Journal of Molecular Structure (Theochem), 166 (1988) 487–492
Elsevier Science Publishers B.V., Amsterdam — Printed in The Netherlands

CNDO ENERGIES AND STABILITY OF HYDROGEN-BONDED SELFASSOCIATED PURINE AND OXIPURINE DIMERS.

T. LEO[1] and D. ESCOLAR[2]

[1]Lab. Termodinâmica E.T.S.I.Aeronâuticos. Pza. Cardenal Cisneros,3. 28040 Universidad Politécnica de Madrid. Madrid(Spain)

[2]Dto. Química Física. Fac.Ciencias. Universidad de Cádiz. Apdo.40. Puerto Real(Cádiz). (Spain)

SUMMARY

Interaction energy values of several purine base pairs, selfassociated by hydrogen bonding, have been calculated using the "supermolecule approach". Quantum mechanical calculations are carried out by means of the CNDO/2 method. Hydrogen bond angles and distances have been optimized. In this study, both annular and functional tautomerism has been considered. Relative stability of different in-plane base pairs is discussed. These results make possible to give a theoretical explanation to available experimental data.

INTRODUCTION

Investigations about molecular interactions between nucleic acids bases constitute one of the most important contributions of quantum-mechanical calculations to Molecular Biology. A significative amount of work is devoted to determine relative stabilities of different associated base-pairs, those being originated either by stacking or by hydrogen bonding(1-13). Ab initio calculations have shown to be in good agreement with in vacuo experimental data(14). In this field, it is important to mention the works of Del Bene(13) and that of Langlet et al.(12) on nucleic acids base-pairs.

It has been found that for highly polar bases, ab initio and semiempirical calculations about stabilization energies give similar results(12). In those cases, despite the advances in the field of ab initio computations, the use of simplified procedures for evaluating intermolecular interaction energies of large molecules or large number of molecules becomes specially useful and recommended.

In the present study, hydrogen bond distances and angles of several dimer geometries of selfassociated purine, 2-oxipurine, hypoxanthine and xanthine have been optimized. Solute-solute interaction energies have been computed by means of a semiempirical calculation method. As it will be discussed later, these energy values are in good agreement with those ab initio obtained for similar molecules(12,13). With the help of the obtained results, observed experimental behaviour can be satisfactorily understood.

0166-1280/88/$03.50

METHODS

Interaction energies of in-plane purine-purine base pairs have been calculated on the basis of the so-called "supermolecule approach". CNDO/2 Pople, Santry and Segal' version(15), extended to third period elements, is used to calculate monomers and base-pairs energies.

Dimer geometries optimization has constituted a previous step for calculating solute-solute interaction energies. That is, monomer-monomer hydrogen bond angles and distances have been optimized. For this purpose, CNDO/2 calculations were performed. Bond angles have been varied in 10 steps, whereas 0.025nm increments were considered enough to optimize hydrogen bond distances.

Approximated monomer geometries, taken from crystallographic data and described in a previous work(16), have been used. Both N(7)H and N(9)H tautomeric forms are taken into account in this work. Keto and enol tautomers have also been calculated in the 2-oxipurine case. This is because experimental evidence of the existence of 2-oxipurine enolic forms has been found in nonpolar solvents(17).

RESULTS AND DISCUSSION

Optimized hydrogen bond angles and distances of purine-purine base pairs are shown in Figs. 1 to 5. Table 1 presents total energy values for purine, 2-oxipurine, hypoxanthine and xanthine monomers, calculated by the CNDO/2 method. Table 2 provides the CNDO/2 interaction energy values corresponding to geometries in Figs. 1 to 5. As it was said, our results agree well with ab initio ones computed for similar molecules. So, ab initio stabilization energy for the

TABLE 1

CNDO/2 energies of purine, 2-oxipurine, hypoxanthine and xanthine monomers.

monomer	$-E_{CNDO/2}$(a.u.)	monomer	$-E_{CNDO/2}$(a.u.)
purine N(7)H	85.0066	purine N(9)H	85.0013
2-oxipurine		2-oxipurine	
keto N(3)H-N(7)H	103.2938	keto N(3)H-n(9)H	103.2943
enol N(7)H	103.4093	enol N(9)H	103.4163
hypoxanthine		hypoxanthine	
keto N(1)H-N(7)H	103.3436	keto N(1)H-N(9)H	103.3475
xanthine N(7)H	121.9173	xanthine N(9)H	121.9033

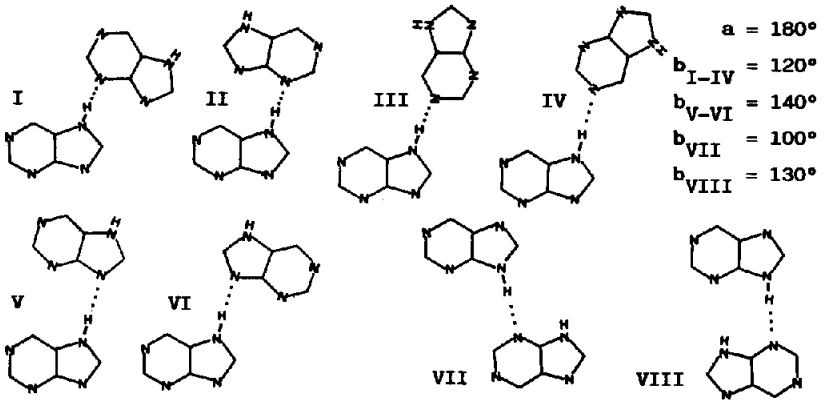

Fig. 1. Purine dimers. Optimized hydrogen-bond geometries. $d_{NH...N}$ = 0.175nm. (a = N-H...N angle; b = H...N-C angle).

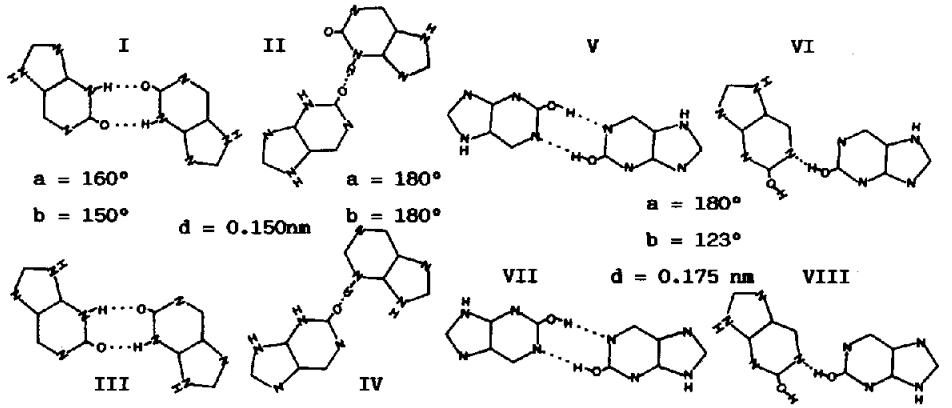

Fig. 2. 2-oxipurine dimers. Optimized hydrogen-bond geometries(a = C-O...H or O-H...N angle; b = N-H...O or C-N...H angle).

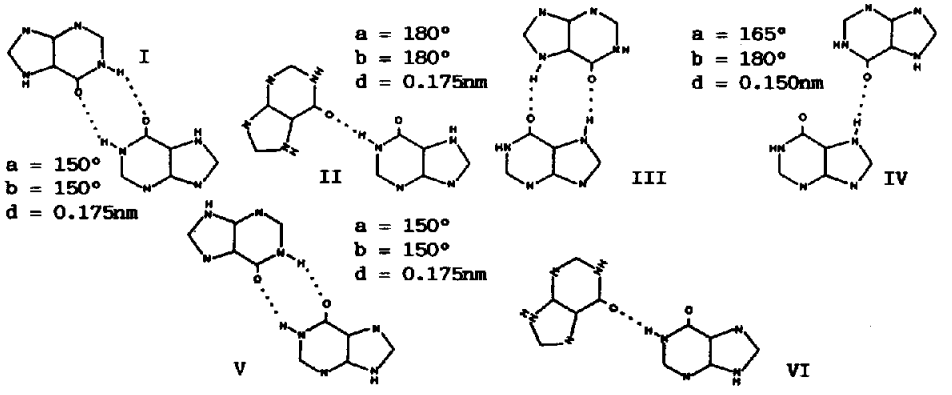

Fig. 3. Hypoxanthine dimers. Optimized hydrogen-bond geometries.(a = N-H...O; b = C=O...H angles).

TABLE 2

Stabilization energies of purines selfassociated by hydrogen bonding.

tautomer	dimer	E_H(a.u.)	E_H(kJ/mol)	tautomer	dimer	E_H(a.u.)	E_H(kJ/mol)
purine(Fig. 1)							
N(7)H	I	0.0080	21.0	N(9)H	VII	0.0076	20.0
	II	0.0085	22.3		VIII	0.0150	39.0
	III	0.0076	20.0				
	IV	0.0067	17.6				
	V	0.0086	22.6				
	VI	0.0086	22.6				
2-oxipurine(Fig. 2)							
keto				keto			
N(3)H-N(7)H	I	0.0152	39.9	N(3)H-N(9)H	III	0.0200	52.5
	II	0.0095	24.9		IV	0.0139	36.5
enol N(7)H	V	0.0314	82.4	enol N(9)H	VII	0.0322	84.5
	VI	0.0144	37.8		VIII	0.0148	38.9
hypoxanthine(Fig. 3)							
keto				keto			
N(1)H-N(7)H	I	0.0150	39.4	N(1)H-N(9)H	V	0.0165	43.3
	II	0.0084	22.1		VI	0.0096	25.2
	III	0.0214	56.2				
	IV	0.0122	32.0				
xanthine		(Fig. 4)				(Fig. 5)	
diketo				diketo			
N(7)H	I	0.0162	42.5	N(9)H	I	0.0151	39.6
	II	0.0165	43.3		II	0.0131	34.4
	III	0.0109	28.6		III	0.0193	50.7
	IV	0.0271	71.2		IV	0.0144	37.8
					V	0.0097	25.5

A-T pair with two hydrogen bonds is shown to be 59 kJ/mol(13), selfassociation of A gives ab initio stabilization energies about 50 kJ/mol and the corresponding ones to U and T were calculated to be about 38 kJ/mol(12).

As it can be deduced from Tables 1 and 2, monomers and dimers stability order seems to be the following:

	dimers	monomers
purine(Fig. 1)		
	VIII > V ≈ VI ≈ II > I > VII ≈ III > IV	P7 > P9
	clsd ----------open----------	

2-oxipurine(Fig. 2)

VII ≈ V > III > I ≈ VIII ≈ VI ≈ IV > II E7>E9≈K39≈K37

------clsd------ -------open-------

hypoxanthine(Fig. 3)

III > V > I > IV > VI > II HX19 > HX17

----clsd---- ----open----

xanthine(Figs. 4 and 5)

X7IV>X9III>X7II>X7I>X9I≈X9IV>X9II>X7III>X9V X7 > X9

where clsd stands for closed dimer geometry and open means it is an open one.

Purine dimers III and IV(Fig. 1), originated by selfassociation of the N(7)H tautomer, are found to be the less stable ones. As it can be seen in Fig. 1, interactions between monomers become fewer than in the other base pairs. In spite of the fact that purine N(7)H tautomer is predicted to be more stable than the N(9)H one, the closed dimer of purine N(9)H (VIII in Fig. 1) results stabilized respect to the other geometries. Then, in few polar or nonpolar solvents, the preponderant existence of purine N(9)H dimers could be expected, as can also be deduced from available experimental data(17).

The most stable monomers and dimers of 2-oxipurine correspond to its enolic forms(Fig. 2). It would be then expected a predominant existence of these species in apolar or few polar media, as it has been found experimentally(17). In polar solvents, solute-solvent interactions can modify tautomeric and association equilibria. So, the keto N(3)H-N(7)H tautomer has been found to be predominant in polar solvents(17), mainly as monomers. This could be theoretically justified since, for this form, solute-solute interaction energies are lower than solute-solvent ones(16).

As in the purine case, the most stable dimer of hypoxanthine is constituted by the less stable monomeric form. That is, dimer III in Fig. 3, corresponding to the N(1)H-N(7)H tautomer, results to be the most stable one whereas N(1)H-N(9)H monomer presents more stability than the N(1)H-N(7)H does. The greater stability of dimer III can be understood since both rings of each base participate in the complex formation.

Dimer IV of xanthine N(7)H (Fig. 4) has shown to be the most stable xanthine dimer. In addition, xanthine N(7)H monomer is more stable than the N(9)H tautomeric form. It could be then expected a predominant existence of N(7)H species. In fact, there exists some experimental evidence for this(17).

CONCLUSIONS

The relative stability order of hydrogen-bonded dimers does not necessarily coincides with that of the monomers one. That is, it has been found that self-association may give rise to changes on relative stabilities of the tautomeric forms of these bases. As described by Del Bene(13), it has been found that the

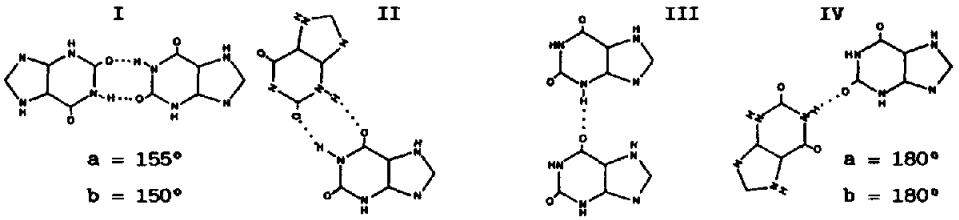

Fig. 4. Xanthine N(7)H dimers. Optimized geometries. $d_{NH...O}$ = 0.150nm.(a = C=O...H angle and b = N-H...O angle in Figs. 4 and 5).

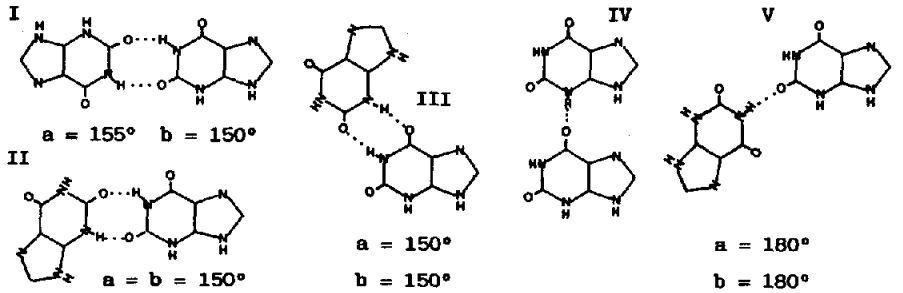

Fig. 5. Xanthine N(9)H dimers. Optimized geometries. $d_{NH...O}$ = 0.150nm.

most stable dimers correspond to the existence of collinearity of the A-H bond with the A-B line whereas the proton acceptor B is colinear with the A-B line.

In spite of the simplicity of the "supermolecule approach" and the method of calculation (CNDO/2), available experimental data have been, at a great extent, explained and theoretically justified.

REFERENCES

1 H. De Voe and I. Tinoco Jr., J. Mol. Biol., 4,500(1962).
2 P. Claverie, B. Pullman and J. Caillet, J. Theor. Biol., 12,419(1966).
3 V.I. Danilov, J. Theor. Biol., 30,559(1971).
4 E. Clementi, J. Mehl and W. von Nissen, J. Chem. Phys., 54,508(1971).
5 F. Jordan and H.D. Sostman, J. Am. Chem. Soc., 95,6544(1973).
6 J. Caillet and P. Claverie, Bioplymers, 13,601(1974).
7 G. Gupta and V. Sasisekharan, Nucleic Acids Res., 5,1639(1978).
8 M. Geller, A. Jaworski and A. Pohorille, Int. J. Quantum Chem., 15,369(1979).
9 M. Geller, B. Lesyng and A. Pohorille, Int. J. Quantum Chem., 17,293(1980).
10 J. Langlet, C. Giessner-Prettre, B. Pullman, P. Claverie and D. Piazzola, Int. J. Quantum Chem., 18,421(1980).
11 J. Langlet, P. Claverie and F. Caron, Intermolecular Forces, B. Pullman(ed.) D.Reidel Pub.Co., 1981. pp397-429.
12 J.Langlet P.Claverie,F.Caron and J.C.Boeuve,Int.J.Quantum Chem.20,299(1981).
13 J.E. Del Bene, J. Mol. Struct.(Theochem), 124,201(1985).
14 I.K. Yanson, A.B. Teplitsky and L.F. Sukhodub, Biopolymers, 18,1149(1979).
15 J.A. Pople, D.P. Santry and G.A. Segal, J.Chem. Phys., 43,S129(1965).
16 T. Leo, D. Escolar, F. Acción and J. Tortajada, Hydrogen bonding distances and energies of several purine-solvent complexes, to be published.
17 T. Leo, Doctoral Thesis, Universidad Complutense de Madrid, Madrid, 1987, pp. 109-214.