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Acidity of Carboxylic Acids: A Rebuttal and Redefinition

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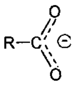
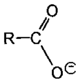
Abstract: A recent theory of ionization of carboxylic acids divided the process of ionization into two steps and attributed the main importance to the electrostatic potential of the acid molecule. The origin of the acidity was thus seen in the high energy of the acid molecule and not in the stabilization of the anion by resonance. In this paper, the theory was revised on the basis of further calculations at an MP2/6-31++G(2d,p) level which followed in two steps the reverse process, protonation of the formate anion. The results were compared to those of the methanolate anion as reference. A contradictory conclusion was obtained: the reason for the acidity is in the electrostatic potential of the anion. As a model compound without resonance, 2,2,2-trifluoroethanol was investigated in the same way. The results were qualitatively similar, although any resonance in the anion is not possible. One can conclude that the acidity of carboxylic acids is due to the low energy of their anions; this follows unambiguously from the isodesmic reactions on the basis of either the experimental enthalpies of formation or the calculated energies. It is more difficult to decide whether this low energy is caused by resonance, because any model of the carboxylate anion without resonance is necessarily imperfect and the whole concept is not exactly defined. Several such models were reexamined and improved by separating the effect operative in the anion from those in the neutral acid molecule. While the electrostatic model did not allow any significant conclusion, two models based on VB calculation and on correlation analysis, respectively, furnished qualitatively concordant results: resonance in the anion is diminished by the resonance in the acid molecule, and both together are responsible for less than one-half of the acidity enhancement as compared to the acidity of alcohols. The ratio is reversed in water solution: resonance is then the more important factor responsible for some two-thirds of the enhanced acidity.

Introduction

The relatively strong acidity of carboxylic acids, particularly evident by comparison with alcohols, has been explained generally by the resonance of their anions: the energy of an anion's real structure (**1A**) is supposed to be lower than that of a structure without resonance (**1B**), which is more similar to the structure of the parent acid. This explanation is presented in most contemporary textbooks.[1]



1A



1B

An alternative theory was suggested by Siggel and Thomas[2] and elaborated in a series of papers by Thomas, Streitwieser, and colleagues.[3] The reason for the high acidity is seen in the high electrostatic potential V of the carboxylic acid molecule, that is, the energy needed for the removal of the proton while the structure of the rest of the molecule is maintained without change. The process of ionization is thus divided into two steps. In the first step, the proton is removed from the carboxylic acid molecule (**2A**) while the structure of the rest of the molecule (**1C**) remains unaltered, eq 1. In the second step, eq 2, **1C** is rearranged into its real lowest-energy structure **1A**, evolving energy R. Quantitative support was furnished by the quantum chemical calculations[3e] for formic acid ($V = 2447$ kJ·mol^{-1},[4] $R = 1017$ kJ·mol^{-1}) and for methanol ($V = 2607$ kJ·mol^{-1},[4] $R = 1013$ kJ·mol^{-1}). Because the two values of V differ significantly, while those of R differ only negligibly, it was concluded that the structure of the acid molecule is responsible for the strong acidity and the contribution from the resonance in the anion is negligible. The Thomas theory was criticized from several points of view[5−7] but was also supported by further

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[1] For instance: (a) March, J. *Advanced Organic Chemistry*, 4th ed.; John Wiley & Sons: New York, 1992; p 264. (b) Solomons, T. W. G. *Organic Chemistry*, 5th ed.; John Wiley and Sons: New York, 1992, Chapter 3.5B. (c) Carey, F. A. *Organic Chemistry*, 3rd ed.; McGraw-Hill: New York, 1996; p 770−771. (d) Walter, W. *Beyer-Walter Lehrbuch der Organischen Chemie*, 22nd ed.; S. Hinzel Verlag: Stuttgart, 1991; p 233−234. Ref 1a,b report also the alternative theory.

[2] Siggel, M. R.; Thomas, T. D. *J. Am. Chem. Soc*. **1986**, *108*, 4360−4363.

[3] (a) Siggel, M. R. F.; Thomas, T. D.; Saethre, L. J. *J. Am. Chem. Soc.* **1988**, *110*, 91−96. (b) Thomas, T. D.; Carroll, T. X.; Siggel, M. R. F. *J. Org. Chem.* **1988**, *53*, 1812−1815. (c) Thomas, T. D.; Siggel, M. R.; Streitwieser, A. *THEOCHEM* **1988**, *165*, 309−318. (d) Siggel, M. R. F.; Ji, D.; Thomas, T. D.; Saethre, L. J. *THEOCHEM* **1988**, *181*, 305−312. (e) Siggel, M. R. F.; Streitwieser, A.; Thomas, T. D. *J. Am. Chem. Soc.* **1988**, *110*, 8022−8028. (f) Ji, D.; Thomas, T. D. *J. Phys. Chem*. **1994**, *98*, 4301−4303. (g) Thomas, T. D. *J. Chem. Soc., Perkin Trans. 2* **1994**, 1945−1948. (h) Wiberg, K. B.; Ochterski, J.; Streitwieser, A. *J. Am. Chem. Soc*. **1996**, *118*, 8291−8299.

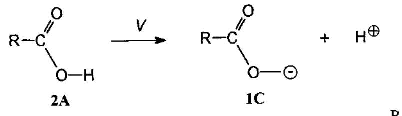
[4] At variance with ref 3a,e, we give here V with a positive sign, because eq 1 is endothermic.

[5] Exner, O. *J. Org. Chem.* **1988**, *53*, 1812−1815.

[6] (a) Dewar, M. J. S.; Krull, K. L. *J. Chem. Soc., Chem. Commun.* **1990**, 333−334. (b) Perrin, C. L. *J. Am. Chem. Soc.* **1991**, *113*, 2865−2868. (c) Bordwell, F. G.; Satish, A. V. *J. Am. Chem. Soc.* **1994**, *116*, 8885−8889.

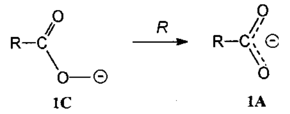
10.1021/ja003665+ CCC: $20.00

calculations,[8] and intermediate opinions were offered,[3e,9−11] assigning less than one-half of the observed effect to resonance. Comparison with similar classes of compounds, such as enols,[3e,g,h,6a,c,9a] phenols,[5,11] and substituted aliphatic alcohols[3a,e,7,10,11] was also important. Final agreement has not been reached.



(1)

R = H $V = 2442$ kJ.mol^{-1}



(2)

R = H $R = -984$ kJ.mol^{-1}

In our opinion, the main misunderstanding has been in the definition of the two terms “resonance” and “electrostatic potential”. In this communication, we attempt to define them with more precision and to formulate the problem in two ways, as two questions with separate answers. The heart of the problem is then in separating the structural effects in the anion and in the acid molecule. In our opinion, a clear statement of the problem is needed more at the present stage than further sophisticated calculations. Nevertheless, we tried to support our opinion by quantum chemical calculations of two kinds. First, we added to the process outlined in eqs 1 and 2 a reverse process in which the formate anion is tranformed into the formic acid molecule in two steps, see later, eqs 7 and 8. Second, we carried out similar calculations on 2,2,2-trifluoroethanol. This compound was chosen as a model in which resonance is not possible but the acidity is considerably strengthened by substitution. Ultimately, we reconsidered some previously suggested models,[3b,10,11] refined them by separating the effects in the anion and in the acid, and extended them to the behavior in water solution. We always focused attention on real molecules and their observable properties.

Problem Statement

In our opinion, the solution of the problem has been prevented by an ambiguous formulation, mixing together two partial questions. We have already formulated[5] these two questions separately:

1. Is the strong acidity of carboxylic acids caused by an extra high energy of the acid molecule or by an extra low energy of the anion? In both cases, the word “extra” means with respect to alcohols used as reference. This part of the problem deals only with real molecules and with observable quantities.

2. If the acidity is caused (at least partially) by the low energy of the anion, one can ask whether this energy is a result of resonance or can be better explained in other terms. This requires us to define exactly the term resonance, to construct an artificial structure of the anion without resonance, or at least to make a quantitative comparison with some related molecules. In this procedure, some fictive structures and/or terms that are not well-defined may be involved.

We shall deal with the two questions in the two following sections.

Energy of the Carboxylic Acid Molecule and of Its Anion

We previously[5] used isodesmic reactions for estimating these energies. If we apply this principle to the simplest compounds, a molecule of formic acid can be built up from methanal and methanol in an isodesmic reaction, eq 3. The formate anion is built up similarly in eq 4. Reaction enthalpies of these reactions in the gas phase, ΔH°_{298}(g), calculated from experimental enthalpies of formation[12] and from gas-phase acidities,[13] are given with eqs 3 and 4. They compare favorably with our calculated Møller−Plesset (MP2) energies, ΔE(MP2): the effect of zero-point energy and of enthalpy increment (heat-content function) is not decisive, as observed already in other isodesmic reactions.[14] Either experimental or calculated reaction enthalpies may be considered as total interaction energies within molecules HCOOH and $HCOO^-$, whether they are attributed to resonance energies or explained differently. No uncertainty in the experimental or calculated values can throw doubt on the fact that the interaction of the CO and OH groups in formic acid is strongly stabilizing. However, the interaction of the CO and O^- groups in formate anion is still more stabilizing. Therefore, the effect of the CO group as a substituent is acid strengthening.[15] Previously, we obtained quite similar results[5] for acetic acid with reference to propanone and 2-methylpropanol using ΔG°_{298} instead of ΔH°_{298}: the results are not sensitive to the choice of compounds and thermodynamic quantities.

$$CH_2O + CH_3OH = HCOOH + CH_4 \qquad (3)$$

$$\Delta E(\text{MP2}) = -146.7\ \text{kJ·mol}^{-1}$$
$$\Delta H^\circ_{298}(\text{g}) = -148\ \text{kJ·mol}^{-1}$$
$$\Delta G^\circ_{298}(\text{aq}) = -127\ \text{kJ·mol}^{-1}$$

$$CH_2O + CH_3O^- = HCOO^- + CH_4 \qquad (4)$$

$$\Delta E(\text{MP2}) = -315.6\ \text{kJ·mol}^{-1}$$
$$\Delta H^\circ_{298}(\text{g}) = -292\ \text{kJ·mol}^{-1}$$
$$\Delta G^\circ_{298}(\text{aq}) = -194\ \text{kJ·mol}^{-1}$$

If in the Thomas theory an opposite conclusion was reached,[2,3] the main reason can be seen in the different understanding of the term electrostatic potential, *V*. When *V* was viewed in purely physical terms as a “property” of the given molecule, its relative

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[7] Burk, P.; Schleyer, P. v. R. *THEOCHEM* **2000**, *505*, 161−167.

[8] (a) Bökman, F. *J. Am. Chem. Soc.* **1999**, *121*, 11217−11222. (b) Godfrey, M. *Tetrahedron Lett.* **1990**, *31*, 5181−5184.

[9] (a) Hiberty, P. C.; Byrman, C. P. *J. Am. Chem. Soc.* **1995**, *117*, 9875−9880. (b) da Motta Neto, J. D.; Nascimento, M. A. C. *J. Phys. Chem.* **1996**, *100*, 15105−15110.

[10] Rablen, P. R. *J. Am. Chem. Soc.* **2000**, *122*, 357−368.

[11] Taft, R. W.; Koppel, I. A.; Topsom, R. D.; Anvia, F. *J. Am. Chem. Soc.* **1990**, *112*, 2047−2052.

[12] (a) Bureš, M.; Holub, R.; Leitner, J.; Voňka, P. *Thermochemické veličiny organických sloučenin [Thermochemical Quantities of Organic Compounds]*; Institute of Chemical Technology: Prague, 1987. (b) Domalski, E. S.; Hearing, E. D. *J. Phys. Chem. Ref. Data* **1993**, *22*, 805−1159.

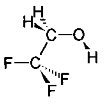
[13] Lias, S. G.; Bartmess, J. E.; Liebman, J. F.; Holmes, J. L.; Levin, R. D.; Mallard, W. G. *J. Phys. Chem. Ref. Data* **1988**, *17*, Supplement 1.

[14] Exner, O. *Prog. Phys. Org. Chem.* **1990**, *18*, 129−161.

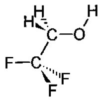
[15] In refs 3b and 10, the significance of isodesmic reactions was questioned, but these reactions were exploited there only to predict the resulting acidity. However, their proper sense for our purpose is to express the interaction energy *separately* for the acid molecule and for the anion. When the effect is stabilizing in the acid molecule, it is not consistent with the picture based on high electrostatic potential. Note still that eqs 3 and 4 are isodesmic but are not homodesmotic in the sense of ref 16, because one C_{sp^3}−O bond is replaced by a C_{sp^2}−O bond. In our opinion, any homodesmotic reaction cannot be constructed in this case. However, eqs 5 and 6 are homodesmotic.

value was attributed to the structure of this molecule. However, in chemical terms, V is the reaction enthalpy belonging to eq 1, and it depends not only on the initial but also on the final state. Its relative value thus depends on the chemically impossible structure **1C** and on a similar structure of the methanolate anion. We shall discuss this structure in the next section to show that it does not represent an anion without resonance and has, in fact, no real meaning.

We searched for a model compound which can be considered a substituted methanol with strengthened acidity but without possibility of resonance. The choice is not easy. Particularly, fluoro derivatives of methanol are unsuitable, because another interaction, called nonbond resonance or negative hyperconjugation, is possible.[17] This excludes all substituents with lone electron pairs in the α-position. Substituents with double bonds, as COX and others, would cause strong hydrogen bonds lowering the energy of the acid. We have chosen 2,2,2-trifluoroethanol, **3**, considered as methanol with CF_3 substituted for one hydrogen atom, as compared with formic acid, in which ═O is substituted for two hydrogen atoms. It turned out that even in **3** a hydrogen bond is possible. There are two stable conformers, **3a** and **3b**, in the MP2 model of which the *sc*-conformer **3a** with a hydrogen bond in a nonplanar cycle (distance F···H 2.565 Å) is more stable by 8.3 $kJ \cdot mol^{-1}$.[18]



3a



3b

Therefore, we have chosen the less stable *ap*-conformer, **3b**, as our model compound; analysis of vibrational frequencies proved that it is a relatively stable molecule at a minimum on the potential-energy surface. The isodesmic reactions, eqs 5 and 6, represent the interaction energy in **3b** and in its anion.

$$CF_3CH_3 + CH_3OH = CF_3CH_2OH(ap) + CH_4 \qquad (5)$$

$$\Delta E(\mathrm{MP2}) = +0.9\ \mathrm{kJ \cdot mol^{-1}}$$
$$\Delta H^\circ_{298}(\mathrm{g}) = -16.4\ \mathrm{kJ \cdot mol^{-1}}$$
$$\Delta G^\circ_{298}(\mathrm{aq}) \approx 0\ \mathrm{kJ \cdot mol^{-1}}$$

$$CF_3CH_3 + CH_3O^- = CF_3CH_2O^-(ap) + CH_4 \qquad (6)$$

$$\Delta E(\mathrm{MP2}) = -97.5\ \mathrm{kJ \cdot mol^{-1}}$$
$$\Delta H^\circ_{298}(\mathrm{g}) = -99.6\ \mathrm{kJ \cdot mol^{-1}}$$
$$\Delta G^\circ_{298}(\mathrm{aq}) \approx -13\ \mathrm{kJ \cdot mol^{-1}}$$

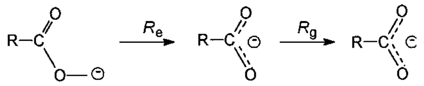
Experimental values of $\Delta H^\circ_{298}(\mathrm{g})$ and $\Delta G^\circ_{298}(\mathrm{aq})$ are based on the enthalpy of formation of CF_3CH_2OH. They are valid for the more stable *sc*-conformer, **3a**, and in addition, they appear to be not very accurate.[19] Nevertheless, it is evident from either experimental or calculated values that stabilization in neutral molecule **3b** is virtually zero, while in the anion it is strong. In terms of organic chemistry, this is attributed to the inductive effect.[20] Note that the interaction energy is not zero for all neutral molecules with an inductive effect; sometimes even relatively small destabilizing effects can be found.[21] In any case, the same finding is valid for substituents with an inductive effect as for those with resonance: the origin of the acidity is to be found in the lowered energy of the anion.

Models for the Carboxylate Anion without Resonance

The foregoing discussion proceeded in terms of real molecules and observable quantities, and we believe that the results are reliable. On the contrary, an answer to our second question requires referring to a model. Either an artificial structure of the carboxylate anion without resonance should be constructed, or the contribution of resonance should be estimated by comparison with other structures in which resonance is not possible. In any case, such a model will always be hypothetical and may adhere only partly to the properties of real molecules. We shall discuss successively four such models suggested in the literature.

(a) Electrostatic Potential of the Carboxylic Acid Molecule. Intuitive feeling would represent an anion without resonance, similar to **1B** with the two C−O bonds of unequal length, one as in the methanolate anion, the other as in acetone. Also, the electron distribution near the O atoms should approximate these two model compounds, respectively. However, near the C atom, the two models will interfere, and the electron density cannot be predicted. When we turn attention to structure **1C**, it approximates the desired model even less: The bond lengths are those present in the acid molecule and are already affected by resonance, but the main defect is in the electron distribution near the O atom. This distribution is very far from that in the methanolate anion and from that in any real molecule. When a similar unnatural structure is constructed also for the methanolate anion, and these two structures are compared,[3e] no conclusion for the real molecules can be derived.

Recently, the relaxation energy, R, was divided[8a] into electronic relaxation R_e and geometric relaxation R_g. When **1C** is submitted to electronic relaxation retaining its geometry, a structure is obtained which is geometrically similar to **1B** but with full electronic relaxation. If it should be represented graphically, it will look like **1D**. The stepwise relaxation is then represented by **1C** → **1D** → **1A**. Even **1D** cannot serve as a model of the anion without resonance. The resonance is only partly reduced as a consequence of the unequal C−O bonds but is still quite strong: the calculated[8a] ΔR_g for the formic acid−methanol pair, 15.9 $kJ \cdot mol^{-1}$, does not represent the actual resonance. In our opinion, a carboxylate anion without resonance cannot be pictured by a formula nor formulated within the framework of MO theory.



1C **1D** **1A**

Ionization is a reversible process, and the structures of the acid molecule and of the anion are of equal importance. Therefore, a similar process to **2A** → **1C** → **1A** can be designed in the opposite direction, that is, starting from the real structure of anion **1A**, proceeding to acid **2C** with the preserved structure

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[16] George, P.; Trachtman, M.; Bock, C. W.; Brett, A. M. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1222−1227.

[17] Schleyer, P. v. R.; Kos, A. J. *Tetrahedron* **1983**, *39*, 1141−1150. We thank Professor Ragué von Schleyer for discussion on this point.

[18] The *g*-conformation **3b** was preferred already in previous lower level calculations: Murto, J.; Rasanen, M.; Aspiala, A.; Lotta, T. *THEOCHEM* **1984**, *17*, 99−112.

[19] Kolesov, V. P.; Ivanov, L. S.; Skuratov, S. M. *Zh. Fiz. Khim.* **1971**, *45*, 547−551. Kolesov et al. give $\Delta_f H^\circ_{298}(\mathrm{s}) = -922.8 \pm 9\ \mathrm{kJ \cdot mol^{-1}}$; $\Delta_f H^\circ_{298}(\mathrm{g})$ calculated from this value is $-888.4\ \mathrm{kJ \cdot mol^{-1}}$ and does not agree with the value calculated on the basis of additivity, $-864.0\ \mathrm{kJ \cdot mol^{-1}}$, ref 12b.

[20] Exner, O.; Charton, M.; Galkin, V. *J. Phys. Org. Chem.* **1999**, *12*, 289.

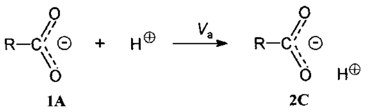
[21] Exner, O. *Org. React. (Tartu)* **1995**, *29*, 1−6.

Table 1. Calculated MP2 Energies of Substituted Alcohols and of Their Deprotonated Forms[a]

	acid, a. u.	anion, a. u.	V, kJ·mol^{-1}	R, kJ·mol^{-1}	V_a, kJ·mol^{-1}	R_a, kJ·mol^{-1}
CH_3OH	−115.472 664	−114.853 164	2604	−978	−923	−704
HCOOH	−189.408 266	−188.853 106	2442	−984	−729	−728
δ(HCOOH−CH_3OH)			−162[b]	−6[b]	+194[c]	−24[c]
CF_3CH_2OH(*ap*), **3b**	−452.020 072	−451.438 041	2523	−995	−818	−710
δ(**3b**−CH_3OH)			−81	−17	+105	−6
CF_3CH_2OH(*sp*), **3a**	−452.023 228					

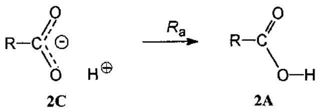
[a] The MP2 energies of the reference compounds are (a. u.): CH_4, −40.389054; CH_2O, −114.268788; CF_3CH_3, −376.936806. [b] Ref 3f gives −160 and −4 kJ·mol^{-1} for V and R, respectively. [c] Ref 7 gives V_a = +115 kJ·mol^{-1} and R_a = +53 kJ·mol^{-1}, calculated at the B3LYP/6-311+G** level, see Discussion.

of the anion, and finally to the acid molecule in its actual structure **2A**. This idea was taken into consideration already by Thomas himself[22] but not elaborated upon. It was presented by us at a meeting[23] and adopted later by Burk and Schleyer.[7]



1A **2C**

(7)



2C **2A**

(8)

While the procedure **1A** → **2C** → **2A** is in principle equivalent to **2A** → **1C** → **1A**, practical realization is less straightforward, because one must design an exact position of the proton in **2C**. We have situated the proton in **2C** at the same distance H−O and the same angle H−O−C as in acid **2A**. The calculated values of V_a and R_a are given in Table 1 and referenced to methanol. (The difference from methanol is denoted by the symbol δ.) There is a great difference between the two compounds in the values of V_a but not of R_a. The result is thus contradictory to that reached from eq 1. The electrostatic potential, V, of the carboxylic acid, rather lower than that of methanol, was considered[2,3e,8a] as proof that the cause of the strong acidity is in the acid molecule. By the same token, the electrostatic potential, V_a, of the carboxylate anion, significantly higher than that of methanolate anion, can be now considered as proof that the cause of acidity is in the anion. Burk and Schleyer[7] calculated a very different value of V_a (Table 1, footnote c). The reason for the disagreement is not likely to be the different theoretical model (B3LYP instead of MP2), because our MP2 acidities of methanol and formic acid are practically the same as their B3LYP data. A more probable explanation is in the different treatment of the geometric parameters. Burk and Schleyer[7] in their calculation of V_a first rearranged the geometry of the anion into that of the neutral acid, and only then, they added a proton without change in the electronic distribution. We preferred the treatment as described here, because it gives V_a as an intrinsic property of the anion and not as a property of a hypothetical structure. Despite this fundamental difference, the qualitative conclusion[7] was the same as ours, that V_a gives an opposite result compared to V.

The same calculations were carried out also for **3b**. The two compounds, formic acid and **3b**, one with and one without resonance, are compared in Figure 1. The main difference is in the stabilization of HCOOH (apparently by resonance, at least partly), which is completely absent in **3b**. Otherwise, the course of stepwise ionization and recombination is rather similar. The inductive effect of the CF_3 substituent in **3b** is weaker than the resonance in HCOOH. If δR should be taken as a measure of resonance in the anion, an absurd result would follow, that the resonance is very small but still somewhat stronger in **3b** than in formic acid.

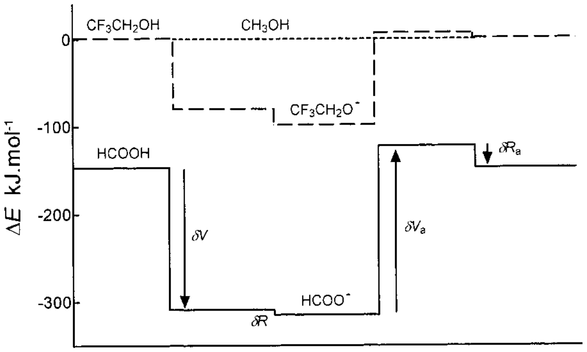


Figure 1. Schematic representation of stepwise deprotonation and protonation of formic acid (solid line), *ap*-2,2,2-trifluoroethanol **3b** (broken line), and methanol as reference (dotted line). Steps from left to right: acids in the real structures, deprotonated acids in the conserved structures, anions in the real structures, protonated anions in the conserved structures, acids in the real structures; *y*-axis provides calculated energies relative to methanol.

(b) Electrostatic Calculations. The electrostatic model has been little elaborated, merely considered as a supporting argument.[3b] Both the anion and acid molecule are modeled as systems of partial charges on the individual atoms. Energy ΔE_{elst} of the ionization process **2A** → **1B** was calculated within the framework of simple electrostatics.[3b] If an approximate agreement with experiment were achieved, one could infer that the resonance in **1A** is negligible. Again comparing formic acid with methanol, eq 9 was derived for the relative electrostatic energy $\delta\Delta E_{elst}$.

$$\delta\Delta E_{elst} = q_O(1/r_{CO(H)} - 1/r_{O\cdot O}) \tag{9}$$

In this equation, $r_{CO(H)}$ and $r_{O\cdot O}$ are the distances C−OH and O···OH, respectively (in Å). The relative permittivity, ϵ_r, was taken as unity and is not included. The charge on the carbonyl oxygen, q_O, was assumed as approximately unity (in electrons, e). With $r_{CO(H)}$ = 1.9627 Å and $r_{O\cdot O}$ = 2.3837 Å (taken from a 3-21+G optimization of acetic acid[22]), $\delta\Delta E_{elst}$ = −125 kJ·mol^{-1} was calculated[3b] in fair agreement with the difference in the experimental gas-phase acidities.[13] However, there is a mistake in the above values in that they are not the distances to the oxygen atom as they were defined in deriving eq 9 but are actually the distances to the OH hydrogen atom, $r_{C\cdot H}$ and $r_{O\cdot H}$. With real experimental values,[24] $r_{CO(H)}$ = 1.363 Å and $r_{O\cdot O}$ = 2.265 Å (insignificantly different from our calculation on formic acid), we get $\delta\Delta E_{elst}$ = −420 kJ·mol^{-1}. When we included even

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[22] Thomas, T. D. Personal communication, 1999.

[23] Exner, O.; Čársky, P. Paper presented at the 5th World Congress of Theoretically Oriented Chemists, WATOC'99, London, August 1−6, 1999.

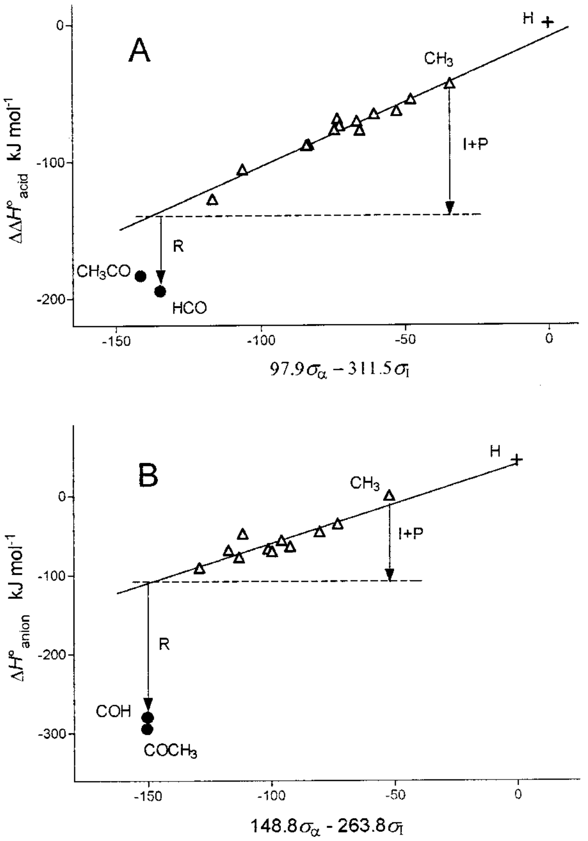

Figure 2. Plots of energies (**A**, gas-phase acidities; **B**, relative energies of the anions) of common oxygen acids XOH vs a blend of substituent constants: aliphatic alcohols and their fluoro- and methoxy-derivatives, △; carboxylic acids, ●; water, +. Arrows show the contributions of resonance (*R*) and of the sum of inductive and polarizability effects (*I* + *P*).

the hydrogen atom into the calculation, we obtained eq 10; with the charge on hydrogen[3g] $q_H = 0.5$ e, we get $\delta\Delta E_{elst} = -309$ kJ·mol^{-1}.

$$\delta\Delta E_{elst} = q_O[1/r_{CO(H)} - 1/r_{O.O} + q_H(1/r_{O.O} - 1/r_{CO(H)} + 1/r_{C.H} - 1/r_{O.H})] \quad (10)$$

The only conclusion is that these electrostatic calculations are of no significance, because they are too sensitive to the input parameters which themselves are rather arbitrary.

(c) Correlation Analysis of Substituent Effects. Taft and coauthors[11] correlated gas-phase acidities of general O-acids by eq 11, which is a linear function of substituent constants σ_α, σ_I, and σ_R , representing polarizability, field-inductive effect, and resonance, respectively.

$$\Delta G°_{acid} = 1608.7 + 97.9\sigma_\alpha - 307.1\sigma_I - 304.6\sigma_R \quad (11)$$

$$R = 0.9995 \quad s = 3.3 \text{ kJ·mol}^{-1} \quad N = 25$$

When eq 11 is applied to formic acid, the contribution of resonance ($304.6\sigma_R$) amounts to 51.8 kJ·mol^{-1}, compared to 6.1 kJ·mol^{-1} found as resonance (hyperconjugation) in ethanol. The difference of 45.7 kJ·mol^{-1} was then compared to the experimental difference in acidity with the result that resonance is of secondary importance[11] (we calculated 36%). However straightforward this reasoning appears to be, it is, though, dependent on many assumptions. First, the accuracy of the correlation, eq 11, is limited, see the standard deviation, *s*. Also, the values of constants σ are loaded with error: an uncertainty of 0.03 σ units represents 9 kJ·mol^{-1}. In our opinion, the most important factor is that eq 11 was derived partly from carboxylic acids themselves: these were important particularly in determining the coefficient at σ_R. We modified the procedure in such a way that the correlation equation was only derived from compounds without resonance: aliphatic alcohols, their fluoro derivatives, and 2-methoxyethanol, assuming simply $\sigma_R = 0$ for all these compounds. We obtained eq 12. The regression coefficients differ only slightly from eq 12, although the correlation is somewhat worse.

$$\Delta G°_{acidity} = 1604.0 + 97.9\sigma_\alpha - 311.5\sigma_I \quad (12)$$

$$R = 0.987 \quad s = 5.1 \text{ kJ mol}^{-1} \quad N = 14$$

When eq 12 is applied to formic or acetic acid, the difference between the calculated and experimental values represents the contribution of resonance. In the graphical representation (Figure 2A), this contribution appears as deviation from the regression line. In this approach, no resonance constants are necessary. The contribution of resonance is estimated to be 31% or 30% for formic acid or acetic acid, respectively.

This procedure can be refined by evaluating separately the effects in the acid molecule and in its anion. The effect in the acid is expressed by the isodesmic reaction, eq 13; its reaction enthalpies $\Delta_{13}H°$ were obtained from experimental enthalpies of formation.[12] The effect in the anion is described by eq 14; its reaction enthalpies $\Delta_{14}H°$ were obtained from $\Delta_{13}H°$ and from the gas-phase acidities.[13]

$$XH + CH_3OH = XOH + CH_4 \quad (13)$$

$$XH + CH_3O^- = XO^- + CH_4 \quad (14)$$

The effects in the anion, $\Delta_{14}H°$, were correlated by eq 15. The fit is worse than in eq 12; the main reason is a reduced number of data.[25]

$$\Delta_{14}H° = 1605.0 + 148.8\sigma_\alpha - 263.8\sigma_I \quad (15)$$

$$R = 0.901 \quad s = 11.8 \text{ kJ mol}^{-1} \quad N = 11$$

As shown in Figure 2B, the points for carboxylic acids deviate from eq 15 still more than from eq 12. The resonance contribution in the anion, related to the methanolate anion, would be estimated to be 65% or 63% in the formate or the acetate anion, respectively. The contribution of resonance to the acidity is then given by a difference of the resonance in the anion and in the neutral acid; the inductive effect is operative essentially in the anion. We can express very approximately these effects for formic acid by eq 16. For the sake of simplicity, the inductive effect and polarizability were taken together under the symbol *I*; their separation is, in any case, somewhat doubtful. This *I* effect in the uncharged acid molecule seems to be slightly destabilizing. Note that the effects in the neutral acid molecule are less certain and have been obtained only from a difference.[25]

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(24) Tam, H. S.; Choe, J.-I.; Harmony, M. D. *J. Phys. Chem.* **1991**, *95*, 9267−9272.

(25) The reduced number of data in eq 15 as compared to eq 12 is due to the lack of certain experimental enthalpies of formation. Moreover, substituent R = H must be excluded, because eqs 13 and 14 would not be isodesmic. Differences between $\Delta H°$ and $\Delta G°$ are immaterial. Substituent effects in undissociated acids, eq 13, are relatively small and less regular (as observed already in the case of the pure inductive effect, ref 26). They correlate poorly with substituent constants and had to be estimated in an indirect way.

Nevertheless, destabilizing inductive effects are possible, because they were observed in other uncharged molecules.[26] In any case, the terms in eq 16 are very approximate and sensitive to small uncertainties in the calculation.

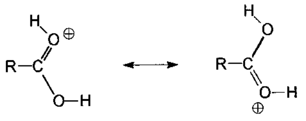
$$\begin{aligned}&\Delta G^\circ_{\text{acidity}}(\text{HCOOH}-\text{CH}_3\text{OH}) =\\ &\qquad R_{\text{anion}} - R_{\text{acid}} + I_{\text{anion}} - I_{\text{acid}}\\ &\qquad -196 + 153 \quad - 98 \quad - 9 \quad = -151\ (\text{kJ mol}^{-1})\end{aligned} \tag{16}$$

A similar approach[10] within the framework of correlation analysis was based on unstable compounds $X_nH_{3-n}COH$ ($X = F, OH, NH_2$), that is, on substitution in the immediate vicinity of the hydroxyl group. Instead of constants σ_α and σ_I, the electronegativity χ of the first atom F, O, or N was used in eq 17.

$$\Delta E_{\text{elst}} = 46.0\Sigma(\chi_i - \chi_C)\ \text{kJ}\cdot\text{mol}^{-1} \tag{17}$$

This simple reaction works well within the given set of compounds whose ionization energies spread over 400 kJ·mol^{-1}. Resonance in carboxylic acids is estimated similarly as in the preceding approach from the deviation when a double bonded oxygen atom is introduced for X2. The contribution of resonance to acidity was estimated at 37%, in remarkable agreement with the preceding value. Effects in the anion and in the the neutral molecule were not separated.

In another approach[10] related to the principles of correlation analysis, the acidity of carboxylic acids was compared with their basicity. The effects of resonance were assumed to be equal, with the electrostatic effect twice greater for the acidity than for the basicity (double-bonded oxygen atom compared to single-bonded OH). The contribution of resonance was estimated to be 20%. In our opinion, both assumptions are rather far from reality. For instance, resonance in the cation must be weaker, because the two structures **4A** and **4B** are not equivalent,[28] while, in the anion, resonance is represented by two identical structures **1B**. Despite all shortcomings, the results based on the correlation analysis are in fair agreement.



4A **4B**

(d) VB Model with Fixed Orbitals. In section a, we offered the opinion that a satisfactory model of the carboxylate anion without resonance cannot be constructed within the framework of MO theory. Hiberty and Birman[9a] described a model based on the valence-bond theory in which one of the π orbitals is doubly occupied and localized on the oxygen atom and the other π orbital is delocalized. The molecule of formic acid is treated in the same way. In our opinion, this is the physically most straightforward model available. It corresponds better to the concept of resonance than the structure required by Burk and Schleyer:[7] "a Lewis structure where all electron pairs are completely localized". However, even in the VB model, the C−O bond does not resemble the C−O bond in an alkanoate anion. This defect should be compensated for by modeling the ethanolate anion in a similar way, using pseudo-π fragment orbitals. Results for the two molecules are then subtracted, but the treatment of the two is not strictly comparable. By comparison with the experimental acidities, Hiberty and Birman[9a] estimated the contribution of delocalization (resonance) as 48% of the total acidity enhancement.

We tried even in this case to separate the effects operating in the anion and in the acid molecule. We used the calculated[9a] delocalization energies for individual species and determined the relative contribution as in the preceding section, on the basis of eqs 13 and 14. The results are given in eq 18. There is only a qualitative agreement with eq 16. Using another reference alcohol is immaterial; the difference is mainly in the resonance in formic acid.

$$\begin{aligned}&\Delta G^\circ_{\text{acidity}}(\text{HCOOH}-\text{C}_2\text{H}_5\text{OH}) =\\ &\qquad R_{\text{anion}} - R_{\text{acid}} + I_{\text{anion}} - I_{\text{acid}}\\ &\qquad -107 \quad + 45 \quad - 115 \quad + 37 \quad = -140\ \text{kJ mol}^{-1}\\ &\qquad\qquad\qquad\qquad\qquad\qquad (\text{exptl value})\end{aligned} \tag{18}$$

The above results[9a] were amended by more sophisticated calculations by da Motta Neto and Nascimento.[9b] In these calculations, avoidance of delocalization in the two classical structures A and B (corresponding to two formulas **1b**) was achieved by means of a GVB(PP) procedure with localized molecular orbitals. The off-diagonal π elements were only calculated in the last iteration and set to zero in all previous iterations. The introduction of delocalization was done by means of a CI-type wave function, $C_A\Psi_A + C_B\Psi_B$, where Ψ_A and Ψ_B were wave functions for the resonance structures A and B. The relative contribution of resonance was estimated to be 51% for the formic acid−methanol pair, or to be 69% for acetic acid−ethanol. Separation of the effects in the anion and in the acid molecule was not attempted. [9b] Compared with the previous treatment,[9a] the final result is little changed and agreement with the approach of correlation analysis (previous paragraph) remained merely qualitative.

Acidity in Water Solution

Up to now, our discussion has been devoted to calculated acidities of isolated molecules or to experimental values in the gas phase. However, most classic reasoning and the concept of resonance were originally based on acidities in water. The simplest way to transfer the above isodesmic reactions into water is to assume[21] that their ΔH°_{298}(g) and ΔG°_{298}(g) values are approximately equal. Then, one can proceed to ΔG°_{298}(aq) by adding the Gibbs energies of hydration[29] $\Delta G^\circ_{298}(\text{g}\rightarrow\text{aq})$ for all compounds involved. We obtained the values given in eqs 3 and 5. The values for the isodesmic reactions of the anions, eq 4 or 6, were then obtained from the pK values in water.[30] As expected, all the values in water are smaller than in the gas phase, but the attenuation is relatively weak. The result is qualitatively similar to that for isolated molecules and quantitatively still more clear-cut: The anion is strongly stabilized, but this effect is partly counterbalanced by a stabilization of the acid molecule which is also rather strong.

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[26] Exner, O.; Nauš, P. *J. Phys. Org. Chem.* **2000**, *13*, 693−698.

[27] The values of $\Delta G^\circ_{298}(\text{g}\rightarrow\text{aq})$ were taken from ref 28. The value for formic acid in eq 3 was estimated assuming that the differences between an aldehyde and the corresponding carboxylic acid are constant (−13.4 kJ·mol^{-1}). The uncertainty in this procedure should not exceed 1 kJ·mol^{-1}.

[28] The basicity of carboxylic acids would deserve a detailed treatment and will not be discussed here. The asymmetrical conformation of the cation **4A↔4B** follows both from the B3LYP/6-31+G** calculations, ref 10, and from the NMR spectra: Hogeveen, H.; Bickel, A. F.; Hilbers, C. W.; Mackor, E. L.; MacLean, C. *J. Chem. Soc., Chem. Commun.* **1996**, 898−899.

[29] (a) Cabani, S.; Gianni, P.; Mollica, V.; Lepori, L. *J. Solution Chem.* **1981**, *10*, 563−595. (b) Abraham, M. H.; Andonian-Haftvan, J.; Whiting, G. S.; Leo, A.; Taft, R. S. *J. Chem. Soc., Perkin Trans. 2* **1994**, 1777−1791.

[30] *Tables of Rate and Equilibrium Constants of Heterolytic Organic Reactions*; Palm, V. A., Ed.; VINITI: Moscow, 1975; Vol. 1(1).

Calculating the relative contribution of resonance is more difficult for the aqueous solution. Quantum chemical models are not very promising but an estimate based on correlation analysis is possible. We rewrote eq 16 for water and got eq 19.

$$\begin{array}{l}\Delta G^\circ_{\text{acidity}}(\text{HCOOH}-\text{CH}_3\text{OH})^{\text{w}} = \\ \quad R^{\text{w}}_{\text{anion}} - R^{\text{w}}_{\text{acid}} + I^{\text{w}}_{\text{anion}} - I^{\text{w}}_{\text{acid}} \\ \quad -171 \quad +129 \quad -20 \quad -2 \quad = -64\ (\text{kJ}\cdot\text{mol}^{-1})\end{array} \qquad (19)$$

The terms in eq 19 were estimated as follows. R^{w} and I^{w} are bound by the constraints already derived (eqs 3 and 4): $R^{\text{w}}_{\text{anion}} + I^{\text{w}}_{\text{anion}} = -191$ and $R^{\text{w}}_{\text{acid}} + I^{\text{w}}_{\text{acid}} = -127$. Assignment of all values is possible in two ways. First, we can assume that the terms I_{anion} and I_{acid} in eq 16 are reduced in water to some 20% to give $I^{\text{w}}_{\text{anion}} - I^{\text{w}}_{\text{acid}}$ in eq 19; this rather strong reduction is expected according to the attenuation of the pure inductive effect in compounds of similar size.[26] The terms given for eq 19 were calculated in this way. Second, these estimates may be tested by the same procedure as in eq 12 and Figure 2A, applied to the acidities of various alcohols in water. This was more difficult than for the gas phase, because few dependable p*K* values are available[30] and these are not sufficiently different. The resulting correlation, eq 20, reveals a good fit, but the choice of compounds was not quite consistent. Instead of restricting the choice to primary alcohols, we were obliged to include some secondary and tertiary alcohols.

$$\Delta G^\circ_{\text{acidity}}(\text{XOH})^{\text{w}} = 79.1 + -79.4\sigma_{\text{I}} \qquad (20)$$

$$R = 0.962 \quad s = 4.1\ \text{kJ mol}^{-1} \quad N = 14$$

Nevertheless, when eq 20 is applied to formic acid, one gets a resonance contribution to acidity of 35 $\text{kJ}\cdot\text{mol}^{-1}$, in reasonable agreement with that of 42 $\text{kJ}\cdot\text{mol}^{-1}$ in eq 19.

No doubt the terms in eq 19 are only rough estimates. However, they yield a rather consistent picture, and the following conclusions seem to be safe. The contribution of resonance to the acidity enhancement of formic acid is stronger in water (66%) than in the gas phase (31%). Because the classic explanation was derived from the acidity in water, it was more justified than if it followed from quantum chemical calculations.[3e,7,9,10] The reason is that the inductive effect is much more strongly attenuated in water (say to 20%) than the resonance (87% or 84% in the anion or in the acid molecule, respectively). A smaller attenuation of resonance compared to the inductive effect was observed with substituted phenols and called specific substituent solvation assisted resonance.[31] In our opinion, it would be better to say that resonance is not "solvation assisted" but less attenuated than the inductive effect.

Conclusions

In our opinion, there are no doubts that the acidity of carboxylic acids is related to the low energy of the anion, not to a high energy of the acid molecule, because even the latter is lowered compared to alcohols. This statement can be supported quantitatively with reliability and with some precision. On the other hand, the importance of resonance can be only estimated. The result will always depend on the definition and on the model applied; every model either operates with artificial structures or transfers some properties from one molecule to another. Nevertheless, several models agree in qualitative results that resonance as traditionally meant represents a factor responsible for a part of acidity enhancement, less than one-half. We wanted particularly to stress two findings. First, resonance is strong both in the carboxylate anion and in the carboxylic acid molecule; the effect on acidity is given by the difference. Every discussion restricted only to this difference is thus incomplete and may be misleading. Second, the relative importance of resonance is changed significantly when going from the isolated molecules to the water solution; in water, resonance is the deciding factor.

The whole concept of resonance seems at present somewhat obsolete and has mainly a pedagogic significance: it means that certain very imperfect structural formulas can be somewhat improved using the resonance structures. Even in its imperfect form, this principle can correctly predict the structure of the carboxylate anion (equivalence of the oxygen atoms, equal bond lengths) and its low energy; calculations of the resonance energy based on more sophisticated models do not seem to be dependable.

Calculations

All the data were obtained by MP2/6-311++G(2d,p) calculations.[32] Choice of the theoretical model is not critical. Basically, the same results are obtained by HF, MP2, and MP4 calculations, as shown by Ji and Thomas[3e] on the data given in the footnotes to their Table 1. Electrostatic potentials *V* were calculated by the procedure described.[3e]

The potential, V_{a}, for **2C** was evaluated on the basis of eq 7, in which the structure **2C** was constructed from **1A** in such a way that a proton was located at a position corresponding to the O−H bond length and C−O−H bond angle in **2A**. Using this geometry, the MP2 energies of **2C** were calculated from the frozen molecular wave function of **1A**; that is, the SCF procedure for **2C** was not allowed to iterate, and the basis set was extended to include the Gaussians on the hydroxyl hydrogen, but their molecular orbital expansion coefficients were set to zero. Because the correlation energy in **1A** and **2C** is the same, V_{a} is given by the difference between the Hartree−Fock energies of **2C** and **1A** at optimum MP2 geometries.

The V_{a} potentials for methanol and $\text{CF}_3\text{CH}_2\text{OH}$, **3b**, were obtained in the same way.

Acknowledgment. Thanks are due to Professor T. D. Thomas for important discussions. The work was supported by the Grant Agency of the Czech Republic, Grant 203/99/1454 (to O.E.).

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[31] Fujio, M.; McIver, R. T., Jr.; Taft, R. W. *J. Am. Chem. Soc.* **1981**, *103*, 4017−4029.

[32] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Head-Gordon, M.; Gonzales, C.; Pople, J. A. *Gaussian 94*, revision C.3; Gaussian, Inc., Pittsburgh, PA, 1995.