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Editorial Additions

~~**Editorial Deletions**~~

COMMENTS

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A Comprehensive Self-Consistent Spectrophotometric Acidity Scale of Neutral Brønsted Acids in Acetonitrile

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For the first time, the self-consistent spectrophotometric acidity scale of neutral Brønsted acids in acetonitrile (AN) spanning 24 orders of magnitude of acidities is reported. The scale ranges from pK_a 3.7 to 28.1 in AN. The scale includes 93 acids that are interconnected by 203 relative acidity measurements (ΔpK_a measurements) and contains compounds with gradually changing acidities, including representatives from all of the conventional families of OH (alcohols, phenols, carboxylic acids, sulfonic acids), NH (anilines, diphenylamines, disulfonimides), and CH acids (fluorenes, diphenylacetonitriles, phenylmalononitriles). The CH acids were particularly useful in constructing the scale because they do not undergo homo- or heteroconjugation processes and their acidities are rather insensitive to traces of water in the medium. The scale has been fully cross-validated: the relative acidity of any two acids on the scale can be found by combining at least two independent sets of ΔpK_a

measurements. The consistency standard deviation of the scale is 0.03 pK_a units. Comparison of acidities in many different media has been carried out, and the structure–acidity relations are discussed. The large variety of the acids on the scale, its wide span, and the quality of the data make the scale a useful tool for further acidity studies in acetonitrile.

Introduction

Acidity data in nonaqueous solutions are of continuing interest to chemists. One of the most popular solvents in this respect is acetonitrile (AN). Experimental measurements of pK_a values in acetonitrile started from the classic papers of the groups of Kolthoff[1–3] and Coetzee[4,5] in the 1960s, and a considerable amount of acidity data for various acids in AN has been accumulated to date.[4,6–11] Literature analysis shows that acidity data for different compounds in the pK_a range of 4–28 exist in AN. However, the data are scattered, and large discrepancies exist between the data of different groups. For example, the literature pK_a values of 2,4-dinitrophenol range from 15.34[12] to 18.40[13] units.

Recently, a comprehensive UV–vis spectrophotometric self-consistent basicity scale in AN was published containing a thorough analysis of the literature and setting a solid foundation for further basicity studies in AN.[14] In this work, we set out to accomplish the same for acidity measurements in AN.

We report in this paper a reliable, continuous, self-consistent acidity scale covering the pK_a range of approximately 3.7 to 28.1, i.e., the whole domain of

conventional acidities in AN. The scale contains compounds with gradually changing acidities, including representatives from all of the conventional families of OH (alcohols, phenols, carboxylic acids, sulfonic acids), NH (anilines, diphenylamines, disulfonimides), and CH acids (fluorenes, diphenylacetonitriles, phenylmalononitriles). The scale has been fully cross-validated: the relative acidity of any two acids on the scale can be found combining at least two independent sets of ΔpK_a measurements.

The majority of measurements reported in the literature have been carried out using potentiometric and conductometric methods. In the present work, the spectrophotometric method was used. We will compare our data with the data reported in the literature to make conclusions about the contraction or expansion effects and other systematic deviations between this scale and the literature data.

The advances in the computational methods during the recent years have encouraged computational approaches to the prediction of pK_a values in the nonaqueous solutions. There have been several works published on theoretical pK_a calculations for the DMSO solution[15] and, to the best of our knowledge, only one for AN solution.[16] At this stage of development, the theoretical solution pK_a values are not as accurate as experimental data (because of the complications in taking the solvation and other effects into account appropriately) and rely heavily on the experimental data (most of the published theoretical pK_a prediction works involve correlations with experimental pK_a values). Experimental data are also essential for improvement of the theoretical calculation methods.

AN has many properties that make it a suitable medium for acid–base studies. It

has low basicity and a very low ability to solvate anions.[4] The low basicity gives AN an advantage in studies of strong acids over the other very popular solvent for acid–base studies, DMSO, which is considerably more basic (stronger hydrogen bond acceptor). As AN also has a high dielectric constant (D = 36.0[4]), it also favors the dissociation of ion pairs into free ions. The autoprotolysis constant of AN is very low, $pK_{auto} \geq 33$,[17,18][17–18] which makes it a good differentiating solvent. Additionally, the advantages of AN are its transparency for UV radiation down to 190 nm and relative ease of purification.

Acidity of an acid HA in a solvent S refers to the equilibrium<pick;equ1;none;suspend></qa>

$$HA + S \rightleftharpoons A^- + SH^+$$ <id;reqid;1>

<nopara>and is expressed as dissociation constant K_a or more commonly its negative logarithm pK_a.<pick;equ2;none;suspend></qa>

$$K_a = \frac{a(SH^+)a(A^-)}{a(HA)}$$ <frx><id;reqid;2>

Because of the complications of measuring the acidity of the medium, $a(SH^+)$, in nonaqueous solvents, we use a method that eliminates the need for its determination. Our method of acidity measurements is based on measuring relative acidities of the acids HA_1 and HA_2 according to the following equilibrium:<pick;equ3;none;suspend></qa>

$$HA_2 + A_1^- \rightleftharpoons A_2^- + HA_1$$ <id;reqid;3>

The relative acidity of the two acids HA_1 and HA_2 (ΔpK_a) is

defined:<pick;equ4;none;suspend></qa>

$\Delta pK_a = pK_a(HA_2) - pK_a(HA_1) = -\log K = \log$ <fr>$a(A_1^-)\cdot a(HA_2)$<fd>$a(HA_1)\cdot a(A_2^-)$<frx> <id;reqid;4>

The method consists of UV–vis spectrophotometric titration of a solution, where both of the acids are present, with a transparent acid or base. As can be seen from eq 4, there is no need for the determination of $a(SH^+)$ anymore.

The acid–base equilibria (1) in weakly solvating solvents such as AN are more complex than those in water. In addition to the equilibrium 1, there are other equilibria present in the system.[4] In AN, the poorly solvated anions vigorously form hydrogen-bonded complexes with hydrogen-bond donors present in the solution. When the donor is the conjugate acid of the anion, then the homoconjugation[19] process takes place:<pick;equ5;none;suspend></qa>

A^- + AH <aw;⇄;none;none>K_{AHA^-}<au><awx> $A^- \cdots$HA<id;reqid;5>

K_{AHA^-} is the homoconjugation constant.<pick;equ6;none;suspend></qa>

K_{AHA^-} = <fr>$a(A^- \cdots HA)$<fd>$a(A^-)\cdot a(HA)$<frx><id;reqid;6>

If the donor is some other acid, then the heteroconjugation process is present. These side reactions have to be suppressed or taken into account if the accurate acidity data are to be obtained.

Results

The results of the measurements are presented in Table 1

<pick;tblI;;float>

. With all of the acids in the scale, at least two independent ΔpK_a measurements to two different acids have been made and the relative acidity of any pair of acids can be obtained by combining at least two independent sets of measurements. This multiple overlapping cross-validates the whole scale and makes it more reliable. Together with the previously published measurements,[6,20][20] a self-consistent acidity scale with pK_a values spanning from 3.7 to 28.1 (span of 24 orders of magnitude) in AN has been created. The scale covers the acidity range starting from weak acids such as substituted diphenylamines and diphenylacetonitriles down to true superacids—sulfonimides modified by using the Yagupolskii principle: =O → =N–SO_2CF_3 (i.e., replacement of double-bonded oxygen by an azatrifyl group). The anchoring point of the scale is picric acid with a pK_a value of 11.00. This value has been determined very carefully by the Kolthoff group using three independent methods.[2]

The pK_a values of individual acids were found as in previous work[6] by minimizing the sum of squares of differences between directly measured ΔpK_a values and the assigned pK_a values, denoted as u:<pick;equ7;none;suspend></qa>

$$u = \sum_{i=1}^{n_m} \{\Delta pK_a^i - [pK_a(HA_2) - pK_a(HA_1)]\}^2$$ <id;reqid;7>

The sum u is taken over all n_m measurements. The ΔpK_a^i is the result of the relative acidity measurements of the acids HA_1 and HA_2 involved in the i-th measurement. The pK_a values of all the acids (except the reference acid, picric acid, pK_a = 11.0) are found by the least squares procedure minimizing the sum u.

The precision and the consistency of the results can be assessed by using the consistency standard deviation (consistency criterion) defined as follows:<pick;equ8;none;suspend></qa>

s = <rl;;><fr>u<fd>n_m – n_c<frx><rlx><id;reqid;8>

The whole acidity scale in AN has a total number of measurements n_m = 203, a number of pK_a values determined n_c = 93–1 = 92, and the consistency of measurements as s = 0.03. This estimate of precision must be interpreted as the average precision of ΔpK_a measurements and not the precision of absolute pK_a values, because (a) different acids have different properties and therefore yield different precisions and (b) different distances from the anchor point of the scale—picric acid—cause different numbers of measurements that have to be summed up for getting the acidity of a particular acid and therefore different precisions.

The calculation of the ΔpK_a values involving the acids **10** and **19** was not quite straightforward because of the high homoconjugation constants and no appropriate spectra. Therefore, ΔpK_a measurements involving these two acids were left out of the above-described minimization procedure, and the pK_a values of these acids were found afterward without affecting the absolute pK_a values of the other acids on the scale. The same method was used earlier[20] to calculate pK_a values of *N*-aryltrifluromethanesulfon-amides (**57**, **58**, **61**, **63**, **64**, and **69**) and *N*,*N*′-bis(trifluoromethanesulfonyl)benzamidines (**78**, **79**, **81**, **83**, **84**, and **88**). In this work, these two families of compounds were included also in the minimization

procedure. This is the reason some absolute pK_a values are different from pK_a values of previous works.[6,20]

For several acids belonging to the scale, the pK_a values in AN have been reported in the literature. From Table 3

<pick;tblII;;float>

<pick;tblIII;;float>

and Figure 1

<pick;fig1;;float>

, it is clearly seen that above picric acid, the weaker the acid the greater the difference of pK_a values of literature and this work. Also, it is seen that the literature values form a more contracted acidity scale. As a broad generalization, most of the error sources in nonaqueous pK_a measurements, most importantly traces of water in the solvent, lead to a contraction (and not expansion) of the scale. The rationale is simple. Traces of water stabilize the anions that are poorly solvated in AN. In somewhat simplified terms: the less stable the anion the stronger the concentration of negative charge in it and the stronger the stabilizing effect of water. Thus, the effect of solvation by water molecules is stronger for the anions of the weaker acids, and therefore, the acid strength of weaker acids is increased by water molecules relatively more than the acid strength of stronger acids. Since the effect of traces of water is dependent on the degree of charge localization in the anion, the susceptibility of the acid strength to alteration by water molecules decreases in the following row: OH acids > NH acids > CH acids. The CH acids are the least

sensitive to the traces of water. This is also a strong point in favor of our scale, since in particular above picric acid there are many CH acids, and most of the ΔpK_a values have been measured in pairs where at least one of the acids is a CH acid. Moreover, the OH acids with the strongest charge localization in the anion (**10** and **19**) have not been included in the scale during the minimization step (their pK_a values were found later, using the already fixed scale), and thus, they have in no way influenced the span of the scale. A further favorable property of CH acids as building blocks for the scale is their tendency to give very intense UV–vis spectra for the anion, thus enabling high-accuracy spectrophotometric measurement.

Contrary to this, a great bulk of literature data[4,7–10] are for the OH acids whose behavior in AN is complicated. Due to the localized charge in their anions, these compounds are strongly influenced by traces of water and form homoconjugation and heteroconjugation complexes easily.

In the pK_a range below picric acid there are too little data in the literature to make any generalizations.

Discussion

Many compounds investigated in this work have also been studied in DMSO, 1,2-dimethoxyethane (DME), and heptane (C7) solutions and in the gas phase (see Table 4

<pick;tblIV;;float>

).

To evaluate the effect of structure and solvent on the acidity of studied acids

upon changing from AN solution to other media (DMSO, DME, C7, gas phase), the statistical analysis of the data from Table 2 was performed. Equation 9 describes the correlation between pK_a values in AN and in other media, where *a* and *b* are constants.<pick;equ9;none;suspend></qa>

pK_a(AN) = *b* + *a*pK_a(other media)<id;reqid;9>

The results of this analysis are given in Table 4.

Also, analysis of the relative contributions of resonance and field-inductive effects to the acidities in AN solution, as characterized by eq 10, where pK_a^0, ρ_F, and ρ_R are the constants and σ_F and σ_R are, respectively, the substituents' field-inductive and resonance effects,[21–43] was made.<pick;equ10;none;suspend></qa>

pK_a(AN) = pK_a^0 + $\rho_F\sigma_F$ + $\rho_R\sigma_R$<id;reqid;10>

The results of this analysis are given in Table 5

<pick;tblV;;float>

. It is seen that the sensitivity of the acidity of ethyl aryl cyanoacetates to field-inductive (σ_F) and resonance effect (σ_R) of the substituents is the lowest (of first four series in the Table 5), which indicates weaker delocalization of the negative charge of carbanionic forms of these compounds. In the case of phenols, an opposite pattern appears—delocalization of the negative charge into the ring is considerable.

Acetonitrile versus Dimethyl Sulfoxide. In Figure 2

<pick;fig2;;float>

, the pK_a values of the studied acids are plotted against the corresponding acidities in DMSO. A narrow line corresponds to the overall correlation (see also Table 4, series 1) where the compounds **71** and **74** have been eliminated due to the very large deviations, –4.6 and –6.4 pK_a units, in AN, respectively. The acidities of these very strong acids are leveled up in DMSO solution and cannot be reliably determined. The dashed line corresponds to the correlation of all CH acids (Table 4, series 1.2) where the compounds **47**, **51**, and **74** have been eliminated. The thick solid line corresponds to the OH acids (series 1.1) and dotted line to the NH acids (series 1.3).

Compound **46** deviates from the regression line of OH acids (by 1.2 units), and compounds **47** and **51** deviate from the regression line of CH acids (1.3 and 1.9 pK_a units in AN, respectively). All of these compounds containing a perfluoro-4-pyridinyl group are stronger acids in AN solution than could be expected from the correlation.

2-Nitrophenol (**12**) also deviates significantly from the correlation: it is 1.3 units weaker acid in AN than could be expected from the correlation. One possible explanation is that this is due to the intramolecular hydrogen bond in the neutral **12** that is more efficient in AN than in DMSO because DMSO is a much stronger hydrogen bond acceptor than AN.[3,40] In the case of picric acid (**62**) and 2,4-dinitrophenol (**40**) the deviation is absent. The nitro groups in the para and ortho position have strong resonance acceptor abilities. Therefore, the negative partial charge on the single *o*-nitro group of compounds **62** and **40** is not so extensive, and

thus, the intramolecular hydrogen bond in AN is not so strong.[8] Another possibility is that in stronger acids as **40** and **62** the hydroxyl group is a better hydrogen bond donor than in **12**, thus forming a more efficient hydrogen bond in DMSO. In AN—a weaker hydrogen bond acceptor—this effect is less pronounced.

With this work, the number of acid pK_a values in AN has come closer to the number of pK_a values in DMSO solution, where several hundred pK_a values[21,10] are available. Still, further measurements in both solutions are necessary. With the different correlation parameters of CH acids, OH acids, and NH acids (as seen from Figure 2) and with some deviations from the correlation line there is evidence of their different properties.

Acetonitrile versus Gas Phase. In Figure 3

<pick;fig3;;float>

, the correlation of pK_a values in AN and the acidities in the gas phase have been plotted. The narrow line corresponds to the overall correlation (see also Table 4, series 4), dashed line to the NH acids (series 4.6), dotted line to the OH acids (series 4.1 and 4.2), and the thick solid lines to the correlations of different groups of CH acids—diarylacetonitriles (series 4.3), ethyl aryl cyanoacetates (series 4.5), and arylmalononitriles (series 4.4).

As expected, the value of the slope of the regression line indicates that in the gas phase the acidities are substantially more sensitive to the structural changes of the compounds than in any of the condensed phases (see Table 4). Unlike in the DMSO solution, individual correlation lines are found for all the different classes of

compounds. Also in heptane (see below), the sensitivity of the acidities of the studied compounds toward the structural variations is considerable as compared to that in AN, DMSO, and DME but not as extensive as in the gas phase.

From Figure 3 and Table 4 it is evident that the ethyl aryl cyanoacetates are the family of acids having the most pronounced decrease of the sensitivity of acidities toward the substituents in the aromatic ring on transfer from the gas phase to AN solution. The decrease of sensitivity is the least pronounced in the case of diphenyl acetonitriles.

In the case of OH acids (except carboxylic acids), the correlation is fair at best. Compounds **26**, **30**, and **40** strongly deviate and have been excluded from the correlation.

Other Media. Table 4, series 2, describes the correlation between pK_a values of all compounds (except **11**) in AN and 1,2-dimethoxyethane (DME). Compound **11** deviates from the correlation having 6.5 units higher acidity in DME than if calculated from the correlation. The reason for this apparent acidity increase is the strong stabilization of the carbanion $C_6F_5C(COOEt)_2^-$ in DME by formation of a contact ion pair with lithium cation that is efficiently chelated by the two ester groups.[34] All of the correlations (series 2, 2.1, 2.2, 2.3) show similar sensitivity of acidities of compounds in AN and in DME.

Heptane (C7) is by a factor of 1.3 a more differentiating solvent than AN as seen from Table 4, series 3, but not as differentiating as the gas phase. In C7, because of the solubility, only the compounds that have delocalized charge in the anion can be

investigated. Due to this structurally very homogeneous family of compounds, the correlation between pK_{ip} values in C7 and pK_a values in AN is good with no deviating compounds.

***p*-Fluoro Substituent.** It is interesting to compare different classes of compounds with polyfluorinated aromatic rings in terms of 4-F and 4-H substituents. For phenylmalononitriles, the pK_a value of the 4-H-substituted compound **53** is slightly (by 0.03 pK_a units) lower than the pK_a value of the 4-F-substituted compound **52**. This difference has been confirmed by two independent direct measurements by different operators and also by two indirect sets of measurements (via compounds **51** and **54**) that all lead to the same order of acidities of **52** and **53**. For diphenylacetonitriles (**17** and **18**) and phenols (**23** and **24**), the pK_a values of two compounds are practically equal. However, for ethyl phenyl cyanoacetates (**33** and **36**) the difference is 0.3 units, the 4-F compound being more acidic. It seems that the more extensive the delocalization of negative charge into the ring (e.g., phenols, diarylacetonitriles) the smaller the acidity difference between these different para-substituted compounds. The effect that 4-H- and 4-F-substituted compounds have practically equal acidities if the other positions of the aromatic ring are fluorinated does not appear only in AN but also in DME[34] (see Table 2) and in water,[30,11] but not in the gas phase.[36]

The reason for this might be that although fluorine is an electronegative substituent, it is also a weak resonance donor.[43] The fluorine is in the para position to the acidity center, which means that the inductive/field effect is weakened by the distance but not the resonance effect. The final factor is the strong electron

deficiency of the perfluorinated ring that still weakens the inductive/field effect by saturation. An explanation based on MO theory is that because the short bond of fluorine appears to overlap the *p*-orbitals of fluorine and π-orbitals of the ring, this gives more electron density to the ring and lowers the acidity of 4-F-substituted compounds.

Yagupolskii's Substituents. A principle of building strong electron-acceptor substituents with extensive conjugated chains was first introduced by Yagupolskii and co-workers.[44][44] Also, a general principle of designing strong neutral superacidic systems has been developed.[45][45] *N*-Benzoyltrifluoromethanesulfonamides **57**, **58**, **61**, **63**, **64**, and **69** and *N*,*N*′-bis(trifluoromethanesulfonyl)benzamidines **78**, **79**, **81**, **83**, **84**, and **88** may be formally considered as derivatives of benzoic acids.[20] It is seen (Table 1) that on replacement of one oxygen atom by the =N-Tf group in benzoic acid its acidity increases by 10.4 pK_a units, whereas the second replacement of oxygen atom leads to a further increase by 4.9 pK_a units. The total acidifying effect of introduction of =N-Tf substituents and transfer from OH acids (benzoic acids) to NH acids (benzamidines analogues of benzoic acids) is thus 15.3 units.

Compounds **87**, **91**, and **93** can be considered as derivatives of sulfonimides **60**, **65**, and **70**, respectively, where an oxygen atom of a sulfonyl group adjacent to the NH acidity center is replaced by a =N-Tf fragment. The acidifying effects of that substitution in this row of compounds are 5.8, 5.7, and 5.4 pK_a units, respectively. Differently from previous examples of introduction of the =N-Tf group into benzoic acids and its derivates, in this case, the comparisons refer to the same

reaction center, the NH group.

The sulfonimides **80**, **86**, and **90** can formally be compared with sulfonic acids **71**, **75**, and **77**, where fragment =O is replaced with =N-Tf. Differences of pK_a values between these compounds are 2.3, 1.8, and 2.2 units, respectively. The reason these differences are not similar to those for benzenesulfonimides (previous section) is that the replacement of oxygen atom in the sulfonyl group of sulfonic acids with =N-Tf leads to structures that tautomerize to NH acid.[6,46] Contrary to sulfonic acids, sulfonamides do not undergo similar tautomerization. In 4-toluenesulfonamide, the effect of replacement of one =O by =N-Tf is 8.3 pK_a units (in DMSO solution).[47]

Comparison of CH Acids and Phenols. Arylmalononitriles, ethyl aryl cyanoacetates, and diarylacetonitriles with similar substituent patterns in the aromatic ring have been studied in this work. Some of the studied phenols also have the same substituents as those above-mentioned CH acids. From the correlations between the pK_a values of aryl(perfluorophenyl)acetonitriles, arylmalononitriles, ethyl aryl cyanoacetates, and substituted phenols, one can deduce the general order of sensitivity of the pK_a values of these compound families toward changes in substituents. The sensitivity increases in the following row: ethyl aryl cyanoacetates < arylmalononitriles < aryl(perfluorophenyl)acetonitriles < phenols. The squared correlation coefficients of these correlations (r^2) were between 0.95 and 1.00. The worst correlation was between phenols and ethyl aryl cyanoacetates: $r^2 = 0.95$. The most deviating compounds were the respective 2-perfluoronaphthyl and perfluorophenyl derivatives. Figure 4

<pick;fig4;;float>

illustrates the changes of acidity accompanying the structural changes in these compound families. The numbers on the vertical arrows (changes in pK_a values) indicate the ability of the respectively substituted aromatic ring (that changes along the vertical columns) to delocalize the negative charge of the anion. In the case of the same acidity center, the perfluoro-4-pyridinyl group delocalizes negative charge best, followed by the 2-perfluoronaphthyl group and then by the perfluorophenyl group. The numbers on the horizontal arrows indicate the ability of the other groups attached to the acidity center (excluding the aromatic group that changes along the vertical columns) to delocalize the negative charge of anion. Using Figure 4, it is possible to approximately but quickly predict the acidity of similar compounds.

Homoconjugation. In the case of phenols, the homoconjugation constant has to be taken into account in the measurements under our experimental conditions if the pK_a value is equal to or higher than ~15. The strongest phenols in the scale **85** and **89** do not form homoconjugation complexes under our experimental conditions. The stabilities of homoconjugation complexes of phenols increase as the acid strength decreases.[10] There are some exceptions. 2-Nitrophenol (**12**) has no remarkable ability to form homoconjugation complex. Substitution of phenol with a nitro group in the ortho position to the hydroxy group reduces homoconjugation mainly due to intramolecular hydrogen bond of the neutral molecule. Compounds **21**, **34** and **35** also do not form homoconjugation complexes, probably chlorine and bromine in the ortho position are responsible for that. Fluorine substituent in the ortho position does not prevent homoconjugation (e.g., compounds **23**, **24**, and **46**).

The reason 1- and 2-perfluoronaphthols (**26** and **30**) have lower homoconjugation constants than, e.g., perfluorophenol (**24**) or 2,3,5,6-tetrafluorophenol (**23**), is that these substances have a stronger ability to delocalize the anionic negative charge than perfluorophenol. 1-Perfluoronaphthol may have lower homoconjugation constant than 2-perfluoronaphthol because of steric hindrance, but not due to *peri*-interaction between hydroxyl group and fluorine.[7]

The Scale as a Tool for Further Acid–Base Studies. The scale as a collection of reference compounds with reliably known pK_a values can be used as the basis for measuring the pK_a values of a large variety of acids. The AN basicity scale[14] has already found useful application for measuring pK_a values of calixarenes.[48][48] The same UV–vis spectrophotometric method has been used for measuring pK_a values of azobenzene dyes.[49][49] We envisage that the present scale could also be a valuable tool for future researchers in acid–base chemistry in AN. The scale has been compiled using primarily compounds with favorable spectral properties and low tendency to homoconjugation, such as arylmalononitriles, diarylacetonitriles. The potential users are advised to use first of all the compounds from the families of arylmalononitriles, diarylacetonitriles, fluorenes, ethyl aryl cyanoacetates, some phenols (picric acid (**62**), 2,4,6-Tf_3-phenol (**89**)), and diarylamines as reference compounds for their measurements. The rest of the phenols, benzoic acids, and sulfonic acids should be used only if no suitable compound is found from the above compound families. Small samples of some of the compounds for such research are available from the authors on request.

Experimental Section

Chemicals. Solutions of trifluoromethanesulfonic acid (TfOH) (99+%) or perchloric acid ($HClO_4$) were used as acidic titrant and solutions of triethylamine (99%); phosphazene bases *t*-BuP_1(pyrr) (≥98%) or EtP_2(dma) (>98%) were used as basic titrants.[14]

Commercial AN with water concentration stated by producer below 0.005% (determined in our laboratory by coulometric Karl Fischer titration below 0.004%) was used for new measurements and in the case of measurements published previously.[20] AN for measurements published in ref 6 was distilled from phosphorus pentoxide (P_2O_5), and its dryness was checked by KFT (visual endpoint detect).

The origin and purification of previously used compounds are described: **40**, **43**, **48**–**50**, **52**–**56**, **59**, **60**, **62**, **65**–**68**, **70**–**77**, **80**, **82**, **86**, **87**, **89**–**93**;[6] **57**, **58**, **61**, **63**, **64**, **69**, **78**, **79**, **81**, **83**, **84**, **88**.[20] Preparation of the following compounds has been previously described: **1**;[24] **2**, **13**, **14**;[50][50] **3**;[51] **4**, **17**, **18**, **20**, **31**;[52][51–52] **5**, **6**;[53][53] **11**, **33**, **36**, **39**, **42**, **44**, **47**, **51**;[54][54] **22**;[55][55] **25**, **28**, **38**, **45**;[56][56] **29**;[57][57] **46**, **26** (additionally was sublimed), **30** (additionally was sublimed twice);[7] **24**[58][58] and commercial, 99+%; **27**;[59][59] **32**.[60][60]

Samples **7**–**9** and **16** were donated by the late Prof. R. W. Taft. Sample **37** was provided by E. M. Arnett[61][61] and sample **85** by L. M. Yagupolskii.[62][62]

The following chemicals were commercial origin. Some of these were purified prior to use: **12** (> 99%) was sublimed once; **21** (“pure”) was sublimed twice; **35** (95%) was recrystallized from ethanol and water mixture; **23** (97%) and **41** (95%) were distilled under reduced pressure. Compounds **10** (“pure for analysis”), **15** (Elemental Analysis Standard), **19** (99%) and **34** (99+ %) were used without additional purification.

Experimental Setup. The spectrophotometric titration method used in this work is mostly the same as described earlier.[6,20,63][63–65] The method is based on UV–vis spectrophotometric titration of a mixture of two acids with a nonabsorbing base to obtain neutral and anionic forms of the solution of mixture. Both acids were also titrated separately to obtain spectra of neutral and ionized forms. From the titration data the relative acidity of the two compounds—the difference of their pK_a values (ΔpK_a)—is obtained.

The reversibility of the protonation–deprotonation process was tested for all compounds. The protonation–deprotonation process was reversible with all acids in the scale. Equilibria were reached in a little longer time (up to one minute) in the case of weak CH acids (fluorenes and diarylacetonitriles).

Sharp isosbestic points were usually obtained during titrations, indicating that the measured compounds did not contain significant amounts of impurities. Fluoro-substituted phenols (**23**, **24**, **32**, and **41**) and compound **46** did not have a sharp isosbestic point at a shorter wavelength range due to homoconjugation processes. The use of a longer wavelength range used for calculation of the pK_a values from the UV–vis spectra was not uncommon.

Calculation Methods. Different calculation methods for ΔpK_a were used:

(1) The general method was described previously.[6,63] All data for the calculations of the ΔpK_a values were obtained from the UV–vis spectra of measured acids. Details are given in the Supporting Information.

(2) In the case of some acids (**15**, **23**, **24**, **26**, **30**, **32**, **41**, and **46**), it was necessary to take homoconjugation into account. It is possible if only one of the acids in equilibrium forms homoconjugation complex. The calculation method has been described earlier.[6] Details are given in the Supporting Information.

(3) Both of the acids form homoconjugation complexes. In this case, we assume that they also form heteroconjugation complexes. We assume that for all the sulfonic acids (**71**, **73**, **75**, **76**, and **77**) the homoconjugation constants are very close and also all the heteroconjugation constants are very close to the homoconjugation constants. In this case, it can be shown that the four species, HA_1, HA_2, A_1^-, and A_2^-, are consumed proportionally to their concentrations for the formation of the homo- and heteroconjugation complexes, and the relative decrease of their concentrations will cancel out so that the formation of the complexes can be ignored when calculating ΔpK_a.

(4) If the one of the acids (**10** and **19**) had no suitable spectra (small difference in the spectra of neutral and deprotonated form or no spectra in the suitable wavelength range) for calculations described in paragraph 1 and 2, then it is possible to use the calculation method where the exact amount of moles of the compounds and added titrant in titration vessel were used for calculations

of ΔpK_a.[20] For these two acids, it was also necessary to take homoconjugation into account.

AN has very low solvating ability for anions. This is the main reason homoconjugation of some anions is extensive in AN. In Table 6

<pick;tblVI;;float>

are represented homoconjugation constants used in this work in calculations and constants reported in the literature. In the case of weak acids, larger values for homoconjugation constants were found in this work than reported in the literature.

The homoconjugation constants used in the ΔpK_a calculations of this work were obtained by minimizing the standard deviation between the parallel ΔpK_a values (corresponding to different solution acidities) that were calculated from the same titration experiment. It was observed that the small variations in homoconjugation constant values do not have significant influence on the calculated ΔpK_a values. For example, the variation of the ΔpK_a value between compounds **32** and **38** when varying the $\log K_{AHA^-}$ from 3.8 to 4.2 is only 0.02 pK_a units (the $\log K_{AHA^-}$ value 4.0 was used for the calculations). This is about the average sensitivity, and one of the largest that we observed was 0.06 units, when $\log K_{AHA^-}$ is varied 0.5 units. In this case, around 10% of the acid was in the form of the homoconjugation complex. From this it can be seen that at used concentrations (10^{-5} M) the homoconjugation constants in the range of 10^3 cannot be estimated reliably. The values of homoconjugation constants were estimated on the basis of values of the literature, still some of the literature values were not suitable for the calculations (see Table 6). As the homoconjugation constants used in this work were not measured directly but estimated, they have to be treated with caution.

The concentrations of the nitro-substituted phenols were too low during the measurements to determine any homoconjugation with our method. The published and estimated values are given in Table 6.

This section tagged Acknowledgment

This work was supported by the Grant Nos. 5800, 6699, and 6701 from the Estonian Science Foundation.

This section tagged Supporting Information

Detailed description of the calculation methods of ΔpK_a. This material is available free of charge via the Internet at http://pubs.acs.org.

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The value of pK_{auto} of AN may be even higher by several pK_a units. However, no experimental evidence to this has been presented to date.

IUPAC suggests using the terms homoassociation (heteroassociation) instead of homoconjugation (heteroconjugation), but in our opinion the term homoconjugation (heteroconjugation) is more appropriate to describe this effect.

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{/PICK;fig1;84480n;;block;;;;yes;2;;4224n;;;;}

Figure 1. Correlation of acidities of the studied acids and acidities reported in the literature. Narrow line corresponds to the ideal correlation with zero intercept and unity slope. The thick line corresponds to the actual situation. The correlation is: pK_a(lit.) = 0.72 + 0.930pK_a(this work); s(intercept) = 0.34, s(slope) = 0.017, n = 12, r^2 = 0.997, S = 0.209.

{/PICK;fig2;84480n;;block;;;;yes;2;;4224n;;;;}

Figure 2. Correlation of the acidities of the studied acids in AN and DMSO. Narrow line corresponds to the overall correlation except compounds **71** and **74**, dashed line to the correlation of CH acids, dotted line to the NH acids, and thick solid line to the OH acids.

{/PICK;fig3;84480n;;block;;;;yes;2;;4224n;;;;}

Figure 3. Correlation between pK_a values in AN and pK_a(GP) values. Narrow line corresponds to the overall correlation, thick solid lines to the correlation of CH acids (diarylacetonitriles, ethyl aryl cyanoacetates, and arylmalononitriles), dashed line to the NH acids, and dotted line to the phenols (compounds **26**, **30**, and **40** have been excluded from the correlation). (pK_a(GP) = 2.30GA/RT = GA/1.364.)

{/PICK;fig4;84480n;;block;;;;yes;2;;4224n;;;;}

Figure 4. Changes in the pK_a values between the some polyfluorinated compounds of the diphenylacetonitrile, ethyl aryl cyanoacetate, and phenol families. The numbers on the arrows indicate the changes in the pK_a values on the hypothetical

transformations of one compound to another. Vertical transformations account for changes in the aromatic parts of the molecules; horizontal transformations account for changes in the acidity centers.

{/PICK;tblI;177408n;;page;;;;yes;1;;4224n;;;;}

Table 1. <tblttl;2>Continuous Self-Consistent Acidity Scale of Neutral Acids in Acetonitrile

<tgr>

[a]Absolute pK_a values (see the Results).

[b]The numbers on the arrows are the experimental ΔpK_a values from this work and previous works.[6,20]

[c]Tos denotes 4-Me-$C_6H_4SO_2$–.

[d]Tf denotes CF_3SO_2–.

{/PICK;tblII;177408n;;page;;;;yes;1;;4224n;;;;}

Table 2. <tblttl;2>Acidity Data of the Acids Studied in This Work Reported in the Literature for Different Media

no.	acid	pK_a values in DMSO	pK_a values in H_2O [l]	pK_{ip} values in heptane[o]	pK_a values in DME [p]	GA[r] (kcal/ mol)
1	9-C_6F_5-fluorene	14.7[a]			15.2[d]	
2	(4-Me-C_6F_4)(C_6H_5)CHCN	13.2[b]				328.2[b]
3	(4-NC_5F_4)(C_6H_5)NH	14.5[c]				323.5[c]
4	(C_6F_5)(C_6H_5)CHCN	12.8[b]			11.8	325.6[b]
5	(4-Me_2N-C_6F_4)(C_6F_5)NH	13.6[d]				
6	(4-Me-C_6F_4)(C_6F_5)NH	13.3[d]		7.04		320.0[c]
7	octafluorofluorene	10.8[e]				317.3
8	fluoradene	10.5[f]		6.40		324.9[b]
9	9-COOMe-fluorene	10.35[e]			9.2[q]	
10	acetic acid	12.3[e] 12.6[g]	4.75			341.1[s]
11	(C_6F_5)CH($COOEt$)$_2$				3.2	

12	2-NO_2-phenol	11.0[g]	7.21 7.23[h]			329.5[t]
13	(4-Me-C_6F_4)$_2$CHCN			4.61		
14	(4-Me-C_6F_4)(C_6F_5)CHCN			3.29	7.1	316.1[b]
15	benzoic acid	11.0[e] 11.1[g]	4.25			330.0[e]
16	9-CN-fluorene	8.3[e]			7.9[q]	321.4[b]
17	(4-H-C_6F_4)(C_6F_5)CHCN				6.7	
18	(C_6F_5)$_2$CHCN	7.95[e]		1.85	6.4	312.4
19	(CF_3)$_3$COH	10.7[e] 10.4[h]	5.4[m]			324.0[u]
20	(4-Cl-C_6F_4)(C_6F_5)CHCN	7.5[b]		1.09	5.4	311.8[b]
22	(2,4,6-Cl_3-C_6F_2)(C_6F_5)CHCN			1.10		
24	2,3,4,5,6-F_5-phenol	8.9[i]	5.53[i]			320.8
25	(2-$C_{10}F_7$)(C_6F_5)CHCN				5.5	
26	1-$C_{10}F_7$OH	8.9[i]	7.05			314.0
27	2,4,6-(SO_2F)$_3$-aniline	7.8[c]	ca. 7[b]			307.5
28	(2-$C_{10}F_7$)$_2$CHCN			−0.68		
29	9-C_6F_5-octafluorofluorene			0.00	5.3[d]	301.8
30	2-$C_{10}F_7$OH	7.9[i]				312.4
31	(4-CF_3-C_6F_4)(C_6F_5)CHCN	4.9[b]		−1.39	3.9	307.5
33	(4-H-C_6F_4)CH(CN)COOEt	4.9[b]				315.6[b]
34	2,3,4,5,6-Cl_5-phenol	7.2[i]	5.26[i]			
36	(C_6F_5)CH(CN)COOEt	4.7[b] 5.1[e]			3.5	313.5
37	4-Me-C_6H_4CH(CN)$_2$	4.85[b]				315.7
38	(2-$C_{10}F_7$)CH(CN)COOEt				3.3	
39	(4-Cl-C_6F_4)CH(CN)COOEt	4.5[b]			3.1	312.5[b]
40	2,4-(NO_2)$_2$-phenol	5.4[e,j]	4.10			308.6
42	(4-NC_5F_4)(C_6F_4)CHCN	3.3[b]			2.2	305.7
43	(4-CF_3-C_6F_4)$_2$CHCN	3.3[b]				302.1
44	(4-CF_3-C_6F_4)CH(CN)COOEt	3.0[b]				307.8[b]
45	(4-NC_5F_4)(2-$C_{10}F_7$)CHCN				1.9	
46	4-NC_5F_4-OH	5.4[i]				311.3
47	(4-NC_5F_4)CH(CN)COOEt	3.2[b]				303.5
48	3-CF_3-C_6H_4CH(CN)$_2$					307.0
49	saccharin	4.0[e]	1.8[n]			

50	4-Me-$C_6F_4CH(CN)_2$			308.0
51	$(4\text{-}NC_5F_4)_2CHCN$	2.4[b]		302.2
52	$C_6F_5CH(CN)_2$	0.3[b]		303.6
53	4-H-$C_6F_4CH(CN)_2$			305.5
54	2-$C_{10}F_7CH(CN)_2$			301.8
56	4-NO_2-$C_6H_4CH(CN)_2$	–1.8[b]		299.5
62	picric acid	–1.0[g]	0.3[i,l]	302.8
66	4-CF_3–$C_6F_4CH(CN)_2$			301.5
71	TosOH	0.90[k]		
73	1-$C_{10}H_7$-SO_3H		0.68	
74	$C_6H_5CHTf_2$	2.0[b]		301.3
89	2,4,6-$(Tf)_3$-phenol			291.8

[a] Reference 21.

[b] Reference 22.

[c] Reference 23.

[d] Reference 24.

[e] Reference 25.

[f] Reference 26.

[g] Reference 27.

[h] Reference 28.

[i] Reference 7.

[j] Reference 8.

[k] Reference 29.

[l] Reference 30.

[m] Reference 31.

[n] Reference 32.

[o]Reference 33, in reference to acid **29**.

[p]Reference 34.

[q]Reference 35.

[r]Reference 36.

[s]Reference 37.

[t]Reference 38.

[u]Reference 39.

{/PICK;tblIII;84480n;;block;;;;yes;1;;4224n;;;;}

Table 3. Comparison of the pK_a Values in AN Determined in This Work with Those Reported in the Literature

		pK_a values in AN		
no.	acid	this work	lit.	difference
10	acetic acid	23.51	22.3[a]	+1.2
			22.31[b]	+1.20
12	2-NO_2-phenol	22.85	22.0[c]	+0.9
			22.1[d]	+0.8
15	benzoic acid	21.51	20.7[a]	+0.8
16	9-CN-fluorene	21.36	20.8[e]	+0.6
24	2,3,4,5,6-F_5-phenol	20.11	19.5[f]	+0.6
26	1-$C_{10}F_7OH$	19.72	19.4[f]	+0.3
30	2-$C_{10}F_7OH$	18.50	17.8[f]	+0.7
34	2,3,4,5,6-Cl_5-phenol	18.02	17.2[f]	+0.8
40	2,4-$(NO_2)_2$-phenol	16.66	15.34[g]	+1.32
			16.0[c]	+0.7
			18.40[b]	–1.74
46	4-NC_5F_4-OH	15.40	15.2[f]	+0.2
62	picric acid [k]		11.0[h]	
71	TosOH	8.6	8.01[i]	+0.6
			8.73[b]	–0.1
92	2,3,5-tricyanocyclopentadiene	4.16	3.00[j]	+1.16

[g]Reference 27.

[b]Reference 13.

[c]Reference 4.

[d]Reference 40.

[e]Reference 41.

[f]Reference 7.

[g]Reference 12.

[h]Reference 2.

[i]Reference 29.

[j]Reference 42.

[k]Anchor compound of the present scale.

{/PICK;tblIV;177408n;;page;;;;yes;1;;4224n;;;;}

Table 4. <tblttl;2>Statistical Analysis of Data from Table 2 in Terms of eq 9

no.	series		a	b	$s(a)$	s(b)	S	r^2	n	compounds
1	**DMSO**	all acids, except **71** and **74**	0.980	12.31	0.044	0.38	1.167	0.933	36	1–10, 12, 15, 16, 18–20, 24, 26, 27, <ind;1>30, 31, 33, 34, 36, 37, 39, 40, <ind;1>42–44, 46, 47, 49, 51, 52, 56, 62
1.1		OH acids, except **12** and **46**	0.884	11.80	0.036	0.32	0.406	0.989	9	10, 15, 19, 24, 26, 30, 34, 40, 62
1.2		CH acids, except **47** and **51**	1.038	12.91	0.013	0.10	0.247	0.997	19	1, 2, 4, 7–9, 16, 18, 20, 31, 33, 36, <ind;1>37, 39, 42–44, 52, 56
1.3		NH acids	1.083	10.60	0.047	0.54	0.428	0.994	5	3, 5, 6, 27, 49
2	**DME**	All acids, except **11**	0.941	14.58	0.036	0.25	0.494	0.980	16	1, 4, 9, 14, 16–18, 20, 25, 29, 31, <ind;1>36, 38, 39, 42, 45
2.1		diarylacetonitriles and <ind;1>ethyl aryl cyanoacetates	1.044	14.21	0.029	0.16	0.262	0.993	12	4, 14, 17, 18, 20, 25, 31, 36, 38, <ind;1>39, 42, 45
2.2		diarylacetonitriles	1.034	14.30	0.036	0.22	0.300	0.992	9	4, 14, 17, 18, 20, 25, 31, 42, 45
2.3		fluorenes	0.927	14.25	0.084	0.84	0.609	0.984	4	1, 9, 16, 29
3	**C7**	all acids	0.756	19.39	0.036	0.13	0.315	0.982	10	6, 8, 13, 14, 18, 20, 22, 28, 29, 31

4	**GP**	all acids	0.559	−110.27	0.058	13.37	2.834	0.702	41	2−4, 6−8, 10, 12, 14−16, 18−20, <ind;1>24, 26, 27, 29, 30, 31, 33, 36, <ind;1>37, 39, 40, 42, 43, 44, 46−48, <ind;1>50−54, 56, 62, 66, 74, 89
4.1		OH acids, except **10**, **15**, **26**, **30**	0.635	−129.53	0.060	13.87	1.422	0.957	7	12, 19, 24, 40, 46, 62, 89
4.2		OH acids, except also **40**	0.651	−133.87	0.029	6.70	0.679	0.992	6	12, 19, 24, 46, 62, 89
4.3		diarylacetonitriles	0.643	−127.15	0.048	11.00	0.943	0.962	9	2, 4, 14, 18, 20, 31, 42, 43, 51
4.4		arylmalononitriles	0.559	−111.78	0.084	18.82	0.830	0.880	8	37, 48, 50, 52−54, 56, 66
4.5		ethyl aryl cyanoacetates	0.369	−67.29	0.014	3.12	0.098	0.996	5	33, 36, 39, 44, 47
4.6		NH acids	0.571	−109.17	0.006	1.38	0.052	1.000	3	3, 6, 27

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Table 5. <tblttl;2>Statistical Analysis of Data from Table 1 in Terms of eq 10

no.	series	pK_a^0	ρ_F	ρ_R	$s(pK_a^0)$	$s(\rho_F)$	$s(\rho_R)$	S	r^2	n	compounds
1	ethyl aryl cyanoacetates 4-X-$C_6F_4CH(CN)COOEt$	18.08	−3.41	−4.86	0.00	0.01	0.01	0.00	1.000	4	33, 36, 39, 44
2	aryl malononitriles 4-X-$C_6F_4CH(CN)_2$	12.90	−4.31	−7.73	0.08	0.23	0.39	0.12	0.998	4	50, 52, 53, 56
3	diarylacetonitriles (4-X-C_6F_4)(C_6F_5)CHCN	20.98	−4.47	−8.03	0.10	0.27	0.45	0.14	0.996	5	14, 17, 18, 20, 31
4	phenols 4-X-C_6F_4OH	19.96	−5.19	−9.28	0.13	0.38	0.60	0.20	0.994	5	23, 24, 32, 41 and [a]
5	*N*-aryltrifluoromethanesulfonamides 4-X-$C_6H_4C(=O)NHTf$	11.09	−2.09	−2.34	0.12	0.25	0.33	0.16	0.976	5	57, 58, 61, 63, 64, 69
6	*N*,*N*′-bis(trifluoromethanesulfonyl)-<ind;1>benzamidines 4-X-$C_6H_4C(=NTf)NHTf$	6.15	−1.35	−1.50	0.10	0.21	0.28	0.13	0.960	5	78, 79, 81, 83, 84, 88

[a] 4-Me-C_6F_4OH pK_a value in AN 20.3[7] units, in correlation used revised value 21.0, that led to significantly improvement correlation. Revised value calculated with correlation at Figure 1.

{/PICK;tblVI;84480n;;block;;;;yes;1;;4224n;;;;}

Table 6. Homoconjugation Constants of the Acids Used for Calculations in This Work and Other Values Found from the Literature

log K_{AHA}

no.	compd	used for calculations in this work[a]	other values from the literature
10	acetic acid	4.5	3.67[b]
			3.70[c]
12	2-NO_2-phenol		2.0[d,e]
			2.20[f]
			2.36[g]
15	benzoic acid	3.9	3.60[b,c,h]
19	$(CF_3)_3COH$	4.8	
23	2,3,5,6-F_4-phenol	4.2	
24	2,3,4,5,6-F_5-phenol	4.2	
26	1-$C_{10}F_7OH$	3.3	
30	2-$C_{10}F_7OH$	3.8	
32	4-C_6F_5-2,3,5,6-F_4-phenol	4.0	
40	2,4-$(NO_2)_2$-phenol		2.0[d,e]
			2.08[f]
			2.14[g]
41	4-CF_3-2,3,5,6-F_4-phenol	3.6	
46	4-NC_5F_4-OH	3.6	
62	Picric acid		0[d]
			0.30[f]
71	TosOH	2.9[i]	2.95[j]
73	1-$C_{10}H_7SO_3H$	2.9[k]	
75	4-Cl-C_6H_4-SO_3H	2.9[k]	
76	3-NO_2-C_6H_4-SO_3H	2.9[k]	
77	4-NO_2-C_6H_4-SO_3H	2.9[k]	

[a] Values obtained in this work if not indicated otherwise.

[b] Reference 27.

[c] Reference 64.

[d] Reference 5.

[e] Reference 4.

[f] Reference 2.

[g]Reference 40.

[h]Reference 65.

[i]Reference 29.

[j]Reference 13.

[k]Due to the structural similarity of the compound **71**, the same value of logK_{AHA} was used.

This paper needs a title running head (TRH).

65 references have been flagged (there are apparently 65 references)

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