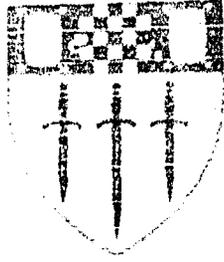


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Scales of Hydrogen-bonding

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Workshop

London, 1st - 3rd July 1987

Sponsored by the Office of Naval Research Branch Office, London

Final Report

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19 ABSTRACT (Continue on reverse if necessary and identify by block number) About 25 chemists took part in the ONRL-sponsored workshop, "Scales of Hydrogen-bonding," held in London from 1 through 3 July 1987. The purpose of the gathering was to discuss current activities in setting up scales of both solute and solvent hydrogen-bond strength. The importance of solute hydrogen-bond scales in the understanding and prediction of effects in such diverse areas as solubilities in water and in blood, water-solvent partition coefficients, toxicological studies, and the response of chemical microsensor coatings to vapors. Work on scales of solute hydrogen-bond acidity and basicity is well advanced. Most of these scales are based on log K values for hydrogen-bond complexation in dilute solution - that is, they are nearly always Gibbs energy related scales. Theoretical work by I.H.Hillier (University of Manchester, UK) has demonstrated that such scales are likely to be more easily handled than scales based on enthalpies of complexation. Not so much work is ongoing in the area of solvent scales, and what work there is seems to be exclusively oriented to solvent hydrogen-bond basicity. P.-C. Maria and J.-F. Gal (University of Nice, France) described their multivariate analysis that leads to an angle θ , descriptive of the electrostatic:covalent ratio in the base:reference acid complex. M.H. Abraham (University of Surrey, UK) showed that it was possible to demonstrate the virtual equivalence of a solute scale and a solvent scale of hydrogen-bond basicity for nonassociated compounds, provided that the reference acids in each case led to θ values that were almost the same - around 65°.					
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It is a pleasure to acknowledge the support of the Office of Naval Research Branch Office, London, without whose help the workshop could not have been held, and especially the contribution of the Scientific Director, Dr. David L. Venezky. The help of the secretarial staff at the Office of Naval Research Branch Office, London, over the organisation of the workshop in London, and of the secretarial staff at the University of Surrey in the general administration of the workshop is gratefully acknowledged.

Finally, I would like to thank all the participants for their individual contributions that helped to make the workshop so successful.

Michael H. Abraham

INTRODUCTION

Over the past few years, a large amount of work has been carried out on the correlation and prediction of solvent effects and, more recently, on solute effects. One of the most powerful methods used in this work has been that of multiple regression analysis, in which some solvent effect, or solute effect, is correlated with a number of parameters. In the case of a solvent effect, the most widely applicable and successful multiple regression equation is that based^{1,2} on the solvatochromic parameters of Kamlet and Taft:

$$XYZ = XYZ_o + s. \pi_1^* + a. \alpha_1 + b. \beta_1 + h. \delta_H^2 \quad (1)$$

Here, XYZ is some property to be correlated, and π_1^* , α_1 , β_1 , and δ_H are the solvent dipolarity, hydrogen-bond acidity, hydrogen-bond basicity, and Hildebrand solubility parameter respectively. The constants XYZ_o , s, a, b, and h are found by multiple regression analysis. Although the δ_H parameter is available through calorimetric enthalpies of vaporisation of solvents, or alternatively from vapour pressures, the so-called solvatochromic parameters π_1^* , α_1 , and β_1 need to be determined. By now, numerous values have been obtained, but there is still need for new values and for re-evaluation of already determined values of these parameters.

A similar situation exists in the correlation of a solute property, SP, with parameters characteristic of the solute (the solvent now being a fixed quantity). Two general equations are currently in use, one being used for processes in condensed phases, equation (2)^{3,4} and the other for processes involving solute vapour \rightarrow solute in a condensed phase, equation (3).⁵

$$SP = SP_o + s. \pi_2^* + a. \alpha_2 + b. \beta_2 + m. V_2 \quad (2)$$

$$SP = SP_o + s. \pi_2^* + a. \alpha_2 + b. \beta_2 + l. \log L^{16} \quad (3)$$

Now π_2^* , α_2 , β_2 , and V_2 denote the solute dipolarity, hydrogen-bond acidity, hydrogen-bond basicity, and volume, and L^{16} is the solute Ostwald solubility coefficient on n-hexadecane at 298K. For general application of equations (2) or (3), these parameters must be available for a wide range of solutes. It is already the case that many such applications cannot be carried out fully because of lack of data especially in connection with the very important solute hydrogen-bond acidity and basicity scales, α_2 and β_2 .

The aim of the present workshop was to draw together workers who were active in the construction of solute scales of hydrogen-bond acidity and basicity, or in the improvement of the already existing solvent scales, in the hope that some general agreement or *co-operation* could be achieved that would enable progress in these areas to be made. In addition to those chemists engaged on the various scales as such, a number of workers who were concerned with the use of hydrogen-bond scales were invited in order that their views could also be aired at the workshop.

A list of lectures follow, together with summaries kindly supplied by the lecturers. There was a considerable amount of discussion after each lecture, as well as an extended general discussion on the last day of the workshop. Much of the discussion after some of the lectures, especially those devoted to the detailed construction of hydrogen-bond scales, was repeated and extended in this general discussion. Hence a brief summary of the main discussion points is given for five lectures that were rather self-contained (those of Kamlet and Doherty, Morris and Taylor, Grate, Hillier and Gould, and Abboud), and the entire discussion following the remaining four lectures (those of Maria and Gal, Laurence and Nicolet, Prior, and Abraham, Grellier and McGill) is contained in the general discussion that follows the lecture summaries.

1. M.J. Kamlet, J.-L.M. Abboud, M.H. Abraham, and R.W. Taft, *J. Org. Chem.*, 1983, 48, 2877.
2. M.H. Abraham, R.M. Doherty, M.J. Kamlet, J.M. Harris, and R.W. Taft, *J. Chem. Soc. Perkin Trans. II*, 1987, 913.
3. M.J. Kamlet, R.M. Doherty, R.W. Taft, M.H. Abraham, G.D. Veith, and D.J. Abraham, *Envir. Sci. Tech.*, 1987, 21, 149.
4. M.J. Kamlet, R.M. Doherty, M.H. Abraham, P.W. Carr, R.F. Doherty, and R.W. Taft, *J. Phys. Chem.*, 1987, 91, 1996.
5. M.H. Abraham, P.L. Grellier, R.A. McGill, R.M. Doherty, M.J. Kamlet, T.N. Hall, R.W. Taft, P.W. Carr, and W.J. Koros, *Polymer*, 1987 in the press.

LECTURES

MORTIMER J. KAMLET AND RUTH M. DOHERTY

Parameter estimation rules for LSER

PIERRE-CHARLES MARIA AND JEAN-FRANCOIS GAL

Multivariate analysis of different kinds of basicity scales:
contribution to the understanding of the hydrogen-bond interaction.

JEFFREY J. MORRIS AND PETER J. TAYLOR

Hydrogen-bonding scales for use in QSAR

CHRISTIAN LAURENCE AND PIERRE NICOLET

Hydrogen-bond basicity of alcohols

DAVID V. PRIOR

Construction of scales of solute hydrogen-bond acidity and basicity

JAY W. GRATE

The relevance of solute solubility properties to the absorption of
vapours into chemical microsensor coatings

IAN H. HILLIER AND I.R. GOULD

Ab-initio MO calculations of hydrogen-bonding: comparison with
experimental measurements

JOSE-LOUIS M. ABOUD

The hydrogen-bonding basicity of oxygen and sulphur compounds

MICHAEL H. ABRAHAM, PRISCILLA L. GRELLIER AND R ANDREW MCGILL

A scale of solvent basicity, using only solvatochromic measurements

PARAMETER ESTIMATION RULES FOR LINEAR SOLVATION ENERGY RELATIONSHIPS

Mortimer J. Kamlet

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Ruth M. Doherty

Naval Surface Weapons Center, White Oak Laboratory, Silver Spring,
MD, 20910, USA

We have recently devised a set of rules for estimation of V_I , π^* , β_m , and α_m of polycyclic aromatic hydrocarbons, polychlorinated benzenes and biphenyls, alkyl and halo-substituted phenols, anilines, and benzoic acids, and aliphatic carboxylic acids. These are consistent with earlier published experimental solvatochromic parameters, and have significantly expanded the data base of solubility, partition, HPLC, and toxicological properties that can be correlated by equation (1).

$$XYZ = XYZ_O + mV_I/100 + s\pi^* + d\delta + b\beta_m + a\alpha_m [+ w(mp - 25)] \quad (1)$$

Recent correlations of the expanded data sets by equation (1) are summarized in Table 1; underlined values are not statistically significant at the 95% confidence level.

Some examples of the parameter estimation rules are given below, and an illustration of the effectiveness of these rules, used with equation (1), in correlating the aqueous solubility of a large number of environmentally important liquids and solids is shown in the Figure, where S_w is the molar solubility.

In equation (1), V_I is the solute intrinsic volume, π^* is the solute dipolarity, δ is a polarisability correction term, and α_m and β_m are the solute monomeric hydrogen-bond acidity and basicity. The latter are sometimes denoted as α_2 and β_2 .

SIMPLE PARAMETER ESTIMATION RULES

Polychlorobenzenes

- Chlorobenzene: $V_I = 58.1$, $\pi^* = 0.71$, $\beta = 0.07$
- 1,2-Dichlorobenzene: $V_I = 67.1$, $\pi^* = 0.80$, $\beta = 0.03$
- Other polychlorobenzenes: Add 9.0 to V_I for each chlorine. If additional chlorine increases dipole moment, add 0.05 to π^* ; If it decreases dipole moment, subtract 0.05. Subtract 0.04 from β for each addition Cl to minimum of 0.0

Polychlorobiphenyls

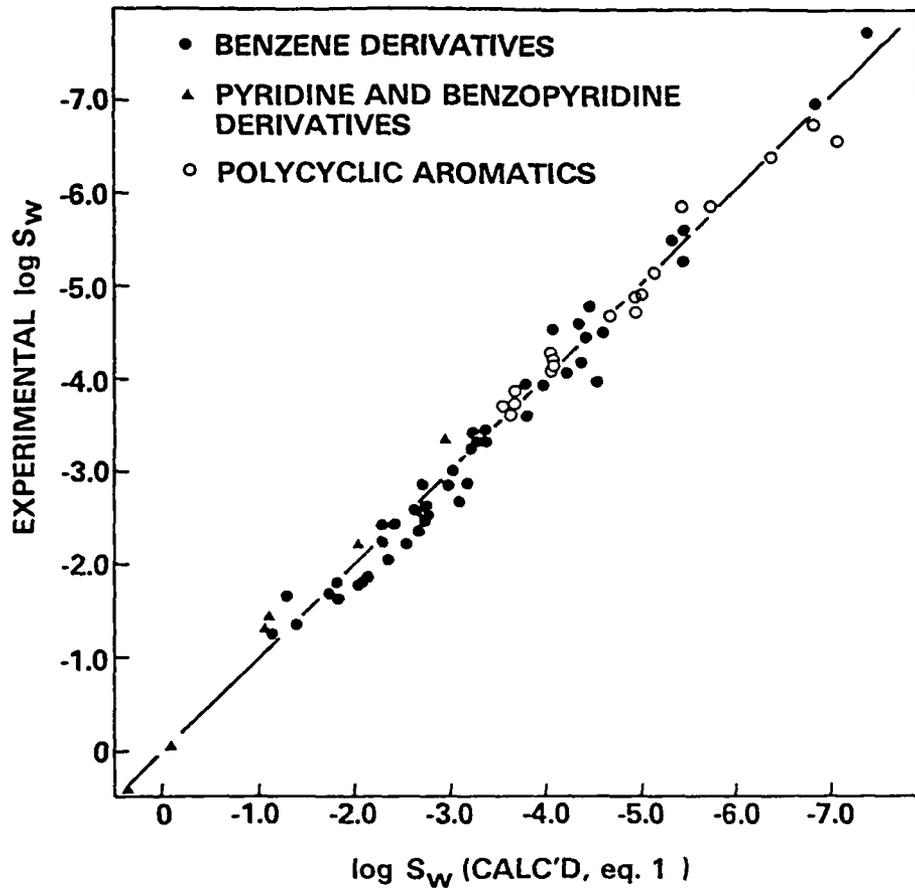
- $V_I = 92.0$ for biphenyl, add 9.0 to V_I for each chlorine.
- Calculate π^* and β separately for each ring, and use summation of π^* , δ , and β values; i.e., $\delta = 2.0$ for biphenyl derivatives

Polycyclic Aromatic Hydrocarbons

- Naphthalene: $V_I = 75.3$, $\pi^* = 0.70$, $\beta = 0.15$
- Add 6.55 to V_I for each additional C or CH in fused ring, e.g., add 26.2 for naphthalene to anthracene or phenanthrene; add 52.4 for naphthalene to triphenylene; add 36.3 for naphthalene to chrysene.
- For each additional fused aromatic ring, add 0.10 to π^* ; add 0.05 to β .
- For addition of methyl, add 9.8 to V_I ; add 0.01 to β ; subtract 0.04 from π^*

TABLE 1. APPLICATION OF EQUATION (1) TO A NUMBER OF SOLUTE PROPERTIES

Property	XYZo	m	s	d	b	a	w	n	r	sd
Aqueous solubility, liquid aliphatic solutes (ex strong HBD)										
	0.05	-5.85	+1.09		+5.23			115	0.9944	0.153
Aqueous solubility, liquid and solid aromatic solutes (ex strong HBD)										
	0.24	-5.30	<u>-0.08</u>		+3.99		-0.0096	147	0.9903	0.337
Octanol/water partition										
	0.32	+5.35	-1.04	+0.35	-3.84	-0.10		245	0.9959	0.131
Cyclohexane/water partition										
	0.27	+6.73	-1.89	+0.64	-5.06	-3.88		70	0.9932	0.187
CCl ₄ /water partition										
	0.36	+6.35	-0.65	<u>-0.01</u>	-5.26	-3.26		50	0.9950	0.140
CHCl ₃ /water partition										
	0.11	+6.18	<u>+0.03</u>	<u>+0.04</u>	-3.61	-3.26		57	0.9934	0.163
Benzene/water partition										
	0.13	+6.27	<u>-0.17</u>	+0.29	-4.93	-3.02		54	0.9955	0.111
Diethyl ether/water partition										
	0.33	+5.79	-0.55	+0.24	-4.90	-0.29		46	0.9923	0.131
Tadpole narcosis										
	-0.67	-4.87	-0.48		+4.57	-0.65		39	0.9899	0.168
Nerve blocking, frog muscle										
	+4.04	-5.09	-0.56		+1.32	-0.28		20	0.9907	0.163



DISCUSSION ON KAMLET AND DOHERTY'S LECTURE

Laurence asked if results using the general solvatochromic equations had been compared to results using other possible combinations of parameters. Doherty replied by stating that for the correlation of solute effects there was almost no comparison to be made, but that in terms of solvent effects a few comparisons have been published (J. Org. Chem., 1981, 46 3053). Doherty stressed, however, that in comparing results from one set of parameters with those from another set, the general interpretation of the correlation was probably more important than minor statistical differences in the goodness-of-fit.

MULTIVARIATE ANALYSIS OF DIFFERENT KINDS OF BASICITY SCALES: CONTRIBUTION
TO THE UNDERSTANDING OF THE HYDROGEN-BOND INTERACTION

Pierre-Charles Maria and Jean-Francois Gal

Laboratoire de Chimie Physique Organique, Universite de Nice -
Parc Valrose 06034 Nice Cedex, France

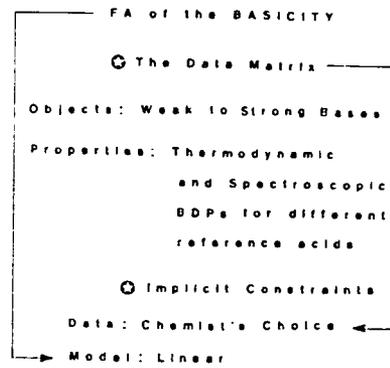
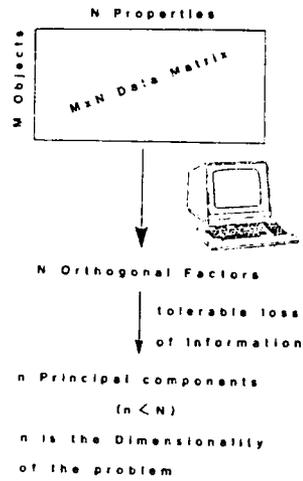
Different kinds of basicity scales related to hydrogen bonding, proton transfer and interactions with hard and soft Lewis acids, including our $-\Delta H_{\text{BF}_3}^\circ$ scale,¹ have been analysed by use of Principal Component Analysis. The first two factors account for about 95% of the total variance of the data, and may be used to quantify electrostatic/covalent contributions to the acid-base interaction².

In the first instance, these contributions depend on the studied physical property: ΔG° , ΔH° , ΔS° , spectroscopic shifts ... and on the nature of the reference acid.

For a particular physical property, even when we focus on hydrogen-bonding interactions, significant variations in the electrostatic/covalent behaviour arise from changes in the reference acid/solvent system. The medium effect shows up as a small electrostatic contribution.

Our multivariate analysis, based on Principal Component Analysis and Information Theory, allowed us to sort out many basicity scales, including various measures of the hydrogen-bond acceptor affinities, and to shed light on their relationships.

1. For molecules commonly used as solvents see :
P.C. Maria and J.F. Gal, J. Phys. Chem., 1985, 89, 1296-1304.
A more comprehensive list of about 300 $-\Delta H_{\text{BF}_3}^\circ$ is available from the authors.
2. P.C. Maria, J.F. Gal, J. de Franceschi and E. Fargin, J. Am. Chem. Soc., 1987, 109, 483-492.



Independent Factors in the Space Generated by the Five Most Informative Scales

Factors F	dimensionality				
	1	2	3	4	5
% variance	82.14	92.18	94.51	99.00	100.00
cumulated % variance	82.14	92.18	94.51	99.00	100.00

variable	correlation coeff.	
	f_1	f_2
$-\Delta H^\circ_{\text{aq}}$	0.92	0.02
pK_{HB}	0.69	0.72
$\Delta_{\text{H}}^{\text{H}}$	0.95	-0.18
$-\Delta H_f$	0.96	-0.19
$\Delta_{\text{H}}^{\text{OH}}$	0.97	-0.17

SOLUTION/GAS PHASE
RELATIONSHIPS

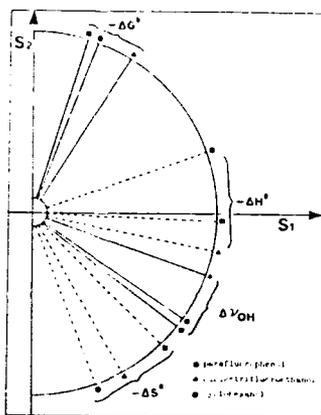
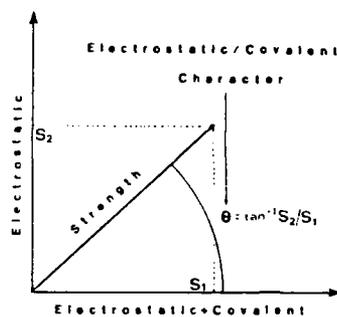
Significance of F_1 and F_2

- F_1 is linear with Proton Affinities
(corrected for polarizability)
- COVALENT+ELECTROSTATIC
contribution
- F_2 is linear with K^+ Affinities
- ELECTROSTATIC contribution

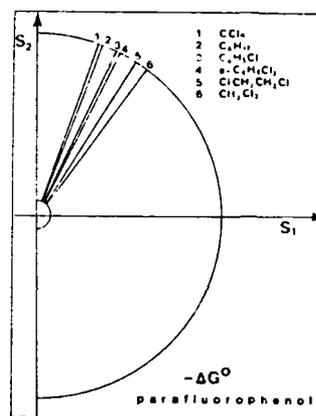
How to use F_1 and F_2
for the study of H-Bonding

$$BDP - BDP_0 = S_1 F_1 + S_2 F_2$$

If a BDP is known for only
a few bases S_1 and S_2 are
significant as long as F_1
and F_2 are orthogonal

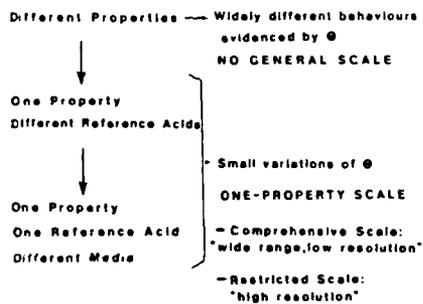


From M.H. Abraham et al. J. Am. Chem. Soc. 107, 1987, 107



From M.H. Abraham et al.

H-BONDING SCALES



HYDROGEN BONDING SCALES FOR USE IN QSAR

J.J. Morris and P.J. Taylor

(ICI Pharmaceuticals Division, Alderley Park,
Macclesfield, Cheshire, SK10 4TG, UK)

In the multi-parameter Hansch equation (1) as used in QSAR, the electronic term is commonly modelled by Hammett's σ . This is entirely appropriate when varying the substituent affects either some general molecular property, eg. pK_a , or interaction with the receptor through a remote functional group. It is not appropriate when the substituent itself interacts with the receptor, eg. by formation of a hydrogen bond.

$$\log 1/C = a \log P - b(\log P)^2 + c(\text{electronic}) + d(\text{steric}) + \dots \quad (1)$$

We have therefore attempted to generate substituent scales of hydrogen bonding for use in QSAR. At the time this work began, in about 1979, it had no precedent and four chief problems quickly became apparent. Firstly, an unequivocal free energy scale is required to allow congruence with equation (1): it is not altogether clear from their derivation whether the Taft-Abboud-Kamlet (TAK) solvent α and β scales are true free energies or some blend of ΔH with ΔG . Hence we need to measure equilibrium constants, though because of arguments which suggest that ΔS may be nearly a constant for the replacement of one (small) substituent by another, the ability simultaneously to generate enthalpy-based quantities could be an advantage. Secondly, we have to avoid solute self-association, since it is abundantly clear that, for example, α and β for bulk alkanols is no guide to the likely behaviour of OH in isolation. Thirdly, a single donor probe (for acceptors) and acceptor probe (for donors) is required that will place all members of each class on a common scale; it is inconvenient and could be misleading to use a range of standards. And fourthly, we need to work in a medium whose polarity is realistic in a biological context and that will dissolve the highly polar molecules that interest us; previous standard solvents, eg. CCl_4 and cyclohexane, fail in both respects. This problem has been solved by the use, for the first time in such studies, of 1,1,1-trichloroethane (TCE); the high polarity ($D=7.53$) of this otherwise totally inert solvent is on a par with octanol, has helped to

minimise solute self-association, and has allowed us to examine a much wider range of highly polar molecules than has hitherto been possible.

Proton acceptor strength ($\log K = pK_B$) has been measured using p-nitrophenol (PNP) as standard probe. At the same time, we have derived a solute β (β_{sm}) scaled to TPPO as unity. This methodology possesses features, therefore, derived both from TAK and the earlier Taft-Schleyer pK_{HB} scale. There was no useful precedent for a proton donor methodology. Here we use N-methylpyrrolidinone (NMP) in excess over the proton donor (this will generally destroy any residual self-association), measuring K ($\log K = pK_a$) either from the change in free A_{OH} or A_{NH} or by a titrational calorimetric technique (Drs M H Abraham and P P Duce, University of Surrey). Simultaneously we measure $\Delta \nu_{C=O}$ as a putative enthalpy - based quantity. In each series, the results are derived by a rigorous non-linear fitting procedure.

Many results for acceptors parallel previous investigations, though it is encouraging, for example, that alcohols and ethers now possess similar pK_B values. However, there are many new results: for example, sulphones are much weaker than sulphoxides and imides than amides, both being roughly on a level with esters. The known range of hetero-cycles has been greatly extended; here there is a partial correlation with basicity but with positive deviations due, at least in some cases, to the "alpha effect".

Among proton donors, most NH acids are weak, but the triazoles are as strong as phenol while tetrazole possesses the highest pK_a value yet to be measured. Unexpectedly, simple carboxylic acids are no stronger than phenol; while anion resonance in CO_2^- may contribute to the explanation, the anomalous weakness of sulphonamides where this cannot be important suggests that the crucial factor may be lone pair repulsion between CO or SO_2 and the incoming proton acceptor. For OH or heterocyclic NH, this will be absent. These anomalies apart, pK_a relates much more simply than pK_B to pK_A , with alkanols and most NH donors lying close to a single line. Phenols however behave quite differently - the two lines cross; so far, this is not understood.

There is no single relation between pK_B and the general pK_B^H scale of Abraham et al.; dipolar acceptors (P = O and S = O), carbonyl, and heterocyclic N lie on three lines of increasing relative pK_B value and possibly

increasing slope (Figure 1). We regard this as an example of "solvent-induced partial ionisation" as identified by Taft in 1972, and since analysed as due to a solvent-dependent balance between electrostatic and covalent forces. Its effect is to make results in TCE unique so that our biochemically-targetted scales are not, except within limited series, interchangeable with others. There is even less of a single relation between pK_{β} and β_{sm} or between pK_{α} and $\Delta v_{C=O}$. In the former (Figure 2), pK_{β} for a given β_{sm} is much less favourable for sp^2 -nitrogen than for sp -oxygen. Since heterocycles possess a single, highly directional lone pair whereas the stereochemistry for the latter class is much less demanding, this strongly suggests an entropic origin for the difference, in which case β_{sm} may be a measure of internal enthalpy. Deviations within series also suggest an entropic explanation. Similarly, while unhindered OH and NH donors fall on lines of different slope (Figure 3), negative deviations from either (lower pK_{α} for a given $\Delta v_{C=O}$) appear to be associated with severe steric hindrance or stereoelectronic repulsion. Within series, therefore, $\Delta v_{C=O}$ may also be a measure of internal enthalpy. The difference in the lines may relate to the expected difference in bond length between any NH...B and OH...B pair (B=base); the latter should be the shorter, hence the greater responsiveness of $\Delta v_{C=O}$.

Finally we show a plot of pK_{α} and pK_{β} vs. σ_p (Figure 4): the result, a scattergram, may help to explain why the electronic term has appeared in so few successful correlations according to equation (1). We believe that its replacement by pK_{α} or pK_{β} may open up new possibilities for the medicinal chemist.

Figure 1

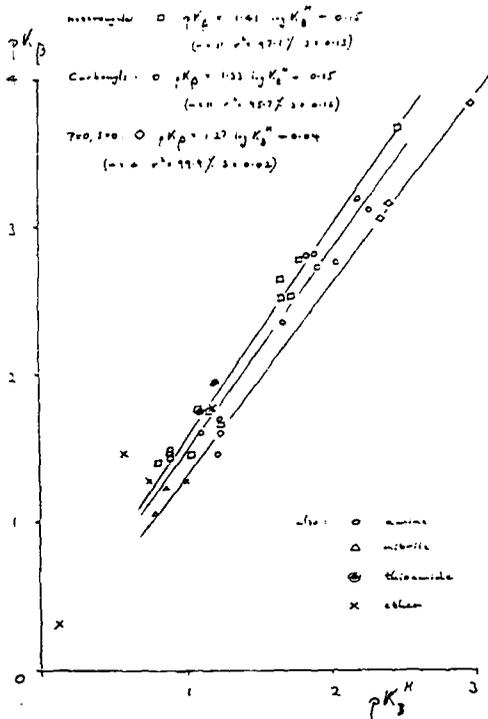


Figure 2

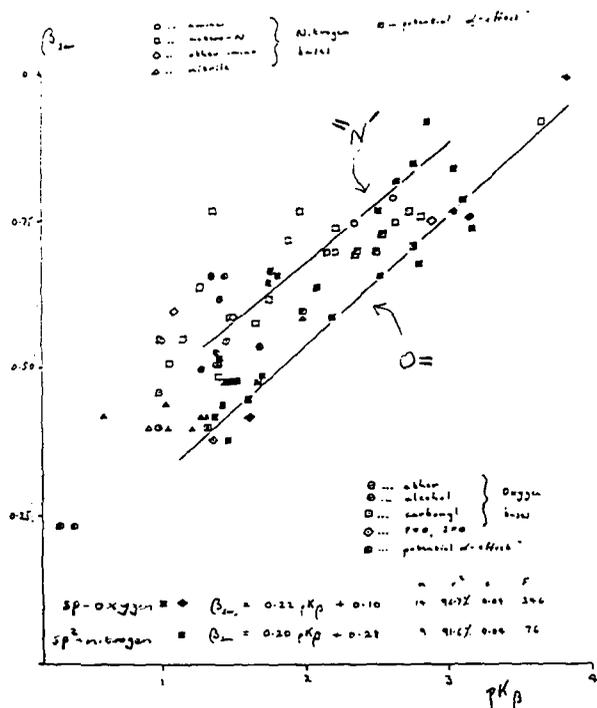


Figure 3

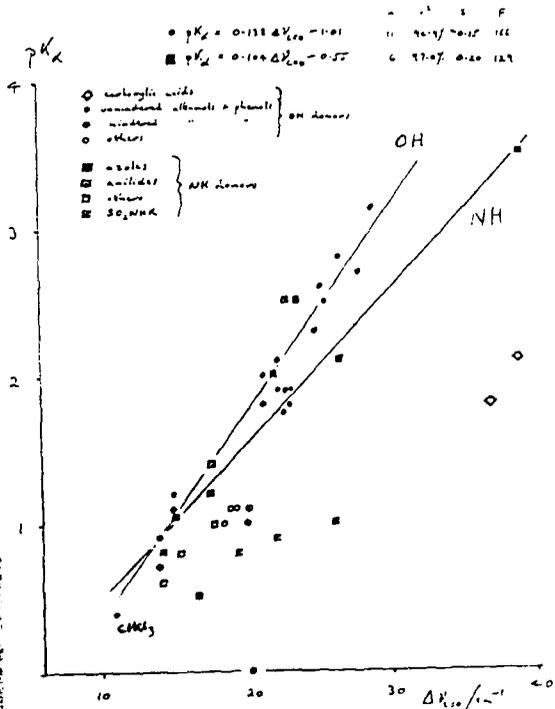
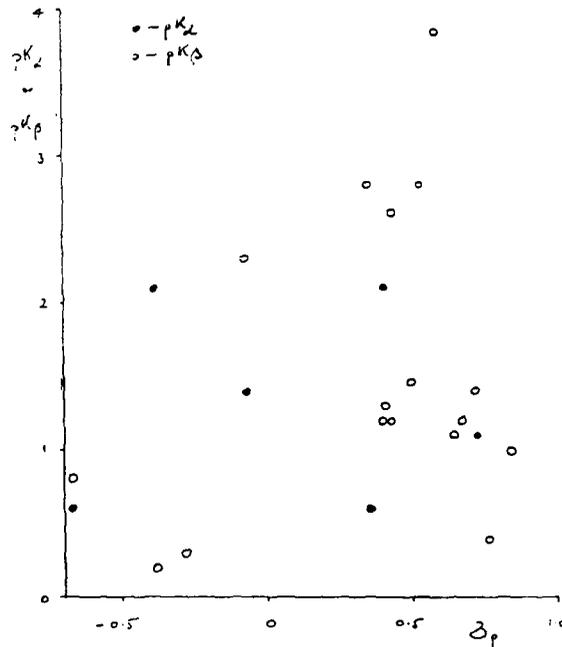


Figure 4



DISCUSSION ON MORRIS AND TAYLOR'S LECTURE

Gal asked if there was any complication from proton transfer when using 4-nitrophenol in TCE. Morris replied that no phenoxide ion can be seen, but if the solvent is made rather more polar, for example CH_2Cl_2 , then phenoxide is indeed formed. Gal also enquired why the existing pK_{HB} scale was not used by Taylor, rather than developing a new pK_{β} scale, but Taylor indicated that the use of a solvent such as TCE meant that many more interesting compounds of use to the medicinal chemist could be studied than with CCl_4 , and that TCE is probably a better measure of receptor environment than is CCl_4 . However, because of the solvent dependence of $\log K$ values, ICI would need to continue to use their pK_{α} and pK_{β} scales as distinct scales of solute hydrogen-bonding from those set up by Prior, for example.

Both Gal and Laurence were concerned with problems over polyfunctional compounds and multisite bases. Morris felt that there must be a new initiative set up to deal with the specific problem of what happens to the hydrogen-bond tendency of one site in a molecule after hydrogen-bonding to another site in the same molecule.

During his lecture, Taylor had shown a plot of pK_{α} vs $\nu_{\text{C=O}}$ for complexation of acids with NMP in TCE. Abraham asked if such a plot showed family dependencies, and Morris replied in some detail indicating that within families where there was no steric hindrance, very good linear plots were obtained that could be used for the estimation of pK_{α} values. Morris also noted that pyridines and ethers were much more susceptible to steric hindrance to hydrogen-bond complexation than were ketones, for example. Taylor followed this up by noting a very important set of results by Hine et al. (J. Org. Chem., 1986, 51, 577) that suggested that whereas ketones could form two hydrogen-bonds, pyridines, trialkylamines, and (very surprisingly) ethers formed only one hydrogen bond, in dilute solution in CCl_4 .

HYDROGEN BONDING BASICITY SCALE OF ALCOHOLS

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Water and alcohols are probably the most important of all solvents and their basicities are of great importance from practical viewpoints. There are, however, few thoroughly acceptable values for the basicities of the alcohols and water in solution. For example, by using hydrogen bonding to study basicity, Kamlet, Taft and co-workers have defined a β scale of hydrogen bondacceptor basicity of a great number of organic solvents, but are particularly uncertain about the β values for the alcohols and water. The differing β values in the 1976-1986 literature are summarized in table I.

Table I. β values of alcohols and water

Alcohols	1976 ¹	1983 ²	1985 ³	1986 ⁴	1986 ⁵
t-BuOH	0.95 (0.91)	~1.01	~1.0		
i-PrOH	0.92 (0.80)	~0.95	~0.9	0.95	0.95
n-BuOH	0.85 (0.80)	~0.88			
EtOH	0.77 (0.73)	~0.77	~0.8	0.77	0.77
MeOH	0.62 (0.70)	~0.62	~0.6	0.62	0.62
PhCH ₂ CH ₂ OH	0.64	~0.61			
Ph CH ₂ C ₆ H ₅	0.56	~0.50			
HOCH ₂ CH ₂ OH	0.51 (0.60)	~0.52			
H OH	0.14 (0.47)	~0.18	~0.5	~0.4	0.18
C ₆ H ₅ CH ₂ CH ₂ OH	0.31 (0.53)	~0.31			
CF ₃ CH ₂ OH		0.00	~0.0	~0.05	
(CF ₃) ₂ CHOH		0.00	0.0		

¹ M.J. Kamlet and R.W. Taft, JACS, 1976, 98,377. The first value refer to p- nitroaniline and the second to p-nitrophenol (vide infra).

² M.J. Kamlet, J.L.M. Abboud, M.H. Abraham and R.W. Taft, J. Org. Chem., 1983, 48, 2877.

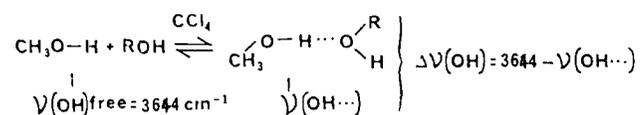
³ R.W. Taft, J.L.M. Abboud, M.J. Kamlet and M.H. Abraham, J. Sol. Chem. 1985, 14, 153.

⁴ M.J. Kamlet, R.M. Doherty, J.L.M. Abboud, M.H. Abraham and R.W. Taft, Chemtech., 1986; 16, 66.

⁵ M.H. Abraham, R.M. Doherty, M.J. Kamlet and R.W. Taft, Chemistry in Britain, 1986, June, p.551.

The reasons for these unprecise values are (i) that the determination of these parameters involves unraveling three types of effects (polarity, acidity and basicity) and (ii) that the HBA basicity of water and alcohols depends on the extent of their self-association. It is well known that monomeric alcohols (existing in dilute solutions in an inert solvent) are much less basic than polymeric alcohols existing in the bulk solvent. Kamlet, Taft and co-workers have defined a β_m scale for monomeric alcohols as solutes while the β scale is valid for alcohols as solvents.

We have first measured the HBA basicity of monomeric alcohols in very dilute solution in CCl_4 from the frequency shift $\Delta\nu(\text{OH})$ of MeOH. In the presence of a hydrogen bond acceptor stronger than MeOH, the MeOH probe behaves as a hydrogen bond donor in the following equilibrium :



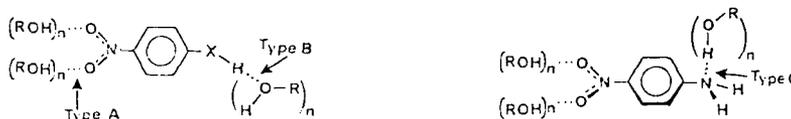
The $\Delta\nu(\text{OH})$ values are in the order expected from the inductive and polarizability effects of the R group, except for phenylethanol and glycol where intramolecular hydrogen bonding seems to increase the HB basicity. They agree well with (i) a $\Delta\nu(\text{OH})$ phenol scale in CCl_4 (M.H. Aslam, G. Collier, J. Shorter, J.C.S. Perkin II, 1981, 1572), (ii) a $\Delta\nu(\text{HF})$ scale in the gas phase (A.C. Legon, D.J. Millen, O. Schrems, J.C.S. Faraday, 1979, 592), and (iii) a thermodynamic $\log K$ scale for the association of 3,4-dinitrophenol with monomeric alcohols in cyclohexane (J.L.M. Abboud, K. Sraïdi, G. Guiheneuf, A. Negro, M.J. Kamlet and R.W. Taft, J. Org. Chem. 1985, 50, 2870).

For the measurement of HBA basicity of alcohols less basic than methanol, we have chosen perfluoro-t-butanol, a very strong HBD alcohol, and a very inert medium (a perfluorinated compound, FC-75), hoping to attain the basicity of $\text{CF}_3\text{CH}_2\text{OH}$ and $(\text{CF}_3)_2\text{CHOH}$. The frequency shifts of the 3618 cm^{-1} $\nu(\text{OH})$ band of perfluoro-t-butanol, $\Delta\nu(\text{OH})$ pFtB, are significantly correlated with the σ^* Taft's constant, and show clearly that $\text{CF}_3\text{CH}_2\text{OH}$ and $(\text{CF}_3)_2\text{CHOH}$ keep a residual HBA basicity.

The HBA basicity of pure alcohols has been measured by Kamlet and Taft by means of their solvatochromic comparison method (results in table I). We have revisited their results and measured new alcohols, with the following homomorphs



Three types of hydrogen bonding, A (bathochromic), B (bathochromic) and C (hypsochromic) can be considered (X = O,NH) :



The thermosolvatochromic comparison plots for 1-2 (fig. 1) and 3-4 (fig. 2) show that 1-2 are better indicators of type B hydrogen bonding than 3-4 : $-\Delta\Delta\nu(1-2)_{\text{O}_2\text{N}}$ is

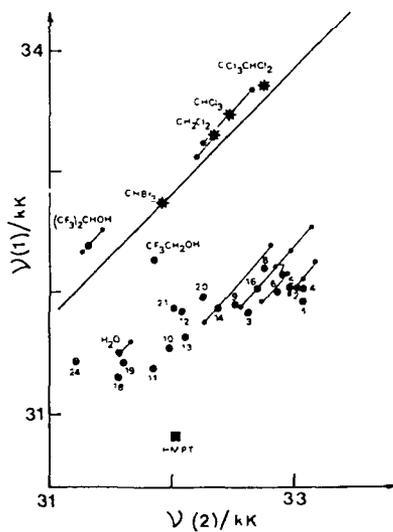


Fig. 1

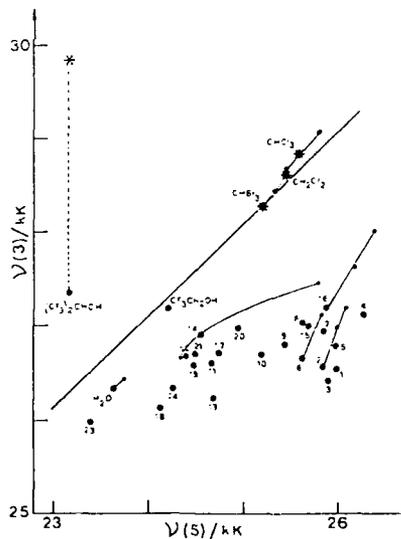
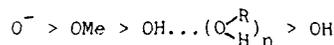
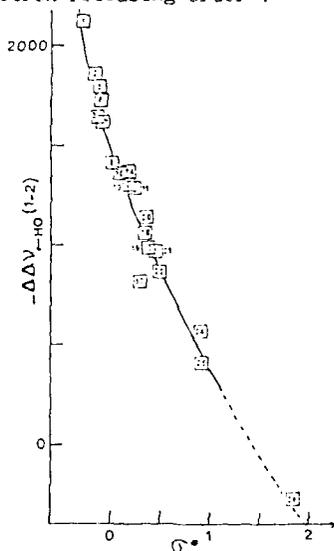
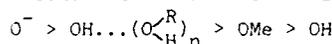


Fig. 2

lower than $-\Delta\Delta v(3-4)_{+O_2N}^A$ for $(CF_3)_2CHOH$ and $-\Delta\Delta v(1-2)_{+HO}^B$ values are less underevaluated for CF_3CH_2OH and H_2O than $-\Delta\Delta v(3-4)_{+H_2N}^B$. Another factor detrimental to the choice of 3-4 is the occurrence of type C hydrogen bond in 3 with CF_3CH_2OH and $(CF_3)_2CHOH$. However $-\Delta\Delta v(1-2)_{+HO}^B$ are certainly underevaluated for weakly basic alcohols because of the electron-releasing order :



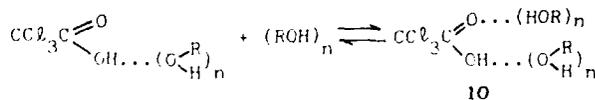
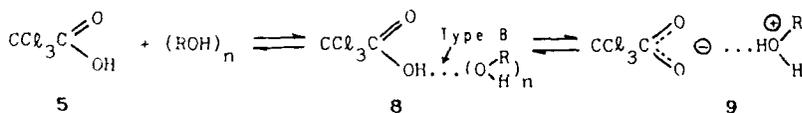
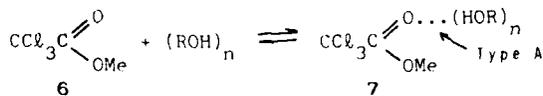
It is possible that for strongly basic alcohols this order becomes :



which causes $-\Delta\Delta v(1-2)_{+HO}^B$ to be overevaluated for these alcohols. These over and underevaluations of $-\Delta\Delta v(1-2)_{+HO}^B$ might explain the curvature of the $-\Delta\Delta v(1-2)$ vs. σ^* correlation (fig. 3).

These imperfect evaluations of HBA basicity of alcohols originate in the amphoteric nature of indicators 1 and 3. Since we want to reveal the basicity of alcohols, we have turned to a very

acidic and very weakly basic indicator, trichloroacetic acid 5, which we have compared to methyl trichloroacetate 6 to unravel polarity from basicity effects of alcohols. In fact the carbonyl stretching wavenumber of 5 is lowered by type B hydrogen bonding $CCl_3COOH \dots (O \begin{smallmatrix} R \\ \diagup \\ H \end{smallmatrix})_n$. The infrared carbonyl stretching absorption of 5 and 6 in alcohols (exemplified in figs. 4 and 5) can be understood on the basis of the following equilibria for solutions of 5 and 6 in pure alcohols :



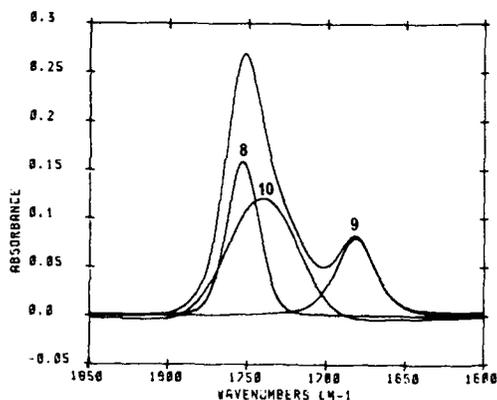


Fig. 4 - Infrared spectrum of CCl_3COOH in methanol from 1900 to 1600 cm^{-1} .

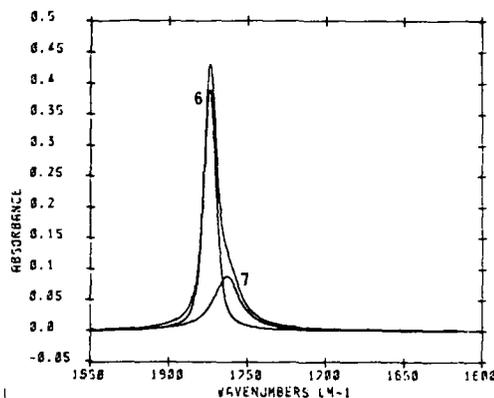


Fig. 5 - Infrared spectrum of CCl_3COOMe in methanol from 1900 to 1600 cm^{-1} .

An "infrared comparison method" allows to calculate the wavenumber shift $\Delta\nu(\text{CO})(5-6)_{+\text{HO}}^{\text{B}}$ from the equation (P. Nicolet, C. Laurence, M. Luçon, J.C.S. Perkin II, 1987, 483)

$$\Delta\nu(\text{CO})(5-6)_{+\text{HO}}^{\text{B}} = (1.1715 \nu_6 - 292.8) - \nu_8$$

They are satisfactorily correlated to σ^*_R . Unfortunately the CCl_3COOH probe does not allow to study $(\text{CF}_3)_2\text{CHOH}$ (only 7 and 10 are observed) and H_2O (because of decarboxylation and protontransfer).

Acronyms and symbols. Hydrogen bond acceptor (HBA), Hydrogen bond donor (HBD). $-\Delta\Delta\nu(1-2)_{+\text{HO}}^{\text{B}}$ denotes an enhanced bathochromic effect for compound 1 relative to compound 2 attributable to type B hydrogen bonding by OH protons to solvent. $+O_2N$ indicates hydrogen bonding by solvent to nitro oxygen. (Kamlet and Taft's nomenclature).

Acknowledgements : We are indebted to Professor M. Berthelot for providing us with unpublished results and Mrs Luçon, Helbert and Sraïdi for assistance in the measurements.

CONSTRUCTION OF SCALES OF SOLUTE HYDROGEN-BOND
ACIDITY AND BASICITY

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Although the hydrogen-bonding ability of solutes is known to be of vital importance in numerous physiochemical and biochemical processes,¹ no scale of hydrogen-bond strength has been constructed, for acids. We now find that hydrogen-bond complexation constants, as $\log K$ values, of a series of acids against reference bases in solvent CCl_4 can be used to define a scale of hydrogen-bond acidity. If $\log K$ values for a series of acids against a given base are plotted vs $\log K$ values for a series of acids against any other reference base, there results a set of lines that intersect at a point corresponding to $\log K = -1.1$, when complexation constants are defined in terms of concentration in mol dm^{-3} . An exactly similar result is obtained when a scale of hydrogen-bond basicity is constructed from $\log K$ values for a series of bases against reference acids in solvent CCl_4 . We then generate a number of equations (1), where $\log K^i$ represents hydrogen-bond complexation constants of a series of acids against a reference base in CCl_4 .

$$\log K^i = L_B \cdot \log K_A^{Hi} + D_B \quad (1)$$

The constants L_B and D_B are characteristic of the reference base, and the $\log K_A^{Hi}$ values characterise the acids. These latter values thus constitute a scale of solute hydrogen-bond acidity. Forty-five equations of type (1) were constructed in which $\log K^i$ values for 89 acids against 45 reference bases were used. The forty-five equations contained a total of 738 data points ($\log K^i$ values): only acids that appeared in at least two equations were used in this primary set. All the 45 equations were constrained to intersect at the magic point with $\log K^i = \log K_A^H = -1.1$, and the resulting equations reproduced the 738 data points with a standard deviation of only 0.089 log units. The set of 45 equations and the 89 primary $\log K_A^H$ values define a reasonably general scale of solute hydrogen-bond acidity. A quite large number of secondary $\log K_A^H$ values may be obtained, usually from single point det-

erminations, giving a total of over 150 available $\log K_A^H$ values. Certain combinations of acids and reference bases are excluded from the present analysis, specifically acids with Maria-Gal² θ values greater than about 75 degrees in combination with pyridines, aliphatic amines, and aliphatic ethers. These acids are usually weak acids such as pyrrole, indole, 5-fluoroindole, Ph_2NH , CHCl_3 , etc.

In order to develop a hydrogen-bond basicity scale, we now set up a series of equations (2), where $\log K^i$ is the complexation constant for a series of bases (i) against a reference acid in CCl_4 . The constants L_A and D_A characterise the reference acid, whilst the $\log K_B^{Hi}$ values characterise the bases and thus represent a reasonably general scale of solute hydrogen-bond basicity.

$$\log K^i = L_A \cdot \log K_B^{Hi} + D_A \quad (2)$$

The scale is not completely general, because of the exclusion of certain acid-base combinations, as specified above. Using literature data on $\log K$ values in CCl_4 we set up a system of 32 equations (2), containing 937 $\log K$ values pertaining to no less than 194 bases (only bases that appeared in two or more equations were allowed in this primary set). As found for the corresponding equations leading to an acidity scale, all the 32 generated equations intersect at a given point, with $\log K = -1.1$ units. On forcing (slightly) all the equations through this magic point ($\log K = \log K_B^H = -1.1$) the 937 $\log K^i$ values could be reproduced with a standard deviation (sd) of only 0.079 log units. From the set of 32 equations, it is possible to obtain a large number of secondary $\log K_B^H$ values for bases that appear in only one equation, giving a total of over 500 $\log K_B^H$ values. Together with the 32 equations (2), it is now possible to predict some 16,000 $\log K$ values in CCl_4 to around 0.08 log units. The 500 $\log K_B^H$ values represent the first scale of solute hydrogen-bond basicity for which the generality is well-defined (c.f. the $\text{p}K_{\text{HB}}$ scale of Taft et al.³).

We can show also that our acidity and basicity scales are fully compatible by noting that L_B in equation (1) is related to $\log K_B^{Hi}$ in equation (2), and that L_A in equation (2) is related to $\log K_A^{Hi}$ in equation (1), a clear demonstration of the importance of setting up general solute hydrogen-bond acidity and basicity scales along the same lines.

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THE RELEVANCE OF SOLUTE SOLUBILITY PROPERTIES TO THE SORPTION
OF VAPORS INTO CHEMICAL MICROSENSOR COATINGS

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A key component of many gas sensors is the chemical coating material which absorbs and concentrates the gas to be detected. Absorption of the gas can be modelled as a solute-solvent interaction, where the gas is the solute and the sensor coating is the solvent. This model has been very useful in understanding the behavior of surface acoustic wave (SAW) vapor sensors, which detect the mass of vapor absorbed into a soft polymeric stationary phase coating.

The solute hydrogen bonding properties, in particular, have been indicated as an important factor in determining the sensitivity and selectivity of SAW vapor sensors. Using pattern recognition techniques, the data from a variety of coating materials on SAW devices exposed to vapors with a full range of solubility properties were examined. Hierarchical cluster analysis demonstrated that vapors which could accept or donate hydrogen bonds were distinguished from non-hydrogen bonding vapors.

A better understanding of the factors influencing the sorption of gases and vapors into sensor coating materials would facilitate the development of gas sensors for specific applications. Indeed, one of the attractive features of sensors employing thin absorbent films is their potential to be adapted to a wide variety of gas phase analytical problems by strategic design or selection of the coating material. However, full realization of this potential will require methods to quantify, understand, and ultimately, to predict, the vapor/coating interactions responsible for vapor sorption.

Quantification of the equilibrium distribution of vapor between the gas phase and a sensor coating (stationary phase) can be achieved using a partition coefficient, K , which gives the ratio of the concentration of the vapor in the stationary phase, C_s , to the concentration of the vapor in the gas phase, C_v (equation 1).

$$K = C_s / C_v \quad (1)$$

Partition coefficients are a particularly useful concept for thinking about SAW sensor responses because the sensors response, a frequency shift, can be directly related to the partition coefficient by equation 2.

$$f_v = f_s C_v K / p \quad (2)$$

In this equation, f_v is the frequency shift caused by vapor absorbed into the coating, f_s is the frequency shift caused by the application of the coating to a bare device (and provides a measure of the amount of coating applied), C_v is the concentration of the vapor in the gas phase, K is the partition coefficient, and p is the coating material density. With this simple equation, partition coefficients can be calculated from SAW sensor data. Alternatively, if K is known from GLC measurements or solvatochromic correlation equations, then SAW sensor responses can be predicted.

The relationship between partition coefficients and SAW sensor responses was experimentally tested using the coating material 'fluoropolyol', which has proven in repeated testing to be a very well behaved and reproducible sensor coating. Polymer/gas partition coefficients calculated from sensor responses were compared with the same partition coefficients determined independently by GLC measurements, using fluoropolyol as the column stationary phase. The results are in good agreement, confirming the solubility model above.

The importance of solute solubility properties can be easily seen simply by examining the magnitudes of the partition coefficients for the vapors examined. The lowest K values were those of isooctane, a solute which is not dipolar, and cannot accept or donate hydrogen bonds. Somewhat more strongly sorbed are vapors such as dichloroethane and toluene, which are polarizable. However, these solutes are still incapable of hydrogen bonding. The vapors with the largest partition coefficients are exclusively those which are capable of hydrogen bonding.

Sorption isotherms can also be used to investigate solubility interactions. For the vapor dimethyl methylphosphonate, the sorption isotherm provides strong evidence for site-specific sorption of this

hydrogen bond acceptor vapor at hydrogen bond donating sites on the polymer.

A more complete and quantitative understanding of the solubility interactions responsible for vapor sorption into sensor coatings requires a numerical scale of vapor solubility properties, which is the subject of this workshop, and a means to quantitatively characterize the solubility properties of the coating materials. The latter problem is being addressed using equations of the form in equation (3).

$$\log K = \text{constant} + s.\pi_2^* + a.\alpha_2 + b.\beta_2 + l.\log L^{16} \quad (3)$$

The equation correlates partition coefficients with vapor solubility properties. The coefficients s , a , b , and l characterize the solubility properties of the stationary phase. The individual terms in the equation allow individual solubility interactions to be sorted out and evaluated. In addition, these types of equations allow partition coefficients, and hence SAW sensor responses, to be predicted.

Full characterisation of fluoropolyol and a variety of other sensor phases by equations of the form shown in equation (3) is well underway, and we hope to report more on this work soon. The final numerical values will be dependent on the establishment of standard scales for solute hydrogen bond donor strength and solute hydrogen bond acceptor strength. Thus, the subject of this workshop is very important to the full characterization and prediction of the behavior of gas-absorbing coating materials used on chemical microsensors.

Acknowledgements

The GLC measurements and development of correlation equations are carried out at the University of Surrey by Michael Abraham, R. Andrew McGill, and Pnina Sasson. SAW sensor research is carried out through the Naval Research Laboratory, and includes work by Arthur Snow, Susan Rose-Pehrsson, David Ballantine, and Hank Wohltjen.

DISCUSSION ON GRATE'S LECTURE

Morris asked if anything was known about the conformation of polymers used as sensor and GLC phases - are all polymer sites available for hydrogen-bonding on absorption of vapours? Abraham suggested that -OH groups in a polymer, for example, might act independently or might still be associated in some way in the polymer. In reply, Grate noted that both sensor and GLC results were obtained at low solute concentration (approx. zero for the GLC results) and that for the polymers studied probably nearly all the sites were available, since the experimental temperature was always above the polymer T_G value; the polymers might usefully be studied by FTIR to determine the nature of the -OH group. McGill suggested that many of the materials used by Grate would offer advantages as selective GLC phases. Grate agreed, saying that GLC phases now used were not very selective.

AB INITIO MOLECULAR ORBITAL CALCULATIONS OF HYDROGEN-BONDING: COMPARISON
WITH EXPERIMENTAL DATA

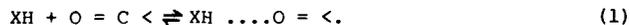
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Ab Initio molecular orbital (MO) calculations can now be used to study an increasing range of molecular systems and to predict, to a chemical accuracy, microscopic properties of such systems. In the case of hydrogen-bonding studies, these theoretical methods may be used

- i) to determine the structure and energetics of hydrogen-bonded complexes;
- ii) to determine spectroscopic properties of hydrogen-bonded complexes, particularly vibrational frequencies
and
- iii) to provide data to allow for the inclusion of solvent effects using suitable models.

We have studied, from a theoretical viewpoint the system



The proton donors (XH) studied include phenols, alcohols, carboxylic acids and anilides. The proton acceptor used here, formaldehyde, is taken to model N-methylpyrrolidinone. Calorimetric data for reaction (1) for these systems have been obtained by Abraham et al.¹, using 1,1,1-trichloroethane and tetrachloromethane as solvent.

For the simplest example of reaction (1), (XH = H₂O), experimental data have been obtained for the vibrational frequencies of the hydrogen-bonded complex in an inert gas matrix at low temperature². In Table 1 we show the shifts in the frequencies of the vibrational modes of the proton donor and acceptor which occur on complex formation, obtained from ab initio MO calculations using various basis sets³, together with the corresponding experimental values. Although the overall agreement between theory and

experiment is improved by basis set expansion, at the minimal basis level (STO-3G), the shift in the C=O stretching frequencies is well produced. With a range of proton donors of varying strengths, complexing with formaldehyde, we find, at the STO-3G level, that there is a linear relationship between the calculated intrinsic hydrogen bond strength and the calculated shift in the C=O frequency (see Figure 1) thus giving theoretical support for the use of this spectroscopic quantity as a measure of intrinsic hydrogen bond strength.

Turning now to the influence of solvent on the predicted enthalpy of the reaction (1), we use the reaction field continuum model⁴ to estimate the solvation energy of the proton donor (HX) and of the hydrogen bonded complex. We ignore the solvation of the common proton-acceptor, since this will not affect the relative values of ΔH , for different proton donors. In this simple model, the interaction energy (G) is given as

$$G = \frac{-f\mu^2}{2(1-f\alpha)}$$

Where

$$f = \frac{2(\epsilon - 1)}{(2\epsilon + 1)a_s^3}$$

Here α is the solute polarizability (estimated from atom additivity values⁵), μ the solute dipole moment (obtained from the MO calculation), ϵ the solvent dielectric constant, and a_s , the radius of the cavity in the solvent containing the solute (estimated from molecular dimensions).

The combination of solvation energies, calculated in this way, with the intrinsic hydrogen-bond strengths from the ab initio MO calculations, leads to the results shown in Figure 2. Here, pK_a is \log_{10} of the experimental equilibrium constant for reaction (1). The trends shown in Figure 2 are in good agreement with the experimental data and help to rationalize data, which at first sight, are apparently somewhat random. These calculations have been further extended to explain the differing behaviour of measured enthalpies¹ for reaction (1) in the two solvents CCl_4 and CH_2Cl_2 .

This work was carried out in collaboration with ICI (Pharmaceuticals Division). We are particularly grateful for numerous discussions with Mr. P.J. Taylor, who suggested a theoretical investigation of the systems studied herein.

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TABLE 1 CALCULATED AND EXPERIMENTAL FREQUENCY SHIFTS (cm^{-1}) FOR WATER-FORMALDEHYDE COMPLEX

Mode	Expt. ²	Calculated			SV 6-31G**
		STO-3G	SV 3-21G	SV 6-31G	
C=O stretch	-5.2	-7.6	-34.8	-22.5	-20.7
C-H asymmetric stretch	16.8	12.1	78.6	44.3	46.0
C-H symmetric stretch	17.6	9.1	37.6	24.8	24.2
CH ₂ deformation	0.0	-11.3	-23.7	-10.9	-4.4
CH ₂ rotation	0.5	-1.0	-5.4	5.3	6.7
CH ₂ waggle	5.3	7.3	24.3	15.8	14.5
O-H asymmetric stretch	-25.0	14.0	-10.6	-15.6	-26.5
O-H symmetric stretch	-55.2	18.8	-11.1	-37.5	-34.6
OH ₂ deformation	21.6	20.9	24.7	11.0	21.2
R.m.s. error in calculated shift		28.3	30.2	14.4	13.8

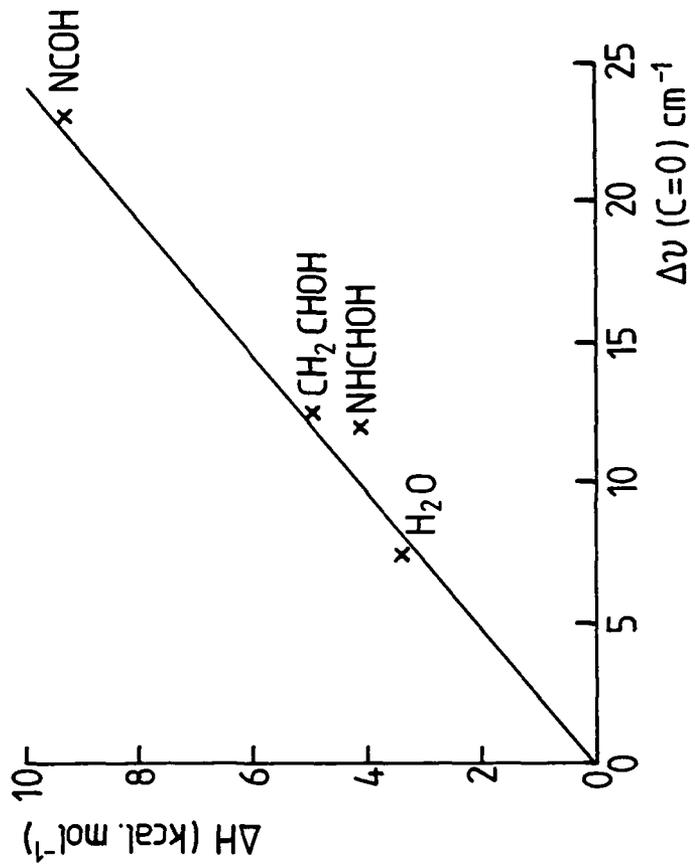


Figure 1

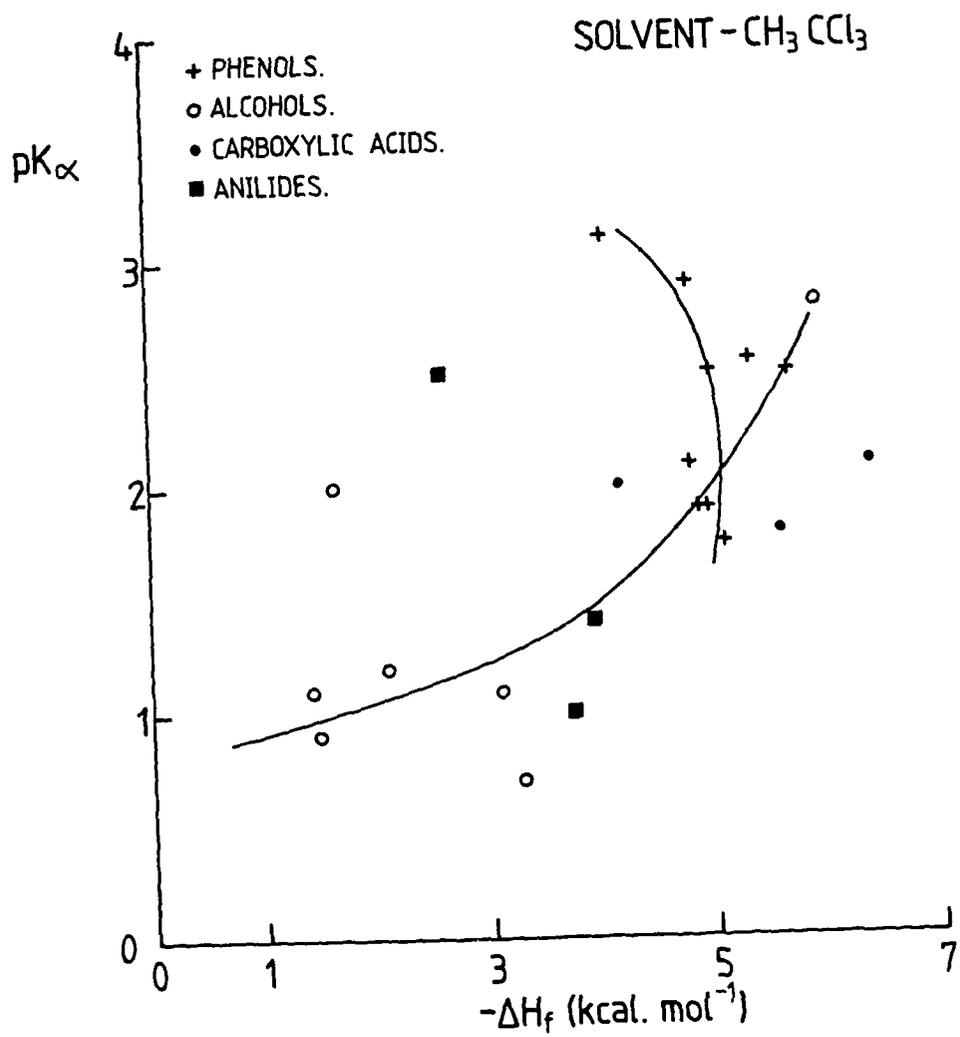


Figure 2

DISCUSSION ON HILLIER AND GOULD'S LECTURE

Taylor pointed out that the results of Hillier show that on transfer from a solvent such as CCl_4 to a solvent like 1,1,1-trichloroethane (TCE), measured enthalpies of hydrogen-bond complexation no longer have the same meaning. And this obtains even when calorimetrically determined ΔH° values are used, let alone van't Hoff enthalpies. Hence it must be very much more difficult to generate a general hydrogen-bond acidity scale based on ΔH° than on ΔG° .

The results of Hillier indicated that polar solvents interact with the proton donors (i.e. the phenols) producing large effects on ΔH° . Prior then referred to work carried out jointly by ICI Pharmaceuticals and the University of Surrey that confirmed experimentally the theoretical results of Hillier - on transfer from CCl_4 to TCE there were large changes in enthalpies of transfer of the phenols themselves with change in substituent, but little such effect on the phenol/NMP complexes.

THE HYDROGEN BONDING BASICITY OF OXYGEN AND SULPHUR COMPOUNDS

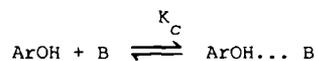
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The hydrogen-bonding (H.B.) basicity parameters, β_m , for various "monomeric" alcohols and thiols as well as for a variety of carbonyl and thiocarbonyl amphiprotic bases have been determined. Also determined were the H.B. basicity parameters, β , for a series of aprotic carbonyl and thiocarbonyl bases ($\beta_m = \beta$ for these materials). The analysis of the data for a set of 62 compounds provides the basis for a comparison of structural effects on the H.B. basicity of oxygen and sulphur bases.

In general, the H.B. basicity of sulphur bases is lower than that of their oxygen homologues. Within families, structural effects on the basicity of oxygen and sulphur bases are proportional. Our results show the contributions from polarizability, field/inductive and resonance effects to the basicity of these compounds. Also, some differential contributions from steric hindrance and hybridization changes have been singled out.

The β_m values have been obtained from the equilibrium constants, K_c pertaining to the formation of 1:1 complexes between these bases and phenols (ArOH):



in CCl_4 and/or cyclohexane.

The relationship between β_m and K_c is as follows:

$$\log K_c = a + b.\beta_m + c.\mu$$

where a , b and c are constants and μ stands for the molecular dipole moment of the base. Data for 3,4-dinitrophenol (1) in C_6H_{12} at 23.3°C, phenol (2), 4-fluorophenol (3) and *p*-chlorophenol (4) in CCl_4 at 25°C have been used.

The analysis of the β_m values shows that in the case of amphiprotic thioamides, cyclic 1:1 complexes between these bases and p-chlorophenol can be formed. It is then possible to decompose the apparent β_m values in two terms: one, β_{tr} , reflects the "true" (intrinsic) basicity of the thiocarbonyl group, while the other, β_{cyc} , provides a measure of the relative stability of the cyclic structures.

DISCUSSION ON ABBOUD'S LECTURE

In the lecture, Abboud had shown that complexing constants in CCl_4 , as $\log K$, could be correlated through a simple plot against $\alpha_2 \cdot \beta_2$ where the latter represent the solute hydrogen-bond acidity and basicity. Prior noted that the plot seemed to include acid/base combinations such as pyridine/chloroform that were now known through the work of Maria and Gal to lie outside the general applicability of such plots. Abboud replied that the error in the predicted $\log K$ values was only around 0.07 log units, but Prior felt that in any extended application of the $\alpha_2 \cdot \beta_2$ equation, careful attention must be given to acid/base combinations that are known to be irregular.

A SCALE OF SOLVENT HYDROGEN-BOND BASICITY USING ONLY SOLVATOCHROMIC MEASUREMENTS

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The original solvent solvatochromic β scale of Kamlet and Taft¹ has been used in the correlation and prediction of a large number of solvent effects. More recently, β values for nonassociated compounds have been used in the construction of a solute hydrogen-bond basicity scale, it being assumed that for such nonassociated compounds solute and solvent hydrogen-bond basicity can be put on the same (β) scale². In order to test such an assumption it is necessary to compare two separate sets of hydrogen-bond basicities, (a) derived only from solvent properties, and (b) derived only from solute properties. Although a set of solute hydrogen-bond basicities is now available, obtained from log K values for hydrogen-bond complexation of monomeric solutes with reference bases in CCl_4 ,³ there is no set of solvent values that has been obtained only from solvent properties. It should be noted that the original β scale was constructed from five properties, two of which were solvatochromic solvent properties, and three of which were actually solute properties.¹ It seemed therefore useful to attempt to construct a solvent β_1 scale based entirely on solvatochromic solvent properties, and then to compare such a scale with the already available solute hydrogen-bond basicity scale (denoted as β_2^H).

Following the work of Maria and Gal,⁴ it is evident that two basicity dependent properties will only show a family independent relationship if their Maria and Gal θ -values are the same, or nearly the same. Hence a match between any solvent β_1 solvatochromic scale and the solute β_2^H scale is only possible if the β_1 scale leads to a θ value of around 68° (the value corresponding to the general solute β_2^H scale). Now it is already known⁴ that the solvatochromic indicator (4-nitrophenol/4-nitroanisole) leads to a value of only 2° , whereas the indicator (4-nitroaniline/4-nitrodimethylaniline) gives rise to a θ value of 66° . Hence for the purpose of matching solute and solvent β scales, the technically better indicator 4-nitrophenol cannot be used. Rather than basing our solvent scale on just one aniline indicator, we used a double regression method based on equation (1).

$$v(i) = v_o(i) + s.\pi_1^* + b.\beta_1 \quad (1)$$

We start with known values of π_1^* for the solvents concerned, and set up n equations of type (1), one for each indicator (note that results from two different workers using the same indicator are used to set up two separate equations). Results were available to yield β_1 values for 45 non associated solvents using eleven equations for ArNH_2 indicators, and to give β_1 values for 39 nonassociated solvents using seven equations for ArNHR indicators. In all cases, our β_1 scale was set with reference compounds cyclohexane (0.00), acetone (0.48), and HMPT (1.00). For consistency we calculated π_1^* values using only the results of Laurence and Nicolet⁵ on 4-nitroanisole and 4-nitrodimethylaniline. Values of π_1^* obtained using 4-nitroanisole gave extraordinary β_1 values from equation (1), and these π_1^* values were not further used. However, π_1^* values calculated from the indicator 4-nitrodimethylaniline yielded reasonable values of β_1 via equation (1) and we shall discuss only results using this latter indicator.

Our first finding is that β_1 values obtained using the ArNH_2 indicators differed from those using the N-alkylated ArNHR indicators. We analysed both sets of results using the Maria-Gal⁴ equation (2),

$$\text{BDP} = (\text{BDP})_o + S_1 F_1 + S_2 F_2 \quad (2)$$

For the same fourteen nonassociated solvent β_1 values, the resultant S_1 and S_2 values yielded θ values as follows: 71° (from ArNH_2 indicators), and 49° (from ArNHR indicators), as compared to a value of 68° using the same fourteen compounds as solutes in β_2^H . Hence there is little point in comparing β_1 (ArNHR) with β_2^H , but it is possible the β_1 (ArNH_2) is essentially the same scale as β_2^H . Some comparisons are made in Table 1.

It can be seen from these, and other values that the two β scales are, indeed, virtually identical - thus demonstrating that for nonassociated compounds the solvatochromic β_1 (ArNH_2) solvent scale can be matched to the hydrogen-bond β_2^H solute scale. However, there are a number of exceptions, the most outstanding being acetonitrile (0.30, 0.44) and tri-n-butylamine (0.42, 0.59). Even granted an error in β_1 (ArNH_2) of around 0.05, these β_1 (ArNH_2) values are much too low.

Table 1. A COMPARISON OF SOLVENT β_1 (ArNH_2) AND SOLUTE β_2^{H} VALUES

compound	β_1 (ArNH_2)	β_2^{H}
chlorobenzene	0.09	0.13
toluene	0.15	0.15
1-bromobutane	0.14	0.20
anisole	0.23	0.27
diethylether	0.42	0.44
acetone	0.48	0.49
DMSO	0.76	0.77
HMPT	1.00	1.00
pyridine	0.63	0.62
triethylamine	0.54	0.66

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2. M.J. Kamlet, R.M. Doherty, J.-L. M. Abboud, M.H. Abraham, and R.W. Taft, *Chem. Tech.*, 1986, 566.
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4. P.-C. Maria, J.-F. Gal, J. de Franceschi, and E. Fargin, *J. Am. Chem. Soc.*, 1987, 109, 483.
5. P. Nicolet and C. Laurence, *J. Chem. Soc. Perkin Trans. II*, 1986, 1071; C. Laurence, P. Nicolet and M. Helbert, *J. Chem. Soc. Perkin Trans. II*, 1986, 1081.

GENERAL DISCUSSION

Throughout the discussion, considerable use was made of the results of Maria and Gal et al.^{1,2} who had analysed various basicity dependent properties, BDP, in terms of the principal component parameters F_1 and F_2 , obtained from multivariate analysis of different kinds of basicity.

$$\text{BDP} = (\text{BDP})_0 + S_1 F_1 + S_2 F_2 \quad (1)$$

Here, F_1 and F_2 characterise a number of bases, and the constants $(\text{BDP})_0$, S_1 and S_2 are obtained by multiple linear regression of some BDP against F_1 and F_2 . Then S_1 and S_2 are used to define an angle $\theta = \tan^{-1} (S_2/S_1)$ that reflects the relative electrostatic: covalent ratio in the complexes of the series of bases against the reference acid used to establish the BDP. The importance of the angle θ is that two BDP's will only be linear with each other (i.e. will show family independent characteristics) if their respective θ values are the same, or nearly the same. Some values of θ for various BDP's are given in Table 1.

Table 1. Maria - Gal θ values

$-\Delta\Delta v$ (4-nitroaniline, 4-nitrodimethylaniline)	66
$-\Delta\Delta v$ (4-nitrophenol, 4-nitroanisole)	2
logK against 4-nitrophenol in CCl_4	67
logK against 4-fluorophenol in CCl_4	70
logK against phenol in CCl_4	67
logK against ethanol in CCl_4	67
logK against water in CCl_4	69

Another topic that influenced the general discussion considerably was that of methodology. Laurence argued that the best method of setting up any particular scale was to select a given reference compound as a primary standard. Thus if a solute scale of hydrogen-bond basicity is to be constructed, one given acid (suggested to be 4-fluorophenol) should be used as the primary standard. Both Prior and Abraham replied against this view. Prior pointed out that if such a method was adopted, any errors in the initial results with the primary standard could not be rectified.

Abraham claimed that such a method did not make use of all the available data, and that a much better method was the matrix method, in which a series of equations using (in the present example) results for bases against a number of acids is solved by an iterative method.

A possible resolution of this argument is as follows. If it is quite clear that for some technical reason one particular reference compound is much better than any other reference compound, then the methodology preferred by Laurence should be used. On the other hand, if there is no technical reason for choosing one particular reference compound out of a number of possible reference compounds, then the methodology advocated by Prior and by Abraham should be used.

Scales of solute hydrogen-bond acidity and basicity

Three scales of solute hydrogen-bond acidity were described at the workshop, (1) the general matrix-generated scale of the University of Surrey/ICI Group described by Prior, (2) the special scale of Abboud using the reference system pyridine-N-oxide/cyclohexane, and (3) the special scale of Taylor and Morris using the reference system NMP/TCE. Taylor pointed out that the latter scale (pK_a) was used exclusively in QSAR work, and that the relationship between pK_a and Prior's scale had yet to be worked out; there should be no confusion between the two scales and, indeed, ICI would use Prior's scale for general (non-QSAR) purposes.

Unlike the construction of a solute hydrogen-bond acidity scale, that of a solute hydrogen-bond basicity scale can logically be based on the results of Maria and Gal.^{1,2} Nearly all the use of multiple regression analysis via equations (2) and (3) in the introduction is concerned with solute bases hydrogen-bonded to oxygen acids, for example water, octanol, octanol/water, ethylene glycol, etc. Now all these acids give rise to Maria-Gal θ values of around 60-70°, and hence the reference acid or acids used in the construction of a solute hydrogen-bond basicity scale should lead also to a similar θ value. If not, then some extra parameter will be needed to match up the derived scale to the experimental values to be analysed - an inconvenient procedure, to say the least. In the event, two scales were described, each giving rise to suitably useful θ values. Laurence advocated a scale tied exclusively to 4-fluorophenol as a reference

acid in CCl_4 ; using $\log K$ values for hydrogen-bond complexation a θ value of 70° is found. Prior put forward a general scale, again using $\log K$ values for hydrogen-bond complexation in CCl_4 , but now generated from a large number of reference acids by the matrix method. This scale gives rise to a θ value of 68° so that for practical purposes, as pointed out by Abraham, the two scales are almost equivalent.

It was agreed that Laurence and Abraham would investigate the possibility of setting up just one solute hydrogen-bond basicity scale, using $\log K$ values for complexation in CCl_4 . Following any firm decision would be subsequent possible work on secondary (non-thermodynamic) processes that might conceivably be matched to the above solute scale.

Scales of solvent hydrogen-bond acidity and basicity

There was practically no discussion on solvent acidity scales, but considerable argument over solvent basicity scales. Abraham, McGill, and Grellier had shown by the matrix method that it was possible to construct a purely solvatochromic solvent hydrogen-bond basicity scale for nonassociated compounds using aniline (ArNH_2) indicators. This scale gave a θ value of 71° , quite close to the θ value for the solute scale described by Prior (68°). Although there were rather large error limits for the solvent scale, the solvent and solute scales could be reasonably well matched and, indeed, could be matched to the β scale used by Kamlet for nonassociated compounds.

Laurence argued strongly that any solvent β scale should be based on 4-nitrophenol indicator and not on aniline indicators, since 4-nitrophenol was technically by far the best indicator to use (because there is less fine structure, the peak maximum is much easier to locate, and the peak shape is more Gaussian). Furthermore, use of 4-nitrophenol indicator enables much more accurate β values to be obtained for solvents water and alcohols. Of course, use of only 4-nitrophenol means that the homomorphism method has to be used, using 4-nitroanisole, but Laurence argued that this "one-indicator" method was still technically the best method.

Abraham pointed out that because the 4-nitrophenol indicator gives rise to $\theta = 2^\circ$ (see Table), whereas ArNH_2 indicators lead to a θ value of 71° , a solvent basicity scale using 4-nitrophenol indicator would show family dependencies against a solvent basicity scale using

ArNH_2 indicators (and for nonassociated compounds similar family dependencies against the general solute scale described by Prior). Sasson asked whether the difference in the two solvent scales was large enough to reverse the order of solvent basicity, and Prior replied that that was indeed the case. McGill pointed out that because of overlapping peaks, 4-nitrophenol could not be used with all solvents, so that ArNH_2 indicators would still have to be used as secondary standards. Shuely suggested that in future, solvent basicity scales with $\theta = 2^\circ$ and with $\theta = 70^\circ$ might both be needed, depending on the process to be studied; Gal agreed, citing proton transfer as a case in point. Abboud then attempted to resolve the problem by the suggestion that if a primary solvent basicity scale was constructed using the homomorphism method with 4-nitrophenol/4-nitroanisole, transfer rules could be set up (e.g. by use of the Kamlet/Taft ξ parameter) to convert this scale with $\theta = 2$ to the secondary solvent basicity scale with $\theta = 68^\circ$. It was agreed that Laurence would set up such a primary scale and that Abboud and Abraham in conjunction with Kamlet, Doherty, and Taft would attempt to convert the scale, through transfer rules as outlined above, to a solvent basicity scale giving rise to θ around 70° .

Finally, it should be noted that indicators of type ArNHR give rise to a solvent basicity scale with θ of about 49° . Abboud suggested that ArNHR indicators were technically better than ArNH_2 indicators. Abraham pointed out that a solvent hydrogen-bond basicity scale using ArNHR indicators would still show family dependences against the ArNH_2 established scale, and Laurence noted again that 4-nitrophenol indicator was to be preferred over the ArNHR indicators so that use of the ArNHR indicators would still give rise to the difficulties mentioned previously with the ArNH_2 indicators.

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