# DESTRUCTIVE HYDRAZINOLYSIS OF [1,2,4]TRIAZOLO[3,4-b]-[1,3,4]THIADIAZOLE DERIVATIVES

I. Ya. Postovskii, A. D. Sinegibskaya, and E. G. Kovalev

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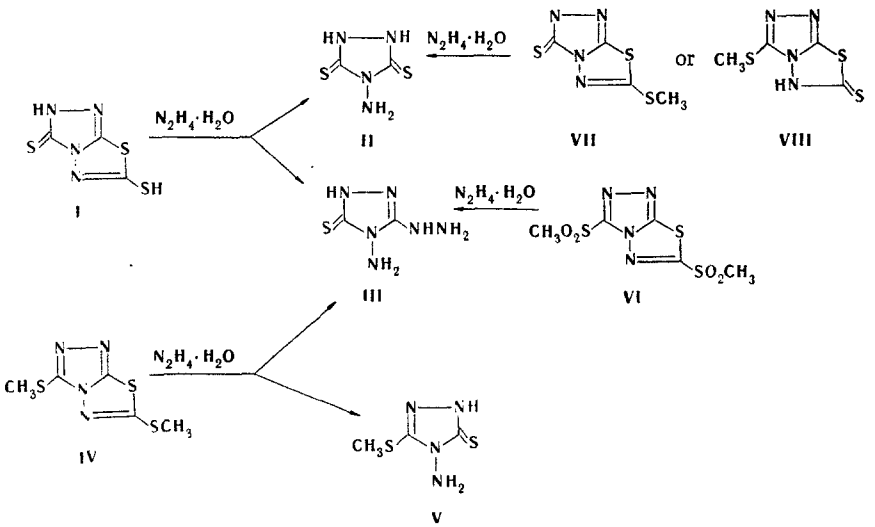
The hydrazinolysis of 2-mercapto[1,2,4]triazolino[3,4-b][1,3,4]triadiazole-5-thione and its S-methyl and disulfonyl derivatives leads to opening of the thiadiazole ring during attack by the nucleophile on the bridge carbon atom. A study of the structures of the reaction products and calculations by the Hückel MO and Pariser–Parr–Pople (PPP) method makes it possible to draw a conclusion regarding the mechanism of the hydrazinolysis.

In our preceding paper [1] we showed that the 2,4-dimercapto[1,2,4]triazolo[3,4-b]-[1,3,4]thiadiazole described in [2] is actually a thione-thiol — 2 mercapto[1,2,4]triazolino—[3,4-b][1,3,4]thiadiazole-5-thione (I) — in the crystalline state and in aprotic solvents.

It is known that some cyclic thioamides readily exchange the sulfur atom of the thioamide group for a hydrazine residue. Continuing our investigation of thioamide I, we set out to obtain hydrazine derivatives by similar transformations in order to extend its synthetic possibilities by utilizing such transformations.

In connection with the fact that the two-ring skeleton of the investigated system contains four nitrogen atoms, it might have been expected that it would have high electron-deficient character and, as a consequence of this, the possibility of facile replacement of the exocyclic sulfur atoms by a hydrazine residue during nucleophilic attack of the ring carbon atoms by hydrazine hydrate. However, heating I with hydrazine hydrate gave an unexpected result — destructive hydrazinolysis of the thiadiazole ring to give two triazole compounds of known structure. 4-Amino-1,2,4-triazolidine-3,5-dithione (II) (85% yield; isolated from the reaction mixture in the form of the hydrazinium salt) and 3-hydrazino-4-amino-1,2,4-triazoline-5-thione (III) [3] (13% yield) were obtained.




S. M. Kirov Urals Polytechnic Institute, Sverdlovsk. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 566-570, April, 1975. Original article submitted May 14, 1974.

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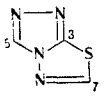
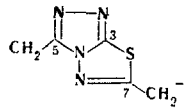
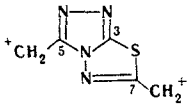
TABLE 1. Reactivity Indexes

| Structure | Atom No. | $Q_r$ | $f_r^+$ | $f_r^-$ | $F_r$ | $L_r^+$ | $Lo_r$ | $L_r^-$ |
|---|---|---|---|---|---|---|---|---|
|  | 3 | −0,073 | 0,015 | 0,153 | 0,140 | 2,155 | 2,454 | 2,754 |
| | 5 | −0,149 | 0,420 | 0,368 | 0,555 | 1,550 | 2,022 | 2,494 |
| | 7 | −0,092 | 0,006 | 0,583 | 0,483 | 1,833 | 2,084 | 2,335 |
|  | 3 | −0,126 | 0,014 | 0,579 | 0,221 | 1,817 | 2,344 | 2,870 |
| | 5 | −0,061 | 0,015 | 0,228 | 0,142 | 2,160 | 2,676 | 3,193 |
| | 7 | −0,042 | 0,009 | 0,289 | 0,082 | 2,343 | 2,710 | 3,078 |
|  | 3 | −0,034 | 0,296 | 0,079 | 0,348 | 2,119 | 2,119 | 2,119 |
| | 5 | +0,009 | 0,067 | 0,000 | 0,140 | 2,781 | 2,781 | 2,781 |
| | 7 | −0,018 | 0,000 | 0,014 | 0,096 | 2,795 | 2,795 | 2,795 |

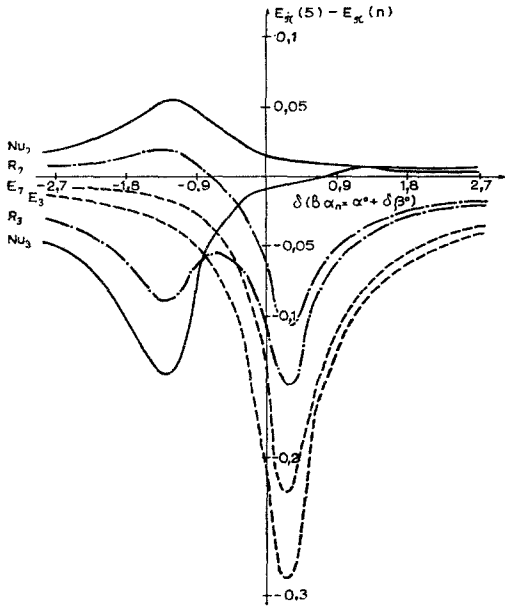



Fig. 1. Dependence of the relative π-electron energy on the nature of the reagent.

Inasmuch as it is known that S-methyl groups are exchanged by a hydrazine group more readily than the thione group, the reaction with hydrazine hydrate was carried out with the dimethyl derivative (IV) [2]. However, the thiadiazole ring is cleaved in this case also, and the chief reaction product is III, which is formed, as presented above, from I in low yield. In addition, hydrazinolysis of IV also gives 5-methylthio-4-amino-1,2,4-triazoline-3-thione (V).

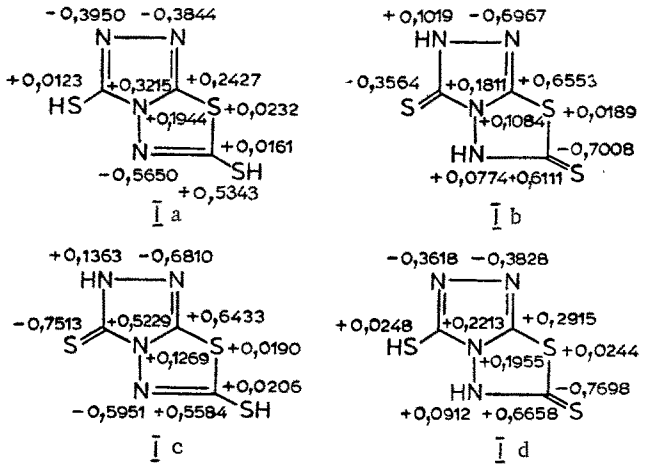
In connection with the fact that sulfonyl groupings are strong acceptors and are therefore usually easily exchanged by hydrazine residues, we expected that the use of disulfonyl derivative VI in the hydrazinolysis would lead to the desired result. In fact, the carbon atom of the triazole ring undergoes attack by hydrazine hydrate, and the sulfonyl group is replaced by a hydrazine group; however, the thiadiazole ring is cleaved during hydrazinolysis here also to give a single reaction product — III.

The somewhat unexpected course of the reaction of two-ring compounds I, IV, and VI with hydrazine hydrate compelled us to occupy ourselves with the establishment of the mechanism of the cleavage reaction in order to discover the reason for the vulnerability of the thiadiazole fragment of the two-ring system in reaction with hydrazine hydrate. With this end in mind, we used the Hückel MO method (with the parameters in [4]) to calculate the static and dynamic reactivity indexes. The results of the calculations of the unsubstituted two-ring systems (Table 1) show that the thiadiazole $C_7$ atom is the most reactive with respect to the nucleophilic agent, whereas the most favorable site for attack by radical and electrophilic agents is the triazole ring $C_5$ atom. Practically analogous conclusions follow from an analysis of the delocalization model [5]. Figure 1 illustrates the increased reactivity of the thiadiazole $C_7$ atom as compared with the other carbon atoms, which is particularly distinctly manifested when the nucleophilic strength of the agent ($\delta$) is −1.2. However, the intersection of the curve of $Nu_3$ with the axis of abscissas constitutes evidence that when $\delta > 0.6$, the $C_3$ bridge carbon atom is more active with respect to the nucleophilic agent than the triazole $C_5$ atom. Insofar as radical attack is concerned, only reagents with $\delta < -0.63$ are capable of attacking the thiadiazole carbon, whereas "hard" agents preferably attack the triazole $C_5$ atom.

Interesting conclusions follow from an examination of the reactivities of disubstituted derivatives of the two-ring system in which $CH_2^-$ — donor substituents — model dimethyl derivative II, and $CH_2^+$ — acceptors — model disulfonyl derivative VI. The data in Table 1 for

the model structures show that, regardless of the nature of the substituent, the most active with respect to any type of attack is the bridge $C_3$ atom, i.e., substitution causes a shift in the reaction center. This result, i.e., such a pronounced substituent effect, is observed quite rarely, inasmuch as the reactivity in the condensed compound is preferably determined by the topology of the systems themselves rather than by the substituents.

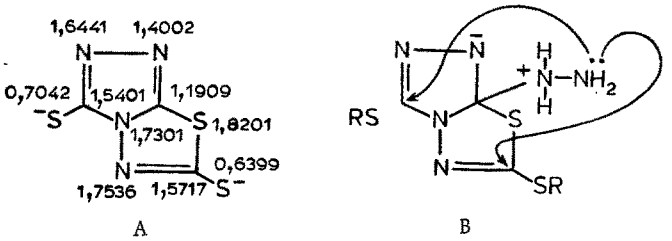
The electron-density distribution in real tautomeric forms Ia-d, calculated by the Pariser–Parr–Pople (PPP) method (with the parameters in [1]), also indicates that the bridge $C_3$ atom is the most active with respect to nucleophiles in the derivatives of the cyclic system.




I a I b I c I d

In connection with the fact that I is a very strong acid [1], its reactivity in basic (hydrazine) media is probably determined by the anionic form. Inasmuch as the electronic spectrum of I in alkaline media is close to the spectrum of fixed dimethyl compound IV, of the four mesomeric forms of the dianion, the structure with negative charges localized on the exocyclic sulfur atoms was used for the calculation. The calculation of the electron densities of this dianion (A) shows (Hückel MO, $\delta_{S^-} = -1.5$) that the bridge $C_3$ atom is the most electrophilic center in this case.

Thus an analysis by the method of calculations of the reactivities of the derivatives of the two-ring system gives us a basis to suppose that the bridge carbon atom undergoes initial attack by hydrazine. The hydrazine added initially to this carbon atom is capable of being incorporated either into the triazole or thiadiazole ring by attacking the unshared pair of electrons of the nitrogen atom or the carbon atom in the triazole ring, or the carbon atom in the thiadiazole ring (B). The ease of secondary attack is determined by the charge on these carbon atoms.




A B

Judging from the charge distribution, the formation of II from I and VII can be represented as the result of primary attack at the bridge carbon atom with subsequent attack of the unshared pair of electrons of the nitrogen atom of hydrazine at the carbon atom of the triazole ring. In this case the ease of secondary attack is determined by the charge on the triazole carbon atom. In I in basic media the proton of the thiol group attached to the triadiazole ring is cleaved, and delocalization of the charge leads to an increase in the electron density on the thiadiazole carbon; this somewhat hinders nucleophilic attack at it and is reflected in the yields of II obtained from I and VII.

A similar pattern is observed in the formation of hydrazine III from disulfonyl derivative VI. However, in this case the sulfonyl group attached to the triazole ring is subject to prior substitution by a hydrazine group, and a second molecule of hydrazine readily cleaves the thiadiazole ring, the carbon of which is rendered strongly positively charged by the adjacent electron-acceptor sulfonyl grouping.

In the hydrazinolysis of IV, a hydrazine derivative that partially undergoes reductive demethylation [6] to give product III and intramolecular hydrazinolysis to give product V is formed as a result of nucleophilic attack at the bridge carbon atom.

In our preceding paper [1] we reported that the product of partial methylation of I and partial demethylation of IV has structure VII rather than structure VIII. Using the destructive hydrazinolysis described here we were able to confirm the structure of this substance by chemical means. In fact, its hydrazinolysis gives II, which can only be obtained from a compound that does not contain a methyl group attached to the triazole ring. Consequently, the S-methyl group was bonded to the thiadiazole ring, and structure VII should be assigned to the monomethyl compound.

## EXPERIMENTAL METHOD

Reactions of Triazolothiadiazole Derivatives with Hydrazine Hydrate. A) A 1-g (5.3 mmole) sample of I [2] was refluxed for 8 h in 10 ml of hydrazine hydrate, after which the solvent was removed by distillation to give 0.1 g (13%) of colorless 3-hydrazino-4-amino-1,-2,4-triazoline-5-thione (III) with mp 224-225° (from water) [3]. The mother liquor was evaporated to give 0.8 g (84%) of hydrazinium salt II wiht mp 228-229° (from water). Found: C 13.6; H 4.5; N 46.6%. $C_2H_8N_6S_2$. Calculated: C 13.3; H 4.5; N 46.6%. Acidification of the aqueous solution with concentrated hydrochloric acid precipitated a colorless substance that was identical to II obtained by the method in [2].

B) Under similar conditions, 1 g (4.6 mmole) of IV [2] yielded 0.3 g (45%) of III (mp 224-225°) and 0.17 g (23%) of V with mp 182-183° (from water) [2].

C) A 0.5-g (1.8 mmole) sample of VI [1] was refluxed in 6 ml of hydrazine hydrate for 5 h, after which the solvent was removed by distillation, and the viscous mass was treated with water. The resulting precipitate was removed by filtration to give 0.15 g (58%) of III with mp 224-225° (from water).

D) A 0.35-g (1.7 mmole) sample of VII [1] was refluxed in 6 ml of hydrazine hydrate for 8 h, after which the excess hydrazine hydrate was removed by distillation, and the residue was dissolved in water. The aqueous solution was acidified with concentrated hydrochloric acid, and the resulting precipitate was removed by filtration to give 0.17 g (68%) of II, which was identical to the product described in [2].

## LITERATURE CITED


1. E. G. Kovalev, A. D. Sinegibskaya, I. Ya. Postovskii, and S. L. Mertsalov, Khim. Geterotsikl. Soedin., 349 (1975).
2. J. Sandström, Acta Chem. Scand., 15, 1209 (1961).
3. R. G. Dickensons and N. W. Jacobson, Anal. Chem., 41, 1324 (1969).
4. E. G. Kovalev and I. Ya. Postovskii, Khim. Geterotsikl. Soedin., 1138 (1970).
5. I. Arriau, O. Chalvet, A. Dargelos, and G. Maury, J. Heterocycl. Chem., 10, 659 (1973).
6. A. D. Sinegibskaya, E. G. Kovalev, and I. Ya. Postovskii, Khim. Geterotsikl. Soedin., 1708 (1973).