Supplementary Materials

On Prototropy and Bond-Length Alternation in Neutral and Ionized Pyrimidine Bases and Their Model Azines in Vacuo

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Table S1. Relative Gibbs energies (ΔG)[a] for neutral, positively and negatively ionized tautomers-rotamers of phenol and mono-hydroxy aromatic azines.

Compound	Isomer	ΔG		
		Neutral	**Radical cation**	**Radical anion**
Phenol[b]	**a**	0.0	0.0	0.0
	b/d	16.7	26.6	−19.8
	c	16.3	31.6	−11.1
2-Hydroxypyridine[c]	**2HOPY-a1**	0.0	0.0	0.0
	2HOPY-a2	5.2	6.3	5.2
	2HOPY-b	−0.9	−11.0	−11.4
	2HOPY-c	23.0	30.7	−1.0
	2HOPY-d	23.6	30.0	−13.7
4-Hydroxypyridine[c]	**4HOPY-a**	0.0	0.0	0.0
	4HOPY-b/d	17.5	23.8	−20.3
	4HOPY-c	1.2	−11.4	−6.9
2-Hydroxypyrimidine[c]	**2HOPM-a1/a2**	0.0	0.0	0.0
	2HOPM-b/d	0.9	−7.9	−10.3
	2HOPM-c	24.7	17.9	3.0
4-Hydroxypyrimidine[c]	**4HOPM-a1**	0.0	0.0	0.0
	4HOPM-a2	5.2	4.0	4.9
	4HOPM-b	−2.1	−17.2	−12.3
	4HOPM-c	7.0	−9.7	5.2
	4HOPM-d	24.5	15.0	−14.0

[a] ΔG (in kcal mol^{-1}) refers to difference between G of **a**-**d** and that of **a** (or **a1**) estimated at the DFT(B3LYP)/6-311+G(d,p) level at 298.15 K. [b] As in ref. [18]. [c] As in ref. [49].

Table S2. Relative Gibbs energies (ΔG)[a] for neutral, positively and negatively ionized tautomers-rotamers of aniline and mono-amino aromatic azines.

Compound	Isomer	ΔG		
		Neutral	Radical cation	Radical anion
Aniline[b]	**a**	0.0	0.0	0.0
	b1/d2	28.2	43.1	−4.7
	b2/d1	28.4	43.0	−3.4
	c	26.5	47.9	4.6
2-Aminopyridine[c]	**2APY-a**	0.0	0.0	0.0
	2APY-b1	16.7	7.5	5.3
	2APY-b2	13.9	3.9	2.0
	2APY-c1	28.8	50.2	7.9
	2APY-c2	32.8	51.2	11.6
	2APY-d1	30.4	50.4	−4.2
	2APY-d2	35.0	52.9	0.6
4-Aminopyridine[c]	**4APY-a**	0.0	0.0	0.0
	4APY-b1/d2	30.4	39.8	−3.4
	4APY-b2/d1	29.8	39.8	−4.6
	4APY-c	16.4	−1.9	8.3
2-Aminopyrimidine[d]	**2APM-a**	0.0	0.0	0.0
	2APM-b1/d2	24.1	14.7	10.2
	2APM-b2/d1	17.4	6.5	3.5
	2APM-c	36.4	44.0	15.6
4-Aminopyrimidine[e]	**4APM-a**	0.0	0.0	0.0
	4APM-b1	16.2	4.8	4.6
	4APM-b2	13.3	1.5	1.5
	4APM-c1	18.2	1.8	14.3
	4APM-c2	22.2	6.2	18.0
	4APM-d1	32.2	42.4	−4.9
	4APM-d2	36.8	43.0	−0.3

[a] ΔG (in kcal mol^{-1}) refers to difference between G of **a**-**d** and that of **a** estimated at the DFT(B3LYP)/6-311+G(d,p) level at 298.15 K. [b] As in ref. [22]. [c] As in ref. [58]. [d] As in ref. [59]. [e] As in refs [60,61].

Table S3. Relative Gibbs energies (ΔG)[a] for neutral, positively and negatively ionized tautomers-rotamers of pyrimidine bases.

		ΔG		
Compound	**Isomer**	**Neutral**	**Radical cation**	**Radical anion**
Uracil[b]	**U13**	–13.9	–11.5	–22.8
	U17a	15.2	9.8	7.1
	U17b	5.6	0.9	5.8
	U18a	–1.6	–4.8	–11.3
	U18b	5.1	1.8	–5.0
	U35	2.7	25.3	–24.9
	U37a	–2.3	–9.0	–6.8
	U37b	5.1	–1.7	nf
	U38a	9.8	0.9	–4.2
	U38b	7.3	–0.5	–4.2
	U57a	21.4	24.2	–12.6
	U57b	19.8	24.2	–14.1
	U58a	20.3	23.0	–1.7
	U58b	27.8	29.3	4.6
	U78aa	0.0	0.0	0.0
	U78ab	5.3	6.8	6.3
	U78ba	1.1	0.6	1.0
	U78bb	5.3	7.9	5.7
Cytosine[c]	**C13a**	2.5	2.4	–4.9
	C13b	0.8	1.3	–7.9
	C17aa	26.7	14.5	15.8
	C17ab	31.0	18.1	20.1
	C17ba	17.6	5.8	18.0
	C17bb	21.0	9.4	20.7
	C18	–1.4	0.2	–10.4
	C35a	17.7	nf	–11.3
	C35b	17.3	37.2	–11.9
	C37aa	15.9	5.9	10.0
	C37ab	13.1	3.1	7.8
	C37ba	23.3	14.6	13.5

	C37bb	20.5	10.8	nf
	C38	5.6	–0.4	–7.3
	C57aa	30.8	38.6	–2.9
	C57ab	35.9	nf	1.9
	C57ba	29.9	39.2	–3.6
	C57bb	34.2	nf	0.4
	C58	20.0	25.2	–1.3
	C78a	0.0	0.0	0.0
	C78b	0.7	0.4	0.9
Isocytosine[d]	**iC13a**	7.8	14.5	–4.5
	iC13b	6.5	11.6	–5.6
	iC17	10.4	17.0	1.9
	iC18aa	21.4	14.1	8.4
	iC18ab	28.2	20.0	14.8
	iC18ba	15.2	7.0	2.6
	iC18bb	21.2	12.0	8.2
	iC35a	15.0	37.8	–11.9
	iC35b	20.1	nf	–5.8
	iC37	0.8	–1.6	–8.8
	iC38aa	25.7	15.3	9.1
	iC38ab	23.3	12.8	nf
	iC38ba	33.2	24.0	15.2
	iC38bb	29.9	20.6	nf
	iC57	16.8	26.7	–15.1
	iC58aa	31.1	44.2	10.7
	iC58ab	39.1	50.8	17.0
	iC58ba	31.7	44.6	12.0
	iC58bb	38.7	50.8	17.4
	iC78a	0.0	0.0	0.0
	iC78b	4.4	5.4	4.5

[a] ΔG (in kcal mol^{-1}) for **U**, **C**, and **iC** relative to G of **U78aa**, **C78a**, and **iC78a**, respectively, estimated at the DFT(B3LYP)/6-311+G(d,p) level at 298.15 K (nf – structure not found). [b] As in refs [62,63]. [c] As in ref. 64]. [d] As in refs [28,57,65].

Table S4. HOMED6[a,b] and HOMED7[b,c] indices for neutral, positively and negatively ionized tautomers-rotamers of phenol and mono-hydroxy aromatic azines.

Compound	Isomer	Neutral		Radical cation		Radical anion	
		HOMED6	HOMED7	HOMED6	HOMED7	HOMED6	HOMED7
Phenol[d]	**a**	0.999_7	0.920	0.918	0.927	0.994	0.916
	b/d	0.374	0.470	0.518	0.606	0.455	0.567
	c	0.403	0.498	0.613	0.685	0.503	0.609
2-HO-pyridine[e]	**2HOPY-a1**	0.995	0.943	0.919	0.933	0.880	0.782
	2HOPY-a2	0.996	0.935	0.908	0.922	0.908	0.802
	2HOPY-b	0.803	0.812	0.808	0.807	0.745	0.792
	2HOPY-c	0.332	0.425	−0.023	0.083	0.477	0.586
	2HOPY-d	0.342	0.428	0.166	0.233	0.432	0.541
4- HO-pyridine[e]	**4HOPY-a**	0.999	0.937	0.979	0.970	0.972	0.907
	4HOPY-b/d	0.358	0.454	0.305	0.394	0.483	0.587
	4HOPY-c	0.754	0.782	0.944	0.955	0.832	0.855
2- HO-pyrimidine[e]	**2HOPM-a1/a2**	1.000	0.961	0.990	0.989	0.856	0.776
	2HOPM-b/d	0.785	0.744	0.788	0.789	0.730	0.774
	2HOPM-c	0.259	0.350	0.087	0.154	0.454	0.558
4- HO-pyrimidine[e]	**4HOPM-a1**	0.995	0.957	0.983	0.977	0.870	0.790
	4HOPM-a2	0.996	0.950	0.983	0.977	0.892	0.801
	4HOPM-b	0.774	0.782	0.824	0.823	0.731	0.778
	4HOPM-c	0.681	0.706	0.937	0.949	0.795	0.816
	4HOPM-d	0.313	0.401	0.060	0.153	0.491	0.584

[a] HOMED6 for six-membered ring (six bonds). [b] Calculated for structures optimized at the DFT(B3LYP)/6-311+G(d,p) level. [c] HOMED7 for entire molecule (eight bonds). [d] Data taken from ref. [18]. [e] Data taken from ref. [49].

Table S5. HOMED6[a,b] and HOMED7[b,c] indices for neutral, positively and negatively ionized tautomers-rotamers of aniline and mono-amino aromatic azines.

Compound	Isomer	Neutral		Radical cation		Radical anion	
		HOMED6	HOMED7	HOMED6	HOMED7	HOMED6	HOMED7
Aniline[d]	**a**	0.998	0.948	0.926	0.942	0.994	0.952
	b1/d2	0.384	0.486	0.711	0.760	0.490	0.597
	b2/d1	0.353	0.459	0.670	0.725	0.470	0.582
	c	0.413	0.511	0.680	0.747	0.514	0.595
2-H_2N-pyridine[e]	**2APY-a**	0.994	0.996	0.929	0.944	0.923	0.846
	2APY-b1	0.767	0.791	0.913	0.925	0.714	0.772
	2APY-b2	0.802	0.818	0.927	0.937	0.786	0.829
	2APY-c1	0.356	0.453	0.669	0.721	0.535	0.605
	2APY-c2	0.352	0.454	0.722	0.779	0.486	0.595
	2APY-d1	0.365	0.453	0.697	0.755	0.500	0.599
	2APY-d2	0.324	0.424	0.200	0.266	0.448	0.560
4-H_2N-pyridine[e]	**4APY-a**	0.996	0.969	0.947	0.958	0.983	0.956
	4APY-b1/d2	0.334	0.440	0.587	0.659	0.498	0.602
	4APY-b2/d1	0.373	0.470	0.683	0.742	0.520	0.618
	4APY-c	0.744	0.779	0.936	0.949	0.820	0.849
2-H_2N-pyrimidine[f]	**2APM-a**	0.995	0.986	0.939	0.951	0.870	0.812
	2APM-b1/d2	0.743	0.760	0.925	0.917	0.701	0.758
	2APM-b2/d1	0.790	0.795	0.945	0.955	0.779	0.819
	2APM-c	0.298	0.397	0.173	0.248	0.489	0.596
4-H_2N-pyrimidine[g]	**4APM-a**	0.991	0.981	0.950	0.960	0.904	0.843
	4APM-b1	0.737	0.756	0.924	0.936	0.712	0.767
	4APM-b2	0.707	0.736	0.938	0.949	0.775	0.818
	4APM-c1	0.664	0.701	0.917	0.934	0.777	0.805
	4APM-c2	0.663	0.702	0.921	0.936	0.773	0.804
	4APM-d1	0.346	0.435	0.122	0.226	0.557	0.640
	4APM-d2	0.170	0.297	0.106	0.210	0.470	0.574

[a] HOMED6 for six-membered ring (six bonds). [b] Calculated for structures optimized at the DFT(B3LYP)/6-311+G(d,p) level. [c] HOMED7 for entire molecule (eight bonds). [d] Data from ref. [22]. [e] Data from ref. [58]. [f] Data from ref. [59]. [g] Data from refs [60,61].

Table S6. HOMED6[a,b] and HOMED8[b,c] indices for neutral, positively and negatively ionized tautomers-rotamers of pyrimidine bases.

		Neutral		Radical cation		Radical anion	
Compound	**Isomer**	**HOMED6**	**HOMED8**	**HOMED6**	**HOMED8**	**HOMED6**	**HOMED8**
Uracil[d]	**U13**	0.698	0.688	0.571	0.553	0.567	0.659
	U17a	0.650	0.649	0.913	0.924	0.773	0.777
	U17b	0.741	0.728	0.933	0.942	0.770	0.762
	U18a	0.788	0.762	0.789	0.796	0.763	0.701
	U18b	0.770	0.738	0.836	0.839	0.768	0.684
	U35	0.342	0.402	0.464	0.521	0.336	0.469
	U37a	0.769	0.755	0.807	0.806	0.600	0.592
	U37b	0.754	0.739	0.785	0.787	nf	nf
	U38a	0.771	0.747	0.709	0.720	0.748	0.680
	U38b	0.788	0.758	0.765	0.768	0.749	0.681
	U57a	0.337	0.429	0.194	0.323	0.500	0.515
	U57b	0.384	0.466	0.200	0.331	0.496	0.515
	U58a	0.281	0.370	−0.017	0.116	0.416	0.460
	U58b	0.217	0.320	0.032	0.155	0.380	0.413
	U78aa	0.995	0.926	0.893	0.914	0.859	0.690
	U78ab	0.994	0.918	0.875	0.898	0.880	0.691
	U78ba	0.996	0.925	0.903	0.924	0.843	0.674
	U78bb	0.996	0.920	0.984	0.976	0.864	0.678
Cytosine[e]	**C13a**	0.688	0.690	0.727	0.714	0.582	0.670
	C13b	0.709	0.706	0.745	0.730	0.634	0.708
	C17aa	0.629	0.636	0.916	0.925	0.760	0.772
	C17ab	0.622	0.633	0.915	0.920	0.753	0.766
	C17ba	0.671	0.680	0.924	0.933	0.762	0.762
	C17bb	0.671	0.683	0.930	0.935	0.762	0.757
	C18	0.785	0.791	0.850	0.866	0.756	0.703
	C35a	0.351	0.415	nf	nf	0.363	0.494
	C35b	0.331	0.402	0.150	0.276	0.381	0.507
	C37aa	0.734	0.731	0.902	0.912	0.625	0.611
	C37ab	0.777	0.767	0.923	0.931	0.704	0.674
	C37ba	0.714	0.752	0.878	0.890	0.798	0.797

	C37bb	0.768	0.755	0.902	0.912	nf	nf
	C38	0.799	0.794	0.749	0.754	0.727	0.692
	C57aa	0.351	0.439	0.647	0.734	0.548	0.550
	C57ab	0.296	0.400	nf	nf	0.509	0.523
	C57ba	0.395	0.473	0.650	0.737	0.549	0.553
	C57bb	0.344	0.438	nf	nf	0.512	0.529
	C58	0.267	0.391	−0.017	0.129	0.434	0.501
	C78a	0.990	0.943	0.896	0.917	0.853	0.660
	C78b	0.992	0.944	0.912	0.929	0.849	0.662
Isocytosine[f]	**iC13a**	0.700	0.695	0.717	0.714	0.571	0.662
	iC13b	0.705	0.701	0.715	0.706	0.568	0.660
	iC17	0.694	0.710	0.896	0.920	0.792	0.810
	iC18aa	0.757	0.744	0.928	0.939	0.726	0.680
	iC18ab	0.723	0.706	0.925	0.934	0.726	0.658
	iC18ba	0.795	0.771	0.947	0.952	0.785	0.721
	iC18bb	0.777	0.747	0.945	0.948	0.788	0.703
	iC35a	0.371	0.437	0.428	0.491	0.422	0.542
	iC35b	0.355	0.426	nf	nf	0.365	0.501
	iC37	0.810	0.795	0.794	0.794	0.682	0.675
	iC38aa	0.796	0.773	0.902	0.913	0.787	0.717
	iC38ab	0.803	0.777	0.931	0.937	nf	nf
	iC38ba	0.733	0.722	0.864	0.883	0.728	0.672
	iC38bb	0.753	0.737	0.906	0.917	nf	nf
	iC57	0.361	0.476	0.179	0.326	0.504	0.548
	iC58aa	0.327	0.414	0.634	0.722	0.469	0.511
	iC58ab	0.272	0.362	0.561	0.666	0.432	0.463
	iC58ba	0.331	0.418	0.636	0.724	0.459	0.502
	iC58bb	0.280	0.369	0.580	0.680	0.423	0.456
	iC78a	0.994	0.946	0.919	0.930	0.867	0.715
	iC78b	0.991	0.936	0.916	0.924	0.903	0.740

[a] HOMED6 for six-membered ring (six bonds). [b] Calculated for structures optimized at the DFT(B3LYP)/6-311+G(d,p) level (nf – structure not found). [c] HOMED8 for entire molecule (eight bonds). [d] Data from refs [62,63]. [e] Data from ref. [64]. [f] Data from refs [28,57,65].

Table S7. Composition of isomeric mixtures for neutral mono-hydroxy aromatic azines estimated at the G2 level.

Derivative	Amount of isomer (x_i in %)					Ref.
	a1	**a2**	**b**	**c**	**d**	
2HOPY	73[b]	$2\ 10^{-2}$	27	$1\ 10^{-14}$	$2\ 10^{-15}$	[49]
4HOPY	99		$1\ 10^{-11}$	1	$1\ 10^{-11}$	[49]
2HOPM	99		1	$5\ 10^{-15}$	1	[49]
4HOPM	20	$1\ 10^{-2}$	80	$5\ 10^{-5}$	$9\ 10^{-16}$	[49]

Figure S1. Twenty-one tautomers-rotamers possible for **iC**. Two labile protons indicated in bold red color.

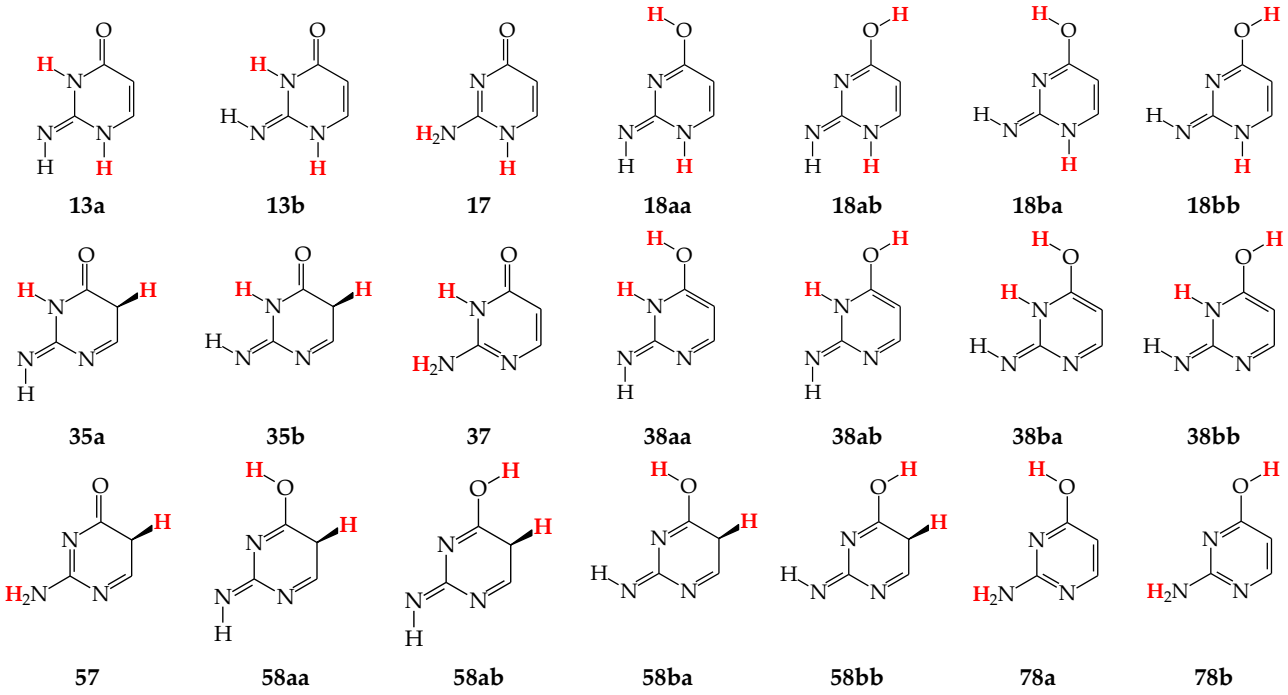


Figure S2. Plots between ΔGs of all tautomers-rotamers of neutral pyrimidine bases. DFT data taken from refs [62,64,65].

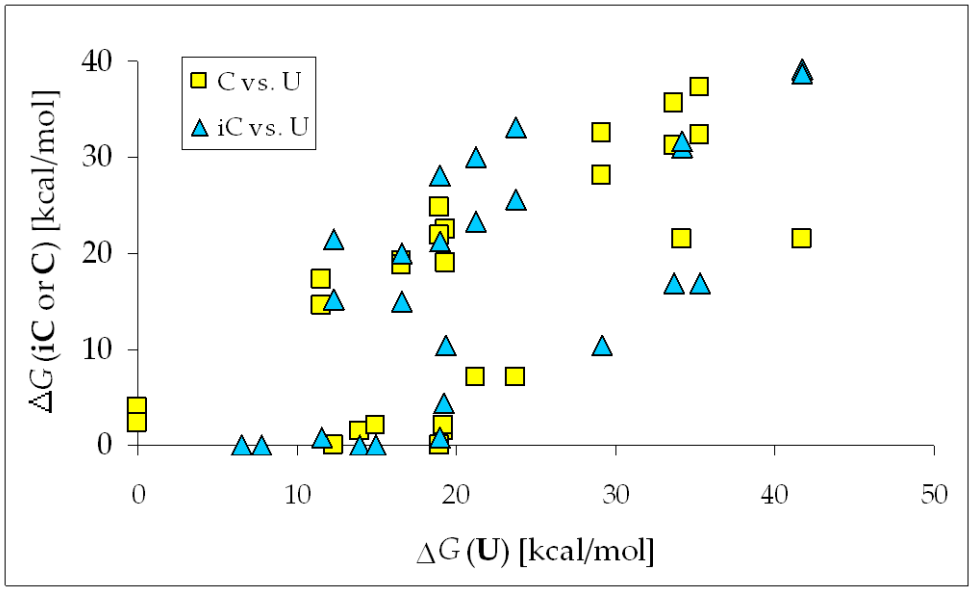
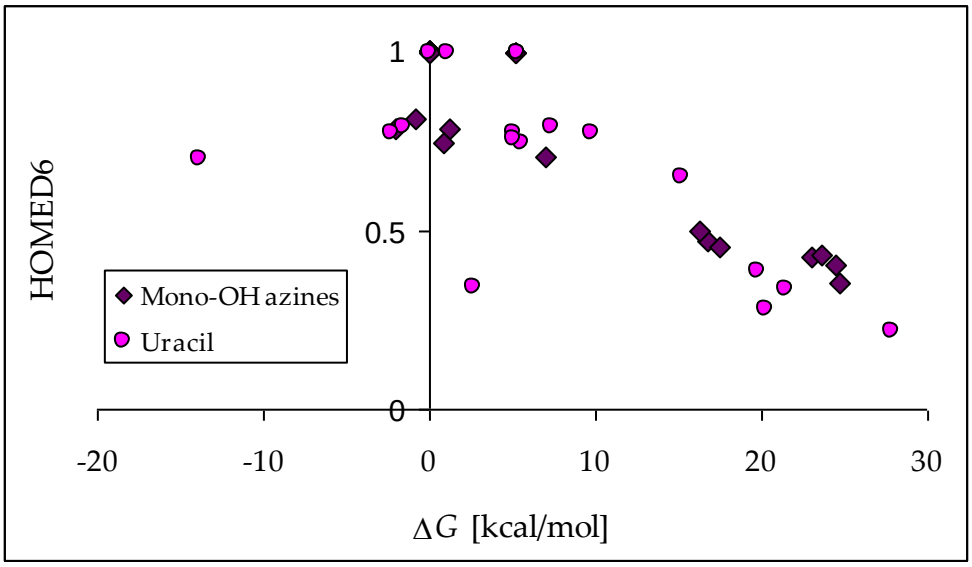


Figure S3. Plots between HOMED6s and ΔGs of all tautomers-rotamers of mono-hydroxy aromatic azines (including phenol) and uracil containing one and two exo OH, respectively (a), and also for all isomers of cytosine and isocytosine containing one exo OH and one exo NH_2 (b). DFT data taken from refs [18,44,62,64,65].

(a) Mono-hydroxy azines (including phenol) and uracil



(b) Cytosine and isocytosine

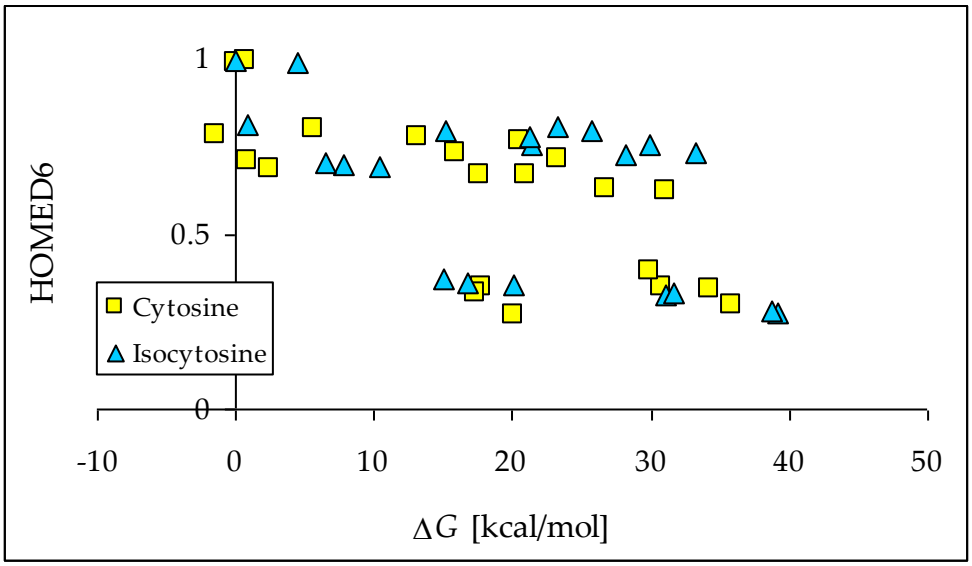


Figure S4. Plots between HOMED8s and ΔGs of all tautomers-rotamers of neutral pyrimidine bases. DFT data taken from refs [62,64,65].

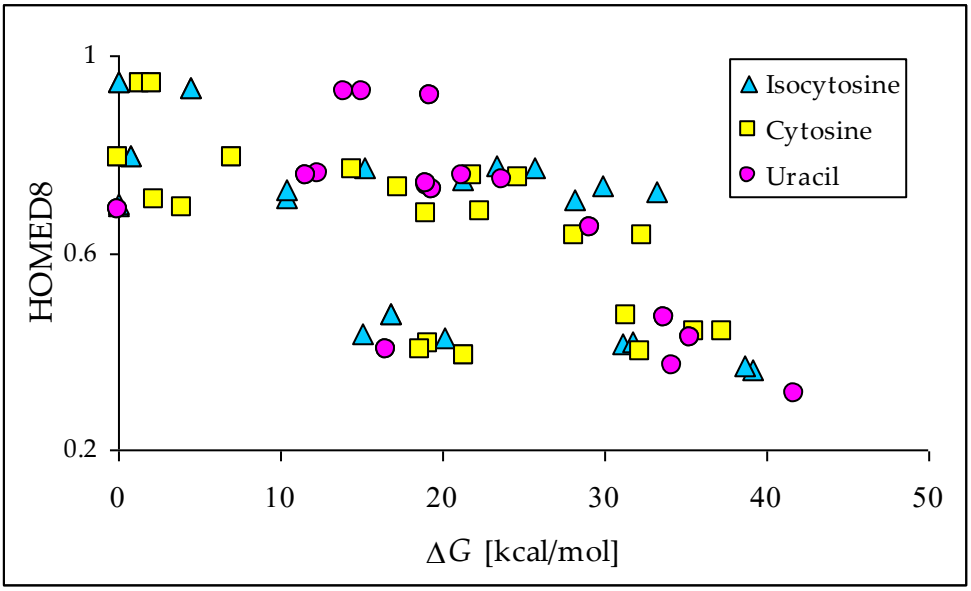
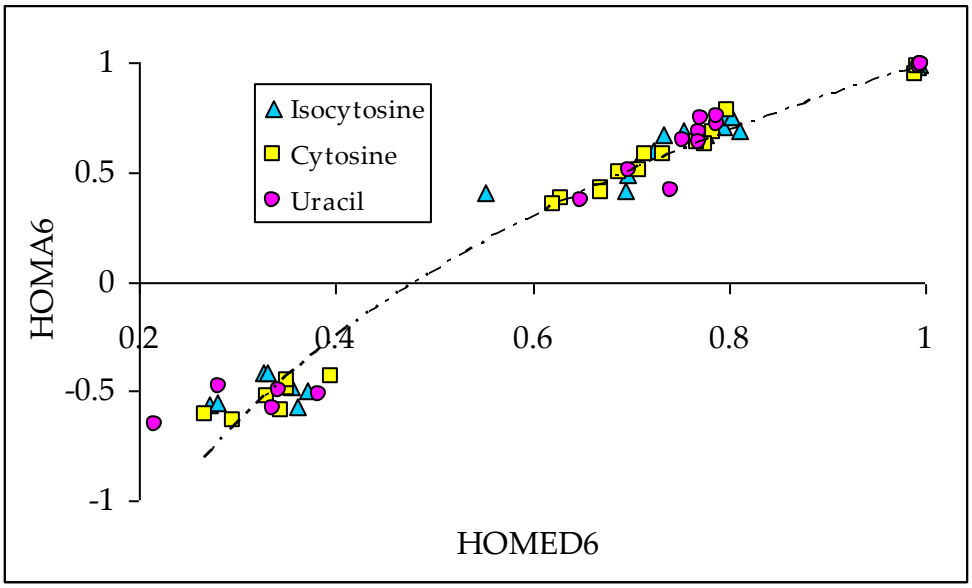


Figure S5. Lack of linear relations between the reformulated HOMA and HOMED indices estimated for all tautomers-rotamers of neutral pyrimidine bases in the six-membered ring (a) and in the entire molecule (b). DFT-calculated geometric parameters taken from refs [65,68].

(a) Six-membered ring



(b) Entire molecule

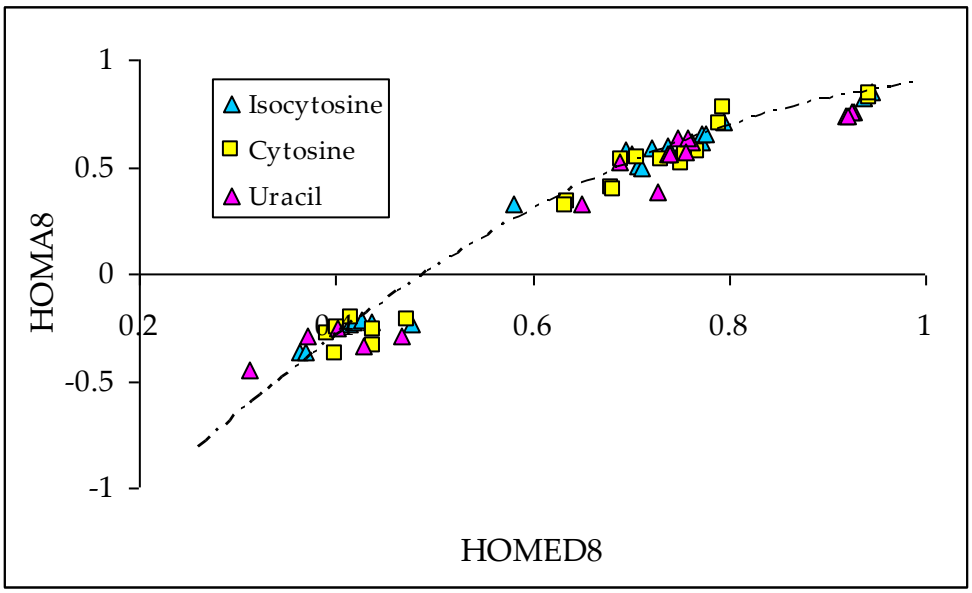
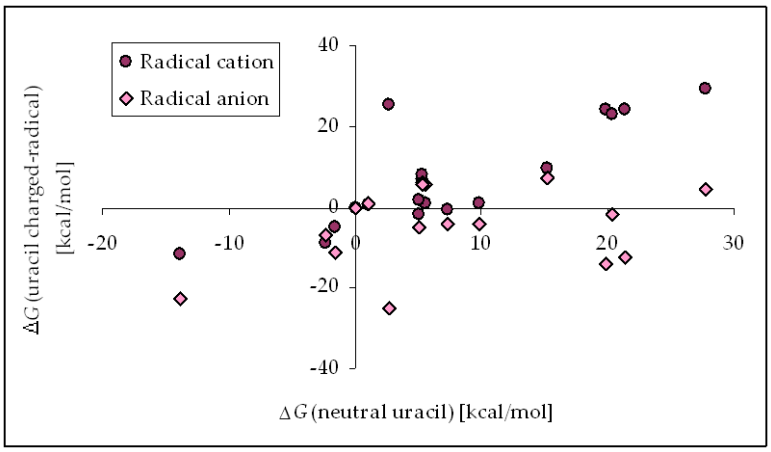
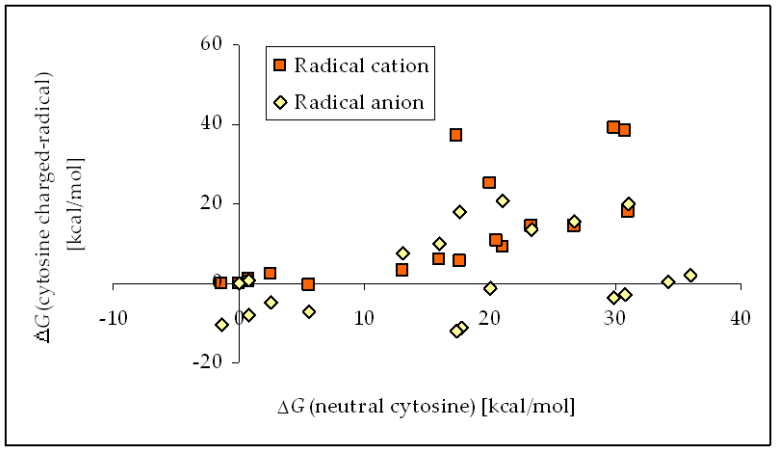


Figure S6. Plots between ΔGs of neutral and ionized tautomers-rotamers of uracil (a), cytosine (b), and isocytosine (c). DFT data taken from refs [28,57,62,63,64,65].

(a) Uracil



(b) Cytosine



(c) Isocytosine

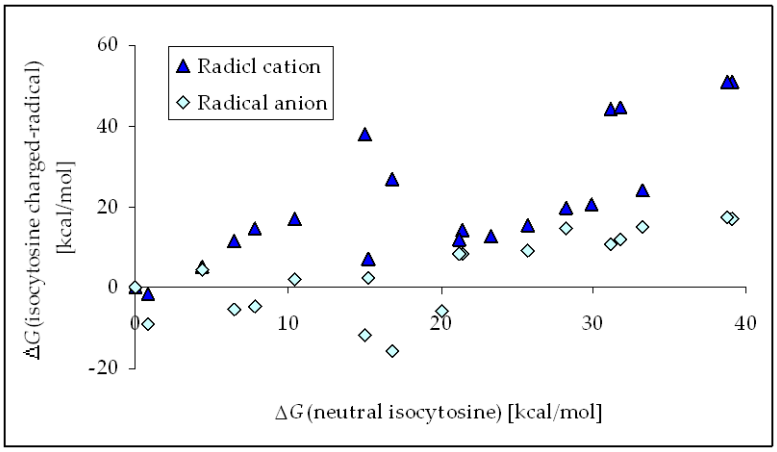
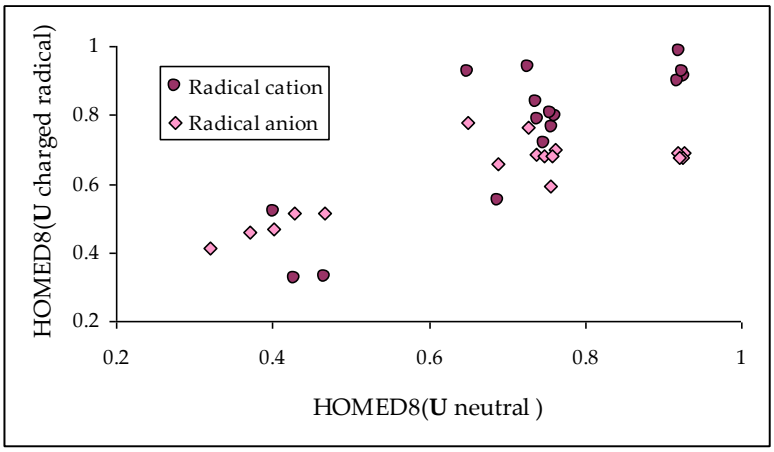
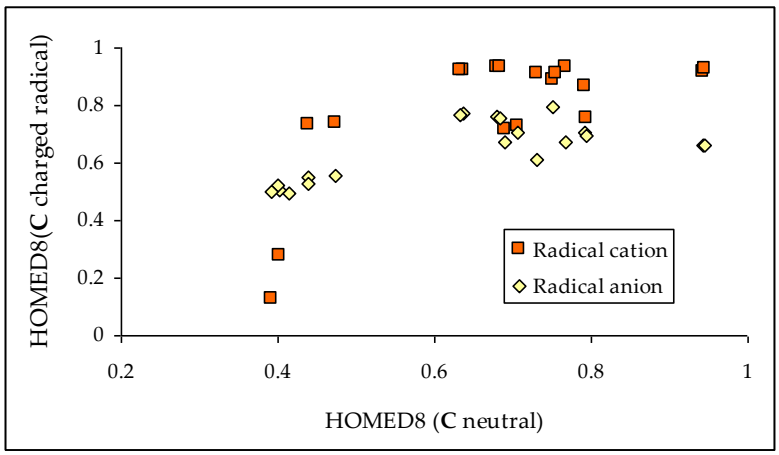


Figure S7. Plots between HOMED8s of neutral and ionized tautomers-rotamers of uracil (a), cytosine (b), and isocytosine (c). DFT data taken from refs [28,57,62,63,64,65].

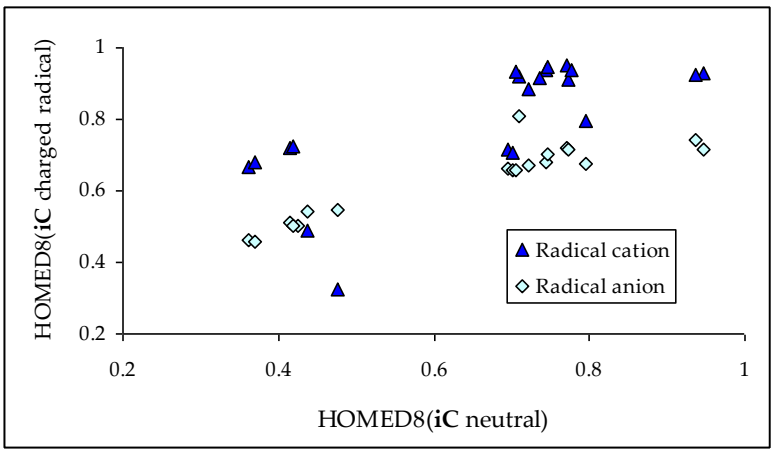
(a) Uracil



(b) Cytosine



(c) Isocytosine



List of abbreviations applied in the main text

2APM	2-aminopyrimidine
4APM	4-aminopyrimidine
5APM	5-aminopyrimidine
2APY	2-aminopyridine
3APY	3-aminopyridine
4APY	4-aminopyridine
2HOPM	2-hydroxypyrimidine
4HOPM	4-hydroxypyrimidine
5HOPM	5-hydroxypyrimidine
2HOPY	2-hydroxypyridine
3HOPY	3-hydroxypyridine
4HOPY	4-hydroxypyridine
A	adenine
α	normalization constant
AM1	Austin Model 1
B3LYP	Becke-style three-parameter hybrid exchange functional with non-local correlation functional of Lee, Yang, and Parr
C	cytosine
CASSCF	complete active space self-consistent field
CCSD(T)	coupled cluster method including single-, double- and triple-excitation
CID	collision-induced dissociation
DFT	density functional theory
E	energy
EA	electron affinity
ESR	electron spin resonance
FT-MW	Fourier transform microwave
G	guanine
G	Gibbs energy
G2	Gaussian-2 theory
G2(MP2)	MP2 variant of Gaussian-2 theory
G4	Gaussian-4 theory
G*n*	Gaussian-*n* theory
HX	hypoxanthine
H	enthalpy
HF	Hartree-Fock self-consistent field
HOMA	harmonic oscillator model of aromaticity
HOMED	harmonic oscillator model of electron delocalization
HX	hypoxanthine
iC	isocytosine
ICR	ion cyclotron resonance
IE	ionization energy
IR	infrared
IRMPD	infrared multiple-photon dissociation
IUPAC	International Union of Pure and Applied Chemistry

K	equilibrium constant
LA-MB-FT-MW	laser-ablation molecular-beam Fourier-transform microwave
LFER	linear free-energy relationship
M	molecule
MNDO	modified neglect of diatomic overlap
MP2	second-order Møller-Plesset (perturbation theory)
MPn	n-order Møller-Plesset (perturbation theory)
MS	mass spectrometry
MW	microwave
n	number of bonds
NMR	nuclear magnetic resonance
PM3	parametric method 3
PES	photoelectron spectroscopy
QCISD(T)	quadratic configuration interaction method including single-, double- and triple-excitation
R	molar gas constant
REMPI	resonantly enhanced multiphoton ionization
R_d	double bond-length
R_i	bond-length in investigated compound
R_o	optimum bond-length
R_s	single bond-length
RNA	ribonucleic acid
S	entropy
T	thymine
T	temperature
TD-DFT	time-dependent density functional theory
U	uracil
UA	uric acid
UV	ultraviolet
UVPD	UV-vis photodissociation
X	xanthine
ZEKE	zero kinetic energy