LITERATURE CITED

1. S. M. Ramsh, S. Yu. Solov'eva, and A. I. Ginak, Khim. Geterotsikl. Soedin., No. 7, 928 (1983).
2. Yu. G. Basova, Candidate's Dissertation, Chemical Science, Leningrad (1980).
3. S. M. Ramsh, N. A. Smorygo, E. S. Khrabrova, and A. I. Ginak, Khim. Geterotsikl. Soedin., No. 4, 544 (1986).
4. R. Baibl, Interpretation of Nuclear Magnetic Resonance Spectra, Atomizdat, Moscow (1969) p. 77.
5. A. I. Kol'tsov and G. M. Kheifets, Usp. Khim., 41, 875 (1972).
6. B. É. L'vovskii and G. B. Erusalimskii, Koord. Khim., 2, 1221 (1976).
7. V. Armithalingam and K. V. Muralidharan, Acta Cryst., 28B, 2417
8. S. M. Ramsh, n. A. Smorygo, and A. I. Ginak, Khim. Geterotsikl. Soedin., No. 8, 1066 (1984).
9. S. M. Ramsh, A. I. Ginak, N. A. Smorygo, Yu. G. Basova, and E. G. Sochilin, Zh. Org. Khim., 14, 1327 (1978).
10. I. P. Gregerov, V. K. Pogorelyi, and I. F. Franchuk, The Hydrogen Bond and Rapid Proton Exchange [in Russian], Naukova Dumka, Kiev (1978), p. 204.
11. R. V. Hoffmann, Mechanisms of Chemical Reactions [Russian translation], Khimiya, Moscow (1979), p. 258.

ACID DEUTERIUM EXCHANGE IN BENZAZOLES

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

UDC 547.72+546.11.02.2:541.127

The kinetics of acid deuterium exchange in benzazoles carrying electron-donor substituents in the 5-, 6-, or 7-positions have been studied. Mass spectrometric studies have shown that exchange in 5-methoxy-1,2-dimethylbenzimidazole takes place exclusively at one position in the benzene ring, in 5-chloro-, 7-chloro-, 5-methoxy-2-methylbenzothiazole and 6-methoxy-2-methylbenzoxazole simultaneously in two positions, and in 6-methoxy-2-methylbenzothiazole the hydrogen at all three possible positions is exchangeable. Using quantum chemical reactivity indices (CNDO/2) in dynamic and state approximations, the orientational features of the reaction have been ascertained. The lack of agreement between the reactivities of the most reactive sites to exchange in heteroaromatic bicycles of similar structure and electrophilic localization energies is explained by differences in the energy profile of the reaction.

Continuing studies of proton-deuterium exchange (H—D exchange) in bicyclic heteroaromatic systems [1], we have measured the rate constants for the reactions of some substituted benzazoles. The acid-initiated H—D exchange reaction in condensed five- and six-membered aromatic heterocycles with two heteroatoms in the ring has received considerably less attention [2, 3] than, for example, in quinolines and isoquinolines [4-6], and no such studies have been carried out in benzazoles. However, for the elucidation of factors governing changes in electrophilic reactivity, such studies are of considerable interest for theoretical heterocyclic chemistry as a whole.

The π-electron deficient parent compounds of this series (benzothiazole N-methylbenzimidazole, and benzoxazole) appear to be totally inert to acid H—D exchange in the benzene ring. In order to facilitate the occurrence of exchange reactions we introduced into the benzene ring, as on a previous occasion [1], an activating substituent (chloro- or methoxy-) in the 5-, 6-, or 7-position of the benzazole nucleus. In addition, in order to be able to

State Institute of Applied Chemistry, Leningrad. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 679-687, May, 1986. Original article submitted February 18, 1985.

0009-3122/86/2205-0557$12.50

TABLE 1. Experimental Results for Acid H–D Exchange in Chlorobenzothiazoles*

Compound	T, °C	Time, h	Deuterium distribution, %				Σd_i, %	$K_D \cdot 10^5$, † sec^{-1}
			d_0	d_1	d_2	(d_3)		
I	140	24	70	28,0	2,0		16,0	0,24
	140	30	70,3	36,8	2,9		16,2	0,19
	140	40	58,2	38,4	6,4		24,0	0,22
	160	6,0	78,6	21,4	—		10,8	0,62
	160	10	65,7	30,7	3,6		18,9	0,68
	160	16	54,4	39,5	6,1		25,8	0,61
	180	2,0	56,6	36,5	6,9		25,2	4,8
	180	6,0	29,9	46,9	22,0	(1,2)	47,4	4,3
	200	1,0	34,0	45,9	18,8	(1,3)	43,8	
II	140	24	89,4	10,5	0,1		5,4	0,080
	140	48	80,7	19,3	—		9,6	0,067
	160	10	60,3	33,8	5,9		22,8	0,84
	160	16	47,3	41,5	11,2		32,1	0,80
	160	20	41,0	44,7	14,3		36,6	0,76
	180	6,0	54,3	39,0	6,7		26,1	1,6
	180	8,0	40,8	44,2	14,7	(0,3)	37,2	1,9

*$\overline{\Sigma d_i}$ and K_D values relate to the two replaceable atoms.

†In calculating K_D from the first-order equation, allowance was made for the equilibrium concentration of deuterium (88%).

compare the results of measurements of H–D exchange in benzazoles with those reported in [1] for quinolines, the reaction medium employed was a mixture of CF_3COOD, $DClO_4$, and D_2O in the same molar proportions as in [1] (91.8 moles of CF_3COOD, 2.5 moles of $DClO_4$, and 5.7 moles of D_2O). Comparison with quinolines was necessary in order to obtain information on the nature of changes in electronic interactions consequent upon replacement of a vinylene CH=CH group in the conjugated bicyclic system by a sulfur or oxygen atom, or the NCH_3 group.

The subjects of the study, experimental conditions, the isotopic composition of the benzazoles following H–D exchange from mass spectrometric data, and the rate constants calculated from the first order reaction equation are shown in Tables 1 and 2.

Since compounds deuterated in a given position in the heteroaromatic ring are extremely difficult to obtain, we measured the H–D exchange rates in benzazoles of natural isotopic composition with a deuterated solvent ("direct" exchange). These was no possibility of H–D exchange in the 2-position in these compounds, since it was protected by the methyl group, but the use of this method involved difficulties of interpretation as to which of the nonequivalent sites in the condensed benzene ring was the most reactive.*

As a result of the inadequacy of chemical information on the orientation of electrophilic reagents in the benzazole ring when activated by electron-donor substituents, we had recourse, in analyzing the experimental findings for H–D exchange, to quantum chemical calculations of reactivity indices: the π-electron charge on the ring carbon atoms ($q_\pi(C_i)$) and the electrophilic localization energy $L_e(C_i)$. These indices were calculated by the standard PPDP/2 method. All calculations of the q_π and L_e values were carried out for compounds unsubstituted in the 2-position by a methyl group, since in their ability to undergo electrophilic condensations in the condensed benzene ring these compounds are similar to their 2-methyl derivatives (see, e.g., [7]). The reactivity indices for these benzazoles in respect of H–D exchange are shown in Tables 3 and 4.

The compounds under study were divided into two groups in accordance with the results obtained: 1) 5- and 7-chloro-2-methylbenzothiazoles (I) and (II), which have a lesser tendency to undergo acid H–D exchange, since the unshared electron pairs of the chlorine participate insufficiently effectively in the p_π conjugation with the π-electrons of the ring, and 2) 5- and 6-methoxy-2-methylbenzothiazoles (III) and (IV), 1,2-dimethyl-5-methoxybenzimidazole (V), and 2-methyl-6-methoxybenzoxazole (VI), in which as a result of stronger p_π conjugation the heterocyclic system is less π-deficient and hence more reactive in H–D exchange.

*Attempts to identify directly the site of isotripic substitution by ^1H NMR and IR spectroscopy did not provide unambiguous information

TABLE 2. Experimental Results for Acid H—D Exchange in Methoxybenzazoles*

Compound	T, °C	Time, h	Deuterium distribution, %				Σd_i, %	$K_D \cdot 10^5$,† sec^{-1}
			d_0	d_1	d_2	d_3		
III	90	16	67,8	31,1	1,1	—	16,5	0,43
	95	12	55,7	43,8	0,5	—	22,5	0,69
	95	16	51,1	41,5	7,4	—	28,4	0,68
	95	24	29,5	52,2	18,3	—	44,3	0,82
	110	8,0	10,3	46,8	42,9	—	66,2	5,0
	110	12	8,3	42,4	49,3	—	70,5	3,8
	110	20	7,4	39,6	53,0	—	73,0	2,5
	120	1,0	66,0	31,4	2,6	—	18,5	6,6
	120	2,0	36,9	49,6	13,8	—	38,2	7,9
	120	4,0	18,1	52,6	29,3	—	55,7	8,6
	125	1,0	35,0	49,4	14,6	—	39,6	17
IV	120	30	58,6	37,1	4,3	—	22,9	0,4
	140	6,0	61,4	32,5	6,1	—	22,5	1,5
	140	10	51,9	39,0	8,7	0,4	28,8	1,2
	140	16	36,7	55,5	7,8	—	31,5	0,87
	140	24	24,2	61,4	14,4	—	45,0	0,95
	160	2,0	67,7	28,6	3,7	—	18,0	3,5
	160	6,0	25,8	43,0	24,9	6,3	37,2	[2,9]
	160	8,0	14,3	39,9	33,4	12,4	48,3	[3,2]
	180	1,0	20,9	41,2	28,6	9,3	42,3	[21]
V‡	50	10	79,9	20,1	—	—	20,1	0,82
	50	16	73,1	26,9	—	—	26,9	0,72
	50	24	60,0	39,8	—	—	39,8	0,80
	60	4,0	76,3	23,7	—	—	23,7	2,5
	60	8,0	60,7	39,3	—	—	39,3	2,4
	60	18	33,1	62,6	4,3	—	35,5	
	70	1,5	74,7	25,3	—	—	25,3	7,0
	70	2,0	67,8	31,9	0,3	—	32,4	7,3
	70	8,0	26,1	65,5	8,4	—	—	—
VI	120	4,0	72,3	23,7	4,0	—	16,2	1,5
	120	6,0	66,9	30,0	3,1	—	18,0	1,1
	120	7,5	61,2	33,7	5,1	—	22,0	1,1
	140	1,0	70,2	26,5	3,3	—	16,6	6,1
	140	2,0	47,9	42,4	9,7	—	31,0	6,3
	140	4,0	28,6	50,9	20,6	—	46,0	5,4
	160	3,0	28,7	48,4	22,9	—	47,2	23
	160	1,0	8,7	41,4	49,4	0,4	70,6	(16)
	160	4,0	6,6	37,0	55,5	0,9	75,0	(15)

*The $\sum_i d_i$ and K_D values for (III), (IV) (partially for the latter), and (VI) relate to two exchangeable atoms, and in (V) to a single atom.

†H—D exchange in (III), (IV), and (VI), the equilibrium concentration of deuterium was 80%. The values of K_D in square brackets are for three exchangeable atoms.

‡The activation parameters of the Arrhenius equation were E = 23.6 kcal/mole, log A = 10.5, and the logarithm of the rate constant at 120°C log K_D = −2.6.

1. The total inactivity of 5- and 6-chloroquinolines in H—D exchange in CF_3COOD with added aqueous $DClO_4$ has been demonstrated previously [1] (no H—D exchange occurs at T 200°C and heating for 8-10 h). In contrast, (I) and (II) undergo exchange quite extensively (by 40-50%) at 180°C (Table 1). This difference in the behavior of heteroaromatic bicycles is explicable in terms of a general increase in the π-electron density in the condensed benzene ring in benzothiazole as compared with the benzene ring in quinoline.

The task of determining the orientation of the electrophilic reagent in H—D exchange in isomers (I) and (II) was complicated by the fact that here isotope substitution takes place in two positions in the benzene ring. In fact, to judge from the low-voltage mass spectra of samples of (I) and (II) following the experiments (Table 1), the strongest molecular ion peaks d_1 and d_2 (m/z 184 and 185) are one or two units stronger than the molecular ion peak d_0 corresponding to the nondeuterated compound, whereas when the extent of deuteration is fairly high (180-200°C) the isotopic forms d_1 and d_2 are present in comparable concentrations Consequently, the reactivities of each of the exchangeable positions in the ring in

TABLE 3. Calculated Reactivity Indices for H–D Exchange in Chlorobenzothiazoles (PPDP/2 method)

Compound	Atom No.	Localization energy, eV		π-electron charges on atoms, e		$-\lg K_D$ at 180°
		neutral molecule	N-protonated form	neutral molecule	N-protonated form	
I	4	13,5024	8,3747	−0,0400	−0,0400	4,35
	6	12,9689	8,1099	−0,0532	−0,0096	
	7	13,2534	—	−0,0050	+0,0209	
II	4	13,1920	8,1736	−0,0192	−0,0175	4,75
	5	12,6254	7,8261	−0,0018	+0,0463	
	6	12,8055	8,0199	−0,0175	+0,0241	

(I) and (II) may differ, but not to such an extent that H–D exchange in each can be clearly differentiated.

From the quantum chemical point of view, the directivity of the H–D exchange reaction remains unclear in respect of which form, uncharged (neutral) species of the cyclic nitrogen-protonated forms of these compounds are involved in the exchange reaction. For this reason, calculations of the electrophilic localization energies in (I) and (II) were carried out in two versions, in one of which H–D exchange in the neutral molecule is considered, and in the other, the benzothiazolium cations. Calculations of both types were carried out on the sp-basis for the sulfur and chlorine atoms.

As will be seen from Table 3, protonation of (I) and (II) does not result in any changes in the predicted orientation of the electrophilic agent. In both versions of the calculation, position 4 has the lowest localization energy, followed by position 6, where strictly speaking attack of the deuteron should occur during H–D exchange in (I) and (II).

The calculated values for the π-electron charges on the atoms both in the neurral molecules and their N-protonated forms are in qualitative agreement with those predicted from the reactivity indices: The L_e for values positions 4 and 6 correspond to the most effective π-charges.

In order to be able to relate the relative reactivities of different positions in the carbocyclic ring of the benzothiazole nucleus with the fine structure of the annelated rings, we turned to the π-isoelectronic analog of (I), 2-chloronaphthalene. The H–T exchange reaction has been studied in detail [8] for the latter compound. In particular, it follows from this study that the rate constant for the reaction with 2-chloronaphthalene-1-T is some 8-10 times greater than with 2-chloronaphthalene-T-3. It appears that approximately the same ratio of $K_D(C_{(4)})$ to $K_D(C_{(6)})$ is maintained in the benzazole analog of 2-chloronaphthalene, namely (I). This is shown indirectly by the isotopic composition of samples of (I) following H–D exchange carried out under conditions favoring low and high extents of deuteration. For example, at 140°C for 24-30 h, when the rate of exchange of the less active position should not be immeasurably great, the mass spectra contain a relatively strong d_1 peak (m/z 184), corresponding in all likelihood to the 4-deuterated compound (I). Under more severe conditions (180-200°C), as already indicated, a mixture of the d_1 and d_2 forms is seen.

These findings therefore argue in favor of the absence of significant changes in the relative reactivities when passing from the carbocycle to its benzothiazole analog, and also of a marked shift of π-electron density from the condensed benzene ring to the azole ring [in contrast to (I) and (II), in 1- and 2-chloronaphthalene the hydrogen atom undergoes exchange in anhydrous CF_3COOH (an acid of "moderate" strength) even at 70°C].

2. From the point of view of elucidating the mechanism of the mutual effect of the rings, of considerable value are quantitative data describing the ratios for the H–D exchange rate constants in separate positions in the benzene ring in methoxybenzothiazoles, benzimidazoles, and benzoxazoles. We did not have at our disposal entire series of isologous benzazoles with methoxy-substituents in the same position in the condensed benzene ring, and for the comparison of relative reactivities we were obliged to study the kinetics of H–D exchange in pairs of 5-substituted (III, V), 6-substituted (IV, VI), and 5- and 6-methoxybenzothiazoles (III, IV).

Consideration of mass spectral measurements for (III) (Table 2) shows that the rate of H–D exchange in this compound is similar in the two positions of the benzene ring. It is

TABLE 4. Calculated Reactivity Indices in H–D Exchange for Methoxybenzazoles (PPDP/2 method)

Compound*	Atom No.	Localization energy		π-Electron charges on atoms, e		$-\lg K_D$ at 120°
		neutral molecule	N-protonated form	neutral molecule	N-protonated form	
III	4	13,8570	8,8306	−0,0765	−0,0785	4,2
		(13,7675)	—	(−0,0928)	—	
	6	13,3715	8,5311	−0,0614	−0,0189	
		—	—	(−0,0680)	—	
	7	13,3612	8,3815	+0,0069	+0,0296	
		—	—	(+0,0453)	—	
IV	4	13,2824	8,0489	+0,0048	+0,0125	
		(13,1734)	—	(−0,0082)	(−0,0120)	
	5	12,4983	8,1125	−0,0511	−0,0077	
		(12,5712)	(7,6506)	(−0,0212)	(+0,0350)	
	7	13,9065	9,0938	−0,0742	−0,0610	
		(13,8008)	(8,9184)	(−0,0395)	(−0,0203)	5,6
V	4	13,5430	8,4654	−0,0710	−0,0728	2,6
	6	13,1540	8,2672	−0,0587	−0,0154	
	7	12,8847	7,8499	−0,0276	+0,0001	
VI	4	13,0005	7,6775	−0,0042	+0,0012	
	5	13,2468	8,3525	−0,0556	−0,0090	4,9
	7	13,0321	8,2515	−0,0830	−0,0735	

*For (III) and (IV), calculations are given on the sp-basis for the sulfur atom, calculated values on the spd-basis being given in brackets.

assumed that as in (I), and for the same reason, isotope substitution takes place in positions 4 and 6. Calculations of L_e and q_π, carried out both on the sp- and the spd-basis for the sulfur atom, confirm these conclusions as to the sites of initial attack.*

In contrast to (III), H–D exchange in (V) is highly selective; prolonged heating at 60-70°C resulted in only one hydrogen being involved in H–D exchange (a strong peak with m/z 177 is seen in the mass spectrum). CNDO/2 calculations in this case also favor the preferential orientation of the attacking electrophile in the 4-position, both from the localization energies and from the π-electron charges (Table 4).

As will be seen from Table 2, the reactivities in H–D exchange of the most reactive position in (V) and (III) are in the ratio of nearly $10^{1.6}$:1. Such a marked drop in reactivity on passing from (V) to (III) is undoubtedly due to the relatively great π-deficiency of the penzothiazole system, and the increased influx of π-electrons from the azole to the benzene ring in the benzimidazole system. The latter is in accordance with the general chemistry of benzimidazole, which is characterized by electrophilic rather than nucleophilic substitution in the benzene ring.

The high positional selectivity of H–D exchange in (V) reflects the known naphthalene-like bond localization in the benzimidazole nucleus. It is worth mentioning in passing that the further loss of conjugation between the benzene and azole rings which appears to occur in 1-benzyl-5,6-dimethylbenzimidazole as a result of steric hindrance created by the adjacent methyl groups favors even more strongly accelerated acid H–D exchange. In contrast to (V) the exchange products of which contain predominantly monodeuterated compounds, samples of the former compound contain mono-, di- and trideuterated compounds (at 140°C for 8 h, $K_D = 2.3 \cdot 10^{-5}$ sec^{-1}; mass distribution d_0 40.9; d_1 37.8; d_2 18.0; d_3 3.3%).

Concluding the comparison of the results for (III) and (V), it may be concluded that both the quantum chemical approaches used (dynamic and static) provide explanations of the directivity of H–D exchange within a single molecule. Unfortunately, these approaches do not provide information on the changes in the rate of the most "reactive" position depending on the nature of the second heteroatom in the azole ring. It has in fact been found experi-

*Bearing in mind that all the methoxy-compounds (III-VI) possess basic properties, and that H–D exchange takes place in a strongly proton-donating medium, we calculated, as in the case of the chlorobenzothiazoles (I) and (II), the reactivity indices L_e and q_π for the neutral molecule and for the ring nitrogen-protonated form.

mentally that in (III) the reaction proceeds at a measurable rate at temperatures 50-60°C higher than in the case of (V), whereas all our calculations predict that the anlogous benzothiazole system should be more reactive. In our view, this discrepancy is due to the different energy profile of the reaction. It is considered to be likely that in the case of (III) the relatively low rate of reaction is due to the formation of a stable σ-complex which requires high temperatures for its aromatization. On the other hand, in the case of (V) a transition state with partial charge transfer is formed, the reason for the high reaction rate being perhaps optimum coupling of ease of addition of a deuteron and elimination of a proton at the intermediate stage.

Turning now to a consideration of the experimental findings for H–D exchange in the 6-substituted benzazoles (IV) and (VI), the stepwise nature of the exchange reaction in (IV) is noteworthy. As will be seen from Table 2, in the products of H–D exchange carried out under relatively mild conditions (140°C, 6-24 h), deuterium is distributed with nearly equal probability between the two positions of the benzothiazole ring, whereas after more extensive exchange under more severe conditios (160-180°C) a mixture of three isotopic modifications (d_1, d_2, and d_3) is formed. This equalization of the reactivities of the individual positions in the ring, in our opinion, is evidence of the fact that (IV) is more highly aromatic than the other benzazoles studied.

Calculations of the reactivity indices for (IV) in two forms (nonprotonated and protonated) and in two versions (sp and spd) lead to the conclusion that positions 7 and 4 are relatively highly-activated towards H–D exchange, and that position 5 is very weakly activated. This is not in accordance with our experimental findings of the small differences in reactivity between positions 7, 4, and 5.

Attempts to obtain a monodeuterated product from H–D exchange with (VI) by carrying out the reaction at low temperatures (120°C) were unsuccessful (Table 2). As in the case of (IV), two atoms in the condensed ring undergo exchange in CF_3COOD, but in this instance the third hydrogen atom is not exchanged for deuterium even under the most severe conditions (160°C, 4 h). The calculated localization energies show that in H–D exchange the electrophile must attack (VI) predominantly in the 5-position, i.e., the β-like-position, rather than the α-position as in (IV). On the other hand, calculations of π-electron charges appear to indicate maximum attack in the 7-position. The directivity of attack in the acid H–D exchange reaction in (VI) will require further investigation.

Before discussing the differences in reactivity in the isomeric methoxybenzothiazoles, it is also worth pointing out that according to its calculated L_e and q_π values (IV) should be more reactive in respect of acid H–D exchange than (VI) (Table 4), but this is clearly not in accordance with the experimental findings (Table 2).

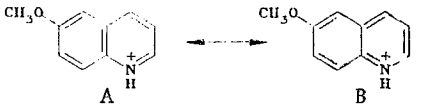
Comparison of the rates of exchange in the isomers (III) and (IV) shows that the 5-methoxy substituent is scarcely more effective than the 6-methoxy substituent. This appears to be due to the fact that the methoxy-substituent in the 6-position of the benzothiazole nucleus is conjugated with the nitrogen atom, resulting in an additional shift of π-electron density from the annealated benzene ring to the heterocyclic part of the molecule (it is also possible that the smaller activating effect of the 6-methoxy substituent is due not only to its direct electronic effect, but also to its ability to facilitate protonation of the pyridine nitrogen, which in turn facilitates the reaction of (IV) with the electrophile as the conjugate acid). In contrast, the 5-methoxy substituent, which is located meta to the nitrogen atom, exerts its π-donor influence to a greater extent on the nearest atom $C_{(4)}$, on which a higher negative charge is concentrated. This modifies the π-electron charge on the most reactive positions in (III) and (IV), but not their localization energies L_e (Table 4).

In order to evaluate more fully the properties conferred on the isoelectric analogs of 6-methoxyisoquinoline by the second heteroatom, it was of interest to compare the observed changes in the exchange capacity of (VII) and benzazoles (III) and (V) (formally obtained by replacing the carbon-carbon double bond in (VII) by sulfur or NCH_3) with theoretical assessments of electrophilic reactivity in H–D exchange. Such comparisons were made with the localization energies and the π-electron charges on $C_{(5)}$ in (VII) (the values of L_e and q are given in [1]), and $C_{(4)}$ in (III) and (V) (Table 4), these being the most active reaction sites in these molecules. The rate constants K_D show the following order of increasing reactivity: (VII) < (III) < (V). According to their L_e indices, these compounds are arranged in a different sequence: (V) < (III) < (VII) (calculated values of L_e for H–D exchange in the neutral molecules). The relative reactivities of the same positions in (III), (V), and (VII) are

similarly not correlated with the π-electron charges on the atoms: (VII) < (V) < (III). A possible reason for these discrepancies is the structure of the transition state, intermediate between a π-complex and the original reaction state (see above).

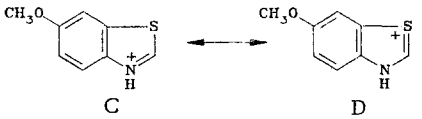
In order to provide a qualitative explanation of the observed changes in the reactivity of the most reactive positions in the heteroaromatic ring in these compounds, we employed the concepts of the valence scheme method. According to this, a measure of the relative stability of the transition state in H–D exchange is provided by the humber of principal resonance structures, characterizing the extent of localization–delocalization of the π-electron in the heterocycle.

The transition state in H–D exchange in (VII) is the system with the least delocalized π-electron density, since this can be described by only one canonical formula (A), which retains unchanged the arrangement of double bonds in the heteroaromatic nucleus; the other canonical form (B) has a quinoid structure, and its contribution to the resonance hybrid must be considerably smaller.



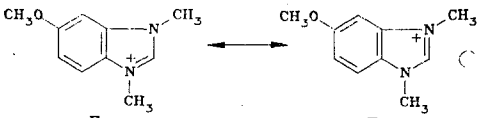
A B

The slightly greater π-electron delocalization in the transition state in H–D exchange in (III) may be due to the fact that here two energetically nonequivalent canonical forms (C) and (D) are possible, which retain unchanged the π-system of the benzene ring.



C D

Finally, the considerable stabilization of the transition state for H–D exchange in (V) is the result of yet more delocalization of π-electrons, due to the superimposition of two energetically nearly equivalent resonance structures, (E) and (F):



E F

It is worthy of mention that the above sequence of increasing reactivities of methoxy-substituted heteroaromatic bicycles with respect to H–D exchange is also the sequence of decreasing CH-acidities of the methyl groups in quaternary salts of 2-methylquinoline and 2-methylbenzazoles, obtained from base H–D exchange in aqueous media [9]. The interpretation proposed by these workers [9] for the changes in CH-acidity is similar to that adopted here, bearing in mind that those factors which promote stabilization of the transition state in acid H–D exchange destabilize the transition state in base H–D exchange, and vice versa.

EXPERIMENTAL

The synthesis and purification of the compounds studied were carried out by standard methods as described in [10-12]; see also reviews [13, 14]. Mass spectra were obtained on a Soviet-made MI-1305 instrument with a modified system for introducing the sample directly into the ion source, ionizing electron energy 14-16 for (I)-(IV) or 20 eV for (V). Cathode emission current 0.45-0.50 mA. Inlet temperature 20°C. Kinetic measurements of H–D exchange were carried out as described in [1]. CNDO/2 calculations were carried out using previously described geometric parameters for the azole systems in their protonated forms [1, 15]. The geometric parameters chosen for the substituents were standard [16].

LITERATURE CITED

1. I. F. Tupitsyn, N. N. Zatsepina, A. I. Belyashova, and A. A. Kane, Khim. Geterotsikl. Soedin., No. 5, 636 (1986).
2. A. El-Anani, S. Clementi, A. R. Katritzky, and L. N. Yakhontov, J. Chem. Soc., Perkin 2, No. 7, 1072 (1973).

3. S. Clementi, S. Lepri, G. Sebastiani, S. Gronowitz, C. Westerlund, and A. Hernfeldt, J. Chem. Soc., Perkin 2, No. 9, 861 (1978).
4. U. Bressel, A. R. Katritzky, and J. R. Lea, Chem. Soc., B, No. 6, 4 (1971).
5. U. Bressel, A. R. Katritzky, and J. R. Lea, Chem. Soc., B, No. 6, 11 (1971).
6. V. P. Lezina, F. U. Stepanyants, L. D. Smirnov, N. A. Andronova, and K. M. Dyumaev, Khim. Geterotsikl. Soedin., No. 12, 1647 (1972).
7. D. J. Evans, H. F. Thimm, and B. A. Coller, J. Chem. Soc., Perkin 2, No. 9, 865 (1978).
8. C. Eaborn and P. Golburn, J. Chem. Soc., B, No. 10, 1112 (1968).
9. M. Bolga, A. Barabás, V. Dénes, and F. Chiraleu, J. Label. Comp., 13, 11 (1977).
10. C. DiModica, E. Barni, and M. Delle, Gazz. Chim. Ital., 95, 432 (1965).
11. K. Tries and A. Wolter, Liebigs Ann., 527, 66 (1937).
12. Y. Mizumo and K. Adachi, J. Pharm. Soc. Japan, 72, 745 (1952).
13. R. Elderfield (ed.), Heterocyclic Compounds [Russian translation], Vol. 5, Izd-vo Inostr. Lit., Moscow (1961), p. 217.
14. P. N. Preston, Chem. Rev., 74, 279 (1974).
15. N. N. Zatsepina, I. F. Tupitsyn, A. A. Kane, and G. N. Sudakova, Khim. Geterotsikl. Soedin., No. 9, 1192 (1977).
16. A. Gordon and R. Ford, Chemist's Companion [Russian translation], Mir, Moscow (1976).

BENZAZOLIN-2-THIONES IN THE MICHAEL REACTION.

2.* REACTION OF BENZOTHIAZOLIN- AND BENZOXAZOLIN-2-THIONES WITH ACRYLONITRILE, ACRYLAMIDE, AND METHYL ACRYLATE IN THE PRESENCE OF BASIC CATALYSTS

K. V. Anan'eva and N. K. Rozhkova†

UDC 547.339.1'371'398.1'787.3'789.6.04

Depending on the structure of the reagents and the kind of basic catalyst, the addition of benzazolin-2-thiones to an activated double bond takes place at either nitrogen or sulfur. Acrylonitrile, regardless of the catalyst, reacts at the nitrogen atom. In the presence of sodium methylate, addition to acrylamide takes place only, and to methyl acrylate predominantly at nitrogen. In the presence of triethylamine, a mixture of compounds with a high content of S-derivatives forms.

As is well known [2, 3], under conditions of basic catalysis azolin-2-thiones react as ambidentate anions, and depending on conditions and reagent structure can give either S- or N-derivatives. Thus benzothiazolin-2-thione reacts reacts with methacryloyl chloride in alkaline medium at the sulfur atom [4]. Addition of benzoxazolin-2-thione to methyl acrylate in the presence of Triton B takes place at the nitrogen atom [5]. The products of the reaction of benzothiazolin- and benzoxazolin-2-thiones with acrylonitrile in basic medium have been assigned the structures of both S-derivatives [6, 7] and N-derivatives [2, 5] by various authors.

In order to elucidate the dependence of the course of benzazolin-2-thione addition to an activated double bond on reagent structure and kind of basic catalyst, we have studied the reactions of benzothiazolin- and benzoxazolin-2-thiones (Ia, b) with acrylonitrile (IIa), acrylamide (IIb) and methyl acrylate (IIc) in the presence of triethylamine (TEA) and sodium methylate. The reaction was carried out at an equimolar ratio of reagents and catalyst in dry

*For 1, see [1].
†Deceased.

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 688-690, May, 1986. Original article submitted February 13, 1985.

 0009-3122/86/2205-0564$12.50