REACTIONS OF AZIDES AND CONDENSED TETRAZOLES WITH ORGANOMAGNESIUM HALOGEN AND ORGANOLITHIUM COMPOUNDS

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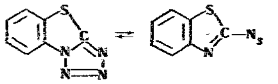
Reactions of azides and condensed tetrazoles, containing electropositive and electronegative substituents, with organomagnesium halogen compounds and organolithium compounds have been studied. The results obtained, like the study of the IR spectra carried out previously, permit the conclusion that the condensed tetrazoles are tautomeric compounds and the course of the reaction depends on the position of the azido-tetrazole equilibrium, which is affected by the nature of the substituent in the nitrogen-containing ring and the chemical nature of the reagent acting.

It is known [1–3] that organic azides react with organomagnesium halogen compounds with the formation of disubstituted triazenes. Triazenes are also formed by the reaction of organolithium compounds with azides [4–5].

In 1951, V. Ya. Pochinok et al. [2] showed for the first time that tetrazolobenzothiazole and its derivatives give triazenes with phenylmagnesium bromide and also under the action of sodium or potassium cyanide. This permitted the assumption of the existence in this type of compounds of an azido-tetrazole tautomerism, and this was confirmed by the special investigations of V. Ya. Pochinok and L. F. Avramenko [6, 7] using UV and IR spectra and also simultaneously and independently from one another by Soviet [8–11] and foreign authors [12–19].



In view of the fact that organometallic compounds, and also sodium and potassium cyanides, react only with the azide form of the compounds mentioned, we set ourselves the aim of studying in detail the reactions of various types of condensed tetrazoles with organomagnesium and organolithium compounds and sodium cyanide. In the reaction we used $BrMgC_6H_5$, $BrMgC_4H_9$-n, $IMgCH_3$, $ClMgCH_2C_6H_5$, LiC_6H_5, LiC_4H_9-n and the condensed tetrazoles listed in the table.

The reactions were carried out in a polar solvent (diethyl ether) and in a nonpolar solvent (benzene).

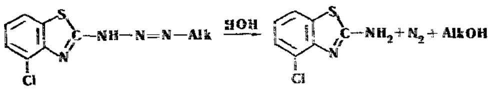
We found that the tetrazoles V and VII do not react with organometallic compounds in ether and benzene solutions. We observed the same thing for 6-methylthiazolo[2,3-e]tetrazole (I). If, however, instead of the methyl group an electronegative substituent (phenyl) is introduced into the latter, the formation of triazenes with $BrMgC_6H_5$, LiC_6H_5, and even with HalMgAlk takes place readily. It is obvious that the phenyl radical, abstracting electrons from the nucleus, thereby favors the opening of the tetrazole ring and the production of the azide form. It has also been found that the tetrazoles III, IV, and VI form triazenes only with $BrMgC_6H_5$ [2, 3] and LiC_6H_5. So far as HalMgAlk and LiAlk are concerned, the formation of aliphatic-aromatic triazenes does not take place either in ether or in benzene solutions on boiling or in the cold—the initial tetrazoles are recovered almost quantitatively. Apparently not only the presence of a nonpolar solvent, favoring the production of the azide form but also a definite electronegativity of the organic residue in the organometallic compound, which also affects the position of the azido-tetrazole equilibrium, are necessary.

Condensed Tetrazole Used in Reactions with Organometallic Compounds

Compound	Name	Decomp. p., °C
I	6-Methylthiazolo[2,3-e]tetrazole	119—120[3]
II	6-Phenylthiazolo[2,3-e]tetrazole	102—103[5]
III	Tetrazolo[1,5-b]benzothiazole	110—112[2]
IV	6-Methyltetrazolo[1,5-b]benzothiazole	121—122[2]
V	4-Methyltetrazolo[1,5-b]benzothiazole	133[2]
VI	6-Chlorotetrazolo[1,5-b]benzothiazole	123[3]
VII	Pyridinotetrazole	156[20, 21]
VIII	4-Chloro-2-azidobenzothiazole	103[5]

2-Azido-4-chlorobenzothiazole (VIII) behaves in a completely opposite manner. Here, under the influence of the negative inductive effect of the chlorine atom, the formation of a tetrazole ring is quite impossible [6]. This compound exists only in the form of the azide, which reacted with organometallic compounds in both polar and nonpolar solvents forming triazenes. Only phenyl(4-chlorobenzothiazol-2-yl)triazene proved to be stable, and the aliphatic-aromatic triazenes could not be isolated because of their instability. As a result of the reaction, 2-amino-4-chlorobenzothiazole was isolated in almost quantitative yield, as was confirmed by the results of the analyses and a mixed melting point.

Apparently, cleavage of the alkyl(4-chlorobenzothiazole-2-yl)triazenes takes place in the following way:



The tetrazoles shown in the table, apart from pyridinotetrazole, readily form cyanotriazenes with sodium cyanide in ethanolic solution [3, 22]. We have obtained a cyanotriazene with tetrazole V for the first time.

The data that we have obtained and the investigations of the IR spectra of the tetrazoles mentioned above that have been given previously [6–19] show that condensed tetrazoles are tautomeric compounds. On the basis of the reactions of various condensed tetrazoles with organometallic compounds and sodium or potassium cyanide we have shown that the course of the reaction depends on the state of the azido-tetrazole equilibrium, which is affected by the nature of the substituent in the heterocycle and also by the chemical nature of the reagent acting on the condensed tetrazole.

EXPERIMENTAL*

Phenyl(4-phenylthiazol-2-yl)triazine. With stirring, an equivalent amount of phenylmagnesium bromide in 20 ml of ether (the yield of C_6H_5MgBr was determined by titration with hydrochloric acid) was added dropwise over half an hour to a solution of 2 g (0.01 mole) of 6-phenylthiazolo[2,3-e]tetrazole (II) in 200 ml of absolute ether. An orange precipitate formed. To complete the reaction, the mixture was heated in the water bath for 30 min. Then it was decomposed with 150 ml of 25% NH_4Cl solution with the addition of a small amount of ammonia. The triazene was extracted with ether and the ethereal extract was washed with water and dried with anhydrous sodium sulfate. After the ether had been distilled off, the yield of yellow crystalline substance was 1.82 g (65%). Crystallization from ethanol gave orange crystals with decomposition at 159–160° C. The triazene is insoluble in water and soluble in ether, benzene, and acetone in the cold and in ethanol on heating. It is decomposed by acids with the evolution of nitrogen. Found, %: N 20.00, 20.50. Calculated for $C_{15}H_{12}N_4S$, %: N 19.98.

b) A solution of 1 g (0.005 mole) of II in 200 ml of absolute ether was added dropwise with vigorous stirring to an equimolecular amount of phenyllithium. The reaction was carried out in a current of dry nitrogen at $-5°$ C. The mixture became yellow-orange and a precipitate deposited. Stirring was continued for an hour with the temperature of the reaction mixture rising gradually to room temperature. Then it was decomposed with ice water with stirring. The triazine formed was extracted with ether, and the ethereal extract was washed until the wash-waters were neutral to litmus. The solution was dried with anhydrous sodium sulfate. After the ether had been distilled off, a yellow-orange crystalline substance remained. The yield was qualitative. After recrystallization from ethanol, a mixture with the triazene obtained by method (a) gave no depression of the melting point.

Phenyl(4-chloro-2-benzothiazolyl) triazine. a) An equivalent amount of $MgBrC_6H_5$ in 25 ml of absolute ether was added dropwise with stirring to a solution of 2 g (0.01 mole) of 2-azido-4-chlorobenzothiazole in 25 ml of absolute ether. The reaction took place in the cold, the mixture acquiring a bright orange color. After standing 10 hr at room temperature, it was decomposed with 100 ml of 10% NH_4Cl solution with the addition of ammonia. The triazene deposited in the form of an orange precipitate, which was filtered off, washed with water, and dried. The yield of crude reaction product was 2.6 g (almost quantitative). The product consisted of yellow-orange needles with decomposition at 174° C (from ethanol). The triazene is insoluble in water, sparingly soluble in ether and petroleum ether, readily soluble in toluene and acetone, and soluble in ethanol on heating; with acids it decomposed with the evolution of bubbles of nitrogen. Found, %: N 19.52, 19.65. Calculated for $C_{13}H_9ClN_4S$, %: N 19.04.

b) Phenyl(4-chlorobenzo-2-thiazolyl)triazine was obtained by organolithium synthesis in a similar manner to phenyl(4-phenyl-2-thiazolyl)triazine from 2.1 g (0.01 mole) of VIII and an equimolecular amount of phenyllithium at —10° C in an atmosphere of dry nitrogen. The yield of substance recrystallized from ethanol was 1.8 g (62.7%). A mixture with the material obtained by method (a) gave no depression of melting point.

n-Butyl(4-phenyl-2-thiazolyl)triazine. a) With stirring, a solution of 1.6 g of n-butylmagnesium bromide in 15 ml of ether was added, over a 10 min period, to a solution of 1 g (0.005 mole) of II in 150 ml of absolute ether. The reaction took place rapidly, the mixture becoming slightly warm and forming a bright yellow precipitate. It was stirred for another 10 min, after which it was decomposed with 200 ml of 10% ammonium chloride solution with the addition of a small amount of ammonia. The ethereal extract was washed with water and dried with calcined sodium sulfate. After evaporation of the ether, the residue was crystallized from petroleum ether. The product consisted of yellow needles with decomposition at 88° C. Yield 0.72 g (54%). It gives a vigorous explosion with concentrated H_2SO_4, which is characteristic for aliphatic-aromatic triazenes. The triazene is readily soluble in many organic solvents. Found, %: N 21.42, 21.68. Calculated for $C_9H_6N_4S$, %: N 21.51.

b) An equivalent amount of butyllithium in benzene was added dropwise with stirring, over a 20 min period, to a solution of 1 g (0.005 mole) of II in 50 ml of dry benzene cooled to —10° C. The reaction mixture became yellow-orange. It was stirred for another hr, with the temperature being gradually raised to that of the room, after which the mixture was decomposed with ice water with stirring and with the addition of another 50 ml of benzene. The benzene extract was washed with water and dried with anhydrous calcium chloride. After the evaporation of the benzene in vacuum, the solid residue was crystallized from petroleum ether. The melting point of a mixture of the substance obtained with the n-butyl(4-phenylbenzothiazol-2-yl)triazine prepared by method (a) gave no depression.

2-Amino-4-chlorobenzothiazole*. With stirring, an equivalent amount of n-butylmagnesium bromide was added dropwise, over a 30 min period, to a solution of 2.1 g (0.01 mole) of VIII in 50 ml of absolute ether at room temperature. The mixture immediately became yellow and deposited a precipitate. Stirring was continued for another 20 min. After standing for 2 hr, the reaction mixture was decomposed with 100 ml of 10% ammonium chloride solution with cooling. The yellow precipitate immediately became colorless and bubbles of gas were evolved. The precipitate was filtered off, washed with water, and dried. Yield 95%. The product, after recrystallization from toluene, consisted of colorless crystals. A mixture with authentic 2-amino-4-chlorobenzothiazole melted at 208° C. Found, %: N 15.19, 15.29. Calculated for $C_7H_5ClN_2S$, %: N 15.17.

Cyano(4-methylbenzothiazol-2-yl)triazine. Over a 30 min period 1.9 g (0.01 mole) of V was added to a solution of 2 g of sodium cyanide and 0.2 g of caustic soda in 40 ml of 75% ethanol, and the mixture was heated in the water bath under reflux. The solution was poured into 100 ml of water and the mixture was filtered and made acid with 50% acetic acid. The resulting precipitate was filtered off, carefully washed with water, and dried. After recrystallization from ethanol it formed small bright yellow needles with decomposition at 157° C. Yield 1.63 g (79%). Found, %: N 32.43, 31.97. Calculated for $C_9H_8N_5S$, %: N 32.08.

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*With the participation of L. A. Mel'nichenko.

*2-Amino-4-chlorobenzothiazole was obtained similarly by the reaction of VIII with CH_3MgI and $C_6H_5CH_2MgCl$ in ether and with LiC_4H_9 in benzene solution.

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