Effect of Molecular Motion and Solvent Interactions on Nitrogen-15 Relaxation in Anilines

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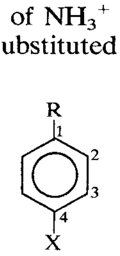
Dipolar relaxation of ^{15}N in anilines and anilinium ions is influenced by overall motion of the molecule, by rotation about the aryl—nitrogen bond, by inversion of the aniline nitrogen and by interactions of the NH_2 or NH_3^+ group with the solvent. These factors are assessed by comparison of the ^{13}C and ^{15}N dipolar relaxation times as a function of *para*-substitution on the aryl ring. In the anilines (solvent $CDCl_3$), electron withdrawal brings about faster relative motion of the amine side-chain, contrary to expectation from consideration of C–N rotation but in agreement with the effects from nitrogen inversion. The ^{15}N dipolar relaxation time correlates with the Hammett σ_p. For the anilinium ions (solvent Me_2SO-d_6), there is no correlation with σ_p and no qualitative relationship with either C–N rotation or N inversion. Nitrogen-15 relaxation, corrected for overall motion as judged by ring ^{13}C relaxation, correlates with the inductive parameter σ_I. Electron withdrawal through induction reduces hydrogen bonding and increases side-chain mobility. For most of the anilines and for all of the anilinium ions, solvent interactions cause the nitrogen side-chain to be less mobile than the aryl ring. Under these circumstances, the Woessner approach cannot be used to calculate barriers. The hydrogen bond donor properties of the anilines are reduced in the absence of electron-donating substituents, and the first barriers to NH_2 rotation/inversion were calculated by this procedure: aniline in $CDCl_3$ 3.5 kcal/mol, *p*-chloroaniline in $CDCl_3$ 3.4 kcal/mol and *p*-nitroaniline in acetone 3.8 kcal/mol.

Measurement of ^{13}C spin–lattice relaxation times has provided a new approach to the study of extremely rapid rotation of methyl groups and of segmental motion of alkyl chains, through application of the theories of Woessner and co-workers.[1–4] Although there now are numerous quantitative applications of the Woessner method to the derivation of the barrier to methyl or deuteriomethyl rotation,[3] the method has otherwise been applied only to the trifluoromethyl group.[5] The nitrogen analogue of methyl is the ammonium group, NH_3^+. The neutral amino group, NH_2, has added complexity and interest from its capability to undergo two related dynamic processes, rotation and inversion. It is possible that both processes contribute to spin–lattice relaxation. Amine rotational barriers determined by independent methods have been related to ^{15}N chemical shifts,[6] and ^{15}N spin–lattice relaxation times have been used to describe overall molecular motion in anilines,[7] but no quantitative studies have been reported on the derivation of barriers for rotation about amino or ammonium groups.

Substitution on the aromatic ring perturbs amine rotation and inversion in a reasonably predictable fashion. An electron-withdrawing group at the *para* position increases double bond character between the aromatic ring and the amino nitrogen, thereby increasing the rate of nitrogen inversion but decreasing the rate of C–N rotation. Conversely, an electron-donating group at the *para* position slows inversion but speeds rotation. Because increased relative motion of the magnetic dipoles causes longer dipolar relaxation times, the inversional and rotational perturbations of *para* substituents should have opposing effects on relaxation times. The effects of substitution on overall motion can be factored out by comparison of ^{15}N relaxation times with ^{13}C relaxation times for the aromatic carbons in the same molecule.

Protonation to form the anilinium ion removes the inversional component, so that the effect of substitution on ^{15}N relaxation might resemble that for ^{13}C relaxation in substituted toluenes.[8] The positive charge on anilinium and the hydrogen bonding abilities of the N—H bonds, however, provide substantial differences from the toluene series.

In order to understand the relative importance of inversion and rotation in amine ^{15}N relaxation and in order to understand the differences in the relaxation processes of NH_3^+ and CH_3, we have studied a series of *para*-substituted anilines and anilinium salts, **1**.



$R = NH_2, {}^+NH_3$;

$X = CH_3O, CH_3, H, Cl, NO_2$

1

RESULTS

As a compromise between spectrometer time and cost of ^{15}N, the substrates were prepared with an enrichment of 5.1% ^{15}N, approximately one order of

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Table 1. Relaxation parameters for *para*-substituted anilines (1, R = NH_2) in $CDCl_3$[a]

X	Atom	T_1(s)	η	T_1(DD)(s)
CH_3O	C-2	5.21±0.08	1.79±0.17	5.8±0.6
	C-3	5.31±0.05	1.73±0.20	6.1±0.8
	$C_{\alpha}{}^{b}$			5.9±0.7
	NH_2	4.8±0.4	−2.81±0.13	8.4±1.1
CH_3	C-2	9.3±0.3	1.66±0.17	11.1±1.5
	C-3	9.4±0.3	1.58±0.10	11.8±1.1
	$C_{\alpha}{}^{b}$			11.5±1.3
	NH_2	6.8±0.4	−1.95±0.23	17.2±3.1
H	C-2	10.8±0.1	1.72±0.19	12.5±1.5
	C-3	10.7±0.1	1.79±0.19	11.9±1.4
	$C_{\alpha}{}^{b}$			12.1±1.5
	C-4	9.31±0.19	1.77±0.15	10.5±1.1
	NH_2	9.4±0.5	−2.21±0.07	21.0±1.8
Cl	C-2	7.66±0.07	1.60±0.13	9.5±0.9
	C-3	7.63±0.13	1.62±0.16	9.4±1.1
	$C_{\alpha}{}^{b}$			9.4±1.0
	NH_2	12.1±0.5	−2.36±0.07	25.3±1.8

[a] Errors are reported as the 90% confidence limits.

[b] Average of the data for C-2 and C-3.

magnitude above natural abundance (0.36%). Commercially available *para*-substituted benzoic acids were converted to the acid chlorides, which were allowed to react with $^{15}NH_3$ to produce the labeled amides. The Hofmann rearrangement of the amides yielded the five desired anilines. The synthesis of the nitrile failed in the final step because the cyano group underwent hydrolysis under the conditions of the rearrangement. The anilinium chlorides were prepared by reaction of the anilines with hydrogen chloride in diethyl ether.

Chemical shifts (^{13}C and ^{15}N) are in agreement with the literature.[9] Spin-lattice relaxation times (T_1) were measured by the inversion recovery method in $CDCl_3$ for the anilines and in $(CD_3)_2SO$ for the anilinium ions. Details are given under Experimental. Carbon-13 relaxation measurements were carried out on proton-decoupled spectra; ^{15}N measurements were obtained with gated proton decoupling in order to avoid unfavorable nuclear Overhauser effects. Overhauser effects were measured for both nuclei in order to calculate dipolar relaxation times according to the equation $T_1(\mathrm{DD}) = (\eta_{\max}/\eta_{\mathrm{obs}})T_1(\mathrm{obs})$,[3] in which $\eta_{\max}$ is 1.988 for ^{13}C and −4.93 for ^{15}N. The relaxation times and nuclear Overhauser effects are reported for the anilines in Table 1 and for the anilinium ions in Table 2. Error estimates are given for the 90% confidence level.

p-Nitroaniline was insufficiently soluble in chloroform for relaxation measurements, and its hydrochloride was not soluble in Me_2SO. Acetone was considered as the solvent for all neutral substrates, but unfortunately some of the substrates were unstable in acetone because of imine formation. Data in acetone could be obtained, however, for the *p*-nitro and *p*-chloro derivatives, and these results are collected in Table 3. Comparison of the *p*-chloro data in Tables 1 and 3 reveals a large solvent effect, so that the *p*-nitro results cannot be compared directly with the rest of the series. Further data were also obtained in CD_2Cl_2 for the *p*-chloro and parent aniline (Table 3).

Table 2. Relaxation parameters for *para*-substituted anilinium chlorides (1, R = $NH_3{}^+$) in $(CD_3)_2SO$[a]

X	Atom	T_1(s)	η	T_1(DD)(s)
CH_3O	C-2	0.51±0.16	1.82±0.06	0.56±0.04
	C-3	0.51±0.08	1.75±0.04	0.58±0.04
	$C_{\alpha}{}^{b}$			0.57±0.04
	$NH_3{}^+$	0.40±0.04	−4.73±0.09	0.42±0.05
CH_3	C-2	1.21±0.04	1.81±0.05	1.33±0.08
	C-3	1.22±0.04	1.90±0.23	1.28±0.20
	$C_{\alpha}{}^{b}$			1.31±0.14
	$NH_3{}^+$	0.64±0.14	−4.44±0.16	0.71±0.18
H	C-2	1.23±0.03	1.9±0.6	1.3±0.4
	C-3	1.25±0.02	1.9±0.3	1.3±0.3
	$C_{\alpha}{}^{b}$			1.3±0.3
	C-4	0.40±0.01	1.99±0.20	0.40±0.05
	$NH_3{}^+$	0.85±0.04	−4.93±0.16	0.85±0.07
Cl	C-2	0.53±0.02	1.69±0.10	0.62±0.05
	C-3	0.53±0.02	1.84±0.17	0.57±0.08
	$C_{\alpha}{}^{b}$			0.59±0.07
	$NH_3{}^+$	0.57±0.03	−4.9±0.3	0.57±0.07

[a] Errors are reported as the 90% confidence limits.

[b] Average of the data for C-2 and C-3.

Table 3. Relaxation parameters for *para*-substituted anilines (1, R = NH_2)[a]

X	Solvent	Atom	T_1(s)	η	T_1(DD)(s)
NO_2	Acetone-d_6	C-2	5.5±0.3	1.82±0.19	6.0±1.0
		C-3	5.48±0.13	1.62±0.16	6.7±1.1
		$C_{\alpha}{}^{b}$			6.3±1.0
		NH_2	9.0±0.3	−2.74±0.04	16.2±0.9
Cl	Acetone-d_6	C-2	5.96±0.14		
		C-3	5.80±0.12		
		NH_2	23.6±1.1		
Cl	CD_2Cl_2	C-2	7.45±0.20		
		C-3	7.55±0.17		
		NH_2	14.8±0.9		
H	CD_2Cl_2	C-2	14.3±0.5	1.79±0.08	15.9±1.3
		C-3	14.1±0.6	1.81±0.11	15.5±1.6
		$C_{\alpha}{}^{b}$			15.7±1.4
		C-4	12.5±0.5	1.88±0.01	13.2±0.6
		NH_2	11.6±0.4	−1.87±0.10	30.6±2.6

[a] Errors are reported as the 90% confidence limits.

[b] Average of the data for C-2 and C-3.

CORRELATION OF RELAXATION PROPERTIES WITH SUBSTITUENT EFFECTS

The dipolar relaxation time is given by Eqn (1), where n is the

$$1/T_1(\mathrm{DD}) = n\gamma_X{}^2\gamma_H{}^2\hbar^2 r_{XH}{}^{-6}\tau_c \qquad (1)$$

number of protons attached to the relaxing nucleus, γ is the gyromagnetic ratio, $\hbar$ is Planck's constant divided by 2π, r is the distance from the relaxing nucleus X to the attached protons in the present case and τ_c is the effective motional correlation time. Comparison of ^{15}N relaxation times from one substituted

Table 4. Correlation times for *para*-substituted anilines (1, R = NH$_2$) in CDCl$_3$

X	Atom	$\tau_c \times 10^{12}$(s)	τ(C)/τ(N)
CH$_3$O	C$_\alpha$	7.4	0.73
	NH$_2$	10.2	
CH$_3$	C$_\alpha$	3.6	0.73
	NH$_2$	4.9	
H	C$_\alpha$	3.6	0.88
	NH$_2$	4.1	
Cl	C$_\alpha$	4.7	1.38
	NH$_2$	3.4	
NO$_2$^{a}	C$_\alpha$	7.1	1.34
	NH$_2$	5.3	

^{a} In acetone-d_6.

system to the next includes both intramolecular (rotation and inversion of the amino group) and intermolecular (overall molecular tumbling) factors. The intermolecular factors should affect carbon and nitrogen relaxation in an analogous fashion. Thus the ratio of correlation times, τ(C)/τ(N), should provide a purer measure of the intramolecular motion of the amino group. The ratio is crude, however, because overall motion is probably anisotropic. For τ(C), we use the average value for C-2 and C-3. The values of τ and of the ratios are given in Tables 4 and 5 for the anilines and the anilinium ions, respectively. The values for *p*-NO$_2$ are from acetone and are not compared with the other substituents.

Nitrogen dipolar relaxation times in the anilines increase monotonically in the order CH$_3$O < CH$_3$ < H < Cl. Thus, electron withdrawal (in the σ_p sense) increases the relaxation times and must provide greater mobility. This order is consistent with inversion rather than rotation as the source of the motion. Thus 4-chloro substitution provides the longest T_1(N) and also the fastest inversion. The ratio of correlation times follows a similar order, so that effects of overall motion are not masking intramolecular effects. Correlation between the ^{15}N T_1(DD) and σ_p ($r = 0.93$) or σ_p^+ (0.99) is good. The ratio τ(C)/τ(N) also correlates ($r = 0.94$ for σ_p). The one bond $J(^{15}N^1H)$ ($r = 0.93$) and the ^{15}N chemical shift ($r = 0.98$) were also found to correlate with σ_p.[9,10] The dependence of the ^{15}N chemical shifts and coupling constants on substitution was related to the inversional properties of nitrogen.[9,10] Thus it is possible that nitrogen inversion gives rise to the primary motional process that determines ^{15}N dipolar relaxation. Alternatively, electron donation could enhance the hydrogen bond acceptor properties of the NH$_2$ group so that, at the CH$_3$O extreme, rotational motion is slowed by intermolecular interactions.

Table 5. Correlation times for *para*-substituted anilinium chlorides in (CD$_3$)$_2$SO (1, R = NH$_3^+$)

X	Atom	$\tau_c \times 10^{11}$(s)	τ(C)/τ(N)
CH$_3$O	C$_\alpha$	7.8	0.54
	NH$_3^+$	14.4	
CH$_3$	C$_\alpha$	3.4	0.40
	NH$_3^+$	8.5	
H	C$_\alpha$	3.4	0.48
	NH$_3^+$	7.1	
Cl	C$_\alpha$	7.5	0.71
	NH$_3^+$	10.6	

The ratio of correlation times, τ(C)/τ(N), is greater than unity (Table 4) for *p*-Cl but less than unity for the remaining substituents, excluding *p*-NO$_2$. Hence only for the electron-withdrawing *p*-Cl (and *p*-NO$_2$ in acetone) is nitrogen mobility greater than ring mobility. This result has ramifications for the calculation of barriers to intramolecular motion (next section).

The anilinium ions, of course, have no contribution to intramolecular motion from nitrogen inversion, and the relative order for substituents (Table 2) no longer follows the inversion order. At NMR concentrations, these salts are undoubtedly aggregated or hydrogen bonded to the solvent. As a result, overall motion may dominate intramolecular contributions, particularly if hydrogen bonding of NH with solvent slows C–N rotation. Indeed, the ratio τ(C)/τ(N) is less than unity for all substituents, indicating that motion of the aryl ring is more rapid than C–NH$_3^+$ rotation. Fraenkel and Kim[11] have shown that anilinium ions can coordinate with up to three hydrogen bond acceptors. Electron withdrawal from the *para*-substituent should promote hydrogen bonding and decrease mobility. The order of ^{15}N dipolar relaxation times is CH$_3$O < Cl < CH$_3$ ≈ H, approximating the inverse order of inductive electron withdrawal. After correction for carbon mobility [τ(C)/τ(N)] (Table 5), the mobility order is CH$_3$ < H < CH$_3$O < Cl, an even better inductive series. Indeed, τ(C)/τ(N) correlates well with σ_I ($r = 0.96$). Hence it appears that mobility in anilinium ions is controlled primarily by intermolecular factors such as hydrogen bonding, which are modulated by substituent inductive effects. As a result, we found no relationship between T_1($^+$NH$_3$) in three anilinium ions and T_1(CH$_3$) in toluenes.[8]

BARRIERS TO INTRAMOLECULAR MOTION OF THE AMINO AND AMMONIUM GROUPS

Because C–N rotation is extremely rapid for primary amines and ammonium ions, NMR line shape methods have not been applied to barrier determination. Vibrational[12–14] and rotational[15] methods have been more successful. The best value for the barrier in aniline from vibrational studies appears to be 3.45 kcal/mol.[12] We applied the NMR method of Dorie *et al.*[6b] to the ^{15}N chemical shift data of Sibi[9c] to give barriers for the series *p*-XC$_6$H$_4$NH$_2$. The figures vary from 5.81 kcal/mol for X = OCH$_3$ to 6.60 kcal/mol for H and 9.62 kcal/mol for NO$_2$. The order for substituents is clearly correct, but the absolute numbers seem high.

The Woessner method[1,2] for the derivation of methyl barriers[3] has not been applied to NH$_2$ or NH$_3^+$, although anisotropic analyses have been reported for 6-X-benzonorbornyl systems, in which X was CH_3, NH_2 and NH_3^+.[16] According to the Woessner formulation for a molecule with the approximate shape of an ellipsoid, anisotropic tumbling can be described by two distinct axes of overall rotation, with diffusion rates about these axes of D_1 and D_2. The spin–lattice relaxation is then given by Eqn (2),[1,3] in which the

$$1/T_1(\mathrm{DD}) = n\gamma_X{}^2\gamma_H{}^2\hbar^2 r_{XH}{}^{-6} \times \left(\frac{A}{6D_2} + \frac{B}{D_1+5D_2} + \frac{C}{4D_1+2D_2}\right) \quad (2)$$

correlation time of Eqn (1) has been expanded to include anisotropic diffusion, with geometric factors A, B and C given by $0.25\,(3\cos^2\Delta - 1)^2$, $0.75\sin^2 2\Delta$ and $0.75\sin^4\Delta$, respectively (Δ is the angle between the NH or CH bond in the rotor and the internal rotation axis). When the small group (CH_3, etc.) is rotating rapidly but not freely, an additional term D_i is added to diffusion about the internal rotation axis, as in Eqn (3),[2,3] in which $\sigma = D_1/D_2$, $D' =$

$$1/T_1(\mathrm{DD}) = n\gamma_X{}^2\gamma_H{}^2\hbar^2 r_{XH}{}^{-6} D_2{}^{-1} \times \left(\frac{A}{6} + \frac{B}{5+\sigma+\mathrm{a}D'} + \frac{C}{2+4\sigma+amD'}\right) \quad (3)$$

D_i/D_2, a and m are statistical factors ($a = 1$, $m = 4$ for a stochastic process; $a = r/2$, $m = 1$ for an r-fold jump process). Once D_i is known, the rotational barrier V_0 can be calculated from $D_i = D_{i0}\exp(-V_0/RT)$, where D_{i0} is the rotational rate of a freely rotating group. For determination of the three diffusion coefficients, D_1, D_2 and D_i, we followed the method developed by Platzer.[8,17].

It is not clear to what degree the Woessner formulation[1,2] can be applied to the internal motion of the NH_2 group. The operations of inversion and rotation can have identical beginning and ending states, even though the mechanisms of movement are different. Moreover, the motion may involve a single operation with both inversional and rotational character. Consequently, we have treated NH_2 as if it were a purely rotational process for the Woessner analysis.

Values for the geometric factors from literature structural data for unsubstituted aniline[18] are $\Delta = 115.9°$, $A = 0.0457$, $B = 0.4632$ and $C = 0.4911$. Platzer's method gave $\sigma = 1.5$ and $D_2 = 3.93 \times 10^{10}\ s^{-1}$ from the ^{13}C data in Table 1. From literature data under slightly different conditions,[7] we calculated $\sigma = 1.6$ and $D_2 = 4.1 \times 10^{10}\ s^{-1}$. For the unsubstituted anilinium ion, the HNH bond angle was estimated from the ^{15}N–^{1}H coupling constant[19] to give $\Delta = 107.6°$. Anisotropic analyses then gave $\sigma = 9.7$ and $D_2 = 1.51 \times 10^{9}\ s^{-1}$ from the ^{13}C data in Table 2. The same calculation from literature data on anilinium trifluoroacetate[7] gave $\sigma = 8.7$ and $D_2 = 1.25 \times 10^{9}\ s^{-1}$. Thus aniline diffuses relatively isotropically, but anilinium very anisotropically.

Application of the Woessner approach to these data does not give a physically real solution in three of these four cases. Negative values of D' are obtained because the dipolar correlation time of the aryl portion of the ring is shorter than that for the amine substituent (see Tables 4 and 5). In effect, the amine side-chain is being held by the solvent, and the aryl rings is undergoing rotation. We can mimic this behavior in toluene. Our data for toluene[8] gave a correlation time of 0.37×10^{-12} s for the CH_3 group and 2.07×10^{-12} s for the ring. Clearly, the methyl group is reorienting more rapidly than the ring. If we artificially reduce T_1(DD) for the methyl group, corresponding to slowing of its motion, at $T_1 = 7.1$ s the methyl correlation time would be 2.31×10^{-12}, a value larger than that of the aryl ring, and D' becomes negative. The literature value for aniline relaxation[7] translates to $V_0 = 3.5$ kcal/mol for a six-fold barrier or 2.5 kcal/mol for a two-fold barrier. The best experimental value was 3.45 kcal/mol from the vibrational study.[12]

We conclude that hydrogen bonding to the solvent, particularly in the anilinium ions, hinders C–N rotation and removes the barrier from the region to which the Woessner method applies. Placement of an electron-withdrawing group at the *para* position in neutral anilines decreases the availability of the nitrogen lone pair for hydrogen bonding. For the two cases of *p*-chloroaniline in $CDCl_3$ and *p*-nitroaniline in acetone (Table 4), the ^{15}N dipolar correlation time is shorter than that for ^{13}C. Woessner analysis of these systems consequently should give physically real solutions. For *p*-nitroaniline, the angle Δ was calculated to be 118.3° from the literature structure.[20] The geometry for *p*-bromoaniline[20] had to be used as an approximation to that for *p*-chloroaniline, $\Delta = 114.9°$. Application of the Platzer method was not possible for these *para*-substituted anilines, because there are too few ^{13}C data. Consequently, the barrier was calculated for values of σ ranging from 1.0 to 10.0. Because the barrier proved to be relatively insensitive to the choice of σ, the calculation appears to be useful. For *p*-chloroaniline, the six-fold barrier was found to range from 3.50 ($\sigma = 1.0$) to 3.33 kcal/mol ($\sigma = 10.0$) (average value 3.4 kcal/mol); the two-fold barrier ranged from 2.82 to 2.67 kcal/mol over the same range. For *p*-nitroaniline, the six-fold barrier ranged from 3.82 to 3.80 and the two-fold barrier from 3.16 to 3.15 kcal/mol. These *p*-chloro and *p*-nitro values cannot be compared with each other because they are from different solvents. Judging from the aniline result, the six-fold result is probably more appropriate.

CONCLUSIONS

para-Substitution in anilines and anilinium ions alters the motional properties and solvent interactions of the NH_2 and NH_3^+ groups. Electron withdrawal in the σ_p sense results in longer ^{15}N dipolar relaxation and hence faster relative motion of the NH_2 group, in the order $CH_3O < CH_3 < H < Cl$ in $CDCl_3$ as solvent. When overall motion is taken into consideration by analysis of ^{13}C dipolar relaxation, the order is essentially unchanged, $CH_3O \approx CH_3 < H < Cl$. Electron withdrawal results in higher C—N double bond character, so that the observed faster motion cannot be the result only of C–NH_2 rotation. The order is in agreement with the effects of nitrogen inversion, the rate of which increases with electron withdrawal. Solvent effects also may play a role, because electron donation would make the NH_2 group a better Lewis base and hydrogen bond acceptor, and these intermolecular interactions may also inhibit motion. Both the ^{15}N dipolar relaxation time and the ratio of ^{13}C to ^{15}N correlation times correlate reasonably well with σ_p, $r = 0.93$ and 0.94, respectively.

The anilinium ions in Me_2SO behave in a different fashion, showing no correlation between σ_p and either the ^{15}N dipolar relaxation time or the ratio of ^{13}C to ^{15}N correlation times. The ^{15}N relaxation times themselves exhibit no simple substituent dependence, but the ratio of ^{13}C to ^{15}N correlation times, which takes into account effects that are common to the aromatic ring and the NH_3^+ group, shows a good correlation with σ_I ($r = 0.96$). Resonance effects should be minimal in the case of the anilinium ions, but inductive effects can alter the hydrogen bond donor properties of the NH_3^+ group. Electron withdrawal through induction reduces hydrogen bonding and increases the mobility of the ammonium group.

Application of the Woessner approach to the determination of barriers to rotation confirms that there are strong interactions between solvent and the NH_2 or NH_3^+ groups, in contrast to our observations with analogous *para*-substituted toluenes.[8] Hydrogen bonding of the nitrogen functionalities to the solvent decreases the mobility of the side-chain to the point that the aryl groups reorientate more rapidly than the nitrogen side-chains, i.e. $\tau(C) < \tau(N)$. In the anilines, this effect is maximal for electron-donating substituents, which augment the hydrogen bond acceptor properties of the NH_2 group. Barriers to Ar–NH_2 rotation/inversion could be calculated only for cases lacking such groups: aniline in $CDCl_3$, 3.5 kcal/mol; *p*-chloroaniline in $CDCl_3$, 3.4 kcal/mol; and *p*-nitroaniline in acetone, 3.8 kcal/mol; assuming a sixfold rotation model. All the anilinium ions showed faster aryl ring than NH_3^+ mobility, presumably because of hydrogen bonding to the solvent.

EXPERIMENTAL

Melting and boiling ranges are uncorrected. Melting ranges were obtained on a Hirschberg apparatus or on a Fisher–Johns hot-stage apparatus. Proton NMR spectra were obtained at 60 MHz on Varian T60, Varian EM360 or Perkin-Elmer R20B spectrometers. Carbon-13 NMR spectra were obtained at 20 MHz on a Varian CFT20 spectrometer at 27 °C or at 22.5 MHz on the JEOL FX90Q spectrometer at 30 °C. Nitrogen-15 NMR spectra were obtained at 9.04 MHz on the JEOL FX90Q spectrometer at 30 °C. No significant difference in ^{13}C data was observed for the two temperatures. Proton chemical shifts (δ) were measured in parts per million downfield from tetramethylsilane ($\delta = 0.00$). Carbon chemical shifts were measured from the center peak of $CDCl_3$ ($\delta = 77.0$) or from the center peak of dimethyl-d_6 sulfoxide ($\delta = 39.5$) and were converted to ppm downfield from Me_4Si. Infrared spectra were recorded on a Perkin-Elmer 283 spectrometer. Ammonium chloride enriched to the 5.1% level in ^{15}N was purchased from Prochem/Isotopes, Summit, NJ, USA. Any necessary solvent and reagent purifications were performed as suggested by Perrin *et al.*[21]

Acid chlorides

Substituted benzoyl chlorides were prepared by refluxing 0.1 mol of the appropriate benzoic acid in 2 ml of thionyl chloride. The excess of thionyl chloride was removed *in vacuo*, and the acid chloride was distilled under reduced pressure. *p*-Nitrobenzoyl chloride (Aldrich) was recrystallized from hexane.

[^{15}N]Benzamides

para-Substituted benzamides, enriched to the 5.1% level with ^{15}N, were synthesized via the method of Axenrod *et al.*[10] A solution of 5.1% enriched [^{15}N]ammonium chloride (6.0 g, 0.11 mol) in 100 ml of water was equilibrated at 95 °C. A 125-ml volume of 1 N NaOH solution was added with stirring over 20 min and the generated $^{15}NH_3$ was swept from the reaction flask with a slow flow of nitrogen. It was passed through a KOH drying tube and bubbled into a solution of acid chloride (0.05 mol) in diethyl ether (600 ml) cooled to −78 °C. The gas flow was continued for 6 h. The reaction was stirred at −78 °C overnight, warmed to room temperature and suction filtered. The solvent was removed *in vacuo*. The precipitated $^{15}NH_4Cl$ was washed with acetone until no further [^{15}N]benzamide was obtained. The combined product was recrystallized from ethanol–water if necessary. [^{15}N]*p*-Methoxybenzamide, 5.7 g (75%), m.p. 164–165 °C (lit.[22] 162–163 °C); [^{15}N]*p*-methylbenzamide, 2.1 g (31%), m.p. 154–158 °C (lit.[22] 160 °C); [^{15}N]benzamide, 2.4 g (40%), m.p. 127–129 °C (lit.[22] 130 °C); [^{15}N]*p*-chlorobenzamide, 2.6 g (33%), m.p. 176 °C (lit.[22] 179 °C); [^{15}N]*p*-nitrobenzamide, 1.0 g (12%), m.p. 195–196 °C (lit.[22] 198 °C).

[^{15}N]Anilines

The substituted [^{15}N]anilines were synthesized from the appropriate [^{15}N]benzamide by the Hofmann rearrangement.[23] The bases used to effect the rearrangement were sodium hypobromite (*p*-CH_3, *p*-NO_2), potassium hypobromite (H, *p*-Cl) and sodium hypochlorite (*p*-OCH_3). A 20% excess of the hypohalite was used in each reaction. All base solutions were prepared immediately prior to use. Correct conditions for the rearrangements were established with unenriched benzamides. For each mole of substituted [^{15}N]benzamide reacted with NaOBr or KOBr, 1.2 mol of Br_2 was added to a solution of NaOH or KOH (5 mol) in water (1667 ml) cooled to 0 °C. The solution was stirred at 0 °C for 30 min and then used. For the preparation of 0.5 N NaOCl solution, chlorine was generated by adding concentrated HCl (18 ml) dropwise to solid $KMnO_4$ (1.62 g). The chlorine was bubbled into a solution of NaOH (10 g) in water (90 ml) cooled to 0 °C. The solution was stirred at 0 °C for 1 h, and then used. The substituted [^{15}N]benzamide was added to the hypohalite solution at 0 °C and stirred at this temperature until the [^{15}N]benzamide dissolved. The solution was heated (80–95 °C) in a previously equilibrated oil bath (20–40 min). The reaction mixture was cooled to room temperature and extracted five times with diethyl ether. The combined extracts were washed once with water and twice with saturated NaCl solution and dried (Na_2SO_4). The drying agent was filtered off, and the solvent was removed *in vacuo*. The resulting product was purified by distillation, sublimation or recrystallization. [^{15}N]*p*-Methoxyaniline, 0.61 g (50%), m.p. 56 °C (lit.[22] 57 °C); [^{15}N]*p*-methylaniline, 0.56 g (35%), m.p. 42–43 °C (lit.[22] 44 °C); [^{15}N]aniline, 0.59 g (53%), b.p. 47 °C (2mmHg); [^{15}N]*p*-chloroaniline, 0.81 g (66%), m.p. 71–73 °C (lit.[22] 72.5 °C); [^{15}N]*p*-nitroaniline, 0.44 g (53%), m.p. 145–146 °C (lit.[22] 149 °C).

[^{15}N]Anilinium chlorides

The ^{15}N-enriched aniline was dissolved in 20 ml of anhydrous diethyl ether. Hydrogen chloride gas, generated by adding concentrated H_2SO_4 to a slurry of NaCl in concentrated HCl, was bubbled through concentrated H_2SO_4, and was allowed to flow into the flask containing the ether solution. A precipitate formed immediately. The solution was stirred for 2 h while continuing the flow of the HCl gas. The solvent was removed by passing dry nitrogen over the mixture. No further purification was done.

Sample preparation

Samples were prepared by adding enough solvent ($CDCl_3$ for neutral compounds, dimethyl-d_6 sulfoxide for salts) to the compound to give an approximately 2 M solution. The solution was added to a 10 mm O.D. glass NMR tube after passing through a pad of neutral alumina to remove any dissolved paramagnetic species, ethanol or water. The sample was degassed by the freeze–pump–thaw method. At least two additional cycles were performed after no bubbling occurred upon thawing. A Sargent–Welch Model 1392 oil diffusion pump was used. Typical pressures were 10^{-3}–10^{-4} mm as measured by a McLeod mercury manometer. The tubes were then sealed under vacuum.

Spin–lattice relaxation time and nuclear Overhauser enhancement measurements

The inversion recovery method was used, $(180°\text{–}\tau\text{–}90°\text{–AT–}D)_n$. Ten spectra, with increasing values of τ, were run consecutively. For each sample, the measurements were made three or four times, the sample was opened and degassed again and the measurements were repeated. A pulse delay D of $5T_1$ was used. The ^{13}C measurements were carried out with proton decoupling. The ^{15}N measurements were carried out with gated decoupling to avoid unfavorable nuclear Overhauser effects. The Overhauser enhancement factors were measured by comparing peak intensities of gated decoupled spectra with those of constantly decoupled spectra. A pulse delay of $10T_1$ was used for these measurements. The T_1 data given in Tables 1 and 3 for neutral anilines are accurate to at least 5%, the data in Table 2 for the salts have even smaller errors. The NOE factors in the tables are accurate to at least 10%. The relaxation times were calculated with the DSSLRT program, a revision of the Basic program DNTICAL.[8] The program calculates the best exponential curve from a least squares fit to $M = M_0[1-2\exp(-\tau/T_1)]$ by adjusting the experimental intensity after the 90° pulse and the T_1. Input data are the observed signal intensities and the waiting time τ. The program calculates T_1, peak intensities for each τ, differences between observed and calculated intensities, standard deviation for the best fit and the 90% error for T_1 and M_0.

Anisotropic motion analysis

Program ANISO3 is a revision by Finzel of Nienhuis's ANISO2 program.[8] The program is in Fortran and calculates D_1/D_2, D_2 and Sumdif [the sum of the differences between observed and calculated values for T_1(DD)] using Platzer's anisotropic motion analysis.[17] Input data consist of observed values of T_1(DD) for all rigid carbon atoms, the C—H bond length and the range of angles to be swept through to find the principal rotation axis.

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