Rotational Spectra and Gas Phase Structure of the Maleimide – Formic Acid Doubly Hydrogen Bonded Dimer

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Abstract

Rotational transitions were measured for the maleimide – formic acid doubly hydrogen bonded dimer using a Flygare-Balle type pulsed-beam Fourier transform microwave spectrometer. No splittings caused by possible concerted double proton tunneling motion were observed. Experimental rotational constants (MHz), quadrupole coupling constants (MHz), and centrifugal distortion constants (kHz) were determined for the parent and three deuterium substituted isotopologues. The values for the parent are $A = 2415.0297(10)$, $B = 784.37494(38)$, $C = 592.44190(33)$, $D_J = 0.0616(64)$, $D_{JK} = -0.118(35)$, $D_K = -1.38(15)$, $1.5\chi_{aa} = 2.083(14)$, and $0.25(\chi_{bb} - \chi_{cc}) = 1.1565(29)$. The hydrogen bond lengths were determined using a nonlinear least squares structure fitting program. Rotational constants for this complex are consistent with a planar structure, with an inertial defect of $\Delta = -0.528 \text{ amu } \text{\AA}^2$. The B3LYP calculation yielded rotational constants within 0.1% of the experimental values.

1. Introduction

Hydrogen bonding interactions play key roles in DNA replication and transcription, protein folding, and many other areas of biology and biochemistry. Hydrogen bonded complexes with two or three hydrogen bonds are important models for the hydrogen bonding properties and dynamics of the A-T and G-C base pairs in DNA. Hydrogen-bonded dimers are not static structures. Several doubly hydrogen-bonded dimers have been shown to exhibit concerted proton tunneling dynamics. These dimers include complexes such as propiolic acid - formic acid^{1,2,3} and acetic acid - formic acid⁴. The doubly hydrogen bonded carboxylic acid dimers that exhibited the tunneling motion had $C_{2v}(M)$ symmetry and a symmetric double-well potential for the tunneling motion. Proton tunneling between identical molecules has also been observed for the homodimers of 3-fluoro-benzoic acid⁵ and acrylic acid.⁶

Calculations have been reported for the problem of tunneling in the asymmetric double-well potentials.^{7,8,9} It appears the tunneling frequencies tend to decrease and the probability of observing tunneling splittings in the spectra becomes less as the potential becomes more asymmetric. No tunneling splittings were observed for formic acid-formamide,¹⁰ 1,2-cyclohexanedione-FA¹¹ or cyclopropanecarboxylic acid-FA.¹² No evidence for proton tunneling was observed in the present work on the Maleimide – Formic Acid complex.

In this study, microwave spectra for the maleimide – formic acid (Mal-FA) doubly hydrogen bonded dimer were measured. It is important to also characterize the dimers with nitrogen containing groups, as tunneling dynamics may be different from the cases with the oxygen containing species. It has been suggested that this proton tunneling

motion may be associated with point mutations in DNA,^{13,14} so studying small benchmark systems, as the ones described, that model the DNA base pairing is critical to better understand the tunneling process in larger biologically active molecules. Information about the dynamics of this tunneling motion, such as barrier height of the potential energy surface, can be determined through the analysis of the microwave spectroscopic data.

2. Calculations, Microwave Measurements and Data Analysis

Ab initio calculations were performed on the Mal-FA dimer in order to obtain preliminary rotational and quadrupole coupling constants for this system, allowing for the pure rotational transitions to be predicted using Pickett's SPCAT¹⁵ program. A B3LYP method was used with an aug-cc-pVTZ basis using the Gaussian 09 suite¹⁶ on the HPC system at the University of Arizona. Additional simple calculations were performed to predict the rotational constants of the singly deuterated isotopologues. This was done by first determining the ratio between the parent experimental and calculated rotational constants. Following this calculation, the ratio was multiplied by the calculated rotational constants of the deuterated isotopologues, which were calculated using Kisiel's PMIFST program¹⁷ after changing the mass of the respective substituted H atom in the calculated structure. Usually the corrected values of the rotational constants for the singly substituted isotopologues are very close to experimental values for ¹³C substituted isotopologues. In the case of these D substituted isotopologues in this Mal-FA dimer, the H atoms are distant from the principle axes, thus making the effect of changing the mass of H to D larger when recalculating the moments of inertia.

This resulted in predicted rotational constants that did not agree very well with the fit experimental values and so significant scanning was needed to measure these singly D substituted transitions.

The rotational transitions were measured for the parent in the 4.9 – 10 GHz range using a Flygare-Balle type pulsed-beam Fourier transform microwave spectrometer that has been previously described.^{18,19} The maleimide sample was purchased from Sigma Aldrich (99%) and was used without further purification. The pressure inside the vacuum cavity was maintained at 10^{-6} to 10^{-7} Torr prior to the pulsed injection of the molecular sample. The Ne carrier gas was maintained at ~ 1 atm. In order to obtain sufficient vapor pressure of the maleimide sample, the sample and pulsed valve (General Valve Series 9) were heated to ~ 70 °C. To prepare the doubly hydrogen bonded dimer, the maleimide and formic acid samples were transferred to separate glass sample cells. Within the Ne gas line, the cooled formic acid (-8 °C) sample cell was placed before the maleimide sample and the temperature of the FA was maintained at -8 °C using a Peltier cooling device. The temperature of maleimide sample cell and the pulsed valve were maintained at 70 °C with a variac heating coil. All measured rotational transitions for the parent are shown in Table 1 and the transitions measured of each of the singly D substituted isotopologues are shown in Table 2. There was no evidence of the concerted proton tunneling motion observed for this dimer. Since many b-type transitions were measured without observing any spectral splittings (which would be present if tunneling was observed), it is reasonable to conclude this dimer did not exhibit tunneling. If proton tunneling was present, the b-type transitions

will be significantly split by hundreds of MHz and a ro-vibrational coupling analysis would be needed to fit the split transitions from each of the tunneling states.

The experimental rotational, quadrupole coupling and centrifugal distortion constants were determined from the assigned rotational transitions for each of the isotopologues using Pickett's SPFIT¹⁵ program and these values are shown in Table 3. The calculated values are within 0.1% of the experimental values. During the microwave fits for the isotopologues, the centrifugal distortion constants were held fixed to the values obtained from the parent. The experimental inertial defect was $\Delta = -0.528 \text{ amu } \text{\AA}^2$, indicating the molecular structure is consistent with a planar structure with a value close to zero. The small negative nonzero value of this inertial defect indicates the presence of out of plane vibrations within this dimer.²⁰ Compared with the inertial defect of the maleimide monomer ($\Delta = -0.0536 \text{ amu } \text{\AA}^2$),²¹ the magnitude of the inertial defect of the dimer is larger, suggesting more out of plane vibrational modes in the hydrogen bonded dimer. This may be a result of the complex being weakly bound, allowing for these additional out of plane vibrations.

From the rotational constants of the parent and each singly D substituted isotopologue, a nonlinear least squares fit was performed to determine the best fit gas phase hydrogen bond lengths of this dimer. This fitting program varies the Cartesian coordinates of the atoms within the molecules to obtain a structure that calculates moments of inertia, or rotational constants, closest to the experimentally determined values. During the fit, the atomic coordinates of Mal were held fixed to previously obtained values²¹ and the structure of formic acid was held fixed to what was obtained from the work of Gerry *et al.*²² Because the structure of the Mal monomer is an

averaged structure of both equilibrium and ground state atomic coordinates, the obtained structure of the dimer is also a vibrationally averaged structure. We believe the differences are small and this best fit structure reasonably represents this dimer in the ground state. There were 2 varied parameters during the structure fit which varied the coordinates of FA in the molecular (a-b) plane. A third parameter, ϕ , was the rotation of the formic acid coordinates within this molecular plane using a standard rotation matrix. ϕ was not varied, but was set to a value that provided the smallest standard deviation in the structure fit, which was 1.09 MHz. This best fit structure can be seen in Figure 1 and the hydrogen bond lengths from the B3LYP calculation and the best fit structure are compared in Table 4. The best fit structure seemed to correlate with the formic acid moiety slightly rotated to increase the length of $r(\text{H}_6\text{-O}_{13})$ and decrease the length of $r(\text{O}_{12}\text{-H}_{10})$. The center of mass separation, determined through the use of the parallel axis theorem, of the monomer units remained unchanged from the calculation and the experimentally determined rotational constants.

The principle axes coordinates of the best fit structure are shown in Table 5 along with the Kraitchman determined coordinates for the single D substituted H atoms, which were calculated using Kisiel's KRA²³ program. The Kraitchman determined coordinates only give the magnitudes and so the absolute values of the coordinates are shown. The D substituted coordinates do not agree very well with the best fit structure, indicating a large change of the molecular structure upon the isotopic substitution. The change in structure upon substitution agrees with the fact that the rotational constants of these D isotopologues could not be predicted very accurately by changing the mass of each of these substituted atoms. Since the nonlinear least squares fitting program

assumes the structure does not change upon isotopic substitution to obtain the best fit structure, this current structure can be refined with the measurement of transitions from singly substituted ^{13}C and ^{15}N isotopologues to obtain more accurate hydrogen bond distances, but these hydrogen bond distances are not expected to significantly change with these additional measurements.

3. Conclusions

Rotational transitions were measured for the maleimide – formic acid doubly hydrogen bonded dimer and three single D substituted isotopologues. There was no evidence of the double concerted proton tunneling in the measurement of the rotational transitions of this dimer, further suggesting that $\text{C}_{2v}(\text{M})$ symmetry is required to observe this tunneling effect. The best fit gas phase structure is an averaged structure of equilibrium and ground state atomic coordinates, but is a reasonable representation of the ground state of this dimer. The current structure can be further refined with the measurement of additional isotopologue transitions.

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Figure 1. Best fit structure of the maleimide – formic acid dimer, showing the hydrogen bond distances in Å.

Table 1. Measured rotational transitions of the maleimide – formic acid heterodimer and the differences (ν_{o-c}) from the calculated values in the fit. Values shown are in MHz.

J'	K_a'	K_c'	F'	J''	K_a''	K_c''	F''	ν_{obs}	ν_{o-c}
2	2	0	2	2	1	1	2	4907.953	0.006
4	1	4	5	3	1	3	4	5093.764	0.002
4	1	4	4	3	1	3	3	5093.864	-0.006
3	1	3	4	2	0	2	3	5287.475	0.005
3	1	3	3	2	0	2	2	5288.088	0.001
4	0	4	5	3	0	3	4	5353.787	-0.004
4	0	4	4	3	0	3	3	5353.961	0.003

4 2 3 3	3 2 2 2	5494.710	0.002
4 2 3 5	3 2 2 4	5494.768	0.006
4 2 3 4	3 2 2 3	5494.978	0.006
5 0 5 5	4 1 4 4	5632.969	-0.002
5 0 5 6	4 1 4 5	5633.204	-0.004
5 0 5 4	4 1 4 3	5633.323	-0.000
4 1 3 3	3 1 2 2	5856.487	-0.002
4 1 3 5	3 1 2 4	5856.553	0.005
4 1 3 4	3 1 2 3	5856.633	0.001
3 2 2 3	3 1 3 3	5764.425	-0.001
3 2 2 4	3 1 3 4	5765.572	0.004
5 1 5 6	4 1 4 5	6342.525	0.006
5 1 5 5	4 1 4 4	6342.597	-0.008
5 0 5 4	4 0 4 3	6593.400	-0.001
5 0 5 5	4 0 4 4	6593.573	0.001
5 2 4 5	5 1 5 5	6671.616	0.000
5 2 4 6	5 1 5 6	6672.609	-0.003
5 2 4 4	5 1 5 4	6672.816	0.001
5 2 4 6	4 2 3 5	6848.564	-0.000
5 2 4 5	4 2 3 4	6848.697	0.002
5 3 3 6	4 3 2 5	6930.662	-0.005
5 3 3 5	4 3 2 4	6930.853	-0.001
6 1 6 6	5 1 5 5	7578.725	0.001
6 0 6 7	5 0 5 6	7793.394	0.005
6 0 6 6	5 0 5 5	7793.556	-0.003
2 2 1 3	1 1 0 2	7837.498	-0.004
2 2 1 2	1 1 0 1	7837.952	-0.005
5 3 2 5	5 2 3 4	8267.066	0.002
5 3 2 5	5 2 3 6	8267.096	-0.008
5 3 2 6	5 2 3 6	8267.188	0.007
3 2 2 4	2 1 1 3	9022.316	-0.002
3 2 2 2	2 1 1 3	9022.316	-0.002
3 2 2 3	2 1 1 3	9022.316	-0.002
3 2 2 3	2 1 1 2	9022.830	-0.009
3 2 2 2	2 1 1 2	9022.830	-0.009
3 2 1 3	2 1 2 2	9676.429	-0.001
3 2 1 4	2 1 2 3	9677.607	0.007
3 2 1 2	2 1 2 1	9678.211	0.001

Table 2. Measured rotational transitions of the isotopologues of the Mal-FA dimer and the differences (ν_{o-c}) from the calculated values in the fit. Values shown are in MHz.

Rotational Transitions		Mal – (D)FA		Mal(ND) – FA		Mal – FA(OD)	
J' K _a ' K _c ' F'	J'' K _a '' K _c '' F''	ν_{obs}	ν_{o-c}	ν_{obs}	ν_{o-c}	ν_{obs}	ν_{o-c}
2 2 0 1	2 1 1 1	4926.610	-0.001			4897.0811	-0.003
2 2 0 3	2 1 1 3	4926.645	0.000			4897.1440	0.005
4 1 4 5	3 1 3 4	4984.640	-0.006	5088.241	-0.006	5055.5005	-0.004
4 1 4 4	3 1 3 3	4984.742	-0.004	5088.347	-0.002	5055.6011	0.000
3 1 3 2	2 0 2 1	5217.600	0.010	5271.962	0.001	5256.7998	0.005
3 1 3 4	2 0 2 3	5217.708	-0.001	5272.074	-0.001	5256.9155	-0.003
3 1 3 3	2 0 2 2	5218.325	0.001				
4 0 4 5	3 0 3 4	5238.871	-0.006			5313.5459	-0.007
4 0 4 4	3 0 3 3	5239.036	0.000	5348.165	0.001	5313.7095	-0.003
5 0 5 5	4 1 4 4	5469.778	-0.002	5636.195	-0.005	5581.7734	0.004
5 0 5 6	4 1 4 5	5470.032	-0.002	5636.430	-0.002	5582.0132	0.001
5 0 5 4	4 1 4 3	5470.153	0.004	5636.546	0.004	5582.1284	0.006
4 1 3 3	3 1 2 2	5717.417	-0.007			5809.5996	-0.006
4 1 3 5	3 1 2 4	5717.487	0.004	5853.249	0.002	5809.6655	0.001
4 1 3 4	3 1 2 3	5717.567	0.008	5853.324	0.000		
5 1 5 6	4 1 4 5	6207.899	0.002	6335.367	0.000	6295.1514	0.002
5 1 5 4	4 1 4 3	6207.954	0.009	6335.420	0.006		
5 0 5 6	4 0 4 5			6585.264	-0.002		
5 0 5 4	4 0 4 3	6456.280	-0.007			6544.7793	-0.006
5 0 5 5	4 0 4 4	6456.449	-0.004	6585.437	-0.002	6544.9556	0.004
6 1 6 7	5 1 5 6			7569.764	0.003	7522.3765	0.009
6 1 6 5	5 1 5 4	7419.320	0.003	7569.798	0.005		
6 1 6 6	5 1 5 5	7419.359	0.004	7569.839	0.006	7522.4468	0.011
6 0 6 5	5 0 5 4	7635.267	-0.004	7782.922	0.004	7736.7603	-0.003
6 0 6 7	5 0 5 6	7635.267	0.002				
6 0 6 6	5 0 5 5	7635.427	-0.004	7783.064	-0.014	7736.9170	-0.005

Table 3. Fit rotational, centrifugal distortion, and quadrupole coupling constants of the Mal – FA dimer. Also shown is the B3LYP/aug-cc-pVTZ calculated values.

	Parent	B3LYP/aug -cc-pVTZ	-ND	D-FA	FA-OD
A/MHz	2415.0297(11)	2414.7720	2403.7960(43)	2402.0396(22)	2405.0404(22)
B/MHz	784.37494(41)	784.34024	784.16342(70)	764.72770(54)	777.87629(55)
C/MHz	592.44190(36)	592.04019	591.65013(28)	580.42763(25)	588.13551(25)
$1.5\chi_{aa}/\text{MHz}$	2.083(15)	2.150	1.86(11)	1.860(44)	1.694(40)
$0.25(\chi_{bb} - \chi_{cc})/\text{MHz}$	1.1565(32)	1.1865	1.118(17)	1.136(10)	1.117(12)
D_J/kHz	0.0616(69)		0.0616*	0.0616*	0.0616*
D_{JK}/kHz	-0.118(38)		-0.118*	-0.118*	-0.118*
D_K/kHz	-1.38(16)		-1.38*	-1.38*	-1.38*
N	45		19	24	20
σ/kHz	4		5	5	5

* Centrifugal distortion constants were held fixed to the experimental parent isotopologue values during the microwave fits of each isotopologue.

Table 4. Hydrogen bond distances and center of mass separation of the monomers in the best fit structure compared with the B3LYP/aug-cc-pVTZ calculated values, shown in Å.

Interatomic Distance	Microwave Fit Value	Calculated (B3LYP) Value
$r(\text{H}_6\text{-O}_{13})$	2.027	1.874
$r(\text{O}_{12}\text{-H}_{10})$	1.634	1.685
COM Separation	4.06	4.06

Table 5. Best fit atomic coordinates (Å) of the best fit structure compared with the Kraitichman determined coordinates of the substituted D isotopes. The Kraitichman values only show the magnitudes of the COM coordinates.

Atom	a	b	Krait- a	Krait- b
C1	0.469	-1.006		
C2	1.868	-1.542		
C3	2.726	-0.481		
C4	1.908	0.775		
C5	-3.095	0.642		
H6	-0.200	1.007	0.4042(38)	0.9895(15)
H7	2.091	-2.601		
H8	3.808	-0.477		
H9	-4.143	0.944	4.06138(38)	1.0843(14)
H10	-2.005	-0.871	2.31736(66)	0.9384(16)
O11	2.313	1.918		
O12	-0.564	-1.642		
O13	-2.184	1.425		
O14	-2.958	-0.691		
N15	0.586	0.371		

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Graphical Abstract