Quality-Controlled pK_a Data in Polar Aprotic Solvents

Sofja Tshepelevitsh,[1] Ivo Leito,[1] Ivari Kaljurand,[1] Mare Piirsalu,[1] Jonathan Wenyuan Zheng,[2] Martí Rosés,[3] Jean-François Gal[4]

[1]University of Tartu, Institute of Chemistry [2]TU Wien, Faculty of Technical Chemistry [3]Departament de Química Analítica, Universitat de Barcelona [4]CNRS, Institut de Chimie de Nice, Université Côte d'Azur

e-mail: sofja.tsepelevits@ut.ee

Database of **>9500 quality-assessed pK_a values of >5000 acids** in 7 organic solvents, freely available in Zenodo repository, continually upkept and updated.

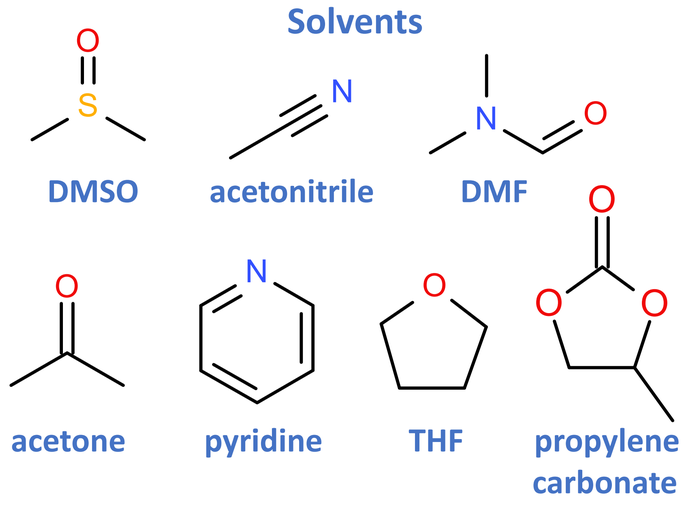
Acid dissociation process

$$(HA)_S + S \rightleftharpoons (SH^+A^-)_S \rightleftharpoons (SH^+)_S + (A^-)_S$$

$$K_a = \frac{a(SH^+)a(A^-)}{a(HA)}$$

$$pK_a = -\log_{10}(K_a)$$

Solvents

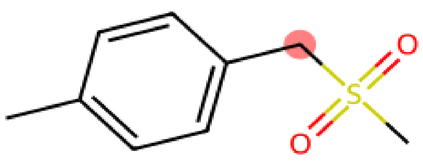


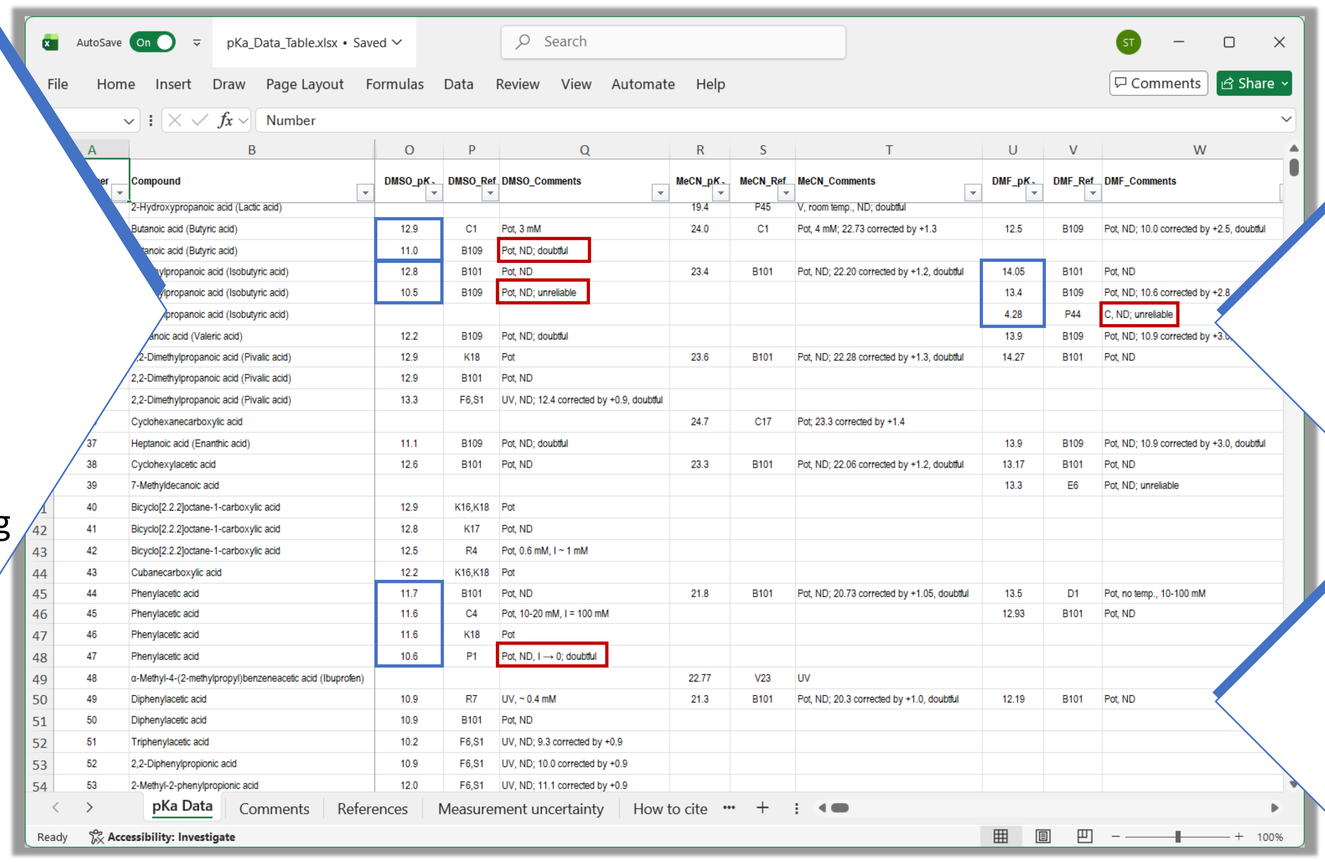
Compound classes

- **OH acids**: carboxylic acids, phenols, alcohols, sulfonic acids …
- **NH acids**: amines, amides, sulfonamides, guanidines, hydrazines, aromatic heterocycles …
- **CH acids**: methylaromatics, fluorenes, carbonyls, sulfones, nitriles …
- **Other**: metal hydrides, SH, PH …

Cheminformatics features

- Systematic names and **CAS** Registry Numbers
- **InChI**, canonical **SMILES**, atom-mapped SMILES with indicated ionization center
- Separate "dictionary" file with automatically generated 2D structures
- Optimised for machine-learning





	Compound	DMSO_pKa	DMSO_Ref	DMSO_Comments	MeCN_pKa	MeCN_Ref	MeCN_Comments	DMF_pKa	DMF_Ref	DMF_Comments
	2-Hydroxypropanoic acid (Lactic acid)				19.4	P45	V, room temp., ND; doubtful			
	Butanoic acid (Butyric acid)	12.9	C1	Pot, 3 mM	24.0	C1	Pot, 4 mM; 22.73 corrected by +1.3	12.5	B109	Pot, ND; 10.0 corrected by +2.5, doubtful
	anoic acid (Butyric acid)	11.0	B109	Pot, ND; doubtful						
	ylpropanoic acid (Isobutyric acid)	12.8	B101	Pot, ND	23.4	B101	Pot, ND; 22.20 corrected by +1.2, doubtful	14.05	B101	Pot, ND
	ypropanoic acid (Isobutyric acid)	10.5	B109	Pot, ND; unreliable				13.4	B109	Pot, ND; 10.6 corrected by +2.8
	ypropanoic acid (Isobutyric acid)							4.28	P44	C, ND; unreliable
	anoic acid (Valeric acid)	12.2	B109	Pot, ND; doubtful				13.9	B109	Pot, ND; 10.9 corrected by +3.0
	2-Dimethylpropanoic acid (Pivalic acid)	12.9	K18	Pot	23.6	B101	Pot, ND; 22.28 corrected by +1.3, doubtful	14.27	B101	Pot, ND
	2,2-Dimethylpropanoic acid (Pivalic acid)	12.9	B101	Pot, ND						
	2,2-Dimethylpropanoic acid (Pivalic acid)	13.3	F6,S1	UV, ND; 12.4 corrected by +0.9, doubtful						
	Cyclohexanecarboxylic acid				24.7	C17	Pot; 23.3 corrected by +1.4			
37	Heptanoic acid (Enanthic acid)	11.1	B109	Pot, ND; doubtful				13.9	B109	Pot, ND; 10.9 corrected by +3.0, doubtful
38	Cyclohexylacetic acid	12.6	B101	Pot, ND	23.3	B101	Pot, ND; 22.06 corrected by +1.2, doubtful	13.17	B101	Pot, ND
39	7-Methyldecanoic acid							13.3	E6	Pot, ND; unreliable
40	Bicyclo[2.2.2]octane-1-carboxylic acid	12.9	K16,K18	Pot						
41	Bicyclo[2.2.2]octane-1-carboxylic acid	12.8	K17	Pot, ND						
42	Bicyclo[2.2.2]octane-1-carboxylic acid	12.5	R4	Pot, 0.6 mM, I ~ 1 mM						
43	Cubanecarboxylic acid	12.2	K16,K18	Pot						
44	Phenylacetic acid	11.7	B101	Pot, ND	21.8	B101	Pot, ND; 20.73 corrected by +1.05, doubtful	13.5	D1	Pot, no temp., 10-100 mM
45	Phenylacetic acid	11.6	C4	Pot, 10-20 mM, I = 100 mM				12.93	B101	Pot, ND
46	Phenylacetic acid	11.6	K18	Pot						
47	Phenylacetic acid	10.6	P1	Pot, ND, I → 0; doubtful						
48	α-Methyl-4-(2-methylpropyl)benzeneacetic acid (Ibuprofen)				22.77	V23	UV			
49	Diphenylacetic acid	10.9	R7	UV, ~ 0.4 mM	21.3	B101	Pot, ND; 20.3 corrected by +1.0, doubtful	12.19	B101	Pot, ND
50	Diphenylacetic acid	10.9	B101	Pot, ND						
51	Triphenylacetic acid	10.2	F6,S1	UV, ND; 9.3 corrected by +0.9						
52	2,2-Diphenylpropionic acid	10.9	F6,S1	UV, ND; 10.0 corrected by +0.9						
53	2-Methyl-2-phenylpropionic acid	12.0	F6,S1	UV, ND; 11.1 corrected by +0.9						

Labels reflect uncertainty estimates

Preferred (~500 values): 0.1-0.2 units
--no label--: 0.2-0.5 units
Doubtful (~1900 values): 1-3 units
Unreliable (~800 values): 3-10 units

Metadata

Measurement technique, temperature, water content, ionic strength, applied corrections …

References:

- I. Leito, I. Kaljurand, M. Piirsalu, S. Tshepelevitsh, J. W. Zheng, M. Rosés, J.-F. Gal, *Pure Appl. Chem.* **97**, 973 (2025).
- I. Leito, I. Kaljurand, M. Piirsalu, S. Tshepelevitsh, J. W. Zheng, M. Rosés, J.-F. Gal, "Acid dissociation constants in selected dipolar non-hydrogen-bond-donor solvents" (dataset), available from https://doi.org/10.5281/zenodo.12608876.

Acknowledgements:

The work has been carried out in the framework of the IUPAC project 2015-020-2-500 and additionally funded by numerous sources, most importantly the EMPIR programme (project 17FUN09 "UnipHied", www.uniphied.eu), by the Estonian Research Council grants (PRG690, PRG2557) and by the Estonian Ministry of Education and Research (TK210).