

Computational Determination of Aqueous pK_a Values of Protonated Benzimidazoles (Part 1)

Trevor N. Brown and Nelaine Mora-Diez*

Supporting Information

(Tables S1 to S5 and Appendix; Total pages: 15)

* Corresponding author. E-mail: nmora@tru.ca

Table S1:

Raw data (energies in atomic units and G_{solv} in kcal/mol) for the aqueous pK_a calculations (at 298.15 K) of protonated benzimidazole at different levels of theory. The data provided corresponds to benzimidazole (Neutral), protonated benzimidazole (Cation), 2-methylbenzimidazole (2-met), protonated 2-methylbenzimidazole (2-met cat), water, and the hydroxide and the hydronium ions.

Level of Theory	Species	$E_{\text{gas}}^{\text{total}}$	$E_{\text{aq}}^{\text{total}}$	ZPC	TCG	q	G_{solv}
MP2/6-31+G(d,p)//AM1 PCM gas-phase	Neutral	-378.74762	-378.76641	0.12090	0.09049	9.725E+13	-12.34
	Cation	-379.11859	-379.21623	0.13298	0.10265	8.949E+13	-62.69
	2-met	-417.93933	-417.95584	0.14880	0.11553	1.994E+15	-10.10
	2-met cat	-418.31628	-418.40600	0.16054	0.12655	4.318E+15	-55.96
	OH^-	-75.60144	-75.76218	0.00827	-0.00794	2.862E+07	-104.11
	H_2O	-76.23301	-76.24557	0.02045	0.00280	1.307E+08	-7.35
	H_3O^+	-76.50610	-76.68268	0.03193	0.01378	2.247E+08	-111.27
	MP2/6-31+G(d,p)//AM1 COSMO gas-phase	Neutral	-378.74762	-378.76477	0.12090	0.09049	9.725E+13
Cation		-379.11857	-379.21270	0.13298	0.10265	8.924E+13	-55.49
2-met		-417.93933	-417.95600	0.14880	0.11554	1.983E+15	-5.53
2-met cat		-418.31628	-418.40569	0.16054	0.12655	4.318E+15	-50.73
OH^-		-75.60144	-75.74549	0.00827	-0.00794	2.862E+07	-91.11
H_2O		-76.23301	-76.24646	0.02045	0.00280	1.307E+08	-6.76
H_3O^+		-76.50610	-76.65233	0.03193	0.01378	2.247E+08	-89.88
HF/6-31+G(d,p) PCM aqueous-phase		Neutral	-	-377.51876	0.12606	0.09618	5.567E+13
	Cation	-	-377.97933	0.13962	0.10966	6.059E+13	-
	2-met	-	-416.56593	0.15489	0.12259	7.193E+14	-
	2-met cat	-	-417.02977	0.16849	0.13566	1.257E+15	-
	OH^-	-	-75.55361	0.00495	-0.01139	3.270E+07	-
	H_2O	-	-76.04349	0.02225	0.00465	1.251E+08	-
	H_3O^+	-	-76.48230	0.03127	0.01314	2.181E+08	-
	HF/6-31+G(d,p) PCM aqueous-phase	Neutral	-377.49987	-377.51836	0.12689	0.09696	5.836E+13
Cation		-377.88239	-377.97891	0.14170	0.11174	6.027E+13	-59.73
2-met		-416.54784	-416.56555	0.15581	0.12359	6.636E+14	-9.71
2-met cat		-416.93821	-417.02926	0.17057	0.13787	1.100E+15	-55.90
OH^-		-75.38396	-75.55276	0.00928	-0.00693	2.881E+07	-104.81
H_2O		-76.03123	-76.04336	0.02312	0.00555	1.215E+08	-6.93
H_3O^+		-76.31104	-76.47943	0.03686	0.01882	2.002E+08	-105.96
MP2/6-31+G(d,p) PCM aqueous-phase		Neutral	-	-378.77078	0.11719	0.08677	9.832E+13
	Cation	-	-379.22145	0.12997	0.09945	1.092E+14	-
	2-met	-	-417.96333	0.14509	0.11111	4.257E+15	-
	2-met cat	-	-418.41657	0.15797	0.12445	2.602E+15	-
	OH^-	-	-	-	-	-	-
	H_2O	-	-76.24580	0.02069	0.00302	1.346E+08	-
	H_3O^+	-	-76.68311	0.02798	0.00977	2.381E+08	-
	MP2/6-31+G(d,p) PCM gas-phase	Neutral	-378.75295	-378.77044	0.11839	0.08797	9.865E+13
Cation		-379.12617	-379.22098	0.13240	0.10194	1.022E+14	-60.08
2-met		-417.94632	-417.96300	0.14639	0.11296	2.376E+15	-10.24
2-met cat		-418.32585	-418.41600	0.16051	0.12748	1.563E+15	-56.26
OH^-		-75.60211	-75.76593	0.00873	-0.00754	3.020E+07	-105.89
H_2O		-76.23311	-76.24566	0.02165	0.00401	1.306E+08	-7.34
H_3O^+		-76.50826	-76.67956	0.03516	0.01706	2.110E+08	-107.89
MP2/6-31+G(d,p) COSMO gas-phase		Neutral	-378.75295	-378.77025	0.11840	0.08798	9.851E+13
	Cation	-379.12617	-379.22072	0.13242	0.10197	1.015E+14	-55.79
	2-met	-	-	-	-	-	-
	2-met cat	-	-	-	-	-	-
	OH^-	-75.60211	-75.74610	0.00873	-0.00754	3.020E+07	-91.04
	H_2O	-76.23311	-76.24650	0.02165	0.00401	1.306E+08	-6.70

	H ₃ O ⁺	-76.50826	-76.65306	0.03516	0.01706	2.110E+08	-88.97
B3LYP/6-31+G(d,p) PCM aqueous-phase	Neutral	-	-379.91054	0.11738	0.08723	7.320E+13	-
	Cation	-	-380.36464	0.13011	0.09988	8.055E+13	-
	2-met	-	-419.23715	0.14456	0.11170	1.289E+15	-
	2-met cat	-	-419.69447	0.15735	0.12401	2.164E+15	-
	OH ⁻	-	-	-	-	-	-
	H ₂ O	-	-76.44637	0.02041	0.00274	1.351E+08	-
	H ₃ O ⁺	-	-76.88220	0.02733	0.00911	2.409E+08	-
B3LYP/6-31+G(d,p) PCM gas-phase	Neutral	-379.89326	-379.91020	0.11820	0.08801	7.677E+13	-9.39
	Cation	-380.26974	-380.36416	0.13224	0.10202	7.971E+13	-58.24
	2-met	-419.22050	-419.23683	0.14550	0.11280	1.100E+15	-8.67
	2-met cat	-419.60428	-419.69394	0.15954	0.12631	1.923E+15	-54.87
	OH ⁻	-75.80343	-75.96619	0.00855	-0.00771	3.021E+07	-100.87
	H ₂ O	-76.43405	-76.44624	0.02129	0.00364	1.312E+08	-6.94
	H ₃ O ⁺	-76.70777	-76.87848	0.03432	0.01621	2.143E+08	-107.28
B3LYP/6-31+G(d,p) COSMO gas-phase	Neutral	-379.89326	-379.91014	0.11820	0.08801	7.677E+13	-5.14
	Cation	-380.26975	-380.36423	0.13224	0.10202	7.966E+13	-53.88
	2-met	-419.22050	-419.23693	0.14550	0.11280	1.100E+15	-3.81
	2-met cat	-419.60428	-419.69364	0.15954	0.12631	1.923E+15	-49.57
	OH ⁻	-75.80343	-75.94683	0.00855	-0.00771	3.021E+07	-87.75
	H ₂ O	-76.43405	-76.44697	0.02129	0.00364	1.312E+08	-6.13
	H ₃ O ⁺	-76.70777	-76.85202	0.03432	0.01621	2.143E+08	-88.70
B3LYP/6-311++G(d,p) PCM gas-phase	Neutral	-379.96718	-379.98416	0.11774	0.08754	7.755E+13	-9.45
	Cation	-380.34301	-380.43735	0.13172	0.10149	8.064E+13	-58.23
	2-met	-	-	-	-	-	-
	2-met cat	-	-	-	-	-	-
	OH ⁻	-75.82733	-75.98977	0.00855	-0.00770	2.998E+07	-100.70
	H ₂ O	-76.45846	-76.47021	0.02129	0.00365	1.303E+08	-6.67
	H ₃ O ⁺	-76.73107	-76.90166	0.03429	0.01618	2.131E+08	-107.21
B3LYP/6-311++G(2df,2p) COSMO gas-phase	Neutral	-379.99260	-380.00868	0.11808	0.08792	7.428E+13	-4.73
	Cation	-380.36986	-380.46377	0.13204	0.10183	7.801E+13	-53.62
	2-met	-	-	-	-	-	-
	2-met cat	-	-	-	-	-	-
	OH ⁻	-75.82979	-75.97237	0.00856	-0.00770	2.988E+07	-87.24
	H ₂ O	-76.46262	-76.47381	0.02136	0.00372	1.297E+08	-5.06
	H ₃ O ⁺	-76.73458	-76.87852	0.03438	0.01629	2.114E+08	-88.52
B3LYP/aug-cc-pvdz PCM gas-phase	Neutral	-379.91494	-379.93122	0.11797	0.08782	7.395E+13	-8.96
	Cation	-380.29046	-380.38432	0.13191	0.10170	7.823E+13	-57.87
	2-met	-	-	-	-	-	-
	2-met cat	-	-	-	-	-	-
	OH ⁻	-75.81693	-75.97257	0.00851	-0.00775	3.020E+07	-96.41
	H ₂ O	-76.44464	-76.45471	0.02123	0.00358	1.316E+08	-5.60
	H ₃ O ⁺	-76.71473	-76.88486	0.03402	0.01591	2.141E+08	-106.90

$E_{\text{gas}}^{\text{total}}$: total gas-phase energy; $E_{\text{aq}}^{\text{total}}$: total aqueous-phase energy; ZPC: zero-point energy correction; TCG: thermal correction to the Gibbs energy; q: total molecular partition function; G_{solv} : Gibbs free energy of solvation (286.15 K).

When the *gas-phase* label is indicated: $E_{\text{gas}}^{\text{total}}$, ZPC, TCG (TCG_{gas}) and q were taken from the gas-phase geometry optimization and frequency calculation; $E_{\text{aq}}^{\text{total}}$ and G_{solv} were taken from the single-point calculation including solvent effects.

When the *aqueous-phase* label is indicated: $E_{\text{aq}}^{\text{total}}$, ZPC, TCG (TCG_{aq}) and q were taken from the aqueous-phase geometry optimization and frequency calculation.

Table S2:

Raw data (energies in atomic units and G_{solv} in kcal/mol) for the aqueous pK_a calculations (at 298.15 K) of the protonated benzimidazoles under study at the MP2/6-31+G(d,p)//AM1-COSMO(sp) level of theory. The data provided corresponds to the neutral, the tautomer (taut., when applicable), the protonated benzimidazole (cat.), water and the hydroxide and hydronium ions.

Species	$E_{\text{gas}}^{\text{total}}$	$E_{\text{aq}}^{\text{total}}$	ZPC	TCG_{gas}	q	G_{solv}
OH ⁻	-75.60144	-75.74549	0.00827	-0.00794	2.86E+07	-91.11
H ₂ O	-76.23301	-76.24646	0.02045	0.00280	1.31E+08	-6.76
H ₃ O ⁺	-76.50610	-76.65233	0.03193	0.01378	2.25E+08	-89.88
5-nitrobenzimidazole	-582.75753	-582.78051	0.12576	0.09109	8.80E+15	-10.91
5-nitrobenzimidazole taut.	-582.75780	-582.77991	0.12568	0.09099	9.05E+15	-10.45
5-nitrobenzimidazole cat.	-583.11010	-583.22016	0.13758	0.10284	9.53E+15	-67.62
2-chlorobenzimidazole	-837.77056	-837.78561	0.11189	0.07937	9.11E+14	-4.30
2-chlorobenzimidazole taut.	-	-	-	-	-	-
2-chlorobenzimidazole cat.	-838.13407	-838.22405	0.12408	0.09165	8.27E+14	-51.28
benzimidazole	-378.74762	-378.76477	0.12090	0.09049	9.73E+13	-6.88
benzimidazole taut.	-	-	-	-	-	-
benzimidazole cat.	-379.11857	-379.21270	0.13298	0.10265	8.92E+13	-55.49
1-methylbenzimidazole	-417.92576	-417.94055	0.14837	0.11495	2.34E+15	-3.92
1-methylbenzimidazole taut.	-	-	-	-	-	-
1-methylbenzimidazole cat.	-418.30353	-418.38993	0.15982	0.12515	8.84E+15	-49.29
1-ethylbenzimidazole	-457.11225	-457.12691	0.17730	0.14169	2.40E+16	-2.53
1-ethylbenzimidazole taut.	-	-	-	-	-	-
1-ethylbenzimidazole cat.	-457.49059	-457.57510	0.18876	0.15291	3.08E+16	-46.96
4-methylbenzimidazole	-417.93634	-417.95278	0.14861	0.11545	1.77E+15	-5.23
4-methylbenzimidazole taut.	-417.93543	-417.95235	0.14858	0.11533	1.96E+15	-5.54
4-methylbenzimidazole cat.	-418.30892	-418.40047	0.16047	0.12648	4.29E+15	-52.69
5-methyl benzimidazole	-417.93346	-417.95055	0.14861	0.11482	3.51E+15	-5.72
5-methylbenzimidazole taut.	-417.93367	-417.95085	0.14861	0.11490	3.21E+15	-5.73
5-methylbenzimidazole cat.	-418.30803	-418.39965	0.16060	0.12711	2.55E+15	-52.78
5,6-methylbenzimidazole	-457.11935	-457.13668	0.17671	0.14159	1.43E+16	-4.94
5,6-methylbenzimidazole taut.	-	-	-	-	-	-
5,6-methylbenzimidazole cat.	-457.49699	-457.58658	0.18862	0.15361	1.27E+16	-50.70
2-methylbenzimidazole	-417.93933	-417.95600	0.14880	0.11554	1.98E+15	-5.53
2-methylbenzimidazole taut.	-	-	-	-	-	-
2-methylbenzimidazole cat.	-418.31628	-418.40569	0.16054	0.12655	4.32E+15	-50.73
5-aminobenzimidazole	-433.95488	-433.97837	0.13828	0.10615	5.98E+14	-10.39
5-aminobenzimidazole taut.	-433.95538	-433.97906	0.13832	0.10628	5.45E+14	-10.29
5-aminobenzimidazole cat.	-434.33285	-434.42571	0.15022	0.11816	5.57E+14	-54.51
2-ethylbenzimidazole	-457.12177	-457.13819	0.17771	0.14232	1.89E+16	-4.23
2-ethylbenzimidazole taut.	-	-	-	-	-	-
2-ethylbenzimidazole cat.	-457.50046	-457.58692	0.18950	0.15445	1.32E+16	-47.84
2-isopropylbenzimidazole	-496.30781	-496.32408	0.20602	0.16898	1.09E+17	-2.81
2-isopropylbenzimidazole taut.	-	-	-	-	-	-
2-isopropylbenzimidazole cat.	-496.68768	-496.77235	0.21792	0.18111	8.61E+16	-45.22
2-aminobenzimidazole	-433.96078	-433.98201	0.13827	0.10607	6.46E+14	-9.01
2-aminobenzimidazole taut.	-	-	-	-	-	-
2-aminobenzimidazole cat.	-434.33663	-434.43394	0.14885	0.11627	9.66E+14	-55.86

$E_{\text{gas}}^{\text{total}}$: total gas-phase energy; $E_{\text{aq}}^{\text{total}}$: total aqueous-phase energy; ZPC: zero-point energy correction; TCG_{gas} : thermal correction to the Gibbs energy; q: total molecular partition function; G_{solv} : Gibbs free energy of solvation (286.15 K). The ZPC, TCG_{gas} and q were taken from the gas-phase frequency calculation at the AM1 level of theory. $E_{\text{gas}}^{\text{total}}$ was taken from the gas-phase single-point calculation at the MP2/6-31+G(d,p) level of theory. $E_{\text{aq}}^{\text{total}}$ and G_{solv} were taken from the aqueous-phase single-point calculation at the MP2/6-31+G(d,p)-COSMO level of theory.

Table S3:

Raw data (energies in atomic units) for the aqueous pK_a calculations (at 298.15 K) of the protonated benzimidazoles under study at the HF/6-31+G(d,p)-PCM(opt) level of theory. The data provided corresponds to the neutral, the tautomer (taut., when applicable), the protonated benzimidazole (cat.), water and the hydroxide and hydronium ions.

Species	E ^{total} _{aq}	ZPC	TCG _{aq}	q
OH ⁻	-75.55361	0.00495	-0.01139	3.27E+07
H ₂ O	-76.04349	0.02225	0.00465	1.25E+08
H ₃ O ⁺	-76.48230	0.03127	0.01314	2.18E+08
5-nitrobenzimidazole	-581.00237	0.12945	0.09543	4.41E+15
5-nitrobenzimidazole taut.	-581.00135	0.12940	0.09539	4.39E+15
5-nitrobenzimidazole cat.	-581.45379	0.14291	0.10879	4.97E+15
2-chlorobenzimidazole	-836.41138	0.11581	0.08387	4.93E+14
2-chlorobenzimidazole taut.	-	-	-	-
2-chlorobenzimidazole cat.	-836.85869	0.12927	0.09724	5.41E+14
benzimidazole	-377.51876	0.12606	0.09618	5.57E+13
benzimidazole taut.	-	-	-	-
benzimidazole cat.	-377.97933	0.13962	0.10966	6.06E+13
1-methylbenzimidazole	-416.54817	0.15590	0.12387	5.38E+14
1-methylbenzimidazole taut.	-	-	-	-
1-methylbenzimidazole cat.	-417.00972	0.16947	0.13752	4.98E+14
1-ethylbenzimidazole	-455.58875	0.18599	0.15207	3.99E+15
1-ethylbenzimidazole taut.	-	-	-	-
1-ethylbenzimidazole cat.	-456.05059	0.19950	0.16564	3.76E+15
4-methylbenzimidazole	-416.55913	0.15531	0.12334	5.04E+14
4-methylbenzimidazole taut.	-416.55909	0.15526	0.12330	4.99E+14
4-methylbenzimidazole cat.	-417.01978	0.16882	0.13672	5.80E+14
5-methyl benzimidazole	-416.55762	0.15503	0.12269	7.46E+14
5-methylbenzimidazole taut.	-416.55798	0.15503	0.12268	7.57E+14
5-methylbenzimidazole cat.	-417.01945	0.16863	0.13625	7.89E+14
5,6-methylbenzimidazole	-455.59566	0.18460	0.15112	2.49E+15
5,6-methylbenzimidazole taut.	-	-	-	-
5,6-methylbenzimidazole cat.	-456.05823	0.19820	0.16463	2.75E+15
2-methylbenzimidazole	-416.56593	0.15489	0.12259	7.19E+14
2-methylbenzimidazole taut.	-	-	-	-
2-methylbenzimidazole cat.	-417.02977	0.16849	0.13566	1.26E+15
5-aminobenzimidazole	-432.55773	0.14346	0.11193	3.16E+14
5-aminobenzimidazole taut.	-432.55896	0.14348	0.11202	2.97E+14
5-aminobenzimidazole cat.	-433.02107	0.15699	0.12548	3.13E+14
2-ethylbenzimidazole	-455.60343	0.18539	0.15118	5.41E+15
2-ethylbenzimidazole taut.	-	-	-	-
2-ethylbenzimidazole cat.	-456.06800	0.19904	0.16466	6.50E+15
2-isopropylbenzimidazole	-494.64073	0.21505	0.17878	4.81E+16
2-isopropylbenzimidazole taut.	-	-	-	-
2-isopropylbenzimidazole cat.	-	-	-	-
2-aminobenzimidazole	-432.57857	0.14224	0.11083	2.81E+14
2-aminobenzimidazole taut.	-	-	-	-
2-aminobenzimidazole cat.	-433.04403	0.15533	0.12357	4.09E+14

E^{total}_{aq}: total aqueous-phase energy; ZPC: zero-point energy correction; TCG_{aq}: thermal correction to the Gibbs energy; q: total molecular partition function; G_{solv}: Gibbs free energy of solvation (286.15 K). E^{total}_{aq}, ZPC, TCG_{aq} and q were taken from the aqueous-phase geometry optimization and frequency calculation at the HF/6-31+G(d,p)-PCM(opt) level of theory.

Table S4:

Raw data (energies in atomic units and G_{solv} in kcal/mol) for the aqueous pK_a calculations (at 298.15 K) of the protonated benzimidazoles under study at the B3LYP/6-31+G(d,p)-COSMO(sp) level of theory. The data provided corresponds to the neutral, the tautomer (taut., when applicable), the protonated benzimidazole (cat.), water and the hydroxide and hydronium ions.

Species	$E_{\text{gas}}^{\text{total}}$	$E_{\text{aq}}^{\text{total}}$	ZPC	TCG_{gas}	q	G_{solv}
OH ⁻	-75.80343	-75.94683	0.00855	-0.00771	3.02E+07	-87.75
H ₂ O	-76.43405	-76.44697	0.02129	0.00364	1.31E+08	-6.13
H ₃ O ⁺	-76.70777	-76.85202	0.03432	0.01621	2.14E+08	-88.70
5-nitrobenzimidazole	-584.40386	-584.42860	0.12065	0.08623	6.80E+15	-8.77
5-nitrobenzimidazole taut.	-584.40414	-584.42795	0.12069	0.08631	6.51E+15	-8.19
5-nitrobenzimidazole cat.	-584.76039	-584.87340	0.13431	0.09980	7.44E+15	-64.22
2-chlorobenzimidazole	-839.48516	-839.49948	0.10850	0.07610	8.02E+14	-2.89
2-chlorobenzimidazole taut.	-	-	-	-	-	-
2-chlorobenzimidazole cat.	-839.85222	-839.94231	0.12227	0.08984	8.28E+14	-50.44
benzimidazole	-379.89326	-379.91014	0.11820	0.08801	7.68E+13	-5.14
benzimidazole taut.	-	-	-	-	-	-
benzimidazole cat.	-380.26975	-380.36423	0.13224	0.10202	7.97E+13	-53.88
1-methylbenzimidazole	-419.20682	-419.22151	0.14609	0.11360	8.83E+14	-2.54
1-methylbenzimidazole taut.	-	-	-	-	-	-
1-methylbenzimidazole cat.	-419.58951	-419.67666	0.15997	0.12761	7.67E+14	-48.07
1-ethylbenzimidazole	-458.52644	-458.54102	0.17457	0.14007	7.44E+15	-1.20
1-ethylbenzimidazole taut.	-	-	-	-	-	-
1-ethylbenzimidazole cat.	-458.91115	-458.99627	0.18836	0.15395	6.77E+15	-45.57
4-methylbenzimidazole	-419.21568	-419.23171	0.14569	0.11311	9.65E+14	-3.54
4-methylbenzimidazole taut.	-419.21480	-419.23153	0.14569	0.11334	7.55E+14	-3.91
4-methylbenzimidazole cat.	-419.59443	-419.68614	0.15970	0.12721	8.80E+14	-51.01
5-methyl benzimidazole	-419.21333	-419.23017	0.14545	0.11251	1.42E+15	-4.07
5-methylbenzimidazole taut.	-419.21359	-419.23042	0.14547	0.11254	1.40E+15	-4.07
5-methylbenzimidazole cat.	-419.59379	-419.68553	0.15952	0.12673	1.20E+15	-51.12
5,6-methylbenzimidazole	-458.53282	-458.54973	0.17332	0.13933	4.32E+15	-3.19
5,6-methylbenzimidazole taut.	-	-	-	-	-	-
5,6-methylbenzimidazole cat.	-458.91649	-459.00602	0.18731	0.15327	4.58E+15	-48.84
2-methylbenzimidazole	-419.22050	-419.23693	0.14550	0.11280	1.10E+15	-3.81
2-methylbenzimidazole taut.	-	-	-	-	-	-
2-methylbenzimidazole cat.	-419.60428	-419.69364	0.15954	0.12631	1.92E+15	-49.57
5-aminobenzimidazole	-435.25296	-435.27592	0.13454	0.10264	4.72E+14	-8.30
5-aminobenzimidazole taut.	-435.25388	-435.27688	0.13460	0.10275	4.49E+14	-8.32
5-aminobenzimidazole cat.	-435.63970	-435.73237	0.14792	0.11523	1.08E+15	-52.15
2-ethylbenzimidazole	-458.53712	-458.55329	0.17423	0.13868	2.25E+16	-2.43
2-ethylbenzimidazole taut.	-	-	-	-	-	-
2-ethylbenzimidazole cat.	-458.92317	-459.00950	0.18828	0.15322	1.34E+16	-46.76
2-isopropylbenzimidazole	-497.85440	-497.87026	0.20221	0.16478	1.63E+17	-1.03
2-isopropylbenzimidazole taut.	-	-	-	-	-	-
2-isopropylbenzimidazole cat.	-498.24200	-498.32663	0.21645	0.17958	9.06E+16	-44.23
2-aminobenzimidazole	-435.26303	-435.28478	0.13489	0.10304	4.44E+14	-7.54
2-aminobenzimidazole taut.	-	-	-	-	-	-
2-aminobenzimidazole cat.	-435.64709	-435.74398	0.14771	0.11531	7.96E+14	-54.75
5-chlorobenzimidazole	-839.48670	-839.50432	0.10859	0.07620	7.88E+14	-4.93
5-chlorobenzimidazole taut.	-839.48689	-839.50414	0.10859	0.07620	7.91E+14	-4.70
5-chlorobenzimidazole cat.	-839.85659	-839.95504	0.12247	0.09006	8.03E+14	-55.72
2-methoxybenzimidazole	-494.42148	-494.44339	0.15018	0.11579	6.52E+15	-6.94
2-methoxybenzimidazole taut.	-	-	-	-	-	-
2-methoxybenzimidazole cat.	-494.80783	-494.89654	0.16422	0.13013	4.80E+15	-48.77

$E_{\text{gas}}^{\text{total}}$: total gas-phase energy; $E_{\text{aq}}^{\text{total}}$: total aqueous-phase energy; ZPC: zero-point energy correction; TCG_{gas} : thermal correction to the Gibbs energy; q: total molecular partition function; G_{solv} : Gibbs free energy of solvation

(286.15 K). $E_{\text{gas}}^{\text{total}}$, ZPC, TCG_{gas} and q were taken from the gas-phase geometry optimization and frequency calculation at the B3LYP/6-31+G(d,p) level of theory. $E_{\text{aq}}^{\text{total}}$ and G_{solv} were taken from the aqueous-phase single-point calculation at the B3LYP/6-31+G(d,p)-COSMO level of theory.

Table S5:

Raw data (energies in atomic units) for the aqueous pK_a calculations (at 298.15 K) of the protonated benzimidazoles under study at the B3LYP/6-31+G(d,p)-PCM(opt) level of theory. The data provided corresponds to the neutral, the tautomer (taut., when applicable), the protonated benzimidazole (cat.), water and the hydroxide and hydronium ions.

Species	E ^{total} _{aq}	ZPC	TCG _{aq}	q
OH ⁻	-76.04416	0.01366	-0.00339	6.91E+07
H ₂ O	-76.44637	0.02041	0.00274	1.35E+08
H ₃ O ⁺	-76.88220	0.02733	0.00911	2.41E+08
5-nitrobenzimidazole	-584.42805	0.11966	0.08516	7.40E+15
5-nitrobenzimidazole taut.	-584.42752	0.11965	0.08520	7.03E+15
5-nitrobenzimidazole cat.	-584.87239	0.13229	0.09762	8.78E+15
2-chlorobenzimidazole	-839.50023	0.10767	0.07534	7.40E+14
2-chlorobenzimidazole taut.	-	-	-	-
2-chlorobenzimidazole cat.	-839.94309	0.12034	0.08792	8.12E+14
benzimidazole	-379.91054	0.11738	0.08723	7.32E+13
benzimidazole taut.	-	-	-	-
benzimidazole cat.	-380.36464	0.13011	0.09988	8.06E+13
1-methylbenzimidazole	-419.22073	0.14542	0.11301	8.12E+14
1-methylbenzimidazole taut.	-	-	-	-
1-methylbenzimidazole cat.	-419.67553	0.15819	0.12581	7.76E+14
1-ethylbenzimidazole	-458.54070	0.17366	0.13918	7.26E+15
1-ethylbenzimidazole taut.	-	-	-	-
1-ethylbenzimidazole cat.	-458.99584	0.18635	0.15188	7.19E+15
4-methylbenzimidazole	-419.23175	0.14485	0.11245	8.01E+14
4-methylbenzimidazole taut.	-419.23185	0.14485	0.11252	7.42E+14
4-methylbenzimidazole cat.	-419.68634	0.15759	0.12510	8.81E+14
5-methyl benzimidazole	-419.23059	0.14455	0.11170	1.28E+15
5-methylbenzimidazole taut.	-419.23085	0.14456	0.11163	1.40E+15
5-methylbenzimidazole cat.	-419.68604	0.15730	0.12439	1.37E+15
5,6-methylbenzimidazole	-458.55021	0.17235	0.13842	4.04E+15
5,6-methylbenzimidazole taut.	-	-	-	-
5,6-methylbenzimidazole cat.	-459.00662	0.18508	0.15101	4.68E+15
2-methylbenzimidazole	-419.23715	0.14456	0.11170	1.29E+15
2-methylbenzimidazole taut.	-	-	-	-
2-methylbenzimidazole cat.	-419.69447	0.15735	0.12401	2.16E+15
5-aminobenzimidazole	-435.27606	0.13337	0.10155	4.34E+14
5-aminobenzimidazole taut.	-435.27703	0.13344	0.10166	4.13E+14
5-aminobenzimidazole cat.	-435.73408	0.14603	0.11416	4.57E+14
2-ethylbenzimidazole	-458.55393	0.17324	0.13842	1.04E+16
2-ethylbenzimidazole taut.	-	-	-	-
2-ethylbenzimidazole cat.	-459.01198	0.18610	0.15126	1.06E+16
2-isopropylbenzimidazole	-497.87109	0.20104	0.16345	1.95E+17
2-isopropylbenzimidazole taut.	-	-	-	-
2-isopropylbenzimidazole cat.	-	-	-	-
2-aminobenzimidazole	-435.28837	0.13289	0.10108	4.25E+14
2-aminobenzimidazole taut.	-	-	-	-
2-aminobenzimidazole cat.	-435.74990	0.14465	0.11216	8.75E+14
5-chlorobenzimidazole	-839.50504	0.10769	0.07534	7.62E+14
5-chlorobenzimidazole taut.	-839.50521	0.10762	0.07526	7.63E+14
5-chlorobenzimidazole cat.	-839.95623	0.12030	0.08784	8.52E+14
2-methoxybenzimidazole	-494.44287	0.14949	0.11538	4.89E+15
2-methoxybenzimidazole taut.	-	-	-	-
2-methoxybenzimidazole cat.	-494.89652	0.16210	0.12787	5.60E+15

$E_{\text{aq}}^{\text{total}}$: total aqueous-phase energy; ZPC: zero-point energy correction; TCG_{aq} : thermal correction to the Gibbs energy; q : total molecular partition function (286.15 K). $E_{\text{gas}}^{\text{total}}$, ZPC, TCG_{aq} and q were taken from the aqueous-phase geometry optimization and frequency calculation at the B3LYP/6-31+G(d,p)-PCM(opt) level of theory.

Appendix 1: Examples of pK_a Calculations

Constants:

Gas Constant	(R)	:	8.314 J K ⁻¹ mol ⁻¹
Temperature	(T)	:	298.15 K
Avogadro's Constant	(N _A)	:	6.022 × 10 ²³
Molar Volume at STP	(V _m)	:	24.46 L
Auto-ionization Constant of Water	(K _w)	:	1.00 × 10 ⁻¹⁴
Concentration of Water	[H ₂ O]	:	55.5 mol L ⁻¹

Unit Conversions:

$$1 \text{ au} = 2.62550 \times 10^6 \text{ J}$$
$$1 \text{ kcal} = 4.184 \times 10^3 \text{ J}$$

Experimental Free Energy Values:

G _{gas} H ⁺	-2.62755 × 10 ⁴ J mol ⁻¹
G _{solv} H ⁺	-1.10458 × 10 ⁶ J mol ⁻¹
G _{gas} OH ⁻	6.75214 × 10 ⁵ J mol ⁻¹
G _{solv} OH ⁻	-4.45178 × 10 ⁵ J mol ⁻¹
G _{gas} H ₂ O	-9.56462 × 10 ⁵ J mol ⁻¹
G _{solv} H ₂ O	-2.64429 × 10 ⁴ J mol ⁻¹
G _{gas} H ₃ O ⁺	-1.66306 × 10 ⁶ J mol ⁻¹
G _{solv} H ₃ O ⁺	-4.32835 × 10 ⁵ J mol ⁻¹

Note:

In the results presented in the paper the calculations carried all digits in each step, instead of rounding at each step as is done in these sample calculations to save space. This practice results in a few noticeable differences between some of the pK_a values calculated here and those presented in the paper.

MP2/6-31+G(d,p)//AM1-COSMO(sp): Scheme 1, Equation 9^(a): benzimidazole

Free Energies:

$$\begin{aligned}G_{\text{gas}}(\text{Bz}) &= (E_{\text{gas}}^{\text{total}} + \text{TCG}) \times 2.62550 \times 10^6 \text{ J mol}^{-1} \text{ au}^{-1} \\G_{\text{gas}}(\text{Bz}) &= (-378.74762 + 0.09049) \times 2.6255 \times 10^6 \text{ J mol}^{-1} \\G_{\text{gas}}(\text{Bz}) &= -9.94164 \times 10^8 \text{ J mol}^{-1}\end{aligned}$$

$$\begin{aligned}G_{\text{solv}}(\text{Bz}) &= G_{\text{solv}} \times 4.184 \times 10^3 \text{ J mol}^{-1} \text{ kcal}^{-1} \\G_{\text{solv}}(\text{Bz}) &= (-6.88) \times 4.184 \times 10^3 \text{ J mol}^{-1} \\G_{\text{solv}}(\text{Bz}) &= -2.87859 \times 10^4 \text{ J mol}^{-1}\end{aligned}$$

$$\begin{aligned}G_{\text{gas}}(\text{HBz}^+) &= (-379.11857 + 0.10265) \times 2.6255 \times 10^6 \text{ J mol}^{-1} \\G_{\text{gas}}(\text{HBz}^+) &= -9.95106 \times 10^8 \text{ J mol}^{-1}\end{aligned}$$

$$\begin{aligned}G_{\text{solv}}(\text{HBz}^+) &= (-55.49) \times 4.184 \times 10^3 \text{ J mol}^{-1} \\G_{\text{solv}}(\text{HBz}^+) &= -2.32170 \times 10^5 \text{ J mol}^{-1}\end{aligned}$$

$$\begin{aligned}\Delta G_{\text{aq}} &= G_{\text{gas}}(\text{Bz}) + G_{\text{solv}}(\text{Bz}) + G_{\text{gas}}(\text{H}^+) + G_{\text{solv}}(\text{H}^+) - G_{\text{gas}}(\text{HBz}^+) - G_{\text{solv}}(\text{HBz}^+) \\ \Delta G_{\text{aq}} &= (-9.94164 \times 10^8) + (-2.87859 \times 10^4) + (-2.62755 \times 10^4) + (-1.10458 \times 10^6) \\ &\quad - (-9.95106 \times 10^8) - (-2.32170 \times 10^5) \\ \Delta G_{\text{aq}} &= 1.45286 \times 10^4 \text{ J mol}^{-1}\end{aligned}$$

Tautomeric Population:

$$\begin{aligned}K_{\text{Taut}} &= 1 \\f_1 &= 1 / (K_{\text{Taut}} + 1) \\f_1 &= 1 / ((1) + 1) \\f_1 &= 0.5\end{aligned}$$

Equilibrium pK:

$$\begin{aligned}\text{pK} &= \Delta G_{\text{aq}} / (RT \ln(10)) \\ \text{pK} &= (1.45286 \times 10^4) / (RT \ln(10)) \\ \text{pK} &= 2.55\end{aligned}$$

pK_a Corrected for Tautomerism and Scheme 1:

$$\begin{aligned}\text{pK}_a &= \text{pK} + \log(f_1) \\ \text{pK}_a &= 2.55 + \log(0.5) \\ \text{pK}_a &= 2.25\end{aligned}$$

MP2/6-31+G(d,p)//AM1-COSMO(sp): Scheme 2, Equation 5^(b): benzimidazole

Zero-point Energies:

$$E_{0K}(\text{Bz}) = (E_{\text{aq}}^{\text{total}} + \text{ZPC}) \times 2.62550 \times 10^6 \text{ J mol}^{-1} \text{ au}^{-1}$$
$$E_{0K}(\text{Bz}) = (-378.76477 + 0.12090) \times 2.62550 \times 10^6 \text{ J mol}^{-1} \text{ au}^{-1}$$
$$E_{0K}(\text{Bz}) = -9.94129 \times 10^8 \text{ J mol}^{-1}$$

$$E_{0K}(\text{HBz}^+) = (-379.21270 + 0.13298) \times 2.62550 \times 10^6 \text{ J mol}^{-1} \text{ au}^{-1}$$
$$E_{0K}(\text{HBz}^+) = -9.95274 \times 10^8 \text{ J mol}^{-1}$$

$$E_{0K}(\text{H}_2\text{O}) = (-76.24646 + 0.02045) \times 2.62550 \times 10^6 \text{ J mol}^{-1} \text{ au}^{-1}$$
$$E_{0K}(\text{H}_2\text{O}) = -2.00131 \times 10^8 \text{ J mol}^{-1}$$

$$E_{0K}(\text{H}_3\text{O}^+) = (-76.65233 + 0.03193) \times 2.62550 \times 10^6 \text{ J mol}^{-1} \text{ au}^{-1}$$
$$E_{0K}(\text{H}_3\text{O}^+) = -2.01167 \times 10^8 \text{ J mol}^{-1}$$

$$\Delta E_{0K} = E_{0K}(\text{Bz}) + E_{0K}(\text{H}_3\text{O}^+) - E_{0K}(\text{HBz}^+) - E_{0K}(\text{H}_2\text{O})$$
$$\Delta E_{0K} = (-9.94129 \times 10^8) + (-2.01167 \times 10^8) - (-9.95274 \times 10^8) - (-2.00131 \times 10^8)$$
$$\Delta E_{0K} = 1.09000 \times 10^5 \text{ J mol}^{-1}$$

Molecular Partition Functions:

$$q(\text{Bz}) = 9.73\text{E}+13$$
$$q(\text{HBz}^+) = 8.92\text{E}+13$$
$$q(\text{H}_2\text{O}) = 1.31\text{E}+08$$
$$q(\text{H}_3\text{O}^+) = 2.25\text{E}+08$$

Tautomeric Population:

$$K_{\text{Taut}} = 1$$
$$f_1 = 1 / (K_{\text{Taut}} + 1)$$
$$f_1 = 1 / ((1) + 1)$$
$$f_1 = 0.5$$

Equilibrium pK:

$$\text{pK} = -\log \left\{ \frac{[q(\text{Bz}) \times q(\text{H}_3\text{O}^+) / (q(\text{HBz}^+) \times q(\text{H}_2\text{O}))] e^{[-(\Delta E_{0K}) / (RT)]}}{1} \right\}$$
$$\text{pK} = -\log \left\{ \frac{[(9.73\text{E}+13) \times (2.25\text{E}+08)] / [(8.92\text{E}+13) \times (1.31\text{E}+08)] e^{[-(1.09000 \times 10^5) / (RT)]}}{1} \right\}$$
$$\text{pK} = 18.82$$

pK_a Corrected for Tautomerism and Scheme 2:

$$\text{pK}_a = \text{pK} + \log(f_1) - \log[\text{H}_2\text{O}]$$
$$\text{pK}_a = 18.82 + \log(0.5) - \log(55.5)$$
$$\text{pK}_a = 16.77$$

MP2/6-31+G(d,p)//AM1-COSMO(sp): Scheme 2, Equation 9^(b): 1-methylbenzimidazole

Free Energies:

$$G_{\text{gas}}(\text{Bz}) = (-417.92576 + 0.11495) \times 2.6255 \times 10^6 \text{ J mol}^{-1} = -1.09696 \times 10^9 \text{ J mol}^{-1}$$
$$G_{\text{solv}}(\text{Bz}) = (-3.92) \times 4.184 \times 10^3 \text{ J mol}^{-1} = -1.64013 \times 10^4 \text{ J mol}^{-1}$$

$$G_{\text{gas}}(\text{HBz}^+) = (-418.30353 + 0.12515) \times 2.6255 \times 10^6 \text{ J mol}^{-1} = -1.09793 \times 10^9 \text{ J mol}^{-1}$$
$$G_{\text{solv}}(\text{HBz}^+) = (-49.29) \times 4.184 \times 10^3 \text{ J mol}^{-1} = -2.06229 \times 10^5 \text{ J mol}^{-1}$$

$$G_{\text{gas}}(\text{H}_2\text{O}) = (-76.23301 + 0.00280) \times 2.6255 \times 10^6 \text{ J mol}^{-1} = -2.00142 \times 10^8 \text{ J mol}^{-1}$$
$$G_{\text{solv}}(\text{H}_2\text{O}) = (-6.76) \times 4.184 \times 10^3 \text{ J mol}^{-1} = -2.82838 \times 10^4 \text{ J mol}^{-1}$$

$$G_{\text{gas}}(\text{H}_3\text{O}^+) = (-76.50610 + 0.01378) \times 2.6255 \times 10^6 \text{ J mol}^{-1} = -2.00831 \times 10^8 \text{ J mol}^{-1}$$
$$G_{\text{solv}}(\text{H}_3\text{O}^+) = (-89.88) \times 4.184 \times 10^3 \text{ J mol}^{-1} = -3.75723 \times 10^5 \text{ J mol}^{-1}$$

$$\Delta G_{\text{aq}} = G_{\text{gas}}(\text{Bz}) + G_{\text{solv}}(\text{Bz}) + G_{\text{gas}}(\text{H}_3\text{O}^+) + G_{\text{solv}}(\text{H}_3\text{O}^+) - G_{\text{gas}}(\text{HBz}^+) - G_{\text{solv}}(\text{HBz}^+) - G_{\text{gas}}(\text{H}_2\text{O}) - G_{\text{solv}}(\text{H}_2\text{O})$$
$$\Delta G_{\text{aq}} = (-1.09696 \times 10^9) + (-1.64013 \times 10^4) + (-2.00831 \times 10^8) + (-3.75723 \times 10^5)$$
$$\quad - (-1.09793 \times 10^9) - (-2.06229 \times 10^5) - (-2.00142 \times 10^8) - (-2.82838 \times 10^4)$$
$$\Delta G_{\text{aq}} = 1.23388 \times 10^5 \text{ J mol}^{-1}$$

Tautomeric Population:

$$K_{\text{Taut}} = 0$$
$$f_1 = 1 / (K_{\text{Taut}} + 1)$$
$$f_1 = 1 / ((0) + 1)$$
$$f_1 = 1$$

Equilibrium pK:

$$\text{pK} = \Delta G_{\text{aq}} / (RT \ln(10))$$
$$\text{pK} = (1.23388 \times 10^5) / (RT \ln(10))$$
$$\text{pK} = 21.62$$

pK_a Corrected for Tautomerism and Scheme 2:

$$\text{pK}_a = \text{pK} + \log(f_1) - \log[\text{H}_2\text{O}]$$
$$\text{pK}_a = (21.62) + \log(1) - \log(55.5)$$
$$\text{pK}_a = 19.88$$

B3LYP/6-31+G(d,p)//PCM(opt): Scheme 3, Equation 5^(b): 5-nitrobenzimidazole

Zero-point Energies:

$$E_{0K}(\text{Bz}) = (-584.42805 + 0.11966) \times 2.62550 \times 10^6 \text{ J mol}^{-1} \text{ au}^{-1} = -1.534101678 \times 10^9 \text{ J mol}^{-1}$$
$$E_{0K}(\text{Bz}_T) = (-584.42752 + 0.11965) \times 2.62550 \times 10^6 \text{ J mol}^{-1} \text{ au}^{-1} = -1.534100313 \times 10^9 \text{ J mol}^{-1}$$
$$E_{0K}(\text{HBz}^+) = (-584.87239 + 0.13229) \times 2.62550 \times 10^6 \text{ J mol}^{-1} \text{ au}^{-1} = -1.535235133 \times 10^9 \text{ J mol}^{-1}$$

$$E_{0K}(\text{Bz}_1) = (-379.91054 + 0.11738) \times 2.62550 \times 10^6 \text{ J mol}^{-1} \text{ au}^{-1} = -9.97147 \times 10^8 \text{ J mol}^{-1}$$
$$E_{0K}(\text{HBz}_1^+) = (-380.36464 + 0.13011) \times 2.62550 \times 10^6 \text{ J mol}^{-1} \text{ au}^{-1} = -9.98306 \times 10^8 \text{ J mol}^{-1}$$

$$\Delta E_{0K} = E_{0K}(\text{Bz}) + E_{0K}(\text{HBz}_1^+) - E_{0K}(\text{HBz}^+) - E_{0K}(\text{Bz}_1)$$
$$\Delta E_{0K} = (-1.534101678 \times 10^9) + (-9.98306 \times 10^8) - (-1.535235133 \times 10^9) - (-9.97147 \times 10^8)$$
$$\Delta E_{0K} = -2.5545 \times 10^4 \text{ J mol}^{-1}$$

Molecular Partition Functions:

$$q(\text{Bz}) = 7.40\text{E}+15$$
$$q(\text{Bz}_T) = 7.03\text{E}+15$$
$$q(\text{HBz}^+) = 8.78\text{E}+15$$
$$q(\text{Bz}_1) = 7.32\text{E}+13$$
$$q(\text{HBz}_1^+) = 8.06\text{E}+13$$

Tautomeric Population:

$$K_{\text{Taut}}(\text{Bz}) = [(q(\text{Bz}_T))/(q(\text{Bz}))]e^{[-(\Delta E_{0K})/(RT)]}$$
$$K_{\text{Taut}}(\text{Bz}) = [(7.03\text{E}+15)/(7.40\text{E}+15)]e^{[-((-1.534100313 \times 10^9) - (-1.534101678 \times 10^9))/(RT)]}$$
$$K_{\text{Taut}}(\text{Bz}) = 0.548$$

$$f_1(\text{Bz}) = 1 / (K_{\text{Taut}} + 1)$$
$$f_1(\text{Bz}) = 1 / ((0.548) + 1)$$
$$f_1(\text{Bz}) = 0.646$$

$$K_{\text{Taut}}(\text{Bz}_1) = 1$$
$$f_1(\text{Bz}_1) = 0.5$$

Equilibrium pK:

$$pK = -\log \{[(q(\text{Bz}) \times q(\text{HBz}_1^+))/(q(\text{HBz}^+) \times q(\text{Bz}_1))]e^{[-(\Delta E_{0K})/(RT)]}\}$$
$$pK = -\log \{[(7.40\text{E}+15) \times (8.06\text{E}+13)]/[(8.78\text{E}+15) \times (7.32\text{E}+13)]e^{[-(-2.5545 \times 10^4)/(RT)]}\}$$
$$pK = -4.44$$

pK_a Corrected for Tautomerism and Scheme 3:

$$pK_a = pK + \log(f_1(\text{Bz})) - \log(f_1(\text{Bz}_1)) + pK_a(\text{Bz}_1)$$
$$pK_a = (-4.44) + \log(0.646) - \log(0.5) + 5.41$$
$$pK_a = 1.08$$

B3LYP/6-31+G(d,p)//PCM(opt): Scheme 3, Equation 9^(b): 5-nitrobenzimidazole

Free Energies:

$$\begin{aligned}G_{\text{aq}}(\text{Bz}) &= (-584.42805 + 0.08516) \times 2.6255 \times 10^6 \text{ J mol}^{-1} = -1.534192258 \times 10^9 \text{ J mol}^{-1} \\G_{\text{aq}}(\text{Bz}_T) &= (-584.42752 + 0.08520) \times 2.6255 \times 10^6 \text{ J mol}^{-1} = -1.534190761 \times 10^9 \text{ J mol}^{-1} \\G_{\text{aq}}(\text{HBz}^+) &= (-584.87239 + 0.09762) \times 2.6255 \times 10^6 \text{ J mol}^{-1} = -1.535326159 \times 10^9 \text{ J mol}^{-1}\end{aligned}$$

$$\begin{aligned}G_{\text{aq}}(\text{Bz}_1) &= (-379.91054 + 0.08723) \times 2.6255 \times 10^6 \text{ J mol}^{-1} = -9.97226 \times 10^8 \text{ J mol}^{-1} \\G_{\text{aq}}(\text{HBz}_1^+) &= (-380.36464 + 0.09988) \times 2.6255 \times 10^6 \text{ J mol}^{-1} = -9.98385 \times 10^8 \text{ J mol}^{-1}\end{aligned}$$

$$\begin{aligned}\Delta G_{\text{aq}} &= G_{\text{aq}}(\text{Bz}) + G_{\text{aq}}(\text{HBz}_1^+) - G_{\text{aq}}(\text{HBz}^+) - G_{\text{aq}}(\text{Bz}_1) \\ \Delta G_{\text{aq}} &= (-1.534192258 \times 10^9) + (-9.98385 \times 10^8) - (-1.535326159 \times 10^9) - (-9.97226 \times 10^8) \\ \Delta G_{\text{aq}} &= -2.5099 \times 10^4 \text{ J mol}^{-1}\end{aligned}$$

Tautomeric Population:

$$\begin{aligned}K_{\text{Taut}}(\text{Bz}) &= e^{[-(-1.534190761 \times 10^9) - (-1.534192258 \times 10^9)] / (RT)} = 0.547 \\ f_1(\text{Bz}) &= 1 / ((0.547) + 1) = 0.646\end{aligned}$$

$$\begin{aligned}K_{\text{Taut}}(\text{Bz}_1) &= 1 \\ f_1(\text{Bz}_1) &= 1 / ((1) + 1) = 0.5\end{aligned}$$

Equilibrium pK:

$$\begin{aligned}pK &= \Delta G_{\text{aq}} / (RT \ln(10)) \\ pK &= (-2.5099 \times 10^4) / (RT \ln(10)) \\ pK &= -4.40\end{aligned}$$

pK_a Corrected for Tautomerism and Scheme 2:

$$\begin{aligned}pK_a &= pK + \log(f_1(\text{Bz})) - \log(f_1(\text{Bz}_1)) + pK_a(\text{Bz}_1) \\ pK_a &= (-4.40) + \log(0.646) - \log(0.5) + 5.41 \\ pK_a &= 1.12\end{aligned}$$