

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/41722552>

# Theoretical investigation of hydrogen atom transfer in the adenine–thymine base pairits coupling with the electronic rearrangement. Concerted vs. stepwise mechanism

ARTICLE *in* PHYSICAL CHEMISTRY CHEMICAL PHYSICS · MARCH 2010

Impact Factor: 4.49 · DOI: 10.1039/b917672a · Source: PubMed

---

CITATIONS

18

---

READS

28

## 1 AUTHOR:



Giovanni Villani

Italian National Research Council

63 PUBLICATIONS 699 CITATIONS

SEE PROFILE

# Theoretical investigation of hydrogen atom transfer in the adenine–thymine base pair and its coupling with the electronic rearrangement. Concerted *vs.* stepwise mechanism

Giovanni Villani

Received 27th August 2009, Accepted 23rd December 2009

First published as an Advance Article on the web 27th January 2010

DOI: 10.1039/b917672a

Two different mechanisms to obtain the imino–enol tautomer of the adenine–thymine base pair, a concerted hydrogen atom transfer and a stepwise process, have been studied and compared. The first mechanism includes both the concerted movement of two hydrogen atoms, in the bridges that bond the two bases, and an electronic reorganisation of the bonds. The stepwise mechanism is the simplest one where there is a correlation between the movement of the hydrogen atoms, but two or more steps can be identified. In this study, a different behaviour has been found when the first atom to move is the hydrogen in the N–N bridge or that in the N–O one.

## 1. Introduction

Hydrogen bonds occurring in the adenine–thymine, AT, and cytosine–guanine, CG, base pairs play a key role in genetic molecular recognition and structure determination of nucleic acid base pairs. It is well known that each base pair may be converted to its minor, but often reasonably stable, enol–imine tautomer by a double proton transfer (prototropic tautomerism). The rare imino/enol tautomers of Watson–Crick pairs are thought to be responsible for genetic instabilities. The transfer of two or more hydrogen atoms can be accomplished by two different mechanisms: concerted and stepwise (step-to-step) multiple-hydrogen transfer. In these reactions, the motions of plural hydrogens may couple each other and/or they couple with the motions of the solvent molecules, because a correlation may exist between the moving atoms. Such dynamical effects cannot exist in the single-hydrogen transfer reaction of course, but they may also be unimportant in the step-to-step process.

A naïve idea of the generation of these tautomers is the following: when a hydrogen atom moves from a base to the other in a bridge of the AT (or CG) base pair, the opposite motion in another H-bridge can be induced. These atom movements are coupled also with the changes of some bond orders, and therefore with the change of the electronic configuration, and both nucleobases remain electrically neutral. There is also the possibility of a non-concerted movement of these two hydrogen atoms and hence a stepwise mechanism. The goal of this paper is to study these processes in order to determine if it is more accurate to speak of a concerted or a stepwise mechanism or if a mix of these two mechanisms can be supposed for the adenine–thymine system.

The interrelation between charge transfer (CT) and proton transfer (PT) in DNA has been experimentally demonstrated by Giese and Wessely.<sup>1</sup> When the proton-transfer and hole-transfer events are separated, the first reaction step is

energetically unfavorable; because of that a concerted process, proton-coupled electron transfer (PCET), often occurs.<sup>2–4</sup> Thorp and co-workers observed a deuterium kinetic isotope effect for electron transfer in several DNA systems and suggested that PCET occurs in DNA.<sup>5</sup> It has been recognized that charge migration in DNA can be accompanied by proton transfer. Sevilla *et al.*<sup>6</sup> demonstrated that both proton transfer from G to the cytosine radical anion ( $C^{\bullet-}$ ) forming neutral hydrogenated cytosine radical ( $CH^{\bullet}$ ) and PT from the guanine radical cation ( $G^{\bullet+}$ ) to C forming neutral dehydrogenated guanine radical ( $G(-H^{\bullet})$ ) show slow electron and hole transfer rates in DNA. Hole transfer to a nucleobase will change its  $pK_a$  value and thereby can enforce rapid deprotonation of the base due to proton transfer between the nucleobase and its surroundings. For instance, a guanine radical cation formed after charge transfer to G exhibits a  $pK_a$  value of 3.9.<sup>7</sup> Due to their low ionization potentials, purines are the most probable sites in DNA where electron holes are localized. The formation of a radical cation changes the acidic properties of the nucleobases and can be associated with proton transfer from purine to pyrimidine bases. Transfer of the first proton may be followed by the subsequent PT (in the opposite direction) leading to double PT structures.

Double-hydrogen transfer is the most basic multiple-hydrogen transfer reaction, and has been observed in the electronic ground state of the dual hydrogen-bonded dimers such as formic acid dimer,<sup>8–12</sup> benzoic acid dimer,<sup>13–15</sup> and (2-pyridone)–(2-hydroxypyridine) dimer.<sup>16–18</sup> These molecules exhibit reversible excited-state double-hydrogen transfer reactions due to tunnelling while, on the other hand, several dual hydrogen-bonded dimers undergo irreversible transfer reactions.<sup>19–23</sup> Proton transfer (PT) within base pairs has attracted much attention. Florián and Leszczynski carried out *ab initio* calculations of several tautomers of CG<sup>24</sup> involving the canonical pair, tautomers formed from this pair by simultaneous transfer of two protons, and ion pairs produced by single proton transfer between the nucleobases. The relative stabilities and dissociation energies of the base pairs were determined at the

Istituto per i Processi Chimico-Fisici, IPCF-CNR, Via G. Moruzzi, 1, I-56124 Pisa, Italy. E-mail: villani@ipcf.cnr.it

MP2/6-31G\*\*//HF/6-31G\* level. The computations indicated that the electron correlation is important for reliable estimation of the relative energy of the tautomers. It was demonstrated that one ion pair and one neutral pair resulting from single- and double-PT within CG are energetically accessible.<sup>24</sup> All stable tautomers of the AT and CG Watson–Crick pairs (at the B3LYP/6-31G\*\* level) have been recently reported by Hayashi and Mukamel.<sup>25</sup> As was demonstrated by Bertran *et al.*<sup>26</sup> and Li *et al.*,<sup>27</sup> among several types of single and double PT that might occur in the radical cations of Watson–Crick pairs (WCPs), just one single proton transfer (SPT) and one double PT (DPT) reactions are feasible for each WCP. No stationary point corresponding to the DPT structure was found for CG<sup>+</sup>.

A recent model study<sup>28</sup> shows that the analytical solution of the transfer dynamics can be obtained by instanton techniques for arbitrary coupling strength if the hydrogen bonds are represented by quartic potentials. In this case, the concerted transfer always takes place and it occurs by synchronous 1D tunnelling in the low-temperature limit. As a consequence, tunnelling splittings can be assigned exclusively to this mechanism. Asynchronous 2D tunneling is prevalent when the temperature is close to the point of crossover to the classical regime, provided the coupling is sufficiently weak. These are precisely the conditions where stepwise transfer provides an alternative mechanism. Otherwise, entropically the synchronous concerted motion will be very unlikely<sup>29–33</sup> and it was emphasized earlier that the one-dimensional picture of proton transfer is inappropriate and the dynamics of concerted and non-concerted motions are the consequences of symmetric and asymmetric nuclear vibrations, respectively.<sup>34</sup>

## 2. Results and discussion

In the following, we would like to study the movement of the hydrogen atoms in the bridges coupled with the electronic reorganisation, under the assumption of overall neutrality throughout the process.

Fig. 1 shows the concerted processes of hydrogen atom transfer and the electronic reorganisation in the A–T system in a schematic manner, where only the important atoms are considered (the numeration is that of ref. 3). This is a complex process where two hydrogen atoms move in the H-bridges and some atomic distances (and charges) change from single to double bonds and *vice versa*. If these changes are not found in the computation, or a large amount of energy is necessary for this process, the non-concerted movement becomes the more probable mechanism also in the generation of the imino–enol neutral tautomer.

One should take care that the terms *stepwise* and *concerted* in multiple-hydrogen reactions are used as a similar meaning of *asynchronous* and *synchronous* reactions.<sup>33,34</sup> We distinguish among these terms. In our view, concerted multiple-hydrogen transfer refers to a single chemical reaction step involving the transfer of all hydrogen atoms. Concerted in this context means that the reaction occurs without an intermediate. In the *stepwise* reaction, a stable intermediate state exists and the potential energy surface (PES) exhibit a stable intermediate with a well deep enough to support a bound state (which is the

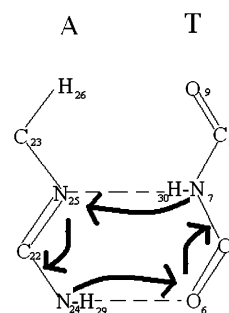
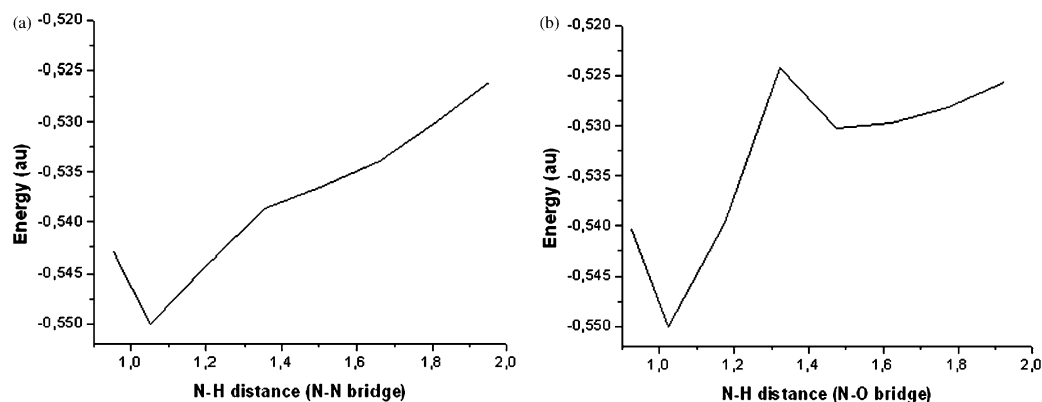


Fig. 1 Schematic representation of the concerted double hydrogen atom migration and electron transfer in the A–T base pair.

origin of the double-exponential decay profiles of the femto-second transients<sup>18</sup>), whereas the *asynchronous* reaction occurs without the intermediate state on the potential surface. Of course, the intermediate possibilities can be obtained. Two well known cases can be a concerted process which is not completely synchronic and a case where the PES does not show a minimum as such but a region with small inclination (and in the time-dependent calculation it can be computed a significant probability that the system is trapped in this region). This means that while the two extreme cases of concerted or step-to-step mechanisms can be clearly identified, the real mechanism may be more complex. As a consequence, although we study the specific process of hydrogen movement and electronic reorganisation in the AT base pair, some results can be more general.

As in our previous papers,<sup>3,4,36–38</sup> this theoretical investigation of the adenine–thymine (A–T) base pair is based (in Gaussian 2003 package<sup>39</sup>) on the density functional theoretical (DFT) approach (b3lyp) in cc-pVDZ basis set (twelve equidistant points in the range of [eq – 0.10 to eq + 1.0] Å for each bridge). In order to study the correlation between the movement of a hydrogen atom in a bridge with the positions of the other atoms, we have optimised the positions of all atoms of the AT system at each fixed position of this hydrogen atom. This is different from the method followed in my previous papers. In those cases, in fact, I had in mind the construction of the multidimensional PES (two-dimensional for AT and three-dimensional for GC system) as a function of the different hydrogen positions in all bridges and, hence, optimised the positions of all the other atoms of this system at each fixed position of these two (or three) hydrogen atoms in the H-bridges.

In this paper, four types of properties have been analyzed: the potential energy curves, selected interatomic distances, that must change considerably in this process, the atomic charges (Mulliken) of the main atoms involved in the process and, finally, the global dipole moment of these systems. Fig. 2–7 in which these results are summarized comprise two parts since there are two hydrogen bridges in the A–T base pair: (a) one is related to the movement of the hydrogen atom in the N–N bridge and the other (b) to the movement in the N–O one. On the *x*-axis, we show the N(T)–H and the N(A)–H distances, obtained from the different positions of the hydrogen atoms in the direction of the N–H bond. Of course, this means to assume a linear bridge, as in previous



**Fig. 2** Potential energy curves as a function of the N–H distance in the N–N (a) and N–O bridge (b). The distances are in Å. In this figure  $-921$  au must be added to the value of energy.

papers,<sup>3,4</sup> and the role of the out-of-plane movement of this hydrogen atom is not included in this study. This simplification is supported in literature and is less expensive in computing time.

Fig. 2 shows the potential energy of the A–T base pair as a function of the hydrogen position in the N(A)–N(T) and N(A)–O(T) bridges. It is evident that these two cases are different. When the hydrogen atom moves from the thymine to the adenine base in the N–N bridge, there exists a region ( $N(T)–H > 1.4$  Å) where the interaction of the H atom with N(A) gives a relative stabilization of this system, but there is not a stable configuration (minimum of PES) with this atom on N(A). In the case of the movement of hydrogen atom in the N–O bridge instead, there is a stable configuration when the hydrogen atom of the adenine reaches the thymine base.

Moreover, there is a general question about the two curves of Fig. 2. These curves of energy are adiabatic, of course, but in a diabatic description is this the energy of only one or more state? We believe that the different behaviour of these two curves can be a consequence of the different number of diabatic states involved: we suppose that, in the case of the movement of the hydrogen atom in the N–N bridge, the energy plotted in Fig. 2(a) is of the same diabatic state for all positions of this atom (one diabatic state), but, when the hydrogen atom moves in the N–O bridge, two diabatic states can be activated. This supposition can be verified with the analysis of the charges of the atoms directly involved in this movement.

In order to compare the two mechanisms of concerted and step to step movement of the two hydrogen atoms in the bridges, we analyze in Fig. 3–5 the modifications of equilibrium distances of the heavy atoms of the H-bridges and of the carbon and nitrogen atoms of the rings that, in the naïve picture of Fig. 1, show change in bonding orders from single to double and *vice versa*. In particular, Fig. 3 shows the distances (in Å) of the atoms of the two bridges: the distance of the heavy atoms of the bridge where the hydrogen atom moves and the change of the atomic distances in the other H-bridge. In the cases studied, the atomic distances of the heavy atoms in the H-bridge with H-movement is similar: a decrease until  $N–H \sim 1.4$ – $1.5$  Å, and then an increase. The behaviour of the atomic distances in the other bridge (indirectly involved in the

hydrogen movement) is, however, different if the hydrogen moves in the N–N or N–O bridge.

In particular, the distance between the heavy atoms decreases monotonically and that of the corresponding hydrogen atom changes only little (a small increase), when the hydrogen moves in the N–N bridge. Instead, the distance of the heavy atoms decreases and then increases and the corresponding hydrogen distance has a discontinuity around  $1.3$ – $1.5$  Å, when the hydrogen moves in the N–O bridge. It is evident that, when the hydrogen of a N–O bridge moves from one base to the other, the hydrogen atom in the N–N bridge follows it. As a consequence, also the distance of the heavy atoms of this N–N bridge has the same behaviour (decrease and then increase) of the distance between the heavy atoms of the bridge where the hydrogen atom moves. This behaviour can be interpreted in the following way. The movement of a hydrogen atom in a H-bridge is helped by the decrease of the distance between the corresponding heavy atoms (as we have demonstrated in our previous calculations<sup>3,4</sup>) and afterwards, when this hydrogen atom moves prevalently on the base of arrival, a relaxation to the original distance of the heavy atoms can be found.

Fig. 4 shows the change of the interatomic distance of the four covalent bonds (two single and two double bonds), schematised in Fig. 1, as a function of the hydrogen position in the two bridges, N–N Fig. 4(a) and N–O Fig. 4(b). These bonds must change from single to double and *vice versa* in the concerted mechanism. In Fig. 4 it is evident that the interatomic distance of the two double bonds  $C_5–O_6$  and  $C_{22}–N_{25}$  increase and that of the two single bonds  $C_5–N_7$  and  $C_{22}–N_{24}$  decrease. This behaviour can be easily correlated to the decrease and increase of the bonding order, respectively. In any case, also Fig. 4(a) and (b) show differences. In particular, Fig. 4(b) shows the practically perfect inversion between the two couples of bonds and a discontinuity at about  $N_{24}(A)–H_{29} \sim 1.4$  Å; both characteristics which are not present when we follow the movement of the hydrogen in the N–N bridge (Fig. 4(a)). Also from these figures we obtain the conclusion that the movement of the hydrogen atom in the N–O bridge generates a concerted process, but that of the hydrogen in the N–N bridge can generate only a step-to-step mechanism.

Fig. 5 and 6 show the atomic charges of the atoms in the hydrogen bridges involved directly and indirectly in the

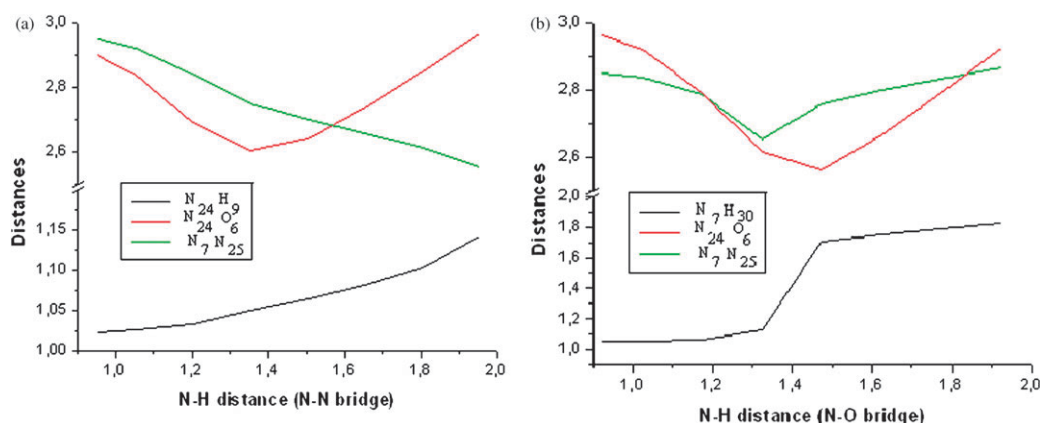


Fig. 3 Atomic distances as a function of the N-H distance in the N-N (a) and N-O bridge (b). The distances are in Å.

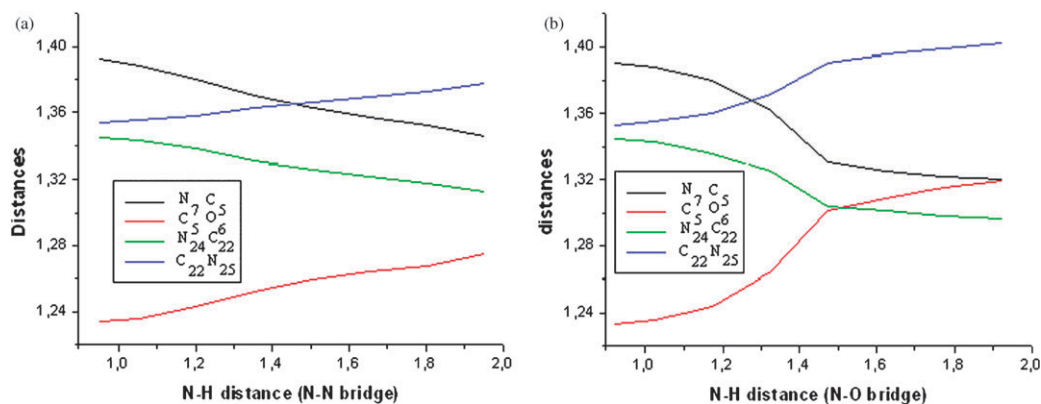


Fig. 4 Atomic distances as a function of the N-H distance in the N-N (a) and N-O bridge (b). The distances are in Å.

movement of the hydrogen atom, respectively. From the comparison between Fig. 5(a) and (b), we can see that the qualitative behaviour of these atomic charges (those of the atoms in the H-bridge where the hydrogen moves) is similar. Two differences are however seen: a discontinuity in the charge variation of Fig. 5(b) (discontinuity similar to that of Fig. 4(b)) and a larger variation of the atomic (N<sub>25</sub>) charge of the atom where the hydrogen arrives in the N-N bridge compared with the oxygen atom (O<sub>6</sub>) of the arrival of the hydrogen movement in the other bridge. Instead, the atomic charges of the atoms in the bridge not directly involved in the hydrogen movement have different variations if the hydrogen atom moves in one bridge or the other. In particular, the atomic charges of N<sub>24</sub>, H<sub>29</sub> and O<sub>6</sub> (when H<sub>30</sub> moves in the N-N bridge) show gradual continuous variations, but those of the atoms N<sub>7</sub>, H<sub>30</sub> and N<sub>25</sub> (when H<sub>29</sub> moves in the N-O) have a discontinuous and larger variations, over all the heavy atoms. This different behaviour can be connected to the different number of diabatic states involved in the two processes: only one diabatic state is involved in the N-N hydrogen transfer, but two in the movement of the hydrogen atom in the N-O bridge.

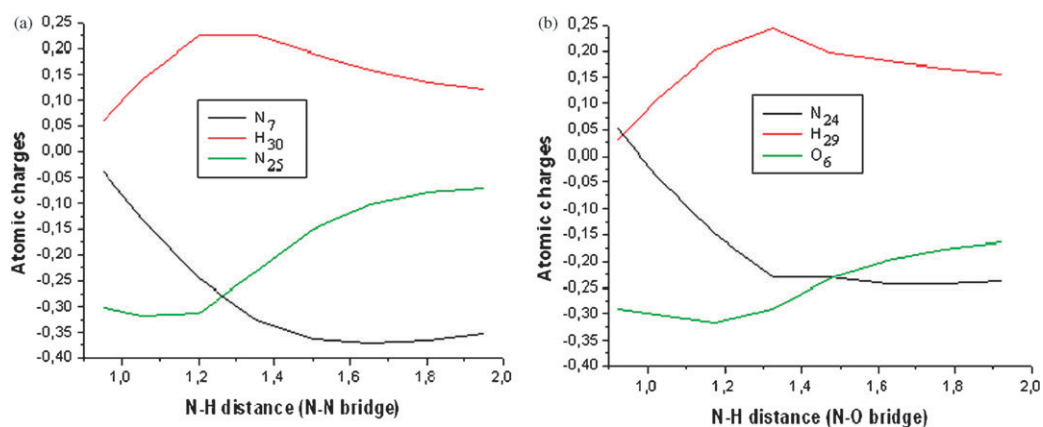
Finally, in Fig. 7 we show the global dipole moment of the A-T system as a function of the hydrogen movement in the N-N and N-O bridges. These figures show very clearly one of the most important results of this paper: the change of the dipole moment, as a function of the hydrogen position in a H-bridge, has a discontinuity when the hydrogen moves in the

N-O bridge (Fig. 7(b)). This means a global change of the atomic charges with the conclusion that one diabatic state is sufficient for describing the movement in the N-N bridge, but not in the N-O one. In this figure, more so than in the previous figures, the discontinuity (N-O bridge, Fig. 7(b)) *versus* the continuity (N-N bridge, Fig. 7(a)) is evident. A discontinuity in the dipole moment close to the transition state region was underlined for the first time in the  $X + \text{CH}_4 \rightarrow \text{HX} + \text{CH}_3$  ( $X = \text{F}, \text{Cl}$ ) reaction.<sup>40</sup>

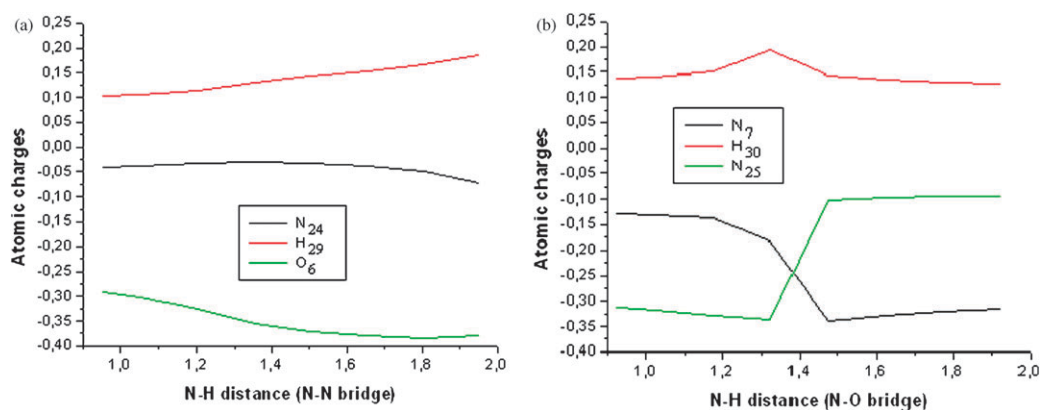
### 3. Conclusion

In this paper we have analysed concerted and stepwise hydrogen atoms transfer and the electronic reorganisation in order to generate the imino-enol form from most stable tautomer of the adenine-thymine base pair (the Watson-Crick structure) under the neutrality restriction which means that the system remains neutral at every moment of the process. This is a very strong restriction that can be assumed as a limiting case. The other limiting case is the completely unrelated movement of each hydrogen atom and also among these atoms and the electrons. In this case a charged system is generated, of course, and the neutrality of this system is obtained only at the end of the process. The information about the real process of generation of the imino-enol form of the A-T base pair can be obtained by a time-dependent analysis, but also by the aid of some static properties (energy, charge, distance

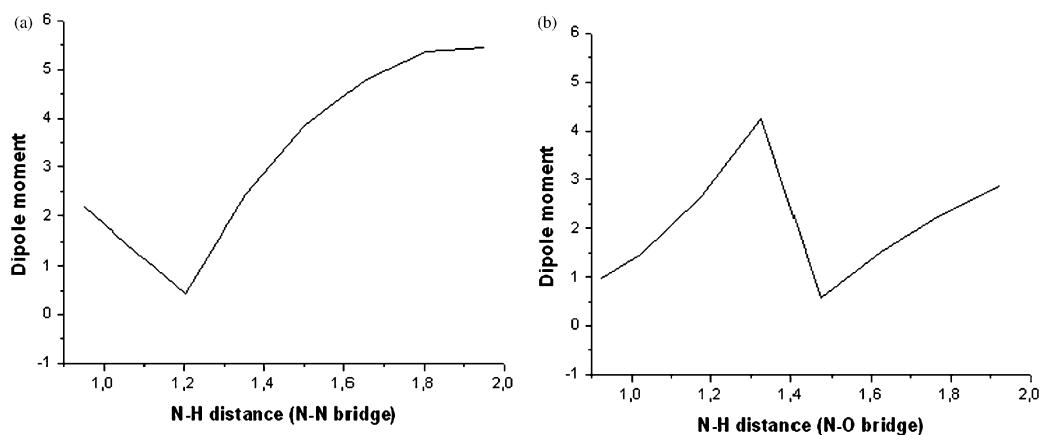




**Fig. 5** Atomic charges as a function of the N–H distance in the N–N (a) and N–O bridge (b) directly involved in the movement. The distances are in Å.



**Fig. 6** Atomic charges as a function of the N–H distance in the N–N (a) and N–O bridge (b) indirectly involved in the movement. The distances are in Å.



**Fig. 7** Dipole moment of the global AT system as a function of the N–H distance in the N–N (a) and N–O bridge (b). The distances are in Å.

of bond, *etc.*) from which some important indications can be obtained. In this paper we have developed the analysis of these properties and some interesting results have been shown. In particular, we can summarize the results as follows:

1. There is a different behaviour if the hydrogen atom moves in the N–N bridge or in the N–O one. From the analysis of Fig. 2–4 we can conclude that the movement of the hydrogen atom in the N–N bridge can generate only a step-to-step

process, while a movement of the hydrogen in the N–O bridge generates a concerted process. In reality also this concerted process is not synchronic since the movement of the first hydrogen does not affect the position of the other hydrogen until the first is completely transferred from one base to the other. Only at that moment, a practically instantaneous movement of the hydrogen atom in the N–N bridge occurs. The two bridges were denoted *hard* (N–N) and *soft* (N–O) in

my previous papers and only the movement of the hydrogen atom in the soft bridge can be followed by the corresponding movement in the hard bridge, but not *vice versa*.

2. In the movement of the hydrogen atom in the N–N bridge only one diabatic state is involved, whereas there are two in the case of hydrogen movement in the N–O bridge. This is evident by the charge variations, as a function of the hydrogen position in the bridge, but, mainly, by the variation of the global dipole moment.

A last question can be related to the problem of an experimental verification of these computational results. Extensive experimental work carried out in past decades have proved the presence of rare tautomers of DNA bases in both polar and nonpolar environments. Unfortunately, very few experimental parameters exist that provide direct evidence of individual hydrogen bonds, with the identification of all atoms involved in this bond (*i.e.* the donor atom, the acceptor atom, as well as the hydrogen atom itself). In fact, the existence of hydrogen bonds is generally inferred *a posteriori* from the spatial proximity and relative orientation of the hydrogen bond donor, the hydrogen, and the hydrogen bond acceptor once the structure of a biomolecule has been solved by either X-ray crystallography or NMR. Moreover, the experimental conditions are important. For example, conventional DNA spectroscopy is dominated by solvent interactions, crystal modes and collective modes of the DNA backbone; in contrast, gas-phase studies can in principle measure interactions between individual molecules in the absence of external effects, but require the vaporisation of the interacting species without thermal degradation. Finally, the experiments could not detect any amount of rare tautomers, due to the limited sensitivity of the methods. The studies of the dynamical processes in this kind of systems are typical problems where a theoretical approach, with reliable calculations, can be very useful.

## References

- 1 B. Giese and S. Wessely, *Chem. Commun.*, 2001, 2108.
- 2 J. Rak, J. Makowska and A. A. Voityuk, *Chem. Phys.*, 2006, **325**, 567.
- 3 G. Villani, *Chem. Phys.*, 2005, **316**, 1.
- 4 G. Villani, *Chem. Phys.*, 2006, **324**, 438.
- 5 S. C. Weatherly, I. V. Yang and H. H. Thorp, *J. Am. Chem. Soc.*, 2001, **123**, 1236.
- 6 Z. Cai, X. Li and M. D. Sevilla, *J. Phys. Chem. B*, 2002, **106**, 2755.
- 7 S. Steenken, *Biol. Chem.*, 1997, **378**, 1293.
- 8 H. Ushiyama and K. Takatsuka, *J. Chem. Phys.*, 2004, **120**, 4561.
- 9 G. V. Mil'nikov, O. Kuhn and H. Nakamura, *J. Chem. Phys.*, 2005, **123**, 074308.
- 10 M. Ortlieb and M. Havenith, *J. Phys. Chem. A*, 2007, **111**, 7355.
- 11 P. Zielke and M. A. Suhm, *Phys. Chem. Chem. Phys.*, 2007, **9**, 4528.
- 12 G. L. Barnes, S. M. Squires and E. L. Sibert, *J. Phys. Chem. B*, 2008, **112**, 595.
- 13 M. V. Vener, O. Kuhn and J. M. Bowman, *Chem. Phys. Lett.*, 2001, **349**, 562.
- 14 M. J. Wójcik, K. Szczeponek and M. Boczar, *Int. J. Mol. Sci.*, 2003, **4**, 422.
- 15 Z. Smedarchina, A. Fernández-Ramos and W. Siebrand, *J. Chem. Phys.*, 2005, **122**, 134309.
- 16 C. S. Tautermann, A. F. Voegelé and K. R. Liedl, *Chem. Phys.*, 2003, **292**, 47.
- 17 M. Meuwly, A. Muller and S. Leutwyler, *Phys. Chem. Chem. Phys.*, 2003, **5**, 2663.
- 18 D. R. Borst, J. R. Roscioli, D. W. Pratt, G. M. Florio, T. S. Zwier, A. Muller and S. Leutwyler, *Chem. Phys.*, 2002, **283**, 341.
- 19 J. Catalán, J. C. del Valle and M. Kasha, *Proc. Natl. Acad. Sci. U. S. A.*, 1999, **96**, 8338.
- 20 J. Catalán, J. C. del Valle and M. Kasha, *Proc. Natl. Acad. Sci. U. S. A.*, 2002, **99**, 5799.
- 21 J. Catalán, J. C. del Valle and M. Kasha, *Chem. Phys. Lett.*, 2000, **318**, 629.
- 22 J. C. del Valle, M. Kasha and J. Catalán, *Int. J. Quantum Chem.*, 2000, **77**, 118.
- 23 H. Y. Chen and I. Chao, *ChemPhysChem*, 2004, **5**, 1855.
- 24 J. Florián and J. Leszczynski, *J. Am. Chem. Soc.*, 1996, **118**, 3010.
- 25 T. Hayashi and S. Mukamel, *Isr. J. Chem.*, 2004, **44**, 185.
- 26 J. Bertran, A. Oliva, L. Rodríguez-Santiago and M. Sadoupe, *J. Am. Chem. Soc.*, 1998, **120**, 8159.
- 27 X. Li, Z. Cai and M. D. Sevilla, *J. Phys. Chem. B*, 2001, **105**, 10115.
- 28 Z. Smedarchina, W. Siebrand and A. Fernández-Ramos, *J. Chem. Phys.*, 2007, **127**, 174513.
- 29 K. Möller and A. H. Zewail, *Chem. Phys. Lett.*, 1998, **295**, 1.
- 30 E. W. G. Diau, O. K. Abou-Zied, A. A. Scala and A. H. Zewail, *J. Am. Chem. Soc.*, 1998, **120**, 3245.
- 31 S. De Feyter, E. W. G. Diau, A. A. Scala and A. H. Zewail, *Chem. Phys. Lett.*, 1999, **303**, 249.
- 32 E. W. G. Diau, S. De Feyter and A. H. Zewail, *Chem. Phys. Lett.*, 1999, **304**, 134.
- 33 T. Fiebig, M. Chachisvilis, M. Manger, A. H. Zewail, A. Douhal, I. García-Ochoa and A. de La Hoz Ayuso, *J. Phys. Chem. A*, 1999, **103**, 7419.
- 34 A. Douhal, S. K. Kim and A. H. Zewail, *Nature*, 1995, **378**, 260.
- 35 S. Miura, M. E. Tuckerman and M. L. Klein, *J. Chem. Phys.*, 1998, **109**, 5290.
- 36 G. Villani, *Chem. Phys.*, 2007, **336**, 143.
- 37 G. Villani, *J. Chem. Phys.*, 2008, **128**, 114306.
- 38 G. Villani, *J. Phys. Chem. B*, 2009, **113**, 2128.
- 39 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, 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, 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. 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 (Revision B. 01)*, Gaussian, Inc., Pittsburgh, PA, 2003.
- 40 A. D. Bandrauk, E. S. Sedick and C. F. Matta, *J. Chem. Phys.*, 2004, **121**, 7764.