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Hydrogen Bonding. 11. A Quantitative Evaluation of the Hydrogen-Bond Acidity of Imides as Solutes

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A reanalysis of equilibrium constants determined by Hine et al. for the 1:1 complexation of imides with various bases in tetrachloromethane has been carried out using our previously reported method. The procedure yields average log $K^{\mathrm{H}}_{\mathrm{A}}$ values for the hydrogen-bond acidity of the imides that can easily be converted into our new hydrogen bond solute acidity parameters, α^{H}_2. It is shown that the hydrogen-bond acidity of activated nitrogen acids, such as imides, can be comparable to that of oxygen acids. Examples of α^{H}_2 values include maleimide (0.50), 2,2,2-trichloroethanol (0.50), tetrafluorosuccinimide (0.89), and dichloroacetic acid (0.90).

Previously, we have used a matrix of some 1300 log K values for 1:1 hydrogen-bond complexation in tetrachloromethane at 298 K to establish scales of solute hydrogen-bond acidity (log $K^{\mathrm{H}}_{\mathrm{A}}$ and α^{H}_2)[1,2] and solute hydrogen-bond basicity (log $K^{\mathrm{H}}_{\mathrm{B}}$, β^{H}_2).[3,4] For the acidity scales, which we first established, log K values for a series of acids against a given reference base B were fitted to a set of equations, eq 1.

$$\log K \text{ (series of acids against base B)} = L_{\mathrm{B}}(\log K^{\mathrm{H}}_{\mathrm{A}}) + D_{\mathrm{B}} \quad (1)$$

Forty-five such equations, one for each of 45 reference bases, were solved to yield values of L_{B} and D_{B}, characteristic of the reference bases, and values of log $K^{\mathrm{H}}_{\mathrm{A}}$, a general solute hydrogen-bond acidity parameter. In this analysis, use was made of the novel observation that all the 45 lines generated by eq 1 intersected within experimental error at a given "magic point" where log K = log $K^{\mathrm{H}}_{\mathrm{A}} = -1.1$, when equilibrium constants are expressed on the molar concentration scale.[1,2]

Similarly, we generated a series of 34 equations, eq 2, where now L_{A} and D_{A} characterize the reference acid, and log $K^{\mathrm{H}}_{\mathrm{B}}$ is a general solute basicity parameter. Again, we

$$\log K \text{ (series of bases against acid A)} = L_{\mathrm{A}}(\log K^{\mathrm{H}}_{\mathrm{B}}) + D_{\mathrm{A}} \quad (2)$$

noted[3,4] that all 34 equations intersected at the same magic point where log K = log $K^{\mathrm{H}}_{\mathrm{B}} = -1.1$, exactly as for the case with eq 1. We then made use of the magic point to define, for the first time,[1-4] scales of solute hydrogen-bond acidity and basicity that could be referenced to a zero origin, simply by shifting the origin from −1.1 to zero, as in the two defining equations, eq 3 and eq 4. The constant of 4.636 serves to establish a convenient spread of α^{H}_2 and β^{H}_2 parameters and also leads to $\beta^{\mathrm{H}}_2 = 1$ for hexamethylphosphoramide (HMPA). Finally,[5] we showed how α^{H}_2 and β^{H}_2 could be regarded as mutually consistent scales through eq 5, where log K refers to hydrogen-bond complexation in tetrachloromethane at 298 K.

Table I. Constants for the Reference Equation, Eq 1[a]

reference base[b]	L_{B}	D_{B}	sd	n
NMP	1.2145	0.2359	0.078	15
DMSO	1.2399	0.2656	0.096	51
TMSO[c]	1.2492	0.2761	0.070	6
HMPA	1.5693	0.6287	0.155	50
THF	0.8248	−0.1970	0.089	23
EtOAc	0.7428	−0.2861	0.117	13

[a] All values from ref 2 except for TMSO. [b] NMP is *N*-methyl-2-pyrollidinone; DMSO is dimethyl sulfoxide; TMSO is tetramethylene sulfone; HMPA is hexamethylphosphoramide; THF is tetrahydrofuran. [c] Obtained using the four log K values in ref 6, together with values for complexation with phenol, ref 7, and with trichloromethane, ref 8.

$$\alpha^{\mathrm{H}}_2 = (\log K^{\mathrm{H}}_{\mathrm{A}} + 1.1)/4.636 \quad (3)$$

$$\beta^{\mathrm{H}}_2 = (\log K^{\mathrm{H}}_{\mathrm{B}} + 1.1)/4.636 \quad (4)$$

$$\log K = 7.354\alpha^{\mathrm{H}}_2\beta^{\mathrm{H}}_2 - 1.094 \quad (5)$$

Using eqs 1 and 3 we obtained log $K^{\mathrm{H}}_{\mathrm{A}}$ and α^{H}_2 values for solutes that were representative of most of the common functionalities, including the imide maleimide,[1] and, later,[2] succinimide as well. At about the same time, Hine et al.[6] set out to obtain the hydrogen-bond acidities of various imides toward oxygen bases by the measurement of hydrogen-bond complexation constants in tetrachloromethane at 298 K. They found that when their log K values were plotted as an equation, eq 6, which is rather analogous to eq 2, there resulted a set of rather randomly intersecting lines.

$$\log K \text{ (series of bases against imide A)} = l \log K \text{ (series of bases against 4-fluorophenol)} + d \quad (6)$$

Hine et al.[6] pointed out that the set of generated lines led to various improbable conclusions, for example that 2-ethyl-2-methylsuccinimide would be a stronger hydrogen bond acid than tetrafluorosuccinimide toward a very weak base, but yet is much the weaker acid towards strong bases. What Hine et al.[6] did not point out is that if eq 6 *does* lead to randomly intersecting lines, then there is actually no

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[1] Abraham, M. H.; Duce, P. P.; Grellier, P. L.; Prior, D. V.; Morris, J. J.; Taylor, P. J. *Tetrahedron Lett.* **1988**, *29*, 1587.

[2] 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.

[3] Abraham, M. H.; Grellier, P. L.; Prior, D. V.; Morris, J. J.; Taylor, P. J.; Laurence, C.; Berthelot, M. *Tetrahedron Lett.* **1989**, *30*, 2571.

[4] Abraham, M. H.; Grellier, P. L.; Prior, D. V.; Morris, J. J.; Taylor, P. J. *J. Chem. Soc., Perkin Trans. 2*, submitted.

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Table II Calculation of log K^H_A Values from the Data of Hine et al.,[6] Using Eq 1[a]

	reference base							average α^H_2
	NMP	DMSO	TMSO	HMPA	THF	EtOAc	average	
2-ethyl-2-methylsuccinimide	1.022	1.242	1.265	1.148			1.169 ± 0.110	0.489 ± 0.024
2-chloro-3-methylmaleimide	1.415	1.507	1.504	1.435			1.465 ± 0.047	0.553 ± 0.010
2,3-dichloro-2-methylsuccinimide	1.880	1.948	1.979	2.037			1.961 ± 0.065	0.660 ± 0.014
tetrafluorosuccinimide	3.005	2.901	2.981	3.202	3.124	2.997	3.035 ± 0.109	0.892 ± 0.024

[a] With the regression constants given in Table I.

Table III. Calculation of α^H_2 from the Data of Hine et al.,[6] Using Eq 5[a]

	reference base (β^H_2)						
	NMP (0.765)	DMSO (0.775)	TMSO (0.788)	HMPA (1.00)	THF (0.510)	EtOAc (0.446)	average
2-ethyl-2-methylsuccinimide	0.457	0.509	0.509	0.479			0.489 ± 0.025
2-chloro-3-methylmaleimide	0.542	0.566	0.561	0.540			0.552 ± 0.013
2,3-dichloro-2-methylsuccinimide	0.642	0.662	0.663	0.669			0.659 ± 0.012
tetrafluorosuccinimide	0.885	0.870	0.879	0.918	0.926	0.925	0.900 ± 0.025

[a] Reference base β^H_2 values from ref 4.

possibility of obtaining any general quantitative measure of the hydrogen-bond acidity of the various imides investigated.

We now reanalyze the data of Hine et al.[6] in terms of our general equations, eqs 1–5, in order to realize the objective of Hine et al.,[6] namely to determine quantitative hydrogen bond acidity parameters, viz log K^H_A and α^H_2. For four of the reference bases used by Hine et al.[6] we already have the constants in eq 1;[3,4] values of L_B, D_B, and standard deviation of observed and calculated log K values (sd), and the number of acids used in the construction of the equation (n), are listed in Table I. For the remaining base, tetramethylene sulfone (TMSO), we constructed an equation from known equilibrium constants[7,8] together with those reported by Hine et al.,[6] see Table I. We now use the log K values for the various imides,[6] together with eq 1, to obtain log K^H_A values. These are shown in Table II, together with the α^H_2 values obtained through eq 3. We can also calculate α^H_2 directly via eq 5, and give details in Table III. There is excellent agreement between the two sets of α^H_2 values; in either set the α^H_2 values are good to around 0.01–0.02 units. It is very satisfying to note that α^H_2 for 2-ethyl-2-methylsuccinimide, 0.49, is perfectly compatible with our previous value for succinimide itself, also 0.49 units.[4] Note that we have (quite properly) used the log K values of Hine et al.[6] to derive eq 1 for TMSO but have then (not quite properly) reused the log K values to deduce the log K^H_A values under TMSO in Table II. This makes an insignificant difference to the final result, but does show the excellent consistency of the measurements of Hine et al.[6] (see the log K^H_A values in Table II).

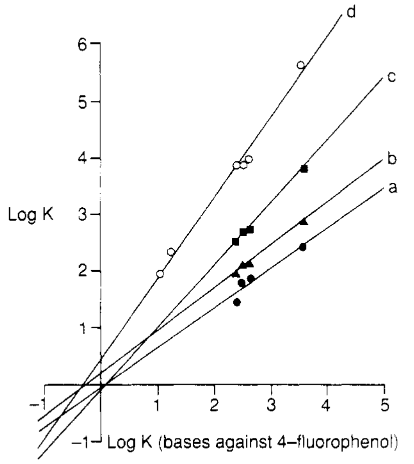

Figure 1. Plots of log K values for hydrogen bonding of various bases against imides vs log K values for hydrogen bonding against 4-fluorophenol. (a) 2-Ethyl-2-methylsuccinimide (●), (b) 2-chloro-3-methylmaleimide (▲), (c) 2,3-dichloro-2-methylsuccinimide (■), (d) tetrafluorosuccinimide (○).

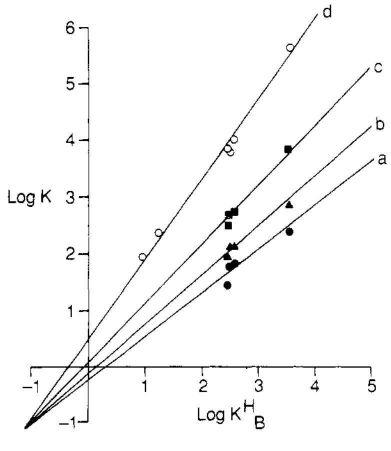

Figure 2. Plots of log K values for hydrogen bonding of various bases against imides vs log K^H_B, forced through the magic point. (a) 2-Ethyl-2-methylsuccinimide (●), (b) 2-chloro-3-methylmaleimide (▲), (c) 2,3-dichloro-2-methylsuccinimide (■), (d) tetrafluorosuccinimide (○).

We can simply illustrate the difference between our procedure and that of Hine et al.[6] by a comparison of Figures 1 and 2. Figure 1 is essentially as given by Hine et al.[6] except that the axes have been extended to cover the magic point. As pointed out above, the various intersecting lines in Figure 1 lead to the awkward conclusion that the relative acidity of the imides depends on the choice of reference base. In Figure 2 are shown plots carried out according to eq 2, with all the lines forced through the magic point. If the plots of log K versus log K^H_B were not constrained in this way then another set of rather randomly intersecting lines would be obtained. There is now no difficulty at all with respect to any change in relative acidity, this will always be in the order d > c > b > a, no matter whether the reference base is weak or strong. It is important to note that the difference between Figures 1 and 2 does not lie with the variables log K (bases against 4-fluorophenol) and log K^H_B. Only a very detailed analysis of all available data[1-4] has uncovered the "magic point" and hence has allowed us to make use of it in the

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Table IV. The Hydrogen-Bond Acidity, α^H_2, of Imides: Comparison with Some Other Solutes[a]

solute	α^H_2	solute	α^H_2
tetrafluorosuccinimide	0.89	dichloroacetic acid	0.90
$(NO_3)_3CCH_2CH_2NHNO_2$	0.78	perfluoro-*tert*-butyl alcohol	0.86
2,3-dichloro-2-methylsuccinimide	0.66		
$EtOCONHNO_2$	0.61	phenol	0.60
$PrNHNO_2$	0.57		
2-chloro-3-methylmaleimide	0.55	acetic acid	0.55
maleimide	0.50	2,2,2-trichloroethanol	0.50
succinimide	0.49		
2-ethyl-2-methylsuccinimide	0.49		
N-methylacetamide	0.38	methanol	0.37
dialkylamines	0.00	alkanes	0.00

[a] Values of α_2^H from Table II and refs 1 and 2.

fits, as shown in Figure 2. The plots shown in Figure 1 indicate that unless extremely accurate log K values are obtained over a wide range of base strength, simple plots will invariably lead to randomly intersecting lines. We have analyzed the lines shown in Figure 1 and can confirm that within experimental error, all four lines could indeed intersect at the magic point. We can conclude that our analysis of hydrogen-bond complexation constants in tetrachloromethane, as summarized by eqs 1 and 2, where in each case all the equations intersect at the "magic point" of −1.1, does lead to a rigorous method for the quantitative determination of solute hydrogen-bond acidity and hydrogen-bond basicity.

It might be argued that the randomly intersecting lines of Figure 1 are "correct", and that we have artificially constructed the plots shown in Figure 2. We point out, however, that a detailed analysis of 45 equations of the type given as eq 1,[1,2] and of 34 equations of the type given as eq 2,[3,4] show conclusively that there is indeed a point of intersection. We have no reason to believe that the four imides studies by Hine et al.[6] behave any differently to the 34 reference acids used before, and which included the imides maleimide and succinimide as well as other nitrogen acids and, of course, oxygen acids.

Finally, we compare in Table IV the hydrogen-bond acidity parameter, $\alpha^H{}_2$, for a variety of nitrogen and oxygen acids. Simple alkylamines or dialkylamines have zero acidity,[1,2] but incorporation of an α-carbonyl group, as in amides, leads to substantial acidity with $\alpha^H{}_2 = 0.38$ for *N*-methylacetamide.[1,2] The second α-carbonyl group, as with the imides succinimide and maleimide, increases the hydrogen-bond acidity yet again, but only from $\alpha^H{}_2 = 0.38$ to $\alpha^H{}_2 = 0.49$ units; this is possibly another example of the effect of lone pair/lone pair repulsion between α-carbonyl groups and the incoming base.[9] Other electronegative substituents such as NO_2 in $PrNHNO_2$ increase the NH hydrogen-bond acidity even more than the CO group, as might be expected from the σ_I values for CO and NO_2.[2] By comparison with oxygen acids, the activated NH acids are quite strong—compare maleimide with 2,2,2-trichloroethanol, or tetrafluorosuccinimide with dichloroacetic acid.[2] Even tetrafluorosuccinimide is not the strongest hydrogen-bond nitrogen acid known; we have observed[9] that a tetrazole is of about the same hydrogen-bond acidity as trifluoroacetic acid. Although we have not yet been able to assign an exact $\alpha^H{}_2$ value for the tetrazole, it is clear that the span of hydrogen-bond acidities of nitrogen acids is quite comparable to that of oxygen acids.

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Registry No. $(NO_3)_3CCH_2CH_2NHNO_2$, 125453-66-9; $EtOCONHNO_2$, 626-37-9; $PrNHNO_2$, 627-07-6; MeCONHMe, 79-16-3; Cl_2CHCO_2H, 79-43-6; $(F_3C)_3COH$, 2378-02-1; PhOH, 108-95-2; $MeCO_2H$, 64-19-7; Cl_3CCH_2OH, 115-20-8; MeOH, 67-56-1; 2-ethyl-2-methylsuccinimide, 77-67-8; 2-chloro-3-methylmaleimide, 69636-50-6; 2,3-dichloro-2-methylsuccinimide, 69636-49-3; tetrafluorosuccinimide, 377-33-3; maleimide, 541-59-3; succinimide, 123-56-8.

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