Multinuclear Solid-State Nuclear Magnetic Resonance and Density Functional Theory Characterization of Interaction Tensors in Taurine

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ABSTRACT: A variety of experimental solid-state nuclear magnetic resonance (NMR) techniques has been used to characterize each of the elements in 2-aminoethane sulfonic acid (taurine). A combination of 15N cross-polarization magic angle spinning (CPMAS), 17O ultrawideline, and 18O overtone experiments enabled a determination of the relative orientation of the nitrogen electric field gradient and chemical shift tensors. 17O spectra recorded from an isotopically enriched taurine sample at multiple magnetic fields allowed the three nonequivalent oxygen sites to be distinguished, and NMR parameters calculated from a neutron diffraction structure using density functional theory allowed the assignment of the 17O parameters to the correct crystallographic sites. This is the first time that a complete set of 17O NMR tensors are reported for a sulfonate group. In combination with 1H and 13C MAS spectra, as well as a previously reported 33S NMR study, this provides a very broad set of NMR data for this relatively simple organic molecule, making it a potentially useful structure on which to test DFT calculation methods (particularly for the quadrupolar nuclei 14N, 17O, and 33S) or NMR crystallography approaches.

1. INTRODUCTION

Solid-state nuclear magnetic resonance (NMR) spectroscopy is one of the premier techniques for the structural characterization of materials, capable of providing detailed information on the local structure and dynamics in a broad range of systems. For the study of crystalline samples, a combination of solid-state NMR experiments and density functional theory (DFT) calculations can be particularly powerful. Gauge-including projector augmented wave (GIPAW) methods that take into account the infinite periodic lattice can be used to calculate NMR parameters to a high degree of accuracy, thereby allowing the exquisite sensitivity of the measured NMR parameters to the crystal or molecular structure to be fully exploited, for example to refine an X-ray diffraction structure. Such approaches are now often referred to as NMR crystallography. Spin-half nuclei such as 1H, 13C, or 29Si have been used to refine structures via their isotropic chemical shifts, chemical shift anisotropies, or spin diffusion properties. Parameters measured from quadrupolar nuclei have also been used to refine crystal structures, but due to various associated difficulties such as low sensitivities or large anisotropic interactions, such nuclei are far more seldom used in NMR crystallography. This is unfortunate, since quadrupolar nuclei are capable of providing a wealth of local structural information. In particular, the electric field gradient (EFG) offers a probe of the local electronic environment that is highly sensitive to the surrounding structure, particularly hydrogen bonding arrangements.

Herein, we present multinuclear solid-state NMR measurements for taurine, which features three challenging quadrupolar nuclei: 14N (nuclear spin I = 1), 17O (I = 5/2), and 33S (I = 3/2). This is therefore a potentially useful system on which to test out new experimental or computational methodologies. By use of a combination of 15N and 14N methods, we obtain a full set of NMR parameters for the nitrogen site, including a determination of the relative orientation of the EFG and chemical shift (CS) tensors. Parameters for the three nonequivalent oxygen sites are also obtained from an isotopically enriched sample and assigned to the correct crystallographic sites with the aid of DFT calculations. Solid-state 1H and 13C NMR spectra are also presented, which, in combination with a previous 33S study, constitutes a near-complete set of NMR results for this model system.

2. EXPERIMENTAL DETAILS

a. Sample Details. For the solid-state 1H, 13C, 14/15N NMR experiments, a natural abundance sample of taurine (>99% pure, purchased from Sigma Aldrich) was used. For the 17O NMR experiments, 17O-enriched taurine was synthesized in the following manner. Sodium sulfite (300 mg, 2.38 mmol) was dissolved in [17O]-water (1.16 g, 41%17O-enriched, purchased from CortecNet). The solution was kept at room temperature for 23 h. 2-Bromoethylamine hydrochloride (585 mg, 2.86 mmol) was then added to the solution. The mixture was stirred at 65 °C in an oil bath for 13 h. The [17O]-water was recovered.

The residual material was refluxed in methanol (30 mL) for 30 min, cooled to room temperature, collected (filtration), washed through sintered glass. Ethanol (35 mL) was then added to the solution. The mixture was stirred at 80 °C for 30 min, cooled to room temperature, collected (filtration), washed with ethanol (2 × 10 mL), and dried at 80 °C. The crude product was dissolved in 1 mL of 40% hydrobromic acid and filtered through sintered glass. Ethanol (35 mL) was added to the filtrate to precipitate out the product. The solid material was then washed...
with ethanol (4 × 10 mL) and dried at 80 °C, giving 220 mg of white solid (74% yield). The 17O enrichment of the product was determined to be 23% by solution 17O NMR.

b. Solid-State NMR Experiments. The 1H, 13C, and 15N NMR spectra were recorded on an 11.7 T Bruker Avance III spectrometer using Varian double-resonance probes with a 3.2 mm rotor diameter and 20 kHz MAS rate for the 1H experiment and a 4.0 mm rotor diameter and 10 kHz MAS rate for the 13C and 15N experiments. The 1H spectrum was acquired using a windowed DUMBO pulse sequence for homonuclear decoupling, with a 2.8 μs π/2 pulse, a 24 μs DUMBO pulse length (ν1 = 71 kHz), a recycle delay of 5 and 4 scans acquired. For the 13C experiment, a 2 μs excitation pulse was applied with continuous-wave 1H decoupling of ~40 kHz power, a recycle delay of 2 min and 32 scans acquired. The 15N spectrum was acquired with cross-polarization from the 1H nuclei using a 1H π/2 pulse of 4 μs, 1.5 ms constant-amplitude contact pulses (ν1 = 55 kHz), a recycle delay of 2.5, and 1000 scans acquired. The 1H and 13C spectra are referenced to tetramethylsilane and the 15N spectrum to solid NH4Cl.

The 14N overtone NMR spectrum was recorded on a 21.1 T Bruker Avance II spectrometer (Ultrahigh-field NMR Facility for Solids, Ottawa, Canada) using a home-built double-resonance static probe with a 7.0 mm inner-diameter coil size. A 25-μs on-resonance excitation pulse (ν1 = 80 kHz as measured on the "H nucleus, which is close in frequency to the 14N overtone transition) was used with continuous-wave 1H decoupling of ~80 kHz power, a recycle delay of 1 s, and 50,000 scans acquired. The spectrum is referenced such that 0 kHz corresponds to exactly twice the 14N fundamental (single-quantum) frequency of solid NH4Cl.

The 17O NMR spectra were recorded at 11.7 and 21.1 T on Bruker Avance and Bruker Avance II spectrometers, respectively. The static and 1D MAS spectra were acquired using a spin–echo pulse sequence (π/2–τ–π/2–acquire). At 11.7 T, both nonspinning and MAS experiments were performed on a Bruker 4.0 mm double resonance MAS probe, the latter with a MAS rate of 12.0 kHz and 512 scans acquired with a recycle delay of 1 s. To obtain a high-quality static spectrum at this field, 8854 scans were acquired with a recycle delay of 5 s. At 21.1 T, nonspinning experiments were performed on a home-built static probe with the sample packed in a 5.0 mm Teflon tube, while MAS and 3QMAS experiments were performed on a Bruker 4.0 mm MAS probe with the sample packed in a Si3N4 rotor spinning at 12.5 kHz. For both MAS and static spectra, a spin–echo sequence was used with a pulse delay of 50 μs, 256 scans acquired and a recycle delay of 20 s. In the 3QMAS experiment, the t1 increment was synchronized with the sample spinning and a total of 48 t1 increments were collected with 192 scans each and a recycle delay of 15 s.

Spectral processing was carried out using the NUTS software (Acorn NMR). The 17O spectra were simulated using Dmfit. The 14N overtone powder pattern was simulated using RMNSim.

c. DFT Calculations. DFT calculations were carried out on a neutron diffraction structure (CCSD code TAURIN03) using the CASTEP software and the Materials Studio 4.3 program (Accelrys) running on a Linux server with 8 processing cores and 32 GB of RAM. Perdew, Burke, and Ernzerhof (PBE) functionals were used with a plane wave basis set cutoff of 610 eV and a 3 × 1 × 2 Monkhorst-Pack k-space grid. Electric field gradient and chemical shielding tensors were
calculated for all nuclei. Because of the relatively high degree of accuracy for this crystal structure, no geometry optimization was performed. DFT optimizations of the proton positions in this structure have previously been shown to yield calculated $^{14}$N and $^{33}$S NMR parameters that agree less well with experimental values than those obtained from the unoptimized structure. $^{11}$

Calculated isotropic shielding values $\sigma_{\text{calc}}$ for $^1$H, $^{13}$C, and $^{17}$O were converted to isotropic chemical shifts $\delta_{\text{calc}}$ using the expression $\delta_{\text{calc}} = \sigma_{\text{ref}} - \sigma_{\text{calc}}$, with values for $\sigma_{\text{ref}}$ previously reported as $\sigma_{\text{ref}}(^1$H) = 30.8 ppm, $\sigma_{\text{ref}}(^{13}$C) = 170.0 ppm, and $\sigma_{\text{ref}}(^{17}$O) = 265 ppm. $^9$ For $^{14}$N, the relation $\delta_{\text{calc}} = 201.4 - 1.05\sigma_{\text{calc}}$ was used, having been determined in a previous study. $^{17}$

To attempt to account for thermal vibrations in the DFT calculations of the NMR parameters, a molecular dynamics simulation was also carried out using the CASTEP software $^{16}$ following a procedure recently reported. $^{18}$ This used a cutoff energy of 550 eV and a $3 \times 1 \times 2$ Monkhorst Pack grid. The temperature was set at 290 K using a Nose thermostat in the NVT ensemble. The time step was set to 1 fs with a total time of 6 ps.

3. RESULTS AND DISCUSSION

3.1. $^1$H and $^{13}$C NMR Spectra. The zwitterionic molecular structure of 2-aminoethane sulfonic acid (taurine) in its crystalline form is shown in Figure 1. The crystal structure is monoclinic with four molecules per unit cell and a cell volume of 486 Å$^3$. $^{15}$ The asymmetric unit contains a single molecule, so all atoms in the molecule are crystallographically distinct, resulting in seven hydrogen sites, two carbon sites, three oxygen sites, and a single nitrogen and sulfur site.

A $^1$H MAS NMR spectrum obtained from taurine at 11.7 T is shown in Figure 2a. Two peaks are observed and are assigned to the NH$_3$ protons (7.6 ppm) and CH$_2$ protons (3.3 ppm) on the basis of the isotropic chemical shifts calculated from the crystal structure (Table 1). The calculated shifts for the four crystallographically distinct CH$_2$ protons are clustered within 0.5 ppm of each other, and the experimental $^1$H NMR peaks are not individually resolved even with the use of the DUMBO

Table 1. $^1$H and $^{13}$C Isotropic Chemical Shift Values for the Seven Crystallographically Distinct Hydrogen Sites and Two Distinct Carbon Sites in Taurine, Calculated from the Crystal Structure Using DFT$^9$

<table>
<thead>
<tr>
<th>site</th>
<th>calculated $\delta_{\text{iso}}$/ppm</th>
<th>experimental $\delta_{\text{iso}}$/ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>H1</td>
<td>8.1</td>
<td>7.6(1)</td>
</tr>
<tr>
<td>H2</td>
<td>5.8</td>
<td></td>
</tr>
<tr>
<td>H3</td>
<td>6.4</td>
<td></td>
</tr>
<tr>
<td>H4</td>
<td>3.2</td>
<td>3.3(1)</td>
</tr>
<tr>
<td>H5</td>
<td>3.7</td>
<td></td>
</tr>
<tr>
<td>H6</td>
<td>3.4</td>
<td></td>
</tr>
<tr>
<td>H7</td>
<td>3.4</td>
<td></td>
</tr>
<tr>
<td>C1</td>
<td>43.9</td>
<td>46.5(1)</td>
</tr>
<tr>
<td>C2</td>
<td>32.9</td>
<td>35.8(1)</td>
</tr>
</tbody>
</table>

*Because of peak overlap, experimental $^1$H isotropic chemical shift values correspond to the peak maxima for the two groups of sites indicated.

Figure 3. (a) $^{15}$N CPMAS NMR spectrum of taurine at 11.7 T, (b) $^{14}$N overtone spectrum obtained from a static powder sample at 21.1 T, (c) simulation of the overtone powder pattern made using the parameters given in Table 2 (including the quadrupolar interaction and the chemical shift anisotropy), and (d) simulation neglecting the effects of the chemical shift anisotropy.
homonuclear decoupling pulse sequence. The three NH₃ protons are also unresolved in the experimental spectrum, despite the calculated isotropic shift values being spread over a range of 2.3 ppm. The convergence of the NH₃ proton chemical shifts to a single, relatively sharp peak is due to the rotational dynamics of this amine group which are unaccounted for in the DFT calculations. There have been a large number of NMR studies of NH₃ group rotations in crystalline amino acids, particularly H relaxation measurements and ²H line shape studies, and typically, jump rates for the NH₃ groups in these systems are on the order of 10⁹ s⁻¹ at room temperature. The molecular dynamics simulation carried out on this structure showed considerable librational motion of the NH₃ group, but interchange of the hydrogen sites was not observed due to the extremely short time scale of the simulation (6 ps). To account for these fast thermal motions in our calculations, a new set of NMR parameters for all nuclei were obtained from the MD simulation by averaging the tensor elements calculated from 46 individual frames spaced 50 fs apart. This approach was successfully used previously to improve calculated ¹³C chemical shift anisotropies; however, in this case it did not result in an improved agreement with our experimental values for this system, and these parameters are therefore not shown.

The two carbon sites are well-resolved in the ¹³C NMR spectrum with isotropic chemical shifts of 46.5 and 35.8 ppm (Figure 3), and on the basis of the calculated values (Table 1) these can be assigned to sites C1 and C2, respectively. This assignment is consistent with the observation of a much shorter spin–lattice relaxation time for the peak at 35.8 ppm. The C2 carbon is directly bonded to a nitrogen site; therefore all C₂ found elsewhere. Parameters for the ³³S nucleus are reported in reference 11.

### Table 2. Experimental (Bold) and Calculated NMR Parameters for the Nitrogen and Three Nonequivalent Oxygen Sites in Taurine

<table>
<thead>
<tr>
<th></th>
<th>δiso/ppm</th>
<th>Ω/ppm</th>
<th>κ</th>
<th>CQ/MHz</th>
<th>ηQ</th>
<th>α/deg</th>
<th>β/deg</th>
<th>γ/deg</th>
</tr>
</thead>
<tbody>
<tr>
<td>¹⁴N exptl</td>
<td>6.0(2)</td>
<td>18(5)</td>
<td>0.16(30)</td>
<td>1.19(1)</td>
<td>0.18(1)</td>
<td>270(50)</td>
<td>77(3)</td>
<td>90(15)</td>
</tr>
<tr>
<td>¹⁴N calc</td>
<td>9.1</td>
<td>12</td>
<td>0.05</td>
<td>1.29</td>
<td>0.36</td>
<td>251</td>
<td>86</td>
<td>352</td>
</tr>
<tr>
<td>¹⁷O (O1) exptl</td>
<td>170(4.2)</td>
<td>88(10)</td>
<td>0.75(10)</td>
<td>6.70(2)</td>
<td>0.14(4)</td>
<td>90(10)</td>
<td>20(2)</td>
<td>90(10)</td>
</tr>
<tr>
<td>¹⁷O (O1) calc</td>
<td>178.2</td>
<td>115</td>
<td>0.36</td>
<td>−7.17</td>
<td>0.08</td>
<td>266</td>
<td>−15</td>
<td>250</td>
</tr>
<tr>
<td>¹⁷O (O2) exptl</td>
<td>179.0(2)</td>
<td>88(10)</td>
<td>0.68(10)</td>
<td>6.65(2)</td>
<td>0.16(4)</td>
<td>0(10)</td>
<td>2(2)</td>
<td>0(10)</td>
</tr>
<tr>
<td>¹⁷O (O2) calc</td>
<td>187.3</td>
<td>88</td>
<td>0.53</td>
<td>−6.97</td>
<td>0.16</td>
<td>123</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>¹⁷O (O3) exptl</td>
<td>187.4(2)</td>
<td>78(10)</td>
<td>0.69(10)</td>
<td>6.80(2)</td>
<td>0.05(4)</td>
<td>0(10)</td>
<td>2(2)</td>
<td>2(2)</td>
</tr>
<tr>
<td>¹⁷O (O3) calc</td>
<td>190.8</td>
<td>65</td>
<td>0.67</td>
<td>−6.76</td>
<td>0.04</td>
<td>10</td>
<td>−11</td>
<td>17</td>
</tr>
</tbody>
</table>

*Calculated isotropic shielding values were converted to chemical shifts δiso based on previously reported empirical relations for nitrogen and oxygen. Also shown are the span (Ω) and skew (κ) of the CS tensor, the quadrupolar coupling constant (CQ) and asymmetry parameter (ηQ), and the Euler angles (α, β, and γ) describing the relative orientations of the CS and EFG tensors. Definitions of these parameters are standard and can be found elsewhere. Parameters for the ³³S nucleus are reported in reference 11.*

### 3.2. ¹⁴N and ¹⁵N NMR Spectra

An accurate isotropic chemical shift for the nitrogen site (−6.0 ppm) was obtained from the ¹⁴N CPMAS spectrum (Figure 3a). Along with the quadrupolar coupling constant (CQ) and asymmetry parameter (ηQ) that were recently determined using ultrawide line ¹⁴N techniques, this provides constraints for the fitting of the ¹⁴N overtone powder pattern obtained at 21.1 T (Figure 3b). ¹⁴N overtone NMR spectra, in which the nuclei are irradiated at approximately twice the Larmor frequency in order to directly excite and observe the Doppler 2 “overtone” transitions, are insensitive to the first-order quadrupolar interaction, which for ¹⁴N is typically on the order of several MHz. The ¹⁴N overtone powder pattern widths are therefore typically on the order of kHz, and perturbations due to both the second-order quadrupolar interaction and chemical shift anisotropy can be resolved, particularly at high field strengths where the effects of the CSA are more pronounced. Such experiments therefore provide a potentially straightforward way of determining the relative orientations of the nitrogen EFG and CS tensors from a powder sample. The simulated ¹⁴N overtone powder pattern of (a) nitrogen, (b) sulfur, and (c) the three oxygen sites in the molecular frame of taurine.
shown in Figure 3c was fitted to the experimental spectrum by manually adjusting the CS tensor parameters (the span $\Omega$ and skew $\kappa$) and Euler angles ($\alpha$, $\beta$, and $\gamma$) while keeping $\delta_{ij}$, $C_{ij}$, and $\eta_{ij}$ fixed to their experimental values. The resultant, complete set of $^{14}$N interaction parameters are presented in Table 2. Experimental uncertainties are larger for certain parameters than others, indicating that these parameters had a relatively minor effect on the shape of the simulated overtone powder pattern (e.g., the pattern shape was extremely sensitive to the value of the Euler angle $\beta$, but far less so to $\alpha$). Overall, the agreement between the experimental and calculated $^{14}$N parameters is reasonably good. The overestimation of the calculated $C_Q$ by 100 kHz is of the same magnitude observed in a previous $^{14}$N study. The fitting of the static overtone powder pattern using constraints from $^{15}$N and ultrawideline $^{14}$N experiments represents a more straightforward approach that is analogous to the way Euler angles are commonly determined for half-integer quadrupolar nuclei, where static central-transition powder patterns are fitted using constraints from MAS spectra (vide infra).

DFT calculations allow the (calculated) orientations of the EFG and CS tensors to be visualized in the molecular frame, and this is illustrated for the nitrogen site in Figure 4a. The largest principal component of the EFG tensor ($V_{33}$) and the least shielded component of the CS tensor ($\delta_{11}$) are predicted to be aligned approximately parallel to the N–C bond. These orientations are consistent with previous DFT studies of amino groups. The correct CS tensor orientation for the $^{33}$S nucleus, which was mislabeled in a previous publication, is also shown in Figure 4b for completeness. The least shielded component of

Figure 5. Experimental MAS (a and b) and static (c and d) $^{17}$O NMR spectra (black) obtained from an isotopically enriched sample of taurine at the magnetic field strengths shown. Spectra (a) and (b) were recorded at 12.5 and 12.0 kHz MAS, respectively. Asterisks denote spinning sidebands. Red traces show fitted simulations, with the individual simulated lineshapes for sites O1, O2, and O3 shown below in green, purple, and blue, respectively.
the $^{35}$S CS tensor ($\delta_{11}$) lies approximately parallel to the S–C bond.

3.3. $^{17}$O NMR Spectra. Taurine has three inequivalent oxygen sites in similar structural environments, but despite considerable overlap of the $^{17}$O powder patterns, these sites could be distinguished on the basis of multiple-field MAS and static NMR spectra (Figure 5). EFG parameters and isotropic chemical shifts were measured from the MAS spectra and then fixed during fits of the static spectra, allowing the CS tensors and Euler angles to be quantified. The calculated $^{17}$O parameters for these sites show reasonably good agreement with the experimental values, allowing the assignment of the NMR parameters to the correct crystallographic sites. The EFG and CS tensor orientations for all three oxygen sites are shown in Table 2.

To further confirm the accuracy of the $^{17}$O NMR parameters, we obtained a 3QMAS spectrum from the enriched taurine. As seen from Figure 6, three well-resolved peaks are observed in the isotropically enriched sample of taurine at 21.1 T. G.W. thanks the National Ultrahigh-Field NMR Facility for Solids, Ottawa (www.nmr900.ca). We are grateful to Drs. Eric Ye and Victor Terskikh for assistance in setting up the $^{1}H$ DUMBO experiment and for helpful discussions. Access to the 21.1 T NMR instrument was provided by the National Ultrahigh-Field NMR Facility for Solids, Ottawa (www.nmr900.ca).

4. SUMMARY

Experimental NMR parameters have been obtained for $^{1}H$, $^{13}$C, $^{14/15}$N, and $^{17}$O in crystalline taurine. The use of a combination of $^{13}$C CP MAS, $^{14}$N static ultraslowine, and $^{14}$N overtone NMR spectroscopy provided a relatively straightforward method for determining the relative orientation of the nitrogen EFG and CS tensors. $^{17}$O NMR parameters were also measured for the three nonequivalent oxygen sites using multiple-field static, MAS, and 3QMAS experiments. Along with a previous $^{35}$S study, this constitutes a large and varied set of data on this relatively simple crystalline structure, making it a potentially useful system on which to test DFT calculation methods or NMR crystallography approaches, particularly for the quadrupolar nuclei. NMR parameters calculated from an unoptimized neutron diffraction structure showed a good overall agreement with experimental values, though there appears to be some room for improvement. This may come from an improved crystal structure, more accurate computational methods (e.g., improved pseudopotentials or methods that account for dynamics), or a combination of the two. Ultimately, it is anticipated that more accurate DFT calculations for quadrupolar nuclei will allow a refinement of crystal structures such as this using the broad range of experimental NMR parameters available from such nuclei.

ASSOCIATED CONTENT

Supporting Information

Further examples of simulated $^{14}$N static overtone powder patterns. This material is available free of charge via the Internet at http://pubs.acs.org.

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REFERENCES