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Computational study of three dimensional potential energy surfaces in intermolecular hydrogen bonding of *cis*-urocanic acid

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ABSTRACT

The interamolecular hydrogen bond (IMHB) of the neutral, cationic, and anionic *cis*-urocanic acid (*cis*-UCA, (Z)-3-(I'*H*-imidazol-4'(5')-yl)propenoic acid) were investigated in the gas phase within ab-initio calculations. To determine the energy and molecular structures, all the compounds were initially optimized at B3LYP and MP2 methods by use of 6-31G* and 6-31G** level of theory. Suitable single-point calculations have been subsequently done. Two dimensional energy curves have been obtained, and by adding a geometrical parameter, the potential energy surface is also plotted. The three-dimensional potential energy surface for proton motion within the molecule in the direction posses the lowest possible energy has been determined. These results show that the properties of hydrogen bonds are significantly different in the three forms of the investigated cis-urocanic acid. For instance, the bond strength in ionic molecules (cationic and anionic) is about twice of that of the neutral molecule. Evaluation of the potential energy versus distance curve is performed by mentioned methods and a single potential barrier curve which is relatively symmetrical is gained. The removal of potential barrier can be attributed to the high magnitude of hydrogen bonding strength.

Keywords: Ab initio calculation; Intermolecular hydrogen bond; Potential energy surface; cis-Urocanic acid

INTRODUCTION

Urocanic acid (2-propenoic acid, 3-[IH-imidazol-4(5)-yl], UA) is one of the smallest molecules to have stimulated global interest among biologists, environmentalists, photochemists, photobiologists, medicinal chemists and immunologists [1]. The study of the hydrogen bond has long been a topic of intensive scientific research due to its relevance in materials science, biochemistry, organic chemistry, inorganic chemistry, solid-state physics, and molecular medicine [2-6]. In recent years, the short-strong hydrogen bond, usually referred as the lowbarrier hydrogen bond (LBHB), has attracted considerable attention because of its possible role in enzyme catalysis [7-10]. It has been suggested that LBHB can supply up to 20 kcal/mol to stabilize the transition states in

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enzymatic reactions [7]. However, the importance of LBHBs in enzyme catalysis has been a controversial issue [11,12]. Although the LBHBs have been shown to be involved in several enzyme systems [13,14].

The formation of an interamolecular hydrogen bond (IMHB) in *cis*-UCA and its derivatives has been demonstrated by various experimental methods in solutions [15-17] and by theoretical calculations in the gas phase [18]. The IMHB in *cis*-UCA has a more general interest than just making part of the chemistry of UCA itself. It is analogous to the N-H···O=C type of hydrogen bond that plays an essential role in determining the conformation of many important bio-organic molecules, such proteins and nucleic acids [19]. Especially, *cis*-UCA is regarded as one of the best model compounds for the interamolecular hydrogen bond prevailing in the catalytic triad of serine proteases [20,21].

Within this work, the properties of internal hydrogen bonds have been computationally investigated among the neutral, cationic and anionic forms of *cis*-urocanic acid. The neutral *cis*-urocanic acid has two conformational structures, and both structures have been investigated. The properties including the energies have been evaluated from the optimized structures. Moreover, two and three dimensional diagrams based on calculated energies versus the bond angles or distances have been also evaluated for the investigated models.

COMPUTATIONAL METHODS

cis-UCA structures **1-4** (Fig. 1) were optimized up to the MP2/6-31G** [22] level of theory. Calculations have been performed based on the B3LYP and MP2 methods and 6-31G* and 6-311G** standard basis sets as implemented in the Gaussian 03 program [23]. To achieve our propose, the changes of distance and angles of internal hydrogen bonding atoms (O−H···N and N−H···O) of *cis*-UCA have been followed at different positions. The energies for each step of overall changes have been recorded for plotting two and three dimensional diagrams; energies vs. geometries. These diagrams were plotted by GaussView, Ver. 5 [24]. It is noteworthy that properties of three forms of *cis*-UCA have been investigated including neutral, cationic and anionic forms.

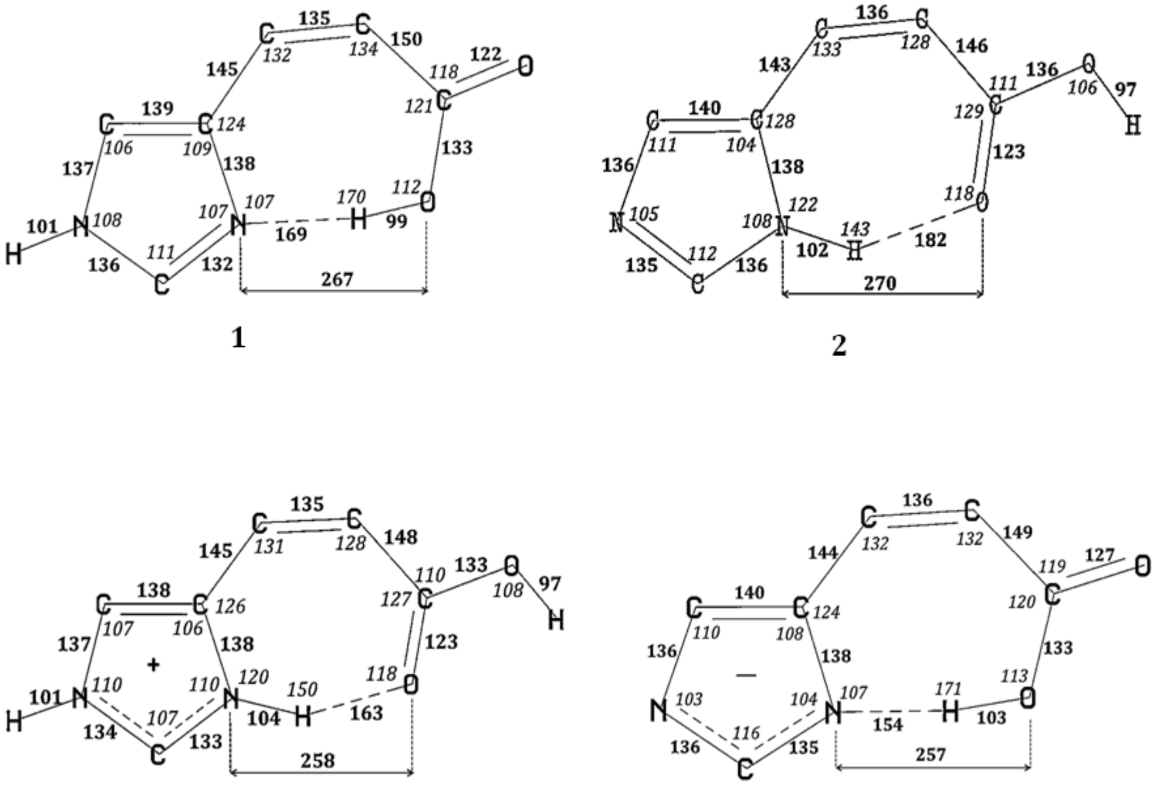
The interamolecular hydrogen bond formation energy was determined according to equation 1:

$$E_{HB} = E_e(\text{with HB}) - E_e(\text{without HB}) \quad (1)$$

Before detecting the changes of interamolecular hydrogen bonds, the optimized structures have been evaluated for the investigated models of study. The parameters of energies have been evaluated for the investigated structures.

RESULTS AND DISCUSSION

The optimized forms in all four molecules (both neutral, cation and anion) can be seen in Figure 1 which were optimized at MP2/6-31G ** level of theory by the described methods .For convenience, the neutral (OHN), Neutral (NH···O), cation and anion molecules, have been labeled **a**, **b**, **c** and **d**, respectively. The bond lengths and bond angles were obtained by different methods. Energy (in kcal/mol) of all four molecules is given in Table 1.



1

2

3

4

Fig. 1. The optimized geometries of the neutral (**1**, **2**), cationic (**3**) and anionic (**4**) cis-UCA structures. The bond lengths (bold face) are given in pm and the angles (italic) in degree. All structures were optimized by MP2/6-31G** level of theory.

Table 1. The energy (in kcal/mol) of four *cis*-UCA molecules in different methods

Physical Properties	Methods/Basis sets	(a) Neutral (O−H···N)	(b) Neutral (N−H···O)	(c) Cationic	(d) Anionic
Energy (au)	*B3LYP/6-31G**	-308851.10	-308858.64	—	—
	*B3LYP/6-31G***	-308861.15	-308868.05	-309109.64	-308522.30
	*MP2/6-31G***	-307980.51	-307986.41	-308227.37	-307641.28

In this stage the minimum energy path must be investigated. We know that the hydrogen atom is moving between the nitrogen and oxygen atoms. Thus, the single-point calculations used to determine the energy changes associated with changes in the distance and the angles due to movements of hydrogen atom between the oxygen and nitrogen atoms. Since the *cis*-UCA is a circular molecule and hydrogen with nitrogen and carbon atoms are in angled, an energy series as a function of the distance that can be achieved within the original optimum angles, and the other based on a distance that is achieved through the 180-degree angle. The energy changes depending on the changing the angle that hydrogen can be between the nitrogen and carbon atoms, has been examined, and ultimately lowest energy and the strongest hydrogen bonds in the molecule was obtained.

The structures have been optimized at MP2/6-31G** level of theory are shown in Fig. 2. In such structures, the potential energy curves as a function of the desired angles were studied using quantum methods. In all four molecules studied, it is impossible to directly change the NHO angle, and so changing the angle of the carbon atom attached to the oxygen and hydrogen (in **a** and **d** molecules) and the angle of the carbon atom attached to the nitrogen and hydrogen (in **b** and **c** molecules) were used for this purpose.

Therefore the C_8-O_{10}-H_{16} angle has been scanned within 83.22 to 143.22 degrees with 1 degree intervals and its potential energy is measured in each case (totally 61 cases). However the optimized angle was 113.22 degree. The two-dimensional potential energy curve is plotted as a function of the angle, is obtained, where there are two important points (Fig. 3). The first point where the curve is proportional to the minimum potential energy, resulting in a stable state of the molecule is located (-492.20 hartree, 308855.5 kcal/mol). The second point is where the angle is closest to 180 degree position (179.8) and in each of the previous and next modes of the angle, is 180 away. This energy is equal to -492.20 hartree (308855.5 kcal/mol). All these works have been done on three other molecules that results are summarized in Table 2.

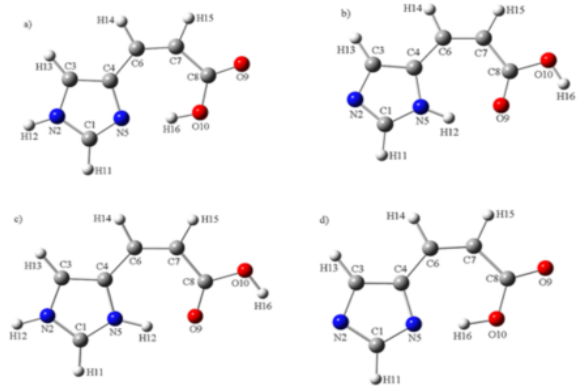


Fig. 2. All structures of *cis*-UCA optimized in MP2/6-31G**.

In the study of potential energy vs. distance curve, two states are considered. First state is the optimized angle has been fixed at 180 degrees between the three atoms forming hydrogen bonds and the next state, when the angle depending on the distance between the two atoms is changed during the optimization. In molecule **a**, the first diagram (Fig. 4, a), was plotted in fixed angle of 180 degrees of N_5-H_{16}-O_{10}. In this curve, the distance between O_{10} to H_{16} from 0.6 Å with steps of 0.01 to 2.06 Å that totally 147 state is obtained has increased which in each of these states, the amount of measured energy in the two-dimensional potential energy versus distance curve is obtained. The second diagram (Fig. 4, b), was plotted in optimized angle. In this curve, the distance between O_{10} to H_{16} has increased from 0.5 Å with steps of 0.01 to 2.5 Å that totally 201 state is obtained. These works have been done on three other molecules and results obtained in two mentioned methods.

To calculate the interamolecular hydrogen bond energy (IMHB), the method chosen here is a method that response on all four molecules. In this way, the C_6-C_7 bond *in* all molecules, rotated by 180 degrees and subsequently the resulting structure has lack of interamolecular hydrogen bond. All new structures were optimized again by the previous method. With the new energy and using equation (1) the hydrogen bond energy can be obtained (Table 3). Figure 5 shows that the rotated C_6-C_7 bonds for four molecules.

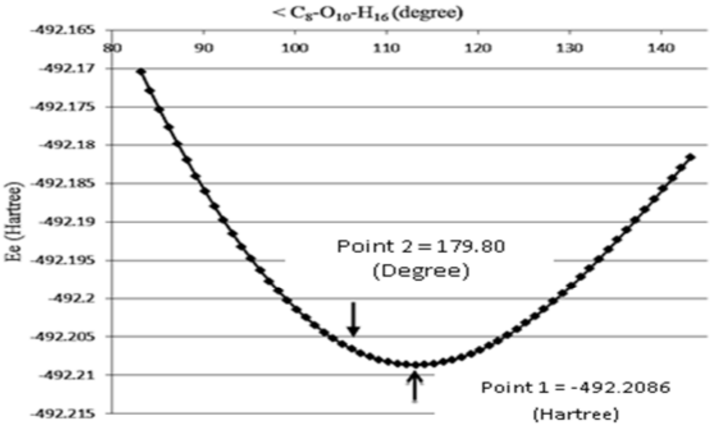
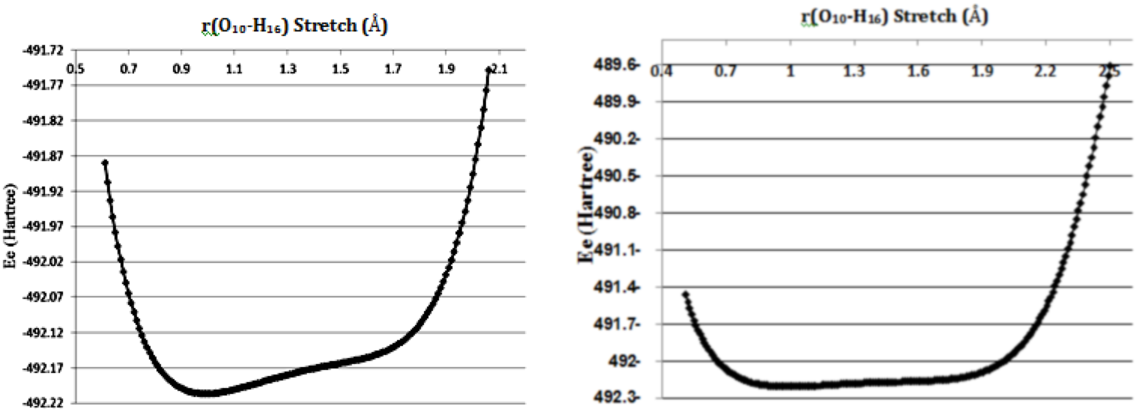


Fig. 3. Two-dimensional potential energy curve, potential energy (hartree) vs. angle (degree) in **a** molecule as calculated using the B3LYP/6-31G** method. Point 1 is proportional to the minimum potential energy and point 2 is where the $O - H \cdots N$ angle is closest to 180 degree position

Table 2. Properties of important point in 2D potential energy vs. angle in 4 molecules

Molecules	a	b	c	d
Point 1 (Degree, kcal/mol)	$<C_8$-O_{10}-H_{16} 113.22°	$<C_4$-N_5-H_{12} 121.54°	$<C_4$-N_5-H_{12} 118.65°	$<C_8$-O_{10}-H_{16} 113.87°
	-308860.94	-308868.19	-309109.43	-308522.12
Point 2 (Degree, kcal/mol)	$<O_{10}$-H_{16}-N_5 179.80°	$<N_5$-H_{12}-O_9 179.78°	$<N_5$-H_{12}-O_9 179.54°	$<O_{10}$-H_{16}-N_5 179.40
	-308859.63	-308854.77	-309100.46	-308520.52



a b

Fig. 4. Two-dimensional potential energy curve, potential energy (hartree) vs. distance (angstrom) in a molecule as calculated using the B3LYP/6-31G** method. The curve a, is in fixed N_5-H_{16}-O_{10} angle and the curve b, is in optimized angle were plotted.

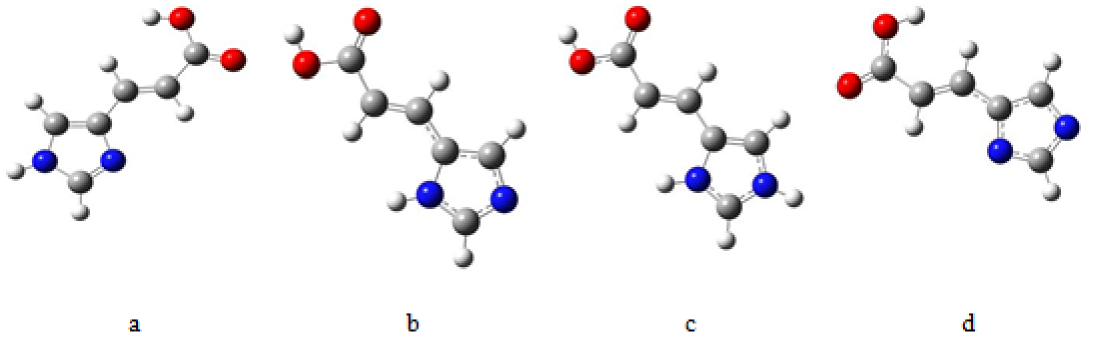


Fig. 5. The rotated C_6-C_7 bonds for four molecules.

Table 3. Interamolecular hydrogen bond energy in four structures with two methods

Structure / Methods	a	b	c	d
B3LYP/6-31G**	−0.017	−0.014	−0.028	−0.031
MP2/6-31G**	−0.018	−0.012	−0.025	−0.033

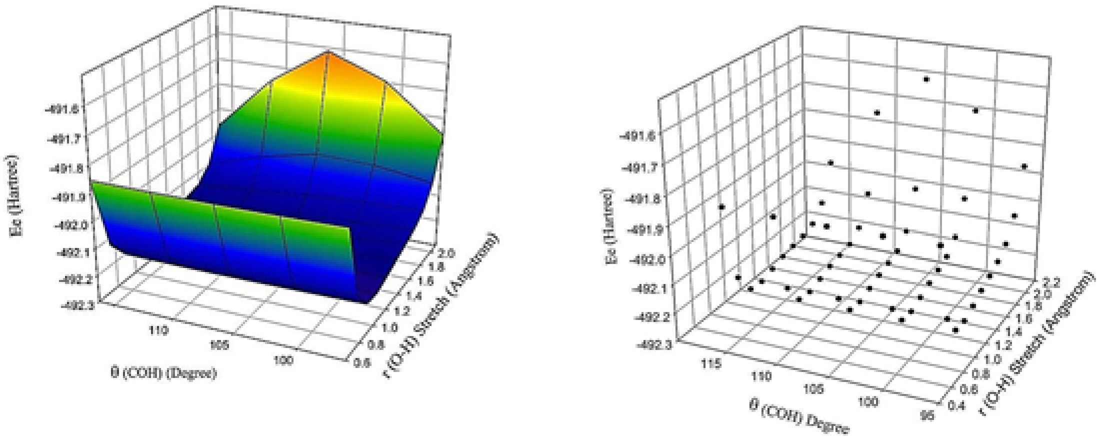


Fig. 6. Mesh graph (left) and scatter (right) three-dimensional potential energy in a molecule, calculated with B3LYP/6-31G**. (Energy, angle and distance in hartee, degrees are angstrom respectively.)

Table 4. Properties of molecules that have the lowest potential energy. Distance, angle and energy in angstrom, degree and kcal/mol, respectively

		a	b	C	d
B3LYP/6-31G**	distance	O_{10}-H_{16} 1.05	N_5-H_{12} 1.05	N_5-H_{12} 1.05	O_{10}-H_{16} 1.10
	angle	C_8-O_{10}-H_{16} 111.35	C_4-N_5-H_{12} 108.70	C_4-N_5-H_{12} 106.90	C_8-O_{10}-H_{16} 113.23
	energy	-308858.45	-308864.22	-309108.00	-308521.42
MP2/6-31G**	distance	O_{10}-H_{16} 1.05	N_5-H_{12} 1.05	N_5-H_{12} 1.05	O_{10}-H_{16} 1.10
	angle	C_8-O_{10}-H_{16} 111.00	C_4-N_5-H_{12} 109.00	C_4-N_5-H_{12} 112.02	C_8-O_{10}-H_{16} 112.00
	energy	-307979.13	-۳۰۷۹۸۲,۲۰	-۳۰۸۲۲۶,۳۱	-۳۰۷۶۴۱,۴۸

In this section, three-dimensional potential energy curves as a function of angle and distance are studied. This means that at a fixed angle, distance was changed and in any of these points, the potential energy is recorded and the angle is changed again, and in new angle, also distance was changed and Potential energy in each point was recorded and so it is repeated. Thus in the three-dimensional curves, one dimension is energy in hartree (or kcal/mol), one dimension is distance in angstrom (Å) and the last dimension is the angle in degrees. In fact, we have investigated the different pathways for proton transfer between electronegative atoms.

In the molecule a, H_{16} proton between O_{10} and N_5 atoms was changing. Proton toward to the oxygen atom number 10 is placed at fixed distance. At this distance, the $<C_8$-O_{10}-H_{16} angle was changed, provided that only proton (H_{16}) displaced. In this state, the proton was migrating in the surrounding area of $N_5 \cdots O_{10}$. In other words, proton transfer between two atoms of oxygen and nitrogen, and in this transfer, proton placed at fixed intervals of O_{10} atom and at a fixed distance, the surrounding environment will be examined. Since the constant distance, the protons are located in different places, so at a constant distance, there will be various structures for molecule a, that during the proton transfer between oxygen and nitrogen atoms, these structures would be immense. In these calculations, the proton from 6.0 to 1.2 Å with 0.15 Å steps is displaced, and at a fixed distance, the $<C_8$-O_{10}-H_{16} angle from 96.35 to 116.35 with five degree steps has changed. On the other hand, the potential energy calculation of

each structure by using quantum mechanical calculation with B3LYP/6-31G ** method were performed. Since the potential energy is a function of two variables, the distance between the proton and the O_{10} atom and the $<C_8$-O_{10}-H_{16} angle, Thus the potential energy curve will be three-dimensional (Fig. 6). All calculations and graphs in other 3 molecules were obtained at B3LYP/6-31G ** and MP2/6-31G ** levels of theory.

CONCLUSIONS

All *cis*-UCA structures by B3LYP/6-31G** and MP2/6-31G** have been optimized and geometrical and structural parameters have been obtained. In study of two dimensional potential energy as a function of angle, two important points were obtained. The first point where the curve is proportional to the minimum potential energy and the second point is where the 3 atoms were involved in hydrogen bond have an angle is closest to 180 degree position.

Evaluation of the potential energy curve versus distance is performed by mentioned methods and the resulting is the singlet relatively symmetrical without potential barrier curves. A minimum level valley with highly structural population is observed that this could be due to highly strength of hydrogen bonding that the potential barrier is removed. Also there were some very minor of potential barrier in some molecules (**b** and **c**) that can be attributed to the curve of the binary symmetric potential barrier where the hydrogen bond energy is slightly reduced compared to the previous case.

According to academic sources [25], the energy of interamolecular hydrogen bonds of the type O−H···N, that structures **a** and **d** are of this type, there are about 7 kcal/mol. Accordingly, with conversion values in Table 3 to kcal/mol, the bond strength values of B3LYP and MP2 methods, respectively, in **a** molecule are 10.66 and 11.29 and about the **d** molecule are 19.45 and 20.70 kcal/mol. Also in **b** molecule by B3LYP and MP2 methods 8.78 and 7.53 is obtained, respectively. In **c** structure, these values are 17.57 and 15.58, respectively. As is clearly identified the bond strength in ionic molecules (cationic and anionic) is about twice that of the neutral molecule.

Our aim of changing the angle and distance and plotting the three-dimensional curve and investigating the hydrogen bond strength, is to find the minimum binding energy and determine the hydrogen path way in which the hydrogen bond strength is greater. The minimum energy in 3D curve obtained and other characteristics and, the distances and angles, have been derived in table 4.

One of the Applications of our results can be design anticancer drugs. When a cell becomes cancerous whatever reason, the hydrogen bonding between paired bases were loos and eventually breaks, and due to breaking of bonds that cancer cells start to proliferate, and this mechanism probably can be controlled and avoided by use of the drugs that make the intramolecular hydrogen bond more strength. So the knowledge about hydrogen bond nature and characteristics can be useful in these cases.

REFERENCES

[1]. M. Norval, N. K. Gibbs, J. Gilmour, Photochem. Photobiol. 62 (1995) 209.

[2]. Jeffrey, G. A. An Introduction to Hydrogen Bonding; Oxford University Press: New York, 1997.

[3]. Scheiner, S. Hydrogen Bonding; Oxford University Press: New York, 1997.

[4]. Desiraju, G. R.; Steiner, T. The Weak Hydrogen Bond; Oxford University Press: Oxford, U.K., 1999.

[5]. Steiner, T. Angew. Chem., Int. Ed. Engl. 41 (2002) 41, 48.
[6]. Hobza, P.; Havlas, Z. Chem. ReV. 100 (2000) 100, 4253.
[7]. Gerlt, J. A.; Gassman, P. G. Biochemistry. 32 (1993) 11943.
[8]. Cleland, W. W.; Kreevoy, M. M. Science 264 (1994) 1887.
[9]. Frey, P. A.; Whitt, S. A.; Tobin, J. B. Science 264 (1994) 1927.
[10]. Shan, S. O.; Loh, S.; Herschlag, D. Science 272 (1996) 97.
[11]. Scheiner, S.; Kar, T. J. Am. Chem. Soc. 117 (1995) 6970.
[12]. Guthrie, J. P. Chem. Biol. 3 (1996) 163.
[13]. Warshel, A.; Papazyan, A. Proc. Natl. Acad. Sci. U.S.A. 93 (1996) 13665.
[14]. Zhao, Q.; Abeygunawarana, C.; Talalay, P.; Mildvan, A. S. Proc. Natl. Acad. Sci. U.S.A. 93 (1996) 8220.
[15]. R. Quinn, J. Mercer-Smith, J.N. Burstyn, J.S. Valentine, J. Am.Chem. Soc. 106 (1984) 4136.
[16]. H. Mawlawi, M.C. Monje, A Lattes, J. Rivie`re, J. Heterocyclic Chem. 29 (1992) 1621.
[17]. J.R. Roberts, C. Yu, C. Flanagan, T.R. Birdseye, J. Am. Chem. Soc. 104 (1982) 3945.
[18]. A. Lahti, M. Hotokka, K. Neuvonen, P.J. A¨ yra¨s, J. Mol. Struct. (Theochem) 331 (1995) 169.
[19]. V. Bertolasi, L. Nanni, P. Gilli, V. Ferretti, G. Gilli, Y.M. Issa, O.E Sherif, New J. Chem. 18 (1994) 251.
[20]. S.C. Zimmerman, J.S. Korthals, K.D. Cramer, Tetrahedron 47 (1991) 2649.
[21]. P.A. Frey, S.A. Whitt, J.B. Tobin, Science 264 (1994) 1927.
[22]. Hehre, W.J., Radom, L., Schleyer, P.V.R., Pople, J. Wiley, New York, 1986.
[23]. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Rob, J. R. Cheeseman, J. A. Montgomery Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, and J. A. Pople, Gaussian 03 (Gaussian, Inc., Wallingford, CT, 2003). [24] GaussView, Version 5, Roy Dennington, Todd Keith and John Millam, Semichem Inc., Shawnee Mission KS, 2009.
[24]. J. Am. Chem. Soc., vol. 126, no. 50 (2004) 16310–16311..