Electronic Supplementary Information (ESI) for:

Novel physico-chemical mechanism of the mutagenic tautomerisation of the Watson-Crick-like A·G and C·T DNA base mispairs: a quantum-chemical picture

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Table S1. Energetic characteristics of the investigated DNA base mispairs and TSs of their tautomerisation *via* the sequential DPT obtained at the different levels of theory for the geometry calculated at the B3LYP/6-311++G(d,p) level of theory.

Complex	Level of theory							
	MP2/6-311++G(2df,pd)		MP2/6-311++G(3df,2pd)		MP2/cc-pVTZ		MP2/cc-pVQZ	
	ΔG^a	ΔE^b	ΔG^a	ΔE^b	ΔG^a	ΔE^b	ΔG^a	ΔE^b
A·G(WC)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
$A{\cdot}G^*_{\downarrow}(w)$	3.27	5.70	3.63	6.06	3.88	6.31	3.76	6.19
$A{\cdot}G^*_{\uparrow}(w)$	6.14	7.34	6.36	7.56	6.34	7.54	6.28	7.48
$A^*{\cdot}G_{\uparrow}(w)$	14.16	13.96	14.11	13.91	14.03	13.83	14.29	14.09
$TS^{A^{+}\cdot G^{-}}_{A\cdot G(WC)\leftrightarrow A\cdot G^*\downarrow(w)}$	16.88	16.94	16.79	16.86	17.73	17.79	17.01	17.07
$A^*{\cdot}G_{\downarrow}(w)$	21.01	22.54	20.73	22.26	21.39	22.92	21.11	22.65
$TS^{A^{+}\cdot G^{-}}_{A\cdot G(WC)\leftrightarrow A^*\cdot G\uparrow(w)}$	24.95	24.05	25.01	24.11	25.46	24.56	25.29	24.39
$TS^{A^{-}\cdot G^{+}}_{A\cdot G(WC)\leftrightarrow A\cdot G^*\uparrow(w)}$	25.48	25.37	25.97	25.86	25.35	25.23	25.79	25.68
$TS^{A^{-}\cdot G^{+}}_{A\cdot G(WC)\leftrightarrow A^*\cdot G\downarrow(w)}$	49.23	49.70	48.94	49.41	49.53	50.00	49.20	49.67
C·T(WC)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
$C^*{\cdot}T_{\uparrow}(w)$	0.66	0.64	0.58	0.57	0.42	0.41	0.52	0.50
$C^*{\cdot}T_{\downarrow}(w)$	3.31	3.42	2.97	3.08	3.09	3.20	3.08	3.20
$C{\cdot}T^*_{O2\uparrow}(w)$	6.17	6.50	6.40	6.74	6.31	6.64	6.25	6.58
$TS_{C^*\cdot T\uparrow(w)\leftrightarrow C\cdot T^*O2\uparrow(w)}$	6.33	8.95	6.74	9.36	6.72	9.33	6.67	9.28
C*·T*(WC)	8.97	8.81	9.27	9.10	8.82	8.66	9.13	8.97
$TS_{C\cdot T(WC)\leftrightarrow C^*\cdot T^*(WC)}$	9.08	10.91	9.56	11.39	9.36	11.19	9.53	11.36
$C{\cdot}T^*_{\downarrow}(w)$	11.84	14.34	12.10	14.60	12.06	14.56	12.05	14.56
$C{\cdot}T^*_{\uparrow}(w)$	15.60	16.97	15.94	17.31	15.64	17.02	15.69	17.06
$TS^{C^{+}\cdot T^{-}}_{C^*\cdot T^*(WC)\leftrightarrow C^*\cdot T\uparrow(w)}$	17.35	17.66	17.13	17.44	17.36	17.68	17.03	17.34
$TS^{C^{+}\cdot T^{-}}_{C^*\cdot T^*(WC)\leftrightarrow C\cdot T^*\downarrow(w)}$	26.71	25.39	26.69	25.37	27.15	25.83	26.62	25.31
$TS^{C^{-}\cdot T^{+}}_{C\cdot T(WC)\leftrightarrow C^*\cdot T\downarrow(w)}$	34.41	35.70	34.27	35.57	34.66	35.95	34.39	35.68
$TS^{C^{-}\cdot T^{+}}_{C\cdot T(WC)\leftrightarrow C\cdot T^*\uparrow(w)}$	46.51	47.72	46.88	48.09	46.66	47.87	46.74	47.95

[a]The relative Gibbs free energy of the investigated complexes ($\Delta G_{A\cdot G(WC)/C\cdot T(WC)}$=0.00; T=298.15 K), kcal·mol^{-1}

[b]The relative electronic energy of the investigated complexes ($\Delta E_{A\cdot G(WC)/C\cdot T(WC)}$=0.00), kcal·mol^{-1}

Table S2. Interbase interaction energies (in kcal·mol^{-1}) for the investigated DNA base mispairs and TSs of their conversions *via* the sequential DPT obtained at the MP2/6-311++G(3df,2pd)//B3LYP/6-311++G(d,p) level of theory.

Complex	$-\Delta E_{int}$[a]	ΣE_{HB}[b]	$\Sigma E_{HB}/\lvert\Delta E_{int}\rvert$, %	$-\Delta G_{int}$[c]
A·G(WC)[§]	17.54	12.87	73.4	3.57
A·G*$_{\uparrow}$(w)	10.40	9.72	93.5	-2.34
A·G*$_{\downarrow}$(w)	12.41	9.83	79.2	0.90
A*·G$_{\uparrow}$(w)	15.24	11.00	72.2	2.83
A*·G$_{\downarrow}$(w)	7.28	3.60	49.5	-3.40
$TS^{A-\cdot G+}_{A\cdot G(WC)\leftrightarrow A\cdot G^{*}\uparrow(w)}$	143.62	26.60	18.5	128.29
$TS^{A+\cdot G-}_{A\cdot G(WC)\leftrightarrow A\cdot G^{*}\downarrow(w)}$	117.62	14.63	12.4	105.01
$TS^{A+\cdot G-}_{A\cdot G(WC)\leftrightarrow A^{*}\cdot G\uparrow(w)}$	111.19	14.63	13.2	97.62
$TS^{A-\cdot G+}_{A\cdot G(WC)\leftrightarrow A^{*}\cdot G\downarrow(w)}$	115.33	15.72	13.6	100.59
C·T(WC)[§§]	13.86	11.84	85.4	1.54
C*·T$_{\uparrow}$(w)	14.43	12.58	87.2	2.84
C*·T$_{\downarrow}$(w)	11.34	9.92	87.5	-0.12
C·T*$_{O2\uparrow}$(w)	27.55	17.65	64.1	15.17
C*·T*(WC)	21.01	17.54	83.5	9.16
C·T*$_{\downarrow}$(w)	11.26	9.16	81.4	1.36
C·T*$_{\uparrow}$(w)	8.28	8.32	100.5	-2.74
$TS^{C+\cdot T-}_{C^{*}\cdot T^{*}(WC)\leftrightarrow C^{*}\cdot T\uparrow(w)}$	118.41	13.70	11.6	106.83
$TS^{C+\cdot T-}_{C^{*}\cdot T^{*}(WC)\leftrightarrow C\cdot T^{*}\downarrow(w)}$	114.18	16.58	14.5	100.97
$TS^{C-\cdot T+}_{C\cdot T(WC)\leftrightarrow C^{*}\cdot T\downarrow(w)}$	136.14	17.93	13.2	124.04
$TS^{C-\cdot T+}_{C\cdot T(WC)\leftrightarrow C\cdot T^{*}\uparrow(w)}$	136.11	23.17	17.0	123.93

[a]The BSSE-corrected electronic interaction energy

[b]The total energy of the intermolecular H-bonds (see Table 1)

[c]The BSSE-corrected Gibbs free energy of interaction (T=298.15 K)

[§,§§]Data are taken from the works [Brovarets' O.O., Zhurakivsky R.O., Hovorun D.M. (2014). Is the DPT tautomerisation of the long A·G Watson-Crick DNA base mispair a source of the adenine and guanine mutagenic tautomers? A QM and QTAIM response to the biologically important question. *Journal of Computational Chemistry, 35*, 451-466] and [Brovarets', O.O., & Hovorun, D.M. (2013). Atomistic understanding of the C·T mismatched DNA base pair tautomerization *via* the DPT: QM and QTAIM computational approaches. *Journal of Computational Chemistry, 34*, 2577-2590], respectively.

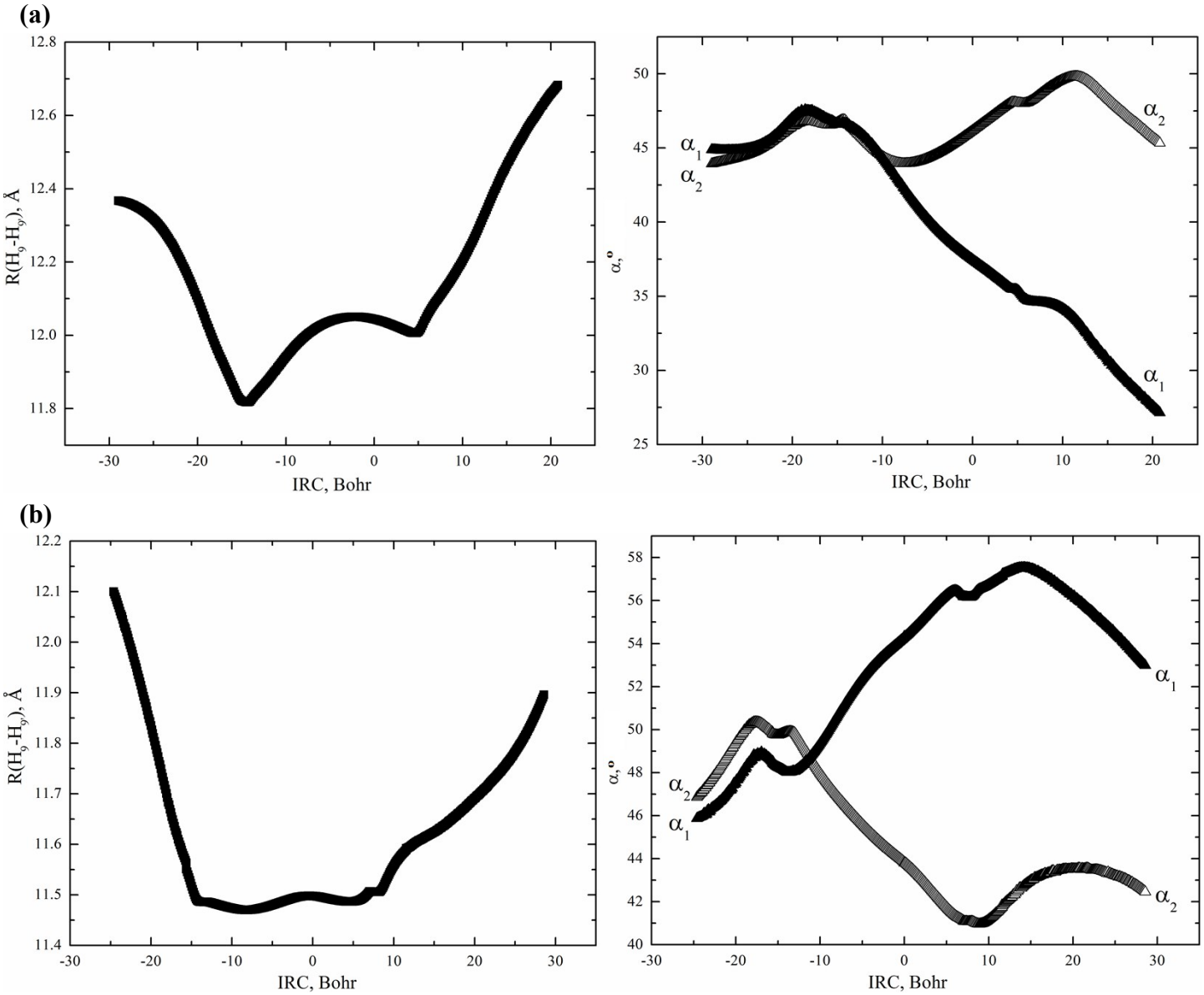
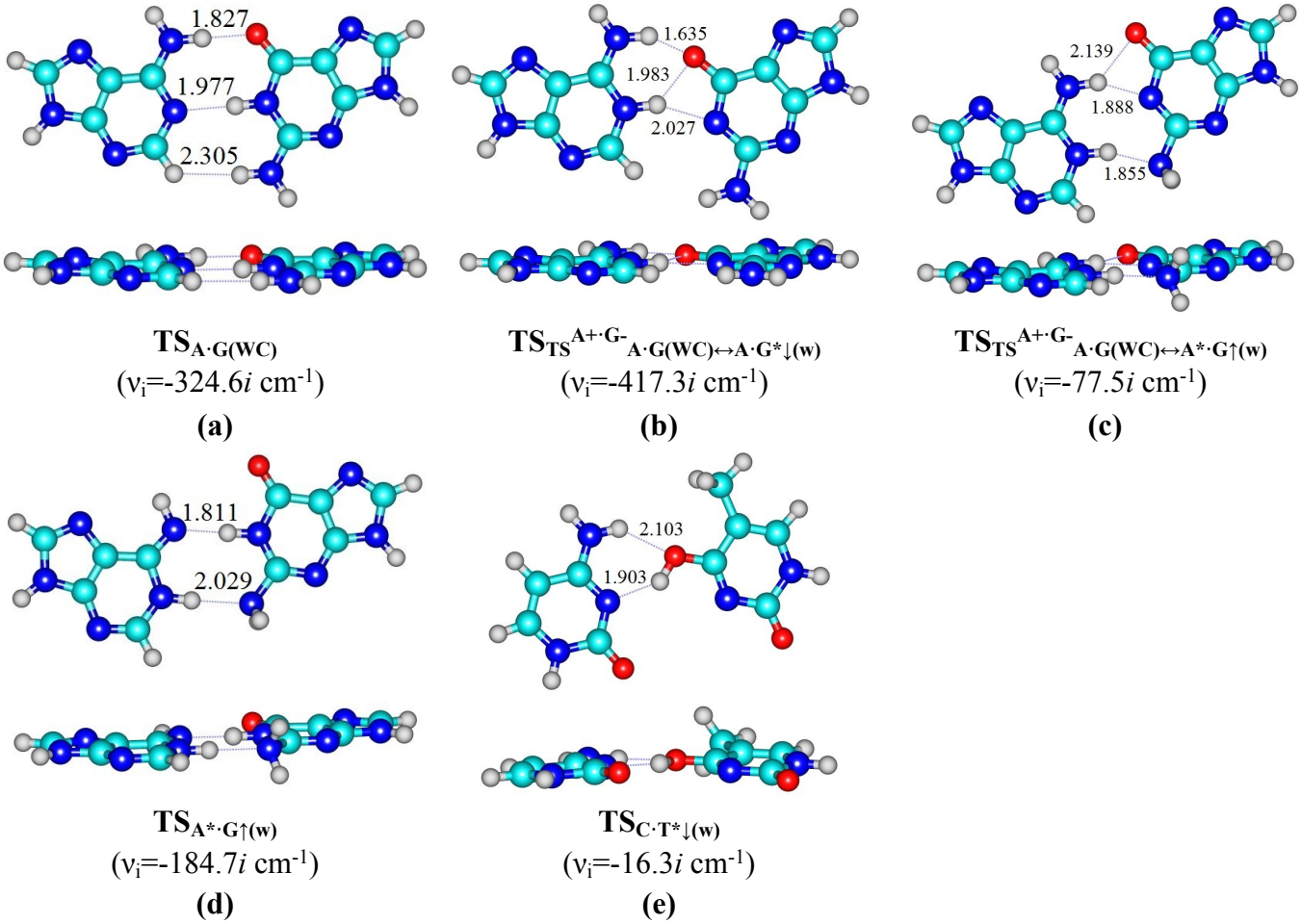


Fig. S1. Profiles of the R(H_9-$H_{9'}$) distances between the H_9 and $H_{9'}$ glycosidic hydrogens and the α_1 (∠N9H_9(G)$H_{9'}$(A)) or α_2 (∠N9$H_{9'}$(A)H_9(G)) glycosidic angles of the G and A DNA bases, respectively, along the IRC of the (**a**) A·G(WC)↔A·G*$_{\downarrow}$(w) and (**b**) A·G(WC)↔A*·G$_{\uparrow}$(w) tautomerisations *via* the sequential DPT obtained at the B3LYP/6-311++G(d,p) level of theory (see Figs. 1 and 2).



$TS_{A\cdot G(WC)}$ (ν_i=-324.6*i* cm^{-1}) **(a)**

$TS_{TS}^{A+\cdot G-}{}_{A\cdot G(WC)\leftrightarrow A\cdot G^*\downarrow(w)}$ (ν_i=-417.3*i* cm^{-1}) **(b)**

$TS_{TS}^{A+\cdot G-}{}_{A\cdot G(WC)\leftrightarrow A^*\cdot G\uparrow(w)}$ (ν_i=-77.5*i* cm^{-1}) **(c)**

$TS_{A^*\cdot G\uparrow(w)}$ (ν_i=-184.7*i* cm^{-1}) **(d)**

$TS_{C\cdot T^*\downarrow(w)}$ (ν_i=-16.3*i* cm^{-1}) **(e)**

Fig. S2. Transition states of the conformational interconversions of the mirror-symmetric enantiomers of the **(a)** A·G(WC), **(b)** $TS^{A+\cdot G-}{}_{A\cdot G(WC)\leftrightarrow A\cdot G^*\downarrow(w)}$, **(c)** $TS^{A+\cdot G-}{}_{A\cdot G(WC)\leftrightarrow A^*\cdot G\uparrow}(w)$, **(d)** $A^*\cdot G_{\uparrow}(w)$ and **(e)** $TS_{C\cdot T^*\downarrow(w)}$ biologically important complexes. Dotted lines indicate AH···B H-bonds (their lengths are presented in angstroms). Carbon atoms are in light-blue, nitrogen – in dark-blue, hydrogen – in grey and oxygen – in red. ν_i – imaginary frequency.

Table S3. Energetic, vibrational, kinetic and geometric characteristics of the conformational interconversions of the mirror-symmetric enantiomers of the biologically important DNA base mispairs and TSs of their tautomerisation *via* the sequential DPT calculated at the MP2/cc-pVQZ//B3LYP/6-311++G(d,p) level of theory.

Transition state of the interconversion	$\Delta\Delta G_{TS}$[a]	$\Delta\Delta E_{TS}$[b]	$\tau_{99.9\%}$[c]	ν_i[d]	β[e]
$TS_{A\cdot G(WC)}$	1.99	1.56	$1.60\cdot10^{-11}$	-324.6*i*	∠C6N1(G)N1C6(A)=±21.9
$TS_{TS}^{A+\cdot G-}{}_{A\cdot G(WC)\leftrightarrow A\cdot G^*\downarrow(w)}$	2.99	2.81	$8.66\cdot10^{-11}$	-417.3*i*	∠C6N1(G)N1C6(A)=±39.9
$TS_{TS}^{A+\cdot G-}{}_{A\cdot G(WC)\leftrightarrow A^*\cdot G\uparrow(w)}$	2.81	2.34	$6.42\cdot10^{-11}$	-77.5*i*	∠C6N1(G)N1C6(A)=±7.1
$TS_{A^*\cdot G\uparrow(w)}$	7.27	7.16	$1.19\cdot10^{-7}$	-184.7*i*	∠C6N1(G)N1C6(A)=±93.5
$TS_{C\cdot T^*\downarrow(w)}$	4.69	2.33	$1.53\cdot10^{-9}$	-16.3*i*	∠C5N3(T)C2N3(C)=±34.3

[a]The Gibbs free energy barrier of the conformational interconversion under normal conditions, kcal·mol^{-1}

[b]The electronic energy barrier of the conformational interconversion, kcal·mol^{-1}

[c]The time necessary to reach 99.9% of the equilibrium concentration between the mirror-symmetric enantiomers, s

[d]Imaginary frequency in the transition state of the conformational interconversion, cm^{-1}

[e]Dihedral angle that characterize the non-planarity of the complex, degree; signs "±" correspond to the mirror-symmetric enantiomers

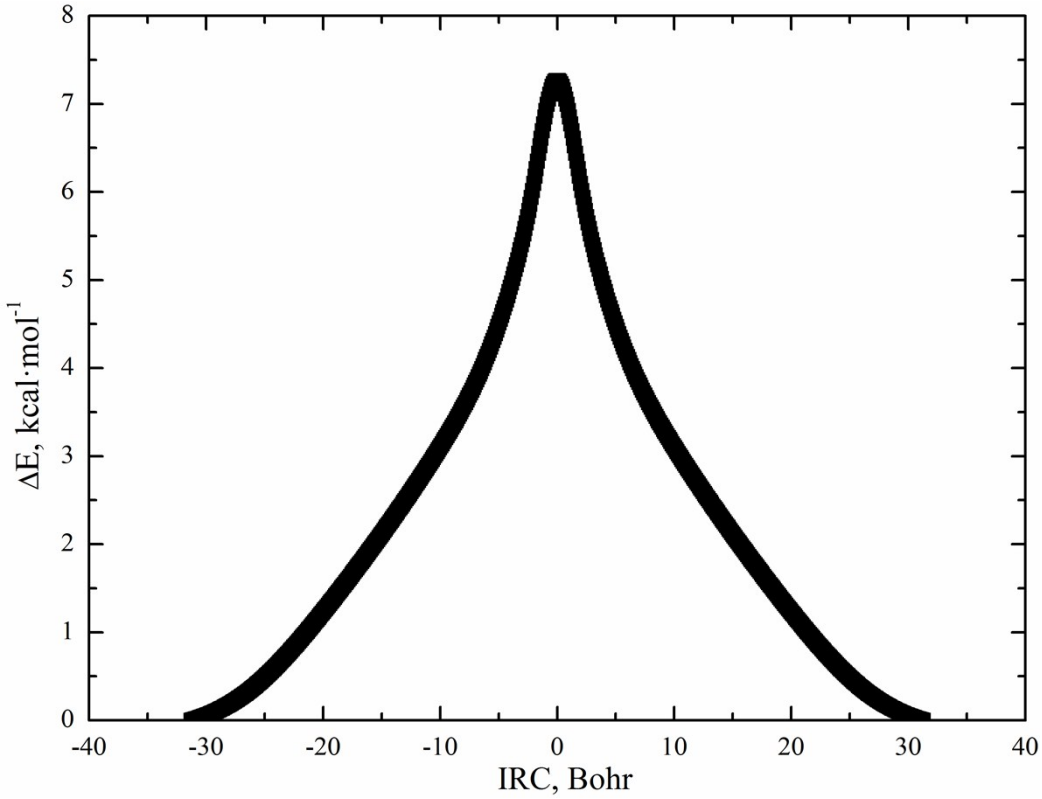
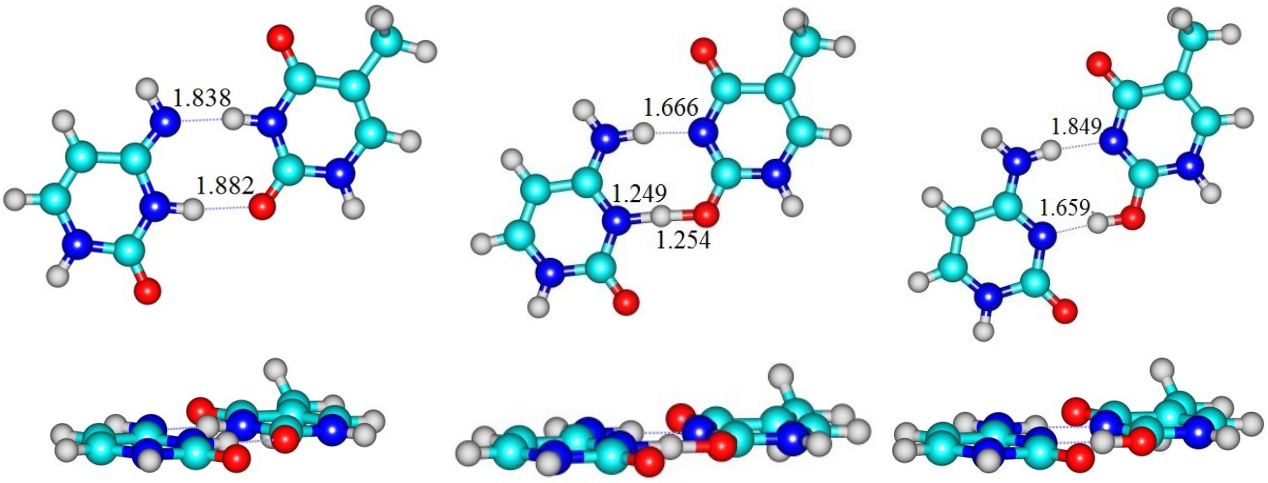


Fig. S3. Profile of the relative electronic energy ΔE of the conformational interconversion of the mirror-symmetric enantiomers of the A*·$G_{↑}$(w) base mispair *via* the rotation of the NH_2 amino group of the G base along the IRC obtained at the B3LYP/6-311++G(d,p) level of theory.



C*·T↑(w) **TS$_{C^{*}\cdot T\uparrow(w)\leftrightarrow C\cdot T^{*}O2\uparrow(w)}$** ($\nu_i$=-807.1*i* cm^{-1}) **C·T*$_{O2\uparrow}$(w)**

Fig. S4. Structures corresponding to the stationary points on the reaction pathway of the C*·T$_{\uparrow}$(w)↔C·T*$_{O2\uparrow}$(w) conversion *via* the sequential DPT obtained at the B3LYP/6-311++G(d,p) level of theory. Dotted lines indicate AH···B H-bonds and continuous lines – loosened A-H-B covalent bridges (their lengths are presented in angstroms). Carbon atoms are in light-blue, nitrogen – in dark-blue, hydrogen – in grey and oxygen – in red. ν_i – imaginary frequency.

Table S4. Energetic and kinetic characteristics of the C*·T$_{\uparrow}$(w)↔C·T*$_{O2\uparrow}$(w) tautomerisation *via* the sequential DPT obtained at the different levels of theory for the geometry calculated at the B3LYP/6-311++G(d,p) level of theory.

Level of theory	ΔG^a	ΔE^b	$\Delta\Delta G_{TS}^c$	$\Delta\Delta E_{TS}^d$	$\Delta\Delta G^e$	$\Delta\Delta E^f$	$\tau_{99.9\%}^g$
MP2/6-311++G(2df,pd)	5.51	5.86	5.67	8.30	0.16	2.44	$9.21\cdot10^{-13}$
MP2/6-311++G(3df,2pd)	5.83	6.17	6.16	8.79	0.33	2.62	$1.23\cdot10^{-12}$
MP2/cc-pVTZ	5.88	6.23	6.30	8.93	0.41	2.69	$1.41\cdot10^{-12}$
MP2/cc-pVQZ	5.71	6.05	6.12	8.75	0.42	2.70	$1.42\cdot10^{-12}$

[a]The Gibbs free energy of the product relatively the reactant of the tautomerisation reaction ($\Delta G_{C^{*}\cdot T\uparrow(w)}$=0.00 kcal·mol^{-1}; T=298.15 K), kcal·mol^{-1}

[b]The electronic energy of the product relatively the reactant of the tautomerisation reaction ($\Delta E_{C^{*}\cdot T\uparrow(w)}$=0.00 kcal·mol^{-1}), kcal·mol^{-1}

[c]The Gibbs free energy barrier for the forward reaction of tautomerisation, kcal·mol^{-1}

[d]The electronic energy barrier for the forward reaction of tautomerisation, kcal·mol^{-1}

[e]The Gibbs free energy barrier for the reverse reaction of tautomerisation, kcal·mol^{-1}

[f]The electronic energy barrier for the reverse reaction of tautomerisation, kcal·mol^{-1}

[g]The time necessary to reach 99.9%of the equilibrium concentration between the reactant and the product of the tautomerisation reaction, s

See also summary Table S1 for the Gibbs and electronic energies of the DNA mispairs and TSs relatively the global minimum – the short Watson-Crick-like C·T(WC) DNA base mispair.

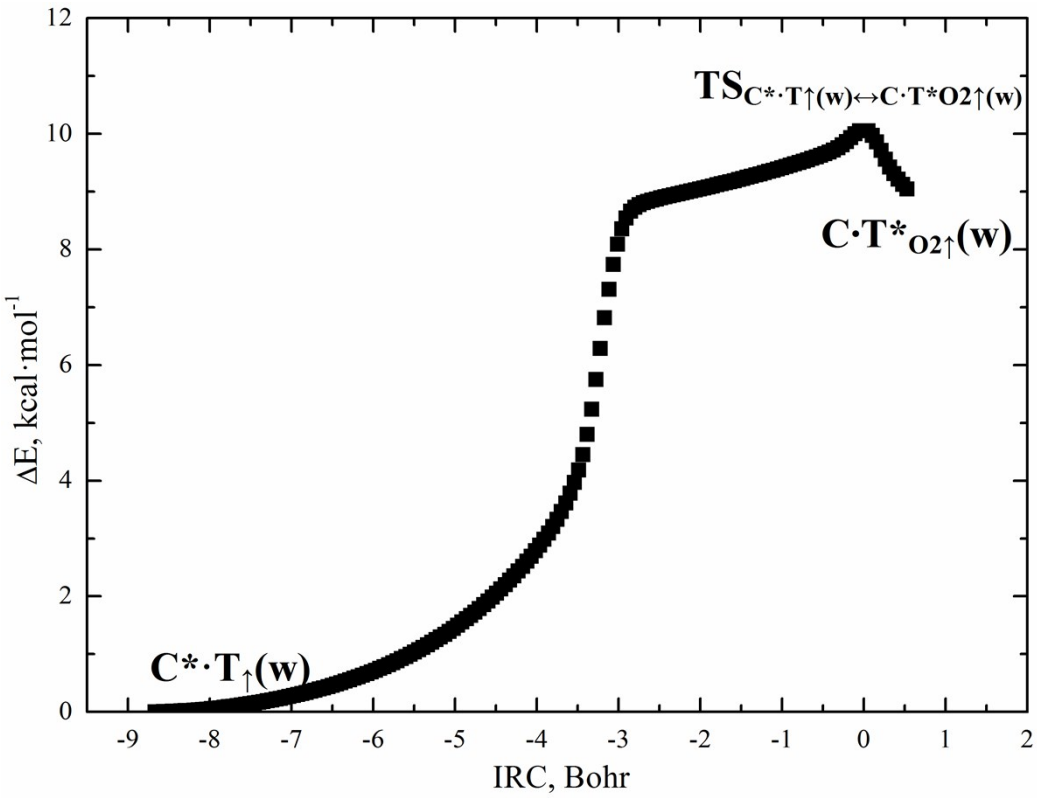


Fig. S5. Profile of the relative electronic energy ΔE of the DNA base mispair along the IRC of the $C^*{\cdot}T_{\uparrow}(w) \leftrightarrow C{\cdot}T^*_{O2\uparrow}(w)$ tautomerisations *via* the sequential DPT obtained at the B3LYP/6-311++G(d,p) level of theory.

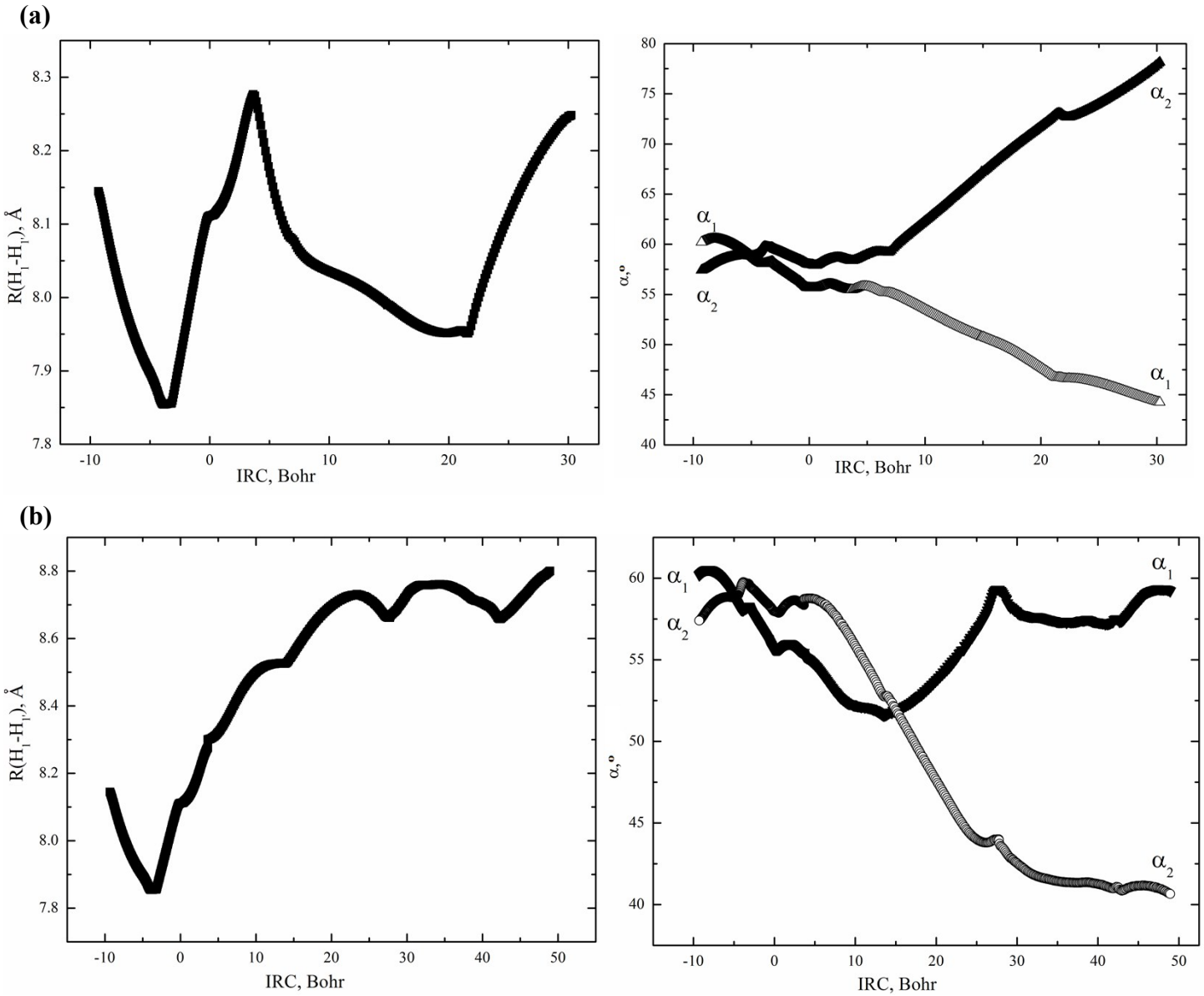


Fig. S6. Profiles of the $R(H_1\text{-}H_{1'})$ distances between the H_1 and $H_{1'}$ glycosidic hydrogens and the α_1 ($\angle N1H_1(C)H_{1'}(T)$) or α_2 ($\angle N1H_{1'}(T)H_1(C)$) glycosidic angles of the C and T DNA bases, respectively, along the IRC of the (**a**) C·T(WC)↔C*·T$_{\uparrow}$(w) and (**b**) C·T(WC)↔C·T*$_{\downarrow}$(w) tautomerisations *via* the sequential DPT obtained at the B3LYP/6-311++G(d,p) level of theory (see Figs. 4 and 5).