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Energy of Crowded Molecules: 3,4,5-Trimethoxybenzoic Acid

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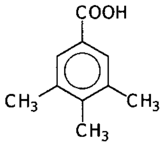
The enthalpy of combustion and enthalpy of sublimation of 3,4,5-trimethoxybenzoic acid (**2**) were measured, and the gas-phase enthalpy of formation at 298.15 K was calculated. Ab initio energies at the B3LYP/6-311+G(d,p) level were calculated for this compound, some mono- and dimethoxybenzoic acids, and a similar series of methyl-substituted benzoic acids. Intramolecular interaction (called the buttressing effect) of the groups COOH and OCH_3 (or CH_3) was defined in terms of isodesmic homodesmotic reactions. Steric crowding raises the energy of **2** in relation to monomethoxybenzoic acids, but no further effect is observed in comparison with 3,4-dimethoxybenzoic acid, on either calculated or experimental values. Similar results were obtained with 3,4,5-trimethylbenzoic acid (**1**); a previous claim of interaction of remote groups in the *meta* position was based on inaccurate enthalpies of formation of reference compounds.

1. Introduction

The effect of steric crowding has been investigated by us on the enthalpies of formation ($\Delta_f H°$) of benzene derivatives, particularly polymethylbenzoic,[1] isopropylbenzoic,[2] *tert*-butylbenzoic,[3] and dimethoxybenzoic[4] acids. Most evident was the effect of *ortho* substitution, which raised $\Delta_f H°$ over the value predicted by the additive scheme[5−7] or over $\Delta_f H°$ of the isomers by 7−22 kJ mol^{-1}, according to the size of the substituent.[1−4] In addition, finer effects were observed. When three substituents are present in the 1,2,3-positions (e.g., in 2,3-dimethylbenzoic acid), $\Delta_f H°$ is raised[1,5] by an additional 4 kJ mol^{-1} over the value expected on the basis of related bis derivatives, in agreement with the classic concept of the buttressing effect (BE).[8] We redefined this effect in a more general way, for any trisubstituted compound and for any observable quantity.[9,10] Then the acronym BE can stand for boost energy.[11] It can be observed more easily on $\Delta_f H°$ than on the acidobasic properties, and in the gas phase more easily than in solution.[10,12] We claimed this effect, although small, even in the case of more distant substituents,[10] not only in the 1,2,3-positions. The most important example was 3,4,5-trimethylbenzoic acid (**1**) since its excessive energy (with reference also to 1,2,3-trimethylbenzene) could be explained only by a steric interaction between the carboxyl group and the distant methyl groups in the *meta* position.[10] Such an interaction would be at variance with the common space-filling models or with the molecular mechanics.[13] We have believed that our value of $\Delta_f H°$ cannot be so much in error to pretend an apparent BE. However, doubts have appeared from another side, viz., from the value of $\Delta_f H°(298,g)$ of the reference benzoic acid. The value used by us,[10] −290.2 kJ mol^{-1}, has been given in both classical[14] and recent[15] data collections, but the most critical review[5] gives −295.4 kJ mol^{-1}. When we proceed from the reviews back to the primary sources, we see that the problem is in the enthalpy of sublimation $\Delta_{sub}H°(298)$. The probably best calorimetric determination[16] preferred by Pilcher[5] agrees well with the value obtained earlier by us[17] as well as with other determinations from the vapor pressure[18] but not with the previous work[19] used in other reviews.[14,15] For this reason, the BE of **1** seemed doubtful, and its confirmation and/or investigation of another model compound appears desirable. In this paper, we present experimental determination of $\Delta_f H°$ of 3,4,5-trimethoxybenzoic acid (**2**) and extensive quantum chemical calculations on both **1** and **2** as well as on a series of reference compounds. The problem is whether there is an additional effect of steric crowding as compared with simpler derivatives, particularly with 1,2,3-trimethylbenzene or 1,2,3-trimethoxybenzene, respectively.



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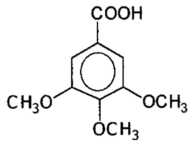

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2. Experimental Section

Purity and Phase Transition Control. The commercial material (Aldrich, mass fraction 0.98) was carefully dried and used without further purification. Determination of purity, assessed by DSC by the fractional fusion technique,[20] showed that the mass fraction of impurities was $<1 \times 10^{-3}$. The sample was studied by DCS over the temperature range $T = 260$ K to its melting point, and no phase transitions were found.

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TABLE 1: Physical Properties at $T = 298.15$ K

compound	empirical formula	M/(g mol^{-1})	ρ/(g cm^{-3})	$(\delta V/\mathrm{d}T)_p \times 10^{-7}$/(dm^3 g^{-1} K^{-1})	c_p/(J K^{-1} g^{-1})
vaseline	$(CH_2)_n$	14.0269	0.87	8.374[23]	2.22[24]
cotton	$C_{1.000}H_{1.740}O_{0.871}$	27.700	1.5	9.69[25]	1.48
3,4,5-trimethoxybenzoic acid	$C_{10}H_{12}O_5$	212.1993	1.31	3.354	1.15

Calorimetry. An isoperibol calorimeter equipped with a static bomb and an isothermal water jacket was used for the measurements of the energy of combustion. The apparatus and procedure have been described in ref 21. Calorimetric temperatures were measured to within $\pm 1 \times 10^{-4}$ K by means of a 25 Ω platinum resistance thermometer, at time intervals of 15 s, using a calibrated resistance bridge (model F26, Authomatic System Laboratories Ltd.) interfaced to a microcomputer programmed to calculate the adiabatic temperature change and a Wilkins 25.00000 Ω resistor calibrated at the U.K.'s National Physical Laboratory.

The combustion was produced by electrical discharge through a platinum wire of 0.05 mm diameter to which a cotton thread had been tied. The initial temperature of the combustion experiments was 296.95 K, and the energy of reaction was always referred to the final temperature of 298.15 K. Combustion is initiated by a device connected to the computer that automatically fires the ignition circuit at the programmed time. The initial, main, and after periods were about 20, 16, and 20 min, respectively. The combustion bomb was flushed and filled with oxygen to a pressure of 3.04 MPa, $T = 298.15$ K. The energy equivalent of the calorimeter ϵ(calor) was determined from the combustion of benzoic acid, NIST standard reference sample 39j, having a massic energy of combustion $\Delta_c u$ under the conditions specified on the certificate of $-(26434 \pm 3)$ J g^{-1}. From 10 calibration experiments $\epsilon(\text{calor}) = 14272.3 \pm 2.1$ J K^{-1}, where the uncertainty quoted is the standard deviation of the mean. Frequent calibration experiments were made throughout the series of combustion experiments.

The energy of combustion of 3,4,5-trimethoxybenzoic acid was determined by burning the solid samples in pellet form in oxygen inside the bomb, with 1 cm^3 of water added. The combustion bomb was flushed and filled with oxygen, previously freed from combustible impurities. Due to the high reactivity of 3,4,5-trimethoxybenzoic acid, many difficulties were found in obtaining combustions with no carbon deposit on the bomb's internal walls. After many trials, the compound was burned using vaseline as auxiliary material and with the bomb filled with oxygen to a pressure of $p = 2.03$ MPa. In these conditions no carbon (soot) or CO was obtained. The massic energy of combustion of vaseline used was $-(46086 \pm 5)$ J g^{-1}.[22] The empirical formula and massic energy of combustion of our cotton-thread fuse, $C_{1.000}H_{1.740}O_{0.870}$ and $-(17410 \pm 37)$ J g^{-1}, were determined in our laboratory. The nitric acid content in the bomb liquid was determined by titration with 0.1 mol dm^{-3} NaOH(aq). The corrections for nitric acid formation were based on -59.7 kJ mol^{-1} for the standard molar energy of formation of 0.1 mol dm^{-3} HNO_3(aq) from N_2(g), O_2(g), and H_2O(l). All samples were weighed with a Mettler AT-21 microbalance, and corrections of apparent mass to mass were made. After disassembly of the calorimeter, the bomb gases were slowly released and the absence of CO was checked with Dragër tubes (the sensitivity level was approximately 1×10^{-6} mass fraction). For the correction of apparent mass to mass, conversion of the energy of the actual bomb process to that of the isothermal process, and correction to standard states, we have used the values of density ρ, massic heat capacity c_p, and $(\mathrm{d}V/\mathrm{d}T)_p$, respectively, given in Table 1. Heat capacities were determined by DSC.

Corrections to standard states were made according to Hubbard et al.[26] The atomic weights of the elements were those recommended by IUPAC in 1995.[27]

A differential scanning calorimeter (Perkin-Elmer, Pyris 1) equipped with an Intracooler unit was used in this research to measure the heat capacities of the compound, to control the purity, and to study the phase transitions of the sample. Its temperature scale was calibrated by measuring the melting temperature of the recommended high-purity reference materials: benzoic acid, tin, and indium.[28] The power scale was calibrated with high-purity indium (mass fraction >0.99999) as reference material.[28] Heat capacities were determined following the method described in ref 29. Synthetic sapphire and benzoic acid were used as standard materials[30] for checking all the processes. The heat capacity values were the average of three experiments done for every interval of temperature, 268.15−308.15, 303.15−343.15, 338.15−379.15, and 373.15−386.15 K. Fresh samples of mass of approximately 8−12 mg were scanned using a heating rate of 0.17 K s^{-1}. The accuracy of the molar heat capacities $C_{p,\mathrm{m}}$ was between 0.01 and 0.02, and the standard deviation of the mean of the experimental results was ± 0.009 J g^{-1} K^{-1}.

Knudsen-Effusion Method. The vapor pressures as a function of temperature of the 3,4,5-trimethoxybenzoic acid were measured by a mass-loss Knudsen-effusion method, using the improved and tested technique and procedure previously described (benzoic acid and naphthalene as reference materials).[31] The Knudsen cell was placed in a stainless steel sublimation chamber, which was connected to a high-vacuum system (1×10^{-4} Pa) and immersed in a bath thermostatically controlled to ± 0.005 K. The temperature for each experiment, T, was measured with a calibrated platinum resistance thermometer. The mass loss of the sample, Δm, during each effusion experiment was measured by weighing the cell before and after each effusion time period, t.

The vapor pressure, p, for each temperature, T, was calculated by means of the equation (1) where a is the area of the effusion

$$p = (\Delta m/W_a a T)(2\pi RT/M)^{1/2} \tag{1}$$

orifice, W_a the corresponding Clausing coefficient[32]

$$W_a = [0.0147(l/r)^2 + 0.3490(l/r) + 0.99982]^{-1} \tag{2}$$

(l is the thickness of the effusion hole, and r is the radius), R the gas constant, and M the molar mass of the studied compound. The thickness of the effusion hole was (0.021 ± 0.004) mm, the area of the hole was (0.669 ± 0.001) mm^2, and the Clausing coefficient was (0.986 ± 0.003).

3. Results

The results of the combustion experiments are given in Table 2.

The symbols in this table have the same meanings, and the experimental values have been derived, as in ref 33. The massic energy of combustion of the compound is referred to the final temperature of the experiments, 298.15 K. The uncertainties of the standard molar energy and enthalpy of combustion are twice

TABLE 2: Results of Combustion Experiments of 3,4,5-Trimethoxybenzoic Acid at T = 298.15 K[a]

m'(compd)/g[b]	0.54217	0.50730	0.50863	0.50883	0.59729	0.36879	0.54902	0.54970	0.54897
m''(vaseline)/g[b]	0.12342	0.12176	0.12577	0.12994	0.08479	0.20873	0.10494	0.11323	0.12087
m'''(fuse)/g*b*	0.00223	0.00229	0.00233	0.00225	0.00219	0.00240	0.00214	0.00217	0.00209
$\Delta T_c/\mathrm{K} = (T_f - T_i + \Delta T_{corr})/\mathrm{K}$	1.2597	1.1994	1.2131	1.2268	1.2219	1.2611	1.2096	1.2383	1.2616
ϵ(calor)($-\Delta T_c$)/kJ[c]	−17.9754	−17.1146	−17.3096	−17.5059	−17.4390	−17.9948	−17.2601	−17.6695	−18.0025
ϵ(cont)($-\Delta T_c$)/kJ[d]	−0.0164	−0.0155	−0.0157	−0.0159	−0.0200	−0.0164	−0.0157	−0.0161	−0.0165
ΔU_{ign}/kJ[e]	0.0004	0.0004	0.0004	0.0004	0.0004	0.0004	0.0004	0.0004	0.0004
$\Delta U_{dec}(HNO_3)$/kJ[f]	0.0012	0.0010	0.0009	0.0009	0.0012	0.0018	0.0009	0.0009	0.0012
ΔU(corr to std states)/kJ[g]	0.0074	0.0070	0.0070	0.0071	0.0107	0.0062	0.0073	0.0074	0.0075
$-m''\Delta u$(vaseline)/ kJ	5.6882	5.6116	5.7963	5.9885	3.9079	9.6288	4.8366	5.2183	5.5705
$-m'''\Delta u$(fuse)/kJ	0.0389	0.0399	0.0405	0.0393	0.0381	0.0419	0.0374	0.0378	0.0364
$\Delta_c u°$(compd)/(kJ g^{-1})	−22.6049	−22.6103	−22.5708	−22.5726	−22.6033	−22.5931	−22.5733	−22.5956	−22.5932
$\langle\Delta_c u°$(compd)$\rangle$/(kJ g^{-1})	−(22.5908 ± 0.0050)								

[a] For the definition of the symbols see refs 26 and 33. T_{th} = 298.15 K; V_{bomb} = 0.380 l; p^i_{gas} = 2.03 MPa; m^i_{water} = 1.00 g. [b] Corrected masses obtained from weight by calculating the buoyancy. [c] ϵ(calor) is the energy equivalent of the whole system minus the contents of the bomb. [d] ϵ(cont) is the energy equivalent of the contents of the bomb, $\epsilon(\mathrm{cont})(-\Delta T_c) = \epsilon^i_{con}(T_i - 298.15\ \mathrm{K}) + \epsilon^f_{con}(298.15\ \mathrm{K} - T_f + \Delta T_{corr})$. [e] Experimental energy of ignition. [f] Experimental energy of formation of HNO_3. [g] ΔU(corr to std states) is the sum of items 81−85, 87−90, 95, and 94 in ref 26.

TABLE 3: Energy and Enthalpies of Combustion and Formation of 3,4,5-Trimethoxybenzoic Acid at T = 298.15 K

$\Delta_c U°_m$(cr)/(kJ mol^{-1})	$\Delta_c H°_m$(cr)/(kJ mol^{-1})	$\Delta_f H°_m$(cr)/(kJ mol^{-1})
−4793.8 ± 2.9	−4795.1 ± 2.9	−855.0 ± 3.2

TABLE 4: Molar Heat Capacities $C_{p,m}$ of 3,4,5-Trimethoxybenzoic Acid

T/K	$C_{p,m}$/(J K^{-1} mol^{-1})	T/K	$C_{p,m}$/(J K^{-1} mol^{-1})	T/K	$C_{p,m}$/(J K^{-1} mol^{-1})
268.2	245.59	305.2	274.97	350.2	300.19
270.2	247.35	310.2	278.12	355.2	303.37
275.2	251.31	315.2	281.41	360.2	305.99
280.2	255.13	320.2	284.49	365.2	309.03
285.2	259.45	325.2	288.52	370.2	311.93
290.2	263.62	330.2	292.06	375.2	317.90
295.2	267.44	335.2	296.23	380.2	322.17
298.15	269.49	340.2	296.80	385.2	325.67
300.2	271.19	345.2	297.08		

the final overall standard deviation of the mean and were estimated as outlined by Olofsson.[34]

Table 3 gives the standard molar energy and enthalpy of combustion referred to the combustion reaction

$$C_{10}H_{12}O_5(\mathrm{cr}) + 2\,1/2O_2(\mathrm{g}) \rightleftarrows 10CO_2(\mathrm{g}) + 6H_2O(\mathrm{l}) \quad (3)$$

The values for the standard molar enthalpies of formation of H_2O(l) and CO_2(g) at T = 298.15 K are −(285.830 ± 0.042) and −(393.51 ± 0.13) kJ mol^{-1}, respectively, and were taken from CODATA.[35]

The molar heat capacities for 3,4,5-trimethoxybenzoic acid from T = 268.15 K to near its melting temperature T = 385.15 K are given in Table 4.

The results of our Knudsen-effusion experiments, calculated by means of eq 1, are summarized in Table 5, where p represents the vapor pressure and Δm the mass loss during the time t, at temperature T. The highest percentage error for the vapor pressure in this table is 0.05 arising from all quantities in eq 1.

The Clausius−Clapeyron equation

$$\ln(p/\mathrm{Pa}) = -B(T/\mathrm{K})^{-1} + A \quad (4)$$

was fitted to the results of Table 5 by the least-squares method, where $B = \Delta_{sub}H°_m\langle T_m\rangle/R$. In this table, the quantities $\delta p/p$ are the fractional deviations of the experimental vapor pressures from those computed using eq 4. The standard molar enthalpy of sublimation at the mean temperature of the experimental temperature range was computed from the corresponding B value. The parameters A and B for eq 4 are 39.6 ± 0.3 and −(15386.1 ± 98.3), respectively. The molar enthalpy of sublimation, corresponding to the mean temperature $\langle T_m\rangle$ = 363.17 K of its experimental range, is $\Delta_{sub}H_m$ = (127.9 ± 0.8) kJ mol^{-1}. The uncertainty assigned to the value of $\Delta_{sub}H_m$ is based on the standard deviation of the B value.

The sublimation enthalpy at the temperature T = 298.15 K was derived using the equation

$$\Delta_{sub}H°_m(298.15\ \mathrm{K}) = \Delta_{sub}H°_m(\langle T_m\rangle) + \int_{T_m}^{298.15}[C^\circ_{p,m}(\mathrm{g}) - C^\circ_{p,m}(\mathrm{cr})]\,\mathrm{d}T \quad (5)$$

where

$$C^\circ_{p,m}(\mathrm{g}) = 14.67 + 0.82T - (4.2 \times 10^{-4})T^2 \quad (6)$$

and

$$C^\circ_{p,m}(\mathrm{cr}) = 78.3 + 0.612T + (1 \times 10^{-5})T^2 \quad (7)$$

$C^\circ_{p,m}$(g) has been calculated by using the group contribution scheme of Rihani[36] and $C^\circ_{p,m}$(cr) has been taken from the experimental results given in Table 4. The standard molar enthalpies of sublimation and formation in crystalline and gaseous states of 3,4,5-trimethoxybenzoic acid at T = 298.15 K are given in Table 6.

No experimental enthalpies of combustion, sublimation, and formation for this compound have been found in the literature for comparison with our results.

4. Calculations

Calculations at a B3LYP/6-311+G(d,p) level were performed exploiting the GAUSSIAN94 program[37] according to the original proposal.[38] Full geometry optimization and vibrational analyses were carried out in all cases. In the case of **2** and other polymethoxy derivatives, we searched not only for the least-energy conformation, but also for the other, less populated conformations by preliminary calculations within the framework of the AM1 method.[39] One dihedral angle, C−C−O−C, was always fixed and the energy optimized for all other geometric parameters. All secondary minima found in this way were successively introduced as starting geometries into the B3LYP/6-311+G(d,p) calculation. The existence of a secondary minimum at the potential energy surface was always confirmed by vibrational analysis. Calculated energies of all conformers found and the most important features of their geometry are listed in Table 7.

The sum of electronic and thermal enthalpies, $\Delta H°(298)$, was also calculated at the B3LYP/6-311+G(d,p) level. Vibrational

TABLE 5: Vapor Pressures *p* of 3,4,5-Trimethoxybenzoic Acid

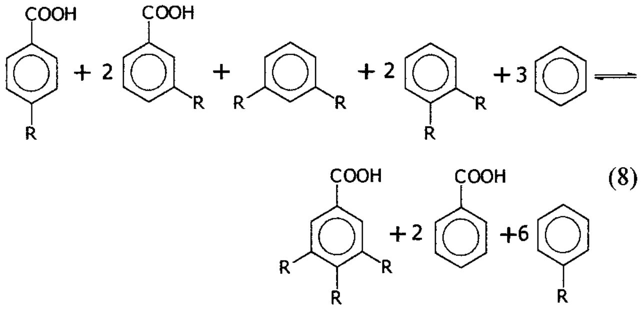
T/K	t/s[a]	Δm/mg[b]	p/Pa[c]	$10^2(\delta p/p)$[d]	T/K	t/s[a]	Δm/mg[b]	p/Pa[c]	$10^2(\delta p/p)$[d]
354.11	28260	1.31	0.0208	−3.93	366.22	21540	4.21	0.0888	−0.257
357.12	27600	1.83	0.0298	1.24	369.24	23460	6.38	0.124	−0.596
360.30	18540	1.80	0.0437	3.52	372.23	21600	8.00	0.170	−1.58
363.10	21180	2.90	0.0619	2.94					

[a] Time for the experiment. [b] Mass of the sublimed substance. [c] Vapor pressure. [d] δp denotes the deviations of the experimental vapor pressures from the values computed using eq 4.

analysis and calculation of $\Delta H°(298)$ was repeated once more according to the recent suggestion,[40] viz., omitting all internal rotational modes. The results were not improved, and the resulting values have not been listed.

5. Discussion

In our original concept,[9,10] the excessive energy of a molecule is called the boost energy (BE) and is equivalent to the former term buttressing effect. It is defined in terms of isodesmic reactions.[41,42] In our case, for the molecule **1** or **2**, the isodesmic reaction, eq 8, is not only isodesmic but also homodesmotic.[43]

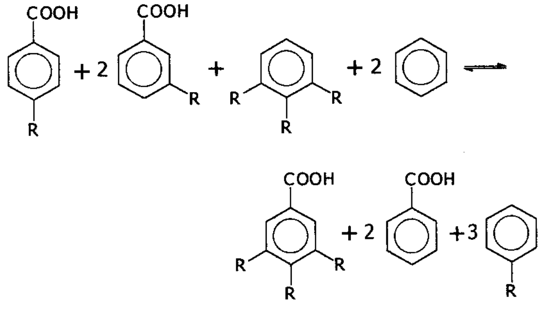


(8)

$R = CH_3$: $\Delta_8H°(g) = 2.4$ $\Delta_8E(DFT) = -3.3$

$R = OCH_3$: $\Delta_8H°(g) = 38.0(?)$ $\Delta_8E(DFT) = -0.5$ (kJ mol^{-1})

The reaction is rather complex, but its purpose is to present all pairwise interactions on the left-hand side. Its reaction enthalpy, $\Delta_8H°(g)$, then represents the excessive energy in a tetrasubstituted molecule. This also includes interaction between the three neighboring methyl (or methoxyl) groups which would take place even without the presence of the carboxyl group. If we are interested particularly in a possible long-range interaction between the carboxyl group and methyl or methoxyl groups, it is better to take these groups together as a block; BE is then expressed by eq 9.



(9)

$R = CH_3$: $\Delta_9H°(g) = -0.4$ $\Delta_9E(DFT) = 0.3$

$R = OCH_3$: $\Delta_9E(DFT) = 1.7$ (kJ mol^{-1})

TABLE 6: Experimental Standard Molar Enthalpies of Sublimation and Formation in the Crystalline and Gaseous States at T = 298.15 K of 3,4,5-Trimethoxybenzoic Acid

$\Delta_fH°_m$(cr)/(kJ mol^{-1})	$\Delta_{sub}H°_m$/(kJ mol^{-1})	$\Delta_fH°_m$(g)/(kJ mol^{-1})
−855.0 ± 3.2	131.2 ± 0.8	−723.8 ± 3.3

When we apply these equations to **1**, no long-range effect is observed according to eq 9 and at most a quite small BE within the block of methyl groups according to eq 8. Agreement of experimental and calculated values is reasonable. Note that the experimental uncertainty may be considerable since eqs 8 and 9 contain 18 or 12 molecules, respectively, and the errors are added. Assuming the uncertainty (2 standard deviations) of one measured $\Delta_fH°$ to be ±2 kJ mol^{-1}, we get for the uncertainty of $\Delta_8H°(g)$ or $\Delta_9H°(g)$ ±9 or ±7 kJ mol^{-1}, respectively. As mentioned in the Introduction, particularly the experimental error in $\Delta_fH°(g)$ of benzoic acid may be critical since this molecule is involved twice in eqs 8 and 9. This is an evident drawback of all complicated isodesmic reactions. Their reaction enthalpies have a clear physical meaning, but their experimental uncertainty increases when they involve too many molecules. We conclude that no long-range interaction is observed in **1** when the new value of $\Delta_fH°(g)$ of benzoic acid has been introduced. Our previous calculations[44] of BE in methyl-substituted benzoic acids must be corrected. All values become smaller: some of them are now within the experimental uncertainties; nevertheless, all remain positive.

When we proceed to the methoxy derivative **2**, we encounter problems with both the calculated and experimental values. Calculations revealed several conformers of **2** representing secondary minima on the potential energy surface (Table 7). Some of them possess very near energies and differ also rather little in geometry. Their occurrence made the calculations more complex since it was desirable to find all conformers; for comparison with experiment, one must calculate the effective $\Delta H°$ of the actual equilibrium mixture at 298 K. However, the resulting effect on energy is very small since conformers with higher energy are little populated. We calculated the assumed population of the conformers of **2** with the common approximation $\Delta G° \approx \Delta H°$: the resulting effective enthalpy was only 0.6 kJ mol^{-1} higher than that of the lowest-energy conformer. The reaction energies Δ_8E(DFT) and Δ_9E(DFT) given with eqs 8 and 9 refer to the conformer of the lowest energy.

Evidently the main problem is striking disagreement between theory and experiment for **2** in eq 8 while in eq 9 the experimental enthalpy of formation of 1,2,3-trimethoxybenzene is not available. Since $\Delta_8H°(298,g)$ of 38 kJ mol^{-1} seemed to be well outside the experimental uncertainty, we tried first to improve the calculations. However, calculation of the thermal enthalpies (Table 7) brought only negligible changes even when these were calculated according to the modification suggested recently.[40] For this reason, we derive further conclusions simply from the electronic energies ΔE(DFT). In our opinion, the cause of disagreement must be sought in the experimental enthalpies of formation, not of methoxybenzoic acids but of methoxybenzenes used as reference compounds in eq 8. We tried to test

TABLE 7: Calculated Energies of Methoxy- and Methylbenzoic Acids and of Some Reference Compounds

				conformation^{a,b}			
compound	E(DFT)/au^a	rel energy/(kJ mol^{-1})	ΔH°(298)/au^a	ϕ	τ_1	τ_2	τ_3
benzoic acid	−420.9481463		−420.822609	0			
3-methylbenzoic acid	−460.2759880			0			
4-methylbenzoic acid	−460.2766550			0			
3,4,5-trimethylbenzoic acid (**1**)	−538.9284252			0			
3-methoxybenzoic acid	−535.5050952		−535.346985	0	0		
4-methoxybenzoic acid	−535.5068031		−535.348702	0	0		
3,4-dimethoxybenzoic acid	−650.0584625			0	0	180	
3,5-dimethoxybenzoic acid	−650.0614712	0		0	0	180	
	−650.0611997	0.7		0	0	0	
	−650.0607725	1.8		0	180	0	
	−650.0590214	6.4		0	180	180	
3,4,5-trimethoxybenzoic acid (**2**)	−764.6067456	0		0	−3	76	−178
	−764.6067151	0.1		0	−2	107	−177
	−764.6052423	3.9		0	−2	72	−71
	−764.6045858	5.7		0	−112	110	−178
	−764.6015962	13.5	−764.374126	0	108	−78	70
benzene	−232.3112375		−232.20 3638				
methylbenzene	−271.6387778						
1,2-dimethylbenzene	−310.9637708						
1,3-dimethylbenzene	−310.9662298						
1,2,3-trimethylbenzene	−350.2900552						
methoxybenzene	−346.8675611		−346.72 7282		0		
1,2-dimethoxybenzene	−461.4165585		−461.24 1430		−3	70	
1,3-dimethoxybenzene	−461.4243734		−461.24 9198		0	0	
1,2,3-trimethoxybenzene	−575.9669207		−575.75 6972		−2	73	−66

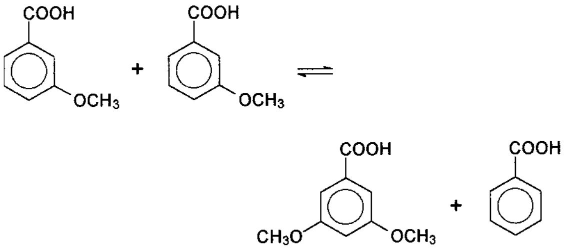
[a] Level B3LYP/6-311+G(d,p)//B3LYP/6-311+G(d,p). [b] ϕ is the torsion angle between the carboxyl group and the ring plane ($\phi = 0$ corresponds to C═O oriented toward the substituents), τ_1 τ_2 and τ_3 are the torsion angles of the methoxy groups given as dihedral angles C−C−O−CH$_3$ in a direction from COOH; $\tau = 0$ thus means the methyl group position nearest to the carbonyl group.

the literature values[45,46] of $\Delta_f H°(298,g)$ in simple isodesmic reactions, relating them to mono- or dimethoxybenzoic acids. Good agreement of experiment and calculation, within 1.6 kJ mol^{-1} at worst, was obtained in the case of methoxybenzene[45] or even for the estimated[4] $\Delta_f H°(298,g)$ of 1,3-dimethoxybenzene. However, $\Delta_f H°(298,g)$ of 1,2-dimethoxybenzene[46] seems to be in error: a less negative value, by more than 20 kJ mol^{-1}, would be required. If this error were present, it would also influence our previous calculations of BE in dimethoxybenzoic acids:[4] actually the calculated BEs of 2,3- and 3,4-dimethoxybenzoic acids were too great. We conclude that no long-range interaction and even no BE was revealed in **2** on the basis of calculated values; a confirmation from experimental values was not possible.

When we cannot use the experimental $\Delta_f H°(298,g)$ of 1,2-dimethoxybenzene in the isodesmic reaction, we can attempt an evaluation based only on methoxybenzoic acids, without reference to simpler molecules. This can be done first by an additive scheme. In this approach,[5,6,7,47] the simple reference compounds are not completely absent but are involved in the values of group parameters (increments) derived statistically. A single experimental error has no great consequence in this approach. However, the results of this approach depend strongly on the system and on special corrections applied. Thus, for the acid **1**, one obtains in the Cox system[47] −384.0 (all values in kJ mol^{-1}), but this value may be questioned. On one hand, it was suggested[5,47] that the correction for *ortho* substitution should be omitted in the case of two methyl groups; on the other hand, Pilcher[5] used in addition a correction for 1,2,3-substitution. (However, he himself used corrections for *ortho* substitution, although he cited Cox,[47] saying that these should be omitted.) Accordingly, the predicted value could be between −392.0 and −380.0. The system of Domalski and Hearing[7] consists of more specialized parameters and of additional corrections; their use is not always unambiguous. For **1**, these authors calculated −390.2 with two corrections for *ortho* substitution and one (why not three?) for *meta* substitution. For **2**, one gets in the Cox system −734.9 with two corrections for *ortho* substitution and one for 1,2,3-substitution. In the system of Domalski and Hearing, the *ortho* corrections between methoxyl groups are not available and must be estimated. One could get values between −753.0 and −740.9. Comparison with our experimental value would suggest a destabilization, but this could not be estimated quantitatively.

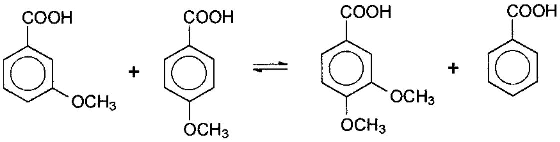
In the following, we shall restrict our consideration to methoxybenzoic acids and use simple isodesmic reactions. This approach is straightforward and simple but can be more sensitive to a single experimental error than was the case in an additive scheme. Also the interpretation need not always be unambiguous.

The relation of mono- and dimethoxybenzoic acids is expressed by eqs 10 and 11.



(10)

$\Delta_{10}H°(g) = -0.1 \quad \Delta_{10}E(\mathrm{DFT}) = 1.5 \quad (\mathrm{kJ\ mol^{-1}})$

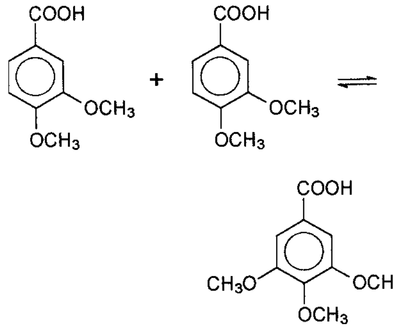


(11)

$\Delta_{11}H°(g) = 18.4 \quad \Delta_{11}E(\mathrm{DFT}) = 13.9 \quad (\mathrm{kJ\ mol^{-1}})$

Agreement of experimental and calculated reaction enthalpies is reasonable. In eq 10, the zero enthalpy means that there is no BE and evidently no steric effect in 3,5-dimethoxybenzoic acid as expected. In 3,4-dimethoxybenzoic acid, eq 11, a steric interaction between the two methoxyl groups is evident, but it cannot be equated with BE since it would still be necessary to subtract the interaction in 1,2-dimethoxybenzene. BE could be obtained only from calculated energies and would be zero or even negative.

When we go on to 3,4,5-trimethoxybenzoic acid (**2**), the increase of energy may be expressed by eq 12.



(12)

$\Delta_{12}H°(g) = -8.3 \quad \Delta_{12}E(\mathrm{DFT}) = 8.8 \quad (\mathrm{kJ\ mol^{-1}})$

The disagreement of experimental and calculated values is rather bad in this case; the calculated energy seems more reasonable. In any case, it follows from both values that there is no gradation of steric effects. On the contrary, introducing an additional methoxyl group is connected with weaker interaction than in the case of 3,4-methoxybenzoic acid. The *para* standing methoxyl group is coplanar with the ring in 3,4-dimethoxybenzoic acid but twisted by 76° in **2** (Table 7, conformation). Therefore, one would expect a raised energy due to steric inhibition of resonance. Its magnitude could be estimated from comparison of the energies of 4-methoxybenzoic and 3-methoxybenzoic acids[4] to 4 kJ mol^{-1}. However, this effect is not observed.

When a buttressing effect was not observed in the energy of **2**, we still searched for some evidence in the conformation of the methoxyl groups. It was observed in some cases that geometry was more sensitive to slight effects than energy.[49] Only one stable conformation of 1,2,3-trimethoxybenzene was found (see Table 7, conformation) similar to but not identical with the conformation derived from experimental dipole moments.[48] In **2**, similar conformations of the methoxyl groups do exist but not in the most stable conformers. In these the outer methoxyl groups are situated nearer to the ring plane: they seem to be attracted rather than repelled by the carboxyl group. One cannot discuss any evident long-range interaction.

6. Conclusions

No long-range effects were proven in the acid **1** or **2**. The buttressing effect in **1** is evidently due to crowding within the block of the three methyl groups; in **2** even this effect cannot be proven. Previous findings[10,44] based on experimental enthalpies of formation should be corrected, and all such values reported from different laboratories and in different times must be taken with utmost caution for more detailed calculations. In our opinion, quantum chemical results may be more dependable in such cases.

Nevertheless, a long-range effect from the *meta* position may exist; it was assumed for instance when interpreting the experimental gas-phase acidity of *tert*-butylbenzoic acid.[50]

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