

# Specific Effects of Dimethyl Sulfoxide on the Relative Basicities of Aliphatic Amines

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The base strength of amines in solvent systems containing dimethyl sulfoxide ( $\text{Me}_2\text{SO}$ ) is studied. Equilibrium constants for the Bronsted acid-base reaction of various amines with *p*-nitrophenol in benzene/ $\text{Me}_2\text{SO}$  solvent systems indicate that all such reactions are favored by increased  $\text{Me}_2\text{SO}$  concentration but that the effect is far greater for primary and secondary amines. NMR studies indicate that hydrogen bonds are forming between primary or secondary amines and  $\text{Me}_2\text{SO}$ . It is proposed that such hydrogen bonds increase amine basicity.

## Introduction

As part of a study of phenol-amine interactions, we observed that in dimethyl sulfoxide ( $\text{Me}_2\text{SO}$ ) solutions the log  $K$  for the ionization of *p*-nitrophenol was considerably higher for *n*-butylamine than for triethylamine although the two amines were considered to be similar in base strength.<sup>1</sup> At that time we proposed that the basicity of the primary amine, *n*-butylamine, was enhanced by the formation of hydrogen bonds between the amine protons and  $\text{Me}_2\text{SO}$ . Present extensions of these studies focus on specific solute-solvent interactions investigating both how solvent influences the reaction and whether the reaction can serve as a probe of the structure of mixed solvent systems.<sup>2</sup> We have returned to this earlier observation to investigate the mechanism of enhancement of basicity both for its own sake and for comparison with solvent systems whose behavior is more complex, particularly aqueous systems.

## Experimental Section

**Materials.** Diethylamine, *n*-butylamine, and triethylamine (Eastman reagent grade) were distilled before use. *p*-Nitrophenol (Eastman indicator grade) was recrystallized from benzene. Dimethyl sulfoxide was spectro grade from Eastman. Benzene was spectro grade from Mallinckrodt.

**UV-Visible Spectrophotometry.** All solutions were assembled by weight. The absorption spectra from 550 to 350 nm were determined by using matched 1-cm silica cells in a Beckman DK-2A, the temperatures of both sample and reference cells being maintained at 25 °C. The concentration of *p*-nitrophenol was  $1.8\text{--}2.2 \times 10^{-5}$  M. For each amine in each solvent system the *p*-nitrophenol spectrum was recorded for no amine and for four or five different amine concentrations. Three solvent systems were studied with all amines: 3:7, 1:1, and 9:1  $\text{Me}_2\text{SO}$ /benzene (vol:vol). Amine concentrations were varied as required to provide useful data, ranging as follows: 3:7  $\text{Me}_2\text{SO}$ /benzene,  $6 \times 10^{-4}\text{--}6 \times 10^{-2}$  M; 1:1  $\text{Me}_2\text{SO}$ /benzene,  $1 \times 10^{-4}\text{--}6 \times 10^{-4}$  M; 9:1  $\text{Me}_2\text{SO}$ /benzene,  $2 \times 10^{-5}\text{--}7 \times 10^{-5}$  M. The method of Rose and Drago<sup>3</sup> was used to calculate equilibrium constants from the absorbances of *p*-nitrophenol in the presence of the various amine concentrations. The array of constants obtained from each calculation was subjected to Chauvenet's criterion to reject extreme values, and the remaining values were averaged. Data were taken and calculated at three different wavelengths for each experimental procedure.

**NMR Spectroscopy.** Solutions for study by NMR were prepared by weighing pure substances directly. Amine self-association was studied by using a range of concentrations of the amines in benzene. The effect of  $\text{Me}_2\text{SO}$

TABLE I: Ionization Reactions for *p*-Nitrophenol and Amines

amine	wave-length, nm	log $K$ in $\text{Me}_2\text{SO}$ /benzene:		
		3:7	1:1	9:1
<i>n</i> -butylamine	410	$2.36 \pm 0.08$	$3.18 \pm 0.19$	$4.09 \pm 0.04$ $4.14 \pm 0.14$
	430	$2.31 \pm 0.15$	$3.19 \pm 0.11$	$4.11 \pm 0.08$ $4.12 \pm 0.07$
	450	$2.26 \pm 0.22$	$3.24 \pm 0.14$	$3.99 \pm 0.13$ $4.12 \pm 0.13$
diethylamine	410	$2.33 \pm 0.21$	$3.14 \pm 0.12$	$3.80 \pm 0.19$
	430	$2.35 \pm 0.17$	$3.25 \pm 0.08$	$3.86 \pm 0.05$
	450	$2.52 \pm 0.23$	$3.25 \pm 0.13$	$3.86 \pm 0.10$
triethylamine	410	$1.09 \pm 0.15$	$1.30 \pm 0.13$	$2.47 \pm 0.16$
	430	$1.24 \pm 0.04$	$1.40 \pm 0.11$	$2.43 \pm 0.17$
	450	$1.22 \pm 0.13$	$1.55 \pm 0.23$	$2.50 \pm 0.15$

was observed by holding the amine concentration constant and varying the relative proportions of  $\text{Me}_2\text{SO}$  and benzene. Mixtures of  $\text{Me}_2\text{SO}$  and benzene without amine were also prepared to measure the effect of  $\text{Me}_2\text{SO}$  concentration on its NMR spectrum. The spectra of these solutions were obtained with a JEOLCO C-60 H1 high-resolution NMR spectroscope, using tetramethylsilane as a standard for determining chemical shift.

The theory developed by Gutowsky and Saika<sup>4</sup> was applied to the data obtained by varying the amine concentration in benzene. A computer program was written to obtain the best value for the equilibrium constant for self-association by the primary and secondary amines.

## Results

The equilibrium constants for the ionization of *p*-nitrophenol by *n*-butylamine, diethylamine, and triethylamine in the various solvent systems are recorded in Table I and are plotted in Figure 1.

The NMR studies are summarized in Figure 2 for *n*-butylamine in benzene, in Figure 3 for diethylamine in benzene, in Figure 4 for *n*-butylamine in  $\text{Me}_2\text{SO}$ /benzene mixtures, and in Figure 5 for diethylamine in  $\text{Me}_2\text{SO}$ /benzene mixtures.

## Discussion

The purpose of this research is to establish that  $\text{Me}_2\text{SO}$  when present in a solvent system does increase the effective basicity of primary and secondary amines. Furthermore, if this occurs, we wish to establish whether the formation of hydrogen bonds between amine hydrogens and  $\text{Me}_2\text{SO}$  is a reasonable explanation for the occurrence. Figure 1 demonstrates that the log  $K$  for the ionization of *p*-nitrophenol by an amine increases for all amines as the pro-

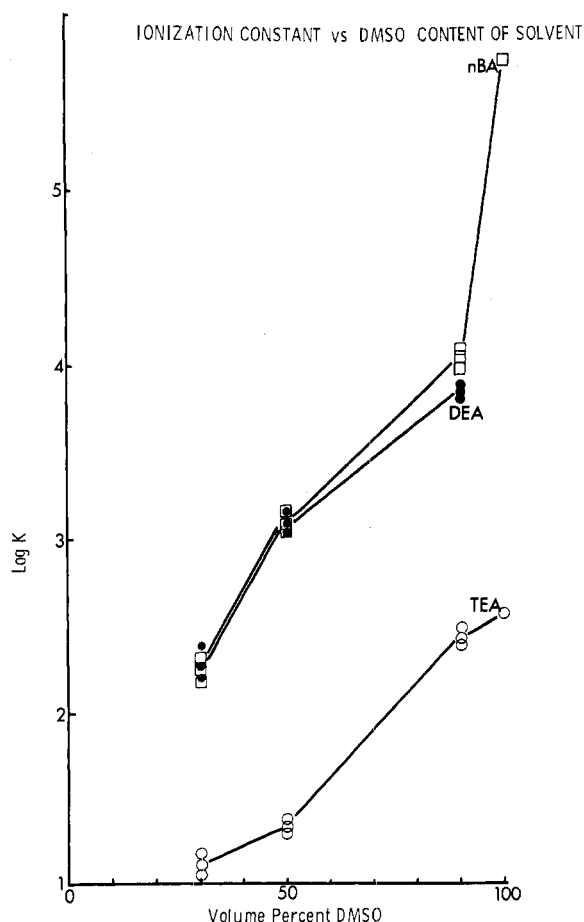


Figure 1. The logarithm of the equilibrium constant obtained spectrophotometrically at 25 °C for the conversion of *p*-nitrophenol to *p*-nitrophenolate ion by *n*-butylamine (nBA), diethylamine (DEA), and triethylamine (TEA) is plotted here against the proportion of Me<sub>2</sub>SO in the solvent.

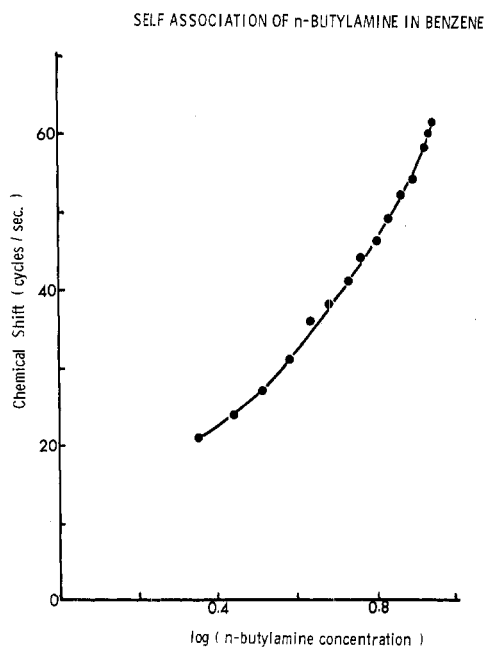


Figure 2. The NMR chemical shifts for amine-group protons in various concentrations of *n*-butylamine in benzene reflect the degree of self-association of the *n*-butylamine by intermolecular hydrogen bonding.

portion of Me<sub>2</sub>SO in the solvent is increased. However, the increase is relatively greater for the primary and secondary amines. This result supports our proposal if we can also establish that the fundamental base strengths of

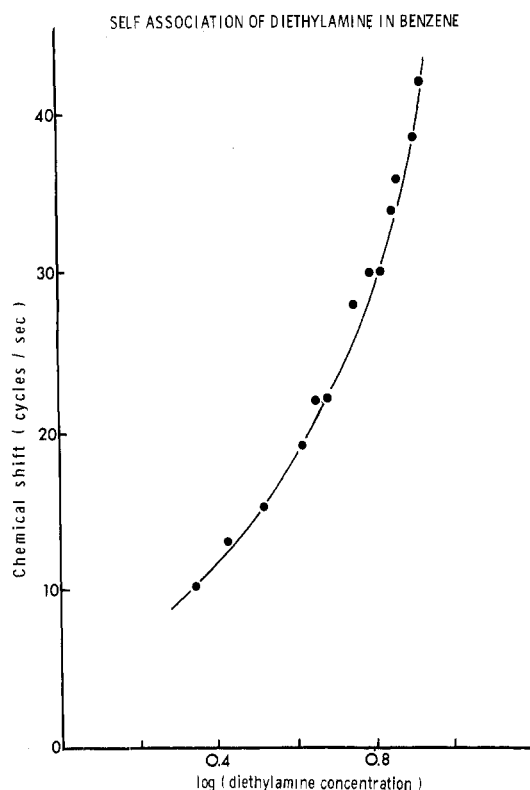


Figure 3. As in Figure 2, the NMR chemical shifts reflect self-association of the amine by hydrogen bonds.

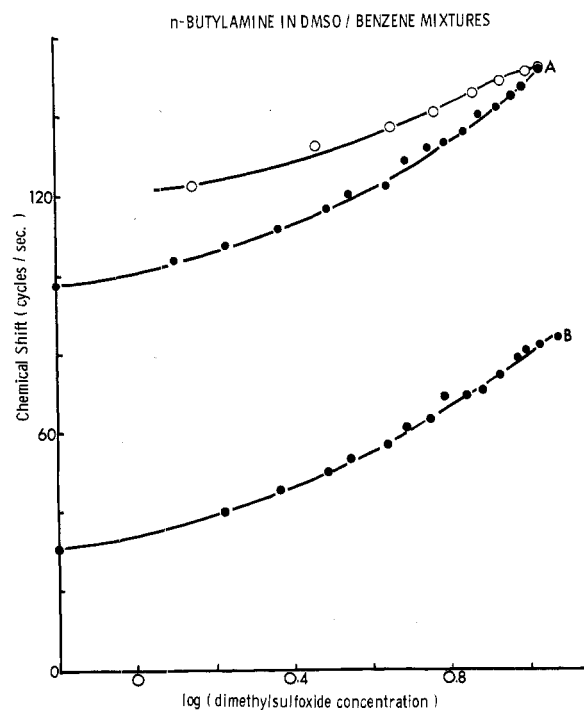


Figure 4. (A) The NMR chemical shifts for the protons of Me<sub>2</sub>SO are plotted against Me<sub>2</sub>SO concentration in the absence (open circles) and presence (solid circles) of a fixed concentration of *n*-butylamine. (B) The NMR chemical shifts for the *n*-butylamine amine-group protons are plotted against Me<sub>2</sub>SO concentration.

three amines are similar enough to warrant direct comparison of the data.

The most commonly used measure of the strength of amines as Brønsted bases is the aqueous  $pK_a$ . The literature values of 10.66 for *n*-butylamine, 10.98 for diethylamine, and 10.75 for triethylamine<sup>5</sup> imply that the three amines have similar base strength, the initial reason for their selection for this study. However, because of the

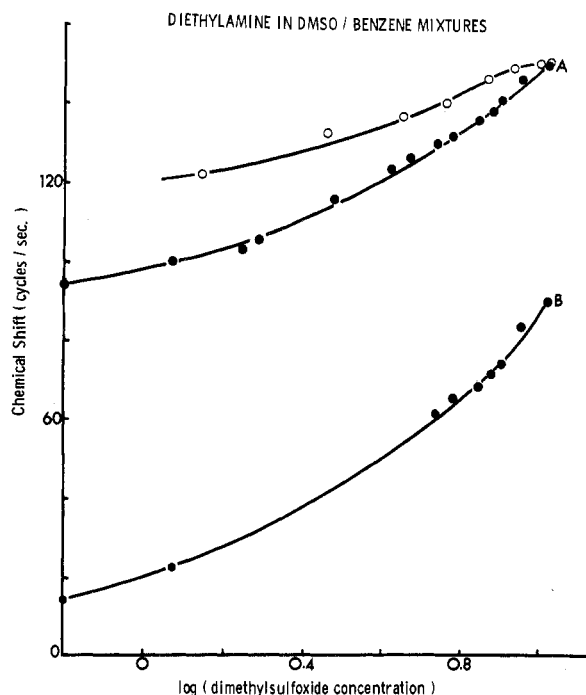


Figure 5. As Figure 4, substituting diethylamine for *n*-butylamine.

TABLE II: Equilibrium Constants for Hydrogen-Bond Formation between Phenols and *n*-Butylamine, Diethylamine, and Triethylamine in Cyclohexane

	log <i>K</i>			ref
	triethyl-amine	diethyl-amine	<i>n</i> -butyl-amine	
<i>p</i> -nitrophenol	3.05		3.25	9
<i>p</i> -cresol	1.79		1.77	8
<i>o</i> -cresol	1.65	1.94	1.89	8
<i>o</i> - <i>sec</i> -butylphenol	1.66	1.99	2.01	8
<i>p</i> -chlorophenol	3.09		3.24	7

possibility of hydrogen bonding between water and amine hydrogens, the effect of the aqueous solvent on base strength may be questioned, and data based on use of an inert solvent is welcomed for comparison.

The equilibrium constants for hydrogen bond formation between these amines and a series of phenols are of interest since cyclohexane was the solvent in each case (Table II). It has been established by using *p*-fluorophenol as the proton donor that Bronsted base strength and ability to accept a proton to form a hydrogen bond are in direct proportion within a family of compounds of identical functional group.<sup>6</sup> In the case of *o*-cresol and *o*-*sec*-butylphenol, the log *K* values for hydrogen bond formation with diethylamine and *n*-butylamine are very similar, while in each case triethylamine is slightly less reactive. The three *p*-substituted phenols reported display log *K* values for hydrogen bonding involving triethylamine that are either the same or slightly lower than the values for *n*-butylamine. This difference may be due to steric effects rather than to base strength. Steric interference in the formation of a hydrogen bond between a tertiary amine and phenol has been proposed,<sup>7,8</sup> although triethylamine is shown in these studies to deviate from expected behavior less than tertiary amines with larger alkyl groups such as tripropylamine and tributylamine.

In the ionization reaction where the reactants do not remain bonded together, steric blockage of the tertiary amine would be expected to have less effect than would be the case for formation of the intermolecular hydrogen bond. More acidic phenols can be ionized in low-dielectric

TABLE III: Equilibrium Constants for the Ionization of Phenols by *n*-Butylamine and Triethylamine in a Variety of Solvent Systems

phenol	solvent system	log <i>K</i>		ref
		triethyl-amine	<i>n</i> -butyl-amine	
<i>p</i> -nitrophenol	1-butanol	1.57	2.45	1
<i>p</i> -nitrophenol	dimethyl-formamide	1.90	3.30	1
<i>p</i> -nitrophenol	4:1 1-butanol/cyclohexane	1.32	2.66	1
<i>p</i> -nitrophenol	1:1 dimethyl-formamide/benzene	1.24	1.57	1
<i>p</i> -nitrophenol	dimethyl sulfoxide	2.61	5.73	1
<i>p</i> -nitrophenol	7:3 dioxane/water	3.19	3.78	11
<i>p</i> -nitrophenol	4:1 dioxane/water	1.50	2.21	11
<i>p</i> -nitrophenol	9:1 dioxane/water	1.71	3.28	11
<i>p</i> -nitrophenol	9:1 acetone/water	2.80	2.82	11
<i>p</i> -nitrophenol	19:1 acetone/water	2.21	2.37	11
<i>p</i> -nitrophenol	4:1 <i>tert</i> -butyl alcohol/water	2.30	5.03	11
<i>p</i> -chlorophenol	1:1 dioxane/water	3.23	3.23	12
		3.19	3.25	
2,6-dinitrophenol	dioxane	4.55	5.23	13
3,4-dinitrophenol	benzene	3.49	3.35	10

solvents, as exemplified by 3,4-dinitrophenol in benzene.<sup>10</sup> Equilibrium constants for that reaction mirror the aqueous  $pK_a$  values strikingly (Table III). In conclusion, we estimate that these amines vary little in their fundamental basicity.

Ionization reactions involve a separation of charge and are therefore facilitated by solvents of higher dielectric constant.<sup>1,11</sup> On this basis alone, one would expect the ionization equilibrium constant for the reaction of *p*-nitrophenol with any amine to increase as the proportion of  $Me_2SO$  in the solvent system increases, and this we observe (Figure 1). However, the increases observed for *n*-butylamine and diethylamine are very much greater than for triethylamine. We interpret the increase in log *K* observed for triethylamine as representing the increase in base strength resulting from the increased solvent dielectric. The additional increase in log *K* exhibited by diethylamine and *n*-butylamine we attribute to specific  $Me_2SO$ -amine interactions dependent on the amine-group hydrogens of primary and secondary amines.

We have proposed that the  $Me_2SO$  is attracting the amine hydrogens to form an amine- $Me_2SO$  hydrogen bond. When the electron density around the amine nitrogen is thus raised, its basicity is increased. NMR studies in which the amine concentration is held constant while the relative proportions of  $Me_2SO$  and benzene are altered (Figures 4 and 5) reveal the amine proton signal shifting with changes in  $Me_2SO$  concentration. This could be due to an interaction with  $Me_2SO$  or could represent an increase in self-hydrogen-bonding as the dielectric constant of the solvent is increased by addition of  $Me_2SO$ . However the signal for the methyl-group hydrogens is also plotted for various benzene/ $Me_2SO$  mixtures both with and without amine. At higher  $Me_2SO$  concentrations the  $Me_2SO$  is present very much in excess of the amine concentration, and any effect of  $Me_2SO$ -amine interaction is overwhelmed by the signal from noninteracting  $Me_2SO$ . However at lower concentrations the  $Me_2SO$  methyl groups are clearly affected by the presence of amine, indicating that inter-

action is occurring between these species.

When one looks for support in previously reported results (Table III), the case of 3,4-dinitrophenol in benzene shows the two amines to be equivalent when the solvent does not hydrogen bond. Hydrogen-bonding solvents such as 1-butanol, dimethylformamide, dioxane, and dioxane/water mixtures generally increase log *K* for *n*-butylamine to a value significantly higher than that for triethylamine. Some surprising results are observed. The amines are roughly equivalent in acetone/water mixtures and in 1:1 dioxane/water, and in the case of 4:1 *tert*-butyl alcohol/water the log *K* for *n*-butylamine is much larger than one would have anticipated, when compared to the other results. Reasons for this behavior are presently under study. The previous study in pure Me<sub>2</sub>SO supports our present study and in fact has been included in Figure 1.

An alternative explanation for the results obtained lies in the possibility that Me<sub>2</sub>SO is breaking up hydrogen-bonded *n*-mers or polymers of the primary or secondary amine. In the studies of diethylamine, Springer and Meek<sup>14</sup> reported that, as the concentration of diethylamine in cyclohexane is increased, the amine forms a cyclic hydrogen-bonded structure containing four amine molecules per unit. To the extent that such structures form, the concentration of amine available to react with phenol is reduced. Me<sub>2</sub>SO, by forming a hydrogen bond with the primary or secondary amine, would prevent the cyclic structure from forming without blocking the amine from interacting with the phenol.

On the assumption that diethylamine favors a tetramer, Feeney and Sutcliffe<sup>15</sup> determined the equilibrium constant for tetramer formation at 25 °C in carbon tetrachloride to be  $2.5 \times 10^{-4} \text{ M}^{-3}$ . Springer and Meek repeated the work in cyclohexane at 40 °C and obtained an equilibrium constant of  $1.75 \times 10^{-3} \text{ M}^{-3}$ .

Our study of diethylamine and *n*-butylamine in benzene was treated in the same fashion as the above reports. Assuming a size for the self-hydrogen-bonded complex (*n*-mer), we calculated the value for the equilibrium constant that would predict a curve that fit the experimental data most closely. The equilibrium constants obtained were  $K_4 = 1 \times 10^{-4} \text{ M}^{-3}$  for diethylamine and  $K_4 = 1.7 \times 10^{-5} \text{ M}^{-3}$  for *n*-butylamine both at 25 °C, in each case assuming for purposes of comparison with previously reported values that the self-hydrogen-bonded form is a tetramer. Plotting calculations done for dimer, tetramer, hexamer, decamer, and even higher *n*-mers revealed that the correspondence of the curve to experimental values when optimally fitted by adjusting the value of  $K_n$  varied very little with changing assumptions of *n*-mer size. The numerical value of  $K_n$  changed as expected, but the cal-

culated concentrations of non-hydrogen-bonded amine altered from one assumption to the next only at very high concentrations of amine. Furthermore, at low amine concentrations all calculations predict less than 1% of the amine to be involved in self-hydrogen-bonding. In conclusion we established that for both amines studied the degree of self-hydrogen-bonding was essentially negligible at most amine concentrations, and we were unable to build a case for one specific size of *n*-mer predominating. The proposal that Me<sub>2</sub>SO could be providing a higher concentration of amine to react with *p*-nitrophenol by breaking up self-hydrogen-bonding by the amine seems to be quantitatively unimportant.

### Summary

The effect of dimethyl sulfoxide on the basicity of primary, secondary, and tertiary amines has been studied. When *p*-nitrophenol is used as the acid and Me<sub>2</sub>SO/benzene mixtures as the solvent, all equilibrium constants for ionization increases when the proportion of Me<sub>2</sub>SO in the solvent is increased, but the effect is far greater in the case of primary and secondary amines. NMR studies of the self-hydrogen-bonding of *n*-butylamine and diethylamine in benzene confirm earlier work in CCl<sub>4</sub> and cyclohexane indicating that the degree of such hydrogen bonding is slight. NMR studies of amines in Me<sub>2</sub>SO/benzene mixtures indicate that hydrogen bonding is occurring between Me<sub>2</sub>SO and the amines. The special effect of Me<sub>2</sub>SO on primary and secondary amines is therefore attributed to the formation of a hydrogen bond between Me<sub>2</sub>SO and the amine-group hydrogen.

### References and Notes

- (1) R. M. Scott, O. DePalma, and S. N. Vinogradov, *J. Phys. Chem.*, **72**, 3192 (1968).
- (2) A. B. Miller and R. M. Scott, *Spectrochim. Acta, Part A*, **36**, 459 (1980).
- (3) N. J. Rose and R. S. Drago, *J. Am. Chem. Soc.*, **81**, 6138 (1959).
- (4) H. S. Gutowsky and A. Salka, *J. Chem. Phys.*, **21**, 1319 (1953).
- (5) D. D. Perrin, "Dissociation Constants of Organic Bases in Aqueous Solution", Butterworths, London, 1965.
- (6) R. W. Taft, D. Gurka, L. Joris, P. von R. Schleyer, and J. W. Rakshys, *J. Am. Chem. Soc.*, **91**, 4801 (1969).
- (7) M. L. Lin and R. M. Scott, *J. Phys. Chem.*, **76**, 587 (1972).
- (8) L. Farah, G. Gilles, D. Wilson, A. Ohno, and R. M. Scott, *J. Phys. Chem.*, **83**, 2455 (1979).
- (9) R. A. Hudson, R. M. Scott, and S. N. Vinogradov, *Spectrochim. Acta, Part A*, **26**, 337 (1970).
- (10) R. A. Hudson, R. M. Scott, and S. N. Vinogradov, *J. Phys. Chem.*, **76**, 1989 (1972).
- (11) R. M. Scott and S. N. Vinogradov, *J. Phys. Chem.*, **73**, 1890 (1969).
- (12) M. L. Lin and R. M. Scott, unpublished data.
- (13) S. N. Vinogradov, R. A. Hudson, and R. M. Scott, *Biochim. Biophys. Acta*, **214**, 6 (1970).
- (14) G. Springer and D. Meek, *J. Phys. Chem.*, **70**, 481 (1966).
- (15) J. Feeney and L. H. Sutcliffe, *J. Chem. Soc.*, 1123 (1962).