The immense acidifying effect of the supersubstituent $=NSO_2CF_3$ on the acidity of amides and amidines of benzoic acids in acetonitrile

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The pK_a values of acidic dissociation of the conjugate acids of derivatives of benzoate anions, where one or two oxygen atoms are replaced by an $=NSO_2CF_3$ group, *N*-aroyltrifluoromethanesulfonamides **1a**–**f** and previously unreported *N,N′*-bis(trifluoromethylsulfonyl)benzamidines **4a**–**f**, were measured in acetonitrile. In the case of the parent compound, the incorporation of the first $=NSO_2CF_3$ group instead of the oxygen atom leads to a sharp (by 9.6 pK_a units) increase in the acidity, whereas the replacement of the second oxygen atom results in a further huge increase in the acidity by 4.9 powers of ten. It was found that the sensitivity of the reaction series under consideration towards substituent effects (in the benzene ring) decreases in the following order: benzoic acids > benzamides (**1a**–**f**) > benzamidines (**4a**–**f**). The results of this work carry potentially important implications for the design of new types of superacids and catalytic materials.

Introduction

The principle of building novel very strong electron-acceptor substituents with extensive conjugated chains was suggested by one of us[1–3] some time ago. It uses the creation of superstrong electron-acceptor substituents by replacing double bonded sp^2 oxygen or sulfur atoms in different (*e.g.* acidic) systems by $=NSO_2CF_3$, $=NSO_2F$, or similar groups.

Since then, a large variety of compounds including those with new superstrong electron-acceptor substituents has been synthesized.[4–6]

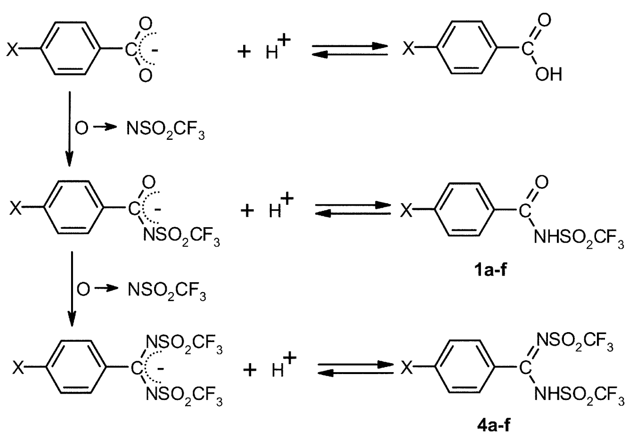
In order to increase the acidity of an acid by changing its structure, it is necessary to either increase the stability of the anion or decrease the stability of the neutral form. By introducing suitable strong electron-acceptor substituents into the acid it is possible to increase the stability of the anion—these substituents contribute to the delocalisation of the charge of the anion.

The introduction of electron-acceptor supersubstituents like $=NSO_2CF_3$, $=NSO_2F$, *etc.* into acidic systems is indeed predicted to lead to very significant increase in their acidity.[7–9] In some cases this has also been observed experimentally[10,11] but nevertheless, the number of experimental studies of the acidity of these novel potentially highly acidic compounds is very limited.

Recently the enormous acidifying effect of the supersubstituent $=NSO_2CF_3$ on the acidity of derivatives of toluene-*p*-sulfonamide in the gas phase and in dimethyl sulfoxide (DMSO) solution was studied by some of us.[10,11] In particular, it was shown that in the gas phase the replacement of the first $=O$ fragment in the sulfo group of $4\text{-Me-}C_6H_4SO_2NH_2$ by $=NSO_2CF_3$ increases its acidity by 23.6 kcal mol^{-1} whereas the substitution of the second $=O$ by the same group leads to an additional acidity increase of 10.7 kcal mol^{-1}. This means that the total acidity is 34.3 kcal mol^{-1} or 25 powers of ten! In DMSO solution the total acidity increase is 13 pK_a units (or 17.7 kcal mol^{-1}).

These observations provide a basis for the further increase of the Brønsted acidity of organic compounds and the creation of new types of superacids and superacidic catalysts.

In the present paper we report the results of studies on the acidity (in acetonitrile solution) of two series of compounds: $ArC(O)NHSO_2CF_3$ and $ArC(=NSO_2CF_3)NHSO_2CF_3$. The deprotonated forms of these compounds could be formally derived from benzoate anions by consecutive replacement of two oxygen atoms (see Scheme 1) and therefore these compounds themselves can also be regarded as derivatives of benzoic acids. The synthetic routes to the compounds **1a**–**f** and **4a**–**f** are presented in Scheme 2.



Scheme 1 The relationship between substituted benzoic acids, their anions, the compounds **1a**–**f** and **4a**–**f** and their anions.

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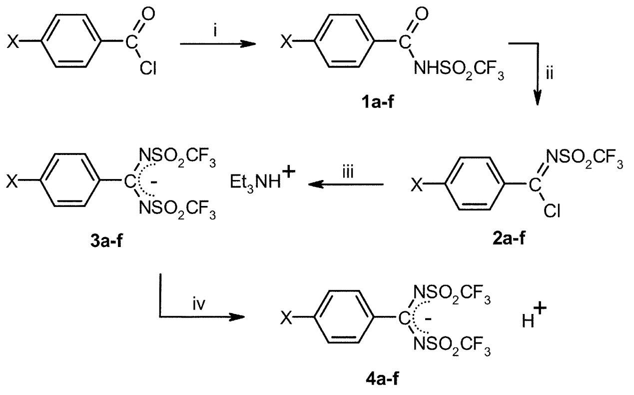


X = OCH_3 (**a**), CH_3 (**b**), H (**c**), F (**d**), Cl (**e**), NO_2 (**f**)

Scheme 2 *Reagents and conditions*: i) $CF_3SO_2NH_2$, Et_3N, CH_3CN, 25 °C. ii) PCl_5, $POCl_3$(4 mmol), reflux. iii) $CF_3SO_2NH_2$, Et_3N, CH_3CN, 25 °C. iv) H_2SO_4, CH_2Cl_2, 0 °C.

Acetonitrile (AN) has many properties that make it suitable for pK_a measurements of strong acids. It has a low basicity and a very low ability to solvate anions.[12] The low basicity gives AN an advantage in studies of strong acids over the other very popular solvents for acid–base studies—water and DMSO—which are considerably more basic (stronger acceptors of hydrogen bonds) and therefore act as levelling solvents for strong acids. AN has a high relative permittivity (D = 36.0[12]) and hence favors the dissociation of ion pairs into free ions. The autoprotolysis constant K_{auto} of AN is very low: p$K_{auto} \geq 33$[13] (even values of pK_{auto} as high as 44 have been suggested[14,15]). All these properties put together make it a good differentiating solvent for strong acids. Additional advantages of AN are its transparency down to 190 nm and relative ease of purification.

The acidity of an acid HA in solvent S refers to the equilibrium:

$$HA + S \rightleftarrows A^- + SH^+ \qquad (1)$$

and is expressed as the equilibrium constant K_a or its negative logarithm pK_a:

$$K_a = \frac{a(SH^+)a(A^-)}{a(HA)} \qquad (2)$$

where a is the activity of the corresponding species. The acid–base equilibria in weakly solvating solvents like acetonitrile are more complex than in water. In addition to the equilibrium (1) there are other equilibria present in the system.[12] In AN the poorly solvated anions eagerly form hydrogen-bonded complexes with hydrogen-bond donors present in the solution. When the donor is the conjugate acid of the anion, the homoconjugation process takes place:

$$A^- + HA \xrightleftharpoons{K_{AHA}} A^- \cdots HA \qquad (3)$$

K_{AHA} (the homoconjugation constant) is the constant of formation of the homoconjugate complex $A^- \cdots HA$:

$$K_{AHA} = \frac{a(A^- \cdots HA)}{a(A^-)a(HA)} \qquad (4)$$

If the donor is some other acid HX then a heteroconjugation process is present:

$$A^- + HX \xrightleftharpoons{K_{AHX}} A^- \cdots HX \qquad (5)$$

These side-reactions have to be suppressed or taken into account if accurate acidity data are to be obtained.

Because of the problems with measuring the acidity of the medium—$a(H^+)$—in non-aqueous solutions, we use a method that eliminates the need for its determination. Our method of acidity measurement gives relative acidities of the acids HA_1 and HA_2 according to the following equilibrium:

$$HA_2 + A_1^- \rightleftarrows A_2^- + HA_1 \qquad (6)$$

$$\Delta pK_a = pK_a(HA_2) - pK_a(HA_1) = \log \frac{a(A_1^-)a(HA_2)}{a(A_2^-)a(HA_1)} \qquad (7)$$

The method consists of UV–Vis spectrophotometric titration of a solution, where both of the acids are present, with a transparent acid or base.[11,16,17]

Experimental

Synthesis

The N,N'-bis(trifluoromethylsulfonyl)benzamidines **4a**–**f** and their triethylammonium salts **3a**–**f** have been synthesized and characterized for the first time. Their synthesis is based on the interaction of N-(trifluoromethylsulfonyl)carboximidoyl chlorides **2a**–**f** with trifluoromethanesulfonamide in the presence of triethylamine in acetonitrile to yield the triethylammonium salts of the N,N'-bis(trifluoromethylsulfonyl)benzamidines **3a**–**f** (see Scheme 2). The starting materials, N-aroyltrifluoromethanesulfonamides[18] and the N-(trifluoromethylsulfonyl)carboximidoyl chlorides **2** have been described earlier[19] with the exception of the compound **2a**, which has been synthesized and described in this work.

In the ^{19}F NMR spectra of the salts **3a**–**f** in $CDCl_3$ and in acetone-d_6 in the range of −79.6 to −79.8 ppm there is a sharp singlet signal from the fluorine nuclei of the trifluoromethyl groups. This provides evidence for the delocalization of the negative charge between the two nitrogen atoms, which carry strong electron-acceptor $-SO_2CF_3$ groups (σ_p = 1.04).[20]

The triethylammonium salts **3a**–**f** are crystalline compounds. They are readily soluble in acetonitrile, methylene chloride, chloroform and benzene. They are insoluble in hexane. Upon treatment of the salts with concentrated H_2SO_4 at 0 °C and extraction with CH_2Cl_2 the N,N'-bis(trifluoromethylsulfonyl)benzamidines **4a**–**f** are obtained in high yields (Scheme 2). In the ^{19}F NMR spectra of **4a**–**f** a sharp singlet peak is present in the range of −76.8 to −79.14 ppm. This could be explained by the equivalence of the two nitrogen atoms due to the fast migration of the proton between those atoms.

General. Moisture-sensitive reactions were carried out under dry argon using flame-dried glassware. All chemicals were of reagent grade or were purified by standard methods before use. Solvents were distilled from the appropriate drying agents immediately prior to use. All reactions were monitored by thin-layer chromatography (TLC) on precoated silica gel Kieselgel 60 F/UV_{254} plates (Merck); spots were visualized with UV light. ^1H and ^{19}F NMR spectra were recorded at 299.5 MHz and 282.2 MHz respectively with a Varian VXR-300 spectrometer, and chemical shifts are given in ppm relative to Me_4Si and CCl_3F, respectively, as internal standards. Coupling constants are given in Hz. IR spectra were recorded with a UR-20 instrument (KBr). Melting points were determined in open capillaries and are uncorrected. Elemental analysis was performed in the Analytical Laboratory of the Institute of Organic Chemistry, NAS of Ukraine, Kiev.

4-Methoxy-N-(trifluoromethylsulfonyl)benzimidoyl chloride (2a). A mixture of carboxamide **1a** (1 g, 2.61 mmol), PCl_5 (0.62 g, 2.98 mmol), and $POCl_3$ (4 ml) was stirred and heated to reflux until evolution of HCl ceased. Once the reaction was complete, $POCl_3$ was distilled off *in vacuo* and the residue was purified by vacuum distillation to give the pure imidoyl chloride **2a** in 81% yield.

Mp 55–56 °C; bp 113–115 °C (0.03 Torr); ^{19}F NMR ($CDCl_3$) δ_F −79.37 (s, 3F, SO_2CF_3) (Calc. for $C_9H_7ClF_3NO_3S$: C, 35.83; H, 2.34; N, 4.64; Cl, 11.75. Found: C, 35.91; H, 2.41; N, 4.63; Cl, 11.78%).

General procedure for the synthesis of triethylammonium salts of *N*,*N*′-bis(trifluoromethylsulfonyl)benzamidines 3a–f. 3 mmol of triethylamine were added to 4 ml of AN solution containing 1.5 mmol of $CF_3SO_2NH_2$. The solution was stirred for 10 minutes and a solution of 1.5 mmol *N*-(trifluoromethylsulfonyl)carboximidoyl chloride **2** in AN was added in batches at 0 °C. The solution was stirred at 0 °C for 0.5 hours. The solution was then warmed up to 25 °C and stirred at that temperature. Completion of the reaction was checked by thin layer chromatography (benzene : ethyl acetate 5 : 2). The solvent was then evaporated *in vacuo*. A 10% solution of HCl was added to the resulting oil. The mixture was extracted with CH_2Cl_2. The combined extracts were washed with water, with 5% solution of $NaHCO_3$ and then again with water. The solution was dried with $MgSO_4$. After removal of the solvent the pure triethylammonium salt **3** was obtained.

*Triethylammonium salt of 4-methoxy-N,N′-bis(trifluoromethylsulfonyl)benzamidine (**3a**).* Colorless solid (yield 73%), mp 66–70 °C; ^{1}H NMR ($CDCl_3$) δ_H 1.34 (t, J = 7.2 Hz, 9H, 3CH_3), 3.22 (m, 6H, 3CH_2), 3.84 (s, 3H, OCH_3), 6.88 (m, 2H, C_6H_4), 7.43 (s, 1H, NH), 8.02 (m, 2H, C_6H_4); ^{19}F NMR ($CDCl_3$) δ_F −79.45 (s, 6F, $2SO_2CF_3$) (Calc. for $C_{16}H_{23}F_6N_3O_5S_2$: C, 37.28; H, 4.50; N, 8.15. Found: C, 37.64; H, 4.72; N, 8.27%).

*Triethylammonium salt of 4-methyl-N,N′-bis(trifluoromethylsulfonyl)benzamidine (**3b**).* Colorless solid (yield 68%), mp 61–65 °C; ^{1}H NMR ($CDCl_3$) δ_H 1.33 (t, J = 7.2 Hz, 9H, 3CH_3), 2.38 (s, 3H, CH_3), 3.24 (m, 6H, 3CH_2), 7.20 (m, 2H, C_6H_4), 7.43 (s, 1H, NH), 7.90 (m, 2H, C_6H_4); ^{19}F NMR ($CDCl_3$) δ_F −79.59 (s, 6F, $2SO_2CF_3$) (Calc. for $C_{16}H_{23}F_6N_3O_4S_2$: C, 38.47; H, 4.64; N, 8.41. Found: C, 38.47; H, 4.56; N, 8.50%).

*Triethylammonium salt of N,N′-bis(trifluoromethylsulfonyl)-benzamidine (**3c**).* Colorless solid (yield 80%), mp 51–55 °C; ^{1}H NMR ($CDCl_3$) δ_H 1.29 (t, J = 7.8 Hz, 9H, 3CH_3), 3.19 (m, 6H, 3CH_2), 7.20 (s, 1H, NH), 7.39–7.99 (m, 5H, C_6H_5); ^{19}F NMR ($CDCl_3$) δ_F −79.69 (s, 6F, $2SO_2CF_3$) (Calc. for $C_{15}H_{21}F_6N_3O_4S_2$: C, 37.11; H, 4.36; N, 8.66. Found: C, 37.23; H, 4.56; N, 8.61%).

*Triethylammonium salt of 4-fluoro-N,N′-bis(trifluoromethylsulfonyl)benzamidine (**3d**).* White solid (yield 67%), mp 83–86 °C; ^{1}H NMR ($CDCl_3$) δ_H 1.21 (t, J = 7.8 Hz, 9H, 3CH_3), 3.49 (m, 6H, 3CH_2), 7.19 (m, 2H, C_6H_4), 7.50 (s, 1H, NH), 7.89 (m, 2H, C_6H_4); ^{19}F NMR ($CDCl_3$) δ_F −79.67 (s, 6F, $2SO_2CF_3$), −109.30 (s,1F, C_6H_4F) (Calc. for $C_{15}H_{20}F_7N_3O_4S_2$: C, 35.78; H, 3.98; N, 8.35. Found: C, 35.69; H, 3.55; N, 8.18%).

*Triethylammonium salt of 4-chloro-N,N′-bis(trifluoromethylsulfonyl)benzamidine (**3e**).* White solid (yield 88%), mp 96–100 °C; ^{1}H NMR ($CDCl_3$) δ_H 1.37 (t, J = 7.5 Hz, 9H, 3CH_3), 3.24 (m, 6H, 3CH_2), 7.46 (s, 1H, NH), 7.60 (m, 2H, C_6H_4), 7.98 (m, 2H, C_6H_4); ^{19}F NMR ($CDCl_3$) δ_F −79.64 (s, 6F, $2SO_2CF_3$) (Calc. for $C_{15}H_{20}ClF_6N_3O_4S_2$: C, 34.65; H, 3.88; N, 8.08. Found: C, 34.70; H, 3.98; N, 8.11%).

*Triethylammonium salt of 4-nitro-N,N′-bis(trifluoromethylsulfonyl)benzamidine (**3f**).* Colorless solid (yield 64%), mp 44–48 °C; ^{1}H NMR ($CDCl_3$) δ_H 1.38 (t, J = 7.7 Hz, 9H, 3CH_3), 3.25 (m, 6H, 3CH_2), 7.86 (s, 1H, NH), 8.13 (m, 2H, C_6H_4), 8.23 (m, 2H, C_6H_4); ^{19}F NMR ($CDCl_3$) δ_F −79.65 (s, 6F, $2SO_2CF_3$) (Calc. for $C_{15}H_{20}F_6N_4O_6S_2$: C, 33.96; H, 3.80; N, 10.56. Found: C, 33.90; H, 3.76; N, 10.80%).

General procedure for the synthesis of *N*,*N*′-bis(trifluoromethylsulfonyl) substituted benzamidines 4a–f. 1 mmol of triethylammonium salt of a substituted *N*,*N*′-bis(trifluoromethylsulfonyl)benzamidine **3** was slowly added to 1 ml of concentrated H_2SO_4 at 0 °C. The solution was stirred at that temperature for 15 minutes, warmed to the room temperature and extracted eight times with CH_2Cl_2 (6 ml of the solvent was used each time). The combined extracts were dried with $MgSO_4$ and the solvent was evaporated *in vacuo*. The residue was crystallized from benzene : hexane (1 : 2).

*4-Methoxy-N,N′-bis(trifluoromethylsulfonyl)benzamidine (**4a**).* White solid (yield 83%), mp 150–152 °C; ν_{max} (KBr)/cm^{-1} 3200 (NH), 1620 (C=N); ^{1}H NMR (acetone-d_6) δ_H 3.98 (s, 3H, OCH_3), 7.20 (m, 2H, C_6H_4), 7.99 (m, 2H, C_6H_4); ^{19}F NMR (acetone-d_6) δ_F −76.83 (s, 6F, $2SO_2CF_3$) (Calc. for $C_{10}H_8F_6N_2O_5S_2$: C, 28.99; H, 1.95; N, 6.76. Found: C, 29.02; H, 1.77; N, 6.90%).

*4-Methyl-N,N′-bis(trifluoromethylsulfonyl)benzamidine (**4b**).* White solid (yield 92%), mp 159–160 °C; ν_{max} (KBr)/cm^{-1} 3350 (NH), 1620 (C=N); ^{1}H NMR (acetone-d_6) δ_H 2.48 (s, 3H, CH_3), 7.48 (m, 2H, C_6H_4), 7.87 (m, 2H, C_6H_4); ^{19}F NMR (acetone-d_6) δ_F −76.86 (s, 6F, $2SO_2CF_3$) (Calc. for $C_{10}H_8F_6N_2O_4S_2$: C, 30.15; H, 2.02; N, 7.03. Found: C, 30.12; H, 1.65; N, 7.04%).

*N,N′-Bis(trifluoromethylsulfonyl)benzamidine (**4c**).* White solid (yield 79%), mp 136–138 °C; ν_{max} (KBr)/cm^{-1} 3170 (NH), 1610 (C=N); ^{1}H NMR (acetone-d_6) δ_H 7.65–7.93 (m, 5H, C_6H_5); ^{19}F NMR (acetone-d_6) δ_F −77.02 (s, 6F, $2SO_2CF_3$) (Calc. for $C_9H_6F_6N_2O_4S_2$: C, 28.13; H, 1.57; N, 7.29. Found: C, 28.46 H, 1.87; N, 7.15%).

*4-Fluoro-N,N′-bis(trifluoromethylsulfonyl)benzamidine (**4d**).* White solid (yield 95%), mp 137–139 °C; ν_{max} (KBr)/cm^{-1} 3200 (NH), 1615 (C=N); ^{1}H NMR (acetone-d_6) δ_H 7.44–8.09 (m, 4H, C_6H_4); ^{19}F NMR (acetone-d_6) δ_F −79.14 (s, 6F, $2SO_2CF_3$), −108.14 (s, 1F, C_6H_4F) (Calc. for $C_9H_5F_7N_2O_4S_2$: C, 26.87; H, 1.25; N, 6.96. Found: C, 26.90 H, 1.26; N, 6.94%).

*4-Chloro-N,N′-bis(trifluoromethylsulfonyl)benzamidine (**4e**).* White solid (yield 88%), mp 141–143 °C; ν_{max} (KBr)/cm^{-1} 3280 (NH), 1630 (C=N); ^{1}H NMR (acetone-d_6) δ_H 7.69 (m, 2H, C_6H_4), 7.97 (m, 2H, C_6H_4); ^{19}F NMR (acetone-d_6) δ_F −78.02 (s, 6F, $2SO_2CF_3$) (Calc. for $C_9H_5ClF_6N_2O_4S_2$: C, 25.81; H, 1.20; N, 6.69. Found: C, 25.74; H, 1.24; N, 6.64%).

*4-Nitro-N,N′-bis(trifluoromethylsulfonyl)benzamidine (**4f**).* White solid (yield 65%), mp 125–127 °C; ν_{max} (KBr)/cm^{-1} 3270 (NH), 1620 (C=N); ^{1}H NMR (acetone-d_6) δ_H 8.10 (m, 2H, C_6H_4), 8.40 (m, 2H, C_6H_4); ^{19}F NMR (acetone-d_6) δ_F −78.29 (s, 6F, $2SO_2CF_3$) (Calc. for $C_9H_5F_6N_3O_6S_2$: C, 25.18; H, 1.17; N, 9.79. Found: C, 25.30; H, 1.30; N, 9.61%).

pK_a measurements

Experimental setup. The spectrophotometric titration method from previous work[16,11] was used. All weighing operations (except the weighing of TfOH for the standard acid solution), preparation of all solutions, titration and spectrophotometric measurements were carried out in an MBraun UNILab glovebox in an argon atmosphere. The measurements were carried out in an external sample compartment situated in the glove-box and connected to the spectrometer (situated outside the glovebox) by means of a fiber-optic accessory. The concentrations of individual acids were usually in the 10^{-5} M range and their total concentration never exceeded 1×10^{-4} M. All solutions were made fresh daily. The rest of the details are the same as in ref. 16.

Chemicals. Solutions of trifluoromethanesulfonic acid (TfOH) (Aldrich, 99+%) and triethylamine (Et_3N) (REAKHIM, pure for analysis) were used as acidic and basic titrants, respectively.

Solvent. AN (>99.9%, Super Purity Solvent (far UV), water content <0.005%) was purchased from Romil (Cambridge, UK) and used without further purification. It was stored in dark bottles in the glovebox and/or refrigerator. It has low absorbance in the UV region down to 200 nm, and its absorbance did not change upon addition of acidic or basic titrant.

Calculation method. The ΔpK_a calculation methods in AN are similar to those of previous work[11,16] only the essentials are given here.

When two partially protonated acids HA_1 and HA_2 are in the same solution, then the following equation holds for absorbance A at wavelength λ (1 cm path length):

$$A^{\lambda} = [HA_1]\,\varepsilon^{\lambda}_{HA_1} + [A_1^-]\,\varepsilon^{\lambda}_{A_1^-} + [HA_2]\,\varepsilon^{\lambda}_{HA_2} + [A_2^-]\,\varepsilon^{\lambda}_{A_2^-} \quad (8)$$

The molar absorptivities ε can be found separately from the spectra of the free acids and fully protonated acids. If we use concentrations that are normalized to 1 then we may write: $[HA_1] = 1 - [A_1^-]$ and $[HA_2] = 1 - [A_2^-]$. After mathematical transformation of eqn. (8) we get:

$$\frac{A^{\lambda} - \varepsilon^{\lambda}_{HA_1} - \varepsilon^{\lambda}_{HA_2}}{(\varepsilon^{\lambda}_{A_2^-} - \varepsilon^{\lambda}_{HA_2})} = [A_1^-]\frac{(\varepsilon^{\lambda}_{A_1^-} - \varepsilon^{\lambda}_{HA_1})}{(\varepsilon^{\lambda}_{A_2^-} - \varepsilon^{\lambda}_{HA_2})} + [A_2^-] \quad (9)$$

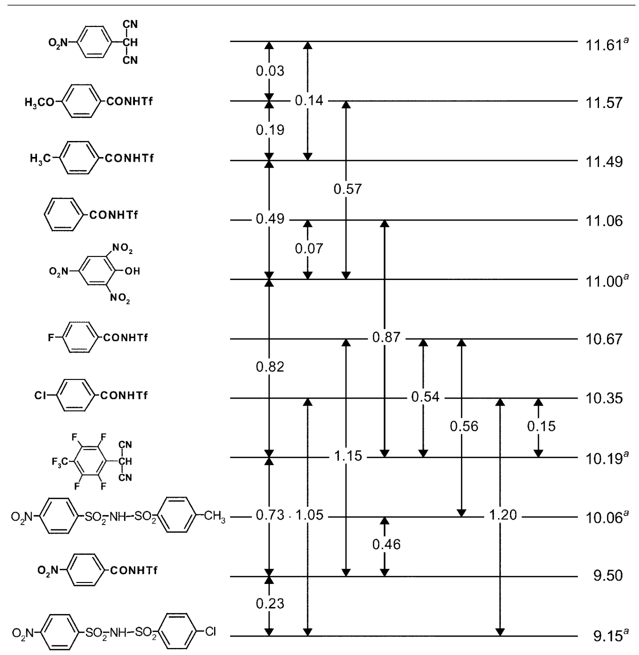
If the spectra are recorded over a range of wavelengths then $[A_1^-]$ and $[A_2^-]$ can be found from eqn. (9) as the slope and intercept of a regression line. Knowing $[A_1^-]$ and $[A_2^-]$ the calculation of ΔpK_a of the acids is straightforward. In many cases (for example, when the acids have absorption maxima in different wavelength ranges) it was possible to use various simpler calculation procedures (see refs 11 and 17). The mixture of acids as well as both acids separately was titrated with an optically transparent acid and/or base and the data for ΔpK_a calculations were obtained from UV–Vis spectra. From each titration experiment, the ΔpK_a was determined as the mean of 4–17 values.

In some cases (4-F-C_6H_4CONHTf) the calculations were carried out on molar basis. The solution containing a mixture of known amounts (in moles) of an "invisible" and a "visible" acid was titrated with a titrant of known concentration. From the added titrant mass and its concentration the amount (in moles) of the titrant in the cell was found. Combining the spectra of solutions containing both acids in fully deprotonated, fully protonated and the mixture of protonated and deprotonated forms the indicator ratio of the visible acid was calculated and knowing the amounts of the visible acid and titrant added, the indicator ratio for the "invisible" acid was calculated. The ΔpK_a calculation is then straightforward (see ref. 16 for details).

Results

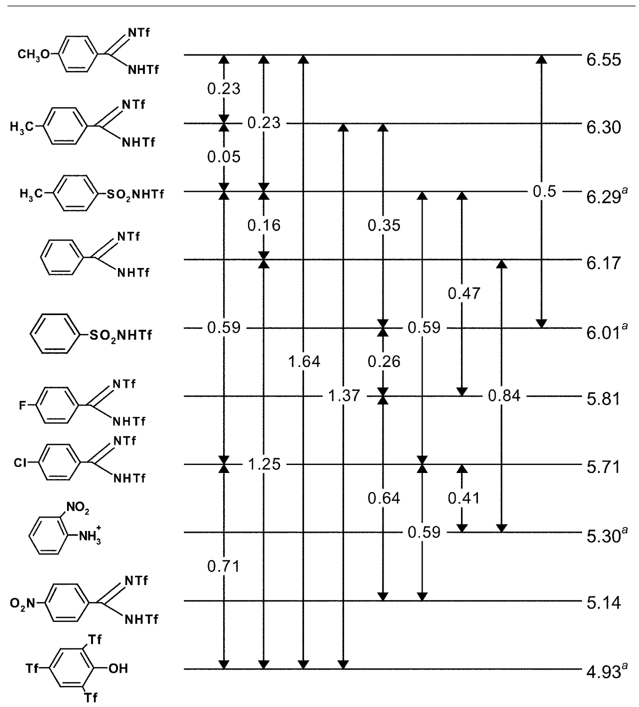
All in all, 35 individual relative acid–base equilibrium measurements between 21 acids were carried out (see Tables 1 and 2). With each of the acids of the families **1a–f** and **4a–f** the ΔpK_a values were determined relative to at least two reference acids with known pK_a values.[11] The reference acids are indicated in Tables 1 and 2. The consistency of the ΔpK_a values with the pK_a values of the reference acids is very good in all cases. The absolute pK_a values were assigned as mean values of pK_a values obtained from individual measurements.

Table 1 Directly measured ΔpK_a values of compounds **1a–f** relative to various reference acids with known pK_a values in AN



[a] Reference acids. pK_a values of the reference acids are from ref. 11.

Table 2 Directly measured ΔpK_a values of compounds **4a–f** relative to various reference acids with known pK_a values in AN



[a] Reference acids. pK_a values for the reference acids are from ref. 11.

Discussion

The anions of *N*-aroyltrifluoromethanesulfonamides **1a–f** and *N*,*N*′-bis(trifluoromethylsulfonyl)benzamidines **4a–f** are derivatives of the benzoate anions in which one or two atoms of oxygen are replaced by $=NSO_2CF_3$ (or rather $\cdots NSO_2CF_3$ groups), thus the corresponding neutrals can be formally considered derivatives of benzoic acids. It is therefore interesting to compare the pK_a values of these compounds to those of substituted benzoic acids.

The summary of the pK_a values (AN) for *N*-aroyltrifluoromethanesulfonamides **1a–f** and *N*,*N*′-bis(trifluoromethylsulfonyl)benzamidines **4a–f** are given in Tables 1 and 2; the pK_a data of substituted benzoic acids available from the literature are given in Table 3.

Table 3 pK_a values of substituted *N*-aroyltrifluoromethanesulfonamides **1a**–**f**, *N*,*N'*-bis(trifluoromethylsulfonyl)benzamidines **4a**–**f** and benzoic acids in AN and the Hammett σ_p constants for the same substitution

X	*p*-$XC_6H_4CONHTf$ pK_a [a]	*p*-$XC_6H_4C(=NTf)NHTf$ pK_a [a]	*p*-XC_6H_4COOH pK_a	σ_p [e]
$(CH_3)_2N$			23.0 [b]	−0.83
CH_3O	11.57	6.55		−0.27
CH_3	11.49	6.30		−0.17
H	11.06	6.17	20.7 [c]	0
Br			20.3 [d]	0.23
F	10.67	5.81		0.06
Cl	10.35	5.71		0.23
NO_2	9.50	5.14	18.7 [c]	0.78

[a] This work. [b] Ref. 21. [c] Ref. 22. [d] Ref. 23. [e] Ref. 20.

One can see that the replacement of only one oxygen atom in the benzoate anion (X = H) by an $-NSO_2CF_3$ group increases the acidity of its conjugate NH acid (compound **1c**) by 9.6 powers of ten whereas the replacement also of the second oxygen atom (compound **4c**) leads to a further significant increase (by 4.9 pK_a units) of acidity: thus the total acidifying effect of going from benzoic acid to its benzamidine analog, another NH acid **4c**, reaches 14.5 powers of ten!

Simple Hammett-type correlations pK_a *vs.* σ_p are found to describe the dependence of the measured pK_a values for all three reaction series in AN (see Table 3 and Fig. 1): (a) *N*-trifluoromethylsulfonylbenzamides (**1a**–**f**) *p*-$XC_6H_4CONHSO_2CF_3$: p$K_a = (10.99 \pm 0.07) - (2.04 \pm 0.20)\sigma_p$; $r^2 = 0.965$; $s = 0.16$; $n = 6$; (b) *N*,*N'*-bis(trifluoromethylsulfonyl)benzamidines *p*-$XC_6H_4C(=NSO_2CF_3)NHSO_2CF_3$: p$K_a = (6.08 \pm 0.06) - (1.31 \pm 0.16)\sigma_p$; $r^2 = 0.945$; $s = 0.13$; $n = 6$; (c) benzoic acids *p*-XC_6H_4COOH: p$K_a = (20.79 \pm 0.05) - (2.64 \pm 0.09)\sigma_p$; $r^2 = 0.998$; $s = 0.11$; $n = 4$.

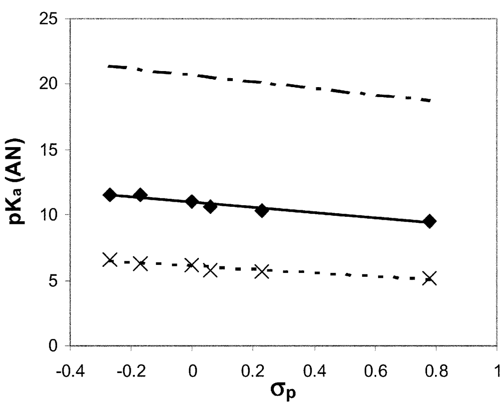


Fig. 1 Plot of pK_a(AN) *versus* Hammett σ_p (data from Table 3) for the following series substituted at the *para* position: benzoic acids (-·-), 4-$XC_6H_4CONHTf$ (——) and 4-$XC_6H_4C(=NTf)NHTf$. (···).

One can see that the sensitivity of these different reaction series towards the substituent effects (in acetonitrile) decreases in the following order: benzoic acids > amides **1a**–**f** > amidines **4a**–**f** which is reflected by the declining ρ values, 2.64 > 2.04 > 1.31, respectively.

However one has to recall that direct comparison of these ρ values is not justified because the reaction series a and b represent NH acids and series c represents OH acids. Also, the immediate surroundings of the deprotonation center in the case of these two series of NH acids are different ($-CONHSO_2CF_3$ and $-C(=NSO_2CF_3)NHSO_2CF_3$).

Due to those circumstances and similar to the earlier findings (the non-additivity of consecutive substitution effects of the oxygen atoms of the SO_2 group by $=NSO_2CF_3$ in the reaction series of the acidic dissociation of substituted toluenesulfonamides in DMSO solution),[10] the effect of replacement of oxygen atoms in carboxylic groups by $=NSO_2CF_3$ is also non-additive. The effect of the replacement of the first oxygen atom in the carboxylic function is by 4.7 pK_a units or 9.6/4.9 = 1.96 times larger than the acidifying effect of the second oxygen atom replacement.

Still, leaving aside the questions of comparability of the absolute ρ values these quantities clearly reflect the increasing degree of delocalization of the negative charge in the anionic center when moving from benzoate anions to the deprotonated compounds **4a**–**f**.

Conclusions

The pK_a values of *N*-aroyltrifluoromethanesulfonamides **1a**–**f** and previously unreported *N*,*N'*-bis(trifluoromethylsulfonyl)-benzamidines **4a**–**f** were measured in acetonitrile by spectrophotometric techniques. It was shown that the replacement of the oxygen atoms in the benzoate anions leads to an extraordinarily strong increase in the acidity of the respective conjugate acids. These findings can be used for the design of novel organic superacids and catalysts.

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References

1 N. V. Kondratenko, V. I. Popov, O. A. Radchenko, N. V. Ignat'ev and L. M. Yagupolskii, *Zh. Org. Khim.*, 1986, **22**, 1716.
2 L. M. Yagupolskii, V. I. Popov, N. V. Pavlenko, R. Y. Gavrilova and V. V. Orda, *Zh. Org. Khim.*, 1986, **22**, 2169.
3 L. M. Yagupolskii, *Aromatic and Heterocyclic Compounds with Fluorine-Containing Substituents*, Naukova Dumka, Kiev, 1988.
4 V. N. Boiko, N. V. Kirii and L. M. Yagupolskii, *J. Fluorine Chem.*, 1994, **67**, 119.
5 L. M. Yagupolskii, R. Yu. Garlyauskajte and N. V. Kondratenko, *Synthesis*, 1992, 749.
6 L. M. Yagupolskii, N. V. Kondratenko and S. V. Iksanova, *Zh. Org. Khim.*, 1995, **31**, 747.
7 I. A. Koppel, R. W. Taft, F. Anvia, N. V. Kondratenko and L. M. Yagupolskii, *Zh. Org. Khim.*, 1992, **28**, 1764.
8 P. Burk, I. A. Koppel, I. Koppel, L. M. Yagupolskii and R. W. Taft, *J. Comput. Chem.*, 1996, **17**, 30.
9 I. A. Koppel, R. W. Taft, F. Anvia, S.-Z. Zhu, L.-Q. Hu, K.-S. Sung, D.-D. DesMarteau, L. M. Yagupolskii, Y. L. Yagupolskii, N. V. Ignat'ev, N. V. Kondratenko, A. Y. Volkonskii, V. M. Vlasov, R. Notario and P.-C. Maria, *J. Am. Chem. Soc.*, 1994, **116**, 3047.
10 I. A. Koppel, J. Koppel, I. Leito, I. Koppel, M. Mishima and L. M. Yagupolskii, *J. Chem. Soc., Perkin Trans. 2*, 2001, 229.
11 I. Leito, I. Kaljurand, I. A. Koppel, L. M. Yagupolskii and V. M. Vlasov, *J. Org. Chem.*, 1998, **63**, 7868.
12 J. F. Coetzee, *Prog. Phys. Org. Chem.*, 1967, **4**, 45 and references therein.

13 I. M. Kolthoff and M. K. Chantooni Jr., *J. Phys. Chem.*, 1968, **72**, 2270.
14 R. Schwesinger and H. Schlemper, *Angew. Chem., Int. Ed. Engl.*, 1987, **26**, 1167.
15 C. F. Bernasconi, A. E. Leyes, M. L. Ragains, Y. Shi, H. Wang and W. D. Wulff, *J. Am. Chem. Soc.*, 1998, **120**, 8632.
16 I. Kaljurand, T. Rodima, I. Leito, I. A. Koppel and R. Schwesinger, *J. Org. Chem.*, 2000, **65**, 6202.
17 I. Leito, T. Rodima, I. A. Koppel, R. Schwesinger and V. M. Vlasov, *J. Org. Chem.*, 1997, **62**, 8479.
18 G. G. Moore, A. C. Conway, Minnesota Mining and Manufacturing Co., *US Pat.* 3705185 (*Chem. Abstr.*, 1973, **78**, 58095m).
19 L. M. Yagupolskii, S. V. Shelyazhenko, I. I. Maletina, V. N. Petrik, E. B. Rusanov and A. N. Chernega, *Eur. J. Org. Chem.*, 2001, 1225.
20 C. Hansch, A. Leo and R. W. Taft, *Chem. Rev.*, 1991, **91**, 165.
21 *Tables of Rate and Equilibrium Constants of Heterolytic Organic Reactions*, ed. V. A. Palm, VINITI, Moscow-Tartu, 1975–1985.
22 I. M. Kolthoff and M. K. Chantooni, Jr., *J. Phys. Chem.*, 1966, **70**, 856.
23 M. K. Chantooni, Jr. and I. M. Kolthoff, *J. Phys. Chem.*, 1973, **77**, 527.