BRIEF COMMUNICATIONS

NEW CASES OF TETRAZOLE—AZIDE TAUTOMERIC TRANSFORMATIONS

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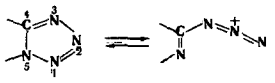
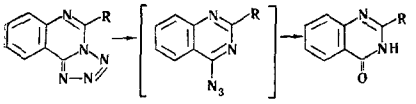
It has been shown that when 5-phenyl- and 5-methyltetrazolo[c]-quinazolines and 6-pyrrolidinotetrazolo[b]pyridazine are dissolved in trifluoroacetic acid, they are converted into the corresponding azides, in the last case with measurable velocity. In the form of the picrate and hydrochloride, 7-piperidinotetrazolo[c]pyrimidine exists as the axide in the crystalline state. These cases of tetrazole-azide transformations evidently take place through the protonation of the initial compounds.

In a study of the properties of N-heterocyclic compounds containing fused tetrazole rings, it was noted that some of these compounds are capable of tautomeric transformations of the tetrazole-azidoazomethine type [1].



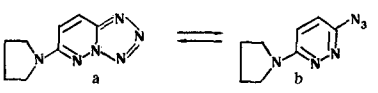
The tendency to this type of transformation depends on the electron-donating capacity of the hetero ring. The lower the electron-donating capacity of the hetero ring to which the tetrazole ring is fused, the weaker is the N_5—N_1 bond and the less stable is the ring-closed tetrazole form. If the energy of the N_5—N_1 bond is low and is close to the energy of solvation, when such a compound is dissolved the fused tetrazole ring opens forming the linear azide group (the product of ring-opening, containing the polar and readily polarized azide group is solvated more strongly than the initial compound containing the fused tetrazole ring). A shift in the tetrazole-azidoazomethine equilibrium in the azide direction can take place not only through dissolution but also through a decrease in the electron-donating nature of the hetero ring to which the tetrazole ring is fused. The electron-donating capacity of the hetero ring can be decreased: 1) by the introduction of electron-accepting substituents into the heterocyclic compound [2]; and 2) by the protonation of the heterocyclic base under the action of acids. Thus, we have observed that 5-substituted tetrazolo[c]quinazolines, which exist in the tetrazole form in the crystalline state and in solutions, give 2-substituted 4-quinazolones on being boiled in hydrochloric acid [3, 4]. Although the intermediate products were not isolated, the formation of 4-quinazolones cannot take place other than through the stage of the opening of the fused tetrazole ring with subsequent hydrolytic splitting off of the azide group by a nucleophilic mechanism.



R = Phenyl-, cycloalkylamino-.

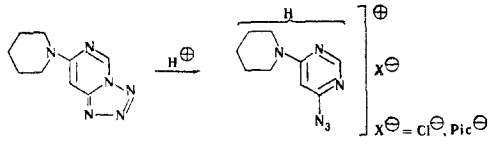
The protonation of a nitrogen atom in the ring of tetrazolo[c]quinazoline that takes place in an acid medium is accompanied by the delocalization of the positive charge over the whole quinazoline ring, in consequence of which the electron-donating capacity of the quinazoline ring falls, the strength of the N_5—N_1 bond decreases, and the transformation of the tetrazole into the azide becomes possible. Protonation takes place even when the substances are dissolved in trifluoroacetic acid in the cold (similar cases of the influence of trifluoroacetic acid on fused tetrazole rings have recently been reported [5]). Thus, we have found that 5-phenyl- and 5-methyltetrazolo[c]quinazolines which, according to the results of IR spectroscopy, exist only in the form of the tetrazolo isomers in the crystalline state and in solutions, exhibit strong azide bands in trifluoroacetic acid solutions at 2172 cm^{-1} for the phenyl derivative and 2147 cm^{-1} for the methyl derivative, with overtones at 2218 and 2210 cm^{-1}, respectively. Apparently, here as a result of protonation the opening of the tetrazole ring takes place even at room temperature.

Some compounds of the pyridazine series behave peculiarly. For example, 6-pyrrolidinotetrazolo[b]-pyridazine is the tetrazole (a) in the crystalline state and in solutions, according to the results of IR spectroscopy. In the IR spectrum of a freshly-prepared solution of this compound in trifluoroacetic acid there are barely detectable azide bands (2131 and 2154 cm^{-1}) the intensity of which increases after some time and becomes constant after 3 days. As far as we are aware, this is the first time that such a type of slow opening of the tetrazole ring to form the azide (b) has been observed.



We may mention that in all the cases referred to, after the evaporation and complete elimination of the trifluoroacetic acid the initial tetrazoles were recovered.

Since, in the cases mentioned, in addition to protonation a decisive role in the opening of the tetrazole rings was also played by solvation, it was impossible to exclude the role of the latter completely. In view of this, it appeared important to determine whether protonation (not in solution but in the solid phase) could lead to the opening of the tetrazole ring. To settle this question, 7-piperidinotetrazolo[c]pyrimidine, which exists in the crystalline state in the form of the tetrazole and in solutions in the form of the azide [6], was converted into the picrate. The IR spectrum of the crystalline picrate was found to have a strong azide band at 2135 cm^{-1}, which convincingly showed that the formation of the picrate is accompanied by the tetrazole—azide transformation. However, it is possible that in this case the reduction in the basicity of the heterocycle is due not only to protonation but also to the formation of a donor-acceptor complex between the 7-piperidinotetrazolo[c]pyrimidine and the picric acid. In view of this, we prepared the hydrochloride of this compound and studied the IR spectrum of its crystals. In complete agreement with this hypothesis, it was found that the hydrochloride, like the picrate, exhibited a strong azide band at 2145 cm^{-1}, and the intensity of the bands assigned to the absorption of the tetrazole ring had decreased considerably. It is characteristic that the absorption bands of 7-piperidinotetrazolo[c]pyrimidine picrate (in fact representing the 6-azido-4-piperidinopyrimidine picrate) and 6-chloro-4-piperidinopyrimidine picrate (a substance with a similar structure to the former, but containing a halogen instead of the pseudohalogen azide group) in the 1100–700 cm^{-1} region of the IR spectrum coincide almost completely, and this can serve as a convincing proof of the absence of the formation of the tetrazole ring in 6-azido-4-piperidinopyrimidine picrate. The hydrochloride of the latter does not exhibit the strong bands at 788 and 1069 cm^{-1} present in the initial tetrazole [6], either.



Thus, the opening of a fused tetrazole ring to form an azidoazomethine in the production of a crystalline salt (hydrochloride, picrate)has been observed for the first time. Subsequently an investigation must be made as to how far the tetrazole—azidoazomethine tautomeric equilibrium, as one of the cases of ring-chain tautomerism, can be regarded as a peculiar acid-base equilibrium [7]:

Lewis base—tetrazole ⇌ Lewis acid—azide.

EXPERIMENTAL

7-Piperidinotetrazolo[c]pyrimidine picrate. A solution of picric acid (0.25 g in 3 ml of methanol) was added to 0.2 g (~1 mM) of 7-piperidinotetrazolo[c]pyrimidine [6], mp 77°–78° C, in 3 ml of methanol. The mixture was boiled for 5 min and cooled. The precipitate was filtered off and crystallized from ethanol, to give yellow needles with mp 136° C (decomp.), weight 0.3 g (75%). Found, %: N 29.06. Calculated for $C_{15}H_{15}N_9O_7$, %: N 29.09.

6-Chloro-4-piperidinopyrimidine picrate. This was obtained by the method described above from 6-chloro-4-piperidinopyrimidine, mp 79° C. Yield 80%, mp 145° C. Found, %: N 19.36. Calculated for $C_9H_{11}N_3Cl \cdot C_6H_3(NO_2)_3OH$, %: N 19.69.

7-Piperidinotetrazolo[c]pyrimidine hydrochloride. A small amount of dry hydrogen chloride was carefully passed through an ice-cooled solution of 0.2 g (~1 mM) of 7-piperidinotetrazolo[c]pyrimidine in 100 ml of diethyl ether. The white crystalline precipitate (needles) that formed was filtered off and dried in the air. Weight 0.1 g (42%), mp 133°–134° C (decomp.). Found, %: Cl 14.98. Calculated for $C_9H_{12}N_6 \cdot HCl$, %: Cl 14.73.

6-Pyrrolidinotetrazolo[b]pyridazine. A solution of 6-chlorotetrazolo[b]pyridazine [9] (0.01 mole) and pyrrolidine (0.02 mole) in benzene was boiled for 1 hr. The precipitate was filtered off and crystallized from ethanol in the form of colorless prisms, mp 195°–196° C. Yield 83%. Found, %: N 44.31. $C_8H_{10}N_6$, %: N 44.21.

The IR spectra of the substances were recorded on a IKS-14 spectrometer.

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