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STRUCTURE OF 1,2,6-THIADIAZINE 1,1-DIOXIDES

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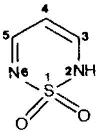
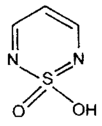
***Ab initio* theoretical calculations were carried out on the three tautomers, NH, OH and CH, of 1,2,6-thiadiazine 1,1-dioxides. Different basis sets were employed in order to obtain an adequate description of these cyclic sulphamide derivatives. A coherent picture is obtained which includes relative stability of tautomers (NH > CH > OH), non-planarity of NH and CH tautomers and electronic distribution (Boys' localized orbitals).**

INTRODUCTION

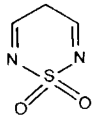
Aromaticity[1–5] and, particularly, heteroaromaticity[2,4] are attracting increasing interest. Continuing with our research on the synthesis and physico-chemical properties of 1,2,6-thiadiazine 1,1-dioxides,[6] we decided to carry out an *ab initio* theoretical study of this potentially aromatic six-membered ring incorporating the N—SO_2—N moiety. In order to discuss the problem of its structure, the three possible tautomeric forms in which the ring can exist have to be considered:



1 (2(6)-NH)



2 (1-OH)



3 (4-CH)

According to x-ray and NMR data in solution, tautomer **1** is the predominant form in 3,5-alkyl- or aryl-thiadiazines whereas **3** is more stable in compounds bearing functional groups such as OH or NH_2 at C-3 and/or C-5.[6] The 1-OH tautomer (**2**) has never been observed experimentally, and only one O-substituted derivative has been claimed.[7]

Many x-ray structures of 1,2,6-thiadiazine 1,1-dioxides have been determined,[6] most of them being non-planar e.g. the simple 3,5-dimethyl derivative shows the sulphur atom 0·405 Å above the mean plane formed by the remaining five atoms[8]). However, at least one derivative, 5-amino-4,4-dibenzyl-3-one, is planar.[9]

In this paper, the problem of the structure and tautomerism of 1,2,6-thiadiazine 1,1-dioxides is considered on the basis of criteria derived from theoretical calculations such as energy values, charge distributions and an analysis of canonical and localized molecular orbitals.

COMPUTATIONAL DETAILS

It is well established that polarization functions are crucial to the correct description of the bonding of sulphur. Unfortunately, a geometry optimization of the system under investigation at the 6–31G* level of accuracy is economically prohibitive, so cheaper alternatives must be considered. Among the most popular ones are the 3–21G(*) and 6–31G(*) basis,[10] which are of split-valence character and include d functions exclusively on the second-row atoms. However, we have recently shown[11] that these basis sets do not reproduce the pyramidalization of the nitrogen atoms directly bonded to the SO_2 moiety of sulphamide. Therefore, and taking into account that the possible pyramidalization of the nitrogen of thiadiazines is one of the problems we want to analyse, we shall carry out single point 3–21G(*) and 6–31G(*) calculations on fully optimized STO-3G* structures. These computational schemes, which will be referred hereafter as 3–21G(*)//STO-3G* and 6–31G(*)//STO-3G*, respectively, have proved to be fairly reliable because the STO-3G* basis reproduces reasonably well the most important structural features

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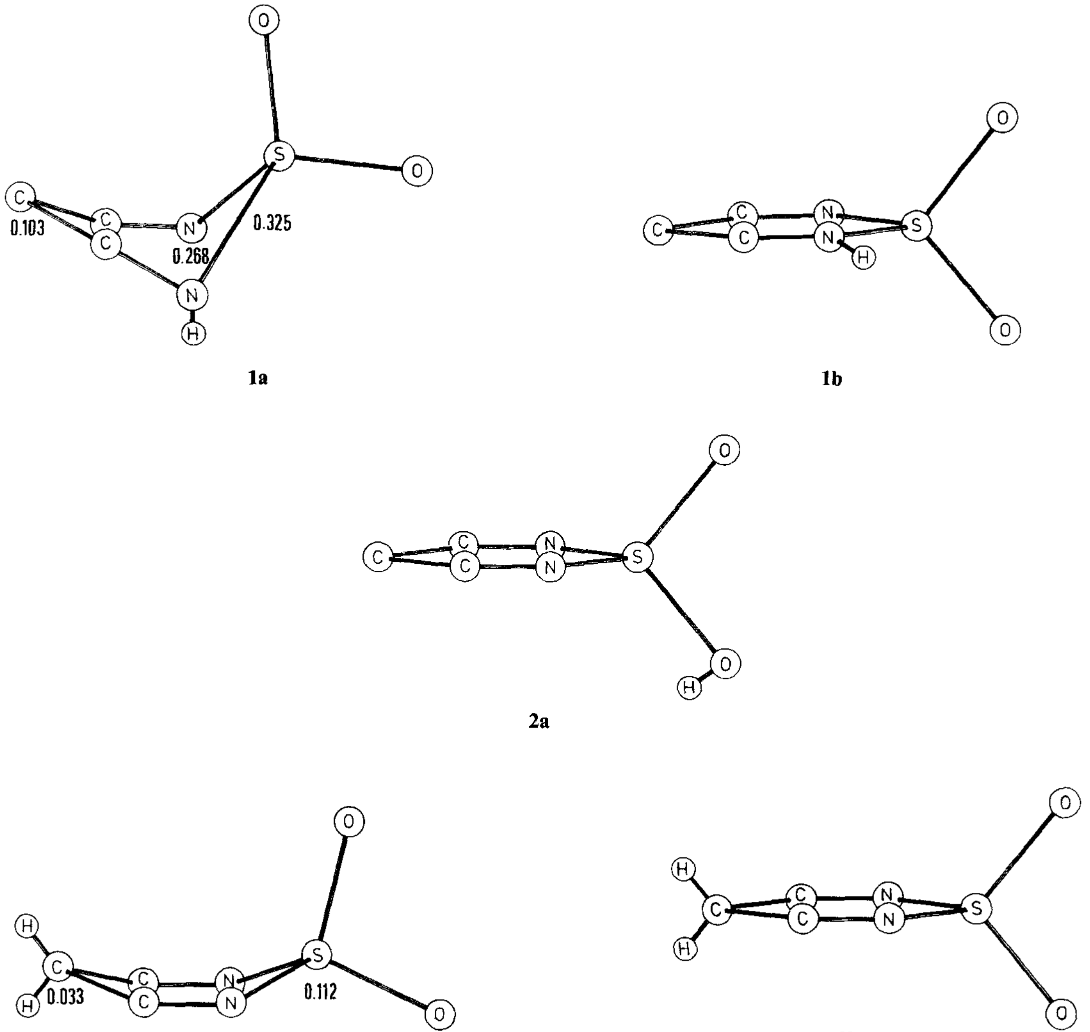
obtained at the 6–31G* level[12] for this kind of compound and the split-valence character of the 3–21G(*) or 6–31G(*) corrects some of the deficiencies of the minimal basis, as we shall illustrate later. All calculations were carried out using the Gaussian 80 series of programs (IBM version).[12]

To characterize better the bonding of the tautomers considered we shall obtain the corresponding localized MOs using the method of Boys.[13]

RESULTS AND DISCUSSION

The optimized geometries (bond lengths and dihedral angles) of the three tautomers together with the experimental data are given in Table 1 and the energies, dipole moments and atomic charges in Table 2. From these results, it is clear that the most stable structure is planar only in the case of tautomer **2**, whereas for tautomers **1** and **3** boat forms are obtained (see Figure 1).

There is acceptable agreement between the experimental and calculated results as seen from the comparison between **1a** and the x-ray coordinates of 3,5-dimethyl-2*H*-1,2,6-thiadiazine 1,1-dioxide (**1′**):[8] the SO_2 group lies 0·405 Å (experimental) and 0·325 Å out of the plane (calculated). The worst accordance concerns the S—N bond lengths (calculated for **1a**, 1·71 Å; observed in **1′** 1·62 Å). It is necessary to keep



1a

1b

2a

3a

3b

Figure 1. Planar and non-planar forms of the three tautomers of 1,2,6-thiadiazine 1,1-dioxide

Table 1. Structural parameters for the different conformers of the tautomers of thiadiazine, calculated with STO-3G* basis

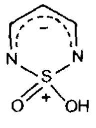
Compound	S-1—O-7	S-1—O-8	S-1—N-2	S-1—N-6	N-2—C-3	N-6—C-5	C-3—C-4	C-5—C-4	S-1—N-2—C-3—C-4	N-2—C-3—C-4—C-5	C-3—C-4—C-5—N-6	C-4—C-5—N-6—S-1
1a	1·451	1·443	1·710	1·712	1·416	1·294	1·472	1·327	7·389	10·563	2·864	−32·097
1b	1·450	1·450	1·705	1·705	1·397	1·292	1·330	1·464	−0·020	0·000	−0·028	0·020
1′	1·426	1·426	1·591	1·640	1·358	1·310	1·407	1·355	9·367	10·005	−7·295	−13·700
2a	1·620	1·443	1·635	1·635	1·346	1·346	1·389	1·389	0·119	0·000	0·000	−0·115
3a	1·450	1·443	1·730	1·730	1·276	1·276	1·524	1·524	2·713	2·894	−2·899	−2·709
3b	1·447	1·447	1·729	1·729	1·276	1·276	1·524	1·524	0·000	0·000	0·000	0·000

Table 2. Energy values, dipole moments and atomic charges calculated of the different conformers of the tautomers of thiadiazine

Basis	Structure	E(hartrees)	Dipole moment (D)	Atomic charge								ΔE (kcal mol^{-1})	
				S-1	N-2	N-6	C-3	C-5	C-4	O-7	O-8		
STO-3G*//STO-3G*	**1a**	−762·884951	4·833	15·507	7·236	7·331	5·906	5·920	6·114	8·242	8·232	1·49,	1·49
	1b	−762·880610	5·033	15·496	7·243	7·344	5·903	5·904	6·127	8·241	8·237	4·22	
	2a	−762·859491	4·360	15·488	7·296	7·297	5·902	5·902	6·165	8·230	8·218	17·47,	17·47
	3a	−762·887333	5·916	15·526	7·221	7·221	5·912	5·912	6·139	8·230	8·224	0·00,	0·0
	3b	−762·885375	5·910	15·524	7·221	7·221	5·912	5·912	6·139	8·224	8·229	1·23	
3–21G(*)//STO-3G*	**1a**	−768·038775	7·052	14·382	7·702	7·931	5·838	5·851	6·398	8·571	8·564	4·61,	0·0
	1b	−768·046125	7·418	14·365	7·720	7·988	5·826	5·786	6·429	8·571	8·564	0·00	
	2a	−768·006017	6·914	14·412	7·746	7·746	5·869	5·869	6·444	8·649	8·534	25·17,	20·55
	3a	−768·017974	8·769	14·433	7·653	7·653	5·845	5·845	6·615	8·565	8·553	17·66,	13·05
	3b	−768·018305	8·770	14·431	7·652	7·652	5·846	5·846	6·615	8·563	8·555	17·46	
6–31G(*)//STO-3G*	**1a**	−771·786846	7·709	14·673	7·567	7·901	5·891	5·835	6·292	8·507	8·491	4·13,	0·0
	1b	−771·793427	8·086	14·646	7·577	7·973	5·889	5·768	6·324	8·502	8·493	0·00	
	2a	−771·748787	7·712	14·734	7·610	7·610	5·918	5·918	6·314	8·632	8·461	28·01,	23·88
	3a	−771·764622	9·640	14·736	7·510	7·510	5·892	5·893	6·469	8·498	8·481	18·07,	13·94
	3b	−771·764920	9·649	14·735	7·510	7·510	5·893	5·893	6·468	8·495	8·485	17·89	

these differences in mind when discussing the energies associated with the different tautomers.

Assuming a proportionality between bond lengths and bond orders,[2] it can be concluded that all forms show a localization of the double and single bonds except **2a**, which can be regarded as an ylide form. In this case there is a delocalization in the N—C—C—C—N fragment and the S—N distances correspond to single bonds.


2a

Since deviations from planarity are very important when discussing the structure of the 1,2,6-thiadiazine system, planar forms (by Z matrix) of tautomers **1** and **3** (**1b** and **3b**) have also been calculated.

Examination of the energy values at the STO-3G*//STO-3G* level shows that, as expected, planar forms of **1** and **3** are unstable with respect to the non-planar forms (**1**, $\Delta E = 2{\cdot}7$ kcal mol^{-1}; **3**, $\Delta E = 1{\cdot}2$ kcal mol^{-1}).

At this level of accuracy, the order of stability of the optimized structures is that **3a** is 1·5 and 17·5 kcal mol^{-1} more stable than **1a** and **2a**, respectively. The great energy difference between tautomer **2a** and tautomers **1a** and **3a** can account for the fact that **2a** has never been found experimentally. However, at this level of calculation tautomer **3a** is more stable than **1a**, which is in contradiction with the experimental evidence, as already mentioned. We shall discuss this point later.

The relatively low stability of tautomer **2a** is a direct consequence of the changes in the bonding of the SO_2 moiety. First, it must be noted that the structure of the ring does not change dramatically with respect to that of conformer **1a**. However, the S—O bond to which the proton is attached becomes 0·17 Å longer. This geometrical change is significant and is responsible for the low stability of this tautomer. As has been found for sulphamide,[11] the S—O bonds in species **1a** and **3a** are the result of a σ-type interaction between the corresponding AOs of oxygen and sulphur and π-type delocalizations involving the oxygen lone pairs on the one hand and p and d orbitals of sulphur on the other. As a consequence, we cannot strictly speak of an S—O double bond since actually the S—O bonds appear as the result of a σ-type S–O interaction and p_π–d_π back-bonding involving the three oxygen lone pairs. This description is not consistent with the conclusion of Fraenkel *et al.*[14] about the conjugative interaction of a nitrogen lone pair and an SO_2 group through a system of C—C double bonds. As we have discussed in a preceding paper,[11] this conjugation does not play any significant role in the behaviour of the N–SO_2 group. The nature of the S—O bond is confirmed by the characteristics of the localized molecular orbitals of all species studied (see Figure 2), which show that for conformers **1a**, **1b**, **3a** and **3b**, oxygen retains practically three lone pairs and it is the polarization of them toward the S that is largely responsible for the multiple bond character of the S—O linkage. This bonding scheme, however, is considerably altered in conformer **2a**, because one of the oxygen lone pairs becomes a σ-bonding orbital involved in the O—H linkage. Accordingly, the S—O bonding becomes considerably weakened and the system globally destabilizes. Again, the LMOs of this conformer (see Figure 2) clearly show this effect and its ylide character.

More subtle is the difference between conformers **1a** and **1b** and between **3a** and **3b**. The first conspicuous fact in Table 2 is that the energy difference between planar and non-planar forms is small and that, as expected, the 6–31G(*) and 3–21G(*) bases predict the planar conformers to be more stable than the non-planar conformers.

It must be noted, however, that the deviation from planarity is very small in both instances. As a consequence, changes in the electronic structure of the systems are very small and, therefore, difficult to quantify properly. Nevertheless, an inspection of the MOs of conformers **1a** and **1b** obtained at the STO-3G* level reveals that the most significant changes affect the HOMO. This is similar to the behaviour described by Alcamí *et al.*[15] regarding nitrogen inversion processes of three-membered rings, where the inversion barrier parallels the destabilization of the HOMO. On going from **1a** to **1b** the energy of the HOMO (see Figure 3) rises about 7 kcal mol^{-1}. It may be observed that this is a π-type MO in the planar form with a strong contribution from the atomic orbitals of N-2. When the S atom is not in the plane of the ring, the s character of the nitrogens directly bonded to it, especially that of N-2, increased noticeably and the MO stabilizes. A similar effect is observed in another inner-lying π-type MO where the strongest contribution comes from the atomic orbitals centered at N-6 (see Figure 3). Obviously there are other smaller changes affecting the remaining MOs, but they almost cancel each other, so that those affecting the just mentioned π-type obitals seem to be responsible for the stabilization of the non-planar form.

It must also be noted that, as mentioned above, no significant changes in the electronic structure of the system should be expected. This is clearly reflected by the corresponding charge distributions (see Table 2), which are almost unaffected by the loss of planarity and by the corresponding LMOs. Actually, comparison of the localized molecular orbitals of **1a** and **1b** reveals the absence of any significant differences between them, and only the nitrogen lone pairs of **1b** appear slightly

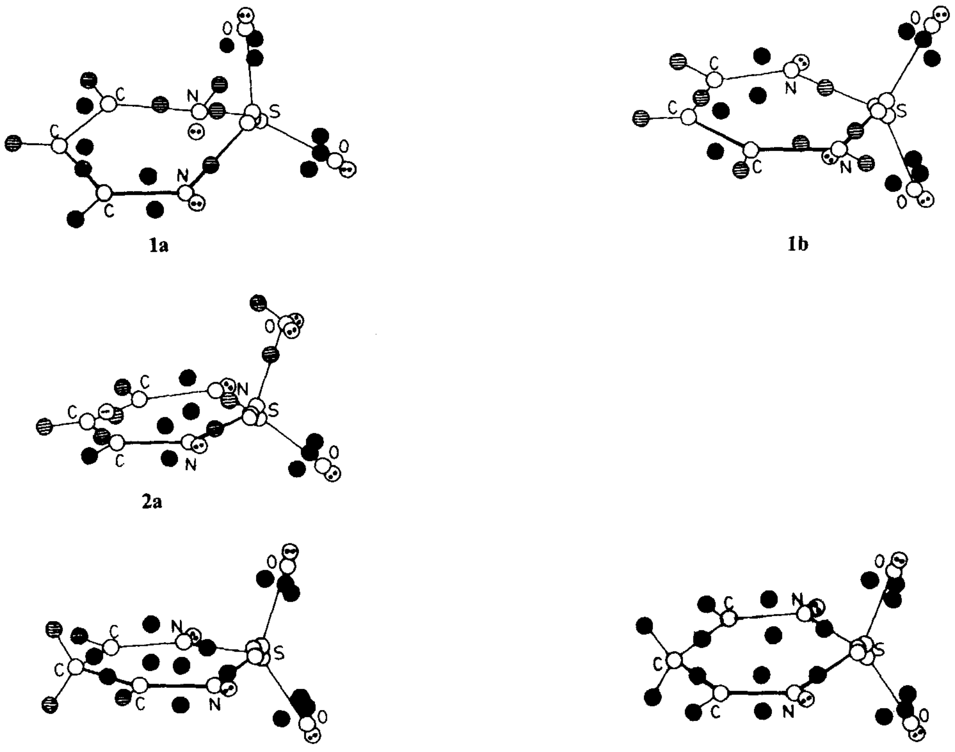


Figure 2. Boys' localized orbitals of the planar and non-planar forms of 1,2,6-thiadiazine 1,1-dioxide tautomers (black circles, π-type orbitals; hatched circles, σ-type orbitals)

reoriented with respect to those of **1a**. A similar situation is found on comparing the LMOs of **3a** and **3b**.

The fact that a 6–31G(*) or a 3–21G(*) basis predicts the planar form as the most stable may be an artifact of the basis. Actually, it is well known[15,16] that an adequate description of the pyramidalization at the nitrogen atoms requires the inclusion of polarization functions on them. On the other hand, a proper polarization of the sulphur atom by including a second set of (diffuse) d functions may also be important, namely when it is bonded to very electronegative atoms.

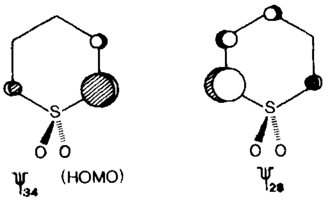


Figure 3. Schematic representation of the π-type MOs most sensitive to puckering in the NH tautomer

To investigate this particular point, we carried out single-point calculations using two different sets of polarized 6–31G basis, defined as follows: set A includes in a 6–31G scheme one set of d functions on sulphur ($\alpha_D = 0{\cdot}65$) and on both nitrogen atoms ($\alpha_D = 0{\cdot}80$) and set B includes a set of d functions on sulphur ($\alpha_D = 0{\cdot}65$), on both nitrogens ($\alpha_d = 0{\cdot}80$) and on both oxygens ($\alpha_D = 0{\cdot}80$). In all cases, STO-3G* fully optimized structures were employed and no-geometry optimization was attempted. The results obtained predict again the planar forms as the most stable, but now the energy differences between conformers **1a** and **1b** are much smaller (0·7 and 0·4 kcal mol^{-1}) when sets A and B are employed, respectively.

We may conclude that although an amelioration of the description of the polarization of sulphur or nitrogen atoms does not change the trend observed at the 6–31G(*) or 3–21G(*) level, the energy difference between the two tautomers becomes so small that a proper geometry optimization or the inclusion of polarization functions on the remaining heavy atoms and on hydrogens or electron correlation effects could be sufficient to stabilize the non-planar conformation. Similarly, the possibility that the intermolecular interactions that take place in the crystal could be responsible for the non-planarity of the ring cannot be ruled out. In this respect, it is significant that according to our results the energetic barrier between the two forms is fairly low, so that in the gas phase a rapid interconversion between the two situations, with the S above and below the ring plane, could probably occur under normal conditions.

More significant is the fact that **1a** is predicted to be considerably more stable than **3a** when a 6–31G(*) or 3–21G(*) basis is employed. This finding reflects the lack of flexibility of a minimal STO-3G basis to describe adequately no-direct bonding interactions such as that which takes place in **1a** between the amino proton and the oxygen lone pairs. A split valence basis is much more flexible as it is possible to populate independently the inner and the outer shells of each heavy atom. It may be observed, in fact, that whereas at the STO-3G* level both nitrogens of **1a** have almost the same electronic population, at the 6–31G(*) level it is considerably greater for the nitrogen bonded to the hydrogen atom. As a consequence, this proton becomes more acidic (its positive charge increases from +0·22 to +0·42). Simultaneously and for the same reasons, the net negative charge on the oxygens of the SO_2 moiety also increases and the coulombic interaction between them and the amino proton considerably stabilizes the system.

However, the STO-3G* basis not only underestimates the stability of tautomer **1a** for the aforementioned reasons, but also overestimates the stability of the **3a** conformer. In **3a** the N—H bond is substituted by a σ lone pair, and the stabilizing interaction between the NH proton and the oxygen lone pairs is changed in a repulsive interaction between the nitrogen and oxygen lone pairs. Since the total electronic population is underestimated at the STO-3G* level, so is the population at the lone pairs and the repulsion between them. In summary, regarding the relative stabilities of the conformers **1a** and **3a**, the description at the 6–31G(*) or 3–21G(*) level seems more realistic and is in agreement with the experimental evidence. As would be expected, the low stability of tautomer **2a** is not changed at this higher level of accuracy.

CONCLUSIONS

From all these calculations the following conclusions can be drawn. In principle, regarding aromaticity, we conclude that neither form **1a** nor **3a** can be aromatic since their optimized conformations are non-planar. However, the energy gap between forms **1a** and **1b** and between **3a** and **3b** is so small that even if non-planar structures are the most stable in the gas phase, the flipping movement of the SO_2 moiety above and below the molecular plane should proceed very rapidly.

On the other hand, the puckering of the ring, in either **1a** or **3a**, is so small that the perturbation of the MOs of the forms **1b** or **3b** is also very small. It should be taken into account, however, that all these species have very large dipole moments, which means that in the crystal the intermolecular interactions must be significant. These interactions may favour a puckering of the ring and the flipping movement might be prohibited.

The most stable ring conformation for the OH tautomer (**2a**) is planar and, according to this criterion, this tautomer could be aromatic. However, an examination of its electronic distribution (see Figure 2) clearly reveals the ylide nature of the OH tautomer.

In contrast to 2-pyrimidinones, 1,2,6-thiadiazine 1,1-dioxides resulting from the replacement of the CO by the SO_2 groups are non-aromatic, which explains the difference in stability of pyrimidinone tautomers ($NH > OH \gg CH$)[17] compared with those of 1,2,6-thiadiazine 1,1-dioxide ($NH > CH \gg OH$).[6]

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