

# Crystallographic study and molecular orbital calculations of 1,2,5-thiadiazole 1,1-dioxide derivatives

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**ABSTRACT:** Single-crystal x-ray diffraction studies are reported for 3,4-dimethyl (I), 3-methyl-4-phenyl (II) and 3,4-diphenyl (III) derivatives of 1,2,5-thiadiazole 1,1-dioxide. *Ab initio* MO calculations on the electronic structure, conformation and reactivity of I, II and III are also reported and compared with the x-ray results. The structural data are related to previous kinetic and electrochemical experimental results on these compounds. © 1998 John Wiley & Sons, Ltd.

**KEYWORDS:** 1,2,5-thiadiazole; 1,1-dioxide derivatives; single-crystal x-ray diffraction; *ab initio* MO calculations; structure; conformation; reactivity

## INTRODUCTION

Organic heterocycles are systems of growing interest in materials science. Several potentially conducting polymers, optically non-linear polymers and biomaterials contain heterocyclic structures. Thiadiazoles are the structural basis of some of these polymeric materials.<sup>1</sup> Furthermore, 1,2,5-thiadiazole derivatives exhibit interesting pharmacological properties.<sup>2</sup>

Following our previous studies on kinetics,<sup>3,4</sup> UV–VIS and NMR spectra<sup>5</sup> and electrochemistry<sup>6,7</sup> of several 3,4-disubstituted 1,1-dioxide derivatives of 1,2,5-thiadiazole, we report here single-crystal x-ray diffraction studies on

the molecular structure of 3,4-dimethyl (I), 3-methyl-4-phenyl (II) and 3,4-diphenyl (III) derivatives. *Ab initio* HF/6–31G\*\* Hartree–Fock LCAO molecular orbital (MO) calculations were also performed for all these compounds.

## MO THEORETICAL CALCULATIONS AND COMPUTATIONAL METHODS

The density functional theory (DFT)<sup>8</sup> provides a convenient theoretical framework for calculating global and local indices that quantitatively describe the inherent reactivity of chemical species. In particular, the Fukui and local softness functions<sup>9–11</sup> can be employed to determine the nature of the reactive sites in a given molecule and, from this information, to draw inferences about some aspects of the behavior of the molecule when reacting with other species.

The condensed Fukui functions, which are determined by a Mulliken population analysis,<sup>12,13</sup> can also be employed to determine the relative softness of each atom in the molecule. The corresponding integrated functions are given by<sup>14</sup>

$$f_k^+ = q_k(N + 1) - q_k(N) \text{ (for nucleophilic attack) (1)}$$

$$f_k^- = q_k(N) - q_k(N - 1) \text{ (for electrophilic attack) (2)}$$

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**Table 1.** Crystal data, data collection details and structure refinement results for 3,4-substituted 1,2,5-thiadiazolx 1,1-dioxide derivatives **I–III**

Parameter	C <sub>4</sub> H <sub>6</sub> N <sub>2</sub> O <sub>2</sub> S ( <b>I</b> )	C <sub>9</sub> H <sub>8</sub> N <sub>2</sub> O <sub>2</sub> S ( <b>II</b> )	C <sub>14</sub> H <sub>10</sub> N <sub>2</sub> O <sub>2</sub> S ( <b>III</b> )
Molecular weight	146.17	208.2	270.3
Space group	C2/c	P2 <sub>1</sub> /n	P2 <sub>1</sub> /c
<i>a</i> (Å)	11.803(3)	10.033(3)	10.115(1)
<i>b</i> (Å)	7.326(1)	8.060(3)	8.125(1)
<i>c</i> (Å)	8.174(3)	12.990(3)	16.168(2)
β (°)	106.70(2)	111.18(1)	98.24(1)
<i>V</i> (Å <sup>3</sup> )	677.1(3)	980(1)	1314.9(5)
<i>Z</i>	4	4	4
<i>D<sub>c</sub></i> (g cm <sup>-3</sup> )	1.124	1.412	1.365
Absorbance (μ mm <sup>-1</sup> )	0.304	0.29	0.233
Independent reflections	886	2291	3493
Reflections <i>I</i> > 3σ( <i>I</i> )	662	1263	2610
<i>R</i> -factor	0.041	0.050	0.045

$$f_k^0 = \frac{q_k(N+1) - q_k(N-1)}{2} \text{ (for radical attack)} \quad (3)$$

where  $q_k$  is the gross charge of atom  $k$  in the molecule.

To distinguish the behavior of the different atoms in a molecule by employing equations (1)–(3), it is necessary to obtain the electronic densities of the molecule as a neutral entity and also the corresponding anionic and cationic moieties. These densities may be calculated within the *ab initio* Hartree–Fock LCAO approximation employing the 6–31G\*\* basis set, while the net atomic charges of the anion, cation and neutral molecule are obtained through a Mulliken population analysis. In conjunction with the nuclear charges at the equilibrium configuration, the electronic distribution determines the molecular electrostatic potential.<sup>15</sup> This potential, in turn, provides a guide to finding the reaction sites on the molecule: positively (negatively) charged reagents, i.e. electrophilics (nucleophilics), tend to attack at places where the electrostatic potential is strongly negative (positive).

All the MO calculations were performed with the Gaussian 94W series of programs.<sup>16</sup> Single determinantal wavefunctions of the restricted Hartree–Fock (RHF) type were used for the closed-shell system, and those of the unrestricted Hartree–Fock (UHF) type were considered for the open-shell systems, with orbitals being the solutions of the Roothaan equations.<sup>17</sup> The equilibrium conformation of the neutral molecule was calculated by the gradient method.

## EXPERIMENTAL

Single crystals of **I** and **III** were grown from ethanolic solutions and **II** from a benzene solution.

Single-crystal fragments of **I–III** were mounted on an Enraf-Nonius CAD-4 x-ray diffractometer. In all cases, 15 centered reflections using least-squares refinement

**Table 2.** Fractional atomic coordinates and isotropic temperature parameters (Å<sup>2</sup>) for 3,4-dimethyl-1,2,5-thiadiazole 1,1-dioxide (**I**)

Atom	<i>X/a</i>	<i>Y/b</i>	<i>Z/c</i>	<i>B<sub>iso</sub></i>
S	0	0.1291(1)	0.25	4.18(3)
N	−0.1119(2)	−0.0196(3)	0.2037(3)	4.37(7)
O	0.0036(2)	0.2293(2)	0.1032(2)	6.25(7)
C(1)	−0.0667(2)	−0.1778(3)	0.2235(3)	3.32(6)
C(2)	−0.1350(3)	−0.3512(4)	0.1982(4)	5.4(1)
H(1)	−0.1191(1)	−0.4256(1)	0.3109(1)	11.0(8)
H(2)	−0.2079(1)	−0.3237(1)	0.1712(1)	11.0(8)
H(3)	−0.1183(1)	−0.4295(1)	0.0988(1)	11.0(8)

**Table 3.** Fractional atomic coordinates and isotropic temperature parameters (Å<sup>2</sup>) for 3-methyl-4-phenyl-1,2,5-thiadiazole 1,1-dioxide (**II**)

Atom	<i>X/a</i>	<i>Y/b</i>	<i>Z/c</i>	<i>B<sub>iso</sub></i>
S	0.1589(1)	0.1292(1)	0.2288(1)	2.92(2)
O(1)	0.0833(3)	−0.0217(3)	0.2195(3)	4.41(9)
O(2)	0.0797(3)	0.2797(3)	0.2123(3)	4.32(9)
N(1)	0.2539(3)	0.1265(4)	0.1468(2)	4.42(9)
N(2)	0.2934(3)	0.1359(4)	0.3508(3)	3.45(9)
C(1)	0.3856(3)	0.1303(4)	0.2083(3)	2.59(8)
C(2)	0.4094(3)	0.1369(5)	0.3313(3)	2.73(8)
C(3)	0.4997(3)	0.1397(5)	0.1634(3)	3.13(9)
C(4)	0.4801(5)	0.2353(7)	0.0712(4)	4.8(1)
C(5)	0.5867(7)	0.2428(9)	0.0269(5)	6.8(2)
C(6)	0.7109(6)	0.1558(9)	0.0726(5)	6.5(2)
C(7)	0.7304(5)	0.0594(7)	0.1636(6)	6.1(2)
C(8)	0.6267(4)	0.0485(6)	0.2104(4)	4.5(1)
C(9)	0.5523(5)	0.1494(6)	0.4202(3)	4.5(1)

**Table 4.** Fractional atomic coordinates and isotropic temperature parameters ( $\text{\AA}^2$ ) for 3,4-diphenyl-1,2,5-thiadiazole 1,1-dioxide (**III**)

Atom	X/a	Y/b	Z/c	$B_{\text{iso}}$
S	0.9141(1)	0.0376(1)	0.7640(1)	2.89(1)
O(1)	0.8607(2)	0.1809(2)	0.7971(1)	4.19(5)
O(2)	0.8361(1)	-0.1083(2)	0.7576(1)	4.01(5)
N(1)	1.0647(2)	0.0010(2)	0.8177(1)	2.77(4)
N(2)	0.9593(2)	0.0791(2)	0.6710(1)	3.21(5)
C(1)	1.1513(2)	0.0190(2)	0.7670(1)	2.37(4)
C(2)	1.0868(2)	0.0608(2)	0.6776(1)	2.59(5)
C(3)	1.2949(2)	0.0066(2)	0.7978(1)	2.57(4)
C(4)	1.3376(2)	-0.1020(3)	0.8632(1)	3.69(6)
C(5)	1.4714(2)	-0.1093(3)	0.8957(2)	4.60(8)
C(6)	1.5629(2)	-0.0088(4)	0.8636(2)	4.54(7)
C(7)	1.5215(2)	0.0983(3)	0.8000(2)	4.04(7)
C(8)	1.3870(2)	0.1068(3)	0.7660(1)	3.18(5)
C(9)	1.1559(2)	0.0790(3)	0.6044(1)	3.12(5)
C(10)	1.2572(3)	-0.0297(3)	0.5902(2)	4.01(7)
C(11)	1.3176(3)	-0.0134(4)	0.5196(2)	5.24(9)
C(12)	1.2796(3)	0.1093(5)	0.4630(2)	6.3(1)
C(13)	1.1798(4)	0.2176(5)	0.4767(2)	6.5(1)
C(14)	1.1157(3)	0.2015(3)	0.5469(2)	4.70(8)

gave the unit cell dimensions and the orientation matrix for data collection. Intensities were measured by the  $\omega$ - $2\theta$  scan technique at a rate between 2.85 and 20.0°  $\text{min}^{-1}$  determined by a fast pre-scan of 20.0°  $\text{min}^{-1}$ . Reflections were collected in the range  $0 < \theta < 30^\circ$  using graphite-monochromated Mo K $\alpha$  radiation. Crystal data,

**Table 5.** Interatomic bond distances ( $\text{\AA}$ ) and angles ( $^\circ$ ) for **I**<sup>a</sup>

Bonds	Experimental	HF/6-31G**
S—N	1.670(2)	1.682
S—O	1.418(2)	1.418
N—C(1)	1.267(3)	1.255
C(1)—C(2)	1.487(4)	1.499
C(1)—C(1')	1.508(5)	1.537
C(2)—H(1)	1.040(3)	1.083
C(2)—H(2)	0.849(3)	1.080
C(2)—H(3)	1.058(3)	1.083
O—S—N	111.1(1)	109.1
O—S—O'	117.6(1)	121.1
O—S—N'	108.4(1)	109.1
N—S—N'	98.5(1)	98.6
S—N—C(1)	106.9(2)	108.9
N—C(1)—C(2)	124.9(2)	121.7
N—C(1)—C(1')	113.8(2)	112.8
C(2)—C(1)—C(1')	121.3(2)	125.5
C(1)—C(2)—H(1)	111.8(3)	112.9
C(1)—C(2)—H(2)	107.6(3)	109.0
C(1)—C(2)—H(3)	110.9(2)	112.9
H(1)—C(2)—H(2)	105.4(3)	108.9
H(1)—C(2)—H(3)	111.7(3)	107.9
H(2)—C(2)—H(3)	109.1(3)	108.9

<sup>a</sup> Primed atoms are obtained from the corresponding symmetry-related and unprimed atoms through the space group operation:  $-x, y, 1/2 - z$ .

**Table 6.** Interatomic bond distances ( $\text{\AA}$ ) and angles ( $^\circ$ ) for **II**.

Bonds	Experimental	HF/6-31G**
S—O(1)	1.415(3)	1.418
S—O(2)	1.423(3)	1.418
S—N(1)	1.666(3)	1.667
S—N(2)	1.670(3)	1.673
N(1)—C(1)	1.274(5)	1.261
N(2)—C(2)	1.277(5)	1.255
C(1)—C(2)	1.529(5)	1.558
C(1)—C(3)	1.462(5)	1.486
C(2)—C(9)	1.484(6)	1.506
C(3)—C(4)	1.377(6)	1.391
C(3)—C(8)	1.405(6)	1.400
C(4)—C(5)	1.387(8)	1.386
C(5)—C(6)	1.365(9)	1.381
C(6)—C(7)	1.368(9)	1.388
C(7)—C(8)	1.384(7)	1.378
C—H	1.090	1.083
O(1)—S—O(2)	117.8(2)	120.8
O(1)—S—N(1)	110.3(2)	109.3
O(1)—S—N(2)	109.5(2)	109.2
O(2)—S—N(1)	109.4(2)	109.3
O(2)—S—N(2)	109.3(2)	109.2
N(1)—S—N(2)	98.9(2)	96.2
S—N(1)—C(1)	107.6(2)	110.5
S—N(2)—C(2)	107.1(3)	109.9
N(1)—C(1)—C(2)	113.0(3)	111.4
N(1)—C(1)—C(3)	122.4(3)	125.0
C(2)—C(1)—C(3)	124.5(3)	129.8
N(2)—C(2)—C(1)	113.4(3)	112.1
N(2)—C(2)—C(9)	122.6(3)	117.5
C(1)—C(2)—C(9)	123.9(3)	130.4
C(1)—C(3)—C(4)	119.3(4)	116.7
C(1)—C(3)—C(8)	121.1(4)	125.0
C(4)—C(3)—C(8)	119.5(4)	118.2
C(3)—C(4)—C(5)	119.7(5)	120.8
C(4)—C(5)—C(6)	121.1(6)	120.3
C(5)—C(6)—C(7)	119.4(6)	119.7
C(6)—C(7)—C(8)	121.3(6)	120.1
C(3)—C(8)—C(7)	118.9(4)	120.8

data collection details and structure refinement results for **I–III** are summarized in Table 1.

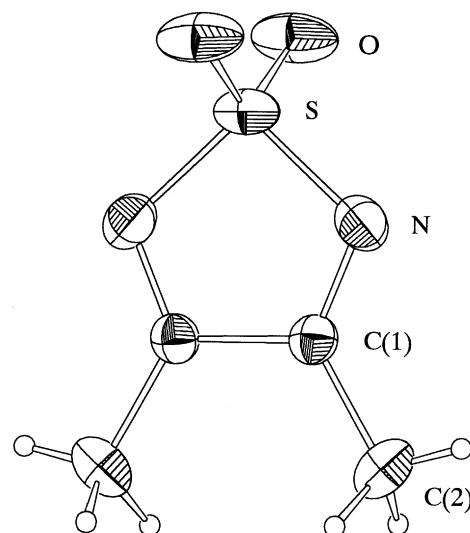
The intensity of one standard reflection selected for each compound was essentially constant over the duration of the experiments. Data were corrected by Lorentz and polarization effects but not for absorption or extinction. Scattering factors taken from Cromer and Waber<sup>18</sup> and the corresponding anomalous dispersion coefficients from Cromer and Liberman<sup>19</sup> were used in the calculations. These were performed with the SHELX<sup>20</sup> and SDP<sup>21</sup> systems of programs. The molecular models shown were drawn with the program ORTEP.<sup>22</sup>

The structures were solved by standard centrosymmetric direct methods and Fourier techniques and refined by full-matrix least-squares methods with anisotropic thermal parameters for all non-hydrogen atoms.

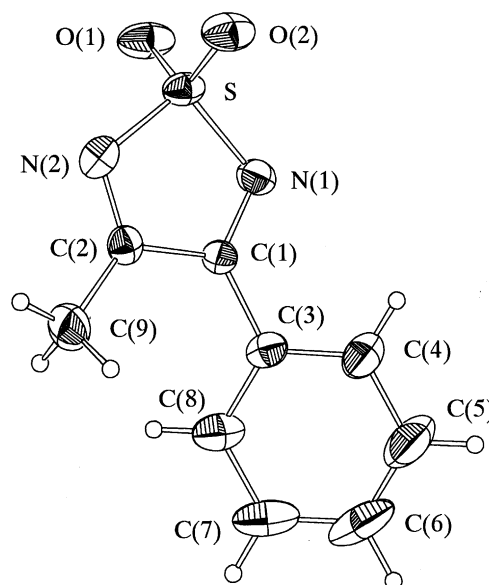
**Table 7.** Interatomic bond distances (Å) and angles (°) for **III**

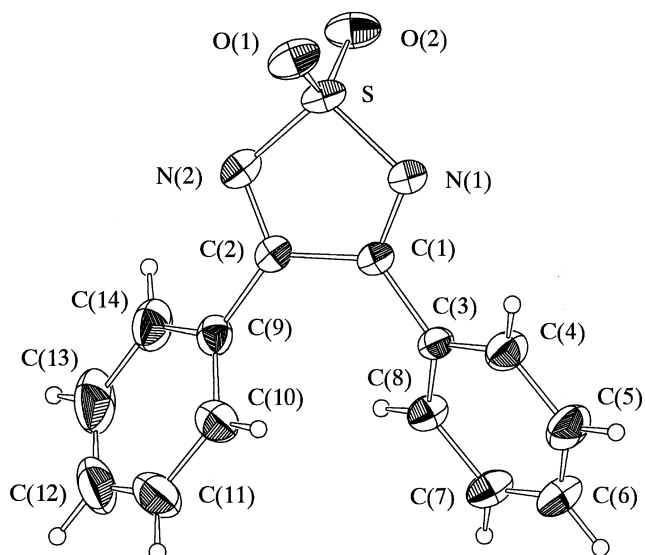
Bonds	Experimental	HF/6-31G**
S—O(1)	1.420(2)	1.419
S—O(2)	1.419(2)	1.419
S—N(1)	1.668(2)	1.672
S—N(2)	1.668(2)	1.672
N(1)—C(1)	1.291(2)	1.266
N(2)—C(2)	1.287(2)	1.267
C(1)—C(2)	1.536(3)	1.559
C(1)—C(3)	1.470(2)	1.464
C(2)—C(9)	1.466(3)	1.464
C(3)—C(4)	1.397(3)	1.390
C(3)—C(8)	1.390(3)	1.391
C(4)—C(5)	1.381(3)	1.381
C(5)—C(6)	1.389(4)	1.381
C(6)—C(7)	1.366(4)	1.385
C(7)—C(8)	1.394(3)	1.391
C(9)—C(10)	1.396(3)	1.391
C(9)—C(14)	1.383(3)	1.391
C(10)—C(11)	1.376(4)	1.380
C(11)—C(12)	1.370(5)	1.387
C(12)—C(13)	1.381(5)	1.385
C(13)—C(14)	1.392(4)	1.391
C—H	1.090	1.088
O(1)—S—O(2)	118.3(1)	121.2
O(1)—S—N(1)	108.56(9)	109.1
O(1)—S—N(2)	110.02(9)	109.6
O(2)—S—N(1)	110.21(9)	109.6
O(2)—S—N(2)	108.93(9)	109.1
N(1)—S—N(2)	99.06(8)	95.1
S—N(1)—C(1)	107.5(1)	111.4
S—N(2)—C(2)	107.6(1)	111.4
N(1)—C(1)—C(2)	112.8(1)	111.0
N(1)—C(1)—C(3)	120.3(2)	122.4
C(2)—C(1)—C(3)	126.8(1)	126.6
N(2)—C(2)—C(1)	112.9(2)	111.0
N(2)—C(2)—C(9)	120.6(2)	122.4
C(1)—C(2)—C(9)	126.5(2)	126.6
C(1)—C(3)—C(4)	118.9(2)	118.5
C(1)—C(3)—C(8)	121.1(2)	121.5
C(4)—C(3)—C(8)	119.9(2)	119.9
C(3)—C(4)—C(5)	119.7(2)	120.0
C(4)—C(5)—C(6)	120.1(2)	120.0
C(5)—C(6)—C(7)	120.5(2)	120.1
C(6)—C(7)—C(8)	120.3(2)	120.1
C(3)—C(8)—C(7)	119.5(2)	119.8
C(2)—C(9)—C(10)	121.0(2)	121.5
C(2)—C(9)—C(14)	119.2(2)	118.5
C(10)—C(9)—C(14)	119.8(2)	119.8
C(9)—C(10)—C(11)	119.9(2)	119.9
C(10)—C(11)—C(12)	120.6(3)	120.0
C(11)—C(12)—C(13)	119.9(3)	120.1
C(12)—C(13)—C(14)	120.5(3)	119.9
C(9)—C(14)—C(13)	119.3(3)	120.1

All methyl hydrogen atoms of **I** were located from a difference Fourier map and were included fixed at these locations in the final structure factor calculation with a common temperature factor which refined to  $U = 0.14(1) \text{ \AA}^2$ . The molecule is at a special position on a crystallographic twofold axis.

**Figure 1.** Molecular structure of 3,4-dimethyl-1,2,5-thiadiazole 1,1-dioxide (**I**)

Most hydrogen atoms of **II** and **III** were also located from difference Fourier maps. However, they were positioned on stereochemical grounds and incorporated in the final molecular model. The positions of the hydrogen atoms were refined in **II** with a common isotropic temperature parameter that converged to  $U = 0.098(7) \text{ \AA}^2$ . All phenyl hydrogens in **III** were treated similarly with a common isotropic temperature parameter which converged to  $U = 0.071(3) \text{ \AA}^2$ . The hydrogen positions were refined by fixing bond distances to the corresponding atoms at their accepted values.

**Figure 2.** Molecular structure of 3-methyl-4-phenyl-1,2,5-thiadiazole 1,1-dioxide (**II**)



**Figure 3.** Molecular structure of 3,4-diphenyl-1,2,5-thiadiazole 1,1-dioxide (**III**)

## RESULTS AND DISCUSSION

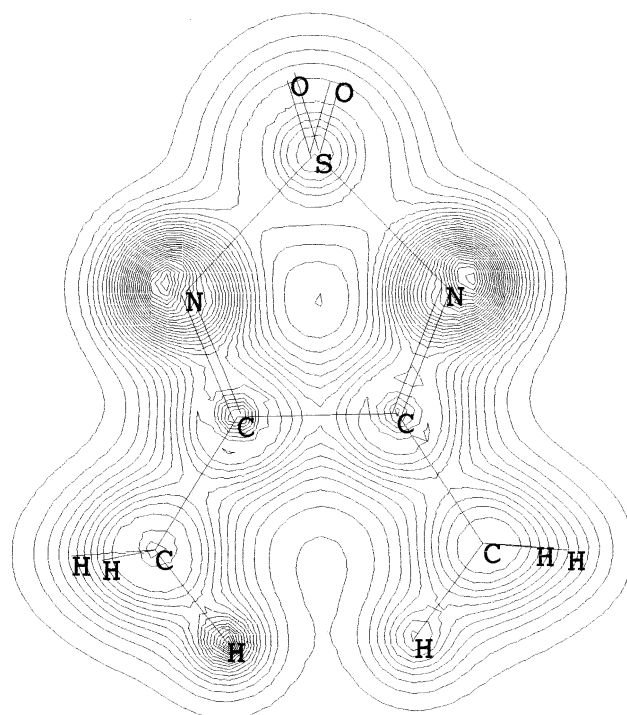
### Crystallography

Fractional coordinates and equivalent isotropic temperature parameters<sup>23</sup> for the non-H atoms in **I–III** are given in Tables 2–4. Relevant bond distances and angles are given in Tables 5–8 and ORTEP molecular drawings showing the labelling of the atoms and their vibrational ellipsoids are shown in Figures 1–3.

The structural details in Tables 5–7 allow comparisons among these compounds and with reported studies on related compounds, such as thiadiazines,<sup>24–28</sup> a thiadiazoline,<sup>29</sup> a thiadiazole 1-dioxide<sup>30</sup> and a thiadiazole,<sup>31</sup> and suggest relationships with their experimental chemical behavior that will be discussed below.

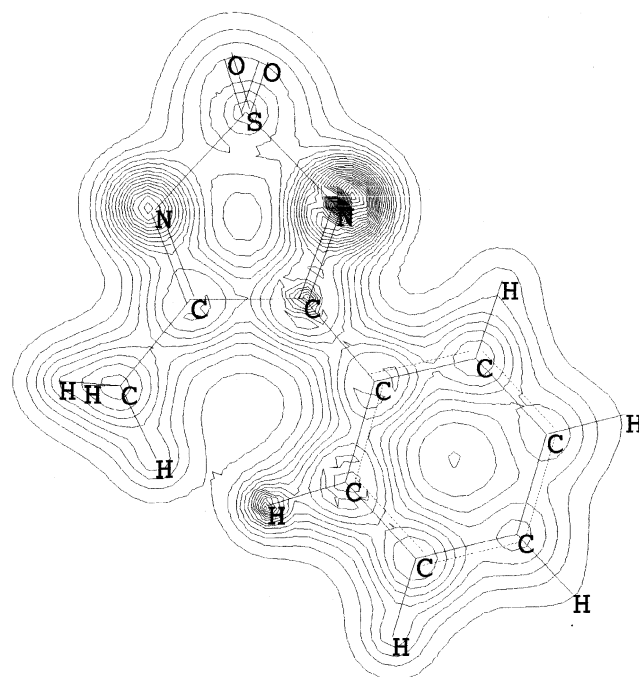
As already found in the related six-membered heterocyclic compounds 1,2,6-thiadiazine 1,1-dioxides,<sup>24–28</sup> the geometry around the S atom corresponds to a distorted tetrahedron, with the O—S—O angle larger than the other bond angles around S. The S—O bond lengths average 1.419(1) Å, being slightly shorter than those reported for thiadiazole 1,1-dioxide<sup>31</sup> (mean = 1.428 Å) and thiazine 1,1-dioxides [mean = 1.428(2) Å]. The S—N bond lengths average 1.669(2) Å and are intermediate between the corresponding bond lengths of the thiazines (*ca* 1.59 Å) and those of thiadiazole 1-oxide (1.712 Å), and similar to those of the 1,1-dioxide<sup>31</sup> (mean = 1.656 Å).

The C=N double bond lengths vary from 1.267 to 1.291 Å, that is, within *ca* 3 $\sigma$  ( $\sigma$  = 0.004 Å) of the mean value for all compounds. Similar bond lengths were found for the thiadiazole 1-oxide (1.280 Å) and 1,1-dioxide (1.303 Å) derivatives.

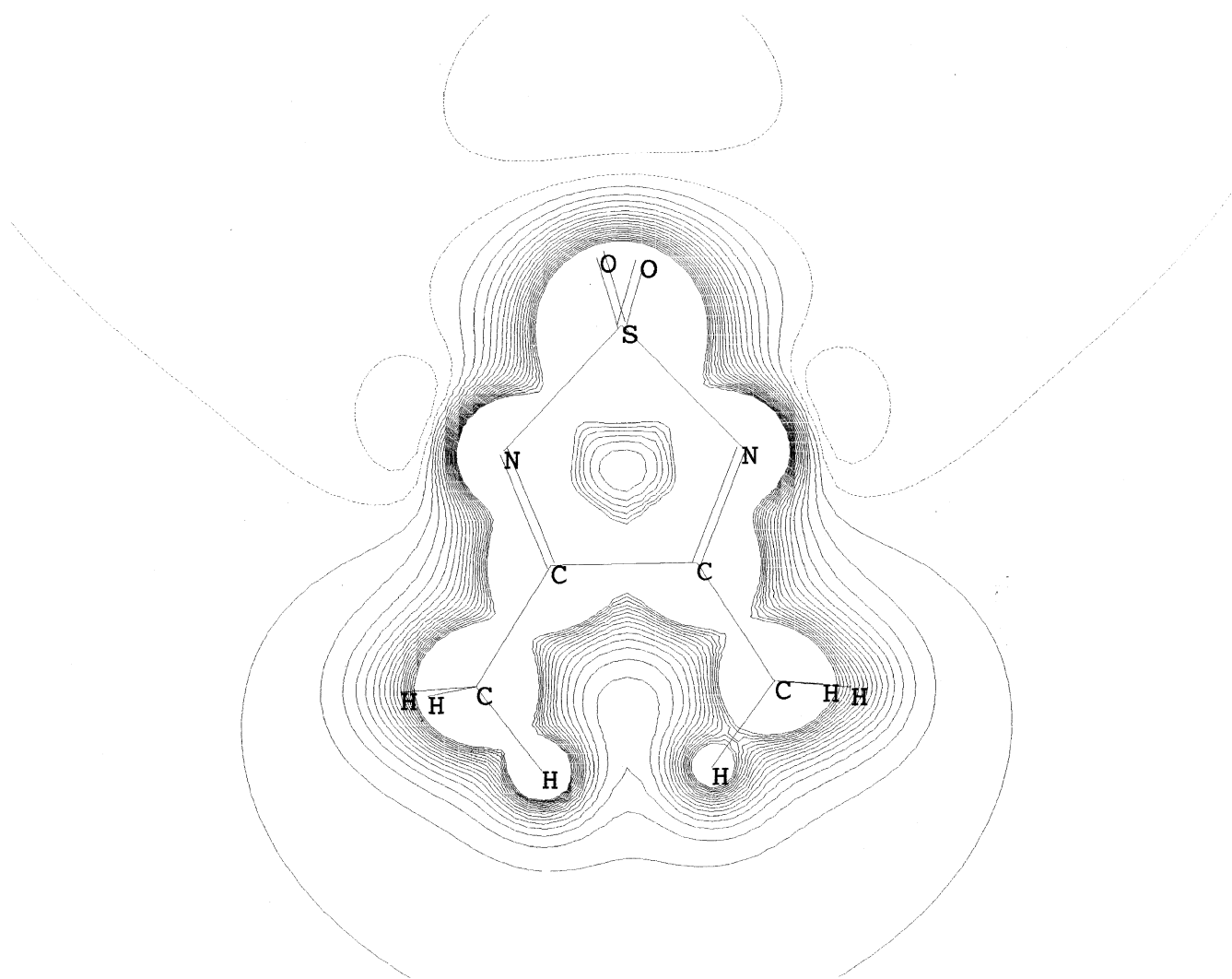


**Figure 4.** HF/6-31G\*\* electron density of 3,4-dimethyl-1,2,5-thiadiazole 1,1-dioxide (**I**) on the molecular plane

The heterocycle ring is planar within the experimental accuracy for **I** and **II** and deviates only slightly (maximum deviation *ca* 10 $\sigma$ ,  $\sigma$  = standard error) from



**Figure 5.** HF/6-31G\*\* electron density of 3-methyl-4-phenyl-1,2,5-thiadiazole 1,1-dioxide (**II**) on the molecular plane



**Figure 6.** HF/6-31G\*\* electrostatic potential of 3,4-dimethyl-1,2,5-thiadiazole 1,1-dioxide (**I**) on the molecular plane

the mean plane in the case of **III**. The phenyl rings in **II** and **III** are planar within  $3\sigma$ .

The methyl carbon atoms are in the plane of the heterocycle in **I**. The phenyl plane in **II** forms a dihedral angle of  $40.9(2)^\circ$  with the heterocycle plane, and in **III** the phenyl-heterocycle dihedral angles are  $43.1(2)$  and  $41.4(1)^\circ$  and the phenyl-phenyl dihedral angle is  $51.9(1)^\circ$ .

Clearly, the phenyl rings in **II** and **III** rotate out of the heterocycle plane to avoid steric strain, but this occurs at the expense of reducing the delocalization energy available through the interaction of the phenyl  $\pi$ -system and the C=N double bond(s). The experimental dihedral angles indicate that the methyl group in **II** exerts nearly the same steric repulsion as a phenyl group (as in **III**) over the neighboring phenyl substituent.

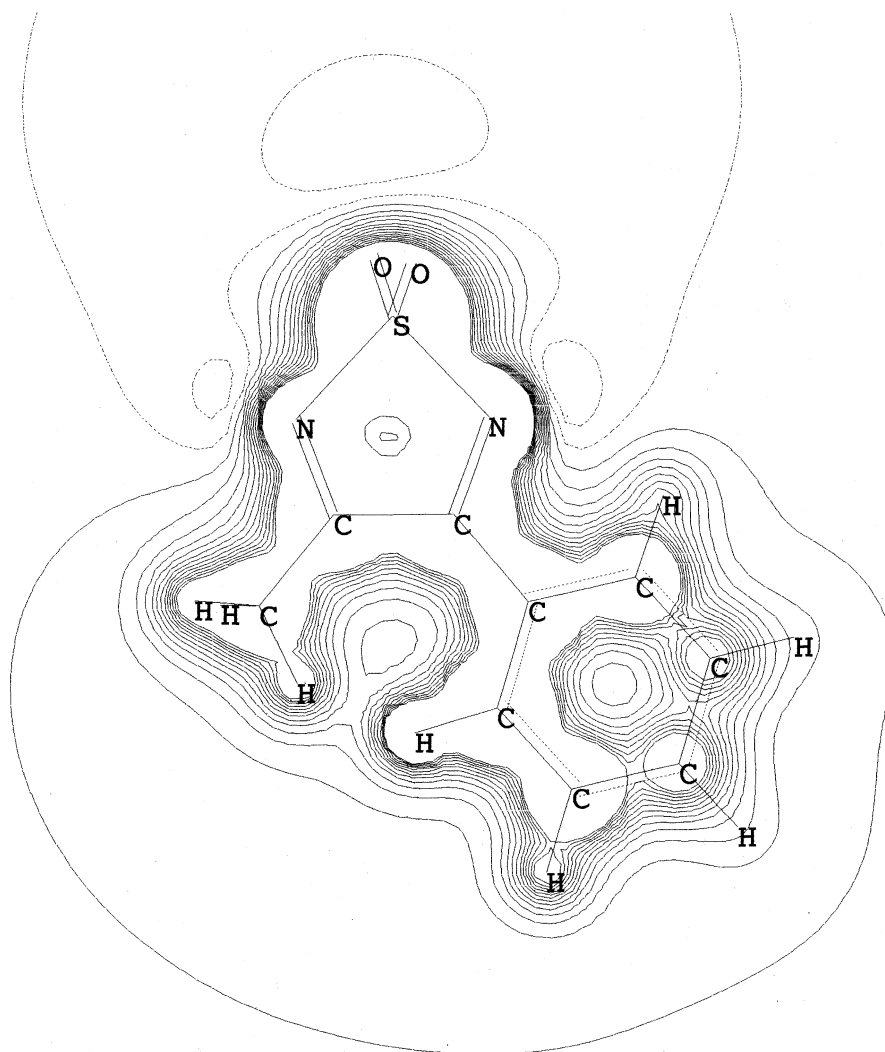
The resonant C—C bond length has a mean value of  $1.383 \text{ \AA}$  ( $\sigma = 0.003$ ); however, the *ortho* bonds are longer (mean =  $1.391 \text{ \AA}$ ) than the *meta* bonds (mean =  $1.387 \text{ \AA}$ ), and the *para* bonds are the shortest (mean  $1.373 \text{ \AA}$ ),

indicating that the phenyl rings are slightly distorted. It is interesting that the longest bond distance corresponds to the C(3)—C(8) bond of **II**, which faces the neighboring methyl substituent.

### Theoretical calculations

The results for the equilibrium conformation of the neutral molecules **I** and **II** (HF/LCAO with 6-31G\*\* basis set) are included in Tables 5–7 along with the experimental x-ray results. The agreement is in general good for these *ab initio* calculations (the standard error of the differences between the experimental and the calculated bond lengths is  $ca 4 \times 10^{-3} \text{ \AA}$  for all methods. The corresponding value for the bond angles is  $0.3^\circ$ ).

Equations (1)–(3) can be applied, as has been shown in previous work,<sup>31–34</sup> to the study of the behavior of substances under nucleophilic or electrophilic attack. Figures 4 and 5 display a planar representation of the calculated



**Figure 7.** HF/6-31G\*\* electrostatic potential of 3-methyl-4-phenyl-1,2,5-thiadiazole 1,1-dioxide (**II**) on the molecular plane

electron densities of **I** and **II** and Figures 6 and 7 show the corresponding electrostatic potential. While Figure 4 and 6 (**I**) are obviously symmetric, Figures 5 and 7 (**II**) show that electrophilic attack would occur preferentially at N(1) and nucleophilic attack at C(2).

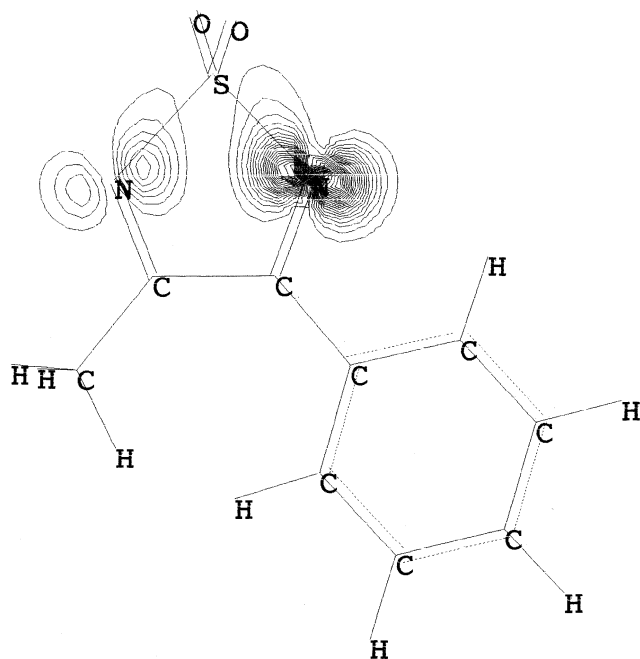
These reactive sites can also be identified by an analysis based on frontier orbitals.<sup>8,35</sup> Figures 8 and 9 show a map of the HOMO electron density on the molecular plane of **I** and **II** and Figures 10 and 11 exhibit the corresponding LUMO electron density for the same molecules. In contrast with the symmetry of **I**, it can be seen that the HOMO presents its largest wave amplitude (corresponding, generally, to the site of electrophilic attack) for **II** at N(1) (Figure 9), whereas the LUMO has its lowest density at C(2) (Figure 11).

Tables 8–10 show the net atomic charges of the neutral molecules for **I**, **II** and **III**, respectively, by a Mulliken population analysis, and the  $f^+$ ,  $f^-$  and  $f^0$  Fukui functions calculated with Equations (1)–(3). These values confirm that for **II**, the site for electrophilic attack is N(1)

(where  $f^-$  is a maximum). The site for potential nucleophilic attacks would depend on the values of  $f^+$  of the atoms with a positive charge density. Although the net positive charge on the sulfur atom is larger than that on the heterocycle carbons, the value of  $f^+$  on carbon atoms C(1) and C(2) are much larger than the corresponding value on the sulfur atom. Therefore, in these molecules, the heterocycle carbon atoms would be more susceptible than sulfur to nucleophilic interactions. Furthermore, from Table 9 it is possible to employ the Fukui function to differentiate the reactivity of C(1) and C(2) in **II**. From the  $f^+$  values, C(2) is more susceptible than C(1) to nucleophilic attack.

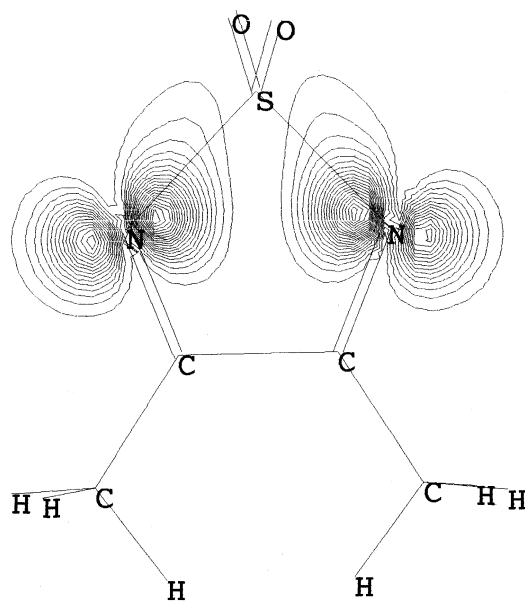
### General discussion

The structural features described above can be correlated with the chemical and electrochemical properties that we have experimentally measured for these molecules. In



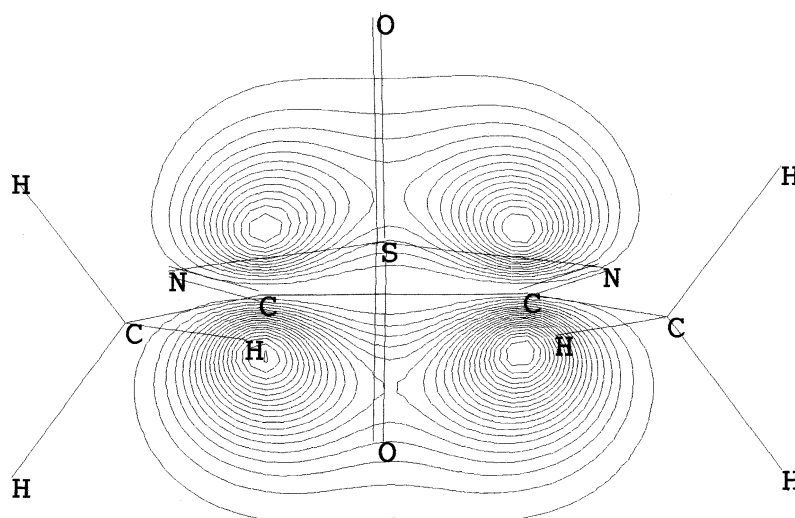
**Figure 8.** HF/6-31G\*\* HOMO electron density of 3,4-dimethyl-1,2,5-thiadiazole 1,1-dioxide (**I**) on the molecular plane

our studies on the nucleophilic addition of alcohols to the C=N double bond of 1,2,5-thiadiazole 1,1-dioxide derivatives, we have found that the addition reaction takes place at a measurable rate for **I**, **II**<sup>36</sup> and **III**.<sup>5</sup> The addition occurs preferentially on C(2) for **II**. We have also observed that **II** and **III** hydrolyze at a measurable rate depending on the experimental conditions. The hydrolysis reaction of **III**<sup>3,4</sup> begins with an electrophilic attack on the heterocyclic N atoms at low pH values and with a nucleophilic attack on the heterocyclic C atoms at higher pH values.



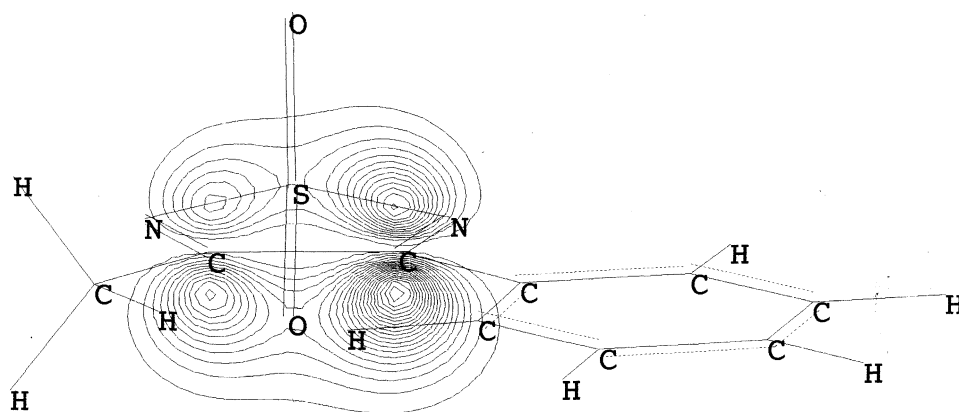
**Figure 9.** HF/6-31G\*\* HOMO electron density of 3-methyl-4-phenyl-1,2,5-thiadiazole 1,1-dioxide (**II**) on a plane located 0.3 Å over the molecular surface

It is well known that C(1) and C(2) are active reaction sites for nucleophilic attack in 1,2,5-thiadiazole 1,1-dioxides owing to the high electron-withdrawing effect of the SO<sub>2</sub> group. Obviously, 3,4-substituents that provide a delocalized  $\pi$ -system that includes the C=N double bond would lower the reactivity of the molecule towards nucleophilic addition. The preferential nucleophilic attack on C(2) in **II** may indicate that the slight mesomeric effect of the phenyl substituent on C(1) predominates over the inductive effect of the methyl substituent on C(2), although steric or kinetic effects may also play a role.



**Figure 10.** HF/6-31G\*\* LUMO electron density of 3,4-dimethyl-1,2,5-thiadiazole 1,1-dioxide (**II**) on a plane located 1 Å over the molecular surface





**Figure 11.** HF/6-31G\*\* LUMO electron density of 3-methyl-4-phenyl-1,2,5-thiadiazole 1,1-dioxide (**II**) on a plane located 0.05 Å over the molecular surface

**Table 8.** Net atomic charges and Fukui functions for the ring atoms of 3,4-dimethyl-1,2,5-thiadiazole 1,1-dioxide (**I**)

Atom	$q$	$f^+$	$f^-$	$f^0$
S	1.614	0.054	0.004	0.029
O	-0.608	0.073	0.094	0.083
N	-0.576	0.068	0.200	0.143
C(1)	0.233	0.162	0.048	0.105

**Table 9.** Net atomic charges and Fukui functions for the ring atoms of 3-methyl-4-phenyl-1,2,5-thiadiazole 1,1-dioxide (**II**)

Atom	$q$	$f^+$	$f^-$	$f^0$
S	1.618	0.050	0.014	0.032
O	-0.609	0.064	0.041	0.052
N(1)	-0.634	0.114	0.059	0.086
N(2)	-0.574	0.146	0.081	0.113
C(1)	0.246	0.023	0.005	0.014
C(2)	0.269	0.126	0.038	0.082

**Table 10.** Net atomic charges and Fukui functions for the ring atoms of 3,4-diphenyl-1,2,5-thiadiazole 1,1-dioxide (**III**)

Atom	$q$	$f^+$	$f^-$	$f^0$
S	1.625	0.051	0.015	0.032
O	-0.609	0.060	0.035	0.047
N	-0.607	0.087	0.046	0.061
C	0.249	0.112	0.009	0.060

We have also studied the electroreduction properties of **I**,<sup>36</sup> **II**<sup>36</sup> and **III**<sup>6,7</sup> in acetonitrile (ACN) solution. The experimental potential (vs Ag/Ag<sup>+</sup> in ACN; scan rate of 0.1 V s<sup>-1</sup>) of the electroreduction voltammetric peaks are -1.10 V (**I**), -0.90 V (**II**) and -0.79 V (**III**). As

expected, owing to the electron-withdrawing characteristics of the SO<sub>2</sub> group, the electroreduction of these compounds is much easier than either the parent heterocyclic ring or the hydrocarbon substituents, which have normal electroreduction potentials that are more negative than -2.3 V.<sup>37,38</sup> The extra electron of the radical anion of the substrates should favor a location associated with the electron-deficient C(1) or C(2) carbon atoms. No charge delocalization possibilities are offered there in **I**, which is the most difficult to reduce. In the radical anion of **III**, the higher stabilization energy potentially available through increased delocalization of the extra charge on one phenyl ring should favor a smaller heterocycle-phenyl dihedral angle on the molecular side on which the electron has been added. The concerted rotation of the other phenyl ring can provide the necessary room at the cost of reducing, although not eliminating, the energy gain. Hence **III** has a less negative  $E^0$  than **I**. It has been mentioned above that the experimental structural results indicate that the methyl group in **II** is as effective as the phenyl group as a steric hindrance; however, it cannot rotate out of the way to allow increased resonance in the other side of the molecule. This might be related to the intermediate position of **II** with regard to the value of  $E^0$ .

## SUPPLEMENTARY MATERIAL

A list of atomic anisotropic thermal parameters (Table 11), of hydrogen atoms positions (Table 12), and listings of observed and calculated structure factor amplitudes (Table 13) can be obtained from the authors on request.

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