the secondary frequency that occurs in this same emission may be associated with that bending mode which involves all three carbonyls but not with that one which is associated only with the isolated carbonyl. Clearly, the emission is associated with the dicarbonyl portion of PA, and the assignment made earlier, namely $^3B_2 \rightarrow {}^1A_1$, coincides with the predictions inherent in Figure 8.

A comparison of the properties associated with the $^1A_1 \leftarrow {}^1A_1$ transition (*i.e.*, the $\pi_{\oplus}\pi_{+}{}^*$ configuration) in *cis*-oxamide and PA shows, as expected, that the two differ in certain aspects. Although λ_{max} values are almost identical for PA and the similarly substituted *cis*-oxamide, 2,3-diketopiperazine, ϵ_{max} for PA is about twice as large as that for oxamide; alkyl substitution produces very similar red shifts but reduces the ϵ_{max} value of PA only slightly while effecting a 50% increase for the oxamide. The very limited solubility of 2,3-diketopiperazine in anything but water precludes solvent shift comparisons; however, the red shift of ~1 mμ recorded for the alkyl-substituted *cis*-oxamide[2] in acetonitrile relative to water is very similar to the behavior recorded for PA and DPPA in Figure 3. A similar comparison for the $^1B_1 \leftarrow {}^1A_1$ transition (*i.e.*, the $\pi_{\ominus}\pi_{+}{}^*$ excitation) is not possible because the corresponding absorption[2] is ill resolved for the *cis*-oxamides.

Finally, a comparison of the emission characteristics of oxamides and parabanic acids also substantiates the importance of the $^1\Gamma_{n\pi^*}/{}^1\Gamma_{\pi\pi^*}$ separation in the determination of emission properties. The luminescence of oxamides, both cis and trans, has been rationalized[2] in terms of an emissive state of mixed $^3\Gamma_{n\pi^*}/{}^3\Gamma_{\pi\pi^*}$ character. In terms of excited electronic configurations, the union of a carbonyl and *cis*-oxamide to produce PA stabilizes the $n\pi^*$ configuration more than the $\pi\pi^*$ configurations and leads to a "pure" $^3\Gamma_{n\pi^*} \rightarrow {}^1\Gamma_1$ emission. Alkylation of PA again reduces the $n\pi^*/\pi\pi^*$ separation and, with DMPA and DPPA, emission properties which are quite similar to those of oxamides and which must also be associated with a $^3\Gamma_{n\pi^*}/{}^3\Gamma_{\pi\pi^*}$ mixed state become apparent.

Spectroscopic Studies of Lewis Acid–Base Interactions. Nuclear Magnetic Resonance Hydrogen Bonding Chemical Shifts[1a]

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Abstract: Hydrogen bonding chemical shifts ($\Delta\omega^0$), defined as the difference in chemical shift between complexed and free acid, were measured for a series of hydrogen bonding Lewis acids interacting with various donors in "inert" solvents such as cyclohexane. The corresponding enthalpies of adduct formation ($-\Delta H$) were measured either calorimetrically, by the nmr technique, or calculated employing the double scale enthalpy equation: $-\Delta H = C_AC_B + E_AE_B$ (I). Linear correlations between $-\Delta H$ and $\Delta\omega^0$ were obtained for a given base interacting with a series of hydrogen bonding Lewis acids when the base was quinuclidine, tetrahydrothiophene, or 1-phospha-2,6,7-trioxa-4-ethylbicyclo[2.2.2]octane. Similar linear relationships could not be established when the base was acetonitrile, tetrahydrofuran, and diethyl ether or when the base contained strongly magnetically anisotropic groups as with pyridine or acetone. In light of the lack of generality for a constant base $-\Delta H$ *vs.* $\Delta\omega^0$ correlation, the $\Delta\omega^0$ values were accounted for in terms of an electric field model based on one originally proposed by Buckingham: $\Delta\omega^0 = K\alpha_{||a}E_B{}^2$ (II), where $\alpha_{||a}$ is the polarizability of the acid along the X–H bond and E_B is some "average" electric field originating on the lone pair electrons of the donor. The values of $\alpha_{||a}$ for the acids studied here were obtained from their corresponding C_A and E_A parameters appearing in eq I. For a given base interacting with a series of acids for which $\alpha_{||a}$ values were available, a linear relationship was obtained when $\Delta\omega^0$ was plotted *vs.* $\alpha_{||a}$. In all cases, except where the base contributed appreciably to $\Delta\omega^0$ from its neighbor anisotropy effect, a straight line resulted, even where no linear ΔH *vs.* $\Delta\omega^0$ constant base relationship could be established. From the slopes of these $\Delta\omega^0$ *vs.* $\alpha_{||a}$ plots, the "average" electric fields for the bases were obtained using eq II. The information about these donor "average" electric fields was found to be incorporated in their corresponding C_B and E_B parameters of eq I. Utilizing eq I and II, the linear $-\Delta H$ *vs.* $\Delta\omega^0$ correlations and their exceptions were accounted for, either when the base was kept constant and the acid varied, or when the acid was kept constant and the base varied.

It has been well established that the position of a hydrogen bonded proton in a nmr spectrum is different from the position of the "free" proton.[2] The resonance usually shifts to lower field unless the donor involved in the hydrogen bonding interaction has a large magnetic anisotropy. Benzene is such a donor and causes a net upfield shift in the hydrogen bonded proton upon adduct formation.

The hydrogen bonding chemical shift, $\Delta\omega^0$, defined as the difference in chemical shift between complexed

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(1) (a) Abstracted in part from the Ph.D. Thesis of F. L. Slejko, University of Illinois, Urbana, Illinois, Aug 1972. (b) National Science Foundation Predoctoral Fellow, 1969–1972.

(2) See, for instance, J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution NMR," Pergamon Press, Oxford, 1965.

and free proton ($\Delta\omega^0 = \omega_{\text{complex}} - \omega_{\text{free}}$) has been used as a measure of the strength of the hydrogen bonding interaction. Eyman and Drago[3] found a linear relationship between the enthalpy of adduct formation ($-\Delta H$) for phenol interacting with a series of Lewis bases and the corresponding change in chemical shift of the phenolic -OH proton. Corrections had to be made for donor anisotropy effects in several of the systems studied. Similarly, correlations of $-\Delta H$ with $\Delta\omega^0$ were reported for 1,1,1,3,3,3-hexafluoro-2-propanol[4] (HFIP), 2,2,2-trifluoroethanol,[5] and chloroform.[6] Trends between $-\Delta H$ and $\Delta\omega^0$ were also observed for hydrazoic acid (HN_3), isocyanic acid (HNCO), and isothiocyanic acid (HNCS).[7,8]

We have recently pointed out the difficulty in assessing a meaningful correction for the donor anisotropy contribution to $\Delta\omega^0$ and have suggested that a more accurate approach would involve a correlation of $-\Delta H$ *vs.* $\Delta\omega^0$ for a system in which the base (quinuclidine) was held constant and the hydrogen bonding Lewis acids[9] varied. In these constant base studies, care must be taken not to use $\Delta\omega^0$ values obtained by simultaneously measuring the equilibrium constant and $\Delta\omega^0$ in solvents which may interact with the proton whose chemical shift is being measured.[6,9]

In this investigation, we shall examine valid values for hydrogen bonding chemical shifts in the light of these correlations. Valid values for $\Delta\omega^0$ are those obtained directly in pure strongly basic nonpolar media, or those in a solvent that does not hydrogen bond at all and in which the data are evaluated by a simultaneous determination of the equilibrium constant, K, and $\Delta\omega^0$.[6] Using data that satisfy these requirements, one finds many donors and acceptors obeying this correlation but a considerable number that do not. The primary objective of this study is to establish a physically meaningful model which rationalizes the $-\Delta H$ *vs.* $\Delta\omega^0$ correlation. This model would, hopefully, explain not only the qualitative trends but also quantitatively account for the slopes and intercepts of the $-\Delta H$ *vs.* $\Delta\omega^0$ linear relationships as well as account for the anomalous behavior reported for several donors and acceptors.

The factors which give rise to the downfield shift of the hydrogen bonded proton are not clearly elucidated. Several attempts have been made to explain these shifts on the basis of the electric field effect model originally proposed by Buckingham.[10-18]

This model is based on eq 1 and applies for a molecule X-H in the presence of a uniform electric field.

$$\Delta\omega_{\text{E}} = (K_{\text{E}} \times 10^{-12})\mathbf{E}_z - (K_{\text{E}}' \times 10^{-18})\mathbf{E}^2 \quad (1)$$

The electric field is assumed to arise primarily from the electron density of the donor's lone electron pair. Here $\mathbf{E}_z$ is the component of the electric field along the X-H bond and $\mathbf{E}$ is the total electric field, K_{E} and K_{E}' being related to the ease of distortion of the electronic charge around the proton.[15] Berkeley and Hanna[12] used the original Buckingham values calculated for the hydrogen atom together with estimated electric fields in an attempt to calculate hydrogen bond lengths for various chloroform-base adducts. Nevertheless, much ambiguity remains in the literature regarding the physical meaning of the constants K_{E} and K_{E}'. Furthermore, there seems to be even less agreement whether both linear and quadratic terms are necessary or whether just one of these is predominant in the case of hydrogen bonding situations.[16]

In a recent publication,[9] we suggested that for one base interacting with a series of hydrogen bonding Lewis acids, X-H, a linear relationship should exist between $\Delta\omega^0$ and $\alpha_{||\text{a}}$, the parallel component of the polarizability for the X-H bond. This linear relationship (eq 2) would hold only if the donor does not contribute differently in the various adducts to $\Delta\omega^0$ from neighbor anisotropy effects.

$$\Delta\omega^0 = a\alpha_{||\text{a}} + b \quad (2)$$

There appears to be some confusion in the literature as to which of the coefficients of eq 1, K_{E}' or K_{E}, depends on the X-H bond polarizability and which depends on the dipole moment at the hydrogen atom in the X-H bond. In either case, for a constant base experiment described above, eq 2 would hold. In one case, the constant a appearing in eq 2 would contain information about $\mathbf{E}^2$, whereas if the other were operative, the constant a would depend on $\mathbf{E}_z$.

As we will show in this work, there is sufficient evidence to favor the case where the coefficient a of eq 2 depends on $\mathbf{E}^2$. This is consistent with the expression

$$\Delta\omega_{\text{E}} = \frac{881}{216}\frac{a_0{}^3}{emc^2}\mathbf{E}^2$$

derived for the hydrogen atom[10-12,14] in the presence of an electric field $\mathbf{E}$, where the polarizability for the hydrogen atom is taken[19] to be $4.5a_0{}^3$. Then, if $\alpha_{||\text{a}}$ is given in units of 10^{-25} cm^3 and $\mathbf{E}_{\text{B}}$ in units of 10^6 esu/cm^2, eq 2 rearranges to

$$\Delta\omega^0(\text{ppm}) = 0.111\alpha_{||\text{a}}\mathbf{E}_{\text{B}}{}^2 + b \quad (3)$$

Here, a positive $\Delta\omega^0$ indicates a downfield shift in the resonance of the hydrogen bonded proton. It might be pointed out here that the coefficient b of eq 3 would depend on the electric field of the base and the permanent dipole at the proton.[16] If one considers only a series of closely related hydrogen bonding Lewis acids, the permanent atomic dipole is not expected to differ significantly and the coefficient b of eq 3 would remain fairly constant for these acids.

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Table I. Nmr Hydrogen Bonding Chemical Shifts and Enthalpies of Adduct Formation for Several Lewis Acid–Base Systems

Acid	Base	Solvent	No. of solns	K, l./mol[c]	Temp, °C	$\Delta\omega^0$,[c] ppm	$-\Delta H$,[b] kcal/mol
m-Fluorophenol	$CH_3CH_2C(CH_2O)_3P$	Cyclohexane	5	8.8 ± 1.2	25		5.55 ± 0.3
1*H*-Perfluoroheptane	$CH_3CH_2C(CH_2O)_3P$	Cyclohexane	5	2.0 ± 0.37	7.5	0.30 ± 0.04	
	Quinuclidine	Cyclohexane	5	1.5 ± 0.2	9.0	1.30 ± 0.11	4.4 ± 0.2
	Pyridine	Cyclohexane	6	1.47 ± 0.07	9.0	1.27 ± 0.04	4.2 ± 0.3
	Acetone	Binary	9	3.73 ± 0.25 (2.0 ± 0.6)[a]	30	0.83 ± 0.18 (0.67)[a]	3.3 ± 0.3 (2.5 ± 0.5)[a]
	Triethylamine	Binary	10	No fit (1.5 ± 0.5)[a]		No fit (0.49)[a]	No fit (4.9 ± 0.9)[a]
	Diethyl ether	Binary	10	1.19 ± 0.47 (0.6 ± 0.2)[a]	30	0.70 ± 0.15 (0.38)[a]	2.1 ± 0.2 (1.7 ± 0.4)[a]
	3-Pentanone	Binary	11	4.38 ± 0.39 (2.2 ± 0.6)[a]	30	0.85 ± 0.02 (0.68)[a]	2.4 ± 0.2 (1.8 ± 0.4)[a]
p-Chlorophenol	Tetrahydrothiophene	Cyclohexane	5	10.0 ± 1.6	25	2.30 ± 0.11	
	$CH_3CH_2C(CH_2O)_3P$	Cyclohexane	6	17.5 ± 1.9	25	2.39 ± 0.08	
	Tetrahydrofuran	Cyclohexane	6			3.80 ± 0.05	
p-*tert*-Butylphenol	Tetrahydrothiophene	Cyclohexane	5	3.36 ± 0.22	25	2.15 ± 0.07	
	$CH_3CH_2C(CH_2O)_3P$	Cyclohexane	4	9.89 ± 0.37	25	1.88 ± 0.02	
	Tetrahydrofuran	Cyclohexane	5	24.7 ± 1.8	25	3.14 ± 0.05	
1,1,1,3,3,3-Hexafluoro-2-propanol	Tetrahydrothiophene	Cyclohexane	5	14.7 ± 1.9	25	2.84 ± 0.10	
	$CH_3CH_2C(CH_2O)_3P$	Cyclohexane	4	16.2 ± 1.7	25	3.17 ± 0.08	

[a] Values in parentheses are those obtained by Alley and Scott using their method for evaluating the data (see S. K. Alley, Jr., and R. L. Scott, *J. Phys. Chem.*, **67**, 1182 (1963)). Equilibrium constants are given in mole fraction units at 30.0°. The other values for each base are those calculated using their data and our method (see ref 6) for simultaneously calculating $\Delta\omega^0$ and K. [b] Except for the *m*-fluorophenol–TMPPE system, all enthalpies were measured by the nmr technique.[6] The *m*-fluorophenol–TMPPE system was measured calorimetrically; see text. [c] Errors given are the marginal standard deviation. For a discussion of the procedure employed in the determination of these errors, see ref 6.

Experimental Section

Purification of Materials. Baker Analyzed reagent carbon tetrachloride and Baker Analyzed reagent gc–spectrophotometric quality cyclohexane were dried over Linde 4A molecular sieves and used without any further purifications. 1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP), phenol, *p*-chlorophenol, *p*-*tert*-butylphenol, and quinuclidine were purified as previously described.[9] 1*H*-Perfluoroheptane (PCR Inc.) was purified by distilling at 96–97° and atmospheric pressure on a 6-in. Vigreaux column and dried further over Linde 4A molecular sieve before using.

1-Phospha-2,6,7-trioxa-4-ethylbicyclo[2.2.2]octane (TMPPE), $CH_3CH_2C(CH_2O)_3P$ (Arapahoe Chemicals), was purified by resubliming at 0.05 Torr. All handlings of this material were done in a N_2-filled drybag. Tetrahydrofuran (Mallinckrodt Reagent) was dried over Linde 4A molecular sieves and distilled from sodium immediately before use.

Chloroform, tetrahydrothiophene, and pyridine were purified as previously described.[6]

Apparatus and Procedure. Nuclear magnetic resonance spectra were measured with a Varian Associates HA-100 high resolution nmr as described in our previous paper.[9] Solutions of the acids and bases were prepared by the method previously described.[6,9] The hydrogen bonding chemical shifts were determined by either plotting the measured chemical shift ($\Delta\omega_{\text{obsd}}$) *vs.* base concentration and extrapolating to $[B^0] = 1.0$ (mol/fraction) or by simultaneously solving for the equilibrium constant K and $\Delta\omega^0$ using a computer fit procedure.[6]

The temperature dependence of the equilibrium constant was used to determine the enthalpy of adduct formation ($-\Delta H$) as previously described.[6]

The calorimetric procedure is similar to that used in our previous paper.[9] The acid, *m*-fluorophenol, was added to a solution containing different amounts of the base and the heat evolved was measured.

Results

Calorimetry. See the paragraph at the end of the paper regarding supplementary material. The results are summarized in Table I.

Nuclear Magnetic Resonance. The hydrogen bonding chemical shifts, $\Delta\omega^0$, for a series of Lewis acid–base systems measured in the course of this work are also summarized in Table I, together with the enthalpies of adduct formation for 1*H*-perfluoroheptane interacting with quinuclidine and pyridine. When no equilibrium constant is given, the hydrogen bonding chemical shift was obtained by plotting $\Delta\omega^0_{\text{obsd}}$ *vs.* $[B^0]$ and extrapolating to infinite base concentration as previously described.[9] For those systems where $\Delta\omega^0$ and the equilibrium constant were solved simultaneously, the original data, consisting of acid and base concentrations, observed chemical shifts, and temperatures, appear immediately following this article in the microfilm edition.

Discussion

1*H*-Perfluoroheptane. A similar study of 1*H*-perfluoroheptane interacting with various Lewis bases was made by Alley and Scott.[20] Their method of evaluating the nmr data, however, was not sufficiently accurate to determine correct values for the equilibrium constant, $\Delta\omega^0$ and $-\Delta H$. Using our procedure[6] to evaluate their data, different results were obtained. These are shown in Table I.

In view of the fact that the systems studied by Alley and Scott were in pure base, the enthalpies of adduct formation cannot be used in any of our correlations because of possible complications arising from solvation effects. The $\Delta\omega^0$ values are probably meaningful as they are probably not affected appreciably by these solvation effects. We are, therefore, limited in considering only the enthalpies of adduct formation of 1*H*-perfluoroheptane with quinuclidine and pyridine (see Table I).

We were interested in incorporating this acid into the double scale enthalpy equation[21] (eq 4) originally proposed by Drago and Wayland.[21a]

$$-\Delta H = C_A C_B + E_A E_B \qquad (4)$$

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Table II. Compilation of Hydrogen Bonding Chemical Shifts and Enthalpies of Adduct Formation

Base	Acid	$\Delta\omega^0$,[a] ppm	Ref	$-\Delta H$,[b] kcal/mol	Ref
$HC(CH_2CH_2)_3N$	C_6H_5OH	6.10 ± 0.03	*t*	9.03	*t*
	p-tert-BuC_6H_4OH	5.33 ± 0.03	*t*	8.0	*d*
	p-FC_6H_4OH	6.35 ± 0.03	*t*	8.8	*d*
	p-ClC_6H_4OH	6.65 ± 0.03	*t*	9.4	*d*
	p-BrC_6H_4OH	6.52 ± 0.03	*t*	9.4	*e*
	p-IC_6H_4OH	6.44 ± 0.03	*t*	9.0	*e*
	CF_3CH_2OH	5.90 ± 0.05	*t*	8.6	*d*
	$(CF_3)_2CHOH$	7.97 ± 0.05	*t*	11.4	*f*
	$C_4H_4NH^g$	2.83 ± 0.05	*t*	5.55	*t*
	$CHCl_3$	1.15 ± 0.12	*t*	4.1	*s*
	$CF_3(CF_2)_5CF_2H$	1.30 ± 0.11	*t*	4.4	*c*
$CH_3CH_2C(CH_2O)_3P$	*p-tert*-BuC_6H_4OH	1.88 ± 0.02	*c*	4.7	*d*
	p-ClC_6H_4OH	2.39 ± 0.08	*c*	5.5	*d*
	$(CF_3)_2CHOH$	3.17 ± 0.08	*c*	6.3	*d*
	$CHCl_3$	0.19 ± 0.05	*s*	2.7	*s*
	$CF_3(CF_2)_5CF_2H$	0.30 ± 0.04	*c*	2.7	*d*
$(CH_2)_4S$	*p-tert*-BuC_6H_4OH	2.15 ± 0.07	*c*	4.5	*h*
	p-ClC_6H_4OH	2.30 ± 0.11	*c*	5.3	*h*
	$(CF_3)_2CHOH$	2.84 ± 0.10	*c*	5.8	*h*
	$CHCl_3$	0.75 ± 0.03	*s*	2.4	*s*
$(CH_3CH_2)_3N$	C_6H_5OH	6.9 ± 0.3	*i, j*	9.1	*h*
	$C_4H_4NH^g$	3.02 ± 0.02	*k, l*	5.9	*h*
	$CHCl_3$	1.51 ± 0.04	*s*	4.5	*s*
$(CH_3CH_2)_2O$	C_6H_5OH	3.35 ± 0.04	*i, j, m*	6.0	*h*
	$C_4H_4NH^g$	1.74 ± ?	*k*	3.4	*d*
	$CHCl_3$	0.605 ± ?	*j*	3.4	*d*
	$CF_3(CF_2)_5CF_2H$	0.68 ± 0.13	*c*	3.1	*d*
$(CH_2)_4O$	C_6H_5OH	3.70 ± ?	*i*	6.0	*h*
	p-tert-BuC_6H_4OH	3.14 ± 0.05	*c*	5.6	*d*
	p-ClC_6H_4OH	3.80 ± 0.05	*c*	6.3	*d*
	$C_4H_4NH^g$	1.89 ± ?	*k*	3.7	*d*
	$CHCl_3$	0.84 ± 0.02	*s*	3.6	*s*
$C_5H_5N^p$	C_6H_5OH	6.65 ± 0.15	*i, j*	8.0	*h*
	$C_4H_4NH^g$	3.71 ± 0.06	*c*	4.9	*q*
	$CHCl_3$	1.36 ± 0.07	*s*	4.6	*d*
	$CF_3(CF_2)_5CF_2H$	1.27 ± 0.04	*c*	4.2	*c*
CH_3CN	C_6H_5OH	2.33 ± 0.23	*i, j*	4.6	*h*
	$C_4H_4NH^g$	1.20 ± 0.02	*k, l*	2.7	*d*
	$CHCl_3$	0.48 ± 0.04	*n, r*	2.9	*d*
$(CH_3)_2CO$	C_6H_5OH	3.7 ± 0.1	*i, j*	5.1	*h*
	$C_4H_4NH^g$	2.00 ± 0.02	*k, l*	3.2	*d*
	$CHCl_3$	0.96 ± 0.01	*s*	3.5	*s*
	$CF_3(CF_2)_5CF_2H$	0.87 ± 0.17	*c*	2.9	*d*
$(CH_3)_2SO$	C_6H_5OH	5.16 ± ?	*o*	6.9	*h*
	p-$CH_3C_6H_4OH$	5.00 ± ?	*j*	6.8	*d*
	p-BrC_6H_4OH	5.52 ± ?	*o*	7.2	*d*
	p-IC_6H_4OH	5.52 ± ?	*o*	7.2	*d*
	p-FC_6H_4OH	5.37 ± ?	*o*	6.6	*h*
	$C_4H_4NH^g$	3.76 ± 0.02	*m*	4.2	*d*
$(CH_3CH_2)_2S$	C_6H_5OH	2.61 ± ?	*m*	4.6	*h*
	$CHCl_3$	0.77 ± 0.09	*s*	2.2	*d*
$O(CH_2)_4O$	$C_4H_4NH^g$	1.50 ± ?	*k, l*	3.5	*d*
$HCON(CH_3)_2$	$C_4H_4NH^g$	2.90 ± ?	*l*	3.9	*d*
$CH_3CON(CH_3)_2$	C_6H_5OH	5.38 ± ?	*j*	6.8	*h*
$CH_3COOCH_2CH_3$	C_6H_5OH	3.6 ± 0.2	*i, j*	4.8	*h*
	$CHCl_3$	0.66 ± 0.06	*s*	3.2	*d*

[a] Errors given are the marginal standard deviations when $\Delta\omega^0$ and K are determined simultaneously. When more than one literature value exists, the average is listed and the error is the deviation. [b] Unless otherwise noted, these are the experimental values. [c] This work. [d] Calculated from eq 4 and E and C parameters from reference 21b, or those determined in this work. [e] Tentative E and C parameters based on enthalpies of adduct formation for these phenols with various Lewis bases predicted from correlations with Hammett substituent constants (see ref 9): *p*-BrC_6H_4OH, $C_A = 0.478$, $E_A = 4.34$; *p*-IC_6H_4OH, $C_A = 0.45$, $E_A = 4.4$. [f] R. M. Guidry and R. S. Drago, submitted for publication. [g] Pyrrole. [h] See ref 21b. [i] See ref 14. [j] G. Socrates, *Trans. Faraday Soc.*, **63**, 1083 (1967). [k] F. Strohbusch and H. Zimmermann, *Ber. Bunsenges. Phys. Chem.*, **71**, 567 (1967). [l] H. Saito and K. Nukado, *J. Amer. Chem. Soc.*, **93**, 1072 (1971). [m] See ref 25. [n] See R. L. Lichter and J. D. Roberts, *J. Phys. Chem.*, **74**, 912 (1970). [o] G. Socrates, *Trans. Faraday Soc.*, **66**, 1052 (1970). [p] Pyridine. [q] See ref 23b. [r] P. Jouve, *Ann. Phys. (Paris)*, **1**, 127 (1966). [s] See ref 6. [t] See ref 9.

In this equation, the subscripts A and B indicate acceptor and donor, respectively, while E and C are two empirically derived parameters assigned to each. Crudely, the product of E_A and E_B includes the contribution to the bonding from electrostatic interactions, while C_A times C_B includes the contribution to the bonding from covalent interactions. A comprehensive listing of these parameters has been recently published.[21b] Based on these two enthalpies, we can calculate C_A to be 0.20 and E_A to be 2.5. It should be emphasized that these parameters are only tentative since they are based on only two enthalpies with no additional enthalpies being available as a check. However, since the C_B/E_B ratios for the two donors used in establishing C_A and E_A are sufficiently different, it is safe to assume that these parameters are fairly accurate.

By a similar procedure, TMPPE was incorporated into the double scale enthalpy equation. An enthalpy of adduct formation for the 4-methyl derivative of TMPPE with $B(CH_3)_3$ of 14.4 kcal/mol has been reported in the literature.[22] If it is assumed that the basicity of the 4-methyl derivative is not significantly different from TMPPE (which has an ethyl group in the 4 position), including the enthalpies with chloroform and *m*-fluorophenol (Table I) enables the calculation of $C_B = 6.41$ and $E_B = 0.548$ for this donor. With these parameters, the calculated enthalpies (eq 4) for all three acids are in excellent agreement with experiment.

Hydrogen Bonding Chemical Shifts. In our previous publications,[6,9] we have discussed difficulties in certain $\Delta\omega^0$ values appearing in the literature. In our present work, we have shown, as in the case of Alley and Scott's data for 1*H*-perfluoroheptane, that when the equilibrium constant (K) is small, the correct method of evaluating the data is by simultaneously solving for K and $\Delta\omega^0$, using our "best-fit" procedure.[6] This is dramatically shown in the case of the system pyrrole–pyridine in cyclohexane studied by Happe.[23a] By using an incorrect method of evaluating the data, he calculated $\Delta\omega^0$ to be 3.5 ppm at 33°. He also observed $\Delta\omega^0$ to be temperature dependent and determined the enthalpy of adduct formation to be 4.3 kcal/mol. Evaluating his data by our procedure gave a value $\Delta\omega^0$ of 3.74 ± 0.06 ppm which was *not* temperature dependent. The recalculated enthalpy is 4.9 ± 0.2 kcal/mol, which is in excellent agreement with a reported[23b] calorimetric value of 5.0 ± 0.3 kcal/mol in the same solvent. Similarly, for the binary system pyrrole–DMSO, the $\Delta\omega^0$ value was found to be 3.75 ± 0.02 ppm opposed to Porter and Brey's[24] value of 3.05 ppm evaluated by the same incorrect procedure used by Happe. The ether–phenol system in carbon tetrachloride[25] was treated correctly and the reported value of 3.10 ppm for $\Delta\omega^0$ agrees perfectly with a value of 3.13 ± 0.04 ppm obtained by our method.

The second point to consider is the solvent used for the nmr experiment. The "free" -OH proton in phenol, for example, is shielded in cyclohexane 0.22 ppm relative to the "free" -OH in carbon tetrachloride.[26] We have pointed out the dangers of interpreting $\Delta\omega^0$ values which were obtained in CCl_4 or CH_2Cl_2.[6,9] Unfortunately, since most of the nmr data were not treated in terms of competing equilibria in these solvents, the ω_{AB} values[3-5] are not meaningful for our present purposes.

Finally, the values for $\Delta\omega^0$ obtained in pure base for the most part agree well with those obtained in an inert solvent when a correct procedure was employed in the treatment of the data. In all cases, these shifts (ω_{AB}) are referenced to ω_{free} measured in an inert solvent such as cyclohexane. Table II is a compilation of all the pertinent literature values of $\Delta\omega^0$ which we are considering in our present work. In all cases, when more than one value appears for the same system, the average is reported with the uncertainty being the spread in the reported values.

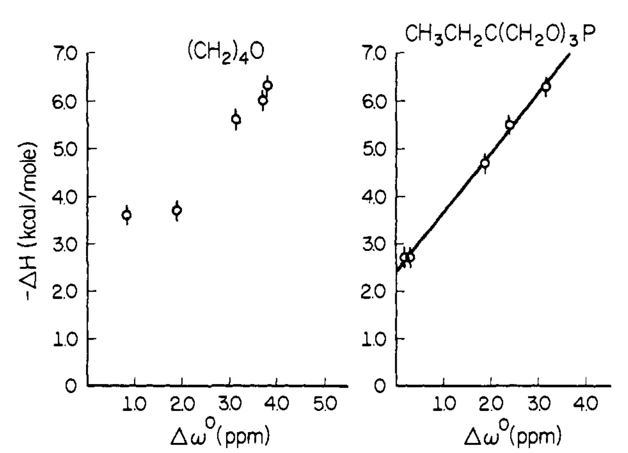

Figure 1. $-\Delta H$ *vs.* $\Delta\omega^0$ plots for various donors interacting with hydrogen bonding Lewis acids.

$-\Delta H$ *vs.* $\Delta\omega^0$ Constant Base Plots. In our earlier paper,[9] we reported a straight line correlation between $-\Delta H$ and $\Delta\omega^0$ for quinuclidine interacting with a series of hydrogen bonding Lewis acids. It would be worthwhile to see if this correlation holds for other donors, for which sufficient data are available (Table II). Figure 1 shows a plot of $-\Delta H$ *vs.* $\Delta\omega^0$ for two of these bases interacting with a series of hydrogen bonding Lewis acids. Straight line, constant base relationships are obtained for $CH_3CH_2(CH_2O)_3P$, $(CH_2)_4S$, and $(CH_3CH_2)_3N$ but not for the other donors. We shall now address ourselves to the question, why isn't the constant base, $-\Delta H^0$ *vs.* $\Delta\omega^0$, linear relationship a general one?

Evaluation of Polarizability Components for Lewis Acceptors. Equation 3 requires that if one assumes that an "average" electric field can be associated with a given donor for hydrogen bonding interaction, in the absence of neighbor anisotropy effects, the $\Delta\omega^0$ values for a series of Lewis acids should be linearly related to the polarizability component of the acceptor along the hydrogen bond. Unfortunately, these polarizability components are not known for a large number of acids. In our previous study involving quinuclidine interacting with a series of Lewis acids,[9] we proposed that the information regarding these polarizability components may be incorporated into our E and C parameters (eq 4).

Equation 4 is most readily described in matrix notation by assigning the acid parameters to a vector $\mathbf{X}_A$ and the base parameters to a vector $\mathbf{Y}_B$, *i.e.*

$$\mathbf{X}_A = \begin{bmatrix} C_A \\ E_A \end{bmatrix} \text{ and } \mathbf{Y}_B = \begin{bmatrix} C_B \\ E_B \end{bmatrix}$$

and allowing the enthalpy of adduct formation, $-\Delta H$, to be a scalar function of the vector.

$$-\Delta H = \mathbf{Y}_B{}^T\mathbf{X}_A = [C_B E_B]\begin{bmatrix} C_A \\ E_A \end{bmatrix} = C_AC_B + E_AE_B \tag{5}$$

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[22] J. G. Verkade, R. W. King, and C. W. Heitsch, *Inorg. Chem.*, 3, 884 (1964).

[23] (a) J. A. Happe, *J. Phys. Chem.*, 65, 72 (1961); (b) M. S. Nozari and R. S. Drago, *J. Amer. Chem. Soc.*, 92, 7086 (1970).

[24] D. M. Porter and W. S. Brey, Jr., *J. Phys. Chem.*, 72, 650 (1968).

[25] J. Chojnowski and W. W. Brandt, *J. Amer. Chem. Soc.*, 90, 1384 (1968).

[26] T. Gramstad and E. D. Becker, *J. Mol. Struct.*, 5, 253 (1970).

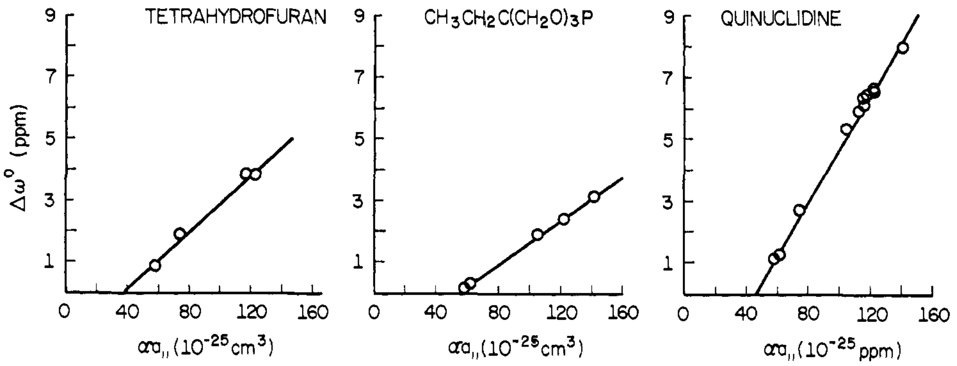

Figure 2. $\Delta\omega^0$ *vs.* $\alpha_{\|a}$ plots for various donors interacting with hydrogen bonding Lewis acids.

Equation 5 applied to a series of adducts has an infinite number of "best-fit" solutions for E_A, C_A, E_B, and C_B, each of which predicts exactly the same $-\Delta H$ for every interaction. This can be shown by defining a 2 × 2 transformation matrix **A** which leads to the new vectors $\mathbf{X}_A'$ and $\mathbf{Y}_B'$ in the following way

$$\begin{aligned} -\Delta H &= \mathbf{Y}_B{}^T[\mathbf{A}^{-1}\mathbf{A}]\mathbf{X}_A \\ &= [\mathbf{A}^{-1T}\mathbf{Y}_B]^T[\mathbf{A}\mathbf{X}_A] \\ &= \mathbf{Y}_B{}'^T\mathbf{X}_A{}' \end{aligned}$$

Once certain parameters are specified, a set of parameters can be obtained which gives a best fit between experimental enthalpies of adduct formation and those calculated from eq 5 using the determined parameters. One can then attempt to impose any model on the system by finding the transformation matrix **A** which allows one to map the vectors ($\mathbf{X}_A$, $\mathbf{Y}_A$) of one solution respectively onto those ($\mathbf{X}_A'$, $\mathbf{Y}_B'$) of another. Imposing a model corresponds to finding a solution for which the *E* or *C* parameters, or some function of them, correspond to some physical property.

In the case of the electric field effect on the hydrogen bonding chemical shift, it was of interest to look for elements of the **A** matrix which might map the C_A and E_A parameters of the acids onto their corresponding polarizability components $\alpha_{\|a}$. This effect might currently be contained in some combination of our present *E* and *C* parameters. This is equivalent to taking a linear combination of these parameters as follows

$$\begin{aligned} a_cC_{A_1} + a_eE_{eA_1} &= \alpha_{\|a_1} \\ a_cC_{A_2} + a_eE_{eA_2} &= \alpha_{\|a_2} \\ &\vdots \\ a_cC_{A_i} + a_eE_{A_i} &= \alpha_{\|a_i} \end{aligned}$$

where C_{A_i}, E_{A_i}, and $\alpha_{\|a_i}$ refer to the *i*th acid. Once the transformation constants are fixed for two acids, the elements of the transformation matrix (a_c and a_e) are defined and the polarizabilities for any acid whose *E* and *C* numbers are known may be calculated. Unfortunately, literature values for these polarizability *components* are not available for many acids for which we know the corresponding E_A and C_A parameters. Chloroform has been found to have a value of $\alpha_{\|a}$ of 58.8 × 10^{-25} cm^3,[27] and $\alpha_{\|a}$ for iodine may be estimated to be 174.3 × 10^{-25} cm^3 from its average polarizability by assuming that the ratio of its parallel and perpendicular components is the same as for chlorine. This latter approximation has been used successfully by Hanna to account for the ir spectra of charge-transfer complexes of iodine.[19b] Fortunately, $CHCl_3$ and I_2 are good standard acids for defining the transformation matrix since they have widely differing C_A/E_A ratios. The elements of the transformation matrix may then be calculated to be a_c = 163.44 and a_e = 10.87, where the polarizability components are then given in units of 10^{-25} cm^3.

Having these transformation matrix elements defined, we are able to calculate the polarizability components for all hydrogen bonding acids in our *E* and *C* correlation. The results are given in Table III. It is encouraging to note that the values of these polarizability components for our substituted phenols (107–135 × 10^{-25} cm^3) agree well with an average value of 125 × 10^{-25} cm^3 given by LeFèvre for similar phenol derivatives.[28]

Table III. Polarizability Components for Hydrogen Bonding Lewis Acids

Acid	E_A[a]	C_A[a]	$\alpha_{\|a}$[b]
p-tert-Butylphenol	4.06	0.387	107.4
p-Methylphenol	4.18	0.404	111.4
Phenol	4.33	0.442	119.2
p-Fluorophenol	4.17	0.446	118.1
p-Chlorophenol	4.34	0.478	125.2
p-Bromophenol	4.34[c]	0.478[c]	125.3
p-Iodophenol	4.4[c]	0.45[c]	121.4
m-Fluorophenol	4.42	0.506	130.7
m-Trifluoromethylphenol	4.48	0.530	135.4
tert-Butyl alcohol	2.04	0.300	71.2
1,1,1-Trifluoroethanol	4.00	0.434	114.5
1,1,1,3,3,3-Hexafluoro-2-propanol	5.56	0.509	143.7
Pyrrole	2.54	0.295	75.9
Chloroform	3.02[d]	0.159[d]	58.8
1*H*-Perfluoroheptane	2.51[e]	0.200[e]	59.9

[a] See reference 21b and the Experimental Section. [b] Given in units of 10^{-25} cm^3. [c] Tentative values, see ref 9. [d] See ref 6. [e] This work.

Figure 2 shows plots of $\Delta\omega^0$ *vs.* $\alpha_{\|a}$ for those donors with which we earlier attempted $-\Delta H$ *vs.* $\Delta\omega^0$ plots (see Figure 1) and also quinuclidine. Except for pyridine, acetone, and dimethyl sulfoxide, good straight lines are obtained, even for those donors which do not

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(27) C. G. LeFèvre and R. J. W. LeFèvre, *J. Chem. Soc.*, 4041 (1953).

(28) R. J. W. LeFèvre and A. J. Williams, *ibid.*, 1825 (1960).

Table IV. Donor Average Electric Fields

Donor	$\mathbf{E}_{B(exptl)}$[c]	$\mathbf{E}_{B(calcd)}$[a]	E_B[b]	C_B[b]	Slope[g]	Intercept,[g] ppm
C_5H_5N (pyridine)		0.846	1.1652	6.4039		
NH_3		0.840	1.3608	3.4627		
CH_3NH_2		0.900	1.3005	5.8841		
$(CH_3)_2NH$		0.891	1.0853	8.7252		
$(CH_3)_3N$		0.849	0.8078	11.5373		
$CH_3CH_2NH_2$		0.937	1.3660	6.0238		
$(CH_3CH_2)_2NH$		0.780	0.8659	8.8341		
$(CH_3CH_2)_3N$	0.897	0.929	0.9914	11.0945	0.0893 ± 0.0003	−3.75 ± 0.03
CH_3CN	0.518	0.513	0.8864	1.3438	0.0298 ± 0.0035	−1.18 ± 0.31
$CH_3CON(CH_3)_2$		0.786	1.3200	2.5841		
$HCON(CH_3)_2$		0.737	1.2338	2.4847		
$CH_3COOCH_2CH_3$		0.574	0.9749	1.7402		
CH_3COCH_3		0.603	0.9869	2.3331		
CH_3SOCH_3		0.808	1.3438	2.8529		
$(CH_3CH_2)_2O$	0.636	0.624	0.9625	3.2489	0.0449 ± 0.0044	−1.93 ± 0.36
$(CH_2)_4O$	0.638	0.669	0.9782	4.2658	0.0452 ± 0.0030	−1.70 ± 0.30
$(CH_3)_4C_5H_6NO$		0.709	0.9152	6.2111		
CH_3COOCH_3		0.532	0.9030	1.6137		
$O(CH_2)_4O$		0.660	1.0929	2.3835		
$(CH_3CH_2)_2S$		0.451	0.3389	7.4000		
$(CH_3)_2NCN$		0.644	1.1032	1.8109		
$ClCH_2CN$		0.511	0.9403	0.5304		
C_5H_5NO		0.866	1.3359	4.5208		
$CH_3C_5H_4NO$		0.895	1.3591	4.9866		
$CH_3OC_5H_4NO$		0.931	1.3725	5.7661		
$(CH_2)_4SO$		0.841	1.3837	3.1579		
$(CH_2)_4S$	0.467	0.471	0.3408	7.9014	0.0242 ± 0.0024	−0.62 ± 0.27
$(CH_3)_2S$		0.455	0.3427	7.4567		
$(CH_2)_5S$		0.470	0.3748	7.4011		
$(CH_3)_3P$		0.681	0.8378	6.5504		
C_6H_6		0.300	0.525[f]	0.681[f]		
$[(CH_3)_2N]_2CO$		0.741	1.1981	3.1018		
$(CH_2)_3S$		0.437	0.3519	6.8408		
$(CH_3)_3C_6H_3$		0.382	0.5744	2.1908		
$(n\text{-}C_4H_9)_2O$		0.676	1.0595	3.3031		
$(i\text{-}C_3H_7)_2O$		0.700	1.1087	3.1915		
$p\text{-}(CH_3)_2C_6H_4$		0.284	0.4160	1.7840		
$(CH_2)_5O$		0.641	0.9487	3.9133		
$HC(CH_2CH_2)_3N$	0.854	0.856	0.7040	13.1848	0.0809 ± 0.0017	−3.46 ± 0.19
$C_6H_{10}O$[d]		0.703	1.0771	3.7637		
$(CH_3)_2Se$		0.422	0.2168	8.3342		
$CH_3CH_2C(CH_2O)_3P$	0.553	0.524	0.548[e]	6.409[e]	0.0339 ± 0.0010	−1.78 ± 0.11
$[(CH_3)_2N]_3PO$		0.925	1.518[f]	3.548[f]		

[a] Calculated from corresponding E_B and C_B parameters using $\mathbf{E}_B = 0.037C_B + 0.523E_B$, expressed in units of 10^6 esu/cm². [b] Unless otherwise noted, see ref 21b. [c] $\mathbf{E}_{B(exptl)}$ determined from slopes of $\Delta\omega^0$ *vs.* $\alpha_{||a}$ plots using eq 3. Units of $\mathbf{E}_{B(exptl)}$ are 10^6 esu/cm². [d] 7-Oxabicyclo[2.2.1]heptane. [e] This work, see text. [f] Reevaluated E_B and C_B parameters based on more accurate enthalpy data than previously published in reference 21b. [g] These quantities are obtained from the least-squares fit of the $\Delta\omega^0$ *vs.* $\alpha_{||a}$ plots, some of which are shown in Figure 2.

obey the $-\Delta H$ *vs.* $\Delta\omega^0$ linear relationship. The results of the least-squares fit are given in Table IV together with the "average" electric fields of the donors, $\mathbf{E}_B$, which may be calculated from the slopes of the $\Delta\omega^0$ *vs.* $\alpha_{||a}$ plots (eq 3).

It is interesting to see that the only donors which do not obey the linear $\Delta\omega^0$ *vs.* $\alpha_{||a}$ correlation, namely pyridine, acetone, and dimethyl sulfoxide, are those which have strongly anisotropic groups which may contribute to $\Delta\omega^0$ from the neighbor anisotropy effect.

Donor "Average" Electric Fields E_B. It is quite surprising that our model, which assumes that a uniform electric field can be identified with each donor, should work as well as it does. *A priori*, one would expect to find a field gradient to be associated with the electric field of the base such that at various distances from the donor molecule the field would vary, thus invalidating our simplified approach. Our success implies that either the electric field is uniform over the range of distance encompassed by the hydrogen bonding systems studied here or that some average distance factor is incorporated into the parameters and deviations from this average give rise to errors comparable to experimental error. We have been able to show that interatomic distances R_{AB} can be fit fairly well for a wide range of systems with an equation of the type $R_{AB} = r_Ar_B$[29] Thus, this distance information may be incorporated into our current set of E and C parameters, *i.e.*, $E_A = \mu_{eff}A/r_A$. Consequently, we shall refer to $\mathbf{E}_B$ as the "average" electric field. This is to say that $\mathbf{E}_B$ is not the actual electric field gradient but some parameter which should be interpreted relative to the limitations just described.

We should be able to extract these apparent electric fields, $\mathbf{E}_B$, from the C_B and E_B parameters of the donors. To do this, as for the polarizabilities of the Lewis acids (*vide supra*), we only need two $\mathbf{E}_B$ values of two donors for which we know the corresponding C_B and E_B parameters. Table IV indicates that we have seven such values. Since we must find elements of a transformation matrix which will map the C_B and E_B param-

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(29) R. A. Kabler and R. S. Drago, unpublished results.

eters of the seven donors onto their respective $\mathbf{E}_B$ values, we have the classical problem of seven equations with two unknowns.

$$\begin{array}{c}
b_c C_{B_1} + b_e E_{B_1} = \mathbf{E}_{B_1} \\
b_c C_{B_2} + b_e E_{B_2} = \mathbf{E}_{B_2} \\
\vdots \quad \vdots \quad \vdots \\
b_c C_{B_7} + b_e E_{B_7} = \mathbf{E}_{B_7}
\end{array}$$

or in matrix notation.

$$(b_c b_e)\begin{bmatrix} C_B \\ E_B \end{bmatrix} = \mathbf{E}_B$$

These equations may be solved using a computer program similar to that used for calorimetry,[21b] for nmr association constants and $\Delta\omega^0$,[6] or for the E and C parameters of a new acid or new base.[21b]

In this case, no unique set of transformation matrix elements exists which will map the C_B and E_B parameters for all seven donors into the corresponding slopes of eq 2. However, if the square roots of the slopes are taken first, an excellent fit for all seven donors results (Table IV). Here, the best fit was obtained using $b_c = 0.037$ and $b_e = 0.523$. Table IV also lists the calculated $\mathbf{E}_B$ values for all of the donors currently in our E and C scheme. It is encouraging to note that the seven donors used to establish the best-fit transformation matrix elements have widely differing C_B/E_B ratios. This is a necessary requirement in order to obtain best values for both b_c and b_e. The fact that the square root of the slopes must be taken in order to find a unique matrix for transforming the C_B and E_B parameters suggests that the coefficient of the term in eq 1, which is quadratic in the base average electric field (K_E'), contains the acid polarizability component. This conclusion presupposes, of course, that the E_B and C_B parameters contain information about the base average electric field and not its square root, $\mathbf{E}_B^{1/2}$. Unfortunately, until a deeper insight into the physical meaning of the E and C equation is obtained, this question shall remain unresolved.

The acid polarizability components, $\alpha_{\|a}$ (Table III), and the calculated average electric fields, $\mathbf{E}_B$ (Table IV), may be used to calculate the induced dipole moment for the $(CH_3CH_2)_3N-HCCl_3$ adduct.

$$\boldsymbol{\mu}_{ind} = \alpha_{\|(CHCl_3)}\mathbf{E}_{(CH_3CH_2)_3N} = 0.5 \text{ D}$$

This is to be compared with the experimental value of 0.4 D.

Intercepts of $\Delta\omega^0$ *vs.* $\alpha_{\|a}$ Plots. With every donor studied so far, the intercepts of the $\Delta\omega^0$ *vs.* $\alpha_{\|a}$ plots are negative, corresponding to shielding. The magnitude of this intercept increases with base $\mathbf{E}_B$ value. An explanation for the sign and magnitudes observed (Table IV) is in order. We have already mentioned the possibility of the term linear in the electric field in eq 1 contributing to the intercept of the $\Delta\omega^0$ *vs.* $\alpha_{\|a}$ plot. The sign given to this term in eq 1 would cause a negative intercept.

An additional contribution may account for the large magnitude of the intercept. In the proximity of a donor molecule, the electron density in the X–H bond is polarized toward X, consequently giving rise to deshielding about that proton. The $\Delta\omega^0$ value is the difference between the "free" X–H molecule and that in the complex. If a bond is not polarizable, there is no mechanism for deshielding the proton and the net effect of the base electron density is to shield the proton (giving rise to the intercept of the $\Delta\omega^0$ *vs.* $\alpha_{\|a}$ plot). A physically analogous situation for $\alpha = 0$ would correspond to that of the bare proton having no electron density around it. In this case, the proton in BH^+ would be shielded relative to the bare proton and $\Delta\omega^0$ (the intercept) would correspond to the difference in chemical shift between the bare proton and $B{:}H^+$.

It would be nice to confirm this prediction with experimental values for chemical shifts of protons in protonated donors; however, such measurements cannot be readily made in inert solvents due to solubility problems and ion pairing. Furthermore, studies in polar solvents may not be meaningful as the chemical shift would be strongly solvent dependent. However, for the sake of completeness, mention should be made of several studies which were made under nonideal conditions but, nevertheless, provide support of our model. Gutowsky and Saika[30] give the difference in chemical shift between the bare proton and H_3O^- as 1.65 ± 0.05 ppm (the H_3O^+ being more shielded). This is to be compared with our intercepts obtained for tetrahydrofuran, 1.70 ± 0.30 ppm, and diethyl ether, 1.93 ± 0.36 ppm. A similar comparison may be made between our value for protonated quinuclidine (3.46 ± 0.19 ppm) and that for protonated DABCO (1,4-diazabicyclo[2.2.2]octane) estimated to be 4.3 ppm.[31] It should be emphasized that these values for the protonated donors, which do show the expected shielding behavior, were obtained under less than ideal conditions and should be taken only as order of magnitude approximations to the true value expected in the absence of ion pairing or adverse solvent effects.

$\Delta\omega^0$ *vs.* $\Delta\omega^{0\prime}$ Correlations. It has been shown[4,5] that if $\Delta\omega^0$ for a given acid interacting with a series of donors is plotted *vs.* $\Delta\omega^0$ for phenol (or any other reference acid) interacting with the same donors, a straight line results. This may be accounted for in terms of eq 3 as will be shown with the following arguments. A careful inspection of the data in Table IV reveals a rough relationship between the slope and the intercept of the $\Delta\omega^0$ *vs.* $\alpha_{\|a}$ plots. Because of the large error in the intercept, an accurate determination of the relationship between the slope and the intercept cannot be made; however, we can say that roughly the slope is directly proportional to the intercept, $\Delta\omega^0 = K\alpha_{\|a}\mathbf{E}_B^2 + I$, where K is the proportionality constant defined in eq 3 and I is the intercept. We then have $I = K''\cdot(K\mathbf{E}_B^2)$, where K'' is a proportionality constant which may be evaluated from the data in Table IV to be $\sim 44 \times 10^{-25}$ cm³. Upon rearranging this gives

$$\Delta\omega^0 = (\alpha_{\|a} + K'')K\mathbf{E}_B^2 \qquad (6)$$

when $\Delta\omega^0$ of a given acid with a series of bases is plotted *vs.* $\Delta\omega^{0\prime}$ of a reference acid (prime indicating reference acid) with the same bases, one arrives at the following equation.

$$\Delta\omega^0 = \frac{(\alpha_{\|a} + K'')}{(\alpha_{\|a}' + K'')}\Delta\omega^{0\prime}$$

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(30) H. S. Gutowsky and A. Saika, *J. Chem. Phys.*, **21**, 1688 (1953).

(31) R. J. Arhart and J. C. Martin, Department of Chemistry, University of Illinois, private communications.

This, then, predicts and confirms the experimental findings of a linear relationship between $\Delta\omega^0$ and $\Delta\omega^{0\prime}$ for a reference acid, the slope of the line being related to the polarizabilities of the acids.

$-\Delta H$ *vs.* $\Delta\omega^0$ Constant Base Correlations. The question arises whether eq 3 can account for the anomalous behavior of pyrrole in the constant base $-\Delta H$ *vs.* $\Delta\omega^0$ plots of Figure 1. Equation 3 may be written to include the intercept I.

$$\Delta\omega^0 = K\alpha_{||\mathrm{a}}\mathbf{E}_{\mathrm{B}}{}^2 + I \tag{7}$$

Combining this equation with eq 4, our double scale enthalpy equation, and substituting the matrix transformation elements relating $\alpha_{||\mathrm{a}}$ to C_{A} and E_{A}, we obtain

$$-\Delta H = \left(\frac{E_{\mathrm{B}}}{10.87K\mathbf{E}_{\mathrm{B}}{}^2}\right)\Delta\omega^0 - \frac{E_{\mathrm{B}}I}{10.87K\mathbf{E}_{\mathrm{B}}{}^2} + C_{\mathrm{A}}\left(C_{\mathrm{B}} - \frac{163.44}{10.87}E_{\mathrm{B}}\right) \tag{8}$$

We can see that for a constant base plot of $-\Delta H$ *vs.* $\Delta\omega^0$ a linear relationship results only if the term $C_{\mathrm{A}}\cdot(C_{\mathrm{B}} - (163.44/10.87)E_{\mathrm{B}})$ is zero or constant for a series of acids (*i.e.*, similar C_{A} parameters). For donors having large $C_{\mathrm{B}}/E_{\mathrm{B}}$ ratios, this term becomes very small. For example, quinuclidine gives $(C_{\mathrm{B}} - (163.44/10.87)/E_{\mathrm{B}}) \sim 2.0$ and tetrahydrothiophene $\sim$2.5. However, for donors having relatively small $C_{\mathrm{B}}/E_{\mathrm{B}}$ ratios, this term becomes rather large and negative, *ca.* -12.7 for acetonitrile and *ca.* -11.2 for tetrahydrofuran. For these donors, the dependency of $-\Delta H$ on C_{A} becomes important and, hence, a linear relationship is obtained only for those acids having nearly similar C_{A} parameters. The C_{A} parameter of pyrrole is not close to those for the substituted phenols and thus the linear $-\Delta H$ *vs.* $\Delta\omega^0$ correlation breaks down. We can, using the data given in Tables III and IV, calculate the term $C_{\mathrm{A}}(C_{\mathrm{B}} - (163.44/10.87)E_{\mathrm{B}})$ for all interactions studied here and subtract it from the left-hand side of eq 8 to give a corrected enthalpy of adduct formation.

$$-\Delta H_{\mathrm{corr}} = -\Delta H - C_{\mathrm{A}}\left(C_{\mathrm{B}} - \frac{163.44}{10.87}E_{\mathrm{B}}\right) = \left(\frac{E_{\mathrm{B}}}{10.87K\mathbf{E}_{\mathrm{B}}{}^2}\right)\Delta\omega^0 - \frac{\mathbf{E}_{\mathrm{B}}I}{10.87K\mathbf{E}_{\mathrm{B}}{}^2} \tag{9}$$

When this quantity ($-\Delta H_{\mathrm{coor}}$) is plotted *vs.* $\Delta\omega^0$ for a constant base experiment, a straight line should result. This is indeed found to be the case for all systems studied here. The constant base plots for tetrahydrofuran and TMPPE shown in Figure 1 are redrawn in Figure 3, using the $-\Delta H_{\mathrm{corr}}$ value obtained using 9. Again these are just representative systems and the data reported here can be plotted to see the generality of this equation. Furthermore, the magnitudes of the slopes and intercepts calculated from the least-squares fit of the data compare favorably with the values predicted by eq 9. Consequently, we are in a position to predict the constant base lines and proton chemical shifts for any base in the E and C correlation. Exceptions can be used as evidence for donor neighbor anisotropic contributions.

A constant base correlation between ω_{AB} and the Hammett substituent constant for DMSO interacting with a series of substituted phenols has been reported in the literature.[32] In view of a previously reported straight line correlation between $-\Delta H$ and the substituent constant[33] for a series of substituted phenols interacting with a given base, the above observation would imply a straight line $-\Delta H$ *vs.* ω_{AB} correlation. According to the model described here, such a result would not be expected because DMSO has a small $C_{\mathrm{B}}/E_{\mathrm{B}}$ ratio (2.12). However, it should be kept in mind that for most substituted phenols the C_{A} values are comparable in magnitude and, hence, the term $C_{\mathrm{A}}(C_{\mathrm{B}} - (163.44/10.87)E_{\mathrm{B}})$ appearing in eq 9 would be approximately the same for all of those acids resulting in an apparent linear $-\Delta H$ *vs.* ω_{AB} correlation.

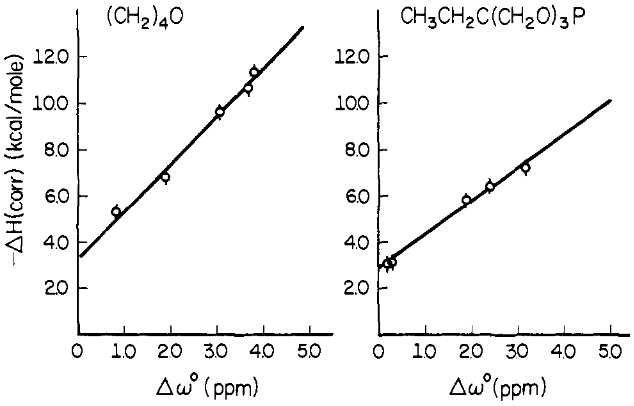

Figure 3. $-\Delta H_{\mathrm{corr}}$ *vs.* $\Delta\omega^0$ plots for various donors interacting with hydrogen bonding Lewis acids.

Donor Anisotropy Effects. So far our discussion has been centered around donors which do not contain strongly anisotropic groups, such as aromatic rings or double bonds. The use of eq 6 together with the calculated apparent electric fields for these anisotropic donors should give the contribution to the total hydrogen bonding chemical shift due to electric field effects only. The difference between this and the experimental value may then be attributed solely to donor anisotropy effects. Recently, work by Lichter and Roberts[34] showed that donor anisotropy effects on the proton chemical shift of chloroform were negligible except for, perhaps, benzene. It was of interest to use our model to evaluate the anisotropic contribution to the proton shift in the benzene–chloroform adduct.

Using the data in Table IV, the constant K'' in eq 6 is found to be approximately -44×10^{-25} cm^3. This predicts a $\Delta\omega^0$ value for the CHCl$_3$–benzene complex to be 0.15 ppm (deshielding), to be contrasted with an experimental value of -1.58 ± 0.03 ppm (shielding). Using eq 10 for the donor anisotropy effect,[3] where $\Delta\chi$ is the anisotropy of the benzene ring[35] and θ being 180° (since the C–H bond of chloroform is perpendicular to the ring and directly over the center), we calculate a distance, R, of 3.0 Å between the center of the ring and the proton. This is to be compared with the value of 3.1 Å calculated by Reeves and Schneider[36] from their nmr investigations of hydrogen bonded chloroform.

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Supplementary Material Available. The concentrations, measured heats, and calculated thermodynamic parameters will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 20 × reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N. W., Washington, D. C. 20036. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche, referring to code number JACS-73-6935.

Nuclear Magnetic Resonance Studies of the Solution Chemistry of Metal Complexes. IX. The Binding of Cadmium, Zinc, Lead, and Mercury by Glutathione[1]

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Abstract: The binding of cadmium, zinc, lead, and mercury ions by the tripeptide glutathione has been investigated by carbon-13 magnetic resonance spectroscopy. Binding to the potential coordination sites was monitored as a function of solution conditions by observing the chemical shifts of the carbon atoms of glutathione. The results indicate that each of these metal ions binds to the potential coordination sites of glutathione with a high degree of specificity, with the actual sites involved in metal binding being dependent on the metal ion and the solution pD, with the exception of mercury which binds only to the sulfhydryl group at a mercury to glutathione ratio up to 0.5. At a metal to glutathione ratio of 0.5, Cd^{2+} and Zn^{2+} bind to both the sulfhydryl group and the amino group, the extent of binding to the two different sites being a function of pD, while Pb^{2+} binds only to the sulfhydryl group. Some binding of the glutamyl and glycyl carboxylic acid groups to cadmium, zinc, and lead was detected in certain pH regions. The chemical shift data for the carbonyl carbons of the two peptide linkages suggest zinc-promoted ionization of the peptide protons with subsequent binding of zinc to the ionized peptide nitrogen at pD greater than 10.5, while no evidence for this metal-promoted reaction was observed in the cadmium, lead, and mercury complexes. The results are discussed in terms of the possible structures of the complexes.

The binding of metal ions by peptides and proteins is of fundamental interest in view of the importance of metal ions in biological systems. Peptides and proteins are comprised of a number of functional groups, many of which are potential coordination sites as shown by studies on metal binding by simple amino acids and other model compounds.

Proton magnetic resonance (pmr) spectroscopy has proven useful for elucidating, at the molecular level, the binding of selected metal ions by simple peptides, particularly polyglycine peptides. The functional groups involved in coordination to diamagnetic cadmium, zinc, lead,[2] and nickel[3,4] have been established from changes in the chemical shifts of carbon-bonded protons close to the binding site, while those involved in coordination to paramagnetic copper and nickel[4,5] have been identified from the dependence of the pmr line widths on their proximity to the binding sites. The application of pmr is limited, however, to relatively simple peptides because of the need for distinct, well-resolved resonances for monitoring interactions at the potential binding sites. The pmr spectra of peptides comprised of more than three or four amino acid residues are characterized by overlapping resonances which are of little use in metal binding studies, particularly if proton–proton coupling is present as, for example, in the pmr spectra of cysteinyl, glutamyl, and lysyl residues.

Carbon-13 magnetic resonance (cmr) spectroscopy should be more useful than pmr for elucidating the binding of metal ions by peptides and proteins; single lines are obtained for nonequivalent carbons in proton-decoupled cmr spectra and the range of chemical shifts is at least an order of magnitude greater. Thus, by cmr it may be possible to elucidate metal binding by larger peptides and by peptides which contain amino acid residues difficult to study by pmr due to proton–proton coupling. In additon, carbon atoms are bonded directly to the potential binding sites making cmr potentially more sensitive as a probe for studying binding at the molecular level.

In the present paper, the results of a cmr study of the binding of cadmium, zinc, lead, and mercury by the tripeptide glutathione (γ-L-glutamyl-L-cysteinylglycine) are reported. This peptide, which is widely distributed in nature, was chosen to evaluate the potential of cmr for the elucidation of metal binding by peptides because there is a lack of agreement as to which of the six potential coordination sites are involved in binding to

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