$), but as the solvent becomes a stronger HBA, the scatter increases and ρ^+ becomes more negative, for example, in anisole $\rho^+ = -2.8_1$ ($r^2 = 0.99$) and in HMPA $\rho^+ = -3.9_7$ ($r^2 = 0.93$), see Figure 4. It is clear that KSEs can have a significant effect on ρ^+ for the ArOH + DPPH$^\bullet$ reaction and these effects should always be taken into account when trying to assess the significance of different ρ^+ values for different ArOH + Y$^\bullet$ reactions.

Scheme 3



(iv) Phenolic O−H BDEs Estimated from Measurements in Solution. A 1995 paper from this laboratory[6] reported photoacoustic calorimetric (PAC) measurements of phenol's O−H bond dissociation enthalpy in a number of solvents, BDE-(O−H)^{sol}, from which gas-phase BDEs were derived by (among other things) correcting for the enthalpies of H-bonding by phenol in the different solvents, BDE(O−H)^{gas} mean 87.4 (later corrected to 87.3)[55d] kcal mol^{-1} in good agreement with various gas-phase values of ~87 kcal mol^{-1}. It was pointed out[6] that "there are some limitations to the EC (electrochemical cycle) method which result from the attempt to use solution *free-energy* measurements to obtain gas-phase *enthalpies*". For some EC work on phenol in DMSO[59] it was also noted that an empirical equation had been used which "failed to properly account for the solvent effect" and the reported "gas phase" O−H BDE of 89.9 kcal mol^{-1} was recalculated as 86.4 kcal mol^{-1}. Furthermore, it was concluded[6] that there were "likely to be systematic errors for BDE(O−H) values measured by the EC method in DMSO" for a series of phenols having various pK_a's simply because the constant in the above-mentioned empirical equation "C^{DMSO}(ArOH) will *not be constant.*" These criticisms were vigorously rebutted and "gas-phase" O−H BDEs for 15 phenols were calculated using the same empirical equation and constant, for example, for phenol 90.4, 4-methoxyphenol 84.6 and 4-cyanophenol 94.2 kcal mol^{-1}.[60] However, from literature data,[38] the free energy changes, $\Delta G°$, for the DMSO/4-methoxyphenol and DMSO/4-cyanophenol hydrogen bonds can be calculated to be smaller by 0.2 and greater by 1.5 kcal mol^{-1}, respectively, than ΔG^0 for the DMSO/phenol H-bond. These differences in free energies for the hydrogen bonds are, presumably, essentially identical to the enthalpy differences which implies that the O−H BDE of 4-methoxyphenol was overestimated by 0.2 kcal mol^{-1}, and that of 4-cyanophenol was underestimated by 1.5 kcal mol^{-1}. Indeed, if 1.5 kcal mol^{-1} is added to the EC ΔBDE(4-NCC_6H_4O−H − PhO−H) value of 3.8 kcal mol^{-1},[60] the ΔBDE rises to 5.3 kcal mol^{-1}, in much better agreement with our earlier PAC measurement of this quantity, viz., 5.0 kcal mol^{-1}. [55d]

Application of the General KSE Equation to Proton Transfer. As noted in the Introduction,[10,11] our work on KSEs for H-atom abstraction from phenols was foreshadowed by Nielsen's work on proton transfer from phenols to an aromatic radical anion. Scheme 3 appears reasonable for proton transfer and is essentially identical to Scheme 1 for H-atom transfer. Provided the three assumptions regarding H-atom abstraction (see Introduction) apply to proton transfer, the KSE equation for proton transfer should identical to that for atom transfer, that is,

$$\log(k^{S}_{XH/Y^-}/M^{-1}\ s^{-1}) = \log(k^{O}_{XH/Y^-}/M^{-1}\ s^{-1}) - 8.3\ \alpha_2^H\beta_2^H \tag{xiii}$$

To check this equation we make use of the best available data, viz., Nielsen and Hammerich's[11b] rate constants for deproto-

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[55] *Experiment*: (a) Lind, J.; Shen, X.; Eriksen, T. E.; Merényi, G. *J. Am. Chem. Soc.* **1990**, *112*, 479−482. (b) Jonsson, M.; Lind, J.; Eriksen, T. E.; Merényi, G. *J. Chem Soc., Perkin Trans. 2* **1993**, 1567−1568. (c) Bordwell, F. G.; Zhang, X.-M.; Satish, A. V.; Cheng, J.-P. *J. Am. Chem. Soc.* **1994**, *116*, 6605−6610. (d) Wayner, D. D. M.; Lusztyk, E.; Ingold, K. U.; Mulder, P. *J. Org. Chem.* **1996**, *61*, 6430−6433. (e) See also, Lucarini, M.; Pedrielli, P.; Pedulli, G. F.; Cabiddu, S.; Fattuoni, C. *J. Org. Chem.* **1996**, *61*, 9259−9263. *Theory*: (f) Wu, Y.-D.; Lai, D. K. W. *J. Org. Chem.* **1996**, *61*, 7904−7910. (g) Wright, J. S.; Carpenter, D. J.; McKay, D. J.; Ingold, K. U. *J. Am. Chem. Soc.* **1997**, *119*, 4245−4252. (h) DiLabio, G. A. *J. Phys. Chem. A* **1999**, *103*, 11414−11424.

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[57] For 4-methoxyphenol the rate constant was initially measured in DMSO ($\beta_2^H = 0.78_0$), $k^{DMSO} = 4.7_8 \times 10^{-2}$ M^{-1} s^{-1}, which gave a calculated $k^o = 174$ M^{-1} s^{-1}, in excellent agreement with a subsequently measured value of 240 M^{-1} s^{-1} in *n*-heptane.

[58] DFT calculations indicate that the transition state for H-atom abstraction from 2-methoxyphenol differs from that for 4-methoxyphenol.[39] Its Arrhenius A-factor will therefore be different from that of 3- and 4-substituted phenols (i.e., break down of the Evans−Polanyi principle) and thus it does not properly "belong" in Figure 4.

Table 5. Rate Constants (M^{-1} s^{-1}) for Deprotonation of Phenol and 2,4,6-Trimethyl-phenol by the Anthracene Radical Cation at 25 °C

		$10^{-3}\, k^{S}_{ArOH/An\bullet-}$ [b]	
solvent	β_2^{H} [a]	phenol	2,4,6-$Me_3C_6H_2OH$
MeCN	0.44 (0.41)	281	17.1
PC[c]	0.50[d] (0.47)	126	5.92
DMF	0.66 (0.68)	5.77	1.53
DMSO	0.78 (0.78)	3.41	0.656

[a] From ref 23a except as noted. Numbers in parentheses are β_2^{H} values calculated from the reported[11] equilibrium constants for H-bond formation by phenol, a "calibrated" HBD for which $L_{PhOH} = 0.946$ and $D_{PhOH} = -0.057$ (ref 23a), these β_2^{H} values being calculated from the relationships, $\log K_2^{H} = (\log K - D_{PhOH})/L_{PhOH}$ and $\beta_2^{H} = (\log K_2^{H} + 1.1)/4.636$. [b] From ref 11b. [c] Propylene carbonate. [d] From ref 61.

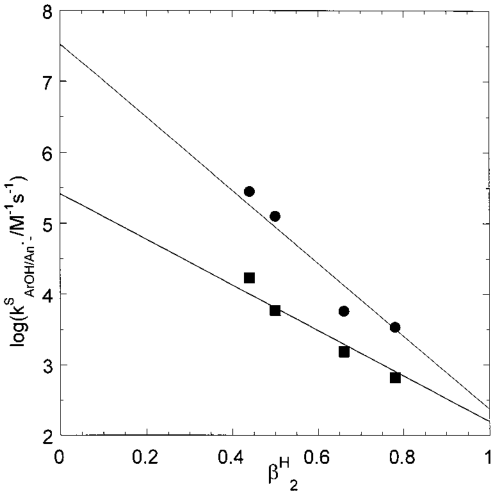

Figure 5. Nielsen and Hammerich's[11b] kinetic data for proton transfer from phenol (●) and 2,4,6-trimethylphenol (■) to the anthracene radical anion plotted against literature values of β_2^{H} for the four solvents employed. The data are from Table 5, and the two straight lines have the same slopes as those found for H-atom abstraction by CumO$^\bullet$, viz., $M_{XH} = -5.1_5$ for phenol and -3.2_2 for trimethylphenol (see Table 4).

nation of phenol and 2,4,6-trimethylphenol by the anthracene radical anion, $k^{S}_{ArOH/An\bullet-}$, in the four solvents they employed (see Table 5). Values of β_2^{H} calculated from the reported[11] equilibrium constants for hydrogen-bond formation between phenol and these four HBAs were in good agreement with literature values[23a,61](see Table 5). Plots of $\log(k^{S}_{ArOH/An\bullet-})$ versus the literature β_2^{H} values are shown in Figure 5. The two straight lines have been drawn with slopes *identical* to those for H-atom abstraction from phenol ($M_{PhOH} = -5.1_5$) and 2,4,6-trimethylphenol ($M_{Me_3C_6H_2OH} = -3.2_2$). The good fit of these lines to experiment is a fairly strong indication that H-atom transfer and proton transfer from the same substrate have the same KSE.

Conclusions

Rate constants at room temperature for H-atom (and proton) abstraction from substrates, XH, in solvents, S, can be correlated by one single equation:

$$\log(k^{S}/M^{-1}\ s^{-1}) = \log(k^{O}/M^{-1}\ s^{-1}) - 8.3\alpha_2^{H}\beta_2^{H} \quad \text{(xiv)}$$

where k^{S} and k^{O} are the rate constants in solvent S and in a saturated hydrocarbon, respectively, α_2^{H} and β_2^{H} are Abraham's parameters which describe the ability of XH to act as a HBD and S as a HBA, respectively. KSEs due to H-bonding can play an important role in determining the products of a reaction, the antioxidant activities of phenols, the magnitude of p^{+} in Hammett type correlations and, no doubt, in numerous other areas. The ability to forecast their magnitude should have far reaching consequences.

Experimental Section

Materials. The following solvents, of the purest grade available, were used as received: acetonitrile, tetrachloromethane and ethyl acetate (OmniSolve); acetic acid, benzene, heptane, octane, pentane, methyl acetate, methyl formate, and *tert*-butyl alcohol (Aldrich). Chlorobenzene (BDH) was purified by repeated washings with concentrated H_2SO_4, H_2O, aqueous sodium bicarbonate, and H_2O, followed by drying over $CaCl_2$ and finally by distillation from P_2O_5. Anisole (Aldrich) was washed with equal volumes of 2 M NaOH (×2) and H_2O (×2), dried over $CaCl_2$, and then distilled from sodium taking the center cut. γ-Valerolactone (Aldrich) was purified as described previously.[12] With one exception, the phenols used in this work were from Aldrich. They were purified by recrystallization from pentane or pentane/ether, followed by sublimation. The 4-methoxyphenol also had to be decolorized with charcoal. 2*R*,4′*R*,8′*R*-α-Tocopherol (natural vitamin E, Chemalog) was purified by chromatography as described previously.[12]

Diphenylpicrylhydrazyl, DPPH$^\bullet$ (BDH, Poole, U.K.) was 98% pure.[12] Di-*tert*-butyl peroxide (Aldrich, 98%) was percolated through activated basic alumina, and dicumyl peroxide (Aldrich) was purified by recrystallization from methanol.

High purity acetophenone, cumyl alcohol, and 1,4-dichlorobenzene (Aldrich) were used as received. Dimethyl sulfoxide (Aldrich) was dried over calcium hydride prior to use.

Laser Flash Photolysis (LFP). The equipment and experimental procedures have been thoroughly described in earlier papers from this laboratory.[62] *Tert*-butoxyl and cumyloxyl radicals were generated by 308 nm LFP of solutions of 0.22 M di-*tert*-butyl peroxide and 0.13 M dicumyl peroxide, respectively. (These concentrations give an OD ≈ 0.3 at the laser wavelength in the 7 × 7 mm^2 Suprasil quartz cells.) All solutions of peroxide and phenol (or other H-atom donor) were deoxygenated by purging with nitrogen for >5 min prior to LFP. Pseudo-first-order rate constants (k^{S}_{exptl}) were determined at 298 ± 2 K using digitally averaged decay or growth curves (from up to 10 laser flashes). Absolute second-order rate constants ($k^{S}_{XH/Y\bullet}$) were calculated by least-squares fitting of plots of k^{S}_{exptl} vs [XH] for at least five different XH concentrations.

Cumyloxyl Radical Kinetics by Product Analysis. Dicumyl hyponitrite, synthesized by a literature procedure,[63] was decomposed at 25 °C in the dark in argon-purged, sealed Pyrex vessels for 10 days in the chosen solvent and known concentrations of an H-atom donor (e.g., 4-methoxyphenol). Yields (absolute and relative) of acetophenone and cumyl alcohol were then determined by GC/FID on a Hewlett-Packard 5890 instrument using a 25 m × 0.02 mm (i.d.) HP-Ultra-2 column and using 1,4-dichlorobenzene as the internal standard. The mass balance in each experiment (ignoring the dicumyl peroxide formed by collapse of the geminate cumyloxyl radical pairs in the solvent cage which was not determined) was calculated as 100× ([acetophenone] + [cumyl alcohol])/ [hyponitrite], see Supporting Information. The

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mean mass balances in chlorobenzene, benzene, anisole, acetic acid, and acetonitrile were 94, 95, 90, 90, and 97%, respectively. If the yields of dicumyl peroxide are assumed to be same as Kiefer and Traylor's[64] measured yields of di-*tert*-butyl peroxide formed in the thermal decomposition of di-*tert*-butyl hyponitrite in solvents of the same viscosities, viz., 0.772, 0.601, 1.25, 1.15, and 0.345 cP, respectively, for the solvents mentioned above, the estimated total mass balances rise to 108, 103, 109, 108, and 106%, respectively. It would appear that cage escape during hyponitrite decomposition of geminate cumyloxyl radicals is more efficient than escape of geminate *tert*-butoxyl radicals.

Infrared Measurements of α_2^H. Experiments were done in CCl_4 (distilled over P_2O_5) using DMSO (dried with CaH_2) as the hydrogen-bond acceptor and a Bomem FTIR spectrophotometer 120 series using a CaF_2 cell with a path length of ~2.5 mm. The concentration of non-H-bonded XH was determined via a calibration curve (i.e., no DMSO). This curve was constructed to ensure that experiments with DMSO were carried out only at XH concentrations below those where measurable self-association occurred, that is, at concentrations where the Beer–Lambert law obtained. At least five different $[XH]_{total}/[DMSO]_{total}$ ratios were used to determine the equilibrium constant for H-bond formation (from the slopes of the straight lines obtained by plotting $[(XH\cdots DMSO)]_{H-bonded}/[XH]_{free}$ against $[DMSO]_{free}$). Values of α_2^H were calculated using the relation:

$$\log K = L_{DMSO} \log K_A^H + D_{DMSO}$$

and

$$\alpha_2^H = \frac{(\log K_A^H + 1.1)}{4.636}$$

where $L_{DMSO} = 1.2399$ and $D_{DMSO} = 0.2656$ (see ref 38).

Kinetic Measurements with DPPH$^\bullet$ Radicals. The experimental procedure has been described in earlier publications from this laboratory.[12,65] Briefly, the concentration of DDPH$^\bullet$ was monitored at its band maximum (512–530 nm, solvent-dependent) relative to an isosbestic point in a 10 × 10 mm^2 quartz cuvette placed in a Hewlett-Packard 8425A diode array spectrophotometer equipped with an HP 98090A programmable heater. Concentrated, deoxygenated stock solutions of more reactive phenols were rapidly mixed with thermostated, deoxygenated solutions of DPPH$^\bullet$. For less reactive phenols, concentrated deoxygenated stock solutions of DPPH$^\bullet$ were rapidly mixed with thermostated, deoxygenated solutions of XH. Values of k^S_{exptl} were measured for at least five different phenol concentrations, and absolute second-order rate constants, $k^S_{XH/DPPH^\bullet}$, were calculated by least-squares fitting of plots of k^S_{exptl} vs [XH].

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Supporting Information Available: Derivation of the general KSE eq viii from Scheme 1 and Abraham's thermodynamic equations for hydrogen bonding, plot of $\log(k^O_{ArOH/DPPH^\bullet}/M^{-1}\ s^{-1})$ for nine phenols versus $\sum\sigma^+$ for their substituents (Figure S1), detailed kinetic data for the reactions of CumO$^\bullet$ with three selected phenols in various solvents: 2,4,6-Me_3, 4-Cl and 3,5-Cl_2-phenol (Tables S1–S3), product data for the reactions of CumO$^\bullet$ with 4-MeO-phenol in various solvents and with c–C_6H_{12} in anisole (Table S4), data from which α_2^H values were calculated (Table S5), values of $k^S_{XH/CumO^\bullet}$ in various solvents (mainly from the literature) for XH = *tert*-butyl hydroperoxide, aniline and 2-methoxyphenol (Table S6), detailed kinetic data for the reactions of DPPH$^\bullet$ with eight phenols in heptane and 4-MeO phenol in DMSO (Table S7), and calculated rate constants for reactions of DPPH$^\bullet$ with 19 phenols in an alkane, benzene, anisole, pyridine, and HMPA (Table S8) (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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