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Cooperative Enhancement of Water Binding to Crownophane by Multiple Hydrogen Bonds: Analysis by High Level ab Initio Calculations

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Abstract: The intermolecular interaction energy of the model system of the water−crownophane complex was analyzed. The water molecule has four hydrogen bonds, with the two hydrogen-donating phenolic hydroxy groups and two hydrogen-accepting oxygen atoms of the poly-oxyethylene chain of the crownophane in the complex. The MP2/6-311G(2d,2p) level calculations of the model system of the complex (hydrogen donating unit + hydrogen accepting unit + water) indicate that the binding energy of the water is 21.85 kcal/mol and that the hydrogen bond cooperativity increases the binding energy as much as 3.67 kcal/mol. The calculated interaction energies depend on the basis set, while the basis set dependence of the cooperative increment is negligible. Most of the cooperative increment is covered by the HF level calculation, which suggests that the major source of the hydrogen bond cooperativity in this system has its origin in induction. The BLYP/6-311G** and PW91/6-311G** level interaction energies of the model system are close to the MP2/6-311G** interaction energies, which suggests that the DFT calculations with these functionals are useful methods to evaluated the interactions of hydrogen bonded systems.

Introduction

The phenomenon of cooperativity is important in a variety of molecular recognition processes.[1−15] The study of cooperative enhancement of binding is a topic of great current interest because it plays an important role in the determination of the stability of many systems such as DNA duplexes, folded proteins, and ligand−receptor complexes. The structures of these systems are stabilized by networks of weak interactions. Detailed information on the cooperativity is important for understanding of the structures and properties of biological systems and for rational design of drugs and artificial host molecules.

Different types of mechanisms, for example hydrogen bond cooperativity,[2,8,16,17] conformational changes,[1,15] secondary electrostatic effects,[3,18] and structure tightening,[10,11] exist for cooperative binding. The hydrogen bond cooperativity is the mutual enhancement of multiple hydrogen bonds.[2,8,10,16,17] The additional hydrogen bonds are enhanced by an already formed hydrogen bond and the additional hydrogen bonds also enhance the already formed hydrogen bond. Host−guest complexes often have multiple hydrogen bonds. Estimation of the size of the hydrogen bond cooperativity is significantly important for the understanding of the host−guest binding of these complexes and for the design of artificial host molecules. The magnitude of hydrogen bond cooperativity in a few small systems has been studied. High-level ab initio calculations of the water and methanol clusters have been carried out to evaluate the magnitude of the cooperative enhancement of the binding.[16,17,19−23]

Recently, Hiratani and co-workers reported that the crownophane which has phenolic hydroxy groups and a poly-oxyethylene chain has a strong binding affinity for a water.[24] The crystal structure of the water−crownophane complex shows that the water molecule has four hydrogen bonds with the two hydrogen-donating phenolic hydroxy groups and the two hydrogen-accepting oxygen atoms of the poly-oxyethylene chain (arrowed in Figure 1).[24] The structure suggests that the hydrogen bond cooperativity enhances the water binding. However, the magnitude of the cooperative enhancement of the binding has not yet been analyzed. It is not an easy task to evaluate the

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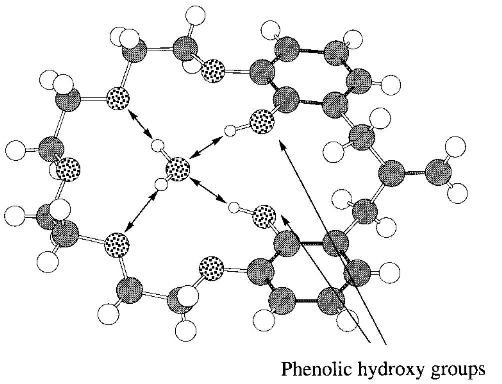

Figure 1. The X-ray structure of the water−crownophane complex.

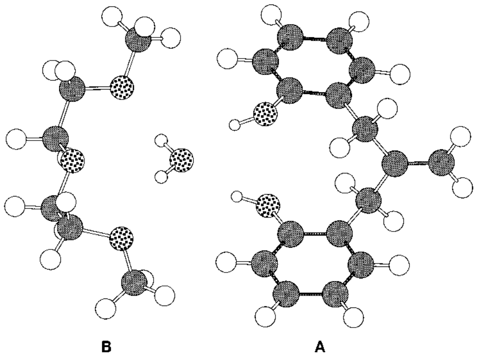

Figure 2. The model system used for this work.

magnitude of the enhancement only by experimental measurements. In this paper we have carried out high-level ab initio calculations of a model system of the water−crownophane complex (Figure 2) for the quantitative evaluation of the cooperative enhancement and for the purpose of understanding the origin of the enhancement. Our ab initio calculations have shown that the hydrogen bond cooperativity significantly increases the binding energy and that the major source of the enhancement has its origin in induction (induced polarization). We would like to emphasize that recent remarkable improvements of the methodologies of molecular orbital calculations and computer hardware enable us to apply computationally demanding high-level ab initio molecular orbital calculations to study the binding of the host−guest complex and that ab initio calculation is now becoming a very powerful tool for studying host−guest interactions.

Computational Method

The Gaussian 98 program[25] was used for all the ab initio molecular orbital calculations. The basis sets implemented in the program were used. Electron correlation was recovered by the second-order Mϕller−Plesset perturbation (MP2) method.[26,27] Basis set superposition error (BSSE)[28] was corrected for all calculations by using the counterpoise method.[29] The trimer basis set (hydrogen donating unit + hydrogen accepting unit + water) of the model system was used for all the calculations of the interaction energies. The geometry of the model system (Figure 2) was taken from the structure of the water−crownophane complex in crystal[24] and capping hydrogen atoms were added. The positions of all hydrogen atoms were optimized at the HF/6-31G* level. The Becke's exchange and Lee, Yang, and Parr's correlation functionals (BLYP),[30,31] Becke's 3 parameter functional combined with Lee, Yang, and Parr's correlation functional (B3LYP),[31,32] and Perdew and Wang's exchange and correlation functionals (PW91)[33] were used for the density functional calculations.

Results and Discussion

Basis Set and Electron Correlation Correction. It is well-known that the calculated intermolecular interaction energies determined with the ab initio method depend on the basis set and electron correlation correction procedure.[34−36] The effects of basis set are large in the calculations of van der Waals systems (rare gas dimers and hydrocarbon dimers),[35−37] in which dispersion is the dominant attractive interaction, while the basis set effects are relatively small in the calculations of hydrogen bonded systems,[38−40] in which electrostatic is the dominant attractive interaction. Electron correlation substantially increases the calculated bonding energies of hydrogen bonded systems,[38−40] while the effects of electron correlation beyond MP2 are not large. Recently reported CCSD(T) calculations of the five hydrogen bonded systems (H_2O−MeOH, H_2O−Me_2O, H_2O−H_2CO, MeOH−MeOH, and HCOOH−HCOOH complexes) with the cc-pVTZ basis set show that the ΔCCSD(T) values (the difference between the CCSD(T) and MP2 interaction energies) are negligible (less than 0.2 kcal/mol).[40]

The interaction energies of the A−H_2O and B−H_2O systems (Figure 2) were calculated with the 6-31G*, 6-311G**, 6-311G(2d,p), and 6-311G(2d,2p) basis sets to evaluate the basis set effects. The interaction of the A−H_2O system corresponds to the interaction between the water and the hydrogen-donating groups of the crownophane. The interaction of the B−H_2O system corresponds to the interaction between the water and the hydrogen-accepting groups of the crownophane. The calculated MP2 interaction energies depend on the basis set as summarized in Table 1. The small 6-31G* basis set overestimates the attraction compared to other basis sets. However, the basis set dependence of the MP2 interaction energies is not large, if basis

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Table 1. The Calculated Interaction Energies of the Model System of the Water−Crownophane Complex[a]

method	$E(A-H_2O)$	$E(B-H_2O)$	$E(AB-H_2O)$	E_{coop}[b]
HF/6-311G**	−7.46 (3.97)	−7.35 (5.48)	−18.44 (5.61)	−3.62
HF/6-311G(2d,2p)	−6.25 (4.02)	−6.36 (5.73)	−16.23 (5.66)	−3.62
MP2/6-31G*	−10.43 (5.99)	−9.21 (8.58)	−23.58 (9.17)	−3.93
MP2/6-311G**	−9.40 (7.58)	−8.72 (10.19)	−21.76 (10.47)	−3.64
MP2/6-311G(2d,p)	−9.55 (7.40)	−8.80 (9.88)	−21.99 (9.88)	−3.63
MP2/6-311G(2d,2p)	−9.20 (7.58)	−8.98 (10.37)	−21.85 (10.34)	−3.67
BLYP/6-311G**	−8.45 (7.18)	−6.87 (9.55)	−19.52 (9.84)	−4.20
B3LYP/6-311G**	−9.51 (6.09)	−8.18 (8.19)	−21.72 (8.45)	−4.03
PW91/6-311G**	−11.03 (6.84)	−9.34 (9.11)	−23.84 (9.49)	−3.48

[a] Energies in kcal/mol. BSSE-corrected interaction energies. The values in parentheses are BSSE values. The geometry of the model system is shown in Figure 2. [b] The cooperative increment of the binding energy. $E_{coop} = E(AB-H_2O) - [E(A-H_2O) + E(B-H_2O)]$.

sets larger than the 6-311G** are used. The Hartree−Fock (HF) interaction energies of the $A-H_2O$ and $B-H_2O$ systems with the 6-311G(2d,2p) basis set are −6.25 and −6.36 kcal/mol, respectively. The MP2 ones are −9.20 and −8.98 kcal/mol, respectively. The HF calculations underestimate the attraction as much as 2.95 and 2.62 kcal/mol, respectively, as the HF calculation cannot evaluate the attractive dispersion interaction.[34,41] The largest part of the attractive interactions in these systems are covered by the HF calculations, which indicates that dispersion is not important and that electrostatics are mainly responsible for the attraction in these systems.

Cooperative Enhancement of the Water Binding. The calculated MP2/6-311G(2d,2p) interaction energy of the $A-H_2O$ system [$E(A-H_2O) = -9.20$ kcal/mol] is not largely different from that of the $B-H_2O$ systems [$E(B-H_2O) = -8.98$ kcal/mol]. The $E(A-H_2O)$ and $E(B-H_2O)$ values are approximately twice as large as the bonding energy (D_e) of the water dimer (5 kcal/mol).[39,42] The interaction energy of the $AB-H_2O$ system [$E(AB-H_2O)$] was also calculated. The $E(AB-H_2O)$ is the bonding energy of H_2O with the AB complex (hydrogen-donating and -accepting units of the crownophane). The $E(AB-H_2O)$ is given by

$$E(AB-H_2O) = E(ABH_2O) - [E(AB) + E(H_2O)]$$

The $E(ABH_2O)$, $E(AB)$, and $E(H_2O)$ are the calculated energies of the ABH_2O and AB complexes and H_2O, respectively. The $E(AB-H_2O)$ calculated at the MP2/6-311G(2d,2p) level is −21.85 kcal/mol. The $E(AB-H_2O)$ is larger (more negative) than the sum of the $E(A-H_2O)$ and $E(B-H_2O)$ (−18.18 kcal/mol). The hydrogen bond cooperativity significantly increases the binding energy of the water. The cooperative increment (E_{coop}) is given by

$$E_{coop} = E(AB-H_2O) - [E(A-H_2O) + E(B-H_2O)]$$

The E_{coop} value calculated at the MP2/6-311G(2d,2p) level is −3.67 kcal/mol. Although the $E(A-H_2O)$, $E(B-H_2O)$, and $E(AB-H_2O)$ values substantially depend on the basis set, the basis set dependence of the E_{coop} is very small (less than 0.3 kcal/mol). The E_{coop} value is about 70% of the bonding energy of the water dimer (5 kcal/mol). The large E_{coop} value shows that the cooperative enhancement is significantly important for the stabilization of the water−crownophane complex. The similar amounts of cooperative enhancement of the binding have been reported from the MP2/6-311+G(2d,2p) level calculations of the water and methanol homo trimers by Masella and Flament.[22] They reported that the three-body terms of these trimers (cooperative increments) were 2.9 and 3.2 kcal/mol, respectively. The calculations show that hydrogen bond cooperativity is significantly important for the stabilization of the water−crownophane complex. It should be noted, however, that structural tightening would occur in the complex by the formation of the hydrogen bonds and therefore some of the cooperative binding would originate also in structural tightening in the real system.

It is interesting to note that most of the E_{coop} is covered by the HF level calculations. The HF/6-311G(2d,2p) level E_{coop} is −3.62 kcal/mol. This result suggests that the major source of the hydrogen bond cooperativity in this system has its origin in induction (induced polarization). The calculated charge distributions also indicate that the water molecule is strongly polarized by the hydrogen bonds. Mulliken population analysis[43] was carried out by using the HF/6-311G** wave functions. The calculated charges on the oxygen and the two hydrogen atoms of the water in the ABH_2O complex are −0.61, 0.32, and 0.31 e ($1e = 1.602 \times 10^{-19}$ C), respectively, while those of an isolated water (HF/6-31G* geometry) are −0.50, 0.25, and 0.25 e, respectively.

Density Functional Calculations. Although MP2 calculations provide sufficiently accurate interaction energies of hydrogen bonded systems,[38−40] MP2 calculations are still too computationally demanding to study the interactions of large systems such as the biological systems. If density functional calculations, which require nearly the same amount of computer resources as HF calculations, can provide sufficiently accurate interaction energies, we can apply density functional calculations for the quantitative analysis of large biological systems such as protein and DNA.

The $E(A-H_2O)$, $E(B-H_2O)$, and $E(AB-H_2O)$ were also calculated by the density functional methods by using the BLYP, B3LYP, and PW91 functionals. The 6-311G** basis set was used for the calculations. The calculated interaction energies are compared with the MP2 interaction energies to evaluate the accuracy of the density functional calculations as summarized in Table 1. The interaction energies calculated with these functionals are close to the MP2 interaction energies. The calculated E_{coop} values by the density functional calculations (−4.20, −4.03, and −3.48 kcal/mol for the BLYP, B3LYP, and PW91, respectively) are not largely different from the MP2/6-311G** value (−3.64 kcal/mol). Surprisingly good performance of the density functional calculations suggests that the density functional calculations are potentially useful methods for studying hydrogen bonded systems and that these methods would be the only possibility for evaluating interactions of large systems, where MP2 calculations are too demanding.[44,45]

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Conclusion

Our ab initio calculations indicate that the hydrogen bond cooperativity significantly increases the binding of the water with the crownophane which has the two hydrogen-donating phenolic hydroxy groups and the hydrogen-accepting polyoxyethylene chain. The calculated cooperative increment of the binding energy is 3.67 kcal/mol. The calculated interaction energies of the model system depend on the basis set, while the basis set dependence of the cooperative increment is negligible. Most of the cooperative increment is covered by the HF calculation, which suggests that the major source of the hydrogen bond cooperativity in this system has its origin in induction (induced polarization). The calculated atomic charge distributions of the water molecule in the model system also show that the water is strongly polarized in the complex.

The calculated B3LYP and PW91 interaction energies are close to the MP2 interaction energies. The good performance suggests that the DFT calculations with these functionals are potentially useful methods for studying hydrogen bonded systems and that these methods would be the only possibility for evaluating the interactions of large systems where MP2 calculations are too demanding. We would like to emphasize that recent remarkable improvements of the methodologies of molecular orbital calculations and computer hardware enable us to apply computationally demanding high-level ab initio molecular orbital calculations for studying the binding of the host−guest complex and that ab initio calculation is now becoming a very powerful tool in the study of host−guest interactions.

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Supporting Information Available: Table of geometries and energies of the complexes (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(44) Recently reported DFT calculations of small hydrogen bonded systems with the BLYP, B3LYP, and PW91 functionals show that the bonding energies by the PW91 are close to those by MP2 and CCSD(T) and that BLYP and B3LYP substantially underestimate the bonding energies.

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