# TOWARDS A UNITARY DESCRIPTION OF THE PHOTOCHEMICAL ISOMERIZATION REACTIONS IN PENTAATOMIC AROMATIC HETEROCYCLES: THE CASE OF FURAN, THIOPHENE, PYRROLE, ISOXAZOLE, IMIDAZOLE, AND PYRAZOLE DERIVATIVES

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***Abstract*** - The photochemical behaviour of furan, thiophene, pyrrole, isoxazole, imidazole, and pyrazole derivatives appears to be very complex and, apparently, no common description of the reactivity of these heterocycles is possible. On the basis of PM3-RHF-CI semiempirical calculations an unitary description of the behaviour of these molecules can be made.

Some years ago, in a text on the heterocyclic chemistry, Newcome and Paudler reported that the photochemical isomerization in π excessive heterocycles was restricted to furan and thiophene derivatives, while pyrrole did not give this type of reaction. Furthermore, the mechanisms reported for the reactivity of furans and thiophenes are quite different, giving the impression that the reactivity of these two heterocycles was completely different.[1] Gilchrist reported the photochemical isomerization of the thiophene while furan and pyrrole can not be treated in his book. Furthermore, two mechanisms are reported for this isomerization, inducing the reader to consider this field in a confused status.[2] Actually, the descriptions of the photochemical isomerization of furan, thiophene, and pyrrole derivatives were reported separately (see below) and no attempt was made to give an unitary explanation of the different behaviour of these molecules. Similar situations can be described for other pentaatomic aromatic heterocycles.

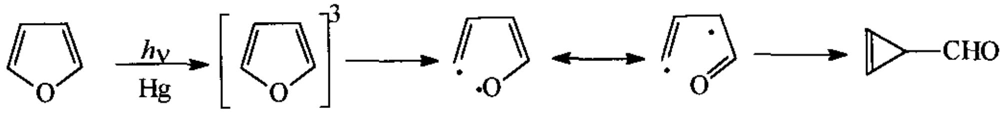
In this article we want to report a first unitary description of the photochemical isomerization of these π excessive heterocycles by using semiempirical calculations. We do not consider it a definitive explanation but only a first attempt to understand the photochemistry of these heterocycles.

In the gas phase photolysis at 254 nm of furan derivatives in the presence of mercury vapour cyclopropene derivatives were obtained as the main products.[3-7]

Liquid phase photolysis of furan was in agreement with the formation of cyclopropene-3-carbaldehyde.[8] The direct flash photolysis of furan gave, on the contrary, a different behaviour. MS fragments corresponding to $C_4H^+$, $C_4H_2^+$, $C_4H_3^+$, and $C_4H_4^+$ were observed together with the formation of cyclopropene-3-carbaldehyde.[9] This behaviour can be explained assuming that Dewar furan is the precursor of the cyclopropene derivative. Dewar furan can be obtained also by the photolysis of furan in argon matrices at 10 K.[10]

In the direct irradiation, cyclopropene derivatives were obtained in lower yields while isomeric furans appeared.[6,11] It is noteworthy that the ring contraction showed a high selectivity. Calculation on the excited state of the substrates showed that the direction of the ring contraction can be predicted, on the basis of the mechanism depicted in Scheme 1, if the weakest bond in the excited furan derivative is known.[12,13] Nevertheless, we have to note that cyclopropene-3-carbaldehyde can be obtained also by thermal rearrangement from the Dewar furan.[14-16]

Scheme 1

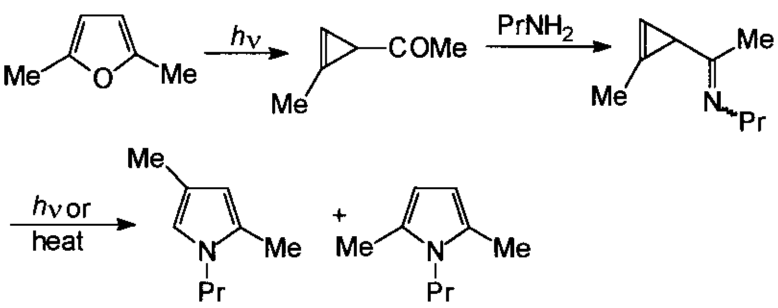


All the reactions described above were reported to be effective in vapour phase, while no reaction occurred in solution. Only a few reactions are described in pentane solution. 2,5-Di-*t*-butylfuran, irradiated in pentane, gave the corresponding cyclopropenyl ketone, 2,4-di-*t*-butylfuran, and an allene.[17,18]

More recently, the same reaction was attempted with 2-trimethylsilylfuran, which gave an allene derivative in 68% yield.[19] The formation of this type of products can be explained assuming the presence of a cyclopropyl intermediate that was converted into the allene. Such a cyclopropyl intermediate can be isolated in the reaction of furan-2-carbonitrile in the presence of methanol. In this case, the reaction gave a mixture of three isomeric products containing MeO substituents.[20,21] These products clearly were obtained from the cyclopropenyl intermediate through a Michael addition of methanol.

The irradiation of furan derivatives in propylamine led to the formation of the corresponding pyrrole. The reaction mechanism can be explained as depicted in Scheme 2.[22,23] It is noteworthy, however, that, when the tetrakis(trifluoromethyl)cyclopropene derivative of the proposed imine was synthesised, it could not be converted into the corresponding pyrrole. In this case the observed behaviour can be explained assuming the formation of a Dewar furan intermediate.[24]

Scheme 2



We performed our calculations by using PM3-RHF-CI semiempirical method. We have calculated the relative energy of the first excited singlet state, the energy of the first excited triplet state, the relative energy of the Dewar heterocycles in their singlet state, and finally, the relative energy of the biradical deriving from the fission of the bond between the heteroatom and C-1. This intermediate is supposed in the isomerisation process leading to the formation of the cyclopropenyl derivatives.

Considering the furan, the data collected in Table 1 and Figure 1 fit the experimental results. In the case of the sensitised reaction, when the excited triplet state is populated, only the formation of the radical intermediate is allowed. This intermediate can evolve to the corresponding cyclopropenyl derivative or to the decomposition products. In a previously reported mechanism the decomposition products resulted from the excited cyclopropenyl derivative. In our hypothesis the formation of both the decomposition products and the cyclopropenyl derivatives can be considered as competitive reactions.

In the case of the direct irradiation, the singlet excited state is populated and, then, the formation of the Dewar furan is energetically possible (Figure 1). This result is in agreement with both the evidences about the formation of the Dewar furan in the direct irradiation and with the formation of isomeric furans.

In the case of 2-methylfuran our data are in agreement with the experimental results. In fact, we can obtain the ciclopropenyl intermediate. When 2-trifluoromethyl is used in our calculation we can see that the diradical intermediate can not be formed starting from the triplet state of the molecule. On the basis of these data, the population of the triplet state, in this case, should not give any interesting result. We do not know any experimental result on this molecule. The irradiation of 2-cyanofuran can give the cyclopropenyl intermediate in agreement with the experimental results, while this type of intermediate can not be present in the photoisomerization of 2-phenylfuran.

Vapours of pyrrole and pyrrole derivatives were irradiated at 214 nm at room temperature showing that some decomposition products were obtained.[25,26] It should be noted that author identified only decomposition products, while they did not find isomerisation products, as in vapour phase photochemistry of furan. To confirm these experimental data, Dewar pyrrole, generated by photofragmentation of a suitable substrate, showed to be very unstable in comparison to similar compounds obtained with furans or thiophenes.[27]

**Table 1** - *Relative energy of both some heterocyclic derivatives and reactive intermediates related to the photoisomerization of furan*

| Chemical Species | Electronic state | Relative energy [kcal mol$^{-1}$] |
|---|---|---|
| Furan | $S_1$ | 129 |
| Furan | $T_1$ | 74 |
| Dewar Furan | $S_0$ | 78 |
| Diradical Intermediate | $T_1$ | 73 |
| | | |
| 2-Methylfuran | $S_1$ | 114 |
| 2-Methylfuran | $T_1$ | 59 |
| Dewar 2-Methylfuran | $S_0$ | 74 |
| Diradical Intermediate | $T_1$ | 59 |
| | | |
| 2-Trifluoromethylfuran | $S_1$ | 117 |
| 2-Trifluoromethylfuran | $T_1$ | 46 |
| Dewar 2-Trifluoromethylfuran | $S_0$ | 75 |
| Diradical Intermediate | $T_1$ | 70 |
| | | |
| 2-Cyanofuran | $S_1$ | 111 |
| 2-Cyanofuran | $T_1$ | 64 |
| Dewar 2-Cyanofuran | $S_0$ | 73 |
| Diradical Intermediate | $T_1$ | 64 |
| | | |
| 2-Phenylfuran | $S_1$ | 107 |
| 2-Phenylfuran | $T_1$ | 53 |
| Dewar 2-Phenylfuran | $S_0$ | 68 |
| Diradical Intermediate | $T_1$ | 62 |

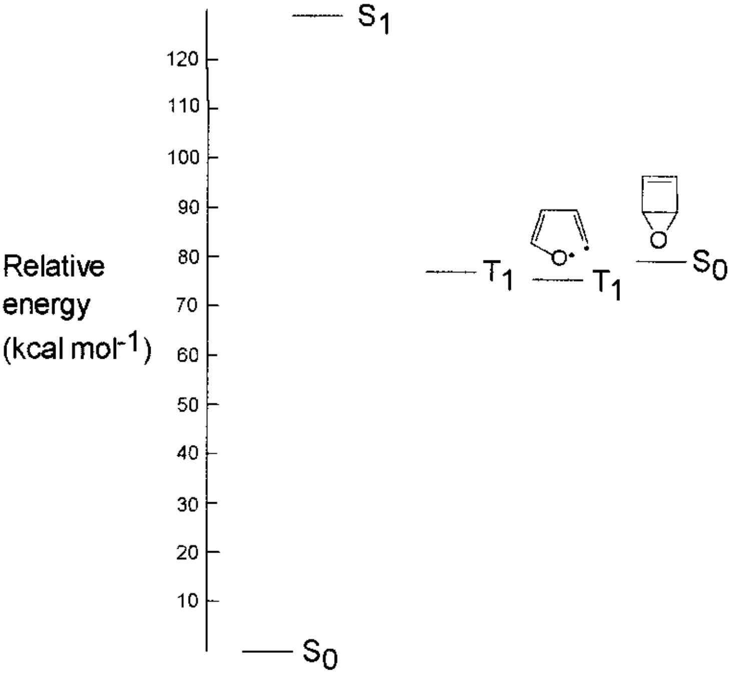
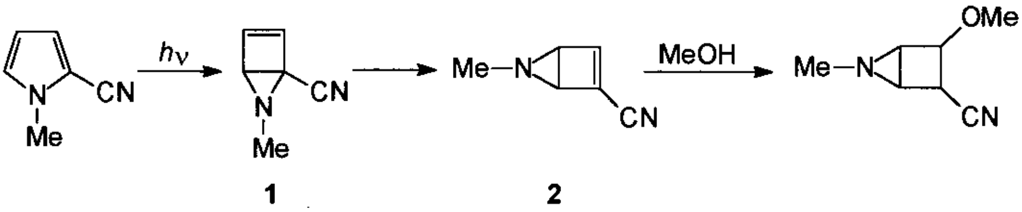


**Figure 1** - *Relative energies of the excited states of furan and of some reactive intermediates*

In 1970 Hiraoka reported that 2-cyanopyrrole, irradiated in methanol with a low pressure mercury arc for 20 h, gave a mixture of 3-cyanopyrrole and pyrrole-2-carbaldehyde.[28] Theoretical calculations showed that strong electron donor or acceptor substituents allowed this behaviour.[29] 1-Methyl-2-cyanopyrrole also gave this reaction.[30] In this case the author isolated the product of the isomerisation, the product of the shift in C-2 of the *N*-methyl group, and a third product that be assumed to be derived from the addition of methanol to the Dewar pyrrole.[31] The reaction depends on the temperature used : in fact, no reaction occurred when the reaction was performed at -68°C. This datum is in agreement with the presence of a thermal activated step.[31]

All these data seem to be in agreement with a mechanism depicted in Scheme 3, where the thermal activated step is the 1,2-sigmatropic shift between **1** and **2**.

Scheme 3



Similar results were obtained using methyl substituted 2-cyanopyrroles.[32] Recently, the 1,3-sigmatropic shift on 2-cyanopyrrole was studied by using the SINDO1 semiempirical method.[33] This study showed that the reaction occurred *via* a $\pi,\pi^*$ transition and that some biradical intermediates are probably involved in the reaction.

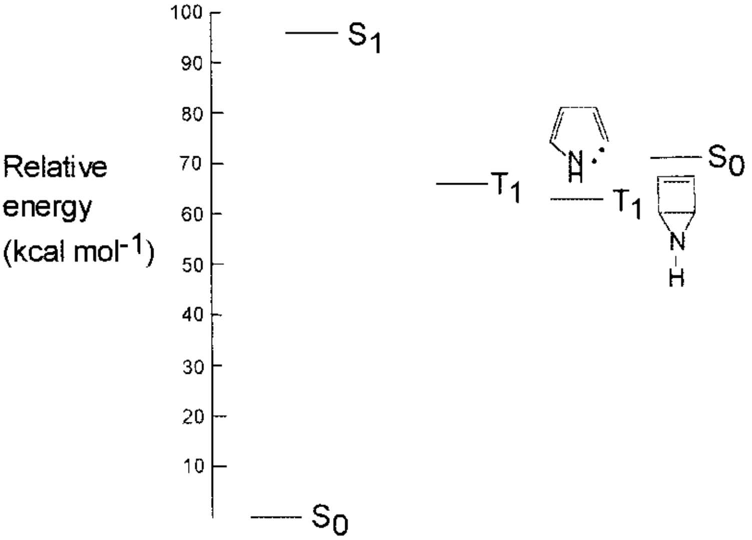


**Figure 2** - *Relative energies of the excited states of pyrrole and of some reactive intermediates*

When pyrrole is irradiated only decomposition products were obtained. Our data can fit this statement (Table 2, Figure 2). In fact, the direct irradiation populates the excited singlet state which can be converted into the Dewar pyrrole or into the corresponding triplet state. Clearly, the intersystem crossing to the triplet state allows to reach the lowest energy state.

The excited triplet state can give the biradical intermediate, and this intermediate can give or the decomposition products only, or the cyclopropenyl derivative that thermally evolves to give the decomposition products as reported in Ref. 24.

On the contrary, when the irradiation is performed on 2-cyanopyrrole, the isomeric products are observed. In fact, in this case, the corresponding Dewar pyrrole shows a lower energy than in the previous case, allowing the formation of the isomeric products (Table 2, Figure 3). When 2-methylpyrrole is used as substrate, the formation of the triplet state is favored, but this triplet state can not evolve through the formation of the diradical intermediate. The same behaviour was observed when 2-trifluoromethylpyrrole and 2-phenylpyrrole were used in our calculation.

**Table 2** - *Relative energy of both some heterocyclic derivatives and reactive intermediates related to the photoisomerization of pyrrole*

| Chemical Species | Electronic state | Relative energy [kcal mol$^{-1}$] |
|---|---|---|
| Pyrrole | $S_1$ | 96 |
| Pyrrole | $T_1$ | 66 |
| Dewar Pyrrole | $S_0$ | 73 |
| Diradical Intermediate | $T_1$ | 63 |
| | | |
| 2-Methylpyrrole | $S_1$ | 107 |
| 2-Methylpyrrole | $T_1$ | 68 |
| Dewar 2-Methylpyrrole | $S_0$ | 77 |
| Diradical Intermediate | $T_1$ | 88 |
| | | |
| 2-Trifluoromethylpyrrole | $S_1$ | 107 |
| 2-Trifluoromethylpyrrole | $T_1$ | 66 |
| Dewar 2-Trifluoromethylpyrrole | $S_0$ | 82 |
| Diradical Intermediate | $T_1$ | 94 |
| | | |
| 2-Cyanopyrrole | $S_1$ | 99 |
| 2-Cyanopyrrole | $T_1$ | 75 |
| Dewar 2-Cyanopyrrole | $S_0$ | 71 |
| | | |
| 2-Phenylpyrrole | $S_1$ | 104 |
| 2-Phenylpyrrole | $T_1$ | 56 |
| Dewar 2-Phenylpyrrole | $S_0$ | 74 |
| Diradical Intermediate | $T_1$ | 84 |

The irradiation of the thiophene in gas phase yields ethylene, allene, methylacetylene, carbon disulphide, and vinylacetylene. No Dewar thiophene or cyclopropene derivatives were isolated.[34] The irradiation in liquid phase gave the Dewar thiophene which can be trapped as a Diels-Alder adduct with furan.[35] The Dewar thiophene and cyclopropene-3-thiocarbaldehyde can be obtained by irradiation in argon matrices at 10 K.[10] Finally, the Dewar thiophene can be obtained by irradiation of tetrakis(trifuoromethyl)-thiophene.[36-40]

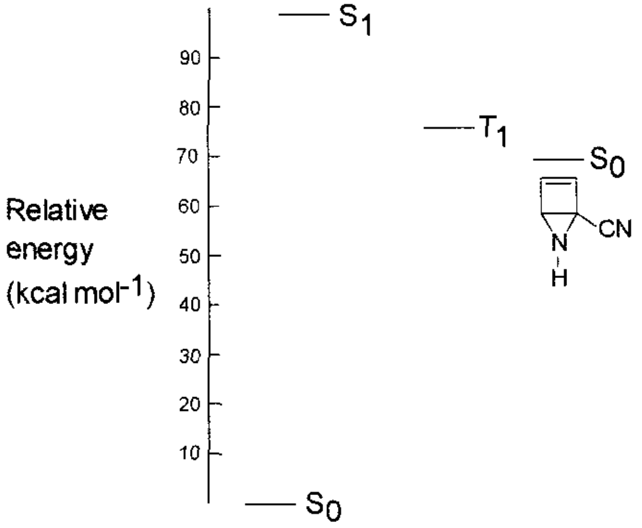
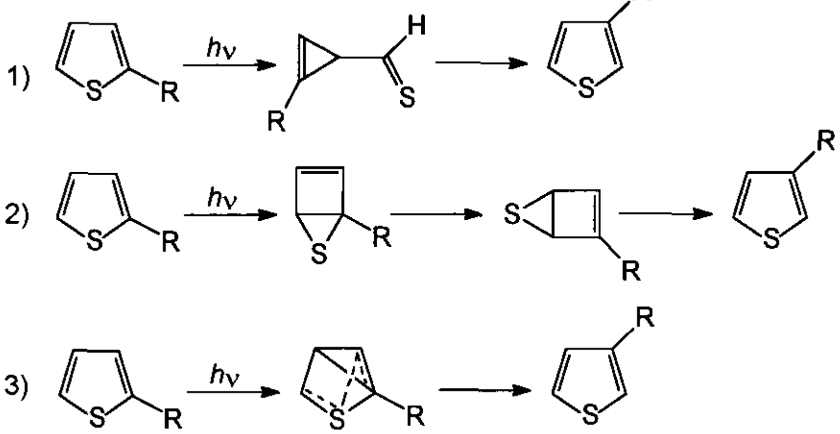


**Figure 3** - *Relative energies of the excited states of 2-cyanopyrrole and of some reactive intermediates*

The most interesting reaction in this field has been discovered by Wynberg in 1965. The irradiation of 2-substituted thiophenes gave the corresponding 3-substituted derivatives.[41] In the first experiments, only arylthiophenes were used as substrates.[41-46] The dithienyls gave this reaction efficiently while 2-(2-pyridyl)thiophene and 2-(2-furyl)thiophene did not give this reaction in a reasonable yield.[47,48] The alkylthiophenes reacted also but they showed a lower reactivity.[49] Carbonyl and olefinic substituents inhibit the rearrangement.[50-58] Several studies have been accomplished on the mechanism of this photoisomerisation showing that the reaction takes place from the singlet excited state of the molecule,[59] that the interchange between $C_2$ and $C_3$ occurs without the concomitant interchange between $C_4$ and $C_5$, and that the bonds between ring carbons and the substituents are not broken.[60] Three mechanisms have been proposed (Scheme 4) and Wynberg preferred the third. More recently several studies showed that the mechanism two is the most probable.[61,62] Furthermore, in the photoisomerisation reaction of cyanothiophene derivatives, a Dewar thiophene was isolated and it showed to be an intermediate in the isomerisation reactions.[63,64]

As reported for the furan derivatives, also thiophenes, when irradiated in the presence of an amine gave the corresponding pyrroles.[22,23] The authors proposed the formation of a cyclopropenyl intermediate, but, successively, a Dewar thiophene derivative, treated with aniline, gave the corresponding pyrrole showing that, probably, it is the true intermediate in this reaction.[24]

Scheme 4



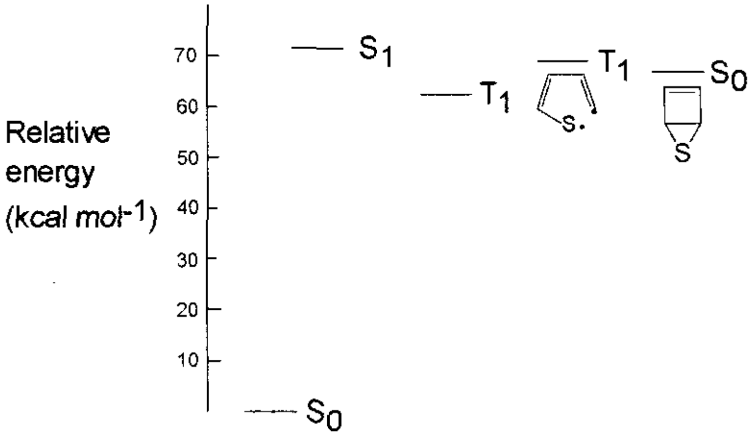


**Figure 4** - *Relative energies of the excited states of thiophene and of some reactive intermediates*

The direct irradiation of thiophene derivatives gives the isomeric product only. The cyclopropenyl derivatives were not observed. Also in this case our calculation results fit the experimental data (Table 3, Figure 4). In fact, the singlet excited state can evolve giving the Dewar thiophene (and, then, isomeric thiophenes) or the corresponding excited triplet state. This triplet state can not be converted into the biradical intermediate because this intermediate shows a higher energy than the triplet state, thus preventing the formation of the cyclopropenyl derivatives. The low reactivity towards photoisomerization of 2-methylthiophene can be explained considering the data reported in Table 3. In fact, in this case, Dewar thiophene can not be obtained, thus preventing the isomerization reaction. The same behavior was observed using 2-trifluoromethylthiophene as substrate.

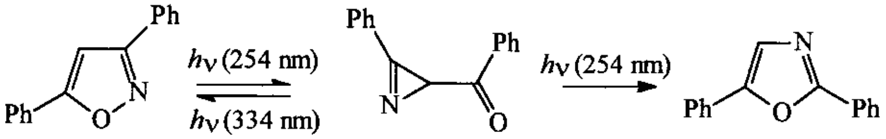
**Table 3** - *Relative energy of both some heterocyclic derivatives and reactive intermediates related to the photoisomerization of thiophene*

| Chemical Species | Electronic state | Relative energy [kcal $mol^{-1}$] |
|---|---|---|
| Thiophene | $S_1$ | 71 |
| Thiophene | $T_1$ | 62 |
| Dewar Thiophene | $S_0$ | 65 |
| Diradical Intermediate | $T_1$ | 69 |
| Zwitterionic Intermediate | $S_0$ | 114 |
| 2-Methylthiophene | $S_1$ | 89 |
| 2-Methylthiophene | $T_1$ | 59 |
| Dewar 2-Methylthiophene | $S_0$ | 68 |
| Diradical Intermediate | $T_1$ | 55 |
| 2-Trifluoromethylthiophene | $S_1$ | 94 |
| 2-Trifluoromethylthiophene | $T_1$ | 61 |
| Dewar 2-Trifluoromethylthiophene | $S_0$ | 72 |
| Diradical Intermediate | $T_1$ | 61 |
| 2-Cyanothiophene | $S_1$ | 88 |
| 2-Cyanothiophene | $T_1$ | 62 |
| Dewar 2-Cyanothiophene | $S_0$ | 71 |
| Diradical Intermediate | $T_1$ | 63 |
| 2-Phenylthiophene | $S_1$ | 86 |
| 2-Phenylthiophene | $T_1$ | 58 |
| Dewar 2-Phenylthiophene | $S_0$ | 68 |
| Diradical Intermediate | $T_1$ | 60 |

When 2-cyanothiophene is used in our calculation, the results fit the experimental results. In fact, in this case, the formation of the triplet state of 2-cyanothiophene can not allow the formation of the diradical intermediate allowing the formation of the Dewar thiophene. The same results were obtained with 2-phenylthiophene.

The photorearrangements of isoxazoles are well known reactions. It is known that 3,5-diphenylisoxazole, when irradiated at 254 nm gave 2,5-diphenyloxazole *via* the corresponding azirine (Scheme 5).

Scheme 5



The azirine can be isolated and the irradiation at 254 nm gave the oxazole while the irradiation at 334 nm gave the isoxazole.[65-70] It is noteworthy that in this case the formation of Dewar isoxazoles can not explain the obtained products.

In this case we have an evidence for the presence of the azirine as the intermediate of this reaction. The azirine is stable and it is the actual first photoproduct of the reaction, such us in the reaction of *t*-butylfuran derivatives.

The fact that it is able to interconvert photochemically and thermally into the oxazole could be an accident. Also in this case we can calculate the energy of the possible intermediate. In the case of 3,5-diphenylisoxazole, the cleavage of the O-N bond should be nearly concerted with N-C4 bond formation;[70] nevertheless, the formation of this intermediate can not be excluded. The results of our calculations are reported in Table 4 and Figure 5.

**Table 4** - *Relative energy of both some heterocyclic derivatives and reactive intermediates related to the photoisomerization of 3,5-diphenylisoxazole*

| Chemical Species | Electronic State | Energy (kcal mol$^{-1}$) |
|---|---|---|
| 3,5-Diphenylisoxazole | $S_1$ | 101 |
| 3,5-Diphenylisoxazole | $T_1$ | 53 |
| Dewar 3,5-Diphenylisoxazole | $S_0$ | 60 |
| Diradical Intermediate | $T_1$ | 20 |

In this case the excited singlet state can interconvert into a dewar or into the triplet state. The conversion into the triplet state is favoured allowing the formation of the diradical intermediate. The same results were obtained using as substrate 3-phenyl-5-methylisoxazole[71] and 3,5-dimethylisoxazole[72] (Table 5).

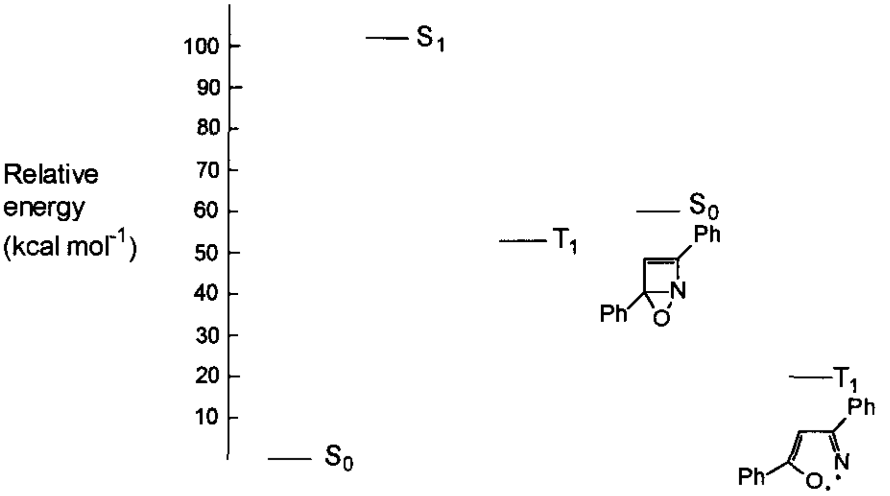


**Figure 5** - *Relative energies of the excited states of 3,5-diphenylisoxazole and of some reactive intermediates*

**Table 5** - *Relative energy of both some heterocyclic derivatives and reactive intermediates related to the photoisomerization of isoxazole*

| Chemical Species | Electronic State | Energy (kcal mol$^{-1}$) |
|---|---|---|
| 3-Phenyl-5-methylisoxazole | $S_1$ | 107 |
| 3-Phenyl-5-methylisoxazole | $T_1$ | 57 |
| Dewar 3-Phenyl-5-methylisoxazole | $S_0$ | 60 |
| Diradical Intermediate | $T_1$ | 21 |
| | | |
| 3,5-Dimethylisoxazole | $S_1$ | 118 |
| 3,5-Dimethylisoxazole | $T_1$ | 57 |
| Dewar 3,5-Dimethylisoxazole | $S_0$ | 66 |
| Diradical Intermediate | $T_1$ | 27 |
| | | |
| 3,5-Diphenyl-4-benzoylisoxazole | $S_1$ | 106 |
| 3,5-Diphenyl-4-benzoylisoxazole | $T_1$ | 52 |
| Dewar 3,5-Diphenyl-4-benzoylisoxazole | $S_0$ | 56 |
| Diradical Intermediate | $T_1$ | 79 |

The only problem to be solved in our hypothesis is that the reaction should occur through the triplet state of the molecules involved, as reported in the furan. On the contrary, both some experimental data[68] and theoretical calculations[70] are in agreement with a singlet state mechanism. The use of sensitizers does not solve the question, because they were used in order to invoke both singlet[68] and triplet sensitization.[67] On the contrary, the evidence that 3,5-diphenyl-4-benzoylisoxazole, a compound with a high intersystem crossing quantum yield, does not react, could be a proof for a singlet state process.

We tested these compounds and the results are reported in Table 5. We can see that the triplet state can be formed but it can not evolve to the high energy triplet diradical intermediate. In conclusion, we think that there is no evidence for a singlet state process in this isomerization.

Scheme 6

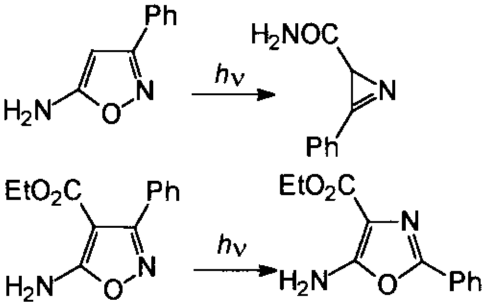


**Table 6** – *Relative energy of both some heterocyclic derivatives and reactive intermediates related to the photoisomerization of 5-aminoisoxazoles*

| Chemical Species | Electronic State | Energy (kcal mol$^{-1}$) |
|---|---|---|
| 3-Phenyl-5-aminoisoxazole | $S_1$ | 100 |
| 3-Phenyl-5-aminoisoxazole | $T_1$ | 45 |
| Dewar 3-Phenyl-5-aminolisoxazole | $S_0$ | 59 |
| Diradical Intermediate | $T_1$ | 14 |
| | | |
| 3-Phenyl-4-carboethoxy-5-aminoisoxazole | $S_1$ | 93 |
| 3-Phenyl-4-carboethoxy-5-aminoisoxazole | $T_1$ | 57 |
| Dewar 3-Phenyl-4-carboethoxy-5-aminoisoxazole | $S_0$ | 58 |
| Diradical Intermediate | $T_1$ | 17 |

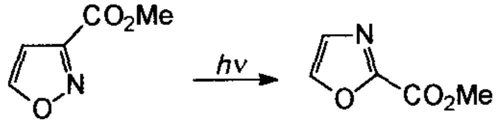
In the photochemical isomerization of isoxazoles some data were obtained from amino derivatives. In a work 5-aminoisoxazole derivatives gave the corresponding azirine (Scheme 6),[73] while, when a 4-

carboethoxy substituted derivative was used, the azirine was not isolated and the oxazole was obtained as the only product (Scheme 6).[74]

The results of our calculation are in agreement with the formation the azirine as intermediate (Table 6). In all the cases the formation of excited triplet state is favoured and this intermediate can evolve to the formation of the azirine *via* the diradical intermediate.

Then I tested some other cases where the azirine intermediates were isolated and some other where this type of intermediates were not detected. The irradiation of 3-carbomethoxyisoxazole gave the corresponding oxazole in very low yields (5-8%) without the isolation of the corresponding azirine (Scheme 7).[75]

Scheme 7



The results of the semiempirical calculations for this reaction are reported in Table 7.

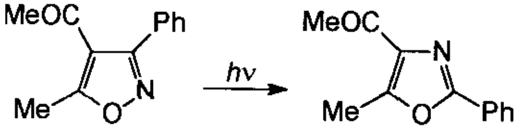
**Table 7** – *Relative energy of both some heterocyclic derivatives and reactive intermediates related to the photoisomerization of 3-carbomethoxyisoxazole*

| Chemical Species | Electronic State | Energy (kcal mol$^{-1}$) |
|---|---|---|
| 3-Carbomethoxyisoxazole | $S_1$ | 117 |
| 3-Carbomethoxyisoxazole | $T_1$ | 57 |
| Dewar 3-Carbomethoxyisoxazole | $S_0$ | 63 |
| Diradical Intermediate | $T_1$ | 22 |
| 2-Carbomethoxyazirine-3-carbaldeide | $S_0$ | 41 |

Also in this case the results of our calculations show that the energy of the triplet state allows the formation of the diradical intermediate and, then, of the azirine. However, the low yields of the conversion can be explained considering that the transformation of the diradical intermediate into the azirine is and endothermic reaction.

In the case of 3-phenyl-4-acetyl-5-methylisoxazole the irradiation of this substrate led to the isolation of isomeric oxazole (Scheme 8).[76]

Scheme 8



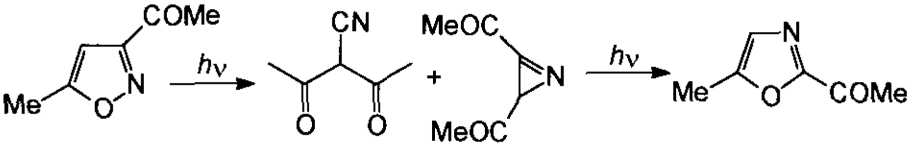
The results of calculations are reported in Table 8. Also in this case the reaction involves the formation of the diradical intermediate starting from the triplet state, in agreement with the presence of the azirine derivative in the reaction mixture.

**Table 8** – *Relative energy of both some heterocyclic derivatives and reactive intermediates related to the photoisomerization of 3-phenyl-4-acetyl-5-methylisoxazole*

| Chemical Species | Electronic State | Energy (kcal mol$^{-1}$) |
|---|---|---|
| 3-Phenyl-4-acetyl-5-methylisoxazole | $S_1$ | 110 |
| 3-Phenyl-4-acetyl-5-methylisoxazole | $T_1$ | 56 |
| Dewar 3-Phenyl-4-acetyl-5-methylisoxazole | $S_0$ | 60 |
| Diradical Intermediate | $T_1$ | 44 |

It is noteworthy that, by using a very similar substrate, 3-acetyl-5-methylisoxazole, the formation of the azirine was detected (Scheme 9).[77]

Scheme 9



The results of our calculations (Table 9) showed that the triplet state allows the formation of the diradical intermediate and, then, of the azirine.

Finally, the photoisomerization of 3-hydroxyisoxazoles gave the corresponding 2-oxazolones without the isolation the of the azirine (Scheme 10).[78] Also in this case calculations are in agreement with the experimental results (Table 10).

In the pyrazole photoisomerization three mechanisms were be invoked. The ring contraction–ring expansion mechanism was used to justify the photoisomerization of 1-methylpyrazole to 1-methylimidazole (Scheme 11).[79]

**Table 9** – *Relative energy of both some heterocyclic derivatives and reactive intermediates related to the photoisomerization of 3-acetyl-5-methylisoxazole*

| Chemical Species | Electronic State | Energy (kcal mol$^{-1}$) |
|---|---|---|
| 3-Acetyl-5-methylisoxazole | $S_1$ | 78 |
| 3-Acetyl-5-methylisoxazole | $T_1$ | 49 |
| Dewar 3-Acetyl-5-methylisoxazole | $S_0$ | 62 |
| Diradical Intermediate | $T_1$ | 23 |

Scheme 10

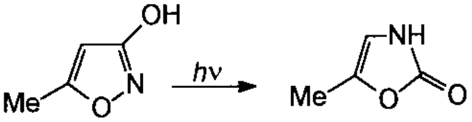


**Table 10** - *Relative energy of both some heterocyclic derivatives and reactive intermediates related to the photoisomerization of 3-hydroxy-5-methylisoxazole*

| Chemical Species | Electronic State | Energy (kcal mol$^{-1}$) |
|---|---|---|
| 3-Hydroxy-5-methylisoxazole | $S_1$ | 101 |
| 3-Hydroxy-5-methylisoxazole | $T_1$ | 62 |
| Dewar 3-Hydroxy-5-methylisoxazole | $S_0$ | 68 |
| Diradical Intermediate | $T_1$ | 20 |

Furthermore, the formation of Dewar pyrazole was invoked in the photoisomerization of 1,3,5-trimethylpyrazole or in the isomerization of cyanopyrazoles (Scheme 11).[80-82] Finally, a zwitterionic intermediate was proposed.[83]

The results of our calculation are reported in Table 11. We can exclude the formation of the zwitterionic intermediate, because it could be formed, but it should evolve *via* the formation of the Dewar isomer, at a higher energy. Between ring-contraction ring-expansion mechanism and the mechanism involving the formation of the Dewar pyrazole, we can see that the energy of triplet state is quite lower than that of the Dewar pyrazole (Figure 6). Probably, the reaction can be explained, as in isoxazole chemistry, assuming the formation of the azirine intermediate.

Scheme 11

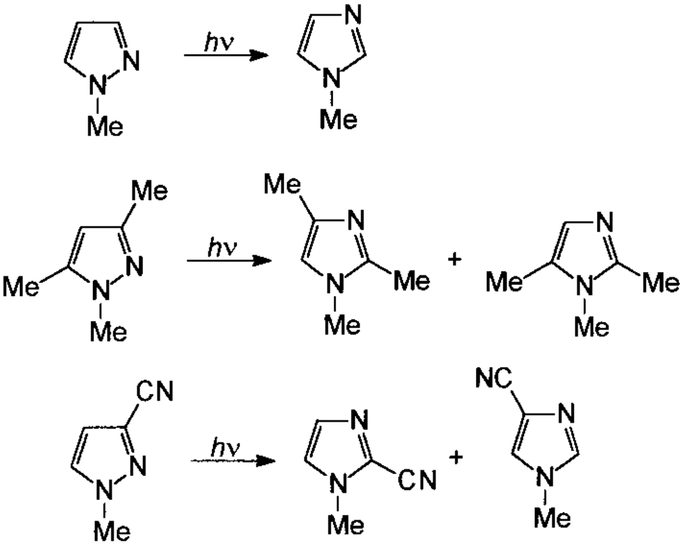


**Table 11** - *Relative energy of both some heterocyclic derivatives and reactive intermediates related to the photoisomerization of pyrazoles*

| Chemical Species | Electronic State | Energy (kcal $mol^{-1}$) |
|---|---|---|
| 1-Methylpyrazole | $S_1$ | 112 |
| 1-Methylpyrazole | $T_1$ | 63 |
| Dewar 1-Methylpyrazole | $S_0$ | 75 |
| Diradical Intermediate | $T_1$ | 58 |
| Zwitterionic Intermediate | $S_0$ | 61 |
| | | |
| 1,3,5-Trimethylpyrazole | $S_1$ | 106 |
| 1,3,5-Trimethylpyrazole | $T_1$ | 51 |
| Dewar 1,3,5-Trimethylpyrazole | $S_0$ | 73 |
| Diradical Intermediate | $T_1$ | 60 |
| | | |
| 1-Methyl-3-cyanopyrazole | $S_1$ | 112 |
| 1-Methyl-3-cyanopyrazole | $T_1$ | 56 |
| Dewar 1-Methyl-3-cyanopyrazole | $S_0$ | 77 |
| Diradical Intermediate | $T_1$ | 61 |

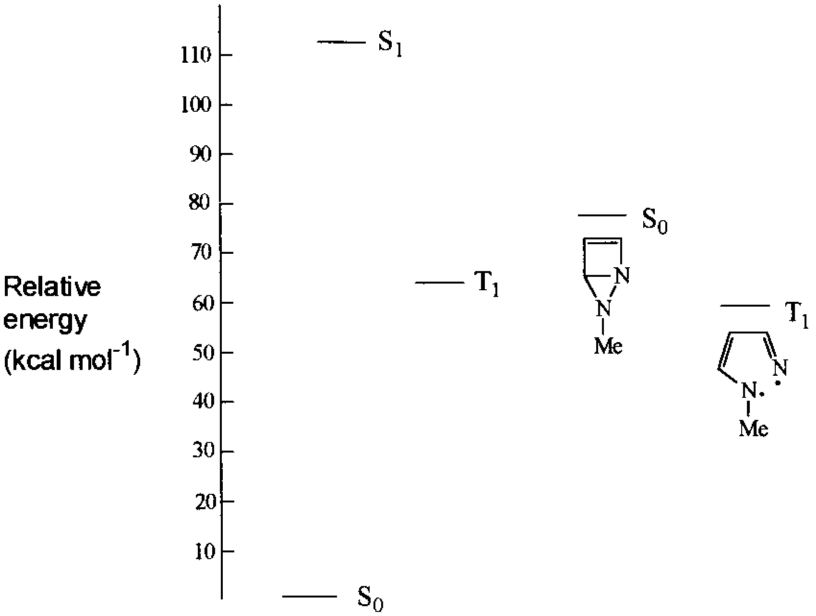


**Figure 6** - *Relative energies of the excited states of 1-methylpyrazole and of some reactive intermediates*

In the case of more substituted pyrazoles, the triplet state can not be converted into the diradical intermediate at higher energy, and the isomerization reaction can occur *via* the Dewar intermediate (Figure 7).

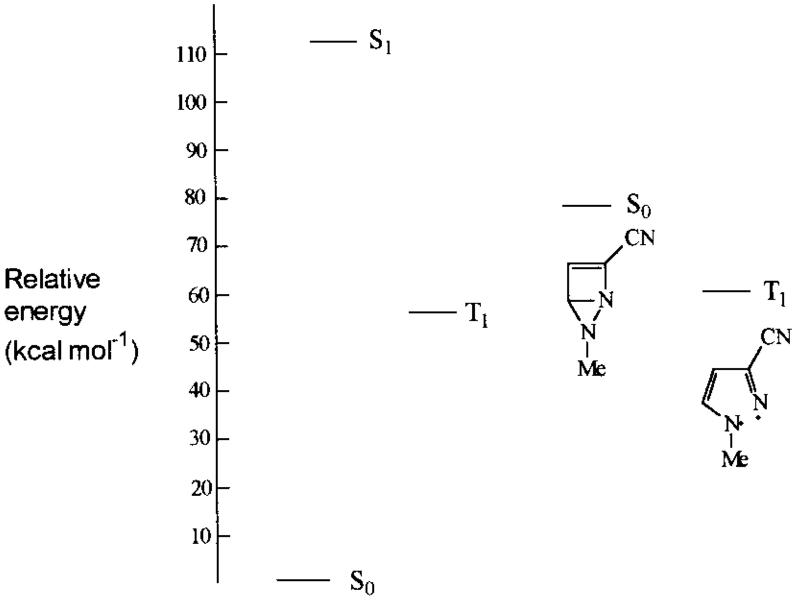
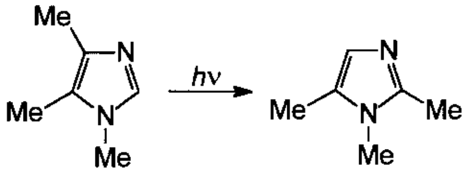


**Figure 7** - *Relative energies of the excited states of 1-methyl-3-cyanopyrazole and of some reactive intermediates*

Finally, Dewar isomers are invoked to justify the photochemical behaviour of imidazoles (Scheme 12).[80,81]

Scheme 12



In the case of 1,4,5-trimethylimidazole the results of calculations are reported in Table 12. The only pathway admitted for the isomerization if the formation of the Dewar isomer through the singlet state. The formation of the triplet state is energetically favoured but it can not evolve to the diradical intermediate at higher energy.

**Table 12**– *Relative energy of both some heterocyclic derivatives and reactive intermediates related to the photoisomerization of 1,4,5-trimethylimidazole*

| Chemical Species | Electronic State | Energy (kcal mol$^{-1}$) |
|---|---|---|
| 1,4,5-Trimethylimidazole | $S_1$ | 100 |
| 1,4,5-Trimethylimidazole | $T_1$ | 52 |
| Dewar 1,4.5-Trimethylimidazole | $S_0$ | 76 |
| Diradical Intermediate | $T_1$ | 73 |

In conclusion, we can see that the complex reactivity observed in the photochemical behaviour of pentaatomic aromatic heterocycles can be easily explained in terms of the relative energies of the corresponding reactive intermediate. We think that our approach represents only the first attempt to rationalise the photochemistry of these compounds and that work must be done in order to improve the method and its confidence. Nevertheless, our first results allow us to discuss the photochemistry of π excessive heterocycles in satisfactory manner.

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