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Benzylidene–oxazolones as photoswitches: photochemistry and theoretical calculations

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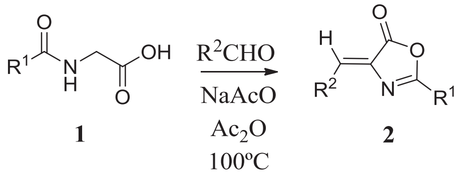
ABSTRACT

The photophysics and photochemistry of a family of compounds proposed as efficient molecular photoswitches is presented. The effect of different light sources, substituents and solvents in the photostationary state has been explored. A detailed mechanistic description is also discussed.

1. Introduction

The synthesis and application of molecular devices has attracted much attention in the last years.[1–3] Among the different types of molecular devices, the use of switches to modify the properties of complex systems has been extensively studied.[4] Molecular switches could be classified based on the stimulus used to induce the nuclear motion (light, chemical or electrochemical energy) or the reaction that take place (ring-closing/opening or bond isomerization in most cases). For the many different families of molecular devices, light-activated switches that perform a C=C photosiomerization[5] have been the most used. Azobenzenes,[6] overcrowded alkenes[7] and retinal-based switches[8] have been applied in many different technological applications and comprehensively studied from both the experimental and the computational point of view. However, the generalization of the photoswitch concept and the development of new applications will require the design, synthesis and study of alternatives to these three main types of compounds.

We have recently reported[9] a new family of switches inspired in the green fluorescent protein (GFP). GFP was obtained from Aequorea victoria jellyfish and its optical properties are determined by a photoexcitable green-light emitter chromophore.[10] When the GFP chromophore is outside the protein cavity it may also undergo *Z*/*E* photoisomerization.[11–13] Chemically related to the GFP chromophore, benzylidene–oxazolones (Scheme 1) have been used as precursor for the synthesis of GFP derivatives and their photoisomerization is already known.[14,15] However, little is known about their photophysical and photochemical properties.[16–18] The application of benzylidene–oxazolones for different uses will first require a careful study of the efficiency on the light use and a detailed knowledge of the molecular processes that affect the photoisomerization. Thus, we present here our recent results on the photophysics and photochemistry of benzylidene–oxazolones, especially in those aspects relevant for an efficient photoisomerization including the effect of different irradiation wavelengths and the fluorescence deactivation. Besides, a complete theoretical study would allow for the description at the molecular



R^1= Me, Ar
R^2=Ar

Scheme 1.

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level of the photoisomerization, the comparison with the well-known GFP chromophore and the design of modifications for new switches.

2. Results and discussion

2.1. Wavelength dependence

Benzylidene–oxazolones **2** are good candidates for efficient photoswitches as they are easily synthesized, feature good photoisomerization quantum yields and are thermally stable.[9] We have previously shown that the irradiation wavelength affects the photostationary state (PSS) in this type of compounds. Also, in our preliminary tests, we detected the presence of side-products in the reaction crude in some cases when using a medium-pressure Hg lamp as the standard light source. These competing reactions took place when an electron-withdrawing group was placed in the phenyl of R^2. Thus, we aimed for the use of light of different wavelengths in order to diminish the contribution of side reactions. Therefore, we irradiated at 360 nm a 2.2×10^{-3} M solution of compound **2a** (R^1=Me, R^2=*p*-BrPh) in $CDCl_3$ in a quartz cuvette with a monochromator, and followed the photoisomerization process by ^{1}H NMR, until the photostationary state was reached. The value for the isomers ratio at the PSS was 54% (*Z*)/46% (*E*), which greatly differed from the result obtained when irradiating in a 125-W medium-pressure Hg lamp and a Pyrex filter [85% (*Z*)/15% (*E*)] used in our previous reaction conditions.[9] The different absorption of the *E* and *Z* isomers in these diverse irradiation conditions explains the experimental outcome. In addition, there were no signals in the ^{1}H NMR spectra of side reactions so the photoisomerization process was taking place exclusively. This implies a considerable improvement over the previous irradiation conditions used in the case of compounds yielding partial decomposition. Therefore, we decided to repeat the irradiation process of different compounds using a light source with emission wavelength centred at 350 nm to compare the two irradiation methods. For this purpose, we prepared 0.01 M solutions of different photoswitches **2** in acetonitrile, placed them in Pyrex test tubes in a carrousel in a photoreactor, and irradiated them using lamps with emission wavelength centred at 350 nm (14 lamps×8-W/lamp) until the PSS was reached. Depending on the compound, the irradiated mixture took from 1 to 2 h to reach the PSS and the reaction was followed by ^{1}H NMR. The results are shown in Table 1.

Table 1
Photostationary state for molecular photoswitches **2** irradiated at 350 nm

Entry	R^1	R^2	Compound	Ratio at PSS	
				% *Z*	% *E*
1	Me	*p*-BrPh	**2a**	54	46
2	Me	*p*-Tol	**2b**	75	25
3	Me	*p*-MeOPh	**2c**	42	58
4	Me	*o*-MeOPh	**2d**	41	59
5	Me	*p*-NO_2Ph	**2e**	76	24
6	Me	*p*-CNPh	**2f**	62	38
7	Me	Ph	**2g**	70	30
8	Ph	*p*-BrPh	**2h**	36	64
9	Me	*o*-Br	**2i**	40	60
10	Ph	*p*-NO_2Ph	**2j**	80	20
11	Ph	*p*-CN	**2k**	55	45

The following trends can be inferred from the results in Table 1. If the substituent of the phenyl group in R^2 is an electron-donor group, such as methoxy (switch **2c**, entry 3), the percentage of *E* isomer at the PSS increases with respect to **2b**. The effect is the same whether the substituent is in *para* or *ortho* (switch **2d**, entry 4) position. However, when having an electron-withdrawing group, such as nitro (switch **2e**, entry 5), there is no significant change in the isomers ratio compared with **2b**. Alternatively, if there is a bromine (switch **2a**, entry 1), the percentage of *E* isomer at the PSS also increases. Moreover, if substituent R^1 is modified from Me (switch **2a**, entry 1) to Ph (switch **2h**, entry 8) and R^2 remains the same, the percentage of *E* isomer at the PSS significantly increases. Therefore, the value of the isomers ratio at the PSS can vary depending on the substituents R^1 and R^2, which represent a great advantage. Even more important is that all of the values for the isomers ratio have improved with respect to the values obtained for each switch when irradiated with a 125-W medium-pressure Hg lamp since the percentage of *E* isomer has increased in all cases. In addition to this, there was no decomposition of the switches when irradiated under these conditions, so no side reactions occurred during the irradiation time intervals, which is a further betterment upon the previous conditions used.

Irradiating under these improved conditions, mixtures of *Z* and *E* isomers of different compounds bearing electron-withdrawing groups were subsequently separated to individually characterize and study them. With this aim, we irradiated a 0.01 M solution of compound **2a** (100% *Z* isomer at t=0 min) in acetonitrile in a photoreactor with lamps (14 lamps×8-W/lamp) with emission wavelength centred at 350 nm, until the PSS was reached. Then, the resulting mixture of isomers was separated by flash chromatography on silica gel, using hexane/ethyl acetate (10:1) as eluent. We then studied the kinetics of the isomerization reaction under these conditions. The photoisomerization reaction was followed by ^{1}H NMR at short irradiation intervals. Showing the isomers ratio versus irradiation time, we obtained the two graphs in Fig. 1(a) corresponding to the sample with 100% of **_Z_-2a** isomer at the beginning of the reaction, and (b) corresponding to the sample with 100% of **_E_-2a** isomer at t_{irrad}=0 min.

As shown in Fig. 1, the value of the isomers ratio at the PSS for these two processes is 51% (*Z*)/49% (*E*), which is reached after ca. 85 min of irradiation. In addition, we can calculate the values for the kinetic constants of each process from the first points of each graph, and therefore determine the value of the relative kinetic constant that relates the rate of both processes. If we consider $k_{Z\rightarrow E}$=1, then $k_{E\rightarrow Z}\approx$1, which means that the $E\rightarrow Z$ isomerization process is almost as fast as the $Z\rightarrow E$ reaction, so there is no difference in rate.

In addition, there are slight differences in the absorption spectra with solvents of different polarities. Thus, to determine if there is any noticeable effect in the values of the isomers ratio at the PSS, we irradiated **2a** in different solvents. Discernible differences in the values for the isomers ratio at the PSS were found (see Table S1). However, the differences between these results were unrelated to the polarity of the solvents according to the varying polarity indices reported in literature, such as $E_{\mathrm{T}}^{\mathrm{N}}$, ε, or π^* (Taft).[19]

2.2. Photophysics

We have previously reported[9] that these photoswitches are quite efficient as the quantum yield of the reaction using the two isomers of **2g** were found to be $\Phi_{Z\rightarrow E}=0.25\pm0.01$ starting from the *Z* isomer and $\Phi_{E\rightarrow Z}=0.11\pm0.02$ from the *E* isomer. Different deactivation processes, such as fluorescence among others could diminish the efficiency of these photoswitches. Therefore, we measured the emission and excitation spectra of two illustrative photoswitches: the two isomers (*Z* and *E*) of compound **2g** (R^1=Me, R^2=Ph, see Fig. 2), and compound **2a** (R^1=Me, R^2=*p*-BrPh) (only the *Z* isomer). A 3.6×10^{-5} M solution of **_Z_-2g** in deoxygenated acetonitrile at 298 K was measured in a spectrofluorimeter. Only a weak emission band centred at 380 nm was obtained when exciting from 250 to 340 nm (Fig. 2).