RESEARCH ON 2,3-POLYMETHYLENEQUINOLINES. XXI.* IONIZATION CONSTANTS OF 4-CHLORO-6-R-2,3-POLYMETHYLENEQUINOLINES

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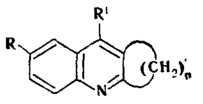
UDC 541.132:547.831

The ionization constants of 4-chloro-6-R-2,3-polymethylenequinolines in 98% methanol were found and it was established that they correlate with the σ_{epi} substituent constants for quinoline. It is shown that the pK_a values of 2,3-tetra- and 2,3-pentamethylenequinolines are close to one another, whereas the pK_a values of 2,3-trimethylenequinolines are one order of magnitude lower; this is a result of the angular strain in the ring system of the latter.

Insufficient study has been devoted to the ionization constants of 2,3-polymethylenequinolines. Only the pK_a values of 2,3-dimethylene-, 2,3-trimethylene-, and 2,3-tetramethylenequinolines, which are, respectively, 4.55, 5.45, and 6.41 units [2], as well as the pK_a values of 4-amino-2,3-tetramethylenequinoline [3] and 6-R-4-butylamino- [4] and 6-R-4-morpholino-2,3-trimethylenequinoline [5], are known. The considerably lower basicity of 2,3-dimethylenequinoline (more than one order of magnitude) as compared with dimethylquinoline (pK_a 5.99) is explained [2] by the high angular strain in the former.† At the same time, the data presented above show that the pK_a values of 2,3-trimethylene- and 2,3-tetramethylenequinolines also differ by one order of magnitude, although the strain in 2,3-trimethylenequinoline should not be as high as in 2,3-dimethylenequinoline. In this connection, it seemed of interest to compare the basicities of 2,3-polymethylenequinolines that differ from one another with respect to the length of the polymethylene chain. For this, we determined the ionization constants in 98% methanol of three reaction series of 4-chloro-6-R-2,3-polymethylenequinoles with the general formula I and three to five methylene groups (Table 1).



I

The data show that the pK_a values of the compounds of the first reaction series (n = 3) are lower by a factor of ~10 than the pK_a values of the compounds of the second series (n = 4). This provides evidence for rather significant strain in 2,3-timethylenequinolines, which arises as a consequence of the fact that their cyclopentene ring, which is fused with a quinoline ring, has a planar structure (compare with indan [6]). Moreover, the angle between the C_2-CH_2 or C_3-CH_2 and C_2-C_3 bonds in these compounds is forced to be reduced from the normal angle for aromatic compounds (120 deg) to 108 deg. In addition to the angular strain in the cyclopentene ring, torsion strain is also present. The strained character of the cyclopentene ring gives rise to changes in the pyridine ring condensed with it, and this evidently leads to a change in the bond lengths in the latter and in its aromatic character and basicity.

The inductive effect of the polymethylene chain makes a definite contribution to the increase in the basicity on passing from compounds of the first series to compounds of the second series, but this contribution is not a decisive one. The fact that the basicities of compounds of the third reaction series (n = 5) are almost the

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*See [1] for communication XX.

†The authors thank L. E. Kholodov for directing their attention to papers dealing with strained heterorings.

Perm Pharmaceutical Institute, Perm 614600. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 506-507, April, 1977. Original article submitted June 22, 1976.

TABLE 1. Ionization Constants of 4-Chloro-6-R-2,3-polymethylenequinolines

Reaction series No.	n	R	R'	pK_a	$pK_a - \Sigma\sigma_{epi}$ correlation parameters
1	3	H	H	3,74±0,03	ρ — 6,47 pK^0 calc 3,51 r 0,980 s 0,14
	3	H	Cl	2,40±0,03	
	3	CH_3	Cl	2,67±0,06	
	3	Cl	Cl	1,54±0,03	
	3	Br	Cl	1,50±0,03	
	3	CH_3O	Cl	2,49±0,03	
2	4	H	H	4,67±0,03	ρ — 7,59 pK^0 calc 4,58 r 0,995 s 0,087
	4	H	Cl	3,30±0,03	
	4	CH_3	Cl	3,61±0,04	
	4	Cl	Cl	2,28±0,04	
	4	Br	Cl	2,10±0,02	
3	5	H	H	4,58±0,03	ρ — 6,97 pK^0 calc 4,57 r 0,999 s 0,01
	5	H	Cl	3,42±0,04	
	5	Cl	Cl	2,39±0,02	
	5	Br	Cl	2,32±0,02	
	5	CH_3	Cl	3,78±0,03	

same as those of compounds of the second series serves as a confirmation of this.

The pK_a values that we found for 2,3-tri- and 2,3-tetramethylenequinolines in 98% methanol are considerably lower than the pK_a values of the same compounds in water [2]; this is due to the lower dielectric permebility of methanol as compared with water.

In order to make a quantitative evaluation of the effect of substituents on the ionization constants we ascertained the correlation of the pK_a values of 2,3-polymethylenequinolines with the total substituent constants (σ_{epi}) for quinoline [7] for substituents in the 4 and 6 positions. Additivity of the constants of substituents in the 4 and 6 positions of quinolines was established in [8]. It was found that a good correlation is observed and that the parameters of this correlation show that the σ_{epi} constants for quinoline can be used successfully for the evaluation of the effect of substituents on the reactivities of 2,3-polymethylenequinolines. At the same time, an attempt to correlate the basicities of I with the σ and σ^0 constants did not give positive results. It follows from this that the mechanism of transmission of electronic effects in 2,3-polymethylenequinolines is similar to the mechanism in quinolines.

EXPERIMENTAL

The ionization constants were determined for analytically pure samples of 4-chloro-6-R-2,3-polymethylenequinolines, which we previously obtained in [9], by potentiometric titration of 0.01 M solutions of bases I in 98% methanol with a 0.1 N hydrochloric acid solution at 25 ± 1 deg with an LPH-01 potentiometer with glass and silver chloride electrodes. The calculations were made by the usual method for eight points corresponding to 10-90% neutralization.

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