Kinetic Solvent Effects on Hydrogen Atom Abstraction from Phenol, Aniline, and Diphenylamine. The Importance of Hydrogen Bonding on Their Radical-Trapping (Antioxidant) Activities[1]

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Absolute rate constants for hydrogen atom abstraction by alkoxyl radicals from phenol, aniline, and diphenylamine have been measured in 14 solvents at room temperature by laser flash photolysis. For all three substrates the rate constants decline as the solvent becomes a stronger hydrogen-bond acceptor (HBA). Thus, on changing the solvent from CCl_4 to CH_3CN the rate constants decline by factors of 148, 7.1, and 4.7 for PhOH, $PhNH_2$, and Ph_2NH, respectively. The kinetic solvent effect for phenol correlates rather well with Abraham's β_2^H scale of relative HBA activities of the solvents we have employed as measured as solutes in CCl_4 solvent. This correlation is not quite so good with aniline and it is almost nonexistent for diphenylamine. With all three substrates the "deviant" solvents produce higher rate constants than would be expected from the β_2^H value of the solvent and, generally, these are the solvents in which steric hindrance to hydrogen-bond formation would appear probable. The kinetic data for the three substrates can be most readily interpreted in terms of specific hydrogen bonding rather than being due to some generalized weakly dipolar interaction. It is concluded, for example, that hydrogen bonding involves the π-electron cloud in benzene but the chlorine atom in chlorobenzene.

Nontertiary aromatic amines and phenols are highly effective radical-trapping antioxidants which retard the rates of oxidative degradation of organic materials of commercial and biological importance.[3] This antioxidant activity arises from the fact that peroxyl and alkoxyl radicals ($Y^•$) abstract hydrogen from the heteroatom of the antioxidant (ArXH, reaction 1) much more rapidly

$$Y^• + ArXH \xrightarrow{k_1} YH + ArX^• \qquad (1)$$

than they abstract hydrogen from hydrocarbons (RH, reaction 2).[4] Although the rate of reaction 2 would appear to be uninfluenced by the nature of the solvent,[5] we recently discovered a dramatic solvent effect on the

$$Y^• + RH \xrightarrow{k_2} YH + R^• \qquad (2)$$

rate of reaction 1.[6] In the latter study,[6] phenol was used as ArXH with the cumyloxyl radical ($CumO^•$) as $Y^•$ and it was found that k_1 declined by a factor of more than 100 on changing the solvent from carbon tetrachloride to acetonitrile or *tert*-butyl alcohol. The observation that k_2 is solvent independent[5] and that k_1 is solvent dependent[6] is obviously relevant to the abilities of antioxidants to fulfill their role in the different environments likely to be encountered both in commercial applications and in the living world. In the present paper, we extend our studies of kinetic solvent effects, KSEs, on reaction 1 to two prototypical synthetic aromatic amine antioxidants, aniline and diphenylamine.[7] The radical-trapping abilities of these two amines have been measured in 14 solvents, and our earlier work on phenol[6] has been extended to cover the same 14 solvents. Our results are likely to be relevant to a number of biologically important secondary amines which have an NH group adjacent to a π-electron system, e.g., tryptophan, reduced flavin adenine dinucleotide, and tetrahydrobiopterin, and to phenols, e.g., tyrosine and vitamin E.

The KSE on the cumyloxyl radical/phenol reaction was attributed to hydrogen bond formation between the phenol as the hydrogen bond donor (HBD) and hydrogen bond accepting (HBA) solvents, S.[6,8] The stronger the hydrogen bond, PhOH- - -S, the smaller k_1 becomes. The strength of ArXH- - -S hydrogen bonds obviously depends on the HBA ability of S and the HBD ability of ArXH. Smaller KSEs are to be expected with the amines since aromatic amines are weaker acids than phenols. This has been found to be the case. However, there is no

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(3) Reviews: Mahoney, L. R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 547−555. Howard, J. A. in *Free Radicals*; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. 2, Chapter 12. Burton, G. W.; Ingold, K. U. *Acc. Chem. Res.* **1986**, *19*, 194−201. Berger, H.; Bolsman, T. A. B. M.; Brouwer, D. M. *Dev. Polym. Stab.* **1983**, *6*, 1−27. Pospisil, J. *Dev. Polym. Stab.* **1984**, *7*, 1−61.

(4) See, e.g.: Howard, J. A.; Ingold, K. U. *Can. J. Chem.* **1962**, *40*, 1851−1864. Howard, J. A.; Ingold, K. U. *Can. J. Chem.* **1963**, *41*, 2800−2806. Brownlee, I. T.; Ingold, K. U. *Can. J. Chem.* **1966**, *44*, 861−868. Brownlee, I. T.; Ingold, K. U. *Can. J. Chem.* **1967**, *45*, 2419−2425. Das, P. K.; Encinas, M. V.; Steenken, S.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 4162−4166. Burton, G. W.; Ingold, K. U. *J. Am. Chem. Soc.* **1981**, *103*, 6472−6477. 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. Evans, C.; Scaiano, J. C.; Ingold, K. U. *J. Am. Chem. Soc.* **1992**, *114*, 4589−4593 and references cited.

(5) Avila, D. V.; Brown, C. E.; Ingold, K. U.; Lusztyk, J. *J. Am. Chem. Soc.* **1993**, *115*, 466−470.

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

(7) Because of the high temperatures encountered in gas turbine (jet aircraft) engines, the preferred lubricants are synthetic esters (e.g., pentaerythrytol tetraheptanoate) which are best protected from oxidative degradation by ca. 0.75 wt % of a diarylamine (e.g., 4,4′-dioctyldiphenylamine), see: Nicholas, P. P.; Luxeder, A. M.; Brooks, L. A.; Hammes, P. A. *Kirk-Othmer Encyclopedia of Chemical Technology*, 3rd ed.; Wiley: New York, 1978, Vol. 3, pp 128−148.

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

monotonic relationship between the pK_a of phenol, aniline, and diphenylamine and the magnitudes of their KSEs, probably because of steric hindrance to hydrogen-bond formation in the case of diphenylamine. For experimental reasons we examined the KSEs for aniline and diphenylamine using *tert*-butoxyl radicals and the technique of laser flash photolysis, LFP. However, the results obtained should apply *on a 1:1 basis*[8,9] to hydrogen abstraction from these two amines by almost any other radical, including the radicals important in autoxidation processes.

Results

In our earlier KSE studies on the reactions of alkoxyl radicals with phenol[6,8] and α-tocopherol,[8] the alkoxyl radicals were generated by 308 nm LFP of their parent peroxides. This procedure proved to be impractical with aromatic amines because these compounds absorb too strongly at 308 nm. For the amines we therefore employed 337 nm LFP and generated *tert*-butoxyl radicals (BO$^\bullet$) from di-*tert*-butyl peroxide (used at a concentration of 1.0 M which gives an optical density of 0.3 at 337 nm in our 7 × 7 mm^2 reaction cell). Absolute rate

$$\underset{\text{(BOOB)}}{Me_3COOCMe_3} \xrightarrow[337\ nm]{h\nu} 2\underset{\text{(BO}^\bullet\text{)}}{Me_3CO^\bullet} \qquad (3)$$

constants for the reaction of the BO$^\bullet$ radicals with the two amines were determined by monitoring the pseudo-first-order growth of the aminyl radical at 400 nm for $PhN\dot{H}$[10] and at 750 nm for $Ph_2\dot{N}$[10] in 14 different solvents at ambient temperatures (295 ± 2 K), i.e.,[11]

$$k^S_{exptl} = k^S_o + (k_{PhN(X)H/BO})\,[PhN(X)H] \qquad (X = H, Ph)$$

$$BO^\bullet + PhNH_2 \xrightarrow{k^S_{PhNH_2/BO}} BOH + Ph\dot{N}H \qquad (4)$$

$$BO^\bullet + Ph_2NH \xrightarrow{k^S_{Ph_2NH/BO}} BOH + Ph_2N^\bullet \qquad (5)$$

The derived values of $k^S_{PhNH_2/BO}$ and $k^S_{Ph_2NH/BO}$ in the 14 solvents are given in Table 1. Included in this table for purposes of comparison are the measured rate constants for hydrogen abstraction from phenol by the cumyloxyl radical, $k^S_{PhOH/CumO}$, in the same solvents. Some of these phenol rate constants have been reported previously,[6] but most were measured in the present work.

Table 1. Measured Rate Constants for the Hydrogen Abstraction Reactions from Phenol by Cumyloxyl and from Aniline and Diphenylamine by *tert*-Butoxyl Radicals in Various Solvents at 295 ± 2 K together with the β_2^H Values for Each Solvent

solvent	$10^{-7}k_{PhOH/CumO}$ (M^{-1} s^{-1})	$10^{-8}k_{PhNH_2/BO}$ (M^{-1} s^{-1})	$10^{-8}k_{Ph_2NH/BO}$ (M^{-1} s^{-1})	β_2^H [a]
1 CCl_4	86[b]	4.7	14	0
2 PhCl	48[b]	3.6	9.9	0.09
3 PhH	28[b]	2.8	15	0.14
4 $PhOCH_3$	5.6[b]	1.5	6.8	0.26
5 $CH_3C(O)OCH_3$	0.95	0.97	4.8	0.40
6 $CH_3C(O)OC_2H_5$	0.75	1.2	8.3	0.45
7 $CH_3C(O)OC(CH_3)_3$	1.4	2.1	11	0.45[c]
8 $(CH_3)_3C(O)OCH_3$	1.3	2.1	6.2	0.45[c]
9 $HC(O)OCH_3$	1.0	0.82	4.5	0.38
10 CH_3CN	0.58[b]	0.66	3.0	0.44
11 $(CH_3)_3CCN$	0.98	1.1	5.0	0.44[d]
12 PhCN	1.9	1.4	7.5	0.42
13 $(CH_3)_3COH$	0.36[b]	1.7	11	0.49
14 CH_3CO_2H	1.8[b]	0.53	6.5	0.42[e]

[a] The values quoted are from ref 18a. [b] Values taken from ref 6. [c] Assumed equal to β_2^H for ethyl acetate. [d] Assumed equal to β_2^H for acetonitrile. [e] Value for butyric acid.

Discussion

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.[12] There are a large number of parameters which purport to measure the relative HBA abilities of different solvents,[12] but it seems probable that many of these empirical parameters are "contaminated" by contributions from other types of solvent effects such as dipolarity, polarizability, etc.[13] The most reliable scales of relative HBA activities of common organic solvents would appear to be the 1983 β-constants of Taft and coworkers[15] and the various "sons of β" which have mainly been fathered by Abraham and co-workers in subsequent years.[16] All of the many β-scales of solvent or solute hydrogen-bond basicity were derived (along with several other parameters which measure other solvent properties) by averaging multiple normalized solvent effects on a variety of properties involving many diverse types of indicators.[15−22] Fortunately, the various β values for a specific HBA are

(9) We have predicted that the magnitude of the KSE in solvents A and B, i.e., k_1^A/k_1^B, would generally be independent of the nature of radical Y$^\bullet$.[6] This prediction has now been confirmed using both phenol itself and the phenol, α-tocopherol (α-TOH, vitamin E).[8] For the experiments with α-TOH, the *tert*-butoxyl (BO$^\bullet$) and 2,2-diphenyl-1-picrylhydrazyl (DPPH$^\bullet$) were chosen as Y$^\bullet$ radicals because, in the same solvent, the absolute magnitudes of k_1 differed by more than a million, i.e., k_1^S(α-TOH/BO)/k_1^S(α-TOH/DPPH) ≈ 1.6 × 10^6. However, for a range of kinetic solvent effects of about 60, for any pair of solvents

(k_1^A(α-TOH/BO)/k_1^B(α-TOH/BO)/
k_1^A(α-TOH/DPPH)/k_1^B(α-TOH/DPPH)) ≈ 1.0

Similar, but even more dramatic results were obtained with phenol for which k_1 values in the same solvent differed by a factor of ~10 billion (10^{10}) between Y$^\bullet$ = cumyloxyl and Y$^\bullet$ = DPPH.[8]

(10) Leyva, E.; Platz, M. S.; Niu, B.; Wirz, J. *J. Phys. Chem.* **1987**, *91*, 2293−2298.

(11) All plots of k $^S_{exptl}$ vs [ArN(X)H] gave straight lines with ⟨r⟩ ≥ 0.99. At the amine concentrations employed irradiation at 337 nm in the absence of BOOB did not produce any transient absorption in the visible or near UV.

(12) Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*; Verlag Chemie: Weinheim, Germany, 1988.

(13) For example, this would appear to be the case for Swain *et al.*'s[14] solvent "basity", *B*, parameter. For an interesting discussion of this point, see: Taft, R. W.; Abboud, J.-L. M.; Kamlet, M. J. *J. Org. Chem.* **1984**, *49*, 2001−2005. Swain, C. G. *J. Org. Chem.* **1984**, *49*, 2005−2010.

(14) Swain, C. G.; Swain, M. S.; Powell, A. L.; Alunni, S. *J. Am. Chem. Soc.* **1983**, *105*, 502−513.

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

(16) There would appear to be at least seven "sons of β": β_m, for monomeric (non-self-associated) material;[17] β_2^H, a general, thermodynamically related, scale of solute hydrogen-bond basicities in CCl_4;[18] β_1(general), β_1(special), two scales of solvent hydrogen-bond basicity;[19] β_2 (pK_{HB}), a special solute scale for hydrogen-bond complexation of bases with 4-fluorophenol in CCl_4;[19] β_{sm}, a basicity scale based on extrapolation to infinite dilution;[20] and $\Sigma\beta_2$, a scale of effective or summation hydrogen-bond basicity appropriate for situations in which a solute is surrounded by solvent molecules.[21,22]

(17) Taft, R. W.; Abboud, J.-L. M.; Kamlet, M. J.; Abraham, M. H. *J. Solution Chem.* **1985**, *14*, 153−175.

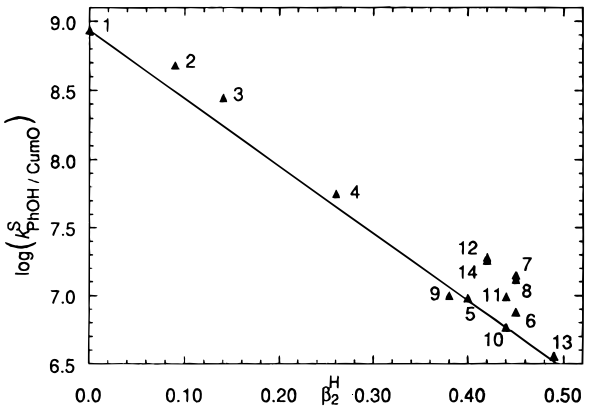


Figure 1. Plot of log $k^S_{PhOH/CumO}$ vs β_2^H. The numbers beside the points correspond to the solvents indicated in Table 1.

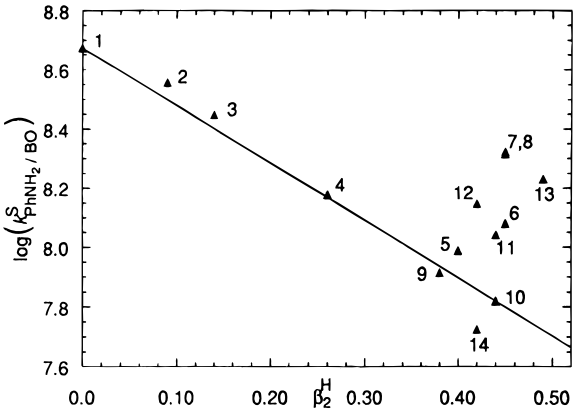


Figure 2. Plot of log ($k^S_{PhNH_2/BO}$) vs β_2^H. The numbers beside the points correspond to the solvents indicated in Table 1.

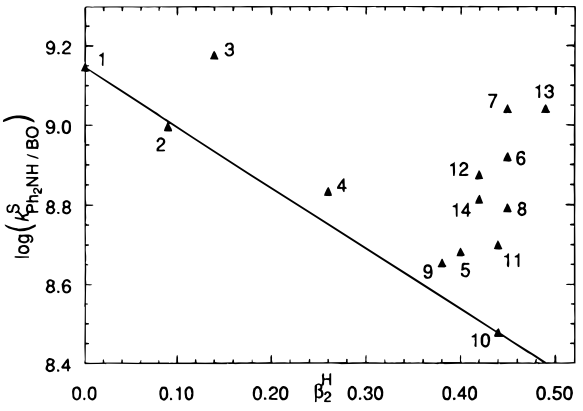


Figure 3. Plot of ($k^S_{Ph_2NH/BO}$) vs β_2^H. The numbers beside the points correspond to the solvents indicated in Table 1.

generally quite similar and, indeed, are often identical. We have chosen, therefore, to correlate our kinetic data with β_2^H, despite the fact that this is a scale of solute hydrogen-bond basicities in CCl_4,[18] rather than a scale for neat solvents. This choice was made simply because the β_2^H-scale is the most extensive of all the β-scales. Plots of log ($k^S_{ArXH/Y}/M^{-1}$ s^{-1}) vs β_2^H for the three reactants are shown in Figures 1−3. It should be noted that the straight lines drawn in these three figures simply connect the rate constant measured in CCl_4 (**1**) with that measured in CH_3CN (**10**), i.e., these lines are not least-squares correlations.

The kinetic data for phenol correlates rather well with β_2^H, although the rate constants in *tert*-butyl acetate (**7**), methyl pivalate (**8**), benzonitrile (**12**), and acetic acid (**14**) are somewhat greater than might have been predicted (see Figure 1). Most of the kinetic data for aniline also correlates reasonable well with β_2^H (see Figure 2). However, "enhanced" rate constants are observed not only in *tert*-butyl acetate, methyl pivalate, and benzonitrile but also in ethyl acetate (**6**), pivalonitrile (**11**), and *tert*-butyl alcohol (**13**). With diphenylamine the rate constants in all solvents except chlorobenzene (**2**) are higher than would be predicted from their β_2^H values and the rate constants measured in CCl_4 (**1**) and CH_3CN (**10**) (see Figure 3). The slopes of the lines shown in Figures 1−3 are −4.9 for phenol, −1.9 for aniline and −1.5 for diphenylamine. These results are at odds with any simple reactant/solvent hydrogen-bond model for KSE's, i.e.,

$$Y^\bullet + ArXH/S \xrightarrow{k^S_{ArXH/Y}} YH + ArX^\bullet + S \qquad (6)$$

The problem is that diphenylamine is more acidic than aniline and hence would be expected to be the better HBD. Thus, any simple model would imply that the magnitude of the KSE should decrease from phenol (pK_a = 18.0),[23] to diphenylamine (pK_a = 25.0),[23] to aniline (pK_a = 30.6).[23,24]

The disagreement between the expected and observed changes in the magnitude of the KSEs for phenol, aniline, and diphenylamine lead us to believe that the simple model shown in reaction 6 is sometimes confounded by steric hindrance to hydrogen-bond formation, particularly when hydrogen-bond formation involves an amino hydrogen atom and a bulky solvent molecule. Steric hindrance is, naturally, more severe for diphenylamine than for aniline, and as a result, the former compound exhibits the smaller KSE despite its higher acidity.[28]

The effect of solvent "size" on the rates of hydrogen atom abstraction from phenol, aniline and diphenylamine was examined for a closely related series of HBA solvents,

(18) (a) Abraham, M. H.; Grellier, P. L.; Prior, D. V.; Morris, J. J.; Taylor, P. J. *J. Chem. Soc., Perkin Trans. 2* **1990**, 521−529. (b) See also, Abraham, M. H.; Grellier, P. L.; Prior, D. V.; Taft, R. W.; Morris, J. J.; Taylor, P. J.; Laurence, C.; Berthelot, M.; Doherty, R. M.; Kamlet, M. J.; Abboud, J.-L. M.; Sraidi, K.; Guihéneuf, G. *J. Am. Chem. Soc.* **1988**, *110*, 8534−8536. Abraham, M. H.; Grellier, P. L.; Prior, D. V.; Morris, J. J.; Taylor, P. J. *Tetrahedron Lett.* **1989**, *30*, 2571−2574. Laurence, C.; Berthelot, M.; Helbert, M.; Sraidi, K. *J. Phys. Chem.* **1989**, *93*, 3799−3802. Abraham, M. H.; Lieb, W. R.; Franks, N. P. *J. Pharm. Sci.* **1991**, *80*, 719−724.

(19) Abraham, M. H.; Buist, G. J.; Grellier, P. L.; McGill, R. A.; Prior, D. V.; Oliver, S.; Turner, E.; Morris, J. J.; Taylor, P. J.; Nicolet, P.; Maria, P.-C.; Gal, J.-F.; Abboud, J.-L. M.; Doherty, R. M.; Kamlet, M. J.; Shuely, W. J.; Taft, R. W. *J. Phys. Org. Chem.* **1989**, *2*, 540−552.

(20) Abraham, M. H.; Duce, P. P.; Prior, D. V.; Barratt, D. G.; Morris, J. J.; Taylor, P. J. *J. Chem. Soc., Perkin Trans. 2* **1989**, 1355−1375.

(21) Abraham, M. H. *J. Phys. Org. Chem.* **1993**, *6*, 660−684.

(22) For reviews of various β scales, see: Abraham, M. H. *Port. Electochim. Acta* **1992**, *10*, 121−134. Abraham, M. H. *Chem. Soc. Rev.* **1993**, 73−83. Abraham, M. H. *NATO ASI Series C* **1994**, *426*, 63−78.

(23) In dimethyl sulfoxide at 25 °C, see: Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456−463.

(24) In this connection, it is worth noting that the equilibrium constants for hydrogen-bond formation by phenol, diphenylamine, and aniline with ethyl acetate in CCl_4 as solvent also do not follow the order which would be expected on the basis of their acidities. That is, for PhOH, Ph_2NH and $PhNH_2$, the equilibrium constants for H-bonding with EtOAc are 8.9 M^{-1} (25 °C),[25] 0.58 M^{-1} (32 °C),[26] and 1.5 M^{-1} (25 °C),[27] respectively. We could not find a complete set of equilibrium constants with any other HBA.

(25) Powell, D. L.; West, D. L. *Spectrochim. Acta* **1964**, *20*, 983−991.

(26) Werner, R. L.; Quinn, J. M.; Haken, J. K. *Spectrochim. Acta* **1982**, *38A*, 887−897.

(27) Lady, J. H.; Whetsel, K. B. *J. Phys. Chem.* **1967**, *71*, 1421−1429.

the esters,[29] methyl acetate (**5**), ethyl acetate (**6**), *tert*-butyl acetate (**7**), methyl pivalate (**8**), and methyl formate (**9**). In order to examine solvent "size" effects it is important to recognize and allow for the fact that an increase in "size" must produce a concomitant decrease in the molar concentration of the functional part of the ester which makes these molecules hydrogen-bond acceptors (the carbonyl oxygen atom, *vide infra*). This correction for the effect of ester molarity can be calculated using the simplified kinetic equation derived previously[6] which relates the rate constant measured in CCl_4 to that measured in solvent S via the equilibrium constant, for hydrogen bond formation in CCl_4 as solvent between dilute ArXH and dilute S. That is,

$$(k^{CCl_4}_{ArXH/Y})_{meas} = (k^{S}_{ArXH/Y})_{meas}(1 + K^{S}_{ArXH}[S]) \quad (7)$$

and

$$ArXH/CCl_4 + S \overset{K^{S}_{ArXH}}{\rightleftharpoons} ArXH\text{- - -}S + CCl_4 \quad (8)$$

First, the measured rate constants in CCl_4 and the least hindered ester, methyl formate (**9**), are used to calculate an effective equilibrium constant for hydrogen bond formation between the substrate, ArXH, and the ester moiety, $(K^{ester}_{ArXH})_{effective}$. Second, this equilibrium constant is used to calculate the rate constants which would be expected in methyl acetate, ethyl acetate, *tert*-butyl acetate, and methyl pivalate on the basis of the molarities of the neat esters. A detailed calculation is given below for phenol in methyl acetate (**5**), and the results of all the calculations are summarized in Table 2 where they are also compared with the experimental rate constants.

From eq 7 (where **1** = CCl_4 and **9** = $HC(O)OCH_3$ and **5** = $CH_3C(O)OCH_3$)

$$k^{\mathbf{1}}_{PhOH/CumO} = k^{\mathbf{9}}_{PhOH/CumO}(1 + K^{ester}_{PhOH}[\mathbf{9}])$$

$$86 \times 10^7 = 1.0 \times 10^7(1 + K^{ester}_{PhOH}[16.2])$$

$$(K^{ester}_{PhOH})_{effective} = 5.25\ M^{-1}$$

$$k^{\mathbf{1}}_{PhOH/CumO} = (k^{\mathbf{5}}_{PhOH/CumO})_{calcd}(1 + K^{ester}_{PhOH}[\mathbf{5}])$$

$$86 \times 10^7 = (k^{S}_{PhOH/CumO})_{calcd}(1 + 5.25\ [12.6])$$

$$(k^{\mathbf{5}}_{PhOH/CumO})_{calcd} = 1.3 \times 10^7\ M^{-1}\ s^{-1}$$

Examination of the data in Table 2 shows that with phenol, which forms a rather strong hydrogen bond with esters (effective $K^{ester}_{PhOH} = 5.25\ M^{-1}$), there is relatively poor agreement between the calculated and experimental rate constants with the latter being noticeably smaller than the former. In fact, the measured rate constants in methyl formate (**9**), methyl acetate (**5**) and ethyl acetate (**6**) decrease monotonically along this series rather than increase as would be expected on the basis of the trend in ester molarities. This decrease does, however, correspond to the increase in the hydrogen bond accepting abilities of these compounds as exemplified by their β_2^H values (viz., 0.38, 0.40, and 0.45, respectively). For *tert*-butyl acetate (**7**) and methyl pivalate (**8**) the β_2^H values are not available, but if they are assumed to be the same as for ethyl acetate, then the increased rate constants in **7** and **8** relative to the rate constant in ethyl acetate are certainly consistent with the decreased molar concentration of the OC(O) ester moiety.

Table 2. Calculated Equilibrium Constants (M^{-1}) for Hydrogen-Bond Formation and Calculated and Measured (in Parentheses) Rate Constants ($M^{-1}\ s^{-1}$) in Esters and Nitriles[a]

	phenol	aniline	diphenylamine
$(K^{ester}_{ArXH})_{effective}$	5.25	0.29	0.13
$10^{-7}k^{\mathbf{5}}_{ArXH}$	1.3 (0.95)	10 (9.7)	53 (48)
$10^{-7}k^{\mathbf{6}}_{ArXH}$	1.6 (0.75)	12 (12)	60 (83)
$10^{-7}k^{\mathbf{7}}_{ArXH}$	2.2 (1.4)	15 (21)	71 (110)
$10^{-7}k^{\mathbf{8}}_{ArXH}$	2.2 (1.3)	15 (21)	71 (62)
$(K^{nitrile}_{ArXH})_{effective}$	7.7	0.32	0.19
$10^{-7}k^{\mathbf{11}}_{ArXH}$	1.2 (0.98)	12 (11)	51 (50)
$10^{-7}k^{\mathbf{12}}_{ArXH}$	1.2 (1.9)	11 (14)	49 (75)

[a] See text for details of the calculations.

In contrast to phenol, the calculated rate constants for aniline (a weak HBD) are in excellent agreement with experiment in methyl acetate and ethyl acetate (see Table 2). Only with *tert*-butyl acetate and methyl pivalate is there poor agreement, and in these cases the measured rate constants are larger than the calculated values, which is consistent with a sterically-induced decrease in the extent of hydrogen bond formation. Aniline is known to form both 1:1 and 1:2 complexes with HBAs.[27,30] Indeed, it is possible that the calculated equilibrium constants for hydrogen-bond formation with esters and nitriles are larger for aniline than for diphenylamine (see Table 2) simply because the weaker acid, aniline, is capable of forming two hydrogen bonds whereas diphenylamine can form only a single hydrogen bond. However, in the two bulky esters (**7** and **8**) steric effects might hinder the formation of two hydrogen bonds by aniline with a consequent enhancement of its reactivity in these two esters relative to its reactivity in sterically less demanding esters. Thus, it would appear that in neat ester solvents the rate constants for a strong HBD, phenol, correlate better with β_2^H than with the molarity of the ester functionality whereas the rate constants for a weak HBD, aniline, correlate better with molarity than with β_2^H.[28]

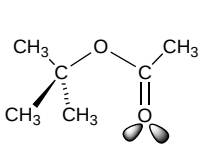
With diphenylamine, which according to our kinetic data forms even weaker hydrogen bonds than aniline, the calculated and experimental rate constants are in satisfactory agreement only in methyl acetate and methyl pivalate. In ethyl and *tert*-butyl acetate it seems likely that steric hindrance of the HBA site causes the measured rate constants to be notably larger than the calculated values (see Table 2). That is, hydrogen bond donors have been demonstrated experimentally to preferentially complex with the carbonyl oxygen atom rather

(28) Abraham has frequently pointed out that OH and NH donors tend to rank proton acceptors differently.[18−22] Unfortunately, those β-scales which have employed amines as hydrogen bond donors[19] do not cover many of the solvents we have investigated and it is partly for this reason we employed the β_2^H scale. Furthermore, even if the basicity scales for OH and NH donors differ this would not explain why the magnitude of the KSE for diphenylamine is less than that for aniline.

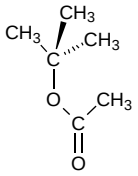
(29) Esters were chosen because of their ubiquitous use in gas turbine engines in conjunction with diarylamine antioxidants.[7]

(30) See, e.g.: Dyall, L. K. *Spectrochim. Acta* **1969**, *25A*, 1423−1435. Brink, G.; Bayles, J. W. *Spectrochim. Acta* **1974**, *30A*, 835−843. Borisenko. V. E.; Filarovski, A. I. *J. Mol. Struct.* **1989**, *196*, 353−370. Wawer, I.; Krysiak, T.; Kecki, Z. *J. Mol. Struct.* **1994**, *326*, 163−170.

than with the alkoxyl oxygen atom.[31] Molecular mechanics calculations[32] on *tert*-butyl acetate yielded structure **A** as the ground state and structure **B** as a transition state. The *tert*-butyl group obviously shields the carbonyl oxygen, and more significantly, it shields the lone pair of electrons on the carbonyl group which is in the *cis*-position with respect to the alkoxy group. It is this *cis* lone pair which is markedly more involved in hydrogen-bonding than the *trans* lone pair.[31f] Steric shielding may also play a role in ethyl acetate but it should be less important in methyl acetate and methyl pivalate and, indeed, the measured rate constants in these two methyl esters are smaller than in ethyl acetate (see Table 1).



A



B

Steric hindrance to hydrogen bond formation with acetonitrile (**10**) must be minimal, and it was for this reason that we decided to draw the lines on the figures between the data points in this solvent and CCl_4. The rate constant ratio, k^{10}/k^{11}, is 1.68 ± 0.01 with phenol, aniline, and diphenylamine (cf. Table 1) which suggests that steric hindrance to hydrogen bond formation also plays no role in pivalonitrile (**11**). This would appear to be reasonable since the *tert*-butyl group in pivalonitrile is far removed from the hydrogen bond (see **C**). By

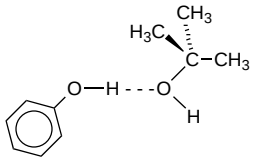
C

implication, these two nitriles should be equally good HBAs at a molecular level, i.e., once allowance has been made for the lower effective molarity of the nitrile group in pivalonitrile relative to acetonitrile. Using the measured rate constants in CCl_4 and CH_3CN, we can calculate values for $(K^{\text{nitrile}}_{\text{ArXH}})_{\text{effective}}$ and $k^{\mathbf{11}}_{\text{ArXH}}$ as described above for the esters. These data are given in Table 2, where it can be seen that the calculated rate constants for phenol, aniline and diphenylamine in pivalonitrile are in excellent agreement with the measured values.

In benzonitrile the calculated rate constants are slightly smaller (21−37%) than the measured rate constants (see Table 2) with all three substrates. We attribute these small deviations to the fact that, according to its β_2^H value (0.42), benzonitrile is a weaker HBA than alkyl cyanides (0.44).

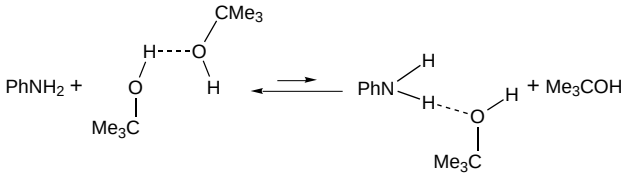
Alcohols and carboxylic acids were represented only by *tert*-butyl alcohol (**13**)[33] and acetic acid (**14**). In the latter solvent the measured rate constant for aniline correlates with the acid's β_2^H value (see Figure 2). However, with phenol and diphenylamine the measured rate constants are somewhat greater than might have been expected from β_2^H (see Figures 1 and 3).

The results with tert-butyl alcohol are particularly interesting. The rate constant for phenol in *tert*-butyl alcohol correlates very well with β_2^H (Figure 1) which implies that there is no steric hindrance to hydrogen bond formation from phenol to *tert*-butyl alcohol, **D**.



D

However, the rate constants for aniline and diphenylamine in *tert*-butyl alcohol are considerably greater than would have been expected (see Figures 2 and 3). It is difficult to see how this could be attributed to steric factors for aniline. That is, formation of a single hydrogen bond between aniline and *tert*-butyl alcohol should suffer no more hindrance than that for phenol and *tert*-butyl alcohol. Even the formation of two hydrogen bonds from aniline to two *tert*-butyl alcohol molecules would also appear to be free of steric hindrance. We therefore suggest that, in contrast to phenol, aniline is simply too weak as a hydrogen-bond donor to compete with *tert*-butyl alcohol and disassociate *tert*-butyl alcohol dimers and oligomers.[34] This suggestion is consistent



with the relative HBD abilities of phenol, *tert*-butyl alcohol, and aniline as defined, for example, by Abraham's α_2^H scale,[36,37] viz., 0.60, 0.32, and 0.26, respectively. Diphenylamine($\alpha_2^H = 0.32$) is as good a HBD as *tert*-butyl alcohol, but steric hindrance of the amino hydrogen atom might prevent the formation of a hydrogen bond from diphenylamine to *tert*-butyl alcohol.

Hydrogen abstraction from diphenylamine occurs more rapidly than would be expected in benzene (**3**), ethyl acetate (**6**), *tert*-butyl acetate (**7**), methyl pivalate (**8**), benzonitrile (**12**), *tert*-butyl alcohol (**13**), and acetic acid (**14**) (see Figure 3). Indeed, even in anisole (**4**), methyl acetate (**5**), and methyl formate (**9**) the rates are somewhat larger than might have been predicted, presumably for steric reasons. The fact that the rate with diphenylamine is higher in benzene than in chlorobenzene whereas the reverse is the case for phenol and aniline suggests that the preferred mode of hydrogen bonding is with the π-electron cloud in benzene, **E**, but with the chlorine atom of chlorobenzene, **F**. The former will obviously be more subject to steric hindrance than the

(31) (a) Fraenkel, G. *J. Chem. Phys.* **1961**, *33*, 1466−1467. (b) Olah, G. A.; O'Brien, D. H.; White, A. M. *J. Am. Chem. Soc.* **1967**, *89*, 5694−5700. (c) Wells, C. F. *J. Phys. Chem.* **1973**, *77*, 1994−1996. (d) Vanderheyden, L.; Zeegers-Huyskens, T. *J. Mol. Liquids* **1983**, *25*, 1−11. (e) Vanderheyden, L.; Zeegers-Huyskens, T. *Bull. Soc. Chim. Belg.* **1985**, *94*, 319−326. (f) Huyskens, P. L.; Marchal, H.; Zeegers-Huyskens, T. *J. Mol. Struct.* **1987**, *158*, 379−385.

(32) MM+ molecular force field in Hyperchem, using the Fletcher−Reeves algorithm.

(33) Other alcohols (such as MeOH) are too reactive toward alkoxyl radicals to make very useful solvents.

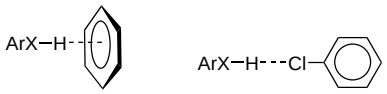
(34) The monomer−dimer and dimer−oligomer equilibrium constants for *tert*-butyl alcohol at 300 K in octane are 7.50 and 12.77, respectively,[35] which implies that in neat *tert*-butyl alcohol the mole fraction of monomer is only 0.08.

(35) Griller, D.; Liu, M. T. H.; Scaiano, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 5549−5551.

(36) 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.

(37) Abraham, M. H.; Duce, P. P.; Grellier, P. L.; Prior, D. V.; Morris, J. J.; Taylor, P. J. *Tetrahedron Lett.* **1988**, *29*, 1587−1590.

latter, and it implies that aromatic amines form specific, directed hydrogen bonds even to very weak HBAs. This conclusion is consistent with the acidic nature of aromatic amines (*vide supra*), but it would stand in contrast to the situation with aliphatic primary and secondary amines for which $\alpha_2^H = 0$. Indeed, Abraham[20,36] has pointed out that complexes involving such aliphatic amines even with strong proton acceptors lie "at the limit where hydrogen bonding per se fades into a generalized weakly dipolar interaction".



E **F**

Conclusions

The ability of phenols and aromatic amines to act as radical traps (antioxidants) declines as the reaction medium becomes a better HBA. This phenomenon has clear relevance to the efficiencies of both commercial and biological antioxidants in non-hydrocarbon media. For phenol the kinetic data in neat solvents correlate rather well with the HBA abilities of the solvents, as measured by Abraham's β_2^H values, provided steric hindrance to hydrogen-bond formation is minimal (see Figure 1). For aniline, which is a much weaker acid than phenol, the kinetic data can again be correlated with β_2^H but steric hindrance to hydrogen bonding becomes more pronounced (see Figure 2). With diphenylamine the kinetic data are very strongly influenced by steric hindrance to hydrogen bonding (see Figure 3 and Discussion).

Our results with both aniline and diphenylamine in esters and nitriles and with diphenylamine in benzene imply that aromatic amines form specific, directed hydrogen bonds even with weak HBAs.

Experimental Section

Materials. Solvents were of the highest purity available. Carbon tetrachloride, chlorobenzene, benzene, ethyl acetate, acetonitrile (Omnisolv), anisole, acetic acid (BDH Chemicals), and *tert*-butyl alcohol (Fisher Scientific) were used without purification. *tert*-Butyl acetate, methyl pivalate, pivalonitrile (Aldrich), and benzonitrile (Kodak) were distilled prior to use. Methyl formate and methyl acetate (Aldrich) were washed with a strong aqueous solution of sodium carbonate, dried, and distilled. Aniline (Aldrich) was distilled and immediately stored under nitrogen. Diphenylamine (BDH Chemicals) and phenol (Aldrich) were recrystallized twice from methanol and cyclohexane, respectively. Dicumyl peroxide (Aldrich) was recrystallized from methanol. Di-*tert*-butyl peroxide (Aldrich, 98%) was passed through a column of neutral alumina to remove *tert*-butyl hydroperoxide.

Laser Flash Photolysis. The apparatus has been described previously.[38] *tert*-Butoxyl radicals were generated by 337 nm LFP of solutions of the amine containing 1.0 M di-*tert*-butyl peroxide and cumyloxyl radicals by 308 nm LFP of solutions of phenol containing 0.13 M dicumyl peroxide. These concentrations of the two peroxides gave an optical density of 0.3 at the laser wavelength. All samples were deoxygenated by purging with nitrogen prior to LFP (up to ten laser flashes). Second-order rate constants were calculated by least-squares fitting of plots containing at least five pseudo-first-order rate constants versus substrate concentration (ranges: 1 to 200 mM for phenol, 0.4 to 20 mM for aniline, and 0.4 to 10 mM for diphenylamine).

Acknowledgment. We thank the Association for International Cancer Research and the National Foundation for Cancer Research for partial support of this work.

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(38) See, e.g.: Scaiano, J. C. *J. Am. Chem. Soc.* **1980**, *102*, 7747–7753. Chatgilialoglu, C.; Ingold, K. U.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 7739–7742. Scaiano, J. C.; Tanner, M.; Weir, D. *J. Am. Chem. Soc.* **1985**, *107*, 4396–4403. Kazanis, S.; Azarani, A.; Johnston, L. J. *J. Phys. Chem.* **1991**, *95*, 4430–4435.