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Influence of N−H···O and C−H···O Hydrogen Bonds on the ^{17}O NMR Tensors in Crystalline Uracil: Computational Study

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We report a computational study for the ^{17}O NMR tensors (electric field gradient and chemical shielding tensors) in crystalline uracil. We found that N−H···O and C−H···O hydrogen bonds around the uracil molecule in the crystal lattice have quite different influences on the ^{17}O NMR tensors for the two C═O groups. The computed ^{17}O NMR tensors on O4, which is involved in two strong N−H···O hydrogen bonds, show remarkable sensitivity toward the choice of cluster model, whereas the ^{17}O NMR tensors on O2, which is involved in two weak C−H···O hydrogen bonds, show much smaller improvement when the cluster model includes the C−H···O hydrogen bonds. Our results demonstrate that it is important to have accurate hydrogen atom positions in the molecular models used for ^{17}O NMR tensor calculations. In the absence of low-temperature neutron diffraction data, an effective way to generate reliable hydrogen atom positions in the molecular cluster model is to employ partial geometry optimization for hydrogen atom positions using a cluster model that includes all neighboring hydrogen-bonded molecules. Using an optimized seven-molecule model (a total of 84 atoms), we were able to reproduce the experimental ^{17}O NMR tensors to a reasonably good degree of accuracy. However, we also found that the accuracy for the calculated ^{17}O NMR tensors at O2 is not as good as that found for the corresponding tensors at O4. In particular, at the B3LYP/6-311++G(d,p) level of theory, the individual ^{17}O chemical shielding tensor components differ by less than 10 and 30 ppm from the experimental values for O4 and O2, respectively. For the ^{17}O quadrupole coupling constant, the calculated values differ by 0.30 and 0.87 MHz from the experimental values for O4 and O2, respectively.

1. Introduction

Since the very early days of NMR spectroscopy, one of the primary rationales for utilizing ^{17}O as a nuclear probe is that ^{17}O NMR parameters are remarkably sensitive to hydrogen-bonding (HB) interaction, and thus are potentially useful in the study of biological systems.[1] Over the past 40 years, general trends in ^{17}O NMR parameters as a function of HB interaction have been known from both solution ^{17}O NMR and nuclear quadrupole resonance (NQR) studies. In contrast, our knowledge regarding the dependence of ^{17}O NMR *tensors* on HB interaction is still limited. A number of recent solid-state ^{17}O NMR studies have accumulated a considerable amount of experimental data on the tensorial aspect of the ^{17}O NMR parameters.[2−14] In parallel to experimental studies, attention has also been paid to theoretical prediction of ^{17}O NMR tensors.[12,13,15−20] The purpose of performing first-principle calculations on ^{17}O NMR tensors is not only to check the validity of computational methodology, but also to provide a useful tool for interpreting experimental NMR data in relation to HB interaction, molecular structure, and dynamics. This combined theoretical/experimental approach represents a trend that has become increasingly important in solid-state NMR. From recent solid-state NMR studies, it has become clear that the accuracy of ^{17}O NMR tensor calculation depends not only on the computational methodology, but also critically on the molecular model used in the calculation. In particular, if the molecule of interest is involved in intermolecular interactions, calculations for an isolated, gas-phase molecule are often incapable of reproducing experimental ^{17}O NMR tensors, which are measured for molecules in the condensed phase. One recent example from our laboratory is the case of crystalline urea.[5] In the crystal lattice, each urea molecule is linked to six neighboring urea molecules by forming eight N−H···O hydrogen bonds. The target oxygen atom is directly involved in four hydrogen bonds. We found that, to reproduce the experimentally determined ^{17}O NMR tensors to a satisfactory degree of accuracy, it is necessary to include the complete HB network (a total of six urea molecules) in the molecular cluster model.[5] Similar observations have been made for ^{17}O NMR tensors in several O−H···O hydrogen bonds.[11,21,22] Although it has been recognized that strong N−H···O and O−H···O hydrogen bonds must be considered in the calculations, little is known about the influence of weak hydrogen bonds such as C−H···O on ^{17}O NMR tensors.

In a recent solid-state ^{17}O NMR study of crystalline uracil, we found that the computed ^{17}O NMR tensors at O2 and O4 atoms in crystalline uracil show quite different behaviors in various cluster models.[13] In particular, the calculated ^{17}O NMR tensors at O4 show substantial sensitivity to the choice of molecular models and are in reasonably good agreement with the experimental results once the molecular model includes the HB network. In contrast, the calculated ^{17}O NMR tensors at O2 are in much poorer agreement with experimental data. Uracil crystallizes in monoclinic form (space group $P2_1/a$).[23] As seen from Figure 1, each uracil molecule in the crystal lattice is involved in a HB network. O4 is strongly hydrogen bonded via two N−H···O bonds ($r_{\mathrm{N1}\cdots\mathrm{O4}} = 2.865$ Å, $\angle$N1−H1···O4 = 171.5°; $r_{\mathrm{N1}\cdots\mathrm{O4}} = 2.864$ Å, $\angle$N3−H3···O4 = 171.2°) to two neighboring molecules, but O2 is only involved in two weak

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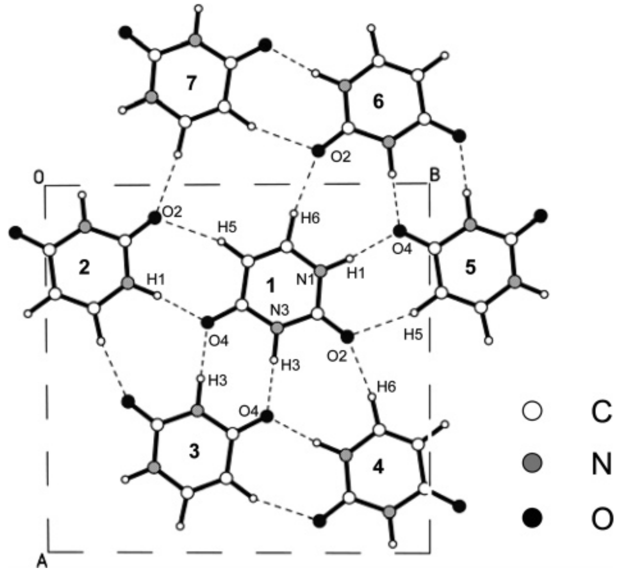

Figure 1. Atomic numbering and hydrogen bonding network in crystalline uracil.

C−H···O hydrogen bonds ($r_{C5\cdots O2} = 3.319$ Å, $\angle$C5−H5···O2 = 162.8°; $r_{C6\cdots O2} = 3.247$ Å, $\angle$C6−H6···O2 = 162.8°). In our original ^{17}O NMR study, we constructed a three-molecule model (consisting of molecules 1, 2, and 3 as defined in Figure 1) to describe the HB environment for crystalline uracil.[13] This cluster model is adequate for predicting ^{17}O NMR tensors at O4. However, the fact that this cluster model does not yield accurate ^{17}O NMR tensors for O2 may suggest that the weak C−H···O hydrogen bonds should also be included in the cluster model. Because crystalline uracil is a classic example for the existence of weak C−H···O hydrogen bonds[24] and C−H···O hydrogen bonds are known to be present in RNA structures such as noncanonical UU base pairing[25−27] and formation of a U-quartet,[28] we decided to use crystalline uracil to further investigate the influence of weak C−H···O hydrogen bonds on ^{17}O NMR tensors.

Another possible source for inaccurate NMR calculations in our previous study is related to the issue of hydrogen atom positions. It is well-known that X-ray diffraction studies (especially early X-ray diffraction studies) do not yield reliable hydrogen atom positions. In our original study, we simply used standard N−H (1.030 Å) and C−H (1.100 Å) bond lengths in the cluster model. This is certainly a very crude approximation. In this study we attempt to find a suitable way of defining hydrogen atom positions for a cluster of hydrogen-bonded molecules. Finally, as the size for a molecular cluster increases, computational cost increases drastically. In many instances, it is desirable to reduce computational cost, while maintaining a reasonable degree of accuracy, so that larger molecular systems can be considered. In this study, we use crystalline uracil as an example to test a locally dense (LD) basis set method[29] in computing ^{17}O NMR tensors.

2. Computational Aspects

All quantum chemical calculations were performed using the Gaussian 98 suite of programs[30] on a SunFire 6800 symmetric multiprocessor system. Each of the four nodes is equipped with a 24 × 1.05 GHz (8 MB E-Cache) UltraSPARC-III processor and 96 GB of RAM. To calculate ^{17}O electric field gradient (EFG) and chemical shielding tensors, a density functional theory (DFT) approach using B3LYP exchange functional was employed. The near basis set limit was tested using numerous standard all-electron basis sets including 6-31G, 6-31G(d), 6-311G, 6-311G(d), 6-311G(d,p), 6-311+G, 6-311++G, 6-311++G(d,p), 6-311G(3df), and cc-pVTZ for all atoms. In the LD basis set calculations, various basis sets including 6-311G(d), 6-311++G(d,p), 6-311G(3df), cc-pVTZ, cc-pVQZ, cc-pV5Z, aug-cc-pVTZ, aug-cc-pVQZ, and aug-cc-pV5Z were used on the target atoms while 6-31G(d) basis set was used for other atoms. The model clusters used in this study were constructed from an experimental X-ray crystal structure for uracil.[23] Since hydrogen atom positions are generally inaccurate in X-ray diffraction studies, two partial geometry optimizations were performed at the B3LYP/6-311G(d,p) level to optimize the hydrogen atom positions; details will be presented in the next section.

The gauge including atomic orbital (GIAO) approach[31,32] was used for chemical shielding calculations. To make direct comparison between the calculated chemical shielding, σ, and the observed chemical shift, δ, we used the new absolute ^{17}O chemical shielding scale established by Wasylishen and Bryce:[33]

$$\delta = 287.5\ \text{ppm} - \sigma \qquad (1)$$

To compare computational EFG tensors with experimental quadrupole parameters, the following equation was used to convert the EFG tensor components, q_{ii}, in atomic units (au) to the quadrupolar coupling constant, C_Q, in MHz:

$$C_Q = e^2 Q q_{zz} h^{-1} = -2.3496 Q q_{zz} \qquad (2)$$

where Q is the nuclear quadrupole moment of the ^{17}O nucleus (in fm^2), and the factor of 2.3496 results from unit conversion. In the present study, we use a standard value of $Q(^{17}\text{O})$, −2.558 fm^2.[34] Another important parameter for the quadrupole interaction is the asymmetry parameter (η_Q): $\eta_Q = (q_{xx} - q_{yy})/q_{zz}$.

3. Results and Discussion

3.1. Cluster Model Building. In our previous solid-state ^{17}O NMR study of crystalline uracil,[13] we calculated the ^{17}O chemical shielding and EFG tensors using a molecular cluster model consisting three uracil molecules (molecules 1, 2 and 3 as labeled in Figure 1). As mentioned earlier, this three-molecule model does not take into consideration the fact that O2 is involved in two weak C−H···O hydrogen bonds. In this study, we build a larger cluster model to include four additional uracil molecules (molecules 4, 5, 6, and 7) to complete the HB network around the target uracil molecule. This seven-molecule model will be the primary cluster model used in this study. Before we can calculate ^{17}O NMR tensors for the target uracil molecule using this new model, we must address the issue regarding hydrogen atom positions. In the original three-molecule cluster model used in our previous study, we used standard N−H (1.030 Å) and C−H (1.100 Å) bond lengths to generate hydrogen atoms. This is clearly an oversimplification. In this study, we further examine two different ways of defining hydrogen atoms. In the first approach, we fully optimize the geometry of a single uracil molecule (in the absence of any HB interaction), and then use this optimized "gas-phase" molecule to generate the symmetry-related molecules in the seven-molecule model. In the second method, we build a cluster model consisting of the target molecule (molecule 1) and four surrounding molecules (molecules 2, 3, 5, and 6). The positions of H1, H3, H5 and H6 on the central molecule are allowed to fully relax during the optimization, while all other atoms remained fixed. In this model, molecules 2, 3, 5 and 6 serve as "anchor" molecules

TABLE 1: Results of Partial Geometry Optimization To Determine Hydrogen Atom Positions in Crystalline Uracil

hydrogen atom	method	X−H (Å)	X−H···O (deg)	H···O (Å)
N1−H1	experimental X-ray[a]	0.836	171.5	2.034
	partially opt. 1 molecule	1.011	167.5	1.868
	partially opt. cluster	1.025	173.4	1.842
N3−H3	experimental X-ray[a]	0.878	171.2	1.995
	partially opt. 1 molecule	1.014	173.0	1.857
	partially opt. cluster	1.029	175.6	1.839
C5−H5	experimental X-ray[a]	0.931	162.8	2.418
	partially opt. 1 molecule	1.081	160.0	2.282
	partially opt. cluster	1.082	160.9	2.279
C6−H6	experimental X-ray[a]	0.958	162.8	2.317
	partially opt. 1 molecule	1.086	159.6	2.205
	partially opt. cluster	1.085	162.0	2.195

[a] From ref 23.

that fix the heavy atom positions involved in hydrogen bonds. Once the optimized positions for H1, H3, H5, and H6 are found, we use molecule 1 and crystallographic symmetry elements to generate other molecules to build the seven-molecule model mentioned earlier. It is quite clear that there is no physical basis for the first approach to succeed. The only reason we did this was to provide a comparison with the results from the second approach that may illustrate the importance of including heavy atom positions in partial geometry optimization. The results for these two methods are summarized in Table 1.

Since to a very good approximation uracil molecules lie in a plane, we can describe the geometry of the hydrogen bond using three parameters: X−H bond length (where X = C or N), X−H···O bond angle, and H···O distance. As seen from Table 1, the primary difference between the two methods for the two N−H···O hydrogen bonds is related to the direction of the hydrogen bonds. For geometry optimization with the cluster model, the two N−H···O bond angles increase substantially from the corresponding X-ray diffraction values (by 2−4°), making each of the four N−H···O hydrogen bonds closer to a perfect linear arrangement. Increases in the N−H···O bond angle simultaneously shorten the H···O bond distance. On the other hand, the geometry optimization with the isolated uracil molecule shows a decrease of 4° in the N−H···O bond angle for H1, but a small increase of 1.8° for H3, compared with the corresponding X-ray diffraction values. This highlights the argument that it is important to include heavy atoms in partial geometry optimization. It is interesting to note that the correctly optimized N−H bond lengths, 1.025 and 1.029 Å, are actually quite similar to the standard value, 1.030 Å, used in our original study. However, as discussed in the next section, improvement in the calculated ^{17}O NMR tensors using the optimized molecular model over the original model is significant. This illustrates the importance of directionality of N−H···O hydrogen bonds.

As is also seen in Table 1, the C−H···O hydrogen bonds show some different trends when compared to the situations in strong N−H···O hydrogen bonds. For example, there is essentially no difference in the C−H bond length from the two methods. This observation is consistent with the results of a recent computational study where Hobza et al. found that, at the MP2/6-31G(d) level of geometry optimization, the C5−H5 bond is lengthened by only 0.003 Å upon UU7 dimer formation.[35] We should point out that, in our cluster model, molecules 1 and 2 can be considered as a UU7 dimer. We also see from Table 1 that the optimized C−H···O bond angles show very small changes (<2°) compared to the corresponding X-ray diffraction values. This may not be surprising because C−H···O hydrogen bonds are weak (typically less than 4 kcal mol^{-1}). As will be discussed in detail in the next section, although the structural changes at O2 are small in the seven-molecule cluster model, the model does show improvement in the calculated ^{17}O NMR tensors for O2.

3.2. Calculation of ^{17}O NMR Tensors. In this section, we focus on comparison of calculated ^{17}O NMR tensors from four different molecular models. The first model consists of a single uracil molecule with its structure fully optimized. This represents a gas-phase molecule. This model provides a baseline for the ^{17}O NMR tensors in uracil. The second model is the original three-molecule model used in our previous study. In this model, standard N−H (1.030 Å) and C−H (1.100 Å) bond lengths are used to localize hydrogen atom positions. The third model is an improved three-molecule model, where H1 and H3 positions are obtained from partial geometry optimization using “anchor” molecules. The fourth model is an optimized seven-molecule model, where all four hydrogen atoms of interest, H1, H3, H5, and H6, are optimized using “anchor” molecules. The calculated ^{17}O NMR tensors from these models are summarized in Table 2 and depicted in Figures 2 and 3. In the discussion that follows, we examine ^{17}O chemical shielding tensors and electric field gradient tensors separately.

3.2.1. Chemical Shielding Tensors. As seen clearly from Figure 2, the ^{17}O chemical shielding tensors for O2 and O4 show quite different responses to different cluster models. More specifically, the calculated ^{17}O chemical shielding tensor for O4 exhibits consistent and significant improvement as the description for the HB network at O4 becomes more complete on going from the isolated-molecule model to the seven-molecule cluster model. With the seven-molecule model, all individual ^{17}O chemical shielding tensor components differ less than 10 ppm from the experimental values at the B3LYP/6-311++G(d,p) level of computation. It is remarkable to see that the isotropic ^{17}O chemical shift for O4 changes by more than 100 ppm depending on whether the uracil molecule is in gas phase or in crystal lattice. This change is much larger than those seen in secondary amides (ca. 30 ppm for one N−H···O hydrogen bond)[4] and in benzamide (ca. 70 ppm for two N−H···O hydrogen bonds),[2] and even larger than that seen in crystalline urea (ca. 80 ppm for four N−H···O hydrogen bonds).[5] This suggests that the HB interaction at O4 in crystalline uracil is quite strong. Similar to the previous cases, change in the isotropic ^{17}O chemical shift for O4 is also accompanied by a reduction in the span of the chemical shielding tensor by approximately 250 ppm. On the basis of the significant improvement in computational accuracy from the optimized three-molecule model over the original three-molecule model, it can be concluded that, when the target oxygen atom is involved in strong N−H···O hydrogen bonds,

TABLE 2: Comparison of Calculated NMR Parameters for Different Model Clusters of Uracil at the B3LYP/6-311++G(p,d) Level

model		δ_{iso} (ppm)	δ_{11} (ppm)	δ_{22} (ppm)	δ_{33} (ppm)	C_Q (MHz)	η_Q
optimized 1-molecule[a]	O2	286	446	398	11	8.60	0.33
	O4	387	688	485	−12	9.82	0.02
original 3-molecule	O2	290	493	416	−20	9.32	0.25
	O4	320	564	410	−14	9.49	0.36
optimized 3-molecule	O2	294	472	411	−2	9.01	0.27
	O4	296	500	380	7	8.44	0.54
optimized 7-molecule	O2	258	409	362	3	8.48	0.44
	O4	279	467	361	10	8.15	0.61
experimental[a]	O2	245	400	330	10	7.61	0.50
	O4	275	470	350	10	7.85	0.55

[a] From ref 13.

obtaining accurate hydrogen atom positions in the cluster model is an important step toward producing reliable theoretical ^{17}O chemical shielding tensors. The further improvement seen in the seven-molecule model over the optimized three-molecule model reflects an indirect effect from a large number of neighboring hydrogen bonds.

In contrast, the ^{17}O chemical shielding tensor for O2 shows much less sensitivity to different cluster models. In fact, the calculated ^{17}O chemical shielding tensors for O2 from the first three models are essentially the same and are in obvious disagreement with the experimental results. The seven-molecule model where the two C−H···O hydrogen bonds are included indeed yields an improved ^{17}O chemical shielding tensor for O2. Now the largest discrepancy between experimental and calculated data occurs at the δ_{22} tensor component, ca. 30 ppm. However, it should be pointed out that this discrepancy is much larger than those seen for the ^{17}O chemical shielding tensor components at O4 (vide infra).

3.2.2. Electric Field Gradient Tensors. As seen from Figure 3, the calculated ^{17}O EFG tensors for O2 and O4 show some trends parallel with those discussed in the ^{17}O chemical shielding tensors. The strong HB interaction at O4 induces a reduction of 1.67 MHz in the ^{17}O quadrupole coupling constant. Again, this change is much larger than those observed for secondary amides (ca. 0.6 MHz for one N−H···O hydrogen bond),[4] benzamide (ca. 1.4 MHz for two N−H···O hydrogen bonds),[2] and crystalline urea (ca. 1.0 MHz for four N−H···O hydrogen bonds).[5] Another significant improvement is in the asymmetry parameter. For example, while the EFG tensor at O4 is axially symmetric, $\eta_Q \approx 0$, for an isolated "gas-phase" uracil molecule, this tensor becomes quite asymmetric for uracil in the seven-molecule cluster, $\eta_Q \approx 0.61$. This increase in η_Q with an increase of the strength of HB interaction has been observed in our

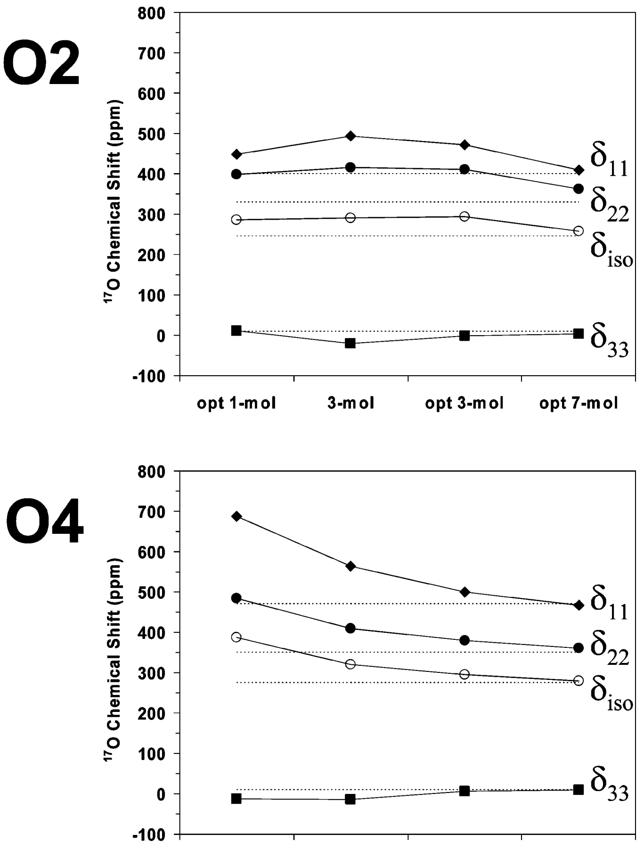

Figure 2. Calculated (symbols) and experimental (dotted lines) ^{17}O chemical shielding tensors for O2 and O4 using different molecular models. All calculations are at the B3LYP/6-311++G(d,p) level.

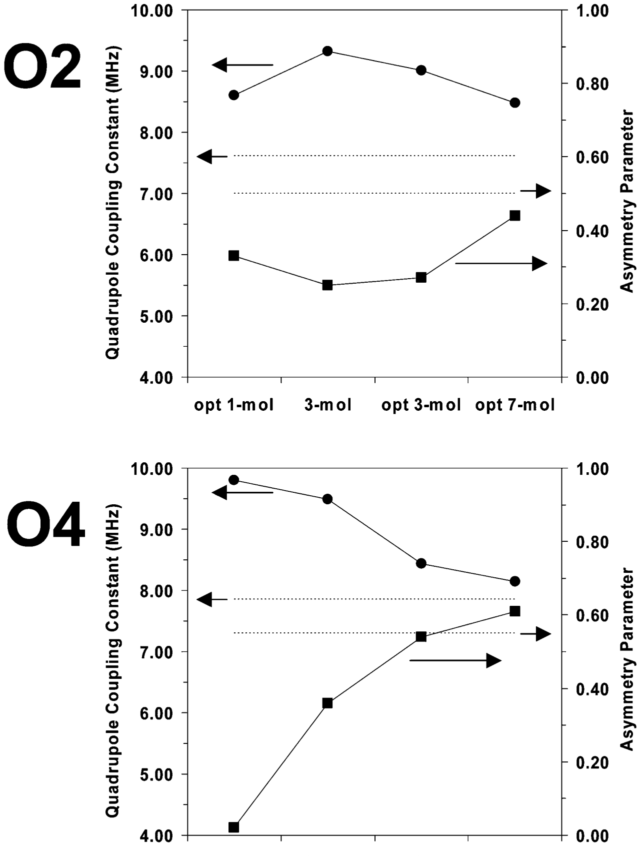

Figure 3. Calculated (symbols) and experimental (dotted lines) ^{17}O quadrupole coupling constant and asymmetry parameter for O2 and O4 using different molecular models. All calculations are at the B3LYP/6-311++G(d,p) level.

TABLE 3: Comparison between Computational Results for the ^{17}O NMR Tensors in Uracil Using Full Basis Set and LD Basis Set Methods[a]

basis set	basis functions	primitive Gaussians	$\delta_{iso}{}^b$ (ppm)	$\delta_{11}{}^b$ (ppm)	$\delta_{22}{}^b$ (ppm)	$\delta_{33}{}^b$ (ppm)	CPU (h)	$C_Q{}^b$ (MHz)	$\eta_Q{}^b$	CPU (h)
6-311G(d)										
full	1092	1932	251, 264	401, 445	354, 347	−1, 0	13.1	8.39, 7.96	0.48, 0.68	1.7
LD	848	1688	253, 265	409, 452	355, 349	−5, −5	7.2	8.37, 7.91	0.48, 0.69	1.4
6-311++G(d,p)										
full	1428	2268	258, 280	409, 467	362, 361	3, 10	82	8.48, 8.15	0.44, 0.61	21.4
LD	856	1696	252, 272	398, 458	354, 352	2, 6	7.6	8.38, 8.10	0.46, 0.62	1.5
cc-PVTZ										
full	2072	3444	253, 271	398, 451	357, 354	4, 9	302.9	8.18, 7.82	0.41, 0.60	39.5
LD	872	1730	249, 263	398, 445	351, 346	−3, −1	15.5	8.14, 7.76	0.43, 0.63	2.4

[a] In all calculations, the seven-molecule optimized model was used. [b] The first number in the column is for O2, and the second number is for O4.

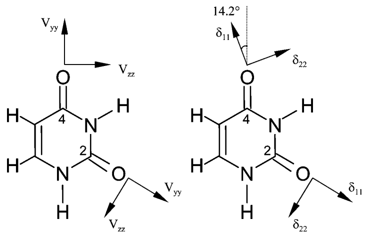

Figure 4. Illustration of orientations of the ^{17}O EFG and chemical shielding tensors for uracil in the molecular frame of reference.

previous study.[4] With the seven-molecule model, the calculated EFG tensor at O4 is in good agreement with the experimental results.

For the EFG tensor at O2, the seven-molecule model also shows improvement, although not as dramatic as the one seen for O4. In addition, the improvement seems to be more pronounced for the asymmetry parameter than for the quadrupole coupling constant. It is also noted that, with the seven-molecule model, the discrepancy between the calculated and experimental ^{17}O quadrupole coupling constants is considerably larger for O2 than for O4, similar to the trend observed in the ^{17}O chemical shielding tensors for these two atoms. As will be shown in the next section, this trend seems to be independent of the basis sets used in the calculation. It is unclear at this time whether this trend reflects a particular difficulty of quantum mechanical calculation in handling weak C−H···O hydrogen bonds or is due to some long-range interactions.

3.3. Orientations of the ^{17}O NMR Tensors. One of the benefits of quantum mechanical calculations is that they yield orientation information for NMR tensors in the molecular frame of reference. In the previous section, we have seen that the magnitude of the ^{17}O NMR tensors (i.e., tensor components) is sensitive to the HB interaction. Here we further examine whether the ^{17}O NMR tensor orientations show any dependence on the HB interaction. The ^{17}O NMR tensor orientations obtained for the optimized seven-molecule model are shown in Figure 4. For both O2 and O4, the largest EFG tensor component lies in the molecular plane and is perpendicular to the C═O bond. The smallest EFG tensor component lies along the norm of the molecular plane. Such an EFG tensor orientation is in agreement with the results found for other functional groups containing a C═O bond, e.g., amide,[2,4] carboxylic acid,[11,36] acid salt,[21] urea,[5] ketone,[37] and aldehyde.[38] We also obtained an identical EFG tensor orientation for the optimized one-molecule (gas-phase) model of uracil. This suggests that the EFG tensor orientation at the oxygen atom in a C═O bond is determined solely by the nature of the C═O double bond, showing no dependence on the HB environment. This makes the EFG tensor useful as an internal reference. That is, if the relative orientation between EFG and chemical shielding tensors is determined experimentally, we can infer the chemical shielding tensor orientation in the molecular frame.

As is also seen from Figure 4, the orientations of the chemical shielding tensors at O2 and O4 are slightly different. At O2, the δ_{11} component is along the C═O bond, and at O4, it is tilted by 14.2° away from the C═O bond. For both O2 and O4, the δ_{33} component is along the norm of the molecular plane. For the optimized single uracil molecule, the ^{17}O chemical shielding tensor orientation is the same for O2 as illustrated in Figure 4, but is slightly different for O4 (the tilt angle between δ_{11} and the C═O bond is 8.5°). Similar to the case for EFG tensors, we can also conclude that the HB interactions in crystalline uracil have little effect on the orientation of the ^{17}O chemical shielding tensor. The tensor orientation seen in uracil is also similar to other functional groups containing a C═O bond such as amide,[2,4] carboxylic acid,[11] ketone,[37] and aldehyde.[38] However, it is also important to point out two notable exceptions, urea[5] and potassium hydrogen dibenzoate,[21] where the δ_{11} component is actually perpendicular to the C═O bond. In these two cases, one may argue that the C═O bond has more single-bond character, because of strong hydrogen bonding in the former case and charge delocalization in the latter case.

3.4. Calculations Using a Locally Dense Basis Set Method. In this study, we chose a DFT approach over Hartree−Fock (HF) theory and other post-HF methods to calculate ^{17}O NMR tensors as a compromise for computational accuracy and efficiency. Because our optimized seven-molecule model consists of 84 atoms, post-HF methods such as coupled-cluster theory, configuration mixing methods, and perturbation theory are not practical with our current computation resources. To further explore ways for achieving both accuracy and efficiency, we utilized a locally dense basis set method.[29] In the LD basis set calculations, we chose three basis sets, 6-311G(d), 6-311++G(d,p), and cc-pVTZ, for the target oxygen atom and a smaller basis set, 6-31G(d), for the remaining atoms in the seven-molecule model. For comparison, we also performed calculations with the full basis set method where the same basis set is used for all atoms. The calculated results for ^{17}O NMR tensors are shown in Table 3. The data in Table 3 show quite clearly that for the basis sets tested in this study, the accuracy from the LD basis set approach is similar to that achieved with the full basis set method. Meanwhile the computational cost for the LD basis set calculations is reduced by a factor of 20. For example, the computational time on our SunFire 6800 computer for chemical shielding calculation using cc-pVTZ basis set for all 84 atoms in the seven-molecule model is 302.9 h. When the LD basis set method is used, i.e., cc-pVTZ for O2 and O4 and 6-31G(d) for other atoms, the computational time is only 15.5 h. Yet the largest discrepancies between these two methods are

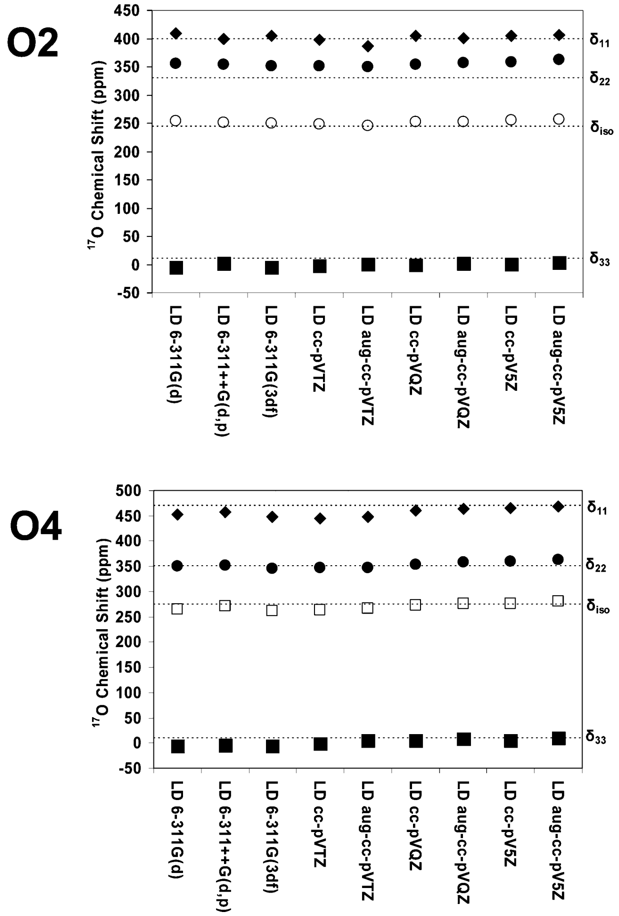

Figure 5. Calculated (symbols) and experimental (dotted lines) ^{17}O chemical shielding tensors for O2 and O4 using different basis sets. The optimized seven-molecule model is used in these calculations.

8 ppm in the chemical shielding tensor components, 0.06 MHz in the ^{17}O quadrupole coupling constant, and 0.03 in the asymmetry parameter.

Because we have just established the validity of the LD basis set approach, it is now possible to investigate whether the accuracy of ^{17}O NMR tensor calculations for crystalline uracil can be further improved by increasing the size of the basis set used for the target oxygen atoms. Here we tested a series of standard split-valence basis sets and Dunning's correlation consistent basis sets. The results are shown in Figures 5 and 6.

For ^{17}O chemical shielding tensors, it seems that the accuracy of the calculations does not improve even with a very large basis set, aug-cc-pV5Z. In fact, the calculations show very little change beyond 6-311G(d). On the other hand, the ^{17}O EFG calculations converge much more slowly. As seen in Figure 6, the calculated asymmetry parameter for both O2 and O4 levels off at cc-pVTZ. This is quite surprising and counterintuitive, because it is generally believed that chemical shielding calculations are much more difficult to perform than EFG calculations. Nonetheless, our results suggest that, to make reliable predictions for both ^{17}O chemical shielding and EFG tensors in systems similar to crystalline uracil, one can use the LD basis set approach with a cc-pVTZ basis set as a minimal level of computation.

4. Conclusion

In this study we have shown that quantum mechanical calculations using an optimized seven-molecule model can yield reliable ^{17}O NMR tensors for O2 and O4 in crystalline uracil. We found that it is important to optimize hydrogen atom positions with a cluster model that includes all neighboring hydrogen-bonded molecules as "anchors". We have also shown that full basis set calculations using B3LYP coupled with 6-311++G(d, p), 6-311G(3df), and cc-pVTZ basis sets are suitable for calculating ^{17}O NMR tensors. In comparison, LD basis set calculations using a cc-pVTZ/6-31G(d) combination are equally reliable, but require a fraction of the computational time. Such an approach can yield a reasonably high degree of accuracy with relatively inexpensive computing resources, provided that a properly designed cluster model is used. Another interesting finding of this study is that, compared to strong N−H···O hydrogen bonds, there seems to exist a particular difficulty in handling weaker C−H···O hydrogen bonds. Compared to experimental ^{17}O NMR data, the accuracy in both calculated EFG and ^{17}O chemical shielding tensors is approximately 3 times better for O4 than for O2. It is possible that both the early crystal structure and experimental ^{17}O NMR data for crystalline uracil are not accurate enough. Further investigation is clearly required. Nonetheless, our results set an upper limit for computational accuracy in these hydrogen-bonded systems. It is possible that a LD basis set approach at the cc-pVTZ/6-31G(d) level can produce useful results for ^{17}O NMR tensors for large molecular systems such as proteins and nucleic acids.

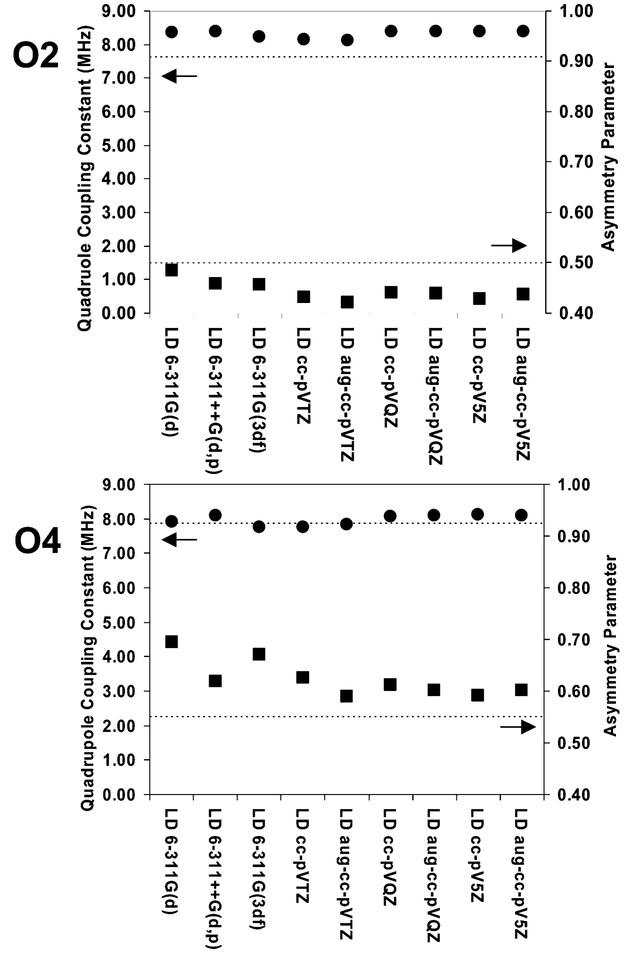

Figure 6. Calculated (symbols) and experimental (dotted lines) ^{17}O quadrupole coupling constant and asymmetry parameter for O2 and O4 using different basis sets. The optimized seven-molecule model is used in these calculations.

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