J. Am. Chem. Soc. **1995,** *117,* 9535–9541

Discrete Secondary Isotope Effects in Zero-Field NMR: Their Relationship to Halide Ion Coordination

Ming-Yuan Liao, Raymond Templin, and Gerard S. Harbison*

Contribution from the Department of Chemistry, University of Nebraska, Lincoln, Nebraska 68588-0304

Received June 15, 1994. Revised Manuscript Received July 14, 1995[⊗]

Abstract: Zero-field magnetic resonance spectra of halogen nuclei in amine and amino acid hydrohalides, partially deuterated at the exchangeable positions, show multiple spectral lines, each one corresponding to a particular pattern of deuteron replacement in the coordinating protonated groups. We have analyzed this isotope perturbation using two-dimensional ^{127}I zero-field NMR spectroscopy (NQ-COSY). The principal values of the electric field gradient tensor for each isotopomer are obtained from the corresponding resonance frequencies of two connected transitions. The difference between the electric field gradient tensor for isotopomers differing by a single isotope substitution is treated as an axially symmetric perturbation along the hydrogen bond between the substituted proton and the halide: under this assumption, we have determined the orientation of the electric field gradient tensor principal axis system.

Introduction

Zero-field NMR spectroscopy, conventionally if inaccurately called nuclear quadrupole resonance or NQR, has recently experienced a rebirth of interest, and there is hope that it can be used to study biological macromolecules, as well as the low molecular weight materials to which it has hitherto been applied. It is most useful for observing quadrupolar nuclei in sites with large electric field gradients and low symmetry, which make high-field NMR spectroscopy difficult. Halide nuclei in particular are silent over most of the electromagnetic spectrum, from the ultraviolet to the microwave region, and our understanding of halogenated materials, and of biological molecules which bind, transport, and metabolize halide ions, has probably suffered accordingly.

While zero-field NMR may well have the intrinsic sensitivity to enable study of protein-bound species, there remains to be answered the important question of how much information can be obtained from the zero-field spectra of such materials. The sort of global structural information available from high-field protein NMR of small macromolecules is clearly not attainable; nonetheless, one might aspire to determining more than a single resonance frequency, which is all that is available from simple one-pulse NMR of spin 3/2 nuclei.

With the goal of expanding the repertory of NMR experiments, we have been extending the technique of two-dimensional Fourier transform spectroscopy to zero-field NMR. We have developed nutation methods for the determination of the full quadrupole coupling tensor for spin 3/2 species,[1] and correlation spectroscopic methods for the assignment of complex zero-field spectra of spin higher than 3/2 and for eliminating inhomogeneous line widths.[2] However, applied to typical zero-field spectra, with one or at most a modest number of resonances, such techniques can only be pushed so far. To obtain detailed molecular information about chemical systems requires spectral multiplicity. Such multiplicity is available from isotope substitution.

It has long been known that secondary isotope effects in zero-field NMR can be substantial; many researchers have compared the resonance frequencies of halogens in ordinary protonated compounds, with the same spin transition in deuterated or partially deuterated materials, and found there to be significant differences (on the order of 1%) in the resonance frequencies. These differences are easily measurable at zero field, where the resonance frequencies are typically tens of megahertz, while line widths are a few kilohertz. Smith[3] reported that substitution of the exchangeable protons with deuterons in alkylammonium bromides decreases the ^{79}Br NQR frequency by about 350–400 kHz. The isotope shifts of the ^{127}I frequency in alkylammonium iodides are typically −350 kHz for the 3/2−1/2 transition and −700 kHz for the 5/2−3/2 transition. These shifts were attributed to shrinkage of the lattice in the deuterated material. Weiss[4] reported a similar shift (−416 kHz) in the ^{79}Br resonance of anilinium hydrobromide, when the exchangeable protons on the ammonium group were replaced with deuterons; however, isotope substitution of the aromatic ring hydrogens caused only a −34 kHz shift. This shows that hydrogen bonding is apparently necessary in producing large secondary isotope effects.

Curiously, however, no observations of partially deuterated materials have apparently been reported. An ionic solid, partially deuterated on exchangeable positions, may be expected to contain a plethora of differently isotope substituted environments for the halide ion. In this paper, we show for the first time that isotopomerism in the coordination environment of bromide and iodide ions leads to zero-field NMR spectra with distinct resonance lines for each isotopomer. The effects of isotope substitution appear to be additive; as might be expected, the distribution of isomers is statistical, and where accurate quadrupole tensors can be obtained, these tensors can be used to obtain structural information about the halide ion environment.

[⊗] Abstract published in *Advance ACS Abstracts,* August 15, 1995.

(1) (a) Harbison, G. S.; Slokenbergs, A.; Barbara, T. M. *J. Chem. Phys.* **1989**, *90*, 5292–5298. (b) Harbison, G. S.; Slokenbergs, A. *Z. Naturforsch.* **1990**, *45A*, 575–580.

(2) (a) Liao, M.-Y.; Harbison, G. S. *J. Magn. Reson.* **1992**, *99*, 198–200. (b) Liao, M.-Y.; Harbison, G. S. *J. Chem. Phys.* **1994**, *100*, 1895–1901.

(3) Jugie, G.; Smith, J. A. S. *J. Chem. Soc., Faraday Trans. 2* **1978**, *74*, 994–1004.

(4) Pies, W.; Weiss, A. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 1051–1061.

0002-7863/95/1517-9535$09.00/0

Experimental Section

I. Materials. Glycine hydrobromide[5] was obtained by slowly cooling a saturated solution of glycine (Sigma) in warm concentrated hydrobromic acid (Aldrich, 48%). Partially deuterated glycine hydrobromide was obtained by crystallizing from H_2O/D_2O mixtures of the appropriate composition. Preparation of crystalline amine hydrohalides in general followed the prescriptions of Wagner,[6] who characterized these salts by optical goniometry. Alkylammonium bromides and iodides[6,7] were prepared by dissolving commercial alkylamines in hydrobromic acid or hydriodic acid (Aldrich, 57%). $[^2H_9]$Trimethylammonium bromide was prepared by the method of Adams and Marvel.[8] Trimethylammonium salts were recrystallized from a 1:1 mixture of chloroform/methanol solution. The ethylammonium salts were recrystallized from a 1:1 mixture of chloroform/ethanol solution, giving flat crystalline plates. Partially deuterated alkylammonium halides were obtained by dissolving alkylammonium halides in a H_2O/D_2O mixture of appropriate composition, and then recrystallizing from a chloroform and alcohol mixture containing the O-deuterated alcohol and alcohol in the same ratio.

II. Spectroscopy. The experiments were carried out using a home-built pulsed solid-state NMR spectrometer at zero magnetic field, using a broad-band double-tuned probe.[9] The resonance frequencies of the halide ion in these crystalline compounds were obtained from the literature.[5,7] Samples were packed into a glass sample tube (10 mm diameter by 40 mm long), without crushing. The temperature was maintained at 24.5 ± 0.5 °C by air cooling. A simple $\pi/2-\tau-\pi-\tau-$Hahn-echo pulse sequence was used to measure the resonance frequency of each transition. Measurements were carried out over the full ranges where the partially deuterated salts show significant signal intensity. Typically 4096 transients were averaged at a rate of 5 transients/s, each with 512 digitized complex data points at a rate of 2 μs/point, with $\tau = 30\ \mu$s.

We have been very conservative in our data acquisition rates to minimize the possibility of rf heating of our samples. Bromine and iodine T_1 values are typically on the order of 1 ms at room temperature, and spectra with good signal to noise ratios can be acquired from some amino acid derivatives by averaging 256 transients in 1 s of total data acquisition. Thus, the intrinsic sensitivity is good enough to make NQR of macromolecules quite feasible.

In the two-dimensional experiments on ^{127}I in ethylammonium iodide, the nominal $\pi/2$ pulse length was 2.5 μs for the 5/2−3/2 transition and 1.8 μs for the 3/2−1/2 transition. A series of measurements were carried out over the range where the sample shows significant signal intensity, i.e., between 31.39 and 32.38 MHz for the 5/2−3/2 transition and between 19.83 and 20.68 MHz for the 3/2−1/2 transition. The basic pulse sequence for two-dimensional zero-field NMR correlation spectroscopy has been discussed previously.[2] The two-dimensional spectra were taken by averaging 8192 transients at $\tau = 30\ \mu$s, with the same digitization rate and number of points as previously used. Sixty-four free induction decays were collected for both real and imaginary quadrature components, zero filling to 128 in the first dimension, with a t_1 increment of 2 μs.

Results and Discussion

I. Isotope Effect on the Bromine Resonance Frequency of Amine and Amino Acid Hydrobromides. Crystalline amine or amino acid hydrohalides generally have low but observable halogen quadrupole resonance frequencies at zero magnetic field, arising from the interaction between the halogen nuclear quadrupole moment and the electric field gradient at the nucleus. In these compounds the major effect of the electric field gradient around the halide ion binding site derives from hydrogen bonding. Deuteration on the exchangeable protons of the ammonium group in these halide compounds in general causes a decrease in the magnitude of the electric field gradient (EFG), which in turn causes a change in the halogen resonance frequency measured by zero-field NMR.

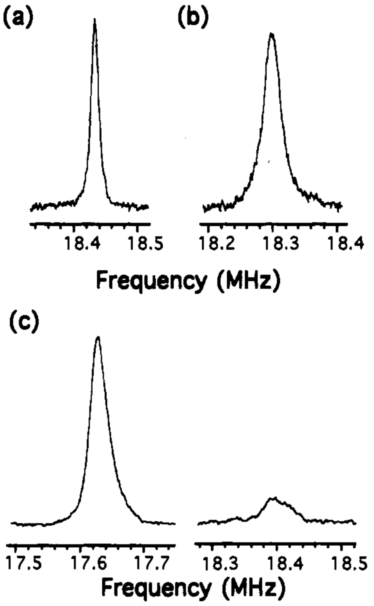

Figure 1. One-dimensional ^{79}Br NQR spectra of trimethylammonium bromide: (a) 100%-protonated, (b) 100%-deuterated on the methyl groups, (c) 80%-deuterated on the ammonium group.

Alkylammonium bromides typically have bromine resonance frequencies between 10 and 20 MHz.[7] The most straightforward examples are the tertiary amine salts, since these have simple structures,[10a] in which the halide ions in all cases have a single linear hydrogen bond to a NH group. This leads to a halide ion environment with approximate axial symmetry, and as would be expected, the EFG asymmetry parameters of these materials are almost zero.

Partial deuteration on the exchangeable position of the ammonium group gives spectra with only two resonance lines, as shown in Figure 1. In the case of trimethylammonium bromide these are at 18.398 and 17.630 MHz; they have been assigned to the two isotopomers $(CH_3)_3NHBr$ and $(CH_3)_3NDBr$, respectively, giving an isotope frequency shift of −768 kHz. The relative intensities of these two resonances are directly proportional to the percentage of deuteration.

We have also examined $[^2H_9]$trimethylammonium bromide, $(CD_3)_3NHBr$. This compound has a bromine resonance frequency of 18.300 MHz, which is 98 kHz lower than that of the fully protonated material. This shift, corresponding to −10.9 kHz per proton, is comparable to the −6.8 kHz deuteration shift at the aromatic ring positions in the anilinium hydrohalides,[4] and is almost 2 orders of magnitude smaller than the isotope shift at hydrogen-bonded positions. Non-hydrogen-bonded protons therefore seem to show only small isotope frequency shifts, making it clear that the shift is largely a local phenomenon. Data for the trimethylammonium halides are summarized in Table 1.

In primary and secondary amine hydrohalides, which have more complex hydrogen-bonding patterns, the spectra of partially deuterated samples become much more complicated. Significant asymmetry parameters are also observed, reflecting the absence of an effective local symmetry axis in the

---

(5) (a) Fleck, S.; Weiss, A. *Ber. Bunsen-Ges. Phys. Chem.* **1984**, *88*, 956−963. (b) Kehrer, A.; Fleck, S.; Weiss, A. *Ber. Bunsen-Ges. Phys. Chem.* **1987**, *91*, 1176−1182.

(6) Wagner, L. *Z. Kristallogr. Mineral.* **1907**, *43*, 148−201.

(7) Frausto Da Silva, J. R.; Vilas Boas, L. F. *Rev. Port. Quim.* **1972**, *14*, 115−116.

(8) Adams, R.; Marvel C. S. *Organic Synthesis*, 2nd ed.; Wiley: New York, 1948; Vol. I, pp 531−533.

(9) Liao, M.-Y.; Yu, H.; Harbison, G. S. Manuscript in preparation.

(10) (a) Sheldrick, G. M.; Sheldrick, W. S. *Acta Crystallogr.* **1970**, *B26*, 1334−1338. (b) Jellinek, F. *Acta Cryst.* **1958**, *11*, 626−631. (c) Hendricks, S. B. *Z. Kristallogr.* **1928**, *67*, 106−118.

Table 1. Measured ^{79}Br and ^{127}I Frequencies and Scaled Intensities of Both 100%-Deuterated and 100%-Protonated Isotopomers in Partially Deuterated Trimethylammonium Halides

isotopomer	ν(3/2−1/2), MHz	*I*(calcd)	*I*(exptl)
80%-Deuterated Trimethylammonium Bromide			
100%-deuterated	17.629 592	1	1
100%-protonated	18.397 574	0.2500	0.2653
90%-Deuterated Trimethylammonium Iodide			
100%-deuterated	18.041 527	1	1
100%-protonated	18.709 246	0.1111	0.1114

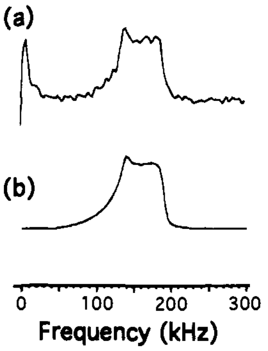

Figure 2. Experimental (a) and simulated (b) ^{79}Br nutation spectrum of ethylammonium bromide at zero field. The spectrum was obtained and simulations done by methods described previously.[1]

compounds in the crystalline state. Figure 2 shows the ^{79}Br nutation spectrum of ethylammonium bromide, obtained by previously published methods.[1] The positions of the singularities indicate an asymmetry parameter of 0.464 ± 0.012. This value has not previously been measured, but it is in good agreement with published measurements on the isomorphous iodides.[7]

From the crystal structure,[10b] there are four ammonium groups close to the bromide ion. Three of them are apparently hydrogen bonded to the anion; the orientation of the fourth makes a hydrogen bond unlikely. Two of these hydrogen bonds are along the *b* axis of the unit cell (orientation **a**), and the other one lies in the *ac* plane and perpendicular to the plane containing the other two hydrogen bonds (orientation **b**). Because of the rapid rotation of the ammonium group (which we have confirmed by ^{2}H NMR[11]), there are effectively six equivalent protons, and thus seven isotopomers, at site **a**, and three protons, or four isotopomers, at site **b**. Therefore, partial deuteration on the exchangeable protons of the ammonium group in ethylammonium bromide can lead to a total of 28 possible isotopomers. However, not all of these will have significant intensity.

Figure 3 shows the ^{79}Br NQR spectra of ethylammonium bromides with both high and low levels of deuteration on the ammonium groups. In the 5%-deuterated sample there are three significant peaks. The main peak corresponds to bromides whose environment is fully protonated, and has essentially the same frequency as unlabeled ethylammonium bromide. The other two peaks correspond to a single isotope substitution at either the **a** or the **b** site. The low deuteron enrichment makes more highly substituted species unlikely. If we assume equilibrium isotope effects to be negligible, the relative intensities of these three resonances can be calculated from the percentage of deuteration and the number of hydrogen bonds of each type. Experimental and calculated results are shown in Table 2. The shift due to a substitution at site **a**, corresponding to the hydrogen bond along the crystal *b* axis, is −52 kHz, while that due to substitution at site **b**, corresponding to the hydrogen bond in the crystal *ac* plane, is −23 kHz. Assuming six protons at site **a** and three protons at site **b**, and that the shifts are additive, we can estimate a total isotope frequency shift for the fully deuterated material of −381 kHz, which is in excellent agreement with the observed frequency difference between the fully protonated (18.477 MHz) and the fully deuterated (18.098 MHz) ethylammonium bromide.

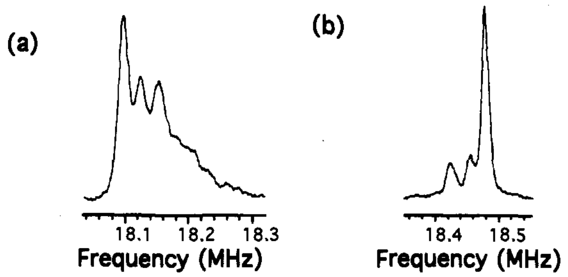

Figure 3. One-dimensional ^{79}Br NQR spectra of ethylammonium bromide with partial deuteration on the exchangeable protons: (a) 90% deuteration, (b) 5% deuteration. Samples were prepared by recrystallizing ethylammonium bromide from H_2O/D_2O mixtures of appropriate composition.

Table 2. Measured ^{79}Br Frequencies and Scaled Intensities of 100%-Protonated and Single Isotope Substitution Isotopomers at Different Sites in 5%-Deuterated Ethylammonium Bromide

isotopomer	ν(3/2−1/2), MHz	*I*(calcd)	*I*(exptl)
100%-protonated	18.476 676	1	1
substitution at **a**	18.424 522	0.3158	0.2786
substitution at **b**	18.453 926	0.1579	0.1352

Halide salts of amino acids have resonance frequencies which fall in the range 10−50 MHz, and generally possess three hydrogen bonds to the halide ion. The geometry found in leucine hydrobromide is fairly typical: the halide ion is coordinated by two $-NH_3^+$ protons and one −COOH proton. The three hydrogen bonds form a T shape around the bromide ion. The crystal structure of glycine hydrobromide has not been determined, but NQR results suggest it is similar to leucine hydrobromide.[5] Since the two $-NH_3^+$ sites are likely to be inequivalent, partial deuteration of the exchangeable positions can lead to a total of 32 isotopomers.

Figure 4 shows the ^{81}Br spectra of glycine hydrobromide with 90% and 15% deuteration at the exchangeable positions. Spectra at very low or very high levels of deuteration show four lines, one of which appears as a shoulder on the main peak, indicating three different types of single isotope substitution, with intensity ratios of 3:3:1. The weakest resonance is shifted the most, by −459 kHz, while the other two shifts are −86 and +39 kHz. At higher levels of deuteration, such as those shown in Figure 4, signals due to double isotope substitution are seen for the two smallest shifts, but no resonance can be observed at 2 × −459 kHz. For this reason, and because of the intensity ratios, the largest shift is assigned to an isotope substitution at the carboxyl group, which can only be singly substituted, while the two smaller shifts are attributed to replacement of protons on the amino groups. Each substitution on an amino group corresponds with effective replacement of 1/3 of a proton with a deuteron, and so the shifts are expected to be smaller than those for the carboxyl group: however, even accounting for this, the carboxyl shift is considerably larger, which is caused by a stronger hydrogen bond between bromide ion and the carboxyl group. The total isotope shift on full deuteration is about −600 kHz, close to the frequency difference between the fully protonated (20.866 MHz) and the fully deuterated (20.289 MHz) glycine hydrobromide.

---

(11) Liao, M.-Y.; Templin, R.; Harbison, G. S. Manuscript in preparation.

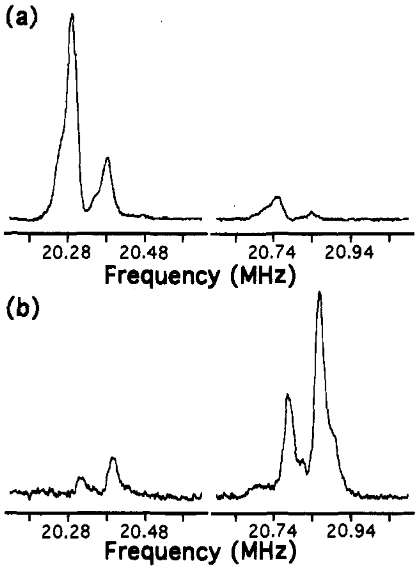

Figure 4. One-dimensional ^{81}Br NQR spectrum of glycine hydrobromide with partial deuteration on the exchangeable protons: (a) 90% deuteration, (b) 15% deuteration. In spectrum a the strongest line is assigned to the fully deuterated resonance; weaker lines derive from singly protonated species. In spectrum b the strongest line is fully protonated, and the weaker lines derive from singly deuterated species.

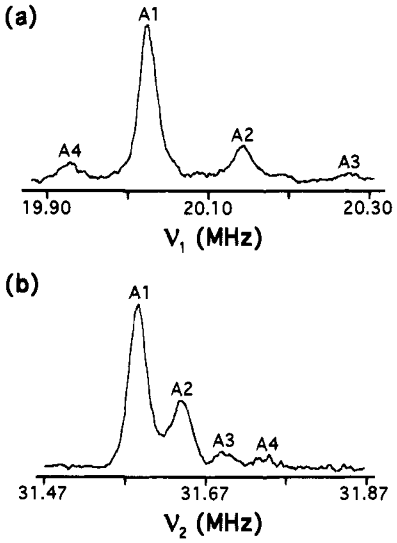

Figure 5. One-dimensional ^{127}I NQR spectrum of ethylammonium iodide with 97% deuteration on the ammonium group. Spectrum a depicts the region of the 3/2−1/2 transition, while spectrum b shows the spectral range around the 5/2−3/2 transition.

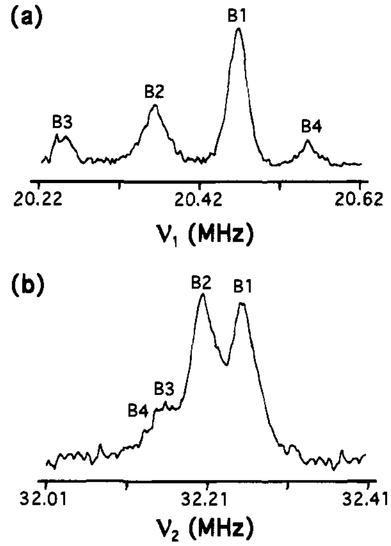

Figure 6. One-dimensional ^{127}I NQR spectrum of ethylammonium iodide with 15% deuteration on the ammonium group. As for Figure 5, spectrum a depicts the region of the 3/2−1/2 transition, while spectrum b shows the spectral range around the 5/2−3/2 transition.

Isotope shifts of the magnitude observed here, while large compared with those seen in high-field NMR, are only on the order of 1% of the full quadrupolar frequency. Unfortunately, for spin 3/2 nuclei, 1% changes in the asymmetry parameter are very difficult to detect, since this quantity can be obtained only from Zeeman-perturbed NQR[12] or nutation spectroscopy,[1] both of which typically have intrinsic errors of 2% or greater. It is therefore difficult to relate bromide isotope shifts to specific changes in the quadrupolar tensor.

Nuclei of spin higher than 3/2, in contrast, have more than one transition frequency at zero field: with two or more observable transitions, the principal values of the quadrupolar interaction tensor can be obtained directly from the NQR frequencies. These frequencies can be measured with considerably better relative precision than can the nutation spectra of spin 3/2 nuclei, and for such higher spin nuclei the limitation of measuring isotope shift tensor changes is the ability to resolve isotopomer resonances. Since NQR line widths typically fall in the range of 1−10 kHz, isotope shifts of as small as 1 part in 10^4 can be detected. We have therefore turned to iodide salts to obtain more detailed information about isotope shifts.

II. Quantitative Analysis of Ethylammonium Iodide. Ethylammonium iodide shows two ^{127}I transitions at zero field; the two-dimensional NQR correlation spectrum shows these are connected transitions of a single species. Partial deuteration of the exchangeable protons of the ammonium group in ethylammonium iodide will produce as many isotopomers as in ethylammonium bromide, since the two structures are isomorphous.[10] As expected several ^{127}I lines are observed for both spin transitions in partially deuterated material, as shown in Figures 5 and 6. The ν_1 axis corresponds to the 3/2−1/2 transition and the ν_2 axis to the 5/2−3/2 transition. Full deuteration of the exchangeable hydrogens in ethylammonium iodide shifts the resonance frequency of iodine by −385 kHz for the 3/2−1/2 transition and by −718 kHz for the 5/2−3/2 transition. In material of a low degree of deuteration there exists, in addition to the resonance from the fully protonated material, two isotope shifted resonances, perturbed by +100 and −115 kHz for the 3/2−1/2 transition and −135 and −51 kHz for the 5/2−3/2 transition. These shifted lines have an approximate 1:2 ratio of intensities, indicating two distinct types of coordinating ammonium protons in a 1:2 ratio. The crystal structure indeed confirms that there are two types of coordinating ammonium groups, which we call types **a** and **b**, in a 2:1 ratio. The two shifted peaks we therefore attribute to a single isotope substitution at either the **a** or the **b** site.

On cooling to liquid nitrogen temperature, the measured isotope frequency shift of iodine for the 5/2−3/2 transition increases from −51 kHz, at 32.21 MHz at room temperature, to −155 kHz at 35.37 MHz at 77 K for the 5/2−3/2 spin transition. The intensity of the shifted resonance also decreases by a factor of 3. This indicates that the hopping motion of the ammonium group is frozen out at 77 K and therefore presents a full isotope effect. The Pake splitting in the high-field ^{2}H NMR spectrum of N-deuterated ethylammonium iodide is only

---

(12) Morino, Y.; Toyama, H. *J. Chem. Phys.* **1961**, *35*, 1289−1296.

(13) (a) Schmidt, P. C.; Sen, K. D.; Das, T. P.; Weiss, A. *Phys. Rev.* **1980**, *B22*, 4167−4179. (b) Weast, R. C. *Handbook of Chemistry and Physics*, 62nd ed.; The Chemical Rubber Co., Boca Raton, FL, 1981; pp E67−E69.

Table 3. Measured ^{127}I Frequencies and Scaled Intensities of Some Isotopomers in Partially Deuterated Ethylammonium Iodide

isotopomer	ν(3/2−1/2), MHz	*I*(calcd)	*I*(exptl)
	97%-Deuterated Ethylammonium Iodide		
A1 + A5	20.114 497	1	1
A2	20.242 320	0.1824	0.1625
A3	20.376 779	0.0282	0.0295
A4	20.015 764	0.0912	0.0894
	15%-Deuterated Ethylammonium Iodide		
B1 + B5	20.486 986	1	1
B2	20.364 259	0.6784	0.6606
B3	20.254 450	0.5986	0.5038
B4	20.588 182	0.3392	0.3201
	10%-Deuterated Ethylammonium Iodide		
B1 + B5	20.486 986	1	1
B2	20.364 259	0.5454	0.5162
B3	20.254 450	0.3030	0.3003
B4	20.588 182	0.2727	0.2704

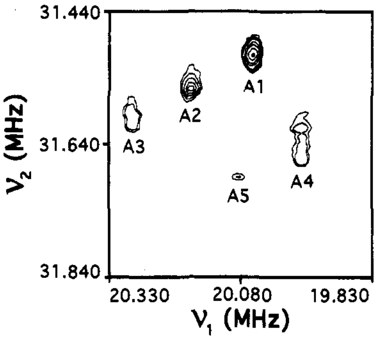

Figure 7. Two-dimensional ^{127}I NQR correlation spectrum of ethylammonium iodide with 97% deuteration on the ammonium group, obtained using the NQ-COSY pulse sequence.[2]

36.8 kHz, consistent with the ammonium group undergoing a three-site jump motion at room temperature. The effect of this hopping motion is to reduce the isotope shift by a factor of 3, while increasing the intensity of the shifted resonance by the same factor (in the limit of low isotope substitution).

In addition to the two singly shifted peaks, in 15% deuterated ethylammonium iodide an additional, weaker peak is seen, shifted by −230 kHz for the 1/2−3/2 transition and by −100 kHz for the 5/2−3/2 transition, or approximately twice the frequency of the **a** site shifted peak. We attribute this to a double substitution at the **a** site. If we assume equilibrium isotope effects to be negligible, the intensities of each isotopomer can be calculated from the percentage of deuteration and the number of hydrogen bonds of each type via a simple binomial distribution. The calculated and experimental data for the 3/2−1/2 transition of 97%-, 15%-, 10%-deuterated samples are listed in Table 3.

Assuming six protons at site **a** and three protons at site **b**, and that the shifts are additive, we can estimate a total isotope frequency shift of −390 kHz in the 3/2−1/2 transition and −711 kHz in the 5/2−3/2 transition for the fully deuterated material, which is in excellent agreement with the observed frequency difference between fully protonated and fully deuterated ethylammonium iodide. These results confirm that the isotope shifts are additive, and that the intensity of each isotopomer exists in a statistical distribution which can be calculated from the crystal structure.

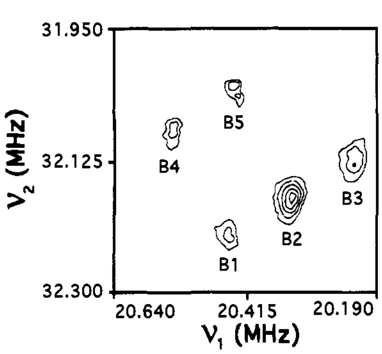

Figure 8. Two-dimensional ^{127}I NQR correlation spectrum of ethylammonium iodide with 15% deuteration on the ammonium group, obtained as for Figure 7.

Table 4. Assigned Environment of the Iodide Ion of Each Isotopomer in Ethylammonium Iodide, Partially Deuterated on the Exchangeable Protons of the Ammonium Group

isotopomer	environment of the iodide ion
A1	$(ND_3^+,ND_3^+)_a(ND_3^+)_b$
A2	$(ND_3^+,ND_2H^+)_a(ND_3^+)_b$
A3	$(ND_3^+,NDH_2^+)_a(ND_3^+)_b$; $(ND_2H^+,ND_2H^+)_a(ND_3^+)_b$
A4	$(ND_3^+,ND_3^+)_a(ND_2H^+)_b$
A5	$(ND_3^+,ND_2H^+)_a(ND_2H^+)_b$
B5	$(NH_3^+,NH_2D^+)_a(NH_2D^+)_b$
B4	$(NH_3^+,NH_3^+)_a(NH_2D^+)_b$
B3	$(NH_3^+,NHD_2^+)_a(NH_3^+)_b$; $(NH_2D^+,NH_2D^+)_a(NH_3^+)_b$
B2	$(NH_3^+,NH_2D^+)_a(NH_3^+)_b$
B1	$(NH_3^+,NH_3^+)_a(NH_3^+)_b$

Two-dimensional correlation spectroscopy allows us to connect each pair of spin transitions. These correlated spectra are shown in Figures 7 and 8. The ν_1 and the ν_2 dimensions correspond to the 3/2−1/2 and 5/2−3/2 transitions, respectively. This experiment allows us to confirm the assignment of connected transitions in the partially deuterated material, and in addition it permits us to visualize the peak due to substitution in both **a** and **b** sites, which is overlapped with other peaks for both the 3/2−1/2 and 5/2−3/2 transitions, but is well separated in the two-dimensional spectrum. Thus, there are five resolved peaks in the two-dimensional spectrum. The two-dimensional spectra of the 97% (Figure 7) and 15% (Figure 8) deuterated material are almost mirror images of each other. Each peak in the two-dimensional spectrum gives a pair of frequencies; the assignment for those isotopomers in 97%- and 15%-deuterated ethylammonium iodide is summarized in Table 4.

The two-dimensional experiment has an additional advantage: because NQR spectra are highly temperature sensitive, sequential measurement of the two transition frequencies may result in inaccuracies arising for a change in temperature between the two measurements. Such inaccuracies could be comparable in magnitude to the isotope shifts, leading to significant errors. In contrast, the two-dimensional spectra measure the two transition frequencies simultaneously, eliminating such systematic errors. From each pair of frequencies, an asymmetry parameter and quadrupolar coupling constant can be determined. These are listed in Tables 5 and 6. The mean values for the Q_{xx}, Q_{yy}, and Q_{zz} elements of the isotope shift tensor in different orientations are shown in Table 7. We calculate a full set of principal values for each isotopomer by adding the perturbed isotope shift tensor elements to those of the unperturbed isotopomer. The differences between the calculated and the experimental values of Q_{xx} and Q_{yy} for the 100%-deuterated isotopomer are +0.069 716 and −0.021 181 MHz, respectively. The slight difference can arise from the isotope effect of those non-hydrogen-bonded protons on the fourth ammonium group which affects the local environment of the iodide ion.

For a free iodide ion, the charge distribution is spherically symmetric and the electric field gradient tensor is zero.

Table 5. Correlated ^{127}I Spin Transition Frequencies, Asymmetry Parameters (η), Quadrupolar Tensor Elements, and Isotope Shift Tensor Elements of 97%-Deuterated Ethylammonium Iodide

Transition Frequency (MHz) and Asymmetry Parameter (η)

isotopomer	$\nu_2(5/2-3/2)$	$\nu_1(3/2-1/2)$	η
A1	31.505 071	20.054 880	0.477 766
A2	31.552 919	20.169 713	0.482 774
A3	31.596 938	20.284 545	0.487 872
A4	31.635 215	19.954 402	0.466 777
A5	31.688 803	20.078 803	0.472 223

Quadrupolar Tensor Elements (MHz)

isotopomer	Q_{xx}	Q_{yy}	Q_{zz}
A1	−28.553 186	−80.797 080	109.350 267
A2	−28.343 418	−81.254 402	109.597 819
A3	−28.124 593	−81.709 690	109.834 283
A4	−29.227 122	−80.397 379	109.624 501
A5	−29.000 802	−80.897 187	109.897 989

Table 6. Correlated ^{127}I Spin Transition Frequencies, Asymmetry Parameters (η), Quadrupolar Tensor Elements, and Isotope Shift Tensor Elements of 15%-Deuterated Ethylammonium Iodide

Transition Frequency (MHz) and Asymmetry Parameter (η)

isotopomer	$\nu_2(5/2-3/2)$	$\nu_1(3/2-1/2)$	η
B1	32.222 967	20.439 761	0.473 545
B2	32.171 053	20.329 952	0.469 007
B3	32.125 837	20.220 144	0.464 168
B4	32.078 947	20.534 498	0.484 430
B5	32.042 105	20.424 689	0.479 404

Quadrupolar Tensor Elements (MHz)

isotopomer	Q_{xx}	Q_{yy}	Q_{zz}
B1	−29.421 481	−82.350 792	111.772 273
B2	−29.607 559	−81.910 182	111.517 741
B3	−29.814 276	−81.467 926	111.282 202
B4	−28.730 718	−82.721 747	111.452 466
B5	−28.955 846	−82.285 407	111.241 254

Table 7. Average Values of the Isotope Shift Tensor Elements (MHz) of Iodine in Ethylammonium Iodide with Isotope Substitution at Different Orientations of the Ammongium Group around the Iodide Ion

orientation	ΔQ_{xx}	ΔQ_{yy}	ΔQ_{zz}
a	−0.210 414	0.457 387	−0.246 973
b	0.687 019	−0.389 809	−0.297 210

Table 8. Nuclear Quadrupole Moments and Sternheimer Antishielding Factors Assumed in the Present Work[13]

nucleus	iodine	bromine
quadrupole moment ($\times 10^{-28}$ m^2)	0.69	0.33
Sternheimer antishielding factor	−162.42	−85.517

Table 9. Calculated Quadrupole Coupling Constants and ^{79}Br Resonance Frequencies of Each Isotopomer in Partially Deuterated Ethylammonium Bromide

environment of bromide	QCC, MHz	ν, MHz
$(NH_3^+, NH_3^+)_a(NH_3^+)_b$	32.5899	16.8930
$(NDH_2^+, NH_3^+)_a(NH_3^+)_b$	32.5156	16.8433
$(NH_3^+, NH_3^+)_a(NDH_2^+)_b$	32.4966	16.8719
$(ND_3^+, ND_3^+)_a(ND_3^+)_b$	31.8837	16.5372
$(NHD_2^+, ND_3^+)_a(ND_3^+)_b$	31.9561	16.5871
$(ND_3^+, ND_3^+)_a(NHD_2^+)_b$	31.9639	16.5522

However, the intermolecular hydrogen bonds in ethylammonium iodide distort the charge distribution around the iodide ion, changing the electric field gradient tensor. Substitution of a hydrogen-bonded proton by a deuterium changes the size of this tensor, presumably because the root-mean-cubed distance between the deuterium and the iodide ion is different from that of a proton as a result of zero-point motion. One might expect, therefore, that the isotope shift should be uniformly negative and axially symmetric along the hydrogen-bonding direction.

However, the isotope shift tensor is a small perturbation on a much larger quadrupolar tensor, and as a result only the diagonal elements of the shift tensor in the frame of reference of the quadrupolar principal axis system can contribute to the overall frequency shift. Therefore, the isotope effect on the quadrupolar tensor will depend on the orientation of the isotope-substituted hydrogen bond with respect to the quadrupolar principal axis system. Since the full isotope shift tensor is unknown, and only its projection onto the quadrupolar axis system can be determined, it is impossible to unambiguously determine the orientation of the quadrupolar tensor relative to a single hydrogen bond. However, because in this case we have two different orientations of hydrogen bonds whose relative orientation can be inferred approximately from the crystal structure, we can infer the overall quadrupolar tensor orientation.

The additivity of the isotope frequency shifts is also explained by the fact that the isotope shift tensors are small perturbations on a much larger quadrupolar frequency tensor. Since the change in orientation of the quadrupolar tensor upon isotope substitution can be neglected to first order, successive substitutions have identical effects on the overall tensor, and in particular substitution on two different **a** ammonium groups has the same effect as double substitution on the same **a** ammonium group. This would not be the case if the isotope replacement were not a small perturbation, since the hydrogen bonds to the two groups are not collinear. The truncated shift tensor is approximately axially symmetric along the quadrupolar z axis in trimethylammonium iodide so that we can assume the hydrogen bond is along the quadrupolar z axis. The unique principal value of the measured untruncated full shift tensor (defined as the difference between the protonated and deuterated quadrupole coupling constants) is 4.55 MHz. The lengths of the hydrogen bonds in ethylammonium iodide at the site **a** and site **b** directions are 2.6 and 2.5 Å, respectively, which is comparable to that of the hydrogen bond in trimethylammonium iodide. It is likely, therefore, that the magnitude of the untruncated shift tensor in ethylammonium iodide should be approximately equal to one-third of that in trimethylammonium iodide (due to the three-site hopping motion). Tilting the hydrogen bond from the quadrupolar z axis into the xy plane scales the truncated shift tensor element ΔQ_{zz} by $(1 - 3\cos^2\theta)/2$ and ΔQ_{xx} by $(1 - 3\sin^2\theta\cos^2\phi)/2$. As a result, the polar angles θ and ϕ relating the quadrupolar principal axis system to the hydrogen bond vector in ethylammonium iodide at site **a** are approximately 47° and −25°, or 47° and −155°, and at site **b** are approximately 46° and 80°. This gives an angle of 71° or 80° between two hydrogen bonds of the **a** and **b** sites, which is in excellent agreement with the crystallographic estimate of 76°.

III. Calculation of Resonance Frequencies in Isomorphous Structures. In isomorphous crystals, equivalent halide sites may be expected to have identical or nearly identical electric field gradients. The small difference in the volume of the unit cells can be corrected for (to first order) by assuming that the EFG scales proportional to the inverse of the volume. The (dimensionless) asymmetry parameters for the two isomorphs can therefore be expected to be almost identical, while the quadrupolar coupling constants will be related by the ratio of the products of nuclear quadrupole moments and the Sternheimer antishielding factors. Using the coupling constants and asymmetry parameters for each of the iodide isotopomers, and the quadrupole moments and Sternheimer factors shown in Table 8, we can therefore calculate the quadrupolar frequencies for the corresponding bromide isotopomers, for which accurate asymmetry parameters are not independently available. These calculated results are listed in Table 9. The agreement is excellent; calculated frequencies fall within 10% of the experimental values listed in Table 2. Thus, while it is not presently feasible to obtain full isotope tensors for spin 3/2 ions such as bromide, indirect estimation of the isotope shifts using data from the corresponding iodide ions allows us to reproduce the shifts accurately.

Conclusion

Halogen resonance frequencies are very sensitive to the binding site of the nucleus and its coordinating groups at zero field. Secondary isotope shifts are sensitive to the nature of the coordinating groups and to their geometry. The halogen resonance frequency and the intensity for each isotopomer can also be predicted by simple statistical analysis. Quantitative analysis of ethylammonium iodide using two-dimensional correlation spectroscopy not only provides an excellent prediction of the quadrupolar tensor elements of each isotopomer, but also gives a good approach to understand the geometry of the hydrogen bonds. These spectra potentially provide a new way to explore the structure of halide ion binding sites in biological systems.

Acknowledgment. We thank Hongyue Yu and Andris Slokenbergs who worked on the early glycine data, Dr. Mieng-Hua Wann who provided [$^2H_9$]trimethylammonium bromide, and Dr. Adilgiry Kusov and Raju Subramanian for informative discussions. This research was supported by grants from the Procter and Gamble Co. in conjunction with an NSF Presidential Young Investigator Award to G.S.H. (Grant DOB 9057765), by a Dreyfus Foundation Teacher Scholar Award (also to G.S.H.), and by the National Institutes of Health (Grant GM-39071).

JA941883V