SYNTHESIS OF 2,5-SUBSTITUTED 1,3,4-THIADIAZOLES FROM 3-PHENYL-5-METHYL-4- ISOXAZOLYLHYDRAZIDE

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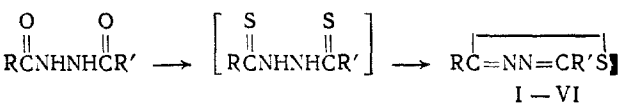
In [1], a synthesis of diacylhydrazines from 3 phenyl-5-methyl-4-isoxazolylhydrazide has been proposed. Considering that different cyclization reactions with the formation of the corresponding heterocycles are inherently specific for disubstituted hydrazines, we used diacylhydrazines for the synthesis of 2,5-disubstituted 1,3,4-thiadiazoles I-VI, which are potentially biologically active compounds.

The most convenient method for the synthesis of both symmetric and asymmetric 1,3,4-thiadiazoles from diacylhydrazines is cyclodehydration of the latter by phosphorus pentasulfide [2, 5]. The reaction proceeds with the formation of thiodiacylhydrazines as intermediate products.



I–VI

I-VI: R'= 3-phenyl-5-methyl-4-isoxazolyl; I: R = 3-phenyl-5-methyl-4-isoxazolyl; II: R = 2-furyl; III: R = 5-nitro-2-furyl; IV: R = 5-bromo-2-furyl; V: R = (2-furylvinyl); VI: R = (5-nitro-2 furylvinyl).

Compound I was obtained by cyclodehydration of the corresponding symmetric diacylhydrazine by phosphorus pentasulfide in dioxane at a temperature of 80°C. Either increase or decrease of the temperature leads to a decrease in the yield of the product.

The cyclodehydration of diacylhydrazines containing a furan ring was carried out in tetrahydrofuran.

The individual state and the structure of the compounds obtained was confirmed by thin-layer chromatography, elemental analysis, and IR spectroscopy.

In the IR spectra, there is an absorption band in the 1600 cm^{-1} region characterizing the vibrations of the thiadiazole ring, and a band in the 750 cm^{-1} region corresponding to the deformational vibrations of this ring [3, 4].

Examination of the biological activity of the compounds obtained showed that they do not exhibit any pronounced antifungal or antibacterial action. The antiviral activity was studied on developing chicken embryos and on mice. The value of the index of protection did not exceed 40%.

EXPERIMENTAL

The course of the reaction and the individual state of the compounds obtained were controlled by thin layer chromatotraphy on "Silufol UV-254" plates in a 10:1 benzene–MeOH system. The spots were developed in UV light at the wavelength of 254 nm and by iodine vapors. The IR spectra were run on UR-20 spectrophotometer in KBr tablets.

2,5-Bis(3'-phenyl-5'-methyl-4'-isoxazolyl)-1,3,4-thiadiazole (I). A 2.2 g portion (0.01 mole) of a thoroughly ground phosphorus pentasulfide is added at 80°C to a solution of 4.0 g

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TABLE 1. Characteristics of 2,5-Disubstituted 1,3,4-Thiadiazoles I-VI

Compound	Yield, %	Mp, °C	Found, %				Empirical formula	Calculated, %				R_f
			C	H	N	S		C	H	N	S	
I	83.7	197–9	65.88	3.75	14.07	8.09	$C_{22}H_{14}N_4O_2S$	65.98	4.03	13.98	7.99	0.66
II	94.8	153–5	62.0	3.40	13.63	10.05	$C_{14}H_{11}N_3O_2S$	62.12	3.58	13.58	10.34	0.63
III	71.6	190–2	54.64	2.82	15.48	8.77	$C_{16}H_{10}N_4O_4S$	54.23	2.84	15.80	9.05	0.63
IV	69.2	153–5	49.73	2.80	10.37	7.85	$C_{15}H_{10}N_3O_2BrS$	49.49	2.59	10.82	8.25	0.57
V	81.1	138–9	64.62	4.11	12.58	9.12	$C_{18}H_{13}N_3O_2S$	64.46	3.90	12.53	9.56	0.65
VI	71.4	185–7	57.05	3.64	14.61	8.97	$C_{18}H_{12}N_4O_4S$	56.83	3.17	14.72	8.42	0.65

Note. Compound IV. Found, %: Br 20.16. Calculated, %: Br 20.47. Compound I was crystallized from ethanol, compounds II-VI from a 5:1 ethanol–dioxane mixture.

(0.01 mole) of 1,2-bis(3'-phenyl-5'-methyl-4'-isoxazolyl)hydrazine in 20 ml of dioxane. The reaction mixtures is held at this temperature for 2 h with stirring, then filtered, and the filtrate cooled. The precipitate is separated. Yield 3.33 g of compound I.

2-(3'-phenyl-5'-methyl-4'-isoxazolyl)-5-furyl-1,3,4-thiadiazole (II). A 4.0 g portion (0.013 mole) of 1-(3'-phenyl-5'-methyl-4'-isoxazolyl)-2-furoylhydrazine is dissolved with heating in 70 ml of tetrahydrofuran, and 2.85 g (0.013 mole) of ground phosphorus pentasulfide are added. The reaction mixture is stirred at the boiling point for 3 h, filtered, and the filtrate cooled, The product obtained is separated. Yield, 3.76 g of compound II.

Compounds III-VI were synthesized in a similar way as compound II. The experimental results and the data of analyses are given in Table 1.

LITERATURE CITED

1. G. V. Andosova, V. N. Konyukhov, Z. V. Pushkareva, et al., Khim.-farm. Zh., No. 8, 63-66 (1978).
2. W. J. Chombers and D. D. Coffman, J. Org. Chem., 26, 4410 (1961).
3. J. Joerdeler, J. Ohm, and O. Tegtmeyer, Chem. Ber., 89, 1534 (1956).
4. A. B. Karitzky and A. Boulton, J. Spectrochim. Acta, 171, 238 (1961).
5. R. Stolle, J. Parkt. Chem., 69, 145 (1904).