3. F. B. Stocker, J. L. Kurtz, B. L. Gilman, and D. A. Forsyth, J. Org. Chem., 35, 883 (1970).
4. C. S. Kim, K. G. Lec, and J. B. Chac, J. Heterocycl. Chem., 20, 1417 (1983).
5. A. E. Onishik, Zh. Obshch. Khim., 25, 984 (1955).
6. M. V. Rubtsov and A. G. Baichikov, Synthetic Pharmaceutical-Chemical Preparations [in Russian], Meditsina, Moscow (1971).

1,2,4-TRIAZOLO[1,5-a]BENZIMIDAZOLES: TAUTOMERISM AND ALKYLATION

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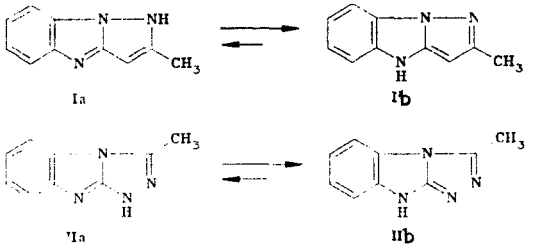
The position of the tautomeric equilibrium in unsubstituted 1,2,4-triazolo[1,5-a] benzimidazole, as well as in its 2-methyl and 2-phenyl derivatives, was investigated by UV, IR, and PMR spectroscopy and by determination of the ionization constants. In all cases the amount of the 4H tautomer in the equilibrium mixture is two to three orders of magnitude greater than the amount of the 3H tautomer, while signs of the existence of the 1 H form are not observed. The synthesis of unsubstituted triazolo [1,5-a]-benzimidazole was accomplished for the first time. The alkylation of the indicated triazolo [1,5-a]benzimidazoles was studied and a relationship between the regiospecificity of this reaction and the position of the tautomeric equilibrium was established.

In recent years the attention of researchers has been directed to condensed systems based on benzimidazole in which another zole ring is attached at the 1–2 bond of the benzimidazole molecule [1]. The principal reason for this interest is the high biological activities of some imidazo[1,2-a]benzimidazoles [2, 3], as well as the complex mutual effect of the condensed rings, the study of which is important for the development of the theoretical chemistry of heterocycles. One of the chief manifestations of this effect is the position of the tautomeric equilibrium in azolobenzimidazoles. Up until now it has been studied for 2-methylpyrazolo[1,5-a]benzimidazole (I) [4] and 3-methyl-1,2,4-triazolo[4,3-a]benzimidazole (II) [5]; it was demonstrated by PMR spectroscopy and measurement of the dipole moments that the 4H tautomer (Ib) dominates in the first case, whereas the 1H tautomer (IIa) dominates in the second case.



The aim of the present research was to study the tautomerism of 1,2,4-triazolo[1,5-a] benzimidazoles III–V. This heterocyclic system contains within itself the features of the structural properties both with I and with azoles II, but the existence of not two but rather three tautomeric forms is possible for it. From a theoretical point of view the following

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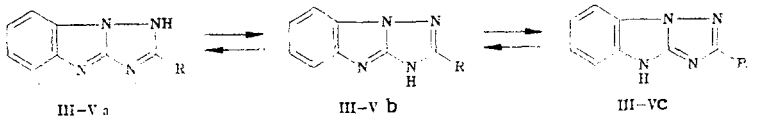
question seemed of interest: where will the NH proton primarily be found: in the central (as in Ib) or side (as in IIa) ring?

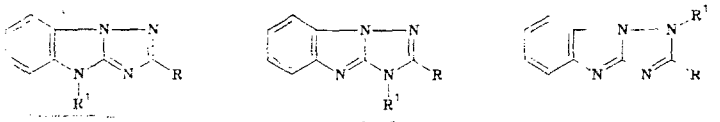


III-V a III-V b III-V c

III—V a R=H; · R=CH_3; c R=C_6H_5

Synthesis of the Starting Compounds

As the subjects of the investigation we selected unsubstituted 1,2,4-triazolo[1,5-a] benzimidazole (III) and its 2-methyl and 2-phenyl derivatives IV and V. The previously undescribed parent compound III of the series was obtained in 66% yield by refluxing 1,2-diaminobenzimidazole (IX) with formamide. Compounds IV and V were previously obtained by heating the corresponding 2-amino-1-acetamidobenzimidazoles with acetic or benzoic anhydride with subsequent hydrolysis of the initially formed 4-acyl-1,2,4-triazolo[1,5-a]benzimidazoles [6]. We showed that this synthesis can be realized successfully and directly from diamine IX; the yields of IV and V reach 90%.

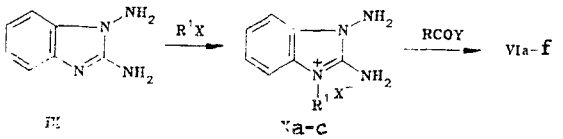


VIa-f VIIa, b,d,e VIII

VI, VII a R=H, $R^1=CH_3$; b R=H, $R^1=C_2H_5$; VI c R=H, $R^1CH_2C_6H_5$; VI, VII R=$R^1=CH_3$; e R=C_6H_5, $R^1=CH_3$; VI f R=C_6H_5, $R^1=CH_2C_6H_5$

In order to study the tautomerism it was also necessary to synthesize the fixed model forms of tautomers III—V. As substituents attached to the nitrogen atoms we used methyl, ethyl, and benzyl groups.

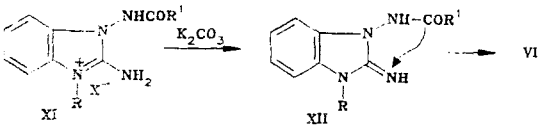
4-Substituted triazolo[1,5-a]benzimidazoles VIa-f were synthesized from diamine IX:



IX XIa-c VIa-f

X a $R^1=CH_3$, X=I; b $R^1=C_2H_5$, X=I; c $R^1=CH_2C_6H_5$, X=Cl

Salts X were cyclized by means of formamide or acetic or benzoic anhydride. It should be noted that the same scheme was used by Japanese chemists to obtain VId,e, but they synthesized salts of the X type by treating 2-amino-1-methylbenzimidazole with mesitylsulfonylhydroxylamine [7]. In addition, cyclization by them was carried out by brief heating at 200°C of salts X (X = MesO) with acetic anhydride or benzoyl chloride; the yields of VId,e were 64 and 50%, respectively. We found that it is more convenient to carry out the cyclization by means of acetic or benzoic anhydride in the presence of potassium carbonate. This makes it possible to obtain VId,e in 90% and 88% yields, respectively. The role of potassium carbonate probably consists in conversion of the intermediately formed salt XI to imine XII, which, as a consequence of the high nucleophilicity of the imine nitrogen atom [8], undergoes cyclization readily.



XI XII VI

We described the preparation of 3-methyl- (VIIa) and 2,3-dimethyl-3H-1,2,4-triazolo[1,5-a] benzimidazole (VIId) in 19% and 62% yields in a previous communication [9]. In the present research we found that it is more convenient to obtain VIIa (29% yield) by cyclization of 1-amino-2-methylaminobenzimidazole with formamide. Let us emphasize, however, that the indicated

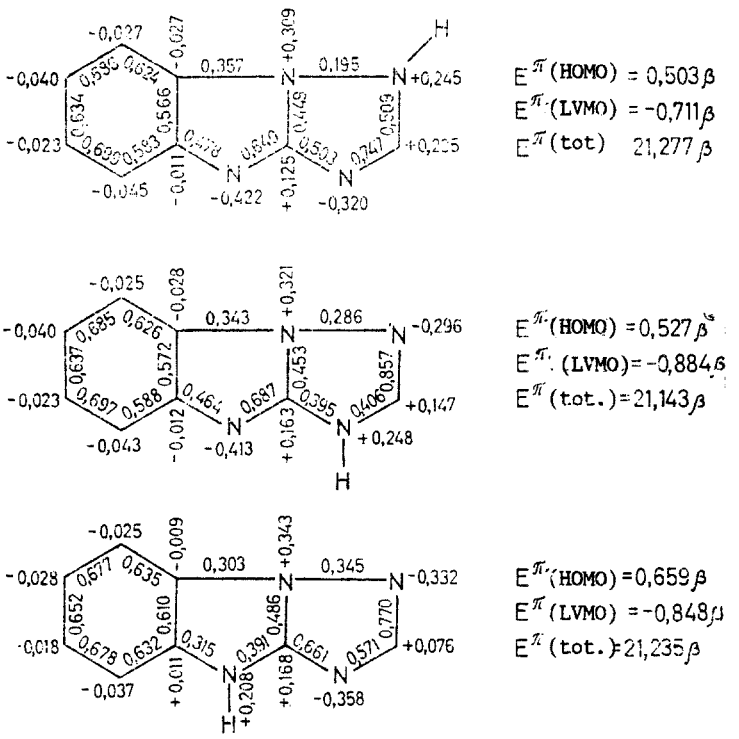
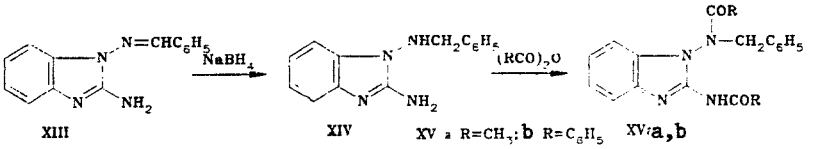


Fig. 1. Effective π charges and orders of the π bonds of the 1H, 3H, and 4H forms of triazolo[1,5-a]benzimidazole.

methods of synthesis of VIIa,d are of value only as a means of obtaining models of the tautomers with a precisely fixed position of the substituents. From a preparative point of view, VIIa,b,d,e, like VI, are obtained more simply by alkylation of the NH forms III-V in a neutral or alkaline medium (see the experimental section).

For the synthesis of 1H-triazolo[1,5-a]benzimidazole derivatives VIII we used, as the starting compound, 2-amino-1-benzylaminobenzimidazole (XIV), which was obtained by reduction of 2-amino-1-benzylideneaminobenzimidazole (XIII) with sodium borohydride. However, except for partial resinification, nothing happens when XIV is heated with formamide. When diamine XIV is heated with acetic or benzoic anhydride, the final product is the corresponding diacetyl derivative XVa,b. Complete resinification is observed when the cyclization of XV in polyphosphoric acid (PPA) is attempted.



Compound VIII also is not obtained in the alkylation of 1,2,4-triazolo[1,5-a]benzimidazoles (see below). All of this evidently constitutes evidence for their instability; the results of calculation by the Hückel MO method may serve as a confirmation of this (Fig. 1). These results show that the 1H form of triazolo[1,5-a]benzimidazole, in contrast to the 3H and 4H forms, has a low order of the $N_{(1)}$–$N_{(9)}$ π bond and a very high positive charge on the $C_{(2)}$ atom; this should lead to facile attack at this position even by weak nucleophiles.

Tautomerism

Although we had only two of the three fixed tautomeric forms of triazolo[1,5-benzimidazoles at our disposal, this proved to be sufficient to establish the position of the tautomeric equilibrium by means of a number of physicochemical methods in conjunction with quantum-mechanical calculations and alkylation data.

The only method that did not make it possible to draw even a qualitative conclusion regarding the preponderance in solution of one or another tautomeric form was electronic

TABLE 1. Physicochemical Characteristics of 1,2,4-Triazolo-[1,5-a]benzimidazoles III-VII

Compound	mp, °C	R_f	UV spectrum, λ_{max}, nm (log ε)	IR spectrum, cm^{-1}
III	228...229	0,10	282 (3,42), 289 (3,46)	1496 (m) 1594 (vs), 1625* (m)
IV	258...259	0,20	282 (3,40), 288 (3,43)	1496 (s) 1595 (s) 1628* (m)
V	309...310	0,15	239 (3,99), 271 (3,92)	1605* (s)
VIa	103...105	0,60	284 (3,42), 291 (3,48)	1508 (s) 1608 (vs) 1648 (m)
VIb	64...66	0,85	†	1496 (s) 1580 (vs) 1626 (m)
VId	100...101	0,80	283 (3,34), 290 (3,39)	1512 (m) 1597 (s) 1622 (s)
VIe	138...140	0,70	246 (4,03), 273 sh (3,77)	1495 (s) 1518 (m) 1610 (vs) 1622 (vs)
VIIa	149...150	0,35	285 (3,22), 293 (3,24)	1535 (s) 1576 (s) 1605 (s) 1658 (vs)
VIIb	128...130	0,80	†	1520 (s) 1558 (s) 1590 (s) 1630 (vs)
VIId	201...202	0,50	282 (3,29), 291 (3,32)	1575 (s) 1580 (s) 1611 (s) 1665 (s)
VIIe	178...179	0,55	246 (4,03), 273 sh (3,77)	1510 (s) 1594 (s) 1621 (s)

*There is also a broad ν_{NH} band at 2500-3200 cm^{-1}.
†The UV spectra were not measured.

spectroscopy. The UV spectra of III-V and fixed forms VI and VII virtually did not differ from one another with respect to the number of absorption maxima and their positions and intensities (Table 1). However, the other characteristics of VI and VII are extremely different. The quantum-mechanical calculations (Fig. 1) showed that the 1H, 3H, and 4H forms have substantially different distributions of the π-electron density. The 4H form is the least polar form. For it the middle ring is characterized by the greatest π-surplus character (in it there are seven π electrons for five atoms), from which carrying away of part of the π-electron density, chiefly to the triazole ring, occurs. This leads to equalization of the π-electron density in the two rings and, in particular, to a decrease in the positive charge on the $C_{(2)}$ atom. In the 1H and 3H forms the most π-surplus ring is formally the triazole ring, and this results in the principal shift of the π-electron density to the imidazole ring. This shift, in conjunction with the electron-acceptor character of the three nitrogen atoms, leads to the development on the $C_{(2)}$ atom of a high positive charge and to an increase in the polarity of the molecule. This fact is manifested distinctly in the physical properties of VI and VII (Table 1). Thus, as compared with their 4H isomers VI, 3H-triazolo[1,5-a benzimidazoles VII have lower chromatographic mobilities and higher melting points and they are much less soluble in nonpolar organic solvents.

A consequence of the high polarities of the aromatic C=C and C=N aromatic bonds is the presence in the IR spectra of 3H-triazolo[1,5-a]benzimidazoles VII of a series (usually four) of very strong absorption bands at 1500-1700 cm^{-1}. At the same time, there are three such bands in the spectra of 4H isomers VI; the higher-frequency band at 1630 cm^{-1} has moderate intensity. The IR spectra of compounds with a free NH group are very similar to the spectra of 4H forms VI. On the basis of this it might be concluded that III–V exist in the 4H form (IIIc-Vc) in the crystalline state.

The PMR spectra showed that this conclusion is also qualitatively valid for solutions. A common multiplet of $H_{(6)}$ and $H_{(7)}$ protons is found in the spectra of triazolo[1,5-a]benzimidazoles (Table 2) at strongest field at 7.1-7.3 ppm. Next, at 7.5-7.7 ppm, one observes signals of $H_{(5)}$ and $H_{(8)}$ protons, which are sometimes separated and sometimes merge to form one multiplet – probably as a function of the anisotropic effect of the $N_{(1)}$ and $N_{(4)}$ atoms. The assignment of the signals of the $H_{(5)}$ and $H_{(8)}$ protons was made in analogy with the PMR spectra of benzimidazoles [10]. The indicator signal, from the position of which one can form a judgment regarding the tautomerism, is the singlet of the $H_{(2)}$ proton at weakest field. The position of this signal (∿8.1 ppm) is almost independent of the solvent in the case of unsubstituted III and the fixed 4H form (VIa,b), while for the 3H form (VIIa,b) on passing from the nonpolar deuterochloroform to polar d_6-DMSO the signal of the $H_{(2)}$ proton is shifted to weak field by almost 1 ppm and goes up to 8.6-8.7 ppm. This is undoubtedly due to complexing of the 3H-triazolo[1,5-a]benzimidazoles and DMSO in which the negative end of the dipole of the molecule of the latter is situated above the electron-deficient $C_{(2)}$ atom; this leads to deshielding of the $H_{(2)}$ proton. Unfortunately, this method cannot be used for 2-substituted triazolo[1,5-a]-benzimidazoles IV and V, regarding the existence of which in the 4H form one can form a judgment only by analogy.

TABLE 2. PMR Spectra of 1,2,4-Triazolo[1,5-a]benzimidazoles, δ, ppm

Compound	Solvent	$H_{(2)}$ (s)	$H_{(5)}$ (m)	$H_{(6,7)}$ (m)	$H_{(8)}$ (m)	N—CH_3
III	$CDCl_3$	8,14	7,56*1	7,41	7,90*1	12,47*2 s
III	d_6-DMSO	8,15	7,55*1	7,30	7,83*1	12,43*2 s
VIa	$CDCl_3$	7,95	7,25	7,25	7,70	3,73 s
VIa	d_6-DMSO	8,15	7,72	7,35	7,72	3,80 s
VIa	CF_3COOH	8,23	7,35	7,35	7,65	3,73 s
VIb	d_6-DMSO	8,13	7,73	7,33	7,73	1,43*3 t 4,30 q
VId	$CDCl_3$	2,45*4	7,20	7,20	7,60	3,65 s
VIe	$CDCl_3$	— *5	7,15	7,15	7,68	3,60 s
VIIa	$CDCl_3$	7,70	7,69	7,23	7,69	3,65 s
VIIa	d_6-DMSO	8,63	7,72	7,25	7,72	3,75 s
VIIa	CF_3COOH	8,13	7,33	7,33	7,63	3,73 s
VIIb	d_6-DMSO	8,73	7,75	7,25	7,75	1,55*3 t 4,20 q
VIId	$CDCl_3$	2,33*4	7,65	7,18	7,65	3,53 s
VIIe	$CDCl_3$	7,45...7,85		7,25	7,45...7,85	3,75 s

*Tentative assignment.
**The NH proton.
***The N—C_2H_5 group, J = 8 Hz.
****The CH_3 group.
*****The C_6H_5 group: 7.40 (3H, m, m-H and p-H); 8.18 ppm (2H, m, o-H).

TABLE 3. Basicity Constants (pK_a, Acetonitrile, 20°C) and Tautomeric Equilibrium Constants (K_T) of III—V and the Corresponding Fixed Forms VI and VII (the nos. of the compounds are given in parentheses)

R	R'			K_T
	H	3-CH_3	4-CH_3	
	pK_a values			
H	9,90 (III)	12,40 (VIIa)	9,37 (VIa)	$1,07 \cdot 10^3$
CH_3	10,85 (IV)	12,85 (VIId)	10,23 (VId)	$4,18 \cdot 10^2$
C_6H_5	8,20 (V)	11,87 (VIIe)	8,38 (VIe)	$2,09 \cdot 10^3$

For an approximate quantitative evaluation of the position of the tautomeric equilibrium in III—V we measured their basicity constants in acetonitrile, as well as the basicity constants of fixed forms VI and VII. It is apparent from Table 3 that the basicities of 3H-triazolo[1,5-a]benzimidazoles VII are 2.5-3.5 orders of magnitude greater than the basicity of the corresponding 4H form VI. This is completely understandable if one takes into account the above-noted tendencies for a shift of the π-electron density in the 3H and 4H forms, as well as the known considerably lower basicity of the triazole ring as compared with the imidazole ring. It is also evident that protonation of the 3H form proceeds at the $N_{(4)}$ atom where the 4H form proceeds at the 3H atom (for example, see the electron densitities on these atoms presented in Fig. 1).

The pK_a values of unsubstituted III—V are close to the pK_a values of the 4H forms. This indicates substantial preponderance of the IIIc—Vc 4H tautomers over the IIIb—Vb 3H forms. In addition, an evaluation of the tautomeric equilibrium constant K_T carried out by means of the formula $K_T = K_a(4\text{-}CH_3)/K_a(3\text{-}CH_3)$ [11] (Table 3) showed that the concentration of the 3H form for 2-methyltriazolo[1,5]benzimidazole (IV) exceeds its amount in III and V. This fact may be due to the positive inductive effect of the 2-CH_3 group, which, naturally, increases the electron density on the $N_{(3)}$ atom to a greater degree than on the $N_{(4)}$ atom. For a similar reason (the —I effect of the phenyl group) in V the concentration of the 4H form is higher by a factor of two than in III.

Alkylation

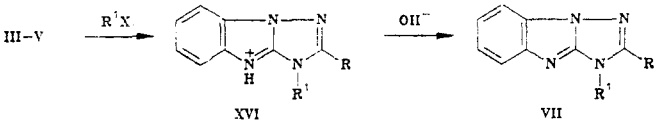
On the basis of the general principles of the alkylation of heteroaromatic tautomeric systems [11, 12] one may predict that the alkylation of the anions of III—V will lead to the

TABLE 4. Results of Alkylation of 1,2,4-Triazolo[1,5-a]-benzimidazoles in Acetone

Expt. no.	Substrate	Type of particle being alkylated	Reagent	Yield,* %	VI/VII isomer ratio †
1	III	Anion	CH_3I	99	96 : 4
2	III	Anion	$(C_2H_5)_2SO_4$	86	75 : 25
3	III	Neutral molecule	$(CH_3)_2SO_4$	78	Only VIIa
4	III	Neutral molecule	$(C_2H_5)_2SO_4$ ‡	85	Only VIIb
5	IV	Anion	CH_3I	70	93 : 7
6	IV	Neutral molecule	$(CH_3)_2SO_4$	71	1 : 99
7	V	Anion	CH_3I	84	Only VIe
8	V	Anion	$C_6H_5CH_2Cl$**	98	Only VIf
9	V	Neutral molecule	$(CH_3)_2SO_4$	40	Only VIIe
10	V	Neutral molecule	$C_6H_5CH_2Cl$**	50	80 : 20

*Overall yield of the N-alkylation products.
†In experiments 1, 3, 5, and 6 the isomer ratios were determined by GLC, while in experiments 2 and 10 they were determined by PMR spectroscopy. In the remaining experiments only one isomer was obtained according to TLC.
‡Without a solvent.
**In DMF.

formation of primarily 4-substituted azoles VI, while the alkylation of the neutral molecule will give almost exclusively 3-substituted VII through the intermediately formed salt XVI:



This prognosis was confirmed satisfactorily (Table 4). The alkylation was carried out with alkyl halides or dialkyl sulfates in dipolar aprotic solvents (acetone, DMF) and in one case without a solvent. A mixture of 4- and 3-methyl-substituted VIa and VIIa is formed in the alkylation of the potassium salt of III with methyl iodide in an overall yield of 99%, but the percentage of VIIa in it is only 4%. The percentage of 3-substituted VIId (7%) is somewhat higher in the methylation, under the same conditions, of 2-methyltriazolobenzimidazole IV; this is in agreement with the tendency for an increased percentage of the 3H form in it. In the ethylation of the anion of III with diethyl sulfate the ratio of the 4- and 3-ethyl-substituted compounds is 3:1. One may attempt to explain the increase in the yield of the latter by steric hindrance, which the condensed benzene ring exerts with respect to the incorporation of the more bulky ethyl radical in the 4 position. In the alkylation of the anion of 2-phenyltriazolo[1,5-a]benzimidazole V the only reaction products are the corresponding 4-subtituted azoles. It is evident that this result is facilitated not only by the increased electron density on the $N(_4)$ atom as compared with the $N(_3)$ atom but also by the pronounced steric shielding of the latter by the phenyl group.

Only 3-substituted azoles VII are always formed in the alkylation of the neutral molecules of III–V. An exception is the benzylation of V with benzyl chloride in DMF, for which the ratio of the 4- and 3-substituted compounds is 4:1. The reaction in this case evidently proceeds in part through the anion (the proton-acceptor ability of dimethylformamide is well known); in addition, the steric effect of the phenyl group also plays a role. It should be noted that the preparation of 3-substituted triazolo[1,5-a]benzimidazoles VII by alkylation of III–V under neutral conditions is simpler than the cyclization of 2-alkyl-amino-1-amino-benzimidazoles [9], which is accompanied by pronounced resinification. The synthesis of 4-substituted VI by alkylation of the corresponding anions of III–V also has preparative value.

An investigation of the reaction mixtures obtained in the alkylation of III–V by GLC, TLC, and PMR showed that the formation of 1-alkyltriazolo[1,5-a]benzimidazoles VIII is not observed in a single case, whereas Ho and Day [6] assigned the 1-benzyl-2-phenyl-1H-1,2,4-triazolo[1,5-a]benzimidazole structure to the product of benzylation of V in an alkaline medium. According to our data, the substance that they obtained is identical to the product of cyclization of salt Xc by benzoic anhydride, i.e., it is 4-benzyl-substituted VIf. Just as erroneously, Ho and Day [6] assigned the 1-acyl-substituted structure XVIII to the products

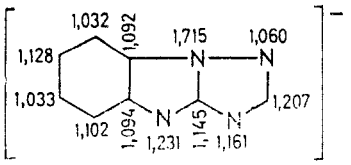
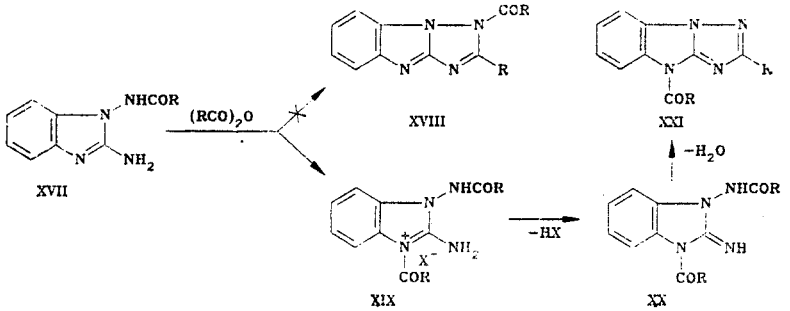
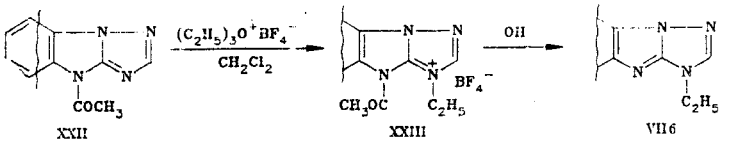


Fig. 2. π-Electron densities in the 1,2,4-triazolo[1,5-a]benzimidazole anion.

of cyclization of 2-amino-1-acylaminobenzimidazoles XVII under the influence of acid anhydrides (identical products were also obtained in the acylation of IV and V with acetic anhydride). The basis for this assignment was provided by uncoupling of one of the signals of the protons of the benzene ring to weak field (δ 8.5 ppm), which supposedly could occur only for the $H(_8)$ proton under the influence of the anisotropic effect of the 1-acyl group. However, it is known [13] that the same shift to weak field under the influence of an N-acetyl group is characteristic for the $H(_7)$ proton in 1-acetylbenzimidazole, which corresponds to the $H(_5)$ proton in 4-acetyltriazolo[1,5-a]-benzimidazoles XXI. Another argument in favor of structure XVIII in [6] consisted in the fact that the position of the N-acetyl group in starting compounds XVII should also be retained in the cyclization products. However, cyclization most likely proceeds through salt XIX and then through imine XX, in which ring closure can be realized through the acyl group bonded to the exocyclic nitrogen atom.



In fact, the substances obtained in [6] are 4-acyl-4H-1,2,4-triazolo[1,5-a]benzimidazoles, which we demonstrated in the case of 4-acetyl-4H-1,2,4-triazolo[1,5-a]benzimidazole (XXII). 3-Ethyl-3H-1,2,4-triazolo[1,5-a]benzimidazole (VIIb) was obtained in 85% yield by the action on it of triethyloxonium tetrafluoroborate with subsequent treatment of quaternary salt XXIII with ammonia. It is evident that if the acetyl group in the starting compound were attached to the $N(_1)$ atom, the principal product of this reaction would be 4-ethyl-substituted VIb.



Thus our investigation has shown that the stabilities of the tautomeric forms of triazolo[1,5-a]benzimidazoles III—V change in the following order: 4H > 3H >> 1H. It is known that prototropy can be regarded as an acid-base process, in the course of which the tautomers are converted into one another through the intermediately formed ambident anion; the concentrations of the tautomeric forms (disregarding solvation factors) are directly proportional to the magnitudes of the electron densities on those centers at which the addition of a proton may occur [11]. In our case calculation of the anion of triazolo[1,5-a]benzimidazole (Fig. 2) by the Hückel MO method showed that the π-electron densities on the $N(_1)$, $N(_3)$, and $N(_4)$ atoms are 1.060, 1.161, and 1.231, respectively. This is in good agreement with both the position of the tautomeric equilibrium and with the specificity of alkylation of the anion. And although in the general case one must also take into account the σ-electron charges, such good agreement between the calculated values and the experimental data can be regarded as an indication that the distribution of the charges in the triazolo[1,5-a]benzimidazole anion is determined primarily by π-electron factors.

EXPERIMENTAL

The IR spectra of suspensions of the compounds in mineral oil were recorded with a UR-20 spectrometer. The UV spectra of solutions in methanol were recorded with a Specord M-40 spectrophotometer. The PMR spectra were obtained with a Tesla BS-487 spectrometer (80 MHz) with hexamethyldisiloxane as the external standard; the chemical shifts were reckoned with respect to the signal of tetramethylsilane (TMS). The ionization constants were measured by potentiometric titration in acetonitrile at 20°C by the method in [14]. The analysis of the mixture of products of alkylation of III–V by GLC was carried out with a Tsvet-101 chromatograph with a flame-ionization detector; the column dimensions were 1 m by 3 mm, the packing was 5% OV-17 on Chromaton N-Super (0.16-0.20 mm), and the column temperature was 250°C, the vaporizer temperature was 300°C, and the carrier-gas (helium) flow rate was 30 ml/min. The ratios of the isomers were calculated by the method of internal normalization with respect to the areas of the peaks. The emergence times were as follows: 4 min and 4 sec for VIa, 9 min and 15 sec for VIIa, 2 min and 15 sec for VId, and 5 min and 15 sec for VIId. The results of elementary analysis for C, H, and N were in agreement with the calculated values.

The quantum-chemical calculations were carried out by the Hückel MO method with the Streitwieser parameters [15]; $k_{N-N} = 0.8$ in all cases. In the calculation of the 1,2,4-triazolo[1,5-a]-benzimidazole anion the parameters for the $N_{(1)}$, $N_{(3)}$, and $N_{(4)}$ atoms, between which the negative charge is delocalized, were assumed to be $h = -0.33$ and $k_{C-N} = 1.0$. The course of the reaction and the purity of the compounds were monitored by TLC on plates with activity II Al_2O_3; the eluent was chloroform, and development was realized by means of iodine vapors. The melting points were determined in sealed capillaries with a PTP apparatus and were uncorrected.

1,2,4-Triazolo[1,5-a]benzimidazole (III, $C_8H_6N_4$). A solution of 3.0 g (20 mmole) of amine IX in 30 ml of formamide was refluxed for 30 min, after which it was cooled, and the precipitate was removed by filtration and washed with water to give 2.1 g (66%) of colorless prisms with mp 228-229°C (from water).

2-Methyl-1,2,4-triazolo[1,5-a]benzimidazole (IV). A solution of 5 g (34 mmole) of amine IX in 50 ml of acetic anhydride was refluxed for 4 h, after which the acetic anhydride was removed by evaporation under reduced pressure, and the residue was treated with 50 ml of water. The precipitated acetyl derivative (7 g) was removed by filtration and suspended in 40 ml of concentrated HCl, and the suspension was refluxed for 3 h. It was then cooled and neutralized with 22% NH_4OH, and the precipitate was removed by filtration and washed with water to give 5.4 g (85%) of colorless crystals with mp 258-259°C (dec., from alcohol), in agreement with the data in [6].

2-Phenyl-1,2,4-triazolo[1,5-a]benzimidazole (V). A mixture of 3.0 g (20 mmole) of amine IX and 15 g (66 mmole) of benzoic anhydride was heated at 185-190°C with stirring for 3 h. The cooled melt was heated in 50 ml of 10% NaOH to decompose the excess benzoic anhydride and the N-benzoyl derivative, after which the mixture was cooled and acidified to pH 3-4 with concentrated HCl. The precipitate, which was a mixture of benzoic acid and V, was removed by filtration and washed with water, and the dried precipitate was suspended in 100 ml of ether (to separate the benzoic acid). The product was removed by filtration to give 4.2 g (90%) of colorless prisms with mp 309-310°C (from aqueous DMF), in agreement with the data in [6].

4-Methyl-4H-1,2,4-triazolo[1,5-a]benzimidazole (VIa, $C_9H_8N_4$). A solution of 2.1 g (7.2 mmole) of iodide Xa in 15 ml of formamide was refluxed for 2 h, after which it was cooled and treated with 20 ml of water and (in portions) with 15 g (0.27 mmole) of KOH (to decompose the formamide). The mixture was extracted with chloroform (two 25-ml portions), and the solution was passed through a column packed with Al_2O_3 (chloroform) with collection of the first fraction to give 0.9 g (72%) of colorless needles with mp 103-105°C (from heptane with benzene).

4-Ethyl-4H-1,2,4-triazolo[1,5-a]benzimidazole (VIb, $C_{10}H_{10}N_4$). This compound was obtained in 65% yield by a procedure similar to that in the preceding experiment. The colorless prisms had mp 64-66°C (from hexane).

4-Benzyl-4H-1,2,4-triazolo[1,5-a]benzimidazole (VIc, $C_{15}H_{12}N_4$). A solution if 1.7 g (6 mmole) of chloride Xc in 10 ml of formamide was refluxed for 2 h. The isolation and purification were similar to the procedures used in the case of VIa. Workup gave 0.9 g (61%) of colorless crystals with mp 64-65°C (from isooctane). PMR spectrum ($CDCl_3$): 5.30 (2H, s, CH_2), 7.25 (8H, m, aromatic), 7.70 (1H, m, $H_{(8)}$), and 8.25 ppm (1H, s, $H_{(2)}$).

2,4-Dimethyl-4H-1,2,4-triazolo[1,5-a]benzimidazole (VId, $C_{10}H_{10}N_4$). A mixture of 0.8 g (2.8 mmole) of iodide Xa and 0.4 g (2.9 mmole) of potassium carbonate in 10 ml of acetic anhydride was refluxed for 7 h, after which it was cooled and treated with 50 ml of water, and the aqueous mixture was neutralized with dry $NaHCO_3$. The resulting precipitate was extracted with chloroform (two 20-ml portions) and purified by chromatography with a column packed with Al_2O_3 (chloroform) to give 0.46 g (90%) of colorless needles with mp 100-101°C (from heptane), in agreement with the data in [7].

4-Methyl-2-phenyl-4H-1,2,4-triazolo[1,5-a]benzimidazole (VIe, $C_{15}H_{12}N_4$). A) A mixture of 1.45 g (5 mmole) of iodide Xa and 0.7 g (5.1 mmole) of potassium carbonate was refluxed for 3 h in 10 ml of benzoyl chloride (the solution became markedly dark), after which the benzoyl chloride was removed by distillation in the vacuum created by a water aspirator (20 mm Hg), and the black residue was treated with 15 ml of 22% NH_4OH and extracted with chloroform (two 25-ml portions). It was then purified with a column packed with Al_2O_3 (chloroform). The dark-brown oil was dissolved in 20 ml of acetone, concentrated HCl was added dropwise to pH 1, and the colorless precipitate was removed by filtration. The precipitate was treated with aqueous ammonia (~4 ml) and washed with water to give 0.5 g (40%) of colorless prisms with mp 138-140°C (from isooctane), in agreement with the data in [7].

B) A mixture of 1.45 g (5 mmole) of iodide Xa, 0.7 g (5.1 mmole) of potassium carbonate, and 10 g (44 mmole) of benzoic anhydride was heated for 3 h at 190-200°C, after which the excess anhydride was decomposed by heating with 30 ml of 10% KOH, and the resulting oil was extracted with chloroform and purified as in method A to give 1.1 g (88%) of colorless prisms with mp 138-140°C (from isooctane). No melting-point depression was observed for a mixture of this product with the sample from experiment A.

4-Benzyl-2-phenyl-4H-1,2,4-triazolo[1,5-a]benzimidazole (VIf, $C_{21}H_{16}N_4$). A mixture of 1.1 g (4 mmole) of chloride Xc, 0.56 g (4 mmole) of potassium carbonate, and 5 g (22 mmole) of benzoic anhydride was heated for 3 h at 180-190° with stirring, after which the excess anhydride was decomposed as in the preceding experiment, and the precipitate was removed by filtration and washed with water to give 1.0 g (77%) of colorless needles with mp 138-139°C (from ethyl acetate). IR spectrum: 1590, 1610, 1625 cm^{-1}. PMR spectrum ($CDCl_3$): 5.4 (2H, s, CH_2), 7.28 (11H, m, aromatic), 7.83 (1H, m, $H_{(8)}$), and 8.28 ppm (2H, m, o-H in C_6H_5).

3-Methyl-3H-1,2,4-triazolo[1,5-a]benzimidazole (VIIa, $C_9H_8N_4$). A solution of 0.8 g (5 mmole) of 1-amino-2-methylaminobenzimidazole [9] in 2 ml of formamide was heated for 10 h at 160°C, after which the formamide was decomposed, and the mixture was extracted with 30 ml of chloroform. The chloroform was evaporated, the residue was dissolved in 10 ml of acetone, and the solution was acidified to pH 1 with concentrated HCl. The resulting precipitate was separated and treated with 22% NH_4OH. The ammonia was evaporated, and the precipitate was removed by filtration to give 0.25 g (29%) of colorless crystals with mp 149-150°C (from heptane), in agreement with the data in [9].

3-Ethyl-3H-1,2,4-triazolo[1,5-a]benzimidazole (VIIb, $C_{10}H_{10}N_4$). A solution of 1.0 g (3.1 mmole) of unpurified tetrafluoroborate XXIII in 4 ml of 22% NH_4OH was evaporated at 20°C, after which the residue was dissolved in 20 ml of chloroform, and the solution was passed through a column packed with Al_2O_3 (chloroform) with collection of the fraction with R_f 0.80. The yield of VIIb was 0.5 g (85%). The colorless prisms had mp 128-130°C (from benzene).

The fraction with R_f 0.10 was eluted with ethyl acetate; after trituration with water it began to crystallize. The yield of III was 0.02 g (4%). The colorless crystals had mp 228-229°C (from water). No melting-point depression was observed for a mixture of this product with a genuine sample of III.

1,2-Diaminobenzimidazole (IX). A neutralized (with dry $NAHCO_3$) solution of 30 g (0.24 mole) of hydroxylamine-O-sulfonic acid in 50 ml of water was added in portions in the course of 5-7 min to a solution of 20 g (0.15 mole) of 2-aminobenzimidazole and 21 g (0.38 mole) of KOH in 200 ml of water at 40-45°C (the temperature of the reaction mixture), after which the mixture was stirred at this temperature for 30 min. It was then cooled, and the resulting precipitate was removed by filtration and washed with water to give 19 g (86%) of colorless prisms with mp 257-259°C (from water), in agreement with the data in [16]. IR spectrum: 1620, 1660, 3290, 3412 cm^{-1}.

1,2-Diamino-3-methylbenzimidazolium Iodide (Xa, $C_8H_{11}IN_4$). This compound was obtained by refluxing 0.5 g (3.4mmole) of amine IX and 0.5 ml (8 mmole) of methyl iodide in 10 ml of alcohol for 2 h. The yield was 0.85 g (86%). The colorless needles had mp 247-248°C (dec., from alcohol).

1,2 Diamino-3-ethylbenzimidazolium Iodide (Xb, $C_9H_{13}IN_4$). A solution of 1.5 g (10 mmole) of amine IX and 1 ml (12.3 mmole) of ethyl iodide in 10 ml of DMF was heated for 3 h on a water bath, after which it was cooled, and the precipitate was removed by filtration and washed with acetone to give 2.95 g (97%) of colorless prisms with mp 193-195°C (dec., from alcohol). IR spectrum: 1665, 3108, 3145, 3297 cm^{-1}.

1,2-Diamino-3-benzylbenzimidazolium Chloride (Xc, $C_{14}H_{14}ClN_4$). A mixture of 1.48 g (10 mmole) of amine IX and 1.24 ml (11 mmole) of benzyl chloride in 15 ml of alcohol was refluxed for 3 h, after which it was cooled, and the precipitate was removed by filtration and washed with alcohol. The mass of the precipitate was 1.5 g. Evaporation of the alcohol yielded another 1.1 g of chloride Xc. The yield was 2.6 g (95%). The colorless crystals had mp 237-238°C (dec., from alcohol).

2-Amino-1-benzylideneaminobenzimidazole (XIII, $C_{14}H_{12}N_4$). A solution of 1.48 g (10 mmole) of amine IX and 1.21 ml (12 mmole) of benzaldehyde containing three drops of perchloric acid in 20 ml of alcohol was refluxed for 2 h, after which it was cooled, and the resulting precipitate was removed by filtration and washed with alcohol and ether to give 2.2 g (93%) of colorless fibrous needles with mp 207-208°C (from alcohol).

2-Amino-1-benzylaminobenzimidazole Monohydrate (XIV, $C_{14}H_{14}N_4 \cdot H_2O$). A 1-g (26 mmole) sample of $NaBH_4$ was added in portions to a solution of 1.8 g (7.6 mmole) of amine XIII in 40 ml of methanol at such a rate that gentle refluxing of the solution was maintained. The mixture was then refluxed for another 15 min and poured into 100 ml of water, and the precipitate was separated. To remove the unchanged starting amine XIII the dried precipitate was refluxed for a few minutes in 50 ml of benzene, and the precipitated product was removed by filtration in the hot state. The yield was 1.55 g (86%). The colorless prisms had mp 178-179°C (from alcohol). IR spectrum: 1638, 2800-3200, 3265, 3412 cm^{-1}. PMR spectrum (d_6-DMSO): 4.2 (2H, d, J = 6 Hz, CH_2), 6.43 (2H, broad s, NH_2, vanished after deuteration), 6.73 (1H, t, NH, vanished after deuteration), 7.0 (2H, m, aromatic), 7.35 ppm (7H, m, aromatic).

2-Acetamido-1-(N-benzylacetamido)benzimidazole (XVa, $C_{18}H_{18}N_4O_2$). A solution of 0.24 g (1 mmole) of XIV in 10 ml (10.5 mmole) of acetic anhydride was refluxed for 5 h, after which the excess anhydride was removed by distillation in the vacuum created by a water aspirator, and the residue was crystallized from aqueous alcohol to give 0.3 g (94%) of slightly pink prisms with mp 177-179°C. IR spectrum: 1685, 1708 (C=O), 3240 cm^{-1} (NH). PMR spectrum ($CDCl_3$): 1.78 (3H, s, $COCH_3$), 2.18 (3H, s, $COCH_3$), 4.78 (1H, d, J = 14 Hz, CH_2), 5.1 (1H, d, J = 14 Hz, CH_2), 6.70 (1H, broad s, NH, vanished after deuteration), 7.15 ppm (9H, m, aromatic).

2-Benzamidol-1-(N-benzylbenzamido)benzimidazole (XVb, $C_{28}H_{22}N_4O_2 \cdot H_2O$). A mixture of 0.48 g (2 mmole) of amine XIV and 1.36 g (6 mmole) of benzoic anhydride was stirred for 3 h at 180-190°C, after which it was cooled, 10 ml of water and 1.5 g (2.7 mmole) of KOH were added, and the mixture was warmed slightly. The lilac-colored precipitate was removed by filtration and washed with water to give 0.65 g (71%) of prisms that melted over the range 100-135°C (from alcohol). IR spectrum: 1695 (C=O), 3150 (NH), 3450, 3550 cm^{-1} (H_2O). PMR spectrum ($CDCl_3$): 4.79 (1H, d, J = 14 Hz, CH_2), 5.58 (1H, d, J = 14 Hz, CH_2), 6.88-7.53 (18H, m, aromatic and NH), 8.35 ppm (2H, m, aromatic).

4-Acetyl-4H-1,2,4-triazolo[1,5-a]benzimidazole (XXII, $C_{10}H_8N_4O$). A solution of 2.1 g (13 mmole) of III in 20 ml of acetic anhydride was refluxed for 2 h, after which the excess anhydride was removed by distillation in the vacuum created by a water aspirator, and the residue was triturated with ether. The solid material was removed by filtration to give 2.5 g (94%) of a product, which was purified with a column packed with Al_2O_3 (chloroform) with collection of the fraction with R_f 0.80. The colorless needles had mp 149-151°C (from alcohol). IR spectrum: 1710 cm^{-1} (C=O). PMR spectrum (d_6-DMSO): 2.88 (3H, s, $COCH_3$), 7.53 (2H, m, $H_{(6)}$ and $H_{(7)}$), 7.85 (1H, m, $H_{(8)}$), 8.33 (1H, s, $H_{(2)}$), 8.38 ppm (1H, m, $H_{(5)}$).

4-Acetyl-3-ethyl-1,2,4-triazolo[1,5-a]benzimidazolium Tetrafluoroborate (XIII, $C_{12}H_{13}N_4O \cdot BF_4$). A solution of 1.0 g (5 mmole) of acetyl derivative XXII and 1.15 g (6 mmole) of triethyloxonium tetrafluoroborate in 10 ml of dry methylene chloride was stirred for 24 h at 20°C. After 1 h, we observed the beginning of the formation of a colorless precipitate, which was separated and washed with methylene chloride to give 1.3 g (82%) of colorless needles with mp 220-222°C (dec., from alcohol). IR spectrum: 1560, 1742 (C=O), 3112 cm^{-1}.

Alkylation of III (Table 4). A) Methylation of the anion. A solution of 0.8 g (5 mmole) of III and 0.35 g (6.2 mmole) of KOH in 2 ml of water was evaporated to dryness, after which the residue was suspended in 10 ml of acetone and treated with 0.4 ml (6.4 mmole) of methyl iodide. The mixture was stirred for 2 h at 20°C, the acetone was evaporated, and the residue was treated with 20 ml of chloroform and passed through a column packed with Al_2O_3 (chloroform). Evaporation of the solvent have 0.85 g (99%) of a mixture of methyltriazolo [1,5-a]benzimidazoles VIa and VIIa.

B) Ethylation of the anion. A 0.86-ml (6.4 mmole) sample of diethyl sulfate in 10 ml of acetone was added to a suspension of 5 mmole of the potassium salt of III, obtained as in the preceding experiment, and the mixture was stirred at 20°C for 3 h. The isolation and purification were carried out via the preceding method. The yield of the mixture of VIb and VIIb was 0.8 g (86%).

C) Methylation in a neutral medium. A mixture of 0.5 g (3.2 mmole) of III and 0.3 ml (3.2 mmole) of dimethyl sulfate was refluxed for 2 h in 10 ml of acetone. After 30 min, the starting substance dissolved completely. The mixture was cooled, and the resulting precipitate was separated, triturated with dilute ammonium hydroxide, dried, and purified by chromatography on Al_2O_3 (chloroform). The yield was 0.4 g (78%). According to TLC data, the product was 3-methyl-3H-1,2,4-triazolo[1,5-a]-benzimidazole (VIIa). The colorless prisms had mp 148-150°C (from heptane).

D) Ethylation in a neutral medium. A mixture of 0.5 g (3.2 mmole) of III and 0.43 ml (3.3 mmole) of diethyl sulfate was heated for 30 min at 140-150°C. At 130°C the mixture melted; after cooling, the melt was treated with 3 ml of 22% ammonium hydroxide and evaporated to dryness. The residue was dissolved in 20 ml of chloroform and purified with a column packed with Al_2O_3 (chloroform) to give 0.5 g (85%) of product. According to TLC data, the product was 3-ethyl-3H-1,2,4-triazolo[1,5-a]benzimidazole (VIIb). The colorless prisms had mp 128-130°C (from benzene).

Alkylation of IV (Table 4). A) Methylation of the anion. A solution of 0.56 g (3.3 mmole) of IV and 0.2 g (3.6 mmole) of KOH in 2 ml of water was evaporated to dryness, and 0.23 ml (3.6 mmole) of methyl iodide and 10 ml of acetone were added to the residue. The suspension was stirred for 2 h at 20°C, after which the product was isolated and purified in the usual way. The yield was 0.42 g (70%).

B) Methylation in a neutral medium. A mixture of 0.51 g (3 mmole) of IV and 0.3 ml (3.2 mmole) of dimethyl sulfate in 10 ml of acetone was refluxed for 3 h. Workup gave 0.4 g (71%) of the product.

Alkylation of V (Table 4). A) Methylation of the anion. A suspension of 0.8 g (2.9 mmole) of the potassium salt of V, obtained by evaporation of equimolar amounts of KOH and V in 2 ml of water, and 0.3 ml (4.5 mole) of methyl iodide in 10 ml of acetone was stirred for 2 h at 20°C. Workup gave 0.52 g (84%) of product. According to TLC data, the product was 4-methyl derivative VIe.

B) Benzylation of the anion. A suspension of 0.8 g (2.9 mmole) of the potassium salt of V and 0.38 ml (3.1 mmole) of benzyl chloride in 5 ml of absolute DMF was refluxed for 2 h. The yield of 4-benzyl-2-phenyl-4H-1,2,4-triazolo[1,5-a]benzimidazole (VIf) was 0.8 g (98%). The colorless prisms had mp 138-139°C (from ethyl acetate). No melting-point depression was observed for a mixture of this product with a genuine sample of VIf.

C) Methylation in a neutral medium. A mixture of 0.46 g (2 mmole) of V and 0.2 ml (2.1 mmole) of dimethyl sulfate in 5 ml of absolute DMF was heated with stirring for 2 h at 100°C. Workup gave 0.2 g (40%) of a substance that, according to TLC data, was 3-methyl-2-phenyl-3H-1,2,4-triazolo[1,5-a]benzimidazole (VIIe). The colorless needles had mp 178-179°C (from ethyl acetate). A 0.15-g (32%) sample of starting azole V was regenerated from the reaction mixture.

D) Benzylation in a neutral medium. A mixture of 0.25 g (1 mmole) of V and 0.5 ml (4 mmole) of benzyl chloride in 3 ml of DMF was refluxed for 1 h. Workup gave 0.16 g (50%) of product. According to the results of PMR spectroscopy of a solution in d_6-DMSO, the product was a mixture of 4-benzyl- (VIf) and 3-benzyl-2-phenyl-3H-1,2,4-triazolo[1,5-a]benzimidazole in a ratio of 4:1.

LITERATURE CITED

1. J. P. Paolini, Special Topics in Heterocyclic Chemistry, edited by A. Weissberger and E. C. Taylor, Interscience, New York–London– (1977), p. 1.
2. A. M. Simonov, A. A. Belous, V. A. Anisimova, and S. V. Ivanovskaya, Khim.-farm Zh., No. 1, 7 (1969).
3. H. Ogura, H. Takayanagi, Y. Yamazaki, S. Yonezawa, H. Tagaki, S. Kobayashi, T. Kamioka, and K. Kamoshita, J. Med. Chem., 15, 923 (1972).
4. J. Elguero, A. Fruchier, L. Knutsson, R. Lazaro, and J. Saudström, Can. J. Chem., 52, 2744 (1974).
5. J. P. Fayet, M. C. Vertut, P. Mauret, J. de Mendoza, and J. Elguero, J. Heterocycl. Chem., 12, 197 (1975).
6. R. I-fu Ho and R. Day, J. Org. Chem., 38, 3084 (1973).
7. Y. Tamura, H. Hayashi, J.-H. Kim, and M. Ikeda, Chem. Pharm. Bull., 27, 2521 (1979).
8. A. F. Pozharskii, I. S. Kashparov, Yu. P. Andreichikov, A. I. Buryak, A. A. Konstantinchenko, and A. M. Simonov, Khim. Geterotsikl. Soedin., No. 6, 807 (1971).
9. T. A. Kuz'menko, V. V. Kuz'menko, A. F. Pozharskii, and A. M. Simonov, Khim.Geterotsikl. Soedin., No. 8, 1070 (1988).
10. P. J. Black and M. L. Hefferman, Aust. J. Chem., 15, 862 (1962).
11. J. Elguero, C. Marzin, A. R. Katritzky, and P. Linda, The Tautomerism of Heterocycles, Academic Press, New York (1976), p. 20.
12. A. F. Pozharskii, The Theoretical Foundations of the Chemistry of Heterocycles [in Russian], Khimiya, Moscow (1985), p. 156.
13. J. L. Aubagnac, J. Elguero, and R. Robert, Bull. Soc. Chim. France, 2868 (1972).
14. V. I. Minkin and V. A. Bren', Reactivities of Organic Compounds [in Russian], Vol. 4, 112 (1967).
15. E. Streitwieser, Molecular Orbital Theory [Russian translation], Mir, Moscow (1965), p. 126.
16. A. V. Zeiger and M. M. Joullie, J. Org. Chem., 42, 542 (1977).