Supplementary Information:

Model calculations for the misincorporation of nucleotides opposite five-membered exocyclic DNA adduct: $N^{2,3}$-ethenoguanine

Venkatesan Srinivasadesikan, Prabhat K. Sahu and Shyi –Long Lee*

Department of Chemistry and Biochemistry, National Chung Cheng University, Chia-Yi, 621 TAIWAN

*E-mail: chesll@ccu.edu.tw

Table S1 (a). Hydrogen bond (Å) and bond angles (Degree) for $N^{2,3}$-ethenoguanine-Adenine complexes in gas phase (aqueous phase) using different DFT levels/6-31+G*.

Table S1 (b). Hydrogen bond (Å) and bond angles (Degree) for $N^{2,3}$-ethenoguanine-Thymine complexes in gas phase (aqueous phase) using different DFT levels/6-31+G*.

Table S1 (c). Hydrogen bond (Å) and bond angles (Degree) for $N^{2,3}$-ethenoguanine-Guanine complexes in gas phase (aqueous phase) using different DFT levels/6-31+G*.

Table S1 (d). Hydrogen bond (Å) and bond angles (Degree) for $N^{2,3}$-ethenoguanine-Cytosine complexes in gas phase (aqueous phase) using different DFT levels/6-31+G*.

Table S2 (a): Total energy (a.u.) for the different conformations of $N^{2,3}$-ethenoguanine adduct and DNA bases in gas phase at different DFT schemes using 6-31+G* basis set.

Table S2 (b): Total energy (a.u.) for the different conformations of $N^{2,3}$-ethenoguanine adduct and DNA bases in aqueous phase at different DFT schemes using 6-31+G* basis set.

Table S2 (c): Hydrogen bonding strength (kcal/mol) for the different conformations of $N^{2,3}$-ethenoguanine adduct and DNA bases in gas phase at different DFT levels/6-311++G//DFT levels/6-31+G*. BEcp: BSSE corrected hydrogen bonding strength (kcal/mol).**

Table S2 (d): Hydrogen bonding strength (kcal/mol) for the different conformations of $N^{2,3}$-ethenoguanine adduct and DNA bases in aqueous phase at different DFT levels/6-311++G//DFT levels/6-31+G*.**

Table S3: Relative binding energies (kcal/mol) for the $N^{2,3}$-ethenoguanine adduct and adenine complexes at different DFT levels/6-311++G// DFT levels/6-31+G* in gas phase (RBE_g and aqueous phase (RBE_{aq}).**

Table S4: Relative binding energies (kcal/mol) for the 1 $N^{2,3}$-ethenoguanine adduct and thymine complexes at different DFT levels/6-311++G// DFT levels/6-31+G* in gas phase (RBE_g and aqueous phase (RBE_{aq}).**

Table S5: Relative binding energies (kcal/mol) for the $N^{2,3}$-ethenoguanine adduct and guanine complexes at different DFT levels/6-311++G// DFT levels/6-31+G* in gas phase (RBE_g and aqueous phase (RBE_{aq}).**

Table S6: Relative binding energies (kcal/mol) for the $N^{2,3}$-ethenoguanine adduct and cytosine complexes at different DFT levels/6-311++G// DFT levels/6-31+G* in gas phase (RBE_g and aqueous phase (RBE_{aq}).**

Table S7 (a): Computed reaction enthalpy values (kcal/mol) for the $N^{2,3}$-ethenoguanine adduct and DNA bases at different DFT levels in gas phase at 298.15 K.

Table S7 (b): Computed reaction enthalpy values (kcal/mol) for the $N^{2,3}$-ethenoguanine adduct and DNA bases at different DFT levels in aqueous phase at 298.15 K.

Hydrogen Bonding Parameters for N^2, 3-ethenoguanine adduct and DNA nucleotides complexes:

1.a N^2, 3-ethenoguanine adduct and Adenine (εG-A) Complexes:

The optimized hydrogen bond distances and bond angles for the several different conformations of N^2, 3-ethenoguanine adduct and adenine complexes; εG-A(1), εG-A(2), εG-A(3), εG-A(4), εG-A(5), εG-A(6) and εG-A(7) are listed in Table S1 (a). From Table.S1 (a) and Fig 1, it can be observed that four different types of hydrogen bonds (N-H·····N, N-H·····O, C-H·····O and C-H·····N) are playing vital role for the stabilization of different εG-A complexes. For all these different complexes, based on both B3LYP and M06 computations, the N-H·····N type and N-H·····O type hydrogen bonds are found to be shorter and the corresponding bond angles are more linear, associated with strong interaction as compared to the weak hydrogen bond interaction of C-H·····N type and C-H·····O type. εG-A(1), εG-A(4), εG-A(7) complexes have been found to be stabilised by two C-H·····N type weak hydrogen bonds (more than 2.4 Å at aqueous phase and the corresponding bond angles are less than 150º) (see Table S1 (a). εG-A(3) complex has been found to be stabilised by one strong N-H·····N type (N12-H61 2.00 Å at M06 level compared to 2.03 Å at B3LYP level) and one weak C-H·····N type hydrogen bonds, N1-H11 2.53 Å at M06 level compared to 2.90 Å at

B3LYP level. εG-A(2) complex has been found to be stabilised by strong N-H·····N type (N1-H1 1.85 Å at M06 level compared to 1.89 Å at B3LYP level) and strong N-H·····O type (O6-H61 1.94 Å at M06 level compared to 1.92 Å at B3LYP level) with one weak C-H·····N type hydrogen bond (N12-H2 2.94 Å at M06 level compared to 3.07 Å at B3LYP level). εG-A(5) and εG-A(6) complexes have been found to be stabilised by two strong N-H·····N type hydrogen bonds and one weak C-H·····O type hydrogenbonds (more than 2.8 Å at aqueous phase and the corresponding bond angles are less than 135º at both M06 and B3LYP level) (see Table 1 (a). The two strong N-H·····N type hydrogen bonds are N1-H1 1.85 Å and N12-H61 2.03 Å at M06 level (1.90 Å and 2.01 Å respectively at B3LYP level) for εG-A(5) complex and N7-H1 1.83 Å and N12-H62 2.04 Å at M06 level (1.88 Å and 2.03 Å respectively at B3LYP level) for εG-A(6) complex (see Table S1(a)).

1.b N^2, 3-ethenoguanine adduct and Thymine (εG-T) Complexes:

The optimized hydrogen bond distances and bond angles for the several different conformations of N^2, 3-ethenoguanine adduct and thymine complexes; εG-T(1), εG-T(2), εG-T(3), εG-T(4), εG-T(5) are listed in Table S1 (b). From Table.S1 (b) and Fig 1, it has been noticed that two hydrogen bonds (each of either N-H·····N, N-H·····O or C-H·····O) are stabilizing all these different εG-T complexes. Among all these different complexes, εG-T(1) complex has been found to be stabilised by one strong N-H·····N type (N7-H3 1.99 Å at M06 level compared to 2.03 Å at B3LYP level) and one weak C-H·····O type hydrogen bonds, O2-H8 2.29 Å at M06 level compared to 2.41 Å at B3LYP level. εG-T(2) and εG-T(5) complexes have been found to be stabilised by two strong N-H·····O type hydrogen bonds with around 1.85 Å at both M06 and B3LYP level. εG-T(3) complex has been found to be stabilised by one strong N-H·····O type (O4-H1 1.83 Å at M06 level compared to 1.89 Å at B3LYP level) and one weak C-H·····O type hydrogen bonds, O6-H71 2.47 Å at M06 level

compared to 2.68 Å at B3LYP level. εG-T(4) complex has been found to be stabilised by one strong N-H·····N type (N12-H3 1.90 Å at M06 level compared to 1.93 Å at B3LYP level) and one strong N-H·····O type (O2-H1 1.85 Å at M06 level compared to 1.87 Å at B3LYP level).

1.c N^2, 3-ethenoguanine adduct and Guanine (εG-G) Complexes:

The optimized hydrogen bond distances and bond angles for the several different conformations of N^2, 3-ethenoguanine adduct and guanine complexes; εG-G(1), εG-G(2), εG-G(3), εG-G(4), εG-G(5), εG-G(6) and εG-G(7) are listed in Table S1 (c). From Table.S1 (c) and Fig 1, it has been noticed that εG-G(1) and εG-G(4) complexes have been found to be stabilised by both strong N-H·····O type and N-H···N type hydrogen bonds with additional weak C-H·····O type hydrogen bonds for only εG-G(1) complex, O6-H8 2.79 Å at M06 level compared to 2.86 Å at B3LYP level. The two strong N-H·····O type and N-H·····N type hydrogen bonds are N7-H1 1.91 Å and O6-H21 1.93 Å at M06 level (1.94 Å and 1.93 Å respectively at B3LYP level) for εG-G(1) complex and N12-H1 1.93 Å and O6-H1 1.80 Å at M06 level and 1.95 Å and 1.80 Å, respectively at B3LYP level for εG-G(4) complex (see Table 1(c)). εG-G(2) complex has been found to be stabilised by two strong N-H·····O type hydrogen bonds with O6-H1 1.82 Å and O6-H1 1.79 Å at both M06 and B3LYP level. εG-G(5) and εG-G(6) complexes have been found to be stabilised by one strong N-H·····N type and one weak C-H·····O type hydrogen bonds as compared to εG-G(3) complex, which is stabilised by one strong N-H·····N type and one weak C-H·····N type hydrogen bonds (see Table S1(c)). εG-G(7) complex has been found to be stabilised by two weak C-H·····N type hydrogen bonds.

1.d N^2, 3-ethenoguanine adduct and Cytosine (εG-C) Complexes:

The optimized hydrogen bond distances and bond angles for the several different conformations of N^2, 3-ethenoguanine adduct and cytosine complexes; εG-C(1), εG-C(2), εG-C(3), εG-C(4) are listed in Table S1 (d). From Table.S1 (d) and Fig 1, it has been noticed that εG-C(1) complex has been found to be stabilised by one strong N-H·····O type O6-H42 1.89 Å at M06 level (1.92 Å at B3LYP level) and one weak C-H·····N type hydrogen bond. Similarly, εG-C(3) complex has been found to be stabilised by one strong N-H·····N type N7-H41 2.02 Å at both M06 and B3LYP level with another weak C-H·····N type hydrogen bond (> 2.4 Å). εG-C(2) complex has been found to be stabilised by one strong N-H·····N type (N3-H1 1.91 Å at M06 level compared to 1.99 Å at B3LYP level) and one strong N-H·····O type (O6-H41 1.91 Å at M06 level comparedto 1.89 Å at B3LYP level). εG-C(4) complex has been found to be stabilised by two strong N-H·····N type hydrogen bonds. The two strong N-H·····N type hydrogen bonds are N12-H4 1.92 Å and N3-H1 2.12 Å at M06 level (1.94 Å and 2.22 Å respectively at B3LYP level) (see Table S1 (d).

Table S1 (a). Hydrogen bond (Å) and bond angles (Degree) for $N^{2,3}$-ethenoguanine-Adenine complexes in gas phase (aqueous phase) using different DFT levels/6-31+G*.

Parameter	B3LYP	M06
εG-A1		
N12-H8	2.439 (2.482)	2.308 (2.556)
H11-N7	2.627 (2.997)	2.461 (2.374)
∠N12H8C8	145.7 (150.6)	145.8 (141.8)
∠C11H11N7	141.4 (134.6)	142.7 (146.0)
εG-A2		
N12-H2	3.019 (3.078)	2.933 (2.945)
H1-N1	1.850 (1.893)	1.824 (1.854)
O6-H61	1.906 (1.922)	1.912 (1.947)
∠N12H2C2	133.5 (132.9)	134.0 (134.0)

∠N1H1N1	178.4 (178.2)	179.2 (179.6)
∠O6H61N6	174.4 (176.1)	173.7 (175.1)
εG-A3		
N12-H61	2.067 (2.032)	2.024 (2.009)
H11-N1	2.531 (2.903)	2.397 (2.532)
∠N12H61N6	173.6 (176.3)	171.6 (171.2)
∠C11H11N1	141.6 (129.9)	143.2 (136.0)
εG-A4		
N12-H2	2.621 (2.816)	2.473 (2.509)
H11N1	2.620 (2.734)	2.416 (2.471)
∠N12H2C2	149.9 (151.5)	150.2 (152.8)
∠C11H11N1	145.0 (149.1)	147.2 (148.5)
εG-A5		
H1-N1	1.854 (1.905)	1.835 (1.859)
N12-H61	2.057 (2.016)	2.046 (2.031)
O6-H2	2.865 (3.000)	2.816 (2.869)
∠N1H1N1	177.5 (175.9)	177.0 (176.4)
∠N12H61N6	173.2 (174.3)	172.5 (172.9)
∠O6H2C2	134.2 (133.2)	134.9 (135.0)
εG-A6		
H1-N7	1.817 (1.884)	1.789 (1.833)
N12-H62	2.118 (2.030)	2.124 (2.043)
O6-H8	2.777 (3.018)	2.681 (2.878)
∠N1H1N7	176.9 (179.9)	175.7 (178.8)
∠N12H62N6	171.0 (169.6)	170.1 (169.6)
∠O6H8C8	124.0 (121.6)	124.7 (123.0)
εG-A7		
N7-H8	2.387 (2.701)	2.276 (2.418)
H8-N7	2.558 (2.521)	2.397 (2.389)
∠N7H8C8	140.5 (135.5)	141.4 (139.6)
∠C8H8N7	134.1 (141.3)	136.7 (140.0)

Table S1 (b). Hydrogen bond (Å) and bond angles (Degree) for $N^{2,3}$-ethenoguanine-Thymine complexes in gas phase (aqueous phase) using different DFT levels/6-31+G*.

Parameter	B3LYP	M06
εG-T1		
N7-H3	2.104 (2.031)	2.075 (1.998)
H8-O2	2.213 (2.415)	2.155 (2.294)
∠N7H3N3	160.7 (167.6)	157.8 (166.8)
∠C8H8O2	135.0 (131.8)	131.9 (133.6)
εG-T2		
H1-O4	1.828 (1.832)	1.828 (1.822)
O6-H3	1.853 (1.855)	1.844 (1.831)
∠N1H1O4	171.4 (175.7)	170.1 (176.9)
∠O6H3N3	171.3 (176.8)	170.6 (178.4)
εG-T3		
H1-O4	1.890 (1.893)	1.853 (1.852)
O6-H71	2.424 (2.689)	2.349 (2.470)
∠N1H1O4	179.8 (172.9)	179.9 (170.8)
∠O6H71C7	163.0 (163.0)	161.0 (157.6)
εG-T4		
N12-H3	1.904 (1.934)	1.887 (1.907)
H1-O2	1.911 (1.872)	1.896 (1.857)
∠N12H3N3	170.5 (172.8)	170.0 (173.3)
∠N1H1O2	165.8 (170.9)	164.5 (170.4)
εG-T5		
H1-O2	1.847(1.853)	1.831(1.834)
O6-H3	1.870(1.851)	1.869(1.846)
∠N1H1O2	170.5(175.1)	168.3(176.4)
∠O6H3N3	168.6(175.0)	165.7(176.1)

Table S1 (c). Hydrogen bond (Å) and bond angles (Degree) for $N^{2,3}$-ethenoguanine-Guanine complexes in gas phase (aqueous phase) using different DFT levels/6-31+G*.

Parameter	B3LYP	M06
εG-G1		
H8-O6	2.506 (2.867)	2.441 (2.793)
N7-H1	1.896 (1.942)	1.867 (1.915)
O6-H21	2.107 (1.931)	2.074 (1.934)
∠C8H8O6	123.6 (118.9)	122.7 (118.8)
∠N7H1N1	170.3 (174.4)	168.2 (173.6)
∠O6H21N2	170.1 (165.4)	171.0 (165.5)
εG-G2		
H1-O6	1.810 (1.824)	1.823 (1.829)
O6-H1	1.766 (1.797)	1.761 (1.797)
∠N1H1O6	174.7 (177.1)	175.4 (178.7)
∠O6H1N1	177.9 (178.2)	175.3 (175.9)
εG-G3		
N12-H8	2.374 (2.561)	2.262 (2.452)
H1-N7	2.040 (1.965)	2.023 (1.924)
∠N12H8C8	135.4 (132.1)	136.0 (131.6)
∠N1H1N7	162.9 (168.7)	160.7 (167.1)
εG-G4		
N12-H1	1.971 (1.958)	1.939 (1.938)
H1-O6	1.819 (1.809)	1.820 (1.801)
∠N12H1N1	176.7 (176.2)	178.2 (178.2)
∠N1H1O6	171.6 (174.0)	171.4 (175.5)
εG-G5		
H1-N7	2.011 (1.957)	2.002 (1.911)
O6-H8	2.213 (2.448)	2.149 (2.381)
∠N1H1N7	163.7 (169.0)	161.8 (168.5)
∠O6H8C8	128.1 (130.5)	134.3 (130.5)

εG-G6		
N12-H1	2.104 (2.122)	2.030 (2.014)
H11-O6	2.236 (2.329)	2.181 (2.287)
∠N12H1N1	175.6 (172.9)	177.6 (176.2)
∠C11H11O6	149.5 (144.3)	151.4 (146.0)
εG-G7		
N12-H8	2.524 (2.543)	2.387 (2.365)
H11-N7	2.466 (2.742)	2.343 (2.576)
∠N12H8C8	138.1 (144.6)	139.3 (145.7)
∠C11H11N7	142.9 (140.3)	143.7 (140.8)

Table S1 (d). Hydrogen bond (Å) and bond angles (Degree) for $N^{2,3}$-ethenoguanine-Cytosine complexes in gas phase (aqueous phase) using different DFT levels/6-31+G*.

Parameter	B3LYP	M06
εG-C1		
N7-H5	2.663 (2.502)	2.594 (2.427)
O6-H42	1.990 (1.926)	1.968 (1.899)
∠N7H5C5	178.1 (178.0)	169.6 (172.0)
∠O6H42N4	172.2 (167.0)	179.0 (176.5)
εG-C2		
O6-H41	1.832 (1.897)	1.850 (1.910)
H1-N3	1.980 (1.992)	1.907 (1.913)
∠O6H41N4	175.6 (175.4)	173.0 (173.0)
∠N1H1N3	169.4 (171.7)	169.2 (171.5)
εG-C3		
N7-H41	2.023 (2.029)	2.015 (2.024)
H8-N3	2.325 (2.662)	2.256 (2.429)
∠N7H41N4	165.7 (172.9)	162.3 (167.0)
∠C8H8N3	131.7 (128.8)	128.8 (129.2)
εG-C4		
N12-H41	1.935 (1.941)	1.948 (1.921)
H1-N3	2.167 (2.224)	2.054 (2.121)

∠N12H41N4	177.1 (179.5)	173.3 (174.2)
∠N1H1N3	164.0 (167.1)	162.6 (163.4)

Table S2 (a): Total energy (a.u.) for the different conformations of $N^{2,3}$-ethenoguanine adduct and DNA bases in gas phase at different DFT schemes using 6-31+G* basis set.

Complexes	B3LYP	M06
εG-A1	-1086.1070632	-1085.4264499
εG-A2	-1086.1237247	-1085.4432836
εG-A3	-1086.1118086	-1085.4310600
εG-A4	-1086.1046709	-1085.4239322
εG-A5	-1086.1218951	-1085.4415914
εG-A6	-1086.1238394	-1085.4429812
εG-A7	-1086.1099056	-1085.4293980
εG-T1	-1072.9290721	-1072.2775708
εG-T2	-1072.9365487	-1072.2842342
εG-T3	-1072.9282893	-1072.2760726
εG-T4	-1072.9391917	-1072.2876231
εG-T5	-1072.9356739	-1072.2834692
εG-G1	-1161.3663087	-1160.6621197
εG-G2	-1161.3661341	-1160.6611491
εG-G3	-1161.3480018	-1160.6437841
εG-G4	-1161.3586280	-1160.6542011
εG-G5	-1161.3519517	-1160.6475040
εG-G6	-1161.3514974	-1160.6476024
εG-G7	-1161.3444310	-1160.6400827
εG-C1	-1013.7250566	-1013.1006494
εG-C2	-1013.7315852	-1013.1090906

εG-C3	-1013.7322096	-1013.1095971
εG-C4	-1013.7271260	-1013.1045988

Table S2 (b): Total energy (a.u.) for the different conformations of $N^{2,3}$-ethenoguanine adduct and DNA bases in aqueous phase at different DFT schemes using 6-31+G* basis set.

System	B3LYP	M06
εG-A1	-1086.1460187	-1085.4643748
εG-A2	-1086.1577913	-1085.4767766
εG-A3	-1086.1502361	-1085.4684185
εG-A4	-1086.1454405	-1085.4637175
εG-A5	-1086.1578917	-1085.4768457
εG-A6	-1086.1582988	-1085.4766852
εG-A7	-1086.1462925	-1085.4648408
εG-T1	-1072.9694747	-1072.3172303
εG-T2	-1072.9764425	-1072.3231832
εG-T3	-1072.9688375	-1072.3157833
εG-T4	-1072.9786200	-1072.3261546
εG-T5	-1072.9758012	-1072.3225911
εG-G1	-1161.4073849	-1160.7020912
εG-G2	-1161.4088746	-1160.7032025
εG-G3	-1161.4014785	-1160.6966450
εG-G4	-1161.4084379	-1160.7031304
εG-G5	-1161.4018347	-1160.6965643
εG-G6	-1161.3999275	-1160.6949010
εG-G7	-1161.3948394	-1160.6893278
εG-C1	-1013.7707427	-1013.1454507

ε□G-C2	-1013.7757518	-1013.1527137
εG-C3	-1013.7700626	-1013.1461689
εG-C4	-1013.7753215	-1013.1515846

Table S2 (c): Hydrogen bonding strength (kcal/mol) for the different conformations of $N^{2,3}$-ethenoguanine adduct and DNA bases in gas phase at different DFT levels/6-311++G//DFT levels/6-31+G*. BEcp: BSSE corrected hydrogen bonding strength (kcal/mol).**

Complexes	B3LYP//B3LYP		M06//M06	
	BE	BEcp	BE	BEcp
εG-A1	-3.23	-2.96	-4.80	-4.40
εG-A2	-13.65	-12.94	-15.85	-15.15
εG-A3	-6.16	-5.78	-7.90	-7.43
εG-A4	-1.46	-1.20	-3.19	-2.83
εG-A5	-12.73	-12.06	-15.00	-14.31
εG-A6	-13.78	-13.10	-15.76	-15.01
εG-A7	-4.99	-4.70	-6.62	-6.19
εG-T1	-6.99	-6.47	-8.75	-8.13
εG-T2	-11.44	-10.71	-13.02	-12.30
εG-T3	-6.38	-4.83	-7.82	-7.26
εG-T4	-13.34	-12.58	-15.40	-14.59
εG-T5	-10.97	-10.26	-12.59	-11.87
εG-G1	-17.28	-16.59	-19.58	-18.79
εG-G2	-17.01	-16.27	-18.94	-18.21
εG-G3	-6.29	-5.74	-8.46	-7.79
εG-G4	-12.81	-12.07	-15.22	-14.43
εG-G5	-8.45	-7.92	-10.31	-9.70
εG-G6	-8.27	-7.78	-10.64	-10.04
εG-G7	-3.86	-3.57	-5.64	-5.22
εG-C1	-8.01	-7.62	-9.15	-8.65
εG-C2	-12.34	-11.52	-14.99	-14.07
εG-C3	-12.60	-12.09	-14.77	-14.16

εG-C4	-9.77	-9.03	-12.39	-11.63

Table S2 (d): Hydrogen bonding strength (kcal/mol) for the different conformations of $N^{2,3}$-ethenoguanine adduct and DNA bases in aqueous phase at different DFT levels/6-311++G//DFT levels/6-31+G*.**

Complexes	B3LYP//B3LYP	M06//M06
εG-A1	-0.64	-2.20
εG-A2	-8.10	-10.54
εG-A3	-3.25	-4.93
εG-A4	-0.26	-1.74
εG-A5	-8.30	-10.74
εG-A6	-8.43	-10.56
εG-A7	-0.80	-2.51
εG-T1	-3.98	-6.05
εG-T2	-8.19	-9.91
εG-T3	-3.52	-5.16
εG-T4	-9.75	-12.03
εG-T5	-7.82	-9.59
εG-G1	-8.22	-10.65
εG-G2	-9.06	-11.23
εG-G3	-4.70	-7.07
εG-G4	-9.07	-11.47
εG-G5	-4.84	-6.88
εG-G6	-3.70	-6.04
εG-G7	-0.44	-2.13
εG-C1	-3.90	-5.32
εG-C2	-7.24	-10.19
εG-C3	-3.51	-5.71
εG-C4	-6.96	-9.53

Table S3: Relative binding energies (kcal/mol) for the $N^{2,3}$-ethenoguanine adduct and adenine complexes at different levels/6-311++G// DFT levels/6-31+G* in gas phase (RBE_g) and aqueous phase (RBE_{aq}).**

Complexes	B3LYP		M06		MP2//B3LYP		MP2//M06	
	RBEg	RBEaq	RBEg	RBEaq	RBEg	RBEaq	RBEg	RBEaq
εG-A1	10.55	7.79	11.05	8.54	11.64	9.31	11.61	9.21
εG-A2	0.13	0.34	0.00	0.20	0.87	0.77	0.85	0.74
εG-A3	7.62	5.18	7.94	5.82	8.75	6.46	8.78	6.50
εG-A4	12.32	8.17	12.66	9.00	13.98	9.69	13.42	9.69
εG-A5	1.05	0.13	0.85	0.00	1.37	0.38	1.38	0.40
εG-A6	0.00	0.00	0.09	0.18	0.00	0.00	0.00	0.00
εG-A7	8.79	7.63	9.23	8.23	9.80	9.05	9.80	9.05

Table S4: Relative binding energies (kcal/mol) for the $N^{2,3}$-ethenoguanine adduct and thymine complexes at different DFT levels/6-311++G// DFT levels/6-31+G* in gas phase (RBE_g and aqueous phase (RBE_{aq}).**

Complexes	B3LYP//B3LYP		M06//M06		MP2//B3LYP		MP2//M06	
	RBEg	RBEaq	RBEg	RBEaq	RBEg	RBEaq	RBEg	RBEaq
εG-T1	6.35	5.77	6.66	5.98	6.76	6.37	6.77	6.41
εG-T2	1.89	1.56	2.38	2.12	3.16	2.41	3.18	2.45
εG-T3	6.96	6.23	7.58	6.87	8.07	7.20	8.06	7.16
εG-T4	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
εG-T5	2.37	1.93	2.81	2.44	3.55	2.75	3.64	2.78

Table S5: Relative binding energies (kcal/mol) for the 1 $N^{2,3}$-ethenoguanine adduct and guanine complexes at different levels/6-311++G// DFT levels/6-31+G* in gas phase (RBE_g and aqueous phase (RBE_{aq}).**

Complexes	B3LYP//B3LYP		M06//M06		MP2//B3LYP		MP2//M06	
	RBEg	RBEaq	RBEg	RBEaq	RBEg	RBEaq	RBEg	RBEaq
εG-G1	0.00	0.85	0.00	0.82	0.00	1.21	0.00	1.19
εG-G2	0.26	0.01	0.64	0.24	1.15	0.67	1.18	0.71
εG-G3	10.99	4.37	11.12	4.41	10.12	4.61	10.25	4.58
εG-G4	4.46	0.00	4.37	0.00	3.81	0.00	3.81	0.00
εG-G5	8.83	4.23	9.28	4.59	7.74	3.76	7.90	3.85
εG-G6	9.00	5.37	8.94	5.43	8.99	5.99	8.94	5.85
εG-G7	13.42	8.63	13.94	9.34	13.91	10.03	13.90	9.98

Table S6: Relative binding energies (kcal/mol) for the $N^{2,3}$-ethenoguanine adduct and cytosine complexes at different DFT levels/6-311++G// DFT levels/6-31+G* in gas phase (RBE_g and aqueous phase (RBE_{aq}).**

Complexes	B3LYP//B3LYP		M06//M06		MP2//B3LYP		MP2//M06	
	RBEg	RBEaq	RBEg	RBEaq	RBEg	RBEaq	RBEg	RBEaq
εG-C1	4.59	3.34	5.84	4.87	5.96	5.35	6.23	5.77
εG-C2	0.26	0.00	0.00	0.00	0.00	0.00	0.00	0.00
εG-C3	0.00	3.73	0.23	4.48	0.70	5.48	0.97	5.76
εG-C4	2.83	0.28	2.60	0.66	2.38	1.26	2.77	1.65

Table S7 (a): Computed reaction enthalpy values (kcal/mol) for the $N^{2,3}$-ethenoguanine adduct and DNA bases at different DFT levels in gas phase at 298.15 K.

Complexes	B3LYP	M06
εG-A1	-1.79	-3.13
εG-A2	-11.53	-12.91
εG-A3	-4.03	-5.22
εG-A4	-0.36	-2.13
εG-A5	-10.43	-12.45
εG-A6	-11.58	-12.90
εG-A7	-3.53	-4.93
εG-T1	-5.55	-8.06
εG-T2	-10.19	-11.13
εG-T3	-5.06	-5.98
εG-T4	-11.33	-12.60
εG-T5	-9.72	-10.55
εG-G1	-16.36	-18.23
εG-G2	-16.54	-17.82
εG-G3	-5.39	-7.70
εG-G4	-11.94	-14.01
εG-G5	-7.00	-8.56
εG-G6	-7.35	-9.16
εG-G7	-3.06	-4.57
εG-C1	-5.99	-6.68
εG-C2	-10.37	-12.10
εG-C3	-10.47	-12.93
εG-C4	-8.16	-9.96

Table S7 (b): Computed reaction enthalpy values (kcal/mol) for the $N^{2,3}$-ethenoguanine adduct and DNA bases at different DFT levels in aqueous phase at 298.15 K.

Complexes	B3LYP	M06
εG-A1	0.61	-0.62
εG-A2	-6.22	-7.52
εG-A3	-1.37	-2.34
εG-A4	0.36	-0.70
εG-A5	-6.16	-8.23
εG-A6	-6.47	-7.73
εG-A7	0.43	-0.84
εG-T1	-3.33	-4.20
εG-T2	-6.94	-7.80
εG-T3	-2.90	-3.74
εG-T4	-7.90	-9.23
εG-T5	-6.53	-8.01
εG-G1	-7.59	-9.17
εG-G2	-8.49	-10.31
εG-G3	-4.59	-5.70
εG-G4	-8.26	-9.56
εG-G5	-3.44	-5.02
εG-G6	-2.96	-4.61
εG-G7	0.28	-0.96
εG-C1	-2.44	-3.17
εG-C2	-5.74	-7.91
εG-C3	-2.86	-3.60
εG-C4	-5.30	-7.10