Acetic Acid Dimer in the Gas Phase, Nonpolar Solvent, Microhydrated Environment, and Dilute and Concentrated Acetic Acid: Ab Initio Quantum Chemical and Molecular Dynamics Simulations

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Theoretical study of the acetic acid dimer, its microhydration and its behavior in water and chloroform solution was performed. To characterize the system, we adopted ab initio methods at the DFT and RI MP2 (the resolution of the identity approximation MP2) levels for the gas-phase calculations, PCM (polarizable continuum model) approximation using the polarizable conductor calculation model (COSMO) for description of solvent, and constant energy (*NVE*) and constant temperature (*NVT*) molecular dynamics simulations for gas phase and explicit solvent calculations, respectively. The cyclic structure of the acetic acid dimer is the most stable in the gas phase only. During microhydration, the water molecules are incorporated in the dimer leading to water-separated structures. This conclusion is based on ab initio quantum chemical calculations, as well as on molecular dynamics simulations. The fact that the cyclic structure does not appear in water solution is in agreement with previous theoretical and experimental results. Extending the search also on other acetic acid dimer structures, we concluded that acetic acid does not form any dimer structure in water solution. The cyclic structure is also supposed to be stable in chloroform solution.

I. Introduction

Acetic acid forms in the gas phase the well-known cyclic structure with two very strong O−H···O hydrogen bonds. Evidence on the cyclic structure of the dimer was obtained from IR spectroscopy, as well as other experiments,[1−9] and dimerization energy, dimerization entropy, and free energy of dimerization (298 K) were theoretically, as well as experimentally, estimated to be about −15 kcal/mol, −36 cal/(K·mol), and −4 kcal/mol, respectively.[10] Formation of the O−H···O hydrogen bond leads to very large red shift of O−H stretch vibration frequencies (619 and 744 cm^{-1} for symmetric and antisymmetric vibrations, respectively). Experimental findings on structure, stabilization energy, and vibration shift agree well with various theoretical calculations.[1,6,7,10] The potential energy surface (PES) of the dimer contains a number of energy minima, and besides the global minimum (cyclic structure), other linear structures possessing O−H···O or C−H···O hydrogen bonds (or both of these bonds simultaneously) are supposed to exist.[1,6] All of these structures are expected to be considerably less stable, and reliable theoretical calculations confirmed this conclusion.[6] The situation is basically not changed when passing from a gas phase to the nonpolar solvent, and the cyclic structure remains the global minimum. Here, again, theoretical calculations agree with experiments.[10,11] The evidence is, however, indirect and is based on agreement between calculated formation free energy for the cyclic structure in the solvent and experimental value. Introduction of the water solvent brings, however, unexpected problems resulting in confusing information on the structure of the dimer in water solution. Two theoretical papers[10,11] appeared recently in which the formation free energy of the dimer in water was investigated using continuous and discrete models. In both cases, clear evidence was found that the cyclic structure cannot be present in the water because the calculated formation free energies were much higher than those found experimentally. Surprisingly, authors of both papers did not answer the crucial question—what is then the structure of the acetic acid dimer? If it is not the expected cyclic structure, which are the next candidates? And we can even ask, is there any dimer structure existing in the water environment. Searching the extended literature, we find various suggestions, from linear open dimer with one O−H···O H-bond or one C−H···O H-bond through trimers, tertramers, and chain structures[1,6] up to hydrophobic structure[3,4] having the methyl−methyl contact. Clear experimental evidence on the structure of a dimer in the water environment is missing, and also quantum chemical calculations do not yield an unambiguous answer. It must be, however, mentioned that the way in which the dimer structure is theoretically determined, that is, calculation of the formation free energy for some selected structure followed by its comparison with experiment, is not adequate. Structure of the dimer in a relevant environment should result from suitable theoretical investigation and not be presupposed.

The situation in a gas phase is clear, and quantum chemical optimization is without doubts a suitable tool. But even here care should be paid to the fact that quantum chemical optimization depends on the starting structure and leads to the nearest stationary point. In the case of a more complicated potential energy surface (PES), it is thus not guaranteed that all minima are considered, and some effective searching procedure should be adopted. Upon introduction of a solvent, quantum chemical calculations became less applicable first because the temperature should be considered. But even in the microhydrated environment (in which the temperature is very low), the static approach is no longer adequate and dynamic calculations are required.

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The ideal solution represents the ab initio molecular dynamics (MD) simulations, but their use for the present problem is limited because (mostly) using the density functional methods, they do not consider properly the London dispersion energy. Some structures of the acetic acid dimer are supposed to be stabilized also by a dispersion energy. The only applicable procedure is thus classical MD simulations using an empirical force field properly covering all energy contributions including the dispersion one. Providing the empirical potential describes the energetics of a dimer properly, the trajectory obtained from MD simulations contains information on all possible structures of the dimer realized during the (sufficiently long) MD run.

The aim of the present paper is to study the structure of the acetic acid dimer in various environments (gas phase, nonpolar solvent, microhydrated environment, dilute and concentrated acetic acid) using correlated ab inito quantum chemical calculations and molecular dynamics simulations based on Cornell et al.[12] empirical field. Formic acid dimer was recently studied in the gas phase, as well as in the aqueous solution, for which Monte Carlo technique using the Miertus−Scrucco−Tomasi model was adopted.[13]

II. Strategy of Calculations

The PES of the acetic acid dimer was sampled using the quenching technique[14] (MD/Q), which is a combination of molecular dynamics and minimization. This technique was used previously for sampling PESs of DNA base pairs,[15] and details about the technique can be found in ref 15. The MD/Q method is combined with the Cornell et al. empirical force field.[12] After locating all energy minima at the PES, the energy-lowest structures were selected and recalculated at DFT/B3LYP/6-31G** level of theory. The performance of the DFT/B3LYP/6-31G** calculations, used for optimization of complex structures, was verified by performing the optimization at the RI MP2 (resolution of the identity MP2)[16−18] level using the TZVPP ([5s3p2d1f/3s2p1d]) and augTZVPP basis sets ([6s4p3d2f/4s3p2d]).

In the case of microhydration of the acetic acid dimer, the MD/Q technique is no longer applicable because the number of the energy minima increases dramatically. Further, we are in fact not interested in the detailed knowledge of the complex structure but more in the way that the acetic acid dimer structure changes upon the (gas-phase) microhydration. Therefore, we used the constant energy molecular dynamics (*NVE*) simulations with the force field of Cornell et al.,[12] and complex structures will be obtained from the analysis of respective trajectories. We are, however, aware of the fact that several important phenomena (such as ionization, proton transfer) cannot be studied at the level of an empirical potential and use of ab initio MD is required. The atomic charges for these vacuum-like simulations were derived from the RESP (restrained electrostatic potential) fitting procedure at DFT/B3LYP/aug-cc-pVTZ level.

To perform the MD simulations in solution, we passed from the *NVE* simulations, which are suitable for gas-phase studies, to the constant temperature molecular dynamics (*NVT*) technique using the periodic boundary conditions and force field of Cornell et al.[12] Similarly to the previous case, the atomic charges were derived by RESP[19,20] fitting procedure. But in contrast, the input charges for RESP were calculated at HF/6-31G* level of theory because the simulations are performed in a liquid environment now and larger atomic charges compensate for missing polarization. Charges on acetic acid (HCHHCOOH) and water used in the gas-phase (*NVE*) and in the liquid-phase (*NVT*) simulations are following: (0.109, −0.315, 0.109, 0.109, 0.814, −0.607, −0.686, 0.447; 0.471, −0.942, 0.471), (0.094, −0.252, 0.094, 0.094, 0.681, −0.547, −0.557, 0.395; 0.339, −0.678, 0.339). Besides the discrete solvent model simulations, we also used the polarized continuum solvent model using the polarizable conductor calculation model (COSMO).[21,22] The solute molecule is placed in a cavity surrounded by an infinite polarizable dielectric.

III. Methods

A. Ab Initio Quantum Chemical Calculations. *Gas-Phase Calculations.* The structures of acetic acid dimer and acetic acid dimer−water complexes suggested by MD/Q and MD calculations were optimized at the DFT/B3LYP/6-31G** level. Final stabilization energies were corrected for the basis set superposition error (BSSE)[23] and the deformation energies of the monomers. For comparison, the energies of dimerization were evaluated also using the standard optimization at the RI MP2/TZVPP[16−18] level of theory, and the single-point interaction energies were obtained adopting augTZVPP basis set on the RI MP2/TZVPP optimized geometries. The thermochemical properties were determined for the optimized geometries using Gaussian 98.[24] All values were determined at the DFT/B3LYP/6-31G** level of the theory. All calculations mentioned in this paragraph were performed employing Gaussian 98[24] and Turbomole[25] packages.

Calculations in Solution. The free energy of dimerization in solution (ΔG^{sol}) was determined by the addition of the value of the free energy of dimerization in the gas phase (ΔG^{g}) to the difference ($\Delta\Delta G_{\mathrm{solv}}$) in the free energy of solvation (ΔG_{solv}) between the monomers and the dimer, which was computed using the COSMO[21,22] model. A correction term accounting for the change of reference state from gas phase to 1 M solution is added at last.

$$\Delta G^{\mathrm{sol}} = \Delta G^{\mathrm{gas}} + \Delta\Delta G_{\mathrm{solv}} + RT\ln(1/22.4)$$

$$\Delta\Delta G_{\mathrm{solv}} = \Delta G_{\mathrm{solv}}(\mathrm{dimer}) - 2\Delta G_{\mathrm{solv}}(\mathrm{monomer})$$

For details, see ref 10. Water and chloroform were considered as solvents, and COSMO calculations were done at the DFT/B3LYP/6-31G** level of theory using Gaussian 98[24] code. Room temperature was considered in all calculations. Geometries of monomer and all dimers were optimized in a solvent, that is, geometry coordinates were relaxed in a specific solvent.

B. Constant Energy (*NVE*) Molecular Dynamics Simulations. The acetic acid dimer and the acetic acid dimer in complexes with 1, 2, 4, 8, 16, and 216 water molecules were studied applying the *NVE* molecular dynamics. Simulation ran at the average energy corresponding to the room temperature (300 K) with 0.5 fs time step. The length of the runs was 0.1 μs.

The trajectories were analyzed employing carnal and ptraj modules from the AMBER[24] package. Dynamics of hydrogen bonding in acetic acid dimer was described using distances between sp^2 and sp^3 carbons. We are aware that usage of radial distribution function would be more appropriate, but we do not expect any significant change. Hydrogen bond analysis was also performed. The results were also checked visually using VMD[27] and Moil-view[28] programs.

C. Constant Temperature (*NVT*) Molecular Dynamics Simulations. The acetic acid in water solutions corresponding to the concentrations 0.3, 1.0, and 10 mol/L and the neat acetic acid were investigated using the *NVT* molecular dynamics simulations with periodic boundary conditions. The acetic acid

TABLE 1: Values of Interaction Energies (Δ*E*), Free Energies of Dimerization in Gas Phase (Δ*G*^{g}), Free Energies of Solvation (Δ*G*$_{solv}$), Free Energies of Dimerization in Solution (Δ*G*^{sol}), and Dipole Moments of Various Structures of Acetic Acid and Hydrated Acetic Acid[a]

	B3LYP/6-31G**			RI MP2/ TZVPP	RI MP2/ augTZVPP	COSMO/B3LYP/ 6-31G** (H_2O)		COSMO/B3LYP/ 6-31G** ($CHCl_3$)	
structure[b]	Δ*E*	Δ*G*^{g}	*μ*	Δ*E*	Δ*E*	Δ*G*$_{solv}$	Δ*G*^{sol}	Δ*G*$_{solv}$	Δ*G*^{sol}
ac[c]	*d*	*d*	1.61	*d*	*d*	−6.52	*d*	−2.17	*d*
I	−15.85	−3.35	0.01	−14.74	−15.85	−1.47	6.376	0.05	−0.85
II	−7.01	5.29	3.45	−6.88	−7.69	−3.38	13.11	−0.69	7.74
III	−8.00	0.99	1.68	−8.06	−8.75	−6.12	6.08	−1.29	1.51
IV	−5.03	6.82	2.16	−5.46	−6.21	−6.21	11.07	−1.30	7.97
V	−4.41	2.42	3.92	−4.41	−5.20	−8.30	5.32	−2.28	2.60
VI	−1.19	8.55	0.00	−3.32	−4.11	−8.79	10.96	−1.69	9.36
ac1W	−23.90	−1.49	1.30	−21.41	*e*	−3.54	15.240	*d*	*d*
ac2W	−35.05	1.02	2.56	−30.38	*e*	−3.54	21.856	*d*	*d*
ac+w	−19.99	*d*	*d*	*d*	*d*	*d*	*d*	*d*	*d*
ac+2w	−23.88	*d*	*d*	*d*	*d*	*d*	*d*	*d*	*d*
H_2O	*d*	*d*	2.04	*d*	*d*	−5.67	*d*	*d*	*d*

[a] Energy units are kcal/mol; dipole moments are in D. [b] See Figures 1 and 2. [c] Isolated monomer. [d] Not calculated. [e] Not calculated because the system is too extensive.

dimer in chloroform solution was also subjected to the *NVT* molecular dynamics simulation in periodic boundary conditions. Details of the simulations are following: time step of 1 fs, temperature of 300 K, normal pressure, and total time of simulation of 0.2 *μ*s. The density was checked during the simulations to control the appropriate conditions. The box sizes (in Å) and number of molecules for various solutions were as follows: 0.3 M (41.9 × 36.0 × 31.9; seven acetic acid molecules); 1.0 M (44.1 × 38.45 × 27.3; 21 acetic acid molecules); 10 M (48.3 × 41.5 × 34.6; 447 acetic acid molecules); 99.8 M (84.1 × 82.3 × 81.0; one water molecule), $CHCl_3$ (59.7 × 45.7 × 45.3; two molecules of acetic acid).

The trajectory analysis was done using carnal and ptraj packages in a similar way as in the previous case.

IV. Results and Discussion

A. Ab Initio Quantum Chemical Calculations. *Gas-Phase Results.* The stabilization energies and free energies of the structures considered in this study are summarized in Table 1. One can see that the most stable structure (the global minimum) at the potential energy surface of the acetic acid dimer and also at its free energy surface (FES) is the sructure with the cyclic arrangement containing two O−H···O hydrogen bonds. This is in agreement with previous theoretical, as well as experimental, studies.[6,10] Comparing the DFT/B3LYP/6-31G** interaction energies to the interaction energies evaluated using RI MP2/TZVPP method (Table 1), one can see that they agree rather well for all structures studied with the exception of structure **VI** (see Figure 1). As an example, let us mention MP2 stabilization energy for structure **I** calculated[10] with aug-cc-pVTZ basis set (−15.8 kcal/mol), which agrees very well with our B3LYP/6-31G** and RI MP2/augTZVPP values (−15.9 kcal/mol). Serious difference in the stabilization energy is found for the structure **VI** for which the B3LYP stabilization energy is smaller by more than 2 kcal/mol than the RI MP2 one. This is clearly due to neglecting the dispersion energy at B3LYP calculations. This result is a warning. Care should be paid for the general application of B3LYP method even in the case of the interaction of such a strongly polar system like acetic acid. It is worth mentioning the open structure **V**. This isomer of acetic acid dimer has a favorable free energy of solvation in the water environment (see later); however, it does not exist as a stable minimum in the gas phase. Standard gradient optimization (exactly the same conditions as in the case of the other structures) changes its structure gradually to the conformation **IV**. Because for the subsequent treatment we need the gas-phase formation free energy, we evaluated the stabilization energy and free energy for the structure optimized in water environment (see later). It must be emphasized that the dimerization energy and the free energy values calculated under these conditions are not optimal and the final value of the free energy of dimerization in solution will be affected, most probably in an unfavorable direction. Following expectation, entropy strongly disfavors dimerization and Δ*G* values are significantly larger than the Δ*E* values. The largest difference is found for structures **I**, **VI** and **V** (for the latter structure, see, however, the note given above).

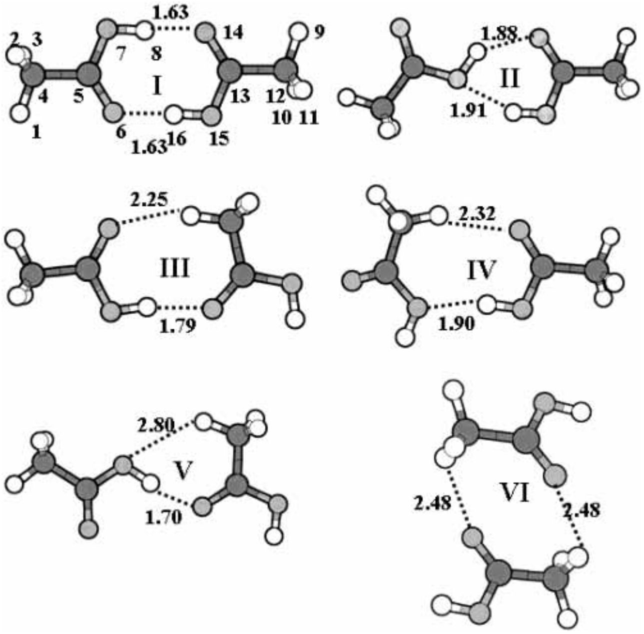

Figure 1. Structures of acetic acid dimer.

Cyclic structure **I** is extremely stable, and the question arises whether the approaching water (or waters) is able to break it. The unambiguous answer is only obtained by performing the MD simulations (see later). Using ab initio calculations, we optimized two structures of the acetic acid dimer···water cluster (cf. Figure 2). Table 1 shows that higher stabilization energy is obtained for the system in which the water molecule is incorporated into the cyclic structure. An even larger difference in stabilization energy (more than 10 kcal/mol) was obtained for two structures of the acetic acid dimer···(water)$_2$ cluster (cf.

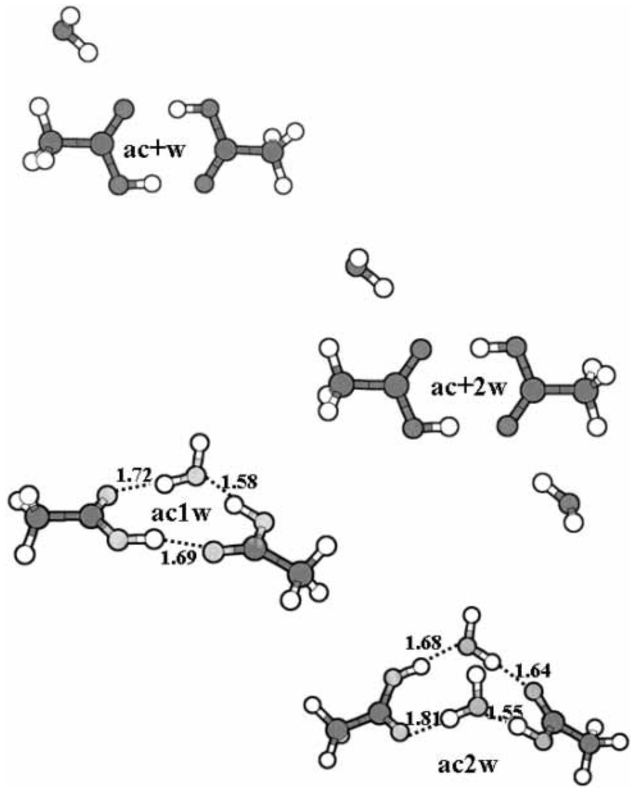

Figure 2. Structures of hydrated acetic acid dimer.

TABLE 2: Distances (Å) between sp^2-Hybridized Carbons (d_1) and between sp^3-Hybridized Carbons (d_2) in Various Structures of Acetic Acid and Hydrated Acetic Acid Optimized at the DFT/B3LYP/6-31G Level of Theory**

structure[a]	d_1	d_2
I	3.82	6.83
II	4.42	6.91
III	4.20	5.57
IV	4.34	5.59
V	4.45	5.81
VI	3.67	4.71
ac1w	4.60	7.33
ac2w	5.35	7.89

[a] See Figures 1 and 2.

TABLE 3: Vibrational Frequencies (cm^{-1}) of the OH Group Calculated at B3LYP/6-31G Level of Theory**

structure[a]	ν(OH)					
ac	3753[b]					
I	3137[d]	3009[e]				
II	3608[f]	3482[g]				
III	3747[b]	3443[g]				
IV	3750[b]	3583[f]				
V	3748	3501				
VI	3753[b]	3752[b]				
ac1w	3869[c]	3448[h]	3314[g]	2934[i]		
ac2w	3868[c]	3722[c]	3565[g]	3274[j]	3160[j]	2749[i]

[a] See Figures 1 and 2. [b] Free OH group in acetic acid. [c] Free OH group in water. [d] OH from acetic acid connected to O in the other acetic acid, antisymmetric mode. [e] OH from acetic acid connected to O in the other acetic acid, symmetric mode. [f] OH from acetic acid connected to OH in the other acetic acid. [g] OH from acetic acid connected to O in the other acetic acid. [h] OH from water connected to O in the acetic acid. [i] OH from acetic acid connected to O in water. [j] Coupled vibrational mode; OH from acetic acid bonded to O in water, OH in water bonded to the other acetic acid; first is the antisymmetric and the latter one is the symmetric mode.

Figure 2). The distances between carbonyl sp^2 carbons (d_1) and between sp^3 carbons (d_2) in optimized structures are presented in Table 2. The ab initio calculations thus clearly favor such structures in which water molecule (molecules) breaks the C═O···O−H H-bonds of the cyclic acetic acid dimer and forms water-separated structures.

The calculated harmonic vibrational frequencies of the acetic OH group are collected in Table 3. The red shift of this frequency upon dimerization is large and, following expectation, is largest for the cyclic structure **I**. The stacked structure **VI** contains unperturbed OH groups, and therefore, their stretch frequencies are the same as that in the isolated monomer.

Results in Solution. The formation free energy of the acetic acid dimer was evaluated in water and chloroform solutions for the structures investigated in the gas phase. The COSMO free dimerization energy in water and chloroform, the COSMO free solvation energy of dimer and monomer, and the values of the dipole moment are presented in Table 1. The COSMO results for the acetic acid monomer and the cyclic dimer **I** were compared to the previous results evaluated by other techniques. Colominas et al.[10] used Monte Carlo free energy perturbation (MC-FEP) and self-consistent reaction field (SCRF) methods and obtained ΔG_{solv} of the acetic acid monomer in the range −5.4 to −8.0 kcal/mol and −5.4 to −7.3 kcal/mol, respectively. These values agree well with the experimental value of −6.7 kcal/mol.[10] The present COSMO result (−6.5 kcal/mol, cf. Table 1) thus agrees well with both computational procedures, as well as with the experiment. In the case of the cyclic dimer structure **I**, the following ΔG_{solv} results were obtained: MC-FEP values by Colominas et al.[10] range from −2.1 to −4.7 kcal/mol depending on basis set and ab initio method used and the SCRF estimates are in range −3.7 to −3.9 kcal/mol, while the present COSMO calculations give −1.5 kcal/mol at the level used in our calculations. Finally, the free energy of dimerization in solution (ΔG^{sol}), reported[11] to be 7.5 kcal/mol, agrees well with the present COSMO model (6.4 kcal/mol). To summarize, we can conclude that COSMO model is suitable for calculations of the free energy of dimerization in solution.

Table 1 shows that all ΔG^{sol} values (seventh column) are positive and high. It unambiguously means that none of the acetic acid dimer structures investigated throughout this study are present in a water solution. The finding that the cyclic dimer **I** is not stable in water solution is in accord with experimental findings,[1,3,4] as well as other theoretical results.[10,11] Although the other structures of the acetic acid dimer have higher dipole moments (see Table 1), which induce more favorable values of the free energy of solvation of dimer (ΔG_{solv}), it is still not enough to overcome the disadvantageous effects coming from the free energy of solvation of monomer.

When chloroform is used as solvent, the situation is different. Investigating ΔG^{sol} in Table 1, we found a negative value for the structure **I**, which gives clear evidence that this dimer exists in the chloroform solution. However, when compared with the experimental value of −4.63 kcal/mol and the value of −4.14 kcal/mol obtained using MC-FEP calculations, it is obvious that COSMO provides a qualitative answer only.[29,30] In contrast, the structures with higher dipole moments are found not to be stable in chloroform environment.

B. Constant Energy (*NVE*) Molecular Dynamics Simulations. *MD/Q Calculations.* The lowest-energy structures of the acetic acid dimer located during MD/Q simulation are depicted in Figure 1 (structures marked **I**−**VI**), and these structures were subjected to further calculations. The other acetic acid dimer structures, differing from the dimers **I**−**VI** by the rotation of the methyl group only, were not considered in subsequent ab initio calculations.

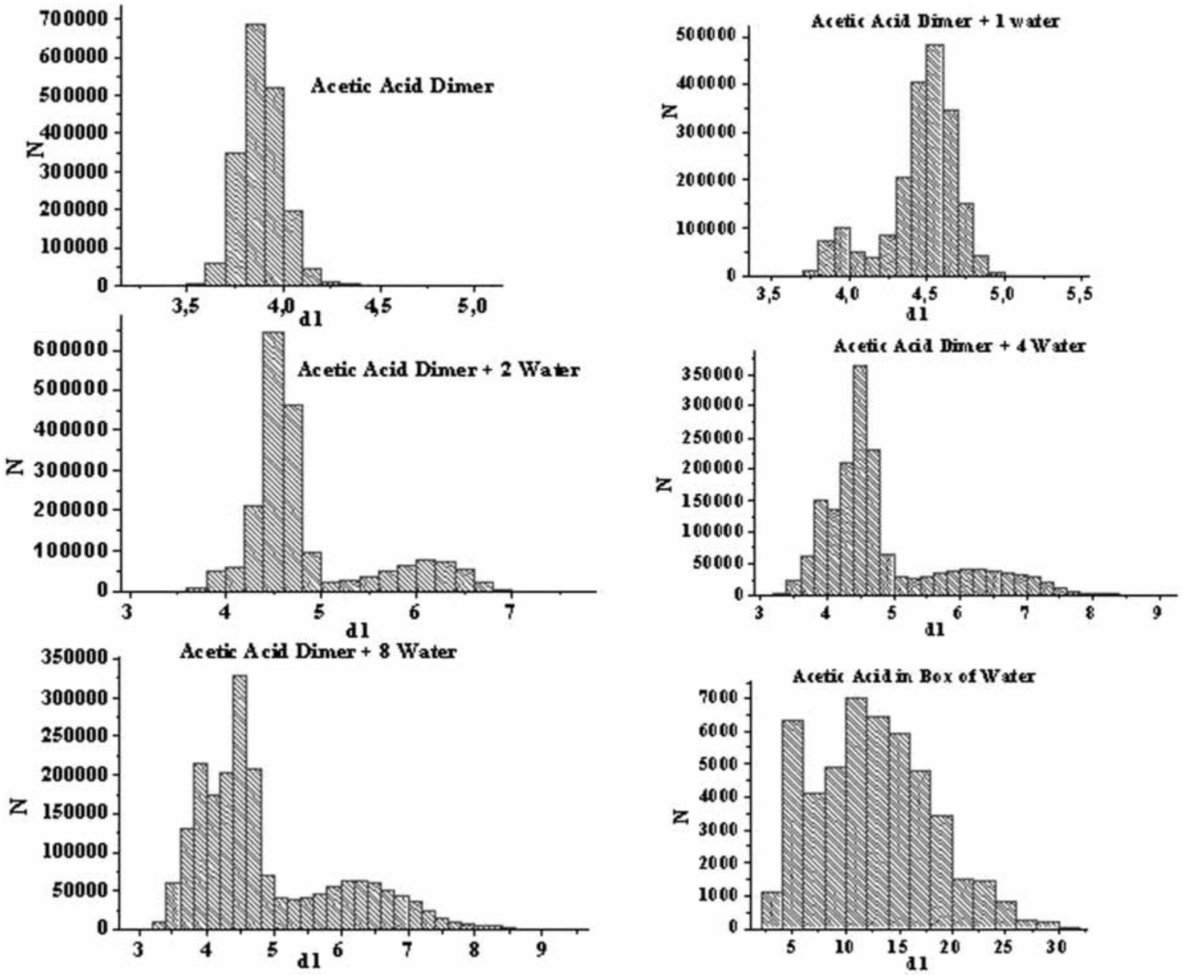

Figure 3. Histograms of acetic acid dimer, acetic acid···(water)$_n$, and acetic acid in water solution, showing distribution of d_1 distances (between sp^2 carbons; Å). Scale of *x*-axes in various histograms are different because of better understanding of individual diagrams.

TABLE 4: Average Values of Distances d_1 (between sp^2 Carbons) and d_2 (between sp^3 Carbons) Measured through the MD Simulations

system	d_1	d_2
0[a]	4.03	6.64
1[a]	4.46	7.09
2[a]	4.84	7.28
4[a]	4.84	6.92
8[a]	4.87	6.68
16[a]	5.11	6.55
216[a]	13.58	14.66
0.3 M[b]	9.54	16.57
1.0 M[b]	8.03	14.00
10.0 M[b]	8.60	10.20
99.8 M[b]	6.36	8.83
$CHCl_3$[c]	3.85	6.78

[a] Number of water molecules per acetic acid dimer. [b] Concentration of the acetic acid solution. [c] Chloroform as solvent. Values in Angstroms (Å).

TABLE 5: Simultaneous Occupancy (%) of Different H-bonds in the Acetic Acid Dimer Occurring at the Same Time during the MD Simulations

H-bond[a]	ac	ac1w	ac2w	ac4w	ac8w	ac16w	ac216w
7−8···14 and 15−16···6	80.5	14.5	3.9	3.4	2.9	2.1	0.4

H-bond	0.3 M	1.0 M	10.0 M	99.8 M	$CHCl_3$
7−8···14 and 15−16···6	0.1	0.1	9.8	25.3	99.7

[a] Numbering of the atoms is explained in Figure 1.

To obtain more information about microhydration, we performed the *NVE* molecular dynamics simulations of the acetic acid dimer and the acetic acid dimer hydrated by 1, 2, 4, 8, 16, and 216 water molecules. Figure 3 shows the histograms of the distribution of the distance between the sp^2 carbons, while Table 4 collects the average distances between two sp^2-hybridized carbons and two sp^3-hybridized carbons obtained from MD simulations with different amounts of water molecules. Further evidence about the dimer structure can be obtained by analyzing the H-bonds in the dimer. Table 5 summarizes the occupancies of both O−H···O bonds in the dimer appearing at the same time together. Bringing together the results from Tables 4 and 5 and Figure 3, we can conclude that the structure occurring most in pure acetic acid dimer simulation is the cyclic structure characterized by distances $d_1 = 3.82$ Å and $d_2 = 6.83$ Å (in its optimal conformation). When one water molecule is added, one of the hydrogen bonds in the cyclic dimer is broken and the geometry of this complex is changed to the structure **ac1w** (cf. Figure 2) with d_1 and d_2 equal to 4.60 and 7.33 Å (in its optimal conformation), respectively. Clear evidence about it follows from the histogram for the **ac1w** structure. The situation becomes more complicated if one more water molecule is added. Two acetic acid molecules and two water molecules can form various structures. Complexes known from the previous case frequently appear (first shoulder below 5 Å in the corresponding histogram in Figure 3). The second more widespread shoulder corresponds to the structure having both water molecules incorporated into the complex so that both hydrogen bonds from cyclic acetic acid dimer are broken (structure **ac2w** in Figure 2). The minor structural patterns represent clusters with one hydrogen bond between acetic acids and one hydrogen bond disturbed by two water molecules.

Upon increase of the hydration number, the simulation gets to be even more complicated and difficult to describe. Focusing in Tables 2 and 4, we can compare the optimized distances d_1 and d_2 (isolated dimers) to their average values in the course of MD simulations with various number of water molecules. The average distance d_1 remains almost the same during the simulations starting with 2 water molecules up to 16 water molecules. In contrast, the average d_2 distance begins to decrease. Additional information about the preferred structure of the dimer is obtained by performing the H-bond analysis. It means that we checked the presence of O−H···O bonds during the molecular dynamics course. The occupancy of O−H···O bonds is summarized in Table 5. The presence of bonds between atoms 7−8···14 and 6···16−15 (for numbering see Figure 1) at the same time is characteristic for the structure **I**; however, in the case that these bonds are not formed at the same time, some other structure is created. The data in Table 5 give us unambiguous evidence that the cyclic structure does not exist when the dimer is hydrated. On the other hand, the cyclic structure is the only one that is presented in chloroform and the major structure in a vacuum.

From the Table 5, it is thus evident that the presence of cyclic structure **I** can be excluded in the hydrated dimers because of nonexistence of two O···H−O hydrogen bonds at the same time. Finally, addition of 216 water molecules to the acetic acid dimer leads to its dissociation.

C. Constant Temperature (*NVT*) Molecular Dynamics Simulations. Systems corresponding to the 0.3, 1.0, and 10.0 mol/L water solutions of acetic acid and neat acetic acid were studied using the *NVT* molecular dynamics under standard conditions (i.e., room temperature, 1 atm pressure). The acetic acid dimer in chloroform environment was also explored under the same conditions. The situation in the liquid chloroform is transparent and will be discussed first. Table 4 shows that the average distances d_1 and d_2 are very similar to those in the gas-phase cyclic structure **I** (cf. Table 2). Further, from the Table 5, it becomes evident that both H-bonds exist simultaneously, which clearly supports the existence of the cyclic structure **I**. Putting both evidences together, we can conclude that the only structure detected during the MD simulation of acetic acid in chloroform is the cyclic structure **I**.

Water solution induces a much more complicated situation, and a different picture results for diluted and concentrated acetic acid. In the 0.3 and 1.0 M water solutions, the acetic acid is dissociated. Analyzing the average distances d_1 and d_2 (cf. Table 4), we found that they both are very large, much larger than any of these distances in various dimer structures (cf Table 2). Also the population of both H-bonds (Table 5) is close to zero, which supports the full dissociation of the dimer. Upon increase of the concentration of the acetic acid (10 M solution), the situation is changed and the H-bond analysis (Table 5) indicates the nonnegligible occurrence of both H-bonds. This result is, however, not supported by analyzing the average distances d_1 and d_2, which are in fact not much shorter than those in 0.3 and 1 M solutions. This may be caused by the fact that the amount of dimers is not high enough to change the average distances dramatically. Therefore, we believe that the H-bond analysis is more reliable in this complicated situation. In the case of neat acetic acid, the average distances d_1 and d_2 are shorter than those in 0.3, 1.0, and 10.0 M solutions, which clearly indicates the presence of some bound dimers. Because the population of both H-bonds is about 25% (cf. Table 5), we can deduce some form of open dimer structures, for example, the chainlike structures. In the case of neat acetic acid, chainlike structures are created. These structures possess more H-bonds than cyclic structures, which might be the reason for their creation.

V. Conclusions

(i) The most stable structure of acetic acid dimer in the gas phase has cyclic arrangement with two strong O−H···O bonds. The other structures are significantly less stable. The cyclic structure is also the most abundant conformer in *NVE* molecular dynamics simulations. (ii) Acetic acid dimer in chloroform was explored using MD simulations, and the only structure detected during the run has the same arrangement as that in the gas phase. (iii) Microhydration of the acetic acid dimer was studied by DFT/B3LYP and RI MP2 methods and using *NVE* molecular dynamics simulations. One water molecule causes breaking of one O−H···O bond, and water is incorporated into the dimer (structure **ac1w**, Figure 2). The situation becomes more complicated as we add more water molecules. The second water molecule usually breaks the other O−H···O bond in such a way that structure **ac2w** is formed (Figure 2). Also some other structures having one or both water molecules incorporated into one O−H···O bond can be formed. These structures do not frequently appear during the simulation. As more and more water molecules are added, more different water-separated complexes of acetic acid dimer are composed; the most frequently appearing complexes correspond, however, to **ac1w** and **ac2w** structures. (iv) Exploring water solutions of acetic acid of different concentrations (*NPT* molecular dynamics), we came to the conclusion that at low concentrations no dimer structure exists. This result is in good agreement with the study of Colominas et al. on formic acid dimer.[13] At higher concentrations of acetic acid, some kind of bound structure is present, but it does not correspond to the cyclic structure known from the gas phase and chloroform. The open structures are more likely to be in such a solution. From MD simulations, we deduced that neat acetic acid contains preferably chainlike structures, which is in agreement with results of a Raman spectral study.[6]

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