Quantum mechanics/molecular mechanics studies on mechanistic photophysics of epigenetic C5-halogen DNA nucleoside: 2′-deoxy-5-chlorocytidine and 2′-deoxy-5-bromocytidine in aqueous solution

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1. Active Orbitals

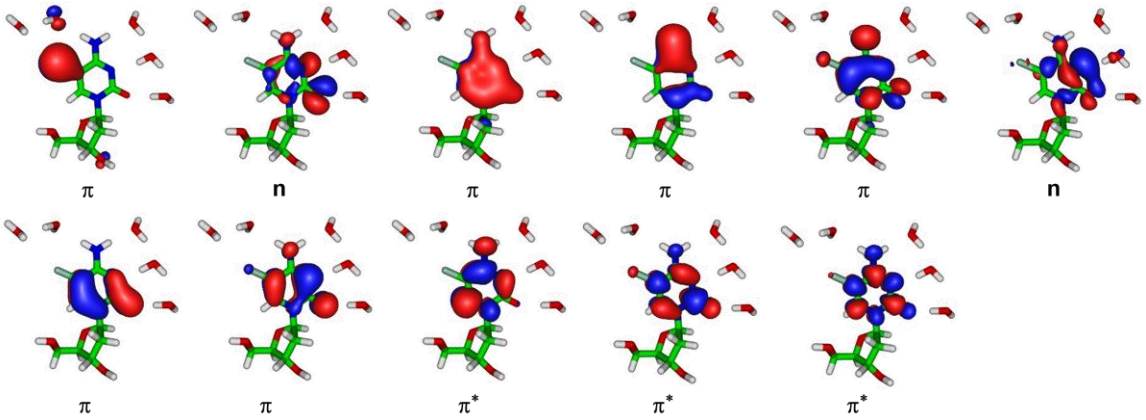

Figure S1. Molecular orbitals included in the active space for 5CldCyd used for QM/MM calculations.

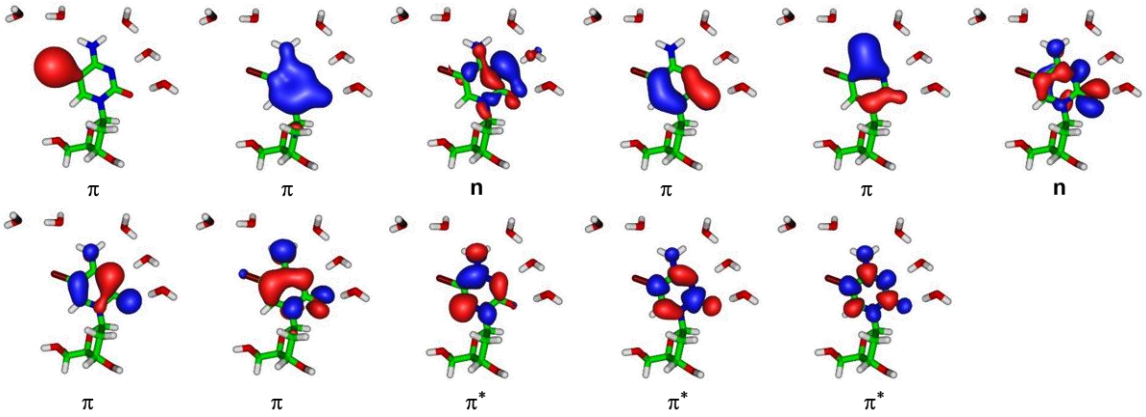

Figure S2. Molecular orbitals included in the active space for 5BrdCyd used for QM/MM calculations.

2. The Effective Spin–Orbit Couplings Expression

Spin-orbit couplings are obtained at the QM(CASPT2)/MM level within the atomic mean-field (AMFI) approximation. The effective spin-orbit couplings are expressed as follows:

$$< \psi_I | H_{eff}^{so} | \psi_J > = \sqrt{\frac{| < \psi_I | H_x^{so} | \psi_J > |^2 + | < \psi_I | H_y^{so} | \psi_J > |^2 + | < \psi_I | H_z^{so} | \psi_J > |^2}{3}}$$

in which ψ_I and ψ_J are the perturbatively modified electronic wave functions of the corresponding singlet and triplet states; H_x^{so}, H_y^{so}, H_z^{so} are the *x*, *y*, and *z* components of the spin-orbit operator.

3. Bond-Length Difference and Dihedral Angles of Minima and Conical Intersections and Crossing Points

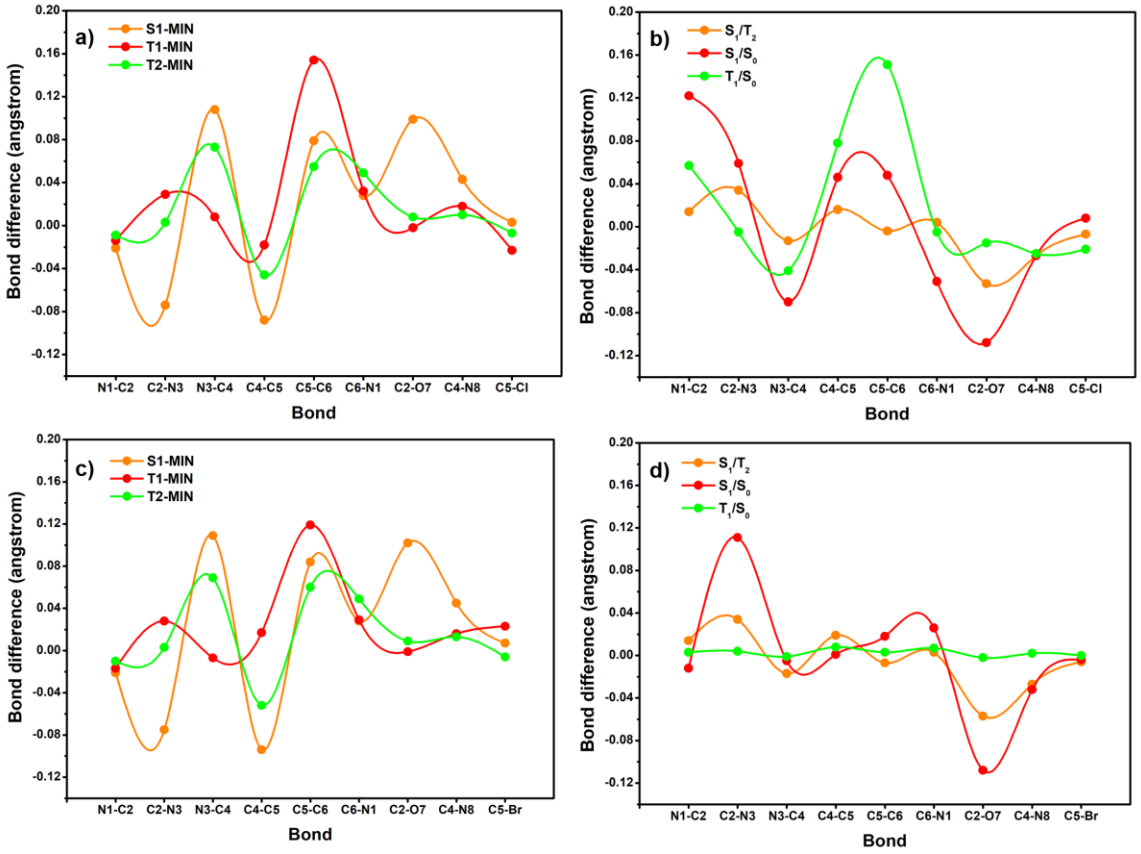

Figure S3. QM(CASSCF)/MM computed bond-length difference (in Å) of excited-state minima compared with the counterparts of the S_0 minimum S0-MIN (a) for 5CldCyd and (c) for 5BrdCyd. The positive and negative values mean they are longer and shorter than those of S0-MIN, respectively. Bond-length difference (in Å) of crossing structures compared with the counterparts of the corresponding excited-state minimum (b) for 5CldCyd and (d) for 5BrdCyd, respectively.

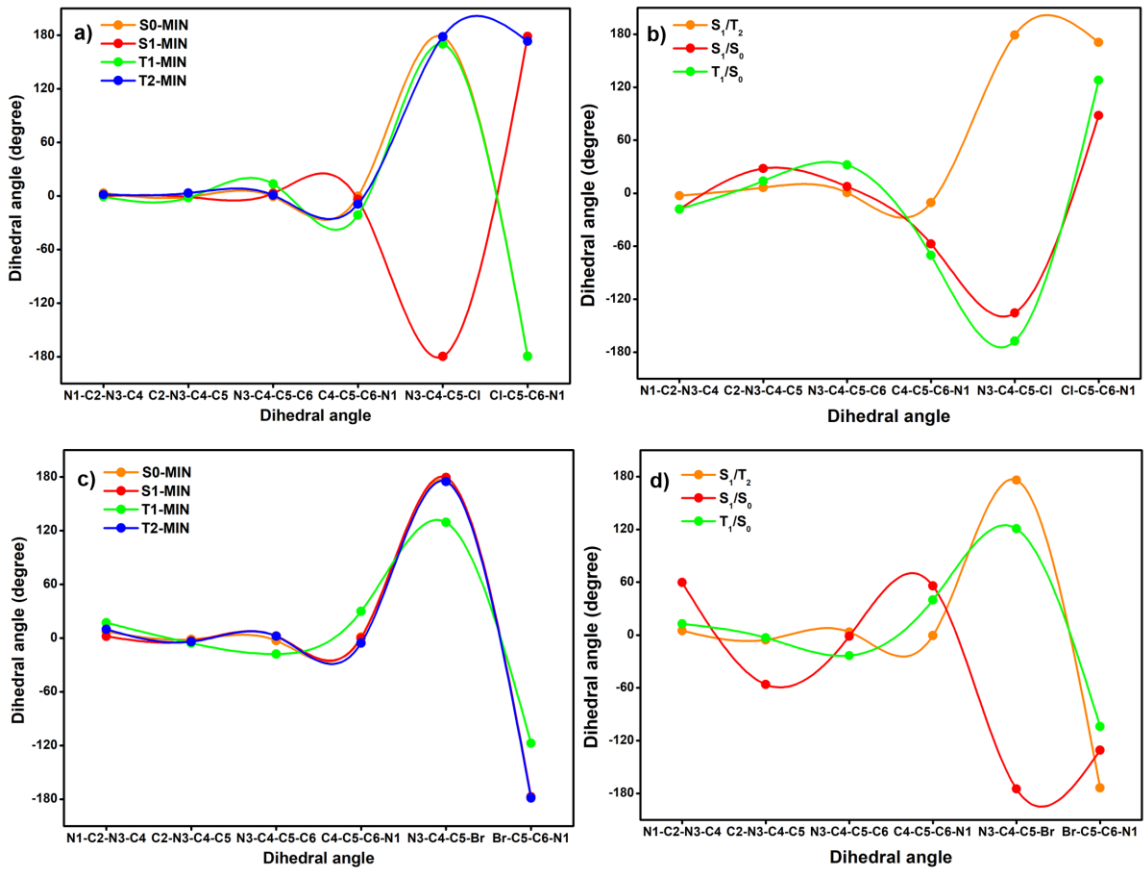

Figure S4. QM(CASSCF)/MM computed dihedral angles (in °) of minima and conical intersections and crossing points (a and b) for 5CldCyd and (c and d) for 5BrdCyd, respectively.

4. Tables

Table S1 Computed vertical excitation energies (in eV) of the low-lying excited singlet states at the S0-MIN of 5ClC/5BrC and 5ClCyd/5BrCyd in gas phase and in aqueous solution, and the experimental absorption maxima (in eV [nm]) of the lowest-energy absorption bands in aqueous solution

	Computed Values[a]		Exp.[a]
	gas	water	water
5ClC/5BrC	4.58/4.56	4.66/4.64	
5ClCyd/5BrCyd	4.66/4.64	4.69/4.66	4.32 [287]/4.30 [288]

a. J. Phys. Chem. B 2020, 124, 2560-2567.

Table S2 Computed vertical excitation energies (in eV [nm]) of the S_1 state at the S0-MIN of 5mC[a] and 5hmC[a] in gas phase, and 5mdCyd[b,c], 5hmdCyd[b], 5fdCyd[b], and 5cadCyd[b] in aqueous solution

	Computed Values		Computed Values
	$S_1(\pi\pi^*)$		$S_1(\pi\pi^*)$
5mC[a]	4.77 [260]	5fdCyd[b]	4.36 [284]
5hmC[a]	4.79 [259]	5cadCyd[b]	4.46 [278]
5mdCyd[b]	4.54 [273]	5mdCyd[c]	4.19 [296]
5hmdCyd[b]	4.56 [272]		

a. J. Phys. Chem. B 2018, 122, 10424−10434.
b. J. Phys. Chem. Lett. 2021, 12, 11070−11077.
c. J. Am. Chem. Soc. 2017, 139, 7780−7791.

Table S3 Computed adiabatic excitation energies (in kcal/mol [eV]) of S1-MIN, T1-MIN, S1S0, and S1T1 of 5mC[a], 5hmC[a], 5fC[b], and 5caC[b] in gas phase, and 5mdCyd[c,d], 5hmdCyd[c], 5fdCyd[c], and 5cadCyd[c] in aqueous solution

	S1-MIN	T1-MIN	S1S0	S1T1
5mC[a]	96.68 [4.19]	78.37 [3.40]	100.67 [4.37]	115.25 [5.00]
5hmC[a]	93.11 [4.04]	77.51 [3.36]	109.23 [4.74]	98.16 [4.26]
5fdC[b]	86.99 [3.77]	77.50 [3.36]	103.13 [4.47]	97.97 [4.25]
5cadC[b]	94.89 [4.11]	80.38 [3.49]	105.13 [4.56]	101.28 [4.39]
5mdCyd[c]	81.9 [3.55]	60.9 [2.64]	89.9 [3.90]	-
5hmdCyd[c]	86.5 [3.75]	70.3 [3.05]	93.4 [4.05]	-
5fdCyd[c]	77.7 [3.37]	61.8 [2.68]	62.3 [2.70]	-
5cadCyd[c]	95.2 [4.13]	-	92.2 [4.00]	-
5mdCyd[d]	91.8 [3.98]	-	78.4 [3.40]	-

a. J. Phys. Chem. B 2018, 122, 10424−10434.
b. J. Phys. Chem. B 2018, 122, 2704−2714.
c. J. Phys. Chem. Lett. 2021, 12, 11070−11077.
d. J. Am. Chem. Soc. 2017, 139, 7780−7791.