Table VI. Values of m' and b Parameters of Equation 2

Solvent	m'	b
$c\text{-}C_6H_{12}$	1.21	−1.21
CCl_4	1.25	−1.28
C_6H_5Cl	1.17	−0.75
$o\text{-}C_6H_4Cl_2$	1.33	−1.16
$Cl(CH_2)_2Cl$	1.43	−1.63
CH_2Cl_2	1.25	−1.50

Table VII. Values of the m'' Parameter of Equation 3

Solvent	m''
$c\text{-}C_6H_{12}$	1.08
CCl_4	(1.00)
C_6H_5Cl	1.00
$o\text{-}C_6H_4Cl_2$	0.81
$Cl(CH_2)_2Cl$	0.76
CH_2Cl_2	0.80

Δ value than that expected by eq 3 might be the result of interaction between the negative phenolic oxygen and the positive sulfur of the DMSO in the hydrogen-bonded complex. This interaction, which would increase log K_f and decrease the Δ value as observed, would also be expected to "fade away" with increased solvent polarity. Decreasing self-association of DMSO in solvents of greater polarity may be an alternate explanation for this observation. However, it is difficult with this explanation to see why the self-association should always lead to decreased apparent values of Δ and increased apparent values of log K_f. No evidence of the effects of self-association has been obtained as a concentration dependence on K_f values.[4,6]

Table VI gives the m' and b constants obtained with the use of eq 2. Table VII gives values of the m'' coefficients of eq 3. The mean value of m' for all six aprotic solvents is 1.27 ± 0.07. The individual values adhere very well to this mean. The somewhat higher value obtained in 1,2-dichloroethane is probably not significant. Values of the intercept, b, in eq 2 show no recognizable pattern of behavior. The m'' values of Table VII show the same general behavior as the m values of eq 1 (*cf.* Table III), *i.e.*, decrease with increasing solvent polarity. All of the Δ *vs.* Δ_{CCl_4} plots pass through the origin, except for the solvent chlorobenzene. In this solvent an intercept of −0.52 is obtained, which apparently reflects some constant magnetic contribution to the Δ values in this solvent. In general, however, the very similar pattern of behavior of m and m'' values, as well as the nearly constant value of m', support the use of F nmr shielding parameters as a free-energy measure (*cf.* eq 2).

Summary

Linear free-energy relationships in the form of eq 1 describe generally the effects of aprotic polar solvents on the formation of hydrogen-bonded complexes of p-fluorophenol with weak pK_A bases. Both m and c values in eq 1 tend to decrease with increasing solvent polarity. Similar linear relationships are found for the F nmr shifts, Δ, eq 3. The effects of aprotic polar solvents on Δ values are correlated well by the corresponding log K_f values, eq 2. The essentially constant value of m' (1.27 ± 0.07) in eq 2 indicates, as previously found, that about 1.8 kcal in the standard free-energy charge corresponds to 1.0 ppm in the F nmr shift in hydrogen-bonded complex formation with $p\text{-}C_6H_4OH$. Strong bases (amines and pyridines) are found to give positive deviations from eq 1 and 3. The deviations increase in magnitude with increasing pK_A of the base and with increasing polarity of the aprotic solvent. Solvent-induced partial ionization in the hydrogen-bonded complexes of these strong pK_A bases is considered to permit the complex to more favorably compete with the free acid and base in solvation by the aprotic polar solvent.

Hydrogen-Bonded Complex Formation with 5-Fluoroindole. Applications of the pK_{HB} Scale[1]

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Abstract: The formation of the hydrogen-bonded complexes of 5-fluoroindole with 27 bases of widely differing types have been studied in CCl_4 at 25° using F nmr and ir methods. The formation constants, K_f, and F nmr shifts, Δ, for this N–H proton donor are found to correlate satisfactorily with the pK_{HB} scale, which is based upon the reference acid, $p\text{-}FC_6H_4OH$. Other generalized correlations with the pK_{HB} scale are summarized.

Linear free-energy relationships were shown recently to have broad applicability in the formation of hydrogen-bonded complexes of various OH reference acids.[2] A scale of proton acceptor strengths in hydrogen-bonded complex formation based upon p-fluorophenol in CCl_4 solution was defined as the pK_{HB} parameter and values of this parameter for numerous bases were tabulated. The pK_{HB} scale bears little or

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(1) This work was supported in part by the Public Health Service, Project No. GM14078.

(2) R. W. Taft, D. Gurka, L. Joris, P. von R. Schleyer, and J. W. Rakshys, *J. Amer. Chem. Soc.*, **91**, 4801 (1969).

no relationship to aqueous pK_A values for the various organic functional groups. However, a generally satisfactory correlation was found[3] between pK_{HB} values and the fluorine nuclear magnetic resonance (F nmr) shift, Δ, for formation of the complex with p-FC_6H_4OH.

The pK_{HB}–Δ correlation has been interpreted as indicating that the strength of the hydrogen-bonding interaction (as measured by the standard free-energy change) is determined, approximately, by the available electron density at the site of complexing in the free base.[3] Evidently, the electron density environment of the proton in the hydrogen-bonded complexes involves a very different scale of base strengths than that experienced by the proton in the conjugate acids of the bases.[4]

In the present study, the applicability of the pK_{HB} scale to an N–H proton donor has been investigated. The results are of interest in connection with biological systems, *e.g.*, the nucleic acids. Values of the formation constants, K_f, in carbon tetrachloride solutions at 25°, and Δ values have been obtained for 5-fluoroindole by application of the previously described F nmr method.[3] Formation constants have also been obtained by application of the ir method[5] and are found to be in satisfactory accord with the values obtained by F nmr. The bases chosen for study with 5-fluoroindole represent a substantial number of different nitrogen and oxygen base functions and their substituted members.

The Δ values for 5-fluoroindole are well correlated by pK_{HB} values[2] (for p-FC_6H_4OH). The values of log K_f for 5-fluoroindole also are correlated by pK_{HB} values but the correlation is limited by base type. This behavior is discussed and interpretations are suggested. In this paper generalized correlations with pK_{HB} have been extended and summarized.

Experimental Section

5-Fluoroindole. This was obtained from the Aldrich Chemical Co. and was freshly sublimed before use, mp 42–43°. ***N*-Methyl-5-fluoroindole** was prepared by methylation with methyl iodide of the conjugate base formed in $NaNH_2$–NH_3. Bases, solvent, and solutions were prepared for use as previously described.[3,5]

F Nmr Method. The same procedure as described for p-FC_6H_4OH was employed with 5-fluoroindole.[3] The observed time-averaged shifts were obtained using 0.01 *M* *N*-methyl-5-fluoroindole as the internal reference standard. The signal for this latter compound in CCl_4 is upfield by 0.76 ppm from that for free 5-fluoroindole (0.01 *M*). The 5-fluoroindole is upfield 11.80 ppm from internal fluorobenzene.

For weak complexes, concentrations of base covering the approximate range 0.05–0.50 *M* were used. For stronger complexes, the concentration range was approximately 0.01–0.20 *M*. With HMPA, 0.001–0.04 *M* solutions were used. These concentrations gave rise to a range of shifts of from about 0.2 to 1.0 ppm (or greater). The observed shifts were fitted to eq 1 of ref 3 by the previously described computer program to obtain values of K_f and Δ. Fittings were of excellent quality, with no evidence of a concentration effect on either of the latter parameters. The generally good accord between the K_f values (*cf.* Table I) obtained by the F nmr and ir methods supports the accuracy of K_f values to a precision of about ±15%.

Ir Method. The same procedure was followed as reported previously for p-FC_6H_4OH.[5] A Perkin-Elmer Model 521 double beam grating spectrophotometer was used with the 1-cm jacketed cell previously described.[5] The N–H stretching frequency of 5-fluoroindole in CCl_4 is at 3495 cm^{-1}. Some unidentified minor absorption occurred at *ca.* 3470 cm^{-1}. However, the absorption of the 5-fluoroindole at 3495 cm^{-1} follows Beer's law in the concentration range 0.0003–0.003 *M*. Using approximately 0.0015 *M* 5-fluoroindole in all experiments, no systematic variation in the value of K_f was found for any of the bases. With weak complexes, the range of base concentrations used was 0.03–0.30 *M*, whereas for the stronger complexes 0.01–0.10 ranges (or smaller) were used.

Table I. Summary of Results

	Base	F nmr, K_f	Ir, K_f	Log K_f[a]	Δ, ppm
1.	Hexamethylphosphoramide	225	213	2.31	2.09
2.	Triphenylphosphine oxide		112	2.05	
3.	*sym*-Tetramethylguanidine	46	45.2	1.65	1.94
4.	Trimethyl phosphate	32	31.1	1.49	1.49
5.	Dimethyl sulfoxide	32	30.6	1.49	1.48
6.	*N*,*N*-Dimethylacetamide	30	29.3	1.47	1.59
7.	Tetramethylurea	30	26.3	1.43	1.60
8.	4-Dimethylaminopyridine	29	25.1	1.41	1.75
9.	*N*,*N*-Dimethylformamide	19.5	17.5	1.25	1.42
10.	Diphenyl sulfoxide		15.5	1.19	
11.	*N*,*N*-Dimethylchloroacetamide	9.0	12.1	1.06	1.15
12.	Quinuclidine	6.1		0.79	1.54
13.	Cyclohexanone	5.3	5.6	0.75	1.04
14.	Pyridine	5.7	5.6	0.75	1.18
15.	*N*,*N*-Dimethylcyclohexylamine		5.4	0.73	
16.	DABCO		5.4[b]	0.73	
17.	*p*-Methoxyacetophenone		5.3	0.72	
18.	Triethylamine	3.7	3.3	0.53	1.32
19.	Benzaldehyde		2.7	0.43	
20.	Tri-*n*-butylamine	2.6	2.7	0.42	1.17
21.	3-Bromopyridine	2.0	2.7	0.42	0.90
22.	Benzonitrile		2.2	0.35	
23.	Tetrahydrofuran	2.9	2.2	0.34	1.01
24.	Diethyl ether		1.71	0.23	
25.	*N*,*N*-Dimethylaniline		1.47	0.17	
26.	Triallylamine		1.38	0.14	
27.	3,5-Dichloropyridine		0.97	−0.01	

[a] Selected best value. [b] Statistical correction has been applied.

Results

Values of K_f and F nmr Δ values obtained for 27 bases with 5-fluoroindole in CCl_4 at 25° are summarized in Table I. The Δ value for complete ionization of 5-fluoroindole (the anion is obtained with NaH in HMPA) is ~9.0 ppm. Consequently all of the Δ values of Table I correspond to an apparent per cent proton transfer[6] (<20%) which is characterized by only hydrogen-bonded complex formation. That is, no measurable extent of ionization is found.

Discussion

In Figure 1 are shown the log K_f values for 5-fluoroindole plotted *vs.* pK_{HB} (for p-FC_6H_4OH) in CCl_4 at 25°. Figure 2 shows a similar figure for the F nmr Δ values for 5-fluoroindole plotted *vs.* pK_{HB} values. Both plots display satisfactorily linear relationships. However, the log K_f plot is limited by base type, whereas the Δ plot appears as a single general linear relationship. In the former (Figure 1) the results may be described by three essentially parallel lines: the upper line for carbonyl and oxide bases, the middle line for pyridines and tetramethylguanidine, and the lower line for tertiary aliphatic amines. Not shown in Figure 1 are the results for diethyl ether and tetrahydrofuran, which

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(3) D. Gurka and R. W. Taft, *J. Amer. Chem. Soc.*, **91**, 4794 (1969).

(4) H. B. Yang and R. W. Taft, *ibid.*, **93**, 1310 (1971).

(5) E. M. Arnett, L. Joris, E. Mitchell, T. S. S. R. Murty, T. M. Gorrie, and P. von R. Schleyer, *ibid.*, **92**, 2365 (1970).

(6) D. Gurka, R. W. Taft, L. Joris, and P. von R. Schleyer, *ibid.*, **89**, 5957 (1967).

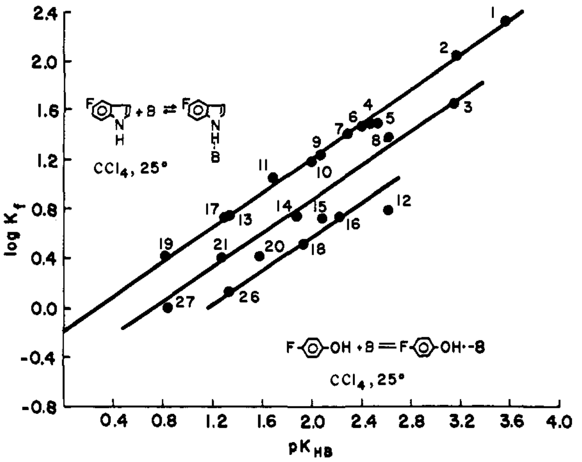

Figure 1. Limited linear free-energy relationship for formation of hydrogen-bonded complexes of 5-fluoroindole and *p*-fluorophenol: ordinate, log K_f, 4-fluoroindole, CCl_4, 25°; abscissa, log $K_f \equiv pK_{HB}$, $p\text{-}FC_6H_4OH$, CCl_4, 25°. Numbers refer to bases as listed in Table I. The upper line represents carbonyl and oxide bases, the middle line pyridine and quanidine bases, and the lower line tertiary aliphatic amine bases.

fall close to the pyridine family line; benzonitrile, which falls close to the oxide line; and *N*,*N*-dimethylaniline, which does not fall near any of these family lines. The line separations are not large, amounting to 0.6 log unit between the upper and lower lines.

The qualitative family behavior found in Figure 1 is reminiscent of similar behavior in plots of aqueous pK_A values for bases *vs.* pK_{HB} values[2] or of ir $\Delta\nu_{NH}$ shifts for hydrogen-bonded complex formation with pyrrole *vs.* corresponding $\Delta\nu_{OH}$ shifts for the methanol complexes.[7] However, in view of the single linear relationship of Figure 2 it seems very unlikely these three examples of family linear relationships have a common origin. It has been demonstrated in the work with $p\text{-}FC_6H_4OH$ that K_f values are much more sensitive to the steric requirements of the base than are the corresponding F nmr Δ values.[3] For example, pK_{HB} and Δ values, respectivly, both decrease in the sequence quinuclidine[8] (2.63, 2.96), triethylamine (1.93, 2.66), and tri-*n*-butylamine (1.57, 2.50), with the greater dependence of log K_f values on increasing steric requirements clearly evident. While the quinuclidine point falls on the general linear correlation between log K_f *vs.* Δ, the triethyl- and tri-*n*-butylamine points show increasing deviations.[3]

The scatter of tertiary aliphatic amine points along the amine family line of Figure 1 does not correspond, however, to the steric requirements of the base. Consequently, we believe the three family lines of Figure 1 do not originate with steric requirements of the bases, at least as usually considered. The origin could, however, result from a steric entropy effect[9] (as opposed to a potential energy effect) associated with characteristic bond lengths for each class of hydrogen bond framework, *i.e.*, different for each type, $OH\text{---}O_{oxide}$, $OH\text{---}N_{ar}$, and $OH\text{---}N_{aliph}$. The notion that there is no potential energy effect giving rise to the separate family lines of Figure 1 is supported not only by the single linear relationship of Figure 2 (the root-mean-square deviation of points is 0.07 ppm and the ratio of this deviation to the root-mean-square of the data points is 4.7%), but by a single linear relationship between Δ values for 5-fluoroindole and corresponding Δ values for $p\text{-}FC_6H_4OH$. This plot (not shown) gives a single regression line of slope 0.61, with points scattering over a breadth of about 0.2 ppm for a range of $p\text{-}FC_6H_4OH$ Δ values of nearly 2.0 ppm. The slope is essentially the same as that of the family line of Figure 1, *i.e.*, approximately 0.70.

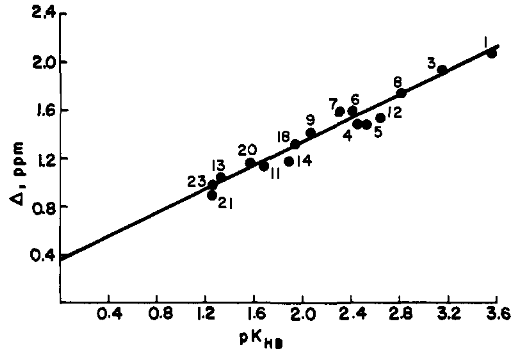

Figure 2. Correlation of F nmr shifts for hydrogen-bonded complex formation with 5-fluoroindole with pK_{HB} parameters: ordinate, Δ, ppm; abscissa, pK_{HB}. Numbers refer to bases as listed in Table I.

In accord with these results, the linear SEE relationship[3] for 5-fluoroindole, *i.e.*, the plot (not shown) of log K_f *vs.* corresponding Δ values, takes the same form as Figure 1. That is, the results may be described as three essentially parallel lines for families of carbonyl and oxide bases, pyridine and guanidine bases, and tertiary aliphatic amine bases with a slope essentially identical with that observed[8] for the OH proton donor $p\text{-}FC_6H_4OH$, in both polar and nonpolar aprotic solvents.

We conclude that the potential energy effects in the formation of N–H hydrogen-bonded complexes of 5-fluoroindole, as apparently measured by F nmr Δ values or by the contributions to $\Delta G°$ values, follow the same scale of base strengths as that for O–H proton donors, *i.e.*, the pK_{HB} scale.

Generalized correlations with pK_{HB} values, eq 1, have been extended and are summarized in Table II. The correlations given in Table II are in addition to the previously reported correlations of log K_f values for 1:1 complex formation between bases and various OH reference acids in CCl_4.[2,10]

$$P = m(pK)_{HB} + c \qquad (1)$$

where P = parameters correlated, as listed in Table II. Values of m, c, SD, and $f \equiv$ SD/RMS (where SD = the standard deviation and RMS = the root-mean-square of the data points) for these correlations are given in Table II. Also included in Table II is a listing of the bases included in each correlation by eq 1 and the literature references.

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[7] L. J. Bellamy and R. J. Pace, *Spectrochim. Acta, Sect. A*, 25, 319 (1969).

[8] L. Joris, J. Mitsky, and R. W. Taft, *J. Amer. Chem. Soc.*, 94, 3438 (1972).

[9] R. W. Taft in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., Wiley, New York, N. Y., 1956, p 652.

[10] Correlation of K_f values for $p\text{-}C_6H_4OH$ and various bases in polar aprotic solvents is reported separately; *cf.* ref 8.

Table II. Correlations with pK_{HB} Parameters

	Parameters correlated by eq 1	m	c	SD	f	Bases[a]
1.	L_s, F nmr pure solvent shifts for alkyl and aryl *p*-fluorophenyl onium ions[b]	0.895	2.20	0.13	0.030	1,4,5,6,7,9,14,28
2.	pK_s, solubility parameters for $(C_6H_5)_4As^+B(C_6H_5)_4^-$[c]	−0.805	−2.92	0.29	0.060	1,5,6,9,28
3.	Δ, F nmr shifts for H-bonded complex formation with 5-fluoroindole, CCl_4, 25°[d]	0.489	0.35	0.07	0.047	1,3,4,5,6,7,8,9,11,12, 13,14,18,20,21,23
4.	Log K_f, H-bonded complex formation with HNCO, CCl_4, 25°[e]	0.816	−0.03	0.03	0.028	14,23,24,28,35
5.	ΔJ_{HSn}, coupling constant shift for formation of complex with Me_3SnCl, pure base[f]	3.096	3.62	0.70	0.072	1,5,6,14,28,29,31
6.	$-\Delta H_f$, complex formation with Me_3SnCl, CCl_4, 26°[g]	1.903	3.28	0.22	0.030	1,5,6,14,28,29
7.	$-\Delta H_f$, H-bonded complex formation with *p*-FC_6H_4OH, CCl_4, 25°[h]	1.297	4.06	0.67	0.106	1,2,8,10,13,14,21,23, 25,30,34,36,37,38
8.	$-\Delta H_f$, H-bonded complex formation with HNCO, CCl_4, 25°[i]	1.590	2.25	0.25	0.063	9,14,24,28,35
9.	$-\Delta H_f$, H-bonded complex formation with HNCS, CCl_4, 25°[j]	2.462	3.33	0.55	0.107	23,24,28,31,35,39,40
10.	$-\Delta H_f$, H-bonded complex formation with C_6H_5OH, pure base[h]	1.931	3.33	0.69	0.107	5,6,9,14,18,23,24,30, 32,34,36,37,41
11.	Drago E_B parameters[k]	0.275	0.64	0.12	0.108	5,6,7,9,14,18,23,24, 28,30,31,32,33

[a] Numbers designate base as listed in Table I. Additional bases are numbered as follows: 28, acetonitrile; 29, acetone; 30, 1,4-dioxane; 31, diethyl sulfide; 32, ethyl acetate; 33, pyridine *N*-oxide; 34, di-*tert*-butyl sulfide; 36, anisole; 37, dibenzyl ether; 38, cyclopropylamine; 39, di-*n*-butyl sulfide; 40, di-*n*-butyl ether; 41, 4-methylpyridine. [b] J. W. Rakshys, Jr., and R. W. Taft, Abstracts of Papers, 154th National Meeting of the American Chemical Society, Sept 1967, No. V-39; J. W. Rakshys, Jr., Ph.D. Thesis, University of California, Irvine, Calif., June 1967. [c] R. Alexander and A. J. Parker, *J. Amer. Chem. Soc.*, **89,** 5549 (1967). [d] This paper. [e] J. Nelson, *Spectrochim. Acta, Sect. A*, **26,** 337 (1970). [f] T. F. Bolles and R. S. Drago, *J. Amer. Chem. Soc.*, **88,** 5730 (1966). [g] T. F. Bolles and R. S. Drago, *ibid.*, **88,** 3921 (1966). [h] E. M. Arnett, L. Joris, E. Mitchell, T. S. S. R. Murty, T. M. Gorrie, and P. von R. Schleyer, *ibid.*, **92,** 2365 (1970). [i] J. Nelson, *Spectrochim. Acta, Sect. A*, **26,** 109 (1970). [j] T. M. Barakat, J. Nelson, S. M. Nelson, and A. D. E. Pullen, *Trans. Faraday Soc.*, **65,** 41 (1969). [k] R. S. Drago and B. B. Wayland, *J. Amer. Chem. Soc.*, **87**, 3571 (1965); the E_B parameters used were taken from a recent compilation; private communication from Professor R. S. Drago.

Summary

The log K_f values obtained in this study of hydrogen-bonded complex formation with 5-fluoroindole give three essentially parallel family base lines when plotted *vs.* pK_{HB} values. However, the corresponding F nmr Δ values are correlated satisfactorily by pK_{HB} values, eq 1, as a single general linear correlation. It is suggested that the family relationships in the former plot may originate from a steric entropy effect. Further generalized correlations with pK_{HB} values have been found and are summarized in Table II.

The wide variety of electron-pair donors and acceptors which follow eq 1 supports the idea that the pK_{HB} scale is applicable for relatively weak interactions (in contrast to strong covalent bond formation) between bases and a strongly shielded center of positive charge.[2] The inclusion of F nmr Δ values for both *p*-FC_6H_4OH[3] and 5-fluoroindole complexes (as well as the L_s values) supports the view that pK_{HB} values measure, approximately, the electron densities available to the strongly shielded centers of positive charge at the (only slightly perturbed) base center in the free base.