53. Preferential Solvation of the Sodium Cation in Binary Mixtures of Tetrahydrofuran with Unidentate Nitrogen Ligands

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Summary

^{23}Na-chemical shifts for the $NaClO_4$ solute depend markedly upon the composition of binary solvent mixtures of THF with amines (pyridine, piperidine, pyrrolidine, aniline, propylamine, and isopropylamine). These changes, analyzed in a novel application of the *Hill* formalism, show equality of the intrinsic equilibrium constant K for the successive steps, upon displacement of THF from sodium coordination by one of these amines. The results, which are entirely consistent with tetracoordination of the sodium cation by these solvents, also indicate proportionality of the K values to the amine chemical shifts.

Introduction. - Important technological processes such as electrolysis, and liquid-liquid extraction, depend critically upon the influence of dissolved salts on phase equilibria [1-3]. Indeed, much effort is applied to obtain a better understanding of the preferential solvation of ions in solvent mixtures [4-8]. NMR. methods appear especially well-suited for such investigations [6-17]. Chemical shifts and relaxation rates, of the solvent molecules, and also of quadrupolar ions themselves, are function of solvent composition.

Interpretation of the quadrupolar ion relaxation rates is model-dependent. For example, does NMR. relaxation occur in a well-defined and persistent chemical complex [15-17], or does it arise from fluctuations of solvent dipoles in the vicinity of the ion [18-24]? We earlier [15-17] accounted successfully for the observed changes in *both* the ^{23}Na-chemical shifts and linewidths arising from competition for tetracoordination of the sodium cation by organic solvents such as tetrahydrofuran (THF), glymes, and pyridine [25][26]. Pyridine shows interesting anomalies: in a number of cases [27-29], its effective donor ability is markedly inferior to that predicted on the basis of its *Gutmann* donor number [30]. More generally, what is the relation between the *Gutmann* donicity of a solvent molecule A, and its performance when in competition with another solvent molecule B?

Our approach to this question, and to that of the relaxation mechanism, is to consider *jointly* the chemical shift and the relaxation rate, which are the two

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observable parameters [15-17] [31] [32]. The approach is further characterized, in this and in the accompanying article [33], by what we believe to be an original application of the *Hill* formalism [34] to the problem of preferential solvation. *Hill* plots enjoy widespread use in biochemical studies of phenomena such as cooperative oxygen binding to hemoglobin [35]. Mathematically, preferential solvation of a tetracoordinated ion, and binding of a ligand to one of four sites in a biomolecule, constitute one and the same problem. The *Hill* formalism, hitherto neglected in studies of preferential solvation, provides a better understanding of the phenomenon than the existing and sometimes less powerful formalisms [6] [36]. We study here unidentate ligands, which will serve as references for determining the magnitude of the chelate effects present with bidentate and polydentate ligands [33].

Experimental Part

All the solvents used were the best commercial grades *(Aldrich, Baker)* available. THF was redistilled from $LiAlH_4$ or CaH_2 under dry argon prior to use. Pyridine was dried over KOH for 12 h, distilled, and transferred under Ar. The amines were refluxed 4 h over NaOH pellets (10% *W/W*), then transferred and refluxed 3 h over Na (2% *W/W*) distilled and transferred under Ar. $NaClO_4$ (*Merck* and *UCB*, for analysis) was dried under vacuum at 120° for 24 h. All the solutions were made by weighing stock solutions of 10^{-2}M $NaClO_4$. NMR. spectra were obtained on a *Bruker* WP-80 instrument in the FT mode, with an external benzene d_6-lock. Sample temperatures were maintained at 303 ± 1 K. The ^{23}Na-spectra were obtained at 21.16 MHz, using a spectral window of 6024 Hz, 8 K data points, and an 8.5 µs pulse length. The chemical shifts are measured to ± 0.15 ppm and uncorrected for the negligible differences in magnetic susceptibility with the reference [15-17]. Accumulation was continued until the signal-to-noise was better than 60:1, in the THF-rich solutions, and better than 20:1, in amine-rich solutions. Chemical shifts were measured with respect to a 3M aqueous NaCl-solution reference with an external benzene-d_6 lock, and are reported with respect to aqueous NaCl-solution extrapolated to infinite dilution.

Results and Analysis. - The two components of the binary solvent mixture compete for solvation of the Na^+-cation. If they share the same solvation number *n* towards Na^+, (n + 1) complexes can be formed in succession. The relative amounts of these solvates will obviously depend upon the composition of the binary mixture. In order to provide a complete description of the system, one has to study therefore the following series of successive equilibria:

$$\begin{tikzcd}
nL_A+Na^+(L_B)_n \arrow[r, shift left, "K_1"] & (n-1)L_A+L_B+Na^+(L_B)_{n-1}(L_A) \arrow[l, shift left] \arrow[d, shift right, "K_2"'] \\
 & \cdots\cdots \arrow[u, shift right] \arrow[d, shift right, "K_{n-1}"'] \\
nL_B+Na^+(L_A)_n \arrow[r, shift left, "K_n"] & L_A+(n-1)L_B+Na^+(L_B)(L_A)_{n-1}. \arrow[l, shift left] \arrow[u, shift right]
\end{tikzcd} \tag{1}$$

Inserting the relevant statistical factors leads to the *intrinsic* equilibrium constants K_i, defined from the relation:

$$\text{apparent } K_i = \frac{n-i+1}{i} \cdot \mathrm{K}_i . \tag{2}$$

These intrinsic equilibrium constants K_i measure the ease of displacement of the solvent L_B by the solvent L_A, for each step in the process that is being studied.

We shall limit our analysis to tetracoordination ($n=4$), a reasonable assumption for the cases studied here (see also the Discussion).

Hence, the question addressed is best rephrased as how to determine the intrinsic constants K_1, K_2, K_3, K_4 from the study of the variation of the sodium chemical shift with composition of the binary solvent mixture. For this purpose, we use the *Hill* formalism [34] [35], Y being the fraction of sites on the Na^+-cation occupied by an amine ligand L_A.

Defining $X=[L_A]/[L_B]$; $\beta_0=1$; $\beta_i=K_1 \cdot K_2 \ldots K_i$ and with

$$D=\sum_{i=0}^{4} \beta_i X^i \tag{3}$$

the mole fraction a_i of the $Na^+(L_B)_{4-i}(L_A)_i$ species is given by:

$$a_i=\beta_i \frac{X^i}{D} \tag{4}$$

The definition of Y is such that:

$$Y=\sum_{i=1}^{4} \frac{i a_i}{4}=\sum_{i=1}^{4} \frac{i \beta_i X^i}{4D} \tag{5}$$

And a *Hill* plot is a representation of $\ln(Y/1-Y)$ as a function of $\ln X$. It allows one to determine quickly and accurately the values of the K_1, K_2, K_3, K_4 constants [35]. In the case of equality of all these intrinsic constants, *i.e.* under the absence of cooperativity, the *Hill* plot becomes linear; indeed, setting

$$K_i=K \quad \text{for each i value} \tag{6}$$

equations 2, 3 and 5 lead to:

$$Y=\frac{KX}{1+KX} \tag{7}$$

so that

$$\ln\left(\frac{Y}{1-Y}\right)=\ln K+\ln X \tag{8}$$

Thus, in the case of equality of the k_i's, the *Hill* plot is indeed a straight line of unit slope, whose intersection with the horizontal axis yields directly the value of the intrinsic constant K caracteristic of each and every step in the successive equilibria of equation 1. Hence, the mere appearance of the *Hill* plot (linear with unit slope or not) is sufficient for stating the (absence or presence of) cooperativity in the successive steps of displacement by L_B of L_A (equ. 1). Whenever the process is devoid of cooperativity and the *Hill* plot is linear, it will also yield the value of the intrinsic constant K describing the L_A *vs.* L_B competition.

In order to produce a *Hill* plot, we have to know, on one hand, the saturation fraction Y, and, on the other hand, the concentration ratio of the *free* L_A and L_B ligands $X=[L_A]_f/[L_B]_f$. The chemical shift provides the former. It can be expressed as:

$$(\delta_{obs}-\delta_0)=\sum_{i=1}^{4} a_i(\delta_i-\delta_0) \tag{9}$$

where δ_i is the chemical shift of the *i*-th species, the $Na^+(L_B)_{4-i}(L_A)_i$ solvate. Introducing here the standard assumption of additive chemical shifts [6], which is successfully tested in another study [32], we find:

$$Y = (\delta_{obs} - \delta_0)/(\delta_4 - \delta_0) \tag{10}$$

since

$$\delta_i - \delta_0 = \frac{i}{4}(\delta_4 - \delta_0) \tag{11}$$

Use of a very small (10^{-2} M) Na^+-concentration ensures that:

$$X = \frac{[L_A]_f}{[L_B]_f} = \frac{[L_A]_t - 4Y[Na^+]_t}{[L_B]_t - 4(1-Y)[Na^+]_t} \simeq \frac{[L_A]_t}{[L_B]_t} \tag{12}$$

where $[L_A]_t$ and $[L_B]_t$ are the total L_A and L_B concentrations.

Therefore, the experimental curve of the ^{23}Na-chemical shift as a function of the L_A mol-fraction *(Fig. 1)* can be directly translated into a *Hill* plot *(Fig. 2)*. For all the unidentate ligands studied here, viz. aniline, pyridine, piperidine, pyrrolidine, propylamine, and isopropylamine, pitted in competition with tetrahydrofuran (THF), these *Hill* plots are linear, with unit slope, and yield directly the intrinsic solvation constants K *(Table)*. The values of K listed in *Table* are those obtained by simple inspection. They agree nicely with those resulting from a least-squares linear regression: for instance K = 4.31 ± 0.79 for propyl- and K = 2.99 ± 0.25 for *i*-propylamine.

A useful visualization of the results is obtained by plotting the a_i-values as a function of ln $[L_A]/[L_B]$, as shown for propylamine in *Figure 3*. Note that, due to the remarkable symmetry of these curves with respect to $L_B \rightleftarrows L_A$ interchange, the point

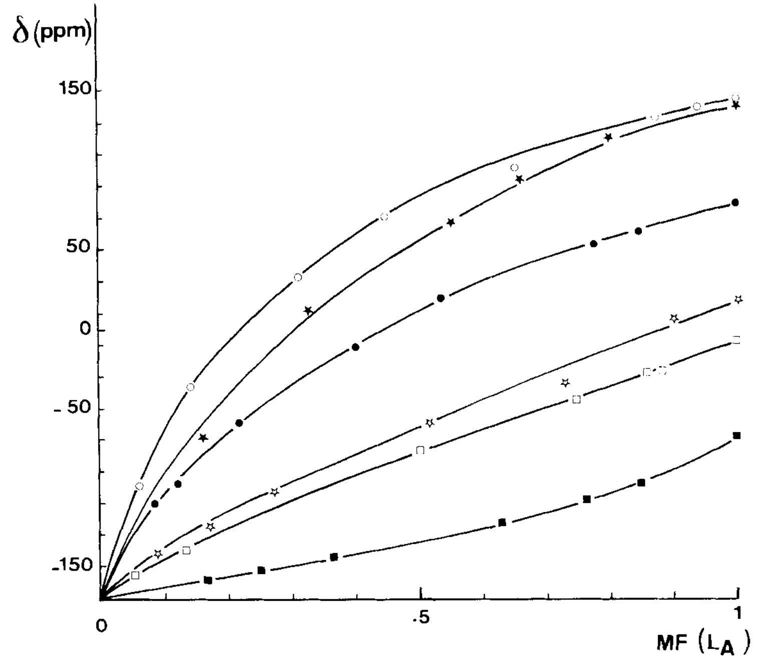

Fig. 1. *Variation of the ^{23}Na-chemical shift δ against mol-fraction of the amine, for the binary mixtures of aniline (▪), pyridine (□), piperidine (✫), pyrrolidine (•), propylamine (○), and i-propylamine (✶) with THF*

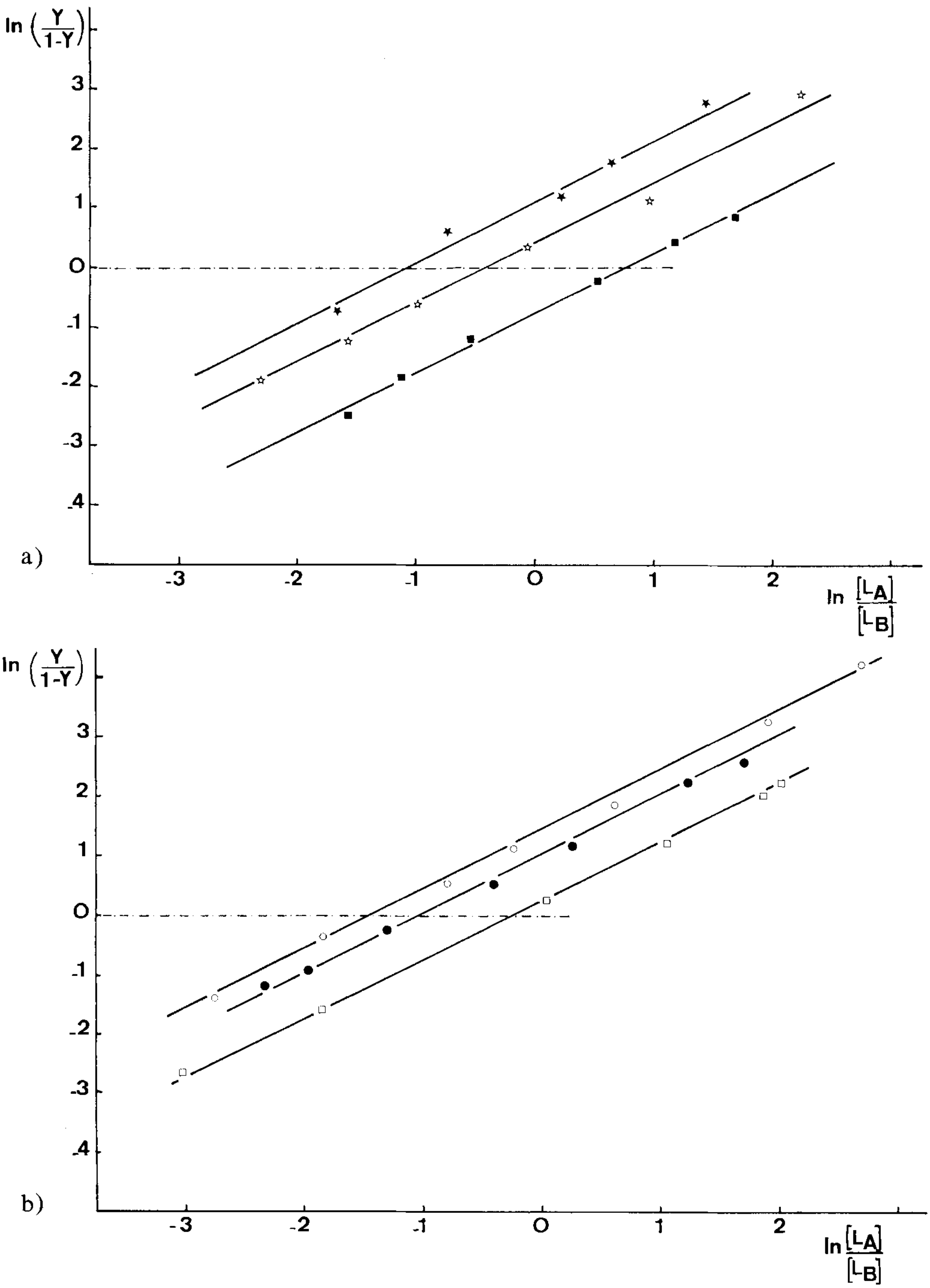

Fig. 2. Hill *plots for the binary mixtures of* a) *aniline* (■), *piperidine* (☆), i-*propylamine* (✶); b) *pyridine* (□), *pyrrolidine* (●), *propylamine* (○) *with THF*

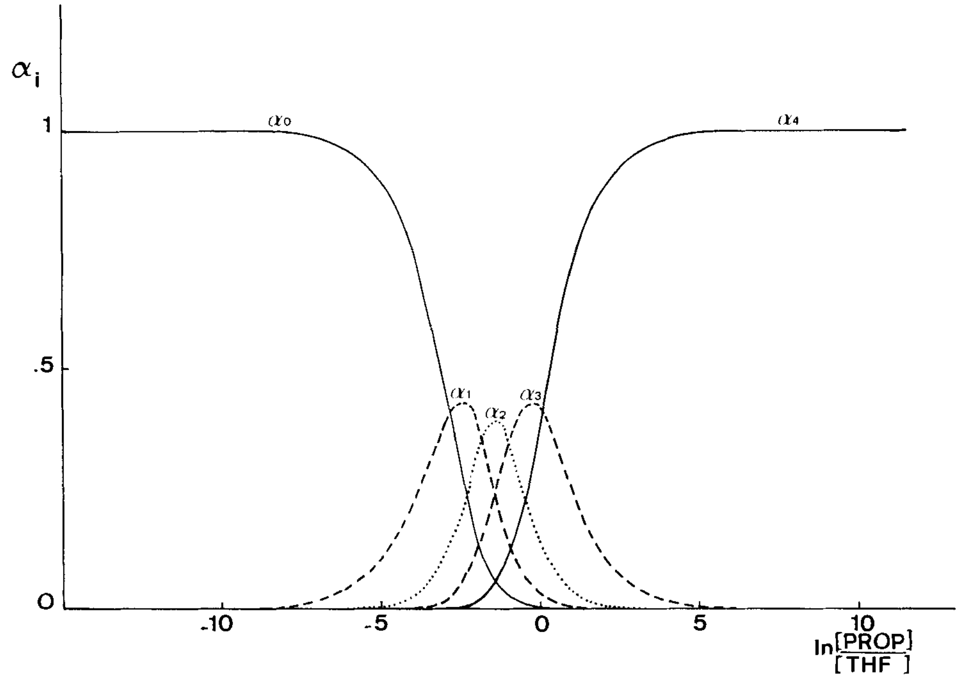

Fig. 3. *A plot of the relative fractions* α_i (i = 0-4) *for each of the intermediate solvates, in the propylamine/THF system*

Table. *Slope of the* Hill *plots* (the linear correlation coefficients are all above 0.996 for at least 6 points), *values of the intrinsic equilibrium constants; and chemical shifts for* $^{23}Na^+ClO_4^-$ (10^{-2} M) *in each solvent measured with respect to aqueous NaCl-solution extrapolated to infinite dilution*

Solvent	δ_4 (ppm)	*Slope of the* Hill *plot*	*Intrinsic constant* K
Aniline ($C_6H_5NH_2$)	− 3.39	1.00	0.46
Pyridine (C_5H_5N)	− 0.45	0.96	1.3
Piperidine ($C_5H_{10}NH$)	0.89	1.03	1.5
Pyrrolidine (C_4H_8NH)	3.67	0.96	2.8
i-Propylamine (*i*-$C_3H_7NH_2$)	6.80	1.12	3.0
Propylamine ($C_3H_7NH_2$)	6.73	0.97	4.4

for half-saturation in the *Hill* plot ($\ln(Y/1-Y)=0$) occurs at the same position ($\ln[L_A]/[L_B] = -1.5$) in the *Hill* plot as the position for the maximum of a_2 in the curves giving the distribution of the mol-fractions for the coexisting solvates (*Fig. 3*). The symmetry of the curves follows necessarily from the model used, of tetra-coordination combined with equality of the intrinsic equilibrium constants.

Discussion. - A first point concerns possible anomalies resulting from use of pyridine as one of the solvents in the binary mixtures [27-29]. We did not find any such anomalies in the present work. Perhaps the discrepancies noticed by other workers [27] [28] between the apparent donicities of pyridine as the pure solvent or as a component in a solvent mixture arise from changes in ion pair structures with solvent composition.

One has to be wary of the possibility of ^{23}Na-chemical shifts being determined in part by changes in the types of ion pairs present: the choice of the perchlorate anion, together with the low (cM) concentration of the salt, ensure that this factor is kept constant. Presumably, in the solvent mixtures studied here, only *loose* ion pairs can be present. We have indeed checked that, in propylamine solution, the ^{23}Na-chemical shift is quasi-invariant with concentration in the whole range of 5.10^{-3} M–0.5 M. With other counter ions (I^-, $B(C_6H_5)_4^-$), tight and loose ion pairs can coexist in amine solvents such as studied here [37].

A crucial assumption for applicability of the *Hill* plot formalism [34] is for THF, used as the reference solvent, and for the unidentate nitrogen ligands studied here to have the same solvation numbers towards the Na^+-cation. Nevertheless it happens to be true, as shown by the vast majority of solvation numbers that have been determined for Na^+ in a variety of organic solvents including some of those studied here. Tetracoordination has been found for THF [38–40] and pyridine, as well as for ammonia [41] in the gas phase. To quote from a study by *Davidson & Kebarle* [42] on Na^+-solvation by acetonitrile: "the large decrease of stability for the addition of the fifth molecule can be very directly observed in the (...) *van't Hoff* plots, where the very big gap between the 3,4 and 4,5 lines is very noticeable (...) the relatively large weakening of interaction with the fifth molecule is due to crowding of molecules in the first 'shell'". Thus, tetracoordination of all the unidentate nitrogen ligands studied here appears to be enforced by a combination of the dipole-dipole repulsions in the coordination sphere, and of the steric congestion preventing coordination of an additional ligand.

Observation of unit slope lines in the *Hill* representation [34] proves that replacement in the Na^+-coordination shell of THF by one of the nitrogen ligands studied here occurs with no cooperativity whatsoever: entry of the first, second, third, ... solvent molecules is equally easy. The *Hill* formalism [34] allows us to determine the intrinsic equilibrium constants K *(Table)*. It is more powerful than existing treatments. For instance, the *Covington* equations [6] are merely a particular case of the *Hill-Adair* [43] equations under the absence of any positive or negative cooperativity. In order to apply the *Covington* equations [6], one has to make restrictive assumptions about the equality of the K_i values. The merit of the *Hill* representation is to provide a clean and easy graphic access to the intrinsic equilibrium constants, while at the same time testing for the absence of cooperativity in the system.

The most important finding from our results is the correlation between the K-values *(Table)* and the chemical shifts δ_4 measured for Na^+ in the pure amine solvents. It may appear surprising that a thermodynamic quantity (the intrinsic equilibrium constant K) is related to a chemical shift, *i.e.* to an electronic distribution. However, there is precedence in such an observation: the ^{23}Na-chemical shifts are linearly correlated to another thermodynamic quantity, the *Gutmann* donicity of the solvent, when a salt such as $NaBPh_4$ is dissolved in a series of O- and N-donor solvents [44]. Furthermore, it is to be expected that the ease of introduction of a ligand in the coordination shell (as measured by K) should be related to the characteristics of the ligands as an electron-donor (as measured by δ_4). The strength of the (predominantly electrostatic) chemical bond between Na^+ and nitrogen increases with nitrogen basicity, which is measured indirectly by the δ_4 values.

The two crucial assumptions made in this study are the additivity of the chemical shifts δ_i, for which there is ample empirical support [6] [32], and tetracoordination of the sodium cation in these solutions of THF and amines: we shall examine critically the latter assumption in the next article in this series.

The *Hill* treatment, for which we suggest an original application here, has been successfully exploited in other areas, such as equilibria involving polyelectrolytes [45].

Conclusion. - In this first article, we show that *Hill* plots provide a useful representation of ^{23}Na-chemical shifts for dilute solutions of sodium salts in binary solvent mixtures of THF with unidentate amines. We find, in all six cases studied here (aniline, pyridine, piperidine, pyrrolidine, propylamine, and isopropylamine), that these amines displace THF from Na^+-coordination with a complete lack of cooperativity: each of the successive displacement steps is equally easy, as measured by the intrinsic equilibrium constants K_i. For such cases, in the absence of cooperativity, the *Hill* treatment [34] is superior to the widely-applied *Covington* treatment [6] in making no prior assumption about equality of the K_i-values: the equality of K_i-values reported here is not an assumption, but a consequence of the experimental observations. The real strength of the *Hill* treatment [34] however is in the application to complex cases in which the K_i-values differ from one another: the next paper [33] gives examples, from studies on polyamines.

Secondly, and most surprisingly, the intrinsic equilibrium constants K (corrected for the appropriate statistical factors) can be provided simply on the basis of a chemical shift measurement: the K-values are proportional to the difference in ^{23}Na-chemical shift between the amine solvent and THF. Were it to prove to be general, this finding would become of central importance to the study of preferential solvation phenomena.

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