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A Solid-State ¹⁷O NMR Study of Carboxylic Acid Dimers: Simultaneously Accessing Spectral Properties of Low- and High-Energy Tautomers

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Abstract

We report a solid-state ¹⁷O NMR study of several crystalline carboxylic acids. We found that, while each of these compounds forms discrete hydrogen-bonded dimers in the crystal lattice, their solid-state ¹⁷O magic-angle spinning (MAS) NMR spectra display quite different features and different temperature dependences. We showed that experimentally observed ¹⁷O NMR spectral behaviors can be explained as due to thermal averaging between the two tautomers that are produced as a result of concerted double hydrogen hopping dynamics within each dimer. In general, the two tautomers have different energies due to intramolecular interactions and crystal packing. From an analysis of variable-temperature ¹⁷O MAS NMR spectra, energy asymmetry between the two tautomers was experimentally determined for each of the carboxylic acid compounds studied. The same data analysis also offers an opportunity to simultaneously assess ¹⁷O NMR parameters in both low- and high-energy tautomers. We concluded that the periodic plane-wave DFT calculations can produce reliable ¹⁷O NMR parameters (chemical shift and quadrupolar coupling tensors) for both tautomers. The same periodic DFT calculations have also produced reasonable energy asymmetry values for the studied carboxylic acid dimers. We have also observed substantial H/D isotope shifts in solidstate ¹⁷O NMR.

1. Introduction

Simple carboxylic acids are known to have great tendency to form hydrogen-bonded dimers in the solid state.¹⁻² Within each dimer, the two protons can undergo concerted double-jumps to produce two tautomers or configurations, A and B, as illustrated in From the carbon-oxygen bonding perspective, the consequence of Figure 1. interchanging the A and B tautomers is to interchange the C–O with C=O bonds. For an isolated carboxylic acid dimer, the two tautomers would have identical energies. In the solid state, however, the two tautomers will generally have different energies due to crystal packing. In some extreme cases, both intra- and inter-molecular interactions strongly favour one tautomer over the other. While in principle the double proton transfer occurs in a two-dimensional (2D) potential energy surface, it is often instructive to think of the problem by using an over-simplified 1D double-well potential energy curve as shown in Figure 1. The energy barrier is defined as V_0 and the energy asymmetry between the two tautomers is usually denoted as ΔE (it is sometimes defined as A). In the past several decades, a large number of investigations have been conducted to probe the dynamics of the concerted double hydrogen hopping process in this type of hydrogen-bonded systems.³⁻⁴⁰ At high temperatures (e.g. > 50 K), the double proton transfer can be considered to be a classic Arrhenius-type over-the-barrier process. At low temperatures, however, the proton transfer dynamics is largely due to incoherent quantum tunnelling between the two vibrational ground states, $v_A^{(0)}$ and $v_B^{(0)}$. Thus, at low temperatures below 50 K, the rate of proton transfer is still on the order of 10^8 s⁻¹ and does not display any temperature dependence. This proton jump rate can be as high as 10¹² s⁻¹ at high temperatures. Because the proton jump rate is almost always much faster

than the NMR timescale, any observed NMR spectral parameter corresponds to the averaged value between those in the two tautomers. That is, the two tautomers are not accessible separately in systems where ΔE is small. While most previous studies have focused on the quantum tunnelling nature of the proton transfer dynamics in carboxylic acid dimers, little attention has been paid to the evaluation of the observed NMR properties and their links to those in both low- and high-energy tautomers. The main objective of this study is to investigate whether we can infer the ¹⁷O NMR properties of the two tautomers by examining the temperature dependence of the experimental ¹⁷O NMR parameters, which are only the averaged results between the two tautomers. It should be noted that early ¹⁷O nuclear quadrupole resonance (NQR) studies by Smith and co-workers^{5, 9} provided perhaps the strongest evidence to support the double proton transfer model in carboxylic acid dimers. The advantage of solid-state ¹⁷O NMR over NQR is that it can produce information about both ¹⁷O magnetic shielding and quadrupole coupling (QC) tensors.

In this work, we conducted a comprehensive solid-state ¹⁷O NMR study of several carboxylic acid dimers where the carboxylate groups are labeled by ¹⁷O: [1,2-¹⁷O₂]benzoic acid (BA), [1,2-¹⁷O₂]salicylic acid (SA), [1,2-¹⁷O₂]Aspirin (ASA), [1,2-¹⁷O₂]cinnamic acid (CA), [1,2-¹⁷O₂]-4-methoxycinnamic acid (MCA). The crystal structures of these compounds indicate that they all form the same basic carboxylic acid dimer structure in the solid state.⁴¹⁻⁴⁵ While solid-state ¹⁷O NMR has been used to study many organic compounds in the past 20 years,⁴⁶⁻⁵⁰ only some preliminary solid-state ¹⁷O NMR data were reported previously for carboxylic acid dimers such as BA, SA, ASA, ibuprofen, and terephthalic acid.⁵¹⁻⁵⁴ In particular, Kong et al.⁵³ found that the ¹⁷O MAS

NMR spectra of ASA and SA exhibit very different temperature dependencies. In the present work, we further examined the temperature dependence of ¹⁷O MAS NMR spectra for this class of compounds. To aid spectral analysis, we employed periodic plane-wave DFT computations to evaluate the ¹⁷O NMR parameters in both low- and high-energy tautomers. Finally, we will address how the experimental variable-temperature ¹⁷O NMR data can be properly interpreted to obtain new information about ¹⁷O NMR spectral properties in low- and high-energy tautomers.

2. Experimental section

2.1 Synthesis

Preparations of $[1,2^{-17}O_2]BA$ -H, $[1,2^{-17}O_2]SA$, $[1,2^{-17}O_2]ASA$, and $[1,2^{-17}O_2]MCA$ were described previously.^{51, 53, 55} $[1,2^{-17}O_2]BA$ -D was obtained by dissolving $[1,2^{-17}O_2]BA$ in an acetone/D₂O mixture. $[1,2^{-17}O_2]CA$ was prepared in the following fashion. $[1^{7}O_4]Malonic$ acid (250 mg, 18% ¹⁷O-enrichment, prepared by heating malonic acid in 40% ¹⁷O-enriched water) was mixed with benzaldehyde (252 mg) and piperidine (two drops) in 4 mL pyridine. The mixture was heated at reflux (oil bath temperature 90 \Box C)

for 12 h. After the solution was cooled to room temperature, solvent was then evaporated on a rotary evaporator to give a paste. This material was dissolved in 1.5 mL ethanol. Upon addition of cold 0.5 M HCl (10 mL), precipitates formed, which were collected by filtration, first washed with cold 0.5 M HCl (8 mL) and then with water (2×5 mL). The solids were initially air dried and then further dried on vacuum. The final product was obtained as a white solid with a distinct honey-like smell (270 mg). The ¹⁷O-enrichment

level in $[1,2-{}^{17}O_2]CA$ was estimated to be 18% based on the ${}^{17}O$ NMR signal integral with respect to that of the solvent (acetone-d₆).

2.2 Solid-state NMR experiments

Preliminary ¹⁷O MAS NMR experiments were performed at 14.1 T (Queen's University) and 21.1 T (National Ultrahigh Field NMR Facility for Solids, Ottawa, Canada). Variable-temperature (VT) ¹⁷O MAS NMR spectra were obtained at 21.1 T at the National High Magnetic Field Laboratory (Tallahassee, Florida, USA) with a 900 MHz Bruker Avance console and a 3.2 mm home-built MAS ¹H-X transmission line probe. Sample temperatures were adjusted for rotor frictional heating under the 20-kHz MAS condition by using solid Pb(NO₃)₂ for temperature calibration.⁵⁶⁻⁵⁸ The actual sample temperature range of the VT MAS probe was between 363 and 129 K. A liquid H₂O sample was used for both RF power calibration and ¹⁷O chemical shift referencing ($\delta = 0$ ppm). All spectral simulations were performed with DMfit.⁵⁹

2.3 Data analysis

Analysis of the isotropic ¹⁷O *chemical shifts.* As mentioned earlier, the proton dynamics in crystalline carboxylic acid dimers occurs on the order of 10¹⁰-10¹² s⁻¹ within the temperature range examined in this study (between 129 and 363 K). As a result, NMR observables such as ¹⁷O chemical shift and QC tensors will be the averaged values between the two possible tautomers A and B. This situation is distinctly different from other cases where solid-state ¹⁷O NMR was used to extract energetic information about dynamic processes.⁶⁰⁻⁶⁶ Following a simple "Arrhenius approach" developed in previous

¹H and ¹³C NMR studies,^{4, 6, 22} we can treat the averaging effect on the ¹⁷O *isotropic* chemical shifts as a simple "thermal averaging" between the two tautomers:

$$\delta_1 = P_A \delta^A_{\mathcal{C}=0} + (1 - P_A) \delta^B_{\mathcal{C}=0H} \tag{1}$$

$$\delta_2 = P_A \delta^A_{C-OH} + (1 - P_A) \delta^B_{C=O} \tag{2}$$

where

$$P_A = \frac{e^{\frac{\Delta E}{RT}}}{1 + e^{\frac{\Delta E}{RT}}}$$
(3)

In the above equation, ΔE refers to the energy asymmetry of the double-well potential curve between tautomers A and B. A schematic diagram showing this averaging is depicted in Figure 2. In this study, we are particularly interested in the temperature dependence of the averaged ¹⁷O isotropic chemical shift values because they can be determined precisely from the experimental spectra. As also illustrated in Figure 2, there are two general types of temperature dependencies. In the first type, as seen in cases (i)-(iii), the separation between the two averaged ¹⁷O NMR signals increases as the temperature is decreased. In the second type, the signal separation initially decreases as the temperature is decreased, and then increases after a "cross-over" point where the two types of temperature dependencies shown in Figure 2 are produced with the same set of ¹⁷O isotropic chemical shifts but different ΔE values, it is also possible to generate these two types with the same value of ΔE but different sets of ¹⁷O isotropic chemical shifts for the two tautomers (vide infra).

Analysis of the ¹⁷O QC tensors. Unlike the aforementioned treatment of ¹⁷O isotropic chemical shifts, averaging of the ¹⁷O QC tensors involved in low- and high-energy

tautomers is not so straightforward. This is because one has to consider the tensor orientations in the molecular frame of reference between the two tautomers. Fortunately, in the case of carboxylic acids, the ¹⁷O QC tensor orientations are well established.^{48, 67-69} Figure 3 shows typical orientations of the ¹⁷O QC tensors found for the C=O and C-OH groups of carboxylic acids. For the C=O group, the largest ¹⁷O QC tensor component, χ_{zz} , is perpendicular to the C=O bond and lies within the O=C-OH plane, whereas the smallest component, χ_{xx} , is perpendicular to the plane. In contrast, while χ_{zz} of the C-OH group also lies within the O=C-OH plane, it is along the C-O bond. In addition, χ_{xx} is now in-plane and perpendicular to the C-O bond. Another important feature to consider is the sign of each ¹⁷O QC tensor component. For carboxylic acids, it is also well known that the sign of $C_Q(^{17}O)$ for the C=O group is positive, which means $\chi_{zz} > 0$, $\chi_{yy} < 0$, $\chi_{xx} < 0$. For the C-OH group, $C_Q(^{17}O)$ is known to be negative, so $\chi_{zz} < 0$, $\chi_{yy} > 0$, $\chi_{xx} > 0$. It should be noted that, while the sign of C_Q cannot be easily determined by solid-state NMR, it can be reliably accessed by quantum chemical computations.

It is interesting to note that, for carboxylic acid dimers, the *directions* of the three principal axes of the ¹⁷O QC tensor are entirely defined by the C-O (or C=O) bond and the O=C-OH plane; see Figure 3. As a result, averaging between A and B tautomers will not change the *directions* of the principal axes. Using this feature, we can define the three principal axes of the averaged QC tensor within the molecular frame as χ_{\parallel} (inplane and along to the C-O bond), χ_{\perp} (in-plane but perpendicular to the C-O bond), and χ_{π} (perpendicular to the O=C-OH plane or out-of-plane). As seen from Figure 3(a), the averaged tensor components for A(C=O) \leftrightarrow B(C-OH) can then be readily calculated:

$$\chi_{\parallel} = P_A \chi_{yy}^A + (1 - P_A) \chi_{zz}^B \tag{4}$$

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$$\chi_{\perp} = P_A \chi_{ZZ}^A + (1 - P_A) \chi_{XX}^B \tag{5}$$

$$\chi_{\pi} = P_A \chi_{xx}^A + (1 - P_A) \chi_{yy}^B \tag{6}$$

A similar set of equations can be obtained for $A(C-OH) \leftrightarrow B(C=O)$. So, in general, two averaged QC tensors will be produced.

Figure 3(b) also shows an example to illustrate the temperature dependence of the averaged ¹⁷O QC tensor. In this case, we assumed the following ¹⁷O QC tensors: A, tautomer, $C_Q = 7.00$ MHz, $\eta_Q = 0.5$ for C=O ($\chi_{zz} = 7.00$, $\chi_{yy} = -5.25$, $\chi_{xx} = -1.75$ MHz) and $C_Q = -6.00$ MHz, $\eta_Q = 0.1$ for C-OH ($\chi_{zz} = -6.00$, $\chi_{yy} = 3.30$, $\chi_{xx} = 2.70$ MHz); B tautomer, $C_Q = 8.00$ MHz, $\eta_Q = 0.3$ for C=O ($\chi_{zz} = 8.00$, $\chi_{yy} = -5.20$, $\chi_{xx} = -2.80$ MHz) and $C_Q = -7.00$ MHz, $\eta_Q = 0.2$ for C-OH ($\chi_{zz} = -7.00$, $\chi_{yy} = 4.20$, $\chi_{xx} = 2.80$ MHz). As seen from Figure 3(b), the averaging of the QC tensors between the two tautomers will lead to two averaged QC tensors. At the high-temperature limit, both averaged QC tensors display $\eta_0 \approx 1.0$. This can be understood by examining the individual tensor components. For example, let us look at χ_{π} of the averaged tensor for A(C=O) \leftrightarrow B(C-OH) at the high-temperature limit. Because $\chi^A_{xx} = -1.75$ MHz and $\chi^B_{yy} = 2.80$ MHz nearly cancel each other when $P_A \rightarrow 0.5$ at $T \rightarrow \infty$, χ_{π} would be very small, resulting in an averaged QC tensor with $\eta_0 \approx 1.0$. At the low-temperature limit, however, the averaged tensors have $\eta_0 \approx 0$ and $\eta_0 \approx 0.5$, which resemble those in the A tautomer alone. This is because $P_A \rightarrow 1$ when $T \rightarrow 0$.

2.4 Quantum Chemical Computations

Plane-wave pseudo-potential DFT calculations of the NMR magnetic shielding and quadrupole coupling parameters were performed using Materials Studio CASTEP software version 4.4 (Accelrys)⁷⁰ on a HP xw4400 workstation with a single Intel Dual-Core 2.67 GHz processor and 8 GB DDR RAM. The Perdew, Burke, and Ernzerhof (PBE) functionals were used in all calculations in the generalized gradient approximation (GGA) for the exchange correlation energy. On-the-fly pseudo potentials were used as supplied with NMR CASTEP with a plane wave basis set cut-off energy of 550 eV and the Monkhorst-Pack *k*-space grid sizes of $4 \times 4 \times 4$ (16 *k*-points used). The most recent crystal structures of BA,⁴¹ SA,⁴² ASA,⁴³ CA,⁴⁴ and MCA⁴⁵ were used as starting structures and then geometry optimization was performed for both low- and high-energy tautomers using the BFGS method without the cell optimization. Following convergence tolerance parameters were used in the geometry optimization process: total energy 10⁻⁵ eV/atom, maximum displacement 0.001 Å, maximum force 0.03 eV/Å, and maximum stress 0.05 GPa.

3. Results and discussion

Figure 4 shows the ¹⁷O MAS NMR spectra obtained for several carboxylic acid dimers at 21.1 T. While these carboxylic acid dimers have very similar hydrogen bonding geometries, their ¹⁷O MAS NMR spectra are quite different. For example, two wellresolved ¹⁷O NMR signals are observed for [1,2-¹⁷O₂]SA, but the two signals from [1,2-¹⁷O₂]BA are nearly indistinguishable. Further examination of the spectral details reveals more differences in the ¹⁷O quadrupole parameters among these carboxylic acid dimers. For example, the two signals in the ¹⁷O MAS NMR spectrum of [1,2-¹⁷O₂]SA have the

following ¹⁷O NMR parameters: signal-1, $\delta_{iso} = 281$ ppm, $C_Q = 7.0$ MHz, $\eta_Q = 0.45$; signal-2, $\delta_{iso} = 164$ ppm, $C_Q = 7.5$ MHz, $\eta_Q = 0.16$. The corresponding parameters for [1,2-¹⁷O₂]BA are: signal-1, $\delta_{iso} = 234$ ppm, $C_Q = 5.8$ MHz, $\eta_Q = 0.8$; signal-2, $\delta_{iso} = 227$ ppm, $C_Q = 5.9$ MHz, $\eta_Q = 0.8$. From the ¹⁷O MAS NMR spectra shown in Figure 4, two general features are note worthy. First, the C_Q values are considerably larger in SA than in BA. Second, while the two signals in SA have very different η_Q values, both of which are less than 0.5, the two signals in BA have the same high η_Q value. In general, as seen from Figure 4, the η_Q values of both signals increase from SA, ASA, CA, to MCA and BA.

To better understand the origin of the spectral differences observed for different carboxylic acid dimers, we obtained VT ¹⁷O MAS NMR spectra for these compounds. Figure 5 shows the results for [1,2-¹⁷O₂]ASA, [1,2-¹⁷O₂]CA, and [1,2-¹⁷O₂]MCA. We should note that the ¹⁷O MAS NMR spectra from [1,2-¹⁷O₂]SA, as reported previously,⁵³ did not display any temperature dependence. As seen from Figure 5, the ¹⁷O MAS NMR spectra of [1,2-¹⁷O₂]ASA change as a function of temperature in three aspects. First, the separation between the two signals decreases as the temperature of the sample is increased. Second, the values of η_Q appear to increase with the temperature for both signals. Third, the C_Q values for the two signals also decrease slightly as the temperature is increased. The spectra of [1,2-¹⁷O₂]CA display similar temperature dependencies as described for [1,2-¹⁷O₂]MCA. In contrast, a quite difference temperature dependence is observed for [1,2-¹⁷O₂]MCA. That is, the separation of the two signals increases with the temperature, and the values of neither C_Q nor η_Q appear to be sensitive to the temperature. Thus, in terms of the signal separation, the general spectral behaviors observed for $[1,2-{}^{17}O_2]ASA$ and $[1,2-{}^{17}O_2]CA$ are similar to those in cases (i)-(iii) shown in Figure 2, but $[1,2-{}^{17}O_2]MCA$ displays a temperature dependence similar to case (iv).

Now in order to interpret the VT ¹⁷O NMR results shown in Figure 5, it is necessary to have some general ideas about the ¹⁷O NMR parameters in both low- and high-energy tautomers. To this end, we decided to perform periodic plane-wave DFT computations to obtain information about both energetic and spectral properties of the two tautomers. For each compound, we started from the best crystal structure available in the literature. Then we obtained the optimized structures for both A and B tautomers. In this step, we obtained the energy asymmetry between the two tautomers. Finally, we computed ¹⁷O NMR tensors for both tautomers. Table 1 shows the computational results. In general, the computations suggest that the ¹⁷O NMR parameters for the carboxylic acid functional group in the two tautomers are quite similar, even when there is a large energy asymmetry between the two tautomers. This is not a total surprise because the ¹⁷O NMR parameters of the -COOH group should be largely determined by the hydrogen bonding interaction within the dimer, whereas the energy asymmetry is mainly influenced by crystal packing. Further, the computations have also confirmed the ¹⁷O QC tensor orientations depicted in Figure 3 as well as the aforementioned signs of $C_0(^{17}\text{O})$ for both C=O and C-OH groups.

Using the computational results listed in Table 1 as initial inputs, we were able to obtain best-fit results for the experimental VT ¹⁷O NMR data (δ_{iso} , C_Q and η_Q) as well as for the energy asymmetry, ΔE . Figure 6 shows the comparison between the experimental and best-fit data for ASA, CA, and MCA. The best-fit parameters are summarized in Table 2. As seen from Figure 6, the overall agreement between the experimental and

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best-fit curves is satisfactory. Because the ¹⁷O MAS NMR spectrum of $[1,2-^{17}O_2]SA$ does not show any temperature dependence, as mentioned earlier, we estimated that ΔE in SA must be greater than 15 kJ mol⁻¹. We will further discuss the results shown in Table 2 in a later section.

For now we turn our attention to a different aspect of carboxylic acid dimers. Previous studies have shown significant H/D isotope effects in these systems.^{12, 19, 21, 23, 32} In particular, many studies have established that the H hopping dynamics within the hydrogen-bonded carboxylic acid dimer is significantly slowed down when H is replaced by D.^{19, 32} In this study, we set out to investigate whether there is any H/D isotope effect on the ¹⁷O NMR parameters as well as their temperature dependence. Figure 7 shows the VT ¹⁷O MAS spectra of [1,2-¹⁷O₂]BA-H and [1,2-¹⁷O₂]BA-D; the detailed spectral fittings for BA-H and BA-D are given in the Supporting Information (Figures S1 and S2). Immediately, one sees that the two compounds display quite different spectral behaviors with BA-D being more sensitive to the temperature than BA-H. At 357 K, the separation between the two signals is about 3 ppm for BA-H. In comparison, for BA-D at 349 K, the signal separation is about 5 ppm. This H/D isotope effect gets amplified at low temperatures. For example, a signal separation of 34 ppm is observed for BA-H at 129 K, which is compared with 55 ppm for BA-D at 137 K. A close inspection of the ¹⁷O isotropic chemical shifts observed for BA-H and BA-D at the lowest temperatures reveals that the high- and low-frequency signals display an apparent H/D isotope shift of -4 and 17 ppm, respectively. Note that the isotope shift is defined as $\Delta^{17}O(H/D) = \delta^{17}O(H) - \delta^{17}O(H)$ $\delta^{17}O(D)$. In the present case, these isotope shifts are the averaged values between the two tautomers. Nonetheless, these H/D isotope shifts are quite substantial as compared with those reported for other hydrogen-bonded systems.⁷¹⁻⁷² Figure 8 shows the experimental and best-fit ¹⁷O NMR results for BA-H and BA-D. Again, the general trends are similar to those shown in Figure 6 for other carboxylic acid dimers. The best-fit ¹⁷O NMR parameters are also listed in Table 2. Indeed, BA-H and BA-D do exhibit different ¹⁷O NMR parameters in both A and B tautomers. Again, substantial isotope shifts, $\Delta^{17}O(H/D)$, are seen for both the C=O and C-OH groups; however, we caution that the uncertainties in the best-fit ¹⁷O NMR parameters shown in Table 2 are quite large. For this reason, we will not further discuss these ¹⁷O isotope shifts. Another interesting finding with regard to the H/D isotope effect is that the energy asymmetry in BA-D is nearly twice that in BA-H. Since the error in ΔE is relatively small, the observed difference between BA-H and BA-D is significant (vide infra).

After analysing all the VT ¹⁷O NMR data, we can now compare the best-fit data reported in Table 2 with those from DFT computations summarized in Table 1. Figure 9 shows the direct comparisons for both ¹⁷O chemical shift/shielding constant and quadrupole parameters. The general agreement is consistent with other studies dealing with ¹⁷O NMR parameters in organic solids. Furthermore, the periodic plane-wave DFT computations appear to have treated the two tautomers equally well. This seems reasonable since the two tautomers indeed have very similar ground-state energies in the first place. This is an important conclusion because the two tautomers in carboxylic acid dimers cannot be separately assessed by NMR. Thus, this study represents a very rare case where information about ¹⁷O NMR parameters from high-energy tautomers are indirectly evaluated.

Finally we will discuss the energy asymmetry ΔE values found for carboxylic acid dimers. Table 3 shows a partial compilation of ΔE values determined for carboxylic acid dimers by various techniques including NMR relaxation measurement (¹H and ²H), neutron/X-ray diffraction data analysis, IR spectral analysis, NOR, and solid-state NMR measurement. The hydrogen bonding lengths, $d_{0\cdots0}$, for the carboxylic acid dimers listed in Table 3 fall in a narrow range between 2.570 and 2.654 Å. In general, the ΔE values are not related to the hydrogen bonding lengths. Rather, ΔE should depend on crystal packing and inramotlecular interactions other than the hydrogen bonding. For example, the compound with the largest ΔE value among those listed in Table 3 is SA. In the A tautomer of SA, the 2-OH group forms an intramolecular hydrogen bond of the type O- $H \cdots O = C$. This makes the C=O group to be the common acceptor of two hydrogen bonds. In the B tautomer, however, the hydrogen bonding arrangement becomes O- $H \cdots O - H \cdots$ where the central OH group serves as both acceptor and donor. Apparently, the A tautomer has significantly lower energy than the B tautomer in SA. It is interesting to note that, in the case of ASA, where the 2-OH group is modified to lose the capability as a hydrogen bond donor, the ΔE value, 3 kJ mol⁻¹, is considerably smaller than that in SA, > 15 kJ mol⁻¹. Another interesting *ortho*-substituted BA derivative where a relatively large ΔE was found is 2NBA ($\Delta E = 5.8 \text{ kJ mol}^{-1}$). The crystal structure of 2NBA shows that both the nitro and carboxylic acid functional groups are significantly out of the benzene plane to avoid $O \cdots O$ contact.⁷³

For the H/D isotope effect, the ΔE value generally increases on going from H to D, except for the case of BA. As seen from Table 3, BA is the most studied carboxylic acid dimer. However, there are some discrepancies among the literature data. As mentioned

earlier, we determined the ΔE values for BA-H and BA-D to be 0.6 and 1.2 kJ mol⁻¹, respectively. Our results are in agreement with those reported by Agaki et al.,¹² by Stöckli et al,¹⁹ and by Takeda and Tsuzumitani.²⁸ In contrast, Heuer and Haeberlen²¹ reported that $\Delta E = 0.72$ kJ mol⁻¹ for BA-D. Xue et al.³² also found that BA-H and BA-D exhibit the same ΔE value, 0.71 kJ mol⁻¹. The exact reason for these discrepancies is unclear to us at this time.

4. Conclusions

We have recorded VT solid-state ¹⁷O NMR spectra at 21.1 T for several carboxylic acid dimers. One important feature found in these compounds is that their ¹⁷O MAS NMR spectra exhibit very different temperature dependences. This temperature effect can be rationalized by considering the thermal averaging of ¹⁷O NMR tensors between the two tautomers associated with double proton hopping within the hydrogen-bonded carboxylic acid dimer. Since the proton transfer dynamics in carboxylic acid dimers is much faster than the NMR timescale, only the averaged results are experimentally accessible. We showed that the best-fit ¹⁷O NMR parameters obtained for the two tautomers are in reasonable agreement with those from plane-wave DFT calculations. Since energy asymmetry values are usually less than a few kJ mol⁻¹ in most systems studied, quantum chemical computations to this degree of accuracy are not to be expected from the current DFT methodologies. Nonetheless, we found that the periodic DFT calculations are in qualitative agreement with the experimental results. We have also presented an interesting case of H/D isotope effects on both ¹⁷O NMR parameters and

energy asymmetry. Further studies on the H/D isotope effects on ¹⁷O NMR parameters in hydrogen-bonded systems are underway in this laboratory.

Supporting Information Available. Two figures showing experimental and simulated ¹⁷O MAS spectra for BA-H and BA-D at different temperatures.

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Figure Captions



Figure 1. (Top) Illustration of the two tautomers generated from concerted double proton hopping within a hydrogen-bonded carboxylic acid dimer in the solid state. (Bottom) Simplified 1D potential curve where the energy difference between the two energy minima is defined as the energy asymmetry (ΔE).





Figure 2. (a) Illustration of the averaging effect for ¹⁷O isotropic chemical shifts between tautomers A and B. (b) General types of temperature dependence of the averaged ¹⁷O isotropic chemical shift. The following ¹⁷O isotropic chemical shifts are used in the calculations: A tautomer, 280 ppm (C=O) and 180 ppm (C-OH); B tautomer, 300 ppm (C=O) and 150 ppm (C-OH). As examples, calculations using four different ΔE values are shown: (i) 10; (ii) 5; (iii) 2; (iv) 0.5 kJ mol⁻¹. Calculations were based on Eqs. (1)-(3). See text for discussion.



Figure 3. (a) ¹⁷O QC tensor orientations in the molecular frame of reference in tautomers A and B. (b) General temperature dependence of the averaged ¹⁷O QC tensor components (solid lines for the δ_1 signal and dashed lines for the δ_2 signal). The following ¹⁷O quadrupole parameters are used in the calculations: A tautomer, $C_Q = 7.0$ MHz, $\eta_Q = 0.5$ for C=O and $C_Q = -6.0$ MHz, $\eta_Q = 0.1$ for C-OH; B tautomer, $C_Q = 8.0$ MHz, $\eta_Q = 0.3$ for C=O and $C_Q = -7.0$ MHz, $\eta_Q = 0.2$ for C-OH. The ΔE value used in the calculations was 2 kJ mol⁻¹. Calculations were based on Eqs. (4)-(6). See text for discussion.



Figure 4. Experimental (black trace) and simulated (colored traces) ¹⁷O MAS NMR spectra of (a) $[1,2-^{17}O_2]BA$, (b) $[1,2-^{17}O_2]MCA$, (c) $[1,2-^{17}O_2]CA$, (d) $[1,2-^{17}O_2]ASA$, and (e) $[1,2-^{17}O_2]SA$. All spectra were obtained at 295 K and at 21.1 T. The sample spinning frequencies were: (a, b) 15 kHz; (c) 18 kHz; (d, e) 20 kHz. The signals marked with * are spinning sidebands.



Figure 5. Experimental (blue trace) and simulated (colored traces) ¹⁷O MAS NMR spectra of (a) $[1,2^{-17}O_2]ASA$, (b) $[1,2^{-17}O_2]CA$, and (c) $[1,2^{-17}O_2]MCA$ at different temperatures. All spectra were obtained at 21.1 T.



Figure 6. Experimental (data symbols) and best-fitted (solid lines) ¹⁷O isotropic chemical shift and quadrupole parameters (C_Q and η_Q) for (a) [1,2-¹⁷O₂]ASA, (b) [1,2-¹⁷O₂]CA, and (c) [1,2-¹⁷O₂]MCA as a function of temperature. The calculations were based on Eqs. (1)-(6) with parameters given in Table 2. The error bars for experimental δ_{iso} (¹⁷O) values (± 1 ppm) are not shown for clarity.



Figure 7. Experimental ¹⁷O MAS NMR spectra of (a) BA-H and (b) BA-D at different temperatures. All spectra were obtained at 21.1 T. The signals marked with * are spinning sidebands. Simulated spectra are not shown for clarity; they are given in the Supporting Information.



Figure 8. Experimental (data symbols) and best-fitted (solid lines) ¹⁷O (a) isotropic chemical shift and (b) quadrupole parameters (C_Q and η_Q) for [1,2-¹⁷O₂]BA-H and [1,2-¹⁷O₂]BA-D as a function of temperature. The calculations were based on Eqs. (1)-(6) with parameters given in Table 2. The error bars for experimental δ_{iso} (¹⁷O) values (± 1 ppm) are not shown for clarity.



Figure 9. Comparison between experimental and computed ¹⁷O NMR parameters for tautomers A (open circles) and B (filled circles) in several carboxylic acids. (a) Experimental δ_{iso} versus computed σ_{iso} . (b) Experimental χ_{ii} versus computed χ_{ii} where ii = xx, yy, and zz.

Table 1. Periodic plane-wave DFT computed ¹⁷O NMR parameters (magnetic shielding constant, quadrupole coupling constant, and asymmetry parameter) for low- and high-energy tautomers (A and B) and energy asymmetry (ΔE) in several crystalline carboxylic acids.

		Tautomer A		Ta				
Compound		σ_{iso}/ppm	C_Q/MHz	η_Q	 σ_{iso}/ppm	$C_{\rm Q}/{\rm MHz}$	η_Q	$\Delta E/\mathrm{kJ}~\mathrm{mol}^{-1}$
BA-H								pprox 0
	C=O	-29	7.616	0.44	-24	7.477	0.47	
	СОН	79	-7.336	0.10	75	-7.252	0.07	
MCA								0.8
	C=O	-9	7.171	0.61	-44	7.556	0.51	
	СОН	66	-7.331	0.14	88	-7.507	0.18	
CA								1.3
	C=O	-15	7.278	0.57	-49	7.644	0.45	
	СОН	61	-7.175	0.08	83	-7.476	0.11	
ASA								3.7
	C=O	-35	7.682	0.45	-49	7.802	0.40	
	СОН	66	-7.402	0.08	74	-7.489	0.10	
SA								18.0
	C=O	-3	6.628	0.78	-14	7.074	0.62	
	СОН	86	-7.576	0.17	77	-7.224	0.23	

Table 2. Experimental ¹⁷ O NMR parameters (chemical shift, quadrupolar coupling
constant, and asymmetry parameter) ^{<i>a</i>} for low- and high-energy tautomers (A and B) and
energy asymmetry (ΔE) values ^b used in the analysis of ¹⁷ O VT NMR data obtained for
several crystalline carboxylic acids.

		Tautomer A		T				
Compo	und	$\overline{\delta_{iso}}/ppm$	$C_{\rm Q}/{\rm MHz}$	η_Q	 δ_{iso}/ppm	C _Q /MHz	η_Q	$\Delta E/kJ \text{ mol}^{-1}$
BA-H								0.6
	C=O	300	7.5	0.3	314	8.0	0.3	
	СОН	158	-6.5	0.0	152	-7.3	0.3	
BA-D								1.2
	C=O	290	7.0	0.5	355	8.5	0.0	
	СОН	145	-6.5	0.0	140	-7.0	0.4	
MCA								0.5
	C=O	278	6.5	0.6	315	7.0	0.1	
	СОН	180	-7.5	0.0	150	-6.0	0.2	
CA								2.5
	C=O	292	6.5	0.5	330	7.7	0.1	
	СОН	170	-6.2	0.0	155	-7.5	0.4	
ASA								3.0
	C=O	302	7.8	0.2	340	6.0	0.1	
	СОН	170	-7.4	0.0	160	-7.5	0.60	
SA								>15
	C=O	280	7.1	0.5			_	
	СОН	165	-7.4	0.2		—	_	

^{*a*}The uncertainties in the ¹⁷O isotropic chemical shifts and QC tensor components are estimated to be \pm 10 ppm and \pm 1.0 MHz, respectively. Note that, because these quantities were extracted from the best-fit plots shown in Figures 6 and 8, the uncertainties were rather large.

^{*b*}The uncertainty in ΔE is estimated to be ± 0.2 kJ mol⁻¹, except for the case of SA.

Table 3. Summary of experimental hydrogen-bond O····O distances determined by X-
ray/or neutron diffraction and energy asymmetry (ΔE) values determined by various
techniques in crystalline carboxylic acid dimers.

BA-H2.608 0.42 ± 0.04 ^{13}C NMR and $^{1}H T_1$ 4 0.79 ± 0.06 $^{1}H T_1$ 19 0.418 ± 0.128 2D spin diffusion22 0.50 ± 0.04 Neutron diffraction39 0.2 ^{17}O NQR26 0.75 $^{1}H T_1$ 28 0.71 ± 0.02 $^{1}H T_1$ 32 0.6 ± 0.2 ^{17}O SSNMRThis workBA-D 1.3 ± 0.1 IR12 1.5 ± 0.1 $^{2}H T_1$ 21 3.0 $^{2}H T_1$ 28	
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BA-D 1.3 ± 0.1 IR 1.5 ± 0.1 $^{2}H T_{1}$ 0.72 $^{2}H T_{1}$ 3.0 $^{2}H T_{1}$ 28	
$\begin{array}{ccccccc} 1.5 \pm 0.1 & {}^{2}\text{H} T_{1} & 19 \\ 0.72 & {}^{2}\text{H} T_{1} & 21 \\ 3.0 & {}^{2}\text{H} T_{2} & 28 \\ \end{array}$	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
3.0 ² H T_1 28	
0.71 ${}^{1}\text{H} T_{1}$ 32	
1.2 ± 0.2 ¹⁷ O SSNMR This work	
IA-D 2.623 0.66 $^{2}\text{H}T_{1}$ 21	
DA-D 2.631 1.31 ${}^{2}\text{H}T_{1}$	
FA-D 2.634 0.12 2 H T_{1}	
TA $2.630 1.0 \pm 0.2 {}^{1}\text{H} T_1 6$	
4-ClBA 2.608 1.66 ± 0.12 Neutron diffraction 34	
GA-H 2.69 3.3 ${}^{1}\text{H}T_{1}$ 12	
GA-D 5.8 ${}^{2}\text{H} T_{1}$	
4-FormBA-H 2.57 1.4 ${}^{1}\text{H}T_{1}$	
4-FormBA-D 2.8 $^{2}\text{H}T_{1}$	
4-DABA 2.622 2.0 X-ray diffraction 35	
3,5-DNBA 2.653 0.8	
4-HBA 2.634 0.16 ± 0.02 ¹⁷ O NQR 26	
4-NBA 2.674 1.25 ± 0.02	
4-FBA 2.609 1.25 ± 0.17 ¹ H T_1 30	
4-ClBA $2.608 1.55 \pm 0.04$	
4-BrBA 2.580 1.41 ± 0.08	
4-IBA 2.610 1.41 ± 0.04	
2-NBA 2.661 5.8 ¹⁷ O NQR 27	
β-9AC 2.634 2.63 ± 0.84 X-ray diffraction 37	
4A35ClBA 2.601 0.83 1 H T_{1} and 35 Cl NQR 39	
4A35IBA 2.581 0.22	
MCA $2.614 0.5 \pm 0.2 {}^{17}\text{O} \text{ SSNMR} \text{This work}$	
CA $2.630 2.5 \pm 0.2$	
ASA 2.642 3.0 ± 0.2	
SA 2.654 > 15	

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4	^{<i>a</i>} Abbreviations of compounds: BA: benzoic acid: IA: m-iodobenzoic acid: DA: 2.3-
5	dimethovybenzoic acid: EA: Eaist's acid: TA: n toluic acid: A CIBA: A chlorobenzoic
6	includy you acid, I'A. Petst S acid, I'A. p-toluic acid, 4-CIDA. 4-CIDOCOULZOIC
7	acid; GA: glutaric acid; 4-FormBA: 4-formylbenzoic acid; 4-DABA: 4-
8	dimethylaminobenzoic acid; 3,5-DNBA: 3,5-dinitrobenzoic acid; 4-HBA: 4-
9	hydroxybenzoic acid; 4-NBA: 4-nitrobenzoic acid; 4-FBA: 4-fluorobenzoic acid; 4-
10	BrBA: 4-bromobenzoic acid: 4-IBA: 4-iodobenzoic acid: 2-NBA: 2-nitrobenzoic acid: β-
11	9AC: B-9-anthracene carboxylic acid: 1A35CIBA: 1-amino-3.5-chlorobenzoic acid:
12	A 25 ID A 4 aming 2.5 is dehensels asid, MCA a methowsingenia asid, CA a singenia
13	4A55IBA: 4-amino-5,5-iodobenzoic acid; MCA: p-methoxycinnamic acid; CA: cinnamic
14	acid; SA: salicylic acid;
15	^b The "-H" and "-D" notations indicate whether the acid proton is protonated and
16	deuterated, respectively.
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TOC graphics







 χ_{zz}

′́≘_H ^χ_{yy}

 $\chi_{\rm xx}$

χ_{yy}

 $\eta_Q\approx 0$

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