

**First Principles pK_a Calculations on Carboxylic Acids using
the SMD Solvation Model: Effect of Thermodynamic Cycle,
Model Chemistry, and Explicit Solvent Molecules**

Supporting Information

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Table S1: Mean Signed Error																
G_{gas}		B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	M052X/ AUG-cc-pVTZ	G3SX(MP3)				G3SX					average
ΔG_{solv}		B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	M052X/ AUG-cc-pVTZ	B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	M052X/ AUG- cc-pVTZ	
NO	D	10.87	5.81	0.43	2.35	0.23	0.37	-0.33	1.23	0.35	1.81	0.08	1.63	0.75	1.83	1.97
	PX	-17.99	-17.60	-8.11	-12.52	-7.91	2.34	1.50	-4.25	1.46	1.76	-0.12	-5.88	-0.16	-6.32	-5.19
	SD	-18.10	-17.56	-0.76	-11.76	0.08	2.24	1.54	3.10	2.22	1.65	-0.08	1.47	0.60	1.67	-2.72
ALL	D	10.56	5.48	0.58	2.13	0.21	-0.41	-0.41	1.01	-0.23	0.36	0.10	1.52	0.27	1.07	1.63
	PX	-18.30	-17.93	-7.96	-12.74	-7.92	1.57	1.42	-4.47	0.88	0.31	-0.10	-5.99	-0.65	-7.08	-5.53
	SD	-18.41	-17.89	-0.61	-11.98	0.07	1.46	1.46	2.88	1.64	0.20	-0.06	1.36	0.11	0.91	-3.06
AQ	D	11.11	5.84	0.77	2.36	0.29	0.61	-0.29	1.57	0.35	2.06	0.11	1.97	0.76	1.89	2.12
	PX	-17.75	-17.56	-7.77	-12.52	-7.85	2.59	1.54	-3.91	1.46	2.01	-0.08	-5.54	-0.16	-6.26	-5.04
	SD	-17.85	-17.52	-0.42	-11.76	0.14	2.48	1.58	3.44	2.22	1.90	-0.04	1.81	0.60	1.73	-2.57
AN	D	9.14	4.19	1.31	2.04	0.99	1.70	2.59	4.04	2.31	2.02	2.62	4.06	2.34	3.03	3.03
	PX	-19.71	-19.21	-7.22	-12.83	-7.14	3.68	4.42	-1.44	3.43	1.97	2.43	-3.44	1.43	-5.11	-4.13
	SD	-19.82	-19.18	0.12	-12.07	0.84	3.57	4.46	5.91	4.18	1.86	2.46	3.91	2.18	2.87	-1.66
average		-8.85	-10.26	-2.47	-7.44	-2.33	1.85	1.63	0.76	1.69	1.49	0.61	-0.26	0.67	-0.81	

Table S2: Mean Unsigned Error																
G_{gas}		B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	M052X/ AUG-cc-pVTZ	G3SX(MP3)				G3SX					average
ΔG_{solv}		B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	M052X/ AUG-cc-pVTZ	B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	M052X/ AUG- cc-pVTZ	
NO	D	10.87	5.81	1.28	2.51	1.07	1.55	1.31	1.62	1.18	2.58	1.34	1.88	1.34	2.00	2.64
	PX	17.99	17.60	8.11	12.52	7.91	2.76	2.24	4.25	1.92	2.55	1.29	5.88	1.01	6.32	6.62
	SD	18.10	17.56	1.07	11.76	0.99	2.68	2.27	3.10	2.49	2.47	1.30	1.76	1.23	1.89	5.14
ALL	D	10.56	5.48	0.77	2.13	0.66	0.96	0.98	1.13	0.62	1.00	0.93	1.52	0.68	1.10	2.11
	PX	18.30	17.93	7.96	12.74	7.92	1.77	1.78	4.47	1.08	0.98	0.93	5.99	0.70	7.08	6.35
	SD	18.41	17.89	0.61	11.98	0.59	1.69	1.81	2.88	1.65	0.96	0.93	1.36	0.64	0.98	4.72
AQ	D	11.11	5.84	0.91	2.36	0.63	1.32	0.98	1.57	0.82	2.40	1.02	1.97	0.97	1.89	2.45
	PX	17.75	17.56	7.77	12.52	7.85	2.59	1.87	3.91	1.54	2.37	0.97	5.54	0.60	6.26	6.37
	SD	17.85	17.52	0.47	11.76	0.60	2.50	1.90	3.44	2.22	2.29	0.98	1.81	0.87	1.73	4.94
AN	D	9.14	4.19	1.58	2.16	1.39	2.07	2.85	4.04	2.41	2.35	2.83	4.06	2.39	3.03	3.19
	PX	19.71	19.21	7.22	12.83	7.14	3.68	4.42	1.44	3.43	2.31	2.69	3.44	1.71	5.11	6.86
	SD	19.82	19.18	0.94	12.07	1.30	3.57	4.46	5.91	4.18	2.23	2.72	3.91	2.27	2.87	6.35
average		15.80	13.81	3.22	8.95	3.17	2.26	2.24	3.15	1.96	2.04	1.50	3.26	1.20	3.35	

Table S3: Max Unsigned Error																
G_{gas}		B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	M052X/ AUG-cc-pVTZ	G3SX(MP3)				G3SX					average
ΔG_{solv}		B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	M052X/ AUG-cc-pVTZ	B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	M052X/ AUG- cc-pVTZ	
NO	D	12.94	7.37	2.38	4.02	2.51	3.66	4.77	2.38	2.94	5.06	4.19	2.79	2.36	3.02	4.41
	PX	20.99	21.19	10.92	15.52	10.65	4.08	3.30	7.06	2.93	5.01	4.38	8.50	3.28	8.84	9.06
	SD	21.10	21.15	3.57	14.76	2.66	3.97	3.34	4.25	3.69	4.90	4.34	2.63	2.52	2.86	7.15
ALL	D	11.81	6.79	1.20	3.38	1.39	2.76	3.26	1.86	1.93	2.14	2.64	2.34	1.31	1.84	3.29
	PX	19.70	19.59	9.25	14.27	9.53	2.65	2.82	5.96	1.76	2.19	2.83	7.37	2.22	8.25	7.70
	SD	19.81	19.55	1.90	13.51	1.54	2.54	2.86	3.73	2.52	2.30	2.79	2.18	1.46	1.68	5.90
AQ	D	12.61	6.76	1.32	3.34	1.05	1.96	3.16	2.10	1.43	4.73	2.58	2.42	1.44	2.34	3.45
	PX	19.29	19.58	9.07	14.01	9.19	3.92	2.69	5.21	2.24	4.68	2.78	6.66	1.76	7.37	7.78
	SD	19.40	19.54	1.72	13.25	1.20	3.81	2.73	3.97	3.00	4.57	2.74	2.26	1.29	2.19	6.11
AN	D	10.61	5.45	2.41	3.27	2.17	3.15	4.09	5.06	3.53	3.81	4.06	5.07	3.45	3.98	4.32
	PX	21.91	21.67	9.62	15.35	9.72	5.13	5.93	3.94	4.65	3.77	3.87	5.79	2.54	7.25	8.76
	SD	22.02	21.63	2.28	14.59	2.03	5.02	5.96	6.93	5.40	3.65	3.90	4.91	3.29	3.82	7.82
average		17.68	15.85	4.64	10.77	4.47	3.56	3.74	4.37	3.00	3.90	3.43	4.41	2.24	4.45	

Table S4: Standard Deviation in Signed Error																
G_{gas}		B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	M052X/ AUG-cc-pVTZ	G3SX(MP3)				G3SX					average
ΔG_{solv}		B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	M052X/ AUG-cc-pVTZ	B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	M052X/ AUG- cc-pVTZ	
NO		1.90	1.86	1.45	1.51	1.37	1.95	2.00	1.25	1.54	2.60	1.92	1.19	1.46	1.15	1.69
ALL		0.91	0.96	0.65	0.86	0.82	1.22	1.35	0.71	0.85	1.26	1.29	0.66	0.79	0.57	0.95
AQ		1.11	1.05	0.68	0.76	0.70	1.39	1.38	0.57	0.88	1.95	1.30	0.50	0.80	0.48	1.01
AN		1.32	1.30	1.21	1.26	1.25	1.52	1.66	1.13	1.24	1.61	1.59	1.06	1.17	0.95	1.33
average		1.31	1.29	1.00	1.10	1.03	1.52	1.60	0.91	1.13	1.86	1.52	0.85	1.06	0.79	

Table S5: Acetic acid calculated pK_a values

G _{gas}		G3SX(MP3)				G3SX					
ΔG _{solv}		B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	M052X/ cc-pVTZ	AUG
NO	D	5.28	4.77	6.53	5.47	5.60	5.09	6.84	5.78	7.07	
	PX	7.26	6.60	1.05	6.58	5.55	4.89	-0.67	4.86	-1.07	
	SD	7.15	6.64	8.40	7.34	5.45	4.93	6.68	5.62	6.92	
ALL	D	3.87	3.99	5.46	4.04	4.40	4.53	5.99	4.58	5.49	
	PX	5.85	5.82	-0.02	5.16	4.35	4.33	-1.51	3.66	-2.66	
	SD	5.74	5.86	7.33	5.91	4.24	4.37	5.84	4.42	5.33	
AQ	D	4.95	4.15	6.37	4.88	5.27	4.47	6.68	5.20	6.65	
	PX	6.93	5.98	0.89	5.99	5.22	4.27	-0.83	4.28	-1.50	
	SD	6.82	6.02	8.24	6.75	5.12	4.31	6.52	5.04	6.49	
AN	D	6.33	7.27	8.89	6.99	6.39	7.33	8.96	7.05	7.87	
	PX	8.31	9.10	3.42	8.11	6.34	7.13	1.45	6.14	-0.27	
	SD	8.20	9.14	10.76	8.86	6.23	7.17	8.80	6.90	7.72	

Table S6: Chloroacetic acid calculated pK_a values

G _{gas}		G3SX(MP3)				G3SX					
ΔG _{solv}		B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	M052X/ cc-pVTZ	AUG-
NO	D	4.10	3.21	4.31	3.37	4.42	3.52	4.63	3.68	4.72	
	PX	6.08	5.04	-1.17	4.48	4.36	3.32	-2.88	2.77	-3.43	
	SD	5.97	5.08	6.18	5.24	4.26	3.36	4.47	3.53	4.56	
ALL	D	3.22	3.03	4.28	2.98	3.65	3.45	4.71	3.40	4.20	
	PX	5.20	4.86	-1.20	4.09	3.60	3.26	-2.80	2.49	-3.95	
	SD	5.09	4.90	6.15	4.85	3.49	3.30	4.55	3.25	4.04	
AQ	D	4.79	3.58	4.95	3.67	5.11	3.90	5.27	3.98	5.04	
	PX	6.77	5.41	-0.53	4.78	5.06	3.70	-2.24	3.07	-3.10	
	SD	6.66	5.45	6.82	5.54	4.95	3.74	5.11	3.83	4.89	
AN	D	5.17	5.97	7.13	5.33	5.13	5.92	7.08	5.29	5.98	
	PX	7.15	7.80	1.66	6.45	5.08	5.73	-0.42	4.37	-2.17	
	SD	7.04	7.84	9.00	7.20	4.97	5.76	6.93	5.13	5.82	

Table S7: Cyanoacetic acid calculated pK_a values

G _{gas}		G3SX(MP3)				G3SX					
ΔG _{solv}		B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	M052X/ cc-pVTZ	AUG-CC
NO	D	2.33	1.60	3.01	2.45	2.69	1.97	3.37	2.81	3.75	
	PX	4.30	3.43	-2.47	3.56	2.64	1.77	-4.13	1.90	-4.39	
	SD	4.20	3.47	4.88	4.32	2.53	1.81	3.22	2.66	3.59	
ALL	D	1.90	1.74	3.28	2.38	2.37	2.22	3.76	2.85	3.60	
	PX	3.87	3.57	-2.20	3.49	2.32	2.02	-3.75	1.94	-4.55	
	SD	3.77	3.61	5.15	4.25	2.21	2.06	3.60	2.70	3.44	
AQ	D	3.43	2.39	3.99	3.28	3.79	2.76	4.36	3.64	4.50	
	PX	5.40	4.22	-1.49	4.39	3.74	2.56	-3.15	2.73	-3.65	
	SD	5.30	4.26	5.86	5.15	3.64	2.60	4.20	3.48	4.34	
AN	D	3.57	4.43	5.92	4.49	3.59	4.44	5.94	4.50	5.15	
	PX	5.55	6.26	0.45	5.60	3.54	4.25	-1.56	3.59	-2.99	
	SD	5.44	6.30	7.79	6.36	3.43	4.28	5.78	4.34	4.99	

Table S8: Formic acid calculated pK_a values

G_{gas}		G3SX(MP3)				G3SX				
ΔG_{solv}		B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	M052X/ cc-pVTZ AUG
NO	D	2.81	2.82	5.11	3.37	6.13	3.35	5.64	3.91	5.58
	PX	4.78	4.65	-0.37	4.48	6.08	3.16	-1.86	2.99	-2.57
	SD	4.68	4.69	6.98	5.24	5.97	3.20	5.49	3.75	5.42
ALL	D	2.47	2.93	4.81	3.03	4.62	3.50	5.37	3.59	4.74
	PX	4.45	4.76	-0.67	4.14	4.57	3.30	-2.14	2.67	-3.41
	SD	4.34	4.80	6.68	4.90	4.46	3.34	5.21	3.43	4.58
AQ	D	2.87	2.46	5.48	3.31	6.19	3.00	6.01	3.84	5.69
	PX	4.84	4.29	0.00	4.42	6.14	2.80	-1.50	2.93	-2.46
	SD	4.74	4.33	7.35	5.18	6.03	2.84	5.85	3.68	5.53
AN	D	4.87	6.17	8.05	5.81	6.52	6.28	8.16	5.92	6.91
	PX	6.85	8.00	2.58	6.93	6.48	6.08	0.66	5.00	-1.23
	SD	6.74	8.04	9.92	7.68	6.37	6.12	8.00	5.76	6.75

Table S9: Hexanoic acid calculated pK_a values

G_{gas}		G3SX(MP3)				G3SX				
ΔG_{solv}		B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	M052X/ cc-pVTZ AUG
NO	D	6.98	6.35	6.95	6.70	9.47	6.66	7.26	7.01	7.46
	PX	8.96	8.18	1.47	7.81	9.42	6.47	-0.25	6.09	-0.69
	SD	8.85	8.22	8.82	8.57	9.31	6.51	7.10	6.85	7.30
ALL	D	5.54	5.53	6.35	5.33	6.47	5.99	6.81	5.79	6.21
	PX	7.52	7.36	0.87	6.44	6.42	5.79	-0.70	4.87	-1.93
	SD	7.41	7.40	8.22	7.20	6.31	5.83	6.65	5.63	6.05
AQ	D	6.59	5.74	6.71	6.01	9.07	6.05	7.02	6.32	6.91
	PX	8.57	7.57	1.23	7.12	9.02	5.86	-0.49	5.41	-1.23
	SD	8.46	7.61	8.58	7.88	8.92	5.90	6.86	6.17	6.75
AN	D	8.03	8.97	9.83	8.41	8.42	8.89	9.75	8.33	8.62
	PX	10.01	10.81	4.36	9.53	8.38	8.70	2.25	7.42	0.48
	SD	9.90	10.84	11.70	10.28	8.27	8.73	9.59	8.17	8.46

Table S10: Oxalic acid calculated pK_a values

G_{gas}		G3SX(MP3)				G3SX				
ΔG_{solv}		B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	M052X/ cc-pVTZ AUG
NO	D	-2.43	-3.54	-0.35	-1.71	-1.86	-2.96	0.23	-1.13	0.54
	PX	-0.46	-1.71	-5.83	-0.60	-1.91	-3.15	-7.27	-2.05	-7.61
	SD	-0.56	-1.67	1.52	0.16	-2.01	-3.11	0.08	-1.29	0.38
ALL	D	-1.53	-2.03	0.74	-0.70	-0.91	-1.41	1.37	-0.08	1.12
	PX	0.44	-0.20	-4.73	0.41	-0.96	-1.60	-6.14	-0.99	-7.02
	SD	0.34	-0.16	2.61	1.17	-1.07	-1.56	1.21	-0.23	0.96
AQ	D	-0.73	-1.93	1.50	-0.20	-0.15	-1.35	2.08	0.38	2.00
	PX	1.24	-0.10	-3.98	0.91	-0.20	-1.55	-5.43	-0.53	-6.14
	SD	1.14	-0.06	3.37	1.67	-0.31	-1.51	1.92	0.22	1.84
AN	D	-0.26	0.19	2.76	0.85	-0.08	0.37	2.94	1.03	2.12
	PX	1.73	2.02	-2.71	1.96	-0.13	0.17	-4.56	0.11	-6.02
	SD	1.61	2.06	4.63	2.72	-0.24	0.21	2.78	0.87	1.96

Table S11: Pivalic acid calculated pK_a values										
G_{gas}		G3SX(MP3)				G3SX				
ΔG_{solv}		B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	M052X/ cc-pVTZ AUG
NO	D	6.98	5.98	6.81	6.43	10.09	6.38	7.21	6.83	7.46
	PX	8.96	7.81	1.33	7.54	10.04	6.18	-0.29	5.91	-0.69
	SD	8.85	7.85	8.68	8.30	9.93	6.22	7.05	6.67	7.30
ALL	D	5.55	5.50	6.26	5.36	6.88	5.97	6.73	5.83	6.29
	PX	7.53	7.33	0.78	6.47	6.83	5.77	-0.78	4.91	-1.85
	SD	7.42	7.37	8.13	7.23	6.72	5.81	6.57	5.67	6.13
AQ	D	6.65	5.59	6.47	5.93	9.76	5.99	6.87	6.33	6.91
	PX	8.63	7.42	0.99	7.04	9.71	5.79	-0.64	5.41	-1.24
	SD	8.52	7.46	8.34	7.80	9.60	5.83	6.71	6.17	6.75
AN	D	7.88	8.62	9.57	8.14	8.84	8.61	9.56	8.12	8.53
	PX	9.86	10.46	4.10	9.25	8.80	8.42	2.05	7.21	0.39
	SD	9.75	10.49	11.44	10.01	8.68	8.45	9.40	7.97	8.37

Table S12: Propanoic acid calculated pK_a values										
G_{gas}		G3SX(MP3)				G3SX				
ΔG_{solv}		B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	B3LYP/ 6-31G(2df,p)	M052X/ 6-31G*	M052X/ 6-31+G**	M052X/ cc-pVTZ	M052X/ cc-pVTZ AUG
NO	D	6.69	6.00	7.25	6.53	7.76	6.42	7.66	6.95	7.89
	PX	8.67	7.83	1.77	7.64	7.71	6.22	0.15	6.03	-0.26
	SD	8.56	7.87	9.12	8.40	7.61	6.26	7.50	6.79	7.73
ALL	D	5.54	5.86	6.73	5.52	5.18	6.34	7.21	6.01	6.71
	PX	7.52	7.69	1.25	6.63	5.13	6.14	-0.30	5.09	-1.44
	SD	7.41	7.73	8.60	7.39	5.02	6.18	7.05	5.85	6.55
AQ	D	6.15	5.49	6.87	5.75	7.22	5.90	7.28	6.16	7.21
	PX	8.13	7.32	1.39	6.86	7.17	5.70	-0.23	5.25	-0.93
	SD	8.02	7.36	8.74	7.62	7.07	5.74	7.12	6.01	7.06
AN	D	7.78	8.92	9.93	8.28	7.15	8.93	9.94	8.29	8.85
	PX	9.76	10.76	4.46	9.40	7.11	8.74	2.44	7.38	0.71
	SD	9.65	10.79	11.80	10.15	7.00	8.77	9.78	8.13	8.69