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SYNTHESIS AND STRUCTURE OF DIHYDRAZONES OBTAINED FROM THE DIHYDRAZIDE OF 1,3,4-THIADIAZOLE-2,5-DITHIOGLYCOLIC ACID

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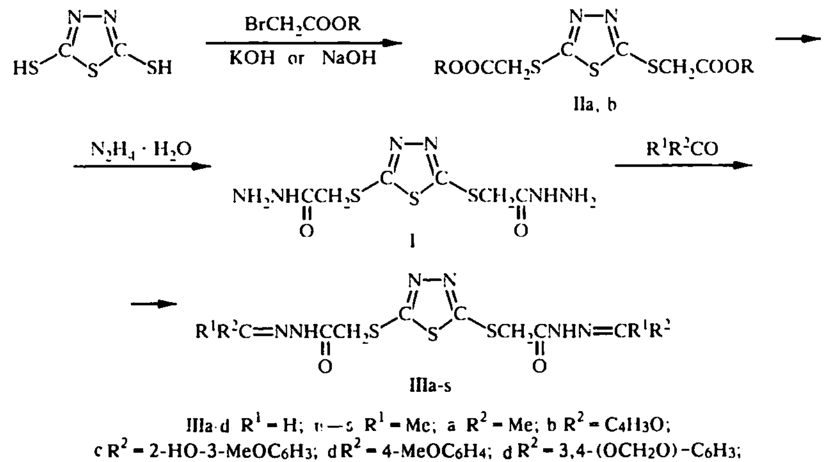
Using PMR spectroscopy we have established that dihydrazones, obtained by condensation of the dihydrazide of 1,3,4-thiadiazole-2,5-dithioglycolic acid with aldehydes, ketones, or b-dicarbonyl compounds, exist in solutions as a mixture of stereoisomeric forms due to conformational and geometric isomerism.

E′,Z′-conformational (rotational) isomerism as a result of hindered rotation about the N–CO amide bond and *E,Z*-geometric *syn-*, *anti*-isomerism relative to the N=C bond in hydrazones [1, 2] and aroylhydrazones [3] have been studied in sufficient detail. However, no data are available in the literature on such a phenomenon in ambifunctional compounds containing two hydrazone groups. With the goal of filling in the existing gap in this area, we synthesized and studied the structure of dihydrazones based on the dihydrazide of 1,3,4-thiadiazole-2,5-dithioglycolic acid (I).

In patent [4], the starting dihydrazide (I) is obtained by esterification of the corresponding acid followed by condensation of the diester formed (IIa) with hydrazine hydrate.

We proposed a more convenient and simple method for synthesis of dihydrazide I. The diesters IIa, b were obtained as a result of direct alkylation of 2,5-dimercapto-1,3,4-thiadiazole by the corresponding esters of monobromoacetic acid in the presence of potassium hydroxide, both in an isopropanol medium and in water under phase transfer catalysis conditions in the presence of triethylbenzylammonium chloride (TEBA). Compounds IIa, b easily react in isopropanol with hydrazine hydrate, forming dihydrazide I, the condensation of which with aldehydes or ketones leads to dihydrazones (IIIa-s). Their characteristics are presented in Tables 1 and 2.



IIIa-d $R^1 = H$; e–s $R^1 = Me$; a $R^2 = Me$; b $R^2 = C_4H_3O$;
c $R^2 = 2\text{-HO-3-MeOC}_6H_3$; d $R^2 = 4\text{-MeOC}_6H_4$; d $R^2 = 3,4\text{-}(OCH_2O)\text{-}C_6H_3$;
f $R^2 = 2,4\text{-}(HO)_2C_6H_3$; g $R^2 = 3,4\text{-}(HO)_2C_6H_3$; h $R^2 = 4\text{-Me}_2NC_6H_4$; i $R^2 = 2,3\text{-}(MeO)_2C_6H_3$;
j $R^2 = 2\text{-HOC}_6H_4$; k $R^2 = CH_2CH(OH)CH_3$; n $R^2 = Me$; o $R^2 = CH_2CH_2CH{=}CH_2$;
p $R^2 = CH{=}C(CH_3)_2$; q $R^2 = Ph$; r $R^2 = 2\text{-OHC}_6H_4$; s $R^2 = 4\text{-HOC}_6H_4$
l $R^1 + R^2 = (\text{-}CH_2\text{-})_5$; m $(R^1 + R^2)$ =N- methylpiperidone

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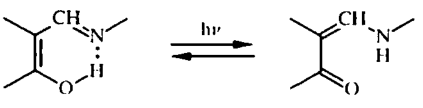
TABLE 1. Characteristics of Hydrazones IIIa-s, IV-VI

Compound	Found, %			Empirical formula	Calculated, %			mp, °C	Yield, %
	C	H	S		C	H	S		
IIIa	34,76	4,09	27,82	$C_{10}H_{14}N_6O_2S_3$	34,67	4,07	27,76	190 - 191	89
IIIb	42,76	3,05	21,53	$C_{16}H_{14}N_6O_4S_3$	42,66	3,13	21,35	176 - 177	83
IIIc	47,21	4,06	16,82	$C_{22}H_{22}N_6O_6S_3$	46,96	3,94	17,10	182 - 183	80
IIId	49,66	4,31	18,28	$C_{22}H_{22}N_6O_4S_3$	49,79	4,18	18,13	176 - 178	72
IIIe	47,39	3,35	17,10	$C_{22}H_{18}N_6O_6S_3$	47,30	3,24	17,22	215 - 217	95
IIIf	44,82	3,54	18,24	$C_{20}H_{18}N_6O_6S_3$	44,93	3,38	17,99	224 - 227	84
IIIg	44,99	3,31	18,15	$C_{20}H_{18}N_6O_6S_3$	44,93	3,38	17,99	140(decomp.)	51
IIIh	51,70	5,02	17,44	$C_{24}H_{28}N_8O_2S_3$	51,78	5,07	17,28	213 - 214	81
IIIi	49,15	4,24	16,10	$C_{24}H_{24}N_6O_6S_3$	48,96	4,11	16,34	217 - 218	92
IIIj	47,58	3,80	18,91	$C_{20}H_{18}N_6O_4S_3$	47,80	3,61	19,14	214 - 215	91
IIIk	38,52	5,27	22,32	$C_{14}H_{22}N_6O_4S_3$	38,70	5,10	22,13	182 - 183	46
III*l*	47,50	5,69	21,08	$C_{18}H_{26}N_6O_2S_3$	47,56	5,76	21,16	149 - 151	86
IIIm	44,49	6,05	19,68	$C_{18}H_{28}N_8O_2S_3$	44,61	5,82	19,84	97 - 98	71
IIIn	38,70	4,68	25,42	$C_{12}H_{18}N_6O_2S_3$	38,49	4,84	25,68	195 - 196	86
IIIo	47,48	5,79	21,41	$C_{18}H_{26}N_6O_2S_3$	47,55	5,76	21,16	94 - 95	87
IIIp	47,58	5,68	21,36	$C_{18}H_{26}N_6O_2S_3$	47,55	5,76	21,16	159 - 160	80
IIIq	53,25	4,31	19,20	$C_{22}H_{22}N_6O_2S_3$	53,05	4,45	19,31	221 - 222	46
IIIr	49,72	4,35	17,92	$C_{22}H_{22}N_6O_4S_3$	49,80	4,18	18,13	144 - 145	68
IIIs	49,53	4,28	18,39	$C_{22}H_{22}N_6O_4S_3$	49,80	4,18	18,13	184 - 185	58
IV	43,78	4,02	22,09	$C_{16}H_{18}N_6O_2S_3$	43,61	4,11	21,84	140 - 141	34
V	41,56	5,22	18,36	$C_{18}H_{26}N_6O_6S_3$	41,69	5,05	18,55	170 - 171	85
VI	53,67	4,68	16,71	$C_{26}H_{26}N_6O_4S_3$	53,59	4,50	16,51	134 - 135	62

Based on data in [1], we can hypothesize that dihydrazones IIIa-s exist in the form of four stereoisomeric forms as a result of *E′*,*Z′*-conformational and *E*,*Z*-geometric isomerism. We have established that these compounds exist in DMSO and DMF solutions as a mixture of two stereoisomers, which follows from the splitting of the signals from protons of the CH_2CO, =CH, and NH groups in PMR spectra, which coalesce when the indicated solutions are heated up to 120°C.

According to literature data [1, 5, 6], the signals from the protons of the CH_2CO and NH groups of the *Z′*-conformer in dihydrazones IIIa-s are found upfield while the signal from the proton of the =CH group is found downfield from the corresponding signals of the *E′* conformer. From Table 2 we see that in solutions of strongly polar solvents DMSO or DMF, the equilibrium of all the dihydrazones except IIIc, f, j is shifted toward the *E′* isomer.

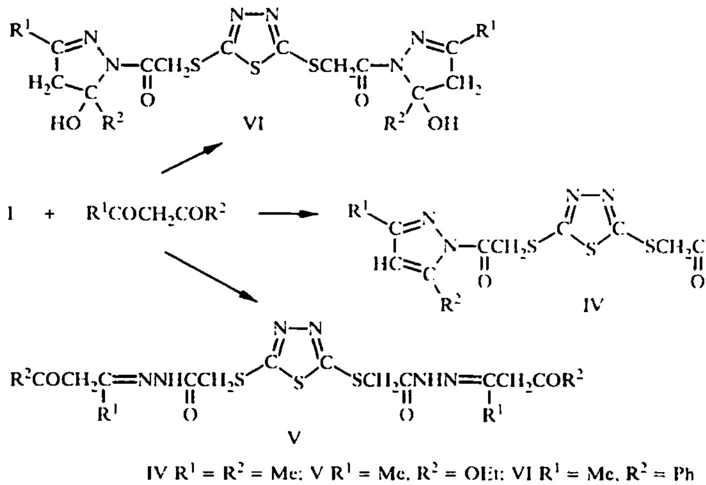


A

We know that the acylhydrazones both in the *E′* and *Z′* forms can form intermolecular hydrogen bonds, and only in the *E′* form can cyclic dimers be obtained [3, 5]. However, in dihydrazones IIIc, f, j obtained from 2-hydroxybenzaldehydes, the *Z′* isomer clearly predominates. These compounds exhibit luminescence, which can be explained by the formation in the azomethines of a rigid group (A) which bonds the electron pair of the azine nitrogen with the proton [7] and which can clearly preferentially arise in the predominant *Z′* isomer. In our case, weak luminescence is also noted for hydrazones having conformational isomers in which a certain part of the absorbed energy is used up in conversion of the conformers [8].

Data are available in the literature indicating that the products of reaction of β-dicarbonyl compounds with hydrazides of acids form systems with a tautomeric hydrazone, 5-hydroxypyrazoline or pyrazole form [1, 9]. We established that the reaction of dihydrazide I with different β-dicarbonyl compounds occurs regiospecifically and in each case one condensation product is formed. Thus in the case of acetylacetone, we isolated dipyrazole (IV), heating of which in DMF solution does not cause coalescence of the signals from the protons of the CH_2CO group. The N–CO amide bond in pyrazole IV is probably found in a state of conjugation with the pyrazole ring, which sharply raises the barrier to rotation about this bond compared with other dihydrazones. Conjugation of the system is also supported by the shift of the absorption band from the carbonyl group in the IR spectrum up to 1715 cm^{-1}, while the absorption bands for the carbonyl group in the remaining dihydrazones are found in the region 1660-1680 cm^{-1}.

The reaction of dihydrazide I with acetoacetic ester leads to formation of compound (V) with a linear hydrazone structure, which is supported by PMR and IR spectra. In the PMR spectrum of dihydrazone V, the signal from the methyl group (R^1) is found at 1.84 ppm, the signals from the OC_2H_5 (R^2) group are found at 1.13 ppm (CH_3) and 3.98 ppm (CH_2). In the IR spectrum of this compound, we observe two intense absorption bands at 1667 and 1707 cm^{-1}, corresponding to stretching vibrations (ν) of the CO group in the $CONH^-$ and COO^- groups respectively, and also a strong absorption band at 3160 cm^{-1}, corresponding to the ν of the NH group.



IV $R^1 = R^2 = Me$; V $R^1 = Me$, $R^2 = OEt$; VI $R^1 = Me$, $R^2 = Ph$

Study of the PMR spectrum of the production of condensation of dihydrazide I with benzoylacetone showed that the dihydrazone (VI) is formed, having a 5-hydroxypyrazoline structure. The signal from the CH_2 group of the pyrazoline ring is found at 3.04 ppm, while the signal from the proton of the hydroxyl group is found at 7.00 ppm. The latter, as we should expect, disappears when trifluoroacetic acid is added. We can hypothesize that cleavage of water from the hydroxypyrazoline V under these conditions is hindered due to the $-I$ effect of the phenyl substituent, which prevents cleavage of the hydroxyl group. On condensation with acetylacetone, the methyl group, having a $+I$ effect, promotes cleavage of water and the reaction does not stop at the 5-hydroxypyrazoline but rather goes on to formation of the dipyrazole IV.

EXPERIMENTAL

The IR spectra were obtained on a UR-10 spectrometer for KBr pellets. The PMR spectra were obtained on a Hitachi R-22 spectrometer (90 MHz), internal standard HMDS. Quantitative determinations were made on the basis of the PMR spectra with five integrations of the signal from the CH_2CO group.

The characteristics of the synthesized compounds are presented in Table 1. The PMR spectral data are presented in Table 2.

Esters of 1,3,4-Thiadiazole-2,5-dithioglycolic Acid (IIa, b). A. A solution of 28.6 g (0.51 moles) potassium hydroxide in 15 ml water was added to a mixture of 400 ml isopropanol and 37.5 g (0.25 moles) 2,5-dimercapto-1,3,4-thiadiazole. Then 85.2 g (56.6 ml, 0.51 moles) ethyl ester of monobromoacetic acid was added dropwise with stirring at a temperature of 35°C. After this, the mixture was stirred for 1.5 more hours at 65-70°C and then diluted with water. The precipitated crystals of the diethyl ester IIb were filtered off and washed with water. Yield 70%. T_{mp} 57-58°C. Lit. T_{mp} 59-60°C [4]. Similarly, from the methyl ester of monobromoacetic acid we obtained the dimethyl ester IIa. Yield 59%. T_{mp} 73-74°C. Lit. T_{mp} 73-74°C [4].

B. Sodium hydroxide (16.8 g, 0.42 moles) and 0.5 g TEBA were dissolved in 200 ml water, and 30 g (0.2 moles) 2,5-dimercapto-1,3,4-thiadiazole was added. Also 61.2 g (38 ml, 0.4 moles) of the methyl ester of monobromoacetic acid was added dropwise at a rate so that the temperature never rose above 30°C. After this, the mixture was stirred for one more hour at room temperature. The precipitated crystals of product IIa were filtered off and repeatedly washed with water. Yield 70%. T_{mp} 72-73°C.

Dihydrazide of 1,3,4-Thiadiazole-2,5-dithioglycolic Acid (I). Hydrazine hydrate (50 ml)was added dropwise to a solution of 29.4 g (0.1 moles) of the dimethyl ester IIa in 350 ml isopropanol at a temperature of 30-40°C. The abundant amorphous precipitate of product I was filtered off and washed with isopropanol. Yield 98%. T_{mp} 154°C. Lit. T_{mp} 164°C [4].

Dihydrazide I was obtained similarly from diethyl ester IIb. Yield 96%. T_{mp} 152-153°C. Found, %: C 24.60, H 3.54, S 32.83. $C_6H_{10}N_6O_2S_3$. Calculated, %: C 24.48, H 3.42, S 32.68.

1,3,4-Thiadiazole-2,5-dithioglycolylhydrazone of Acetaldehyde (IIIa). A mixture of 2.94 g (10 mmoles) dihydrazide I, 50 ml dioxane, and 3 ml acetaldehyde was stirred for 1 h at 70°C. The dioxane was partially driven off, and the crystals of product IIIa were filtered off and washed with acetone.

1,3,4-Thiadiazole-2,5-dithioglycolylhydrazone of 2-Furaldehyde (IIIb). A mixture of 2.94 g (10 mmoles) dihydrazide I, 50 ml dioxane, 5 ml water, and 1.92 g (20 mmoles) 2-furaldehyde was stirred for 1.5 h at 80°C. The dioxane was partially driven off and the crystals of product IIIb were recrystallized from dioxane.

1,3,4-Thiadiazole-2,5-dithioglycolylhydrazone of 2-Hydroxy-3-methoxybenzaldehyde (IIIc) was obtained as for compound IIIb from 2.94 g (10 mmole) dihydrazide I, 50 ml dioxane, 5 ml water, and 3.04 g (20 mmoles) 2-hydroxy-3-methoxybenzaldehyde.

1,3,4-Thiadiazole-2,5-dithioglycolylhydrazone of 4-Methoxybenzaldehyde (IIId). A mixture of 2.94 g (10 mmoles) dihydrazide I, 40 ml dioxane, 5 ml water, and 2.72 g (20 mmoles) 4-methoxybenzaldehyde was stirred for 1 h at 75°C and then cooled. The crystals of product IIId were filtered off and washed with ether.

1,3,4-Triadiazole-2,5-dithioglycolylhydrazone of 3,4-Methylenedioxybenzaldehyde (IIIe). A mixture of 2.94 g (10 mmoles) dihydrazide I, 40 ml dioxane, 5 ml water, and 3 g (20 mmoles) 3,4-methylenedioxybenzaldehyde was stirred for 1.5 h at 85°C. The dioxane was partially driven off and the residue was diluted with petroleum ether. The crystals of product IIIe were filtered off and washed with petroleum ether.

1,3,4-Thiadiazole-2,5-dithioglycolylhydrazone of 2,4-Dihydroxybenzaldehyde (IIIf). A mixture of 2.94 g (10 mmoles) dihydrazide I, 50 ml dioxane, 5 ml water, and 2.8 g (20 mmoles) 2,4-dihydroxybenzaldehyde was stirred for 2 h at 85°C. The dioxane was driven off and the oily residue was triturated in petroleum ether. The precipitated crystals of product IIIf were filtered off and washed with petroleum ether.

TABLE 2. PMR Spectral Data for Compounds IIIa-s, IV-VI

Compound	Solvent	Chemical shifts, δ, ppm				E'-isomer, %
		$CH_2C=O$, s	=CH, s	NH, s	Other signals	
IIIa	DMSO-D_6	3,91 (Z'), 4,27 (E')	7,24 (1H, m)	11,07 (Z'), 11,11 (E')	1,76 (3H, d, CH_3)	65
IIIb	DMSO-D_6	4,03 (Z'), 4,41 (E')	7,75 (E'), 7,95 (Z')	11,44 (Z'), 11,51 (E')	—	64
IIIc	DMSO-D_6	4,05 (Z'), 4,43 (E')	8,20 (E'), 8,27 (Z')	11,20 (Z'), 11,50 (E')	8,93 (1H, s, OH), 3,71 (3H, s, CH_3)	40
IIId	DMF -D_7	4,11 (Z'), 4,53 (E')	8,01 (E'), 8,15 (Z')	11,33 (Z'), 11,58 (E')	3,71 (3H, s, CH_3)	61
IIIe	DMF -D_7	4,13 (Z'), 4,47 (E')	7,96 (E'), 8,11 (Z')	11,38 (Z'), 11,60 (E')	6,00 (2H, s, OCH_2O)	62
IIIf	DMF -D_6	4,02 (Z'), 4,38 (E')	7,96 (E'), 8,07 (Z')	10,82 (Z'), 11,13 (E')	9,60 (1H, d, OH), 11,44 (1H, s, OH)	31
IIIg	DMSO-D_7	4,04 (Z'), 4,47 (E')	7,78 (E'), 7,89 (Z')	—	—	67
IIIh	DMSO-D_6	3,96 (Z'), 4,38 (E')	7,69 (E'), 7,87 (Z')	11,13 (Z'), 11,20 (E')	2,84 (6H, s, $2CH_3$)	62
IIIi	DMSO-D_6	4,01 (Z'), 4,40 (E')	8,13 (E'), 8,29 (Z')	11,42 (Z'), 11,58 (E')	3,67 (6H, d, $2CH_3$)	63
IIIj	DMSO-D_6	4,07 (Z'), 4,47 (E')	8,24 (E'), 8,33 (Z')	11,51 (Z'), 11,82 (E')	—	47
IIIk	DMSO-D_6	3,98 (Z'), 4,33 (E')	7,38 (1H, m)	10,82 (Z'), 10,90 (E')	0,98 (3H, d, CH_3), 2,18 (2H, t, $CH\underline{CH_2}$), 3,67 (1H, m, $\underline{CH}CH_3$)	73
III*l*	DMSO-D_6	3,96 (Z'), 4,27 (E')	— —	10,18 (Z'), 10,31 (E')	—	52
IIIm	DMSO-D_6	4,04 (Z'), 4,38 (E')	—	10,51 (Z'), 10,64 (E')	2,13 (3H, s), 2,33 (8H, m, $(CH_2)_2C(CH_2)_2$)	57
IIIn	DMSO-D_6	4,01 (Z'), 4,31 (E')	—	10,14 (Z'), 10,27 (E')	1,79 (s, CH_3) (E), 1,82 (s, CH_3) (Z)	55
IIIo	DMSO-D_6	4,02 (Z'), 4,31 (E')	—	10,13 (Z'), 10,31 (E')	1,75 (s, CH_3) (E), 1,81 (s, CH_3) (Z)	58
IIIp	DMSO-D_6	4,07 (Z'), 4,33 (E')	—	10,17 (Z'), 10,33 (E')	1,73 (s, CH_3) (E), 1,84 (s, CH_3) (Z), 5,59 (1H, s, =CH)	56
IIIq	DMSO-D_6	4,11 (Z'), 4,33 (E')	—	10,57 (Z'), 10,80 (E')	2,18 (3H, s, CH_3)	64
IIIr	DMSO-D_6	3,87 (Z'), 4,00 (E')	—	10,96 (E',Z')	2,27 (3H, s, CH_3), 12,62 (1H, s, OH)	61
IIIs	DMSO-D_6	4,18 (Z'), 4,47 (E')	—	10,49 (Z'), 10,62 (E')	2,11 (3H, s, CH_3), 9,64 (1H, s, OH)	65
IV	DMF -D_7	4,07 (Z'), 4,86 (E')	6,02	—	2,09 (3H, s, $CH_3C=C$), 2,36 (3H, s, $CH_3C=N$)	65
V	DMSO-D_6	4,31 (E')	—	10,42 (Z'), 10,60 (E')	1,13 (3H, t, $\underline{CH_3}CH_2$), 1,84 (3H, s, CH_3), 3,98 (q, $\underline{CH_2}CH_3$)	*
VI	DMSO-D_6	4,47 (E')	—	—	1,95 (3H, s, CH_3), 3,04 (2H, s, $C-CH_2-C$), 7,00 (1H, s, OH)	100

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[*] The ratio of E', Z' conformers is not calculated due to superposition of the signal from CH_2CO of the Z' conformer onto the signal from the $\underline{CH_2}CH_3$ group.

1,3,4-Thiadiazole-2,5-dithioglycolylhydrazone of 3,4-Dihydroxybenzaldehyde (IIIg) was obtained from 2.94 g (10 mmoles) dihydrazide I, 50 ml dioxane, 5 ml water, and 2.8 g (20 mmoles) 3,4-dihydroxybenzaldehyde according to the procedure described for dihydrazone IIIf. The crystals obtained were dissolved in acetone and the solution was filtered. The filtrate was evaporated and the oily residue was triturated in water. The crystals of product IIIg were filtered off.

1,3,4-Thiadiazole-2,5-dithioglycolylhydrazone of 4-Dimethylaminobenzaldehyde (IIIh) was obtained from 2.94 g (10 mmoles) dihydrazide I, 50 ml dioxane, 5 ml water, and 2.98 g (20 mmoles) 4-dimethylaminobenzaldehyde according to the procedure described for dihydrazone IIIe.

1,3,4-Thiadiazole-2,5-dithioglycolylhydrazone of 2,3-Dimethoxybenzaldehyde (IIIi) was obtained from 2.94 g (10 mmoles) dihydrazide I, 50 ml dioxane, 5 ml water, and 3.32 g (20 mmoles) 2,3-dimethoxybenzaldehyde according to the procedure described for dihydrazone IIIe.

1,3,4-Thiadiazole-2,5-dithioglycolylhydrazone of 2-Hydroxybenzaldehyde (IIIj). A mixture of 2.94 g (10 mmoles) dihydrazide I, 50 ml dioxane, 5 ml water, and 2.42 g (20 millimoles) 2-hydroxybenzaldehyde was stirred for 3 h at 85°C. The dioxane was partially driven off, and then the crystals of product IIIj were filtered off and washed with water.

1,3,4-Thiadiazole-2,5-dithioglycolylhydrazone of 3-Hydroxybutanal (IIIk) was obtained from 2.94 g (10 mmoles) dihydrazide I, 50 ml dioxane, 5 ml water, and 1.74 g (20 mmoles) 3-hydroxybutanal according to the procedure for obtaining dihydrazone IIIj.

1,3,4-Thiadiazole-2,5-dithioglycolylhydrazone of Cyclohexanone (III*l*) was obtained from 2.94 g (10 mmoles) dihydrazide I, 50 ml dioxane, 5 ml water, and 1.96 g (20 millimoles) cyclohexanone according to the procedure for obtaining dihydrazone IIIb.

1,3,4-Thiadiazole-2,5-dithioglycolylhydrazone of N-Methylpiperidone (IIIm) was obtained from 2.94 g (10 mmoles) dihydrazide I, 50 ml dioxane, 5 ml water, and 2.3 g (20 mmoles) N-methylpiperidone according to the procedure for obtaining dihydrazone IIIj.

1,3,4-Thiadiazole-2,5-dithioglycolylhydrazone of Acetone (IIIn). A mixture of 2.94 g (10 mmoles) dihydrazide I and 100 ml acetone was boiled for 3 h. The acetone was partially driven off. The crystals of product IIIn were filtered off and washed with ether.

1,3,4-Thiadiazole-2,5-dithioglycolylhydrazone of 5-Hexen-2-one (IIIo) was obtained from 2.94 g (10 mmoles) dihydrazide I, 50 ml dioxane, 5 ml water, and 1.96 g (20 mmoles) 5-hexen-2-one according to the procedure for synthesis of dihydrazone IIIb.

1,3,4-Thiadiazole-2,5-dithioglycolylhydrazone of 4-Methyl-3-penten-2-one (IIIp). A mixture of 2.94 g (10 mmoles) dihydrazide I, 50 ml dioxane, 5 ml water, and 1.96 g (20 mmoles) 4-methyl-3-penten-2-one was stirred for 2 h at 80°C. The dioxane was partially driven off. The crystals of product IIIp were filtered off and washed with dioxane and methanol.

1,3,4-Thiadiazole-2,5-dithioglycolylhydrazone of Acetophenone (IIIq) was obtained from 2.94 g (10 mmoles) dihydrazide I, 50 ml dioxane, 5 ml water, and 2.4 g (20 mmoles) acetophenone according to the procedure for synthesis of dihydrazone IIIj.

1,3,4-Thiadiazole-2,5-dithioglycolylhydrazone of 2-Hydroxyacetophenone (IIIr) was obtained from 2.94 g (10 mmoles) dihydrazide I, 50 ml dioxane, 5 ml water, and 2.5 g (20 mmoles) 2-hydroxyacetophenone according to the procedure for synthesis of dihydrazone IIIj.

1,3,4-Thiadiazole-2,5-dithioglycolylhydrazone of 4-Hydroxyacetophenone (IIIs) was obtained from 2.94 g (10 mmoles) dihydrazide I, 50 ml dioxane, 5 ml water, and 2.5 g (20 mmoles) 4-hydroxyacetophenone according to the procedure for synthesis of dihydrazone IIIj.

1,3,4-Thiadiazole-2,5-dithioglycolyl-3,5-Dimethylpyrazole (IV). A mixture of 2.94 g (10 mmoles) of dihydrazide I and 50 ml acetylacetone was held for 2 h at 105°C. The acetylacetone was partially driven off and the viscous crystalline mass was dried. Product IV was isolated by recrystallization from acetone.

1,3,4-Thiadiazole-2,5-dithioglycolylhydrazone of Acetoacetic Ester (V). Acetoacetic ester (2.6 g, 20 mmoles) was added to a solution of 2.94 g (10 mmoles) dihydrazide I in 100 ml water at 80°C. The mixture was stirred at the same temperature for 3 h. Then the crystals of product V were filtered off and washed with ethanol.

1,3,4-Thiadiazole-2,5-dithioglycolyl-3-methyl-5-phenyl-5-hydroxypyrazoline (VI). A mixture of 2.94 g (10 mmoles) dihydrazide I, 50 ml dioxane, 5 ml water, and 3.22 g (20 mmoles) benzoylacetone was stirred for 3 h at 85°C. The dioxane was partially driven off and the crystals were filtered off. The filtrate was evaporated, 10 ml ethanol was added, and after 24 h the precipitated crystals of product VI were filtered off and washed with ethanol.

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