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Conformation and Steric Effects in Mono- and Dimethoxybenzoic Acids

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The conformation of mono- and dimethoxybenzoic acids in solution was determined from their IR spectra and ^{13}C and ^{1}H NMR spectra. The main feature is a strong intramolecular hydrogen bond in all 2-methoxy derivatives that persists even in polar aprotic solvents but not in methanol. The methyl groups are mostly coplanar with the ring plane, the two planar conformations are almost equally abundant, and their conformation is not responsible for some enhanced values of the enthalpy of formation. The hydrogen bond (and possibly dimerization) is the reason for differences in the relative acidities ($\delta pK = pK - pK^H$) measured either in dimethyl sulfoxide or in methanol and also for the differences between δpK values of methoxybenzoic acids and corresponding methylbenzoic acids. Nevertheless, it was possible to separate with good approximation the polar and steric effects on the acidity. The steric effects in methanol are then parallel for methyl- and methoxybenzoic acids despite variable conformation of the latter. Steric effects in dimethyl sulfoxide are smaller and less regular. The acidity enhancement by *ortho* substituents is better described as electrostatic induction in the anion rather than a steric hindrance.

Introduction

For the complete series of methyl-substituted benzoic acids, we have investigated steric effects both in isolated molecules[1−3] and in solution.[4−6] At least three different experimentally verifiable mechanisms were revealed: (a) Steric hindrance to resonance exists only in acid molecules with two *ortho* methyl groups whose nonplanar conformation can be proven.[4] (b) Primary steric effect is observed mainly on the enthalpies of formation.[1] (c) Steric effect on the acidity is not caused by a higher energy of the acid molecule (van der Waals tension) but merely by lower energy of the anion[6] (interaction pole-induced dipole), and in solution this effect is attenuated.[5] The effects are generally not additive (buttressing effect[2,7]), but in polyderivatives they tend toward saturation.[3] The methyl group in these studies served as the simplest substituent of approximately spherical shape[8] and defined polarizability.[6] Its polar effects are small and predictable and can be subtracted. In the literature, many scales of steric effects have been suggested including substituents of unsymmetrical shape and those with strong polar effects.[9,10] A unified scale hardly seems possible even in the restricted region of aromatic *ortho* derivatives; we accept merely the description of the so-called steric effects as a composition of different interaction mechanisms.[8]

In this communication, we are dealing with mono- and dimethoxybenzoic acids. The unsymmetrical methoxy substituent can show particularly steric effects on conformation,[8] and its polar effect is by far not negligible. Previously, we interpreted gas-phase enthalpies of formation of these compounds with respect to the conformation of the methoxy groups.[11] Gas-phase acidities are known only for mono derivatives and were interpreted in terms of inductive effect, resonance, and pole-induced dipole interaction.[12] Few data are available on the acidities in water[13] or in mixed aqueous solvents.[14,15] In 2-methoxybenzoic acid, any steric effect on the acidity was rebutted in favor of an enhanced polar effect from the near position.[9] Attempts to determine gas-phase acidities of dimethoxybenzoic acids were not successful.[16] We report here the acidities in methanol and in dimethyl sulfoxide (DMSO) and a study of conformation based on IR spectra and the nuclear Overhauser effect (NOE) in the ^{1}H NMR spectra. For interpretation within the

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Table 1. Carbonyl and Hydroxyl Stretching Vibrations of Mono- and Dimethoxybenzoic Acids (cm^{-1}; tetrachloromethane, $c = 0.000\,12$ mol dm^{-3})

		ν(O−H) monomer				ν(C═O) monomer				
				asymmetry				asymmetry		
no.	methoxyl position	ν apparent	$\Delta\nu_{1/2}$	AF[a]	(α)[b]	ν apparent	$\Delta\nu_{1/2}$	AF[a]	(α)[b]	ν(C═O) dimer[c]
1	H	3540.7	27.7	0.4	−2.2	1742.7	11.5	2.6	−2.4	1696vs
2	3	3540.0	27.7	0	−1.5	1740.6	13.0	3.1	−3.5	1696vs
3	4	3543.6	27.0	2.3	−5.0	1735.8	11.9	3.4	−4.5	1695s
4	3,4	3543.0	27.6	−0.7	−1.3	1733.1	14.8	0	0	1690vs
5	3,5	3539.2	27.7	−1.1	+1.5	1741.7	15.3	11.1[d]	+17.5[d]	1687s
6	2	3365.8	102.4	8.3	−32.5	1749.8	14.8	−4.1[e]	+10.0[e]	1705w
7	2,3	3266.5	101.7	5.4	−29.3	1754.4	11.5	0	0	1700w
8	2,4	3385.9	68.7	11.5	−34.9	1746.3	13.2	2.3	−3.6	1691w
9	2,5	3340.1	91.3	6.8	−40.3	1748.1	15.9	1.9	0.8	1709vw
10	2,6	3521.9	26.8	0.7	−3.0	1754.2	13.6	−0.7	0.7	1711s

[a] Asymmetry factor as defined in ref 4. [b] Asymmetry angle, ref 4. [c] Concentration 0.003 mol dm^{-3}. [d] Satellite band (inflex) ≈ 1736 cm^{-1}. [e] Satellite band (inflex) ≈ 1764 cm^{-1}.

Table 3. Proton NMR Data of Mono- and Dimethoxybenzoic Acids

		proton chemical shifts						proton	interproton coupling constants							
no.	OMe position	H-2	H-3	H-4	H-5	H-6	irrad. OMe[a]	(% NOE)[b]	J(2,3)	J(3,4)	J(4,5)	J(5,6)	J(2,4)	J(2,6)	J(3,5)	J(4,6)
1	(H)	8.132	7.488	7.625	7.488	8.132			7.9	7.4	7.4	7.9	1.3	0.5	1.3	1.3
2	3	7.633		7.166	7.390	7.727	3.875 (3)	H-2 (10.2)			8.2	7.6	2.7	1.5		1.0
								H-4 (3.6)								
3	4	8.072	6.952		6.952	8.072	3.884 (4)	H-3,H-5 (9.0)	9.1			9.1		∼2.2	∼2.7	
4	3,4	7.600			6.928	7.779	3.953 (3)	H-2(13.2)				8.5		2.0		
							3.964 (4)	H-5 (11.1)								
5	3,5	7.243		6.698		7.243	3.845 (3,5)	H-2,6 (9.9)					2.4			2.4
								H-4 (5.4)								
6	2		7.070	7.586	7.156	8.203	4.092 (2)	H-3 (8.7)		8.4	7.4	7.8			1.0	1.9
7	2,3			7.166	7.206	7.725	4.090 (2)				8.2	7.8				1.8
							3.933 (3)	H-4 (9.6)								
8	2,4		6.539		6.652	8.142	4.049 (2)	H-3 (10.5)				8.8			2.4	
							3.886 (4)	H-3 (3.9)								
								H-5 (8.4)								
9	2,5		7.009	7.129		7.694	4.051 (2)	H-3 (10.5)		9.1						3.3
							3.930 (5)	H-4 (2.4)								
								H-6 (9.9)								
10	2,6		6.608	7.344	6.608		3.889 (2,6)	H-3,5 (12.3)		8.4	8.4					

[a] Chemical shift of methoxy hydrogens irradiated in a NOE experiment (in parentheses, position of this methoxyl). [b] Relative to one-third of the total intensity of the signal of the irradiated methyl group.

framework of correlation analysis, it is not possible to compare with the gas-phase acidities; however, of importance will be the correlation with methyl-substituted benzoic acids. Of the many correlations carried out, we report only the most important.

Experimental Section

Compounds **2**−**10** (Table 1) were described in a previous work.[11]

Infrared spectra were measured in the same way as previously[4] in tetrachloromethane solution at concentrations of 0.003 and 0.000 12 mol dm^{-3}. Asymmetry of the bands was evaluated according to two arbitrary measures, previously suggested and defined in detail:[4] AF is the deviation of the band maximum divided by the band half-width, and α is the angle of the band axis from the perpendicular direction. The C═O and N−H bands are described in Table 1, and further vibrational frequencies are in Table 2 in the Supporting Information.

The NMR spectra were measured at 500 (^{1}H) or 125.7 (^{13}C) MHz in $CDCl_3$ at 20 °C and referenced to internal tetramethylsilane. Characteristic chemical shifts, coupling constants, and/or substituent effects were used for structural assignment of proton signals (Table 3). NOE enhancements were determined from 1D difference NOE ^{1}H NMR spectra obtained by subtraction of two spectra acquired at identical conditions except for irradiation frequency, which was placed (1) "on" and (2) "off" the 100 Hz resonance position of the methoxy group signal for 5 s before data acquisition. NOE enhancements were related to the intensity of the signal of the corresponding methoxy group. In Table 3 are given the position of the irradiated methoxyl group, chemical shift of its protons, positions of the affected ring protons, and their NOE in percent. ^{13}C NMR spectra were accumulated with a broad-band proton decoupling. Characteristic chemical shifts, relative intensities, and known substituent effects were used for structural assignment of carbon signals. The results are given in Table 4 in the Supporting Information.

The pK values in methanol and in DMSO were measured potentiometrically with a glass electrode; the technique has been described in some detail.[17] All values were obtained relative to a literature reference value for benzoic acid[17] and are sufficient for further discussion. Experimental pK values are listed in Table 5.

Results and Discussion

Conformation on the Carboxyl Group. According to the conformation on the carboxyl group, the methoxybenzoic acids can be classified into three groups:

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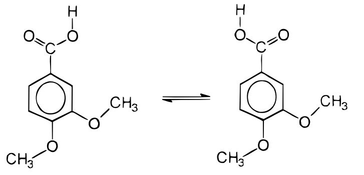
Table 5. p*K* of Mono- and Dimethoxybenzoic Acids in Methanol and Dimethyl Sulfoxide and Derived Quantities

		p*K*		$\delta\Delta G°$		SE		ΔBE	
no.	methoxyl position	MeOH	DMSO	MeOH	DMSO	MeOH	DMSO	MeOH	DMSO
1	(H)	9.41[a]	11.00[a]	0	0	0	0	0	0
2	3	9.30[b]	10.92	−0.6	−0.5	0	0	0	0
3	4	9.79[c]	11.38	2.2	2.2	0	0	0	0
4	3,4	9.60[d]	11.40	1.1	2.3	−0.5	0.6	0.5	−0.6
5	3,5	9.27[e]	10.71[e]	−0.8	−1.7	0.4	−0.6	−0.4	0.6
6	2	9.23	11.21[f]	−1.0	1.2	−3.2	−1.0	0	0
7	2,3	9.04	10.89	−2.1	−0.6	−3.7	−2.3	0.5	1.3
8	2,4	9.90	11.48	2.8	2.7	−1.6	−1.7	−1.6	0.7
9	2,5	9.15	10.92	−1.5	−0.5	−3.1	−2.2	−0.1	1.2
10	2,6	8.83	11.22	−3.3	1.2	−7.7	−3.2	1.3	1.2
uncertainty (2 SD)		0.06	0.12	0.3	0.6	0.4	0.8	0.4	0.8

[a] Reference standard values, ref 17. [b] Reference 34. [c] Reference 34 gives 9.75. [d] Reference 35 gives 9.54. [e] Reference 36. [f] Reference 31b.

(a) Derivatives without any *ortho* standing substituents, **1**−**5** (Table 1), can exist in principle in an equilibrium of two rotamers, as shown in the formulas **4A** ⇌ **4B**. However, in the case of the symmetrical compounds (**1**, **3**, and **5**), the equilibrium is degenerate, and in the remaining compounds, **2** and **4**, the two rotamers differ only in the position of a *meta* methyl group, which has practically no effect on the carboxyl. Two bands, C=O or O−H, have never been observed, and even the asymmetry of the bands is negligible (Table 1). Essentially the same result was obtained for the corresponding methylbenzoic acids,[4] but in the present case, the measures of asymmetry were less useful. For example, AF of **3** is somewhat large for an apparently symmetrical compound.

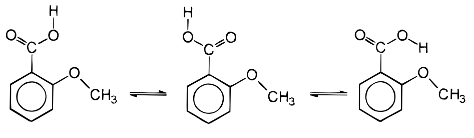


4A **4B**

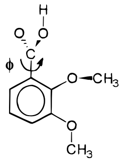
In all compounds, the dimeric form prevails at the higher concentration (0.003 mol dm^{-3}); at the lower concentration (0.000 12 mol dm^{-3}), either the monomeric form prevails or the abundance of the two forms is comparable.

(**b**) Derivatives with one *ortho* methyl group, **6**−**9**, exist in tetrachloromethane solution predominantly in the hydrogen-bonded form, such as **6C**. The band of the free hydroxyl is very weak. It proves the presence of a small amount of the nonbonded form, **6A** and/or **6B**, but does not allow measurement of its asymmetry and estimation of the abundance. In the case of compound **6**, the intramolecular hydrogen bond was already observed, both in the gas phase[18] and in solutions.[19] The hydrogen bond is medium strong,[20] as estimated from the shifts $\Delta\nu$ with reference to benzoic acid (155−201 cm^{-1} in **6**, **8**, and **9**); in **7** the hydrogen bond is stronger, $\Delta\nu = 274$ cm^{-1} (buttressing effect). In contrast, this hydrogen bond is stable even in more polar solvents. Its breaking could not be achieved at various conditions usable in IR work such as in chloroform or acetonitrile solution or in tetrachloromethane in the presence of methanol (a 10-fold concentration compared to the concentration of **6**). Only in the presence of DMSO (in the same concentration) is the hydrogen bond partly broken, and the forms **6A**−**C** can be observed in addition to the dimer. Remarkably, DMSO in a still higher concentration (100-fold the concentration of **6**) almost eliminates **6C**, but the prevailing form now is not **6A,B** but the dimer. At these conditions it was not possible to prove the separate existence of **6A** and **6B** from the band asymmetry as was done previously in the case of similar methylbenzoic acids.[4] (Great values of the asymmetry factors AF and α for **6**−**9** belong to the hydrogen-bonded forms such as **6C**.) We deduce that in pure DMSO, at the conditions of p*K* measurement, the dimeric form prevails. In methanol, IR spectral proofs were impossible but prevalence of the forms **6A,B** seems probable. From the ^{1}H NMR shifts, their abundance was estimated to be 57% on the basis of the assumption that it is 100% in water.[19b]

In the crystalline phase, **7** forms dimers[21] with a nonplanar conformation (**7D** with the torsion angle $\phi = 36°$), whereas **3**−**5** are in planar dimers.[22−24] An intermediate case[25] is **6** ($\phi = 6°$).

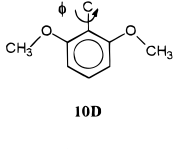


6A **6B** **6C**



7D

(**c**) Compound **10** with two *ortho* standing methoxy groups evidently exists in one nonplanar conformation, **10D**; the low values of asymmetry factors would be compatible with a single form, either planar or nonpla-



10D

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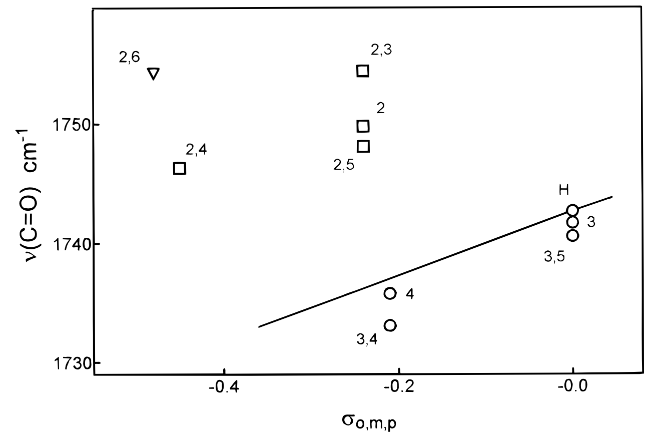
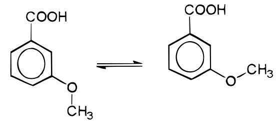


Figure 1. Plot of the carbonyl frequency of methoxybenzoic acids vs substituent constants σ: ○ *meta* and *para* derivatives (planar molecules), □ *ortho* derivatives (planar molecules with a hydrogen bond), ▽ 2,6-dimethoxybenzoic acid (nonplanar); the line was determined on methylbenzoic acids, ref 4.

nar. In the crystalline phase, this molecule is nonplanar[26] ($\phi = 57°$). In the case of methylbenzoic acids, the main proof of a planar or nonplanar conformation was obtained[4] from plotting ν(C=O) frequency against the sum of substituent constants σ. In the present case, such a convincing proof is not possible because of the smaller number of compounds and the shortage of reliable values of σ. Of them, the σ_{ortho} can be of only limited scope and should be determined at the same conditions as σ_m and σ_p. (in a less polar solvent). With the σ values derived from electrochemical reduction of aryl tosylates in acetonitrile,[27] we obtained Figure 1. *Meta* and *para* derivatives **1**−**5** are situated near the same straight line valid also for formethylbenzoic acids, following approximately the Hammett equation. The remaining derivatives deviate upward, **6**−**9** because of the intramolecular hydrogen bond, and **10** because of its nonplanarity.

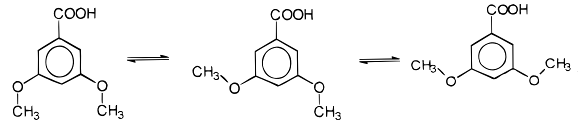
An additional possibility of distinguishing planar and nonplanar conformations in a purely empirical way is from the ^{13}C NMR spectra (Table 4 in Supporting Information). The shifts of the carboxyl carbon atom are between 170.5 and 172.4 when the carboxyl group is coplanar (**1**−**5**). In the nonplanar molecule of **10**, it is only 169.3, but it is lowered still more by the hydrogen bond (to 165.3−165.5 in **6**−**9**). Exploiting this regularity for assignment of conformation would require more compounds for comparison.

Conformation on the Methoxy Groups. We can assume that the methoxy groups tend to take a coplanar position with the benzene ring unless they are in *ortho* position to each other.[28] Therefore, the conformation of methoxy groups is unambiguous in **6** and **10**; in **3** and **4**, the two conformations differ only in the position of the carboxyl group (see **4A** $\rightleftharpoons$ **4B**) and are practically indistinguishable. In the case of compounds **2**, **5**, **8**, and **9**, the conformation can be deduced from NOE in the ^{1}H NMR spectra (Table 3). In the two conformations such as **2A** and **2B**, the distance of the methyl hydrogen atoms from the adjoining ring hydrogen are equal; hence, the NOE values can be taken directly as the relative abundance of the two forms. It follows that an equilibrium takes place in all cases. In **2** and **9**, the conformers with the methoxy group nearer to the carboxyl group (as in **2B**) prevail in a ratio of 3:1.



2A **2B**

A similar ratio (4:1) can be inferred for each methoxy group of the acid **5**. This case is complex because the two methoxyls cannot be distinguished in NMR, although they are not equivalent with respect to the unsymmetrical carboxyl group. Hence, one cannot evaluate directly the amount of the conformers. When we estimate the ratio of the two conformations at 4:1 on each methoxy group, the relative abundance of **5A**, **5B**, and **5C** would be 1:8:16 and the ratio of NOE in the position 2(6) and 4 should be 2:1, in reasonable agreement with experiment. All the results are somewhat unexpected; in no case is the conformation controlled by any kind of direct interaction (e.g., steric hindrance) from the carboxyl group in the *meta* position. At first sight, one would expect **2A** to be more stable than **2B**, but just the opposite is found.[29] In **8**, the conformer with more remote methoxy groups is preferred (2:1), as one could expect.



5A **5B** **5C**

In compounds **6** and **8**, the position of 2-OCH$_3$ is unambiguous, but the NOE is somewhat weaker than one could expect from the sum of NOE in **2**. Although the intensity of NOE in different molecules can be compared only with a rough approximation, we suggest that this lower intensity could mean a certain deviation of the 2-OCH$_3$ group from planarity. The most probable conformations would probably be similar to **7D** found in the crystalline phase. This would also be in accord with the assumed conformation of 1,2-dimethoxybenzene.[28] In **10**, the NOE is somewhat stronger and the planarity of the methoxy groups is preserved as in **10D**. The acid **4** is a limiting case; the 3-OCH$_3$ group is possibly coplanar, and the 4-OCH$_3$ is somewhat rotated out.

In the discussion of enthalpies of formation,[11] we found unexpected high values for **4** and **7** and attempted to explain them by conformation of these compounds. Steric crowding should compel a less favorable conformation than that preferred in simpler derivatives. For instance,

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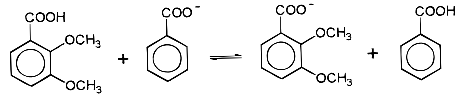
[29] A steric interaction of groups in the *meta* positions is not impossible. This was proven particularly by the enthalpies of formation (in the gas phase) of some polymethylbenzoic acids, refs 2 and 3. In **2B** the methyl group is nearer to the carboxyl than, for example, in 3,4,5-trimethylbenzoic acid, but an interaction is not observed (in nonpolar solution).

in **4A** or **4B** the conformation of the 3-methoxyl should be less favorable than that in **2A**. However, we have had no direct proof of the conformation **2A**. This previous interpretation is not confirmed by the present results, because **2A** is not the preferred conformation of **2**. On the contrary, **2B** is more abundant. We are now of the opinion that seemingly high interaction energies of **4** and **7** were an artifact caused by the high (probably not exact) value of enthalpy of formation of 1,2-dimethoxybenzene[30] which was used as reference.

Acidity in Solution. The pK values of methoxybenzoic acids in methanol and in DMSO (Table 5) are not parallel and seem to be controlled by rather different substituent effects. Their mutual dependence reveals a correlation coefficient of only $R = 0.611$; a plot is not shown. From relative values of pK, the overall substituents effects $\delta\Delta G^\circ$ were calculated (Table 5) which represent the Gibbs energies of an isodesmic reaction.[1-3] (On both sides of the equation, there is the same number of bonds of each kind.) For instance, with 2,3-dimethoxybenzoic acid, this reaction reads



$$\delta\Delta G^\circ_{\mathrm{MeOH}} = -2.1\ \mathrm{kJ\ mol^{-1}}$$

$$\delta\Delta G^\circ_{\mathrm{DMSO}} = -0.6\ \mathrm{kJ\ mol^{-1}} \qquad (1)$$

The salient feature of substituent effects is strong electron releasing by a methoxy group in the *para* position, which corresponds with the Hammett constant[10] $\sigma_p = -0.28$ and makes the 4-methoxybenzoic acid **3** weaker than benzoic acid. This effect is repeated in acids **4** and **8**. An attempt to analyze the substituent effects was done in the same way as in the case of methylbenzoic acids.[1,3] It assumes that the overall substituent effect can be decomposed into polar effect PE and steric effect SE:

$$\delta\Delta G^\circ = \mathrm{PE} + \mathrm{SE} \qquad (2)$$

Polar effect PE is then assumed equal in the *ortho* and *para* positions. This may be a somewhat crude approximation, because the polar effect in the *ortho* position was estimated[31] both stronger and weaker than that in *para*. Our approach was nevertheless confirmed by all available information in the case of methylbenzoic acids.[3] The explanation could be that polar effects of the methyl group are very weak. With methoxybenzoic acids, this approximation could be less satisfactory because the polar effects of the methoxy group are stronger. It is here used as an assumption which must be supported by its consequences. When the approximation is accepted, the steric effect, for example, of 2,3-dimethoxybenzoic acid is calculated by the simple equation:

$$\mathrm{SE}(2,3) = \delta\Delta G^\circ(2,3) - \delta\Delta G^\circ(3) - \delta\Delta G^\circ(4) \qquad (3)$$

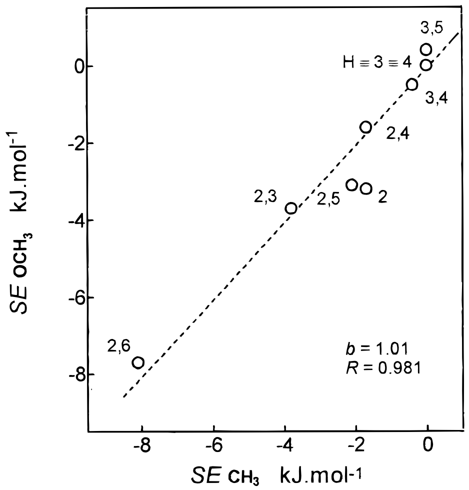
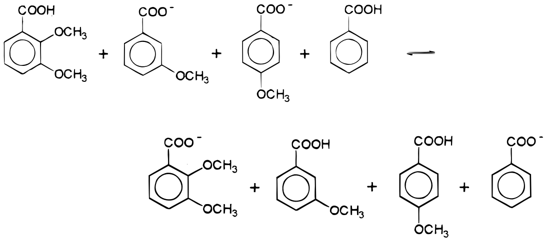


Figure 2. Plot of steric effects SE (defined according to eq 3) on the ionization in methanol: methylbenzoic acids (x-axis) vs methoxybenzoic acids (y-axis).

The value of SE may be also understood as ΔG° of an isodesmic reaction. These reactions are rather complex. An example is given here only to show that SE can be given a strict physical meaning if necessary:



$$\delta\Delta G^\circ_{\mathrm{MeOH}} = -3.7\ \mathrm{kJ.mol^{-1}}$$

$$\delta\Delta G^\circ_{\mathrm{DMSO}} = -2.3\ \mathrm{kJ.mol^{-1}} \qquad (4)$$

Of many correlations attempted, the most telling is the plot of SE of the acidity in methanol of methoxybenzoic acids vs that of methylbenzoic acids (Figure 2). The linear dependence is rather close ($R = 0.981$), much better than it would be for the pertinent unresolved values of $\delta\Delta G^\circ$ ($R = 0.785$). This gives a posteriori evidence that the definition of SE was meaningful. Although the polar effects of the CH_3 and OCH_3 groups are rather different, their steric effects appear to be practically equal in the same positions. This is not incompatible with the description of the steric effect on acidity as a pole-induced dipole interaction in the anion.[6,12] Within the framework of this model, the induction in the atoms of carbon or oxygen should be not equal because of their different polarization,[32] but the influence of more remote atoms (hydrogens of the methyl group) is difficult to estimate because of the great dependence on the distance. In any case, the unity slope in Figure 2 may arise by an accidental compensation.

In DMSO, a more complicated picture is obtained. In Figure 3, steric effects on acidity are compared in the two solvents. For methylbenzoic acid, a reasonable correlation was obtained with points separated into several

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[30] Cass, R. C.; Fletcher, S. E.; Mortimer, C. T.; Quincey, P. G.; Springall, H. D. *J. Chem. Soc.* **1958**, 2595−2597.

[31] (a) Charton, M. *J. Org. Chem.* **1971**, *36*, 882−887. (b) Pytela, O.; Liška, J. *Collect. Czech. Chem. Commun.* **1994**, *59*, 2005−2021. (c) Thompson, H. W.; Steel, G. *Trans. Faraday Soc.* **1956**, *52*, 1451−1457.

[32] Polarizability α may be represented by the increments of molar refraction, 2.59 for the C atom, 1.76 for O in ethers (in cm^3 mol^{-1}): Vogel, A. I. *J. Chem. Soc.* **1948**, 1833−1855.

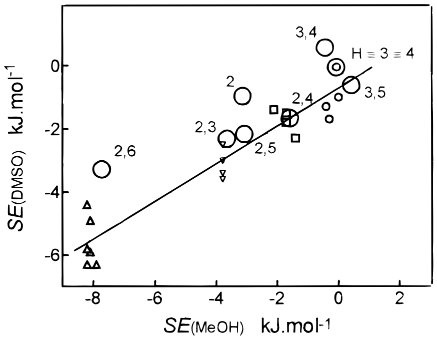


Figure 3. Plot of the steric effects SE (defined according to eq 3) on the ionization of benzoic acids, in methanol (*x*-axis) and in DMSO (*y*-axis): ○ (large) mono- and dimethoxybenzoic acids, ○ (small) methylbenzoic acids without *ortho* substituents, □ methylbenzoic acids with one *ortho* methyl, ▽ methylbenzoic acids with 2,3-dimethyl substitution, Δ methylbenzoic acids with two *ortho* methyls; the regression line is valid for methylbenzoic acids.

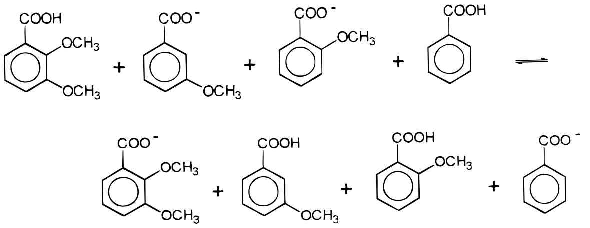
groups.[5] Its overall slope was interpreted that solvation of the carboxylate group in DMSO is more effective than in methanol. However, there were greater differences in DMSO than in methanol within each group of similar compounds (i.e., having the same number of *ortho* substituents). This was explained that the molecules of methanol can better separate the sterically interacting groups and eliminate finer steric effects of more remote substituents.[5] Most methoxybenzoic acids are shifted in this graph in the direction toward weaker acids in DMSO, i.e., this solvent is less effective in solvating the anion in the presence of methoxy groups. Solvent effects in DMSO are generally more complex, and the experimental values are less dependable.[5] Also, formation of dimers (first section) is a complicating factor.

Buttressing Effect. The buttressing effect BE was recently generalized and redefined[2] as excess energy of a trisubstituted compound that exceeds the energy which could be estimated from the individual bis derivatives.[33] In the enthalpies of formation of dimethoxybenzoic acids, a significant BE was found only for **4** and **7**.[11] However, this finding is doubtful because of the questionable value[30] of $\Delta_f H°$ of 1,2-dimethoxybenzene as discussed in the second section.

In the case of an ionization process, some terms in the definition equation cancel. For instance, for 2,3-dimethoxybenzoic acid, the differential buttressing effect ΔBE is given as

$$\Delta\mathrm{BE}(2,3) = -\delta\Delta G°(2,3) + \delta\Delta G°(2) + \delta\Delta G°(3) \quad (5)$$

Within the framework of isodesmic reactions, ΔBE can be defined as in eq 6; the sign in eqs 5 and 6 is chosen to obtain positive values (stronger acids) in the case of a steric hindrance.



$$\delta\Delta G°_{\mathrm{MeOH}} = 0.5\ \mathrm{kJ\ mol^{-1}}$$

$$\delta\Delta G°_{\mathrm{DMSO}} = 1.3\ \mathrm{kJ\ mol^{-1}} \quad (6)$$

The values of ΔBE for compounds **4**, **5**, and **7**−**10** (Table 5) were more often positive than negative as anticipated, but in absolute values all are less than 1.6 kJ $\mathrm{mol^{-1}}$. Strong attenuation of BE in solution is a common feature.[2]

Conclusions

The steric effects of methoxy groups in mono- and dimethoxybenzoic acids as measured on several observable quantities are of moderate intensity and are strongly attenuated in solution. The effect of conformation is much weaker than anticipated, and the steric effects of methoxy groups are often quite similar to those of methyl groups in the same positions. The hydrogen bond in all *ortho* derivatives strongly influences infrared spectra but is little manifested in the enthalpies of formation and p*K* values in solution.

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Supporting Information Available: Infrared spectra of compounds **1**−**10** (additional characteristic bands) (Table 2) and ^{13}C NMR spectra of compounds **1**−**10** (Table 4). This material is available free of charge via the Internet at http://pubs.acs.org.

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(33) Our new definition of BE is more general and more exact than the original one, ref 2, but leads to the same results in the classical examples. It follows that the term buttressing effect is somewhat out-of-date, particularly for more remote groups. In all cases, it is possible to read the acronym BE as "Boost Energy". We are thankful to Dr. J. Shorter for suggesting this term, which is applicable and physically correct in all examples.

(34) Ludwig, M.; Baron, V.; Kalfus, K.; Pytela, O.; Večeřa, M. *Collect. Czech. Chem. Commun.* **1986**, *51*, 2135−2142.

(35) Pytela, O.; Kulhánek, J.; Ludwig, M.; Říha, V. *Collect. Czech. Chem. Commun.* **1994**, *59*, 627−638.

(36) Pytela, O.; Kulhánek, J.; Ludwig, M. *Collect. Czech. Chem. Commun.* **1994**, *59*, 1637−1644.