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Photoisomerization of fluorinated 1,3-dimethyl-5-propenyl uracils

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ABSTRACT

We investigated the photo-induced *cis*/*trans* isomerization of double bonds in fluorinated derivatives of 1,3-dimethyl-5-propenyl uracils. When 1,3-dimethyl-5-(*E*-1,2,3,3,3-pentafluoropropenyl)uracil was irradiated by light $\lambda > 300$ nm, we obtained the photostationary state involving equilibration with 1,3-dimethyl-5-(*Z*-1,2,3,3,3-pentafluoropropenyl)uracil where the more sterically congested isomer *Z* was the major product (*E*:*Z* = 1:1.5). Irradiation of *Z* isomer as the starting material also led to the identical photostationary state. In the case of 1,3-dimethyl-5-(1,3,3,3-tetrafluoropropenyl)uracil the more sterically congested isomer *E* was even more abundant (*Z*:*E* = 1:7.5). The results of DFT calculations suggest that photo-induced *cis*/*trans* isomerization of these compounds can run through the formation of allyl-methylene biradical species, which are the transition states produced during photoexcitation. Preference of the formation of more sterically hindered isomers in photostationary state one can rationalize on the basis of the difference in oscillator strength and the role of equilibration between conformers *s-cis*/*s-trans*.

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1. Introduction

One of the classic problems of photochemistry is the photoisomerization of compounds changing the relative position of substituents attached to the double bond, which has been a subject of intense research for long time [1]. The *cis–trans* photoisomerization of dienes provides a prototypical system for studying the coupling between electronic excitation and atomic motion [2] so as connected with the idea of nano-motors [3] it is of considerable interest in virtually all such studies. It is generally accepted that the photochemical *cis–trans* isomerization of arylethenes usually takes place in the excited state through the rotation around the C=C double bond [4].

Recently, we studied extensively synthetic methodology to access 5-fluorinated alkenyl uracils as well as to determine their structural properties [5–10]. We have reported photochemical isomerization of such derivatives where the more sterically hindered isomers were the major products in the observed photostationary states. The aim of this work is to explain the observed stereoselectivity of the studied reactions. On the basis of the DFT calculations we propose the reaction mechanism rationalizing the observed product yields based on the oscillator strengths of the substrates. We have shown that the preference of the formation of the more sterically hindered isomers may stem from the difference in oscillator strengths of various *cis*/*trans* stereoisomers and the role of the equilibration processes between *s-cis* and *s-trans* conformers.

2. Results and discussion

Recently we have reported our observations dealing with isomerization of fluorinated derivatives of 1,3-dimethyl-5-propenyl uracils [5], assuming electrocyclic mechanism of such transformations. The torquoselectivity concept has been considered as a dominant factor governing the thermal ring opening process [11–13]. However at this stage of research we could not determine the role of radical concept as a potential competitive mechanisms.

As had been shown previously [11] the thermal ring opening of perfluoro-3-methylcyclobutene leads exclusively to the formation of Z-isomer (Scheme 1).

The observed $\Delta H^{\neq}$ difference of transition states for outward vs inward rotation of CF_3 is about 13 kcal mol^{-1}, what practically excludes the presence of the E isomer in the reaction mixture. In our case, photoisomerization of 1,3-dimethyl-5-(*Z*-1,2,3,3,3-pentafluoropropenyl) uracil led to the photostationary state where the more sterically congested isomer *Z* was the major product (*E*:*Z* = 1:1.5). Similarly, in the case of 1,3-dimethyl-5-(1,3,3,3-tetrafluoropropenyl)uracil the more sterically congested isomer *E* was even more abundant (*Z*:*E* = 1:7.5). These data, although showing the preference of the formation of more sterically congested isomer (what is in a good agreement with torquoselectivity concept) does not clearly explain expected relatively large $\Delta H^{\neq} \approx 10$ kcal mol^{-1} difference of transition states

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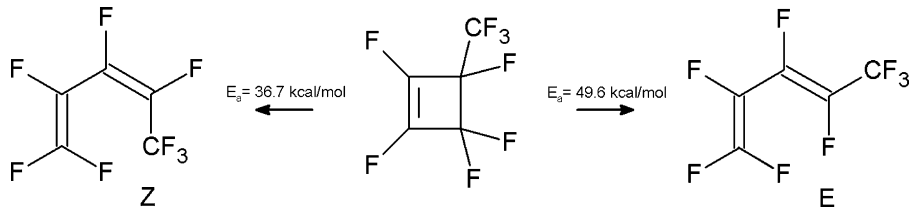
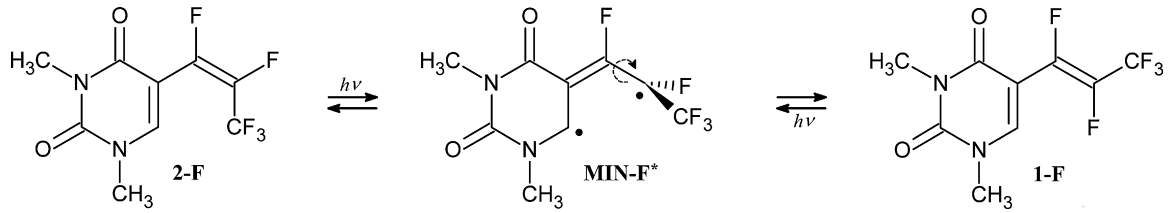
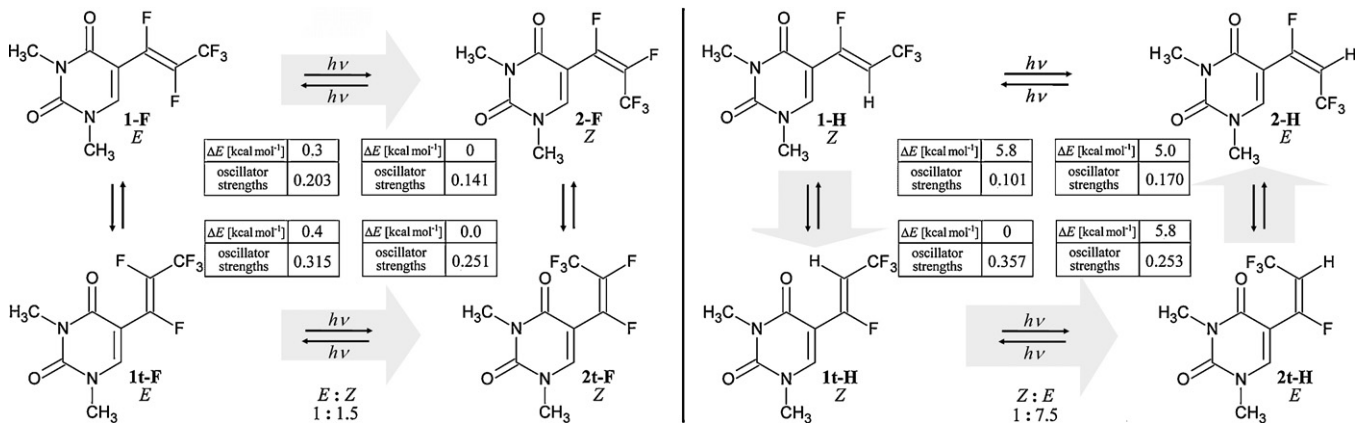


Scheme 1. Dramatic kinetic differences for the inward vs outward rotation of a perfluoro-3-methylcyclobutene.



Scheme 2. Suggested mechanisms of radical isomerization of *s-cis*-1,3-dimethyl-5-(1,2,3,3,3-pentafluoropropenyl)uracil.



Scheme 3. Photochemical isomerization of 1,3-dimethyl-5-(1,2,3,3,3-pentafluoropropenyl)uracil (left) and 1,3-dimethyl-5-(1,3,3,3-tetrafluoropropenyl)uracil (right). Comparison of the calculated thermodynamic stabilities and oscillator strengths (tables).

for isomerization processes. It can be explained by the fact that the mechanism of electocyclization is different than in case of perfluoro-3-methylcyclobutene (because in our case the only possible direction of conrotation to open the cyclobutene ring is governed by the rotation of N-1 atom of uracil, which must rotate outward to re-create flat structure of uracil ring) or we are dealing with another, competitive process. The DFT calculation could provide additional insights on radical mechanism showing that the energy of the allylmethylene biradical (transition state between isomers *E* and *Z*) corresponds to the local minimum on the S_1 potential energy surface. The presented results showed how much the radical process could be competitive to the proposed electrocyclic mechanism.

In this article the photochemical properties of fluorinated derivatives of 1,3-dimethyl-5-propenyl uracils were studied assuming a radical mechanism [14] of the observed isomerization (Scheme 2), competitive to the electrocyclic mechanism which we recently proposed [5]. Still we tried to explain observed transformation overpassing electrocyclization.

It should be noted that the both isomers exist in two conformational forms (*s-cis* and *s-trans*) [15]. The *s-cis* conformers (**1-F**, **2-F**) are in the equilibrium with the *s-trans* conformers (**1t-F**, **2t-F**). Results of DFT calculations for 1,3-dimethyl-5-(1,2,3,3,3-pentafluoropropenyl)uracil do not show significant differences in thermodynamic stabilities between them. The calculated energy differences are less than 0.6 kcal mol^{-1} (Scheme 3 and Table 1).

In the case of 1,3-dimethyl-5-(1,3,3,3-tetrafluoropropenyl) uracil (**1-H**, **2-H**, **1t-H** or **2t-H**), the calculated energy differences are larger up to 5.8 kcal mol^{-1} (Table 3). The isomer *Z* is present almost exclusively as a conformer *s-trans* (**1t-H**), which displays the conformation not favorable for pericyclic reaction [5]. However such effect will be less significant in aqueous solution.

The irradiation of a water solution of 1,3-dimethyl-5-(*E*-1,2,3,3,3-pentafluoropropenyl)uracil **1-F** (**1t-F**) led to a photostationary state being equilibrium with 1,3-dimethyl-5-(*Z*-1,2,3,3,3-pentafluoropropenyl)uracil **2-F** (**2t-F**), where the more sterically congested isomer *Z* was the major product (HPLC ratio *E*:*Z* = 1:1.5) [8]. Irradiation of *Z* isomer **2-F** (**2t-F**) as the starting material also led to the identical photostationary state.

Table 1
Calculated energies and oscillator strengths for 1,3-dimethyl-5-(1,2,3,3,3-pentafluoropropenyl)uracil. Relative energy values obtained with reference to the energy of **2-F**.

S_0		ΔE [kcal mol^{-1}]	Vertical excitation [cm^{-1}]	Oscillator strengths
s-cis	**1-F**	0.3	35,954	0.203
	MIN-F	71.6	3276	0.005
	2-F	0.0	36,903	0.141
s-trans	**1t-F**	0.4	35,844	0.315
	MINt-F	71.1	3250	0.005
	2t-F	0.0	35,870	0.251

Table 2
Calculated relative energies for the first excited state (S_1). Relative energy values obtained with reference to the energy of **2-F**. Structures **1-F** and **2-F** (**1t-F** and **2t-F**) are unstable in the excited state. Their optimization at CIS/6-31G(d) level leads to the structure **MIN-F** (**MINt-F**).

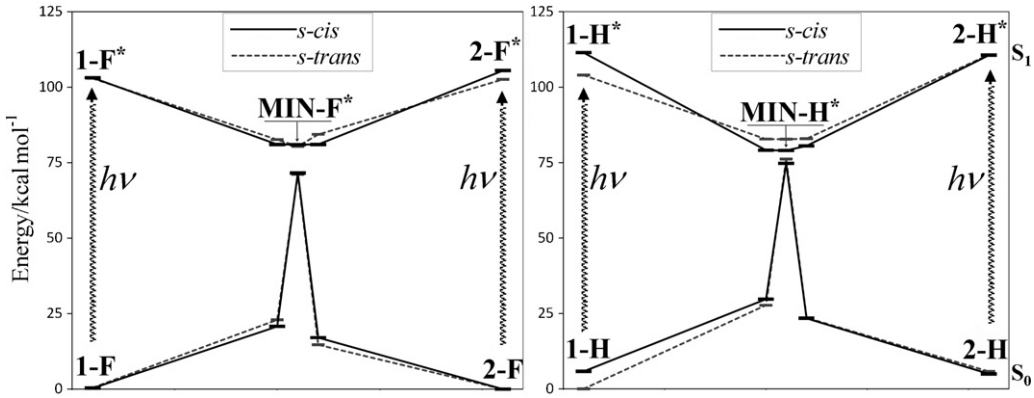
S_1		ΔE [kcal mol^{-1}]
s-cis	**1-F***	103.1
	MIN-F*	80.9
	2-F*	105.5
s-trans	**1t-F***	102.9
	MINt-F*	80.4
	2t-F*	102.6

Table 3
Calculated energies and oscillator strengths for 1,3-dimethyl-5-(1,3,3,3-tetrafluoropropenyl)uracil. Relative energy values obtained with reference to the energy of **1t-H**.

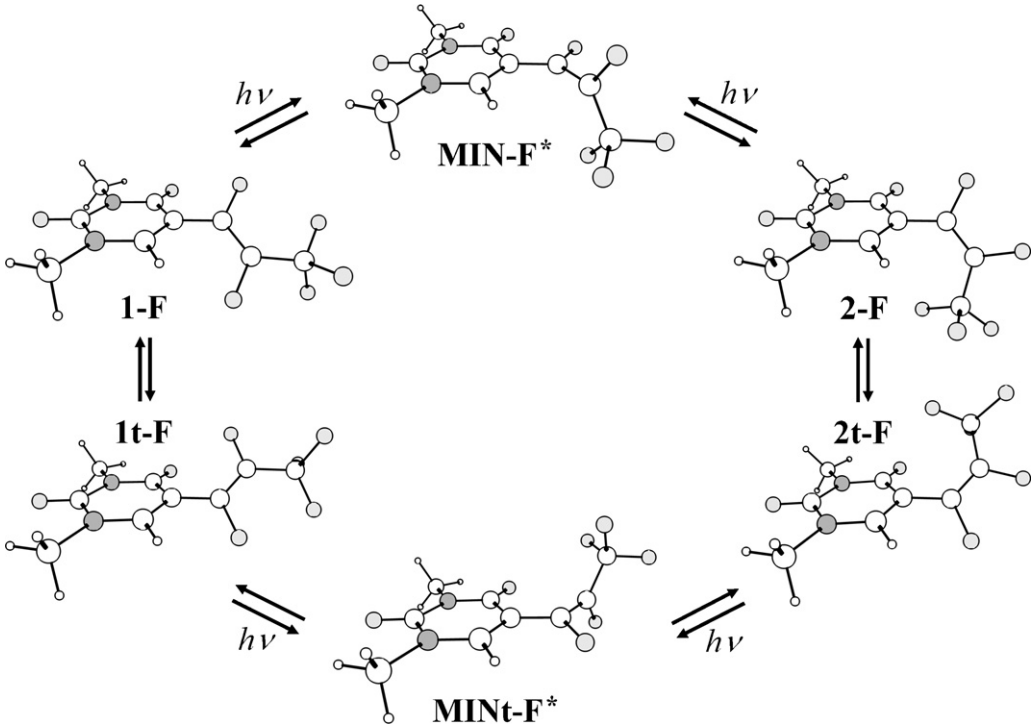
S_0		ΔE [kcal mol^{-1}]	Vertical excitation [cm^{-1}]	Oscillator strengths
s-cis	**1-H**	5.8	36,952	0.101
	MIN-H	74.7	1497	0.001
	2-H	5.0	36,960	0.170
s-trans	**1t-H**	0.0	36,378	0.357
	MINt-H	76.2	2302	0.002
	2t-H	5.8	36,707	0.253

In the case of 1,3-dimethyl-5-(1,3,3,3-tetrafluoropropenyl) uracil (**1-H**, **2-H**, **1t-H** or **2t-H**) the more sterically congested isomer *E* is even more abundant (HPLC ratio *Z*:*E* = 1:7.5).

The DFT calculation could provide additional insights into radical mechanism showing that the S_1 energy minimum **MIN-F**(**H**) (or **MINt-F**(**H**)) corresponds to the transition state between **1-F**(**H**) and **2-F**(**H**) (or **1t-F**(**H**) and **2t-F**(**H**)) providing the channel mediating radiationless deactivation and photochemical reaction (Scheme 4 and Tables 2 and 4). However, relatively low computational level prohibits detailed discussion on the actual nature of this surface



Scheme 4. Energy diagram for radical isomerization. Potential energy hypersurfaces of the ground (S_0) and first excited states (S_1). Values obtained at the TD-DFT level. Potential energy hypersurfaces for the structures **1-F**(**H**), **2-F**(**H**) and **MIN-F**(**H**) are shown by solid line. Potential energy hypersurfaces for the structures **1t-F**(**H**), **2t-F**(**H**) and **MINt-F**(**H**) are shown by dash line.



Scheme 5. Photochemical isomerization of 1,3-dimethyl-5-(1,2,3,3,3-pentafluoropropenyl)uracil. Structures optimized at the DFT level.

Table 4
Calculated relative energies for the first excited state (S_1). Relative energy values obtained with reference to the energy of **1t-H**. Structures **1-H** and **2-H** (**1t-H** and **2t-H**) are unstable in the excited state. Their optimization at CIS/6-31G(d) level leads to the structure **MIN-H** (**MINt-H**).

S_1		ΔE [kcal mol^{-1}]
s-cis	**1-H***	111.5
	MIN-H*	79.0
	2-H*	110.6
s-trans	**1t-H***	104.0
	MINt-H*	82.8
	2t-H*	110.8

* Excited state.

crossing process (conical intersection vs avoided crossing). Preference of the formation of more sterically hindered isomer (**2-F**, **2t-F**) in photostationary state one can rationalize on the basis of the difference in oscillator strengths. Less sterically hindered isomers (**1-F**, **1t-F**), display larger probability to be shifted to the excited state (Scheme 3 and Table 1). Therefore, less sterically hindered isomers (**1-F**, **1t-F**) should isomerize faster than the more sterically congested ones. This would be a "kinetic factor" determining the composition of the reaction mixture in photostationary state (Scheme 5).

In the case of 1,3-dimetylo-5-(1,3,3,3-tetrafluoropropenyl) uracil significant preference of more congested isomer *E* (more sterically hindered **2-H** and **2t-H**) is supported by the fact that isomer *Z* is present almost exclusively as a conformer *s-trans* (**1t-H**), which could be easily excited (oscillator strength 0.357); thus it isomerizes fast yielding compound **2t-H**. Contrary to that, compound **2t-H** is transformed to more stable conformer **2-H**, which excitation ability is characterized by much lower oscillator strength (oscillator strength 0.170) (Scheme 3 and Table 3).

3. Conclusions

The results of our calculations suggest that photo-induced *cis*/*trans* isomerization of fluorinated derivatives of 1,3-dimethyl-5-propenyl uracils can run through the formation of allylmethylene biradical species, which are the transition states produced during photoexcitation. Despite the possibility of electrocyclic mechanism as competitive, we were able to explain observed photostationary states assuming radical mechanism of the discussed isomerization using DFT calculations with taking into consideration the role of equilibration between conformers *s-cis*/*s-trans* as well as a differences in oscillator strengths. However we did not determined the role of proposed radical mechanism in competition with electrocyclization.

4. Quantum mechanical calculations

Information on the electronic structure and geometry of the compounds was obtained with the use of quantum-chemical density-functional theory (DFT) calculations. The calculations were performed using the B3LYP functional [16] in conjunction with a split-valence polarized basis set 6-31G(d) for the C, H atoms and the 6-31G + (2df) for the F, N, O atoms as more flexible basis set is generally recommended for strongly electronegative atoms [17]. Full optimization of the geometrical parameters of the molecules produced a ground-state potential energy minima. A transition state connecting these minima was also found, and IRC (intrinsic reaction coordinate) calculations followed by full geometry optimization (pseudo-IRC) verified that the obtained transition state indeed connects these energy minima. The vertical excitation energies and oscillator strengths were computed using time dependent (TD) approach as implemented in the Gaussian 03 program [18]. Predicted lowest energy singlet–singlet transitions of the compounds, S_0 f S_i, were calculated for the ground-state geometry. The excitation energies computed using TD-B3LYP level of theory are estimated to be accurate within 2000–3000 cm^{-1}, usually requiring a shift toward the red to reproduce experimental spectra. To gain insight into geometry relaxation of the first excited state, crude calculations at CIS/6-31G(d) level were carried out. A local minimum was located for the first excited state during geometry optimization with CIS method (configuration interaction with single excitations), whose geometry closely resembled the S_0 transition state.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jphotochem.2012.01.010.

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