2-Dimethylamino-4,4-dimethyl-5-methylenethiazoline (IIc). This compound was isolated by fractional distillation of the product of thermolysis of quaternary salts IIIc-IVc. The colorless liquid had n_D^{25} 1.5400. Found: C 56.7; H 8.4; N 16.2%. $C_8H_{14}N_2S$. Calculated: C 56.5; H 8.2; N 16.5%.

2-Dimethylamino-4-methyl-4-ethyl-5-methylenethiazoline (IId). This compound was obtained by fractional distillation of the product of thermolysis of quaternary salts IIId and IVd. The colorless liquid had n_D^{25} 1.5410. Found: C 58.5; H 8.8; N 15.5; S 16.9%. $C_9H_{16}N_2S$. Calculated: C 58.7; H 8.7; N 15.2; S 17.4%.

2-(Methyl)amino-4-methyl-4-ethyl-5-methylenethiazoline (IIe). This compound was isolated from the mixture of isomers obtained in the thermolysis of methiodides IIIe and IVe. The product had n_D^{25} 1.5410. Found: C 60.4; H 9.0; N 14.3; S 16.3%. $C_{10}H_{18}N_2S$. Calculated: C 60.6; H 9.1; N 14.1; S 16.2%.

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RING-CHAIN TAUTOMERISM OF β-KETO ESTER THIOBENZOYLHYDRAZONES

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The products of condensation of thiobenzhydrazide with methyl acetoacetate and its α-alkyl-substituted homologs have the structure of the corresponding 2,3-dihydro-1,3,4-thiadiazoles; only the derivative of α-isopropylacetoacetic acid ester has the open hydrazone form. The products of the reaction of thiobenzhydrazide with the methyl esters of 2-oxocyclopentane- and 2-oxocyclohexanecarboxylic acid are mixtures of enehydrazine and thiadiazoline forms; the percentage of the latter decreases in polar solvents.

Thiobenzhydrazide — the most accessible of the thiohydrazides — is a promising reagent that can be used for the realization of various types of tautomeric equilibria in the products of its condensation with carbonyl compounds. Thus the products of condensation of thiobenzhydrazide with aldehydes and ketones serve as an example of hydrazone—1,3,4-thiadiazoline ring-chain tautomerism [1], whereas the product of the reaction with acetylacetone serves as an example of 1,3,4-thiadiazoline—5-hydroxypyrazoline ring—ring tautomerism [2]. In the case

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TABLE 1. β-Keto Ester Thiobenzoylhydrazones I-VI*

Compound	R	R′	R_f	Found, %		Empirical formula	Calc., %	
				C	H		C	H
I	CH_3	H	0,75	57,5	5,5	$C_{12}H_{14}N_2O_2S$	57,6	5,6
II	CH_3	CH_3	0,74	59,3	6,0	$C_{13}H_{16}N_2O_2S$	59,1	6,1
III	CH_3	C_2H_5	0,77	60,3	6,4	$C_{15}H_{18}N_2O_2S$	60,4	6,5
IV	CH_3	i-C_3H_7	0,75	61,5	6,9	$C_{15}H_{20}N_2O_2S$	61,6	6,9
V	$(CH_2)_3$		0,77	66,6	5,6	$C_{14}H_{16}N_2O_2S$	60,8	5,8
VI	$(CH_2)_4$		0,78	65,2	6,3	$C_{15}H_{18}N_2O_2S$	62,1	6,3

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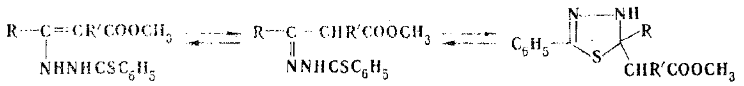
*Compounds I-IV and VI are viscous uncrystallizable liquids for which one cannot determine the densities or refractive indexes; they also decompose during vacuum distillation. Compound V is a crystalline substance with mp 117°C.

of the products of condensation of β-keto esters with thiobenzhydrazide (I-VI) that we investigated (with allowance for the fact that the hydrazones of these β-dicarbonyl compounds display the ability to undergo hydrazone—enehydrazine linear tautomerism [3-4]) one might, in principle, have expected a tautomeric equilibrium with the participation of three forms, viz., hydrazone (A), enehydrazine (B), and 1,3,4-thiadiazoline (C).



B A C

I—VI

I $R=CH_3$, $R'=H$; II $R=R'=CH_3$; III $R=CH_3$, $R'=C_2H_5$; IV $R=CH_3$, $R'=i\text{-}C_3H_7$;
V $R—R'=—(CH_2)_3—$; VI $R—R'=—(CH_2)_4—$

First of all, let us point out that only the reaction of acetoacetic ester with thiobenzhydrazide [5], as a result of which, instead of the expected alkylidene derivative of a β-keto ester, acetone thiobenzoylhydrazone, which, according to refined data, is 2,2-dimethyl-5-phenyl-2,3-dihydro-1,3,4-thiadiazole [6], was isolated, has been previously described. However, we obtained the desired products of condensation of selected β-keto esters (I-VI, Table 1) when we carried out the reaction under mild conditions.

According to the results of a spectroscopic study, the β-keto ester derivatives of the open series I-IV exist in a single tautomeric form that has the 1,3,4-thiadiazoline structure in media with different polarities (CCl_4, $CDCl_3$, and d_6-DMSO). Thus absorption bands at 1620 and 1745 cm^{-1}, which should be assigned to the stretching vibrations of the C=N bond and an unconjugated ester grouping, and an absorption band at 3360 cm^{-1}, which is due to NH stretching vibrations, are observed in their IR spectra recorded for the substances in the condensed state and for solutions in CCl_4 and $CHCl_3$. One should particularly note the absence of absorption at 1650-1680 cm^{-1}, which is characteristic for the enehydrazine form of β-keto ester hydrazones [3, 4].

The high-field position of the signals of the CH_3 group (1.56-1.89 ppm) and of the NH proton (6.0-7.0 ppm) in the PMR spectra (Table 2), which is characteristic for 1,3,4-thiadiazolines [2, 6], serves as further proof of the structure. In addition, the anisochronicity of the protons of the CH_2 group of I is significant; this is associated with the presence of an asymmetric carbon atom in 1,3,4-thiadiazoline form C. Finally, the unambiguous conclusion that this compound has the thiadiazoline structure follows from its ^{13}C NMR spectrum; the characteristic signals in it are the signals at 79.5 and 145.5 ppm, which should be assigned to the carbon atoms in the 2 and 5 positions of the thiadiazoline ring (the signals of the carbon atoms of the methyl groups are found at 25.8 and 44.8 ppm, while the signal of the methylene group is located at 51.1 ppm, and the signal of the C=O group is found at 169.9 ppm).

Compounds II-IV, which have two chirality centers, are represented by pairs of diastereomers with 1,3,4-thiadiazoline form C, which follows from doubling of most of the signals in their PMR spectra (Table 2; the ratios of the diasteromers in the II-IV series are 58:42, 57:43, and 65:35, respectively).

TABLE 2. PMR Spectra of β-Keto Ester Thiobenzoylhydrazones I-VI (solutions in $CDCl_3$)*

Compound	Chemical shift, ppm (J, Hz)				
	OCH_3	H	R	R′	CH
I	3,66	6,83	1,87	2,73 d (1H); 3,08 d (1H) (J_{AB}=17,6 Hz)	
II	3,62; 3,61	6,52; 6,54	1,60; 1,68	1,26 d (7,2); 1,30 d (7,2)	3,02 q (7,2) 2,78 q (7,2)
III	3,62	6,66	1,63	1,60—1,92 m (CH_2); 0,81 t (CH_2, 7,0)	2,44—2,82 m
	3,61	6,26	1,56	1,60—1,92 m (CH_2); 0,81 t (CH_2, 7,0)	2,44—2,82 m
IV	3,63	6,06	1,65	0,91 d (CH_3, 7,0); 1,07 d (CH_3, 7,0); 1,84—2,12 m (CH)	2,86 d (6,6)
	3,63	6,52	1,65	0,90 d (CH_3, 7,0); 1,03 d (CH_3, 7,0); 1,84—2,12 m (CH)	2,63 d (6,0)
V	3,72	7,10		1,70—2,20 m, 2,50—2,78 m	2,80—3,20 m
VI	3,72; 3,74	6,88; 7,10		1,30—1,97 m, 2,04—2,28 m; 2,66—2,70 m	3,20—3,38 m

*In II-IV the 1,3,4-thiadiazoline form is represented by two diastereomers. Compounds V and VI are tautomeric mixtures of the enehydrazone and 1,3,4-thiadiazoline forms; data for only the latter are presented. Enehydrazine form of V: 3.52 ppm (methoxy group protons) and 11.30 ppm (NH protons). Enehydrazine form of VI: 3.61 ppm (methoxy group protons) and 12.17 ppm (NH protons).

Compound IV occupies a somewhat special position. The PMR spectrum of a solution of IV in d_6-DMSO contains, in addition to the signals of diastereomers of 1,3,4-thiadiazoline form C, additional signals at 1.96, 3,55, and 12.20 ppm, which most likely correspond to hydrazone form A (protons of a methyl group, the methoxy group, and the NH bond). The development of enehydrazine form B here is extremely unlikely, since, according to the data on the tautomerism of β-keto ester hydrazones, introduction of an isopropyl grouping into the α position leads to a complete shift of the equilibrium to favor precisely the hydrazone tautomer [3]. The percentage of the open tautomeric form in a solution of IV in d_6-DMSO does not exceed 10%. Its development in the case of IV can be explained by an increase in the spatial population in the zone of the C=N bond, which hinders the formation of a cyclic tautomer [7].

The products of the reaction of cyclic β-keto esters with thiobenzhydrazide (V and VI) exist in solutions as mixtures of the enehydrazine and 1,3,4-thiadiazoline forms ($B \rightleftarrows C$). In addition to the absorption band at 1745 cm^{-1}, which is due to the stretching vibrations of the C=O bond of an unconjugated ester grouping of cyclic form C, absorption bands at 1680 (for V) and 1660 cm^{-1} (for VI) are observed in the IR spectra of their solutions in CCl_4; the latter bands correspond to the stretching vibrations of the C=O bond of strongly conjugated enehydrazine form B. The percentage of enehydrazine form B, estimated from the PMR data (Table 2), in a solution of V in CCl_4 is 51%, as compared with 26% for VI. The percentage of enehydrazine tautomer B increases when more polar solvents (d_6-DMSO and d_7-DMF) are used.

The development of the B form on passing from β-keto ester derivatives of the open series (I-IV) to cyclic β-keto ester derivatives V and VI is in agreement with data on the hydrazone—enehydrazine tautomerism of β-keto esters [8] and the ring-chain equilibrium of the products of condensation β-keto esters with amino alcohols [9], according to which the introduction of a cyclic element in the β-dicarbonyl component favors the conjugated enehydrazine or enamine form.

Two resonance signals of a methoxy group at 3.72 and 3.74 ppm in the PMR spectrum of VI are due to 1,3,4-thiadiazoline form C; this indicates that the cyclic tautomer is represented by two diastereomers (the ratio of the diastereomers is 70:30). One signal at 3.72 ppm in the spectrum of V belongs to the methoxy group of form C, and its broad form makes it possible to assume that superimposition of the corresponding signals of the diastereomers of this form occurs in this case. In fact, two sets of resonance signals correspond to 1,3,4-thiadiazoline form C in the ^{13}C NMR spectrum of V; for example, two signals of comparable intensity at 75.0 and 77.1 ppm correspond to the quaternary carbon atoms in the 3 position of the thiadiazoline ring. All of this leads to the conclusion that the 1,3,4-thiadiazoline form exists in the form of two diastereomers also in the case of V.

Thus the products of the reaction of β-keto esters with thiobenzhydrazide, like the corresponding derivatives of other carbonyl compounds [1, 10], have a tendency to exist in the ring 1,3,4-thiadiazoline form; however, tautomeric conversion to the hydrazone or enehydrazine form can be realized by a directed change in the structure of the β-dicarbonyl component.

EXPERIMENTAL

The IR spectra of 1% solutions of the compounds in $CHCl_3$ and CCl_4 and of suspensions in mineral oil were recorded with a UR-20 spectrometer. The PMR spectra of 10% solutions in $CDCl_3$, d_6-DMSO, or d_7-DMF were recorded with a Tesla BS-497 spectrometer (100 MHz). The ^{13}C NMR spectra of 10% solutions in $CDCl_3$ were recorded with a CFT-20 spectrometer (20 MHz) under pulse conditions with Fourier transformation under conditions of noise decoupling of the protons and with hexamethyldisiloxane as the internal standard. The tautomeric and configurational compositions were determined by integration of the signals of the corresponding tautomeric or configurational forms; the accuracy in the determination was ±3%. The solutions were allowed to stand for no less than 24 h to establish equilibrium. Thin-layer chromatography was carried out on L 40/100 μm silica gel with hexane–ether (1:1) as the eluent.

β-Keto Ester Thiobenzoylhydrazones (I-VI). A mixture of 25 mmole of thiobenzhydrazide and 25 mmole of the corresponding β-keto ester in 25 ml of methanol was allowed to stand for 24 h, after which the condensation product was isolated by TLC. Data on I-VI, the yields of which were no less than 80%, are presented in Table 1.

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