

Probing Hydrogen Bonding Environments: Solvatochromic Effects on the CN Vibration of Benzonitrile

Daniel J. Aschaffenburg and Richard S. Moog*

Department of Chemistry, Franklin and Marshall College, Lancaster, Pennsylvania 17604-3003

Received: June 19, 2009; Revised Manuscript Received: August 3, 2009

The energy of the nitrile stretching mode in benzonitrile is known to be solvent-dependent. Kamlet–Taft solvatochromic parameters π^* and α are used to model this dependence in both protic and aprotic solvents using multivariable linear regressions. Aprotic solvents induce red shifts that are shown to be proportional to π^* . In protic solvents, the positions of the two bands attributed to distinct solvation states, F and H, are both fit to the Kamlet–Taft solvatochromic equation. The inclusion of an α term yields excellent correlations with the H band, indicative of the strong influence of hydrogen bonding interactions occurring at the nitrile nitrogen in this solvation state. The F band also is best fit by inclusion of the α term, albeit with a weaker overall dependence and a much poorer fit than that for the H band. DFT calculations on simple single-molecule complexes with benzonitrile are consistent with the presence of π -H bonds to the nitrile group as a possible source of the F band dependence on α .

Introduction

Nitriles have recently gained attention as useful monitors of the local solvent environment. The nitrile stretching vibration is an ideal probe for such investigations because its motion is generally considered to be substantially decoupled from the rest of the molecule, and the IR transition gives rise to a narrow absorption band with a high extinction coefficient in a region of the spectrum that is free of competing absorptions from other functional groups.^{1–6} This vibration has also been shown to be sensitive to subtle changes in the electrostatic environment and to hydrogen bonding interactions.^{7,8} Thus, the nitrile group can provide a direct probe of the local solvation status^{4,8–12} including fast solvation dynamics.^{13–15}

Of particular note is the use of the nitrile stretch in the investigation of systems of biological interest such as peptides,^{3,7} DNA oligomers,¹⁶ nucleic acids,¹⁷ enzymes,¹⁸ and proteins.^{1,19–21} Nitriles have also been used as environmental probes through the vibrational Stark effect due to their high sensitivity to electric fields.² This method has been used to detect electric fields in proteins²⁰ and in the active site of human aldose reductase.¹⁸ Recently, nitrile-derivatized amino acids such as cyanoalanine (Ala_{CN}) and cyanophenylalanine (Phe_{CN}) have been recognized as useful probes for studying the structure and dynamics of biological systems; Phe_{CN} is of particular interest because it can be readily incorporated into peptides and proteins.^{3,7,19,21,22} Getahun et al. studied Ala_{CN} and Phe_{CN} in water, THF, and water–THF mixtures as models of the hydrophilic, hydrophobic, and mixed environments found in proteins.³ They attributed the relatively broad nitrile peak in water to a direct hydrogen bonding interaction between a water molecule and the CN group, which increases the CN bond order and results in a higher vibrational frequency. Huang et al. investigated the temperature dependence of the energy of the nitrile vibration of Phe_{CN} in water.⁴ The observed nitrile IR absorption was deconvolved into two components, a lower-energy peak attributed to “free” CN groups (F) and a higher-energy peak corresponding to hydrogen-

bonded CN species (H). This shift to higher energy in the presence of hydrogen bond donation to the nitrile nitrogen has been observed in nitriles previously, both experimentally and computationally.^{5,6,11,23} Hochstrasser and co-workers have recently reported 2D IR experiments concerning the dynamics of forming and breaking hydrogen bonds for several nitriles in methanol.^{13–15} Their results are well modeled by this two-solvation-state model, with an equilibrium $H \rightleftharpoons F$ between the two states, and interconversion occurring on a time scale of a few picoseconds. They propose that the F state corresponds to a solvation environment in which the methanol molecules are hydrogen-bonded to each other but not directly to the nitrile nitrogen.

There have been many efforts to understand explicitly how the solvent influences the nitrile stretch and to correlate the experimental data with properties of the solvent. An early attempt was the Kirkwood–Bauer–Magat equation,^{24,25} eq 1, which modeled the shift of an IR peak ($\Delta\nu$) from that in the gas phase as a function of the dielectric constant, ϵ_0 .

$$\frac{\Delta\nu}{\nu_s} = C \frac{\epsilon_0 - 1}{2\epsilon_0 + 1} \quad (1)$$

Here, ν_s is the peak position in the given solvent and C is a proportionality constant.²⁶ Allerhand and Schleyer later studied solvent effects on IR vibrations involving hydrogen bonding.²⁷ They proposed an empirical linear free energy relationship

$$\frac{\Delta\nu}{\nu_s} = aG \quad (2)$$

where a is characteristic of the particular vibration and its solvent sensitivity and G is an empirical scale based on the observed shifts of the carbonyl stretches of dimethylformamide and benzophenone and the sulfonyl band of dimethylsulfoxide.²⁸ In 1990, Nyquist⁹ observed “pseudo-linear” correlations between the nitrile stretches of acetonitrile and benzonitrile with Gut-

* To whom correspondence should be addressed. Tel: 717-291-3804. Fax: 717-291-4343. E-mail: rick.moog@fandm.edu.

mann's acceptor number (AN).²⁹ Fawcett and co-workers¹¹ expanded on this effort to show that the solvent-induced shift of acetonitrile correlated reasonably well with not only the solvent AN but also the solvent basicity as expressed as Gutmann's donor number (DN). Kolling¹⁰ characterized the fundamental vibrational peak of the nitrile in benzonitrile using various reaction field models^{24,30,31} for aprotic solvents. Fits to these models were generally good when aromatic solvents were removed from the analysis. More recently, several computational studies have also investigated the solvation of nitrile solutes in an effort to understand more specifically how the solvent influences the nitrile absorption.^{5,6,8,23}

An approach that may have potential to correlate the nitrile vibrational energy with solvent properties for a wide range of solvents is the empirical linear solvation energy relationship

$$XYZ = XYZ_0 + s\pi^* + a\alpha + b\beta \quad (3)$$

originally proposed by Kamlet, Abboud, and Taft³² and widely used to characterize solvent effects on numerous solute physical properties.³³ Empirical solvatochromic parameters are used to characterize the solvent in terms of its dipolarity/polarizability (π^*), hydrogen bond acidity (α), and hydrogen bond basicity (β).^{32,34–36} The coefficients s , a , and b are parameters that are characteristic of the solute, and XYZ is some experimental observable such as a rate constant, equilibrium constant, free energy change, NMR coupling constant, or the position of maximum intensity of an absorption band. Though this model is empirical in nature, the parameters themselves represent physical interactions, such as the solvent's ability to donate a proton, α . One advantage of this approach is that, unlike many other models, this approach specifically separates the effects of hydrogen bonding interactions (α , β) from those characteristic of the bulk solvent (π^*).

Previous work has shown that the Kamlet–Taft solvatochromic equation, eq 3, can be used to describe solvent effects on a vibrational transition. For example, Kamlet et al. studied the shift of O–H stretching frequencies of phenols upon complexation with several different bases in carbon tetrachloride solution. They found that the observed shifts attributed to the hydrogen bonding interaction correlated with the solvent β values.^{28,37,38} In addition, eq 3 has been used to describe the effects of hydrogen bond donation at a nitrile group on an electronic transition. Wu and co-workers³⁹ examined the solvatochromism of fluorescence from 4-(*N,N*-dimethylamino)benzonitrile in a wide range of solvents, both protic and aprotic. The emission maximum was observed to follow the Kamlet–Taft solvatochromic equation with very high correlation ($R^2 = 0.99$) when terms involving both π^* and α were included. Thus, eq 3 may provide an excellent model for investigating the solvent-dependent shifts of the nitrile vibrational energy.

Numerous previous experimental and computational studies have shown that the solvent induces a shift in the fundamental nitrile vibrational energy and that in protic solvents two distinct solvation states (F and H) are observed. In this investigation, we examine the solvent effects of both protic and aprotic solvents on the nitrile vibration in benzonitrile, a model for the biologically important derivatized amino acid Phe_{CN}. The data will be analyzed using a variety of solvent polarity scales including the Kamlet–Taft solvatochromic equation in an attempt to correlate the energies of the IR absorptions, including the F and H bands, with solvent properties. Our goal is to better understand the factors that influence the energies of these absorptions, particularly in protic solvents, in an effort to provide

greater insight into the use of the nitrile absorption energy as a probe of the local solvent structure and environment.

Experimental Methods

All chemicals were obtained from Aldrich and were anhydrous or spectroscopic grade or, otherwise, of the highest purity available. They were all distilled over calcium hydride in a nitrogen atmosphere prior to use, except for benzonitrile, decalin, butyl ether, and 1-propanol, which were used as received. Formamide was distilled under vacuum. All samples were prepared under a nitrogen atmosphere, and sample concentrations of benzonitrile were approximately 100 mM to avoid dimerization observed at higher concentrations.^{9,10}

Infrared absorption spectra were collected at 25.0 ± 0.1 °C from 1500 to 3000 cm^{-1} on a Bruker Tensor 37 FT-IR spectrometer at 256 scans per sample with 1 cm^{-1} resolution and a path length of 100 μm . All spectra were post-zero filled with a factor of 4 and baseline corrected.

The observed peaks were fitted using the pseudo-Voigt function, eq 4, which is a linear combination of a Gaussian and a Lorentzian distribution.¹²

$$y = A \left[m_L \frac{2}{\pi} \frac{\text{FWHM}}{4(\tilde{\nu} - \tilde{\nu}_{\text{max}})^2 + \text{FWHM}^2} + (1 - m_L) \frac{\sqrt{4 \ln 2}}{\sqrt{\pi} \text{FWHM}} \exp\left(-\frac{4 \ln 2}{\text{FWHM}^2} (\tilde{\nu} - \tilde{\nu}_{\text{max}})^2\right) \right] \quad (4)$$

Here, FWHM is the full width at half-maximum for both the Gaussian and Lorentzian functions; m_L is the fraction of Lorentzian character ($m_L = 1$ indicates a pure Lorentzian and $m_L = 0$ indicates a pure Gaussian); A is an arbitrary amplitude parameter; and $\tilde{\nu}_{\text{max}}$ is the fitted central frequency of the band. For solvents where $\alpha \neq 0$, two pseudo-Voigt functions were used to deconvolve the band into two separate components, as described further below. The line shape analyses were performed using the Solver function in Microsoft Excel. The parameters were adjusted to obtain the best individual fit to each spectrum; other than $\tilde{\nu}_{\text{max}}$, none of the fit parameters are necessarily considered to have any physical significance concerning the solvation of benzonitrile within the model considered here.

Assessing the validity of including additional parameters in fits using eq 3 involves the analysis of variance (ANOVA). The test statistic used to assess the quality of a fit for any number of fit parameters, p , is the F ratio as defined by⁴⁰

$$\text{SS}(\text{fit}) = \sum_i (y_i^{\text{obs}} - y_i^{\text{fit}})^2 \quad (5)$$

$$\text{SS}(\text{data}) = \sum_i (y_i^{\text{obs}} - \bar{y})^2 \quad (6)$$

$$F \equiv \frac{\{\text{SS}(\text{data}) - \text{SS}(\text{fit})\}/(p - 1)}{\text{SS}(\text{fit})/(N - p)} \quad (7)$$

where y_i^{obs} is the experimentally observed energy, y_i^{fit} is the energy calculated from a fit to the data, \bar{y} is the mean experimental energy of a given data set, and N is the number of data points. F measures the extent to which the proposed model accounts for the observed variation in the data, where an increase in F represents a stronger model including a

consideration of the total number of fit parameters. All statistical analyses were performed with DataDesk 6.2.

Results and Discussion

The IR absorption spectrum of benzonitrile was measured in 17 solvents. Central frequencies and overall band profiles were found to be reproducible within the experimental uncertainty of the instrument. In all cases, the fitted values for $\tilde{\nu}_{\max}$ from distinct measurements in a given solvent differed by less than 0.15 cm^{-1} , and for the vast majority of solvents, the difference was less than 0.10 cm^{-1} . The observed bands all lie within a narrow region of the spectrum, roughly $2227\text{--}2236\text{ cm}^{-1}$. For spectra taken in aprotic solvents, the peak was generally fairly symmetric; however, in protic solvents, noticeable broadening was clearly apparent on the high-energy side. As described previously, this broadening can be attributed to the presence of two distinct solvation states when hydrogen bond donation from the solvent is possible, a higher-energy component (H) attributed to benzonitrile with a “linear” σ -type hydrogen bond involving the nitrogen and a lower-energy component (F) arising from “free” benzonitrile, that is, benzonitrile surrounded by a solvent configuration which explicitly excludes a σ -hydrogen bond to the nitrogen. Thus, spectra in aprotic solvents ($\alpha = 0$) were assumed to have a single average solvation state and are fitted to one pseudo-Voigt function, whereas protic solvents ($\alpha > 0$) are fitted to two pseudo-Voigts functions to model these two distinct solvation states. The data in acetone were treated uniquely because of its small, but nonzero, value for α , 0.08. This α value is so small that any hydrogen bonding interaction with acetone would be expected to produce an H component that would be unresolvable from the F component based on the analysis described below. For this reason, the nitrile band in acetone was fit to only a single pseudo-Voigt function, but it was not included in the $\alpha = 0$ fitting analysis. However, the single fit value for $\tilde{\nu}_{\max}$ was included in the overall fits to both the H and the F bands described below.

Typical fits for each solvent type are shown in Figure 1. For $\alpha = 0$ solvents, the band shape is predominantly Lorentzian; the fractional Lorentzian component, m_L , ranged from 0.60 to 0.88. The deconvolution of 2-propanol ($\alpha > 0$) clearly shows the presence of two bands with the higher-energy band (H) being significantly broader, as was the case for all of the strongly protic solvents. The H bands are all either pure Gaussian or nearly pure Gaussian. The F bands for the primary alcohols had $m_L \approx 0.40$; for 2-propanol and formamide, m_L was much lower. (The full set of fit parameters for all solvents is provided in the Supporting Information.)

On the basis of the values of the central frequencies of the two component bands that are observed in the various alcohols, one might conclude that the spectra in these solvents are essentially the same in all cases. For example, as shown in Table 1, 1-butanol and ethanol have the same central frequencies for the F and H bands. However, the spectra are in fact noticeably different, as shown in Figure 2. Although the fit central frequencies are the same, the relative amplitudes, widths, and m_L values of the components are not the same, leading to clear differences in the overall band shape.

Correlations with the Central Frequency. The central frequencies for the fits to the 17 solvents are presented in Table 1. Experimental values of $\tilde{\nu}_{\max}$ are in good agreement with previously reported values.^{9,10} Table 1 also includes the relevant values for several scales that attempt to quantify nonspecific effects due to solvent polarity and polarizability. A common theoretical construct based on a dielectric continuum model is

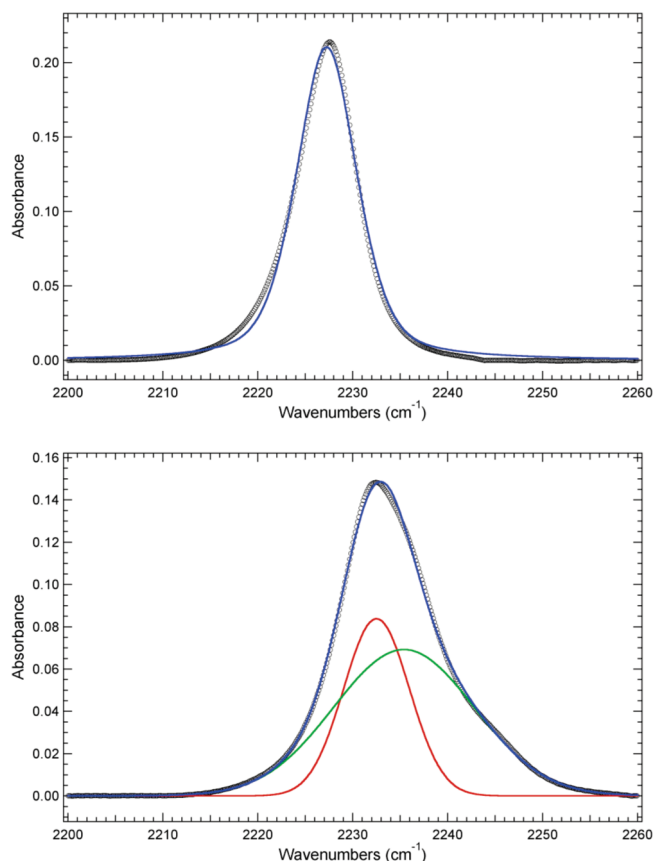


Figure 1. Top: CN stretching band of 100 mM benzonitrile in DMSO is in open circles; the PV fit (eq 4) is in blue. Bottom: CN stretching band of 100 mM benzonitrile in 2-propanol is in open circles with two PV fits in red (F) and green (H). The global fit is in blue.

the reaction field approach,^{41–44} in which the solvent effect is characterized by a function of the dielectric constant (ϵ_0) and the index of refraction (n), in eq 8.

$$F(\epsilon_0, n) = \frac{\epsilon_0 - 1}{\epsilon_0 + 2} + \frac{n^2 - 1}{n^2 + 2} \quad (8)$$

Table 1 also includes several empirical scales based on the observed solvatochromism of a single measurement. These include Dong–Winnick’s P_y scale^{45,46} based on the fluorescence of pyrene, SPP^{47–49} [relative solvatochromism of the electronic absorption spectra of 2-(*N,N*-dimethylamino)-7-nitrofluorene and 2-fluoro-7-nitrofluorene], Reichardt’s E_T^N scale⁵⁰ [electronic absorption of 2,6-diphenyl-4-(2,4,6-triphenyl-1-pyridiniumyl)phenoxide], and Gutmann’s acceptor number AN^{29} [NMR shifts of triethylphosphine oxide]. Finally, two empirical solvent polarity scales based on the average of several measurements are presented, Drago’s S' unifying solvent polarity scale⁵¹ and Kamlet and Taft’s π^* ,^{32,36} the dipolarity/polarizability of the solvent.

We now investigate the extent to which each of these approaches provides a correlation with the central frequency for the CN stretch of benzonitrile through linear regression. Because each of these models involves a single fit parameter (the proportionality constant relating $\tilde{\nu}_{\max}$ to the scale under investigation), the R^2 value can be used to directly compare the quality of the fits. We begin by examining the relative effectiveness of the various models to describe the solvent effect for the subset of solvents with $\alpha = 0$. The leftmost column of

TABLE 1: Experimental and Fitted Parameters for the CN Stretch of Benzonitrile and Solvatochromic Parameters for 17 Solvents

solvent	π^{*b}	α^b	β^b	ϵ_0^b	n^b	$F(\epsilon_0, n)^b$	P_y^e	S'^e	SPP^e	E_T^{Nb}	AN^f	$\tilde{\nu}_{\max}$ (cm ⁻¹)
hexane	-0.11	0	0	1.88	1.370	0.00	0.58	0.68	0.519	0.009	0.0	2233.0
heptane	-0.06	0	0	1.92	1.385	0.00		0.79	0.526	0.012	0.0	2232.9
MCH ^a	0	0	0	2.02	1.424	0.00				0.006		2232.4
decalin	0.09	0	0	2.15	1.480	-0.01				0.015		2231.8
butyl ether	0.18	0	0.46	3.08	1.397	0.17				0.071		2231.3
diethyl ether	0.24	0	0.47	4.20	1.350	0.30	1.02	1.73	0.694	0.117	3.9	2231.1
ethyl acetate	0.45	0	0.45	6.02	1.370	0.40	1.37	2.15	0.795	0.228	9.3	2230.4
THF ^a	0.55	0	0.55	7.58	1.405	0.44	1.35	2.08	0.838	0.207	8.0	2229.3
DMF ^a	0.88	0	0.69	36.71	1.428	0.67	1.81	2.80	0.954	0.386	16.0	2228.0
DMSO ^a	1.00	0	0.76	46.45	1.478	0.66	1.95	3.00	1.000	0.444	19.3	2227.2
acetone	0.62	0.08	0.48	20.56	1.356	0.65	1.64	2.58	0.881	0.355	12.5	2229.7

											$\tilde{\nu}_F$ (cm ⁻¹)	$\tilde{\nu}_H$ (cm ⁻¹)	
1-butanol	0.47	0.79	0.88	17.51	1.397	0.61	1.06	2.74	0.837	0.586	36.8	2231.6	2235.4
1-propanol	0.52 ^g	0.78 ^g	0.90 ^c	20.45	1.384	0.63	1.09	2.68	0.847	0.617	37.3	2231.7	2235.5
ethanol	0.54	0.83	0.77	24.55	1.359	0.67	1.18	2.80	0.853	0.654	37.1	2231.6	2235.4
methanol	0.60	0.93	0.62	32.66	1.327	0.71	1.35	2.87	0.857	0.762	41.3	2231.5	2235.8
2-propanol	0.48	0.76	0.95	19.92	1.375	0.63	1.09	2.66	0.848	0.546	33.5	2232.5	2235.4
formamide	0.97	0.71	0.48 ^d	111.00	1.447	0.71				0.775	39.8	2230.8	2232.4

^a Abbreviations are MCH, methylcyclohexane; THF, tetrahydrofuran; DMF, dimethylformamide; DMSO, dimethylsulfoxide. ^b Reference 40. ^c Reference 44. ^d Reference 33. ^e Reference 47. ^f References 29 and 33. ^g Reference 36.

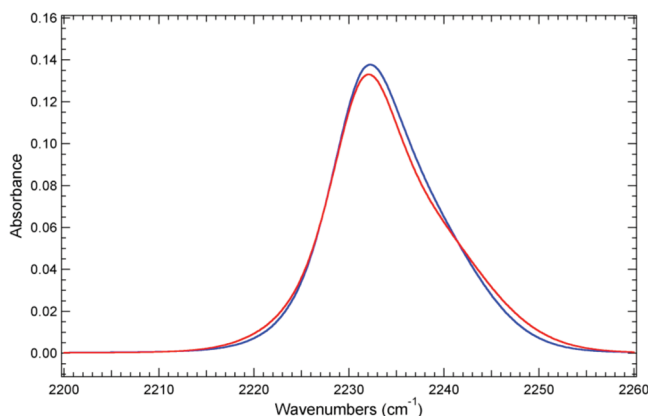


Figure 2. Blue: CN stretching of 100 mM benzonitrile in 1-butanol. Red: CN stretching of 100 mM benzonitrile in ethanol.

TABLE 2: R^2 Values for Correlations of Various Solvent Polarity Scales with $\tilde{\nu}_{\max}$ Values^a

scale	$\alpha = 0$	all solvents with F bands	all solvents with H bands
π^*	0.99 (10)	0.59 (17)	0.09 (16)
ϵ_0	0.78 (10)	0.13 (17)	0.00 (17)
ϵ_{02}	0.87 (7)	0.05 (14)	0.00 (14)
n	0.19 (10)	0.15 (17)	0.23 (17)
$F(\epsilon_0, n)$	0.93 (10)	0.27 (17)	0.00 (17)
P_y	0.97 (6)	0.84 (12)	0.46 (12)
S'	0.96 (7)	0.27 (13)	0.00 (13)
SPP	0.99 (7)	0.54 (13)	0.07 (13)
E_N^T	0.94 (10)	0.04 (17)	0.15 (17)
AN	0.94 (7)	0.01 (14)	0.35 (14)

^a Values in parentheses represent the number of solvents in regression; see Table 1; ϵ_{02} excludes hexane, heptane, and MCH.

values in Table 2 provides R^2 values for linear correlations with each of the listed solvent polarity scales.

As can be seen in Table 2, several of the solvent scales [$F(\epsilon_0, n)$, P_y , S' , SPP, E_N^T , and AN] all offer good correlations to $\tilde{\nu}_{\max}$. The two best correlations for modeling the central frequency for solvents with $\alpha = 0$ are π^* and SPP. The high quality of the fit with π^* is shown graphically in Figure 3. (Analogous plots for the other solvent scales are available in the Supporting Information.) Thus, in the absence of specific

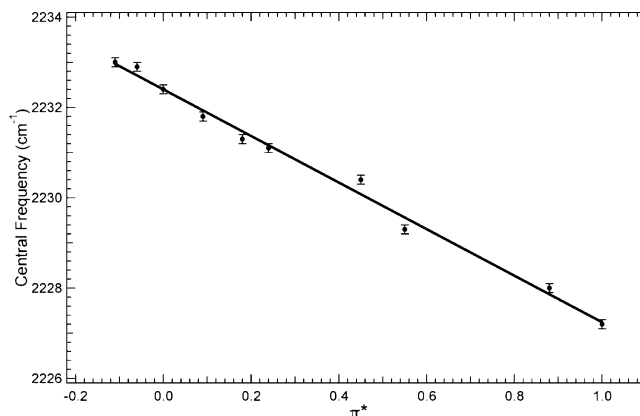


Figure 3. Plot of central frequencies ($\tilde{\nu}_{\max}$) versus π^* for $\alpha = 0$ solvents. Error bars represent the reproducibility of the measurements.

solvent–solute interactions, the transition energy is observed to be linearly dependent on a mixture of solvent polarity and polarizability, with π^* and SPP providing the best measure of the appropriate relative contributions. However, when the protic solvents are included in the regression analysis, none of the above single parameter scales provide nearly as good of a correlation with either the F or H peaks, as shown in Table 2. For the fits that include the F peaks, only P_y has R^2 greater than 0.80. For the fits that include the H peaks, all of the R^2 values are quite low. Thus, none of these single parameter scales provide a strong quantitative correlation with the CN stretching frequency for both protic and aprotic solvents. However, for the Kamlet–Taft solvatochromic model, eq 3, additional parameters related specifically to hydrogen bonding interactions may be included, providing a possible method of characterizing the observed peaks in protic solvents. Thus, this approach may provide a single, consistent model that can be used to describe the solvatochromism of the F and H nitrile bands in protic solvents, possibly providing some additional insight into the factors responsible for the observed solvent effects.

Regression Analysis Using the Solvatochromic Equation. As discussed previously, the F ratio can be used to determine whether or not the inclusion of an additional parameter in a

TABLE 3: Regression Fitting Results for $\tilde{\nu}_{\max}$ Using Equation 3^a

	$\tilde{\nu}_0$	s	a	b	F
$\alpha = 0$ solvents	2232.4(±0.2)	-5.2(±0.3)			1021
	2232.4(±0.2)	-4.9(±0.8)		-0.4(±1.0)	477
all solvents with H	2233.2(±2.2)	-2.3(±3.9)			1.41
	2232.4(±0.1)	-5.2(±0.3)	7.1(±0.2)		1863
	2231.9(±2.1)	-6.8(±4.7)		6.6(±4.9)	4.54
	2232.4(±0.2)	-5.3(±0.4)	7.0(±0.3)	0.2(±0.5)	1212
all solvents with F	2232.6(±0.9)	-3.6(±1.7)			17.3
	2232.3(±0.4)	-4.8(±0.8)	2.8(±0.7)		87
	2232.2(±1.0)	-5.0(±2.3)		2.0(±2.4)	11.1
	2232.4(±0.4)	-4.3(±1.0)	3.1(±0.8)	-0.8(±1.3)	61.6

^a The values in parentheses represent the 95% confidence limits. Each line represents a different fit; the bold entry in each group is the best fit.

model equation provides a significantly better fit to the data. When the F ratio increases in response to an additional fit parameter, the inclusion of that parameter is considered significant in providing an improved fit to the data. In this case, the fitted central frequencies were first fit to eq 3 containing only the constant term and the π^* term; this result was then compared to fits in which additional solvatochromic parameters (α and/or β) were included. Table 3 contains the results of these analyses, with the parameter set giving rise to the largest F ratio in each case presented in bold.

As shown in Table 3, the following solvatochromic equations are obtained using this procedure

$$\tilde{\nu}_{\max}(\text{cm}^{-1}) = 2232.4 - 5.2\pi^* \quad (\text{for } \alpha = 0 \text{ solvents}) \quad (9)$$

$$\tilde{\nu}_{\text{H}}(\text{cm}^{-1}) = 2232.4 - 5.2\pi^* + 7.1\alpha \quad (10)$$

$$\tilde{\nu}_{\text{F}}(\text{cm}^{-1}) = 2232.3 - 4.8\pi^* + 2.8\alpha \quad (11)$$

Equation 9 was obtained from the fit to all of the solvents for which $\alpha = 0$. When the H components from protic solvents are included (along with acetone), eq 10 results. A fit including all solvents with the F bands from the protic solvents produces eq 11. Note that the $\tilde{\nu}_{\max}$ values for $\alpha = 0$ solvents are, as expected, best fit by a solvatochromic equation including π^* only.⁵² The negative coefficient in the π^* term indicates that an increase in π^* causes a decrease in $\tilde{\nu}_{\max}$. Equation 10 shows that when all of the solvents are analyzed including the H band from the protic solvents, the best fit involves an additional term depending on α . The magnitude of the coefficient a (7.1) reflects the large relative impact of the hydrogen bonding interaction on the energy of the absorption, and its positive value indicates that the hydrogen bonding interaction with the solvent causes a blue shift of the band, consistent with previous reports.^{10,14} This result is also fully consistent with the previous assignment of the high-energy band to a solvation state that includes hydrogen bond donation from the solvent. When a term involving β , the solvent hydrogen-bond-accepting ability, is included in any of the regressions, the F ratio decreases (as expected) because benzonitrile is not a hydrogen bond donor. Thus, no β term is included in any of the best-fit equations.

If the F bands truly correspond to solvation states in which there is no hydrogen bonding to the nitrile taking place, then one might reasonably expect that the best solvatochromic equation to describe the energies of these bands would not

include the α term. However, as shown in Table 3, when a regression involving only π^* is conducted including all solvents and the F peaks from the spectra in protic solvents, the F ratio dramatically decreases from its value with only the aprotic solvents from 1021 to 17.3. This resulting small value of F indicates a very poor fit and suggests that the solvation giving rise to the F bands is not well characterized solely by the π^* parameter. Somewhat surprisingly, the F band data is best fit to a solvatochromic equation including both π^* and α . Notably, with an F value of only 87, this result represents a significantly poorer overall correlation than that for the H bands or that for the $\alpha = 0$ solvents alone. In addition, the a coefficient in eq 11 is relatively small (2.8), indicating a weaker dependence on α than was seen for the H band. Still, the values of $\tilde{\nu}_{\text{F}}$ predicted by eq 11 for the alcohols are all within 0.7 cm^{-1} of the experimental values. (See the Supporting Information for a graphical depiction of the relative quality of the fits for H and F bands.) Thus, this apparent dependence of the F band on the hydrogen-bond-donating ability of the solvent seems to contradict the assignment of the band to solvation states involving “free” benzonitrile, that is, benzonitrile molecules which are *not* involved in hydrogen bonding interactions with the solvent.

To further investigate the apparent dependence of the F band positions on the solvent α value, we examined the extent to which the deviation from the values predicted by eq 9 are linearly dependent on α for the protic solvents. Note that for the H bands, this is clearly true; eq 10 resulted in identical fit parameters for the constant term (2232.4 cm^{-1}) and the s coefficient (5.2 cm^{-1}) as were obtained in the fit to the aprotic solvents only (eq 9). Therefore, the displacement of the H band from the energy predicted by eq 9 is very well quantified as 7.1α . For the F bands in protic solvents (excluding acetone), the relevant data were thus fit to the equation $\tilde{\nu}_{\text{F}} = 2232.4 - 5.2\pi^* + a\alpha$, with the a coefficient as the only fit parameter. The resulting relationship is

$$\tilde{\nu}_{\text{F}} = 2232.4 - 5.2\pi^* + 3.0(\pm 0.6)\alpha \quad (12)$$

where the parentheses indicate the 95% confidence interval for the fit value. This fit results in an increase of only about 15% in the sum of squares of residuals over the three-parameter fit reported in eq 11. The coefficient a is essentially identical in eqs 11 and 12, and the two equations predict $\tilde{\nu}_{\text{F}}$ values that are within $\pm 0.1 \text{ cm}^{-1}$ of each other for all but two of the solvents, which differ by 0.3 cm^{-1} . (See Supporting Information for full details.) Thus, both approaches suggest that the energy of the F band in the protic solvents depends upon both the solvent polarity/polarizability and (more weakly) the solvent's ability as a hydrogen bond donor. The possible implications of this result will be discussed further in the following section.

Because of the interest in the use of Phe_{CN} as a probe of the local environment in peptide-containing biological systems, we now investigate the usefulness of eqs 10 and 11 (or 12) in predicting the solvent effect of water on benzonitrile, a reasonable model for Phe_{CN}. For water, $\pi^* = 1.09$ and $\alpha = 1.17$.³⁶ These values result in predictions of $\tilde{\nu}_{\text{F}} = 2230.3 \text{ cm}^{-1}$ (or 2230.2 cm^{-1} using eq 12) and $\tilde{\nu}_{\text{H}} = 2235.0 \text{ cm}^{-1}$. Hochstrasser and co-workers^{14,15} report that the best fit to the absorption profile of benzonitrile in water requires at least three components (one F and two H bands) and that the interconversion of different solvation states in water is occurring more rapidly than that in methanol. These observations suggest that the solvation environment is more complicated than that in the protic solvents examined in this study. Unfortunately, we were

TABLE 4: Effective π^* Values, π^*_{eff} , for Protic Solvents Estimated From $\tilde{\nu}_F$ (cm^{-1}) and Equation 9

solvent	$\tilde{\nu}_F$	π^*_{eff}
1-butanol	2231.6	0.16
1-propanol	2231.7	0.14
ethanol	2231.6	0.16
methanol	2231.5	0.18
2-propanol	2232.5	-0.02
formamide	2230.8	0.31

unable to obtain a useful spectrum of benzonitrile in water due to solubility issues. However, the reported peak of the IR absorption of benzonitrile in water is at about 2235 cm^{-1} ,¹⁴ with observable asymmetric broadening to higher energy, suggesting that there are significant components with energies higher than that of the predicted $\tilde{\nu}_H$ band. Thus, water appears to provide a unique solvent effect on the nitrile stretch compared to that of the protic solvents examined here, perhaps due to the extended nature of the hydrogen bond network in this solvent.

Possible Interpretations. The two components observed in the IR absorption spectra of benzonitrile in protic solvents have been independently fit to solvatochromic equations. The high-energy band (H) is very well described by this approach when both π^* and α terms are included. The lower-energy band (F) is much less well described by the solvatochromic equation, although the best fit also includes the hydrogen-bond-donating ability of the solvent. Still, this dependence of the F band position on both π^* and α raises some questions concerning the interpretation of all of the fits to the Kamlet–Taft solvatochromic equation.

We consider four possible explanations for this result. The first is that the solvatochromic model is not appropriate for describing solvent effects on the nitrile stretching band in benzonitrile. A second possibility is that the assumption that the spectra are well characterized by one or two pseudo-Voigt functions is too simplistic to appropriately model the solvation states of benzonitrile in these solvents. However, two results argue strongly against both of these possibilities. There is an excellent correlation of π^* with $\tilde{\nu}_{\text{max}}$ for the $\alpha = 0$ solvents; in addition, the fit to the H band using the solvatochromic equation is also extremely good, with an increased F ratio for the inclusion of the α term in the fit. Thus, it seems unlikely that either of the first two possibilities is the best interpretation.

A third possibility is that the F band does correspond to “free” benzonitrile but that the value of π^* for these solvation states is not the same as that for the bulk solvent. If the molecules giving rise to the F band are in fact specifically *not* involved in hydrogen bond interactions with the solvent, then clearly, some possible solvation states are not represented in the ensemble producing this band. To the extent that π^* represents an average solvent polarity/polarizability effect *including solvation states that involve hydrogen bonding*, the benzonitrile molecules contributing to the F band can be considered to be experiencing an *effective* π^* (π^*_{eff}). Table 4 contains π^*_{eff} values for the protic solvents calculated from $\tilde{\nu}_F$ and eq 9. The four normal alcohols all have approximately the same value for π^*_{eff} (0.14–0.18); this is roughly equal to the π^* value for butyl ether. This makes some sense chemically as solvation states involving normal alcohols that explicitly exclude hydrogen bonding to the solute could result in solvent–solute interactions that are generally “ether-like”. This analysis in terms of π^*_{eff} is consistent with the notion that the average solvation environment giving rise to the F band is solvent-independent for the four small normal alcohols.^{6,8} For formamide, $\pi^*_{\text{eff}} = 0.31$, a value that is between

those of the ethers and ethyl acetate. This is not completely unreasonable as those solvation arrangements that exclude hydrogen bonding to formamide would likely involve dipolar interactions with the carbonyl group, analogous to those present in the ester. However, using this model to explain the results for 2-propanol is somewhat more problematic. For 2-propanol, $\pi^*_{\text{eff}} = -0.02$, a value most typical of alkanes. It is difficult to imagine that the solvation shell around benzonitrile would consist exclusively of 2-propanol molecules with the alkyl groups oriented toward the solute. Thus, overall, the suggestion that an effective π^* can be used to describe the solvation of the F state species may have some merit, although questions remain regarding its applicability in all cases.

The last and possibly most interesting explanation is that the dependence of the F band energy on α represents a true dependence on the hydrogen bonding ability of the solvent but that the nature of that dependence does not involve σ -H bonds with the nitrogen atom of the nitrile. Note that the value of a in eq 11 is much smaller than that in eq 10 (2.8 versus 7.1), indicating that the relative impact of the solvent hydrogen-bond-donating ability is substantially reduced for the F band compared to the impact on the H band. Thus, a weaker hydrogen bonding interaction arising from an alternative configuration may be the source of this dependence. For example, the observed gas-phase 1:1 complex of benzonitrile and methanol reported by Borst et al.⁵³ does not involve a σ -H bond interaction. The dominant component of the binding energy arises from dipolar interaction, but two types of hydrogen bonding interaction are also present. One of the interactions involves the donation of a hydrogen bond from methanol to the π system of the nitrile triple bond, and the other involves acceptance of a hydrogen bond from one of the phenyl ring hydrogens to the methanol oxygen. Interactions of this type could conceivably influence the nitrile stretching frequency in a manner that depends on the hydrogen-bond-donating ability of the complexing solvent.

To further examine this possibility, density functional theory (DFT) calculations were performed using Gaussian03 at the B3PW91/6-31++G(d,p) level for an isolated benzonitrile molecule and for several different geometries involving a single “solvent” molecule, as shown in Figure 4. This model is clearly greatly simplified from the actual situation in solution and does not provide the more complete picture that a more sophisticated molecular dynamics simulation would provide. However, our goal here is simply to investigate whether or not it is plausible that there could be solvation states which do not involve σ -H bonds to the nitrile nitrogen but do provide a red shift of the vibrational energy relative to that of isolated benzonitrile. We also can examine if such states could also produce an appropriate dependence on the α value of the solvent.

As shown in Figure 4a, optimization of an isolated benzonitrile yielded a nitrile stretching energy, $\tilde{\nu}_{\text{CN}}$, of 2346.8 cm^{-1} . When a single methanol molecule was added and optimized in a “linear” hydrogen bonding geometry (Figure 4b), the DFT-calculated $\tilde{\nu}_{\text{CN}}$ shifted to 2355.9 cm^{-1} . This increase (of about 9 cm^{-1}) is the same as that recently reported by Ghosh et al.¹⁴ and is qualitatively consistent with the blue shifts observed for the H bands experimentally, although the magnitude of the effect in the calculation is much larger. For 2-propanol and formamide (see Supporting Information), the “linear” complex with optimal hydrogen bonding directly to the N atom gave $\tilde{\nu}_{\text{CN}} = 2354.5$ and 2353.0 cm^{-1} , respectively. These values are consistent with the experimental ordering of the $\tilde{\nu}_H$ values for formamide, 2-propanol, and methanol. Conversely, when the hydroxyl group in a methanol molecule is oriented “parallel” to the nitrile

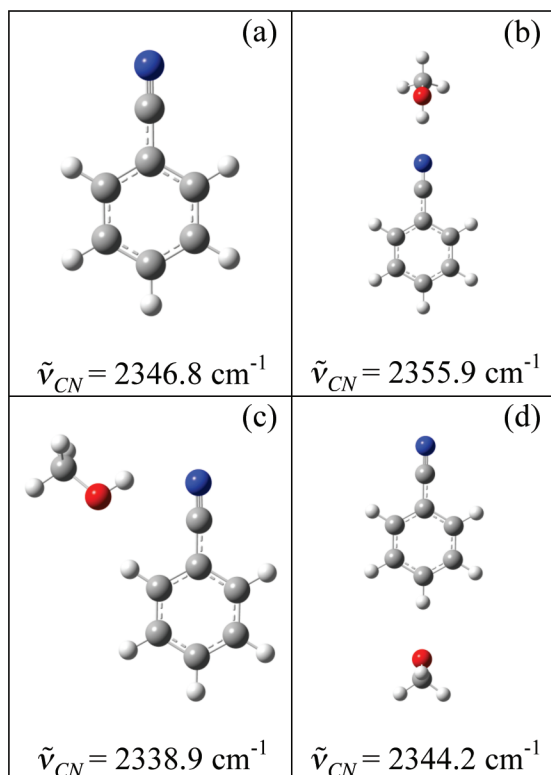


Figure 4. B3PW91/6-31++G(d,p)-optimized gas-phase structures for benzonitrile and complexes with a single methanol molecule; (a) benzonitrile, (b) benzonitrile with methanol in a “linear” or σ -H bond geometry, (c) benzonitrile with methanol in a “parallel” or π -H bond geometry, and (d) benzonitrile with methanol interacting with the *para*-hydrogen.

(Figure 4c), the peak shifts to 2338.9 cm^{-1} , a red shift of about 8 cm^{-1} . This result is qualitatively consistent with a previous report by Choi et al.⁵ involving analogous calculations of complexes of acetonitrile and water and has a structure that is very similar to the gas-phase 1:1 complex reported by Borst and co-workers.⁵³ Choi et al. also describe the “parallel” arrangement (Figure 4c) as a π -H bond because the complex “is stabilized by the hydrogen bonding interaction between the water H atom and the nitrile’s π orbitals”.⁵ When calculations involving this type of π -H bond interaction are performed with 2-propanol and formamide (see Supporting Information), the resulting energies are 2339.4 and 2341.3 cm^{-1} , respectively. All of these values are significantly lower than the energy of the isolated benzonitrile stretch. This result supports the proposal that the impact of solvation states that include π -H bonds could result in red-shifted absorption bands. However, because the dipole moments (and π^* values) of the three solvent molecules vary substantially and the strong dipolar interaction in this configuration can influence the fundamental vibrational energy, we are unable to draw any conclusions from these calculations concerning the dependence of the stretching frequency on α for π -H-bonded species. However, it is plausible that there could be a weak α dependence arising from these types of structures involving hydrogen bond donation to the nitrile π system.

In our calculations, the “linear” (σ -type) hydrogen bond configuration with methanol (Figure 4b) has a N–H distance of 2.08 \AA , whereas the N–H distance in the “parallel” arrangement in Figure 4c is 2.32 \AA . Interestingly, this π -H bond distance is roughly the same as the O–H distance (2.35 \AA) between the oxygen atom of methanol and the H in the *para* position on the phenyl ring shown in Figure 4d, where a single

methanol molecule interacts with the phenyl ring far from the nitrile group. In this case, $\tilde{\nu}_{\text{CN}}$ is also red shifted relative to the isolated benzonitrile, albeit by a much smaller amount (2.6 cm^{-1}). However, if this apparent hydrogen-bond-accepting interaction of the alcohol with the phenyl hydrogen were significant in determining the overall energy of the nitrile vibration, it would be characterized by a dependence on the solvent β parameter. Because no significant dependence on β was observed, this interaction is unlikely to be dominant in determining the central frequency value in any solvent.

Choi et al. noted that for the acetonitrile–water system, collections of solvent molecules need to be taken into consideration in order to accurately estimate the frequency shifts associated with different solvation states.⁵ The same caveat certainly applies in the cases that we are considering here. However, these calculations provide evidence that interactions between protic solvents and benzonitrile can lead to both red and blue shifts. Thus, two important conclusions can be reached. First, the assignment of the higher-energy component of the nitrile band in protic solvents to a σ -type hydrogen-bonded solvation state is supported further. Perhaps more significantly, another important conclusion that can be reached is that a π -H bond can lead to a red shift in the nitrile vibrational energy, and it is plausible that this shift could depend on the hydrogen-bond-donating ability of the solvent. Therefore, the F band observed in protic solvents could be attributed to solvation states in which these types of interactions dominate, and the observed dependence on α could be indicative of the presence of this type of local environment.

Conclusion

We have shown that solvent effects on the CN stretch of benzonitrile can be characterized by the solvatochromic model of Kamlet and Taft. For aprotic solvents, the observed absorption energy is linearly dependent on a mixture of the solvent polarity and polarizability, a relationship that is well characterized by the solvatochromic parameter π^* . Other solvent models also provide reasonable correlations for the aprotic solvents, although π^* in general provides a superior fit. For protic solvents, the absorption can be characterized as arising from two solvation states, H and F, as has been described previously. The energy of the H band is very well predicted by a solvatochromic equation that involves both π^* and α , the solvent hydrogen-bond-donating ability. In addition, the best fit to the data for the F band also includes a term involving α , although the dependence on α is weaker, and the fit is not nearly as good. However, this result, combined with some simple DFT calculations, suggests that the average solvation state giving rise to the F band may include some π -H bond interactions with protic solvents.

Given their structural similarity, the results reported here for benzonitrile are likely applicable in a general way to Phe_{CN} also. Thus, additional insight into the local solvent structure or protein dynamics may be gained through the application of a Kamlet–Taft solvatochromic analysis to the observed nitrile IR absorption of Phe_{CN} in peptides and proteins.

Acknowledgment. The authors thank Professor Scott Brewer of Franklin and Marshall College for numerous helpful and insightful discussions and for assistance in the use of Gaussian03 for DFT calculations. The authors also acknowledge the helpful comments of a reviewer in clarifying the interpretation of some of the DFT calculations. Financial support was provided by Franklin and Marshall College through the Hackman Scholars program and the Committee on Grants.

Supporting Information Available: Full details of pseudo-Voigt fitting parameters, a graphical representation of the quality of the fits using eqs 10 and 11, comparison of predicted $\tilde{\nu}_F$ values using eqs 11 and 12, DFT calculations of benzonitrile complexes with formamide and 2-propanol, and correlations of the central frequency with several solvent scales for $\alpha = 0$ solvents. This material is available free of charge via the Internet at <http://pubs.acs.org>.

References and Notes

- Schultz, K. C.; Supekova, L.; Ryu, Y. H.; Xie, J. M.; Perera, R.; Schultz, P. G. *J. Am. Chem. Soc.* **2006**, *128*, 13984.
- Andrews, S. S.; Boxer, S. G. *J. Phys. Chem. A* **2000**, *104*, 11853.
- Getahun, Z.; Huang, C. Y.; Wang, T.; De Leon, B.; DeGrado, W. F.; Gai, F. *J. Am. Chem. Soc.* **2003**, *125*, 405.
- Huang, C. Y.; Wang, T.; Gai, F. *Chem. Phys. Lett.* **2003**, *371*, 731.
- Choi, J. H.; Oh, K. I.; Lee, H.; Lee, C.; Cho, M. *J. Chem. Phys.* **2008**, *128*, 134506.
- Oh, K. I.; Choi, J. H.; Lee, J. H.; Han, J. B.; Lee, H.; Cho, M. *J. Chem. Phys.* **2008**, *128*, 154504.
- Mukherjee, S.; Chowdhury, P.; DeGrado, W. F.; Gai, F. *Langmuir* **2007**, *23*, 11174.
- Reimers, J. R.; Hall, L. E. *J. Am. Chem. Soc.* **1999**, *121*, 3730.
- Nyquist, R. A. *Appl. Spectrosc.* **1990**, *44*, 1405.
- Kolling, O. W. *Appl. Spectrosc.* **2000**, *54*, 890.
- Fawcett, W. R.; Liu, G. J.; Kessler, T. E. *J. Phys. Chem.* **1993**, *97*, 9293.
- Maienschein-Cline, M. G.; Londergan, C. H. *J. Phys. Chem. A* **2007**, *111*, 10020.
- Kim, Y. S.; Hochstrasser, R. M. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 11185.
- Ghosh, A.; Remorino, A.; Tucker, M. J.; Hochstrasser, R. M. *Chem. Phys. Lett.* **2009**, *469*, 325.
- Kim, Y. S.; Hochstrasser, R. M. *J. Phys. Chem. B* **2009**, *113*, 8231.
- Krummel, A. T.; Zanni, M. T. *J. Phys. Chem. B* **2008**, *112*, 1336.
- Watson, M. D.; Gai, X. S.; Gillies, A. T.; Brewer, S. H.; Fenlon, E. E. *J. Phys. Chem. B* **2008**, *112*, 13188.
- Webb, L. J.; Boxer, S. G. *Biochemistry* **2008**, *47*, 1588.
- Liu, J.; Strzalka, J.; Tronin, A.; Johansson, J. S.; Blasie, J. K. *Biophys. J.* **2009**, *96*, 4176.
- Suydam, I. T.; Boxer, S. G. *Biochemistry* **2003**, *42*, 12050.
- Tucker, M. J.; Getahun, Z.; Nanda, V.; DeGrado, W. F.; Gai, F. *J. Am. Chem. Soc.* **2004**, *126*, 5078.
- Miyake-Stoner, S. J.; Miller, A. M.; Hammill, J. T.; Peeler, J. C.; Hess, K. R.; Mehl, R. A.; Brewer, S. H. *Biochemistry* **2009**, *48*, 5993.
- Lindquist, B. A.; Corcelli, S. A. *J. Phys. Chem. B* **2008**, *112*, 6301.
- Kirkwood, J. G. *J. Chem. Phys.* **1934**, *2*, 351.
- Bauer, E.; Magat, M. *J. Phys. Radium* **1938**, *8*, 319.
- West, W.; Edwards, R. T. *J. Chem. Phys.* **1937**, *5*, 14.
- Allerhand, A.; Schleyer, P. V. *J. Am. Chem. Soc.* **1962**, *85*, 371.
- Kamlet, M. J.; Abboud, J. L.; Taft, R. W. An Examination of Linear Solvation Energy Relationships. In *Progress in Physical Organic Chemistry*; Taft, R. W., Ed.; John Wiley & Sons: New York, 1981; Vol. 13; p 485.
- Gutmann, V. *The Donor-Acceptor Approach to Molecular Interactions*; Plenum Press: New York, 1978.
- Block, H.; Walker, S. *Chem. Phys. Lett.* **1973**, *19*, 363.
- McRae, E. G. *J. Phys. Chem.* **1957**, *61*, 562.
- Kamlet, M. J.; Abboud, J. L.; Taft, R. W. *J. Am. Chem. Soc.* **1977**, *99*, 6027.
- Marcus, Y. *Chem. Soc. Rev.* **1993**, *22*, 409.
- Kamlet, M. J.; Taft, R. W. *J. Am. Chem. Soc.* **1976**, *98*, 377.
- Taft, R. W.; Kamlet, M. J. *J. Am. Chem. Soc.* **1976**, *98*, 2886.
- Kamlet, M. J.; Abboud, J. L. M.; Abraham, M. H.; Taft, R. W. *J. Org. Chem.* **1983**, *48*, 2877.
- Kamlet, M. J.; Solomonovici, A.; Taft, R. W. *J. Am. Chem. Soc.* **1979**, *101*, 3734.
- Taft, R. W.; Gramstad, T.; Kamlet, M. J. *J. Org. Chem.* **1982**, *47*, 4557.
- Wu, Y. G.; Tabata, M.; Takamuku, T. *J. Solution Chem.* **2002**, *31*, 381.
- Moog, R. S.; Kim, D. D.; Oberle, J. J.; Ostrowski, S. G. *J. Phys. Chem. A* **2004**, *108*, 9294.
- Ooshika, Y. *J. Phys. Soc. Jpn.* **1954**, *9*.
- Lippert, E. *Z. Naturforsch.* **1955**, *A10*.
- McRae, E. G. *J. Phys. Chem.* **1957**, *61*.
- Horng, M. L.; Gardecki, J. A.; Papazyan, A.; Maroncelli, M. *J. Phys. Chem.* **1995**, *99*, 17311.
- Dong, D. C.; Winnik, M. A. *Photochem. Photobiol.* **1982**, *35*, 17.
- Dong, D. C.; Winnik, M. A. *Can. J. Chem.* **1984**, *62*, 2560.
- Catalan, J. *J. Org. Chem.* **1997**, *62*, 8231.
- Catalan, J.; Lopez, V.; Perez, P. *Liebigs Ann. Chem.* **1995**, *793*.
- Catalan, J.; Lopez, V.; Perez, P.; Martinvillamil, R.; Rodriguez, J. G. *Liebigs Ann. Chem.* **1995**, *241*.
- Reichardt, C. *Chem. Rev.* **1994**, *94*, 2319.
- Drago, R. S. *J. Chem. Soc., Perkin Trans. 2* **1992**, 1827.
- Slightly different values of π^* for some of the solvents may be obtained from ref 36. Regression analyses using these values produced comparable correlations for which the fit parameters are the same within the 95% confidence intervals. For example, using the values from ref 36 for the $\alpha = 0$ solvents gives the following regression $\nu_{\max} = 2232.5(\pm 0.3) - 5.1(\pm 0.5)\pi^*$ with F ratio = 424.
- Borst, D. R.; Pratt, D. W.; Schafer, M. *Phys. Chem. Chem. Phys.* **2007**, *9*, 4563.

JP905802A