STERIC EFFECTS AND STERIC INHIBITION OF RESONANCE IN ISOPROPYLBENZOIC ACIDS IN THE GAS PHASE AND IN SOLUTION

Pavel FIEDLER[a], Jiří KULHÁNEK[b], Michèle DECOUZON[c], Jean-François GAL[c],
Pierre-Charles MARIA[c] and Otto EXNER[a,*]

[a] Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, 166 10 Prague 6, Czech Republic; e-mail: uochb@uochb.cas.cz

[b] Department of Organic Chemistry, University of Pardubice, 532 10 Pardubice, Czech Republic; e-mail: kulhanek@hlb.upce.cz

[c] GRECFO – Chimie Physique Organique, Université de Nice–Sophia Antipolis, 06108 Nice, Cedex 2, France; e-mail: gal@unice.fr

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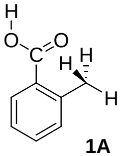
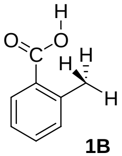
The substituent effects of the isopropyl group in 2-, 3- and 4-isopropylbenzoic acids were investigated on the enthalpies of formation, gas-phase acidities, acidities in methanol and in dimethyl sulfoxide, and on the IR spectra in tetrachloromethane. Particular attention was given to the influence of variable conformation on the observed steric effect. In contrast to 2-*tert*-butylbenzoic acid and similarly to 2-methylbenzoic acid, 2-isopropylbenzoic acid exists in two planar conformations in equilibrium. Due to this conformational freedom, the steric effects of the isopropyl group on the conformation of the carboxyl group or on the gas-phase acidity are relatively small, rather close to that of a methyl group. The gas-phase acidity can be qualitatively described in terms of pole/induced dipole interaction in the anion. The latter effect is observable with a lower intensity even in 3-isopropylbenzoic acid: in this action from a more remote position, the isopropyl group resembles more the *tert*-butyl than the methyl group. In methanol and dimethyl sulfoxide solutions, the steric effects and particularly the pole/induced dipole interaction are attenuated and effect of isopropyl acquires intermediate values between methyl and *tert*-butyl. Solvent effects are thus deciding for the position of the isopropyl substituent on the scale of steric substituent constants.

Key words: Steric effects; Substituent effects; IR spectroscopy; Inhibition of resonance; Conformation analysis; Benzoic acids; Acidity; Induced dipole.

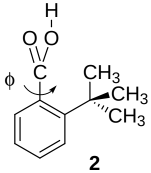
The classic concepts of steric inhibition of resonance and of steric effect on acidity[1] were reinvestigated by us on the isolated molecules[2–5], referring to the gas-phase enthalpies of formation and to the gas-phase acidities. As model systems, we used mono- and polymethylbenzoic acids[2–4] and mono-*tert*-butylbenzoic acids[5]. The main result was that the steric inhibition of resonance does not exist[2] in all compounds in which it has been assumed[6] since certain pertinent molecules are planar: planar or nonplanar conformation must be carefully distinguished in each individual example. For instance, 2-methylbenzoic acid and polymethylbenzoic acids with only one *ortho* methyl group are in planar conformations[2,3] as in **1A**$\rightleftharpoons$**1B**, at variance with classic[1b,1c] and recent[6] literature reports. 2,6-Dimethylbenzoic acid and higher-methylated benzoic acids, as well as 2-*tert*-butylbenzoic acid (**2**) are nonplanar. Even in these compounds, the calculated steric inhibition of resonance may make only a lesser part of the observed effect[4]: the so-called "steric" effect on acidity is better explained in terms of pole/induced dipole interaction[4,7]. In these examples, determinations of conformation were accomplished experimentally mainly from the IR spectra[3,5], and confirmed also by *ab initio* calculations[4]. Subsequently, some acidities of these compounds in solution were also reinvestigated, mainly in pure non-aqueous solvents[5,8]: the interpretation retained its validity but all observed effects were strongly attenuated.



1A



1B



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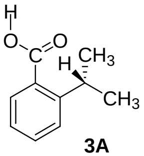
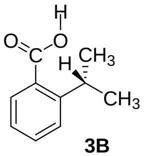
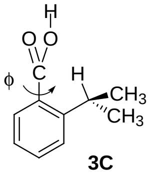
In this work, we are dealing with the isopropyl group as substituent. In contrast to the methyl group[2] and *tert*-butyl group[5] investigated previously, isopropyl group is axially unsymmetrical and can acquire conformations with very different steric requirements. Importance of conformation was stressed in a recent analysis of steric effects[9]. However, in isolated molecules, only substituent effects in methoxybenzoic acids have been investigated so far[10]: in these compounds, conformation is controlled by strong hydrogen bonds. Considering 2-isopropylbenzoic acid as a simple model, various conformations as **3A**–**3C** must be taken into account, differing both



3A



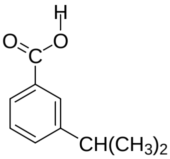
3B



3C

in the position of the isopropyl group and of the carboxyl group. According to the actual conformation, the isopropyl substituent may appear either as small as the methyl group, or as large as the *tert*-butyl group. In the common scales of steric effects[11], isopropyl is placed between methyl and *tert*-butyl, nearer to the former in a ratio of *ca* 2 : 1; these scales have been based mainly on solution reactivity.

In this communication, we investigated the three isomeric isopropylbenzoic acids **3**–**5**, using the same techniques as previously[2,5]. Infrared spectroscopy served to determine conformation, substituent effects in the isolated molecules were evaluated from the known gas-phase enthalpies of formation[12] and from the gas-phase acidities. For comparison, p*K* values in methanol and dimethyl sulfoxide (DMSO) were measured. Previous physico-chemical investigations of **3**–**5** have been scarce[13], and have been restricted mostly to p*K* values in mixed solvents[13a–13c].



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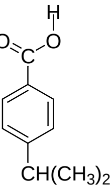

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EXPERIMENTAL

2-Isopropylbenzoic acid (**3**) was prepared from 2-isopropylaniline[15]. 3-Isopropylbenzoic acid (**4**) was from the batch for determining the enthalpy of formation[12], it was kindly given us by Dr P. Jiménez. 4-Isopropylbenzoic acid (**5**) was a commercial product.

The gas-phase acidities were determined by Fourier-Transform Ion Cyclotron Resonance (FT-ICR) as described previously[2]. We used 3-(trifluoromethyl)phenol as the reference acid for all measurements with the aim to obtain strictly comparable results: the exact anchoring on the acidity scale was of less importance for our purposes. Values of $\Delta G^{\circ}_{\text{acid}}$ were converted to $\Delta H^{\circ}_{\text{acid}}$ as previously[2], taking into account only the symmetrical part of the entropy. The results are given in Table I, lines 4–6, the primary measurements of relative acidities in the footnotes *c*–*e*.

The p*K* values in methanol and in DMSO were measured potentiometrically with a glass electrode[8]. The results were related to standard values for benzoic acid and are thus strictly comparable with the previous ones[5,8]. The p*K* values are given in Table I, lines 10 and 13.

Infrared absorption spectra were recorded in tetrachloromethane as previously described[3] at a concentration of 0.00012 mol l^{-1}, and are comparable to previous measurements[3,5] at 0.0006 (O–H) or 0.00012 (C=O) mol l^{-1}. Wavenumbers of the bands assigned to the carboxyl group are given in Table I, lines 16–27. Asymmetry of the ν(C=O) and ν(O–H) bands was expressed by the asymmetry factor *AF* as defined previously[3] (lines 18 and 21).

TABLE I
Physical properties of isopropylbenzoic acids[a]

Line	Quantity	2-Isopropyl **3**	3-Isopropyl **4**	4-Isopropyl **5**
1	$\Delta_f H°$(g) enthalpy of formation, ref.[12]	–359.2	–375.5	–382.7
2	$\Delta_1 H°$(g) substituent effect in $\Delta_f H°$(g)[b]	9.9	–6.4	–13.6
3	SE_4(g) steric effect in $\Delta_f H°$(g)[b]	23.5	0	0
4	ΔG^{o}_{acid}(g) gas-phase acidity	1 389.8[c]	1 390.6[d]	1 393.8[e]
5	$\Delta_2 G°$(g) substituent effect in ΔG^{o}_{acid}(g)[b]	–3.5	–2.8	1.5
6	$\Delta_2 H°$(g) substituent effect in ΔH^{o}_{acid}(g)[b]	–3.2	–2.8	1.5
7	SE_6(g) steric effect in ΔH^{o}_{acid}(g)[b]	–4.7	0	0
8	$\Delta_3 H°$(g) substituent effect in $\Delta_f H°$(g) of the anion[b]	6.7	–9.2	–12.1
9	SE_5(g) steric effect in $\Delta_f H°$(g) of the anion[b]	18.8	0	0
10	p*K* (methanol)	9.07	9.47	9.59
11	$\Delta_2 G°$(methanol)[b]	–1.9	0.3	1.0
12	SE_8(me) steric effect in $\Delta_2 G°$(methanol)[b]	–2.9	0	0
13	p*K* (DMSO)	10.96	11.14	11.34
14	$\Delta_2 G°$(DMSO)[b]	–0.2	0.8	1.9
15	SE_8(DMSO) steric effect in $\Delta_2 G°$(DMSO)[b]	–2.1	0	0
16	ν(O–H) (monomer) in CCl_4, cm^{-1}	3 535.2	3 540.8	3 541.7
17	$\Delta\nu_{1/2}$ of the O–H band, cm^{-1}	31.2	28.3	26.4
18	Asymmetry factor *AF* of the O–H band[f]	5	1	0
19	ν(C=O) (monomer) in CCl_4, cm^{-1}	1 738.7	1 741.3	1 739.1
20	$\Delta\nu_{1/2}$ of the C=O band, cm^{-1}	13.4	14.2	12.1
21	Asymmetry factor *AF* of the C=O band[f]	4	5	2
22	β(COH) (monomer) in CCl_4, cm^{-1}	1 342	1 338	1 342
23	ν(C–O) (monomer) in CCl_4, cm^{-1}	1 119	1 165	1 173
24	ν(O–H) (dimer) in CCl_4, cm^{-1}	2 648 2 553	2 671 2 554	2 674 2 592 2 551
25	ν_{as}(C=O) (dimer) in CCl_4, cm^{-1}	1 694	1 695	1 694
26	β(COH) + ν(C–O) (dimer) in CCl_4, cm^{-1}	1 405 1 300	1 414 1 291	1 425 1 410 1 290 1 283
27	γ(COH) (dimer) in CCl_4, cm^{-1}	931 br	931 br	936 br

[a] 298 K, energies in kJ mol^{-1}. [b] These quantities are denoted by a subscript identical with the number of the defining equation. [c] The acid **3** was found to be stronger than the reference acid 3-(trifluoromethyl)phenol (ΔG^{o}_{acid}(g) = 1391 kJ mol^{-1} according to ref.[14]) by –1.24(0.21) kJ mol^{-1}. [d] **4** was found to be a stronger acid than 3-(trifluoromethyl)phenol by –0.45(0.08) kJ mol^{-1}. [e] **5** was found to be a weaker acid than 3-(trifluoromethyl)phenol by +3.79(0.36) kJ mol^{-1}. [f] The asymmetry factor *AF* is defined in ref.[3]

RESULTS AND DISCUSSION

Conformation

Planar or nonplanar conformation of alkyl substituted benzoic acids was of utmost importance for explaining the nature of steric effects, in particular the possibility of steric inhibition of resonance. This conformation was deduced from AM1 (ref.[2c]) or *ab initio*[4] calculations, and agrees with the scarce X-ray data[16]. However, the most efficient method[3] was based on a Hammett plot of the ν(C=O) wavelengths *versus* the σ constants. The points corresponding to the planar acid molecules are situated near a straight line and are controlled by the polar effect of the methyl groups. The points corresponding to the nonplanar acids (bearing two *ortho* methyl groups) deviate very strongly in the direction toward higher wavelengths, due to the inhibition of resonance. Now, when we plot the points for the isopropylbenzoic acids **3**–**5** (Table I) into the same graph, Fig. 1 is obtained. All these points lie near the Hammett line and reveal planar conformation; they behave similarly to monomethylbenzoic acids[3], but differently than *tert*-butylbenzoic acids[5]. One *tert*-butyl group in **2** is able to twist the carboxyl group out of the ring plane, but one isopropyl group in **3** is not sufficiently bulky to do it. In this respect, the isopropyl group appears to be effectively of similar size as the methyl group.

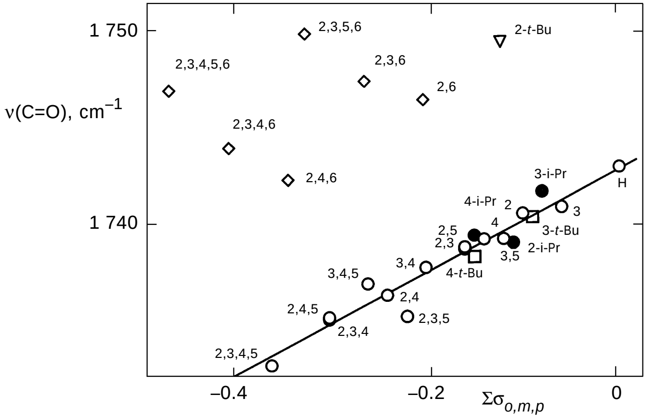


FIG. 1

Hammett plot of the carbonyl stretching frequencies of substituted benzoic acids *vs* the sum of substituent constants σ: ❍ methyl derivatives with no or one *ortho* methyl group, ✧ with two *ortho* methyl groups, ❑ *tert*-butyl derivatives with no *ortho tert*-butyl group, ∇ 2-*tert*-butylbenzoic acid, ● isopropylbenzoic acids

In constructing the above plot (Fig. 1), there could be problems in choosing a suitable value of σ_o for isopropyl in an *ortho* position; similar problems were encountered previously with the *ortho tert*-butyl group[5]. For the latter group, we previously used[5] an estimate $\sigma_o = -0.12$. In this paper, we have made now an estimate of $\sigma_o = -0.11$ for the isopropyl group. Note that the conclusions drawn from Fig. 1 do not rely on the accuracy of σ values: one could obtain a satisfactory proof even by plotting ν(C=O) *versus* the mere number of alkyl groups.

The values of ν(C=O) appear as the quantity most sensitive to the inhibition of resonance. Nevertheless, rather similar graphs were obtained when plotting the data for **3**–**5** into the plots ν(O–H) *versus* σ (see Fig. 3 of ref.[3]), or ν(O–H) *versus* its half-width (not shown), or ν(C=O) monomer *versus* ν(C=O) dimer (Fig. 2 in this paper). The last plot is simple and has the merit of being based only on directly measured quantities. In all cases, 2-*tert*-butylbenzoic acid (**2**) is grouped together with 2,6-dimethylbenzoic and with higher-methylated acids, while 2-isopropylbenzoic acid (**3**) is grouped together with 2-methylbenzoic acid (**1**) and with other acids bearing only one *ortho* methyl group. Remarkably, the amount of dimer decreases in the sequence **5** > **4** > **3**, so that a kind of weak steric hindrance can be taken into consideration even in the *meta* position. The same observation was made also with *tert*-butylbenzoic acids[5].

Conformation of **3** has not been completely determined, at least one can consider an equilibrium **3A**$\rightleftharpoons$**3B**. In this respect, we can refer to the asym-

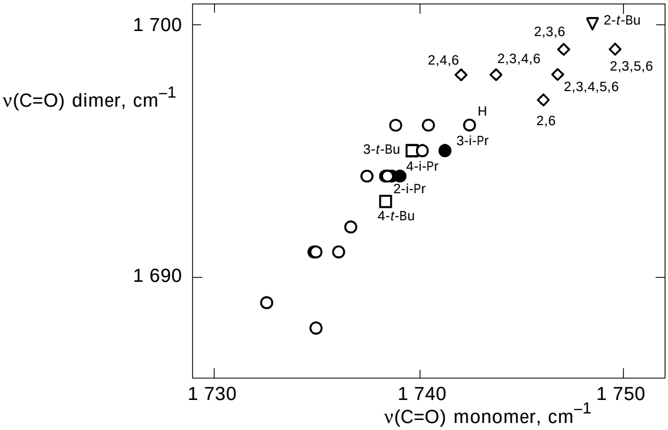


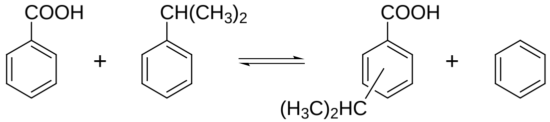
FIG. 2
Plot of the carbonyl stretching frequencies of substituted benzoic acids, monomer vs dimer; the points are denoted as in Fig. 1

metry factor[3] *AF* of the ν(O–H) band (Table I, line 18). A zero value of *AF* is expected in the case of planar symmetrical (or almost symmetrical) structures, as in **5** or **4**, respectively, as well as in the case of one nonplanar conformation as in **2**. Only in the case of an equilibrium of strongly different forms, as in **1A**$\rightleftharpoons$**1B**, a strongly unsymmetrical band is observed (*AF* approximately 5) indicating the presence of two conformers even when the two bands cannot be resolved. According to this criterion, the conformational equilibrium of **3** would be shifted similarly to that in **1** for which the abundances of **1A** and **1B** were estimated[4] to be 80 : 20. *AF* of ν(C=O) (Table I, line 21) is less reliable for this purpose as in previous cases[5].

Summarizing, the steric effect of the isopropyl substituent on the immediately adjoining groups depends strongly on its possibility to take up a suitable conformation. Effectively, this effect will then appear more similar to that of the methyl substituent than of the *tert*-butyl one.

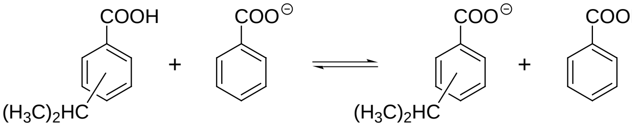
Substituent Effects in the Gas Phase

The substituent effect of the isopropyl group on the carboxyl group (or *vice versa*) can be expressed[2a] by the reaction enthalpy, $\Delta_1H°$, of the isodesmic reaction:



(1)

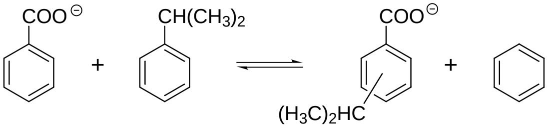
The values of $\Delta_1H°$ were calculated from the enthalpies of formation[12,17] $\Delta_fH°$ and are given in Table I, line 2. In an independent way, the substituent effect can be also estimated from the gas-phase acidities. Relative values of these acidities relate to proton transfer from the substituted to the unsubstituted acid in an isodesmic reaction:



(2)

Our experimental values of $\Delta_2H°$ of this reaction are given in Table I, line 6. The two definitions of the substituent effect do not describe the same process and the values obtained differ. When they were plotted against each other for various alkyl substituents[2c,5], an approximate linear dependence was expected for *meta* and *para* methyl derivatives according to the Hammett equation. Most of the *ortho* methyl derivatives were also situated near this line while 2-*tert*-butyl- and even 3-*tert*-butylbenzoic acids deviated in a direction toward stronger acidity. The effect of *ortho tert*-butyl on $\Delta_1H°$ is to be classified as steric (recently called van der Waals interaction), while that on $\Delta_2H°$ is better represented[4,5] by an electrostatic model as pole/induced dipole interaction[7] in the anion. The latter explanation is also applicable to the weaker effect of *meta tert*-butyl on $\Delta_2H°$. Such "steric" interactions of more distant groups, not understandable in terms of space-filling (Stuart–Briegleb) models, were observed several times on isolated molecules in the gas phase[2]. When we now plot the isopropylbenzoic acids into this graph, we get Fig. 3. In this figure, 2-isopropylbenzoic acid (**3**) behaves similarly to 2-methylbenzoic acid (**1**) as follows from the planar conformation of both. Both 3- and 4-isopropylbenzoic acids (**4** and **5**) show similar deviations as already observed on the corresponding *tert*-butylbenzoic acids, **5** seems to deviate even more. Somewhat anomalous value of $\Delta_fH°$ of **5** was already pointed out[12].

Substituent effect in the anion can be observed separately applying a thermodynamic cycle: summation of Eqs (*1*) and (*2*) yields Eq. (*3*). The values of $\Delta_3H°$ are given in Table I, line 8.



(3)

The three scales of substituent effects $\Delta_1H°$, $\Delta_2H°$ and $\Delta_3H°$ are not proportional (Table I); the classic explanation is an interaction of polar effects present in all positions and steric effects predicted mainly in the *ortho* position.

In first approximation, one can summarize that steric effects of the isopropyl group are intermediate between those of the methyl group and of the *tert*-butyl group. This behaviour is conditioned by a conformational freedom. In the proximity of another group, the conformation of the isopropyl group is forced and its effect, particularly on the gas-phase acidity, appears smaller, near to that of a methyl.

Separation of Polar and Steric Effects

A simple separation, attempted in our previous work[2], assumes that polar effects are equal in the positions *ortho* and *para*, and steric effects negligible in the positions *meta* and *para*. In spite of its simplicity, this separation yielded reasonable results at least for the weakly polar methyl group[2,8]. In the case of *tert*-butyl group, the assumption of zero steric effects in the *meta* position was evidently poor but comparison of *ortho* and *para* derivatives was still possible[5]. In **3**, there is a single *ortho*-standing group: the steric effect *SE* is then defined by simple difference between the *ortho* and the *para* derivatives, Eq. (*4*) for an acid molecule or Eq. (*5*) for the anion. The steric effect on acidity, SE_6, is given by a difference of relative acidities, Eq. (*6*). According to the experience with *tert*-butylbenzoic acids[5], we can expect that the steric effect in the *ortho* position will be reproduced reasonably by these equations; the much weaker steric effect in the position *meta* cannot be evaluated within the framework of this approach.

$$SE_4 = \Delta_1H°(ortho) - \Delta_1H°(para) \tag{4}$$

$$SE_5 = \Delta_3H°(ortho) - \Delta_3H°(para) \tag{5}$$

$$SE_6 = \Delta_2H°(ortho) - \Delta_2H°(para) \tag{6}$$

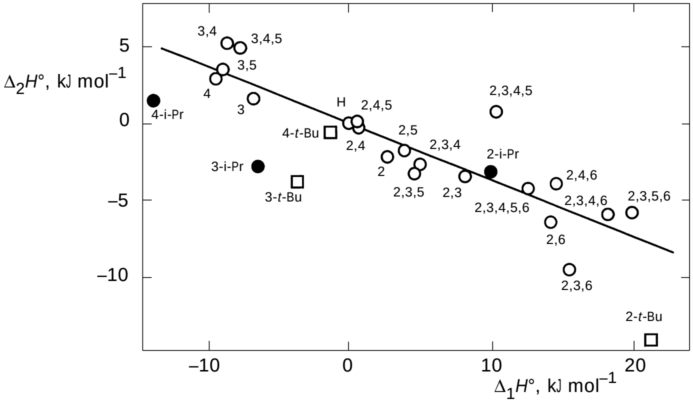


FIG. 3

Plot of the cumulative substituent effects in substituted benzoic acids: *x*-axis, substituent effect on the enthalpy of formation, $\Delta_1H°$(g), Eq. (*1*); *y*-axis, substituent effect on the gas-phase acidity, $\Delta_2H°$(g), Eq. (*2*); ❍ methyl derivatives, ❑ *tert*-butyl derivatives; ● isopropyl derivatives; the regression line determined on methyl derivatives

The values of SE_4, SE_5 and SE_6 for 2-isopropylbenzoic acid are given in Table I, lines 3, 9, and 7, respectively. Their interpretation is best carried out by comparing with the well investigated[2] methyl substituted benzoic acids. When we plotted the steric effects of their anions (SE_5) *versus* the steric effects of the acids (SE_4), we obtained[2c,5] the pattern shown in Fig. 4. The right interpretation is based on the fact that the geometries of the COOH and COO^- groups are very similar[4]. This is expressed by the straight lines of the unity slope. The actual steric effects (van der Waals interaction) are thus equal in the acid molecule and in the anion. The greater stability of the anions bearing *ortho* methyl groups is best explained[4,5] by pole/induced dipole interaction[7]. The latter is represented by the distance between the lines in Fig. 4 and is twice greater for two *ortho* methyl groups than for one *ortho* methyl group. Very approximately, it can be expressed by an electrostatic equation[7] as a function of the charge of the ion q and polarizability of a polarizable group α. In its corrected form[4,5] the equation reads:

$$\Delta E = -\alpha q^2 \Big/ 32\pi^2 \varepsilon_0^2 \varepsilon_{\mathrm{eff}}^2 r^4 \; . \qquad (7)$$

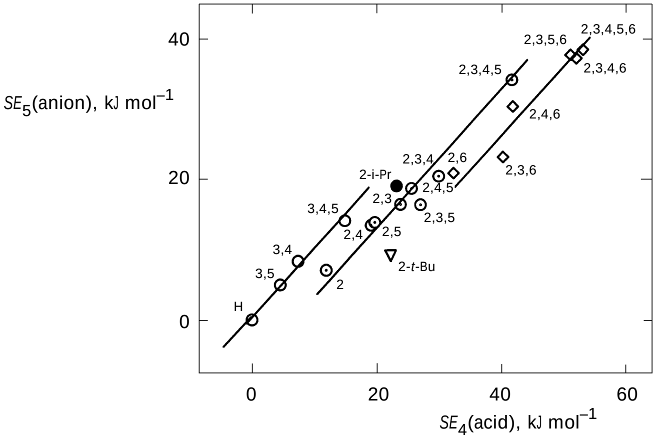


FIG. 4

Dependence of steric effects in substituted benzoic acids (SE_4) and in their anions (SE_5) in the gas phase: ❍ methyl derivatives with no *ortho* methyl group, ⊙ with one *ortho* methyl group, ✧ with two *ortho* methyl groups, ∇ 2-*tert*-butylbenzoic acid, ● 2-isopropylbenzoic acid

This expression is very sensitive to the distance *r* and also to the effective relative permittivity $\varepsilon_{\mathrm{eff}}$: the polarizability α can be obtained from molar refraction[18]. The values of ΔE calculated according to Eq. (*7*) correspond roughly to the distances of lines in Fig. 4: any additional effect of inhibited resonance is not evident[4]. Nor Fig. 3 reveals any evident steric inhibition of resonance in 2,6-dimethyl derivatives. We assume that this effect largely cancel in the acid molecule and in the anion as supported by quantum chemical calculations of some fixed molecules[4].

Position of 2-*tert*-butylbenzoic acid (**2**) in Fig. 4 is in agreement with its nonplanar conformation: the pole/induced dipole interaction is similar to that for 2,6-dimethylbenzoic acid merely by chance. On the other hand, 2-isopropylbenzoic acid (**3**) is ranged together with planar methyl derivatives. While the van der Waals interaction of isopropyl is distinctly greater than that of methyl (distance of the two points), the pole/induced dipole interaction is approximately equal (position of the two points on the same straight line). The latter fact is understandable when the conformation is near to **3A**: the end methyl groups have little effect. On the other hand, a slight distortion of the COOH group from coplanarity is possible. In 2,3-dimethylbenzoic acid, the van der Waals interaction may be of similar magnitude and the distortion from planarity was recently estimated[19] to be 12°. Values of this order still allow classifying[3] these molecules as "approximately planar".

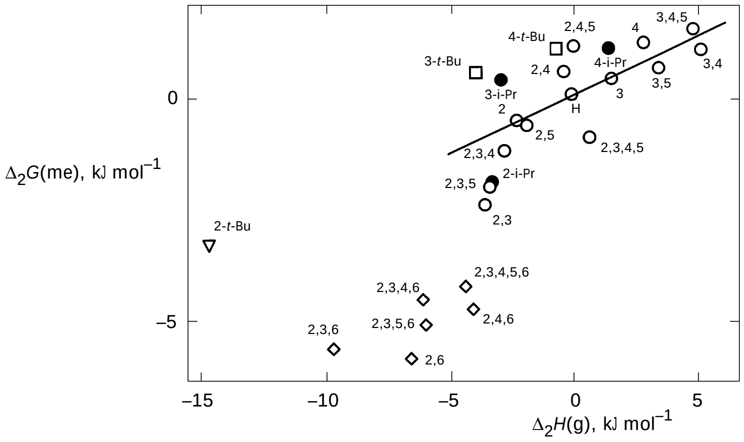


FIG. 5
Plot of the acidities of substituted benzoic acids in methanol *vs* their acidities in the gas phase; the points are denoted as in Fig. 1

Acidities in Solution

The relative acidities, related to benzoic acid, are expressed by the isodesmic reaction, Eq. (*2*). For practical reasons, we compared previously gas-phase acidities[2] in terms of $\Delta_2 H°$ and acidities in solution[5,8] in terms of $\Delta_2 G°$. Figure 5 compares acidities in the gas phase and in methanol. Methylbenzoic acids without *ortho* substituents determine a straight line in agreement with the Hammett equation. Its slope, 0.26, is a measure of the attenuation in solution. Methylbenzoic acids with one *ortho* methyl group deviate moderately, the nonplanar derivatives with two *ortho* methyl groups deviate strongly in the direction of stronger acidity in methanol. This was explained[8] by a better solvation of a nonplanar carboxyl group, making the acids stronger. 2-Isopropylbenzoic acid (**3**) behaves in this respect similarly to acids with a moderate steric hindrance. The *meta* and *para* *tert*-butylbenzoic acids, and to a lesser extent *meta* and *para* isopropylbenzoic acids, deviate from the Hammett line in the opposite direction: they are weaker acids in methanol. Explanation by steric hindrance to solvation seems evident. Remote bulky groups can thus hinder solvation of the anion and make the acid weaker while the same groups in a near position have in adition an acid-strengthening effect classified as pole/induced dipole interaction.

The last statement can be made more clear by separation of steric effect carried out in the same way as in the gas phase. Instead of Eq. (*6*), we have the same expression in terms of ΔG^{o}_{acid}:

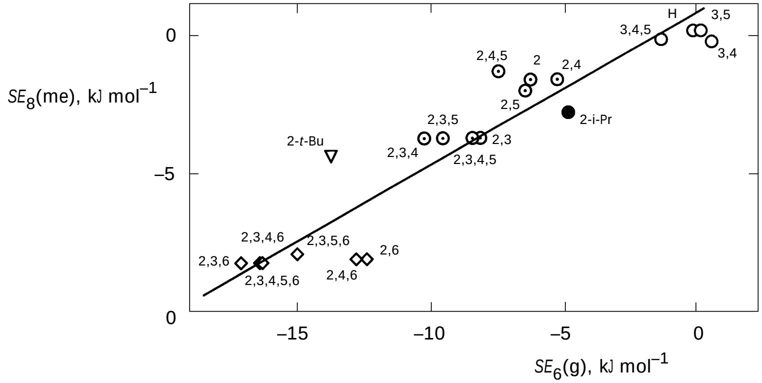


FIG. 6

Plot of the steric component *SE* of the substituent effect in the acidities of substituted benzoic acids, in methanol *vs* that in the gas phase: the points are denoted as in Fig. 4

$$SE_8 = \Delta G^{\mathrm{o}}_{\mathrm{acid}}(ortho) - \Delta G^{\mathrm{o}}_{\mathrm{acid}}(para)\ . \qquad (8)$$

Steric effects in solution, SE_8, are compared with steric effects in the gas phase, SE_6, in Fig. 6. Separate groups of methyl substituted benzoic acids are obtained: within each group, the smaller effects of more remote substituents are observable in the gas phase but this effect is absent in solution. The solvent eliminates the influence of more remote groups, in agreement with Eq. (*7*), by a higher value of $\varepsilon_{\mathrm{eff}}$. 2-Isopropylbenzoic acid (**3**) behaves differently than 2-*tert*-butylbenzoic acid (**2**). The main difference is observed in the gas phase, where the nonplanar molecule **2** is the stronger acid. In methanol, the acidities of **2** and **3** are nearer due to the steric hindrance to solvation in **2**, the same ratio being observed in aqueous methanol solvents[13a–13c].

In DMSO, the dependence of $\Delta_2 G°$(DMSO) and $\Delta_2 H°$(g) (not shown) is similar to that shown in Fig. 5 but with a greater scatter; the dependence of SE_8(DMSO) and SE_6(g) is similar to that in Fig. 6. In all cases, the plots of steric effects are more significant and simpler to understand than plots of the unresolved quantities, $\Delta_2 G°$(solvent) *versus* $\Delta_2 H°$(g). This confirms again the physical meaning of simple separation of steric and polar effects as it is given by Eqs (*4*)–(*6*).

The whole discussion of substituent effects in solution reveals the great complexity of the problem: values of pK in solution are complex quantities and are not suitable for evaluation of steric effects in isolated molecules. Still more complex are the acidities in mixed solvents as already seen from great differences between the behaviour in 50% methanol[13b,13c] and 50% ethanol[13a]; the explanation by steric inhibition of resonance[13b] has not been proven.

CONCLUSIONS

The isopropyl group behaves as a substituent of intermediate size and exhibits usually steric effects of an intensity between methyl and *tert*-butyl: it shows even detectable effects from more remote positions (in the gas phase). The variable conformation of the isopropyl group manifests itself only in the *ortho* position and in the gas phase: in this case the sterically more advantageous conformation is strongly preferred and the isopropyl group has an almost equal effect on the acidity (pole/induced dipole interaction) as the methyl group. In other cases, the steric effect of the isopropyl group can be expressed by an intermediate steric constant ("effective" size) without respect to the variable conformation.

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