Empirical Method for Description of Solvent Effect on the Ionization Constants of NH Acids

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Abstract—An empirical method was used to calculate 192 ionization constants of 24 NH acids in 8 solvents. The relative error in the calculations did not exceed 10%, and the average error was no higher than 3.5%. The calculated values were compared with those obtained by quantum-chemical and other up-to-date methods for the determination of acid ionization constants in various solvents.

Solvent effects on chemical reactions and physical and chemical properties of compounds attract persistent researchers' interest, as follows from a large number of studies in this field reported during the past decade and recently published monographs [1–3]. One of the most important aspects of this problem is solvent effect on protonation (deprotonation) equilibria, i.e., variation of basicity (acidity) constants in going from one solvent to another. In the past five years, the error in the calculation of acidity parameters in the gas phase (molecular proton affinities ΔH_H and basicities ΔG_H) attained a level of less than 1% [4–10]. Advances in the development of calculation procedures made it possible to reliably predict sites of protonation of multicenter species in agreement with the experimental data [11–14].

Comparative analysis of up-to-date quantum-chemical methods for the calculation of acid ionization constants pK_a (mostly in aqueous medium) on the basis of experimental or theoretical data for the gas phase and various solvation models (to calculate energies of solvation ΔG_{solv} for species involved in equilibrium) was performed by us previously [15]. These methods ensured 5–40% deviation (εpK_a) of the calculated pK_a values from those determined experimentally.

In the present article we demonstrate the application of empirical approach proposed by us previously [15–18] to the calculation of ionization constants of NH acids in various solvents on the basis of experimental parameters of the substrates and solvents. The use of exclusively experimental parameters constitutes

the principal difference from the empirical QSPR approach which relates a given molecular parameter to other molecular parameters (or parameters of molecular fragments) calculated by quantum-chemical methods (mostly semiempirical). Joint application of QSPR and nonempirical quantum-chemical methods for the calculation of ΔH_H and ΔG_H were described in [19, 20] where theoretical or experimental values of ΔG_{solv} for molecules, anions, and proton or their combinations were used as descriptors. The QSPR approach was directly used to calculate pK_{BH^+} values in [6, 7, 21, 22]. The correlations obtained in [6] were characterized by r^2 values ranging from 0.915 to 0.945 for 5 descriptors. The condition $\varepsilon pK_{BH^+} < 10\%$ was met for 28 calculated pK_{BH^+} values of 36 anilines. Pankratov et al. [23] used simple semiempirical PM3 procedure to calculate ΔH_H and ΔG_H values, but the correlation coefficient with pK_{BH^+} was as poor as 0.791 for 63 anilines, though 49 of the 126 calculated pK_{BH^+} values met the condition $\varepsilon pK_{BH^+} < 10\%$. Likewise, the use of three descriptors calculated by the AM1 method gave a correlation coefficient of 0.88 for 188 pK_{BH^+} values [22]. The best results obtained by the QSPR method were reported in [21]: εpK_{BH^+} did not exceed 10% for 31 of 36 anilines. A four-parameter correlation included descriptors based on the Bader "atoms in molecules" (AIM) approach and quantum topological molecular similarity.

In the present article we considered only publications concerning calculations of pK_{BH^+} values of NH acids [6–10, 19–21, 23–32]. By *NH acid* we mean two

kinds of molecular entities: (1) NH^+ *acids* that include protonated amines (primary, secondary, and tertiary) and heterocyclic compounds protonated at pyridine-type nitrogen atom and (2) NH^0 *acids* that are nitrogen-containing heterocycles having a labile proton on the pyrrole-type nitrogen atom.

As in our previous publications [15–18], ionization constant $pK_{BH^+}^{jk}$ of some acid (k) in some solvent (j) was calculated using linear Eq. (1):

$$\delta pK_{BH^+}^{jk} = a_k \delta X_{jk} + b_k, \qquad (1)$$

where a_k and b_k are constants. The quantity $\delta pK_{BH^+}^{jk}$ is linearly related to the ionization constant through the parameter Y_j [Eq. (2)]:

$$\delta pK_{BH^+}^{jk} = pK_{BH^+}^{jk} - Yj, \qquad (2)$$

and δX_{jk} is experimental solvent parameter $X_{ex,j}$ minus contribution of atoms:

$$\delta X_{jk} = X_{ex,j} - X_k \sum_i g_{ij} X_i. \qquad (3)$$

Here, g_{ij} is the number of ith atoms in jth solvent molecule, X_i is the contribution of ith atom to the molecular solvent parameters, and X_k is a dimensionless coefficient.

Unlike previous studies [16–18], here, as well as in [15], Eqs. (1)–(3) interrelate molecular parameters of different substances. The coefficient Y_j was taken as a constant of jth solvent (though it implicitly includes substrate parameters), and the coefficient X_k at atom contributions to solvent parameter was taken as a constant of kth NH acid.

Taking into account the results of application of the described procedure to carboxylic acids [15], as molecular parameter of solvent we selected the Dimroth–Reichardt solvatochromic parameter E_T^{30}. In this case, the physical sense of atom contribution X_i is not obvious (cf. [15]), for the quantity E_T^{30} is nonadditive. Therefore, atom contributions for E_T^{30} were fit empirically. Preliminary calculations showed that the second appropriate molecular parameter may be molecular volume (V_M). It might be expected that volumes of the corresponding atoms would be apt to approximate X_i; however, the results showed that this is not the case. Moreover, we succeeded in selecting atom contributions that were similar for both E_T^{30} and V_M. The experimental values of E_T^{30} and V_M were taken from [1, 33].

Though there are numerous experimental pK_{BH^+} values of NH acids in various individual (not mixed) solvents [34–59], integration of data from different sources into a single array suitable for further processing constituted a particular analytical problem. The main reasons were the following.

(1) Different methods were used for the determination of pK_{BH^+} values: spectrophotometric, potentiometric, and conductometric; the two latter cannot be used to determine pK_{BH^+} in weakly polar media [58];

(2) Some authors measured different parameters characterizing acidity in nonaqueous solution and used different mathematical models for the calculation of pK_{BH^+} values from the measurement data and for their processing;

3) In some cases, the acidity was characterized by results of measurements, from which pK_{BH^+} values cannot be calculated;

4) Experiments were usually performed with large (but specific for each particular study) series of compounds and 1 to 2 solvents. As a result, the number of pK_{BH^+} values for the same compound in different solvents does not exceed 2, which is too small to draw a correlation;

5) The quantity pK_{BH^+} in weakly polar aprotic solvents makes no rigorous physical sense, while measurable equilibrium constants for formation of ion pairs with proton transfer depend on the nature of the conjugate base [34].

As a result of the first two factors, pK_{BH^+} values of the same compound in the same solvent, determined by different authors, may differ by 5 log units.

If three or more pK_{BH^+} values for the same compound in the same solvent were available, those differing by more than 0.5 log units from the others were excluded. If such situation was observed for more than half of the total number of values given in a particular publication, all data given therein were excluded. Thus the data of [35, 36] were discarded: the acidity constants obtained by converting the given basicity constants through ionic products of the corresponding solvents [1, 42] strongly deviated from analogous values given in other publications. No calculation procedure and initial measurement data were given in [35, 36]; therefore, it was impossible to restore acidity constants from the initial data.

We also discarded the data of [37] where only half-neutralization potentials obtained by potentiometric titration were given, which are specific for measure-

ment conditions. The data of [46] on the acidity of a series of anilines in methanol and ethanol were excluded for the same reason: the relative acidity constants were referenced to indicators: Methyl Yellow and 4-methyl-3-nitroaniline, and pK_{BH^+} values could not be restored. Four pK_{BH^+} values for 100% dioxane [38] were excluded from consideration since measurement of pK_{BH^+} was not the main goal of this study and the measurements were likely to be performed at a low accuracy level. In addition, anomalous effect of dioxane on pK_{BH^+} in dioxane–water mixtures containing more than 70% of the former was noted in [59]. The pK_{BH^+} values given in [50–58] were obtained in a single solvent, and no other data for the examined substrates (mainly nitrogen-containing heterocycles) were available; these publications were also discarded.

The pK_{BH^+} values given in [39–41, 48] for the same substrate in DMSO are consistent within 0.05–0.09 log unit; therefore, average values were used if more than

Table 1. Constants Y_j for solvent parameters E_T^{30} and V_M

j	Solvent	Y_j	
		V_M	E_T^{30}
1	Acetone	8.77	8.21
2	DMSO	5.91	6.01
3	Acetonitrile	12.7	11.8
4	Nitromethane	9.82	9.75
5	Ethanol	8.86	9.63
6	Methanol	10.7	10.5
7	Formamide	6.36	7.73
8	Water	11.1	11.1

two values were available. The data of [42, 43] for the acidity of the same substrate in methanol differed considerably, by 0.25 log unit. If two pK_{BH^+} values were available, we selected that given in [43], for this study was specially aimed at measuring pK_{BH^+} in aque-

Table 2. Coefficients for the calculation of pK_{BH^+}, numbers of solvents N, and maximal relative errors $\max(\varepsilon pK_{BH^+})$ for 24 NH acids in the calculations with E_T^{30} as solvent parameter

k	Compound	a	b	X_k	$\max(\varepsilon pK_{BH^+})$	N
1	NH_4^+	−0.392	23.0	−0.234	1.91	4
2	$EtNH_3^+$	−0.400	25.1	−0.509	0.41	4
3	$BuNH_3^+$	−0.391	24.5	−0.463	0.36	4
4	1-Naphthylammonium	−0.177	4.19	0.307	9.19	4
5	$Et_2NH_2^+$	−0.382	24.5	−1.00	9.49	5
6	$Bu_2NH_2^+$	−0.375	24.1	−0.856	0.13	4
7	Bu_3NH^+	−0.424	25.9	−1.07	1.88	4
8	$PhNH_3^+$	−0.288	12.1	−0.553	8.44	8
9	$4\text{-}MeC_6H_4NH_3^+$	−0.296	13.1	−0.475	9.37	7
10	$3\text{-}MeC_6H_4NH_3^+$	−0.299	12.8	−0.555	6.88	6
11	$4\text{-}ClC_6H_4NH_3^+$	−0.283	11.1	−0.525	5.87	8
12	$4\text{-}BrC_6H_4NH_3^+$	−0.282	10.6	−0.438	1.63	5
13	$3\text{-}ClC_6H_4NH_3^+$	−0.289	10.9	−0.566	6.14	6
14	$3\text{-}O_2NC_6H_4NH_3^+$	−0.262	8.02	−0.407	0.51	5
15	$4\text{-}ON_2C_6H_4NH_3^+$	−0.290	8.31	−0.250	9.63	4
16	$Ph(Me)NH_2^+$	−0.290	12.3	−0.820	4.48	6
17	$Ph(Et)NH_2^+$	−0.318	14.2	−0.912	7.96	6
18	$PhMe_2NH^+$	−0.307	13.7	−1.14	5.59	5
19	$PhEt_2NH^+$	−0.337	16.8	−1.32	9.58	5
20	Pyridinium $C_5H_5N^+$	−0.368	17.2	−0.934	9.09	8
21	$2\text{-}MeC_5H_5N^+$	−0.363	18.0	−1.03	4.31	6
22	Piperidinium	−0.392	24.8	−0.776	9.91	7
23	Quinolinium	−0.357	16.8	−1.05	5.13	4
24	Codeine·H^+	−0.0198	−2.39	22.3	9.39	4

Table 3. Coefficients for the calculation of pK_{BH^+}, numbers of solvents N, and maximal relative errors $\max(\varepsilon pK_{BH^+})$ for 24 NH acids in the calculations with V_M as solvent parameter

k	Compound	a	b	X_k	$\max(\varepsilon pK_{BH^+})$	N
1	NH_4^+	0.166	–4.67	1.59	0.05	4
2	$EtNH_3^+$	0.168	–3.16	2.24	2.30	4
3	$BuNH_3^+$	0.165	–3.06	2.12	2.17	4
4	1-Naphthylammonium	0.118	–8.93	2.00	9.20	6
5	$Et_2NH_2^+$	0.167	–2.68	3.34	8.46	5
6	$Bu_2NH_2^+$	0.158	–2.40	3.06	1.40	4
7	Bu_3NH^+	0.178	–3.96	3.59	4.25	4
8	$PhNH_3^+$	0.130	–8.40	2.42	9.88	8
9	$4\text{-}MeC_6H_4NH_3^+$	0.128	–8.01	2.11	9.61	7
10	$3\text{-}MeC_6H_4NH_3^+$	0.130	–8.44	2.27	8.44	6
11	$4\text{-}ClC_6H_4NH_3^+$	0.127	–9.12	2.37	9.87	8
12	$4\text{-}BrC_6H_4NH_3^+$	0.120	–9.35	1.91	6.01	5
13	$3\text{-}ClC_6H_4NH_3^+$	0.131	–9.75	2.42	9.59	6
14	$3\text{-}O_2NC_6H_4NH_3^+$	0.109	–10.5	1.92	1.72	5
15	$4\text{-}O_2NC_6H_4NH_3^+$	0.122	–12.2	1.57	9.09	4
16	$Ph(Me)NH_2^+$	0.123	–8.28	2.89	7.71	6
17	$Ph(Et)NH_2^+$	0.132	–8.21	3.12	5.89	6
18	$PhMe_2NH^+$	0.134	–8.16	3.60	7.81	5
19	$PhEt_2NH^+$	0.133	–6.81	4.08	9.32	5
20	Pyridinium $C_5H_5N^+$	0.150	–8.65	3.21	7.75	8
21	$2\text{-}MeC_5H_5N^+$	0.163	–7.83	3.50	6.56	6
22	Piperidinium	0.175	–3.29	2.78	9.96	7
23	Quinolinium	0.170	–8.80	3.59	5.36	4
24	Codeine·H^+	0.168	–6.03	2.70	8.61	6

ous methanol (volume fraction 0–100%). If some values were absent in [43], the corresponding values were taken from [42]. The data of [43, 45] on the acidity in ethanol showed a better agreement with each other. If pK_{BH^+} values for the same substrate differed by no more than 0.1 log unit, average values were taken; if the difference was larger, preference was given to the data of [45] where pK_{BH^+} values in aqueous ethanol (0–100 wt %) were specially measured. Likewise, if pK_{BH^+} values in water [41–47, 49] differed by no more than 0.1 log unit, average values were used; otherwise, those given in [49] were taken as the most recent compilation of pK_{BH^+} in water for 2156 substances. The data on pK_{BH^+} in acetonitrile were taken from [39, 41, 47]. Only triethylamine revealed discrepancy by more than 0.1 log unit; in this case, the pK_{BH^+} value from the latest publication [41] was taken. The basicity constants pK_{BH^+} in nitromethane were given only in [40, 41], and in formamide,

only in [42]. Insofar as it was impossible to check their validity, these values were taken as such.

As a result, we have obtained an array including 105 substrates, each being characterized by pK_{BH^+} values in at least two solvents, which were taken from [39–45, 47–49]. The pK_{BH^+} values were determined mainly by potentiometric method. However, among the substrates included, only 52 were characterized by pK_{BH^+} values in three or more solvents, and 24, in four or more solvents. Since analysis of correlations derived from three points seems to be insufficiently correct and calculation of pK_{BH^+} from such correlations seems to be poorly reliable, we selected 24 substrates characterized by four and more (maximally 8) pK_{BH^+} values in different solvents.

The coefficients a_k, b_k, X_k, X_i, and Y_j were determined by minimization of the sum of the squared relative deviations of the calculated [using Eqs. (1–3)]

and experimental (denoted with the index "ex") ionization constants of kth NH acid in the selected solvents:

$$E_k = \sum_j \left[\frac{pK_{BH^+}^{ex,jk} - pK_{BH^+}^{jk}}{pK_{BH^+}^{ex,jk}} \right]^2. \qquad (4)$$

Advantages of using the above criterion instead of correlation coefficients calculated by traditional least-squares procedure were considered in [17].

The minimum condition for any j and k was written as follows:

$$\frac{\partial \sum_k E_k}{\partial a_k} = \frac{\partial \sum_k E_k}{\partial b_k} = \frac{\partial \sum_k E_k}{\partial X_k} = \frac{\partial \sum_k E_k}{\partial Y_k} = 0 \qquad (5)$$

However, numerical solution gave $a_k < 10^{-6}$ for about a half of the examined substrates, which corresponds to degenerate Eq. (6).

$$pK_{BH^+}^{jk} = Y_j + b_k, \qquad (6)$$

Obviously, Eq. (6) includes no experimental solvent parameters. Modification of Eq. (1) with a constant coefficient a_k for all substrates (i.e., for any k) resulted in persistently nondegenerate solutions, but the relative error in the calculation exceeded 20%. Therefore, minimum condition (5) for all solvents was simplified so as to obtain Eq. (7), and it was used to determine numerically all coefficients X_k, a_k, and b_k.

$$\frac{\partial \sum_k E_k}{\partial a_k} = \frac{\partial \sum_k E_k}{\partial b_k} = \frac{\partial \sum_k E_k}{\partial X_k} = 0. \qquad (7)$$

The algorithm for fitting X_i and Y_j was described by us previously [15]. The atom contributions X_i for C, H, O, N, and S were 1.88, 1.22, −1.75, −6.10, and 0.50, respectively. The values of Y_i are listed in Table 1. The program for the calculation of X_k, a_k, and b_k from known X_i and Y_j was given in [60]. The X_k, a_k, and b_k values obtained with the use of E_T^{30} and V_M as solvent parameters are collected in Tables 2 and 3, respectively.

Using the coefficients given in Tables 2 and 3, pK_{BH^+} values were calculated by Eq. (8) which directly follows from Eqs. (1)–(3):

$$pK_{BH^+}^{jk} = a_k \left[X_{ex,j} - X_k \sum_i g_{ij} X_i \right] + Y_j + b_k. \qquad (8)$$

The calculated and experimental pK_{BH^+} values were given in [60]. Table 4 shows an example of comparison of pK_{BH^+} values calculated by Eq. (8) for three NH acids with the experimental data. We calculated pK_{BH^+} values for NH acids and solvents for which no experimental data were given in [39–45, 47–49] (Table 5). The experimental pK_{BH^+} values in water ($j = 8$) are available for all 24 substrates.

The relative error for pK_{BH^+} calculated in the present work and given in [39–45, 47–49] was less than 10%. Taking into account this result, the accuracy

Table 4. Experimental and calculated pK_{BH^+} values for anilinium, pyridinium, and piperidinium

NH acid	pK_{BH^+}	$j = 1$	$j = 2$	$j = 3$	$j = 4$	$j = 5$	$j = 6$	$j = 7$	$j = 8$
Anilinium	Experimental [39–45, 47]	5.92	3.69	10.6	9.10	5.70	6.00	4.10	4.61
	Calculated (E_T^{30})	6.42	3.60	10.6	9.24	5.35	5.86	3.95	4.92
	εpK_{BH^+}, % (E_T^{30})	8.44	2.33	0.04	1.54	6.22	2.40	3.74	6.65
	Calculated (V_M)	6.44	3.66	10.8	9.69	5.14	6.01	3.85	4.83
	εpK_{BH^+}, % (V_M)	8.77	0.76	1.48	6.44	9.88	0.16	6.07	4.83
Pyridinium	Experimental [40, 42, 44]	5.77	3.40	12.3	12.0	4.30	5.54	4.48	5.21
	Calculated (E_T^{30})	6.02	3.23	11.8	11.34	4.51	5.54	4.89	4.78
	εpK_{BH^+}, % (E_T^{30})	4.30	5.10	4.70	5.70	5.00	0.00	9.10	8.20
	Calculated (V_M)	5.84	3.24	11.4	11.26	4.53	5.76	4.83	4.84
	εpK_{BH^+}, % (V_M)	1.14	4.82	7.63	6.37	5.39	3.98	7.75	7.05
Piperidinium	Experimental [40, 42, 44, 49]	12.2	10.6	–	18.2	12.5	11.0	11.1	11.0
	Calculated (E_T^{30})	13.1	10.2	18.3	17.7	11.3	12.0	11.1	10.9
	εpK_{BH^+}, % (E_T^{30})	6.90	4.10	–	2.70	9.90	9.50	0.10	1.00
	Calculated (V_M)	13.0	10.3	18.0	17.9	11.3	12.1	11.2	10.6
	εpK_{BH^+}, % (V_M)	5.89	2.84	–	1.48	9.74	9.96	0.71	3.62

Table 5. Experimental[a] and calculated[b] pK_{BH^+} values of NH acids in some solvents

k	Compound	Me$_2$CO	DMSO	MeCN	MeNO$_2$	EtOH	MeOH	HCONH$_2$
1	NH$_4^+$	13.7/13.4	10.5	16.5	15.2	11.4/11.5	11.3/11.5	8.78/8.94
2	EtNH$_3^+$	14.1/13.8	11.0	18.4	17.1	12.0/12.1	12.3/12.5	10.6/10.8
3	BuNH$_3^+$	14.2/14.0	11.1	18.3	16.9	12.2/12.2	12.4/12.6	10.5/10.7
4	1-Naphthylammonium	5.42	3.00/3.10	9.70/9.70	8.10/8.20	5.10	5.66	3.00/2.70
5	Et$_2$NH$_2^+$	11.2	10.5	18.8	17.9	10.7/10.8	11.9/12.0	11.5/11.6
6	Bu$_2$NH$_2^+$	12.8/12.6	10.0	18.3	17.8	11.2/11.2	12.1/12.3	11.3/11.4
7	Bu$_3$NH$^+$	11.1/10.8	8.31	18.1	17.7	9.30/9.40	10.6/10.8	10.7/11.0
8	PhNH$_3^+$	5.92	3.69	10.6	9.10	5.70	6.00	4.10
9	4-MeC$_6$H$_4$NH$_3^+$	6.57	4.5	11.2	9.80	6.24	6.60	4.30/4.10
10	3-MeC$_6$H$_4$NH$_3^+$	6.15	3.70/3.80	10.8	9.70	5.78	6.20	4.00/3.80
11	4-ClC$_6$H$_4$NH$_3^+$	5.34	2.98	9.56	8.00	4.66	4.90	3.26
12	4-BrC$_6$H$_4$NH$_3^+$	5.60/5.70	2.70/2.90	9.42	7.90	4.54	4.80	2.70/2.30
13	3-ClC$_6$H$_4$NH$_3^+$	4.85	2.30/2.40	9.30/9.50	7.70	4.25	4.50	2.75
14	3-O$_2$NC$_6$H$_4$NH$_3^+$	3.97	1.18	7.76	6.10	3.10/2.90	3.40/3.60	1.20/0.70
15	4-O$_2$NC$_6$H$_4$NH$_3^+$	3.52	0.50/0.50	6.17	5.20	2.20/2.00	2.30/2.50	0.40
16	Ph(Me)NH$_2^+$	5.60/5.60	2.82	10.5	9.80	4.86	5.45	4.10/3.80
17	Ph(Et)NH$_2^+$	5.80/5.70	3.18	10.9	10.2	4.30	5.80	4.60/4.40
18	PhMe$_2$NH$^+$	4.91	2.40/2.60	11.0/11.0	11.0	4.40	5.20	4.90/4.60
19	PhEt$_2$NH$^+$	6.26	3.20/3.20	12.6/12.2	12.1	4.37	6.85	6.50/6.10
20	Pyridinium C$_5$H$_5$N$^+$	5.77	3.40	12.3	12.0	4.30	5.54	4.48
21	2-MeC$_5$H$_5$N$^+$	6.64	4.00	13.1	12.5/13.1	5.54	6.24	6.10/6.30
22	Piperidinium	12.2	10.6	18.3/18.0	18.2	12.51	11.0	11.1
23	Quinolinium	5.41	3.00/3.20	12.4	11.5/12.7	4.58	5.50/5.80	5.10/5.70
24	Codeine·H$^+$	13.7/13.4	10.5	16.5	15.2	11.4/11.5	11.3/11.5	8.80/8.90

[a] Single value per cell.
[b] Two values separated by slash per cell; the first corresponds to E_T^{30} as solvent parameter, and the second, to V_M.

Table 6. Comparison of the results of quantum-chemical calculations of pK_{BH^+} with those obtained in the present work

Solvent	Calculation method[a]	Substrates	Total number of compounds[b]	Number of pK_a values matching the condition εpK_a <10%	Z_1[c]	Z_2[d]	Reference[e]
Water	QSPR	Carboxylic acids, protonated amines	76 (76)	57[f]	8	5	[21]
Water	CPCM, QSPR	Various compounds	64 (64)	42[f]	0	0	[19]
Water	CPCM, Cluster, QSPR	Carboxylic acids, phenols, pyridinium salts	64 (64)	53[f]	7	4	[20]
DMSO	PCM	Various compounds	42 (42)	28[f]	1	1	[24]
Water	Cluster	Phenols, imidazole, methanol	5 (19)	12[f]	0	0	[25]
Water	QSPR	Protonated anilines	36 (36)	28[f]	8	2	[6]
Water	PCM, SE	Protonated pyridines	15 (15)	7	1	1	[7]

Table 6. (contd.)

Solvent	Calculation method[a]	Substrates	Total number of compounds[b]	Number of pK_a values matching the condition $\varepsilon pK_a <10\%$	Z_1[c]	Z_2[d]	Reference[e]
DMSO	IPCM	Various compounds	36 (36)	12	1	0	[8]
DMSO	Cluster	Various compounds	106 (212)	98	4	0	[9]
Water, DMSO, MeCN	PCM	Mineral and carboxylic acids, phenols, protonated amines	8 (144)	23	2 (6)	0	[10]
Water	PCM, Cluster	Various compounds	17 (17)	5	1	0	[26]
Water	CPCM	Imidazoles	36 (38)	9	0	0	[27]
Water	CPCM	Tetrazoles	9 (144)	38	0	0	[28]
Water	CPCM	Mineral and carboxylic acids, nucleotides, imidazoles	9 (60)	0	0	0	[29]
Water	PCM	Protonated amines and imines, heterocycles	25 (72)	18	8 (21)	1	[30]
Water	SE, QSPR	Protonated anilines	63 (126)	49	12 (24)	1	[23]

[a] PCM stands for polarizable continuum model, CPCM stands for conductor-like polarizable continuum model, IPCM stands for integral polarizable continuum model, cluster denotes the model taking into account geometric parameters of the solvate–solvent complex, QSPR stands for the quantitative structure–property relationship (which was used to process the results and/or calculate the energy of solvation or deprotonation), and SE denotes that the calculations were performed in part by semiempirical method.

[b] The number of pK_{BH^+} values calculated by different methods is given in parentheses.

[c] The number of NH acids for which pK_{BH^+} values were calculated in the present work and in the corresponding referenced study; the total number of pK_{BH^+} values calculated for these acids by different methods is given in parentheses.

[d] The number of pK_{BH^+} values (see note [c]) for which the relative error was lower than the best result obtained in the present work.

[e] The data of [31, 32] were not included, for only correlation parameters were given therein while calculated pK_{BH^+} values were lacking or experimental data required for comparison were absent.

[f] The number of pK_{BH^+} values matching the condition $\varepsilon pK_{BH^+} < 10\%$ exceeds the half of the total number of calculated values.

criterion for the calculation procedures was set at 10% relative error (εpK_{BH^+}). Among publications (during the past decade) in which pK_{BH^+} of organic compounds, including NH acids, in solution were calculated by quantum-chemical methods, the best agreement with the experimental data was reached in [6, 19–21, 24]. The efficiencies of different calculation procedures are compared in Table 6.

The total number of pK_{BH^+} values calculated in [6–10, 19–21, 23–30] and in the present work is 74. Comparison with the sum of Z_2 (Table 6) shows that only 15 pK_{BH^+} values from [6–10, 19–21, 23–30] are better consistent with the experimental data than those calculated by Eq. (8).

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