

In order to evaluate the influence of substituents in position 5 of indole and in the para position of phenyl on the stability of 2-ethoxycarbonylindole-3-indolyphenylmethyl cations (IPMCs) we have experimentally determined by a spectrophotometric method the values of the acidity constants ( $pK_{R^+}$ ) of the IPMCs in  $H_2SO_4$  solutions. The IPMCs were generated from 3-( $\alpha$ -chlorobenzyl)-2-ethoxycarbonylindoles by dissolving them in sulfuric acid with a concentration of 55-93%. Two reaction series were studied. In the first, the correlation equation  $pK_{R^+} = -5.18\sigma - 10.5$  was obtained for substituents in the para position of the phenyl ring. In the second series we evaluated the influence of substituents in position 5 of the indole ring:  $pK_{R^+} = -2.6\sigma - 11.3$ . The lower influence of substituents on the stability of the IPMCs from position 5 as compared with the para position of the phenyl ring is due to the delocalization of the charge in the heterocycle of the indole system. It was established that in sulfuric acid solutions di(2-ethoxycarbonylindol-3-yl)phenylmethanes dissociate with the formation of IPMCs and 2-ethoxycarbonylindoles.

It is known that in reaction with aromatic aldehydes under conditions of acid catalysis indoles form not only addition products [3-( $\alpha$ -X-benzyl)indoles (I)] but also condensation products [di(indol-3-yl)phenylmethanes (II)] [1, 2]. The formation of structures (I) and (II) takes place through the indolyphenylmethyl cation K, which interacts with all the nucleophiles present in the solution in accordance with the following scheme:

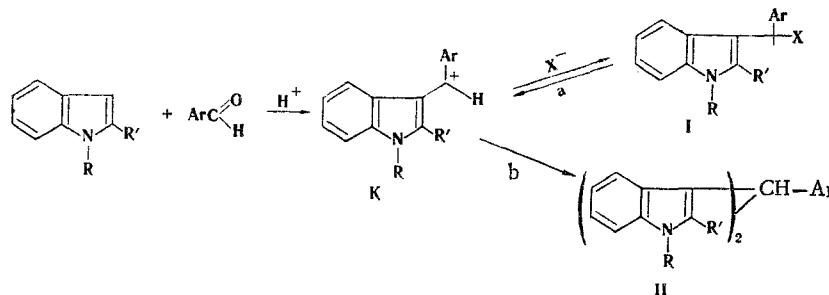


TABLE 1. Characteristics of the Equilibria (1), (2), and (8)

Compound	Series	Y	Z	$pK_{R^+}$	r	s	$\lambda_{max}$	$\epsilon \cdot 10^4$
Ia	(2)	H	H	$-11,3 \pm 0,5$	0,97	0,08	460	1,65
Ib	(2)	H	CH <sub>3</sub>	$-11,3 \pm 0,4$	0,98	0,09	460	1,46
Ic	(2)	H	OCH <sub>3</sub>	$-10,9 \pm 0,5$	0,96	0,11	460	1,33
Id	(2)	H	Cl	$-11,6 \pm 0,4$	0,98	0,09	460	2,22
Ie	(2)	H	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> O	$-10,7 \pm 0,4$	0,95	0,10	470	1,66
If	(2)	H	NO <sub>2</sub>	$-12,4 \pm 0,4$	0,97	0,10	460	1,78
Ig	(1)	<i>o</i> -Cl	H	$-8,1 \pm 0,4$	0,99	0,09	460	2,00
Ih	(1)	H	H	$-10,7 \pm 0,4$	0,98	0,09	460	1,80
Ii	(1)	NO <sub>2</sub>	H	$-13,0 \pm 0,8$	0,95	0,10	440	1,20
Ij	(1)	Cl	H	$-10,6 \pm 0,4$	0,98	0,09	460	3,50
Ik	(1)	<i>m</i> -NO <sub>2</sub>	H	$-13,9 \pm 0,4$	0,96	0,11	425	1,14
IIa	(8)	H	H	$-10,5 \pm 0,5$	0,98	0,12	460	2,00
IIb	(8)	OCH <sub>3</sub>	H	$-8,1 \pm 0,5$	0,96	0,08	460	1,11
IIc	(8)	<i>o</i> -Cl	H	$-8,2 \pm 0,3$	0,97	0,12	470	2,10

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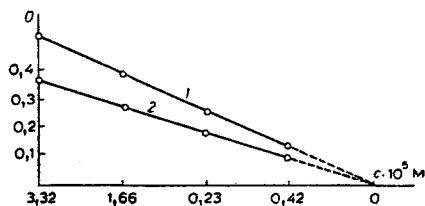


Fig. 1

Fig. 1. Observance of the Lambert-Beer law in 84%  $H_2SO_4$  for compounds (Ib) (1) and (Ik) (2). The conversion into the cation was about 80%.

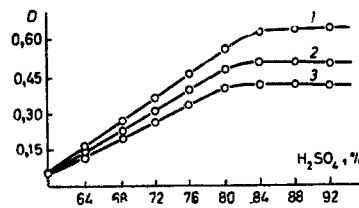


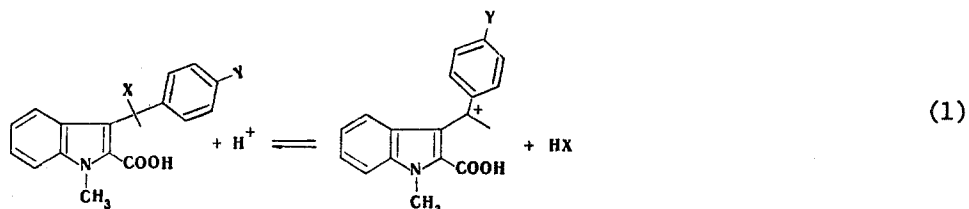
Fig. 2

Fig. 2. Dependence of the optical density  $D$  of solutions of compounds (Ia) (1), (Id) (2) and (Ic) (3) on the concentration of  $H_2SO_4$ .

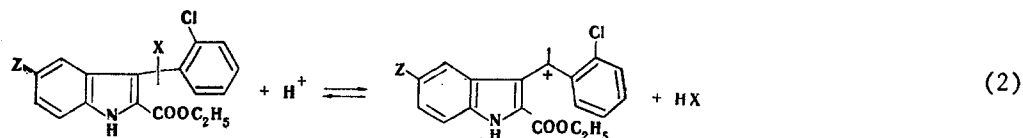
Kinetic control of the process leads to compounds (I) and thermodynamic control to the diindolylphenylmethanes (II), which are stable under the conditions of the reaction. An important role in the position of the equilibrium  $\alpha$  is played by the solvent. The low solubility of compounds in ether saturated with HCl leads to their separation from the solution, while in  $CH_3COOH-CH_3COCl$  (1:1 by volume), compounds (II) are isolated exclusively [3] (Table 1).

As was to be expected, a rise in the temperature shifts the equilibrium  $\alpha$  in the direction of structures (II). Experimental investigations of the conditions of formation of compounds (I) and (II) have shown a large role of the substituents in the indole reactant and, particularly, in the aldehyde reactant. It appeared necessary to make a quantitative estimate of the influence of substituents in the indole and phenyl radicals on the stability of the cation K and to compare the  $pK_R^+$  values of the cations with the values of  $pK_R^+$  in the series of benzyl, diphenylmethyl, and triphenylmethyl cations.

We selected two reaction series, the first of which permitted us to evaluate the influence of substituents Y in the para position of the phenyl radical in the equilibrium (1):



The second series characterized the influence of substituents Z in position 5 of the indole ring on equilibrium (2):



Equilibria (1) and (2) were studied in  $H_2SO_4$  solutions by a method which we have described previously [7]. The replacement of the group  $X=OH$  by Cl had no appreciable influence on the position of the equilibrium as has also been established in the benzhydrol series [4], and also for 3-( $\alpha$ -X-benzyl)indoles [7]. In view of the high concentration of water, as compared with the concentration of chloride ion, one must consider a basic equilibrium in which the cation K participates — its interaction with water:



The appearance of the cation K in  $H_2SO_4$  solution was recorded in the UV spectra from the appearance of a characteristic coloration having a maximum absorption in the 440–460 nm range. Solutions of the cation K obey the Lambert-Beer law over the range of concentrations studied (Fig. 1). The molar extinction of the cation K can be found if the initial carbinol is converted completely into the cation. For this purpose, the optical density  $D$  of a solution of the carbinol (I) is plotted against the concentration of  $H_2SO_4$  in the region of  $\lambda_{max}$  of the

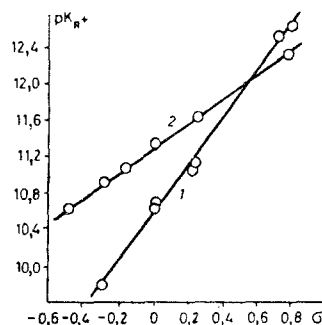


Fig. 3. Correlation relationship  $pK_{R^+} = f(\sigma)$  for the equilibria (1) and (2).

corresponding cation. The sloping sections in Fig. 2 correspond to the partial, and the horizontal sections to the complete, conversion of the carbinol into the cation. In view of the fact that the absorption of the initial carbinol in the 440–460 nm region is negligibly small in comparison with the absorption of the cation K, the indicator ratio Q can be calculated from the relation

$$Q = \frac{R^+}{ROH} = \frac{D_i}{D_{\max} - D_i},$$

where  $D_{\max}$  is the optical density of the solution when all the carbinol has been converted to the cation K. Thus, knowing the acidity of  $H_2SO_4$  solutions over a wide range of concentrations from the literature [5] and determining experimentally the value of Q it is possible to find the value of  $pK_{R^+}$  of different cations from the equation

$$pK_{R^+} = C_0 + \log Q, \quad (4)$$

where  $C_0$  is the acidity of the  $H_2SO_4$  solution, which has been found for the diphenyl carbinol series [5].

Compounds (I) are weak bases appreciable ionization of which begins in 50%  $H_2SO_4$  and above. To evaluate the  $pK_{R^+}$  values of such substances use is made of a set of "overlapping" indicators — compounds of the same class but ionizing already in very dilute solutions of acids. In view of the fact that we had no complete set of compounds (I) ionizing in dilute  $H_2SO_4$ , we used the acidity function  $C_0$  obtained by the method of "overlapping" indicators for a series of diphenyl carbinols [5]. Although the acidity function constructed for a series of alkylindoles is known [6], its use for estimating  $pK_{R^+}$  of indole-3-ylphenyl carbinols is impermissible because of a basic difference in the mechanisms of the protonation of the alkylindoles of the indolylphenylmethanols (I).

Figure 3 shows the correlation relationship  $pK_{R^+} = f(\sigma)$  for para-phenyl-substituted cations K (curve 1) and 5-substituted cations K (curve 2). The first relationship is described by equation (5), and the second by equation (6)

$$pK_{R^+} = -5.18\sigma - 10.5 \quad (5)$$

$$pK_{R^+} = -2.62\sigma - 11.3. \quad (6)$$

The corresponding equation for diphenyl carbinols substituted in the para position [4] has the form:

$$pK_{R^+} = -5.63\sigma - 13.2 \quad (7)$$

A comparison of equations (5) and (7) shows the very slight difference in the transfer of the electronic effect of substituents in the para positions of the phenyl radicals of the cation of K and in the diphenylmethyl cations,  $\rho_5 = -5.18$ ,  $\rho_7 = -5.63$ . The stability of a carbonium ion containing an indolyl radical is higher than that of a carbonium ion containing a phenyl radical by 2.7 pK units, i.e., almost 1000-fold.

A comparison of Eqs. (5) and (6) shows a weakening of the transmission of the electronic effect from position 5 of the indole system as compared with the para position of the phenyl radical by a factor of  $\rho_5/\rho_6 = 5.1/2.6 \approx 2$ . Although the distance from a substituent in po-

sition 5 of the indole nucleus to the reaction center (CHX) is the same as from the para position of the phenyl ring (4 C-C bonds), the transmission effect is halved because of the delocalization of the charge in the heterocycle of the indole system.

Under the conditions of equilibrium (1), it was impossible to obtain 3-( $\alpha$ -X-benzyl)indoles when the aldehyde contained electron-donating substituents, e.g., p-methoxybenzaldehyde. Because of the stability of the carbonium ion K arising, the equilibrium is displaced in the direction of the formation of di(indol-3-yl)-p-methoxyphenylmethane (compound (IIb), Table 1). In a previous investigation [7], on the basis of cryoscopic measurements and TLC results we found that di(indol-3-yl)phenylmethanes (II) are also capable of generating indolylphenylmethyl cations K in aqueous solutions of H<sub>2</sub>SO<sub>4</sub> by the following scheme:



Subsequent experiments showed that the addition of one of the reaction products — 1-methylindole-2-carboxylic acid — to the solution did not change the concentration of the cation K. From this it may be concluded that the cation K generated by Scheme (8) then participates in equilibrium (3), since water is a more active nucleophile and its concentration is considerably higher than that of the 1-methylindole-2-carboxylic acid. An additional confirmation of this conclusion is the agreement within the limits of experimental error of the values of pK<sub>R</sub><sup>+</sup> of the carbocations K generated both from 3-( $\alpha$ -X-benzyl)indoles (I) [compounds (Ig) (pK<sub>R</sub><sup>+</sup> = -8.1 ± 0.4) and (Ih) pK<sub>R</sub><sup>+</sup> = -10.7 ± 0.4] and from the di(indol-3-yl)phenylmethanes (II) [compounds (IIc) (pK<sub>R</sub><sup>+</sup> = -8.2 ± 0.3) and (IIa) pK<sub>R</sub><sup>+</sup> = -10.5 ± 0.5]. Consequently, the di(indol-3-yl)phenylmethanes (II), just like the 3-( $\alpha$ -chlorobenzyl)indoles (I), are capable of dissociating in media with a high acidity to form the cations K. The same conclusion has recently been drawn [8] in a study of the exchange of indole radicals in diindolylphenylmethanes in concentrated solutions of perchloric acid.

#### EXPERIMENTAL

The determination of the pK<sub>R</sub><sup>+</sup> values of compounds (Ia-f) (Table 1) was made by the method of Deno et al. [4], and the pK<sub>R</sub><sup>+</sup> values of compounds (Ig-IIc) were taken from our previous paper [7]. The synthesis of compounds (Ia, c, d) has been described previously [3].

Ethyl 3-( $\alpha$ ,o-Dichlorobenzyl)-5-methoxyindole-2-carboxylate (Ib). With stirring, 20 ml of ether saturated with HCl was added to a mixture of 2.04 g (10 mmole) of o-chlorobenzaldehyde [sic] at 0°C. After rapid dissolution, a precipitate of compound (Ib) began to deposit. After 1 h, it was filtered off washed with heptane, and dried in the air. Yield 2.9 g (80%), mp 144-145°C. Found: C 19.0; N 3.7%. C<sub>19</sub>H<sub>18</sub>Cl<sub>2</sub>NO<sub>2</sub>. Calculated: Cl 19.4; N 3.8%.

Ethyl 5-benzyloxy-3-( $\alpha$ ,o-dichlorobenzyl)indole-2-carboxylate (Ie) was obtained similarly. The reaction was carried out in boiling ether for 10 min. Yield 70%, mp 158-160°C (from acetonitril). Found: Cl 15.8; N 2.9%. C<sub>25</sub>H<sub>22</sub>Cl<sub>2</sub>NO<sub>2</sub>. Calculated: Cl 16.1; N 3.2%.

Ethyl 3-( $\alpha$ ,o-Dichlorobenzyl)-5-nitroindole-2-carboxylate (If). This was obtained in a similar manner to compound (Ie). Yield 40%, mp 183-186°C. Found: Cl 17.6; N 6.6%. C<sub>18</sub>H<sub>15</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>4</sub>. Calculated: Cl 18.1; N 7.1%.

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