THE AZIDO-TETRAZOLE EQUILIBRIUM IN THE THIAZOLO[2,3-e]TETRAZOLE SERIES

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Khimiya Geterotsiklicheskikh Soedinenii, Vol. 4, No. 3, pp. 423–427, 1968

UDC 547.796.1'789.1:543.422.4

Thiazolo[2,3-e]tetrazole and its derivatives with electropositive and electronegative substituents have been synthesized. The bromination, thiocyanation, and nitration reactions of some thiazolo[2,3-e]tetrazoles have been studied. By means of the IR spectra, the structure of the compounds synthesized in the crystalline state and in solutions has been determined. The influence of substituents and the polarity of solvents on the position of the azido-tetrazole equilibrium in the thiazolo[2,3-e]tetrazole series has been studied.

In a number of tetrazoles condensed with nitrogen-containing heterocycles the phenomenon of azido-tetrazole tautomerism is observed. The position of the azido-tetrazole equilibrium A $\rightleftarrows$ T depends on the nature of the nitrogen-containing heterocycles with which the tetrazole ring is condensed, on the electronic nature of the substituents in the ring, on the polarity of the solvents, and on the temperature [1–18].

In an extension of our study of the azido-tetrazole equilibrium in the tetrazolo[1,5-b]benzothiazole series we have synthesized thiazolo[2,3-e]tetrazole (I) and its derivatives (II-XIII) with various substituents in the thiazole ring (see Table 1). We studied the bromination, thiocyanation, and nitration of several thiazolo[2,3-e]tetrazoles. The reaction of 6-methyl- (II) and 6-phenyl-(VII)-thiazolo[2,3-e]tetrazoles with N-bromosuccinimide in chloroform leads to the bromination of the initial tetrazoles in position 5 of the thiazole ring. The bromine derivatives isolated were identical, respectively, with the 5-bromo-6-methylthiazolo[2,3-e]tetrazole (V) and the 2-azido-5-bromo-4-phenylthiazole (XI) obtained from diazonium salts and nitrous acid. This is confirmed by the results of analysis, IR spectra, and mixed melting points.

The reaction of the tetrazoles II and VII with ammonium thiocyanate in acetic acid in the presence of bromine led to the thiocyanation of the initial substances and the formation of, respectively, 6-methyl-5-thiocyanatothiazolo[2,3-e]tetrazole (VI) and 2-azido-4-phenyl-5-thiocyanatothiazole (XII).

The nitration of VII led to 2-azido-5-nitro-4-phenylthiazole (XIII). The structure of the compounds synthesized in the crystalline state and in solutions was established by means of IR spectra. The existence of a substance in the azide form was judged from the presence in its spectrum of a band in the 2100–2170 cm^{-1} region [9, 19, 20]. The bands relating to the vibrations of the tetrazole ring lie in the 720, 760, and 952–1250 cm^{-1} regions [21]. In the IR spectrum of tetrazolo [1,5-b] benzothiazole, bands at 1390, 1465 and 1480 cm^{-1} also characterize the vibrations of the tetrazole ring [7,8].

In view of the fact that the thiazole ring gives bands in the 1000–1100 and 1400–1500 cm^{-1} regions [22], the identification of the tetrazole structure in the range of these frequencies becomes unreliable and it is necessary to be cautious in drawing conclusions about the structure of the substance.

If in the crystalline state, as we have observed in the case of compounds XI–XIII (see Table 1), the bands of the azido group appear in the 2100–2170 cm^{-1} region and the positions and intensities of all the other bands in the spectrum remain constant for the crystalline state and solutions ($CHCl_3$, CH_3CN, CCl_4), it can be stated that under the given conditions these substances exist in the azide form.* The presence of electronegative groups in the thiazole ring makes the existence of a condensed tetrazole ring impossible or greatly lowers its stability. It is possible to explain in this way the fact that the bromination, thiocyanation, and nitration of 6-phenylthiazolo[2,3-e]tetrazole (VII) forms the 2-azido derivatives XI–XIII.

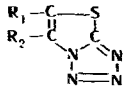
In the IR spectra of the phenyl derivatives VII–X in the crystalline state the characteristic frequency of the stretching vibrations of the azido group is absent. Consequently, in the crystalline state VII–X have a cyclic structure. For the assignment of the tetrazole bands, the spectra of these compounds were compared with the spectra of the azides XI–XIII. A comparison was also made of the frequencies and intensities of the bands in various solvents and in the crystalline state for each of these compounds. It was established that in the IR spectra of X in the crystalline state there are bands at 1185, 1200, 1375, 1385, and 1460 cm^{-1} which can be ascribed to the skeletal vibrations of the tetrazole ring. This is substantiated by the following facts: a) the assignment of the bands made in a number of papers [6–8, 11, 14] for tetrazolo[1,5-b]benzothiazole; b) the absence of absorption bands from these parts of the spectrum in the case of the azides XI–XIII; and c) the disappearance of the characteristic bands of the tetrazole ring in the spectra of solutions of X in chloroform and carbon tetrachloride and the appearance of the azide band (see Table 1).

Thus, in the crystalline state X has the cyclic structure and under the influence of solvents the tetrazole is converted into the isomeric azide form. A similar situation is observed in the IR spectra of the other phenyl derivatives (VII–IX). In un-

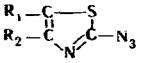
*In considering the spectra of XII, it must be borne in mind that the doublet of bands from the stretching vibrations of the thiocyanato group is also located in the 2100–2170 cm^{-1} region [23]. In the spectrum of XII in the crystalline state, this band has a frequency of 2138 cm^{-1} and in solutions it fuses with the strong azide band.

Table 1

IR Spectra of the Compounds Synthesized*



I–X



XI–XIII

Compound	R_1	R_2	Medium	Bands of the azido group, cm^{-1}	Bands of the tetrazole ring, cm^{-1}
I	H	H	KBr	—	1208 s., 1235 s., 1331 m., 1378 m.
			$CHCl_3$	2135 v. s.	—
			CCl_4	2135 v. s.	—
II	H	CH_3	KBr	—	1190 m., 1238 m.
			CH_3CN	2138 v. s.	1179 m., 1239 m.
			$CHCl_3$	2138 v. s.	1176 w., 1238 m.
			CCl_4	2136 v. s.	—
III	CH_3	H	KBr	—	1208 s., 1229 s., 1399 s.
			$CHCl_3$	2135 v. s.	1203 m., 1231 m., 1400 s.
			CCl_4	2135 v. s.	—
IV	CH_3	CH_3	KBr	—	1200 s., 1392 m., 1402 m.
			$CHCl_3$	2128 v. s.	1197 m., 1380 w., 1406 m.
			CCl_4	2128 v. s.	1199 w., 1380 v. w., 1400 w.
V	Br	CH_3	KBr	—	1090 w., 1230 m., 1433 m., 1455 w.
			CH_3CN	2136 v. s.	—
			$CHCl_3$	2134 v. s.	—
			CCl_4	2134 v. s.	—
VI	SCN	CH_3	KBr	—	1088 w., 1170 w., 1420 m.
			$CHCl_3$	2134 v. s.	—
			CCl_4	2135 v. s.	—
VII	H	C_6H_5	KBr	—	1178 m., 1378 v. w.
			CH_3CN	2140 v. s.	—
			$CHCl_3$	2137 v. s.	—
			CCl_4	2137 v. s.	—
VIII	H	(*n*) CH_3—C_6H_4	KBr	—	1183 m., 1202 w., 1387 w., 1459 m.
			CH_3CN	2142 v. s.	—
			$CHCl_3$	2140 v. s.	—
			CCl_4	2140 v. s.	—
IX	H	(*n*) Cl—C_6H_4	KBr	—	1180 m., 1200 w., 1375 w., 1457 m.
			$CHCl_3$	2138 v. s.	—
			CCl_4	2138 v. s.	—
X	H	(*n*) Br—C_6H_4	KBr	—	1185 m., 1200 v. w., 1375 w., 1385 w., 1460 m.
			$CHCl_3$	2137 v. s.	—
			CCl_4	2136 v. s.	—
XI	Br	C_6H_5	KBr	2149 s.	—
			CH_3CN	2145 v. s.	—
			$CHCl_3$	2145 v. s.	—
			CCl_4	2140 v. s.	—
XII	SCN	C_6H_5	KBr	2135—2158 v. s.	—
			$CHCl_3$	2140 v. s.	—
			CCl_4	2140 v. s.	—
XIII	NO_2	C_6H_5	KBr	2133 v. s.	—
			$CHCl_3$	2135 v. s.	—
			CCl_4	2135 v. s.	—

*Intensities of the bands: v.s. is very strong, s. is strong, m. is medium, w. is weak, v.w. is very weak.

substituted thiazolo[2,3-e]tetrazole (I) bands at 1208, 1235, 1331, and 1387 cm^{-1} (in the crystalline state) are ascribed to the tetrazole ring. Under the influence of solvents, the opening of the ring and the isomerization of I into 2-azidothiazole take place. If the tetrazole form is preserved at all, it is in such small amounts that it cannot be detected spectroscopically.

Table 2

Characteristics of the Compounds Synthesized

Compound	Decomp. P, °C	Emprical formula	Found N, %	Calculated N, %
V	110	$C_4H_3BrN_4S$	25.31 25.40	25.58
VI	70	$C_5H_3N_5S_2$	35.20 35.07	35.50
VIII	69	$C_{10}H_8N_4S$	25.71 26.09	25.90
IX	86	$C_9H_5ClN_4S$	23.32 23.43	23.67
X	84	$C_9H_5BrN_4S$	19.60 19.79	19.92
XI	43	$C_9H_5BrN_4S$	20.05 19.98	19.92

The assignment of the characteristic bands of the tetrazole ring in the 1475–1350 and 1350–1175 cm^{-1} regions for the methyl derivatives II–VI is complicated by the fact that in these parts of the spectrum strong and medium-intense bands of the deformation vibrations of the C—H bonds of the methyl groups and of the skeletal C—CH_3 vibrations appear [22]. A more reliable section for the assignment of the absorption bands of the tetrazole ring is the 952–1250 cm^{-1} regions, in spite of the fact that vibrations of the thiazole ring are also found in the same region; in this section the vibrations of the latter are reliably determined. In the crystalline state, compounds II–IV have the cyclic structure (see Table 1). In solutions, they are converted into the isomeric azides, while in the case of II and III in polar solvents (CH_3CN and $CHCl_3$) the equilibrium A $\rightleftarrows$ T is established, this equilibrium being displaced in the direction of the azide form in a nonpolar solvent (CCl_4). Even in the nonpolar carbon tetrachloride, the dimethyl derivative IV isomerizes into the azide incompletely. The existence of the equilibrium A $\rightleftarrows$ T for a solution of IV in carbon tetrachloride is shown by bands at 1199 and 1380 cm^{-1}, which are characteristic for the tetrazole ring, and by a band at 2128 cm^{-1}, which is characteristic for the azido group. Thus, the methyl derivatives of thiazolo[2,3-e]tetrazole II–IV are more stable than unsubstituted thiazolo [2,3-e]tetrazole and its phenyl derivatives VII–X, which are connected with the action of the electropositive methyl groups.

Compounds V and VI, which are tetrazoles in the crystalline state, are converted completely into the isomeric azides in solution.*

*In the IR spectrum of VI in the crystalline state there is a doublet in the 2100–2170 cm^{-1} region due to the stretching vibrations of the thiocyanate group. In solvents, these bands fuse with the intense band of the stretching vibrations of the azido group.

The decrease in the stability of the condensed tetrazole rings in this case is caused by the introduction into position 5 of the thiazole ring of the electronegative bromine and thiocyanate groups.

Thus, the stability of the thiazolo[2,3-e]tetrazoles and the 2-azidothiazoles isomeric with them, and also the position of the azido-tetrazole equilibrium A $\rightleftarrows$ T between them are determined to a considerable extent by the electronic nature of the substituents in the thiazole ring and by the polarity of the solvent.

Electropositive substituents stabilize the condensed tetrazole ring, while electronegative substituents lower the stability of the latter and facilitate the formation of the isomeric azides.

Any solvent decreases the stability of the condensed tetrazole ring and favors the production of the isomeric azide forms, but nonpolar solvents exert a considerably greater effect than polar ones. In carbon tetrachloride, all the compounds studied apart from IV, which contains two electropositive methyl groups, are converted completely into the isomeric azides. In polar solvents the existence of an azido-tetrazole equilibrium is possible in most cases where the tetrazole ring is stabilized by electropositive methyl groups (II–IV).

These results are in complete harmony with those obtained previously [5–18].

EXPERIMENTAL

The synthesis of the tetrazoles I–IV and VII has been described in preceding papers [4, 5]. Compounds V, VI and VIII–XI were obtained similarly with yields of about 15% by diazotizing the corresponding 2-aminothiazoles and then treating the diazonium salts with nitrous acids. The characteristics of the compounds obtained are given in Table 2.

Bromination of 6-methylthiazolo[2,3-e]tetrazole (II). With stirring, a solution of 1.78 g (0.01 mole) of N-bromosuccinimide in 25 ml of chloroform was added dropwise during 20 minutes at room temperature to a solution of 1.4 g (0.01 mole) of II in 30 ml of chloroform. Stirring was continued for another 15 min, after which the chloroform was evaporated off in vacuum and the solid residue was crystallized from methanol. The product obtained was identical with the V synthesized from the diazonium salt. Yield 7%, mp 110° C. Found, %: N 25.42, 25.63. Calculated for $C_4H_3BrN_4S$, %: N 25.58.

Bromination of 6-phenylthiazolo[2,3-e]tetrazole (VII) was carried out under analogous conditions. The product isolated has the structure of 2-azido-5-bromo-4-phenylthiazole. Yield 23%, decomp. p. 43° C. Found, %: N 20.02, 20.05. Calculated for $C_9H_5BrN_4S$, %: N 19.92.

Thiocyanation of 6-phenylthiazolo[2,3-e]tetrazole (VII). With stirring, a solution of 1.8 g(0.012 mole) of bromine in 30 ml of glacial acetic acid was added dropwise over 30 minutes at room temperature to a solution of 2.02 g (0.01 mole) of VII and 2.8 g (0.05)mole) of ammonium thiocyanate in 50 ml of glacial acetic acid. Stirring was continued for another 30 minutes after which the reaction mixture was poured onto ice and the product was extracted with chloroform. The chloroform was evaporated in vacuum and the solid residue was crystallized from methanol. On the basis of the results of analysis and the IR spectrum, the compound obtained can be ascribed the structure of 2-azido-4-phenyl-5-thiocyanatotetrazole (XII). Yield 14%, decomp. p. 68° C. Found, %: 27.33, 27.46. Calculated for $C_{10}H_5N_5S_2$, %: N 27.00.

Thiocyanation of 6-methylthiazolo[2,3-e]tetrazole (II) was carried out under the same conditions. Here the bulk of the II was recovered from the reaction mixture in the unchanged state. A product with decomp. p. 70° C, identical with the 6-methyl-5-thiocyanatothiazolo[2,3-e]tetrazole (VI) synthesized from the diazonium salt was also obtained in very low yield (3%). Found, %: N 34.99, 34.94. Calculated for $C_5H_3N_5S_2$, %: N 35.50.

Nitration of 6-phenylthiazolo[2, 3-e]tetrazole (VII). In small portions, 1.01 g (0.05 mole) of **VII** was added to 15 ml of concentrated sulfuric acid cooled to −10° C. The resulting solution was treated in drops with nitrating mixture (1 ml of nitric acid, sp. gr. 1.5, and 1 ml of concentrated sulfuric acid) in such a way that the temperature did not rise above −5° C. The mixture was left in ice for 30 minutes and then at room temperature for 2 hr, after which it was poured onto ice. The precipitate that deposited was filtered off, washed with ice water to neutrality to Congo Red, and crystallized from methanol. This gave 2-azido-5-nitro-4-phenylthiazole in the form of yellowish needles. Yield 20%, decomp. p. 115° C, found, %: N 28.46, 28.72. Calculated for $C_9H_5N_5O_2S$, %: N 28.34.

REFERENCES

1. V. Ya. Pochinok, Khimicheskii Sbornik KGU, 7, 175, 1956.

2. V. Ya. Pochinok, Naukovii shchorichnyk Kyivs'kogo derzhavnogo universytetu, 91, 1957.

3. V. Ya. Pochinok and S. D. Zaitseva, Ukr. khim. zh., 26, 351, 1960.

4. V. Ya. Pochinok, S. D. Zaitseva, and R. G. El'gort, Ukr. khim. zh., 17, 509, 1951.

5. V. Ya. Pochinok and L. F. Avramenko, Ukr. khim. zh., 28, 513, 1962.

6. L. F. Avramenko, V. Ya. Pochinok, and Yu. S. Rozum, ZhOKh, 33, 980, 1963.

7. Yu. N. Sheinker, I. Ya. Postovskii, N. P. Bednyagina, L. B. Senyavina, and L. F. Lipatova, DAN, 141, 1388, 1961.

8. I. Ya. Postovskii, N. P. Bednyagina, L. B. Senyavina, and Yu. N. Sheinker, Izv. AN SSSR, OFN, 36, 1298, 1962.

9. I. Ya. Postovskii and I. N. Goncharova, ZhOKh, 33, 2334, 1963.

10. I. Ya. Postovskii and N. B. Smirnova, DAN, 166, 1136, 1966.

11. J. H. Boyer and E. J. Miller, J. Am. Chem. Soc., 81, 4671, 1959.

12. J. H. Boyer, M. S. Chang, and R. F. Reinish, J. Org. Chem., 25, 286, 1960.

13. J. H. Boyer and H. W. Hyde, J. Org. Chem, 25, 458, 1960.

14. G. A. Reynolds, J. A. Van Allan, and J. F. Tinker, J. Org. Chem, 24, 1205, 1959.

15. H. Behringer and H. J. Fischer, Chem. Ber., 95, 2546, 1962.

16. C. Temple and J. H. Montgomery, J. Am. Chem. 86, 2946, 1964.

17. C. Temple and J. H. Montgomery, J. Org. Chem., 30, 826, 1965.

18. C. Temple and J. H. Montgomery, J. Org. Chem., 30, 829, 1965.

19. Yu. N. Sheinker, L. B. Senyavina, and V. N. Zheltova, DAN, 160, 1339, 1965.

20. L. Bellamy, Infrared Spectra of Complex Molecules [Russian translation], IL, Moscow, 379, 392, 1963.

21. E. Lieber, D. Levering, and L. Patterson, Anal. Chem. 23, 1594, 1951.

22. M. P. V. Mijovik and J. Walker, J. Chem. Soc., No. 8, 3381, 1961.

23. N. S. Ham and B. Willis, Spectro chim. acta, 16, 297, 1960.

12 May 1966

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