ACYLATION AND IODINATION OF 5-(p-R-PHENYL)-1,2,4-TRIAZOLE-3-THIONES

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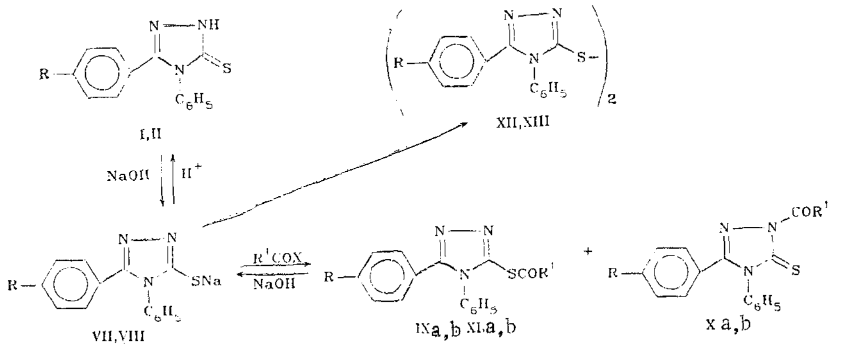
The acylation of 5-(p-R-phenyl)-1,2,4-triazole-3-thiones was studied. It was shown that the reaction depends on the nature of the group in the para position of the 5-phenyl substituent. Iodination of the sodium salts of 1,2,4-triazole-3-thiones is accompanied by the formation of disulfides, whereas 1,2,4-triazole-3-thiones that contain an unsaturated substituent with an allylic bond in the 4 position of the ring are iodinated to give condensed thiazolotriazole systems.

It has been previously shown that, inasmuch as they have dual reactivity, 1,2,4-triazole-3-thiones form S- and N-derivatives in substitution and addition reaction [1-4]; the substituent in the 5 position of the ring has a significant effect on the direction of the reaction. Condensed thiazolo[2,3-c]triazole systems are formed in the bromination of 4-allyl-5-phenyl-(benzyl)-1,2,4-triazole-3-thiones [3, 5].

The aim of the present research was to study the acylation of 1,2,4-triazole-3-thiones that contain in the 5 position a phenyl group with electron-donor (I) and electron-acceptor (II) substituents in the para position and to study the iodination of 1,2,4-triazole-3-thiones that have an unsaturated grouping with an allylic double bond in the 4 position of the ring (III-V).

Treatment of bases I and II with sodium hydroxide solution gave the corresponding sodium salts VII and VIII, which were acylated with acid chlorides. Acylation of the sodium salt (VII) of 4-phenyl-5-(p-tolyl)-1,2,4-triazole-3-thione leads in both cases to the formation of S- and N-derivatives (IXa, b and Xa, b) in a ratio of 1:4, respectively, whereas only S-derivatives XIa,b are formed in the acylation of the sodium salt (VIII) of 4-phenyl-5-(p-nitrophenyl)-1,2,4-triazole-3-thione:



I, VII, IXa, b Xa,b, XII $R=CH_3$; II, VIII, XIa,b, XIII $R=NO_2$; a $R^1=CH=CHC_6H_5$;
b $R^1=C_6H_5$

Compounds VII and VIII have thiol structures; the negative charge is probably concentrated primarily on the sulfur atom, and attack by electrophilic reagents in the initial step therefore takes place at the sulfur atom. However, substituent R in the para position of the 5-phenyl ring of the triazolethiones, which, because of the presence of conjugation, can increase the electron density on the nitrogen atom of the $-N-\underset{|}{C}-S^{\ominus}$ triad (VII, $R = CH_3$) or, on the other hand, can decrease it on the nitrogen atom (VIII, $R = NO_2$), has a significant effect on the formation of the final reaction products and their ratio. In the first case the final

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products of acylation consist of a mixture with preponderance of the N-derivatives (Xa, b, 80%), which are formed due to S,N-transacylation of the electrophilic particles, as well as a smaller amount of the S-derivatives (IXa,b, 20%).

In the second case, because of a decrease in the electron density on the nitrogen atom, S,N-transacylation does not occur, and the final products are only S-derivatives XIa,b.

S,N-Transacylation of triazolethiones upon heating has been previously observed [4].

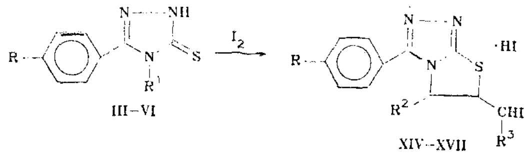
According to our data (Table 1), replacement of the hydrogen atom in the para position of the 5-phenyl substituent of 1,2,4-triazole-3-thiones by a group of some kind affects their acidities. It is apparent from Table 1 that a nitro group, which displays strong electron-acceptor properties, increases the acidities of triazolethiones, whereas the electron-donor methyl group decreases the acidities. These results are in agreement with the data in [2].

The hydrolysis of S- and N-acyl derivatives IXa,b-XIa,b with a 2 N aqueous alcohol solution of alkali at room temperature leads to the starting sodium salts VII and VIII, the acidification of which gave the corresponding bases I and II.

Disulfides XII and XIII are formed by the action of iodine on sodium salts VII and VIII.

It is known that the bromination and iodination of N-allylthioureas are accompanied by cyclization with the formation of a thiazoline ring [6,7].

In III-V an N-allylthiourea residue is bonded to the triazolethione ring, and compounds that contain a condensed system made up of triazole and thiazole rings (XIV-XVII) are therefore formed when they are iodinated:



III–VI

XIV–XVII

III, IV, V R^1=—$CH_2CH:CH_2$; VI R^1=  III, XIV R=CH_3; IV, XV R=Br; V, XVI R=NO_2; VI, XVII R=H; XIV, XV, XVI R^2=R^3=H; XVII R^2+R^3=—$(CH_2)_3$—

Compounds XIV-XVII are hydriodides, and this indicates that the iodination of III-VI proceeds with ring formation.

The IR spectra of S-derivatives IXa,b and XIa,b contain absorption bands that are characteristic for C—S—C vibrations at 750 cm^{-1} and C=N vibrations at 1660 cm^{-1}. The IR spectra of N-derivatives Xa,b contain absorption bands of a C=S group at 1330 cm^{-1}. An intense absorption band of a C=O group at 1670-1690 cm^{-1} is characteristic for all acyl derivatives IXa,b-XIa,b. The spectra of III-VI contain an absorption band at 1620-1680 cm^{-1}, which is characteristic for the C=C bond; this band vanishes in the spectra of their iodination products (XIV-XVII), but absorption bands that are characteristic for the C—I bond (540 cm^{-1}) and for the C—S—C grouping (750 cm^{-1}) appear in the spectra.

Thus we have shown that the acylation reaction depends on the electronic nature of the group in the para position of the 5-phenyl substituent of 1,2,4-triazole-3-thiones; this group also has a significant effect on their acidities.

Therefore, a new condensed derivative of the thiazolo[2,3-c]triazoles was obtained, which is of interest in connection with a study of their physiological activity.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-10 spectrometer. The acidity constants were determined by the method in [8].

4-R-5-(p-R-Phenyl)-1,2,4-triazole-3-thiones (I-VI). We synthesized these compounds for the first time by the method in [9]. Data on the synthesized compounds are presented in Table 2.

4-Phenyl-5-(P-tolyl)-1,2,4-triazole-3-thione Sodium Salt (VII). A mixture of 2.67 g (10 mmole) of I and 0.4 g (10 mmole) of sodium hydroxide in aqueous alcohol [water—alcohol

TABLE 1. Acidity Constants of 4,5-Diphenyl-1,2,4-triazole-3-thione [4] and I and V

Compound	$K_a \times 10^8$
4,5-Diphenyl-1,2,4-triazole-3-thione	1,91 [4]
I	9,12
V	11,5

TABLE 2. Characteristics of the Compounds Obtained

Compound	mp,[a] °C	Empirical formula	S, %		Yield, %
			found	calc.	
I	251—252	$C_{15}H_{13}N_3S$	11,8	12,0	92
II	252—254	$C_{14}H_{10}N_4O_2S$	10,7	10,7	80
III	138—140	$C_{12}H_{13}N_3S$	13,7	13,8	85
IV	158—160	$C_{11}H_{10}BrN_3S$	10,7	10,8	95
V	180—181	$C_{11}H_{10}N_4O_2S$	12,1	12,2	63
VI	165—167	$C_{14}H_{15}N_3S$	12,4	12,4	93
VII	150—151	$C_{15}H_{12}N_3NaS$	14,4[b]	14,5[b]	95
VIII	>300	$C_{14}H_{19}N_4NaO_2S$	10,0	10,0	75
IXa	191—193	$C_{24}H_{19}N_3OS$	7,9	8,1	20
IXb	198—200	$C_{22}H_{17}N_3OS$	8,5	8,6	20
Xa	234—236	$C_{24}H_{19}N_3OS$	8,0	8,1	80
Xb	240—241	$C_{22}H_{17}N_3OS$	8,4	8,6	80
XIa	205—207	$C_{23}H_{16}N_4O_3S$	7,4	7,5	96
XIb	185—187	$C_{21}H_{14}N_4O_3S$	7,9	8,0	98
XII	243—244	$C_{30}H_{24}N_6S_2$	11,9	12,0	97
XIII	255—256	$C_{28}H_{18}N_8O_4S_2$	10,7	10,8	95
XIV	191—192	$C_{12}H_{13}I_2N_3S$	6,6 26,0[c]	6,6 26,2[c]	81
XV	281—282	$C_{11}H_{10}BrI_2N_3S$	5,9 22,8[c]	5,8 23,1[c]	70
XVI	251—253	$C_{11}H_{10}I_2N_4O_2S$	6,3	6,2	60
XVII	148—149	$C_{14}H_{15}I_2N_3S$	8,4[b]	8,2[b]	75

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[a] The following solvents were used to crystallize the compounds: ethanol for I, III, VI, XIb, XII, and XIV-XVII, DMF—water (15:1) for II and V, ethanol—water (5:1) for VII, water for VIII, carbon tetrachloride for IXa, benzene for IXb and Xa,b, dioxane for XIa, dioxane—water (12:1) for IV, and DMF for XIII. [b] Nitrogen. [c] Iodine.

(1:3)] was heated on a boiling water bath for ~15 min until the solid material had dissolved completely. The solution was cooled, and the precipitate was separated and washed with cold ethanol.

4-Phenyl-5-(p-nitrophenyl)-1,2,4-triazole-3-thione Sodium Salt (VIII). This compound was obtained by a method similar to that used to prepare VII.

2-Cinnamoyl-4-phenyl-5-(p-tolyl)-1,2,4-triazole-3-thione (Xa) and 3-Cinnamoylthio-4-phenyl-5-(p-tolyl)-1,2,4-triazole (IXa). A mixture of 2.67 g (10 mmole) of VII, 1.66 g (10 mmole) of cinnamoyl chloride, and 40 ml of dry benzene was stirred thoroughly at room temperature for 50 min, after which the precipitated Xa was removed by filtration, washed with water, and dried. Evaporation of the benzene from the filtrate gave IXa.

2-Benzoyl-4-phenyl-5-(p-tolyl)-1,2,4-triazole-3-thione (Xb) and 3-Benzoylthio-4-phenyl-5-(P-tolyl)-1,2,4-triazole (IXb). These compounds were obtained from VII and benzoyl chloride by a method similar to that used to prepare Xa and IXa.

3-Cinnamoylthio-4-phenyl-5-(p-nitrophenyl)-1,2,4-triazole (XIa). A mixture of 3.2 g (10 mmole) of VIII, 1.66 g (10 mmole) of cinnamoyl chloride, and 50 ml of dry benzene was stirred thoroughly at room temperature for 50 min, after which the precipitated sodium chloride was removed by filtration, and 35 ml of ether was added to the filtrate. The precipitate was removed by filtration and dried.

3-Benzoylthio-4-phenyl-5-(p-nitrophenyl)-1,2,4-triazole (XIb) was similarly obtained from VIII and benzoyl chloride.

Bis[4-phenyl-5-(p-tolyl)-1,2,4-triazol-3-yl] Disulfide (XII). A solution of 1.3 g (5 mmole) of iodine in 50 ml of ethanol was added dropwise with thorough stirring and ice cooling in the course of 30 min to a solution of 2.89 g (10 mmole) of VII in 25 ml of ethanol. After all of the iodine had been added, the reaction mixture was stirred at room temperature for another 30 min. The resulting precipitate was separated by filtration.

Similar iodination of VIII gave bis[4-phenyl-5-(p-nitrophenyl)-1,2,4-triazol-3-yl] disulfide (XIII).

4-Iodomethyl-4,5-dihydro-6-(p-tolyl)thiazolo[2,3-c]-1,2,4-triazole Hydriodide (XIV). A solution of 2.54 g (10 mmole) of iodine in 100 ml of ethanol was added dropwise with thorough stirring and ice cooling to a solution of 2.31 g (10 mmole) of III in 15 ml of ethanol. After all of the iodine solution had been added, the reaction mixture was stirred for another 30 min at room temperature. The precipitate was removed by filtration and washed with ether.

Thiazolo[2,3-c]triazoles XV-XVII were similarly obtained by iodination of IV-VI.

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SYNTHESIS OF 2-(4'-METHYL-1',3'-IMIDAZOLIDON-1'-YL)-sym-TRIAZINES

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N-Cyano-N-allylamino-sym-triazines, which were synthesized by the reaction of allyl bromide and the potassium salts of cyanoamino-sym-triazines, were converted to 2-(4'-methyl-1',3'-imidazolidon-1'-yl)-sym-triazines by the action of hydrogen peroxide in an alkaline medium. A similar transformation occurred in hydrochloric acid or under the influence of hydrogen chloride in alcohol. The structures of the products were confirmed by IR and mass-spectral data and alternative synthesis.

sym-Triazine derivatives have great practical value as chemical agents for the protection of plants. Epoxypropylamino-sym-triazines could be of definite interest as herbicides if one takes into account their structural similarity to the preparation "metoprotrin" [2-methylmercapto-4-isopropylamino-6-(3-methoxypropylamino)-sym-triazine], which displays pronounced selectivity with respect to grain crops [1].

In order to study the possibility of obtaining epoxypropylamino derivatives of sym-triazines we synthesized N-cyano-N-allylamino-sym-triazines and studied their behavior under epoxidation conditions. The synthesis of N-cyano-N-allylamino-sym-triazines I-IX (see Table 1) was accomplished by the reaction of the potassium salts of cyanoamino-sym-triazines with allyl bromide.

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