

COMPUTATIONAL STUDY OF ION-MOLECULE INTERACTIONS

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By

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Declaration

I hereby declare that the matter embodied in this report is the result of investigation carried out by me in the Department of Chemistry, Indian Institute of Technology Hyderabad under the supervision of Dr. Bhabani Shankar Mallik.

In keeping with general practice of reporting scientific observations, due acknowledgement has been made wherever the work described is based on the findings of other investigators.

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Thank You.

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Dedicated to
My Parents

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ABSTRACT

The interaction of ions with neutral molecules was studied by computational methods in this project. Two types of systems were studied; the first one being triethyloxonium ion with water molecules and the second one is N-methylacetamide (NMA) with alkyl ammonium ions and carboxylate ions in the presence of water molecule. It was found that the interaction energy of first two water molecules to oxonium ion Et_3O^+ is mainly contributed by hydrophobic interactions. With the addition of more water molecules, the interaction energy was found to be increasing and it comes from the stability gained due to H-bonds among water molecules. The lowest energy isomers of the clusters for 3, 4 and 5 water molecules, are found to have cyclic structures of water molecules. The cyclic water tetramer also stabilizes the clusters with more water molecules, indicating that it is the most stable cyclic structure of water molecules. Et_3O^+ ion is found to be stabilized in basic medium, and got destabilized in acidic medium. When compared for the hydrophobic nature, Et_3O^+ is found to be slightly more hydrophobic than its analogous carbon counterpart Et_3C^+ .

NMA, being amide, has nucleophilic as well as electrophilic centre. So, it can interact with charged and neutral chemical entities. Based on the interactions of NMA with protonated amines, carboxylates and water molecules, it was found that NMA can interact more with electrophiles than nucleophiles. Transfer of two protons took place, when protonated amine and carboxylate interacted with NMA simultaneously. One proton transfer took place from protonated amine to NMA, and second one from NMA to carboxylate ion. When these cations and anions were made to interact separately with NMA in the presence of water molecule, the cations and anions didn't undergo proton transfer. This finding can be exploited in stabilizing the peptides as well as proteins by using suitable ion- pairs in aqueous solution.

1 Introduction and Motivation

In this project we have studied the interactions of ions and molecules to understand their behaviour towards each other. For this we considered two systems: one being the oxonium ion-water system and the second one is ionic liquid-water system. Ionic liquid-water system contains N-methylacetamide with the ionic species, protonated amines and carboxylate ions in the presence of water molecule. We have taken triethyloxonium ion for the model oxonium ion and studied its interaction with water. We have also compared these interactions with carbocation-water interactions. We also studied these interactions by taking water molecules with protonic defects. For both the systems we have used DFT methods to optimize the structures and calculating energetics of the clusters employing B3LYP/6-311+G(2d,p) level.

1.1 What is Oxonium ion?

Oxonium ion contains positive trivalent oxygen with an octet of electron. It is a very reactive species and can be divided into two classes. The first category with three oxygen-ligand bonds is called saturated oxonium ions having the general formula R_3O^+ where R can be hydrogen or hydrocarbon part. When $R = H$, it is called hydronium ion (H_3O^+); it is the simplest oxonium ion known.¹ Saturated oxonium ions involve many other species like protonated alcohols² (also called alkyl oxonium ions) which are important intermediates in the acid-catalyzed dehydration of alcohols, protonated ethers² (which are called dialkyloxonium ions) and the cationic part of Meerwein's salts which is called trialkyloxonium ion, because it contains three C-O single bonds. The second category of oxonium ions are unsaturated oxonium ions which have at least a double or triple bond between oxygen and other species mainly carbon atom. The oxonium ions with double bond between oxygen and carbon are called oxocarbenium ions. Oxocarbenium ions are important intermediates of the reactions involving aldehydes and ketones, like acid-catalyzed hydration and nucleophilic addition of carbonyl compounds, etc. The intermediate of these reactions are protonated aldehydes and ketones, which come under the category of oxocarbenium ions. The direct evidence of oxocarbenium ion as intermediate, was first reported in 1992 in the asymmetric cleavage of chiral acetals.³ Then it was reported as an intermediate in Lewis acid mediated reactions of acyclic acetals.⁴ Since

then it is a very interesting topic on which research is being carried out. Trialkyloxonium ions are the most widely known oxonium ions. They are very useful synthetic reagents^{5,6} due to their general stability and alkylating properties as Meerwein's salts. The alkylation by Meerwein's salts was done previously in organic solvents most commonly dichloromethane, and due to this restriction they had to use inappropriate solvents for the reactions. Then it was reported in 1986 that triethyloxonium tetrafluoroborate ($\text{Et}_3\text{O}^+ \text{BF}_4^-$) can be used as ethylating agent in aqueous solution.⁷ Nowadays these salts are being used extensively as alkylating agents in Inorganic and Organic chemistry. Oxonium ions don't exist independently however trialkyloxonium salts are stable at low temperature in ethereal media. For example $\text{Et}_3\text{O}^+ \text{BF}_4^-$ is a white crystalline solid. Oxonium salts are very reactive and can react with almost all nucleophiles. It reacts with water to undergo hydrolysis at ambient and high temperatures. Although at low temperatures, water cannot react with these ions, as their hydrolysis is an endothermic process. Oxatriquinane and Oxatriquinacene are unusually stable oxonium ions, first described in 2008.⁸ Oxatriquinane does not react with boiling water or with weak nucleophiles like alcohols, thiols, halide ions or amines, although it does react with strong nucleophiles such as hydroxide, cyanide and azide.

1.2 Need of the study of Oxonium ion-Water interactions

Oxonium ions have been extensively studied previously by different methods like IR⁹, ¹⁷O NMR¹⁰ and ¹³C NMR¹¹ and much information have been gathered about their structural and electronic properties.^{2,12} However there are not many studies, in particular, to stabilize these ions despite the enormous usefulness of these ions. Non-covalent interactions like H-bonding and van der Waals forces can play an important role in stabilizing the structures of ions and molecules. Nowadays, water is being studied for research purposes as it is a green solvent. Keeping the fact in mind, we intended to study oxonium ion-water interactions as water molecules have the ability to solvate ions through hydrogen bonds. It can serve as a good medium to stabilize these ions though only at low temperatures. Triethyloxonium ion is taken as the model oxonium ion as it is the smallest alkyloxonium ion whose experimental data is available to compare the structure and the bond lengths. Its three C-O bond lengths are found to be 1.506 Å⁸ with the pyramidal geometry centered on oxygen. Since this

ion have medium sized ethyl group as the substituents, it can serve as a good model for studying hydrogen bonding interactions as well as hydrophobicity.

1.3 Importance of Hydrogen bonding in polypeptides and proteins

Amides are present as peptide linkage in polypeptides and proteins, and are very important from the biological point of interest to understand many of the biological functions.

They have unique properties, as they have both the proton acceptor site (carbonyl oxygen) and proton donor site (amine part NH). Hydrogen bonding interactions are very important in determining the structural features of proteins. As per the studies, about 90% of the polar groups of the main chain of globular protein participate in hydrogen bonds¹³ whereas surface polar groups interact mainly with the surrounding solvent. The importance of hydrogen bonding capacity of polypeptides was also postulated by Pauling and Corey long before by proposing that α - helices and β - sheets play an important role in proteins.^{14,15} In particular, hydrogen bonding between the carboxyl oxygen and amine hydrogen atom in the protein backbone is responsible for stabilizing β -sheets and other motifs.¹⁶ The polypeptide chains are always associated on accord of these interactions. The concept of hydrogen bonding is mainly based on the preferred spatial orientation of polar groups involving donor and acceptor atoms. Apart from the H-bond interactions in proteins, water also plays a significant role in influencing the structure and functions of these biological molecules. A lot of research is going on for understanding the structural and functional features of proteins.¹⁷⁻²⁷

1.4 NMA as a model for molecule for peptides

An efficient way of developing general models of hydrogen bonding of this peptide linkage with water and other species without directly involving the complexity of macromolecules is offered by a simple fragment N-methylacetamide (NMA, C_3H_7NO). It contains a single peptide group ($O=C-N-H$), which is connected to methyl moieties on carbonyl oxygen and amine nitrogen. Therefore its internal degree of freedom and intermolecular bonding is similar to those of polypeptide segments. NMA is a good model for studying the interactions of peptides and proteins because it is also economical for simulations and experimental techniques.

1.5 Need of the study of interaction between Ions and NMA in aqueous solution

In regard of interactions between water molecules and NMA and their self-association, an interesting study has been done. The simulations of these interactions predicted that bulk water structure is significantly disrupted by the addition of even small quantities of NMA. In contrast, when water is added to pure NMA, the hydrogen bonded intermolecular chains of NMA tend to break only at linear section, but not at branching points and therefore they show significant self-association even at very low concentration.²⁵

We have studied the interaction of NMA with different cations and anions of biological interest taking protonated amines as cations and carboxylates as anions by computational methods. We also studied these interactions in the presence of water to stabilize NMA. For this we took various cations and anions with different alkyl and hydroxyl substituted alkyl group so that our study can have good range of substituents.

1.6 Computational Details

Computational studies have been performed using DFT method to optimize, and calculate energetics of different chemical species under consideration. All calculations have been carried out with Gaussian [09]²⁸ suite of programs. We have used Gauss View package for visualization of optimized geometries and analysis of computational results. The computations are done at B3LYP/6-311+G(2d,p) level.^{29,30} This level of electronic structure calculation gives satisfactory geometries as those found with other theoretical levels³¹, but with a much reduced execution time. We computed the structure and energetics of each cluster. After obtaining the optimized structure for each species, we calculated the frequency for each chemical entity at the same level of optimization. We have used the thermal corrected values for calculating the interaction energy. We calculated the interaction energy (I.E.) by the following relation.

I.E. = Energy of the interacted cluster – sum of the energies of the individual species.

The energy of each chemical entity includes zero-point energy and thermal energetics from 0 K to 298 K.

2 Oxonium Ion-Water Interactions

In this chapter we have focused upon the interactions of oxonium ion with water molecules by changing the number of water molecule in the cluster. In addition to that we have compared the structural and electronic properties of oxonium ion with that of a carbocation and a neutral alkane. We have also compared the oxonium ion and carbocation for the hydrophobicity. We also studied the interaction of oxonium ion and water with protonic defects.

2.1 Comparative studies of oxonium ion and Hydrocarbon species

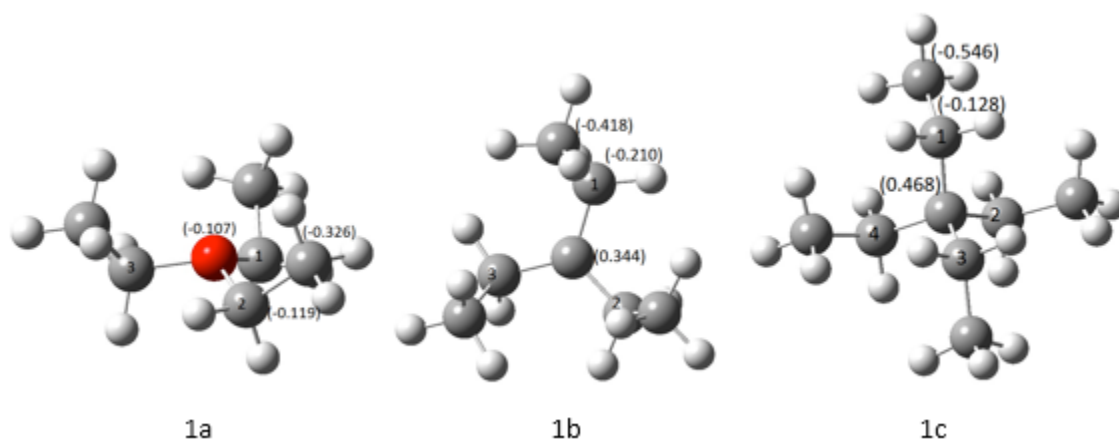


Figure 1. Structures of Et_3O^+ , Et_3C^+ and Et_4C (left to right) optimized at B3LYP/6-311+G(2d,p) level; Colour codes red, grey and light grey for Oxygen, Carbon and Hydrogen respectively (the same coding follows).

Our ion of interest triethyloxonium ion (1a) is found to have pyramidal structure when we optimized it. The three ethyl groups get projected in pyramidal geometry. All the O-C bond lengths are found to be equal to 1.51 Å which is very close to the earlier reported value 1.506 Å. All the bond angles C-O-C are found to be 113.90° which shows the deviation from the normal tetrahedral angle.

Coming to the similar looking species Et_3C^+ (1b) we found that it is a planar molecule with the tertiary carbon sp^2 hybridised as it is characteristics of carbocation. All C^+-C bondlengths are equal to 1.47 Å which is less than the O-C bondlength of the oxonium ion. This can be explained on the basis of hybridisation, as oxygen is sp^3 hybridised in Et_3O^+ , whereas tertiary carbon in Et_3C^+ is sp^2 hybridised. The more s-character in the bonding orbitals of the carbocation is responsible for shortening of

bondlength as compared to oxonium ion where s-character is less in the bonding orbitals.

The alkane 3,3-diethylpentane $\text{C}_{10}\text{H}_{22}$ (1c) shows a tetrahedral geometry with all the C-C bond lengths equal to 1.55 Å. The steric hindrance of the ethyl groups along with the sp^3 hybridisation of quaternary carbon makes the bondlength longer as compared to the bondlengths in Et_3O^+ and Et_3C^+ .

Focussing on the charge distribution of the oxonium ion, we found that O-atom bears partial negative charge of -0.107. This can be explained on the basis of electronegativity difference as oxygen is more electronegative than carbon and hence can withdraw the electron density from the attached carbon atoms which in turn is withdrawing electron density from hydrogen atoms. This leads to partial negative charges on oxygen and carbon atoms while all the positive charges end upon hydrogen atoms. In the carbocation Et_3O^+ (1b), we see that tertiary carbon is positively charged because it cannot withdraw electron density from the other carbons attached to it. The remaining carbon atoms are negatively charged as they are more electronegative than H-atoms and the H-atoms are positively charged. Following the same line for the molecule 3,3-diethylpentane (1c) the quaternary carbon is positively charged and all other C-atoms are negatively charged and the positive charges on the H- atoms.

2.2 Oxonium ion-water system

Three different modes of interaction of water with Oxonium ion can be seen (figure 2). These geometrical arrangements are designated as 2a, 2b and 2c. In the structure, 2a, the water molecule interacts with the ion from an equatorial position having O-O distance of 4.18 Å. In the second isomer, water molecule interacts with the ion from the site, where the lone pair of electrons of oxygen is supposed to be occupied and hence it will experience some repulsion. This is reflected in the longer O-O distance (4.36Å). The third isomer, 2c, is the most stabilized structure among them. In this isomer, water interacts with oxonium oxygen from the opposite side to that in the second isomer. It also interacts with methylene hydrogen which leads to greater stabilization of the system and shows the minimum of O-O distance (3.58 Å). It is the

most stable isomer for OXW. No any appreciable change has been noted in the O-C bond lengths of oxonium ion in the presence of water molecule. The structure bears the partial negative charge on oxygen and carbon atoms while all the partial positive charges on hydrogen atoms. The oxonium oxygen, even in the vicinity of water molecule, has a very small value of negative charge, which is not significantly changed when compared to isolated oxonium ion (1a).

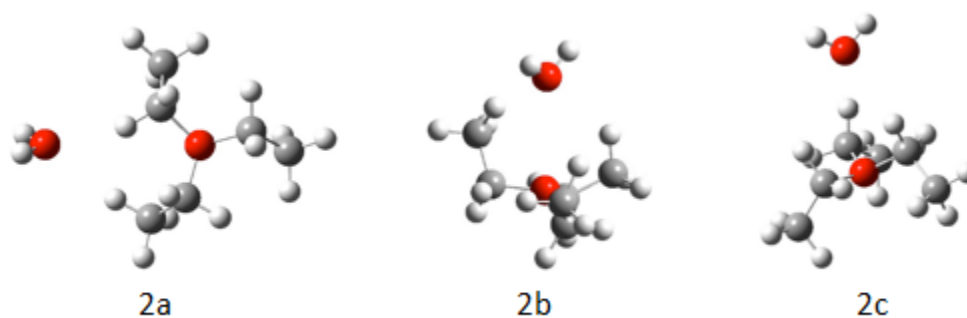


Figure 2. Geometries of different isomers of OXW cluster.

When two water molecules are made to interact with oxonium ion, we got several structures with different arrangement and orientations of water molecules (figure 3). In the isomers 3a, 3b, 3c, and 3d, the two water molecules interact with the ion from different positions though all of them have different orientations of water molecules. In the structures, 3a and 3b the two water molecules interact with the ion from the positions between the ethyl groups. In the third isomer, 3c, one water is interacting above while the other is in the middle of the two ethyl groups. In the fourth isomer the oxygen atoms of water molecules and oxonium oxygen form a bent structure with an angle of 146° . The isomers 3e, 3f and 3g contain hydrogen bonded water molecules and only one of the two water molecules interact with the ion. These isomers are found to be more stabilized than other isomers. The extra stability of these isomers can be attributed to the hydrogen bond operating between the water molecules. Despite the fact that all these isomers contain hydrogen bonded water molecules 3e is the most stable isomer among them. The water molecule in this isomer interacts from that side where it can have interactions with the methylene hydrogen. We can see that the isomer, 3e, is just derived from the most stable isomer for one water cluster, 2c. The structure, 3e, contains two water molecules where the second one is having H-bond interactions with the first one. OXW₂ isomers do not show appreciable change in the O-C bond lengths compared to isolated ion as well as OXW isomers. The

nearest water molecule is 3.37 Å from the oxonium oxygen and the second water molecule is hydrogen bonded with the first one. The H- bond as well as the ion- water interaction is responsible for its greater stability compared to OXW complex, which lacks hydrogen bond. The charge distribution is not much affected due to the presence of second water molecule.

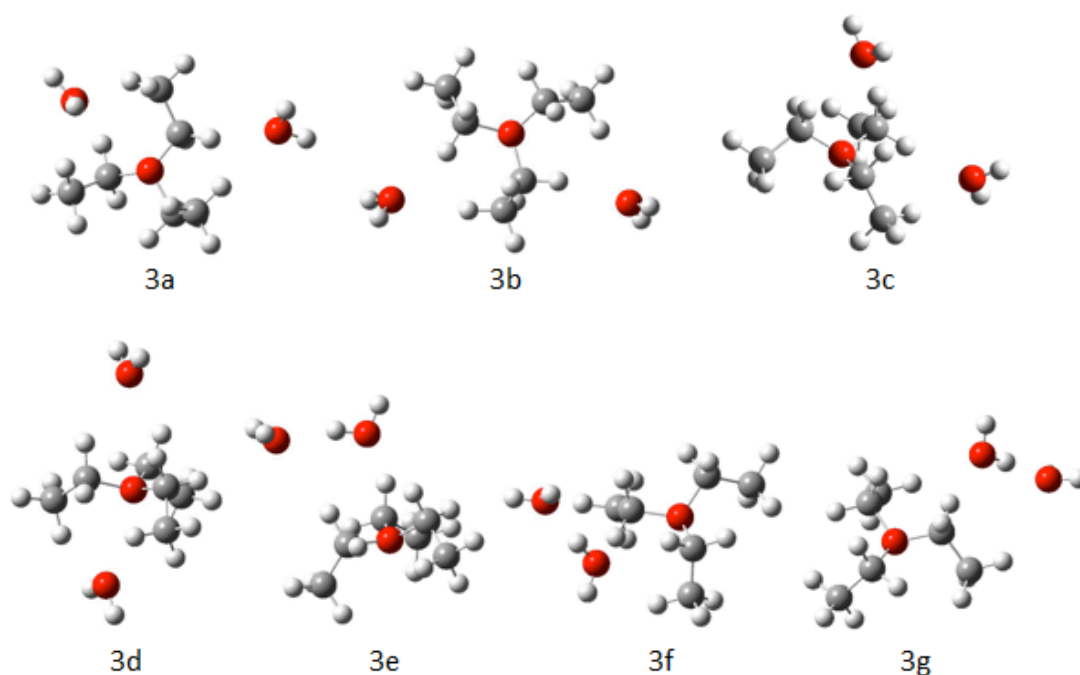


Figure 3. Geometries of different isomers of OXW₂ cluster.

With 3 water molecules, we got eight isomers namely 4a, 4b, 4c, 4d, 4e, 4f, 4g and 4h (figure 4). In first four isomers 4a to 4d, the three water molecules are interacting separately with oxonium ion from different positions thus only having the hydrophobic interactions. 4b is the most symmetric structure among them as it have all the three water molecules at equal distances from the oxonium oxygen. It is also the most stabilized structure among them. The isomers 4a, 4c and 4d may appear structurally same, and their interaction energies vary by very small value but the water molecules in those isomers are in different orientation. The isomers 4e, 4f and 4g contain chains of three water molecules formed via H-bonds and only one of them is close enough to interact with the oxonium oxygen. These isomers are different from each other because the water chain is interacting from different positions with the ion. The isomer 4h has a cyclic trimer of water molecules and it is the most stabilized

isomer for OXW_3 . The higher stability of 4h than that of 4b can be attributed to the H-bond interactions operating between water molecules. In this isomer all the water molecules interact with the ion with the same strength and they also interact with methylene hydrogen. It is shown as figure 7c containing a trimer of water (making a cyclic structure through H-bonds) interacting with the ion. All the water molecules are at a distance of 4.07 Å from the ion. The three ethyl carbon atoms of oxonium ion bear equal negative charge and the oxygen atoms of the three water molecules also bear equal negative charge making the structure symmetric.

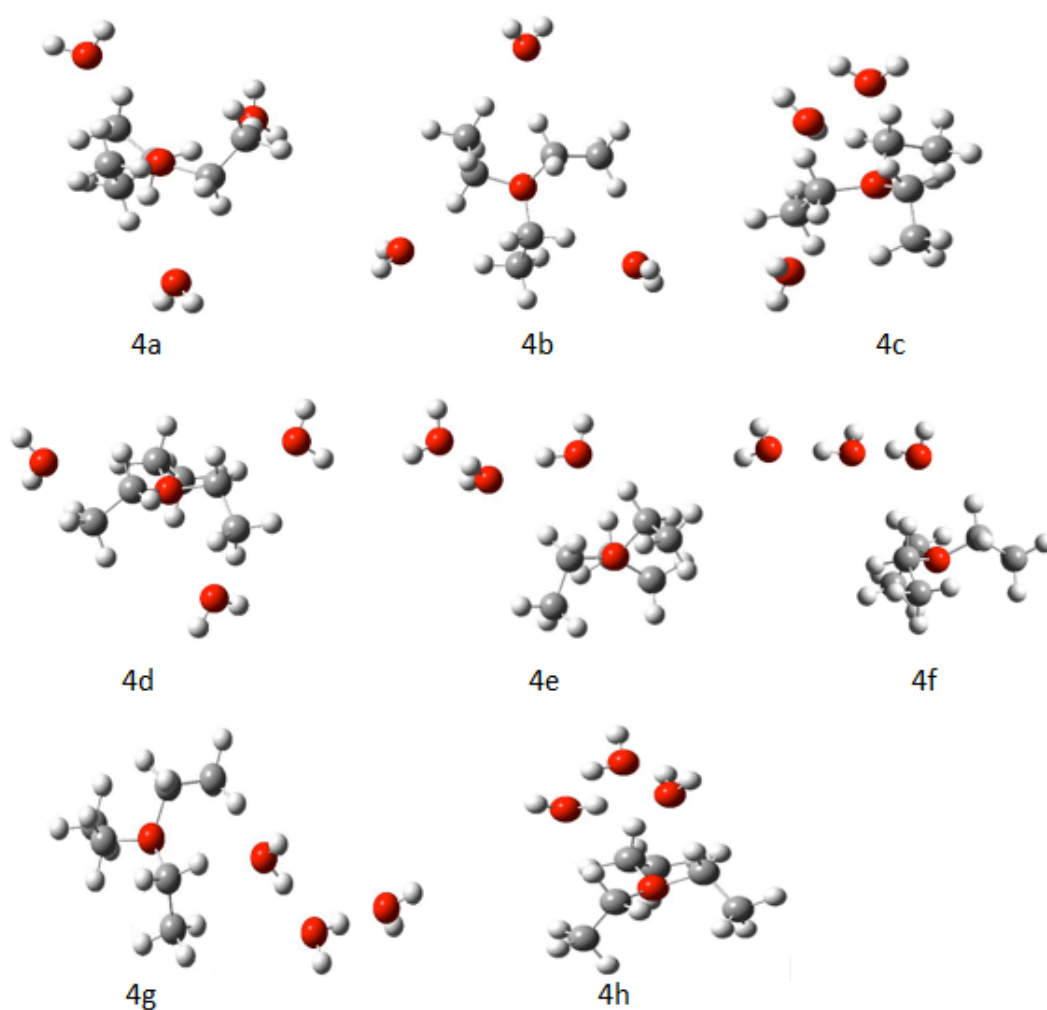


Figure 4. Geometries of different isomers of OXW_3 cluster.

Among the different isomers of OXW_4 (figure 5), 5a and 5c may look similar to each other as the oxonium ion is surrounded by the four water molecules but they vary in their orientation and energy values. 5b, 5d and 5e have hydrogen bonding between water molecules and they are more stabilized than those isomers, which lack hydrogen bonds among water molecules. This indicates that the extra stabilization of

these isomers results due to hydrogen bonding. The isomer, 5d, having maximum hydrogen bonding among water molecules, has maximum negative value of interaction energy. The isomer, 5b, having only one H- bond in its structure has minimum negative value, and 5e has the intermediate of these two energies. 5f and 5g have tetramer of water molecules interacting with the ion though the tetramers interact from the opposite side in 5f to 5g. 5g have greater stabilization even though the two structures have the same hydrogen bonding and cyclic tetramer of water molecules. The underlying reason can be the difference in the position of the water ring. In 5f the tetramer will experience repulsion from the lone pair electrons of oxonium oxygen while in 5g the water ring being on the opposite side will not experience the same and in addition to that water molecules can interact with methylene hydrogen. This trend is continuously observed from one water to four water clusters that hydrogen bonding among water molecules and their interaction with methylene hydrogen is leading to greater stability. The structure, 5g, is the most stable isomer for OXW_4 (figure 7d) and it contains a tetramer of water molecules interacting among themselves through hydrogen bonds. The nearest water molecule is at 3.97 Å from the oxonium oxygen; the rest three are at approximate distances only. The stabilization of this isomer is mainly contributed due to the formation of cyclic structure of water molecules not through the ion-water interactions, as the other isomers lacking this water structure are far less stable. The charge distribution of the cluster does not follow any order with the addition of water molecules and it solely depends upon the arrangement of the water molecules around the ion and how it is interacting with it.

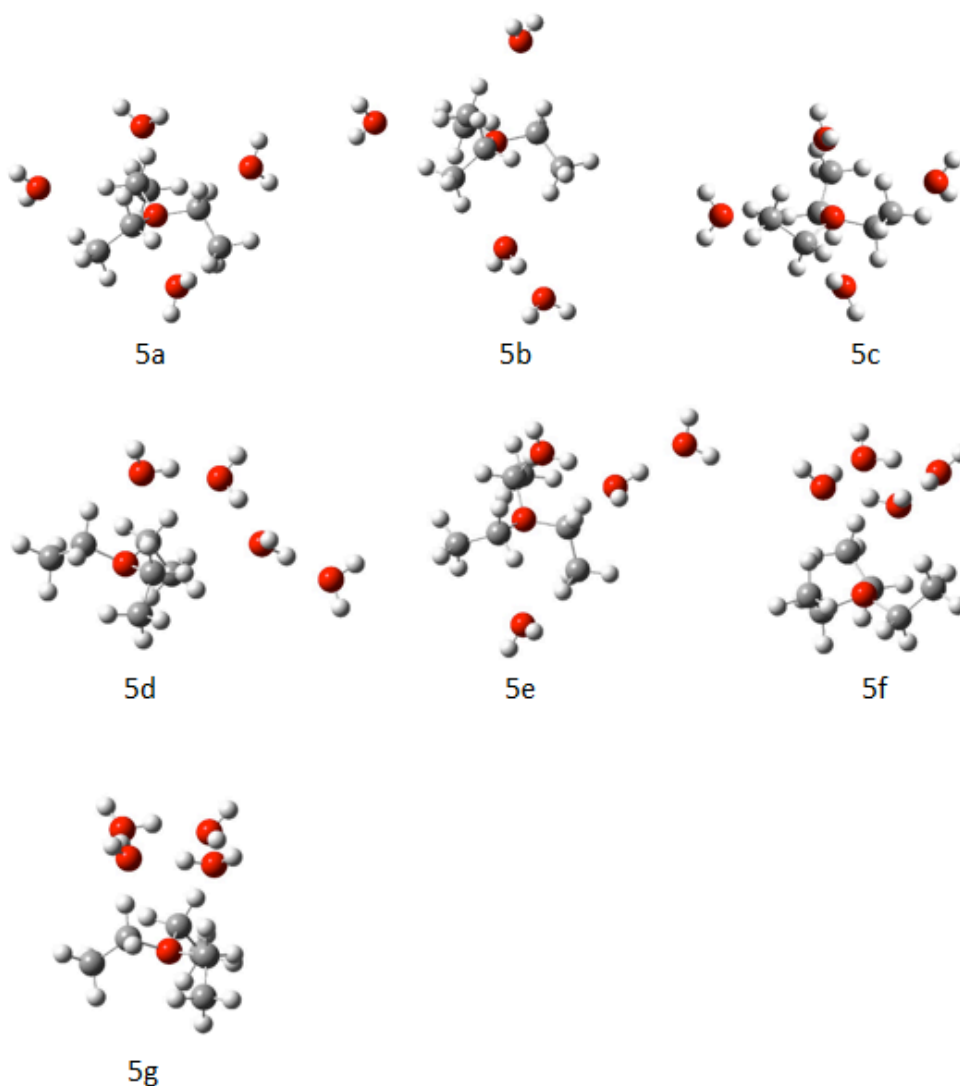


Figure 5. Optimized geometries of different isomers of OXW₄ cluster.

The five water-ion complex also have different isomers (see figure 6). Water molecules make a solvation shell surrounding the ion as shown by 6a and 6c structures. These two structures are different in the position of the water chain as they are on the two opposite sides of the oxonium ion. The water molecules in 6c are oriented in such a manner that they can interact with methylene hydrogen imparting it more stability than that of 6a. 6b has the least interaction energy, which can be due to the less number of hydrogen bonds in this structure. The most stable structure is 6d, which has a water ring of five molecules. Apart from the hydrogen bonds among water molecules, the interaction with methylene hydrogen is the factor, which make this isomer the most, stable among them. The greater stabilization of these structures mostly comes through the H- bonds operating between water molecules. The nearest

water molecule from the oxonium oxygen is at 4.6 Å distance (figure 7e). The charge distribution when compared to 7d is not affected much.

The ion- water interactions are prevalent in the one water and two water clusters as there is no other interaction significantly contributing whereas the clusters with higher number of water molecules are mainly stabilized due to the cooperative interactions among water molecules and the oxonium ion. The binding energy for all the isomers of the clusters is tabulated in table 1.

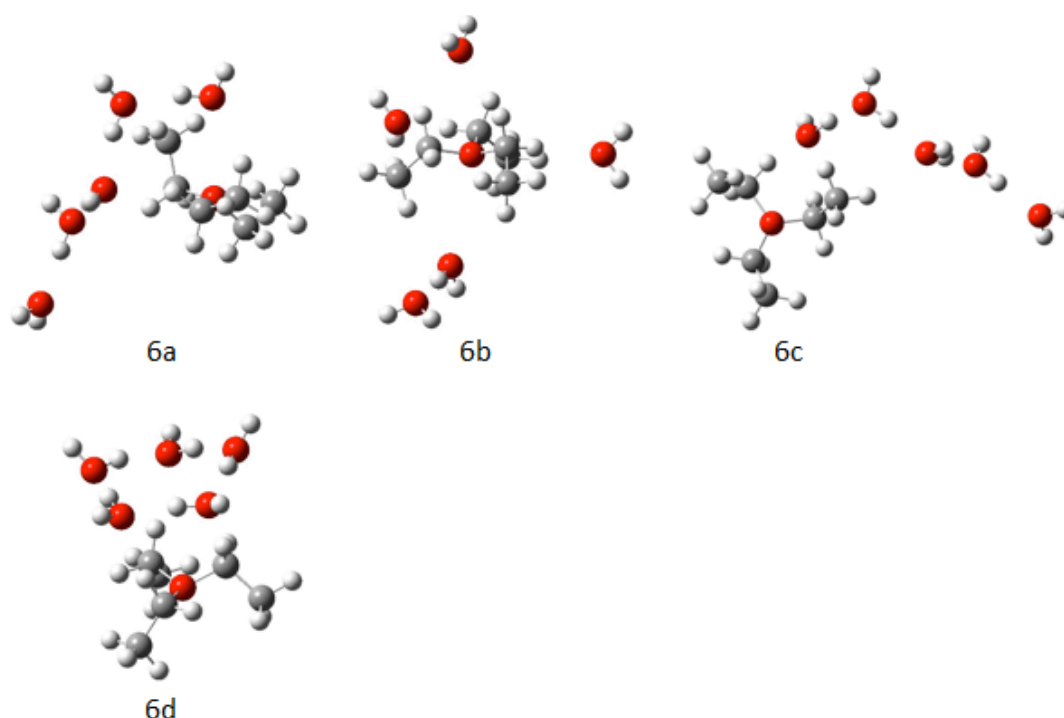


Figure 6. Optimized geometries of different isomers of OXW₅ clusters.

Table 1: Interaction Energy values and bond lengths for all the isomers of OXW_n (n = 1 to 5) water clusters.

OXW _n (n = 1 to 5)	Interaction Energy (kcalmol ⁻¹)	Smallest O ⁺ -O distance (Å)	Smallest O ⁺ -C bond distance (Å)
2a	-6.9	4.18	1.50
2b	-5.0	4.36	1.51
2c	-7.0	3.58	1.51
3a	-11.4	3.85	1.50
3b	-13.2	4.20	1.50

3c	-13.2	3.59	1.51
3d	-11.6	3.53	1.50
3e	-16.0	3.37	1.51
3f	-15.3	3.80	1.50
3g	-15.1	4.07	1.50
4a	-17.3	3.62	1.51
4b	-18.9	4.22	1.51
4c	-18.8	3.64	1.51
4d	-16.8	3.85	1.50
4e	-24.9	3.34	1.51
4f	-24.9	3.36	1.51
4g	-22.9	4.00	1.50
4h	-24.7	4.07	1.51
5a	-23.8	3.63	1.50
5b	-24.1	3.70	1.50
5c	-22.1	3.88	1.50
5d	-33.3	3.36	1.51
5e	-30.0	3.38	1.51
5f	-32.8	4.17	1.51
5g	-36.3	3.97	1.51
6a	-36.4	3.79	1.49
6b	-28.9	3.63	1.50
6c	-38.8	3.74	1.49
6d	-45.3	4.06	1.51

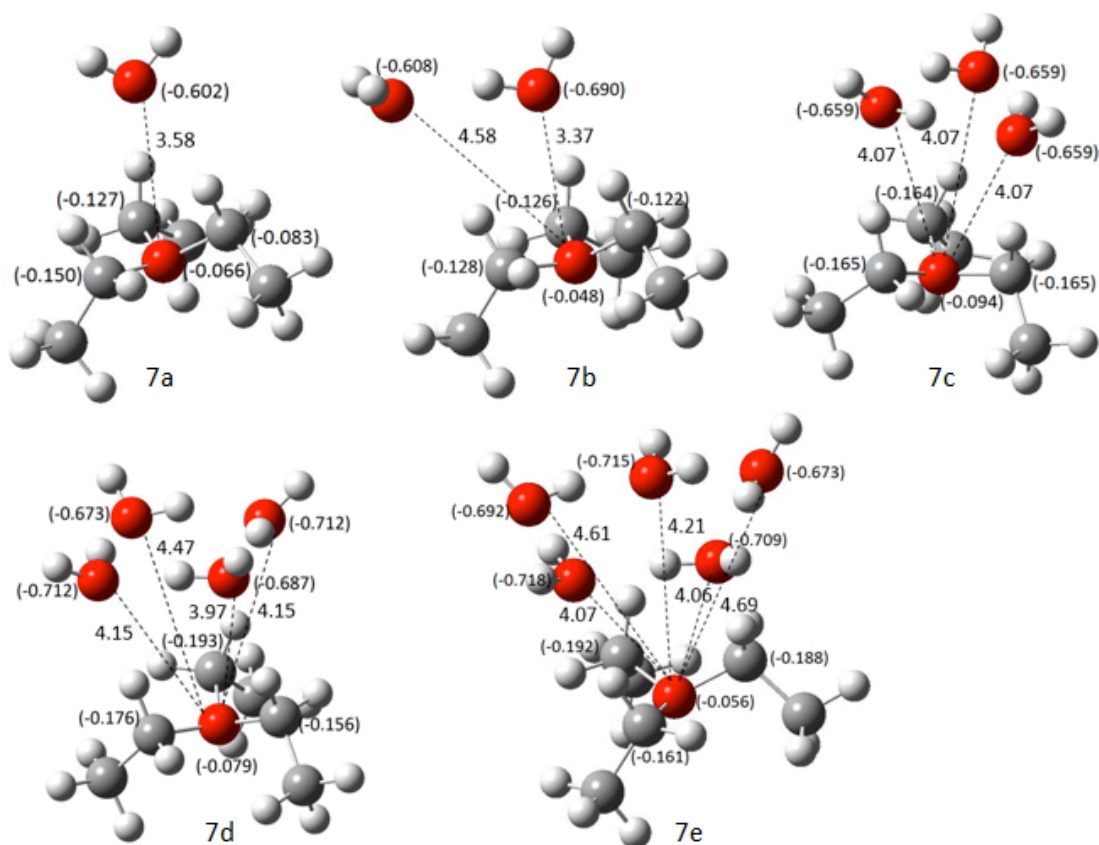


Figure 7. Lowest energy isomers of $\text{Et}_3\text{O}^+(\text{H}_2\text{O})_n$ clusters calculated at the B3LYP/6-311+G(2d,p) level. Bond lengths are in angstroms, the atomic charges are in parentheses.

Figure 7 displays the optimized structures for the most stable isomers of $\text{Et}_3\text{O}^+(\text{H}_2\text{O})_n$ where $n = 1-5$.

2.3 Hydrophobicity of oxonium ion and carbocation:

In order to study the hydrophobicity of oxonium ion and comparing it with that of carbocation we optimized the respective ions with three water molecules and found that oxonium ion is slightly more hydrophobic than the carbocation. The minimum distance between oxonium oxygen and water molecule in oxonium-water cluster is 4.07 Å (figure 8a) whereas the minimum distance between the tertiary carbon of the carbocation and water molecules is 4.04 Å (figure 8b). Even the substituents on the central atom for both the ion is same, the difference in contribution of steric factor cannot be neglected as they are projected in space in different geometries. The charges on central atom also make contribution to their hydrophobic properties. The oxygen atom is slightly negatively charged and the pyramidal geometry of the ethyl

groups in oxonium ion repel the water molecules more than that compared to carbocation which is planar in geometry and also the central carbon bears partial positive charge.

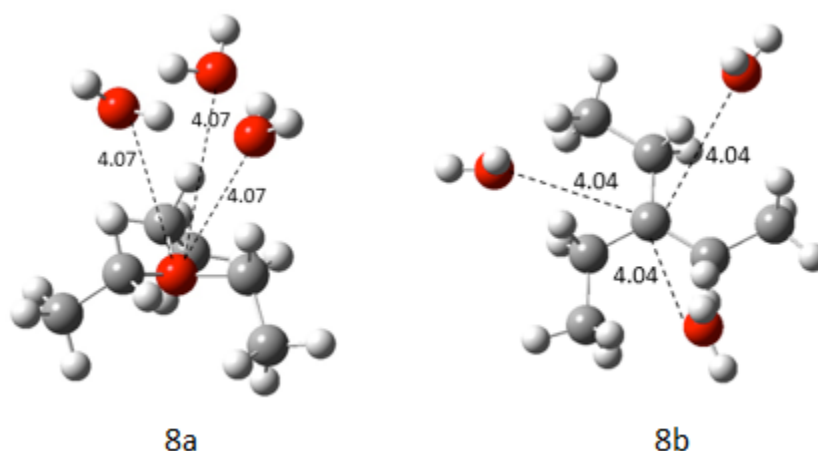


Figure 8. Structure of $\text{Et}_3\text{O}^+\text{W}_3$ and CET_3^+W_3 .

2.4 Oxonium ion with more water molecules

In cluster of ion with six water molecules, the water molecules arranged themselves in a chain surrounding the ion (figure 9a). The four water molecules make a solvation cell around the ion and the other two molecules going farther which shows that hydrophobic interactions are prevalent because of the ethyl groups, which repel water. With seven water molecules, the chain makes a shape (figure 9b) such that the first, fourth and seventh water molecule gets closer to the oxonium oxygen as compared to other molecules. The farther molecules of the chain are distant from the oxonium oxygen because of the hydrophobicity of the ethyl substituents. The addition of one more water molecule to the cluster with seven water molecules, leads to altogether different shape of the water chain. The eight water cluster (figure 9c) forms a tetramer of water making a cyclic structure, which is interacting with the water chain of the closer three water molecules through H- bonds. These three water molecules interact with methylene hydrogen and surround the ion whereas the tetramer is far from the oxonium oxygen as hydrophobic ethyl group repels it and the remaining water molecules are hydrogen bonded to the tetramer and are more distant from the concerned oxygen. The cluster with nine water molecules (figure 9d) can be seen as an extension to OXW_7 cluster as it almost surrounds the ion by making a continuous single chain through H- bonds among themselves. It can be seen from the figure that

some water molecules are farther compared to others as the ethyl groups repel them, and the other water molecules are so oriented that they occupy the spaces between the ethyl groups and so they are nearer to the oxygen of the ion. The ten water cluster OXW_{10} (figure 9e) shows a similar structure to OXW_8 as it forms two clusters containing tetramer of water molecules. The two tetramers are connected to each other through H-bonds and the remaining two molecules are also making H-bonds to them. It can be seen from the figure that one tetramer has occupied the space such that it is able to interact with methylene hydrogen and the second tetramer is farther as it is close to the ethyl group and got repelled due to the hydrophobic nature of ethyl groups and the rest two are surrounding the ion and hence are relatively closer to the oxonium ion.

These structures reveal that in gas phase the orientation of water molecules around oxonium ion can have two tendencies to form the solvation shell; either they can form a linear chain or can have the cyclic tetramer structure in the shell. It depends upon the position and orientation of water molecules as well as the nature of alkyl groups attached to the oxygen atom. As hydrophobic ethyl groups repel the water molecules and the farther water molecules get arranged in cyclic tetramer structure through H-bonds stabilizing themselves instead of interacting with the oxonium ion.

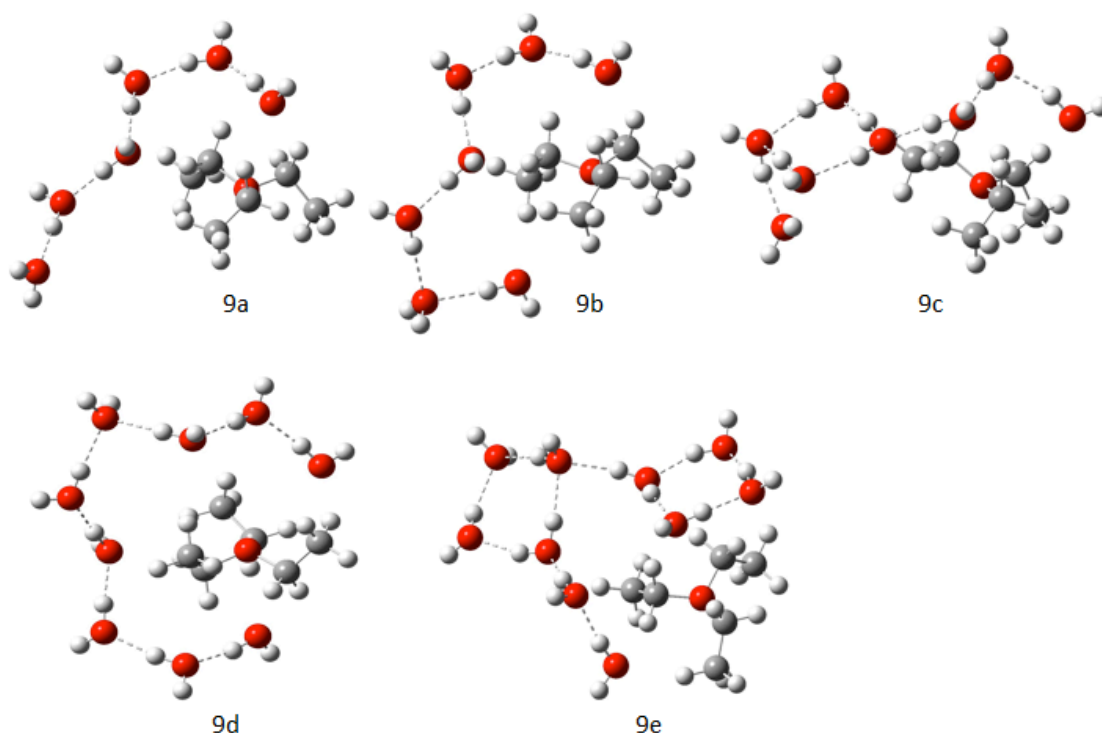


Figure 9. Structures of OXW_n ($n = 6$ to 10).

2.5 Oxonium ion in the vicinity of water molecules with protonic defects

Oxonium ion is surrounded with water molecules putting one hydroxide ion and one hydronium ion in the chain to study the interaction of oxonium ion in basic and acidic medium respectively. In neutral environment water molecules forms a chain around oxonium ion. In the presence of hydroxide ion, all the water molecules surround the ion and hydroxide ion is closest to oxonium oxygen, which is because the oxonium ion, being positively charged, will attract the negatively charged hydroxide ion. When we optimized the structure putting a hydronium ion along with neutral water molecules, water molecules along with hydronium ion showed a repulsion from oxonium ion which is expected according to the rule that like charges repel and opposite charges attract. It indicates that as compared to neutral medium, acidic environment is less stabilizing for the oxonium ion. On the other hand, basic environment stabilize the ion more than the neutral water molecules.

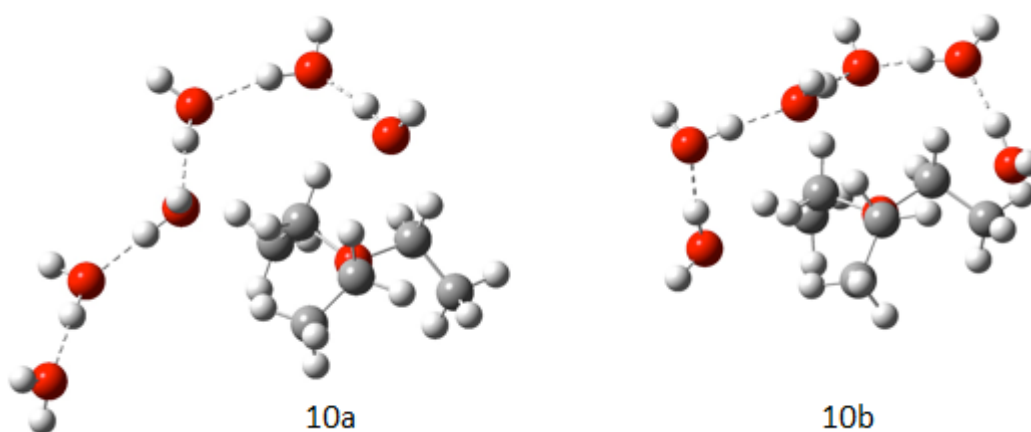


Figure 10. Orientation of water molecules in neutral conditions (10a) and in presence of one hydroxide ion (10b)

3 Ionic Liquid-Water System

In this chapter we have studied the interactions of N-methylacetamide with different cationic and anionic species to check whether these interaction can stabilize those ions. We also studied these clusters after including one water molecule to know the effect of water molecule on the interaction.

3.1 NMA-Cation Interactions

We have a number of alkyl ammonium ions and carboxylates substituted with different alkyl and hydroxyl substituted alkyl groups. We have mentioned the alkyl ammonium ions as cations, which are shown in figure 11, and the carboxylate ions as anions, which are shown in figure 12.

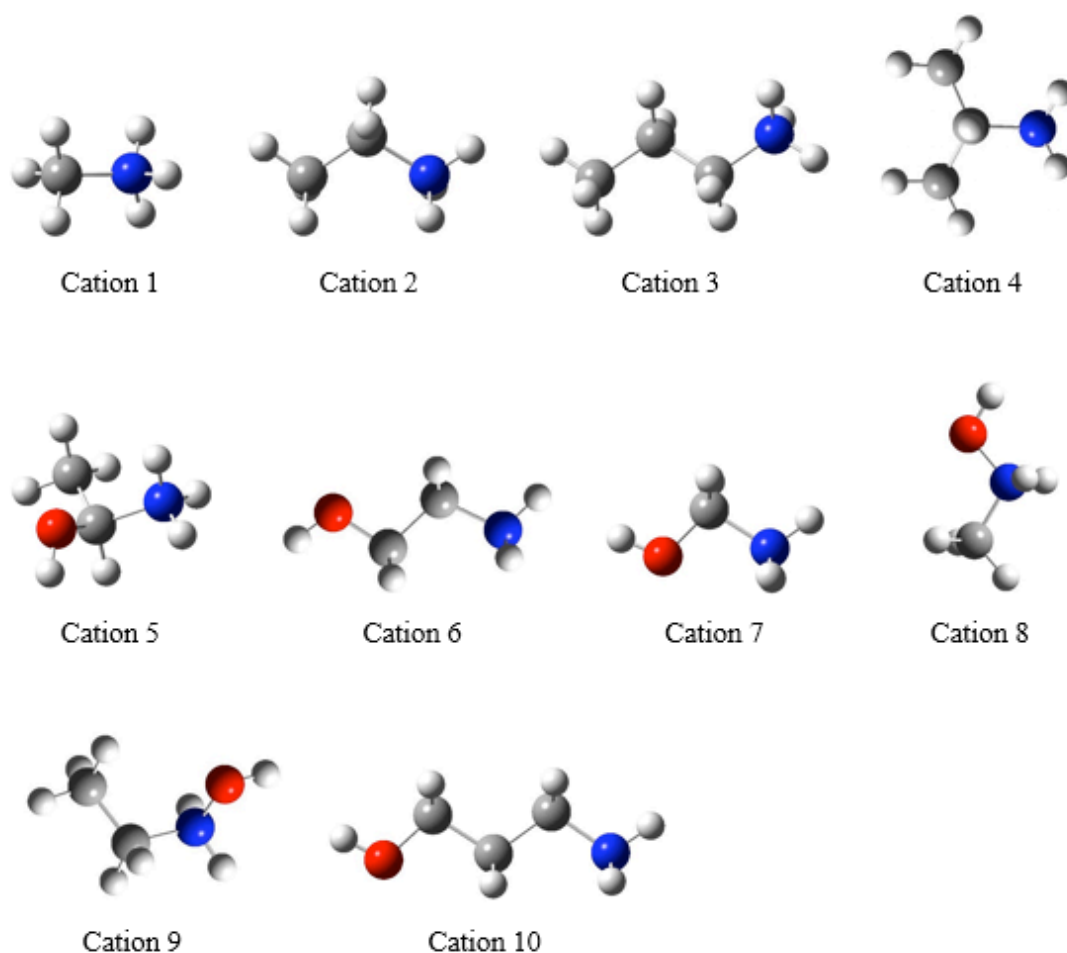


Figure 11. Structure of Cations; Colour codes are red, grey, blue and light grey for Oxygen, Carbon, Nitrogen and Hydrogen respectively (the same coding follows).

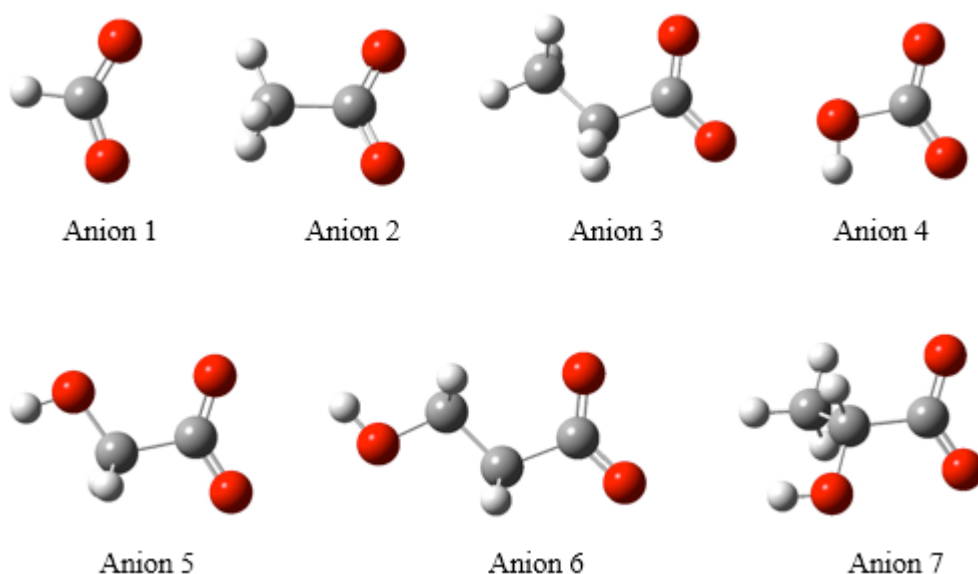


Figure 12. Structure of Anions

These cations contain positively charged tetravalent nitrogen atom attached to at least one hydrogen, because of which they can act as hydrogen bond donor (HBD) and interact with N-methylacetamide (NMA) via H-bonding where NMA can act as hydrogen bond acceptor (HBA) through the carbonyl oxygen. Thus this interaction is accepting-donating interaction. The optimized geometries of NMA and that of interacted clusters are shown in figure 13 and the interaction energy and hydrogen bond distance for the concerned interactions are tabulated in table 2. Cations of the form $R-NH_3^+$ interact differently with NMA on account of R. The first four cations having R as methyl, ethyl, n-propyl and isopropyl show regular decrease in interaction energy. Cation 1 having R as methyl group is stabilized by an amount of $31.250 \text{ kcalmol}^{-1}$ when it interacts with NMA. This stabilization energy decreases when R is changed to ethyl group for the case of cation 2. This can be explained on the basis that the R group with electron donating capacity, if connected to NH_3^+ , will stabilize the cation by donating electrons to positively charged nitrogen due to which interaction with NMA is minimized, hence less I.E. is observed.

This is also supported by the values of interaction energy for Cation 3 and Cation 4 as the value decreased to 29.116 and $28.238 \text{ kcalmol}^{-1}$ respectively. Cation 3 with R as n-propyl stabilizes the cation more effectively than ethyl and methyl group and hence Cat 3- NMA interactions is expected be lesser. Isopropyl group in Cation 4 is more electron donating than n-propyl group therefore stabilizes the cation more which will make the cat 4- NMA interaction least of the four.

The hydroxyl substitution on alkyl part of the cation destabilizes the cation because of $-I$ effect of hydroxyl group, which results in greater cation- NMA interactions. Cation 5 and cation 6 has $-OH$ group on ethyl part at 1, 2- position respectively and their interaction energy is greater than that for cation 2, which has ethyl group as R. The same trend is observed for the case of cation 7 as it has hydroxyl substitution on methyl group. It interact more with NMA than cation 1, which have methyl group as alkyl part. Following the same line the hydroxyl substitution on propyl group (cation 10) causes more interaction with the amide when compared to Cat 3-NMA interactions.

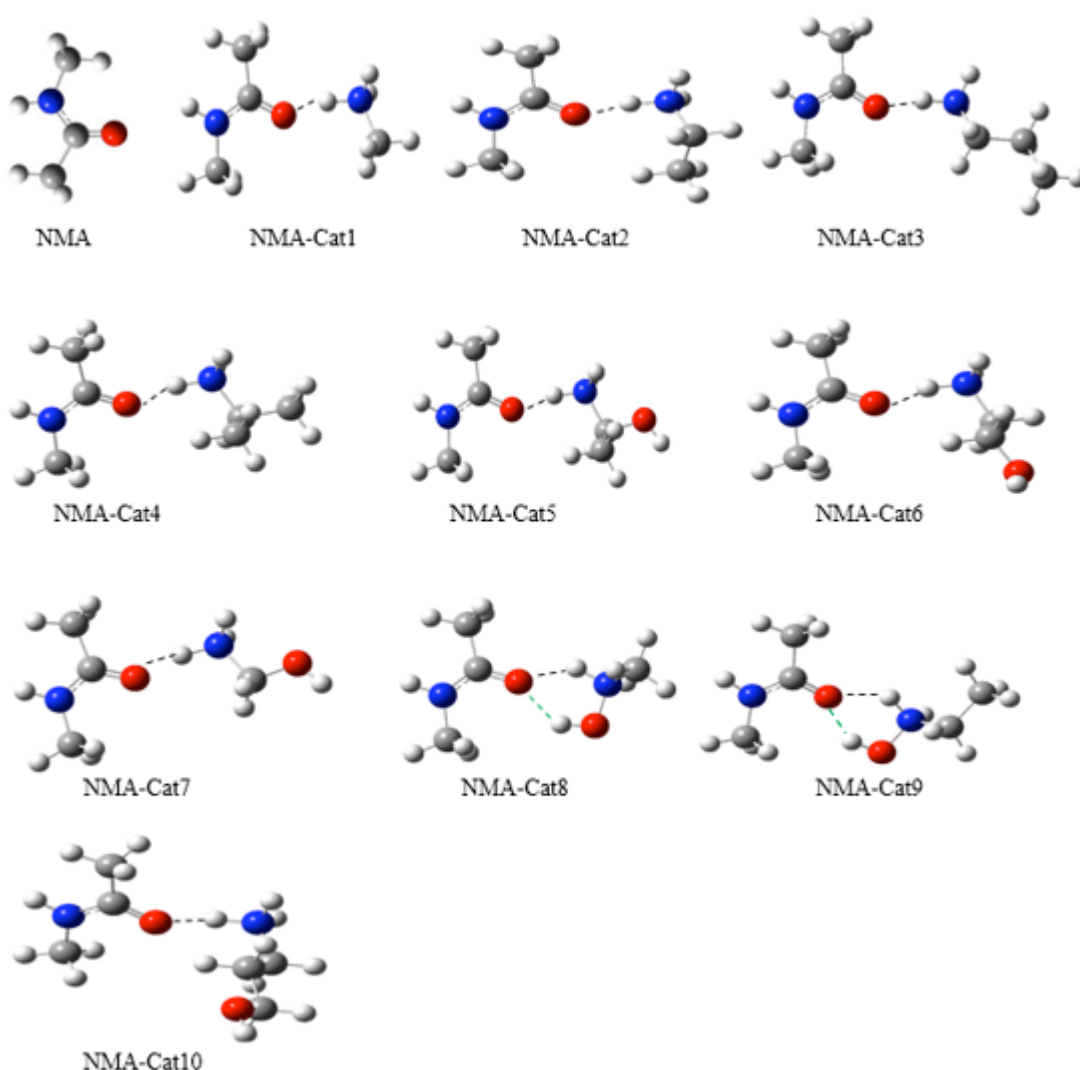


Figure 13. Structures of NMA and NMA-Cation interacted clusters optimized at B3LYP/6-311+G(2d,p) level.

There are two cases in which hydroxyl group is attached to nitrogen atom itself as can be seen for the cases of cation 8 and cation 9. The hydroxyl substitution on nitrogen

destabilizes the cation more than the hydroxyl substitution on alkyl part and therefore these cations are more susceptible to interact with NMA. The -OH substitution on nitrogen not only destabilizes the cation but also provides the possibility for the second hydrogen bond between the carbonyl oxygen of NMA and hydrogen of the hydroxyl group which is indicated in the figure 1 by green dotted bonds for cation 8 and cation 9. These two effects result in the higher values for Cat 8-NMA and cat 9-NMA interactions.

Table 2: Interaction Energy values and hydrogen bond distance for Cation-NMA clusters.

NMA-Cation cluster (fig. 13)	Interaction Energy (kcalmol ⁻¹)	H-bond distance (Å)
1	-31.2	1.52
2	-29.4	1.55
3	-29.1	1.55
4	-28.2	1.57
5	-29.5	1.54
6	-30.3	1.54
7	-31.7	1.51
8	-35.6	1.74
9	-34.3	1.83
10	-29.3	1.55

3.2 NMA-Anion Interactions

The carboxylates contain negatively charged oxygen atom which can act as HBA while NMA can act as HBD through the NH proton. The optimized structures of the interacted product of different anions with NMA are shown in figure 14, and the interaction energy for the clusters and the corresponding hydrogen bond distance are tabulated in table 3. The Carboxylate ions being electron rich species can interact with the proton-donating site of NMA. The higher the electron density on O-atom, the more it will interact with amide. Anion 1, anion 2 and anion 3 have hydrogen, methyl and ethyl group respectively connected to COO⁻. Formate ion (anion 1) interacts with

NMA via H-bond between its carbonyl oxygen and the NH hydrogen of the amide and the interacted product gets stabilized by $24.2 \text{ kcalmol}^{-1}$. The ethanoate ion (anion 2) is more reactive because the methyl group attached to COO^- will enhance the electron density on carbonyl oxygen so it will interact more with NMA which is supported by the larger value ($24.7 \text{ kcalmol}^{-1}$) of I.E. for anion 2. Anion 3 interacts less with NMA, which may be due to the steric effect of the longer alkyl chain.

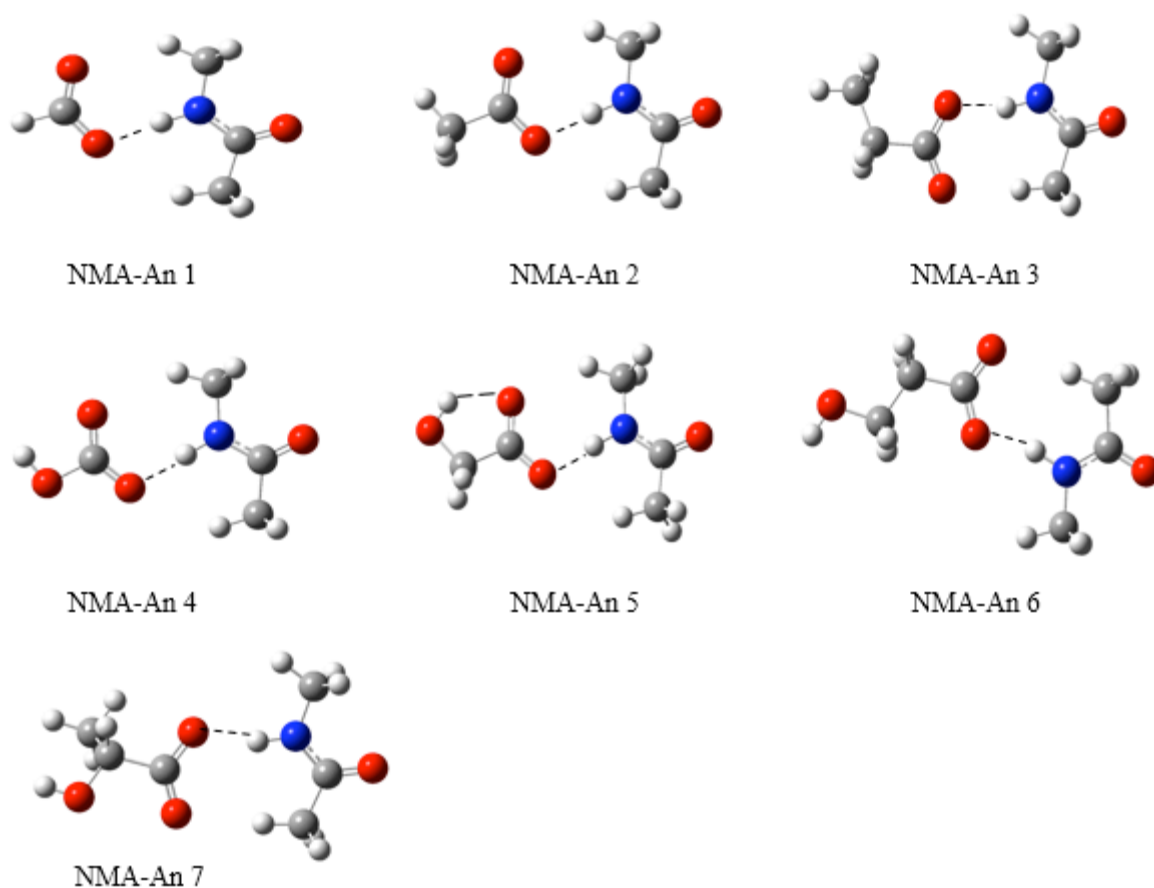


Figure 14. Optimized structures of NMA- Anion Interacted clusters.

The anions 4, 5, 6 and 7 with hydroxyl substitution on alkyl part will be stabilized than the parent ions because the hydroxyl group being electron withdrawing reduces the electron density from the carbonyl oxygen. As a result of which these anions will interact less than the anions having the same alkyl group without hydroxyl substitution. We found that I.E. for anion 4, anion 6 and anion 7 reflects the trend. Anion 1 when substituted with hydroxyl group becomes anion 4 and it has I.E. of lesser value ($22.7 \text{ kcalmol}^{-1}$) than that of anion 1. Anions 6 and 7 are hydroxyl derivatives of anion 3 and show lesser interaction with NMA than anion 3. Anion 5 interact more with NMA in comparison to other anions. This much higher interaction

energy for anion 5 can be attributed to the extra intra-molecular H-bond (1.89 Å) formed in the carboxylate ion, which is shown in the structure of NMA-An5 (figure 14) in addition to the intermolecular hydrogen bond between the anion and amide.

Table 3: Interaction Energy values and hydrogen bond distance for NMA-Anion clusters.

NMA-Anion cluster (fig. 14)	Interaction Energy (kcalmol ⁻¹)	H-bond distance (Å)
1	-24.2	1.75
2	-24.7	1.74
3	-23.6	1.76
4	-22.7	1.77
5	-36.3	1.78
6	-22.8	1.77
7	-23.0	1.76

3.3 Comparison of interactions of cis- and trans-NMA with cation and anion

Figure 15 shows the interaction of cis- NMA with cation 1 and anion 1. The structure 15a is cis-NMA and 15b and 15c show its interacted cluster with cation 1 and anion 1 respectively. The I.E. of cation 1 with cis- NMA (-32.191 kcalmol⁻¹) is found to be greater than that with trans- NMA (-31.250 kcalmol⁻¹). On the contrary anion 1 interacts less with cis- NMA corresponding to the value of 19.641 kcalmol⁻¹ whereas the I.E. of anion 1 with trans form is -24.159 kcalmol⁻¹.

The more interaction of cation 1 with cis-NMA than the trans one can be explained on the basis that cis form is less stable, so when it forms H-bond with the cation it gets more stabilized than that of trans form. The reverse case is observed with the anion as it interacts more with trans NMA than cis-NMA. It can be due to the steric repulsion of the cis form to the carboxylate ion, which is reflected in the longer H- bond length (1.83 Å) than that for trans NMA (1.75 Å). The cation interact more with NMA than the anion as suggested by the energy values and it is well supported by the lengths of H-bond formed by cation 1 with cis- NMA and trans- NMA are of lengths 1.53 and 1.52 Å respectively while anion form longer H-bonds.

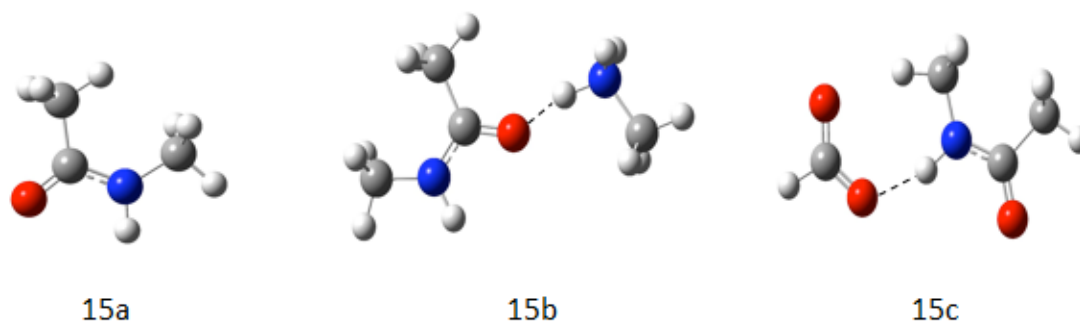


Figure 15. Structure of cis- NMA and its interacted cluster with cation 1 and anion 1.

3.4 Exploring the cations and anions for their proton transfer behaviour with NMA in presence of water

The proton transfer from cation to anion takes place when they are in close proximity resulting in neutral amine and carboxylic acid and they are connected via H- bond. We found that proton transfer from cation to anion takes place when the anion is HCOO^- and the cation is Me-NH_3^+ , Et-NH_3^+ , Pr-NH_3^+ and i-Pr-NH_3^+ as shown in figures 16a, 16b, 16c and 16d respectively. When cation 1 interacted with carboxyl oxygen of NMA and anion 1 with amide proton, two proton transfers took place; one from the cation to NMA and second from NMA to carboxylate ion resulting in neutral amine, hydroxyl substituted imine and carboxylic acid which interacted via hydrogen bonds (figure 16e).

While exploring the interaction of NMA with water first as HBA and then as HBD (as shown in 16f and 16g) we found that NMA act as good HBA but poor HBD which is supported by the hydrogen bond length of 1.87 and 2.07 Å respectively for 16f and 16g. The more I.E. value for 16f ($-7.2 \text{ kcalmol}^{-1}$) than that for 16g ($-4.1 \text{ kcalmol}^{-1}$) also reflect that carbonyl oxygen of NMA is more effective in hydrogen bond interactions.

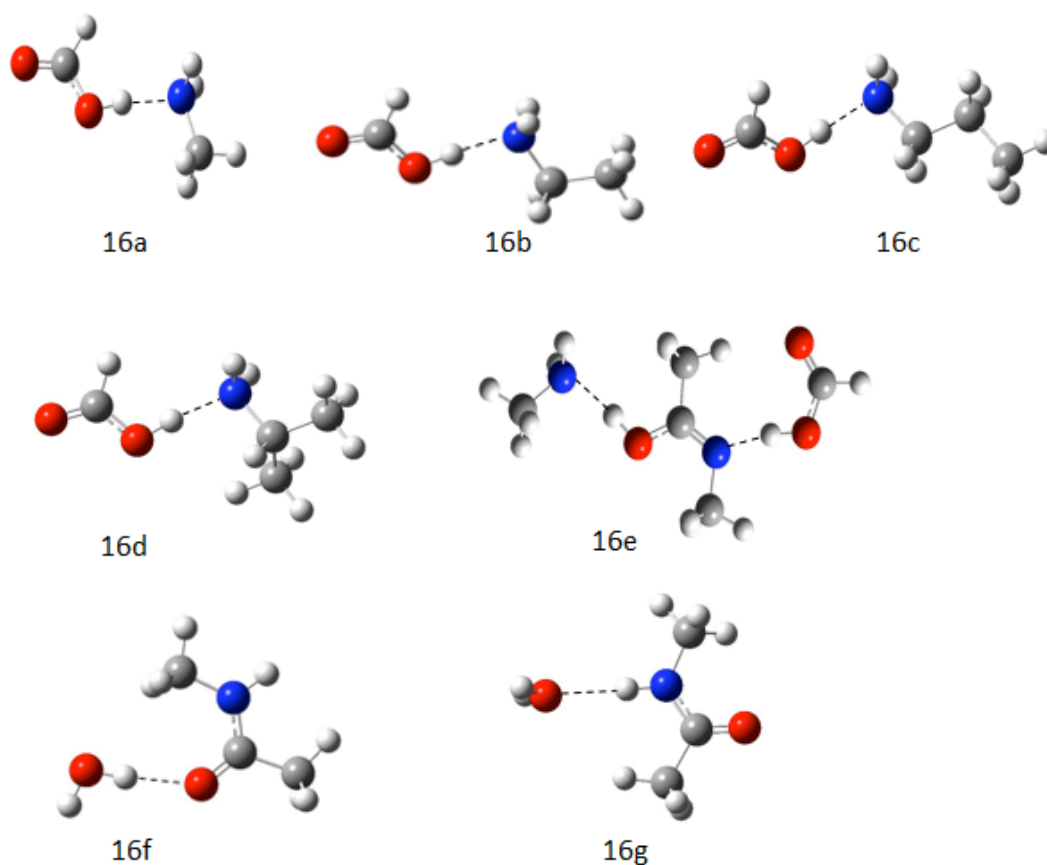


Figure 16. Structure of clusters showing different interactions.

When cations are interacted with carbonyl oxygen of NMA and, water molecule with amine proton of NMA the cluster was found to be not stable for the case of cation 1, 2, 3 and 9. However cation 4, which is isopropyl ammonium ion, when interacted with NMA in the presence of water (figure 17a) is found to be stable. This observation can be explained on the basis that isopropyl ammonium ion is more stable than methyl, ethyl and n-propyl substituted ammonium ion, which makes the cluster stable. Cations 5 and 8 also make stable cluster while interacting with NMA in presence of water as shown in figure 17b and 17e respectively. These cations don't transfer proton as carbonyl oxygen is involved in two hydrogen bond interactions and cannot accept a proton from the cation. Cations 6, 7, and 10 also show the interaction with NMA in the presence of water and don't transfer protons to NMA. These clusters are shown in figure 17c, 17d and 17f respectively.

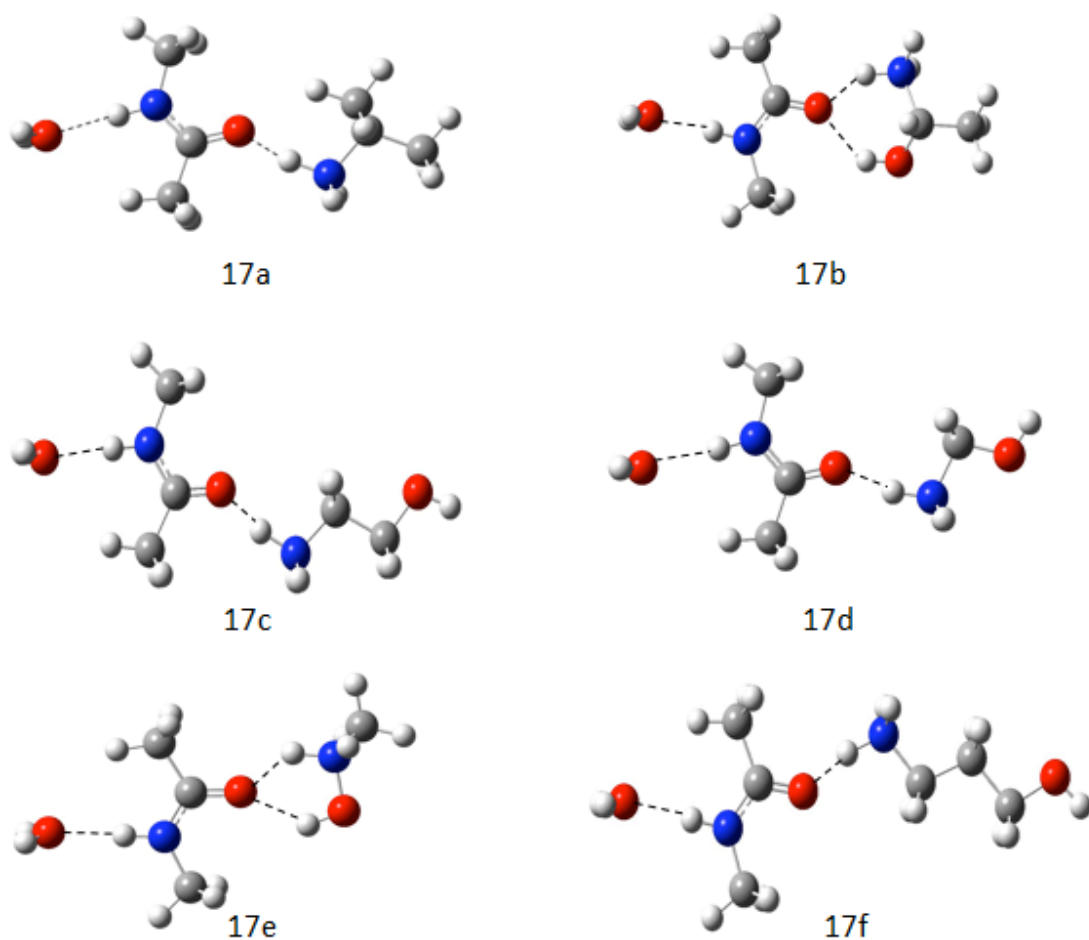


Figure 17. Optimized geometries of cation- NMA- water interacted clusters.

The interaction energy values of the cations with NMA in the presence of water are listed in table 4.

Table 4: Interaction energy values and hydrogen bond distance for Cation-NMA in Cation-NMA-Water clusters.

Cation-NMA-Water Cluster (fig. 17)	Interaction Energy in the presence of water molecule (kcalmol^{-1})	H-bond Distance (\AA)
17a	-32.4	1.53
17b	-35.0	1.66
17c	-35.3	1.47
17d	-36.7	1.45
17e	-40.0	1.66
17f	-34.6	1.50

Figure 18a shows that the proton transfer does not take place when anion 1 interacts with amine proton of NMA while water interacts with carbonyl oxygen of NMA. Two hydrogen bonds are operating in the cluster and the bond between NMA and anion is 1.71Å while the other one is 1.81Å showing that anion interacts strongly with NMA than that of water. As anion 1 is stabilized in the presence of water interacting with NMA, the same effect is observed with anion 2 (figure 18b) and anion 3 (figure 18c). These anions show the same hydrogen bond interactions with NMA in presence of water. We found that anions bearing hydroxyl group like anion 4, anion 5, anion 6 and anion 7 are also stabilized with NMA in the presence of water as proton transfer does not take place. These clusters are shown in figures 18d, 18e, 18f and 18g respectively.

Table 5: Interaction energy values and hydrogen bond distance for Anion-NMA in Anion-NMA-Water clusters.

Anion-NMA-Water cluster (fig. 18)	Interaction Energy in the presence of water molecule (kcalmol ⁻¹)	H-bond distance (Å)
18a	-27.4	1.71
18b	-28.6	1.69
18c	-26.4	1.70
18d	-25.0	1.72
18e	-26.8	1.72
18f	-26.7	1.71
18g	-26.0	1.72

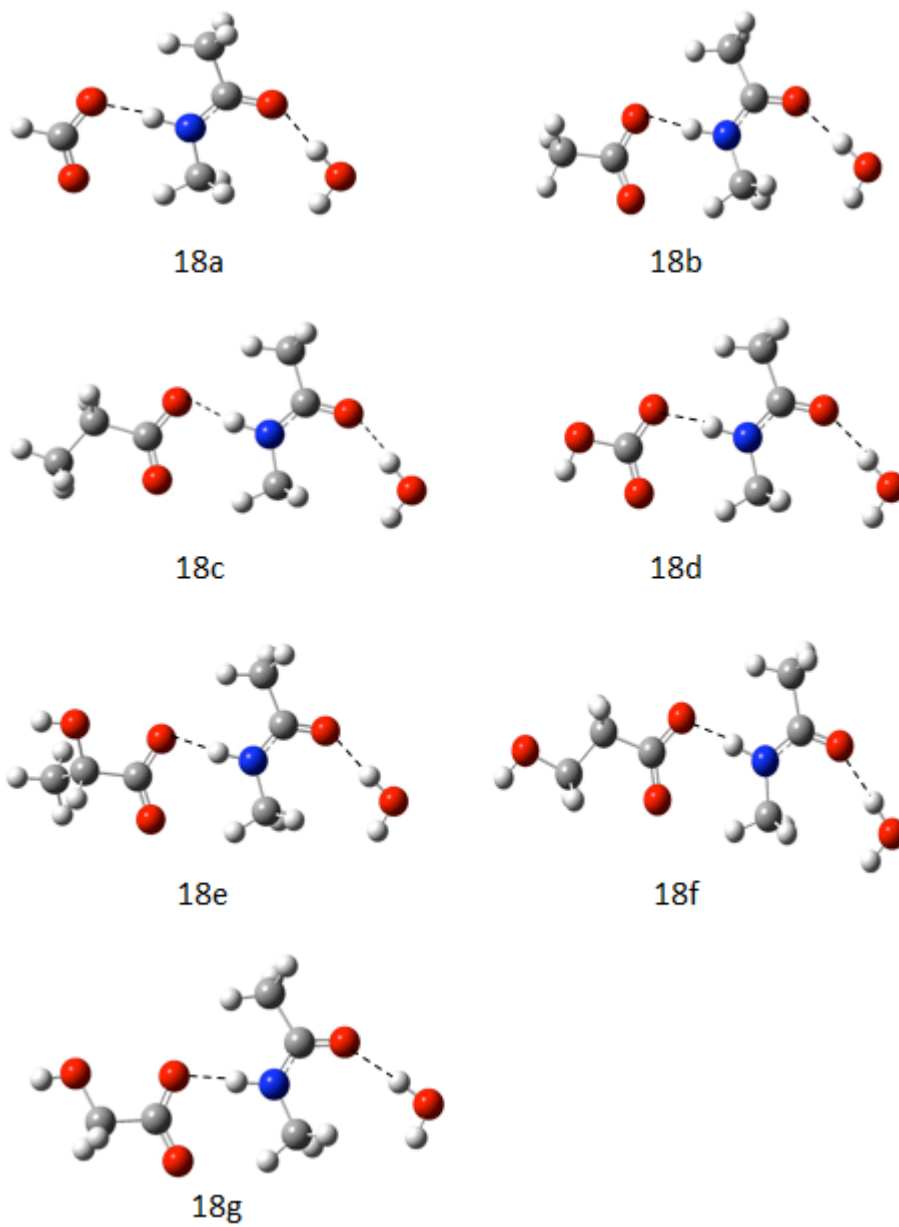


Figure 18. Optimized geometries of anion- NMA- water interacted clusters.

4 CONCLUSION

From our studies it is concluded that Oxonium ion-water clusters are stabilized as a cooperative effect of hydrogen bond interactions and hydrophobic interactions. When compared with carbocation, oxonium ion is found to be slightly more hydrophobic. We also conclude that basic medium is more stabilizing than neutral water molecules for the oxonium ion-water cluster whereas acidic medium destabilizes the cluster. We also noted one interesting activity of water molecules to form a solvation shell around the ion either in the form of linear chain or forming cyclic tetramer of water molecules in the chain. The finding that, oxonium ion can be stabilized in these clusters due to H-bond interactions, can be employed further if needed.

From the ionic liquid-water part, we conclude that NMA acts as better HBA as it interacts more with protonated amines than carboxylates. This means that carbonyl oxygen is more effective in hydrogen bond interactions and this is also supported by the interaction energy values of NMA-water interactions. The interaction energy is found to be greater when NMA acts as HBA and water as HBD. The stabilization of all the anions with NMA in the presence of water also supports the idea because anions interact via amine proton of NMA and proton transfer does not take place but some of the cations undergo proton transfer to give neutral amine molecules as they interact via carbonyl oxygen of the amide. The interaction of different cations and anions with NMA depends upon their chain length and substitution. Cations with longer alkyl chain length interact less while anions with longer alkyl chain length do not show any appreciable change in the interaction energy values. The presence of electron withdrawing group, like $-OH$, stabilizes the cation-NMA cluster while it destabilizes the anion-NMA cluster. The appropriate combination of cations and anions, which don't undergo proton transfer reactions while interacting with NMA in the presence of water, can serve as ionic media for NMA in aqueous solution. The properties of this model system can be further exploited in relevance to the aqueous proteins and long chain peptides for biological studies.

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