THE NATURE OF THE INTERACTION OF THE PHENYL AND IMIDAZOLE RINGS IN THE N-ARYLIMIDAZOLES

III. Ionization Constants and Menshutkin Rate Constants in a Series of N-Substituted Imidazoles and Benzimidazoles*

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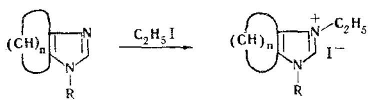
The ionization constants in 50% aqueous ethanol at 20° C and the rates of interaction with ethyl iodide in acetone at 50° C of the N-methyl, N-benzyl, and N-phenyl derivatives of imidazole and benzimidazole have been measured. It has been shown that in N-phenylbenzimidazole, the phenyl group departs from the plane of the molecule by an angle of about 40°. Because of this, the influence of the N-phenyl group on the reactivity of the imidazole ring is greater in the imidazole series than in the benzimidazole series.

An interpretation of the electronic interaction of the phenyl and imidazole nuclei in the N-phenylimidazoles has been given previously on the basis of certain reactions [1], physical characteristics [2, 3], and the molecular orbital calculations [4]. In the present work, to study this question further we have measured the ionization constants in 50% ethanol at 20° C and the rates of the reaction with ethyl iodide in acetone at 50° C of a number of N-substituted imidazoles and benzimidazoles (R = CH_3, $C_6H_5CH_2$, C_6H_5):



imidazoles (n = 0) benzimidazoles (n = 4)

As is well known, the Menshutkin reaction belongs to the S_E2 type and its rate is proportional to the basicity of the tertiary nitrogen atom. Consequently, imidazoles, as stronger bases, react 2-4 times faster than benzimidazoles. In both the imidazole and the rates of the reaction differ little from one another for the N-methyl and N-benzyl derivatives. The slightly lower values of the rate constants and pK_a for the latter are connected with -I effect of the benzyl group. However, the rates of the reaction and the pK_a values for the N-phenyl-substituted derivatives are considerably lower in both reaction series. These results, in agreement with the conclusions drawn previously [1-4], show that the phenyl group in the N-phenylimidazoles is an electron acceptor both in the static state and in the course of the reaction and therefore does not exhibit the +E effect that is sometimes characteristic for it in electrophilic reactions [6]. The influence of the phenyl group is considerably greater in the imidazole series than in the benzimidazole series. This conclusion follows both from a comparison of the rate constants and ionization constants K_{CH_3} and K_{Ph} within each reaction series and also from the fall in the value of K_{imid}/K_{bzm} and ΔpK_a on passing from the N-methyl to the N-phenyl derivatives (Table 1)*.

The phenomenon mentioned may be due to two factors: 1) the acoplanarity of the molecule of N-phenylbenzimidazole [2] with the consequent decrease in resonance interaction between the N-phenyl and the imidazole rings, and 2) the higher conduction of the electron effects through the pyrrole N atom of the imidazole as compared with the benzimidazole. There are grounds for assuming that the imidazole ring in various heterocyclic systems is characterized by approximately the same polarizability (see, for example [7]). If this is so, the difference found in the reaction rate constants between the N-methyl and N-phenyl derivatives in the imidazole and benzimidazole series can be used to evaluate the angle of rotation of the phenyl group of N-phenylbenzimidazole relative to the plane of the molecule. It is known [8] that Braude's formula $M = M_0 \cdot \cos^2 \varphi$ approximately connects the fall in the mesomeric effect with the angle of rotation, φ, of the conjugated groups relative to one another, while very diverse physical parameters may act as measures of the mesomeric effect M (in a sterically hindered molecule) and M_0 (in a plane molecule, M = 0° C). Taking as M and M_0 the

Table 1

Ionization Constants and Rate Constants of the Reaction with Ethyl Iodide of N-Substituted Imidazoles and Benzimidazoles

R	K ×10⁵, l • mole-1 • sec-1			pK_a (magnitude of K_a)		ΔpK_a
	imidazoles	benzimidazoles	K_{imid}/K_{bzm}	imidazoles	benzimidazoles	
CH_3	3.87	1.03	3.76	6.56 (2.75×10^{-7})	4.98 (1.05×10^{-5})	1.58
$C_6H_5CH_2$	3.35	0.95	3.53	6.09 (8.13×10^{-7})	4.49 (3.24×10^{-5})	1.60
C_6H_5	1.57	0.76	2.1	5.10 (7.94×10^{-6})	3.73 (1.85×10^{-4})	1.37

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*For part II, see [3].

*Ph = C_6H_5, imid = imidazolyl, bzm = benzimidazolyl.

Table 2

Angle of Rotation, φ, of the N-Phenyl Group in N-Phenylbenzidazole Relative to the Plane of the Benzimidazole Ring

Stuart model	van der Waals model	Dipole moments	Ionization constants	Rate constants of the Menshutkin reaction	Mean
40°	39°	41—43°	39°	40°	40°

ratio K_{CH_3}/K_{Ph} in the benzimidazole and imidazole series, respectively, we found $\varphi = 42°$.

An analogous treatment [in this case, in order to satisfy the condition $M_0 > M$, we must take the ratio $K_a(Ph)/K_a(CH_3)$] of the ionization constants, K_a, gives a value $\varphi = 39°$. These values of the angle of rotation agree satisfactorily with the figures that we calculated from the dipole moments of the N-phenylimidazoles [2] and also those obtained from Stuart and van der Waals models of the molecule (Table 2)*. Such a close agreement of the values of the angle φ found from very different data shows the well-foundedness of the assumption that we made of the approximate identity of the polarizabilities of the pyrrole N atoms in imidazole and benzimidazole.

The departure of the phenyl group from the plane of the molecule by 40° (mean value) damps the mesomeric effect by approximately 25%. The residual difference in the reactivities of the 1-methyl- and 1-phenylbenzimidazoles must be mainly due to the 75% fraction of the mesomeric interaction. It is obvious that the inductive interaction of the phenyl and imidazole rings in the molecules of the N-phenylimidazoles is extremely small.

EXPERIMENTAL

The starting materials were obtained and purified by known methods [5]. The acetone and ethyl iodide were rendered absolute and were then twice redistilled. The ionization constants were measured on a LPU-01 pH-meter with glass electrodes and saturated silver chloride flow electrodes. In the pH measurements, a 0.001 M solution of the base was titrated with 0.01 M HCl. The ionization constants were calculated by means of Henderson's equation on the basis of 8-9 measurements. The maximum deviation did not exceed ±0.05 pK_a.

For the kinetic measurements, an ~0.1 M solution of the base and an ~0.2 M solution of ethyl iodide in acetone were prepared. The cooled solutions of the reactants (2.5 ml each) were mixed in tubes which were then sealed and placed in a thermostated vessel. The time when a temperature of 50 ± 0.05° C had become established in the thermostated vessel was taken as the beginning of the reaction. From the results of an analysis of one tube at this moment a correction was introduced for the error connected with the occurrence of the reaction before the establishment of the desired temperature. Subsequently, the remaining tubes were opened at predetermined intervals of time and their contents were transferred into a separating funnel containing distilled water (60 ml) and petroleum ether (20 ml). The unchanged ethyl iodide passed into the ethereal layer and the imidazolium salt formed into the aqueous layer. The ethereal layer was washed twice more with water (30-ml portions) and the iodine produced, which was present in the wash-waters, was titrated potentiometrically. The titrating agent used was an acidified 0.05 M solution of silver nitrate. The reaction was carried out to 35-70% conversion. The rate constants of the reactions, proceeding by a second-order law, were calculated from the equation: $K = 2.3/ /[(a-b)r] \cdot [(a-x)b]/[(b-x)a]$ ($l \cdot mole^{-1} \cdot sec^{-1}$). The final rate constant was arrived at by averaging the results of 5-7 measurements. The figures for the rate constants and ionization constants obtained are given in Table 1.

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*In the calculation of φ from dipole moments, as M and M_0 we took the values of the extra π-moments in the benzimidazole and imidazole series which are, respectively, 0.35-0.40 D and 0.65-0.70 D [2]. On considering the van der Waals model (cf. [2]), the radius of the hydrogen atom was taken not as 1.07 Å but as 1.01 Å [9].