Contents lists available at ScienceDirect

Journal of Photochemistry and Photobiology A: Chemistry

journal homepage: www.elsevier.com/locate/jphotochem

# Effect of the positional isomerism on the photoreactivity of styryloxazoles



Photochemistry

Photobiology

# V. Botti<sup>a</sup>, F. Elisei<sup>a</sup>, U. Mazzucato<sup>a,\*</sup>, I. Šagud<sup>b</sup>, M. Šindler-Kulyk<sup>b,\*</sup>, A. Spalletti<sup>a</sup>

<sup>a</sup> Department of Chemistry, Biology and Biotechnology and Centro di Eccellenza sui Materiali Innovativi Nanostrutturati (CEMIN), University of Perugia, via Elce di Sotto 8, Perugia 06123, Italy

<sup>b</sup> Department of Organic Chemistry, Faculty of Chemical Engineering and Technology, University of Zagreb, Marulićev trg 19, Zagreb 10000, Croatia

#### ARTICLE INFO

Article history: Received 16 July 2015 Received in revised form 20 October 2015 Accepted 25 October 2015 Available online 29 October 2015

# ABSTRACT

This paper describes the results obtained in the study of the photobehaviour of heteroanalogs of stilbene bearing an oxazole ring. The competitive relaxation processes (fluorescence, isomerization and cyclization) of the excited states of *n*-styryloxazoles (n = 2 and 4) were investigated and compared with the behaviour previously reported for n = 5. After preparation of the unknown compound with n = 4 and of its positional isomer with n = 2 (the latter with a new method of synthesis), their photobehaviour was firstly investigated in preparative conditions by NMR analysis to measure the chemical yields of their photoproducts. The study was then continued in mild irradiation conditions to measure the quantum yields of the competitive photoreactions in the primary irradiation steps.

The effects of the position of the styryl group at the oxazole ring, the relative abundance of the various conformers and the possible formation of intramolecular H—bonds on the deactivation pathways are described. Quantum-mechanical Hyperchem calculations proved to be very useful to describe the conformational equilibria and the role of conformers on photoreactivity while more refined DFT calculations on the Z isomers allowed to explain the structure dependent competition between their isomerization/cyclization processes. The effect of the replacement of the phenyl ring with a second heteroaromatic group of electron donor character was investigated for the 5-(2-(furan-2-yl) ethenyl) oxazole.

© 2015 Elsevier B.V. All rights reserved.

# **1. Introduction**

The two main photoreactions (isomerization and cyclization) of stilbene have been under continuous investigation over many decades [1-13]. However, some mechanistic insights are still deeply debated in the modern literature [14-18]. In comparison, stilbene-like compounds bearing one or more heteroaryl groups have been less deeply investigated. The study of structural effects on their photobehaviour is then interesting since the presence and position of the heteroatom(s) can affect sensibly their relaxation pathways.

In a previous paper [19] the photobehaviour of the *trans* (E) and *cis* (Z) isomers of 5-styryloxazole (**5-StOx**) and their *p*-OMe derivatives was investigated in cyclohexane in mild conditions (room temperature, short and moderate-intensity irradiation times and low concentration) to measure reliable quantum yields of the competitive relaxation pathways of the excited states (fluorescence,  $E \rightarrow Z$  and  $Z \rightarrow E$  isomerization and cyclization) [19].

\* Corresponding author.

 $\label{eq:http://dx.doi.org/10.1016/j.jphotochem.2015.10.022 \\ 1010-6030/ @ \ 2015 \ Elsevier \ B.V. \ All \ rights \ reserved.$ 

No contribution of other pathways, such as dimerization and intersystem crossing (ISC), were observed. Internal conversion (IC) was likely operative in the case of the *E*-OMe derivative and in both Z isomers because the sum of emission and isomerization yields did not account for all the absorbed quanta [19].

The reversible photoisomerization was reported to occur in the singlet manifold by the well known diabatic mechanism [1,2]. Starting from the *trans* isomer, it involves twisting around the ethenic bond towards an energy minimum at the perpendicular configuration (at about 90°, <sup>1</sup>perp\*) followed by a  $S_1 \rightarrow S_0$  IC and relaxation to the ground-state E and Z isomers in roughly a 1:1 branching ratio [<sup>1</sup>E\*  $\rightarrow$  <sup>1</sup>perp\*  $\rightarrow$  <sup>1</sup>perp  $\rightarrow$  a<sup>1</sup>Z+(1  $- \alpha$ )<sup>1</sup>E], where the partitioning factor  $\alpha$  is generally assumed to be ~0.5 [1,2].

The cyclization photoreaction, which starts from the *Z* isomer and is generally accepted to occur in the singlet manifold [3– 13,20], led, as usual, to the unstable coloured intermediate (4a,4bdihydrophenanthrene-type, DHP) which, in the presence of an oxidant (generally oxygen), lost the two hydrogen atoms in *trans* stereochemistry to give the stable polynuclear phenanthrene-type (P) arene [19]. It should be recalled that two different cyclization intermediates (DHP and DHP') have been sometimes reported in the literature since the initial DHP, generally in anaerobic



*E-mail addresses:* ugo.mazzucato@unipg.it (U. Mazzucato), msindler@fkit.hr (M. Šindler-Kulyk).

conditions, can produce an isomer DHP' (through an intramolecular 1,*n*-hydrogen shift) which does not revert to Z and loses the hydrogen atoms to give the final P-type product [3,4]. Moreover, relatively good reactivity predictions about the cyclization path were reported in the literature on the basis of the sum of the free valence numbers of the excited state for the reacting C atom pair ( $\Sigma F_r^*$ ) [3]. Even better results were obtained with an alternative method where differences in the electronic overlap population (EOP) in the ground and excited states were used as general reactivity indices for photocyclization [3].

As to the quantum yields of the competing relaxation pathways of the parent **5-StOx** compound, a modest fluorescence yield ( $\phi_F$  of ~7%) was measured for the E isomer whereas, as usual, no emission was detected for the Z isomer in these experimental conditions. Photoisomerization was the largely prevailing deactivation pathway, particularly for the E isomer ( $\phi_{E\to Z}$  = 0.57). For the reverse reaction of the Z isomer, a smaller yield, smaller than that of stilbene (0.35) [1,2,18], was reported ( $\phi_{Z\to E}$  = 0.15). A small formation of DHP, with  $\lambda_{max}$  = 378 nm and  $\tau$  = 210 min in deaerated solution, was obtained. In the presence of oxygen DHP led to the stable cyclization product (naphtho[1,2-*d*]oxazole, NPh[1,2-*d*]Ox) with a yield  $\phi_{Z\to DHP}$  of 0.013 [19].

Similar results were reported for the *p*-OMe derivative which displayed slightly smaller isomerization and higher cyclization yields. The ratio  $\phi_{Z\rightarrow E}/\phi_{Z\rightarrow DHP}$  decreased from the value of 11.54 for **5-StOx** to 8.9 for the *p*-OMe derivative, in favour of the cyclization process [19].

In conclusion, the photobehaviour of the two *E*-styryloxazoles previously investigated was found to be rather similar to that of stilbene [1–13] while that of the Z isomers showed a reduced reactivity, particularly for cyclization. It should be noted that even the few quantitative data of relaxation quantum yields available in the literature for *E*-styryl-substituted five-membered heteroaryl units (such as thiophene [4,21], pyrrole [22] and indole [22]) show a similar photobehaviour, namely efficient isomerization and weak fluorescence. On the other hand, the cyclization was reported to generally display lower yield than stilbene and in some cases not to be operative at all.

Since the study of stilbene-like compounds with heterocyclic groups replacing one or both phenyl rings is important from various points of view (synthesis of polycyclic compounds [23], fluorescence sensors [24] and preparation of candidates for potential applications in non-linear optics [25] and for the therapy of human pathologies [26]), the present work aims to investigate the effects of the position of the styryl group at the oxazole ring on the photobehaviour of *n*-styryloxazoles (n=2, 4 and 5) and the effect of the replacement of the phenyl ring with a second heteroaromatic group on the photobehaviour of 5-(2-(furan-2-yl) ethenyl) oxazole (**2-FEt-50x**) (Scheme 1).

# 2. Experimental

# 2.1. Synthesis and irradiation of 2-StOx, 4-StOx and 2-FEt-5Ox

Two approaches were applied to synthesize the investigated compounds (Scheme 2). The furyl derivative **2-FEt-5Ox** was prepared by the Van Leusen reaction from the corresponding carbaldehyde and *p*-tolylsulfonyl)methyl isocyanide (TosMIC) as



**Scheme 1.** Compounds investigated: *E*-2- and *E*-4-styryloxazole (E-*n***-StOx** with n = 2 and 4) and *E*-5-(2-(furan-2-yl) ethenyl) oxazole (**2-FEt-5Ox**).



**Scheme 2.** Synthesis of *E*/*Z*-2-styryloxazole (**2-StOx**), *E*/*Z*-4-styryloxazole (**4-StOx**) and *E*-5-(2-(furan-2-yl) ethenyl) oxazole (**2-FEt-5Ox**).

described [23], while the novel **4-StOx** was prepared by Wittig reaction from oxazole-4-carbaldehyde [27] and benzyltriphenylphosphonium salt. To prepare **2-StOx** [28] we developed a new "one pot" procedure which includes formylation of oxazole and the Wittig reaction.

Preparative irradiation experiments were performed under aerobic conditions and addition of iodine in benzene solution in a Rayonet reactor equipped with 300 nm lamps as described for **5-StOx** [23]. Irradiation of **n-StOx** (n = 2, 4 and 5) was also performed in deuterated benzene in NMR tubes in aerobic conditions not purged with oxygen (oxygen from the air present in the tube) and the process followed by <sup>1</sup>H NMR (Bruker, AV300 and AV600) spectrometry. Further details are given in the Supplementary Information.

# 2.1.1. Synthesis of 2-StOx

To a solution of oxazole (0.9 g, 13.05 mmol) in dried ether under nitrogen at  $-70^{\circ}$ C *n*-BuLi (1.6 M, 8 mL, 15.6 mmol) was added dropwise and the mixture was stirred for 30 min. To this mixture 1 mL of dried DMF (0.96 g, 13.05 mmol) was added, stirred for 30 min and then left to warm to room temperature. Benzyltriphenylphosphonium bromide (4 g, 9.2 mmol) was added in portions of 0.5 g and the mixture stirred overnight. The reaction mixture was poured on ice water and extracted with benzene. Organic layers were combined and dried over anhydrous MgSO<sub>4</sub>, filtered and concentrated under vacuum. By multiple extraction with petroleum ether 0.434 g (16%) of product [28] is gained as a mixture of Zand E-**2-StOx** (Z:E=9:1). The crude material was purified by column chromatography (petroleum ether/ether variable ratio).

**Z-2-StOx:** Oil,  $R_f(PE/E = 10:2) = 0.60$ ; IR  $\nu_{max}/cm^{-1}$ : 3128, 3068, 1632, 1507, 1499, 1164, 1108, 918; UV (EtOH)  $\lambda_{max}/nm$  ( $\epsilon/dm^3$  mol<sup>-1</sup> cm<sup>-1</sup>): 220 (11248), 294 (12824); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz):  $\simeq/ppm$  7.66–7.63 (m, 2H, H-ar), 7.52/d,  $J_{4,5} = 0.59$  Hz, 1H, H-5), 7.39–7.31 (m, 3H, H-ar), 7.17 (d,  $J_{4,5} = 0.59$  Hz, 1H, H-4), 6.86 (d,  $J_{et} = 12.85$  Hz, 1H, H-et), 6.44 (d,  $J_{et} = 12.85$  Hz, 1H, H-et); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz):  $\simeq/ppm$  160.51 (s), 137.88 (d, C-5), 136.39 (d, C-et), 135.67 (s), 129.42 (d, C-ar), 128.51 (d, C-ar), 128.20 (d, C-4), 128.02 (d, C-ar), 114.65 (d, C-et). HRMS (MALDI-TOF/TOF) za C<sub>19</sub>H<sub>17</sub>NO: (M+K)<sup>+</sup><sub>calcd</sub> = 210.0316 (M+K)<sup>+</sup><sub>exp</sub> = 210.0315.

**E-2-StOx:** Yellow powder, mp 52-54 °C;  $R_f$  (PE/E = 10:2) = 0.40; UV (EtOH)  $\lambda_{max}/nm$  (ε/dm<sup>3</sup> mol<sup>-1</sup> cm<sup>-1</sup>): 221 (8741), 227 (8569), 234 (Sh 5526), 302 (25,193), 313 (Sh 23516); IR  $\nu_{max}/cm^{-1}$ : 3201, 1643, 1539, 1448, 1106, 966; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz):  $\delta$ /ppm 7.63 (d,  $J_{4,5}$  = 0.60 Hz, 1H, H-5), 7.47 (d,  $J_{et}$  = 16.40 Hz, 1H, H-et), 7.55–7.52 (m, 2H, H-ar), 7.40–7.32 (m, 2H, H-ar), 7.35–7.32 (m, 1H, H-ar), 7.19 (d,  $J_{4,5}$  = 0.60 Hz, 1H, H-4), 6.97 (d,  $J_{et}$  = 16.40 Hz, 1H, H-et); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz):  $\delta$ /ppm 161.80 (s), 138.15 (d, C-5), 136.16 (d, C-et), 135.55 (s), 129.16 (d, C-ar), 128.86 (d, C-ar), 128.55 (d, C-4), 127.18 (d, C-ar), 113.99 (d, C-et); MS *m/z* (EI): 171 (100%), 109 (10%).

# 2.1.2. Synthesis of 4-StOx

Synthesis of **4-StOx**: To an absolute ethanol solution of benzyltriphenylphosphonium bromide (3.08 g, 7.1 mmol, 50 mL) NaOEt in ethanol was added dropwise and simultaneously with a solution of oxazole-4-carbaldehyde (0.69 g, 7.1 mmol) [27] and the reaction mixture was stirred for 24 h. After removal of the solvent the residue was dissolved in water and extracted with benzene. Organic layers were dried over anhydrous MgSO<sub>4</sub>, filtered and the solvent was removed under reduced pressure. By multiple extractions with petroleum ether 0.673 g (56%) of product was obtained as a mixture of Z- and E-**4-StOx** (Z:E = 3:2). By multiple column and thin layer chromatography, 0.411 g of Z-**4-StOx** was isolated (contaminated with 11% of *E*-**4-StOx**).

**Z-4-StOx:** Oil,  $R_f$  (PE/E = 3:1) = 0.41; IR  $\nu_{max}/cm^{-1}$ : 3024, 1517, 1097, 1065, 910; UV (EtOH)  $\lambda_{max}/nm$  ( $\epsilon/dm^3 mol^{-1} cm^{-1}$ ): 275 (8719); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz):  $\delta/ppm$  7.78 (s, 1H, H-2), 7.38–7.33 (m, 5H, H-ar), 7.28 (s, 1H, H-5), 6.72 (d, 1H,  $J_{et}$  = 12.0 Hz, H-et), 6.44 (d,  $J_{et}$  = 12.0 Hz, 1H, H-et); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta/ppm$ : 150.1 (d, C-2), 137.6 (s), 136,71 (s), 136.2 (d, C-5), 132.2 (d, C-et), 128.5 (d, C-Ar), 128.3 (d, C-Ar), 127.6 (d, C-Ar), 120.0 (d, C-Ar); HRMS (MALDI–TOF/TOF) for C<sub>11</sub>H<sub>9</sub>NO: (M+K)<sup>+</sup><sub>calcd</sub> = 210.0316, (M+H)<sup>+</sup><sub>exp</sub> = 210.0311.

*E*-4-StOx: Oil,  $R_f$  (PE/E = 3:1) = 0.40; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz) δ/ppm (values are derived from the spectrum of mixture of isomers): 7.88 (s, 1H, H-2), 7.68 (s, 1H, H-5), 7.50 (d,  $J_{ar}$  = 7.3 Hz, 1H, H-ar), 7.38–7.33 (m, 2H, H-ar), 7.36 (d,  $J_{et}$  = 16.0 Hz, H-et), 7.29–7.28 (m, 1H, H-ar), 6.94 (d,  $J_{et}$  = 12.0 Hz, 1H, H-et).

# 2.1.3. Synthesis of NPh[2,1-d]Ox

Irradiation of **4-StOx** gave naphtho[2,1-d]oxazole (**NPh[2,1-d] Ox**) [29]: 92% yield, colorless crystals, mp 50–51 °C;  $R_f$  (PE/ E = 10:2) = 0.43; UV (EtOH)  $\lambda_{max}/nm$  (e/dm<sup>3</sup> mol<sup>-1</sup> cm<sup>-1</sup>): 222 (29,823), 233 (31,946), 311 (1545), 326 (2098); IR  $\nu_{max}/cm^{-1}$ : 3099, 2921, 1498, 1261, 1087, 1066; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz): d/ ppm 8.26 (d,  $J_{ar}$  = 8.6 Hz, 1H, H-ar), 8.25 (s, 1H, H-2), 8.00 (d,  $J_{ar}$  = 8.2 Hz, 1H, H-ar), 7.86 (d,  $J_{et}$  = 8.7 Hz, 1H, H-et), 7.82 (d,  $J_{et}$  = 8.7 Hz, 1H, H-et), 7.67–7.64 (m, 1H, H-ar), 7.59–7.56 (m, 1H, Har); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz): d/ppm 151.2 (d), 145.6 (s), 136.1 (s), 131.4 (s), 128.1 (d), 126.5 (d), 125.5 (d), 125.0 (d), 120.0 (s), 119.8 (d), 118.4 (d).

#### 2.2. Spectral and photoreactivity measurements

For the spectroscopic and photoreaction measurements, cyclohexane (CH) from Fluka, spectrophotometric grade, was used as solvent. In some experiments also acetonitrile (MeCN), benzene and a mixture of 9/1 (v/v) methylcyclohexane/3-methylpentane (MCH/3MP) from Fluka were used after further purification by standard procedures.

PerkinElmer Lambda 800 and Cary 4E Varian spectrophotometers were used for the absorption measurements. The fluorescence spectra were measured with a Spex Fluorolog-2 F112AI spectrofluorimeter. Dilute solutions (absorbance <0.1 at the excitation wavelength,  $\lambda_{exc}$ ) were used for fluorimetric measurements. The fluorescence quantum yields ( $\phi_F$ ) were determined at  $\lambda_{exc}$ corresponding to the maximum of the first absorption band ( $\lambda_{max}$ ). 2-(1-naphthyl)-5-phenyl-3,4-oxadiazole ( $\alpha$ -NPD) in CH was used as fluorometric standard ( $\phi_F$ = 0.70 in deaerated solvent) [30].

For photochemical measurements (potassium ferrioxalate in water as actinometer) a 150 W high pressure xenon lamp coupled with a monochromator and a 500 W mercury lamp and an interference filter at 313 nm were used. The photoreaction (solute concentrations  ${\sim}10^{-4}$  M) was monitored by HPLC using a Waters apparatus equipped with analytical Gemini C18 (4.6  ${\times}$  250 mm; 5  ${\mu}$ m) and Prontosil 200-3-C30 (4.6  ${\times}$  250 mm; 3  ${\mu}$ m) columns and an UV diode-array detector.

The procedure used to measure the  $E \rightarrow Z$  photoreaction quantum yields was as follows: diluted solutions of the E isomers in de-aerated (by bubbling nitrogen) CH were irradiated up to a maximum conversion percentage of ~10% to minimize competition of the back photoreaction. To follow the photoreactions of the Z isomers (not available as pure separated compounds) irradiation was initially performed at 313 nm to reach a photostationary state enriched in the Z isomer (in the presence of a side source of visible light to destroy DHP and avoid P formation at this stage) and then at 254 nm where the absorption of the Z isomer largely prevails. Samples of the irradiated solutions, analyzed immediately after the removal of the irradiating source by combined HPLC and spectrophotometric techniques, generally contain four components: E, Z, DHP and small amounts of the P-type dehydrogenated compound. The air-equilibrated solutions were then left overnight in the dark to allow the decay of the DHP intermediates to go to completion. The residual components were separated by HPLC (using MeCN/water mixtures as eluent) and identified spectrophotometrically. Only in the case of 4-StOx the irradiation was carried out on a pure Z sample, previously separated from the E isomer by HPLC.

The thermal stability of DHPs at room temperature was measured by following spectrophotometrically the disappearance of the visible absorption band in both oxygenated and de-aerated CH (by bubbling oxygen and nitrogen, respectively). The quantum yields reported in the Tables are generally averages of two/three independent experiments with mean deviations of *ca.* 10% for  $\phi_{E\rightarrow Z}$ . Higher uncertainty (15–20%) was found in the more delicate measurements of the photoreaction yields starting from the Z isomer ( $\phi_{Z\rightarrow E}$  and  $\phi_{Z\rightarrow P}$ ), particularly in the presence of very small cyclization yield (<2%).

Quantum-mechanical calculations were carried out using the HyperChem computational package (version 7.5). Total energies and dipole moments were obtained for geometries optimized by HF ab initio method (3-21-G level). The computed transition energies and oscillator strengths were obtained by ZINDO/S at the optimized geometries, the configuration interaction including 400  $(20 \times 20)$  single excited configurations.

More refined quantum-mechanical calculations on Z isomers were carried out in CH at the B3LYP/6-311G + (2d,p) level of theory [31] using the Gaussian 09 package [32]. The geometry optimizations were undertaken using tight convergence limits and with no symmetry constraints. The final energies for each optimized structure, the electron density changes and the frontier molecular orbitals were calculated using the CPCM model [33] to simulate the dielectric medium effect.

# 3. Results and discussion

#### 3.1. n-Styryloxazoles

The initial part of the photochemical work, carried out at the Zagreb laboratory, was particularly aimed to optimize the



Fig. 1. Graphical presentation of irradiation of (E/Z)-4-StOx in NMR tubes in C<sub>6</sub>D<sub>6</sub>.



Scheme 3. Photoreactions of Z-4-StOx.

cyclization process. It started from irradiation of the E isomer or mixtures of E/Z isomers under suitable conditions for a preparative work (high light intensity, long irradiation times of tenths of hours, concentrated solutions and addition of iodine as efficient oxidant). The evolution of the photoreactive pathways in aerobic conditions (see experimental), measured in the present work also for the previously investigated **5-StOx**, was followed by NMR analysis, as shown in Fig. 1 for n = 4, as an example, and in Figs SI.1 and SI.2 in the Supplementary Information for the other two isomers.

The results thus obtained gave interesting information on the photobehaviour. Irradiation of *E*-**2-StOx** showed only the E–Z isomerization which led to photostationary state (E:Z=3:1) after 40 min. Irradiation of **4-StOx** (E:Z=1:1) showed the E–Z isomerization and the photostationary state (E:Z=3:1) was reached after  $\approx$ 2.5 h followed by the electrocyclization after  $\approx$ 8 h. The **5-StOx**, measured for the sake of comparison, displayed a photobehaviour similar to **4-StOx** with the more effective process of electrocyclization. The long induction period for the formation of the cyclised P product recorded by NMR can be explained by slow formation of the DHP intermediate due to the competition of its return to the starting Z isomer by thermal and mainly photochemical processes. It should also be noted that the final P product should accumulate enough before the sensitivity of the NMR method allows its detection.

The experimental work was then continued at the Perugia laboratory under mild experimental conditions to follow the photobehaviour in the first stages of irradiation with the main aim



**Fig. 2.** Absorption and normalized emission spectra of the E isomers of **2-** and **4- StOx** in CH compared with n = 5 from Ref. [19].

to characterize the absorption/emission spectral properties and to measure the quantum yields of the competing relaxation processes.

The different position of the styryl group with respect to the oxygen atom in the five-membered ring is expected to change the electronic distribution and affect in some way the competition of the different relaxation pathways. Scheme 3 shows the photoreactions of these compounds for **4-StOx**, as an example. The spectral properties of the E isomers are shown in Fig. 2 and collected in Table 1.

The E isomers of 2- and 5-StOx absorb in the same spectral region with the tail of 2-StOx broadened towards the red and a more structured shape for n = 5; the spectrum of **4-StOx** is shifted towards the blue as also predicted by calculations (see below, Table 3). The absorption coefficients of the E isomers were measured directly, those of the polycyclic final products were assumed equal to those in ethanol (see spectra of Fig. SI.3) and those of the Z isomers and DHP intermediates were obtained by normalization at the E/Z and DHP/P isosbestic points, respectively. For n=2, no sign of formation of the DHP intermediate and its dehydrogenation product P was observed. It should be noted that the spectral shape of Z-2-StOx is unusually structured (see Fig. SI.4) indicating a planar and more conjugated geometry favoured by an interaction of H-bond type between the N atom of the oxazole ring and a H atom of the phenyl group, as also suggested by the computed results (see below). The naphtho[2,1-d]oxazole (NPh [2,1-d]Ox), polycyclic product formed under irradiation of Z-4-**StOx**, shows the structured spectrum typical of these compounds while its DHP precursor has a bell-shaped band shifted towards 400 nm because of the extended conjugation in the non-aromatic  $\pi$ -system typical of these intermediates (Fig. 3).

The almost specular absorption/emission spectra are structured and the excitation spectra are practically superimposed to the absorption spectra (Figs SI.5 and SI.6). Deviations are within the experimental uncertainty due to the weak signal and the use of low transmittance filters to avoid photodegradation. In the case of the compound with n = 4 (as previously found for **5-StOx**) [19], no  $\lambda_{exc}$ effects on the emission spectra were observed (Fig. SI.7) whereas changes in the spectral shape were found for n = 2, consistent with the presence (confirmed by calculations) of conformational equilibria among fluorophores with slightly different spectral properties (Fig. SI.8).

Since these flexible molecules exist in solutions as mixtures of conformers [34,35] due to rotation of the aryl groups around the quasi-single bond with the ethenic bridge (see Scheme 4 for Z-**4**-**StOx** as an example), calculations of total energies were performed to evaluate their relative abundances in the ground state and spectral properties. Tables 2 and 3 show the results obtained for the two compounds. The last column shows the experimental

#### Table 1

Spectral properties and stokes shifts  $(\Delta \tilde{v}_s)$  of two positional isomers of **2-** and **4-StOx** in two solvents. Data for n=5 from ref. 19 are also reported for comparison purposes.<sup>a</sup>

n	solvent	$\lambda_{abs}^{max} \; (nm)$	$\epsilon^{max}$ (M <sup>-1</sup> cm <sup>-1</sup> )	$\lambda_F^{\max}(nm)$	$\Delta \\ \tilde{v}_{\rm S}({ m cm}^{-1})$
2	СН	325 309 299	28800	334 352 369	5040
	EtOH	328 312 302	25300		
4	СН	306 286 278	25650	312 327 341	5390
	MeCN	304 285 277	25500		
5	СН	322 307 296	25200	327 343 360	3420
	MeCN	318 304 293	28600		

<sup>a</sup> The main maxima are underlined.

maxima for comparison: there is good agreement for the conformers of the E isomer, less for those of the Z isomers. In the case of E-**2-StOx**, both conformers are abundant while one largely prevails for the Z isomer, namely that one where C and N atoms are faced at the reaction center (see below).

For **4-StOx**, one conformer largely prevails for both E and Z isomers. Similar results were reported for n = 5 [19].

The two *n***-StOx** isomers with n = 2 and 4 display a rather similar behaviour, the main difference being that n = 4 cyclizes with a good yield, similar to that of stilbene ( $\phi_{Z \rightarrow DHP} = 0.1$ ) [6,18], whereas n = 2 does not cyclize at all. The comparison with n = 5 indicates that the latter is characterized by a larger  $E \rightarrow Z$  isomerization yield while the Z isomer is less reactive, particularly in the cyclization pathway (almost one order of magnitude smaller). Perusal of data in Table 4 indicates that, contrary to the case of the E isomers with n = 5 and n = 4, where isomerization, with a small additional contribution of fluorescence, accounts for all excitation quanta (assuming  $\alpha \approx 0.5$ , the partitioning factor towards E and Z for the decay from the <sup>1,3</sup>perp\* configuration in the diabatic mechanism) [1], internal conversion (IC) contributes to the relaxation of n = 2. A more



Fig. 3. Absorption spectra of E-4-StOx and its photoproducts in CH.



Scheme 4. Conformational equilibrium of Z-4-StOx.

significant contribution of IC is found for the Z isomers, particularly for n = 4 and n = 5. The isomer with n = 4 displays a cyclization yield almost one order of magnitude higher than that of n = 5. It should be noted that the metastable DHP intermediate is characterized by three deactivation pathways: under irradiation it undergoes ring opening and reverts to Z while in the dark it is thermally oxidized to P or undergoes H-shift [4] followed by dehydrogenation to P even in the absence of oxidant. Therefore, the cyclization yield depends obviously on three rate constants,  $k_{Z \to DHP}k_{DHP \to Z}$  and  $k_{DHP \to P}$  the latter representing the oxidation rate,  $k_{ox}$ . From the information of the chromatographic analysis we assume  $k_{DHP \to P} >>$  $k_{DHP \to Z}$  in the presence of the oxidant and then  $\phi_{Z \to DHP}$ approximates  $\phi_{Z \to P}$  the formation photoefficiency of the final product P (Fig. 4).

The thermal evolution of the absorption spectrum of DHP for n=4 (Fig. 5) was followed in the dark in deaerated (nitrogen atmosphere) and aerated (oxygen atmosphere) CH and MeCN solutions. In deaerated solution,  $\tau_{DHP}$  = 210 and 160 min in CH and MeCN, respectively (Table 4) were derived from the initial rates of the DHP disappearance (Fig. 5B for n = 4). These lifetimes, reduced by 50% by bubbling oxygen, are very similar to those reported for 5-StOx and slightly longer than the value of stilbene in aerated solution (140 min) [3]. A rough estimation of  $k_{ox}$  in CH (5.6 × 10<sup>-3</sup> and  $8.9 \times 10^{-3} \,\mathrm{M^{-1} \, s^{-1}}$  for *n* = 4 and 5, respectively) was derived by the lifetimes in Table 4, showing the importance of the presence of an oxidant to accelerate the  $DHP \rightarrow P$  process. In deaerated solutions the disappearance kinetics of DHP is probably due to different contributions, namely the thermal DHP  $\rightarrow$  Z cycloreversion and formation of P by oxygen traces not completely removed by bubbling nitrogen. However, production of P in anaerobic conditions cannot be excluded [20].

Some preliminary experiments on the effect of temperature and solvent on the relaxation properties were carried out for 4-StOx. The experiments at different T on the E isomer evidenced, as expected, the coupling between the reactive and emissive deactivations since in the rigid matrix, when the isomerization is inhibited, the fluorescence yield approximates a value of 100%. An investigation on the solvent effect carried out on Z-4-StOx showed that polar solvents favour the isomerization to the detriment of cyclization  $(\phi_{Z \rightarrow DPH}$  decreases from 0.063 in CH to 0.014 in MeCN). Similar results were described also for Z-stilbene where the cyclization is particularly affected (two-three times smaller in polar solvents)[8]. We tried to explain the different cyclization yields for the conformers of Z-**n-StOx** able to cyclize and for those indicated by the Hyperchem calculations as the most abundant species (see above) by performing DFT calculations with the CAM-B3LYP/6-311G + (2d,p) method, simulating the solvent effect by the CPCM model. The results reproduced satisfactorily the experimental trend of the absorption properties and showed that the spectral band is assignable to the first  $S_0 \rightarrow S_1$  transition, described ~97% by the HOMO  $\rightarrow$  LUMO,  $\pi \rightarrow \pi^*$ -type, configuration.

The computed changes in electron density (EDC) on going from S0 to S1 under excitation (Table 5) are interesting. Indeed, they showed, in addition to the well-known decrease of the ethenic bond order, responsible for the twisting towards the E isomer, a density increase between the two carbon atoms implied in the ring closing process (reaction center) for the isomers with n = 5 and 4, particularly for the latter. This indicates that the Franck–Condon state reached by irradiation is already disposed towards DHP

#### Table 2

Computed dipole moment ( $\mu$ ) and total energy ( $E_{TOT}$ ), derived relative abundance (%) at room temperature, transition energy ( $\lambda$ ) and oscillator strength (f) of the conformers of the E and Z isomers of **2-StOx**.<sup>a</sup>

Conformer		$\mu(D)$	E <sub>TOT</sub> (kcal mol-1)	% (293K)	λ(nm)	f		λ <sub>exp</sub> (nm)
No No	E(A)	0.72	-343868.531	36	312 279 260 241 217	0.94 0.0003 (TC) 0.009 ( <i>n</i> ,π <sup>*</sup> ) 0.09 0.37	S <sub>1</sub> S <sub>2</sub> S <sub>3</sub> S <sub>4</sub> S <sub>6</sub>	299 227
	E(B)	1.67	-343868.875	64	311 278 257 241 217	0.91 0.0003 (TC) 0.01 ( <i>n</i> , <i>π</i> *) 0.13 0.37	S <sub>1</sub> S <sub>2</sub> S <sub>3</sub> S <sub>4</sub> S <sub>6</sub>	299 227
	Z(A)	0.81	-343865.125	99	318 280 279 245 221	0.71 0.002 (TC) 0.01 ( <i>n</i> ,π*) 0.13 0.3	S <sub>1</sub> S <sub>2</sub> S <sub>3</sub> S <sub>4</sub> S <sub>6</sub>	294 224
∩ ∩ N	Z(B)	1.75	-343862.625	1				

<sup>a</sup> The last column shows the experimental transition energies for comparison.

formation and reflects the experimental results (highest  $\phi_{Z \rightarrow DHP}$  for n = 4). As said above, for n = 2, where the N atom of the oxazole ring is faced to the C atom of the phenyl ring at the reaction center, no cyclization was observed. CN bond formation has been described in a limited number of cases (see, for example, the earliest case of the formation of benzimidazo[1,2-a]quinoline from

2-styrylimidazoles [36] and the recent deep investigation on 2styrylquinolines [37]. However, no sign of CN cyclization was found in the present case.

A planar structure was computed for the latter isomer (see Table SI.1), probably stabilized by a H—bond between N and the ortho H atom of the phenyl ring, as suggested by the computed

#### Table 3

Computed dipole moment ( $\mu$ ) and total energy ( $E_{\text{TOT}}$ ), derived relative abundance (%) at room temperature, transition energy ( $\lambda$ ) and oscillator strength (f) of the conformers of the E and Z isomers of **4-StOx**.<sup>a</sup>

Conformer		μ (D)	$E_{\rm TOT}$ (kcal mol <sup>-1</sup> )	% (293 K)	λ (nm)	f		$\lambda_{exp}$ (nm)
N= O	E (A)	1.05	-343865.750	99	285 280 275 251 215	1.01 0.11(TC) 0.08 0.01 ( <i>n</i> ,π*) 0.41	S <sub>1</sub> S <sub>2</sub> S <sub>3</sub> S <sub>4</sub> S <sub>7</sub>	286 278
N	E (B)	1.40	-343863.188	1				
N NO	Z (A)	1.32	-343859.656	2				
	Z (B)	1.68	-343861.875	98	268 266 249 244 196 195	0.006 (Ph) 0.06 (H–L) 0.01 ( <i>n</i> ,π*) 0.45 0.76 0.75	$S_1 \\ S_2 \\ S_3 \\ S_4 \\ S_{11} \\ S_{12}$	272 220

<sup>a</sup> The last column shows the experimental transition energies for comparison.



**Fig. 4.** Spectral evolution of E-2-StOx in CH at increasing irradiation times  $(\lambda_{exc}=299 \text{ nm})$  up to the photostationary state.

distance between N and H (2.1 Å) and N— $\hat{H}$ —C angle (147°), both values typical of a "real" H-bond formation [38]. It should be noted that Z-**2-StOx** displays the highest reactivity towards the E isomer (Table 4).

It is difficult to compare the photoreaction quantum yields measured at the first stages of irradiation with the results obtained by prolonged irradiation in preparative conditions (where the  $E \rightarrow Z \rightarrow DHP$  consecutive process is followed), as described above. Anyway the comparison shows that Z-**2-StOx** does not cyclize in both conditions.

#### Table 4

Quantum yields of the radiative and reactive processes and lifetime of the DHP intermediate for the positional isomers of *n*-styryloxazole in deaerated CH.

n-StOx	n=2	n = 4	$n = 5^{a}$
$\phi_{\rm F}$ (E isomer)	0.010	0.036	0.072
$\phi_{\mathrm{E} ightarrow\mathrm{Z}}$	0.38	0.48	0.57
$\phi_{Z  ightarrow E}$	0.40	0.18	0.14
$\phi_{Z  ightarrow DPH}$	Not observed	0.06	0.014
$\tau_{\rm DHP}$ (min)		210 (116) <sup>b</sup>	200 (90) <sup>b</sup>

<sup>a</sup> Data for **5-StOx** from Ref. [19] reported for comparison.

<sup>b</sup> Data in parenthesis refer to oxygenated solutions.





Fig. 6. Absorption spectra of E- and E-2-FEt-5Ox in CH.



Scheme 5. Conformational equilibrium of Z-2-FEt-5Ox.

# 3.2. E-5-(2-(furan-2-yl) ethenyl) oxazole (2-FEt-50x)

Replacement of the phenyl group of **5-StOx** with another heteroaromatic group of different electron donor/acceptor (D/A) properties can modify the photobehaviour. We examined the effect of an electron rich furyl group (the E isomer is shown in Scheme 1).

It should be noted that the D/A character of the oxazole group is rather ambiguous and depends on the attachment position. Its second heteroatom (the tertiary nitrogen) contributes one electron to the aromaticity of the ring and the lone pair of electrons in the molecular plane lowers the  $\pi$ -orbital energy level. The oxazole is



**Fig. 5.** Spectral evolution of the DHP formed from **4-StOx** in deaerated CH kept 1040 min in the dark at room temperature (A) and corresponding kinetics in deaerated and oxygenated solutions (B) (at short wavelengths the formation of the first peak of the final P product at 325 nm can be also observed).

#### Table 5

 Z
 π<sub>it</sub>
 π',
 EDC

 St
 <td

Frontier molecular orbitals and changes in electron density (EDC, isodensity = 0.0004) for the  $S_0 \rightarrow S_1$  transition (violet and light-blue colours refer to an increase and a decrease in the ED, respectively) obtained by TDDFT calculations.

then characterized by higher ionization potentials (9.83 eV) and displays weaker electron donor properties with respect to furan (8.88 eV) and other  $\pi$ -rich analogues [39]. In any case the electron density map of the oxazole ring indicates that it still remains a weak  $\pi$  donor [40,41]. In any case, the nature of the two side heteroaryl groups of **2-FEt-50x** suggests a very weak charge transfer (CT) character of the S<sub>0</sub>  $\rightarrow$  S<sub>1</sub> transition and the probable absence of further intramolecular (ICT) processes in the excited state.

The weak CT character is in agreement with the absence of important changes of the absorption spectrum (Fig. 6) with solvent polarity, the  $\lambda_{max}$  in MeCN being shifted by only 2 nm towards the blue (321 nm) with respect to CH (323 nm). The fluorescence yield was found to be very low ( $\phi_F$  = 0.007 in CH) and the fluorescence spectrum did not shift on going from CH to anisole and MeCN pointing to the absence of any fluorosolvatochromism. In principle, four conformers (Scheme 5) are expected for *Z*-**2-FEt-50x**.

The calculations of Table SI.2 indicate that the most stable ones are those where OH intramolecular H-bonds can favour planar structures (B and C rotamer in Scheme 5). However, they cannot lead to a ring closure which would imply formation of a new CC bond, as confirmed by the DFT calculations on the C conformer (Table 5) showing the absence of electron density at the reaction center. The computed distance between O and H (2.2 Å) and OĤC angle (125°) of the C conformer indicate also in this case, similarly to what described above for 2-StOx, the formation of a strong interaction of Hbond character. The only conformer (A) suitable to a ring closure (see the sizable electron density in Table 5) has a distorted structure owing to severe steric interactions (Table SI.1). The consequent rather higher energy level of this isomer implies in practice its absence in the conformational equilibrium at room temperature and could then explain why no trace of DHP was found in our experiments (see below).

The  $\phi_{F \rightarrow 7}$  value (0.38) was found slightly smaller than those previously reported for **5-StOx** and its p-OMe derivative [19]. Considering also the very low emission yield, a non-negligible part of the excited molecules probably decays by IC. However, a contribution of ISC to the triplet manifold cannot be excluded. The  $\phi_{Z \rightarrow E}$  value (0.24) is similar to that measured for the analogous **5**-StOx bearing the donor *p*-OMe substituent [19]. Despite the absence of DHP and P (P = furobenzoxazole, FBOx) formation in the mild conditions used for our irradiations (short irradiation time, low conversion, low light dose and low concentration), the experiments on preparative scale, using iodine as oxidant and performed in benzene at  ${\sim}40\,^{\circ}\text{C}$  until full conversion of the starting reagents ( $\sim$ 24h of irradiation), led to FBOx with a notable chemical yield of 63% [23]. Evidently the presence of iodine, able to accelerate the oxidation rate  $(k_{ox})$  to P to detriment of the ring opening of DHP, was crucial for the formation of the final product.

## 4. Conclusions

The results obtained allowed some aspects of the excited state behaviour of 1,2-(di-aryl) ethenes, where one aryl group is a fivemembered oxazole ring, to be clarified.

The photobehaviour of **2-** and **4-StOx**, investigated with the aim of comparing it with that of the positional isomer **5-StOx** [19,23], indicated that the E isomers of the three compounds emit a very weak fluorescence while isomerisation to Z is the largely prevalent relaxation pathway, at least for n = 4 and 5, similarly to the parent hydrocarbon, E-stilbene.

A reduced reactivity was found for the Z isomers with both the  $Z \rightarrow E$  and  $Z \rightarrow DHP$  quantum yields smaller with respect to those of Z-stilbene, indicating a non-negligible role of IC on the deactivation process. An interesting result was found for Z-**2-StOx**, which displayed a good isomerization yield but no formation of the cyclized compound.

In short, the effect of the position of the styryl group at the oxazole ring was found to be rather modest but the comparison of the experimental results, supported by quantum-mechanical calculations, allowed some interesting information to be obtained.

The first series of calculations, performed with the 7.5 Hyperchem packet was useful in evaluating the relative abundance of the possible conformers, to confirm the experimental spectral data and to determine the energy of the  $n,\pi^*$  states introduced by the nitrogen heteroatom with respect to that of the lowest S<sub>1</sub> state, responsible for emission and reactivity. In fact, the upper  $n,\pi^*$  states of both E/Z geometrical isomers were found to lie far enough in energy (particularly for n=2 and 5) thus not explaining the derived IC contributions on the basis of proximity effects only.

Calculations on the Z isomers with the more refined DFT method were very useful in interpreting the cyclization quantum yields. The computed increase in electron density between the C atoms at the reaction centre, found already in the Franck–Condon excited state, allowed to explain well the observed differences in the efficiency of the cyclization pathway of the three compounds.

In some cases the M.O. calculations allowed the role of intramolecular H-bond on the photocyclization to be highlighted.

The 2-furyl derivative showed that the *trans/cis* photoisomerisations occur with a yield not very different from those of the phenyl analogue, **5-StOx**, but did not cyclize. The only conformer suitable to the formation of a CC bond has a distorted structure owing to severe steric interactions thus explaining the absence of the ring closing reaction.

# Acknowledgements

The authors thank the Ministero per l'Università e la Ricerca Scientifica e Tecnologica, MIUR (Rome, Italy) [PRIN "Programmi di Ricerca di Interesse Nazionale" 2010–2011 (2010FM738P) as well as the Ministry of Science, Education and Sports of the Republic of Croatia (grant nos. 125-0982933-2926) for fundings.

The authors thank also Mr. Danilo Pannacci for his technical assistance in HPLC measurements.

# Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jphotochem.2015.10.022.

#### References

 J. Saltiel, Y.-P. Sun, Photochromism: Molecules and Systems, in: H. Dürr, H. Bouas-Laurent (Eds.), Elsevier, Amsterdam, 1990, pp. 64–162 and references therein.

- [2] D.H. Waldeck, Chem. Rev. 91 (1991) 415-436 and references therein.
- [3] K.A. Muszkat, Top. Curr. Chem. 88 (1980) 91–143 and references cited therein.
- [4] F.B. Mallory, C.W. Mallory, Organic Reactions, vol. 30, John Wiley and Sons, New York, 1984, pp. 1–456.
- [5] W.H. Laarhoven, Photochromism, Molecules and Systems, in: H. Dürr, H. Bouas-Laurent (Eds.), Elsevier, Amsterdam, 1990, pp. 270–313 chapter 7 and references therein.
- [6] K.A. Muszkat, E. Fischer, J Chem. Soc. B 66 (1967) 2–678 and references therein.
   [7] S.T. Repinec, R.J. Sension, A.Z. Szarka, R.M. Hochstrasser, J. Phys. Chem. 95
- (1991) 10380–10385.
- [8] J.M. Rodier, A.B. Myers, J. Am. Chem. Soc. 115 (1993) 10791-10795.
- [9] M.J. Bearpark, F. Bernardi, S. Clifford, M. Olivucci, M.A. Robb, T. Vreven, J. Phys. Chem. A 101 (1997) 3841–3847.
- [10] Y. Dou, R.E. Allen, J. Mod. Opt. 51 (2004) 2485–2491.
- [11] M. Greenfield, S.D. McGrane, D.S. Moore, J. Phys. Chem. A 113 (2009) 2333–2339 and references therein.
- [12] T. Wismontski-Knittel, G. Fischer, E. Fischer, J. Chem. Soc. Perkin Trans. II (1974) 1930–1940.
- [13] H. Petek, K. Yoshihara, Y. Fujiwara, Z. Lin, J.H. Penn, J.H. Frederick, J. Phys. Chem. 94 (1990) 7539–7543 and references cited therein.
- [14] M. Boggio-Pasqua, M. Ravaglia, M.J. Bearpark, M. Garavelli, M. Robb, J. Phys. Chem. A 107 (2003) 11139–11152.
- [15] J. Quennevile, T.J. Martinez, J. Phys. Chem. 107 (2003) 829-837.
- [16] C.-W. Jiang, R.-H. Xie, F.-L. Li, R.E. Allen, Chem. Phys. Lett. 487 (2010) 177–182 and references therein.
   [17] T. Nakamura, S. Takeuchi, T. Taketsugu, T. Taahara, Phys. Chem. Chem. Phys. 14
- (2012) 6225–6232. [18] Y. Harabuchi, K. Keipert, F. Zahariev, T. Taketsugu, M.S. Gordon, J Phys. Chem. A
- 118 (2014) 11987–11998 and references therein. [19] I. Šagud, M. Šindler-Kulyk, A. Spalletti, U. Mazzucato, Croat. Chem. Acta 87
- (2014) 327–333. [20] U. Mazzucato, A. Spalletti, J. Phys. Chem. A 113 (2009) 14521–14529 and
- references therein. [21] G. Bartocci, G. Galiazzo, G. Ginocchietti, U. Mazzucato, A. Spalletti, Photochem. Photobiol. Sci. 3 (2004) 870–877.
- [22] G. Galiazzo, G. Gennarí, P. Bortolus, Gazz. Chim. Ital. 121 (1991) 67–71.
   [23] I. Šagud, F. Faraguna, Ž. Marinić, M. Šindler-Kulyk, J. Org. Chem. 76 (2011)
- 2904–2908.
- [24] T. Deligeorgiev, A. Vasilev, S. Kaloyanova, J.J. Vaquero, Color. Technol. 126 (2010) 55–80.
- [25] E.M. Breitung, C.-F. Shu, R.J. McMahon, J. Am. Chem. Soc. 122 (2000) 1154–1160.
   [26] C.G. Fortuna, V. Barresi, C. Bonaccorso, G. Consiglio, S. Failla, A. Trovato-Salinaro, G. Musumarra, Eur. J. Med. Chem. 47 (2012) 221–227.
- [27] J.T. Reeves, J.J. Song, Z. Tan, H. Lee, N.K. Yee, C.H. Senanayake, Org. Lett. 9 (10) (2007) 1876–1878.
- [28] F. Besselievre, S. Lebrequier, F. Mahuteau-Betzer, S. Piguel, Synthesis (2009) 3511–3518.
- [29] E. Boyland, D. Manson, Biochem. J. 99 (1966) 189–199.
- [30] G. Bartocci, F. Masetti, U. Mazzucato, A. Spalletti, I. Baraldi, F. Momicchioli, J. Phys. Chem. 91 (1987) 4733–4743.
- [31] A. Jankowiak, E. Obijalska, P. Kaszynski, Beilstein J. Org Chem. 9 (2013) 1873–1880.
- [32] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G.A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H.P. Hratchian, A.F. Izmaylov, J. Bloino, G. Zheng, J.L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J.A. Montgomery Jr., J.E. Peralta, F. Ogliaro, M. Bearpark, J.J. Heyd, E. Brothers, K.N. Kudin, V.N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J.C. Buran, S.S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J.M. Millam, M. Klene, J.E. Knox, J.B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, R.L. Martin, K. Morokuma, V.G. Zakrzewski, G.A. Voth, P. Salvador, J.J. Dannenberg, S. Dapprich, A.D. Daniels, O. Farkas, J.B. Foresman, J.V. Ortiz, J. Cioslowski, D.J. Fox, Gaussian 09, Revision B.01, Gaussian, Inc., Wallingford CT, 2010.
- [33] V. Barone, M. Cossi, J. Phys. Chem. A 102 (1998) 1995-2001.
- [34] U. Mazzucato, F. Momicchioli, Chem. Rev. 91 (1991) 1679-1719.
- [35] G. Bartocci, A. Spalletti, U. Mazzucato, Conformational Analysis of Molecules in Excited States, in: J. Waluk (Ed.), Wiley-VCH, New York, 2000 chapter 5 and references therein.
- [36] G. Cooper, W.J. Irwin, J. Chem. Soc. Perkin I (1976) 75-80.
- [37] E.N. Gulakova, D.V. Berdnikova, T.M. Aliyeu, Y.V. Federov, I.A. Godovikov, O.A. Fedorova, J. Org. Chem. 79 (2014) 5533–5537 and references therein.
- [38] I. Baraldi, A. Spalletti, D. Vanossi, Spectrochim. Acta A 59 (2003) 75–86.
   [39] M. Montalti, A. Credi, L. Prodi, M.T. Gandolfi, Handbook of Photochemistry,
- Third Edition, CRC Press, 2006, pp. 500.
   [40] J. Revuelta, F. Madetti, S. Cicchi, Modern Heterocyclic Chemistry, vol. 1, in: J. Alvarez-Builla, J.J. Vaquero, J. Barluenga (Eds.), Wiley-VCH, 2011, pp. 809–813
- ch. 10.
  [41] V.K. Arora, T. Philip, S. Huang, Y.Z. Shu, Drug Metab. Dispos. 40 (2012) 1668–1676.