Russian Journal of General Chemistry, Vol. 72, No. 9, 2002, pp. 1468–1472. Translated from Zhurnal Obshchei Khimii, Vol. 72, No. 9, 2002, pp. 1557–1561.

To Estimation of pK_a for Spiropyrans of the Indoline Series

A. V. Chernyshev, M. S. Chernov'yants, E. N. Voloshina, and N. A. Voloshin

Research Institute of Physical and Organic Chemistry, Rostov State University, Rostov-on-Don, Russia
Rostov State University, Rostov-on-Don, Russia

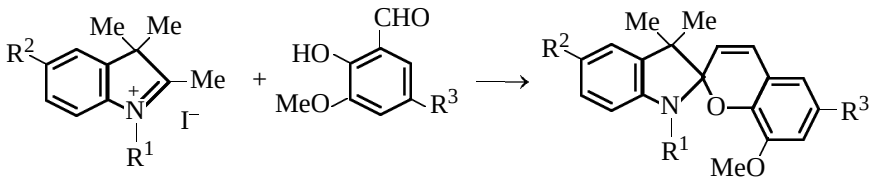
Received November 30, 2000

Abstract — A mathematically substantiated approach to estimating acid–base characteristics of spiropyrans of the indoline series with account for the ring–chain tautomerism of these compounds was proposed. The pK_a values of spiropyrans of various basicity were estimated.

Spiropyrans of the indoline series are among the most effective and, therefore, sufficiently thoroughly studied class of organic photochromic compounds capable of forming, under UV irradiation, colored quinoid zwitter-ionic structures whose reversible rearrangement into the initial spiro form occurs spontaneously or under visible light [1–3]. Recently complex formation of the colored merocyanine form of spiropyran with metal ions in aprotic or aqueous-organic media have received researcher's attention. Spiropyrans are considered as promising organic reagents for photometric and fluorescent analysis of metal ions [4–7]. The existence in solutions of the analytically active merocyanine form of spiropyrans is associated with the basicity of the donor oxygen atom, which depends on substituents and can be measured by the protolytic equilibrium constant. There have been only a few works on this topic. Dzhaparidze [8] has reported pK_a values for spiropyrans to illustrate a correlation between the stability of their open-chain form and the basicity of the pyran oxygen atom. Drumond and Furlog [9] have studied the photochromic and protolytic properties of spiropyrans in aqueous-organic media.

Spiropyrans **I**–**V** were obtained by reactions of 1-R^1-2,3,3-trimethyl-5-R^2-3*H*-indolium iodide with 2-hydroxy-3-methoxy-5-R^3-benzaldehydes in the presence of a base.

Scheme 1.



I–**V**

I, R^1 = Me, R^2 = R^3 = H; **II**, R^1 = Me, R^2 = H, R^3 = CHO; **III**, R^1 = Me, R^2 = OMe, R^3 = CHO; **IV**, R^1 = CH_2Ph, R^2 = H, R^3 = Br; **V**, R^1 = CH_2Ph, R^2 = H, R^3 = NO_2.

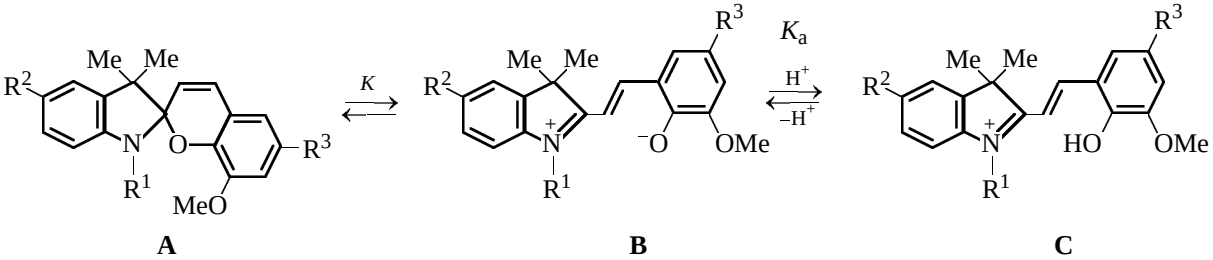
In the present work we performed a first potentiometric and spectrophotometric study of the protolytic properties of spiropyrans of the indoline series (compounds **I**–**V**) with account for the existence in solutions of an equilibrium between the cyclic (**A**), merocyanine (**B**), and protonated (**C**) forms of these compounds. This equilibrium in aqueous-organic media can be represented by Scheme 2.

Thermodynamic stability of the open-chain merocyanine form **B** depends on solvent polarity, possibility of hydrogen bonding between the charged centers of the molecule (formation of solvate bridge), and electronic effects of substituents in the indoline and pyrane moieties [2].

In view of Scheme 2, the protolytic equilibrium of

1070-3632/02/7209-1468 $27.00

Scheme 2.



A **B** **C**

spiropyrans (L) in the solution can be represented by Eq. (1) and quantitatively described by the apparent equilibrium constant K'_a [Eq. (2)].

$$LH^+ + H_2O \rightleftarrows L_m + L_c + H_3O^+, \quad (1)$$

$$K'_a = [H_3O^+][L']/[LH^+]. \quad (2)$$

Here $[LH^+]$, $[L_m]$, and $[L_c]$ are the equilibrium concentrations of the protonated, merocyanine, and cyclic forms, and $[L'] = [L_m] + [L_c]$ is the sum of the equilibrium concentrations of nonprotonated forms of spiropyrans. The K'_a value reported by Drumond and Furlog [9] is considered apparent in view of the fact that in determining [L'] the authors did not estimate the equilibrium concentrations of forms **A** and **B**.

The protonation constant of the merocyanine form (K_a) can be determined is this form is present in appreciable amounts [Eq. (3)].

$$K_a = [H_3O^+][L_m]/[LH^+]. \quad (3)$$

Based of the material balance equation (4), the law of mass action [Eq. (2)], and the ring–chain equilibrium equation (5), we come to Eq. (6) which relates K_a to K'_a in normal or logarithmic forms [Eq. (7)].

$$c_L = [LH^+] + [L_m] + [L_c], \quad (4)$$

$$K = [L_m]/[L_c], \quad (5)$$

$$K'_a = K_a(1 + 1/K), \quad (6)$$

$$pK'_a = pK_a - \log(1 + 1/K). \quad (7)$$

Here c_L is the total concentration of the spiropyran forms in the solution.

The ring–chain equilibrium constants K were determined by a known procedure [10] from the ^{1}H NMR spectra of spiropyrans **I**–**V** in a mixture of $(CD_3)_2CO$ and D_2O, deuterated analogs of the media where the pK_a values were estimated. The molar fractions of the open-chain and cyclic forms in the solution were found from the intensity ratio of the proton signals of indicator groups (formyl and/or *gem*-dimethyl). Spiropyrans **I** and **IV**, according to ^{1}H NMR and UV spectral data, are present in the cyclic form exclusively. The K value for spiropyran **V** could not be determined by ^{1}H NMR spectroscopy because of the poor solubility of this compound. The ring–chain equilibrium constants K of spiropyrans **II** and **III** are 0.87 and 6.25, respectively.

Equation (10) for estimating pK'_a from potentiometric titration data (it is this value which is determined experimentally) was derived from the material balance equation (8) and the solution electroneutrality equation (9).

$$c_L = [LH^+] + [L'], \quad (8)$$

$$[Na^+] + [H^+] + [LH^+] = [OH^-] + [Cl^-], \quad (9)$$

$$pK'_a = pH + \log \frac{(1 - a)c_L - [H^+]}{ac_L + [H^+]}. \quad (10)$$

Here $[Cl^-] = c_L$ and $[Na^+] = ac_L$ ($a = c_{NaOH}/c_L$ is the neutralization degree of the solution).

The pK_a values were calculated by Eq. (7).

The potentiometric technique, while being universal, involves a number of limitations. In titration of dyes, for instance, the latter may well be adsorbed on the membrane of the glass electrode, thus affecting the potential measured [11]. At concentrations of about 10^{-2}–10^{-3} M (working concentrations in potentiomeric titration), dimeric structures may form.

Preliminary analysis of the electronic absorption spectra of spiropyrans in neutral and acidic aqueous-acetone (1:1) solutions showed that spiropirans **II**, **III**, and **V** are present in all the three forms **A**–**C** (Fig. 1). The merocyanine form selectively absorbs in the long-wave region (λ 545, 546, and 570 nm, respectively). Spiropyrans **I** and **IV** (Fig. 2) are present only in forms **A** and **B**, and the latter selectively absorbs at λ 400 nm. In view of the specific behavioral features of spiropyrans in solutions, the approaches to estimating pK_a from the absorption of

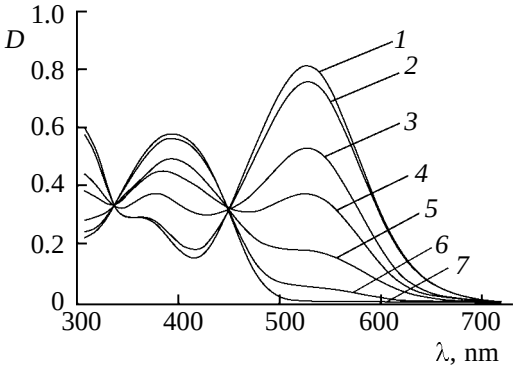


Fig. 1. Absorption spectra of spiropyran **III** at various pHs of the aqueous-acetone (1 : 1) solutions. pH: (*1*) 7.0, (*2*) 6.4, (*3*) 5.3, (*4*) 4.9, (*5*) 4.4, (*6*) 3.7, and (*7*) 2.0 ($c_{\mathbf{III}}$ 2.5×10^{-5} M).

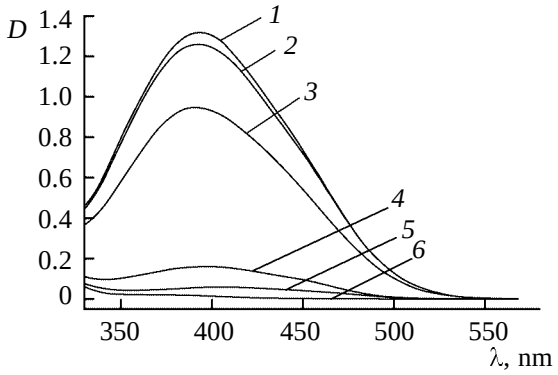


Fig. 2. Absorption spectra of spiropyran **I** at varios pHs of the aqueous-acetone (1 : 1) solution. pH: (*1*) 1.40, (*2*) 2.05, (*3*) 5.20, (*4*) 6.60, (*5*) 7.20, and (*6*) 7.70 ($c_{\mathbf{I}}$ 4.2×10^{-5} M).

form **B** (spiropyrans **II**, **III**, and **V**) or form **C** (spiropyrans **I** and **IV**) should be different.

The calculations were based on the optical density additivity equation (11) and the material balance equation (4).

$$\begin{cases} A = \varepsilon c_L l, \\ A = (\varepsilon_m[L_m] + \varepsilon_c[L_c] + \varepsilon_{LH^+}[L_{LH^+}])l. \end{cases} \quad (11)$$

Here l = 1 cm is the absorbing layer thickness, $\varepsilon = \varepsilon_m\Phi_m + \varepsilon_c\Phi_c + \varepsilon_{LH^+}\Phi_{LH^+}$ is the mean molar extinction coefficient, $\Phi_i = [L_i]/c_L$ are the molar fractions of the correponding spiropyran forms, ε_m, ε_c, ε_{LH^+} are the molar extinction coefficients of the forms at the working wavelength, and A is the optical density.

For spiropyrans **I** and **IV**, $[L_m] = 0$, and Eq. (11) takes form (12).

Protolytic equilibrium constants for spiropyrans **I**–**V** in aqueous acetone (1 : 1)

Comp. no.	Potentiometric titration		Spectrophotometry	
	pK'_a	pK_a	pK'_a	pK_a
I	5.52 ± 0.06	–	5.72 ± 0.08	–
II	4.62 ± 0.03	4.95 ± 0.03	4.37 ± 0.08	4.70 ± 0.08[a]
			4.64 ± 0.08	4.97 ± 0.08[b]
III	–	–	5.00 ± 0.10	5.06 ± 0.10[a]
			4.98 ± 0.20	5.04 ± 0.23[b]
IV	3.61 ± 0.20	–	3.94 ± 0.04	–
V	3.31 ± 0.10	–	3.30 ± 0.05	–

[a] Calculated by Eq. (17). [b] Calculated by Eq. (18).

$$\varepsilon([LH^+] + [L_c]) = \varepsilon_{LH^+}[LH^+] + \varepsilon_c[L_c]. \quad (12)$$

With $[L_m] = 0$, the apparent rate constant K'_a can only be determined [Eq. 13].

$$K'_a = [H_3O^+]\frac{(\varepsilon - \varepsilon_{LH^+})}{(\varepsilon_c - \varepsilon)}. \quad (13)$$

Optical density measurements are convenient to perform at the λ_{max} of the protonated form. In view of the fact that spiropyrans completely pass from the cyclic to LH^+ form at the maximum acidity of the solution, $A_{max} = \varepsilon_{LH^+}c_L$. Then Eq. (13) can be brought into form (14) which is convenient for calculations.

$$pK'_a = pH - \log\frac{(A_{max} - A_i)}{(A_i - A_{min})}. \quad (14)$$

Here A_{max}, A_{min}, and A_i are the maximal, minimal, and current optical densities for a given spectral series.

The absorption spectra of compound **I** at varied pHs of the solution are presented in Fig. 2. The pK'_a values calculated by Eq. (14) are listed in the table.

To calculate pK_a values for the merocyanine forms of spiropyrans **II** and **III** in cases where the concentrations of the open-chain and cyclic forms are comparable (Fig. 1), the optical density additivity equation (11) can be transformed into Eq. (15).

$$\varepsilon([LH^+] + [L_m] + [L_c]) = \\ = \varepsilon_{LH^+}[LH^+] + \varepsilon_m[L_m] + \varepsilon_c[L_c]. \quad (15)$$

Substituting Eq. (15) into Eq. (3) and taking the logarithm, we obtain Eq. (16).

$$pK_a = pH - \log\frac{(\varepsilon - \varepsilon_{LH^+})}{[(\varepsilon_c/K + \varepsilon_m) - \varepsilon(1 + 1/K)]}. \quad (16)$$

When one works at the absorption maximum of the merocyanine form ($\varepsilon_c = 0$, $\varepsilon_{LH^+} = 0$), Eq. (16) transfors into Eq. (17).

$$pK_a = pH + \log \frac{\varepsilon_m c_L - A_i(1 + 1/K)}{A_i}. \qquad (17)$$

The molar extinction coefficients of the merocyanine forms of spiropyrans **II** and **III** (4.66×10^4 and 3.85×10^4 l mol^{-1} cm^{-1}, respectively) were determined by the formula $\varepsilon_m = A_{max}(1 + K)/(c_L K)$.

When one works at the absorption maximum of the LH^+ form, Eq. (16) transforms into Eq. (18).

$$pK_a = pH - \log \frac{(A_{max} - A_i)}{[A_i(1 + 1/K) - A_{min}]}. \qquad (18)$$

The pK'_a values were calculated by Eq. (7).

Using the ring–chain and protolytic equilibrium constants, we constructed pH dependences of the distrubution of the cyclic and open-chain (merocyanine and protonated) forms of spiropyrans (Fig. 3). The molar fractions of the forms (Φ_i) were calculated by Eq. (19).

$$\Phi_i = \frac{B_i}{K_a + KK_a + K[H_3O^+]}. \qquad (19)$$

Here $B_i = KK_a$, K_a, and $K[H_3O^+]$ for the merocyanine, cyclic, and protonated forms.

The basicity of form **B** is higher than the estimate from the apparent protolytic equilibrium constant. Probably, the larger the fraction of form **B** (spiropyran **III**), the closer the pK_a and pK'_a values to each other.

EXPERIMENTAL

The ^{1}H NMR spectra (300 MHz) we measured on a Varian Unity-300 spectrometer in the ^{2}H stabilization mode. The electronic absorption spectra were obtained on a Specord M-40 spectrophotomer in quartz cells (*l* 1 cm). Potentiometric titration of 0.1 mmol of spiropyran **I**–**V** preliminarily protonated by treatment with equivalent amount of hydrochloric acid was performed with a 0.1 M solution of NaOH (μ 0.1, NaCl). The pHs of the solutions were measured on an EV-74 pH-meter with a glass electrode. Acetone of special purity and twice distilled water were used.

Spiropyrans I–V. A mixture of 1 mmol of 1-R^1-2,3,3-trimethyl-5-R^2-3*H*-indolium iodide, 1 mmol of 2-hydroxy-3-methoxy-5-R^3-benzaldehyde, and 1 mmol of piperidine in 5 ml of 2-propanol was heated under reflux for 2 h. The solvent was removed in a vacuum, and the residue was subjected to chromatography on a column of Al_2O_3 (eluent chloroform)

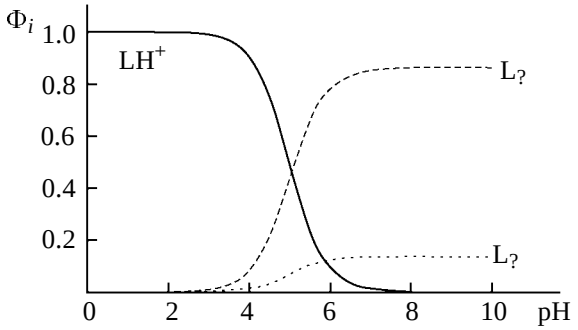


Fig. 3. Distribution of various forms of spiropyran **III** vs. pH of the aqueous-acetone (1 : 1) solution.

and additionally purified by recrystallization from heptane.

8-Methoxy-1',3',3'-trimethylspiro(2*H*-1-benzopyran-2,2'-indoline) (I), yield 54%, mp 120–121°C (mp 120°C [12]). **6-Formyl-8-methoxy-1',3',3'-trimethylspiro(2*H*-1-benzopyran-2,2'-indoline) (II),** yield 75%, mp 150–151°C (mp 151°C [12]). **6-Formyl-5',8-dimethoxy-1',3',3'-trimethylspiro(2*H*-1-benzopyran-2,2'-indoline) (III),** yield 84%, mp 180.5–181.5°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.16 s (3H, 3'-CH_3), 1.26 s (3H, 3'-CH_3), 2.68 s (3H, 1'-CH_3), 3.70 s (3H, 8-OCH_3), 3.77 s (3H, 5'-OCH_3), 5.74 d (1H, 3-H, *J* 10.3 Hz), 6.42 d (1H, 7'-H, *J* 9.1 Hz), 6.66–6.69 m (2H, 4'-H, 6'-H), 6.86 d (1H, 4-H, *J* 10.3 Hz), 7.21 d (1H, 5-H, *J* 2.0 Hz), 7.25 d (1H, 7-H, *J* 2.0 Hz), 9.77 s (1H, 6-CHO). Found, %: C 72.24; H 6.47; N 3.72. $C_{22}H_{23}NO_4$. Calculated, %: C 72.31; H 6.34; N 3.83. **1'-Benzyl-6-bromo-8-methoxy-3',3'-dimethylspiro(2*H*-1-benzopyran-2,2'-indoline) (IV)**, yield 62%, mp 139– 140°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.24 s (3H, 3'-CH_3), 1.32 s (3H, 3'-CH_3), 3.67 s (3H, 8-OCH_3), 4.22 d (1H, 1'-CH_2Ph, *J* 16.7 Hz), 4.53 d (1H, 1'-CH_2Ph, *J* 16.7 Hz), 5.75 d (1H, 3-H, *J* 10.2 Hz), 6.25 d (1H, 7'-H, *J* 7.7 Hz), 6.66 d (1H, 4-H, *J* 10.2 Hz), 6.78 d (1H, 5-H, *J* 2.1 Hz), 6.80 t.d (1H, 5'-H, *J* 7.4 and 0.9 Hz), 6.82 d (1H, 7-H, *J* 2.1 Hz), 7.00 t.d (1H, 6'-H), 7.07 d.d (1H, 4'-H, *J* 7.3 and 1.1 Hz), 7.19–7.28 m (5H, 1-CH_2Ph). Found, %: C 67.65; H 5.16; N 3.12. $C_{26}H_{24}BrNO_2$. Calculated, %: C 67.54; H 5.23; N 3.03. **1'-Benzyl-8-methoxy-3',3'-dimethyl-6-nitrospiro(2*H*-benzopyran-2,2'-indoline) (V)**, yield 64%, mp 165– 166.5°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.27 s (3H, 3'-CH_3), 1.32 s (3H, 3'-CH_3), 3.76 s (3H, 8-OCH_3), 4.26 d (1H, 1'-CH_2Ph, *J* 16.7 Hz), 4.52 d (1H, 1'-CH_2Ph, *J* 16.7 Hz), 5.86 d (1H, 3-H, *J* 10.3 Hz), 6.31 d (1H, 7'-H, *J* 7.7 Hz), 6.80 d (1H, 4-H, *J* 10.3 Hz,), 6.84 t.d (1H, 5'-H, *J* 7.4 and 0.9 Hz), 7.04 t.d (1H, 6'-H, *J* 7.7 and 1.1 Hz), 7.09 d.d (1H, 4'-H, *J* 7.3 and 1.1 Hz), 7.20–7.28 m

(5H, 1-CH_2Ph), 7.59 d (1H, 5-H, *J* 2.3 Hz), 7.65 d (1H, 7-H, *J* 2.5 Hz). Found, %: C 72.73; H 5.74; N 6.70. $C_{26}H_{24}N_2O_4$. Calculated, %: C 72.88; H 5.65; N 6.54.

ACKNOWLEDGMENTS

The work was financially supported by CRDF and the Ministry of Education of the Russian Federation (grant REC-004).

REFERENCES

1. Barachevskii, V.A., Lashkov, G.I., and Tsekhomskii, V., *Fotokhromizm i ego primenenie* (Photochromism and Its Application), Moscow: Khimiya, 1977.
2. *Photochromism. Molecules and Systems*, Duerr, H. and Bouas-Laurent, H., Eds., Amsterdam: Elsevier, 1990.
3. *Photochromism. Technology of Chemistry*, Brown, G.B., Ed., New York: Wiley, 1971.
4. Phillips, J.P., Mueller, A., and Przystal, F., *J. Am. Chem. Soc.*, 1965, vol. 87, no. 17, p. 4020.
5. Atabekyan, L.S., Chibisov, A.K., and Roitman, G.P., *Zh. Anal. Khim.*, 1982, vol. 37, no. 3, p. 389.
6. Atabekyan, L.S. and Chibisov, A.K., *Zh. Anal. Khim.*, 1988, vol. 43, no. 10, p. 1787.
7. Winkler, J.D., Bowen, C.M., and Michlet, V., *J. Am. Chem. Soc.*, 1998, vol. 120, no. 13, p. 3237.
8. Dzhaparidze, K.G., *Spirokhromeny* (Spirochromenes), Tbilisi: Mitsniereba, 1979.
9. Drumond, C.J. and Furlog, D.N., *J. Chem. Soc., Faraday Trans.*, 1990, vol. 86, p. 3613.
10. Pozzo, J.-L., Samat, A., Guglielmetti, R., and Keukeleire De, D., *J. Chem. Soc., Perkin Trans. 2*, 1993, no. 7, p. 1327.
11. Ramenskaya, L.M., Borodin, V.A., Vasil'ev, V.P., and Kozlovskii, E.V., *Zh. Fiz. Khim.*, 1999, vol. 73, no. 6, p. 1029.
12. Hinnen, A., Audic, C., and Gautron, R., *Bull. Soc. Chim. Fr.*, 1968, no. 5, p. 2066.