had mp 162-163°C (from isopropyl alcohol). Found: Cl 11.1%. $C_{17}H_{18}N_4 \cdot HCl$. Calculated: Cl 11.3%.

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ACIDITIES OF 1-INDOLYLACETIC AND CARBAZOLYLACETIC ACIDS. INDUCTIVE CONSTANTS OF INDOLYL AND CARBAZOLYL GROUPS

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The pK_a values of 1-indolylacetic, 3-(9-ethyl)carbazolylacetic, and a number of 3,6-disubstituted 9-carbazolylacetic acids in aqueous ethanol solutions were determined by potentiometry. The inductive constants of the corresponding heterocyclic fragments were calculated from the values obtained. It is shown that annelation of the benzene ring with the pyrrole ring of indole gives rise to a decrease in the negative inductive effect of the heteroring. A linear relationship between the acidic properties of carbazoles and the corresponding 9-carbazolylacetic acids was established.

We have previously shown [1, 2] that the terminal sp^2-hybridized atom in the 9-alkenylcarbazole series is appreciably less shielded in the ^{13}C NMR spectra as compared with N-vinyl derivatives of pyrrole [3]. This fact indicates the smaller effect of $p-\pi$ conjugation of the p electrons of the nitrogen atom of the carbazolyl ring with the π electrons of the C=C bond. However, the possibility that deshielding of the terminal vinyl atom on passing from 1-vinylpyrrole (chemical shift 95.89 ppm [4]) and 1-vinylindole (96.0 ppm [5]) to 9-vinylcarbazole (101.18 ppm [1]) may be determined by (in addition to steric reasons) an increase in the negative inductive effect of the heterorings in the same order is not excluded; whereas in ordinary enamines the effects of conjugation prevail over the negative inductive effects of the aminoalkyl or aminocycloalkyl groups [6], in the N-vinylamines under discussion, in addition to $p-\pi$ conjugation, one observes the competitive and conjugation-weakening delocalization of the p electrons in the heterocyclic fragments, which may appreciably increase the role of inductive effects in the distribution of the electron densities of the C=C groups and their contribution to the reactivity. It is only natural that quantitative data on the σ_I constants of the indicated heterocycles not only are necessary for a solution of the problem noted above but are also of fundamental importance for an understanding of the chemistry of heterocycles of the pyrrole series.

In the present research to determine the inductive constants of 1-indolyl and carbazolyl groups we determined the pK_a values in aqueous ethanol of a number of acetic acids that contain a heterocyclic fragment, viz., 1-indolylacetic (I), 9-carbazolylacetic (IIa-e), and 3-(9-ethylcarbazolyl)acetic (III) acids.

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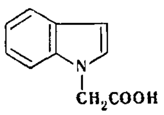
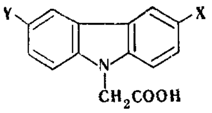
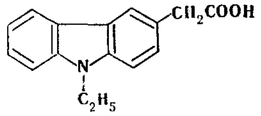


I



II a-e



III

IIa $X=Y=H$; b $X=C_2H_5$, $Y=H$; c $X=COCH_3$, Y=[illegible]; d $X=NO_2$, $Y=H$; e $X=Y=Cl$

The method for the determination of the inductive constants of various groups from the pK_a values of substituted acetic acids is well known, and, of particular importance in our case, steric factors do not have an appreciable effect on the σ_I constants obtained [7].

The thermodynamic pK_a values of acids I-III (Table 1) were determined by potentiometry [8] at 25 ± 0.5°C. The pK_a values found for acids IIa-e in 50 and 60% aqueous ethanol are linearly related to the $\sigma°$ constants of the X and Y substituents [Eqs. (1) and (2), respectively]:

$$pK_a=4{,}63-0{,}38\sigma_p^0;\ S=0{,}02;\ r=0{,}990 \tag{1}$$

$$pK_a=4{,}92-0{,}54\sigma_p^0;\ S=0{,}03;\ r=0{,}985, \tag{2}$$

where ρ is the reaction constant, S is the standard deviation, and r is the correlation coefficient. The decrease in the ρ value as the fraction of ethanol in solution decreases for acids II is a characteristic feature also for substituted phenylacetic acids: the ρ values in 75, 50, and 10% aqueous ethanol are, respectively, 0.83, 0.71, and 0.54 [9]. A comparison of the ρ values for acids IIa-e and phenylacetic acids in 50% ethanol indicates appreciably lower sensitivity of the dissociation constants of 9-carbazolylacetic acids to the effect of the substituents, i.e., the less pronounced transmission properties of the carbazolyl ring as compared with the phenyl group. A study of the effect of the composition of the medium on the strength of acid Ia showed that as the fraction of ethanol is increased from 50% to 95%, the acid properties of Ia become weaker; the dependence of the pK_a on the percentage of ethanol has approximately linear character [Eq. (3)]:

$$pK_a=3{,}43+0{,}025\%\ \text{EtOH};\ S=0{,}07;\ r=0{,}980 \tag{3}$$

Measurement of the acidity of acid Ia in more dilute ethanol solutions is not possible because of its limited solubility. The effect of the medium on the strength of acid IIa is similar to its effect on the strength of other aliphatic carboxylic acids [10]. From the pK_a values of acids I and IIa in a 56% by volume solution of ethanol (mass content 50%) by means of the equation in [11]

$$\sigma^*=8{,}18-1{,}13\,pK_a \tag{4}$$

we calculated the Taft inductive constants for the 9-carbazolyl (σ^* = 1.55 ± 0.05) and 1-indolyl (σ^* = 1.75 ± 0.05) groups. We also calculated the σ_I constants from the expression $\sigma_I = \sigma^*/6.23$: 0.25 ± 0.01 (9-carbazolyl) and 0.28 ± 0.01 (1-indolyl). It is interesting to note that extrapolation of the dissociation constant of acid IIa to a purely aqueous solution by means of Eq. (3) (although such extrapolation is not theoretically substantiated) gives a pK_a value of 3.43. The use of the Charton correlation relationship between the pK_a values and the σ_I constants for aqueous solutions of substituted acetic acids at 25°C, viz., $\sigma_I = 1.186 - 0.25\ pK_a$ [7], leads to a σ_I constant of 0.32 for the 9-carbazolyl group. This value does not differ much from the σ_I value of 0.25 obtained from Eq. (4), and this to a certain extent confirms the correctness of the constant for the 9-carbazolyl group. However, the chief significance of the pK_a value obtained by extrapolation consists in the fact that it makes it possible to make an approximate comparison of the strength of acid IIa with the strengths of other carboxylic acids, the acidities of which in very many cases have been determined in aqueous solutions.

The effect of the substituents in the carbazolyl ring on the strengths of acids IIa-e coincides qualitatively with the effect of the same substituents on the NH acidities of carbazoles in DMSO [12]. (The pK_a values of 3-methylcarbazole, carbazole, 3-nitrocarbazole, and 3,6-dichlorocarbazole are, respectively, 17.29, 16.55, 14.10, and 15.23.) An approximate linear relationship exists between the pK_a values of acids IIa, d, e (in 60% ethanol) and 3-methyl-9-carbazolylacetic acid, the pK_a of which was calculated from Eq. (2), and the pK_a values of the carbazoles indicated above [Eq. (5)]:

$$pK_{a\,\text{acid}}=1{,}98+0{,}17\,pK_{a\,\text{carbazole}};\ S=0{,}22;\ r=0{,}984 \tag{5}$$

TABLE 1. pK_a Values of 1-Indolyl- (I) and Carbazolylacetic (IIa-e, III) Acids in Aqueous Ethanol Solutions at 25°C

Compound	pK_a for various volume fraction of aqueous ethanol, %					
	50	56	60	75	80	95
I		4,75±0,04				
IIa	4,65±0,04	4,91±0,03	4,93±0,03	5,19±0,02	5,31±0,02	5,88±0,03
IIb	4,67±0,04	5,00±0,03	5,01±0,01			
IIc	4,45±0,04		4,73±0,03			
IId	4,32±0,03		4,48±0,04			
IIe			4,59±0,03			
III		6,17±0,03		6,31±0,02		

It is important to note that indolylacetic acid I is somewhat stronger than acid IIa; however, at the same time, the equilibrium NH acidity of indole is appreciably lower than that of carbazole [12, 13]. Consequently, annelation of the pyrrole ring of indole with a benzene ring gives rise, on the one hand, to an increase in the stabilization of the carbazole anion and, on the other, leads to a decrease in the —I effect of the neutral heterocyclic ring. The conclusion regarding the smaller —I effect of the 9-carbazolyl group is also in agreement with the ^{13}C NMR spectroscopic data for N-methyl derivatives of indole and carbazole. It has been shown that the inductive effects of the substituents make the chief contribution to the ^{13}C NMR chemical shifts of a number of methyl derivatives (CH_3X) [14]. The chemical shift of the methyl group of 1-methylindole is 32.1 ppm [15]. However, the signal of the CH_3 group of 9-methylcarbazole is shifted almost 5 ppm to stronger field: NCH_3 28.20, C_1 107.87, C_2 125.18, C_3 118.54, C_4 119.96, C_{10} 140.61, and C_{11} 122.56 ppm. Thus the experimental data obtained indicate unambiguously that the deshielding of the terminal vinyl atom and, consequently, the decrease in the electron density on this atom in series of N-vinyl derivatives of indole and carbazole are not determined by inductive factors but rather by resonance factors, i.e., by a decrease in the p—π conjugation, since otherwise one should have expected the reverse pattern because of the large —I effect of the 1-indolyl group.

It is interesting to compare the strengths of acids IIb and III. The σ^* and σ_I constants were calculated for the 9-(3-ethyl)carbazolyl (1.43 ± 0.02 and 0.23 ± 0.01) and 3-(9-ethyl)carbazolyl (0.15 ± 0.02 and 0.02 ± 0.01) groups from Eq. (4). It is absolutely clear that the decrease in the electron-acceptor properties in this series is associated with the greater electronegativity of the nitrogen atom as compared with the carbon atom. In addition, the decrease in the electron-acceptor properties of the 3-(9-ethyl)-carbazolyl group as compared with the phenyl group (the pK_a value of phenylacetic acid in 50% ethanol is 5.47 [9]) is a consequence of the increase electron density on the carbon atoms of carbazole (a π-surplus heterocycle [16]) as compared with benzene.

EXPERIMENTAL

The ^{13}C NMR Fourier spectra of solutions in CCl_4 were recorded with a Brucker HX-90 spectrometer (22.63 MHz) under conditions of complete suppression of spin—spin coupling of ^{13}C with the protons.

9-Carbazolylacetic acids IIa-e were synthesized by reaction of the corresponding carbazoles with chloroacetic acid in DMF in the presence of KOH [17]. The same method was used to obtain 1-indolylacetic acid (I) from bromoacetic acid. 3-(9-Ethyl)carbazolylacetic acid was obtained by the method in [18]. All of the acids were chromatographically pure after isolation and recrystallization from ethanol.

The pK_a values of the investigated acids were determined by potentiometric titration [8, 10] with a pH-673 pH meter calibrated with respect to phthalate and borate buffers and equipped with glass and silver chloride electrodes in a thermostatted cell in an argon atmosphere. Titration of aqueous ethanol solutions of the acids was carried out with 0.1 and 0.005 N solutions of KOH purified to remove carbonates. Concentrations of 0.01 mole/liter were used for acids I, IIa-c, and III in greater than 50% ethanol. In all the remaining cases the concentrations of the acids were 0.005 mole/liter. To reduce the experimental pK_a values to thermodynamic values we used the following δ corrections (a combination of the diffusion potential and the effect of the medium): 0.15 for 50% aqueous ethanol [19], 0.21 for 56% aqueous ethanol [20], 0.22 for 60% aqueous ethanol [21], 0.29 for 75% aqueous ethanol [19], 0.27 for 80% aqueous ethanol [21], and 0.25 for 95% aqueous ethanol [21]. Each of the pK_a values presented in Table 1 was obtained by averaging five to eight measurements. The accuracy of the method was verified by measuring the pK_a value of a purified sample of phenylacetic acid, which was found to be 5.40 ± 0.04 (5.47 [9]).

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