tion with hexane. PMR spectrum: 2.14 (6H, m, aliphatic), 4.10 (1H, m), 4.65 (1H, m), and 7.40 (4H, m, aromatic).

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INVESTIGATION OF THE STEREOCHEMICAL DIRECTION OF THE CYANOETHYLATION OF SIX-MEMBERED HETEROCYCLIC KETONES AS A FUNCTION OF THE NATURE OF THE HETEROATOM

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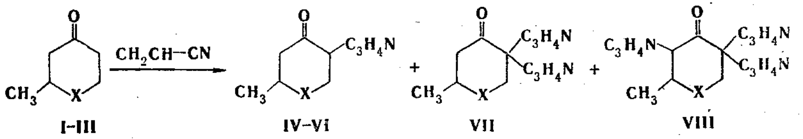
Only a mono(cyanoethyl) compound is formed from thiopyranone in the cyanoethylation of six-membered heterocyclic ketones that contain a methyl group attached to the C_2 atom of the heteroring, whereas primarily bis- and tris(cyanoethyl) derivatives are obtained from pyranone due to the effect of the heteroatom.

We have previously studied [1, 2] the cyanoethylation of some N-substituted 2,5-dimethyl-4-piperidones and 2,5-dimethyltetrahydro-4-thiopyranone. Continuing these studies, we have carried out the cyanoethylation of 1,2-dimethyl-4-piperidone (I), 2-methyltetrahydro-4-pyranone (II), and 2-methyltetrahydro-4-thiopyranone (III) with acrylonitrile in equimolar ratios in the presence of potassium hydroxide.



I, IV, VIII X=N–CH$_3$; II, V, VII X=O; III, VI X=S

From piperidone I we obtained 1,2-dimethyl-5-(β-cyanoethyl)-4-piperidone (IV) and 1,2-dimethyl-3,5,5-tris(β-cyanoethyl)-4-piperidone (VIII) in 1 and 84% yields, respectively, from tetrahydropyranone II we obtained 2-methyl-5-(β-cyanoethyl)tetrahydro-4-pyranone (V) and 2-methyl-5,5-bis(β-cyanoethyl)tetrahydro-4-pyranone (VII) in 2 and 73% yields, respectively, whereas from tetrahydrothiopyranone III we obtained only 2-methyl-5-(β-cyanoethyl)tetrahydro-4-pyranone (VI) in 20% yield.

Thus tris(cyanoethylation) product VIII is primarily formed from piperidone I, bis(cyanoethyl) derivative VII is primarily formed from pyranone II, and only mono(cyanoethylated) compound VI is obtained from thiopyranone III. This difference in the behavior of heterocyclic ketones in cyanoethylation is apparently explained by the different effects of the hetero-

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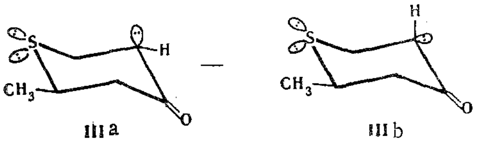
TABLE 1. Cyanoethylated Compounds IV-VIII

Compound	bp, °C (mm)	mp, °C	n_D^{20}	d_4^{20}	IR spectrum, cm-1			Found, %			Empirical formula	Calc., %		
					C=O	C≡N	N—CH$_3$	C	H	N		C	H	N
IV	140 (3)	—	1,4903	1,0604	1710	2250	2795	66,8	9.0	5,4	$C_{10}H_{16}N_2O$	66,2	8,9	5,6
VIII	—	110	—	—	1710	2247	2800	67,6	7,6	9,8	$C_{16}H_{22}N_4O$	67,0	7,7	9,6
V	135 (3)	—	1,4730	1,0886	1710	2246	—	64,5	8,0	8,5	$C_9H_{13}NO_2$	64,7	7,8	8,4
VII	—	80	—	—	1705	2250	—	65,7	7,3	2,5	$C_{12}H_{16}N_2O_2$	65,4	7,3	2,7
VI	160 (2)	—	1,5230	1,1463	1712	2250	—	59,2	7,0	7,5	$C_9H_{13}NOS$*	59,0	7,0	7,6

*Found: S 7.3%. Calculated: S 7.5%.

atoms on the conformations of the intermediately formed carbanions.

Carbanions, the electron pair of which is axially oriented, since it is known [3] that an axial hydrogen atom is more easily removed from a ketone, are formed from ketones I-III in an alkaline medium; interaction of the orbitals of the unshared pairs of electrons of the ring heteroatom and the axial electron pair of the carbanion becomes possible in this case; this interaction will depend on the nature of the heteroatom. In the case of thiopyranone III repulsion of the unshared pairs of electrons of sulfur and the axial electron pair of carbanion IIIa leads to conformation IIIb with an equatorial electron pair.



IIIa IIIb

As a consequence of this, the cyanoethyl group enters the equatorial position, and mono(cyanoethyl) derivative VI, which, like the trans isomer of 2,5-dimethyltetrahydro-4-thiopyranone [2], will undergo further cyanoethylation with difficulty, is formed. This effect is a modification of the "hockey stick effect," which consists in interaction of the orbitals of the unshared pairs of the electrons of the ring heteroatom and the axial substituent [4, 5]. This effect is not observed in the case of piperidone I and pyranone II, and their cyanoethylation reactions do not differ from the cyanoethylation of alicyclic ketones.

EXPERIMENTAL

Starting ketones I and II were synthesized by known methods, while ketone III was obtained through the methiodide of I. The IR spectra of the compounds in the form of drops in CCl_4 and KBr pellets were recorded with a UR-20 spectrometer.

1,2-Dimethyl-5-(β-cyanoethyl)-4-piperidone (IV) and 1,2-Dimethyl-3,5,5-tris(β-cyanoethyl)-4-piperidone (VIII). A 5.3-g (0.1 mole) sample of acrylonitrile in 20 ml of dry ether was added dropwise at 20°C to a mixture of 2.72 g (0.1 mole) of I and 0.2 g of powdered KOH in 50 ml of dry ether. At the end of the addition, a brown precipitate began to form. Stirring was continued at 20°C for another 4 h, after which the ether was decanted, and the precipitate was washed several times with ether. The ether extracts were combined and dried with Na_2SO_4, and the residue was distilled to give 5 g of piperidone I and 0.3 g of piperidone IV [the hydrochloride had mp 158°C (from alcohol)]. The precipitate was recrystallized several times from alcohol—acetone (1:1) to give 8 g of piperidone VIII [the hydrochloride had mp 233°C (from alcohol)].

2-Methyl-5-(β-cyanoethyl)tetrahydro-4-pyranone (VII). A 6-g (0.114 mole) sample of acrylonitrile was added at 20°C to a mixture of 13.5 g (0.114 mole) of pyranone II in 50 ml of dry ether and 0.2 g of powdered KOH, after which the mixture was stirred at 20°C for 4 h. The precipitated crystals were removed by filtration, washed several times with ether, and recrystallized from alcohol to give 7.1 g of pyranone VII. The combined ether extracts were dried with Na_2SO_4, the ether was removed by distillation, and the residue was distilled to give 4 g of pyranone II and 0.3 g of pyranone V.

2-Methyl-5-(β-cyanoethyl)tetrahydro-4-thiopyranone (VI). A solution of 6.1 g (0.115 mole) of acrylonitrile in 20 ml of ether was added dropwise at 20°C to a mixture of 15 g (0.115 mole) of thiopyranone III in 50 ml of dry ether and 0.2 g of powdered KOH, after which the mixture was stirred at 20°C for 4h and neutralized. The ether was removed by distillation, and the residue was distilled to give 10.8 g of thiopyranone III and 4.3 g of thiopyranone VI.

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SYNTHESIS AND TRANSFORMATIONS OF CHLORO DERIVATIVES OF 4,7-DIOXOBENZO-2,1,3-THIADIAZOLE

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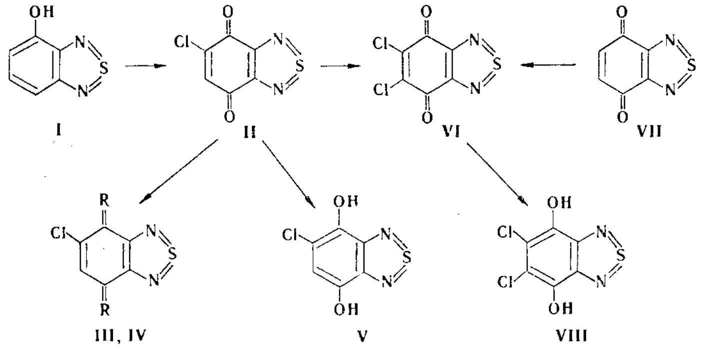
5-Chloro-4,7-dioxo- and 5,6-dichloro-4,7-dioxobenzo-2,1,3-thiadiazoles were synthesized, and their reduction to the corresponding dihydroxy derivatives was studied. The bis(semicarbazone) and bis(thiosemicarbazone) of the 5-chloro derivative were obtained, and their antivirus activities were determined.

We have previously [1, 2] reported the synthesis and chemical transformations of 4,7-dioxo- and 5-methyl-4,7-dioxobenzo-2,1,3-thiadiazoles. The present paper is a continuation of these studies and is devoted to the synthesis and proof of the structures of chloro derivatives of 4,7-dioxobenzo-2,1,3-thiadiazole.

The reaction of 4-hydroxybenzo-2,1,3-thiadiazole (I) with a 30% solution of hydrogen peroxide in the presence of an acid gives 5-chloro-4,7-dioxobenzo-2,1,3-thiadiazole (II), which reacts with 2 moles of semicarbazide or thiosemicarbazide to give, respectively, bis(semicarbazone) III and bis(thiosemicarbazone) IV.

Thiadiazole II is readily reduced by sulfur dioxide or sodium hydrosulfite to 5-chloro-4,7-dihydroxybenzo-2,1,3-thiadiazole (V).



III R=N—NH—CO—NH$_2$; IV R=N—NH—CS—NH$_2$

A C=O absorption band at 1707 cm^{-1} is present in the IR spectrum of II; this band is absent in the spectrum of V, but an absorption band of OH stretching vibrations appears at 3540 cm^{-1}.

The chlorination of II with gaseous chlorine in acetic acid gives 5,6-dichloro derivative VI in high yield; this product is identical to the quinone formed in the chlorination of 4,7-dioxobenzo-2,1,3-thiadiazole (VII) with a known structure [2].

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