Organic and Biological Chemistry

Studies of Hydrogen-Bonded Complex Formation. III. Thermodynamics of Complexing by Infrared Spectroscopy and Calorimetry[1,2]

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Abstract: Formation constants (K_f) and heats of formation (ΔH_f) are determined for the hydrogen-bonded complexes between p-fluorophenol and 35 bases. The formation constants are used in conjunction with heats of reaction of the phenol and base at low concentration in carbon tetrachloride to give ΔH_f by the high dilution method (I). A second method, the pure base method (II), which we believe is novel, involves measuring the molar heat of reaction of a small increment of p-fluorophenol in the pure base as solvent where all of the phenol is complexed. Model compounds, chiefly p-fluoroanisole, are used to correct for solvent–solute interactions other than hydrogen bonding. Extensive data for heats of solution of p-fluorophenol, phenol, p-fluoroanisole, anisole, n-butyl alcohol, n-butyl chloride, and some related compounds in a variety of organic solvents are tabulated. These data are used to determine ΔH_f for hydrogen bonding of p-fluorophenol, phenol, and n-butyl alcohol to these solvents as acceptors. Although method II is theoretically dubious, agreement with method I and with reliable values from other laboratories is good for the systems reported here. Attempts at extrathermodynamic correlations of $\Delta G_f°$ vs. ΔH_f or ΔH_f vs. $\Delta S_f°$ lead to general scatter diagrams which may be partially resolved into separate trends for different groups of bases. This behavior was also observed for $\Delta G_f°$ vs. the aqueous pK_a's for protonation of these bases. We note in particular that the free energies of hydrogen-bond formation for the pyridines as one class and for the dipolar oxides and amides as another class are in each case controlled entirely by ΔH_f with no entropy contribution to the substituent effects. This contrasts with the behavior of the other types of bases studied here. The infrared and calorimetric data are used to test the correlation of $\Delta\nu$ vs. $\Delta H_f°$. Although the trend is clear, no good general correlation is found.

The structural theory of modern organic chemistry deals with the relationship between the geometry of covalent bonds in organic molecules and their energies. Although a detailed knowledge of intramolecular bonding has developed over the last century, no corresponding progress has been made in relating the energies and geometrical requirements of those intermolecular and interfunctional forces which do not involve covalent bond formation. Since very few of the organic reactions which take place in solution also occur in the gas phase, it is clear that interactions of organic molecules with their neighbors in the condensed phase can play a deciding role in their reactivity.

Of all the various types of intermolecular and interionic forces which have been proposed[3-7] the hydrogen bond occupies a special position, being strong enough to have a profound effect on the reactivity of the molecules engaged in it, yet weak enough to prevent their permanent conversion into other compounds. Hydrogen bonds have, therefore, occupied a key position in the interpretation of biophysical processes.[5,8,9] Because of its importance and ubiquity as the locus of interaction between molecules and between nearby functions in the same molecule, the hydrogen bond offers special promise for the study of such interactions. It has been known for many years[3,10-12] that the readily observed stretching frequency of a covalently bound hydrogen atom is perturbed in a characteristic way when that atom participates in hydrogen bonding to an acceptor group. Such infrared shifts are studied so handily that we have a broad and detailed knowledge of the geometrical requirements for hydrogen bonding—both intermolecular and intramolecular.[13]

However, although many energy measurements for this interaction have been reported, there is a serious dearth of values which are sufficiently reliable to take full advantage of the structural information. The problem lies in the difficulty of finding good data which

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(2) Most of the work presented here is derived from the doctoral theses of T. S. S. R. Murty, University of Pittsburgh, 1967, and L. Joris, Princeton University, 1967.

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permit direct comparison of a wide range of donor or acceptor molecules under the same conditions. Furthermore, those cases which can be compared often show serious disagreement between the results obtained by different workers studying the same system by different methods. In view of the fact that most hydrogen bonds have energies falling between 3 and 10 kcal/mole, discrepancies amounting to 2 or 3 kcal/mole can reduce the utility of such energy measurements to the vanishing point.

Reliable hydrogen bonding values are necessary not only for chemical and biophysical theory, but also for testing such extrathermodynamic relationships as the Badger–Bauer[14,15] correlation of hydrogen bond enthalpy with infrared shift, a correlation which has been assumed by some workers and challenged by others. The relationship between hydrogen bonding and complete proton transfer as manifested in heats of protonation or pK_a's of bases against aqueous acids is closely related to the whole concept of "basicity"—an idea which is as fundamental and nearly as vague as "aromaticity."

Against this background, we, in collaboration with Taft's group,[16] have undertaken an extensive study of hydrogen bond energies through a number of independent methods for a clearly characterized system which is relevant to many previous reports. We have chosen p-fluorophenol (PFP) as the standard donor and carbon tetrachloride at 25° as the standard condition. In view of the many previous studies of phenols in this solvent, our results should be relatable to those of other workers. p-Fluorophenol provides a singular opportunity to study the hydrogen-bonding interaction from two spectroscopic vantage points: through the O–H infrared (ir) stretching frequency of the hydroxyl group and through the ^{19}F chemical shift of the fluorine atom at the opposite end of the molecule. Through these spectroscopic methods, the equilibrium constants for hydrogen bond formation may be determined. The temperature coefficients of these equilibrium constants could be used to estimate heats of formation. However, in view of the well-recognized shortcomings of the van't Hoff method for studying weak interactions,[17,18] we have chosen to use solution calorimetry for the determination of hydrogen bond enthalpies.

If the heat of formation is taken as a function of concentration, it is frequently possible[19–23] to determine the free energy of an interaction provided that the equilibrium is measurably displaced over the range of concentrations studied. One, therefore, can compare

calorimetrically determined equilibrium constants with those found by the two spectroscopic methods in order to determine how clearly and consistently the energy of hydrogen bonding is defined by the different operations. In this paper, we shall describe in detail the infrared and calorimetric methods outlined in our previous communication.[24] In a companion paper[25] our collaborators have described in greater detail their ^{19}F method and results. In subsequent articles, we shall discuss solvent effects on hydrogen bonding and the relationships between different measures of hydrogen bond strengths both with each other and with corresponding properties for complete proton transfer.

Experimental Section

Materials. Carbon tetrachloride (Baker reagent or spectroscopic grade) was distilled from calcium hydride or phosphorus pentoxide and was either used at once or stored over Molecular Sieves (4A) beads. p-Fluorophenol (Eastman) was distilled or sublimed under vacuum and stored briefly in a desiccator prior to preparation of solutions. Because phenols are quite hygroscopic, they must be protected carefully for hydrogen-bonding work in aprotic media. Phenol was also vacuum distilled and stored in a desiccator.

All other compounds were obtained from commercial sources in the highest possible grade and were purified as recommended in authoritative texts until the boiling point, melting point, or refractive index agreed with the best literature values.[26] In many cases purity was also checked by glpc analysis.

Further details of purification and comparison of our physical constants with literature values may be found in the theses of Murty and Joris.

Methods

A. Spectroscopic (Joris, Gorrie, and Schleyer). Apparatus. All ir spectra were taken with a Perkin-Elmer 421 double beam grating spectrophotometer. A 1-cm path length, infrared silica, constant-temperature cell was used for the samples, and a 1-cm path length, infrared silica cell served as a reference. The slit width was 0.02 μ and the chart speed was 15 cm^{-1}/min.

Solution Preparation. Standard phenol solutions were prepared by transferring about 1 g of pure, dry phenol to a calibrated, dried 100-ml volumetric flask. The flask was reweighed and filled to the mark with pure, dry CCl_4.

Different amounts of base were added to five 50-ml volumetric flasks and then reweighed. About 40 ml of CCl_4 was added to each flask to minimize the evaporation of base. Aliquots (2 ml) from the standard phenol solution were transferred to the five flasks containing base and to one empty 50-ml volumetric flask. Into another empty 50-ml volumetric flask was placed 1 ml of standard phenol solution. Each flask was filled to the 50-ml mark with CCl_4 and the room temperature was noted.

Fifteen minutes were allowed for the solution to equilibrate to 25.0° (in the constant-temperature infrared cell) before the spectrum was recorded.

Experimental Procedure for the Determination of K_f by Infrared Spectroscopy. If dimerization of the hydrogen bond donor and acceptor are negligible,

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Table I. Data and Results for Hydrogen Bonding of p-Fluorophenol to Diphenyl Sulfoxide in CCl₄ at 25.0° ([A₀] = 0.003058 M; 1/ε = 4.42 × 10⁻³)

Concn of (Ph)₂SO, [B₀]	0.00182	0.00372	0.00644	0.00787	0.01051
Absorbance	0.604	0.528	0.477	0.408	0.355
[A] × 10³, M	2.66	2.33	2.10	1.80	1.57
[C] × 10³, M	0.40	0.73	0.96	1.25	1.49
K_f, M^{-1}	106	105	105	106	103

K_f average = 105 ± 1 M^{-1}

K_f is given by the expression

$$K_f \ (\text{in } M^{-1}) = \frac{[C]}{[A]([B_0] - [C])} = \frac{[A_0] - [A]}{[A]([B_0] - [A_0] + [A])} \quad (1)$$

The concentration of hydrogen bonded complex [C] is equal to the initial concentration of proton donor [A₀] minus the equilibrium concentration of free donor [A]. The concentration of free base [B] is equal to the initial concentration of base [B₀] minus [C]. The infrared bonded peak, because it occurs at a much lower frequency, does not contribute to the absorbance of the free peak. Since [A₀] and [B₀] are known quantities, K_f can be calculated by eq 1.

We first investigated the possibility that the proton donor was partially dimerized at the working concentration. Appreciable dimerization of phenol would result in a nonlinear Beer's law correlation of absorbance vs. [A₀]. Fortunately, in the range of phenol concentrations used in this study (1–4 × 10⁻³ M), dimerization is negligible (see Figure 1), dimer concentration being only 0.5% of the free phenol concentration at 4 × 10⁻³ M. For p-fluorophenol, the dimerization constant (K_d) is probably even lower (K_d for p-chlorophenol is 15% lower than that of phenol).[27] In addition, no dimer absorption (ca. 3400 cm⁻¹) was detected in the spectrum of 4 × 10⁻³ M p-fluorophenol. Independent evidence against dimerization at low phenol concentration is given in the calorimetric section below.

When a bonded peak occurs in a spectrum, the base line obviously must be estimated from the high-frequency side of the free OH peak. However, absorption of atmospheric water vapor is sufficiently strong on the high-frequency side so that the base line cannot be found directly. Accordingly, the transmittance difference between the minimum near 3670 cm⁻¹ and the base line for phenol solutions was determined for various free OH peak heights and the appropriate corrections to the base lines for spectra with bonded peaks were estimated.

The concentrations of phenols were adjusted so that a majority of the absorbances fell within the range of 0.3–0.6 absorbance unit.[28]

No significant dependence of K_f on base concentration was observed even for DMSO, the base which we expect would be most prone to dimer formation. At the maximum concentration 3 × 10⁻² M, the fraction of dimeric DMSO is about 7%.[29] Evidently, this

partial conversion to dimer is insufficient to create an observable "concentration effect" in K_f.

In a typical run, the absorbances of two different phenol solutions were measured to compute ε_{ArOH} (the molar absorptivity) and also to check Beer's law; then the spectra of five ArOH–base solutions were scanned from which K_f was computed. After a series of four or more consecutive runs were completed, the ε's were averaged. Using this average ε, the concentration of free proton donor [A], and ultimately K_f, were calculated. Data for [B₀], [A₀], and absorbance and calculated results ([A], [C], and K) for a typical run are given in Table I.
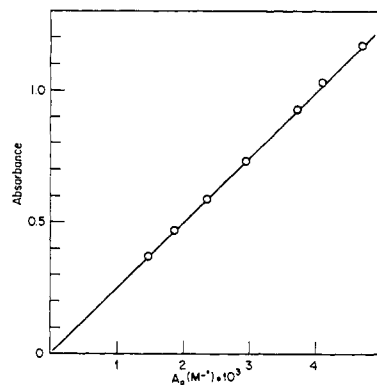

Figure 1. Correlation between absorbance of the free OH peak with initial concentration of phenol [A₀].

B. Calorimetric Methods (Arnett, Murty, and Mitchell).

The various calorimetric procedures presented below all employ the type of solution calorimeter and procedures described previously by the Pittsburgh group.[30] A 250-ml dewar flask was used for the calorimeter. All heat measurements were calibrated electrically before and after introduction of each sample from an airtight syringe. All measurements were made at 25 ± 1° and the samples allowed to reach thermal equilibrium in the calorimeter before injection.

Pure, dry carbon tetrachloride (see above) was drawn into dried 1-l. volumetric flasks containing a carefully weighed sample of the phenol. The solvent had been stored in a sealed 4-l. bottle with delivery buret (Scientific Glass, Inc., JB-6990) over a large bed of Molecular Sieves 4A.

Systematic errors were avoided by frequent checks of the calorimeter against well-accepted values for the heat of solution of KCl[31] or ethanol[32] in water.

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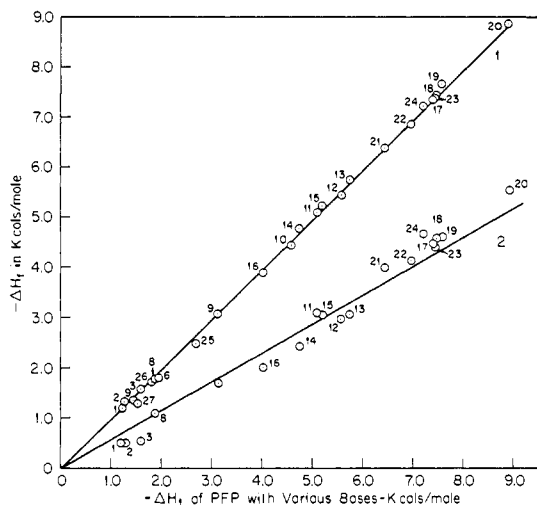(32) F. Franks and B. Watson, J. Sci. Instrum., [2] 1, 940 (1968).

Figure 2. Plot 1, $-\Delta H_f$ of PFP vs. $-\Delta H_f$ of phenol; plot 2, $-\Delta H_f$ of PFP vs. $-\Delta H_f$ of n-butyl alcohol. Bases used are (1) benzene; (2) toluene; (3) mesitylene; (4) cumene; (5) cyclohexyl chloride; (6) cyclohexyl bromide; (7) cyclohexyl iodide; (8) diphenyl ether; (9) anisole; (10) dibenzyl ether; (11) dioxane; (12) ether; (13) tetrahydrofuran; (14) ethyl acetate; (15) 2-butanone; (16) N,N-dimethylaniline; (17) pyridine; (18) quinoline; (19) 4-picoline; (20) triethylamine; (21) N-methylformamide; (22) N,N-dimethylformamide; (23) N,N-dimethylaniline; (24) dimethyl sulfoxide; (25) n-butyl chloride; (26) n-butyl bromide; (27) n-butyl iodide.

The precision of the heat measurements depends primarily upon the magnitude of the recorder pen

deflection. This in turn is a function of several factors such as the amount of base used, the amount of proton donor, the ΔH_f and K_f of hydrogen bond formation, the heat of solution of the solute in the solvent, and the heat capacity of the system.

For the dilute solution method (method I), in the case of weak bases such as anisole, where the heats produced are small, the standard deviation in the calculated ΔH_f may be as high as 0.5 kcal/mole. In the case of strong bases (pyridine, THF, etc.), which produce larger heats, the standard deviations of ΔH_f are usually ±0.1–0.2 kcal/mole.

Using the pure base method (method II), which involves measuring four heats of solution, the standard deviations of ΔH_f are in the range of ±0.10 to ±0.15 kcal/mole.

The number of measurements made depended on the compounds under study and the experimental limitations. In some cases, only two measurements were made and in some others as many as 15 using various acid and base concentrations. In one case (DMSO), we made 25 measurements. In some instances of particular importance, two or three duplicate measurements were made at each acid and base concentration.

To check the overall reproducibility of the results, many of the measurements were repeated after a time lapse of 3 months to 1 year with fresh solutions and freshly purified solutes.

Method I. The High Dilution Method. If a small quantity of a base B (from 50 to 300 μl) is injected into a dilute solution of the hydrogen bonding acid A (*e.g.*, PFP) to produce a 1:1 complex C, the observed heat of interaction, ΔH_{obsd}, is related to the enthalpy of hydrogen bond formation (ΔH_f) by the expression

$$\Delta H_{obsd} = \Delta H_f[C]V \qquad (2)$$

where V = volume in liters of the solution in the calorimeter (usually 0.19 or 0.20 l.), and [C] = molar concentration of C at equilibrium.

ΔH_{obsd} is determined experimentally by subtracting the heat of solution for a given quantity of base in the pure solvent from its heat of solution in the same amount of solvent containing the proton donor at the molar concentration $[A_0]$.

The equilibrium involved can be written as A + B $\rightleftarrows$ C so that

$$K_f = \frac{[C]}{([A_0] - [C])([B_0] - [C])} \qquad (3)$$

Equation 3 can be written as

$$K_f([A_0][B_0] - [A_0][C] - [B_0][C] + [C]^2) = [C] \qquad (4)$$

and solved for [C] by inserting the appropriate values for $[A_0]$, $[B_0]$, and K_f into the quadratic and solving it[24] through eq 5

$$[C] = \frac{-\left([A_0] + [B_0] + \dfrac{1}{K_f}\right) \pm \sqrt{\left([A_0] + [B_0] + \dfrac{1}{K_f}\right)^2 - 4[A_0][B_0]}}{2} \qquad (5)$$

one of whose roots is always absurd.

Linear expression 2 yields ΔH_f when ΔH_{obsd} is plotted vs. ([C]V) (*e.g.*, ref 24, Figure 2). Excellent linearity based on 15 measurements of ΔH_{obsd} for PFP concentrations 0.02, 0.01, and 0.005 M and pyridine concentrations from 3.44×10^{-3} to 18.57×10^{-3} M, coupled with the fact that the ΔH_f value determined using the pure base method (method II) is the same within experimental error as ΔH_f by method I, lend very strong support to the applicability of the 1:1 complex treatment to these systems. A typical set of results is presented in Table II.

Because pyridine has been widely studied by many workers, we have used it as a standard for a number of the calibration experiments cited below. It should be noted that it does not form perfect solutions[33] in carbon tetrachloride and is also very hygroscopic. Reactions of amines with carbon tetrachloride and other halomethanes are heavily documented.[34,35] Evidence that these reactions did not interfere with our measurements is provided by (a) clean, linear recorder tracings following injection of the base into the solvent; (b) good agreement between ΔH_f values for amines determined

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Table II. Determination of ΔH_f for Hydrogen Bonded Complex of Pyridine (B) and PFP (A)

[A₀] × 10³, moles/l.	Volume of B, μl	[B₀] × 10³, moles/l.	[C] × 10³,ᵃ moles/l.	[C]V × 10³, moles	−ΔH₀ᵦₛᵈ,ᵇ cal	−ΔHf, kcal/mole
20.00	198.6	12.27	6.24	1.25ᶜ	8.77	7.0
	203.7	13.26	6.69	1.27ᵉ	9.37	7.4
	297.9	18.42	8.53	1.71ᶜ	12.0	7.0
	302.7	19.70	8.95	1.70ᵉ	12.4	7.3
10.00	96.8	6.137	2.26	0.441ᵈ	3.16	7.2
	106.2	6.911	2.49	0.473ᵉ	3.45	7.3
	135.8	8.837	3.04	0.578ᵉ	4.14	7.2
	136.2	8.636	2.98	0.581ᵈ	4.24	7.3
	194.5	12.33	3.88	0.757ᵈ	5.46	7.2
	198.6	12.28	3.88	0.776ᶜ	5.55	7.2
10.00	203.7	13.26	4.08	0.775ᵉ	5.48	7.1
	292.8	18.57	5.04	0.983ᵈ	7.15	7.3
	297.9	18.42	5.02	1.00ᶜ	6.96	7.0
5.00	135.8	8.837	1.74	0.331ᵉ	2.29	6.9
	198.6	12.27	2.16	0.432ᶜ	2.98	6.9
					Av 7.2 ± 0.2	

ᵃ K_f^{298} used = 75.0 l./mole. ᵇ ΔH_{obsd} is corrected for $\Delta \bar{H}_s$ of pyridine in carbon tetrachloride. $\Delta \bar{H}_s$ used = +0.36 kcal/mole. ᶜ Volume of solutions used: V = 0.20 l. ᵈ Volume of solutions used: V = 0.195 l. ᵉ Volume of solutions used: V = 0.19 l.

by method I in carbon tetrachloride and method II in which the base does not contact the solvent.

In the discussion of ir spectroscopic procedures above, we demonstrated that our phenols are not associated in carbon tetrachloride at concentrations below 0.02 M. A calorimetric study confirmed this conclusion, as can be seen from Table III. The

Table III. Heat of Solution of p-Fluorophenol in Carbon Tetrachloride

PFP added Milligrams	Millimolesᵃ	ΔH_{obsd}, cal	$\Delta \bar{H}_s$, kcal/mole
21.5	0.192	1.353	7.05
52.4	0.467	3.260	6.98
63.2	0.564	4.055	7.19
87.0	0.776	5.426	6.94
93.2	0.831	5.820	7.00
96.5	0.861	5.984	6.95
116.7	1.041	7.220	6.94
164.0	1.462	10.37	7.09
194.5	1.735	12.00	6.92
254.6	2.271	16.06	7.07
349.4	3.117	21.85	7.01
413.0	3.684	25.53	6.93
667.6	5.955	41.60	6.99
1017.0	9.072	63.45	6.99
1311.9	11.703	81.55	6.97
		Av +7.00 ± 0.07	

ᵃ The volumes of solvent used varied. They are 190, 200, and 210 ml.

$\Delta \bar{H}_s$ values are constant within experimental error, up to 0.03 M, and a plot of millimoles of the phenol injected into the calorimeter *vs.* observed heat of solution in calories is linear through the origin.[24] This proves the absence of calorimetrically significant solute–solute interactions and $\Delta \bar{H}_s$, therefore, corresponds to the value at infinite dilution.

The most serious limitations of the high dilution method are (a) its dependence on another method (in our case, ir) for values of K_f; (b) the fact that ΔH_f is very sensitive to errors in K_f when the latter is small. With strong bases like pyridine, etc., the K_f's are large (50 l./mole and above) so that an error of ±2 l./mole in K_f does not affect the calculated ΔH_f. However, for weaker bases like THF, ether, etc., (K_f of 20 l./mole

or less), an error of ±2 l./mole in K_f changes ΔH_f drastically. For much weaker bases like anisole, diphenyl ether, π bases, etc., this method is almost useless because the K_f values themselves are 5 l./mole and less. Table IV lists the sensitivity of ΔH_f to K_f for some typical cases.

Table IV. Demonstration of Sensitivity of ΔH_f to K_f

Base	Proton donor	ΔHf, kcal/mole Using an accurate Kf Kf	−ΔHf	Using an assumed but wrong Kf Kf	−ΔHf
Pyridine	PFP	75	7.2 ± 0.2	55	8.5 ± 0.1
Pyridine	Phenol	49.7	7.2 ± 0.2	55	6.8 ± 0.2
Anisole	PFP	2.3	3.1 ± 0.2	1.2	5.7 ± 0.3
Diphenyl ether	PFP	2.2	1.9 ± 0.4	0.8	4.9 ± 1.0
Ethyl acetate	PFP	12.3	4.9 ± 0.2	10.0	5.8 ± 0.2
Tetrahydrofuran	PFP	17.7	6.0 ± 0.3	16.0	6.5 ± 0.3

Method II. The Pure Base Method. In order to avoid the difficulties cited above resulting from the need for accurate K_f values at high dilution, a totally different approach was attempted under conditions where complete complexing of the hydrogen bond donor and acceptor could usually be assured—namely, a dilute solution of the phenol in pure, liquid base as solvent.

When a small quantity (50–300 mg) of hydrogen bonding acid (say PFP) is injected into a large excess of base as solvent, there are two obvious heat terms involved: (1) the heat due to hydrogen bonding interaction, and (2) the heat term that might occur if there were no hydrogen bonding.

Assuming a 1:1 complex (*i.e.*, that under these conditions, each molecule of the phenol is hydrogen bonded to one molecule of B), other interactions between the phenol and the surrounding B molecules will also occur. If, however, it is possible to choose a proper model compound to correct completely for these other interactions, the hydrogen bonding energy can be isolated. The model compounds which we tried were p-fluoroanisole for p-fluorophenol (p-difluorobenzene was also tried as a model), anisole for

phenol (fluorobenzene and chlorobenzene were also tried), and n-butyl chloride for n-butyl alcohol.

When the model compound is injected into the pure base as solvent, the observed heat of solution is a sum of (1) the heat of solution which it might be expected to give in an inert solvent, and (2) special interactions. To correct for the heats of solution of our acids and model compounds, carbon tetrachloride was used as the reference inert solvent. Other reference solvents were cyclohexane, methylcyclohexane, n-hexane, carbon disulfide, chloroform, dichloromethane, and isooctane.

The determination of ΔH_f is then simply a matter of measuring (i) $\Delta \bar{H}_s$ of the acid (A) in pure base, (ii) $\Delta \bar{H}_s$ of the model (M) in pure base, (iii) $\Delta \bar{H}_s$ of the acid (A) in the reference solvent, and (iv) $\Delta \bar{H}_s$ of the model (M) in the reference solvent. Then

$$(\Delta H_f)_{A...B} = (\Delta \bar{H}_s{}^A - \Delta \bar{H}_s{}^M)_{base} - (\Delta \bar{H}_s{}^A - \Delta \bar{H}_s{}^M)_{ref\ solv}$$

This method has the advantage of giving ΔH_f directly, since if all A molecules are converted to 1:1 complex, no estimate of K_f is needed. Infrared spectra showed no free hydroxyl frequency for phenol (at 3610 cm^{-1}) even in a base as weak as benzene. One may argue further that the 1:1 complex assumption is valid because ΔH_f values obtained by the pure base method agree within experimental error with those obtained by method I, except, of course, when the bases are highly associated (e.g., dimethyl sulfoxide and dimethylacetamide). Other important experimental advantages of this method are: (1) the much larger and, therefore, more precisely measurable molar heats that are produced by complete complexing, and (2) the reduced need for careful temperature control since ΔH_f has a much smaller temperature coefficient than does K_f.

The experimental advantages of this method would be completely overruled if there were a large medium effect on ΔH_f itself. So, a systematic study of the sensitivity of ΔH_f to solvent composition in binary mixtures intermediate between CCl$_4$ and pure base was carried out for a few carefully selected bases. The results, which will be reported in a subsequent article, indicate that ΔH_f is relatively invariant to solvent composition, except in the case of highly associated liquids with high dielectric constants. This important conclusion has already been suggested by the agreement between methods I and II and justifies the original assumptions of method II.

A typical calculation for this method is as follows using p-fluorophenol as the proton donor and pyridine as the base: (i) $\Delta \bar{H}_s$ of p-fluorophenol in pure pyridine = -1.01 ± 0.06 kcal/mole, (ii) $\Delta \bar{H}_s$ of p-fluoroanisole in pure pyridine = $+0.06 \pm 0.01$ kcal/mole, (iii) $\Delta \bar{H}_s$ of p-fluorophenol in carbon tetrachloride = $+7.00 \pm 0.07$ kcal/mole, and (iv) $\Delta \bar{H}_s$ of p-fluoroanisole in carbon tetrachloride = $+0.67 \pm 0.02$ kcal/mole; $\Delta \bar{H}_f = (-1.01 \pm 0.06 - 0.06 \pm 0.01) - (+7.00 \pm 0.07 - 0.67 \pm 0.02) = -7.40 \pm 0.09$ kcal/mole. This may be compared with the result obtained by method I using $K_f = 75$ which is -7.2 ± 0.2 kcal/mole.

Results

In Table V are presented the combined results for the systems we have studied to date.

Their precision is suggested by the error limits shown in the table and the following comments. Infrared shifts ($\Delta \nu$) of the 3610 cm^{-1} band of p-fluorophenol in carbon tetrachloride were extrapolated to zero concentration with an error of ± 2 or 3 cm^{-1}. Unless cited otherwise, all equilibrium constants (K_f) and the free energies derived from them ($\Delta G_f{}^\circ$) were obtained by the infrared method. In several cases where very weak complexes are formed, K_f was obtained from calorimetric data alone by variation of base concentration; this method will be described fully in a later article. In all cases, the thermodynamic standard state is high dilution in carbon tetrachloride at 25° for the process of complex formation [acid (A) + base (B) $\rightleftharpoons$ complex (C)] using molarity (M) concentration units. Reported enthalpy values (ΔH_f) are given with errors expressed as standard deviations. Those determined by the high dilution method were usually derived from 10 to 15 heat measurements while those by the pure base method employed 2 to 5. The accuracy of these results will be considered in the Discussion where their internal consistency and agreement with the work of others shall be compared.

The actual stretching frequency of a hydrogen bond falls at a rather low frequency (100–200 cm^{-1}) and so might have a great enough heat capacity to make ΔH_f sensitive to temperature. That this is not so is demonstrated by good linear van't Hoff plots of log K_f vs. $1/T$ obtained for several systems by Taft's group and by a complete determination of ΔH_f for the pyridine–PFP complex at 34 ± 0.5° and at 12 ± 1° using ΔH_f at 25° to calculate K_f at these temperatures by the van't Hoff equation from K_f at 25°. The values obtained are $\Delta H_f{}^{34} = -7.1 \pm 0.4$ kcal/mole from $K_f{}^{34} = 52.5$ l./mole and $\Delta H_f{}^{12} = -7.2 \pm 0.2$ kcal/mole from $K_f{}^{12} = 130.6$ l./mole.

A wealth of thermochemical data was generated in the course of the calorimetric study. These data are summarized in Table VI where the partial molar heats of solution ($\Delta \bar{H}_s$) of p-fluorophenol, p-fluoroanisole, phenol, anisole, n-butyl alcohol, and n-butyl chloride in the 29 bases which were studied by the pure base method are reported. In Table VII are listed the corresponding heats of solution ($\Delta \bar{H}_s$) of many of these compounds in carbon tetrachloride, these measurements having been made in the course of the high dilution study. Most of the liquid solutes which are devoid of hydrogen-bonding sites give small heats of solution (less than 1 kcal/mole) in each other as would be expected for nearly perfect solutions. Large negative $\Delta \bar{H}_s$ generally represent exothermic hydrogen-bond formation between solvent and solute. Positive (endothermic) $\Delta \bar{H}_s$ values are found when work must be done against cohesive forces in the solute, such as association if it is liquid, or lattice energy if it is a solid.

Discussion

In the preceding sections, we presented two independent approaches for determining the heat of hydrogen bond formation. In the high dilution method the observed heat of reaction of the hydrogen bond donor and acceptor is measured as a function of concentration at relatively high dilution in an "inert" solvent. The molar heat evolved depends on the fraction of donor and acceptor molecules which are complexed and this

Table V. Summary of Infrared Spectroscopic ($\Delta\nu$ and K_f) and Calorimetric Results for Hydrogen Bond Complexes of p-Fluorophenol (PFP), Phenol, and Methanol with Various Acceptor Bases at 25° in Carbon Tetrachloride

Acceptor base	$\Delta\nu$, cm^{-1} (PFP)	$\Delta\nu$, cm^{-1} (MeOH)	K_f, l./mole[a] (PFP)	K_f, l./mole (phenol)	$-\Delta H_f$, kcal/mole (high diln, PFP)	$-\Delta H_f$, kcal/mole (pure base, PFP)	$-\Delta G_f°$, kcal/mole	$-\Delta S_f°$ cal/mole deg
Benzene	49[l]	28[l]				1.23 ± 0.11		
Toluene	57[l]	31[l]				1.27 ± 0.11		
Mesitylene	76[l]	47[l]				1.60 ± 0.11		
Cyclohexyl chloride	71[l]	26 ± 5[l]				2.12 ± 0.11		
Cyclohexyl bromide	90[l]	32 ± 5[l]				1.96 ± 0.10		
Cyclohexyl iodide	95[l]	38 ± 5[l]				1.46 ± 0.11		
n-Butyl chloride	62[l]	27 ± 5[l]				1.93 ± 0.08		
n-Butyl bromide	71[l]	35 ± 5[l]				1.82 ± 0.07		
n-Butyl iodide	78[l]	50[l]				1.55 ± 0.11		
Diphenyl ether	43 ± 5[b,l] / 132[l]	28 ± 5[b,l] / 66 ± 5[l]	1.9 ± 0.2[c]		1.9 ± 0.4	1.89 ± 0.10	0.38 ± 0.06	5.1 ± 1.3
Anisole	43 ± 5[b] / 169	32 ± 5[b,l] / 75[l]	2.3 ± 0.2[c]		3.1 ± 0.2	3.13 ± 0.08	0.49 ± 0.05	8.8 ± 0.6
N,N-Dimethylaniline	83[b,l] / 382 ± 10[h,l]	41[b,l] / 212 ± 10[h,l]	3.5 ± 0.4[c]		4.0 ± 0.4	4.02 ± 0.08	0.74 ± 0.07	10.9 ± 1.3
Dibenzyl ether	38 ± 5[b,l] / 249[l]	24 ± 5[b,l] / 126[l]	6.3 ± 0.6[c]		4.5 ± 0.3	4.59 ± 0.09	1.09 ± 0.05	11.4 ± 1.0
Dioxane	252	122 ± 5				5.10 ± 0.11		
Diethyl ether	285	139[d]	10.3 ± 1.0[c]		5.6 ± 0.1	5.57 ± 0.12	1.38 ± 0.05	14.2 ± 0.3
Ethyl acetate	142/201 199 ± 5[f,l]	69/102 102 ± 5[f,l]	12.3 ± 0.4	9.0 ± 0.4		4.74 ± 0.12	1.49 ± 0.02	10.9 ± 0.3[e]
2-Butanone	138/246 221 ± 5[f,l]	71/116 113 ± 5[f,l]	15.6 ± 0.5	10.6 ± 0.4		5.20 ± 0.13	1.63 ± 0.02	12.0 ± 0.3[e]
N,N-Dimethylaminopropionitrile	164[g] / [h,i]	76[g] / 356 ± 5[h]	17.1 ± 0.9		5.8 ± 0.1		1.68 ± 0.03	13.8 ± 0.3
Anthrone	156/234 218 ± 5[f,l]	71/115 112 ∓ 5[f,l]	17.6 ± 0.2		5.6 ± 0.4		1.70 ± 0.01	13.1 ± 1.3
Tetrahydrofuran	292	150	17.7 ± 0.5	13.3 ± 0.4	5.6 ± 0.1	5.75 ± 0.08	1.70 ± 0.02	13.1 ± 0.3
3-Bromopyridine	421	228	20.3 ± 0.9		6.2 ± 0.2		1.78 ± 0.03	14.8 ± 0.7
Cyclohexanone	141/250 229 ± 5[f,l]	95/159 147 ± 5[f,l]	20.5 ± 0.7		5.8 ± 0.2	5.68 ± 0.09	1.79 ± 0.02	13.4 ± 0.7
Quinoline	498 ± 10	284	72.3 ± 1		7.35 ± 0.1	7.47 ± 0.09	2.54 ± 0.01	16.1 ± 0.3
Pyridine	485 ± 10	268	76.2 ± 1.1	49.7 ± 1.0	7.1 ± 0.1	7.40 ± 0.09	2.56 ± 0.01	15.2 ± 0.3
Triethylamine	i	410	85.2 ± 1.9			8.92 ± 0.09	2.63 ± 0.02	21.0 ± 0.3[e]
N-Methylformamide	271 ± 10	122 ± 10	90.0 ± 5.6		5.5 ± 0.1	6.44 ± 0.08	2.67 ± 0.03	9.5 ± 0.3
Diphenyl sulfoxide	311 ± 5	160	105 ± 1		6.3 ± 0.3		2.76 ± 0.01	11.9 ± 1.0
4-Picoline	495 ± 10	285	109 ± 5		7.3 ± 0.1	7.59 ± 0.08	2.78 ± 0.03	15.2 ± 0.3
N,N-Dimethylformamide	239/318 308 ± 5[f,l]	131/165 157 ± 5[f,l]	116 ± 3	75.5 ± 2.0	6.6 ± 0.1	6.97 ± 0.11	2.81 ± 0.01	12.7 ± 0.3
N,N-Dimethylacetamide	261/363 356 ± 5[f,l]	153/215 203 ± 5[f,l]	260 ± 12	134 ± 3.0		7.44 ± 0.13	3.29 ± 0.03	13.9 ± 0.3[e]
Dimethyl sulfoxide	367	199	346 ± 8	202 ± 2.0	6.6 ± 0.1	7.21 ± 0.08	3.46 ± 0.02	10.9 ± 0.3
Triphenylphosphine oxide	422 ± 5	237	1456 ± 80		7.4 ± 0.1		4.32 ± 0.01	10.3 ± 0.3
Hexamethylphosphoramide	479 ± 10	269	~3600		8.0 ± 0.1	8.73 ± 0.11	4.85 ± 0.02	10.6 ± 1.3
Cyclopropylamine	i	304 ± 5	44 ± 2[j]		7.5 ± 0.3		2.24 ± 0.01	17.6 ± 1.0
4-Dimethylaminopyridine	i	352[k]	650 ± 90[j]		7.8 ± 0.1		3.79 ± 0.01	13.4 ± 0.3

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a Compare with value obtained by ^{19}F nmr in companion paper. *b* Represents hydrogen bonding of donor to phenyl ring. *c* K_f determined using calorimetric data alone. *d* A. Allerhand and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **85**, 371 (1963). *e* Calculated using $-\Delta H_f$ (pure base). *f* There is a problem in reporting $\Delta\nu$ for compounds which give more than one bonded band or give an asymmetric peak. Traditionally, $\Delta\nu$ is measured to the point of maximum absorption. It would be preferable to report not only a $\Delta\nu$ for each component band, but also a composite $\Delta\nu$ based on the weighted average of the areas (in per cent absorbance) of the individual component bands. This has been done for the cases indicated. *g* Represents hydrogen bonding of donor to nitrile group. *h* Represents hydrogen bonding of donor to amino group. *i* Value extremely difficult to obtain accurately due to interference with C-H stretching region of donor. A reasonable approximation is $\Delta c_{C_6H_5OH} = 1.85 \cdot \Delta\nu_{MeOH}$: L. Joris, Ph.D. Thesis, Princeton University, 1968. *j* Measured by Taft and Gurka using ^{19}F nmr. *k* L. Joris and P. v. R. Schleyer, *Tetrahedron*, **24**, 5991 (1968). *l* Values were obtained by using a Du Pont 310 curve resolver to resolve peak(s).

Table VI. Summary of Thermochemical Results for Determining Heats of Hydrogen Bonding (ΔH_f) by the Pure Base Method

Base	$\Delta\bar{H}_s$ of PFP*a* in base, kcal/mole	$\Delta\bar{H}_s$ of PFA*b* in base, kcal/mole	$-\Delta H_f$*c* (PFP),*a* kcal/mole	$\Delta\bar{H}_s$ of phenol in base, kcal/mole	$\Delta\bar{H}_s$ of anisole in base, kcal/mole	$-\Delta H_f$,*c* kcal/mole	$\Delta\bar{H}_s$ of *n*-butyl alcohol in base, kcal/mole	$\Delta\bar{H}_s$ of *n*-butyl chloride in base, kcal/mole	$-\Delta H_f$,*c* kcal/mole
Benzene	+5.10 ± 0.09	0	1.23 ± 0.11	+4.72 ± 0.01	0	1.18 ± 0.07	+3.93 ± 0.08	+0.08 ± 0.01	0.50 ± 0.14
Toluene	+4.94 ± 0.05	−0.12 ± 0.07	1.27 ± 0.11	+4.51 ± 0.03	−0.06 ± 0.03	1.33 ± 0.08	+3.56 ± 0.11	−0.29 ± 0.04	0.50 ± 0.16
Mesitylene	+4.78 ± 0.08	+0.05 ± 0.01	1.60 ± 0.11	+4.62 ± 0.13	+0.29 ± 0.01	1.57 ± 0.15	+3.62 ± 0.01	−0.19 ± 0.04	0.54 ± 0.12
Cumene				+4.47 ± 0.08	+0.12 ± 0.01	1.55 ± 0.11	+3.64 ± 0.07	−0.16 ± 0.01	0.55 ± 0.13
n-Butyl chloride	+4.81 ± 0.03	+0.41 ± 0.02	1.93 ± 0.08	+4.52 ± 0.06	+0.33 ± 0.02	1.71 ± 0.10			
n-Butyl bromide	+4.73 ± 0.10	+0.22 ± 0.02	1.82 ± 0.07	+4.39 ± 0.03	+0.20 ± 0.02	1.71 ± 0.08			
n-Butyl iodide	+5.65 ± 0.03	+0.87 ± 0.07	1.55 ± 0.11	+5.18 ± 0.18	+0.54 ± 0.13	1.3 ± 0.2			
Cyclohexyl chloride	+4.85 ± 0.07	+0.64 ± 0.03	2.12 ± 0.11	+4.38 ± 0.10	+0.51 ± 0.04	2.03 ± 0.13			
Cyclohexyl bromide	+5.14 ± 0.06	+0.77 ± 0.04	1.96 ± 0.10	+4.60 ± 0.03	+0.51 ± 0.04	1.81 ± 0.09			
Cyclohexyl iodide	+5.73 ± 0.07	+0.86 ± 0.06	1.46 ± 0.11	+5.10 ± 0.04	+0.55 ± 0.10	1.35 ± 0.13			
Diphenyl ether	+4.66 ± 0.06	+0.22 ± 0.04	1.89 ± 0.10	+4.20 ± 0.10	+0.11 ± 0.01	1.81 ± 0.12	+3.50 ± 0.03	+0.25 ± 0.07	1.10 ± 0.14
Anisole	+3.20 ± 0.04	0	3.13 ± 0.08	+2.82 ± 0.11	0	3.08 ± 0.13	+2.82 ± 0.07	+0.16 ± 0.03	1.69 ± 0.14
Dibenzyl ether	+1.65 ± 0.06	−0.09 ± 0.01	4.59 ± 0.09	+1.51 ± 0.07	+0.04 ± 0.02	4.43 ± 0.10			
Dioxane	+1.01 ± 0.09	−0.22 ± 0.01	5.10 ± 0.11	+0.85 ± 0.04	+0.06 ± 0.01	5.11 ± 0.08	+1.72 ± 0.01	+0.48 ± 0.01	3.11 ± 0.11
Ether	+0.41 ± 0.09	−0.35 ± 0.04	5.57 ± 0.12	+0.45 ± 0.04	0	5.45 ± 0.08	+1.15 ± 0.04	−0.24 ± 0.05	2.96 ± 0.13
Tetrahydrofuran	−0.17 ± 0.01	−0.75 ± 0.01	5.75 ± 0.08	−0.36 ± 0.10	−0.51 ± 0.02	5.75 ± 0.12	+1.06 ± 0.02	−0.23 ± 0.01	3.06 ± 0.11
Ethyl acetate	+1.13 ± 0.09	−0.46 ± 0.04	4.74 ± 0.12	+0.98 ± 0.01	−0.17 ± 0.01	4.75 ± 0.08	+2.13 ± 0.07	+0.21 ± 0.01	2.43 ± 0.13
2-Butanone	+0.70 ± 0.11	−0.43 ± 0.01	5.20 ± 0.13	+0.48 ± 0.06	−0.19 ± 0.01	5.23 ± 0.09	+1.50 ± 0.07	+0.20 ± 0.01	3.05 ± 0.13
N,N-Dimethylaniline	+2.00 ± 0.01	−0.31 ± 0.04	4.02 ± 0.08	+1.93 ± 0.04	−0.08 ± 0.01	3.89 + 0.08	+2.24 ± 0.03	−0.09 ± 0.03	2.02 ± 0.12
Pyridine	−1.01 ± 0.06	+0.06 ± 0.01	7.40 ± 0.09	−1.41 ± 0.07	+0.03 ± 0.01	7.34 ± 0.10	+0.30 ± 0.03	+0.42 ± 0.01	4.47 ± 0.12
Quinoline	−1.14 ± 0.06	0	7.47 ± 0.09	−1.61 ± 0.03	−0.07 ± 0.01	7.44 ± 0.08	−0.07 ± 0.04	+0.15 ± 0.03	4.57 ± 0.12
4-Picoline	−1.53 ± 0.04	−0.27 ± 0.01	7.59 ± 0.08	−1.76 ± 0.01	0	7.66 ± 0.08	−0.09 ± 0.01	+0.18 ± 0.07	4.62 ± 0.13
Triethylamine	−2.31 ± 0.05	+0.28 ± 0.01	8.92 ± 0.09	−2.41 ± 0.01	+0.54 ± 0.03	8.85 ± 0.08	−1.14 ± 0.02	+0.04 ± 0.01	5.53 ± 0.11
N-Methylformamide	0	+0.11 ± 0.02	6.44 ± 0.08	0	+0.48 ± 0.01	6.38 ± 0.07	+0.79 ± 0.03	+0.43 ± 0.02	3.99 ± 0.12
N,N-Dimethylformamide	−1.13 ± 0.08	−0.49 ± 0.02	6.97 ± 0.11	−1.06 ± 0.02	−0.10 ± 0.03	6.86 ± 0.08	+0.74 ± 0.03	+0.53 ± 0.01	4.14 ± 0.11
N,N-Dimethylacetamide	−1.76 ± 0.11	−0.65 ± 0.01	7.44 ± 0.13	−1.67 ± 0.04	−0.21 ± 0.01	7.36 ± 0.08	+0.28 ± 0.07	+0.36 ± 0.01	4.43 ± 0.13
Dimethyl sulfoxide	−0.66 ± 0.03	+0.22 ± 0.01	7.21 ± 0.08	−0.72 ± 0.01	+0.59 ± 0.03	7.21 ± 0.08	+0.93 ± 0.01	+1.24 ± 0.01	4.66 ± 0.11
Cyclohexanone	+0.23 ± 0.01	−0.42 ± 0.02	5.68 ± 0.09						
Hexamethylphosphoramide	−4.12 ± 0.08	−1.71 ± 0.05	8.78 ± 0.11						

a PFP is *p*-fluorophenol. *b* PFA is *p*-fluoroanisole. *c* Values in this column are obtained by subtracting the following values from the difference between the two terms in the two columns to its left: $(\Delta\bar{H}_s{}^{PFP} - \Delta\bar{H}_s{}^{PFA})_{CCl_4} = 6.33 \pm 0.07$; $(\Delta\bar{H}_s{}^{phenol} - \Delta\bar{H}_s{}^{anisole})_{CCl_4} = 5.90 \pm 0.07$; $(\Delta\bar{H}_s{}^{BuOH} - \Delta\bar{H}_s{}^{BuCl})_{CCl_4} = 4.35 \pm 0.11$ [*e.g.*, for pyridine with PFP; $\Delta H_f(PFP) = (-1.01 - 0.06 - 6.33 = -7.40)$].

Table VII. Partial Molar Heats of Solution at High Dilution ($\Delta \bar{H}_s$) for Various Compounds in Carbon Tetrachloride at 25°

Compound	$\Delta \bar{H}_s$, kcal/mole
1. Hexamethylphosphoramide	-1.41 ± 0.05
2. Triethylamine	-0.68 ± 0.02[a]
3. Tetrahydrofuran	-0.60 ± 0.02
4. Diethyl ether	-0.42 ± 0.01
5. 4-Picoline	-0.05 ± 0.01
6. Ethyl acetate	$+0.014 \pm 0.004$
7. n-Butyl chloride	$+0.08 \pm 0.01$
8. Cyclohexanone	$+0.09 \pm 0.01$
9. N,N-Dimethylaniline	$+0.12 \pm 0.01$
10. Chlorobenzene	$+0.15 \pm 0.02$
11. Diphenyl ether	$+0.17 \pm 0.03$
12. 3-Bromopyridine	$+0.23 \pm 0.03$
13. Fluorobenzene	$+0.26 \pm 0.03$
14. Dibenzyl ether	$+0.30 \pm 0.02$
15. Pyridine	$+0.36 \pm 0.02$
16. Anisole	$+0.37 \pm 0.02$
17. N,N-Dimethylacetamide	$+0.41 \pm 0.02$
18. 2-Butanone	$+0.43 \pm 0.01$
19. p-Difluorobenzene	$+0.45 \pm 0.02$
20. Quinoline	$+0.46 \pm 0.01$
21. p-Fluoroanisole	$+0.67 \pm 0.02$
22. Cyclopropylamine	$+0.76 \pm 0.03$
23. Acetophenone	$+0.79 \pm 0.01$
24. N,N-Dimethylformamide	$+0.87 \pm 0.01$
25. N,N-Dimethylaminopropionitrile	$+1.03 \pm 0.11$
26. Dimethyl sulfoxide	$+1.76 \pm 0.04$
27. Acetonitrile	$+1.81 \pm 0.03$
28. Triphenylphosphine oxide	$+4.15 \pm 0.23$
29. n-Butyl alcohol	$+4.43 \pm 0.11$
30. 4-Dimethylaminopyridine	$+5.16 \pm 0.20$
31. Diphenyl sulfoxide	$+5.23 \pm 0.10$
32. Flavone	$+5.33 \pm 0.30$
33. Anthrone	$+5.58 \pm 0.15$
34. 2,6-Dimethyl-γ-pyrone	$+6.06 \pm 0.13$
35. Phenol	$+6.27 \pm 0.07$
36. p-Fluorophenol	$+7.00 \pm 0.07$

[a] Triethylamine is known to react with carbon tetrachloride.[34]

fraction may be small at high dilution. Therefore, it is necessary to know the equilibrium constant for complexing and this we have obtained by infrared spectroscopy. These equilibrium constants may be used to derive entropies of formation when combined with corresponding enthalpies. The chief drawback of this method for weak complexes is the extreme sensitivity of ΔH_f to the magnitude and precision of K_f.

The second approach, the pure base method, has the great advantage of being quite independent of K_f. Here a small amount of the hydrogen-bonding acid is injected directly into a large excess of the pure base as solvent so that for all except the weakest interactions total complexing may be assumed. Correction is then made for all other thermochemically significant interactions by using an aprotic model compound for the hydrogen bond donor. In view of the fact that this is, to our knowledge, a novel method *and is theoretically unsupported, it should be regarded with skepticism. Accordingly, we have subjected it to the tests described below.*

For this method to be accepted as giving reliable and accurate values for ΔH_f, we believe the following conditions should be satisfied.

(1) ΔH_f's from method II should agree well with those determined by the high dilution method using well-established K_f's, and with reliable data from other laboratories.

(2) The model compounds used (anisole for phenol and p-fluoroanisole for p-fluorophenol) should correct for all interactions other than hydrogen bonding.

(3) The medium effect should be negligible in most cases and in those cases (polar solvents) where it is important, a reasonable estimate of the effect must be obtainable.

Table V allows comparison for 14 bases of ΔH_f values determined by the two methods. They are almost identical within experimental error for all bases except DMSO, DMF, N-methylformamide, and hexamethylphosphoramide. For the first three of these, the differences are not large. For hexamethylphosphoramide, it is about 10%.

In Table VIII our results are compared with a number of the most reliable published values for about 20 well-documented cases. Agreement of our K_f's obtained by infrared measurements with the ^{19}F nmr numbers is demonstrated elsewhere.[36] The general conformity of our ΔH_f values with reliable ones obtained by other workers using other methods lends further support to our own techniques.

In Figure 2, ΔH_f for complexing of 27 bases with p-fluorophenol is compared with the corresponding values for phenol and n-butyl alcohol. The excellent correlation between data for the two phenols in this wide variety of media supports the method further and is useful for estimating ΔH_f values for bases measured with one phenol but not the other. The poorer correlation of n-butyl alcohol, especially for hindered bases (points 16 and 20), probably reflects different steric requirements between the aliphatic and aromatic alcohols.

Table VI shows that the ΔH_f's for complexing of phenol and p-fluorophenol are very similar, with the values of PFP running slightly higher as expected. Moreover, it is seen that there is a considerable difference between the heats of transfer of phenol and p-fluorophenol from carbon tetrachloride to any basic solvent as is also found for the corresponding properties of anisole and p-fluoroanisole (the respective model compounds). However, when the heats for each pair of phenol and ether are combined as shown, the ΔH_f's compare extremely well for phenol and PFP.

$$(\Delta H_f) = [(\Delta \bar{H}_s{}^{acid} - \Delta \bar{H}_s{}^{methyl\ ether}{}_{base}) -$$

$$(\Delta \bar{H}_s{}^{acid} - \Delta \bar{H}_s{}^{methyl\ ether}{}_{CCl_4})$$

Further evidence that p-fluorophenol is a slightly stronger hydrogen-bond donor than phenol is provided by the infrared shifts in Table IX. The fact that p-fluorophenol is also slightly more acidic ($pK_a = 9.91$) than phenol ($pK_a = 9.95$) in water might be noted although it is not necessarily relevant to hydrogen bonding.

The fact that the pure base method gives such good agreement with the high dilution method is itself the strongest argument both for the use of the methyl ether as a model for the phenol and also for the relative unimportance of solvent effects. Further evidence on the first point follows from Table VII where it is seen that chlorobenzene, fluorobenzene, and p-difluorobenzene which might be considered as alternative

(36) D. Gurka and R. W. Taft, *J. Am. Chem. Soc.*, **91**, 4794 (1969); R. W. Taft, D. Gurka, L. Joris, P. von R. Schleyer, and J. W. Rakshys, *ibid.*, **91**, 4801 (1969).

Table VIII. Comparison of Our Results with Those from the Literature. All Values are for Hydrogen Bonding to Phenol

Acceptor base	Δν, cm⁻¹	Cited values		$K_f(25°)$, l./mole	Cited values
Benzene	46[a]	49[b]	49 ± 1[c]		
Toluene	56[a]	58[b]	56 ± 1[c]		
Mesitylene	75[a]	78[b]			
Cyclohexyl chloride	68	66[f]			
Cyclohexyl bromide	89	82[f]			
Cyclohexyl iodine	95	86[f]			
Dioxane	237[a]	234[cc]			
Diphenyl ether	43 ± 5[a,ee]; 132[a]	119;[h] 125 ± 5;[c] 130[i]			
Anisole	46 ± 5[a,ee]; 160[a]	150[b]	165 ± 3[c]	(2.1)[k]	1.20[c]
Dibenzyl ether	39 ± 5[a,ee]; 234[a]	237;[h] 230 ± 7;[c] 233[i]			
Ether	275[a]	279;[l] 279 ± 7;[c] 271[i]		(8.5)[k]	9.73;[c] 8.83[bb]
Tetrahydrofuran	285	285[n]	283[i]	13.3 ± 0.4	13.5 ± 0.5;[n] 11.0;[i,t] 16.2[j]
Ethyl acetate	145, 207 } 193 ± 5[a,ff]	164;[n] 163;[bb] 164[q]		9.0 ± 0.4	7.2 ± 0.4;[n] 9.3 ± 0.3;[q] 8.7;[i,t] 10.1[bb]
2-Butanone	125, 216 } 205 ± 5[a,ff]	198[bb]		10.6 ± 0.4	8.9;[i,t] 12.3[bb]
Pyridine	471	465 ± 10;[n] 465;[r] 475 ± 5;[s] 492[u]		49.7 ± 1	42.0;[s] 49;[t,u] 43[q,t]
Quinoline	489 ± 10	498[u]			
4-Picoline	485 ± 10	500[u]			
Triethylamine	dd			(59.7)[k]	58;[s] 89 ± 4[q]
N,N-Dimethylformamide	209, 304 } 297 ± 5[a,ff]	294[q]	292[v]	75.5 ± 2	64 ± 1;[v] 68;[q,t] 67[t,v]
Dimethyl sulfoxide	357	350[z]		202 ± 4	182 ± 1,[d] 183[z]
N,N-Dimethylacetamide	256 344 ± 5[a,ff]; 348	345[n]		134 ± 3	107 ± 15;[n] 134 ± 3[aa]

[a] Values obtained by using DuPont 310 curve resolver to resolve peak(s). [b] Z. Yoshida and E. Ōsawa, *J. Am. Chem. Soc.*, **88**, 4019 (1966). [c] B. Wayland and R. S. Drago, *ibid.*, **86**, 5240 (1964). [d] R. S. Drago, B. Wayland, and R. L. Carlson, *ibid.*, **85**, 3125 (1963). [e] R. West, International Symposium on Molecular Structure and Spectroscopy, Tokyo, Sept 1962, P.D. 117-1. [f] R. West, D. L. Powell, L. S. Whatley, M. K. T. Lee, and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **84**, 3221 (1962). [g] H. Fritsche, *Ber. Bunsenges. Physik. Chem.*, **68**, 459 (1964). [h] E. Ōsawa, T. Kato, and Z. Yoshida, *J. Org. Chem.*, **32**, 2803 (1967). [i] T. Gramstad, *Spectrochim. Acta*, **19**, 497 (1963). [j] R. West, D. L. Powell, M. K. T. Lee, and L. S. Whatley, *J. Am. Chem. Soc.*, **86**, 3227 (1964). [k] Estimated using relationship: log $K_{f(phenol)}$ = 0.92 log $K_{f(PFP)}$; see T. S. S. R. Murty, Thesis. [l] R. West, 139th National Meeting of the American Chemical Society, St. Louis, Mo., March 1961. [m] R. J. Niedyielski, R. S. Drago, and R. L. Middaugh, *J. Am. Chem. Soc.*, **86**, 1694 (1964). [n] T. D. Epley and R. S. Drago, *ibid.*, **89**, 5770

Table IX. Comparison of Δν Values in Dilute Carbon Tetrachloride Solution for Phenol and PFP

Base	Δν to phenol, cm⁻¹	Δν to PFP, cm⁻¹
Benzene	46	49
Cyclohexyl iodide	95	95
Dioxane	237	252
Ether	275	285
Tetrahydrofuran	285	292
Dimethyl sulfoxide	357	367
Quinoline	489	498

Table X. Comparison of the Enthalpy of Solution of Fluorobenzene, Chlorobenzene, p-Difluorobenzene, Anisole, and PFA in Various Solvents at 25°

Solvent	Model compd	$\Delta \bar{H}_s$, kcal/mole	Ether	$\Delta \bar{H}_s$, kcal/mole
Carbon disulfide	Fluorobenzene	+0.94	Anisole	+0.99
n-Hexane		+0.92		+1.45
Methylcyclohexane		+0.92		+1.34
Carbon disulfide	Chlorobenzene	+0.54		+0.99
Carbon disulfide	p-Difluorobenzene	+1.35	PFA	+1.44
n-Hexane		+0.95		+1.37
Methylcyclohexane		+1.19		+1.63

models have nearly the same $\Delta \bar{H}_s$ in carbon tetrachloride as do anisole and p-fluoroanisole. Correspondingly, their $\Delta \bar{H}_s$ values relative to the ether models are shown in Table X. The lack of thermochemically important solvent effects on the hydrogen bonded complex from the pure base to dilute carbon tetrachloride solution is also supported by $\Delta \bar{H}_s$ results in a number of binary mixtures intermediate between CCl₄ and the pure base. These show ΔH_f values identical with those at the two extremes, pure CCl₄ or pure base, except in the cases where there is a slight difference between results in the two media. In those cases, ΔH_f is a linear function of mole fraction composition.

Extrathermodynamic Correlations of Hydrogen-Bonding Properties. The linear free energy correlations of K_f with pK_a's in aqueous media and other proton-

transfer properties have been dealt with elsewhere.[36] One of our principle goals is to examine the relationship between enthalpies, entropies, and infrared shifts in hydrogen bonded systems. Although those presented in this report are incomplete, they are sufficiently provocative to merit comment at this time, especially since they will influence the direction of our future researches.

Isokinetic Relationships. The ΔH_f's and $\Delta S_f°$'s presented in Table V are mostly based on independent enthalpy and free energy measurements. Their correlation[37,38] may therefore be pursued without the nagging

(37) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley & Sons, Inc., New York, N. Y., 1963.
(38) M. G. Evans and M. Polanyi, *Trans. Faraday Soc.*, **32**, 1333 (1936).

$-\Delta H_f$, kcal/mole (pure base method)	Cited values				$-\Delta S_f^\circ$, cal/mole deg	Cited values
1.18 ± 0.07		1.82[e]				
1.33 ± 0.08	1.89[e]					
1.57 ± 0.15	2.46[e]					
2.03 ± 0.13	2.21[f]					
1.81 ± 0.09	2.05[f]					
1.35 ± 0.13	1.72[f]					
5.11 ± 0.08	5.00 ± 0.22[g]					
1.81 ± 0.12	2.6[i]	2.6[e]				
3.08 ± 0.13	3.5[j]	3.5[e]	3.3[c]			
4.43 ± 0.10	4.6[i]	4.6[e]	4.28 ± 0.11[j]			
5.45 ± 0.08	5.1 ± 0.5[m]	5.6[e]	5.1[i]	5.41 ± 0.06[j]		
5.6 ± 0.2[o]	5.30 ± 0.06[n]	5.3[j]	5.7[i]	5.5[p]	13.3 ± 0.7	12.2[i]
4.75 ± 0.08	4.77 ± 0.1[n]	4.7;[e] 4.45[bb]	4.2[i]		11.7 ± 0.3	6.3 ± 1.6[q]
5.23 ± 0.09	5.2[i]	6.5[e]	4.7[p]	5.34[bb]	12.8 ± 0.3	12.9[bb]
7.0 ± 0.2[o]	7.5[r]		7.0[u]	6.5[x]	15.7 ± 0.7	17.4;[r] 14.4;[s] 15.6;[u] 14.0[x]
7.44 ± 0.08	7.2[u]	6.74[w]				
7.66 ± 0.08	6.6[u]	6.72[w]	6.4[x]			
8.85 ± 0.08	7.8[u]	8.4[p]	9.1[s]			
6.86 ± 0.08	5.4[v]	6.2[p]			13.6 ± 0.3	
7.21 ± 0.08					16.5 ± 0.3	11.7 ± 0.6[aa]
7.36 ± 0.08	6.84 ± 0.1[n]					

(1967). [o] Done in dilute solution. [p] H. Dunken and H. Fritsche, *Z. Chem.*, **1**, 127, 249 (1961); **2**, 345 (1962). [q] M. D. Joesten and R. S. Drago, *J. Am. Chem. Soc.*, **84**, 3817 (1962). [r] G. Aksnes and T. Gramstad, *Acta Chem. Scand.*, **14**, 1485 (1960). [s] S. Singh and C. N. R. Rao, *Can. J. Chem.*, (129) **44**, 2611 (1966). [t] Calculated from K_f 20° using $\ln(K_2/K_1) = -\Delta H[T_2 - T_1]/RT_1T_2$. [u] T. Gramstad, *Acta Chem. Scand.*, **16**, 807 (1962). [v] T. Gramstad, *ibid.*, **16**, 1369 (1962). [w] D. Neerinck and L. Lamberts, *Bull. Soc. Chim. Belges*, **75**, 484 (1966). [x] J. Rubin and G. S. Panson, *J. Phys. Chem.*, **69**, 3089 (1965). [y] M. Joesten and R. S. Drago, *J. Am. Chem. Soc.*, **84**, 2696 (1962). [z] T. Gramstad, *Spectrochim. Acta*, **19**, 829 (1963). [aa] M. D. Joesten and R. S. Drago, *J. Am. Chem. Soc.*, **84**, 2037 (1962). [bb] D. L. Powell and R. West, *Spectrochim. Acta*, **20**, 983 (1964). [cc] A. Allerhand and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **85**, 371 (1963). [dd] See footnote i, Table V. [ee] See footnote b, Table V. [ff] See footnote f, Table V.

fear[18,37,39,40] that we are merely generating error contours from two sets of numbers (ΔH and ΔS) extracted from treatment of the same free energy values—a basic hazard in the van't Hoff–Arrhenius–Eyring methods of analyzing temperature dependence of equilibria and rates.

In Figures 3 and 4, ΔH_f is plotted first against ΔG_f° and then against $T\Delta S_f^\circ$. Naturally, since $\Delta G^\circ = \Delta H - T\Delta S^\circ$, the two correlations are related directly, and both give scatter diagrams.

Some resolution of the random dispersion is achieved by noting a fairly good correlation of ΔH_f with the other two properties for points 1, 2, 3, 4, 5, 6, 7, 8, 10, 13, and 22. In contrast, the pyridines (points 9, 11, 12, 16, and 23) in Figure 3 show a trend toward a ΔG_f° *vs.* ΔH_f correlation line which is nearly of unit slope and crudely parallel to that for the strongly dipolar amines and oxides (points 14, 15, 17, 18, 19, 20, 21). The logical consequence is portrayed in Figure 4 where we see that the large changes in K_f, ΔG_f°, and ΔH_f for the pyridines and for the dipolar oxides and amides are nearly independent of entropy changes in each class. This isoentropic behavior is a clear departure from that of the other acceptors studied by us and from that reported by other workers. For all three groups of

compounds, the entropy of complexing falls around − 15 eu as might be expected from the loss of translation entropy from the combination of two molecules to make a unit.

We also note[36] that the correlation of ΔG_f° *vs.* pK_a for the protonation in aqueous solution of a number of the bases discussed above also shows scatter which can be analyzed into a series of nearly parallel lines for amines, pyridines, ketones, sulfoxides, etc. Unfortunately, at this writing there is no obvious relationship between the grouping of bases in the two instances.

The Relationship between $\Delta\nu$ and ΔH. Badger and Bauer[41] noted very early that, for a few compounds, there appeared to be a relationship between ΔH_f and ir shifts, but they doubted the generality of their findings. In their definitive 1960 review, Pimentel and McCellan[11] concluded, "Unhappily, the data do not substantiate the proposed relation of Badger and Bauer ...."; other, more recent workers with more data to work with have generally been similarly critical.[42−55] The con-

(39) R. F. Brown, *J. Org. Chem.*, **27**, 3010, 3015 (1962).
(40) C. D. Ritchie and W. F. Sager, "Progress in Physical Organic Chemistry," Vol. 2, Interscience Publishers, New York, N. Y., 1964, p 323.

(41) R. M. Badger and S. H. Bauer, *J. Chem. Phys.*, **5**, 839 (1937); S. H. Bauer, *ibid.*, **8**, 288 (1940).
(42) T. Gramstad and J. Sandström, *Spectrochim. Acta*, **25A**, 31 (1969), and previous articles in the same series.
(43) E. D. Becker, *ibid.*, **17**, 436 (1961).
(44) S. Wada, *Bull. Chem. Soc. Japan*, **35**, 707 (1962).
(45) R. West, D. L. Powell, L. S. Whatley, M. K. T. Lee, and P. von R. Schleyer, *J. Am. Chem. Soc.*, **84**, 3221 (1962); R. West, D. L. Powell, M. K. T. Lee, and L. S. Whatley, *ibid.*, **86**, 3227 (1964); D. L. Powell and R. West, *Spectrochim. Acta*, **20**, 883 (1964).
(46) D. A. K. Jones and J. G. Watkinson, *J. Chem. Soc.*, 2366 (1964).

Table XI. Comparison of Calculated (Equation 6) and Experimental Enthalpies (kcal/mole)

Compd	$-\Delta H^{\text{phenol}}_{\text{calcd}}$ [a]	$-\Delta H^{\text{phenol}}_{\text{exptl}}$ [b]	$-\Delta\Delta H^d$	$-\Delta H^{\text{PFP}}_{\text{calcd}}$ [a]	$-\Delta H^{\text{PFP}}_{\text{exptl}}$ [c]	$-\Delta\Delta H^d$
Anisole[e]	4.73	3.08	+1.65	4.82	3.13	+1.69
Dimethylaniline[e]				7.01	4.02	+2.99
Dioxane	5.52	5.11	+0.41	5.68	5.10	+0.58
Dibenzyl ether[e]	5.49	4.43	+1.06	5.64	4.59	+1.05
Ether	5.91	5.45	+0.46	6.02	5.57	+0.46
Tetrahydrofuran	6.03	5.6	+0.43	6.09	5.75	+0.34
3-Bromopyridine				7.42	6.2	+1.22
Dimethylformamide	6.14	6.86	−0.72	6.25	6.97	−0.72
Dimethylacetamide	6.62	7.36	−0.74	6.75	7.44	−0.69
Pyridine	7.93	7.0	+0.93	8.12	7.40	+0.72
Dimethyl sulfoxide	6.76	7.21	−0.45	6.86	7.21	−0.35
Quinoline	8.12	7.44	+0.68	8.21	7.47	+0.74
4-Picoline	8.08	7.66	+0.42	8.18	7.59	+0.59

[a] Calculated from data in Tables V and VIII by eq 6. [b] Table VIII. [c] Table V, pure base data. Use of the high dilution data from Table V gives virtually the same results. [d] Difference between experimental and calculated values. [e] These compounds are multisite hydrogen bond acceptors as shown by the more than one $\Delta\nu$ obtained (Tables V and VIII). The experimental $-\Delta H$ must be composite values due to hydrogen bonding to these different sites. In this table, we have followed convention and have the largest $\Delta\nu$ value (generally to the strongest hydrogen bonding site) for comparison with $-\Delta H$ observed. A modification of this procedure, taking in account the multisite problem, will be discussed in the future.

sensus seems to be that no general relationship between ΔH_f and $\Delta\nu$ exists, although in a few limited series of closely similar compounds, correlations are found.

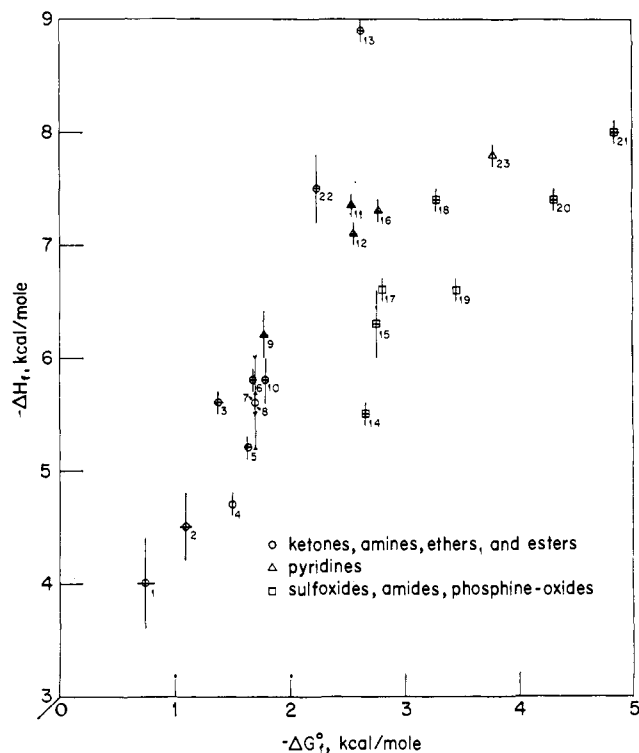However, Drago and his associates[14,15] have defended a general enthalpy–spectral shift relationship. After

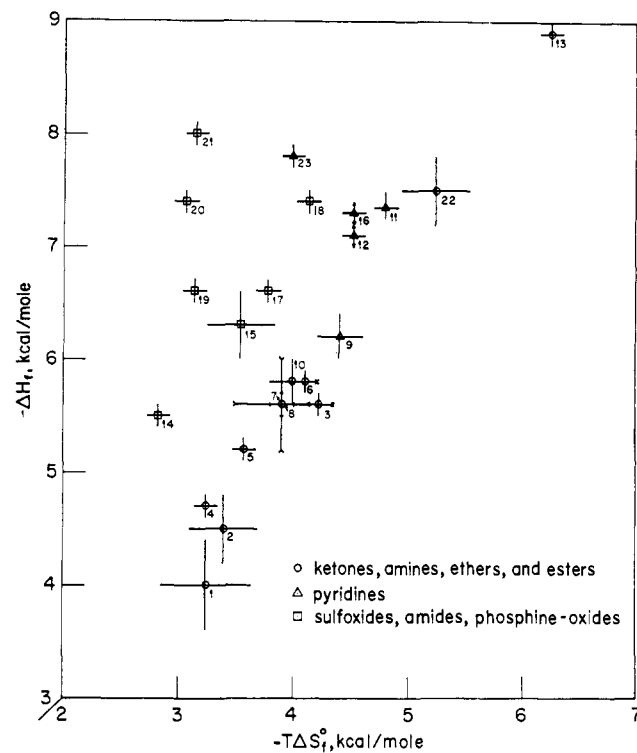Figure 3. $-\Delta G_f°$ of hydrogen bonding with PFP vs. $-\Delta H_f°$ of hydrogen bonding with PFP.

Figure 4. $-T\Delta S_f°$ of hydrogen bonding with PFP vs. $-\Delta H_f°$ of hydrogen bonding with PFP. Bases used are (1) N,N-dimethylaniline; (2) dibenzyl ether; (3) diethyl ether; (4) ethyl acetate; (5) 2-butanone; (6) N,N-dimethylaminopropionitrile; (7) anthrone; (8) tetrahydrofuran; (9) 3-bromopyridine; (10) cyclohexanone; (11) quinoline; (12) pyridine; (13) triethylamine; (14) N-methylformamide; (15) diphenyl sulfoxide; (16) 4-picoline, (17) N,N-dimethylformamide; (18) N,N-dimethylacetamide; (19) dimethyl sulfoxide; (20) triphenylphosphine oxide; (21) hexamethylphosphoramide; (22) cyclopropylamine; (23) 4-dimethylaminopyridine. Compounds 1, 2, and 6 have two acceptor sites as shown by infrared. Therefore, their positions on these figures may be deceptive.

(47) S. Ghersetti and A. Lusa, Spectrochim. Acta, 21, 1067 (1965); P. Besarini, G. Galloni, and S. Ghersetti, ibid., 20, 267 (1964).

(48) H. Fritzsche, Ber. Bunsenges. Phys. Chem., 68, 459 (1964); Z. Naturforsch., 19a, 1132 (1964).

(49) T. M. Barakat, M. J. Nelson, S. M. Nelson, and A. D. E. Pullin, Trans. Faraday Soc., 62, 2674 (1966).

(50) S. Singh, A. S. N. Murthy, and C. N. R. Rao, ibid., 62, 1056 (1966); A. S. N. Murthy and C. N. R. Rao, Appl. Spectrosc. Rev., 2, 69 (1968); S. Singh and C. N. R. Rao, J. Am. Chem. Soc., 88, 2142 (1966).

(51) Z. Yoshida and E. Ōsawa, ibid., 88, 4019 (1966); 87, 1467 (1965); E. Ōsawa and Z. Yoshida, Spectrochim. Acta, 23A, 2029 (1967).

(52) A. V. Jogansen and B. V. Rassadin, Zh. Prikl. Spectrok., 6, 492 (1967).

(53) T. Kito and C. H. Jarboe, J. Org. Chem., 32, 407 (1967).

(54) G. Aksnes and P. Albriktsen, Acta Chem. Scand., 22, 1866 (1968).

(55) H. E. Hallam, J. Mol. Struct., 3, 43 (1969).

undergoing two revisions,[14] eq 6 had been proposed for use with phenol and substituted phenols.[15]

$$-\Delta H \text{ (kcal/mole)} = 0.0103\Delta\nu_{OH} \text{ (cm}^{-1}) + 3.08 \quad (6)$$

Since we intend a full discussion of the $\Delta\nu-\Delta H$ relationship subsequently, it will suffice here to test eq 6 rather superficially against some of the data reported in Tables V and VIII. Since eq 6 obviously cannot be used for hydrogen bonds whose enthalpies are less than 3 kcal/mole, we have restricted our comparison between experimental and calculated (eq 6) values (Table XI) to the stronger hydrogen bonds. Even in this re-

stricted range, the average difference between calculated and experimental values is 0.84 kcal/mole. Since the whole range of enthalpies treated is only 5.1 kcal/mole (3.1–8.2 kcal/mole, Table XI), eq 6 is not a very satisfactory method for providing reliable ΔH_f data.[56]

(56) Professor Drago, private communication, has criticized this test of eq 6. As is indicated by footnote *e*, Table XI, some of the bases have more than one hydrogen-bonding site. The use of only the larger $\Delta\nu$ to compute ΔH may lead to inaccuracies. Drago argues that the pure base method may be imprecise, especially with the more polar bases. We concede this possibility, although for DMSO the agreement between calculated and experimental ΔH's is fairly good. We plan a rigorous and direct test of the validity of eq 6, free from these and other objections.

The Evaluation of Strain in Hydrocarbons. The Strain in Adamantane and Its Origin[1,2]

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Abstract: Many group-increment and bond-energy additivity schemes, *e.g.*, the frequently employed one by Franklin, devised for calculation of heats of formation of acyclic alkanes, are inadequate for cyclic systems. Even those schemes which treat cyclic molecules well are not applicable to the problem of defining hydrocarbon strain energies. Group increments, derived from the heats of formation of the acyclic alkanes in completely skew-free conformations, are presented: CH_3, -10.05 kcal; CH_2, -5.13 kcal; CH, -2.16 kcal; C, -0.30 kcal. These "single-conformation" increments are recommended for the evaluation of strain in hydrocarbons and tables of such strain estimates are provided. A modest strain in cyclohexane (1.35 kcal/mol) and *trans*-decalin (1.79 kcal/mol) is indicated. More important and surprising is the finding of 6.48 kcal/mol of strain in adamantane, thought previously to be a "strain-free" molecule. This strain can be accounted for quantitatively in terms of angle strain and C···C nonbonded repulsions from which the rigidity of adamantane skeleton allows no escape, provided rather hard C···C nonbonded potential functions are employed in computer conformational analysis calculations. Softer C···C nonbonded functions appear to be less satisfactory, as they do not reproduce well the energies and geometries of bridged hydrocarbons. Special cage effects need not be invoked in interpreting the strain in adamantane, nor, presumably, in other bridged polycyclic molecules.

Adamantane has generally been assumed to be a strain-free molecule[6] since the structural features are thought to be "ideal": all angles are tetrahedral, or nearly so, the bond lengths are normal, and adjacent carbon atoms are held in the staggered, torsionally most favorable conformation.[7]

However, analysis of the recently available thermochemical data for adamantane reveals that adamantane

(1) This work was supported by grants from the National Institutes of Health (AI-07766), the National Science Foundation, and the Petroleum Research Fund, administered by the American Chemical Society.

(2) A preliminary account of this work was presented at the Conference on Stereochemistry, Bürgenstock, Switzerland, May 1967. Some of the calculations have been published in a review.[3]

(3) J. E. Williams, P. J. Stang, and P. v. R. Schleyer, *Ann. Rev. Phys. Chem.*, **19**, 531 (1968).

(4) National Science Foundation Predoctoral Fellow, 1965–1969; Ph.D. Thesis, Princeton University, 1969.

(5) National Science Foundation Predoctoral Fellow, 1961–1965; Ph.D. Thesis, Princeton University, 1966.

(6) Review: R. C. Fort, Jr., and P. v. R. Schleyer, *Chem. Rev.*, **64**, 277 (1964).

(7) Studies of the structure of adamantane: ref 6 and J. Donohue and S. H. Goodman, *Acta Crystallogr.*, **22**, 352 (1967); C. E. Nordman and D. L. Schmitkons, *ibid.*, **18**, 764 (1965). *Cf.* also the structure of diamantane ("congressane"), I. L. Karle and J. Karle, *J. Amer. Chem. Soc.*, **87**, 919 (1965), and of 1-biadamantane, R. A. Alden, J. Kraut, and T. G. Traylor, *ibid.*, **90**, 74 (1968).

is, in fact, far from being strain free. This paper establishes this surprising result and provides an interpretation. It is necessary first to define what is meant by "strain" and then to establish the extent to which adamantane is "strained." This involves the estimation of a strain-free heat of formation for adamantane. A critical analysis shows that many of the methods commonly used for estimating such heats of formation have serious flaws which render them inapplicable to cyclic compounds. A new method, free from these defects, is required. Finally, the reason for the unexpected strain in adamantane needs to be found.

Definition of Strain. The concept of strain in organic molecules, although inexact, is conceptually useful. Certain molecules with higher energies than "normal" are found to have distorted structures. This relationship between energy and structure permits a chemist to predict easily which compounds will be strained. For example, molecules with bond angles deviating from the normal values, with atoms approaching each other too closely, or with eclipsed conformations will typically be strained. Since adamantane appears to possess none of these defects, it has long been expected to be strain free.