REACTION OF ACID HYDRAZIDES WITH SOME THIAZOLIDONES

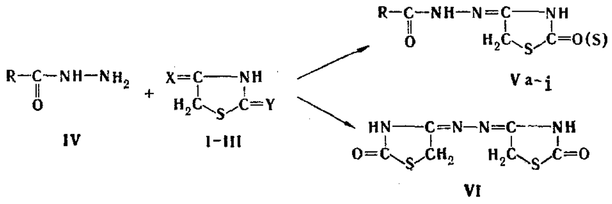
P. G. Sekachev

UDC 547.789.3:543.422.4.6:541.69

Thiazolidone 4-acylhydrazones are obtained by reaction of hydrazides of aromatic, aromatic sulfonic, and aliphatic acids with 4-thiono- and 4-imino-2-thiazolidones. The reaction of aliphatic hydrazides with 4-thiono-2-thiazolidone gives 4,4'-azino-2-dithiazolidone. Condensation of 4-imino-2-thiazolidone with formylhydrazine gives pyrazolo[3,4-d]-2-thiazolidinone.

The high reactivity of the thione group in the 4 position of the recently obtained isorhodanine (4-thiono-2-thiazolidone) [1] (I), thiorhodanine (2,4-dithionothiazolidine) [2] (II), and 2,4-dithionothiazine [3] makes it possible to use them for the synthesis of the previously inaccessible products of condensation with amino compounds; 4-amino-2-thiazolidone (III) is also active in these reactions. In the present investigation, we have studied the reaction of hydrazides (IV) with I, II, and III in order to compare the activity of the thione and imino groups and to obtain new hydrazine derivatives as potential biologically active compounds [4].

It was found that the course of the reaction depends, on the one hand, on the substituent in the 4 position of the thiazolidone and, on the other hand, on the character of radical R in IV; this can be represented by the following scheme:



I X=S, Y=O; II X=Y=S; III X=NH, Y=O

Aromatic IV react readily with I and II to give 4-acylhydrazonothiazolidones (Va-i). In this case, IV (R = p-$NH_2C_6H_4$) reacts with the hydrazine group. We were unable to introduce hydrazides of sulfonic acids into reaction with I.

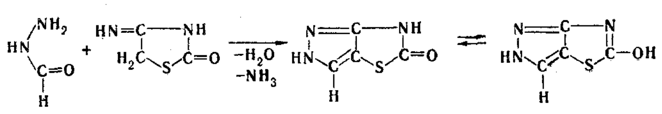
Aliphatic IV react with I to give 4,4'-azino-2-dithiazolidone (VI). 4-Acylhydrazonothiazolidones are not detected in these reactions. Compound VI was also isolated, along with Vc, from the condensation of I with IV (R = p-$CH_3C_6H_4$).

We introduced imino compound III into reaction with IV; this made it possible to eliminate the possible side effect of the liberated hydrogen sulfide. In this case, we obtained 4-acylhydrazonothiazolidones with both aromatic and aliphatic IV. The products of the reaction of IV with III were identical to the corresponding 4-acylhydrazonothiazolidones obtained by reaction of IV with I. The fact that azine VI, which is not obtained in the reaction of a number of 4-acylhydrazonothiazolidones with I, is not formed in this reaction provides a basis for assuming that the formation of the azine occurs only in the case of condensation of labile IV with thio compound I and is caused by the action of hydrogen sulfide on the C – N bond.

The reaction of formylhydrazine IV (R = H) and III occurs with subsequent closing of the pyrazole ring to give a two-ring product – pyrazolo[3,4-d]-2-thiazolidone (VII) via the scheme

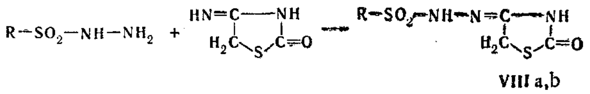
---

Central Scientific-Research Institute of Paper, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1351-1353, October, 1973. Original article submitted November 22, 1972.



VII

The use of III makes it possible to also introduce hydrazides of sulfonic acids into the reaction to give products VIIIa,b:



VIII a,b

The characteristics of the synthesized substances are presented in Table 1.

The IR spectra of the compounds have intense absorption bands of carbonyl groups. Moreover, the absorption of the $C_{(2)}=O$ stretching vibrations for the majority of the compounds differs only slightly from the corresponding band of the spectra of thiazolidine-2,4-dione (1690 cm^{-1}) and 4-imino-2-thiazolidone (1695 cm^{-1}). This band is shifted to ~1728 cm^{-1} for compounds in which conjugation of the aromatic ring with the heteroring and disruption of the conjugation in the ring $-\underset{|}{N}=\underset{|}{C}=O$ grouping are possible. Amide carbonyl absorption is observed at 1670 cm^{-1}.

The character of the $C=N$ bond of V-VII differs considerably from its state in 4-imino- and 4-phenylimino-2-thiazolidone. The spectra of the latter have an intense absorption band at 1525 cm^{-1} from a strongly polarized $C=N$ bond. Polarization of this bond in 4-phenylhydrazono-2-thiazolidone is lowered due to the adjacent nitrogen atom (1605 cm^{-1}). The presence of a carbonyl group in the substituent of V and of an SO_2 group in VIII increases the absorption band frequency to 1640 cm^{-1}.

The formation of a pyrazole ring is confirmed by a number of characteristic absorption bands: 3072, 1540, 1242, 1040, 920, and 800 cm^{-1} [5]. The absorption at 3662 and 1191 cm^{-1} confirms the presence of a tautomeric form containing a hydroxyl group [6].

Absorption at ~1245 cm^{-1} is characteristic for thiazolidines with a free methylene group in the 5 position. This band is found in the spectra of more than 15 compounds at 1235 to 1248 cm^{-1} and corresponds to the $-CH_2-S-$ grouping [7]. The absence of this band is apparently a good characteristic of 5-substituted thiazolidones.

The electronic spectra of the compounds are represented by three absorption bands at 230, 260, and 290 nm. In addition, absorption at 311 nm, caused by the thione chromophore [8], appears in the spectrum of Vb.

EXPERIMENTAL

The acid hydrazides were obtained by known methods from the corresponding esters, amides, or acid chlorides.

The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrophotometer. The UV spectra of solutions ($1 \cdot 10^{-4}$ mole/liter in ethanol and saturated solutions in heptane) were obtained with a Unicam-SP-800 scanning spectrophotometer (layer thickness 1 cm).

TABLE 1. Products of the Condensation of Thiazolidones with Hydrazides of Carboxylic and Sulfonic Acids

Comp.	mp, °C	Empirical formula	Found, %		Calc., %		Yield, %
			N	S	N	S	
Va	202	$C_{10}H_9N_3O_2S$	17,5	13,3	17,9	13,6	28
Vb	250—252	$C_{10}H_9N_3OS_2$	16,5	25,4	16,8	25,5	40
Vc	188	$C_{11}H_{11}N_3O_2S$	16,7	12,5	16,9	12,8	20
Vd	208—209	$C_{10}H_{10}N_4O_2S$	22,1	13,1	22,4	12,8	30
Ve	196—197	$C_{10}H_8BrN_3O_2S$	13,5	—	13,4	—	32
Vf	173	$C_{11}H_{11}N_3O_2S$	17,0	12,8	16,9	12,9	25
Vg	214—215	$C_{14}H_{11}N_3O_3S$	13,6	10,2	14,0	10,6	29
Vh	203—204	$C_{14}H_{12}N_6O_4S_2$	21,1	15,9	21,4	16,3	38
Vi	192—193	$C_5H_7N_3O_2S$	24,7	19,0	24,2	18,5	80
VI	234 (dec.)	$C_6H_6N_4O_2S_2$	23,9	27,9	24,3	27,8	26
VII	191	$C_4H_3N_3OS$	30,2	23,2	29,8	22,7	92
VIIIa	195	$C_9H_9N_3O_3S_2$	15,9	24,0	15,5	23,6	44
VIIIb	191	$C_{10}H_{11}N_3O_3S_2$	14,5	22,4	14,8	22,5	32

4-Benzoylhydrazono-2-thiazolidone (Va). A 3.99 g (0.03 mole) sample of isorhodanine and 4.08 g of benzoic acid hydrazide were refluxed in 30 ml of ethanol for 1 h, after which the mixture was cooled and treated with an equal volume of water. The precipitate was removed by filtration to give 1.9 g (28%) of colorless needles with mp 202° (from water).

Similarly obtained were the following compounds: Vc by reaction of isorhodanine with p-toluic acid hydrazide, Vd by reaction of isorhodanine with p-aminobenzoic acid hydrazide, Ve by reaction of isorhodanine with p-bromobenzoic acid hydrazide, Vf by reaction of isorhodanine with phenylacetic acid hydrazide, Vg by reaction of isorhodanine with 3-hydroxy-2-naphthoic acid hydrazide, and Vh by reaction of isorhodanine with isophthalic acid dihydrazide. Reaction of thiorhodanine with benzoic acid hydrazide by this method gave Vb.

4-Acetylhydrazono-2-thiazolidone (Vi). A mixture of 1.16 g (0.01 mole) of 4-imino-2-thiazolidone and 0.74 g of acetylhydrazine in 10 ml of absolute ethanol was refluxed for 10 h. The precipitate was removed by filtration to give 1.38 g (80%) of a white hygroscopic substance with mp 191-192° (from dioxane).

The following compounds were similarly obtained: VIIIa by reaction of 4-imino-2-thiazolidone with benzenesulfonic acid hydrazide, VIIIb by reaction of 4-imino-2-thiazolidone with p-toluenesulfonic acid hydrazide, IX by reaction of 4-imino-2-thiazolidone with formic acid hydrazide, and Va by reaction of 4-imino-2-thiazolidone with benzoic acid hydrazide.

LITERATURE CITED

1. A. P. Grishchuk, I. D. Komaritsa, and S. N. Baranov, Khim. Geterotsikl. Soed., 706 (1966).
2. A. P. Grishchuk, Khim. Geterotsikl. Soed., 372 (1966).
3. A. P. Grishchuk and G. I. Roslaya, Khim. Geterotsikl. Soed., 537 (1966).
4. Taniyama Yasui Utida, J. Pharm. Soc. Japan, 74, 374 (1954).
5. C. R. Hauser and C. E. Cain, J. Org. Chem., 23, 1142 (1958).
6. L. Bellamy, Infrared Spectra of Complex Molecules, Wiley (1958).
7. G. F. Bol'shakov, E. A. Glebovskaya, and Z. G. Kaplan, Infrared Spectra and X-Ray Diffraction Patterns of Heteroorganic Compounds [in Russian], Khimiya, Moscow (1967), p. 4.
8. G. F. Bol'shakov, V. S. Vatago, and F. B. Agrest, Ultraviolet Spectra of Heteroorganic Compounds [in Russian], Khimiya, Moscow (1969), p. 18.