MP2 and Density Functional Studies of Hydrogen Bonding in Model Trioses: D-(+)-Glyceraldehyde and Dihydroxyacetone

Marek Lozynski* and Danuta Rusinska-Roszak

Poznan Technical University, Institute of Chemical Technology and Engineering, Pl. M.Sklodowskiej-Curie 2, 60965 Poznan, Poland

Hans-Georg Mack*

Institut für Physikalische und Theoretische Chemie der Universität Tübingen, Auf der Morgenstelle 8, 72076 Tübingen, Germany

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Among the conformers of the title compounds, all stable structures found reveal hydrogen bonding to an sp^2 oxygen atom in five- or six-membered rings and usually cooperative effects. Nonlocal density functional calculations using different functionals prove the applicability of DFT to study geometries of systems containing intramolecular hydrogen bonds. The hydrogen bond parameters obtained applying the B3LYP approximation exhibit perfect agreement with those calculated at the MP2 level. The local gradient correction does not provide encouraging results.

Introduction

Until recently there existed no precise and efficient quantum mechanical methods to describe the subtle hydrogen-bonding effects in relative large biomolecules like carbohydrates or oligopeptides. The density functional theory (DFT) methods seem to be the first chance to precisely assess self-assembling properties or affinity of biomolecules for other macromolecules, especially for their high-affinity binding sites. Density functional theory belongs to the class of methods that proved to be an alternative to classic ab initio calculations, because they provide more economic procedures for calculating both structural and energetic properties. The most important aim of this work is to compare DFT parameters of intramolecular hydrogen bonds with those obtained from Møller−Plesset (MP2) calculations.

D-(+)-Glyceraldehyde (**1**) and achiral dihydroxyacetone (**2**) (see Figure 1) as isolated molecules, possessing free carbonyl functions, are ideal models for studying the effect of electron correlation on energy differences and hydrogen bonding. These compounds (dihydroxyacetone as phosphate) are formed from fructose 1-phosphate by enzymatic cleavage and are important compounds in the glycolytic pathway.[1] The first molecule is the simplest aldose with a chiral center at the C2 carbon atom. Dihydroxyacetone, being an isomer of glyceraldehyde, is a three-carbon ketose and possesses no asymmetric carbon. In glyceraldehyde, two hydroxyls acting as proton donors may form both five- and six-membered, hydrogen bonded rings with the carbonyl oxygen atom as an acceptor. Moreover, a cooperative phenomenon could be found. The prochirality of sp^3 oxygen atoms may double the number of stable conformations. Structural features of dihydroxyacetone allow the formation of a hydrogen bridge in a six-membered ring, if hydroxyls act as proton donor and proton acceptor, but do not engage with carbonyl groups. Thus, these two monosaccharides may be chosen as model compounds to investigate the intramolecular hydrogen bonding and to furnish more data about the performance of the tested density functionals.

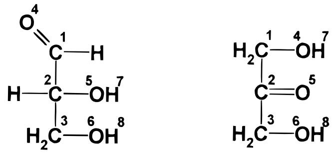

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Figure 1. Atom numbering for D-(+)-glyceraldehyde (**1**) and dihydroxyacetone (**2**).

In earlier publications it has been shown that the gradient-corrected density functional BP86 or better B3LYP gave an excellent description for the water dimer,[2,3] in contrast to the local spin density (LSD) approximation to the exchange-correlation functional, which was inadequate for describing hydrogen bonding. The nonlocal density approximation using BP86 and BLYP functionals was applied to the study of small water clusters (up to water hexamers).[4,5] The last functional has been found to yield very good agreement with experimental results for hydrogen-bonded complexes[6,7] or networks in an infinite water polymer.[8] The structure, interaction energy, and proton transfer features of the $(H_5O_2)^+$ complex[9] and of the water cluster containing $(H_3O)^+$ and $(OH)^-$ [10] were also investigated using the above functionals. The B3LYP functional was applied to assess the proton transfer process in the $(HFH)^-$ anion.[11] However, it is not known how well density functional theory will be suited for describing intramolecular hydrogen bonded systems in organic compounds. The geometric parameters obtained for 1,2-ethanediol show an excellent agreement with those calculated at the MP2 level of theory.[12]

Unfortunately, a direct assessment of the quality of the theoretical results for the geometry of both trioses is not possible. Experimental, i.e. X-ray data, are available for the stable, cyclic D,L-glyceraldehyde dimer only,[13,14] due to the reactivity of both carbonyl and hydroxyl groups directed toward the six-membered (bishemiacetal) ring formation.[1] Although in aqueous solution the monomeric, noncyclic structures are considered to be present in negligible amounts only, they nevertheless are responsible for the biochemical behavior of the aldehyde and ketone due to free carbonyl functions. Thus, this means that the molecular structures, energetically preferable conformations, and energy differences between the isomeric D-(+)-glyceraldehyde and dihydroxyacetone are central for the understanding of a variety

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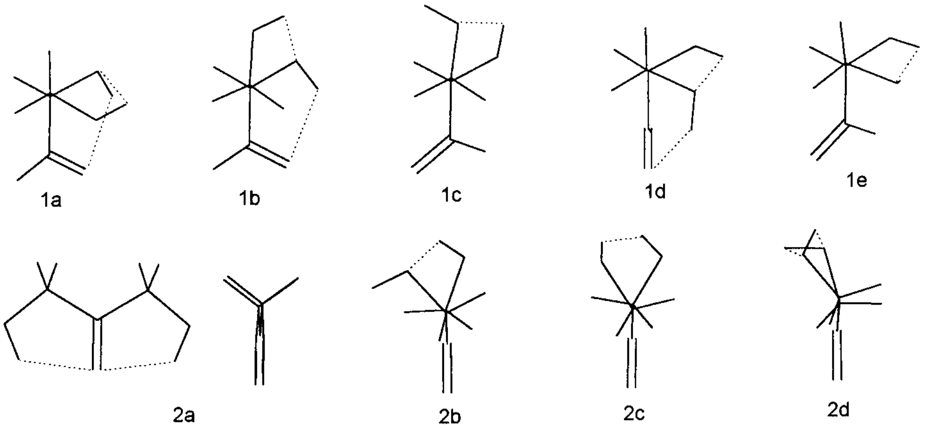

Figure 2. Newman projections of D-(+)-glyceraldehyde **1a**−**1e** and projections of dihydroxyacetone **2a**−**2d** MP2 conformers. For conformer **2a**: (left) view perpendicular to the carbonyl plane; (right) view in the direction of C(3)−C(1). Dotted lines denote hydrogen bond contacts.

of physical and chemical properties of carbohydrates. All this emphasizes the importance of reliable theoretical studies.

Method

The standard, moderate-sized 6-31G(d,p) contracted Gaussian basis set for the classic ab initio Hartree−Fock (HF) method and for many-body perturbation theory (MP2) as implemented into the GAUSSIAN 92/DFT[15] was used. The results of DFT calculations were obtained applying the B3LYP functional formed by combining Becke's three-parameter exchange functional[16] and the nonlocal correlation functional of Lee, Young, and Parr.[17] In the case of calculations labeled BP86 the nonlocal exchange functional of Becke[18] and the gradient-corrected correlation potential of Perdew[19] have been employed; similarly in the nonlocal BLYP method Becke's exchange functional[18] is combined with the correlational potential provided by Lee et al.[17] The SVWN functional, used for performing LSD functional calculations, combines Slater's exchange functional[20] and the correlation functional of Vosko, Wilk, and Nusair.[21]

The most commonly used basis sets for ab initio calculations of hydrogen-bonded systems are 6-31G(d,p), 6-311++G(d,p), cc-pVDZ, and aug-cc-pVTZ. The series of calculations performed for *small* hydrogen-bonded complexes indicated a strong basis set effect for DFT methods.[22] On the other hand, the addition of diffuse functions did not improve the hydrogen-bonded geometries in the case of DFT calculations.[23] The O···O distance obtained for the water dimer at the MP2/6-31G(d,p) level of theory is 2.910 Å,[24] in close agreement with the experimental value of 2.946 Å,[25] and the binding energies are −5.35 (with counterpoise correction)[24] and −5.44(7) kcal mol^{-1}, respectively.[26] In the MP2/aug-cc-pVDZ and MP2/aug-cc-pVTZ approximations the following structural and binding parameters are obtained:[3] 2.918 and 2.908 Å for the O···O distance, −5.26 and −5.18 kcal mol^{-1} for ΔE. These values are very similar to those predicted by the computationally less demanding MP2/6-31G(d,p) procedure. For these reasons, Pople's 6-31G(d,p) basis set was accecpted as an optimal choice for all the density functional methods in this study.

In the DFT calculations, the Coulomb and exact exchange integrals were evaluated analytically, and the integrals over the exchange and the correlation functionals were done over numerical grids, using the default grid options (50 radial shells, 194 angular points per shell, pruned to about 3000 points per atom) [cf. ref 6].

All ab initio and DFT calculations were performed on a Cray Y-MP8/832 computer (KFA, Jülich, Germany) as follows. Various conformers obtained at the semiempirical level of theory with PM3 parametrization were used as input for HF/3-21G structure optimizations. Subsequently, full geometry optimizations at the higher HF, MP2, and DFT levels were done for the HF/3-21G optimized structures.

Results and Discussion

Geometries of MP2 Structures. Trioses **1** and **2** as acyclic sugars have carbonyl oxygen atoms, which can be only acceptors for hydrogen bonding. The presence of the "acceptor-only" oxygen atom in ketotrioses prevents the formation of the cooperative chain. On the other hand, the central position of the ketone function makes proton donor or proton acceptor properties of O(1)H and O(3)H hydroxy groups equal or similar to O(α)H hydroxyls, depending on the conformer's symmetry. In the case of aldotrioses we deal with two different hydroxyls: O(α)H, affected by a formyl group, due to the peculiarity of the α-position, and O(*β*)H. The vicinity of the carbonyl group leads to a preference for the eclipsed over the gauche conformation, when the hydrogen bond to the carbonyl is formed. Therefore, the notation of Radom et al.[27] used to specify rotational isomers of vicinal dihydroxy compounds should to be extended. We suggest the e ($\Phi = 120°$) and e− ($\Phi = -120°$) symbols to decribe the orientation of H(α) with respect to the O(α)−C(α) bond, specifying the H7O5C2C3 dihedral angle (Figure 2). It is obvious that for structural reasons the notation could not be applied to **2** (1,3-dihydroxy compound).

Comparison with the results of many-body perturbation theory calculations shows that the second-order MP2 approximation closely reproduces available experimental data, such as hydrogen bond parameters as well as the dipole moment of the linear trans water dimer.[3] Therefore, it seems reasonable to compare the quality of a wide range of DFT methods to MP2 calculations, even using smaller basis sets, for example 6-31G(d,p). Considering the results of the MP2/6-31G(d,p) approximation, one can learn that for **1a** and **1b** the O5−H7 (i.e. in the O(α)H···O^{sp2} system) bond length is 0.972 Å, that is 0.05 Å longer than the O6−H8 bond (i.e. for O(*β*)H···O^{sp3}), while for **2a** (C_2 symmetry conformer) this bond amounts to 0.970 Å (Tables 1 and 2). It shows the strongest interaction of the O(α)H groups involved in the cooperative system. The value of the oxygen−hydrogen bond length not engaged in hydrogen bonding is 0.965 Å for both O(α)H and O(*β*)H (cf. **2b**−**2d** and **1c**), and the shortest O(*β*)−H bond (0.963 Å) is obtained for the **1e** conformer. Similarly, the aldehyde group engaged in hydrogen bonding possesses a C1=O4 bond length that is slightly longer: 1.226 Å for **1b** and **1d** or 1.223 Å for **1a**, but only 1.221 Å for **1e**. For the isomeric ketone, the carbonyl bond length C2=O5 is 1.230 Å in the case of **2a**, which is 0.007 Å longer than that for **1a**. For carbonyls not affected by hydrogen bonding the

TABLE 1: Selected Bond Lengths and Intramolecular Hydrogen Bond Optimized Parameters of D-(+)-Glyceraldehyde Conformers[a]

	HF/ 3-21G	HF/ 6-31G**	MP2/ 6-31G**	BP86/ 6-31G**	BLYP/ 6-31G**	B3LYP/ 6-31G**	SVWN/ 6-31G**	hydrogen bond type
				Conformer **1a**				
C2−O5	1.434	1.391	1.413	1.418	1.427	1.410	1.392	
O5−H7	0.971	0.948	0.972	0.990	0.988	0.975	0.998	
C1═O4	1.209	1.189	1.223	1.226	1.227	1.213	1.217	
C3−O6	1.434	1.394	1.416	1.419	1.428	1.412	1.391	cooperative system
O6−H8	0.969	0.945	0.968	0.982	0.982	0.970	0.987	5-memb. ring to
H7···O4	2.084	2.121	2.020	1.970	2.019	2.024	1.830	sp^2 oxygen
O5−H7···O4	113.3	113.7	119.3	122.1	120.7	119.2	124.4	5-memb. ring to
H8···O5	2.278	2.433	2.291	2.224	2.293	2.308	2.017	sp^3 oxygen
O6−H8···O5	107.2	103.5	110.1	114.0	112.1	110.1	118.9	
				Conformer **1b**				
C2−O5	1.434	1.392	1.413	1.418	1.426	1.410	1.391	
O5−H7	0.970	0.947	0.972	0.988	0.987	0.974	0.996	
C1═O4	1.211	1.189	1.226	1.228	1.230	1.215	1.220	
C3−O6	1.431	1.391	1.412	1.416	1.424	1.409	1.387	cooperative system
O6−H8	0.969	0.945	0.967	0.981	0.981	0.969	0.985	5-memb. ring to
H7···O4	2.094	2.115	2.039	2.007	2.056	2.050	1.869	sp^2 oxygen
O5−H7···O4	114.4	114.9	119.1	120.6	119.3	118.4	122.7	5-memb. ring to
H8···O5	2.200	2.369	2.251	2.229	2.281	2.284	2.011	sp^3 oxygen
O6−H8···O5	110.1	105.2	110.8	112.2	111.0	109.9	117.2	
				Conformer **1c**				
C2−O5	1.430	1.394	1.413	1.418	1.426	1.411	1.388	
O5−H7	0.969	0.945	0.968	0.983	0.983	0.970	0.988	
C1═O4	1.209	1.188	1.222	1.122	1.223	1.211	1.211	
C3−O6	1.449	1.405	1.427	1.435	1.443	1.425	1.408	
O6−H8	0.966	0.943	0.965	0.977	0.979	0.967	0.977	
H7···O6	2.169	2.319	2.202	2.113	2.179	2.205	1.960	5-memb. ring to
O5−H7···O6	114.2	110.0	115.8	119.8	118.2	116.0	122.3	sp^3 oxygen
				Conformer **1d**				
C2−O5	1.439	1.398	1.424	1.437	1.445	1.424	1.411	
O5−H7	0.972	0.947	0.971	0.988	0.986	0.973	0.997	
C1═O4	1.212	1.191	1.226	1.230	1.231	1.216	1.223	
C3−O6	1.446	1.402	1.426	1.435	1.442	1.424	1.411	cooperative system
O6−H8	0.967	0.945	0.967	0.984	0.983	0.970	0.992	5-memb. ring to
H7···O6	2.148	2.334	2.182	2.116	2.178	2.213	1.912	sp^3 oxygen
O5−H7···O6	115.7	110.9	117.1	120.2	118.6	116.3	124.5	6-memb ring to
H8···O4	2.328	2.454	2.219	2.086	2.139	2.204	1.878	sp^2 oxygen
O6−H8···O4	115.6	116.0	124.4	131.0	129.8	125.9	134.9	
				Conformer **1e**				
C2−O5	1.429	1.393	1.415	1.420	1.429	1.413	1.392	
O5−H7	0.970	0.946	0.968	0.982	0.982	0.970	0.987	
C1═O4	1.208	1.187	1.221	1.221	1.122	1.210	1.211	
C3−O6	1.448	1.406	1.429	1.439	1.448	1.429	1.413	
O6−H8	0.964	0.942	0.963	0.974	0.975	0.964	0.972	
H7···O6	2.043	2.228	2.133	2.076	2.136	2.137	1.902	5-memb ring to
O5−H7···O6	114.8	110.5	114.6	117.8	116.2	114.8	121.0	sp^3 oxygen

[a] Bond lengths in angstroms, angles in degrees.

trend is the same as in the aldehyde case, with the difference ranging from 0.004 to 0.006 Å. The most striking effect of hydrogen bonding is observed for carbon−oxygen single bonds. The typical value ranges from 1.412 Å for **1b** to 1.416 Å in **1a** (or from 1.413 to 1.419 Å for **2b** and **2d**, respectively) for hydroxyls forming hydrogen bonds. The extreme values of 1.403 Å for **2a** and 1.424 and 1.426 Å in the case **1d** are pronounced exceptions easily explained by unusual geometries of the considered systems (*vide infra).*

Indeed, the detailed analysis of the hydrogen bond lengths strongly suggests that there are two predominant factors that govern their strength: the size of the ring, in which hydrogen bonding is arranged, and the hybridization of the oxygen atom toward which the hydrogen bond is directed. The five-membered ring and O^{sp2} acceptor atom or the six-membered ring and O^{sp3} acceptor possess the shortest hydrogen bridge. The conformers **1a** (eG−g), **1b** (eGg−), and **2a** (twice) illustrate the former case. In fact, hydrogen bonds in a cooperative system are shorter (2.020 and 2.039 Å for **1a** and **1b**, respectively) than those in **2a** (2.042 Å). The bonds in **2c** with 2.022 Å, in **2b** with 2.048 Å, and in **2d** with 2.064 Å are examples of the latter case. It is evident that the strain introduced into the molecule, due to hydrogen bond formation, can be minimized more easily where hybridization and ring size are compatible. The predicted strain for the five-membered ring drops to near zero with respect to its flat conformation due to the participation of the carbon−oxygen double bond. Similarly, the puckered (chair or boat shape) form of the six-membered ring due to participation of tetrahedral atoms (including proton acceptor oxygen) entirely reduces angle strain. Thus, it is reasonable to assume that planar five- and nonplanar six-membered rings involved in hydrogen bonds can be strainless or at least have no angle strain in the tested molecules, and therefore, these hydrogen bonds are the shortest; that is they are the strongest.

In the case of the **1d** (gG−g−) conformer (six-membered ring and sp^2 oxygen) the hydrogen bond is much longer, 2.219 Å, like the five hydrogen bonds in the **1a**−**1e** conformers, where

TABLE 2: Selected Bond Lengths and Intramolecular Hydrogen Bond Optimized Parameters of Dihydroxyacetone Conformers[a]

	HF/ 3-21G	HF/ 6-31G**	MP2/ 6-31G**	BP86/ 6-31G**	BLYP/ 6-31G**	B3LYP/ 6-31G**	SVWN/ 6-31G**	hydrogen bond type
Conformer **2a**								
C1−O4	1.425	1.383	1.403	1.406	1.414	1.399	1.378	
O4−H7	0.970	0.947	0.970	0.985	0.985	0.973	0.990	
C2═O5	1.215	1.196	1.230	1.237	1.237	1.222	1.229	
C3−O6	1.425	1.383	1.403	1.406	1.414	1.399	1.378	
O6−H8	0.970	0.947	0.970	0.985	0.985	0.973	0.990	
H7···O5	2.093	2.107	2.042	2.014	2.053	2.047	1.898	5-memb. ring
O4−H7···O5	114.8	115.1	119.3	120.6	119.6	118.6	122.1	to sp^2 oxygen
H8···O5	2.092	2.108	2.042	2.014	2.053	2.047	1.898	5-memb. ring
O6−H8···O5	114.8	115.1	119.3	120.6	119.6	118.6	122.1	to sp^2 oxygen
Conformer **2b**								
C1−O4	1.427	1.392	1.413	1.417	1.426	1.410	1.389	
O4−H7	0.969	0.945	0.968	0.983	0.983	0.971	0.989	
C2═O5	1.209	1.192	1.225	1.226	1.228	1.215	1.216	
C3−O6	1.449	1.407	1.433	1.445	1.454	1.432	1.419	
O6−H8	0.966	0.943	0.965	0.976	0.978	0.966	0.975	
H7···O6	1.919	2.174	2.048	1.959	2.037	2.019	1.790	6-memb. ring
O4−H7···O6	129.2	124.2	130.1	136.5	133.2	132.9	140.0	to sp^3 oxygen
Conformer **2c**								
C1−O4	1.428	1.393	1.416	1.419	1.429	1.412	1.391	
O4−H7	0.969	0.944	0.967	0.984	0.983	0.970	0.989	
C2═O5	1.209	1.191	1.224	1.225	1.227	1.214	1.215	
C3−O6	1.448	1.406	1.431	1.441	1.449	1.429	1.415	
O6−H8	0.965	0.943	0.964	0.975	0.976	0.965	0.974	
H7···O6	1.913	2.143	2.022	1.929	1.988	2.000	1.776	6-memb. ring
O4−H7···O6	127.8	123.4	129.2	135.8	133.7	131.3	139.0	to sp^3 oxygen
Conformer **2d**								
C1−O4	1.430	1.395	1.419	1.423	1.432	1.416	1.395	
O4−H7	0.968	0.943	0.966	0.982	0.981	0.969	0.986	
C2═O5	1.211	1.192	1.226	1.227	1.228	1.215	1.217	
C3−O6	1.444	1.400	1.427	1.438	1.446	1.426	1.411	
O6−H8	0.967	0.943	0.965	0.977	0.978	0.967	0.978	
H7···O6	1.896	2.229	2.064	1.988	2.030	2.043	1.842	6-memb. ring
O4−H7···O6	131.9	115.3	125.4	129.1	128.6	127.3	130.1	to sp^3 oxygen
H8···O4	2.860	2.734	2.703	2.645	2.679	2.726	2.439	6-memb. ring
O6−H8···O4	67.3	82.1	81.9	84.2	83.8	80.7	87.6	to sp^3 oxygen

[a] Bond lengths in angstroms, bond angles in degrees.

we find five-membered rings and O^{sp3} oxygen (the bond lengths are 2.291, 2.251, 2.202, 2.182, and 2.133 Å, respectively). One can infer that the O(α)H bonds and bonds involved in cooperativity or both (see **1d**) are distinctly shorter.

For 1,2-ethanediol the available experimental[28,29] as well as the theoretical results[30−33] predict similar stabilities for the tGg− and gGg− conformers. Relative energies for four glycerol conformers (MP2/6-311G** level) exhibit distinct stabilities for the structures of forms with three or two internal hydrogen bonds.[34] The global minimum (g−G−g, g−Gg−) conformer, according to the correlated calculations, is the structure with three hydrogen bonds arranged in three puckered rings within the molecule. In this structure, where "cyclic cooperativity" exists, one ring is six-membered with the hydrogen bond directed to the O^{sp3} acceptor and with a nonbonded distance of 2.069 Å, the shortest one found in this conformer. For another conformer of glycerol (tG−g, g−Gg), where such a 1,6-interaction occurs, torsional repulsion is probably also relatively small and the shortest hydrogen bond is observed (1.951 Å).[34] The hydrogen bond lengths in five-membered rings to sp^3 oxygen are always longer, and these results are in full agreement with our data.

A recent study[35] of the hydroxymethyl rotamers of β-D-glucose demonstrates a considerable agreement with the above-depicted effects. The [ttttTg+] may, in fact, serve as a model for studying cooperativity in a finite chain system containing four hydrogen bonds. One may observe that the cooperative interaction within substantially reduces the lengths of the hydrogen bonds from 2.446 to 2.360 Å (for the third one) at the MP2/6-31G(d) level of theory. The fourth hydogen bond arranged in the six-membered ring (O^{sp3} as acceptor) forms the shortest contact: only 1.970 Å. The contraction of this bond is also observed for the [ttttG+g−] conformation, but it is substantially smaller by 0.29 Å in the five-membered ring.[35] Further theoretical investigations of such hydrogen-bonding properties may contribute to the understanding of the intramolecular interactions underlying hybridization and stereochemical phenomena.

Geometry Performance in DFT. Additional work has been done to determine how well various exchange and correlation functionals within DFT model the title compounds. Linear least squares analysis of selected *atomic* bonds, i.e. that of single and double carbon−oxygen and oxygen−hydrogen bonds, reveals very good consistency of all investigated methods. For HF/6-31G(d,p), all nonlocal, and SVWN functionals the correlation (with respect to a correlation coefficient r) with MP2 results is perfect (Table 3). The slope value (a scale factor) is almost 1, and the intercept (an additive constant) is very small, except for the SVWN method, where values of 0.913 and 0.102 Å, respectively, were obtained. One can see that linear scaling considerably improves rms fits both for the HF/6-31G(d,p) and for the SVWN method, but the HF/3-21G results are independent of the scaling procedure. The detailed discussion of the relative accuracy of each DFT method in determining the *hydrogen* bond parameters of **1** and **2** follows below.

TABLE 3: Linear Least-Squares Analysis of Carbon−Oxygen and Oxygen−Hydrogen Atomic Bond Lengths for Conformers 1 and 2 at Different Levels of HF and DFT Theory[a]

method	*r*	max err.[b]	rms err.[b]	slope	intercept[b]	max fit[b]	rms fit[b]
HF/3-21G	0.999	0.022	0.008	1.034	−0.036	0.021	0.005
HF/6-31G(d,p)	1.000	0.037	0.029	0.998	−0.023	0.012	0.001
BP86/6-31G(d,p)	1.000	0.018	0.005	0.982	0.031	0.008	0.001
BLYP/6-31G(d,p)	1.000	0.021	0.008	1.000	0.012	0.011	0.001
B3LYP/6-31G(d,p)	1.000	0.011	0.001	0.989	0.011	0.009	0.001
SVWN/6-31G(d,p)	1.000	0.026	0.015	0.913	0.102	0.009	0.001

[a] Compared to MP2/6-31G(d,p). [b] In angstroms.

TABLE 4: Linear Least-Squares Analysis of Hydrogen Bond Lengths for Conformers 1 and 2 at Different Levels of HF and DFT Theory[a]

method	*r*	max err.[b]	rms err.[b]	slope	intercept[b]	max fit[b]	rms fit[b]
HF/3-21G	0.937	0.168	0.119	1.242	−0.533	0.134	0.092
HF/6-31G(d,p)	0.961	0.235	0.218	0.949	0.225	0.123	0.032
BP86/6-31G(d,p)	0.985	0.133	0.070	0.976	−0.011	0.067	0.012
BLYP/6-31G(d,p)	0.988	0.080	0.011	0.974	0.046	0.069	0.010
B3LYP/6-31G(d,p)	0.996	0.033	0.005	1.053	−0.111	0.027	0.004
SVWN/6-31G(d,p)	0.956	0.343	0.788	0.856	0.079	0.103	0.030

[a] Compared to MP2/6-31G(d,p). [b] In angstroms.

TABLE 5: D-(+)-Glyceraldehyde (1) Conformers[a]

method	absolute energy **1a**	relative energies **1a**	**1b**	**1c**	**1d**	**1e**
HF/3-21G	−339.746 873 7	0.00	1.73	2.48	−0.43	0.46
HF/6-31G (d,p)	−341.673 581 2	0.00	1.60	2.81	1.01	2.14
MP2/6-31G (d,p)	−342.649 010 9	0.00	1.95	4.29	1.50	3.55
BP86/6-31G (d,p)	−343.581 241 4	0.00	0.95	4.37	1.46	4.71
BLYP/6-31G (d,p)	−343.481 459 0	0.00	0.88	3.95	1.21	4.28
B3LYP/6-31G (d,p)	−343.579 823 2	0.00	1.13	3.93	1.57	3.86
SVWN/6-31G (d,p)	−341.833 061 5	0.00	1.47	6.90	1.48	6.76

[a] Absolute energy of **1a** (in hartrees) and relative energies of **1a**−**1e** (in kcal mol$^{-1)}$ as obtained by the various computational procedures.

BP86. Even though absolute values of bond distances and angles can differ significantly at the BP86 and MP2 levels of theory, the geometric trends obtained reasonably well reflect all features of the systems investigated. The BP86 optimized H···O bond lengths reported in Tables 1 and 2 (for atom numbering see Figure 1) differ from the MP2 values, and they are always shorter. Hydrogen bond angles relax in response to the enhancement of interaction. One can see that the BP86 optimized O−H···O angles are more obtuse than the MP2 values in order to bring the H···O atoms closer together. As expected for BP86 hydrogen bond lengths, Table 4 reveals a remarkable slope value and a small, although negative, intercept (0.976 and −0.011, respectively). Therefore, it is possible to scale the BP86 results to obtain relatively good lengths. It is seen that reoptimization of HF/3-21G results with BP86 leads to a considerable improvement with respect to the agreement with the highest level results (*r* value increases from 0.937 to 0.985).

BLYP. Table 4 shows that the initial maximum error in bond length is only 0.080 Å and the rms error amounts to 0.011 Å, a much better result than in the case of the BP86 functional. As expected, when linear scaling is applied, only a small improvement in accuracy is obtained. BLYP, like the B3LPY approximation, does agree very well with the highest level of theory.

B3LYP. This nonlocal method including Becke's three-parameter exchange functional produces results that are virtually identical to the full MP2 optimized values. The maximum error in the hydrogen bond length is only 0.033 Å, and the linear scaling does not change the results at all. A slightly worse agreement is found for hydrogen bond angles: *r* is 0.997, slope is 1.074, and intercept is equal to −8.34°; initial maximum error decreases from 2.80° to 1.57° after the fit procedure. For bond parameters the B3LYP approach appears to be accurate enough to model hydrogen bonding, at least in compounds containing oxygen proton donors and proton acceptors.

SVWN. The results suggest that this local DFT method should not be used to examine molecules with hydrogen bridges like glyceraldehyde or dihydroxyacetone. However, despite the rms error of 0.788, it is possible to scale SVWN results to obtain reasonably good parameters for bond lengths. Linear scaling improves the rms error relative to the highest level of theory (Table 4).

Very recently, Csonka, Elias, and Csizmadia performed an extensive study for the pyranose chair form of D-glucose applying DFT methods.[23] They reported a full agreement between the hydrogen-bonding geometries as predicted by the B3LYP method and the corresponding MP2 results. Moreover, their calculations indicate that the BP86 functional follows the trend of the present work. The correct description of all O−H···O contacts demonstrates the usefulness of the gradient-corrected results, although the basis set is important to obtain well-optimized geometries.[23]

A comparison reveals a surprising agreement between HF/3-21G and MP2/6-31G(d,p) lengths and angles of hydrogen bonds, probably better than for HF/6-31G(d,p). The initial errors given in Table 4 are pronounced. Always, the sp^3 oxygen in O^{sp3}···H bond lengths are too short (by about 0.01−0.17 Å), while the O^{sp2}···H bonds are too long (usually by ca. 0.05 Å; Tables 1 and 2). Obviously, this remarkable accuracy results from some cancellation of errors due to basis set deficiency (HF/3-21G → HF/6-31G(d,p) leads to bond shortening) and neglect of electron correlation (HF/6-31G(d,p) → MP2/6-31G(d,p) leads to lengthening of the bonds). Nevertheless, Table 4 suggests that the HF/3-21G level of theory may provide an approximate representation of the geometries of equilibrium structures for larger carbohydrate molecules (than simple trioses [cf. ref 35]). In contrast to this, the HF/6-31G(d,p) level of theory works reasonably well in describing hydrogen bonds, but only after scaling, which considerably improves the results.

Relative Energies. The results for the D-(+)-glyceraldehyde conformers, as obtained by the various DFT functionals and by the ab initio approaches, are summarized in Table 5. In Table 6 the corresponding data for four dihydroxyacetone conformers are collected. A cursory inspection of Tables 5 and 6 reveals that all DFT approximations used properly predict the most stable conformers for both D-(+)-glyceraldehyde and

TABLE 6: Dihydroxyacetone (2) Conformers[a]

method	absolute energy **2a**	relative energies **2a**	**2b**	**2c**	**2d**
HF/3-21G	−339.746 873 7	0.00	−1.50	−1.20	1.73
HF/6-31G (d,p)	−341.676 472 6	0.00	2.55	2.53	4.63
MP2/6-31G (d,p)	−342.648 693 7	0.00	2.54	2.87	4.61
BP86/6-31G (d,p)	−343.586 028 8	0.00	4.78	5.53	6.13
BLYP/6-31G (d,p)	−343.485 549 1	0.00	4.14	4.82	5.30
B3LYP/6-31G (d,p)	−343.583 981 0	0.00	4.06	4.52	5.52
SVWN/6-31G (d,p)	−341.838 260 8	0.00	6.72	7.47	8.35

[a] Absolute energy of **2a** (in hartrees) and relative energies of **2a**−**2d** (in kcal mol$^{-1)}$ as obtained by the various computational procedures.

dihydroxyacetone. The MP2/6-31G(d,p) energy difference between **1** and **2** amounts to −0.20 kcal mol^{-1} for the respective most stable conformers. This value changes to 3.00, 2.57, and 2.61 kcal mol^{-1} for DFT calculations at the BP86, BLYP, and B3LYP levels, respectively. Hartree−Fock calculations performed in the HF/3-21G approximation demonstrate that it is not possible to obtain, at this level of theory, a proper prediction of the relative energies for the stable conformations of the hydroxyaldehyde and of the hydroxyketone derivative. In contrast to this, the more advanced HF/6-31G(d,p) calculations, as compared to the MP2 results, reproduce the sequence of the relative energies fairly well. The comparison of HF and MP2 results demonstrates that inclusion of electron correlation has a major influence on the relative energies in the case of **1**. For D-(+)-glyceraldehyde we found that the **1a** rotamer is the most stable one, even though it is 1.95 kcal mol^{-1} lower in energy than **1b** (MP2 approximation). In both conformers the hydrogen atom of the proton acceptor hydroxyl group (i.e. of the hydroxyl group at the epimeric carbon atom) is also engaged in an intramolecular interaction with the oxygen atom of the carbonyl group. This means that the rotational freedom of the proton acceptor hydroxyl is entirely limited, and geometrical constraints, increase the energy, apparently more in **1b**, although the cooperative interaction still works. The energy of the third cooperative system, **1d**, is somewhat lower than that of **1b** (1.50 kcal mol^{-1} at the MP2 level, relative to **1a**).

In general, the best agreement between DFT and MP2 energies is obtained in the case of the B3LYP and BLYP methods. However, it is typical that the relative stabilities of conformers **1b** and **1d** depend on the theoretical approximations applied. The DFT approaches predict that **1d** is significantly less stable than conformation **1b**. One cannot exclude that this is due to the cooperativity of the hydrogen bonds in the more polar aldehyde molecule **1**, in contrast to the symmetric ketone structure **2**, where such inner interactions cannot exist. Moreover, the application of nonlocal density functionals dramatically affects the depths of the energy minima in compound **2**, but the predicted energy ranking **2b** < **2c** < **2d** is not at variance with the energies of the MP2 optimized geometries. The observed effect is not understood, because the DFT results of hydrogen-bonding interactions in intermolecular complexes result in rather low interaction energies when the LYP functional is used.[35] It is interesting enough that also the inclusion of the VWN local correlation functional decreases the interaction energy, in good agreement with previous calculations.[22]

Conclusion

These several model calculations on a few triose conformers show that cooperative interactions of neighboring hydroxyl groups may play a significant role in modeling structural properties of carbohydrates and their derivatives. Finally, our calculations demonstrate that the stability of different conformations appears to be a consequence of the number of hydrogen bridges formed. On the other hand, hydrogen bond geometries predominantly depend on both the ring size and hybridization of the acceptor atom involved, being sensitive to the spatial arrangement of the oxygen lone pairs. The position of the proton donor hydroxyl relative to the carbonyl function is a less substantial factor.

It is clear that the participation of cooperative phenomena in hydrogen bonding is essential for the energy of the carbohydrate conformers. Cooperativity is strong enough to have a possible influence on their real structures. For this reason it is important to investigate the contribution of cooperativity to overall behavior of such systems. Our studies demonstrate that the nonlocal density functional approximation appears to be accurate enough to describe the intramolecular hydrogen bonding of D-(+)-glyceraldehyde and dihydroxyacetone. Calculations for different conformers of these trioses show that the B3LYP and, to a somewhat less degree, the BLYP procedures result in hydrogen bond geometries that are in excellent accordance with those obtained from full MP2 calculations. It is also observed that BP86 calculations carried out with the same basis set lead to hydrogen bond lengths that are evidently shorter. The SVWN method (only LSD approximation) results in geometries that provide a distinct divergence from the data obtained by nonlocal procedures. However, our results reveal that, in some cases, B3LYP and MP2 can lead to different relative stabilities for structures that are close in energy. It is not quite clear why the relative energies for one set of conformers (namely, for dihydroxyacetone) are predicted to be essentially higher by all nonlocal DFT approximations, while for the other set (the aldehyde case) the correlation is quite satisfactory. Generally, our studies confirm that electron correlation effects are especially important in modeling hydrogen bonding.

To conclude, it is possible that DFT calculations, which are much less computationally demanding than MP2, may be used for the vicinal heteroatom system, which is able to form hydrogen bonds,[34−39] and also for larger systems, which mimic biochemical structures, especially those with intimate involvement of hydrogen bonds.

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References and Notes

(1) Lehninger, A. L.; Nelson, D. L.; Cox, M. M. *Principles of Biochemistry*, 2nd ed.; Worth Publishers: New York, 1993.
(2) Ortiz, G.; Ballone, P. *Phys. Rev. B* **1991**, *43*, 6376.
(3) Kim, K.; Jordan, K. D. *J. Phys. Chem.* **1994**, *98*, 10089.
(4) Lee, C.; Chen, H.; Fitzgerald, G. *J. Chem. Phys.* **1994**, *101*, 4472.
(5) Laasonen, K.; Parrinello, M.; Car, R.; Lee, C.; Vanderbilt, D. *Chem. Phys. Lett.* **1993**, *207*, 208.
(6) Abashkin, Y.; Mele, F.; Russo, N.; Toscano, M. *Int. J. Quantum Chem.* **1994**, *52*, 1011.
(7) Kaschner, R.; Seifert, G. *Int. J. Quantum Chem.* **1994**, *52*, 957.
(8) Suchai, S. *J. Phys. Chem.* **1995**, *99*, 1172.
(9) Mijoule, C.; Latajka, Z.; Borgis, D. *Chem. Phys. Lett.* **1993**, *208*, 364.
(10) Lee, C.; Sosa, C.; Novoa, J. J. In preparation.
(11) Latajka, Z.; Bouteiller, Y.; Schreiner, S. *Chem. Phys. Lett.* **1995**, *234*, 159.
(12) Csonka, G. I.; Csizmadia, I. G. *Chem. Phys. Lett.* **1995**, *243*, 419.
(13) Senma, M.; Taira, Z.; Osaki, K.; Taga, T. *J. Chem. Soc., Chem. Commun.* **1973**, 880.
(14) Lehmann, C. W.; Luger, P. *Z. Kristallogr.* **1991**, *195*, 49.

(15) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Wong, M. W.; Foresman, J. B.; Robb, M. A.; Head-Gordon, M.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. *Gaussian 92DFT*, Revision G; Gaussian, Inc.: Pittsburgh, PA, 1993.

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

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

(18) Becke, A. D. *Phys. Rev A* **1988**, *38*, 3098.

(19) Perdew, J. P. *Phys. Rev. B* **1986**, *33*, 8822.

(20) Slater, J. C. *The Self-Consistent Field for Molecules and Solids, Quantum Theory of Molecules and Solids*; McGraw-Hill: New York, 1974; Vol. 4.

(21) Vosko, S. H.; Wilk, L.; Nusair, M. *Can. J. Phys.* **1980**, *58*, 1200.

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

(23) Csonka, G. I.; Elias, K.; Csizmadia I. G. *Chem. Phys. Lett.* **1996**, *257*, 49.

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

(25) Odutola, J. A.; Dyke, T. R. *J. Chem. Phys.* **1980**, *72*, 5062.

(26) Curtiss, L. A.; Frurip, D. J.; Blander, M. *J. Chem. Phys.* **1979**, *71*, 2703.

(27) Radom, L.; Lathan, W. A.; Hehre, W. J.; Pople, J. A. *J. Am. Chem. Soc.* **1973**, *95*, 693.

(28) Kristiansen, P.-E.; Marstokk, K.-M.; Møllendal, H. *Acta Chem. Scand.* **1987**, *A41*, 403.

(29) Takeuchi, H.; Tasumi, M. *Chem. Phys.* **1983**, *77*, 21.

(30) Cramer, C. J.; Truhlar, D. G. *J. Am. Chem. Soc.* **1994**, *116*, 3892.

(31) Oie, T.; Tapiol, I. A.; Burt, S. K. *J. Phys. Chem.* **1994**, *98*, 1121.

(32) Cabral, B. J. C.; Albuquerque, L. M. P. C.; Fernandes, F. M. S. S. *Theor. Chim. Acta* **1991**, *78*, 271.

(33) Bultinck, P.; Goeminne, A.; Van de Vondel, D. *J. Mol. Struct. (THEOCHEM)* **1995**, *357*, 19.

(34) Teppen, B. J.; Cao, M.; Frey, R. F.; van Alsenoy, C.; Miller, D. M.; Schäfer, L. *J. Mol. Struct. (THEOCHEM)* **1994**, *314*, 169.

(35) Barrows, S. E.; Dulles, F. J.; Cramer, C. J.; French, A. D.; Truhlar, D. G. *Carbohydr. Res.* **1995**, *276*, 219.

(36) Luke, B. T. *J. Comput. Chem.* **1994**, *15*, 1176.

(37) Bultinck, P.; Goeminne, A.; Van de Vondel, D. *J. Mol. Struct. (THEOCHEM)* **1995**, *339*, 1.

(38) Bultinck, P.; Goeminne, A.; Van de Vondel, D. *J. Mol. Struct. (THEOCHEM)* **1995**, *334*, 101.

(39) Buemi, G. *J. Chem. Soc., Faraday Trans.* **1994**, *90*, 1211.