A KNOWLEDGE BASED ADVISORY SYSTEM FOR ACID/BASE TITRATIONS IN NON-AQUEOUS SOLVENTS

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sept 1995, to be published in Anal.Chim.Acta

Abstract

A computer program was developed that can give advice on the choice of solvent and titrant for acid/base titrations in non-aqueous media. It is shown that the feasibility of a titration in a given solvent can be calculated from solvent properties and intrinsic acid/base properties of the sample components. A consistent set of properties for various solvents and a large number of acidic and basic compounds was calculated from literature data with the use of a genetic algorithm. Test results show that the system works well for titrations in various classes of solvents

INTRODUCTION

Titrations in non-aqueous solvents have been traditionally an important tool for the accurate determination of various pharmaceuticals [1], the analysis of industrial process streams, the analysis of polymers [2], etc. The successful development of a new titration method in this field is strongly dependent on a thorough understanding of the

chemical equilibria involved in the titrations and the relationship between the equilibrium constants and the properties of the solvent used for the titration. The bulk of this knowledge has been acquired in the sixties [3-6] and has been applied since then to numerous practical problems [7].

Recent developments in the field of titrations in non-aqueous solvents concern the generalization of equilibrium data with the use of quantified solvent properties like basicity, dielectric constant, etc.[8-10] This paper describes an attempt to put this knowledge to use in a computer program that can assist in the development of titration procedures for new sample/solvent combinations. The design of such a knowledge based system generally requires the structuring of the knowledge in a database of facts and a set of reasoning rules that can be used by a so-called inference engine that does the reasoning[3]. In the program that was developed in this work the required knowledge is structured in three forms: (1) a database, (2) a set of reasoning rules and (3) procedures that calculate the quality of the titration of a proposed sample/solvent/titrant combination. The database contains solvent properties and intrinsic acid/base strengths of various compounds and functional groups. The reasoning rules are of a qualitative nature and are based on the Brønsted/Lowry theory of acids and bases and the solvent classification scheme of Brønsted [4]. A special feature of the system developed in this work is that it also contains a quantitative physico-chemical model of the phenomena it deals with. This procedural knowledge concerns the calculation of actual acid/base strengths of samples in specific solvents, the calculation of the titration curve and the calculation of the accuracy of the titration. These calculations are not restricted to single components systems, but can deal with samples that consist of a mixture of acids and bases.

The data needed to fill the database of the system is not available in the required form in literature, so part of the paper is devoted to the description of a method to obtain a consistent dataset with properties of solvents, acids and bases that enables the calculation of the needed equilibrium constants. For this goal a genetic algorithm [13-15] was used to extract the wanted data from published tables of pKa-values in various solvents because these algorithms are known to be efficient in the search of the large parameter space that in this problem consists of the properties of all solvents and acids and bases that the system

has to deal with.

The procedure for the calculation of the titration curve of a specific system has to be efficient because it has to be used very frequently to rank the solutions suggested by the qualitative reasoning processes. For this goal the EQUIL software [5] was rewritten in the language C and extended with routines that can identify the compounds causing the different inflection points and that calculate the accuracy with which these points can be determined.

Because of the hybrid nature of the system to be developed, in the sense that it should accomodate declarative as well as procedural knowledge, CLIPS [6] was thought to be the ideally suited development tool as this expert system development environment allows easy mixing of procedural and declarative coding styles together with the possibility of using an object oriented language that very nicely fits the natural way of thinking in the field of titrations in non-aqueous solvents, i.e. solvent classes, compound classes, etc.

A major point of concern in the design of software is the user interface. This point is closely connected with the choice of the platform(s) the software is to be developed for. UNIX together with the X11 windowing system is a generally accepted platform for scientific applications and we decided to use the public domain version **Linux** [7] running on INTEL based PC's together with the **Tk** [8] user interface package that builds on the functionality offered by X11 and provides all the kinds of menus needed for the user interaction of this advisory system. With this choice the software that is developed can easily be ported to any workstation that runs UNIX/X11. Another aspect of this choice is that in the development of the complete system it is easy to use existing software packages, i.e. for plotting curves, the user interface and formatting the output for printing without the need for any changes by integrating them in a so-called shell script.

THEORY

Choice of candidate solvents

The choice of the solvent for the titration of a specific sample is first of all governed by the solubility of the sample. To be able to carry out the titration of a sample in a given medium, the sample should be

dissolved in this medium. Solubility data are not kept in the system, so this information has to be provided by the user and the system uses this information in such a way that it starts to look at solvents for which it is known that they dissolve the sample. Only in case that none of these solvents turns out to produce a suitable titration curve the system falls back on other solvents from its internal list on which it has data available. Media in which the sample is said to be insoluble are simply not taken into consideration.

Within the constraints of solubility as described above, the choice of the solvent is dependent on the nature of the sample component(s) to be titrated (acidic or basic), the number of components in the sample and in case of a multicomponent sample, whether the titration should provide the result for all components separately or as their sum only. Based on the solvent classification given by Brønsted and shown in Table 1 the heuristics for the distinction between solvents that should be taken into account and those than can be disregarded are: (1) if possible use a solvent with a high dielectric constant, (2) take the amphiprotic solvents from classes I and V into consideration for every kind of titration problem, (3) for total acid determination look at the basic solvents from the classes III and VII, (4) for total base determination look at the acidic solvents from the classes II and VI, (5) for a differential titration of a mixture of acids look at the inert and acidic solvents from classes IV, II and VI, (6) for a differential titration of a mixture of bases look at the inert and basic solvents from classes IV, III and VII, (7) if nothing else works look at the solvents from class VIII, the inert solvents with a low dielectric constant and (8) if the matrix of the sample is not inert then look at solvents similar to the matrix.

The rationale behind the heuristics (1) and (7) is that it is rather difficult to obtain stable pH-readings with ordinary glass-electrodes in solvents with a low dielectric constant, especially if they are completely inert and/or inmiscible with water. The heuristics 3-6 all concern the phenomenon of *levelling*[9] in which all acids (or bases) exceeding a certain strength in a particular solvent appear to have the same strengths in that solvent. For differential titrations leveling should not occur, whereas for titrations of the total amount of acids or bases in a mixture this leveling is advantageous. Heuristic (2) is based on the fact that amphiprotic solvents like the alcohols are generally more comfortable to work with and less toxic than solvents from the other

classes.

Using these heuristics the candidate solvents for a given titration problem can be classified as **preferred**, **uncomfortable** and **last-resort** solvents as shown in Table 2.

pKa-values

Based on the theory described earlier [10] [11] the dissociation constant of an acidic compound in a specific solvent can be described in terms of the intrinsic acidity constant of the compounds, the solvent basicity and an electrical part that can be described by the Born theory.

$$(pKa)_{solvent} = (pKa)_{intrins} - solventbasicity + \Delta U_{electrical} \qquad (1)$$

Strictly spoken this electrostatic term is specific for a given compound / solvent combination. In this work this term is neglected for cationic acids with a charge of +1 and taken to be a constant that is characteristic for any other charge type/solvent combination. With this simplification the dissociation constant of a compound can be found for any solvent if its intrinsic acidity constant is known together with the solvent basicity and the electrical term for the solvent.

Fitting equation (1) to tables of available pKa-data for various solvents using a genetic algorithm[12] delivers the required tables of intrinsic acidity constants, the solvent basicities and the electrical terms. The procedure needs a reference point for the basicity data as well as the electrical data. Arbitrarily these terms were set to zero for the solvent water. This makes it easy to incorporate a new compound into the system when its aqueous pKa-value is known, which is often the case.

Titration curve calculations

To evaluate the feasibility of a titration in a candidate solvent it is necessary to calculate the titration curve based on the pKa-data obtained in approximated form as described above. When this curve is available the accuracy of the analysis of the compounds in the sample can be calculated from its steepness in the equivalence points. Three categories of quality ratings are introduced in this respect: a rating of 100 for accuracies better than 0.3 %, 90 for accuracies between 0.3 and 0.5 % and a rating of 50 for an accuracy between 0.5 and

1.0 %. To calculate the quality rating of an equivalence point it is assumed that the inflection point can be determined to $\pm$ 0.1 pH-units. Of course, the real concentrations of the sample components are unknown in this stage, so the calculations have to be performed for standard conditions, which were taken as: titrant strength 0.1 M, sample concentration 0.006 M, and volume at the start of the titration 60 mL.

For the evaluation of titration of samples consisting of mixtures of acids or bases it is very convenient if the breaks in the titration curve have been identified. This identification can be carried out by calculating the titration curve for a given sample with varying initial concentrations of each of the sample components and determining the shifts of the various inflection points. The position of these inflection points can be established by determining the extrema in the first derivatives of the titration curves which, in their turn, can be calculated with the Savitzky/Golay procedure [13].

SOFTWARE

Figure 1 shows the general dataflow diagram of the system. The system has two input externals, the solubility data and the sample data which have to be provided by the user and one output external, the advice on the solvent and titrant combination that can be used for the given problem. The solubility data consists of two parts: a list of solvents in which the sample is known to dissolve and a list of media in which the sample is insoluble.

The advice on a suitable solvent/titrant combination also includes a graph of the expected titration curve, an expected rating of the quality of the analysis and the identification of the endpoints in the curve.

B The three processes depicted in the dataflowdiagram, "read user input", "reasoning system" and "evaluate accuracy" are implemented as separate programs. The communication between the processes is via diskfiles, in the diagram depicted as the datastores "reas.system input" and "candidate solvents". The other datastores are tables that contain the factual knowledge of the system. These tables are internal to the programs that use them.

The reasoning system controls the operation of the system after

it is provided with its necessary input from the user input interface. This user interface has 5 pull-down menus: "Solvents", "Non-Solvents", "Func.Groups", "Sample-Matrix", "Analysis Type" and "Sample Identification". The "Solvents" and "Non-Solvents" menus both show a list of solvents. Items on these lists can be activated by mouse clicks, thus generating the solubility data needed in the reasoning system. Table 3 shows the solvents the system can deal with. The same menu technique is used for the input of components to be titrated in the "Func.Groups" menu. Table 4 shows the list of compounds that are known to the system. In the "Sample-Matrix" menu only one item can be chosen from the possibilities "Inert", "Weak Acidic", "Strong Acidic", "Weak Basic" and "Strong Basic". The "Analysis Type" menu offers the choice between "total acid", "differential acid", "total base" and "differential base". Finally the "Sample Identification" menu presents a form to be filled out with filing data like sample identifcation, date, customers name , etc.

Based on this input data the reasoning system chooses various solvent/titrant combinations and has them evaluated by the "evaluate accuracy" system. It continues to do so until either a suitable solution to the problem has been found or until its possibilities are exhausted. The data needed for this evaluation consists of a symbolic representation of all the chemical equilibria that play a role during the titration together with the equilibrium constants of these reactions. All are provided by the reasoning system.

Every solvent evaluation that the system performs is presented to the user in the form of a titration curve and its quality rating. The curves are plotted with the public domain software package **gnuplot** [14]. In this way the user can decide what to do when a less than perfect solution is the best that the system can come up with.

The software is available upon request by e-mail from m.bos@ct.utwente.nl.

EXPERIMENTAL

Chemicals

The chemicals tert-butanol, benzoic acid, imidazol, hydroxylammoniumchloride, phenol, n-butanol, acetonitril (AN) and pyridine were from Merk, quality Zur Analyse and used as received. Dimethyl-

sulphoxide (DMSO) (zur Analyse) and n-butylamine (zur Synthese) were from Merck-Schuchardt and also used as received. The titrants used were trifluoromethanesulphonic acid (0.1 M) (TMFS) and tetrabutylammoniumhydroxyide (TBUOH) and were both dissolved in isopropanol. Hydrochloric acid used in the acidic samples to be titrated was prepared from a stock solution that was obtained by solving gaseous hydrochloric acid (Baker) in tert-butanol.

Equipment

The titrations were carried out with automatic titration equipment from Schott, type TR250 with burette T100 and a combined glass/reference electrode from Orion, type 81-72BN. This electrode was not standardized for the various solvents in which it was used, so the pH-scales in the curves presented should be considered as relative.

Titrations

Titrations were performed on 50 mL samples of a test mixture of acids, consisting of 0.3 mmol of each of the compounds benzoic acid, hydroxylammoniumchloride, hydrochloric acid and phenol and on 50 mL samples of a test mixture of bases, consisting of 0.3 mmol of pyridine, imidazol and n-butylamine.

RESULTS AND CONCLUSIONS

Calculation of a consistent set of solvent properties and intrinsic acidities

Equation (1) is the basis to obtain the intrinsic acidities of sample components to be titrated and the solvent properties basicity and the Born term. This equation is first applied to acids with charge type +1 for which the electrical term ΔU can be neglected. Table 5 shows the literature [4,25-28] data which was used to fit the intrinsic acidity and solvent basicity parameters in such a way that the sum of squared differences between the pKa-values calculated with the equation (1) and the pKa-values given in literature is minimized. These calculations are performed with the Genetic Algorithm package Genitor [12].

The results are given in the Tables 6 and 7. In the last table also the aqueous pKa-values haven been entered. As the reference value for the basicity of water was set to zero, the intrinsic values can be compared directly with these values and generally they agree within $\pm$ 0.5 pK-units. The only exception is for p-anisidine-H^+, but for this compound only its pKa-values for water and acetic acid were available. Similar comparisons of literature pKa-values and those calculated with equation (1) and based on the data of Table 6 and 7 have been made and show the same general picture.

The next step is to use the solvent basicities from Table 6 and pKa-data of electrically neutral acids in the full equation (1) to find the electrical term for the various solvents for the dissociation of this type of acids in the various solvents together with the intrinsic acidities of the acids involved. Table 8 shows the literature data [3,4,25-27,29] used in this procedure and the Tables 9 and 10 show the results.

The ΔU_{elec} term in Table 9 does not strictly increase in absolute sense with a decrease in the dielectric constant of the solvents. This can be explained by the fact that upon dissociation of an acid in a given solvent there will also be a change in the entropy, due to solvation processes of the species involved. Equation (1) only takes care of the enthalpy part of the dissociation. The entropy change upon dissociation caused by differences in solvation, especially stabilization of the anion of a dissociating electrically neutral acid, will be lumped with the ΔU term. For solvents that poorly solvate these anions the absolute magnitude of this term will be much higher as can be seen from the comparison of the solvents methanol and acetonitril, resp. m-cresol and pyridine. This does not impair the accuracy of the use of equation (1) as long as the ΔU terms are determined from experimentally established pKa-data, but unfortunately it prevents the calculation of this term directly from the dielectric constant of a solvent.

A comparison of the intrinsic pKa-values of the compounds in Table 10 with their pKa(H_2O) counter parts shows greater deviations than for the cationic acid from Table 7. This can be due to specific solvation phenomena for some of the compounds. Surprisingly the discrepancies are rather large for the carboxylic acids acetic acid and benzoic acid in the solvent water, although the intrinsic acidity of these compounds fits the model of equation (1) very well for the other solvents (see table 11). Nevertheless the accuracy of the pKa-

values calculated with equation (1) is sufficient to determine whether a titration is feasible or not.

Test titrations

The complete system incorporates more solvents and compounds than the ones listed in the previous section for which a consistent set of properties was established. The data for these other compounds and solvents was estimated from pKa(H_2O) values and analogies between solvents based on dielectric constant, hydrogen bonding capacity and basicity. It is expected that the quality of the advice of the system on the titration procedure for these compounds and solvents sometimes will be less than for the compounds and solvents for which sufficient data was avaliable. Future work will be devoted to a self-learning mode of the system in which actual experimental titration data will be compared with the titration curves generated in the evaluation of the quality of the titration in specific solvents to adjust numerical data on intrinsic acidities or solvent properties in the knowledge base of the system.

Figures 2 and 3 show the actual curves and the ones predicted by the system for the titration of a mixture of benzoic acid, phenol, hydroxylammoniumchloride and hydrochloric acid in the solvents dimethylsulphoxide (DMSO) and acetonitril (AN) that are suggested by the system for the differential titration of this mixture. Vertical displacement of the experimental curves along the pH-axis has no meaning in these figures, as the glass electrode was not calibrated. Slight differences in the position of the inflection points on the volume axis can be caused by a small difference between the strength of the titration used in the calculations (0.1000 M) and the actual strength of the titrant used as well as impurities in the sample components.

For both solvents the first inflection point is identified as belonging to hydrochloric acid. For DMSO the second inflection point in the predicted curve is for the sum of benzoic acid and hydroxylammoniumchloride and the third is for phenol. In acetonitrile the second inflection point is for hydroxylammoniumhydrochloride, the third for the carboxylic acid and no inflection point can be discerned for phenol. For DMSO the quality of the inflection points in the experimentally determined curve is somewhat less than calculated, for AN the quality of the second inflection point of the experimental curve is somewhat

better than predicted, whereas the quality of the third inflection point in the experimental curve is somewhat worse than predicted. Nevertheless it can be seen from these curves that the agreement between the predicted and actual curves is such that the quality of the titrations can fairly be estimated.

For the titration of the total amount of acid in this sample the system suggest a titration in n-butylamine and predicts a titration curve showing a clear inflection point when all components have been titrated. The actual titration curve also shows an inflection point at this position, although with a much smaller pH-jump, indicating that the estimated data on n-butylamine should be improved. A comparison of the two curves is given in figure 4.

To assess the performance of the system for the titration of bases a test mixture of n-butylamine, imidazol and pyridine was used. For the differential titration the system suggests n-butanol, for the titration of the total amount of bases it choses acetic acid. The predicted and actual curves are given in the figures 5 and 6 . One can see that the quality of the titration in n-butanol estimated by the system agrees very well with the one that can be realized in practice. For the titration in acetic acid this is not the case. Here the predicted curve shows inflections for all three components of the sample mixture. In the actual curve there is only a single inflection point in the curve at the position where all three components haven been titrated. This means that the basicities of the sample components have been estimated too low by the system. In the system the values of the formation constants of the protonation of bases are calculated as the reciprocal of the dissociation constant of the conjugate acids. In their turn these are calculated from the intrinsic strengths of these conjugate acids and solvent properties, in this case the basicity of acetic acid from Table 6. Further experiments should show whether this is in error or that the differences between the actual and predicted titration curve is caused by using overall dissociation constants instead of separate ioniziation and ionpair dissociation constants.

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Captions to the figures

Figure 1
Dataflow diagram of knowledge based advisory system for titrations in non-aqueous solvents

Figure 2
Titration of 0.3 mmol HCL, 0.3 mmol benzoic acid, 0.3 mmol hydroxylammoniumchloride and 0.3 mmol phenol in 50 mL of DMSO. Titrant 0.1 M TBUOH in iso-propanol. (+) experimental curve (pH-scale uncalibrated),
($\diamond$) curve estimated by system.

Figure 3
Titration of 0.3 mmol HCL, 0.3 mmol benzoic acid, 0.3 mmol hydroxylammoniumchloride and 0.3 mmol phenol in 50 mL of Acetonitril. Titrant 0.1 M TBUOH in iso-propanol. (+) experimental curve (pH-scale uncalibrated), ($\diamond$) curve estimated by system.

Figure 4
Titration of 0.3 mmol HCL, 0.3 mmol benzoic acid, 0.3 mmol hydroxylammoniumchloride and 0.3 mmol phenol in 50 mL of n-butylamine. Titrant 0.1 M TBUOH in iso-propanol. (+) experimental curve (pH-scale uncalibrated), ($\diamond$) curve estimated by system.

Figure 5
Titration of 0.3 mmol n-butylamine, 0.3 mmol imidazol and 0.3 mmol pyridine in 50 mL n-butanol. Titrant 0.1 M TMFS in iso-propanol. (+) experimental curve (pH-scale uncalibrated) , ($\diamond$) curve estimated by system.

Figure 6
Titration of 0.3 mmol n-butylamine, 0.3 mmol imidazol and 0.3 mmol pyridine in 50 mL acetic acid. Titrant perchloric acid in acetic acid. (+) experimental curve (pH-scale uncalibrated), ($\diamond$) curve estimated by system.

Table 1: Solvent classes according to Brønsted

Class nr.	dielectric constant	relative acidity	relative basicity
I	+	+	+
II	+	+	-
III	+	-	+
IV	+	-	-
V	-	+	+
VI	-	+	-
VII	-	-	+
VIII	-	-	-

Table 2: Suitability of solvents for specific titrations based on their Brønsted class number

Suitability	titr. of total acid	titr. of total base	titr. of acid diff.	titr. of base diff
preferred	III, I, IV	II, I, IV	IV, II, I	IV, III, U
uncomfortable	VII, V	VI, V	VI, V	VII, V
last resort	VIII	VIII	VIII	VIII

Table 3: Solvents in knowledge base

methanol	n-butylamine	dimethylsulphoxide
ethanol	n-propylamine	acetic acid anhydride
isopropanol	triethylamine	dimethylformamide
n-propanol	ethylenediamine	acetone
t-butanol	ethanolamine	pyridine
m-cresol	formic acid	acetic acid
o-cresol	sulphuric acid	dichloroethane
benzylalcohol	acetonitril	benzene

Table 4: Sample compounds in knowledge base

carboxylic acid	iodoacetic acid	sec-amine
hydrochloric acid	2,4-dinitrophenol	tert-amine
phenol	3,6-dinitrophenol	acetamide
prim-amine-H^+	4-nitrophenol	aniline
sec-amine-H^+	3-nitrophenol	n-butylamine
tert-amine-H^+	2-nitrophenol	strychnine
bisulphate	4-picolinium	imidazol
picric acid	prim-amine	pyridine

Table 5: Literature pKa-values cationic acids

Compound	pKa H2O	pKa DCLE	pKa m-Cres	pKa HAc	pKa Pyr	pKa AN	pKa MeOH	pKa DMSO
strychnine-H^+	8.0	16.0	13.0					
morpholine-H^+	9.6	15.0	12.1		3.5			
n-butylamine-H^+	10.6	17.0	13.9		5.5	18.3	11.1	
triethylamine-H^+	10.8	17.7	14.2		3.8	18.5	10.9	9.0
tetramethylguanidine-H^+	13.6	21.5			9.6	23.3	13.2	
4-picoline-H^+	6.0				13.65	6.09		
acetamide-H^+	-0.5			3.95				
p-anisidine-H^+	5.29			3.85				
N,N-diethylaniline-H^+	6.56		9.3					
N.N-dimethylaniline-H^+	5.06			8.9				
1,3-diphenylguanidine-H^+	10.0			9.3				
o-nitro-aniline-H^+	0.0			3.4				
pyridine-H^+	5.2			8.48		12.3		3.4
urea-H^+	0.2			4.27				
benzylamine-H^+	9.3							
methylamine-H^+	10.64					18.4	11.0	
dimethylamine-H^+	10.72					18.7	11.2	
trimethylamine-H^+	9.74					17.6	9.8	
ethylamine-H^+	10.6					18.4	11.0	
NH_4^+	9.2					16.5		10.5
diethylamine-H^+	11.0					18.8		10.5
dibutylamine-H^+	11.3					18.3		10.0
tributylamine-H^+	10.9					18.1		8.4
aniline-H^+	4.6					10.6		3.6

Table 6: Fitted solvent basicities

solvent	fitted basicity
acetonitril (AN)	-7.74
dichloro-ethane (DCLE)	-6.94
m-cresol (m-Cres)	-3.83
acetic acid (HAc)	-2.63
methanol (MeOH)	-0.62
water (H2O)	0.0[1]
dimethylsulphoxide (DMSO)	0.65
pyridine (Pyr)	5.31

[1] reference value

Table 7: Fitted intrinsic pKa-values

Compound	Intrins. pKa	pKa(H2O)
strychnine-H^+	8.29	8.0
morpholine-H^+	8.43	9.6
n-butylamine-H^+	10.36	10.6
triethylamine-H^+	9.94	10.8
tetramethylguanidine-H^+	14.10	13.6
4-picoline-H^+	5.46	6.0
acetamide-H^+	0.55	-0.5
p-anisidine-H^+	3.27	5.29
N,N-diethylaniline-H^+	6.59	6.56
N.N-dimethylaniline-H^+	5.64	5.06
1,3-diphenylguanidine-H^+	8.38	10.0
o-nitro-aniline-H^+	0.33	0.0
pyridine-H^+	4.81	5.2
urea-H^+	0.97	0.2
benzylamine-H^+	9.32	9.3
methylamine-H^+	10.12	10.64
dimethylamine-H^+	10.57	10.72
trimethylamine-H^+	9.26	9.74
ethylamine-H^+	10.72	10.6
NH_4^+	9.43	9.2
diethylamine-H^+	10.88	11.0
dibutylamine-H^+	10.63	11.3
tributylamine-H^+	9.86	10.9
aniline-H^+	3.55	4.6

Table 8: Literature pKa-values electrically neutral acids

Compound	pKa H2O	pKa DCLE	pKa m-Cres	pKa HAc	pKa Pyr	pKa AN	pKa DMSO	pKa MeOH
picric	0.38	13.7						
iodoacetic	3.12	17.6	13.0					
m-nitrobenzoic	3.5					19.2		
p-nitrobenzoic	3.44					18.7		
o-nitrobenzoic	2.21					18.2		
3,5-dinitrobenzoic	2.82					16.9	7.4	
2,4-dinitrobenzoic	1.42					16.1		
2,6-dihydroxybenzoic	1.2					12.6	3.1	
4-chloro-2,6-dinitrophenol	3.0					15.3	3.5	
2,6-dinitrophenol	3.6					16.45	4.9	
salicylic	3.0					16.7	6.8	
2,6-di-t-butyl-4-nitrophenol	7.2					19.0	7.6	
3,5-dinitrophenol	6.7					20.5	10.6	
p-nitrophenol	7.2					20.7	11.0	11.15
o-nitrophenol	7.2					22.0	11.0	
5,5-diethylbarbituric	8.0					23.4	13.0	
hydriodic		7.9	4.4					
hydrobromic		8.7	4.4			5.51		
hydrochloric		10.8	6.4	8.55		8.94		
benzenesulphonic		12.1	6.3					
benzoic	4.2	20.0	15.0		11.0	20.7	11.1	9.4
perchloric				4.87				
acetic	4.75		16.0		12.0	22.3	12.6	
sulphuric(1)						7.32		
nitric					8.89			
3,4-dimethylbenzoic	4.4					21.2		
p-hydroxybenzoic	4.5					20.8		
m-bromobenzoic	3.86					19.5		
3,4-dichlorobenzoic						19.0		
3,5-dichlorobenzoic						18.7		
3-nitro-4-chlorobenzoic						16.9		
phenol	9.98					27.2	16.4	14.2

Table 9: Born term for the dissociation of HX type acids

Solvent	ΔU_{elec}	dielectric constant
water (H2O)	0.00[1]	78.2
methanol (MeOH)	-1.89	32.6
dimethylsulphoxide (DMSO)	-3.70	46.7
acetonitril (AN)	-5.12	37.5
m-cresol (m-Cres)	-5.51	11.75
dichloro-ethane (DCLE)	-6.87	10.4
acetic acid (HAc)	-8.05	6.2
pyridine (Pyr)	-9.48	12.3

[1] reference value

Table 10: Intrinsic pKa-values

Compound	pKa (H2O)	pKa (intrins)
picric	0.38	-1.13
iodoacetic	3.12	2.84
m-nitrobenzoic	3.5	4.32
p-nitrobenzoic	3.44	4.06
o-nitrobenzoic	2.21	2.78
3,5-dinitrobenzoic	2.82	3.02
2,4-dinitrobenzoic	1.42	1.61
2,6-dihydroxybenzoic	1.2	-0.26
4-chloro-2,6-dinitrophenol	3.0	1.32
2,6-dinitrophenol	3.6	2.19
salicylic	3.0	2.76
2,6-di-t-butyl-4-nitrophenol	7.2	5.27
3,5-dinitrophenol	6.7	6.49
p-nitrophenol	7.2	6.94
o-nitrophenol	7.2	7.39
5,5-diethylbarbituric	8.0	8.64
hydriodic		-6.44
hydrobromic		-7.16
hydrochloric		-4.59
benzenesulphonic		-3.55
benzoic	4.2	5.54
perchloric		-8.28
acetic	4.75	6.67
sulphuric(1)		-6.73
nitric		-5.37
3,4-dimethylbenzoic	4.4	7.14
p-hydroxybenzoic	4.5	6.64
m-bromobenzoic	3.86	5.30
3,4-dichlorobenzoic		4.83
3,5-dichlorobenzoic		4.64
3-nitro-4-chlorobenzoic		4.44
phenol	9.98	11.92

Table 11: Calculated and experimental pKa-values for benzoic acid

	pKa-calc.	pKa-exp
water	7.53	4.19
dichloro-ethane	20.4	20.0
m-cresol	15.78	15.0
pyridine	11.37	11.0
acetonitril	19.78	20.7
dimethylsulphoxide	10.39	11.1
methanol	8.5	9.4