Adenine−Hydrogen Peroxide System: DFT and MP2 Investigation

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Theoretical calculations have been performed for different possible hydrogen bonding complexes between adenine and hydrogen peroxide (AHP). The studied complexes (**1**−**6**) were cyclic ones showing two hydrogen bonds of different strength. All of the structures have been characterized at the B3LYP/6-31G(2d,p) and MP2(full)/6-31G(2d,p) levels, yielding only real frequencies (minima) at the B3LYP/6-31G(2d,p). The binding energies have been carried out for all of the structures, taking into account the so-called BSSE and yielding for the most stable structure **6** values of −11.53 and −11.95 kcal/mol at the B3LYP and MP2 levels, respectively. BSSE-free PES calculations were also performed for several complexes. The Bader analyses were also applied to investigate the hydrogen bonding electronic properties.

I. Introduction

Hydrogen peroxide (HP) has proven of considerable interest in many fields such as atmospheric chemistry,[1] photodissociation dynamics,[2] and oxidation reactions.[3] Also, HP is a byproduct of several metabolic pathways, giving significant quantities of HP detectable in the human blood.[4] HP generates highly reactive radicals by different mechanisms such as the Fenton reaction, the Haber−Weiss reaction, or reactions with ascorbic acid.[5] These free radicals may damage several molecules including DNA. Different modified DNA bases have been identified by treating mammalian cells with HP,[6] and it has been proven that the biological effect of HP is mediated by hydrogen bonded HP adducts,[7] which could be due to the enhanced HP stability by adduct formation. In addition, neutral HP adducts seem to cross the cell membrane, carrying extracellular HP to intracellular targets.

The above findings justify the interest of studying all HP···DNA base adducts. In the literature, theoretical investigations on several adenine complexes were reported.[8,9] Moreover, Serra[10] and co-workers experimentally determined the X-ray structure of the adenine···HP adduct (AHP).

Theoretical methods, including DFT methods,[12−16] proved to be accurate enough in describing hydrogen bonding complexes.[11] Moreover, the accuracy of DFT results still has to be compared with other correlated methods. In this context Lozynski proposed B3LYP as the shortest way to MP2 results in hydrogen bonded systems.[17] The topology of electron density as described by Bader[18,19] is an adequate tool in the hydrogen-bonded species.[12,20−22]

Recently, the results of a number of studies, dealing with hydrogen peroxide complexes, have been published using the ab initio molecular orbital theory and paying particular attention to the basis set superposition error (BSSE) and its corrections by the counterpoise (CP) method[23,24] to the interaction energies and to the vibrational spectra of the HP dimer,[25−27] HP···water,[20,28] HP···hydrogen halides,[21] and recently HP···urea[12] complexes.

Until now, the CP correction has been done only at the uncorrected equilibrium geometry, except in complexes where only one intermolecular parameter was needed for the definition of the system.[29] However, a method for the calculation of the BSSE-free potential energy surface (PES) has been proposed recently by S. Simón, M. Duran, and J. J. Dannenberg.[30] In this context, BSSE-free PES investigations have been very recently performed.[31] In all of the complexes investigated by our group, the BSSE was corrected by the CP method[23,24] at the HF, MP2, or DFT level. The CP method is based on the assumption that the energy is minimized if the same basis set is used for the description of both the supermolecule and its fragments. Although the validity of this approach has been discussed for many years in the literature,[32,33] recent calculations have shown that the CP method converges with other a priori procedures. Therefore, reliable results for intermolecular complexes can be obtained,[34] and its usefulness has been pointed out recently.[32,33,35]

In this paper, we are going to expand our studies on hydrogen peroxide to the AHP complexes. The MP2 level has been used together with DFT method, whose utility for the description of the physical and chemical molecular properties,[36−41] including hydrogen bond systems[13−16] has been demonstrated. The goal of the present work is to characterize the different AHP complexes (to our knowledge, the first theoretical investigation) and to report the structures, interaction energies, vibrational analyses, and electronic properties of these systems. In addition, BSSE-free PES geometries have been obtained for several complexes.

II. Methods of Calculation

Calculations have been carried out with the Gaussian 94 and Gaussian 98 packages of programs[42,43] at the B3LYP/6-31G(2d,p)//B3LYP/6-31G(2d,p) and MP2(full)/6-31G(2d,p)//MP2(full)/6-31G(2d,p) levels. The AHP complexes were fully optimized at both levels, without any symmetry constraint. A vibrational analysis was carried out in order to check the nature of the stationary points, and all of the structures **1**−**6** presented no imaginary frequencies (true minima) at the B3LYP/6-31G(2d,p)//B3LYP/6-31G(2d,p) level. The BSSE was estimated

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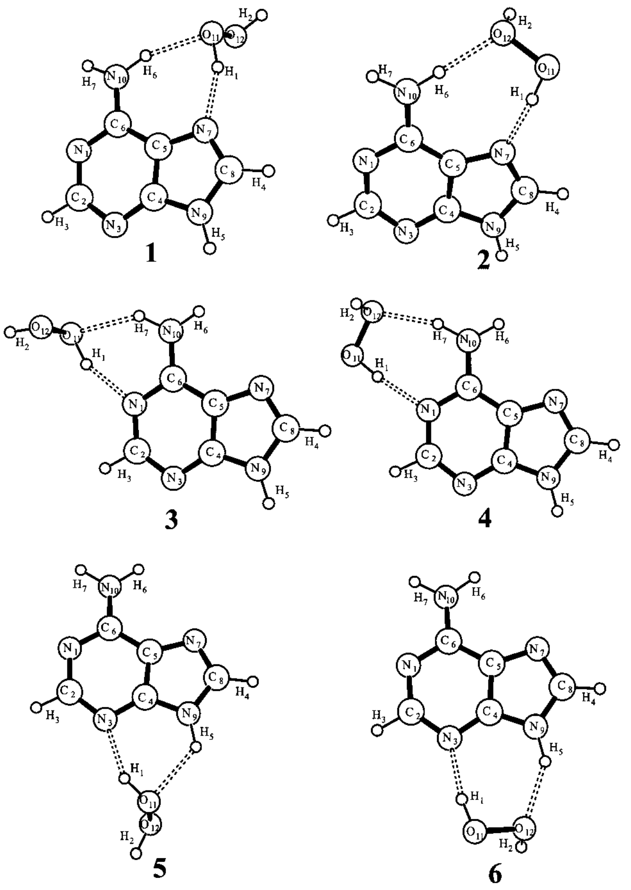

Figure 1. The adenine−hydrogen peroxide (AHP) complexes (**1**−**6**) with the corresponding atom numbering.

using the full counterpoise method[24] as it was previously described.[12,20,21,25]

The energy and gradients with respect to the geometrical parameters have been calculated for the complex, monomers, and monomers in the whole basis set (ghost orbitals) at every point using the Gaussian 98 package.[43] BSSE-free PESs have been constructed as shown in refs 30, 31. For the location of the minima geometries, Pulay's direct inversion in the iterative subspace (DIIS)[44] with BFGS[45] updating procedure for the inverse Hessian has been implemented. Initial guess for the inverse Hessian has proven to be essential for the optimization procedure. Uncorrected initial inverse Hessian has been obtained from HF/3-21G frequency calculations. The convergence criterion has been set to $10E^{-5}$ a.u. in the RMS of the gradient.

The Bader analyses have been performed with the AIMPAC series of programs[46] using the B3LYP wave function as input, as it was described in *"Atoms in Molecules"* Theory (AIM).[18,19] A brief overview of the AIM terminology is explained elsewhere.[47,48]

III. Results and Discussion

A. Molecular Structure and Hydrogen Bonding. The calculated structures **1**−**6** were cyclic with two hydrogen bonds (see Figure 1). For the different structures, one of the HP oxygens, N_1, N_3, and N_7 atoms behave as electron donors, while one of the HP hydrogen, H_5, H_6, and H_7 atoms of adenine behave as electron acceptors. In structures **1**, **3**, and **5**, one of the HP hydroxyls participates in both hydrogen bonds, while in **2**, **4**, and **6**, both HP hydroxyls participate in hydrogen bond formation, one with its hydrogen as electron acceptor and the other with its oxygen as electron donor.

The optimized geometrical parameters are listed in Tables 1 and 2, in which the DFT and MP2 results were compared with the experimental structure related to **1**. As reflected in Table 1, the DFT and MP2 results for **1** were very similar and in good agreement with the experimental structure. In general, the geometrical parameters for the adenine moiety were mainly invariable within the different studied complexes. The main differences came in the HP geometry, especially the HP torsion angle; this angle in **1** remained the same as in the HP monomer equilibrium geometry. Small variations were found for **3** and **5**. For these complexes (**1**, **3**, and **5**), only one HP hydroxyl participates in the hydrogen bond formation. Larger deviations (> 10°) appeared for **2**, **4**, and **6** in which both hydroxyls participated in the hydrogen bond formation.

All the structures **1**−**6** showed two hydrogen bonds with geometries that corresponded to a medium hydrogen bond strength, giving complexes with very similar energies (see Table 3). The hydrogen bond distances moved between 2.1 and 1.8 Å, and the angles ranged from 126° to 177°, but the hydrogen bond geometries were very similar for the different structures. The nature of the hydrogen bond was analyzed by studying the electron density topological behavior of the complexes. The numerical parameters for the different critical points in $\rho(r)$ are listed in Table 4, and the graphical contour plots of $\nabla^2\rho(r)$ are presented in Figure 2.

Table 4 summarizes $\rho(r)$, $\nabla^2\rho(r)$, hydrogen bond lengths and angles for the bond critical points (BCPs), and the corresponding ring critical points (RCPs). In Figure 2, detailed $\nabla^2\rho(r)$ contour plots on the hydrogen bonding plane are presented for complexes **1**−**6**. The nature of the hydrogen bonded complexes is clearly cyclic, showing two BCPs corresponding to the two hydrogen bonds; in addition, an RCP was also present for each structure. The two hydrogen bond CPs, represented as a solid square in Figure 2, were located in the positive $\nabla^2\rho(r)$ region, indicating the electrostatic type of interaction for both bonds. The numerical values were also in accordance (small $\rho(r)$ values and positive $\nabla^2\rho(r)$ values). Two different hydrogen bonds were identified. One was formed between the HP hydroxyl and an adenine nitrogen atom (Hbond1), and the other is formed by an adenine N−H with the HP oxygen atom (Hbond2). The former hydrogen bonds were stronger than the latter ones, showing larger $\rho(r)$ and $\nabla^2\rho(r)$ values in the CPs (see Table 4, for $\rho(r)$ values of ca. 0.04 and 0.025 e/a_0^3 for Hbond1 and Hbond2, respectively, and for $\nabla^2\rho(r)$ values ca. 0.1 and 0.06 e/a_0^5, for Hbond1 and Hbond2, respectively). The hydrogen bond geometrical parameters yielded bond lengths smaller for the Hbond1 than for Hbond2 (ca. 1.8 Å or ca. 2.0 Å, respectively).

The importance of the optimization on the BSSE-free PESs, for the intermolecular complexes, has been pointed out recently,[30,31] especially for systems with large BSSE. In this context, BSSE-free PES optimization[30] at the B3LYP/6-31G(2d,p) level was carried out for the minimum energy complexes **6** and **1** (of which experimental data are available) for comparison. The results are also summarized in Tables 1 and 2. The BSSE-free PES geometrical parameters of HP and adenine within the complexes **1** and **6** remained almost unchanged as the uncorrected PES values. The main differences appeared in the intermolecular parameters (hydrogen bond lengths). Moreover, the O···HN and OH···N lengths became 0.05 Å longer, giving looser complexes and better agreement with the intermolecular experimental parameters for **1** (see Table 1). These results illustrate the importance of the BSSE-free PES calculations.

TABLE 1: Geometrical Parameters (Å and degrees) for the Adenine (A), Hydrogen Peroxide (HP) Monomers, and AHP Complexes (1, 3, and 5) at the Different Theoretical Levels

	B3LYP/6-31G(2d,p)					MP2(full)/6-31G(2d,p)					exptl[a]
	1	**3**	**5**	**A**	**HP**	**1**	**3**	**5**	**A**	**HP**	**AHP**
N_1-C_2	1.338(1.340)	1.343	1.337	1.342		1.344	1.349	1.345	1.345		1.343
N_1-C_6	1.347(1.344)	1.352	1.344	1.342		1.337	1.342	1.336	1.334		1.348
C_2-N_3	1.336(1.333)	1.329	1.335	1.334		1.334	1.329	1.333	1.335		1.325
N_3-C_4	1.334(1.332)	1.339	1.342	1.336		1.332	1.336	1.338	1.330		1.349
C_4-C_5	1.395(1.396)	1.396	1.395	1.398		1.395	1.396	1.395	1.396		1.380
C_4-N_9	1.380(1.382)	1.375	1.369	1.376		1.374	1.374	1.363	1.376		1.371
C_5-C_6	1.416(1.412)	1.409	1.407	1.407		1.408	1.404	1.401	1.401		1.411
C_5-N_7	1.388(1.388)	1.383	1.383	1.385		1.390	1.374	1.373	1.377		1.395
C_6-N_{10}	1.344(1.344)	1.345	1.355	1.359		1.344	1.344	1.356	1.360		1.334
N_7-C_8	1.311(1.308)	1.309	1.312	1.308		1.321	1.322	1.324	1.322		1.315
C_8-N_9	1.370(1.371)	1.378	1.376	1.379		1.360	1.368	1.365	1.365		1.359
H_3-C_2	1.088(1.088)	1.086	1.087	1.087		1.083	1.094	1.079	1.082		0.968
H_4-C_8	1.080(1.081)	1.080	1.080	1.081		1.080	1.077	1.077	1.077		1.013
H_5-N_9	1.009(1.008)	1.008	1.016	1.008		1.009	1.005	1.013	1.006		0.924
H_6-N_{10}	1.017(1.012)	1.006	1.007	1.007		1.011	1.003	1.004	1.004		0.900
H_7-N_{10}	1.007(1.003)	1.014	1.007	1.008		1.001	1.008	1.005	1.003		0.836
$\angle N_1-C_2-N_3$	129.0(129.1)	128.3	128.5	129.0		129.1	128.8	128.3	129.0		128.94
$\angle C_2-N_3-C_4$	110.7(110.6)	111.3	111.7	111.1		110.5	110.7	111.9	110.7		111.07
$\angle N_3-C_4-C_5$	127.4(127.5)	127.0	126.4	126.9		127.4	127.3	126.1	127.3		126.40
$\angle C_4-C_5-C_6$	116.1(115.9)	116.5	115.9	115.8		116.2	116.3	116.1	115.8		117.24
$\angle C_5-C_6-N_1$	118.0(118.0)	117.6	119.0	118.9		118.1	117.9	119.3	119.0		117.36
$\angle C_2-N_1-C_6$	118.8(118.8)	119.3	118.4	118.2		118.8	119.0	118.3	118.2		118.95
$\angle N_9-C_4-C_5$	104.9(104.7)	104.6	105.2	104.5		104.8	104.4	105.3	104.2		106.02
$\angle C_4-C_5-N_7$	110.4(110.6)	111.4	110.8	111.3		110.7	112.0	111.5	111.9		110.21
$\angle C_5-N_7-C_8$	104.9(104.7)	104.2	104.0	104.0		104.4	103.3	103.2	103.3		103.72
$\angle N_7-C_8-N_9$	112.9(113.0)	113.2	113.5	113.5		112.8	113.6	113.8	113.5		113.83
$\angle C_4-N_9-C_8$	107.0(107.0)	106.7	106.4	106.7		107.3	106.7	106.5	107.0		106.22
$\angle N_1-C_6-N_{10}$	118.6(118.6)	119.3	118.6	118.9		118.8	119.9	119.0	119.3		118.82
$O_{11}-O_{12}$	1.451(1.451)	1.448	1.448		1.449^b	1.469	1.467	1.470		1.464^b	1.4592
H_1-O_{11}	0.989(0.990)	0.993	0.993		0.968^b	0.988	0.986	0.987		0.966^b	1.000
H_2-O_{12}	0.966(0.968)	0.967	0.970		0.968^b	0.966	0.965	0.966		0.966^b	1.047
$\angle H_1-O_{11}-O_{12}$	101.2(101.1)	101.3	101.6		100.3^b	98.8	99.0	98.8		98.9^b	101.04
$\angle H_2-O_{12}-O_{11}$	100.4(100.1)	100.5	100.3		100.3^b	98.8	98.9	99.2		98.9^b	95.74
$\angle H_1-O_{11}-O_{12}-H_2$	−110.0(−112.0)	−108.6	−106.8		111.9^b	−111.1	−107.6	−107.6		112.3^b	−111.94
$H\cdots O_{11}$	1.976(2.028)	2.079	2.138			1.969	2.082	2.132			2.137
$\angle N-H\cdots O_{11}$	159.9(160.6)	140.9	128.4			160.3	140.1	126.2			163.49
$H_1\cdots N$	1.788(1.837)	1.817	1.854			1.776	1.795	1.824			1.812
$\angle O_{11}-H_1\cdots N$	159.7(159.7)	156.5	152.3			160.3	157.4	152.2			152.03

[a] AHP X-ray values from ref 10. [b] Values from ref 51.

The nature of the different stationary points obtained for **1**−**6** was tested with the frequency calculations, giving only real frequencies for all of the structures. The numerical results obtained at the B3LYP/6-31G(2d,p) level are presented in Table SI-I (available as Supplementary Information), also including the adenine frequencies at the same level.

Table 5 summarizes some interesting vibrational modes directly related to hydrogen bonds for the AHP complexes. The analysis of these modes let us characterize the different hydrogen bond for the complexes. The selected modes were the $\nu(O-H)$ (HP) and $\nu(N_9-H)$, $\nu(N_{10}-H)$ (adenine) stretchings. All of the AHP complexes used one hydroxyl hydrogen from the HP in the hydrogen bonds; this was clearly observed for the $\nu(O-H)$ (HP) modes. The $\nu(O_{12}-H_2)$, for all of the complexes, was ca. 3765 cm^{-1}. However, a large red shift was observed for the $\nu(O_{11}-H_1)$ (hydrogen bonded) mode of ca. 500 cm^{-1}.

Complexes **1**−**4** involved the NH_2 group at C_6 in the hydrogen bonding. Nevertheless, the N_9-H bond participated only in complexes **5** and **6**. Two stretchings were associated with the NH_2 group at C_6, “symmetric” and “asymmetric” ones as was observed for the adenine monomer. A small red shift ca. 20 cm^{-1} was observed for the “asymmetric” mode. However, the “symmetric” one experienced a large red shift (> 100 cm^{-1}), for complexes **1**−**4**.

On the other hand, the $\nu(N_9-H_5)$ remained unchanged for **1**−**4** in comparison with the adenine monomer. Complexes **5** and **6** showed a large red shift for this mode (> 100 cm^{-1}). In addition, this red shift was higher for **6** (ca. 180 cm^{-1}), illustrating the stronger hydrogen bond character for this complex. The corresponding “asymmetric” $\nu(NH_2)$ mode for **5** and **6** remained unchanged compared with adenine.

B. Binding Energy and BSSE. Table 3 shows the binding energy (corrected and uncorrected for the BSSE), the BSSE, the relative energy, and the dipole moment at the two levels of theory used. The corresponding BSSE-free PES values for **1** and **6** are also listed.

The B3LYP functional was chosen as a suitable method to describe different molecular properties,[49,50] including hydrogen bonding.[12−16] The basis set chosen was the 6-31G(2d,p), which provided an appropriate description of the hydrogen peroxide geometry, together with the B3LYP functional.[12,51] To test the quality of the results, we also performed the MP2(full)/6-31G(2d,p) calculations.

As shown in Table 3, the results obtained at the DFT and MP2 levels agree with the resulting structure **6** as the global minimum. Moreover, the relative stability for all of the structures was within ca. a 2.0 kcal/mol range, and the ZPVE within ca. a 0.1 kcal/mol range (see Tables 3 and SI−I). This energy range is easily released from the packing forces, in addition to the

TABLE 2: Geometrical Parameters (Å and degrees) for the AHP Complexes (Structures 2, 4, and 6) at the Different Theoretical Levels

	B3LYP/6-31G(2d,p)			MP2(full)/6-31G(2d,p)		
	2	**4**	**6**	**2**	**4**	**6**
N_1-C_2	1.336	1.344(1.336)	1.336	1.344	1.352	1.341
N_1-C_6	1.344	1.351(1.346)	1.344	1.338	1.340	1.338
C_2-N_3	1.339	1.328(1.336)	1.336	1.335	1.328	1.335
N_3-C_4	1.332	1.339(1.341)	1.339	1.333	1.334	1.340
C_4-C_5	1.395	1.395(1.393)	1.393	1.397	1.396	1.396
C_4-N_9	1.378	1.374(1.368)	1.370	1.374	1.373	1.366
C_5-C_6	1.412	1.410(1.408)	1.405	1.407	1.406	1.403
C_5-N_7	1.388	1.383(1.381)	1.383	1.379	1.374	1.371
C_6-N_{10}	1.344	1.342(1.352)	1.352	1.340	1.340	1.352
N_7-C_8	1.310	1.309(1.311)	1.311	1.325	1.325	1.326
C_8-N_9	1.373	1.378(1.374)	1.377	1.361	1.367	1.365
H_3-C_2	1.088	1.087(1.088)	1.088	1.084	1.082	1.084
H_4-C_8	1.081	1.080(1.083)	1.080	1.079	1.077	1.078
H_5-N_9	1.005	1.008(1.019)	1.022	1.007	1.004	1.017
H_6-N_{10}	1.014	1.006(1.004)	1.007	1.009	1.003	1.003
H_7-N_{10}	1.006	1.018(1.007)	1.006	1.003	1.011	1.004
$\angle N_1-C_2-N_3$	129.1	128.6(128.5)	128.3	129.1	128.6	128.6
$\angle C_2-N_3-C_4$	110.6	111.1(111.6)	111.7	110.3	110.8	111.3
$\angle N_3-C_4-C_5$	127.4	127.1(126.5)	126.4	127.5	127.3	126.4
$\angle C_4-C_5-C_6$	116.1	116.5(116.1)	116.1	116.1	116.3	116.1
$\angle C_5-C_6-N_1$	118.0	117.5(118.7)	118.8	118.1	118.0	119.0
$\angle C_2-N_1-C_6$	118.8	119.3(118.6)	118.6	118.8	119.0	118.5
$\angle N_9-C_4-C_5$	104.9	104.5(105.2)	105.4	104.8	104.2	105.2
$\angle C_4-C_5-N_7$	110.4	111.5(111.0)	110.8	110.9	112.1	111.5
$\angle C_5-N_7-C_8$	104.9	103.8(103.8)	104.0	104.2	103.2	103.1
$\angle N_7-C_8-N_9$	112.7	113.5(113.7)	113.5	113.0	113.5	114.0
$\angle C_4-N_9-C_8$	107.0	106.7(106.3)	106.2	107.2	107.0	106.2
$\angle N_1-C_6-N_{10}$	118.6	119.5(118.8)	118.6	119.2	119.7	119.2
$O_{11}-O_{12}$	1.448	1.450(1.450)	1.447	1.462	1.465	1.459
H_1-O_{11}	0.989	0.996(0.992)	0.996	0.984	0.990	0.988
H_2-O_{12}	0.989	0.970(0.967)	0.967	0.964	0.965	0.966
$\angle H_1-O_{11}-O_{12}$	100.4	100.6(101.4)	101.6	99.3	99.3	100.5
$\angle H_2-O_{12}-O_{11}$	101.0	101.0(100.8)	101.3	99.4	99.3	99.8
$\angle H_1-O_{11}-O_{12}-H_2$	−100.0	−102.1(−102.9)	−99.3	−99.7	−101.5	−97.3
$H\cdots O_{12}$	1.948	1.948(2.003)	1.965	1.949	1.956	1.939
$\angle N-H\cdots O_{12}$	174.9	161.2(147.6)	146.9	174.7	160.7	146.7
$H_1\cdots N$	1.811	1.813(1.879)	1.828	1.805	1.809	1.822
$\angle O_{11}-H_1\cdots N$	177.1	175.3(169.5)	169.0	177.4	173.8	168.8

TABLE 3: Binding Energies (without, ΔE, and with BSSE Correction, ΔE_{corr}), BSSE, Relative Energy, E_r, and Dipole Moment, μ, for the AHP Complexes (1−6) at the Different Theoretical Levels

	ΔE (kcal/mol)		ΔE_{corr} (kcal/mol)		BSSE (kcal/mol)		E_r (kcal/mol)		μ (Debye)	
	B3LYP	MP2	B3LYP	MP2	B3LYP	MP2	B3LYP	MP2	B3LYP	MP2
1	−14.09	−15.53	−10.11 (−10.20)	−10.00	3.98 (3.82)	5.53	1.10 (1.43)	1.51	3.83	4.30
2	−14.12	−15.40	−10.49	−10.22	3.64	5.18	1.07	1.64	2.86	3.04
3	−13.13	−14.62	−9.09	−9.20	4.03	5.42	2.06	2.42	2.90	3.30
4	−14.43	−15.70	−10.65	−10.52	3.77	5.18	0.76	1.34	4.16	4.30
5	−13.75	−16.16	−9.87	−10.83	3.88	5.32	1.44	0.88	0.77	0.63
6	−15.19	−17.04	−11.53 (−11.63)	−11.95	3.66 (3.46)	5.09	—[a] (—[c])	—[b]	2.39	2.15

[a] Reference energy value (−618.9145099 a.u.) and the corresponding ones (−151.5515192 and −467.3387843 a.u.) for hydrogen peroxide and adenine, respectively. [b] Reference energy value (−617.4247375 a.u.) and the corresponding ones (−151.2158999 and −466.1816833 a.u.) for hydrogen peroxide and adenine, respectively. [c] Reference energy value (−618.9088417 a.u.).

larger dipolar moments and the possibility of other additional hydrogen bonds from the neighboring complexes, yielding structure **1** as the experimental one. This had physiological relevance in DNA damage, because in nucleic acids the N_1, N_9, and H_7 sites are involved in the N-glycosidic linkage or Watson−Crick base pair, leaving only the N_7 and H_6 sites accessible for additional linkages.

The study of the binding energy in the intermolecular complexes was affected by the so-called BSSE. This error increased in importance as the quality of the basis set decreased. From our previous studies of the hydrogen peroxide complexes,[12,20,21,25] we concluded that the binding energy using the 6-31G(2d,p) basis has to be corrected for the BSSE, and especially for the electron correlation methods.

The BSSE, for structures **1−6**, was estimated with the full counterpoise procedure defined as:

$$\mathrm{BSSE} = E(\mathrm{X})_{\mathrm{X}} - E(\mathrm{X})_{\mathrm{XY}} + E(\mathrm{Y})_{\mathrm{Y}} - E(\mathrm{Y})_{\mathrm{XY}} \quad (1)$$

where $E(\mathrm{X})_{\mathrm{XY}}$ and $E(\mathrm{X})_{\mathrm{X}}$ represent the energy of X which is calculated using its geometry within the dimer and the basis functions of X plus Y in the former and those of X alone in the

TABLE 4: Hydrogen Bond Geometrical Parameters, Charge Density, $\rho(r)$, and the Laplacian of the Charge Density, $\nabla^2\rho(r)$ for the AHP Complexes (1−6) at the B3LYP/6-31G(2d,p)//B3LYP/6-31G(2d,p) Level

critical points	definition[a]	$\rho(r)$ (e/a_0^3)	$\nabla^2\rho(r)$ (e/a_0^5)	bond length (Å)	angle (degree)
		1			
(3,−1)	Hbond1 ($O_{11}-H_1\cdots N_7$)	0.0425	0.1070	1.788	159.7
(3,−1)	Hbond2 ($O_{11}\cdots H_6-N_{10}$)	0.0261	0.0677	1.976	159.9
(3, 1)	ring	0.0061	0.0299		
		2			
(3,−1)	Hbond1 ($O_{11}-H_1\cdots N_7$)	0.0405	0.1001	1.811	177.1
(3,−1)	Hbond2 ($O_{12}\cdots H_6-N_{10}$)	0.0268	0.0732	1.948	174.9
(3, 1)	ring	0.0043	0.0192		
		3			
(3,−1)	Hbond1 ($O_{11}-H_1\cdots N_1$)	0.0410	0.0995	1.817	156.5
(3,−1)	Hbond2 ($O_{11}\cdots H_7-N_{10}$)	0.0216	0.0593	2.079	140.9
(3, 1)	ring	0.0110	0.0556		
		4			
(3,−1)	Hbond1 ($O_{11}-H_1\cdots N_1$)	0.0415	0.0976	1.813	173.5
(3,−1)	Hbond2 ($O_{12}\cdots H_7-N_{10}$)	0.0271	0.0736	1.948	161.2
(3, 1)	ring	0.0071	0.0338		
		5			
(3,−1)	Hbond1 ($O_{11}-H_1\cdots N_3$)	0.0367	0.0935	1.854	152.3
(3,−1)	Hbond3 ($O_{11}\cdots H_5-N_9$)	0.0196	0.0566	2.138	128.4
(3, 1)	ring	0.0096	0.0495		
		6			
(3,−1)	Hbond1 ($O_{11}-H_1\cdots N_3$)	0.0391	0.0950	1.828	169.0
(3,−1)	Hbond3 ($O_{12}\cdots H_5-N_9$)	0.0260	0.0732	1.965	146.9
(3, 1)	ring	0.0059	0.0289		

[a] The atom numbering is depicted in Figure 1.

TABLE 5: Selected Harmonic Vibrational Frequencies[a] (cm^{-1}) for the AHP Complexes 1−6, Adenine and HP Monomers, at the B3LYP/6-31G(2d,p)//B3LYP/6-31G(2d,p) Level

descript	HP	adenine	**1**	**3**	**5**	**2**	**4**	**6**
ν ($O_{12}-H_2$)	3769		3770	3769	3767	3762	3762	3765
$\nu a(NH_2)$		3724	**3695**	**3710**	3734	**3695**	**3708**	3733
$\nu(N_9-H_5)$		3668	3668	3666	**3553**	3668	3666	**3485**
$\nu s(NH_2)$		3596	**3467**	**3509**	3602	**3470**	**3456**	3602
$\nu(O_{11}-H_1)$	3769		**3273**	**3274**	**3335**	**3313**	**3246**	**3287**

[a] Modes (in bold) were involved in hydrogen bond formation.

latter. The full CP correction can be taken as an upper bound estimate of the BSSE and is known to work generally well at the SCF level, except when minimal basis sets were used.[25,52,53] We have taken into account that the correction of the BSSE for the interaction energy should be performed at the BSSE corrected equilibrium geometry. This can be easily achieved in systems where only one intermolecular parameter was needed for the definition of the system.[29] However, when there are two or more intermolecular parameters, and when the relaxation of the monomers is pronounced, it is difficult and expensive to perform that correction. Therefore, energy correction at the uncorrected equilibrium geometry has been performed for **1**−**6**.

There are conflicting views[54,55] on whether one should implement BSSE correction at the correlated level. The use of the full counterpoise correction method for correlated methods is questionable, since in the calculation of the $E(X)_{XY}$, and analogously $E(Y)_{XY}$, excitations from occupied orbitals of X to the *occupied* orbitals of Y are allowed, and may lead to a spurious overcorrection. The *occupied* orbitals of Y are not accessible for electrons of X in the supermolecule calculation. Attempts to utilize only the virtual spaces of X and Y have led to discouraging results.[56] However, recently the BSSE correction at the correlated level has been performed to study the hydrogen bonding.[12,14] The resulting values are presented in Table 3, remaining in the same magnitude of order as the binding energy, corroborating the necessity of this correction.

All the complexes investigated yielded attractive corrected binding energies, with values of around −12.0 kcal/mol for the most stable structures (i.e., structure **6**, see Table 3). This result was compatible with a medium strength contribution for a hydrogen bond.

As was previously stated, the intermolecular complex calculations should be done on the BSSE-free PES. In this work we have carried out such calculations for **1** and **6**. The corrected binding energies obtained were similar to the uncorrected PES values (differences < 0.1 kcal/mol). Therefore, these BSSE-free PESs also yielded values which were similar to the uncorrected ones for the BSSE (see Table 3). All of the above agreed with the strength of the hydrogen bond for these complexes.

IV. Conclusions

Five new AHP cyclic complexes were characterized in addition to the experimental complex (structure **1**) by the ab initio MP2 and DFT methods, and the results indicated that they were true minima stationary points.

The DFT methods showed good agreement in reproducing the geometrical parameters and the energetics compared to the MP2 and the experimental results. Moreover, the BSSE obtained with the DFT methods (ca. 3.5 kcal/mol) was smaller than the MP2 values; hence, the BSSE correction was required to obtain accurate binding energies.

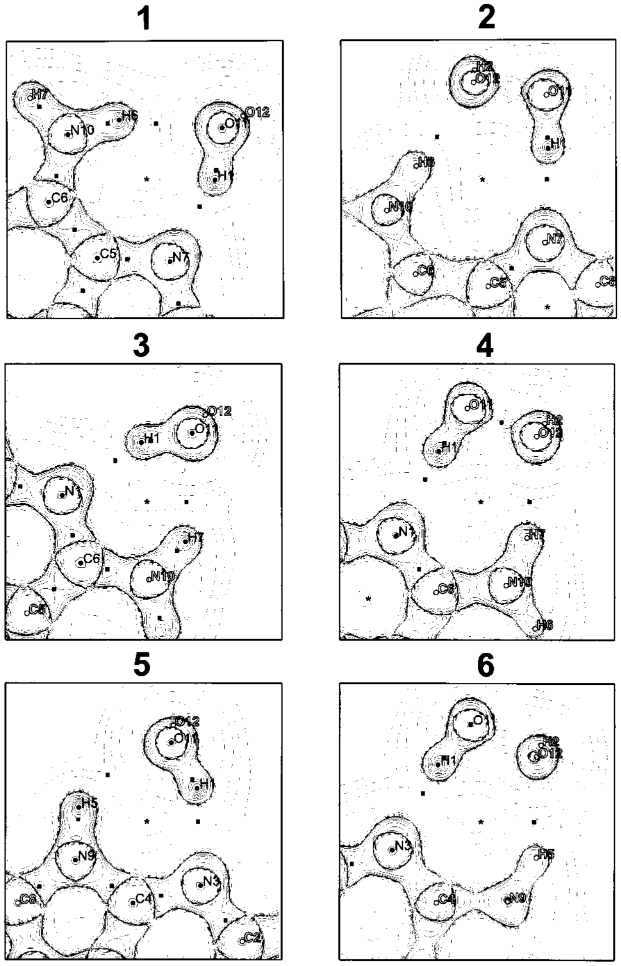

Figure 2. $\nabla^2\rho(r)$ contour map for the hydrogen bonding in the molecular plane obtained using the MORPHY program.[57] The contours begin at zero and they increase (solid contours) and decrease (dashed contours) in steps of ± 0.02, ± 0.04, ± 0.08, ± 0.2, ± 0.4, ± 0.8, ± 2.0, ± 4.0, ± 8.0. The thick solid lines represent the molecular graph that joins the nuclei (solid circles) and the BCP (solid squares), and also represent the zero flux surface and the RCP (asterisk).

All of the theoretical results described the six complexes with values of the relative energy within ca. 2.0 kcal/mol range.

All of the stretching modes (ν(NH) and ν(OH)) involved in the hydrogen bonding formation experienced a large, red shift in comparison to adenine and HP monomers. BSSE-free PES calculations showed its importance in the intermolecular hydrogen bond description. However, the binding energies for the corrected and uncorrected BSSE-free PESs values were similar.

The existence of structure **1** in the solid state was explained by means of the packing forces, the larger dipolar moment, and the presence of additional hydrogen bonds, giving this structure possible physiological significance in DNA damage.

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Supporting Information Available: Table SI-I containing the harmonic vibrational frequencies for the AHP complexes and adenine. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Wayne, R. P. *Chemistry of Atmospheres*; Clarendon Press: Oxford, 1991.

(2) Zhang, D. H.; Zhang, J. Z. H. *J. Chem. Phys.* **1993**, *98*, 6276.

(3) Cooper, M. S.; Heaney, H.; Newbold, A. J.; Sanderson, W. R. *Synlett* **1990**, 533.

(4) Varma, S. D.; Devamanoharan, P. S. *Free Radical Res. Commun.* **1991**, *14*, 125.

(5) Rowley, D. A.; Halliwell, B. *Clin. Sci.* **1983**, *64*, 649.

(6) Dizdaroglu, M.; Nackerdien, Z.; Chao, B. C.; Gajewski, E.; Rao, G. *Arch. Biochem. Biophys.* **1991**, *285*, 388.

(7) Schubert, J.; Wilmer, J. W. *Free Radical Biol. Med.* **1991**, *11*, 545.

(8) Gould, I. R.; Kollman, P. A. *J. Am. Chem. Soc.* **1994**, *116*, 2493.

(9) Schoone, K.; Smets, J.; Houben, L.; Vanbael, M. K.; Adamowicz, L.; Maes, G. *J. Phys. Chem. A* **1998**, *102*, 4863.

(10) Serra, M. A.; Dorner, B. K.; Silver, M. E. *Acta Crystallogr. C* **1992**, *48*, 1957.

(11) Schneiner, S. *Reviews in Computational Chemistry*; Lipkowitz, K. B., Boyd, D. B., Eds.; VCH: New York, 1991; Vol. 2, p 165.

(12) Dobado, J. A.; Molina, J.; Portal, D. *J. Phys. Chem. A* **1998**, *102*, 778.

(13) Latajka, Z.; Bouteiller, Y. *J. Chem. Phys.* **1994**, *101*, 9793.

(14) Novoa, J. J.; Sosa, C. *J. Phys. Chem.* **1995**, *99*, 15837.

(15) Pudzianowski, A. T. *J. Phys. Chem.* **1996**, *100*, 4781.

(16) Hamann, D. R. *Phys. Rev. B* **1997**, *55*, 10157.

(17) Lozynski, M.; Rusinska-Roszak, D.; Mack, H.-G. *J. Phys. Chem. A* **1998**, *102*, 2899.

(18) Bader, R. F. W. *Atoms in Molecules: a quantum theory*; Clarendon Press: Oxford, 1990.

(19) Bader, R. F. W. *Chem. Rev.* **1991**, *91*, 893.

(20) Dobado, J. A.; Molina, J. *J. Phys. Chem.* **1994**, *98*, 1819.

(21) Dobado, J. A.; Molina, J. *J. Phys. Chem.* **1994**, *98*, 7819.

(22) Espinosa, E.; Molins, E.; Lecomte, C. *Chem. Phys. Lett.* **1998**, *285*, 170.

(23) Jansen, H. B.; Ross, P. *Chem. Phys. Lett.* **1969**, *3*, 140.

(24) Boys, S. F.; Bernardi, F. *Mol. Phys.* **1970**, *19*, 553.

(25) Dobado, J. A.; Molina, J. *J. Phys. Chem.* **1993**, *97*, 7499.

(26) Mo, O.; Yañez, M.; Rozas, I.; Elguero, J. *J. Chem. Phys.* **1994**, *100*, 2871.

(27) Gonzalez, L.; Mo, O.; Yañez, M. *J. Comput. Chem.* **1997**, *18*, 1124.

(28) Mo, O.; Yañez, M.; Rozas, I.; Elguero, J. *Chem. Phys. Lett.* **1994**, *219*, 45.

(29) Xantheas, S. S. *J. Chem. Phys.* **1996**, *104*, 8821.

(30) Simón, S.; Duran, M.; Dannenberg, J. J. *J. Chem. Phys.* **1996**, *105*, 11024.

(31) Daza, M. C.; Dobado, J. A.; Molina, J. M.; Salvador, P.; Duran, M.; Cardoso, J. L. V. *J. Chem. Phys.*, in press.

(32) Schwenke, D. W.; Truhlar, D. G. *J. Chem. Phys.* **1985**, *82*, 2418; **1986**, *84*, 4113; **1987**, *86*, 3760.

(33) Frisch, M. J.; Del Bene, J. E.; Binkley, J. S.; Schaefer, H. F., III. *J. Chem. Phys.* **1986**, *84*, 2279.

(34) Paizs, B.; Salvador, S.; Duran, M.; Suhai, S. *J. Comput. Chem.*, accepted.

(35) Novoa, J. J.; Planas, M.; Rovira, M. C. *Chem. Phys. Lett.* **1996**, *251*, 33.

(36) Parr, R. G.; Yang, W. *Density functional theory of atoms and molecules*; Oxford University Press: Oxford, 1989.

(37) Jones, R. O.; Gurnnarsson, O. *Rev. Mod. Phys.* **1990**, *61*, 689.

(38) Kryachko, E. S.; Ludeña, E. V. *Energy Density Functional Theory of Many Electron Systems*; Kluwer Academic: London, 1990.

(39) Labanowski, J., Ed. *Density Functional Methods in Chemistry*; Springer: New York, 1991.

(40) Ziegler, T. *Chem. Rev.* **1991**, 651.

(41) Dobado, J. A.; Molina, J.; Portal, D. *J. Mol. Structure (THEOCHEM)* **1998** *433*, 181.

(42) Gaussian 94, revision C.2. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J.; Cioslowski, B. B.; Stefanov, A.; Nanayakkara, M.; Challacombe, J. B.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. Gaussian Inc.: Pittsburgh, PA, 1994.

(43) Gaussian 98, Revision A.4. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.;

Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. Gaussian Inc.: Pittsburgh, PA, 1998.

(44) Pulay, P. *J. Comput. Chem.* **1982**, *3*, 556.

(45) Fletcher, R. *Practical Methods of Optimization*; Wiley: New York, 1980; Vol. 1.

(46) Biegler-König, F. W.; Bader, R. F. W.; Tang, T. H. *J. Comput. Chem.* **1982**, *3*, 317.

(47) Dobado, J. A.; Molina, J.; Martínez-García, H.; Sundberg, M. R. *J. Am. Chem. Soc.* **1998**, *120*, 8461.

(48) Bader, R. F. W. In *Encyclopedia of Computational Chemistry*, Schleyer, P. v. R., Ed.; Wiley & Sons: Chichester, 1998.

(49) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.

(50) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.

(51) Dobado, J. A.; Molina, J.; Portal, D. *J. Mol. Structure (THEOCHEM)* **1998**, *433*, 181.

(52) Carsky, P.; Urban, M. *Ab initio Calculations. Methods and Applications in Chemistry. Lecture Notes in Chemistry*; Springer: Berlin, 1980; Vol. 16.

(53) Hobza, P.; Zahradnik, R. *Weak intermolecular interactions in Chemistry and Biology*; Academia: Prague; Elsevier: Amsterdam, 1980.

(54) Hobza, P.; Zahradnik, R. *Chem. Rev.* **1988**, *88*, 871.

(55) (a) van Lenthe, J. H.; van Duijneveldt-van de Rijdt, J. G. C. M.; van Duijneveldt, F. B. *Adv. Chem. Phys.* **1987**, *69*, 521. (b) Schwenke, D. W.; Truhlar, D. G. *J. Chem. Phys.* **1985**, *82*, 2418. (c) Dykstra, C. E. *Ab initio Calculations of the Structures and Properties of Molecules;* Elsevier: Amsterdam, 1988. (d) Mayer, I. *Theor. Chim. Acta* **1987**, *72*, 207. (e) Mayer, I. *Int. J. Quantum Chem.* **1983**, *23*, 341. (f) Loushin, S. K.; Liu, S.; Dykstra, C. E. *J. Chem. Phys.* **1986**, *84*, 2720.

(56) Gutowski, M.; van Lenthe, J. H.; Verbeek, J.; van Duijneveldt, F. B.; Chalasinski, G. *Chem. Phys. Lett.* **1986**, *124*, 370.

(57) Popelier, P. L. A. *Comput. Phys. Commun.* **1996**, *93*, 212.