DISSERTATIONES CHIMICAE UNIVERSITATIS TARTUENSIS

78

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AGNES KÜTT

Studies of acid-base equilibria in non-aqueous media

TARTU UNIVERSITY
PRESS

Institute of Chemistry, Faculty of Science and Technology, University of Tartu, Estonia

Dissertation is accepted for the commencement of the Degree of Doctor of Philosophy in Physical and Analytical Chemistry on April 24th, 2008 by the Doctoral Committee of the Institute of Chemistry, University of Tartu.

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Commencement: June 25th 2008 at 11:00, 18 Ülikooli St., room 204

Publication of this dissertation is granted by University of Tartu

ISSN 1406–0299
ISBN 978–9949–11–853–3 (trükis)
ISBN 978–9949–11–854–0 (PDF)

Tartu Ülikooli Kirjastus
www.tyk.ee
Tellimus nr. 174

OK, so you’re a PhD. Just don’t touch anything.

CONTENTS

LIST OF ORIGINAL PUBLICATIONS

This thesis consists of seven articles listed below and a review. The articles are referred in the text by Roman numerals I–VII. The review summarizes and supplements the articles.

I Ivari Kaljurand, **Agnes Kütt**, Lilli Sooväli, Toomas Rodima, Vahur Mäemets, Ivo Leito, and Ilmar A. Koppel. Extension of the Self-Consistent Spectrophotometric Basicity Scale in Acetonitrile to a Full Span of 28 pK_a Units: Unification of Different Basicity Scales. *J. Org. Chem.* **2005**, *70*, 1019–1028.

II Mirjana Eckert-Maksić, Zoran Glasovac, Pavle Trošelj, **Agnes Kütt**, Toomas Rodima, Ivar Koppel, and Ilmar A. Koppel. Basicity of Guanidines with Heteroalkyl Side Chains in Acetonitrile. Submitted to *Eur. J. Org. Chem.*

III Alexander A. Kolomeitsev, Ilmar A. Koppel, Toomas Rodima, Jan Barten, Enno Lork, Gerd-Volker Röschenthaler, Ivari Kaljurand, **Agnes Kütt**, Ivar Koppel, Vahur Mäemets, and Ivo Leito. Guanidinophosphazenes: Design, Synthesis, and Basicity in THF and in the Gas Phase. *J. Am. Chem. Soc.* **2005**, *127*, 17656–17666.

IV **Agnes Kütt**, Ivo Leito, Ivari Kaljurand, Lilli Sooväli, Vladislav M. Vlasov, Lev M. Yagupolskii, and Ilmar A. Koppel. A Comprehensive Self-Consistent Spectrophotometric Acidity Scale of Neutral Brønsted Acids in Acetonitrile. *J. Org. Chem.* **2006**, *71*, 2829–2838.

V **Agnes Kütt**, Valeria Movchun, Toomas Rodima, Timo Dansauer, Eduard B. Rusanov, Ivo Leito, Ivari Kaljurand, Juta Koppel, Viljar Pihl, Ivar Koppel, Gea Ovsjannikov, Lauri Toom, Masaaki Mishima, Maurice Medebielle, Enno Lork, Gerd-Volker Röschenthaler, Ilmar A. Koppel, and Alexander A. Kolomeitsev. Pentakis(trifluoromethyl)-phenyl, a Sterically Crowded and Electron-withdrawing Group: Synthesis and Acidity of Pentakis(trifluoromethyl)benzene, -toluene, -phenol, and -aniline *J. Org. Chem.* **2008**, *73*, 2607–2620.

VI Ivo Leito, **Agnes Kütt**, Eva-Ingrid Rõõm, and Ilmar Koppel. Anions $N[C(CN)_2]_3^-$ and $P[C(CN)_2]_3^-$ and the Superacidic Properties of Their Conjugate Acids. *THEOCHEM* **2007**, *815*, 41–43.

VII **Agnes Kütt**, Ivar Koppel, Ilmar A. Koppel, and Ivo Leito. Boratabenzene Anions $C_5B(CN)_6{}^-$ and $C_5B(CF_3)_6{}^-$ and the Superacidic Properties of Their Conjugate Acids. Submitted to *Angew. Chem., Int. Ed.*

Author's contribution

Paper I: Perfomed a large part of measurements and calculations of pK_a values, contributed to writing the text.

Paper II: Perfomed all measurements and calculations of pK_a values, contributed to writing the text.

Paper III: Perfomed calculations of pK_ip and pK_α values, contributed to writing the text.

Paper IV: Main person responsible for planning and writing the manuscript. Perfomed large part of measurements and calculations of pK_a values.

Paper V: Main person responsible for planning and writing the manuscript. Perfomed large part of the synthesis and all of the measurements and calculations of pK_a values in acetonitrile.

Paper VI: Helped to prepare the manuscript. Performed some of the theoretical calculations.

Paper VII: Main person responsible for writing the manuscript.

ABBREVIATIONS

α	Empirical parameter for solvent HBA acidity
AN	Acceptor number
AN	Acetonitrile
AU	Absorbance unit
B	Neutral base
β	Empirical parameter for solvent HBA basicity
CIP	Contact ion pair
DCE	1,2-Dichloroethane
DME	1,2-Dimethoxyethane
DMSO	Dimethyl sulfoxide
DFT	Density Functional Theory
ΔG_{acid}	Gas-phase acidity
ΔG_{base}	Gas-phase basicity
ΔG	Standard molar Gibbs free energy change
dma	*N*,*N*-dimethylamino group
DN	Donor number
ϵ_{r}	Relative permittivity
EPA	Electron-pair acceptor
EPD	Electron-pair donor
f	Activity coefficient
GP	Gas phase
HA	Neutral acid
HBA	Hydrogen bond acceptor
HBD	Hydrogen bond donor
HF	Hartree-Fock
IMME	(1,3-dimethylimidazolidin-2-ylidene)imine
imme	(1,3-dimethylimidazolidin-2-ylidene)amino group
K	Equilibrium constant
K_{a}	Acid dissociation constant
K_{AHA}	Homoconjugation constant
K_{α}	An estimate of K_{a} value
K_{d}	Ion pair dissociation constant
λ	Wavelength

n	Number of points in statistical analysis
NMR	Nuclear magnetic resonance
ΔpK_a	Difference of pK_a values, relative acidity
pK_auto	Autoprotolysis constant
pK_a	Negative logarithm of acid dissociation constant
PA	Proton affinity
π^*	Empirical parameter for overall solvent polarity
p	Negative logarithm
pyrr	*N*-pyrrolidino group
r	Correlation coefficient in statistical analysis
s	Standard deviation in statistical analysis
SSIP	Solvent-separated ion pair
Tf	Trifluoromethanesulfonyl group, F_3C-SO_2-
Tos	*Para*-toluenesulfonyl group, 4-CH_3-C_6H_4-SO_2-
THF	Tetrahydrofuran
TMG	*N*,*N*,*N'*,*N'*-tetramethyl guanidine
tmg	*N*,*N*,*N'*,*N'*-tetramethyl guanidino group
UV	Ultraviolet
vis	Visible
WCA	Weakly coordinating anion

1. INTRODUCTION

The first more or less contemporary theory of acids and bases was proposed by Arrhenius in 1880: acids are substances delivering hydrogen cations (often simply called just proton) to the solution (water). In 1923 Brønsted and Lowry, inspired by the work of Arrhenius, independently extended and generalized the definitions of acids and bases: acids are substances from which a proton can be dissociated; bases are substances that bind protons – there are no bases without acids and no acid exists without a base. According to this theory any compound capable of binding the proton can be considered as a base. All compounds can be therefore considered as bases, since virtually any compound can bind protons. The question is, what binds the proton more strongly? This question can be resolved with precise measurements of the strength of acids and bases. The strength of an acid characterizes its proton-donatong ability and the strength of a base characterizes its proton-accepting ability.[1]

The first and the most important medium for investigation of acid-base properties is, of course, water. Thousands of pK_a values of different compounds have been measured in water. But as the water itself has acidic and basic properties then measuring of stronger acids and stronger bases than water itself, is complicated in water and the strengths of strong acids and strong bases are levelled. All these acids and bases will be fully dissociated and pK_a values of those compounds are very difficult to measure. The strength of many strong acids have been measured in water which contains more hydronium ions than ordinary water. However, in this case we cannot talk about water as medium anymore. Also solubility of some compounds in water can be a problem.[2]

The other possibility is to investigate acids and bases in such media that do not possess that strong acid-base properties themselves. For example, dimethyl sulfoxide (DMSO) and acetonitrile (AN) are very common media for acid-base studies. In the present work, AN is mainly used as a medium to measure pK_a values, or to be more precise – to compare acid-base properties of different compouns – to measure ΔpK_a values. AN is a good solvent for moderately strong acids and bases but in the presence of superbases and superacids, AN also acts as an acid or base. For superbases, tetrahydrofuran (THF) is used because of its weaker acidic properties. For superacids 1,2-dichoroethane (DCE) is used because of its very weak basic properties. The only medium which has no limitations for measuring as strong acids or bases as one can get, is the gas phase (GP). It is also easy to perform quantum chemical calculations of the strengths of acids and bases in the gas phase. The quantum chemical calculations in solution phase are much more complicated. The influence of different media on different compounds depends on many factors and it is difficult to take all of those into account. Nowadays, several theoretical methods are used to predict strength of acids and bases in solution. All these computational and predicted values support measurements in GP and in solution phase. Still, real measurements are always essential, especially in solution phase where the accuracy of calculations is still significantly lower than the accuracy of measurements.

It has a great practical value to know the exact strength of acids and bases. Obtained values are used in many areas of chemistry, biology, medicine, materials science, *etc.*, in both reasearch and industrial fields.[3,4] Superacids and their anions – weakly coordinating anions (WCAs) are mainly used as catalysts and the knowledge of exact pK_a values are essential for further developments.[5] Many bases have biological importance, their pK_a values are helping properties, for example, for drug design.[6] Also, the study and synthesis of receptors, which recognize anions or cations in solution, can advance only with known pK_a values of those compounds.[7,8]

The main goal of the present work is to reach self-consistency between measured pK_a values and to provide more values with higher quality. In this work two comprehensive self-consistent scales of pK_a values in AN have been composed – for the acids and for the bases. These scales have been compiled using a measurement method permitting to obtain values of high consistency and are therefore useful tools for measuring pK_a values of all kinds of other compounds – as it is demonstrated in this work. Not only AN, but also DCE, THF and GP as reaction media have been used in this work to measure the acid-base properties of superacids, superbases and many other different compounds.

2. GENERAL ASPECTS

2.1. Brønsted-Lowry Acid-Base Equilibria

Acid-base chemistry is one of the most fundamental areas in chemistry. Proton transfer covers substantial part of all topics studied in chemistry. Therefore, the investigation of acid-base equilibria has significant importance.

According to the Brønsted-Lowry definition, acidity of a neutral acid (z = -1) or a cationic acid (z = 0) $\mathrm{HA^{z+1}}$ in solvent S is defined using equation 2.1 and is expressed as the acid dissociation constant (in this work the more general term – dissociation constant – is often used) K_a (equation 2.2) or more commonly as the negative logarithm of dissociation constant – pK_a.

$$\mathrm{HA^{z+1}} + \mathrm{S} \overset{K_\mathrm{a}}{\leftrightarrows} \mathrm{A^{z}} + \mathrm{SH^{+}} \tag{2.1}$$

$$K_\mathrm{a} = \frac{a(\mathrm{SH^{+}}) \cdot a(\mathrm{A^{z}})}{a(\mathrm{HA^{z+1}})} \tag{2.2}$$

$$\mathrm{p}K_\mathrm{a} = -\log\frac{a(\mathrm{SH^{+}}) \cdot a(\mathrm{A^{z}})}{a(\mathrm{HA^{z+1}})} \tag{2.3}$$

In the case of a neutral base, the bacicity of that base is defined *via* the acidity of a cationic acid, the conjugate acid of that base. The main reason for that is the need to have comparable dissociation constants for neutral acids and neutral bases. In this work, the terms "acidity of cationic acid" and "basicity of neutral base" (or just a base) are used interchangeably. Note that dissociation of a cationic acid involves only rearragangement of the the cationic charge between different species in solution while dissociation of a neutral acid involves generation and separation of two charged species. For the requirement of electroneutrality, it would be correct to write the dissociation of a base in another way, with the presence of anion. The equation 2.1 is a simplified way to describe the process. The process described with the equation 2.1 occurs only in polar solvents such as water, MeOH, DMSO, *etc.* (*vide infra*).[9,10]

In non-aqueous solvents, the measurements of activity of solvated hydrogen ion $a(\mathrm{SH^+})$ are problematic, especially in solvents of low polarity. To exclude the necessity to measure the activity of solvated hydrogen ion $a(\mathrm{SH^+})$, the equilibrium between two acids $\mathrm{HA_1^{z+1}}$ and $\mathrm{HA_2^{z+1}}$ can be studied:

$$\mathrm{A_2^z} + \mathrm{HA_1^{z+1}} \overset{\Delta K_\mathrm{a}}{\leftrightarrows} \mathrm{HA_2^{z+1}} + \mathrm{A_1^z} \tag{2.4}$$

This equilibrium refers to the relative acidity of the two acids $\mathrm{HA_1^{z+1}}$ and $\mathrm{HA_2^{z+1}}$ which is expressed as $\Delta\mathrm{p}K_\mathrm{a}$ and is defined as follows:

$$\Delta\mathrm{p}K_\mathrm{a} = \mathrm{p}K_\mathrm{a}(\mathrm{HA_2^{z+1}}) - \mathrm{p}K_\mathrm{a}(\mathrm{HA_1^{z+1}}) = \log\frac{a(\mathrm{HA_2^{z+1}}) \cdot a(\mathrm{A_1^z})}{a(\mathrm{HA_1^{z+1}}) \cdot a(\mathrm{A_2^z})} \tag{2.5}$$

As can be seen, the component $a(\mathrm{SH^+})$ is not appearing anymore in the equation 2.5. If it is assumed that the ratio of activity coefficients $f(\mathrm{HA^{z+1}})/f(\mathrm{A^z})$ is the same for both species[11] then the equation 2.5 can be transformed into the following form:

$$\Delta\mathrm{p}K_\mathrm{a} = \mathrm{p}K_\mathrm{a}(\mathrm{HA_2^{z+1}}) - \mathrm{p}K_\mathrm{a}(\mathrm{HA_1^{z+1}}) = \log\frac{[\mathrm{HA_2^{z+1}}] \cdot [\mathrm{A_1^z}]}{[\mathrm{HA_1^{z+1}}] \cdot [\mathrm{A_2^z}]} \tag{2.6}$$

The species in square brackets are now equilibrium concentrations which can be measured directly.

Before it was mentioned that the process according to the equation 2.1 is the simplified way to describe an acid-base equilibria. The dissociation as a process according to a solvent may consist of several steps and can be described with consecutive equilibria 2.7. The following equations are written only for neutral acids and square brackets indicate solvent cage of species, not the equilibrium concentrations anymore.

$$\mathrm{HA} + \mathrm{S} \overset{K_1}{\leftrightarrows} [\mathrm{AH} \cdots \mathrm{S}] \overset{K_2}{\leftrightarrows} [\mathrm{A^-HS^+}] \overset{K_3}{\leftrightarrows} [\mathrm{A^-}][\mathrm{HS^+}] \overset{K_4}{\leftrightarrows} \mathrm{A^-} + \mathrm{SH^+} \tag{2.7}$$

The first step K_1 is the initial complex formation between acid and solvent. This complex is held together by hydrogen bond or non-specific van der Waals forces (can be also both of those). Hydrogen bond is usually absent in the case of steric restrictions or if the charges of the formed ions are well delocalized and the H–A bond in $[\mathrm{HA} \cdots \mathrm{S}]$ is weakly polar.

The second step K_2, also called primary ionization step, is proton transfer from the acid to the solvent with a formation of a *contact ion pair* (CIP) complex $[\mathrm{A^-SH^+}]$, with no solvent molecules between ions. This complex is usually hydrogen-bonded, but again, it can be held together with electrostatic forces.

When solvatation increases, the bonding decreases and *solvent-separated ion pair* (SSIP) $[\mathrm{A^-}][\mathrm{SH^+}]$ forms (K_3), which is held together by electrostatic forces. This ion pair can dissociate into free ions (K_4). K_a is the overall product of all of these equilibrium constants: $K_1 \cdot K_2 \cdot K_3 \cdot K_4 = K_\mathrm{a}$.

Steps K_2 and K_3 are called ionization steps – ion pairs form but dissociation has not yet occured. The term ionization is often used instead of dissociation, but using this term is correct only if the dissociation process is not complete.

The extent of the dissociation of the compound depends mainly on the relative permittivity (ϵ_r) of the solvent. Usually in solvents having ϵ_r larger than 20 (water, DMSO, AN, MeOH, EtOH, *etc.*) the process proceeds to the formation of free solvated ions in the solvent. The extent of ionization of the acid depends not as much on ϵ_r but mainly on electron-pair donating and accepting properies (see section 2.3. for more profound review).

For a neutral base the similar process to the equation 2.7 can be written. According to the properties of the solvent and the neutral acid from what the base gets its proton, the molecule of the neutral base binds the proton either from the neutral acid, ion-paired complex or protonated solvent molecule (see equation 2.7). In the case of a weaker acid in a weakly polar solvent with rather low solvating ability, the proton comes from the ion-paired complex or from the neutral acid (as it is written in the following equation):

$$\mathrm{B} + \mathrm{HA} \overset{K_1}{\leftrightarrows} [\mathrm{B} \cdots \mathrm{HA}] \overset{K_2}{\leftrightarrows} [\mathrm{BH^+A^-}] \overset{K_3}{\leftrightarrows} [\mathrm{BH^+}][\mathrm{A^-}] \overset{K_4}{\leftrightarrows} \mathrm{HB^+} + \mathrm{A^-} \qquad (2.8)$$

Again, the first step K_1 is the initial complex formation between an acid and a base. The reaction proceeds to formation of CIP (K_2), then SSIP (K_3) between acid anion and protonated base, and if favorable, two ions are eventually separated and dissociated into solution (K_4). The overall result of all of these equilibrium constants indicates the proton distribution equilibrium between neutral and cationic acid. The relative concentrations of the different species in equation 2.8 depend on the polarity of solvents, EPD and EPA properties, properties of ions, *etc.*

Sometimes only K_{ip} is studied (*e.g.* in sections 4.3. and 5.3. and III). In this case only ionization equilibrium (K_2 or K_3, in equations 2.7 and 2.8) is experimentally determined. While equation 2.4 is describing the equilibirium of proton distribution between two fully dissociated species, then the equation 2.9 describes the proton distribution between two ion-paired species:

$$\mathrm{HA_1} + [\mathrm{HB^+A_2^-}] \overset{\Delta K_{\mathrm{ip}}}{\leftrightarrows} \mathrm{HA_2} + [\mathrm{HB^+A_1^-}] \tag{2.9}$$

It is possible to write this model equation using equilibrium steps containing dissociated species as well as ion-paired species:

$$\begin{aligned}\mathrm{HA_1} + [\mathrm{HB^+A_2^-}] \overset{K_{\mathrm{d}}^{[\mathrm{HB^+A_2^-}]}}{\leftrightarrows} \quad \mathrm{HA_1} + \mathrm{A_2^-} + \mathrm{HB^+} \overset{\Delta K_\alpha}{\leftrightarrows} \\ \mathrm{HA_2} + \mathrm{A_1^-} + \mathrm{HB^+} \overset{1/K_{\mathrm{d}}^{[\mathrm{HB^+A_1^-}]}}{\leftrightarrows} \quad \mathrm{HA_2} + [\mathrm{HB^+A_1^-}]\end{aligned} \tag{2.10}$$

The constants K_{d} are the dissociation constants of respective ion pairs and the constant ΔK_α is the estimate of the dissociation constant of the relative free acid. Estimated K_α is used because often the true dissociation constants K_{a} cannot be measured (also with UV-vis spectrophotometry method used in this work). From equations 2.9 and 2.10 it is possible get $\Delta\mathrm{p}K_{\mathrm{ip}}$:

$$\begin{aligned}\Delta\mathrm{p}K_{\mathrm{ip}} = \mathrm{p}K_{\mathrm{ip}}(\mathrm{HA_2}) - \mathrm{p}K_{\mathrm{ip}}(\mathrm{HA_1}) = \\ = \log\frac{a([\mathrm{HB^+A_1^-}])\cdot a(\mathrm{HA_2})}{a([\mathrm{HB^+A_2^-}])\cdot a(\mathrm{HA_1})} = \log\frac{\Delta K_\alpha \cdot K_{\mathrm{d}}^{[\mathrm{HB^+A_2^-}]}}{K_{\mathrm{d}}^{[\mathrm{HB^+A_1^-}]}}\end{aligned} \tag{2.11}$$

If the K_{d} values are measured or estimated[12] (as in this work), then the ΔK_α can be found as follows:

$$\Delta\mathrm{p}K_\alpha = \mathrm{p}K_\alpha(\mathrm{HA_2}) - \mathrm{p}K_\alpha(\mathrm{HA_1}) = \Delta\mathrm{p}K_{\mathrm{ip}} - \log\frac{K_{\mathrm{d}}^{[\mathrm{HB^+A_1^-}]}}{K_{\mathrm{d}}^{[\mathrm{HB^+A_2^-}]}} \tag{2.12}$$

The convenient and common experimental technique to study ion-pairing is conductometry, often in combination with other methods.[13] In this work (see III) in the case of neutral bases the estimation was made using the Fouss equation:[14]

$$K_{\mathrm{d}} = \frac{3000e^{\frac{-e^2}{aDkT}}}{4\pi N a^3} \tag{2.13}$$

where N is Avogadro's number ($N = 6.02 \cdot 10^{-23}$ 1/mol), a is the distance of ion centres in cm ($a = r^{+}+r^{-}$), e is the charge of electron, $e = 4.80{\cdot}10^{-10}$ esu (1 esu $= 1.60{\cdot}10^{-19}$ C), k is Boltzmann constant, $k = 1.38{\cdot}10^{-16}$ erg/K ($1.38{\cdot}10^{-23}$ J/K), T is temperature in K.

2.2. Side Reactions of Acid-Base Equilibria

Many solvents (in particular polar non-HBD solvents) have poor ability to solvate either anions or cations or both species of ions. In this case different side reactions may appear during the measurements.[15] Formation of homoconjugate and heteroconjugate complexes is the most common of them. *Homoconjugate complex* is the hydrogen-bonded complex between the acidic and basic form of the same compound:

$$\mathrm{HA}_1^{\mathrm{z}+1} + \mathrm{A}_1^{\mathrm{z}} \overset{K_{\mathrm{AHA}}}{\leftrightarrows} \mathrm{HA}_1 \cdots \mathrm{A}_1{}^{2z+1} \tag{2.14}$$

Heteroconjugate complex is the complex between the acidic and basic forms of different compounds:

$$\mathrm{HA}_1^{\mathrm{z}+1} + \mathrm{A}_2^{\mathrm{z}} \overset{K_{\mathrm{A'HA}}}{\leftrightarrows} \mathrm{HA}_1 \cdots \mathrm{A}_2{}^{2z+1} \tag{2.15}$$

Self-association is complex-formation between two or more neutral, anionic or cationic species. The equation 2.16 is written only for neutral acid:

$$n\mathrm{HA} \overset{K_{\mathrm{HA}2}}{\leftrightarrows} (\mathrm{HA})_2 \overset{K_{\mathrm{HA}n}}{\leftrightarrows} (\mathrm{HA})_n \tag{2.16}$$

Also, larger aggregates (joined conjugate complexes, associate complexes and ion pairs) may appear in the solution during the measurements.[15] Those complexes have been connected *via* hydogen bond and electrostatic forces and they may grow so large that they start to scatter visible light. This appear especially in solvents of low polarity.

It is generally observed that the extent of homoconjugation and association increase if the processes studied involve ions with poorly delocalized charge and not well hindered protonation-deprotonation centre. It is also observed that upon increase of the number of acidic protons in the compound the extent of formation of conjugate complexes increases.[16]

Measuring both, acids and bases in AN, it was observed that many neutral acids formed homoconjugate complexes but none of the bases. It is known that AN solvates anions poorly[15] and due to the different dissociation proccess of acids (formation of two oppositely charged particles) the formation of homoconjugate complexes was observed (see IV and V). In any other solvents, associate and conjugate complex-formation were not observed with those compounds which were under investigation in those solvents. The easiest way to decrease the influence of forming homoconjugate complexes without changing the medium is to use method that allows to work with rather diluted solutions.

2.3. Selection of Solvents

Everyone who has measured pK_a values in different non-aqueous solvents, has found that AN is a good solvent for acid-base measurements. Measuring acid-base properties in DCE and THF is significantly more challenging. Why is that so? That is caused not as much by compounds under investigation as by the properties of solvents. Not only the physical properties (boiling point – that determines largely ease of purification, viscosity, UV absorbance window, *etc.*) and chemical properties (stability against common impurities and oxidation, UV radiation, electrochemical stability, *etc.*) of the solvent are important. Several other properties of solvents have important influence on the acid-base reactions also. It has been commonly accepted that three main components that determine non-specific and specific solvent-solute interactions can be interpreted as polarity, polarizability and acid-base properties of solvents.[17]

According to Reichardt,[17] polarity of a solvent is the overall solvatation capability of the solvent, which in turn depends on the action of all possible, nonspecific and specific intermolecular interactions between solute and solvent molecules. These interactions in turn depend on the Brønsted-Lowry and Lewis acid-base properties, polarity, polarizability, and other properties of the involved molecules.

One physical constant that is the most commonly used parameter to describe polarity of a solvent is relative permittivity ϵ_r (IUPAC suggest to use the term relative permittivity instead of dielectric constant). ϵ_r experesses the ability of a solvent to decrease the interactions between charged particles by orienting its dipoles. ϵ_r characterizes well the dissociating power of solvents. Solvents of large ϵ_r ($\epsilon_\mathrm{r} > 40$) are called *polar solvents* and ionic species are fully dissociated in those solvents. In solvents of intermediate ϵ_r (ϵ_r = 15–40) the ratio between free and ion-paired ions depends on the structure of the solvent and solute (ion size, charge distribution, hydrogen bonding abilites, *etc.*), their interactions and the concentration of the solute. Solvents of low ϵ_r are called *apolar* or *nonpolar* solvents and ions are ion-paired in these solvents. Only solvents with sufficiently high ϵ_r will be capable to reduce the strong electrostatic attraction between oppositely charged ions to such an extent that ion pairs can dissociate into free solvated ions. These solvents are usually called *dissociating solvents.* The importance of ϵ_r over the other criteria due to the simplicity have become a useful measure of solvent polarity.

Dipole moment μ (unit C·m or D) is a measure of polarity of a single molecule. Electrically neutral molecules with an unsymmetrical charge distribution possess a permanent dipole moment μ. Only molecules possessing a permanent dipole moment should be called *dipolar molecules.*[17] Although in order to have high relative permittivity the solvent has to have molecules with high dipole moment, these two quantities are not strictly correlated. ϵ_r depends also on the polarizability of the solvent, its HBD and HBA properties, *etc.*

ϵ_r as well as μ are often used for the quantitative characterization of solvent polarity but neither of the two describe very well the the specific intermolecular interactions that are also an intrinsic component of solvent polarity. There are many empirical polarity parameters, which may describe more adequately polarity, polarizability, acidity, basicity, hyrogen bonding, *etc.*

Polarizability shows the ease of distortion of the electron cloud of a molecular entity by an electric field, which may be caused by the presence of a nearby ion or dipole. Solvents of high polarizability are often good solvators for anions which also possess high polarizability. The polarizability is connected with the index of refraction n (or n_D if index of refraction is given for the centre of the yellow sodium double emission) – molecules with a more easily polarizable electron cloud more intenesely reduce the speed of light inside the medium and have larger index of refraction.

Acid-base properties of the solvent are very important properties in terms of acid-base studies. These properties become even more important if compounds under investigation are extremly strong or weak acids or bases. Brønsted-Lowry acid-base properties of a solvent describe the ability of solvent molecule to donate (equation 2.17) or accept proton (equation 2.18):

$$\mathrm{SH} \leftrightarrows \mathrm{H}^+ + \mathrm{S}^- \tag{2.17}$$

$$\mathrm{SH} + \mathrm{H}^+ \leftrightarrows \mathrm{SH}_2^+ \tag{2.18}$$

A combination of these two processes is described quantitatively by the autoprotolysis constant (K_{auto}) of the solvent:

$$2\mathrm{SH} \overset{K_{\mathrm{auto}}}{\leftrightarrows} \mathrm{SH}_2^+ + \mathrm{S}^- \tag{2.19}$$

$$K_{\mathrm{auto}} = a(\mathrm{SH}_2^+) \cdot a(\mathrm{S}^-) \tag{2.20}$$

The lower the K_{auto} value (or the higher the pK_{auto} value) the wider is the range of strengths of acids or bases that can exist in this solvent without being fully dissociated or protonated. The strongest acid that can exist in the solvent is the lyonium ion SH_2^+ and the strongest base is the lyate ion S^-.

There are solvents which do not have proton at all. This kind of solvents are called *aprotic* solvents. Most of solvents have protons in their molecules, but the equilibria according to the equation 2.17 are insignificant (not observable experimentally). These kind of solvents are also called aprotic. If the dissociation of the solvent proceeds to a measurable extent then the solvent is called *protic*. Usually pK_{auto} value 20 is considered to be the limit between aprotic and protic solvents. However, the term aprotic is rather misleading, since, for example, solvents commonly referred to as dipolar aprotic (*e.g.* DMSO, AN) are in fact not aprotic. In reactions where strong bases are employed, their protic character can be recognized. Therefore, the term aprotic solvents should be replaced by *non-HBD* solvents (*vide infra*). In *amphiprotic* solvents both reactions (equations 2.17 and 2.18) are present. Water is the prototype of amfiprotic solvents.

Solvents can be divided also according to their acidity and basicity. *Protogenic* solvents have more pronounced acidic than basic character, *protophilic* solvents have more pronounced basic than acidic character. If a solvent has low acidity and basicity, then it is a good *differentiating* solvent. Solvents can be also good differentiating solvens for example only for strong bases and weak acids but at the same time not for weak bases and and strong acids, or *vice versa.* Solvents having significantly acidic or basic nature are called *levelling* solvent for bases or acids, respectevly. The terms amfiprotic, protic and levelling are connected – if solvent is protic, then it is usually levelling.

Hydrogen bonding plays significant role in acid-base studies. When a covalently bound hydrogen atom forms a second bond to another atom, then the second bond is called *hydrogen bond.* Often hydrogen bonding can be regarded as a preliminary step on a Brønsted-Lowry acid-base reaction (see equations 2.7 and 2.8). Solvents containing proton-donor groups are designated protic solvents or *hydrogen bond donating* (HBD) solvents, solvents containing proton-acceptor groups are called *hydrogen bond accepting*

(HBA) solvents. Amphiprotic solvents can act both as HBD and as HBA solvents simultaneously. The stronger the HBA properties of the solvents, the better it stabilizes cations. The stronger the HBD properties, the better it stabilizes anions. This is one reason why for example AN and THF solvates better cations.

One approach – solvatochromic comparison method – was employed and further developed by Kamlet, Abboud and Taft *et al.*[18–20] It is used to evaluate a β scale of solvent HBA basicities, an α scale of solvent HBD acidities and a π^* scale of solvent dipolarity-polarizability using UV-vis spectral data of solvatochromic compounds. π^* values measure the ability of the solvent to stabilize a charge or a dipole by virtue of its dielectric effect and therefore characterize the overall solvent polarity.

Lewis acid-base properties of solvents describe solvents power to donate or accept electron pair. As *dissociating power* of solvents depends mainly on ϵ_r, then *ionizing power* depends on the ability of the solvent to be *electron-pair acceptor* (EPA) or *electron-pair donor* (EPD). These properties can be empirically described *e.g.* with acceptor number (AN) or donor number (DN). Higher values mean that solvent has higher ability to ionize neutral acid molecules and to stabilize the formed ions.

Koppel and Palm[21] and Koppel and Paju[22] have defined an empirical solvent scale of Lewis basicity B and B', respectevly. B' scale is based on the O-H streching frequencies of phenol, which has formed the complex with the HBA molecules in CCl_4. Koppel and Palm also presented an empirical parameter E to describe solvent Lewis acidity, P as a measure of solvent polarizability and Y as a measure of solvent polarity. Y and P are considered as non-specific and E and B' (B) as specific characteristics of the solvent.

If the solvent is good EPD but poor EPA, then it stabilizes cations efficiently but anions poorly. Therefore, anions tend to form aggregates with cations or neutrals. The term HBA refers to the acceptance of the proton of a hydrogen-bond. Therefore, HBA solvents are also EPD solvents. HBD refers to the donation of the proton. Therefore, HBD solvents behave as protic solvents. Solvents of higher acidity and basicity solvate ions better. Therefore, it is necceary to find a compromise between ionizing power and acid-base properties. For example, DCE has the $DN = 0$ (it is the reference solvent for DN-s), but is one of the few possible choices for measuring acidities of superacids, because most of the other common solvents are either too basic and protonate in the presence of superacids or are so nonpolar that neither the acids nor the salts are soluble in those solvents. Because of the low ϵ_r and nonexistent EPD abilities and we have to consider the ion pairs and formation of associates during the measurements.

In the present work, different media were used for measurements and for comparison of pK_a values. Media referred during the entire study are following:[17]

Water is by far the most popular solvent for investigation of acid-base equilibria. With its high EPD-EPA ability ($AN = 54.8$; $\alpha = 1.17$ and $\beta = 0.18$ here and afterward from reference 20) and high polarity ($\epsilon_\mathrm{r} = 78.30$, $\pi^* = 1.09$) it is good ionizing and dissociating solvent, but at the same time it has quite high acidity and basicity (p$K_\mathrm{auto} = 14.00$) and is therefore levelling solvent for stronger bases and acids. Water forms hydrogen bonded complexes with compounds under investigation and thus it masks the intrinsic acid-base properties of acids and bases. Water is also not a good solvent for nonpolar molecules. Many important compounds cannot therefore be studied because of the solubility problems.

Acetonitrile (AN) has many good properties to make it a suitable solvent for acid-base studies. It has low basicity and almost negligible acidity, thus it has very low ability to solvate anions. This causes weaker acids with no sterically hindered protonation site to form larger aggregates. AN is sufficiently polar ($\epsilon_\mathrm{r} = 35.94$, $\pi^* = 0.75$) to favor dissociation of ion pairs into free ions. The extent of autoprotolysis is significantly lower (p$K_\mathrm{auto} \geqslant 33$) than that of water, but very similar to THF and DMSO. AN is a sufficiently differentiating solvent. AN is a weak HBD and EPD ($DN = 14.1$, $\beta = 0.31$) and moderate EPA ($AN = 18.9$, $\alpha = 0.19$), thus AN is good solvent for measuring especially strong acids. AN has also one disadavantage – in the presence of strong bases it starts to oligomerize due to the deprotonation of AN molecule. Still, in AN it is possible to work with bases in the range of basicities covering almost all conventional superbases (approximately 8 units above pK_a value of DBU, see section 4.1. and I).

Tetrahydrofuran (THF) has much lover polarity ($\epsilon_\mathrm{r} = 7.58$, $\pi^* = 0.58$) than AN but very similar differentiating ability (p$K_\mathrm{auto} = 34.7$). THF solvates cations ($DN = 20.0$, $\beta = 0.55$) even better than AN but anions ($AN = 8.0$, $\alpha = 0.00$) even more poorly. THF is much stronger base compared to AN. According to these properties THF is a good solvent for measurements of strong bases. In this work THF was selected as the medium for measuring superbases which were not possible to measure in AN. At present, approximately 6 pK_a units higher basicities have been measured in THF than in AN (see I and III). Differently from AN, in THF the ion-pair basicities are measured. Generally, THF is very popular and widely used solvent for measuring both acids[23–25] and bases.[12,26]

1,2-Dichloroethane (DCE) is with its polarity ($\epsilon_\mathrm{r} = 10.36$, $\pi^* = 0.81$) similar to the THF. After examined all the other properties, we found DCE to be markedly different from all the previously mentioned solvents. Observable autoprotolysis according to the Brønsted-Lowry definition is missing and therefore it sets virtually no limits for choice of compounds. Nevertheless, it is possible that in the presence of the strongest acids known (carborane acids) it may protonate and HCl could therefore be detached. Also it has been determined in this work that after standing for one day in the presence of superbases (t-BuP$_4$(dma)) the measurements cannot be carried out anymore. DCE has rather acidic properties (AN = 16.7, α = 0.00) and basicity (DN = 0.0, β = 0.00) is virtually nonexistent. In fact, DCE is used as the reference solvent for measuring EPD properties. Because of the low polarity and small DN in DCE only ion-pair acidities are measured. DCE is not a very common solvent for acid-base studies even though it is widely used in organic syntehsis.

Heptane is a very interesting solvent for acid-base studies. Ionic compounds have extremly low solubility in such a nonpolar solvent (ϵ_r = 1.92, α = 0.00, β = 0.00, π^* = -0.08) but in spite of that, several pK_{ip} values (still till now only relative pK_{ip} values) have been measured in heptane. The trick is in choosing the compounds that on deprotonation (acids) or protonation (bases) give ions with highly delocalized charges. Nevertheless, during the measurements in heptane, ions and neutrals form ion pairs, complexes and higher aggregates. In order to avoid an extremely complex and difficult to interpret picture, very low concentrations are used, at which it can be assumed that ions with delocalized charges exist only as ion pairs and no higher aggregates are formed. Heptane does not undergo autoprotolysis and possesses no electron-pair accepting or donating properties. With its very low polarity, heptane is a kind of half-way between polar sovents and GP. Acidity data in solvents of low polarity are very valuable.

Gas-Phase (GP) is the least polar (ϵ_r = 1) and the most differentiating medium possible.[17,21] It is a much more differentiating medium than water, AN and THF. The intrinsic acid-base properties of molecules can be studied in the gas phase. No solvent effects are disturbing. GP as a medium itself does not set any limits for the strength of acids and bases. The problems that are encountered with many compounds are practical – the insufficient volatility and availability as free neutral acids and bases. In the gas phase theoretical calculation methods are much more successful than in any of the condendsed media and often accuracy of theoretical results can rival the accuracy of experiment.[27]

Dimethyl sulfoxide (DMSO) is highly polar (ϵ_r = 46.45, π^* = 1.00) non-HBD solvent with rather high basicity (DN = 29.8, β = 0.76) and low acidity (AN = 19.3, α = 0.00). Its autoprotolysis constant is similar to that of AN and THF, pK_{auto} = 35.[28] DMSO dissolves both polar and nonpolar compounds easily and is a widely used solvent in organic synthesis. It is certainly one of the most popular non-aqueous solvent for acidity measurements where hundereds of pK_a values have been measured.[28,29]

1,2-Dimethoxyethane (DME) is used in synthesis as a highly boiling alternative to THF and diethyl ether. It has similar properties to THF. DME has been chosen for measuring several acidities of CH acids with well delocalized charge.[30–32] DME forms chelate complexes with cations and acts as a bidentate ligand and is by this property different from all previously mentioned solvents. DME is a basic solvent ($AN = 10.2$, $\alpha = 0.00$, $\beta = 0.41$, $\pi^* = 0.53$) with moderate differentiating ability.

2.4. Selection of Method

There are several methods developed to study quantitatively acid-base equilibria. Undesirable side-reactions and effects of impurities, the information provided by the method, the number of approximations necessary to get the results, compatibility of the method with the medium and with the compounds under study, available equipment, *etc.* are some of the factors to consider when choosing the method. The parallel use of different methods gives the most reliable results.[33] However, to study, to use and to install a method may often be time-consuming and take much effort. In this section only the main methods are shortly discussed and their positive and negative features in terms of acid-base investigations in non-aqueous media will be considered.

Potentiometic titration has been widely used for acid-base studies[13,33,34] especially in water and other protic solvents. Numerous pK_a values in literature have been measured using this method, even though it needs repeated measurements and particularly prudent handling of equipment because pontentiometric signals from glass electrodes in non-aqueous media are not as reliable as in water, mainly due to the low conductivity of solutions, high liquid junction potentials and drift of the properties of the potentiometric system in time (caused *e.g.* by small changes of water content in the solutions). Potentiometric approach cannot be extended to very low and high pK_a regions.[35] Procedure itself is somewhat inconvenient with its standardization and calibration steps. Concentrations of the acids and bases under investigation must be relatively high during the measurements and in non-aqueous media this may lead to formation of conjugate complexes and ion pairs. Impurities may easily affect the results. Also, a relatively large amount of sample is required which can be a problem with determining pK_a values of newly sunthesized and rare compounds.

UV-vis spectrophotometry has been also widely used and is often the most preferred method due to the possibility to work with low concentrations (less associate and conjugate complexes) and small amounts of compounds. The genuine spectrophotometric method means that in solution there is an indicator compound whose absorption spectrum is sensitive to the proton activity and using the spectum of this indicator and the amount of protonated and deprotonated forms of the investigated compound in the solution, the pK_a value of the compound (usually with no absorption spectra in the UV-vis region) is found. This means prior knowledge of pK_a values of indicators in the given solvent and this method may suffer from serious errors if the solvent, impurities or the compounds under investigation exhibit considerable absorbance in the same spectral region as the indicator. The method used in the pesent work to investigate acid-base properties of compounds is a modification of this UV-vis spectrophotometric method. The variation from the genuine method is that in our case, differences of pK_a values – ΔpK_a – of two compounds are measured the way that no amounts of compounds and titrants are needed, only the spectral data are used. This sets some specific requirements to the compounds under study – mainly, both compounds have to have spectra in the UV-vis region and the spectra have to be sensitive to the proton activity. The advatntage of this method is its "clearness" – the method allows to detect formation of associate and conjugate complexes, non-reversibility and other problems which may appear during the study.

Conductometry is also a widely used method for acid-base studies.[13] Conductance of pure solvent is usually poor but if there are ions in the solution, the conductance increases considerably. The conductance of such electrolytic solutions depends on the concentration of the ions and also on their nature (charge, size and mobilty). Dissociation constants of acids can be determined by measuring limiting conductance as a function of concentration of the ions formed by the dissociation. Using this method, also values of homoconjugation constants logK_AHA can be measured, even though it is not very accurate. Combination of potentiometry and conductometry is widely used in apolar solvents where ion pairs and associates often appears. Ion-pair acidities are measured using potentiometry and the incomplete dissociation of acids is taken account using conductometric method.

Nuclear magnetic resonance (NMR) spectrometry[12,36] has been used for measuring ΔpK_a values. From proton NMR spectra of mixture of two pure compounds and step by step protonated or deprotonated mixture, it is possible to calculate ΔpK_a values of these two compounds. The main drawback of the NMR method is the necessity to use higher concentrations that in less polar solvents can lead to formation of ion pairs. The advantage of NMR is the richness of information it offers. It is possible to observe side processes, get information about protonation site, *etc.*

All kinds of other methods are used – voltammetry,[37] high-performance liquid chromatography (HPLC)[38] , electrophoresis,[39,40] *etc.* Whatever property of a compound can be measured that is dependent on its protonation or deprotonation could be used for acidity-basicity measurements. Often it is simpler to compare acidities of different compounds – to measure ΔpK_a values. However, using this approach, known pK_a values in a given solvent must be available if absolute pK_a values of the investigated compounds are desired.

Previous methods were all for investigation of acid-base properties in solutions. Another important field is to measure acid-base properties of compounds in the gas phase. For this also several methods have been developed.

Fourier transform ion cyclotron resonance mass spectrometry (FT-ICR MS) is one of the main methods for measuring the gas-phase acidity (ΔG_{acid}) and the gas-phase basicity (ΔG_{base}) values.[41,42] The principle of the method is simple. The ratio of abundances of ionic species can be obtained from the signal intensities of respective ions in mass spectra (recorded after some reaction time is allowed for the species in order to reach equilibrium) and the concentrations of neutrals can be obtained from partial pressures of the respective species, which can be measured separately for both compounds. The main problems are the necessity to use free acids and bases (not salts of those compounds) and that the acids and bases must possess some volatility. Different techniques, such as the use of direct insertion probes have been developed to overcome these problems.[42]

High-pressure mass-spectrometry[43,44] and flowing afterglow techniques are also widely used. More limited is the use of the extended kinetic method of Cooks[45,46] which can measure directly only approximate values of proton affinities (PA). The gas-phase PA of a molecule is defined as the enthalpy change of protonation reaction. The GP acidity is defined as a change of Gibbs free energy of protonation reaction. The entropy must be calculated or measured to get the ΔG_{base} values from PA values.

Quantum chemistry and correlation methods are a type of entirely different methods to predict the acid-base properties of compounds in condensed media and in the GP. Quantum chemical calculations at different levels of ab initio and DFT theories are extensively and successfully used for the calculation and prediction of GP acidities and basicities of neutral and cationic acids. Less successful in reproducing and predicting the solution pK_a data are numerous computational methods (see *e.g.* the Gaussian User's Reference[47]) which use either various modifications of the dielectric theory or its combinations with the super-molecule approach or statistical thermodynamic approach.

2.5. Method Used in This Work – "Pure" UV-vis Spectrophotometric Method

It was mentioned in previous section that UV-vis spectrophotometric method is one of the many methods used to study acid-base properties of compounds. It has several advantages compared to other methods. From equations 2.6 it is evident that there is an approach which allows to exclude the measurement of proton activity in the solvent. In this work this knowledge has been applied and the UV-vis spectrophotometric method is used to measure relative acidities of compounds. The principle of this method is very simple – we titrate simultaneously two compounds dissolved in the same solution, which have UV-vis spectra, with acidic or basic titrant. The titrants themselves do not absorb in the analytically important wavelength range (it is the wavelength range where the compounds under investigation absorb). In the area of analytical wavelengths a set of complex spectra forms. These spectra are superpositions of spectra of the four species – the protonated and deprotonated forms of the two compounds. Using the calculation methods described in section 3.1. it is possible to calculate the relative acidity of these two compounds quite accurately. This method, because there are two compounds in the same solution, eliminates many possible sources of errors or reduces their influence. The advantages of this method are:

1. The disturbing effects (water, impurities, interference in spectrophotometer, *etc.*) affect both compounds with the same magnitude and are expected to cancel out. The influence can be somewhat different if the types of simultaneously measured acids or bases have significantly different protonation-deprotonation centre (*e.g.* CH acid *vs.* OH acid).

2. Low concentrations (one of the adavantages of UV-vis spectrophotometric method) allow to use very weak buffering with this method. If a minor acidity change of a solution occurs, it will have influence for the spectra on both compounds.

3. No need to measure the acidity of the medium.

4. No concentrations of compounds are needed for measurements. This allow us to use very small amounts of compounds and solvents.

This method has also some disadvantages:

1. The relative acidity of the two compounds, which are simultaneously titrated, can vary only within a narrow range – up to 2 pK_a units. This means that we have to compile ladders to cover the whole acidity area which is quite hard work and may take years. If we have no reference compounds in a certain acidity area, no other compounds can be measured there.
2. Relative acidities and basicities can only be measured. This means that in order to obtain absolute values, the scales have to be anchored to a reference compound with known acidity (basicity).
3. Both compounds should have UV-vis spectra and spectra of acidic and basic form should be relatively different.

See section 3.1. for the description of different calculation methods for ΔpK_a values.

2.6. Isodesmic Reactions Approach

An isodesmic reaction is a chemical reaction (actual or hypothetical) where the same number of chemical bonds of the same type are broken and formed in the initial compounds and in the reaction products.[48] In the present work the isodesmic reactions approach was used to explore the origin and trends of acidity in pentakis(trifluoromethyl) derivatives (see section 5.2. and V). The principle of this method is to calculate of enthalpy changes (or if the number of particles is the same on the both sides of the reactions and no intramolecular cyclization is involved, then it is possible to use also Gibbs free energy changes) of both sides of a reaction which gives liberation or demand of energy during this reaction. The isodesmic reactions approach allows to obtain data that are often experimentally inaccessible. It is possible to calculate energetic effects rearranging the carbon skeleton of molecules, shifts of substituents within molecules and between molecules, *etc.* The obtained data can in turn be used for estimating energetic contributions of different electronic and steric effects. More detailed discussion about pentakis(trifluoromethyl) derivatives can be found in section 5.2. and in paper V.

3. EXPERIMENTAL

3.1. Calculation Methods for $\Delta \mathrm{p}K_\mathrm{a}$ Values

According to the above described method (see section 2.5.) whereby the relative acidity (basicity) of two acids or bases is measured, it is necessary to measure also the spectra of the basic and acidic forms of both pure compounds. To confirm the purity of the measured compounds, it would be good also to measure some spectra between the fully acidic and basic forms to assess the sharpness of the isosbestic points (the absorbance of protonated and deprotonated forms is the same). On Figure 3.1 there are spectra of two pure compounds measured separately.

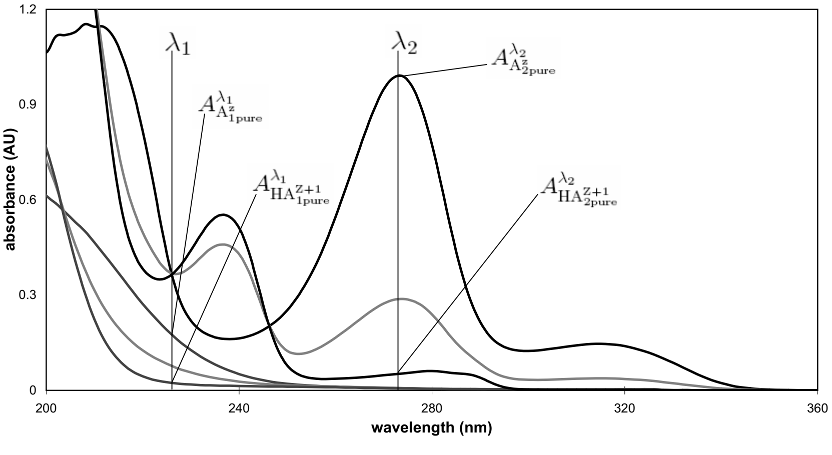


Figure 3.1: Spectra of two pure compounds

After measuring the spectra of the pure compounds, the spectra of their mixture at different dissociation levels are measured. On Figure 3.2 the spectra of mixture of the same two compounds have been indicated.

The principle of calculation of $\Delta \mathrm{p}K_\mathrm{a}$ values from spectral data is to get (using different approximations, if necessary) the dissociation level α of each acid (or protonation level of each base) in the solution at each titration point when titrating the mixture of acids (bases).

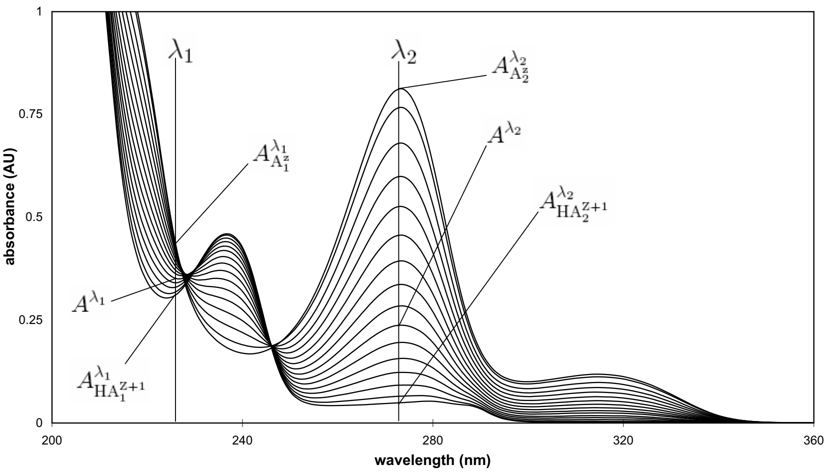


Figure 3.2: Spectra of mixture

Dissociation level α of an acid $\mathrm{HA}^{\mathrm{z}+1}$ is defined *via* following equation:

$$\alpha = \frac{[\mathrm{A}^{\mathrm{z}}]}{[\mathrm{HA}^{\mathrm{z}+1}] + [\mathrm{A}^{\mathrm{z}}]} \tag{3.1}$$

The approximations which have been taken into account in the case of every calculation methods are:

- The normalized concentrations for compounds are used – the sum of equilibrium concentrations of the acidic and basic form of a compound are normalized to unity:

$$[\mathrm{HA}_1^{\mathrm{z}+1}] + [\mathrm{A}_1^{\mathrm{z}}] = 1 \text{ and } [\mathrm{HA}_2^{\mathrm{z}+1}] + [\mathrm{A}_2^{\mathrm{z}}] = 1 \tag{3.2}$$

- The optical path length, 1 cm, is equal for all substances and is included in A^{λ} and absorbance caused by solvent is compensated.
- Concentrations are used instead of activities. See equations 2.5 and 2.6 in section 2.1.

$\Delta \mathrm{p}K_{\mathrm{a}}$ values are calculated according to equation 3.3 in the case of almost all calculation methods, if not indicated differently.

$$\Delta \mathrm{p}K_{\mathrm{a}} = \log \frac{\alpha_1 (1 - \alpha_2)}{\alpha_2 (1 - \alpha_1)} \tag{3.3}$$

$\Delta \mathrm{p}K_{\mathrm{a}}$ values are found from every titration point during the titration of mixture. Points with dissociation levels between 5% to 95% for both acids are usually used. In THF and in DCE the dissociation level range 10% to 90% was often used. Therefore, to get as many $\Delta\mathrm{p}K_\mathrm{a}$ values as possible from one measurement, the acidity of the mixture should be changed only in small steps. 10 to 20 spectra for one $\Delta\mathrm{p}K_\mathrm{a}$ measurement were usually measured. From UV-vis spectrophotometric data it is possible to calculate with good confidence level $\Delta\mathrm{p}K_\mathrm{a}$ values up to 2 units. Usually the $\Delta\mathrm{p}K_\mathrm{a}$ values obtained using different data treatment methods agreed well.

Method A – The least-squares of linear combination method.

When two partially dissociated compounds are in the same solution, the Lambert-Beer Law for the net absorbance at wavelength λ can be written:

$$A^\lambda = [\mathrm{A}_1^\mathrm{z}]\epsilon^\lambda_{\mathrm{A}_1^\mathrm{z}} + [\mathrm{A}_2^\mathrm{z}]\epsilon^\lambda_{\mathrm{A}_2^\mathrm{z}} + [\mathrm{HA}_1^{\mathrm{z}+1}]\epsilon^\lambda_{\mathrm{HA}_1^{\mathrm{z}+1}} + [\mathrm{HA}_2^{\mathrm{z}+1}]\epsilon^\lambda_{\mathrm{HA}_2^{\mathrm{z}+1}} \tag{3.4}$$

ϵ^λ values are normalized concentration absorptivities of the respective species at a given wavelength. Equation 3.4 can be rearranged:

$$A^\lambda = \epsilon^\lambda_{\mathrm{HA}_1^{\mathrm{z}+1}} + \epsilon^\lambda_{\mathrm{HA}_2^{\mathrm{z}+1}} + [\mathrm{A}_1^\mathrm{z}](\epsilon^\lambda_{\mathrm{A}_1^\mathrm{z}} - \epsilon^\lambda_{\mathrm{HA}_1^{\mathrm{z}+1}}) + [\mathrm{A}_2^\mathrm{z}](\epsilon^\lambda_{\mathrm{A}_2^\mathrm{z}} - \epsilon^\lambda_{\mathrm{HA}_2^{\mathrm{z}+1}}) \tag{3.5}$$

If there is a spectrum of a mixture where both compounds are in basic form, then the net absorbance of the solution is defined as follows:

$$A^\lambda = [\mathrm{A}_1^\mathrm{z}]\epsilon^\lambda_{\mathrm{A}_1^\mathrm{z}} + [\mathrm{A}_2^\mathrm{z}]\epsilon^\lambda_{\mathrm{A}_2^\mathrm{z}} \tag{3.6}$$

The terms on the right side of this equation can be expressed *via* absorbances of pure compounds in basic form multiplied by coefficients c_1 and c_2, which are the ratios of concentrations in mixture and solutions of pure compounds:

$$[\mathrm{A}_1^\mathrm{z}]\epsilon^\lambda_{\mathrm{A}_1^\mathrm{z}} = c_1 A^\lambda_{\mathrm{A}^\mathrm{z}_{1\mathrm{pure}}} \text{ and } [\mathrm{A}_2^\mathrm{z}]\epsilon^\lambda_{\mathrm{A}_2^\mathrm{z}} = c_2 A^\lambda_{\mathrm{A}^\mathrm{z}_{2\mathrm{pure}}} \tag{3.7}$$

If both compounds are in the basic form, then in the case of normalized concentrations $[\mathrm{A}_1^\mathrm{z}] = 1$ and $[\mathrm{A}_2^\mathrm{z}] = 1$ and equation 3.7 can be written:

$$\epsilon^\lambda_{\mathrm{A}_1^\mathrm{z}} = c_1 A^\lambda_{\mathrm{A}^\mathrm{z}_{1\mathrm{pure}}} \text{ and } \epsilon^\lambda_{\mathrm{A}_2^\mathrm{z}} = c_2 A^\lambda_{\mathrm{A}^\mathrm{z}_{2\mathrm{pure}}} \tag{3.8}$$

Coefficients c_1 and c_2 are constant over the wavelength range where values of ϵ^λ are not equal to zero. If equations 3.6 and 3.7 are combined then it is possible to calculate the coefficients c_1 and c_2 from the spectrum of every mixture of compounds in basic form and from the spectra of both pure compounds in basic form by using the least squares minimization over a wavelength range for S^2:

$$S^2 = \sum_{\lambda} (A^{\lambda} - c_1 A^{\lambda}_{\mathrm{A}^{\mathrm{z}}_{1\mathrm{pure}}} - c_2 A^{\lambda}_{\mathrm{A}^{\mathrm{z}}_{2\mathrm{pure}}})^2 \tag{3.9}$$

The same way as indicated above, if both compounds are in solution only in the acidic form, we can write:

$$A^{\lambda} = [\mathrm{HA}_1^{\mathrm{z}+1}]\epsilon^{\lambda}_{\mathrm{HA}_1^{\mathrm{z}+1}} + [\mathrm{HA}_2^{\mathrm{z}+1}]\epsilon^{\lambda}_{\mathrm{HA}_2^{\mathrm{z}+1}} \tag{3.10}$$

Taking into account also normalized concentrations, ϵ^{λ} values on the right side of equation 3.10 can be expressed:

$$\epsilon^{\lambda}_{\mathrm{HA}_1^{\mathrm{z}+1}} = c_1 A^{\lambda}_{\mathrm{HA}^{\mathrm{z}+1}_{1\mathrm{pure}}} \text{ and } \epsilon^{\lambda}_{\mathrm{HA}_2^{\mathrm{z}+1}} = c_2 A^{\lambda}_{\mathrm{HA}^{\mathrm{z}+1}_{2\mathrm{pure}}} \tag{3.11}$$

Analogously, the absorbance of the solution where the both compounds are simultaneously in acidic or basic form, can be derived by combining equations 3.5, 3.8 and 3.11 and by introducing dissociation level α_1 and α_2 of compounds $\mathrm{HA}_1^{\mathrm{z}+1}$ and $\mathrm{HA}_2^{\mathrm{z}+1}$, respectively:

$$\begin{aligned} A^{\lambda} = {} & c_1 A^{\lambda}_{\mathrm{HA}^{\mathrm{z}+1}_{1\mathrm{pure}}} + c_2 A^{\lambda}_{\mathrm{HA}^{\mathrm{z}+1}_{2\mathrm{pure}}} + \\ & + \alpha_1 c_1 (A^{\lambda}_{\mathrm{A}^{\mathrm{z}}_{1\mathrm{pure}}} - A^{\lambda}_{\mathrm{HA}^{\mathrm{z}+1}_{1\mathrm{pure}}}) + \alpha_2 c_2 (A^{\lambda}_{\mathrm{A}^{\mathrm{z}}_{2\mathrm{pure}}} - A^{\lambda}_{\mathrm{HA}^{\mathrm{z}+1}_{2\mathrm{pure}}}) \end{aligned} \tag{3.12}$$

This equation can be rewritten as a two-parameter (α_1 and α_2) linear regression model as follows:

$$\begin{aligned} & A^{\lambda} - c_1 A^{\lambda}_{\mathrm{HA}^{\mathrm{z}+1}_{1\mathrm{pure}}} - c_2 A^{\lambda}_{\mathrm{HA}^{\mathrm{z}+1}_{2\mathrm{pure}}} = \\ & = \alpha_1 c_1 (A^{\lambda}_{\mathrm{A}^{\mathrm{z}}_{1\mathrm{pure}}} - A^{\lambda}_{\mathrm{HA}^{\mathrm{z}+1}_{1\mathrm{pure}}}) + \alpha_2 c_2 (A^{\lambda}_{\mathrm{A}^{\mathrm{z}}_{2\mathrm{pure}}} - A^{\lambda}_{\mathrm{HA}^{\mathrm{z}+1}_{2\mathrm{pure}}}) \end{aligned} \tag{3.13}$$

By using the least squares minimization for S over the wavelength range described in equation 3.14, the respective α_1 and α_1 for the compounds in solutions with different acidities are found as regression coefficients:

$$\begin{aligned} S^2 = \sum_{\lambda} [& A^{\lambda} - c_1 A^{\lambda}_{\mathrm{HA}^{\mathrm{z}+1}_{1\mathrm{pure}}} - \\ & - c_2 A^{\lambda}_{\mathrm{HA}^{\mathrm{z}+1}_{2\mathrm{pure}}} - \alpha_1 c_1 (A^{\lambda}_{\mathrm{A}^{\mathrm{z}}_{1\mathrm{pure}}} - A^{\lambda}_{\mathrm{HA}^{\mathrm{z}+1}_{1\mathrm{pure}}}) - \\ & - \alpha_2 c_2 (A^{\lambda}_{\mathrm{A}^{\mathrm{z}}_{2\mathrm{pure}}} - A^{\lambda}_{\mathrm{HA}^{\mathrm{z}+1}_{2\mathrm{pure}}})]^2 \end{aligned} \tag{3.14}$$

Alternatively, intercept b_0 can be introduced and the following three-parameter regression can be used:

$$A^{\lambda} - c_1 A^{\lambda}_{\mathrm{HA}^{z+1}_{1\mathrm{pure}}} - c_2 A^{\lambda}_{\mathrm{HA}^{z+1}_{2\mathrm{pure}}} = \\ = \alpha_1 c_1 (A^{\lambda}_{\mathrm{A}^{z}_{1\mathrm{pure}}} - A^{\lambda}_{\mathrm{HA}^{z+1}_{1\mathrm{pure}}}) + \alpha_2 c_2 (A^{\lambda}_{\mathrm{A}^{z}_{2\mathrm{pure}}} - A^{\lambda}_{\mathrm{HA}^{z+1}_{2\mathrm{pure}}}) + b_0 \quad (3.15)$$

Normally the models 3.13 and 3.15 give very similar results. Model 3.15 permits to take into account slight baseline shifts that have occurred between the measurements of spectra of pure compounds and mixtures. Using the α_1 and α_2 values, the $\Delta\mathrm{p}K_\mathrm{a}$ values are calculated according to the equation 3.3.

From experiments it comes out that if the compounds have similar shape of absorbance spectra but the difference in absorbance maxima is at least 6 nm, then this calculation method is usually well applicable.

Method B – The general method using only the spectra of mixture.

A frequent situation is that for one compound (compound 1) a convenient wavelength range can be found where the difference between the absorbances of the acidic and basic form is large and the other compound (compound 2) has an isosbestic point within the same wavelength range. Usually in this case neither of the forms of the compound 1 have absorbance within a longer wavelength range, where compound 2 has large difference in absorbances of the acidic and basic forms. This situation was observed for example in the case of all guanidine bases measured in paper II and alkyl substituted phosphazene bases measured in papers III and I. Those compounds (compounds 1 according to the above classification) have suitable spectral properties in the wavelength range of 215–235 nm, but do not have any absorbance at longer wavelengths (starting from *ca* 250 nm). Most of aryl-substituted phosphazene bases (compounds 2) have an isosbestic point in the range of 220–230 nm in AN and THF solution (*e.g.* Figures 3.1 and 3.2). Therefore the wavelength of the isosbestic point of the aryl-phosphazene base (compound 2) can be used for measuring the protonation level of the guanidine and alkyl-phosphazene bases (compound 1) in the solutions.

The wavelength (denoted as λ_1) at which the compound 2 (denoted as HA_2^{z+1} and A_2^{z}) has the isosbestic point is selected as the first analytical wavelength. The absorbance of protonated and deprotonated forms of the compound 1 (denoted as HA_1^{z+1} and A_1^{z}) are different at that wavelength. Thus the absorbance of the solution in that wavelength λ_1 is:

$$A^{\lambda_1} = [\mathrm{HA}_1^{z+1}]\epsilon^{\lambda_1}_{\mathrm{HA}_1^{z+1}} + [\mathrm{A}_1^{z}]\epsilon^{\lambda_1}_{\mathrm{A}_1^{z}} + \epsilon^{\lambda_1}_{\mathrm{A}_2^{z}} \quad (3.16)$$

In the spectrum of the mixture where both compounds are in the basic form, $[\mathrm{HA}_1^{z+1}]$=0 and $[\mathrm{A}_1^{z}]$=1 (in the case of normalized concentrations). The absorbance of the solution at wavelength λ_1 is:

$$A^{\lambda_1}_{\mathrm{A}_1^{z}} = \epsilon^{\lambda_1}_{\mathrm{A}_1^{z}} + \epsilon^{\lambda_1}_{\mathrm{A}_2^{z}} \tag{3.17}$$

In the spectum of the mixture where both compounds are in the acidic form, $[\mathrm{HA}_1^{z+1}]$=1 and $[\mathrm{A}_1^{z}]$=0 and the absorbance of the solution at wavelength λ_1 is:

$$A^{\lambda_1}_{\mathrm{A}_1^{z}} = \epsilon^{\lambda_1}_{\mathrm{HA}_1^{z+1}} + \epsilon^{\lambda_1}_{\mathrm{A}_2^{z}} \tag{3.18}$$

In the case of normalized concentrations the dissociation level (α) of compound 1 is equal:

$$\alpha_1 = [\mathrm{A}_1^{z}] \tag{3.19}$$

From equations 3.16, 3.17 and 3.18 the $[\mathrm{A}_1^{z}]$ can be obtained as a funcion of absorbances:

$$\alpha_1 = \frac{A^{\lambda_1}_{\mathrm{A}_1^{z}} - A^{\lambda_1}}{A^{\lambda_1}_{\mathrm{A}_1^{z}} - A^{\lambda_1}_{\mathrm{HA}_1^{z+1}}} \tag{3.20}$$

The dissociation level of the compound 2 is found at longer wavelength λ_2 where compound 1 does not absorb. The absorbance at λ_2 is expressed as:

$$A^{\lambda_2} = [\mathrm{HA}_2^{z+1}]\epsilon^{\lambda_2}_{\mathrm{HA}_2^{z+1}} + [\mathrm{A}_2^{z}]\epsilon^{\lambda_2}_{\mathrm{A}_2^{z}} \tag{3.21}$$

The dissociation level for HA_2^{z+1} can be written:

$$\alpha_2 = \frac{[\mathrm{HA}_2^{z+1}]}{[\mathrm{HA}_2^{z+1}] + [\mathrm{A}_2^{z}]} = \frac{A^{\lambda_2}_{\mathrm{A}_2^{z}} - A^{\lambda_2}}{A^{\lambda_2}_{\mathrm{A}_2^{z}} - A^{\lambda_2}_{\mathrm{HA}_2^{z+1}}} \tag{3.22}$$

The calculation of $\Delta \mathrm{p}K_\mathrm{a}$ is according to the equation 3.3.

Method C – The method to take homoconjugation into account if the spectrum of the homoconjugate complex can be approximated as the sum of the spectra of the neural acid and its anion.

In the case of some acids (perfluorinated phenols and sulfonic acids), it was necessary to take homoconjugation into account (see IV). Let us denote the compound that forms a homoconjugate complex as compound 1 (HA_1^{z+1}) and the compound that does not form a homoconjugate complex as compound 2 (HA_2^{z+1}). In this case the analytical concentration C_1 of the compound HA_1^{z+1} can be expressed as follows:

$$C_1 = [\mathrm{A}_1^{\mathrm{z}}] + [\mathrm{HA}_1^{\mathrm{z}+1}] + [\mathrm{HA}_1 \cdots \mathrm{A}_1^{2\mathrm{z}+1}] \tag{3.23}$$

We assume that the molar absorption coefficient ϵ^{λ} of the homoconjugate complex $\mathrm{HA}_1 \cdots \mathrm{A}_1^{2\mathrm{z}+1}$ between protonated form of $\mathrm{HA}_1^{\mathrm{z}+1}$ and its deprotonated form $\mathrm{A}_1^{\mathrm{z}}$ can be expressed as a sum:

$$\epsilon(\mathrm{HA}_1 \cdots \mathrm{A}_1^{2\mathrm{z}+1}) = \epsilon(\mathrm{A}_1^{\mathrm{z}}) + \epsilon(\mathrm{HA}_1^{\mathrm{z}+1}) \tag{3.24}$$

Now using the least-squares of linear combination method (see method A) and models 3.13 or 3.15, we can calculate apparent dissociation level α_{app}, which is:

$$\alpha_{\mathrm{app}} = \frac{[\mathrm{A}_1^{\mathrm{z}}] + [\mathrm{HA}_1 \cdots \mathrm{A}_1^{2\mathrm{z}+1}]}{C_1} \tag{3.25}$$

α_{app} contains also analytical concentration of homoconjugate complex $[\mathrm{HA}_1 \cdots \mathrm{A}_1^{2\mathrm{z}+1}]$.

It is known, that K_{AHA} (the homoconjugation constant) is the constant of formation of the homoconjugate complex $\mathrm{HA}_1 \cdots \mathrm{A}_1^{2\mathrm{z}+1}$ and from equation 2.14 we can write:

$$K_{\mathrm{AHA}} = \frac{a(\mathrm{HA}_1 \cdots \mathrm{A}_1^{2\mathrm{z}+1})}{a(\mathrm{A}_1^{\mathrm{z}}) \cdot a(\mathrm{HA}_1^{\mathrm{z}+1})} \tag{3.26}$$

We assume that the activities in equation 3.26 can be replaced with concentrations and for now on we use only concentrations instead of activities:

$$K_{\mathrm{AHA}} = \frac{[\mathrm{HA}_1 \cdots \mathrm{A}_1^{2\mathrm{z}+1}]}{[\mathrm{A}_1^{\mathrm{z}}] \cdot [\mathrm{HA}_1^{\mathrm{z}+1}]} \tag{3.27}$$

Combining the equations 3.23, 3.25, 3.27 and 3.26, then the relative concentration of the complex $\mathrm{HA}_1 \cdots \mathrm{A}_1^{2\mathrm{z}+1}$ can be found:

$$\frac{[\mathrm{HA}_1 \cdots \mathrm{A}_1^{2\mathrm{z}+1}]}{C_1} = \frac{1 + \frac{1}{C_1 \cdot K_{\mathrm{AHA}}}}{2} - \sqrt{\left(\frac{1 + \frac{1}{C_1 \cdot K_{\mathrm{AHA}}}}{2}\right)^2 - \alpha_{\mathrm{app}} \cdot (1 - \alpha_{\mathrm{app}})} \tag{3.28}$$

Now $[\mathrm{A}_1^{\mathrm{z}}]/[\mathrm{HA}_1^{\mathrm{z}+1}]$ can be calculated:

$$\frac{[\mathrm{A}_1^{\mathrm{z}}]}{[\mathrm{HA}_1^{\mathrm{z}+1}]} = \frac{\alpha_{\mathrm{app}} - \frac{[\mathrm{HA}_1 \cdots \mathrm{A}_1^{2\mathrm{z}+1}]}{C_1}}{1 - \alpha_{\mathrm{app}} - \frac{[\mathrm{HA}_1 \cdots \mathrm{A}_1^{2\mathrm{z}+1}]}{C_1}} \tag{3.29}$$

With known $[\mathrm{A}_1^{\mathrm{z}}]/[\mathrm{HA}_1^{\mathrm{z}+1}]$ the calculation of $\Delta\mathrm{p}K_{\mathrm{a}}$ is as follows:

$$\Delta\mathrm{p}K_{\mathrm{a}} = \log\frac{[\mathrm{A}_1^{\mathrm{z}}](1-\alpha_2)}{[\mathrm{HA}_1^{\mathrm{z}+1}]\alpha_2} \tag{3.30}$$

Method D – The method to take homoconjugation into account if the spectrum of the homoconjugate complex cannot be approximated as sum of the spectra of the neural acid and its anion.

If a neutral acid forms homoconjugate complex with its anion extensively and if the protonation site is directly bound to an aromatic ring (*e.g.* phenols) then the spectrum of the homoconjugate complex is different from that of the sum of spectra of the anion and the neutral. This leads to abnormalities in UV-vis spectra during the titration of the pure compound. In particular the spectra do not have isosbestic points anymore evidencing that there is a more complex equilibrium in the solution than just between two forms of a compound. In this case, it is possible to calculate from the titration data of the pure compound the spectrum of the homoconjugate complex using the concentration of the compound, amount of moles of basic titrant added and the homoconjugation constant K_{AHA}.

The compound that forms a homoconjugate complex is $\mathrm{HA}_1^{\mathrm{z}+1}$ and the compound that does not form a homoconjugate complex is $\mathrm{HA}_2^{\mathrm{z}+1}$. We assume that the two compounds do not form a heteroconjugate complex (this assumption holds if $\mathrm{HA}_2^{\mathrm{z}+1}$ is a CH or NH acid with hindered acidity center and giving a charge-delocalized anion on deprotonation).

At a given point of the titration the concentrations of the protonated form $\mathrm{HA}_1^{\mathrm{z}+1}$ and deprotonated form $\mathrm{A}_1^{\mathrm{z}}$ in solution, which we can calculate directly from the mass of added titrant to the solution are apparent concentrations, because a part of the species are bound into the homoconjugate complex:

$$[\mathrm{HA}_1^{\mathrm{z}+1}]_{\mathrm{app}} = [\mathrm{HA}_1^{\mathrm{z}+1}] + [\mathrm{HA}_1\cdots\mathrm{A}_1^{2\mathrm{z}+1}] \tag{3.31}$$

and

$$[\mathrm{A}_1^{\mathrm{z}}]_{\mathrm{app}} = [\mathrm{A}_1^{\mathrm{z}}] + [\mathrm{HA}_1\cdots\mathrm{A}_1^{2\mathrm{z}+1}] \tag{3.32}$$

The same apparent concentrations can be found *via* the analytical concentration C_1 of $\mathrm{HA}_2^{\mathrm{z}+1}$ and its apparent dissociation level $\alpha_{1\mathrm{app}}$:

$$[\mathrm{HA}_1^{\mathrm{z}+1}]_{\mathrm{app}} = (1-\alpha_{1\mathrm{app}})\cdot C_1 \text{ and } [\mathrm{A}_1^{\mathrm{z}}]_{\mathrm{app}} = \alpha_{1\mathrm{app}}\cdot C_1 \tag{3.33}$$

The apparent dissociation level $\alpha_{1\mathrm{app}}$ is the ratio of mass of titrant added up to the current point and the total mass of titrant added to the solution by the end of the titration. The apparent dissociation level is the dissociation level which does not distinguish between free deprotonated form and protonated form of the compound and those bound into the homoconjugate complexes.

Using equations 3.27 and 3.31 we get the quadratic equation:

$$\begin{aligned}&[\mathrm{HA_1 \cdots A_1^{2z+1}}]^2 - \\ &\quad - ([\mathrm{A_1^z}]_{\mathrm{app}} + [\mathrm{HA_1^{z+1}}]_{\mathrm{app}} + \frac{1}{K_{\mathrm{AHA}}}) \cdot [\mathrm{HA_1 \cdots A_1^{2z+1}}] + \\ &\qquad + [\mathrm{A_1^z}]_{\mathrm{app}} \cdot [\mathrm{HA_1^{z+1}}]_{\mathrm{app}} = 0 \end{aligned} \tag{3.34}$$

The concentration of the complex $\mathrm{HA_1 \cdots A_1^{2z+1}}$ can be found:

$$\begin{aligned}[\mathrm{HA_1 \cdots A_1^{2z+1}}] &= \frac{\frac{1}{K_{\mathrm{AHA}}} + [\mathrm{HA_1^{z+1}}]_{\mathrm{app}} + [\mathrm{A_1^z}]_{\mathrm{app}}}{2} + \\ &+ \frac{\sqrt{([\mathrm{A_1^z}]_{\mathrm{app}} + [\mathrm{HA_1^{z+1}}]_{\mathrm{app}} + \frac{1}{K_{\mathrm{AHA}}})^2 - 4 \cdot [\mathrm{A_1^z}]_{\mathrm{app}} \cdot [\mathrm{HA_1^{z+1}}]_{\mathrm{app}}}}{2}\end{aligned} \tag{3.35}$$

After we know $[\mathrm{HA_1 \cdots A_1^{2z+1}}]$, from equations 3.31 it is possible to calculate the real concentrations of $[\mathrm{HA_1^{z+1}}]$ and $[\mathrm{A_1^z}]$. Using the analytical concentration C_1 of acid $\mathrm{HA_1^{z+1}}$ it is possible to get the relative concentrations of the species $\mathrm{HA_1^{z+1}}$, $\mathrm{A_1^z}$ and $\mathrm{HA_1 \cdots A_1^{2z+1}}$ in the solutions with different dissociation levels (corresponding to different points of the titration). The relative concentrations $[\mathrm{HA_1^{z+1}}]_{\mathrm{rel}}$, $[\mathrm{A_1^z}]_{\mathrm{rel}}$ and $[\mathrm{HA_1 \cdots A_1^{2z+1}}]_{\mathrm{rel}}$ show how large is the proportion of the corresponding species in the solution. From these relative concentrations and the spectral data it is now possible to calculate the spectrum of the homoconjugate complex. The spectrum of the same species (ie the homoconjugate complex) has to be the same in solutions of different dissociation levels. The expression for total absorbance of the solution at any dissociation level using relative concentration of particles at wavelength λ is:

$$\begin{aligned}A^{\lambda}_{1\mathrm{pure}} &= [\mathrm{A_1^z}]_{\mathrm{rel}} A^{\lambda}_{\mathrm{A^z_{1pure}}} + [\mathrm{HA_1^{z+1}}]_{\mathrm{rel}} A^{\lambda}_{\mathrm{HA^{z+1}_{1pure}}} + \\ &\quad + [\mathrm{HA_1 \cdots A_1^{2z+1}}]_{\mathrm{rel}} A^{\lambda}_{\mathrm{HA_1 \cdots A_1^{2z+1}}}\end{aligned} \tag{3.36}$$

The A_1^{λ} values are the absorbances of the respective individual species at concentration C_1 and wavelength λ. From the equation 3.36 we get the absorbance $A^{\lambda}_{\mathrm{HA_1\cdots A_1^{2z+1}}}$ of the hypothetical solution containing only the homoconjugate complex $\mathrm{HA_1\cdots A_1^{2z+1}}$ at concentration C_1:

$$A^{\lambda}_{\mathrm{HA_1\cdots A_1^{2z+1}}} = \frac{A^{\lambda}_{\mathrm{1pure}} - [\mathrm{A_1^z}]_{\mathrm{rel}} A^{\lambda}_{\mathrm{A^z_{1pure}}} - [\mathrm{HA_1^{z+1}}]_{\mathrm{rel}} A^{\lambda}_{\mathrm{HA^{z+1}_{1pure}}}}{[\mathrm{HA_1\cdots A_1^{2z+1}}]_{\mathrm{rel}}} \tag{3.37}$$

The spectra of the homoconjugate complexes were calculated from different titration points in the middle of the titration run (where the concentration of the homoconjugate complex is the highest) and were averaged. The averaged spectrum was used for calculation of the $\Delta \mathrm{p}K_a$ value as described below.

To calculate the $\Delta \mathrm{p}K_a$ value from a titration point of the mixture was first necessary to find the coefficients c_1 and c_2, which show the ratios of concentrations in the titrated mixture of two acids $\mathrm{HA_1^{z+1}}$ and $\mathrm{HA_2^{z+1}}$ and in the separate titrations of the pure acids. The calculation of these two coefficients are described at method A. The absorbance of the solution containing mixture of the two acids at wavelength λ can be calculated as follows:

$$A^{\lambda} = A^{\lambda}_1 + A^{\lambda}_2 \tag{3.38}$$

Where A^{λ}_1 and A^{λ}_2 are the absorbences of $\mathrm{HA_1^{z+1}}$ and $\mathrm{HA_2^{z+1}}$ in mixture. A^{λ}_1 can be expressed as the sum of absorbences of the pure forms multiplied by their relative concentrations in the mixture:

$$\begin{aligned} A^{\lambda}_1 = c_1([\mathrm{A_1^z}]_{\mathrm{rel,mix}} A^{\lambda}_{\mathrm{A^z_{1pure}}} + [\mathrm{HA_1^{z+1}}]_{\mathrm{rel,mix}} A^{\lambda}_{\mathrm{HA^{z+1}_{1pure}}} + \\ + [\mathrm{HA_1\cdots A_1^{2z+1}}]_{\mathrm{rel,mix}} A^{\lambda}_{\mathrm{HA_1\cdots A_1^{2z+1}}}) \end{aligned} \tag{3.39}$$

The absorbance of acompound 2 at a certain dissociation level can be also written using absorbances of the pure forms of compound 2:

$$A^{\lambda}_2 = c_2[\alpha_2 A^{\lambda}_{\mathrm{A^z_{2pure}}} + (1-\alpha_2) A_{\mathrm{HA^{z+1}_{2pure}}}] \tag{3.40}$$

Dissociation level of compound 2 is found at a longer wavelength where the compound 1 does not absorb:

$$A^{\lambda}_2 = \frac{A^{\lambda}_{\mathrm{x}}}{A^{\lambda}_{\mathrm{A^z_2}}} \tag{3.41}$$

The apparent concentrations of $\mathrm{HA_1^{z+1}}$ and $\mathrm{A_1^z}$ in the mixture are found from the apparent dissociation level of $\mathrm{HA_1^{z+1}}$ in the mixture $\alpha_{\mathrm{1app,mix}}$ as follows:

$$[\mathrm{HA}_1^{\mathrm{z}+1}]_{\mathrm{app,mix}} = (1-\alpha_{1\mathrm{app,mix}})\cdot c_1 \cdot C_1 \tag{3.42}$$

and

$$[\mathrm{A}_1^{\mathrm{z}}]_{\mathrm{app,mix}} = \alpha_{1\mathrm{app,mix}}\cdot c_1 \cdot C_1 \tag{3.43}$$

The concentration of the homoconjugate complex $[\mathrm{HA}_1\cdots\mathrm{A}_1^{2\mathrm{z}+1}]_{\mathrm{mix}}$ is found as follows:

$$\begin{aligned}[\mathrm{HA}_1\cdots\mathrm{A}_1^{2\mathrm{z}+1}]_{\mathrm{mix}} = {} & \frac{\frac{1}{K_{\mathrm{AHA}}} + [\mathrm{HA}_1^{\mathrm{z}+1}]_{\mathrm{app,mix}} + [\mathrm{A}_1^{\mathrm{z}}]_{\mathrm{app,mix}}}{2} + \\ & + \frac{\sqrt{([\mathrm{A}_1^{\mathrm{z}}]_{\mathrm{app,mix}} + [\mathrm{HA}_1^{\mathrm{z}+1}]_{\mathrm{app,mix}} + \frac{1}{K_{\mathrm{AHA}}})^2 - 4\cdot[\mathrm{A}_1^{\mathrm{z}}]_{\mathrm{app,mix}}\cdot[\mathrm{HA}_1^{\mathrm{z}+1}]_{\mathrm{app,mix}}}}{2}\end{aligned} \tag{3.44}$$

The real equilibrium concentrations of $\mathrm{HA}_1^{\mathrm{z}+1}$ and $\mathrm{A}_1^{\mathrm{z}}$ in the mixture are found as follows:

$$[\mathrm{HA}_1^{\mathrm{z}+1}]_{\mathrm{mix}} = [\mathrm{HA}_1^{\mathrm{z}+1}]_{\mathrm{app,mix}} - [\mathrm{HA}_1\cdots\mathrm{A}_1^{2\mathrm{z}+1}]_{\mathrm{mix}} \tag{3.45}$$

and

$$[\mathrm{A}_1^{\mathrm{z}}]_{\mathrm{mix}} = [\mathrm{A}_1^{\mathrm{z}}]_{\mathrm{app,mix}} - [\mathrm{HA}_1\cdots\mathrm{A}_1^{2\mathrm{z}+1}]_{\mathrm{mix}} \tag{3.46}$$

The relative concentrations $[\mathrm{HA}_1^{\mathrm{z}+1}]_{\mathrm{rel,mix}}$, $[\mathrm{A}_1^{\mathrm{z}}]_{\mathrm{rel,mix}}$ and $[\mathrm{HA}_1\cdots\mathrm{A}_1^{2\mathrm{z}+1}]_{\mathrm{rel,mix}}$ can be found from the respective absolute concentrations:

$$[\mathrm{HA}_1^{\mathrm{z}+1}]_{\mathrm{rel,mix}} = \frac{[\mathrm{HA}_1^{\mathrm{z}+1}]_{\mathrm{mix}}}{C_1} \tag{3.47}$$

and

$$[\mathrm{A}_1^{\mathrm{z}}]_{\mathrm{rel,mix}} = \frac{[\mathrm{A}^{\mathrm{z}}{}_1]_{\mathrm{mix}}}{C_1} \tag{3.48}$$

After combining equations 3.38, 3.39 and 3.40 we get:

$$\begin{aligned}A^{\lambda} = {} & c_1([\mathrm{A}_1^{\mathrm{z}}]_{\mathrm{rel,mix}} A^{\lambda}_{\mathrm{A}^{\mathrm{z}}_{1\mathrm{pure}}} + \\ & + [\mathrm{HA}_1^{\mathrm{z}+1}]_{\mathrm{rel,mix}} A^{\lambda}_{\mathrm{HA}^{\mathrm{z}+1}_{1\mathrm{pure}}} + [\mathrm{HA}_1\cdots\mathrm{A}_1^{2\mathrm{z}+1}]_{\mathrm{rel,mix}} A^{\lambda}_{\mathrm{HA}_1\cdots\mathrm{A}_1^{2\mathrm{z}+1}}) + \\ & + c_2[\alpha_2 A^{\lambda}_{\mathrm{A}^{\mathrm{z}}_{2\mathrm{pure}}} + (1-\alpha_2) A^{\lambda}_{\mathrm{HA}^{\mathrm{z}+1}_{2\mathrm{pure}}}]\end{aligned} \tag{3.49}$$

Equation 3.49 models the spectrum of the mixture of compounds $\mathrm{HA}_1^{\mathrm{z}+1}$ and $\mathrm{HA}_2^{\mathrm{z}+1}$ *via* the spectra of the pure forms of the acids and the concentrations of the species in the mixture. Least squares minimization procedure between two different spectra - experimental and modeled spectra (see equations 3.50 and 3.51) can be used.

$$S^2 = \sum_{\lambda} (A^{\lambda}_{\mathrm{exp}} - A^{\lambda})^2 \tag{3.50}$$

This equation can be rewritten as:

$$\begin{aligned} S^2 = \sum_{\lambda} [A^{\lambda}_{\mathrm{exp}} - c_1([\mathrm{A}_1^-]_{\mathrm{rel,mix}} A^{\lambda}_{\mathrm{A}^{\mathrm{z}}_{1\mathrm{pure}}} + \\ + [\mathrm{HA}_1^{\mathrm{z}+1}]_{\mathrm{rel,mix}} A^{\lambda}_{\mathrm{HA}^{\mathrm{z}+1}_{1\mathrm{pure}}} + [\mathrm{HA}_1 \cdots \mathrm{A}_1^{2\mathrm{z}+1}]_{\mathrm{rel,mix}} A^{\lambda}_{\mathrm{HA}_1 \cdots \mathrm{A}_1^{2\mathrm{z}+1}}) + \\ + c_2(\alpha_2 A^{\lambda}_{\mathrm{A}^{\mathrm{z}}_{2\mathrm{pure}}} + (1 - \alpha_2) A^{\lambda}_{\mathrm{HA}^{\mathrm{z}+1}_{2\mathrm{pure}}})]^2 \end{aligned} \tag{3.51}$$

The dissociation level α_2 of $\mathrm{HA}_2^{\mathrm{z}+1}$ and the apparent dissociation level $\alpha_{1\mathrm{app}}$ of $\mathrm{HA}_1^{\mathrm{z}+1}$ corresponding to the minimum difference between the experimental spectra and those calculated by equation 3.49 are found by least squares minimization of S^2 over the used wavelength range using the two α values as adjustable parameters. The concentrations $[\mathrm{HA}_1^{\mathrm{z}+1}]_{\mathrm{rel,mix}}$, $[\mathrm{A}_1^{\mathrm{z}}]_{\mathrm{rel,mix}}$ and $[\mathrm{HA}_1 \cdots \mathrm{A}_1^{2\mathrm{z}+1}]_{\mathrm{rel,mix}}$ are linked to $\alpha_{1\mathrm{app}}$ by equations 3.42 to 3.47. The real protonation level α_1 is found as follows:

$$\alpha_1 = \frac{[\mathrm{A}_1^{\mathrm{z}}]_{\mathrm{mix}}}{[\mathrm{A}_1^{\mathrm{z}}]_{\mathrm{mix}} + [\mathrm{HA}_1^{\mathrm{z}+1}]_{\mathrm{mix}}} \tag{3.52}$$

In the case of phenols, the minimization procedures were usually carried out in the wavelength range 250–290 nm. In this range the difference of the spectra of the corresponding phenol and phenolate anion is the largest. Using the α_1 and α_2 values, the $\Delta \mathrm{p}K_{\mathrm{a}}$ value at the given titration point can be calculated according to equation 3.3.

Method E – Calculation method using concentrations.

In some cases ("invisible compound" (for example, aliphatic amines, alkyl-phospazenes, alkyl-alkohols, *etc.*) *vs.* "visible" aromatic compounds) the calculations have been carried out on a molar basis. The solution containing a mixture of known amounts (in moles) of "invisible" and "visible" compounds was titrated with titrant of known concentration. From the added titrant mass and its concentration, the amount (in moles) of titrant in the cell was found. The dissociation level of the "visible" compound was calculated from the spectra of the mixture, using fully protonated and fully deprotonated spectra of that compound. The calculation is the same as described at the method B. Knowing the amounts of the "visible" compound, its dissociation level and titrant added, the dissociation level for "invisible" compound was calculated. The ΔpK_a calculation is then straightforward according to equation 3.3. This method is based on the original method from Kolthoff *et al.*[49] It is not as accurate as other mothods but usually a good agreement between other methods (if it is possible to use) have been found. It is possible to use the same method if "invisible" compound forms homoconjugate complex.

3.2. Absolute pK_a Values, their Consistency and Uncertainty

The pK_a values for individual acids were found by minimizing the sum of squares of differences between directly measured ΔpK_a values and the assigned pK_a values (including pK_a value of the anchor compound of the scale):

$$u = \sum_{i=1}^{n_m} [\Delta pK_a^i - (pK_a(HA_2^{z+1})) - (pK_a(HA_1^{z+1}))]^2 \tag{3.53}$$

The sum is taken over the measurements between all compounds included in the scale whereby $pK_a{}^i$ is the result of a relative acidity measurement of acids HA_1^{z+1} and HA_2^{z+1} (HA_2^{z+1} is the acid with higher pK_a value). $pK_a(HA_1^{z+1})$ and $pK_a(HA_2^{z+1})$ are the absolute pK_a values for the two acids as found by the least squares procedure (with different i values different acids are involved). The precision and the consistency of the results can be assessed using a standard deviation as defined by equation 3.54:

$$s = \sqrt{\frac{u}{n_m - n_c}} \tag{3.54}$$

where n_m is the total number of measurements, n_c is the number of pK_a values determined. The consistency parameter s has been given for every measured acidity and basicity scale in this work.

Uncertainty estimation for measured pK_a values have been carried out for neutral bases in AN solution.[50] The uncertainties of the pK_a values are defined in different ways. One approach is based on the ISO GUM[51] methodology and involves careful analysis of the uncertainty sources and quantifying the respective uncertainty components. The second approach is based on the standard deviation that has been used for characterization of the consistency of the scale (equation 3.54). Also, the uncertainty of pK_a value of the anchor compound has been either taken into account or not. It comes out that uncertainty of the pK_a values is the larger the farther away the compound is removed from the anchor compound on the scale. The uncertainty of the pK_a of the first and last compound on the scale is around two times larger than the uncertainty of the pK_a value of that to adjacent to the anchor compound. In the case of neutral bases in AN, the uncertainty ranges are 0.12–0.22 and 0.12–0.14 pK_a units at standard uncertainty level for different bases using the ISO GUM and statistical approach, respectively, if the uncertainty of pK_a value of pyridine is taken into account. If the uncertainty of pK_a value of pyridine is not taken into account, the ranges of uncertainty values are 0.04–0.19 and 0.02–0.08 pK_a units, respectively. In the case of neutral acids in AN, the uncertainty values may be higher – the homoconjugation should be taken into account and water and other impurities may influence measured ΔpK_a values of acids more than those of bases. In other solvents (DCE, THF) the uncertainty values are most probably still higher. In the solvents with lower polarity the influence of water and impurities to ΔpK_a values is higher and probability to form associate and conjugate complexes is very high.

3.3. Chemicals and Solvents

The origin and synthesis of the used compounds have been described in publications I–V. In the case of commercially available chemicals the purity was the most important criterion in choosing the vendor. The solvent suitable for our work must be very dry and the concentration of any acidic and basic impurities and those that absorb UV radiation must be very low. The commercial AN, THF and DCE were used (Romil, Super Purity Solvent, assay 99.9%, water content <0.005%). AN was used as recieved. The water content determined by coulometric Karl Fisher titration was below 0.004%. DCE was additionally dried before use with molecular sieves (3Å, 8–12 mesh) for at least 2 days. The water content determined was up to 0.0005%. THF was distilled from $LiAlH_4$ under argon before every measurement. The best way to assess the solvent purity (apart from water content) with our method is to examine the sharpness of the low-wavelength isosbestic points in the spectra of compounds during the titrations.

3.4. Experimental Setup

All procedures involved preparation of solutions and acid-base titrations were carried out in a commercial glovebox under an atmosphere of argon.

The atmosphere in the glovebox was constantly circulated through a purification system containing activated carbon, molecular sieves and activated copper for removing residues of volatile organics, water vapor and oxygen, respectevly. The residual concentrations of water and oxygen in the atmosphere of the glovebox were constantly monitured and they were usually under 1 ppm.

For spectrophotometric titration, a commercial UV-vis spectrophotometer equipped with an external sample compartment positioned in the glovebox was used. The external sample compartment was connected to the spectrophotometer *via* quartz fiber-optic cables. The temperature in the external sample compartment was monitored and it was between 23–27°C.

Working solutions were preapared gravimetrically by dilution of the stock solution using mainly syringe technique. Vials and pipettes used in this work were washed with ethanol before heating in an oven at 150°C for at least 6 hours and were then immediately transferred to the glovebox. Usually all solutions were used within 3 days. The solution of $\mathrm{EtP_2(dma)}$ in AN cannot be used for longer than one day.

3.5. Theoretical Gas-Phase Acidity and Basicity Calculations

ΔG_{acid} of an acid HA is the Gibbs free energy change on deprotonation of the acid according to the following equilibrium:

$$\mathrm{HA} \overset{\Delta G_{\mathrm{acid}}}{\leftrightarrows} \mathrm{A}^- + \mathrm{H}^+ \tag{3.55}$$

Gas-phase basicity ΔG_{base} and proton affinity ($PA = \Delta H_{\mathrm{base}}$) of a base B refer to the following equilibrium:

$$\mathrm{B} + \mathrm{H}^+ \overset{\substack{\Delta G_{\mathrm{base}} \\ \Delta H_{\mathrm{base}}}}{\leftrightarrows} \mathrm{HB}^+ \tag{3.56}$$

The ΔG_{acid} and ΔG_{base} values were calculated taking zero-point energies, finite temperature (298 K) correction and the pressure-volume work term into account. Density functional theory (DFT) calculations at B3LYP 6-311+G** level were used. The Gaussian 03 system of programs was used.[52] Full geometry optimizations were carried out for all neutrals, anions and cations. Several different starting geometries were used in doubtful cases. In order to confirm that calculated structures correspond to true minima, frequency calculations were run in all cases and the absence of imaginary frequencies ($N_{\mathrm{imag}} = 0$) was taken as the criterion of the stability of the species.

4. BASES

According to the Brønsted-Lowry definition, bases are compounds which are able to bind proton. The stronger the base, the more stable is the conjugate acid of that base. Neutral bases have great practical use in synthesis but ionic bases are widely used. Anionic superbases are for example alkyl lithium compounds, lithium dialkylamides, potassiom alkoxides, hydrides and mixtures of those compounds. Inorganic superbases – alkali metal hydroxides and oxides and nitrides are also widely used. But it is not always possible to use ionic bases. The insufficient solubility in many solvents, instability of many of them and harshness are the main problems using ionic bases. Nonionic superbases have the advantage that, unlike strong ionic bases, unwanted side reactions are minimized or eliminated completely. Well-known nonionic superbases are DBU, TMG, Proton Sponges, *etc.* but these bases are too weak compared to the alkyl and aryl metal, metal amide and other ionic superbases (ΔG_{base} of DBU is 243 kcal/mol, but for t-Bu$^-$ 406 kcal/mol). Therefore, organic neutral superbases which would be easy to handle and at the same time would have base strength approaching that of the ionic superbases would be very useful for many chemists.

During the recent years, Verkade and his group have developed a series of derivatives of bicyclic phosphines, proazaphosphatranes.[53] These bases are stronger than any known amines, DBU, TMG, *etc.* but not as strong as Schwesinger's phosphazene base t-BuP$_4$[54–56] whose pK_{a} value in AN is predicted to be 43 units. Basicities of phosphazene bases (or phosphorus imines or iminophosphoranes, see Figure 4.2 for the main structures of phosphazene bases) and their analogues, phosphorus ylides can be tuned by varying the number of phosphorus atoms and substituents (see sections 4.1. and 4.3. and I and III). Using this approach a large and diverse family of extremely strong noncharged organic bases – P$_1$–P$_5$ phosphazene bases[26] have been developed. In the present work a new family of neutral organic superbases – guanidinophosphazenes have been introduced (see section 4.3. and III). These hydrolytically stable bases starts to become rather useful organic reagents. Besides the enhanced basicity, they combine high solubility in apolar to moderately polar organic solvents, easy handling and easier workup through cleaner reactions, low sensitivity to moisture and oxygen, and the possibility to operate at lower temperature and higher selectivity.

N,*N*,*N'*,*N'*-tetramethyl guanidino (tmg) group has been useful building block for designing a plenty of new superbases (see also sections 4.2. and 4.3. and III and II). Proton Sponges, polyguanides and other compounds containing tmg groups have been published.[57–59]

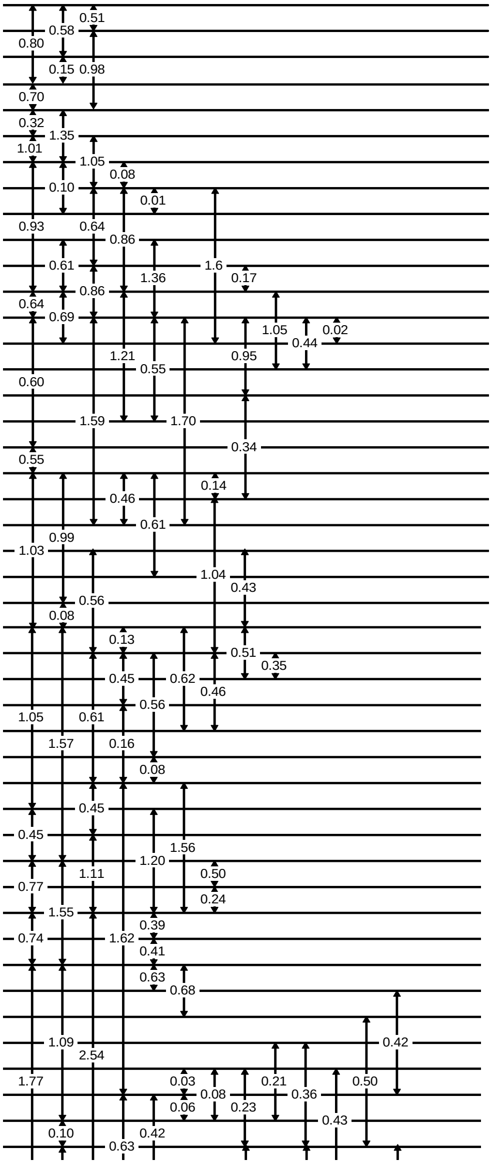
Designing such nonionic superbases whose protonated forms would have well delocalized positive charge and neutral forms would be stable, is essential of high interest for many chemists. To allow optimal use of the bases, the pK_a values of many conventional bases and superbases have been measured in AN and in THF. The measurements of strength of bases, including superbases, are necessary for their optimal use, for design of new bases and for advancing the general understanding of acid-base chemistry.

4.1. Comprehensive Basiciy Scale in Acetonitrile

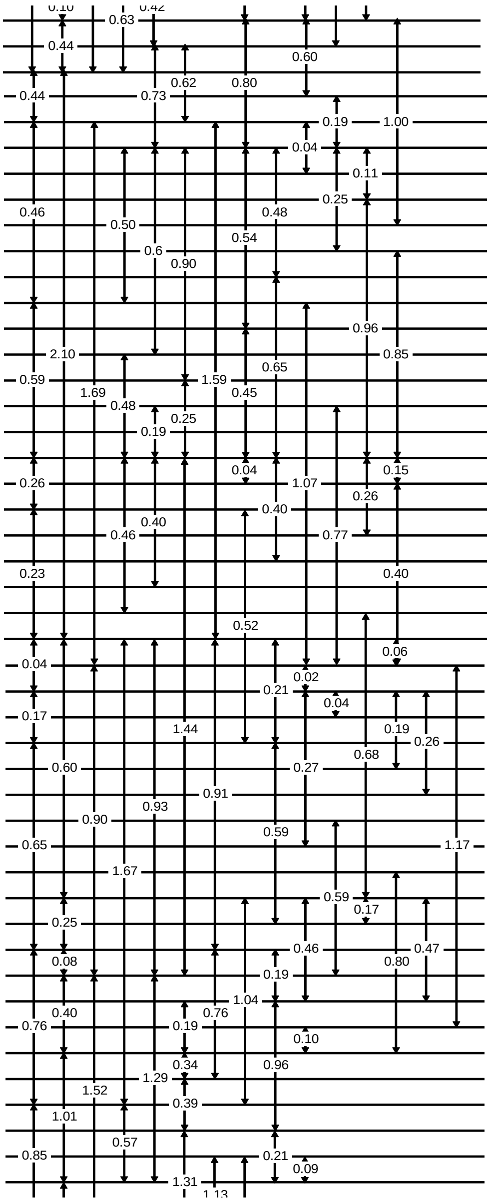
The primary goal of this part of the work (see I) was to expand significantly the existing self-consistent scale toward superbasic direction and also toward weaker basicity area for several pK_a units. Second, due to the abundant new data, we are now in the position to critically review the absolute basicity values assigned to the bases in earlier works using pyridine as the reference base.[60–62] We will now compare our data with the data of 13 different research groups. On the basis of this comparison, we can shift the reference point of our scale (which is a relative scale) and reassign new absolute values to the compounds in such a way that the agreement between our data and the data of the other authors is the best possible.

The earlier compiled self-consistent spectrophotometric basicity scale in AN[60] was expanded to range from 3.8 to 32.0 pK_a units, that is 28 orders of magnitude. Altogether 302 relative basicity measurements (ΔpK_a measurements) were carried out and 136 compounds are currently present on the scale. The scale contains now bases from very different families of compounds – phosphazenes, bispidines,[63] alkylamines and alkyldiamines,[64] substituted guanidines (see section 4.2. and paper II), porphyrines,[61] pyridines, anilines, *etc.* The relative basicity of any two bases in the scale can be obtained by combining at least two independent sets of measurements. Multiple overlapping measurements make the results more reliable. The overall consistency (as defined earlier) of the measurements is $s = 0.04$ pK_a units.

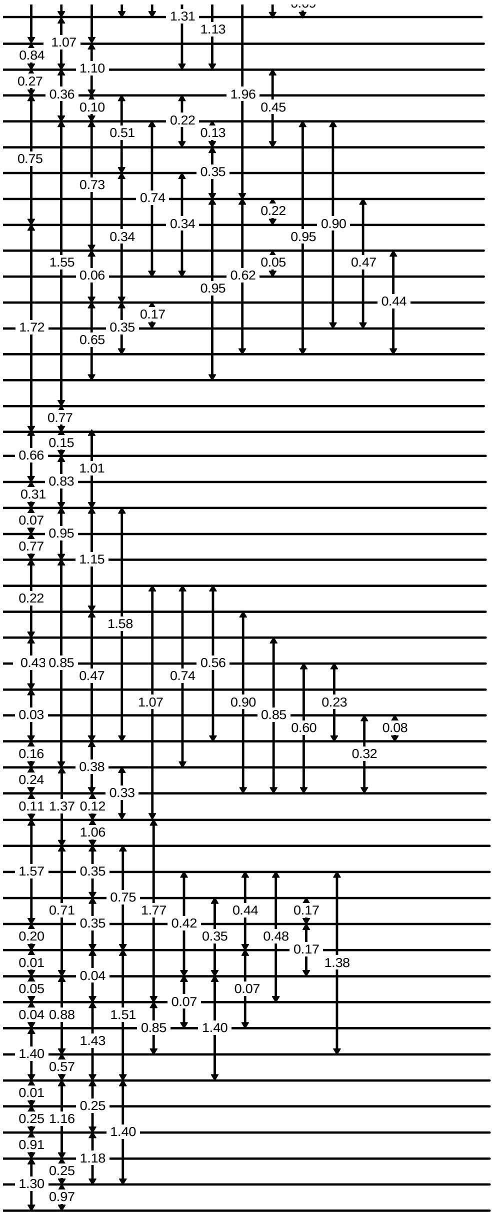
Table 4.1: Continuous Self-Consistent Basicity Scale of Neutral Bases in AN

	Base	pK_a(AN)	Directly measured ΔpK_a values
BA1	4-MeO-$C_6H_4P_3$(dma)	**31.99**	
BA2	PhP_3(dma)	**31.48**	
BA3	PhP_1(tmg)	**31.38**	
BA4	2-Cl-$C_6H_4P_3(pyrr)_6NEt_2$	**31.19**	
BA5	4-CF_3-$C_6H_4P_3$(pyrr)	**30.50**	
BA6	2-Cl-$C_6H_4P_3(dma)_6NEt_2$	**30.16**	
BA7	2,5-Cl_2-$C_6H_3P_3(pyrr)_6NEt_2$	**29.16**	
BA8	4-CF_3-$C_6H_4P_3$(dma)	**29.10**	
BA9	$PhP_1(tmg)_2$dma	**29.07**	
BA10	EtP_1(pyrr)	**28.88**	
BA11	*t*-BuP_1(pyrr)	**28.42**	
BA12	4-MeO-$C_6H_4P_2$(pyrr)	**28.23**	
BA13	PhP_2(pyrr)	**27.55**	
BA14	MeP_1(dma)	**27.52**	
BA15	*N*,*N′*,*N″*-$[(CH_2)_3NMe_2]_3$-guanidine	**27.15**	
BA16	HP_1(pyrr)	**27.01**	
BA17	*t*-BuP_1(dma)	**26.98**	
BA18	*N*,*N′*-$[(CH_2)_3NMe_2]_2$,*N″*-propylguanidine	**26.63**	
BA19	PhP_2(dma)	**26.46**	
BA20	4-Br-$C_6H_4P_2$(pyrr)	**26.32**	
BA21	TBD	**26.03**	
BA22	HP_1(dma)	**25.85**	
BA23	*N*-$[(CH_2)_3NMe_2]$,*N′*,*N″*-dipropylguanidine	**25.85**	
BA24	MTBD	**25.49**	
BA25	2-Cl-$C_6H_4P_2$(pyrr)	**25.42**	
BA26	4-CF_3-$C_6H_4P_2$(pyrr)	**25.29**	
BA27	*N*,*N′*,*N″*-tripropylguanidine	**24.92**	
BA28	*N*,*N′*-$[(CH_2)_3OMe]_2$,*N″*-propylguanidine	**24.84**	
BA29	*N*-$[(CH_2)_3OMe]$,*N′*,*N″*-dipropylguanidine	**24.81**	
BA30	*N*,*N′*,*N″*-$[(CH_2)_3OMe]_3$-guanidine	**24.74**	
BA31	$PhP_1(dma)_2$tmg	**24.68**	
BA32	DBU	**24.34**	
BA33	2-Cl-$C_6H_4P_2$(dma)	**24.23**	
BA34	4-NMe_2-$C_6H_4P_1$(pyrr)	**23.88**	
BA35	TMG	**23.37**	
BA36	4-MeO-$C_6H_4P_1$(pyrr)	**23.12**	
BA37	*N*,*N′*-Me_2-Bispidine	**22.74**	
BA38	PhP_1(pyrr)	**22.34**	
BA39	(-)-Sparteine	**21.66**	
BA40	Bispidine	**21.55**	
BA41	*N*,*N′*-Bn_2-Bispidine	**21.38**	
BA42	*N*,*N′*-(CHMePh)2-Bispidine	**21.25**	
BA43	PhP_1(dma)	**21.25**	
BA44	4-Br-$C_6H_4P_1$(pyrr)	**21.19**	
BA45	$PhP_1(dma)_2$Me	**21.03**	

BA45	PhP$_1$(dma)$_2$Me	**21.03**	
BA46	PhTMG	**20.84**	
BA47	1-NaphtP$_1$(pyrr)	**20.61**	
BA48	*N*,*N*′-Me$_2$-1,3-Diaminopropane	**20.39**	
BA49	2-Cl-C$_6$H$_4$P$_1$(pyrr)	**20.17**	
BA50	4-CF$_3$-C$_6$H$_4$P$_1$(pyrr)	**20.16**	
BA51	*N*,*N*,*N*′,*N*′-Me4-1,3-Diaminobutane	**20.09**	
BA52	*N*-Me-1,3-Diaminopropane	**20.04**	
BA53	*N*,*N*,*N*′,-Me3-1,3-Diaminopropane	**20.01**	
BA54	*N*,*N*,*N*′,*N*′-Me4-1,4-Diaminobutane	**19.93**	
BA55	1,3-Diaminopropane	**19.70**	
BA56	2-Tol-1-BG	**19.66**	
BA57	*N*,*N*-Me2-1,3-Diaminopropane	**19.57**	
BA58	Pyrrolidine	**19.56**	
BA59	Piperidine	**19.29**	
BA60	*N*,*N*,*N*′,*N*′-Me4-1,3-Diaminopropane	**19.27**	
BA61	Homopiperazine	**19.10**	
BA62	2-Cl-C$_6$H$_4$P$_1$(dma)	**19.07**	
BA63	MePrNH	**18.92**	
BA64	Et$_3$N	**18.82**	
BA65	*i*-Pr$_2$NH	**18.81**	
BA66	Piperazine	**18.69**	
BA67	*N*,*N*,*N*′,*N*′-Me4-1,2-Diaminoethane	**18.68**	
BA68	Proton Sponge	**18.62**	
BA69	2,6-Cl$_2$-C$_6$H$_3$P$_1$(pyrr)	**18.56**	
BA70	2,5-Cl$_2$-C$_6$H$_3$P$_1$(pyrr)	**18.52**	
BA71	4-NO$_2$-C$_6$H$_4$P$_1$(pyrr)	**18.51**	
BA72	PrNH$_2$	**18.43**	
BA73	4-Pyrr-Pyridine	**18.33**	
BA74	Me$_2$EtN	**18.33**	
BA75	Pr$_3$N	**18.25**	
BA76	*N*-Me-Piperidine	**18.25**	
BA77	Me$_2$BuN	**18.24**	
BA78	*N*-Me-Piperazine	**18.07**	
BA79	4-NMe$_2$-Pyridine	**17.95**	
BA80	*N*,*N*′-(CHPh$_2$)$_2$-Bispidine	**17.79**	
BA81	2-NO$_2$-4-Cl-C$_6$H$_3$P$_1$(pyrr)	**17.68**	
BA82	4-NH$_2$-Pyridine	**17.62**	
BA83	9-O-1,5-Me2-*N*,*N*′-Bn$_2$-Bispidine	**17.48**	
BA84	*N*,*N*′-Me$_2$-Piperazine	**17.36**	
BA85	2-NO$_2$-5-Cl-C$_6$H$_3$P$_1$(pyrr)	**17.27**	
BA86	9-O-*N*,*N*′-Bn$_2$-Bispidine	**16.95**	
BA87	PhCH$_2$NH$_2$	**16.91**	
BA88	2-NO$_2$-4-CF$_3$-C$_6$H$_3$P$_1$(pyrr)	**16.54**	
BA89	2-NH$_2$-Acridine	**16.39**	
BA90	2-NH$_2$-1-Me-Benzimidazole	**16.31**	



BA90	2-NH$_2$-1-Me-Benzimidazole	**16.31**
BA91	2-NH$_2$-Benzimidazole	**16.08**
BA92	2,3-(NH$_2$)$_2$-Pyridine	**15.24**
BA93	2,4,6-Me$_3$-Pyridine	**14.98**
BA94	2,4-(NO$_2$)$_2$-C$_6$H$_3$P$_1$(pyrr)	**14.88**
BA95	2,6-(NH$_2$)$_2$-Pyridine	**14.77**
BA96	2-NH$_2$-Pyridine	**14.47**
BA97	2,6-Cl$_2$-4-NO$_2$-C$_6$H$_2$P$_1$(pyrr)	**14.43**
BA98	4-MeO-Pyridine	**14.23**
BA99	3-NH$_2$-Pyridine	**14.17**
BA100	2,6-Me$_2$-Pyridine	**14.13**
BA101	2,6-NO$_2$-C$_6$H$_3$P$_1$(pyrr)	**14.12**
BA102	*N*,*N′*-Ph$_2$-Bispidine	**13.97**
BA103	9-O-1,5-(COOMe)$_2$-*N*,*N′*-Bn$_2$-Bispidine	**13.81**
BA104	9-O-1,5-*N*,*N′*-(CHPh$_2$)$_2$-Bispidine	**13.48**
BA105	2-Me-Pyridine	**13.32**
BA106	Pyridine	**12.53**
BA107	OEP	**12.37**
BA108	4-MeO-Aniline	**11.86**
BA109	2-methylkinolin-8-amine	**11.54**
BA110	*N*,*N*-Me$_2$-Aniline	**11.43**
BA111	Aniline	**10.62**
BA112	2-Me-Aniline	**10.50**
BA113	TPP	**10.41**
BA114	5-NO$_2$-Benzimidazole	**10.39**
BA115	TMP	**10.15**
BA116	MePh$_2$P	**9.96**
BA117	TCPP	**9.94**
BA118	2-MeO-Pyridine	**9.93**
BA119	1-Naphthylamine	**9.77**
BA120	3-Cl-Pyridine	**9.55**
BA121	4-Br-Aniline	**9.43**
BA122	2,4-F$_2$-Aniline	**8.39**
BA123	9-O-1,5-(COOMe)$_2$-*N*,*N′*-Ph$_2$-Bispidine	**8.11**
BA124	4-CF$_3$-Aniline	**8.03**
BA125	2-Cl-Aniline	**7.86**
BA126	3-NO$_2$-Aniline	**7.68**
BA127	4-F-3-NO$_2$-Aniline	**7.67**
BA128	2,6-(MeO)$_2$-Pyridine	**7.64**
BA129	Ph$_3$P	**7.61**
BA130	2-Cl-Pyridine	**6.79**
BA131	4-NO$_2$-Aniline	**6.22**
BA132	2,5-Cl$_2$-Aniline	**6.21**
BA133	Ph$_2$NH	**5.97**
BA134	2,6-Cl$_2$-Aniline	**5.06**
BA135	2-NO$_2$-Aniline	**4.80**
BA136	4-Cl-2-NO$_2$-Aniline	**3.80**



Some of the measurements have been omitted for clarity

Anchoring the Scale. Thorough analysis of all of experimental data (pK_a values of this and earlier works) and experimental pK_a data in AN available in the literature (works from the groups of Coetzee and Padmanabhan, Kolthoff and Chantooni, Jr., the Schwesinger group, Bren' *et al.* and some others, altogether 19 papers) was carried out.

Basicity scale in AN has been previously[60] anchored to the pK_a value of pyridine: 12.33 determined by Coetzee and Padmanabhan.[16] In light of the new data obtained in this work it is now reasonable to reexamine this anchor point.

Available pK_a data in AN for the bases studied in this work have been collected. There are seven major papers where pK_a values for bases in AN have been published: The paper on basicities of amines (including aniline and pyridine) by Coetzee and Padmanabhan,[16] the papers of basicities on weak bases by Kolthoff *et al.*,[9,49,65,66] the contribution from the Schwesinger group on simple alkylphosphazenes, amidines and guanidines,[54] substituted pyridines from Augustin-Nowacka and Chmurzynski,[67] pyridines and anilines from Pawlak *et al.*[68,69] anilines from Bren' *et al.*[70] and arylphosphazenes using ^{13}C and ^{1}H NMR from Rodima *et al.*[36] There are still some other contributions[12,71–76] that contain less data. If we correlate the literature pK_a values from particular research group in AN with the values from our present work (anchor compound pyridine, pK_a value 12.33) we can make the following observations:

1. A correlation series of the present data with literature values from particular author(s) shows in some cases (works of Coetzee,[16] Kolthoff,[9,49,65,66] Bren',[70] Zvezdina,[75] Schwesinger[54] and Augustin-Nowacka[67]) close to unity slope (deviation is less than 0.03 units), whereas others differ more significantly (more than 0.07 units) from unity (works of Pawlak[68,69] and Rodima[36]).

2. The same correlations show that in some cases (works of Coetzee,[16] Kolthoff,[9,49,65,66] Bren',[70] Zvezdina,[75] Schwesinger[54]) the standard deviations of the regression line are small (less than 0.17 pK_a units), whereas in some cases (works of Pawlak,[68,69] Augustin-Nowacka,[67] Rodima[36]) the standard deviations of the regression line are larger (more than 0.23 pK_a units).

These two observations lead to the following conclusions. First, the pK_a values from groups that give in correlation of our data regression line with slope close to unity give confidence, that our scale has no contraction or expansion with respect to the data of other authors due to the different experimental conditions (temperature, composition of medium, effects arising from impurities, ionic association, *etc.*). Second, as our basicity scale is

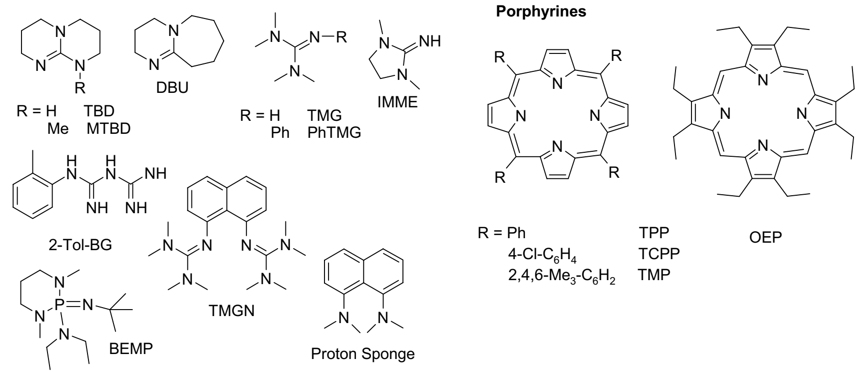


Figure 4.1: Compounds in Tables 4.1 and 4.4

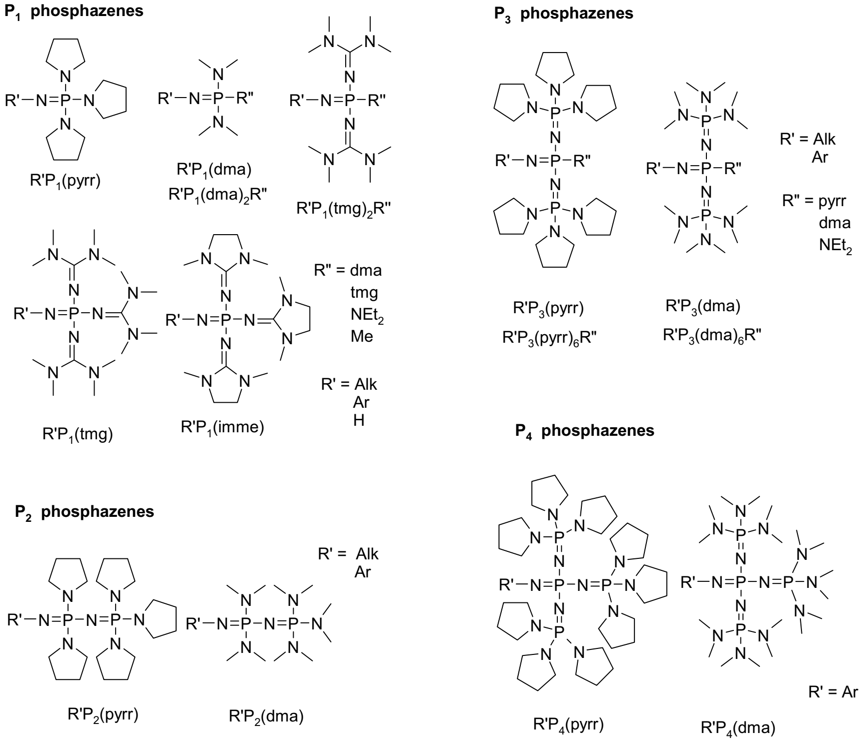


Figure 4.2: Substituted phosphazenes in Tables 4.1 and 4.4

self-consistent by its nature, the pK_a values from a particular group that give on correlation with our results regression lines with relatively small standard deviations are truly close to self-consistency by themselves and can thus be considered reliable.

Thus, the experiments by Coetzee,[16] Kolthoff,[9,49,65,66] Bren',[70] Zvezdina[75] and Schwesinger[54] for measurement of pK_a values can be considered to be carried out at nearly the same conditions as ours and are self-consistent. These works have altogether 26 common pK_a values of bases with our work (compounds **BA10**, **BA11**, **BA14**, **BA17**, **BA21**, **BA24**, **BA32**, **BA58**, **BA64**, **BA82**, **BA87**, **BA91**, **BA96**, **BA106**, **BA108**, **BA111**, **BA121**, **BA124**, **BA126**, **BA131**, **BA135**, **BA136**). In addition, there are two works[73,74] that both have only one common compound (**B68**) with our scale, but for which we are not able to find a reason to leave these values out from the sample. The overall correlation of all these literature pK_a values with our pK_a values anchored to the pK_a value of pyridine 12.33 gives the following equation:

$$\mathrm{p}K_\mathrm{a}(\mathrm{lit.}) = 0.25 + 0.995\mathrm{p}K_\mathrm{a}(\mathrm{this\ work}) \tag{4.1}$$

$$s(\mathrm{intercept}) = 0.05, s(\mathrm{slope}) = 0.003, n = 28, r^2 = 1.000, S = 0.11$$

The average value of our pK_a values (scale anchored to pyridine pK_a value 12.33) of the range what has common part with literature pK_a values is 16.14 pK_a units. At this point the difference between the hypothetical literature pK_a value described by the regression line and our average value is 0.18 pK_a units. The difference of hypothetical literature pK_a value at our anchor point value (pyridine, pK_a = 12.33) described by the regression line and our value (12.33) is 0.19 pK_a units. We see, that these two approaches yield virtually identical corrections. Hence, we have corrected all our values increasing them by 0.20 pK_a units. This way very good agreement between our relative data and the absolute pK_a values of the abovementioned authors was obtained. The resulting corrected pK_a values of the bases are indicated in the Table 4.1.

Comparison of pK_a Values of Anilines and Phosphazenes. It is of interest to compare the basicities of the substituted $\mathrm{PhP_1(pyrr)}$ bases with corresponding anilines. pK_a values of substituted anilines in AN correlate well with pK_a values of $\mathrm{PhP_1(pyrr)}$ in AN:

$$\mathrm{p}K_\mathrm{a}(\mathrm{PhP_1(pyrr)}) = 14.61 + 0.706\mathrm{p}K_\mathrm{a}(\mathrm{Aniline}) \tag{4.2}$$

$$s(\mathrm{intercept}) = 0.38, s(\mathrm{slope}) = 0.047, n = 9, r^2 = 0.970, S = 0.35$$

For only 4-C_6H_4 substitution the correlation is as follows:

$$\mathrm{p}K_\mathrm{a}(\mathrm{PhP_1(pyrr)}) = 13.46 + 0.824\mathrm{p}K_\mathrm{a}(\mathrm{Aniline}) \tag{4.3}$$

$$s(\mathrm{intercept}) = 0.26, s(\mathrm{slope}) = 0.027, n = 5, r^2 = 0.997, S = 0.12$$

As seen from Figure 4.3 and from equations 4.2 and 4.3, the basicity of $\mathrm{PhP_1(pyrr)}$ is less sensitive toward substitution in the aromatic ring than basicity of anilines. Lower sensitivity can be due to the contribution of the ylenic structure in the substituted $\mathrm{PhP_1(pyrr)}$ series[60] and delocalization of the positive charge of the protonated form into the large phosphorane moiety.

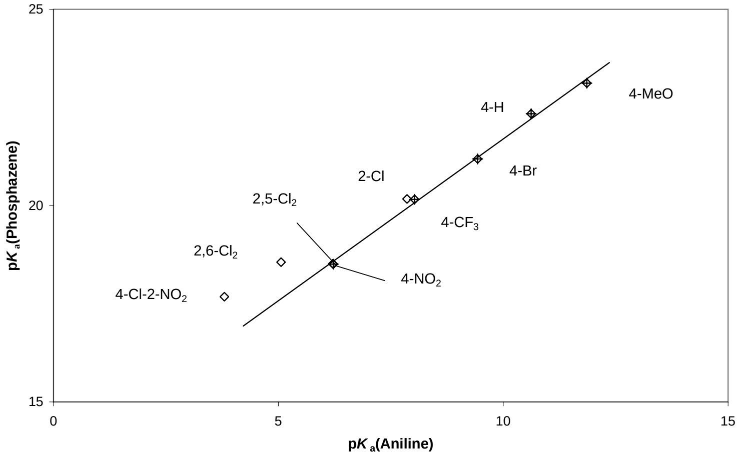
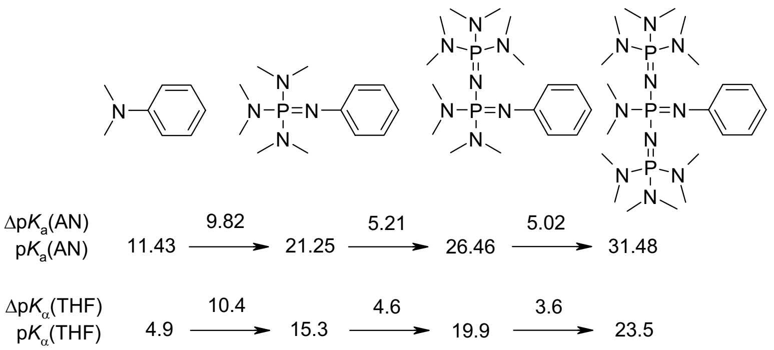


Figure 4.3: Correlation of pK_a values in AN of phenylsubstituted anilines and $\mathrm{PhP_1(pyrr)}$ phosphazenes. The line corresponds to the correlation equation of the *para*-substituted compounds. The most deviating points belong to the 2,6-Cl_2- (**BA69** and **BA87**) and 4-Cl-2-NO_2-substituted (**BA81** and **BA89**) compounds.

Basicity of Phosphazenes. If we follow the change in free ion basicities of $\mathrm{PhP}_n\mathrm{(dma)}$ ($n = 0 \cdots 3$, compounds **BA110**, **BA43**, **BA19**, **BA2**) in AN and THF we observe the following base strengthening effect upon addition of phosphazene groups into a molecule, in AN: 9.82; 5.21; 5.02 pK_a units and in THF: 10.4; 4.6; 3.6 pK_a units, respectively. The addition of first $\mathrm{N{=}P(dma)_2}$ subunit into the amine **BA110** molecule is more expressed in THF (ratio 0.94). The addition of second and third $\mathrm{N{=}P(dma)_2}$ subunit into the molecules **BA43** and **BA19**, respectively, the basicity is 1.16 and 1.36 times stronger expressed in AN than in THF. Schwesinger[26] reports in the row t-$\mathrm{BuP}_n\mathrm{(dma)}$ ($n = 0 \cdots 5$) the following base strengthening effect upon addition of phosphazene N=P(dma)$_2$ subunits into a molecule in AN: approximately 8.5, 6.61, 5.1, 4.1, 2.6 pK_a units, last three being extrapolated from experiments in other solvents. This row is quite similar to the findings of this work.



(4.4)

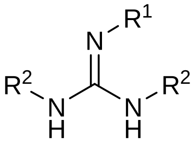
4.2. Basicity of Guanidines with Heteroalkyl Side Chains

Guanidine derivatives continue to attract interest among organic chemists due to their versatile chemistry and interesting biochemical properties.[77] Guanidine moiety is an important substructure in many molecules of biological importance such as arginine, creatine phosphate and purines.[78] Due to their strong basic properties guanidines also serve as useful catalysts in a wide range of base-catalyzed organic reactions.[79–83] Guanidine fragment has been employed as an essential building block in computational tailoring and synthesis of strong organic superbases[59,84–88] (see also section 4.3. and III). Particularly interesting in this regard were found to be guanidines substituted with flexible heteroalkyl chains capable of forming multiple intramolecuar hydrogen bonds.

The pK_a values of seven novel guanidine derivatives, six of them possesing heteroalkyl substituents capable of forming intramolecular hydrogen bonds, are determined in AN and presented in this section and in the paper II. The obtained pK_a values range from 24.7 to 27.2 pK_a units. The most basic among the studied guanidines was found to be by *ca* 4 pK_a units more basic than the well-known superbase TMG.

Compound **1** (see Table 4.2 for numbering) possesses a propyl group at each of the guanidine nitrogen atoms and cannot form hydrogen bonds neither in the neutral nor the protonated form. Hence, its basicity is mainly governed by the resonance effect in the guanidine moiety of the protonated form coupled with contribution associated with polarizability of the alkyl

Table 4.2: Numbering of Guanidines with Heteroalkyl Side Chain

	no.	R^1	R^2	no. in Table 4.1
	**1**	$(CH_2)_2CH_3$	$(CH_2)_2CH_3$	**BA27**
	2	$(CH_2)_3NMe_2$	$(CH_2)_2CH_3$	**BA23**
	3	$(CH_2)_2CH_3$	$(CH_2)_3NMe_2$	**BA18**
	4	$(CH_2)_3NMe_2$	$(CH_2)_3NMe_2$	**BA15**
	5	$(CH_2)_3OMe$	$(CH_2)_2CH_3$	**BA29**
	6	$(CH_2)_2CH_3$	$(CH_2)_3OMe$	**BA28**
	7	$(CH_2)_3OMe$	$(CH_2)_3OMe$	**BA30**

groups. Thus, it is expected that its basicity should be similar to that of previously studied poly-alkyl-substituted guanidine derivatives. This is indeed found to be a case. The measured pK_a value 24.92 is very close to the pK_a values of TBD (**BA21**) and TMG (**BA35**) in AN are (26.0 and 23.4, respectevly). Replacement of the propyl groups with the dimethylaminopropyl or the methoxypropyl chains opens possibility of forming intramolecular hydrogen bonds which, as discussed earlier,[84] could additionally stabilize the protonated forms and increase the basicity of the parent base. Comparison of the pK_a value of **1** with those of its heteroalkyl analogues shows that replacement of the propyl group at the imino nitrogen in **1** by the 3-dimethylmetylaminopropyl chain (compound **2**) increases its pK_a value by 0.93 units. Similarly, replacement of the propyl groups at the amino nitogen atoms with the 3-dimethylaminopropyl groups (compound **3**) results an increase of pK_a value by 1.71 units. This corresponds to 0.86 units per amino nitrogen which is slightly less than in the case of imino nitrogen. Finally, the compound **4** containing three 3-dimethylaminopropyl groups is found to be more basic than **1** by 2.23 units. This makes compound **4** the most basic guanidine derivative in acetonitrile measured so far. It is also interesting to note that replacement of the first propyl chain with a 3-dimetylaminopropyl group in **1** influences basicity signficanly, more than going from **3** to **4**. On the other hand, the pK_a values of the methoxypropyl substituted guanidines **5** to **7** appear to be slightly lower than the pK_a value of **1**. Thus, on passing from **1** to **7** a decrease in total basicity of 0.18 units is observed. To be more specific, replacement of the propyl groups at the amino nitrogens with 3-methoxypropyl chains in **1** leading to **6** results in a decrease in basicity of 0.1 units which is slightly less than on going from **1** to **5** with the 3-methoxypropyl group attached to the imino nitrogen. This in turn, results in the basicity order change relative to dimethylaminopropyl-substituted guanidines **2** to **4**. The trend of changes in pK_a values on passing from **1** to a series of 3-methoxypropyl

Table 4.3: Calculation Results and Experimental pK_a Values of Studied Guanidine Derivatives in AN

compound	*PA*^{a} (kcal/mol)	pK_a (calcd)	pK_a (exp)	ΔpK_a
1H$^+$	290.6	24.3	24.92	-0.7
2H$^+$	293.5	25.7	25.85	-0.2
3H$^+$	296.1	27.0	26.63	0.4
4H$^+$	299.7	28.7	27.15	1.6
5H$^+$	292.0	25.0	24.81	0.2
6H$^+$	294.2	26.0	24.84	1.2
7H$^+$	295.5	26.7	24.74	2.0
5H$^+$**(oc)**	289.4	23.7	24.81	-1.1
6H$^+$**(oc)**	287.7	22.8	24.84	-2.0
7H$^+$**(oc)**	287.2	22.6	24.74	-2.1

[a] *PA* of conjugate bases **1**–**7** and open-chain structures **5(oc)**–**7(oc)**.

guanidine derivatives strongly implies that formation of the intramolecular hydrogen bonds in these bases in AN is questionable.

Computational (polarized continuum model in combination with B3LYP 6-311+G**//HF 6-31G* method) *PA* values of bases **1** to **7** in AN were calculated (see Table 4.3). Theoretical pK_a values were obtained from the correlation equation found from the correlation between experimental pK_a values *vs.* computational *PA* values (in AN) of large number of strong nitrogen bases. The comparison of obtained values are presented in the Table 4.3. For bases **5** to **7** calculations were carried out for the cyclic, as well as for the open-chain (in the Table 4.3 indicated as "oc") structures.

Analysis of the results in Table 4.3 reveals that the calculated pK_a values are in fair accordance with the experimental ones. However, there are some larger deviations, like those in the molecules **4** and **7**, where the number of intramolecular hydrogen bonds increases upon protonation. This indicates that a part of the disagreement might have its origin in neglecting the entropy contribution. In such systems the entropy change upon protonation occurring due to the entropy of the incoming proton remains fairly constant across the series of structurally similar compounds. On the other hand, the structures with the heteroalkyl chains considered here are stabilized by one or more intramolecular hydrogen bonds. This holds true in particular for the protonated forms, which as a rule exhibit stronger hydrogen bonds than their parent bases. The next point of interest is that the trend of calculated pK_a on passing from **1** to the 3-methoxypropyl derivatives **5** to **7** does not follow the order of the measured pK_a values. This is not surprising as the *PA* values used are calculated for the GP geometries, implying that structural features of the considered species (including the geometry of the intramolecular hydrogen bonds) in the gas phase and AN are the same. Therefore, in the case of 3-methoxypropyl guanidine derivatives where this assumption apparently does not hold, larger deviations between calculated and the measured $\mathrm{p}K_\mathrm{a}$ values can be expected. It is interesting to note within this context that the AN $\mathrm{p}K_\mathrm{a}$ values of bases **5** to **7**, when calculated for open-chain isomers reproduce qualitatively the experimentally obtained order of $\mathrm{p}K_\mathrm{a}$ values, but in this case larger $\Delta\mathrm{p}K_\mathrm{a}$ values are encountered.

4.3. Basicity of Guanidinophosphazenes

A principle for creating a new nonionic superbases – guanidinophosphazenes – is presented in this section (see III). The main idea for construction of the new family of superstrong uncharged bases of the guanidinophosphazene type (see Figure 4.4 and also Figure 4.1) is to apply, instead of the dialkylamino and tris(dimethylamino)phosphazeno fragments as building blocks, the strongly electrondonating and presumably less toxic[88,89] tmg,[57,87,90] (1,3-dimethylimidazolidin-2-ylidene)amino (imme) or bis(tetraalkylguanidino)carbimino fragments to the phosphorus atom of the iminophosphorane group. TMG combines strong basic (**BT44**, $\mathrm{p}K_\mathrm{ip}(\mathrm{THF}) = 17.0$, $\mathrm{p}K_\alpha(\mathrm{THF}) = 15.5$, see Table 4.4) and nucleophilic properties. Therefore, it is advantageous to apply this compound and its easily available cyclic analogue, 1,3-dimethylimidazolidine-2-imine (**BT43**, $\mathrm{p}K_\mathrm{ip}(\mathrm{THF}) = 17.2$, $\mathrm{p}K_\alpha(\mathrm{THF}) = 15.9$) (derived from nontoxic 1,3-dimethyl-2-imidazolidone), as building blocks for designing new cheap organic superbases for common use in organic synthesis. The enormous basicity-increasing effect according to this principle is experimentally verified for the tmg and imme groups in the THF medium: the basicity increase when moving from t-BuP$_1$(dma) (**BT37**, $\mathrm{p}K_\alpha = 18.9$) to t-BuP$_1$(tmg) (**BT3**, $\mathrm{p}K_\alpha = 29.1$) is 10 orders of magnitude.

To be synthetically useful, an organic superbase (along with having high intrinsic basicity) has to be a hydrolytically stable compound. This requirement also applies to its protonated form. We assume that significant delocalization of the positive charge over the tmg groups due to the conjugation of guanidino moieties with either a phosphorus atom of guanidinophosphazene or a phosphonium center will reduce the electrophilic character of phosphorus, providing the respective bases and phosphonium salts with high hydrolytic stability. This assumption is supported by previous results on the use of TMG for synthesizing a new generation of robust phase-transfer catalysts with delocalized lipophilic cations.[91,92] The introduction

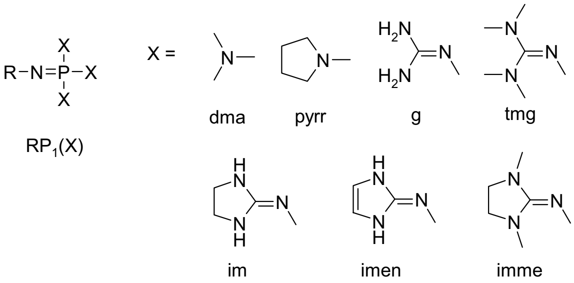


Figure 4.4: Designations of the substituents

of one electron-donating tmg group into carbonium or phosphonium centers and three tmg substituents to a sulfonium center provided cations with enhanced stability under extreme conditions (*e.g.* high temperature, strongly basic media, powerful nucleophiles).[93,94] This led to expect similar hydrolytic stability also for the tmg-substituted carbimines and phosphazenes.

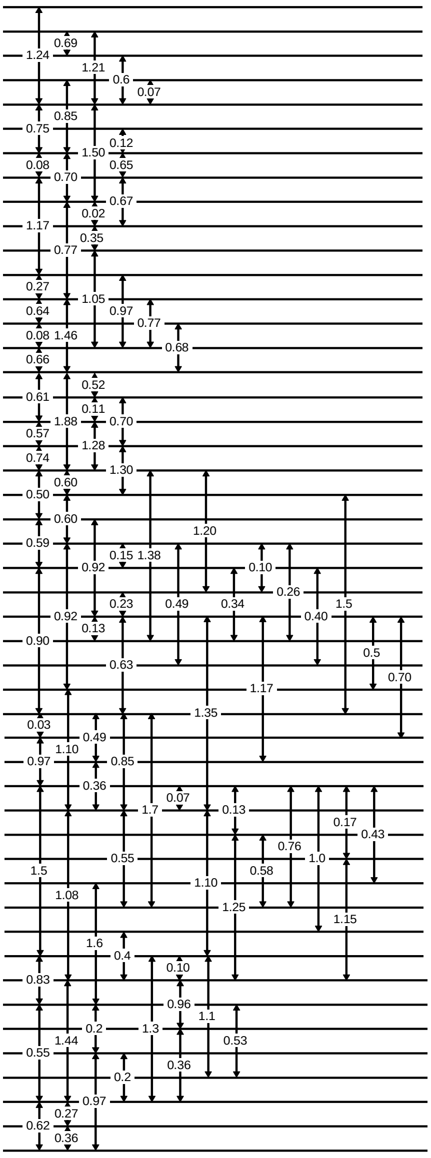
Using the novel guanidino-phosphazenes (and some other bases) the self-consistent basicity scale in THF medium[62,95] has been expanded, now spanning 24 orders of magnitude (Table 4.4). Basicity of eight nonionic superbasic phosphazene bases, tetramethylguanidino-substituted at the P atom, have been the key building blocks for expanding the basicity scale in THF (basicity of three of those have been mesured also in AN, see Table 4.1 in section 4.1.).

In the papers of Raab *et al.*[57] it was found that in AN solution the basicity of Alder's Proton Sponge increased by *ca* 6.9 pK_a units when the 1,8-bis(dimethylamino) substituents in the naphthalene ring were replaced with 1,8-bis(tetramethylguanidino) groups. As evidenced in this work, in THF solution a similar change of the substituents in the naphthalene ring results in a somewhat more modest (by 5.8 pK_a units) increase in the basicity of the Proton Sponge. In THF, changing all three dimethylamino groups in *t*-BuP$_1$(dma), PhP$_1$(dma), and HP$_1$(dma) phosphazenes (see refs 95 and 62 for the pK_α values in THF for thos compounds not presented in Table 4.4) to tetramethylguanidino groups increases the basicity enormously: by 10.2, 9.0, and 8.9 powers of 10, respectively. The basicity increase in the pyrrolidinyl phosphazenes – *t*-BuP$_1$(pyrr), PhP$_1$(pyrr), and HP$_1$(pyrr) – initially somewhat stronger, is 8.9, 8.3, and 7.8 pK_a units, respectively.

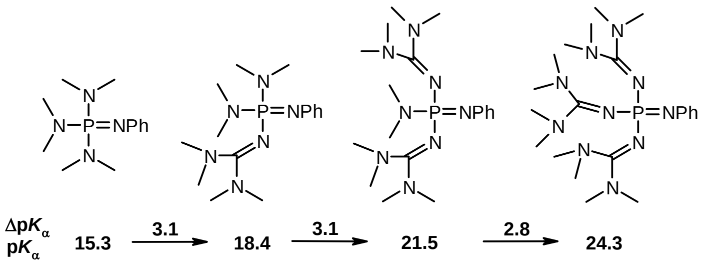
Table 4.4: Stronger Basicity Area of the Self-Consistent Basicity Scale of Neutral Bases in THF

	Base	pK_{ip}(THF)	pK_{α}(THF)
BT1	S(-) CH(Ph)(Me)P_1(imme)	**29.1**	**29.5**
BT2	R(+) CH(Ph)(Me)P_1(imme)	**29.1**	**29.5**
BT3	*t*-BuP_1(tmg)	**28.4**	**29.1**
BT4	HP_1(tmg)	**27.9**	**28.6**
BT5	4-MeO-$C_6H_4P_4$(pyrr)	**27.8**	**28.9**
BT6	(+/-) CH(Ph)(Me)P_1(tmg)	**27.2**	**27.6**
BT7	PhP_4(pyrr)	**27.1**	**28.1**
BT8	4-MeO-$C_6H_4P_4$(dma)	**27.0**	**27.7**
BT9	*t*-BuP_1(tmg)$_2$NEt$_2$	**26.4**	**26.8**
BT10	PhP_4(dma)	**26.3**	**27.0**
BT11	EtP_2(pyrr)	**25.9**	**26.6**
BT12	4-Br-$C_6H_4P_4$(pyrr)	**25.8**	**26.9**
BT13	2-Cl-$C_6H_4P_4$(pyrr)	**25.6**	**26.6**
BT14	EtP_2(dma)	**24.9**	**25.3**
BT15	4-MeO-$C_6H_4P_3$(pyrr)	**24.9**	**25.7**
BT16	PhP_3(pyrr)	**24.2**	**25.1**
BT17	PhP_1(tmg)	**23.7**	**24.3**
BT18	4-MeO-$C_6H_4P_3$(dma)	**23.6**	**24.1**
BT19	PhP_3(dma)	**23.0**	**23.5**
BT20	4-CF_3-$C_6H_4P_3$(pyrr)	**22.3**	**23.2**
BT21	TBD	**21.7**	**21.0**
BT22	EtP_1(pyrr)	**21.8**	**21.8**
BT23	4-CF_3-$C_6H_4P_3$(dma)	**21.2**	**21.7**
BT24	2-Cl-$C_6H_4P_3$(pyrr)$_6$NEt$_2$	**21.1**	**22.0**
BT25	PhP_1(tmg)$_2$dma	**21.1**	**21.6**
BT26	4-MeO$C_6H_4P_2$(pyrr)	**20.9**	**21.5**
BT27	HP_1(pyrr)	**20.9**	**20.9**
BT28	MeP_1(dma)	**20.7**	**20.7**
BT29	2-Cl-$C_6H_4P_3$(dma)$_6$NEt$_2$	**20.4**	**20.9**
BT30	PhP_2(pyrr)	**20.3**	**20.9**
BT31	*t*-BuP_1(pyrr)	**20.3**	**20.3**
BT32	HP_1(dma)	**19.7**	**19.7**
BT33	PhP_2(dma)	**19.4**	**19.9**
BT34	2,5-Cl_2-$C_6H_3P_3$(pyrr)$_6$NEt$_2$	**19.3**	**20.2**
BT35	4-Br-$C_6H_4P_2$(pyrr)	**19.3**	**20.0**
BT36	BEMP	**19.3**	**19.0**
BT37	*t*-BuP_1(dma)	**18.9**	**18.9**
BT38	MTBD	**18.7**	**18.0**
BT39	*t*-OctP_1(dma)	**18.5**	**18.5**
BT40	DBU	**18.1**	**16.9**
BT41	PhP_1(dma)$_2$tmg	**18.1**	**18.4**
BT42	4-Me_2N-$C_6H_4P_1$(pyrr)	**17.3**	**17.3**
BT43	IMME	**17.2**	**15.9**
BT44	TMG	**17.0**	**15.5**
BT45	2-Cl-$C_6H_4P_2$(pyrr)	**16.9**	**17.6**
BT46	4-MeO-$C_6H_4P_1$(pyrr)	**16.8**	**16.8**
BT47	TMGN	**16.5**	**16.8**
BT48	PhP_1(pyrr)	**16.1**	**16.1**

Directly measured ΔpK_{ip} values



The following pattern of basicity change is observed in the THF solution:



(4.5)

The basicity increase is nearly additive: the consecutive replacements of dma groups by tmg fragments contribute 34.4, 34.4, and 31.2%, respectively, to the total basicity increase of 9 pK_a units. The comparison of differences (*ca* 2.3 pK_α units) in pK_α values between two pairs of compounds with sterically more demanding *t*-Bu groups on the imino nitrogen, **BT3** and **BT9** on one hand and **BT17** and **BT25** on the other hand, indicates that the introduction of the first two tmg groups accounts for *ca* 70–80% of the overall basicity increase when going from the *t*-BuP$_1$(dma) and PhP$_1$(dma) to their double tmg-substituted analogues.

Comparison of phosphazenes with tmg and imme substituents are possible. The 1-methylphenethyl substituted phosphazenes containing tmg as well as imme groups were measured. These phosphazenes are chiral compounds, it was found out that the basicity does not depend on the type of chiral center. CH(Ph)(Me)P$_1$(imme) (in Table 4.4 compounds **BT1** and **BT2**) is 2 pK_a units stronger base than CH(Ph)(Me)P$_1$(tmg) (**BT6**). At the same time, the basicity of TMG (**BT44**) and IMME (**BT43**) differs by only 0.4 units – for three substituents the maximum change would be 1.2 units. The larger basicity change comes probably from the slightly smaller size of the imme group and the planarity of the cyclic guanidino-moiety (as opposed to the twisted geometry of the tmg fragment). This leads to more efficient delocalization of the positive charge in the protonated form of the base.

N,*N*,*N'*,*N'*-tetramethylguanidino moiety is a very good building block for designing stronger bases. Two papers – II and III have been presented in this work based on the basicity measurements of compounds with unit and in paper I several good reference compounds, phosphazenes with tmg substituents have been investigated.

5. ACIDS

The use of acids in synthetic chemistry is as widespread as that of different bases.[4] For example, superacids are used either as different catalysts[96] and their anions as counterions in the role of WCAs[97–101] in the case of stereoselective catalysts, materials for highly effective electrochemical power sources (Li-ion batteries, electrochemical double layer capacitors, fuel cells, *etc.*).

The definition of superacids is simple – all acidic systems stronger than 100% sulfuric acid are considered to be superacids. Since 1930's the strongest known acids were developed[102,103] – triflic acid (TfOH) and fluorosulfonic acid (FSO_3H) and superacidic media – Magic Acid, fluoroantimonic acid and related acids were later also developed. These acids (and media) are by 10^7 to 10^{19} times stronger[104] than sulfuric acid. These developments opened new horizons for the chemistry of superacids. Nowadays the strongest known neutral superacid (most probably) was developed by Reed *et al.* – $H(CHB_{11}Cl_{11})$[101] – a representative of the carborane acids. It is a strong but gentle acids which is able to protonate even C_{60} fullerene without breaking it.[105,106] Much older but worth of its reputation is pentacyanocyclopentadiene and other polycyano acids originally discovered by Webster.[107]

The generalized principle for designing superacids has been published.[108] The principle is based on the generalization of the Yagupolskii's principle to design superacids, which is known since the 70's of the previuos century. The generalized principle in this paper[108] is based on the scheme where double-bonded sp^2 oxygen in carbonyl, sulfonyl, *etc.* groups is replaced by a bivalent electron-attractive substituent, such as =NCN, $=C(CN)_2$, $=NSO_2F$, *etc.* In the case of the Yagupolskii's substituent, the =O is replaced by =N-Tf. The Yagupolskii's substituent is a powerful acidifying tool – replacement of an oxygen atom by =N-Tf group in sulfonimides increases their acidity by approximately 5 $\mathrm{p}K_\mathrm{a}$ units in condensed media. The sulfonimides modified according to the Yagupolskii's principle have proven to be stable also as free acids.[109] Many neutral superacids are stable only in solution or it is very difficult to get free acid.

In addition to the Yagupolskii's substituent and its generalized versions, the cyano group[110] has many positive sides for designing superacids.[107] It has strong electron-withdrawing power combined with the lowest steric demand among strong electron-acceptor substituents. The small size is a property that gives the opportunity to add many cyano groups to the parent molecule. It is in this respect drastically different from other strongly electronegative substituents as nitro or alkyl- or aryl-sulphonyl groups. Cyano group have also some disadvantages. The cyano group has nucleophilic properties and makes many acids therefore much weaker than could be assumed. It was recently established that the free acid pentacyanocyclopentadiene has a polymeric structre with protons attached to the cyano groups of two anions simultaneously thus linking them into a polymeric chain.[111] This polymeric substance is not soluble in AN. Carborane acid with single cyano group – $H(CHB_{11}H_{10}CN)$ – is weaker than the nonsubstituted carborane acid because the preferred protonation site is introduced with the cyano group – on the nitrogen with its free electron pair on it.

Trifluoromethyl group has electron-withdrawing power inferior to that of cyano group. Trifluoromethyl group is also bulkier than cyano group. Due to the lower resonance effect (hypergonjugation) of trifluoromethyl group, the molecule or ion does not have to be planar for this group to work well. Due to the bulkiness of trifluoromethyl group, poly-trifluoromethyl compounds have like a shield made of inert fluorine atoms. If the whole anion is shielded with fluorines, then the proton has no favorable protonation site and the acidity of the conjugate acids of such anions can be higher than of polycyano acids. It is not like this with conventional compounds (phenol, phenylmalononitrile, toluene, *etc.* – pentacyanated compounds are approximately 10 pK_a units stronger than pentakis(trifluoromethylated) compounds – see V) but for example, the strongest designed superacid is the fully per(trifluoromethylated) carborane acid $CHB_{11}(CF_3)_{12}$.[104] The difference between these conventional acids and the carborane acid is that the conventional acids have certain known protonation site and cyano group wins in terms of electron-withdrawing power. The anion of this kind of carborane acid has a fluorine-shield and not definite protonation site. Trifluoromethyl group is therefore very useful in avoiding introduction of protonation sites into the anions of superacids. Compounds with trifluoromethyl group are usully volatile enough which is a good property for preparing neutral free acids *via* sublimation.

Up to now it has not been possible to set up an equilibrium acidity scale of truly superacidic molecules in a solvent of constant composition. The strongest measured superacid in the GP is sulfonimide $(C_4F_9SO_2)_2NH$.[112] Estimates of solution acidities of the famous cyanocarbon acids and other superacids have also been published.[107] Reed and his group measured shifts of the infrared (IR) NH stretch absorption bands of trioctylammonium for comparison of superacids.[113] The easiest way to get estimates of acidity is calculations. Computational acidity data for a large number of acids have been reported, among them also for superacids. But still, the real directly measured equilibrium acidities of superacids are very much needed.

Not only the strength of the strong acids but also of weaker acids and very weak acids has been under study and is of interest.[114–116] Acidities of the most common organic acids – acetic acid, benzoic acid, phenols, *etc.* – are in the weaker acidity area but their pK_a values would be still interesting to measure in different condensed media. The problem with investigation of weak acids in non-aqueous media is their tendency to form associates due to the localized charge (usually this kind of acid anions have rather localized charge). Also the traces of water have great influence to their pK_a values.

In the present work the comprehensive acidity scale in AN spanning mor ethan 25 pK_a units is composed. A large variety of different acids were measured (see section 5.1. and IV). As it comes out, most of the older literature pK_a values differ from the pK_a values measured in this work and the weaker the acid the larger the difference. Evidence is presented in favor of the present results compared to the older results from literature and the acidity scale presented in this work could be considered as the most correct acidity scale in AN up to now.

Also, the first achievements on the way towards an equilibrium acidity scale of superacids in DCE are presented in this work (see section 5.3.). The scale currently spans *ca* 10 orders of magnitude and is the most acidic equilibrium acidity scale in a medium of constant composition.

5.1. Comprehensive Acidity Scale in Acetonitrile

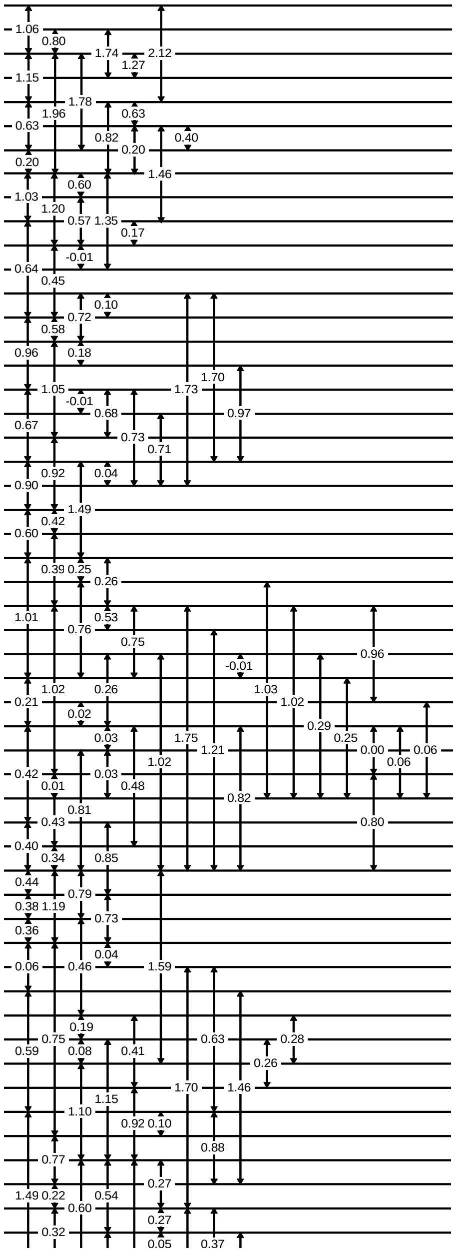
Acidity data in non-aqueous solutions are of continuing interest to chemists. One of the most popular solvents in this respect is AN. Experimental measurements of pK_a values in AN started from the classic papers of the groups of Kolthoff[33,49,115] and Coetzee[15,117] in the 1960's, and a considerable amount of acidity data for various acids in AN has been accumulated to date.[15,29,71,107,118–122] Literature analysis shows that acidity data for different compounds in the pK_a range of -2–28 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[123] to 18.40[124] units.

In this work (see IV), the self-consistent spectrophotometric acidity scale of neutral Brønsted acids in AN spanning more than 25 orders of magnitude of acidities is reported. The scale ranges from pK_a 3.6 to 29.1 in AN.

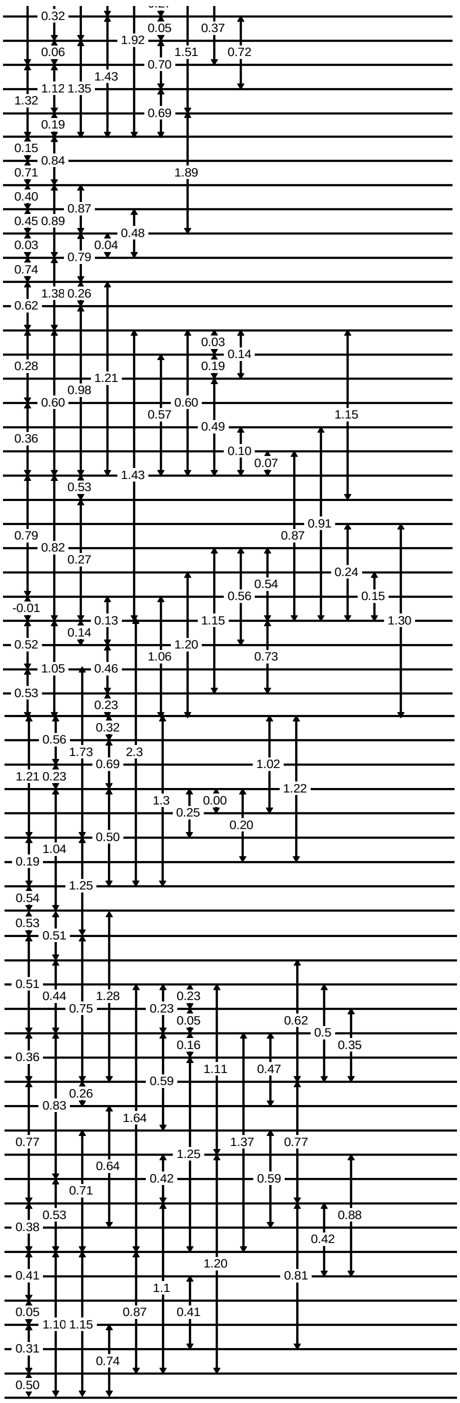
Table 5.1: Continuous Self-Consistent Acidity Scale of Neutral Acids in AN

	Acid	pK_a (AN)	logK_{AHA}
AA1	Phenol	**29.14**	**5.0**
AA2	2,3,4,5,6-$(CF_3)_5$-Toluene	**28.7**	
AA3	9-C_6F_5-Fluorene	**28.11**	
AA4	$(4\text{-}NC_5F_4)(4\text{-}Me\text{-}C_6H_4)NH$	**26.96**	
AA5	$(4\text{-}Me\text{-}C_6F_4)(C_6H_5)CHCN$	**26.96**	
AA6	3-CF_3-Phenol	**26.50**	**5.0**
AA7	$(4\text{-}NC_5F_4)(C_6H_5)NH$	**26.34**	
AA8	$(C_6H_5)(C_6F_5)CHCN$	**26.14**	
AA9	4-CF_3-Phenol	**25.54**	**5.0**
AA10	$(4\text{-}Me_2N\text{-}C_6F_4)(C_6F_5)NH$	**25.12**	
AA11	$(4\text{-}Me\text{-}C_6F_4)(C_6F_5)NH$	**24.94**	
AA12	2-CF_3-Phenol	**24.88**	**5.0**
AA13	2,3,4,5,6-$(CF_3)_5$-Aniline	**24.59**	
AA14	Octafluorofluorene	**24.49**	
AA15	Fluoradene	**23.90**	
AA16	3,5-$(CF_3)_2$-Phenol	**23.78**	**5.0**
AA17	9-COOMe-Fluorene	**23.53**	
AA18	Acetic acid	**23.51**	**4.5**
AA19	$(C_6F_5)CH(COOEt)_2$	**22.85**	
AA20	2-NO_2-Phenol	**22.85**	
AA21	$(4\text{-}Me\text{-}C_6F_4)_2CHCN$	**22.80**	
AA22	$(4\text{-}Me\text{-}C_6F_4)(C_6F_5)CHCN$	**21.94**	
AA23	Benzoic acid	**21.51**	**3.9**
AA24	9-CN-Fluorene	**21.36**	
AA25	$(4\text{-}H\text{-}C_6F_4)(C_6F_5)CHCN$	**21.11**	
AA26	$(C_6F_5)_2CHCN$	**21.10**	
AA27	$(CF_3)_3COH$	**20.55**	**4.8**
AA28	$(4\text{-}Cl\text{-}C_6F_4)(C_6F_5)CHCN$	**20.36**	
AA29	2,4,6-Br_3-Phenol	**20.35**	
AA30	2,3,4,5,6-$(CN)_5$-Toluene	**20.14**	
AA31	$(2,4,6\text{-}Cl_3\text{-}C_6F_2)(C_6F_5)CHCN$	**20.13**	
AA32	2,3,5,6-F_4-Phenol	**20.12**	**4.2**
AA33	2,3,4,5,6-F_5-Phenol	**20.11**	**4.2**
AA34	$(2\text{-}C_{10}F_7)(C_6F_5)CHCN$	**20.08**	
AA35	1-$C_{10}F_7OH$	**19.72**	**3.3**
AA36	2,4,6-$(SO_2F)_3$-Aniline	**19.66**	
AA37	$(2\text{-}C_{10}F_7)_2CHCN$	**19.32**	
AA38	9-C_6F_5-Octafluorofluorene	**18.88**	
AA39	2-$C_{10}F_7OH$	**18.50**	**3.8**
AA40	$(4\text{-}CF_3\text{-}C_6F_4)(C_6F_5)CHCN$	**18.14**	
AA41	4-C_6F_5-2,3,5,6-F_4-Phenol	**18.11**	**4.0**
AA42	$(4\text{-}H\text{-}C_6F_4)CH(CN)COOEt$	**18.08**	
AA43	2,3,4,5,6-Cl_5-Phenol	**18.02**	
AA44	2,3,4,5,6-Br_5-Phenol	**17.83**	
AA45	$(C_6F_5)CH(CN)COOEt$	**17.75**	
AA46	4-Me-$C_6H_4CH(CN)_2$	**17.59**	
AA47	$(2\text{-}C_{10}F_7)CH(CN)COOEt$	**17.50**	
AA48	$(4\text{-}Cl\text{-}C_6F_4)CH(CN)COOEt$	**17.39**	
AA49	2,4-$(NO_2)_2$-Phenol	**16.66**	
AA50	4-CF_3-2,3,5,6-F_4-Phenol	**16.62**	**3.6**
AA51	$(4\text{-}NC_5F_4)(C_6F_5)CHCN$	**16.40**	
AA52	$(4\text{-}CF_3\text{-}C_6F_4)_2CHCN$	**16.13**	

Directly measured ΔpK_a values



AA52	(4-CF$_3$-C$_6$F$_4$)$_2$CHCN	**16.13**	
AA53	(4-CF$_3$-C$_6$F$_4$)CH(CN)COOEt	**16.08**	
AA54	(4-NC$_5$F$_4$)(2-C$_{10}$F$_7$)CHCN	**16.02**	
AA55	4-NC$_5$F$_4$-OH	**15.40**	
AA56	(4-NC$_5$F$_4$)CH(CN)COOEt	**14.90**	
AA57	3-CF$_3$-C$_6$H$_4$CH(CN)$_2$	**14.72**	
AA58	Saccharin	**14.57**	
AA59	4-Me-C$_6$F$_4$CH(CN)$_2$	**13.87**	
AA60	(4-NC$_5$F$_4$)$_2$CHCN	**13.46**	
AA61	C$_6$F$_5$CH(CN)$_2$	**13.01**	
AA62	4-H-C$_6$F$_4$CH(CN)$_2$	**12.98**	
AA63	2-C$_{10}$F$_7$CH(CN)$_2$	**12.23**	
AA64	Tos$_2$NH	**11.97**	
AA65	4-NO$_2$-C$_6$H$_4$CH(CN)$_2$	**11.61**	
AA66	4-MeO-C$_6$H$_4$C(=O)NHTf	**11.60**	
AA67	4-Me-C$_6$H$_4$C(=O)NHTf	**11.46**	
AA68	(C$_6$H$_5$SO$_2$)$_2$NH	**11.34**	
AA69	4-Cl-C$_6$H$_4$SO$_2$NHTos	**11.10**	
AA70	C$_6$H$_5$C(=O)NHTf	**11.06**	
AA71	Picric acid	**11.00**	
AA72	4-F-C$_6$H$_4$C(=O)NHTf	**10.65**	
AA73	2,3,4,5,6-(CF$_3$)$_5$-Phenol	**10.46**	
AA74	2,3,4,6-(CF$_3$)$_4$-C$_6$HCH(CN)$_2$	**10.45**	
AA75	4-Cl-C$_6$H$_4$C(=O)NHTf	**10.36**	
AA76	(4-Cl-C$_6$H$_4$SO$_2$)$_2$NH	**10.20**	
AA77	4-CF$_3$-C$_6$F$_4$CH(CN)$_2$	**10.19**	
AA78	4-NO$_2$-C$_6$H$_4$SO$_2$NHTos	**10.04**	
AA79	4-Cl-3-NO$_2$-C$_6$H$_3$SO$_2$NHTos	**9.71**	
AA80	4-NO$_2$-C$_6$H$_4$C(=O)NHTf	**9.49**	
AA81	4-NO$_2$-C$_6$H$_4$SO$_2$NHSO$_2$C$_6$H$_4$-4-Cl	**9.17**	
AA82	2,3,4,5,6-(CF$_3$)$_5$C$_6$CH(CN)$_2$	**8.86**	
AA83	TosOH	**8.5**	**2.9**
AA84	(4-NO$_2$-C$_6$H$_4$SO$_2$)$_2$NH	**8.19**	
AA85	2,4,6-(SO$_2$OCH$_2$CF$_2$CF$_2$H)$_3$-Phenol	**8.17**	
AA86	2,4,6-(SO$_2$OCH$_2$CF$_3$)$_3$-Phenol	**7.97**	
AA87	1-C$_{10}$H$_7$SO$_3$H	**7.89**	**2.9**
AA88	C$_6$H$_5$CHTf$_2$	**7.85**	
AA89	4-Cl-C$_6$H$_4$SO$_3$H	**7.2**	**2.9**
AA90	3-NO$_2$-C$_6$H$_4$SO$_3$H	**6.65**	**2.9**
AA91	4-NO$_2$-C$_6$H$_4$SO$_3$H	**6.60**	**2.9**
AA92	4-MeO-C$_6$H$_4$C(=NTf)NHTf	**6.41**	
AA93	4-Me-C$_6$H$_4$C(=NTf)NHTf	**6.18**	
AA94	TosNHTf	**6.17**	
AA95	C$_6$H$_5$C(=NTf)NHTf	**6.03**	
AA96	C$_6$H$_5$SO$_2$NHTf	**5.89**	
AA97	4-F-C$_6$H$_4$C(=NTf)NHTf	**5.66**	
AA98	4-Cl-C$_6$H$_4$C(=NTf)NHTf	**5.56**	
AA99	2,4,6-(SO$_2$F)$_3$-Phenol	**5.53**	
AA100	4-Cl-C$_6$H$_4$SO$_2$NHTf	**5.33**	
AA101	4-Cl-C$_6$H$_4$SO(=NTf)NHTos	**5.13**	
AA102	4-NO$_2$-C$_6$H$_4$C(=NTf)NHTf	**4.99**	
AA103	2,4,6-Tf$_3$-Phenol	**4.79**	
AA104	C(CN)$_2$=C(CN)OH	**4.69**	
AA105	4-NO$_2$-C$_6$H$_4$SO$_2$NHTf	**4.39**	
AA106	4-Cl-C$_6$H$_4$SO(=NTf)NHSO$_2$C$_6$H$_4$-4-Cl	**4.34**	
AA107	2,4-(NO$_2$)$_2$-C$_6$H$_3$SO$_3$H	**4.30**	
AA108	2,3,5-tricyanocyclopentadiene	**4.02**	
AA109	4-Cl-C$_6$H$_4$SO(=NTf)NHSO$_2$C$_6$H$_4$-4-NO$_2$	**3.62**	



The scale includes 109 acids that are interconnected by 273 relative acidity 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, phenylethylcyanoacetates, toluenes). 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 $\Delta \mathrm{p}K_\mathrm{a}$ measurements. The consistency standard deviation of the scale is $s = 0.06$ (or $s = 0.04$ if some of the measurements of the weakest acids are left out) $\mathrm{p}K_\mathrm{a}$ units. 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 AN.

Comparison of the literature pK_a values with those measured in this work. For several acids belonging to the scale, the $\mathrm{p}K_\mathrm{a}$ values in AN have been reported in the literature. From Table 5.2 and Figure 5.1, it is clearly seen that above picric acid, the weaker the acid the greater the difference of $\mathrm{p}K_\mathrm{a}$ 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 non-aqueous $\mathrm{p}K_\mathrm{a}$ 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 in general 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, CH acids actually form the backbone of the scale and most of the $\Delta \mathrm{p}K_\mathrm{a}$ 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 (**AA1**, **AA6**, **AA9**, **AA12**, **AA16**, **AA18**, **AA27**) have not been included in the scale during the minimization step (their $\mathrm{p}K_\mathrm{a}$ 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

Table 5.2: Comparison of the pK_a Values in AN Determined in This Work with Those Reported in the Literature

no.	acid	pK_a values in AN this work	lit.	difference
AA1	phenol	29.14	27.2[a]	+1.9
			26.6[b]	+2.5
AA18	acetic acid	23.51	22.3[a]	+1.2
			22.31[c]	+1.20
AA20	2-NO_2-phenol	22.85	22.0[b]	+0.9
			22.1[d]	+0.8
AA23	benzoic acid	21.51	20.7[a]	+0.8
AA24	9-CN-fluorene	21.36	20.8[e]	+0.6
AA33	2,3,4,5,6-F_5-phenol	20.11	19.5[f]	+0.6
AA35	1-C_10F_7OH	19.72	19.4[f]	+0.3
AA39	2-C_10F_7OH	18.50	17.8[f]	+0.7
AA43	2,3,4,5,6-Cl_5-phenol	18.02	17.2[f]	+0.8
AA49	2,4-$(NO_2)_2$-phenol	16.66	15.34[g]	+1.32
			16.0[b]	+0.7
			18.40[c]	–1.74
AA55	4-NC_5F_4-OH	15.40	15.2[f]	+0.2
AA71	picric acid[k]		11.0[h]	
AA83	TosOH	8.5	8.01[i]	+0.5
			8.73[c]	–0.2
AA108	2,3,5-$(CN)_3$-cyclopentadiene	4.02	3.00[j]	+1.02

[a] Reference 125. [b] Reference 15 [c] Reference 124. [d] Reference 126. [e] Reference 127. [f] Reference 118. [g] Reference 123. [h] Reference 33. [i] Reference 128. [j] Reference 107. [k] Anchor compound of the present scale.

acids as building blocks for the scale is their tendency to give very intense UV-vis spectra for the anions that are strongly different from the spectra of neutrals, thus enabling high-accuracy spectrophotometric measurement. Contrary to this, a great bulk of literature data[15,29,118–121] 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. The pK_a values in the lower end of the scale (below pK_a = 9) of paper IV have been corrected downwards by 0.1 to 0.15 pK_a units because of re-evaluation of some of the original experimental data.

Homoconjugation. AN has very low solvating ability for anions. This is the main reason homoconjugation of some anions is extensive in AN. Values of homoconjugation constants $\log K_{AHA}$ used in this work have been indicated in Table 5.1. The homoconjugation constants used in the ΔpK_a

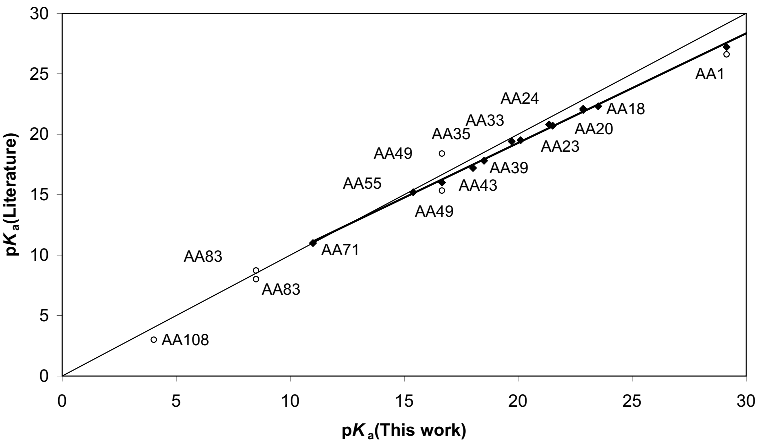


Figure 5.1: Correlation of acidities of the studied acids and acidities reported in the literature. Narrow line corresponds to the ideal correlation with zero intercept and unity slope. The thick line corresponds to the actual situation. Compounds indicated by empty circles have been left out from the correlation. The correlation is: pK_a(lit.) $= 1.17 + 0.906$ pK_a(this work); s(intercept) $= 0.33$, s(slope) $= 0.016$, $n = 13$, $r^2 = 0.997$, $S = 0.244$.

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 **AA41** and **AA47** when varying the logK_AHA from 3.8 to 4.2 is only 0.02 pK_a units (the logK_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 logK_AHA is varied by 0.5 units. In this case, around 10% of the acid was in the form of the homoconjugate complex. From this it can be seen that at used concentrations (n$\cdot 10^{-5}$ M) the homoconjugation constants in the range of n$\cdot 10^3$ cannot be estimated reliably. The values of homoconjugation constants were estimated taking the literature values as initial guesses, still some of the literature values were not suitable for the calculations. It has to be stressed that as the homoconjugation constants used in this work were not measured directly but just estimated, they have to be treated with caution.

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 units . The stronger phenols in the scale **AA71**, **AA73**, **AA85**, **AA86**, **AA99** and **AA103** do not form homoconjugate complexes under our experimental conditions. The stabilities of homoconjugate complexes of phenols increase as the acid strength decreases.[29] There are some exceptions. 2-Nitrophenol (**AA20**) has no remarkable ability to form homoconjugate 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 **AA29**, **AA43** and **AA44** also do not form homoconjugate complexes, probably chlorine and bromine in the *ortho* position are responsible for that. Fluorine substituent in the *ortho* position does not prevent homoconjugation (for example, compounds **AA32**, **AA33**, **AA41**, **AA50** and **AA55**). The reason 1- and 2-perfluoronaphthols (**AA35** and **AA39**) have lower homoconjugation constants than, for example perfluorophenol (**AA33**) or 2,3,5,6-tetrafluorophenol (**AA32**), 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.[118]

Connecting pK_a Scales of Acids of Different Charge Type in AN. In this work self-consistent acidity and basicity scales in AN have been set up (see section 4.1.). The scales of neutral acids and cationic acids are in fact subunits of one and the same common acidity scale. They have been treated separately because of the simplicity of calculating ΔpK_a values for acids of identical charge type. Proton transfer reaction between neutral acid and neutral base according to equation 5.1 leads to the equation 5.2 for ΔpK_a values:

$$\mathrm{HA} + \mathrm{B} \overset{\Delta K_a}{\leftrightarrows} \mathrm{A}^- + \mathrm{HB}^+ \tag{5.1}$$

When calculating the relative acidity of a neutral and cationic acid according to equation 5.1 then the assumption that the ratios of the activity coefficients are equal is not valid any more and the ΔpK_a value is calculated using activities:

$$\Delta \mathrm{p}K_a = \mathrm{p}K_a(\mathrm{AH}) - \mathrm{p}K_a(\mathrm{HB}^+) = \log \frac{a(\mathrm{HA}) \cdot a(\mathrm{B})}{a(\mathrm{HB}^+) \cdot a(\mathrm{A}^-)} \tag{5.2}$$

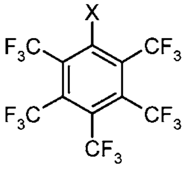
Attempt was made to connect the set up acidity scale with the revised basicity scale. ΔpK_a measurements between neutral and cationic acids were carried out. The average difference between the directly measured ΔpK_a value and the differences calculated from the assigned pK_a values is 0.05 pK_a units, meaning that the pK_a scale of bases (cationic acids) is shifted by 0.05 pK_a units downwards relative to the pK_a scale of neutral acids. However, the root mean square (rms) difference is 0.10 pK_a units. In general, the individual differences are less than 0.10 pK_a units. The most deviating measurements are those that involve compounds with rather localized negative charge on the anion (sulfonic acids). As a conclusion, the two scales can be considered satisfactorily interconnected. The interconnection has some uncertainty that is the best estimated from the rms difference. This means that when the pK_a value of a compound is estimated from measurements with references of different charge type, an additional uncertainty of *ca* 0.1 pK_a units (at standard deviation level) has to be taken into account.

The Scales as a Tool for Further Acid-Base Studies. The acidity and basicity scales as a collections 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 (see section 4.1.) has already found useful application for measuring pK_a values of calixarenes.[129] The same UV-vis spectrophotometric method has been used for measuring pK_a values of azobenzene dyes.[130] We envisage that the present acidity 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 (**AA71**), 2,3,4,5,6-$(CF_3)_5$-phenol (**AA73**), 2,4,6-Tf_3-phenol (**AA103**)), 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.

5.2. Syntehsis, Structure and Acidity of Some Poly(trifluoromethyl)phenyl Derivatives

Fluorination of organic compounds is gaining more and more importance in drug design, materials development, *etc.*[131–133] A particularly interesting group of fluorinated compounds are the polytrifluoromethylated compounds. Compared to polyfluorination, polytrifluoromethylation of aromatic compounds significantly increases molecular size and steric strain. Bulky 2,6-bis(trifluoromethyl)phenyl and 2,4,6-tris(trifluoromethyl)phenyl substituents have proved very useful in stabilizing reactive species and have allowed the isolation and characterization of several free radicals, carbenes, carbenoids and WCAs.[98,134–143] Due to the buttressing effect of the two *meta*-CF_3 substituents (presence of *meta*-CF_3 groups prevents the *ortho*-CF_3 groups from bending), pentakis(trifluoromethyl)phenyl ($C_6(CF_3)_5$) group has to be superior over 2,6-bis(trifluoromethyl)phenyl and 2,4,6-tris-(trifluoromethyl)phenyl substituents as kinetic stabilizer. The same effect of $C_6(CF_3)_5$ group should also lead to increased electron donating ability of the fluorine lone pairs of the *ortho*-CF_3 substituents to the electron-deficient center. On the other hand, the general electron-withdrawing effect of the $C_6(CF_3)_5$ group has to be superior to that of 2,6-bis(trifluoromethyl)phenyl and 2,4,6-tris(trifluoromethyl)phenyl substituents.

Table 5.3: Numbering of Pentakis(trifluoromethyl) Derivatives



1 $X = OH$
1a $X = O^-$
1b $X = O\cdot$
2 $X = CF_3$
3 $X = H$
3a $X = (\cdot\cdot)^-$
4 $X = Cl$
5 $X = NH_2$
5a $X = NH^-$
6 $X = CH_3$
6a $X = CH_2^-$
7 $X = CH(CN)_2$
7a $X = C(CN)_2^-$

A general route to functionalized $C_6(CF_3)_5$ derivatives (see Table 5.3 for numbering), promising building blocks for designing novel carbenes, superacids, WCAs and other practically and theoretically useful species, is shortly presented in this section (see V). A general approach for introduction of perfluoroakyl groups into different compounds has been published[144–149] and a number of polytrifluoromethylated aromatic compounds are known[150–154] but no general method to synthesize pentakis(trifluoromethyl) arenes has not been published to date. In this work a pertrifluoromethylation route was developed that proceeds *via* conveniently pregenerated (trifluoromethyl)copper (CF_3Cu) species in DMF, stabilized by addition of 1,3-dimethyl-2-imidazolidinone (DMI) or N-methyl-2-pyrrolidinone (NMP). Pregeneration of CF_3Cu species is based on Ruppert-Prakash reagent CF_3SiMe_3 as the source of CF_3 group. These species react with hexaiodobenzene C_6I_6 at ambient temperature to give the potassium pentakis-(trifluoromethyl)phenoxide ($\mathbf{1a{\cdot}K^+}$) along with hexakis(trifluoromethyl)-benzene (**2**) and pentakis(trifluoromethyl)benzene (**3**) in a combined yield of 80%. Vacuum sublimation from the mixture of $\mathbf{1a{\cdot}K^+}$ and concentrated sulfuric acid affords hitherto unknown highly acidic and hindered pentakis(trifluoromethyl)phenol (**1**). **1** gives rise to easily functionalized pentakis(trifluoromethyl)chlorobenzene (**4**) and pentakis(trifluoromethyl)-aniline (**5**). Pertrifluoromethylation of pentaiodochlorobenzene and pentaiodotoluene allows straightforward access to pentakis(trifluoromethyl)-chlorobenzene (**4**) and pentakis(trifluoromethyl)toluene (**6**), respectively (see Figure 5.2).

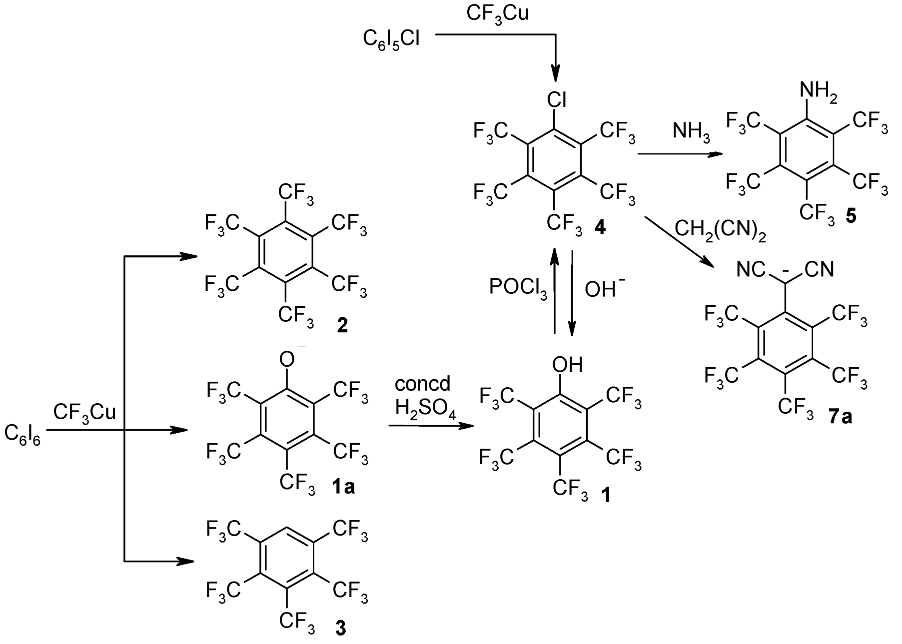


Figure 5.2: General Synthesis Route to Pentakis(trifluoromethyl)aryl Compounds

XRD structures of several $C_6(CF_3)_5$ derivatives were determined and compared with the calculated structures. Due to the steric crowding the aromatic rings in all $C_6(CF_3)_5$ derivatives are significantly distorted. The gas-phase acidities and pK_a values in different solvents (AN, DMSO, water) for these compounds and a number of related compounds have been measured. The origin of the acidifying effect of the $C_6(CF_3)_5$ group has been explored using the isodesmic reactions approach. Introduction of five CF_3 groups into moderately to weakly acidic compounds, such as phenol, aniline and toluene significantly increases their acidity.

Structure of pentakis(trifluoromethyl)derivatives. In 1976, when the XRD structure of $C_6(CF_3)_6$ was determined,[155] the first time it was noticed that benzene ring is distorted due to the bulky substituents. CF_3 groups are bent up and down by 12° from the plane formed by the ring atoms. The structure of pentakis(trifluoromethyl) derivatives – **1** and **1a**; **5** and **5a**; **6** and **6a** (XRD and computational study) is very similar, benzene ring is slightly bent, the rings in the anions are more distorted than in neutrals. The molecules have chair-like conformation, The CF_3 groups are alternately twisted out of the aromatic plane up to 27°, whereas in the case of neutrals the *para*-CF_3 group is the most distotred and in the case of anions *ortho*-CF_3 groups are the most distorted. *Ipso*-*ortho* bondlengths

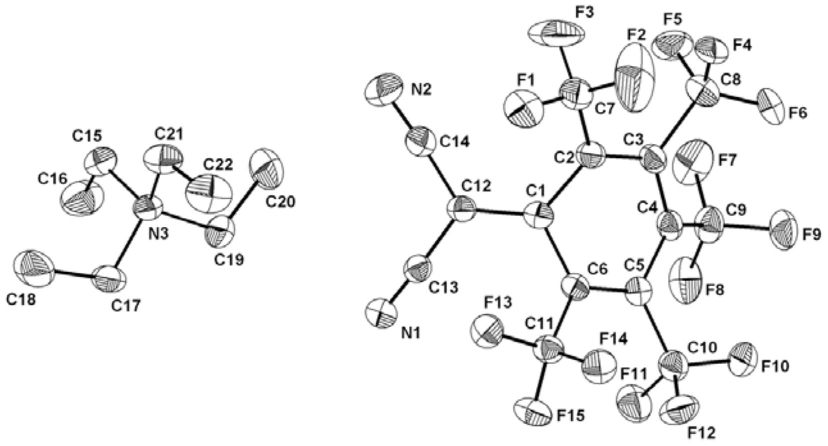


Figure 5.3: Molecular structure of $\mathbf{7a} \cdot \mathbf{Et_4N^+}$ with 50% thermal ellipsoids (hydrogen atoms of $\mathbf{Et_4N^+}$ cation are omitted for clarity. Selected bond distances (Å), angles (deg) and dihedral angles (deg): C1-C12 1.390(2), C1-C2 1.447(2), C1-C6 1.452(2), C2-C1-C6 112.15(12), C3-C4-C5 116.87(13), C13-C12-C14 112.25-(12), C14-C12-C1-C2 -4.27(24), C1-C2-C3-C4 -11.92(21), C1-C6-C5-C4 9.09(20).

in aromatic ring is considerably elongated compared to the other ring bond lengths even by up to 0.10 Å, it is especially apparent in the case of anions. One of the C-F bonds in CF_3 group is longer at the expense of the other two. The nearest F-F distances between the adjacent CF_3 groups are in 2.5 Å range, which is less than 2.70 Å, twice the generally accepted value for the fluorine van der Waals radius (1.35 Å). Generally, the geometries of the anions are similar to each other and the geometries of the neutrals are similar to each other.

Contrary to the anions **1a**, **5a** and **6a**, the computational geometry of the anion **3a** is not chairlike, but strongly twisted. The twist is so strong that it is impossible to define any plane similar to one defined for the other compounds. This strong distortion renders it impossible to rigorously assess the out-of-plane distortion of the CF_3 groups. The closer look reveals the tendency of the *ortho*-CF_3 groups to assume perpendicular orientation and indicates somewhat allenic character of the *ipso*-carbon.

The anion **7a** (Figures 5.3 and 5.4) has significantly more deformed aromatic ring than **1a**. In particular, the malononitrile fragment $C(CN)_2^-$ together with the *ipso*-carbon C1 are strongly forced out of the C2-C3-C5-C6 (the numeration is indicated in Figure 5.3) plane by the two *ortho*-CF_3 groups: the angle between this and the C1-C2-C6 plane is 35.3°. At the same time, the angle between the C1-C2-C6 plane and the bond C1-C12 is

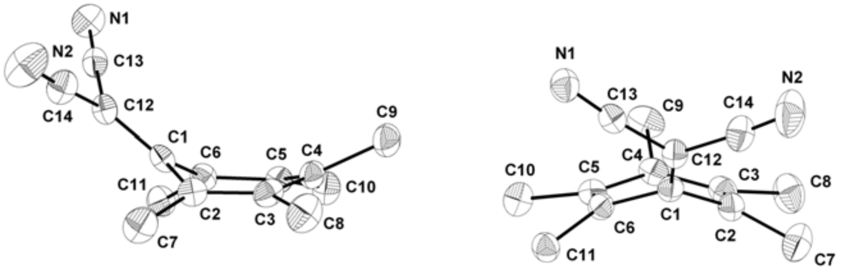


Figure 5.4: Molecular structure of **7a** · $\mathbf{Et_4N^+}$ with 50% thermal ellipsoids to demonstrate non-planarity of the aromatic ring and out of plane positions of the CF_3 groups ($\mathbf{Et_4N^+}$ cation and all fluorine atoms are omitted for clarity).

only 3.8° and the whole C1-C2-C6-C12-C13-C14-N1-N2 moiety (see Figure 5.3) is nearly planar. This is the reason for the abovementioned strong deformation – there is strong resonance within this moiety. Bonds C1-C2 and C1-C6 are considerably longer compared to the other bonds in aromatic ring, being 1.45 Å, whereas the other bonds in the ring are in range of 1.39–1.42 Å. The angle of C2-C1-C6 is also lower than is typical to aromatic ring: 112.1(1)°. The locations of the CF_3 groups are slightly different from **1a**: instead of being displaced alternately up and down from the ring the four *ortho-* and *meta-*CF_3 groups are on the opposite side of the aromatic ring with respect to the $C(CN)_2^-$ fragment while the *para-*CF_3 group is on the same side. Differently from **1a**, the aromatic ring in this case is not chairlike but boatlike. The bond lengths and angles in the CF_3 groups are not much different from **1a**. The differences between the XRD and computational geometries of **7a** are more pronounced. The ring of the computational structure of **7a**, differently from the boat geometry observed by XRD, displays an asymmetric chair geometry: C1 is out of the C2-C3-C5-C6 plane by 0.371 Å (0.468 Å according to XRD), while C4 is out of the plane to the opposite side by only 0.043 Å (0.232 Å to the same side according to XRD). Concurrently, differently from the XRD geometry, the computational structure of **7a** has alternating displacement of the CF_3 groups from the C2-C3-C5-C6 plane. The computed geometry of the moiety composed of the C1-C2-C6 fragment and the $C(CN)_2^-$ group is rather similar to the experimental one. The structure of neutral **7** is similar to the other neutral compounds. The aromatic ring is only slightly distorted, the CF_3 groups are slightly out of plane. When comparing the $C(CN)_2^-$ and $CH(CN)_2$ groups in **7a** and **7** it is evident that two CN groups in **7** are not on the same plane with aromatic ring but oriented almost perpendicularly to the ring to incur the least possible steric destabilization.

Acidity. The results of experimental and computational acidity determination of **1**, **5**, **6**, **7** and a number of related compounds in different media are given in Table 5.4 and Table 5.1 (all compounds measured in AN have been included into the AN acidity scale Table 5.1 and have been numbered differently than in this section, **1** = **AA73**, **5** = **AA13**, **6** = **AA2**, **7** = **AA82**). pK_a measurement of **3** was unsuccessful in all condensed media except in DMSO. It is interesting to compare the acidity of compounds containing $C_6(CF_3)_5$ group with acidities of compounds containing pentacyano- and trinitrophenyl groups. From Tables 5.1 and 5.6 it is seen that three nitro groups and five CF_3 groups have nearly the same influence to an acidity but much less compared to five cyano groups (we can compare phenols, **AA71**, **AA73** and **AD7** (approximately 3.5 pK_a units in AN) and toluenes, **AA2** and **AA30**).

Acidities of 1, 5, 6 and 3 in the Gas Phase. As is seen from Table 5.4 the acidities of the $C_6(CF_3)_5$ substituted compounds decrease in the following order in all media where comparison is possible: **1** > **5** > **6** > **3**. The acidity differences between the three consecutive pairs of compounds **1**, **5**; **5**, **6**; and **6**, **3** are significantly smaller (12.9, 8.1 and 13.7 kcal/mol in the gas phase, respectively) than in the case of the unsubstituted parent compounds (16.8, 14.6 and 19.5 kcal/mol in the gas phase, respectively), reflecting the decrease of importance of the first atom of the protonation center compared to the substituted aromatic nucleus. The only condensed phase, where similar comparison can be carried out, is DMSO. In DMSO the same differences between pairs **1**, **5** and **5**, **6** (data for **3** are not available) in the case of substituted compounds are 10.48 and 2 pK_a units and in the case of unsubstituted compounds 12.6 and 12.4 pK_a units. Particularly noteworthy is the remarkable strength of **6** in this solvent compared to **5**; the latter is only by 2 pK_a units stronger.

Normally the effect of stepwise introduction of multiple electron-acceptor substituents into the phenol aromatic ring of phenol does not display additive behavior; the gross effect of the introduction of the substituents is usually smaller than the sum of single substituent effects. This is attributable to the saturation of the substituent effects and has been extensively discussed, *e.g.* in ref 112. For small substituents, notably fluorine, it can also be observed that the gross acidifying effect of multiple substituents in polysubstituted compounds is larger than the additive sum of single substituent effects. There are five bulky substituents in the molecules of **1**, **3**, **5** and **6**. Thus, there is every reason to expect a less-than-additive behavior. In the gas-phase this is really the case for **1**, **3**, **5** and **6**: according to both experimental and computational results the gross acidifying effect of the

Table 5.4: Results of Experimental and Computational (DFT B3LYP 6-311+G**) Acidity Determinations in Different Media[a]

compound	ΔG_{acid} (exp)	ΔG_{acid} (calcd)	pK_{a} (AN)	pK_{a} (DMSO)	pK_{a} (water)
Phenols					
$C_6(CF_3)_5OH$ (**1**)	298.7	290.2	10.46	3.1	1.32
4-CF_3-phenol	330.1[b]	325.2	25.54	14.6	8.68[c]
3-CF_3-phenol	332.4[b]	328.2	26.50	15.1	8.95[c]
2-CF_3-phenol	332.2	327.1	24.88	14.4	8.42
3,5-$(CF_3)_2$-phenol	322.9[b]	318.3	23.78	13.2	8.26
phenol	342.3[b]	339.2	29.14	18.0[d]	9.95[c]
Anilines					
$C_6(CF_3)_5NH_2$ (**5**)	310.8[b]	312.2	24.59	12.5	
4-CF_3-aniline	346.0[b]	345.1		27.0[e]	
3-CF_3-aniline	349.6[b]	348.8		28.2[e]	
2-CF_3-aniline		347.1			
3,5-$(CF_3)_2$-aniline	340.6[b]	338.7		25.7[e]	
aniline	359.1	359.4		30.6[d]	
Toluenes					
$C_6(CF_3)_5CH_3$ (**6**)	318.9	317.6	28.7[g]	13.9	
4-CF_3-toluene	359.8	357.7			
3-CF_3-toluene	362.0	363.0			
2-CF_3-toluene		359.9			
3,5-$(CF_3)_2$-toluene	354.3	352.0			
toluene	373.7	374.9		43[d]	
Benzenes					
$C_6(CF_3)_5H$ (**3**)	331.1[f] 328.4[h]	332.4		20[g]	
4-CF_3-benzene		380.1			
3-CF_3-benzene		380.8			
2-CF_3-benzene	379.0[i]	378.2			
1,3-$(CF_3)_2$-benzene	365.0[i]	363.6			
benzene	390.9[b]	393.3			
Phenylmalononitriles					
$C_6(CF_3)_5CH(CN)_2$ (**7**)		280.9	8.86		
2,3,4,6-$(CF_3)_4$-$C_6HCH(CN)_2$		286.8	10.45		

[a] This work, if not specified otherwise. [b] Reference 156. [c] Reference 122. [d] Reference 28. [e] Reference 157. [f] Approximate value from one single measurement (± 1 kcal/mol). [g] Approximate value (± 1 pK_{a} units). [h] Value obtained from the correlation of pK_{a} value of THF/Et_2O/DME *vs.* ΔG_{acid} value. [i] Reference 158.

five CF_3 substituents forms around 80% of the sum of the acidifying effects of the single substituents in **1**, **5** and **6**. In **3** there is 88% additivity. It is of interest to analyze the acidifying effect of the five CF_3 substituents in order to get some insight into the acidity of these rather peculiar molecules. We use the method of isodesmic reactions.[159] The acidity of a $C_6(CF_3)_5$ substituted derivative $C_6(CF_3)_5X$, denoted as $\Delta G_{\text{acid}}(C_6(CF_3)_5X)$, can be calculated from the acidity of the unsubstituted compound $\Delta G_{\text{acid}}(C_6H_5X)$ and the acidifying-deacidifying effects of different interactions as follows:

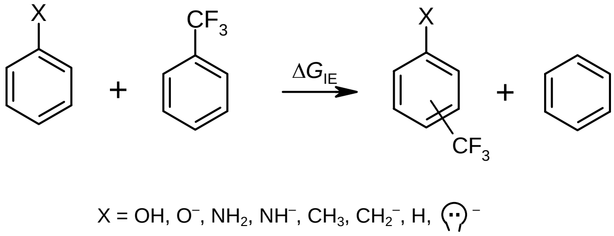
$$\begin{aligned}\Delta G_{\text{acid}}(\mathrm{C_6(CF_3)_5X}) = \Delta G_{\text{acid}}(\mathrm{C_6H_5X}) + \Delta\Delta G_{\text{GAIE}} + \\ + \Delta\Delta G_{\text{S}} + \Delta\Delta G_{\text{RCC}} + \Delta\Delta G_{\text{RCX}}\end{aligned} \tag{5.3}$$

The $\Delta\Delta G$ value in equation 5.3 are defined as follows:

$$\Delta\Delta G = \Delta G(\text{anion}) - \Delta G(\text{acid}) \tag{5.4}$$

- ΔG_{GAIE} (defined *via* equation 5.6) is the estimate of the gross interaction energy between the reaction center and the CF_3 substituents in the idealized pentasubstituted molecule where there are no steric or other interactions between the CF_3 groups and the interactions between the CF_3 groups and the reaction center are just as strong as in the respective monosubstituted molecules. The steric interaction in twice the extent present in 2-CF_3-C_6H_4X is also included in ΔG_{GAIE}.
- ΔG_{S} is the energy contribution due to saturation of the substituent effects.
- ΔG_{RCC} is the energy contribution due to steric repulsion between the CF_3 groups.
- ΔG_{RCX} is the energy contribution due to additional steric repulsion between the two CF_3 groups in position 2 and the group X (or its deprotonated form). The additional contribution has two reasons: (1) in the pentakis-substituted derivative there are simultaneously two CF_3 groups in positions 2 and 6, and (2) there are CF_3 groups also in positions 3 and 5 that reduce the flexibility of the 2- and 6-CF_3 groups.

The ΔG_{GAIE} contributions can be estimated from the following series of reactions:

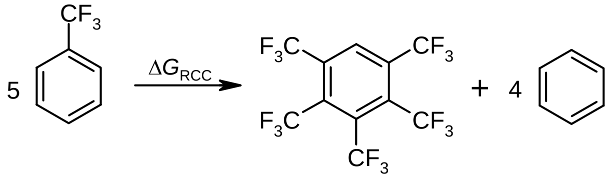


(5.5)

The energy effects of this reaction with the 1,2-, 1,3- and 1,4-product can be summarized as follows, directly providing the ΔG_{GAIE}:

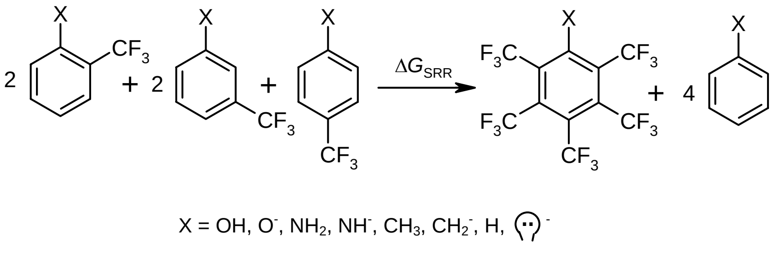
$$\Delta G_{\text{GAIE}} = \Delta G_{\text{IE}}(1,4) + 2\Delta G_{\text{IE}}(1,3) + 2\Delta G_{\text{IE}}(1,2) \tag{5.6}$$

The ΔG_{RCC} is found *via* the following equation:



(5.7)

Since the group X is not involved in this reaction this contribution is the same in all species leading to $\Delta G_{\text{RCC}} = 0$ kcal/mol. No single isodesmic reaction equations can be written for obtaining the remaining two ΔG contributions: the contributions $\Delta G_{\text{S}} + \Delta G_{\text{RCX}}$ can in the framework of this isodesmic reaction approach be estimated only jointly. The following series of reactions was used:



(5.8)

The negative free energy change of these reactions can be expressed as follows:

$$\Delta G_{\text{SRR}} = \Delta G_{\text{S}} + \Delta G_{\text{RCC}} + \Delta G_{\text{RCX}} \tag{5.9}$$

Table 5.5: Results of Analysis According to Equation 5.3 (all Values are in kcal/mol)[a]

	1	**5**	**6**	**3**
Contributions from isodesmic reactions equations 5.6–5.10				
ΔG_{GAIE}(neutral)	3.8	–0.9	6.9	0
ΔG_{GAIE}(anion)	–56.5	–60.9	–63.9	–68.5
ΔG_{GAIE}	–60.3	–60.0	–70.8	–68.5
ΔG_{RCC}(neutral, anion)	56.0	56.0	56.0	56.0
ΔG_{S}(neutral)+ΔG_{RCX}(neutral)	5.0	6.9	6.4	0
ΔG_{S}(anion)+ΔG_{RCX}(anion)	16.3	19.7	20.0	7.6
$\Delta\Delta G_{\mathrm{S}}$+$\Delta\Delta G_{\mathrm{RCX}}$	11.3	12.8	13.5	7.6
Contributions estimated from additional approximations				
ΔG_{S}(neutral)	0	0	0	0
ΔG_{S}(anion)	11.3	12.8	13.6	7.6
ΔG_{RCX}(neutral)	5.0	6.9	6.4	0
ΔG_{RCX}(anion)	5.0	6.9	6.4	0
Gross acidifying effects				
computational	–49.0	–47.2	–57.3	–60.9
experimental	–48.5	–48.3	–54.8	–62.5

[a] Enthalpies would be preferred in the analysis by isodesmic reactions. See section 2.6. for explanation.

From equations 5.7 and 5.9 follows that

$$\Delta G_{\mathrm{S}} + \Delta G_{\mathrm{RCX}} = \Delta G_{\mathrm{SRR}} + \Delta G_{\mathrm{RCC}} \tag{5.10}$$

The results of the analysis according these equations are presented in Table 5.5.

The ΔG_{GAIE} contributions in the anions of **1**, **3**, **5** and **6** are vastly larger than in the neutrals and change monotonously when moving from **1a** to **5a** to **6a** to **3a** indicating increase in stabilization of the anion in the row. It is interesting that the ΔG_{GAIE} in **3a** is by 4.6 kcal/mol more negative than in **6a**, in spite of the seemingly unfavorable geometry (from the point of view of resonance and hyperconjugation[160] stabilization) of the free electron pair of the anion **3a**. When looking at the contributions of the individual substituents then it is evident that this is first of all caused by the large stabilizing interaction with the two CF_3 groups in positions 2 and 6: -15.1 kcal/mol (per one CF_3 group). This value is clearly the most negative in the row followed by -11.8 kcal/mol of **6a**. Most likely, thereason is twofold: (1) the lack of steric repulsion between the deprotonated acidity center and the 2-CF_3 groups and (2) the shorter distance (2 bonds, *vs.* 3 bonds in **1a**, **5a** and **6a**) between the acidity center and the 2-CF_3 substituents.

Contrary to this the gross additive interaction energies of five CF_3 substituents in the neutrals display complex behavior. The effect is destabilizing in the case of **1** and **6**. This is primarily due to the destabilizing effect of the 2-substitution in **1** (1.6 kcal/mol) and **6** (3.2 kcal/mol) and is not compensated by the weak stabilizing effect of 4-substitution (-0.6 and -0.2 kcal/mol, respectively). 3-substitution shows slight destabilizing effect in both **1** and **6** (0.6 and 0.4 kcal/mol, respectively). In **5**, the effect of 2-substitution is weakly destabilizing (0.8 kcal/mol) but it is compensated by the stabilizing effects of 3- (-0.4 kcal/mol) and 4-substitution (-1.6 kcal/mol). As a result, the ΔG_{GAIE} contributions do not change monotonously from **1** to **3**. Instead, the effects of **1** and **5** are very similar and significantly lower than in the case of **6**. From the analysis we may conclude that the acidifying effect in **5** is lower mainly because the interaction energy between the CF_3 substituents and the acidity center -NH_2 is significantly more negative than in the case of -OH or -CH_3. The observed acidifying effects, both experimental and computational, follow the trend. Obviously, as the ΔG_{GAIE} is defined by equation 5.10, $\Delta G_{\mathrm{GAIE}}(\mathbf{3}) = 0$ kcal/mol.

In order to separate the joint contributions $\Delta G_{\mathrm{S}} + \Delta G_{\mathrm{RCX}}$ into components we use the following additional approximations.

1. As seen from the ΔG_{GAIE} values of the neutrals **1**, **3**, **5** and **6**, the interaction energies in them are small. We can therefore assume that the effect of saturation of the interaction energy is still a lot smaller and thus forms a negligible part of the joint contribution $\Delta G_{\mathrm{S}} + \Delta G_{\mathrm{RCX}}$ in the neutrals, that is $\Delta G_{\mathrm{S}}(\text{neutral}) = 0$ kcal/mol.

2. Geometries of the neutrals and anions of **1**, **5** and **6** are similar. Proton abstraction does not markedly change the geometry of **1**, **5** and **6** or release the steric strain. This claim is confirmed by the geometry analysis (see above). Thus we may assume that as a first approximation the steric destabilization effects in the neutrals and the anions are equal: $\Delta G_{\mathrm{RCX}}(\text{neutral}) = \Delta G_{\mathrm{RCX}}(\text{anion})$. The only exception is the anion **3a**.

From the above analysis and from the geometries of the species it is possible to draw the following principal conclusions:

1. The abrupt changes in the acidifying effects of five CF_3 groups in phenol, aniline and toluene are caused by the complex behavior of the neutrals, not the anions.

2. The effect of release of steric strain on deprotonation is of minor importance: the steric distortion of the molecules **1**, **5** and **6** does not change significantly with deprotonation. Instead, the *ca* 80% additivity of the effect of substituents on acidity is primarily caused by saturation of the substituent effects. However, the saturation may well have the steric distortion of the anion as a major cause.

3. The low acidity of **3** is not caused by inefficiency of the substituents in stabilizing the anion as might be expected from the classic substituent effect considerations but by the very low acidity of the parent compound, C_6H_6. The acidifying effect of the five CF_3 substituents in **3** is in fact the highest in the row **1-5-6-3**. This is remarkable because the anion **3a** is the least planar of the anions in the row **1a-5a-6a-3a**.

At the same time, the measured and in this work calculated ΔG_{acid} value of compound **3** is in a very good agreement with the results of gas-phase acidity measurements[156,158] of eight mono- to 1,2,4,5-tetrakis(trifluoromethyl) substituted benzenes for which also the additivity of the substituent effects (**3** included) is observed.

Acidities of 1 and 7 in Condensed Phase. Contrary to the gas phase, the acidity of **1** in all condensed media (no comparison is possible for **5**, **6** and **3** due to lack of data) considered is either close (AN 107%, DMSO 91%) to that predicted from fractional additivity or even surpasses it (H_2O 133%). Surely, all the above-discussed effects are also in operation in condensed phase and the (apparent) additivity has to be caused by solvation. The higher than expected solution acidity can be due to either additional stabilization of the anion or the absence of some factor stabilizing the neutral (in both cases with respect to the respective monosubstituted compounds). It is difficult to see how **1a** can be efficiently stabilized by solvation: the charge is delocalized across the large anion and the phenoxide group is hidden between the bulky CF_3 groups. Contrary to that the neutral **1** has extremely polarized O-H bond and is in principle a powerful hydrogen-bond donor. This hydrogen-bond donating ability, however, is almost lost due to two *ortho*-CF_3 groups. This leaves the neutral poorly solvated compared to the singly substituted phenols. We thus suggest that the higher-than-expected solution acidity of **1** is not due to an extra stabilization effect of **1a** but is caused by the lack of possibility of stabilizing the neutral by hydrogen-bond. This hypothesis is partially supported by the observation that the non-additivity is especially pronounced in H_2O, which is the strongest hydrogen-bond acceptor of the three solvents. The acidity of **7** is lower than would be expected based on the acidity data of different substituted phenylmalononitriles (lack of data does not allow exact calculation of additivity). The lower than expected acidity is easily rationalized considering that the aromatic ring is only slightly distorted in the neutral and is very strongly distorted in the anion. The reasons leading to lowered acidity are destabilization of the anion *via* reduced aromaticity of the ring and less-than-optimal resonance delocalization of the negative charge.

In conclusions it is possible to say that five trifluoromethyl groups in a phenyl ring lead to a considerable increase of acidity compared to unsubstituted derivatives. Calculations show that their influence is practically the same as that of three nitro groups but definitely weaker than that of five cyano groups.

5.3. Acidity Scale in 1,2-Dichloroethane

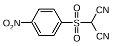
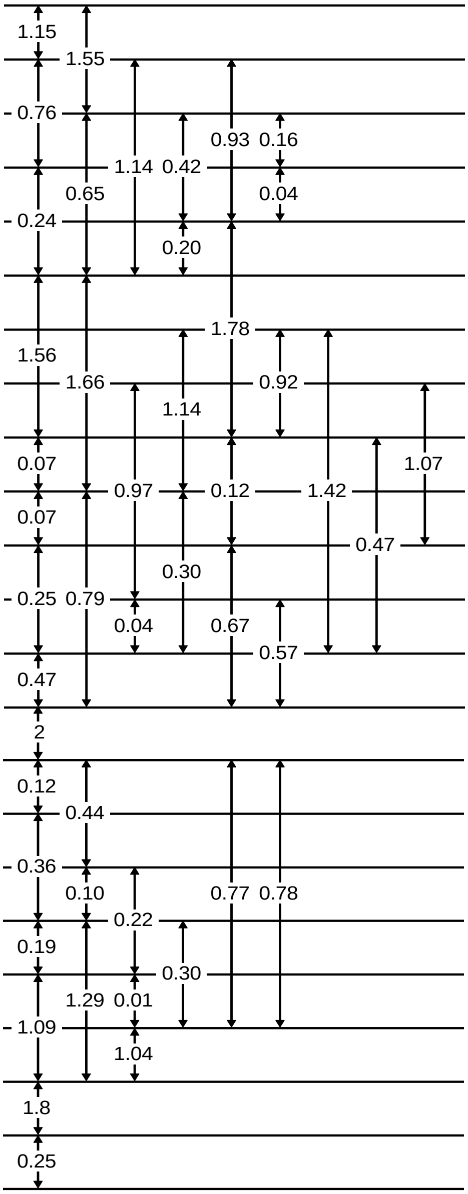
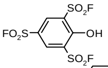
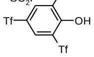
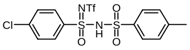
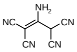
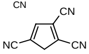
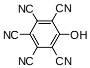
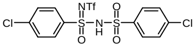
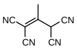
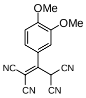
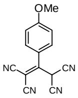
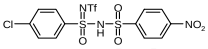
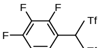
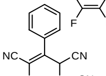
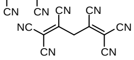
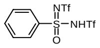
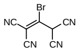
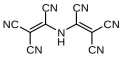
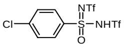
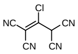
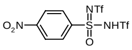
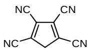
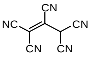
Acids of very high strength and their derivatives are receiving increasing attention.[96,161] Anions of superacids (WCAs) are of key importance as counterions in catalysts and charge carriers in electrochemical power sources.[99,100] Although, not many consistent acidity-basicity data are available for acid-base equilibria involving superacids.[28,29,122] For many traditional superacids there are acidity estimates (usually H_0 values) available, for most of the novel superacids there are none. In addition, the H_0 value of every acid refers to a different medium (usually neat acid or its mixture with water, HF, *etc.*). While very useful for characterizing the acidity of the acids as media the H_0 values are less suitable for characterizing the acids as individual compounds or for analysing of dependence of acidity on molecular structure. The available data are fragmentary and often serious discrepancies exist between the data from different laboratories (see section 5.1. and IV for examples). Recently an IR-spectroscopic scale of ion-pairing ability of superacid anions with trioctylammonium ion was reported by the Reed group.[113] Although being very useful in characterizing anions of superacids and providing implications of the acidity of the parent acids, that scale is not an equilibrium acidity scale and characterizes the anions rather than their parent acids. Accurate self-consistent scales of superacids in different solvents of constant composition would be desirable as these would enable rigorous analysis of structure and solvent effects on acidity. Such scales are available but mostly for acids of moderate strength and do not extend into the realm of superacids. In this work (see section 5.1.) extensive self-consistent acidity scale in AN including also a dozen of superacids is presented. However, due to basicity of AN this solvent cannot be used for expanding the scale towards stronger superacids.

Search for a suitable solvent for setting up a self-consistent acidity scale of superacids has led us to DCE. This solvent is inert, has very low basicity and at the same time is one of the most polar chloroalkanes ($\epsilon_\mathrm{r} = 10.6$), thus suitable for studies of ionic equilibria involving superacids. It is readily available and has good solvent properties, also for many ionic compounds. At the same time the inertness of DCE is expected to invoke several problems in acidity measurements: side-processes like ion pair formation and homoconjugation are expected to be much more extensive in DCE than in AN. The acidities directly measured in DCE are ion-pair acidity measurements. DCE is also more likely affected by impurities like traces of water. In the course of this work it was established that it is possible to use the UV-Vis spectrophotometric method studing of acid-base equilibria in DCE and that it is possible to compose self-consistent scale of $\mathrm{p}K_\mathrm{ip}$ in DCE. The first segment of the scale spanning for 10 $\mathrm{p}K_\mathrm{ip}$ units and containing 23 acids has been created. *Till now it is the most acidic equilibrium acidity scale that has been composed in a medium of constant composition.* The consistency parameter of the whole scale is $s = 0.11$ units, this value will decrease to $s = 0.04$ units if compounds with pyridinium counterion **AD4**, **AD8**, **AD12** and pentacyanophenol **AD7** (due to the impurity in this compound) are left out. In future we expect to extend the available self-consistent acidity data towards stronger superacids in DCE by several orders of magnitude and fill the gaps which right now are present in this scale (two approximately 2 $\mathrm{p}K_\mathrm{ip}$ unit gaps). We also plan to measure in the framework of this scale some of well-known common acids (TfOH, HBr) and derivatives of carborane acids ($\mathrm{CB_{11}H_{12}H}$), *etc.*

Compiling the scale. From the practical measurement standpoint an important difference was found between DCE and AN. In AN acids can easily be studied as salts with relatively small cations such as triethylammonium, pyridinium, *etc.* The same is not directly possible in DCE due to strong specific interactions between the acid anion and the cation. In this work a workaround was found for this problem: the salts must be first titrated into neutral form and then the neutral acid can be titrated with a base forming a large and delocalized cation on protonation (phosphazene base t-BuP$_1$(pyrr) was used). Still, later we found out, that only compounds with tetraalkylammonium counterions or free acids are suitable to get consistent results with other measurements. It was also found out that this reversible titration method is still necessary for titration of compounds with tetraaklylammonium counterions to have more consistent results.

The concentration of studied compounds during the titrations should be lower (1–$2{\cdot}10^{-5}$) than concentrations in AN (up to $5{\cdot}10^{-4}$), especially in the case of stronger acids with many cyano groups. Some of the relative measurements between poly-cyano acids were not successful, probably due to the formation of higher aggregates. It would be very good, if the partners for the measurement of poly-cyano acids would be an aromatic sulfonimides

Table 5.6: Continuous Self-Consistent Acidity Scale of Neutral Acids in DCE

	Acid	pK_{ip}(DCE)	Directly measured ΔpK_{ip} values
AD1		**10.5**	
AD2		**9.4**	
AD3		**9.0**	
AD4		**8.7**	
AD5		**8.5**	
AD6		**8.3**	
AD7		**7.7**	
AD8		**6.9**	
AD9		**6.7**	
AD10		**6.6**	
AD11		**6.5**	
AD12		**6.2**	
AD13		**6.3**	
AD14		**5.8**	
AD15		**3.8**	
AD16		**3.7**	
AD17		**3.4**	
AD18		**3.3**	
AD19		**3.1**	
AD20		**3.1**	
AD21		**2.0**	
AD22		**0.2**	
AD23		**0.0**	

or a tris(sulfonyl)methanes or other types of acids containing not many cyano groups. Aromatic sulfonimides are good because of their acidity can be tuned by varying either substituents in the benzene ring or replacing =O with the Yagupolskii's substituent =N-Tf.

Anchoring the scale and obtaining absolute pK_{ip} values is problematic in DCE. In this work the scale is anchored to the strongest acid measured and its pK_{ip} is arbitrarily essigned to zero (in order to prevent negative pK_{ip} values). There are 16 pK_{a} values of neutral acids reported in the literature[162] which have been measured in DCE using potentiometric titration and conductometry. Several of those acids (TfOH, HI, HBr) are expected to be in the acidity realm covered by our acidity scale and could thus be used as anchor compounds. The authors of reference 162 also report their acidities to be not ion-pair acidities but free ionic acidities. This claim is based on the results of conductometric measurements. Given the low dielectric constant of DCE and its negligible ability to solvate anions, the validity of this claim has to be carefully studied before accepting it. It may well be that it is the impurities in the solvent (first of all water) that dramatically increase the conductivity. If proved is valid then the potential anchor compound will probably be TfOH which is expected to be in the range between 2–3 pK_{ip} units in the present scale and has pK_{a} value in the literature 7.3 units.[162] The final anchor compound will be chosen after careful study.

Comparison of the acidities of the studied acids in DCE and AN. The correlation of the obtained DCE data with those measured in AN does not give a uniform relationship. There are currently too little data in DCE to make far-reaching conclusions but it can be expected that instead of a single correlation line accommodating all acids several family relationships form. Future studies are necessary. Still 6 compouns have been measured both in AN and DCE.

Three of those compounds are sulfonimides which were used as salts with pyridinium counterion (**AD4**, **AD8**, **AD12**). These sulfonimides are substituted using Yagupolskii's substituent (*vide supra*). The remaining three of those are **AD2**, **AD3**, **AD6** which were used either as free acids or salts with tetraalkylammonium counterion.

The scale of acidities of sulfonimides is much wider in DCE than in AN (see Figure 5.5). It is other way around with other compounds. From Tables 5.1 and 5.6 it is seen, that phenols are in AN relatively stronger and in DCE weaker compared to other acids. It probably comes from less favorable solvatation of phenoxide by DCE. Anions of sulfonimides and polycyanocarbon acids have more delocalized charge and the solvatation ability of those anions by DCE and AN cannot be distinguished.

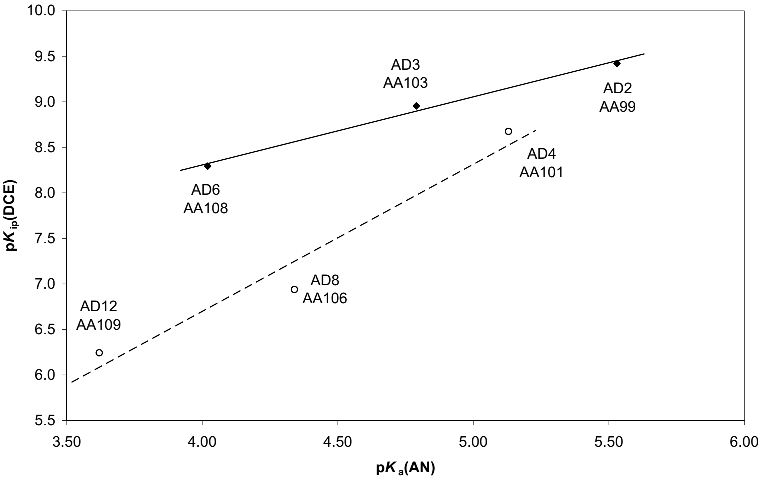


Figure 5.5: Correlation of pK_{ip} values of acids in DCE with pK_{a} values of acids in AN. Dashed line corresponds to the sulfonimides, solid line to the other compounds.

5.4. Some New Superacids

Quantum chemical computations is one of the easiest ways to predict GP acid-base properties of new types of compounds. Many of the new as well as established superacids are estimated to reach ΔG_{acid} values down to the region of 250–280 kcal/mol: 1,1,2,3,3-pentacyanopropene (267 kcal/mol),[104] pentacyanocyclopentadiene (254 kcal/mol). Some superacids, are expected to have ΔG_{acid} values even below 250 kcal/mol (several carborane acids are expected to have acid strength even down to 200–210 kcal/mol).

In the present work (see VI and VII) two types of anions whose protonated forms can be regarded as superacids with acidities below 280 kcal/mol are presented. One type of those anions are derivatives of anions of mineral acids (nitrate and metaphosphate, respectevly) obtained by formal replacement of oxygen atoms by dicyanomethylene fragments (see Figure 5.6). The other type is substituted boratabenzene anions (see Figure 5.8). Neither the anions nor their conjugate acids have been described earlier.

Anions $\mathrm{N[C(CN)_2]_3^-}$ and $\mathrm{P[C(CN)_2]_3^-}$ and the Superacidic Properties of Their Conjugate Acids. It has been suggested that when designing a superacid one should first of all design the anion.[104] According to the common knowledge the charge in the anion should be as delocalized as possible, using electron-accepting substituents with strong field-inductive and resonance-acceptor properties. It is the best if the anion does not have a well-defined protonation site and has instead a symmetric structure with many energetically equivalent protonation sites.

In this section a computational (DFT B3LYP 6-311+G**) design of two novel anions **1A** and **2A** and the superacidic properties of their conjugate acids are presented (See Figure 5.6). The results of acidity calculations are presented in Table 5.7.

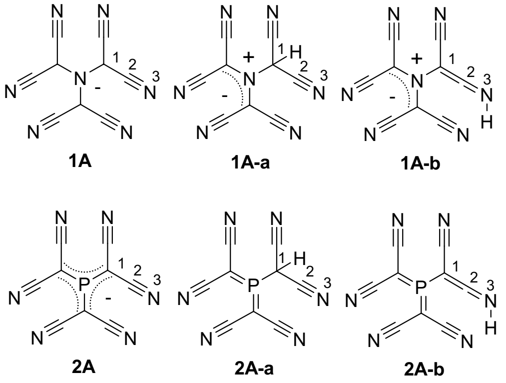


Figure 5.6: Structures of the anions **1A** and **2A** and their protonated forms.

The geometry of the anions **1A** and **2A** is similar (Figure 5.7, images of **2A**, **2A-a** and **2A-b** are presented, the respective forms of **1A** are similar). Both have D_3 symmetry. The most pronounced difference is the length of the bonds between the central atom and the C1 carbon (numbering in Figure 5.6), which for **1A** and **2A** is 1.38 and 1.71 Å, respectively, and the value of the angles between the planes of the central NC_3 or PC_3 moiety and the $C(CN)_2$ fragments: 34° and 30°, respectively. The shorter distance from C1 to the central atom might be the cause of the somewhat stronger distortion of the anion **1A** and one of the factors responsible for somewhat higher acidity of protonated **2A** compared to protonated **1A**.

In the C1-protonated species **1A-a** and **2A-a** the CN groups of the $CH(CN)_2$ fragment are rotated out of the plane of the central moiety, which is still nearly planar in both cases (Fig 5.7). The angles between the plane of the central moiety and the N-C-H and P-C-H planes are 12.5° and 5.9°, respectively. Distortion of this fragment out of the main plane enables the other two $C(CN)_2$ fragments to decrease their angles with respect to the central plane to 21° and 11° for **1A-a** and **2A-a**, respectively. The geometry of the N3 protonated species **1A-b** and **2A-b** is rather similar to the anions (Figure 5.7). The CNH angle is 124° and 127° in **1A-b** and **2A-b**, respectively, and the proton is directed out of the plane of the

Table 5.7: Calculation (DFT B3LYP 6-311+G**) Results of the Acidities of Protonated Forms of Anions **1A** and **2A**

Compounds	ΔH_{acid}	ΔG_{acid}
$N[C(CN)_2]_3^-$, **1A**		
$N[C(CN)_2]_2C(CN)CNH$, **1A-b**	**266.6**	**259.5**
$N[C(CN)_2]_2CH(CN)_2$, **1A-a**	266.5	259.4
$P[C(CN)_2]_3^-$, **2A**		
$P[C(CN)_2]_2C(CN)CNH$, **2A-b**	**263.3**	**256.1**
$P[C(CN)_2]_2CH(CN)_2$, **2A-a**	258.1	252.1

[a] All energies are given in kcal/mol and correspond to the most stable conformations of the species. The results for the most stable protonated species are given in bold.

$C(CN)_2$ fragment to which it is attached towards the nearest CN group of the neighboring $C(CN)_2$.

The protonated forms **1A-a** and **1A-b** have Gibbs free energies differing by only 0.1 kcal/mol (Table 5.7). Thus the anion **1A** provides an example of an anion without a well-defined protonation site – it has nine protonation sites with virtually equal energies! The protonated form **2A-b** is by 4.0 kcal/mol more stable than **2A-a**. The partial Mulliken atomic charge on the central nitrogen in **1A** is +0.84, the partial charge on the central phosphorus atom in **2A** is +0.08. As expected, the negative charge of the anions **1A** and **2A** mainly resides on the nitrogen atoms of the CN groups (partial charges -0.30 in both anions).

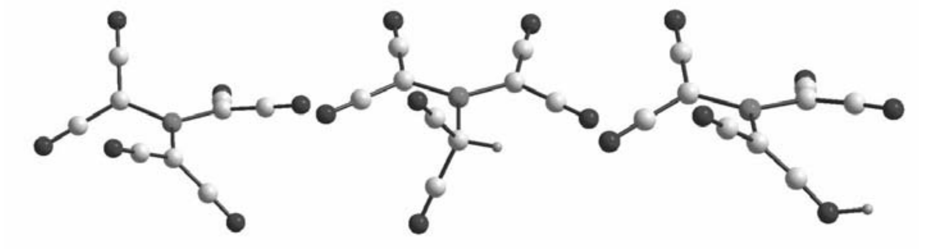
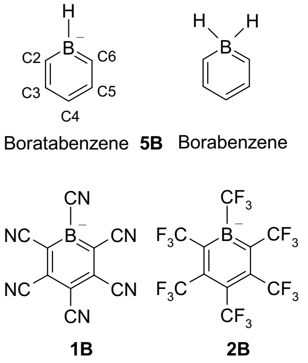


Figure 5.7: Geometries of $N[C(CN)_2]_3^-$ (**2A**), $P[C(CN)_2]_2CH(CN)_2$ (**2A-a**) and $P[C(CN)_2]_2C(CN)CNH$ (**2A-b**).

The acids **1A-b** and **2A-b** are predicted to be by 54.5 and 47.1 kcal/mol more acidic that their "parent" acids HNO_3 and HPO_3,[104] while **2A-b** is by 3.4 kcal/mol more acidic than **1A-b**. These acids are among the strongest noncarborane superacids and confirm the superstrong acidifying effect of incorporation of multiple CN groups into an acidic molecule whose conjugate anion is able to form an extensive conjugated system with the anionic protonation center. The acid **2A-b** is predicted to be in the gas phase stronger than any of the following acids: TfOH, $HAlCl_4$, HPF_6 and the parent carborane acid $CB_{11}H_{12}H$.[104]

Boratabenzene Anions $C_5B(CN)_6^-$ and $C_5B(CF_3)_6^-$ and the Superacidic Properties of their Conjugate Acids. Boratabenzenes and their conjugate acids, borabenzenes (see Figure 5.8) have been known for long time and have been used in organometallic chemistry as π-donating ligands.[163] Substitution of borabenzenes with electron-accepting substituents with highly field-inductive and resonance-acceptor properties is expected to lead to highly acidic compounds, but the potential of these compounds as superacids and WCAs has not been recognized.



Boratabenzene **5B** Borabenzene

1B **2B**

Figure 5.8: Structures of boratabenzene, borabenzene, hexacyanoboratabensene **1B** and hexakis(trifluoromethyl)boratabenzene **2B**.

The results of the calculations of the title compounds and some related structures are presented in Table 5.8. Structures of **1B** and **2B** and their most stable protonated forms are presented in Figure 5.9. To predict the protonation sites and to rationalize the relative stability of the protonated forms analysis of natural charges using the Natural Bond Orbital (NBO) approach was performed for all boratabenzenes and most of the neutral forms.[164]

The conjugate acid of **1B** is by ca 26 kcal/mol more acidic than that of **2B**. The anion **1B** is planar and has C_{2v} symmetry. Protonation to the ring makes the CN group to bend out of the plane by 46° (proton on C2) or 57° (proton on C4). Nevertheless the aromatic rings remain planar. If the proton is attached to a CN nitrogen, then the whole molecule is planar. The anion **2B** has a slightly bent aromatic ring (dihedral angle of B-C2-C3-C4 is 7.9°) with chair conformation - B and C4 are bent from the remaining four carbons which are on the same plane (dihedral angle of C2-C3-C5-C6 is 0°). The anion **2B** has C_s symmetry.

Similarly to unsubstituted boratabenzene, the anion **1B** has the largest negative partial charge on carbons C2 and C6: -0.36 units. The nitrogen of the cyano group attached to the boron atom has also high negative partial charge: -0.35. This is also the most favourable protonation site. C4 has partial charge -0.15 units, C3 and C5 0.06 units and the boron atom +0.31 units.

Anion **2B** has the largest negative partial charge again on carbons C2 and C6: -0.44 units. C4 has partial charge 0.20 units, C3 and C5 0.04 units and the boron atom +0.46 units. F atoms in 2 have quite similar partial charges: -0.33 to -0.37 units. The most negative of these values belong to the CF_3 group attached to the boron atom. Protonation to this CF_3 group leads to the decomposition of the molecule with detachment of HF.

The most favorable protonation site of **2B** is carbon C4. If the proton is attached to C2, then the structure of the resulting borabenzene is quite similar to the structure of the anion but a little more chair-like. The C-H bond in this structure is almost perpendicular to the plane which is formed by four carbon atoms of the aromatic ring (C2-C3-C5-C6, dihedral angle of these atoms is 6.3°). Protonation on C4 leads to a bath-conformation, where the boron atom is much more out of plane and the C4 carbon is almost on the same plane as the other four carbon atoms. The CF_3 group of C4 is not bent to the other side of CF_3 group of boron anymore, but to the same side. The angle between the plane formed by all five carbon atoms and the CH bond is almost the same as the angle of the same plane and the CF_3 group attached to C4 (dihedral angle of C(4-CF_3)-C4-C3-C2 is 137.3° and 129.8°, H-C4-C3-C2 is 112.3° and 119.2°). In the C4-protonated conjugate acid of **2B** the charge is more effectively delocalized (seen from atomic partial charges). The structure in chair-conformation was also calculated and found to be by 7.6 kcal/mol less stable than the bath-conformation. The most negative electrostatic potential in **2B** is where fluorine atoms of CF_3 groups attached to the B and C2 atoms are very close, envisaging a protonated structure where proton is chelated by F atoms of two adjacent CF_3 groups. This structure proved to be unstable: HF was detached.

In comparison of anions **1B** and **2B** it is seen that the total amount of negative charge in the aromatic ring is almost equal (-0.7 units) but the distribution of the charge among different atoms of the ring is different. In the anion **1B** the charges are distributed more evenly. This could be rationalized on the basis of the difference in resonance acceptor and

Table 5.8: Computational (DFT B3LYP 6-311+G**) Acidities of Conjugate Acids of Boratabenzenes in the Gas Phase

	Anion	ΔG_{acid} (kcal/mol)	ΔH_{acid} (kcal/mol)	Protonation site, comments
1B	$BC_5(CN)_6^-$	**250.5**	**257.5**	1-CN
		247.7	254.6	4-CN
		235.2	241.3	C2
		234.9	241.1	C4
2B	$BC_5(CF_3)_6^-$	**276.8**	**280.9**	C4, "bath"
		269.2	274.5	C4, "chair"
		251.7	258.6	C2
		260.0	263.4	Chelate, HF detached
		249.9	253.5	1-CF_3, HF detached
3B	$BC_5(CN)H_5^-$	**308.0**	**314.7**	C2
		307.5	314.4	C4
		293.3	300.5	1-CN
4B	$BC_5(CF_3)H_5^-$	**309.6**	**316.4**	C2
		309.2	316.0	C4
5B	$BC_5H_6^-$	**325.8**	**332.4**	C2
		324.7	331.7	C4
6B	$C_5(CN)_5^-$	**256.3**	**263.4**	1-CN
		250.1	256.6	C1[104]
7B	$C_5(CF_3)_5^-$	**275.5**	**283.8**	C1

field-inductive properties of CF_3 and CN groups (CN is a stronger resonance acceptor group) and, even more importantly, from the planarity of **1B** and non-planarity of **2B**. The stronger resonance acceptor properties of CN cause the more even charge distribution in $BC_5(CN)H_6$ compared to $BC_5(CF_3)H_6$: the resonance effect of the CN group decreases electron density especially at C2, C4 and C6 that in the unsubstituted boratabenzene are the most electron-dense positions. Resonance requires planarity of the whole molecule to delocalize electrons throughout the molecule, field-inductive effects at the same time depend on bond valence and position of functional group and need no planarity to work. CN groups are strong resonance acceptor groups and the whole molecule has to be planar for these groups to work well. CF_3 groups are rather weak resonance acceptors and at the same time bulky. Both these factors have a role in the non-planarity of **2B** and its protonated form.

From Table 5.8 it is also seen that the hexakis-substituted borabenzene and the corresponding pentakis-substituted cyclopentadiene (**1B** and **6B**; **2B** and **7B**) have very similar gas-phase acidities. The conjugate acid of **6B** is by approximately 6 kcal/mol weaker acid, even though the protons are in both cases bound to the nitrogen of a cyano group. Both compounds are planar and the stronger acidity of borabenzene may come from its slightly larger size, one additional CN group and the parent boratabenzene as more stable anion compared to the parent cyclopentadiene. The acidity of **6B** was also calculated using G3(MP2) and both protonation sites (nitrogen of a cyano group and carbon of a cycle) led to almost the same acidities 254.3 kcal/mol and 254.4 kcal/mol, respectively. The geometries of these boratabenzenes and cyclopentadiene anions are similar. Anions **1B** and **6B** are planar. The rings of anions **2B** and **7B** are slightly bent and the CF_3 groups are somewhat bent out of plane.

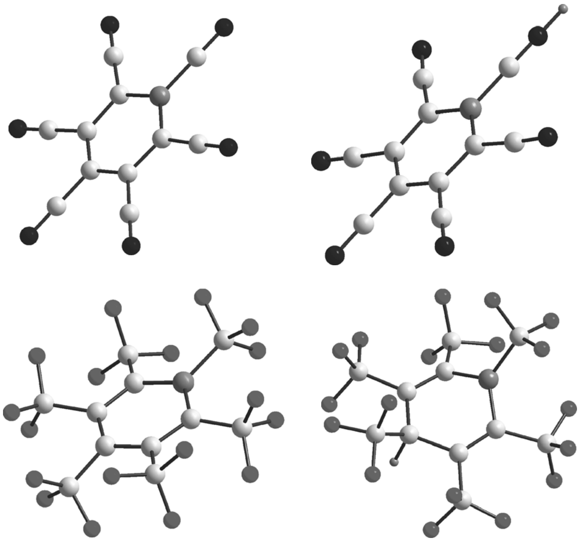


Figure 5.9: Structures of anions **1B** and **2B** and their the most stable protonated forms.

It is expected that the compounds described in this section, would lead to a substantial addition to the compounds suitable for compiling the acidity scales (DCE acidity scale as well GP acidity scale) in the superacidic region.

6. SUMMARY

The main goal of the present work was to study acidic and basic properties of different Brønsted-Lowry acids and bases in non-aqueous media. The work contains two major parts – studies of neutral bases and studies of neutral acids.

The first part of the present work is focused on neutral bases. In this part the comprehensive basicity scale of neutral bases in acetonitrile spanning 28 orders of magnitude is presented. The scale contains 136 bases whose pK_a values have been obtained from over 300 measurements of ΔpK_a values. A useful property of this scale is that it contains many well-behaving compounds with good spectral properties (aryl substituted phospazenes, anilines, pyridines, *etc.*) covering the overall basicity area (can be used as good reference compounds for further studies) and also all kinds of basic compounds from different families – simple alkylamines and diamines, well-known superbases based on guanidine structure, bispidines, porphyrines, *etc.* The scale was critically reviewed by comparing the basicities of this work to the basicities found from literature. As a result, compared to the previous basicity scale, the pK_a values of this scale were increased by 0.20 pK_a units to establish consistency between the pK_a values from literature and the pK_a values presented in this work.

Additionally, the basicities of seven novel and very interesting substituted guanidines were measured in acetonitrile. One of those compounds was found to be the strongest base among the alkyl substituted quanidines known to date. Also, guanidinophosphazenes as a new type of really powerful superbases were presented. These bases are so strong (27–29 pK_ip units in tetrahydrofuran) that they are able to deprotonate acetonitrile. Therefore, tetrahydrofuran which has very low acidity, was used to measure the basicity of those phosphazene bases.

The second part of this work focuses on neutral acids. The comprehensive acidity scale in acetonitrile is presented. The scale includes 109 acids that are interconnected by 273 relative acidity measurements and spanning over 25 orders of magnitude. This scale is composed using well-behaving acids, mainly poly-florinated aromatic CH acids and NH acids. Representatives from all of the conventional families of OH (alcohols, phenols, carboxylic acids, sulfonic acids), NH (anilines, diphenylamines, disulfonimides) and CH acids (fuorenes, diphenylacetonitriles, phenylmalononitriles, phenylethylcyanoacetates, toluenes) have been included to the scale. The scale also includes pentakis(trifluoromethyl)phenol, -aniline, -toluene, -phenylmalononitrile and related compounds. The synthesis and structures of pentakis(trifluoromethyl) derivatives are presented and discussed. Due to the steric crowding, the aromatic rings in all $C_6(CF_3)_5$ derivatives are significantly distorted.

Many of the compounds whose $\mathrm{p}K_\mathrm{a}$ values would be interesting to know are superacids and it is not possible to measure their strength in acetonitrile. 1,2-dichloroethane was chosen to investigate those true superacids. As a result, the most acidic equilibrium acidity scale that has been composed in a medium of constant composition is presented in this work.

Two new types of superacids (cyano-substituted derivatives of mineral acids and substituted borabenzenes, ΔG_acid values are between 260–280 kcal/mol) were also presented in this work and their properties were studied computationally. These superacids would be useful compounds for acidity measurements in solution phase and in the gas phase.

7. SUMMARY IN ESTONIAN

Happe-aluse tasakaalude uurimine mittevesikeskkondades.

Käesoleva töö peamine eesmärk oli uurida erinevate Brønsted-Lowry hapete ja aluste happelis-aluselisi omadusi erinevates mittevesikeskkondades. Töö koosneb kahest osast – neutraalsete aluste uurimine ja neutraalsete hapete uurimine.

Esimene osa käesolevast tööst käsitleb neutraalsete alustega seonduvat. Selles osas on esitatud uus ulatuslik neutraalsete aluste kooskõlaline skaala atsetonitriili keskkonnas ulatusega 28 suurusjärku. Praeguseks on skaalal 136 alust, mille pK_a väärtused on saadud enam kui 300 ΔpK_a väärtuse mõõtmisest. Skaala eeliseks on see, et see sisaldab atsetonitriilis hästi käituvaid heade spektraalsete omadustega aineid (arüül-asendatud fosfaseenid, aniliinid, püridiinid jne.) üle kogu aluselisuse piirkonna (neid aineid saab kasutada heade võrdlusainetena edaspidiseks mõõtmiseks) ja lisaks veel aineid paljudest erinevatest aluste perekondadest – lihtsad alküülamiinid ja diamiinid, guanidiinid, bispidiinid, porfüriinid jne. Skaalal olevaid pK_a väärtusi võrreldi kirjanduses olevate samade ainete pK_a väärtustega ja leiti, et varem koostatud skaalal olevate ainete pK_a väärtusi tuleb tõsta 0.20 pK_a ühiku võrra, et saavutada kooskõla kirjanduse ja käesolevas töös mõõdetud ainete pK_a väärtuste vahel.

Lisaks mõõdeti ära seitsme uue guanidiini pK_a väärtused atsetonitriili keskkonnas. Üks nendest alustest on siiani kõige tugevam alus alküülasendatud guanidiinide seas. Uuriti ka uut tüüpi ülitugevaid superaluseid – guanidinofosfaseene. Need alused on nii tugevad (pK_ip väärtused tetrahüdrofuraani keskkonnas on 27–29 ühikut), et enamik neist deprotoneerib atsetonitriili. Et siiski teada saada nende aluselisusi, uuriti neid tetrahüdrofuraani keskkonnas.

Teine osa tööst on pühendatud hapete uurimisele. Siin koostati kooskõlaline happelisuse skaala atsetonitriili keskkonnas ulatusega 25 suurusjärku. Skaalale on mõõdetud 109 happe pK_a väärtused, mis on saadud 274 ΔpK_a väärtuse mõõtmisest. Ka see skaala on koostatud atsetonitriili keskkonnas hästi käituvatest ainetest – polüfluoreeritud CH ja NH hapetest. Skaalal on esindatud väga paljud erinevad hapete perekonnad – OH happed (alkoholid, fenoolid, karboksüülhapped, sulfoonhapped), NH happed (aniliinid, difenüülaniliinid, disulfoonimiidid) ja CH happed (fluoreenid, difenüülatsetonitriilid, fenüülmaloonnitriilid, fenüületüültsüanoatsetaadid, tolueenid). Samuti on skaalaga seotud pentakis(trifluorometüül)fenool, -aniliin, -tolueen ja -fenüülmaloonnitriil ning nendga sarnased ained. On esitatud pentakis(trifluorometüül)fenüül-ühendite süntees ja struktuuri analüüs. Kuna seda tüüpi ühendid on steeriliselt väga pingestatud, siis leiti, et neil on oluliselt deformeerunud aromaatne tuum.

Paljusid ühendeid, mille pK_a väärtusi oleks huvitav teada, pole nende ülikõrge happelisuse tõttu võimalik mõõta atsetonitriili keskkonnas. Seetõttu on 1,2-dikloroetaan valitud keskkonnaks, et mõõta superhapete happelis-aluselisi omadusi. Tulemusena on koostatud kõige happelisem tasakaalulise happelisuse skaala konstantse koostisega keskkonnas.

Käesolevas töös esitletakse ka kahte uudset superhapete perekonda (tsüano-asendatud mineraalhapete derivaadid ja asendatud borabenseenid). Nende ainete struktuuri ja happelisust uuriti arvutuslikult ja leiti, et need ained kuuluvad tõeliste superhapete hulka, mille ΔG_acid väärtused jäävad vahemikku 260–280 kcal/mol.

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ACKNOWLEDGMENTS

I wish to experess my sincere gratitude to my supervisors Professor Ivo Leito, Senior Research Fellow Dr. Ivari Kaljurand and Research Professor Ilmar Koppel for their professional guidance, good advice and constant support.

I would like to express my greatest gratitude to Dr. Toomas Rodima who has kindly offered his knowledges about synthesis and has prepared so many useful compounds to our research group.

The greatest thanks to Prof. Dr. Gerd-Volker Röshenthaler and Dr. Alexander A. Kolomeitsev for their advice and support in Bremen.

Many thanks to all of co-authors: Dr. Lilli Sooväli, Dr. Eva-Ingrid Rõõm, Dr. Ivar Koppel, Dr. Vahur Mäemets, Dr. Juta Koppel, Dr. Viljar Pihl, Ms. Gea Ovsjannikov, Dr. Mirjana Eckert-Maksić, Dr. Zoran Glasovac, Dr. Pavle Trošelj, Ms. Valeria Movchun, Dr. Eduard B. Rusanov, Mr. Timo Dansauer, Dr. Enno Lork, Prof. Masaaki Mishima, Dr. Maurice Medebielle and Dr. Jan Barten for their contribution to our joint papers. I also wish tho express my gratitude to Prof. Vladislav M. Vlasov and Prof. Lev M. Yagupolskii for their irreplaceable compounds. I also thank Dr. Lauri Toom for good advice concerning NMR spectroscopy.

I thank Dr. Koit Herodes and Mr. Allan Künnapas for their help with MS measurements. It has been the true help to identify compounds.

The greatest thank also to Ms. Ester Uibopuu and to Ms. Marju Rosenthal for their support.

I also thank Ms. Vera Vogel, Dr. Hanna Skarpos, Ms. Olesya Kasakova, Ms. Katja Vlasov, Dr. Natalya Kalinovich, Ms. Christina Kenst, Dr. Jolanta Ignatowska, Ms. Romana Pajkert, Mr. Krzysztof Cichowicz and Mr. Ovidiu Moldovan for their kind support and friendly atmosphere in Bremen. My greatest gratitude to Dr. Ciprian-Ionut Rat for helping me with NMR measurements, offering his knowledge about crystallography and chemistry in general. I kindly thank Dipl. Ing. Johannes Stelten for the NMR measurements and analysis, Mr. Peter Brackmann for the crystallographic measurements. The greatest thanks to Dr. Thomas Dülcks and Dipl. Ing. Dorit Kempken for the MS measurements and analysis in Bremen.

I am very greatful to all my colleagues for warm and nice atmosphere – Lauri, Eve, Eva-Ingrid, Toomas, Koit, Ester, Marju, Lilli, Viljar, Anneli, Elin, Signe, Kristina, Ivar, Ivo, Ilmar, Ivari...

The last but not the least (*vice versa*) – the greatest gratitude to my family and friends for being beside me all the time – mom, Meelis, granny and Urmas.

The financial support for this work came from Grant Nos 5800, 5226, 5508, 5254, 7374, 6701, 6699, and 7260 from the Estonian Science Foundation, the project Nos 436 EST 17/2/04 and 436 EST 113/3/0-1 from the Deutsche Forschungsgemeinschaft and the project No 098-0982933-2920 from the Ministry of Science, Education and Sport of Croatia.

PUBLICATIONS

Reproduced with permission from *The Journal of Organic Chemistry*, vol. 70, 2005, Ivari Kaljurand, Agnes Kütt, Lilli Sooväli, Toomas Rodima, Vahur Mäemets, Ivo Leito, and Ilmar A. Koppel. Extension of the Self-Consistent Spectrophotometric Basicity Scale in Acetonitrile to a Full Span of 28 pK_a Units: Unification of Different Basicity Scales, pages 1019–1028. Copyright 2005 American Chemical Society.

II

Mirjana Eckert-Maksić, Zoran Glasovac, Pavle Trošelj, Agnes Kütt, Toomas Rodima, Ivar Koppel, and Ilmar A. Koppel. Basicity of Guanidines with Heteroalkyl Side Chains in Acetonitrile. Submitted to *Eur. J. Org. Chem.*

III

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IV

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V

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VI

Ivo Leito, Agnes Kütt, Eva-Ingrid Rõõm, and Ilmar Koppel. Anions $N[C(CN)_2]_3^-$ and $P[C(CN)_2]_3^-$ and the Superacidic Properties of Their Conjugate Acids. *THEOCHEM* **2007**, *815*, 41–43.

VII

Agnes Kütt, Ivar Koppel, Ilmar A. Koppel, and Ivo Leito. Boratabenzene Anions $C_5B(CN)_6^-$ and $C_5B(CF_3)_6^-$ and the Superacidic Properties of Their Conjugate Acids. Submitted to *Angew. Chem., Int. Ed.*

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Attended conferences and meetings

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3. 233rd American Chemical Society National Meeting and Exposition in Chicago, IL, USA. Presented poster: Leito, I.; Kütt, A.; Kaljurand, I.; Rõõm, E.-I.; Rodima, T.; Koppel, I. A. Brønsted Acidity of Neutral and Cationic Acids in Nonaqueous Solvents: Recent Developments. 2007. INOR-1036.

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Osalemine konverentsidel

1. Meetings of Nobel Laureates in Lindau, 18th Lindau Meeting in Chemistry, Lindau, Saksamaa, 2006.
2. 18th International Symposium on Fluorine Chemistry, Bremen, Saksamaa. Esitatud poster: Kütt, A.; Leito, I.; Kaljurand, I.; Soovli, L.; Vlasov, V. M.; Yagupolskii, L. M.; Koppel, I. A. A Comprehensive Self-Consistent Spectrophotometric Acidity Scale of Neutral Brønsted Acids in Acetonitrile. 2006. ORG-090.
3. 233rd American Chemical Society National Meeting and Exposition in Chicago, IL, USA. Esitatud poster: Leito, I.; Kütt, A.; Kaljurand, I.; Rõõm, E.-I.; Rodima, T.; Koppel, I. A. Brønsted Acidity of Neutral and Cationic Acids in Nonaqueous Solvents: Recent Developments. 2007. INOR-1036.

Koostöö

1. November, 2006 – jaanuar, 2007. Polü-perfluoroalküül ühendite süntees ja uurimine. Prof. G.-V. Röschenthaler, Bremeni Ülikool, Anorgaanilise ja Füüsikalise Keemia Instituut
2. Juuli, 2007 – september, 2007. Polü-perfluoroalküül ühendite süntees ja uurimine. Prof. G.-V. Röschenthaler, Bremeni Ülikool, Anorgaanilise ja Füüsikalise Keemia Instituut

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