Supporting Information

Cytosine Iminyl Radical (cytN•) Formation via Electron Induced Debromination of 5-Bromocytosine: A DFT and Gaussian 4 study

Anil Kumar and M. D. Sevilla*

Department of Chemistry, Oakland University, Rochester, Michigan 48309

Contents

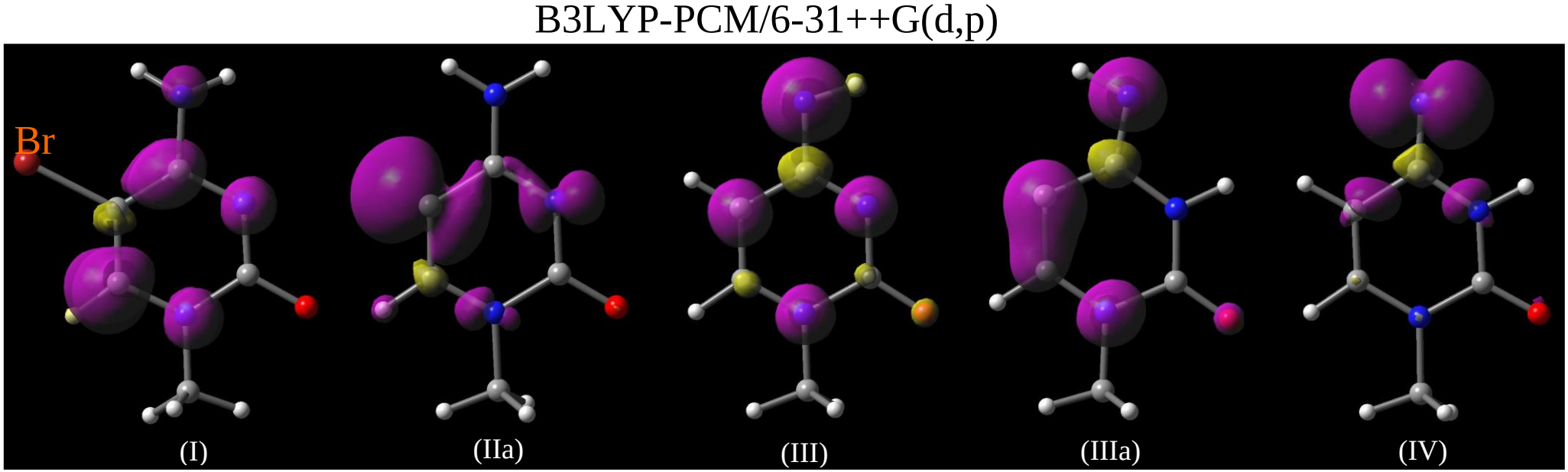


Figure S1- B3LYP-PCM/6-31++G(g,p) calculated spin density plot of 5-Brcyt•⁻ (I), cytosine-5-yl• (IIa), aminyl radical (IIIa) and iminyl radical (IV).

B3LYP-PCM/6-31++G(d,p)

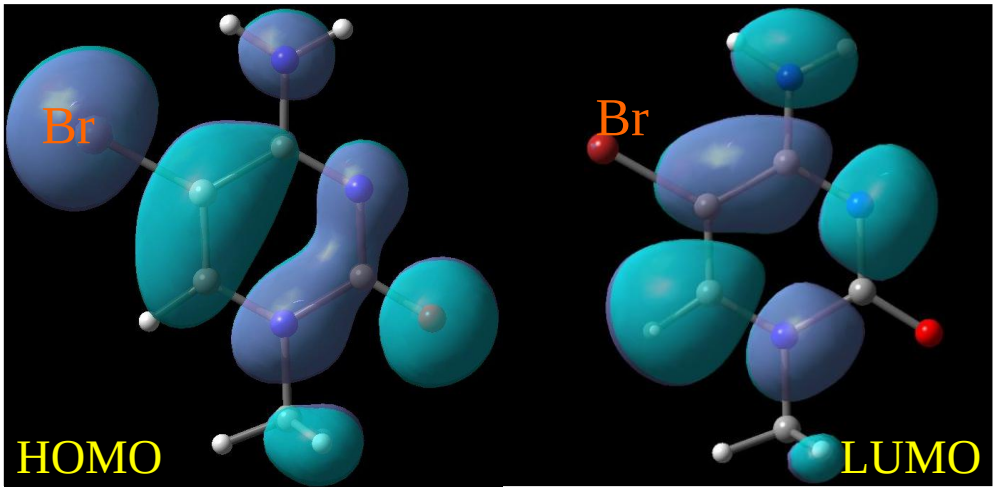


Figure S2- B3LYP-PCM/6-31++G(g,p) calculated highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) of 5-Brcyt.

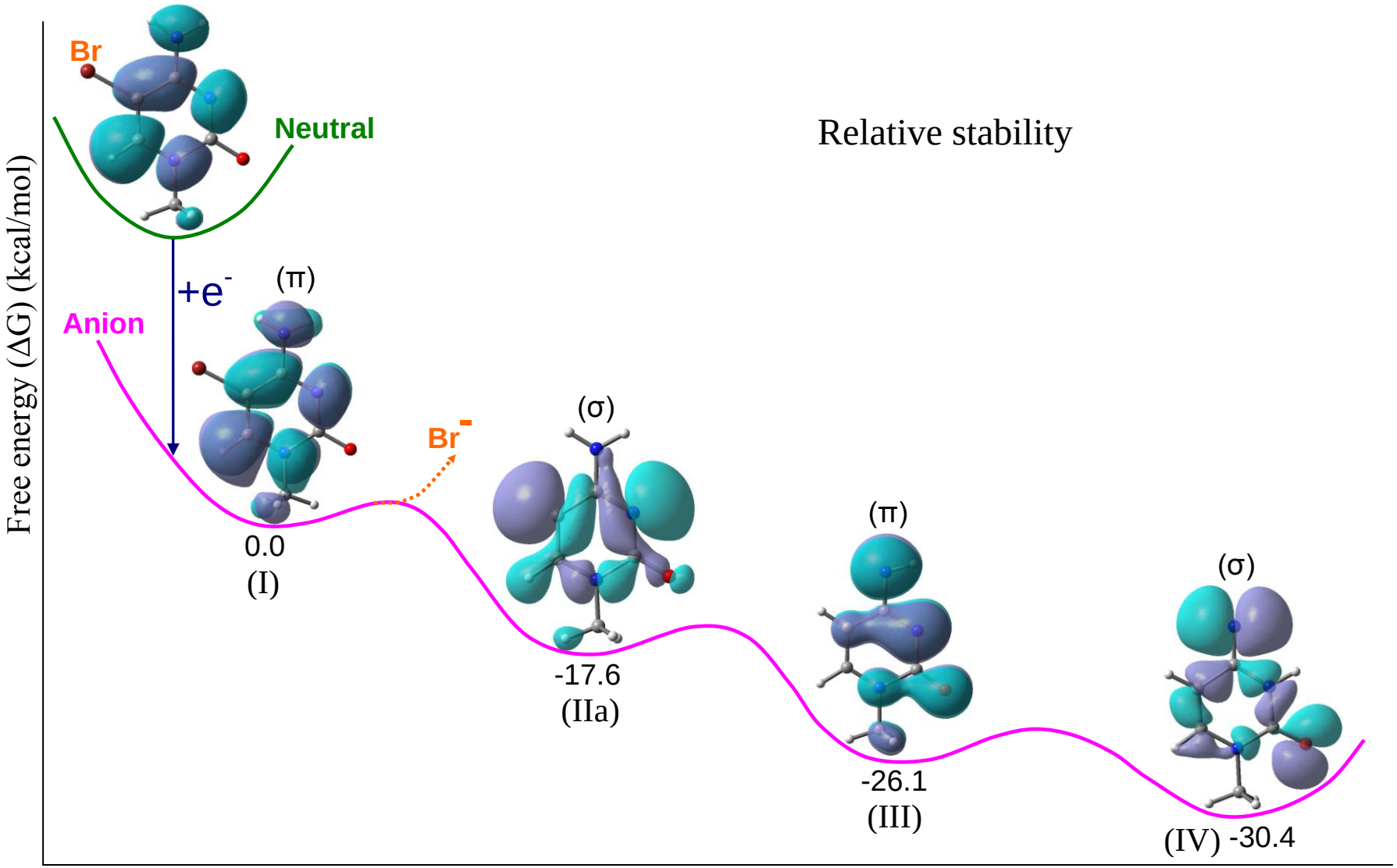


Figure S3- Gaussian 4 calculated relative stabilities of radicals after an electron addition to 5-Brcyt. ΔG of Br^- was added to the free energy of debrominated-radicals for the calculation of the relative stabilities with respect to 5-Brcyt radical anion. Energies in kcal/mol are shown below each figure.

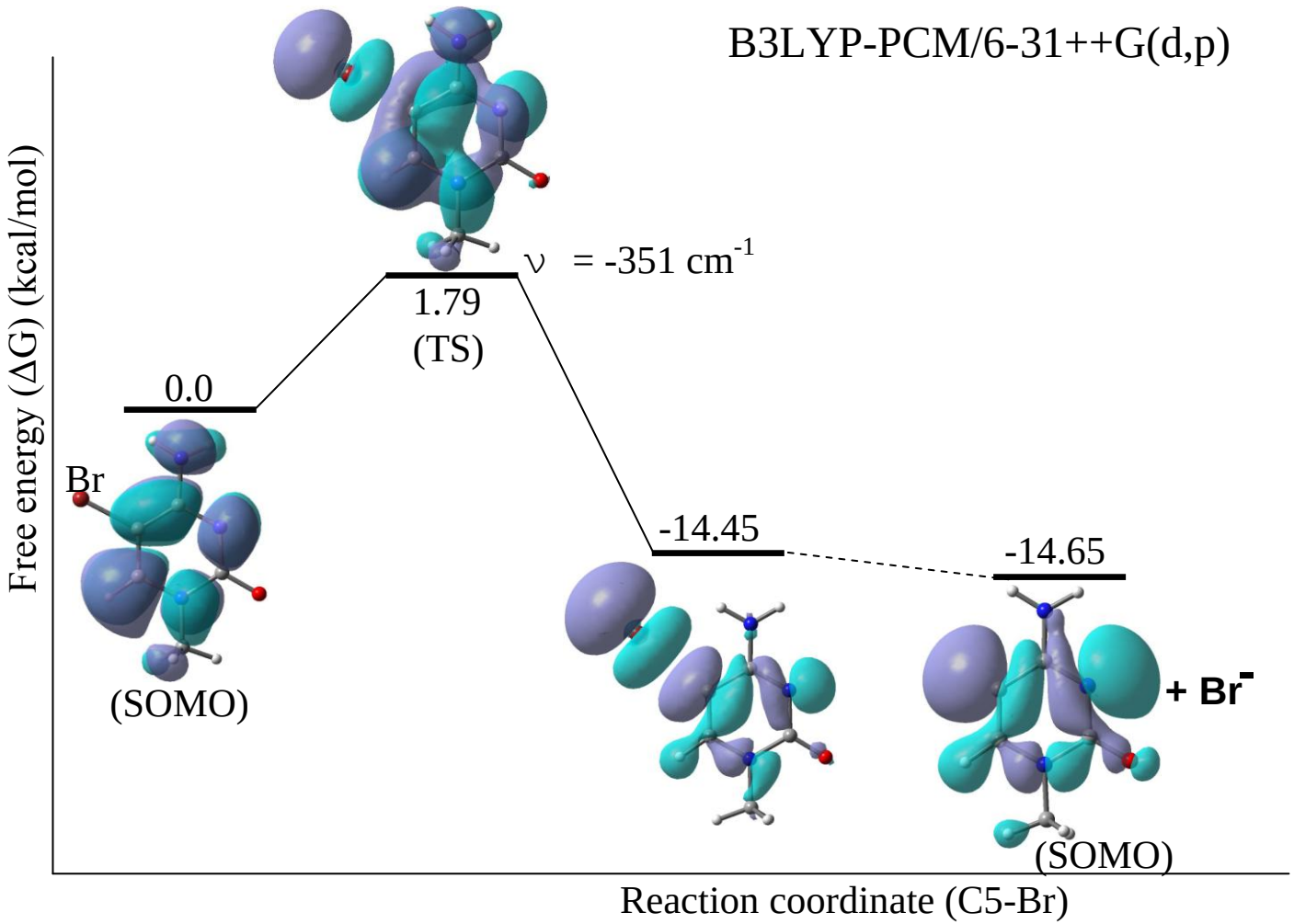
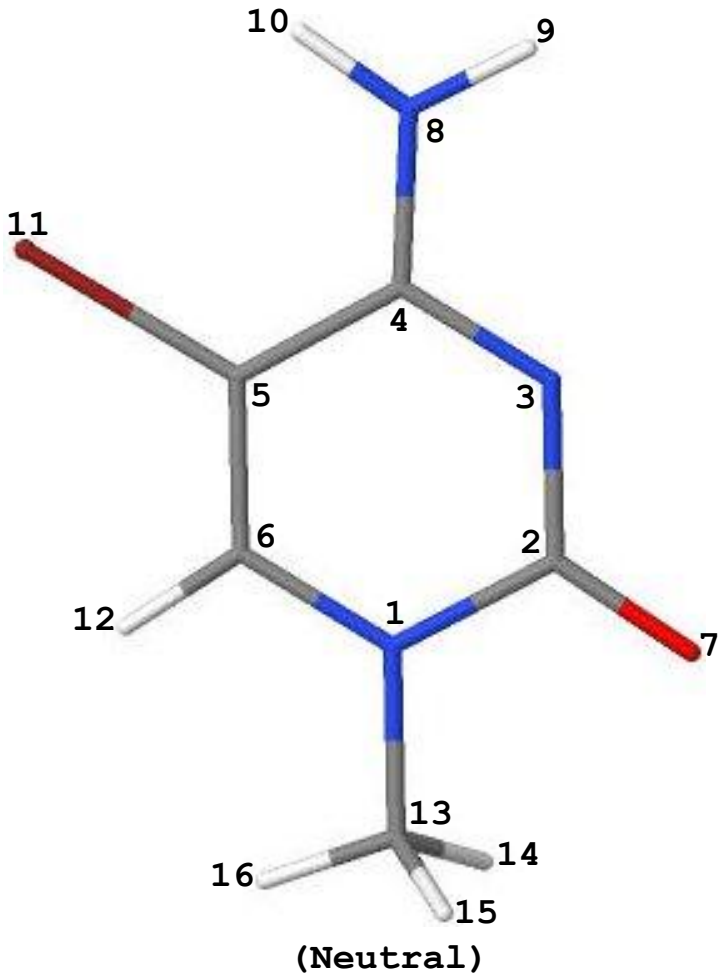


Figure S4- Free energy (ΔG) reaction profile of 5-BrCyt$^{\bullet-}$ → Br$^-$ + cytosine-5-yl• computed at the B3LYP/6-31++G(d,p) level in water using PCM solvation model. Energies are given in kcal/mol. TS = Transition state characterized by a negative frequency.

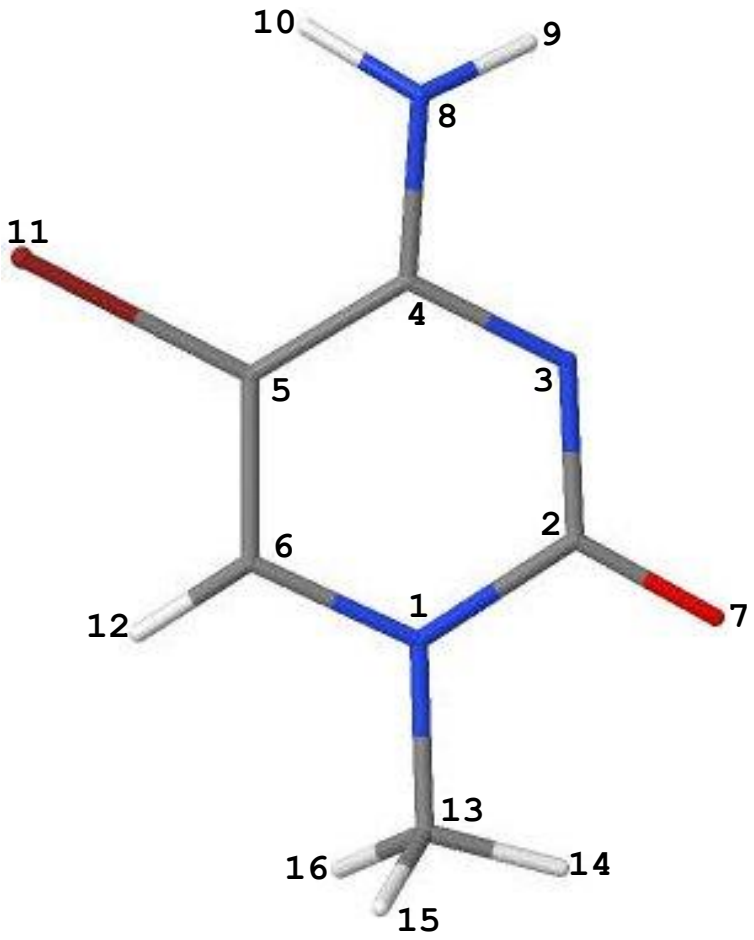
Comparison of geometrical parameters calculated by different methods including PCM



(Neutral)

Neutral				
Distance (Å)	**G4-Theory**	**B3LYP[a]**	**ωB97X[a]**	**M06-2x[a]**
1-2	1.414	1.417	1.405	1.409
2-3	1.361	1.361	1.360	1.359
3-4	1.325	1.332	1.325	1.325
4-5	1.436	1.436	1.436	1.436
5-6	1.358	1.362	1.355	1.357
6-1	1.348	1.356	1.353	1.352
1-13	1.472	1.468	1.461	1.462
2-7	1.226	1.241	1.235	1.233
4-8	1.343	1.346	1.341	1.340
5-11	1.901	1.896	1.873	1.875
Angle (deg.)				
1-2-3	117.8	118.2	118.4	118.2
2-3-4	121.7	121.5	121.1	121.2
3-4-5	121.0	121.0	121.4	121.4
4-5-6	117.6	117.5	117.2	117.2
5-6-1	121.0	121.1	121.2	121.0
6-1-2	120.8	120.7	120.8	121.0

[a]Calculated using 6-31++G(d,p) basis set.



(Anion radical)

Anion Radical				
Distance (Å)	**G4-Theory**	**B3LYP**[a]	**ωB97X**[a]	**M06-2x**[a]
1-2	1.414	1.407	1.398	1.401
2-3	1.352	1.352	1.348	1.349
3-4	1.369	1.379	1.375	1.372
4-5	1.378	1.380	1.374	1.376
5-6	1.406	1.405	1.406	1.404
6-1	1.409	1.413	1.409	1.408
1-13	1.447	1.454	1.449	1.450
2-7	1.245	1.262	1.257	1.253
4-8	1.405	1.405	1.401	1.4
5-11	1.901[b]	1.916	1.888	1.891
Angle (deg.)				
1-2-3	119.1	119.7	120.0	119.7
2-3-4	120.0	120.1	119.6	119.7
3-4-5	121.9	121.5	122.1	122.0
4-5-6	120.6	120.4	120.0	120.2
5-6-1	115.9	116.7	116.6	116.3
6-1-2	122.1	121.3	121.2	121.4

[a]Calculated using 6-31++G(d,p) basis set.
[b]Constraind distance to avoid dissociation during optimization.

ωb97x-PCM/6-31++G(d,p)

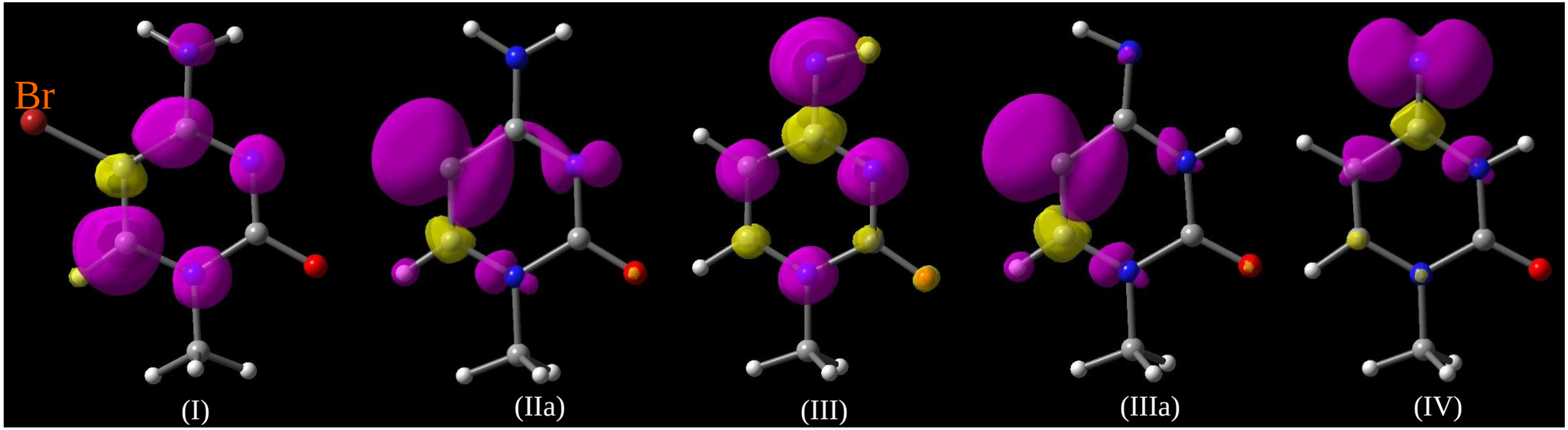


Figure S5- ωb97x-PCM/6-31++G(g,p) calculated spin density plot of 5-Brcyt•− (I), cytosine-5-yl• (IIa), aminyl radical (IIIa) and iminyl radical (IV).

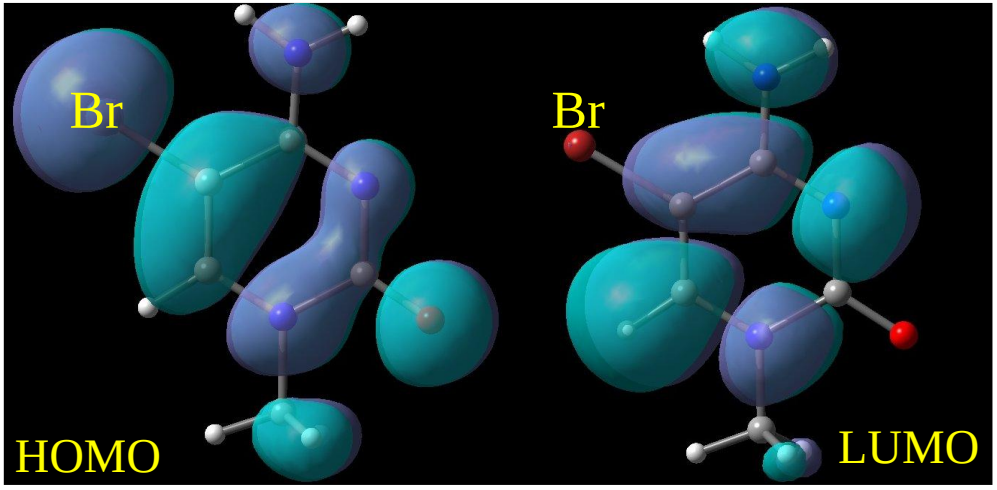


Figure S6- ωb97x-PCM/6-31++G(g,p) calculated highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) of 5-Brcyt.

Potential Energy Surface (PES) for Tautomerization Reaction

The potential energy surfaces (PES) for the tautomerizaton reactions from the NH_2 group of cytosine-5-yl$^{\bullet}$ (IIa) to form the intermediate aminyl radical (III) and finally the iminyl radical (IV) were calculated using the B3LYP-PCM/6-31++G(d, p) level of theory in the presence of four water molecules including full aqueous phase via PCM. We placed two hydrogen-bonded water molecules between N3 and NH_2 sites and the other two hydrogen-bonded water molecules between C5 and NH_2 group of the cytosine-5-yl$^{\bullet}$ and fully optimized the structures. The PES for proton transfer reactions from NH_2 group of cytosine-5-yl$^{\bullet}$ is shown in Figure S7. To calculate the PES, we first transfer a proton from the NH_2 group of the cytosine-5-yl$^{\bullet}$ to C5 atom by scanning the N-H bond from equilibrium bond length of cytosine-5-yl$^{\bullet}$ of 1.02 Å to 1.8 Å in 0.1 Å steps and optimized the structures. At N-H distance of 1.5 Å proton completely transfers to the C5 atom through two hydrogen-bonded water molecules by producing aminyl radical (III) as an intermediate, see Figure S7. From the aminyl radical (III), the second proton was transferred from the NH group of the aminyl radical towards N3 atom also by scanning the N-H bond from equilibrium bond length (1.03 Å) of aminyl radical to 1.8 Å in 0.1 Å steps and optimized the structures. In this case at a N-H distance of 1.43 Å the proton completely transfers to N3 through hydrogen-bonded two water molecules by producing the most stable iminyl radical (IV). The barrier height for first proton transfer from NH_2 group of cytosine-5-yl$^{\bullet}$ to C5 atom was calculated to be ca. 24 kcal/mol (see Figure S7) while the barrier height for the second proton transfer from NH group of aminyl radical to produce was calculated to be ca. 18 kcal/mol.

We also investigated a model for the tautomerization from cytosine-5-yl$^{\bullet}$ (IIa) to aminyl radical (III) in which an hydroxide anion was present in place of a water and solvated by two water molecules, see Figure S8. In the calculation total five water molecules and an hydroxide ion was considered. The geometries were fully optimized using the B3LYP-PCM/6-31++G(d, p) level of theory. In this case, we scanned the N-H bond from equilibrium bond length (1.09 Å) of cytosine-5-yl$^{\bullet}$ to 1.5 Å in 0.05 Å steps and optimized the structures. From PES we find that the proton transfer from NH_2 group of cytosine-5-yl$^{\bullet}$ (IIa) to hydroxide anion takes place with negligible barrier (ca. 0.3 kcal/mol) by producing an anionic intermediate, see Figure S8. From this intermediate the proton transfer from a water molecule hydrogen-bonded to C5 to produce aminyl radical (III) proceeds via a barrier of ca. 5 kcal/mol.

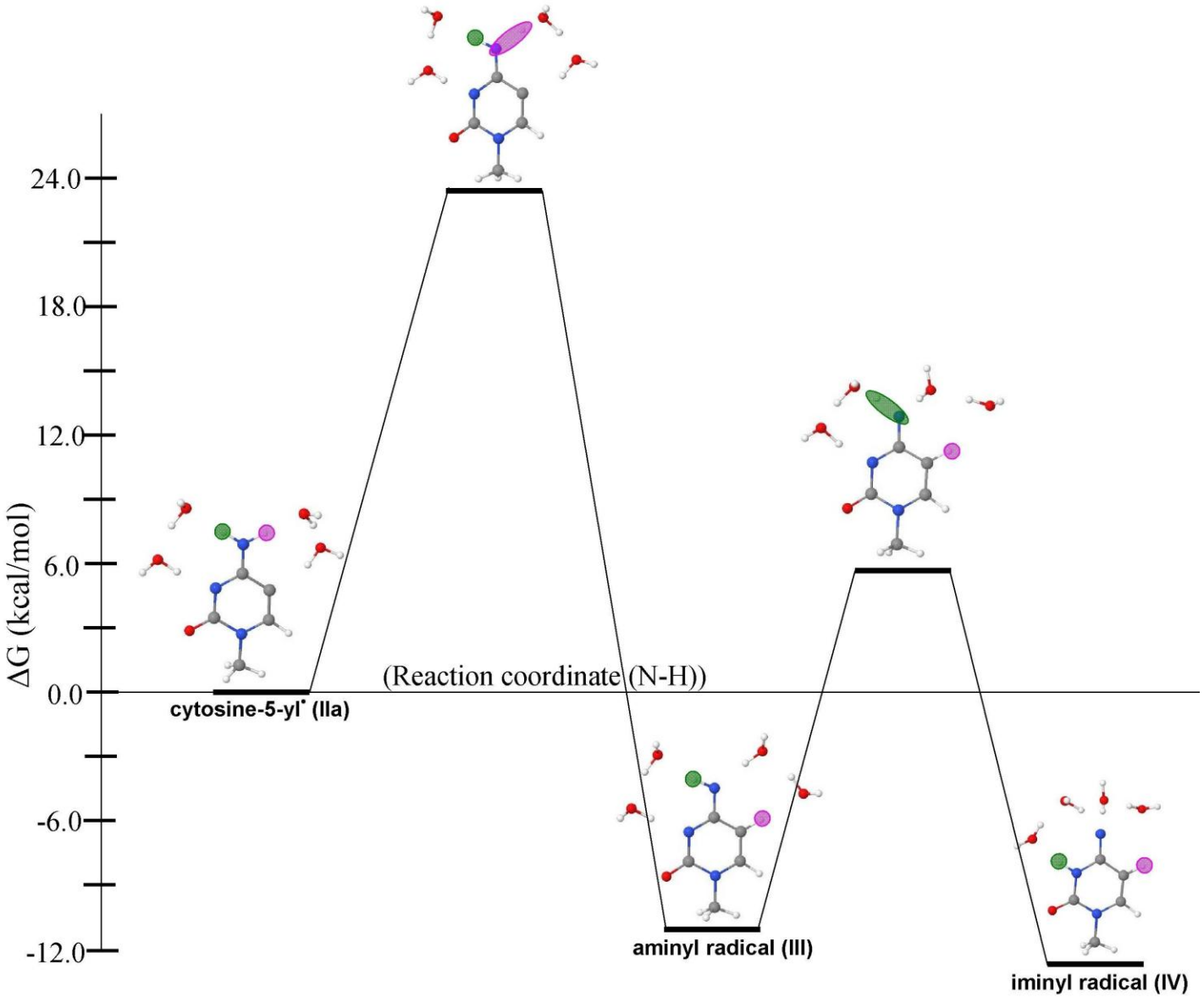


Figure S7- Potential energy surface for deprotonation reactions from cytosine-5-yl• (IIa in scheme 1) to form iminyl radical (IV in scheme 1) via aminyl radical (III in scheme 1). Relative Gibbs free energies calculated by B3LYP-PCM/6-31++G(d, p) are given in kcal/mol. The transferring two protons from NH_2 group of cytosine-5-yl• are highlighted by pink and green colors.

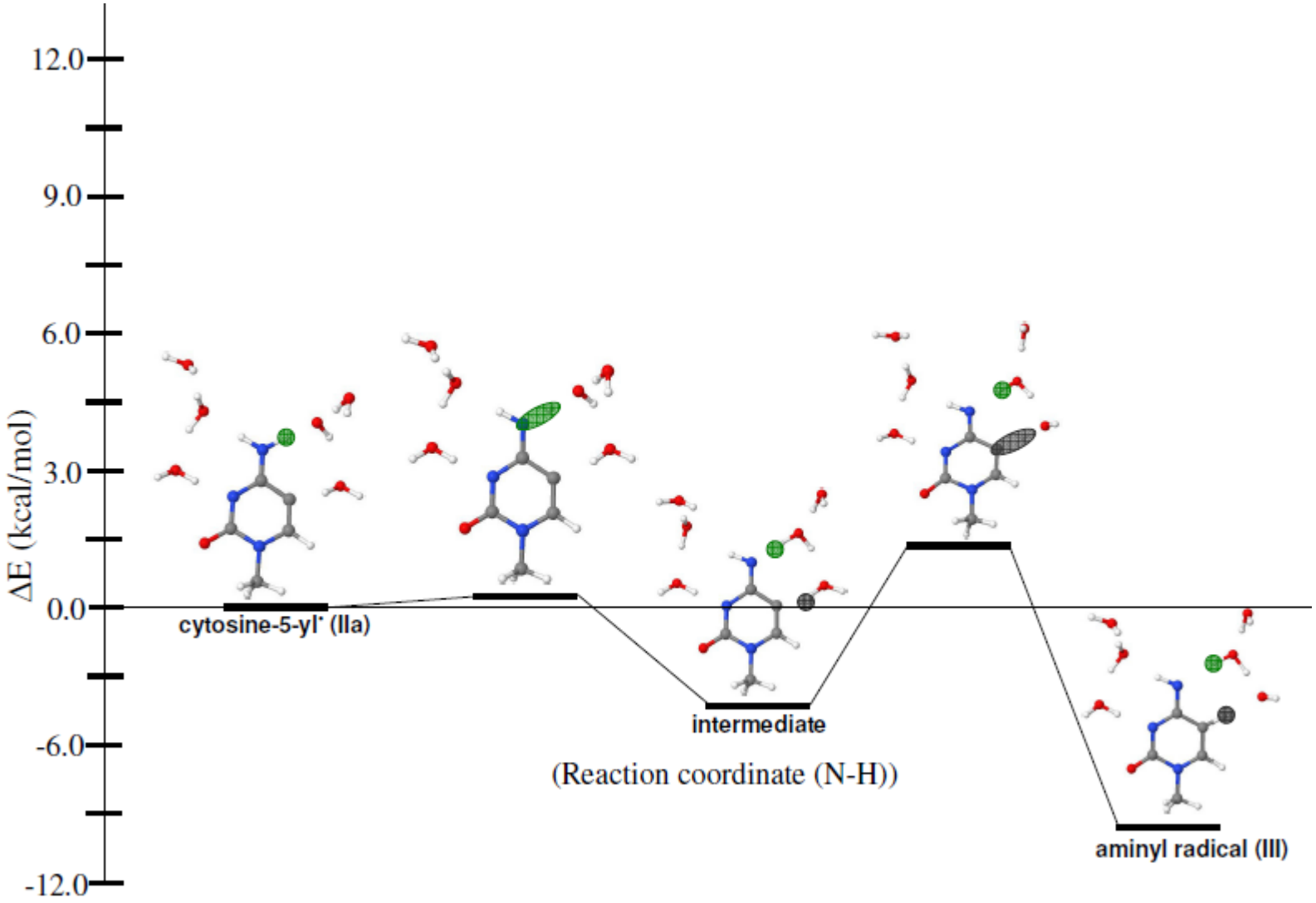


Figure S8- Potential energy surface for deprotonation reactions from cytosine-5-yl• (IIa in scheme 1) to form aminyl radical (III in scheme 1). Relative energies(ΔE) calculated by B3LYP-PCM/6-31++G(d, p) are given in kcal/mol. The transferring protons from NH_2 group of cytosine-5-yl• and water molecule are highlighted by green color and gray colors.

9. Complete Gaussian 09 reference.

Gaussian 09, Revision D.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2013.