Intramolecular and intermolecular interactions in N-methylformamide–water mixture: X-ray scattering and DFT calculation study

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ABSTRACT

X-ray scattering and DFT calculations were performed to study the competitiveness of the formation of hydrogen bond(s) in equal stoichiometric N-methylformamide–water mixture. The experimental data were analyzed to yield the structure factor $S_M(q)$ and the pair correlation function $g(r)$ of the solution. Among a wide variety of some considered clusters, our X-ray measurements clearly showed the possibility of the formation of aggregates containing more than one hydrogen bond.

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1. Introduction

Hydrogen bonding is known to play a significant role in the formation and stabilization of protein structures [1–3]. Hydrogen bonds stabilize peptides' secondary structures such as the α-helix and β-sheet conformations [2]. Simple amide systems have been investigated extensively as models of $O=C-N-H$ peptide bonds because of their presence as a repetitive unit in biological macromolecules [4–8]. On our side, some prototypes such as formamide [9], acetamide [10], N-methylacetamide [11] and N-methylformamide [12–14] were investigated. In the case of N-methylformamide (NMF), which has a biomedical importance [15], the liquid and the amorphous structures were studied by means of X-ray and neutron scattering combined with DFT calculations [12,13]. The trans conformer was shown to dominate the liquid and the amorphous states. Strong hydrogen bonds could be established between the $C=O$ and $N-H$ groups of adjacent NMF molecules to form a linear association similar to the crystalline structure.

For a deeper understanding of the structural properties and biological functions of amides and proteins, it is important to know how they interact with solvents, particularly water. Many macroscopic properties of H-bonded liquids are dramatically linked to their environment. The amide aqueous solutions show strong hydrogen-bonded structures which lead to the strong non-ideal behavior [16,17]. In aqueous media, the hydrogen bond interplayed between water and other organic molecules control many material properties which are important both in nature and in a wide range of technological applications [18]. In this

context, mixtures of water with N-methylacetamide or N-methylformamide are the simplest and most interesting models accessible to accurate quantum chemical investigations. The present paper is aimed at examining in detail the structure of NMF–water mixture with equal concentrations. This mixture system was investigated by theoretical methods [19,20]. Xiaolan et al. [19] and Cordeiro et al. [20] respectively performed *ab-initio* and Monte-Carlo simulations to study the NMF–water mixture. These theoretical investigations show that in the considered mixture, each NMF molecule is connected to two water molecules with strong $N-H^{..}O-H$ and $C=O^{..}H-O$ hydrogen bonds. However, none of the earlier studies has been interested in the experimental characterization of the intermolecular arrangement in NMF–water mixture. This is the reason why the problem of local order in this system is reconsidered in the present paper which is particularly aimed at investigating the intermolecular arrangement in NMF–water mixture by using X-ray scattering in combination with a DFT calculations. The latter technique is a more adapted method for geometry prediction and the investigation into the physicochemical property of amides.

Firstly, the scattering data were analyzed to yield the total structure factor of the mixture and the pair correlation function. Secondly, the optimized geometries of the NMF and H_2O monomers were considered to construct the molecular form factor. Thirdly, to describe the intermolecular associations in NMF–water mixture, a series of molecular models were considered. Some of them have already been reported in the literature [20], while the others are novel models discussed for the first time. Intermolecular distances, particularly the hydrogen bonding parameters, which are generally difficult to determine experimentally, were then deduced via a DFT calculation of the minimum energy structure for the considered models. The distinct

structure factor and/or the pair correlation function constructed for each model was then compared with that extracted from the experimental data. The most probable clusters describing the local order in NMF–water mixture were then deduced.

2. Experimental

Liquid NMF was purchased from Aldrich Chemical (State purity 99$^+$%) and used without further purification and the solution was prepared with deionized water. The X-ray scattering measurements were carried out on a standard (θ–2θ) diffractometer operating in the transmission mode with MoK$_\alpha$ radiation (λ = 0.7093 Å) monochromated by a bent asymmetric quartz. The scattered intensity was measured in steps of 0.25° (2θ) in the 3°–120°. To perform the measurements, the sample was put in a flat sample holder (4 mm thick) equipped with Mylar windows. Several scans were conducted until about 80 000 counts were obtained at each angle.

3. Theoretical considerations

3.1. X-ray diffraction formalism

In our most recent paper [21], the theoretical framework for X-ray scattering by molecular liquids and the correction procedure were presented in details, but only the most relevant details will be reported here. For molecular liquids, the total structure factor S_M(q) can be separated into two terms arising from intramolecular and intermolecular terms:

$$S_M(q) = F_1(q) + D_M(q) \qquad (1)$$

where the molecular form factor $F_1(q)$ is given by:

$$F_1(q) = \sum_{\alpha,\beta=1}^{m} f_\alpha(q)f_\beta(q)J_0\left(qr_{\alpha\beta}\right)\exp\left[-\langle\Delta r_{\alpha\beta}^2\rangle q^2/2\right]/\left(\sum_\alpha^m f_\alpha(q)\right)^2 \quad (2)$$

where $J_0(x) = \sin x/x$ and $\langle\Delta r_{\alpha\beta}^2\rangle^{1/2} = \mu_{\alpha\beta}$ is the root mean square (r.m.s) deviation of the local and instantaneous site-site separation distance of the mean value $r_{\alpha\beta}$. The distinct structure factor $D_M(q)$ includes all the intermolecular interactions and generally decays to zero very rapidly. However, in the case of hydrogen-bonded liquids, the intermolecular structure factor continues to oscillate in the high q-range [22]. Then, it is convenient to split $D_M(q)$ as follows:

$$D_M(q) = D_{inter}^{HB}(q) + D_{inter}^{NHB}(q) \qquad (3)$$

where $D_{inter}^{HB}(q)$ is the H-bond structure function [23] and $D_{inter}^{NHB}(q)$ denotes the intermolecular correlations other than those related to H-bonding.

The pair correlation function $g_L(r)$ of intermolecular terms, may be expressed by:

$$g_L(r) = 1 + \frac{1}{2\pi^2 r\rho}\int_0^\infty qD_M(q)\sin qrdq \qquad (4)$$

where ρ is the molecular density. $g_L(r)$ gives the probability of finding another atom lying in another molecule at a distance r from a given atom. By analogy to Eq. (3), the $g_L(r)$ function can be removed into two terms arising from hydrogen-bonding and non hydrogen-bonding interactions as follows:

$$g_L(r) = g_{inter}^{HB}(r) + g_{inter}^{NHB}(r) \qquad (5)$$

where $g_{inter}^{HB}(r)$ and $g_{inter}^{NHB}(r)$ are respectively the Fourier transformations of $D_{inter}^{HB}(q)$ and $D_{inter}^{NHB}(q)$.

3.2. DFT calculation

To study the relative stability of all possible intermolecular (dimers, trimers, and tetramer) arrangements of the NMF–water mixture in the liquid state, a density functional theory (DFT) calculation was performed using namely the standard TZV basis set [24] augmented by one diffuse (d) function for C, N and O atoms and one polarization (p) function for all H atoms with HONDO7 polarization exponents. All DFT calculations were conducted with the GAMESS2002 series of programs [25]. Becke's hybrid three parameter functional B3LYP [26] was used. Optimization of each structure was considered converged with a maximum gradient less than 0.0001. No frozen coordinates and no symmetry restriction were used.

4. Results and discussion

4.1. Intramolecular structure

It is common that N-methylformamide molecules adopt the trans form in the liquid state [5,27–29]. In our part [12], the cis/trans isomerism was analyzed by means of experimental and theoretical techniques such as X-ray scattering, neutron scattering, and DFT calculations. In the present study, the intramolecular and the intermolecular structures of the NMF–water mixture with respect to the earlier results were investigated.

The intramolecular distances as deduced from DFT calculations for the N-methylformamide monomer before and after mixture with water molecules are given in Table 1. Surveying the obtained results in five complexes M_1, M_2, M_3, M_4 and M_5 which will be detailed below, it can be noticed that changes in the monomer geometries upon complexation are relatively minor. A small elongation of the C_3=O bond and a very small contraction of the C_1–N bond can be mentioned. Other bond lengths are hardly affected by the solvation. These small changes were also noted by Dong-mei Du et al. [30,31] in their density functional theory study of the hydrogen-bonding interaction of mixtures of formamide with hydrogen peroxide and water respectively.

Fig. 1(a) shows the experimental structure factor $S_M(q)$ of NMF–water mixture as deduced from X-ray scattering data after standard corrections [10] of background, polarization, absorption and effective irradiated volume. By a least-square fitting of Eq. (2) to the experimental structure factor $S_M(q)$ data in the large q-range, we have obtained an intramolecular conformation that is compatible with the data fitted. In this calculation and in order to reduce the number of flexible parameters, the intramolecular distances are kept equal to the deduced values from our DFT geometry optimization. Only the Debye–Waller parameters are fitted. Some of the intramolecular parameters as deduced from model M_1 (see Table 1) are summarized in Table 2. A good agreement could be seen between the experimental structure factor $S_M(q)$ and the computed molecular form factor $F_1(q)$ [Fig. 1(a)] beyond q = 7.5 Å^{-1}. Two important points may be addressed here. Firstly, the refinement of the μ_{X-H} factors does not improve the adjustment between $S_M(q)$ and $F_1(q)$. The computed molecular form factors $F_1(q)$ with and without the contribution of the X–H correlations (with X = H, C, N and O) are very similar particularly

Table 1
Some of intramolecular distances r_{ij} (in Angstrom) as deduced from DFT geometry optimization for the pure NMF and for all the considered models of NMF–water mixture.

	Pure NMF	M$_1$	M$_2$	M$_3$	M$_4$	M$_5$
r_{N2-C3}	1.356	1.353	1.350	1.343	1.342	1.336
r_{C1-C3}	2.456	2.464	2.496	2.472	2.493	2.478
$r_{C3=O12}$	1.216	1.218	1.222	1.227	1.230	1.235
r_{N2-O12}	2.279	2.295	2.298	2.298	2.293	2.296
r_{C1-N2}	1.455	1.452	1.459	1.457	1.461	1.458
r_{C1-O12}	2.825	2.870	2.928	2.900	2.920	2.911