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Acid-Base Thermochemistry at Elevated Temperatures

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Abstract: By means of a simple batch calorimeter, heats of reaction were determined for nine nitrogen bases with methanesulfonic acid in tetramethylene sulfone (sulfolane) at 30, 100, and 150, and, in some cases, 200 °C. These data provide the first available information on temperature variation for acid-base processes in nonaqueous media at elevated temperatures. Unlike previous studies in water, the heat capacities of ionization ($d\Delta H_i/dt$) are small or negligible. If this fact is general for homogeneous solutions, it means that (a) extrapolations of acid-base properties from room temperature to the elevated ones common for catalytic industrial processes will be straightforward, and (b) the large and often erratic heat capacities of ionization often found in water probably reflect the peculiarities of that solvent rather than anything characteristic of proton-transfer processes. This leads us to question recent attempts to interpret heat capacities of ionization in water through a multiple-step kinetic scheme.

Introduction

Acid-base reactions are of classic and on-going value for development of structure-reactivity relationships. One need only recall the importance of the dissociation constants of the substituted benzoic acids in water at 25 °C as the original reference point for linear free energy relationships to appreciate the importance of such data. Since most molecules and ions are capable of proton transfer, Brønsted acidity-basicity comparisons can be used to rank an enormous range to species on a common scale of reactivity. Furthermore, the protolysis reaction is of great practical significance, providing the most general of catalytic processes for industrial and biological chemistry.

In addition to being very sensitive to variation in molecular and ionic structure, it is well known that acid-base reactions are affected sharply by changes in solvent and temperature. Thus, there is always cause to doubt whether pK_a values, or even relative acidities, obtained in water at 25 °C will still obtain under other conditions.

Considerable progress has been made in comparing acid-base properties in a wide range of media, including the total removal of solvent in the gas phase.[1] Studies of temperature effects are considerably fewer and have mostly been limited to aqueous solutions over a relatively short temperature range from which ΔH_i° and ΔS_i° can be calculated from the first derivative of pK_a with respect to temperature using the van't Hoff equation. A few such studies of temperature variation done with high precision at a series of temperatures have shown by careful analysis that neither ΔH_i° nor ΔS_i° is constant and their variation implies that rather large heat capacity terms are associated with ionization in water.[2-11] Careful statistical analysis of the best of these data shows that even heat capacities of ionization (ΔC_{pi}'s) are temperature dependent.

Very few data are available which allow comparison of temperature effects on acid-base reactions in nonaqueous systems, especially over a wide range of elevated temperatures. This paper describes such a study of heats of reaction of a series of high-boiling nitrogen bases with methanesulfonic acid, a very strong proton donor, in tetramethylene sulfone (sulfolane) from room temperature to 150 or 200 °C.

This solvent was chosen for its stability at high temperature,[12,13] its low acidity and basicity,[14-16] its high dielectric constant (43 at 30 °C),[17] and several previous studies which provide some useful reference data.[18-23]

Our method for determining heat capacities of ionization is a very simple application of reaction calorimetry through measuring the temperature coefficient of the heat of ionization. This gives results of resonably high precision (±1 cal/mol deg) with much greater ease than through the second derivative of the equlibrium constant, albeit the latter approach provides much more information about free energies and entropies.

Our motivation is both practical and theoretical. Since many industrial processes employ proton transfer at elevated temperatures with both homogeneous and heterogeneous catalysts, enthalpies and heat capacities of ionization are needed for estimating acidity-basicity values at high temperature. From a theoretical view we were interested to see whether the large, and sometimes erratic, ΔC_{pi}'s observed by other workers in water are a manifestation of the peculiarities of that solvent or are a more general pattern for temperature effects on ionization in other solvents.

Experimental Section

Sulfolane Preparation. Sulfolane (Phillips Chemicals) was purified by standard literature procedures.[22,23] First, it was heated at 170-180 °C over NaOH pellets (25 g/L) for 24 h with N_2 bubbling through the solution. Then it was vacuum distilled (~3 mm, 125 °C). Next, the sulfolane was distilled from 96% H_2SO_4 (25 g/L) and stored several days over 4-Å sieves. Finally, the solvent was vacuum distilled from CaH_2 (10 g/L) and stored in a drybox. Sulfolane prepared in this manner had a melting point of 28.4 ± 0.1 °C (lit.[16] mp 28.37 °C). All subsequent transfers of the solvent were made in a drybox.

Chemicals. Imidazole, 4-aminoquinaldine, and 2-aminopyridine (all from Aldrich, 99+%) were used after drying in a vacuum desiccator.

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Table I. Heats of Reaction of Nitrogen Bases with $MeSO_3H$ in Sulfolane Solution from 30 to 200 °C

base	$-\Delta H°(30\ °C)^a$	$-\Delta H°(100\ °C)^a$	$-\Delta H°(100\ °C)^a$	$-\Delta H°(200\ °C)^a$	$\Delta C_{p\ i}^{\circ\ b}$
quinoline	13.6 ± 0.2	13.5 ± 0.2	13.3 ± 0.3		+2
2-methylquinoline	14.5 ± 0.2	14.4 ± 0.2	14.5 ± 0.2		0
4-amino-2-methylquinoline	19.6 ± 0.3	20.6 ± 0.3	20.3 ± 0.2	21.2 ± 0.4	−9
2-aminopyridine	17.0 ± 0.35	17.6 ± 0.3	17.8 ± 0.1		−7
2-amino-3-methylpyridine	17.7 ± 0.2	18.1 ± 0.1	18.3 ± 0.1		−6
4-aminopyridine	19.7 ± 0.35	19.9 ± 0.2	19.9 ± 0.35		−2
1,8-bis(dimethylamino)naphthalene	19.0 ± 0.2		19.3 ± 0.2		−3
imidazole	18.5 ± 0.2	18.3 ± 0.2	18.5 ± 0.2	18.7 ± 0.3	−1
triethanolamine	21.2 ± 0.3[c]	21.3 ± 0.3	21.3 ± 0.2	21.2 ± 0.5	0

[a] In kcal mol^{-1}. [b] In cal mol^{-1} K^{-1}; ±3. [c] 42 °C.

Quinoline, quinaldine, 2-amino-3-methylpyridine, and triethanolamine were stored over 4-Å sieves, then distilled once or twice before use. 4-Aminopyridine was recrystallized from benzene; 1,8-bis(dimethylamino)naphthalene was recrystallized from ligroin.

Methanesulfonic acid was distilled twice (0.5 mm, 110 °C). Titration with standard NaOH showed it to be 99.7 ± 0.2% pure. Sulfuric acid (100%) was made by adding 96% H_2SO_4 to 30% fuming H_2SO_4 until no more fuming occurred under a flow of wet air (fair-and-foggy method).[24] Upon storage, a small amount of water was usually absorbed, so before each use the melting point was checked and a small amount of 30% fuming H_2SO_4 was added to raise the melting point to 10.4 ± 0.1 °C (lit.[25] mp 10.37 °C).

Calorimeter. The isoperibol calorimeter for use near and below room temperture has been described in detail before.[26] Only slight modifications were needed to extend the operating range of the calorimeter up to 200 °C. Teflon TFE insulated wire (Belden No. 83 006) and a high-melting-point solder (Multicore Ersin No. 33F314) were used for connections to the thermistor, calibration heater, and balance heater. Thermistors of varying resistance were used depending on the temperature range: 2 kΩ (25 °C) near room temperature, 10 kΩ (25 °C) at 40–80 °C, 100 kΩ (25 °C) at 100–120 °C, and 500 kΩ (25 °C) at 150–200 °C. These thermistors had resistances of 1–7 kΩ at the operating temperatures. The calorimeter vessel was a 250-mL unsilvered glass Dewar which fitted snugly into a 2-kg brass cannister. The top of the container was coated with GE RTV silicone rubber to prevent leaching of the brass by the hot sulfolane solution.

To maintain constant temperature near ambient temperature, the calorimeter assembly was immersed in a Hotpack water bath capable of maintaining the temperature to ±0.1 °C. Above 40 °C, a Becker Delft Model No. 1452 DPF GC oven was used. The cavity of the oven was modified to securely hold the calorimeter. The oven temperature was constant to ±0.1 °C at all the temperatures used in this study and is rated at this precision up to 400 °C. A rapidly stirred air bath is an essential feature for temperature control.

A brief description of the calorimetric experiment follows; a complete description of the ampoule technique has been given earlier.[26] In a drybox the Dewar was charged with 230 mL of sulfolane plus the base to be used (typically 0.05 M solution of base). The calorimeter contents were kept under a blanket of argon to prevent moisture contamination of the sulfolane solution.

The contents took about 5 h to reach thermal equlibrium at temperatures of 100–200 °C. When equilibrium was attained, two ampules containing neat acid were inserted into the calorimeter through holes drilled in the top of the brass cap. The ampules were connected to 30-cm glass rods with a short piece of Teflon tubing and were lowered gently onto stainless steel rings suspended from the cap inside the Dewar. The rods protruded 20 cm out of the top of the calorimeter and provided the means for breaking the ampules. After the ampules were allowed to equilibrate for 30 min, a calibration heating curve was run by passing a known current through a manganin wire heater of known resistance for a measured length of time. After reattainment of a steady base line, the ampule was crushed by pushing it against the steel ring on which it was resting. After a steady base line was again reached, another heating curve was run. The average of the two calibration heating curves was used to calculate the heat of the acid–base reaction run between the two heating curves. The thermograms were analyzed by the methods described by Challoner et al.[27] and Gunn.[28] The operation of the calorimeter at 25 °C was checked by measuring the heat of protonation of Tham in water. The experimental value of −11.4 ± 0.1 kcal/mol compared well with the accepted value of −11.33 kcal/mol.[29]

Tests for Sulfolane Stability at High Temperature. Sulfolane is reported to decompose slowly at its boiling point, 285 °C,[12] but is reported as stable up to 220[12] or 240 °C.[13] To test its long-term stability, a sample of 0.2 M CH_3SO_3H in sulfolane and one of 0.2 M quinoline in sulfolane were heated at 165 °C for 25 h. Analysis by gas chromatography (28% Pennwalt 223/4% KOH column) and NMR showed no sign of decomposition. Over the course of a calorimetric run taking several hours, no trend in the heats of reaction was observed, which also suggests that calorimetrically significant decomposition of solvent and solute is not occurring at the elevated temperatures.

Product Isolation. Sharp thermograms at all temperatures indicated that the reactions of acid with base were clean, without slow decomposition or side reactions taking place. This was verified in a few cases by isolating the products after completion of the calorimetric measurement by pouring the sulfolane solution into benzene to cause precipitation of the salts. From the reactions at 150 °C of imidazole, quinoline, and 4-aminoquinaldine with $MeSO_3H$, the salts were isolated in 95, 70, and 95% yields, respectively. From the reaction of quinaldine with sulfuric acid at 150 °C, the salt was isolated in 89% yield. The salts had the following physical properties.

Quinolinium methanesulfonate: mp 135–137 °C; NMR (CD_3SOCD_3) δ 2.6 (3 H, s, $CH_3SO_3^-$), 7.7–9.2 (7 H, m, aromatic H), 9.5 (1 H, broad s, ⊕NH).

4-Aminoquinaldinium methanesulfonate: mp 196–199 °C; NMR (CD_3SOCD_3) δ 2.55 (3 H, s, 2-CH_3 group), 2.62 (3 H, s, $CH_3SO_3^-$), 6.68 (1 H, s, 3-H proton), 8.80 (2 H, broad s, NH_2), 7.5–8.5 (4 H, m, aromatic H). The protonated ⊕N–H did not show up.

Imidazolium methanesulfonate: mp 188–190 °C; NMR (CD_3SOCD_3) δ 2.60 (3 H, s, $CH_3SO_3^-$), 7.73 (2 H, s, 4- and 5-H), 9.14 (1 H, s, 2-H), 12.30 (2 H, s, ⊕NH) (agrees with NMR of HCl salt[30]).

Quinaldinium hydrogen sulfate: mp 209–211 °C (lit.[31] mp 211–213 °C); NMR (CD_3SOCD_3) δ 2.9 (3 H, s, CH_3), 7.6–9.0 (6 H, m, aromatic H), 12.5 (1 H, s, ⊕NH).

Results

A. Methanesulfonic Acid. The heats of reaction of nine nitrogen bases with $MeSO_3H$ in sulfolane solution at 30 −200 °C are listed in Table I. For each run, 8–10 aliquots of neat acid were added to an excess of base in the calorimeter by an ampule technique. The values for quinoline, 2-methylquinoline, 4-amino-2-methylquinoline, and imidazole are based on two runs at each temperature; the other values are based on one run. The errors are quoted at the 95% confidence level. The heat capacities of protonation were obtained from the slope of a plot of ΔH vs. T, and we believe they are accurate to ±3 cal mol^{-1} K^{-1}. Since all values were obtained at relatively low concentrations and are concentration independent, they should be considered as partial molar properties referred to a standard state of infinite dilution in sulfolane.

The measured heats of reaction are probably free of thermochemically significant ion-pairing effects at the concentrations used (0.005–0.05 M). Benoit[18] has found no evidence for ion pairing of pyridinium and *o*-anisidinium perchlorates up to 10^{-2} M in sulfolane by conductance measurements, but we recognize (thanks to a perceptive referee) that the methanesulfonate anion

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Table II. Heats of Reaction of Nitrogen Bases with H_2SO_4 in Sulfolane Solution from 30 to 150 °C

base	$-\Delta H°$- (30 °C)[a]	$-\Delta H°$- (100 °C)[a]	$-\Delta H°$- (150 °C)[a]	$\Delta C_p{}^\circ{}_i$ [b]
quinoline	15.3 ± 0.3	14.8 ± 0.3	15.0 ± 0.3	+3
2-methyl-quinoline	15.8 ± 0.3	15.8 ± 0.3	15.8 ± 0.3	0

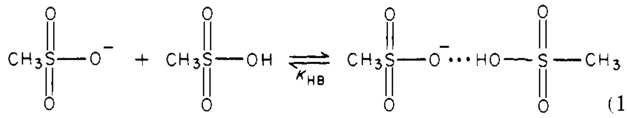
[a] In kcal mol^{-1}. [b] In cal mol^{-1} K^{-1}; ±3.

is superior to perchlorate as a hydrogen-bond acceptor.

The enthalpies of reaction shown in Table I have been corrected for the heat of solution of $MeSO_3H$ in sulfolane (Table III). The negligible heat capacity of solution for the nonelectrolyte in sulfolane agrees with other demonstrations that heat capacities of solution in solvents other than water are small[32] even when the solvents are highly polar. The value of −1.3 kcal/mol for the heat of solution of $MeSO_3H$ in sulfolane at 30 °C is similar to the value found by Benoit of −1.4 kcal/mol for the heat of solution of CF_3COOH.[19] Hydrogen bonding of the weakly basic sulfone oxygens to the acidic hydrogens of these strong acids accounts reasonably for the observed exothermic heats of solution.

Our heats of ionization can be compared most aptly with those of Brown and Holmes,[33] who measured heats of reaction of alkyl-substituted pyridines with $MeSO_3H$ in nitrobenzene at 25 °C. For pyridine they measured a value of −17.1 kcal/mol, slightly more exothermic than we find for quinoline (−13.6 kcal/mol) or 2-methylquinoline (−14.5 kcal/mol) in sulfolane at 30 °C.

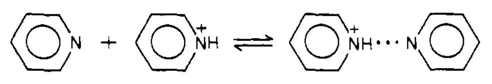
The order of addition (acid into excess base or base into excess acid) is important for these reactions. Brown and Holmes[33] found that addition of base to excess acid caused a trend in the data, with the heats at large acid/base ratios being 6 kcal/mol more exothermic than those near equivalence. We have found similar results in sulfolane at both 30 and 150 °C when adding base to excess acid. Brown and Holmes[33] attributed these results to the occurrence of a second equilibrium (eq 1) to form what would



$$CH_3S(=O)_2-O^- + CH_3S(=O)_2-OH \underset{K_{HB}}{\rightleftharpoons} CH_3S(=O)_2-O^-\cdots HO-S(=O)_2-CH_3 \quad (1)$$

now be called a homoconjugated anion. Recent measurements of K_{HB} for equilibrium 1 in several solvents has substantiated this hypothesis, for K_{HB} values are approximately 10^3 in nonbasic solvents such as CH_3CN, propylene carbonate, and methyl isobutyl ketone.[34]

Addition of acid to excess base caused no perceptible trend in the heats of reaction, either in our work in sulfolane or Brown's work in $PhNO_2$.[33] This indicates that the hydrogen-bond equilibrium such as (2) is not thermochemically important in these



(2)

solvents. Previous work has shown that the equilibria such as (2) are not significant even in the nonpolar solvent CCl_4.[35] Thus, the heats reported in Table I appear to be free of solute–solute effects such as hydrogen bonding and ion pairing.

An estimate of the free energy changes for these reactions can be made from pK_a values in acetonitrile, a solvent of similar properties and basicity to sulfolane. Methanesulfonic acid has a pK_a of 8.36 in CH_3CN,[34] while pyridinium ion has a pK_a of 12.3.[36] From this, a pK_a of 12.0 can be estimated for quinolinium (ΔpK_a between pyridinium and quinolinium is 0.3 in water). Consequently, assuming a ΔpK of 3.6 ($\Delta G° = -5.0$ kcal/mol) for the reaction of quinoline with $MeSO_3H$ in sulfolane, and combining this with the $\Delta H°$ of −13.6 kcal mol^{-1} leads to a $\Delta S°$ value of approximately −30 cal mol^{-1} K^{-1} for the reaction. A large negative entropy is expected for a reaction in which ionic products are formed from neutral reactants owing to the organization of the solvent around the ions.[37]

Table III. Heats of Solution (kcal mol^{-1}) of $MeSO_3H$ and H_2SO_4 in Sulfolane from 30 to 150 °C

$MeSO_3H$		H_2SO_4	
T, °C	$\Delta H_s{}^0$	*T*, °C	$\Delta H_s{}^0$
30	−1.32 ± 0.05	30	−6.0 ± 0.15
150	−1.36 ± 0.06	60	−6.22 ± 0.06
		80	−6.29 ± 0.11
		120	−6.04 ± 0.15
		150	−6.35 ± 0.10

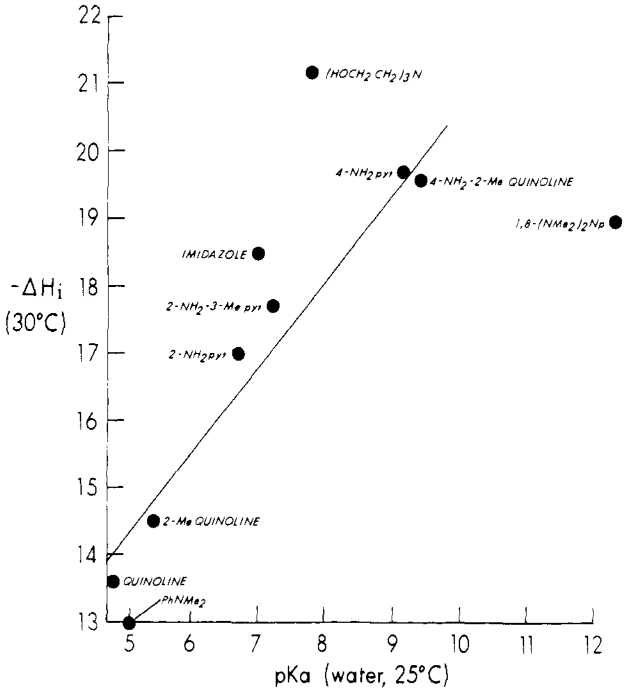


Figure 1. Heats of protonation (ΔH_i) for various nitrogen bases in sulfolane at 30 °C with methanesulfonic acid.

B. Sulfuric Acid. Heats of reaction of quinoline and 2-methylquinoline with 100% H_2SO_4 in sulfolane solution from 30 to 150 °C are shown in Table II. The heats of reaction with H_2SO_4 are only 1–2 kcal/mol more exothermic than those with $MeSO_3H$, which suggests that the acidities of $MeSO_3H$ and H_2SO_4 are similar in sulfolane. This agrees with the small differences in pK_a values for these two acids in Me_2SO and CH_3CN.[38]

As shown in Table III, sulfuric acid has a significant exothermic heat of solution in sulfolane. It is similar in size to the heat of solution of −5.4 kcal/mol for sulfolane into 92% H_2SO_4.[39] At first, this might suggest that H_2SO_4 is a strong enough acid to appreciably protonate sulfolane. However, Benoit[20] and Coetzee[21] have shown that acids much stronger than H_2SO_4 do not fully dissociate in sulfolane, with $HClO_4$ having a pK_a of 3.0[21] (2.7);[20] FSO_3H, 3.3;[20] and $H_2S_2O_7$, 5.0.[20] The large heat of solution is, therefore, probably not due to a heat of protonation of the solvent, but is more likely due to hydrogen bonding to the sulfone oxygens of sulfolane with at most only partial ionization. The unchanging heats of solution with increasing temperature would consequently indicate that heat capacities for hydrogen-bond equilibria are also small in sulfolane.

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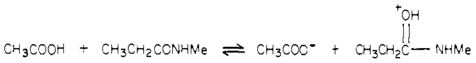
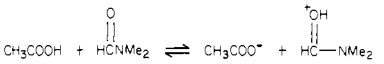
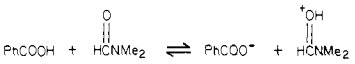
Table IV. Comparisons of Literature Values for $\Delta C_p°$ Reported in Several Solvents for Ionization of Neutral Acids

solvent	reaction	$\Delta C_p°$(25 °C)[a]	ref
water	$2H_2O \rightleftharpoons H_3O^+ + OH^-$	-51	b
MeOH	$2MeOH \rightleftharpoons Me\overset{+}{O}H_2 + MeO^-$	-56	c
$HOCH_2CH_2OH$	$2HO(CH_2)_2OH \rightleftharpoons HO(CH_2)_2\overset{+}{O}H_2 + HO(CH_2)_2O^-$	-29	d
$HO(CH_2)_3OH$	$2HO(CH_2)_3OH \rightleftharpoons HO(CH_2)_3\overset{+}{O}H_2 + HO(CH_2)_3O^-$	-30	d
water	$CH_3COOH + H_2O \rightleftharpoons CH_3COO^- + H_3O^+$	-35	c
$CH_3CH_2CONHMe$	 $CH_3COOH + CH_3CH_2CONHMe \rightleftharpoons CH_3COO^- + CH_3CH_2\overset{\overset{+}{O}H}{\overset{\Vert}{C}}—NHMe$	-24	e
DMF	 $CH_3COOH + H\overset{O}{\overset{\Vert}{C}}NMe_2 \rightleftharpoons CH_3COO^- + H\overset{\overset{+}{O}H}{\overset{\Vert}{C}}—NMe_2$	4500	f
MeOH	$CH_3COOH + MeOH \rightleftharpoons CH_3COO^- + Me\overset{+}{O}H_2$	0	g
water	$PhCOOH + H_2O \rightleftharpoons PhCOO^- + H_3O^+$	-36	c
MeOH	$PhCOOH + MeOH \rightleftharpoons PhCOO^- + MeOH_2$	-39	c
DMF	 $PhCOOH + H\overset{O}{\overset{\Vert}{C}}NMe_2 \rightleftharpoons PhCOO^- + H\overset{\overset{+}{O}H}{\overset{\Vert}{C}}NMe_2$	58	f
water	$PhOH + H_2O \rightleftharpoons PhO^- + H_3O^+$	$+19$	h
water	$PhOH + H_2O \rightleftharpoons PhO^- + H_3O^+$	-32	j
water	$PhOH + H_2O \rightleftharpoons PhO^- + H_3O^+$	-53	i
MeOH	$PhOH + MeOH \rightleftharpoons PhO^- + Me\overset{+}{O}H_2$	-70	g

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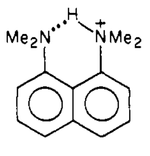
$\Delta G°$ vs. $\Delta H°$ Correlations. Figure 1 shows a plot of the heats of protonation of nitrogen bases with $MeSO_3H$ in sulfolane at 30 °C vs. the aqueous pK_a's of their conjugate acids. A reasonably straight line can be drawn through the six pyridines, with a slope of 1.33, $r = 0.984$. Straight lines of this type have been observed before for heats of protonation in FSO_3H and H_2SO_4.[40] In FSO_3H, bases of several types (anilines, pyridines, aliphatic amines, oxygen bases) plot on only one line. In sulfolane, however, nitrogen bases not of the pyridine family fall off the plot. This is due either to differences in entropies of protonation for pyridines compared to other bases in sulfolane or to a poor correlation between pK$_a$'s in sulfolane and those in water. Both reasons probably contribute to the scatter in the plot since pronounced differences in solvation effects for the hydrogen-bonding solvent water compared to the non-hydrogen-bonding solvent sulfolane will cause differences in $\Delta G_i°$ and $\Delta S_i°$ depending on the nature of the base and its conjugate acid. That such a good correlation exists between $\Delta H_i°$ in FSO_3H and $\Delta G_i°$ in water is probably due to the fact that both are good hydrogen-bonding solvents and thus solvate the base and its conjugate acid similarly.

1,8-Bis(dimethylamino)naphthalene ("Proton Sponge") falls 5 kcal/mol below the pyridine line. This suggests that the high basicity of this compound in water[41] is due in part to a less negative entropy of protonation than for other bases, caused by the relief in strain upon protonation and considerable shielding of the transferred proton from solvation through hydrogen bonding.

Heat Capacities of Protonation. Heats of protonation of nitrogen bases with $MeSO_3H$ and H_2SO_4 in sulfolane vary only slightly with temperature (Tables I and II), resulting in only small partial molar heat capacities of ionization $(\Delta C_p°)_i = [\partial(\Delta H)/\partial T]_p)_i$. This is brought out in Figure 2, which shows a plot of $\Delta H_i°$ at 150 °C vs. $\Delta H_i°$ at 30 °C. The slope of the line is 1.07, $r = 0.987$, which means that, in general, the heats of reaction are scarcely more exothermic at 150 °C than at 30 °C. This linear plot also shows that nitrogen bases of different type all behave similarly, having only small heat capacities of reaction. For quinolines and pyridines, the positive charge that is formed upon protonation can be distributed throughout the molecule. For 1,8-bis(dimethylamino)naphthalene and triethanolamine, the positive charge cannot be delocalized, but internal hydrogen bonding can occur (**1** and **2**). However, interactions of these solutes with sulfolane are apparently nonspecific, such that they cause no major structural changes in solvents that are sensitive to temperature variation.



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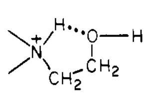

2

Discussion

Heat Capacities of Protonation in Sulfolane. Comparisons with Other Solvents. An examination of Tables I and II shows that heat capacities of protonation of nitrogen bases with CH_3SO_3H and H_2SO_4 in sulfolane from 30 to 150 or 200 °C are small. These results contrast with the heat capacities of dissociation of neutral acids measured in water,[2-11] where the $\Delta C_p°$'s for ionization are generally large and negative and become increasingly negative at higher temperatures. The results in sulfolane are also in contrast to the few heat capacities measured in other solvents, primarily alcohols. Comparisons of heat capacities of ionization of a few acids that have been measured in several solvents are shown in Table IV. Several of these heat capacities were determined by taking the second derivative of the pK_a with respect to temperature, and thus may be less accurate than those from the first derivative of the heat of ionization. Also, the heat capacities are listed at 25 °C in the table, but are known to vary considerably with temperature. Keeping this in mind, a few conclusions can be drawn. The heat capacities of dissociation in the alcohol solvents are negative and are of nearly the same magnitude as in water. Also, the $\Delta C_p°{}_i$ of -24 cal mol^{-1} K^{-1} for the ionization of acetic acid in $CH_3CH_2CONHCH_3$ solvent is of the same magnitude as in water.[42] Only one set of measurements that we know of has

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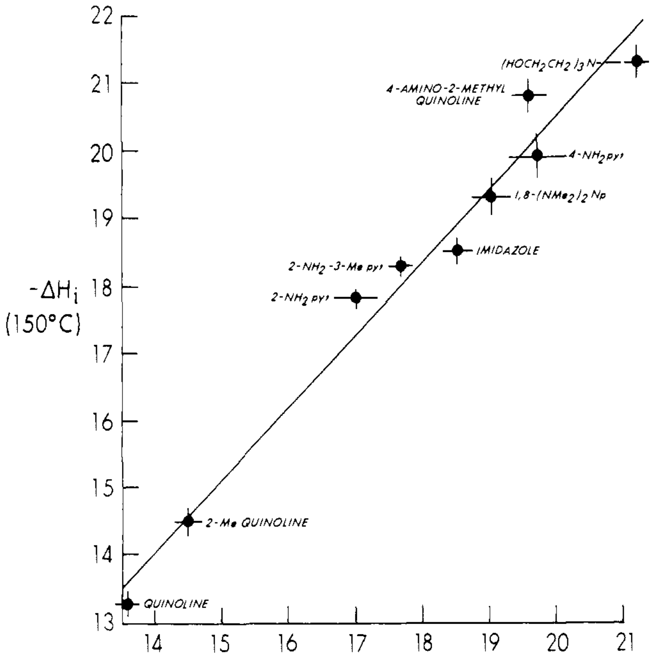

Figure 2. Correlation of heats of protonation at 30 and 150 °C for nitrogen bases in sulfolane.

been reported for the temperature dependence of pK_a in a polar nonacidic solvent, *N,N*-dimethylformamide (DMF),[43] and the heat capacities derived from these values are so large (4500!) as to arouse skepticism. Complications such as ion pairing and homoconjugate hydrogen bonding (known to affect pK_a values in solvents such as Me_2SO, DMF, and CH_3CN)[44] may have caused errors in these measurements, resulting in spurious heat capacities. If so, the results compiled in Table IV and our results in sulfolane solution suggest that large heat capacities of ionization may be restricted to solvents that are structured significantly by hydrogen bonding. This structure can be altered by the addition of solutes, by changing the temperature, or both. In a non-hydrogen-bonded, less structured solvent such as sulfolane, the solvent structure is less sensitive to the addition of solutes or to temperature change. The following analysis of the partial molar heat capacities of the reactants and products of a proton-transfer reaction sheds more light on this matter.

Heat Capacities of Reaction Calculated from Initial and Final States. The molar heat capacity change ($\Delta C_p°$) for any reaction in solution can be calculated from the individual partial molar heat capacities of each product and reactant ($\bar{C}_{p_2}$) by subtracting the sum of the heat capacities of the reactants from the sum of the heat capacities of products (eq 3). For the proton-transfer

$$\Delta C_p°(\text{rxn}) = \sum \bar{C}_{p_2}(\text{products}) - \sum \bar{C}_{p_2}(\text{reactants}) \qquad (3)$$

reaction shown in eq 4, the heat capacity of protonation can be calculated from the individual heat capacities, as shown in eq 5.

$$\text{B} + \text{AH} \rightleftharpoons \text{BH}^+ + \text{A}^- \qquad (4)$$

$$\Delta C_p° = \bar{C}_{p_2}(\text{BH}^+\text{A}^-) - \bar{C}_{p_2}(\text{B}) - \bar{C}_{p_2}(\text{AH}) \qquad (5)$$

In the case of neutral reactants forming ionic products, as in eq 4, heat capacities of proton transfer in water[2-11] and the alcohols[45-47] are generally large and negative. This is to be expected on the basis of 5, because electrolytes generally have negative (or slightly positive) heat capacities in water[48] and the alcohols,[49] while nonelectrolytes have positive heat capacities.[50] Consequently, $\sum \bar{C}_{p_2}$(products) is negative (or slightly positive) and $\sum \bar{C}_{p_2}$(reactants) is positive, so the difference between them (eq 3) gives a large, negative value.

Suspecting that heat capacities of protonation in other solvents would also be largest when charges were either formed or destroyed in the reaction, we began our work on $\Delta C_p°$ in sulfolane solution with neutral nitrogen bases reacting with the neutral acids CH_3SO_3H and H_2SO_4 to form ionic products. The results in Tables I and II show that, even for this type of ionic reaction, the heat capacities of ionization in sulfolane are small. This means that the separate terms in eq 5 must nearly cancel each other, in contrast to the results in CH_3OH and water.

Partial molar heat capacities ($\bar{C}_{p_2}$) of solutes in various solvents provide insight on this question. For nonelectrolytes, a few $\bar{C}_{p_2}°$ values have been reported in solvents other than water, but they can be calculated from the reported heat capacities of solution ($\Delta C_{p_s}°$) and from the heat capacities of the pure solutes (C_p), from eq 6.[51] Heat capacities of solution of nonelectrolytes in dipolar

$$\bar{C}_{p_2} = \Delta C_{p_s}° + C_p \qquad (6)$$

aprotic and alcohol solvents are small: heat capacities of solution of methanol, 1-butanol, and 1-pentanol in Me_2SO, DMF, *N*-methylformamide, and ethylene glycol range from 0 to −9 cal mol^{-1} K^{-1};[32] methanol, ethanol, 1-propanol, and 1-butanol in ethylene glycol from 0 to 2 cal mol^{-1} K^{-1};[52] He, N_2, Ar, and ethane in $CH_3CONHMe$ from 0 to −5 cal mol^{-1} K^{-1}.[53] *N*-Butylacetamide was negligible in MeOH and −1 cal mol^{-1} K^{-1} in EtOH.[54] From eq 6, when the heat capacity of solution ($\Delta C_p°$) is small, the $\bar{C}_{p_2}°$ values will be nearly identical with the heat capacity of the pure compound (C_p). Since heat capacities for all compounds are positive (defined as the amount of heat needed to raise 1 mole of the compound 1K, it follows that $\bar{C}_{p_2}$ values for nonelectrolytes will be positive and nearly equal (for a particular nonelectrolyte) in both alcoholic and dipolar aprotic solvents. The $\bar{C}_{p_2}$ values in water for nonelectrolytes are also positive, but generally larger than in other solvents since the heat capacities for solution of nonelectrolytes in water are positive.

On the other hand, Criss and co-workers[49b,55] have found that partial molar heat capacities ($\bar{C}_{p_2}$) of electrolytes in dimethylformamide are *positive*, in contrast to the negative values for the same electrolytes measured in MeOH[49b] and water.[48] This, then, appears to be the main reason for the small heat capacities of protonation in sulfolane (assuming $\bar{C}_{p_2}$ in sulfolane are positive as they are in DMF) as compared to the negative values in MeOH or water. In sulfolane, the $\bar{C}_{p_2}$ values of both electrolytes and nonelectrolytes are positive, so $\sum \bar{C}_{p_2}$(products) and $\sum \bar{C}_{p_2}$(reactants) will always be positive and the difference between the two ($\Delta C_p°$) is likely to be small. Thus, most reactions (not just proton transfer) are likely to have small heat capacities in dipolar aprotic solvents, regardless of whether ions are formed or destroyed.

Heat Capacities of Protonation at High Temperature. The above discussion has been based on literature values of heat ca-

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pacities mostly measured near room temperature over a fairly small temperature range. It is well known that heat capacities of protonation vary with temperature in both MeOH[45] and water,[3,6] becoming increasingly negative at elevated temperatures. This makes the absence of appreciable heat capacities for proton transfer in sulfolane even more surprising, considering the fairly wide temperture range (from 30 to 150 or 200 °C) of our study.

The primary reason for increasingly negative heat capacities for acid dissociations in water appears to be due to the decrease in dielectric constant of water as the temperature increases.[6,56] In line with this, Wood and Smith-Magowan[57] have shown that partial molar heat capacities of electrolytes in water become enormously negative as the temperature is raised above 150 °C, with $\bar{C}_{p_2}$ for NaCl in water as it approaches the critical point decreasing from -30 cal mol^{-1} K^{-1} at 152 °C to -750 cal mol^{-1} K^{-1} at 327 °C. Again, this was attributed to the large decrease in dielectric constant in this medium from 43.9 to 15.5 between 150 and 330 °C.[57]

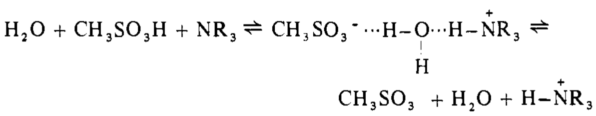
The dielectric constant of sulfolane decreases from 43 to 30 over the temperature range of 30 to 150 °C.[17] This modest decrease probably accounts for the small, negative heat capacities of protonation that were measured over this range (Table I and II). Even at 200 °C, there is no significant difference in $\Delta H°$ of reaction from that at 30 °C. Apparently, much higher temperatures are required for the decrease in dielectric constant to strongly affect the heat capacity of proton transfer in this solvent.

Heat Capacities and Reaction Intermediates. Finally, we would like to comment on a recent proposal that negative heat capacities for ionizations in water are due to proton-transfer reactions occurring by multistage processes through hydrogen-bonded intermediates.[58] The analysis is based on the assumption that, because of these intermediates, precise equilibrium constants in water measured by conductivity or emf measurements do not give a true equilibrium constant between reactants and ionic products, but only the ratio of dissociated to undissociated species. Assuming that proton transfer occurs by two or three-step processes, each of which have constant heats of reaction, the proponents of this view could reproduce the observed negative heat capacities of ionization for several proton-transfer reactions by the judicious choice of parameters for fitting the curves.[58]

Depending on how one views the intermediate in the proton-transfer reaction, our heat capacity measurements in sulfolane can be made either to fit or not fit with this hypothesis. If one assumes that the intermediate encounter complex does not involve the solvent,[58b] (eq 7), then behavior similar to that in water might

$$CH_3SO_3H + NR_3 \rightleftharpoons CH_3SO_3^- \cdots H{-}^+NR_3 \rightleftharpoons CH_3SO_3^- + H{-}^+NR_3 \quad (7)$$

be expected in any dissociating solvent. The negligible heat capacities which we observe in sulfolane, in contrast to those in water[2-11] or MeOH,[45,47] argue against this reasoning. If one assumes that hydrogen bonding by the solvent to the intermediates plays a key role[58c] (eq 8), then we would expect different behavior



$$H_2O + CH_3SO_3H + NR_3 \rightleftharpoons CH_3SO_3^- \cdots H{-}\underset{\substack{|\\H}}{O}\cdots H{-}\overset{+}{N}R_3 \rightleftharpoons CH_3SO_3 + H_2O + H{-}\overset{+}{N}R_3 \quad (8)$$

between reactions in hydroxylic solvents and nonhydroxylic solvents. That we see negligible heat capacities for protonation in sulfolane seems to support this second proposal.

However, from the discussions in previous sections, we have seen that heat capacities of ionization can be determined purely by the individual $\bar{C}_{p_2}$'s of the products and reactants. Since the heat capacity of ionization is a state function (as indeed are $\Delta G_i°$, $\Delta H_i°$, and $\Delta S_i°$) and is not dependent on the mechanistic pathway of the ionization reaction, it should be as readily calculated by adding individual $\bar{C}_{p_2}$'s as through temperature coefficients of pK_a's or of ΔH_i's.

Three groups have actually calculated heat capacities of ionization from the heat capacities of initial and final states,[2,59,60] and the results agree fairly well with values obtained from the second derivative of pK_a with respect to temperature, or from the first derivative of the heat of reaction with respect to temperature, where comparisons can be made. For example, the heat capacity for the ionization of water was measured from initial and final states by Hepler and his students,[2] who obtained a value of -51.39 cal mol^{-1} K^{-1} at 25 °C. From the dependence on temperature of the heat of reaction of HCl with NaOH, Olofsson and Olofsson measured a heat capacity of ionization of water of -51.15 cal mol^{-1} K^{-1} at 25 °C.[61] Finally, from the second derivative of the pK_a with respect to temperature, Sweeton, Mesmer, and Baes[5] determined a $\Delta C_p°$ of -55.21 cal mol^{-1} K^{-1} at 25 °C for the ionization of water. That similar heat capacities can be calculated from measurements on the actual reaction or from measurements only on initial and final states is a simple consequence of the "first law" and implies that the pK_a's from conductance or emf measurements, and the heats of reaction measured calorimetrically, are in fact "true" equilibrium constants and heats of reaction.

No doubt, the individual heat capacities measured for each reactant and product are influenced by the occurrence of hydrogen-bonded equilibria (eq 9). There is little doubt that

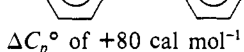
$$Na^+ + OH^- + n(H_2O) \rightleftharpoons Na^+ + HO^- \cdots n(H_2O) \quad (9)$$

equlibria such as (9), which cause the restructuring of water, are responsible for large heat capacity terms for solution in that solvent. However, solvation of ground-state reactants and products can provide no definitive information about intermediates along a reaction path.

We also point out that large heat capacities of reaction in water are not limitied to proton transfers, but can be calculated for numerous other reactions. For example, $\Delta C_p°$ for the methyl transfer reaction, a close analogy to proton transfer but without hydrogen bonding, can be calculated. From the $\bar{C}_{p_2}$ values for $Me_4N^+Br^-$,[62] Me_3N,[63] and MeBr[64] in water, a heat capacity for reaction 10 of -126 cal mol^{-1} K^{-1} is found.

$$Me_3N + MeBr \rightarrow Me_4{}^+NBr^- \quad (10)$$

Large heat capacities of reaction in water can be calculated for other hypothetical reactions where hydrogen-bonding factors, such as those involved in proton transfer, are negligible. For example, from the $\bar{C}_{p_2}$ of reactants and products,[63,64] a $\Delta C_p°$ of -67 cal mol^{-1} K^{-1} may be calculated for reaction 11, while reaction



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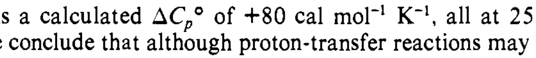

(12)

12 has a calculated $\Delta C_p°$ of +80 cal mol^{-1} K^{-1}, all at 25 °C.

We conclude that although proton-transfer reactions may very well proceed through multistep processes, kinetic analysis of heat capacities of ionization can provide little unequivocal information

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J. Am. Chem. Soc. 1983, 105, 4163-4168

regarding postulated intermediates along the reaction coordinate for proton transfer.

Conclusion

Heat capacities of protonation in sulfolane are negligible over a wide temperature range, 30 to 150 or 200 °C. If this result is general for other nonhydroxylic solvents, it implies that extrapolation of data for acid–base reactions near room temperature to elevated temperatures will be straightforward since large and variable heat capacities will not have to be contended with. Although limited by the present equipment and the stability of sulfolane to temperatures less than 200 °C, we suspect that heat capacities at much higher temperatures would become increasingly negative as the dielectric constant of the solvent decreases. Analysis of partial molar heat capacities of both electrolytes and nonelectrolytes in dipolar nonhydroxylic solvents suggests that most reactions in these media will have small heat capacity changes over wide temperature ranges. Since many types of catalytic processes involve proton transfer at elevated temperatures, it is important to test the generality of this simplifying conclusion.

Acknowledgment. We are pleased to acknowledge the support of this work by the Exxon Educational Foundation and by the U.S. Department of Energy under Grant No. DE-FG22-82PC50807. Professors Robert Wood and Cecil Criss provided helpful advice on the problems of high-temperature calorimetry.

Registry No. Quinoline, 91-22-5; 2-methylquinoline, 91-63-4; 4-amino-2-methylquinoline, 6628-04-2; 2-aminopyridine, 504-29-0; 2-amino-3-methylpyridine, 1603-40-3; 4-aminopyridine, 504-24-5; 1,8-bis(dimethylamino)naphthalene, 20734-58-1; imidazole, 288-32-4; triethanolamine, 102-71-6; methanesulfonic acid, 75-75-2; sulfuric acid, 7664-93-9; sulfolane, 126-33-0.

Cadmium-113 Shielding Tensors of Cadmium–Oxo Compounds. 1. Single-Crystal Studies on $Cd(NO_3)_2 \cdot 4H_2O$ and $3CdSO_4 \cdot 8H_2O$

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Abstract: Diffraction-quality single crystals of $Cd(NO_3)_2 \cdot 4H_2O$ and $3CdSO_4 \cdot 8H_2O$ have been investigated by ^{113}Cd Fourier transform NMR methods in a home-built single-crystal probe. As expected from point group symmetry arguments, the shielding tensors do not exhibit axial symmetry. The ^{113}Cd NMR of $Cd(NO_3)_2 \cdot 4H_2O$ gave rise to two cadmium resonances for the magnetically nonequivalent (but crystallographically equivalent) positions in the unit cell. The principal elements of the symmetry related tensors for $Cd(NO_3)_2 \cdot 4H_2O$ are −174.4, −154.3, and 22.2 ppm for σ_{11}, σ_{22}, and σ_{33}, respectively (the chemical shifts are reported with respect to solid $Cd(ClO_4)_2$). The ^{113}Cd NMR of $3CdSO_4 \cdot 8H_2O$ afforded three resonances as expected from the crystal symmetry. Two of the resonances are assigned to general positions within the lattice. These positions gave rise to symmetry-related tensors, which have principal elements −93.1, −76.7, and 25.5 ppm. The remaining resonance is assigned to cadmium in special position; the corresponding shielding tensor has principal elements −95.6, −85.3, and −3.4 ppm. These data are discussed in terms of the structure of the cadmium salts.

Introduction

Because of our interest in utilizing ^{113}Cd NMR spectroscopy[1] as a probe for calcium sites in biological systems,[2] we have been interested in obtaining a detailed understanding of the structural factors responsible for the isotropic ^{113}Cd chemical shifts in these molecules. In the systems studied (concanavalin A,[3] parvalbumin,[4] troponin C,[5] calmodulin,[6] and insulin[7]), the substitution of cadmium for calcium places cadmium in an environment in which the atoms in the primary coordination sphere are exclusively oxygens. Cadmium has been assumed to be six-coordinate. The isotropic chemical shifts for these compounds[8] fall in a characteristic range from −85 to −130 ppm with respect to 0.1 M $Cd(ClO_4)_2$. To date, there are no model compounds that can be studied in aqueous solution which have isotropic shifts within this range.[9]

If, however, one performs the ^{113}Cd NMR experiments in the solid state,[11] one finds a bewildering array of cadmium–oxo compounds that can be employed to model these biological systems. The coordination number for cadmium in these compounds is

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[1] (a) Maciel, G. E.; Borzo, M. *J. Chem. Soc. Chem. Commun.* **1973**, 394. (b) Peters, C. S.; Codrington, R.; Walsh, H. C.; Ellis, P. D. *J. Magn. Reson.* **1973**, *11*, 431. (c) Kostlenik, R. J.; Bothner-by, A. A. *Ibid.* **1974**, *14*, 141. (d) Cardin, A. C.; Ellis, P. D.; Odom, J. D.; Howard, J. W., Jr. *J. Am. Chem. Soc.* **1975**, *97*, 1672.

[2] A. A. Bothner-By actually proposed performing these experiments on Troponin C and Calmodulin more than 10 years ago. The basic approach is outlined in the Ph.D. thesis of R. J. Kostelnik, 1971, University Microfilms 72-21, 599.

[3] Palmer, A. R.; Bailey, D. B.; Cardin, A. D.; Yang, P. P.; Behnke, W. D.; Ellis, P. D. *Biochemistry* **1980**, *19*, 5063. Bailey, D. B.; Ellis, P. D.; Cardin, A. C.; Behnke, W. D. *J. Am. Chem. Soc.* **1978**, *100*, 5236.

[4] Darkenberg, T.; Lindman, B.; Cavé, A.; Parello, J. *FEBS Lett.* **1978**, *92*, 346. Cavé, A.; Parello, J.; Drakenberg, T.; Thulin, E.; Lindman, B. *Ibid.* **1979**, *100*, 148.

[5] Forsēn, S.; Thulin, E.; Lilja, H. *FEBS Lett.* **1979**, *104*, 123.

[6] Forsēn, S.; Thulin, E.; Drakenberg, T.; Krebs, J.; Seamon, K. *FEBS Lett.* **1980**, *117*, 189.

[7] Sudmeier, J. L.; Bell, S. J.; Strom, M. C.; Dunn, M. F. *Science* **1981**, *212*, 560.

[8] The single exception of this chemical shift range is the shift observed for the calcium site in bovine insulin;[7] its chemical shift is −36 ppm. The X-ray data are definitive in this case for the Ca^{2+} to be six-coordinate: Blundell, T.; Dodson, G.; Hodgkin, D.; Mercola, D. *Adv. Protein Chem.* **1972**, *26*, 279.

[9] The problem arises because of the kinetic lability of the oxo ligands in aqueous solutions. The kinetic lability may be circumvented by employing supercooled aqueous solutions.[10] However, one still has the problem of how to relate those isotropic chemical shifts to structure!

[10] Ackerman, M. J. B.; Ackerman, J. J. H. *J. Phys. Chem.* **1980**, *84*, 3151. Jakobsen, H. J.; Ellis, P. D. *Ibid.* **1981**, *85*, 3367.

[11] (a) Nolle, A. *Z. Naturforsch. A* **1978**, *33*, 666. (b) Ackerman, J. J.; Orr, T. V.; Bartuska, V. J.; Maceil, G. E. *J. Am. Chem. Soc.* **1979**, *101*, 341. (c) Cheung, T. T. P.; Worthington, L. E.; Murphy, L. D.; Murphy, P. D. Gerstein, B. C. *J. Magn. Reson.* **1980**, *41*, 158. (d) Murphy, P. D.; Gerstein, B. C. *J. Am. Chem. Soc.* **1981**, *103*, 3282. (e) Murphy, P. D.; Stevens, W. C.; Cheung, T. T. P.; Lacelle, S.; Gerstein, B. C.; Kurtz, D. M., Jr. *Ibid.* **1981**, *103*, 4400. (f) Mennit, P. G.; Shatlock, M. P.; Bartuska, V. J.; Maciel, G. E. *J. Phys. Chem.* **1981**, *85*, 2087. (g) Inners, R. R.; Doty, F. D.; Garber, A. R.; Ellis, P.D. *J. Magn. Reson.* **1981**, *45*, 503. (h) Ellis, P. D.; Inners, R. R.; Jakobsen, H. J. *J. Phys. Chem.* **1982**, *86*, 1506. (i) Jakobsen, H. J.; Ellis, P. D.; Inners, R. R.; Jensen, C. F. *J. Am. Chem. Soc.* **1981**, *104*, 7442.