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Measurement and *ab initio* modeling of the inelastic neutron scattering of solid N-methylformamide

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Vibrational motions of solid N-methylformamide (NMF) and its N-deuterated analogue are investigated using the inelastic neutron scattering (INS) technique at 15 K. The force field for obtaining the normal vibrational modes of the crystal is based on a quantum chemical calculation and a subsequent transfer of a harmonic force field of a smaller pentameric segment to a fragment of 11 NMF molecules. Two types of hydrogen bonds present in crystalline NMF are also modeled with dimers. The distinct bonding leads to a splitting of the N-hydrogen wagging mode in the spectrum. Although the hydrogen bonding has a profound effect on vibrational frequencies, the results indicate that an occurrence of a double-well potential for bonded hydrogen proposed previously is unlikely. Instead, a limited electronic conjugation along the hydrogen bonds in crystalline NMF is observed. Unlike in previous models, we simulate the relative INS intensity of each vibrational transition separately, which leads to a substantial improvement of the overall profile of the intensity pattern. The modeling allows one to assign most of observed INS bands to vibrational modes and the overall spectral profile that reproduced by the simulation compares well with the experiment. © 1998 American Institute of Physics. [S0021-9606(98)01101-5]

I. INTRODUCTION

N-methylformamide (NMF, HCONHCH_3) is one of the simplest amides that are widely used to investigate basic properties of the peptide linkage, $\text{O}=\text{C}(\text{R})-\text{NH}(\text{R}')$. As in formamide or N-methylacetamide (NMA), strong intermolecular hydrogen bonding is present in the condensed phase of NMF. Traditionally, the bonding was compared to proteins and other molecules present in living matter.^{1,2} Quite recently, for example, NMF was identified as an anticancer agent³⁻⁵ and phase II clinical trials have even been conducted.⁶ Also, other basic biochemical processes (charge transfer, neuron signaling) can be conveniently modeled with simple amides.

The presence of intermolecular hydrogen bonding can also be investigated by conventional ir and Raman spectra, especially in the near ir region ($3000-3500\text{ cm}^{-1}$) where stretching motions of the hydrogen atoms dominate. However, in the lower energy region, either the signal is obscured by vibrational motions of heavier atoms, or it cannot be measured due to the limited spectral window of the spectrometer.

Thus due to the high inelastic neutron scattering cross section for hydrogen, INS offers an attractive alternative to the conventional optical spectroscopy for the studies of hydrogen bonding. In addition, with the lack of symmetry selection rules, all the vibrational modes involving hydrogen can be observed. INS intensities for each vibrational mode are directly proportional to the mean square displacements of the hydrogen atoms and thus can be modeled using standard methods of normal mode analysis. INS studies on the deuterated compounds can be particularly aimed at the hydrogen bonding, since the acidic hydrogen may be easily exchanged. The main drawbacks of the INS method are expensive instrumentation, lower resolution, and a relatively large amount of sample needed.

NMF in the gas, liquid, and solution phases has been extensively studied by means of vibrational spectroscopy,⁷⁻⁹ microwave spectroscopy,¹⁰ and electron diffraction.¹¹ These studies confirm the planar structure of an isolated NMF molecule,¹² stabilized due to the partial double-bond character of the C-N bond. Surprisingly, x-ray crystal structure of NMF was not determined until recently,¹³ while the intermolecular structure of NMF in the liquid phase has been studied by x-ray and neutron diffraction.¹⁴⁻¹⁶ The NMF molecules form helical chains in the crystal, with equal numbers of left-

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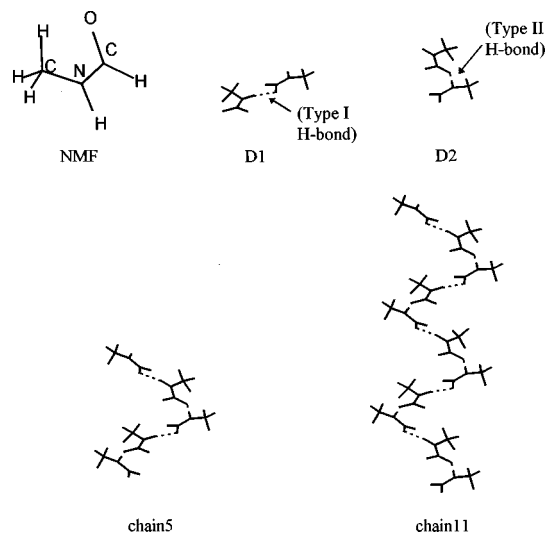


FIG. 1. The models of the NMF crystal: single molecule (NMF), H-bonded dimers D1 and D2, and the polymers chain5 and chain11.

and right-handed helices. In fact, the helical and sheeted structures of proteins are stabilized by similar hydrogen-mediated interactions.

Previously, we studied the INS spectrum of solid formamide (FA).¹⁷ The results confirmed that the strong intermolecular hydrogen bonds have a major effect on the vibrational motions of FA molecules in the lattice. The FA study also showed that the crude ionic model^{18,19} for the hydrogen bonds in amides and peptides was incorrect. In a crystal of the FA, hydrogen atoms participate in two hydrogen bonds, unlike the most usual interactions between peptide groups in a living matter. In this study, we focused on NMF which we consider a more realistic model for the biomolecular interactions. In the case of FA, a model has also been developed, based on *ab initio* quantum chemical calculations, which allows one to assign the peaks observed in the INS spectrum to the vibrational modes of the crystal.¹⁷

The harmonic force field for molecular and crystalline NMF was modeled in numerous studies based on isolated molecules or dimers using a relatively lower level of approximation.^{20–22} In this study, we take advantage of the current computer power and the discovery of modern DFT functionals. The functionals usually provide accurate vibrational frequencies for molecules in the gaseous and liquid state.^{17,23,24} A series of model NMF crystal fragments is proposed as plotted in Figure 1: a single molecule (NMF), two types of dimers derived from the x-ray structure of NMF (D1 and D2) and helical chains of 5 and 11 NMF molecules (referred to as chain 5 and chain 11, respectively).

II. EXPERIMENT

The INS spectra of NMF and N-deuterated NMF were measured using the CHEX inelastic neutron spectrometer at the Intense Pulsed Neutron Source (IPNS) located at Argonne National Laboratory, Illinois. The details of the instrumental design have been described elsewhere.¹⁷ The energy resolution ($\Delta\nu/\nu$) is less than 2% for an energy transfer

smaller than 2000 cm^{-1} . N-methylformamide was purchased from Aldrich and used without further purification. The N-deuteration was carried out by successive exchange with D_2O . The degree of deuteration was determined by NMR measurement to be greater than 95%. An “organ pipe”-like sample cell was made from a row of vertical thin aluminum tubes so that the whole cross section of the incident neutron beam (about $10\times 10\text{ cm}$) was covered. The whole sample assembly was cooled to 15 K for the INS measurements.

III. THEORY OF INS

General theory of INS has already been elaborated in numerous studies.^{25,26} For computer simulations, however, we used a more convenient treatment based on intensities of individual quantum transitions than working with a general formula for an ensemble of harmonic oscillators. Especially, the former approach leads to mathematically simpler expressions which can be directly implemented with a limited number of empirical parameters. In principle, anharmonic vibrational transitions (which are not considered here) can also be included.

The process of the inelastic neutron scattering can be described using basic quantum mechanical rules. Since the neutron-sample interaction is weak, the initial wave function of the sample and neutron beam can be expressed as a product (omitting a normalization constant)

$$\psi_i = \exp(-i\mathbf{k}_i \cdot \mathbf{r}) Q_i = \phi_i Q_i, \quad (1)$$

where ϕ_i and Q_i are the neutron and sample parts, respectively, \mathbf{k}_i is the wave vector of the incident neutron beam, $i = \sqrt{-1}$. The wave vector is related to the neutron current density, \mathbf{I}_i , by

$$\mathbf{I}_i = i(\phi_i^* \nabla \phi_i - \phi_i \nabla \phi_i^*) = 2\mathbf{k}_i. \quad (2)$$

Neglecting the spin, the sample-beam potential can be approximated by a sum²⁵

$$V(\mathbf{r}) = \sum_{\lambda=1\dots N} a_\lambda \delta(\mathbf{r} - \mathbf{r}^\lambda), \quad (3)$$

where \mathbf{r}^λ is the position vector of a nucleus λ and N is the number of atoms. The constant a_λ is proportional to the bound scattering length²⁶ and $(a_\lambda)^2$ is proportional to the INS scattering cross section, σ_λ . Due to the interaction, quantum state (1) becomes

$$\psi_f = \exp(-i\mathbf{k}_f \cdot \mathbf{r}) Q_f, \quad (4)$$

with a neutron current $\mathbf{I}_f = 2\mathbf{k}_f$. The differential cross section σ_f for the process is²⁶

$$\sigma_f = k_f k_i^{-1} |w_f|^2 \quad (5)$$

with

$$\begin{aligned} w_f &= \sum_{\lambda=1\dots N} a_\lambda \langle \psi_f | \delta(\mathbf{r} - \mathbf{r}^\lambda) | \psi_i \rangle \\ &= \sum_{\lambda=1\dots N} a_\lambda \langle Q_f | \exp(i(\mathbf{k}_f - \mathbf{k}_i) \cdot \mathbf{r}^\lambda) | Q_i \rangle \\ &= \sum_{\lambda=1\dots N} a_\lambda \exp(i\Delta \cdot \mathbf{r}_0^\lambda) \langle Q_f | \exp(i\Delta \cdot \mathbf{R}^\lambda) | Q_i \rangle. \end{aligned} \quad (6)$$

The difference $\Delta = \mathbf{k}_f - \mathbf{k}_i$ is commonly known as the momentum transfer since the wave vector is equal to the mo-

momentum in atomic units. In the last expression, nuclear coordinates \mathbf{r}^λ were separated into vibrational deviations, \mathbf{R}^λ , and equilibrium positions, \mathbf{r}_0^λ . The deviations can be further expressed using the normal mode coordinates Q_j ,

$$\mathbf{R}^\lambda = \sum_j \mathbf{S}_j^\lambda Q_j, \quad (7)$$

where \mathbf{S}_j^λ is the normal mode displacement matrix. Except for the highest energy transitions, the product $(\mathbf{\Delta} \cdot \mathbf{R}^\lambda)$ is small and the last exponential term in (6) can be expanded. For example, for a neutron with an energy 300 cm^{-1} , $|\mathbf{\Delta}| \sim 4.2 \text{ \AA}^{-1}$ and the amplitudes \mathbf{R} of the vibrational motion are typically of the order of 0.01 \AA . Using the orthonormality of the vibrational functions, $\langle Q_f | Q_i \rangle = 0$, and Eq. (7), we have

$$w_f = i \sum_{\lambda=1..N} a_\lambda \exp(i \mathbf{\Delta} \cdot \mathbf{r}_0^\lambda) \mathbf{\Delta} \cdot \sum_j \mathbf{S}_j^\lambda \langle Q_f | Q_j | Q_i \rangle + o[(\mathbf{\Delta} \cdot \mathbf{R})^2]. \quad (8)$$

For harmonic vibrational states the nonzero elements are

$$\langle Q_f(n_f) | Q_j | Q_i(n_i-1) \rangle = \delta_{jf} [n_f \hbar / (2 \omega_f)]^{1/2}, \quad (9)$$

where n_f is the vibrational quantum number and ω_f is the fundamental frequency for mode f , \hbar is the Planck's constant. Because of the energy conservation,

$$\hbar \omega_f = \hbar^2 (2m_N)^{-1} (k_i^2 - k_f^2), \quad (10)$$

where m_N is the neutron mass, the cross section from (5) becomes

$$\sigma_f = k_f k_i^{-1} (n \hbar / 2) \omega_f^{-1} \sum_{\lambda=1..N} \sum_{\lambda'=1..N} a_\lambda a_{\lambda'} \times \exp[i \mathbf{\Delta}$$

TABLE I. Geometrical parameters of N-methylformamide.

Bond length (Å)	Single molecule		Crystal		
	Calc.	Expt. ¹¹	D1/D2	Chain5 (I/II) ^a	Expt. (I/II) ¹⁵
C=O	1.220	1.219(5)	1.229/1.228	1.236/1.237	1.231/1.219
N-H	1.009	1.027(6)	1.018/1.018	1.025/1.026	0.750/0.847
C(O)-N	1.359	1.366(8)	1.346-53/1.349-51	1.339/1.333	1.319/1.319
H···O	-	-	1.971/1.970	1.879/1.855	2.166/2.032

^aFor the center molecule in chain5, Roman numerals denote the two types of the H bonding.

the N-hydrogens. In order to match the observed spectra patterns, simulated bandwidths were taken as directly proportional to the transitional frequencies ($\delta = 0.0154\omega + 5.86$ for δ and ω in cm^{-1}), except for Figure 4 where a uniform width of 5 cm^{-1} was used.

IV. RESULTS AND DISCUSSION

A. Geometries

Selected geometrical parameters are listed in Table I. The experimental N-H bond length in the crystal appears unreasonably short which can be attributed to an inaccurate determination of the hydrogen positions by the x-ray diffraction. In fact, an increase of the N-H bond length is expected in solid NMF when compared to the gas phase, as given by the calculations. Similarly, the experimental length of the hydrogen bond (H···O) appears affected by the inaccurate determination of the hydrogen position. On the other hand, the experimentally derived N-H bond length for a single molecule of 1.027 Å^{11} compares well with the theoretical value of 1.009 Å . The N-H bond becomes longer in the clusters as part of its electron cloud participates in the hydrogen bonding. Moreover, we can observe the effect of the long range electron conjugation in the chain of NMF molecules, since the change of the N-H distance is doubled in chain5 if compared to the dimers. This is in agreement with a generally accepted model of the hydrogen bonding as a cooperative process. On the other hand, the N-H bond length (and thus the hydrogen bond strength) depends little on molecular orientation, as apparent from a comparison of D1 and D2. The C=O bond becomes longer in the crystal if compared to an isolated molecule, and the calculated C=O bond length difference of 0.016 Å (for chain5) is greater than the experimental value ($0.000-0.012$). Meanwhile, the N-C bond becomes shorter in the crystal, by 0.047 Å (experimentally determined) or by $0.020-0.026 \text{ Å}$ (theoretically predicted). Since these calculated differences are comparable with the experimental ones within the error, we feel that our model reasonably well describes the hydrogen bonding in solid NMF. Although the N-H bond is substantially weakened due to the H bonding, the covalent character of the N-H bond is conserved. Therefore, the double-well theory of the hydrogen bonding in amides^{18,19} is not consistent with our calculations. Surprisingly, the two different orientations of NMF molecules in D1 and D2 do not have any significant effect on the geometry parameters, unlike the vibrational frequencies given below.

B. INS Spectra

The INS spectra provide a more detailed view into the structure and forces in crystalline NMF than sole geometry parameters. The experimental and simulated spectra of NMF are shown in Figure 3. The vibrational frequencies and assignments based on the normal modes of the chain5 model are listed in Table II. The spectrum of chain11 differs from chain5 mainly due to the signal of the terminal N-H groups. Most of the spectral bands for the single molecule (NMF) can be assigned to observed peaks with approximately correct relative intensities. Calculations for single NMF cannot obviously reproduce the lowest frequency region dominated by signal stemming from the H bonding, which can be improved, however, for the dimers D1 and D2. The spectra of D1 and D2 appear similar, although minor differences in the mode ordering can be seen in Table II. Those differences occur primarily in the C-H stretching ($2863-2952 \text{ cm}^{-1}$) and bending ($1386-1488 \text{ cm}^{-1}$) regions. A far more dramatic effect on the INS intensities has been observed on the

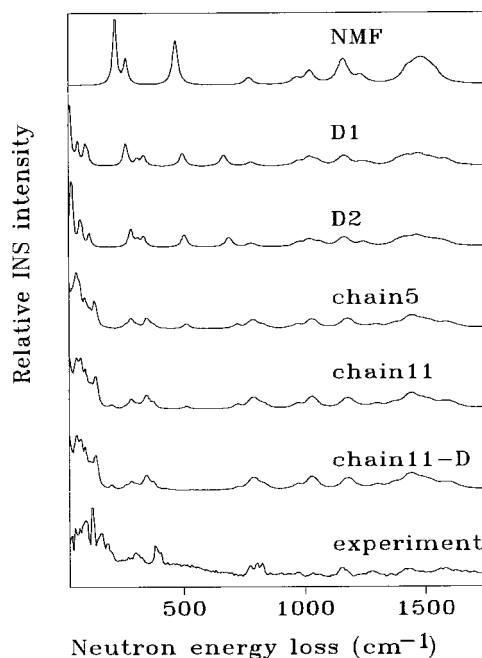


FIG. 3. Simulated and experimental INS spectra of NMF. Top: calculated intensities for the five model systems (see Figure 1, the free acidic hydrogen is replaced by deuterium in chain11-D); bottom: the experimental spectrum of solid NMF, measured at 15 K. Spectra simulated with a variable bandwidth (see the text).

TABLE II. Calculated and experimental vibrational frequencies of N-methylformamide.

Single molecule		Condensed phase				Assignment
NMF	vapor/matrix ^a	D1/D2	chain5	solution/liquid ^b	INS	
3650	3480/3490	3661/3650 3498/3501	3654 3443 3441 3382 3357		~3350	N-H stretch, free N-H stretch, H-bonded
3150	2934/2960	3278/3262 3146/3162	3284 3280 3175 3166 3153		~3120	C-H stretch in CH ₃ , asymmetric
3116	/2944	3097/3119	3133 3120 3107			
3055	2849/2854	3044/3060 3043/3031	3063 3051 3041 3041 3037			C-H stretch in CH ₃ , symmetric
2954	2732/	2983/2991 /2952 2919/ 2882/ /2863	2983 2977 2964 2962 2920 2878 2867		2920	formyl C-H stretch C-H stretch in CH ₃ , asymmetric
1812	1724/1721	1809/1789 1784/1777 1593/1549 1590/ 1600	1809 1792 1780 1769 1758 1623 1608 1601 1600	1687/1675	1778	C=O stretch, free C=O stretch, H-bonded (amide I)
1547	1498/1528	1537/1556	1550		1580	amide II, H-bonded
1490	/1467	1527/1590	1582 1580 1521 1520	1525/1546	1515	amide II, free H C-H bend in CH ₃ , asymm.
	/1458	1489/1521 /1488 /1386	1518 1489 1489		1484	
1515	1411/1410	1478/1462	1459	1450/1455	1440	C-H bend in CH ₃ , symm.
1464		1463/1462	1454 1451 1451 1447			
1429	-/1392	1444/1423 1428/1421	1439 1428 1427 1425 1423	1416/1414	1415	formyl C-H bend, in plane
			1375 1372	1387/1384	1354	CH ₃ , umbrella bend
		1273/1252	1310 1298 1295 1280		1281	amide III, H-bonded
1237	1201/1207	1382/1244	1248	1229/1248		amide III, free

TABLE II. (Continued.)

Single molecule		Condensed phase				Assignment
NMF	vapor/matrix ^a	D1/D2	chain5	solution/liquid ^b	INS	
1171		1242/1176	1194 1194 1184 1184 1184		1159	CH ₃ rocking, in and out of plane
1159	/1148	1179/1171 1170/1155	1180 1170	1149/1150	1154	
		1156/1050	1164 1048		1062	formyl C-H bend, out of plane
1026	785/880	1054/ 1027/1029	1045 1031/1011 1030		1030	
		1023/1017	1026 1025 1023			C(H ₃)-N stretch,
971	946/951	981/979	974 973 971 971 961	956/960	975	
	/761	/690	829 802 791	750/771	824	N-H wag, H-bonded
773		785/788	790 784		802	
		776/779	777 775 770			C-N-C bend
		671/ 493/505	722 512	676/720	774	
471	~500/570 - /368	337/337	375 355 348 345	356/353	400 381 374	N-H wag, H-bonded N-H wag, free N-C(O) torsion
		299/312	311 299		326	
265		265/288	286 283		302	CH ₃ -bend
221		248/282	278 261 200 141 138 131		268 164	
0		<108/<112	<130		124	N-C(O) torsion lattice mode lattice modes

^aReferences 8 and 9.

^bReference 7. Frequencies in cm⁻¹. Assignments are based on a dynamic displacement of vibrational modes as calculated for chain5.

shift of the N-H out of plane wagging mode caused by the hydrogen bonding. This is also observed for the NH₂ out of plane wagging in solid formamide.¹⁷ This mode, calculated for single NMF molecule at 471 cm⁻¹ is shifted to 671 and 690 cm⁻¹ for D1 and D2, respectively. The largest shift to 829 cm⁻¹ calculated for this mode in chain5 corresponds well to the experimental peak observed at 824 cm⁻¹. Moreover, the two types of hydrogen bonds present in crystalline NMF are reflected in the distinct signals of the hydrogen out of plane wagging modes, at 774 and 824 cm⁻¹ (calculated

for chain11 at 724 and 830 cm⁻¹). The relatively large frequency separation can be accounted for by a larger electron conjugation in the second type of the hydrogen bonding (as in D2) assisted by the nearly planar structure of the N-H...O=C system. As apparent from Table II, the mode was found at 771 cm⁻¹ in liquid NMF, which indicates a much stronger, cooperative hydrogen bonding in the crystal. Calculated intensity of the wagging mode of the free terminal hydrogen in chain5 (512 cm⁻¹) becomes lower in

chain11 and the signal disappears entirely when the mass of the hydrogen is set to 2 (chain11-D in Figure 3).

The simulated spectra compares well with the experiment, although individual modes cannot be compared at the lowest energy region below 150 cm^{-1} . The relative intensity simulated for the symmetric C–H bending (around 1450 cm^{-1}) and $-\text{CH}_3$ rocking ($\sim 1050\text{ cm}^{-1}$) appears greater than observed, which can be partially attributed to the neglect of the hydrophobic forces between the helical chains in the crystal. However, these forces have only a minor effect on INS intensities, since our trial model (not shown here) that included those interactions at an empirical level did not lead to any improvement of the spectral pattern. Due to the limited resolution of the spectrometer also the higher frequency modes ($>2000\text{ cm}^{-1}$) cannot be assigned in detail. Nevertheless, the comparison of the calculated frequencies and the experiment for single molecule can still be considered satisfactory, in spite of the fact that large frequency

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signal of the C–H and N–H stretching modes (around 3000 cm^{-1}). Unfortunately, neither of the two models provides an expression for the bandwidths of individual transitions, which must be found empirically. We do not expect that this obstacle involving a solution of the time dependent Schrödinger equation would be solved in the near future using an *a priori* approach.

V. CONCLUSION

The INS spectra of hydrogenated and N-deuterated solid NMF were measured and the overall spectral profile as well as the intensities of most of the observed vibrational transitions were successfully reproduced by the simulation. The modeling was based on the scattering of the neutron beam on a cluster of NMF molecules mimicing the crystal geometry. The *ab initio* harmonic force field could be transferred in Cartesian coordinates onto the larger segment of the crystal, not accessible by the calculation directly. The results reveal strong cooperative hydrogen bonds which stabilize the helical chains in the NMF crystal. The two types of the hydrogen bonding present in crystalline NMF lead to the split of the INS signal assigned to the N-hydrogen out of plane wagging modes. Present findings are consistent with our earlier study on solid formamide, i.e., the N–H bonds are weakened if compared to free molecules, but their character of a covalent single-minimum potential is still conserved.

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