Synthesis and studies of photochromic properties of spirobenzopyran carboxy derivatives and their model compounds as potential markers

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A number of photochromic markers, *viz.*, spirobenzopyrans containing one or two active carboxy groups attached directly or through a spacer, as well as their model derivatives, were synthesized. The obtained compounds were characterized by instrumental methods of analysis. Spectrokinetic methods were used to study the behavior of the spirobenzopyran markers and the model derivatives in solutions in EtOH and toluene.

Key words: spiropyran, Horner—Emmons olefination, Knoevenagel condensation, photochromic markers.

Introduction of photosensitive groups in the molecules possessing biological activity makes possible in prospect the development of optobioelectronic devices. These devices will be used as materials for recording information, photocontrolled highly selective systems of molecular isolation/purification, and therapeutic agents activated in the required zones.[1]

Among other photochromes, spirobenzopyrans are used the most frequently for these purposes.[2—4] In the majority of works devoted to this issue, the addition to the substrate was directed at position N(1) of the indoline fragment of spiropyran molecule modified by an active group.[5—7] In the present work, we have chosen a terminal carboxy group as the active site, since the conjugation of such key derivatives with various substrates is well studied. A carboxy group can be activated by various methods (carbodiimide, azide, carboxyanhydride, using mixed anhydrides, activated esters, *etc.*). As a rule, an attack by an activated carboxy group is directed on the sterically accessible ε-amino groups of amino acid moieties of lysine (the reaction with the serine, threonine, tyrosine moieties is less efficient and, besides, the stability of the ester group under physiological conditions is considerably lower than that of the amide group). The conjugating agent (chemical activation of the carboxy group) should be chosen based on the properties and characteristics of the target molecule, and the conditions of conjugation should not cause destruction or significant loss in activity of the biopolymer. The properties of the substrate can be controlled because of the close spatial interaction of a dye with the active center or due to the change in the hydrophilic-hydrophobic surrounding of the object/active center.[8]

Special attention should be paid to the works, in which biepitopic markers are used. Thus, in the works[9,10] a new spiropyran derivative containing activated β-carboxyethyl spacers with the terminal hydroxysuccinimide ester groups at two position of the molecule were used to control the folding process of the short peptide molecules.

The present work, being a continuation of the earlier started studies,[11] is devoted to the synthesis and studies of properties of photochromic spiropyrans containing various active terminal groups in the indole and pyran fragments of the molecule. These compounds can be of interest for the addition or covalent binding of separate sites of macromolecules between each other and subsequent control of their properties through a photochromic reaction.

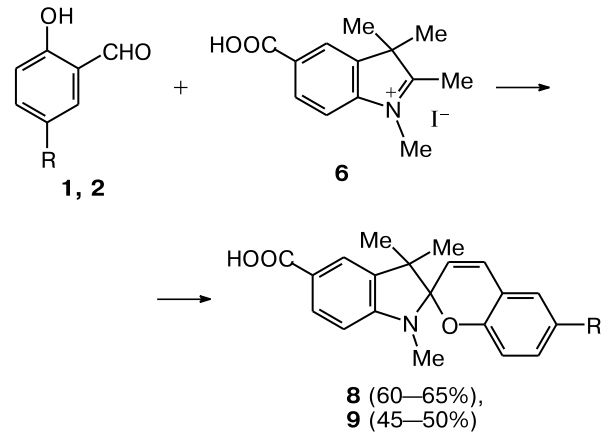
Results and Discussion

Synthesis of spirobenzopyrans. A classic approach to the preparation of spiropyrans is the condensation of 2-hydroxybenzaldehyde derivatives **1**—**5** with substituted 1,2,3,3-tetramethylindoleninium iodide **6** (Scheme 1) or 1,3,3-trimethyl-2-methyleneindolenine **7**[12—20] (Scheme 2).

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 9, pp. 2026—2035, September, 2014.
1066-5285/14/6309-2026

We used this approach to synthesize a number of the target and the intermediate spirobenzopyrans **8**—**14**.

Scheme 1



R = COOH (**1**, **8**), NO_2 (**2**, **9**)

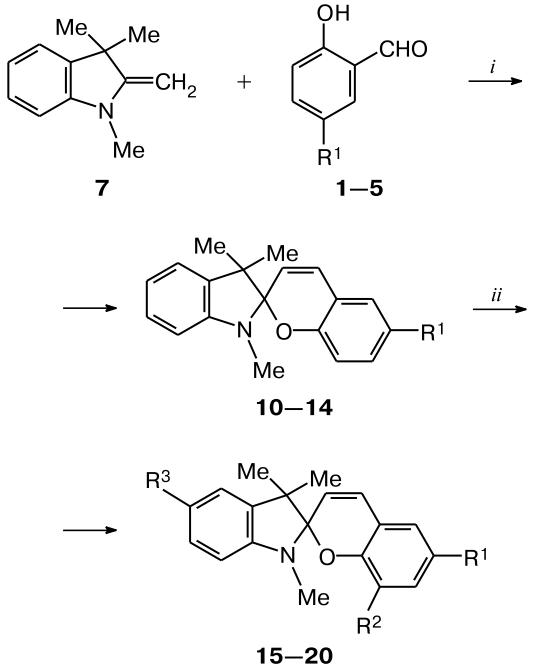
Reagents: *i*. 1) Et_3N, EtOH; 2) HCl.

The carboxy groups were introduced in the structure of spiropyrans either in two steps by olefination of the carbonyl precursor and subsequent saponification of formed esters under standard conditions, or by the Knoevenagel reaction carried out in a mixture of piperidine—pyridine. A general approach to the synthesis of spiropyrans containing carboxy groups is given in Scheme 3. For realization of this synthetic strategy, in the present work we synthesized the formyl precursors of carboxy spiropyrans **15—20** by the Duff reaction, using an approach developed by us earlier[21] (see Scheme 2).

Triethyl phosphonoacetate (C_2-phosphonate) was used for the Horner—Emmons olefination of aldehydes **14** and **16—20**. The phosphonate anions were generated using NaH (a 60% suspension in mineral oil) in THF at 0 °C and the ratio of reagents SP-CHO : C_2-phosphonate : NaH = 1 : 1.2 : 1.2 (method ***A***). This reaction results in the model esters **21**—**26**. Carboxy derivatives **27**—**29** were obtained by saponification of esters **21**—**24** with KOH (2 equiv.) in a mixture of MeOH : water = 5 : 1 (method ***B***) or the heating the starting spiropyrans **14**—**16** and **20** with malonic acid (2 equiv.) in the presence of piperidine (method ***C***). According to the ^{1}H NMR spectroscopy data, the newly formed C=C bonds have predominantly *E*-configuration in all the cases. The data in Table 1 demonstrate that the yields of carboxy derivatives **27**—**29** obtained by the Knoevenagel reaction are higher than those in the two-step procedure.

As a model of photochromic crosslink **30** in the substrate structure the most suitable for biological conditions, we synthesized compound **31**, in which the *n*-butylamide terminal groups serve as the models of the lysine moieties in protein. The model diamide **31** was synthesized in high yield from bis-carboxy derivative **30** using the system of reagents isobutyl chloroformate—*N*-methylmorpholine—*n*-butylamine in anhydrous dichloromethane (method ***D***).

Scheme 2



Reagents: *i*. EtOH; *ii*. Hexamethylenetetramine (HMTA), TFA.

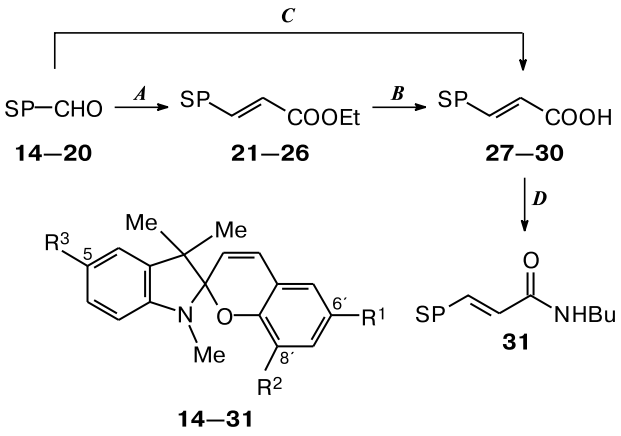
Compounds **1**—**5**, **10**—**14**	R^1	Yields of compounds **10**—**14** (%)
1, **10**	COOH	60—65
2, **11**	NO_2	75—85
3, **12**	COOEt	65—70
4, **13**	COOMe	65—70
5, **14**	CHO	70—75

Compounds **15**—**20**	R^1	R^2	R^3	Yield (%)
15	COOH	H	CHO	45—55
16	NO_2	H	CHO	70—80
17	COOEt	H	CHO	55—60
18	COOMe	H	CHO	45—55
19	COOMe	CHO	CHO	15—20
20	CHO	H	CHO	65—75

The presence of the activated carboxy group not always can assist in the efficient introduction of markers in the substrate because of steric and electrostatic factors in the site of binding. In such cases, the use of markers with different spacer length can prove efficient. In the present work, we suggest a convenient method for the modification of carboxy spacer by its elongation through the amide group (Scheme 4).

The activation of the carboxy group of spiropyran **9** using *N*,*N*-carbonyldiimidazole (CDI) led to the imidazole derivative, which smoothly reacted *in situ* with ethyl

Scheme 3*



Reagents and conditions: ***A***. 1) NaH, THF, 0 °C, 40 min; 2) $(EtO)_2P(O)CH_2COOEt$; ***B***. KOH, MeOH, 50 °C; ***C***. $CH_2(COOH)_2$, pyridine, piperidine, 100 °C; ***D***. 1) isobutyl chloroformate, *N*-methylmorpholine, 4-dimethylaminopyridine (DMAP), –70 °C, 30 min; 2) *n*-butylamine, 0 °C, 2 h.

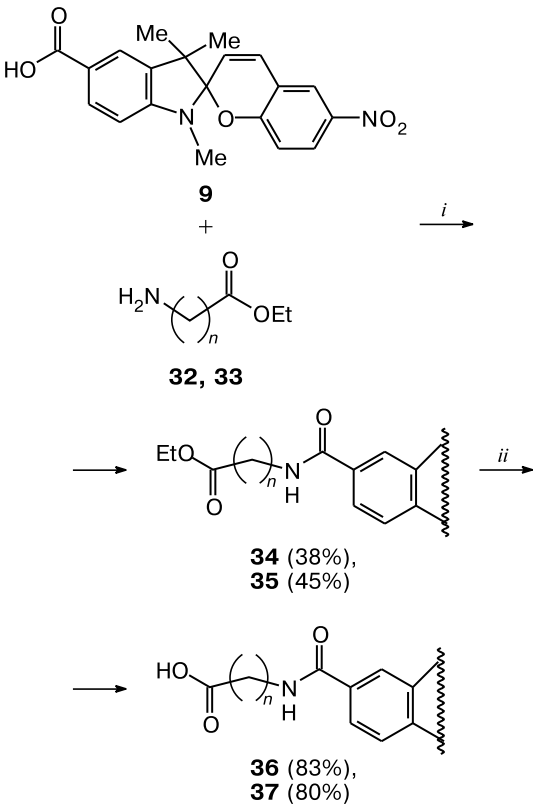
* SP is the spiropyran moiety. Substituents R^1, R^2, and R^3 for spiropyrans **21**—**31** are given in Table 1.

esters of β-alanine **32** or 6-aminohexanoic acid **33** to obtain the intermediate esters **34** and **35** in moderate yields. The saponification of esters **34** and **35** under mild conditions gave the target carboxy-substituted spiropyrans **36** and **37** in high yields.

Spirobenzopyran carboxy-substituted markers **8**, **9**, **27**—**30**, **36**, **37** and their model compounds **12**, **13**, **21**—**26**, **31**, **34**, **35** were obtained in preparative amounts and characterized by instrumental methods of analysis.

Studies of photochromic properties of spiropyrans. Traditionally, we carry out the studies of the photochromism (Scheme 5) of new compounds in solutions in polar ethanol

Scheme 4



n = 2 (**32**, **34**, **36**), 5 (**33**, **35**, **37**)

Reagents and conditions: *i*. CDI, DMF; *ii*. LiOH, THF, H_2O.

(Table 2) and low polar toluene (Table 3). As it was expected, the colorability of spiropyrans possessing no strong electron-withdrawing substituents has proved considerably lower than that of compounds with a nitro group in the pyran ring of the molecule.

Table 1. Synthesis of carboxy derivatives of spiropyrans **21**—**30** and diamide **31**

Spiropyran	R^1	R^2	R^3	Starting compound	Method	Yield (%)
21	CH=CHCOOEt	H	H	**14**	***A***	90—95
22	NO_2	H	CH=CHCOOEt	**16**	***A***	90—95
23	COOEt	H	CH=CHCOOEt	**17**	***A***	90—95
24	COOMe	H	CH=CHCOOEt	**18**	***A***	90—95
25	COOMe	CH=CHCOOEt	CH=CHCOOEt	**19**	***A***	85—90
26	CH=CHCOOEt	H	CH=CHCOOEt	**20**	***A***	85—90
27	CH=CHCOOH	H	H	**21**	***B***	45—50
				14	***C***	30—35
28	NO_2	H	CH=CHCOOH	**22**	***B***	45—50
				16	***C***	50—55
29	COOH	H	CH=CHCOOH	**23** or **24**	***B***	20—25
				15	***C***	45—50
30	CH=CHCOOH	H	CH=CHCOOH	**20**	***C***	40—50
31	CH=CHCONHBn	H	CH=CHCONHBn	**30**	***D***	45—50

Table 2. Spectrokinetic characteristics of spiropyran derivatives in EtOH

Compound	λ_{max}^{A}	λ_{max}^{B}	$\Delta D_B^{phot}{}_{max}$	k_{BA}^{db}/s^{-1}
	nm			
10	290	553	0.040	0.089
12	290	550	0.200	0.064
13	290	550	0.230	0.058
21	348 sh, 318, 265	592	0.080	0.250
22*	347, 260 sh	565	0.250	0.023
23	348	570	0.023	0.220
24	348	570	0.025	0.180
25	347, 281 sh	580	0.023	0.080
26	348, 265 sh	613	0.015	0.390
27	340 sh, 308, 260	592	0.050	0.240
28	342, 262 sh	558	0.230	0.011
29	348	569	0.010	0.190
30	344, 262	613	0.007	0.300
31	340, 310 sh, 261	615	0.025	0.450

Note. Here and in Table 3, λ_{max}^{A} and λ_{max}^{B} are the absorption maxima of the starting (spiro) and photoinduced (merocyanine) forms, respectively; $\Delta D_B^{phot}{}_{max}$ is the maximal photoinduced change of optical density in the absorption maximum of the photoinduced form in the photoequilibrium state with the identical optical density values ($D \approx 0.5$) in the absorption maximum of the starting form; k_{BA}^{db} is the rate constant of the photobleaching reaction; $t_{0.5}$ is the time during which the maximum value of photoinduced optical density in the absorption maximum of the photoinduced form ($D_B^{phot}{}_{max}$) decreases to a one-half under continuous irradiation with nonfiltered light of a Lightingcure LC8 lamp. The increase of $\Delta D_B^{phot}{}_{max}$ indicates an increase in colorability, the increase of k_{BA}^{db} indicates an acceleration of photobleaching, whereas the growth of $t_{0.5}$ indicates an increase in photostability and *vice versa*.

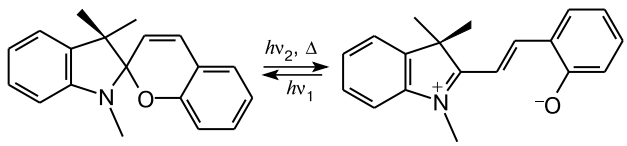
* $t_{0.5}$ = 306 s, for other compounds no decrease of $D_B^{phot}{}_{max}$ was observed during the standard time of the experiment (400 s).

Table 3. Spectrokinetic characteristics of spiropyran derivatives in toluene

Compound	λ_{max}^{A}	λ_{max}^{B}	$\Delta D_B^{phot}{}_{max}$	k_{BA}^{db}	$t_{0.5}$
	nm			s^{-1}	
10	293	608 sh, 572	0.130	0.158	61
12	293	612 sh, 578	0.110	0.162	48
13	294	613 sh, 578	0.150	0.153	46
21	318	655 sh, 608, 566 sh	0.055	0.400	37
22	345	623, 582 sh	0.350	0.051	16
23	345	635 sh, 595	0.005	0.540	90
24	344	640 sh, 595, 530 sh	0.005	0.420	85
25	343	625, 535 sh	0.011	0.046	72
26	345	670 sh, 620, 565 sh	0.007	0.420	60
27	321	654 sh, 608, 560 sh	0.045	0.420	29
28	346	623, 582 sh	0.300	0.061	12
29	410 sh, 345	—*	—*	—*	—*
30	345	670 sh, 620	0.006	0.430	50
31	328	620	0.004	0.440	39

* Values were not determined because of insufficient solubility.

Scheme 5



Spiropyran (SP) Merocyanine (MC)

Comparing the data obtained for the solutions of photochromic compounds shows that on going from ethanol to toluene, the photostability significantly decreases and the dark photobleaching significantly accelerates. In addition, several absorption bands of the photoinduced (PI) form were found in toluene (Figs 1—4). These phenomena are explained by the fact that in ethanol there is a possibility of stabilization of the PI molecule of the merocyanine (MC) form through the formation of hydrogen bonds of the MC form with the solvent molecules, whereas in the low polar aprotic toluene, the polar MC form can exist in various aggregated states.[22—26]

The studies of the photochromic behavior of the photochromic crosslink **30** and its model compounds **26** and **31** showed that, bearing weak electron-withdrawing substituents, these products expectedly undergo insignificant photocoloring. However, when the polarity of the solvent increases on going from toluene to ethanol, the colorability considerably increases; the order of the photocoloring improvement is as follows: acid (**30**) < ester (**26**) < diamide (**31**). It can be predicted that on going to the solu-

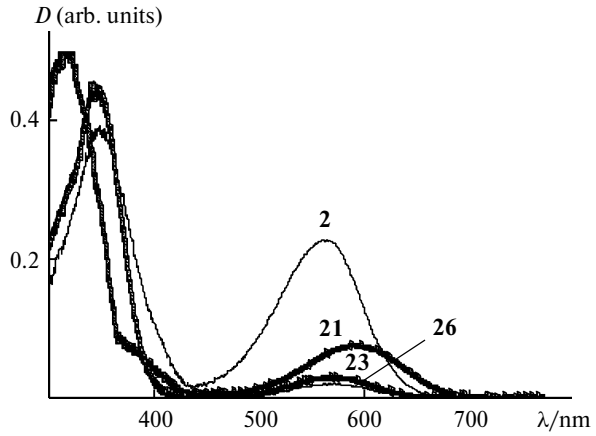


Fig. 1. Absorption spectra of spiropyrans **2**, **21**, **23**, and **26** ($c \approx 1 \cdot 10^{-5}$ mol L^{-1}) after UV irradiation in EtOH, 25 °C.

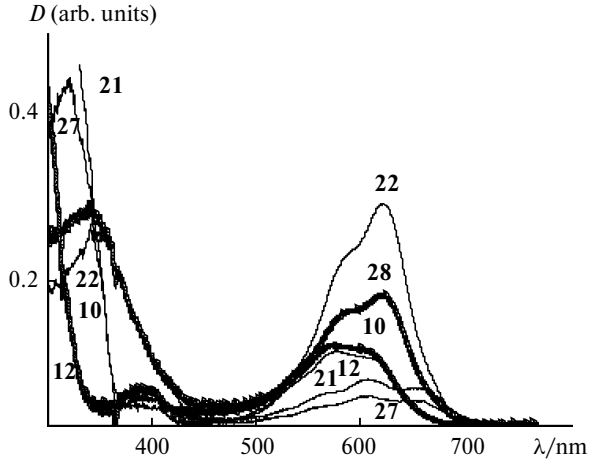


Fig. 2. Absorption spectra of spiropyrans **10**, **12**, **21**, **22**, **27**, and **28** ($c \approx 1 \cdot 10^{-5}$ mol L^{-1}) after UV irradiation in toluene, 25 °C.

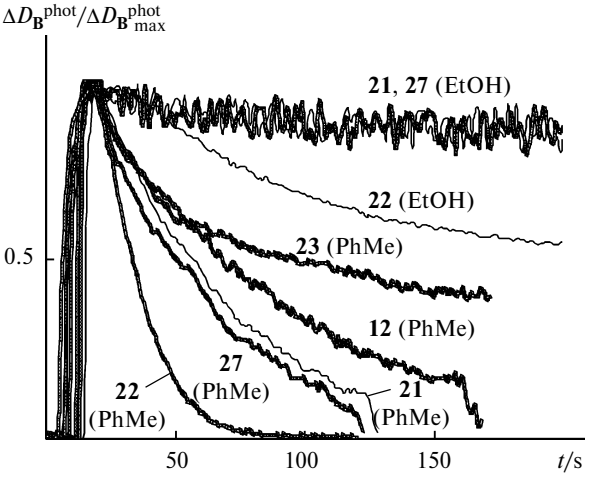


Fig. 3. Normalized curves of photodegradation of spiropyrans **12**, **21**—**23**, and **27** ($c \approx 1 \cdot 10^{-5}$ mol L^{-1}) recorded on the wavelength of the absorption maximum of the PI MC form in EtOH and toluene, 25 °C. Here and in FIg. 4, ΔD_B^{phot} is the change in optical density of the photoinduced form upon UV irradiation.

tions close in properties to physiological media (DMSO, aqueous buffer), the coloring of these compounds will significantly improve. In this case, the cyclic spiropyran form presumably will be the starting form, in contrast to the data in the works,[9,10] according to which the starting photochromes exist in the colored MC form.

We compared the carboxy-containing spiropyrans **27**—**30** and their model derivative **21**—**23** and **26** in toluene and ethanol (Table 2, 3) and found a number of specific features of the photochromic behavior on going to models **21**—**23** and **26**: their colorability and stability increased, whereas bleaching upon storage in dark accelerated in the case of ethanol and retarded in the case of toluene.

We should also mention some regularities observed in the photochromic behavior on going from ethyl esters **10**

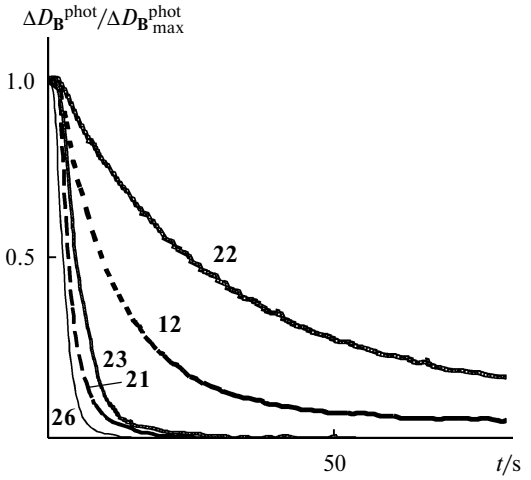


Fig. 4. Normalized kinetic curves of dark bleaching of spiropyrans **12**, **21**—**23**, and **26** ($c \approx 1 \cdot 10^{-5}$ mol L^{-1}) after UV irradiation recorded on the wavelength of the absorption maximum of the PI MC form in EtOH, 25 °C.

and **25** to methyl esters **11** and **22**. Thus, we observed an insignificant improvement of the colorability, a retardation of the dark photobleaching, and a decrease of the photostability. The introduction of an additional ethoxycarbonylpropene fragment in the structure **22** gives product **26**, for which a retardation of the dark photobleaching, a decrease in the photostability, and an improvement of the colorability were observed in toluene and its worsening in EtOH (see Tables 2 and 3).

In conclusion, in the present work we synthesized a number of photochromic markers, which are photochromic spirobenzopyrans containing one or two carboxy groups attached either directly or through a spacer. We showed convenient possibilities of design and modification of the spacer with the terminal carboxy group. The obtained compounds were characterized using instrumental methods of analysis (NMR spectroscopy, electron absorption spectroscopy in UV and visible region, as well as liquid chromatography—mass spectrometry (LC/MS)). Spectrokinetic studies of the behavior of spirobenzopyran markers and model derivatives in solutions in ethanol and toluene were carried out.

Experimental

Thin-layer chromatography was carried out on Sorbfil STKh-1VE UV 254 (Sorbpolymer, Russia) and Kieselgel 60F_{254} (Merck, Germany) plates in the following solvent systems: dichloromethane (A), dichloromethane—methanol, 5 : 1 (B), 30 : 1 (C) (v/v), spots were visualized under UV light ($\lambda = 254$ nm). Preparative column chromatography and flash-chromatography were carried out on Kieselgel 60 silica gel (Merck, Germany) and alumina (activated, Brockmann IV standard grade; Reanal, Hungary). All the spectral studies were performed under identical conditions at 25 °C. ^{1}H NMR spectra were re-

corded on a Bruker DPX-300 (300 MHz) spectrometer (Germany) in $CDCl_3$ and DMSO-d_6. Chemical shifts are given in δ scale with the accuracy of 0.01 ppm relative to the residual signals for the protons of solvents (δ 7.25 ($CDCl_3$) and δ 2.50 (DMSO-d_6)). Spin-spin coupling constants are given with the accuracy to 0.1 Hz. Liquid chromatography—mass spectrometry (LC/MS) were performed on an API-150EX mass spectrometer (Japan) equipped with a Gilson-215 direct automated injector, a source of ions (electrospray ionization, registration of positive ions), ELSD-Sedex-55 and UV-SCL-10A detectors (Shimadzu, Japan), and columns XBridge-C8 (4.6×50 mm, 3.5 μm (column I), 4.6×50 mm, 8.1 μm (column II), eluent acetonitrile—0.1% aqueous TFA). Melting points of compounds under study were determined on an Electrotermal MEL-TEMP heating stage (USA). Elemental analysis was carried out on a Finnigan EA 1112 automated C,H,N-analyzer (Thermo, Italy).

Electron absorption spectra, kinetic data for photocoloring and spontaneous bleaching processes were obtained on a spectrophotometric equipment: an HR-2000+ series model (Ocean Optics, USA) in quartz cells with a 10-mm pathlength with the exposure of solutions to the light of a Lightingcure LC8 lamp (Hamamatsu, Japan) through a UFS-2 light filter (270—380 nm) with stirring on a magnetic stirrer. The concentration of compounds in all the experiments was $1 \cdot 10^{-5}$—$1 \cdot 10^{-4}$ mol L^{-1}. Kinetics of photodegradation of photochromic compounds was studied upon exposure of solutions to nonfiltered irradiation of a Lightingcure LC8 lamp (light intensity 180 mW cm^{-2}). All the spectrokinetic studies were carried out under identical conditions. To evaluate efficiency of photochromic transformations of spiropyrans, we used the value of optical density in the absorption maximum of the PI MC form located in the visible region of the spectrum after the equilibrium was reached between the starting and colored forms of spiropyrans. To obtain comparable values of optical density of PI forms, we chose identical values of absorption ($D \approx 0.5$) in the absorption maximum of the starting form. For this, we plotted dependences of the photoinduced optical density in the absorption maximum of the PI form on the optical density in the absorption maximum of the starting form. Using these dependences, we calculated the PI optical densities ($\Delta D_{\mathbf{B}}{}^{\mathrm{phot}}{}_{\mathrm{max}}$) and the rate constants of photobleaching ($k_{\mathbf{BA}}{}^{\mathrm{db}}$). The photodegradation value ($t_{0.5}$) was determined from the time required for the PI optical density in the absorption maximum of the PI form to drop to a one-half of the maximum value under continuous irradiation with a nonfiltered light. Between experiments, solutions were stored in dark.

Solvents were purified according to the standard procedures. The following reagents were used in the work: isobutyl chloroformate, 4-(dimethylamino)pyridine, 1,1′-carbonyldiimidazole (Merk), triethyl phosphonoacetate (C_2-phosphonate), malonic acid, *n*-butylamine, *N*-methylmorpholine, 1,3,3-trimethyl-2-methyleneindolenine (**6**) (Fischer base), sodium hydride (a 60% suspension in mineral oil) (Aldrich); other reagents were produced in Russia.

Synthesis of spiropyrans **22** and **28** is described in the work.[11] 2-Hydroxybenzaldehyde derivatives were obtained according to the known procedures.[27—30] Carboxy (**1**) and carboxyalkyl (**3** and **4**) derivatives were obtained by formylation of available *para*-substituted carboxyalkyl phenols by the Reimer—Tiemann and Duff reaction, respectively. Nitroaldehyde **2** was synthesized from unsubstituted commercially available salicylaldehyde by nitration with the HNO_3—AcOH (glacial) nitrating system, formyl derivative **5** was prepared in two steps by chloromethylation and transformation of the intermediate product under conditions of the Sommelet reaction. 5-Carboxy-1,2,3,3-tetramethylindoleninium iodide **6** was obtained according to the method described earlier.[12] Formyl-containing spiropyran **14** was obtained by the condensation of freshly distilled 1,3,3-trimethyl-2-methyleneindolenine **7** with 4-hydroxyisophthalic aldehyde **5** upon heating in ethanol similarly to the described methods.[13—20] Formyl-containing spiropyrans **14**—**20** were synthesized according to the method developed by us earlier.[21]

Since the detailed physicochemical characteristics for a number of compounds synthesized in the present work are not specified in the literature, we report them below.

5,6′-Dicarboxy-1,3,3-trimethylspiro[indoline-2,2′-[2*H*]-chromene] (8). Triethylamine (1.1 mL, 7.6 mmol) was added dropwise to a mixture of aldehyde **1** (0.53 g, 3.2 mmol) and 5-hydroxycarbonyl-1,2,3,3-tetramethylindoleninium iodide (**6**) (1.0 g, 2.9 mmol) in ethanol (100 mL) under argon. The reaction mixture was refluxed for 3 h and cooled, followed by addition of 0.1 *M* HCl (100 mL), a precipitate formed was filtered off and washed with water. Then, it was dissolved in 10% aqueous KOH, washed with dichloromethane, and acidified with 0.1 *M* HCl to pH 4. A newly formed precipitate was filtered off, washed with water, and crystallized from EtOH to obtain compound **8** (0.5 g, 47%), R_f 0.24 (B), m.p. 297—299 °C. ^{1}H NMR (DMSO-d_6), δ: 1.12, 1.24 (both s, 3 H each, C(3)Me); 2.74 (s, 3 H, C(1)Me); 5.87 (d, 1 H, H(3′); J = 10.3 Hz); 6.66 (d, 1 H, H(7), J = 8.2 Hz); 6.77 (d, 1 H, H(8′), J = 8.5 Hz); 7.16 (d, 1 H, H(4′), J = 10.3 Hz); 7.66 (s, 1 H, H(4)); 7.70 (d, 1 H, H(6), J = 8.5 Hz); 7.80 (d, 1 H, H(7′), J = 8.3 Hz); 7.83 (d, 1 H, H(5′), J = 1.8 Hz); 12.50 (s, 1 H, COOH). LC/MS (column I), m/z (τ_{ret}/min): 366.5 $[M + 1]^+$ (1.78). Found (%): C, 68.55; H, 5.71; N, 3.95. $C_{21}H_{19}NO_5$. Calculated (%): C, 69.03; H, 5.24; N, 3.83.

5-Carboxy-1,3,3-trimethyl-6′-nitrospiro[indoline-2,2′-(2*H*)-chromene] (9) was obtained similarly. R_f 0.56 (B), m.p. 294—296 °C. LC/MS (column I), m/z (τ_{ret}/min): 367.0 $[M + 1]^+$ (1.68). Found (%): C, 65.33; H, 5.22; N, 7.53. $C_{20}H_{18}N_2O_5$. Calculated (%): C, 65.57; H, 4.95; N, 7.65. ^{1}H NMR (DMSO-d_6), δ: 1.14, 1.25 (both s, 3 H each, C(3)Me); 2.77 (s, 3 H, C(1)Me); 6.02 (d, 1 H, H(3′), J = 10.3 Hz); 6.70 (d, 1 H, H(7), J = 8.3 Hz); 6.92 (d, 1 H, H(8′), J = 9.1 Hz); 7.26 (d, 1 H, H(4′), J = 10.3 Hz); 7.67 (d, 1 H, H(4), J = 1.5 Hz); 7.81 (dd, 1 H, H(6), J = 8.3 Hz, J = 1.6 Hz); 8.02 (dd, 1 H, H(7′), J = 9.0 Hz, J = 2.8 Hz); 8.24 (d, 1 H, H(5′), J = 2.8 Hz); 12.34 (s, 1 H, COOH) (*cf.* Ref. 12).

6′-Carboxy-1,3,3-trimethylspiro[indoline-2,2′-(2*H*)chromene] (10). R_f 0.46 (B), m.p. 109—112 °C. ^{1}H NMR ($CDCl_3$), δ: 1.18, 1.29 (both s, 3 H each, C(3)Me); 2.73 (s, 3 H, C(1)Me); 5.75 (d, 3 H, H(3′), J = 10.3 Hz); 6.54 (d, 1 H, H(7), J = 7.7 Hz); 6.74 (d, 1 H, H(8′), J = 8.4 Hz); 6.86 (t, 1 H, H(5), J = 7.2 Hz); 6.90 (d, 1 H, H(4′), J = 10.6 Hz); 7.07 (d, 1 H, H(4), J = 6.9 Hz); 7.18 (t, 1 H, H(6), J = 7.6 Hz); 7.83 (s, 1 H, H(5′)); 7.85 (dd, 1 H, H(7′), J = 8.6 Hz, J = 2.0 Hz). LC/MS (column II), m/z (τ_{ret}/min): 322.5 $[M + 1]^+$ (5.74). Found (%): C, 74.44; H, 6.11; N, 4.30. $C_{20}H_{19}NO_3$. Calculated (%): C, 74.75; H, 5.96; N, 4.36.

6′-Ethoxycarbonyl-1,3,3-trimethylspiro[indoline-2,2′-(2*H*)-chromene] (12). R_f 0.51 (A), m.p. 101—103 °C. ^{1}H NMR ($CDCl_3$), δ: 1.18, 1.30 (both s, 3 H each, C(3)Me); 1.37 (t, 3 H, $OCH_2C\underline{H}_3$, J = 7.1 Hz); 2.73 (s, 3 H, C(1)Me); 4.33 (q, 2 H, $OC\underline{H}_2CH_3$, J = 7.1 Hz); 5.74 (d, 1 H, H(3′), J = 10.3 Hz); 6.54 (d, 1 H, H(7), J = 7.8 Hz); 6.73 (d, 1 H, H(8′), J = 8.3 Hz); 6.87 (t, 1 H, H(5), J = 7.2 Hz); 6.90 (d, 1 H, H(4′), J = 10.3 Hz); 7.08

(dd, 1 H, H(4); J = 7.1 Hz, J = 1.1 Hz); 7.19 (td, 1 H, H(6), J = 7.7 Hz, J = 1.1 Hz); 7.79 (d, 1 H, H(5′), J = 2.0 Hz); 7.81 (dd, 1 H, H(7′), J = 8.3 Hz, J = 2.0 Hz). LC/MS (column II), m/z (τ_{ret}/min): 350.6 $[M + 1]^+$ (7.09). Found (%): C, 75.42; H, 6.71; N, 4.05. $C_{22}H_{23}NO_3$. Calculated (%): C, 75.62; H, 6.63; N, 4.01.

6′-Methoxycarbonyl-1,3,3-trimethylspiro[indoline-2,2′-(2*H*)chromene] (13). R_f 0.48 (A), m.p. 109—111 °C (*cf.* Ref. 18: m.p. 109 °C and Ref. 19: m.p. 106—108 °C). ^{1}H NMR ($CDCl_3$), δ: 1.18, 1.31 (both s, 3 H each, C(3)Me); 2.73 (s, 3 H, C(1)Me); 3.86 (s, 3 H, OCH_3); 5.73 (d, 1 H, H(3′), J = 10.3 Hz); 6.54 (d, 1 H, H(7), J = 7.7 Hz); 6.72 (d, 1 H, H(8′), J = 9.4 Hz); 6.87 (td, 1 H, H(5), J = 7.3 Hz, J = 0.8 Hz); 6.88 (d, 1 H, H(4′), J = 10.3 Hz); 7.09 (dd, 1 H, H(4), J = 7.3 Hz, J = 0.8 Hz); 7.19 (td, 1 H, H(6), J = 7.3 Hz, J = 0.8 Hz); 7.78 (s, 1 H, H(5′)); 7.82 (dd, 1 H, H(7′), J = 7.3 Hz, J = 2.1 Hz). LC/MS (column I), m/z (τ_{ret}/min): 336.5 $[M + 1]^+$ (2.29). Found (%): C, 75.03; H, 6.41; N, 4.25. $C_{21}H_{21}NO_3$. Calculated (%): C, 75.20; H, 6.31; N, 4.18.

Diethyl (2″*E*,2‴*E*)-3-{1,3,3-trimethylspiro[indoline-2,2′-(2*H*)chromene-5,6′-diyl]}bispropenoate (26). Method *A*. C_2-Phosphonate (180 mg, 0.8 mmol) was added dropwise using a syringe to a suspension of sodium hydride (36 mg, 0.9 mmol; a 60% suspension in mineral oil) in anhydrous THF (10 mL) cooled to 0 °C with vigorous stirring. The mixture was stirred until complete dissolution of sodium hydride (1 h). Then, a solution of 5,6′-diformyl-1,3,3-trimethylspiro[indoline-2,2′-(2*H*)chromene] (**20**) (100 mg, 0.3 mmol) in THF (2 mL) was added dropwise with stirring. After 1 h of stirring, a distilled water (20 mL) was added dropwise to the mixture (pH 10), which was then acidified with 0.1 *M* HCl to pH 6 and extracted with dichloromethane. The extracts were dried with anhydrous Na_2SO_4, the solvent was evaporated *in vacuo*. The target product was isolated by flash-chromatography on Al_2O_3. The fractions containing the target compound were combined, the solvent was evaporated *in vacuo* to obtain compound **26** (125 mg, 88%), R_f 0.18 (A), m.p. 53—55 °C. ^{1}H NMR ($CDCl_3$), δ: 1.16, 1.30 (both s, 3 H each, C(3)Me); 1.31 (both t, 3 H each, $OCH_2C\underline{H}_3$, J = 7.1 Hz); 2.75 (s, 3 H, C(1)Me); 4.25 (q, 4 H, $OC\underline{H}_2Me$, J = 7.1 Hz); 5.71 (d, 1 H, H(3′), J = 10.3 Hz); 6.27, 6.28 (both d, 1 H each, (O)CH, J = 15.9 Hz); 6.49 (d, 1 H, H(7), J = 8.1 Hz), 6.70 (d, 1 H, H(8′), J = 8.4 Hz), 6.87 (d, 1 H, H(4′), J = 10.3 Hz); 7.22 (d, 1 H, H(5′), J = 2.1 Hz); 7.26 (dd, 1 H, H(7′), J = 8.4 Hz, J = 2.1 Hz); 7.27 (d, 1 H, H(4), J = 1.6 Hz); 7.34 (dd, 1 H, H(6), J = 8.1 Hz, J = 1.6 Hz); 7.59, 7.67 (both d, 1 H each, C(O)CHC$\underline{H}$, J = 15.9 Hz). LC/MS (column II), m/z (τ_{ret}/min): 474.4 $[M + 1]^+$ (7.64). Found (%): C, 73.32; H, 6.73; N, 3.09. $C_{29}H_{31}NO_5$. Calculated (%): C, 73.55; H, 6.60; N, 2.96.

Compounds **21—25** were obtained similarly.

Ethyl (2″*E*)-3-{1,3,3-trimethylspiro[indoline-2,2′-(2*H*)-chromen-6′-yl]}propenoate (21). R_f 0.45 (A), m.p. 99—101 °C. ^{1}H NMR ($CDCl_3$), δ: 1.17, 1.30 (both s, 3 H each, C(3)Me); 1.33 (t, 3 H, $OCH_2C\underline{H}_3$, J = 7.1 Hz); 2.73 (s, 3 H, C(1)Me); 4.25 (q, 2 H, $OC\underline{H}_2CH_3$, J = 7.1 Hz); 5.74 (d, 1 H, H(3′), J = 10.3 Hz); 6.28 (d, 1 H, C(O)CH, J = 16.0 Hz); 6.53 (d, 1 H, H(7), J = 7.7 Hz); 6.71 (d, 1 H, H(8′), J = 8.4 Hz); 6.85 (td, 1 H, H(5), J = 7.4 Hz, J = 0.9 Hz); 6.86 (d, 1 H, H(4′), J = 10.3 Hz); 7.07 (dd, 1 H, H(4), J = 7.3 Hz, J = 0.8 Hz); 7.18 (td, 1 H, H(6), J = 7.6 Hz, J = 1.3 Hz); 7.22 (d, 1 H, H(5′), J = 2.1 Hz); 7.28 (dd, 1 H, H(7′), J = 8.5 Hz, J = 2.2 Hz); 7.60 (d, 1 H, C(O)CHC$\underline{H}$, J = 16.0 Hz). LC/MS (column II), m/z (τ_{ret}/min): 376.6 $[M + 1]^+$ (7.28). Found (%): C, 76.62; H, 6.81; N, 3.63. $C_{24}H_{25}NO_3$. Calculated (%): C, 76.77; H, 6.71; N, 3.73.

Ethyl (2″*E*)-3-{1,3,3-trimethyl-6′-nitrospiro[indoline-2,2′-(2*H*)chromen-5-yl]}propenoate (22).[11] R_f 0.34 (A), m.p. 132—134 °C. LC/MS (column I), m/z (τ_{ret}/min): 421.4 $[M + 1]^+$ (3.78). ^{1}H NMR ($CDCl_3$), δ: 1.18, 1.30 (both s, 3 H each, C(3)Me); 1.32 (t, 3 H, $OCH_2C\underline{H}_3$, J = 7.0 Hz); 2.77 (s, 3 H, C(1)Me); 4.24 (q, 2 H, $CH_3C\underline{H}_2O$, J = 7.0 Hz); 5.84 (d, 1 H, H(3′), J = 10.3 Hz); 6.29 (d, 1 H, C(O)CH, J = 16.0 Hz); 6.33 (d, 1 H, H(7), J = 8.1 Hz); 6.76 (d, 1 H, (8′), J = 9.8 Hz); 6.94 (d, 1 H, H(4′), J = 10.3 Hz); 7.28 (d, 1 H, H(4), J = 1.5 Hz); 7.34 (dd, 1 H, H(6), J = 8.1 Hz, J = 1.5 Hz); 7.66 (d, 1 H, C(O)CHC$\underline{H}$, J = 16.0 Hz); 8.0 (s, 1 H, H(5′)); 8.01 (dd, 1 H, H(7′), J = 9.8 Hz, J = 1.7 Hz). Found (%): C, 68.42; H, 5.91; N, 6.55. $C_{24}H_{24}N_2O_5$. Calculated (%): C, 68.56; H, 5.75; N, 6.66.

Ethyl (2″*E*)-3-{6′-ethoxycarbonyl-1,3,3-trimethylspiro[indoline-2,2′-(2*H*)chromen-5-yl]}propenoate (23). R_f 0.21 (A), m.p. 42—44 °C. ^{1}H NMR ($CDCl_3$), δ: 1.17, 1.29 (both s, 3 H each, C(3)Me); 1.32, 1.36 (both t, 3 H each, $OCH_2C\underline{H}_3$, J = 7.1 Hz); 2.76 (s, 3 H, C(1)Me); 4.24, 4.33 (both q, 2 H each, $OC\underline{H}_2CH_3$, J = 7.1 Hz); 5.71 (d, 1 H, H(3′), J = 10.3 Hz); 6.28 (d, 1 H, C(O)CH, J = 15.9 Hz); 6.50 (d, 1 H, H(7), J = 8.1 Hz); 6.72 (d, 1 H, H(8′), J = 8.4 Hz); 6.91 (d, 1 H, H(4′), J = 10.2 Hz); 7.28 (d, 1 H, H(4), J = 1.6 Hz); 7.34 (dd, 1 H, H(6), J = 8.1 Hz, J = 1.6 Hz); 7.66 (d, 1 H, C(O)CHC$\underline{H}$, J = 15.9 Hz); 7.78 (d, 1 H, H(5′), J = 2.1 Hz); 7.81 (dd, 1 H, H(7′), J = 8.4 Hz, J = 2.1 Hz). LC/MS (column II), m/z (τ_{ret}/min): 448.6 $[M + 1]^+$ (7.47). Found (%): C, 72.23; H, 6.70; N, 3.20. $C_{27}H_{29}NO_5$. Calculated (%): C, 72.46; H, 6.53; N, 3.13.

Ethyl (2″*E*)-3-{6′-methoxycarbonyl-1,3,3-trimethylspiro-[indoline-2,2′-(2*H*)chromen-5-yl]}propenoate (24). R_f 0.20 (A), m.p. 44—45 °C. ^{1}H NMR ($CDCl_3$), δ: 1.17, 1.29 (both s, 3 H each, C(3) Me); 1.32 (t, 3 H, $OCH_2C\underline{H}_3$, J = 7.1 Hz); 2.76 (s, 3 H, C(1)Me); 3.87 (s, 3 H, OCH_3); 4.24 (q, 2 H, $OC\underline{H}_2CH_3$, J = 7.1 Hz); 5.71 (d, 1 H, H(3′), J = 10.2 Hz); 6.27 (d, 1 H, C(O)CH, J = 15.9 Hz); 6.50 (d, 1 H, H(7), J = 8.1 Hz); 6.72 (d, 1 H, H(8′), J = 8.3 Hz); 6.91 (d, 1 H, H(4′), J = 10.2 Hz); 7.27 (d, 1 H, H(4), J = 1.7 Hz); 7.34 (dd, 1 H, H(6), J = 8.1 Hz, J = 1.7 Hz); 7.66 (d, 1 H, C(O)CHC$\underline{H}$, J = 15.9 Hz); 7.77 (d, 1 H, H(5′), J = 2.1 Hz); 7.80 (dd, 1 H, H(7′), J = 8.3 Hz, J = 2.1 Hz). LC/MS (column I), m/z (τ_{ret}/min): 434.4 $[M + 1]^+$ (2.87). Found (%): C, 71.81; H, 6.41; N, 3.42. $C_{26}H_{27}NO_5$. Calculated (%): C, 72.04; H, 6.28; N, 3.23.

Diethyl (2″*E*,2‴*E*)-3-{6′-methoxycarbonyl-1,3,3-trimethylspiro[indoline-2,2′-(2*H*)chromene-5,8′-diyl]}bispropenoate (25). R_f 0.16 (A). ^{1}H NMR ($CDCl_3$), δ: 1.12 (t, 3 H, C(5)CH=CHCOOCH$_2$C$\underline{H}_3$, J = 7.1 Hz); 1.19, 1.27 (both s, 3 H each, C(3)Me); 1.31 (t, 3 H, C(8′)CH=CHCOOCH$_2$C$\underline{H}_3$, J = 7.1 Hz); 2.73 (s, 3 H, C(1)Me); 3.87 (s, 3 H, OCH_3); 4.02, 4.23 (both q, 2 H each, $OC\underline{H}_2CH_3$, J = 7.1 Hz); 5.80 (d, 1 H, H(3′), J = 10.3 Hz); 6.18 (d, 1 H, C(5)CH=C$\underline{H}$, J = 16.2 Hz); 6.28 (d, 1 H, C(8′)CH=C$\underline{H}$, J = 15.9 Hz); 6.52 (d, 1 H, H(7), J = 8.0 Hz); 6.93 (d, 1 H, H(4′), J = 10.3 Hz); 7.29 (d, 1 H, H(4), J = 1.6 Hz); 7.34 (dd, 1 H, H(6), J = 8.0 Hz, J = 1.6 Hz); 7.49 (d, 1 H, C(5)C$\underline{H}$=CH, J = 16.2 Hz); 7.65 (d, 1 H, C(8′)C$\underline{H}$=CH, J = 15.9 Hz); 7.76 (d, 1 H, H(5′), J = 2.1 Hz); 7.98 (d, 1 H, H(7′), J = 2.1 Hz). LC/MS (column I), m/z (τ_{ret}/min): 532.3 $[M + 1]^+$ (3.01). Found (%): C, 70.30; H, 6.11; N, 3.02. $C_{31}H_{33}NO_7$. Calculated (%): C, 70.04; H, 6.26; N, 2.63.

(2″*E*)-3-{6′-Carboxy-1,3,3-trimethylspiro[indoline-2,2′-(2*H*)chromen-5-yl]}propenoic acid (29). Method *B*. A 4 *M* solu-

tion of potassium hydroxide in aqueous methanol (10 mL, 40 mmol) was added to a solution of ester **24** (1 g, 2.31 mmol) in methanol (50 mL). The reaction mixture was stirred for 4 h at 50 °C until disappearance of the starting compound. The solvent was evaporated *in vacuo*, the residue was dissolved in distilled water (50 mL) and acidified with aqueous solution of HCl to pH 6. A precipitate formed was filtered off and washed with distilled water. The mother liquor was extracted with dichloromethane, the extracts were combined, dried with anhydrous sodium sulfate, the solvent was evaporated *in vacuo*. The precipitates obtained were combined and subjected to chromatography on a short layer of silica gel. The fractions containing the target compound were combined, the solvent was evaporated, the residue was dried *in vacuo* for 1 h at 0.2 Torr. The product was additionally purified by crystallization from EtOH to obtain compound **28** (0.18 g, 20%), R_f 0.20 (B), m.p. >200 °C. ^{1}H NMR (DMSO-d_6), δ: 1.13, 1.25 (both s, 3 H each, C(3)Me); 2.72 (s, 3 H, C(1)Me); 5.86 (d, 1 H, H(3′), J = 10.2 Hz); 6.34 (d, 1 H, C(O)CH, J = 15.9 Hz); 6.62 (d, 1 H, H(7), J = 8.2 Hz); 6.77 (d, 1 H, H(8′), J = 8.6 Hz); 7.16 (d, 1 H, H(4′), J = 10.2 Hz); 7.41 (dd, 1 H, H(6), J = 8.2 Hz, J = 1.5 Hz); 7.52 (d, 1 H, C(O)CHC<u>H</u>, J = 15.9 Hz); 7.55 (d, 1 H, H(4), J = 1.5 Hz); 7.70 (dd, 1 H, H(7′), J = 8.6 Hz, J = 2.1 Hz); 7.82 (d, 1 H, H(5′), J = 2.1 Hz); 12.30 (s, 1 H, COOH). LC/MS (column I), m/z (τ_{ret}/min): 392.6 $[M + 1]^+$ (1.66). Found (%): C, 70.12; H, 5.91; N, 3.85. $C_{23}H_{21}NO_5$. Calculated (%): C, 70.58; H, 5.41; N, 3.58.

Compounds **27** and **28** were obtained similarly.

(2″*E*)-3-{1,3,3-Trimethylspiro[indoline-2,2′-(2*H*)chromen-6′-yl]}propenoic acid (27). R_f 0.45 (B), m.p. 86—88 °C. ^{1}H NMR ($CDCl_3$), δ: 1.16, 1.29 (both s, 3 H each, C(3)Me); 2.72 (s, 3 H, C(1)Me); 5.75 (d, 1 H, H(3′), J = 10.2 Hz); 6.27 (d, 1 H, C(O)CH, J = 15.9 Hz); 6.53 (d, 1 H, H(7), J = 7.6 Hz); 6.72 (d, 1 H, H(8′), J = 8.4 Hz); 6.85 (t, 1 H, H(5), J = 7.4 Hz); 6.86 (d, 1 H, H(4′), J = 10.2 Hz); 7.07 (d, 1 H, H(4), J = 6.7 Hz); 7.18 (t, 1 H, H(6), J = 7.5 Hz); 7.26 (s, 1 H, H(5′)); 7.30 (d, 1 H, H(7′), J = 8.6 Hz); 7.69 (d, 1 H, C(O)CHC<u>H</u>, J = 15.9 Hz). LC/MS (column II), m/z (τ_{ret}/min): 348.5 $[M + 1]^+$ (5.86). Found (%): C, 75.82; H, 6.21; N, 4.11. $C_{22}H_{21}NO_3$. Calculated (%): C, 76.06; H, 6.09; N, 4.03.

(2″*E*)-3-{1,3,3-Trimethyl-6′-nitrospiro[indoline-2,2′-(2*H*)-chromen-5-yl]}propenoic acid (28).[11] R_f 0.55 (B), m.p. >200 °C. ^{1}H NMR ($CDCl_3$), δ: 1.20, 1.31 (both s, 3 H each, C(3)Me); 2.79 (s, 3 H, C(1)Me); 5.83 (d, 1 H, H(3′), J = 10.4 Hz); 6.30 (d, 1 H, C(O)CH, J = 15.9 Hz); 6.54 (d, 1 H, H(7), J = 8.1 Hz); 6.77 (d, 1 H, H(8′), J = 8.4 Hz); 6.95 (d, 1 H, H(4′), J = 10.4 Hz); 7.31 (s, 1 H, H(4)); 7.39 (dd, 1 H, H(6), J = 8.1 Hz, J = 1.5 Hz); 7.75 (d, 1 H, C(O)CHC<u>H</u>, J = 15.9 Hz); 8.1 (s, 1 H, H(5′)); 8.02 (dd, 1 H, H(7′), J = 8.4 Hz, J = 2.8 Hz). LC/MS (column I), m/z (τ_{ret}/min): 393.3 $[M + 1]^+$ (2.56). Found (%): C, 67.03; H, 5.41; N, 7.05. $C_{22}H_{20}N_2O_5$. Calculated (%): C, 67.34; H, 5.14; N, 7.14.

(2″*E*,2‴*E*)-3-{1,3,3-Trimethylspiro[indoline-2,2′-(2*H*)-chromene-5,6′-diyl]}bispropenoic acid (30). Method *C*. A mixture of spiropyran **20** (100 mg, 0.3 mmol), malonic acid (125 mg, 1.2 mmol), and piperidine (50 μL) in anhydrous pyridine (10 mL) was refluxed with stirring for 3 h. After cooling to room temperature, the reaction mixture was poured onto ice, then carefully acidified with 10% aqueous HCl to pH 6. A precipitate formed was filtered off. The product was isolated by chromatography on a short layer of silica gel and crystallized from ethanol to obtain spiropyran **30** (60 mg, 48%), R_f 0.17 (B), m.p. >200 °C. ^{1}H NMR ($CDCl_3$), δ: 1.19, 1.32 (both s, 3 H each, C(3)Me); 2.78 (s, 3 H, C(1)Me); 5.73 (d, 1 H, H(3′), J = 10.2 Hz); 6.28, 6.29 (both d, 1 H each, C(O)CH, J = 15.8 Hz); 6.52 (d, 1 H, H(7), J = 8.2 Hz); 6.73 (d, 1 H, H(8′), J = 8.4 Hz); 6.90 (d, 1 H, H(4′), J = 10.2 Hz); 7.27 (s, 1 H, H(5′)); 7.30 (s, 1 H, H(4)); 7.32 (d, 1 H, H(7′), J = 8.4 Hz); 7.38 (d, 1 H, H(6), J = 8.1 Hz); 7.69, 7.77 (both d, 1 H each, C(O)CHC<u>H</u>, J = 15.8 Hz). LC/MS (column II), m/z (τ_{ret}/min): 418.5 $[M + 1]^+$ (5.14). Found (%): C, 71.52; H, 5.95; N, 3.05. $C_{25}H_{23}NO_5$. Calculated (%): C, 71.93; H, 5.55; N, 3.36.

Physicochemical characteristics of compounds **27**—**29** obtained by methods ***B*** and ***C*** are similar.

(2″*E*,2‴*E*)-3-{1,3,3-Trimethylspiro[indoline-2,2′-(2*H*)-chromene-5,6′-diyl]}bispropenoic acid dibutylamide (31). Method *D*. Isobutyl chloroformate (40 μL, 0.30 mmol) was added dropwise to a mixture of spiropyran **30** (50 mg, 0.12 mmol), *N*-methylmorpholine (72 μL, 0.64 mmol), and DMAP (10 mg, 0.08 mmol) in anhydrous dichloromethane (10 mL) at –70 °C under argon with stirring. A brown solution formed was stirred for 30 min, the temperature of the mixture was slowly raised to 0 °C, followed by addition of butylamine (100 μL, 1.0 mmol). After 2 h of stirring at room temperature, the reaction mixture was neutralized, washed with 5% aqueous HCl, the extract was dried with anhydrous sodium sulfate, the solvent was evaporated *in vacuo*. The target product was isolated by column chromatography on Al_2O_3 to obtain diamide **31** (30 mg, 47%), R_f 0.55 (C), m.p. 91—92 °C. ^{1}H NMR ($CDCl_3$), δ: 0.91, 0.94 (both d, 3 H each, CH_3, J = 7.3 Hz); 1.13, 1.26 (both s, 3 H each, C(3)Me); 1.37 (sext, 4 H, C<u>H</u>$_2$CH$_3$, J = 7.0 Hz); 1.53 (pentet, 4 H, NHCH$_2$C<u>H</u>$_2$, J = 7.2 Hz); 2.72 (s, 3 H, C(1)Me); 3.36, 3.37 (both q, 2 H each, NHC<u>H</u>$_2$, J = 7.1 Hz); 5.67 (d, 1 H, H(3′), J = 10.2 Hz); 5.68 (t, 1 H, NH, J = 6.0 Hz); 5.79 (t, 1 H, NH, J = 6.0 Hz); 6.24, 6.25 (both d, 1 H each, C(O)CH, J = 15.5 Hz); 6.45 (d, 1 H, H(7), J = 8.1 Hz); 6.70 (d, 1 H, H(8′), J = 8.5 Hz); 6.83 (d, 1 H, H(4′), J = 10.2 Hz); 7.16 (d, 1 H, H(5′), J = 2.0 Hz); 7.21 (d, 1 H, H(4), J = 1.6 Hz); 7.24 (dd, 1 H, H(7′), J = 8.6 Hz, J = 2.2 Hz); 7.30 (dd, 1 H, H(6), J = 8.1 Hz, J = 1.6 Hz); 7.52, 7.59 (both d, 1 H each, C(O)CHC<u>H</u>, J = 15.5 Hz). LC/MS (column II), m/z (τ_{ret}/min): 528.7 $[M + 1]^+$ (6.45). Found (%): C, 75.02; H, 7.71; N, 8.05. $C_{33}H_{41}N_3O_3$. Calculated (%): C, 75.11; H, 7.83; N, 7.96.

{1,3,3-Trimethyl-6′-nitrospiro[indoline-2,2′-(2*H*)chromen-5-yl]}carboxylic acid *N*-(2-ethoxycarbonylethyl)amide (34). *N*,*N*-carbonyldiimidazole (0.29 g, 1.8 mmol) was added to a solution of 5-carboxy-1,3,3-trimethyl-6′-nitrospiro[indoline-2,2′-(2*H*)chromene] (**9**) (0.5 g, 1.4 mmol) in anhydrous dimethylformamide (50 mL) at room temperature under argon with vigorous stirring. After 40 min, β-alanine ethyl ester hydrochloride (**32**) (0.5 g, 3.3 mmol) and triethylamine (1 mL, 6.9 mmol) were added and the reaction mixture was stirred for 4 h, then poured into water (100 mL), and extracted with dichloromethane, the extract was dried with anhydrous sodium sulfate. The target product was isolated by column chromatography on Al_2O_3, eluent dichloromethane—light petroleum (1 : 1). The product obtained was additionally purified by crystallization from a mixture of ethanol—light petroleum (1 : 2) to obtain compound **34** (250 mg, 38%), R_f 0.80 (C), m.p. 115—117 °C. ^{1}H NMR ($CDCl_3$), δ: 1.18 (s, 3 H, C(3a)Me); 1.27 (t, 3 H, OCH$_2$C<u>H</u>$_3$, J = 7.0 Hz); 1.31 (s, 3 H, C(3b)Me); 2.64 (t, 2 H, C(O)CH$_2$, J = 5.9 Hz); 2.78 (s, 3 H, C(1)Me); 3.71 (q, 2 H, NHC<u>H</u>$_2$, J = 7.0 Hz); 4.16 (q, 2 H, OC<u>H</u>$_2$CH$_3$, J = 7.0 Hz); 5.83 (d, 1 H, H(3′), J = 10.3 Hz); 6.51

(d, 1 H, H(7), J = 8.0 Hz); 6.70 (t, 1 H, NH, J = 7.5 Hz); 6.75 (d, 1 H, H(8´), J = 8.5 Hz); 6.94 (d, 1 H, H(4´), J = 10.3 Hz); 7.56 (d, 1 H, H(4), J = 1.8 Hz); 7.60 (dd, 1 H, H(6), J = 8.0 Hz, J = 1.8 Hz); 8.0 (s, 1 H, H(5´)); 8.02 (dd, 1 H, H(7´), J = 8.5 Hz, J = 2.7 Hz). LC/MS (column I), m/z (τ_{ret}/min): 466.3 $[M + 1]^+$ (1.75). Found (%): C, 64.36; H, 6.05; N, 9.10. $C_{25}H_{27}N_3O_6$. Calculated (%): C, 64.51; H, 5.85; N, 9.03.

{1,3,3-Trimethyl-6´-nitrospiro[indoline-2,2´-(2*H*)chromen-5-yl]}carboxylic acid *N*-(5-ethoxycarbonylpentyl)amide (35) was obtained similarly to compound **34**. R_f 0.75 (C), m.p. 74—76 °C. ^{1}H NMR ($CDCl_3$), δ: 1.19 (s, 3 H, C(3a)Me); 1.24 (t, 3 H, $OCH_2C\underline{H}_3$, J = 7.1 Hz); 1.31 (s, 3 H, C(3b)Me); 1.44 (m, 2 H, $NH(CH_2)_2C\underline{H}_2$); 1.65 (m, 4 H, $C(O)CH_2C\underline{H}_2$ and $NHCH_2C\underline{H}_2$); 2.32 (t, 2 H, $C(O)CH_2$, J = 7.3 Hz); 2.78 (s, 3 H, C(1)Me); 3.45 (q, 2 H, $NHC\underline{H}_2$, J = 6.9 Hz); 4.12 (q, 2 H, $OC\underline{H}_2CH_3$, J = 7.1 Hz); 5.83 (d, 1 H, H(3´), J = 10.3 Hz); 6.06 (t, 1 H, NH, J = 6.0 Hz); 6.52 (d, 1 H, H(7), J = 8.0 Hz); 6.75 (d, 1 H, H(8´), J = 8.5 Hz); 6.94 (d, 1 H, H(4´), J = 10.3 Hz); 7.56 (d, 1 H, H(4), J = 1.5 Hz); 7.60 (dd, 1 H, H(6), J = 8.0 Hz, J = 1.8 Hz); 8.0 (s, 1 H, H(5´)); 8.02 (dd, 1 H, H(7´), J = 8.5 Hz, J = 2.8 Hz). LC/MS (column I), m/z (τ_{ret}/min): 508.4 $[M + 1]^+$ (1.92). Found (%): C, 66.04; H, 6.69; N, 8.15. $C_{28}H_{33}N_3O_6$. Calculated (%): C, 66.26; H, 6.55; N, 8.28.

{1,3,3-Trimethyl-6´-nitrospiro[indoline-2,2´-(2*H*)chromen-5-yl]}carboxylic acid *N*-(2-carbonylethyl)amide (36). Lithium hydroxide (25 mg, 1.04 mmol) was added to a mixture of spiropyran **34** (100 mg, 0.22 mmol) in THF (20 mL) and distilled water (10 mL). The mixture was stirred for 6 h, then poured into water (50 mL), acidified with 0.1 *M* HCl to pH 6, and extracted with dichloromethane. The extracts were dried with anhydrous Na_2SO_4, the solvent was evaporated *in vacuo*. The residue was crystallized from a mixture of ethanol—light petroleum (1 : 1) to obtain compound **36** (80 mg, 83%), R_f 0.30 (B), m.p. 222—224 °C. ^{1}H NMR ($CDCl_3$), δ: 1.18, 1.31 (both s, 3 H each, C(3)Me); 2.73 (t, 2 H, $C(O)CH_2$, J = 5.8 Hz); 2.78 (s, 3 H, C(1)Me); 3.73 (q, 2 H, $NHC\underline{H}_2$, J = 5.2 Hz); 5.83 (d, 1 H, H(3´), J = 10.4 Hz); 6.52 (d, 1 H, H(7), J = 8.1 Hz); 6.65 (t, 1 H, NH, J = 6.5 Hz); 6.75 (d, 1 H, H(8´), J = 8.7 Hz); 6.94 (d, 1 H, H(4´), J = 10.4 Hz); 7.56 (d, 1 H, H(4), J = 1.6 Hz); 7.60 (dd, 1 H, H(6), J = 8.1 Hz, J = 1.8 Hz); 8.0 (s, 1 H, H(5´)); 8.02 (dd, 1 H, H(7´), J = 8.7 Hz, J = 2.7 Hz). LC/MS (column I), m/z (τ_{ret}/min): 438.4 $[M + 1]^+$ (1.54). Found (%): C, 62.82; H, 5.70; N, 9.75. $C_{23}H_{23}N_3O_6$. Calculated (%): C, 63.15; H, 5.30; N, 9.61.

{1,3,3-Trimethyl-6´-nitrospiro[indoline-2,2´-(2*H*)chromen-5-yl]}carboxylic acid *N*-(5-carbonylpentyl)amide (37) was obtained similarly to compound **36**. R_f 0.42 (B), m.p. 210—212 °C. ^{1}H NMR ($CDCl_3$), δ: 1.18, 1.31 (both s, 3 H each, C(3)Me); 1.45 (m, 2 H, $NH(CH_2)_2C\underline{H}_2$); 1.66 (m, 4 H, $C(O)CH_2C\underline{H}_2$ and $NHCH_2C\underline{H}_2$); 2.38 (t, 2 H, $C(O)CH_2$, J = 7.3 Hz); 2.78 (s, 3 H, C(1)Me); 3.45 (q, 2 H, $NHC\underline{H}_2$, J = 6.9 Hz); 5.83 (d, 1 H, H(3´), J = 10.3 Hz); 6.07 (t, 1 H, NH, J = 6.5 Hz); 6.52 (d, 1 H, H(7), J = 8.1 Hz); 6.75 (d, 1 H, H(8´), J = 8.7 Hz); 6.94 (d, 1 H, H(4´), J = 10.3 Hz); 7.56 (d, 1 H, H(4), J = 1.5 Hz); 7.60 (dd, 1 H, H(6), J = 8.0 Hz, J = 1.8 Hz); 8.0 (s, 1 H, H(5´)); 8.02 (dd, 1 H, H(7´), J = 8.7 Hz, J = 2.7 Hz). LC/MS (column I), m/z (τ_{ret}/min): 480.3 $[M + 1]^+$ (1.63). Found (%): C, 64.73; H, 6.52; N, 8.51. $C_{26}H_{29}N_3O_6$. Calculated (%): C, 65.12; H, 6.10; N, 8.76.

This work was financially supported by the Council on Grants at the President of the Russian Federation (Program of State Support for Young Scientists-Candidates of Science, MK-6877.2012.4) and the Russian Foundation for Basic Research (Program of State Support for Young Scientists No. 12-04-31190).

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Received September 3, 2013;
in revised form April 4, 2014