Experimental and Computational Thermochemistry of 1,3-Benzodioxole Derivatives

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The standard ($p° = 0.1$ MPa) molar energies of combustion in oxygen, at $T = 298.15$ K, of four 1,3-benzodioxole derivatives (5-oxoethyl-1,3-benzodioxole, 5-cyano-1,3-benzodioxole, 5-nitro-1,3-benzodioxole, and 5-methyl-1,3-benzodioxole) were measured by static bomb calorimetry. The standard molar enthalpies of vaporization or of sublimation, at $T = 298.15$ K, were measured by Calvet microcalorimetry. Combining these results, the standard molar enthalpies of formation of the compounds in the gas phase, at $T = 298.15$ K, have been calculated: 5-oxoethyl-1,3-benzodioxole (−319.3 ± 2.8) kJ·mol^{-1}; 5-cyano-1,3-benzodioxole (−23.2 ± 2.2) kJ·mol^{-1}; 5-nitro-1,3-benzodioxole (−176.0 ± 3.2) kJ·mol^{-1} and 5-methyl-1,3-benzodioxole (−184.7 ± 3.5) kJ·mol^{-1}. The most stable geometries of all the compounds were obtained using the density functional theory with the B3LYP functional and two basis sets: 6-31G** and 6-311G**. The nonplanarity of the molecules was analyzed in terms of the anomeric effect, which is believed to arise from the interaction between a nonbonded oxygen p_π orbital and the empty orbital σ^*_{CO} involving the other oxygen atom. Calculations were performed to obtain estimates of the enthalpies of formation of all the substituted benzodioxoles using appropriate isodesmic reactions. There is good agreement between theoretical and experimental results. This agreement allows us to estimate the enthalpies of formation of some 1,3-benzodioxole derivatives whose experimental study was impossible.

Introduction

Benzodioxole (methylenedioxybenzene) and many of its derivatives play important roles in several areas of industry, in medicine, and in chemistry as well. Thus, benzodioxole itself is an intermediate in pharmaceuticals, fragrances, agrochemicals and other organic products,[1] while safrole (1-allyl-3,4-methylenedioxybenzene) is used for making soaps and perfumes, as a flavoring agent in drugs and foods, and in the manufacture of other derivatives[1] such as piperonal (heliotropin) and piperonyl butoxide that are used in medicine, in perfumes, and as mosquito repellents.[1] Piperonyl butoxide is a synergist used in a wide variety of insecticides.[1] Derivatives like safrole, isosafrole, and dihydrosafrole were found to be carcinogenic in mice and rats.[1] Sesamol (1-hydroxy-3,4-methylenedioxybenzene) is one of the most powerful antioxidants present in the natural sesame oil, which is often used in regular oiling of the skin for slowing the aging process.[2]

Synthetic derivatives are also known and widely used, like 3,4-methylenedioxymethamphetamine, which is better known as the infamous ecstasy drug.[3] In the experimental part of this paper, we report the standard molar enthalpies of formation of 5-oxoethyl-1,3-benzodioxole, 5-cyano-1,3-benzodioxole, 5-nitro-1,3-benzodioxole, and 5-methyl-1,3-benzodioxole in the condensed and gaseous phases. The results of the measurements of combustion energies, using a static bomb calorimeter, and the values for the enthalpies of sublimation or vaporization of the compounds, measured by Calvet microcalorimetry, were combined to yield the standard molar enthalpies of formation in the gaseous phase.

In addition, we also report the results of "theoretical" calculations carried out in the framework of the Density Functional Theory (DFT) for the compounds studied and also for other substituted benzodioxoles not studied experimentally: 5-methanal-1,3-benzodioxole, 5-methylamine-1,3-benzodioxole, and 5-amine-1,3-benzodioxole. In parallel, the values of the gas-phase enthalpies of formation, $\Delta_f H^0_m$(g), for the 1,3-benzodioxole derivatives were calculated using appropriate isodesmic reactions and previous experimental data for all species (exception made to the species we are studying) included in these reactions. There is good agreement between calculated and experimental enthalpies of formation.

In a previous work, we reported the results of experimental and theoretical studies of other derivatives (-OH, -CH_2OH, -COOH, -CH_2COOH) of benzodioxole.[4] In the present work, we are trying to obtain an overall understanding of the conformational behavior of the benzodioxole moiety under the influence of the different substituents we consider and the energetic factors, which can be claimed to determine the most stable conformations.

Experimental Section

Materials. All the compounds are commercial products from Aldrich Chemical Co.: 5-oxoethyl-1,3-benzodioxole [CASRN 3162-29-6, 99.10 % (GC)], 5-cyano-1,3-benzodioxole [CASRN 4421-09-4, 98 % (minimum)], 5-nitro-1,3-benzodioxole [CASRN 2620-44-2, 99.8 % (GLC)], and 5-methyl-1,3-benzodioxole [CASRN 7145-99-5, 98 % (minimum)]. All the samples were purified by repeated distillation or sublimation under reduced

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Table 1. Temperatures of Fusion (T_{fus}), Enthalpies of Fusion ($\Delta_{\mathrm{cr}}^{\mathrm{l}}H_{\mathrm{m}}^{0}(T_{\mathrm{fus}})$), and Mass Fraction of Impurities (x) of the Studied Benzodioxoles

	T_{fus}	$\Delta_{\mathrm{cr}}^{\mathrm{l}}H_{\mathrm{m}}^{0}(T_{\mathrm{fus}})$	
	K	$\mathrm{kJ \cdot mol^{-1}}$	$10^3 \cdot x$
5-oxoethyl-1,3-benzodioxole	358.87 ± 0.03	26.23 ± 0.08	0.4
5-cyano-1,3-benzodioxole	366.26 ± 0.04	20.79 ± 0.12	0.5
5-nitro-1,3-benzodioxole	420.16 ± 0.04	28.20 ± 0.52	1.0

Table 2. Typical Combustion Experiments, at T = 298.15 K[a]

	5-oxoethyl-1,3-benzodioxole	5-cyano-1,3-benzodioxole	5-nitro-1,3-benzodioxole	5-methyl-1,3-benzodioxole
$m(\mathrm{CO_2}, \mathrm{total})/\mathrm{g}$	1.61185	1.64890	1.31628	1.72014
$m(\mathrm{cpd})/\mathrm{g}$	0.66607	0.68681	0.71082	0.61807
$m'(\mathrm{fuse})/\mathrm{g}$	0.00338	0.00380	0.00369	0.00350
$\Delta T_{\mathrm{ad}}/\mathrm{K}$	1.08350	1.09919	0.85551	1.22655
$\epsilon_{\mathrm{f}}/(\mathrm{J \cdot K^{-1}})$	16.14	15.29	15.20	15.95
$\Delta m(\mathrm{H_2O})/\mathrm{g}$	0.0	0.0	−0.1	−0.1
$-\Delta U(\mathrm{IBP})/\mathrm{J}$	17357.49	17607.92	13703.81	19648.55
$\Delta U(\mathrm{fuse})/\mathrm{J}$	54.89	61.71	59.93	56.84
$\Delta U(\mathrm{Melinex})/\mathrm{J}$				1162.34
$\Delta U(\mathrm{HNO_3})/\mathrm{J}$	0.31	26.46	29.49	1.62
$\Delta U(\mathrm{ign.})/\mathrm{J}$	1.20	1.20	1.10	1.19
$\Delta U_{\Sigma}/\mathrm{J}$	12.29	14.68	13.31	12.39
$-\Delta_{\mathrm{c}}u°/(\mathrm{J \cdot g^{-1}})$	25958.23	25487.50	19134.35	29794.94

[a] $m(\mathrm{CO_2}, \mathrm{total})$ is the total mass of $\mathrm{CO_2}$ formed in the experiment. $m(\mathrm{cpd})$ is the mass of compound burnt in the experiment. $m(\mathrm{fuse})$ is the mass of fuse (cotton) used in the experiment. ΔT_{ad} is the corrected temperature rise. ϵ_{f} is the energy equivalent of contents in the final state. $\Delta m(\mathrm{H_2O})$ is the deviation of the mass of water added to the calorimeter from 3119.6 g. $\Delta U(\mathrm{IBP})$ is the energy change for the isothermal combustion reaction under actual bomb conditions. $\Delta U(\mathrm{IBP})$ includes $\Delta U(\mathrm{ign.})$, which is the energy of ignition. $\Delta U(\mathrm{fuse})$ is the energy of combustion of the fuse (cotton). $\Delta U(\mathrm{Melinex})$ is the energy of combustion of Melinex. $\Delta U(\mathrm{HNO_3})$ is the energy correction for the nitric acid formation. ΔU_{Σ} is the energy correction to the standard state. $\Delta_{\mathrm{c}}u°$ is the standard massic energy of combustion.

pressure before being studied. For the solid compounds, the impurity mass fractions (Table 1) were derived from DSC (Setaram DSC 141) analysis by a fractional fusion technique.[5] The samples, hermetically sealed in stainless steel crucibles, were heated at $3.33 \times 10^{-2}\ \mathrm{K \cdot s^{-1}}$. The temperature scale of the calorimeter was calibrated by measuring the melting temperature of three high-purity reference materials (naphthalene, benzoic acid, and indium),[6] and its power scale was calibrated with high-purity indium (mass fraction > 0.99999). The recorded thermograms did not show any phase transition between 298 K and the melting temperature of the compounds studied.

The purity of the liquid compound was evaluated by gas−liquid chromatography. The composition of the samples was also confirmed through the carbon dioxide recovery ratios. 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: 5-oxoethyl-1,3-benzodioxole (1.0001 ± 0.0001), 5-cyano-1,3-benzodioxole (0.9999 ± 0.0002), 5-nitro-1,3-benzodioxole (0.9992 ± 0.0001), and 5-methyl-1,3-benzodioxole (1.0002 ± 0.0003). The densities of the samples were estimated as $1.0\ \mathrm{g \cdot cm^{-3}}$ for the solids and $1.13\ \mathrm{g \cdot cm^{-3}}$ for the liquid.

Combustion Calorimetry. The combustion experiments were performed with a static bomb calorimeter. The apparatus and technique have been described.[7,8] Benzoic acid (Bureau of Analysed Samples, Thermochemical Standard, BCS-CRM-190 p) was used for calibration of the bomb. Its massic energy of combustion is $-\Delta_{\mathrm{c}}u = (26432.3 \pm 3.8)\ \mathrm{J \cdot g^{-1}}$, 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. From six calibration experiments performed, $\epsilon_{\mathrm{cal}} = (16004.8 \pm 1.6)\ \mathrm{J \cdot K^{-1}}$, where the uncertainty quoted is the standard deviation of the mean.

The crystalline compounds were burnt in pellet form. The liquid 5-methyl-1,3-benzodioxole was enclosed in polyester bags made of Melinex, using the technique described by Skinner and Snelson,[9] who determined the specific energy of combustion of dry Melinex as $\Delta_{\mathrm{c}}u° = -(22902 \pm 5)\ \mathrm{J \cdot g^{-1}}$. This value was confirmed in our laboratory. The mass of Melinex used in each experiment was corrected for the mass fraction of water (0.0032), and the mass of carbon dioxide produced from it was calculated using the factor previously reported.[9]

For the cotton-thread fuse, empirical formula $\mathrm{CH_{1.686}O_{0.843}}$, $\Delta_{\mathrm{c}}u° = -16250\ \mathrm{J \cdot g^{-1}}$,[10] this value has been confirmed in our laboratory. The corrections for nitric acid formation $\Delta U(\mathrm{HNO_3})$ were based on $-59.7\ \mathrm{kJ \cdot mol^{-1}}$,[11] for the molar energy of formation of $0.1\ \mathrm{mol \cdot dm^{-3}}$ $\mathrm{HNO_3(aq)}$ from $\mathrm{N_2}$, $\mathrm{O_2}$, and $\mathrm{H_2O(l)}$. As samples were ignited at T = 298.15 K

$$\Delta U(\mathrm{IBP}) = -\{\epsilon_{\mathrm{cal}} + \Delta m(\mathrm{H_2O}) \cdot c_p(\mathrm{H_2O,l}) + \epsilon_{\mathrm{f}}\}\Delta T_{\mathrm{ad}} + \Delta U_{\mathrm{ign}} \quad (1)$$

where $\Delta U(\mathrm{IBP})$ is the energy associated to the isothermal bomb process, ϵ_{f} is the energy of the bomb contents after ignition, and ΔT_{ad} is the adiabatic temperature raise. Table 4 lists the derived standard molar energies and enthalpies of combustion, $\Delta_{\mathrm{c}}U_{\mathrm{m}}^{0}(\mathrm{cr,l})$ and $\Delta_{\mathrm{c}}H_{\mathrm{m}}^{0}(\mathrm{cr,l})$, and the standard molar enthalpies of formation for the compounds in the crystalline or liquid phase $\Delta_{\mathrm{f}}H_{\mathrm{m}}^{0}(\mathrm{cr,l})$ at T = 298.15 K. In accordance with customary 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.[12] In the values of the auxiliary quantities, to derive $\Delta_{\mathrm{f}}H_{\mathrm{m}}^{0}(\mathrm{cr,l})$ from $\Delta_{\mathrm{c}}H_{\mathrm{m}}^{0}(\mathrm{cr,l})$, the standard molar enthalpies of formation of $\mathrm{H_2O(l)}$ and $\mathrm{CO_2(g)}$ at T = 298.15 K, −(285.830 ± 0.042) and $-(393.51 \pm 0.13)\ \mathrm{kJ \cdot mol^{-1}}$,[13] respectively, were used.

Calvet Microcalorimetry. The standard molar enthalpies of sublimation or vaporization were measured using the "vacuum sublimation" drop microcalorimetric method.[14] Samples, about (3 to 5) mg of the crystalline compounds and of (7 to 10) mg of the liquid compound, contained in a thin glass capillary tube sealed at one end, were dropped at room temperature into the hot reaction vessel in a high-temperature Calvet microcalorimeter held at T = 367 K (5-oxoethyl-1,3-benzodioxole and 5-cyano-1,3-benzodioxole), T = 414 K (5-nitro-1,3-benzodioxole), and T = 377 K (5-methyl-1,3-benzodioxole) and then removed from the hot zone by vacuum evaporation. The observed enthalpies of vaporization or sublimation $\Delta_{\mathrm{cr,298.15K}}^{\mathrm{g},T}H_{\mathrm{m}}^{\mathrm{o}}$ were corrected to T = 298.15 K, using the equation:

$$\Delta_{298.15\ \mathrm{K}}^{T}H_{\mathrm{m}}^{\mathrm{o}}(\mathrm{g}) = \int_{298.15\ \mathrm{K}}^{T/\mathrm{K}} C_{p,\mathrm{m}}^{\mathrm{o}}(\mathrm{g})\, \mathrm{d}T \quad (2)$$

where T = 365 K and $C_{p,\mathrm{m}}^{\mathrm{o}}(\mathrm{g})$ were derived as a function of T, from statistical thermodynamics using the vibrational frequencies obtained from the DFT calculations with the B3LYP functional and the 6-31G** basis set. The microcalorimeter was calibrated in situ for these measurements using the reported standard molar enthalpies of sublimation of naphthalene[15] and of vaporization of n-decane.[16]

Computational Details

The geometries of all molecules have been fully optimized using DFT with the Becke three-parameter hybrid exchange[17] and the Lee−Yang−Parr[18] correlation density functionals (B3LYP) and the Pople's split-valence 6-31G** extended basis

Table 3. Individual Values of the Massic Energy of Combustion, at $T = 298.15$ K

5-oxoethyl-1,3-benzodioxole	5-cyano-1,3-benzodioxole	5-nitro-1,3-benzodioxole	5-methyl-1,3-benzodioxole
$-\Delta_c u^\circ/(\mathrm{J \cdot g^{-1}})$			
25942.03	25475.03	19163.11	29721.43
25958.23	25497.32	19147.69	29760.70
25952.66	25489.50	19132.57	29724.42
25947.00	25490.41	19121.06	29745.12
25946.48	25460.56	19134.35	29745.75
25953.56	25470.06	19146.86	29736.98
	25487.50		29703.23
			29794.94
$-<\Delta_c u^\circ \times b0>/(\mathrm{J \cdot g^{-1}})$			
25950.0 ± 2.4	25481.5 ± 5.0	19140.9 ± 6.0	29741.6 ± 9.9

Table 4. Derived Standard ($p^\circ = 0.1$ MPa) Molar Values of the Enthalpies of Formation in the Gas Phase, at $T = 298.15$ K

	$-\Delta_f H_m^0$(cr,l)	$\Delta_{\mathrm{cr,\,l}}^{\mathrm{g}} H_m^0$	$-\Delta_f H_m^0$(g)
	$\mathrm{kJ \cdot mol^{-1}}$	$\mathrm{kJ \cdot mol^{-1}}$	$\mathrm{kJ \cdot mol^{-1}}$
5-oxoethyl-1,3-benzodioxole	423.7 ± 1.8	104.4 ± 2.2	319.3 ± 2.8
5-cyano-1,3-benzodioxole	114.1 ± 2.0	90.9 ± 0.9	23.2 ± 2.2
5-nitro-1,3-benzodioxole	273.4 ± 2.3	97.4 ± 2.2	176.0 ± 3.2
5-methyl-1,3-benzodioxole	239.6 ± 3.3	54.9 ± 1.2	184.7 ± 3.5

set.[19] The optimum structures so obtained were further certified as true minima by constructing and diagonalizing the corresponding Cartesian Hessian matrix, this procedure providing also the harmonic vibrational frequencies which, after properly scaled by the recommended scaling factor 0.9614[20] allow reliable calculations of the thermal corrections to the molecular energy. We have further refined the optimum structures by reoptimizing them using the same methodology with the Pople's split-valence 6-311G** extended basis set.[21]

The NBO analyses have been done on B3LYP/6-31G** wave functions obtained with the B3LYP/6-31G** optimum geometries. All calculations have been performed using the UK version of program GAMESS.[22]

Experimental Results

Enthalpies of Fusion. The temperatures of fusion of the solid compounds were measured using a differential scanning calorimeter. The results (observed at the onset of the calorimetric peaks), T_{fus}, are presented in Table 1 together with the enthalpies of fusion at the temperatures of fusion, $\Delta_{\mathrm{cr}}^{\mathrm{l}} H_m^0(T_{\mathrm{fus}})$, and the mass fraction of impurities, x, of the purified samples. Those values represent the mean values of six independent experiments on fresh samples, and the uncertainties are twice the standard deviation of the mean.

Combustion Calorimetry Results. Table 2 presents the results for a typical combustion experiment of each compound, where $\Delta m(\mathrm{H_2O})$ is the deviation of the mass of water added to the calorimeter from 3119.6 g. Combustion experiments were made in oxygen at $p = 3.04$ MPa, with 1.00 cm^3 of water added to the bomb; ΔU_Σ is the correction to the standard state.[23] The remaining quantities are as described in the Experimental Section. The individual results of all combustion experiments, together with the mean value and its standard deviation, are given for each compound in Table 3.

Microcalorimetric Results. The standard molar enthalpies of sublimation or vaporization correspond to the mean values of six experiments with uncertainties given as their standard deviation. The values are given in Table 4.

Enthalpies of Formation. The standard molar enthalpies of formation, in both the condensed and gaseous phases, at the temperature 298.15 K for the studied compounds are summarized in Table 4.

Theoretical Results and Discussion.

Optimized Geometries. Even though the molecule of 1,3-dioxole lacks the two adjacent CH$_2$ groups, which are believed to be the origin of torsional forces responsible for the nonplanarity of cyclopentene, both experiment[24] and theory[25] indicate that this molecule adopts a nonplanar (puckered) most stable conformation. This anomalous behavior has been attributed to the anomeric effect that is present in molecules with O−C−O linkages. Indeed, the hyperconjugative interactions involving the lone electron pairs of each oxygen atom and the vacant C−O antibonding orbitals (anomeric interactions) are only effective when some puckering of the ring occurs. B3LYP calculations with moderate-sized basis sets predict the 1,3-dioxole ring to be puckered by about 18°. When the more complex 1,3-benzodioxole molecule is considered, an essentially similar conformational behavior is observed, either from experiment or from theory[26−28] but with a considerably lower puckering angle (ca. 13°). Thus an attenuation of the anomeric effect seems to result from the attachment of the aromatic benzene ring to the pentagonal 1,3-dioxole ring. A possible explanation for this is the extended electronic delocalization of the oxygen atoms lone pairs density into the aromatic ring, which leaves a decreased lone pair electron available to participate in anomeric interactions. These two competing interactions are very different in their conformational requirements: anomerism is favored by the puckering of the 1,3-dioxole ring while electronic delocalization is hindered by ring puckering. These factors can thus explain the attenuated anomeric effect in 1,3-benzodioxole.

The structural importance of the anomeric interactions has been stressed, on the basis of thermochemical data, for several sulfur-containing ring compounds,[29−33] but the detailed analysis of the importance of such hyperconjugative orbital interactions can only be appropriately done by natural bond orbital[34−36] (NBO) calculations as shown in previously reported studies of 1,3-dioxole,[25] 1,3-benzodioxole,[28] phthalan,[37] substituted 1,3-dioxane and 1,3-dithiane,[38] 2,4-dioxaheptane, 2,4,6-trioxaheptane,[39] and substituted 1,3-benzodioxoles.[4]

In the framework of the NBO method, the canonical molecular orbitals are transformed into a set of localized hybrids (NBOs) described in terms of an orthogonalized atomic orbital basis set. The resulting filled NBOs describe covalency effects in the molecules while small occupancies of the nominally unoccupied antibonding NBOs are used to describe departures from an idealized Lewis picture and thus represent small noncovalency corrections to the picture of localized covalent bonds. The energy associated with such effects can be numerically assessed by deleting the relevant NBOs from the bond set and then recalculating the total energy, thus determining the associated variational energy lowering. In this way the total energy can be decomposed into components associated with the covalent and selected noncovalent contributions. Deletion of all the virtual NBOs similarly leads to estimates of the overall effect of electron delocalization (ϵ_{del}).

In order to analyze the effect of hyperconjugative orbital interactions on the amount of ring puckering of the most stable conformations of these systems, we have optimized the corresponding planar structures (by restricting the angle θ_{2145} to 0°; Figure 1), and then we have performed comparative NBO analyses for both conformations. Our results indicate that the observed variable degree of ring puckering for the equilibrium structures of the molecules studied result from the relative balance of a large number of individual interactions leading to opposite forces: those favoring a puckering of the pentagonal

Table 5. Variation of Delocalization Energies between Puckered and Planar Conformations of 1,3-Benzodioxole-5-R, $\Delta\epsilon_{del}$, and Main Hyperconjugative Contributions, $n_p \rightarrow \sigma^*_{CO}$ and $n_p \rightarrow \pi^*_{CC}$[a]

			1,3-benzodioxole in conformation of 1,3-benzodioxole-5-**R**		puckered conformation		planar conformation		Δ = puckered − planar	
	Θ_{puck}	$\Delta\epsilon_{del}$	$n_p \rightarrow \sigma^*_{CO}$	$n_p \rightarrow \pi^*_{CC}$	$n_p \rightarrow \sigma^*_{CO}$	$n_p \rightarrow \pi^*_{CC}$	$n_p \rightarrow \sigma^*_{CO}$	$n_p \rightarrow \pi^*_{CC}$	$n_p \rightarrow \sigma^*_{CO}$	$n_p \rightarrow \pi^*_{CC}$
benzodioxole (R = H)	13.1	1.180	4.87	187.77	4.87	187.77	0.0	191.77	4.87	−4.00
5-oxoethyl-1,3-benzodioxole (R = $COCH_3$)	10.2	1.640	3.02	189.23	2.91	196.96	0.0	199.67	2.91	−2.71
5-cyano-1,3-benzodioxole (R = CN)	0.0	3.393	0.0	191.77	3.71[b]	200.79[b]	0.0	205.82	3.71[b]	−5.03[b]
5-nitro-1,3-benzodioxole (R = NO_2)	6.0	0.699	1.05	190.71	0.94	210.10	0.0	210.92	0.94	−0.82
5-methyl-1,3-benzodioxole (R = CH_3)	13.3	0.904	5.01	187.66	5.10	188.81	0.0	193.28	5.10	−4.47
5-methanal-1,3-benzodioxole (R = COH)	8.7	0.314	2.18	189.87	2.02	205.52	0.0	207.37	2.02	−1.85
5-methylamine-1,3-benzodioxole (R = CH_2NH_2)	14.2	1.711	5.68	187.12	5.85	185.03	0.0	189.53	5.85	−4.50
5-amine-1,3-benzodioxole (R = NH_2)	16.0	1.916	7.19	185.91	7.69	182.57	0.0	188.39	7.69	−5.82

[a] All values are in kJ·mol^{-1}. NBO analysis has been done on B3LYP/6-31G** wave functions obtained with the B3LYP/6-31G** optimized geometries. [b] The values reported for 5-cyano-1,3-benzodioxole (R = CN) as the puckered conformation refer to an arbitrary puckering angle of 13.0°.

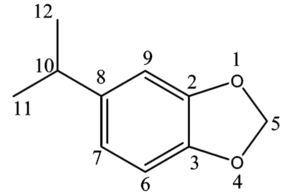


Figure 1. Atom numbering scheme for the geometric results of the benzodioxole derivatives.

Table 6. Calculated Electronic Energies (hartree) and Thermal Corrections, E_{total} (kJ·mol^{-1})

compound	$E_{B3LYP/6-31G^{**}}$	$E_{B3LYP/6-311G^{**}}$	$E_{Total/B3LYP/6-31G^{**}}$[a]
benzodioxole	−420.785961	−420.889175	311.0
5-oxoethyl-1,3-benzodioxole	−573.436949	−573.579543	414.9
5-cyano-1,3-benzodioxole	−513.028347	−513.155858	312.3
5-nitro-1,3-benzodioxole	−625.287228	−625.448933	324.4
5-methyl-1,3-benzodioxole	−460.106001	−460.216713	385.2
5-methanal-1,3-benzodioxole	−534.112677	−534.247422	340.0
5-amine-1,3-benzodioxole	−476.141506	−476.259869	356.9
5-methylamine-1,3-benzodioxole	−515.450508	−515.577360	433.7
methane	−40.524007	−40.534248	121.2
propanone	−193.164211	−193.215443	225.8
cyanomethane	−132.759142	−132.795085	124.2
nitromethane	−245.013374	−245.084723	137.8
ethane	−79.838734	−79.857273	198.2
ethanal	−153.835727	−153.878788	150.6
methanamine	−95.863679	−95.889512	171.1
ethanamine	−135.183374	−135.217931	246.4
phenylformate	−420.808962	−420.916093	309.1
benzene	−232.248664	−232.311529	266.2
acetophenone	−384.882805	−385.000694	370.5
cyanobenzene	−324.500092	−324.577584	267.4
nitrobenzene	−436.750580	−436.870249	279.7
toluene	−271.578779	−271.639558	340.0
benzaldehyde	−345.573444	−345.667340	295.2
aminobenzene	−287.616506	−287.685063	311.6
benzenemethanamine	−326.923297	−327.000185	388.4

[a] E_{total} $(T = 298.15\text{ K}) = E_{trans} + E_{rot} + E_{ZP} + \Delta_{0K}^{298.15K}E_{vib}$.

ring and those that favor the corresponding planar conformation. It is observed from the values of the delocalization energy differences ($\Delta\epsilon_{del}$) between the puckered and the planar conformations (Table 5) that the interactions favoring the puckering of the pentagonal ring are, in all cases, collectively more important than those favoring the planar conformation, thus explaining the larger stability of the puckered conformations. The only exception is found for 5-cyano-1,3-benzodioxole for which the interactions favoring the planar conformation collectively dominate over their opponent, thus leading to a completely planar (non-puckered) most stable conformation.

In addition, a more detailed analysis of individual orbital interactions reveals, as in previous studies of 1,3-dioxole[25] and of 1,3-benzodioxole,[28] that the most important forces favoring ring puckering are those associated with the interaction of each oxygen atom p lone electron pair, n_p, with the antibonding C−O orbital, σ^*_{CO}, involving the other oxygen atom ($n_p \rightarrow \sigma^*_{CO}$), an interaction usually recognized as describing the so-called anomeric effect, while among the forces favoring ring planarity, the interaction between the same oxygen lone electron pair and the antibonding C−C π orbitals of the benzenic ring ($n_p \rightarrow \pi^*_{CC}$) plays a major role.

The last interactions tend to establish an extended delocalized π electron system involving the two rings. Table 5 shows the results for both interactions in the puckered and in the planar conformations of all systems as well as the same interactions for non-substituted benzodioxole in optimized puckered conformations with the same puckering angle as the substituted systems.

On the other hand, when we analyze the values of the variation of the interaction energy for these interactions between the puckered and the planar conformations (columns under Δ in Table 5), we can conclude that the interaction favoring puckered conformations clearly overshadows the interaction favoring planar conformations, the only exception being, as before, 5-cyano-1,3-benzodioxole. In addition the effect of the substituents R is to attenuate both the $n_p \rightarrow \sigma^*_{CO}$ and the $n_p \rightarrow \pi^*_{CC}$ energy differences between the puckered and planar conformations, the only exception occurring for the CH_3 substituent. The corresponding puckering angle clearly follows the above tendency of variation of the interaction energies. In the case of the -CN substituent, a reinforcement of the $n_p \rightarrow \pi^*_{CC}$ interaction energy difference coexists with an attenuation of the $n_p \rightarrow \sigma^*_{CO}$ interaction. Since the reinforcement of the $n_p \rightarrow \pi^*_{CC}$ overshadows the attenuation of the $n_p \rightarrow \sigma^*_{CO}$ interaction, the resulting conformation is planar. The variation in these interaction energy differences, rather than being merely the result of the different puckering angles adopted by the

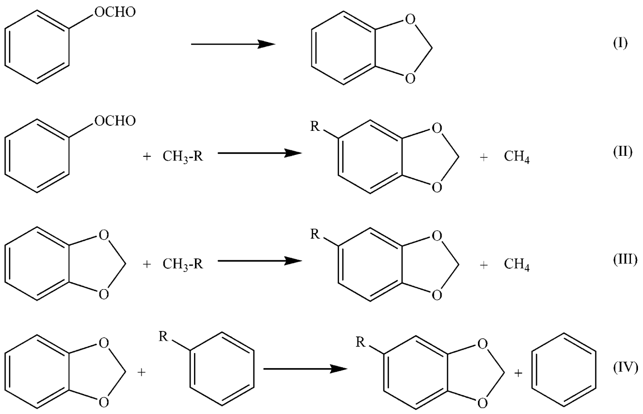
Table 7. Theoretical Estimates of the Standard Enthalpies of Formation in the Gas Phase at $T = 298.15$ K of Benzodioxoles

	$\Delta_f H^0_m$(g)/kJ·mol^{-1}				
	reaction I	reaction II	reaction III	reaction IV	exp
benzodioxole	−143.2				−142.7 ± 2.9[24]
5-oxoethyl-1,3-benzodioxole		−310.7	−310.2	−315.6	−319.3 ± 2.8
5-cyano-1,3-benzodioxole		−11.8	−11.3	−11.1	−23.2 ± 2.2
5-nitro-1,3-benzodioxole		−170.7	−170.2	−160.6	−176.0 ± 3.2
5-methyl-1,3-benzodioxole		−167.3	−166.7	−174.2	−184.7 ± 3.5
5-methanal-1,3-benzodioxole		−271.3	−270.8	−268.4	
5-amine-1,3-benzodioxole		−136.7	−136.2	−130.2	
5-methylamine-1,3-benzodioxole		−130.7	−130.1	−129.2	

systems, seems to be the main factor determining the particular conformations, as can be concluded from a comparison of the interaction energies in substituted benzodioxoles and in non-substituted benzodioxole at the same corresponding puckering angles. Indeed we can observe from the results (columns 4 to 7 of Table 5) that the effect of the substituents R is to reinforce differently the $n_p \rightarrow \pi^*_{CC}$ interactions, while the $n_p \rightarrow \sigma^*_{CO}$ is in general weakened when compared with non-substituted benzodioxole. The only exceptions to this behavior are 5-methyl-1,3-benzodioxole for which the $n_p \rightarrow \sigma^*_{CO}$ is slightly reinforced by the substituent and 5-cyano-1,3-benzodioxole where the substituent has essentially no effect on the $n_p \rightarrow \sigma^*_{CO}$ interaction energy, which remains essentially zero. This behavior results in a null puckering angle for 5-cyano-1,3-benzodioxole and in an (small) increase of the puckering angle, corresponding to a diminished attenuation of the anomeric effect, for 5-methyl-1,3-benzodioxole (Table 5).

Thus, from our actual and previous results, we can describe the influence of the substituents on the conformational behavior of the systems studied as follows. The stabilizing anomeric interactions tend to pucker the dioxole ring to a puckering angle of about 19° in dioxole (at the B3LYP/6-311G** level) whereas the possibility of stabilizing extended electronic delocalization, afforded by the attachment of a benzene ring (1,3-benzodioxole), opposes the puckering tendency, leading to a decrease of the puckering angle to about 13°. This planarization of the molecule reflects a partial suppression of the anomeric effect by the benzene ring. Further introduction of substituents at the benzene ring merely affect the degree of suppression of the anomeric effect, depending on their behavior in relation to π electron exchanges with the ring. Substituents that are π electron donors (-OH, $-CH_2OH$, $-NH_2$, $-CH_2NH_2$) decrease the suppression of anomeric effect by the aromatic ring since the lone pair orbitals of the oxygen atoms no longer need to participate in the extended electronic delocalization with the ring. Thus, a larger fraction of their electronic density becomes available to participate in the anomeric interactions. On the other hand, substituents that are π electron acceptors ($-COCH_3$, -CN, -COOH, -CH2COOH, -CHO, $-NO_2$) induce a π electron deficiency at the aromatic ring, which must then be fulfilled by some of the electronic density of the lone pair orbitals of the oxygen atoms. This process leaves a smaller electron density available to participate in the anomeric interactions and the suppression of the anomeric effect then becomes enhanced. In these cases a decrease of the puckering angle, compatible with a decrease of the importance of the anomeric interactions, is generally observed. Finally, we observe that the methyl substituent, which, incidentally, has no noticeable ability to participate in mesomeric interactions, maintains essentially the puckering angle of non-substituted benzodioxole

Calculated Enthalpies of Formation. In order to estimate the enthalpies of formation of the systems from the calculated energies we used the following set of reactions (I to IV) involving auxiliary systems whose thermochemical properties are well-established experimentally.[40] Reactions III and IV are more likely to produce substantial cancellation of the correlation errors introduced in the calculations since they are of the isodesmic type.



Total energies, identified by the subscripts B3LYP/6-311G**//B3LYP/6-311G**, are reported in Table 6 for the benzodioxole derivatives studied. The optimum geometries, the energies and the thermal corrections for all the auxiliary molecules have also been obtained using the same procedures as described above. The resulting estimates of the enthalpies of formation, at the B3LYP/6-311G**//B3LYP/6-311G** level of calculation, are provided in Table 7, for all reactions used.

We can observe from these results that, even though our calculations reproduce correctly the experimentally observed stability order, the calculated enthalpies of formation are only in moderate agreement with experiment. The average errors are (10.7, 11.2, and 10.4) kJ·mol^{-1}, respectively, for reactions II, III, and IV. The worst results, obtained from reactions II and III, can possibly be traced back to the fact that reaction II is not of the isodesmic type while in reaction III the substituent is bonded to very different substrates in reactants and in products. However, the lack of experimental data precludes the use of more adequate reactions, which, we believe, are the most important starting point to correctly describe the experimentally observed thermochemistry.

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