Supporting Information : Electronic Insights into the Role of Nuclear Quantum Effects in Proton Transfer Reactions of Nucleobase Pairs

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S1. Natural Bond Orbital

Natural Bond Orbital (NBO) is a localized molecular orbital method widely utilized in chemical bond analysis.[1–3] The Natural Atomic Orbital (NAO), which represents the localized orbital of each atom, is generated based on the canonical molecular orbitals obtained from quantum chemical calculations. Combining these defines the NAO, Natural Hybrid Orbital (NHO), and NBO.

$$\text{Canonical MO} \Rightarrow \text{Atomic Orbital} \Rightarrow \text{Natural Atomic Orbital} \Rightarrow$$
$$\text{Natural Hybrid Orbital} \Rightarrow \text{Natural Bond Orbital} \Rightarrow \text{Natural Localized Orbital}$$

As the eigenvalues correspond to the number of electrons occupied, it is possible to discuss the ease with which bonds can be broken. In this study, we examine reactivity concerning the electron occupancy of the N-H antibonding NBO, which represents the reactive site. Moreover, the NBO comprises bonding, antibonding, lone pair, and Rydberg orbitals, and the interaction between them can be calculated. Following the tenets of second-order perturbation theory, the interaction is defined as follows.

$$\Delta E^{(2)}_{\mathrm{D}\rightarrow\mathrm{A}} = q_{\mathrm{D}} \frac{F(\mathrm{D},\mathrm{A})^2}{\epsilon_{\mathrm{D}} - \epsilon_{\mathrm{A}}} \tag{1}$$

Here, D and A, represent donor and acceptor, respectively. In addition, q_{D}, $F(\mathrm{D},\mathrm{A})^2$ and ϵ represent the number of electrons occupying the donor orbitals (2, because it is a closed shell system), the off-diagonal NBO Fock matrix element, and the orbital energy, respectively. In this study, we calculated the interaction between the lone electron pair of the hydrogen-bond acceptor atoms (O, N) and the N-H antibonding NBO.

S2. Time Dependence of The Formation Probability of Tautomers

The probability of generating tautomeric isomers depends on time, as shown in eqn (15) in the main text. Here, we show the convergence of the probability with time. In BO, it took 6.00×10^3 ps to reach equilibrium. In cNEO, it took 5.75 ps to reach equilibrium.

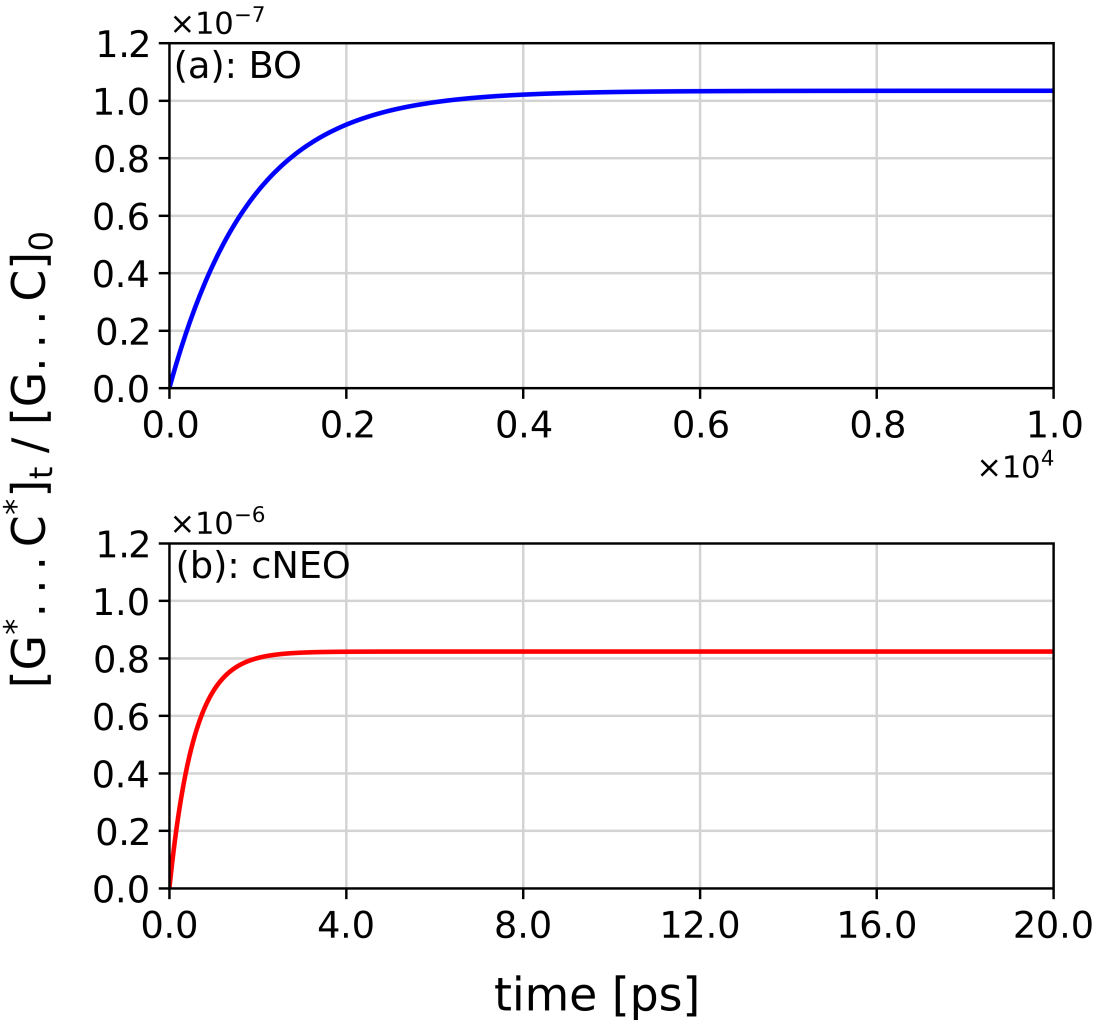

Figure S1: Time dependence of the probability of generating tautomeric forms in C...G.

S3. Hydrogen Bonding Distance

The hydrogen bond distances of C...G are reduced by 0.099 Å and 0.082 Å at the reaction sites (N)H...O and N...H(N), respectively, when compared with BO and cNEO (**Figure S2**). Conversely, the distance at the non-reactive site (O...H(N)) is reduced to 0.062 Å, although to a lesser extent than at the reactive site.

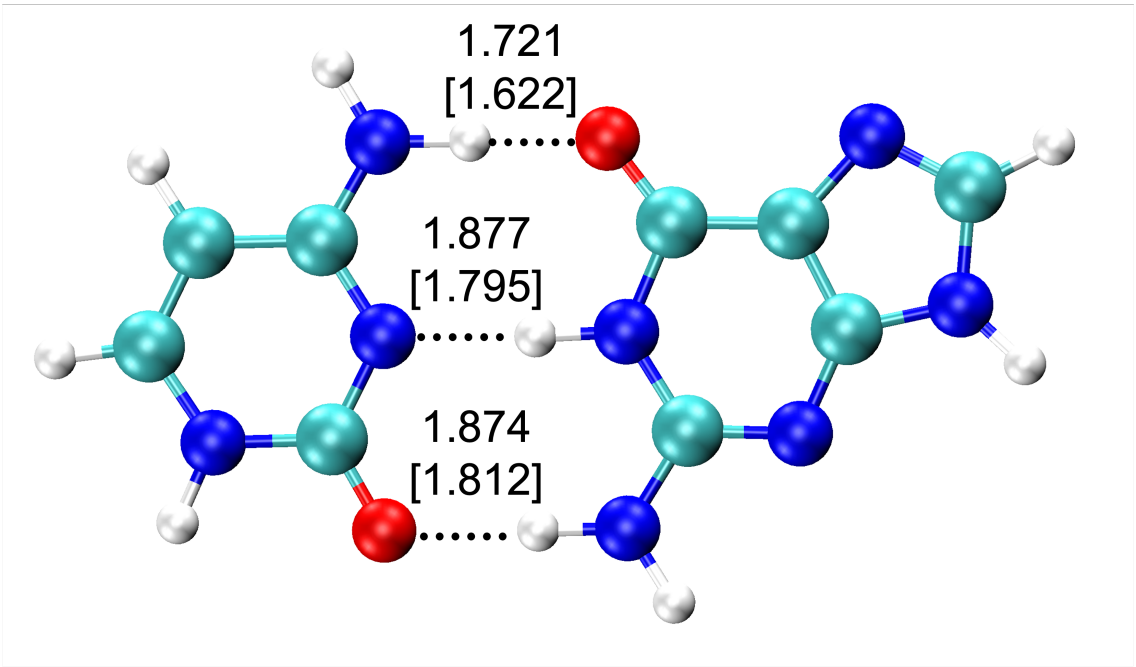

Figure S2: C...G hydrogen bonding distances [Å]. Numbers without parentheses represent BO results, numbers in square brackets represent cNEO results.

S4. Cartesian Coordinates of Reactants and Products

Table S1: C...G Optimized structure (BO) [Å].

symbol	x	y	z
H	-0.343525	0.175463	-0.000019
H	-0.663443	2.427172	0.000001
H	-0.901733	-2.243316	0.000004
H	0.739984	3.490356	0.000060
H	5.248911	1.339208	0.000059
H	5.966772	-1.130347	-0.000002
H	-4.626221	-2.497127	0.000098
H	-6.028657	-0.413323	0.000051
H	-4.903498	1.684812	-0.000035
H	-2.315740	-3.306939	0.000069
C	3.250988	0.635502	0.000021
C	2.814177	-0.685735	-0.000018
C	1.406313	-0.920490	-0.000032
C	1.225139	1.536779	0.000026
C	4.936688	-0.790966	-0.000002
N	0.685785	0.276939	-0.000011
N	2.523000	1.770000	0.000044
N	3.887297	-1.558597	-0.000032
N	4.615039	0.554239	0.000032
O	0.801544	-1.999038	-0.000057
N	0.350942	2.562262	0.000051
C	-4.180295	-1.507335	0.000058
C	-2.749693	-1.323981	0.000026
C	-4.940849	-0.391134	0.000033
N	-1.932516	-2.375648	0.000040
N	-2.199173	-0.109216	-0.000016
C	-2.968340	1.004952	-0.000037
O	-2.516903	2.152080	-0.000071
N	-4.356141	0.835404	-0.000017

Table S2: C...G Optimized structure (cNEO) [Å].

symbol	x	y	Z
H	-0.404307	0.166891	-0.000016
H	-0.709723	2.428371	-0.000000
H	-0.828419	-2.221783	-0.000002
H	0.744951	3.503141	0.000048
H	5.241690	1.345295	0.000052
H	5.960167	-1.156817	0.000004
H	-4.609250	-2.513074	0.000084
H	-6.028024	-0.417508	0.000051
H	-4.892141	1.712151	-0.000021
H	-2.292947	-3.315514	0.000055
C	3.230145	0.627741	0.000019
C	2.788664	-0.692522	-0.000013
C	1.381727	-0.917059	-0.000025
C	1.202868	1.532654	0.000022
C	4.911941	-0.804376	0.000003
N	0.659652	0.273237	-0.000008
N	2.504274	1.761753	0.000037
N	3.859551	-1.569060	-0.000022
N	4.594329	0.543587	0.000029
O	0.778548	-2.003067	-0.000045
N	0.333455	2.561269	0.000042
C	-4.155754	-1.504128	0.000050
C	-2.723046	-1.322410	0.000021
C	-4.919155	-0.389222	0.000033
N	-1.899712	-2.364843	0.000029
N	-2.179437	-0.098987	-0.000013
C	-2.952358	1.010079	-0.000027
O	-2.502051	2.160657	-0.000054
N	-4.337832	0.841143	-0.000008

Table S3: C*...G* Optimized structure (BO) [Å].

symbol	x	y	Z
H	-1.192101	0.102066	-0.000015
H	-0.646930	2.440068	0.000007
H	-0.143258	-2.053792	-0.000015
H	0.781214	3.454389	0.000058
H	5.261672	1.298468	0.000043
H	5.937033	-1.179675	-0.000019
H	-4.557472	-2.514741	0.000097
H	-6.002044	-0.480043	0.000039
H	-4.962190	1.662811	-0.000051
H	-2.221403	-3.210921	0.000077
C	3.247454	0.625922	0.000019
C	2.792429	-0.691707	-0.000016
C	1.395084	-0.847272	-0.000020
C	1.200879	1.474789	0.000036
C	4.911491	-0.825858	-0.000013
N	0.618772	0.242295	0.000004
N	2.510127	1.735754	0.000045
N	3.855433	-1.582916	-0.000035
N	4.613071	0.526000	0.000020
O	0.865732	-2.048160	-0.000047
N	0.363535	2.539410	0.000071
C	-4.131404	-1.516540	0.000055
C	-2.686088	-1.352572	0.000030
C	-4.915648	-0.425109	0.000024
N	-1.801480	-2.286119	0.000043
N	-2.232719	-0.041734	-0.000013
C	-3.015173	1.075033	-0.000044
O	-2.571882	2.215518	-0.000082
N	-4.379265	0.838520	-0.000029

Table S4: C*...G* Optimized structure (cNEO) [Å].

symbol	x	y	Z
H	-1.081035	0.108023	-0.000007
H	-0.706084	2.454873	0.000007
H	-0.245207	-2.080141	-0.000011
H	0.775285	3.475216	0.000053
H	5.235183	1.312978	0.000034
H	5.915738	-1.197286	-0.000019
H	-4.524902	-2.531523	0.000085
H	-5.987476	-0.479202	0.000033
H	-4.925266	1.688758	-0.000044
H	-2.196176	-3.235721	0.000071
C	3.209368	0.622431	0.000016
C	2.751348	-0.693002	-0.000013
C	1.352788	-0.855094	-0.000015
C	1.164027	1.482012	0.000034
C	4.871782	-0.831532	-0.000013
N	0.580246	0.246458	0.000006
N	2.474808	1.735076	0.000039
N	3.812940	-1.586117	-0.000030
N	4.574847	0.522341	0.000015
O	0.821839	-2.044847	-0.000039
N	0.331723	2.548688	0.000066
C	-4.093584	-1.513103	0.000049
C	-2.649609	-1.342670	0.000029
C	-4.879983	-0.421553	0.000021
N	-1.773406	-2.290083	0.000042
N	-2.183441	-0.040819	-0.000008
C	-2.973932	1.067318	-0.000036
O	-2.538742	2.214645	-0.000070
N	-4.339873	0.839215	-0.000024

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(3) Glendening, E. D.; Landis, C. R.; Weinhold, F. NBO 7.0: New vistas in localized and delocalized chemical bonding theory. *J. Comput. Chem.* **2019**, *40*, 2234–2241.