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Unexpected A·T(WC)↔A·T(rWC)/A·T(rH) and A·T(H)↔A·T(rH)/A·T(rWC) conformational transitions between the classical A·T DNA base pairs: A QM/QTAIM comprehensive study

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Abstract

In this study, using QM/QTAIM calculations in the continuum with ε = 1 under normal conditions, we have revealed for the first time the nondissociative A·T(WC)↔A·T(rWC)/A·T(rH) and A·T(H)↔A·T(rH)/A·T(rWC) conformational transitions. It was established that they proceed *via* the essentially nonplanar transition states (C_1 symmetry) through the intermediates, which are wobbled conformers (C_1 symmetry) theoretically predicted in our previous work (Brovarets' et al., *Frontiers in Chemistry*, 2018, 6:8, 10.3389/fchem.2018.00008) of the classical A·T DNA base pairs—Watson–Crick A·T(WC), reverse Watson–Crick A·T(rWC), Hoogsteen A·T(H) and reverse Hoogsteen A·T(rH). At this, the A·T(H)↔A·T(rWC) and A·T(WC)↔A·T(rH) conformational transformations are controlled by the transition states (TSs) stabilized by the participation of the intermolecular (T)N3H···N6(A) H-bond (∼3.70 kcal·mol^{-1}) between the imino group N3H of T and pyramidilized amino group N6H$_2$ of A. Gibbs free energies of activation for these processes consist 12.22 and 11.11 kcal·mol^{-1}, accordingly, under normal conditions. TSs, which control the A·T(WC)↔A·T(rWC) and A·T(H)↔A·T(rH) conformational transitions are stabilized by the participation of the intermolecular (T)N3H···N6(A) H-bond (5.82 kcal·mol^{-1}) and bifurcating intermolecular (T)N3H···N6(A) (5.00) and (T)N3H···N7(A) (0.61 kcal·mol^{-1}) H-bonds, accordingly. Notably, in these two TSs amino group N6H$_2$ of A is significantly pyramidilized; Gibbs free energies of activation for these reactions are 19.07 and 19.71 kcal·mol^{-1}, accordingly.

KEYWORDS

classical A·T DNA base pairs, conformational transformation, quantum-mechanical calculation, transition state, wobble structure

1 | INTRODUCTION

It is well known that the A·T DNA base pair have four classical configurations, which are biologically significant—Watson–Crick A·T(WC), reverse Watson–Crick A·T(rWC), Hoogsteen A·T(H), and reverse Hoogsteen A·T(rH).[1] Plane-symmetric architecture (C_s symmetry) is their characteristic structural feature in free state, while the geometrically isomorphic A·T(H) and A·T(rH) pairs have narrowed (∼ 2 Å) glycoside groove in comparison with the geometrically isomorphic A·T(WC) and A·T(rWC) pairs.[2] All of them are stabilized by the participation of three intermolecular H-bonds, one of which is noncanonical C2H/C8H···O4/O2 H-bond.[2–4]

Notably, that while it is known that DNA double helix contains the canonical Watson–Crick base pairs, which provides storage and precise transfer of the genetic information, their replacement with the non-Watson–Crick base pairs leads to perspective interesting practical applications.[5–11]

Traditional A·T Watson–Crick DNA base pair[12–14] may acquire different conformations with various organization of the H-bonds through the rotation of one of the bases according to the other:

- On 180 ° around the (A)N1–N3(T) axis, leading to the formation of the reverse Watson–Crick A·T(rWC) or so-called Donohue DNA base pair,[1] registered in the bioactive parallel-stranded DNA;[15–21]
- On 180 ° around the (A)C9′-N9 axis from the *anti*- to *syn*-conformation, representing Hoogsteen A·T(H) base pair[22] involved into a number of biologically important processes such as recognition, damage induction, replication;[21–32]
- On 180 ° around the (A)N7–N3(T) axis in the Hoogsteen base pair forming the reverse Hoogsteen A·T(rH) or so-called Haschemeyer–Sobell base pair.[33–36]

Discussed DNA base pairs are not static structures in the composition of DNA.[37,38] Thus, the spontaneous A·T(WC)↔A·T(H) conformational transition has been experimentally registered by the NMR method on the DNA regions enriched by the classical A·T nucleobase pairs.[32] Despite numerous theoretical investigations, microstructural nature of these transitions remains incomprehensible.[30,39]

By the methods of nonempirical quantum chemistry it was investigated only the A·T(WC)↔A·T(rWC) and A·T(H)↔A·T(rH) conformational transitions of the pairs in free state, which occur by turning of the bases relative one to another on the angle of 180 ° around the central (T) N3H···N1/N7(A) H-bond, which is the strongest in all base pairs.[2]

Researchers of DNA converge in one point of view—it takes place the concerted change of the configuration of the base pair and rotation of A around the glycoside bond from the *anti*- into the high-energy *syn*-conformation.[30,39]

It is quite logically to appeal to similar processes occurring in the isolated nucleobase pairs (see work[40] and bibliography presented therein) at the studying of the microstructural nature of the conformational transitions of the DNA base pairs.

Recently, we have theoretically revealed novel high-energetic, significantly nonplanar (symmetry C_1) conformers—A·T(w_{WC}), A·T(w_{rWC}), A·T(w_H), and A·T(w_{rH}) for each of the four biologically important A·T DNA base pairs—A·T(WC), A·T(rWC), A·T(H), and A·T(rH).[40]

It was found that each of these conformers possesses wobble (w) structure and is stabilized by the participation of the two anti-parallel N6H/N6H´···O4/O2 and N3H···N6 H-bonds (the exocyclic N6H′ bond has *trans*-orientation relative to the endocyclic N1C6 bond of A). These specific intermolecular contacts involve pyramidalized amino group of the A DNA base, acting simultaneously as an acceptor and a donor of the H-bonding. The transition states (TSs)—$TS_{A\cdot T(WC)\leftrightarrow A\cdot T(wWC)}$, $TS_{A\cdot T(rWC)\leftrightarrow A\cdot T(wrWC)}$, $TS_{A\cdot T(H)\leftrightarrow A\cdot T(wH)}$, and $TS_{A\cdot T(rH)\leftrightarrow A\cdot T(wrH)}$—controlling the dipole-active transformations of the conformers from the main state of the classical A·T DNA base pairs into the high-energetic, significantly nonplanar state and *vice versa*, have been localized. They also possess wobble structures (symmetry C_1) similarly to the high-energetic conformers and are stabilized by the participation of the N6H/N6H´···O4/O2 and N3H···N6 H-bonds. It was assumed that these conformational transitions are directly related to the thermally driven fluctuational behavior—"breathing" of DNA.[37,38]

In this work, it was established for the first time that just-mentioned novel conformers A·T(w_{WC}), A·T(w_{rWC}), A·T(w_H), and A·T(w_{rH}) are intermediates, controlling biologically important A·T(WC)↔A·T(rWC)/A·T(rH) and A·T(H)↔A·T(rH)/A·T(rWC) conformational transition between the classical A·T DNA base pairs. TSs of these transitions have been localized and their structural, energetical, and polar characteristics have been documented.

2 | COMPUTATIONAL METHODS

Geometries of the main and high-energetic conformers and transition states (TSs) of their mutual conformational transformations, as well as their harmonic vibrational frequencies have been calculated at the B3LYP/6-311++G(d,p) level of theory,[41–45] using Gaussian'09 package[46] in free state. Applied level of theory has successfully proved itself for the calculations of the similar systems.[47–53] A scaling factor that is equal to 0.9668[54–56] has been applied in the present work for the correction of the harmonic frequencies of all conformers and TSs of their conformational transitions. We have confirmed the local minima and TSs, localized by synchronous transit-guided quasi-Newton method,[57] on the potential energy landscape by the absence or presence, respectively, of the imaginary frequency in the vibrational spectra of the complexes. We applied standard TS theory for the estimation of the activation barriers of the conformational transformations.[58] Electronic energy calculations have been performed at the single point at the MP2/aug-cc-pVDZ level of theory,[59,60] which has been successfully applied previously for the similar objects.[61–66]

To model internally inherent conformational transitions between the classical A·T DNA base pairs all calculations have been performed for the isolated H-bonded pairs of nucleotide bases in the continuum with a dielectric constant of ε = 1, which is characteristic for the substantially hydrophobic interfaces of protein–DNA interactions.[67–71] At this, we have relied on the experience received in the previous works[72–74] for the related systems, where the negligibly small impact of the stacking and sugar-phosphate backbone has been shown, and also on the good agreement between theoretical[75–81] and experimental[82–87] data.

The Gibbs free energy *G* for all structures was obtained in the following way:

$$G = E_{el} + E_{corr}, \quad (1)$$

where E_{el}–electronic energy, while E_{corr}–thermal correction.

Electronic interaction energies ΔE_{int} have been calculated at the MP2/6-311++G(2df,pd) level of theory as the difference between the total energy of the base pair and energies of the monomers and corrected for the basis set superposition error (BSSE)[88,89] through the counterpoise procedure.[90,91]

Bader's quantum theory of Atoms in Molecules (QTAIM),[92–96] using program package AIMAll,[97] was applied to analyze the electron density distribution. The presence of the bond critical point (BCP), namely the so-called (3,−1) BCP, and a bond path between hydrogen donor and acceptor, as well as the positive value of the Laplacian at this BCP ($\Delta\rho > 0$), were considered as criteria for the H-bond formation.[98–103] Wave functions were obtained at the level of theory used for geometry optimization.

The energies of the intermolecular AH···B H-bonds were evaluated by the empirical Iogansen's formula:[104]

$$E_{AH\cdots B} = 0.33\cdot\sqrt{\Delta\nu - 40}, \quad (2)$$

where $\Delta\nu$–magnitude of the frequency shift of the stretching mode of the AH H-bonded group involved into the AH···B H-bond relatively the unbound group. The partial deuteration was applied to avoid the effect of vibrational resonances.[105–110]

The atomic numbering scheme for the DNA bases is conventional.[111]

3 | RESULTS AND DISCUSSION

In our previous paper[40] for the first time we have succeed to establish in the classical biologically important A·T DNA base pairs with C_s symmetry—Watson–Crick (WC), reverse Watson–Crick A·T(rWC), Hoogsteen A·T(H) and reverse Hoogsteen A·T(rH) DNA base pairs—novel high-energetic, dynamically stable, mirror-symmetrical A·T$(w_{WC})_{R,L}$, A·T$(w_H)_{R,L}$, A·T$(w_{rWC})_{R,L}$, and A·T$(w_{rH})_{R,L}$ conformational states. Their distinguished feature independently of the pair, in which they are realized, is significantly nonplanar structure (C_1 symmetry), caused by the pyramidal structure of the ≥C6N6H_2 amino fragment of A DNA base, the amino group of which acts simultaneously as a donor and an acceptor of the specific intermolecular interaction with T by two (T)N3H···N6(A) and (A)N6H/N6H′···O4/O2(T) H-bonds. Each of the four A·T DNA base pairs transfers into the aforementioned conformer *via* two mirror-symmetric pathways through the soft $TS_{A\cdot T(WC)\leftrightarrow A\cdot T(wWC)R,L}$, $TS_{A\cdot T(rWC)\leftrightarrow A\cdot T(wrWC)R,L}$, $TS_{A\cdot T(H)\leftrightarrow A\cdot T(wH)R,L}$, and $TS_{A\cdot T(rH)\leftrightarrow A\cdot T(wrH)R,L}$ transition states (C_1 symmetry) with low values of the imaginary frequencies. At this, the structures, which names differ from each other only by the subscripts R and L, are mirror-symmetrical, that is enantiomers. It is well known that enantiomers have identical scalar physico-chemical characteristics and differ only by the direction of the dipole moment.

At this point the question arise, what structural-dynamic consequences cause these unusual conformers of the classical A·T DNA base pairs? To answer on this biologically important question, we initially analyzed at the qualitative stereochemical level possible processes and transition states, which control them, and further verified them by numerical quantum-mechanical calculations.

In this context, it was fixed important result—these conformers are responsible as intermediates for the A·T(WC)↔A·T(rWC)/A·T(rH) and A·T(H)↔A·T(rH)/A·T(rWC) conformational transitions between the classical A·T DNA base pairs (Figure 1, Tables 1–3).

The A·T(H)↔A·T(rWC) and A·T(WC)↔A·T(rH) conformational transformations are controlled by the essentially nonplanar TSs (C_1 symmetry) with low values of the imaginary frequencies (19.9 and 21.9 c_M^{-1}, accordingly) stabilized by the participation of the intermolecular (T)N3H···N6(A) H-bond (∼3.70 kcal·mol^{-1}) between the imino group of T and pyramidilized amino group of A (Figure 1, Table 2). At this, amino group of A is pyramidilized noticeably stronger than in the free base. Gibbs free energies of activation for these processes consist 12.22 and 11.11 kcal·mol^{-1}, accordingly.

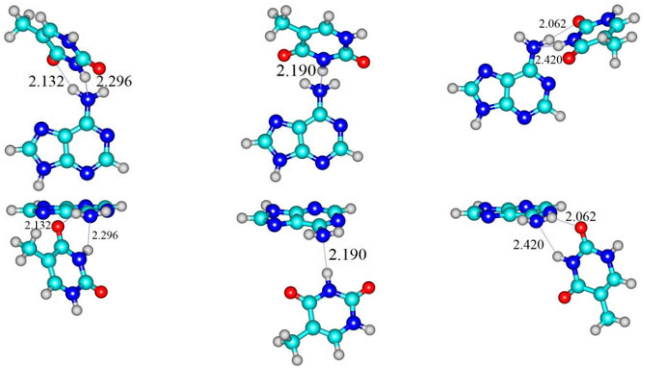
In this case, conformational transformations of the A·T DNA base pairs are realized by the following nondissociative scenario (each of them—by the mirror-symmetric pathways):

A·T(H) (0.00) ↔ $TS_{A\cdot T(H)\leftrightarrow A\cdot T(wH)R,L}$ (9.15) ↔ A·T$(w_H)_{R,L}$ (9.02) ↔ $TS_{A\cdot T(wH)R,L\leftrightarrow A\cdot T(wrWC)R,L}$ (12.22) ↔ A·T$(w_{rWC})_{R,L}$ (7.85) ↔ $TS_{A\cdot T(wrWC)R,L\leftrightarrow A\cdot T(rWC)R,L}$ (9.40) ↔ A·T(rWC) (1.08 kcal·mol^{-1});
and A·T(WC) (0.00) ↔ $TS_{A\cdot T(WC)\leftrightarrow A\cdot T(wWC)R,L}$ (7.28) ↔ A·T$(w_{WC})_{R,L}$ (7.03) ↔ $TS_{A\cdot T(wWC)R,L\leftrightarrow A\cdot T(wrH)R,L}$ (11.11) ↔ A·T$(w_{rH})_{R,L}$ (7.68) ↔ $TS_{A\cdot T(wrH)R,L\leftrightarrow A\cdot T(rH)R,L}$ (9.67) ↔ A·T(rH) (−0.65 kcal·mol^{-1}).

Herewith, some R structures transform into the other R structures, the same concerns L-structures. Saying in other words, pathways of these dipole-active conformational transformations are mirror-symmetric. In fact, the $TS_{A\cdot T(wH)R,L\leftrightarrow A\cdot T(wrWC)R,L}$ and $TS_{A\cdot T(wWC)R,L\leftrightarrow A\cdot T(wrH)R,L}$, which pairwise link the A·T$(w_H)_{R,L}$ with A·T$(w_{rWC})_{R,L}$ and A·T$(w_{WC})_{R,L}$ with A·T$(w_{rH})_{R,L}$ conformers, are transition states of the A·T(H)↔A·T(rWC) and A·T(WC)↔A·T(rH) conformational transformations of the classical A·T DNA base pairs, accordingly.

Essentially nonplanar TSs (C_1 symmetry), which control A·T(WC)↔A·T(rWC) and A·T(H)↔A·T(rH) conformational transitions, possess significantly higher values of the imaginary frequencies (274.7 and 270.8 c_M^{-1}, accordingly) and are stabilized by the participation of the intermolecular (T)N3H···N6(A) H-bond (5.82 kcal·mol^{-1}) for the $TS_{A\cdot T(wWC)R,L\leftrightarrow A\cdot T(wrWC)L,R}$ and bifurcating intermolecular (T)N3H···N6(A) (5.00 kcal·mol^{-1}) and (T)N3H···N7(A) (0.61 kcal·mol^{-1}) H-bonds in the second case for the $TS_{A\cdot T(wH)R,L\leftrightarrow A\cdot T(wrH)L,R}$ (Figure 1, Table 2). Notably, in these two TSs amino group of A is significantly pyramidilized. In this case, pyramidalization of the amino group of A is around the same, as in the case of the TS of

A·T(w$_H$)$_{R,L}$↔A·T(w$_{rWC}$)$_{R,L}$



A·T(w$_H$)$_{R,L}$

(ΔE$_{int}$=-5.69 (0.97)/ ΔG$_{int}$=6.21 / ΔG=0.00 / ΔE=0.00)

TS$_{A\cdot T(wH)R,L\leftrightarrow A\cdot T(wrWC)R,L}$

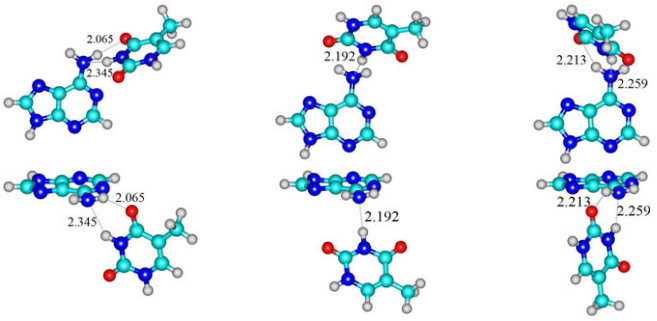
(ν_i=19.9 *i* cm^{-1})

(ΔE$_{int}$=-3.74 (0.99) / ΔG$_{int}$=9.06 / ΔG=3.20 / ΔE=2.30)

A·T(w$_{rWC}$)$_{R,L}$

(ΔE$_{int}$=-6.51 (0.91) / ΔG$_{int}$=4.97 / ΔG=-1.17 / ΔE=-0.74)

A·T(w$_{WC}$)$_{R,L}$↔A·T(w$_{rH}$)$_{R,L}$



A·T(w$_{WC}$)$_{R,L}$

(ΔE$_{int}$=-6.34 (0.98)/ ΔG$_{int}$=5.50/ ΔG=0.00 / ΔE=0.00)

TS$_{A\cdot T(wWC)R,L\leftrightarrow A\cdot T(wrH)R,L}$

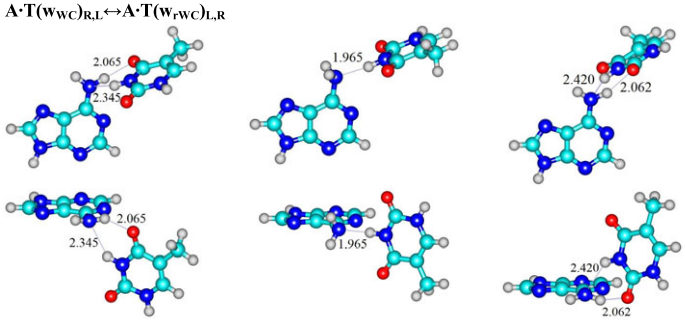
(ν_i=21.9 *i* cm^{-1})

(ΔE$_{int}$=-3.70 (0.99) / ΔG$_{int}$=8.87 / ΔG=4.08 / ΔE=3.34)

A·T(w$_{rH}$)$_{R,L}$

(ΔE$_{int}$=-6.01 (0.87) / ΔG$_{int}$=5.84 / ΔG=0.65 / ΔE=0.65)

A·T(w$_{WC}$)$_{R,L}$↔A·T(w$_{rWC}$)$_{L,R}$



A·T(w$_{WC}$)$_{R,L}$

(ΔE$_{int}$=-6.34 (0.98)/ ΔG$_{int}$=5.50/ ΔG=0.00 / ΔE=0.00)

TS$_{A\cdot T(wWC)R,L\leftrightarrow A\cdot T(wrWC)L,R}$

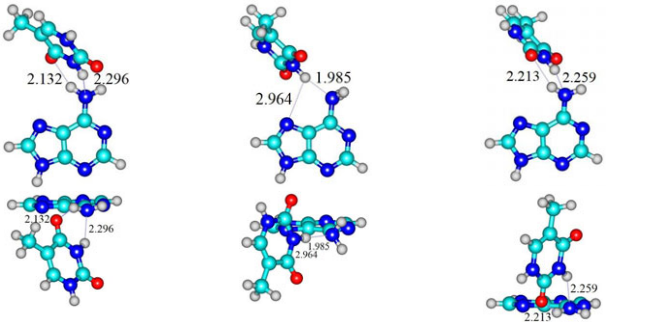
(ν_i=274.7 *i* cm^{-1})

(ΔE$_{int}$=-8.17 (0.71) / ΔG$_{int}$=3.44 / ΔG=12.04 / ΔE=11.18)

A·T(w$_{rWC}$)$_{L,R}$

(ΔE$_{int}$=-6.51 (0.91) / ΔG$_{int}$=4.97 / ΔG=-0.10 / ΔE=0.26)

A·T(w$_H$)$_{R,L}$↔A·T(wrH)$_{L,R}$



A·T(w$_H$)$_{R,L}$

(ΔE$_{int}$=-5.69 (0.97)/ ΔG$_{int}$=6.21 / ΔG=0.00 / ΔE=0.00)

TS$_{A\cdot T(wH)R,L\leftrightarrow A\cdot T(wrH)L,R}$

(ν_i=270.8 *i* cm^{-1})

(ΔE$_{int}$=-8.48 (0.66) / ΔG$_{int}$=3.68 / ΔG=10.69 / ΔE=9.35)

A·T(w$_{rH}$)$_{L,R}$

(ΔE$_{int}$=-6.01 (0.87) / ΔG$_{int}$=5.84 / ΔG=-0.41 / ΔE=-0.35)

TABLE 1 Energetic characteristics (in kcal·mol^{-1}) of the discovered conformational transitions of the four biologically important A·T DNA base pairs obtained at the MP2/aug-cc-pVDZ//B3LYP/6-311++G(d,p) level of QM theory in the continuum with ε = 1 under normal conditions (see Figure 1)

Conformational transition	ν_i[a]	ΔG[b]	ΔE[c]	$\Delta\Delta G_{TS}$[d]	$\Delta\Delta E_{TS}$[e]	$\Delta\Delta G$[f]	$\Delta\Delta E$[g]
$A{\cdot}T(w_H)_{R,L}\leftrightarrow A{\cdot}T(w_{rWC})_{R,L}$	19.9	−1.17	−0.74	3.20	2.30	4.37	3.04
$A{\cdot}T(w_{WC})_{R,L}\leftrightarrow A{\cdot}T(w_{rH})_{R,L}$	21.9	0.65	0.65	4.08	3.34	3.42	2.69
$A{\cdot}T(w_{WC})_{R,L}\leftrightarrow A{\cdot}T(w_{rWC})_{L,R}$	274.7	−0.10	0.26	12.04	11.18	12.15	10.92
$A{\cdot}T(w_H)_{R,L}\leftrightarrow A{\cdot}T(w_{rH})_{L,R}$	270.8	−0.41	−0.35	10.69	9.35	11.10	9.70

[a] Imaginary frequency at the TS of the conformational transition, cm^{-1}
[b] The Gibbs free energy of the product relatively the reactant of the conformational transition (T = 298.15 K)
[c] The electronic energy of the product relatively the reactant of the conformational transition
[d] The Gibbs free energy barrier for the forward conformational transition
[e] The electronic energy barrier for the forward conformational transition
[f] The Gibbs free energy barrier for the reverse conformational transition
[g] The electronic energy barrier for the reverse conformational transition.

its anisotropic rotation around the C6N6 bond in free state.[112] Gibbs free energies of activation for these processes consist 19.07 and 19.71 kcal·mol^{-1}, accordingly.

In this case, R structures transform into the L structures and *vice versa* and A·T(WC)↔A·T(rWC) and A·T(H)↔A·T(rH) conformational transitions of the classical A·T DNA base pairs occur in such a case (each of them—by the mirror-symmetric pathways):

$A{\cdot}T(WC)$ (0.00) ↔ $TS_{A\cdot T(WC)\leftrightarrow A\cdot T(wWC)R,L}$ (7.28) ↔ $A{\cdot}T(w_{WC})_{R,L}$ (7.03) ↔ $TS_{A\cdot T(wWC)R,L\leftrightarrow A\cdot T(wrWC)L,R}$ (19.07) ↔ $A{\cdot}T(w_{rWC})_{L,R}$ (6.92) ↔ $TS_{A\cdot T(wrWC)L,R\leftrightarrow A\cdot T(rWC)L,R}$ (8.47) ↔ A·T(rWC) (0.16 kcal·mol^{-1});
and A·T(H) (0.00) ↔ $TS_{A\cdot T(H)\leftrightarrow A\cdot T(wH)R,L}$ (9.15) ↔ $A{\cdot}T(w_H)_{R,L}$ (9.02) ↔ $TS_{A\cdot T(wH)R,L\leftrightarrow A\cdot T(wrH)L,R}$ (19.71) ↔ $A{\cdot}T(w_{rH})_{L,R}$ (8.61) ↔ $TS_{A\cdot T(wrH)L,R\leftrightarrow A\cdot T(rH)L,R}$ (10.60) ↔ A·T(rH) (0.27 kcal·mol^{-1}) (after each structure in brackets relative Gibbs free energy is presented at the MP2/aug-cc-pVDZ//B3LYP/6-311++G(d,p) level of QM theory in the continuum with ε = 1 under normal conditions).

Interestingly, that among all without exception investigated in this work H-bonded structures, total energy of the intermolecular H-bonds consists only a part of the electron energy of the monomers interactions (see Figure 1). This result agrees with the previously obtained data for the other H-bonded pairs of nucleotide bases.[106–109]

The methyl group of the T DNA base does not change its orientation during all without exception processes of the conformational transformations. Moreover, the heterocycles of the DNA bases remain planar, despite their ability for the out-of-plane bending (Table 3).[113–115]

So, obtained by us results launch the conception of the "mechanics" of the nondissociative, dipole-active A·T(WC)↔A·T(rWC)/A·T(rH) and A·T(H)↔A·T(rH)/A·T(rWC) conformational transitions between the classical A·T DNA base pairs.

Finally, we would like to note the following. In the paper[2] it was shown that the nondissociative A·T(WC)↔A·T(rWC) and A·T(H)↔A·T(rH) conformational transitions are also realized by the rotation of the complementary bases one with respect to another on the angle of 180 ° around the middle intermolecular H-bond, which is involved in the stabilization of these pairs. These transitions are more energetically favorable, than those described in this paper. However, current situation can change in the composition of DNA, since the rotations of the bases around the middle H-bond are more strongly inhibited by the stacking than the conformational transitions described in this article, which is carried out in the flip mode, that is, significantly weakened stacking interactions.[30,39]

4 | CONCLUSIONS

By applying developed by us novel ideas according the high-energetic conformers of the classical A·T DNA base pairs,[40] for the first time we offered novel nondissociative mechanisms of the A·T(WC)↔A·T(rWC)/A·T(rH) and A·T(H)↔A·T(rH)/A·T(rWC) conformational transitions. TSs of these transitions have been localized and their structural, energetical, and polar characteristics have been documented.

We hope that this discovery would encourage experimenters to register it in the composition of DNA using wide arsenal of the modern spectroscopical methods.

FIGURE 1 Discovered new pathways of the conformational transitions of the four biologically important A·T DNA base pairs. Electronic ΔE_{int} (contribution of the total energy of the intermolecular H-bonds) and Gibbs free ΔG_{int} energies of the interaction (MP2/6-311++G(2df,pd)//B3LYP/6-311++G(d,p) level of theory, in kcal·mol^{-1}), relative Gibbs free energies ΔG and electronic energies ΔE (in kcal·mol^{-1}), imaginary frequencies ν_i at the TSs of the conformational transitions (MP2/aug-cc-pVDZ//B3LYP/6-311++G(d,p) level of theory in the continuum with ε = 1 at T = 298.15 K) are presented below complexes in brackets. Dotted lines indicate AH···B H-bonds—their lengths H···B are presented in angstroms (for their more detailed physicochemical characteristics see Table 2); carbon atoms are in light-blue, nitrogen–in dark-blue, hydrogen–in gray, and oxygen–in red

TABLE 2 Electron-topological, geometrical and energetic characteristics of the intermolecular H-bonds in the investigated DNA base pairs and TSs of their conformational transformations obtained at the B3LYP/6-311++G(d,p) level of QM theory (ε = 1; see Figure 1)

Complex	AH···B H-bond	ρ^a	$\Delta\rho^b$	$100\cdot\varepsilon^c$	$d_{A\cdots B}{}^d$	$d_{H\cdots B}{}^e$	∠AH···B^f	$E_{AH\cdots B}{}^g$	μ^h
A·T(w_{WC})$_{R,L}$	N6H···O4	0.020	0.070	4.53	2.990	2.065	150.0	4.84	2.57
	N3H···N6	0.013	0.040	17.05	3.215	2.345	142.8	2.47	
A·T(w_{rWC})$_{R,L}$	N6H···O2	0.020	0.071	4.08	2.993	2.062	151.2	3.79	2.68
	N3H···N6	0.011	0.034	20.35	3.273	2.420	141.0	2.11	
A·T(w_H)$_{R,L}$	N6H′···O4	0.018	0.062	4.93	3.010	2.132	143.5	3.70	5.88
	N3H···N6	0.014	0.043	8.80	3.186	2.296	145.1	2.81	
A·T(w_{rH})$_{R,L}$	N6H′···O2	0.015	0.052	8.40	3.051	2.213	138.8	3.29	6.10
	N3H···N6	0.016	0.047	6.58	3.155	2.259	145.8	2.98	
$TS_{A\cdot T(wH)R,L\leftrightarrow A\cdot T(wrWC)R,L}$	N3H···N6	0.017	0.052	1.51	3.202	2.190	170.2	3.70	3.26
$TS_{A\cdot T(wWC)R,L\leftrightarrow A\cdot T(wrH)R,L}$	N3H···N6	0.017	0.052	1.50	3.203	2.192	169.8	3.69	4.14
$TS_{A\cdot T(wWC)R,L\leftrightarrow A\cdot T(wrWC)L,R}$	N3H···N6	0.030	0.081	0.81	2.993	1.965	173.3	5.82	1.97
$TS_{A\cdot T(wH)R,L\leftrightarrow A\cdot T(wrH)L,R}$	N3H···N6	0.028	0.079	1.26	3.007	1.985	170.9	5.00	4.35
	N3H···N7	0.004	0.015	194.40	3.514	2.964	114.2	0.61	

[a] The electron density at the (3,−1) BCP of the H-bond, a.u.
[b] The Laplacian of the electron density at the (3,−1) BCP of the H-bond, a.u.
[c] The ellipticity at the (3,−1) BCP of the H-bond
[d] The distance between the A and B atoms of the of the AH···B H-bond, Å
[e] The distance between the H and B atoms of the AH···B H-bond, Å
[f] The H-bond angle, degree
[g] Energy of the H-bond, kcal·mol^{-1}
[h] The dipole moment of the complex, D.

TABLE 3 Selected geometrical parameters, characterizing the nonplanarity of the TSs of the discovered conformational transitions, obtained at the B3LYP/6-311++G(d,p) level of theory in the continuum with ε = 1 (see Figure 1)

TS of conformational transition	Dihedral angle, degree
	(A)N7C5(T)N3C4
$TS_{A\cdot T(wH)R,L\leftrightarrow A\cdot T(wrWC)R,L}$	13.3
$TS_{A\cdot T(wWC)R,L\leftrightarrow A\cdot T(wrH)R,L}$	174.1
$TS_{A\cdot T(wWC)R,L\leftrightarrow A\cdot T(wrWC)L,R}$	92.8
$TS_{A\cdot T(wH)R,L\leftrightarrow A\cdot T(wrH)L,R}$	79.4

Note: Signs of the dihedral angles are presented exclusively for one type of enantiomers.

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AUTHOR CONTRIBUTIONS

Proposed the idea of the study, formulated the task and suggested possible pathways of the conformational transitions between the classical A·T DNA base pairs and partly wrote the text of the manuscript: Hovorun

Localized the pathways of the investigated conformational transitions, performed QM/QTAIM calculations, prepared numerical data for Tables and graphical materials for Figures and partly wrote the text of the manuscript: Brovarets'

Performed QM/QTAIM calculations, participated in the preparation of the text of the manuscript. All authors were involved in the proofreading of the final version of the manuscript: Tsiupa

ADDITIONAL INFORMATION

No competing financial and nonfinancial interests were stated by the authors.

CONFLICT OF INTEREST

The author declare that they have no conflicts of interest with the contents of this article.

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