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On Triazoles, IX [1] HMO Calculations of Tautomeric 1,2,4-Triazole Derivatives [2]

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HMO calculations were performed for all possible tautomeric forms of different 1,2,4-triazole derivatives **1**–**4** and their condensed ring analogues **5**–**8**. The resonance energies obtained showed this method useful for the differentiation of the tautomeric structure of the planar monocyclic 1,2,4-triazole derivatives but it did not give satisfactory results in case of their non-planar condensed ring analogues.

(Keywords: Resonance energy; Tautomeric structure; 5-Amino-1,2,4-triazoles; 1,2,4-Triazolo[1,5—a]pyrimidinones; 1,2,4-Triazolo[4,3—a]pyrimidinones)

Über Triazole, 9. Mitt.: HMO-Berechnungen tautomerer 1,2,4-Triazol-Derivate

Die HMO-Methode wurde für alle möglichen tautomeren Formen der 1,2,4-Triazol-Derivate **1**—**4** und deren kondensierte Analogen **5**—**8** verwendet. Die berechneten Resonanzenergien bewiesen, daß die *Hückel*-Methode gute Resultate für die Unterscheidung verschiedener tautomerer Formen der planaren 1,2,4-Triazol-Derivate, aber nicht für deren nicht-planare kondensierte Analogen ergibt.

Introduction

In a previous paper [3] we have stated that the HMO calculations may be useful to decide which of the tautomeric structures of planar condensed-ring heterocyclic compounds is more probable. As the HMO calculations—possibly owing to their simplicity—are still popular to solve different kinds of problems in organic chemistry [4–10] we decided to extend our investigations for different 5-amino-3-R^1-thio-, and 3-R^2-amino-1,2,4-triazoles, their ring-acetylated and acetylamino derivatives and their condensed ring analogues prepared by us earlier [11–16]. The simple, not condensed 1,2,4-triazoles were planar, their condensed ring

analogues were not planar. In this paper we wanted to study how the deviation from planarity affects the theoretical results as compared with the experiments. Thus we have calculated (by using the simple HMO method [17]) the resonance energies of all possible tautomeric forms of the above 5-amino-1,2,4-triazole derivatives and compared them with the stable tautomeric structures deduced previously from different spectral data. It was found that in this class of molecules the conclusions drawn from the theoretical calculations agreed well with the experimental results for the planar molecules but did not agree with the experiments in case of the non-planar analogues.

Calculations

Equation for localised π-bonds given in *Pullman* and *Pullman*'s [18] book was used with *Streitwieser*'s parameters [17]. The following fragments each containing 2π electrons were obtained: —N=C—: 2.5616; —N=N—: 3.0000; —N—: 3.0000; —S—: 3.0000; C=O: 3.2361; CH_3: 2.0000; —C=C—: 2.0000 (all energy values are given in β units $\approx$ 2.4 eV). The localised energies of the π systems were calculated by taking into account the contribution of the localised units of the π electrons for each molecule. The resonance energies used in our study were obtained by substracting the localised energies from the total (*Hückel*) energies.

Results and Discussion

Derivatives **1**

For derivatives **1** the **a**–**e** tautomeric forms (Scheme 1) have to be considered. As no *Streitwieser* parameters were available for the S-alkyl and S-aralkyl substituents they were replaced in the HMO calculations by an SH and SPh group. The results obtained are summarized in Table 1.

Scheme 1

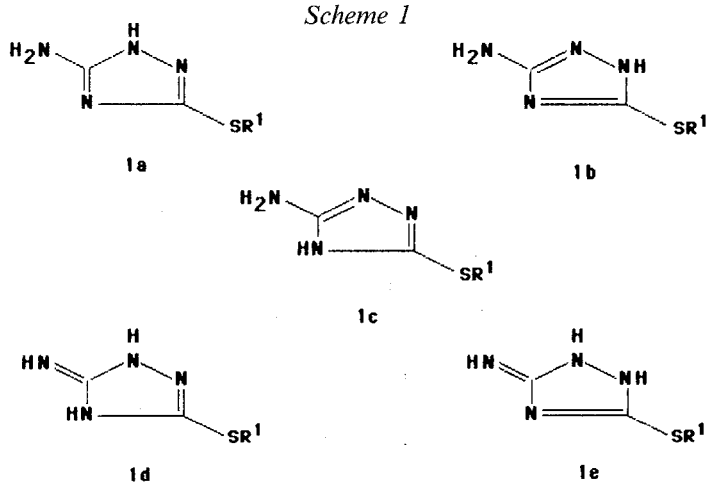


Table 1. *Resonance energies (in β-units) calculated for derivatives* **1**

Compound	R^1 = H	R^1 = *Ph*
1a	2.552	4.933
1b	2.552	4.933
1c	2.509	4.891
1d	2.247	4.629
1e	2.230	4.609

Within each column the order of energies of the tautomers is the same in Table 1. Consequently the S-alkyl or S-aralkyl groups may be replaced either by a H or by a *Ph*. Therefore in all subsequent calculations the replacement by H was used.

According to the calculated total energies derivatives **1** have to exist in the tautomeric mixture of **1a** and **1b**. Our previous results [11, 12] based on the chemical shifts of the triazole carbon atoms in the ^{13}C-NMR indicated in the case of derivatives **1** (R^1 = S-alkyl and S-aralkyl) tautomer **1a** to be predominant in *DMSO* solution. X-ray analysis [19] of the analogues 5-amino-1,2,4-triazole indicated the presence of the tautomeric form **1a** in solid state, too.

Derivatives **2**

For derivatives **2** the tautomeric structures **2a–2h** have to be considered (Scheme 2). The calculated total energies for R^2 = *Ph* and CH_2*Ph* are summarized in Table 2.

As it can be seen from the data of Table 2 structures **2a** and **2b** are again the most probable, being of the same probability (structure **2b** is in case of the benzyl derivatives slightly more probable). This is a theoretical explanation of our previous results [13] showing these derivatives in *DMSO* solution as a mixture of tautomeric forms **2a** and **2b**.

Derivatives **3** *and* **4**

On acetylation at mild conditions the 3-R^1-thio-5-amino-1*H*-1,2,4-triazole derivatives gave 1-acetyl-3-R^1-thio-5-amino-1*H*-1,2,4-triazoles (**3**), which were thermally re-arranged to the corresponding 3-R^1-thio-5-acetylamino-1*H*-1,2,4-triazoles (**4**) [14]. For derivatives **3** tautomeric structures **3a**, **3b** and **3e**, for their isomers **4** the tautomeric structures **4a–4e** (Scheme 3) have to be considered. The total energies were again calculated by replacing R^1 with H. The results are summarized in Table 3.

Scheme 2

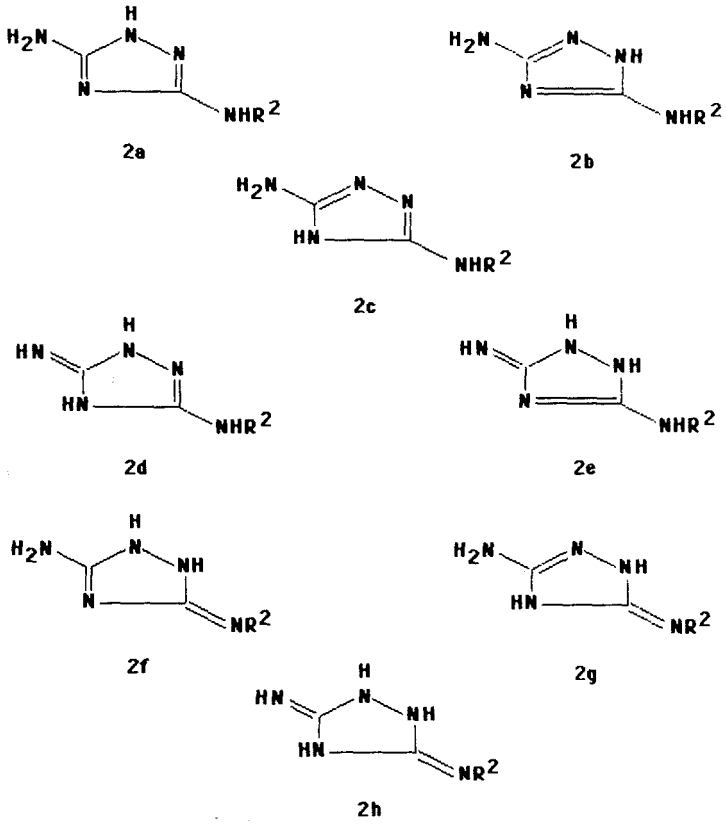


Table 2. *Resonance energies (in β-units) calculated for derivatives* **2**

Compound	$R^2 = Ph$	$R^2 = CH_2Ph$
2a	4.933	6.747
2b	4.933	6.760
2c	4.891	6.717
2d	4.629	6.452
2e	4.609	6.450
2f	4.739	6.562
2g	4.743	6.606
2h	4.496	6.374

Scheme 3

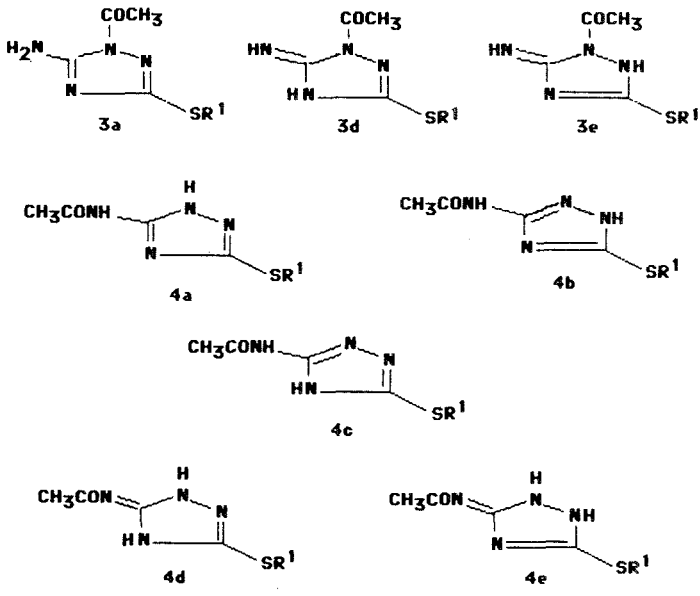


Table 3. *Resonance energies (in β-units) calculated for the planar derivatives* **3**–**4**

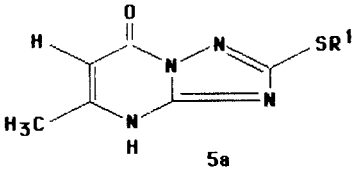
Compound		Compound	
3a	5.286	**4a**	5.350
		4b	5.357
		4c	5.310
3d	5.021	**4d**	5.260
3e	5.028	**4e**	5.288

As it can be seen from the data of Table 3, derivates **3** should exist in tautomeric form **3a** in full agreement with our previous results obtained in *DMSO* solution [14]. Derivatives **4** have to exist in the tautomeric form **4b** which is practically as stable as **4a**. Our previous spectroscopic results [14] showed that **4a** is the predominating tautomeric form in ethanolic and *DMSO* solutions.

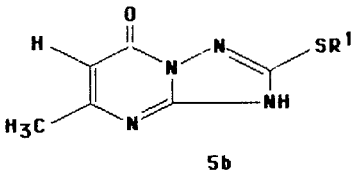
Derivatives **5**–**8**

The four isomeric triazolo-pyrimidone derivatives **5**–**8** derived from the possible reaction of 5-amino-3-methylthio-1*H*-1,2,4-triazole with ethyl acetoacetate may exist in tautomeric forms **5a**–**5c**, **6a**–**6c**, **7a**–**7b** and **8a**–**8b**, respectively [15–16] (Scheme 4).

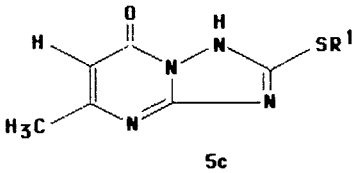
Scheme 4



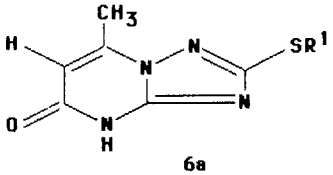
5a



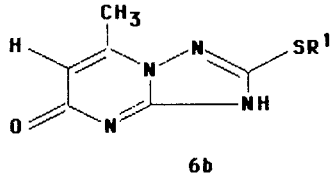
5b



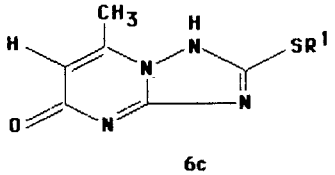
5c



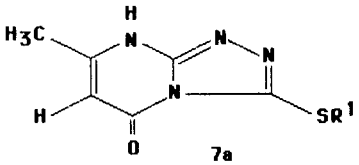
6a



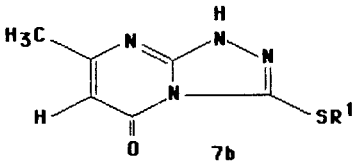
6b



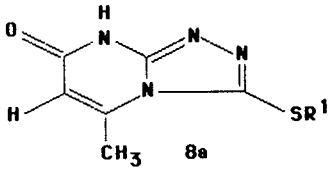
6c



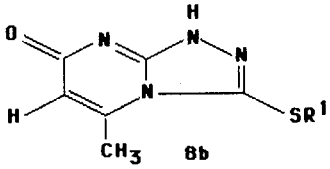
7a



7b



8a



8b

The total energies corresponding to the above tautomers were calculated again by replacing R^1 by H. The results obtained are summarized in Table 4.

Table 4. *Resonance energies (in β-units) calculated for the non-planar derivatives* **5–8**

Compound		Compound	
5a	6.328	**6a**	6.300
5b	6.308	**6b**	6.283
5c	6.345	**6c**	6.321
7a	6.240	**8a**	6.239
7b	6.285	**8b**	6.259

As it can be seen from the data of Table 4 the calculated energies indicate that tautomers **5c**, **6c**, **7b** and **8b** are the most stable ones, respectively. This result contradicts our previous observation [15–16] showing that tautomers **5a**, **6a**, **7a** and **8a** are the predominating ones in *DMSO* solution, respectively. This may be caused by the sp^3 nitrogen atom of the pyrimidone ring, the triazole and pyrimidone rings being not coplanar in derivatives **5–8**. This leads to the stabilisation of tautomers **5a**, **6a**, **7a** and **8a** as compared to the non-aromatic tautomers **5c**, **6c**, **7b** and **8b** in *DMSO* solution. It is very probable that the calculations could be improved if a different set of β-parameters were chosen for the sp^3 nitrogen atoms of the pyrimidone ring.

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