Steric Inhibition of Resonance: A Revision and Quantitative Estimation on the Basis of Aromatic Carboxylic Acids

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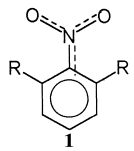
Abstract: The classical concepts of steric inhibition of resonance (SIR) and primary steric effect (van der Waals interactions) were revised with the aid of methyl-substituted benzoic acids. The quantum chemical model was based on the energies of various conformations, calculated at the RHF/6–31+G(d,p) and B3LYP/6–311+G(3df,2pd)//RHF/6–31+G(d,p) levels. The molecule of 2-methylbenzoic acid is planar: no SIR is possible, and van der Waals interaction is practically equal in the acid molecule and in its anion. Therefore, the increased strength of this acid is not due to any steric effect but can be described in terms of electrostatic interaction pole/induced dipole, which lowers the energy of the anion. The molecule of 2,6-dimethylbenzoic acid is nonplanar. SIR is significant in the acid molecule but equal or even greater in the anion. The higher acidity cannot be connected with SIR and can be explained also by electrostatic interaction. In 2,3,5,6-tetramethylbenzoic acid, SIR is greater and may be responsible for one third of the acid-strengthening effect. The concept of SIR is to be applied with caution; even when the nonplanar conformation is proven, SIR need not be responsible for any observable quantity, and particularly not for the acidic and basic properties.

Keywords: acidity · carboxylic acids · hindered resonance · *ortho* effect · steric hindrance

Introduction

The term steric inhibition of resonance (SIR) was used for the first time with aromatic nitro compounds.[1] In the substituted nitrobenzene **1**, conjugation of the nitro group with the benzene ring (resonance) would require a partial double C:N bond, and hence the two oxygen atoms must be coplanar with the ring. If the coplanarity is prevented by the bulky groups R, resonance and some observable substituent effects are decreased.



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Similarly in the methyl-substituted benzoic acids **2** or **5** (Table 1), if the COOH group is rotated out of the ring plane, the resonance of the molecule is lowered, and the acidity is strengthened. The concept of SIR has been incorporated by the English school into classic theory,[2] extended to further compounds and to various observable quantities, and included in contemporary textbooks.[3] In a more sophisticated, quantitative version of the theory,[4] one assumes, for individual derivatives, a variable torsional angle ϕ between the two parts of the conjugated system (benzene ring and substituent). SIR and various observable quantities then depend on $\cos^2\phi$. Substituted benzaldehydes and acetophenones,[4] *N*,*N*-dimethylanilines,[5] benzoic acids,[6] and biphenyls[7] were treated in this way. In more detailed investigations, even an additional effect of more remote substituents (in the *meta* position) was revealed: the buttressing effect.[8] This theory was challenged by us for two reasons. Firstly, some observable quantities, particularly dipole moments,[9] can be explained even without reference to resonance and its inhibition. Secondly and more importantly, certain compounds do not actually possess the conformation postulated by the theory. So we have proven[10] that 2-methylbenzoic acid does not exist in a nonplanar conformation but in an equilibrium of two planar forms **2a** and **2b** (Scheme 1). The same holds for polymethylbenzoic acids with only one *ortho* methyl group.[11] Sterically more hindered compounds such as 2,6-dimethylbenzoic acid **5** (Scheme 2) are nonplanar,[11] but the angles ϕ do not agree with the values formerly anticipated.[6]

We concluded[11] that the principle of SIR must be applied with caution, and the actual conformation must be proven for every molecule involved. In addition, the resonance energy should be estimated at least approximately. It can happen[11a]

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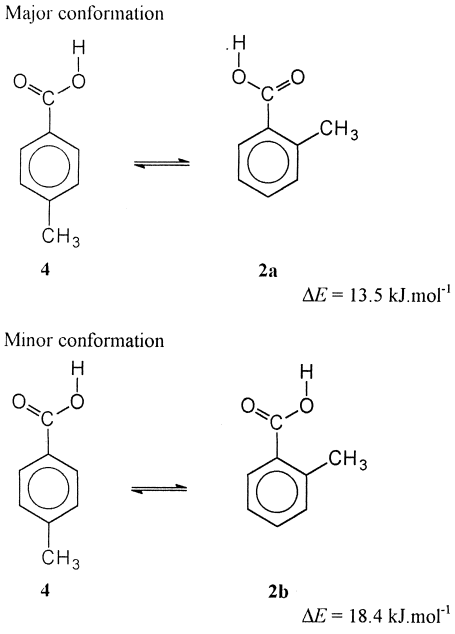
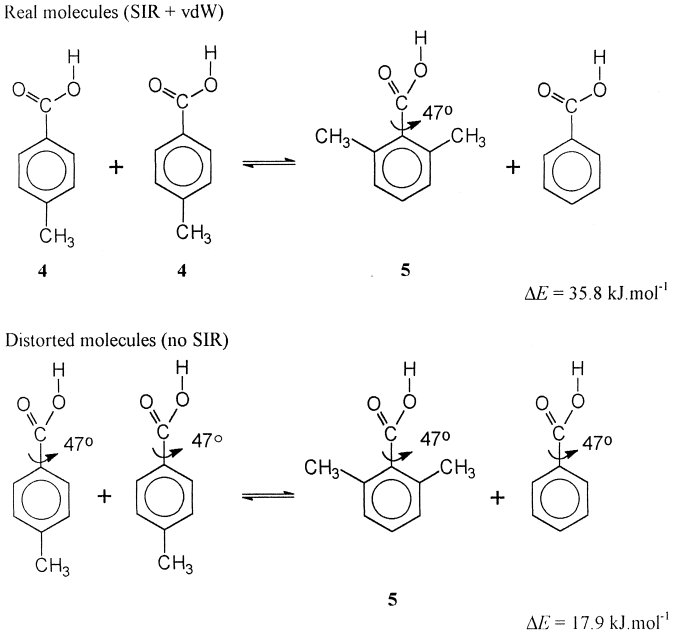
Table 1. Calculated energies of methyl-substituted benzoic acids and their deprotonated forms.[a]

	Conformation, $\phi =$				
	0°	47.4°	77.0°	90°	180°
benzoic acid	– 420.9775082	– 420.9729324	– 420.9679495	– 420.9671761	[b]
	– 418.3530821	*– 418.3474236*	*– 418.3416669*	*– 418.3408138*	[b]
2-methylbenzoic acid (**2**)	– 460.3045151			– 460.2975899	– 460.3026810
	– 457.3887980			*– 457.3805285*	*– 457.3869343*
3-methylbenzoic acid (**3**)	– 460.3082487		– 460.2987344	– 460.2978945	– 460.3081049
	– 457.3929234		*– 457.3817309*	*– 457.3808560*	*– 457.3927523*
4-methylbenzoic acid (**4**)	– 460.3088705	– 460.3036311	– 460.2985177	– 460.2979177	[b]
	– 457.3939507	*– 457.3877107*	*– 457.3817085*	*– 457.3809367*	[b]
2,6-dimethylbenzoic acid (**5**)	– 499.6260387	– 499.6286101		– 499.622681	[b]
	– 496.4186659	*– 496.4211703*		*– 496.4199737*	[b]
2,3,5,6-tetramethylbenzoic acid (**6**)	– 578.2771695		– 578.2845675	– 578.2845775	[b]
	– 574.4861902		*– 574.4943725*	*– 574.4943522*	[b]
	0°	65.2°	79.1°	90°	180°
benzoate anion	– 420.4247473	– 420.4196752	– 420.4188065	– 420.4185927	[b]
	– 417.7892042	*– 417.7813674*	*– 417.7797849*	*– 417.7793496*	[b]
2-methylbenzoate anion	– 459.7505156				[b]
	– 456.8232659				[b]
3-methylbenzoate anion	– 459.7542684		– 459.7460009	– 459.7482143	[b]
	– 456.8279045		*– 456.8188556*	*– 456.8184129*	[b]
4-methylbenzoate anion	– 459.7540193	– 459.7486782	– 459.7477666	– 459.7475512	[b]
	– 456.8278023	*– 456.8196127*	*– 456.8179114*	*– 456.8174466*	[b]
2,6-dimethylbenzoate anion	– 499.072404	– 499.0800938		– 499.0802456	[b]
	– 495.8530977	*– 495.8590471*		*– 495.8586496*	[b]
2,3,5,6-tetramethylbenzoate anion	– 577.7196228		– 577.7348039	– 577.7348356	[b]
	– 573.9183662		*– 573.9312551*	*– 573.9311758*	[b]

[a] E in a.u. B3LYP/6 – 311 + G(3df,2pd)//RHF/6 – 31 + G(d,p); in italics RHF/6 – 31 + G(d,p); the lowest-energy conformation of each species is underlined. [b] Equal as for $\phi = 0°$.



Scheme 1. Isodesmic reactions that represent the steric effect in the molecule of 2-methylbenzoic acid **2**.



Scheme 2. Isodesmic reactions that represent the steric effects in the molecule of 2,6-dimethylbenzoic acid **5**.

that it is smaller that its anticipated inhibition: then the interpretation is evidently wrong. The result of our investigations was that the general term "steric effect" can acquire different meanings even within a series of structurally very similar compounds. In acids with no or one *ortho* methyl group (for example, **2**) we can speak about a primary steric effect in terms of the classical Ingold's theory;[2a] a more modern term would be van der Waals tension (vdW). In the benzoic acids with two *ortho* methyl groups (for example, **5** or **6**), SIR is undoubtedly responsible at least for a part of the observed effects. When this is accepted, we still have to deal with two problems.

a) How should the steric effect in planar molecules be explained, that is, whether the popular term, (primary)

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steric effect, can be called vdW or whether it is described more adequately by another model.

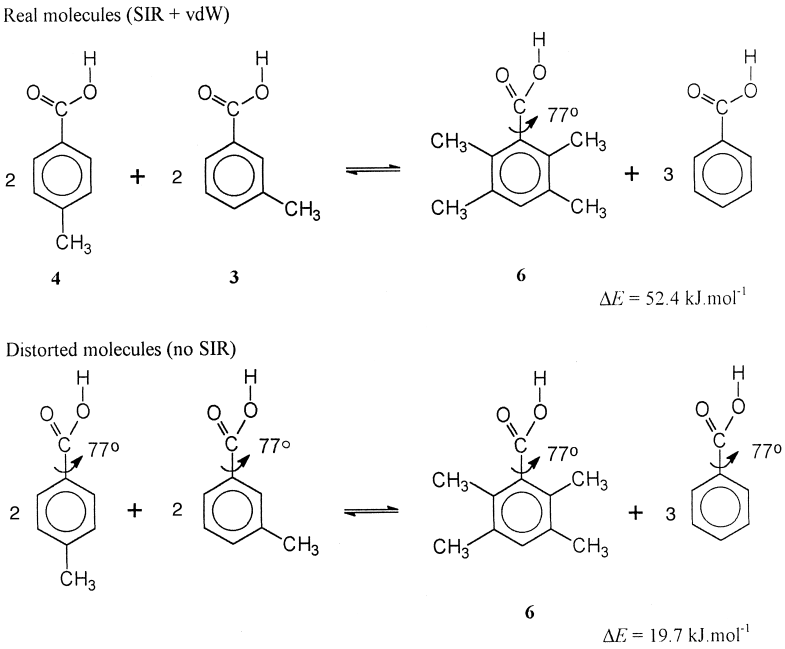
b) In the case of nonplanar molecules, what is the relative contribution of SIR, that is, whether vdW or another effect is not present even in these compounds.

These problems are the subject of the present investigation. Our main tool was ab initio calculations of the energy and geometry of the acids **2**–**6** in different conformations at the levels RHF/6–31+G(d,p) and B3LYP/6–311+G(3df,2pd)//RHF/6–31+G(d,p). These energies were treated in terms of isodesmic (and also homodesmotic) reactions[12] and compared with experimental enthalpies of formation and enthalpies of dissociation wherever possible. Calculations of $\Delta_f H^0_{298}$ or $\Delta_f H^0_0$ would be feasible for the molecules in their minimum-energy conformations, but their values would not be comparable with the calculations on twisted conformers which do not represent real molecules. For this reason and because the comparison with experiments was favorable, we evaluated all substituent effects in terms of the E(RHF) and E(B3LYP) values not combined with the experimental data. According to previous experience,[12b] differences between ΔE(RHF) and $\Delta_f H^0_{298}$ or even $\Delta_f G^0_{298}$ become usually insignificant in isodesmic reactions of this kind.

Results and Discussion

Theoretical and experimental energies: Our calculated energies (Table 1) offer two possibilities for comparison with experiments. Firstly, various isodesmic reactions can be constructed as for instance those in the Schemes 1–3 (the reactions at the top of each scheme). Some of these reactions may represent a kind of substituent effect of the methyl groups. Whatever their physical meaning may be, their ΔH^0_{298} can also be obtained[11a] from the experimental enthalpies of formation, $\Delta_f H^0_{298}$, of all species involved, and compared with the calculated ΔE by means of linear regressions. This was done for nine isodesmic reactions constructed for the compounds **2**–**6**; this includes the reactions in Schemes 1–3. The agreement is almost equally good for the E(RHF) and E(B3LYP) values, with standard deviations of 2.39 and 2.31 kJ mol^{-1}, respectively. In our opinion, any better agreement cannot be expected since the experimental uncertainty of $\Delta_f H^0_{298}$ is hardly better than 2 kJ mol^{-1} for one compound in each reaction.[13] For three important reactions, the agreement of calculations and experiments is shown in Table 2, lines 1–3. However, there is a difference which makes the E(RHF) calculations preferable. The slope of regression b for them does not differ from unity, while for the E(B3LYP) calculations $b = 0.86 \pm 0.05$ (this means that steric hindrance is underestimated in the crowded molecules).

The second possibility for comparison of experimental and calculated values is in the relative acidities[11a] in the gas phase, $\delta\Delta_{acid}H^0_{298}$. They correspond to the isodesmic reaction (Equation (1) in Scheme 4), in which the proton is transferred from



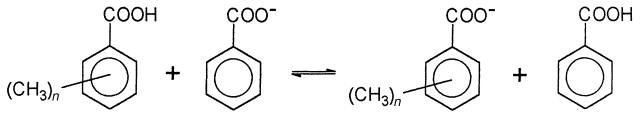
4 **3** **6** **6**

Scheme 3. Isodesmic reactions that represent the steric effects in the molecule of 2,3,5,6-tetramethylbenzoic acid **6**.

Table 2. Analysis of steric effects in methyl-substituted benzoic acids.[a]

	Compound	Isolated molecules			Acidities in methanol		
		SE[b]	SIR	non-SIR[c]	SE[b]	SIR	non-SIR[c]
	acid molecules						
1	**2**	13.5 (*12*)	0	13.5			
2	**5**	35.8 (*33*)	17.9	17.9			
3	**6**	52.4 (*53*)	32.7	19.7			
	anions of						
4	**2**	11.9	0	11.9			
5	**5**	19.3	22.4	−3.1			
6	**6**	32.9	25.3	7.7			
	acidities of						
7	**2**	−1.6 (*−5*)	0	−1.6	(*−2*)	0	−2
8	**5**	−16.5 (*−12*)	4.5	−21.0	(*−8*)	≈3	≈−11
9	**6**	−19.5 (*−15*)	−7.4	−12.0	(*−8*)	≈−5	≈−3

[a] In kJ mol^{-1}, calculated from E(RHF) values; in italics experimental values in terms of ΔH^0_{298}. [b] Total steric effect, experimental values in the gas phase are based on $\Delta_f H^0_{298}$ from ref. [11b], experimental data in solution on $\Delta_{acid}G^\circ$ taken from ref. [17b]. [c] This share is to be interpreted as vdW interaction in the case of acid molecules, as PIDI in the case of acidities, and as both in the case of anions.



(1)

Scheme 4. An isodesmic reaction, in which the proton is transferred from one acid to the anion of another acid.

one acid to the anion of another acid. When the acids **2**–**6** were substituted in this scheme, the agreement was distinctly worse than in the previous case. In particular, the acid **2** deviated even qualitatively since it is stronger than benzoic acid, while both RHF and B3LYP treatments predicted it to be weaker. When this compound is excluded, regression with five points gives the standard deviations 1.66 and 1.11 kJ mol^{-1} for ΔE(RHF) or ΔE(B3LYP), respectively. A disadvantage of B3LYP is again in the slope ($b = 1.66 \pm 0.13$); in this case it overestimates the steric effects, particularly in the acid **5**. When the steric effects are evaluated separately (in the following sections), the agreement with experiments is better, since the errors for the individual acids compensate. The important reactions are given in Table 2, lines 7–9; the disagreement exceeds only slightly the experimental uncertainty (s.d. may acquire 0.7 kJ mol^{-1} for a single compound, 1 kJ mol^{-1} for the reaction). Note particularly that the uncertainty is greatest for the acid **2** and does not affect our main conclusions for **5** and **6**.

The imperfect agreement for the acidities prompted us to calculate the values of $\delta\Delta H^0_{298}$ and $\delta\Delta G^0_{298}$ for Equation (1) in the case of the acid **5**, for which the differences between RHF and B3LYP levels were the greatest. For the RHF treatment, almost perfect agreement was obtained: E(RHF) -4.61, $\delta\Delta H^0_{298}$ -5.20, $\delta\Delta G^0_{298}$ -6.86, and experimental $\delta\Delta G^0_{298}$ or $\delta\Delta H^0_{298}$ -6.5 kJ mol^{-1}, while E(B3LYP) equals -11.54 and is little changed by the statistico-mechanical corrections.

In our opinion, the reliability of our calculations allows us to found the following discussion and evaluation of steric effects exclusively on calculated energies, which are not combined with experimental values.[14] In this way, a conceptually pure model was obtained. Table 2 contains results from RHF calculations; B3LYP calculations yield very similar results, but a scaling correction would be necessary as has been shown from the values of regression slopes.

Conformation: Further results of calculations concern the conformation (Table 3, last column). Calculations predict a nonplanar conformation for **5** and **6** (with $\phi = 47$ and 77°, respectively) and an equilibrium of planar forms, **2a** and **2b** (Scheme 1), for **2**; the ratio for **2a**:**2b** is approximately 4:1. This is in accord with the indirect experimental results from the correlation analysis,[11] with the crystal structures,[10, 15] and with the conformation of the methyl ester of **2**.[16]

The structure of **2a** gives no indication of any weak hydrogen bonds between the methyl hydrogen atoms and the carbonyl oxygen, as was considered possible.[6a] On the contrary, the conformation of the C2–C(H_3) bond shifts these hydrogen atoms as far as possible from the carbonyl.

Steric effects in planar molecules: In the next step, the energy values were used to construct the isodesmic reactions (Schemes 1–3). These reactions may represent a desired "substituent effect" with a better or worse approximation, but the energy values have always a clear physical meaning. They are simply reaction energies (enthalpies) of an isodesmic reaction.

Separation of steric and polar effects was attempted by us with a comparison of *ortho* and *para* derivatives, as expressed in a simplified way by Equation (2).

$$SE = \Delta H^\circ(2) - \Delta H^\circ(4) \qquad (2)$$

In the case of polysubstituted derivatives, two (or more) reference compounds are needed. Together they contain as many *para* substituents as the original compound has *para* and *ortho* substituents; the number of *meta* substituents is retained (Scheme 2 and Scheme 3). The approach assumes that the polar effects mediated through the benzene ring are equal in the *ortho* and *para* positions. The latter approximation can be doubted[17] but has been found sufficient in detailed analyses of the acidities of these compounds in the gas phase[11a, b] and in solution.[17b] In the case of 2-methylbenzoic acid **2**, Equation (2) represents a simple isomerization reaction (Scheme 1). With respect to the two conformations of **2**, the steric effect of one *ortho* methyl group is represented by the reaction enthalpy of either the reaction **4** → **2a** or **4** → **2b** (Scheme 1). Since **2a** is dominant, its calculated reaction energy can be compared with the experimental ΔH^0_{298}[11] derived from the enthalpies of formation (Table 2, line 1). The agreement is better than with ΔH^0_{298} calculated previously[11b] by AM1. By the same procedure, we calculated ΔE(RHF) of the isodesmic reactions between the anions

Table 3. Some calculated bond lengths and bond angles in methyl-substituted benzoic acids.[a]

	C=O	C–OH	C1–C(O)	C1–C2	C1–C6	O=C–O	ϕ
4-methylbenzoic acid **4**	1.192	1.330	1.485	1.393	1.388	121.7	0
2-methylbenzoic acid **2a**	1.193	1.333	1.489	1.406	1.396	120.8	0
2,3-dimethylbenzoic acid[b]	1.193	1.333	1.487	1.406	1.395	120.6	12
2,6-dimethylbenzoic acid **5**	1.191	1.330	1.497	1.401	1.401	121.3	47
2,3,5,6-tetramethylbenzoic acid **6**	1.189	1.330	1.502	1.395	1.395	121.8	77
4-methylbenzoate anion	1.234		1.545	1.390	1.390	129.4	0
2-methylbenzoate anion	1.234		1.554	1.406	1.394	128.7	0
2,6-dimethylbenzoate anion	1.234		1.542	1.399	1.399	129.4	65
2,3,5,6-tetramethylbenzoate anion	1.234		1.541	1.399	1.399	129.4	79

[a] Bond lengths in Å, bond angles in degrees. [b] See ref. [30].

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(similar reactions as in Scheme 1 with COO^- instead of COOH, anions of **2a** and **2b** are identical). If we subtract the reaction energies of the anions and acids, we obtain $\delta\Delta E$(RHF); this represents the enhanced acidity due to the steric effect. This value can be compared with the experimental $\delta\Delta H^0_{298}$ obtained from the gas-phase ionization[11b] (Table 2, line 7).

The acidity of **2** was formerly explained by hindered resonance.[2b, 6a, 6d] When this is not present, one has to refer to the primary steric effect or in more modern terms to the van der Waals interaction (vdW). The traditional interpretation of primary steric effects on acidities[2a, 3a] was simple: the steric effect makes the acid less stable. It was overlooked that the steric effect is also present in the anion, and that the COO^- group is evidently not smaller than COOH. When we started from the standard geometry,[18] we calculated the same distance, C(H_3)–C(O), in the idealized structures of **2a** and of its anion.[19] Within the framework of molecular mechanics and force field[20] MM3, we obtained the assumed van der-Waals repulsion, which was even a little greater for the anion (30.4 kJ mol^{-1}) than for the acid molecule of **2a** (26.1 kJ mol^{-1}). When the COO^- group is not smaller than COOH, it would still be possible that it is "softer", that is, that an interaction from the same distance requires less energy. We can test this hypothesis by comparison of the geometry of an *ortho*-substituted benzoic acid and its anion in their real, fully relaxed geometries. The *ortho* substitution produces deformation of the benzene ring, and in the crystalline state this mainly causes the C(1)–C(2) bond to become longer and the angles C(O)–C(1)–C(2) and C(1)–C(2)–C(H_3) to become wider. Out-of-plane deformations and deformations on the carboxyl group were found to be insignificant.[10] If the above hypothesis was correct, the deformations would be greater in the acid molecule than in the anion. We tried three possible approaches that compared the following: a) a crystal structure of an acid and of its salt, b) a series of crystal structures of various acids and various salts, and c) calculated structures.

a) A detailed search in the Cambridge Structural Database[21] did not reveal a single pair of suitable structures of an *ortho*-substituted benzoic acid and its salt, that is, when the disordered structures and the acid salts had been eliminated. The only example would be 2-hydroxybenzoic acid and its trimethylammonium salt, but the size of the substituent is insufficient, and the structure is influenced by hydrogen bonds.
b) In a series of substituted benzoic acids,[21] the average difference Δl of the bond length C(1)–C(2) was calculated and related to the mean bond length in the benzene ring. For nine approximately planar 2-substituted benzoic acids ($\phi < 6°$) $\Delta l = 0.024$ Å; for two salts of such acids $\Delta l =$ 0.026 Å. For twenty four nonplanar 2,6-disubstitued acids ($\phi > 29°$) $\Delta l = 0.008$ Å; for sixteen such salts $\Delta l = 0.010$ Å. While the difference between 2- and 2,6-derivatives is significant, that between acids and salts is not. Other geometrical parameters were still less telling.
c) The most important results were obtained from the calculations. The calculated geometries of the minimum-energy structures of the acid **2** and of its anion are shown in Figure 1. There is very little difference in the critical parameters, as demonstrated particularly by the equal bond lengths C(1)–C(2).

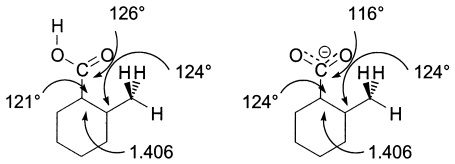

Figure 1. Calculated bond lengths and bond angles of 2-methylbenzoic acid **2** and of its anion.

Previously, we estimated steric effects in polymethyl-substituted benzoic acids, SE_{acid}, according to Equation (1). The same procedure was carried out also for their anions.[11b] When they are plotted against each other, it turned out that SE_{anion} is about 80% of SE_{acid} (Figure 2, broken line). In this

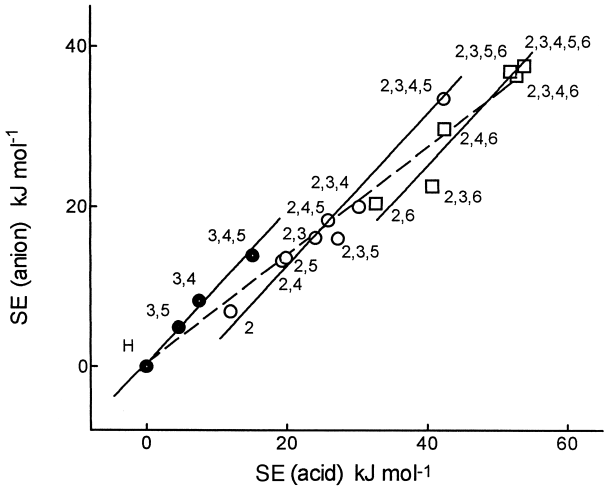

Figure 2. Plot of the steric effects SE, derived from the experimental values of $\Delta_f H^\circ$ and ΔH^0_{acid} for the molecules of methyl-substituted benzoic acids (*x*-axis) and for their anions (*y*-axis): ● acids without *ortho* substituents, ○ with one *ortho* substituent, and □ with two *ortho* substituents. The full lines have unity slope. Data taken from ref. [11b].

way, the apparent steric effect on the acidity could be formally explained. However, this interpretation is misleading as it is known that the groups COOH and COO^- have equal steric requirements. We prefer to divide all methyl-substituted benzoic acids into three groups: those with no *ortho* substituent, those with one *ortho* substituent, and those with two *ortho* substituents, respectively. Then $SE_{acid} = SE_{anion}$ is valid within each group[19] (Figure 2, full lines); the values in different groups are shifted by 6 kJ mol^{-1}. In our opinion, the only reasonable explanation[19] for the substituent effect on the acidity is: that it is not the energy of the acid molecule that is enhanced by steric effects, but it is the energy of the anion that is lowered. A possible model is electrostatic interaction pole/induced dipole (PIDI). This type of interaction[22] has already been considered[23] in the discussion of the gas-phase acidity of **2.** It can be expressed by Equation (3).

$$\Delta E = -\alpha q^2/32\pi^2\varepsilon_O^2\varepsilon_{ef}^2 r^4 \quad (3)$$

Remarkably, the equation has not been reported correctly in the literature: once it was given (in the CGS system, without the factor of $16\pi^2\varepsilon_O^2$) with ε_{ef} instead of ε_{ef}^2,[24] in other papers ε_{ef} was omitted.[22, 23] The polarizability α for one mole (units $cm^3 mol^{-1}$) can be taken from the molar refraction of the CH_3 group,[25] the charge q may be divided over the two oxygen atoms. The main problem is the sensitivity to the estimated distance r (present as r^4) and also to ε_{ef} (present as ε_{ef}^2). With $\varepsilon_{ef}=2$, we obtained $\Delta E=-6.1\ kJ\,mol^{-1}$,[26] in surprising agreement with the SE of **2** derived from experiments,[11] $-5.1\ kJ\,mol^{-1}$, or with the mean value from Figure 2, $-6\ kJ\,mol^{-1}$. With $\varepsilon_{ef}=1$, a value of $\Delta E=-9.6\ kJ\,mol^{-1}$ was calculated,[23] but the value of α was not given (our result for $\varepsilon_{ef}=1$ would be $\Delta E=-24.5\ kJ\,mol^{-1}$). These figures should be evaluated in the light of the limited success with the calculation of substituent effects by pole/permanent dipole interaction;[27] if one reduces the quantum chemical reality to simple electrostatics, this is a great simplification, and the representation of complex charge distribution by separate atomic charges introduces great arbitrariness. We cannot say more than that Equation (3) can be used as a model for the qualitative reproduction of results.

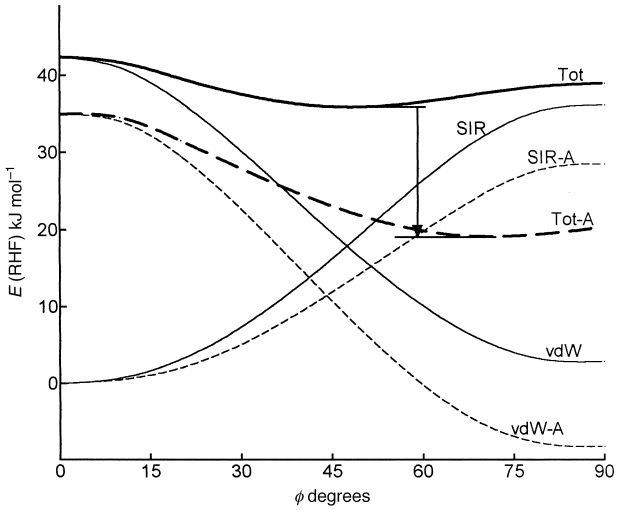

Figure 3. Calculated steric effects (RHF level) in 2,6-dimethylbenzoic acid **5** with a varying torsional angle ϕ: SIR = steric hindrance to resonance in the acid **5** (SIR-A = in its anion), vdW = van der Waals tension in **5**, (vdW-A = van der Waals tension and pole-induced dipole interaction in the anion), and Tot = total steric effect in **5** (Tot-A = in its anion); the arrow shows the steric effect on the acidity as a difference between the minima of the curves Tot and Tot-A.

Inhibited resonance in nonplanar molecules: In the case of the nonplanar molecule of **5** with two *ortho* substituents, the substituents' steric effect on acidity should consist of the same effects as in the preceding paragraph and, in addition, of SIR. We tried to separate these components as shown in Scheme 2. The reference for the two *ortho* methyl groups is two molecules of **4**. The first isodesmic reaction in Scheme 2 involves only real molecules, and its ΔE(RHF) can be considered as a sum of the two named effects. The gist of the matter is in the artificial second reaction, in which all molecules are twisted by the same angle $\phi=47^\circ$, as in the stable conformation of **5**; any SIR is not possible. If we subtract ΔE(RHF) values of the two reactions, we obtain an estimate of SIR in **5** (Table 2, line 2); SIR and vdW contribute equally to the increased energy of the molecule. Qualitatively, this result was expected since the strain energy must be relaxed to all degrees of freedom. In Figure 3, the components of the steric strain in **5** are shown against a varying torsion angle ϕ. SIR increases along a function not much different from the anticipated $\cos^2\phi$[4] (line SIR), vdW decreases along a similar function (line vdW), and the total energy (line Tot) is a delicate balance of the two, with a shallow minimum. Note that SIR at $\phi=90^\circ$ is quite different from the rotational barrier of **5**; the latter is a sum of SIR and vdW and is represented in Figure 3 by the difference between the two end points of the line Tot.

When the above procedure was repeated for the anion of **5**, the lowest energy was obtained at $\phi=65^\circ$. The greater value of ϕ in the anion than in the acid molecule may seem surprising. With respect to the equal vdW effects of COOH and COO^-, this must be explained by the weaker conjugation of COO^- with the benzene ring. Note also that the minima on the curves Tot and Tot-A in Figure 3 are shallow, and the values of ϕ are not definite. The value of SIR for the anion is slightly greater than in the acid molecule, while the share of the non-SIR component is almost zero (Table 2, line 5). The latter represents the sum of negative vdW energy and positive PIDI. In the graphical representation (Figure 3, broken lines for the anion), the PIDI contribution is shown by the difference between the lines vdW and vdW-A. When we subtracted the steric energies of the anion and the acid, we obtained values for the substituent steric effects on the acidity (Table 2, line 8). Remarkably, it is not controlled by SIR; the calculated contribution of SIR would be small and in the opposite direction (acid weakening). The main acid-strengthening effect can again be attributed to PIDI, as in the case of the planar acid **2**. An approximate estimation[26] obtained from Equation 3 for $\phi=65^\circ$ yielded -7.6 or $-30.2\ kJ\,mol^{-1}$ for $\varepsilon_{ef}=1$ or 2, respectively, instead of -21 in Table 2. Figure 3 shows the steric effect on acidity as a difference between the lowest points on the curves for the acid molecule and for the anion, respectively. Both curves are relatively flat as a result of the interplay of SIR, vdW, and PIDI; a further problem is in the unequal angle ϕ in the acid and the anion. The acidity appears as a rather complex quantity, and simple interpretation is not possible.

The above procedure was applied to the acid **6**, and the steric effects are strengthened by the "buttressing effect"[28] of the methyl groups in positions 3 and 5. The results (Scheme 3 and Table 2, lines 3, 6, and 9) are qualitatively similar to those for the acid **5**. The main difference is in the greater twisting angle, ϕ, both in the acid molecule and in the anion (Table 1). For this reason, SIR is also greater. The effects on the acidity are again less easy to understand; they appear as differences between relatively large quantities (Table 2, line 9). In contrast to **5**, SIR is now negative (the acid is strengthened as expected), but most remarkable is the share of PIDI, which is smaller than in the less methylated acid **5**. Calculation according to Equation (3) for $\phi=79^\circ$ yielded -7.9 or $-31.2\ kJ\,mol^{-1}$ for $\varepsilon_{ef}=1$ or 2, respectively, instead of -12 in Table 2. Even in this case, a merely qualitative agreement

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was obtained,[26] but the difference between compounds **5** and **6** cannot be reproduced. In Figure 4, the main difference, in comparison with Figure 3, is the larger angle ϕ at the minimum-energy conformations; this is almost equal in the acid and in the anion. Both lines, Tot and Tot-A, have very shallow minima. Therefore, the angle ϕ is not well determined and could be taken as almost 90° (see also the B3LYP energies in Table 1); then resonance can be considered as virtually inhibited.

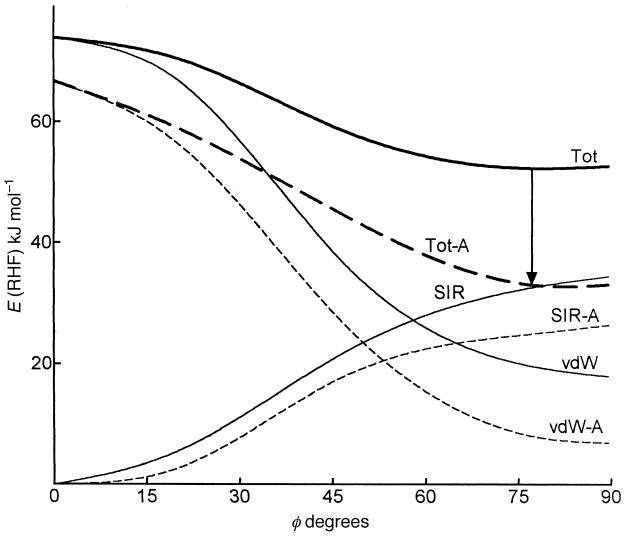

Figure 4. Calculated steric effects in 2,3,5,6-tetramethylbenzoic acid **6** with varying torsional angle ϕ: the same abbreviations are used as in Figure 3.

Inhibited resonance observed in the geometry: Our calculations also offered us the opportunity to search for some proofs of SIR in the geometrical parameters. Our values can be compared with greater reliability than those from the X-ray studies,[30] as these are loaded with considerable errors. In Table 3, the acids are arranged according to increasing SIR. As a reference without SIR, we chose 4-methylbenzoic acid **4**. Most significant is the lengthening of the C1–C(O) bond with decreasing resonance, but a smaller increase in bond length, due to the vdW effect, is observed even in **2**, in which there is no SIR. There is little shortening of the C=O bond with increasing SIR, but it is just observable. Any significant changes in the C–O bond or in the O=C–O angle were not found. In the geometry of the anions, no signs of conjugation or its hindrance can be detected. For a primary steric strain (vdW), the best proof is the increase in the C1–C2 bond length in the aromatic ring, when compared with the C1–C6 bond. It is greatest in **2** and in 2,3-dimethylbenzoic acid;[30] in **5** and **6**, the torsion released the strain, and the bond C1–C2 is less stretched. Besides the large strain, a finer effect[31] is observed in the planar, unstrained acid **4**: different bond lengths for C1–C2 and C1–C6 are observed due to the influence of the extraannular double bond C=O. In summary, geometric parameters are relatively sensitive to conjugation and to its hindrance, and often they were found to be more sensitive than the energies.[32]

Acidities in solution: The above calculations yielded SIR, vdW, and PIDI in terms of the Hartree–Fock energy of isolated molecules. The results can be extended in a qualitative discussion to a relative share of these effects under various experimental conditions; a quantitative estimation is possible only with several approximations. In the literature,[1–6] SIR was applied to solution data and mainly to equilibrium constants; the use of this interpretation may be disputed, or at least with respect to its quantitative aspect. For the compounds **2–6**, dissociation constants in methanol and in dimethyl sulfoxide are available,[17b] but the latter are affected by dimerization. For the former, we attempted a bisection into SIR and PIDI (Table 2, right-hand part). In solution, resonance is usually moderately attenuated.[33] We assumed its reduction to approximately two thirds; it follows that PIDI is reduced more, as anticipated. The difference between PIDI in **5** and **6** is difficult to understand as it was in the case of the gas-phase values. What is sure is that SIR does not play any greater role; this conclusion does not depend on the above assumptions. With regard to the former intuitive interpretation of the acidity in water,[2b, 6a, d] it was correct only in that SIR exists in the isolated acid molecules. However, it does not manifest itself in the solution acidities.

Conclusion

Steric effects were represented here by a model based on quantum chemical calculation of energies. This model is internally consistent and in reasonable agreement with observable quantities. All observations were made on methyl-substituted benzoic acids. Even on this narrow class of compounds, various effects were observed; these differed sometimes very distinctly. We would like to avoid the unwarranted extension of these arguments, but the following statements are valid more generally.

1) SIR is a useful concept that can account for the relative reactivity of many compounds and is supported by further observable quantities (torsional angles, bond lengths, dipole moments). However, it has been applied to many cases, in which it does not exist. In any individual case, two preconditions must be fulfilled: one based on geometry, and the other based on energy. The compound under consideration (sterically hindered) must be actually nonplanar, while the reference compound (nonhindered) is planar. Even when this is true, the steric hindrance to resonance can be responsible only for a smaller part of the observed effect, and an estimate of the resonance energy is necessary in relation to its assumed hindrance.
2) With regard to the carboxylic acids, the traditional explanation of their strength by steric hindrance is not justified, since the effective steric volumes of the carboxyl group and carboxylate groups are practically equal. An ad hoc model, which reproduces qualitatively the experimental facts, is PIDI; this stabilizes the carboxylate anion. It is strong in the gas phase, attenuated in solution.
3) If one considers merely the terminology, it should be noted that some terms used here such as vdW or PIDI do not represent something that exists in the real world. They are simplified mathematical models of the quantum chemical reality, and their reason is for the more or less accurate

reproduction of observable numerical properties. However, the term SIR supposes a definite conformation of the molecule, and this is at least in this part provable in the real world. From this point of view, also the general term steric effect does not seem appropriate: more suitable is the term proximity effect.

Computational methods: The RHF calculations were done with the Gaussian94 program.[34] When the structures of minimum-energy conformations were calculated, full geometry optimization was carried out with redundant internal coordinates. Vibrational analysis was carried out in all cases: all structures belonged to an energy minimum. In the case of conformations with frozen rotation (a fixed torsional angle ϕ), all remaining geometry parameters were optimized with internal coordinates. The B3LYP calculations were done according to the original proposal.[35]

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