

A THEORETICAL STUDY OF THE STRUCTURE AND TAUTOMERISM
OF 1,2,4,6-THIATRIAZINE 1,1-DIOXIDE

José Elguero^{a*}, José Luis G. de Paz^b, Pilar Goya^a,
Juan Antonio Pérez^a, and Isabel Rozas^a

^aInstituto de Química Médica, C.S.I.C.,

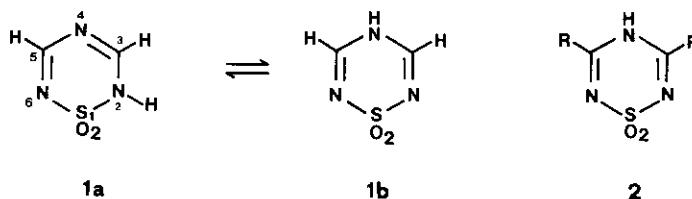
Juan de la Cierva, 3, 28006 Madrid, Spain

^bDepartamento de Química, Facultad de Ciencias,

Universidad Autónoma de Madrid, 28049 Madrid, Spain

Abstract - "Ab initio" theoretical calculations have been used to study the structure and annular tautomerism of 2(4)H-1,2,4,6-thiatriazine 1,1-dioxide. The 4H-tautomer has been found to be the most stable in agreement with ¹H-, ¹³C- and ¹⁵N-nmr data.

The 1,2,4,6-thiatriazine 1,1-dioxide skeleton is present in several structures of considerable biological interest.¹ In spite of this fact, no theoretical calculations have been reported¹ probably owing to the difficulty to correctly describe the hypervalent sulfur atom.² In this paper, we will discuss the structure of the parent 2(4)H-1,2,4,6-thiatriazine 1,1-dioxide 1, with special emphasis on annular tautomerism, *i.e.* tautomerism involving exclusively ring atoms.³



In the case of compound 1, ¹H-, ¹³C- and ¹⁵N-nmr data provide conclusive evidence for the existence of the 4-NH tautomer 1b in DMSO solution.⁴ The 3,5-ditrifluoromethyl derivative presents a unique signal in ¹⁹F-nmr, which is consis-

tent with a 4H structure 2 ($R=CF_3$).⁵ With functional groups at positions 3 and/or 5 ($R=OH$, NH_2), more tautomers are possible, but still the 4-NH ones seem the most stable.¹

Computational details

Polarized basis sets, STO-3G*⁶ and 3-21G(*)⁷ were selected. The calculations were performed using the Gaussian 80 series of programs⁸ and Murtagh-Sargent optimization procedures.⁹ Fully optimization of the geometries was carried out only at the STO-3G* level (noted, as usual, STO-3G*//STO-3G*). On this geometries punctual 3-21G(*) calculations were carried out (3-21G(*)//STO-3G*).

Results:

Geometries

STO-3G* fully optimized geometries of tautomers 1a and 1b are reported in Table 1. In the case of planar structures (less stable, see later), the planarity has been imposed, in order to explore local minima and to estimate ring inversion barriers.

Table 1
Calculated geometries of 1,2,4,6-thiatriazine 1,1-dioxide 1

Bond lengths (Å)	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 -N ₄	C ₅ -N ₄
1a planar	1.448	1.451	1.709	1.696	1.393	1.290	1.294	1.436
1a nonplanar	1.450	1.442	1.709	1.711	1.411	1.291	1.291	1.443
1b planar	1.446	1.446	1.723	1.723	1.281	1.281	1.404	1.404
1b nonplanar	1.450	1.442	1.726	1.726	1.283	1.283	1.413	1.413

Bond angles (°)	O ₇ -S ₁ -O ₈	S ₁ -N ₂ -C ₃	N ₂ -C ₃ -N ₄	C ₃ -N ₄ -C ₅	N ₄ -C ₅ -N ₆	C ₅ -N ₆ -S ₁	N ₂ -S ₁ -N ₆
1a planar	122.3	124.8	126.8	114.9	131.5	122.2	99.8
1a nonplanar	122.6	118.4	125.2	114.7	130.9	118.4	97.7
1b planar	124.1	119.3	126.6	121.1	126.6	119.3	106.9
1b nonplanar	123.7	117.4	126.3	118.9	126.3	117.4	105.4

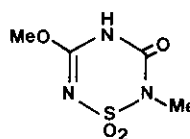
Torsion angles (°)	S ₁ -N ₂ -C ₃ -N ₄	N ₂ -C ₃ -N ₄ -C ₅	C ₃ -N ₄ -C ₅ -N ₆	N ₄ -C ₅ -N ₆ -S ₁
1a planar	0.0	0.0	0.0	0.0
1a nonplanar	-31.9	0.7	13.6	6.3
1b planar	0.0	0.0	0.0	0.0
1b nonplanar	-5.7	-18.5	18.5	5.7

The C-H and N-H bond lengths are 1.095±0.001 Å for all structures and 1.025±0.002 (1a) and 1.020±0.002 Å (1b) respectively. The results obtained indicate that in the case of nonplanar forms tautomer 1a would have a twisted structure and tautomer 1b a boat structure.

Since we have been unsuccessful in obtaining suitable crystals of 1, the calculated geometries of Table 1 are to be compared with literature results on two related structures 3¹⁰ and 4.¹¹

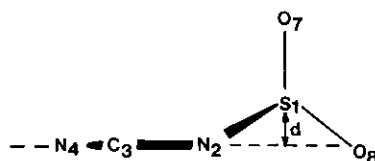


3



4

Both exist in the crystal in folded conformations, corresponding to our "non-planar" structures, with the sulfur atom above the mean plane formed by the five other ring atoms:



$$d(3) = 0.441 \text{ Å}$$

$$d(4) = 0.259 \text{ Å}$$

$$d(1a, np) = 0.615 \text{ Å}$$

$$d(1b, np) = 0.482 \text{ Å}$$

Both are 2H,4H-tautomers (and not 2H,6H-ones). This and the presence of a carbonyl group at C₃ and a substituent on C₅, make comparisons delicate. Theoretical calculations reproduce the fact that S₁-O₇ is longer than S₁-O₈ and yields reasonable N-C distances. On the other hand, S-N distances are overestimated in the calculated geometries (+ 0.09 Å) and the experimental fact^{10,11} that S₁-N₂H is

longer than $S_1-N_6=$ is not reproduced by the calculations. The bond angles are quite different; if we compare the sulfamide fragment of compounds **3** and **4** with that of **1a** ($=N-SO_2-NH-$) i.e. the experimental averaged values for $O_1-S_1-O_8$ (117.0°) and $N_2-S_1-N_6$ (105.0°) with the calculated ones (Table 1), 122.6 and 97.7° , it appears that the calculations enlarge the O-S-O angle at expense of the N-S-N one.

Energies

The values of energies for the four situations described in Table 1 are collected in Table 2.

Table 2
Calculated energies (hartrees) and relative energies (kcal.mol^{-1})
of 1,2,4,6-thiatriazine 1,1-dioxide **1**

Compound	STO-3G*//STO-3G*		3-21G(*)//STO-3G*	
1a planar	-778.6353	8.5	-783.9466	1.8
1a nonplanar	-778.6407	5.1	-783.9389	6.6
1b planar	-778.6480	0.6	-783.9494	0.0
1b nonplanar	-778.6489	0.0	-783.9434	3.8

STO-3G*//STO-3G* values clearly show that the 4H tautomer **1b** is the most stable and that nonplanar structures are slightly more stable than the planar ones (this is particularly true for the 2H tautomer which corresponds to molecules **3** and **4**). 3-21G(*)//STO-3G* energies favor the planar conformations with regard to the STO-3G*//STO-3G* values by kcal.mol^{-1} 8.2 (**1a**) [$(6.6-1.8) - (5.1-8.5)$] and 4.4 kcal.mol^{-1} (**1b**) [$(3.8-0.0) - (0.0-0.6)$]. We have already observed this behaviour of the 3-21G(*) basis set in the related case of 1,2,6-thiadiazine 1,1-dioxides.² Moreover, these calculations being punctual, it is reasonable to assume that they do not correspond to energetic minima.

Atomic charges and dipole moments

We have collected in Table 3 the data corresponding to STO-3G*//STO-3G* calculations of the most stable forms.

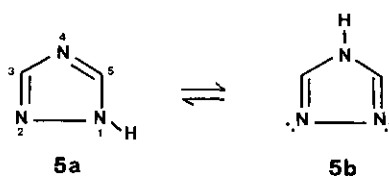
Table 3
Gross atomic population and dipole moments of nonplanar forms
of 1,2,4,6-thiatriazine 1,1-dioxide **1** (STO-3G*//STO-3G*)

Compound	S ₁	N ₂	N ₆	C ₃	C ₅	N ₄	O ₇	O ₈	μ(D)
1a nonplanar	15.504	7.339	7.235	5.808	5.833	7.270	8.232	8.222	3.48
1b nonplanar	15.531	7.246	7.246	5.809	5.809	7.339	8.235	8.227	6.98

No experimental data are available to test the values of Table 3 except for the ¹⁵N-nmr chemical shifts (DMSO) of compound **1b**. In agreement, at least qualitative with the calculations, the signal of N₄ appears at 238.3 ppm whereas those of N₂ and N₆ appear at 142.4 ppm.⁴ The fact that tautomer **1b** has the higher dipole moment would make it even more favoured in solution.

Discussion

Theoretical calculations provide an explanation to the fact that in 1,2,4-triazole 5, tautomer **5a** is much more stable than tautomer **5b**^{3,12} both in gas phase and solution whereas the reverse is true for 1,2,4,6-thiatriazine 1,1-dioxide.



A qualitative explanation of the relative low stability of tautomer **5b** compared with tautomer **1b**, is that in the latter the SO₂ group prevents the lone pair/lone pair repulsion present in **5b** (between N₁ and N₂). We have estimated¹³ that this repulsion amounts to 7.2 kcal.mol⁻¹, which roughly correspond to the shift of the equilibrium from 1,2,4,6-triazole (ΔG=3.9 kcal.mol⁻¹, STO-3G//STO-3G)¹² to 1,2,4,6-thiatriazine 1,1-dioxide (ΔG=-5.1 kcal.mol⁻¹, Table 2).

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