Design and acidity measurements of superacidic molecules

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Munich Jan 2011

Overview

- Brønsted acidity
  - In non-aqueos solutions
  - In the gas phase
  - Measurement of acid strength
- Superacidic molecules
- Design of superacidic molecules

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Acidity of molecules and acidity of media

- Brønsted acidity of a **molecule** refers to its ability to donate proton to other molecules
  - Usually defined in terms of equilibrium constants (K_a, pK_a) or deprotonation energies (GA or ΔG_{acid})
- Brønsted acidity of a **medium** refers to the ability to donate proton to molecules in the medium
  - In aqueous solution: pH
  - Strongly acidic solutions: H_0

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Acidity of molecules in solution

- Acidity of molecules in solution is defined in the framework of the **Brønsted** theory via the **pK_a values**

$$HA + S \underset{}{\overset{K_a}{\rightleftharpoons}} A^- + SH^+$$

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

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Acidity of molecules in the gas phase

- Acidity of molecules in the gas phase is expressed via deprotnation **Gibbs' free energy**

$$HA \underset{}{\overset{K_a}{\rightleftharpoons}} A^- + H^+$$

$$GA = \Delta G_{acid} = -RT \ln K_a$$

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Example of acidity differences in solution and in the gas phase

Acid	**pK_a (water)**	**pK_a (MeCN)**	**ΔG_a (GP) kcal / mol**	**pK_a (GP)**
HBr	ca -9	5.5	318.3	233.4
2,4-Dinitrophenol	3.96	16.7	308.6	226.2

- In water HBr is 10^{13} times **stronger** than 2,4-DNP
- In the gas phase HBr is 10^{7} times **weaker** than 2,4-DNP

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Why do we need acidity data?

- Measurements of pK_a values of newly synthesized acids and bases
- Rationalization and prediction of mechanisms of chemical and industrial processes
- Design of novel acids and bases
- Development of theoretical calculation methods

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Solutions: aqueous vs nonaqueous

- Aqueous solution:
  - Simple and accurate measurements
    - Using the pH scale
  - **Strong acidities cannot be accessed**
    - Water has too high basicity
    - Strong acids are leveled
- Non-aqueous solution:
  - **Very high acidities can be realized and measured**
  - Measurements more complicated

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Non-aqueous pK_a values: not trivial

- Processes are often more complex than simple ionic dissociation
  - Ion-pairing, homoconjugation, ...
- Measurement of $a(SH^+)$ is not trivial
- Traces of moisture can significantly affect results

K. Kaupmees et al, *J. Phys. Chem. A* 2010, *114*, 11788

  - Working in an inert gas atmosphere (glovebox) is necessary

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Acid-base reaction in a non-aqueous solvent

$$(AH)_S + (:B)_S \overset{K_1}{\leftrightarrows} (AH\cdots:B)_S \overset{K_2}{\leftrightarrows} (A^-:\cdots HB^+)_S \text{ v. } (A^-:HB^+)_S \overset{K_3}{\leftrightarrows}$$

HB complex *HB complex* *contact ion pair*

$$\overset{K_3}{\leftrightarrows} (A^-:\,//\,HB^+)_S \overset{K_4}{\leftrightarrows} (A^-:)_S + (HB^+)_S$$

solvent-separated ion pair *free ions*

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Approach: Relative measurement

- Measurement of pK_a **differences**
  - ΔpK_a values
- No need to measure $a(SH^+)$ in solution
- Many of the error sources cancel out, either partially or fully
  - Traces of moisture
  - Impurities in compounds
  - Baseline shifts and drifts
- Technique: UV-Vis spectrometry

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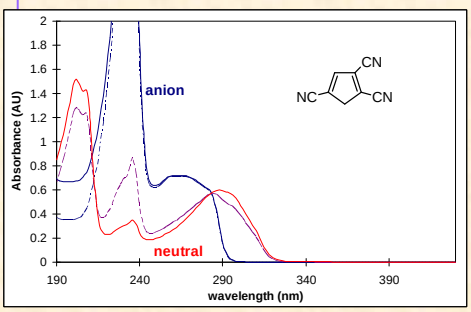
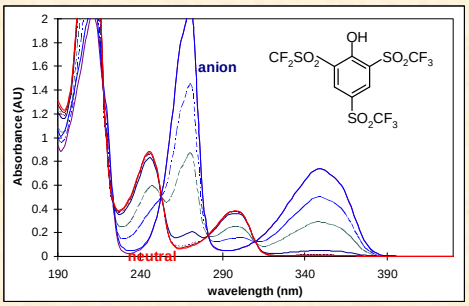
UV-Vis ΔpK_a measurement

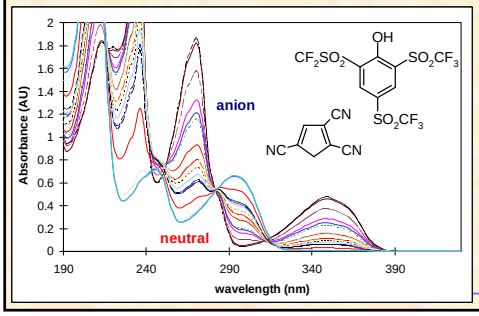
Compound 1



Compound 2



Mixture



$$\Delta pK_a = pK_a(HA_2) - pK_a(HA_1)$$

$$= -\log K = \log \frac{[A_1^-]\cdot[HA_2]}{[HA_1]\cdot[A_2^-]}$$

$$= 0.87$$

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What solvent to use for strongly acidic molecules?

- Desirable properties
  - As low as possible basicity and anion-solvating ability
  - High polarity
  - High pK_{auto}
  - Easy to purify, reasonably inert, electrochemically stable, transparent in UV, readily available, widely used

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Acetonitrile (MeCN)

- Advantages of MeCN:
  - Low basicity (B' = 160), low anion-solvating ability → **quite strong acids measurable**
  - High polarity (ε = 36)
  - High pK_{auto} ($\geq$ 33)
  - Transparent in UV, easy to purify, reasonably inert, electrochemically stable, readily available, widely used
- Limitations:
  - Very strong bases decompose MeCN
    - Already Et-P2(pyrr) slowly decomposes MeCN
  - **Impossible to study the strongest superacids**

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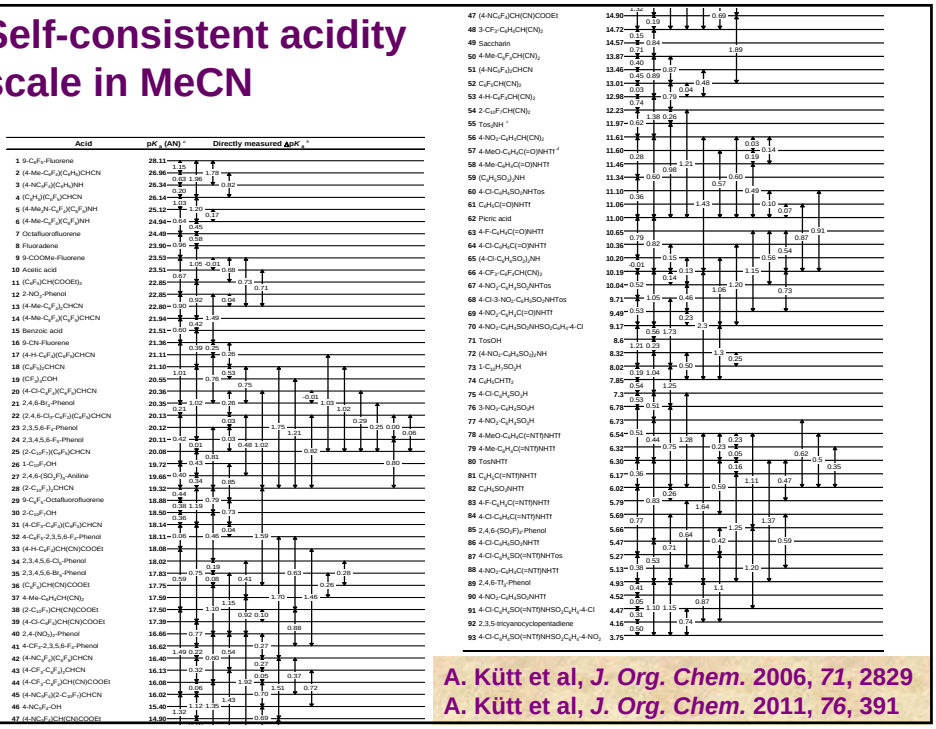
Self-consistent acidity scale in MeCN



A. Kütt et al, *J. Org. Chem.* 2006, *71*, 2829
A. Kütt et al, *J. Org. Chem.* 2011, *76*, 391

Properties of the MeCN acidity scale

- **Consistency**, checked by **circular validation measurements**:
  - 93 acids, 203 relative acidity measurements
  - Consistency standard deviation: 0.03 pK_a units
- Anchored to Picric acid (pK_a = 11.0)
- pK_a range: 3.7 .. 28.1
  - Useful tool for further studies
- Acids in the lower part are **superacids**

What is a superacid?

- Superacidic **medium**:

A Brønsted superacid is a medium, in which the chemical potential of the proton is higher than in pure sulfuric acid

D. Himmel et al, *Angew. Chem. Int. Ed.* 2010, *49*, 6885

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What is a superacid?

- Superacidic **molecule**:

A superacidic molecule in a given medium is one that is more acidic than H_2SO_4 in that medium

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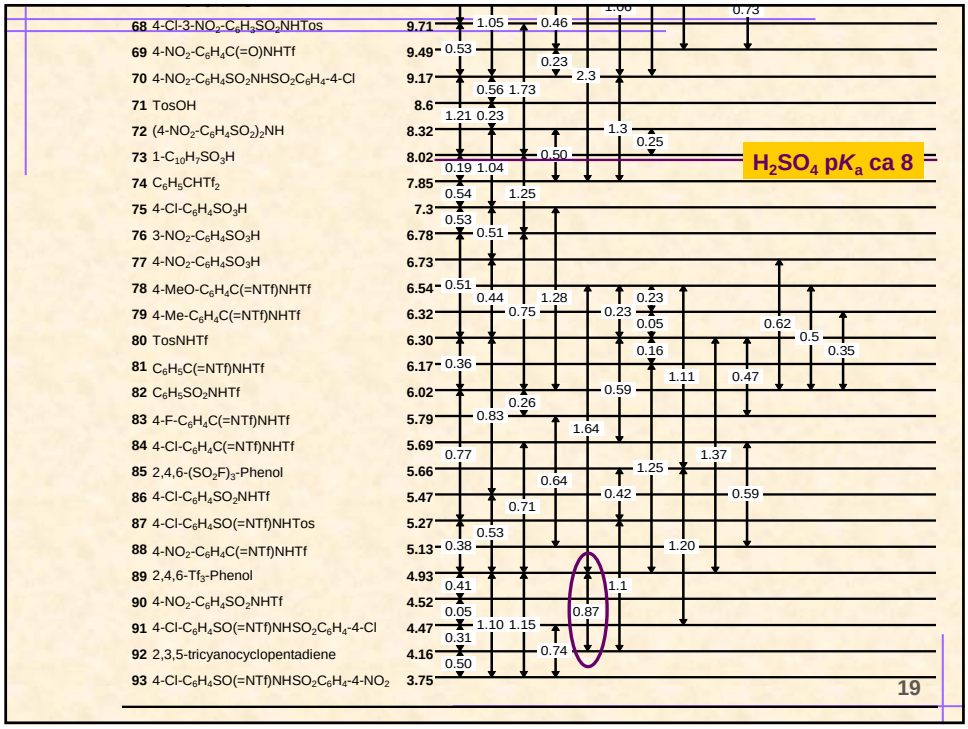

How to measure strengths of even stronger acids?

- The H_0 scale
  - Classical approach
  - Different H_0 values refer to different medium
  - Used to characterise media rather than molecules
- X-H vibrational frequencies
  - Stoyanov, et al *JACS* **2006**, *128*, 8500
  - Indirect: not directly characterising the eq acidity
- Equilibrium pK_a measurements in some low-basicity solvent
  - **Obvious but no reports until recently!**

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Requirements for the solvent

- As low as possible basicity
  - B' << 160
- As high ε as possible
- As high pK_{auto} as possible

- An ideal solvent is not available

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1,2-Dichloroethane

- Advantages of 1,2-DCE:
  - Very low basicity (B' = 40), low anion-solvating ability → **strong superacids are measurable**
  - pK_{auto} unmeasurably high
  - Reasonably inert and stable, readily available, widely used, dissolves also many ionic compounds well
  - Transparent in UV down to 230 nm
- Limitations:
  - ~Low polarity (ε = 10)
    - **Ion-pair acidities**

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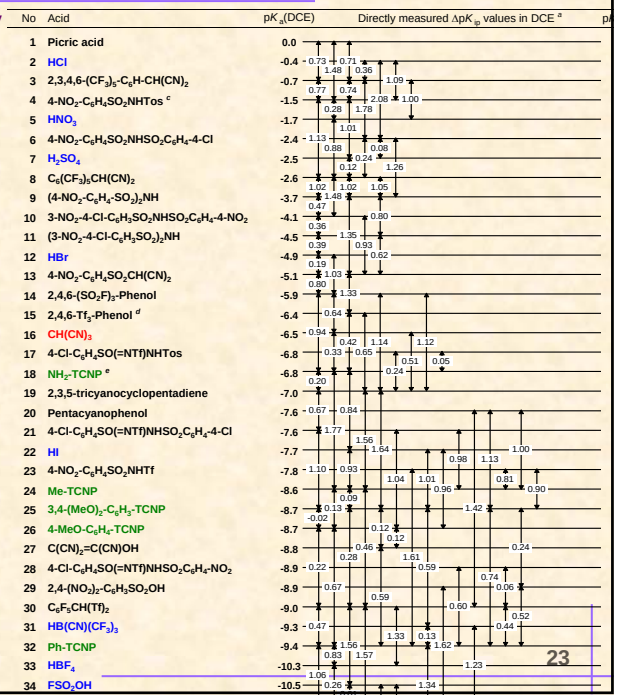
1,2-DCE acidity scale

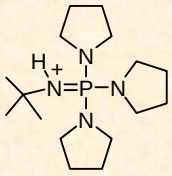
- **The most acidic equilibrium acidity scale in a constant-composition medium**
- Relative acidities
  - Not easy to anchor
  - Some values available in literature, but are doubtful

A. Kütt et al *J. Org. Chem.* 2011, *76*, 391

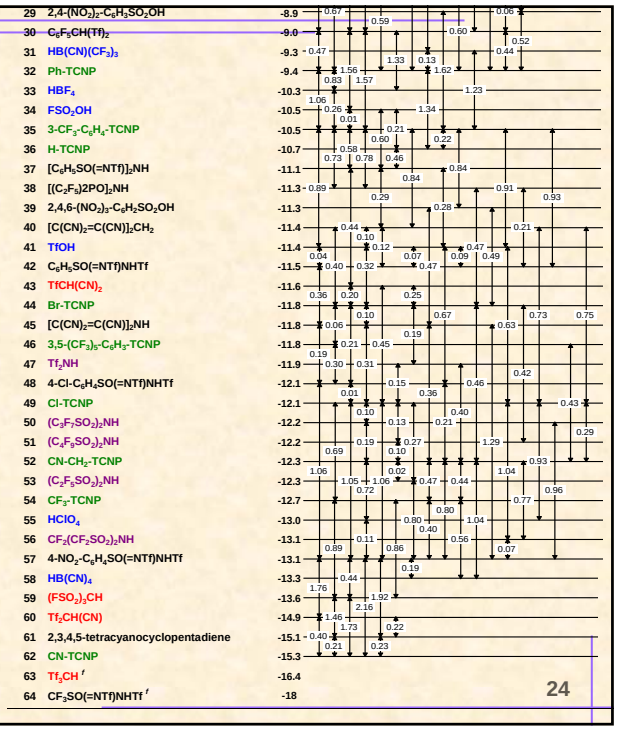


1,2-DCE acidity scale

- Ion pair acidities
- Counter-ion:



- Aqueous pK_a (H_0) values down to -10 .. -15



Important aspects for superacids

- Brønsted acidity
  - As strong as possible
  - "Clean" protonation desirable
  - Lewis acidity is normally not desirable
- Stability under superacidic conditions
- Weak coordinating properties of the anions

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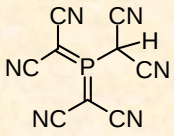
Design of superacidic molecules

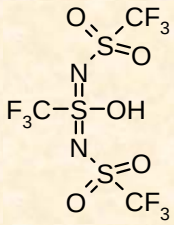
- "Acid-based" approach:
  - Pick a parent acid
  - Introduce substituents
    - electronegative, strong electron acceptors, highly polarizable



$\Delta\Delta G_{acid}$ = **47 kcal/mol**

ΔG_{acid} = 256 kcal/mol
(DFT B3LYP/6-311+G**)

Leito et al *J. Mol. Stru. Theochem*, 2007, *815*, 43



$\Delta\Delta G_{acid}$ = **40 kcal/mol**

ΔG_{acid} = 260 kcal/mol
(DFT B3LYP/6-311+G**)

Koppel, Yagupolskii et al *to be submitted*

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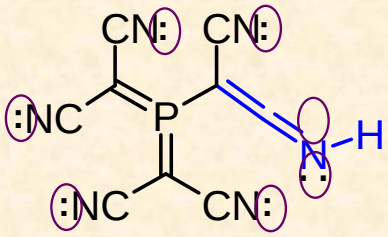
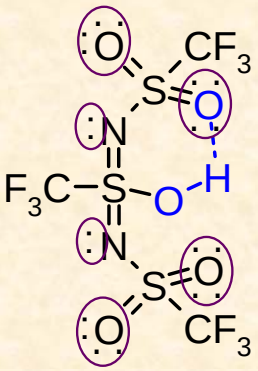
Basicity Centers on Substituents





It is not only about the acceptor power but also about basicity!

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Design: Anion-based approach

- Design an anion, which
  - Has delocalized charge
  - Is as stable as possible
  - Has as few as possible protonation sites and those are of low basicity

Not looking at any particular acidity center

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Fluorine

- Highly electronegative element
  - Decreases the basicity of nearby basicity centers
  - Has very low basicity itself
- Many X-F bonds are extremely strong
  - C-F bond: 484 kJ/mol
  - High stability of fluorinated compounds
- Small size
  - Polyfluorinated compounds have low steric strain

Fluorination is intrinsically suitable for superacid design

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Substituent properties

Substituent	σ_F	σ_R	σ_α
-F	0.57	-0.33	0.13
$-CF_3$	0.46	0.09	-0.25
$-SO_2CF_3$	0.83	0.26	-0.58
-CN	0.54	0.18	-0.46

- Neither –F nor $–CF_3$ seem particularly impressive

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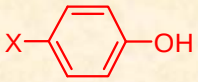
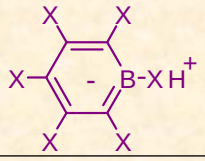
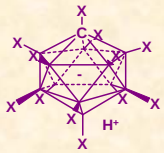
-F and -CF_3 vs -CN

(DFT B3LYP/6-311+G**)

Acid	Gas-phase acidity (kcal/mol)		
	-CN	-F	-CF_3
	325	340	330
	250		277
HBX_4	259	290	244
	225	213	~200

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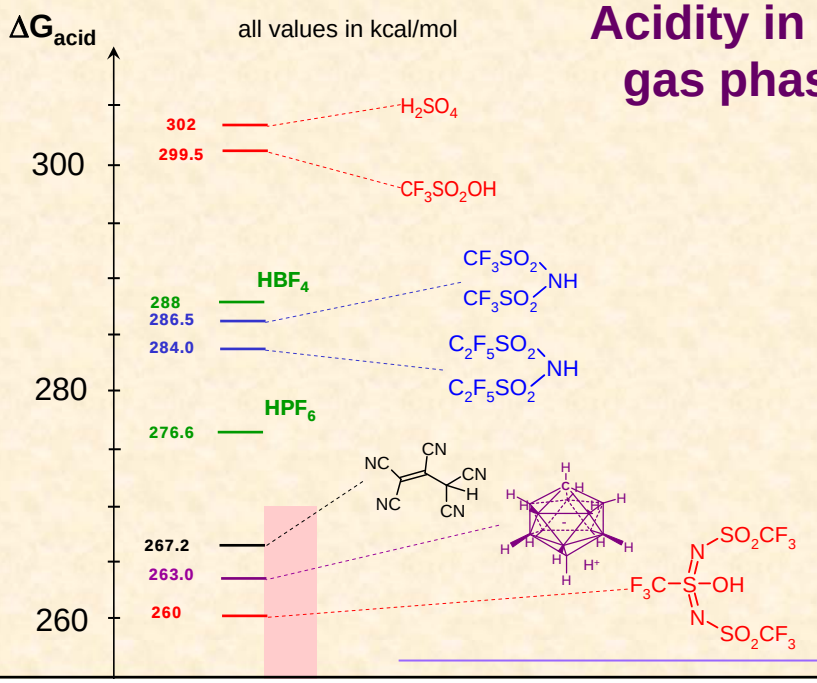
Acidity in the gas phase



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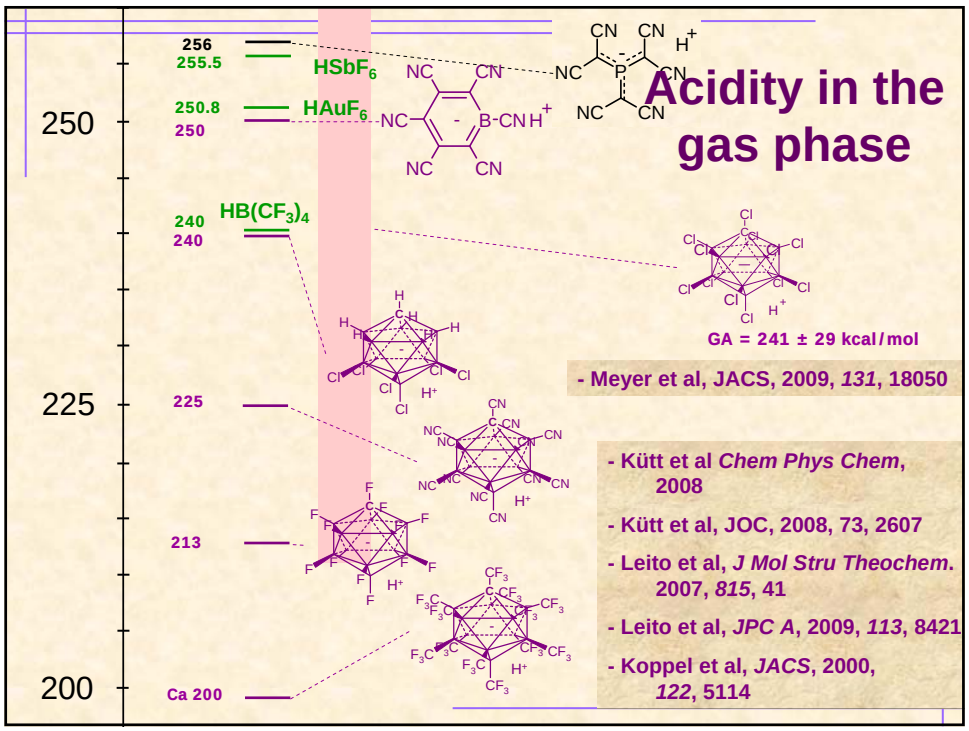
Acidity in the gas phase
256
255.5
250.8
250
240
240
250
225
213
200
Ca 200
HSbF6
HAuF6
HB(CF3)4
GA = 241 ± 29 kcal/mol
- Meyer et al, JACS, 2009, 131, 18050
- Kütt et al Chem Phys Chem, 2008
- Kütt et al, JOC, 2008, 73, 2607
- Leito et al, J Mol Stru Theochem. 2007, 815, 41
- Leito et al, JPC A, 2009, 113, 8421
- Koppel et al, JACS, 2000, 122, 5114


Thanks to all these people!

Collaboration

- Y.L. Yagupolskii
  (IOC, Ukrainian Academy of Sciences, Kiev)
- I. Krossing, D. Himmel
  (Freiburg University)
- A.A. Kolomeitsev, G.-V. Röschenthaler
  (IIPC, University of Bremen)
- V.M. Vlasov (IOC, Russian Academy o Sciences, Novosibirsk)
- M. Mishima (IMCE, Kyushu University)

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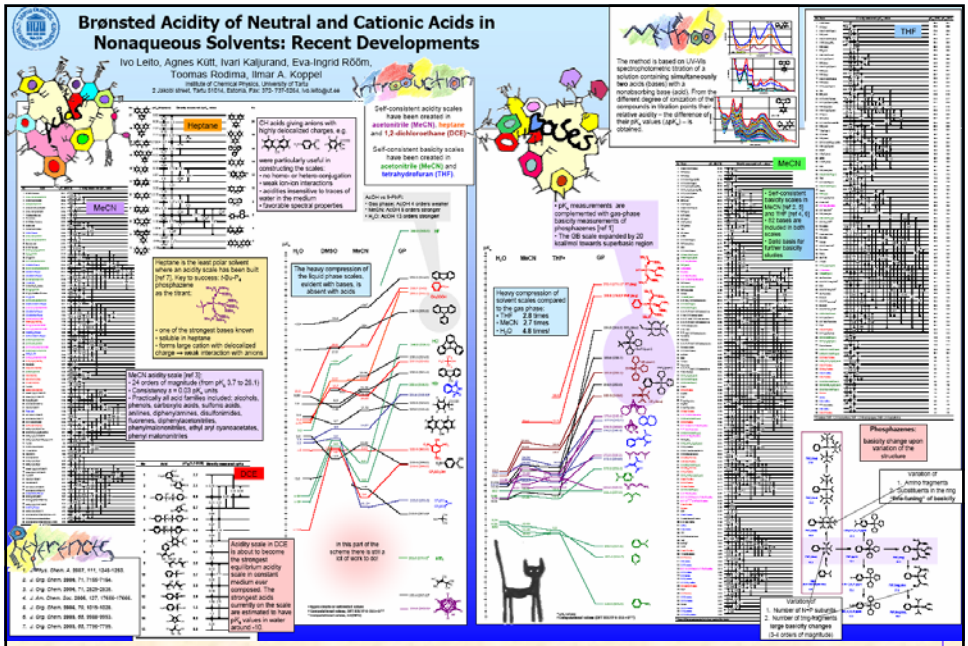

Overview: http://tera.chem.ut.ee/~ivo/HA_UT/

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