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Ab initio study on the photochemical isomerization of thiazole derivatives

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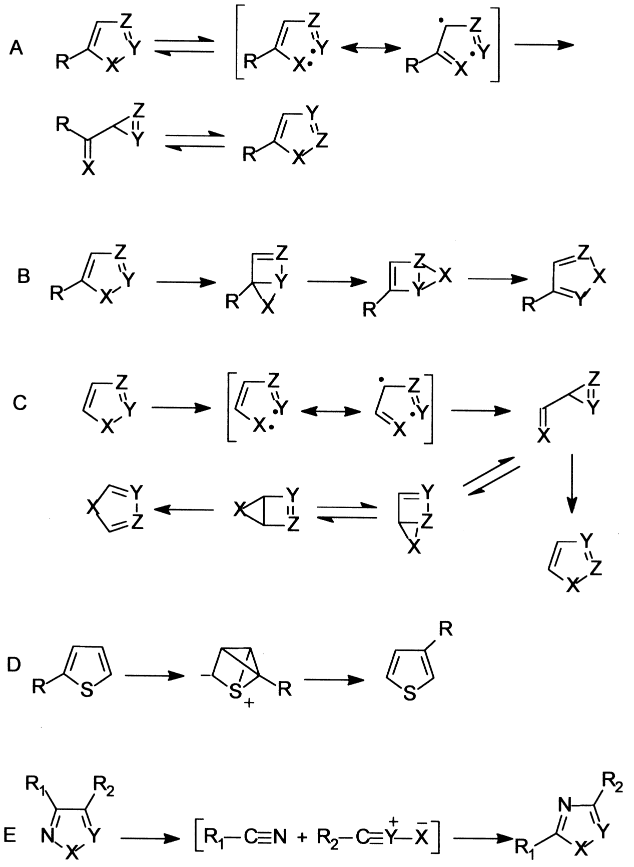
Abstract—The photochemical isomerization reactions of 2-phenyl and 2-acetylthiazole were studied using ab initio methods. The results are in agreement with the previously reported data obtained through semiempirical methods. Triplet excited 2-phenylthiazole is a π,π^* triplet with LSOMO at −9.47 eV and HSOMO at −6.84 eV. In this case, the singlet excited state can evolve giving the Dewar thiazole while the corresponding excited triplet state cannot be obtained. Furthermore, the triplet state cannot be converted into the biradical intermediates because these intermediates show a higher energy than the triplet state, thus preventing the formation of the cyclopropenyl derivatives. Triplet excited 2-acetylthiazole is a π,π^* species. It shows the LSOMO at −10.70 eV and the HSOMO at −8.14 eV. In this case, the direct irradiation involves the population of the excited singlet state, and then the formation of the Dewar isomer is possible. The intersystem crossing to the triplet state can occur; the intersystem crossing quantum yield for this conversion is nearly quantitative. The triplet state cannot convert into Dewar thiazole but it can give the corresponding biradicals. These biradicals are not responsible for the isomerization reactions but they are able to give only decomposition products. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

Five mechanisms can be invoked in order to justify the photochemical isomerization of pentaatomic aromatic heterocycles: (1) the ring contraction–ring expansion route (RCRE) (Scheme 1A); (2) the internal cyclization–isomerization route (ICI) (Scheme 1B); (3) the van Tamelen–Whitesides general mechanism (VTW) (Scheme 1C); (4) the zwitterion–tricycle route (ZT) (Scheme 1D); (5) the fragmentation–readdition route (FR) (Scheme 1E). Recently we reported that the photochemical isomerization of pentaatomic aromatic heterocycles[1] can be described using a unifying hypothesis.[2–6] In this hypothesis, if the first excited singlet state of a molecule is populated, the molecule can convert into the corresponding triplet state or into the corresponding Dewar isomer. The efficiency of these processes will depend on energetic factors. If the Dewar isomer is formed, the isomeric product is obtained. If the triplet state is formed, cleavage of the X–C$_\alpha$ bond can occur to give ring opening products, decomposition products or ring contraction products. However, if the radical formed after the X–C$_\alpha$ cleavage shows a higher energy than the triplet state, the triplet state will not be able to give the biradical with high efficiency, and, then, it will be quenched in radiative and not radiative processes. In this case, the Dewar isomer could be responsible for the isomerization reaction, but the isomerized product will probably be produced in very low quantum yields.



Scheme 1. Proposed mechanisms for photochemical isomerization of pentaatomic aromatic heterocycles.

Keywords: thiazole photoisomerization; ab initio study; 2-acetylthiazole; decomposition products.

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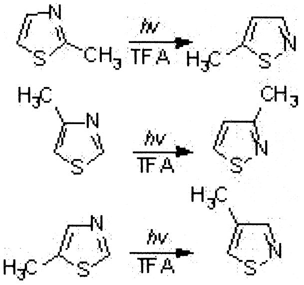


Scheme 2. Photochemical isomerization of alkylthiazole derivatives.

These results were obtained on the basis of both semi-empirical calculations[2–4] and ab initio results on the photochemical isomerization of furan derivatives.[5,6]

In this paper, we want to report our results on thiazole derivatives using ab initio calculations in order to test the validity of the above described hypothesis.

2. Results and discussion

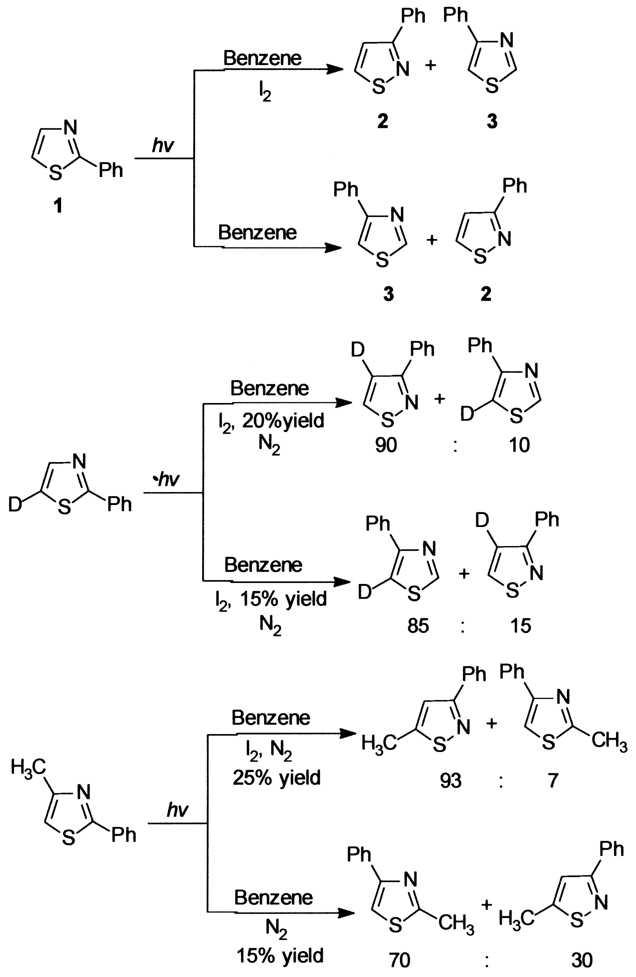
The irradiation of thiazole did not give any interesting product.[7] However, 2-, 4-, and 5-methylthiazole gave the corresponding isothiazoles in low yield when irradiated in trifluoroacetic acid (Scheme 2).[8]

A lot of data have been reported on the reactivity of 2-phenylthiazole. In a pioneering work, the irradiation of this compound led to 4-phenylthiazole and 3-phenylisothiazole; however, while the experimental conditions were provided (benzene, 12–24 h), the yields of the obtained products were not reported.[9] Subsequently, the same authors reported that the irradiation of a benzene solution of 2-phenylthiazole (**1**) (obtained through irradiation of 2-iodothiazole in benzene), in the presence of iodine, leads to **2**, as the major product, in addition to small amounts of **3** (Scheme 3). When the reaction was carried out without iodine, the main product was 4-phenylthiazole (**3**) while 3-phenylisothiazole (**2**) was present in trace quantities.[10,11]

2-Phenyl-5-deuterothiazole and 2-phenyl-4-methylthiazole showed the same behavior (Scheme 3). By contrast, 4-phenylthiazole practically did not react and 5-phenylthiazole gave 4-phenylisothiazole as the main product in very low yield.

Other methyl derivatives were additionally studied: thus, 2-phenyl-5-methylthiazole furnishes mainly 3-phenyl-4-methylisothiazole, 2-methyl-5-phenylthiazole gives 3-methyl-5-phenylisothiazole, 4-methyl-5-phenylthiazole leads to the formation of 3-methyl-4-phenylisothiazole, 2-methyl-4-phenylthiazole gives 3-phenyl-5-methylisothiazole, and, finally, 4-phenyl-5-methylthiazole is converted into 3-phenyl-4-methylisothiazole.[12]

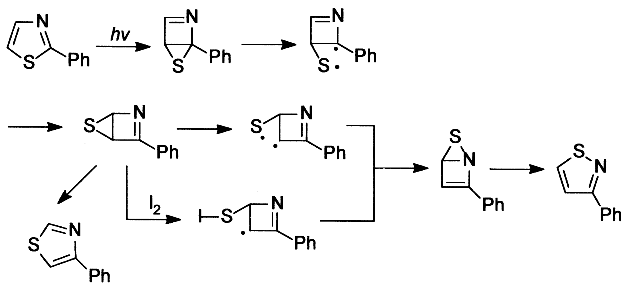
The authors generally considered the above results consistent with an ICI mechanism.[4] In this context, iodine favors intersystem crossing or the opening of the Dewar intermediate as reported in Scheme 4.[10]



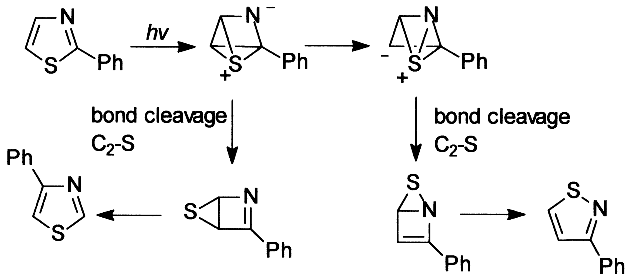
Scheme 3. Photochemical isomerization of phenylthiazoles.

However, such a possible explanation was not convincing for other authors. Maeda and Kojima found that the irradiation of 2-phenylthiazole in ethanol at 80°C led to the same products described before but in a different ratio. Under the same reaction conditions, 5-phenylthiazole gave 4-phenylisothiazole, while 4-phenylthiazole was converted into 3-phenylisothiazole.

The most important observation those authors made was that deuterium incorporation occurred when the reaction was carried out in benzene at 80°C in the presence of deuterium oxide. In fact, 2-phenylthiazole furnished deuterated 3-phenyl-4-deuteroisothiazole and 4-phenylthiazole without any deuterium incorporation.



Scheme 4. Hypothetical mechanism for the photochemical isomerization of phenylthiazole derivatives.

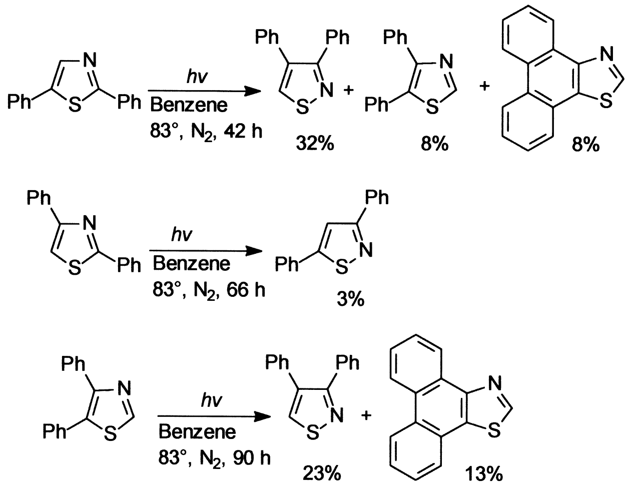


Scheme 5. Alternative mechanism for 2-phenylthiazole photoisomerization.

Likewise, 4-phenylthiazole was converted into 3-phenyl-4-deuteroisothiazole, and instead 5-phenylthiazole did not undergo any deuterium incorporation.[13,14] On the basis of their results the authors put forward a new mechanistic hypothesis based on the ZI route involving the intervention of a polar intermediate (Scheme 5). In fact, the formation of a polar intermediate could justify deuterium incorporation. However, deuterium incorporation could also be explained by using the ICI mechanism.[11]

The same authors discussed the reactivity of diphenylthiazoles. 2,5-Diphenylthiazole, irradiated in benzene at 80°C, gave 3,4-diphenylisothiazole as the major product, together with minor amounts of 4,5-diphenylthiazole and its cyclized derivative (Scheme 5). 2,4-Diphenylthiazole gave only a very low yield of 3,5-diphenylisothiazole, while 4,5-diphenylthiazole was converted into the corresponding cyclized product and into 3,4-diphenylisothiazole (Scheme 6).[14,15] All the data are in agreement with an ICI mechanism.

We investigated the ground state and the lowest triplet state of 2-phenylthiazole the triplet biradical that results from the homolytic cleavage of the S–C$_\alpha$ bond (these biradical intermediates are supposed to occur in the isomerization process leading to the formation of the cyclopropenyl derivatives), and Dewar 2-phenylthiazole in its singlet state. The structural properties of all these compounds and/or intermediates are shown in Fig. 1 and Tables 1 and 2. We do not consider the formation of the zwitterionic intermediate considering that, on the basis of our previous work in this field performed by using semiempirical methods,[4] this intermediate showed higher energy than the Dewar isomer. The formation of this intermediate could be allowed only assuming that the reaction conditions used by Kojima and Maeda allowed the endothermic reaction to give this type of intermediate.



Scheme 6. Photoisomerization of diphenylthiazoles.

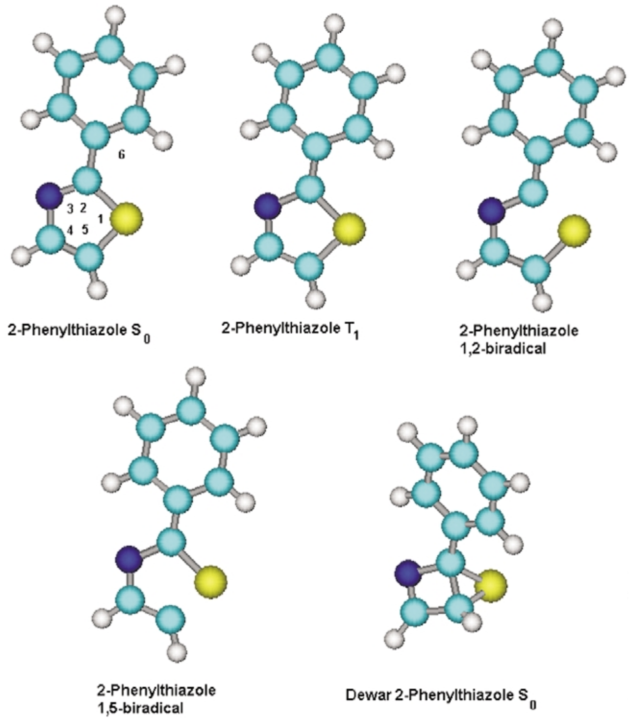


Figure 1. Structures of possible intermediates in the photochemical isomerization of 2-phenylthiazole.

We have to note that while 2-phenylthiazole in the ground state shows a partial dienic character (the C_2–N_3 and C_4–C_5 distances resemble that of a double C=N and C=C bonds, respectively, while the N_3–C_4 one shows an intermediate distance between a single and a double C–N bond), the triplet state is clearly deformed with some inverted distances: in fact, the C_2–N_3 distance resembles that of a single C–N bond, N_3–C_4 is similar to a double C–N bond, and the C_4–C_5 distance is intermediate between those of a single and a double C–C bond. Both S_0 and T_1 states of 2-phenylthiazole are planar.

It is interesting to note that 2-phenylthiazole does not show the behavior observed with furan.[16] The triplet state of furan showed that the C_3–C_4 bond was shorter than the C_2–C_3 one. Furthermore, in the biradical intermediate, the O–C_5 bond was a double bond, while the C_4–C_5 bond resembled a single carbon–carbon bond. We observe the same trend in thiazole, with a difference: S–C$_\alpha$ bond is a single bond. Triplet excited furan was a π,π^* triplet, and the resulting biradical was a σ,π species;[5] triplet excited 2-phenylthiazole is a π,π^* triplet with LSOMO at −9.47 eV and HSOMO at −6.84 eV and the biradical intermediates are π,π species with LSOMO at −9.46 eV and HSOMO at −6.84 eV. The biradicals are very similar to the triplet species.

Table 1. Structural properties and energy of possible intermediates in the photochemical isomerization of thiazole derivatives

Compound	Electronic state	Structural element						Relative energy (kcal/mol)
		S_1–C_2 (Å)	C_2–N_3 (Å)	N_3–C_4 (Å)	C_4–C_5 (Å)	C_5–S_1 (Å)	C_5–C_2 (Å)	
2-Phenylthiazole	S_0	1.7456	1.2803	1.3731	1.3398	1.7260		0
2-Phenylthiazole	T_1	1.7980	1.4490	1.2904	1.4195	1.7522		34
2-Phenylthiazole biradical 1,2	T_1		1.4491	1.2905	1.4195	1.7521		36
2-Phenylthiazole biradical 1,5	T_1	1.7979	1.4488	1.2901	1.4200			36
2-Phenylthiazole dewar	S_0	1.8254	1.4886	1.2635	1.5102	1.8125	1.4806	62
2-Acetylthiazole	S_0	1.7402	1.2773	1.3689	1.3449	1.71745		0
2-Acetylthiazole	T_1	1.7741	1.3352	1.3482	1.3739	1.7367		54
2-Acetylthiazole biradical 1,2	T_1		1.4483	1.2892	1.4228	1.7607		41
2-Acetylthiazole biradical 1,5	T_1	1.7868	1.4483	1.2895	1.4223			41
2-Acetyllthiazole dewar	S_0	1.8059	1.4865	1.2648	1.5150	1.8090	1.4746	41

Table 2. Other structural properties and energy of possible intermediates in the photochemical isomerization of thiazole derivatives

Compound	Angle (°)												
	1–2–3	2–3–4	3–4–5	4–5–1	5–1–2	1–2–6	3–2–6	5–2–3	4–5–2	2–5–1	1–2–5	1–5–4	5–2–6
2-Phenylthiazole S_0	113.77	111.74	115..97	109.49	89.03	122.76							
2-Phenylthiazole T_1	112.26	110.53	118.04	111.11	88.07	125.63							
2-Phenylthiazole biradical 1,2		110.51	118.04	111.12			112.08						
2-Phenylthiazole biradical 1,5	112.25	110.55	118.05			125.65	112.10						
2-Phenylthiazole dewar	110.20	90.10	98.13		48.03			90.11	81.59	66.44	65.53	108.03	131.67
2-Acetylthazole S_0	114.33	111.43	115.71	109.74	89.79	123.03							
2-Acetylthiazole T_1	113.69	111.11	116.66	110.24	88.30	125.86							
2-Acetylthiazole biradical 1,2		119.99	118.22	110.84			121.99						
2-Acetylthiazole biradical 1,5	113.20	109.96	118.23			124.80	122.01						
2-Acetylthiazole dewar	111.47	89.72	98.22		48.14			90.76	81.27	65.81	66.04	108.06	129.07

The relative energies for the five above-mentioned structures are shown in Fig. 2 and Table 1.

The data are in agreement with experimental results. In fact, the singlet excited state (the energy was obtained from the UV spectrum) can evolve giving the Dewar thiazole (and, then, isomeric thiazoles and isothiazoles in agreement with the mechanism depicted in Scheme 4) while the corresponding excited triplet state can be obtained. Furthermore, the triplet state cannot be converted into the biradical intermediates because these intermediates show a higher energy than the triplet state, thus preventing the formation of the cyclopropenyl derivatives.

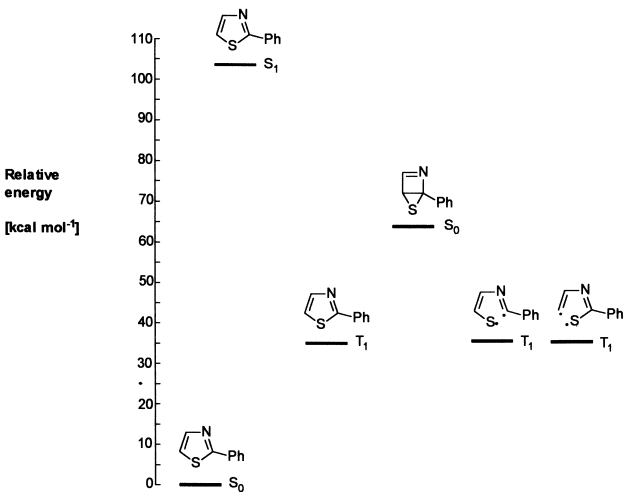


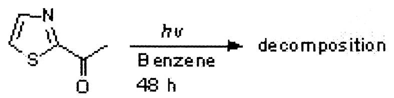
Figure 2. Relative energy of the species involved in the photoisomerization of 2-phenylthiazole.

In order to verify this scheme, we tested the photochemical behavior of 2-acetylthiazole. A 10^{-2} M solution of this compound in benzene was irradiated for 48 h and the resulting mixture was analyzed through GLC. We did not observe the formation of any photoisomerization product but we could observe a slow decomposition of the substrate (Scheme 7).

2-Acetylthiazole shows absorptions at 250 and 310 nm to give the first excited singlet state (S_1). It shows a quantitative intersystem crossing into the triplet state (T_1). Calculations confirm this behavior. The structural properties of all the possible intermediates involved in the photochemical isomerization of 2-acetylthiazole are shown in Fig. 3 and Tables 1 and 2.

We note that in the ground state the bond length is larger for S–C_2 than for S–C_5, and that this feature is maintained in the triplet state.

In the ground state, all the bonds are shorter than in 2-phenylthiazole with the exception of C_4–C_5 bond that is longer than the C_4–C_5 bond in 2-phenylthiazole. In the triplet state, both C_2–N_3 and C_4–C_5 bonds are shorter than in the corresponding state of 2-phenylthiazole. On the contrary, the N_3–C_4 bond is longer than in 2-phenylthiazole.



Scheme 7. Photochemical behavior of 2-acetylthiazole.

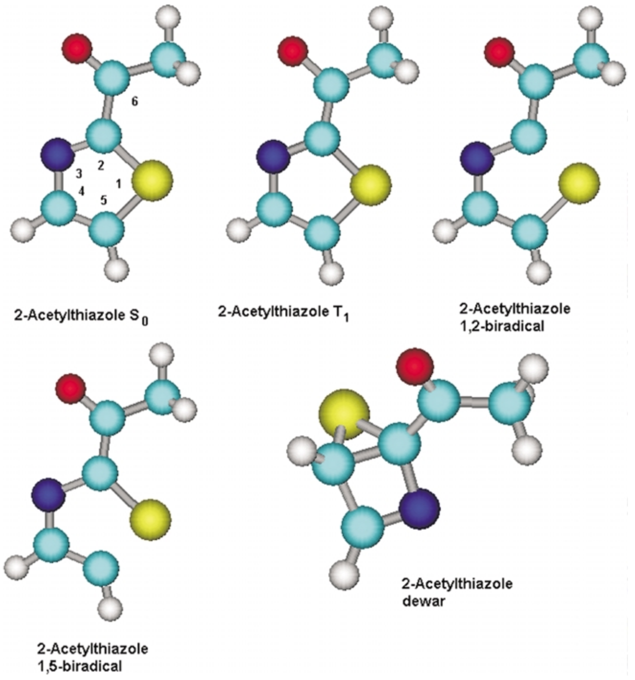


Figure 3. Structures of possible intermediates in the photochemical isomerization of 2-acetylthiazole.

The biradicals that result from the fission of both the $S-C_2$ and $S-C_5$ bonds show the same structure and these structures resemble the triplet state.

Triplet excited 2-acetylthiazole is a π,π^* species. It shows a LSOMO at −10.70 eV and a HSOMO at −8.14 eV. The biradicals are π,π species with LSOMO at −11.87 eV and HSOMO at −7.79 eV. The relative energy of the possible intermediates involved in the photochemical isomerization is shown in Fig. 4 and Table 1.

In this case, direct irradiation involves the population of the excited singlet state (its energy was calculated on the basis of the UV absorption), and then the formation of the Dewar isomer is possible. The intersystem crossing to the triplet state can occur; however, its conversion into the corresponding biradicals can be efficient.

2-Acetylthiazole showed nearly quantitative intersystem crossing: the triplet state cannot convert into Dewar thiazole but it can give the corresponding biradicals. These biradicals are not responsible for the isomerization reactions but they are only able to give decomposition products.

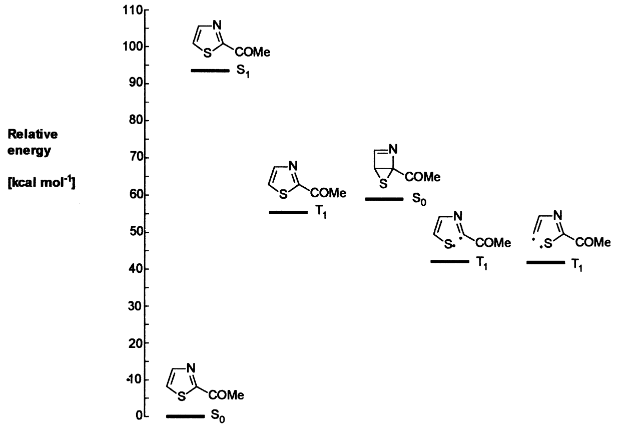


Figure 4. Relative energy of the species involved in the photoisomerization of 2-acetylthiazole.

In conclusion, the results of the above-described ab initio study of the photochemical isomerization of thiazole derivatives are in agreement with experimental results and with previous reported data obtained from semiempirical methods. In this case, the photochemical isomerization involves the formation of the Dewar isomer. The triplet state can be obtained, and, when it can be obtained, it is not able to convert into the corresponding biradicals via $S-C_\alpha$ bond cleavage. When the biradicals can be obtained they do not give isomerization but only decomposition products.

3. Experimental

2-Acetylthiazole (Aldrich) (100 mg) was dissolved in benzene (10 ml) and outgassed with nitrogen for 1 h. The solution was irradiated with a 125 W high-pressure mercury-arc (Helios-Italquartz, Milan) surrounded by a Pyrex water jacket. After 24 and 48 h, the mixture was analyzed by GLC. The analyses were performed with HP6890 plus gas-chromatograph equipped with a Phenomenex Zebron ZB-5 MS capillary column (30 m×0.25 mm ID×0.25 μm FT). As detector we used a HP 5973 Mass Selective Detector, Helium at 0.8 ml/min was used as carrier gas. The injector was splitless at 250°C. Detector was maintained at 230°C. Oven was maintained at 40°C for 2 min, then the temperature increased until 250°C (8°C/min); finally, this temperature was maintained for 10 min.

The intersystem crossing quantum yield for 2-acetylthiazole was determined by using the sensitized isomerization of α-methylstilbene.[17] 2-Acetylthiazole solution in benzene (10 ml, 10^{-2} M) was irradiated at 340 nm in the presence of α-methylstilbene (20 mg) with a high-pressure mercury arc (Helios-Italquartz, 125 W) surrounded by a Pyrex water jacket. The lamp was immersed in 2 M KNO_3 solution in order to cut-off all the emission below 330 nm. The *cis–trans* isomerization was determined via GLC. Benzophenone was used as actinometer.

We performed some ab initio calculations using 6-31G** basis set on Gaussian 94, using UHF method. The calculations were usually done using Møller–Plesset perturbations (MP2). The Polak–Ribiere algorithm with gradient calculations was adopted for geometry optimizations. The open-shell states were treated at the same level of accuracy as the closed state states. We verified that the obtained structures were minima on the potential energy surfaces calculating the frequencies of the optimized structures.

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