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New indoline spiropyrans with highly stable merocyanine forms

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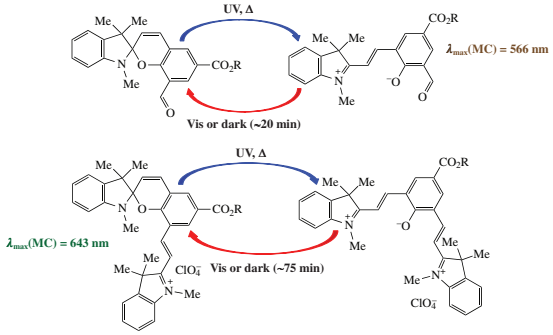
New spiropyrans with chromene and indoline cores bearing alkoxycarbonyl group and cationic π-acceptor in the chromene moiety were synthesized in one step from 1,2,3,3-tetramethylindolinium and isophthalic dialdehyde derivatives. The appending of a 8′-positioned conjugated cationic fragment causes a significant red-shift of the photoinduced isomers absorption maxima and provides them with extremely long lifetimes up to 75 min. The obtained spiropyrans exhibit both positive and negative photochromism in solutions, demonstrating the properties of 'photochromic balance'.

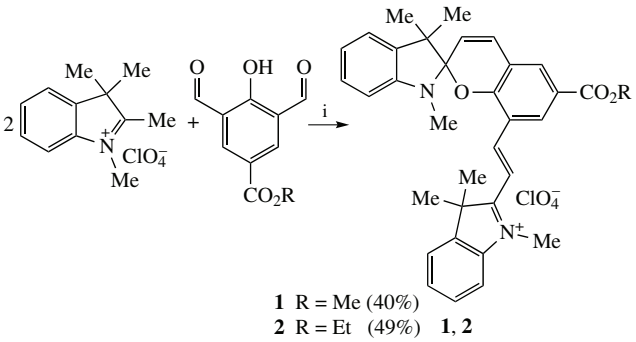


Keywords: spiropyrans, indolinium salts, photochromism, cationic fragment, molecular switch, merocyanine, bathochromic shift.

Currently, enormous attention is paid to the design of materials with controllable properties and the development of the active components of systems allowing reversible switching of their core features. Spiropyrans, the promising compounds of this type, tend to reversibly transform between the spirocyclic (SP) and the open merocyanine (MC) forms under the impact of electromagnetic irradiation, temperature, or action of metal cations. Due to this multi-sensitivity, spiropyrans are widely used as building blocks for creating dynamic materials[1] which can be applied in molecular electronics, chemosensing, bio-imaging and photopharmacology.[2–10] One of the most important requirements for the successful application of spiropyrans as fluorescent probes for bio-imaging[11,12] or photopharmacological agents[13] is the location of their absorption maxima in the long-wavelength region of the spectrum as biological fluids and tissues show the greatest transparency in this optical region. Also, it would be a benefit for the use of these compounds as integral parts in molecular electronics devices.[14–16] To improve the aforementioned characteristic of spiro compounds, we have previously[17,18] developed a single-stage synthesis of spiropyran derivatives containing cationic 3*H*-indolium fragment conjugated with the 2*H*-chromene moiety. Such compounds show a strong bathochromic shift of the absorption and emission maxima of MC in comparison with previously known analogues up to the near-IR region (> 700 nm).[19,20] The second important characteristic of spiropyrans is the lifetime of merocyanine form since the very MC is the active state of the spiropyran-based molecular switch, and it should be appropriately long-living to have an effect both in the context of photopharmacology and electronics. Thus, one of the main challenges nowadays is to increase the stability of photogenerated MC isomer.

In this work, we employed our original procedure[17–20] for the synthesis of new spirocyclic compounds **1**, **2** with an ester group and a cationic fragment in the chromene moiety† (Scheme 1). Their optical properties were also studied.

To comprehensively establish the effect of the substituent at the position 8 on the properties of the compounds, we also synthesized new spiropyrans **3**, **4** with formyl substituent instead of the cationic fragment and known 8-unsubstituted analogues **5**[21] and **6**.[22] The presence of two electron-withdrawing groups (EWGs) in molecules of spiropyrans **1**–**4** allowed us to expect



Scheme 1 *Reagents and conditions*: i, Et_3N, Pr^iOH, reflux, 6 h.

† *2-[(E)-2-(6-Methoxycarbonyl-1′,3′,3′-trimethyl-1′,3′-dihydrospiro[chromene-2,2′-indol]-8-yl)vinyl]-1,3,3-trimethyl-3H-indolium perchlorate* **1**. 1,2,3,3-Tetramethyl-3*H*-indol-1-ium perchlorate (1.641 g, 6 mmol) was added to a solution of 2,6-diformyl-4-(methoxycarbonyl)-phenol (0.624 g, 3 mmol) in propan-2-ol (20 ml). Triethylamine (0.42 ml) was then carefully added dropwise, and the mixture was refluxed for 6 h. Most of the solvent was evaporated, and the residue was left overnight at room temperature for the precipitate forming. The precipitate was filtered off and purified by column chromatography on silica gel using chloroform as the eluent. Recrystallization from ethanol afforded 0.752 g (40%) of dark green crystals, mp 217 °C. For the synthesis of homologue **2** and spectral characteristics, see Online Supplementary Materials.

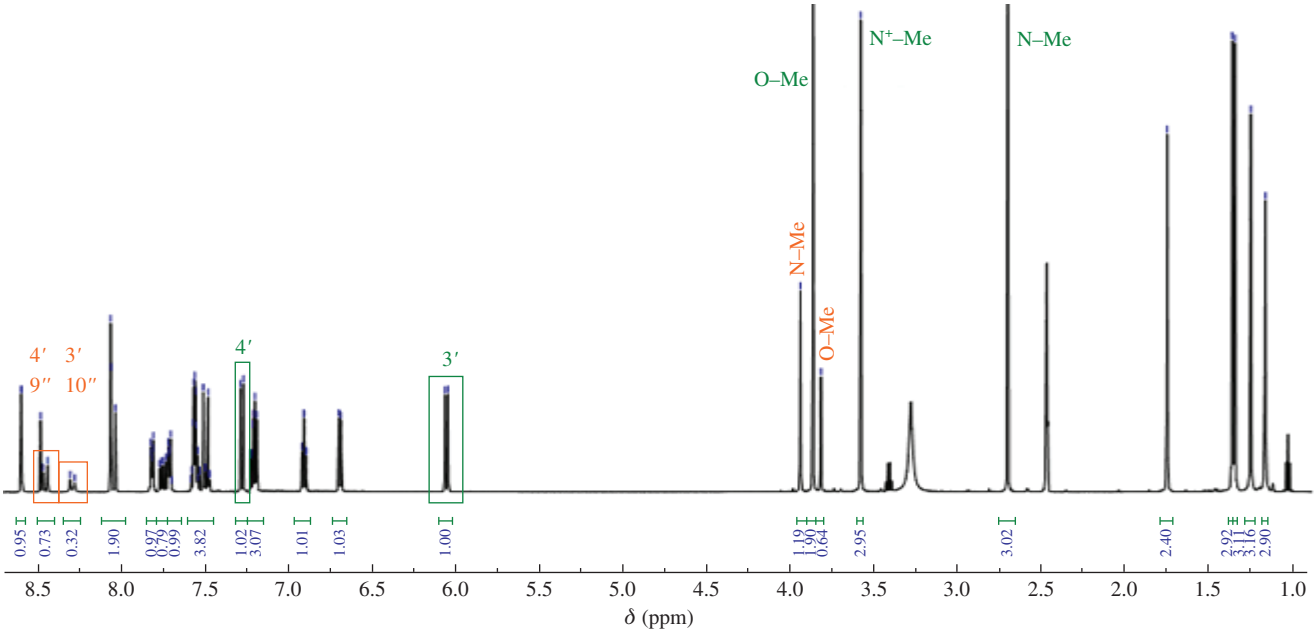
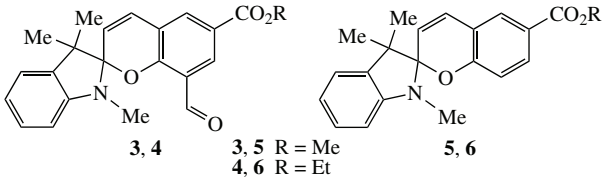


Figure 1 ^{1}H NMR spectrum of spiropyran **1**. The signals for the cyclic SP and the open MC forms are highlighted in green and orange, respectively.

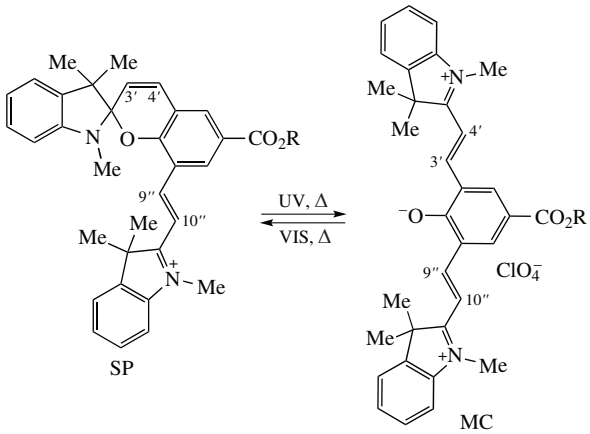
the enhanced stability and the increased lifetimes of their MC forms. The insignificant difference in the structure of the 6-positioned substituent between compounds **1**, **3**, **5** and **2**, **4**, **6** made it possible to estimate the degree of system sensitivity towards small changes in electronic effects.



Usually, under ambient conditions, spiropyran molecules predominately exist in their cyclic SP form. If the MC form turns out to be more stable than the SP one, spiropyran may show negative photochromism.[23] Molecular systems with negative photochromism are of great interest as their switching can be performed by less destructive visible light, which is very important for biomedical applications. Full or partial thermal stabilization of MC in solution was observed for some representatives of spiropyrans containing two strong EWGs in chromene moiety.[24–30] However, this is quite a rare phenomenon for this class of photochromic compounds. Additionally, all of these reported compounds have MC forms with rather short-wavelength absorption maxima ($\lambda_{max} < 600$ nm).

The results of our NMR analysis revealed that spiropyrans **1** and **2** exist in an equilibrium between SP and MC forms in DMSO-d_6 solutions under ambient conditions (Scheme 2). This fact can be explained by delocalization of the excessive negative charge from the phenolate oxygen atom of MC form due to –M-effect of the alkoxycarbonyl substituents and the more efficient distribution of the electron density along the enlarged conjugation chain of the molecule.

There are two sets of signals with an intensity ratio of 5 : 1 and 7 : 1 for SP and MC forms, respectively, in the ^{1}H NMR spectra of compounds **1** and **2** recorded at room temperature (Figure 1). In particular, the spectra contain characteristic doublet signals of *cis*-oriented protons 3′ and 4′ of the SP form with J = 10.5 Hz, as well as *trans*-oriented protons 9″ and 10″ of the vinyl fragment with J = 16.4 Hz as part of the corresponding signal groups. There are also characteristic singlets for the N–Me and N$^+$–Me



Scheme 2 Atom numbering is given for MNR interpretation.

groups at 2.7 and 3.6 ppm, respectively. In the case of the MC isomer, the spectrum contains pronounced two-proton‡ doublets of symmetrically located equivalent vinyl fragments with J = 15.6 Hz, which indicates the *trans*-configuration of the C(3′)=C(4′) and C(9″)=C(10″) bonds. The presence of singlets with a relative intensity of 6H at 3.94 (for **1**) and 3.97 ppm (for **2**) indicates the symmetrical zwitterionic form of the MC isomer. The signals of nonequivalent C(3)–Me groups of the SP form appear as four singlets in the range of 1.16–1.38 ppm, while for the MC form these groups resonate as one 12H singlet at 1.74–1.77 ppm. Also, the spectrum of spiropyran **1** contains two singlets for ester methoxy groups at 3.86 and 3.81 ppm corresponding to the SP and MC forms. The relative integral intensities and multiplicity of other signals correspond to the proposed structures and indicate the above-mentioned ratio of isomeric forms. Spiropyrans **3**–**6** deprived of cationic fragment were found to exist in cyclic forms under the NMR analysis conditions.

The photochromic properties of the compounds obtained were investigated in acetonitrile solutions (Table 1). Spiropyrans **1**–**4** in solution exist in the equilibrium between SP and MC

‡ Further, as well as in the Online Supplementary Materials, the intensities of signals for the SP and MC forms during the analysis of the spectra are indicated in terms of the individual isomeric form.

Table 1 Spectral and kinetic characteristics of spiropyrans **1**–**6**, T = 293 K.

Compound	Solvent	λ_{max}(SP)/nm[a]	λ_{max}(MC)/nm	τ_{MC}/s
1	MeCN	204, 247, 288, 384, 434^{sh}	642	4516.5
	PhMe	393, 425^{sh}	670	324.4
2	MeCN	203, 220,^{sh} 248, 286, 383, 425^{sh}	643	4250.3
	PhMe	392, 425^{sh}	670	295.5
3	MeCN	203, 240, 291, 346	566	1037.9
4	MeCN	203, 241, 290, 348, 358^{sh}	566	1130.5
5	MeCN	204, 242, 291, 319^{sh}	570	17.1
6	MeCN	203, 242, 291, 315^{sh}	–	–

[a] Upper index sh denotes a shoulder.

forms, which is significantly shifted towards the cyclic isomers. The absorption spectra in this case contain absorption bands for both isomers. The SP form of spiropyrans **5**, **6** is characterized by three bands with maxima at 203–204, 240–248, and 286–291 nm. The presence of the 8-positioned formyl group leads to the appearance of a new structured band in the spectrum with a maximum in the region of 346–348 nm, which would undergo a red shift up to the visible region when the formyl substituent is replaced by a cationic one.

During the irradiation of solutions of **1**–**5** with UV light (λ_{irr} = 365 nm), an increase in intensity or an appearance of the absorption bands with maxima in the range of 566–643 nm corresponding to MC was observed (Figure 2). It should be noted that the introduction of the cationic substituent into molecules of **1** and **2** leads to a strong bathochromic shift of their MC forms absorption maxima ($\Delta\lambda_{max}$ = 75–76 nm) compared to spiropyrans **3**–**5**, which can be explained by the growth of the conjugation chain, which was previously[20] confirmed by TD-DFT calculations. However, in comparison with the previously obtained cationic derivatives of this series, these absorption maxima are significantly blueshifted due to the known hypsochromic effect of strong π-acceptor substituents located at the position 6 of indoline spiropyrans.[3]

After irradiation is stopped, solutions of spiropyrans **1**–**5** return to their initial state due to the thermal recyclization. The kinetic curves are in a good agreement with monoexponential function (Figure 3). Thus, the solutions of spiropyrans **1**–**5** demonstrate positive photochromism.

Along with this, due to the existing of reverse photoreaction MC → SP, the studied spiropyrans exhibit the properties of negative photochromism. Thus, irradiation of the initial solutions of spiropyrans **1**–**4** at the absorption band of the MC forms with visible light (λ_{irr} = 578 nm) leads to complete discolouration of the solutions (see Online Supplementary Materials, Figures S37, S42) followed by thermal recovery of the initial equilibrium state. The simultaneous existence of both positive and negative

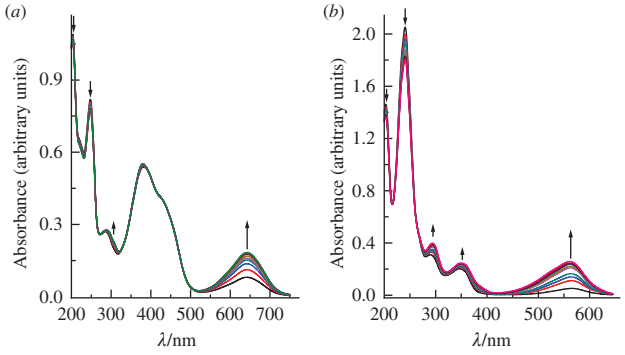


Figure 2 Changes in the absorption spectra of (*a*) compound **2** ($c = 3.6 \times 10^{-5}$ M, dt = 10 s) and (*b*) compound **4** ($c = 4 \times 10^{-5}$ M, dt = 5 s) upon irradiation with UV light (λ_{irr} = 365 nm) in acetonitrile, T = 293 K.

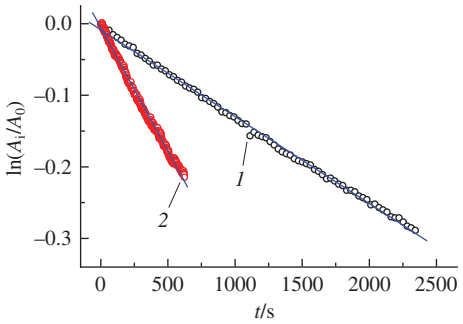


Figure 3 Linear anamorphoses of kinetic curves of thermal relaxation of spiropyrans (*1*) **2** and (*2*) **4** in acetonitrile, T = 293 K.

photochromism in solutions of spiropyrans **1**–**4** indicates that they have quite a rare property of 'photochromic balance', when the photoinduced deviation of the MC isomer content in one or another direction is compensated by the reverse thermal processes. There are few examples of spiropyrans demonstrating such properties.[28,31] In most previously reported cases with compounds existing in an equilibrium of cyclic and open forms, the MC forms are extensively thermally stabilized and the compounds show only negative photochromism.[24–27]

In order to study the effect of solvent polarity on the spectral-kinetic characteristics of isomeric forms of spiropyrans, the photochromic properties of compounds **1** and **2** were explored in non-polar toluene (see Table 1 and Figures S35, S38). In contrast to the acetonitrile solutions, in toluene the equilibrium between the isomeric forms of spiropyrans **1** and **2** is almost completely shifted towards cyclic isomers. It should be noted that the absorption maxima of the open MC forms generated upon irradiation of toluene solutions with UV light (λ_{irr} = 365 nm) are redshifted by 27–28 nm in comparison with the analogous forms in acetonitrile. Moreover, their lifetimes (τ_{MC} = 295.5–324.4 s) in a non-polar solvent decrease by a factor of ~15 in comparison with a polar one. However, even under these conditions the values of the MC lifetimes exceed the longest known one for this type of cationic spiropyrans registered in polar acetonitrile (τ_{MC} = 238.7 s for the 6-bromo-substituted derivative).[20] Along with thermal relaxation, photorecyclization is also observed during irradiation in the absorption bands of MC forms with visible light (λ_{irr} = 578 nm), which leads to complete discolouration of toluene solutions.

The analysis of the obtained data has shown that compounds **1**–**4** containing two π-acceptor substituents in their molecules are characterised by the extremely high lifetimes of the MC forms at room temperature in acetonitrile (τ_{MC} = 1037.9–4516.5 s), while for most representatives of spiropyrans including compound **5** (τ_{MC} = 17.1 s) this value does not exceed several tens of seconds under the same conditions.[3] Moreover, appending the cationic 3*H*-indolium fragment to the position 8 increased the MC lifetimes of compounds **1** and **2** by a factor of ~4 in comparison with the formyl analogues **3**, **4**. In the case of 8-nonsubstituted spiropyran **6**, photochromic activity at room temperature was not detected.

In summary, we have synthesized new spiropyrans with alkoxycarbonyl groups in the chromene moiety demonstrating both positive and negative photochromism and estimated the effect of additional EWGs on their photochromic behaviour and dynamic equilibrium in solution. Compounds **3** and **4** with formyl groups manifest the lifetimes of MC forms up to 17–19 min. Replacement of formyl substituent by the conjugated cationic fragment made the MC isomers of spiropyrans **1**, **2** extremely long-living in acetonitrile (τ_{MC} = 71–75 min), which also caused a redshift of their absorption maxima for more than 70 nm. These facts together make spiropyrans under the study

promising candidates for the creation of materials with controllable properties, especially for biomedical applications.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2021.05.040.

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