# First-Principles Prediction of the Effects of Temperature and Solvent Selection on the Dimerization of Benzoic Acid

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ABSTRACT: We introduce a procedure of quantum chemical calculations (B3P86/6-31G**) to study carboxylic acid dimerization and its correlation with temperature and properties of the solvent. Benzoic acid is chosen as a model system for studying dimerization via hydrogen bonding. Organic solvents are simulated using the self-consistent reaction field (SCRF) method with the polarized continuum model (PCM). The cyclic dimer is the most stable structure both in gas phase and solution. Dimer mono- and dihydrates could be found in the gas phase if acid molecules are in contact with water vapor. However, the formation of these hydrated conformers is very limited and cyclic dimer is the principal conformer to coexist with monomer acid in solution. Solvation of the cyclic dimer is more favorable compared to other complexes, partially due to the diminishing of hydrogen bonding capability and annihilation of dipole moments. Solvents have a strong effect on inducing dimer dissociation and this dependence is more pronounced at low dielectric constants. By accounting for selected terms in the total free energy of solvation, the solvation entropy could be incorporated to predict the dimer behavior at elevated temperatures. The temperature dependence of benzoic acid dimerization obtained by this technique is in good agreement with available experimental measurements, in which a tendency of dimer to dissociate is observed with increased temperatures. In addition, dimer breakup is more sensitive to temperature in low dielectric environments rather than in solvents with a higher dielectric constant.
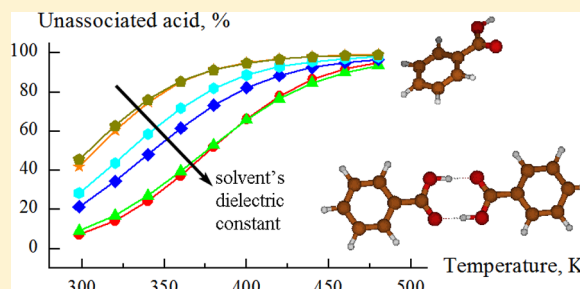
1. INTRODUCTION

It is known that organic acids may dimerize in both aqueous and nonaqueous environments due to hydrogen bonding between two carbonyl and hydroxyl pairs.[1] Hydrogen bonds can be considered as a special case of the electrostatic interaction between dipoles. The self-association by hydrogen bonding between molecular units determines the availability of monomeric species in solution. Hydrogen bonding is, in fact, responsible for many physicochemical phenomena and biological processes through the control of bonding strength, solubility, boiling point, diffusion coefficient and partition properties in solution with mixed solvents.[1] The dimerization of carboxylic acids is a signature system for studying the nature of hydrogen bonds as a function of temperature, pressure, solvation environment and organic substituents.[2]

The observation of carboxylic acid dimers in organic solvents and vapor phase was first reported in the late 19th century[1] and the monomer−dimer equilibrium since then has been extensively studied by different experimental techniques such as infrared,[3−5] ultraviolet,[6] nuclear magnetic resonance,[7] Raman spectra or thermochemical methods, and measurement of electrical conductivity,[8] vapor pressure, freezing point depression,[9] boiling point,[10] magnetic circular dichroism,[11] and partition ratios in mixed solvent systems.[12−14]

In the last 2 decades, with the significant advances in computer resources and theoretical techniques, computation has emerged as an alternative and accurate approach to study the nature of many physical and chemical phenomena at the electronic and atomistic level. In particular, the reliability of *ab initio* quantum chemical methods has been examined for the calculation of hydrogen bonding and dimer formation of simple carboxylic acids.[15−19] Colominas and co-workers analyzed a number of theoretical methods from classical to high-level *ab initio* computations to simulate the dimerization of formic acid.[20] The effect of solvents on hydrogen bonding was well described in terms of dipole moments, solvent-accessible surfaces and cavity volumes by other researchers.[21] Later, the mechanism of formic acid dimerization was reported by Gantenberg et al. as an example of noncovalent reaction[22] and studied by Brinkmann et al. in which the cyclic dimer is formed through an acyclic dimer intermediate.[23] The diversity of formic acid dimers was also evidenced by the theoretical work of Rodziewicz et al. using first-principles molecular dynamics[24] and by Turner's group using Monte Carlo simulations.[25] Recently, several researchers have performed molecular dynamics (MD) simulations on dimer formation of carboxylic acid in gas phase, aqueous solution, nonpolar solvent and microhydration.[26−29] The potentials of mean force obtained by MD simulation can be used to estimate the

binding affinity of hydrogen bonds and dimerization constants.[30]

Ab initio quantum chemical calculations are, therefore, capable of predicting the hydrogen bonding energy, free energy, enthalpy, and Gibbs free energy of dimerization in gas phase quite closely to experimental data.[20] In this work, we present a procedure to compute the free energy of formation of carboxylic acid dimers in various solvents, in which the solvation entropy is extracted for predicting the entropic thermodynamic correction. This technique can be generally applied toward the correction of Gibbs free energy at high temperature for any solute−solvent systems at quantum chemical levels. The high symmetry of benzoic acid dimer makes it a good model to study double hydrogen bonding[6] and experimental reports regarding the thermodynamic data of benzoic acid association have been well documented.[1,3,31−34]

The hydrogen bonding, proton transfer, hydration, partition and dimerization of benzoic acid have been the subject of a vast number of early experimental investigations.[6,14,31,32,35−40] It has been suggested that monomeric acid species are generally in equilibrium with open chain and cyclic dimers. In addition, benzoic acid dimers were also found to be present in monohydrate and dihydrate forms in organic solvents.[12] References to temperature and pressure effects on hydrogen bonding in benzoic acid dimerization were given in a series of publications.[1,3,9,13,41−43] Barraza and his colleagues indicated that increasing pressure favors the formation of dimeric species.[3] There was also evidence that the formation of hydrogen bonds is preferable at reduced temperatures,[41] which is likely to be an entropic effect. The dissociation of benzoic acid dimers in benzene as a function of temperature was well summarized and analyzed in the works of Allen, Barton, Huq, and Wall et al.[10,31,35,36,44] However, early studies were mostly confined to low temperature ranges; capture of the hydrogen bonding effect on electronic absorption spectra can be performed more easily at low temperatures where absorption bands are sharp.[32]

Several groups have reported the solvent effect on benzoic acid dimers. Fujii and co-workers studied the hydration and dimerization by partition and measurement of water in different organic phases containing benzoic acid.[12] Yamada et al. investigated the solvation effect in mixed solvent systems[45] and I'Haya et al. examined the interaction of benzoic acid with a small amount of water in dilute solvent, which is believed to have significant effect on the dimerization equilibrium.[37] It is commonly accepted that the dimerization becomes stronger in lower dielectric medium due to reduced competition by the solvent for the electrostatic nature of hydrogen bonds. It was also suggested that the stability of acid dimers and hydrogen bonds in solution could be also influenced by hydrophobic and hydrophilic interactions. For instance, water or charged ions will prefer a polar medium while the aliphatic or aromatic hydrocarbon chains in general are apolar.[8,21,28]

In this work, we present an investigation of the dimerization behavior of benzoic acid molecules as a function of temperature and solvent. The comparison of the first-principles results with the literature data will be used to provide an estimate of the method's reliability. The next section describes the model system and the specifics of the technique employed in this study. In section 3, the results and interpretation of the calculations are presented.

2. COMPUTATIONAL METHOD

First-principles quantum chemical calculations were performed using the Gaussian 09 software.[46] Free energy are computed mostly at the DFT/B3P86 level of theory using a 6-31G** basis set,[20] unless otherwise noted. Geometry optimizations in solvent medium were obtained and solvation effects were implicitly incorporated using the self-consistent reaction field (SCRF) method with polarized continuum model (PCM),[47] in which the solvents are modeled as continuum of uniform dielectric constant ε. This homogeneous continuum introduces an average effect induced by solvent medium that describe the solute−solvent interactions. The solute molecule or solvation clusters are immersed in a cavity with appropriate shape embedded in an infinite polarizable dielectric medium. Compared to explicit models, the PCM method is less computationally expensive due to its simplicity but still describes well the critical properties of the solvent phase and so can often be used for typical problems such as chemical reaction, geometrical optimization and solvent-shift effect in molecular spectra in solution.[47]

Calculations on Dimer Binding Energy and Dimerization Constant. The Gibbs free energy of the dimerization reaction (ΔG_r) of an acid dimer is obtained by subtracting the total energy of monomer reactants ($G_{monomer}$) from that of dimer product (G_{dimer}). The final dimerization energies were then corrected with basis set superposition error (BSSE)[48] from counterpoise calculations.

$$\Delta G_r^{(gas)} = G_{dimer}^{(gas)} - 2G_{monomer}^{(gas)}$$

$$\Delta G_r^{(sol)} = G_{dimer}^{(sol)} - 2G_{monomer}^{(sol)}$$

where the superscripts *gas* and *sol* denote the *vacuo* (gas phase) and solution, respectively, in which the free energy calculations of monomer and dimer species are performed.

The dimerization constant is then calculated directly from this Gibbs free energy using the following thermodynamic relation

$$K_d = x_{dimer}/x_{monomer}{}^2 = e^{(-\Delta G_r/RT)}$$

where x is the concentration of the indicated species.

Entropy of Cavity Formation in Solutions and Thermal Correction to Gibbs Free Energy. In order to predict the Gibbs free energy of benzoic acid in solvents at elevated temperatures, we propose a technique to account for the thermal correction induced by the change in entropy. The gas-phase entropy $S^{(gas)}$ consists of several terms, including vibrational, electronic, translational and rotational entropies. Upon solvation, the total entropy decreases due to the formation of a cavity that accommodates the solute molecule.[49]

$$S^{(gas)} = S_{vib}^{(gas)} + S_{elec}^{(gas)} + S_{trans}^{(gas)} + S_{rot}^{(gas)}$$

$$S^{(sol)} = S_{vib}^{(sol)} + S_{elec}^{(sol)} + S_{trans}^{(sol)} + S_{rot}^{(sol)} + \Delta S_{solv}$$
$$= S_{vib+elec+trans+rot}^{(sol)} + \Delta S_{solv}$$

where $S^{(gas)}$ and $S^{(sol)}$ denote the total entropy of species in gas phase and solution; $S_{vib}^{(gas)}$, $S_{elec}^{(gas)}$, $S_{trans}^{(gas)}$, $S_{rot}^{(gas)}$ correspond to vibrational, electronic, translational and rotational entropies, respectively, in gas phase; $S_{vib}^{(sol)}$, $S_{elec}^{(sol)}$, $S_{trans}^{(sol)}$, and $S_{rot}^{(sol)}$ denote vibrational, electronic, translational and rotational entropies in solution, respectively; ΔS_{solv} = solvation entropy.

ΔS_{solv} can be regarded as entropy change due to the formation of void volume and the polarization of surrounding solvent medium.[49] In the PCM model, the solvation energy composes of electrostatic term ΔG_{el} and nonelectrostatic term, which includes energies of cavitation ΔG_{cav}, repulsion ΔG_{rep}, dispersion ΔG_{dis} and molecular motion contributions ΔG_{Mm}.[50] The major source inducing the change in entropy upon solvation in this work is taken as cavitation energy ΔG_{cav}, repulsion energy ΔG_{rep} and polarization energy ΔG_{pol} (which is part of the electrostatic term ΔG_{el}). If we assume that these energy terms have little contributions to enthalpy change[49] (i.e., the enthalpies of cavitation, repulsion and polarization are insignificant), the total entropy change ΔS_{solv} can be estimated as follows:

$$\Delta S_{solv} = \Delta S_{cav} + \Delta S_{rep} + \Delta S_{pol} = \frac{1}{T}(\Delta H_{cav} - \Delta G_{cav})$$
$$+ \frac{1}{T}(\Delta H_{rep} - \Delta G_{rep}) + \frac{1}{T}(\Delta H_{pol} - \Delta G_{pol})$$
$$\approx -\frac{1}{T}(\Delta G_{cav} + \Delta G_{rep} + \Delta G_{pol})$$

According to our calculations, it was noted that the major contribution to ΔS_{solv} in the equation above comes from ΔG_{cav} and even if the addition from ΔG_{rep} and ΔG_{pol} is neglected it would not induce significant changes in the final pK_d for a limited range of temperature.

The correction to Gibbs free energy of solute−solvent system from standard conditions (state 1) to a particular temperature (state 2) can be described in the following equations, assuming that the entropy of solvation is independent of temperature:

$$\Delta G_{1 \to 2} = G_2 - G_1 = (H_2 - T_2 S_2^{(sol)}) - (H_1 - T_1 S_1^{(sol)})$$
$$= \Delta H_{1 \to 2} + (T_1 S_{1(vib+elec+trans+rot)}^{(sol)}$$
$$- T_2 S_{2(vib+elec+trans+rot)}^{(sol)}) - \Delta T \Delta S_{solv}$$

In our computations, the thermal corrections to enthalpy and conformational entropy were derived from the frequency calculations with no scale factor applied.

3. RESULTS AND DISCUSSION

3.1. Dimer Structures, Hydration, and Solvation under Normal Conditions.
Numerous studies in literature suggested the possible coexistence of carboxylic acids in monomer, dimer, hydrate, and other complex forms.[22,51] In Figure 1, we depict the optimized structures of several benzoic acid aggregates in aqueous medium using PCM model. The configurations were selectedly chosen, based on suggestion from previous theoretical and experimental studies of carboxylic acid dimers.[1,24,27,49,52] The most common conformation evidenced by both experiments and theoretical calculations is the cyclic dimer that has two hydrogen bonds formed by two carboxyl groups of partner acids (I).[1] Other possible dimer structures are the open dimer, in which the double hydrogen bonds come from the same carbonyl group in of one acid molecule (II) and the side dimer, in which the OH group of the second acid does not participate in hydrogen bonding (III).[52] When acid molecules are surrounded by water, the hydrates could be formed. In a water-rich environment, the monomer hydrate (IV) could be less feasible, since one might argue that the water here would be expected to form the hydrogen bonding with
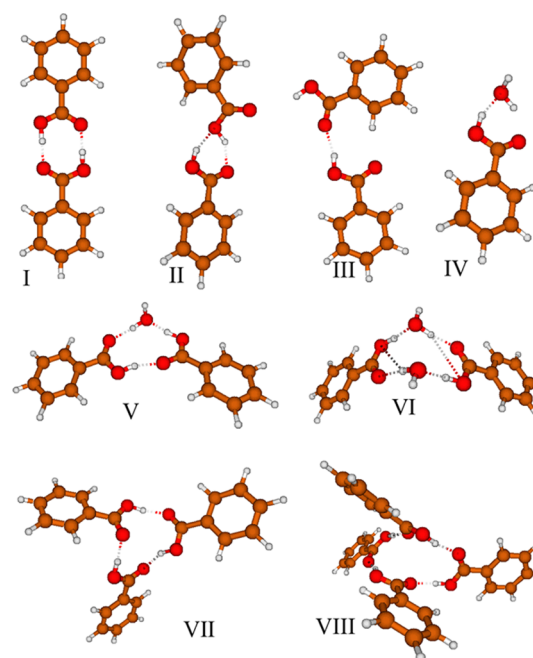

Figure 1. Optimized structures of studied benzoic acid clusters (dimers, hydrates, trimer and tetramer) obtained for aqueous solution, using the PCM model. C atoms are denoted in gray, O in red, and H in white.

other waters as well, instead of forming a close structure with the acid. However, configuration IV was added into our collection to test the idea that the stronger acid molecule would tend to bind to another acid, compared to binding to another water. Even the clustering of the acid molecule with more than one water molecules is possible; in this work we pay more attention to the hydration of acid in the dimer configurations rather than in its monomer form, assuming that the formation of dimer is the center of our work here. The dimer hydrates (V and VI) were therefore selected, according to Chocholousova et al.'s theoretical investigation of acetic acid. In addition, highly aggregated configurations, such as trimer (VII) and tetramer (VIII) were also included to make sure the multiple clustering of more than two acid molecules was not ignored in this study.

As is known to occur in aqueous solution, the acid may dissociate to produce its conjugate ion (base) and proton. However, the conjugate base will be less equipped for dimer/aggregate formation due to the loss of proton-donating capacity from the carboxylic acid group. At the same time, one could consider the formation of aggregates containing the conjugate base form, while remembering that the computation of ionization energies is rather complex, especially when one wishes to extend to a variety of solvents. For this reason, such complexes are considered to be beyond the scope of the present paper. In fact, we have addressed this issue in a separate work, currently in preparation.[53]

The internal energy, enthalpy, and Gibbs free energy of benzoic acid dimer formation in different structures are collected in Table 1. In general, the likelihood for formation of benzoic acid clusters decreases in the order: gas phase > benzene > aqueous water. In other words, it is more energetically favorable to form the complexes in isolated systems (gas phase) than in any solvent. The ΔE calculations also indicate that hydrogen bonds are stronger in gas phase than in solutions.

Table 1. Internal Energy, Enthalpy, and Gibbs Free Energy of Dimerization in Gas Phase, Benzene Solvent, and Aqueous Solution

	ΔE, kcal/mol			ΔH, kcal/mol			ΔG, kcal/mol		
	gas	benzene	water	gas	benzene	water	gas	benzene	water
I (cyclic dimer)	−18.24	−16.00	−13.48	−17.52 (−16.2[a])	−15.34	−12.91	−6.06	−4.03	−1.70
II (open dimer)	−7.68	−6.32	−5.02	−6.45	−5.12	−3.86	3.55	4.85	6.06
III (side-on dimer)	−7.76	−6.51	−5.14	−7.01	−5.79	−4.49	4.65	5.83	7.07
IV (monomer monohydrate)	−11.84	−10.02	−8.00	−10.03	−8.28	−6.42	−0.13	1.59	3.22
V (dimer monohydrate)	−26.07	−22.62	−18.68	−23.61	−20.27	−16.48	−4.15	−0.99	2.92
VI (dimer dihydrate)	−36.19	−31.51	−26.30	−32.33	−27.78	−22.77	−3.79	0.91	6.27
VII (trimer)	−22.58	−19.21	−15.50	−20.74	−17.41	−13.74	0.27	3.69	7.41
VIII (tertamer)	−30.57	−26.06	−21.42	−27.68	−23.22	−18.66	5.02	9.53	13.89

[a]Experimental.[35]

According to calculated formation energies ΔE, strong hydrogen bonds are found in several configurations. However, when big clusters are formed an entropy loss is expected following the decrease in translational and rotational degrees of freedom.[21] For instance, the $T\Delta S$ entropy contributions are approximately −10 kcal/mol and −20 kcal/mol in dimerization and trimerization processes. Because of the large entropy loss, only selected complex structures could be formed and stabilized. It suggests that the cyclic dimer (I) is always more stable than any other noncyclic dimer forms (II and III), regardless of the environment where they are found. Several authors proposed the stepwise mechanism of acetic acid dimerization in which the acyclic dimer is an intermediate step in formation of the cyclic dimer.[23]

In addition, it is shown by our calculations of Gibbs free formation energy that dimer monohydrate V and dimer dihydrate VI are stable complexes in gas phase in case of water availability. This observation is consistent with the study of Chocholousova et al. on stabilization energy of hydrated acetic acid dimers in gas phase.[27] However, it was indicated that cyclic dimer is the only stable structure in solution, according to ΔG values and this conforms with Fuji et al.'s investigation, which stated that unhydrated dimers were more stable than the water bridged acid dimers in solvents.[33] Besides the B3P83/6-31G** functional that was used uniformly throughout this work, an additional set of simulations was also performed to accounts for the dispersion correction to the first-principles calculations. However, it was shown that the energetic ordering of different configurations is the same with what presented in Table 1.

In most of the cases, the cluster formation of benzoic acids results in the reduction of dipole moment, except for open dimer and monomer monohydrate (Table 2). The double hydrogen bonding in cyclic dimer results in a cancellation of the total dipole moment and this, therefore, implies that the cyclic structure will be more stable in a nonpolar solvent. The active hydrogen-bonding capability and its dipole in the polar functional groups of the open and side dimers are responsible for stronger interactions with polar solvents,[20,21] which correspond to a higher contribution to electrostatic energy term in total free energy of solvation. While cyclic dimer has a zero dipole moment, the open dimer II possesses the largest dipole moment compared to others (see Table 2). The dipole moment of species, in general, increases when changing from low to high dielectric environments.

It is shown in Table 3 that the solvation process is more thermodynamically favorable in water solution than in benzene solvent. As described earlier, the solvation energy is composed

Table 2. Dipole Moment (Debye) Calculated for Different Acid Structures in the Gas Phase, Benzene Solvent, and Aqueous Solution

structures	gas phase	benzene	water
acid monomer	1.94	2.20	2.53
I	0.009	0.012	0.002
II	3.50	3.95	4.77
III	1.82	1.71	1.88
IV	2.14	2.36	2.25
V	1.53	1.77	1.87
VI	1.16	1.66	1.70
VII	1.58	1.59	2.07
VIII	1.43	1.57	1.91

Table 3. Enthalpies and Gibbs Free Energies of Solvation in Benzene Solvent and Aqueous Solution under Normal Conditions[a]

	ΔH, kcal/mol		ΔG, kcal/mol	
	benzene	water	benzene	water
monomer	−2.12	−4.75	−2.16	−4.82
I	−1.03	−2.44	−1.15	−2.64
II	−1.46	−3.45	−1.51	−3.57
III	−1.51	−3.49	−1.57	−3.62
IV	−2.46	−5.71	−2.53	−6.06
V	−1.50	−3.47	−1.63	−3.58
VI	−1.94	−4.54	−1.90	−4.37
VII	−1.01	−2.41	−1.02	−2.44
VIII	−1.01	−2.49	−1.03	−2.60

[a]The values for complexes are rescaled to be per benzoic acid unit (divided by the number of acid molecules).

of electrostatic and nonelectrostatic terms and, correspondingly, the solvation effect is determined by a number of factors including dipole moments, cavity volume and surface areas of the solute species.[21] Water is more polar and active than benzene, therefore it induces a more pronounced solute–solvent interaction and a larger amount of energy is released as a result of solvation.

The increase in the absolute value of the solvation energies of multimolecule complexes (dimers, hydrates, oligomers, etc.) is partially due to their large volumes and surface areas. However, the total energy freed during the solvation of a complex is always below the sum of those released by the solvation of corresponding individual species. This is in agreement with other calculations on hydrogen bonding of acetic acid with different organic compounds.[21] In other words, benzoic acid

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favors the solvation in unassociated monomer form than in cluster forms (Table 3).

Table 4 presents the dimerization constant values of different dimers and clusters in gas phase, benzene solvent and aqueous

Table 4. Dimerization Constants of Benzoic Acid in the Gas Phase, Benzene Solvent, and Aqueous Solution (Room Temperature)

dimer structures	$\log(K_d)$		
	gas phase	benzene	water
I	4.44	2.96	1.24
II	−2.61	−3.56	−4.44
III	−3.41	−4.28	−5.18
IV	0.09	−1.17	−2.36
V	3.04	0.73	−2.14
VI	2.78	−0.67	−4.60
VII	−0.20	−2.70	−5.44
VIII	−3.68	−6.99	−10.19

environment. In gas phase, cyclic dimer (I) and hydrated dimers (V and VI) have relatively higher $\log(K_d)$ compared to others. This indicates that if acid molecules are surrounded by a certain amount of water in the vapor phase, those conformers I, V, and VI will be main structures to be formed. However, in solution the cyclic dimer is almost the dominant complex and other conformers exist in only insignificant quantities. Furthermore, for low concentrations of water molecules in the nonaqueous solution phases, entropic factors will tend to disfavor the hydrated dimer forms.

On the basis of calculated dimerization constants, one is able to predict the coexistence profile of free acid monomer, dimers and other oligomers. As mentioned earlier, we will only pay attention to unassociated acid monomer, cyclic dimer I, dimer monohydrate V and dimer dihydrate VI because the K_d values of the ther conformers are too low, which suggests that they will only be present in miniscule (negligible) quantities. In aqueous solution, the low $\log(K_d)$ value of cyclic dimer indicates that its formation is possible but quite limited. In other words, the formation of benzoic acid dimers and clusters are not energetically favorable in dilute water medium. This is consistent with the conclusions made for formic and acetic acids; namely, that formic and acetic acid cyclic dimers are not stable in water solution.[20,27]

Our predictions regarding the relative distribution of benzoic acid dimer complexes in the benzene solvent are shown in Table 5. At an initial acid concentration of 1% wt or 0.08 mol/kg, and selecting some nominal water concentrations up to 5% wt, our calculations suggest that there is around 90% of benzoic acid existing in the double H-bond structure, 8% of benzoic acid staying in monomer form and less than 1.5% of benzoic acid present in other dimeric structures. Since the hydrated dimers are formed in minute quantities in benzene solution, the water concentration turns out to be a trivial factor. This finding indicates that hydration of carboxylic acid appears to be relatively inconsequential in organic solvents and provides a quantitative analysis of the coexistence profile of dimers, trimers and oligomers in solution.[33,51] Several authors have maintained that the monomer mono- and dihydrate and dimer monohydrates of benzoic acid are present in the organic phase.[12,33] Iscan and co-workers suggested that benzoic acid monomer monohydrate is dominant at high temperatures.[13] Some osmometric studies reported the formation of trimers in

Table 5. Calculations on Distribution of Benzoic Acid in Monomer and Dimer Forms in Benzene Solvent at Room Temperature (at Acid Concentration $C_a \approx 1\%$ wt or 0.08 mol/kg)

benzoic acid in benzene solvent	water concentration C_w, % wt.			
	5.0	1.0	0.5	0.1
unassociated acid monomer, %	8.39	8.43	8.44	8.44
acid in cyclic dimer I, %	90.19	91.29	91.42	91.52
acid in monohydrate dimer V, %	1.29	0.26	0.13	0.026
acid in dihydrate dimer VI, %	0.12	5.0×10^{-3}	1.3×10^{-3}	5.0×10^{-5}
amount of free water, %	99.97	99.98	99.98	99.98

addition to dimers of carboxylic acids in solution.[51] However, many other authors just assume monomer and cyclic dimer to be the principal species of the dimerization equilibrium in their study.[1,3,10] Our calculated dimerization constants indicate that the cyclic dimer is the dominant complex also in aqueous solution. In other words, even in infinitely dilute water environment, the formation of hydrated dimers is very limited. Furthermore, our results do not support the formation of substantial amounts of the trimer phase.

Following the finding above, the cyclic dimer (structure I, with double H bond) will be considered as the primary structure that forms in organic solvents, and we will neglect all other cluster conformers while dealing with benzoic acid in solution to this end.

A more competent method to find the possible local minima for cluster formation is through a dynamic aggregation approach without assuming any initial chemical binding and this approach was already successfully used by several authors.[54] This method also allows the estimation of kinetic barriers between local energy minima. However, the kinetic study is beyond the scope of this work, which focuses on the thermodynamics of stable states.

3.2. Further Examination of the Role of Solvent Effects on the Dimerization of Benzoic Acid. Because of the electrostatic nature of hydrogen bonds through which dimers are associated,[21] the dimer stability is influenced by the dielectric properties or polarity of the surrounding environment in which they are found. In Figure 2 dimerization constants of cyclic benzoic acid dimer as a function of solvents at normal temperature are compared to Fuji's data obtained from partition and solubility measurements[33] and I'Haya's data obtained from infrared spectroscopy.[37] The solvents with a larger dielectric constant corresponds to lower $\log(K_d)$ values. This trend of dimerization with respect to solvent was quite well documented. It was explained by the fact that in an active dielectric environment, strong solute−solvent interactions such as dipole or hydrogen bonding would minimize the association of monomer species to each other.[55] It was also suggested by Aquino et al. that some types of hydrogen bonds are weaker in polar solvents than in apolar media.[21]

However, the $\log(K_d)$ do not decrease linearly with increasing dielectric constants ε. It was shown that dimerization constants change by several orders of magnitude within the range of of ε considered. On going to higher dielectric constants, the variation of K_d becomes more flat (Figure 2a).
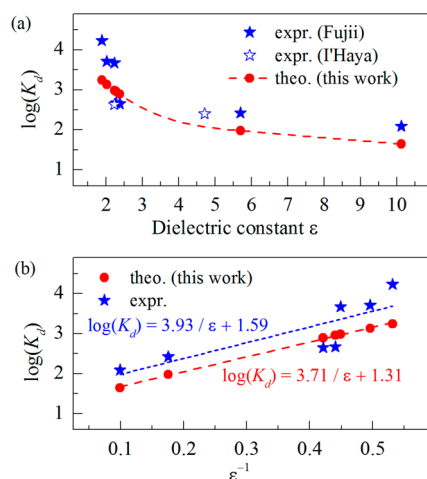
Figure 2. Dimerization constants of cyclic benzoic acid dimer under solvent effects (under normal conditions).

This could be related to the contribution from electrostatic interaction that is inversely proportional to the medium's permittivity, according to Coulomb's law. For that reason, a variation at low permittivity induces more change to electrostatic energy than it does at high permittivity. In Figure 2b, we plot our $\log(K_d)$ results with respect to the inverse of ε and we find that the resulting linearity confirms this hypothesis. The fitting coefficients such as slope and intercept terms are shown on the graph. The former term characterizes the contribution from the electrostatic interaction and also defines how strongly the dimerization is affected by the solvent's permittivity. This term yielded by our calculations (3.71) is close to that obtained from the Fujii data (around 5% of error). In other words, this work is able to reproduce well the dielectric dependence of dimer behavior. The latter term (intercept term in $\log(K_d)$ fitting equation) represents the contribution from all other nonelectrostatic interactions. This term is independent of solvent's dielectric constant and the difference between the experimental and theoretical values only describes the shifting between two sets of data, rather than the sensitivity of dimerization upon solvent's change.

Spectroscopy is a frequently used method to study the dimerization phenomenon in organic species.[56] A pronounced modification is expected in the position and absorptivity in absorption spectra when monomers associate into dimers. As the result of symmetric and antisymmetric combinations of vibration of two monomers, there are more vibrational modes

in the dimer complex. However, the symmetrical vibrations in general either do not cause absorption or have weak intensity.

Table 6 documents the calculated infrared resonant frequencies of C=O stretch (also the same as the in-plane C–O–H bend), which is usually the dominant mode in determining the monomer and dimer species. A red shift of carbonyl vibration $\nu_{C=O}$ to lower frequency is observed once the dimer is formed and this was also found by several authors in their investigation on dimer systems of various organic compounds.[56,57] Because of the hydrogen bonding between hydroxyl and carbonyl groups in dimer complex, the C=O bond distance increases (by about 0.02 Å) and this corresponds to a decreased force constant and bond strength. Similarly, a redshift in C=O vibration is expected with respect to the increase in the environment's permittivity. This trend was also reported in the self-association of acetic acid in some organic solvents.[55] As shown in Table 6, the C=O bond is weaker in strong dielectric medium due to a larger interaction with the active solvent.

3.3. Temperature Dependence of the Dimerization Equilibrium. *3.3.1. Benzoic Acid Dimer in Benzene.* The temperature effect is incorporated[59] into our calculations for the dimerization Gibbs' free energy by accounting for the thermal correction and the entropy of solvation as described in section 2. Figure 3 compares our theoretical dimerization
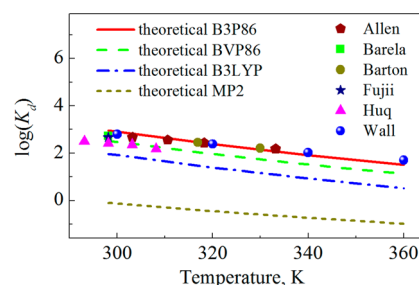

Figure 3. Temperature dependence of dimerization constants $\log(K_d)$ for cyclic benzoic acid dimer in benzene solvent, compared with experiments.

constant calculations for benzoic acid in benzene solvent up to the boiling point of benzene with experimental data reported by Allen, Fujii, Barela, Barton, Huq, and Wall et al.[1,12,31,32,34−36,44] Higher temperatures favor the dissociation of benzoic acid dimers; a fact which is demonstrated by a decline of association constants in both theoretical and experimental measurements. It was suggested that hydrogen bonds are weakened and its

Table 6. Calculated Bond Length and Infrared Resonant Mode of C=O Stretch in Benzoic Acid Monomer and Cyclic Dimer at Normal Conditions (a Scaling Factor of 0.9558 Was Applied to Vibrational Frequency for the B3P86 Functional[58])

		$l_{C=O}$, Å		$\nu_{C=O}$, cm^{-1}	
solvents	ε	monomer	dimer	monomer	dimer
gas phase	1.00	1.213	1.237	1759 (1752[a])	1698 (1709[a])
n-hexane	1.88	1.215	1.238	1748	1686
cyclohexane	2.01	1.215	1.238	1747	1686
carbontetrachloride	2.23	1.215	1.238	1745 (1737[b])	1684 (1692[b])
benzene	2.27	1.215	1.238	1745	1684
toluene	2.37	1.215	1.238	1744	1683
chlorobenzene	5.69	1.216	1.239	1734	1672
dichloroethane	10.12	1.217	1.239	1730	1668

[a]Experimental.[56] [b]Experimental.[37]

length increases with increasing temperature.[60−62] Furthermore, entropy will favor the monomer forms as increasingly high temperatures are applied.

For a comparison between various levels of theory, the results obtained with BVP86, B3LYP, and MP2 were also added in Figure 3. MP2 appears to underestimate the hydrogen bonding. Therefore, dimerization constants yielded by this method are low. B3P86 produces the highest K_d among the methods studied and matches well with the data obtained by experiments. The trends of $\log(K_d)$ variations with respect to temperature predicted by all theoretical levels are relatively parallel with those measured experimentally up to the boiling point of benzene.

If the system is maintained in the liquid phase at higher temperatures (for example, by the application of appropriate pressure controls), the difference between the extrapolation of Wall et al. data and our theoretical B3P86 prediction at 600 K is less than one unit of $\log(K_d)$. It is noteworthy to mention that this corresponds to an error of less than 1.36 kcal/mol in ΔG calculation, which is well below the accuracy expectation and error limit allowed by the present computations.

3.3.2. Benzoic Acid Dimer in Other Solvents. The calculations performed for benzene solvent are quite encouraging and we next studied the thermal effect on benzoic acid dimers in various solvents representing different solute-acid interactions (Figure 4). In going from heptane to higher
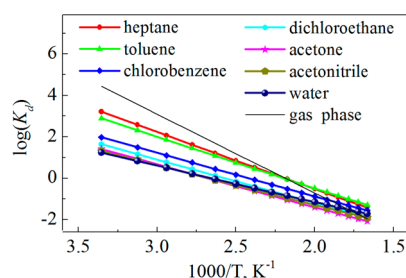

Figure 4. Log(K_d) of cyclic benzoic acid as a function of temperature and solvation environments. The dimerization constant values calculated for organic solvent and aqueous solution are obtained with liquid phase assumption at all temperatures.

dielectric environments such as acetonitrile or aqueous solution, there is a progressive decrease in $\log(K_d)$ and in H bonding strength of benzoic acid dimers, which corresponds to the tendency of the dimer to dissociate. Neither temperature nor solvent dependence of benzoic acid dimerization was observed as a linear change. Instead, the dimerization behavior with respect to temperature could be described in a general form as $\log(K_d) = -A/T + B$, where A factor describes its temperature sensitivity and B characterizes the dimer strength at normal conditions. The enthalpy of formation ΔH could be obtained directly from coefficient A. It was seen that the dimer breakup is more strongly dependent on temperature in low dielectric environments than in stronger dielectric solvents, which corresponds to a decrease in the ΔH values. It also means that the solvent effect on dimerization is less pronounced at high temperatures; this last point is evident by the near-convergence of $\log(K_d)$ values around 500−600 K.

The dimerization of benzoic acid in Figure 4 is investigated up to temperatures that exceed the boiling points of the corresponding solvents. This is meaningful when dealing with processes in which the solute−solvent system is maintained in

the liquid phase. Otherwise, at the boiling of solvent molecules at such elevated temperatures, the dimerization behavior of benzoic acid will become equal to (or very close to) that of the gas phase; i.e., there will be a discontinuity that occurs at the boiling point for the dimerization behavior as a function of temperature.

It should be kept in mind that the electrostatic solute−dielectric interactions described in the PCM model rely on a continuous medium in which the internal properties such as dielectric constant and thermal expansion coefficient are assumed, herein, to be independent of temperature. In reality, these parameters will all be functions of temperature. In addition, the thermal entropic correction introduced earlier to correct the Gibbs free energy at high temperature in our technique has an assumption that the change of solvation entropy with respect to temperature elevation is negligible. Therefore, the interpretation of the dimer behavior in solution at high temperature extent should be taken with these caveats kept firmly in mind.

3.3.3. Prediction of Dimer Dissociation Temperatures in Various Solvents. A monomer−dimer equilibrium profile can be obtained under given conditions of total acid concentration, temperature and surrounding solvents, as well as the computed dimerization constants. It was suggested earlier that cyclic structures are the only dominant dimer to be formed in solution; therefore, all other conformers could be neglected. Figure 5 details the temperature profile of acid dissociation and
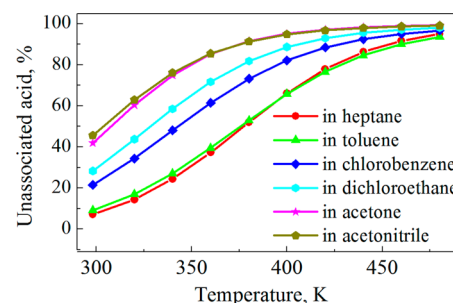

Figure 5. Estimated percentage of unassociated benzoic acid monomer as a function of temperature in different solvents. Data are obtained at benzoic acid concentration of approximately 1% wt in solution.

breakup processes of benzoic acid dimer in different solvents. According to these calculations, at an initial concentration of 1% wt, approximately 90% of benzoic acid molecules are associated in heptane and toluene, while about 50% are associated in acetone and acetonitrile at normal conditions. The dissociation process takes place extensively in the range 300−400 K, and there is an upper temperature limit above which essentially no acid dimers could be found in any solution. The dimer breakup temperatures are lower in higher dielectric media, i.e., given equal conditions; the formation of dimer in higher dielectric solution is less favorable.

4. CONCLUSION

A technique of thermodynamic extraction on solvation entropy and enthalpy was adopted and applied to study hydrogen bonding in dimerization phenomenon of carboxylic acids in solution at elevated temperatures. Benzoic acids form strong hydrogen bonds with each other in different complexes but the cyclic dimer is the most stable configuration. When acid molecules are in contact with water vapor in the gas phase, the

formation of dimer mono- and dihydrate are possible. However, the cyclic dimer is the principal structure to coexist with the unassociated acid monomer in solution.

The dielectric constant is the primary factor to determine the solvent effect on acid dimerization, in which $\log(K_d)$ values could be described as a linear function of the inverse of dielectric constant. Strong dielectric media induce strong interactions and consequently reduce the hydrogen bonding strength of dimers.

The technique used in this work also reproduces well the thermal effect of dimerization process, in which high temperature favors the dissociation of dimers into monomer acid species. The temperature dependence of dimer dissociation is less pronounced in high dielectric solvent than in low dielectric environment.

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Notes
The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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