COVALENT HYDRATION IN THE TETRAZOLO[1,5-c]QUINAZOLINE SERIES (STRUCTURE OF THE PRODUCTS OF HYDRATION OF 5-METHYL(PHENYL)-9-BROMOTETRAZOLO[1,5-c]-QUINAZOLINES)

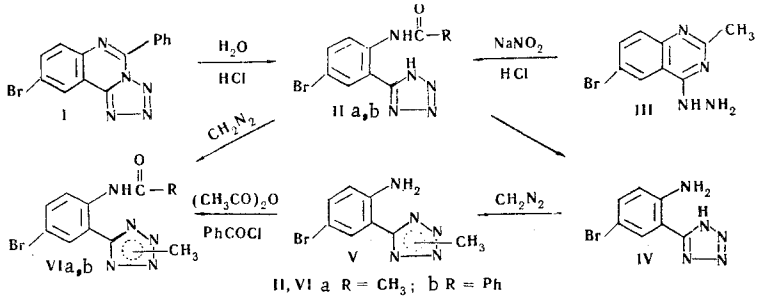
B. V. Golomolzin and I. Ya. Postovskii

UDC 547.856.1:541.623

1(2)-Methyl-5-(2-acylamino-5-bromophenyl)tetrazoles (VIa,b), the structures of which were proved by alternative synthesis, were obtained by the action of diazomethane on the products of covalent hydration of 5-methyl(phenyl)-9-bromotetrazolo[1,5-c]quinazolines. A comparison of the IR and UV spectra of the hydration products and VIa and VIb confirms that the former have the 5-(2-acylamino-5-bromophenyl)tetrazole structure (IIa,b) in the crystalline state and in solution.

In a previous paper [1] it was established that ring-chain tautomerism occurs in the hydration of tetrazolo[1,5-c]quinazoline and that a mixture of 5,6-dihydro-5-hydroxytetrazolo[1,5-c]quinazoline and 5-(2-formylaminophenyl)tetrazole is formed in acidic media. These results served as a basis for an examination of the problem of the structures of the products of hydration of 5-methyl(phenyl)-9-bromotetrazolo[1,5-c]-quinazolines.

We previously reported [2] that 5-phenyl-9-bromotetrazolo[1,5-c]quinazoline (I) in acidic media covalently adds a molecule of water at the $N_{(6)}=C_{(5)}$ bond. Continuing our investigation, we observed that 2-methyl-4-hydrazino-6-bromoquinazoline (III), just as the compound which does not contain a bromine substituent [3], reacts with HNO_2 in hydrochloric acid to form a product of covalent hydration of 5-methyl-9-bromotetrazolo[1,5-c]quinazoline, which turned out to be identical to the product of acetylation of 5-(2-amino-5-bromophenyl)tetrazole (IV) [2].



II, VI a R = CH_3; b R = Ph

The IR spectra of the hydration products (IIa,b) in the crystalline state make it possible to assume that these compounds have a structure with an open pyrimidine ring, viz., 5-(2-acylamino-5-bromophenyl)-tetrazoles. Also evidence in favor of this is the absence of absorption bands for the OH group (3600-3400 cm^{-1}) as well as the presence of bands at 1679 (IIa) and 1665 cm^{-1} (IIb) (amide C=O) and absorption at 3100-3050 cm^{-1} (amide N-H). To confirm this conclusion it was necessary to have model substances with the fixed structure of 5-(2-acylaminophenyl)tetrazoles. With this end in mind, the investigated hydration products were subjected to the action of diazomethane, and their methylated derivatives (VIa,b) were obtained; the structures of the latter were proved by alternative synthesis.

S. M. Kirov Ural Polytechnical Institute, Sverdlovsk. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 133-136, January, 1971. Original article submitted January 17, 1970.

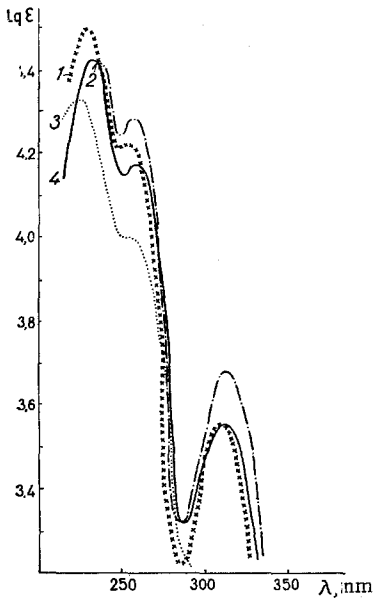


Fig. 1

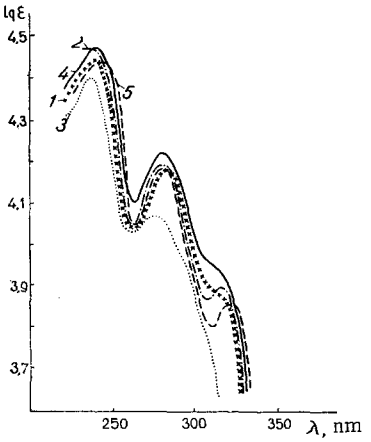


Fig. 2

Fig. 1. UV spectra: 1) VIa in acetic acid and in alcohol; 2) IIa in acetic acid; 3) IIa in 0.1 N aqueous NaOH; 4) IIa in alcohol.

Fig. 2. UV spectra: 1) VIb in acetic acid and in alcohol; 2) IIb in acetic acid; 3) IIb in 0.1 N aqueous NaOH; 4) IIb in alcohol; 5) IIb in dioxane.

5-(2-Amino-5-bromophenyl)tetrazole (IV)* reacts with diazomethane to give 1(2)-methyl-5-(2-amino-5-bromophenyl)tetrazole (V). The fact that methylation here proceeds at the tetrazole ring is confirmed by the IR spectra: on passing from IV to V a series of weak absorption bands at 3130-2640 cm^{-1} (acidic NH group of the tetrazole [4]) disappears, and the intense doublet from the primary amino group at 3471 and 3369 cm^{-1} is preserved.† Acylation of V gave its acetyl (VIa) and benzoyl (VIb) derivatives, which turned out to be identical to the corresponding products of the methylation of IIa and IIb. Thus the products of hydration of 5-methyl(phenyl)-9-bromotetrazolo[1,5-c]quinazolines are methylated by diazomethane toform 1(2)-methyl-5-(2-acylamino-5-bromophenyl)tetrazoles (VIa,b), which may serve as a confirmation of the open pyrimidine ring structure of IIa and IIb.

Intense absorption bands at 1688 cm^{-1} (VIa) and 1676 cm^{-1} (VIb) are observed for VIa and VIb, which contain an amide grouping. At the same time, IV and V, which do not contain an acyl residue, do not have similar bands. This undoubtedly attests to the fact that the indicated bands belong to the carbonyl group. Similar bands for IIa and b (1679 and 1665 cm^{-1}) can also apparently be unambiguously assigned to the carbonyl absorption. It should also be noted that the intensities of the carbonyl bands in the investigated and model compounds are approximately the same. Overall, it can be assumed to be proved that the products of the covalent hydration of 5-methyl(phenyl)-9-bromotetrazolo[1,5-c]quinazolines in the crystalline state have the 5-(2-acylamino-5-bromophenyl)tetrazole structures (IIa,b).

The UV spectra were used to study the structures of IIa and IIb in solution (the IR spectra could not be obtained because of the low solubility of these compounds in suitable solvents). As seen from the graphs (Fig. 1), the UV spectra of IIa in alcohol, dioxane, and acetic acid solutions are almost identical. The small difference in the intensities of the long-wave maxima are most likely associated with the different degree of solvation of molecules of the substance. The spectra of VIa in alcohol and glacial acetic acid are completely identical and almost coincide with the spectra of IIa. The pattern is completely analogous if one examines the curves of the spectra of IIb and VIb (Fig. 2). On the basis of these data it can be concluded with a high degree of probability that IIa and IIb also have an open structure in solution.

*See [1] for the preparation of this compound by alkaline cleavage of IIb.

†The problem of which position the methyl group enters in the tetrazole ring is not of substantial significance in this case and will be examined separately.

Attention is drawn to the fact that while the covalent hydrate of 5-methyltetrazolo[1,5-c]quinazoline exists in crystals as the cyclic tautomer – 5,6-dihydro-5-methyl-5-hydroxytetrazolo[1,5-c]quinazoline [3] – IIa, which contains a bromine atom in the benzene ring, has an open ring structure. Thus the mutual transition of the cyclic and open tautomers, which is accompanied by proton migration from the oxygen atom to the tetrazole ring (electrophilic ring-chain tautomerism), is determined by the effect of the substituent on the benzene ring. The introduction of a bromine decreases the basicity of the oxygen atom, thereby hindering proton transfer to it and stabilizing the open tautomeric form.

EXPERIMENTAL

Preparation of 5-(2-Benzoylamino-5-bromophenyl)tetrazole (IIb). IIb was obtained by hydration of 5-phenyl-9-bromotetrazolo[1,5-c]quinazoline by the method described in [2]. IR spectrum (cm^{-1}): 3082 medium, 3043 strong, 3013 strong (amide N-H), 1665 strong (amide C= O), 1078 medium, 1061 strong, and 1006 (tetrazole).

5-(2-Acetamido-5-bromophenyl)tetrazole (IIa). This was obtained from 2-methyl-4-hydrazino-6-bromoquinazoline (III) via the method described in [3]. IIa was identical to the product formed by the acetylation of 5-(2-amino-5-bromophenyl)tetrazole (IV) [2]. IR spectrum (cm^{-1}): 3146 strong (amide N-H), 1679 strong (amide C = O), 1075 medium, 1059 strong, and 1006 strong (tetrazole).

Methylation of IIa,b and IV. A solution of 0.04-0.05 mole of CH_2N_2 in ether was added in the course of 15 min to a suspension (or solution) of 0.01 mole of IIa,b or IV in 50 ml of ether at 0°. The mixture was held at 0° for 1 h, the ether was removed by distillation, and the products were crystallized from alcohol. VIa: mp 171-173°. Found %: C 40.4; H 3.2. $C_{10}H_{10}N_5OBr$. Calc. %: C 40.6; H 3.4. IR spectrum (cm^{-1}): 1688 strong (amide C=O), 1060 medium, 1052 weak, 1018 weak (tetrazole). VIb: mp 179-180°. Found %: C 50.2; H 3.4. $C_{15}H_{12}N_5OBr$. Calc. %: C 50.3; H 3.4. IR spectrum (cm^{-1}): 1676 strong (amide C=O), 1078 medium, 1052 strong, 1011 medium (tetrazole). V: mp 108-110°. Found %: C 38.0; H 3.2; N 27.6. $C_8H_8N_5Br$. Calc. %: C 37.8; H 3.2; N 27.6. IR spectrum (cm^{-1}): 3369 strong, 3471 strong (NH_2), 1078 weak, 1054 medium, 1011 weak (tetrazole).

Preparation of 5-(2-Amino-5-bromophenyl)tetrazole (IV). This compound was prepared by alkaline cleavage of IIb as described in [2]. IR spectrum (cm^{-1}): 3469 strong, 3357 strong (NH_2), 1075 medium, 1063 medium, 1006 medium (tetrazole).

Acetylation of V. V (0.008 mole) was refluxed in 10 ml of acetic anhydride for 15 min, 10 ml of water was added, and the mixture was refluxed for another 15 min. The reaction mass was cooled, and the precipitate was filtered. The product was identical to VIa formed by methylation of IIa.

Benzoylation of V. V (0.008 mole) was dissolved in 10 ml of pyridine and 0.008 mole of benzoyl chloride was added. The mixture was held at 20° for 30 min. The reaction mass was then poured into water, and the resulting precipitate was filtered and crystallized from alcohol. The sample was identical to VIb obtained by methylation of IIb.

The IR spectra of the compounds in mineral oil pastes (NaCl prism) and perfluorohydrocarbon pastes (LiF prism) were obtained with IKS-14 and UR-20 spectrometers. The UV spectra were obtained with an SF-4 spectrometer.*

LITERATURE CITED

1. N. N. Vereshchagina, I. Ya. Postovskii, and S. L. Mertsalov, Khim. Geterotsikl. Soedin., 1096 (1967).
2. I. Ya. Postovskii and B. V. Golomolzin, Khim. Geterotsikl. Soedin., 100 (1970).
3. I. Ya. Postovskii and N. N. Vereshchagina, Khim. Geterotsikl. Soedin., 944 (1967).
4. I. Ya. Postovskii and V. L. Nirenburg, Zh. Obshch. Khim., 34, 2517 (1964).

*The IR spectra were obtained by I. I. Mudretsova and the UV spectra were obtained by É. A. Maslova.