Studies on Hydroxy Inclusion Complexes.

I. Host-Guest Interaction of the Molecular Complexes of 9-Hydroxy-9-(1-propynyl)fluorene and 1,1-Bis(2,4-dimethylphenyl)-2-butyn-1-ol with Water, Methanol, Ethanol, and *n*-Propanol

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Abstract. Molecular inclusion by hydroxy host systems (9-hydroxy-9-(1-propynyl)fluorene + guest and 1,1-bis(2,4-dimethylphenyl)-2-butyn-1-ol + guest) has been investigated by using an empirical potential function. Water, methanol, ethanol, and *n*-propanol have been employed as guest molecules and their relative stabilities are considered. Alcohol is found to be more suitable than water as a guest molecule in the two tested host molecules. It is also found that the nonbonded interaction is the most important factor in determining the relative stabilities of hydroxy host systems.

Key words: 9-hydroxy-9-(1-propynyl)fluorene, 1,1-bis(2,4-dimethylphenyl)-2-butyn-1-ol, water, methanol, ethanol, *n*-propanol, molecular inclusion, nonbonded interaction, relative stability.

1. Introduction

Molecular inclusion is one of the important physical properties in physical and organic chemistry because one can separate selected species from mixtures and/or solutions.

Various hydroxy host molecules have been found useful in the extraction of alcohols from aqueous solutions of various concentrations [1]. For example, 9-hydroxy-9-(1-propynyl)fluorene (HPF) and 1,1-bis(2,4-dimethylphenyl)-2-butyn-1-ol (BDB) can be used to extract pure alcohols from their aqueous solutions [2].

Recently, the structures of these compounds have been determined by X-ray crystallographic studies [2–5] which have given remarkable information about inclusion phenomena. These studies conclude that all complexes show the presence of strongly hydrogen-bonded hydroxyl groups and that the alkyl group of the alcohol is located in the channel of the crystalline complex. Therefore, the reason molecular inclusion by hydroxy host systems has occurred may be found in a consideration of the hydrogen bond interaction between hydroxyl groups in host and guest molecules, as well as nonbonded interactions between hydrophobic groups.

In this study, we report the results of an investigation using an empirical poten-

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tial function on the properties of hydroxy inclusion complexes such as the HPF and BDB + guests complexes. The use of empirical potentials in the study of inclusion complexes is important because most *ab initio* methods are applied only to small clusters or dimers. Empirical potentials can be applied to larger systems without using excessive computing time, although they usually do not give accurate interaction energy and geometry, but provide considerable information about the systems. The relative stabilities among the several guest molecules in HPF and BDB are calculated and compared with experimental results [1, 2].

2. Model Compounds

The computations have been carried out on model compounds such as HPF and BDB which have relatively simple structures compared with other hydroxy inclusion compounds. In addition, their crystal structures are well known [2]. This information is essential for the explanation of inclusion phenomena because they may not be explained by considering only single pair interactions between host and guest molecule.

In order to make reliable calculations, the structure of the host molecule is obtained from X-ray data [2]. The hydrogen bonded O···O distances range from 2.69 Å to 2.76 Å in HPF and BDB systems. The shapes of HPF and BDB molecules are shown in Figure 1. The BDB host molecule has more bulky aromatic side chains than the HPF host molecule, and two aromatic groups in the BDB host molecule are twisted relative to each other by nearly 90°. For the positions of the hydrogen atoms, 1.09 Å and 1.08 Å were used as bond distances from aliphatic and aromatic carbon atoms, respectively. For the O—H bond length in the host molecule, 0.945 Å was used [6]. The aromatic 6-membered rings are regarded as regular hexagonal planes, so that C—C—H bond angles in these rings are set to 120°. In the initial calculations, we checked the effect of allowing the methyl groups in the host molecules to rotate freely. It was found that this causes no significant effect on the interaction energy. Therefore, the rotation of the methyl group in the host molecule is not considered in order to reduce the computing time.

Water, methanol, ethanol, and *n*-propanol were investigated as guest molecules in HPF and BDB host molecules. These guest molecules are inserted in accordance with X-ray data [2]. The geometries of the rigid monomers are based on their experimental data in [7] for water and [8] for methanol. The geometries of ethanol and *n*-propanol studied here were generated using a "standard" set of bond lengths
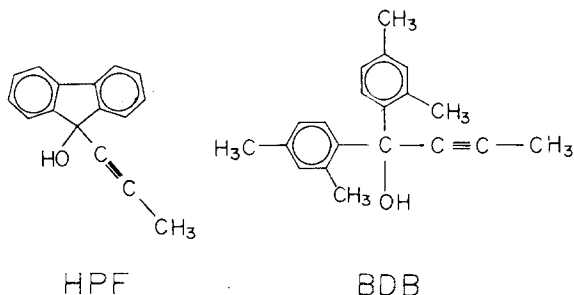

Fig. 1.   Molecular shapes of HPF and BDB.

and bond angles derived from experiment. The values for the "standard" bond lengths and bond angles are well described in [9]. The conformations of ethanol and *n*-propanol were taken from [9 and 10].

3. Methods of Calculations

3.1. POTENTIAL FUNCTION [11, 12]

As noted above, the energy calculation of the host–guest interaction was carried out by using an empirical potential function. The total interaction energy (E_{tot}) was obtained by the sum of terms which are electrostatic (E_{el}), polarization (E_{pol}), non-bonded (E_{nb}), and hydrogen bond energies (E_{hb}), i.e.,

$$E_{tot} = \sum_{\substack{nb\ pairs \\ -hb\ pairs}} (E_{el} + E_{nb}) + \sum_{i} E_{pol} + \sum_{hb\ pairs} E_{hb} \qquad (1)$$

Electrostatic and nonbonded energies are counted all over the interacting pairs except hydrogen bonding pairs.

3.1.1. *Electrostatic Energy*

Each atom in our system is considered as a point charge, so the electrostatic energy is simply the Coulomb potential which is given by

$$E_{el} = q_i q_j / r_{ij} \qquad (2)$$

where r_{ij} is the distance between atom i and j, and q_i and q_j are their partial charges. The atomic partial charges were readily obtained by using the semiempirical methods: the Del Re method [13, 14] for σ-charges and the Hückel method [15, 16] for π-charges.

3.1.2. *Polarization Energy*

The polarization energy is given by

$$E_{pol} = -\tfrac{1}{2} \bar{\alpha}_i |\bar{E}_i|^2 \qquad (3)$$

where $\bar{\alpha}_i$ is the atomic static polarizability [17] of the atom i and $\bar{E}_i$ is the electric field at the atom i by all surrounding atoms in the interacting molecule.

3.1.3. *Nonbonded Energy*

The nonbonded energy is composed of the dispersion energy and short-range repulsion energy, which is a Lennard–Jones type and is given by

$$E_{nb} = -K_6(i, j)/z_{ij}^6 (1 - 0.5/z_{ij}^6) \qquad (4)$$

where

$$K_6(i, j) = C_6(i, j)/\mathring{r}_{ij}^6, \qquad z_{ij} = r_{ij}/\mathring{r}_{ij}$$

and $\mathring{r}_{ij}$ is the sum of the van der Waals radii of the atom i and the atom j [18]. According to the London approximation [19], $C_6(i, j)$ can be written as

$$C_6(i, j) = \tfrac{3}{2} \frac{\overline{\alpha}_i \overline{\alpha}_j I_i I_j}{I_i + I_j} \tag{5}$$

where $\overline{\alpha}_i$ and I_i are the atomic static polarizability and the ionization potential [17], respectively.

3.1.4. Hydrogen Bond Energy

The form of the hydrogen bond potential is

$$E_{hb}(r, \phi) = E^{\circ}_{hb}(r) \cdot A(\phi) \tag{6}$$

where

$$E^{\circ}_{hb}(r) = D_e \{1 - (r/r_e)^n \exp(-a(r/r_e - 1))\}^2 - D_e$$

and

$$A(\phi) = b(\cos^2 \phi - 1) + 1$$

In the $E_{hb}(r)$ term, D_e is the dissociation energy, r is the internuclear distance between atoms directly involved in a hydrogen bond, and r_e is its equilibrium distance. Since there are no experimental values for the hydrogen bonded systems, values of D_e and r_e were obtained from *ab initio* calculations [20], with $a = 2.00$ and $n = 0.01$ [11, 12], which are shown in Table I. In the attenuating factor $A(\phi)$, ϕ is the angle of the hydrogen bond and b is a constant whose value was taken as 0.456 [11]. If the angle ϕ is less than 120° or if the hydrogen bond length is longer than the critical distance r_c, then the two atoms are considered not to form a hydrogen bond.

Table I.   Parameters for hydrogen bond potential

Type	r_e/Å	D_e/kcal mol⁻¹	r_c/Å
—C—O—H···O—H H	1.85	35.566	2.55
—C—O—H···O—C— H	1.85	26.319	2.55
H—O—H···O—C— H	1.85	28.213	2.55

3.2. CALCULATIONAL PROCEDURE

Calculations of interaction energy were carried out by increasing the number of (host + guest) units from one to nine for the HPF system and from one to five for the BDB system according to the X-ray data [2].

Since the guest molecule located in the center of the model compound is energetically the most similar one to the true one, energy calculations were performed with the condition that one guest molecule in the center of the model compound interact with its environments, and interactions between its environments are not considered.
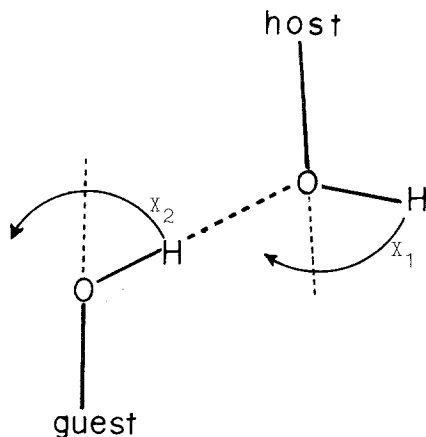
host

guest

Fig. 2. Variables used in calculations.

Therefore, the meaning of the total interaction energy used here is somewhat different from the usual meaning of the "total interaction energy" of the system investigated.

As mentioned in Section 2, geometries of the model compounds were fixed from X-ray data, so that the necessary number of variables for the calculation is reduced as in Figure 2. As shown, the hydroxyl hydrogen atoms and alkyl residues in the guest molecule must be optimized. Optimization of these variables was carried out by using the quasi-Newton–Raphson procedure [21].

4. Results and Discussion

4.1. (HPF + GUEST) SYSTEM

The calculated interaction energy for each guest molecule with the HPF host molecule is shown in Table II and Figure 3. From Figure 3, it can be seen that the magnitudes of interaction energies for all guest molecules increase as the number of (host + guest) units increase. Since there exists another hydrogen bond between the model guest molecule – located in the center of the model compound – and the second HPF host molecule, a sudden increase in the interaction energy is observed when the number of units becomes two. The differences of interaction energies between alcohols and water also increase with increasing numbers of units. Accordingly, if the numbers of units are greater than three, the differences become about 3 kcal/mole.

Table II. Total interaction energies for the (HPF + Guest) system (kcal/mole)

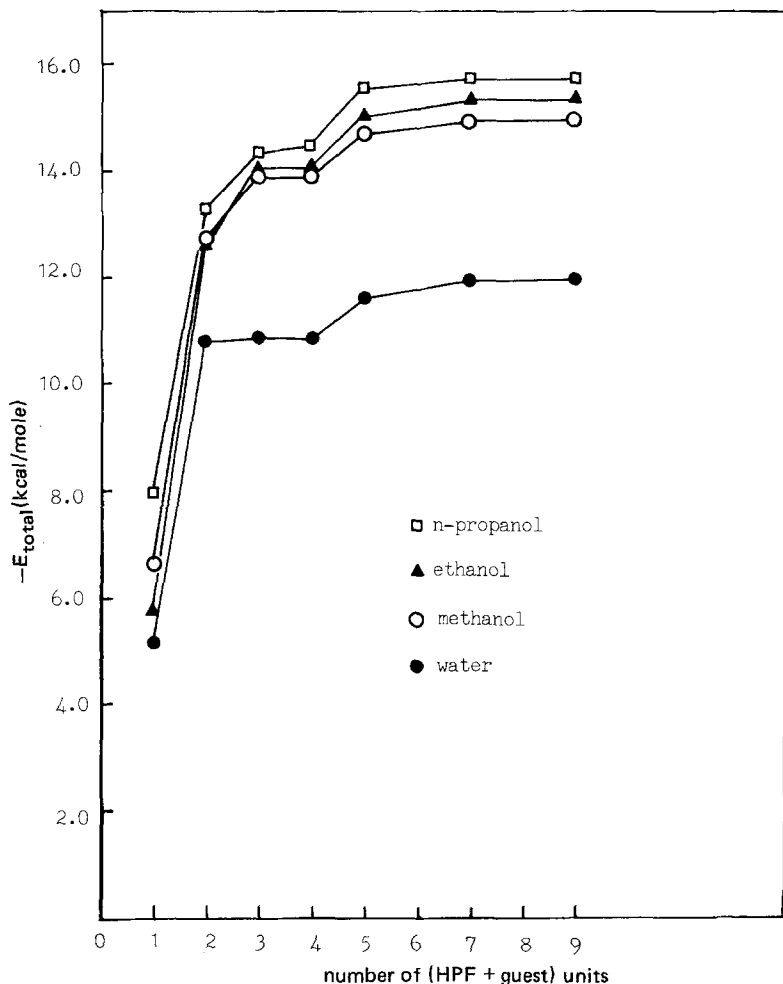| Guest	1^a	2	3	4	5	7	9
water	−5.16	−10.76	−10.88	−10.83	−11.60	−11.98	−11.98
methanol	−6.67	−12.72	−13.92	−14.91	−14.68	−14.93	−14.93
ethanol	−5.74	−12.62	−14.01	−15.02	−15.02	−15.37	−15.37
n-propanol	−7.97	−13.29	−13.36	−14.46	−15.52	−15.68	−15.68

^{a} Number of (HPF + guest) units.

Fig. 3.   Total interaction energy of the (HPF + Guest) system.

As mentioned earlier in Section 3.2, in the calculation of E_{tot}, the interaction between only one model guest and its neighbors was counted. In a real inclusion complex, therefore, the total interaction energy differences between water and alcohol should be much greater. It means that alcohol is more suitable than water as a guest molecule in the HPF host molecule.

In order to investigate the reason why the energy differences between alcohols and water gradually increase with increasing numbers of units, the illustration of each energy component of the potential function is needed, which is shown in Figures 4 to 6. Figure 4 shows simply the sum of the electrostatic and the hydrogen bond interaction, i.e., $E_{el} + E_{hb}$. In this figure, the energy differences are not large enough to affect the total interaction energy differences in Figure 3. Therefore, the sum of the electrostatic and the hydrogen bond interaction energy seems to be not a main factor in the determination of the relative stabilities of the guest molecules in the HPF system. The magnitude of this energy component for n-propanol is, however, slightly smaller than for water.
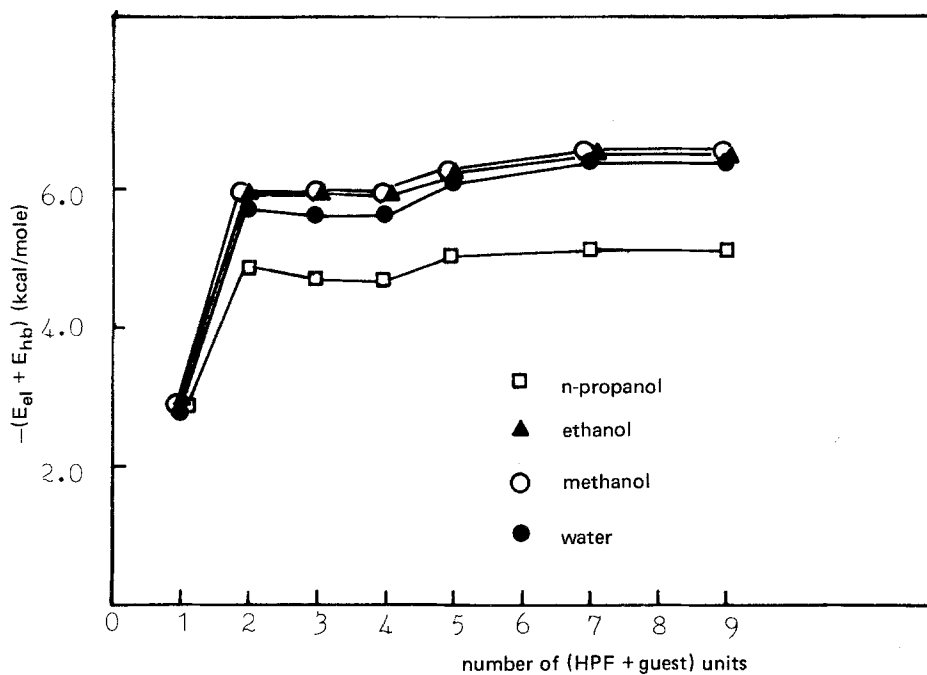
Fig. 4. Electrostatic and hydrogen bond energy of the (HPF + Guest) system.
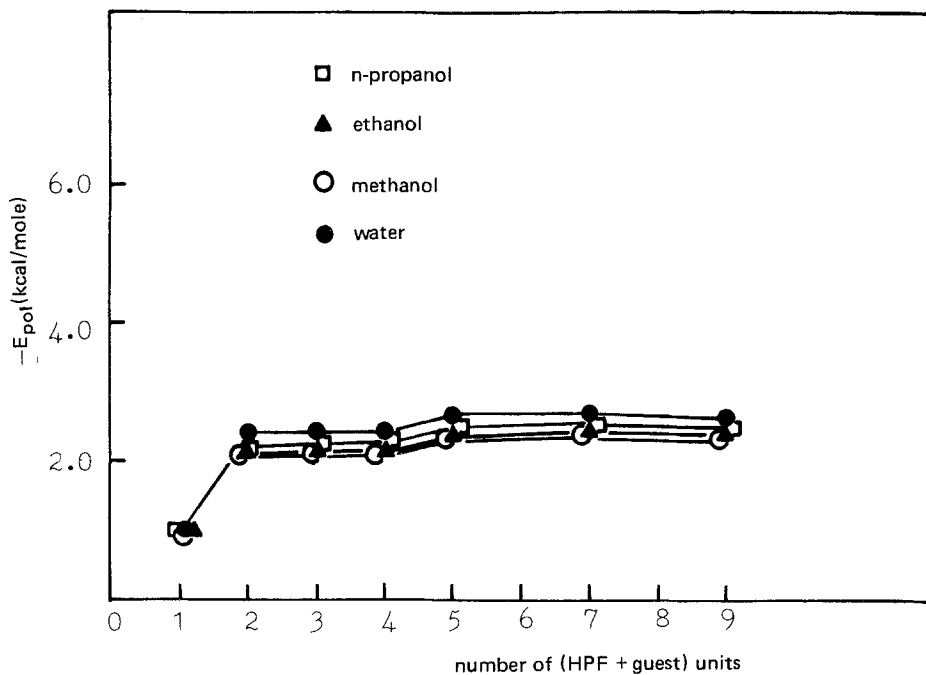
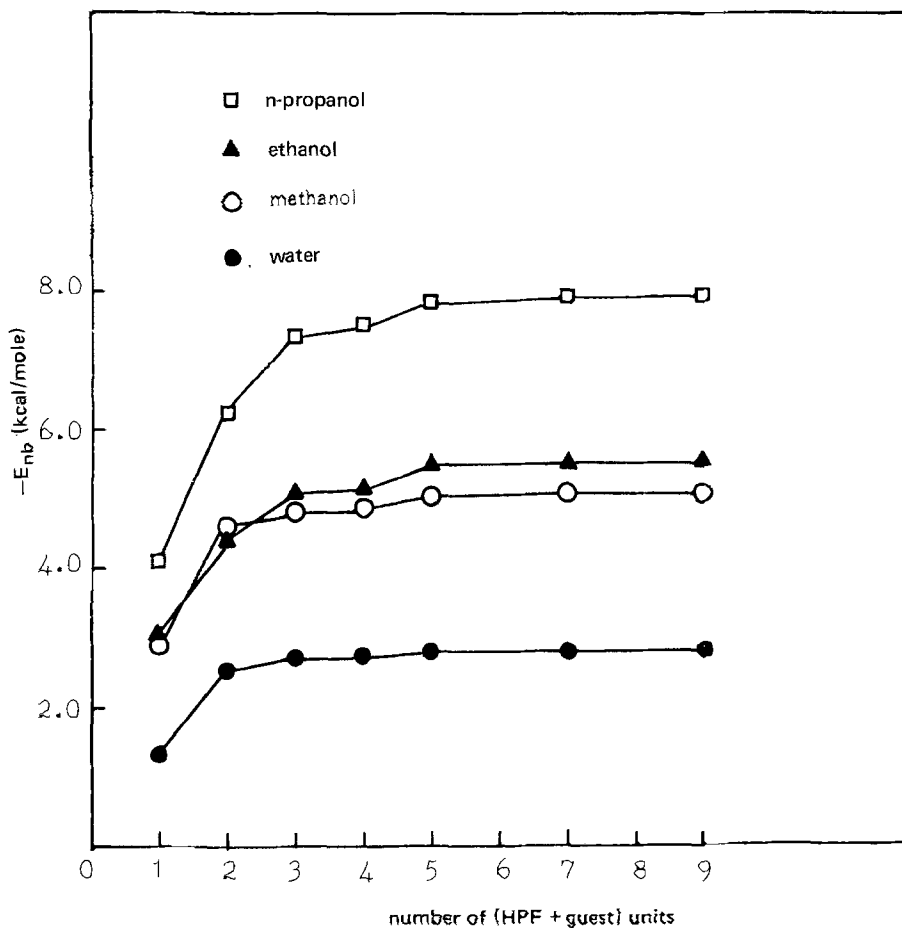

Fig. 5. Polarization energy of the (HPF + Guest) system.

Fig. 6.   Nonbonded energy of the (HPF + Guest) system.

The polarization energy in Figure 5 shows a similar tendency to the electro-static and the hydrogen bond energy in Figure 4. One sees that the difference in polarization energy between alcohol and water is very small.

The nonbonded interaction energy is shown in Figure 6. Here, the difference is quite large and indicates a different origin. In this figure, it is found that the non-bonded energy difference between alcohol and water becomes greater in proportion to the increase of the size of the model compound, which agrees well with the total interaction energy difference in Figure 3. The absolute values of energy provided here need not be taken too seriously, but the relative values may be instructive. The main factor which makes alcohol more suitable than water as a guest molecule is, therefore, the nonbonded interaction energy. The fact that alcohol has a hydroxyl group able to form a hydrogen bond and a hydrophobic alkyl group able to inter-act significantly with the HPF moiety seems to make alchol more suitable. Water is also able to form hydrogen bonds but it does not significantly interact with the hydrophobic groups in HPF. Moreover, for water in solution, there exists an extra stabilization due to the two hydrogen bonds which are not possible in this system.

But for alcohol, in its solution, there exists only one hydroxyl group able to form a hydrogen bond which is also possible in this model compound. In practice, according to *ab initio* calculations [22, 23], the magnitude of the binding energy of a water cluster is greater than that of methanol by approximately 5 kcal/mole.
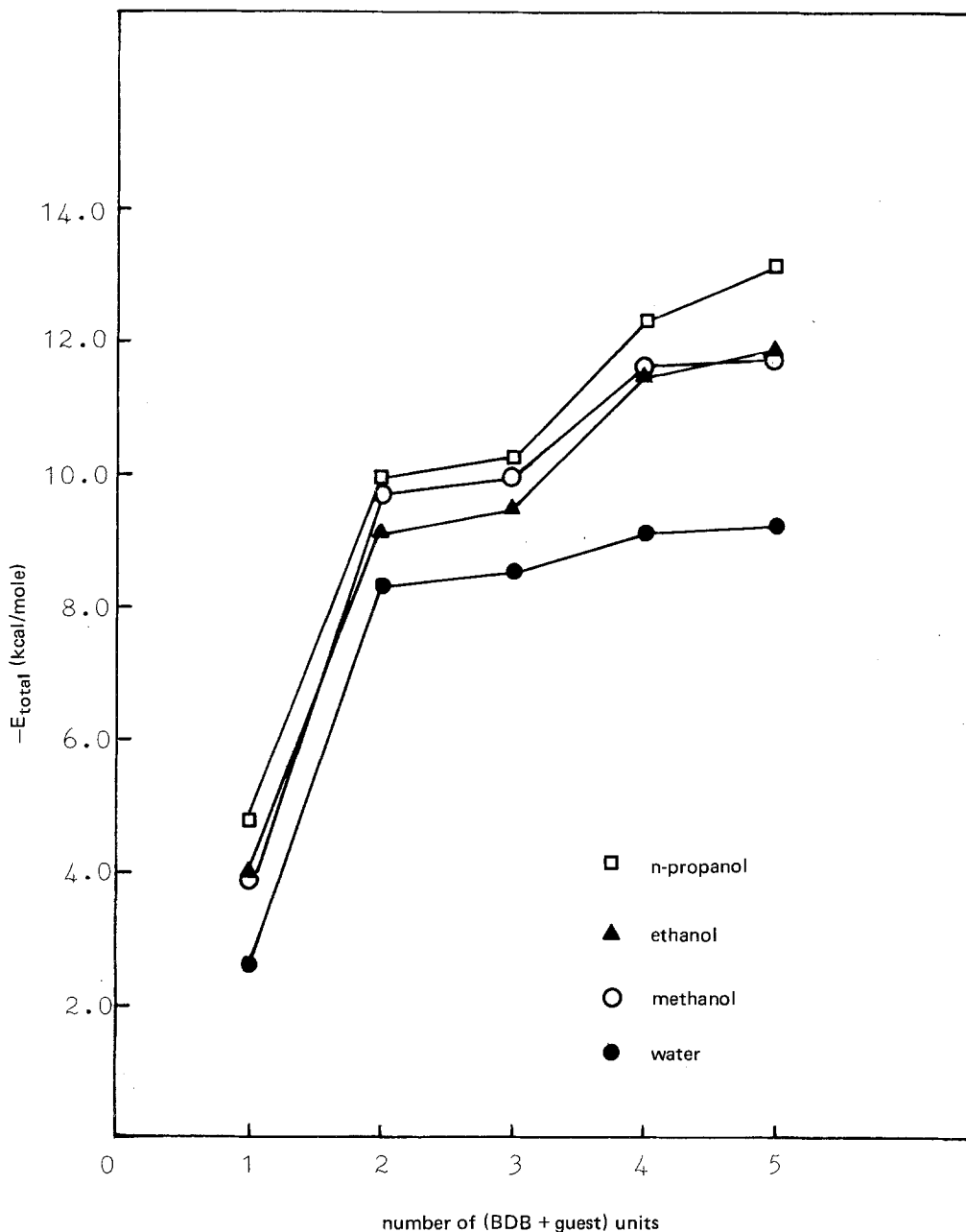

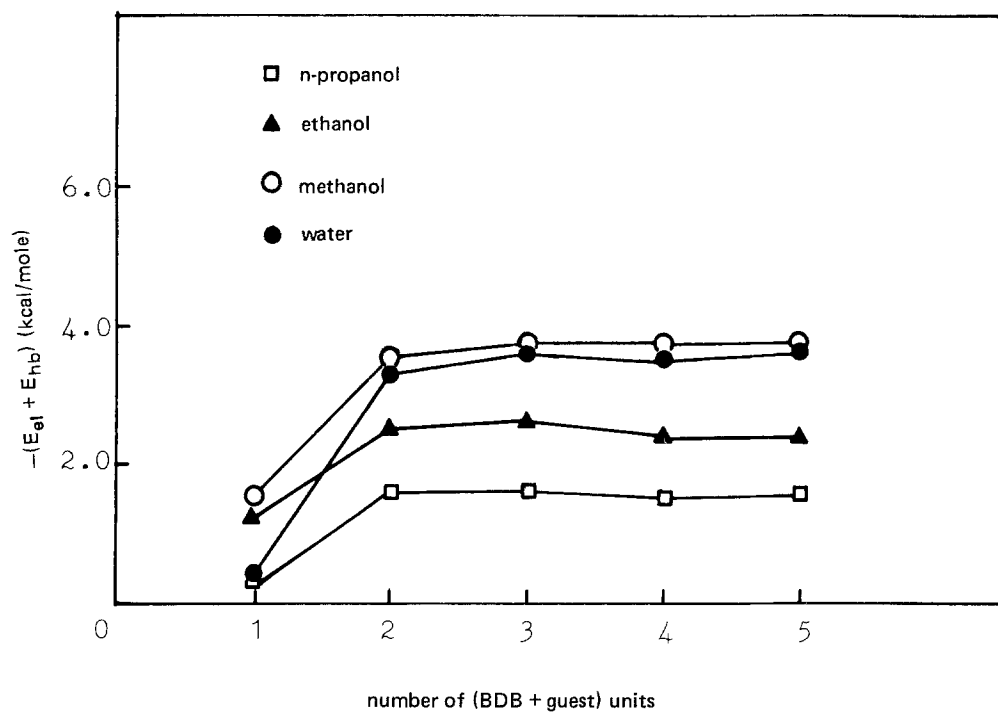Fig. 7. Total interaction energy of the (BDB + Guest) system.

Fig. 8.   Electrostatic and hydrogen bond energy of the (BDB + Guest) system.
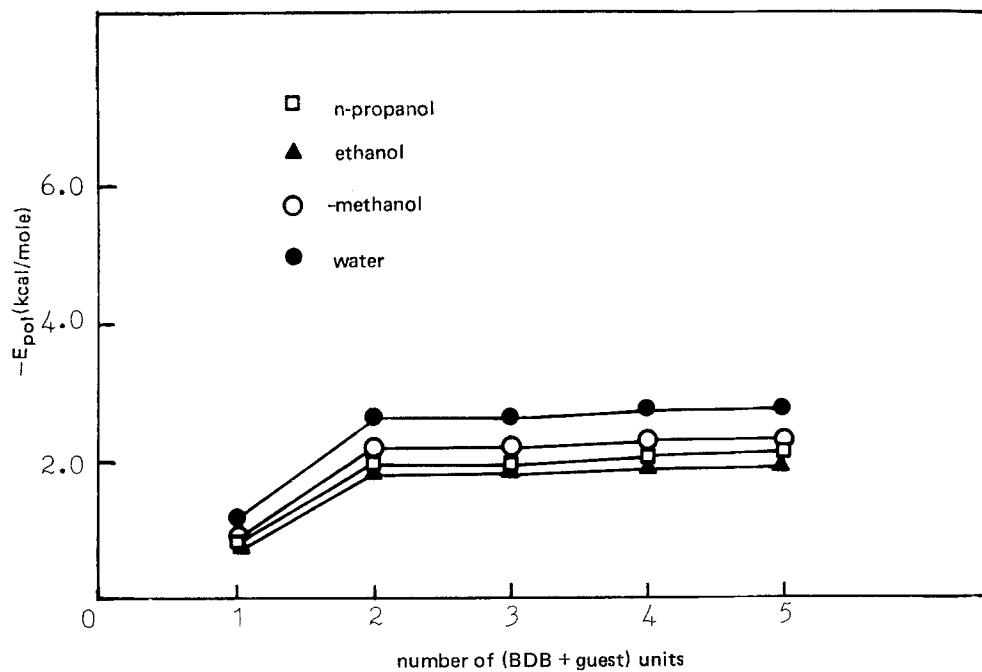

Fig. 9.   Polarization energy of the (BDB + Guest) system.

4.2. (BDB + GUEST) SYSTEM

According to X-ray crystallographic data, the (BDB + ethanol) complex has a cyclic hydrogen bonded $(OH)_4$ ring in its crystal structure. The calculated interaction energy for each guest molecule is depicted in Table III and Figure 7. The results are similar to the HPF system. All energy components for the above inter-

Table III.   Total interaction energies for the (BDB + Guest) system (kcal/mole)

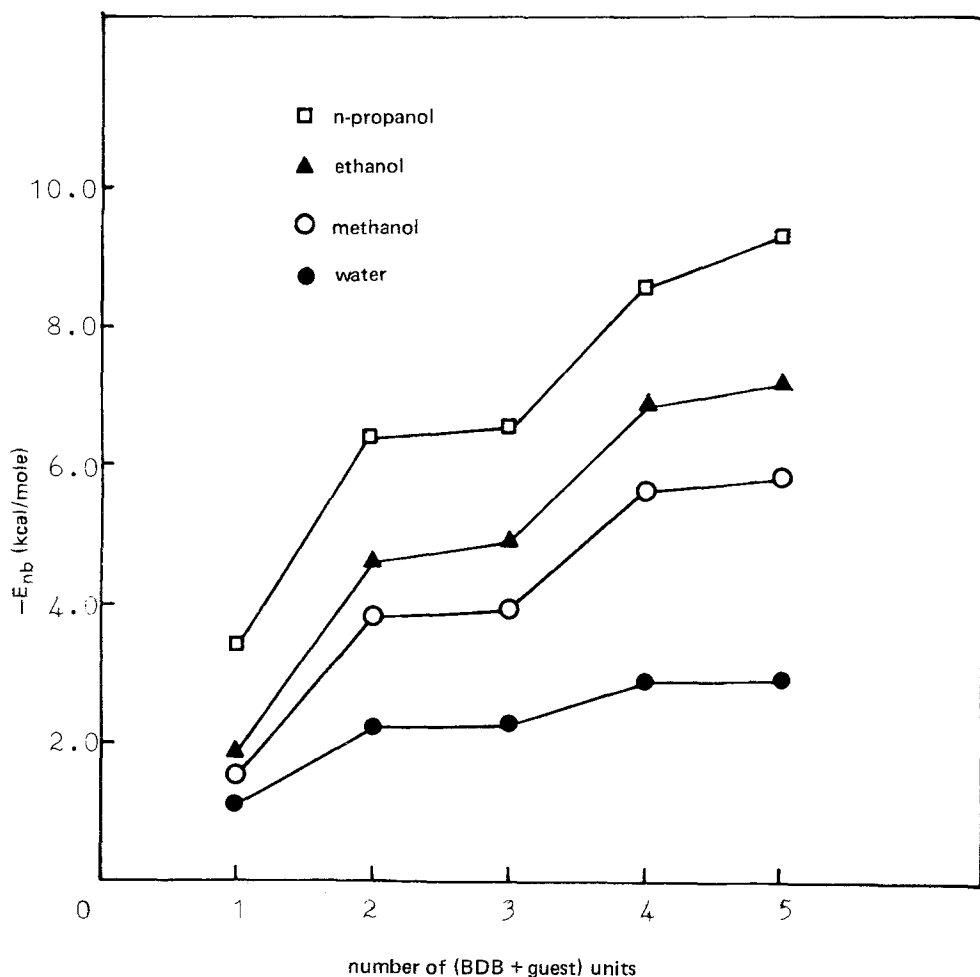| Guest	1^a	2	3	4	5
water	−2.64	−8.31	−8.52	−9.15	−9.24
methanol	−3.88	−9.71	−9.94	−11.61	−11.76
ethanol	−4.00	−9.20	−9.52	−11.53	−11.88
n-propanol	−4.73	−9.96	−10.28	−12.37	−13.12

[a] Number of (BDB + Guest) units.

Fig. 10.   Nonbonded energy of the (BDB + Guest) system.

action energies are shown in Figures 8 to 10 for electrostatic + hydrogen bond, polarization, and nonbonded energy, respectively.

In Figure 7, sudden increases of the total interaction energy when the number of units is two are due to the extra hydrogen bond of the guest molecule with its neighboring BDB host molecule. The trend in the BDB system is practically the same as for the HPF system. In the case of five units, differences of interaction energies between alcohols and water are greater than 2.5 kcal/mole. As mentioned previously, in a real crystal, all guest molecules must be energetically equivalent, so that these energy differences should be very large.

In the electrostatic + hydrogen bond in Figure 8 and the polarization energy in Figure 9, water seems to be more suitable than alcohol, which differs slightly from that of the HPF system. In terms of the nonbonded energy in Figure 10, however, alcohol is much more favorable than water. The magnitude of the nonbonded energy for five units still increases and differences of this energy between water and the alcohols are large enough to overcome the differences of polarization and electrostatic + hydrogen bond energy. Since the guest alcohol which has a more bulky alkyl side chain exhibits not only greater nonbonded interaction with the BDB host molecule, but also weaker electrostatic + hydrogen bond and polarization interaction, it is not easy to evaluate the relative stability between the quest alcohols.

5. Conclusion

The following conclusions may be drawn from this study of both HPF and BDB + water, methanol, ethanol, and *n*-propanol inclusion complexes:

(1) As a guest molecule of HPF and BDB, water is less stable than alcohols, which is in good agreement with experiments.
(2) Nonbonded interactions play a very important role in HPF and BDB + guest systems.
(3) There are no clear correlations in this study for the relative stabilities among the alcohols as guest molecules of HPF and BDB.

Acknowledgement

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