A NEW METHOD OF SYNTHESIZING MESOIONIC 1,2,4-TRIAZOLE-3-THIONES AND THEIR SPECTRA

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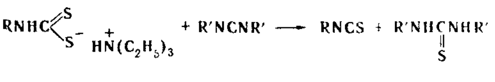
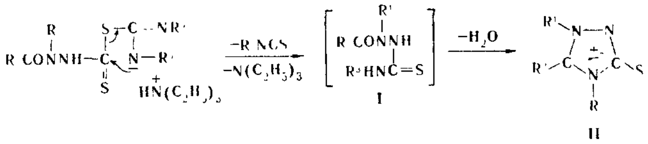
Mesoionic 1,2,4-triazole-3-thiones have been synthesized by the reaction of 1-acyl-1-arylhydrazines and 1-acyl-1-alkylhydrazines with isothiocyanates in the presence of triethylamine. The structure of the compounds obtained has been confirmed by a study of their UV, IR, PMR, and mass spectra.

In the presence of a tertiary amine, dithiocarbamates react with carbodiimides to form isothiocyanates [1].

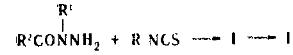


In an attempt to use this method to replace the amino groups of 1-acyl-1-alkylhydrazines by isothiocyanate groups, which should lead after intramolecular cyclization to mesoionic oxathiazole-2-thiones, we found that the reaction took place anomalously. When the carbodiimide used was diphenylcarbodiimide, the reaction product proved to be the mesoionic 1,2,4-triazole-3-thione (II, R^3 = Ph). Phenyl isothiocyanate was present in the reaction mixture: it was identified by its reaction with aniline. It is possible to suggest a reaction mechanism with the intermediate formation of 1,4-disubstituted 1-acylthiosemicarbazides (I).



The possibility of such a reaction in principle is known [2,3]. 1,4-Disubstituted 1-acylthiosemicarbazides cyclize on being heated to their melting points and are also intermediates in the reaction of 1,4-disubstituted thiosemicarbazides (III) with acyl chlorides, leading to salts of mesoionic triazolethiones. The salts are converted into the bases by treatment with pyridine or on heating [3].

On the basis of these facts it appeared possible to develop a simpler and more convenient method for the synthesis of compounds of type (II) from acylhydrazines and isothiocyanates in the following way:



$$R'CO\overset{R'}{N}NH_2 + RNCS \longrightarrow I \longrightarrow II$$

In the reaction of 1-acylhydrazines with isothiocyanates it is fairly difficult to isolate the pure acylthiosemicarbazides (I), since even in their preparation and subsequent recrystallization they partially cyclize into the mesoionic triazolethiones (II), as can be seen from the IR spectra of the reaction products. When triethylamine is added to the reaction mixture, however, cyclization takes place completely and the mesoionic triazoles are produced without the intermediate isolation of the acylthiosemicarbazides.* The

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*When this paper was in press, a communication appeared [9] in which the same method of obtaining mesoionic 1,2,4-triazole-3-thiones is described.

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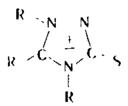
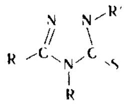
TABLE 1


II


IV

Comp.	R^1	R^2	R^3	Empirical formula	mp, °C	Solvent for recrystallization	ν_{NCS}, cm^{-1}	λ_{max}, nm (log ε)	τ, ppm				Yield, % (method of synthesis)
									CH_3	C_6H_5	5-H	other protons	
II a	C_6H_5	C_6H_5	C_6H_5	$C_{20}H_{15}N_3S$	Does not melt below 350	$HCON(CH_3)_2$ + + $(CH_3)_2CO$	1352 s 1378 m	234 (4,32) 330 (3,38)	—	2,26 (R^1) 2,42 (R^2)	—	—	100 (B) 33 (A)
II b	CH_3	H	C_6H_5	$C_9H_9N_3S$	250—251	$HCON(CH_3)_2$ + + $(CH_3)_2CO$	1345 s	236 (4,02)	5,50	2,05	0,21	—	42 (B)
II c	C_6H_5	C_6H_5	CH_3	$C_{15}H_{13}N_3S$	273—273,5	$HCON(CH_3)_2$ + + CH_3CN	1335 s 1360 m 1370 m	254 (4,33) 326 (3,39)					47 (C)
II d	$C_6H_5CH_2$	H	CH_3	$C_{10}H_{11}N_3S$	224,5—225	CH_3CN	1345 1365	250 (4,24)	5,79	2,24	0,52	4,23 (CH_2)	65 (C) 29 (B)
II e	CH_3	H	CH_3	$C_4H_7N_3S$	235	$CH_3CN + C_2H_5OH$	1345	248 (4,35)	5,59 5,76	—	0,29	—	74 (C)
II f	C_6H_5	C_6H_5	C_4H_9	$C_{18}H_{19}N_3S$	211,5—212	C_2H_5OH	1335 s 1370 m 1380 m	256 (4,46) 324 (3,42)					60 (C)
II g	$C_6H_5CH_2$	H	C_4H_9	$C_{12}H_{15}N_3S$	208,5—209	CH_3CN	1350 s 1375 m	251 (4,49)					36 (C)
II h	CH_3	H	C_4H_9	$C_7H_{13}N_3S$	98—98,5	$C_2H_5OH + (C_2H_5)_2O$	1345 s 1360 m	250 (4,16)	5,52	—	0,24	8,65 (CH_3 in R^3)	70 (B)
IV a	$C_6H_5CH_2$	H	C_6H_5	$C_{15}H_{13}N_3S$	252,5—253	1) $HCON(CH_3)_2 + CH_3CN$ 2) $HCON(CH_3)_2$ †	1340 s 1365 m	306 (3,36)	—	2,30	0,37	4,17 (CH_2)	28 (A)
IV b	C_6H_5	CH_3	C_6H_5	$C_{15}H_{13}N_3S$	242	$CH_3CN + C_2H_5OH$	1330 m 1350 s	308 (3,36)	7,00	2,07	—	—	97 (B)

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* The compositions of the compounds were confirmed by elementary analysis (C, H, N, S).

† After recrystallization, washed with acetone.

TABLE 2. Main Fragments and Their Relative Intensities in the Mass Spectra of Compounds (II) and (IV)

Compound	m/e	Rel. intensity, %	Structure of the ion
IIa	329	19,2	$M^{+\cdot}$
	180	100	$C_6H_5\overset{+}{N}{\equiv}CC_6H_5$
IIb	191	70,7	$M^{+\cdot}$
	190	31,2	$(M-1)^+$
	118	31,2	$C_6H_5N-\overset{+}{N}{\equiv}CH$
	104	36,8	$C_6H_5\overset{+}{N}{\equiv}CH$; $M\xrightarrow{*}104$
	91	100	$C_6H_5N^{+\cdot}$
			$M\xrightarrow{*}91$, $118\xrightarrow{*}91$
	77	79	$C_6H_5^+$, $104\xrightarrow{*}77$
	42	18,4	$CH_3\overset{+}{N}{\equiv}CH$
II c	267	99	$M^{+\cdot}$
	180	16,5	$C_6H_5C{\equiv}\overset{+}{N}C_6H_5$
	164	19,5	$(M-C_6H_5CN)^{+\cdot}$
	118	12,1	$C_6H_5C{\equiv}\overset{+}{N}CH_3$
	91	100	$C_6H_5N^{+\cdot}$
	77	52	$C_6H_5^+$; $180\xrightarrow{*}77$
			$118\xrightarrow{*}77$
II d	205	21,5	$M^{+\cdot}$
	91	100	$C_7H_7^+$
	42	13,4	$CH_3C{\equiv}\overset{+}{N}H$
II e	129	87,9	$M^{+\cdot}$
	88	43,3	$(CH_3NHNCS)^+$; $M\xrightarrow{*}88$
	42	100	$CH_3\overset{+}{N}{\equiv}CH$
II f	309	39	$M^{+\cdot}$
	276	37,3	$(M-SH)^+$; $M\xrightarrow{*}276$
	180	100	$C_6H_5C{\equiv}\overset{+}{N}C_6H_5$
	118	23,9	$C_6H_5C{\equiv}\overset{+}{N}CH_3$
	104	36,5	$C_6H_5C{\equiv}\overset{+}{N}H$
	91	57	$C_6H_5N^{+\cdot}$; $180\xrightarrow{*}91$

TABLE 2 (continued)

Compound	*m/e*	Rel. intensity, %	Structure of the ion
IIf	77	87	$C_6H_5^+$, $180\xrightarrow{*}77$ $118\xrightarrow{*}77$
	41	12,8	$(CH_3CN)^{+\cdot}$
II g	247	17,7	$M^{+\cdot}$
	91	100	$C_7H_7^+$
IIh	171	74	$M^{+\cdot}$
	142	20,5	$(M-CH_8N)^{+\cdot}$
	116	28,8	$(M-CH_3N_2C)^+$
	115	100	$C_4H_9NCS^{+\cdot}$
	57	19,3	$C_4H_9^+$
	56	10,6	$CH_3N_2CH^{+\cdot}$
	42	33	$CH_3\overset{+}{N}\equiv CH$
	41	31,4	$(CH_3NC)^{-\cdot}$
II i	253	43,5	$M^{+\cdot}$
	252	20,6	$(M-1)^+$
	150	19,2	$(M-C_6H_5CN)^{+\cdot}$
	135	11,5	$C_6H_5NCS^+$
	118	53,0	$C_6H_5N_2CH^{+\cdot}$
	104	59,5	$C_6H_5\overset{+}{N}\equiv CH$, $M\xrightarrow{*}104$
	93	46,4	?
	92	18,8	?
	91	43,5	$C_6H_5N^+$, $104\xrightarrow{*}91$
	77	100	$C_6H_5^+$; $104\xrightarrow{*}77$
IVa	267	31,8	$M^{+\cdot}$
	207	27,4	$(M-HS-HCN)^+$
	167	17,7	?
	158	26,4	$(M-C_6H_5S)$; $M\xrightarrow{*}158$
	135	10,0	$(C_6H_5NCS)^+$
	118	9,0	$C_6H_5CH_2NCH^+$ $(C_6H_5NCHN)^+$
	104	10,0	$C_6H_5\overset{+}{N}\equiv CH$
	91	100	$C_7H_7^+$
	77	28,3	$C_6H_5^+$
IV b	267	18,2	$M^{+\cdot}$
	118	100	$C_6H_5C\equiv\overset{+}{N}CH_3$
	91	19,8	$C_6H_5N^{+\cdot}$
	77	53,6	$C_6H_5^+$
	41	19,0	$CH_3CN^{+\cdot}$

solvent used is tetrahydrofuran or dimethyl sulfoxide (Table 1, methods B and C, respectively; the yield is sometimes higher in the latter). It must be noted that the cyclization of the acylthiosemicarbazide takes place almost quantitatively and the losses are connected with the yield, not always high, in the reaction of the acylhydrazine with the isothiocyanate, as can be seen from the literature [3].

The reaction of acylhydrazines with isothiocyanates described in the present paper can be used for the synthesis of compounds of type (II) regardless of the nature of the substituents R^1 and R^2. However, if R^1 = aryl, it is simplest to synthesize the 1,4-disubstituted thiosemicarbazide (III) from the arylhydrazine and then to obtain the (II) after acylation and the elimination of hydrogen chloride [3]. Alkylhydrazines react with isothiocyanates to give mixtures of 1,3- and 1,4-disubstituted thiosemicarbazides [4]. Therefore, when R^1 = alkyl it is fairly difficult to obtain compound (III) in the pure state and it is more convenient to use the method of synthesis described in the present paper.

The IR spectra of the compounds obtained show a characteristic very strong band of the vibrations of the CNS grouping in the 1335-1370-cm^{-1} region; it is split in almost all the compounds. In the spectra of all these compounds there is also a series of bands in the 1400-1550-cm^{-1} region which is probably characteristic for the triazole ring, since on passing from the triazolethiones to the triazolones the relative intensities and the nature of the bands in this series do not change [5].

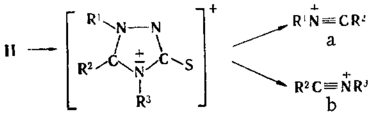
The UV spectra of compounds (II) have absorption maxima at 235-255 nm, while in some of them there is a second absorption maximum at 325-300 nm. Similar spectra are given for other compounds of this type [2, 3].

Compounds (IVa) and (IVb) (Table 1) each have one absorption maximum, at 306 and 308 nm, which sharply distinguishes them from the other triazoles obtained. Compound (IVb) was obtained instead of the expected 5-methyl-1,4-diphenyl-1,2,4-triazole-3-thione when 1-acetyl-1,4-diphenylthiosemicarbazide was heated above its melting point. It has been shown previously [3] that the reaction of 1,4-diphenylthiosemicarbazide with acetyl chloride gives the hydrochloride of the mesoionic 5-methyl-1,4-diphenyltriazole-3-thione, but after the elimination of HCl the base now has the structure (IVb), as was confirmed by independent synthesis. We repeated this synthesis and obtained a substance completely identical with compound (IVb) according to its UV and IR spectra. The purity of the compound (IVb) was checked by TLC. By analogy with (IVb), compound (IVa) was ascribed the structure not of the mesoionic triazolethione but of 2-benzyl-4-phenyl-1,2,4-triazole-3-thione. The nonmesoionic triazole-3-thiones, as described by Duffin et al. [6], have an absorption maximum at 290 nm, which enables them to be distinguished from the mesoionic isomers.

The PMR spectra confirm the structure of the compounds obtained, but it is not possible to make a distinction between compounds of types (II) and (IV). Signals in the spectra in the 7.30-9.00-ppm region show the presence of CH_3 groups. The signals of the $N-CH_3$ group (5.50-5.80 ppm) are in a weaker field than the signals of the $C-CH_3$ group (7.00-7.15 ppm). Similarly, in compound (IIa), the $N-C_6H_5$ group gives a signal in a weaker field than the $C-C_6H_5$ group. The presence of the NCHN fragment is revealed by signals in the weak field (τ from −0.3 to 0.5 ppm). For comparison, we recorded the spectrum of compound (IIi) ($R^1 = R^3 = C_6H_5$, $R^2 = H$) [7], in which τ for the protons of the phenyl group is 2.02 and τ for the proton of $C-H$ group of the triazole ring is −0.28 ppm.

The molecular weights of all the compounds obtained were determined from their mass specta. On considering the mass spectra, a characteristic fairly reproducible fragmentation under the action of electron impact is found (Table 2). The spectra of all the compounds investigated contain the molecular ion and two characteristic fragments (a and b).

Judging from the metastable ions observed in some spectra, the fragments a and b are formed directly from the molecular ion. In compounds having phenyl substituents, strong ions with m/e 77 (phenyl) and 91 are observed. Both these and others, judging from the presence of the corresponding metastable peaks, are formed from the ions a and b. The ions with a mass number of 91, the intensity of which is fairly high, probably have the structure of an azatropylium ion [8]. When $R^1 = C_6H_5CH_2$, the tropylium ion $C_7H_7^+$ is the



strongest in the spectrum, but it is impossible to determine whether it is formed directly from the molecular ion. Attempts to show the mesoionic or nonmesoionic structure of compounds (IVa) and (IVb) proved unsuccessful. In the spectrum of compound (IVb) the fragments a and b are identical and no other characteristic ions are formed. In the spectrum of compound (IVa) there is an ion with a mass number of 104 (C_6H_5NCH) – a fragment showing the position of the phenyl group, which is also confirmed by the presence of an ion with m/e 135 ($C_6H_5NCS^{+\cdot}$). A fragment with m/e 118 may be either $C_6H_5CH_2NCH$ or C_6H_5NCHN, i.e., it is impossible to establish the structure of the compounds of type (IV) unambiguously without the use of high-resolution spectrometry.

EXPERIMENTAL

The melting points were determined with the aid of a heated stage.

The UV spectra of solutions in acetonitrile were taken on an SF-4 spectrophotometer, and the IR spectra of samples in the form of tablets with KBr on a UR-10 spectrophotometer. The PMR spectra of solutions in CF_3CO_2H (c 1 M) were obtained on a YaMR-5535 spectrometer at a frequency of 40 MHz. The trifluoroacetic acid served simultaneously as internal standard (τ = 1.80 ppm).

The mass spectra were obtained on an MKh-1303 spectrometer using a system for the direct introduction of the sample into the ion source. The ionizing voltage was 70 V.

1,4,5-Triphenyl-1,2,4-triazole-3-thione (IIa). A. A mixture of 2.4 g (11 mmoles) of 1-benzoyl-1-phenylhydrazine, 1.4 ml (15 mmoles) of carbon disulfide, 1.8 ml (24 mmoles) of triethylamine, and 30 ml of absolute tetrahydrofuran was boiled for 30 min and then a solution of 2.2 g (11 mmoles) of diphenylcarbodiimide in 50 ml of tetrahydrofuran was added dropwise over 4 h 30 min. After the addition of approximately half the carbodiimide a precipitate began to deposit. The mixture was left overnight and then 1.1 g of compound (IIa) [5] was filtered off; the filtrate was evaporated in vacuum and ether was added, after which an oil separated out. The ether was decanted off and 2 ml of ethanol was added. After the crystallization of the oil another 0.12 g of the triazolethione was obtained. The ethereal solution was treated with 0.5 ml of aniline and left overnight. After elimination of the ether and recrystallization from ethanol, 0.47 g of a colorless substance was obtained; it was identified as diphenylurea by its IR spectrum and a mixed melting point.

B. A solution of 1 g (5 mmoles) of 1-benzoyl-1-phenylhydrazine in 25 ml of absolute tetrahydrofuran was boiled with 0.62 ml (6 mmoles) of phenyl isothiocyanate and 0.5 g (5 mmoles) of triethylamine for 1 h and the precipitate of (IIa) was filtered off. Yield quantitative.

1-Benzyl-4-phenyl-1,2,4-triazole-3-thione (IVa). A. A solution of 1.2 g (7 mmoles) of 1-benzyl-1-formylhydrazine in 10 ml of tetrahydrofuran was added to a mixture of 1.3 g (7 mmoles) of diphenylcarbodiimide, 0.94 g (10 mmoles) of triethylamine, and 1.22 ml (20 mmoles) of carbon disulfide in 20 ml of absolute tetrahydrofuran at a gentle boil, and the resulting mixture was boiled for 4 h. This gave 0.6 g of (IVa). R_f 0.66 on chromatography in acetone on terephthalate plates with a fixed layer of silica gel (Chromogram Sheets, Kodak); the substance was deposited in the form of a solution in dichloroethane and the spots were revealed with iodine vapor.

B. With cooling, 2.7 g (20 mmoles) of phenyl isothiocyanate was added to 3.05 g (20 mmoles) of 1-benzyl-1-formylhydrazine in 20 ml of absolute benzene and the mixture was boiled for 30 min. After cooling, 3.11 g of precipitate was filtered off. This was dissolved in 40 ml of ethanol, the solution was heated to the boil, and 10 ml of a 1 M solution of K_2CO_3 in water was added. After cooling, 2.85 g of compound (IVa) was obtained.

4-Methyl-1,5-diphenyl-1,2,4-triazole-3-thione (IIc, method C). A mixture of 2.9 g (13 mmoles) of 1-benzoyl-1-phenylhydrazine and 1 g (13 mmoles) of methyl isothiocyanate in 10 ml of absolute dimethyl sulfoxide was heated at 100°C for 4 h, after which 1.92 ml (26 mmoles) of triethylamine was added and heating was continued for another 4 h. After dilution with ethanol, 1.72 of compound (IIc) was isolated.

The other compounds (Table 1) were obtained from the corresponding acylhydrazines with CS_2, a carbodiimide, and NEt_3 (method A) or with an isothiocyanate and NEt_3 (methods B and C).

LITERATURE CITED

1. J. C. Jochims, Ber., 101, 1746 (1968).
2. K. T. Potts, S. K. Roy, and D. P. Jones, J. Heterocycl. Chem., 2, 105 (1965).

3. K. T. Potts, S. K. Roy, and D. P. Jones, J. Org. Chem., 32, 2245 (1967).
4. A. N. Kost and R. S. Sagitullin, Usp. Khim., 33, 361 (1967).
5. A. Ya. Lazaris, Zh. Organ. Khim., 4, 1849 (1968).
6. G. F. Duffin, I. D. Kendall, and H. T. I. Waddington, J. Chem. Soc., 799 (1959).
7. M. Busch, J. Prakt. Chem., [2], 67, 249 (1903).
8. R. C. Dougherty, R. L. Folz, and L. B. Kier, Tetrahedron, 26, 1989 (1970).
9. R. Grashey, M. Baumann, and R. Hamprecht, Tetrahedron Lett., 2939 (1972).