

## Molecular Mechanics (MM2) Parameters for Divinyl Ethers and Aromatic Halide Derivatives

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The MM2 force field has now been extended to include divinyl ether derivatives and halo-containing aromatics. Many natural products, synthetic intermediates, structures of theoretical interest, and biologically important compounds contain aromatic halides and furan moieties. As the first necessary step in attempting to understand the stereoelectronic effects in complex and biologically interesting molecular structures such as polychlorinated benzodioxins, furans, and biphenyls, we have examined a variety of compounds with aromatic halides and divinyl ether linkages. Full geometry optimized 6-31G\* calculations on divinyl ether and related compounds were carried out and used to augment available experimental information for the development of a complete MM2 force field capable of handling the title compounds. Our results and a new parameter set are presented. In general, our calculations agree well with the available experimental data.

Advances in computational and molecular modeling methods have been increasingly utilized by organic chemists in attempting to understand both ground-state and transition-state structures. From these theoretical approaches, chemists can gain quantitative insight into molecular behavior and make better predictions of organic and biochemical reactions, as well as drug behavior. Interest in applying these methodologies to biohazards and toxins has been growing over the last few years. Many pharmaceuticals, hazardous chemicals, natural products, and synthetic intermediates contain vinyl and/or aromatic halides. Trying to understand biological activity at the molecular level and to correlate this activity to structural features with molecular mechanics methods is currently a major challenge. Previous to this work, there were no accurately determined MM2 parameters for any halo-benzenes and/or compounds containing vinyl halide linkages, such as halofuran derivatives. In order to have confidence in conformational predictions on complex halo-containing aromatic molecular structures, the development of an accurately parametrized force field capable of handling the fundamental functionalities is a necessity. Any attempt to gain quantitative understanding of conformational preferences without a secure foundation would be suspect. In this case, the development of a new force field capable of handling these widespread and diverse functional groups was first necessary to establish the correct molecular geometry for divinyl and diphenyl ethers as well as various halo derivatives. Where appropriate, ab initio calculations were carried out to augment sketchy or unavailable experimental data. We report our calculations and new molecular mechanics parameters for the title compounds.

Recently, a great deal of attention has been focused on polychlorinated biphenyls (PCB), dibenzo-*p*-dioxins (PCDDs), and dibenzofurans (PCDFs), because of the acute toxic properties exhibited by this large class of compounds. PCDDs and PCDFs are very stable hazardous

environmental contaminants.<sup>1</sup> These compounds are teratogenic, mutagenic, and potentially carcinogenic.<sup>2</sup> The physical, chemical, biochemical, and toxicological properties of these compounds are very similar. Polyhalogenated biphenyls have also received recent critical attention.<sup>3</sup> In addition to biologically important compounds, many natural products, synthetic intermediates, and structures of theoretical interest contain either aromatic halides and/or furans. Derivatives of these classes still remain synthetic challenges for many chemists.

The precise mechanisms of action for many enzymes, drugs, and toxins are poorly understood but presumably depend on conformational and stereoelectronic effects. Today, powerful computational procedures enable chemists to make more accurate quantitative predictions concerning conformational energies with an insight not previously available from experiment alone. In fact, this combination of theoretical and empirical techniques for tackling problems of this type provides the most complete means for obtaining solutions. There are few reports in the literature concerning the applications of molecular modeling in the specific area of health hazards.<sup>4</sup> Table

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(3) (a) McKinney, J. D.; Singh, P. *Chem. Biol. Interact.* 1981, 33, 271. (b) McKinney, J. D.; Chae, K.; Gupta, B. N.; Moore, J. A.; Goldstein, J. A. *Toxicol. Appl. Pharmacol.* 1976, 36, 64. (c) Poland, A.; Glover, E. *Mol. Pharmacol.* 1977, 13, 924.

**Table I. Molecular Mechanics Parameters for Divinyl Ether, Haloethylenes, and Halobenzene Derivatives<sup>a</sup>**

	torsional		
	V <sub>1</sub>	V <sub>2</sub>	V <sub>3</sub>
2-2-41-2	0.000	8.30	-0.800
2-2-41-20	0.000	0.000	0.250
5-2-41-20	0.000	7.500	0.000
5-2-41-2	-0.460	2.700	0.700
41-2-2-41	-2.000	15.000	0.000 <sup>b</sup>
2-2-2-41	0.000	15.000	0.000
5-2-2-41	0.000	15.000	0.000
11-2-2-11	-2.060	15.500	0.000
5-2-2-11	0.000	15.000	0.000
2-2-2-11	0.000	15.000	0.000
1-2-2-12	-1.470	15.500	0.000
6-2-2-12	-1.000	15.500	0.000
12-2-2-41	-1.000	15.500	0.000
2-2-2-12	0.000	15.000	0.000
12-2-2-12	-1.750	15.500	0.000
5-2-2-12	0.000	15.000	0.000
6-2-2-13	0.000	15.250	0.000
13-2-2-41	0.000	15.250	0.000
2-2-2-13	0.000	15.000	0.000
13-2-2-13	-2.150	15.500	0.000
5-2-2-13	0.000	15.000	0.000
11-2-2-12	-1.750	15.000	0.000
	bond stretching		
	K <sub>1</sub>	l <sub>0</sub>	bond moment
2-11	5.40	1.320	1.48
2-12	3.40	1.719	1.58
2-13	2.50	1.881	1.46
2-41	10.00	1.225	0.95 <sup>b</sup>
20-41	4.60	0.600	-0.75 <sup>b</sup>
	bending		
	K <sub>θ</sub>	θ <sub>0</sub>	
2-11	0.05		
2-12	0.05		
2-13	0.05		
2-41-2	0.87	113.95	
2-2-41	0.60	118.10 (type 2) <sup>b</sup>	
2-2-41	0.60	120.00 (type 1) <sup>b</sup>	
5-2-41	0.45	108.00	
2-41-20	0.35	122.20	
5-2-11	0.45	120.00	
2-2-11	0.65	121.00	
5-2-12	0.45	112.60	
2-2-12	0.55	118.80	
5-2-13	0.46	112.10	
2-2-13	0.45	118.10	

<sup>a</sup> MM2 atom types: 1 = C<sub>sp<sup>3</sup></sub>, 2 = C<sub>sp<sup>2</sup></sub> (alkene), 5 = H (alkyl), 6 = O<sub>sp<sup>2</sup></sub>, 41 = O<sub>sp<sup>2</sup></sub> (conjugated, MM2), 11 = F, 12 = Cl, 13 = Br, 20 = lone pair. The units and definitions are those used in the MM2 program (ref 5). These parameters are currently in the MM2(87) force field. <sup>b</sup> These parameters were independently developed by Julia Tai during the course of this investigation and were adopted without modification.

I displays some new MM2 parameters<sup>5</sup> that make it possible to carry out calculations on halo-containing vinyl and aromatic compounds as well as halo-containing furan and pyran derivatives.

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(5) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127 and subsequent papers. The program MM2(85) which is an extended but otherwise unchanged version of MM2 (Allinger, N. L.; Yuh, Y. *QCPE Newsletter* **1980**, *12*, 395) is available from the Quantum Chemistry Program Exchange, Department of Chemistry, University of Indiana, Bloomington, IN 47401, and from Molecular Design, Ltd., 47405 Faralon Drive, San Lenadro, CA 94577.

**Table II. Ab Initio and MM2 Conformational Energies for Divinyl Ether (kcal/mol)**

conformation	4-31G <sup>11</sup>	4-21G <sup>10</sup>	6-31G* <sup>a</sup>	MM2(85)	MM2(87)
[0, 180]			1.36	1.87	1.45
[180, 180]	0.65	1.58	0.46	0.00	0.46
[-28.9, -28.9]	2.39	1.07	2.99	5.03	2.45
[143, -17]	0.00	0.00	0.00	3.99	0.00 <sup>a</sup>

<sup>a</sup> The actual MM2 minimized energy conformation has  $\Psi_1 = 133$  and  $\Psi_2 = -7$ .

Divinyl ether, which until recently was extensively used as an anesthetic, is the simplest compound with the critical C<sub>sp<sup>2</sup></sub>-C<sub>sp<sup>2</sup></sub>-O-C<sub>sp<sup>2</sup></sub> torsion angle that is common to both PCDDs, PCDFs, and related furan derivatives. Divinyl ether has several possible rotameric forms, which may be described by two unique dihedral angles [ $\Psi_1$ ,  $\Psi_2$ ] about the central C<sub>sp<sup>2</sup></sub>-O bond. Some conflicting interpretations have been reported in the literature concerning the conformational preferences for divinyl ether.<sup>6-9</sup> Electron diffraction studies in the gas phase were long ago interpreted as indicating that a near planar [180, 180] conformation was the most stable.<sup>6</sup> Microwave studies<sup>7</sup> point to the [180, -60] conformer as the most stable, whereas infrared and Raman work<sup>8</sup> in the vapor and liquid states have been interpreted in terms of the [0, 180] conformer as the lowest energy rotamer. Later infrared and Raman experiments in the liquid and solid phases indicated that [180, 180] was the lowest energy conformer.<sup>9</sup> Geise and co-workers<sup>10</sup> have critically analyzed all of the previous experiments; they combined all of these techniques and developed an internally consistent model with the additional aid of ab initio calculations at the 4-21G level. Geise concludes that at 300 K the rotameric mixture of divinyl ether consists of 80% [143.5, -17.6] and 20% [180, 180]. Previous quantum mechanical calculations by John and Radom<sup>11</sup> at the STO-3G and 4-31G level gave a different order to the conformational energies, but generally agree with those obtained by Geise. These uncertainties prompted us to investigate the conformational preferences and energies with a higher basis set by using GAUSSIAN 82.<sup>12</sup>

We carried out a series of restricted Hartree-Fock full geometry optimizations with the split valence 6-31G\* basis set. Our results, presented in Table II, are in agreement with John and Radom's 4-31G calculations, with only minor geometric differences. (Also see Table III.) The 6-31G\* calculations indicate a mixture of conformations, principally with [143, -17] and [180, 180], 90% and 10%, respectively.<sup>13</sup> The early MM2 parameters for systems containing C<sub>sp<sup>2</sup></sub>-C<sub>sp<sup>2</sup></sub>-O<sub>sp<sup>2</sup></sub>-C<sub>sp<sup>2</sup></sub> (MM2 atom types: 2-2-41-2)<sup>14</sup> dihedral angles were based entirely on planar

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(11) John, I. G.; Radom, L. *J. Mol. Struct.* **1977**, *39*, 281.

(12) Pople's GAUSSIAN 82 program was used for all of the reported ab initio calculations except where otherwise stated. GAUSSIAN 82 was obtained from Professor Pople, Department of Chemistry, 4400 Fifth Avenue, Carnegie-Mellon University, Pittsburgh, PA 15213.

(13) When several conformations of a single compound have similar steric energies, a Boltzmann calculation should be carried out to determine the mole fraction of each conformer present in the equilibrium mixture. Each mole fraction may then be multiplied by the respective steric energy and summed to determine the average heat content,  $\Delta H$ , present in the system. The entropy of mixing and symmetry may be calculated, multiplied by the temperature, and subtracted from  $\Delta H$  to yield the free energy,  $\Delta G$ . In this case, the [180, 180] is C<sub>2h</sub> with a symmetry number of 2 while the [143, -17] conformer is C<sub>1</sub> with a symmetry number of 1. The latter is also a DL pair. For the conformational conversion of C<sub>2h</sub> to C<sub>1</sub>, the latter is favored by an entropy term of  $R \ln 4$ .

**Table III. Calculated and Experimental Geometries<sup>a</sup> for Divinyl Ethers, Related Derivatives, and Halo-Containing Alkenes and Benzenes<sup>18</sup>**

compound		experiment	MM2
divinyl ether [180, 180] <sup>10</sup>	C-O	1.387 (2)	1.386
	C=C	1.335	1.343
	C-C-O	118.7	120.99 <sup>b</sup>
	C-O-C	118.6	119.20
diphenyl ether <sup>16</sup>	C-O	1.358 (32)	1.388
	C-O-C	115.4 (3.3)	117.54
furan <sup>51</sup>	C-O	1.362 (30)	1.361
	C-O-C	106.55 (20)	106.34
	C-C-O	110.7 (2)	110.84
dioxin (TCDD) <sup>43</sup>	C-O	1.378	1.390
	C-O-C	115.1	
		115.6 <sup>c</sup>	116.99
furan (TCDF)	C-O-C	105.7 <sup>c</sup>	106.12
vinyl chloride <sup>19</sup>	C-Cl	1.726 (5)	1.720
	C-C-Cl	122.3 (5)	122.40
	H-C-Cl		114.19
		1.718 (10)	1.722
<i>cis</i> -1,2-dichloroethylene <sup>20</sup>	C-C-Cl	123.8 (15)	124.91
	C-Cl	1.726 (0.004)	1.721
<i>trans</i> -1,2-dichloroethylene <sup>20</sup>	C-C-Cl	120.7 (0.3)	121.98
	C-C-H	124.1 (1.3)	124.09
	C-Cl	1.711 (15)	1.725
chlorobenzene <sup>21</sup>	C-Cl	1.711 (15)	1.725
	C-C-Cl		119.92
	C-Cl	1.71 (3)	1.730
1,2-dichlorobenzene <sup>22</sup>	C-Cl	1.69 (3)	1.726
1,3-dichlorobenzene <sup>22</sup>	C-Cl	1.69 (3)	1.725
1,4-dichlorobenzene <sup>22</sup>	C-Br	1.882 (2)	1.882
vinyl bromide <sup>23</sup>	C-C-Br	122.7 (2)	122.88
	H-C-Br	113.5 (5)	113.68
	C-Br	1.883 (8)	1.885
1,2-dibromoethylene <sup>24</sup>	C-C-Br	124 (2)	126.37
	C-Br	1.85 (4)	1.890
bromobenzene <sup>25</sup>	C-Br	1.883 (8)	1.898
	<i>d</i>	63.6 (5)	63.90
1,2-dibromobenzene <sup>26</sup>	C-Br	1.88	1.890
	C-F	1.347 (9)	1.322
1,4-dibromobenzene <sup>27</sup>	C-F	1.347 (9)	1.322
	C-C-F	121.2	121.1
	H-C-F	110 (10)	118.7
vinyl fluoride <sup>28</sup>	C-F	1.310 (20)	1.325
	C-C-F	123.7 (25)	121.77
	C-F	1.354 (10)	1.323
fluorobenzene <sup>30</sup>	C-C-F		120.24
	C-F	1.310	1.324
	<i>e</i>	60.4 (20)	60.55
1,3-difluorobenzene <sup>32</sup>	C-F	1.30 (3)	1.323
	C-F	1.329 (20)	1.323
1-fluoro-3-chlorobenzene <sup>33</sup>	C-Cl	1.699 (20)	1.726
	C-F	1.30 (3)	1.323
1-bromo-4-fluorobenzene <sup>34</sup>	C-Br	1.87 (2)	1.890

<sup>a</sup> Bond lengths in angstroms, bond angles in degrees. <sup>b</sup> Ab initio 6-31G\* calculations give C-C-O = 121.5. <sup>c</sup> X-ray crystal value. <sup>d</sup> Effective angle between the two C-Br bonds. <sup>e</sup> Effective angle between the two C-F bonds.

aromatic systems such as furan and did not consider the divinyl ethers. This torsional potential was therefore not

(14) The MM2(85) program is the  $\pi$  atom version of MM2 (Allinger, N. L.; Sprague, J. T.). An approximately linear relationship exists between the bond order and bond lengths. Sufficient experimental data have been determined to also establish a linear correlation between the force constants and bond orders for multiple bonds in conjugated systems. The slope for the force constant, SSLOPE in the MM2 program, of the 2-41 bond type should be 5.44 and not 10.88. The 10.88 SSLOPE constant was incorrectly incorporated into the MM2(85) force field and discovered in the course of this investigation. (It is corrected in MM2(87) and later versions.) When the bond order becomes too small, molecular structures tend to dissociate because the force constants become negative. Thus, in order to calculate acyclic divinyl ether derivatives, the SSLOPE must be changed to 5.44. For more details on MM2, see: Burkert, U.; Allinger, N. L. *Molecular Mechanics*, American Chemical Society: Washington, DC, 1982 and the reference manual. The MM2 program assigns specific atom types to each atom and hybridized state. For example, 1 = C<sub>sp<sup>3</sup></sub>, 2 = C<sub>sp<sup>2</sup></sub>(alkene), 41 = oxygen in conjugation, and 5 = alkyl hydrogen. A more complete listing of the atom types may be found in the MM2 manual.

previously well established, and the values in MM2(85) do not in fact correctly account for the energy and conformational distribution in divinyl ethers. The lowest energy conformer derived with our new molecular mechanics parameters perhaps overestimates the stability of the eclipsed C<sub>sp<sup>2</sup></sub>-C<sub>sp<sup>2</sup></sub>-O<sub>sp<sup>2</sup></sub>-C<sub>sp<sup>2</sup></sub> dihedral angle. Instead of having [143, -17], we obtain [133, -7]. Single point ab initio calculations on the MM2 minimized structures (6-31G\*|| MM2) show that the [133, -7] energy is too stable by approximately 0.4 kcal/mol. This could very well be a deficiency in the force field or a quantum mechanical correlation problem.<sup>15</sup> Nevertheless, this discrepancy is within the margin of errors for both methods.

The C<sub>sp<sup>2</sup></sub>-O<sub>sp<sup>2</sup></sub>-C<sub>sp<sup>2</sup></sub> parameters were adjusted to give the best fit for furan, dibenzofuran, and divinyl ether. By using the torsional potential ( $V_{\text{tor}}$ ) expressed by a three-term truncated Fourier series, the best geometric and energetic fit for divinyl ether was obtained (eq 1). However,

$$V_{\text{tor}} = \frac{1}{2}[V_1(1 + \cos \omega) + V_2(1 - \cos 2\omega) + V_3(1 + \cos 3\omega)] \quad (1)$$

MM2 predicts two other low-energy conformations, [143, 143] and [143, -143], with essentially the same energy and 0.10 kcal lower, respectively, than the [133, -7] MM2 conformer. Fixing both torsion angles  $\Psi_1$  and  $\Psi_2$  in divinyl ether to 143° and allowing all other geometric parameters to be variables, a 6-31G\* optimization was carried out. The energy was 0.60 kcal/mol higher than the [180, 180] conformation. The MM2 results predicting the [143, 143] and [143, -143] conformers as stable are not surprising, since the torsional terms were adjusted to give a minimum near 143° for the C<sub>sp<sup>2</sup></sub>-C<sub>sp<sup>2</sup></sub>-O<sub>sp<sup>2</sup></sub>-C<sub>sp<sup>2</sup></sub> dihedral angle. Nonetheless, for the entire set of compounds, MM2 agrees well with the ab initio and experimental data.

Diphenyl ether is a similar compound that contained the critical C<sub>sp<sup>2</sup></sub>-C<sub>sp<sup>2</sup></sub>-O<sub>sp<sup>2</sup></sub>-C<sub>sp<sup>2</sup></sub> torsion angle that also needed to be examined. The structure of diphenyl ether has been studied by electron diffraction by Naumov and Ziatdinova.<sup>16</sup> Four series of models were analyzed with (1)  $\Psi_1 = \Psi_2$ , (2)  $\Psi_1 = -\Psi_2$ , (3)  $\Psi_1 = 90 - \Psi_2$ , and (4)  $\Psi_1 \neq \Psi_2$ . Naumov and Ziatdinova indicate that when the number of quantities being varied included the basic geometric parameters  $r(\text{C-O})$ , the angle COC,  $\Psi_1$ , and  $\Psi_2$  (the restriction  $\Psi_1 = 90 - \Psi_2$  was removed), the *R* factor was decreased sharply. From this analysis Naumov and Ziatdinova conclude that the conformation with  $\Psi_1 = 29^\circ$ ,  $\Psi_2 = 70^\circ$  shows slightly better agreement with experiment than the conformation with  $\Psi_1 = \Psi_2 = 43^\circ$ . With the new MM2 parameters, which were derived specifically to fit the divinyl ether case, we obtain two diphenyl ether conformations of approximately the same energy with  $\Psi_1 = 17^\circ$ ,  $\Psi_2 = 72^\circ$  and with  $\Psi_1 = 41^\circ$  and  $\Psi_2 = 40^\circ$ . A third diphenyl ether conformation has  $\Psi_1 = \Psi_2 = 89^\circ$  and is 1.5 kcal/mol higher in energy. The two phenyl planes form approximately 80°, 67°, and 64° angles, respectively, for the [17, 72], [41, 40], and [89, 89] diphenyl ether conformers. X-ray diffraction work on a diphenyl ether derivative by Cory et al. indicated a similar conformation for the two phenyl planes.<sup>17</sup>

(15) There seems to be a systematic difference between ab initio and molecular mechanics energies for eclipsed conformations. In general, MM2 is parameterized to fit experimental data, when available. A specific case in point and under study is the Me/Me eclipsed conformation of butane. Ab initio calculations give the barrier to be about 6 kcal/mol, whereas MM2 calculations give a barrier of 4.5 kcal/mol, which is in agreement with experimental data.

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**Table IV. Calculated and Experimental Relative Energies for the Cis-Trans Isomerization of 1,2-Dihaloethylenes and Related Compounds in the Gas Phase<sup>38</sup>**

compound	experiment	MM2
HFC=CFH	0.928 ± 0.029	0.957 <sup>a</sup>
HFC=CHCl	0.780 + 0.020	0.79
HCIC=CClH	0.650 + 0.076	0.20 <sup>a</sup>
HBrc=CBrH	0.320 + 0.200	0.32
HCIC=CHCH3	0.700 + 0.064	0.71

<sup>a</sup> See ref 35.

Table III displays, among other data, the experimental and calculated molecular geometries for some compounds containing the key C-O bond. The bond order and resonance integrals are a function of the torsion angles about the C-O bond. As one would expect, twisting the  $C_{sp^2}-C_{sp^2}-O_{sp^2}-C_{sp^2}$  torsion angle from planarity reduces the overlap, and the MM2 bond orders and resonance integrals reflect this trend.<sup>14</sup> Substituted halobenzenes and haloethylenes are important organic compounds and have never before been quantitatively parametrized with MM2. In order to study more complex halo-containing aromatic derivatives, such as dioxin analogues, the molecular geometries for various halogenated compounds needed to be fitted. Table III also displays the experimental and calculated results for a variety of fluoro-, chloro-, and bromo-substituted compounds. Most of the structural information comes from microwave data and electron diffraction work.<sup>18-34</sup> The calculated geometries are generally within experimental error and appear overall to adequately reproduce known experimental data.

Where possible, we have carried out ab initio calculations to compare the molecular geometries and energies. 6-31G\* calculations do not adequately reproduce the energy differences between *cis/trans*-1,2-difluoroethylene and *cis/trans*-1,2-dichloroethylene.<sup>35,36</sup> It is known experimentally that the *cis* geometry is the most stable. For 1,2-difluoroethylene and 1,2-dichloroethylene, the *cis* isomer is favored by approximately 1.1 and 0.2 kcal/mol, respectively. The 6-31G\* calculations have the reverse energy preference, favoring the *trans*-1,2-difluoro- and 1,2-dichloroethylene by 0.4 and 0.2 kcal/mol, respectively. These problems have been recognized for some time, however, and are attributed to the inadequacy of the basis sets. Higher level calculations with the more flexible 6-31G\*\* basis set seem to remedy the problem.<sup>37</sup> To fit the experimentally determined energy preferences for the *cis*-1,2-dihaloethylenes, we have added a large negative  $V_1$  term to the torsional potential (Table I). For example, the  $V_1$  term for the 1,2-difluoroethylene torsional potential 11-2-2-11 (F- $C_{sp^2}-C_{sp^2}$ -F) was set to -2.06, and the  $V_1$  term for the 1,2-dichloroethylene torsional potential 12-2-2-12 (Cl- $C_{sp^2}-C_{sp^2}$ -Cl) was set to -1.75. Table IV displays the *cis-trans* isomerization energies for some 1,2-dihalo-substituted ethylenes and related compounds.<sup>38</sup> With the development of the fundamental divinyl and halo-containing ethylene parameters it was then possible to calculate some polyhalogenated molecular structures. Our attention was focused on examining structures with both groups present in the same molecule and having some biological importance.

Various experimental techniques have been used to determine bond angles for dibenzodioxins and related compounds. Many of these studies have inferred structures ranging from folded to near planar, with the COC bond angle ranging from approximately 115° to 118°.<sup>39-43</sup> Spectral and structural correlations for dibenzodioxins were recently determined by IR analyses using off-line microsampling dispersive techniques.<sup>44,45</sup> In these studies, characteristics of individual chlorinated dibenzodioxin isomers were deduced from IR data by a valence-bond treatment of electronic and structural contributions to the ether linkage asymmetric stretching frequency.<sup>46</sup> By incorporating the ether linkage vibrational frequencies into valence force field equations, dimethyl ether was determined by this approach to have a COC bond angle of 116°,<sup>47,48</sup> whereas it has been experimentally determined

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to be 112°. Molecular mechanics calculations yield a COC bond angle of 111.78°, more in agreement with experimental data.<sup>49</sup> In-phase ring stretching vibrational frequencies resulting from Raman spectroscopy for cycloalkanes and cyclic aliphatic ethers have been found to be roughly proportional to the bond angle.<sup>47,50</sup> A study on the correlation of planarity of rings with the substitution pattern in chlorinated dibenzodioxin was conducted by Chen, using IR data.<sup>44</sup>

The infrared vapor phase spectrum for 2,3,7,8-tetrachlorodibenzodioxin was recorded, and its COC bond angle ( $\alpha$ ) was calculated from IR data by using mass approximations for the terminal atom in a nonlinear  $XV_2$  model and by neglect of the valence force field equations of the symmetric stretch-bending term. Details of these calculations, describing the molecular geometries using IR data for 2,3,7,8-tetrachloro- and other chlorinated dibenzodioxins and the limiting approximations, are reported elsewhere by Grainger, Reddy, and Patterson.<sup>45</sup> The COC bond angle ( $\alpha$ ) derived for 2,3,7,8-tetrachlorodibenzodioxin was 115.1° compared with 115.6° determined from X-ray diffraction data.<sup>43</sup> In addition, for furan we calculate a COC bond angle of 110.8°, which is in agreement with the experimental value of 110.7 (2)°.<sup>51</sup>

With the new parameter set, we find that a near planar structure is favored for 2,3,7,8-tetrachlorodibenzodioxin. Our calculations indicate that an extreme "butterfly" conformation is not a minimum energy conformation. MM2 gives a COC angle of 116.9°, with one of the phenyl rings bent out of the plane, defined by the other phenyl group, by approximately 5°.

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## Conclusions

MM2 parameters have been developed for divinyl and diphenyl ethers, as well as for a variety of halo-substituted vinyl and aromatic derivatives. Ab initio calculations were used to augment sketchy or lacking experimental data. The new MM2 parameters reasonably reproduce the conformational energies and molecular geometries for a wide variety of structures comprising this general class of organic compounds. Therefore, we recommend that users of MM2 substitute the new divinyl parameters for the ones incorporated into older (1985 and earlier) versions of the program. They should also correct the SSLOPE from 10.88 to 5.44 for the 2-41 atom type<sup>14</sup> and add the new halogen parameters.

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**Registry No.** TCDD, 1746-01-6; TCDF, 51207-31-9; *cis*-HFC=CFH, 1630-77-9; *cis*-HFC=CHCl, 2268-31-7; *cis*-HBrC=CBrH, 590-11-4; *cis*-HCIC=CHCH<sub>3</sub>, 16136-84-8; *trans*-HFC=CFH, 1630-78-0; *trans*-HFC=CHCl, 2268-32-8; *trans*-HBrC=CBrH, 590-12-5; *trans*-HCIC=CHCH<sub>3</sub>, 16136-85-9; divinyl ether, 109-93-3; diphenyl ether, 101-84-8; furan, 110-00-9; vinyl chloride, 75-01-4; *cis*-1,2-dichloroethylene, 156-59-2; *trans*-1,2-dichloroethylene, 156-60-5; chlorobenzene, 108-90-7; 1,2-dichlorobenzene, 95-50-1; 1,3-dichlorobenzene, 541-73-1; 1,4-dichlorobenzene, 106-46-7; vinyl bromide, 593-60-2; 1,2-dibromoethylene, 540-49-8; bromobenzene, 108-86-1; 1,2-dibromobenzene, 583-53-9; 1,4-dibromobenzene, 106-37-6; vinyl fluoride, 75-02-5; 1,2-difluoroethylene, 1691-13-0; fluorobenzene, 462-06-6; 1,2-difluorobenzene, 367-11-3; 1,3-difluorobenzene, 372-18-9; 1-fluoro-3-chlorobenzene, 625-98-9; 1-bromo-4-fluorobenzene, 460-00-4.

## Structurally New Macrocycles from the Resorcinol-Aldehyde Condensation. Configurational and Conformational Analyses by Means of Dynamic NMR, NOE, and $T_1$ Experiments

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The acid-catalyzed condensation of resorcinol with heptanal or dodecanal followed by acetylation produces three stereoisomeric tetrameric macrocycles. The product distribution is controlled by the relative solubilities of the stereoisomeric octols in the reaction medium. These isomers comprise the previously described boat conformation ( $C_{2v}$  symmetry) and chair conformation ( $C_{2h}$  symmetry) plus a new one with a diamond-like conformation ( $C_s$  symmetry). The corresponding relative configurations of the alkyl substituents, determined from NOE enhancements and NMR spectra, are all-*cis*, *cis-trans-trans*, and *cis-trans-cis*. In all three isomers, the alkyl substituents are in the less hindered axial position. The thermodynamically more stable boat octols can be obtained selectively in high yields (50–80%) by heating the crude initial condensation mixtures at reflux for 4 h.

### Introduction

In our search for building blocks for cavitands,<sup>2</sup> we became interested in macrocycles of structure I, which can

be easily obtained in high yield by the acid-catalyzed condensation of resorcinol with aldehydes.<sup>3</sup> Although there are many possible stereoisomers of I, only two have been found experimentally. The configuration and conformation of these two isomers of the octaesters  $R = Ph$

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