Thermochemical Study of the Methoxy- and Dimethoxyphenol Isomers

M. Agostinha R. Matos,*,[†] Margarida S. Miranda,[†] and Victor M. F. Morais[‡]

Centro de Investigação em Química, Departamento de Química, Faculdade de Ciências da Universidade
do Porto, Rua do Campo Alegre, 687, P-4169-007 Porto, Portugal, and Instituto de Ciências Biomédicas
Abel Salazar, da Universidade do Porto, P-4099-003 Porto, Portugal

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The standard ($p° = 0.1$ MPa) molar enthalpies of formation for 2-, 3-, and 4-methoxyphenol and 2,3-, 2,6-, and 3,5-dimethoxyphenol in the gaseous phase were derived from the standard molar enthalpies of combustion, in oxygen, at 298.15 K, measured by static bomb combustion calorimetry, and the standard molar enthalpies of evaporation at 298.15 K, measured by Calvet microcalorimetry: 2-methoxyphenol, −(246.1 ± 1.9) kJ mol^{-1}; 3-methoxyphenol, −(240.4 ± 2.1) kJ mol^{-1}; 4-methoxyphenol, −(229.7 ± 1.8) kJ mol^{-1}; 2,3-dimethoxyphenol, −(386.0 ± 2.2) kJ mol^{-1}; 2,6-dimethoxyphenol, −(381.7 ± 1.9) kJ mol^{-1}; 3,5-dimethoxyphenol, −(399.4 ± 3.0) kJ mol^{-1}. Density functional theory calculations for all the methoxy- and dimethoxyphenols and respective phenoxyl radicals and phenoxide anions were performed using extended basis sets, which allowed the estimation of the gas-phase enthalpies of formation for all compounds. The good agreement of the calculated and experimental gas-phase enthalpies of formation for the closed-shell systems gives confidence to the estimates concerning the isomers which were not experimentally studied and to the estimates concerning the radicals and the anions. Substituent effects on the homolytic and heterolytic O−H bond dissociation energies have been analyzed, the results being in good agreement with available experimental data. Detailed analysis of these effects suggests that electronic exchange phenomena between the substituents dominate the effect the substituents have on these systems.

Introduction

In the sequence of previous work on the thermochemistry of substituted phenols,[1−3] we report the standard molar enthalpies of formation of the three methoxyphenol isomers and of 2,3-, 2,6-, and 3,5-dimethoxyphenols in the gaseous phase, obtained from measurements of standard molar energies of combustion using a static bomb calorimeter and from the values for the standard enthalpies of sublimation or vaporization measured by Calvet microcalorimetry. Additionally, density functional theory was used in order to obtain the most stable geometries for these molecules and for all the remaining dimethoxyphenol isomers and respective phenoxyl radicals and phenoxide anions. Using carefully chosen isodesmic reactions involving the methoxy- or the dimethoxyphenols, the relative stability of the methoxy- and dimethoxyphenols, in the gaseous phase, was derived.

The study of the energetics of phenolic compounds has a considerable practical interest, since this class of chemical compounds includes a large number of synthetic and naturally occurring antioxidants. This antioxidant function is due to the ability of phenols to trap the peroxyl radicals

$$\mathrm{ROO^{\bullet} + ArO{-}H \rightarrow ROO{-}H + ArO^{\bullet}} \qquad (1)$$

and it is directly related to the energetics of the O−H bond. The stability of this bond is affected by the number, nature, and position of the substituents in the aromatic ring.[4] In the present work we try a theoretical interpretation of the influence of the substituents on the dissociation energy of the O−H bond, in the case of the methoxy substitution. Theoretical DFT gas-phase acidities were also calculated, and the agreement with existing experimental values for the methoxyphenols is very good.

Experimental Section

Materials. The methoxyphenols were obtained commercially from Aldrich Chemical Co., and they were purified by repeated distillation or sublimation under reduced pressure until the combustion results were consistent and the carbon dioxide recovery ratios were satisfactory. The average ratios, together with the standard deviation of the mean, of the mass of carbon dioxide recovered to that calculated from the mass of sample were as follows: 2-methoxyphenol (2-MeO−C_6H_4−OH) [90-05-1], (0.9993 ± 0.0001); 3-methoxyphenol (3-MeO−C_6H_4−OH) [150-19-6], (0.9992 ± 0.0002); 4-methoxyphenol (4-MeO−C_6H_4−OH) [150-76-5], (0.9996 ± 0.0002); 2,3-dimethoxyphenol (2,3-(MeO)$_2$−C_6H_3−OH) [5150-42-5], (0.9999 ± 0.0003); 2,6-dimethoxyphenol (2,6-(MeO)$_2$−C_6H_3−OH) [91-10-1], (0.9998 ± 0.0001); 3,5-dimethoxyphenol (3,5-(MeO)$_2$−C_6H_3−OH) [500-99-2], (0.9990 ± 0.0005) (hygroscopic). Additionally, the final purity of the crystalline samples was confirmed from DSC analysis, while for the liquid samples GLC experiments were performed to check the purity of samples. The densities of the samples were as follows: 2-MeO−C_6H_4−OH, $\rho = 1.129$ g cm^{-3};[5] 3-MeO−C_6H_4−OH, $\rho = 1.131$ g cm^{-3};[5] 2,3-(MeO)$_2$−C_6H_3−OH, $\rho = 1.182$ g cm^{-3}.[5] From the dimensions and the mass of the pellets of 4-MeO−C_6H_4−OH, of 2,6-(MeO)$_2$−C_6H_3−OH, and of 3,5-

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* To whom correspondence should be addressed. E-mail: marmatos@fc.up.pt.

[†] Centro de Investigação em Química.

[‡] Instituto de Ciências Biomédicas Abel Salazar.

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Table 1. Typical Combustion Experiments at $T = 298.15$ K

	2-MeOPhOH	3-MeOPhOH	4-MeOPhOH	2,3-$(MeO)_2$PhOH	2,6-$(MeO)_2$PhOH	3,5-$(MeO)_2$PhOH
$m(CO_2$, total)/g	2.12180	2.32843	2.29822	1.76134	1.82657	2.01930
m(compd)/g	0.79812	0.87925	0.92334	0.70948	0.79687	0.88132
m'(fuse)/g	0.00293	0.00262	0.00421	0.00286	0.00414	0.00405
m''(Melinex)/g	0.05957	0.06209		0.05957		
ΔT_{ad}/K	1.52828	1.67508	1.66214	1.27011	1.32580	1.45953
$\epsilon_f/(J\ K^{-1})$	16.89	17.11	16.80	16.65	16.78	16.96
$\Delta m(H_2O)$/g	0.1	0.1	0.2	0.0	0.0	0.0
$-\Delta U$(IBP)/J	24487.76	26840.41	26649.40	20350.45	21242.70	23385.64
$-\Delta U$(Melinex)/J	1364.29	1422.09		1364.29		
$-\Delta U$(fuse)/J	47.58	42.55	68.37	46.45	67.23	65.77
$-\Delta U(HNO_3)$/J	1.82	2.30	1.52	1.71	0.90	6.81
$-\Delta U$(carbon)/J	0.00	0.00	0.00	0.00	0.00	0.00
ΔU(ign)/J	0.95	0.95	0.58	0.58	0.83	0.93
$-\Delta U_\Sigma$/J	15.47	17.20	16.74	12.88	13.22	14.86
$-\Delta_c u°/(J\ g^{-1})$	28891.14	28838.52	28768.14	26674.65	26555.59	26435.57

$(MeO)_2-C_6H_3-OH$, we estimated the values $\rho = 1.10$ g cm^{-3}, 1.04 g cm^{-3}, and 1.12 g cm^{-3}, respectively.

Combustion Calorimetry. The combustion experiments were performed with a static bomb calorimeter. The apparatus and technique have been described elsewhere.[6,7] Benzoic acid (Bureau of Analyzed Samples, Thermochemical Standard, BCS-CRM-190p) was used for calibration of the bomb. Its massic energy of combustion is $\Delta_c u = -(26\ 432.3 \pm 3.8)$ J g^{-1}, under certificate conditions. The calibration results were corrected to give the energy equivalent ϵ_{cal} corresponding to the average mass of water added to the calorimeter: 3119.6 g; $\epsilon_{cal} = (16\ 006.4 \pm 1.4)$ J K^{-1} was used for all measurements except for the combustion experiments involving the $4-MeO-C_6H_4-OH$, where the calibration constant $\epsilon_{cal} = (16\ 015.9 \pm 0.7)$ J K^{-1} was used. The uncertainties quoted are the standard deviations of the mean. Combustion experiments were performed in oxygen at $p = 3.04$ MPa, with 1.00 cm^3 of water added to the bomb. For all experiments, ignition was made at (298.150 ± 0.001) K. The electrical energy for ignition ΔU(ign) was determined from the change in potential difference across a capacitor when discharged through the platinum ignition wire. For the cotton-thread fuse, empirical formula $CH_{1.686}O_{0.843}$, $\Delta_c u° = -16\ 250$ J g^{-1}.[8] This value was confirmed in our laboratory. The corrections for nitric acid formation $\Delta U(HNO_3)$ were based on -59.7 kJ mol^{-1},[9] for the molar energy of formation of 0.1 mol dm^{-3} HNO_3(aq) from N_2, O_2, and H_2O(l). Sealed Melinex bags were used in combustion of the liquids, using the technique described by Skinner and Snelson,[10] who determined the specific energy of combustion of dry Melinex as $\Delta_c u° = -(22\ 902 \pm 5)$ J g^{-1}. That value was confirmed in our laboratory. The mass of Melinex used in each experiment was corrected for the mass fraction of water (0.0032).[10] The mass of the compound m(compound) used in each experiment was determined from the total mass of carbon dioxide $m(CO_2$, total) produced after allowance for that formed from the cotton-thread fuse and Melinex. An estimated pressure coefficient of specific energy $(\partial u/\partial p)_T = -0.2$ J g^{-1} MPa^{-1} (ref 11) at 298.15 K, a typical value for most organic compounds, was assumed. For each compound, the massic energy of combustion, $\Delta_c u°$, was calculated by the procedure given by Hubbard et al.[12] The molar masses used for the elements were those recommended by the IUPAC commission.[13]

Enthalpies of Sublimation and Vaporization. The enthalpies of sublimation and of vaporization were measured using the "*vacuum sublimation*" drop microcalorimetric method,[14] which, in the case of vaporization, was previously tested in the Porto laboratory.[15] Samples, about 3 to 5 mg of each solid compound and 7 to 11 mg of the liquids, contained in thin glass capillary tubes sealed at one end, were dropped, at room temperature, into the hot reaction vessel, in a high-temperature Calvet microcalorimeter held at a convenient temperature T, and then removed from the hot zone by *vacuum* evaporation. The observed enthalpies of evaporation were corrected to $T = 298.15$ K by using the value of $\Delta_{298.15K}^{T} H_m°(g)$ estimated by a group method with values from Stull *et al.*[16] The microcalorimeter was calibrated in situ for these measurements by using the reported enthalpies of sublimation of naphthalene[16] and of vaporization of undecane.[17]

Experimental Results

Results for a typical combustion experiment of each compound are given in Table 1, where $\Delta m(H_2O)$ is the deviation of the mass of water added to the calorimeter from 3119.6 g, and ΔU_Σ is the correction to the standard state. The remaining quantities are as previously defined.[12] As samples were ignited at $T = 298.15$ K, $\Delta U(IBP) = -\{\epsilon_{cal} + \Delta m(H_2O)c_p(H_2O, l) + \epsilon_f\}\Delta T_{ad} + \Delta U(ign)$, where ΔU(IBP) is the energy associated with the isothermal bomb process, ϵ_f is the energy of the bomb contents after ignition, and ΔT_{ad} is the adiabatic temperature raise. The individual results of all combustion experiments, together with the mean value and its standard deviation, are given for each compound in Table 2. Table 3 lists the derived standard molar energies and enthalpies of combustion, $\Delta_c U_m°$(cr, l) and $\Delta_c H_m°$(cr, l), and the standard molar enthalpies of formation for the compounds in the condensed phase, $\Delta_f H_m°$(cr, l) at $T = 298.15$ K. In accordance with normal thermochemical practice, the uncertainties assigned to the standard molar enthalpies of combustion are, in each case, twice the overall standard deviation of the mean and include the uncertainties in calibration[18] and in the values of auxiliary quantities. To derive $\Delta_f H_m°$(cr, l) from $\Delta_c H_m°$(cr, l), the standard molar enthalpies of formation of H_2O(l) and CO_2(g), at $T = 298.15$ K, $-(285.830 \pm 0.042)$ kJ mol^{-1} (ref 19) and $-(393.51 \pm 0.13)$ kJ mol^{-1},[19] respectively, were used. Measurements of the enthalpies of sublimation or of vaporization are given in Table 4 with uncertainties of twice the standard deviation of the mean. The derived enthalpies of formation, in both the condensed and gaseous phases, for all the compounds are summarized in Table 5.

NIST WebBook[20] refers to a value for the enthalpy of formation of crystalline 2,6-dimethoxyphenol, -518.4 kJ mol^{-1}, which does not show any uncertainty, and it is quite different from the value we obtained in this work, $-(480.1 \pm 1.6)$ kJ mol^{-1}. It is noticeable that the same experimentalists have obtained for the enthalpy of formation of crystalline 2,6-dimethylphenol the value -250 kJ mol^{-1}, which is also in significant disagreement with other values determined by other experimentalists and cited in the

Table 2. Individual Values of the Massic Energy of Combustion of the Methoxy- and Dimethoxyphenols, at T = 298.15 K

$-\Delta_c u°/(J\ g^{-1})$					
2-MeOPhOH	3-MeOPhOH	4-MeOPhOH	2,3-(MeO)$_2$PhOH	2,6-(MeO)$_2$PhOH	3,5-(MeO)$_2$PhOH
28 912.88	28 826.26	28 765.88	26 689.32	26 553.25	26 441.00
28 907.39	28 835.45	28 761.50	26 662.68	26 564.77	26 435.57
28 900.81	28 823.15	28 773.75	26 677.25	26 557.15	26 408.34
28 884.69	28 838.52	28 778.33	26 667.03	26 559.23	26 438.48
28 880.53	28 818.95	28 761.87	26 689.33	26 565.02	26 413.97
28 891.08	28 844.60	28 768.14	26 676.32	26 549.65	26 417.12
28 870.65	28 838.28		26 663.76	26 555.59	26 432.79
28 890.23	28 822.57		26 674.65	26 560.80	26 434.52
28 891.14			26 664.77	26 575.09	
28 899.44					
$-\langle\Delta_c u°\rangle$ (J g^{-1})					
28 892.9 ± 4.0	28 831.0 ± 3.3	28 768.2 ± 2.7	26 673.9 ± 3.4	26 560.1 ± 2.5	26 427.7 ± 4.4

Table 3. Derived Standard ($p°$ = 0.1 MPa) Molar Values at T = 298.15 K for the Energy and the Enthalpy of Combustion, $\Delta_c U_m°$ and $\Delta_c H_m°$, and the Enthalpy of Formation, $\Delta_f H_m°$, of the Methoxyphenols in the Condensed Phase

	$-\Delta_c U_m°$(cr, l)	$-\Delta_c H_m°$(cr, l)	$-\Delta_f H_m°$(cr, l)
	kJ mol^{-1}	kJ mol^{-1}	kJ mol^{-1}
2-MeOPhOH(l)	3586.7 ± 1.5	3589.2 ± 1.5	308.7 ± 1.8
3-MeOPhOH(l)	3579.1 ± 1.4	3581.6 ± 1.4	316.3 ± 1.7
4-MeOPhOH(cr)	3571.3 ± 0.9	3573.8 ± 0.9	324.1 ± 1.3
2,3-(MeO)$_2$PhOH(l)	4112.2 ± 1.7	4114.7 ± 1.7	462.5 ± 2.0
2,6-(MeO)$_2$PhOH(cr)	4094.6 ± 1.2	4097.1 ± 1.2	480.1 ± 1.6
3,5-(MeO)$_2$PhOH(cr)	4074.2 ± 1.7	4076.7 ± 1.7	500.5 ± 2.0

NIST WebBook, −(237.4 ± 1.1) kJ mol^{-1} and −(233.1 ± 2.9) kJ mol^{-1}.

Theoretical Calculations

The most stable conformations of all possible methoxy- and dimethoxyphenol isomers as well as of their corresponding phenoxyl radicals and phenoxide anions were obtained using density functional theory (DFT) with the Becke three-parameter hybrid exchange[21] and Lee−Yang−Parr[22] correlation density functional (B3LYP) and the Pople's split-valence 6-31G** extended basis set.[23] Harmonic vibrational frequencies were calculated through construction and diagonalization of the Hessian matrixes at the obtained optimum molecular geometries, using the same basis set. This procedure allowed us to characterize these equilibrium geometries as true minima and to obtain the corrections needed to estimate energies at any temperature different from 0 K. Following standard procedure, the harmonic vibrational frequencies were scaled by the factor[24] 0.96 in order to correct for anharmonicity. More accurate energies were then obtained for all systems by using the B3LYP functional and the Pople's 6-311G** extended basis set.[23,25] Yet another set of accurate calculations, using the nonlocal functionals of Becke[26] (exchange) and Perdew[27] (correlation), were also performed for all systems at their most stable B3LYP/6-31G** geometries. For these calculations, hereafter denoted by the acronym BP, we used a basis set, properly optimized for density functional calculations,[28] which is roughly equivalent in size to the Pople's 6-311G** one and which represents the H atom by a (41/1*) contraction pattern and the first-row atoms by a (7111/411/1*) contraction pattern (using the Huzinaga notation).[29] All calculations were performed using the U.K. version of GAMESS[30,31] and an academic version of the deMon program.[32]

Optimum Conformations

The most stable conformations for these systems are mainly determined by the balance of two antagonistic phenomena: (i) electron conjugation effects involving the aromatic ring and the π-electron donor methoxyl group (These interactions are favored by the coplanarity between the substituents and the ring.) and (ii*)* steric repulsions between *ortho* groups which force the methoxyl group to adopt an out of plane conformation relative to the ring. Table 6 (see Figure 1 for the conventional numbering of the atoms) shows the dihedral angles defining the orientation of the hydroxyl and the methoxyl groups for all these molecules at their optimum B3LYP/6-31G** geometries.

The obtained optimum geometries reflect the general trends which would be expected from the above considerations. Thus, the O−H bonds of the substituted methoxy phenol molecules are found to be in the plane of the aromatic ring, a well-known behavior found earlier for other substituted phenols.[1] This preference evidences the greater effectiveness of the interaction of the π lone-electronic-pair of the oxygen atom with the aromatic ring π orbitals, relative to the corresponding interaction involving the oxygen σ lone-electronic-pair. Nevertheless, for 2,3-dimethoxyphenol, the steric repulsions between the very proximate substituents and the hydroxyl group force the O−H bond to deviate from planarity, as evidenced by the dihedral angle $C_2C_1O_7H_{12}$ of ~3.0°.

The $-OCH_3$ substituents also display a tendency for adopting conformations which are coplanar with the aromatic ring, a fact that can be understood on the basis of considerations similar to the above ones, since this substituent can also exchange π-electrons with the aromatic ring. Note that this preference for planar conformations is observed for the closed-shell as well as for the anionic and radical species. The only noticeable exceptions to this behavior occur, in the case of the closed-shell species, for 2,3-dimethoxyphenol and 3,4-dimethoxyphenol; for these isomers the circumstance of the substituents being very close together or even very close to the −OH group introduces destabilizing factors, dominated by the steric repulsions between the substituents, thus favoring the conformations for which one of the substituents adopts a conformation orthogonal to the aromatic ring. The substituent which adopts such a conformation is the *ortho* one in the case of 2,3-dimethoxyphenol and the *para* one for 3,4-dimethoxyphenol. The stabilization energy which is gained by such a process clearly exceeds the destabilization resulting from a less effective π-electron exchange between the substituents and the ring.

It is also observed that, in the most stable conformation of all phenols having a substituent at the *ortho* position, the H atom of the hydroxyl group points toward the *ortho* methoxyl substituent, a preference that results in further stabilization, since an intramolecular hydrogen bond interaction presumably comes into play. The H···O(CH$_3$)

Table 4. Microcalorimetric Standard ($p° = 0.1$ MPa) Molar Enthalpies of Vaporization and Sublimation at $T = 298.15$ K for the Methoxyphenols

	no. of expts	T K	$\Delta_{\mathrm{cr,l}}^{\mathrm{g},T}H_{\mathrm{m}}^{\circ}$ kJ mol^{-1}	$\Delta_{298.15\mathrm{K}}^{T}H_{\mathrm{m}}^{\circ}(\mathrm{g})$ kJ mol^{-1}	$\Delta_{\mathrm{cr,l}}^{\mathrm{g}}H_{\mathrm{m}}^{\circ}(T = 298.15\ \mathrm{K})$ kJ mol^{-1}
2-MeOPhOH(l)	5	375	74.5 ± 0.5	11.9	62.6 ± 0.5
3-MeOPhOH(l)	7	375	87.8 ± 1.2	11.9	75.9 ± 1.2
4-MeOPhOH(cr)	6	375	106.3 ± 1.2	11.9	94.4 ± 1.2
2,3-$(\mathrm{MeO})_2$PhOH(l)	5	369	89.9 ± 1.0	13.4	76.5 ± 1.0
2,6-$(\mathrm{MeO})_2$PhOH(cr)	5	375	112.9 ± 1.1	14.5	98.4 ± 1.1
3,5-$(\mathrm{MeO})_2$PhOH(cr)	6	368	114.3 ± 2.3	13.2	101.1 ± 2.3

Table 5. Derived Standard ($p° = 0.1$ MPa) Molar Values at $T = 298.15$ K for the Enthalpies of Formation of the Gaseous Isomers

	$-\Delta_{\mathrm{f}}H_{\mathrm{m}}^{\circ}(\mathrm{cr,\ l})$ kJ mol^{-1}	$\Delta_{\mathrm{cr,l}}^{\mathrm{g}}H_{\mathrm{m}}^{\circ}$ kJ mol^{-1}	$-\Delta_{\mathrm{f}}H_{\mathrm{m}}^{\circ}(\mathrm{g})$ kJ mol^{-1}
2-MeOPhOH	308.7 ± 1.8	62.6 ± 0.5	246.1 ± 1.9
3-MeOPhOH	316.3 ± 1.7	75.9 ± 1.2	240.4 ± 2.1
4-MeOPhOH	324.1 ± 1.3	94.4 ± 1.2	229.7 ± 1.8
2,3-$(\mathrm{MeO})_2$PhOH	462.5 ± 2.0	76.5 ± 1.0	386.0 ± 2.2
2,6-$(\mathrm{MeO})_2$PhOH	480.1 ± 1.6	98.4 ± 1.1	381.7 ± 1.9
3,5-$(\mathrm{MeO})_2$PhOH	500.5 ± 2.0	101.1 ± 2.3	399.4 ± 3.0

distances are found to be 2.086 Å, 2.084 Å, 2.098 Å, 2.087 Å, and 2.070 Å, respectively, for 2-methoxyphenol and 2,3-, 2,4-, 2,5-, and 2,6-dimethoxyphenol. These values, being lower than the sum of the oxygen (1.4 Å) and hydrogen (1.2 Å) van der Waals radii, provide further support to the conjecture that an intramolecular hydrogen bond occurs in these systems. Such an intramolecular hydrogen bond has been reported from experimental results[33] for 2-methoxyphenol, but no experimental information is available for phenols with more than one methoxyl substituent. The hydrogen bond energies were calculated as the energy difference between the cis and the trans conformers, assuming that the trans conformation does not allow the occurrence of the hydrogen bond (the trans conformations have also been completely optimized). For 2,6-dimethoxyphenol, however, both conformations allow an hydrogen bond to occur. Thus, using this procedure, the hydrogen bond for this isomer cannot be estimated. The following results were obtained from the B3LYP/6-311G** energies: 2-methoxyphenol, 20.05 kJ mol^{-1}; 2,3-dimethoxyphenol, 22.63 kJ mol^{-1}; 2,4-dimethoxyphenol, 19.51 kJ mol^{-1}; 2,5-dimethoxyphenol, 23.07 kJ mol^{-1}.

The radicals prefer to adopt conformations with the substituents coplanar with the aromatic ring. The only exceptions to this behavior are 2,3- and 3,4-dimethoxyphenoxyl radicals where the effect of the steric repulsions between the proximate methoxyl groups results in the nonplanar conformation of one of the substituents. For both cases, the nonplanar conformation is adopted by the *meta* substituent. This preference is well understood by observing that, since the methoxyl substituent behaves as a π-electron donor whereas the oxygen atom is a π-electron acceptor, they interact cooperatively, thus stabilizing the system; however, as explained below, this interaction is much weaker when the substituent is *meta* relative to the hydroxyl group. On the other hand, the coplanarity of the substituents and the ring favors this type of interactions. Thus, maintaining the *ortho* substituent coplanar with the ring must be energetically more favorable than maintaining the coplanarity of the *meta* one.

The methyl group of the *ortho* methoxyl substituents is always oriented toward the oxygen atom of the radicals, a preference which may presumably result from a stabilizing interaction between this methyl group and the radical oxygen.[33] For 2,6-dimethoxyphenoxyl one substituent points toward and the other points away from the oxygen atom.

For the anionic systems the electronic interactions between the substituents and $-\mathrm{O}^-$ tend to be destabilizing, since now the last group is a very strong π-electron donor. As a consequence, a so-called π-electron saturation effect can manifest itself, and a preference for conformations with the substituents not coplanar with the ring is observed. Exceptions to this behavior occur only for the 3-methoxyphenoxide anion and also for 2,5-, 3,4-, and 3,5-dimethoxyphenoxide anions, which have the *meta* substituent coplanar with the ring. For these systems all the groups attached to the aromatic ring are π-electron donors and σ-electron acceptors, but whereas the $-\mathrm{OH}$ group in the closed-shell systems is a moderate π-electron donor and a very strong σ-electron acceptor, now the $-\mathrm{O}^-$ group is a very strong π-electron donor and a mild σ-electron acceptor. This results in much stronger electronic interactions between the substituents in the anionic species than those in the closed-shell ones. Furthermore, in both classes of systems this interaction results in an attenuation of each individual interaction between the substituents and the ring, since all substituents tend to donate π-electronic charge to the same aromatic ring and to withdraw σ-electrons also from the same ring. The π-electron donation to the ring assumes particular importance, since it depends very strongly on the relative positions occupied by the substituent groups in the ring, contrary to the σ-electron withdrawal, which is essentially independent. Such dependence results from the particular symmetry properties of the ring π higher occupied molecular orbital (HOMO) and π^* lower unoccupied molecular orbital (LUMO) orbitals, which have particularly large contributions from the p_π orbitals of those ring carbon atoms which are in the *para* position relative to the $-\mathrm{OH}$ or $-\mathrm{O}^-$ groups and much smaller contributions from those of the remaining ring carbon atoms. In this way, the interactions between the two π-electron donor groups are much stronger for 4-methoxyphenoxide anion than for the homologous *ortho* and *meta* monosubstituted anions. Thus, for these molecules the above-mentioned saturation effect becomes so important that the π-electron interaction can become really destabilizing. The mechanism thus adopted for minimizing the destabilization is the preference for an orthogonal conformation with the exception of the *meta* $-\mathrm{OCH}_3$ substituent, which interacts very weakly with the $-\mathrm{OH}$ group.

The predicted C$-$(OH) bond lengths do not vary significantly within each class of compounds: substituted phenol molecules, 1.36 to 1.37 Å; substituted phenoxide anions, 1.26 to 1.28 Å; substituted phenoxyl radicals, 1.25 to 1.26 Å. These values are intermediate between the experimental values of the single CO bond length in phenol, 1.375 Å,[34] and the double CO bond length in benzoquinone, 1.225 Å.[35] The observed decrease in the CO bond length relative to the case of unsubstituted phenol is an evidence of the progressive increase of the double-bond character of the

Table 6. Dihedral Angles (deg) Defining the Orientation of the Hydroxyl and Methoxyl Groups in the Methoxy-Substituted Phenols, Phenoxyl Radicals, and Phenoxide Anions

	closed-shell			radical		anion	
substituent	$C_2C_1O_7H_{12}$	$C_bC_bO_8C_9$	$C_bC_bO_{10}C_{11}$	$C_bC_bO_8C_9$	$C_bC_bO_{10}C_{11}$	$C_bC_bO_8C_9$	$C_bC_bO_{10}C_{11}$
H	0.0						
2-MeO	0.0	0.0		180.0		125.0	
3-MeO	180.0	180.0		180.0		180.0	
4-MeO	0.0	180.0		180.0		90.3	
2,3-(MeO)$_2$	−3.0	66.6	−1.3	175.4	−113.3	113.1	−107.1
2,4-(MeO)$_2$	0.0	0.0	0.0	180.0	180.0	119.8	−92.7
2,5-(MeO)$_2$	0.0	0.2	0.0	180.0	0.0	−120.9	1.3
2,6-(MeO)$_2$	0.4	1.6	179.2	179.9	0.0	117.5	−63.4
3,4-(MeO)$_2$	−179.6	−176.5	102.4	−81.5	3.0	−177.6	98.8
3,5-(MeO)$_2$	0.0	180.0	0.0	180.0	0.0	180.0	0.0

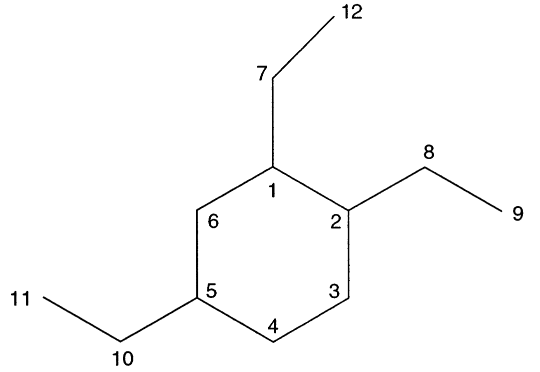

Figure 1. Atom numbering scheme.

CO bond as we consider the methoxy-substituted phenol molecules, the anions, and the radicals, in this order: an increasing which is also consistent with the relative importance, within each class of compounds, of the π-electron interactions with the ring described above.

OH Rotational Barrier. The barrier for internal rotation of the hydroxyl group in phenol and in the methoxy-substituted phenol isomers has been calculated, at the B3LYP/6-311G** level, as the energy difference between the orthogonal and planar conformations (the orthogonal conformations have also been completely optimized). After proper correction for the hydrogen bond interaction for the *ortho*-substituted methoxyphenols (with the exception of 2,6-dimethoxyphenol, for which it is not possible to estimate the hydrogen bond energy), the following estimates were obtained for the intrinsic interaction energies resulting from the electronic delocalization involving the hydroxyl group, the substituents, and the aromatic ring: 15.53 kJ mol^{-1}, 10.51 kJ mol^{-1}, 17.18 kJ mol^{-1}, 11.99 kJ mol^{-1}, 9.22 kJ mol^{-1}, 6.15 kJ mol^{-1}, 8.32 kJ mol^{-1}, 24.43 kJ mol^{-1}, 14.37 kJ mol^{-1}, and 15.45 kJ mol^{-1}, respectively, for phenol and 2-, 3-, 4-, 2,3-, 2,4-, 2,5-, 2,6-, 3,4-, and 3,5-methoxy-substituted phenols. The calculated values for phenol show a very good agreement with the experimental values obtained from microwave spectroscopy in the gas-phase: 13.729 kJ mol^{-1} [36] and 14.130 kJ mol^{-1}.[37] To our knowledge, no experimental values for the height of the OH rotational barrier in methoxy-substituted phenols are available.

It is interesting to note the general trend toward a decrease of the rotational barrier when compared with that for nonsubstituted phenol. This decrease may reflect the destabilizing effect of the substituents which are trying to donate π-electron density to the same aromatic ring to which the hydroxyl group is already donating π-electron density. This lowering of the barrier height is more pronounced when two methoxyl substituents are present, and in the case of monosubstituted phenols, it is obvious its dependence on the position of the substituent, a *meta* substituent, originates an increase instead of a lowering of the barrier height. This reinforcement of the interaction results from the fact that in this case the hydroxyl and methoxyl groups interact with different π-orbitals of the ring.

Stability. To study the stability of these systems, we have considered two different types of isodesmic reactions. The first one, denoted by set I in the tables, involves the reactions

$$\mathrm{MeO{-}C_6H_4{-}OH + CH_4 \rightarrow C_6H_5{-}OH + CH_3OCH_3} \quad (2)$$

$$\mathrm{(MeO)_2{-}C_6H_3{-}OH + 2CH_4 \rightarrow C_6H_5{-}OH + 2CH_3OCH_3} \quad (3)$$

whose energy variations represent the effect of the methoxyl group on the stability of the phenolic ring measured relative to its effect on the stability of methane. The calculated reaction energies ($T = 0$ K) and enthalpies ($T = 298.15$ K), together with the experimental values, are presented in Table 7 (all the necessary experimental values for the auxiliary compounds were taken from ref 17). The theoretical results obtained from this type of reaction are in good agreement with the experimentally observed ones, the largest error obtained being only 11.5 kJ mol^{-1} for the B3LYP results and 12.6 kJ mol^{-1} for the BP calculations.

Also the following isodesmic reactions (set II)

$$\mathrm{MeO{-}C_6H_4{-}OH + C_6H_6 \rightarrow C_6H_5{-}OH + MeO{-}C_6H_5} \quad (4)$$

$$\mathrm{(MeO)_2{-}C_6H_3{-}OH + C_6H_6 \rightarrow C_6H_5{-}OH + (MeO)_2{-}C_6H_4} \quad (5)$$

were considered in this work, the energy variations of which represent the effect of the introduction of the methoxyl group in the phenolic ring measured relative to same effect on the benzene ring. The resulting reaction energies ($T = 0$ K) and enthalpies ($T = 298.15$ K) are also shown in Table 7 together with the corresponding experimental values (all the necessary experimental values for the auxiliary compounds were taken from ref 17, with the exception of the values for the dimethoxybenzene isomers, which were taken from ref 38). The results reproduce very closely the experimental values, with errors not higher than 9.6 kJ mol^{-1} and 9.7 kJ mol^{-1}, respectively, for the B3LYP and BP results.

Table 8 shows the theoretical estimates of the standard enthalpies of formation in the gas phase, obtained from the last set of isodesmic reactions, for all methoxy-substituted phenols, including those not studied experimentally, together with the available experimental values.

Table 7. Calculated Reaction Energies at $T = 0$ K and Enthalpies at $T = 298.15$ K in kJ mol^{-1}

	reaction I					reaction II				
	$\Delta_rE_{T=0K}$		$\Delta_rH^\circ_{T=298.15K}$			$\Delta_rE_{T=0K}$		$\Delta_rH^\circ_{T=298.15K}$		
	B3LYP	BP	B3LYP	BP	exp	B3LYP	BP	B3LYP	BP	exp
2-MeO	44.3	45.0	46.0	46.6	40.0 ± 2.2	4.4	4.0	3.3	3.0	−(0.8 ± 2.4)
3-MeO	41.6	42.2	44.0	44.6	34.3 ± 2.4	1.6	1.2	1.3	0.9	−(6.5 ± 2.5)
4-MeO	32.5	33.6	35.1	36.2	23.6 ± 2.1	−7.5	−7.4	−7.6	−7.5	−(17.2 ± 2.3)
2,3-(MeO)$_2$	71.2	70.2	75.7	74.7	70.2 ± 2.7	13.6	18.0	11.8	16.2	4.6 ± 4.2
2,4-(MeO)$_2$	78.8	79.8	83.2	84.2		−2.7	−2.7	−3.7	−3.6	
2,5-(MeO)$_2$	79.3	79.3	83.7	83.7		6.6	4.6	5.6	3.6	
2,6-(MeO)$_2$	67.4	70.4	72.0	75.0	65.9 ± 2.5	−14.1	−12.1	−14.8	−12.8	−(19.1 ± 3.3)
3,4-(MeO)$_2$	58.0	55.3	63.5	60.8		0.4	3.1	−0.4	2.4	
3,5-(MeO)$_2$	79.6	79.3	84.7	84.5	83.8 ± 3.4	−2.0	−3.2	−2.1	−3.2	−(1.2 ± 4.0)

Table 8. Theoretical Estimates of the Standard Enthalpies of Formation in the Gaseous Phase at $T = 298.15$ K (kJ mol^{-1})

	$\Delta_fH^\circ_m$(calc)		
	B3LYP	BP	$\Delta_fH^\circ_m$(exp)
2-methoxyphenol	−250.2	−249.9	−(246.1 ± 1.9)
3-methoxyphenol	−248.2	−247.8	−(240.4 ± 2.1)
4-methoxyphenol	−239.3	−239.4	−(229.7 ± 1.8)
2,3-dimethoxyphenol	−393.2	−397.6	−(386.0 ± 2.2)
2,4-dimethoxyphenol	−397.1	−397.2	
2,5-dimethoxyphenol	−396.1	−394.1	
2,6-dimethoxyphenol	−386.0	−388.0	−(381.7 ± 1.9)
3,4-dimethoxyphenol	−381.0	−383.8	
3,5-dimethoxyphenol	−398.7	−397.6	−(399.4 ± 3.0)

Table 9. Theoretical Estimates of the Standard Enthalpies of Formation in the Gaseous Phase at $T = 298.15$ K for the Methoxy-Substituted Phenoxyl Radicals and Phenoxide Anions (kJ mol^{-1})

	radical		anion	
	$\Delta_fH^\circ_m$(calc)		$\Delta_fH^\circ_m$(calc)	
	B3LYP	BP	B3LYP	BP
2-methoxyphenoxyl	−110.1	−110.4	−314.2	−309.9
3-methoxyphenoxyl	−102.7	−104.3	−316.6	−314.7
4-methoxyphenoxyl	−112.7	−114.7	−300.6	−296.3
2,3-dimethoxyphenoxyl	−245.6	−250.5	−460.4	−457.6
2,4-dimethoxyphenoxyl	−276.1	−278.3	−455.3	−447.9
2,5-dimethoxyphenoxyl	−258.5	−262.4	−468.2	−461.2
2,6-dimethoxyphenoxyl	−260.3	−263.0	−465.2	−456.6
3,4-dimethoxyphenoxyl	−248.1	−253.5	−452.2	−453.2
3,5-dimethoxyphenoxyl	−258.3	−260.7	−473.8	−470.4

For the radicals and anions we have just considered, the following isodesmic and isogyric reactions, homologous to those in set II above, apply.

$$\mathrm{MeO{-}C_6H_4{-}O^\bullet + C_6H_6 \rightarrow C_6H_5O^\bullet + MeO{-}C_6H_5} \quad (6)$$

$$\mathrm{(MeO)_2{-}C_6H_3{-}O^\bullet + C_6H_6 \rightarrow C_6H_5O^\bullet + (MeO)_2{-}C_6H_4} \quad (7)$$

$$\mathrm{MeO{-}C_6H_4{-}O^- + C_6H_6 \rightarrow C_6H_5O^- + MeO{-}C_6H_5} \quad (8)$$

$$\mathrm{(MeO)_2{-}C_6H_3{-}O^- + C_6H_6 \rightarrow C_6H_5O^- + (MeO)_2{-}C_6H_4} \quad (9)$$

The estimates of the formation enthalpies obtained from both sets of calculations for the phenoxyl radicals and phenoxide anions are collected in Table 9. Even though the lack of experimental information regarding the thermochemistry of these systems prevents the rigorous validation of our results, we believe that these estimates should have a degree of reliability similar to those obtained for the closed-shell systems.

An analysis of the predicted enthalpies of formation for the closed-shell as well as for the radical systems, and a comparison with the known experimental enthalpies of formation of phenol,[17] −96.4 kJ mol^{-1}, and of phenoxyl radical,[39] 54.0 kJ mol^{-1}, shows that the radicals are more stabilized by the presence of the methoxyl substituent when compared to the homologous closed-shell molecules. This observation, which could be anticipated on the basis of the nature of the π-electron interactions between the substituents and the oxygen atom or the hydroxyl group discussed above, allows us to expect a weakening of the O−H bond, relative to homolytic dissociation, resulting from the methoxy substitution. On the other hand, similar arguments lead to the conclusion that the phenoxide anions are destabilized (relative to the homologous closed-shell systems) by the methoxyl substituents, which results now from the unfavorable interaction between the strong π-electron donor oxygen atom and the π-electron donor methoxyl group. Thus, a general trend to a strengthening of the O−H bond, relative to the heterolytic bond dissociation, is expected.

O−H Bond Dissociation Energies. The effect of the methoxyl substituents on the O−H bond strengths of the substituted phenol molecules must reflect the corresponding effect upon the stability of the closed-shell and the homologous radical or anionic systems. The homolytic O−H bond dissociation energy ($T = 0$ K), D_e(O−H), and the corresponding bond dissociation enthalpy ($T = 298.15$ K), D_h(O−H), are defined, respectively, as the energy and enthalpy variations associated with the following bond breaking reactions:

$$\mathrm{MeO{-}C_6H_4{-}OH \rightarrow MeO{-}C_6H_4{-}O^\bullet + H^\bullet} \quad (10)$$

$$\mathrm{(MeO)_2{-}C_6H_3{-}OH \rightarrow (MeO)_2{-}C_6H_3{-}O^\bullet + H^\bullet} \quad (11)$$

Estimates of these properties have been calculated directly from the definition, and the results are collected in Table 10. Our calculations predict the values 350.9 kJ mol^{-1} and 361.0 kJ mol^{-1}, obtained, respectively, from the B3LYP and the BP energies, for the homolytic O−H bond dissociation enthalpy of phenol. The BP estimate is in very good agreement with the value 368.4 kJ mol^{-1} obtained from the experimental formation enthalpies of phenol and phenoxyl radical and is also much closer to the selected experimental value,[4a] (371.3 ± 2.3) kJ mol^{-1}, than the B3LYP estimate.

The effect of the methoxyl substituents is to weaken the O−H bond in what respects to the homolytic bond breaking processes, the calculated decrease, ΔD_h(O−H), ranging from about 2 kJ mol^{-1} to 30 kJ mol^{-1}. The ΔD_h(O−H) values calculated from the two sets of energies are consistent with each other and are also in good agreement with the recommended values by Santos and Simões[4a] and with experimental data obtained from photoacoustic calorimetry measurements.[33] The only noticeable disagreement with

Table 10. Calculated DFT Homolytic O−H Bond Dissociation Energies (kJ mol^{-1})

	D_e(O−H)		D_h(O−H)		ΔD_h(O−H)		ΔD_h(O−H)		D_h(O−H)	
substituent	B3LYP	BP	B3LYP	BP	B3LYP	BP	exp[4a]	exp[33]	B3LYP	BP
H	374.7	384.9	347.5	357.7	0.0	0.0	0.0	0.0		
2-MeO	364.6	374.1	337.6	347.0	−9.9	−10.7	−17 ± 4	1.6	358.1	361.5
3-MeO	370.3	378.5	342.9	351.1	−4.6	−6.6	0 ± 4		363.5	358.1
4-MeO	350.7	358.4	324.6	332.3	−22.9	−25.4	−22 ± 4	−20.5	344.6	342.2
2,3-(MeO)$_2$	372.5	382.1	345.1	354.8	−2.4	−2.9			365.6	365.1
2,4-(MeO)$_2$	346.0	354.0	318.5	326.5	−29.1	−31.2		−19.7	339.0	336.9
2,5-(MeO)$_2$	361.7	366.0	335.0	339.3	−12.6	−18.4			352.2	346.4
2,6-(MeO)$_2$	349.5	358.9	323.2	332.6	−24.3	−25.1	−21 ± 8	−26.4	343.7	343.0
3,4-(MeO)$_2$	356.9	364.3	330.4	337.9	−17.1	−19.8			348.0	345.4
3,5-(MeO)$_2$	365.1	371.8	337.8	344.4	−9.7	−13.2	−7 ± 8		358.4	354.9

Table 11. Parent and Radical Contributions to ΔD_e(O−H) in Methoxy- and Dimethoxyphenols in kJ mol^{-1}

	homolytic bond dissociation						heterolytic bond dissociation			
	B3LYP			BP			B3LYP		BP	
substituent	ΔD_e(O−H)	$\Delta^{pc}D_e$	$\Delta^{rc}D_e$	ΔD_e(O−H)	$\Delta^{pc}D_e$	$\Delta^{rc}D_e$	ΔD_e(O−H)	$\Delta^{ac}D_e$	ΔD_e(O−H)	$\Delta^{ac}D_e$
H	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
2-MeO	−10.1	−4.4	−14.5	−10.8	−4.0	−14.9	1.4	−3.0	5.3	1.3
3-MeO	−4.4	−1.6	−6.1	−6.4	−1.2	−7.6	−4.3	−6.0	−2.9	−4.1
4-MeO	−24.0	7.5	−16.6	−26.5	7.4	−19.1	3.5	10.9	7.8	15.2
2,3-(MeO)$_2$	−2.3	−13.6	−15.8	−2.8	−18.0	−20.8	−1.8	−15.4	5.4	−12.6
2,4-(MeO)$_2$	−28.8	2.7	−26.0	−30.9	2.7	−28.2	7.7	10.4	15.2	17.9
2,5-(MeO)$_2$	−13.0	−6.6	−19.6	−18.9	−4.6	−23.5	−5.6	−12.1	−0.5	−5.1
2,6-(MeO)$_2$	−25.2	14.1	−11.1	−26.0	12.1	−13.9	−13.8	0.3	−3.1	8.9
3,4-(MeO)$_2$	−17.9	−0.4	−18.2	−20.6	−3.1	−23.7	−7.1	−7.5	−5.4	−8.5
3,5-(MeO)$_2$	−9.6	2.0	−7.6	−13.1	3.2	−10.0	−11.3	−9.3	−9.0	−5.9

the experimental available data refers to 2-methoxyphenol, for which the PAC experiments predict a strengthening of about 2 kJ mol^{-1} whereas our results predict a weakening of about 10 kJ mol^{-1}, consistent with the decrease observed for the remaining systems and with the recommended values.[4a] However, since the reported experimental error of the PAC estimates is about 6 kJ mol^{-1}, that obscures whether there is net strengthening or weakening of the O−H bond. On the other hand, we must also stress that a lowering of the homolytic O−H bond dissociation energy is expected on the basis of the phenomena, described above, which determine the relative stabilization of the closed-shell molecules and of the radicals upon methoxyl substitution.

The relative values, ΔD_h(O−H), are presumably more reliable than the corresponding absolute values of the homolytic bond dissociation enthalpies, D_h(O−H); better estimates of this property can however be obtained by using the estimated formation enthalpies for the closed-shell and for the radical systems (Tables 8 and 9). The bond dissociation enthalpies obtained in this way, with the exception of that of nonsubstituted phenol, are reported in the last two columns of Table 10.

The overall substituent effect on the O−H bond dissociation energy can be usefully partitioned into the effect the substituent has in the radicals (radical contribution, rc) and its effect in the closed-shell molecules (parent contribution, pc). The importance of each effect can be evaluated from the energy variation of the reactions

$$\mathrm{MeO{-}C_6H_5 + C_6H_5OH \rightarrow MeO{-}C_6H_4{-}OH + C_6H_6} \qquad (12)$$

$$\mathrm{(MeO)_2{-}C_6H_4 + C_6H_5OH \rightarrow (MeO)_2{-}C_6H_3{-}OH + C_6H_6} \qquad (13)$$

$$\mathrm{MeO{-}C_6H_5 + C_6H_5O^{\bullet} \rightarrow MeO{-}C_6H_4{-}O^{\bullet} + C_6H_6} \qquad (14)$$

$$\mathrm{(MeO)_2{-}C_6H_4 + C_6H_5O^{\bullet} \rightarrow (MeO)_2C_6H_3{-}O^{\bullet} + C_6H_6} \qquad (15)$$

which represent, respectively, the effect of the methoxyl substituent on the stability of the closed-shell molecule and of the radicals, both measured relative to the effect on benzene. The results of this analysis are shown in Table 11 under the headings $\Delta^{pc}D_e$(O−H) and $\Delta^{rc}D_e$(O−H). It can be observed from these results that all phenoxyl radicals are stabilized by the methoxyl substituent and, on the other hand, the closed-shell molecules are either stabilized or destabilized by the methoxyl group. Nevertheless, the observed weakening of the O−H bond dissociation energy is largely determined by the stabilizing effect of the methoxyl group on the phenoxyl radicals and only to a slight extent by the effect on the closed-shell molecules.

The effects observed in the radicals and the closed-shell molecules can be rationalized in terms of the electronic interactions between the substituents and the hydroxyl group, which occur neccessarily through the aromatic ring.

The π-electronic charge density and the spin density transfers for all systems have been calculated using the natural bond orbitals (NBOs) formalism.[40] The results, shown in Tables 12 and 13, allow us to observe that the π-electronic charge density on the oxygen atom of all methoxyphenoxyl radicals increases as a consequence of the methoxyl substitutions, when compared to that of nonsubstituted phenoxyl radical. This increase is associated with the favorable interaction between the π-electron acceptor oxygen atom and the π-electron donor methoxyl substituents, resulting in a reinforcing of both opposite tendencies. For the methoxyphenoxyl radicals having at least a substituent in *meta* position, an attenuation of that cooperation between the two groups occurs, a fact that is associated with the spatial symmetry properties of the higher occupied molecular orbital and the lower vacant molecular orbital of the aromatic ring, as described above. This effect is of particular relevance for 3,5-dimethoxyphenoxyl radical.

Another effect closely connected to the stabilization of the methoxyphenoxyl radicals is the possibility for a greater delocalization of the electronic spin afforded by the methoxyl substituents. Since these radicals are π-radicals, the

Table 12. π-Electronic Charge Density and Spin Density Transfers for All Closed-Shell Systems

	q^{π}_{OH}	q^{σ}_{OH}	$q^{\pi}_{\mathrm{OCH_3}}{}'$ [a]	$q^{\sigma}_{\mathrm{OCH_3}}{}'$ [a]	$q^{\pi}_{\mathrm{OCH_3}}{}''$ [a]	$q^{\sigma}_{\mathrm{OCH_3}}{}''$ [a]	Q^{π}_{ring}	$Q^{\sigma}_{\mathrm{ring}}$
phenol	+0.123	−0.311					−0.121	−0.605
2-methoxyphenol	+0.128	−0.299	+0.134	−0.326			−0.228	−0.090
3-methoxyphenol	+0.123	−0.312	+0.158	−0.325			−0.248	−0.091
4-methoxyphenol	+0.114	−0.308	+0.146	−0.325			−0.224	−0.097
2,3-dimethoxyphenol	+0.148	−0.319			+0.151	−0.324	−0.283	+0.399
2,4-dimethoxyphenol	+0.117	−0.296	+0.137	−0.324	+0.145	−0.326	−0.333	+0.417
2,5-dimethoxyphenol	+0.128	−0.300	+0.125	−0.325	+0.149	−0.324	−0.335	+0.418
2,6-dimethoxyphenol	+0.125	−0.288	+0.132	−0.326	+0.154	−0.314	−0.343	+0.430
3,4-dimethoxyphenol	+0.124	−0.315	+0.157	−0.319			−0.277	+0.389
3,5-dimethoxyphenol	+0.123	−0.312	+0.156	−0.325	+0.157	−0.324	−0.370	+0.425
methoxybenzene			+0.155	−0.327			−0.122	−
1,2-dimethoxybenzene							−0.153	−
1,3-dimethoxybenzene			+0.157	−0.325	+0.155	−0.327	−0.247	−
1,4-dimethoxybenzene			+0.146	−0.325	+0.146	−0.325	−0.223	−
phenoxide	+0.399	−1.144					−0.397	−0.558
2-methoxyphenoxide	+0.370	−1.130					−0.406	−0.084
3-methoxyphenoxide	+0.403	−1.144	+0.130	−0.374			−0.486	−0.065
4-methoxyphenoxide	+0.397	−1.142					−0.393	−0.105
2,3-dimethoxyphenoxide	+0.388	−1.137					−0.427	+0.384
2,4-dimethoxyphenoxide	+0.373	−1.131					−0.389	+0.354
2,5-dimethoxyphenoxide	+0.381	−1.133			+0.131	−0.373	−0.489	+0.409
2,6-dimethoxyphenoxide	+0.350	−1.115					−0.409	+0.382
3,4-dimethoxyphenoxide	+0.399	−1.140	+0.132	−0.364			−0.483	+0.398
3,5-dimethoxyphenoxide	+0.406	−1.143	+0.131	−0.370	+0.131	−0.370	−0.576	+0.432

[a] The notation $q^{\pi}_{\mathrm{OCH_3}}{}'$ means the π-charge at the substituent which is attached to the carbon with lower numbering (see Figure 1).

Table 13. π-Electronic Charge Density and Spin Density Transfers for All Open-Shell Systems

	q^{π}_{O}	q^{σ}_{O}	S_{O}	$q^{\pi}_{\mathrm{OCH_3}}{}'$	$q^{\sigma}_{\mathrm{OCH_3}}{}'$	$S_{\mathrm{OCH_3}}{}'$	$q^{\pi}_{\mathrm{OCH_3}}{}''$	$q^{\sigma}_{\mathrm{OCH_3}}{}''$	$S_{\mathrm{OCH_3}}{}''$	Q^{π}_{ring}	S_{ring}
phenoxyl	−0.292	−0.167	+0.441							+0.293	+0.577
2-methoxyphenoxyl	−0.362	−0.153	+0.391	+0.226	−0.316	+0.114				+0.151	+0.500
3-methoxyphenoxyl	−0.313	−0.164	+0.404	+0.166	−0.317	−0.005				+0.175	+0.623
4-methoxyphenoxyl	−0.332	−0.159	+0.402	+0.201	−0.325	+0.090				+0.155	+0.515
2,3-dimethoxyphenoxyl	−0.371	−0.144	+0.393	+0.219	−0.320	+0.113				+0.099	+0.510
2,4-dimethoxyphenoxyl	−0.386	−0.148	+0.382	+0.208	−0.316	+0.088	+0.190	−0.323	+0.070	+0.031	+0.458
2,5-dimethoxyphenoxyl	−0.398	−0.147	+0.325	+0.230	−0.318	+0.091	+0.171	−0.320	+0.018	+0.039	+0.529
2,6-dimethoxyphenoxyl	−0.368	−0.139	+0.386	+0.197	−0.317	+0.058	+0.210	−0.315	+0.095	+0.004	+0.458
3,4-dimethoxyphenoxyl	−0.352	−0.141	+0.392				+0.199	−0.318	+0.087	+0.098	+0.530
3,5-dimethoxyphenoxyl	−0.324	−0.163	+0.386	+0.162	−0.315	−0.008	+0.162	−0.315	−0.008	+0.055	+0.658

effect the substituents have on the spin delocalization must also be dependent on their π-electron donor capability. Table 13 shows that the unpaired spin, which in nonsubstituted phenoxyl radical is about 56% delocalized, becomes more delocalized for the substituted radicals, with only 32−40% of the unpaired spin remaining localized at the oxygen atom. This enhanced spin delocalization is more important for disubstituted radicals than for the monosubstituted ones, and topological effects are also observed, implying some attenuation of the above effect when the substituents occupy *meta* positions relative to the oxygen atom. The lowering of the unpaired spin density at the oxygen atom is generally paralleled by a corresponding lowering of the unpaired spin density in the ring, suggesting that an important factor determining the enhancement of the spin delocalization is the presence of the methoxyl substituents which can absorb a significant fraction of the unpaired spin density leaving the oxygen atom. However, for 3-methoxyphenoxyl radical and for 3,5-dimethoxyphenoxyl radical an increase of the ring unpaired spin density is observed. For these systems the relative topological situation of the methoxyl substituents and the oxygen atom results in a severely restricted interaction between the π-electron exchange capabilities of both groups, and as a consequence, the methoxyl substituents are no longer effective in absorbing the unpaired spin density lost by the oxygen atom, which appears therefore in the aromatic ring. This effect and the similar behavior observed for the total π-electron density cause the anomalous small stabilization the methoxyl substituents introduce to these radicals.

For the closed-shell systems, since both −OH and $-\mathrm{OCH_3}$ are π-electron donor groups, it is to be expected, on the basis of arguments similar to the above ones, that the introduction of the methoxyl substituents should lead to a decrease of the π-electron donor capability of −OH. However, this expected behavior is only observed for those molecules where the expected attenuation would be more effective, that is, the isomers having one methoxyl substituent at the *para* position relative to the −OH: 4-methoxyphenol and 2,4-dimethoxyphenol (for 3,4-dimethoxyphenol a marginal increase in the π-electron donation of −OH is observed). Incidentally, this effect seems to explain the very large decrease of the homolytic O−H bond dissociation energy for these systems: this large decrease results from a combined stabilization of the radicals by the methoxyl substituents and a significant destabilization of the corresponding closed-shell systems due to the restricted π-electron donation capability of both the −OH and the $-\mathrm{OCH_3}$ substituents.

The enhancement of the π-electron donor capability of −OH observed for the remaining systems results from both the π and σ electron interactions between both substituents. Indeed, since both substituents are σ-electron acceptors ($-\mathrm{OCH_3}$ being a slightly more strong acceptor than −OH, as can be concluded from the σ-charge they display in phenol and in methoxybenzene), a tendency of the ring to become electron deficient would result, unless the −OH group compensates this excess σ-withdrawal by donating more π-electrons to the ring. This seems to be really what occurs for these systems.

The only remaining noticeable behavior occurs for 2,6-dimethoxyphenol, where large destabilizations of about 14 kJ mol^{-1} and 12 kJ mol^{-1} are observed respectively from the B3LYP and BP calculations. This system offers the unique example for which the destabilization of the closed-shell system assumes an importance comparable to or even greater than the stabilization of the radical in the decrease of the O−H bond dissociation energy. We believe that the destabilization of this closed-shell system is the result of strong repulsions between the substituents which are very close together. Indeed, calculations made with Hartree−Fock theory and the 6-31G* basis set predict for this system a geometry with nonplanar arrangement of one of the methoxyl substituents resulting from steric repulsions and a destabilization of about 17 kJ mol^{-1}. Density functional theory is known to weight electron delocalization effects more heavily than Hartree−Fock theory,[41] a fact that explains that the predicted DFT geometry is planar and that the destabilization energy is reduced to only 14 kJ mol^{-1}.

The importance of the above-mentioned electronic exchange phenomena in determining the stability of the closed-shell molecules and of the radicals can be best illustrated through correlation plots of the calculated π-charge or spin density variations on the substituents against the stabilization energies, $\Delta^{pc}D_e$(O−H) and $\Delta^{rc}D_e$(O−H). For the closed-shell systems this correlation is shown in panel a of Figure 2. The coefficients were obtained by a least-squares fitting of the calculated data, and the resulting root-mean-square deviation is 1.5 kJ mol^{-1}. The larger deviation is observed for 2,6-dimethoxyphenol, for which, as said above, a large steric destabilization, not accounted for by this correlation, takes place. For the radicals a correlation involving also the spin-density variation on the oxygen atom is show in panel b of Figure 2, which represents the least-squares fitting of the data with a rmsd of 1.6 kJ mol^{-1}.

Gas-Phase Acidities. The absolute gas-phase acidity of the methoxy-substituted phenols, at T = 298.15 K, defined as the Gibbs function variation for the following heterolytic bond breaking reaction

$$\mathrm{MeO{-}C_6H_4{-}OH \rightarrow MeO{-}C_6H_4{-}O^- + H^+} \quad (16)$$

$$\mathrm{(MeO)_2{-}C_6H_3{-}OH \rightarrow (MeO)_2{-}C_6H_3{-}O^- + H^+} \quad (17)$$

has also been estimated from the thermodynamic equation $\Delta_{\mathrm{acid}}G = \Delta_{\mathrm{acid}}H - T\Delta_{\mathrm{acid}}S$ ($\Delta_{\mathrm{acid}}S$ was obtained using standard statistical thermodynamics formulas), and the results are shown in Table 14. It is worth noting the good agreement between the estimates of the acidity of phenol obtained from both calculations and the experimental values, (1432.0 ± 8.4) kJ mol^{-1} [42] and (1437.0 ± 8.4) kJ mol^{-1} [43] recommended in a compilation by Bartmess.[44] This observation lends some support to the quality of our estimates. The acidity of the substituted phenols relative to phenol was also calculated, and the resulting relative gas-phase acidities, as well as the corresponding available experimental data,[42,45] are also reported in that table. The effect of the methoxyl on the acidity is small and irregular. Despite the differences in the values for absolute gas-phase acidity, the relative values, $\Delta(\Delta_{\mathrm{acid}}G°)$, calculated with both methods are similar and display a very good agreement with the few available experimental values.

A partitioning of the overall substituent effect on the O−H heterolytic bond dissociation energy into the effect of the substituent in the closed-shell molecules and the effect in the anion (anion contribution, ac) can be obtained similarly to what has been done for the homolytic bond breaking processes by using the additional reactions

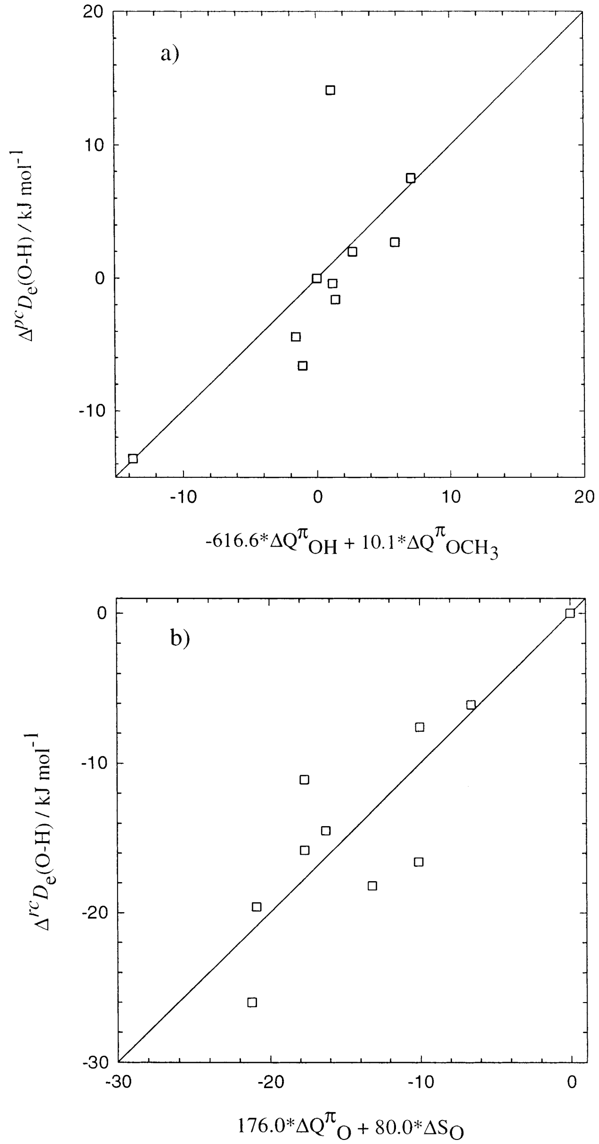

Figure 2. Correlation plots of the charge and spin density variations against stabilization energies for the closed-shell systems (panel a) and for the radicals (panel b).

$$\mathrm{MeO{-}C_6H_5 + C_6H_5O^- \rightarrow MeO{-}C_6H_4{-}O^- + C_6H_6} \quad (18)$$

$$\mathrm{(MeO)_2{-}C_6H_4 + C_6H_5O^- \rightarrow (MeO)_2{-}C_6H_3{-}O^- + C_6H_6} \quad (19)$$

for whom the energy variation represents the effect of the methoxyl substituent on the anion, measured relative to its effect on benzene. The individual contributions are shown in Table 13 under the headings $\Delta^{ac}D_e$(O−H) and $\Delta^{pc}D_e$(O−H). The phenoxide anions are mostly stabilized by the methoxyl substituent, the exceptions being 4-methoxyphenoxide anion, 2,4-dimethoxyphenoxide anion, and also 2,6-dimethoxyphenoxide anion, which is only marginally destabilized by the substituents. The stabilization of the remaining anions is always associated with an enhancement of the π-electron transfers to the ring, which occurs mainly because both substituent groups, −O$^-$ and

Table 14. Calculated DFT Gas-Phase Acidity at $T = 298.15$ K in kJ mol^{-1}

	D_e(O−H)		$\Delta_{acid}G°$		$\Delta(\Delta_{acid}G°)$		$\Delta(\Delta_{acid}G°)^a$	
substituent	B3LYP	BP	B3LYP	BP	B3LYP	BP	exp[45]	exp[42]
H	1511.3	1478.8	1450.5	1418.1	0.0	0.0	0.0	0.0
2-MeO	1512.7	1484.2	1452.6	1424.1	2.1	6.0	−3.8	
3-MeO	1507.0	1476.0	1446.2	1415.2	−4.3	−2.9	−6.3	−4.6
4-MeO	1514.8	1486.6	1452.7	1424.5	2.2	6.5	3.3	5.0
2,3-$(MeO)_2$	1509.5	1484.3	1447.5	1422.3	−3.0	4.2		
2,4-$(MeO)_2$	1519.0	1494.0	1456.1	1431.2	5.6	13.1		
2,5-$(MeO)_2$	1505.8	1478.3	1443.1	1415.7	−7.4	−2.3		
2,6-$(MeO)_2$	1497.6	1475.7	1437.2	1415.3	−13.3	−2.7		
3,4-$(MeO)_2$	1504.2	1473.5	1445.0	1414.3	−5.5	−3.8		
3,5-$(MeO)_2$	1500.1	1469.8	1439.7	1409.4	−10.8	−8.6		

[a] $\Delta_{acid}G°$(O−H) = (1432.0 ± 8.4) kJ mol^{-1} from ref 42, and $\Delta_{acid}G°$(O−H) = (1437.0 ± 8.4) kJ mol^{-1} from ref 43.

$-OCH_3$, act as π-electron donors. Even though a saturation effect could be expected to take place, thus reducing the π-electron donor capability of each group, the σ-accepting ability and polarizability of the methoxy group dominate ($-O^-$ σ-accepting ability is mild), forcing an increase in π-electron donation of both groups to the ring, which would otherwise become excessively electron deficient. For 4-methoxyphenoxide anion and 2,4-dimethoxyphenoxide anion one of the methoxyl substituents is located at the *para* position relative to $-O^-$, and thus, the saturation effect becomes particularly important. The result of the severely restricted π-electron transfers is a decrease of the π-electronic charge of the ring and a consequent destabilization of the anions by about 10 to 11 kJ mol^{-1} and 15 to 18 kJ mol^{-1}, respectively, for the B3LYP and BP calculations.

In the case of the anionic species a correlation between the charge variation at the substitutents and the corresponding stabilization of the anions was revealed to be much less reliable than that for the radicals or the closed-shell systems. Consequently, such a correlation is not shown here, but it is nevertheless interesting to mention that in order to obtain even a crude correlation (rmsd of about 3 kJ mol^{-1}) the σ-charge variation of the substituents should be taken into account in addition to their π-charge variation, a fact that supports our earlier argument concerning the importance of the σ-withdrawing effects in the overall stabilization of the anionic species.

Conclusions

In this work the thermochemistry of six methoxy-substituted phenols has been experimentally determined using combustion calorimetry. In addition, density functional theoretical calculations for the whole class of mono- and disubstituted methoxyphenols have been done, allowing the estimates of their formation enthalpies. The good agreement of the calculated and experimental gas-phase enthalpies of formation gives some confidence to our estimates concerning the isomers which were not experimentally studied. Also, the enthalpies of formation of all radicals and anions have been estimated and the results are believed to be at least as reliable as the estimates obtained for the closed-shell systems. The substituent effects on the homolytic and heterolytic O−H bond dissociation energies of these systems have been analyzed on the basis of the calculated energies, the results being in good agreement with available experimental data. Detailed analysis of the substituent effects suggests that electronic exchange phenomena between the substituents dominate the effect the substituents have on these systems. In particular, a radical stabilization has been observed, resulting from both π-electron and unpaired spin density exchanges between the substituents and the aromatic ring. This radical stabilization accounts for most of the weakening observed in the homolytic O−H bond dissociation energy.

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