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Photochromic behavior of retinal analogs

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Abstract

New dihetarylethenic retinal analogs were synthesized, and their photochromic behavior was studied. The relationship between the compound structures and their spectral and kinetic parameters was determined due to the comparative spectral-kinetic studies of synthesized dihetarylethenes. It was shown, that all synthesized compounds possess expressed photochromic properties and the thermal irreversibility. The best kinetic characteristics for the photocyclization process as well as a low photodegradation were measured for short-chain nitrile.

Keywords: Photochromism; Diarylethenes; Retinal analogs; Retinoids

1. Introduction

Nowadays retinoids play a key role as converters of light energy into physiological signals in living cells. Definite stereoisomers of vitamin A aldehyde – retinal – are part of the chromophoric groups of retinal proteins. This class of proteins is responsible for important biological functions: light-driven proton and chloride ion transport (bacteriorhodopsin and halorhodopsin from *Halobacterium salinarum*), vision (visual pigments–rhodopsins), phototaxis (sensoric, phobo- or protorhodopsins) [1].

On the other hand, organic photochromic compounds attract increasing attention for applications in molecular devices, including sensors, optical switches, signal transducers and optical data storage [2–5]. Among them, diarylethene derivatives, developed by Irie et al., are very promising photochromic compounds due to their excellent fatigue resistance and thermal stability [6–11].

In order to elucidate the influence of terminal polar group nature as well as chain length on the photochromism of diarylethene vinylogs, we present our results of the study of spectral and photochromic properties of new hybrid retinoid derivatives (**I**, **III**–**V**) in this paper. We have developed and synthesized a novel retinoid molecular type, which merged a photochromic diarylethenic moiety with conjugated polyenic chain ending with a terminal formyl group.

2. Experimental

^{1}H NMR spectra were recorded on a Bruker DPX-300 spectrometer in $CDCl_3$ with the working frequency of 300 MHz. Chemical shifts are given in ppm relative to tetramethylsilane or $CDCl_3$ as the internal standards (δ 0.00 ppm and δ 7.24 ppm, correspondently). The spin–spin coupling constants are in Hz.

Electron impact (EI, IE 70 eV) mass spectra were recorded on a Kratos model MS-30.

The qualitative composition of the reaction mixtures and the homogeneity of the compounds were determined by TLC on Kieselgel 60 F_{254} plates (Merck) or on Silufol UV-254 plates (Kavalier) in the following solvent mixture: hexane–ethyl acetate, 4:1. The spots were visualized under UV light.

The preparative adsorption column chromatography was performed on Kieselgel 60 (0.040–0.063 mm, Merck).

All solvents were purified and dried according the standard procedures, and the 1.5 M toluene solution of DIBAL (Aldrich) was used in the experimental work.

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All operations with oxygen-sensitive reagents were carried out under argon atmosphere.

The spectral-kinetic studies were performed in solution in quartz cells with a 0.2 cm thickness, and toluene or ethanol of a high purity grade was used as a solvent. The solution concentrations of photochromic compounds were 2×10^{-4} M.

The UV–vis spectra were recorded on a Cary Bio-50 spectrophotometer (Varian) in the spectral range of 280–800 nm. Photo-induced absorption spectra were obtained after the irradiation with filtered light of lamp LC-4 (Hamamatsu).

The photocoloration and photobleaching kinetic curves were obtained under UV and visible light irradiation separated by the suitable glass filters. The kinetic studies of the photocoloration, the photobleaching and the photodegradation processes of examined compounds solutions were carried out on fiber–optic spectrophotometer model USB2000 (Ocean Optics) and Hg-lamp (DRSH-250).

Maxima of the absorption spectra of the initial $\mathbf{A}(\lambda^{A}_{max})$ and photo-induced $\mathbf{B}(\lambda^{B}_{max})$ forms were measured with the use of the spectrophotometer Cary 50 (Varian). The cyclic form **B** was prepared by UV irradiation (with $\lambda = 313$ nm) of Hg-lamp (DRSH-250) through the glass UV filter. For the comparative analysis of spectral-kinetic parameters all measurements were carried out in the same experimental conditions. The value of photo-induced optical density (ΔD_B), as well as the rate constants for photocoloration (k_{AB}, s^{-1}) and photobleaching (k_{BA}, s^{-1}) were calculated from these curves. Photodegradation processes were studied under unfiltered light of Hg-lamp (DRSH-250). The value of photodegradation was characterized by a decrease of photo-induced optical density for the photostationary state at the absorption maximum of the B form by one half ($t_{0.5}$, s). Solutions were stored in the darkness between measurements.

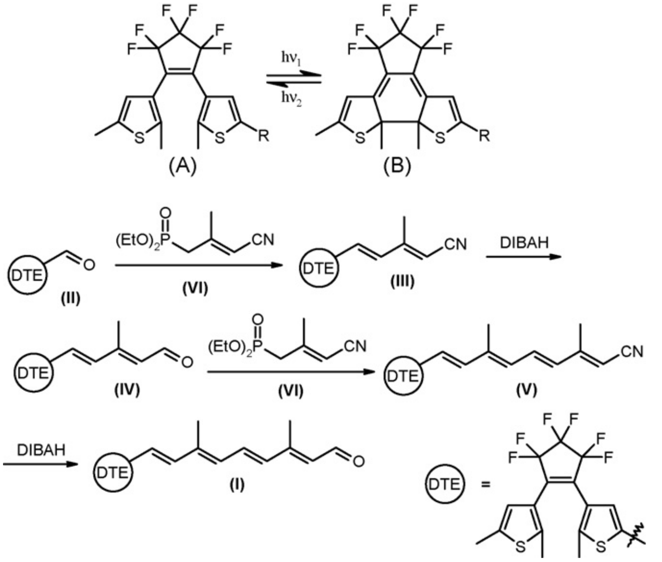
The substituted dihetarylethenes were used as the research subjects.

The starting compound: 1-(2,5-dimethylthien-3-yl)-2-(2-formyl-5-methylthien-3-yl)perfluorocyclopentene (**II**) was prepared according to the previously published procedure [12,13].

Dihetarylethenes (**I**, **III**, **IV**, **V**) were synthesized according to the synthetic route of retinoid derivatives preparation designed by us earlier (Scheme 1) [14–17].

2.1. *(1E,3E)-1-[2-(4-Cyano-3-methyl-1,3-butadien-1-yl)-5-methylthien-3-yl]-2-(2,5-dimethylthien-3-yl)perfluorocyclopentene (**III**)*

A 60% suspension of sodium hydride (25 mg, 0.63 mmol) in mineral oil washed with anhydrous hexane (3 ml × 5 ml) and anhydrous tetrahydrofuran (30 ml) was added to the residue. Then phosphonate (**VI**) (116 mg, 0.54 mmol) was added dropwise using a syringe to the resulting mixture, which was vigorously stirred at 0 °C. After complete NaH disappearance (1 h), a solution of 1-(2,5-dimethylthien-3-yl)-2-(2-formyl-5-methylthien-3-yl)perfluorocyclopentene (**II**) (200 mg, 0.49 mmol) in anhydrous THF (10 ml) was added dropwise using a syringe to the resulting solution. The reaction mixture was cooled for 30 min with permanent stirring and quenched with water (5 ml), acidified with 0.1 M aqueous hydrochloric acid to pH 5 and extracted with chloroform (3 ml × 100 ml). The organic layers were combined, dried and concentrated. The crude product was purified by column chromatography on silica gel using *n*-hexane/ethyl acetate mixture, 3:1 (v/v), as eluent to give pure compound (**III**). Recrystallization from methanol gave compound (**III**) as white crystals (yield: 208 mg, 90%; mp 123–124 °C; R_f 0.60).



Scheme 1. Synthetic route for the preparation of the diarylethenic retinal analog (**I**).

^{1}H NMR data are presented in Table 1.

UV–vis spectrum [λ_{max}, nm, ethanol (log ε)]: 276 (4.41), 338 (4.74).

2.2. *(1E,3E)-1-(2,5-Dimethylthien-3-yl)-2-[2-(4-formyl-3-methyl-1,3-butadien-1-yl)-5-methylthien-3-yl]perfluorocyclopentene (**IV**)*

A solution of (1*E*,3*E*)-1-[2-(4-cyano-3-methyl-1,3-butadien-1-yl)-5-methylthien-3-yl]-2-(2,5-dimethylthien-3-yl)perfluorocyclopentene (**III**) (208 mg, 0.44 mmol) in anhydrous toluene (25 ml) was cooled to −80 °C and a 1.5 M solution of DIBAH in toluene (0.3 ml) was added, then the reaction mixture was stirred until the temperature increased to 0 °C (~40 min). Then the reaction mixture was diluted with methanol (3 ml), the solvent was evaporated, then the residue was poured in water (50 ml), acidified with 10% aqueous sulfuric acid to pH 4, and extracted with dichloromethane (3 ml × 50 ml). The organic layers were combined, dried over anhydrous sodium sulfate and concentrated. The crude product was purified by column chromatography on silica gel using *n*-hexane/ethyl acetate mixture, 3:1 (v/v), as eluent to give pure compound (**IV**) (yield: 94 mg, 45%; mp 117–118 °C; R_f 0.48).

^{1}H NMR data are presented in Table 1.

UV–vis spectrum [λ_{max}, nm, ethanol (log ε)]: 270 (shoulder), 355 (4.78).

Table 1
^{1}H NMR data for compounds (**I**, **III**, **IV**)

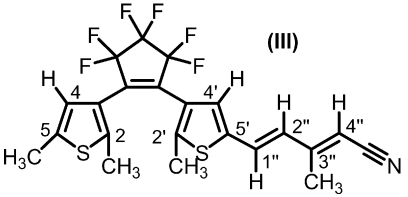
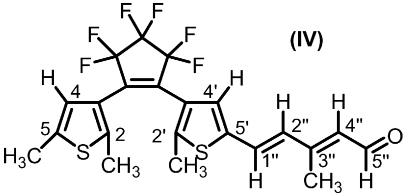
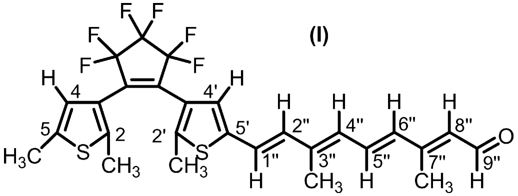
Compound structure		1″–H	2″–H	3″–CH$_3$	4″–H	5″–H	6″–H	7″–CH$_3$	8″–H	9‴–H	Remarks
 **(III)**	δ (ppm)	6.90 d	6.49 d	2.21 s	5.26 s						6.68, 7.08: 4, 4′–H (thienyl); 1.83, 1.89: 2, 5–CH$_3$ (thienyl); 2.39: 2′–CH$_3$ (thienyl)
	J (Hz)	16.0	16.0	–	–						
		1H	1H	3H	1H						
 **(IV)**	δ (ppm)	7.07 d	6.56 d	2.32 s	6.01 d	10.11 d					6.68, 7.09: 4, 4′–H (thienyl); 1.84, 1.89: 2, 5–CH$_3$ (thienyl); 2.40: 2′–CH$_3$ (thienyl)
	J (Hz)	16.0	16.0	–	7.8	7.8					
		1H	1H	3H	1H	1H					
 **(I)**	δ (ppm)	6.75 d	6.59 d	2.06 s	6.33 d	7.12 dd	6.43 d	2.35 s	6.01 d	10.13 d	6.72, 7.00: 4, 4′–H (thienyl); 1.87, 1.89: 2, 5–CH$_3$ (thienyl); 2.43: 2′–CH$_3$ (thienyl)
	J (Hz)	16.0	16.0	–	11.5	11.5/15.1	15.1	–	7.8	7.8	
		1H	1H	3H	1H	1H	1H	3H	1H	1H	

Table 2
Spectral-kinetic characteristics of the synthesized dihetarylethenes (**I**–**V**)

Compounds	λ^{A}_{max} (nm)		λ^{B}_{max} (nm)		ΔD_B[a]	k_{AB}/k_{BA}[a]	$t_{0.5}$ (s)[a]
	Toluene	Ethanol	Toluene	Ethanol			
(**II**)	295	–	380, 580	–	0.4[b]	1.4	340
(**III**)	340	276, 338	585	576	0.2	7.8	660
(**IV**)	353	355	585	580	0.2	5.9	275
(**I**)	390, 400	390, 402	380, 553	392, 409, 579	0.5	2.6	240

Note: λ^{A}_{max} and λ^{B}_{max}, absorption band maxima of the open and closed (cyclic) forms, correspondently; ΔD_B, the amount of photo-induced change in the optical density at the absorption bands maximum of the cyclic form at the VIS spectrum; k_{AB} and k_{BA}, photocoloration and photobleaching rate constants (s^{-1}), correspondingly; $t_{0.5}$ (s), time for irreversible decreasing of photo-induced optical density at the absorption band maximum of the cyclic form for two times under permanent irradiation with unfiltered light from the Hg-lamp (DRSH-250).

[a] In toluene.

[b] At 580 nm.

2.3. (1E,3E,5E,7E)-1-[2-(8-Cyano-3,7-dimethyl-1,3,5,7-octatetraen-1-yl)-5-methylthien-3-yl]-2-(2,5-dimethylthien-3-yl)perfluorocyclopentene (V)

The compound (**V**) was prepared according to a similar synthetic procedure for compound (**III**) from (1*E*,3*E*)-1-(2,5-dimethylthien-3-yl)-2-[2-(4-formyl-3-methyl-1,3-butadien-1-yl)-5-methylthien-3-yl]perfluorocyclopentene (**IV**) (94 mg, 0.20 mmol) (yield: 88 mg, 83%). This compound was used in the next step of the synthesis without an additional purification.(1*E*,3*E*,5*E*,7*E*)-1-[2-(3,7-Dimethyl-8-formyl-1,3,5,7-octatetraen-1-yl)-5-methylthien-3-yl]-2-(2,5-dimethylthien-3-yl)perfluorocyclopentene (**I**)

The compound (**I**) was prepared according to a similar procedure for compound (**IV**) from (1*E*,3*E*,5*E*,7*E*)-1-[2-(8-cyano-3,7-dimethyl-1,3,5,7-octatetraen-1-yl)-5-methylthien-3-yl]-2-(2,5-dimethylthien-3-yl)perfluorocyclopentene (**V**) (88 mg, 0.16 mmol) (yield: 35 mg, 39%; R_f 0.43).

The analytical sample of aldehyde (**I**) was purified by preparative reverse-phase HPLC.

^{1}H NMR data are presented in Table 1.

UV–vis spectrum [λ_{max}, nm, ethanol ($\log \varepsilon$)]: 390 (shoulder), 402 (4.73), 420 (shoulder).

Mass spectrum (m/z; I_{rel}, %): 542 ([M^+] (55)), 527(71), 511(82), 473(84), 380(89).

3. Results and discussions

The dihetarylethenes (**I**–**IV**) represented in Scheme 1 are thermally irreversible photochromic compounds that undergo the reciprocal photo-induced transformations of the "open" (**A**, colorless) form and the cyclic "closed" (**B**, colored) form only. The photocoloration of these compounds takes place under the UV-irradiation absorbed by the "open" form **A**. The photobleaching occurs under the vis-irradiation with spectral distribution which was defined by the cyclic form **B** absorption band.

The results of synthesized retinoids spectral-kinetic studies are presented in Figs. 1–4 and Table 2.

The spectral-kinetic data obtained for the starting compound (**II**) were used for the comparison with other experimental data.

The absorption spectra of the open form **A** and the closed form **B** of this compound during the continuous UV-illumination were shown in Fig. 1 (the curve 1 and the curves 2–7, correspondently).

It was shown that the short-wave band disappeared under the UV-irradiation.

Two new absorption bands with λ_{max} 380 nm and λ_{max} 580 nm, caused by the cyclic form formation, appeared simultaneously.

The replacement of the aldehyde group with polyenic fragment ending with a terminal nitrile group in the molecule of nitrile (**III**) stimulates the appearance of the open form **A** absorption band with λ_{max} 340 nm, which lacked from the spectrum of the aldehyde (**II**) (Fig. 2a). This band intensity decreased under the UV-irradiation, and the cyclic form **B** absorption band appeared synchronously at 585 nm (see Fig. 2a).

The compound (**IV**) with terminal formyl group demonstrated the similar photo-induced spectral changes (Fig. 2b).

It was interesting to show that the spectral characteristics of both the open form **A** and the closed form **B** for dihetarylethenes (**III**, **IV**) slightly depend on the terminal polar group nature, and obviously, that they are defined by the conjugation chain length only. As evident from Table 2, the introduction of the polyenic chain into the molecules of retinoids (**III**, **IV**) shifts the absorption maximum of the open form **A** to the long-wave spec-

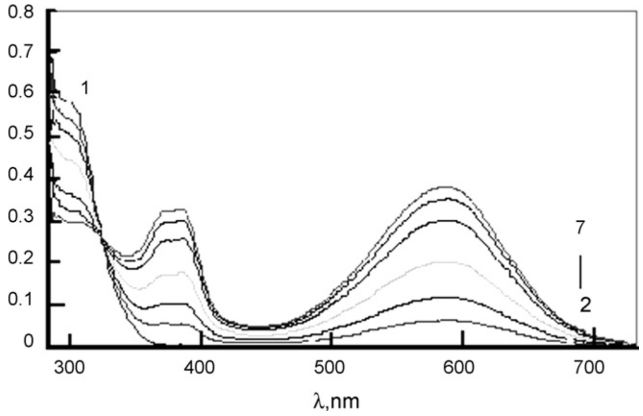


Fig. 1. The absorption spectra of compound (**II**) solution in toluene before (1) and during (2–7) the UV-irradiation.

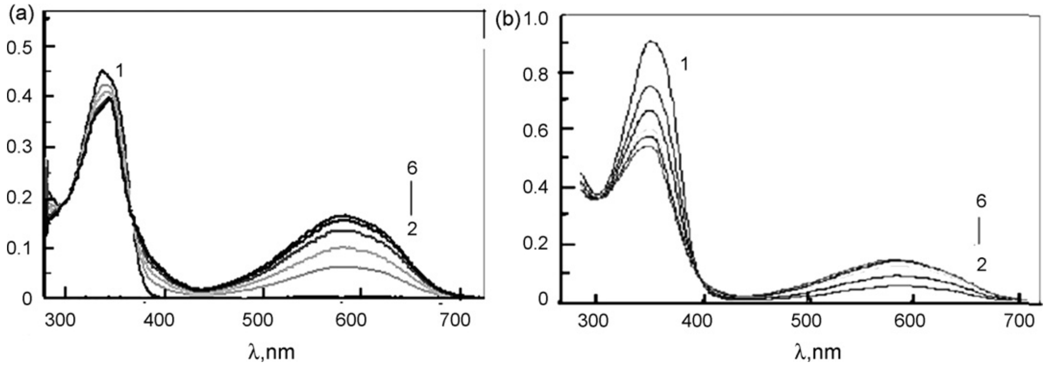


Fig. 2. (a) The absorption spectra of compound (**III**) solution in toluene before (1) and during (2–6) the UV-irradiation. (b) The absorption spectra of compound (**IV**) solution in toluene before (1) and during the UV-irradiation (2–6).

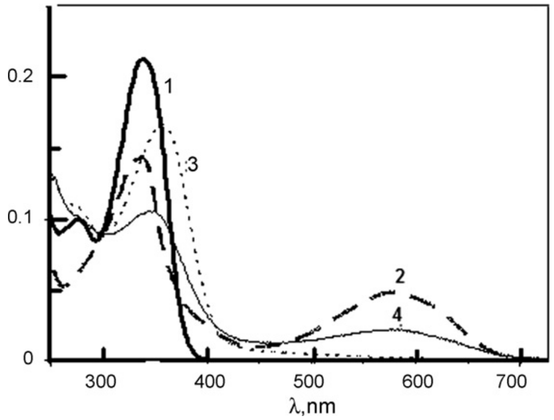


Fig. 3. The absorption spectra of compound (**III**) (curves 1, 2) and (**IV**) (curves 3, 4) solutions in ethanol before (curves 1, 3) and after (curves 2, 4) UV-irradiation.

tral region as compared with aldehyde (**II**). Besides, in contrast to the compound (**II**) which was characterized with the photo-induced absorption band appearance at 380 nm, the decrease in the intensity of the absorption band **A** initially existed in the same spectral region for the compounds (**III**, **IV**) was observed. The distances between the maxima of the absorption bands of **A** and **B** forms were 232–243 nm for the compounds (**III**, **IV**), that agree with the data obtained for the dihetarylethenic derivatives of the carotenoids [11]. The photochromic reactions of all investigated compounds show only slight solvent and wavelength dependences (compare data from Fig. 2a and b with Fig. 3; Fig. 4a with Fig 4b).

The further chain elongation in the polyenal (**I**) stimulated significant changes of the cyclic form **B** absorption spectra (Fig. 4a and b), namely, it resulted in the bathochromic shift of the long-wave absorption band of form **A** for 43–56 nm and the hypsochromic shift of the absorption band form **B** for 32 nm as compared with dihetarylethenes (**III**, **IV**).

In contrast to spectral properties of the short-chain dihetarylethenes (**III**, **IV**) the UV-band absorption intensity of the closed form **B** of polyenal (**I**) increased under the UV-irradiation, that was similar to the photo-induced spectral changes of aldehyde (**II**). The distance between the maxima of the absorption bands of forms **A** and **B** decreased to 156 nm comparing with 232–245 nm for the compounds (**III**, **IV**). In the case of the spectrum of the closed form **B** of polyenal (**I**) in the toluene solution, the conjugation between dihetarylethenic unit and polyenic chain is interrupted due to changes in the polyenic chain–thienyl ring conformation, what leads to hypsochromic shift of the position of the absorption band maximum. This effect is not observed in ethanolic solution (Fig. 4a and b).

The analysis of kinetic data of the photo-transformation processes of these compounds demonstrated the relationship between measured parameters and compound structures (Table 2).

Data in Table 2 demonstrated that the amount of photo-induced optical density of the cyclic form in the photostationary

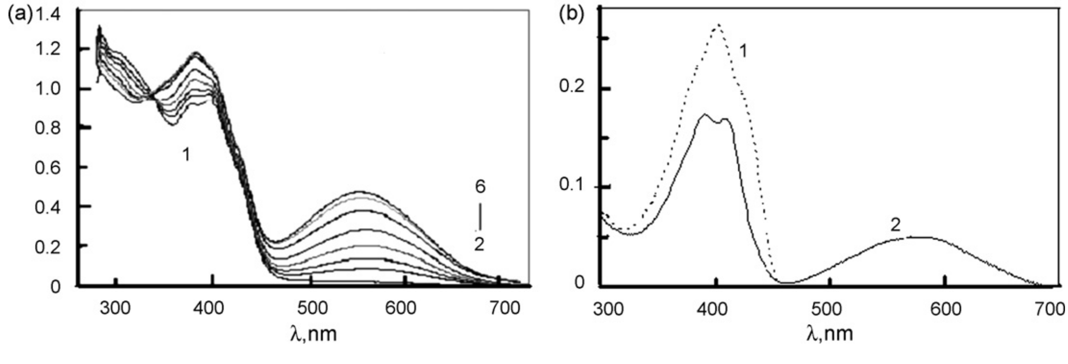


Fig. 4. (a) The absorption spectra of compound (**I**) solution in toluene before (1) and during (2–8) the UV-irradiation. (b) The absorption spectra of compound (**I**) solution in ethanol before (1) and after (2) the UV-irradiation.

state decreased for dihetarylethenes (**III**, **IV**) in comparison with the compound (**II**).

The compound (**I**) was the exception to other tested compounds, because its light-sensitivity value was congruent with the same value for the starting compound (**II**), but the increase of the long-wave absorption band intensity at the UV-range of spectrum was observed for these two compounds (see Fig. 1 and 4a). It can be proposed, that the chemical structure of the compound (**I**) determines its photocoloration efficiency.

The analysis of the ratio between photocoloration and photobleaching constants of studied compounds shows that retinal-containing compounds were characterized with more effective photocoloration rate compared with the compound (**II**), but the photocoloration rate would be decreased when the retinal chain would be elongated.

When photodegradation data of synthesized compounds, represented in Table 2, were compared, it was shown, that compound (**III**) containing the nitrile electron acceptor group possessed the best resistance to fatigue. It was found, that further elongation of retinal chain results in increase in photodegradation efficiency.

4. Conclusion

The relationship between the compounds structures and their spectral and kinetic parameters was determined due to the comparative spectral-kinetic studies of the synthesized retinal-contained dihetarylethenes.

It was shown, that all synthesized compounds possess expressed photochromic properties and thermal irreversibility.

It was found that the introduction of polyenic chain conjugated with diarylethenic moiety leads to bathochromic shift of the absorption maximum of open form **A** ($\Delta\lambda$ 105 nm), as compared with initial aldehyde (**II**). The position of absorption maximum of open form **A** of compounds (**III**, **IV**, **I**) slightly depends on nature of terminal polar group and is defined mostly by conjugated chain length.

For closed isomers, position of absorption maximum depends slightly on the conjugation chain length of the retinoids, most probably, due to changes in polyenic chain–thienyl ring conformation, that leads to hypsochromic shift of the absorption band maximum in toluene solution of polyenal (**I**).

The best kinetic characteristics for the photocyclization process as well as low photodegradation were measured for nitrile (**III**).

Acknowledgments

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