

Orbital SCF Energies in the Double Proton Transfer of the Adenine-Thymine Base Pair (*).

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Summary. — The double-minimum potential generated by the proton motion involved in the two hydrogen bonds of the adenine-thymine base pair can be accounted for through the orbital-energy spectrum. The results show that the greatest interaction between the molecular orbitals is found when the interprotonic distance of the protons is optimum, *i.e.* at the top of the barrier of the double-minimum potential. This raises the question of charge transfer electronic transitions as a possibility of modelling the behaviour of the double proton transfer in the excited states of this base pair.

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1. — Introduction.

Semi-empirical quantum-mechanical calculations have been recently used to determine the double-minimum potential originated by the double-proton-

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transfer (DPT) process in some hydrogen-bonded complexes (¹⁻⁶). The results were qualitatively similar to those obtained by *ab initio* techniques (⁷). In particular, the form of the potential-energy curve and the height of the barrier separating the two minima are sometimes believed to influence the biological behaviour of DNA (⁸). The present paper deals with the interpretation of the double-minimum-potential barrier of the adenine(A)-thymine(T) base pair through an analysis of the SCF orbital energies.

2. - Theory.

Recently RUEDENBERG (⁹) building upon a work by POLITZER (¹⁰) has suggested that the total Hartree-Fock SCF energy

$$(1) \quad E = \sum_k v_k \varepsilon_k + V_{nn} - V_{ee},$$

where ε_k is a SCF orbital energy with occupation number v_k , V_{nn} is the nuclear-nuclear repulsion energy and V_{ee} is the electron-electron repulsion energy, can be approximated by

$$(2) \quad E = c \sum_k v_k \varepsilon_k$$

at equilibrium nuclear separations. Rationalization is thus provided for the extended Huckel method and for discussions of Walsh's rules in which total energies are replaced by orbital sums.

In more recent studies it was shown (¹¹) that relation (2) with $c = 1.55$

(¹) S. ABDULNUR: *Quantum Science, Methods and Structure* (New York, N. Y., 1976), p. 567.

(²) J. MARAÑÓN, O. M. SORARRAIN, H. GRINBERG, S. LAMDAN and C. H. GAOZZA: *J. Theor. Biol.*, **74**, 11 (1978).

(³) H. GRINBERG, A. L. CAPPARELLI, A. SPINA, J. MARAÑÓN and O. M. SORARRAIN: *J. Phys. Chem.*, **85**, 2751 (1981).

(⁴) J. MARAÑÓN and H. GRINBERG: *Theochem.*, **88**, 283 (1982).

(⁵) S. SCHEINER and C. W. KERN: *Chem. Phys. Lett.*, **57**, 331 (1978); *J. Am. Chem. Soc.*, **101**, 4081 (1979).

(⁶) J. LIPINSKI and W. A. SOCALSKI: *Chem. Phys. Lett.*, **76**, 88 (1980).

(⁷) E. CLEMENTI, J. MEHL and W. VON NIESSEN: *J. Chem. Phys.*, **54**, 508 (1971).

(⁸) P. O. LÖWDIN: *Rev. Mod. Phys.*, **35**, 724 (1963); *Adv. Quantum Chem.*, **2**, 213 (1965).

(⁹) a) K. RUEDENBERG: *J. Chem. Phys.*, **66**, 375 (1977); b) E. J. SHAAD, B. H. ROBINSON and B. A. HESS jr.: *J. Chem. Phys.*, **67**, 4616 (1977).

(¹⁰) P. POLITZER: *J. Chem. Phys.*, **64**, 4239 (1976).

(¹¹) a) T. ANNO and Y. SAKAI: *J. Chem. Phys.*, **67**, 4771 (1977); b) E. A. CASTRO: *Int. J. Quantum Chem.*, **15**, 355 (1979); c) T. ANNO: *J. Chem. Phys.*, **72**, 782 (1980).

is still inadequate to discuss geometric molecular stabilities and that any quantity defined as a multiple of $\sum_k v_k \epsilon_k$ does not even show a minimum at least along a stretching co-ordinate within a molecule. Moreover, on using eq. (2) only for valence orbitals, it was predicted that c takes its maximum value when the molecule is in its equilibrium configuration⁽¹²⁾. Further, it was shown that relation (2) is valid with $c = 1$ when all the eigenvalues (valence plus inner orbitals) are included. But, when only the valence eigenvalues are considered, the constant relating the total energy to the sum of the eigenvalues times their occupancy can be used analytically, since it is related to the stability of a given conformer and reflects the bond length variation in nonstable conformers.

From the relation

$$(3) \quad \Delta E = \Delta c \sum_k v_k \Delta \epsilon_k$$

it can be observed that the variation of the molecular energy in DPT processes can be characterized by the orbital-energy shifts $\Delta \epsilon_k$. Therefore, as a continuation of our studies on the double hydrogen bonding in the A-T base pair^(2,4), we wish to present our findings on the SCF orbital-energy correlation and orbital-energy shifts of this particular hydrogen-bonded complex.

3. - Results and discussion.

Computations were performed with the CNDO/S-CI procedure⁽¹³⁾ as described earlier^(2,4). The numbering structure of the hydrogen-bonded system under consideration is shown schematically in fig. 1. Bond lengths and angles were obtained from ref. (14) and references cited there. The interatomic distances for the atoms involved in the hydrogen bonds were taken from ref. (15). The problem in some of these studies is that, since the exact geometries of the rare tautomeric forms are not known experimentally, the energies were determined by using assumed geometries, which retained the ring structure of the normal form for the rare form. Protons H₂₉ and H₃₀ (fig. 1) were allowed to move independently along the lines joining N₁₀ and O₂₂ and joining N₁ and N₁₅, respectively. All other nuclei were held stationary.

⁽¹²⁾ M. A. WHITEHEAD: *J. Chem. Phys.*, **69**, 497 (1978).

⁽¹³⁾ Calculations were performed on an IBM 360/50. The closed-shell CNDO/S program was obtained from the Quantum Chemistry Program Exchange, Indiana University, Bloomington, In. 47401.

⁽¹⁴⁾ L. E. SUTTON: *Chem. Soc., Spec. Publ.*, **11** (1958); **18** (1965).

⁽¹⁵⁾ S. ARNOTT, S. D. DOVER and A. J. WONACOTT: *Acta Crystallogr., Sect. B*, **25**, 2192 (1969).

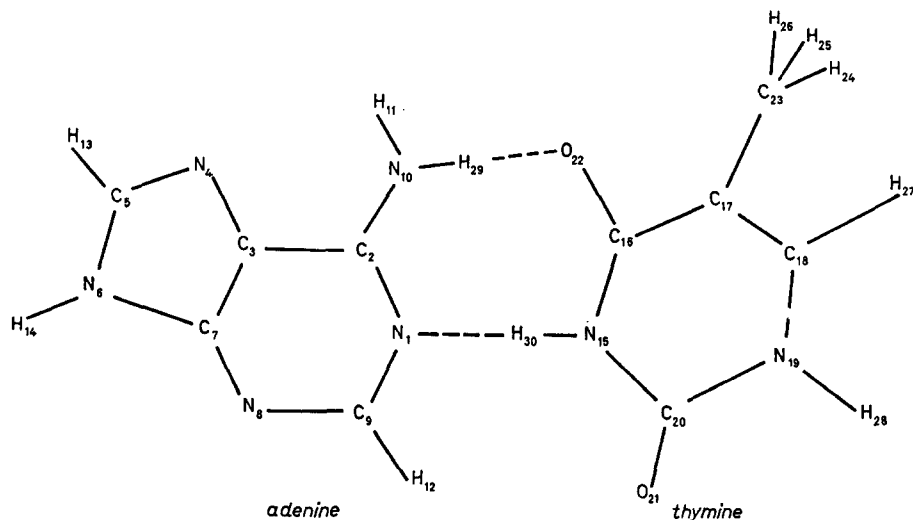


Fig. 1. — Adenine-thymine base pair. Hydrogen bonds are shown as dashed lines.

Figure 2 shows the orbital-energy correlation curves of both normal and tautomeric configurations of the A-T base pair. It can be observed that the behaviour of the σ - and π -MOs is quite different.

The π and π^* orbitals are localized on the same molecule (A or T) through the DPT process. In general, the interaction takes place between pairs of π -orbitals close in energy and localized in different molecules (A \rightarrow A* or T \rightarrow T*).

The maximum interaction is observed at the position of minimum interprotonic distance, which in turn corresponds to the top of the double-minimum-potential well. The behaviour of the MOs is particularly interesting which in the normal form of the base pair correspond to the HOMO-3 and HOMO-4 localized on A and T, respectively. These are correlated with the HOMO-3 and HOMO-4 (π character) localized on T and A, respectively, of the tautomeric configuration. We postulate a nonallowed intercrossing at the position of maximum protonic approach. This behaviour can be rationalized as due to the variation of the lone-pair character of the MOs involved in the hydrogen bonding. The HOMO-3 is localized on the nitrogen of the N—N— —N bridge with 34% of relative localization in the normal configuration; it increases to 39% at the top of the barrier and decreases to 26% at the tautomeric position. The lone-pair character of the HOMO-4 is somewhat modified during the DPT process. In fact, its relative localization at the nitrogen of the other N— —H—O hydrogen bridge is 53% at the tautomeric position, 48% at the top of the barrier and reaches 53% at the normal position.

Similar behaviour show the LUMO and LUMO+1 π virtual eigenvectors. This accounts for the existence of singlet and triplet $\pi^* \leftarrow \pi$ charge transfer

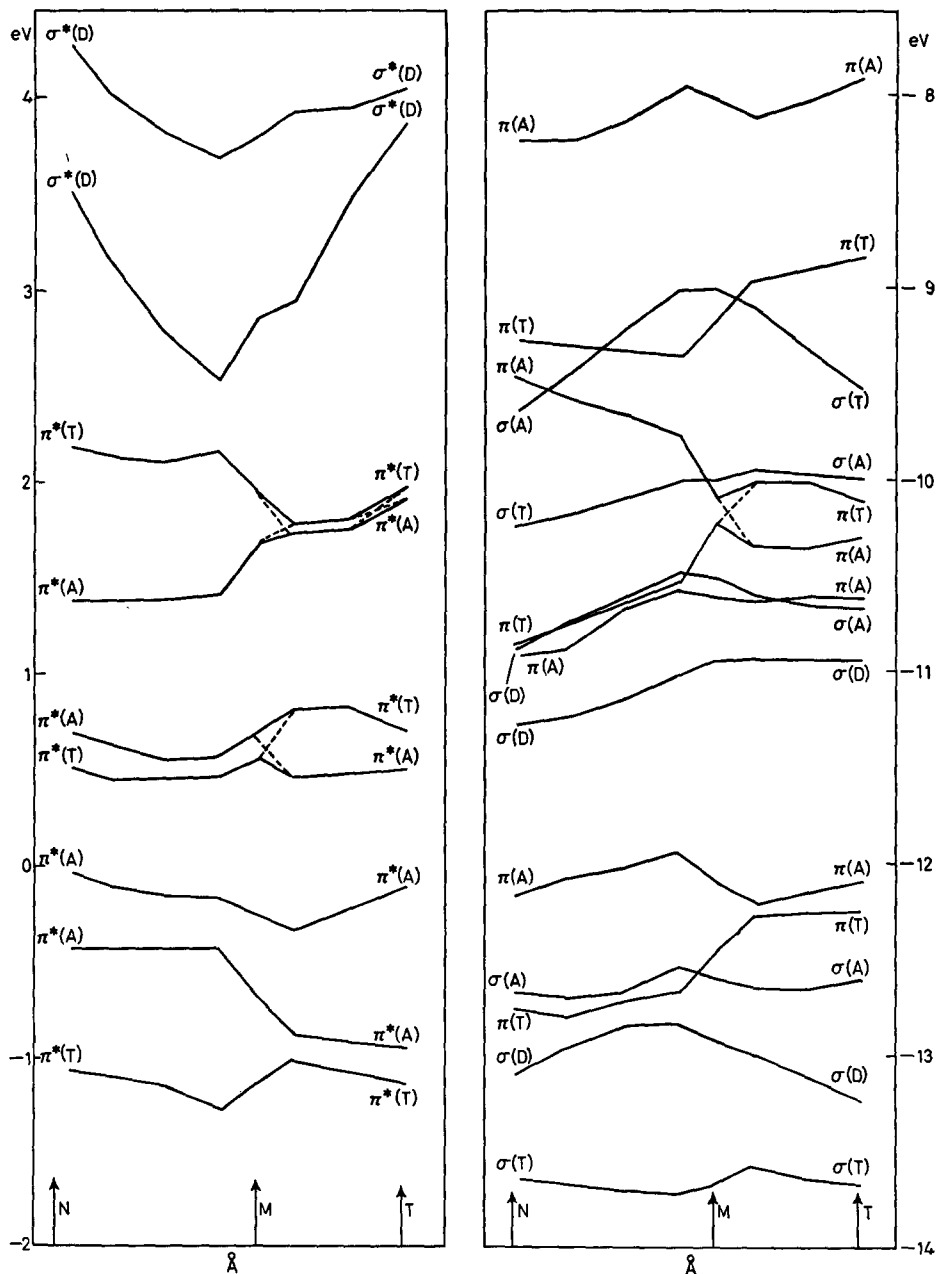


Fig. 2. - Correlation of the SCF orbital energies for the double proton transfer of the adenine-thymine base pair. N normal position, M maximum approach of the protons involved in the double hydrogen bonding, T tautomeric position. (A) adenine, (T) thymine, (D) delocalized.

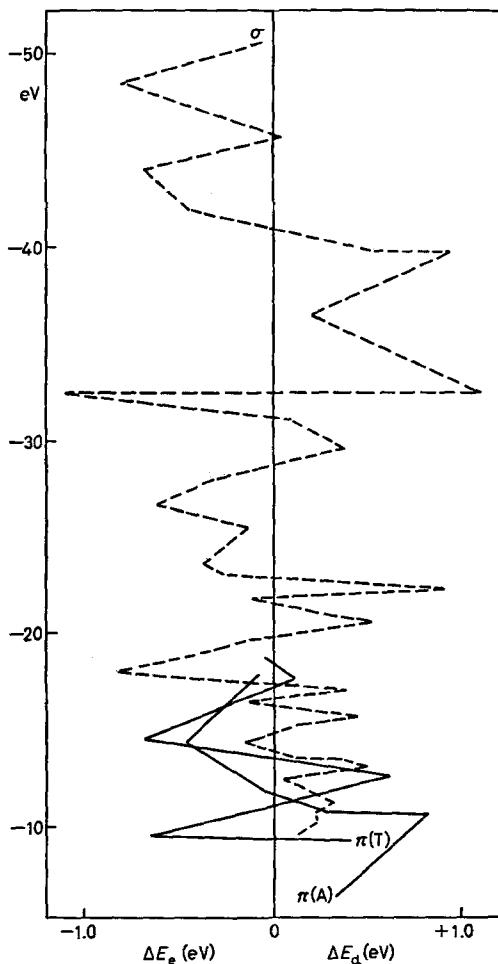


Fig. 3. - SCF orbital-energy shifts for the double proton transfer of the adenine-thymine base pair. ΔE_s stabilization energy, ΔE_d destabilization energy. (A) adenine (T) thymine.

electronic transitions computed through SCF-CNDO/S-CI calculations (^{3,16}).

As to the behaviour of the σ -MOs, it was observed that during the DPT process they modify their relative localization. These MOs were found to be localized on both units of the pair in both normal and tautomeric configurations. It is important to point out that the SCF orbital-energy correlation curves show, in general, a change of the slope at the top of the double-well potential. In particular, this behaviour is neatly observed in the MOs localized in the atoms involved in both hydrogen bonds.

(¹⁶) J. MARAÑÓN, H. GRINBERG and N. S. NUDELMAN: *Int. J. Quantum Chem.*, **22**, 69 (1982).

We have also studied the spectral decomposition of the orbital energy shift (eq. (3)) as a function of the orbital energy at the position of total minimum energy of the normal configuration. The results are shown in fig. 3. We can see the σ -orbitals, that in general are found to be delocalized on both units, show a regular behaviour in three different energy zones: the first zone (deepest energy orbitals), from -32 eV to -51 eV; the second zone, from -18 eV to -32 eV, and the third zone, from -10 eV to -18 eV. In each of them it can be observed that the orbital-energy shift has initially a destabilizing character and terminates with a stabilizing character, but no repetition of this trend was observed in other zones of the orbital-energy spectrum. To the first zone contribute both the $2s$ orbitals of the heavy atoms and the $1s$ orbitals of hydrogens involved in both hydrogen bondings. In the second zone an intercrossing is produced of the $2p$ orbitals, while in the third zone the orbital interaction is regulated by the lone-pair contribution to the eigenvectors. As to the behaviour of the π -orbitals (localized either on A or on T) they do not show a so pronounced regularity as that shown by the σ -MOs in the third zone of orbital energies.

The contribution to the total energy destabilization for the σ -orbitals is

$$\sum_{k \in \sigma} v_k \Delta \varepsilon_k = 1.712 \text{ eV}$$

and for the π -orbitals

$$\sum_{k \in \pi} v_k \Delta \varepsilon_k = 1.078 \text{ eV}.$$

Since the variation of the total energy in the DPT process is 2.289 eV (see table I), the consequence which emerges is that the « overall change » of the SCF orbital energy is the determining factor governing the DPT process.

TABLE I. — *Total energies and sum of the SCF orbital energies for the adenine-thymine base pair. Energies are given in eV.*

Configuration	$-E$ (eq. (1))	$-\sum_k v_k \varepsilon_k$ (eq. (2))	c
A-T (normal form)	1912.176	2150.694	0.8891
A*.T* (tautomeric form)	1909.887	2428.984	0.7863

As to expression (2), it can be observed in the table that the results are consistent with what was previously pointed out ⁽¹²⁾, *i.e.*, since the normal configuration is more stable, its c value has to be greater than that of the tautomeric configuration.

Leaving the conclusions of purely biological interest aside, one result which is relevant for the present study appears. Since the steric conditions are

favourable, the hydrogen bonds do not interrupt the conjugated system entirely. A small amount of conjugation persists.

Finally, it should be emphasized that the co-operative proton motion in multiconnected hydrogen bond system and its coupling with electronic motion plays an important role in ferroelectric systems. This problem, which is sometimes believed to influence the behaviour of the proteins, certainly merits a thorough investigation. Obviously, there is an overall self-consistency between these results and the similar results previously discussed (17).

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The authors are grateful to CONICET, República Argentina, for a research grant in support of this work.

(17) See, for example, S. BRATOZ: *Adv. Quantum Chem.*, **3**, 209 (1967).

● RIASSUNTO (*)

Il potenziale a doppio minimo generato dal movimento dei protoni coinvolti nei due legami a idrogeno della coppia di basi ademina-timina può essere preso in considerazione attraverso lo spettro di energia orbitale. I risultati mostrano che la maggiore interazione tra orbitali molecolari si trova quando la distanza interprotonica dei prodotti è ottimale, cioè nel punto più alto della barriera del potenziale a doppio minimo. Ciò solleva il problema della transizioni elettroniche con trasferimento di carica come una possibilità di regolare il comportamento del doppio trasferimento di protoni negli stati eccitati di questa coppia di basi.

(*) *Traduzione a cura della Redazione.*

Орбитальные SCF энергии в процессе двойного переноса протонов для пары оснований аденина и тимина.

Резюме (*). — Потенциал с двойным минимумом, образованный за счет движения протонов, участвующих в двух водородных связях пары оснований аденина и тимина, может быть объяснен с помощью спектра орбитальной энергии. Результаты показывают, что наибольшее взаимодействие между молекулярными орбиталями возникает, когда расстояние между протонами является оптимальным, т.е. на вершине барьера потенциала с двумя минимумами. При этом возникает вопрос о возможности моделирования поведения двойного переноса протонов в возбужденных состояниях этой пары оснований.

(*) *Переведено редакцией.*