Structure of the Boronic Acid Dimer and the Relative Stabilities of Its Conformers

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Despite the widespread use of boronic acids in materials science and as pharmaceutical agents, many aspects of their structure and reactivity are not well understood. In this research the boronic acid dimer, $[HB(OH)_2]_2$, was studied by second-order Møller−Plesset (MP2) perturbation theory and coupled cluster methodology with single and double excitations (CCSD). Pople split-valence 6-31+G*, 6-311G**, and 6-311++G** and Dunning−Woon correlation-consistent cc-pVDZ, aug-cc-pVDZ, cc-pVTZ, and aug-cc-pVTZ basis sets were employed for the calculations. A doubly hydrogen-bonded conformer (**1**) of the dimer was consistently found to be lowest in energy; the structure of **1** was planar (C_{2h}) at most computational levels employed but was significantly nonplanar (C_2) at the MP2/6-311++G** and CCSD/6-311++G** levels, the result of an intrinsic problem with Pople-type sp-diffuse basis functions on heavy atoms. The dimerization energy, enthalpy, and free energy for the formation of (**1**) from the exo−endo conformer of the monomer were −10.8, −9.2, and +1.2 kcal/mol, respectively, at the MP2/aug-cc-pVTZ level. Several other hydrogen-bonded conformers of the dimer were local minima on the potential energy surface (PES) and ranged from 2 to 5 kcal/mol higher in energy than **1**. Nine doubly OH-bridged conformers, in which the boron atoms were tetracoordinated, were also local minima on the PES, but they were all greater than 13 kcal/mol higher in energy than **1**; doubly H-bridged structures proved to be transition states. MP2 and CCSD results were compared to those from the BLYP, B3LYP, OLYP, O3LYP, PBE1PBE, and TPSS functionals with the 6-311++G** and aug-cc-pVTZ basis sets; the PBE1PBE functional performed best relative to the MP2 and CCSD results. Self-consistent reaction field (SCRF) calculations predict that boronic acid dimerization is less favorable in solution than in vacuo.

Introduction

Organoboronic acids, which contain the -$B(OH)_2$ functional moiety, are powerful and versatile reagents for carbon−carbon bond formation[1−4] and have been widely used for the synthesis of compounds of pharmaceutical interest.[5−7] These acids also serve as chemical sensors for recognizing 1,2- and 1,3-diols,[8−15] as affinity ligands in chromatographic protocols,[16−20] as inhibitors in serine proteases and β-lactamases,[2,21−23] and as building blocks in the development of novel materials.[24−28] For example, orthoboric acid- [$B(OH)_3$-] based nanometer- and micrometer-sized tubes, tips, and rods have been reported, and their application in submicrometer-scale devices has been discussed.[25]

Despite the rapidly increasing use of boronic acids, many aspects of their molecular structures and reaction energetics are not well understood. A survey of crystal structures containing the C−$B(OH)_2$ structural moiety, deposited in the Cambridge Structural Database (CSD),[29,30] shows that organoboronic acids often form hydrogen-bonded dimers.[26] For example, the asymmetric unit in the X-ray crystal structure of phenylboronic acid (PBA) consists of two independent molecules of the acid, each of which has the hydroxyl hydrogen atoms in the expected exo−endo arrangement, linked by a pair of H−O···H bonds.[31] This hydrogen-bonding pattern, in which the boron atoms have a planar trigonal coordination, has also been observed in the crystal structures of other arylboronic acids[1,26−29,32] Interestingly, this motif is similar to that found in dimers formed from the -$CONH_2$ and -COOH functional groups,[33−35] where so-called resonance-assisted hydrogen bonding (RAHB) is an important factor.[36,37] Other hydrogen-bonding patterns, however, have also been observed with organoboronic acids, for example, the crystal structure of 5-pyrimidylboronic acid involves B−O−H···N bonds with ring nitrogen atoms; the nearly centrosymmetric hydrogen-bonding motif that is typically found with other arylboronic acid dimers is not evident in this structure.[38]

Few in-depth computational studies of boronic acid dimers have been reported in the literature. In a 1996 investigation of the hydrolysis of diborane, B_2H_6, McKee[39] reported that the lowest-energy structure of the dimers of boronic acid, $[HB(OH)_2]_2$, and boric acid, $[B(OH)_3]_2$, were planar with C_{2h} symmetry at the MP2(FC)/6-31G* computational level, although no other *stable* forms of these dimers were given by McKee. In the present article, we report results from a high-level computational exploration of the potential energy surface (PES) of the boronic acid dimer, using second-order Møller−Plesset

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perturbation theory[40] and coupled-cluster calculations[41−44] with Pople split-valence[45,46] and Dunning−Woon correlation-consistent basis sets.[47−50] A variety of hydrogen-bonded, OH-bridged, and H-bridged structures have been identified as stationary points on the PES.

Computations using ab initio MP2 or CCSD methodology for more extended organoboronic acids are not yet practical with high-quality basis sets. Density functional theory (DFT) is a viable, economical alternative to these ab initio methods, if its reliability in describing various aspects of boronic acid chemistry can be established; unfortunately, there are already indications that the popular BLYP and B3LYP functionals have problems predicting the strength of B−O and B−N dative bonds.[51−55] To address the DFT reliability issue with respect to the dimerization of boronic acids, we have also compared our MP2 and CCSD results with those obtained with the BLYP, B3LYP, OLYP, O3LYP, PBE1PBE, and TPSS functionals.

Computational Methods

Equilibrium geometries for the structures in this article were obtained by second-order Møller−Plesset (MP2)[40] and coupled cluster calculations with single and double excitations (CCSD);[41−44] the frozen core approximation was employed in most cases. Pople 6-31+G*, 6-311G**, and 6-311++G**[45,46] and Dunning−Woon cc-pVDZ, cc-pCVDZ, aug-cc-pVDZ, cc-pVTZ, and aug-cc-pVTZ basis sets[47−50] were used throughout. Frequency analyses were performed analytically or numerically, depending on the computational efficiency, to confirm that the optimized structures were local minima on the PES and to correct dimerization enthalpies and free energies to 298 K. Dimer stabilization energies (SE) were computed by the supermolecule approach, SE = $E_{\mathrm{dimer}} - \Sigma E_{\mathrm{monomers}}$, and corrected for basis-set superposition errors (BSSEs) using the counterpoise procedure. Calculations were performed with the GAUSSIAN 03[56] or ACESII[57] programs.

DFT geometry optimizations were performed with the following functionals: BLYP and B3LYP, which incorporate the dynamical functional of Lee, Yang, and Parr (LYP)[58] coupled with Becke's pure DFT exchange functional (B);[59] OLYP[60] and O3LYP,[61] constructed from the novel OPTX exchange functional; PBE1PBE,[62,63] which makes use of the one-parameter GGA PBE functional[64] with a 25% exchange and 75% correlation weighting; and TPSS, the nonempirical metageneralized gradient approximation (MGGA) functional recently developed by Staroverov et al.[65]

Self-consistent reaction field (SCRF) calculations were carried out with the integral equation formalism (IEF) polarizable continuum model (PCM)[66−70] as implemented in GAUSSIAN 03[56] with the aprotic solvents carbon tetrachloride ($\epsilon = 2.228$) and acetonitrile ($\epsilon = 36.64$). Boronic acids may be converted to their cyclic ester forms in such aprotic solvents,[71,72] and it is of interest to assess the effects of these solvents on the HB-$(OH)_2$ dimer PES.

Results and Discussion

$HB(OH)_2$ Monomer. Relatively little is known experimentally about the boronic acid monomer, although it has been detected by microwave spectroscopy as an intermediate in the pyrolysis of a mixture of diborane and water.[73,74] At all the MP2, CCSD, and DFT computational levels employed in this study, the lowest-energy form of the $HB(OH)_2$ monomer in vacuo was planar with the two hydroxyl groups in the exo−endo orientation (C_s)[38,75] (Figure 1); this is the same orientation of the hydroxyl groups that is found in the crystal structure of many arylboronic acids.[26,38] Planar conformers of $HB(OH)_2$, with the hydroxyl groups in an anti or a syn arrangement, were also local minima, only 1.0 (1.1) and 3.1 (2.4) kcal/mol higher in energy, respectively, than the exo−endo conformer at the MP2/aug-cc-pVTZ (CCSD/aug-cc-pVTZ) computational levels. Transition states for the conversion of the exo−endo conformer of HB-$(OH)_2$ to the corresponding anti and syn conformers were 10.5 (10.6) and 10.1 (10.3) kcal/mol, respectively, higher in energy than the exo−endo conformer at the MP2/aug-cc-pVTZ (B3LYP/6-311++G**) levels.

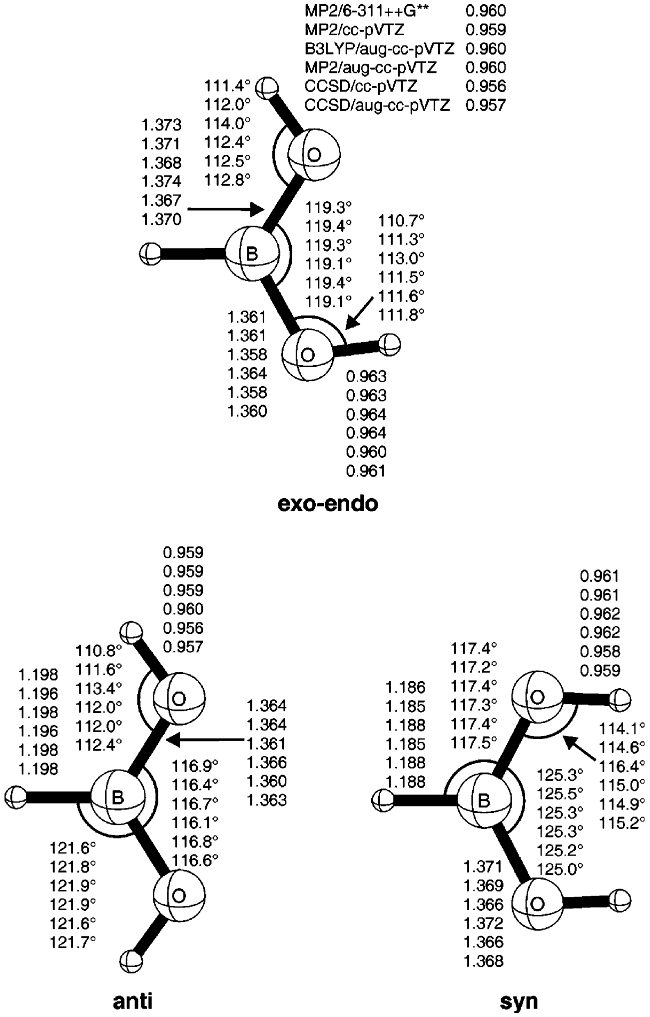

Figure 1. Selected gas-phase geometrical parameters of the optimized *exo−endo*, anti, and syn conformers of the $H{-}B(OH)_2$ monomer. Distances are given in angstroms, and angles are given in degrees.

The computed B−O distances, 1.364 (1.360) and 1.374 (1.370) Å in the exo−endo conformer at the MP2/aug-cc-pVTZ (CCSD/aug-cc-pVTZ) levels are in reasonable agreement with the experimental r_s(B−O) distance, 1.351 Å, for the related compound H_2BOH. The computed B−H distance, 1.190 (1.192) Å, is in good agreement with the reported experimental value of 1.197 Å for $HB(OH)_2$.[73,74] The MP2/aug-cc-pVTZ vibrational frequencies of the exo−endo conformer are listed in Table 1S of the Supporting Information; experimental vibrational data are not available for comparison. It should be noted that both the exo−endo and syn conformers of the monomeric unit have been observed in crystal structures of organoboronic acids.[1,26,31,76]

All three conformers of $HB(OH)_2$ were also optimized in the reaction fields of the aprotic solvents carbon tetrachloride and acetonitrile, by use of a continuum model at the MP2/aug-cc-

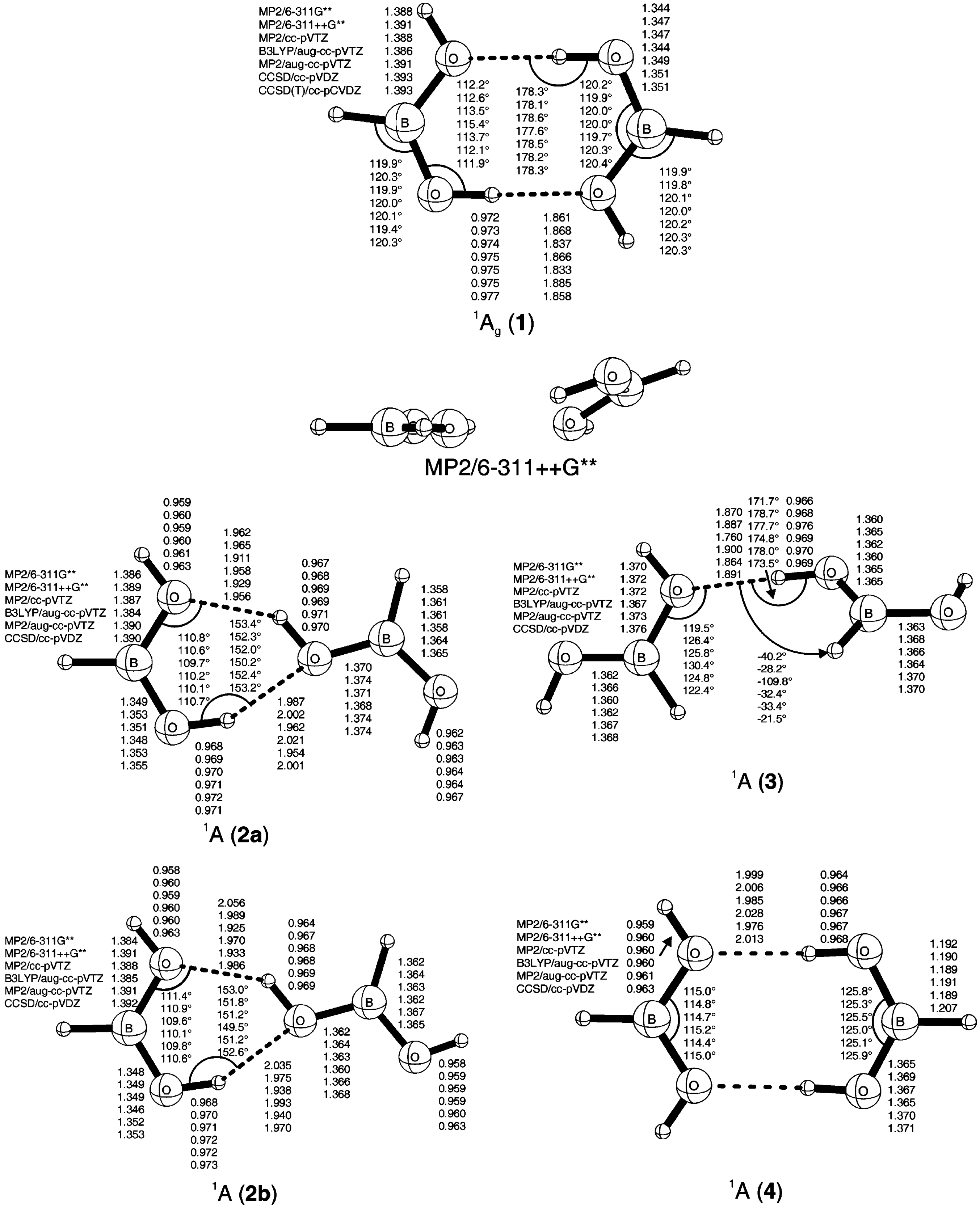

Figure 2. Selected gas-phase geometrical parameters of the optimized hydrogen-bonded conformers **1**−**4** of the $H(BOH)_2$ dimer. Distances are given in angstroms, and angles are given in degrees.

pVTZ level.[66−70] The computed dipole moment of the exo−endo form in vacuo, 1.51 D, is significantly smaller than the dipole moments of the anti and syn forms, 2.33 and 2.63 D, respectively, and thus, it is not surprising that energy differences among these three conformers are lower in CCl_4 ($\epsilon = 2.2$) than in vacuo: the exo−endo form remains lowest in energy in this solvent, but the anti and syn forms are only 0.7 and 2.5 kcal/mol higher in energy. In acetonitrile ($\epsilon = 36.6$), where the dielectric constant is much higher, the anti form is 0.1 kcal/mol *lower* in energy than the exo−endo form; the syn form is

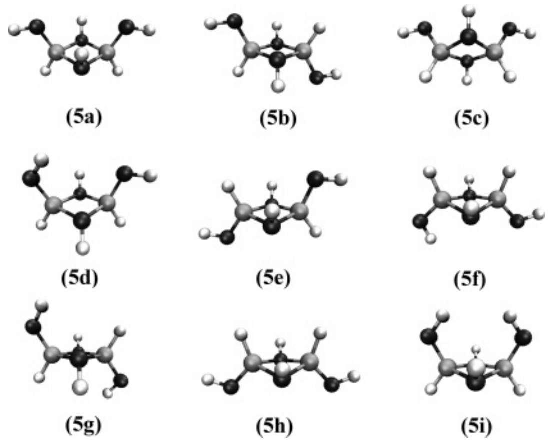

Figure 3. Optimized conformers of the OH-bridged conformers **5a**−**5i**.

only 0.9 kcal/mol higher in energy than **1**.[77] In CH_3CN, transition states for the conversion of the exo−endo conformer to the anti and syn conformers are 9.1 (8.9) and 9.2 (9.0) kcal/mol, respectively, higher in energy than **1** at the MP2/aug-cc-pVTZ (B3LYP/aug-cc-pVTZ) levels, ~1 kcal/mol lower than the corresponding values in vacuo.

$HB(OH)_2$ Dimer. An extensive B3LYP/6-31+G* conformational search of the $[HB(OH)_2]_2$ PES in vacuo was performed initially, and a rich variety of hydrogen-bonded, OH-bridged, and H-bridged stationary points were located, as seen in Table 2S. The planar, doubly hydrogen-bonded (C_{2h}) conformer (**1**) of this dimer, as described by McKee,[39] in which the hydroxyl hydrogens in both monomeric units are in the exo−endo form (Figure 2), was found to be lowest in energy at this level. However, two alternate doubly hydrogen-bonded conformers (C_s), **2a** and **2b**, in which one of the hydroxyl groups acts as both a hydrogen-bond donor and an acceptor in a six-membered ring motif, were only 2.5 and 3.4 kcal/mol, respectively, higher in energy than **1**; a singly hydrogen-bonded conformer (C_1), **3**, composed of two exo−endo monomeric units, was only 4.1 kcal/mol higher in energy than **1**; and a doubly hydrogen-bonded conformer (C_{2v}), **4**, that involves one syn and one anti monomeric unit, was 5.0 kcal/mol higher in energy than **1**. In addition, nine doubly OH-bridged structures **5a**−**5i** (see Figure 3) were also local minima on the PES, although they ranged from 19.6 to 30.2 kcal/mol higher in energy than **1**, and several doubly H-bridged diborane-like structures were identified as transition states at this computational level.

The aforementioned concerns about the reliability of the B3LYP functional to accurately model some aspects of boronic acid chemistry[51−55] prompted us to examine the PES of the $HB(OH)_2$ dimer using ab initio MP2 and CCSD methodology with more complete basis sets. The results of these computations provide more reliable values for the energy differences among the stationary points identified in the B3LYP/6-31+G* conformer search, establish a baseline from which to evaluate the performance of some currently available functionals in describing boronic acid dimerization, and thus guide the choice of functional to be used in studies of more complex organoboronic acids.

Ab Initio MP2 and CCSD Results. Relative energies of the local minima on the $HB(OH)_2$ dimer PES are listed in Table 1 at several MP2 and CCSD computational levels with both Pople and Dunning−Woon basis sets; selected geometrical parameters are shown in Figure 2. Consistent with our preliminary conformational search, the doubly hydrogen-bonded, C_{2h} conformer of **1** was found to be the lowest-energy local minimum at most MP2 and CCSD levels, for example, frequency analyses at the MP2/6-311G**, MP2/aug-cc-pVTZ, and CCSD/cc-pVDZ levels found that this planar conformer was a local minimum on the PES. Vibrational frequencies at the MP2/aug-cc-pVTZ level are listed in Table 1S of the Supporting Information.

Surprisingly, however, vibrational frequency analyses at the MP2(FC or FULL)/ 6-311++G**, MP2(FC or FULL)/6-311++G(df,pd), and CCSD/6-311++G** levels predicted that this planar conformer was a second-order transition state; on the other hand, at the MP2(FC)/6-311++G(2df,2pd) level the planar form was a local minimum. Relaxing symmetry constraints at the MP2/6-311++G** level, and reoptimizing the structure led to a significantly nonplanar, albeit still doubly hydrogen-bonded conformer, with C_2 symmetry, ~0.2 kcal/mol lower in energy than the corresponding planar form (Figure 2). Several attempts to locate *both* a stable C_{2h} and a stable C_2 conformer at the same computational level were not successful. To help resolve this structural issue, the planar form of **1** was also optimized at the CCSD(T)/cc-pCVDZ computational level and a frequency analysis showed it to be a local minimum. Thus, it appears that the 6-311++G** basis set, in conjunction with MP2 and CCSD methodologies, gives an erroneous nonplanar geometry for **1**; including a sufficient number of additional polarization functions, however, seems to remedy the problem.

A variety of additional MP2 optimizations with different Pople-type basis sets clearly showed that the origin of this nonplanarity of **1** was a direct result of including sp-diffuse functions on the heavy atoms in the basis set, rather than any inherent problem with the split-valence nature of the basis set. In Figure 4 we show the results of four optimizations of **1** at the MP2/6-31+G* level in which either an s- or a p-type diffuse function was deleted from the basis set. These calculations suggest that the nonplanarity of **1** at this computational level is the result of an unfavorable interaction between a diffuse p-orbital on the boron atom of one monomer and a diffuse s-orbital on an oxygen atom of the second monomer. Considering the weak nature of such van der Waals interactions, the corresponding energy change is small (~0.02 kcal/mol) and thus it is difficult to quantify the magnitude of the individual orbital contributions. To the authors' knowledge, this effect has not previously been reported in the literature.

As can be seen from Figure 2, the geometrical parameters calculated for **1** at the MP2 and CCSD computational levels employed in this study are in relatively good agreement, although the length of the H···OH bonds are somewhat sensitive to both the methodology and basis set. Interestingly, the two computed hydrogen H···OH bond distances in **1**, which range from ~1.83 to 1.88 Å at the different levels, are significantly shorter than the corresponding values from the X-ray crystallographic study of PBA, 1.96(3) and 2.07(3) Å. For comparison, the H···OH hydrogen bond distance in the water dimer is 1.948 Å.[78] The two calculated H···OH bond angles in vacuo, ~178.5°, are close to those reported for PBA, 176(3)° and 174(3)°.[31] These structural results suggest that hydrogen bonding in the dimeric unit of the crystal structure of PBA is somewhat weaker than hydrogen bonding in the corresponding gas-phase dimer, in which there are no interactions between dimeric units. The calculated values of the two distinct B−O distances in **1** differ by ~0.04 Å at all the MP2 and CCSD computational levels employed, whereas the corresponding difference in the exo−endo form of the monomer is only ~0.01 Å; compare Figures 1 and 2. This is in contrast to what is observed when resonance

TABLE 1: Relative Energies of the Optimized Boronic Acid Dimer Conformers at Various MP2 and CCSD Computational Levels[a]

conf	sym	6-311G**	6-311++G**	cc-pVDZ	cc-pVTZ	aug-cc-pVDZ	aug-cc-pVTZ
				(A) MP2			
1	C_{2h}	0.00 (0.00)	0.00 (0.00)[b,c]	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)
2a	C_s	2.86 (2.53)[b]	2.37 (3.09)	2.61 (2.08)[b]	2.54 (2.22)[b]	2.46 (2.22)	2.58 (2.29)
2b	C_s	3.97 (3.60)	3.31 (3.24)[b]	3.61 (3.15)[b]	3.18 (2.84)	3.05 (2.81)	3.06 (2.74)
3	C_1	4.68 (4.22)	3.94 (4.27)	4.43 (3.16)	4.45 (3.86)	4.29 (3.67)	4.51 (3.83)
4	C_{2v}	5.10 (4.73)	4.69 (4.19)[b]	4.84 (4.15)	4.38 (4.10)	4.15 (3.90)	4.27 (3.99)
5a	C_{2v}	15.09 (15.24)	14.45 (15.84)	15.40 (15.47)	12.83 (13.20)	12.75 (12.99)	12.92
5b	C_i	16.85 (17.02)	16.51 (17.65)	17.18 (17.23)	14.51 (14.83)	14.67 (14.78)	14.62
5c	C_s	17.14 (17.10)	16.52 (17.59)	17.61 (17.42)	14.64 (14.80)	14.85 (14.84)	14.67
5d	C_1	17.61 (17.81)	17.09 (18.30)	17.93 (18.03)	15.30 (15.64)	15.27 (15.49)	15.43
5e	C_s	18.65 (18.68)	18.21 (19.13)	18.81 (18.78)	16.12 (16.14)	16.10 (16.06)	16.13
5f	C_s	19.70 (19.54)	18.75 (19.82)	19.92 (19.56)	16.90 (17.05)	17.09 (17.24)	16.97
5g	C_i	20.23 (20.20)	19.73 (20.81)	20.38 (20.20)	17.66 (17.84)	17.54 (17.61)	17.85
5h	C_{2v}	21.80 (21.34)	20.91 (21.57)	22.33 (21.56)	18.61 (18.51)	18.82 (18.80)	18.46
5i	C_{2v}	26.07 (25.60)	24.97 (25.69)	26.26 (25.71)	22.54 (22.36)	22.06 (21.86)	22.33
				(B) CCSD			
1	C_{2h}	0.00 (0.00)	0.00 (0.00)[b]	0.00			
2a	C_s	2.63 (2.27)[b]	2.21 (2.76)	2.73			
2b	C_s	3.81 (3.41)[b]	3.20 (3.08)[b]	3.83			
3	C_1	4.35 (3.79)	3.64	4.54			
4	C_{2v}	4.87 (4.47)	4.49 (4.02)[b]	4.86			
5a	C_{2v}	16.38 (16.58)	15.62	16.74			

[a] Relative energies E are given in kilocalories per mole. ZPVE-corrected values are given in parentheses. [b] The planar forms of these conformers were transition states. [c] The planar form of **1** was a second-order transition state at the MP2(FULL)/6-311++G** computational level.

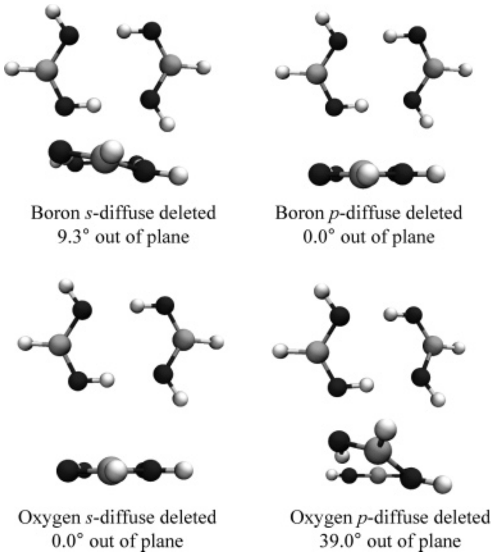
Boron *s*-diffuse deleted 9.3° out of plane
Boron *p*-diffuse deleted 0.0° out of plane
Oxygen *s*-diffuse deleted 0.0° out of plane
Oxygen *p*-diffuse deleted 39.0° out of plane

Figure 4. Effect of Pople-type boron and oxygen *s*- and *p*-diffuse functions on the planarity of conformer **1** for the 6-31+G* basis set.

assistance is involved;[36,37] for example, in the formic acid dimer the C═O and C−O(H) distances in the monomer tend to equalize.

Conformer **1**, however, is not the only local minimum on the boronic acid dimer PES. Consistent with the results of our B3LYP/6-31+G* conformer search, two doubly hydrogen-bonded conformers **2a** and **2b** (Figure 2), in which one of the hydroxyl groups acts as both a hydrogen-bond donor *and* an acceptor, are only 2.6 (2.7) and 3.1 (3.8) kcal/mol higher in energy than (**1**) at the MP2/ aug-cc-pVTZ (CCSD/cc-pVDZ) computational levels (Table 1); correction for zero-point vibrational energies (ZPVEs) lowers these values ∼0.3 kcal/mol. These two conformers differ primarily in the form of the two monomeric units (Figure 2). In contrast to **1**, where the two O−H···O hydrogen bond lengths are the same, the lengths of the two hydrogen bonds in these conformers differ significantly and they are both longer than in **1**; the corresponding O−H···O angles are much smaller.

Although the optimized structures of both **2a** and **2b** were found to be planar during the B3LYP/6-31+G* conformer search, their lowest computed frequencies were extremely small. Nevertheless, at the highest computational level where we could obtain frequencies, MP2/aug-cc-pVTZ, these planar forms were also local minima. However, at some computational levels, for example, MP2/6-311G**, MP2/ 6-311++G**, and MP2/cc-pVDZ, one or both of these planar structures were found to be transition states, although slightly nonplanar (C_1) forms were minima; energy differences between the planar and nonplanar forms were negligible. It is important to note that the correlation between stability and the planarity of these conformers was quite sensitive to the inclusion of diffuse functions, particularly when correlation-consistent basis sets were employed with MP2 methodology. For example, with the cc-pVDZ and cc-pVTZ basis sets the planar form of **2a** was a transition state, whereas with the aug-cc-pVDZ and aug-cc-pVTZ basis sets the planar form was a local minimum.

A nonplanar (C_1), singly hydrogen-bonded conformer (**3**), composed of two exo−endo monomeric units of $HB(OH)_2$ that are twisted ∼54° with respect to each other, was also found to be a local minimum on the PES (Figure 2), structure **3** 4.5 (4.5) kcal/mol higher in energy than **1** at the MP2/aug-cc-pVTZ (CCSD/cc-pVDZ) computational levels; correction for zero-point vibrational energies at the MP2/aug-cc-pVTZ level reduces this to ∼3.8 kcal/mol.

A planar doubly hydrogen bonded (C_{2v}) conformer (**4**) that involves one syn and one anti form of the monomer also proved to be a local minimum (Figure 2), 4.3 (4.9) kcal/mol higher in energy than **1** at the MP2/aug-cc-pVTZ (CCSD/cc-pVDZ) level.[79] Pedireddi and SeethaLekshmi[1] recently showed that supramolecular assemblies of PBA and 4,4′-bipyridine have the hydroxyl groups of PBA in a syn arrangement; the assemblies are held together by OH···N bonds.

Although conformers **2**−**4** of the $HB(OH)_2$ dimer are consistently predicted to be ∼2−5 kcal/mol higher in energy than **1** at all the MP2 and CCSD computational levels employed in this study, preliminary calculations suggest that these conformers are sufficiently close in energy to play a role in various dehydration processes involving boronic acids.[80,81] Indeed, formation of anhydrides of arylboronic acids sometimes occurs if the acids are simply warmed in an anhydrous solvent such as CCl_4.[80−82] Indeed, the novel drug Velcade (*N*-benzoyl-Phe-Ala-boroLeu), a modified dipeptidylboronic acid, approved by the FDA for treatment of multiple myeloma, exists in a cyclic anhydride form as a trimeric boroxine.[83]

In Table 2the dimerization energies, enthalpies, and Gibbs free energies for conformers **1−4** are listed at a variety of MP2 and CCSD computational levels. The values of ΔE, ΔH^0_{298}, and ΔG^0_{298} for the formation of **1** from two exo−endo conformers of the monomer were −10.8, −9.2, and +1.2 kcal/mol, respectively, at the MP2/aug-cc-pVTZ computational level; the corresponding values reported by McKee[39] were −13.0, −11.4, and −1.0 kcal/mol at the MP2/6-31G* level. Correction for BSSE at the MP2/aug-cc-pVTZ level changed these computed values by only ∼1 kcal/mol, to −9.5, −7.9, and +2.4 kcal/mol, respectively. For comparison, we note that ΔE for the analogous dimerizations of formic acid and formamide were −15.2 and −14.2 kcal/mol, respectively, at the MP2/aug-cc-pVTZ//MP2/aug-cc-pVDZ computational level, when corrected for BSSE;[37] these latter two dimers involve resonance-assisted hydrogen bonds[36,37] and, as might be anticipated, their dimerization energies are more exothermic than that for boronic acid.

The nine doubly OH-bridged forms of $[HB(OH)_2]_2$, **5a−5i**, identified as local minima in the B3LYP/6-31+G* conformer search (Figure 4), were also found to be local minima at several MP2 levels; at the MP2/aug-cc-pVTZ level these bridged structures were computed to range from 12.9 to 22.3 kcal/mol higher in energy than **1**, as seen in Table 1. These structures were very compact, for example, the distance between the boron atoms was typically ∼2.23 Å at the MP2/aug-cc-pVTZ level compared to ∼4.18 Å for conformer **1**. The compact nature of these bridged conformers, however, brings the electron density-rich oxygen atoms into relatively close proximity, which leads to significant electrostatic repulsion and contributes to their relatively high energy. The boron atoms in these structures were all tetracoordinated.[84] Interestingly, the energetic ordering of conformers **5a−5i** was relatively insensitive at the MP2 level to the basis set employed (Table 1). However, the magnitude of the relative energies of these conformers above **1** were several kilocalories per mole lower when correlation-consistent basis sets were employed instead of the Pople split-valence basis sets.

No doubly H-bridged, diborane-like structures were found to be local minima on the PES; a conformer with C_{2h} symmetry was found to be a first-order transition state that connected two equivalent forms of the singly hydrogen-bonded conformer **3**. This transition state was computed to be 24.9 kcal/mol higher in energy than **3** at the MP2/aug-cc-pVTZ level.

DFT Results. The relative energies of the various local minima on the $HB(OH)_2$ dimer PES by use of the BLYP, B3LYP, OLYP, O3LYP, PBE1PBE, and TPSS functionals, with the aug-cc-pVTZ basis set, are listed in Table 3; the corresponding results for the 6-311++G** basis set are listed in Table 3S of the Supporting Information; and *xyz* coordinates from a variety of DFT levels are given in Table 4S of the Supporting Information. In general, the values of the geometrical parameters of these conformers are in good agreement with the corresponding MP2 and CCSD results. With all of these functionals, for either the aug-cc-pVTZ or the 6-311++G** basis sets, the planar C_{2h} conformer **1** was consistently predicted to be a local minimum on the PES, and it was lower in energy

TABLE 2: Dimerization Energies,[a] Enthalpies, and Free Energies[b] of Conformers 1−4 at Various MP2 Computational Levels

		6-311G**	6-311++G**	cc-pVDZ	cc-pVTZ	aug-cc-pVDZ	aug-cc-pVTZ
1	ΔE	−11.96 (−8.13) [−6.63]	−10.33 (−8.30) [−7.63]	−12.28 (−7.57) [−6.07]	−10.78 (−8.87) [−7.33]	−10.76 (−8.66) [−7.09]	−10.80 (−9.48) [−7.81]
1	ΔH^0_{298}	−10.41	−10.37	−10.77	−9.24	−9.18	−9.15
1	ΔG^0_{298}	−0.50	+1.77	−0.54	+0.97	+1.05	+1.23
2a	ΔE	−9.10 (−6.10) [−4.93]	−7.96 (−6.10) [−4.70]	−9.32 (−5.49) [−4.34]	−8.25 (−6.67) [−5.45]	−9.46 (−6.55) [−5.23]	−8.22 (−7.22) [−5.84]
2a	ΔH^0_{298}	−8.24	−6.37	−8.50	−7.35	−7.93	−6.67
2a	ΔG^0_{298}	+2.32	+2.55	+2.17	+3.26	+1.02	+2.38
2b	ΔE	−9.52 (−6.85) [−5.51]	−8.45 (−6.94) [−6.30]	−9.96 (−6.11) [−4.91]	−8.82 (−7.24) [−5.99]	−8.87 (−7.10) [−5.73]	−8.78 (−7.78) [−6.41]
2b	ΔH^0_{298}	−8.67	−8.43	−7.03	−7.35	−6.41	−7.23
2b	ΔG^0_{298}	+1.99	+2.72	+3.71	+0.49	+2.68	+1.73
3	ΔE	−7.27 (−4.70) [−3.67]	−6.38 (−4.92) [−3.91]	−7.36 (−4.41) [−3.40]	−6.33 (−5.13) [−4.19]	−6.47 (−5.06) [−4.11]	−6.29 (−5.51) [−4.52]
3	ΔH^0_{298}	−5.79	−4.88	−5.89	−4.90	−5.03	−4.83
3	ΔG^0_{298}	+1.60	+2.17	+1.40	+2.35	+2.32	+2.64
4	ΔE	−12.09 (−9.10) [−7.70]	−10.86 (−9.14) [−8.74]	−12.32 (−8.60) [−7.12]	−10.67 (−9.10) [−7.66]	−10.76 (−8.96) [−7.45]	−10.64 (−9.53) [−7.95]
4	ΔH^0_{298}	−10.46	−10.93	−10.64	−10.44	−9.07	−9.14
4	ΔG^0_{298}	−1.89	+0.14	−1.65	−1.58	+0.03	−0.07

[a] Dimerization energies ΔE are given in kilocalories per mole; counterpoise-corrected values are given in parentheses, and counterpoise- plus ZPVE-corrected values are given in brackets. The energies of the planar forms were used in all cases. [b] Enthalpies, ΔH^0_{298}, and free energies, ΔG^0_{298}, are given in kilocalories per mole.

TABLE 3: Relative Energies[a] of the Optimized Boronic Acid Dimers 1−5 by Use of Various Functionals with the Aug-cc-pVTZ Basis Set

	DFT/aug-cc-pVTZ					
	B3LYP	BLYP	O3LYP	OLYP	PBE1PBE	TPSS
1	0.00	0.00	0.00	0.00	0.00	0.00
2a	2.29 (2.00)	2.22 (1.95)	1.60 (1.25)	1.34 (0.95)	2.40 (2.11)	2.42 (2.07)
2b	2.82 (2.57)	2.73 (2.52)	2.06 (1.72)	1.79 (1.51)	2.87 (2.62)	2.95 (2.68)
3	3.55 (2.89)	3.26 (2.63)	1.66 (1.10)	1.17 (0.68)	3.85 (3.17)	3.63 (3.02)
4	4.22 (3.97)	4.21 (4.00)	3.24 (2.90)	2.94 (2.60)	4.38 (4.12)	4.50 (4.23)
5a	20.45	23.04	19.36	20.68	13.86	14.16
5b	21.80	24.34	20.64	21.88	15.31	15.59
5c	21.79	24.27	20.55	21.74	15.27	15.52
5d	22.61	25.00	21.56	22.75	16.22	16.26
5e	23.35	25.85	22.08	23.27	16.83	17.10
5f	23.90	26.23	22.57	23.66	17.46	17.48
5g	24.89	27.15	23.86	25.01	18.61	18.42
5h	25.40	27.73	23.89	24.94	18.86	19.02
5i	29.55	31.69	28.76	29.85	23.44	22.84

[a] Relative energies E are given in kilocalories per mole.

than any of the other conformers. In fact, at the LDA(SVWN5)/6-311++G**,[85] MPW1PW91/6-311++G**,[86] and PW91PW91/6-311++G**[64] levels, as well as at the HF/ 6-311++G** level, this planar form was found to be a local minimum. Thus, although the 6-311++G** basis set gave anomalous nonplanar geometries for **1** with the MP2 and CCSD methodologies, it did not give similarly anomalous results with any of the density functionals employed, suggesting that the problem with the Pople sp diffuse set affects only pairwise interactions.

The hydrogen-bonded conformers **2a**, **2b**, and **4**, which were found to be planar in the B3LYP/6-31+G* conformational search and at the MP2/aug-cc-pVTZ computational level, were also found to be planar with all the DFT/aug-cc-pVTZ methods employed here. However, at the corresponding DFT/6-311++G** levels, the results were not as consistent; for example, the TPSS functional predicted all three of these planar structures to be transition states. However, removing the planarity constraint and reoptimizing the structures led to stable, slightly nonplanar conformers in which energy differences between the corresponding planar and nonplanar forms were negligible (see Table 3S).

To a large extent, the predicted energy ordering of all the hydrogen-bonded and OH-bridged conformers of the boronic acid dimer was the same at the DFT/6-311++G** and DFT/aug-cc-pVTZ levels as it was at the various MP2 and CCSD levels. The magnitude of the energy differences between the various dimer conformers, however, was less consistent: BLYP, B3LYP, OLYP, and O3LYP all overestimate the energy differences between conformer **1** and the various OH-bridged structures **5a**−**5i**, with either basis set, when compared to the corresponding MP2 differences. OLYP and O3LYP perform poorly even with respect to the relative energies of the hydrogen-bonded conformers **1**−**4**, whereas the PBE1PBE functional does quite well.

In Table 4 we list the $[HB(OH)_2]_2$ dimerization energies, enthalpies, and Gibbs free energies of conformers **1**−**4** from the appropriate monomeric forms at the various DFT/aug-cc-pVTZ computational levels; the corresponding values corrected for BSSE are also given in this table. To a large extent, these DFT results mimic those obtained at the MP2/aug-cc-pVTZ level (compare Tables 2 and 4), although the DFT dimerization energies tend to be ∼2−3 kcal/mol less exothermic than the corresponding MP2 values.

SCRF Results in Aprotic Solvents. Since many reactions of boronic acids have been carried out in aprotic solvents,[51,72,87] we also optimized the geometries of conformers **1**−**5a** in the reaction fields of carbon tetrachloride and acetonitrile. Initially, we performed a variety of DFT calculations in these aprotic solvents using the B3LYP, PBE1PBE, and TPSS functionals with the aug-cc-pVTZ and 6-311++G** basis sets. Planar forms of conformers **1** and **4** were consistently predicted to be local minima in both solvents. Although conformer **1** was still calculated to be lower in energy than **4**, the energy difference between them was smaller in these solvents than in vacuo, for example, at the PBE1PBE/6-311++G**(PBE1PBE/aug-cc-pVTZ) levels in acetonitrile, conformer **1** was only 1.0 (0.9) kcal/mol lower in energy than **4** as compared to 4.9 (4.4) kcal/mol lower in energy when the calculation was carried out in the gas phase; since the dipole moment of **4** is ∼7 D while that of **1** is precisely zero, this finding was only to be expected. Frequency analyses of the optimized planar forms of **2a** in the reaction field of carbon tetrachloride at the B3LYP/aug-cc-pVTZ (PBE1PBE/aug-cc-pVTZ) levels found this structure also to be a local minimum, although it was 2.7 (2.8) kcal/mol higher in energy than **1**, as compared to 2.3 (2.4) in vacuo. The planar form of **2b** was a local minimum at the B3LYP/aug-cc-pVTZ level but a first-order transition state at the (PBE1PBE/aug-cc-pVTZ) level, 3.0 (3.1) kcal/mol higher in energy than **1**, compared to 2.8 (2.9) kcal/mol in vacuo. No stable conformer of the dimer that was similar in structure to **3** could be found in CCl_4 at these computational levels. The OH-bridged structure **5a** was computed to be a local minimum at the B3LYP/aug-cc-pVTZ (PBE1PBE/aug-cc-pVTZ) levels, but it was still high in energy, 18.6 (12.1) kcal/mol above **1**, compared to 20.4 (13.9) kcal/mol in the gas phase.

The above DFT results suggest that the planar conformers **1** and **4** of the boronic acid dimer are lowest in energy in both of these aprotic solvents. Indeed, at the MP2/cc-pVDZ (MP2/aug-cc-pVDZ) levels these conformers were also the two lowest-energy local minima we found; in CCl_4 and CH_3CN, conformer **4** is only 3.1 (2.3) and 1.2 (0.7) kcal/mol, respectively, higher in energy than **1**.

As might be expected, the dimerization reaction energetics for conformers **1** and **4** are sensitive to the solvent. For example, in going from vacuum $\rightarrow CCl_4 \rightarrow CH_3CN \rightarrow H_2O$, the Gibbs free energy for the dimerization process increases from $+2.8 \rightarrow +6.0 \rightarrow +11.6 \rightarrow +11.8$ kcal/mol for **1**, while it increases from $+1.9 \rightarrow +4.8 \rightarrow +10.6 \rightarrow +11.0$ kcal/mol for **4**, when the appropriate conformations of the monomer are used for the calculations at the PBE1PBE/aug-cc-pVTZ computational level. (Of course, use of PCM methodology for water as a solvent does not incorporate the important directional aspects of the

TABLE 4: Dimerization Energies,[a] Enthalpies, and Free Energies[b] of Conformers 1−4 at Various DFT/Aug-cc-pVTZ Computational Levels

		B3LYP	BLYP	O3LYP	OLYP	PBE1PBE	TPSS
1	ΔE	−8.41 (−8.21) [−6.59]	−7.63 (−7.43) [−5.89]	−5.06 (−3.97) [−2.57]	−4.10 (−3.94) [−2.64]	−9.14 (−8.93) [−7.34]	−8.43 (−8.19) [−6.59]
1	ΔH^0_{298}	−6.80	−6.08	−3.47	−2.54	−7.57	−6.88
1	ΔG^0_{298}	+3.59	+4.25	+6.18	+6.77	+2.85	+3.60
2a	ΔE	−6.11 (−5.96) [−4.63]	−5.40 (−5.24) [−3.97]	−3.46 (−3.34) [−2.29]	−2.76 (−2.65) [−1.73]	−6.74 (−6.57) [−5.27]	−6.01 (−5.82) [−4.57]
2a	ΔH^0_{298}	−8.27	−3.89	−1.97	−1.30	−5.22	−4.54
2a	ΔG^0_{298}	+0.48	+4.77	+5.76	+5.42	+3.47	+3.93
2b	ΔE	−6.70 (−6.55) [−5.15]	−5.97 (−5.82) [−4.47]	−3.96 (−3.83) [−2.74]	−3.22 (−3.10) [−2.06]	−7.32 (−7.16) [−5.78]	−6.58 (−6.40) [−5.02]
2b	ΔH^0_{298}	−5.12	−4.43	−2.45	−1.71	−5.77	−5.05
2b	ΔG^0_{298}	+3.88	+4.51	+5.35	+5.86	+3.25	+3.95
3	ΔE	−4.86 (−4.73) [−3.78]	−4.34 (−4.21) [−3.33]	−3.41 (−3.30) [−2.45]	−2.93 (−2.83) [−2.02]	−5.29 (−5.15) [−4.24]	−4.80 (−4.65) [−3.67]
3	ΔH^0_{298}	−3.39	−2.91	−1.96	−1.50	−3.85	−3.33
3	ΔG^0_{298}	+3.75	+3.59	+4.81	+5.06	+3.01	+3.95
4	ΔE	−8.31 (−8.14) [−6.56]	−7.34 (−7.16) [−5.65]	−5.81 (−5.67) [−4.43]	−5.00 (−4.88) [−3.75]	−8.95 (−8.76) [−7.23]	−7.90 (−7.69) [−6.18]
4	ΔH^0_{298}	−6.57	−5.62	−4.18	−3.42	−7.24	−6.19
4	ΔG^0_{298}	+2.59	+3.44	+4.01	+4.37	+1.90	+2.86

[a] Dimerization energies ΔE are given in kilocalories per mole; counterpoise-corrected values are given in parentheses, and counterpoise- plus ZPVE-corrected values are given in brackets. The energies of the planar forms were used in all cases. [b] Enthalpies, ΔH^0_{298}, and free energies, ΔG^0_{298}, are given in kilocalories per mole.

hydrogen bonding for this protic solvent.)[88,89] Thus, these SCRF calculations predict that the thermochemistry of boronic acid dimer formation is less favorable in solution than it is in vacuo.

Concluding Remarks

Despite the rapidly increasing use of boronic acids as pharmaceuticals, chemical sensors, and building blocks for novel materials, many aspects of their structures and reaction energetics are not well established, either experimentally or computationally. A survey of the chemical literature[29,30] showed that organoboronic acids often form (nearly) centrosymmetric hydrogen-bonded dimers that are linked by a pair of H−O···H bonds.[31] In this article the structure and thermochemistry of the simple $HB(OH)_2$ dimer were discussed by use of a variety of MP2, CCSD, and DFT computational methods.

Generally, there was good agreement among a variety of MP2, CCSD, and DFT computational levels that the planar, doubly hydrogen-bonded conformer **1** with C_{2h} symmetry (Figure 2) was the lowest-energy conformer of the boronic acid dimer. The only exceptions to this finding were at the MP2(FC or FULL)/6-311++G**, MP2(FC or FULL)/6-311++G(df,-pd), and CCSD/6-311++G** levels that predicted this planar form to be a second-order saddle point; the MP2(FC)/6-311++G(2df,2pd) level, however, predicted the planar form to be a local minimum. These findings suggest that some care must be exercised in using the popular 6-311++G** basis set in modeling more extended boronic acids, particularly with respect to dimerization processes. The energy, enthalpy, and Gibbs free energy for the formation of **1** from the exo−endo conformer of the monomer were predicted to be −10.8, −9.2, and +1.2 kcal/mol, respectively, at the MP2/aug-cc-pVTZ level; when corrected for BSSE by the counterpoise method, the corresponding values were −9.5, −7.9, and +2.5 kcal/mol. The value of ΔE for the analogous dimerizations of formic acid and formamide at the MP2/aug-cc-pVTZ//MP2/aug-cc-pVDZ computational level (corrected for BSSE), −15.2 and −14.2 kcal/mol, respectively, were more exothermic, presumably as a result of improved electron delocalization.[37]

Four other hydrogen-bonded conformers were identified as local minima on the boronic acid dimer PES, but they ranged from ∼2−5 kcal/mol higher in energy than **1** in vacuo; preliminary B3LYP/6-31+G* calculations suggest that these conformers may play some role in the formation of various anhydrides from the free acids. A variety of compact OH-bridged structures of the $HB(OH)_2$ dimer were also found to be local minima on the PES, but they were more than 12.9 kcal/mol higher in energy than **1** at the MP2/aug-c-pVTZ level. No stable, doubly H-bridged, diborane-like structures were found to be local minima on the PES. It is not clear what role (if any) these bridged forms may play in the chemistry of boronic acids.

In the aprotic solvents carbon tetrachloride and acetonitrile, SCRF PCM calculations, using MP2 or DFT methodology with correlation-consistent basis sets, generally found that the planar conformer **1** was a local minimum on the boronic acid dimer PES. However, the energy difference between conformers **1** and **4** was lower in these solvents than it was in the gas phase. SCRF calculations also predict that the thermochemistry of boronic acid dimerization is less favorable in such solutions than in vacuo.

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Supporting Information Available: Listing of the MP2-(FC)/aug-cc-pVTZ vibrational frequencies of the endo−exo conformer of the monomer and conformer **1** of the dimer (Table 1S), relative energies of the local minima identified during the B3LYP/6-31+G* initial conformer search (Table 2S), DFT/6-311++G** relative energies of the dimers (Table 3S), and *xyz* coordinates of the species studied (Table 4S). This material is available free of charge via the Internet at http://pubs.acs.org.

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