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Basicity of carboxylic acids: resonance in the cation and substituent effects†

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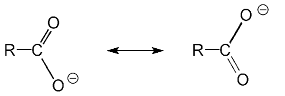
Basic properties of acetic, formic and substituted benzoic acids were investigated by the density functional theory at the levels B3LYP/6-311+G(d,p) and/or B3LYP/6-311++G(2d,2p). The protonated form prefers unsymmetrical conformation *E*,*Z* on the two partially double C–O bonds; only in the case of formic acid the *E*,*E* form is still observable. Lower basicity of carboxylic acids as compared to ketones is due to the higher energy of the cation while the effect in the uncharged acid molecule is negligible. Contribution of resonance and of the inductive effect was approximately estimated by means of relatively sophisticated model compounds. The inductive effect of the hydroxy group in the cation is the deciding factor for the lowered basicity. Resonance in the cation is strong, stronger than in the acid molecule or in the carboxylate anion, but cannot overcome the inductive effect. Relative basicities of *meta*- and *para*-substituted benzoic acids are controlled by the Hammett equation with marked deviations of the *para* donor substituents that have been not observable with the basicities in solution.

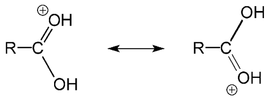
Carboxylic acids are relatively strong bases as isolated molecules or in the gas phase. On the scale of increasing basicity including all organic compounds,[1] acetic acid is almost in the middle (at 46% of the whole range), while on the similar scale of acidity[2] it is only slightly displaced toward the side of strong acids (57% of the scale). In aqueous solutions, the acidity and basicity are attenuated in a different degree.[3] While the acidities are well defined and measured within the pH scale, their basicities are expressed by negative values of the extended pH scale: the measurement is difficult and the results often disagree.[3,4] The name 'carboxylic acids' is thus appropriate for water solutions, while in the gas phase the term 'carboxylic base' would be equally justified.

Recently, basicity of carboxylic acids received attention in two respects, both associated with the concept of resonance and related to the acidity of the same compounds:

(a) Relatively strong acidity of carboxylic acids compared to alcohols has been explained in terms of resonance occurring in the carboxylate anion, **1A** ↔ **1B**.[5] Thomas and colleagues challenged this explanation and attributed the acidity to the high electrostatic potential of the acid molecule.[6] The problem was discussed from several points of view and diverse results were reached at.[7–9] We offered the opinion that two independent problems should be distinguished:[9] By means of suitable isodesmic reactions, one can decide what part of the enhanced acidity is due to the low energy of the anion and what part to the high energy of the acid molecule. This question can be answered unambiguously and quantitatively. On the other hand, one cannot determine exactly what part is due to resonance. This would require defining a model molecule resembling the carboxylate anion but without resonance: this is not exactly possible. Nevertheless, some of the suggested models yielded concordant results:[7b,e,i,8,9b] the contribution of resonance was estimated between 30 and 46%.



1A **1B**



2A **2B**

Basicity of carboxylic acids was only mentioned in this connection.[8,9b] Resonance in the cation, **2A** ↔ **2B**, is at first sight similar to that in the anion, **1A** ↔ **1B** , and it was assumed as the first approximation that it is equally strong.[8] However, the structures **2A** and **2B** are no longer equivalent when their conformation is taken into account;[9] then resonance could be weaker than in **1A** ↔ **1B**. In any case, carboxylic acids are weaker bases than ketones; hence the conclusion[8] was evidently right that resonance **2A** ↔ **2B** is outweighed by the inductive effect of the hydroxy group.

In the present communication, we intended to get more definite results when calculating the substituent effect separately in the cation **2** and in the carboxylic acid molecule in terms of isodesmic reactions, similarly as we proceeded previously[9] with the anion **1**. The contribution of resonance was estimated according to the model developed by Taft for the acidities.[7b] In our case, the basicity of substituted ketones was followed in dependence on some non-conjugated substituents. When the OH substituent was introduced into the series (producing a carboxylic acid molecule), a deviation from the dependence was taken as a measure of resonance. Gas-phase basicities of some reference compounds were available[1] but we were able to design the models more freely when we calculated

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† Electronic supplementary information (ESI) available: Table S1 giving the DFT calculated energies of the carbonyl compounds **8a–e** and the reaction energies of the isodesmic reactions serving for estimating the contribution of resonance to the basicity of acetic acid. Table S2 giving the DFT energies of the substituted alcohols **10a–d** and the reaction energies for estimating the contribution of resonance to the acidity of acetic acid. Appendix describing in detail the latter procedure and presenting it in Figs. S1 and S2. See http://www.rsc.org/suppdata/nj/b4/b411039k/

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all values within the framework of the density functional theory[10] (DFT).

(b) The second problem concerns the conjugation of the whole functional group with the rest of the molecule (group R in **1** and **2**). For instance with *para*-substituted benzoic acids, a donor substituent should be more strongly conjugated in the cation 4-$XC_6H_4COOH_2^+$ than in the acid molecule 4-XC_6H_4COOH or in the anion 4-$XC_6H_4COO^-$ (different separation of charges). This should be apparent when the relative acidities of *meta*- and *para*-substituted benzoic acids (**3**), are correlated with their relative basicities within the framework of the Hammett equation.

$$\underset{\mathbf{3}}{\text{3(4)-X-}C_6H_4COOH} + C_6H_5COO^- = \underset{\mathbf{4}}{\text{3(4)-X-}C_6H_4COO^-} + C_6H_5COOH \tag{1}$$

$$\underset{\mathbf{3}}{\text{3(4)-X-}C_6H_4COOH} + C_6H_5COOH_2^+ = \underset{\mathbf{5}}{\text{3(4)-X-}C_6H_4COOH_2^+} + C_6H_5COOH \tag{2}$$

In terms of isodesmic reactions, the acidities and basicities are represented by eqn. (1) and (2), respectively. The Hammett equation postulates that their reaction energies Δ_1E and Δ_2E are linearly related but *para* substituents directly conjugated with the reaction center can deviate and must be excluded from the range of validity.[11] However, when the pK values in water were plotted, no significant deviations were found.[3] It is true that this result may be partly due by the lower accuracy of measurements in solution, particularly the basicities are less dependable.[3,4] However, significant progress can be in our opinion reached only when the substituent effect is investigated separately in the acid molecule and in the cation. The same procedure was followed in the case of acidity:[12,13] the substituent effect was bisected into the effect in the acid molecule, eqn. (3), and in the anion, eqn. (4).

$$C_6H_4COOH + X\text{-}C_6H_5 = \underset{\mathbf{3}}{\text{3(4)-X-}C_6H_4COOH} + C_6H_6 \tag{3}$$

$$C_6H_4COO^- + X\text{-}C_6H_5 = \underset{\mathbf{4}}{\text{3(4)-X-}C_6H_4COO^-} + C_6H_6 \tag{4}$$

In this communication, we bisected the substituent effect on the basicity of benzoic acids by the same approach, *i.e.* by evaluating separately the effects in the cation (**5**), eqn. (5), from those in the acid molecule (**3**), eqn. (3). Conjugation in the cation **5** was then apparent from the deviations from the Hammett equation.

$$C_6H_4CO_2H_2^+ + X\text{-}C_6H_5 = \underset{\mathbf{5}}{\text{3(4)-X-}C_6H_4CO_2H_2^+} + C_6H_6 \tag{5}$$

Our calculations were carried out within the framework of the DFT theory at the level B3LYP/6-311+G(d,p). This model proved good in our previous work[14] for molecules of similar size, *i.e.* it yielded very reliable relative values within the series of substituted compounds.

Calculations

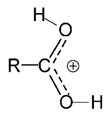
Energies of protonated forms of carboxylic acids and of reference compounds were calculated by the DFT method[10] with the GAUSSIAN 03 program.[15] For various conformations (Table 1) and for substituted benzoic acids **5a**–**5z** (Table 2) the level B3LYP/6-311+G(d,p)//B3LYP/6-311+G(d,p) was chosen as in the previous work,[14] for the smaller molecules of substituted ketones (Table S1†) the preferred level was B3LYP/6-311++G(2d,2p)//B3LYP/6-311++G(2d,2p). There were no significant differences between the results obtained at the two levels. Planarity or any symmetry was never anticipated. All structures were checked by vibrational analysis and behaved as energy minima.

All reasonable conformations were taken into consideration and calculations were started from the pertinent near structures. Particularly in the case of the *meta* derivatives **5b**–**5m** the two conformations around the C(1)–C(O) bond were always taken into account, in the case of unsymmetrical substituents still the two possible conformations on the substituent. Population of conformers was calculated with the approximation that $\Delta G°(298) \cong \Delta E$; with this population the effective ΔE for the equilibrium mixture of conformers was obtained. The energies E(DFT) listed in the Table 2 for molecules with variable conformations relate always to the equilibrium mixture. Energies Δ_5E of the isodesmic reactions of eqn. (5) (Table 2, column 7) were obtained from E(DFT) of **5** and from E(DFT) of the monosubstituted benzene calculated previously.[14a]

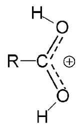
Results and discussion

Conformation of the cation

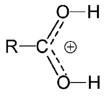
Of the three possible planar conformations **2a**–**c**, the unsymmetrical E,Z form **2a** is evidently the most stable. It was preferred by calculations for protonated acetic[16] or formic[17] acid, and found experimentally in crystals of salts of formic acid[18] and in solution of formic acid at low temperatures.[19] In the latter case it was accompanied by a minor form that was tentatively assigned[19] as **2b**.



2a *E,Z*



2b *E,E*



2c *Z,Z*

Our calculations preferred the E,Z conformations **2a** for both acetic acid and benzoic acid. The energy difference against the

Table 1 Energies and some geometric parameters of protonated carboxylic acids $RCOOH_2^+$ in various conformations[a]

	Substituent R	Conformation[b]	E(DFT)/a.u.	ΔE/kJ mol^{-1}	C–O E/Å	C–O Z/Å	C–C(O)/Å	∠ O–C–O/deg
2a	CH_3	E,Z	−229.473 6264	0	1.288	1.276	1.476	116.7
2b		E,E	−229.468 1362	14.4 (12.4)[c]	1.280		1.484	112.5
2c		Z,Z	−229.466 3619	19.1 (17.4)[c]		1.285	1.472	124.1
5a	C_6H_5	E,Z	−421.273 9883	0	1.302	1.294	1.431	114.7
		E,E	−421.266 7214	19.1	1.292		1.444	111.5[d]
		Z,Z	−421.268 5987	14.2		1.304	1.423	122.0
5t	4-$NH_2C_6H_4$	E,Z	−476.675 0746		1.315	1.306	1.406	113.6
5v	4-$NO_2C_6H_4$	E,Z	−625.814 8933		1.297	1.290	1.440	115.1
6	H	E,Z	−190.126 7463	0	1.273	1.263		120.7
		E,E	−190.119 5597	8.4 (6.7)[c]	1.267			116.2
		Z,Z	−190.124 1821	21.0 (18.9)[c]		1.270		128.4

[a] Calculated at the level B3LYP/6-311+G(d,p)//B3LYP/6-311+G(d,p). [b] Conformation about the two C–O bonds. [c] Calculated at the level B3LYP/6-311++G(2d,2p)//B3LYP/6-311++G(2d,2p). [d] The molecule is not planar with the dihedral angles O–C–C–C 24° and O–C–O–H 172°.

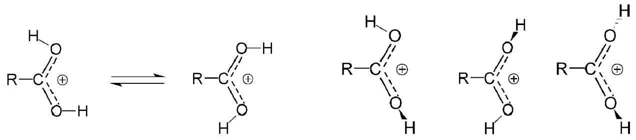
Table 2 Calculated energies and some geometric parameters of protonated forms of substituted benzoic acids **5** and energies of the isodesmic reactions

		ΔE(DFT)/a.u.		$\Delta_i E$/kJ mol^{-1}		
	Substituent	Z^a	E^a	$\Delta_2 E$	$\Delta_3 E^b$	$\Delta_5 E$
5a	H	−421.273 9883		0	0	0
5b	3-CH_3	−460.604 9384	−460.605 2161	−8.64	−0.73	−9.37
5c	3-CH_2Cl	−920.219 3144	−920.219 3964	8.66	2.19	10.85
5d	3-CF_3	−758.410 2939	−758.409 6974	30.00	5.40	35.40
5e	3-CHO *sp*[c]	−534.621 0252	−534.622 9087	20.22	4.24	24.46
	ap[c]	−534.620 0108	−534.619 5914			
5f	3-CN	−513.522 0844	−513.521 9292	41.76	6.81	48.57
5g	3-NH_2	−476.656 9684	−476.658 1267	−18.61	−1.04	−19.65
5h	3-$N(CH_3)_2$	−555.288 9127	−555.290 0021	−31.67	−2.31	−33.98
5i	3-NO_2	−625.817 6942	−625.816 5457	44.52	7.80	52.32
5j	3-OH *sp*[c]	−496.520 8128	−496.519 2250	−1.16	0.51	−0.67
	ap[c]	−496.521 6740	−496.521 9785			
5k	3-F	−520.533 9151	−520.534 0325	19.60	4.13	23.33
5l	3-Cl	−880.888 6324	−880.888 7096	17.55	4.13	21.68
5m	3-SO_2CH_3	−1009.231 1327	−1009.229 3105	24.74	7.43	32.17
5n	4-CH_3	−460.608 5183		−15.88	−2.47	−18.35
5o	4-CH_2Cl	−920.220 8068		5.23	1.82	7.05
5p	4-CF_3	−758.408 7682		32.86	6.01	38.87
5r	4-CHO	−534.619 8181	−534.619 3567	25.80	6.17	31.97
5s	4-CN	−513.522 6726		40.26	6.58	46.84
5t	4-NH_2	−476.675 0746		−54.55	−10.29	−64.84
5u	4-$N(CH_3)_2$	−555.309 3666		−72.88	−12.62	−85.50
5v	4-NO_2	−625.814 8933		50.37	8.61	58.98
5w	4-OH	−496.530 8486	−496.531 3604	−20.28	−5.43	−25.71
5x	4-F	−520.538 8077		10.63	0.02	10.65
5y	4-Cl	−880.893 0973		8.71	1.35	10.06
5z	4-SO_2CH_3	−1009.227 5764		34.52	6.38	40.90

[a] Conformation around the C1–C(O) bond. [b] Ref. 13. [c] Conformation around the bonds C3–C7 or C3–O, respectively.

E,E and *Z,Z* forms is at least 14 kJ mol^{-1} (Table 1). In the case of benzoic acid, the *E,E* conformation is still less stable due to the steric hindrance and planarity of the functional group is distorted (Table 1, footnote *d*). Therefore, presence of other conformers need not be taken into account in further considerations. With substituted acetophenones we revealed protonation on the oxygen atom from two possible sides and the ratio of stereoisomeric cations changed with substitution.[20] In our case, the changes with substitution are negligible. The unsymmetrical form **2a** thus represents an exception from the general rule[21] that equivalent groups tend to take the same conformations.[22] In order to confront our calculations with the low-temperature experiments,[19] we still made calculations with formic acid **6** (Table 1). Even in this case the *E,Z* conformer **2a** (R = H) is preferred but the population of **6b** is no longer negligible (Table 1). We still calculated the conformations of the small molecules at the higher level B3LYP/6-311++G(2d,2p)//B3LYP/6-311++G(2d,2p). The results are still relatively sensitive to the computational level (Table 1, column 4, in the parentheses) but the strong dominance of the protonated form *E,Z* has not changed. For formic acid, calculations now predict 7% of the form *E,E* which is compatible with the observed 23% at 106 K in solution.[19b] In any case we can confirm the tentatively suggested[19b] conformation *E,E*. Relatively higher stability of this minor conformer in the case of formic acid is evidently due to low steric requirement of hydrogen. This is seen for instance from the large angle O–C–O (Table 1, last column).

Both in the gas phase and in solution, the protonated form exists in the degenerate equilibrium **2a** ⇌ **2a′**. The mechanism of the interchange can proceed *via* the conformer **2b** and the transition states **7a** and **7b**, *i.e.* by stepwise rotation of the two OH groups.



2a **2a’** **7a** **7b** **7c**

An alternative mechanism could be simultaneous rotation *via* the transition state near to **7c**. However, calculations prefer the former possibility. In the sequence **2a** → **7a** → **2b** → **7b** → **2a′**, the highest energy is that of the transition state **7B**, by 93 kJ mol^{-1} over **2A**. On the other hand, we were unable to obtain a transition state structure near to **7c**.

Table 3 Acidity and basicity of the carboxy group in acetic acid, estimated contributions of the inductive effect and resonance (in kJ mol^{-1})

	Neutral molecule		Ion		Acidity/basicity		Total effect [a]	R/I
	I effect	resonance	I effect	resonance	I effect	resonance		
Acidity [b]	+69	−146	−8	−180	−77	−34	−111	0.44
Acidity [c]	+18	−95	−73	−115	−91	−20	−111	0.22
Basicity	+19	−96	+82	−131	+63	−35	+28	0.56

[a] Experimental values, ref. 1 and 2. [b] Estimated in ref. 9 from the experimental acidities of model compounds [eqn. (12)] and recalculated now to 2-propanol as reference [eqn. (13)]. [c] Estimated here from eqns. (14) and (18)†, see Figs. S1 and S2 (Supporting Information).

Significance of resonance

We shall proceed in the same way as in the discussion of the acidity of carboxylic acids[9] discriminating two independent questions: (a) whether the basicity is controlled merely by the energy of the cation or by the energy of the acid molecule, and (b) whether it is due mainly or partly by the resonance in the cation. The former question can be answered rigorously by means of isodesmic reactions. The latter question requires an approximate model and can be answered only tentatively. Note that the answers can be less definite than they were in the case of the acidity since the acidity of carboxylic acids is very strong and conspicuous when compared to alcohols while the differences in basicity compared with some reference compounds are less marked.

The basicity of acetic acid is best compared to the basicity of acetone[8,9] using the isodesmic reaction, eqn. (6). Both molecules are of similar size and possible effects of polarizability are minimized.

$$\begin{aligned} &CH_3C(OH^+)CH_3 + CH_3COOH \\ &\quad = CH_3CO_2H_2^+ + CH_3COCH_3 \\ &\Delta_6H^\circ g(298)\ \text{exper.}\ 28.3\ \text{kJ mol}^{-1} \\ &\Delta_6E\ \text{calc.}\ 31.9\ [33.0]\ \text{kJ mol}^{-1} \end{aligned} \tag{6}$$

Acetic acid is a weaker base; hence the effect of resonance cannot be deciding. Our calculations at the B3LYP/6-311++G(2d,2p) level agree with the experimental gas phase basicities[1] ΔH°g(298) within usual limits, at the lower level B3LYP/6-311+G(d,p) the agreement is somewhat worse as given in the square brackets. As in similar cases we did not consider it necessary to calculate the zero-point energy and enthalpy at 298 K since the corrections are mostly negligible in isodesmic reactions[13,14,23] and the calculations are not quite dependable. Rablen received apparently still better results at the levels B3LYP/6-311+G(2df,p)//B3LYP/6-311+G** (30.1 kJ mol^{-1}) or CBS-4 (27.6 kJ mol^{-1}).[8] Note however that the experimental basicities are not reliable with a better accuracy than say 2 kJ mol^{-1}.

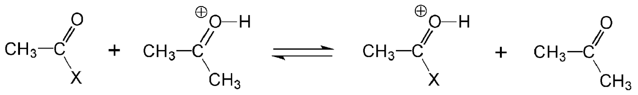
Separation of the substituent effects in the acid molecule and in the cation is represented by the isodesmic reactions in eqns. (7) and (8).

$$\begin{aligned} &CH_3COCH_3 + (CH_3)_2CHOH \\ &\quad = CH_3COOH + (CH_3)_2CHCH_3 \\ &\Delta_7H^\circ(298)\ \text{exp.} -77.0\ \text{kJ mol}^{-1} \\ &\Delta_7E\ \text{calc.} -74.5\ [-73.6]\ \text{kJ mol}^{-1} \end{aligned} \tag{7}$$

$$\begin{aligned} &CH_3C(OH^+)CH_3 + (CH_3)_2CHOH \\ &\quad = CH_3CO_2H_2^+ + (CH_3)_2CHCH_3 \\ &\Delta_8H^\circ(298)\ \text{exp.} -49.0\ \text{kJ mol}^{-1} \\ &\Delta_8E\ \text{calc.} -41.5\ [-41.7]\ \text{kJ mol}^{-1} \end{aligned} \tag{8}$$

Note that eqns. (7) and (8) are isodesmic but not homodesmotic[24] since the bonds C_{sp^3}–C_{sp^2} and C_{sp^3}–O have been replaced by the bonds C_{sp^3}–C_{sp^3} and C_{sp^2}–O. Agreement with experiments might be somewhat worse but still more important are probably the less precise experimental enthalpies obtained from the tabulated[25] values of Δ_fH°g(298). When these values were reliable[26] to ±2 kJ mol^{-1}, the uncertainty in Δ_8H° would be[27] ±5 kJ mol^{-1}. Eqn. (7) reveals that the molecule of acetic acid is stabilized strongly by interaction of the two groups C=O and OH as found in the analysis of its acidity.[9] The protonated form is stabilized less as shown in eqn. (8). The difference causes the weaker basicity of acetic acid as compared to acetone.

The second question is now to what extent the reaction energy of eqn. (8) is due to resonance in the cation, **2A** ↔ **2B**; estimating the effect of resonance on the observed basicity means still subtracting the resonance in eqn. (7). We proceeded similarly as with the problem of acidity;[9b] the fundamental idea originates from Taft.[7b] Relative basicities of carbonyl compounds **8** with a variable group X are represented as the reaction energies Δ_9E of the isodesmic reaction, eqn. (9).

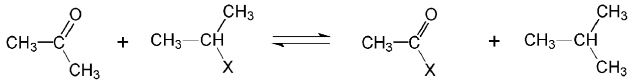


8a–e **9a–e**

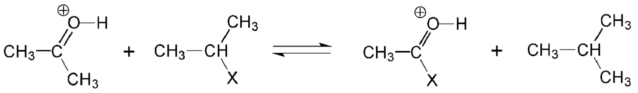
(9)

When Δ_9E is calculated for several substituents X not conjugated with the CO group and plotted *vs.* the inductive constant[28] σ_I, a linear dependence should confirm that the basicity is controlled essentially by the inductive effect of X. When the group OH is introduced as a substituent X, its deviation should represent the resonance. It turned out that the assumptions were fulfilled reasonably. Selection of the groups X is rather restricted: they must not contain lone electron pairs in the α position and should be of variable polarity. For X = CH_3, CH_2F, CF_3, CN and NO_2 (**8a–e**) we obtained (at the higher level of calculation) the energies given in Table S1 (Supporting Information)†. All protonated forms prefer the (*Z*)-configuration on the C=O bond as shown in the formula **9a–e**. The (*E*)-configuration has higher energy by 5 to 24 kJ mol^{-1} and will be neglected in further considerations. The plot of Δ_9E *vs.* the inductive constants[28] σ_I (values recommended specially for the gas phase) is shown in Fig. 1. The correlation is good but the number of points is restricted; nevertheless the deviation of the point for OH is marked. The resonance effect (denoted **R**) in Fig. 1 is estimated to −35 ± 5 kJ mol^{-1}, the inductive effect of the OH group (denoted **I** in Fig. 1) is then 63 ± 5 kJ mol^{-1}. Rablen[8] started from the assumption that resonance in the cation is equally as strong as in the carboxylate anion (not confirmed by our following calculations) and estimated the effect of resonance to −22 kJ mol^{-1}.

In order to resolve the contribution of resonance into the parts operating in the cation and in the neutral molecule, it is necessary to repeat the above analysis for the isodesmic reactions of eqns. (10) and (11).



(10)



(11)

The calculated energies $\Delta_{10}E$ and $\Delta_{11}E$ are given in Table S1,† the last two columns. The reactions of eqns. (10) and (11) are not homodesmotic since one C_{sp^3}–X bond is replaced by C_{sp^2}–X. Therefore, we anticipated somewhat worse correlation with the inductive constants σ_I, particularly for the uncharged particles in eqn. (10). Fig. 2 shows the plot corresponding to eqn. (11) yielding the resonance and inductive component to −131 and +82 kJ mol^{-1}, respectively, with an uncertainty estimated to ±11 kJ mol^{-1}. All estimated contributions to the basicity of acetic acids are summarized in Table 3 and compared to previous similar treatment of the acidity.[9b,29] In spite of the uncertainty in the estimates, one result seems to be evident that the resonance in the cation (**2A** ↔ **2B**) is stronger than in the anion (**1A** ↔ **1B**). When the resonance formulas are written with respect to conformation (**2C** ↔ **2D**), it is

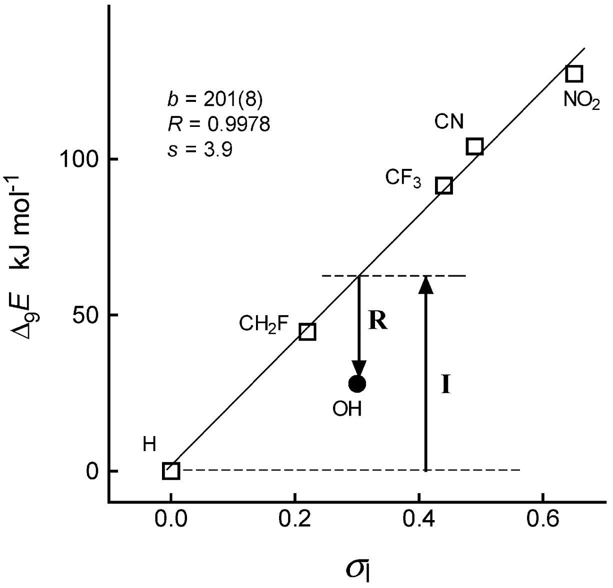
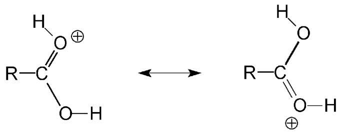


Fig. 1 Plot of the calculated relative basicities of carbonyl compounds CH_3COX [eqn. (9)] *vs.* the inductive constant σ_I, the groups X are denoted at each point. The point ● belongs to X = OH, the arrows show the assumed contribution of resonance **R** and of the inductive effect **I**.

evident that they are not identical.



2C **2D**

This is confirmed also from the calculated bond lengths of the two partially double C–O bonds (Table 1, columns 6 and 7). The bond associated with the *Z* conformation is shorter; hence the form **2D** should be somewhat more represented. This fact does not weaken the resonance markedly: conjugation in a positively charged system is evidently stronger than in a negatively charged system.

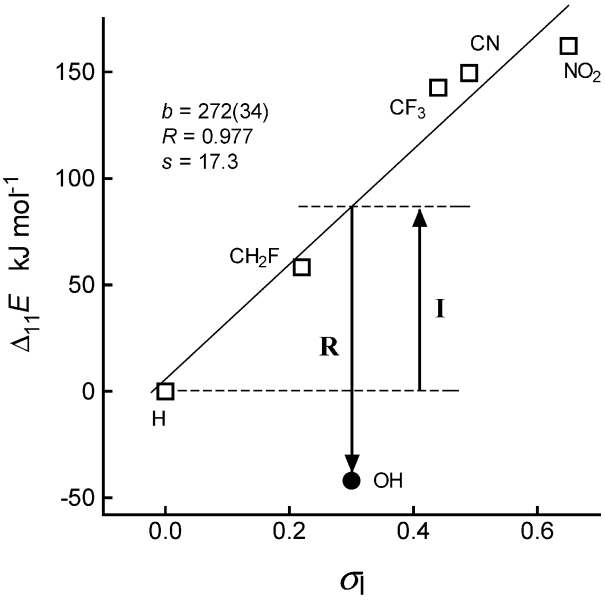


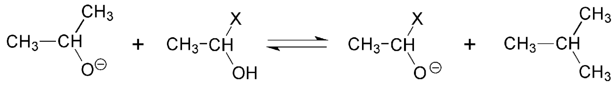
Fig. 2 Plot of the calculated stabilization energies of the protonated carbonyl compounds CH_3COH^+X [isodesmic reaction of eqn. (11)] *vs.* the inductive constant σ_I, the groups X are denoted at each point. The point ● belongs to X = OH, the arrows show the assumed contribution of resonance **R** and of the inductive effect **I**.

Both in the course of the previous analysis of the acidity[9b,29] and of the present analysis of the basicity, the inductive effect and resonance in the molecule of acetic acid itself were estimated. In the former case, they were defined as the substituent effects of the CO group on the OH group, in the latter case *vice versa*. Nevertheless, the values should be equal. However, there was a significant difference particularly in the inductive effect. The reason was evidently a different reference and conditions: in the study of acidity[9b] acetic acid was related to methanol, and the correlation was based on experimental acidities of the compounds of the general formula X–OH [eqn. (12)] while in the present study the reference was acetone and the calculated basicities referred to compounds **8**. [eqn. (9)].

$$CH_3O^- + X\text{–}OH = X\text{–}O^- + CH_3OH \qquad (12)$$

$$(CH_3)_2CHO^- + X\text{–}OH = X\text{–}O^- + (CH_3)_2CHOH \qquad (13)$$

We tried to improve the agreement in two ways. First methanol as reference was replaced by 2-propanol to give eqn. (13). The result is given in Table 2, first line. Second a new model reaction for the acidity was created, as similar as possible to the model reaction for basicity, eqn. (9). We obtained eqn. (14).



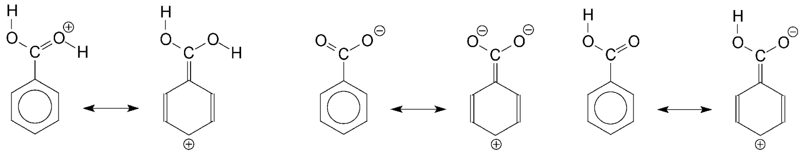
10

(14)

Since this model is somewhat over-sophisticated, the details are given in the Appendix (Supporting Information);† the results are in Table 2, line 2. Agreement of the lines 1 and 2 is bad. With the assumed uncertainty of 5 to 10 kJ mol^{-1}, one could accept the results for the acidity (columns 6 and 7) but separation into effects in the anion (columns 4 and 5) and in the acid molecule (columns 2 and 3) is not dependable and the results depend on the model. We have already stated that evaluation of the resonance requires defining a model without resonance but otherwise quite similar to the molecule investigated. This is principally not possible; hence the results will be only approximate. We would prefer their formulation in a semi-quantitative sense: Resonance in the carboxylate anion is important, nevertheless the strong acidity of carboxylic acids is due in greater part to the inductive effect of the C=O group and in a minor degree to resonance. Reverting to the problem of basicity, we observe much better agreement with the results on acidity when analogous models have been used: the same values were obtained for the uncharged acid molecule (Table 2, lines 2 and 3, columns 2 and 3). The conclusion seems to be reasonably supported that resonance in the cation (**2C** ↔ **2D**) is somewhat stronger than in the anion (**1A** ↔ **1B**). The weaker basicity of carboxylic acids compared to ketones is due to the strong inductive effect of the OH group in the cation. Resonance in the cation is operative in the opposite direction but cannot reverse this effect since it is partly cancelled by the resonance in the uncharged acid molecule.

Conjugation with the benzene ring

Conjugation of the group $COOH_2^+$ with the benzene ring is described within the framework of the classic resonance theory by the formulas **10A** ↔ **10B** and is predicted to be much stronger then the resonance in the anion **11A** ↔ **11B** or in the uncharged molecule of benzoic acid **12A** ↔ **12B** (effect of near charges or of distant charges).



10A **10B** **11A** **11B** **12A** **12B**

Quantitative evaluation can be attempted by means of isodesmic reactions that compare benzoic acid to acetic acid, eqns. (15)–(17).

$$CH_3CO_2H_2^+ + C_6H_6 = C_6H_5CO_2H_2^+ + CH_4$$

$$\Delta_{15}H^\circ\ g(298)\ \text{exper.}\ -52.8\ \text{kJ mol}^{-1}$$

$$\Delta_{15}E\ \text{calc.}\ -60.5\ \text{kJ mol}^{-1} \quad (15)$$

$$CH_3COO^- + C_6H_6 = C_6H_5COO^- + CH_4$$

$$\Delta_{16}H^\circ\ g(298)\ \text{exper.}\ -51.7\ \text{kJ mol}^{-1}$$

$$\Delta_{16}E\ \text{calc.}\ -44.8\ \text{kJ mol}^{-1} \quad (16)$$

$$CH_3COOH + C_6H_6 = C_6H_5COOH + CH_4$$

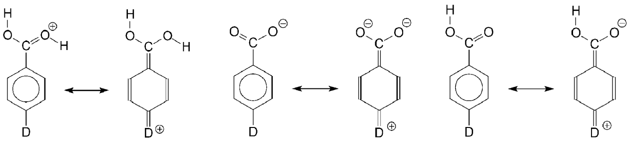
$$\Delta_{17}H^\circ\ g(298)\ \text{exper.}\ -15.4\ \text{kJ mol}^{-1}$$

$$\Delta_{17}E\ \text{calc.}\ -16.1\ \text{kJ mol}^{-1} \quad (17)$$

These reactions are not homodesmotic and also the fit of calculated and experimental values is only fair. Moreover, these reaction energies do not express only resonance. Polarizabilities of the CH_3 and C_6H_5 groups are not equal and $\Delta_{15}E$ to $\Delta_{17}E$ may include some effect of polarization.[14a] Recently the *n*-C_4H_9 group was recommended as standard to which the others should be compared.[30] If methyl derivatives in eqns. (15)–(17) were replaced by *n*-butyl derivatives, $\Delta_{15}E$ to $\Delta_{17}E$ would become smaller in absolute values by a constant quantity of 3.5 kJ mol^{-1}. In any case the result is valid that resonance of the group $COOH_2^+$ with the benzene ring is by some 15 kJ mol^{-1} stronger than that of the COO^- group.

Correlation with the Hammett equation

The conjugated systems in benzoic acid and their ions **10**, **11** and **12** can be extended by a donor substituent in the *para* position to give **13** to **15**. Then the resonance is strengthened and the differences between the three systems are more profound, particularly the resonance **13A** ↔ **13B** should be much stronger than the others.



13A **13B** **14A** **14B** **15A** **15B**

Different resonance can be proven most clearly in terms of the Hammett equation. Since the acidities of substituted benzoic acids, eqn. (1), have been chosen as standard reaction, the basicities, eqn. (2), are compared to them (Fig. 3). Correlation is good for *meta* substituents, although some of them deviate a little. Correlation is not vitiated by *para* acceptor substituents but substituents NH_2 and 4-$N(CH_3)_2$ deviate strongly in the direction of stronger basicity *i.e.* stronger interaction in **13B**. The negative slope *b* means that electron-attracting substituents strengthen the acidity and weaken the basicity; the absolute value of *b* near to unity agrees with the fact that the reaction center in **13** and **14** is equally distant.

The deviations are still more marked when the energies of the cations **13** [eqn. (5)] are compared to the energies of the anions **14** [eqn. (4)] in Fig. 4. The absolute value of b now shows greater sensitivity of the cation to substituent effects. These results confirm once more our opinion[13,14c,31] that the Hammett equation is strictly valid only for *meta* substituents. Introduction of *para* substituents raises deviations, either of

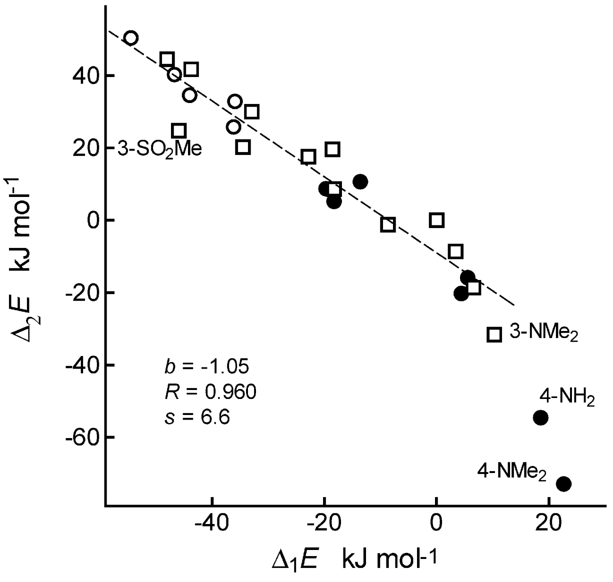


Fig. 3 Hammett plot for the calculated basicities Δ_2E of *meta*- and *para*-substituted benzoic acids, eqn. (2), *vs.* the acidities of the same compounds Δ_1E, eqn. (1); □ *meta* substituents, ○ *para* acceptor substituents, ● *para* donor substituents; the regression line and the statistics relate to the groups □ + ○.

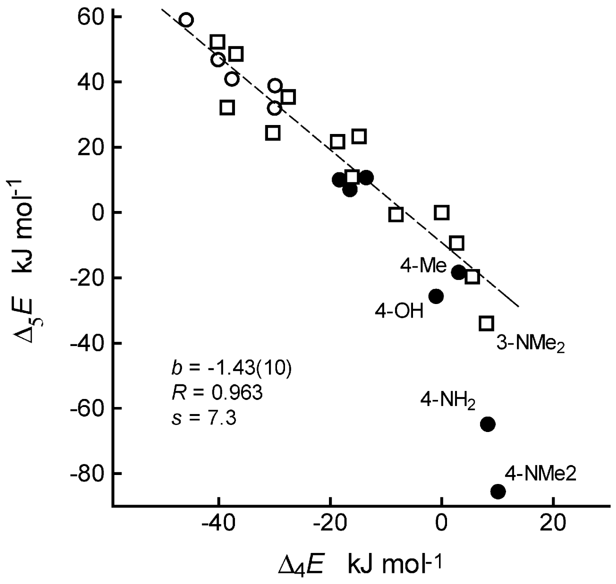


Fig. 4 Hammett plot for the substituent effects in the protonated *meta*- and *para*-substituted benzoic acids, Δ_5E, eqn. (5), *vs.* the substituent effects in their anions, Δ_4E, eqn. (4); denotation of points as in Fig. 3.

donor or of acceptor groups according to the character of the functional group. In the experimental data obtained in solution, these deviations can be partly masked or are not observable at all. For instance, the basicities of the acids 4-$NH_2C_6H_4COOH$ and 4-$N(CH_3)_2C_6H_4COOH$ could not be included into the Hammett correlation[3] since these compounds would be preferentially protonated on nitrogen. Such cases show some merits of the theoretical approach.

Conclusions

Basicity of carboxylic acids in the gas phase is comparable with their acidity and is controlled by the same factors: inductive effect operating in the cation (anion) and resonance. Resonance in the cation (anion) is partly cancelled by the significant resonance in the uncharged acid molecule, hence the effect on the basicity (acidity) is reduced. As a result of these factors it can happen that carboxylic acids are much stronger acids than alcohols and somewhat weaker bases than ketones. All estimations of the resonance contribution are only tentative since they require the defining of a similar reference molecule without resonance.

Protonated carboxylic acids may exist in three forms differing by the conformations on the two partially double C–O bonds. The unsymmetrical *E*,*Z* conformation is preferred always; only in the case of formic acid a minor conformation can be observed.

Acknowledgements

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