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Exploring Hydration Patterns of Aldehydes and Amides: Ab Initio Investigations

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Results of an extensive ab initio level investigation of the hydration patterns and energetics of some carbonyl compounds, viz., formaldehyde, acetaldehyde, formamide, and acetamide, are reported. This study employs restricted Hartree−Fock and density functional theory with the 6-31G(d,p) and 6-31++G(d,p) basis sets for exploring explicit hydration of these substrates with 8, 12, and 16 water molecules. Hydrated structures are seen to be dominated by four- and five-membered rings of water molecules as also exhibited by the $(H_2O)_n$ clusters. Electrostatic guidelines are found to be useful for predicting the growth of the smaller hydrated clusters. Hydration of these molecules leads to the weakening of C═O and N−H bonds as revealed by the corresponding internuclear distances and vibrational frequencies.

I. Introduction

Water is the omnipresent solvent in almost all important chemical and biological processes. It is thus no wonder that the study of molecular hydration, dealing with the interaction of water with solute molecules, has become an area of prime importance in chemistry and biology. With the advent of more sophisticated experimental tools[1] as well as theoretical methods,[2,3] a large number of studies on molecular hydration have been reported in the recent literature. Several investigations describing the hydration of molecules at different levels of sophistication such as Hartree−Fock (HF) and density functional theory (DFT), continuum models of solvation, Møller−Plesset perturbation (MP2), and molecular dynamics/molecular mechanics calculations have been reported[2−9] since 2000. The combined experimental and theoretical investigations[6] on the vibrational spectra of $(\text{benzene})_n\cdots(H_2O)_8$ clusters for $n = 1$ and 2 have revealed that the interacting moiety in these clusters happens to be a water octameric cube. Roth and co-workers[10] through their extensive spectroscopic and theoretical investigations of $\text{phenol}\cdots(H_2O)_n$ for $n = 1-12$ have also concluded that phenol can attach to and insert itself into the water network. Gadre et al.[11a] have employed the molecular electrostatic potential (MESP)-guided ab initio approach to explore the hydration of uracil by up to 15 water molecules. They have observed that water tetramers and octameric cubes are the basic building blocks of hydration.

Hydration studies of amides and their derivatives[13−19] are of great interest since amides can serve as a model for the peptide linkage in biological species. Also, Lewell et al.[14] have pointed out that the double-bonded oxygen atom of the carbonyl group presents an interesting contrast to the hydroxyl of water and other related molecules, as it displays trends quite similar to those of hydrides. The following discussion presents a short review of the hydration studies of various carbonyl compounds.

Kumpf et al.[15a] have reported HF level studies on formaldehyde⋯water systems (1:1 complexes), whereas Dimitrova et al.[15b] have presented the corresponding results at the MP2 level. The results of a further study on the same systems at the CCSD level with the pVTZ basis carried out by Ramelot et al.[15c] are in agreement with those reported by Kumpf and co-workers.[15a] Wolfe et al.[16] in their ab initio level study on the hydration of formaldehyde with up to four water molecules have reported the thermochemical parameters and vibrational frequencies. They[16] have observed a structure for $\text{formaldehyde}\cdots(H_2O)_3$ bearing a similarity to the ring arrangement of a water tetramer. Also, another study on hydration of formamide by up to five water molecules, with a view to explore the barrier to internal rotation, has been reported by Chen et al.[17] They have carried out a comparison of ab initio results with those obtained by the effective fragment potential (EFP) model. Robertson et al.[18] have performed spectroscopic investigations to study stepwise hydration of *N*-benzylformamide (NBFA) clusters by up to three water molecules. They report the preferential sites for water binding, along with the influence of hydration on geometry and electronic structure. The MESP-guided approach assisted by hydration pattern mapping for exploring stepwise hydration of formamide has also been recently reported by Gadre et al.[19]

Although the current literature is rich with several experimental as well as theoretical works addressing the problem of molecular hydration by up to seven water molecules, those dealing with a larger number are rather scarce.[21] While the present study extends the number of water molecules interacting with some model carbonyl compounds (M), the focus here is to obtain molecular level insights into the primitive patterns of the hydration process and not to merely carry out more extensive calculations. The present work is aimed at providing answers to the following queries.

(i) What are the likely basic patterns of hydration and possible changes in them on inclusion of a hydrophobic group (e.g., $-CH_3$)? Can one predict further growth of clusters with 8, 12, and 16 water molecules by employing these patterns as the building blocks?

(ii) Are there any energetically competitive structures close in energy to the most favorable $M\cdots(H_2O)_n$ one with increasing n?

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(iii) How are the properties such as the bond length, spectral frequencies, etc. of the carbonyl molecule affected by hydration?

Two prototype examples each of amides and aldehydes, viz., formamide (FM), acetamide (AM), formaldehyde (FLD), and acetaldehyde (ALD), are considered in the present investigation. It is hoped that this study will provide a better picture of what happens at an intermediate level of hydration, viz., between a solute molecule M interacting with a single molecule of water and the molecule M in bulk water.

II. Methodology

We have used stepwise building up of higher clusters (supermolecule approach) assisted by pattern selection,[11a,19] viz., utilizing the most common motifs of water molecules occurring in smaller clusters, for generating the initial geometries of $M\cdots(H_2O)_n$ ($n \geq 8$). MESP guidelines offered by an electrostatics-based model, viz., electrostatic potential for intermolecular complexation (EPIC), are also employed for generating geometries of hydrated clusters. Further details of the EPIC model can be found elsewhere.[11]

These clusters are optimized at the HF level using the GAUSSIAN 94[21] and GAMESS[22] suites of programs, employing the computationally manageable, yet quite adequate 6-31G(d,p) basis set. The popularity of the DFT-based approach for studying hydrogen-bonded systems[24] may be attributed to the fact that it enables modeling of correlation effects, frequently comparable to or in certain cases[25] even superior to MP2 at a considerably lower cost. Also, our previous studies[26] on weakly bonded systems have brought out excellent agreement with the experimentally measured vibrational frequencies. Taking a cue from these observations, lowest energy structures of each system (for $n = 8$ and 12) were optimized employing the B3LYP functional[7] and a fairly large basis set, viz., 6-31++G(d,p), with all the default options of optimization. For such systems, one may expect several minima on the shallow potential energy surface. Consideration of *all* such geometries is beyond the scope of ab initio treatment at the present scenario of computing technology. However, typically ~30 structures are scanned for each "*n*" to locate the lowest energy ones. It is further ascertained that the structures reported in this study are indeed local minima on the potential energy surface by calculating vibrational frequencies at the appropriate level of theory. The interaction energy, ΔE, is defined as $\Delta E = E_{M\cdots n(w)} - E_M - nE_w$. Also, to predict the extra stability of the hydrated clusters as compared to the corresponding most stable water clusters,[27] the concept of relative stabilization energy[11a,26a] is invoked. ΔE_{rel} is given by

$$\Delta E_{rel} = \Delta E_{M\cdots n(w)} - \Delta E_{n(bw)} = E_{M\cdots n(w)} - E_M - E_{n(bw)}$$

Here, w and bw, respectively, denote free water and the best cluster[27] of *n* water molecules, respectively. A negative value of ΔE_{rel} is indicative of whether the molecule can interact favorably with the corresponding most stable $(H_2O)_n$ cluster. The generation of initial geometries as well as the final visualization of the hydrated clusters is done by using the in-house-developed package UNIVIS-2000.[28]

III. Results and Discussion

Presented below are the results of the study on hydration of FM, AM, FLD, and ALD. This work may be thought of as an extension of the earlier work.[19] However, the main objective here is to carry out more extensive hydration studies of these model carbonyl compounds, providing meaningful answers to the queries given in the Introduction, and to obtain better insights into the explicit hydration process at the molecular level.

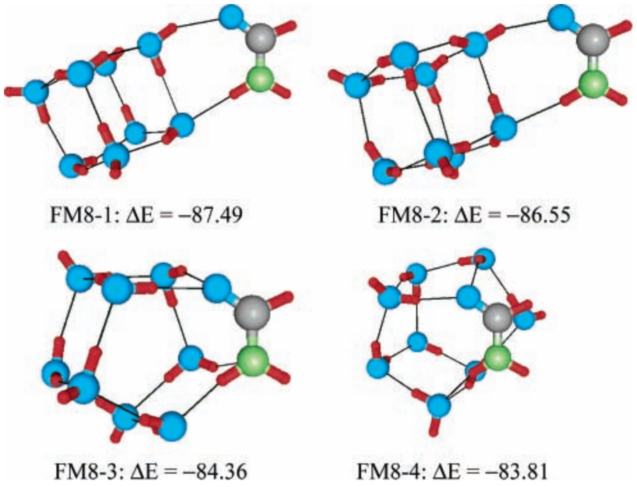


Figure 1. RHF/6-31G(d,p)-optimized geometries of $HCONH_2\cdots(H_2O)_8$ along with the interaction energies (kcal·mol^{-1}). See the text for details.

A. Hydration of Amides. *i.* $FM\cdots(H_2O)_n$ *(n= 8, 12, and 16)*. The lowest energy structures for $n < 8$ from the previous study[19] and the knowledge of the water cluster geometries[27] are used for generating various trial structures for $n = 8$. The structures thus generated have the interaction energy ranging from −87.49 to −83.71 kcal·mol^{-1} at the RHF/6-31G(d,p) level. The four lowest local minima on the potential energy surface are depicted in Figure 1. The energetics and other relevant information are displayed in Table 1. The water octamer in the most stable structure FM8-1 bears a striking structural similarity to that observed earlier for hydrated clusters of benzene[6] and phenol.[10]

To study the effect of correlation on energetics and the molecular geometries, the two lowest energy structures, viz., FM8-1 and FM8-2, have been further optimized at the B3LYP/6-31++G(d,p) level. The vibrational frequency calculations have also been performed at the same level to ascertain the nature of these complexes and to check the effect of zero-point energy (ZPE) correction. The details of ZPE-corrected and -uncorrected interaction energies are given in Table 2 (also see the Supporting Information for B3LYP-optimized geometries). The interaction energies for the complexes FM8-1 and FM8-2 have been found to scale down considerably with ZPE correction.

For higher hydrated clusters, there are several possibilities of generating trial structures by piecing together smaller (e.g., $(H_2O)_4$, $(H_2O)_8$, etc.) water clusters to the smaller hydrated clusters of formamide. To simplify this problem and understand the growth of hydrated clusters, we have explored the MESP of a prototype cluster ($n = 8$). Figure 2 depicts the MESP isosurface for $FM\cdots(H_2O)_8$, viz., FM8-1, of value −50.20 kcal·mol^{-1} at RHF/6-31G(d,p), which is present in four different spatial regions. However, the presence of two large lobes on the diagonally opposite oxygen atoms from the side of the octameric cube may be anticipated to provide the proper seed for further growth of the hydrated cluster. To generate such larger structures, electrostatics-based calculations with the EPIC model[11] have been performed on various possible geometries of the hydrated cluster and an added water tetrameric ring. The EPIC results indicate that growth of the hydrated cluster will be favorable on the B-side (formed by water molecules numbered as 5−8) of the octameric cube. A subsequent follow-up at the RHF/6-31G(d,p) level shows that the energetics

TABLE 1: RHF/6-31G(d,p) Level Interaction (ΔE) and Relative Stabilization (ΔE_{Rel}) Energies (kcal·mol^{-1}) for M···$(H_2O)_n$, $n = 8$, 12, and 16, Clusters[a]

structure code	ΔE	ΔE_{rel}	structure code	ΔE	ΔE_{rel}	structure code	ΔE	ΔE_{rel}	structure code	ΔE	ΔE_{rel}
FM8-1	−87.49	−11.60	AM8-1	−87.44	−11.52	FLD8-1	−82.38	−6.46	ALD8-1	−82.25	−6.33
FM8-2	−86.55	−10.66	AM8-2	−86.56	−10.64	FLD8-2	−81.80	−5.88	ALD8-2	−81.68	−5.77
FM8-3	−84.36	−8.47	AM8-3	−84.79	−8.87	FLD8-3	−79.53	−3.61	ALD8-3	−81.21	−5.29
FM8-4	−83.81	−7.92	AM8-4	−84.52	−8.60	FLD8-4	−78.47	−2.56	ALD8-4	−79.03	−3.11
FM8-5	−83.71	−7.82	AM8-5	−84.02	−8.11	FLD8-5	−77.81	−1.90	ALD8-5	−78.84	−2.93
FM12-1	−134.11	−11.68	AM12-1	−134.01	−11.57	FLD12-1	−128.93	−6.49	ALD12-1	−128.89	−6.46
FM12-2	−133.27	−10.84	AM12-2	−133.28	−10.85	FLD12-2	−128.41	−5.97	ALD12-2	−128.28	−5.84
FM12-3	−131.86	−9.43	AM12-3	−132.78	−10.34	FLD12-3	−126.33	−3.90	ALD12-3	−127.11	−4.68
FM12-4	−131.39	−8.95	AM12-4	−132.58	−10.15	FLD12-4	−126.06	−3.63	ALD12-4	−127.02	−4.59
FM12-5	−131.26	−8.83	AM12-5	−131.33	−8.90	FLD12-5	−125.85	−3.41	ALD12-5	−126.73	−4.29
FM16-1	−180.52	−11.65	AM16-1	−180.48	−11.62	FLD16-1	−175.34	−6.48	ALD16-1	−175.63	−6.76
FM16-2	−179.68	−10.82	AM16-2	−180.30	−11.43	FLD16-2	−175.14	−6.28	ALD16-2	−174.70	−5.83
FM16-3	−179.42	−10.55	AM16-3	−179.69	−10.82	FLD16-3	−173.30	−4.44	ALD16-3	−174.50	−5.63
FM16-4	−176.13	−7.26	AM16-4	−177.01	−8.14	FLD16-4	−171.44	−2.58	ALD16-4	−172.46	−3.59
FM16-5	−176.07	−7.21	AM16-5	−176.28	−7.42	FLD16-5	−171.35	−2.49	ALD16-5	−171.93	−3.07

[a] (M = formamide (FM), acetamide (AM), formaldehyde (FLD), and acetaldehyde (ALD)). Refer to the text for further details.

TABLE 2: Raw[a] **and ZPE-Corrected B3LYP/6-31++G(d,p) Level Interaction Energies of Hydrated Clusters (kcal·mol^{-1})**[b]

n	structure code	ΔE_{raw}	$\Delta E_{ZPE\text{-}corr}$	structure code	ΔE_{raw}	$\Delta E_{ZPE\text{-}corr}$
8	FM8-1	−92.29	−68.70	AM8-1	−92.26	−68.73
	FM8-2	−91.55	−67.50	AM8-2	−91.49	−67.81
12	FM12-1	−140.19	−102.81	AM12-1	−140.11	−103.01
	FM12-2	139.38		AM12-2	−139.33	−102.48
8	FLD8-1	−86.56	−62.17	ALD8-1	−87.13	−62.73
	FLD8-2	−86.03	−63.09	ALD8-2	−86.85	−63.52
12	FLD12-1	−134.41	−97.50	ALD12-1	−134.60	
	FLD12-3	−133.71	−97.89			

[a] Raw interaction energies refer to energies not corrected for ZPE and BSSE. [b] Refer to the text for details.

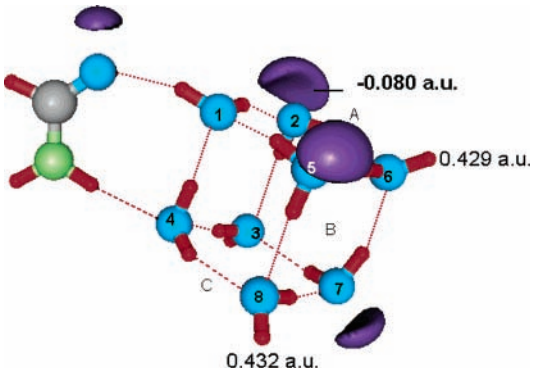


Figure 2. MESP isosurfaces of value −50.20 kcal·mol^{-1} (denoted by bold letters) mapped at RHF/6-31G(d,p) for FM8-1. The values in normal letters indicate the MESP-derived charges of the hydrogen atoms.

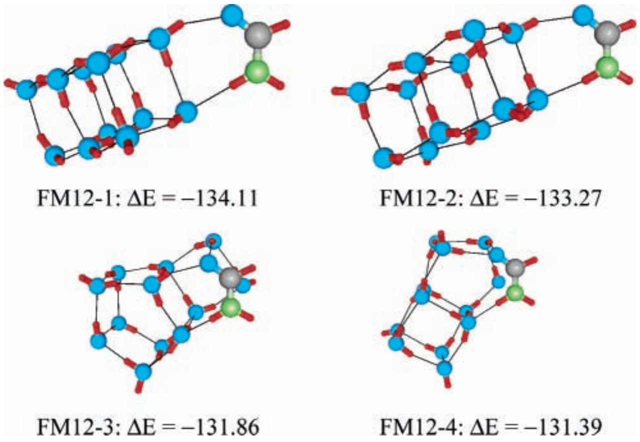

FM12-1: ΔE = −134.11
FM12-2: ΔE = −133.27
FM12-3: ΔE = −131.86
FM12-4: ΔE = −131.39

Figure 3. RHF/6-31G(d,p)-optimized geometries of $HCONH_2$···$(H_2O)_{12}$ along with the interaction energies (kcal·mol^{-1}). See the text for details.

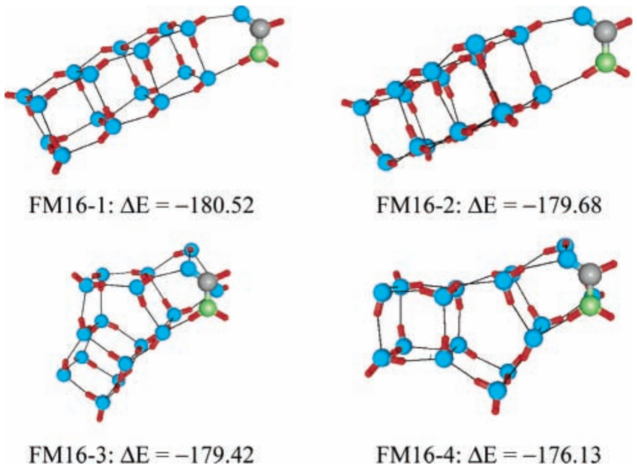
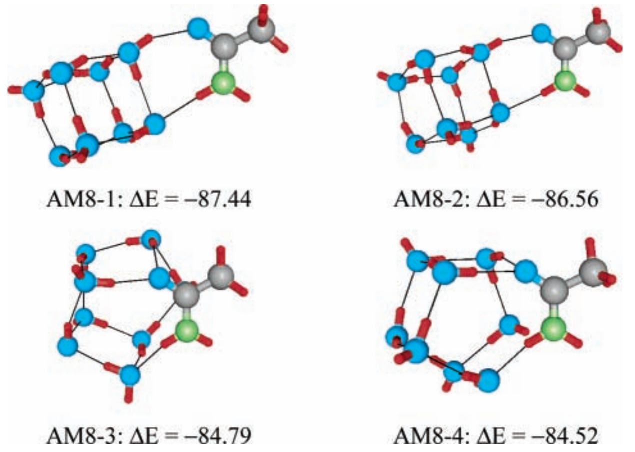

FM16-1: ΔE = −180.52
FM16-2: ΔE = −179.68
FM16-3: ΔE = −179.42
FM16-4: ΔE = −176.13

Figure 4. RHF/6-31G(d,p)-optimized geometries of $HCONH_2$···$(H_2O)_{16}$ along with the interaction energies (kcal·mol^{-1}). See the text for details.

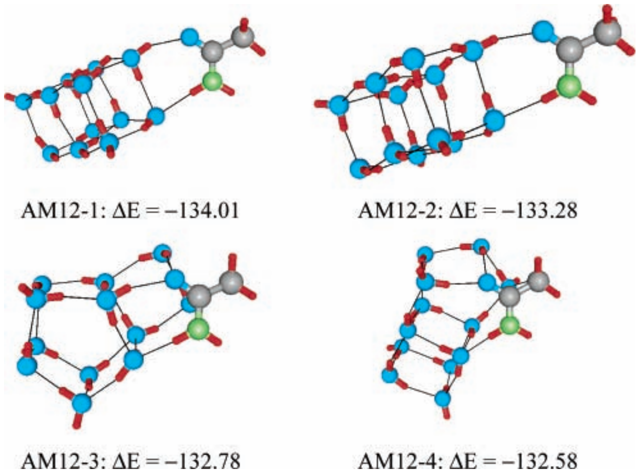
predicted by the EPIC model are in agreement with those observed at the HF level. Some trial structures for $n = 12$ were generated by combining lowest energy structures for $n = 8$ along with the knowledge of the water cluster environment and EPIC guidelines. We have done a fairly extensive scan for several low-lying structures, the four best among which are depicted in Figure 3, and the energetics are provided in Table 1. The hydrated structures for $n = 16$ were also generated using an approach similar to that for the $n = 12$ case. These structures have energies ranging from −180.52 to −176.07 kcal·mol^{-1}. Figure 4 depicts the four energetically best structures, the interaction energies for which are reported in Table 1. It may be noted that basic patterns of hydration for $n = 16$ are still dominated by a cube of water molecules interacting with the solute in combination with the tetrameric and pentameric rings of water molecules. Also, as expected, the average number of hydrogen bonds (n_H) increases from FM8 (14) through FM12 (22) to FM16 (29). It may be qualitatively seen that the average ΔE grows with n_H.

The elongation of the C═O bond length from 1.193 Å (for isolated formaldehyde) to 1.217 Å (mean C═O bond length in


AM8-1: $\Delta E = -87.44$ AM8-2: $\Delta E = -86.56$

AM8-3: $\Delta E = -84.79$ AM8-4: $\Delta E = -84.52$

Figure 5. RHF/6-31G(d,p)-optimized geometries of $CH_3CONH2\cdots(H_2O)_8$ along with the interaction energies (kcal·mol^{-1}). See the text for details.


AM12-1: $\Delta E = -134.01$ AM12-2: $\Delta E = -133.28$

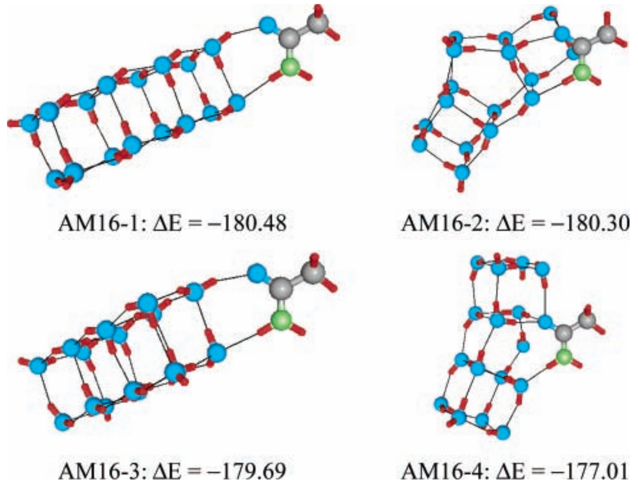
AM12-3: $\Delta E = -132.78$ AM12-4: $\Delta E = -132.58$

Figure 6. RHF/6-31G(d,p)-optimized geometries of $CH_3CONH2\cdots(H_2O)_{12}$ along with the interaction energies (kcal·mol^{-1}). See the text for details.

a hydrated cluster) is also noticed. This can be attributed to the effect of hydration. Also, in certain cases of hydrated structures for $n > 8$ and 12, the $-NH_2$ group is seen to undergo pyramidalization (by an angle between 1° and 13° from its planar configuration), which can be considered as another signature of hydration. The C═O bond length for the most stable cluster is found to be very close to 1.209 Å for all the lowest energy structures with $n = 8$, 12, and 16.

ii. AM···(H₂O)ₙ (n= 8, 12, and 16). The structures for $AM\cdots(H_2O)_n$, $n = 8$, 12, and 16, are generated from the corresponding lowest energy structures of hydrated clusters of formamide as well as by employing the pattern selection approach. AM is seen to show (cf. Table 1) energetic trends akin to those of FM, with the lowest energy structures being almost in the ±0.20 kcal·mol^{-1} range. Figures 5−7 depict the lowest energy hydrated clusters of acetamide, showing structural patterns are also found to be similar to those observed for the case of formamide. However, here water molecules are conspicuous by their absence around the hydrophobic methyl group of AM. The lengthening of the C═O distance from 1.20 Å (isolated AM) to 1.22 Å (average bond length in the hydrated clusters) is also observed. The hydrated clusters also show slight pyramidalization of the NH_2 group, similar to that in the case of formamide.

The follow-up of two lowest energy structures at the B3LYP/6-31++G(d,p) level of theory shows trends similar to those for formamide. Table 2 provides the details of ZPE-uncorrected and -corrected interaction energies of hydrated clusters of acetamide. At this stage, it may be seen that the trends in energetics of these amides remain unaltered by the incorporation of correlation effects and a higher basis set.


AM16-1: $\Delta E = -180.48$ AM16-2: $\Delta E = -180.30$

AM16-3: $\Delta E = -179.69$ AM16-4: $\Delta E = -177.01$

Figure 7. RHF/6-31G(d,p)-optimized geometries of $HCHO\cdots(H_2O)_8$ along with the interaction energies (kcal·mol^{-1}). Refer to the text for details.

TABLE 3: Variation of C═O Stretching Frequencies of Amides and Aldehydes and N−H Stretching Frequencies of Amides at the B3LYP/6-31++G(d,p) Level for *n* = 8 Water Molecules and for the PCM Model[a]

a. C═O Stretching Frequencies (cm^{-1})

no. of water molecules	FM	AM	FLD	ALD
0	1796	1767	1815	1813
8	1778	1758	1792	1782
PCM	1727	1685	1795	1772

b. N−H Stretching Frequencies (cm^{-1})

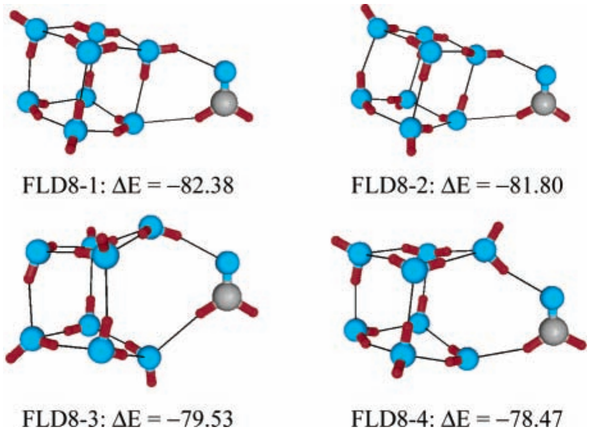
no. of water molecules	FM	AM
0	3738, 3591	3761, 3620
8	3681, 3672, 3404	3683, 3577, 3569
PCM	3390, 3518	3396, 3526

[a] See the text for further details.

The vibrational frequencies at the B3LYP level may be compared with those from the combined spectroscopic and theoretical study of $NBFA\cdots H_2O$, reported by Robertson et al.[18] Since the structure of $NBFA\cdots H_2O$ for the *cis*-conformer matches that of $FM\cdots H_2O$, only the results of the *cis*-form have been used for comparison in the present study. They have observed a progressive shift in the C═O overtone stretching frequencies (viz., 3465, 3429, 3326, and 3314 cm^{-1}) for isolated NBFA, $NBFA\cdots(H_2O)$, $NBFA\cdots(H_2O)_2$, and $NBFA\cdots(H_2O)_3$, respectively. Similar trends have been observed in the present study for the C═O stretching of amides for $n = 8$ water molecules calculated at the B3LYP/6-31++G(d,p) level of theory. The details are given in Table 3a.

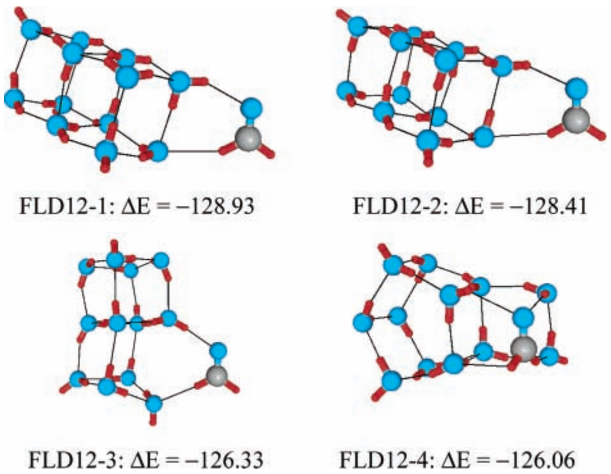
Also, N−H stretching frequencies for NBFA are observed[18] to shift to the high-wavelength side (3443, 3345, 3224, and 3204/3224 cm^{-1}) with increasing number of water molecules from 0 to 3. The results of the frequency analysis for our systems also show similar trends. The details of N−H stretching frequencies are given in Table 3b.

At this juncture, it is felt worthwhile to compare the trends shown by continuum models of solvation. PCM calculations[5] at the B3LYP/6-31++G(d, p) level for isolated molecules of


FLD8-1: ΔE = −82.38 FLD8-2: ΔE = −81.80

FLD8-3: ΔE = −79.53 FLD8-4: ΔE = −78.47

Figure 8. RHF/6-31G(d,p)-optimized geometries of HCHO···$(H_2O)_8$ along with the interaction energies (kcal·mol^{-1}). Refer to the text for details.


FLD12-1: ΔE = −128.93 FLD12-2: ΔE = −128.41

FLD12-3: ΔE = −126.33 FLD12-4: ΔE = −126.06

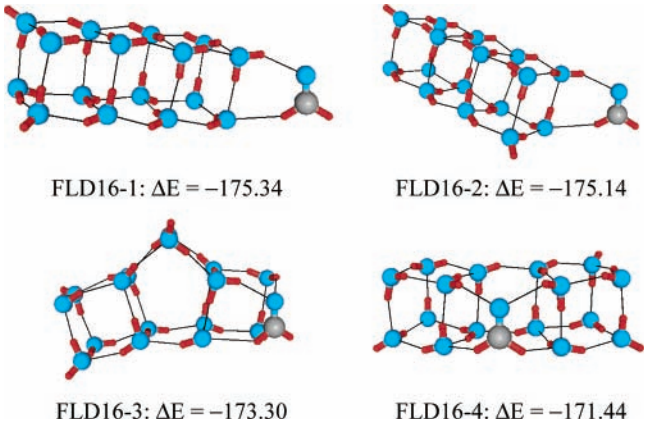
Figure 9. RHF/6-31G(d,p)-optimized geometries of HCHO···$(H_2O)_{12}$ along with the interaction energies (kcal·mol^{-1}). Refer to the text for details.

formamide and acetamide also show the pyramidalization of the −NH_2 group (∼1−13° from the plane of the remaining part of AM) as well as the shift in C═O stretching frequency in a qualitatively fashion similar to that seen earlier in the present study (cf. Table 3).

The interaction energies of formamide and acetamide (for noncuboid geometries FM8-3, FM12-3, AM8-4, etc.) are generally found to decrease with increasing cluster size with reference to the best cuboid structure (ΔE_{diff}) (cf. the Supporting Information, Table 1). This indicates that, at the ambient temperature and for sufficiently large clusters, the coexisting noncuboid structures will be competitive in stability with the respective cuboid ones (FM8-1, FM12-1, etc.).

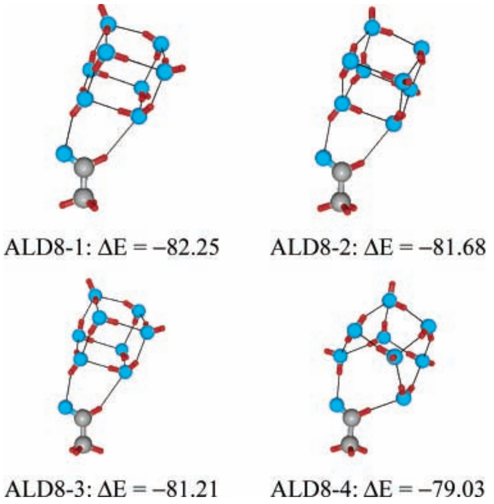
B. Hydration of Aldehydes. This study has been extended to aldehydes to probe the carbonyl group in a different electronic environment and obtain further molecular level insights into the hydration patterns. For this purpose, several low-lying hydrated structures of two model aldehydes, viz., formaldehyde (FLD) and acetaldehyde (ALD), are scanned in detail.

FLD···$(H_2O)_n$ and ALD···$(H_2O)_n$ (n= 8, 12, and 16). The knowledge of FM···$(H_2O)_n$ and the cooperativity of water molecules with an aldehyde molecule is employed for generating the starting geometries for hydrated aldehydes. The details of the energetics for formaldehyde and acetaldehyde are given in Table 1, while Figures 8−13 depict the geometries of the hydrated clusters for $n = 8-16$.


FLD16-1: ΔE = −175.34 FLD16-2: ΔE = −175.14

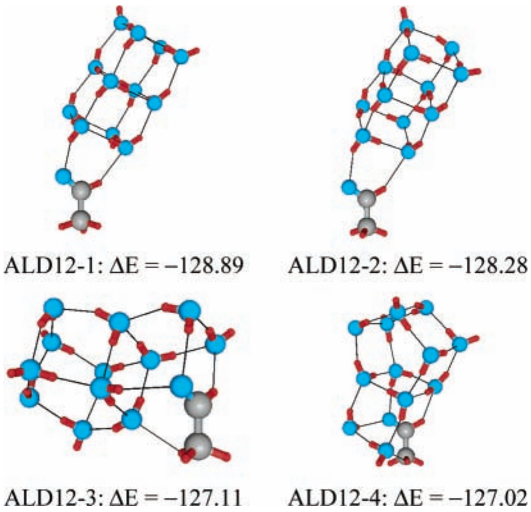
FLD16-3: ΔE = −173.30 FLD16-4: ΔE = −171.44

Figure 10. RHF/6-31G(d,p)-optimized geometries of HCHO···$(H_2O)_{16}$ along with the interaction energies (kcal·mol^{-1}). Refer to the text for details.


ALD8-1: ΔE = −82.25 ALD8-2: ΔE = −81.68

ALD8-3: ΔE = −81.21 ALD8-4: ΔE = −79.03

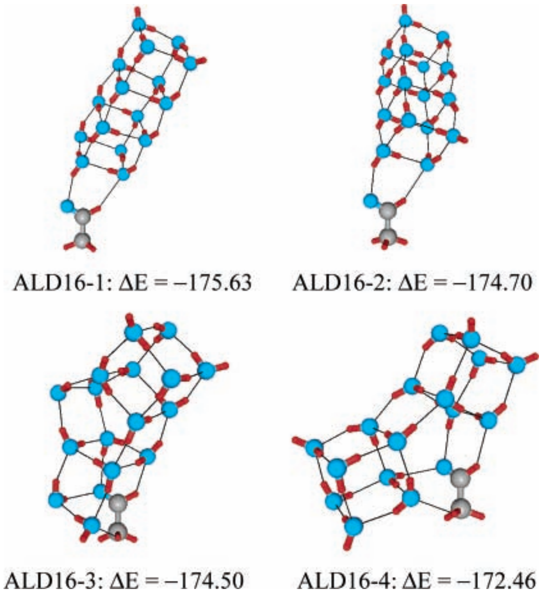
Figure 11. RHF/6-31G(d,p)-optimized geometries of CH_3CHO··· $(H_2O)_8$ along with the interaction energies (kcal·mol^{-1}). See the text for details.


ALD12-1: ΔE = −128.89 ALD12-2: ΔE = −128.28

ALD12-3: ΔE = −127.11 ALD12-4: ΔE = −127.02

Figure 12. RHF/6-31G(d,p)-optimized geometries of CH_3CHO··· $(H_2O)_{12}$ along with the interaction energies (kcal·mol^{-1}). Refer to the text for details.

It has been observed that the structural patterns of the lowest energy cluster of FLD/ALD···$(H_2O)_n$ are similar to those observed earlier for the clusters of amides, where the basic unit is a water octamer and its combinations interacting with the solute molecule. However, for other structures of acetaldehyde,



ALD16-1: $\Delta E = -175.63$ ALD16-2: $\Delta E = -174.70$

ALD16-3: $\Delta E = -174.50$ ALD16-4: $\Delta E = -172.46$

Figure 13. RHF/6-31G(d,p)-optimized geometries of $CH_3CHO\cdots(H_2O)_{16}$ along with the interaction energies (kcal·mol^{-1}). See the text for details.

the water molecules are conspicuous by their absence around the methyl group of ALD, as also noticed earlier in the case of AM.

The follow-up of lowest energy structures for $n = 8$ and 12 at the B3LYP/6-31++G(d,p) level brings out trends similar to those observed for the earlier molecular systems. The raw and ZPE-corrected energies for FLD/ALD$\cdots(H_2O)_n$, $n = 8$ and 12, at the B3LYP level are given in Table 2. It may be noted that, for the present systems, ZPE correction is typically 27% of the corresponding interaction energy (ΔE) and in some cases it alters the trends in energetics as observed earlier in the case of water clusters.[27] The shift in C═O stretching frequency (cf. parts a and b of Table 3) to the high-wavelength side has also been observed along with the corresponding increment in the intensity. It may also be noted that the frequency shift (for C═O stretching) for acetaldehyde is numerically smaller than that for formaldehyde, which may be attributed to the hydrophobic effect of the CH_3 group on acetaldehyde. PCM calculations[5] at the B3LYP/6-31++G(d,p) level (cf. Table 3a) for the formaldehyde and acetaldehyde molecules also show similar trends in C═O shifts.

ΔE_{rel}, viz., the interaction energy of the $(H_2O)_n$ cluster with the amides, is typically -10 kcal·mol^{-1} for $n = 8$, 12, and 16. The corresponding value for the case of aldehydes, however, is pegged at -6 kcal·mol^{-1}. This essentially brings out the difference in the polar nature of the interaction sites in the two classes of compounds. The distance analysis shows the lengthening of C═O from 1.184 to 1.195 Å and from 1.188 Å (isolated molecule) to 1.198 Å (in the hydrated cluster) for formaldehyde and acetamide, respectively.

The trends observed in ΔE_{diff} (cf. the Supporting Information, Table 1) of formaldehyde and acetaldehyde are similar to those observed for amides, where the noncuboid structures are observed well within ~1 kcal·mol^{-1} of the best cuboid one. This further brings out the existence of noncuboid structures quite competitive with the respective cuboid ones, FLD8-1, FLD12-1, etc. Also it may be noticed that the energy difference between the most favorable structure and the best noncuboid structure for compounds with a $-CH_3$ group (AM and ALD) is always numerically smaller than that for the corresponding parent molecules, viz., FM and FLD.

IV. Concluding Remarks

In the present paper we report the results of a systematic investigation of several low-energy hydrated structures of FM, AM, FLD, and ALD at the HF and DFT levels using the 6-31G(d,p) and 6-31++G(d,p) basis sets, respectively. A reasonably good search of such structures has been carried out, and all the structures reported here are ensured to be local minima. The present study also provides satisfactory answers to the queries raised in the Introduction, which are summarized below.

The hydrated structures involving tetrameric, pentameric, and octameric water patterns are found to be energetically more favorable than those involving the water molecules in a spatially distributed manner. Such patterns have also been observed for other molecules in the literature, e.g., benzene$\cdots(H_2O)_n$,[6] phenol$\cdots(H_2O)_n$,[10a] and pyridazine$\cdots(H_2O)_n$.[3a] However, the trends in energetics indicate that, at ambient temperature and for sufficiently large clusters (typically $n > 20$ or so), the noncuboid structures could be competitive with the respective cuboid ones. Also, the structural patterns of water molecules for the carbonyl compound with $-CH_3$, viz., AM and ALD, are quite similar to those in the case of FM and FLD, except for the absence of water molecules around the methyl group. The MESP-based approach[11,19] correctly predicts the favorable direction for the growth of hydrated clusters.

The elongation of the C═O bond and the vibrational shift in C═O as well as N−H stretching to the high-wavelength side may be considered as a signature of hydration. These results are similar to the ones observed by Robertson et al.[18] for hydration of a substituted amide. It may also be noted that the shift of C═O stretching vibrations for the lowest energy structures of the carbonyl molecules with a CH_3 group is always smaller than that for the corresponding unsubstituted one.

The trends in interaction energies at the RHF level (cf. Table 1) suggest that hydration of amides is energetically more favorable than that of the respective aldehydes. Further follow-up at a higher level, viz., B3LYP/6-31G++(d,p), indicates that the overall trends in the energetics remain unaltered on inclusion of correlation. The geometries of the hydrated clusters at the B3LYP level are also similar to those observed at the RHF level (for a comparison, refer to the Supporting Information). These trends are in general similar to the findings for water clusters[27] where the energetic trends (uncorrected for ZPE and BSSE) and the structural patterns are mostly unaltered at various levels of theory and with various basis sets. In general, the interaction energies at the RHF/6-31g(d,p) level are scaled up by ~4−6% at the B3LYP/6-31++G(d,p) level.

It is hoped that the insights into the structure and energetics obtained from the present study, assisted by the advent of computational power, may lead to a better understanding of molecular hydration soon.

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Supporting Information Available: Table of interaction energies (ΔE) and difference in the interaction energies (ΔE_{diff}) of all the clusters at the RHF/6-31G(d,p) level and a comparison of hydrated clusters at the B3LYP/6-31++G(d,p) and RHF/6-

31G(d,p) levels along with the details of vibrational frequency analysis performed at the B3LYP/6-31++G(d,p) level. This material is available free of charge via the Internet at http://pubs.acs.org.

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