Substituent Effects on the Binding Energies of Benzyl Alcohol-H₂O Clusters: *Ab initio* Study[†]

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Computations are presented for the ortho- and para-substituted benzyl alcohol-H₂O clusters. A variety of conformers are predicted, and their relative energies are compared. Binding energies of the clusters are computed, and detailed analysis is presented on the effects of substitution on the strength of the hydrogen bond in the clusters. F- and NH₂- substituted clusters are studied to analyze the effects of electron-withdrawing and electron-pushing groups. In para-substituted clusters, the inductive effects are dominant, affecting the binding energies in opposite way depending on whether the hydroxyl group is proton-donating or -accepting. For ortho-substituted clusters, more direct involvement of the substituting group and the resulting geometry change of the hydrogen bond should be invoked to elucidate complicated pattern of the binding energy of the clusters.

Keywords : Substituent effect, Binding energies.

Introduction

Clusters have been given a lot of attention as intermediary structures lying between the isolated molecules and the fully solvated molecules in solution phase. Many solvent molecules may interact with the solute in solution phase, and the properties of the solute molecule in solution would depend on the configuration of the solvents around it in very complicated fashion. One approach to treat this situation is to employ the approximations based on polarizable continuum model,[1,2] in which the solvent is considered as continuum parametrized by bulk property such as the dielectric constant. Alternatively, the solution phase may be approximated as clusters,[3-17] when only a small number of solvents molecules affect the properties of solute. When a specific functional group of the solute interacts with solvent molecules, the cluster model may serve as good model system of the solution, since the interactions with the solvent molecules in the immediate vicinity of the functional group would largely determine the properties of the solution, while other solvent molecules may safely be considered as "spectators".

The interactions between the hydroxyl group of the organic alcohol and the water molecules in aqueous solution are such case, where the cluster model may be very useful to understand the effects of solvent configurations. Specifically, the binding energies of organic alcohol - water clusters can be very useful guide to elucidate the local arrangement of solvent molecules around the solute in solution phase, and to understand the differential interactions (*i.e.*, hydrogen bonding),[18,19] between a variety of functional groups in the organic alcohol with the water molecules. Combined with the experimental studies based on the infrared (IR) spectroscopy and the supersonic beam technique, computational study of the structures and binding energies of organic alcohol-

water clusters can help reveal valuable information for the configuration of solvent molecules around the solute. Thus, the binding energies of these interesting clusters, when properly computed, can yield direct meaning of the solvent-solute interactions measured, for example, by the chromatographic method[20-23] on molecular scale. Particularly interesting is the role of the differences in the structures of the functional groups in yielding differential hydrogen bonding with the water molecules. For example, in the analysis of the hydrogen bonding in phenol-(H₂O)ₙ and benzyl alcohol-(H₂O)ₙ (n = 1-4) clusters and the corresponding clusters with the methanol molecules, we showed[24] that the differences in the binding energies of these clusters may largely be explained by the differences in the acidity and the hydrogen bonding basicity of the organic alcohols and the "solvent" molecules in the system. This suggests that the electrostatic effects of the functional groups and the water and the methanol molecules are primarily important in determining the interactions. Other effects (such as streric) are considered to play minor role in these systems. However, they may affect the strengths of the hydrogen bonding to a larger degree in other clusters.

In the present study, we investigate the effects of different type of interactions (inductive, steric, intramolecular hydrogen bonding, etc.) on the binding energies of the benzyl alcohol derivative-H₂O clusters by studying the effects of the substitution by functional groups (-F, and -NH₂) at ortho or para positions. In the para-subsituted clusters, for which the effects may be safely considered as mostly inductive, the influence of the substituted functional groups depends on whether the hydroxyl group is proton-donating or accepting: the binding energy of the cluster increases (decreases) by the electron-withdrawing substituent when the OH group is proton-donating (-accepting), and the reverse is true for the elecron-pushing substituents. For ortho substitution, however, the presence of the substituents may significantly alter the local structures of the OH-water interactions, and the effects

of the intramolecular hydrogen bonding and the steric factors may also affect the strengths of the hydrogen bonding in very complicated fashion.

Computational Methods

In this study all the calculations were carried out using the GAUSSIAN 98W set of programs.[25] Bond lengths and angles are computed along with the zero-point energies by employing the HF/6-31+G** basis set. Since we are mostly interested in the difference between the binding energies of the unsubstituted and the substituted benzyl alcohol-water clusters to elucidate the role of substituting group, we employ fairly simple theoretical model (HF/6-31+G**) in the present work. The results presented below indicate that this model could elucidate the role of electron-withdrawing and electron-pushing substituents on the hydrogen bonding in various types of the substituted benzyl alcohol-water clusters in a systematic way. The stationary conformers are obtained by verifying that all the harmonic frequencies be real. The binding energies are computed as the difference between the energy of the clusters and the sum of the energies of the separated fragments, corrected for zero-point energies.

Results

We first compute the binding energies of the unsubstituted benzyl alcohol-water clusters to compare with those of the substituted benzyl alcohol-water clusters. The structures and the binding energies are given in Figure 1 and Table 1, respectively. We find two stationary structures for the benzyl alcohol-water clusters. In the conformer B1, the alcoholic OH group acts as proton donor to the water molecule, while it accepts proton in the second conformer B2. The binding energies of B1 and B2 are 3.67 and 3.17 kcal/mol, respectively. The orientation of the binding water molecule in B1 and B2 are different: In B1, the water molecule lies above
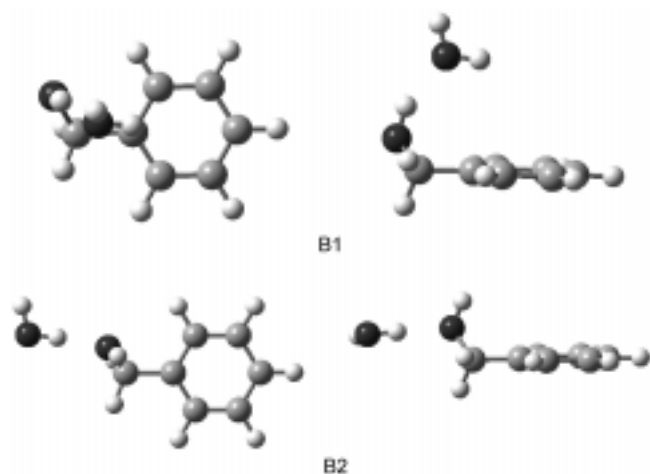

Figure 1. Computed structures of benzyl alcohol-H_2O clusters (B1 and B2).

Table 1. Computed energies, zero point energies (ZPE) and binding energies (BE) of the clusters

	Energy (Hartree)	ZPE (kcal/mol)	BE (kcal/mol)	Role of phenolic OH group
H_2O	-76.03123	14.51		
Benzyl alcohol	-344.61723	89.66		
Benzyl alcohol-H_2O				
(B1)	-420.65694	105.82	3.67	Proton-donating
(B2)	-420.65627	105.89	3.17	Proton-accepting
p-fluorobenzyl-alcohol	-443.47067	84.28		
p-fluorobenzyl-alcohol-H_2O				
(p-FB1)	-519.51043	100.36	3.78	Proton-donating
(p-FB2)	-519.50949	100.52	3.03	Proton-accepting
p-aminobenzyl-alcohol	-399.65334	100.51		
p-aminobenzyl-alcohol-H_2O				
(p-AB1)	-475.69286	117.10	3.45	Proton-donating
(p-AB2)	-475.69283	117.08	3.45	Proton-accepting
o-fluorobenzyl-alcohol	-443.47076	84.44		
o-fluorobenzyl-alcohol-H_2O				
(o-FB11)	-519.51055	100.28	4.04	Proton-donating
(o-FB12)	-519.51030	100.74	3.42	Proton-donating
(o-FB13)	-519.51030	100.63	3.41	Proton-accepting
(o-FB14)	-519.51010	100.55	2.83	Proton-accepting

and almost in perpendicular position relative to the phenyl ring, while it orients parallel to the phenyl ring in B2. The effects of the substituents on the weak interactions in the aromatic alcohol-water clusters may be quite complicated to analyze. First, the substituting group may influence the hydrogen bonding between the hydroxyl and the water molecule through the phenyl ring by inductive effects. In this case, the electron-withdrawing or electron-donating tendency of the substituting group would be the critical factor to affect the strengths of the hydrogen bonds. For para-substituted benzyl alcohol, this effect will be most important, because the substituting group is rather isolated from the hydrogen bond. For ortho-substituted benzyl alcohol, on the other hand, the substituting group is very close to the hydrogen bond between the hydroxyl and the water molecule, and thus may directly interact either with the hydroxyl group or the water molecule. In some instances, it is expected that the substituting group may alter the local structures of the clusters near the hydrogen bond so that they are completely different from those of the phenol-water cluster. Therefore, we first compute the structures and the binding energies of the conformers of para-substituted benzyl alcohol to isolate the inductive effects of the substituting group through the phenyl ring. We investigate the effects of substitution by -F and -NH_2 group at the para position as typical example of electron-withdrawing and electron-donating group, respectively.

The computed structures and the energies of the p-fluoro-benzyl alcohol-H_2O clusters are given in Figure 2 and Table 1. We obtain two isomers (p-FB1 and p-FB2), of which p-FB1 is of lower energy. In this isomer, the hydroxyl group is proton-donor to the water molecule, while in p-FB2, it acts as proton-acceptor. Since the fluorine is at para-position, a direct interaction between hydroxyl and fluorine is extremely unlikely. This indicates that the difference in the binding energy related to that of benzyl alcohol-H_2O clusters signifies the inductive effects of fluorine. It is also worth noting that their local structures of p-FB1 and p-FB2 are quite similar to those of the corresponding benzyl alcohol-H_2O clusters, B1 and B2, shown in Figure 1. The computed binding energies for of p-FB1 and p-FB2 are 3.78 and 3.03 kcal/mole, respectively. This finding suggests that the substitution by fluorine atom at the para position affects the binding energy of the cluster in opposite fashion, depending on weather the hydroxyl group is proton-donating or proton-accepting, since the binding energy of the p-fluorobenzyl alcohol-H_2O cluster p-FB1 is larger than that (3.67 kcal/mole) of the benzyl alcohol-H_2O cluster B1, while the binding energy of p-FB2 is smaller than that (3.17 kcal/mole) of B2. This interesting behavior of the binding energy can be understood by considering that the electron-withdrawing effect of the fluorine at the para-position tends to reduce the partial negative charge of the oxygen atom and to increase the partial positive charge of the hydrogen atom of the hydroxyl group. As the result, the acidity of the hydrogen atom increases and the hydrogen bonding basicity of the oxygen atom of the hydroxyl group decreases. Thus, when the hydroxyl group acts as proton-donor (acid) as in the p-FB1 cluster, the hydrogen bonding is strengthened by the fluorine atom at the para-position, while the reverse is true for p-FB2, in which the hydroxyl group is proton-accepting.

By the same reasoning, the substitution by an electron-*donating* group at the para position would decrease (increase) the bonding energy of the clusters containing the proton-donating (accepting) hydroxyl group. In order to confirm this prediction, we also compute the binding energies of the p-aminobenzyl alcohol-H_2O clusters, in which
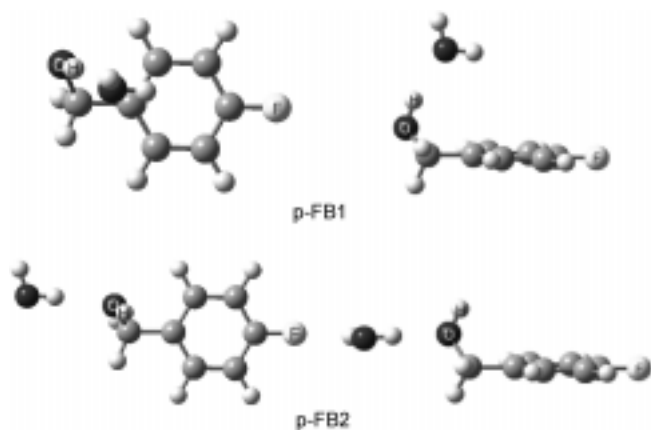

Figure 2. Computed structures of p-fluorobenzyl alcohol-H_2O clusters (p-FB1 and p-FB2).
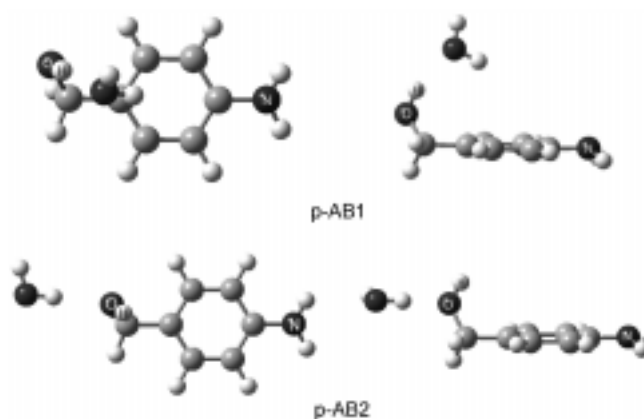

Figure 3. Computed structures of p-aminobenzyl alcohol-H_2O clusters (p-AB1 and p-AB2).

the amino group acts as *electron-donating* substituent. If the change in the binding energy of the p-fluorobenzyl alcohol-water cluster from that of the corresponding fluorobenzyl alcohol-water cluster is indeed due to the inductive effects of the *electron-withdrawing* -F group, then the substitution by -NH_2 at the para position would give changes in the binding energy in exactly the reverse way. Two isomers of the p-aminobenzyl alcohol-H_2O clusters are found (Figure 3). One isomer (p-AB1) is the structure in which the hydroxyl is a proton-donor, while for the other (p-AB2) it is proton-accepting. According to the analysis given above, the binding energy of the cluster would decrease when the hydroxyl acts as proton-donor, and increase when it acts as proton-acceptor. The computed binding energies of p-AB1 and p-AB2 are very similar to each other, being about 3.45, as given in Table 1. As expected, the binding energy of p-AB1 (p-AB2) is smaller (larger) than the corresponding benzyl alcohol-H_2O cluster B1 (B2).

The structures of o-fluorobenzyl alcohol are shown in Figure 4. It can be seen that the structures of o-fluorobenzyl alcohol are rather different from those of p-fluorobenzyl alcohol. In the ortho-substituted isomers, the fluorine atom can directly participate in hydrogen bonding with the hydroxyl group. One isomer (o-FB1) contains intramolecular interactions, while the other (o-FB2) does not. The energies of the two isomers are very similar, the difference being only 0.006 kcal/mole. In order to analyze the binding energies of the ortho-substituted benzyl alcohol-water clusters, the dihedral angle of the carbon-carbon bond connecting the phenyl ring and the -CH_2OH group should be taken into consideration, since the carbon-carbon bond may rotate to form more favorable hydrogen bond. This dihedral angle may depend sensitively on the environment around the functional groups in the molecule. In the bare benzyl alcohol, for example, the dihedral angle is 43.5°, while those of the two isomers of o-fluorobenzyl alcohol are 115.2° (o-FB1) and 21.9° (o-FB2). It indicates that the C-C bond in o-FB1 rotates to form intramolecular hydrogen bond between the fluorine atom and the hydroxyl group. In other words, the increase in energy by forming hydrogen bond overwhelms
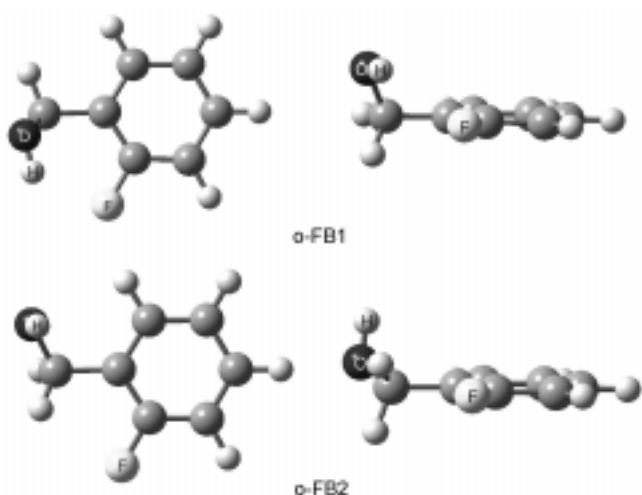
Figure 6. Computed structures of o-fluorobenzyl alcohol-H$_2$O clusters (o-FB13, o-FB14). Proton-accepting OH group.

Figure 4. Computed structures of o-fluorobenzyl alcohol (o-FB1, o-FB2).

the decrease in energy by the rotation of the carbon-carbon bond. The structures of the o-fluorobenzyl alcohol-H$_2$O clusters are shown in Figure 5 and Figure 6. Four structures are found. In the two structures given in Figure 5, o-FB11 and o-FB12, the hydroxyl groups act as proton-donor. In the others two isomers (o-FB13 and o-FB14), they are proton-accepting. The binding energies of o-FB11 and o-FB14, which are of lower energy of the two isomers given in Figure 5 and Figure 6, are 4.04 and 3.41 kcal/mole, respectively. In o-FB14 the OH group displays intramolecular interactions between the proton of the hydroxyl and fluorine atom, while in o-FB11 it does not. Since the binding energies of the o-fluorobenzyl alcohol-H$_2$O clusters can be affected by so many factors, such as the inductive effects, intramolecular hydrogen bond, π-interaction with benzene ring, and the rotation of the C-C bond, etc., it will be quite difficult to resolve the effects of each factor. If the structures
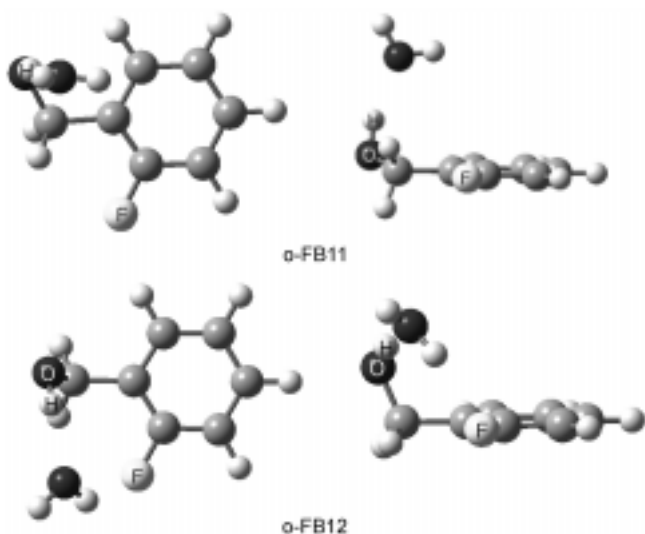
of the unsubtituted and the substituted benzyl alcohol-water clusters are quite similar to each other, it may be possible to assume that the other factors than the inductive effects be similar in both clusters, and it will be easier to analyze the inductive effects. Since the structure of o-FB11 is similar to that of B1, it would be quite useful to compare their binding energies. As given in Table 1, the binding energy of o-FB11 (4.04 kcal/mole) is larger than that (3.67 kcal/mole) of B1. Thus, the binding energy increases to some degree by substitution of fluorine at the ortho-position. On the other hand, the binding energy (2.83 kcal/mole) of o-FB13, whose structure is similar to that of B2, is smaller than that (3.17 kcal/mole) of B2. Since the hydroxyl group is proton-donor in the former case (o-FB11 and B1), while it is proton-accepting in the latter clusters (o-FB13 and B2), this observation is in line with the case of the para-substituted clusters discussed above. Some of the computed binding energies, however, are subtler to analyze. For example, the binding energy of o-FB14 is computed to be larger than that of B2. Since the various factors affecting the binding energy cannot be easily separated in this case, the difference in the binding energies of these two clusters are more difficult to elucidate. However, we can give at least some qualitative explanation for the observation. In the o-FB14 cluster, extended hydrogen bonding network is formed among the fluorine, the hydroxyl group, and water. These three moieties are arranged approximately linearly along the hydrogen bond in the same plane. This configuration may make the hydrogen bond between fluorine and the hydroxyl, and that between water and the hydroxyl rather strong, rendering the binding energy of o-FB14 a little larger than that of B2.

Conclusion

We find that the effects of substitution at the para-position are entirely inductive, and the analysis of the binding energies of the para-substituted benzyl alcohol-H$_2$O clusters is quite straightforward: When electron-withdrawing group is substituted at the para-position, the binding energy of the

Figure 5. Computed structures of o-fluorobenzyl alcohol-H$_2$O clusters (o-FB11, o-FB12). Proton-donating OH group.

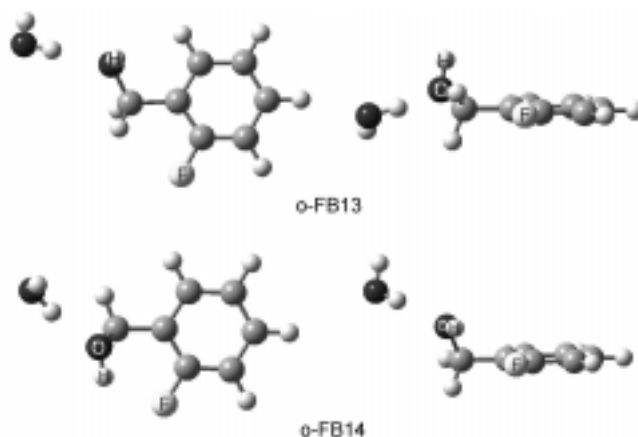cluster containing proton-donating (-accepting) hydroxyl group increases (decreases), while the reverse is true for electron-donating substituents. For the ortho-substitued clusters, the substituents may directly bond with the hydroxyl group or the water molecule, or induce considerable changes in the local structure near the hydrogen bond. Thus, in addition to the inductive effects, other factors such as intramolecular hydrogen bond, π-interaction with benzene ring, and the rotation of the C-C bond may also significantly affect the binding energies of the clusters. The role of the inductive effects may be elucidated only when the structures of the unsubstituted and the substituted clusters are similar. Experimental studies on these clusters will be highly intriguing and desirable.

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