Studies of Hydrogen-Bonded Complex Formation with *p*-Fluorophenol. IV. The Fluorine Nuclear Magnetic Resonance Method[1]

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Abstract: Using 0.01 *M* *p*-$FC_6H_4OCH_3$ as an internal reference standard in CCl_4, the shielding effects of hydrogen-bonded complex formation of 0.01 *M* *p*-FC_6H_4OH have been evaluated quantitatively. Using this method and reference acid, the formation constant, K_f, and limiting F nmr shifts, Δ, for formation of the 1:1 hydrogen-bonded complex have been obtained for 62 bases of widely different structures in CCl_4 at 25°. Some additional formation constants have been obtained in CCl_4 at $-20°$. In general, the van't Hoff enthalpies of complex formation based upon K_f values at 25 and $-20°$ are in satisfactory accord with the calorimetric values obtained in the companion collaborative study. A linear relationship between corresponding values of log K_f and Δ is shown to apply with generally good precision, except for bases of large steric requirements. This empirical relationship provides evidence that the potential energy change in the formation of the hydrogen-bonded complex is approximately proportional to the standard free energy change. The F nmr Δ values are essentially independent of temperature in CCl_4 and are not increased in the polar solvent, $ClCH_2CH_2Cl$, indicating the formation of only hydrogen-bonded complexes (no appreciable contribution from the hydrogen-bonded ion pair, $FC_6H_4O^-$---^+HB). The Δ values are interpreted as showing that a small extent of proton transfer (apparent proton transfer = 10–30%) occurs in the hydrogen-bonded complexes of *p*-FC_6H_4OH. It has been conclusively established that the aqueous pK_A and the log K_f scales of base strengths for common functional groups are unrelated.

In this paper we report results from a collaborative effort to obtain definitive hydrogen-bond parameters. The reference acid, *p*-fluorophenol, was selected for study in hydrogen-bonded complex formation with general bases in very dilute carbon tetrachloride solutions using three methods of investigation: fluorine nuclear magnetic resonance spectroscopy (F nmr), infrared spectroscopy (ir), and calorimetric determinations. Preliminary results of this collaborative work have been communicated.[2,3] The F nmr method is described in detail and the results of its application to 62 bases of widely varying structure are reported herein.

Two major objectives have been explored. First, the applicability of the linear electronic energy shielding (LSEE) relationship[4] to hydrogen-bond formation by *p*-FC_6H_4OH has been determined. Second, a detailed study has been carried out of the effects of molecular structure on base strength as measured by the formation constant of the 1:1 hydrogen-bonded complexes of *p*-FC_6H_4OH. The applicability and limitations of linear free energy and other structure–reactivity relationships to hydrogen-bonded complex formation have been determined. The results of this second major area of interest are reported in paper V of this series.[5]

A key issue in the development of the F nmr method for the present work was the choice of a proper reference standard for evaluating the intramolecular screening effects of hydrogen-bonded complex formation with *p*-FC_6H_4OH. Precise formation constants, K_f, for the 1:1 complex of base and *p*-FC_6H_4OH obtained by the ir method[6] were used to develop a definitive F nmr reference standard. We have found that up to base concentrations of 0.02 *M*, the effects of base on the shielding of 0.01 *M* *p*-FC_6H_4OH in CCl_4 relative to an external reference are (within the experimental error of ±0.02 ppm) due entirely to hydrogen-bonded complex formation. However, with base concentrations above 0.02 *M*, the shifts based upon the external and the internal reference (*cf.* Experimental Section) are measurably different. The shift relative to the external reference is due to contributions from H bonding and general F nmr medium effects.[7,8] Ideally, one would hope to find an internal reference having precisely the same F nmr medium effects (relative to external reference) as that of the *p*-fluorophenol. The F nmr shifts of *p*-fluorophenol measured relative to such an internal reference at base concentrations much larger than 0.02 *M* would then also be quantitative measures of the H-bonding shift.

The use of 0.01 *M* *p*-fluoroanisole as internal reference accomplishes this objective. Previous studies showed that the internal fluorobenzene standard nearly eliminates intermolecular F nmr medium effects and provides the intramolecular shielding effects of *meta* and *para* substituents.[8] Since the intramolecular screening effects of the OCH_3 and OH substituents are very similar, *p*-fluoroanisole is the logical selection for an internal reference which presents to the medium a *p*-F atom very nearly identical with that of *p*-fluorophenol and its hydrogen-bonded complexes. Since 0.01 *M* *p*-fluoroanisole is not expected to give (and the F nmr shielding results do not indicate any) chemical com-

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(2) E. M. Arnett, T. S. S. R. Murty, P. von R. Schleyer, and L. Joris, *J. Am. Chem. Soc.*, **89**, 5955 (1967); paper I of series.

(3) D. Gurka, R. W. Taft, L. Joris, and P. von R. Schleyer, *ibid.*, **89**, 5957 (1967); paper II of series.

(4) R. W. Taft and L. D. McKeever, *ibid.*, **87**, 2489 (1965); **88**, 4544 (1966); C. S. Giam and R. W. Taft, *ibid.*, **89**, 2397 (1967).

(5) R. W. Taft, D. Gurka, L. Joris, P. von R. Schleyer, and J. W. Rakshys, *ibid.*, **91**, 4801 (1969).

(6) E. M. Arnett, L. Joris, E. Mitchell, T. S. S. R. Murty, and P. von R. Schleyer, submitted for publication; paper III of series.

(7) (a) D. F. Evans, *J. Chem. Soc.*, 877 (1960); (b) R. W. Glick and S. Ehrenson, *J. Phys. Chem.*, **62**, 1599 (1958).

(8) R. W. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Andersen, and G. T. Davis, *J. Am. Chem. Soc.*, **85**, 709, 3146 (1963).

binations with any of the bases employed or with the 0.01 *M* p-FC_6H_4OH, the use of this internal reference provides quantitative shifts which satisfy the hydrogen-bonded complex formation equilibrium expression (*cf.* eq 1 following section) up to relatively high base concentrations.

Calorimetric and ir studies by our collaborators show that p-FC_6H_4OH is negligibly self-associated in CCl_4 solutions at the concentrations employed (~0.01 *M*) in this study.[6] They also find that *p*-fluoroanisole is a satisfactory reference for the determination of calorimetric heats of hydrogen-bonded complex formation of p-FC_6H_4OH.[2,6]

Experimental Section

Materials. Carbon tetrachloride and all liquid bases were distilled from calcium hydride immediately before use. Solid bases were recrystallized two to three times until agreement with literature melting points was obtained. *p*-Fluorophenol was sublimed just before use and immediately transferred to purified carbon tetrachloride. All bases used were obtained commercially except those given below. Samples of triphenylphosphine oxide and *p*-nitrophenyl methyl sulfoxide were obtained from Dr. J. R. Rakshys and Professor K. K. Andersen, respectively. N,N-Dimethyltrifluoroacetamide was prepared by the procedure of Bissel and Finger.[9] Di-*t*-butyl ether was prepared by the procedure of Erickson and Ashton.[10] Phenyl methyl sulfoxide was prepared by the procedure of Leonard and Johnson.[11] N,N-Dimethyl-*p*-nitrobenzamide (mp 95–97°; lit.[12] 93–95°) and N,N-dimethyl-α-chloroacetamide (bp 65° (1 mm)) were prepared by the reactions of *p*-nitrobenzoyl chloride and α-chloroacetyl chloride, respectively, with dimethylamine in dry ether.

Apparatus. All spectra were obtained on a Varian HA-60 spectrometer equipped with a Varian 1024 computer of average transients (CAT) and NMR Specialties heteronuclear decoupler, Model SD60-B. The temperature was maintained at either −20 or 25° using the temperature-control probe.

All measurements were made with solutions of purified carbon tetrachloride containing 0.01 *M* p-FC_6H_4OH and 0.01 *M* p-$FC_6H_4OCH_3$ (the internal reference). The nmr tubes contained an inserted capillary of 28 wt % 1,1,2,2-tetrafluoro-3,3,4,4-tetrachlorocyclobutane in CCl_4 as external reference. The ring protons were decoupled and about five CAT scans were employed for each "titration" point. The CAT recorder was calibrated to agree with direct read-out within ±1 cps. All spectra were run at a sweep width of 250 cps and a sweep time of 100 sec.

For base concentrations up to *ca.* 0.02 *M*, the same F nmr shifts, δ (±0.02 ppm), is obtained with either the internal or external references. From 0.02 to 0.7 *M* base only the internal reference gives satisfactory results (*cf.* following section).

Data Treatment

Equilibrium Expression. For the formation of a 1:1 hydrogen-bonded complex between p-FC_6H_4OH and general base, B, the following equilibrium expression applies.

$$p\text{-}FC_6H_4OH + B \rightleftharpoons p\text{-}FC_6H_4OH\text{---}B$$

The formation constant, K_f, is shown in eq 1 where

$$K_f = (\delta/\Delta)A_0/\{A_0[1 - (\delta/\Delta)]\}[B_0 - (\delta/\Delta)A_0] \quad (1)$$

A_0 = initial (total) p-FC_6H_4OH concentration, B_0 = initial (total) base concentration, and δ = the observed time-average F nmr shift in parts per million (ppm) for the equilibrium mixture relative to that for 0.01 *M* p-FC_6H_4OH in CCl_4. Unless otherwise specified the reference standard is internal 0.01 *M* p-$FC_6H_4OCH_3$. Δ = the limiting F nmr shift (ppm), *i.e.*, the shift of the completely formed complex relative to uncomplexed p-FC_6H_4OH.

Validity of Equilibrium Expression. When the value of K_f is known from an independent determination, *e.g.*, the ir method, eq 1 may be rigorously confirmed by the demonstration that the values of Δ calculated for each δ value are a precise constant, *i.e.*, independent of B_0. Alternatively, the observed and calculated values of δ at each base concentration over the range of 30–80% complex formation may be shown to be in agreement (to within the combined experimental errors), based upon the use of the best value of Δ. Using the K_f values provided by the collaborative work of Arnett, Murty, Schleyer, and Joris,[6] this condition was found to hold in every instance. Typical results are illustrated in Table I.

Table I. Typical Fits of F Nmr "Titration Curve" to Equilibrium Eq 1 at 25° in CCl_4

10^2A_0, *M*	10^2B_0, *M*	δ, ppm Obsd	δ, ppm Calcd
	N,N-Dimethylacetamide[a]		
1.126	0.408	0.71	0.70
1.052	0.782	1.22	1.25
0.126	0.816	1.25	1.28
1.052	1.174	1.62	1.62
1.126	1.223	1.65	1.66
1.052	1.565.	1.94	1.93
1.126	1.63	1.96	1.93
1.126	2.04	2.14	2.13
	Ethyl Acetate[b]		
0.934	2.52	0.40	0.40
0.934	4.20	0.59	0.59
0.934	8.40	0.90	0.90
0.934	12.59	1.08	1.09
0.934	16.8	1.22	1.22
0.934	21.0	1.33	1.31

[a] K_f = 242 ± 6; Δ = 2.86 ppm. [b] K_f = 12.0 ± 0.2; Δ = 1.85 ppm.

In view of its widely demonstrated applicability, eq 1 may also be accepted as valid for those bases for which an independent K_f value is not available. The evaluation of the K_f and Δ value for these bases from δ values observed over a range of 30–80% complex formation is described subsequently.

Validity of the Internal Reference. Identical shifts were observed up to 0.02 *M* concentrations of all bases with either the external reference or internal reference. Consequently, the demonstration of the validity of eq 1 with strong bases at concentrations less than 0.02 *M* shows rigorously that the shifts relative to external reference are due entirely to hydrogen-bonded complex formation (no F nmr medium effects). The data for N,N-dimethylacetamide in Table I are typical. Table II lists additional results for strong bases for which eq 1 holds at base concentrations less than 0.02 *M*. The precision of eq 1 is demonstrated by the precision of the Δ value obtained (Table II gives the mean value of $\Delta^{(\text{ext ref})}$ from Δ values calculated at each base concentration for the indicated range; deviations from the mean value are entirely random, showing no trends with B_0).

Table II also lists corresponding values of $\Delta^{(\text{int ref})}$ obtained from direct measurement using 0.01 *M* internal

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[9] E. R. Bissel and M. Finger, *J. Org. Chem.*, **24**, 1256 (1959).

[10] J. L. E. Erickson and W. H. Ashton, *J. Am. Chem. Soc.*, 63, 1769 (1941).

[11] N. J. Leonard and C. R. Johnson, *ibid.*, **84**, 3701 (1962).

[12] A. V. Kirsanov, *Zh. Obshch. Khim.*, **23**, 223 (1953); *Chem. Abstr.*, **48**, 2635*a* (1954).

Table II. Agreement between Calculated Δ Values from Measurements with Partial Conversion Using the External Reference and Observed Δ Values at 97–99% Conversion Using 0.01 *M* Internal p-$FC_6H_4OCH_3$

Base	10^2B_0, *M*	$K_f^{25°}$ (ir)	$\Delta_{calcd}^{(ext\ ref)}$	$\Delta_{obsd}^{(int\ ref)}$
Dimethyl sulfoxide	0.48–1.94	346 ± 8	2.70 ± 0.01	2.74 ± 0.02
2,6-Dimethyl-γ-pyrone	0.30–1.51	318 ± 18	3.07 ± 0.05	2.99 ± 0.02
N,N-Dimethylacetamide	0.41–1.63	260 ± 12	2.83 ± 0.03	2.86 ± 0.02
N,N-Dimethylformamide	0.67–2.05	116 ± 3	2.71 ± 0.01	2.72 ± 0.02
Triethylamine	0.64–1.92	85.2 ± 1.9	2.67 ± 0.02	2.66 ± 0.02
Pyridine	0.69–1.95	76.2 ± 1.1	2.57 ± 0.03	2.51 ± 0.02

Table III. Comparison of Independently Determined Formation Constants, K_f, for p-FC_6H_4OH–Base Complexes, CCl_4, 25.0°

Base	Ir method	F nmr method	Calorimetric method
Dimethyl sulfoxide	346 ± 8	338 ± 7	
N,N-Dimethylacetamide	260 ± 12	242 ± 6	
4-Methoxypyridine	131 ± 4	139 ± 2	
N,N-Dimethylformamide	116 ± 3	115 ± 2	122 ± 9
4-Methylpyridine	109 ± 5	107 ± 2	102 ± 7
Triethylamine	85.2 ± 1.9	82 ± 2	
Pyridine	76.2 ± 1.1	76 ± 1	74 ± 5
Quinoline	72.3 ± 1.0	71 ± 3	73 ± 5
Cyclohexanone	20.5 ± 0.7	21.4 ± 0.5	
Tetrahydrofuran	17.7 ± 0.5	18.4 ± 0.5	19.4 ± 1.0
2-Butanone	15.6 ± 0.5	15.1 ± 0.3	17.0 ± 1.0
Ethyl acetate	12.3 ± 0.3	12.0 ± 0.2	13.0 ± 0.7
Diethyl ether		9.5 ± 0.4	10.3 ± 0.3

p-$FC_6H_5OCH_3$ as reference and high base concentrations (0.1–0.7 *M*) such that the hydrogen-bonded complex is 97–99% formed (with correction to 100%). The substantial agreement shown in Table II between corresponding values of $\Delta^{(int\ ref)}$ and $\Delta^{(ext\ ref)}$ for bases of a wide variety of types establishes the validity of the internal reference procedure. The result is made rigorous by the finding in the collaborative ir determinations[6] that values of K_f are constant (within their precision measures) for similar ranges of base concentrations. Consequently, the agreement between $\Delta^{(ext\ ref)}$ and $\Delta^{(int\ ref)}$ cannot be an accident of coincidental cancellations of F nmr shielding and K_f medium effects.

Further confirmation comes from the fact that eq 1 is also valid for those weak bases which require concentrations appreciably greater than 0.02 *M* in order to achieve 30–80% complex formation. Using shifts based upon 0.01 *M* internal p-$FC_6H_4OCH_3$ and the independently determined K_f values from the ir method,[6] the results for weak bases are found to follow eq 1 to within the combined experimental errors of observed and calculated δ values. The results given in Table I for ethyl acetate are typical in this regard.

Final confirmation is shown by the excellent agreement obtained between the independently determined K_f values, *i.e.*, values based upon only F nmr, ir, or calorimetric determinations. The method employed for independent F nmr determination of the K_f value is given in the following section. The ir and calorimetric methods are reported in the companion paper.[6] A summary showing the excellent agreement obtained by the three methods is given in Table III.

We conclude that 0.01 *M* p-$FC_6H_4OCH_3$ as an internal reference in CCl_4 may be used generally with most types of bases (up to concentrations of ~0.7 *M*) to obtain the F nmr shielding effects for hydrogen bonding with 0.01 *M* p-FC_6H_4OH.

Independent F Nmr Method for Determination of K_f. The shifts, δ, obtained for the range of given base concentrations required to achieve approximately 30–80% complex formation, were analyzed by computer[13] in terms of eq 1 to give best value of the formation constant, K_f, and the corresponding limiting shift, Δ. The analysis is subject to the following considerations in light of the results presented above. The accumulation of error in one parameter necessarily leads to error in the other parameter (*i.e.*, in both K_f and Δ), and, in general, such errors are not readily apparent in a poorer precision of over-all fit of the δ values to eq 1.[3] However, this difficulty can be largely overcome by the direct measurement of Δ in independent experiments. Computer analysis of the δ values with the fixed value of Δ gives a best value of K_f which is relatively precise (*cf.* Table III) and the fit of data is essentially to the experimental error of individual points (±0.02 ppm). All of the bases employed in this study for which apparently satisfactory best values of Δ were obtained (*cf.* following section) gave such results.

Evaluation of Best Values of Δ. Three different determinations of Δ were developed from which a best value was selected. First, values referred to as Δ^{titr} were obtained from the δ values for the range 30–80% complexing (relatively low base concentrations) using computer analysis of best fit to eq 1. If an independently determined K_f value was available (*i.e.*, from ir determination) this value was used as a constraint in the computer analysis for results summarized in Table V. Otherwise, the Δ^{titr} value is that obtained when the computer is free to select best values of both Δ and K_f (as employed to obtain the completely independent F nmr results given in Table III, or as employed in the absence of an ir determination of K_f).

Second, values of Δ were obtained at 25° by direct measurement at the high base concentration (0.1–0.7 *M*) which gives 97–99% complex formation (corrected to 100%). Third, a procedure similar to the second was

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(13) R. W. Taft, G. B. Klingensmith, and S. Ehrenson, *J. Am. Chem. Soc.*, 87, 3620 (1965).

Table IV. Evaluation of Δ_{best}[a] by Three Methods

Base no.[b]	$\Delta_{25°}^{\text{titr}}$	$\Delta_{25°}^{(\text{int rel})}$	$\Delta_{-20°}^{(\text{int rel})}$	Δ_{best}
1		3.71 ± 0.02		3.71 ± 0.02
2	3.58 ± 0.03			3.58 ± 0.03
3	3.40 ± 0.09	3.40 ± 0.02	3.34 ± 0.02	3.37 ± 0.05
4	3.00 ± 0.01	3.00 ± 0.01		3.00 ± 0.02
5	2.90 ± 0.04	2.97 ± 0.02	3.00 ± 0.02	2.96 ± 0.04
6	3.07 ± 0.04	2.98 ± 0.02	2.89 ± 0.02	2.98 ± 0.05
7	2.83 ± 0.02	2.91 ± 0.01	2.84 ± 0.02	2.86 ± 0.04
8	2.82 ± 0.01	2.74 ± 0.02	2.73 ± 0.02	2.77 ± 0.03
9	2.77 ± 0.01	2.75 ± 0.02	2.66 ± 0.02	2.74 ± 0.02
10	2.71 ± 0.01	2.72 ± 0.02		2.72 ± 9.02
11	2.71 ± 0.01	2.74 ± 0.02	2.66 ± 0.02	2.71 ± 0.03
12	2.68 ± 0.03	2.75 ± 0.02		2.71 ± 0.04
13	2.69 ± 0.02	2.71 ± 0.02		2.70 ± 0.02
14	2.71 ± 0.01	2.69 ± 0.02		2.70 ± 0.02
15	2.67 ± 0.01	2.67 ± 0.02		2.67 ± 0.02
16	2.64 ± 0.02	2.65 ± 0.02	2.70 ± 0.02	2.66 ± 0.02
17	2.55 ± 0.02	2.60 ± 0.02	2.52 ± 0.02	2.54 ± 0.04
18	2.53 ± 0.01	2.51 ± 0.02		2.52 ± 0.02
19	2.50 ± 0.06			2.50 ± 0.06
20	2.46 ± 0.01	2.51 ± 0.02		2.49 ± 0.03
21	2.44 ± 0.01	2.46 ± 0.02		2.45 ± 0.02
22		2.41 ± 0.02		2.41 ± 0.04
23	2.40 ± 0.03	2.34 ± 0.02	2.40 ± 0.02	2.40 ± 0.03
24	2.41 ± 0.04	2.34 ± 0.02	2.39 ± 0.02	2.40 ± 0.03
25	2.30 ± 0.03	2.37 ± 0.02		2.33 ± 0.05
26	2.32 ± 0.05			2.32 ± 0.05
27	2.29 ± 0.02			2.29 ± 0.02
28	2.21 ± 0.05		2.23 ± 0.02	2.23 ± 0.04
29	2.22 ± 0.04			2.22 ± 0.04
30			2.16 ± 0.05	2.16 ± 0.05
31	2.18 ± 0.04	2.11 ± 0.02	2.18 ± 0.02	2.16 ± 0.03
32	2.12 ± 0.01	2.17 ± 0.02		2.15 ± 0.03
33	2.14 ± 0.02		2.10 ± 0.02	2.12 ± 0.02
34	2.10 ± 0.03			2.10 ± 0.03
35	2.07 ± 0.03			2.07 ± 0.03
36	2.00 ± 0.00		2.03 ± 0.02	2.02 ± 0.02
37	2.00 ± 0.05		2.02 ± 0.02	2.01 ± 0.03
38	2.02 ± 0.00		1.97 ± 0.02	2.00 ± 0.02
39	1.91 ± 0.04		2.07 ± 0.02	1.99 ± 0.05
40	1.92 ± 0.03		1.92 ± 0.02	1.92 ± 0.02
41	1.88 ± 0.03		1.91 ± 0.02	1.90 ± 0.02
42			1.88 ± 0.02	1.88 ± 0.02
43	1.85 ± 0.03		1.90 ± 0.02	1.88 ± 0.03
44	1.84 ± 0.04	1.89 ± 0.02	1.87 ± 0.03	1.88 ± 0.02
45	1.83 ± 0.01		1.86 ± 0.02	1.85 ± 0.02
46	1.84 ± 0.02			1.84 ± 0.02
47	1.78 ± 0.05		1.87 ± 0.02	1.83 ± 0.05
48	2.17 ± 0.2		1.75 ± 0.02	
49	1.69 ± 0.06		1.72 ± 0.02	1.71 ± 0.03
50	1.64 ± 0.04		1.73 ± 0.02	1.70 ± 0.05
51	1.70 ± 0.04			1.70 ± 0.04
52	1.60 ± 0.02		1.63 ± 0.02	1.62 ± 0.03
53	1.48 ± 0.4		1.42 ± 0.02	1.45 ± 0.04
54	1.40 ± 0.05		1.45 ± 0.02	1.45 ± 0.04
55	1.12 ± 0.10		1.00 ± 0.10	1.10 ± 0.10

[a] In parts per million. [b] Base number refers to the designation given in Table V.

employed at a temperature of −20° where the equilibrium is shifted in favor of further complex formation. The third procedure was especially useful for bases too weak to utilize the second procedure at 25°.

Table IV illustrates the generally good agreement obtained by these methods. Since the potential sources of error for Δ^{titr} are quite different than those for $\Delta^{(\text{int ref})}$, the general agreement achieved offers strong additional support for the conclusions of earlier sections. Except for 2,6-dimethyl-γ-pyrone, trimethyl phosphate, and dimethyl sulfoxide (bases numbered 6, 9, and 11) there appear to be no significant differences between $\Delta_{25°}^{(\text{int ref})}$ and $\Delta_{-20°}^{(\text{int ref})}$. Since $\Delta^{(\text{int ref})}$ is subjected to error if the base is appreciably self-associated at the relatively high concentrations (several tenths molar) employed in this method of determination, it is probably significant that $\Delta_{-20°}^{(\text{int ref})}$ is smaller than $\Delta_{25°}^{(\text{int ref})}$ for each of these three bases. These three bases are of the polar type which tend to show the greatest self-association, and such self-association should be greater at −20 than 25°. Competition with hydrogen bonding would thereby reduce the apparent value of Δ. Values of Δ_{best} for these three bases were therefore taken from the results at 25° only. For all other bases, values of Δ_{best} were selected either by averaging, or, if precision measures were substantially different, by weighting in favor of the more precise individual values.

It is also significant that self-association of a base would be expected to cause deviations from the equilibrium expression, eq 1. Consequently, the fits of the

Table V. Summary of Formation Constants and Limiting Shifts for Hydrogen-Bonded Complex Formation with p-FC_6H_4OH, CCl_4, 25°

No.	Base	Δ, ppm	K_f, M^{-1} [d]	Log K_f
1	Hexamethylphosphoramide	3.71 ± 0.03	3600	3.56 ± 0.06
2	Triphenylphosphine oxide	3.58 ± 0.03	1456 ± 80	3.16 ± 0.06
3	4-Dimethylaminopyridine	3.37 ± 0.05	650 ± 90	2.81 ± 0.06
4	Tetramethylurea	3.00 ± 0.02	261 ± 5	2.42 ± 0.01
5	N,N-Dimethylbenzamide	2.96 ± 0.04	167 ± 16	2.22 ± 0.04
6	2,6-Dimethyl-γ-pyrone	2.98 ± 0.05	318 ± 18	2.50 ± 0.03
7	N,N-Dimethylacetamide	2.86 ± 0.04	242 ± 6	2.38 ± 0.01
8	4-Methoxypyridine	2.77 ± 0.03	139 ± 2	2.14 ± 0.01
9	Trimethyl phosphate	2.74 ± 0.02	250 ± 8	2.40 ± 0.01
10	N,N-Dimethylformamide	2.72 ± 0.02	115 ± 2	2.06 ± 0.01
11	Dimethyl sulfoxide	2.71 ± 0.03	338 ± 7	2.53 ± 0.01
12	N,N-Dimethylcyclohexylamine	2.71 ± 0.04	118 ± 2	2.07 ± 0.01
13	4-Methylpyridine	2.70 ± 0.02	107 ± 2	2.03 ± 0.01
14	Diphenyl sulfoxide	2.70 ± 0.02	106 ± 2	2.03 ± 0.01
15	Phenyl methyl sulfoxide	2.67 ± 0.02	141 ± 4	2.15 ± 0.01
16	Triethylamine	2.66 ± 0.02	85 ± 2	1.93 ± 0.01
17	N,N-Dimethyl-*n*-propylamine	2.54 ± 0.04	95 ± 1	1.98 ± 0.01
18	2-*n*-Butylpyridine	2.52 ± 0.02	76 ± 2	1.88 ± 0.01
19	Tri-*n*-butylamine[c]	2.50 ± 0.06	37 ± 3	1.57 ± 0.03
20	Pyridine	2.49 ± 0.03	76 ± 1	1.88 ± 0.01
21	Flavone	2.45 ± 0.02	98 ± 6	1.99 ± 0.03
22	N,N-Dimethylchloroacetamide	2.41 ± 0.04	48 ± 5	1.68 ± 0.04
23	Quinoline	2.40 ± 0.03	71 ± 3	1.85 ± 0.02
24	Benzylamine	2.40 ± 0.03	56 ± 2	1.75 ± 0.01
25	N,N-Dimethylbenzylamine	2.33 ± 0.05	38 ± 3	1.58 ± 0.03
26	*p*-Nitrophenyl methyl sulfoxide[c]	2.32 ± 0.05	38 ± 5	1.58 ± 0.05
27	Cyclopropylamine[c]	2.29 ± 0.02	44 ± 2	1.64 ± 0.02
28	N,N-Dimethyl *p*-nitrobenzamide	2.23 ± 0.04	48 ± 6	1.62 ± 0.05
29	Triallylamine[c]	2.22 ± 0.04	17 ± 1	1.23 ± 0.03
30	*p*-Dimethylaminobenzonitrile[c]	2.16 ± 0.05	24 ± 3	1.38 ± 0.05
31	Propargylamine	2.16 ± 0.03	30 ± 1	1.48 ± 0.02
32	Acetylferrocene	2.15 ± 0.03	44 ± 1	1.64 ± 0.01
33	Cyclohexanone	2.12 ± 0.02	21.4 ± 0.5	1.33 ± 0.01
34	*p*-Methoxyacetophenone[c]	2.10 ± 0.03	25 ± 1	1.40 ± 0.02
35	2-Bromopyridine[c]	2.07 ± 0.03	8.8 ± 0.5	0.94 ± 0.03
36	2-Butanone	2.02 ± 0.02	15.1 ± 0.3	1.18 ± 0.01
37	Di-*t*-butyl ether	2.01 ± 0.03	5.1 ± 0.4	0.71 ± 0.03
38	Tetrahydrofuran	2.00 ± 0.02	18.4 ± 0.5	1.26 ± 0.02
39	3-Bromopyridine	1.99 ± 0.05	18.1 ± 1.2	1.26 ± 0.03
40	Acetophenone	1.92 ± 0.02	13.6 ± 0.3	1.13 ± 0.01
41	*p*-Methoxybenzaldehyde	1.90 ± 0.02	12.6 ± 0.2	1.10 ± 0.01
42	Acetonitrile[c]	1.88 ± 0.02	11.2 ± 0.6	1.05 ± 0.02
43	Diethyl ether	1.88 ± 0.03	9.5 ± 0.2	0.98 ± 0.01
44	β-Cyanoethyl ethyl ether	1.88 ± 0.03	11.2 ± 0.5	1.05 ± 0.02
45	Ethyl acetate	1.85 ± 0.02	12.0 ± 0.2	1.08 ± 0.01
46	Pyrimidine[c]	1.84 ± 0.02	22.5 ± 0.5	1.05 ± 0.02[a]
47	*p*-Methoxybenzonitrile	1.83 ± 0.05	9.8 ± 0.4	0.99 ± 0.02
48	N,N-Dimethylaniline	(1.75)[b]	2.7 ± 0.2	0.43 ± 0.03
49	Benzonitrile	1.71 ± 0.03	6.1 ± 0.6	0.79 ± 0.04
50	Benzaldehyde	1.70 ± 0.05	6.8 ± 0.2	0.83 ± 0.01
51	Dibenzyl ether[c]	1.70 ± 0.04	5.3 ± 0.2	0.72 ± 0.02
52	3,5-Dichloropyridine	1.62 ± 0.03	5.6 ± 0.2	0.75 ± 0.01
53	β,β,β-Trifluoroethylamine	1.45 ± 0.04	3.9 ± 0.1	0.59 ± 0.01
54	Dioxane	1.45 ± 0.04	10.2 ± 0.6	0.71 ± 0.02[a]
55	Diethyl sulfide	1.10 ± 0.10	1.3 ± 0.2	0.11 ± 0.07

[a] With statistical correction. [b] *Cf.* comments in Experimental Section. [c] Values of K_f are based only upon a single determination of the Δ value; *cf.* Table IV. [d] At 25°.

present data to eq 1 provide no evidence of appreciable self-association in CCl_4 of the bases of Tables IV and V at the concentration levels employed to give 30–80% complex formation with 0.01 M p-FC_6H_4OH.

The results for N,N-dimethylaniline (*cf.* Table IV) are exceptional, as were those obtained with *n*-butylamine. For the latter, eq 1 is well fitted by the best parameters: $\Delta_{25°}^{\text{titr}} = 2.56 \pm 0.03$, $K_f = 129 \pm 6$. However, values of $\Delta_{25°}^{(\text{int ref})} = 2.74 \pm 0.02$ and $\Delta_{-20°}^{(\text{int ref})} = 3.01 \pm 0.02$ were obtained. These results remain anomalous, although there is evidence that N,N-dimethylaniline has two acceptor sites,[14] which might explain its behavior. In the case of *n*-butylamine, alternate possibilities include higher order complexing at high base concentrations (involving N–H proton donation), or absorption of atmospheric carbon dioxide (which was not rigorously excluded). Our results with amines in general need to be confirmed by ir studies. We do not believe that our results are seriously affected by reaction between strongly basic amines and CCl_4 for the following reasons: (a) no precipitates were observed during the time required for the F nmr measurements (although these do form on longer standing), (b) the F nmr shifts are reproducible for up to 5 hr after preparation of the solutions and these shifts obey eq 1.

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(14) L. L. Ferstandig, *Tetrahedron Letters*, 1235 (1963).

Table VI. Formation Constants at −20° and Enthalpies for Hydrogen-Bonded Complex Formation with p-FC_6H_4OH[a]

No.		$K_f^{-20°}$	$K_f^{25°}$	$-\Delta H_f^{\circ b}$	$-\Delta H_f^{\circ c}$	$-\Delta H_f^{\circ d}$
39	3-Bromopyridine	107 ± 7	18.1	5.8	6.2 ± 0.2	
38	Tetrahydrofuran	103 ± 8	18.4	5.7	5.6 ± 0.1	5.8 ± 0.1
36	2-Butanone	64 ± 6	15.1	4.8		5.2 ± 0.1
45	Ethyl acetate	49 ± 2	12.0	4.7		4.7 ± 0.1
54	Dioxane	40 ± 3	10.2	4.6		5.1 ± 0.1
51	Dibenzyl ether	22.0 ± 0.5	5.3	4.7		4.6 ± 0.1
48	N,N-Dimethylaniline	9.8 ± 0.5	2.7	4.2	4.0 ± 0.4	4.0 ± 0.1

[a] In CCl_4; measured in kilocalories/mole. [b] From van't Hoff equation for K_f at −20 and 25°; estimated uncertainty, ±0.3 kcal. [c] Calorimetric value at 25°; *cf.* ref 6. [d] Obtained by pure base method; *cf.* ref 6.

Results

Table V summarizes the best values of the formation constants, K_f, for hydrogen-bonding complex formation of p-FC_6H_4OH with 55 different bases in CCl_4 solution at 25°. Also given are corresponding best values of Δ, the limiting F nmr shift in parts per million (ppm) between complexed and uncomplexed p-FC_6H_4OH.

Table VI summarizes the best values of K_f obtained with eight bases in CCl_4 at −20°, together with values of the van't Hoff enthalpy of complex formation (based upon K_f values at −20 and 25°), $-\Delta H°_f$, and corresponding calorimetric values of $-\Delta H°_f$ (25°) obtained in the collaborative study.[6] Values of K_f at −20° are based upon concentrations corrected for the density change of CCl_4 between 25 and −20°.

Discussion

The molecular composition of the hydrogen-bonded complexes of p-FC_6H_4OH under the conditions of the present investigation is shown rigorously to be 1:1. The fits of δ values to the equilibrium expression 1 are generally within the experimental errors of the individual measurements for a critical region of 30 to 80% complex formation. Similar fits of the ir and calorimetric data to corresponding equilibrium expressions for 1:1 complex formation have also been found.[2,6] It is especially noteworthy that the enthalpy of complex formation, $\Delta H_f°$, has nearly the same value in CCl_4 at high dilution as in the pure base as solvent.[2,6] This result provides striking confirmation that the 1:1 molecular composition does not change with dramatic increases in the base to acid ratio.

Comparison of the values of the formation constant, K_f, determined independently by the three methods (Table III) shows that there are no serious deviations, agreement frequently being within the combined uncertainty limits. In view of the appreciable variety of base types for which this result has been obtained, the F nmr method developed herein may be accepted as a generally useful and precise method for the determination of formation constants.

The results given in Table VI provide a further indication of the high degree of internal consistency in the results obtained by the three methods of investigation employed in our collaborative efforts. There is generally satisfactory agreement between the values of the enthalpies of complex formation, $-\Delta H_f°$, obtained by the van't Hoff equation from K_f values at −20 and 25° and the direct calorimetric measurements at 25°. Calorimetric measurements of $-\Delta H_f°$ over a smaller temperature interval (12, 25, and 34°) show no measurable temperature dependence (*i.e.*, ΔC_p for complex formation is indicated to be small).[6]

The formation constants, K_f, summarized in Table V are not of uniform quality. Values of K_f which are based upon a single determination of the Δ value (*cf.* Table IV) and which have not been confirmed by an independent method should be regarded as having potential uncertainty beyond their indicated precision measures (*cf.* footnote *c* of Table V).

Regarding the Linear SEE Relationship. This relationship involves a linear correlation of the F nmr shift between product and reactant states for a series of closely related chemical reactions with the corresponding thermodynamic standard free energy or enthalpy change.[4] It has been observed in several chemical reactions quite different in character from the present one, in particular, for reactions involving strong rather than weak bond formation. In the systems studied previously the relationship has been found to hold over significant ranges of shifts and thermodynamic properties, and the latter have been taken to provide a reasonably quantitative estimation of the potential or electronic energy change for the reactions.[4]

Figure 1 plots the log K_f *vs.* Δ values for 48 bases of Table V. The number given in Figure 1 refers to the base as designated in Table V. An approximate linear relationship of useful precision (the standard deviation of log K values is 0.09 with a root mean square of 1.76) is obeyed. The correlation covers oxygen, nitrogen, and sulfur bases of a wide variety of types with apparently equal precision. Seven bases from Table V show deviations greater than three times the SD of Figure 1 and have been excluded: (5) N,N-dimethylbenzamide, (11) dimethyl sulfoxide, (19) tri-*n*-butylamine, (29) triallylamine, (35) 2-bromopyridine, (37) di-*t*-butyl ether, and (48) N,N-dimethylaniline. The anomalous behavior of the last amine is discussed in the Experimental Section.

Bases 19, 29, 35, and 37 quite plainly have the common structural feature of very high steric requirements. It is also probably significant that the additional bases of large steric requirements show smaller deviations in the same direction, *i.e.*, triethylamine, 16; diethyl ether, 43; dibenzyl ether, 51. The linear correlation of Figure 1 must be limited, therefore, to bases of small or moderate steric requirements. Deviations for the bases of large steric requirements are all in the direction indicating the F nmr shift has a much smaller dependence upon steric requirements than does the standard free energy change of complex formation. A similar result has been observed by Dr. A. A. Grey in the formation of Lewis acid–base adducts with p-fluorophenylboron dichloride.[15] The significance of these findings is currently under further study.

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(15) A. A. Grey, Ph.D. Thesis, University of California, Irvine, June 1967.

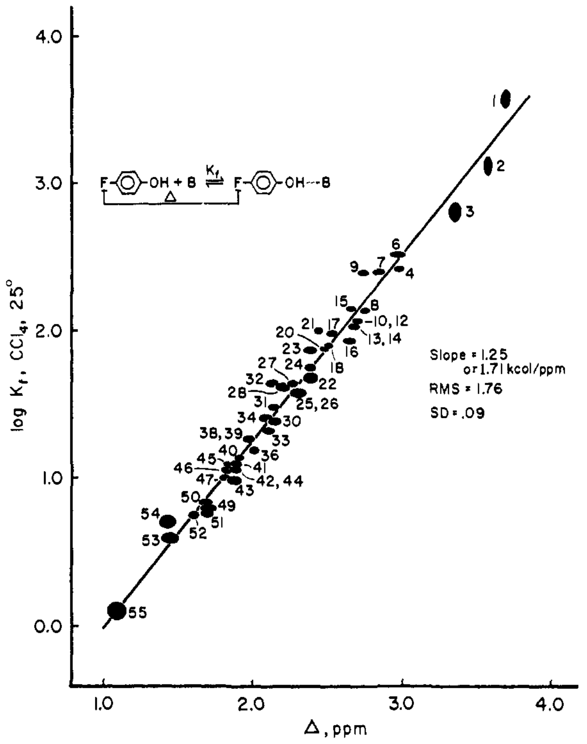
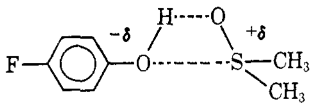


Figure 1. Linear SEE relationship for hydrogen-bonded complex formation with p-FC_6H_4OH, CCl_4, 25°. Numbers refer to bases as designated in Table V.

The deviations of bases 5 and 11 are anomalous and no satisfactory explanation can be given presently. In the case of dimethyl sulfoxide the smaller than expected Δ value might be interpreted as reflecting some O–S interaction in the hydrogen-bonded complex, *i.e.*



However, this possibility is not supported by the behavior of both phenyl methyl sulfoxide and diphenyl sulfoxide which are essentially "normal" in Figure 1.

In Table VII are presented some additional best values of Δ obtained by either the second or third procedure (*cf.* Experimental Section). Using the correlation of Figure 1, estimated values of log $K_f^{25°}$ for these bases have been obtained and are also listed in Table VII.

Table VII. Values of Δ and Estimated Log $K_f^{25°}$ for Some Additional Bases

No.	Base	Δ, ppm	Log $K_f^{25°}$ (est)
56	$Cl^-(n\text{-}C_7H_{15})_4N^+$	4.30[a]	~4.0
57	Tetramethylguanidine	3.78	3.48
58	N-Methylpyrrolidone	2.91	2.37
59	Tetramethylene sulfoxide	2.80	2.22
60	p-Dimethylaminobenzaldehyde	2.30	1.56
61	N,N-Dimethyltrifluoroacetamide	1.97	1.19

[a] Unpublished result of Dr. Jon Lipowitz.

The generally successful correlation of Figure 1 has interesting and significant implications with respect to the standard free energy change of hydrogen-bonded complex formation, $\Delta G_f°$. First, by the basic hypothesis of the SEE relationship,[4] the correlation of Figure 1 implies that $\Delta G_f°$ is approximately proportional to the potential energy change of formation of the hydrogen-bonded complex. It is particularly significant that the correlation includes bases with substantial variations in the entropies of complex formation.[6] Thus, it is suggested that the kinetic energy terms ($-RT \ln \pi Q$) included in $\Delta G_f°$ are of the special kind which, at least approximately, tend to parallel corresponding potential energy changes.[16] It is to be noted that the proportionality constant between the standard free and potential energies is implied to be temperature dependent by the slopes of log K_f *vs.* Δ (1.71 kcal/ppm at 25° and 1.92 kcal/ppm at −20°). Secondly, since the F nmr shift, Δ, has been postulated to be a measure of the "apparent per cent proton transfer" (≅100 Δ/14) in the hydrogen-bonded complex,[3] the correlation of Figure 1 indicates that $\Delta G_f°$ must also be an approximate "measure" of the extent of proton transfer in the complex.

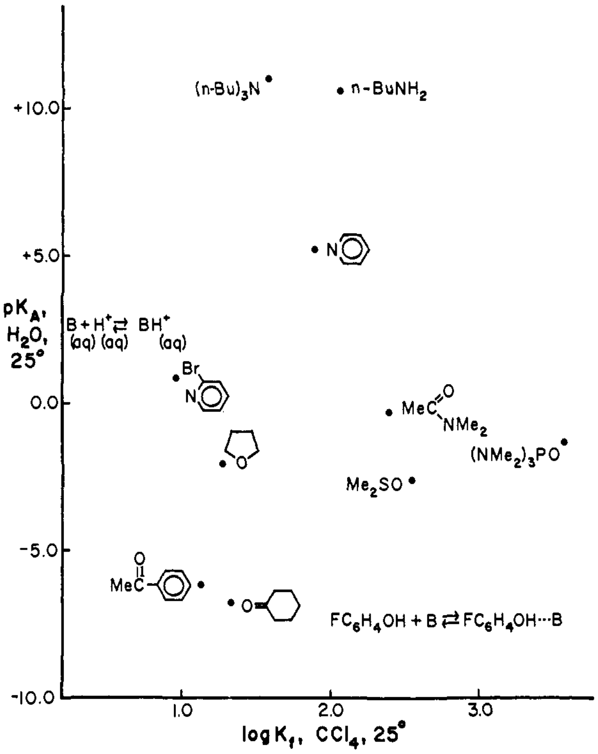


Figure 2. Comparison of base strengths, aqueous H^+ *vs.* p-FC_6H_4OH.

The present F nmr study has provided additional new evidence defining the character of the hydrogen-bonded complexes of p-FC_6H_4OH. It is indeed conceivable in terms of previous concepts and discussions of hydrogen bonding[17] that the observed values of Δ may pertain to a complex mixture of very rapidly interconverting states having appreciably different energy contents and extents of proton transfer (*e.g.*, the hydrogen-bonded complex, the hydrogen-bonded ion pair, and perhaps other states). We believe this possibility is excluded by the present finding that the F nmr shift, Δ, is the same at −20 as

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(16) R. W. Taft in M. S. Newman "Steric Effects in Organic Chemistry," John Wiley & Sons, Inc., New York, N. Y., 1956, p 569.

(17) *Cf.*, for example, R. Scott, D. DePalma, and S. Vinogradov, *J. Phys. Chem.*, 72, 3192 (1968), and references therein.

25°. Preliminary studies[18] in the polar solvent $ClCH_2CH_2Cl$ at 25° with bases 10, 11, 16, 20, 48, and 57 (Tables V and VII) indicate that Δ values are 10 to 20% less than corresponding values in CCl_4, except for triethylamine which is 10% larger. Thus, with the possible exception of the latter, there is no F nmr evidence of an appreciable enhancement in any hydrogen-bonded ion pairs. If the latter were present to a measurable extent in CCl_4, this form should be further increased in the polar $ClCH_2CH_2Cl$ solvent.

We therefore conclude that in CCl_4 p-FC_6H_4OH forms only the hydrogen-bonded complex with all of the bases of Table V. Our results are consistent with these hydrogen-bonded complexes having a rather well-defined and a relatively low extent (up to ~30%) of apparent proton transfer.[3]

In accord with the conclusion that there is a small extent of proton transfer in these hydrogen-bonded complexes is the fact that there is *no* simple correspondence between base strength as measured by the standard free energy of hydrogen-bonded complex formation of p-FC_6H_4OH in CCl_4 and corresponding aqueous pK_A values of base. Figure 2 shows the complete scatter pattern which results from a plot of pK_A[19] *vs.* log $K_f^{25°}$ values for bases having a variety of common functional groups. This subject is considered in detail in paper V of this series.[5]

Acknowledgment. We are pleased to acknowledge the valuable assistance provided for this work by the preliminary studies made with 0.1 M p-FC_6H_4OH by Dr. M. G. Schwartz.[20] We are also pleased to acknowledge the preliminary studies of Mr. Joseph Mitzky in $ClCH_2CH_2Cl$ solutions.

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(18) Unpublished results of Mr. Joseph Mitzky.

(19) The pK_A values shown in Figure 2 for hexamethylphosphoramide (−1.4) and dimethyl sulfoxide (−2.6) are unpublished results of Dr. J. R. Rakshys, obtained by the method of Haake (P. Haake, R. D. Cook, and G. H. Hurst, *J. Am. Chem. Soc.*, **89**, 2650 (1967)).

(20) M. G. Schwartz, Ph.D. Thesis, The Pennsylvania State University, Dec 1965.

Studies of Hydrogen-Bonded Complex Formation with p-Fluorophenol. V. Linear Free Energy Relationships with OH Reference Acids[1]

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Abstract: Linear free energy relationships have been established in the formation of hydrogen-bonded complexes of various OH reference acids with a wide variety of proton acceptors. The effects of temperature, solvent, and substituents have been examined. A unique base parameter, pK_{HB}, has been defined which measures the relative strength of the acceptor in hydrogen-bonded complex formation with any suitable OH reference acid. pK_{HB} values do not correlate with aqueous pK_A values, except within series having a common functional center and variable electronic effects of substituents. pK_{HB} values also are not applicable to reference acids involving internal hydrogen bonding and are presumably not applicable to systems in which there is substantial formation of the hydrogen-bonded ion pair (in mobile equilibrium with the hydrogen-bonded complex). Evidence is presented that the pK_{HB} scale is applicable (at least qualitatively) to other relatively weak interactions between bases and a "shielded" center of positive charge. The highly dispersed family relationships between pK_{HB} and corresponding pK_A values are indicated to be useful in distinguishing the atomic center of complexing in polyfunctional bases.

The effect of molecular structure on the strength of the hydrogen bond is a subject of diverse interests.[2,3a] These include, for example, the structure and reactivity of proteins and many other natural products, solvation effects in many chemical reactions and in spectroscopic measurements, and transition-state characteristics in proton-transfer processes.

There have been in recent years several extensive studies[4] of the effects of structure on base strengths toward a common reference acid, as measured by the formation constant, K_f, for the 1:1 hydrogen-bonded

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(1) This work was supported in part by the Public Health Service, Projects GM14078 (Irvine), AI-07766 (Princeton).

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