

Comparison of Brønsted acidities of neutral CH acids in gas phase and dimethyl sulfoxide

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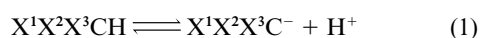
The Brønsted acidities of a number of neutral CH-acids (substituted toluenes, aryl- and diarylacetonitriles, fluorenes, ethyl esters of phenylcyanoacetic acids, substituted methanes, *etc.*) were measured in the gas phase (pulsed FT-ICR spectrometry) and in dimethyl sulfoxide (potentiometric titration). Comparison of the Brønsted acidities of the neutral CH-acids in the gas phase and in dimethyl sulfoxide (DMSO) was also carried out. It was shown that, as a rule, substituent effects on the acidity of the studied compounds are significantly attenuated by the transfer of the reaction series of acidic dissociation of neutral acids from the gas phase into DMSO. The weakest attenuation was monitored in the case of aromatic hydrocarbons, which are the conjugate acids of carbanions with very extensive charge delocalization (fluoradene, substituted fluorenes, aryl-substituted cyclopentadienes and indenenes, toluene, diphenyl and triphenylmethanes, *etc.*). The strongest solvent-induced attenuation of the substituent effects is characteristic of *meta*-substituted phenylacetonitriles and phenylmalononitriles, whose sensitivity towards substituent effects decreases with transfer from the gas phase into DMSO by up to 2.8–3.3 times. At the same time, the reaction series of *para* and/or *ortho*- π -acceptor substituted phenylacetonitriles are less sensitive to a change from the gas phase to DMSO.

In the series of α -cyanosubstituted toluenes the solvent attenuation of substitution effects in the benzene ring increases with the successive inclusion of cyano groups into the α -position.

In the special case of *para*-acceptor substituted phenylacetonitriles it was demonstrated that the specific solvation induced an increase in the acidity of the *para*- and/or *ortho*-acceptor substituted phenylacetonitriles as compared to the behavior of the corresponding *meta*-substituted phenylacetonitriles by up to 3.6 p*K*_a units.

Introduction

Acidic dissociation of neutral Brønsted CH acids X¹X²X³CH occurs according to the scheme:



where X¹, X² and X³ are substituents. This reaction plays an extremely important role in chemical technology, organic synthesis, biochemistry, molecular biology, *etc.* Therefore the study of CH acidity and its dependence upon structure and solvent is of crucial significance for the understanding of mechanisms in a wide variety of chemical, biochemical, *etc.* processes and for the optimization of the technological schemes and synthetic routes in chemical engineering and synthetic chemistry.

So far, various aspects of the influence of structure and solvent (dimethoxyethane, cyclohexylamine, dimethyl sulfoxide) on p*K*_a values of several classes of neutral CH acids have been discussed.^{1–5} In the present work, the comparison of Brønsted acidities of different classes of compounds (substituted toluenes, fluorenes, arylacetonitriles, aryl and diarylmethanes, *etc.*) in the gas phase and DMSO was undertaken. Also, some

aspects of the problems discussed in ref. 1 are revisited and reconsidered with the inclusion of the new experimental data available.

One of our goals was the study of solvent dependence of substituent effects in the toluene family, ArCH₃, on the nature and extent of the substitutions of the α -hydrogen atoms of its methyl group.^{1,2} The electronic structure and number of the α -groups, their donor and acceptor properties and steric demands play the major role in delocalization of the charge of the carbanionic center. The cyano function⁶ is strongly electron-withdrawing and has minimal steric demand for fulfilling the coplanarity conditions for the carbanions.^{7,8} From the practical viewpoint, the introduction of one or more cyano groups into toluene or methane allows the p*K*_a of the resulting cyanocarbon acid (p*K*_a(C₆H₅CH₂CN) = 21.9; p*K*_a(C₆H₅CH(CN)₂) = 4.2) to be measured in DMSO solution.⁹ Therefore comparison of solvent dependence of substituent effects in a series of substituted toluenes, arylacetonitriles and arylmalononitriles is possible.¹⁰

The effect of the introduction of an α -ester group (*e.g.*, COOC₂H₅) into toluene is only somewhat less acidifying (Δ p*K*_a = 20) than the corresponding effect of the introduction of the first CN group (Δ p*K*_a = 21).^{1,2,9,11} At the same time due to the lower electron accepting ability and more pronounced

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steric demands, the consecutive introduction of two CN and COOC₂H₅ groups into CH₄ produces already a more significant difference in the acidities of the resulting molecules (p*K*_a respectively 11.0 and 16.7 in DMSO).

The introduction of an α -phenyl group into toluene leads to a more modest estimated increase of the acidity: (C₆H₅)₂CH₂ is expected to be, by 10.8 p*K*_a units, more acidic than C₆H₅-CH₃.^{1,2,9-11} At the same time, consecutive replacement of the phenyl group in the arylmethanes by the electron-acceptor group(s) is known to lead to further increase (by *ca.* 5–6 p*K*_a units per one substitution) the acidity of the α -C–H bond.¹¹

In DMSO solution the acidifying effect of CF₃ group is stronger than that of phenyl group ((CF₃)₃CH p*K*_a = 12.6;¹² C₆H₅C(CF₃)₂H p*K*_a = 17–18;¹³ see also ref. 11). However, the strongest acidifying effect of the α -substituent belongs to trifluoromethanesulfonyl (triflyl) group: the introduction of a CF₃SO₂ group into α -position of toluene reduces its p*K*_a by 28.4 units.⁹ At the same time in the gas phase the introduction of the first triflyl group into methane increases its acidity by 66.8 kcal mol⁻¹,¹⁴ in DMSO the acidity increase is 37 p*K*_a units.⁹ The second CF₃SO₂ group increases the acidity of the resulting bistriflylmethane by 38.3 kcal mol⁻¹¹⁴ and 16.4 p*K*_a units⁹ respectively.

The fruitful idea about comparison of gas-phase and solution acidities for acids which give highly charge-dispersed carbanions with no heteroatoms, *e.g.* fluoradene, substituted fluorenes, *etc.* was put forward a long time ago.^{15,16} Later it was shown¹⁻⁴ that for some rather narrow selection of acids practically no attenuation of the substituent effects with the transfer from the gas phase into DMSO takes place. One of the goals of this work is to verify the limits of observance of this phenomenon on the basis of a wider selection of the representative CH-acids, and in some cases to revise of the earlier reported data.

A literature analysis^{1,2,5,9,17,18} shows, however, that the acidity data for most compounds are not simultaneously available in the above mentioned media. To partially fill that gap, in the experimental part of this work the gas phase acidity of CH acids (diarylmethanes, substituted toluenes, arylacetonitriles, fluorenes, cyclopentadienes, substituted methanes, *etc.*) was measured by ion cyclotron resonance (ICR) spectrometry. In particular, the gas-phase acidities and/or the p*K*_a values of acidic dissociation in DMSO solution were measured for the series of substituted diarylacetonitriles Ar¹CH(CN)Ar², ethyl esters of substituted (polyfluoro)arylcynoacetic acids XC₆F₄-CH(CN)COOC₂H₅, ring-polysubstituted toluenes, α,α' -bistriflyltoluenes, α,α' -bisfluorosulfonyltoluenes, trifluoroacetyl-substituted methanes and for some other Brønsted CH acids. The gas phase acidities and p*K*_a values in DMSO of substituted toluenes, phenylacetonitriles and fluorenes were also measured.

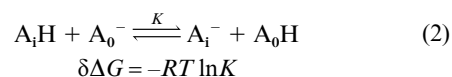
Some of the measured ΔG_{acid} values were, prior to publication, donated by one of us (R. W. T.) to the NIST database of the gas-phase acidities and appeared in NIST tables¹⁸ or in review articles (*e.g.*, ref. 2(*b*)). However the experimental details of those measurements, which are necessary for the correct assessment of the quality and self-consistency of these data, were never made available to a wider audience. This task is fulfilled in the current publication. Simultaneously some noticed mistakes or inconsistencies in the ΔG_{acid} values of the compounds published in NIST tables are revised and corrected.

Experimental

Gas phase acidity measurements

The gas phase acidity measurements reported in this paper were performed at the Chemistry Department of the University of California, Irvine, using either a pulsed FT ion cyclotron resonance mass-spectrometer¹⁴ (IonSpec Corp., Irvine, CA) or a conventional ICR spectrometer (built in-house at the

University of California, Irvine), both with 1 Tesla electromagnets. Part of the measurements were also made at the Institute for Fundamental Research of Organic Chemistry, Kyushu University using an Extrel FT-MS 2001 spectrometer (3 Tesla superconducting magnet). The experimental techniques used for the measurement of the equilibrium constants, *K*, of the proton transfer reaction (2), where A_i refers to the given acid



(A_iH) and A₀ to the standard (reference) compound (A₀H), were largely as described previously.^{14,19} All experiments were performed at a cell temperature of 100 °C. The partial pressures of the compounds were in the 10⁻⁸–10⁻⁷ Torr range. The equilibrium constants were calculated according to the standard procedure using the appropriate correction factors applied to direct ion gauge readings for the different ionization cross section of the various compounds.

The experimental $\delta\Delta G_{\text{acid}}$ values relative to various reference compounds are listed in Table 1.

Several compounds were not stable enough under the ICR conditions to be measured in the gas phase. So, no peak corresponding to the anionic form was monitored for 4-(CF₃)₃-CC₆F₄CH(CN)C₆F₄CF₃. In a similar way, in the case of (2-C₁₀F₇)₂CHCN loss of the C₁₀F₇ fragment took place and no anion with *m/z* = 544 corresponding to the M – 1 ion was observed. The measurements of ΔG_{acid} for several compounds (1,3,5-(CF₃SO₂)₃C₆H₃, 1,3,5-(NO₂)₃C₆H₃, [2,4,6-(CF₃SO₂)₃C₆H₂]₂CH₂) for which we report here p*K*_a values failed as described in ref. 14.

p*K*_a measurements

In DMSO the p*K*_a values of CH acids were measured at 25 °C using the potentiometric titration of the DMSO solution of the acid with the standard *ca.* 0.01 molar solution of Bu₄NOH. Benzoic acid (p*K*_a = 11.0⁹) and 2,6-dinitrophenol (p*K*_a = 4.9⁹) were used as the reference compounds. The p*K*_a values calculated for the different ionization ratios remained constant within 0.02–0.04 p*K*_a units. The average p*K*_a values are reliable within ± 0.2 p*K*_a units. A detailed description of the technique is given in refs. 12 and 20–22.

The acidities of some CH acids (*e.g.* Tf₃CH, (FSO₂)₃CH, (CF₃CO)₃CH, *etc.*) were evidently too high to be measured by this method in DMSO. Their p*K*_a values are assumed to be below the determination limit (*ca.* p*K*_a ≤ 2) of the method of potentiometric titration.

Indeed, the extrapolation of the ΔG_{acid} vs. p*K*_a(DMSO) relationships 8 and 9 from Table 3 for derivatives of methane (see also Fig. 1) to the corresponding ΔG_{acid} values for Tf₃CH, (FSO₂)₃CH, (CF₃CO)₃CH and (NC)₃CH leads to much lower p*K*_a values. In particular, for cyanoform, the use of the relationship 8 from Table 3 and suggested gas-phase value $\Delta G_{\text{acid}} = 293$ ¹⁴ leads to the extrapolated value of p*K*_a = –7.

Chemicals

The following compounds are the same as used in ref. 14: 19, 20, 44–46, 48, 49, 51, 62, 63, 66, 67, 75, 76, 96–100, 102–104, 107–109. The following compounds were synthesized at the Institute of Organic Chemistry of Siberian Branch of Russian Academy of Sciences as described in previous publications: 53,²³ 54–57,²⁴ 58,²³ 59,²³ 60,²⁵ 61,²⁵ 64,²³ 65,²⁶ 69–73,²⁷ 74,²⁸ 105,²⁹ 106.³⁰ Compounds 5, 26, 35, 36, 78, 80, 81, 83, 95 and the substituted fluorenes were a kind donation from Professor F. G. Bordwell to R. W. T. Compound 21 was a kind donation from Professor K. Friedrich (University of Freiburg, Germany) to I. A. K. Toluene 17 was the same as used in ref. 31. Toluene 10 was the same as used in ref. 32. Toluenes 4 and 12 were prepared according to

Table 1 Directly measured $\delta\Delta G_{\text{acid}}$ values^a for proton-transfer equilibria between the studied CH acids A_1H and reference acids A_0H at 373 K

A_1H^b	A_0H	$\Delta G_{\text{acid}}(A_0H)^{c,d}$	$\delta\Delta G_{\text{acid}}^c$
<i>Substituted toluenes</i>			
4-NO ₂	Pr ⁱ SH	347.1	-1.6
	BuSH	346.2	-0.8
4-NO	4-NO ₂ C ₆ H ₄ CH ₃	345.3	-0.2
	4-CH ₃ OCOC ₆ H ₄ NH ₂	345.2	-0.1
4-SO ₂ CF ₃	C ₆ H ₅ OH	342.3	-1.5
	3,5-(CF ₃) ₂ C ₆ H ₄ NH ₂	340.6	0.1
4-COC ₆ H ₅	3-FC ₆ H ₄ NH ₂	353.9	-0.4
4-COCH ₃	4-FC ₆ H ₄ NH ₂	357.0	-2.0
	2-FC ₆ H ₄ NH ₂	355.3	-0.4
	3-FC ₆ H ₄ NH ₂	353.9	0.8
4-COCN	4-FC ₆ H ₄ OH	339.9	-0.9
	2-FC ₆ H ₄ OH	339.0	-0.1
4-COCF ₃	3-CNC ₆ H ₄ NH	345.7	-1.6
	4-CH ₃ OC ₆ H ₄ OH	343.5	0.6
4-CO ₂ CH ₃	2-FC ₆ H ₄ NH ₂	355.3	0.05
	3-FC ₆ H ₄ NH ₂	353.9	1.4
3-NO	CH ₃ COCH ₃	361.9	-0.4
	C ₆ H ₅ NH ₂	359.1	1.5
4-SO ₂ CH ₃	4-ClC ₆ H ₄ NH ₂	353.1	-0.9
	3-ClC ₆ H ₄ NH ₂	351.6	0.4
4-SOCH ₃	4-CH ₃ OC ₆ H ₄ NH ₂	359.8	-0.5
	C ₆ H ₅ NH ₂	359.1	0.2
3-CON(CH ₃) ₂	Bu ⁱ OH	368.0	-0.7
	Bu ⁱ CH ₂ OH	366.0	0.7
4-CON(CH ₃) ₂	C ₆ H ₅ NH ₂	359.1	-0.3
	4-FC ₆ H ₄ NH ₂	357.0	1.1
3,5-(CF ₃) ₂	3-FC ₆ H ₄ NH ₂	353.9	0.3
2,3,4,5,6-(CN) ₅	(CF ₃ CO) ₂ NH	307.5	-5.5
	(CF ₃ SO ₂) ₂ CH ₂	301.5	0.6
<i>Substituted phenylacetonitriles</i>			
3-CF ₃	3-FC ₆ H ₄ OH	336.8	-1.6
	3-ClC ₆ H ₄ OH	335.0	0.3
3-CN	C ₆ H ₅ SH	333.8	-1.5
3-OCH ₃	4-CH ₃ C ₆ H ₄ OH	343.4	-0.7
	C ₆ H ₅ OH	342.3	0.5
4-(CH ₃) ₂ N	Pr ⁱ SH	347.1	-0.6
	Bu ⁱ SH	346.2	0.4
4-OCH ₃	4-CF ₃ C ₆ H ₄ NH ₂	346.0	-1.1
	4-CH ₃ C ₆ H ₄ OH	343.4	1.8
4-CN	CF ₃ CH ₂ COOH	327.7	0.2
	4-SCF ₃ C ₆ H ₄ OH	330.4	-0.5
4-NO ₂	CHF ₂ COOH	323.8	-0.4
	3,5-(CF ₃) ₂ C ₆ H ₃ OH	322.9	0.4
	3-CF ₃ SO ₂ C ₆ H ₄ OH	322.7	0.6
	CHCl ₂ COOH	320.8	2.2
4-F	C ₆ H ₅ OH	342.3	0.0
	3-Pr ⁱ C ₆ H ₄ OH	342.2	0.3
4-CF ₃	3-ClC ₆ H ₄ OH	335.0	-1.9
	3-CF ₃ C ₆ H ₄ OH	332.4	0.5
<i>Ar¹CH(CN)Ar²</i>			
<i>Ar¹</i>	<i>Ar²</i>		
C ₆ H ₅	C ₆ H ₅	3-CF ₃ C ₆ H ₄ CH ₂ CN	335.3 ^f
		(CH ₃ CO) ₂ CH ₂	336.7
		(CF ₃) ₃ COH	324.0 ^e
C ₆ H ₅	C ₆ F ₅	C ₆ F ₅ CH ₂ CN	327.6 ^e
		C ₄ F ₉ SO ₂ NH ₂	315.1 ^e
C ₆ H ₅	4-NC ₅ F ₄	(CF ₃) ₃ CH	326.6 ^e
C ₆ H ₅	4-CH ₃ C ₆ F ₄	(CF ₃) ₃ CH	326.6 ^e
C ₆ H ₅	4-HC ₆ F ₄	C ₆ F ₅ CH(CN)C ₆ H ₅	325.6 ^f
		C ₄ F ₉ SO ₂ NH ₂	315.1 ^e
C ₆ H ₅	4-CF ₃ C ₆ F ₄	4-NC ₅ F ₄ CH(CN)C ₆ H ₅	316.0 ^f
		CF ₃ COSH	312.5 ^e
C ₆ F ₅	4-ClC ₆ F ₄	(CF ₃ CO) ₂ CH ₂	310.3 ^e
C ₆ F ₅	4-COOC ₂ H ₅ C ₆ F ₄	C ₄ F ₉ SO ₂ NH ₂	315.1 ^e
C ₆ F ₅	4-CH ₃ C ₆ F ₄	(CF ₃ CO) ₂ NH	307.5 ^e
C ₆ F ₅	4-NC ₅ F ₄	CF ₃ COSH	312.5 ^e
C ₆ F ₅	4-BrC ₆ F ₄	4-ClC ₆ F ₄ CH(CN)C ₆ F ₅	311.8 ^f
		(CF ₃ CO) ₂ NH	307.5 ^e
4-CF ₃ C ₆ F ₄	4-C ₂ F ₅ C ₆ F ₄		-1.2

Table 1 (Contd.)

A_1H^b	A_0H	$\Delta G_{\text{acid}}(A_0H)^{c,d}$	$\delta\Delta G_{\text{acid}}^e$
<i>X-CH(CN)COOC₂H₅</i>			
C_6H_5	$(CF_3)_3COH$	324.0 ^e	-1.0
	4-NO ₂ C ₆ H ₄ CH ₂ CN	323.3 ^f	-0.2
	CF ₃ COCH ₂ COCH ₃	322.0	0.9
4-HC ₆ F ₄	C ₄ F ₉ SO ₂ NH ₂	315.1 ^e	0.5
4-CH ₃ C ₆ F ₄	C ₄ F ₉ SO ₂ NH ₂	315.1 ^e	1.3
4-CNC ₆ F ₄	(CF ₃ CO) ₂ NH	307.5 ^e	-0.9
	4-CF ₃ C ₆ F ₄ CH(CN)COOEt	307.8 ^f	-1.3
4-CF ₃ C ₆ F ₄	(CF ₃ CO) ₂ NH	307.5 ^e	0.3
4-ClC ₆ F ₄	CF ₃ COSH	312.5 ^e	0.0
4-BrC ₆ F ₄	C ₄ F ₉ SO ₂ NH ₂	315.1 ^e	-1.8
	CF ₃ COSH	312.5 ^e	-0.2
<i>Hydrocarbon acids with highly charge dispersed anions</i>			
(C ₆ H ₅) ₃ CH	3-ClC ₆ H ₄ NH ₂	351.6	-0.9
	3-CF ₃ C ₆ H ₄ NH ₂	349.6	1.0
2,5-(C ₆ H ₅) ₂ CP	3-SCF ₃ C ₆ H ₄ OH	330.4	0.2
	4-CF ₃ C ₆ H ₄ OH	330.1	0.4
1,2,3,4,5-(CH ₃) ₅ CP	2-FC ₆ H ₄ NH ₂	355.3	-0.4
	C ₆ H ₅ COCH ₃	354.5	0.5
1,3-(C ₆ H ₅) ₂ In	4-CF ₃ C ₆ H ₄ OH	330.1	-1.4
	CF ₃ CH ₂ COOH	327.7	1.1
Fl	C ₆ H ₅ CH ₂ CN	344.1	-0.2
	4-CH ₃ C ₆ H ₄ OH	343.4	-0.6
9-Bu ⁱ -Fl	Bu ⁱ SH	346.2	-1.0
	4-CF ₃ C ₆ H ₄ NH ₂	346.0	-0.6
9-C ₆ H ₅ -Fl	3-FC ₆ H ₄ OH	336.8	-1.4
	3-ClC ₆ H ₄ OH	335.0	0.5
9-Pr ⁱ -Fl	4-CH ₃ C ₆ H ₄ OH	343.4	0.0
	4-C ₂ H ₅ C ₆ H ₄ OH	342.9	0.7
9-Bu ⁱ -Fl	4-CH ₃ C ₆ H ₄ OH	343.4	-0.4
	C ₆ H ₅ OH	342.3	0.7
9-Bu ⁱ CH ₂ -Fl	2-FC ₆ H ₄ OH	339.0	0.2
	3-FC ₆ H ₄ OH	336.8	2.0
9-CN-Fl	CF ₃ SO ₂ NH ₂	321.3	0.1
9-CH ₃ -Fl	4-CH ₃ C ₆ H ₄ OH	343.4	0.1
	4-C ₂ H ₅ C ₆ H ₄ OH	342.9	0.7
9-C ₂ H ₅ -Fl	4-CH ₃ C ₆ H ₄ OH	343.4	0.3
	4-C ₂ H ₅ C ₆ H ₄ OH	342.9	0.7
9-SO ₂ CH ₃ -Fl	CF ₃ COCH ₂ COCH ₃	322.0	1.0
2-CH ₃ -Fl	Bu ⁱ SH	346.2	-1.3
	4-CH ₃ C ₆ H ₄ OH	343.4	1.5
9-C ₆ H ₅ -1,2,3,4,-F-Fl fluoradene	(CF ₃) ₃ CH	326.6	-1.6
	4-CNC ₆ H ₄ OH	325.3	-0.4
	CHF ₂ COOH	323.8	1.0
<i>Varia</i>			
C ₆ F ₅ COCH ₂ C ₆ F ₅	C ₆ F ₅ COOH	316.6 ^e	-0.3
	C ₄ F ₉ SO ₂ NH ₂	315.1 ^e	1.2
4-CF ₃ C ₆ F ₄ CH ₂ COC ₆ F ₅	CF ₃ COSH	312.5 ^e	-1.8
	(CF ₃ CO) ₂ CH ₂	310.3 ^e	1.0
(C ₆ F ₅) ₃ CH	C ₄ F ₉ SO ₂ NH ₂	315.1 ^e	2.5
(C ₆ F ₅) ₂ CHC ₆ H ₅	(CF ₃) ₃ CH	326.6 ^e	1.8
	CH ₂ (CN) ₂	328.3	-0.4
4-CF ₃ C ₆ F ₄ CH(C ₆ F ₅) ₂	(CF ₃ CO) ₂ CH ₂	310.3 ^e	0.1
CH ₃ COCN	2-Bu ⁱ C ₆ H ₄ OH	338.3	0.6
	3-FC ₆ H ₄ OH	336.8	0.8
	3-ClC ₆ H ₄ OH	335.0	2.5

^a $\delta\Delta G_{\text{acid}} = \Delta G_{\text{acid}}(A_1H) - \Delta G_{\text{acid}}(A_0H)$. ^b Fl denotes fluorene; Cp denotes cyclopentadiene, In denotes indene. ^c All values are given in kcal mol⁻¹ (1 cal = 4.184 J). ^d $\Delta G_{\text{acid}}(A_0H)$ values taken from ref. 18, if not indicated otherwise. ^e Ref. 14. ^f This work.

the description in ref. 33. Toluene 9 was prepared according to ref. 34. Toluene 18 was prepared from bis(trifluoromethyl)-benzyl bromide by a general method. The rest of the chemicals used in this work were available from various commercial sources and were purified by standard procedures prior to measurements if needed.

Results and discussion

The gas-phase ΔG_{acid} values derived from the $\delta\Delta G$ values and DMSO pK_a values measured in this work are given in Table 2 together with the relevant data available from the literature.

In order to evaluate the effect of structure and solvent on the acidity of neutral CH acids upon changing from the gas phase to DMSO, the statistical analysis of the data from Table 2 was performed in terms of eqn. (3), where a and b are constants.

$$\Delta G_{\text{acid}}(\text{gas phase}) = a + b pK_a(\text{DMSO}) \quad (3)$$

The results of this analysis are given in Table 3. Roughly linear family relationships were established between the acidities of CH-acids in the gas phase and in solution.

In Fig. 1 the respective gas-phase data on intrinsic acidities of CH-acids are plotted against the corresponding acidities in

Table 2 Comparison of CH-acidities of neutral Brønsted acids in the gas phase and dimethyl sulfoxide

Compound ^a		Gas Phase ^b ΔG_{acid}	DMSO ^b pK _a	Compound ^a		Gas Phase ^b ΔG_{acid}	DMSO ^b pK _a	
<i>Substituted toluenes</i>				<i>X-CH(CN)COOC₂H₅</i>				
1	H	373.7 ^c	43.0 ^d	68	C ₆ H ₅	323.0	7.5	
2	4-CN	353.6 ^c	30.7 ^e	69	4-HC ₆ F ₄	315.6	4.9	
3	4-NO ₂	345.2	20.4 ^d	70	4-CH ₃ C ₆ F ₄	316.3	5.3	
4	4-NO	345.1	—	71	4-CF ₃ C ₆ F ₄	307.8	3.0	
5	4-SO ₂ CF ₃	340.7	24.1 ^d	72	4-ClC ₆ F ₄	312.5	4.5	
6	4-SO ₂ C ₆ H ₅	352.1	29.85 ^d	73	4-BrC ₆ F ₄	312.3	4.5	
7	4-COC ₆ H ₅	353.5	26.8 ^e	74	4-CNC ₆ F ₄	306.6	2.8	
8	4-COCH ₃	354.9	—	75	C ₆ F ₅	313.5 ^g	4.7 ^j	
9	4-COCN	339.0	—	76	4-NC ₅ F ₄	303.5 ^g	3.2	
10	4-COCF ₃	344.1	—	<i>Hydrogen acids with highly charge dispersed anions</i>				
11	4-CO ₂ CH ₃	355.4	—	77	(C ₆ H ₅) ₂ CH ₂	358.2 ^c	32.2 ^d	
12	3-NO	361.1	—	78	(C ₆ H ₅) ₃ CH	350.7	30.6 ^d	
13	3-NO ₂	355.7 ^c	33.5 ^f	79	Cp	347.7 ^c	18.0 ^d	
14	4-SO ₂ CH ₃	359.3	—	80	2,5-(C ₆ H ₅) ₂ Cp	330.5	14.3 ^d	
15	4-SOCH ₃	359.3	—	81	1,2,3,4,5-(CH ₃) ₅ Cp	355.0	26.1 ^d	
16	3-CON(CH ₃) ₂	367.0	—	82	In	344.6 ^c	20.1 ^d	
17	4-CON(CH ₃) ₂	367.0	—	83	1,3-(C ₆ H ₅) ₂ In	328.8	13.1 ^k	
18	3,5-(CF ₃) ₂	354.2	—	84	Fl	344.0	22.6 ^d	
19	2,4,6-(NO ₂) ₃	309.0 ^g	10.4	85	9-Bu ^l -Fl	345.2	24.35 ^l	
20	2,4,6-(CF ₃ SO ₂) ₃	305.7 ^g	3.6	86	9-C ₆ H ₅ -Fl	335.5	17.9 ^d	
21	2,3,4,5,6-(CN) ₅	302.1	8.2	87	9-Pr ^l -Fl	343.5	23.2 ^l	
22	2,3,4,5,6-F ₅	354.7 ^g	—	88	9-Bu ^l -Fl	343.0	21.6 ^l	
<i>Substituted phenylacetonitriles</i>				89	9-Bu ^l CH ₂ -Fl	339.2	20.3 ^l	
23	H	344.1 ^c	21.9 ^h	90	9-CN-Fl	321.4	8.3 ^d	
24	3-Cl	337.5 ^c	19.5 ^h	91	9-CH ₃ -Fl	343.5	22.3 ^d	
25	3-CF ₃	335.3	19.2 ^h	92	9-C ₂ H ₅ -Fl	343.6	22.6 ^l	
26	3-CN	332.3	18.7 ^h	93	9-SO ₂ CH ₃ -Fl	323.0	12.75 ^l	
27	3-NO ₂	330.9 ^c	18.1 ^h	94	2-CH ₃ -Fl	344.9	23.1 ^m	
28	3-CH ₃	344.2 ^c	—	95	fluoradene	324.9	10.5 ⁿ	
29	3-OCH ₃	342.8	—	<i>Varia</i>				
30	3-F	344.0 ^c	20.0 ^h	96	C ₆ H ₅ CH(SO ₂ F) ₂	307.0 ^g	3.0	
31	4-(CH ₃) ₂ N	346.6	24.6 ^h	97	C ₆ H ₅ CH(SO ₂ CF ₃) ₂	301.3 ^g	2.0	
32	4-OCH ₃	345.0	23.8 ^h	98	(CF ₃ CO) ₂ CH ₂	310.3 ^g	2.3	
33	4-CH ₃	345.0 ^c	22.9 ^h	99	(FSO ₂) ₂ CH ₂	307.3 ^g	2.4	
34	4-Cl	338.5 ^c	20.5 ^h	100	(CF ₃ SO ₂) ₂ CH ₂	301.5 ^g	2.4	
35	4-CN	327.9	16.0 ^h	101	(CF ₃ SO ₂) ₂ CHK	—	14.7	
36	4-NO ₂	323.3	12.3 ^h	102	(CF ₃ CO) ₃ CH	300.6 ^g	<2	
37	4-F	342.4	22.2 ^h	103	(CF ₃ SO ₂) ₃ CH	289.0 ^g	<2	
38	4-CF ₃	332.9	18.1 ^h	104	(FSO ₂) ₃ CH	—	<2	
39	2,3,4,5,6-F ₅	327.6	15.8 ^d	105	C ₆ F ₅ COCH ₂ C ₆ F ₅	316.3	10.3	
<i>X-CH(CN)₂</i>				106	4-CF ₃ C ₆ F ₄ CH ₂ COC ₆ F ₅	311.0	9.4	
40	C ₆ H ₅	314.3 ^g	4.24 ⁱ	107	1,3,5-(NO ₂) ₃ C ₆ H ₃	—	12.9	
41	4-ClC ₆ H ₄	309.0 ^g	3.14 ⁱ	108	1,3,5-(CF ₃ SO ₂) ₃ C ₆ H ₃	—	7.0	
42	4-CH ₃ C ₆ H ₄	315.7 ^g	4.85 ⁱ	109	[2,4,6-(CF ₃ SO ₂) ₃ C ₆ H ₂] ₂ CH ₂	—	3.0	
43	4-CH ₃ OC ₆ H ₄	315.4 ^g	5.68 ⁱ	110	(CF ₃) ₃ CH	326.6 ^o	12.6 ^o	
44	4-NO ₂ C ₆ H ₄	299.5 ^g	-1.8 ^f	111	CH ₃ COCN	337.6	—	
45	3-ClC ₆ H ₄	308.8 ^g	2.7 ^f	112	C ₆ H ₅ COCH ₂ CN	326.3 ^c	10.2 ^d	
46	C ₆ F ₅	303.6 ^g	0.3 ^f	113	CH ₃ SO ₂ CF ₃	339.8 ^g	18.75 ^d	
47	4-HC ₆ F ₄	305.5 ^g	—	114	CH ₂ (CN) ₂	328.3 ^c	11.0 ^d	
48	3-CNC ₆ H ₄	304.4 ^g	2.2 ^f	115	CH ₃ CN	364.0 ^c	31.3 ^d	
49	3-NO ₂ C ₆ H ₄	303.0 ^g	1.7 ^f	116	CH ₄	408.6 ^c	56.0 ^d	
50	2-C ₁₀ F ₇	301.8 ^g	—	^a Fl denotes fluorene; Cp denotes cyclopentadiene, In denotes indene.				
51	4-CF ₃ C ₆ F ₄	301.5 ^g	1.7 ^f	^b Data from this work, if not indicated otherwise. Gas-phase values are given in kcal mol ⁻¹ (1 cal = 4.184 J). ^c Ref. 18. ^d Ref. 9. ^e Ref. 35. ^f Extrapolated value. See text. ^g Ref. 14. ^h Ref. 7. ⁱ Ref. 38. ^j See also ref. 40.				
<i>Ar^lCH(CN)Ar²</i>				^k Ref. 1. ^l Ref. 41. ^m Ref. 42. ⁿ Ref. 39. ^o Ref. 12.				
<i>Ar^l</i>	<i>Ar²</i>			DMSO. The dashed line with the unity slope (1000b/2.3RT = 1.0; T = 298 K) in Fig. 1 is drawn for comparison through the point of fluoradene – an acid, that is known to form a carbanion with extensive delocalization of negative charge. The latter should result in very weak, if any, solvent attenuation of substituent effects while changing from gas phase into DMSO for the latter type of acid–base equilibria.				
52	C ₆ H ₅	C ₆ H ₅	333.4	17.5 ^h	In ref. 1 it was demonstrated that for a narrow range of the selected aromatic CH-acids (fluoradene, 1,3-diphenylindene, 2,5-diphenylcyclopentadiene, 9-phenylfluorene, 9-neopentylfluorene, 9-isopropylfluorene, 9-tert-butylfluorene and triphenyl-			
53	C ₆ H ₅	C ₆ F ₅	325.6	12.8				
54	C ₆ H ₅	4-NC ₅ F ₄	316.0	7.9				
55	C ₆ H ₅	4-CH ₃ C ₆ F ₄	328.2	13.2				
56	C ₆ H ₅	4-HC ₆ F ₄	325.7	12.8				
57	C ₆ H ₅	4-CF ₃ C ₆ F ₄	315.7	10.0				
58	C ₆ F ₅	C ₆ F ₅	312.4 ^g	7.95 ^d				
59	C ₆ F ₅	4-ClC ₆ F ₄	311.8	7.5				
60	C ₆ F ₅	4-COOC ₂ H ₅ C ₆ F ₄	310.5	—				
61	C ₆ F ₅	4-CH ₃ C ₆ F ₄	316.1	—				
62	C ₆ F ₅	4-CF ₃ C ₆ F ₄	307.5 ^g	4.9				
63	C ₆ F ₅	4-NC ₅ F ₄	305.7 ^g	3.3				
64	C ₆ F ₅	4-BrC ₆ F ₄	312.9	7.5				
65	4-CF ₃ C ₆ F ₄	4-C ₂ F ₅ C ₆ F ₄	306.3	4.7				
66	4-NC ₅ F ₄	4-NC ₅ F ₄	302.2 ^g	2.4				
67	4-CF ₃ C ₆ F ₄	4-CF ₃ C ₆ F ₄	302.1 ^g	3.3				

Table 3 Statistical analysis of data from Table 2 in terms of eqn. (3)

Series	<i>a</i>	1000 <i>b</i> /2.3 <i>RT</i>	<i>s</i>	<i>r</i>	<i>n</i>	Compounds
1	Aromatic hydrocarbons which form carbanions with extensive delocalization of charge					
1.1	311.6(1.1)	0.98(0.04)	1.0	0.995	8	78, 80, 83, 85–87, 89, 95
1.2	309.7(1.1)	1.08(0.03)	1.4	0.994	15	1, 77, 78, 80, 83–89, 91, 92, 94, 95
2	9-Substituted fluorenes					
3	Toluenes					
3.1	292.2	1.39	—	—	2	1, 13
3.2	313.0(7.2)	1.01(0.18)	4.2	0.944	6	1–3, 5–7
4	Arylacetonitriles ArCH ₂ CN					
4.1	262.4(19.4)	2.81(0.73)	2.9	0.888	6	23–27, 30
4.2	267.4(7.0)	2.58(0.26)	1.0	0.985	5	23–27
4.3	281.1(4.7)	2.06(0.17)	1.2	0.977	9	23–27, 33, 34, 37, 38
4.4	295.6(2.3)	1.54(0.08)	1.4	0.988	10	23, 31–39
4.5	294.5(3.7)	1.59(0.14)	2.3	0.954	15	23–27, 30–39
5	Arylmalononitriles ArCH(CN) ₂					
5.1	298.7(1.8)	2.60(0.34)	0.8	0.982	4	40–42, 45
5.2	295.3(1.6)	3.34(0.42)	1.1	0.985	4	40, 45, 48, 49
5.3	303.3(0.9)	1.68(0.16)	1.3	0.982	6	40–45
6	296.5(1.0)	1.61(0.08)	1.7	0.987	14	52, 53, 54–59, 62–67
7	294.9(2.0)	2.85(0.32)	1.8	0.960	9	68–76
8	308.2(1.3)	1.29(0.03)	1.3	0.999	4	113–116
9	303.1(1.4)	1.39(0.05)	3.7	0.993	12	40, 96–100, 110, 112–116

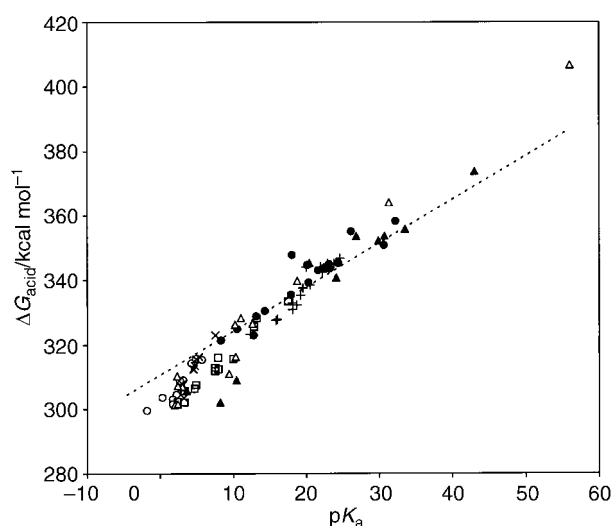


Fig. 1 Plot of gas-phase acidities ΔG_{acid} versus DMSO solution acidities (pK_{a}) of different classes of neutral Brønsted acids. The notation of points is as follows (see Table 2): \blacktriangle substituted toluenes; $+$ substituted arylacetonitriles; \circ substituted arylmalononitriles; \square substituted diarylacetonitriles; \times ethyl esters of cyanosubstituted phenylacetic acids; \bullet hydrocarbon acids with highly charge dispersed anions; Δ varia; The dashed line is drawn with the unity slope ($1000b/2.3RT = 1$) through the point of fluoradene (see text).

methane) a linear correlation with the unity slope $\delta\Delta G_{\text{g}} = 0.1 + 1.01 \delta\Delta G_{\text{DMSO}}$ could be obtained. However, closer analysis shows that this is an exception rather than a general rule. As evidenced in this work, for the wider selection of aromatic hydrocarbons that are believed to lead to carbanions of extensive negative charge delocalization, the slope is already, by 6–8 per cent, higher than unity (see Table 3, series 1.2). This could be due, by at least a modest level of attenuation of the substituent effects, to the change from the gas phase into DMSO. The point for toluene satisfies the equation for series 1.2 (deviation $0.6 \text{ kcal mol}^{-1}$), as well as 9-cyanofluorene (deviation $0.6 \text{ kcal mol}^{-1}$). Indene deviates from the relationship by $5.3 \text{ kcal mol}^{-1}$, cyclopentadiene by $11.5 \text{ kcal mol}^{-1}$.

The separate reaction series for the acidic dissociation of 9-substituted fluorenes also indicates a relatively weak attenuation of the substituent effects by the solvent effects. The

attenuation factor 1.20 ± 0.08 is evidence for extensive delocalization of the negative charge all over the anionic moiety.

Substituted toluenes

Due to the extremely weak acidities, the directly measured experimental pK_{a} values of mono-*meta*-substituted toluenes in DMSO solution ($pK_{\text{a, autoprotolysis}} = 35$) are absent.^{1,2,9,10,17,35} They are either out of scale for this medium ($pK_{\text{a}} \geq 35$) or very difficult to measure accurately enough in close range to the autoprotolysis constant of DMSO. Therefore the estimated value (see footnote to Table 2) for 3-NO₂ derivative ($pK_{\text{a}} = 33.5$), together with the similar value for unsubstituted toluene, was used for a very rough estimate of the solvent attenuation factor of the substituent effects.³⁶ This procedure leads to the attenuation factor $1000b/2.3RT = 1.39$ that is definitely higher than in the case of the above-discussed anions with most extensive negative charge delocalization. On the other hand, this value is significantly lower than the same quantity (2.8) for *meta*-substituted anilines.²²

At the same time scarce data on pK_{a} values in DMSO for only a few *para*-electron-acceptor-substituted toluenes, as well as the pK_{a} values for 2,4,6-trinitrotoluene, pentacyanotoluene and 2,4,6-(CF₃SO₂)₂C₆H₂CH₃ (see Table 2), are available for the comparison with the respective gas-phase data.¹⁴ Plotting the ΔG_{acid} values of the 4-substituted toluenes versus the corresponding DMSO pK_{a} values (Table 3, series 3.2) results in a rather scattered and rough correlation, somewhat different in its slope and intercept from that for the *meta*-substituted derivatives.

The points for the *para*-electron-acceptor substituents deviate from the line defined by the points for toluene and its *meta*-nitro-substituted derivative towards the higher solution acidity or lower DMSO pK_{a} values. In the case of the 4-NO₂ group, such deviations amount up to 7.6 pK_{a} units, whereas for C₆H₅CO this deviation is 5.5 pK_{a} units, for 4-CN 1.7 pK_{a} units and for 4-C₆H₅SO₂ 1.7 pK_{a} units. Such deviations for the *para*- π -electron-acceptor substituents towards higher solution acidity were previously^{1–3,19,22,37} ascribed to substituent solvation assisted resonance (SSAR) effects.

In the case of the simultaneous inclusion also of *ortho* substituents, the deviations from the line defined by *meta*-substituted derivatives have a more complex origin and are additionally caused by field effects (NO₂, SO₂CF₃), steric inhibition of resonance and solvation and by other effects. Therefore

the net outcome of these effects is difficult to predict. In particular, the complex nature of this phenomenon is reflected by the fact that with the relatively close ΔG_{acid} values ($\Delta\Delta G_{\text{acid}} = 3.3$ kcal mol⁻¹), the pK_{a} values of TNT and 2,4,6-(CF₃SO₂)₃C₆H₂CH₃ in DMSO solution differ by almost 7 pK_{a} units. At the same time the deviation of 2,4,6-(CF₃SO₂)₃C₆H₂CH₃ from the expected line for *meta*-substituted derivatives is 3.5 pK_{a} units. Trinitrotoluene and pentacyanotoluene deviate towards weaker solution acidity (the deviations are 1.5 pK_{a} units and 2.9 pK_{a} units, respectively).

Substituted arylacetonitriles

The introduction of a cyano group into the methyl group of toluene acidifies the α -hydrogen sufficiently to allow convenient and accurate pK_{a} measurements of the resulting phenylacetonitrile and its derivatives in DMSO solution. Therefore, in contrast to the family of toluenes, ample data are in hand^{7,9,18} for similar statistical analysis in terms of eqn. (3). The solvent attenuation factor for the series of *meta*-substituted arylacetonitriles is significantly larger ($1000b/2.3RT = 2.6$ for series 4.2 and 2.8 for series 4.1) than in the case of *meta*-substituted toluenes, reflecting the less extensive delocalization of the negative charge to the benzene ring of the ArCHCN⁻ anion.^{2,7,10} The *para*-substituents (4-CH₃, 4-F, 4-Cl, 4-CF₃), which are not able to participate in SSAR type interactions, fit the correlation line whose regression coefficients are somewhat different from those of the *meta* substituents. The calculated attenuation factor (2.06) for this series (Table 3, series 4.3) is slightly smaller than the same quantity for *meta*-substituted anilines.²² In contrast to *meta*-substituted phenylacetonitriles, and by analogy²² with *para*-substituted anilines, *para*-substituted phenylacetonitriles display much weaker attenuation of the substituent effects by DMSO medium ($1000b/2.3RT = 1.54$), whereas the 2,3,4,5,6-F₅ substituted derivative C₆F₅CH₂CN fits the same correlation as the *para*-substituted derivatives.

The derivatives with *para* π -acceptor (4-CN, 4-NO₂) substituents, as expected for the SSAR effects, deviate significantly from the line for the *meta*-substituents towards the decreased solution pK_{a} values (increase of acidity in solution).^{2,22} The SSAR effect for 4-NO₂ is *ca.* 3.6 pK_{a} units and for 4-CN 1.2 pK_{a} units, in close comparison with the similar quantities for the series of anilines.²² However, these SSAR effects are smaller than the similar roughly estimated values for 4-NO₂ and 4-CN toluenes. As expected, similar or somewhat smaller deviations of the *para*-donor substituents (2.1 pK_{a} units for 4-N(CH₃)₂ and 1.8 pK_{a} units for 4-CH₃O) from the line defined for *meta*-substituents are observed in the other direction (relative weakening of the acid in the solution) because their π -electron donor effects are reduced in gas-phase acidities by repulsive interactions by the carbanionic center. The specific solvation of those *para* donor groups in DMSO solution by the positive end of the S–O dipole of DMSO molecules and by hydrogen bonding reduces that repulsion effect relative to the gas phase. The SSAR effect of pentafluorophenyl substituent in this reaction series is rather small (1.3 pK_{a} units) due to the complex role played by the two *ortho*-fluorine substituents.²²

Arylmalononitriles

Partially due to the high acidity of strong electron-acceptor substituted arylmalononitriles, the measurement of their pK_{a} s in DMSO is complicated³⁸ and the data matrix for comparison of gas-phase ΔG_{acid} values with pK_{a} values is rather scarce. Therefore, for the evaluation of the solvent-induced attenuation of the *meta* and *para* substituted derivatives while going from the gas phase into DMSO solution the pK_{a} values for 3-CN (2.2), 3-NO₂ (1.7) and 4-CF₃ (1.7) phenylmalononitriles were derived from linearities of the available pK_{a} values for this reaction series with the corresponding pK_{a} values of substituted phenylacetonitriles⁷ and phenols.¹⁹

It follows from Table 3 that the solvent attenuation factor for the *meta*-substituted arylmalononitriles (series 5.2) is $1000b/2.3RT = 3.34$. Somewhat lower attenuation factors, $1000b/2.3RT = 2.60$, are obtained if one uses only the directly measured pK_{a} values for the unsubstituted compound, together with 3-Cl, 4-CH₃ and 4-Cl derivatives (Table 3, series 5.1). Similar to the reaction series of substituted phenylacetonitriles, SSAR effects for 4-NO₂ derivatives (*ca.* 2.7 pK_{a} units) could be obtained from the data available in Table 2. Also of similar values are the deviations for the 2,3,4,5,6-pentafluorophenyl derivative (*ca.* 1.5 pK_{a} units towards the increased acidity value in DMSO solution) and 4-methoxy substituted derivative (*ca.* 1.3 pK_{a} units towards the weaker solution acidity) in both series.

From the discussion given above one can see that in the succession of reaction series of acidic dissociation of toluenes, phenylacetonitriles and phenylmalononitriles the consecutive introduction of the cyano groups into the α -methyl group results in the stepwise increase of solvent induced attenuation of the substituent effects and in progressively less pronounced delocalization of the anionic charge.

The attenuation factor for the joint reaction series of *meta*- and *para*-substituted arylmalononitriles 1.68 (Table 3, series 5.3) is also the highest in the group of toluenes, phenylacetonitriles and phenylmalononitriles, indicating decreased delocalization of the anionic charge in the benzene ring with successive introduction of the CN groups into the methyl group of toluene.

A similar conclusion could be reached analyzing the relative contributions of resonance, field-inductive and polarizability effects to the gas-phase acidities, ΔG_{acid} , in the case of the above-mentioned three reaction series, in terms of the three-parameter equation^{2,10} [eqn. (4)], where a_0 , ρ_{R} , ρ_{F} and ρ_{a} are

$$\Delta G_{\text{acid}} = a_0 + \rho_{\text{R}}\sigma_{\text{R}} + \rho_{\text{F}}\sigma_{\text{F}} + \rho_{\text{a}}\sigma_{\text{a}} \quad (4)$$

constants and σ_{R} , σ_{F} and σ_{a} are respectively the substituent resonance, field-induction effect and polarizability constants. So, in the case of *para*-acceptor substituents, with the relatively constant contribution of $\rho_{\text{F}}\sigma_{\text{F}}$ term and practical negligibility of the $\rho_{\text{a}}\sigma_{\text{a}}$ term, the $\rho_{\text{R}}\sigma_{\text{R}}$ term increases progressively upon going from phenylmalononitriles ($\rho_{\text{R}} = -19 \pm 9$) (this work) to phenylacetonitriles ($\rho_{\text{R}} = -48 \pm 7$)^{2,10} and to toluenes ($\rho_{\text{R}} = -76 \pm 2.5$).^{2,10} This clearly evidences the increased importance of charge delocalization into the aromatic ring *via* the resonance interactions while going from a series of substituted phenylmalononitriles to a series of substituted phenylacetonitriles and toluenes.

Diarylacetonitriles

As a rule, the reaction series of diarylacetonitriles Ar¹CH(CN)Ar² includes (with the exception of Ar¹ = Ar² = C₆H₅ and a few more compounds where Ar¹ = C₆H₅) two polyfluorophenyl rings, 4-X¹C₆F₄ and 4-X²C₆F₄ which both contain substituents X¹ and X² in the *para*-position to the reaction center. It has been demonstrated (see ref. 11 and references therein) that, as a rule, polyfluoroaryl groups (*e.g.* C₆F₅, 4-NC₅F₄, *etc.*) themselves are rather strong, comparable to CF₃ group, electron-acceptor groups ($0.22 \leq \sigma_{\text{m}} \leq 0.34$; $0.27 \leq \sigma_{\text{p}} \leq 0.45$) (whose behavior significantly depends on the steric orientation of the polyfluorinated ring towards the carbanionic center) and on the nature of the substituents X¹ and X².

One can see from Table 3, by their behavior regarding solvent attenuation of substituent effects while going from the gas phase into DMSO, that this reaction series resembles closely that of *para*-substituted arylacetonitriles ($1000b/2.3RT = 1.54$) and *para*-substituted diarylamines ($1000b/2.3RT = 1.44$).²² Therefore it could be concluded that the introduction of the substituted perfluorophenyl group into the CH₂ fragment of

phenylacetonitriles does not result in a significant change of the solvent attenuation of the substituent effects in the case of those two reaction series.

Ethyl esters of cyano-substituted phenylacetic acids

The conclusion described at the end of the previous subsection is not valid for the case of replacement of the α -hydrogen atom in phenylacetonitriles by the sterically more demanding ethoxycarbonyl group COOC_2H_5 . Indeed, Table 3 (series 7) evidences that the attenuation due to the transfer from the gas phase into DMSO of the *para*-substituent effects in ethyl esters of 4-X substituted polyfluorophenyl cyanoacetic acids $\text{XC}_6\text{F}_4\text{CH}(\text{CN})\text{COOC}_2\text{H}_5$ is the highest of all the *para*-acceptor substituted derivatives of toluenes, arylacetonitriles, arylmalononitriles and diarylacetonitriles considered so far. In fact, the corresponding attenuation factor ($1000b/2.3RT = 2.85$) is between the values for *meta*-substituted arylacetonitriles and arylmalononitriles, which both display a rather modest degree of delocalization of the negative charge in their carbanionic forms. Weaker π -electron demand from the carbanionic center than in the case of acidic dissociation of toluenes, phenylacetonitriles and phenylmalononitriles in the gas phase is also evidenced by treatment of the data for the series of 4- $\text{XC}_6\text{F}_4\text{CH}(\text{CN})\text{COOC}_2\text{H}_5$ from Table 2 in terms of eqn. (4), which indicates lower sensitivities to the resonance ($\rho_{\text{R}} = -14.3 \pm 0.9$) and field inductive ($\rho_{\text{F}} = -12.08 \pm 0.04$) effects than in the case of the three above-mentioned reaction series.

Some simple derivatives of methane

A relatively low solvent substituent effects attenuation factor (1.29 ± 0.03) is characteristic also of the reaction series which consists of CH_4 , its mono cyano and CF_3SO_2 derivatives and malononitrile. It covers *ca.* 80 kcal mol⁻¹ on the ΔG_{acid} scale and 45 pK_a units on the pK_a scale.

The regression parameters change only slightly when a more extensive series of relatively simple CN, SO_2F , SO_2CF_3 , COCF_3 , C_6H_5 , CF_3 and C_6F_5 derivatives of methane (series 9 from Table 3) is considered. This relationship now holds over 105 kcal mol⁻¹ on ΔG_{acid} scale and 54 units of pK_a scale with a standard deviation 3.7 kcal mol⁻¹. It possibly indicates extensive negative charge delocalization in the conjugate carbanions of these acids. At the same time, however, the points for nitromethane and HCN, which were not included in this correlation, deviate by 12 kcal mol⁻¹ and 15 kcal mol⁻¹ from the line towards much stronger than expected solution acidity values (lower pK_a values).

Conclusions

New experimental data on gas-phase acidities (66 compounds) and pK_as in DMSO solution (31 compounds) for several families of CH acids (substituted toluenes, arylacetonitriles, fluorenes, ethyl esters of cyanoarylacetic acids, substituted methanes, *etc.*) were obtained using ICR spectrometry and potentiometric titration techniques.

The analysis of these and literature data reveals that, in the case of acidic dissociation of neutral Brønsted CH-acids, the substituent effects are significantly attenuated by transfer from the gas phase into the DMSO solution. The strongest attenuation was monitored for *meta*-substituted phenylacetonitriles, phenylmalononitriles and ethyl esters of *para*-substituted polyfluorophenyl cyanoacetic acids, whereas all other reaction series considered are characterized by lower attenuation factors.

Contrary to the previous findings it was concluded that in the case of CH acids, which give highly charge-dispersed carbanions, the lack of attenuation of substituent effects by the transfer from the gas phase into DMSO is an exception rather than a general rule and does not hold for a wider selection of the respective aromatic CH acids.

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References

- 1 R. W. Taft and F. G. Bordwell, *Acc. Chem. Res.*, 1988, **21**, 463.
- 2 (a) R. W. Taft, *Prog. Phys. Org. Chem.*, 1983, **14**, 247; (b) R. W. Taft and R. D. Topsom, *Prog. Phys. Org. Chem.*, 1987, **16**, 1.
- 3 (a) V. M. Vlasov and I. A. Oskina, *Org. React.*, 1989, **26**, 19; (b) V. M. Vlasov and I. A. Oskina, *Org. React.*, 1993, **28**, 47.
- 4 I. Koppel, R. Pikver, A. Sügis, E. Suurmaa and E. Lippmaa, *Org. React.*, 1981, **18**, 3.
- 5 (a) A. Streitwieser, Jr., E. Juaristi and L. L. Nebenzahl, in *Comprehensive Carbanion Chemistry. Part A. Structure and Reactivity*, eds. E. Buncl, T. Durst, Elsevier, Amsterdam, 1980, p. 323; (b) I. S. Antipin, R. F. Gareyev, A. N. Vedernikov and A. I. Kononov, *J. Phys. Org. Chem.*, 1994, **7**, 181.
- 6 E. Ciganek, W. J. Linn and O. W. Webster, in *The Chemistry of the Cyano Group*, ed. Z. Rappoport, Wiley, London, 1970.
- 7 F. G. Bordwell, J.-P. Cheng, M. J. Bausch and J. E. Bares, *J. Phys. Org. Chem.*, 1988, **1**, 209.
- 8 (a) J. P. Richard, G. Williams and J. Gao, *J. Am. Chem. Soc.*, 1999, **121**, 715; (b) G. N. Merrill, G. D. Dahlke and S. R. Kass, *J. Am. Chem. Soc.*, 1996, **118**, 4462.
- 9 F. G. Bordwell, *Acc. Chem. Res.*, 1988, **21**, 456.
- 10 R. W. Taft, J.-L. M. Abboud, F. Anvia, M. Berthelot, M. Fujio, J.-F. Gal, A. D. Headley, W. G. Henderson, I. Koppel, J. H. Qian, M. Mishima, M. Taagepera and S. Ueji, *J. Am. Chem. Soc.*, 1988, **110**, 1797.
- 11 V. M. Vlasov and G. G. Yakobson, *Usp. Khim.*, 1974, **43**, 1642.
- 12 I. A. Koppel, V. Pihl, J. Koppel, F. Anvia and R. W. Taft, *J. Am. Chem. Soc.*, 1994, **116**, 8654.
- 13 K. J. Klabunde and D. J. Burton, *J. Am. Chem. Soc.*, 1972, **94**, 820.
- 14 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.
- 15 F. G. Bordwell, J. E. Bartmess, G. E. Drucker, Z. Margolin and W. S. Matthews, *J. Am. Chem. Soc.*, 1975, **97**, 3226.
- 16 W. S. Matthews, J. E. Bares, J. E. Bartmess, F. G. Bordwell, F. J. Cornforth, G. E. Drucker, Z. Margolin, R. J. McCallum, G. J. McCollum and N. R. Vanier, *J. Am. Chem. Soc.*, 1975, **97**, 7006.
- 17 *Tables of Rate and Equilibrium Constants of Heterolytic Organic Reactions*, ed. V. Palm, VINITI, Moscow-Tartu, 1975-1985.
- 18 J. E. Bartmess, *Negative Ion Energetics Data*, eds. W. G. Mallard and P. J. Linstrom, NIST Chemistry WebBook, NIST Standard Reference Database Number 69, August 1997, National Institute of Standards and Technology, Gaithersburg MD, 20899 (<http://webbook.nist.gov>).
- 19 M. Fujio, R. T. McIver, Jr. and R. W. Taft, *J. Am. Chem. Soc.*, 1981, **103**, 4017.
- 20 I. Koppel, J. Koppel, I. Leito, V. Pihl, L. Grehn and U. Ragnarsson, *J. Chem. Res. (S)*, 1994, 212.
- 21 I. Koppel, J. Koppel, F. Degerbeck, L. Grehn and U. Ragnarsson, *J. Org. Chem.*, 1991, **56**, 7172.
- 22 I. Koppel, J. Koppel, P.-C. Maria, J.-F. Gal, R. Notario, V. M. Vlasov and R. W. Taft, *Int. J. Mass Spectrom. Ion Processes*, 1998, **175**, 61.
- 23 V. M. Vlasov and G. G. Yakobson, *Zh. Org. Khim.*, 1973, **9**, 1024.
- 24 V. M. Vlasov, O. V. Zakharova and G. G. Yakobson, *Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk*, 1975, 80.
- 25 V. M. Vlasov and G. G. Yakobson, *Zh. Org. Khim.*, 1974, **10**, 573.
- 26 V. M. Vlasov, O. V. Zakharova and G. G. Yakobson, *J. Fluorine Chem.*, 1977, **9**, 321.
- 27 V. M. Vlasov and O. V. Zakharova, *Zh. Org. Khim.*, 1975, **11**, 785.
- 28 V. M. Vlasov, O. V. Zakharova and G. G. Yakobson, *Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk*, 1977, 127.
- 29 V. P. Molosnova, V. A. Barkhash and N. N. Vorozhtsov, *Zh. Obshch. Khim.*, 1969, **39**, 1774.
- 30 O. V. Zakharova, V. M. Vlasov and G. G. Yakobson, *Zh. Org. Khim.*, 1979, **15**, 2169.
- 31 M. Mishima, N. Shimizu, Y. Tsuno, T. Ariga, K. Isomura, S. Kobayshi and H. Taniguchi, *Mem. Fac. Sci., Kyushu Univ., Ser. C*, 1988, **16**, 217.

- 32 A. Murata, M. Goto, R. Fujiyama, M. Mishima, M. Fujio and Y. Tsuno, *Bull. Chem. Soc. Jpn.*, 1990, **63**, 1129.
- 33 H. E. Baumgarten, A. Staklis and E. M. Miller, *J. Org. Chem.*, 1965, **30**, 1203.
- 34 H. A. Smith, C. A. Buehler, T. A. Magee, K. V. Nayak and D. M. Glenn, *J. Org. Chem.*, 1959, **24**, 1301.
- 35 F. G. Bordwell, D. Algrim and N. R. Vanier, *J. Org. Chem.*, 1977, **42**, 1817.
- 36 The more correct and probably more realistic approach for the direct determination of a reliable solvent attenuation factor for *meta*-substituted toluenes would be the measurement of gas-phase and DMSO acidities of 3,5-dinitro and 3,5-bistriflyl derivatives of toluene. The expected values of ΔG_{acid} and pK_{a} for the latter compound are predicted to be respectively 330 kcal mol⁻¹ and around $pK_{\text{a}}=20$, well within the reach of the experimental techniques.
- 37 M. Mishima, R. T. McIver, Jr., R. W. Taft, F. G. Bordwell and W. N. Olmstead, *J. Am. Chem. Soc.*, 1984, **106**, 2717.
- 38 E. B. Troughton, K. E. Molter and E. M. Arnett, *J. Am. Chem. Soc.*, 1984, **106**, 6726.
- 39 C. D. Ritchie and R. E. Uschold, *J. Am. Chem. Soc.*, 1968, **90**, 2821.
- 40 F. G. Bordwell, J. C. Branca, J. E. Bares, R. Filler, *J. Org. Chem.*, 1988, **53**, 780.
- 41 F. G. Bordwell, G. E. Drucker and G. J. McCollum, *J. Org. Chem.*, 1976, **41**, 2786.
- 42 F. G. Bordwell and G. J. McCollum, *J. Org. Chem.*, 1976, **41**, 2391.