

A Model for Quantitative Evaluation of Equilibrium Constants for Hydrogen Bonding in Polar Aprotic Solvents Based on Incomplete Data Sets Related to Different Solvents

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A general model is proposed for the evaluation of equilibrium constants for hydrogen bonding in polar aprotic solvents between weak acids and (a) solvents, (b) anions and (c) other acid molecules, based on incomplete literature data for hydrogen bonding in polar aprotic solvents or in carbon tetrachloride.

The model is based on the apparent existence of 'unique', solvent-independent equilibrium constants, K_u , for the hydrogen bonding equilibria of interest. It is shown that equilibrium constants for hydrogen bonding between neutrals in carbon tetrachloride may serve as K_u -values, while equilibrium constants for hydrogen bond formation between an anion and a neutral in an aprotic solvent may be converted into a K_u -value if a K_u -value for hydrogen bonding between the neutral and the solvent is known. Application of linear free energy relationships for determination of equilibrium constants unavailable in the literature is demonstrated and used extensively.

Finally, the consequences of the generally strong hydrogen bonding interaction between acids and polar aprotic solvents for interpretation of measured pK -values in these solvents are discussed.

A series of methyl substituted phenols and their anions are used as a general example throughout the paper.

Interference from hydrogen bonding equilibria involving proton donors on the measured rates of proton transfer reactions in polar aprotic solvents has previously been shown to be of importance,¹⁻⁴ and any attempts to interpret the observed rate constants for proton transfer on a microscopic level require a detailed knowledge of the state of the reactants in the solution including specific solute–solute and solute–solvent interactions such as hydrogen bonding.⁵

Experimental determination of the hydrogen bonding equilibrium constants is difficult (in some cases impossible) and time consuming, when series of proton donors and series of solvents are used, and the aim of the present paper is to rationalize quantitatively the relationships between different hydrogen bonding equilibria in order to enable the determination of the required equilibrium constants based on incomplete sets of published experimental data. The analysis of the proposed general model is also based entirely on data available in the literature.

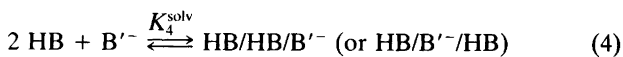
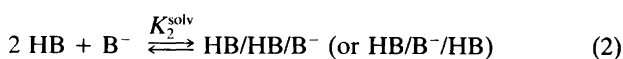
The hydrogen bonding equilibria included in the discussion are (a) 1:1 and 1:2 homoconjugation equilibria in which the corresponding anion of the proton donor, B^- , forms a hydrogen bond with one or two molecules of the parent acid, HB; (b) 1:1 and 1:2 heteroconjugation equilibria in which an anion, B'^- , forms hydrogen bonds with one or two molecules of an acid, HB; (c) dimerization equilibria in which two molecules of the acid form a hydrogen

bonded dimer, and (d) hydrogen bonding between an acid molecule or a dimer of the acid and the solvent.

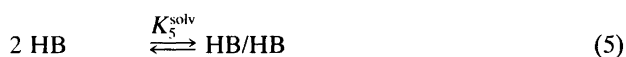
The search for such a quantitative treatment of literature data was prompted by the analysis of an extensive set of kinetic data for the protonation of anthracene anion radical by a series of mono-, di- and trimethyl substituted phenols in a series of polar aprotic solvents, where interpretation of solvent, as well as of substituent, effects seemed to be related to specific interactions between the phenols and (1) the solvents, (2) other phenol molecules and (3) the corresponding phenolate anions.⁵ The determination of equilibrium constants pertinent to the analysis of these kinetic data from existing literature data will be used as the 'case study', but the analysis includes a wider range of proton donors. Most of the results of the analysis are confined to polar aprotic solvents such as hexamethylphosphoric triamide (HMPA), dimethyl sulfoxide (DMSO), *N,N*-dimethylformamide (DMF), *N,N*-dimethylacetamide, (DMA), propylene carbonate (PC), acetonitrile, (MeCN) and benzonitrile (PhCN).

In addition, the consequences of a quantitative knowledge of the equilibrium constants for hydrogen bonding between acids and polar aprotic solvents for the interpretation of measured equilibrium acidities will be discussed for a series of substituted phenols.

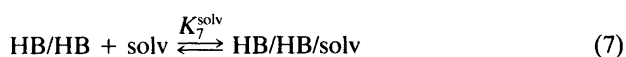
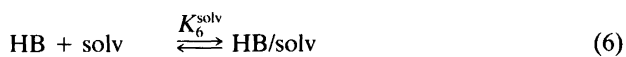
The equilibria and the existing data. In order to clarify whether it is possible to predict from the existing equilibrium data and the stoichiometric concentrations of HB (C_{HB}^0) and B^- ($C_{B^-}^0$) in a given polar aprotic solvent (solv), the distribution of HB and B^- on the species 'free' HB, 'free' B^- , HB/solv, HB/HB, HB/ B^- , HB/HB/ B^- , HB/HB/solv, it is necessary to analyze the comparability of the existing data. (Here and in the following '/' represents a hydrogen bond, and 'free' means non-specifically solvated). For the four homo- and hetero-conjugation equilibria, (1)–(4), values of the corresponding equilibrium constants for different HB, B^- and HB, B'^- pairs have been measured in different polar aprotic solvents, K_i^{solv} (here and in the following the subscript refers to the number of the equilibrium while the superscript refers to the solvent in which the equilibrium constant has been measured). Only for a limited number of HB, B^- and HB, B'^- pairs has K_i^{solv} been determined in more than one solvent. With respect to equilibria (1)–(4) the main question is therefore whether knowledge of $K_i^{\text{solv}_1}$ is sufficient to estimate $K_i^{\text{solv}_2}$ for a given HB, B^- or HB, B'^- pair.



Very limited sets of data are available for equilibrium constants for the formation of hydrogen bonded dimers, eqn. (5), and these data were obtained in apolar solvents such as CCl_4 , CH_2Cl_2 or cyclohexane. In this case the main question is therefore whether it is possible to predict, from e.g. $K_5^{\text{CCl}_4}$ -values, the amount of hydrogen bonded dimer present in polar aprotic solvents.



With respect to hydrogen bonding of HB or HB/HB to the polar aprotic solvents, eqns. (6) and (7), equilibrium constants have only been reported when 'solv' is in fact a solute and the solvent CCl_4 , CH_2Cl_2 or equivalent apolar solvents. Again the question is whether it is possible to estimate from $K_6^{\text{CCl}_4}$ the value of K_6^{solv} when 'solv' is the polar aprotic solvent as well as the hydrogen bond acceptor.



The model and the assumptions. The model for a generalized treatment of hydrogen bonding equilibria is based on the assumption that each hydrogen bond donor molecule, HB, can be the hydrogen bond donor only in one hydrogen bond at a time.

The suggestion is that for each hydrogen bond donor – hydrogen bond acceptor pair there exists a unique, solvent-independent equilibrium constant, K_i , for hydrogen bonding. This unique equilibrium constant should be interpreted as the equilibrium constant, K_i , for equilibrium (i) measured in a hypothetical solvent with a relative permittivity in the range of the polar aprotic solvents but without hydrogen bond donor or acceptor interactions with the solutes, i.e. a pure dielectric-continuum-solvent.

Given these unique equilibrium constants and the stoichiometric concentrations of HB, B^- , B'^- and solv, the distribution of HB, B^- , B'^- and solv on the possible free and hydrogen bonded species can then be calculated from the mutual fulfilment of all the equilibrium conditions.

In the next sections are discussed the possibilities for determining these unique equilibrium constants from available literature data.

Results and discussion

Equilibrium constants for hydrogen bonding to solvents. Application of $K_6^{\text{CCl}_4}$ -values as unique K_6 -values. In order to determine the equilibrium concentrations of a free proton donor in polar aprotic solvents, it is necessary to have access to the value of the equilibrium constant for hydrogen bonding between the proton donor and the hydrogen bond acceptor, when the hydrogen bond acceptor at the same time acts as the solvent. In the case of the methyl-substituted phenols where kinetic measurements were carried out in four different solvents,⁵ this corresponds to 4×14 equilibrium constants, and to the best of our knowledge none of these, or other equilibrium constants of this type, have been determined with the hydrogen bond acceptor as the solvent. This is related to the fact that direct determination of the equilibrium constants for hydrogen bonding between good hydrogen bond donors such as phenols and hydrogen bond acceptors with the latter also acting as the solvent is difficult owing to the very low concentration of the free hydrogen bond donor, when the equilibrium constant is large. However, especially for substituted phenols, a wealth of equilibrium constants for hydrogen bonding to a large group of neutral hydrogen bond acceptors including DMSO, DMF, PC and MeCN (which were used as solvents in the kinetic study applying the methyl-substituted phenols⁵) have been determined in CCl_4 , $K_6^{\text{CCl}_4}$, by spectroscopic methods (IR, NMR, UV), and it is therefore tempting to propose $K_6^{\text{CCl}_4}$ -values as unique K_6 -values, although the dielectric constant, ϵ , for CCl_4 ($\epsilon = 2.2$) is much smaller than that for polar aprotic solvents.

The relationship between the $K_6^{\text{CCl}_4}$ -values and the appropriate 'pure base' values is not known in general, but it has been shown⁶⁻⁸ that there is a remarkably good agreement

Table 1. Data from Ref. 6 for the heat of hydrogen bond formation, ΔH_f , at 25 °C measured calorimetrically either by the pure base method or in dilute CCl_4 solution for phenol and 4-fluorophenol as hydrogen bond donors.

H-acceptor	$\Delta H_f/\text{kcal mol}^{-1}$		$K_6^{\text{CCl}_4}/\text{M}^{-1}$	
	pure base	CCl_4	IR ^a	$\Delta H_f(\text{pure base})^b$
Phenol				
DMF	-6.86 ± 0.08	-6.3 ± 0.2	75.5 ± 2.0	70.0 ± 6.0
THF	-5.75 ± 0.08	-5.7 ± 0.3	13.3 ± 0.4	13.6 ± 0.4
Pyridine	-7.34 ± 0.10	-7.2 ± 0.2	49.7 ± 1.0	48.0 ± 2.0
4-Fluorophenol				
DMF	-6.97 ± 0.11	-6.7 ± 0.2	116.0 ± 3.0	122 ± 9
DMSO	-7.21 ± 0.08	-6.6 ± 0.1^c	346 ± 8^c	
THF	-5.75 ± 0.08	-6.0 ± 0.3	17.7 ± 0.5	19.4 ± 1.0
Pyridine	-7.40 ± 0.09	-7.2 ± 0.2	75.0 ± 1.5	74.0 ± 5.0

^aFrom Ref. 6, equilibrium constant determined from IR measurements in dilute CCl_4 solution. ^bFrom Ref. 6, equilibrium constant calculated from calorimetrically determined ΔH_f^{obs} in dilute CCl_4 at several concentrations of the hydrogen bond donor assuming $\Delta H_f(\text{pure base})$ equal to $\Delta H_f(\text{CCl}_4)$. ^cFrom Ref. 7.

between the heat of complex formation, ΔH_f , in 'pure base' experiments (see Ref. 6 for a description of the method) and in experiments carried out in dilute CCl_4 solutions as demonstrated in Table 1.

This agreement is not *a priori* expected as ΔH_f has been shown to be moderately solvent dependent.⁹ For the hydrogen bonding between 3-fluorophenol and, e.g., ethyl acetate ΔH_f changes from $-6.7 \text{ kcal mol}^{-1}$ in cyclohexane to $-3.7 \text{ kcal mol}^{-1}$ in 1,2-dichloroethane, with the values in CCl_4 , 1,2-dichlorobenzene and benzene in between.⁹ The correspondence between the ΔH_f -values measured in CCl_4 and obtained by the 'pure base' method is therefore difficult to rationalize. Unfortunately, the largest discrepancies between the 'pure base' values and the CCl_4 values are found when the hydrogen bond acceptor is likely to self-associate when neat as e.g. DMSO.⁸ In these cases the ΔH_f -value measured in CCl_4 may overestimate the 'pure base' value due to the energy required to break-up the self-association which accompanies the formation of the hydrogen bond.

With respect to the entropy of complex formation, ΔS_f , it has been shown that for a series of phenols, unsubstituted in the *ortho* position, ΔS_f is practically constant for a common acceptor, as has been reported for DMA,¹⁰ when the experiments are carried out in CCl_4 , i.e. there is a direct relationship between ΔH_f and $K_6^{\text{CCl}_4}$. Similarly, in CCl_4 ΔS_f is practically constant for one phenol (4-fluorophenol), when the acceptor belongs to a series of related compounds, e.g. a series of *N,N*-disubstituted amides or a series of sulfoxides.⁸

On the basis of the considerations above it was decided to use $K_6^{\text{CCl}_4}$ -values as the best available approximation of the unique, solvent-independent K_6 -values as well as of the 'pure base' value, although there is an uncertainty in the relationship between the *absolute* magnitude of $K_6^{\text{CCl}_4}$ (= K_6) and the absolute magnitude of the 'pure base' value,

especially for the values related to DMSO and DMF as acceptors, because these acceptors are the most likely to be self-associated.⁶⁻⁸ On the other hand, the *relative* magnitudes of $K_6^{\text{CCl}_4}$ -values for one acceptor and different, closely related donors seem to be representative of the relative magnitudes of the corresponding 'pure base' values.

Determination of 'missing' $K_6^{\text{CCl}_4}$ -values. Despite the large number of $K_6^{\text{CCl}_4}$ -values available in the literature the situation frequently arises that the $K_6^{\text{CCl}_4}$ -value for a certain HB,solv pair is unknown. In the case of the methyl-substituted phenols, only six of the 4×14 $K_6^{\text{CCl}_4}$ -values required, appear to have been measured previously (cf. Table 2). However, a reliable estimate of the missing $K_6^{\text{CCl}_4}$ -value for unsubstituted phenol, $K_6^{\text{CCl}_4}(\text{PhOH/PC})$, can be obtained by application of the linear free energy relation method of Taft *et al.*^{11,12} which has recently been presented in a more general form,^{13,14} and which, in principle, associates every hydrogen bond donor with a hydrogen bond donor acidity and every hydrogen bond acceptor with a hydrogen bond acceptor basicity. However, for the present purpose the simpler version in eqn. (8)¹⁵ is appropriate.

$$\log K_6^{\text{CCl}_4}(\text{donor}_1/\text{acceptor}_i) = c_1 \log K_6^{\text{CCl}_4}(\text{donor}_2/\text{acceptor}_i) + c_2 \quad (8)$$

Eqn. (8) describes a linear relationship between $\log K_6^{\text{CCl}_4}$ -values for two different hydrogen bond donors, donor₁ and donor₂, and the same series of hydrogen bond acceptors, acceptor_i, where c_1 and c_2 are constants determined by the two donors. Using existing literature data for $K_6^{\text{CCl}_4}$ (primary values), determined for PhOH and for 4-chlorophenol and a series of common hydrogen bond acceptors, the value of $K_6^{\text{CCl}_4}(\text{PhOH/PC}) = 9.8 \text{ M}^{-1}$, (a secondary value), can be found from the known value of

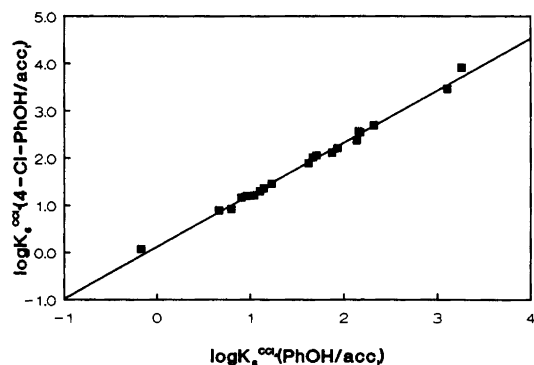


Fig. 1. Regression of $\log K_6^{\text{CCl}_4}(4\text{-chlorophenol/acc})$ vs. $\log K_6^{\text{CCl}_4}(\text{phenol/acc})$; slope = 1.10, intercept = 0.13, $r = 0.996$. The data are from Refs. 6, 7, 10, 16–43.

$K_6^{\text{CCl}_4}(4\text{-chlorophenol/PC}) = 16.3 \text{ M}^{-1}$,¹⁶ and the linear relationship between the logarithm of the two sets of $K_6^{\text{CCl}_4}$ -values, eqn. (8), shown in Fig. 1.

For the methyl-substituted phenols only few (in the range 0–10) primary values for hydrogen bonding to different acceptors can be found in the literature. Consequently, determination of secondary values by application of linear relationships of the type in eqn. (8) between each of the methyl-substituted phenols and, e.g., PhOH will be rather uncertain, and the four $K_6^{\text{CCl}_4}$ -values needed for each of these phenols therefore have to be evaluated by another method. The general linear free energy relation method^{13,14} predicts that a linear relationship similar to eqn. (8) exists for the hydrogen bonding between two different hydrogen bond acceptors, acceptor₁ and acceptor₂, and a common series of hydrogen bond donors, donor₁, eqn. (9), where c_3 and c_4 are constants determined by the two acceptors.

$$\log K_6^{\text{CCl}_4}(\text{donor}_i/\text{acceptor}_1) = c_3 \log K_6^{\text{CCl}_4}(\text{donor}_i/\text{acceptor}_2) + c_4 \quad (9)$$

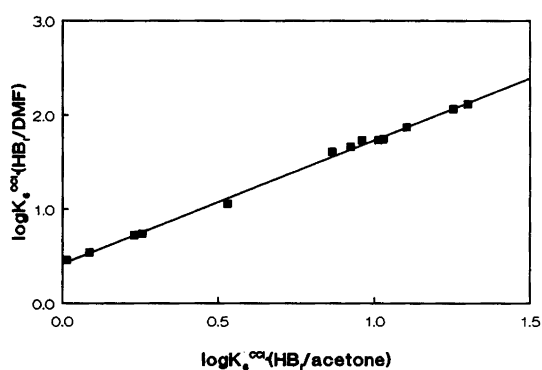


Fig. 2. Regression of $\log K_6^{\text{CCl}_4}(\text{HB/DMF})$ vs. $\log K_6^{\text{CCl}_4}(\text{HB/acetone})$; slope = 1.32, intercept = 0.42, $r = 0.998$. The data are from Refs. 6, 7, 16, 18, 21, 24, 25, 32, 33, 44–52, two secondary values for $\log K_6^{\text{CCl}_4}(\text{HB/DMF})$ and one secondary value for $\log K_6^{\text{CCl}_4}(\text{HB/acetone})$ derived from the regression lines found in the legend to Fig. 5 as described in the text.

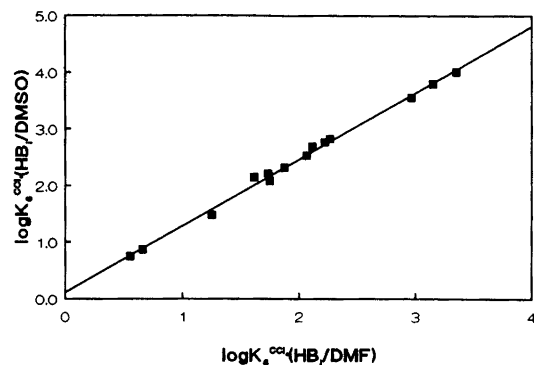


Fig. 3. Regression of $\log K_6^{\text{CCl}_4}(\text{HB/DMSO})$ vs. $\log K_6^{\text{CCl}_4}(\text{HB/DMF})$; slope = 1.18, intercept = 0.12, $r = 0.997$. The data are from Refs. 6, 7, 16, 18, 19, 24, 26, 31, 33, 45–47, 49–51, 53, 54, and four secondary values for $\log K_6^{\text{CCl}_4}(\text{HB/DMF})$ derived from the linear regression lines in the legend to Fig. 5 as described in the text.

Application of eqn. (9) for the determination of the $K_6^{\text{CCl}_4}$ -values for the methyl-substituted phenols and the four polar aprotic solvents as acceptors, requires (1) that $K_6^{\text{CCl}_4}$ -values for *all* the methyl-substituted phenols have been determined for *one* common hydrogen bond acceptor, acceptor₂, and (2) that a correlation of the type shown in eqn. (9) can be established between acceptor₂ and each of the four acceptors needed for our purpose, acceptor₁, through a common set of *other* hydrogen bond donors, donor₁.

The equilibrium constants for hydrogen bonding between acetone and phenol and all the methyl-substituted phenols (except 2,3,6-trimethylphenol) have been measured previously in CCl_4 ,^{21,44} and a correlation between $\log K_6^{\text{CCl}_4}(\text{HB}_i/\text{DMF})$ and $\log K_6^{\text{CCl}_4}(\text{HB}_i/\text{acetone})$ can be established by application of $K_6^{\text{CCl}_4}$ -values for 13 common donors, Fig. 2. For DMSO, PC and MeCN the number of

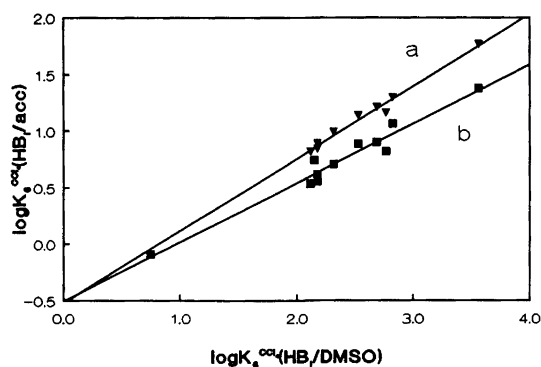


Fig. 4. Regression of (a) $\log K_6^{\text{CCl}_4}(\text{HB/PC})$ vs. $\log K_6^{\text{CCl}_4}(\text{HB/DMSO})$; slope = 0.64, intercept = -0.52 , $r = 0.991$; and (b) $\log K_6^{\text{CCl}_4}(\text{HB/MeCN})$ vs. $\log K_6^{\text{CCl}_4}(\text{HB/DMSO})$; slope = 0.53, intercept = -0.51 , $r = 0.98$. The data are from Refs. 7, 8, 16, 19, 22, 25, 26, 30, 31, 37, 45, 46, 49. Eight secondary values for $\log K_6^{\text{CCl}_4}(\text{HB/PC})$ and six secondary values for $\log K_6^{\text{CCl}_4}(\text{HB/MeCN})$ are derived from the linear regression lines found in the legend to Fig. 5 as described in the text.

$K_6^{CCl_4}$ -values which can be used in a correlation with the acetone data are limited to less than ten common donors, but a correlation of the type in eqn. (9) between $\log K_6^{CCl_4}(\text{HB}_i/\text{DMSO})$ and $\log K_6^{CCl_4}(\text{HB}_i/\text{DMF})$ data can easily be established based on a large number of $K_6^{CCl_4}$ -values in the literature for common hydrogen bond donors, Fig. 3. Therefore, the secondary values for the equilibrium constants for hydrogen bonding between the methylphenols and DMF derived from the correlation in Fig. 2 can be used in the correlation between $\log K_6^{CCl_4}(\text{HB}_i/\text{DMSO})$ and $\log K_6^{CCl_4}(\text{HB}_i/\text{DMF})$ to estimate the equilibrium constants for hydrogen bonding between the methyl-substituted phenols and DMSO.

The same approach was used to obtain the equilibrium constants for hydrogen bonding to PC and to MeCN, Fig. 4, but the $\log K_6^{CCl_4}(\text{HB}_i/\text{PC})$ - and $\log K_6^{CCl_4}(\text{HB}_i/\text{MeCN})$ -values were correlated with the $\log K_6^{CCl_4}(\text{HB}_i/\text{DMSO})$ -values, instead of with the $\log K_6^{CCl_4}(\text{HB}_i/\text{DMF})$ -values, because a larger number of primary values for common donors is available in these cases. Owing to the lack of literature values for $K_6^{CCl_4}(\text{HB}_i/\text{PC})$, all the PC-values used in the correlation with the DMSO-values are based on the reported value of the equilibrium constant for hydrogen bonding between 4-chlorophenol and PC,¹⁶ which, as described above, allows the determination of secondary values for other hydrogen bond donors by application of relations of the type described by eqn. (8). These secondary values of the equilibrium constant for hydrogen bonding between PC and a series of substituted phenols have been determined using PhOH as donor. The regression of $\log K_6^{CCl_4}(4\text{-fluorophenol}/\text{acc}_i)$ vs. $\log K_6^{CCl_4}(\text{PhOH}/\text{acc}_i)$ is shown in Fig. 5, where the regression lines for seven other substituted phenols are also given in the legend.

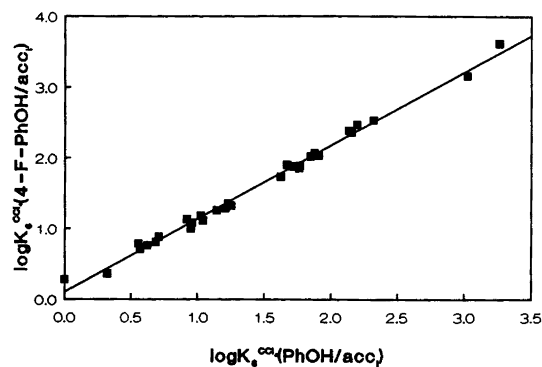


Fig. 5. Regression of $\log K_6^{CCl_4}(4\text{-fluorophenol}/\text{acc}_i)$ vs. $\log K_6^{CCl_4}(\text{phenol}/\text{acc}_i)$ (slope = 1.04, intercept = 0.11, $r = 0.996$). Similar regressions for seven other substituted phenols, $\log K_6^{CCl_4}(X\text{-phenol}/\text{acc}_i)$ vs. $\log K_6^{CCl_4}(\text{phenol}/\text{acc}_i)$ result in the following regression lines: 4-bromophenol (slope = 1.20, intercept = -0.03, $r = 0.997$); 4-methylphenol (slope = 0.96, intercept = -0.06, $r = 0.998$); 4-methoxyphenol (slope = 1.02, intercept = -0.17, $r = 0.998$); 3,4-dimethylphenol (slope = 0.91, intercept = -0.04, $r = 0.995$); 3-methylphenol (slope = 1.00, intercept = -0.17, $r = 0.990$); 3-nitrophenol (slope = 1.38, intercept = 0.22, $r = 0.990$); 4-nitrophenol (slope = 1.36, intercept = 0.36, $r = 0.98$). The data for $\log K_6^{CCl_4}(\text{phenol}/\text{acc}_i)$ are from Refs. 6, 7, 10, 17–20, 22–27, 29–42, 56–63, and the data for the substituted phenols are from Refs. 6–8, 10, 17, 19–21, 23, 36, 41, 45–47, 54, 55, 57, 58, 63–70.

Using the primary $K_6^{CCl_4}$ -values for hydrogen bonding between the methyl-substituted phenols and acetone⁴⁴ and the four correlations of the type given in eqn. (9) described above, the secondary $K_6^{CCl_4}$ -values for the hydrogen bonding between the methyl-substituted phenols and DMSO, DMF, PC and MeCN found in Table 2 were derived. For

Table 2. Secondary values of the equilibrium constant for hydrogen bond formation, $K_6^{CCl_4}$, at 25 °C between 14 phenols and four polar aprotic solvents based on the $K_6^{CCl_4}$ -values for hydrogen bond formation between the same phenols and acetone as described in the text.

Phenol substituent	Acetone ^a	$K_6^{CCl_4}/\text{M}^{-1}$			
		DMSO	DMF	PC	MeCN
None	12.7	210 (210) ^b	75 (75) ^c	9.2 ^d	5.1 (5.1) ^e
2-Methyl	8.5	112	44	6.2	3.7
3-Methyl	10.7	160 (130) ^f	60 (57) ^f	7.8	4.5
4-Methyl	10.6	160 (150) ^g	60	7.7	4.5
2,3-Dimethyl	7.0	84	34	5.1	3.2
2,4-Dimethyl	6.9	82	34	5.0	3.2
2,5-Dimethyl	7.3	89	36	5.3	3.3
2,6-Dimethyl	3.1	24	12	2.3	1.6
3,4-Dimethyl	8.5	110	44	6.2	3.7
3,5-Dimethyl	9.3	130	50	6.8	4.0
2,3,5-Trimethyl	6.3	71	30	4.6	2.9
2,3,6-Trimethyl	2.7 ^h	19	9.7	2.0	1.5
2,4,6-Trimethyl	2.5	17	8.8	1.8	1.4
3,4,5-Trimethyl	7.8	99	40	5.7	3.5

^aData from Ref. 44. ^bAverage of data from Refs. 7, 19, 26, 31. ^cAverage of data from Refs. 6, 7, 18, 24, 33. ^dSecondary value from correlation between PhOH and 4-chlorophenol data, Fig. 2, 9.8 M^{-1} . ^eAverage of data from Refs. 22, 25, 30. ^fData from Ref. 45.

^gData from Ref. 19. ^hEstimated as described in the text.

2,3,6-trimethylphenol, for which no literature data exist for the hydrogen bonding to acetone, the value of the equilibrium constant for hydrogen bonding to acetone was estimated to be 2.7 M^{-1} by evaluation of the average effect of a 3-methyl substituent on the equilibrium constant for phenol, 2-methyl-, 3-methyl-, 4-methyl- and 2,3-dimethylphenol, and the value of the equilibrium constant for 2,6-dimethylphenol.

In Table 2 are given in parentheses the six primary $K_6^{\text{CCl}_4}$ -values found in the literature for hydrogen bonding between the methyl-substituted phenols and the four solvents. By comparison of these primary values with the corresponding secondary values derived as described above, it appears that the error introduced by the application of the secondary values is relatively small. The largest deviation is found for hydrogen bond formation between 3-methylphenol and DMSO (23%), which, however, is almost within the experimental uncertainty of the primary, spectroscopically determined values of $K_6^{\text{CCl}_4}$.⁴⁵

Alternative method for the determination of 'missing' $K_6^{\text{CCl}_4}$ -values. The existence of the linear free energy relationships, eqns. (8) and (9), suggests that for a given hydrogen bond acceptor a Hammett correlation might exist for structurally related hydrogen bond donors such as, e.g., a series of substituted phenols. However, in the following it will be demonstrated that application of this method has severe drawbacks compared with the method described above for the estimation of 'missing' $K_6^{\text{CCl}_4}$ -values.

In order to establish the Hammett relationship, primary $K_6^{\text{CCl}_4}$ -values for the hydrogen bond equilibria between *meta*- and *para*-substituted phenols and the hydrogen bond acceptor in question, are required. Taking again DMSO, DMF, PC and MeCN as examples, the number of available literature values is limited (between one and eleven values) and the regression lines can therefore only be determined with a large uncertainty.

In the example with the methyl-substituted phenols, 2-substituted as well as 2,6-disubstituted phenols were in-

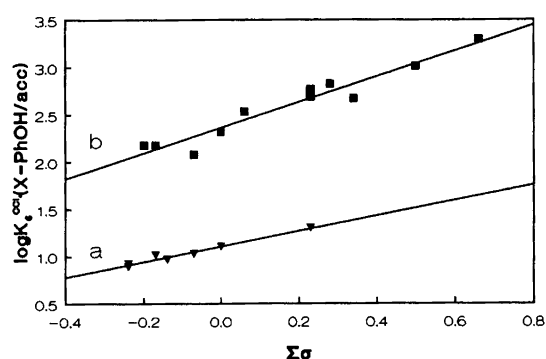


Fig. 6. Hammett plot of (a) $\log K_6^{\text{CCl}_4}(\text{X-phenol/acetone})$ (slope = 0.82, intercept = 1.11, $r = 0.98$) based on seven primary values of $K_6^{\text{CCl}_4}$, Refs. 16, 21, 25, 32, 44 and (b) $\log K_6^{\text{CCl}_4}(\text{X-phenol/DMSO})$ (slope = 1.35, intercept = 2.37, $r = 0.97$) based on 11 primary values of $K_6^{\text{CCl}_4}$, Refs. 7, 16, 19, 26, 31, 45, 46, 71.

Table 3. Comparison of 'best' σ_2 - and $\sigma_{2,6}$ -values for methyl substituents in phenols taken from the literature or estimated from literature data.

Measured quantity	Ref	σ_2^b	$\sigma_{2,6}^b$
Equilibrium constant for hydrogen bonding to acetone in CCl_4	44 ^a	-0.24	-0.75
Equilibrium constant for hydrogen bonding to Et_3N in CCl_4	58	-0.24	-
NMR frequency shift of hydroxy proton in HMPA	72	-0.07	-0.67
NMR frequency shift of hydroxy proton in DMSO	73, 74	-0.12	-0.76

^aThe equilibrium constants are found in Table 2.

cluded in the series. This raises the problem of a meaningful definition of σ -values for the 2-methyl and the 2,6-dimethyl substitution patterns. Utilizing again the data set for hydrogen bonding between acetone and methyl substituted phenols,^{21,44} it is possible to define a Hammett relation based on the *ortho* unsubstituted phenols, Fig. 6(a), and from this regression line to determine the 'best' σ_2 - and $\sigma_{2,6}$ -values for the methyl group with respect to this equilibrium, $\sigma_2^b = -0.24$ and $\sigma_{2,6}^b = -0.75$. Using these values, additivity with respect to additional *meta* or *para* substituents is maintained. The question is how general the applicability of these σ_2^b - and $\sigma_{2,6}^b$ -values is for methyl groups. Table 3 summarizes the 'best' values, σ_2^b and $\sigma_{2,6}^b$, found in the literature or calculated from literature data dealing with equilibrium processes involving 2-methyl and 2,6-dimethyl substituted phenols.

Inspection of the data in Table 3 reveals that the σ_2^b -values found from the two hydrogen bonding studies^{44,58} are identical, indicating that the influence of the 2-methyl substituent in phenol is comparable even for two acceptors, acetone and triethylamine, which structurally are quite different. Furthermore, the rule of additivity of σ for two *ortho* substituents ($\sigma_{2,6}^b = \sigma_2^b + \sigma_6^b$) is not followed in any of the studies, but for the measurements of the chemical shift in HMPA,⁷² which includes a total of 11 methyl-substituted phenols, it appears that once the proper σ_2^b - and $\sigma_{2,6}^b$ -values are chosen, additivity of the σ -values is followed, as is also observed in the case of hydrogen bonding to acetone. The σ_2^b -values corresponding to the NMR studies⁷²⁻⁷⁴ are considerably less negative than those corresponding to the value of the hydrogen bonding equilibrium constants. This difference may be attributed to the quantities measured, where the changes in the values of the chemical shift, contrary to the free energy of complex formation, do not take into account the entropy.

Assuming the σ_2^b - and $\sigma_{2,6}^b$ -values found from the data for hydrogen bonding to acetone are generally applicable in Hammett relations of equilibrium constants for hydrogen bonding of methyl substituted phenols, it is possible to compare the $K_6^{\text{CCl}_4}$ -values for 2-methyl- and 2,6-dimethyl-

Table 4. Secondary values of the equilibrium constant for hydrogen bond formation, $K_6^{\text{CCl}_4}$, at 25 °C between 11 phenols and DMSO determined from the Hammett plot in Fig. 6(b) and with $\sigma_2^o = -0.24$ and $\sigma_{2,6}^o = -0.75$ found from Fig. 6(a) as described in the text.

Phenol substituent	$\Sigma\sigma, \sigma^b$	$K_6^{\text{CCl}_4}/\text{M}^{-1}$
2-Methyl	-0.24	111
2,3-Dimethyl	-0.31	89
2,4-Dimethyl	-0.41	66
2,5-Dimethyl	-0.31	89
2,6-Dimethyl	-0.75	23
3,4-Dimethyl	-0.24	111
3,5-Dimethyl	-0.14	152
2,3,5-Trimethyl	-0.38	72
2,3,6-Trimethyl	-0.82	18
2,4,6-Trimethyl	-0.92	13
3,4,5-Trimethyl	-0.31	89

substituted phenols hydrogen bonding to DMSO determined from the linear relations (8) and (9), with those determined by application of the σ_2^o - and $\sigma_{2,6}^o$ -values and the Hammett relation for hydrogen bonding to DMSO (the only case for which sufficient literature data are available for construction of the Hammett correlation). The Hammett plot in Fig. 6(b) is given by the equation $\log K_6^{\text{CCl}_4}(\text{X-phenol/DMSO}) = 1.35\sigma + 2.37$ from which the $K_6^{\text{CCl}_4}$ -values in Table 4 are found for the 2-methyl- and 2,6-dimethyl-substituted phenols as well as for the other methyl-substituted phenols for which no primary values exist for the equilibrium constant for hydrogen bonding to DMSO. Comparing these values with the corresponding values in Table 2, shows that surprisingly good agreement is obtained. In only three cases, 2,4-dimethyl-, 3,5-dimethyl- and 2,4,6-trimethyl-phenol, do the $K_6^{\text{CCl}_4}$ -values found deviate from the Hammett relation by more than 10 % from the values found by application of eqns. (8) and (9), and the deviations seem to be non-systematic.

This agreement strongly supports the validity of the much more general approach described above, where literature data for *different* types of hydrogen bond donor are used in combination in order to obtain the regression lines defined by eqn. (9).

Evaluation of equilibrium constants for formation of dimers by hydrogen bonding. The existence of hydrogen-bonded dimers has been reported for a few phenols in CCl_4 ,^{23,39,40,58,75-78} as well as for a number of alcohols⁷⁸⁻⁸¹ and carboxylic acids^{75,82-84} but the measured values of $K_5^{\text{CCl}_4}$ may not be directly applicable as unique values as in the case of K_6 , because, in some cases, especially for the carboxylic acids, they have been attributed to a cyclic structure involving two hydrogen bonds per dimeric species,^{77,84} whereas the polarity and the hydrogen bond acceptor strength of the polar aprotic solvents make the cyclic dimer unlikely. However, the $K_5^{\text{CCl}_4}$ -values are the only values available and are therefore chosen as the best – and prob-

Table 5. Literature values of the equilibrium constant for formation of phenol dimers by hydrogen bonding in CCl_4 , $K_5^{\text{CCl}_4}$.

Phenol substituent	$K_5^{\text{CCl}_4}/\text{M}^{-1}$		
	Ref. 58 (30 °C)	Ref. 76 (28 °C)	Ref. 77 (? °C)
None	4.7	1.3	0.72
2-Methyl		0.77	
4-Methyl	4.7		0.80
3,4-Dimethyl	5.0		

ably maximum – estimates of unique equilibrium constants for reaction (5) in the case of phenols.

Again, taking the methyl-substituted phenols as an example, reported values of $K_5^{\text{CCl}_4}$, which include at least two of the phenols^{58,76,77} are found in Table 5. If we compare the values only within a single set of measurements it appears that substitution in the *ortho* position, as may be expected from steric reasons, causes a decrease in the value of $K_5^{\text{CCl}_4}$, while substitution in the 4- and 3,4-positions causes a slight increase in the value. It is assumed that this tendency is independent of the structure of the dimeric species. For the 2,6-dimethyl-substituted phenols no values have been reported, but from the large differences between the K_6 -values for 2,6-dimethyl-substituted phenols and the K_6 -values for other phenols, the values of $K_5^{\text{CCl}_4}$ for 2,6-dimethyl-substituted phenols may well be an order of magnitude smaller than for phenols unsubstituted in the *ortho* position.

The $K_5^{\text{CCl}_4}$ -values from Ref. 58 were chosen, despite the fact that they are obtained at 30 °C, while almost all other $K_5^{\text{CCl}_4}$ -values refer to 25 °C, for two reasons: (1) the $K_5^{\text{CCl}_4}$ -values are found in the only work including three of the phenols of interest; (2) the $K_5^{\text{CCl}_4}$ -values were determined by the same workers who made measurements of equilibrium constants for 1:1 as well as 2:1 hydrogen-bonding complexes involving the same three phenols (and a series of other substituted phenols), and the results from these measurements are used below in order to estimate the stoichiometric effect of hydrogen bonding between dimeric species and solvents.

The results from Ref. 76, cf. Table 5, indicate that methyl substitution in the 2-position leads to a $K_5^{\text{CCl}_4}$ -value which is only 60 % of the value for PhOH, and, assuming that this decrease in $K_5^{\text{CCl}_4}$ by methyl substitution in the *ortho* position can be transferred to the set of data from Ref. 58, this will be equivalent to a $K_5^{\text{CCl}_4}$ -value for 2-methylphenol equal to 2.8 M^{-1} . Based on the apparent effects of substitution in 2-, 4- and 3,4-positions, the values of $K_5^{\text{CCl}_4}$ for the remaining phenols may be estimated to be in the range 3–10 M^{-1} , with the $K_5^{\text{CCl}_4}$ -values for phenols substituted in the *ortho* position in the lower end of the range and with the $K_5^{\text{CCl}_4}$ -values for 3,5-dimethyl- and 3,4,5-trimethyl-phenol in the higher end.

That this is, in fact, the right order of magnitude of the

K_5 -values, and consequently, that the values of $K_5^{\text{CCl}_4}$ are not seriously effected by possible cyclic structures in CCl_4 , may be checked if we approximate the hydrogen bond acceptor property of a phenol with the hydrogen bond acceptor property of a corresponding alkyl phenyl ether. For PhOH the equilibrium constant for hydrogen bonding to methyl phenyl ether in CCl_4 has been determined to be 1.01 M^{-1} ³² and for hydrogen bonding to ethyl phenyl ether in CCl_4 to be 1.12 M^{-1} ³² or 1.22 M^{-1} .²⁹ To the best of our knowledge the analogous values for the methyl-substituted phenols are not available in the literature.

Therefore, also in this case of unique equilibrium constants for the formation of hydrogen-bonded dimers, K_5 , the corresponding equilibrium constants determined in CCl_4 , $K_5^{\text{CCl}_4}$, are chosen as representatives.

Unique equilibrium constants for homo- and hetero-conjugation. Determination of unique K_1 - and K_3 -values from K_1^{solv} -, K_3^{solv} - and K_6 -values. The K_1^{solv} -values found in the literature (solv being a polar aprotic solvent) do not take into account the fact that the hydrogen bond donor, HB, as demonstrated above, is mainly hydrogen bonded to the solvent, HB/solv, and consequently, K_1^{solv} may more precisely be interpreted as in eqn. (10).

$$K_1^{\text{solv}} = \frac{[\text{HB}/\text{B}^-]}{([\text{HB}] + [\text{HB}/\text{solv}])[\text{B}^-]} \quad (10)$$

Knowledge of the values of $K_6^{\text{CCl}_4}(\text{HB}/\text{solv})$ offers the opportunity of calculating a value for the homoconjugation constant which takes into account that only part of the hydrogen bond donor is free and able to form the new hydrogen bond.

$$K_1 = \frac{[\text{HB}/\text{B}^-]}{[\text{HB}][\text{B}^-]} = K_1^{\text{solv}}(1 + K_6^{\text{CCl}_4}[\text{solv}]) \quad (11)$$

K_1 defined in eqn. (11) may be taken as the unique homoconjugation constant quantifying directly the interaction between the hydrogen bond donor and the anion and *not* the competition between the anion and the solvent for

hydrogen bonding with the donor. In that respect K_1 would correspond to the equilibrium constant for equilibrium (1) measured in an inert solvent, e.g. CCl_4 , but $K_1^{\text{CCl}_4}$ -values are not available and, owing to the low relative permittivity of CCl_4 ($\epsilon = 2.2$), such data would be influenced by ion-pairing effects, and consequently the values of K_1 cannot be experimentally verified. However, if determination of K_1 from different K_1^{solv} -values, i.e. from apparent equilibrium constants for homoconjugation measured in different solvents, give similar values of K_1 , it seems appropriate to use these K_1 -values as unique equilibrium constants for equilibrium (1), and it will then be possible from the value of the equilibrium constant for homoconjugation determined in one solvent, solv₁, to determine the value of the equilibrium constant in another solvent, solv₂, if $K_6^{\text{CCl}_4}(\text{HB}/\text{solv}_1)$ and $K_6^{\text{CCl}_4}(\text{HB}/\text{solv}_2)$ are known. In order to test whether this approach is feasible, 4-nitrophenol was used as a model compound, this being the only compound for which literature data are available for homoconjugation in several different polar aprotic solvents.

The equilibrium constants for homoconjugation of 4-nitrophenol determined in the five different solvents DMSO,⁷⁰ DMF,⁸⁵⁻⁸⁷ PC,⁸⁸ MeCN^{64,67,69,70} and PhCN,^{67,89} vary by approximately 2.5 orders of magnitude when the solvent is changed from DMSO to PhCN (Table 6). Unfortunately, only $K_6^{\text{CCl}_4}(4\text{-nitrophenol}/\text{DMSO})$ has been determined,¹⁹ but reliable secondary values of $K_6^{\text{CCl}_4}(4\text{-nitrophenol}/\text{solv})$ when solv is DMF, PC, MeCN or PhCN can be obtained by application of the regression equation given in the legend to Fig. 5 together with the known values of $K_6^{\text{CCl}_4}(\text{PhOH}/\text{solv})$. These secondary values of $K_6^{\text{CCl}_4}(4\text{-nitrophenol}/\text{solv})$ are also found in Table 6.

By application of eqn. (11) and the K_1^{solv} - and $K_6^{\text{CCl}_4}$ -values in Table 6, five independent values of the unique equilibrium constant for homoconjugation of 4-nitrophenol were calculated (cf. Table 6), and when the very different origins of the literature data for K_1^{solv} , as well as for $K_6^{\text{CCl}_4}$, are taken into account, the variation in K_1 is certainly very small – less than a factor of two – indicating that non-specific interactions between the polar aprotic solvents and the solutes are of minor importance for the formation of the homoconjugation complex.

Table 6. Values of the unique equilibrium constant for homoconjugation, K_1 , between 4-nitrophenol and 4-nitrophenolate calculated from eqn. (11) by application of the equilibrium constants for homoconjugation in five polar aprotic solvents, K_1^{solv} , and the equilibrium constants for hydrogen bonding between 4-nitrophenol and the solvents, $K_6^{\text{CCl}_4}$.^a

	DMSO	DMF	PC	MeCN	PhCN
$K_6^{\text{CCl}_4}/\text{M}^{-1}$	3610 ^b	930 ^c	58 ^d	24 ^e	15 ^f
$K_1^{\text{solv}}/\text{M}^{-1}$	40 ^g	70 ^h	3.55×10^3 ⁱ	4.1×10^3 ^j	2.5×10^4 ^k
$K_1 \times 10^{-6}/\text{M}^{-1}$	2.0	2.0	2.4	1.9	3.7

^aAt 25 °C. ^bRef. 19. ^cSecondary value derived from the regression line in the legend to Fig. 5 and primary value of $K_6^{\text{CCl}_4}(\text{PhOH}/\text{DMF})$, Refs. 6, 7, 18, 24, 33. ^dSecondary value derived from the regression line in the legend to Fig. 5 and the secondary value of $K_6^{\text{CCl}_4}(\text{PhOH}/\text{PC})$, see Table 2. ^eSecondary value derived from the regression line in the legend to Fig. 5, and the primary value of $K_6^{\text{CCl}_4}(\text{PhOH}/\text{MeCN})$, Refs. 22, 25, 30. ^fSecondary value derived from the regression line in the legend to Fig. 5 and the primary value of $K_6^{\text{CCl}_4}(\text{PhOH}/\text{PhCN})$, Refs. 22, 59. ^gRef. 70. ^hRefs. 85–87. ⁱRef. 88. ^jRefs. 64, 67, 69, 70. ^kRefs. 67, 89.

Table 7. Values of the unique equilibrium constant, K_3 , for heteroconjugation between 4-bromophenol and five different anions, calculated from eqn. (13), the equilibrium constants for heteroconjugation in three different solvents, K_3^{solv} , and the equilibrium constants for hydrogen bonding between 4-bromophenol and the solvents, $K_6^{\text{CCl}_4}$ (4-bromophenol/solv).^a

Anion	DMSO		DMF		MeCN	
	$K_3^{\text{DMSO}}/\text{M}^{-1}$	K_3/M^{-1}	$K_3^{\text{DMF}}/\text{M}^{-1}$	K_3/M^{-1}	$K_3^{\text{MeCN}}/\text{M}^{-1}$	K_3/M^{-1}
3-BrC ₆ H ₄ COO ⁻	26.3 ^b	2.1×10 ⁵	129 ^b	2.8×10 ⁵	1820 ^c	2.3×10 ⁵
3-NO ₂ -4-ClC ₆ H ₃ COO ⁻	12.9 ^b	1.1×10 ⁵	75.9 ^b	1.7×10 ⁵	955 ^c	1.2×10 ⁵
4-NO ₂ C ₆ H ₄ COO ⁻	17.0 ^b	1.4×10 ⁵	83.2 ^b	1.8×10 ⁵	1100 ^c	1.4×10 ⁵
3,5-di-NO ₂ C ₆ H ₃ O ⁻	19.0 ^d	1.6×10 ⁵	74 ^d	1.6×10 ⁵	1320 ^e	1.7×10 ⁵
4-NO ₂ C ₆ H ₄ O ⁻	24.5 ^d	1.8×10 ⁵	74 ^d	1.6×10 ⁵	710 ^f	0.9×10 ⁵

^a $K_6^{\text{CCl}_4}$ (4-bromophenol/DMSO) = 590 M⁻¹, Ref. 19, and the secondary values $K_6^{\text{CCl}_4}$ (4-bromophenol/DMF) = 170 M⁻¹, $K_6^{\text{CCl}_4}$ (4-bromophenol/MeCN) = 6.6 M⁻¹, determined from the regression line in the legend to Fig. 5. ^bRef. 90. ^cRef. 91. ^dRef. 92. ^eRefs. 64, 69, 92. ^fRefs. 64, 69.

As with the literature values for the equilibrium constants for homoconjugation, literature values for equilibrium constants for heteroconjugation, do not take into account the fact that the hydrogen bond donor, HB, is found mainly as HB/solv. The only difference between the homoconjugation, equilibrium (1), and the heteroconjugation, equilibrium (3), is that the anion, B⁻, of the hydrogen bond donor, HB, is different from the anion, B'⁻, to which the hydrogen bond is formed in the heteroconjugation complex.

Consequently, the literature values, K_3^{solv} , may more precisely be interpreted as in eqn. (12), and analogously to the equilibrium constants for homoconjugation, the measured equilibrium constant for heteroconjugation can be recalculated to a unique equilibrium constant for heteroconjugation taking into account the hydrogen bonding between HB and the solvent by application of eqn. (13).

$$K_3^{\text{solv}} = \frac{[\text{HB}/\text{B}'^-]}{([\text{HB}] + [\text{HB}/\text{solv}])[\text{B}'^-]} \quad (12)$$

$$K_3 = \frac{[\text{HB}/\text{B}'^-]}{[\text{HB}][\text{B}'^-]} = K_3^{\text{solv}}(1 + K_6^{\text{CCl}_4}[\text{solv}]) \quad (13)$$

The equilibrium constants for heteroconjugation of different anions with 4-bromophenol in three different aprotic solvents have been reported,^{64,69,90-92} Table 7. From these

values of K_3^{solv} three independent values of the unique heteroconjugation equilibrium constant, K_3 , can be calculated for each anion, by application of eqn. (13), and in none of the five cases do the three values of K_3 differ by more than a factor of two, Table 7.

The consistency in unique values of homo- and heteroconjugation equilibrium constants determined as described above from the available, solvent specific literature data, supports the applicability of the approach for determination of unknown solvent-specific homoconjugation equilibrium constants, K_1^{solv} .

For the series of phenols in the example, comparison of K_1 -values derived from different K_1^{solv} -values can only be made for unsubstituted phenol, for which K_1^{DMSO} and K_1^{MeCN} have been reported. Application of the values of $K_6^{\text{CCl}_4}$ (PhOH/DMSO) and $K_6^{\text{CCl}_4}$ (PhOH/MeCN) found in Table 2 and the reported K_1^{solv} -values^{69,70,93} in eqn. (11) results in $K_1 = 6.8 \times 10^6 \text{ M}^{-1}$ (DMSO) and $1.1 \times 10^6 \text{ M}^{-1}$ (MeCN). The origin of the substantial difference in this case – a factor of six – is not clear.

On the basis of the four reported values of K_1^{DMSO} for methyl-substituted phenols^{93,94} and the corresponding $K_6^{\text{CCl}_4}$ -values in Table 2, the K_1 -values in Table 8 can be calculated. From Table 8 it appears that the rather small variation in the observed K_1^{DMSO} -values is partly a consequence of a parallel decrease in the values of K_1 and $K_6^{\text{CCl}_4}$ upon methyl substitution in the *ortho* position.

Table 8. Equilibrium constants for homoconjugation in DMF, PC and MeCN, K_1^{solv} , calculated from the values in DMSO, K_1^{DMSO} , the equilibrium constants for hydrogen bonding between the phenols and the solvents, $K_6^{\text{CCl}_4}$, in Table 2 and eqn. (11).^a

Phenol substituent	$K_1^{\text{DMSO}}/\text{M}^{-1}$ ^b	K_1/M^{-1} ^c	$K_1^{\text{DMF}}/\text{M}^{-1}$ ^d	$K_1^{\text{PC}}/\text{M}^{-1}$ ^d	$K_1^{\text{MeCN}}/\text{M}^{-1}$ ^d
None	2.3×10 ³	6.8×10 ⁶	7.0×10 ³	6.3×10 ⁴	6.8×10 ⁴ (1.1×10 ⁴) ^e
2-Methyl	1.4×10 ³	2.2×10 ⁶	3.9×10 ³	3.0×10 ⁴	3.1×10 ⁴
3-Methyl	2.3×10 ³	5.2×10 ⁶	6.7×10 ³	5.7×10 ⁴	6.0×10 ⁴
4-Methyl	2.5×10 ³	5.6×10 ⁶	7.3×10 ³	6.2×10 ⁴	6.5×10 ⁴
2,6-Dimethyl	1.9×10 ³	6.4×10 ⁵	4.2×10 ³	2.3×10 ⁴	1.9×10 ⁴

^aAt 25 °C. ^bFrom Refs. 93, 94. ^cCalculated from eqn. (11). ^dCalculated from eqn. (11) and the values of K_1 . ^eFrom Refs. 69,70.

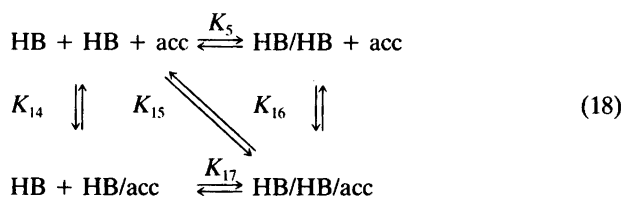
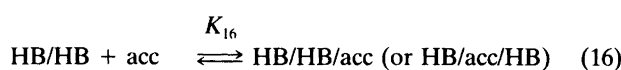
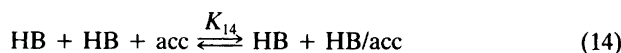
The calculated values of K_1 for PhOH, 2-, 3- and 4-methylphenol and for 2,6-dimethylphenol permit the estimation of K_1^{solv} in DMF, PC and MeCN for these phenols, by application of the $K_6^{\text{Cl}_4}$ -values in Table 2 and eqn. (11), and these estimated values are also found in Table 8.

Inspection of Table 8 also reveals that methyl substitution in 3- and 4-position has a similar and only small diminishing effect on the value of K_1 , contrary to substitution in the 2-position and especially in 2- and 6-position. It therefore seems justified to assign the same K_1 -value as found for 3- and 4-methylphenol (on the average $5.5 \times 10^6 \text{ M}^{-1}$) to 3,4- and 3,5-dimethylphenol and to 3,4,5-trimethylphenol. Similarly, a K_1 -value only a little lower ($2 \times 10^6 \text{ M}^{-1}$) than the one found for 2-methylphenol ($2.3 \times 10^6 \text{ M}^{-1}$), can be assigned to 2,3-, 2,4-, 2,5-dimethylphenol and 2,3,5-trimethylphenol; and a K_1 -value of $6 \times 10^5 \text{ M}^{-1}$ (slightly lower than the one found for 2,6-dimethylphenol, $6.4 \times 10^5 \text{ M}^{-1}$) can be assigned to 2,3,6- and 2,4,6-trimethylphenol.

Determination of unique K_2 -, K_4 - and K_7 -values from K_5 - and K_6 -values. It is well recognized^{23,36,52,58,95,96} that formation of a hydrogen bond to a hydrogen bond acceptor site in a molecule strengthens a hydrogen bond donor site within the same molecule, and the non-cyclic hydrogen bonded dimers are consequently expected to be stronger hydrogen bond donors than the monomers. Therefore, although the unique equilibrium constants for formation of hydrogen bonded dimers, K_5 , as discussed above, are relatively small for the phenols, it is necessary to determine to what extent the dimer, HB/HB, is present hydrogen bonded to the solvent, HB/HB/solv, or to the corresponding anion, HB/HB/B⁻, in order to estimate the distribution of HB on monomeric and dimeric forms.

In general, a hydrogen bonded complex consisting of two molecules of a hydrogen bond donor and one molecule of a hydrogen bond acceptor (acc) may have two different structures, HB/HB/acc or HB/acc/HB, if the acceptor has two possible acceptor sites, i.e. two lone-pairs. For example, in the 2:1 homoconjugation complex, the formulation of the 2:1 complex as HB/B⁻/HB indicates that two monomeric phenols hydrogen bond to the same anion. However, this species differs only in a single proton shift from HB/HB/B⁻, which could be described as a conjugation complex between a hydrogen bonded dimer, HB/HB, and a corresponding anion, B⁻.

If we ignore any possible differences in the structure of the 2:1 complexes formed by two molecules of a hydrogen bond donor and one molecule of a hydrogen bond acceptor, the thermodynamic cycle (18) shows the close relationship between equilibrium (14) [the generalized version of equilibria (1), (3) and (6)], equilibrium (5), equilibrium (15) [the generalized version of equilibria (2) and (4)] and equilibrium (16) [the generalized version of equilibrium (7)], when all the reactions are formulated as solvent independent with the unique equilibrium constants, K_{14} - K_{17} .



Given the unique values K_5 ($= K_5^{\text{Cl}_4}$) and either K_{15} or K_{14} and K_{17} , the unique value, K_{16} , for the equilibrium constant for hydrogen bonding between the dimer and an acceptor can be calculated: $K_{16} = K_{15}/K_5 = K_{14}K_{17}/K_5$.

Equilibrium constants for the overall formation of a 2:1 homoconjugation complex have been reported for PhOH and other *ortho* unsubstituted phenols in MeCN,⁹⁷ $K_2^{\text{MeCN}} = K_{15}^{\text{MeCN}}$. Analogously to the recalculation of the equilibrium constants for homoconjugation, taking into account that only part of the acid is free and able to form new hydrogen bonds, the unique equilibrium constant, $K_2 = K_{15}$, for formation of the 2:1 complex can be calculated by application of eqn. (19) using the corresponding K_6 -values ($= K_6^{\text{Cl}_4}$ -values).

Table 9. Values of the unique equilibrium constant, K_{16} , for hydrogen bonding between PhOH/PhOH and Cl⁻ and between PhOH/PhOH and PhO⁻ calculated from the reported equilibrium constants for 1:1 and overall 2:1 complex formation, K_{14}^{MeCN} and K_{15}^{MeCN} respectively, as described in the text.^a

acc	$K_{14}^{\text{MeCN}}/\text{M}^{-1}$	K_{14}/M^{-1}	$K_{15}^{\text{MeCN}}/\text{M}^{-2}$	K_{15}/M^{-2}	K_{16}/M^{-1}
Cl ⁻	150 ^b	1.5×10^4 ^c	600 ^b	5.7×10^6 ^f	1.2×10^6
PhO ⁻	1.1×10^4 ^b	1.1×10^6 ^d	5.8×10^5 ^e	5.4×10^9 ^f	1.1×10^9

^aAt 25 °C. ^bRefs. 22, 69. ^cCalculated from eqn. (13), $K_{14}^{\text{MeCN}} = K_3^{\text{MeCN}}$. ^dCalculated from eqn. (11), $K_{14}^{\text{MeCN}} = K_1^{\text{MeCN}}$. ^eRef. 97. ^fCalculated from eqn. (19).

$$K_{15} = K_{15}^{\text{soliv}} (1 + K_6[\text{soliv}])^2 \quad (19)$$

For PhOH the values of K_{15}^{MeCN} ($= K_2^{\text{MeCN}}$), K_6 and K_5 result in a unique equilibrium constant for formation of a 2:1 homoconjugation complex between a dimer and an anion $K_7 = K_{16} = K_{15}/K_5 = 1.1 \times 10^9 \text{ M}^{-1}$, cf. Table 9. By application of the same procedure the reported overall equilibrium constant for the hydrogen bonding between two PhOH molecules and Cl^- in MeCN, $K_4^{\text{MeCN}} = K_{15}^{\text{MeCN}}$,⁹⁷ gives the unique value of $K_4 = K_{15}$ found in Table 9 using eqn. (19), K_6 and K_5 .

The corresponding unique equilibrium constants for formation of 1:1 complexes between PhOH and PhO^- , $K_1 = K_{14}$, and between PhOH and Cl^- , $K_3 = K_{14}$, (cf. Table 9) can be used to compare the relative strengths of the dimer and the monomer as hydrogen bond donors. With Cl^- as the hydrogen bond acceptor, the ratio $K_{16}/K_{14} = 80$ tells that the equilibrium constant for hydrogen bonding is 80 times as large for the dimer as for the monomer, whereas the ratio $K_{16}/K_{14} = 10^3$ found when PhO^- is the acceptor, tells that when the hydrogen bond acceptor is the much stronger PhO^- , the relative strength of the dimer compared with the monomer is about an order of magnitude larger than when the acceptor is Cl^- .

For PhOH, 3-methylphenol and 3,4-dimethylphenol the equilibrium constants for formation of 1:1 complexes, K_{14} , with Br^- , I^- , tetramethylurea (TMU) and triethylamine (TEA) in CCl_4 have been reported^{36,52,58,95} together with the equilibrium constants for formation of a second hydrogen bond from another phenol molecule to the 1:1 complex, K_{17} . Br^- and I^- exist as ion pairs in CCl_4 (the tetrabutylammonium salt, $\text{Br}^-/\text{Bu}_4\text{N}^+$ ³⁶ or the tetraheptylammonium

Table 10. Values of the unique equilibrium constant for hydrogen bond formation between four acceptors and the dimer, K_{16} , calculated from the values of the unique equilibrium constants for 1:1 complex formation, K_{14} , and 2:1 complex formation, K_{17} .^a

Phenol substituent	Hydrogen bond acceptor	K_{14}/M^{-1}	K_{17}/M^{-1}	K_{16}/M^{-1}
None	$\text{Br}^-/\text{Bu}_4\text{N}^+$	1.3×10^3 ^b	1.1×10^2 ^b	3.0×10^4
	$\text{I}^-/\text{Hep}_4\text{N}^+$	2.7×10^2 ^b	4.7×10^1 ^b	2.7×10^3
	TMU	1.2×10^2 ^c	1.8×10^1 ^c	4.6×10^2
	Et_3N	4.9×10^1 ^d	2.9×10^1 ^d	2.9×10^2
4-Methyl	$\text{Br}^-/\text{Bu}_4\text{N}^+$	8.3×10^2 ^b	1.3×10^2 ^b	2.2×10^4
	$\text{I}^-/\text{Hep}_4\text{N}^+$	2.2×10^2 ^b	2.7×10^1 ^b	1.3×10^3
	TMU	7.6×10^1 ^c	1.5×10^1 ^c	2.4×10^2
	Et_3N	3.8×10^1 ^d	4.1×10^1 ^d	3.3×10^2
3,4-Dimethyl	$\text{Br}^-/\text{Bu}_4\text{N}^+$	6.5×10^2 ^b	9.4×10^1 ^b	1.2×10^4
	$\text{I}^-/\text{Hep}_4\text{N}^+$	1.7×10^2 ^b	3.6×10^1 ^b	1.2×10^3
	TMU	7.1×10^1 ^c	1.4×10^1 ^c	2.0×10^2
	Et_3N	3.1×10^1 ^d	3.8×10^1 ^d	2.4×10^2

^aAt 25°C. ^bData from Refs. 36, 52. ^cData from Ref. 95. ^dData from Ref. 58.

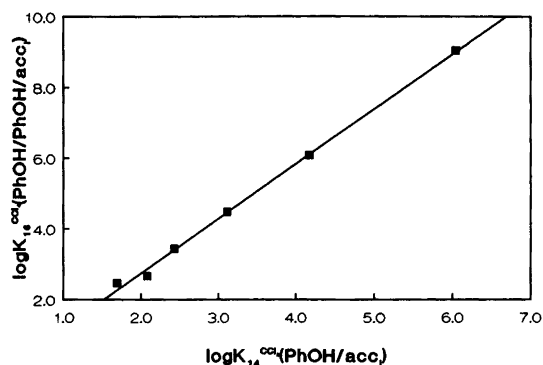


Fig. 7. Regression of $\log K_{16}[(\text{PhOH})_2/\text{acc.}]$ vs. $\log K_{14}(\text{PhOH}/\text{acc.})$ (slope = 1.55, intercept = -0.35, $r = 0.998$). The values of K_{14} and K_{16} are found in Tables 9 and 10.

salt, $\text{I}^-/\text{Hep}_4\text{N}^+$ ⁵²) and consequently, the measured equilibrium constants are *not* equivalent to the unique equilibrium constants for heteroconjugation determined above for Cl^- from data obtained in MeCN. However, the *relative* hydrogen bonding strengths of phenol monomers and dimers toward these ion-paired anions are still valid quantities.

Using the thermodynamic cycle (18) and the values of K_5 , the values of $K_{16} = K_{14}K_{17}/K_5$ found in Table 10 were calculated. For each of the three phenols we now have two sets of values, one set consisting of the unique equilibrium constants for formation of hydrogen bonds between the phenol molecule and a series of hydrogen bond acceptors (Cl^- , PhO^- , $\text{Br}^-/\text{Bu}_4\text{N}^+$, $\text{I}^-/\text{Hep}_4\text{N}^+$, TME and TEA for PhOH and $\text{Br}^-/\text{Bu}_4\text{N}^+$, $\text{I}^-/\text{Hep}_4\text{N}^+$, TME and TEA for 4-methylphenol and 3,4-dimethylphenol), and one set consisting of what formally can be regarded as the unique equilibrium constants for hydrogen bonding between the phenol dimer and the same series of hydrogen bond acceptors. Consequently, we can make a correlation of the type in eqn. (8) for each phenol, with the monomeric phenol as donor₁ and the corresponding dimer as donor₂. For PhOH, where we have six points in the regression, the linearity of the plot is surprisingly good, cf. Fig. 7. From this linear relation and the known values of the equilibrium constants for hydrogen bonding between monomeric PhOH and the four solvents, $K_6 = K_6^{\text{CCl}_4}$, (Table 2) the corresponding equilibrium constants for formation of the 2:1 complexes

Table 11. Estimated unique equilibrium constants, $K_7 = K_{16}$, for hydrogen bonding between hydrogen bonded dimers and the four aprotic solvents.^a

Phenol substituent	K_5/M^{-1} ^b	$K_7 = K_{16}/\text{M}^{-1}$			
		DMSO	DMF	PC	MeCN
None	4.7	1.8×10^3	3.6×10^2	14	5.6
4-Methyl	4.7	1.3×10^3	3.2×10^2	16	7.4
3,4-Dimethyl	5.0	7.6×10^2	2.1×10^2	14	6.9

^aAt 25°C. ^bFrom Ref. 58.

by hydrogen bonding between the dimer and the solvent, $K_7 = K_{16}$, can be estimated, and the values are found in Table 11.

For 4-methylphenol and 3,4-dimethylphenol the same correlations can be made (although only with four points in each), and again the $K_7 = K_{16}$ -values for the four solvents can be estimated. The data are summarized in Table 11.

We believe that the $K_7 = K_{16}$ -values in Table 11 are valid to within half an order of magnitude, but it is important to emphasize that the quality of the data in Table 11 is much lower than the secondary data derived previously because (1) the exact structure of the 2:1 complexes may vary from one hydrogen bond acceptor to another owing to differences in the number of acceptor sites (lone pairs) and to differences in the electronic distribution in the 1:1 complex; (2) the unknown influence of the ion pair structure of $\text{Br}^-//\text{Bu}_4\text{N}^+$ and $\text{I}^-//\text{Hep}_4\text{N}^+$; (3) the number of points in the correlations is small compared with the other applied correlations; (4) the K_5 -values may be uncertain.

For 2-methylphenol the estimate of K_5 was equal to 2.8 M^{-1} and consequently the relative hydrogen bond donor strength of the dimer compared with the monomer is expected to be smaller than for the *ortho*-unsubstituted phenols discussed above, and for the 2,6-dimethyl-substituted phenols, the small values estimated for K_5 indicate that the dimers have a hydrogen bond strength comparable to that of the monomers.

Distribution of acid and anion on different species in solution. Based on the determination of the different equilibrium constants in the previous sections it is now possible to estimate the distribution of neutral acids and anions on the different 'free' and hydrogen bonded species in a polar aprotic solvent, solv. Taking first the case where only neutral acid is present in solution in the stoichiometric concentration C_{HB}° , the stoichiometric equation (20) must be satisfied. Using the equilibrium constants K_5 , K_6 and K_7 , eqn. (20) leads to eqn. (21) from which [HB] can be found.

$$C_{\text{HB}}^{\circ} = [\text{HB}] + [\text{HB/solv}] + 2[\text{HB/HB}] + 2[\text{HB/HB/solv}] \quad (20)$$

$$2K_5(1 + K_7[\text{solv}])[\text{HB}]^2 + (1 + K_6[\text{solv}])[\text{HB}] - C_{\text{HB}}^{\circ} = 0 \quad (21)$$

In the case where the neutral acid as well as the anion is initially present, the two stoichiometric equations (22) and (23) must be fulfilled. Eqns. (22) and (23) may by application of the equilibrium constants K_1 , K_5 , K_6 , K_7 and K_{16} (for hydrogen bonding between the dimer and the anion) be combined to give eqn. (24), from which [HB] can be found.

$$C_{\text{HB}}^{\circ} = [\text{HB}] + [\text{HB/solv}] + 2[\text{HB/HB}] + 2[\text{HB/HB/solv}] + [\text{HB/B}^-] + 2[\text{HB/HB/B}^-] \quad (22)$$

$$C_{\text{B}^-}^{\circ} = [\text{B}^-] + [\text{HB/B}^-] + [\text{HB/HB/B}^-] \quad (23)$$

$$\{2K_{16}K_5^2(1 + K_7[\text{solv}])\}[\text{HB}]^4 + \{2K_1K_5(1 + K_7[\text{solv}]) + K_5K_{16}(1 + K_6[\text{solv}])\}[\text{HB}]^3 + \{K_1(1 + K_6[\text{solv}]) + 2K_5(1 + K_7[\text{solv}]) + K_5K_{16}(2C_{\text{B}^-}^{\circ} - C_{\text{HB}}^{\circ})\}[\text{HB}]^2 + \{(1 + K_6[\text{solv}]) + K_1(C_{\text{B}^-}^{\circ} - C_{\text{HB}}^{\circ})\}[\text{HB}] - C_{\text{HB}}^{\circ} = 0 \quad (24)$$

Interpretation of thermodynamic acidities in polar aprotic solvents. Bordwell and coworkers have reported a large number of equilibrium acidities in DMSO,^{93,94} $\text{p}K^{\text{DMSO}}$. The measurements were made by spectroscopic determination of the concentrations of an indicator acid and its corresponding anion, and the equilibrium constants for, e.g., phenols have been corrected for the influence of homoconjugation. The indicator acids, HIn, are, in general, carbon acids which are unable to form hydrogen bonds either to the solvent or to the corresponding anions,⁹⁸ In^- .

However, the hydrogen bonding between the test acids and the solvent was not taken into account in the calculation of the equilibrium constants, and the reported equilibrium constants are therefore K_{25} , defined in eqn. (25),

Table 12. Literature values of $\text{p}K^{\text{solv}}$ and the corresponding $\text{p}K_{\text{solv}}^{\circ}$ -values corrected for hydrogen bonding between the acid and the solvent calculated from eqn. (27) and the $K_6^{\text{CCl}_4}$ -values in Table 2.^a

Phenol substituent	$\text{p}K^{\text{DMSO } b}$	$\text{p}K_{\text{DMSO}}$	$\text{p}K^{\text{DMF } c}$	$\text{p}K_{\text{DMF}}$	$\text{p}K^{\text{MeCN } d}$	$\text{p}K_{\text{MeCN}}$
None	18.03	14.53	18.0	15.0	27.2	25.2
2-Methyl	18.10	14.89			27.5	25.6
3-Methyl	18.23	14.87				
4-Methyl	18.86	15.51			27.45	25.5
2,6-Dimethyl	18.52	15.99				

^aAt 25 °C. ^bFrom Refs. 93, 94. ^cFrom Ref. 99. ^dFrom Refs. 70, 100.

rather than K_{26} , defined in eqn. (26), which defines the 'true' acidity of the 'free' acid.

$$K_{25} = \frac{[\text{HIn}][\text{B}^-]}{([\text{HB}] + [\text{HB}/\text{solv}])([\text{In}^-])} \quad (25)$$

$$K_{26} = \frac{[\text{HIn}][\text{B}^-]}{[\text{HB}][\text{In}^-]} \quad (26)$$

Consequently, the true thermodynamic acidity of the 'free' acid, HB, in the solvent solv, $\text{p}K_{\text{solv}}$, is related to the measured acidity, $\text{p}K^{\text{solv}}$, by eqn. (27), which shows that the acidity of the acids forming the strongest hydrogen bonds to the solvent are seriously underestimated.

$$\text{p}K_{\text{solv}} = \text{p}K^{\text{solv}} - \log(1 + K_6^{\text{CCl}_4}[\text{solv}]) \quad (27)$$

Returning to the case of the methyl-substituted phenols, the equilibrium acidities, $\text{p}K^{\text{DMSO}}$, have been measured for PhOH, 2-, 3-, 4-methylphenol and 2,6-dimethylphenol by Bordwell and coworkers.^{93,94} These values are listed in Table 12 together with the 'true' $\text{p}K_{\text{DMSO}}$ -values calculated from eqn. (27) and the $K_6^{\text{CCl}_4}$ -values in Table 2. Inspection of Table 12 reveals that although 2-methyl- and 2,6-dimethyl-substitution of the phenol have surprisingly small effects on the measured $\text{p}K^{\text{DMSO}}$ -values, the corrected $\text{p}K_{\text{DMSO}}$ -values are in the order expected from an inductive substituent effect of the methyl groups.

Modification by application of eqn. (27) is also necessary for $\text{p}K^{\text{solv}}$ -values measured in other polar aprotic solvents, because none of them – independent of the method of determination – takes into account the extent to which the phenol is hydrogen bonded to the solvent.

Only the equilibrium acidity of the unsubstituted phenol has, to the best of our knowledge, been determined in DMF and in PC, while in MeCN the acidities of 2-methyl- and 4-methyl-phenol have also been reported,¹⁰⁰ and these values are found in Table 12. The reason for the apparently different change in the $\text{p}K_{\text{MeCN}}$ -values with 2- and 4-substitution compared with the $\text{p}K_{\text{DMSO}}$ -values is probably the fact that the reported values of $\text{p}K^{\text{MeCN}}$ are uncorrected for homoconjugation in contrast with the $\text{p}K^{\text{DMSO}}$ -values.

For the phenols for which no $\text{p}K^{\text{solv}}$ -values have been reported, secondary $\text{p}K_{\text{solv}}$ -values may be determined from Hammett plots of the $\text{p}K_{\text{solv}}$ -values for a series of substituted phenols.

If the measured $\text{p}K^{\text{DMSO}}$ -values for seven of the eight carefully selected phenols in Ref. 93 (PhOH, 3-methyl-, 4-methyl-, 3-fluoro-, 3-chloro-, 4-chloro-, 3-cyano- and 3-nitro-phenol) are all subjected to the correction for hydrogen bonding by eqn. (27) (the $K_6^{\text{CCl}_4}$ -value for 3-cyanophenol is not available) the ρ -value for $-\text{p}K_{\text{DMSO}}$ vs. σ takes the value 6.7, compared with $\rho = 5.3$ (or 5.2 if 3-cyanophenol is omitted here as well) for $-\text{p}K^{\text{DMSO}}$ vs. σ . From the $\text{p}K_{\text{DMSO}}$ -values for 2-methylphenol and 2,6-dimethylphenol

in Table 12 and the Hammett relation we arrive at $\sigma_2^{\text{b}} = -0.08$ and $\sigma_{2,6}^{\text{b}} = -0.24$.

It is interesting now to compare the values of (a) ρ for the unique equilibrium constants for hydrogen bonding between substituted phenols and DMSO, $\rho(\log K_6^{\text{CCl}_4})$, and ρ for the absolute acidities of the same phenols in DMSO, $\rho(-\text{p}K_{\text{DMSO}})$ and (b) the 'best' values, σ_2^{b} and $\sigma_{2,6}^{\text{b}}$, determined for hydrogen bonding and for thermodynamic acidity in DMSO.

First, from the linear relations of the type in eqn. (8) it appears that the stronger the hydrogen bond donor, the stronger the dependence of the strength of the hydrogen bond acceptor on the values of $K_6^{\text{CCl}_4}$. This corresponds for a series of phenols to a larger value of $\rho(\log K_6^{\text{CCl}_4})$ when the strength of the hydrogen bond acceptor is increased. Or, in other words, the stronger the redistribution of charge, the stronger the substituent effect. It is therefore expected, that the value of $\rho(-\text{p}K_{\text{DMSO}})$ is larger than $\rho(\log K_6^{\text{CCl}_4})$ even when the acceptor is as strong as DMSO, owing to the presence of a full charge in the anion, and this is exactly what is found. Second, comparison of the σ_2^{b} and $\sigma_{2,6}^{\text{b}}$ -values for methyl found for hydrogen bonding with those found for complete ionization shows that 'the *ortho* effect' is completely different for the two equilibria. The steric requirements for formation of hydrogen bonds are far larger than those for ionization in DMSO, where no specific solvent interaction with the anion is expected. The effect of 2-methyl- and 2,6-dimethyl-substitution of phenols on σ_2^{b} and $\sigma_{2,6}^{\text{b}}$ and ρ -values for the *rate* of proton transfer from these phenols have been examined in the kinetic study referred to above.⁵

Solvent attenuation of thermodynamic acidities. It is well known that the effect of substituents in series of benzoic acids, phenols, anilines and toluenes, on thermodynamic acidities is attenuated in solution compared with the gas phase,¹⁰¹⁻¹⁰³ as expressed by the lower values of ρ for Hammett plots of $\text{p}K^{\text{solv}}$. For the three polar aprotic solvents DMSO, DMF and MeCN a common value of $\rho(-K^{\text{solv}}) = 4.4 \pm 0.1$ has previously been reported,⁹² and the attenuating effect has primarily been ascribed to solvation of the anions.¹⁰¹⁻¹⁰³ However, in the previous section it was found that the ρ -value for the 'true' thermodynamic acidities in DMSO, $\text{p}K_{\text{DMSO}}$, of a small series of substituted phenols was considerably larger, $\rho(-\text{p}K_{\text{DMSO}}) = 6.7$, than the ρ -value for the measured acidities of the same series of phenols, $\rho(-\text{p}K_{\text{DMSO}}) = 5.2$, and in the following it will be shown that in the four aprotic solvents DMSO, DMF, PC and MeCN a varying fraction of the attenuation is due to the hydrogen bonding of the parent acid.

From eqns. (28)–(30) it follows that the $\rho(-\text{p}K_{\text{solv}})$ -value can be found by application of eqn. (31) for *ortho*-unsubstituted phenols, because the approximation $1 + K_6[\text{solv}] \approx K_6[\text{solv}]$ is valid in all cases, i.e., the ρ -values for the thermodynamic acidity of 'free' phenols, $\rho(-\text{p}K_{\text{solv}})$, can be determined as the sum of $\rho(\log K_6)$ and the ρ -value for the *measured* equilibrium acidities, $\rho(-\text{p}K^{\text{solv}})$.

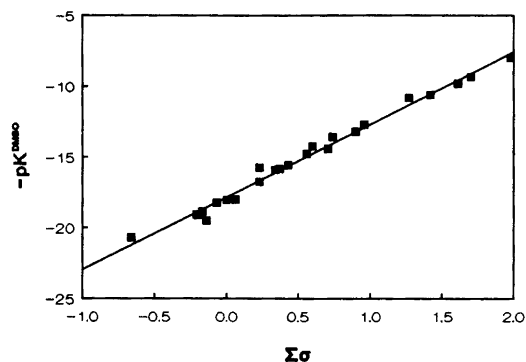


Fig. 8. Hammett plot of $-pK^{\text{DMSO}}$ (slope = 5.14, intercept = -17.81, $r = 0.994$), data from Refs. 92–94 and Refs. cited therein.

$$\log K_6(\text{X-phenol/solv}) = \rho(\log K_6) \sigma + \log K_6(\text{PhOH/solv}) \quad (28)$$

$$-pK^{\text{solv}}(\text{X-phenol}) = \rho(-pK^{\text{solv}}) \sigma - pK^{\text{solv}}(\text{PhOH}) \quad (29)$$

$$pK_{\text{solv}}(\text{X-phenol}) = pK^{\text{solv}} - \log(1 + K_6[\text{solv}]) \quad (30)$$

$$-pK_{\text{solv}}(\text{X-phenol}) = \{\rho(-pK^{\text{solv}}) + \rho(\log K_6)\} \sigma - pK_{\text{solv}}(\text{PhOH}) \quad (31)$$

The excellent correspondence between K_6 -values determined from linear relations of the type in eqns. (8) and (9) and from the Hammett plot found for the hydrogen bonding between substituted phenols and DMSO, Fig. 6(b) and Table 4, allow the inclusion of secondary K_6 -values determined by application of (8) and (9) in the construction of Hammett plots for hydrogen bonding between substituted phenols and the aprotic solvents for which insufficient primary data exist. The $\rho(\log K_6)$ -values for DMSO, DMF, PC and MeCN are summarized in Table 13.

A Hammett plot of $-pK^{\text{DMSO}}$ for 24 substituted

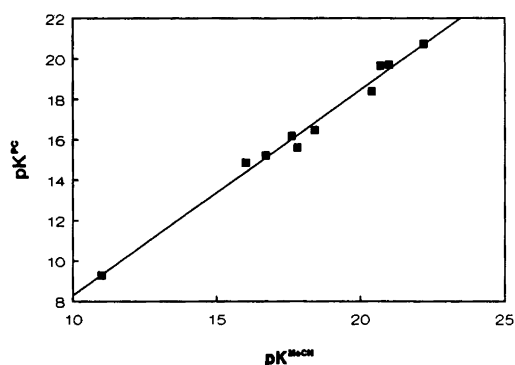


Fig. 9. Regression of pK^{PC} vs. pK^{MeCN} (slope = 1.02, intercept = -1.87, $r = 0.993$), data from Refs. 88, 92, 104 and Refs. cited therein.

Table 13. Summary of Hammett ρ -values obtained by correlation of equilibrium constant for hydrogen bonding, $K_6^{\text{Cl}_4}$, measured equilibrium acidity, pK^{solv} , and equilibrium acidity corrected for hydrogen bonding of the acids, pK_{solv} .

	DMSO	DMF	PC	MeCN
$\rho(\log K_6^{\text{Cl}_4})$	1.4 ^a	1.2 ^b	0.8 ^c	0.6 ^d
$\rho(-pK^{\text{solv}})$	5.1 ^e	4.5 ^f	4.5 ^g	4.4 ^h
$\rho(-pK_{\text{solv}})$ ⁱ	6.5	5.7	5.3	5.0

^aData from Refs. 7, 16, 19, 26, 31, 46, 71 and four secondary values from Table 2; std. error on $\rho \approx 0.1$. ^bData from Refs. 6, 7, 16, 18, 24, 33, 46, 47 and eight secondary values from Table 2 and the regression lines in the legend to Fig. 5; std. error on $\rho \approx 0.06$. ^cData from Ref. 16 and 11 secondary values from Table 2 and the regression lines in the legend to Fig. 5; std. error on $\rho \approx 0.05$. ^dData from Refs. 8, 22, 25, 30, 55 and six secondary values from Fig. 1, Table 2 and the regression lines in the legend to Fig. 5; std. error on $\rho \approx 0.06$. ^eData from Fig. 8, std. error on $\rho \approx 0.1$. ^fData from Ref. 92 and Refs. cited therein; std. error on $\rho \approx 0.2$. ^gFrom correlation of pK^{PC} against pK^{MeCN} , Fig. 9. ^hData from Ref. 92 and Refs. cited therein; std. error on $\rho \approx 0.1$. ⁱ $\rho(-pK_{\text{solv}}) = \rho(-pK^{\text{solv}}) + \rho(\log K_6^{\text{Cl}_4})$.

phenols (mono- as well as di- and tri-substituted) yields $\rho(-pK^{\text{DMSO}}) = 5.1$, Fig. 8, resulting in $\rho(-pK_{\text{DMSO}}) = 6.5$. This value is slightly lower than the value found directly from the seven pK_{DMSO} -values ($r = 0.999$) partly due to the difference between the $\rho(-K^{\text{DMSO}})$ -value for the seven phenols used above ($\rho = 5.2$, $r = 0.995$), and the $\rho(-pK^{\text{DMSO}})$ -value for the larger set of phenols ($\rho = 5.1$, $r = 0.994$), and partly due to the scatter in the correlation of $\log K_6$ vs. σ ($r = 0.98$).

Application of the same procedure to literature values for pK^{DMF} and pK^{MeCN} resulted in the $\rho(-pK_{\text{solv}})$ -values in Table 13. For PC too few literature data for substituted phenols were found to obtain a reliable $\rho(-K^{\text{PC}})$ -value. However, by including different types of acid a linear relationship between pK^{PC} and pK^{MeCN} was established, $pK^{\text{PC}} = 1.02 pK^{\text{MeCN}} - 1.87$, Fig. 9, and from that relation $\rho(-pK^{\text{PC}}) = 4.3$ was found, cf. Table 13.

Inspection of Table 13 reveals that correction of the measured pK^{solv} -values with respect to the hydrogen bonding of the phenols to the solvent leads to differences in the sensitivity of the equilibrium acidity of the 'free' phenols toward substitution, due to the differences between the solvents with respect to substitution effects on the $\log K_6$ -value.

Acknowledgements. Professor Bordwell is gratefully acknowledged for making available Ref. 94.

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