SYNTHESIS AND PROPERTIES OF SPIROPYRANS THAT ARE CAPABLE OF REVERSIBLE OPENING OF THE PYRAN RING (REVIEW)

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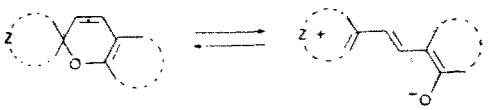
UDC 547.816'72'8.07

The review is devoted to spiropyrans in which the pyran ring can be opened reversibly to give a completely conjugated colored isomer. Methods for the preparation of spiropyrans from various heterocyclic systems, their chemical properties, and the effects of various factors on the relative stabilities of the spiropyrans and the isomeric merocyanines are examined.

Diverse heterocyclic compounds that contain a 2H-pyran ring, the α-carbon atom of which as a spiro atom belongs simultaneously to some other heteroring, belong to the class of spiropyrans that are capable of reversible opening of the pyran ring. They are usually named in conformity with the IUPAC rules for nomenclature of heterocyclic spiro compounds, although the widely known 2H-chromene derivatives are often regarded as 2H-1-benzopyran derivatives.



The first 2,2'-spirobi(2H-chromenes) were synthesized at the beginning of our century [1, 2]. However, they attracted attention only in 1926, when three groups of researchers simultaneously observed that colorless solutions of spirodinaphthopyran in inert solvents are capable of becoming intensely colored when they are heated and of becoming colorless again when they are cooled [3-6]. This discovery served as an impetus for the search for new compounds with thermochromic properties, as a result of which a number of different spirobipyran derivatives were synthesized in the following decade. The study of these compounds made it possible to establish some structural factors that determine the development of thermochromic properties. Dilthey and co-workers also substantiated their dipolar structure of the colored isomer of spirobipyrans [3, 4] that is formed due to heterolytic cleavage of the C-O bond (see [7] for a review of these studies).

Wizinger and Wenner [8] arrived at the conclusion that the ease of thermal ionization should be determined by the ease of transmission of electrons from the spiro carbon atom to the oxygen atom. In conformity with this, thermochromism is not a feature of only spirobipyrans but also can be observed in the case of various 2,2 derivatives of the pyran series. Wizinger's conclusions were confirmed experimentally in the case of 2,2-diaryl-2H-chromenes and spiropyrans that contain various nitrogen heterocycles. He obtained substances for which the thermal equilibrium was shifted either to favor the colorless isomer or to favor the colored isomer.

A new stage in the investigation of spiropyrans began after the detection of the photochromic properties of these compounds, i.e., their ability to undergo conversion to a colored form under the influence of UV irradiation and their ability to be decolorized in the dark or under the influence of visible light [9]. This property of spiropyrans has attracted special attention, since it could be used in the most diverse areas of technology: variable-density light filters, protective devices from powerful sparks, copying materials, materials for the optical recording of information, and many others. More than 500 papers, including several reviews [10-19], of which the last one is the most nearly complete, have been published in the last 20 years. More than 1000 spiropyrans have been synthesized thus far, but, if one disregards the small section in [19], no reviews have been devoted to the methods for their

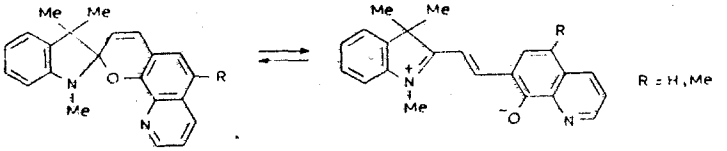
Lensovet Leningrad Technological Institute, Leningrad 198013. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 435-459, April, 1979. Original article submitted June 23, 1978.

0009-3122/79/1504-0351$07.50

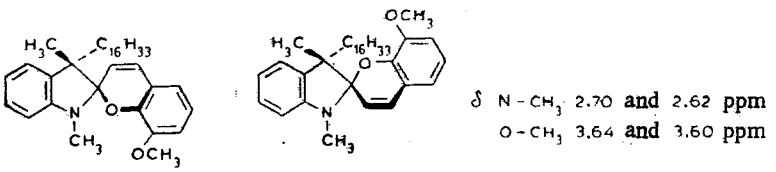
synthesis and their chemical properties. In the present review we will examine the most important research dealing with these problems.

Structure and Spectra of Spiropyrans

The results obtained by Wizinger during his study of the thermochromism of spiropyrans [8] stimulated the search for new photochromic substances among spiro compounds based on the most diverse heterocycles. Most of the spiropyrans known today are colorless or slightly colored crystalline substances (form A) that are insoluble in water, only slightly soluble in alcohol and aliphatic hydrocarbons, and quite soluble in aromatic hydrocarbons and haloalkanes. Their solutions in nonpolar solvents are usually colorless, whereas in polar solvents (alcohols) they may be more or less intensely colored, depending on the structure and the nature of the substituents because of thermal equilibrium conversion to the mercyanine-like isomer (form B). Both isomer B (from polar solvents) and spiro form A (from nonpolar solvents) can be isolated in the crystalline state in the case of some compounds [20]:



The spiran structure of the colorless form (A) is confirmed unambiguously by spectral methods. The IR spectra contain characteristic stretching vibrations of a C_{spiro}-O bond, an intense band at 940-960 cm^{-1}, and a band of the double bond of the pyran ring at ∿1640 cm^{-1}, which is not present in the spectra of the colored isomers [21-25]. In the PMR spectra of 1,3,3-trimethylspiro(indoline-2,2'-[2H]chromenes) the methyl groups in the 3 position give two singlets at ∿1.2 and 1.3 ppm as a consequence of their nonequivalence because of the orthogonality of the indoline and pyran rings. The signal of the N-methyl group is found at ∿2.7-2.8 ppm, while the 3' and 4' protons (attached to the double bond of the pyran ring) show up in the form of two doublets at ∿5.6-5.8 and 6-6.8 ppm (J ≈ 10 Hz) [22, 26-28]. Similar data have been reported for spiropyrans of benzoselenazole [29], benzoxazole [30], and benzothiazole [31-33]. The existence of two stereoisomers in equilibrium at a concentration ratio of 1.7 was established recently [34] for indoline spiropyrans with an asymmetric $C_{(3)}$ atom by PMR spectroscopy of solutions in CCl_4.

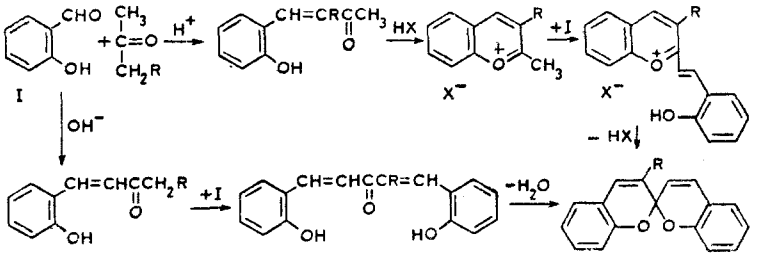


The structures of the colored isomers (B) are also confirmed by their PMR spectra. Thus, the geminal methyl groups attached to $C_{(3)}$ of the colored forms of indoline spiropyrans give one six-proton signal due to the planar structure of the open form, while the signal of the N-methyl group is shifted to weak field (∿4 ppm) because of considerable localization of the positive charge on the nitrogen atom [22, 27, 28]. The difference in the spectra of the A and B isomers makes it possible to identify them when both are present. The trans configuration, increased polarity, and higher positive charge on the β-carbon atom of the vinyl group than on the α atom were established during a study of the open forms of benzothiazoline spiropyrans by ^1H and ^{13}C NMR spectroscopy [37].

To a first approximation, the electronic absorption spectra of the spiropyrans coincide with the sum of the spectra of the fragments, since the spiro atom prevents conjugation between them [14, 19]. In contrast to this, in the case of the B isomer the entire molecule is joined by a single conjugation chain similar to the chromophore system of dimethylidenemerocyanines. It is precisely this circumstance that explains the existence of long-wave absorption in the visible portion of the spectrum in the case of the B isomers. The spectra of the B isomers, like those of ordinary merocyanines, depend markedly on the polarity of the solvent (solvatochromism) [33] and also on the temperature and concentration of the solutions because of association of the molecules [36]. The spectra of spiropyrans and the corresponding colored isomers and discussed in many experimental [19, pp. 102-119] and theoretical [38, 39] papers devoted to the study of photochromism.

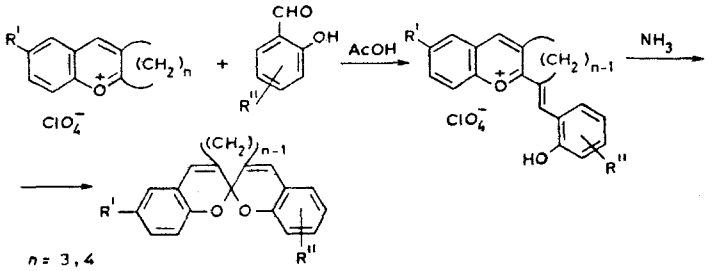
Synthesis of Spirobipyrans

The most general method for the preparation of spirobipyrans is based on the condensation of aromatic o-hydroxy aldehydes with pyrylium salts that have activated methylene groups. Both benzopyrylium salts and their precursors, i.e., o-hydroxystyryl ketones, aromatic o-hydroxy aldehydes, and aliphatic ketones can be used for the synthesis of compounds of the spirobipyran type:

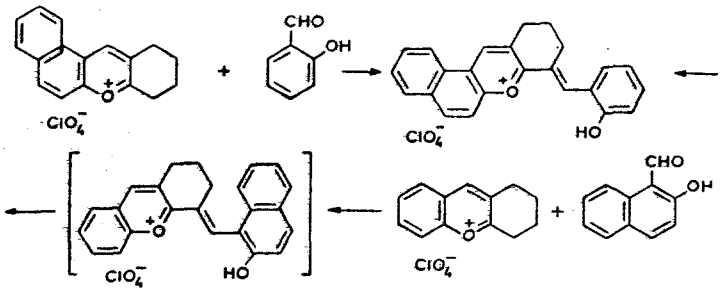


The condensation of hydroxy aldehydes with ketones in alkaline media leads to mono- or bis(o-hydroxystyryl) ketones, which are converted to the corresponding pyrylium salts when they are treated with acid. In acidic media the final reaction product is the α-hydroxystyrylpyrylium salt, which can be obtained without isolation of the intermediates [40]. The salt is converted to the corresponding spirobi(pyran) on treatment with bases. Unsymmetrical methyl alkyl ketones react with aldehydes in acidic media through the methylene group [41], whereas they react through the methyl group in the presence of bases [7]. The methylene group initially undergoes condensation in any media in the case of ketones with an activated methylene group (methyl benzyl ketone and phenoxyacetone) [42-44].

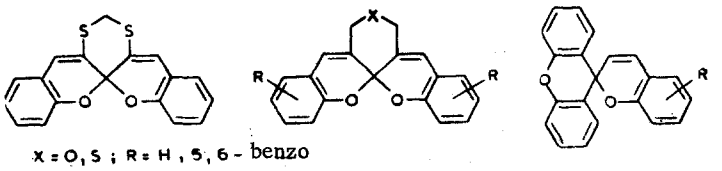
Spirobi(pyrans) in which the 3 and 3' positions arejoined by hydrocarbon bridges are obtained from cyclic saturated ketones [45, 46]. Similar compounds were obtained by condensation in acidic media of 2,3-polymethylenechromylium salts (n = 3, 4) with o-hydroxy aldehydes [25, 47,48]; however, 2,3-penta- and 2,3-hexamethylenebenzo[f]chromylium perchlorates did not react with aldehydes [47].



Unsymmetrical compounds can also be obtained from 2,3-polymethylenechromylium salts, during which the same o-hydroxystyrylpyrylium salt is formed in acidic media, regardless of the synthetic scheme selected [25].



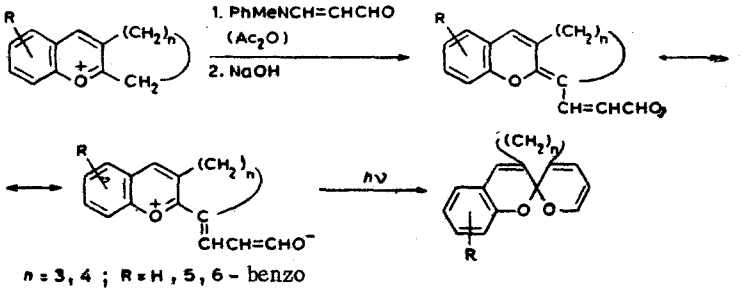
Spirobipyrans that contain a heteroatom in the chain between the 3 and 3' positions have been synthesized by condensation of salicylaldehyde with 1,3-dithian-5-one in the presence of piperidine [49] and of salicylaldehyde and 2-hydroxynaphthaldehyde with tetrahydro-γ-pyrone [50] and tetrahydro-γ-thiopyrone [51] in a refluxing alcohol solution of hydrogen chloride with subsequent treatment of the resulting salts with ammonia.



X = O, S ; R = H, 5,6 - benzo

The condensation of o-hydroxy aldehydes with γ-methyl-substituted benzopyrylium salts has been used for the preparation of the so-called "isospiropyrans," i.e., 2,4'-spirobi-(pyrans) [40, p. 239] in which the spiro carbon atom is bonded to only one heteroatom. Many of them also have photochromic and thermochromic properties; this is particularly true of spiropyrans of the xanthene series (40, p. 370; 52].

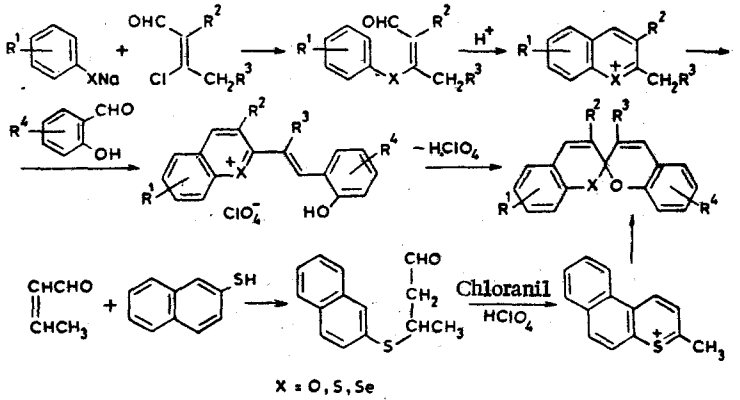
In all of the spirobipyrans that are known today both fragments of the molecule are at least two-ring systems (spirobichromenes). It has not beem possible to obtain compounds in the spiran form in which at least one pyran ring is not annelated with a benzene ring or some heteroring. In contrast to chromylium salts, opening of the pyrylium ring rather than intramolecular cyclization occurs when 2-(o-hydroxystyryl)4,6-diphenylpyrylium salts are treated with bases [48]. A method for the preparation of the valence tautomers of such compounds — formylvinyl derivatives of 2-methylenechromene — was developed to study the possibility of their synthesis [53].



n = 3, 4 ; R = H, 5,6 - benzo

It has been shown that these vinylformyl derivatives exist in the dipolar form (λ_{max} 410 nm); however, they can be converted to spiropyrans when they are irradiated [54].

Analogs of spirobi(chromenes) in which there is a sulfur [54, 55] or selenium [54] atom in place of the oxygen atom in one of the heterorings are of great interest. These compounds could not be obtained by condensation with o-mercapto- or o-hydroselenobenzaldehydes, and an original synthetic scheme that includes aldovinylation of thio- and selenophenols, cyclization in acidic media to 1-thia- and 1-selenanaphthalenium salts, and condensation with 2-hydroxynaphthaldehyde to give o-hydroxystyryl derivatives was developed for them. The o-hydroxystyryl derivatives were converted to spiro compounds by treatment with dry ammonia in ether. Salicylaldehyde and o-vanillin could be subjected to condensation only in the form of the cyclic acetals.

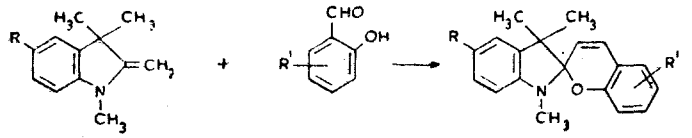


X = O, S, Se

Synthesis of Benzazole Spiropyrans

Indoline derivatives occupy the central position among spirans in which the 2H-chromene ring is connected by a spiro bond with a five-membered nitrogen heteroring [12-19]. The

first indoline spiropyrans were obtained by Wizinger [8] in high yields by condensation of 1,3,3-trimethyl-2-methyleneindoline (the Fischer base) and its 5-methoxy derivatives with salicylaldehyde and 2-hydroxynaphthaldehyde by heating in methanol.*



R = H, OCH_3 R' = H, benzo

This method was subsequently used most frequently [57-61], since the various derivatives of the Fischer base are completely accessible, although they are relatively unstable. The yield of the spiropyran increases with a simultaneous decrease in the yield of the side product (from 2 moles of the methylene base with 1 mole of the aldehyde) as the temperature is raised and the reaction time is increased (the recommended conditions are heating for 5 h in methanol at 65°C or for 1 h at 140°C) [60]. The fraction of the side product is lower in low-polarity solvents, but the degree of conversion is also lower. In a number of cases considerably higher yields of the indoline spiropyrans are obtained by condensation in dimethylformamide (DMF) [62].

The method has been used successfully for the preparation of compounds with various alkyl [62-66] (including 3,3-pentamethylene [65, 66] and 1,7-trimethylene) and aryl [59, 66-69] groups in the 1 and 3 positions of the indoline ring and diverse substituents in the benzene rings of the indoline and chromene fragments [60, 61], for the preparation of a spirothiopyran by condensation with o-mercaptobenzaldehyde [70], and for the synthesis of 6'-nitro-1,3,3-trimethylspiro(indoline-2,2'-chromene) labeled in the 1 (1-*CH_3), 1', and 3' positions with ^{14}C, ^{18}O, and ^{13}C isotopes, respectively [71].

The corresponding quaternary indolenine salts in the presence of an equimolar amount of base (usually piperidine) can be used as the starting compounds [72-74].† A second variant in the condensation (without isolation of the methylene bases) has been used much more often for the preparation of spiropyrans of the benzothiazoline [75-79], benzoselenazoline [29], and benzoxazoline [30] series. This condensation was also carried out under heterogeneous conditions for the preparation of 3'-alkoxy and 3'-aryloxybenzothiazoline spiropyrans: by heating a suspension of benzothiazolium toluenesulfonate in toluene with equimolar amounts of aldehyde and piperidine [75]. In all of these cases the colorless spiropyran forms are produced only when a substituent whose role in the simplest case is explained by destabilization of the corresponding merocyanine because of disruption of its coplanarity is present in the 3' position [72]. The large hypsochromic shift of the absorption maximum of the 3-methyl-2-(2-oxido-5-nitrostyryl)benzothiazolium ion when a hydrogen atom attached to the α-methylidyne group is replaced by a methyl group (~50 nm in polar solvents and 20 nm in low-polarity solvents) may serve as a confirmation of this point of view [33].

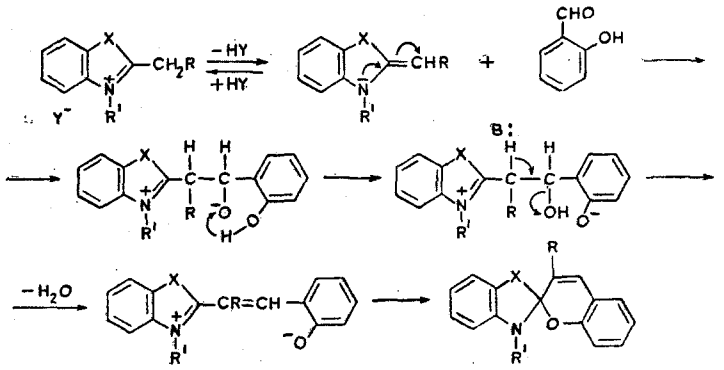
The mechanism of the formation of spiropyrans was examined in the case of derivatives of the benzothiazoline series [76] and is assumed to be identical for all benzazoles [29-30].

A stoichiometric amount of base (piperidine) is required for the condensation of the 2-ethyl-3-methylbenzothiazolium salt with salicylaldehyde, while catalytic amounts are sufficient for the reaction with benzaldehyde [76]. It is therefore assumed that the initially formed methylene base undergoes condensation with the hydroxy aldehyde. Subsequent dehydration, which may be catalyzed by base (piperidine or the methylene base) leads to the merocyanine-like compounds. The ability of the latter to undergo spontaneous cyclization depends on the nature of X, R, and the substituents in both parts of the molecule.

The nature of the anion of the quaternary salt (I^- or TsO^-) has virtually no effect on the results of the condensation. Replacement of the methyl group attached to the nitrogen atom by an ethyl group lowered the yield of the spiropyran somewhat, evidently because of the steric effect and the stronger electron-donor effect of the ethyl group [76]. 3,3'-Dimethylspiro(benzothiazoline-2,2'-2H-chromene) was obtained in virtually the same yield

*Of course, it was later established that Wizinger obtained a product of condensation of two molecules of the Fischer base with one molecule of the aldehyde rather than a spiropyran in the case of salicylaldehyde [56].

†The melting points of the 6'- and 8'-nitro derivatives are confused in [72] (see [58]).

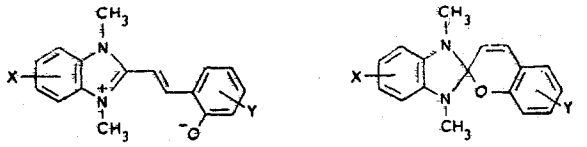


X = C(Alk)$_2$, S, O, Se ; R = Alk, Ar, OAlk, OAr, SMe, SPh

B = molecule of the base

when the corresponding quaternary salt and piperidine was used and from 2-ethylidene-3-methylbenzothiazoline when the condensation was carried out in alcohol. When alcohol is replaced by pyridine, as recommended in a patent [80, 81], the yield of 8'-methoxy-6'-nitro derivative is approximately halved in both cases [76]. However, better results were obtained in pyridine for benzoxazoline spiropyrans and the failures to obtain some compounds of this series were explained by the lower stability of the benzoxazolium salts, as a consequence of which the hydrolysis of the latter competed with the condensation. To avoid hydrolysis, the condensation with hydroxy aldehydes was carried out in the presence of neutral drying agents (Na_2SO_4) [30].

The pronounced effect of substituents in the benzazole part of the molecule on the possibility of intramolecular cyclization was demonstrated in the case of merocyanines of the benzimidazole series. When there were no substituents in the α position relative to the heteroring, these compounds, like other benzazoles [72], were stable only in the merocyanine form [84], but their derivatives with nitro groups in the 5 or 5 and 6 positions of the benzimidazole ring were also isolated in the spiropyran form [85]. The basic condensation of 5,6-dinitro-1,2,3-trimethylbenzimidazolium salts with hydroxy aldehydes was accompanied by considerable hydrolysis of the cation because of its increased electrophilicity. The condensation took place more cleanly in acetic anhydride [85].



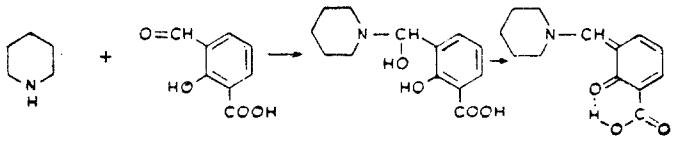
X = 5-NO_2 or 5,6-$(NO_2)_2$; Y = H, 5,6-benzo, 3,5-Br_2, 5-NO_2, 5-OCH_3

X = 5-NO_2, Y = H ; X = 5,6-$(NO_2)_2$, Y = H, 6'-OCH_3

It is difficult to make any correlations regarding the effect of the substituents in benzothiazolium derivatives on basic condensation. Only a certain decrease in the yields for 6-carboxy derivatives has been noted [76]. The nature of the substituents in the o-hydroxy aldehydes has a stronger effect. As expected, the highest yields are obtained with aldehydes that are activated by electron-acceptor groups (NO_2 and CN) [58, 76]. It should be noted that up until now not one case of successful condensation with aliphatic-aromatic o-hydroxy ketones has been reported.

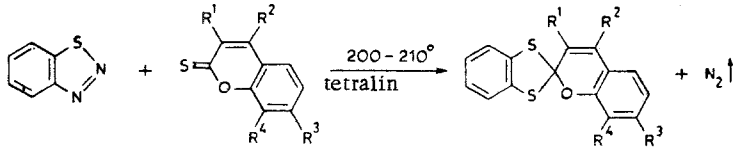
An unsuccessful attempt to obtain benzothiazoline spiropyrans from a 3-methyl-2-ethylbenzothiazolium salt and 3-carboxysalicylaldehyde (3-formylsalicylic acid) in the presence of piperidine has been reported, although 3-methoxycarbonylsalicylaldehyde reacted normally [32]. Condensation was also not observed in the case of excess piperidine but proceeded readily in a neutral alcohol medium with the same aldehyde and 3-methyl-2-ethylidenebenzothiazoline, as well as with Fischer bases [86]; condensation in a neutral medium did not interfere with the possible conversion of the methylene bases to quaternary salts in this case. Dumenil and co-workers [32] explained the lack of a reaction by deactivation of piperidine by the carboxylic acid. In fact, piperidine and the carboxylic acid can form a buffer system with insufficient basicity for ionization of the methylene group of the quaternary salt. However, it is more likely that the carboxyl group stabilizes the product of the reaction of piperidine withthe formyl group, thereby making the aldehyde inert. However, this

does not interfere with the reaction with the more active 2,3-dimethylbenzothiazolium salt (the reaction products is a merocyanine).



Synthesis of Spiropyrans with Other Five-Membered Heterocycles

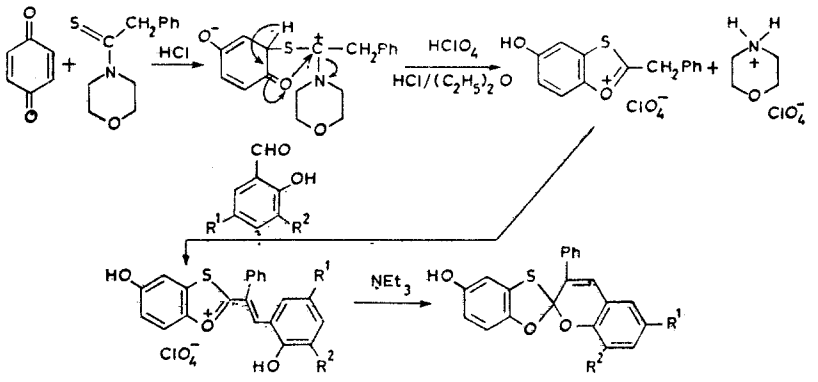
Reports regarding the synthesis of spiropyrans from 1,3-benzodithiolium [87-91] and 1,3-benzoxathiolium [92] salts have been recently published. The first representatives of benzodithiolium derivatives were obtained by condensation of 2,5-dimethyl-1,3-benzodithiolium perchlorate with 5-nitrosalicylaldehyde and 2-hydroxynaphthaldehyde in acetic acid in the presence of $HClO_4$, with subsequent treatment of the salts of hydroxy styryl compounds with ammonia in ether [87]. In contrast to benzothiazoline spiropyrans, the cyclic forms of these compounds were stable also when there were no substituents in the 3' position. Shortly thereafter, an original method for the synthesis of analogous compounds that made it possible to obtain derivatives with substituents in the 4' position, which are inaccessible by means of the classical method because of the inert character of the alkyl aryl ketones, was described [89].



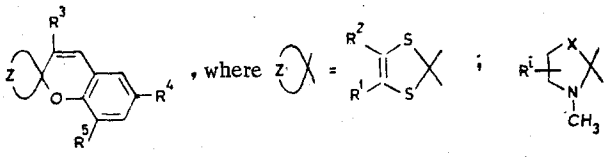
a $R^1=CH_3$; b $R^1=CH_3$, $R^4=OCH_3$; c $R^2=CH_3$; d $R^2=CH_3$, $R^3=OCH_3$; e $R^2=Ph$; remainder R=H

It is true that this method was found to be unsuitable for the synthesis of 6'-nitro derivatives because of the low activities of the corresponding 6-nitrothiochromones. A two-step method [90, 91] similar to the method indicated in [87] was therefore subsequently used for the preparation of nitro derivatives that are of greatest interest as photochromic compounds. The proposed mechanism of the condensation [91] assumes the prior formation of a methylene base (with the participation of acetic acid as the proton carrier) as in the case of basic catalysis of the condensation of quaternary salts of benzazoles [76]. A number of spiropyrans with alkyl, aryl, and aralkyl groups in the 3' position have been described [91].

A one-step method in which the formation of the quaternary 5-hydroxy-2-benzyl-1,3-benzoxathiolium salt and its condensation with hydroxy aldehydes were carried out simultaneously in ether in the presence of HCl and $HClO_4$ has been used for the preparation of 5-hydroxy-1,3-benzoxathiolium salts of spiropyrans [92].



Spiropyrans of a number of mononuclear heterocycles — 1,3-dithiole [93], oxazolidine [94], and thiazolidine [95] — were recently obtained.



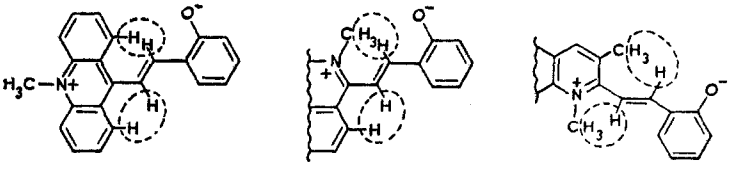
R^1, R^2 = H, Ph, p-PhC_6H_4; R^3 = Ph, CH_3; R^4, R^5 = OCH_3, NO_2; R^i = H, CH_3; X = O, S

The condensation of dithiolium salts with aldehydes was carried out in ether in the presence of $HClO_4$ and HCl, since the yields were very low in acetic acid [93]. The merocyanine isomers of these spirans undergo cyclization exceptionally rapidly, approximately two orders of magnitude faster than their benzodithiole analogs. The rate constant of dark decolorization (35 sec^{-1} in toluene at 25°C) has been determined for only one compound (R^1 = R^3 = Ph, R^2 = H, R^4 = OCH_3, and R^5 = NO_2).

Oxazolidine derivatives were obtained by condensation of the corresponding quaternary salts in the presence of piperidine both in alcohol solution and in absolute benzene with the addition of anhydrous sodium sulfate [94]. One thiazolidine spiropyran was obtained not only by the classical method but also (although in only 10% yield) by quaternization of the corresponding 2-(o-hydroxystyryl)-1,3-thiazol-2-ine with subsequent splitting out of acid on treatment with a base [95].

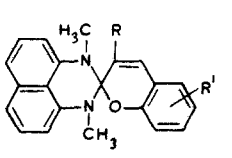
Synthesis of Spiropyrans with Six-Membered Heterorings

Spiropyrans of the acridine series were first obtained by Wizinger [8] from 9,10-dimethylacridinium salts. Repeated but unsuccessful attempts to synthesize pyridine and quinoline derivatives were subsequently made [97-99]. The reports by Schiele and Kalinowski [100, 101] in 1966 regarding the synthesis of quinoline spiropyrans and their explanation for the failure of other investigators (because of the reaction of the aldehydes with the N-methyl groups of the quaternary salts [98]) were found to be erroneous [99, 102]. The question of the possibility of intramolecular cyclization of o-oxidostyryl derivatives of the heterocyclic cations of the pyridine series and the stabilities of the spiropyran forms was examined by means of the MO LCAO method within the Hückel approximation [103]. It was concluded that these properties depend on the magnitude of the positive charge on the carbon atom of the quaternary salt, due to which a pyran ring is formed, and on the difference in the π-electron energies of the quaternary salt and the corresponding dihydro derivative (the "localization energy" of the reaction center; this approach on the basis of more refined MO methods has been used for a large number of heterocycles [39]). In conformity with the results of the calculations, spiropyrans of phenanthridine [99, 104] and mono- and bisspiropyrans of 4,9-diazapyrene [103, 105] have been found to be readily obtainable. In addition, in an examination of acridine spiropyrans [103] it was assumed that there is a certain amount of destabilization of the corresponding merocyanines because of disruption of their coplanarity by the hydrogen atoms in the 1 and 8 positions of acridine (in [103] these atoms are designated 4 and 5).

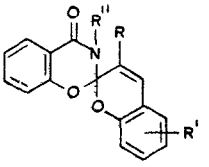


Similar destabilization of merocyanines should also have been expected for derivatives of other heterocycles with a similar geometry in the vicinity of the cyclization center, particularly phenanthridine and isoquinoline. This effect is evidently extremely significant, since colorless spiropyrans, in contrast to compounds of the quinoline series, actually could be obtained for 1-(o-oxidostyryl)-2-methylisoquinoliniums [106] and their 3,4-dihydro derivatives [107]. With respect to the ease of opening the pyran ring under the influence of polar solvents, dihydroisoquinoline spiropyrans are close to phenanthridine spiropyrans and are considered more stable than the isoquinoline analogs [108]. In this connection, one might have expected a similar increase in the stabilities of spiropyrans based on quinaldine and lepidine under the influence of a substituent in the 3 position. Even a methyl group may be a substituent of this type, despite its electron-donor effect, since the position in space of one of its hydrogen atoms coincides with the position of the peri-hydrogen atom in the compounds examined above [109].

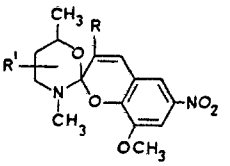
Spiropyrans based on perimidine [110], 1,3-benzoxazin-4-one [111], and mononuclear perhydro-1,3-oxazine [112] have been recently described. All of them were obtained from the quaternary salts of the corresponding heterocycles (in the latter case the reaction could be realized only in benzene with piperidine and removal of the water with anhydrous magnesium sulfate; see [75, 94]). These heterocations sufficiently activate not only methyl groups but also ethyl groups (R = CH_3), although the 2-ethyl-1,3-dimethylperimidinium cation reacted with aldehydes in the presence of piperidine only in pyridine [110].



R = H, Me
R = H, 5,6-benzo



R = H, Me; R' = H, 5,6-benzo, 6'-OMe; R'' = H, Alk



R = H, Me, Ph; R' = H, Me

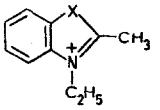
Comparison of the Activities of C-Alkyl Groups Bonded to Heterocyclic Cations and Stabilities of the Corresponding Spiropyrans

Since the principal methods for the preparation of spiropyrans utilize the condensation of the alkyl groups of the quaternary salts of heterocycles or the corresponding methylene bases, it is interesting to compare the activities of these compounds. Although there is no single method for systematic physicochemical studies for them, a qualitative comparison is possible. In agreement with the magnitudes of the Brooker proportional deviation [113] (Table 1), the most stable spiropyrans correspond to the most acidic quaternary salts (indolinium salts) and are not formed at all in the case of the pyridinium and benzimidazolium ions. The stabilities of the methylene bases of these quaternary salts in which the nitrogen atom is in the same valence state as in spiropyrans also decrease in parallel with the acidities of the C-methyl groups of the salts. Thus the monomeric Fischer base is completely stable at room temperature when oxygen is absent, 1-ethyl-2-methylene-1,3-benzoselenazoline can be stored for several days at 0°C, its sulfur analog can be stored at 0°C for only 2 h, and the 4,5-benzo derivative of the latter is stable only in solution in tetramethylguanidine [114]. When there are substituents in the methylene group, the stabilities of the monomers of the methylene bases are increased considerably [115, 116]. Unfortunately, the pK_a values were measured only for a few compounds. The following values were found for α- and γ-N-methylpicolinium, N-methylquinaldinium, and N-methyllepidinium ions, respectively, in acetonitrole [117]: 24.8, 25.0, 19.7, and 20.6. The acidities of the C-methyl groups decreased in the order V > III > II > IV in alcohol in the case of the N-methylquinaldinium cation (II) and its 3-methyl derivative (III) and the 1,2-dimethylisoquinolinium cation (IV) and its 3,4-dihydro derivative (V) in alcohol [118]. The pK_a values for aqueous solutions, which were found by extrapolation of the results of measurements in aqueous dimethyl sulfoxide (DMSO) were recently determined for cations V, II, and IV, as well as for 1,4- and 1,2-dimethylpyridinium ion (VI and VII) [119] [13.07, 15.76, 15.95, 18.19, and 19.19]; these values are in agreement with the order established for alcohol solutions.

The kinetics of deuterium exchange in the C-methyl groups of heterocyclic cations in neutral media have been studied more extensively. The order of the change in the acidities obtained on the basis of kinetic measurements [120] basically coincides with the order established by Brooker and co-workers. Since the acidities of these groups depend primarily on the magnitude of the positive charge on the carbon atoms, a comparison of the chemical shifts of the carbon nuclei is of interest. It has been shown that the chemical shifts of the ring carbon atoms that bear the methyl groups depend linearly on the densities of the π electrons calculated by the Hückel MO method [121] (^{13}C $\delta = 109.7q_\pi - 49.03$; $r = 0.901$) and are good indicators of the C-H acidities of the methyl groups. When allowance is made for the densities of the π and σ electrons, the correlation is poorer ($r = 0.831$) and there is no correlation for the shift of the carbon atoms of the methyl groups. These conclusions were also confirmed during a study of cations II-V [118].

The kinetics of condensation with p-dimethylaminobenzaldehyde in neutral media were also studied for the alkylheteroammonium cations indicated in Table 1 [122, 123]. It is apparent from the data presented in Table 1 that the activity increases as the C-H acidity increases, although the rate-determining step in this reaction is not ionization but rather is reaction

TABLE 1. Activities of the C-Methyl Groups of Heterocyclic Cations



X	$C(CH_3)_2$	Se	O	S	Sa	CH=CH	b	$N-C_2H_5$
Proportional deviation, % [113]	28,3	35,9	37,5	40,7	58,7	57,1	86,5	100
Deuterium exchange at 70°C in DMSO/D_2O, $\tau_{1/2}$, min [120]	<3	27,0	30,5	36,0	139	341	—	No exchange
$^{13}C_\alpha$ δ in DMSO, ppm from CS_2 [121]	−0,1	2,9	23,9	14,3	—	30,3	—	39.0
$k^{50°} \cdot 10^4$ with p-dimethylaminobenzaldehyde in alcohol, liters/mole·min [122]	—	—	80	64	13,3	2,3	1,0[c]	0,0

a) Naphtho[1, 2-d]-1,3-thiazolium ion; b) 1-ethyl-2-methylpyridinium ion; c) at 70°C in butanol [123].

of the aldehyde with the methylene base that is present in the equilibrium concentration (very low but spectrally observable) [124]. The symbatic character of the condensation rate constants and the C-H acidities is evidently due to the fact that for various heterocycles the equilibrium concentrations of the corresponding methylene bases differ much more markedly than their activities. Thus, various methods for the estimation of the reactivities reveal higher activities of the C-methyl groups bonded to the five-membered heterocations than in the case of those attached to six-membered heterocations. A similar relationship is also observed for other C-alkyl groups. Thus, although the condensations for five-membered heterocations involving substituted methylene groups (CH_2R) with aldehydes proceed quite readily [29, 30, 60, 76-79], in the case of six-membered heterocycles condensation, if it does take place, does so only under much more severe conditions [110, 125-129]. The very low activities of substituted methylene groups in six-membered heterocations is evidently due to not only the low positive charge but to a considerable extent also to steric hindrance because of a decrease in the angle between the bonds with the ring at the adjacent atoms. In [118] the reactivities of the C-methyl groups were investigated for α,N-dimethyl-substituted quinolinium, 3-methylquinolinium,isoquinolinium and tetrahydroisoquinolinium ions. On the basis of a comparison of the acidities of these groups, an estimate of the charges on the carbon atoms of the rings by means of ^{13}C NMR spectroscopy, polarographic reduction of the cations, and the kinetics of the condensation with p-dimethylaminobenzaldehyde it was shown that steric factors have a large effect not only on the rate of reaction with aldehydes but also on the ease of intramolecular cyclization to give spiropyrans.

For the comparison of the activities of the C-methyl groups of the heterocations used in the synthesis of the spiropyrans from the kinetics of the condensation with aldehydes, one should, strictly speaking, have examined the condensation with o-hydroxy aldehydes. It hasalready been noted above that, in contrast to the benzaldehyde, a stoichiometric amount of piperidine is required for the reaction with them in the case of basic catalysis [76]. Moreover, in the presence of a large excess of piperidine (a 100-fold amount) the kinetic parameters of salicylaldehyde in the condensation with 1-ethyl-2-methylpyridinium iodide also differ substantially from the parameters of other benzaldehyde derivatives, including also p-hydroxy-substituted compounds. Under these conditions, the reaction rate did not depend on the piperidine concentration, and the largest second-order reaction constant was found for salicylaldehyde. At the same time the minimal activation energy was observed for it (Table 2) [130]. However, for most heterocations the study of the kinetics of basic condensation with o-hydroxy aldehydes is complicated by acid–base transformations of the condensation products, and the simultaneous spirocyclization evidently did not occur.

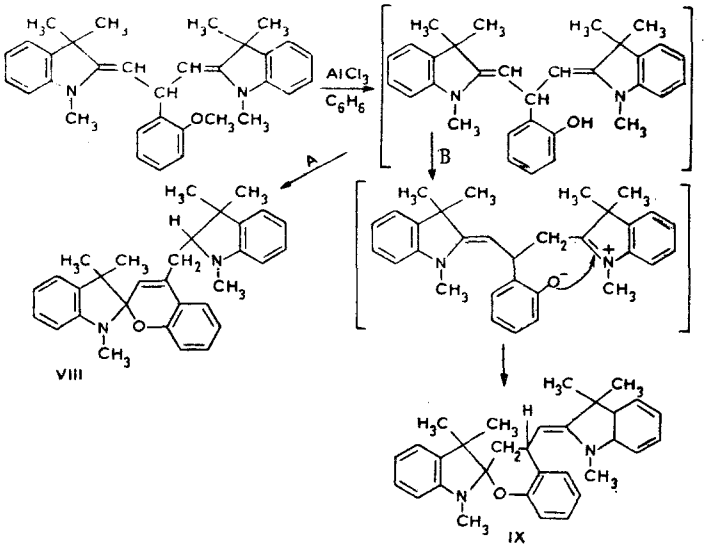
Side Compounds in the Synthesis of Spiropyrans

Side products, which are most often products of condensation of one aldehyde molecule with two molecules of the heterocycle, are formed in addition to the spiropyrans in a number of cases in the condensation of aldehydes with the quaternary salts of heterocycles or the

TABLE 2. Rate Constants and Activation Parameters for the Reaction of 1-Ethyl-2-methylpyridinium Iodide with Substituted Benzaldehydes in Ethanol [130]

X	$k_{eff} \cdot 10^4$, liters/mole·sec				E, kcal/mole	lg A (25°)
	25°	35°	45°	55°		
4-OH-3-OCH_3	3,73	6,45	12,77	21,70	12,08	5,38
4-OH	7,0	21,90	35,50	65,40	11,32	5,10
4-$N(CH_3)_2$	9,0	17,0	33,0	58,0	12,65	6,20
2-OH	57,0	72,0	91,2	116,0	4,75	1,26

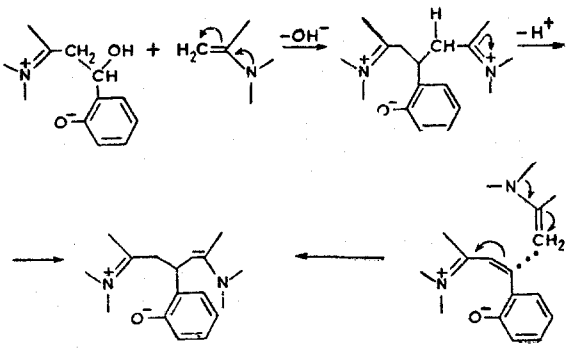
corresponding methylene bases. This was first observed in 1952 in the case of indoline spiropyrans [56]. Donor substituents in the aldehyde molecule [56, 131], a reduced temperature



during the condensation, and a high solvent polarity [60] promote the formation of a side product. The 4'-(2-indolinylmethyl)spiropyran structure (VIII) was proposed for the side product in the condensation of the Fischer base with salicylaldehyde, since the same compound was obtained by demethylation of o-methoxybenzalbis(1,3,3-trimethyl-2-methyleneindoline) [56].

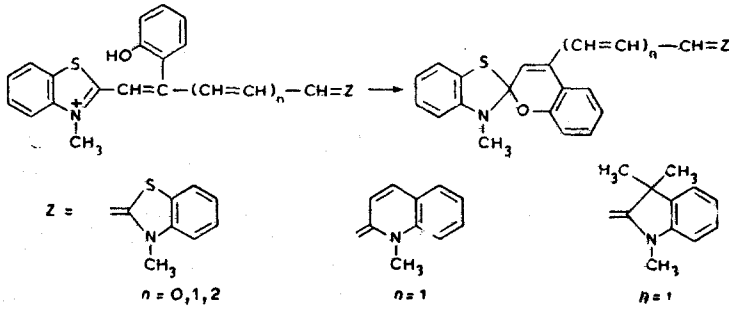
In their examination of the IR spectra of these compounds Schiele and Arnold [132] also assumed 4'-substituted spirochromene structures for them. However, in an analysis of the PMR spectra of the products of concentration of the Fischer base with salicylaldehyde it was demonstrated convincingly that the side compound does not contain a chromene ring and is a 4'-(2-indolinylidenemethyl)spirochroman derivative (IX) [27]. The formation of the latter from o-hydroxybenzalbis(methyleneindoline) is in complete agreement with the properties of enamines (pathway B), while the formation of a substituted spirochromene (VIII) is unlikely. Similar compounds, the structures of which were also established by PMR spectroscopy, were obtained in the condensation of salicylaldehyde and its derivatives with 1,1-diphenylethylene [133] and 1,1-bis(p-dimethylaminophenyl)ethylene ("Michler's ethylene") [134] in the presence of acids, with the 9,10-dimethylacridinium ion (in the presence of bases) [135], and with 9-methyl-9-xanthenol (in acidic media) [52, 136]. In contrast to spirochromenes, compounds of the spirochroman type are not photochromic and have intense fluorescence; this makes it possible to detect very small traces of them [137].

When "discondensed" indoline compounds are heated with acetic acid, they split out a second indoline residue and are converted to salts of ordinary spirochromenes [60]. When it is heated in the presence of an o-hydroxy aldehyde, the liberated indoline is also converted to a spirochromene. It is assumed that "discondensed" compounds are formed either by reaction of the intermediate carbinol with the methylene base [60] or as a consequence of the addition of the latter via a reaction of the Michael type to the merocyanine form of the spiropyran [19, p. 256].



Citing unpublished data, Bertelson [19, p. 256] reports the preparation of "discondensed" compounds by heating indoline spirochromenes with the Fischer base, although Hinnen and coworkers were unable to do this [60]. Similar transformations have been described for spiropyrans of the xanthene series [52] and in the reaction of indoline spiropyrans with Michler's ethylene [138-139]. A methyl group attached to a double bond has a very pronounced effect on such reactions [140]. A homolog of Michler's ethylene — 1,1-bis(p-dimethylaminophenyl)-propene — is much less active than Michler's ethylene and does not react with salicylaldehyde, and reaction with its nitro derivatives gives only 2,2-diaryl-3-methylchromenes (without discondensed compounds). Moreover, Michler's ethylene adds readily not only to indoline spiropyrans but also to 3-methyl-2-(2-oxido-5-nitrostyryl)benzothiazolium ion but does not react at all with its α-methyl derivative.

"Discondensed" compounds possibly can be oxidized to difficult-to-obtain 4'-substituted spiropyrans, but thus far there have been no reports of such attempts. Several 4'-substituted spiropyrans have been obtained only from β-(-o-hydroxyphenyl)-substituted thiacyanines [141].



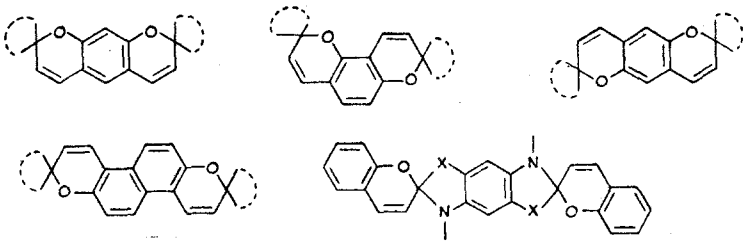
A number of side products, including 1,2,7,8-dibenzoxanthene, are formed in the preparation of spirobichromenes from 2-hydroxynaphthaldehyde with ketones in alcohol solutions of HCl because of the reaction of the aldehyde with alcohols [142].

Methods for the Modification of the Structures and Properties of Spiropyrans

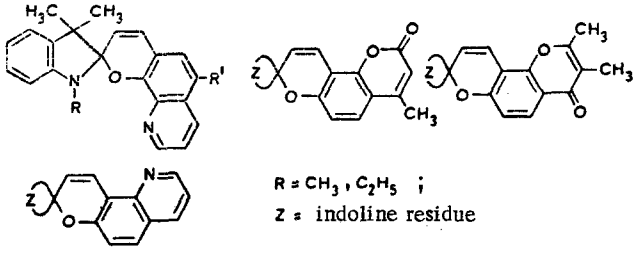
The reasons for the modification of the structures of spiropyrans have been reduced primarily to the following: for a change in the spectral and kinetic characteristics of the photoinduced forms, an increase in the quantum yields and degree of reversibility of photocoloration, an increase in the compatability with polymeric materials, and an explanation of the mutual effect of closely situated photochromic centers (both those in conjugation and those bonded to isolated chains).

Of the many derivatives of spiropyrans one should note several types of compounds synthesized primarily by the usual methods. These include indoline [143-145] and benzothiazoline [144] spiropyrans in which two spiropyran fragments are bonded by one or several (up to 12) methylene groups attached to the nitrogen atoms of a heteroring or the carbon atom of a benzene ring or through an intermediate amide group [144]. These compounds were obtained from the corresponding bifunctional quaternary salts or bis(o-hydroxy aldehydes). Indoline derivatives in which the chain between the nitrogen atoms contain 1,4-phenylene, an oxygen atom, or a double bond (>NCH_2CH-$CHCH_2N$<) [146], as well as compounds in which chromene rings are bonded by carbonyl or sulfonyl groups [147], have been described. In some benzothiazoline and indoline bifunctional spiropyrans the benzene rings of the nitrogen heterocycles

[148] or the chromene fragments [147, 149] are connected directly by a single bond or both pyran rings are annelated with one benzene or naphthalene ring [145, 147, 149, 150].



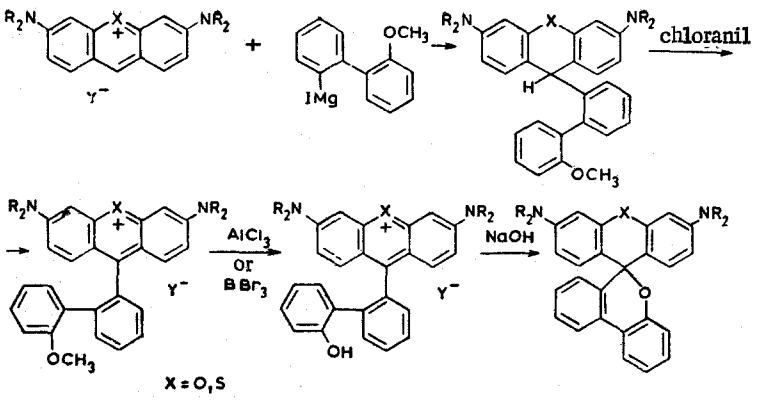
Bisspiropyrans with chromene fragments that are not interconnected were obtained from bisquaternary salts of condensed nitrogen heterocycles such as the above-mentioned 5,10-dimethyl-4,9-diazapyrene [103, 105] and linear and angular benzobisazoles [151]. A number of spiropyrans with functional groups that have a substantial effect on the optical, physical, or chemical properties have been described. Thus a benzoyl group in the chromene ring of indoline [152] and phenanthridine [153] spiropyrans has been proposed as an intramolecular sensitizer, while the presence of a phenylazo group [153, 154] led to a strong bathochromic shift of the absorption of not only the cyclic form but also the merocyanine form as a consequence of interaction of the two chromophores. Water-soluble indoline spiropyrans were obtained from salicylaldehyde derivatives that contain sulfonatomethyl ($-CH_2SO_3Na$), N-pyridiniamethyl, and piperidinomethyl groups in the 6 position [155]. Compounds of the latter type, as well as their analogs with hydroxy- and ethoxymethyl groups, were used for the preparation of photochromic chelate complexes [156, 157]. Spirochromenes with an annelated pyridine ring, the merocyanine isomers of which are capable of forming chelates, have been proposed as analytical reagents [158]. These compounds were obtained by condensation of the Fischer base with 7-formyl-8-hydroxyquinoline and its 5-methyl derivatives. Indoline spiropyrans with heterocycles annelated to the chromene fragment were also obtained from 7-hydroxy-8-formyl-substituted 4-methylcoumarin, 2,3-dimethylchromene, and quinoline [159]. Considerable inhibition of the dark cyclization of the merocyanine forms is characteristic for these compounds.



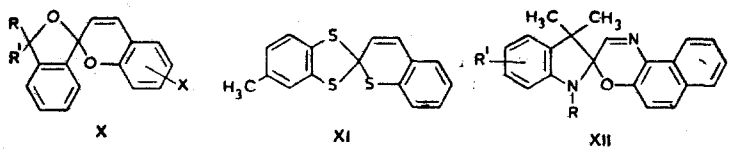
A number of spiropyrans that contain unsaturated groups have been synthesized for the preparation of polymeric photochromic materials. 5-Methacrylamido-3,3'-dimethyl-6'-nitrospiro(benzothiazoline-2,2'-chromene) and its copolymerization with methyl methacrylate, methacrylonitrile, styrene, and 2-vinylnaphthalene have been described [160]. N-Allylbenzothiazoline spiropyrans have been obtained [33]. 6-Methacrylamido derivatives and the copolymer of one of them with methyl methacrylate were later synthesized [161]. Indoline spiropyrans useful as monomers were obtained by acylation of N-β-hydroxyethyl [162-165] and 6-hydroxy derivatives [163] with methacryloyl chloride and by reaction of p-chloromethylstyrene with the sodium salt of 5-carboxy-1,3,3-trimethylspiro(indoline-2,3']benzo[f]chromene) [166]. The photochromic properties of the polymers with covalently bonded photochromic groups have been examined in a review [167].

Concluding our examination of the methods for the synthesis of spiropyrans, let us note the original method proposed for spiro(xanthene-9,6'-6H-benzo[c]chromenes) that have cryochromic properties [168].

The synthesis of spiropyrans of the 2-oxaindane series (X) [169] and spirothiopyran XI, obtained by the reaction of the sodium salt of o-mercaptobenzaldehyde with 2,5-dimethylbenzo-1,3-dithiolium perchlorate was recently described [170]. Spiro(indoline-2,3'-naphtho[2,1-b]-1,4-oxazines) (XII) that have photochromic properties were also obtained by a method similar to that used for spiropyrans by condensation of 1-nitroso-2-naphthol with 2-methyleneindolines



[171] or quaternary salts of 2,3,3-trimethylindolenine in the presence of an equimolar amount of triethylamine [172].



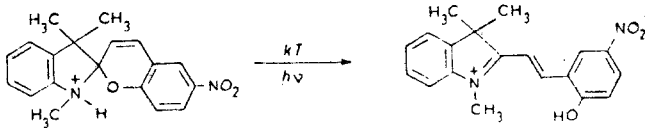
Chemical Properties

One of the most interesting properties of spiropyrans is their reversible conversion to colored merocyanine-like isomers. The position of this equilibrium in dark processes is determined by the relative thermodynamic stabilities of the two isomers, which may vary over a wide range. As a rule, the cyclic forms have low polarities, whereas a considerable charge separation, which brings their electronic structure close to a dipolar structure, is characteristic for the colored forms [36, 173, 174]. The dipolarity of the open forms is confirmed by their pronounced negative solvatochromism [33, 61, 72, 104, 108]. In connection with the dipolarity of the colored forms, they are stabilized by the introduction of substituents that facilitate delocalization of the separated charges, viz., acceptor substituents that are conjugated with a phenoxide oxygen atom and donor substituents that are conjugated with a positive charge of the heteroring [72]. Polar solvents that solvate the much more strongly polar colored forms also promote stabilization of the latter with almost no effect on the stability of the cyclic forms [72]. Partial [175] and even almost complete conversion to the colored isomers [104] is therefore observed in polar solvents for many spiropyrans that form colorless solutions in nonpolar solvents. Using this property in some cases one can isolate both isomers in crystalline form [75, 99, 104, 107, 175]. It was recently shown that the structures of the colored forms of benzodithiol [176] and benzoxathiol [92] spiropyrans are closer to quinoid structures than dipolar structures. The shift of the position of the equilibrium between the two forms as the polarity of the medium changes can be easily detected in aqueous acetone mixtures with various compositions or other binary solvents from the change in the intensity of the long-wave absorption of the colored form [108]. Stabilization of the open forms in polar media is also manifested in the fact that most spiropyrans are converted to colored forms during adsorption; the polarizing effect of sorbents is considerably stronger than that of solvents [74, 177-179]. The formation of 3-methoxy-5-nitrosalicylaldehyde, the amount of which depended on the activity of the sorbent, was also observed in the case of adsorption of 6'-nitro-8'-methoxy-1,3,3-trimethylspiro(indoline-2,2'-[2H]chromene) on silica gel [180].

In alcohols opening of the pyran ring may be accompanied by the addition of a proton from the solvent to the phenoxide oxygen atom of the dipolar form [141, 181, 182]. The analogous reaction of hydroxyl solvents with merocyanine dyes with structures that are close to those of the colored forms of spiropyrans has been previously discussed [182]. The addition of acids to the spiropyrans leads to complete conversion to the corresponding o-hydroxystyryl salts. The formation of salts from both forms has been established for the spiropyrans of nitrogen heterocycles at low temperatures:

$$A + H^+ \rightleftharpoons Y^+ \underset{\text{Visible light at 120°C}}{\overset{\text{UV light}}{\rightleftharpoons}} BH^+ \rightleftharpoons B + H^+$$

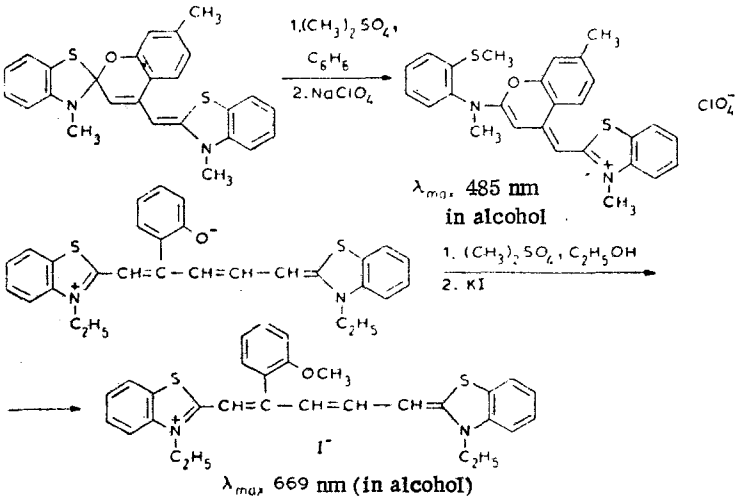
Form A requires a considerably large excess of acid for salt formation. On the basis of the spectral and photochemical data it has been assumed that under conditions where the A ⇄ B interconversion is possible, salts of the BH^+ type are formed due to protonation of open form B. Salts Y^+ and BH^+ are regarded as stereoisomeric salts of open forms, of which Y is the cis isomer [183]. At the same time, the formation of salts of the Y^+ type has not been observed for spirobi(pyrans). In methylcyclohexane at low temperatures for any spiropyrans the spectral changes when acids are added attest to the formation of salts of the cyclic form (AH^+) but not of the Y^+ type [183]. In the case of 6'-nitro-1,3,3-trimethylspiro(indoline-2,2'-chromene) two salts with HCl that differ with respect to their physical properties and behavior under the influence of bases were isolated. The AH^+ structure was assumed for one of them obtained in toluene at −78°C. When it is stored or refluxed for 10 min in alcohol, it is converted completely to the BH^+ isomer. It was assumed that the proton in the AH^+ salt is localized on the indoline nitrogen atom; however, its addition to the oxygen atom and even to the nitro group is possible. The possibility that the site of addition of the proton differs in different derivatives and depends on the substituents present is also not excluded [19, pp. 258, 263]



AH^+ (yellowish) BH^+ (bright yellow)

In the case of spirobi(chromenes) the substituents in the α position relative to the spiro atom hinders opening of the substituted pyran ring because of the sharp decrease in the stability of the corresponding o-oxidostyryl because of disruption of its coplanarity. The pyrylium salt is therefore due to opening of the unsubstituted ring when one substituent is present in the α position in spirobi(benzo[f]chromenes) [184]. However, when two α substituents, even methyl groups, are present, the pyrylium salts cannot be isolated. They can be observed only in solutions from the absorption spectra in strongly acidic media [185]. If both α positions are connected by a polymethylene chain, the pyrylium salt cannot be isolated when there are more than three methylene groups [185].

The cyclic form of 4'-substituted benzothiazoline spiropyrans reacts with dimethyl sulfate at the sulfur atom with opening of the thiazoline ring, whereas the merocyanine form reacts at the oxygen atom [14]:



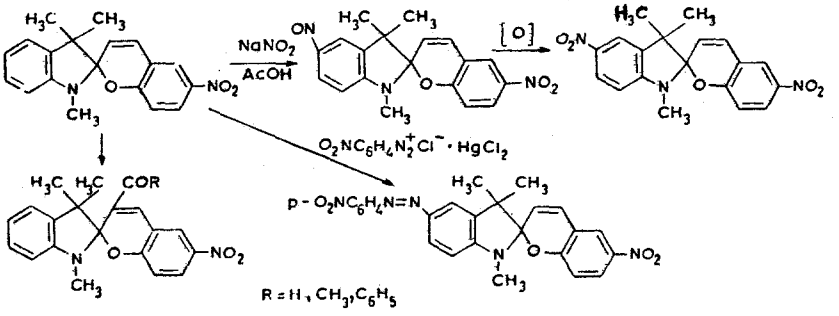
The formation of yellow O-methyl derivatives by the reaction of cyclic forms of indoline spiropyrans with dimethylsulfate (the conditions are not indicated), the structure of which was confirmed by the PMR spectra, was reported in a review [19, p. 267] with a citation to unpublished data.

The cyclic forms of spiropyrans may undergo substitution reactions. Bromine most readily enters the 5 position of the indoline ring in the bromination of 1,3,3-trimethylspiro-(indoline-2,2'-chromene) with N-bromosuccinimide (NBS) in chloroform. Under the influence of excess NBS further substitution takes place simultaneously in the 3' and 6' positions of the chromene ring and the 7 position of the indoline ring to give the tetrabromo derivative [186]. The considerably higher activity of the indoline ring as compared with the chromene ring makes it possible to obtain various 5-bromo derivatives from compounds with known substituents in the chromene ring. If, however, there is a nitro group, which lowers its activity, in the chromene ring, 5,7-dibromo derivatives can also be easily obtained [186].

5-Halo-substituted compounds are also obtained with other halogenating agents such as cupric halides, free halogens, and halogens in the presence of aluminum chloride or boron trifluoride etherate, as demonstrated in the case of 6'-nitro-1,3,3-trimethylspiro(indoline-2,2'-chromene) [187]. In the case of the 5,6'-dinitro derivative a bromine atom entered the 7 position of the indoline ring under the influence of bromine in chloroform [188]. It was found that a bromine atom in the 5 position could be replaced by a cyano group by the action of the copper cyanide complex with pyridine [188].

The action of nitric acid in acetic anhydride or concentrated sulfuric acid on 6'-nitro-1,3,3-trimethylspiro(indoline-2,2'-chromene) leads to the 5,6-dinitro derivative. This dinitro derivative is obtained more smoothly if a NO group is initially introduced in the 5 position by the action of sodium nitrite in acetic acid and it is then oxidized with air oxygen [187].

The high reactivity of the 5 position is also manifested in the ability of the spiropyran to undergo diazo coupling to give the 5-(p-nitrophenylazo) derivative. However, an



acyl group enters the 3' position in the case of Vilsmeier formylation and acylation (with acetic anhydride in the presence of boron trifluoride etherate in chloroform, benzoyl chloride and $AlCl_2$ in CS_2, or benzoyl chloride in dimethylaniline) [189].

Thus, in the case of indoline spiropyrans electrophilic substitution reactions proceed primarily in the 5 position even in those cases in which the spiropyran exists virtually completely in the open salt form and one might have expected a certain amount of deactivation of the heteroring. Samoilova [188] explained this disparity by the fact that the substitution reactions proceed with the closed form that exists in equilibrium with the protonated form. However, without additional studies, particularly studies of the kinetics of substitution reactions, one cannot exclude the possibility of the formation of 5-substituted compounds directly from the protonated form as is observed, for example, in the protonation of anilinium [190] and 1,3-dimethylbenzimidazolium [191] ions.

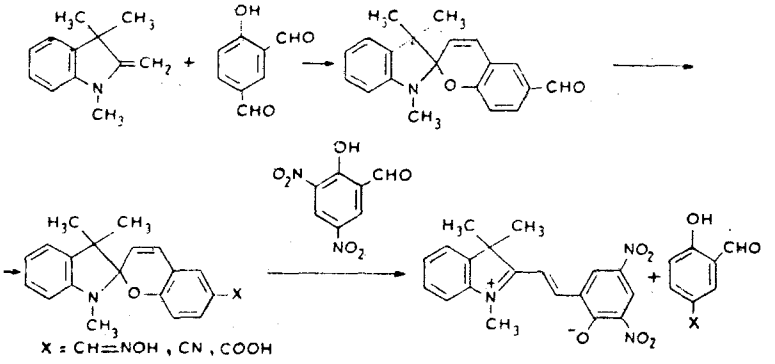
A nitro group in the chromene ring of spiropyrans can be reduced catalytically without involvement of the double bond of the pyran ring [186].

This makes it possible to obtain amino-substituted spirochromenes that heretofore were inaccessible because of the instability of the aminosalicylaldehydes. The amino group in these compounds is easily acetylated under the influence of acetic anhydride [186]. The alkylation and acylation of the hydroxy group in 5-hydroxy derivatives of benzo-1,3-oxathiolium spiropyrans have also been described [92].

The introduction of one or two acylimido- [192] and acylamidomethyl [193] groups in derivatives of indoline benzo- and naphthospiropyrans by the reaction of the corresponding spiropyrans with N-hydroxymethylimides and N-hydroxymethylamides of carboxylic acids in 89% sulfuric acid or in the presence of other condensing agents has been described in patents, but the positions of the entering groups were not established.

The preparation of photochromic monomers by acylation with the chlorides of unsaturated acids of β-hydroxyethyl groups bonded to the nitrogen atoms of the indoline ring [162, 164] and alkylation of 5-carboxy derivatives of indoline spiropyrans with (chloromethyl)styrene has been described [166, 194]. One should also note the report by Namba and Suzuki [195] regarding the modification of the properties of an enzyme (α-amylase) that is covalently bonded to a spiropyran. The anhydride, which was used for the acylation of α-amylase, was obtained by treatment of 1-β-carboxyethyl-3,3-dimethyl-6'-nitro(indoline-2,2-[2H]-chromene) with dicyclohexylcarbodiimide in dioxane. It was found that, in contrast to native amylase, the activity of the spiropyran-modified enzyme depended on irradiation with light. Namba and Suzuki [195] explained this by the change in the hydrophilicity of the enzyme during isomerization of the spiropyran and the attendant affinity for the substrate.

The reversibility of the condensation in alcohol of 2-methyleneindolines (Fischer bases) with most substituted salicylaldehydes is reported in a review [19, p. 257] on the basis of unpublished data of Bertelson. The reaction goes virtually to completion only with 3,5-dinitrosalicylaldehyde because of the very low solubility of the condensation product (it is isolated in the merocyanine form). In this connection, Bertelson used the Fischer base for protection of the o-hydroxyformyl grouping in the case of chemical transformations with the other substituents. This method was used to obtain a number of compounds from 5-formylsalicylaldehyde.



Thus, although the chemical properties of spiropyrans have not yet received adequate study, it is already clear that they make it possible to accomplish the most diverse transformations both in the rings and in the attached substituents.

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SYNTHESIS OF ETHYL 2-ALKYLTHIO-2-OXAZOLINE-5-CARBOXYLATE

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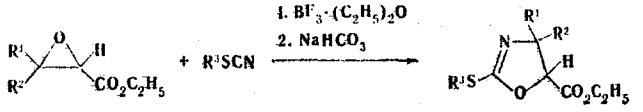
UDC 547.787.07

Glycidic esters react with excess alkyl thiocyanates in the presence of equimolar amounts of boron trifluoride etherate to give esters of 2-alkylthio-2-oxazoline-5-carboxylic acids. The structure of the products was confirmed by the data from the PMR and IR spectra.

It is known that oxiranes react with nitriles [1] and cyanamides [2] to give the corresponding 2-oxazolines. The literature does not contain any data on the reaction of epoxide compounds with alkyl thiocyanates. The aim of the present research was to develop a new method for the preparation of substituted 2-oxazolines in the case of the reaction of glycidic esters with alkyl thiocyanates.

We have found that glycidic esters (I-III) in equimolar amounts with respect to boron trifluoride etherate react at room temperature with excess alkyl thiocyanates to give ethyl 2-alkylthio-2-oxazoline-5-carboxylates (Table 1) in up to 61% yields.



I-III IV-XII

I, IV—VI $R^1=R^2=CH_3$; II, VII—IX $R^1+R^2=-(CH_2)_4-$; III, X—XII $R^1+R^2=-(CH_2)_5-$; IV, VII, X $R^3=CH_3$; V, VIII, XI $R^3=C_2H_5$; VI, IX, XII $R^3=i\text{-}C_3H_7$

Intense absorption bands of the stretching vibrations of C=N (1610-1621 cm^{-1}) and C=O (two bands, 1734-1760 cm^{-1}) groups, as well as a band at ~1150 cm^{-1} due to the vibrations of the C—O—C fragment, are observed in the IR spectra of the synthesized 2-oxazolines IV-XII (Table 2).

The data from the PMR spectra of IV-XII (Table 2) also confirm the structure of IV-XII.

From the presented spectral data one cannot directly establish the position of the ester group (5 or 4) in the 2-oxazoline ring of IV-XII. However, a comparison of the PMR spectra of IV and ethyl 2-methylthio-5,5-dimethyl-2-oxazoline-4-carboxylate [3] (δ 1.33 s and 1.54 s $2CH_3$; 1.29 t and 4.17 q OCH_2CH_3; 2.45 s SCH_3; 4.26 s H) shows that these compounds are isomers and that consequently IV has the ethyl 2-methylthio-4,4-dimethyl-2-oxazoline-5-carboxylate structure; in our case this constitutes evidence for opening of the oxide ring of glycidic ester I on the side of the β-carbon atom.

The structure of V-XII was assumed in analogy with that of IV.

EXPERIMENTAL

The IR spectra of 0.1 M solutions of the compounds in CCl_4 were recorded with a UR-20 spectrometer. The PMR spectra of 10% solutions of the compounds in chloroform were obtained

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 0009-3122/79/1504-0372$07.50