SYNTHESIS AND PROPERTIES OF SOME HYDRAZONES DERIVED FROM 5-METHYL-3-PHENYL-ISOXAZOL-4-YLCARBONYLHYDRAZINE

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Continuing a search for biologically active compounds among 3,5-disubstituted isoxazoles we have obtained a number of hydrazones (II-XI) from 5-methyl-3-phenyl-isoxazol-4-ylcarbonylhydrazine (I) (see Table 1). The synthesis of the hydrazones was performed by condensing the hydrazine (I) with carbonyl compounds as described previously [1]. As the carbonyl components we used aldehydes (resorcylaldehyde, veratraldehyde, cinnamaldehyde, β-bromocinnamaldehyde, imidazolecarbaldehyde [2], p-hydroxybenzaldehyde, p-[di(2-chlorethyl)amino]-benzaldehyde [3], and 5-nitrofurfural), and the ketone furfurylideneacetone [4], the hydrazones of these compounds in other classes [5] being biologically active compounds.

The hydrazones consisted of colorless or light-yellow crystalline substances soluble in organic solvents and insoluble in water. To confirm the chemical structure of the compounds synthesized we studied their IR spectra, which contained the characteristic frequencies of C = N stretching vibrations in the 1650-1625 cm^{-1} region [6].

EXPERIMENTAL

Pharmacological

The study of the antitumoral activity of the hydrazones was performed on random-bred white mice with transplanted tumors. The following strains of tumor were used: sarcoma 180, adenocarcinoma AK-755, Lewis's tumor, and leukemia L-1210. In view of their poor solubility, the preparations were introduced internally in gelatinized starch. The results of the trials showed that compounds (VIII, IX, and X) inhibited the growth of sarcoma 180 by 10-34% and of adenocarcinoma AK-755 by 15-29%.

The study of the antitubercular activity of the compounds was carried out in Soton's synthetic medium without serum, and also with the addition of 10% of normal horse blood serum. The $H_{32}V$ laboratory strain of tuberculosis mycobacteria was used. It was found that compounds (III, VI, and XI) possess a moderate tuberculostatic activity, inhibiting the growth of the tuberculosis mycobacterium in dilutions of 3.1-6.25 μg/ml in the absence of horse serum. On the addition of the serum, the activity disappeared.

The antiviral activity of the substances in relation to the causative agents of A2 and B influenza was studied in experiments on developing chick embryos and mice. The value of the protective index for some compounds was between 30 and 39%.

From the level of activity shown, the substances are of no interest for more detailed study as potential chemotherapeutic agents.

Chemical

The IR spectra were taken on a UR-20 instrument in mineral oil.

5-Methyl-3-phenylisoxazol-4-ylcarbonylhydrazone of Furfurylideneacetone (II). With heating, 2.17 g (0.01 mole) of the hydrazine (I) was dissolved in 20 ml of ethanol, and then 1.36 g (0.01 mole) of furfurylidene-

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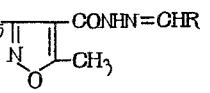
TABLE 1. The Hydrazones (III–XI) 

Compound	R	Yield, %	mp, °C*	Found, % N	Molecular formula	Calculated, % N
III	4-HOC_6H_4	43,4	239—40	12,80	$C_{18}H_{15}N_3O_3$	13,10
IV	2,4-$(OH)_2C_6H_3$	58,9	139—40	12,01	$C_{18}H_{15}N_3O_4$	12,47
V	3,4-$(CH_3O)_2C_6H_3$	78,3	207—8	11,68	$C_{20}H_{19}N_3O_4$	11,82
VI	$CH=CHC_6H_5$	94,1	196—7	13,10	$C_{20}H_{17}N_3O_2$	12,68
VII	$CBr=CHC_6H_5$	94,4	186—7 (decomp.)†	10,42	$C_{20}H_{16}BrN_3O_2$	10,24
VIII	4-$(CH_2CH_2Cl)_2NC_6H_4$	90,33	149—50‡	12,70	$C_{22}H_{22}Cl_2N_4O_2$	12,58
IX	5-NO_2(furyl-2)	93,7	200—1	16,47	$C_{16}H_{12}N_4O_5$	16,46
X	CH=CH(furyl-2)	54,1	188—90	13,32	$C_{18}H_{15}N_3O_3$	13,07
XI	imidazol-5(4)-yl	59,5	222—3	24,01	$C_{15}H_{13}N_5O_2$	23,76

*Compounds (III, V, VI, VIII, and X) were crystallized from ethanol, (IV and XI) from aqueous ethanol, and (VII and IX) from dioxane.
†Found, %: Br 19.52. Calculated, %: Br 19.47.
‡Found, %: Cl 16.32. Calculated, %: Cl 15.92.

acetone and 1-2 drops of hydrochloric acid were added and the mixture was boiled for 1 h. The solution was filtered and cooled, and the precipitate that deposited was separated off and washed with ether. Yield 3.16 g (84.1%), mp 158-9°C (from aqueous ethanol). Found, %: N 12.60. Calculated, %: N 12.52. Compounds (III-XI) were synthesized similarly to (II). The results obtained and the analyses of the products are given in Table 1.

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