

# Concepts of Sterically Hindered Resonance and Buttrressing Effect: Gas-Phase Acidities of Methyl-Substituted Benzoic Acids and Basicities of Their Methyl Esters

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**Abstract:** Two classical terms "Steric Hindrance to Resonance" and "Buttrressing Effect" are revisited on the basis of the gas-phase acidities of nine methyl-substituted benzoic acids and of the gas-phase basicities of their methyl esters, measured using FT-ICR spectrometry. By combining these data with published heats of formation of the neutrals and by using the principle of isodesmic reactions, relative enthalpies of formation were evaluated separately for the acid molecules, their anions (deprotonated), and their protonated cations (substituted by the protonated forms of the corresponding methyl esters). Energies of all species were also calculated at the semiempirical level (AM1). Substituent effects on the gas-phase acidity are similar to those on the acidity in water. All the methyl groups have a stabilizing polar effect, and *o*-methyl groups have a destabilizing steric effect, both effects increasing from the deprotonated forms to the acid molecules and then to the protonated forms. Separation of the two effects was attempted, assuming equal polar effects in the ortho and para positions. The results are internally consistent: their detailed analysis is in favor of a primary steric effect rather than a steric inhibition of resonance. The latter must be relatively weaker and operating only in 2,6-dimethyl derivatives, which are certainly nonplanar. In the literature this concept has been used too broadly, even for compounds for which the nonplanar conformation has not been proven. The concept of buttrressing effect has been confirmed for methyl-substituted benzoic acids, but it is formulated more generally and more exactly. According to the new definition, it can be observed even for nonadjacent substituents.

## Introduction

Steric inhibition of resonance is a well-documented concept that is explained in classical textbooks.<sup>1</sup> Very often, the experimental quantities discussed are the dissociation constants.<sup>2</sup> When applied to aromatic ortho derivatives, this effect has to be separated from several others: inductive, direct steric polarizability, hydrogen bonding, and steric hindrance to solvation. For this reason, an interpretation of the ortho effect has long been difficult.<sup>3-5</sup> In methyl-substituted benzoic acids the steric effect is relatively weak; nevertheless, these compounds were often chosen as a demonstration example.<sup>1a,2-5</sup> The stronger acidity of 2-methylbenzoic acid—compared to benzoic acid—was originally explained<sup>6</sup> by its nonplanar conformation and the resulting weakened resonance of the carboxyl group with the benzene ring. This effect, operating in the neutral molecule, was preferred<sup>6</sup> to another explanation, a stabilizing interaction (weak hydrogen bond) operating in the anion. This interpretation seems to be generally accepted:<sup>1a,d,2-4</sup> the twisting angle,  $\phi$ , was estimated as

11°, 38°, or 29°, respectively,<sup>4,7</sup> and the difference in acidity from that of 4-methylbenzoic acid was even suggested as an estimate of the steric effect of the methyl group ( $\sigma_s$ ).<sup>8</sup> However, in a more recent analysis<sup>5</sup> the primary steric effect on the solvated carboxyl group was ultimately suggested as the most probable explanation. This reasoning was supported by the reversed order of acidities in 35–90% aqueous dimethyl sulfoxide.<sup>9</sup> The explanation by the steric inhibition of resonance was recently challenged also for the reason that 5-nitro-2-methylbenzoic and 2,3-dimethylbenzoic acids are planar in the crystalline state.<sup>10</sup> The conformation of 2-methylbenzoic esters was also discussed, giving preference to an equilibrium of two planar forms,<sup>11</sup> although previous literature claimed twisted conformations with angles of 21° and 40°, respectively.<sup>12,13</sup> These doubts in the interpretation do not apply to 2,6-dimethylbenzoic acid, which is still stronger than 2-methylbenzoic acid<sup>6</sup> and evidently nonplanar: the twisting angle is 53° in the crystal;<sup>13</sup> for the solution, it was estimated<sup>7</sup> as 70° or 55°, and the energy of the interrupted conjugation<sup>3</sup> is estimated as 4 kJ mol<sup>-1</sup>. Remarkably, even 2,3-dimethylbenzoic acid is stronger than 2-methylbenzoic, and moreover it is stronger than 2,5-dimethylbenzoic.<sup>6</sup> The original explanation was in terms

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of valence deflection,<sup>6</sup> but in a more modern approach, one should consider rather a restricted movement of one methyl group in the presence of another one. The phenomenon received the name of buttressing effect.<sup>14</sup> The difference in acidity between a couple of 3-X-2-methylbenzoic and 5-X-2-methylbenzoic acids was also suggested<sup>15</sup> as a measure of purely steric effect of the substituent X.

The two concepts (steric inhibition of resonance and buttressing effect) can be revisited by measuring the gas-phase acidities of various methyl-substituted benzoic acids by Fourier transform ion cyclotron resonance (FT-ICR). The solvent effect can be revealed immediately. Moreover, we can separate the substituent effects, hitherto discussed almost exclusively in terms of ionization equilibria, into the effects operating in the neutral acid molecule and those operating in the anion, both stabilizing and destabilizing. To this end we used the principle of isodesmic reactions and recently determined<sup>16</sup> thermodynamic quantities. The acidities of the three monomethylbenzoic acids in the gas phase were reported but were measured by another experimental technique.<sup>17</sup> Although the sequence of acidities was the same as in water, the differences were attributed to the polarizability effect in the anions: <sup>17</sup> compared to field/inductive and polarizability effects, the resonance effect is generally believed to be of less importance in the gas phase.<sup>17,18</sup>

Additional information could be obtained from gas-phase basicities of the same methylbenzoic acids. Because of technical difficulties (fragmentation of the protonated molecules into the ArCO<sup>+</sup> cations) we determined instead the basicities of the corresponding methyl esters in which this fragmentation is weaker. We assumed that the relative basicities of the acids and the corresponding esters would be parallel. Concerning the basicities in solution, there is one study of the basicities of methylbenzoic acids.<sup>19</sup> Weakening of the basicity by *o*-alkyl groups was explained by a steric hindrance to resonance and by steric hindrance to solvation in the protonated species. However, 2-methylbenzoic acid itself is a base just a little stronger than benzoic acid.<sup>19</sup>

An additional tool used in this work was simple quantum chemical calculations at the AM1 level<sup>20</sup> carried out on the neutral acid molecules and their deprotonated forms as well as the corresponding methyl esters and their protonated forms. The AM1 method was recently found satisfactory for a series of meta- and para-substituted benzoic acids with different polar substituents.<sup>21</sup> In this paper we report only the calculations immediately related to the compounds investigated experimentally: the main purpose was to predict the missing thermodynamical data and to correct them for the presence of conformers. Additional theoretical results in a broader context and on a higher computational level will be published elsewhere.<sup>22</sup>

## Experimental Section

The acids **1**, **2**, and **5–9** (Table I) are commercial products; 2,3,5,6-tetramethylbenzoic acid (**10**) was prepared from 1,2,4,5-tetramethyl-

Table I. Gas-Phase Acidities (in kJ·mol<sup>-1</sup>) of Methyl-Substituted Benzoic Acids (AH)

AH no.	AH substituent	$\Delta\Delta_{\text{acid}}G^\circ$ (338 K) <sup>a</sup>	$\delta\Delta_{\text{acid}}G^\circ$ (338 K) <sup>b</sup>	$\Delta_{\text{acid}}G^\circ$ (AH) <sup>c</sup>
1	H	+2.3 ± 0.1	0	1393.3
2	2-Me	-0.2 ± 0.1	-2.5	1390.8
3	3-Me		+2.9 <sup>d</sup>	1396.2
4	4-Me		+4.6 <sup>d</sup>	1397.9
5	2,3-Me <sub>2</sub>	-1.7 ± 0.3	-4.0	1389.3
6	2,4-Me <sub>2</sub>	+1.7 ± 0.2	-0.6	1392.7
7	2,5-Me <sub>2</sub>	+0.2 ± 0.2	-2.1	1391.2
8	2,6-Me <sub>2</sub>	-4.2 ± 0.8	-6.5	1386.8
9	2,4,6-Me <sub>3</sub>	-1.7 ± 0.8	-4.0	1389.3
10	2,3,4,5,6-Me <sub>4</sub>	-3.6 ± 0.1	-5.9	1387.4

<sup>a</sup> Gibbs energies for the reactions AH + 3-CF<sub>3</sub>C<sub>6</sub>H<sub>4</sub>O<sup>-</sup> = 3-CF<sub>3</sub>C<sub>6</sub>H<sub>4</sub>OH + A<sup>-</sup>; quoted uncertainties correspond to the standard deviation for 3–4 measurements. <sup>b</sup> Gas-phase acidities relative to the unsubstituted compound. <sup>c</sup> Absolute Gibbs energies of acidity (AH → A<sup>-</sup> + H<sup>+</sup>) (at 298 K) anchored to  $\Delta_{\text{acid}}G^\circ(3\text{-CF}_3\text{C}_6\text{H}_4\text{OH}) = 1391 \pm 8$  kJ·mol<sup>-1</sup>.<sup>27</sup> The value obtained for **1** corresponds exactly to the value reported by J. Bartmess (333.0 kcal·mol<sup>-1</sup>) in the unpublished "1987 gas-phase acidity scale" prefiguring the GIANT table.<sup>27</sup> <sup>d</sup> Methyl substituent effects reported in ref 17.

benzene and oxalyl chloride.<sup>23</sup> The methyl esters **2e** and **5e–10e** (Table II) were prepared from pure samples of the acids and diazomethane and were not further purified except by simple distillation.

Proton transfer equilibria were monitored by Fourier transform ion cyclotron resonance (FT-ICR) as described previously for gas-phase acidity<sup>24</sup> and basicity<sup>25</sup> measurements. Ion gauge readings were corrected according to Bartmess and Georgiadis.<sup>26</sup> Gibbs energies of proton transfer between a reference acid (reference base) and the acid (base) under study were determined at 338 K.

Owing to the restricted acidity range, all the acidities of **1–10** could be determined by using the same reference compound, 3-(trifluoromethyl)-phenol, and the corresponding  $\Delta\Delta_{\text{acid}}G^\circ(338\text{K})$  are gathered in Table I. The Gibbs energies of acidity of the substituted benzoic acids **2–10**, relative to benzoic acid (**1**),  $\delta\Delta_{\text{acid}}G^\circ(338\text{K})$ , are also collected in Table I. They were converted to  $\delta\Delta_{\text{acid}}H^\circ(338\text{K})$  by using estimates of  $\delta\Delta_{\text{acid}}S^\circ$ . The entropy took into account only changes in external symmetry and the entropy of mixing (see the Results and Discussion section for details). In the next step we assumed that  $\delta\Delta_{\text{acid}}H^\circ(338\text{K})$  equals  $\delta\Delta_{\text{acid}}H^\circ(298\text{K})$  and we calculated the absolute enthalpies of acidity,  $\Delta_{\text{acid}}H^\circ$  based on  $\Delta_{\text{acid}}H^\circ(\text{PhCOOH}) = 1423$  kJ·mol<sup>-1</sup>.<sup>27</sup> Using the same set of  $\delta\Delta_{\text{acid}}S^\circ$  values we found that  $\delta\Delta_{\text{acid}}G^\circ(298\text{K})$  equals  $\delta\Delta_{\text{acid}}G^\circ(338\text{K})$  with a sufficient approximation. Hence we calculated the absolute values of  $\Delta_{\text{acid}}G^\circ$  (Table I) by adding  $\delta\Delta_{\text{acid}}G^\circ(338\text{K})$  to  $\Delta_{\text{acid}}G^\circ(\text{PhCOOH}) = 1393.3$  kJ·mol<sup>-1</sup> (see footnote c to Table I). The relative enthalpies  $\delta\Delta_{\text{acid}}H^\circ(298\text{K})$  are given in Table III.

Basicities of the corresponding methyl esters (**1E–10E**) span a wider range. Therefore several reference compounds were needed. During the construction of the ladder we noticed some discrepancies in the compiled scale.<sup>27</sup> Hence the relative basicities of some reference compounds were redetermined and found in good agreement with recent data.<sup>28</sup> The relative Gibbs energies of basicity,  $\Delta GB(338\text{K})$ , related to several reference compounds, are reported in Table II. They were converted successively into  $\delta GB(338\text{K})$  and  $\delta PA(338\text{K})$ , relative to benzoic acid (**1**) and to absolute proton affinities and gas-phase basicities at 298K, *PA*, and *GB*, respectively, in principle by the same sequence of steps as in the case of acidity. In fact, however, the calculations are much simpler since the external symmetry numbers are equal for the molecules of ester and their protonated form, and no entropy of mixing was considered (see the Results and Discussion section), hence  $\delta GB$  equals  $\delta PA$  in all cases. As anchor point for the whole ladder we used only the data for acetophenone, *PA* = 878.6 kJ·mol<sup>-1</sup> according to a recent reevaluation of the upper proton-

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Table II. Gas-Phase Basicities (in kJ·mol<sup>-1</sup>) of Methyl-Substituted Methyl Benzoates

B formula or no.	B substituent	Ref formula or no.	$\Delta GB(338\text{ K})^a$	$GB(B)^b$
( <i>i</i> -Pr) <sub>2</sub> O		C <sub>6</sub> H <sub>5</sub> COCH <sub>3</sub>	-0.5 ± 0.1	845.7
( <i>i</i> -Pr) <sub>2</sub> CO		C <sub>6</sub> H <sub>5</sub> COCH <sub>3</sub>	-7.7 ± 0.1	
		( <i>i</i> -Pr) <sub>2</sub> O	-6.8 ± 0.1	838.7
( <i>n</i> -Pr) <sub>2</sub> S		( <i>i</i> -Pr) <sub>2</sub> O	+7.8 ± 0.1	853.5
1E	H	C <sub>6</sub> H <sub>5</sub> COCH <sub>3</sub>	-9.0 ± 0.2	
		( <i>i</i> -Pr) <sub>2</sub> O	-9.5 ± 0.1	
		( <i>i</i> -Pr) <sub>2</sub> CO	-1.9 ± 0.1	836.7
2E	2-Me	C <sub>6</sub> H <sub>5</sub> COCH <sub>3</sub>	-2.6 ± 0.2	
		( <i>i</i> -Pr) <sub>2</sub> O	-1.3 ± 0.1	
		( <i>i</i> -Pr) <sub>2</sub> CO	+5.8 ± 0.2	
		1E	+9.4 ± 0.4	844.7
		2E	+7.0 ± 0.2	851.7
CH <sub>3</sub> COCH <sub>2</sub> COCH <sub>3</sub>				842.5 <sup>c</sup>
3E	3-Me			846.3 <sup>c</sup>
4E	4-Me			
5E	2,3-Me <sub>2</sub>	( <i>n</i> -Pr) <sub>2</sub> S	-3.6 ± 0.1	
		CH <sub>3</sub> COCH <sub>2</sub> COCH <sub>3</sub>	-2.3 ± 0.3	
		C <sub>6</sub> H <sub>5</sub> COCH <sub>3</sub>	+3.2 ± 0.7	
		( <i>i</i> -Pr) <sub>2</sub> O	+3.5 ± 0.1	
		2E	+6.3 ± 0.2	849.8
6E	2,4-Me <sub>2</sub>	( <i>n</i> -Pr) <sub>2</sub> S	+1.5 ± 0.2	
		( <i>i</i> -Pr) <sub>2</sub> O	+9.3 ± 0.1	855.0
7E	2,5-Me <sub>2</sub>	( <i>n</i> -Pr) <sub>2</sub> S	-1.9 ± 0.1	
		C <sub>6</sub> H <sub>5</sub> COCH <sub>3</sub>	+5.6 ± 0.1	
		( <i>i</i> -Pr) <sub>2</sub> O	+5.7 ± 0.1	851.6
8E	2,6-Me <sub>2</sub>	C <sub>6</sub> H <sub>5</sub> COCH <sub>3</sub>	-0.8 ± 0.2	
		( <i>i</i> -Pr) <sub>2</sub> O	-1.7 ± 0.1	
		2E	-1.0 ± 0.1	
		( <i>i</i> -Pr) <sub>2</sub> CO	+4.8 ± 0.1	844.2
9E	2,4,6-Me <sub>3</sub>	( <i>n</i> -Pr) <sub>2</sub> S	-0.2 ± 0.3	
		( <i>i</i> -Pr) <sub>2</sub> O	+7.1 ± 0.2	853.1
10E	2,3,4,5,6-Me <sub>4</sub>	C <sub>6</sub> H <sub>5</sub> COCH <sub>3</sub>	+5.3 ± 0.2	
		( <i>i</i> -Pr) <sub>2</sub> O	+5.5 ± 0.1	851.4

<sup>a</sup> Gibbs energies for the reaction  $BH^+ + \text{Ref} = \text{Ref}H^+ + B$ ; quoted uncertainties correspond to the standard deviation for 3–4 measurements.

<sup>b</sup> Absolute Gibbs energies of basicity ( $BH^+ \rightarrow B + H^+$ ) anchored to  $GB(C_6H_5COCH_3) = 878.6 \text{ kJ}\cdot\text{mol}^{-1}$  (assuming  $S^\circ(BH^+) = S^\circ(B)$ , no temperature correction). <sup>c</sup> From the methyl substituent effects reported in: Mishima, M.; Fujio, M.; Tsuno, Y. *Tetrahedron Lett.* 1986, 27, 951–954.

Table III. Enthalpies for Methyl-Substituted Benzoic Acids and Their Deprotonated and Protonated Forms (kJ·mol<sup>-1</sup>, Ideal Gas State, 298 K)

AH(methyl position)	$\delta\Delta_{\text{acid}}H^\circ$ <sup>a</sup>	$-\delta PA$ <sup>b</sup>	neutral acid molecule		$\Delta_6H^\circ$ <sup>e</sup>	deprotonated form $\Delta_7H^\circ$ <sup>e,f</sup>	protonated form $\Delta_8H^\circ$ <sup>e,g</sup>
			exp <sup>c</sup>	calc <sup>d</sup>			
1 (-)	0	0	-290.2 <sup>h</sup>	-284.34	0	0	0
2 (2-Me)	-2.2	-8.0	-320.1	-310.11	2.9	0.7	-5.1
				(-310.83)		(8.9)	(1.5)
3 (3-Me)	2.9	-5.8	-329.5	-316.21	-6.5	-3.6	-12.3
				(-316.23)		(1.8)	(-2.5)
4 (4-Me)	4.6	-9.6	-332.1	-317.23	-9.1	-4.5	-18.7
						(1.6)	(-8.6)
5 (2,3-Me <sub>2</sub> )	-3.5	-13.1	-345.8	-335.70	10.0	6.5	-3.1
				(-336.39)		(5.2)	(5.9)
				(-332.88)			
6 (2,4-Me <sub>2</sub> )	-0.3	-18.3	-355.0	-342.99	0.8	0.5	-17.5
				(-343.67)		(10.7)	(-6.8)
				(-341.00)			
7 (2,5-Me <sub>2</sub> )	-1.8	-14.9	-351.1	-341.99	4.7	2.9	-10.2
				(-342.67)		(10.6)	(-0.9)
				(-339.95)			
8 (2,6-Me <sub>2</sub> )	-6.5	-7.5	-341.6	-331.87	14.2	7.7	6.7
				(33°)		(14.6)	(8.7)
9 (2,4,6-Me <sub>3</sub> )	-4.0	-16.4	-374.4	-364.34	14.2	10.2	-2.2
				(32°)		(16.6)	(0.9)
10 (2,3,5,6-Me <sub>4</sub> )	-5.9	-14.7	-397 <sup>i</sup>	-387.06	24.4	18.5	9.7
				(73°)		(25.8)	(19.7)

<sup>a</sup> Relative gas-phase acidities; negative values mean a stronger acid, isodesmic reaction 1. <sup>b</sup> Enthalpies of isodesmic reaction 2 (negative relative  $PA$ s); negative values mean a stronger base. <sup>c</sup> Reference 16. <sup>d</sup> Calculated by AM1 (this work). If two conformers are predicted, the effective value according to eq 4 is given together with the individual values for the rotamers (in parentheses); if a nonplanar conformation is predicted, the torsion angle is given in parentheses. <sup>e</sup> Enthalpies of isodesmic reactions, eq 6, 7, or 8, respectively. These values serve for the estimation of the interaction energy between all substituents on the benzene ring. <sup>f</sup> In parentheses: calculated by AM1 (this work). <sup>g</sup> These values correspond to the basicities of the pertinent methyl esters; the substituent effects are assumed to be valid also for the protonated forms of the carboxylic acids. <sup>h</sup> Reference 35. <sup>i</sup> Estimated from the calculated value, see Discussion.

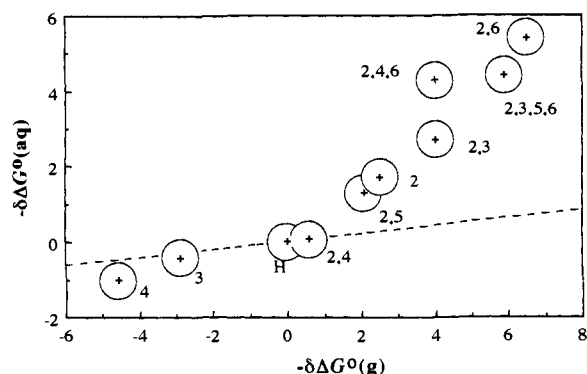
affinity range.<sup>29</sup> An upward revision of about 18 kJ·mol<sup>-1</sup> for  $PA$  of  $NH_3$  was proposed<sup>29</sup> and confirmed (see however Note Added in Proof, ref 41).<sup>30</sup>  $GB$  values are listed in Table II, and proton affinities relative to

methyl benzoate,  $\delta PA$ s, are given in Table III (in fact,  $-\delta PA$ s).

The AM1 calculations were performed using the standard program provided in the AMPAC package,<sup>31</sup> with complete geometry optimization

(29) Meot-Ner (Mautner), M.; Sieck, C. V. *J. Am. Chem. Soc.* 1991, 113, 4448–4460.

(30) Szulejko, J. E.; McMahon, T. B. *Int. J. Mass Spectrom. Ion Processes* 1991, 109, 279–294.



**Figure 1.** Plot of the acidities (in terms of Gibbs energy,  $\text{kJ}\cdot\text{mol}^{-1}$ ) of methyl-substituted benzoic acids (water vs gas phase): the broken line corresponds to meta- and para-substituted benzoic acids with polar substituents (ref 17). Points size, as an indication of accuracy, corresponds to  $\pm 0.5$  kJ, although the acidities in water (ref 6) are more accurate.

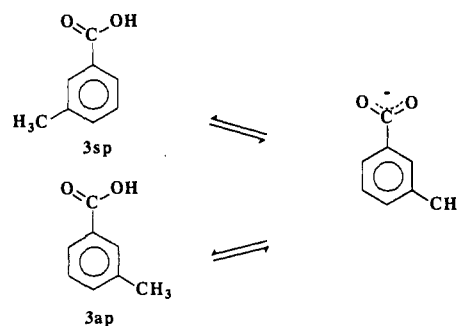
employing the keyword PRECISE which lowers the calculation tolerance by a factor of 100. Particular attention was given to the conformation about the  $\text{C}_{\text{ar}}-\text{C}(\text{O})$  bond. When two energy minima were found for two values of the torsion angle  $\phi$  (in the case of the acids 2, 3, 5, 6, and 7, their esters, and the protonated esters), full geometry optimization was carried out for each conformer, and both values of the energy are given.

## Results and Discussion

**Acidities in the Gas Phase and in Solution.** In Table I are listed the gas-phase acidities (in terms of Gibbs energy) of methyl-substituted benzoic acids 1–10; in Table II are listed the gas-phase basicities of the corresponding methyl esters 1E–10E. It is evident that the differences between individual compounds sufficiently exceed the experimental error. All the ortho-substituted acids are stronger than benzoic acid, and all methyl-substituted esters are stronger bases than methyl benzoate. On first inspection one can say that the acidities are essentially as expected from the values in solution, while the basicities show a different pattern and stronger substituent effects. Let us deal first with the acidities that can be immediately compared to the known acidities in water. For this purpose we preferred a comparison in terms of Gibbs energies since they are, for water solutions, much more accurate than enthalpies.<sup>6,7a</sup>

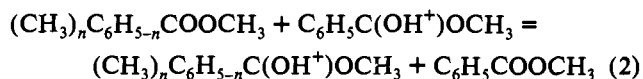
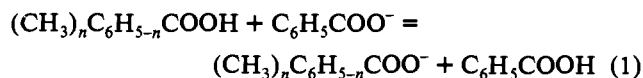
The plot in Figure 1 reveals an evident trend, or say a curvilinear dependence, with one point somewhat deviating: in water the substituent effects are reduced by a factor of 0.6–0.8 (the solvent attenuation factor, SAF) according to their magnitude. A much stronger attenuation was observed on meta- and para-substituted benzoic acids with polar substituents,<sup>17</sup>  $\text{SAF} = 0.1$  (broken line in Figure 1). These facts may be simply rationalized: those ions, in which the charge is more delocalized by substitution, are less effectively solvated; and there is a competition between substituent and solvent effects in stabilizing the anion. When steric effects are operating, solvation is less effective and charge delocalization less important: attenuation is weaker but still observable. The main conclusion from Figure 1 is that the solvent effects both in the anion (steric hindrance to solvation)<sup>1b,c,5</sup> and in the acid molecule (primary steric effect on the hydrated carboxyl groups)<sup>5</sup> are present and proportional in the whole series: they are responsible for the SAF but cannot explain the difference between individual compounds of our set. The reasoning<sup>5</sup> referring to the solvent dependence was based only on the acidities in water and in aqueous dimethyl sulfoxide.<sup>9</sup> We have collected all data available for 26 varying solvent systems.<sup>32</sup> They are of variable precision and the differences are sometimes

## Scheme I



too small, but a generalization is possible: in water, pure alcohols, and more dilute aqueous acetone or ethanol, the same pattern is preserved as in the gas phase—2-methylbenzoic acid and 4-methylbenzoic acid are respectively stronger and weaker than benzoic acid. In more concentrated aqueous ethanol, and particularly in aqueous dioxane or aqueous dimethyl sulfoxide, 2-methylbenzoic acid becomes weaker than benzoic acid, ultimately approaching the strength of the 4-isomer. According to these results, the water solution is a better model for the behavior of isolated molecules than are the mixed solvents.

**Calculation of Relative Enthalpies of Reaction.** For the following analysis the acidities and basicities will be better expressed as enthalpies, in order to be immediately related to the heats of formation of the acids. The relative values  $\delta\Delta_{\text{acid}}H^\circ$  and  $-\delta PA$  listed in Table III correspond to the enthalpies of the isodesmic reactions, eq 1 or 2, respectively.



These values were derived from the experimental Gibbs energies in a relatively complex way, with several approximations, as follows. Considering only the symmetry contribution to entropy is a common approximation for gas-phase reactions.<sup>27</sup> Here we shall introduce also the entropy of mixing arising when one compound is present as a mixture of conformers. This term has been commonly neglected. Among our compounds we expected two planar conformers for the neutral molecules 2, 3, 5, 6, and 7 (see as an example the formulas 3ap and 3sp in Scheme I), while in their anions the conformers are degenerate. For compounds 8–10 single nonplanar conformers were anticipated. Our anticipation was based on observations<sup>10,11</sup> both in the solid state and solution, and it was confirmed by the present AM1 calculations (Table III). These calculations allowed us to evaluate the populations,  $x_1$  and  $x_2 = 1 - x_1$ , of the two conformers 1 and 2 of a species AH, according to eq 3, using their calculated enthalpies of formation,  $\Delta_f H^\circ(1)$  and  $\Delta_f H^\circ(2)$ , instead of the required Gibbs energies as a satisfactory approximation. Then the effective enthalpy of formation of AH is defined by eq 4.

$$x_1 = 1/[1 + \exp\{[\Delta_f H^\circ(1) - \Delta_f H^\circ(2)]/RT\}] \quad (3)$$

$$\Delta_f H^\circ(\text{AH}) = x_1\Delta_f H^\circ(1) + (1 - x_1)\Delta_f H^\circ(2) \quad (4)$$

Enthalpies of dissociation of the neutral acid, AH, can be calculated from eq 5 in which the second term on the right involves the entropy for symmetry changes and the third term the entropy of mixing.

$$\Delta_{\text{acid}}H^\circ(\text{AH}) = \Delta_{\text{acid}}G^\circ(\text{AH}) + RT(x_1 \ln \sigma_1 + x_2 \ln \sigma_2 - \ln \sigma_a) + RT\{x_1 \ln x_1 + (1 - x_1) \ln (1 - x_1)\} \quad (5)$$

When eq 5 is applied to relative values  $\delta\Delta_{\text{acid}}H^\circ$  (as they correspond

(31) Dewar Research Group and Stewart, J. J. P. *QCPE Bull.* 1986, 6, 24. AMPAC (QCPE No. 523) user's manual, Appendix D.

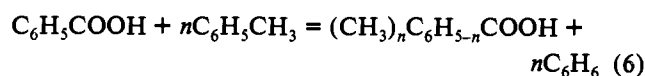
(32) *Tables of Rate and Equilibrium Constants of Heterolytic Organic Reactions*; Palm, V. A., Ed.; VINITI: Moscow, Vol. I, 1975; and Suppl. I, 1984.

e.g. to eq 1), all the species involved are to be taken into account with a proper sign. The external symmetry numbers  $\sigma$  ( $\sigma_1$ ,  $\sigma_2$ , and  $\sigma_a$  for the two conformers and for the anion, respectively) were calculated with the assumptions that the methyl groups possess rotational symmetry and that in the nonplanar stable conformations of **8**, **9**, and **10** the carboxyl group is perpendicular to the ring plane. Then  $\sigma = 2$  for the anions of **1**, **4**, **8**, **9**, and **10**; for the remaining anions, and for all neutral acids, it equals unity. The errors of these approximations should largely, if not completely, be cancelled out on the two sides of eq 1 or 2. The internal numbers of symmetry,  $n$ , were not included in the calculations, in agreement with a recommendation<sup>33</sup> to neglect them as soon as the barrier to rotation is higher than 2 kJ mol<sup>-1</sup>. This suggestion was empirically confirmed by a plot<sup>34</sup> of acidities of 3,5-disubstituted vs 3-substituted benzoic acids: in fact, this plot requires the neglecting of either the internal symmetry numbers or the entropy of mixing. This result is logical since the entropy of mixing presumes that the conformers are relatively stable during the process of ionization, while the internal symmetry numbers presume the opposite. This is seen in the case of compound **3** whose two conformers are very close in energy: then the two entropic terms of eq 5 nearly compensate, and practically the same results is obtained taking into account either the entropy of mixing or the internal symmetry numbers. The heart of the problem is the confidence we can place on our AM1 calculations, predicting planar or nonplanar forms. As a test we have compared the calculated energies for the neutral acids 1–9 to the experimental<sup>16</sup>  $\Delta_f H^\circ$  values (Table III). In the case of compounds for which the theory predicts two rotamers, the effective enthalpy was calculated according to eq 4. All calculated energies are shifted to higher values but a plot (not shown) is linear for the ortho derivatives only, with unit slope (slope  $b = 1.006$ ,  $r = 0.9985$ , s.d. = 1.08) and with 3-methylbenzoic acid and 4-methylbenzoic acid deviating slightly to one side and benzoic acid to the other. Therefore, the calculations are sufficiently reliable for neutral molecules and allow us to calculate, for compound **10**, the  $\Delta_f H^\circ$  value, not available from experiments (Table III, footnote *i*).

In the case of protonated forms we were unable to predict which compound forms a mixture of conformers and which is nonplanar, since the AM1 calculations were not reliable for charged species. In our opinion the best approximation, and probably the only possible one, was to assume simply that both the symmetry and population of the protonated forms are the same as for neutral acids (or esters). This assumption is not critical here, since the observed effects in the case of protonation are much larger than those for deprotonation and cannot be obscured by small entropy terms.

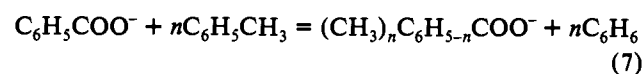
Let us point out that we have contributed to the clarification of a thermodynamic problem very often neglected in the analysis of gas-phase data. However, in the present case, the total entropy contributions are only a few tenths of a kilojoule since the two terms of eq 5 nearly compensate. All the corrections depend very slightly on the AM1 calculations; particularly, they do not depend at all on the calculated angles  $\phi$ . It follows that all the approximations involved cannot affect the results of the following sections.

**Relative Stabilities of the Acid Molecules and Ions.** To proceed a step further in the analysis of substituent effects we attempted to separate the effects in the anion and in the neutral acid molecule. The published heats of formation<sup>16</sup> are collected in Table III. These values now allow the isodesmic reactions to be constructed in which our acids 1–10 are produced from benzoic acid and from several molecules of toluene, eq 6.



The enthalpy of this reaction,  $\Delta_6 H^\circ$ , can be considered as a measure of the mutual interaction between all substituents present. The corresponding values were calculated from the experimental  $\Delta_f H^\circ$  values in Table III, and from  $\Delta_f H^\circ$  values of benzene and toluene;<sup>35</sup> they are given in Table III too. The uncertainty in  $\Delta_6 H^\circ$  originates in the limitations inherent in the isodesmic approach<sup>36,37</sup> and in the experimental error on  $\Delta_f H^\circ$  (estimated<sup>16</sup> to be less than 2 kJ, usual precision<sup>35</sup> for good quality data). It would be unwise to give much weight to values smaller than 4 kJ; nevertheless, even the smaller values of  $\Delta_6 H^\circ$  yield a very consistent picture. All ortho derivatives are destabilized proportionally to the number of ortho interactions (steric hindrance); 3-methyl- and 4-methylbenzoic acids are stabilized (opposite effects of donor and acceptor, or hyperconjugation). In 2,4-dimethylbenzoic acid the two effects compensate one another.

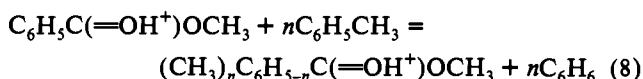
The relative stability of the anions of our acids may be represented by means of another isodesmic reaction, eq 7, an analog of eq 6:



The reaction enthalpy,  $\Delta_7 H^\circ$ , of this reaction is obtained by means of a thermodynamic cycle from  $\Delta_6 H^\circ$  and from the enthalpies of ionization,  $\delta\Delta_{\text{acid}} H^\circ$ . The values given in Table III are somewhat less reliable than  $\Delta_6 H^\circ$  since they are loaded with the approximations made in transforming  $\delta\Delta_{\text{acid}} G^\circ$  into  $\delta\Delta_{\text{acid}} H^\circ$ . The values may be understood as substituent effects in the anions and agree generally with the expectation: they parallel those for the neutral acid molecules, but they are smaller. In a plot of  $\Delta_7 H^\circ$  vs  $\Delta_6 H^\circ$  (not shown) a straight line can be drawn with a slope of 0.73, and the acids without ortho substituents deviate slightly. We can conclude that the stability of the anions is controlled by the same factors as the stability of acid molecules but their effect is smaller. A more significant relationship is obtained for the steric components of  $\Delta_6 H^\circ$  and  $\Delta_7 H^\circ$ , as described in the next section.

The values of  $\Delta_7 H^\circ$  were also compared with AM1 calculations. The calculated values were obtained according to eq 7 by introducing calculated  $\Delta_f H^\circ$  of the anions and experimental<sup>35</sup>  $\Delta_f H^\circ$  for benzene and toluene: the resulting  $\Delta_7 H^\circ$  values are given in table III in parentheses. Agreement with experiment is much worse than in the case of neutral molecules. It seems that AM1 underestimates the conjugation in the anions or overestimates the steric hindrance. We consider further discussion fruitless unless more accurate calculations are available.<sup>22</sup> Note that even a direct prediction of  $\delta\Delta_{\text{acid}} H^\circ$  by AM1 would be much less successful than in the case of meta- and para-substituted benzoic acids.<sup>21</sup>

The relative stabilities of the protonated forms of the esters were calculated in the same way as in the case of the anions. The respective isodesmic reaction reads:



The values of  $\Delta_8 H^\circ$  listed in Table III were calculated in the same way as  $\Delta_7 H^\circ$  values. In discussing them we will assume that there would be no difference between these relative values for the basicity of esters or of the acids. The interpretation is less straightforward than in the case of the anions or neutral acid molecules: all  $\Delta_8 H^\circ$  values are strongly shifted toward negative

(33) Ebersson, L. In *The Chemistry of Carboxylic Acids and Esters*; Patai, Ed.; Interscience: London, 1969; p 220.

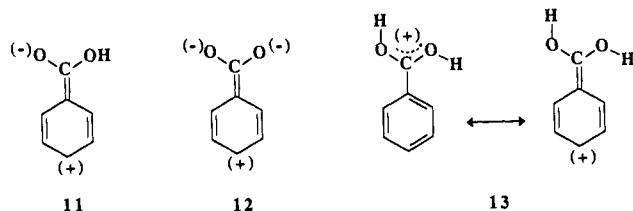
(34) Kalfus, K.; Kroupa, J.; Vecera, M.; Exner, O. *Collect. Czech. Chem. Commun.* **1975**, *40*, 3009–3019.

(35) Bures, M.; Holub, R.; Leitner, J.; Vonka, P. *Sb. Vys. Sk. Chem.-Technol. Prazé, Fys. Chem.* **1987**, *N3*, 5–376.

(36) Exner, O. *Prog. Phys. Org. Chem.* **1990**, *18*, 129–161.

(37) Exner, O. *J. Org. Chem.* **1988**, *53*, 1810–1812.

## Scheme II



values. A plot of  $\Delta_8H^\circ$  vs  $\Delta_6H^\circ$  (not shown) would be scattered. There seems to be a stabilizing effect of the methyl groups in any position, but particularly in the para and the ortho positions. It cannot be simply the polarizability, which is generally considerable in the gas-phase ionizations, but weak for relatively large molecules of benzene derivatives.<sup>18</sup> Moreover, polarizability should be approximately equal in cations and anions.<sup>38</sup> We would use the term conjugation: either hyperconjugation, or simple conjugation of the protonated carbonyl group strengthened by the inductive effect of the methyl group. Again a simpler and more significant relationship is obtained between the steric components of  $\Delta_6H^\circ$  and  $\Delta_8H^\circ$  (next section). A comparison with AM1 calculations (Table III, in parentheses) yields a similar picture, as in the case of anions: stabilizing conjugation is underestimated, and possibly also the destabilizing steric effect is overestimated.

In conclusion, all methyl substituent effects are parallel in neutral acid molecules and in their anions but weaker in the anions. In the protonated forms there is in addition a strong stabilization, mainly in the ortho and para positions.

**Inhibition of Resonance or Primary Steric Effect.** When explaining the enhanced acidity of ortho-substituted benzoic acids, we can first reject two possibilities, hitherto considered not very probable. In the first section of this Discussion (see particularly Figure 1) we showed that the solvation had no decisive effect.<sup>5,9</sup> A possible stabilizing interaction in the anion<sup>6</sup> (say a hydrogen bond) can be rejected now on the basis of  $\Delta_7H^\circ$  values of Table III: the ortho-substituted anions are generally destabilized, particularly when compared to the corresponding para isomers (2-Me compared to 4-Me and 2,6-Me<sub>2</sub> to 2,4-Me<sub>2</sub>). The following two explanations (steric hindrance to resonance and primary steric hindrance) cannot be distinguished so easily.

The concept of steric hindrance to resonance<sup>1,2,6</sup> first assumes that benzoic acid is made weaker, compared to aliphatic carboxylic acids, by the resonance form 11 (Scheme II), while it is simultaneously made stronger by the inductive effect of the phenyl group. The latter effect can be estimated, at least qualitatively, by comparing the acidities of phenylacetic and benzoic acids in water.<sup>1a,d</sup> Secondly, it is assumed that all ortho-substituted benzoic acids are nonplanar with differing torsion angles: according to the value of this angle the resonance is gradually eliminated down to zero. This effect of the *o*-methyl groups is opposed by their acid-weakening polar effect: for this reason ortho derivatives are often compared to their para isomers. The third assumption of the theory was that resonance and its hindrance take place in the acid molecule, the anion being essentially unaffected (12 having practically no weight).

When the above theory is extended to the basicity, one expects still greater resonance in the protonated form 13 and base strengthening. The steric hindrance is base weakening and is again opposed by the polar effect of the alkyl group (here much stronger).

The alternative theory of primary steric hindrance<sup>5</sup> is based on the assumption that the carboxyl group is "effectively" bulkier than the carboxylate group, but without explanations. The reason is hardly the presence of a hydrogen atom but rather the geometrical factors of the OCO skeleton: in solution also the

solvation should be considerable.<sup>5</sup> It follows that the molecules of ortho-substituted benzoic acids are more destabilized than their anions. The concurrence with polar effect is the same as in the former theory: qualitatively, the same picture is predicted.

A decision between the two concepts on the basis of our values of  $\Delta_6H^\circ$ ,  $\Delta_7H^\circ$ , and  $\Delta_8H^\circ$  (Table III) would not be straightforward, although these agree better with the concept of primary steric effect. To obtain a more direct proof we attempted to separate polar and steric effects, returning to the traditional assumption that polar effects are equal in ortho and para positions. The enthalpies of reactions 6–8 are considered as the sum of polar and steric effects.

$$\Delta_iH^\circ = P_{(i)} + S_{(i)} \quad (i = 6, 7, \text{ or } 8; \text{ eqs } 6\text{--}8, \text{ respectively}) \quad (9)$$

In eq 9 the polar effect  $P$  is taken as the sum of substituent effects in the meta (–6.5 kJ), para (–9.1 kJ), and ortho (same value as for para) positions.

At this point we leave the area of thermodynamic calculations, even approximate ones, and enter into the correlation analysis. The results (Table IV) are significant unless they are smaller than say 5 kJ: first of all, they must be checked for their internal consistency. In Figure 2 are plotted the effects in the deprotonated forms,  $S_{(7)}$ , and in the protonated forms,  $S_{(8)}$ , vs the estimated steric substituent effect in the acid molecules,  $S_{(6)}$ . Their proportionality is remarkable as regards the several approximations made and the variety of the experimental data sources.<sup>39</sup> The steric effect in the anion is proportional to that in the acid but weakened to one-half (slope 0.53). The effect in the protonated form is somewhat stronger than that in the acids. The dependence can be represented approximately by a straight line encompassing all 8 points (including the point for the unsubstituted parent, slope  $1.34 \pm 0.07$ ). On the other hand, if we admit the existence of an additional effect for the di-ortho substitution, we can draw a line of slope  $1.06 \pm 0.04$  (five points) for the mono-ortho-substituted compounds with the last three points deviating upward (Figure 2).

There are now at least four objections to the explanation of this picture exclusively by the hindered resonance. First, the values of  $S_{(7)}$  are certainly not zero, although the resonance in the anion (nonrealistic formula 12) should be practically negligible, hence also its hindrance. Second, the steric effect is steadily increasing in all three series (from 2 to 10), although the torsion angle  $\phi$  must be large already in the middle of these series and cannot have any great additional effect. Third, the protonated forms exhibit stronger sensitivity to polar effects of the methyl group than the neutral acids (see  $\Delta_6H^\circ$  and  $\Delta_8H^\circ$  for 4-methylbenzoic acid); one should also expect stronger resonance and stronger hindrance. However, the steric effects,  $S_{(6)}$  and  $S_{(8)}$ , are not so different (Figure 2). This is understandable with respect to the unsymmetrical conformation of the protonated form (13) but less compatible with the concept of gradual out-of-plane deformation. The fourth objection is in our opinion the strongest one. The energy of conjugation, estimated<sup>3</sup> from the solution data as 4 kJ, can be obtained more reliably, for the gas phase, from the isodesmic reaction, eq 10.



From the tabulated data<sup>35</sup> we obtained  $\Delta_{10}H^\circ = -15.35 \text{ kJ}\cdot\text{mol}^{-1}$ . Since the steric hindrance cannot exceed the magnitude of the

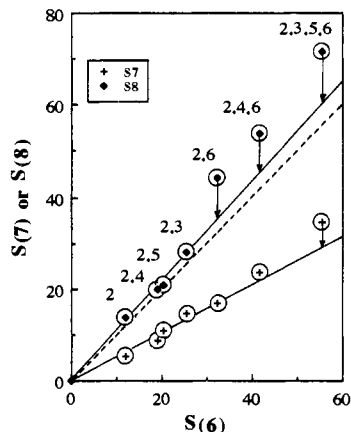
(39) The coordinates in Figures 2 and 3 are each calculated as the algebraic sum of several experimental quantities, some of them appearing in the graph on either axis. (For instance  $S_{(6)}$  and  $S_{(7)}$  have a common component in the difference of two  $\Delta_6H^\circ$  values). This does not impair the physical meaning of the graphs but could have some consequences if some starting data were loaded with big errors; then the errors in some quantities would display the points out of the line, and others would only shift the points along the line and would not disturb the linear dependence. Therefore, the points should not be represented by circles but rather by elliptical curves if one wanted to show the effect of experimental errors.

(38) Taft, R. W.; Taagepera, M.; Abboud, J. L. M.; Wolf, J. F.; DeFrees, D. J.; Hehre, W. J.; Bartmess, J. E.; McIver, R. T. *J. Am. Chem. Soc.* 1978, 100, 7765–7767.

**Table IV.** Separation of Methyl-Substituent Effects in Methyl-Substituted Benzoic Acids into Polar (*P*) and Steric (*S*) Components (kJ·mol<sup>-1</sup>, 298 K)<sup>a,b</sup>

AH	methyl position	neutral acid molecule		deprotonated form		protonated form	
		<i>P</i> (6)	<i>S</i> (6)	<i>P</i> (7)	<i>S</i> (7)	<i>P</i> (8)	<i>S</i> (8)
1	H	0	0	0	0	0	0
2	2-Me	-9.1	12.0	-4.5	5.2	-18.7	13.6
3	3-Me	-6.5	0	-3.6	0	-12.3	0
4	4-Me	-9.1	0	-4.5	0	-18.7	0
5	2,3-Me <sub>2</sub>	-15.6	25.6	-8.1	14.6	-31.0	27.9
6	2,4-Me <sub>2</sub>	-18.2	19.0	-9.0	8.6	-37.4	19.9
7	2,5-Me <sub>2</sub>	-15.6	20.3	-8.1	11.0	-31.0	20.8
8	2,6-Me <sub>2</sub>	-18.2	32.4	-9.0	16.7	-37.4	44.1
9	2,4,6-Me <sub>3</sub>	-27.3	41.5	-13.5	23.7	-56.1	53.9
10	2,3,5,6-Me <sub>4</sub>	-31.2	55.6	-16.2	34.7	-62.0	71.7

<sup>a</sup> Based on the assumption that the steric component is zero for compounds 3 and 4. The accuracy may be estimated as ±2 kJ. <sup>b</sup> The subscripts refer to the isodesmic reactions, eq 6, 7, or 8, respectively, from which the total substituent effect was evaluated.



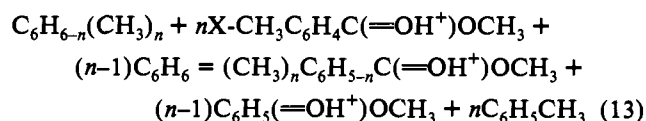
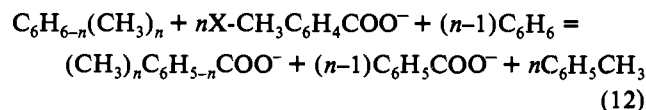
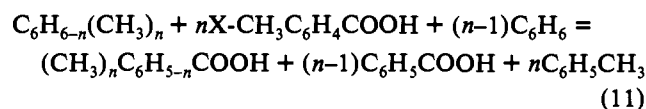
**Figure 2.** Plot of the steric contributions to the substituent effects (in terms of enthalpy, kJ·mol<sup>-1</sup>) in various forms of methylbenzoic acids: *x*-axis, *S*(6) valid for neutral acid molecules; *y*-axis, *S*(7) valid for the anions; *S*(8) valid for the protonated forms. The arrows mean the estimated possible effect of the steric hindrance to resonance; the broken line has unit slope. Point size, as an indication of accuracy, corresponds to ±2 kJ.

resonance itself, the greater part of the values in Figure 2 must be due to another effect. At most the steric hindrance of resonance may be responsible for a part of *S*(8) in the case of protonated forms with two *o*-methyl groups: only in this case is the actual form nonplanar. This possibility is shown in Figure 2: the estimate of the effect of hindered resonance is represented by arrows. In the case of *S*(7) a contribution from the hindered resonance would also be possible but cannot be ascertained, since it would only slightly exceed the uncertainty.

In conclusion, we think that all observed facts are in agreement with the concept of primary steric effect, increasing in the sequence carboxylate anion, carboxylic acid, and protonated acid (or ester). This effect may be combined with the probably-weaker steric hindrance to resonance, operative only in polysubstituted derivatives which are actually nonplanar (compounds 8–10). In the literature, the latter effect was evidently extended even to cases where nonplanarity was not proven. Of course the crucial proof would be the conformation of 2-methylbenzoic acid. According to our AM1 calculations and according to the X-ray results<sup>10</sup> it is planar: a gas-phase experiment is still lacking.

**The Buttressing Effect.** According to the classical definition, this is a steric effect exerted on a functional group by a more distant substituent through another *immediately-adjointing substituent*.<sup>6,14</sup> In the case of benzene derivatives this effect is supposed to be exerted on a functional group in position 1 by a substituent in position 3 through another one present in position 2: in order to eliminate polar effects the 2,3-disubstituted derivative is usually compared with its 2,5-isomer.<sup>6,15</sup> The weakness of this comparison is the assumption that there is no

interaction in the latter. The data in this paper offer the opportunity to define differently, and to evaluate with more precision, the buttressing effect. We suggest, as a definition, that it would be an excess of (steric) energy remaining in a trisubstituted benzene (in fact, one function and two substituents) after subtracting the interaction energies between all pairs of groups (as determined on disubstituted benzenes). In the case of benzene rings bearing more than three groups, one can define the buttressing effect in a similar way. We determine the buttressing effect as the remaining interaction between the carboxyl group and the given assembly of methyl groups when the pairwise interactions between the carboxyl group and each methyl group, taken separately, are subtracted. This definition is expressed by the isodesmic reaction, eq 11, and similarly by eqs 12 and 13 for the anions and for the protonated esters, respectively.



X = 2, 3, 4

The first compound in each reaction represents a polymethylbenzene with methyl groups in the same relative positions as in the acid molecule on the right side. The second term on the left includes several monomethylbenzoic acids with the methyl group in all proper positions as the case may be.

The values of  $\Delta_{11}H^\circ$ ,  $\Delta_{12}H^\circ$ , and  $\Delta_{13}H^\circ$  pertinent to these reactions are given in Table V. They can be rationalized in terms of their essentially steric origin. First, they are certainly not negligible, confirming the known fact that steric effects are generally not additive: particularly in the case of benzene polyderivatives they cannot be reduced to pairwise interactions. As expected, all the values are positive and increase with the number of methyl groups. They are greater when methyl groups are in adjoining positions, although even in the para position the interaction is certainly not zero. The relationships  $\Delta_{12}H^\circ$  and  $\Delta_{13}H^\circ$  vs  $\Delta_{11}H^\circ$  (Figure 3) are similar to *S*(7) and *S*(8) vs *S*(6) in Figure 2; the main difference is in the slopes. Again, the effect is weaker in the anion than in the acid (slope = 0.72); in the protonated esters it is the strongest. The same deviations are observed in Figure 2 when two *o*-methyl groups are present. They

**Table V.** Buttrressing Effect<sup>a</sup> (Excess of Steric Effects) in Methylbenzoic Acids (kJ·mol<sup>-1</sup>, 298 K)

AH	methyl position	neutral acid molecule $\Delta_{11}H^\circ$ <sup>b</sup>	deprotonated form $\Delta_{12}H^\circ$ <sup>b</sup>	protonated form <sup>b</sup> $\Delta_{13}H^\circ$ <sup>b,c</sup>
1, 2, 3, 4		0	0	0
5	2,3-Me <sub>2</sub>	11.8	7.6	12.5
6	2,4-Me <sub>2</sub>	7.0	4.3	6.3
7	2,5-Me <sub>2</sub>	7.5	5.0	6.4
8	2,6-Me <sub>2</sub>	8.4	6.3	16.9
9	2,4,6-Me <sub>3</sub>	18.0	13.8	27.2
10	2,3,5,6-Me <sub>4</sub>	28.5	21.2	41.4
"5-7"		4.3 <sup>d</sup>	2.6 <sup>d</sup>	6.1 <sup>d</sup>

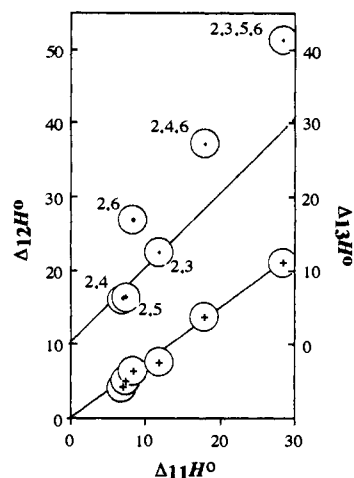
<sup>a</sup> Buttrressing effect redefined in this paper as additional (steric) interaction between several substituents, exceeding the sum of pairwise interactions. <sup>b</sup> Enthalpies of the isodesmic reactions, eq 11, 12, or 13, respectively, according to the subscript. The values may be understood as additional energy arising by introducing the carboxyl group (or carboxylate or protonated carboxyl) into a poly-methylated benzene, exceeding the sum of interactions with the individual methyls. <sup>c</sup> Difference between the enthalpies for 2,3-dimethyl- and 2,5-dimethylbenzoic acids which served in the original definition of the buttrressing effect, refs 6 and 15. <sup>d</sup> Calculated from the data on protonated methyl esters, believed to be valid also for the protonated forms of carboxylic acids.

may be again ascribed to the hindered resonance: in the case of protonated forms these deviations are evident, in the case of anions they hardly exceed the experimental errors.<sup>39</sup>

In the original conception, the buttrressing effect was demonstrated on a comparison of 2,3- and 2,5-dimethyl derivatives.<sup>6,15</sup> This is done also in Table V, last row. The effect has the expected sign; it also increases from anions to the protonated forms, but it is relatively weak since even in the 2,5-dimethyl derivative the effect is not zero; it is only reduced say to one-half. We can thus correct the classical picture in the sense that even the interactions between more distant groups cannot be neglected. Let us stress that, in this conception, the buttrressing effect is no longer connected with the word "buttrress" and does not say more than the interaction energy in trisubstituted systems is generally larger than that predicted from disubstituted systems.<sup>40,41</sup> Of course, our point of view agrees with any quantum chemical description, it is just not compatible with the oversimplified representation by space-filling models. We continued our attempt to calculate

(40) Even in 3,4-dimethyl- and 3,5-dimethylbenzoic acids the effect is not zero. We calculated  $\Delta_{11}H^\circ$  for these compounds as 7.2 and 4.3 kJ·mol<sup>-1</sup>, respectively, the latter value being not far from the limits of the experimental error. Note that these values have been determined from experimental heats of formation<sup>16</sup> and are independent of any assumptions or theoretical calculations.

(41) **Note Added in Proof:** Since submission of this manuscript we have become aware of two new independent papers concerning the revision of the *PA* scale. An experimental work on variable temperature proton-transfer equilibria measurements shows that the previously proposed revision<sup>29,30</sup> does not apply, in fact, to compounds close to acetophenone in terms of *PA*: Szulejko, J. E.; McMahon, T. B. *J. Am. Chem. Soc.* 1993, 115, 7839-7848. These new experimental results are in agreement with ab initio calculations at the G2 level: Smith, B. J.; Radom, L. *J. Am. Chem. Soc.* 1993, 115, 4885-4888.



**Figure 3.** Plot of the buttrressing effect (excess of interaction energy between several substituents in various forms of methylbenzoic acids, in terms of enthalpy, kJ·mol<sup>-1</sup>): x-axis,  $\Delta_{11}H^\circ$  valid for neutral acid molecules; y-axis,  $\Delta_{12}H^\circ$  valid for the anions (bottom);  $\Delta_{13}H^\circ$  valid for the protonated forms (top). Point size, as an indication of accuracy, corresponds to  $\pm 2$  kJ.

the buttrressing effect using reference compounds without a polar group, but the results for polyalkylbenzenes obtained from their heats of formation<sup>35</sup> were not consistent. The probable reason is that the effects are too weak compared to the experimental error, but other model compounds are not at our disposal.

## Conclusions

Previous discussions of acidities (basicities) in water were unable to separate substituent effects on both sides of the equilibrium, viz. in the neutral molecule and in the anion (cation). In addition it was difficult to estimate the effect of the solvent. A combination of gas-phase acidities (basicities) with the principle of isodesmic reaction and thermodynamic data, as described in this paper, is in our opinion promising in reaching both these objectives. We have here generalized and defined with more precision the term buttrressing effect while we have confirmed it as an experimental fact. On the other hand we have objections against the concept of steric inhibition of resonance. Certainly it should not be used unless it is proven that the molecule is actually nonplanar and that in a proper planar reference molecule the resonance is existing, i.e. sufficiently strong compared to its supposed hindrance. In our opinion the concept has been used in the literature too broadly. Even in apparently similar cases the correct interpretation may be different, as shown here for instance on 2-methylbenzoic and 2,6-dimethylbenzoic acids.

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