



Speaker – Prof. Khodonov A.A.

**Structure study of 1',3',3'-trimethylspiro[2H-1-benzopyran-2,2'-indoline]
stable complex with aluminum salts by NMR spectroscopy**

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Introduction

Currently, significant progress has been achieved in the synthesis and study of the properties of polyfunctional photochromic organic compounds of the spiroopyran class.

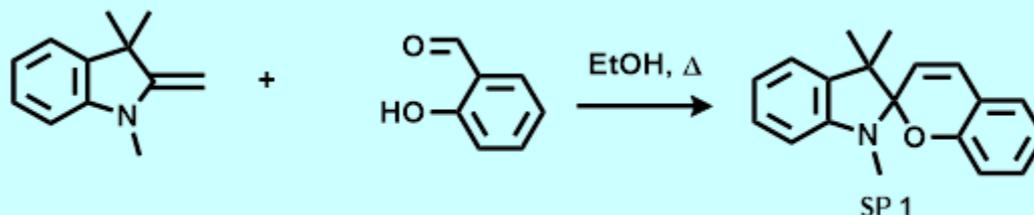
Photocontrolled photochromic ionophores and artificial receptors, which make it possible to control the complexation process and the properties of the resulting products by illuminating the sample with light with a certain wavelength, attract particular interest of researchers in various fields. An additional advantage of spiroopyran-based photochromic ligands is the presence of 2 different types of analytical signals in one molecule (change in absorption in the 450-630 nm region and fluorescence induction at 650 nm in the photoinduced merocyanine form).

The aim of this study was to study the structure of a stable complex of photochromic spiroopyran – 1',3',3'-trimethylspiro[2H-1-benzopyran-2,2'-indoline] (SP1) and aluminum salts by ^1H -, ^{13}C - and 2D- NMR spectroscopy.

Previously, it was shown that substituted derivatives of 1',3',3'-trimethylspiro[2H-1-benzopyran-2,2'-indoline] (BIPS, SP1) form relatively stable complexes with salts of some d- and f-elements. A number of similar photocontrolled cation-complexing systems containing a nitro group at position 6 of the pyran fragment, and as an ionophore or chelatophore unit in a photochrome molecule: carboxy, methoxy or mercapto groups; or fragments of molecules of crown ethers, podands, iminodiacetate, N-heterocycles, bipyridyls, and dendrimers have been described in the literature.

It was found that the spectral properties and parameters of phototransformations of spiroopyrans strongly depend on the nature of the substituents present in the molecule; therefore, directed variation of the substituents makes it possible to purposefully search for new photochromes with specified photochemical characteristics and various stimulus-reacting structural elements and “molecular addresses”.

Method for the preparation of 1',3',3'-trimethylspiro[2H-1-benzopyran-2,2'-indoline] (SP1)



Scheme 1. Synthesis of 1',3',3'-trimethylspiro[2H-1-benzopyran-2,2'-indoline] (SP1)

The target spiroopyran (SP1) was obtained by heating at the boiling point of a solution of 1.0 eq. freshly distilled Fischer base with 1.2 equiv. salicylic aldehyde in anhydrous ethanol under argon. After completion of the reaction, the solvent was removed, the compound (SP1) was isolated by flash chromatography of the residue on silica gel, the solvent was removed from the collected combined fractions containing the target product (SP1), then the crude product was crystallized from anhydrous ethanol. Yield: 97%. Colorless crystals, m.p. 91–92 C, product purity 98% by HPLC. The structure of the target compound (SP1) was proved by a set of modern physico-chemical methods of analysis (UV-, ^1H - and ^{13}C -NMR spectroscopy and mass spectra). LC-MS spectrum (m/z): 278 [M + H]⁺, C₁₉H₁₉NO.

Study of the formation, photochromic behavior and spectral characteristics of the photochromic ligand (SP1) and its complexes with aluminum salts.

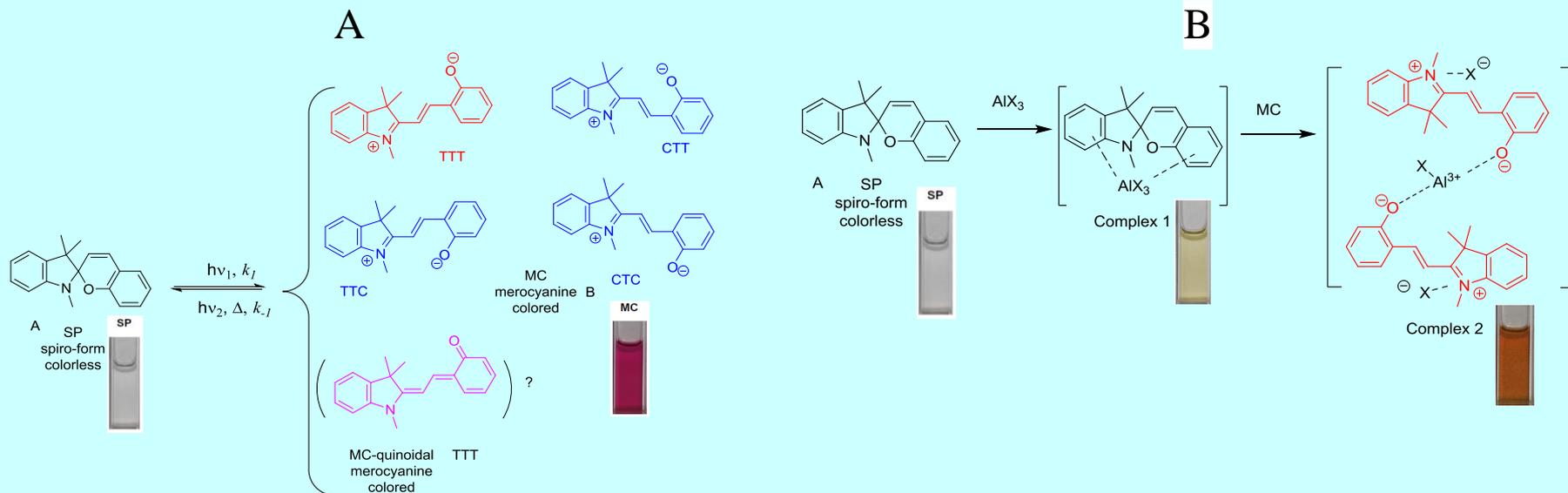


Fig. 1. Scheme of photochemical transformations A - (SP1) and B - the structure of its complexes with aluminum salts

In order to study the mechanism of complexation of spiropyran derivatives with salts of various metals and to determine the contribution of the presence and nature of substituents in the photochrome molecule, we first studied the process of interaction of the **simplest precursor, unsubstituted indoline spiropyran (SP1), with aluminum salts**. The process was studied in solutions of the following solvents: in EtOH, in MeOH, and in a mixture of MeOH + H₂O (up to 20% by volume).

For the first time, a unique phenomenon of the formation of a stable in the dark complex of its MC-form with aluminum salts (Al(NO₃)₃ x 9H₂O or with anhydrous AlCl₃) in a 2: 1 ratio was discovered. The formation occurs in two stages: first, a labile π -complex of aromatic fragments of the spiro-form with an aluminum salt is formed (**complex 1**, 380 nm, Fig. 1 B, lifetime less than 30 s). Its structure was established by the NMR method; water enters into its coordination sphere. Next, **complex 1** reacts with the merocyanine form (MC) (SP1) present in the solution in a low concentration, with the formation of **complex 2 of 2 merocyanine (MC) molecules and 1 aluminum cation**. **Complex 2** (430-434 nm) has a pronounced reverse photochromism. The mechanism of formation of **complexes 1 and 2** was studied in detail. The structure of **complexes 1 and 2** was established by NMR methods, it was shown that the merocyanine form in **complexes 2** is in the form of the trans-TTT isomer (see Fig. 1 B, and Fig. 4-6). For the first time, a unique phenomenon of stabilization of the life time of the MC-form of spiropyran in the dark was discovered: complexation with aluminum cations selectively completely suppresses the reverse thermal reaction of cyclization to the spiro-form, but at the same time, **complex 2** easily transforms into the initial spiro-form when illuminated with light > 400 nm. **Complex 2** is stable (the life time is more than 2 weeks in the dark), but it quickly degrades when an HCl solution or a complexone - EDTA is added. The preliminary results of studying the kinetics of formation and photochemical characteristics of the photochromic ligand (SP1) and its complexes with aluminum salts have published [1].

Study of the structure of the spiro-form of spiropyran (SP1) by NMR spectroscopy

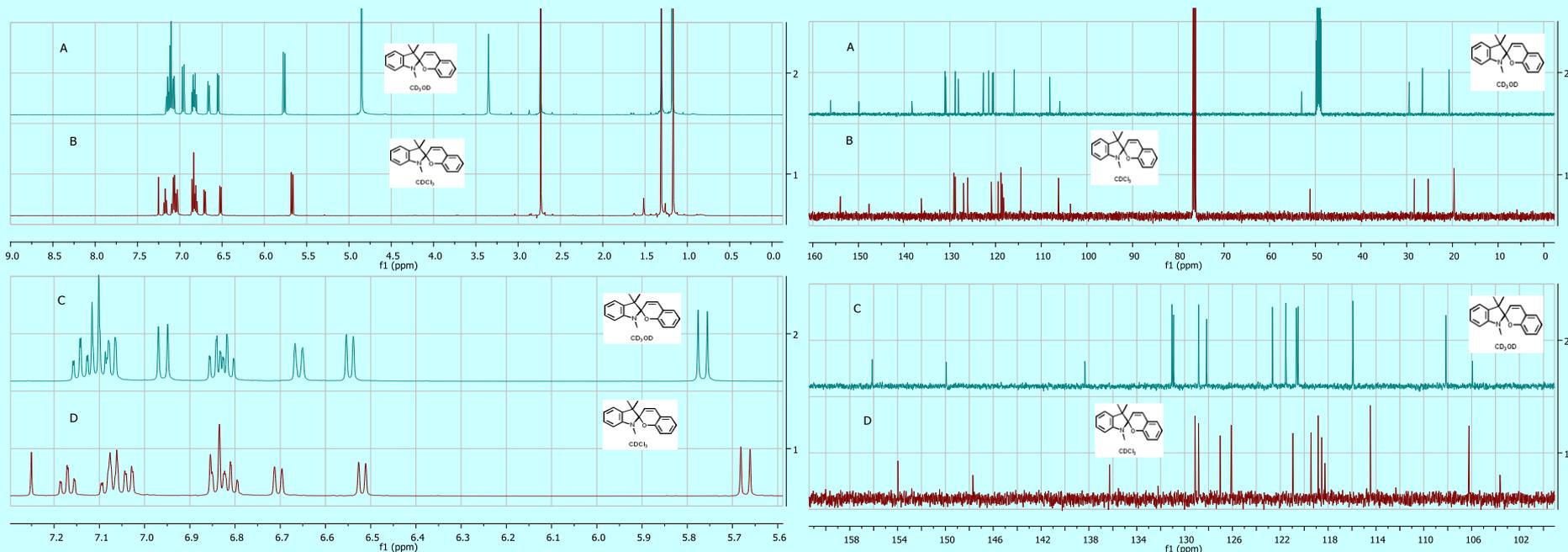


Fig. 2. ^1H - (left panel) and ^{13}C - (right panel) NMR spectra of spiro-form 1',3',3'-trimethylspiro[2H-1-benzopyran-2,2'-indoline] (SP1) in CDCl_3 (the color of the lines of the spectrum is terracotta) and in CD_3OD (the color of the lines of the spectrum is turquoise); where A, B - spectra of the full range of chemical shifts of signals; C, D - fragments of signal spectra of aromatic ring nuclei (indoline and benzopyran)

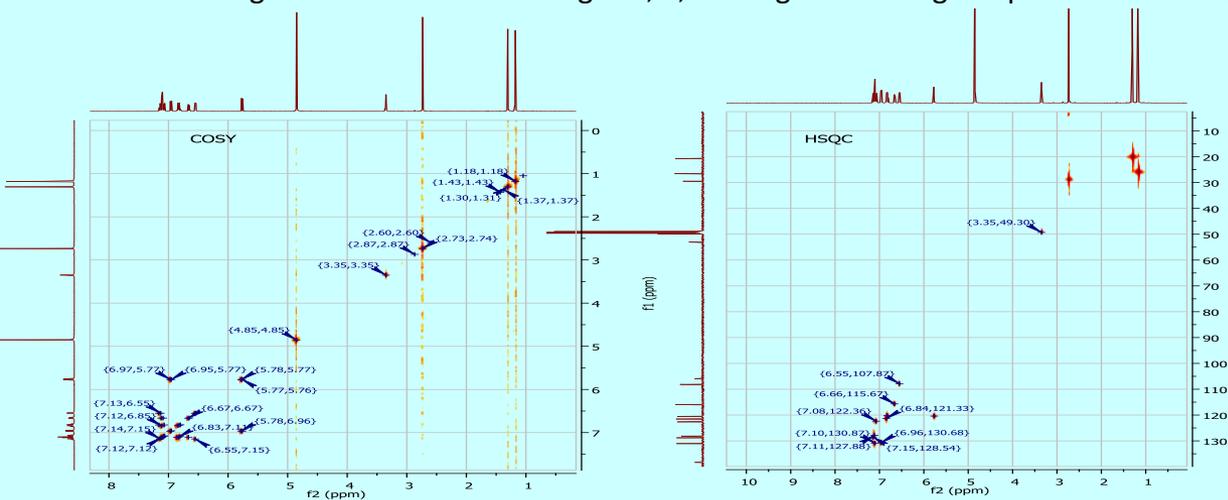


Fig. 3. Fragments of 2D-NMR spectra of spiro-form 1',3',3'-trimethylspiro[2H-1-benzopyran-2,2'-indoline] (SP1) in CD_3OD : (left panel) ^1H - ^1H -Correlation Spectroscopy (COSY) and (right panel) ^1H - ^{13}C -HSQC NMR spectra of free spiropyran (SP1) and its complexes with aluminum salts were recorded in CDCl_3 or in CD_3OD on a Bruker Avance III-500 spectrometer (Germany) with an operating frequency of 500 MHz for protons and 126 MHz for carbon nuclei.

Although spirocyan (SP1) was synthesized more than 70 years ago and its photochemical characteristics were studied in detail by the methods of transient pulsed spectroscopy and laser flash photolysis, the its MC-form lifetime range is from portion a second to several seconds, this technically makes it is impossible to study the composition and structure of its photostationary mixture by standart NMR spectroscopy. Thus, the composition and detailed structure of the photointermediates of its photostationary mixture under illumination with light of 320-350 nm have not yet been proven.

Remained unresolved data:

- the exact configurations of the (SP1) MC-form intermediates and
- the possible presence of quinoid structures.

At the first stage of the work, it was necessary to carry out a detailed analysis and assignment of the signals of the proton and carbon nuclei of the spiro-form (SP1) molecule. The presence in the spiro form of the target molecule (SP1) two fragments of 1,2-substituted benzene with similar magnetic properties of atoms made it very difficult to solve this problem even with a modern device with an operating frequency of 500 MHz for protons, therefore, we first recorded spectra in 2 different solvents and additionally used 2D-NMR spectroscopy with pulse sequences: ^1H - ^1H -Correlation Spectroscopy (COSY) and ^1H – ^{13}C -HSQC. A complete assignment of signals was made for both protons and carbon nuclei of the spiro-form (SP1) molecule.

Study of the structure of the stable complex of spirocyan and aluminum salts by NMR spectroscopy.

Immediately after the introduction of sufficiently large amounts of the Al^{3+} salt in EtOH or MeOH, a new broad absorption band of **complex 1** appears at 380 nm in the UV-Vis region. The formation of **complex 2**, stable in the dark, occurs in two stages: first, a labile short-lived π -complex of aromatic fragments of the spiro-form (SP1) with an aluminum salt (**complex 1**, Fig. 1 B, lifetime less than a minute) is formed, which slowly transforms in the dark into **complex 2**.

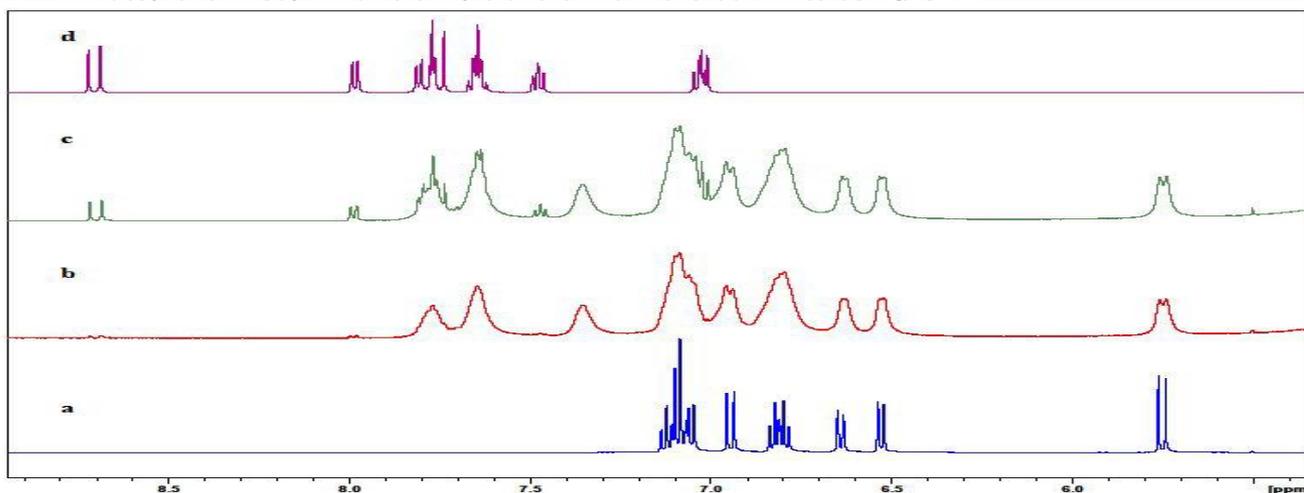


Fig. 4. Fragments of ^1H -NMR spectra of signals of protons of aromatic rings (SP1) SP - ($6.0 \cdot 10^{-2}$ M) in CD_3OD : A - without the addition of $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ (0.2 M) pure spiro form SP; B - complex 1 immediately after adding $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ (0.2 M); C - mixture of complex 1 (63%) and complex 2 (37%) after adding $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ (0.2 M) and holding for 0.5 h; D - complex 2 after adding $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ (0.2 M) and holding for 24 h.

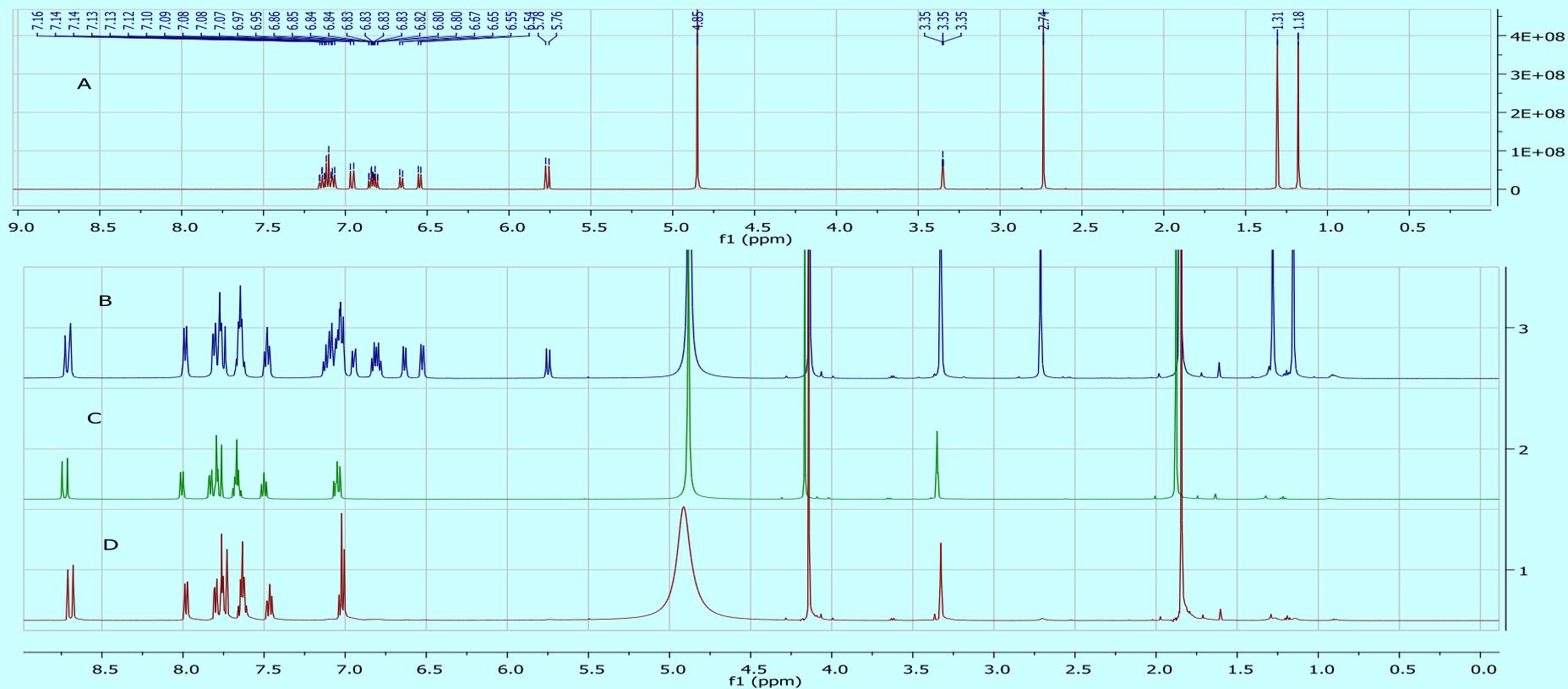


Fig. 5. $^1\text{H-NMR}$ titration: $^1\text{H-NMR}$ spectra (SP1) ($6.0 \times 10^{-2} \text{ M}$) in CD_3OD without adding (A) and after adding a solution of $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ in concentrations, M: (A) - 0; (B) 1.5×10^{-2} ; (C) 3.0×10^{-2} ; (D) 6.0×10^{-2} and keeping samples in the dark for 24 h

We found that the NMR spectra (SP1) change significantly upon the addition of (0.25 -10 eq) $\text{Al}(\text{NO}_3)_3 \times 9\text{H}_2\text{O}$: in the spiro form (SP1) and **complex 1**, the upfield initial signals of protons and carbons of two nonequivalent 3,3-methyl groups in the form of 2 singlets at δ 1.18 ppm / 1.31 ppm (20.8 /26.6 ppm), become equivalent due to the quasi-planar structure of the merocyanine form of **complex 2** and transform with a downfield shift into a single singlet (6H) at δ 1.87 ppm / (27.2 ppm). Similarly, the N-CH₃ signal in the spiro form (SP1) and in complex 1 at δ 2.74 ppm / (29.5 ppm) in the merocyanine form of **complex 2** has a downfield shift at δ 4.16 ppm / (34.8 ppm) due to the presence of a positively charged N-atom. In the spiro form (SP1) and in **complex 1**, the signals of the AB nuclei in the C3-C4 position of the pyran ring in the form of 2 doublets at δ 5.77 ppm/ 6.96 ppm with J 10.2 are also downfield shifted in the spectrum of **complex 2** (δ 8.72 ppm /7.77 ppm J 16.4 Hz), which allows us to unambiguously determine the configuration of the C=C bond in the merocyanine form of **complex 2** as the trans isomer (TTT) (see fig. 1B, and fig. 6). Signal value at 184.5 ppm **complex 2** (the signal of the quaternary protonated C(2)=N⁺ -) in the ¹³C-NMR spectrum clearly indicates the absence of quinoid structures in the composition of **complex 2**. Comparison of the features of the spectra of the spiro-form (SP1) and **complex 1** shows the appearance of two new signals - broadened singlets with integral intensity in ¹H at δ 7.38 ppm and 6.83 ppm with a significant broadening of the shape of all signals in the aromatic range (5.7–7.2 ppm and 7.3–7.9 ppm), a decrease in J from 10.2 to 9.5 Hz, which indicates the presence of coordination interactions between AlX_3 and aromatic fragments of the spiro form (SP1) with the formation of a labile **complex 1**. ¹H-NMR titration (see Fig. 5) tested the formation of **complex 2** in the dark for 24 h and confirmed its final composition of 2 molecules of merocyanine (MC) and 1 molecule of aluminum salt; similar data were obtained by the Job's method according to the data spectrophotometric titration.

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[1]. Levin P.P., Belikov N.E., Levina I.I., Tatikolov A.S., Khodonov A.A., Khudyakov I.V. J. Phys. Org. Chem., 2019, 32 (12), e4012

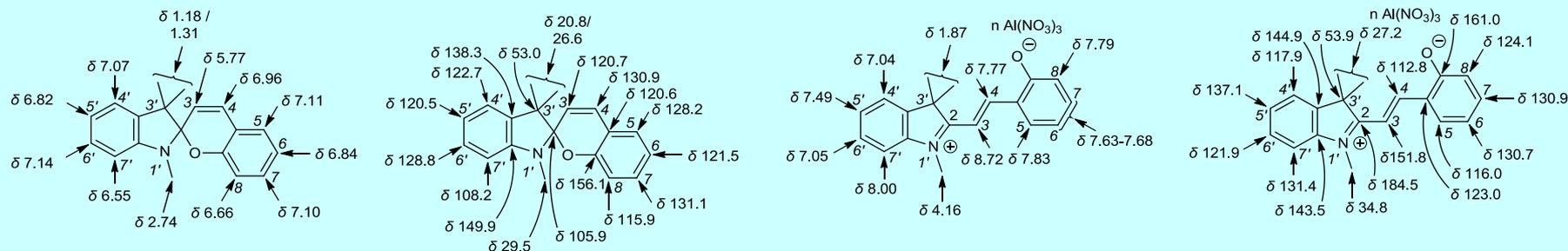


Fig. 6. Chemical shifts of the NMR spectra of spiro-form (A) and **complex 2** (B) (SP1) in CD_3OD : ¹H-NMR (2 left figures) and ¹³C-NMR (2 right figures), n = 1/2.

Research results

Thus, we have established the exact structure of a stable complex of photochromic spiropyran **1',3',3'-trimethylspiro[2H-1-benzopyran-2,2'-indoline] (SP1)** with aluminum salts by methods ¹H-, ¹³C- and 2D-NMR spectroscopy.