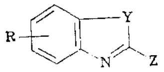
AN INVESTIGATION OF THE TRANSMISSION OF ELECTRONIC EFFECTS IN A SERIES OF 5- AND 6-SUBSTITUTED BENZAZOLES BY THE METHODS OF BASIC DEUTERIUM EXCHANGE AND NMR SPECTROSCOPY

I. F. Tupitsyn, N. N. Zatsepina,
and A. I. Belyashova

UDC 547.78:546.11.02.2:542.422.25:
541.127

The kinetics of deuterium exchange at the methyl groups in 5- and 6-substituted 2-methylbenzothiazoles, 6-substituted 2-methylbenzoxazoles, and 5-substituted 1,2-dimethylbenzimidazoles have been studied. A quantitative estimate of the influence of the substituents on the free energy of activation of deuterium exchange and on the chemical shifts in the ^{1}H, ^{13}C, and ^{19}F NMR spectra of the benzazoles investigated and of the substituted quinolines and naphthalenes used as standard systems has been made with the aid of correlation analysis. It has been shown that the decrease in the transmission capacity of the benzazole nucleus in the transition state of the reaction as compared with the initial state is due to the influence of cross-conjugation effects disturbing the additive nature of the electronic interactions. The question of the probable structure of the transition state of the reaction is discussed.

Features of the transmission of the influence of substituents R to the reaction center Z in benzazoles of type A have been studied previously using various methods [1-11]; however, the question of the interpretation of the experimental results obtained is insufficiently clear and is still the subject of lively discussion.



A

Y=S, O, NH, NCH_3; Z=CH_3, NH_2, SCH_3, CO_2H, Cl

In the present paper, on the basis of the results of a study of the kinetics of deuterium exchange at the methyl groups in 5- and 6-substituted methylbenzazoles and their NMR spectra an attempt is made to determine the differences in the nature of the electronic effects acting during the reaction and specific for the initial (extrareaction) state. We started from the assumption that the changes in the rate constant of the reaction caused by a variation in structural factors does not in itself prevent the possibility of delimiting the influence of substituents in the initial and the transition states expressing their combined, resultant, action. In order to be able to separate the effects of the initial state in determining the rate of the reaction, we selected NMR spectroscopy, assuming that changes in the ^{1}H, ^{13}C, and ^{19}F chemical shifts (CSs) more or less adequately describe the electronic interactions in systems not participating in the reaction.

The conditions of the experiments and the kinetic characteristics of deuterium exchange reactions at methyl groups (k, E_a, log A) are shown in Tables 1-3.

In order to study the transmission of the influence of substituents through the ring in the initial and the transition states, we made use of the method of correlation analysis that is traditional in physical organic chemistry. The results of the treatment of the kinetic and spectral data by the method of least squares are summarized in Tables 4 and 5. In particular, when we substituted the figures of Tables 1 and 2 in the Hammett equation we

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Institute of Applied Chemistry, Leningrad, 197198. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1235-1245, September, 1984. Original article submitted May 9, 1982; revision submitted January 11, 1984.

0009-3122/84/2009-1011$08.50

TABLE 1. Kinetic Parameters and Quantum-Chemical Characteristics of Deuterium-Exchange Reactions in 5- and 6-Substituted 2-Methylbenzothiazoles

R	Temperature, °C	$k\times10^5$ sec^{-1}[a]	Activation energy, E_a, kJ/mole	lg A	$-\lg k$ (20°)	ΔE, eV	Δq_H, a.u
H[b]	−10 0 10	0,6 2,1 6,5	75,4	9,7	3,8	25,153	0,0230
5-NH_2	20 30 40	0,9 3,1 9,6	90,0	11,0	5,0	25,202	0,0253
5-OCH_3	20 30 40	2,0 4,1 24	94,6	12,2	4,7	—	0,0240
5-Cl	−10 0 10	0,6 2,6 9,9	85,4	11,7	3,5	24,931	0,0279
5-NO_2	−20 −10 0	4,7 17 61	74,9	10,5	2,8	24,624	0,0309
6-NH_2	30 40 50	1,5 5,4 16	96,3	11,8	5,4	25,307	0,0230
6-OCH_3	10 20 30	0,7 2,5 8,6	89,6	11,4	4,6	25,170	0,0247
6-Cl	−20 −10 0	1,0 4,5 18	82,9	12,1	2,9	24,947	0,0273
6-NO_2[c]	0 10 20	3,0 6,6 16	55,7	6,1	3,8 (2,1)[d]	24,566	0,0347

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a) In C_2H_5OD at a concentration of C_2H_5OK of 0.57 M.

b) According to [12].

c) Concentration of ethanolate ion 10^{-2} M.

d) Recalculated to a concentration of ethanolate ion of 0.57 M.

TABLE 2. Kinetic Parameters of Deuterium Exchange in 6-Substituted 2-Methylbenzoxazoles (0.57 M solution of C_2H_5OK in C_2H_5OD)

R	Temperature, °C	$k\cdot10^5$ sec^{-1}	Activation energy, E_a, kJ/mole	lg A	$-\lg k$ (20°)
H[a]	−10 0 10	0,82 3,4 11,0	80,0	10,8	3,45
NH_2	40 50 60	2,2 6,8 22,0	100,1	12,0	5,83
OCH_3	0 15 25	0,24 2,1 7,6	93,4	12,2	4,44
NO_2[b]	0 10 20	2,4 5,3 9,2	44,4	3,9	4,0 (2,3)[c]

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a) According to [12]. Calculated by the CNDO/2 method: ΔE = 25.009 eV, Δq_H = 0.0324 a.u.

b) Concentration of ethanolate ion 10^{-2} M.

c) Recalculated to a concentration of ethanolate ion of 0.57 M.

found that for the deuterium exchange reaction in the methyl groups of the 2-methylbenzazoles (series I, II, and V) the best correlations were obtained on using the σ_p-constants, while for deuterium exchange at an aromatic CH bond in the benzothiazoles (series III and IV), the

TABLE 3. Kinetic Parameters of Deuterium Exchange in 5-Substituted 1,2-Dimethylbenzimidazoles (0.57 M solution of C_2H_5OK and C_2H_5OD)

R	Temperature, °C	$k \cdot 10^5$ sec^{-1}	Activation energy, E_a, kJ/mole	lg *A*	−lg *k* (50°)
H[a]	40 55 70	0,24 2,0 13	119,3	15,3	5,0
NH_2	60 70 80	1,6 5,1 15,0	110,5	12,5	5,3
OCH_3	50 60 70	0,65 2,4 8,0	115,6	13,5	5,2
NO_2	0 10 20	1,4 6,1 22,0	91,7	12,6	2,1

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a) According to [12], calculated by the CNDO/2 method: ΔE = 25.320 eV, Δq_H = 0.034 a.u.

TABLE 4. Coefficients of the Equation $\log k = \log k^\circ + \rho\sigma_p$ and the Correlation Parameters of the Rate Constants in the Series of 5- and 6-Substituted Benzazoles

Series	Nature of the compound	Type of σ-constants	ρ	−lg k^0	*r*	*s*	*n*
I	6-Substituted 2-methylbenzothiazoles[a]	σ_n	2,43	3,76	0,976	0,192	5
		σ_n^0	2,88	4,00	0,962	0,270	5
II	5-Substituted 2-methylbenzothiazoles[a]	σ_n	1,64	3,97	0,980	0,165	5
		σ_n^0	1,94	4,13	0,965	0,214	5
III	6-Substituted benzothiazoles[b]	σ_n	1,83	3,69	0,990	0,126	5
		σ_n^0	2,20	3,86	0,999	0,050	5
IV	5-Substituted benzothiazoles[b]	σ_n	2,11	3,82	0,999	0,02	4
		σ_n^0	2,11	3,83	0,999	0,02	4
V	6-Substituted 2-methylbenzoxazoles[a]	σ_n	2,39	3,92	0,976	0,318	4
VI	6-Substituted 2-methylquinolines[c]	σ_n	4,33	5,80	0,982	0,283	5

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a) At 20°C.

b) Deuterium exchange with respect to the aromatic CH bond in position 2 at 25°C [8].

c) At 25°C [13].

rate constants correlated best with the σ°_p constants (Table 4). A comparison of the dependences of the ^1H, ^{13}C, and ^{19}F CSs in the NMR spectra of the benzazoles on the various tapes of σ-constants of the substituents showed that, in agreement with conclusions in the literature [3, 4, 7], a correlation with Hammett's σ_p-constants, which contain a considerable resonance components, is observed (an exception is the X series, where correlation exists with the σ_m constants). The conclusion that the resonance effect predominates somewhat over the induction effect in the case of series for which there is a possibility of using a fairly broad set of substituents (series VIII, XVI, and XVII) is confirmed by a direct calculation of the effects of the substituents on the resonance and induction components using various types of correlations that have been discussed in the literature [4, 17, 18].

Let us pass to a discussion of the experimental material. In accordance with the task of the investigation that was formulated above, let us first consider features of the manifestation of electronic effects in nonreacting molecules. Since the benzazoles under investigation form fairly complex molecular systems for which both a mutual influence of the heteroatoms and nonadditivity of the reaction of heteroatoms with the influence of the substituent are possible, it is appropriate to characterize the electronic effects recorded from the results of measuring the ^1H, ^{13}C, and ^{19}F magnitudes in comparison with the electronic effects for simpler systems — naphthalene and quinoline derivatives, which are the π-isoelectronic

TABLE 5. Connection of the CSs of the ^1H, ^{13}C, and ^{19}F Nuclei with the σ_p Constants of the Substituents in Series of 5- and 6-Substituted Benzazoles, Quinolines, and Naphthalenes

Series	Nature of the compounds	Nucleus observed	ρ_p	δ_o, ppm	r	s	n
VII	6-Substituted-2-methylbenzothiazoles [2]	^1H	0,14	2,79	0,970	0,013	5
VIII	The same [4]	$^{13}C^a$	9,23	155,1	0,994	0,390	11
IX	6-Substituted-2-fluorobenzothiazoles [7]	^{19}F	10,8	85,0	0,987	0,686	5
X	5-Substituted 2-methylbenzothiazoles [4]	$^{13}C^b$	5,92	166,5	0,974	0,305	11
XI	6-Substituted benzothiazoles' [14]	$^1H^a$	0,61	2,86	0,975	0,084	5
XII	6-Substituted 2-methylbenzoxazoles [3]	^1H	0,13	2,59	0,997	0,005	4
XIII	5-Substituted benzimidazoles [10]	$^{13}C^a$	5,97	141,8	0,992	0,254	5
XIV	6-Substituted 2-methylquinolines [15]	^1H	0,14	2,67	0,922	0,018	5
XV	6-Substituted naphthalenes [16]	$^1H^{a,c}$	0,43	7,27	0,999	0,008	8
XVI	The same [17]	$^{13}C^a$	5,14	125,4	0,989	0,347	7
XVII	6-Substituted 2-fluoronaphthalenes [8]	^{19}F	8,40	98,9	0,993	0,388	8

a) CSs of the ring ^1H or ^{13}C nuclei in position 2.

b) Correlation of the magnitudes of $\delta(^{13}C)$ with σ_m constants of the substituents.

c) Correlation of the magnitude $\delta(^1H)$ with the σ°_p-constants of the substituents.

analogs of the benzazoles. One of the methods for such a comparative study is to turn to the transmission coefficients determined as the ratio of the sensitivity constants ρ to the influence of substituents for the CSs of the series of benzazoles studied and for the model series of 6-membered rings. A comparison of the above-mentioned series is completely justified since monotypical correlation relationships (correlations with the σ_p constants; see series XIV-XVII, Table 5) exist in the series of 6-substituted 2-methylbenzazoles, 2-methylquinolines, and 2-methylnaphthalenes and, consequently, the nature of the electronic interactions differs little. We may note, moreover, that, in addition to 6-substituted 2-methylnaphthalenes we are right to assign the 6-substituted 2-methylquinolines to the type of compounds in the molecules of which there are no nonadditive interactions whatever. This follows, for example, from the results of investigations [17, 19-21] according to which the increase in the CSs of the "indicator" carbon atom in position 2 caused by the introduction of identical substituents into position 6 of two π-isoelectronic rings — naphthalene and quinoline — practically coincide.

The pattern of change in the transition capacity of the electronic system of the benzazoles as compared with the "model" systems of the naphthalenes or quinolines in the spectral series studied proved not to be completely clear. For some of these series the magnitude of the transmission coefficient was close to unity, which presupposes an independent influence of the heteroatoms and of the substituent on the reaction center. In particular, in spite of the inadequate reliability of the correlation of the CSs of the protons of the methyl groups of the 6-substituted 2-methylquinoline with the σ_p-constants ($r = 0.922$, series XIV, Table 5), it may nevertheless be concluded from a comparison of series VII and XIV that no appreciable changes take place in the efficiency of the transmission of the influence of substituents on passing from the 6-substituted 2-methylquinolines to the 6-substituted 2-methylbenzothiazoles.

The CSs of the protons of the methyl groups in the series of 6-substituted 2-methylbenzoxazoles reveal a behavior not differing from that which is characteristic for the CSs of their benzothiazole analogs. The transmission coefficient of this system, determined from the results of correlations in series XII and XIV, is 0.97. A comparison of the constants σ_p for correlations of the magnitudes δ_F in series of 6-substituted 2-fluorobenzothiazoles and 2-fluoroethylenes leads to the same conclusion (the ratio ρ_p in series IX and XVII differs only insignificantly from unity).

According to the results of an analysis of other spectral series, the substituents in position 6 of the benzothiazole ring interact with the reaction center more strongly than is the case in the model series of compounds. Thus, judging from the correlations for the magnitudes δ_C in the series of 6-substituted benzothiazoles and naphthalenes (series VIII and XVI), the passage from naphthalene to benzothiazole increases the sensitivity constant ρ_p by a factor of 1.9. The sensitivity to the influence of substituents of the CSs of the hydrogen atoms attached to the benzothiazole ring (series XI) is approximately 1.4 times higher than that of the hydrogen atoms occupying position 2 in the 6-substituted naphthalenes (series XV). However, we do not consider the facts concerning an increase in the sensitivity constants in the benzothiazole system as an indication of the manifestation of an additional interaction between the substituent and the heteroatoms as a consequence of which their combined influence on the CSs becomes nonadditive. A possible explanation of these facts is that the passage from the series VIII and XI investigated to the comparison series XV and XVI is accompanied by an increase in the distance between the substituent and the "indicator" atom, and also by an increase in the angle between the vector of the dipole moment of the substituent and the direction of the C—H bond. As is well known, both these factors should lead to a weakening of the transmission of the electronic influence of substituents, both through the field effect [22] and through the π-induction effect [23]. The observed difference in the behaviors of the ^{13}C and ^{19}F CSs (series VIII and XVI and series IX and XVII) corresponds quantitatively to the proposed explanation, since, in series VIII and XVI, the center of detection (carbon-13) is one of the atoms of the cyclic system that is closer to the substituent than the analogous exocyclic fluorine atom and, consequently, the action of the factors mentioned above on the "carbon" series should be more pronounced.*

Unfortunately, we have no information on the CSs of ^1H, ^{13}C, or ^{19}F nuclei occupying position 2 in the ring of the 5-substituted naphthalenes or quinolines. Consequently, in an analysis of the specific features of the influence of substituents from position 5 of the benzothiazole ring in a reaction center in position 2 we shall not make use of the method of comparing correlations in the series investigated and model series but will have recourse to the criterion of evaluating the relative efficiency of the transmission of electronic effects by two routes in the benzazole system based on Jaffe's relations

$$\text{Substituent R in position 5: } \delta = \rho_N\sigma_m + \rho_S\sigma_p + \delta_o. \tag{1}$$

$$\text{Substituent R in position 6: } \delta = \rho_N\sigma_p + \rho_S\sigma_m + \delta_o. \tag{2}$$

According to [8], a combination of Eqs. (1) and (2) leads to an expression for the constants ρ_N and ρ_S which should be observed and actually are observed [3, 8, 11] only if there are no mutual influences between the two routes for the transmission of the electronic effects: through the cyclic nitrogen atom or through the sulfur atom. Equations (1) and (2) are approximately satisfied for the magnitudes δ_C. This follows directly from the fact that a correlation of the δ_C CSs in 5-substituted benzothiazoles (series X) with the σ_m constants exists (it is true, with a lower constant ρ_m of sensitivity to the nature of the substituent than in the series of 6-substituted compounds; Table 5). Both the σ_p and the σ°_p constants are clearly unsuitable for describing the effect of the substituents. The existence of correlations of the 5-substituent, σ_m, and the 6-substituent, σ_p, constants is equivalent to a simplified form of relations (1) and (2) in which the constant ρ_S assumes a value of zero, i.e., in the reaction series considered, the electronic effects are transmitted to the reaction center almost exclusively through the endocyclic nitrogen atom.

Thus, on the basis of the discussion presented, it may be concluded that the possibilities of correlation analysis, including the idea of the additive and independent influences of the two heteroatoms and the substituent of the reaction center, permit an explanation of the observed changes in the CSs of the ^1H, ^{13}C, and ^{19}F nuclei for benzazole systems.

In attempting to obtain definite information concerning the mutual influence of groups in the reacting molecules, let us consider the transmission capacity of benzazole systems based on the results of a kinetic study of the deuterium exchange reaction at methyl groups

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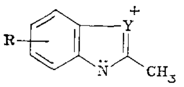
*So far as concerns the interpretation of results of correlations of the protonic CSs (in particular, of series XI and XV), for them, in addition to the facts mentioned above, one must take into account the increase in the contribution of the ring current due to the replacement of a 5-membered sulfur-containing ring by a 6-membered aromatic (heteroaromatic) ring (see, for example, [24]).

in 6-substituted aromatic heterocycles. The invariability of the type of mechanism of the exchange reaction in the series of benzazoles investigated and in a series of model substances (6-substituted 2-methylquinolines and 2-methylnaphthalenes) is indicated by the correlation of the corresponding rate constant by a single set of σ-constants — Hammett's σ_p constants (see Table 4, series I, V, and VI). The values of ρ_p in the correlations for the rate constants of deuterium exchange at the methyl group of various nuclear-substituted 2-methylnaphthalenes and 2-methylquinolines coincide closely ($\rho_p = 6.2$) which permits the conclusion concerning the completely independent (additive) nature of the combined influence of the cyclic nitrogen atom and a remote substituent to be extended to quinoline derivatives even during the reaction act.* On comparing the constants ρ_p of the deuterium exchange series of 6-substituted 2-methylbenzothiazoles and 2-methylbenzoxazoles (series I and V) with the constant ρ_p for the analogous series of 6-substituted 2-methylquinolines (series VI) we find that the transmission coefficient is 0.55, i.e., in the series of compounds investigated a significant weakening of the electronic transmission is observed. This gives grounds for assuming a mechanism of the transmission of the influence of substituents that is different from that in the spectral series. While for the latter, as already mentioned, the influences of the substituents and of the heteroatoms in the initial state of the substituents and heteroatoms in the initial state that is transmitted to the reaction centers through the field or by the π-inductive mechanism are independent, in the reaction series of deuterium exchange the electronic effects of the transmission state are apparently predominant. It may be assumed that in the reaction system an additional resonance interaction takes place between the unshared pairs of electrons and the sulfur or oxygen atom and the nitrogen atom. In this case there is the peculiar "dispersion of the conjugation effect," the existence of which was shown as long ago as 1958 by Izmailskii [25]. The basis for this hypothesis is a conclusion [26] that, in the case of the deuterium exchange reaction at the methyl group in 6-substituted 2,3-dimethylbenzazolium iodides, compounds for which the appearance of limiting canonical structures of type B is more favorable, are characterized by a higher reactivity and a lower sensitivity to electronic influences.



B

In agreement with what has been said, the passage from the benzothiazole derivatives investigated to benzothiazolium salts is accompanied by a further decrease in the transmission properties of the heteroaromatic ring: in the latter series, $\rho_p = 1.96$ [26].

In addition, the value of the constant ρ_p may be influenced by the fact of the conjugation of the electron-donating CH_2^- group in a carbanion with a heteroatomatic ring formed as an intermediate. The effect mentioned is so considerable that it may partially compensate the electronic effect created by a substituent in position 6 and thereby smooth out the differences in the stabilizing influences of substituents. The mechanism of the weakening of transmission capacity because of "cross-conjugation" that has been described is in harmony with the results on the nature of the change in the correlation constants ρ_p for the carbon CSs for the endocyclic $C_{(2)}$ atom in the series of 6-substituted benzothiazoles (series VIII, $\rho_p = 9.23$), 2-methylbenzothiazoles ($\rho_p = 9.68$ [4]), and 2-aminobenzothiazoles ($\rho_p = 6.19$ [4]). As can be seen, the constant of sensitivity to the electronic influence of substituents from position 6 is practically the same when substituents of low polarity (Z = H or CH_3) are present at the "indicator" atom and are decreased by one third if the substituent is an amino group (Z = NH_2), which is similar in its π-donor capacity to the CH_2^- group.

As in the case of the spectral series, for the study of the behavior of the rate constants of deuterium exchange in the series of 5-substituted 2-methylbenzothiazoles we shall make use of an approach based on an investigation of the compatibility of equations of types

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*The slight difference of the constant ρ given in [13] from the analogous constant ρ_p for the deuterium exchange series VI considered here is not surprising if it is borne in mind that in [13] values of the rate constants for 34 aromatic and heteroaromatic compounds were included in the correlation treatment, while series VI consists of only one of the special reaction series into which this total group of kinetic results is divided.

(I) and (II). In this way it is not difficult to show that the rate constants of deuterium exchange at the methyl group do not satisfy Jaffe's criterion (Table 1). The reason apparently lies in the mutually dependent (nonadditive) nature of the influence of a substituent and of both heteroatoms on the reaction center in the transition state of the deuterium-exchange reaction of the 2-methylbenzothiazoles. A difference conclusion must be mentioned which is based [8] on the results of a study of deuterium exchange at the aromatic $C_{(2)}$—H bond of the 5- and 6-substituted benzothiazoles (series III and IV). Assuming that substituents in position 5 simultaneously and independently transmit a meta-influence to the nitrogen atom and a para-influence to the sulfur atom, and substituents in position 6 a para-influence to the nitrogen and a meta-influence to the sulfur atom, Attanasi et al. [8] interpreted the results that they had obtained as an indication of the approximately equal efficacy of the transmission of electronic effects through the S—C and the N—C bonds. The difference observed in the mechanisms of the transmission of electronic influences is connected with a change in the resonance contribution to the stabilization of the transition state: In the exchange reaction at an aromatic C—H bond the negative charge arising on the carbon atom cannot interact sufficiently effectively with the π-system (correlation with the σ°_{p}-constants in series III and IV); conversely, in the exchange reaction at a methyl group, where the transition state apparently has a more pronounced carbanionic nature, the conjugation effect favors the delocalization of the partial negative charge between the CH_2^- group and the ring and thereby intensify the nonactivity of interactions (correlation with σ_p constants in series I and II).

The kinetic investigation that we have performed has revealed a nature of the influence of substituents present in position 5 of the benzimidazole series on the rate constant that is somewhat unusual for benzazole systems. In fact, on the introduction into this position of 1,2-dimethylbenzimidazole of electron-donating substituents (R = NH_2, OCH_3), a very slight weakening of the kinetic CH acidity is observed; at the same time, the introduction of the electron-accepting group NO_2 causes a pronounced acidifying effect (Table 3). Here there is no correlation of the rate constant with any of the sets of σ-constants of the substituents. The reason may be the disturbance of the LFE principle in the transition state of the deuterium exchange reaction of the benzimidazole exchange reaction of the benzimadazole series arising because of the saturation effect. The latter is expressed in a marked decrease in the electron-donating capacity of each of the fragments of the reacting molecule — the electron-donating substituent, the cyclic NCH_3 group (which is a more powerful donor than a sulfur atom), and the reaction center CH_2^- — when they are present together in the benzimidazole system.

In concluding our discussion of the results of correlation analysis, we emphasize that the conclusion concerning the nature of the electronic influences that has been based on the study of the kinetics of the kinetics of deuterium exchange differs from the conclusion from spectral characteristics. The most probable reason for this discrepancy is the fact that the rate constants of deuterium exchange describe predominantly the behavior of the transition state in which electronic influences are exerted nonadditively with the inclusion of perturbing influences of cross-conjugation effects.

Although the complex correlation argument given above enables us to obtain information on the nature of the electronic interactions both in nonreacting and in reacting heteroaromatic bicyclic systems, it nevertheless leaves open the question of the probable position of the transition state along the reaction coordinate between the initial state and the "long-lived" carbanion. From this point of view the use of the quantum-chemical approach may be of some use. At the present time two methods for a theoretical description of the kinetic CH acidity are commonly used which are based on calculations of the quantum-chemical indices of reactivity in the SCF MO LCAO approximation [27-29]. In the first method an index is used that is obtained in the calculation of molecules "outside the reaction": the effective electronic charge on the hydrogen atom attacked ($\Delta q_H = q_H - 1$). In the second method, the reactivity index is determined by calculating the difference in the total energies ΔE of a neutral molecule of the substrate (the initial CH acid) and a hypothetical molecule corresponding to its carbanion. In order to judge the probable position of the transition state of the reaction coordinate, it is necessary to perform an analysis of the applicability of the two indices in each individual series of compounds. A situation is possible, for example, in which there is a correlation between the magnitudes log k and Δq_H while the index ΔE "does not work." In this case it is said that the transition state is formed with a comparatively slight perturbation of the electronic configuration of the initial state. However, the case in which there is no correspondence between the magnitudes log k and Δq_H and the index ΔE

TABLE 6. Logarithms of the Rate Constants and Indices of Reactivity in the Deuterium Exchange Reactions of 6-Substituted 2-Methylquinolines (calculation by the CNDO/2 method)

R	$-\lg k^a$ (20°)	ΔE, eV	Δq_H, a.u
H	5,7	25,618	0,0151
OCH_3	7,6	25,650	0,0139
F	5,8	25,535	0,0157
NO_2	2,5	25,013	0,0203
NO_2^b	4,2	25,264	0,0181

a) At 20°C [13].

b) Substituent in position 5 of the quinoline ring.

gives the correct information on the course of the change in the CH acidity is far more frequent. This presupposes a closeness of the electronic structure of the transition state to the structure of the "long-lived" carbanion.

In order to avoid an indeterminacy of the results of correlation connected with small intervals of change in the values of Δq_H and ΔE in the series of benzazoles investigated, we expanded the range of substances for comparing both quantum-chemical indices with the kinetic characteristics of deuterium exchange by including substituted 2-methylquinolines and some methyl-substituted monocyclic azoles having different types of electronic effects in the molecules (4-methylthiazole, 1,1,2-dimethylimidazole, 4-nitro-1,2-dimethylimidazole, 3,4-dimethyl-1,2,5-oxadiazole, 2,5-dimethyl-1,3,4-oxadiazole, and 2,5-dimethyl-1,3,4-thiadiazole). The calculations were performed with the aid of the CNDO/2 method which, as is well known, serves as a source of fairly correct information on the factors affecting the kinetic CH acidity (see, for example, [27-29]). For sulfur-containing compounds we used the sp basis.

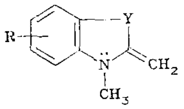
An important question arising in calculations of carbanionic molecules of a transition state is that of the real structure of the reaction center. Although this question has not been definitively answered, a model in which the angles relating to the CH_2^- group are considered to be the same as in the initial CH-acid ("pyramidal" model) is considered to be the best-based at the present time. In view of what has been said, we selected the above-mentioned "pyramidal" model (with retention of the initial geometry of the rest of the molecule).

The results of calculations of the magnitudes Δq_H and ΔE for bicyclic heteroaromatic compounds are given in Tables 1 and 6. The experimental and calculated figures for the monocyclic azoles were taken from the literature [29, 30]. According to these results, among the compounds of the classes considered there is no linear correlation between log k and Δq_H, while the magnitude ΔE qualitatively gives the relative reactivities of the methyl group in the basic deuterium exchange reaction in a fairly satisfactory manner. The relation between log k and ΔE found is described by the equation

$$\lg k = 4.231 \Delta E - 102.244, \quad (3)$$

where $r = 0.951$, $s = 0.69$, $n = 21$.

On the basis of what has been said, it may be concluded that changes in the kinetic CH acid are determined mainly by the energy of the CH bond and the energy of the subsequent stabilization of a transition state close in structure to the "pyramidal" carbanion. We obtained similar results in calculations of a "planar" model of a carbanionic transition state in which there is still more considerable redistribution of the excess charge between the sp^2-hybrid extracyclic carbon atom and the heteroaromatic carbon system than in the "pyramidal" carbanion (these results are not given here). Since a direct quantum-chemical investigation does not permit an unambiguous choice to be made between the models of the carbanions, we have attempted to arrive at such a conclusion by an indirect route, comparing the entropy contributions to the change in the free energy of activation of deuterium exchange in the 2-benzothiazoles and the deuterium exchange reaction of similarly substituted 2,3-dimethylbenzothiazolium iodides in ethanol. A feature of the latter reaction is a transition state of the neutral type characterized by a comparatively weak tendency to solvation, and also the presence in it of a sp^2-hybrid carbon atom and, correspondingly, a considerable delocalization of the π-electron density over the conjugated system [26].



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In the performance of the above-mentioned comparison, we took into account the fact that the "true" rate constant $k_2 = k/[C_2H_5O^-]$ in the quaternary salt series is approximately 10^4-10^5 times higher than in the 2-methylbenzothiazole series. In pure ethanol, the concentration of alcoholate ion is of the order of 10^{-8} M; for C_2H_5OH, pK ~ 16. It follows from Table 1 that the values of the entropy of activation $\Delta S^{\neq}$ in the case of the benzothiazole system investigated are in the range from −5 to −15 e.u. Thus, they are 20-30 e.u. lower than for the deuterium exchange reaction of the 2,3-dimethylbenzothiazolium iodides. As is known, high negative values of $\Delta S^{\neq}$ indicate both the orderedness due to the solvation of the substrate (transition state) by solvent molecules [31] and a high polarity of the transition state of the reaction [32]. Thus, in the case of the substituted 2-methylbenzothiazoles the transition state is highly solvated and is, in all probability, characterized by sp^3-hybridization of the orbitals in the CH bonds of the CH_2^- group, which also ensures a higher degree of localization of the electron density on the anionic carbon atom than in the transition state of the reaction of quaternary salts.

EXPERIMENTAL

The syntheses and the purification of the compounds investigated were performed by the usual methods, which are described in [3, 33-35]. The method of measuring the rate of the deuterium exchange reaction and the treatment of the results of the kinetic experiments have been described in [36]. In the performance of exchange, a 30- to 40-molar excess of solvent was usually taken. For the reason give, and also because the coefficient of distribution of deuterium between its bonds with carbon and oxygen is close to unity, the isotope exchange reaction was described by a first-order equation. The magnitudes E_a and log A were determined by means of the Arrhenius equation from the rate constants of deuterium exchange at three temperatures. The entropy of activation $\Delta S^{\neq}$ was calculated from the formula [37]: $\Delta S^{\neq} = 4.576 \log(\kappa/T) + E_a/T - 46.212$.

The position of the deuterium in the molecules was identified from the IR spectra only on samples of unsubstituted benzazoles obtained after the most prolonged experiments. The appearance of intense bands at 2120-2240 cm^{-1} confirmed that the CH bonds of the methyl group had undergone deuteration, and the absence of bands at 2240-2280 cm^{-1} showed the absence of isotope exchange of the hydrogen of the aromatic ring. The amount of deuterium in the samples analyzed was determined by low-voltage mass spectrometry from the molecular ions.

Calculations by the CNDO/2 method were performed on a BÉSM-6 computer. All the calculations were made on the assumption of a regular hexagonal form of the aromatic rings with interatomic distances $r_{CC} = 1.39$ Å and $r_{CH} = 1.09$ Å; for the 5-membered ring of benzothiazole the geometric parameters used previously in calculations of heteroaromatic monocycles [29] were used; for substituents the idealized-geometry parameters recommended by Pople and Gordon [38] were taken.

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