Electronic Supplementary Material Available:

Insight into the Acidic Group-induced Nitration Mechanism of 2-Methyl-4,6-dihydroxypyrimidine (MDP) with Nitronium

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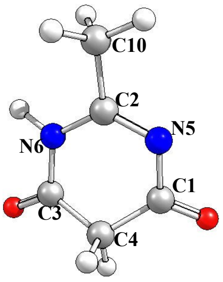
The calculated Mulliken atomic charges (e) of MDP and the relevant intermediate *via* B3LYP/6-311G(d,p). Schematic energy diagram of the direct nitration of MDP with NO_2^+ obtained *via* B3LYP-D3/6-311++G(3df,3pd)//B3LYP/6-311G(d,p). Schematic energy diagram of the HSO_4^--induced nitration of MDP with NO_2^+ obtained *via* B3LYP-D3/6-311++G(3df,3pd)// B3LYP/6-311G(d,p). Schematic energy diagram of the direct H-transfer of mono-nitro substitution product obtained *via* B3LYP-D3/6-311++G(3df,3pd)//B3LYP/6-311G(d,p). Schematic energy diagram of the direct H-transfer of di-nitro substitution product obtained *via* B3LYP-D3/6-311++G(3df,3pd)//B3LYP/6-311G(d,p). Schematic energy diagram of the *trans*-HSO_4^--induced nitration in the second nitration step in path C obtained *via* B3LYP-D3/6-311++G(3df,3pd)//B3LYP/6-311G(d,p). The Hirshfeld atomic charge of the atoms and the Coulomb attraction between the atoms of the pre-intermediates in the step ③ in paths A-C.The *f* and Δ*f* of the atoms of the pre-intermediates in the step ③ in paths A to C (calculated from the Hirshfeld charge). Optimized geometries of species for the rate-limiting step in paths A-C calculated *via* B3LYP/6-311G(d,p) (bond lengths are in angstrom). Free energies (G, Hartree) and active free energies ($\Delta G^{\neq}$, kcal mol^{-1}) for the nitration of MDP with NO_2^+ in the gas (g), formamide (f) and dimethylsulfoxide (d) phases. See DOI: 10.1039/x0xx00000x.

Table S1 The calculated Mulliken atomic charges (e) of MDP and the relevant intermediate *via* DFT-B3LYP/6-311G(d,p).



Species	C1	C2	C3	C4	N5	N6	C10
MDP	0.277	0.290	0.367	-0.342	-0.326	-0.421	-0.286
A1`-IM1	0.343	0.360	0.390	-0.319	-0.453	-0.412	-0.263
A1-IM1	0.302	0.320	0.366	-0.336	-0.390	-0.422	-0.292
A-IM3	0.355	0.428	0.357	-0.333	-0.473	-0.464	-0.322

The Mulliken atomic charges of MDP were calculated *via* the B3LYP/6-311G(d,p) method. The results are shown in Table S1. As is listed in Table S1, the negative charge centers, which may be potentially attacked by NO_2^+ in MDP, should be C4 (C in methylene group), C10 (C in methyl group), N5 and N6. It is clearly shown in our recent work that the C-nitration is much more favorable than N-nitration in the reaction of TO with NO_2^+ in the presence of acidic group of HSO_4^- /NO_3^- (RSC Adv., 2015, 5, 25183). Such calculation result has also been experimentally verified in view that the preponderant products in the nitration systems (such as NO_2^+ with TO (Explos., Pyrotech., 2005, 30, 298) and NO_2^+ with MDP (J. Org. Chem., 2004, 69, 4369; Acta Chim. Sinica, 2004, 62, 295; Org. Process Res. Dev., 2012, 16, 1711)) are found to be exactly relevant to the C-nitration results. Therefore, only the attacking of methylene C4 and methyl C10 in MDP by the nitration reagent of NO_2^+ are discussed in the present work.

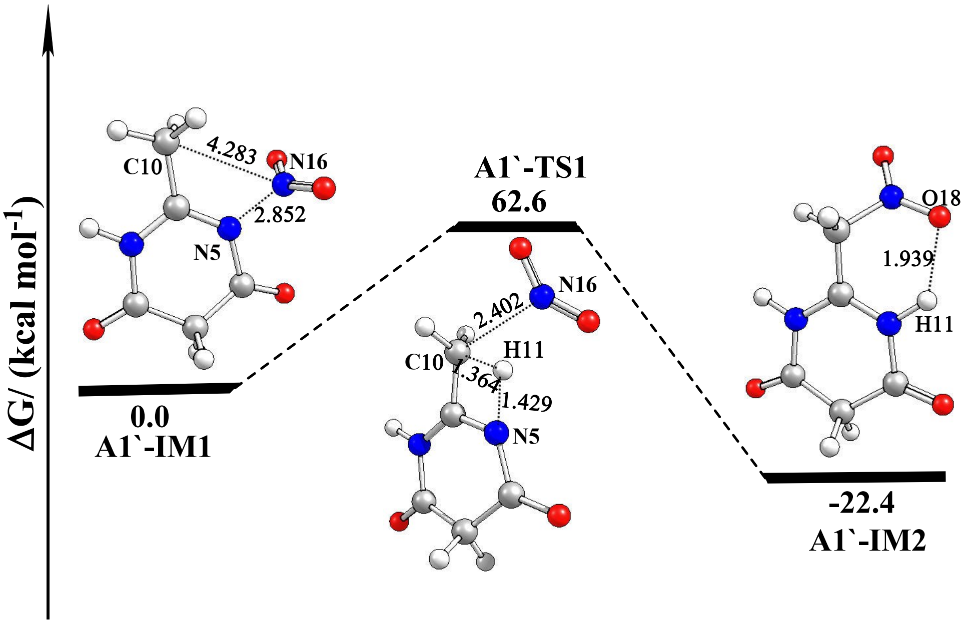


Fig. S1 Schematic energy diagram of the direct nitration of MDP with NO_2^+ obtained *via* B3LYP-D3/6-311++G(3df,3pd)//B3LYP/6-311G(d,p).

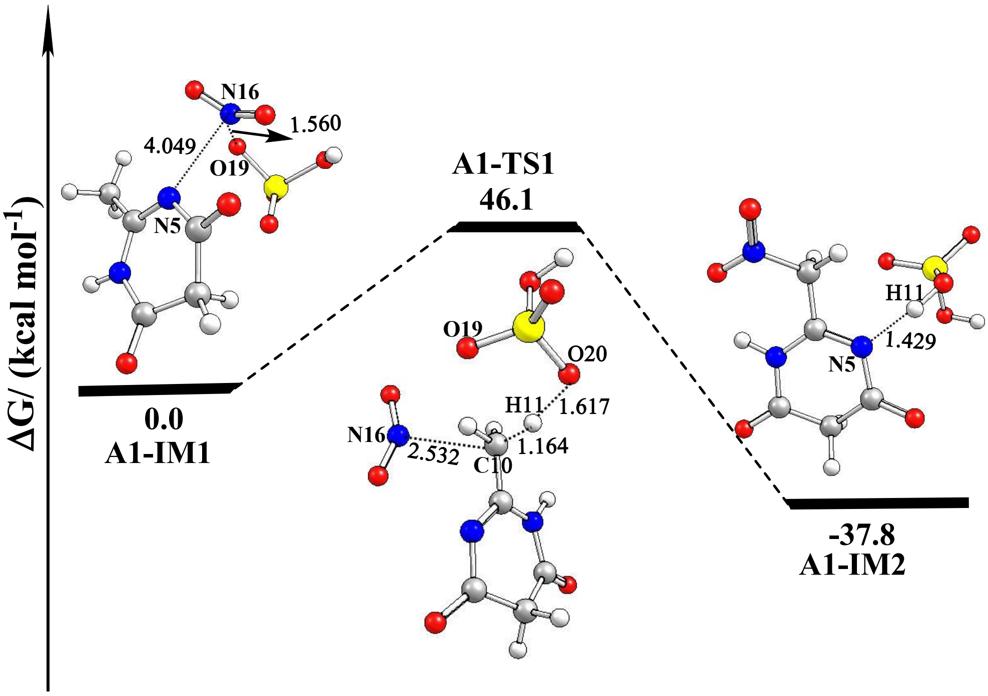


Fig. S2 Schematic energy diagram of the HSO$_4^-$-induced nitration of MDP with NO$_2^+$ obtained *via* B3LYP-D3/6-311++G(3df,3pd)//B3LYP/6-311G(d,p).

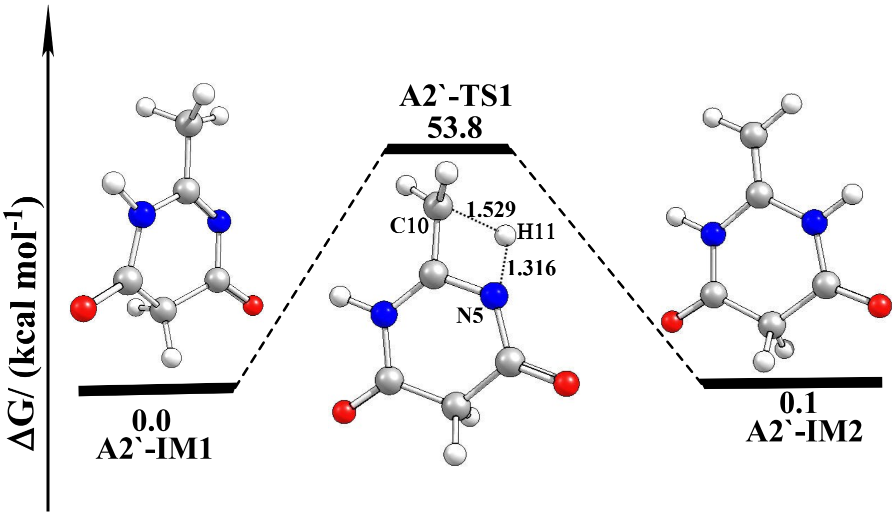


Fig. S3 Schematic energy diagram of the direct H-transfer of MDP obtained *via* B3LYP-D3/6-311++G(3df,3pd)//B3LYP/6-311G(d,p).

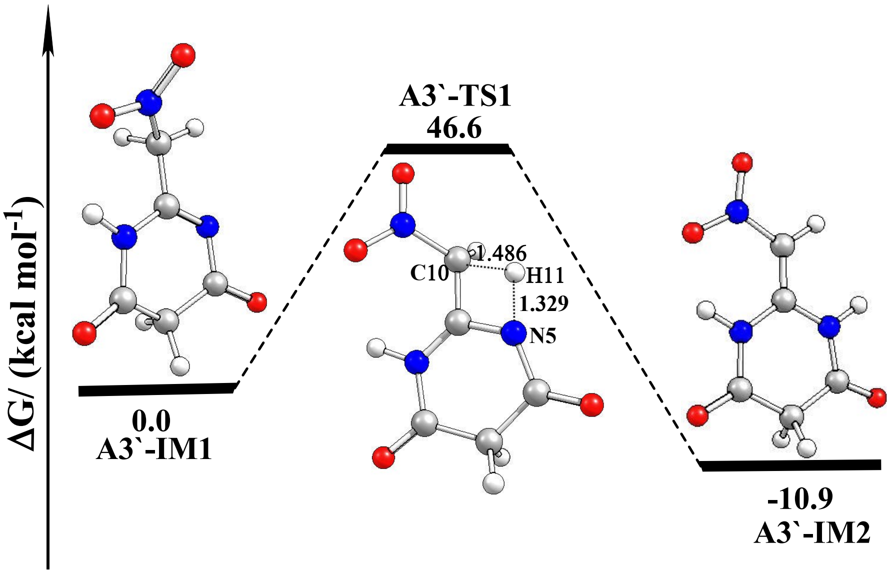


Fig. S4 Schematic energy diagram of the direct H-transfer of mono-nitro substitution product obtained *via* B3LYP-D3/6-311++G(3df,3pd)//B3LYP/6-311G(d,p).

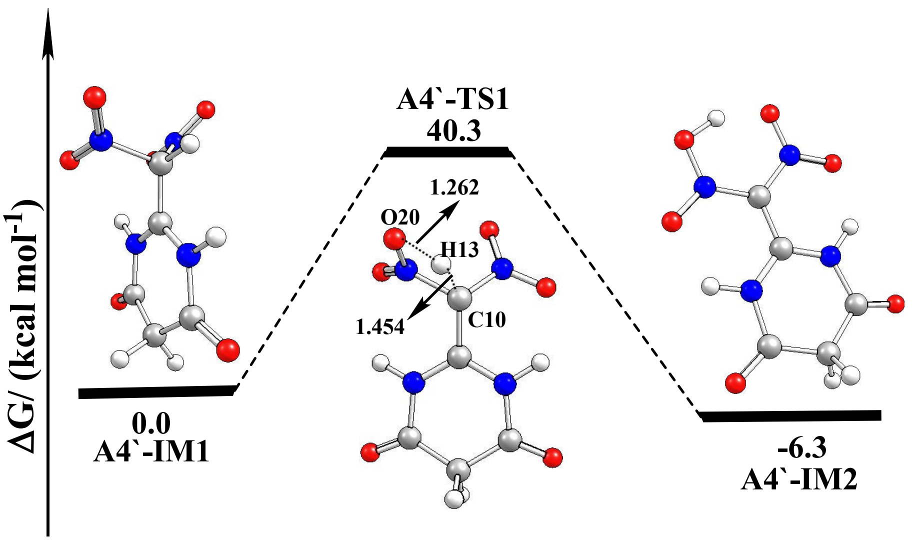


Fig. S5 Schematic energy diagram of the direct H-transfer of di-nitro substitution product obtained *via* B3LYP-D3/6-311++G(3df,3pd)//B3LYP/6-311G(d,p).

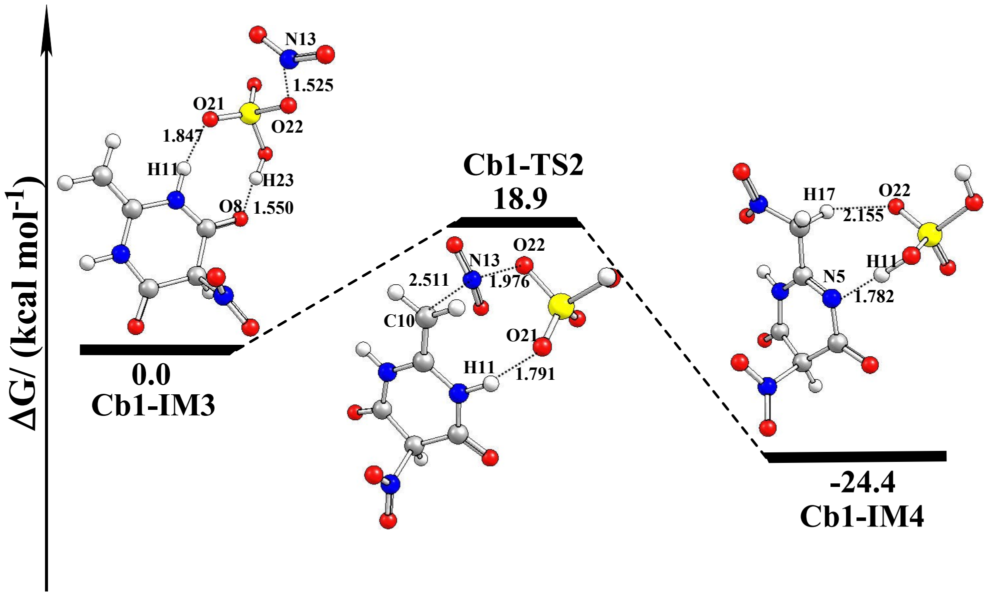


Fig. S6 Schematic energy diagram of the *trans*-HSO_4^--induced nitration in the second nitration step in path C obtained *via* B3LYP-D3/6-311++G(3df,3pd)//B3LYP/6-311G(d,p).

During the second nitration step, a *cis*-transition state, namely Cb-TS2 (Figure 5) and a *trans*-transition state, namely Cb1-TS2 (Figure S6) are obtained, which are associated with two configurations that HSO_4^--induced. It is seen that in the NO_2^+ attacking step ① in path C, the *cis*-HSO_4^--induced nitration (Figure 1, Cb-IM3→Cb-IM4, $\Delta G^{\neq} = 7.9$ kcal.mol^{-1}) is more favorable than the *trans*-HSO_4^--induced one (as shown in Figure S6, $\Delta G^{\neq} = 18.9$ kcal.mol^{-1}). Such calculation is in accordance with the results reported by Zhang et al (Chem. Eur. J., 2014, 20, 1), in which it was reported that *cis*-configuration is more stable than *trans*-configuration for double C60 adducts.

Table S2 The Hirshfeld atomic charge of the atoms and the Coulomb attraction between the atoms of the pre-intermediates in the step ③ in paths A-C.

Methods	Species	Q/e [a]			r/m [b]		F/N [c]	
		C4	N16	O8	C4-N16	O8-N16	C4-N16	O8-N16
Hirshfeld	A-IM13	-0.054	0.313	-0.128	3.325×10^{-10}	1.594×10^{-10}	3.531×10^{-11}	3.642×10^{-9}
	B-IM15	-0.066	0.309	-0.107	3.477×10^{-10}	1.498×10^{-10}	3.896×10^{-11}	3.403×10^{-9}
	Ca-IM5	-0.057	0.311	-0.107	3.475×10^{-11}	1.507×10^{-10}	3.391×10^{-11}	3.384×10^{-9}

a. Q, the atomic charge of the pre-intermediates in the step ③ in paths A to C for the nitration of MDP with NO_2^+ calculated via B3LYP/6-311G(d,p). To calculate the Coulomb force, the charge unit of *e* should be transformed to Coulomb (C) with a relationship as: 1 e=1.602×10^{-19} C; b. *r*, the distance between atoms C4 and N16 or atoms O8 and N16 is calculated *via* B3LYP/6-311G(d,p); c. *F*, the Coulomb attraction between atoms C4 and N16 or atoms O8 and N16 is calculated by Coulomb's law ($F=-kQ_1.Q_2/r^2$), where the constant k is 9.0×10^9 Nm^2/C^2 if other variables take their standard international units.

Table S3 The f and Δf of the atoms of the pre-intermediates in the step ③ in paths A to C (calculated from the Hirshfeld charge).[a]

Species	Atoms	N	N+1	N-1	f^+(r)	f^-(r)	Δf(r)
A-IM13	C4	-0.054	-0.15	0.101	0.096	0.165	-0.069
	N16	0.313	0.242	0.329	0.071	0.016	0.055
	O8	-0.128	-0.188	-0.116	0.06	0.012	0.048
B-IM15	C4	-0.066	-0.159	0.071	0.093	0.137	-0.044
	N16	0.309	0.222	0.329	0.087	0.020	0.067
	O8	-0.107	-0.154	-0.077	0.047	0.030	0.017
Ca-IM5	C4	-0.057	-0.124	0.072	0.067	0.129	-0.062
	N16	0.311	0.252	0.330	0.059	0.019	0.040
	O8	-0.107	-0.139	-0.078	0.032	0.029	0.003

a. Hirshfeld charge in their N, N+1 and N-1 electrons states for the corresponding atoms in the step ③ in paths A to C is calculated and listed in columns 3 to 5. The condensed f^- and f^+ and Δf is calculated and listed in columns 6 to 8.

According to the calculation method (J. Chem. Theory Comput. 2010, 6, 1470; Computers & Chemistry, 2012, 33, 580), the f referred to the difference of atomic charges in two states. f and Δf can be expressed and calculated as

$$f^+(\mathrm{r}) = q_{\mathrm{N}} - q_{\mathrm{N+1}} \qquad (1)$$

$$f^-(\mathrm{r}) = q_{\mathrm{N-1}} - q_{\mathrm{N}} \qquad (2)$$

$$\Delta f(\mathrm{r}) = f^+(\mathrm{r}) - f^-(\mathrm{r}) \qquad (3)$$

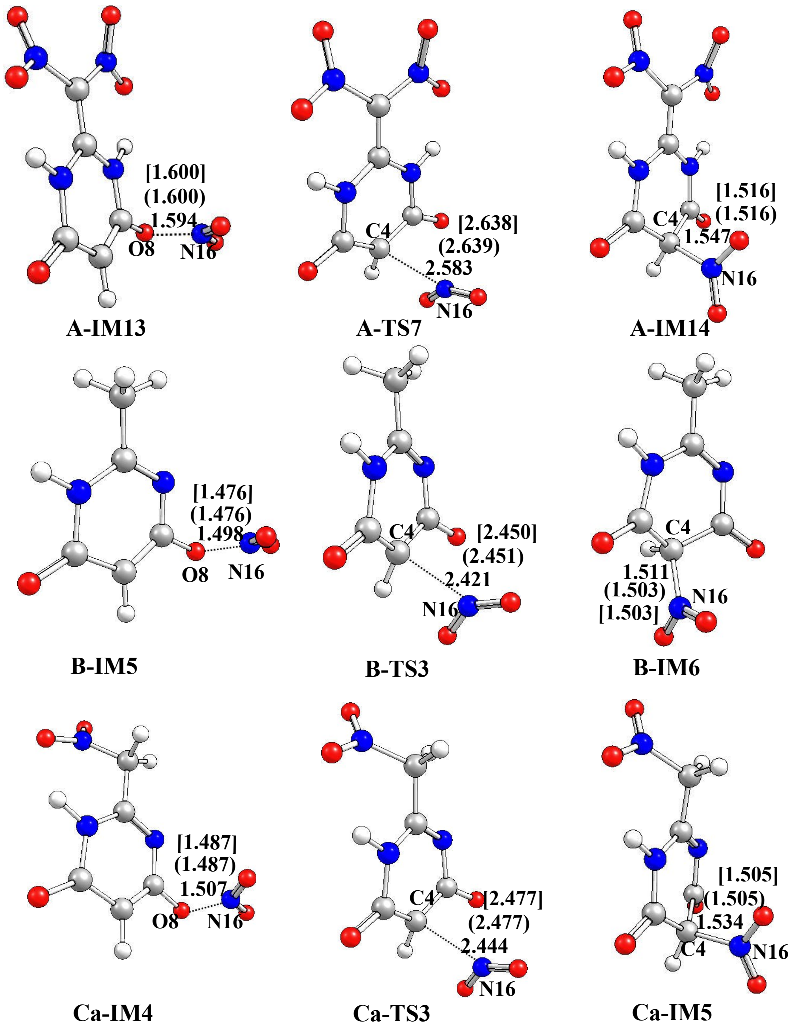


Fig. S7 Optimized geometries of species for the rate-limiting step in paths A-C calculated *via* B3LYP/6-311G(d,p) (bond lengths are in angstrom). For the bond lengths of specicies, no-bracket, bracket and square brackets respect gas, formamide and DMSO phases, respectively.

Table S4 Free energies (G, Hartree) and active free energies ($\Delta G^{\neq}$, kcal mol^{-1}) for the nitration of MDP with NO_2^+ in the gas (g) and formamide (f) and dimethylsulfoxide (d) phases.[a]

System	G(g)	ΔG≠(g)	G(f)	ΔG≠(f)	G(d)	ΔG≠(d)
A-IM13	-1067.868880		-1067.892100		-1067.892111	
A-TS7	-1067.833941		-1067.858344		-1067.858129	
A-IM14	-1067.910558		-1067.934647		-1067.934649	
A-IM13→A-IM14		21.9		21.2		21.3
B-IM5	-658.7420287		-658.7569809		-658.7567593	
A-TS7	-658.6957357		-658.7123957		-658.7121419	
B-IM6	-658.7711167		-658.7960904		-658.7956936	
B-IM5→B-IM6		29.1		27.9		28.0
Ca-IM5	-863.3096296		-863.3276008		-863.3715784	
A-TS7	-863.2636412		-863.2834389		-863.3273402	
Ca-IM6	-863.3395476		-863.3639724		-863.2831436	
Ca-IM5→Ca-IM6		28.9		27.7		27.8

[a] ZPG was obtained *via* DFT at the B3LYP/6-311G(d,p) level. The energy value (ΔG) was obtained *via* DFT at the B3LYP-D3/6-311++G(3df,3pd)//B3LYP/6-311G(d,p) level.