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Tautomerism and Conformational Isomerism of Mercaptoacetylhydrazones of Aliphatic and Aromatic Aldehydes

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Abstract— Mercaptoacetylhydrazones of aliphatic and aromatic aldehydes exist in the solutions as tautomeric mixtures of open-chain and cyclic 1,3,4-thiadiazine forms. The linear hydrazone form consists of a set of isomers due to the configurational and conformational isomerism. At growing bulk of the alkyl substituent at the C=N bond of the aliphatic aldehydes derivatives decreases the fraction of the cyclic tautomer; therewith the logarithms of the constants of the chain-ring tautomeric equilibrium correlate with the steric constants of the alkyl substituents. In the series of the aromatic aldehydes mercaptoacetylhydrazones the linear tautomer prevails, and the equilibrium position is insignificantlyt affected at variation of the electronic characteristics of the substituents in the aromatic ring.

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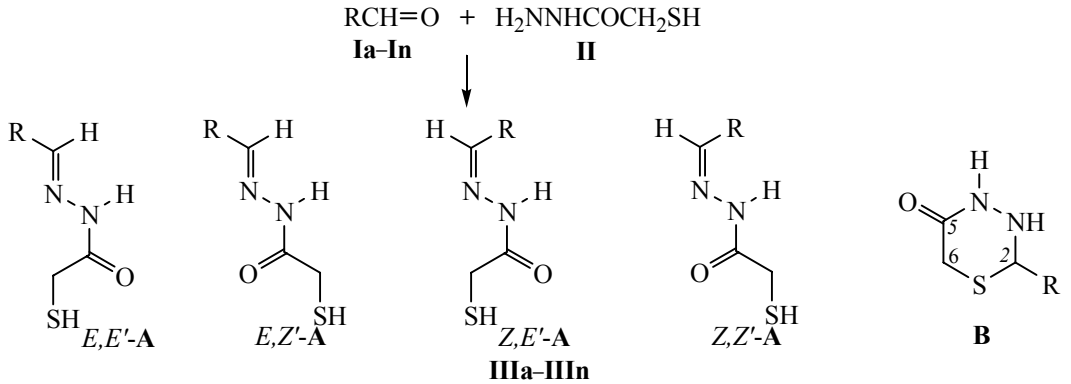
The condensation products of carbonyl compounds with thioglycolic acid hydrazide attract attention as potential tautomeric systems capable to exist either in the linear mercaptoacetylhydrazone (**A**) or in cyclic 1,3,4-thiadiazine (**B**) forms. The latter arises therough an intramolecular nucleophilic addition of the SH group to the C=N bond of the hydrazone fragment. We showed formerly that methyl alkyl ketones mercaptoacetylhydrazones were capable of the ring-chain tautomerism, and the equilibrium position was governed by the steric characteristics of the alkyl substituent [1, 2]. In extension of this research we investigated the ability to ring-chain

Scheme.



R = Me (**a**), Et (**b**), Pr (**c**), Bu (**d**), *i*-Pr (**e**), *i*-Bu (**f**); R = XC_6H_4, X = 4-NO_2 (**g**), 3-NO_2 (**h**), H (**i**), 4-Me (**j**), 4-OH (**k**), 4-MeO (**l**), 4-Me_2N (**m**), 2-HO (**n**).

tautomerism of condensation products of aliphatic and aromatic aldehydes with thioglycolic acid hydrazide (see the scheme).

Compounds **IIIa–IIIn** were obtained in 40–85% yields by short keeping at room temperature in a water-alcoholic solution of equimolar amounts of the thioglycolic acid hydrazide (**II**) and of the appropriate aldehyde (see EXPERIMENTAL).

The variation in time of the ^{1}H NMR spectra of compounds **IIIa–IIIn** suggests that they exist in the crystalline state in the cyclic thiadiazine form **B**. For instance, in the freshly prepared solution of compound **IIIa** in DMSO-d_6 a single set of peaks is observed corresponding just to **B** form. It is indicated by two signals of NH groups protons at 5.77 and 9.00 ppm and by a quartet at 4.48 ppm (H^2), and the ^{13}C NMR spectrum of this form is characterized by the signal of sp^3-hybridized atom C^2 at 63.8 ppm.

Gradually in the ^{1}H NMR spectrum of compound **IIIa** in DMSO-d_6 signals appear corresponding to the stereoisomers of the linear acylhydrazone form **A**: three signals of azomethine protons at 7.16, 7.32, and 7.49 ppm, and also broadened signals of NH protons in the region 11.0 ppm. After some time the spectrum of compound **IIIa** stopped to change indicating that the ring-chain equlibrium was attained where alongside the cyclic thiadiazine form **B** existed three stereoisomeric modifications of the linear form **A**.

Four spatial structures are conceivable for the carbonyl compounds acylhydrazones distinguished by the position of substituents with respect to the C=N bond (geometric *Z,E*-isomerism) and C–N bond of the amide fragment (conformational *Z',E'*-isomerism) [3, 4]. The aldehydes derivatives exist predominantly or totally in the *E*-configuration with respect to the C=N bond.

The assignment of signals to geometric *Z,E*-isomers can be made based on the deshielding effect of the hydrazone fragment on the cis-located azomethine protons observed in the ^{1}H NMR spectra of acylhydrazones [5]. Owing to it the strongest downfield signal at 7.32 ppm in the spectrum of compound **IIIa** should originate from the *E,E'*-isomer, the weakest upfield signal at 7.16 ppm, to the *Z,E'*-isomer, and the signal of intermediate intensity at 7.49 ppm, to *E,Z'*-isomer.

Likewise appear the spectra of solutions in DMSO-d_6 of compounds **IIIb–IIIf**. Going to compounds **IIIe** and **IIIf** containing bulky isopropyl and isobutyl groups leads to the exclusion from the equilibrium of the configurational isomer *Z,E'*-**A** and to the considerable increase in the content in the solution of isomers *E,E'*-**A** and *Z',E'*-**A**. Logs of the constants of the tautomeric equilibria are in linear correlation with the steric constants of Taft E_S [6, 7] and Palm $E_S°$ [6]; the use of Charton steric constants x [8] improves the correlation (Table 1).

Table 1. Correlation of logarithms of the constants of tautomeric equilibria Q_T of compounds **IIIa–IIIf** with the steric constants of Taft E_S, Palm $E_S°$, and Charton x along the equation: $\log K_T = A + B X$; ($n = 6$)

X	A	B	r	s_D
E_S	1.09±0.04	0.82±0.08	0.983	0.057
$E_S°$	1.17±0.06	0.67±0.09	0.964	0.083
υ	1.96±0.09	–1.68±0.13	0.989	0.047

Thus the products of aliphatic aldehydes condensation with thioglycolic acid hydrazide in the crystalline state possess the structure 1,3,4-thiadiazine, and only in solution in strongly polar solvents they partially transform into the open-chain form; consequently, it is only tentatively possible to use the name "mercaptoacetylhydrazone" for such compounds.

Comparing the tautomeric behavior of aldehydes **IIIa–IIIf** mercaptoacetylhydrazones with the previously studied condensation products of thioglycolic acid hydrazide and methyl alkyl ketones [2] it turns out that the aldehydes derivatives tend to be present prevailingly in the cyclic form, and for the methyl alkyl ketones mercaptoacetylhydrazones the equilibrium is considerably shifted to linear forms. This fact is apparently due to the possibility for alkyl substituent in the position *2* of the *chair* conformation of the 1,3,4-thiadiazine ring to be equatorially oriented. In the derivatives of methyl alkyl ketones the methyl or alkyl group are forced to occupy the axial position and to occur in a strong *syn*-axial interaction with a hydrogen atom in the position *4* thus destabilizing the 1,3,4-thiadiazine; therefore the open-chain tautomers successfully compete with the cyclic form.

In aromatic aldehydes mercaptoacetylhydrazones the ring-chain tautomeric equilibrium should shift to the open-chain form **A** for the latter is stabilized by involving the aromatic ring in the system of π-*p*-π-conjugation of the acylhydrazone fragment [3, 4]. This assumption was completely confirmed by the study of NMR spectra of compounds **IIIi–IIIn**.

The ^{1}H NMR spectrum of benzaldehyde mercaptoacetylhydrazone **IIIi** registered just after dissolution in

DMSO-d_6 contained two sets of resonances corresponding to two stereoisomers of the linear form **A**. The major isomer present in 65% fraction in the initial moment gives rise to the following signals: a singlet of the azomethine proton at 8.01 ppm, a doublet of methylene protons at 3.59 ppm, a triplet of the proton of SH group at 2.71 ppm, and a broadened singlet of NH group at 11.44 ppm. The analogous signals of the minor stereoisomer (35%) are observed at 8.18, 3.20, 2.89, and 11.52 ppm respectively. The ^{13}C NMR spectrum also confirms the presence of two isomers of the linear form **A**.

The acylhydrazones of aromatic aldehydes are known to exist prevailingly or completely in the *E*-configuration [3, 9]. Consequently, the observed doubling of the signals in the ^{1}H and ^{13}C NMR spectra of compound **IIIi** is not caused by the configurational equilibrium with respect to the C=N bond, but the presence of the conformational *Z',E'*-isomers with different position of substituents relative to the amide C–N bond.

The assignment of signals belonging to *E,E'*- and *E,Z'*-isomers of linear form **A** was based on the known difference in the chemical shifts of the carbon atoms in the C=N and C=O bonds in the ^{13}C NMR spectra of conformational isomers of monocarbonyl compounds acylhydrazones; the *E'*-isomer signals of these groups were located in the region 145 and 170 ppm, whereas those of *Z'*-isomer, at 150 and 160 ppm respectively [2, 9, 10]. In the ^{13}C NMR spectrum of compound **IIIi** the resonances of the carbon atoms of C=N and C=O bonds of the prevailing isomer appeared at 143.7 and 170.2 ppm, the corresponding signals of the minor stereoisomer were observed at 147.6 and 164.8 ppm. In view of the above the major isomer had *E,E'*-configuration, and the structural arrangement of the minor isomer was *E,Z'*.

Table 2. Tautomeric composition of compound **IIIi** in various solvents registered 48 h after dissolution

Solvent	Form **A**, %		Form **B**, %
	E,E'-	*E,Z'*-	
Chloroform-d_1	91	9	–
Pyridine-d_5	79	20	1
Acetone-d_6	74	23	3
Acetonitrile-d_3	65	32	3
DMSO-d_6	60	34	6
DMF-d_7	61	32	7

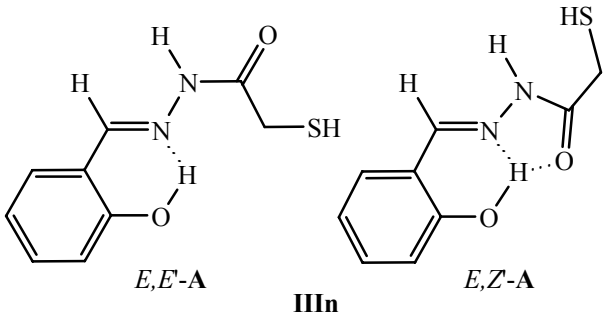
In the ^{1}H and ^{13}C NMR spectra of the compound **IIIi** solution in DMSO-d_6 gradually appeared signals corresponding to the cyclic 1,3,4-thiadiazine form **B**. The typical signals of this form in the ^{1}H NMR spectrum are the peaks of protons H^{2} and NH at 5.45 and 6.20 ppm respectively; diastereotopic protons H^{6} give rise to *AB* system at 3.24 and 3.51 ppm (coupling constant 14.7 Hz), the signal of the sp^3-hybridized C^{2} atom appears in the ^{13}C NMR spectrum at 65.5 ppm. Hence in the compound **IIIi** solution in DMSO-d_6 the ring-chain equilibrium was established between *E,E'*- and *E,Z'*-stereoisomers of **A** form and the cyclic 1,3,4-thiadiazine **B** form.

Mercaptoacetylhydrazones of other aromatic aldehydes **IIIg–IIIn** posses the hydrazone steructure **A** in the crystals, and in DMSO-d_6 solutions exist tautomeric mixtures of open-chain and cyclic forms. The tautomeric equilibrium in the series of aromatic aldehydes derivatives is shifted to the open-chain tautomer **A**, and the fraction of the thiadiazine tautomer does not exceed 5% excluding any conclusions on the effect of the electronic properties of the substituent in the aromatic ring.

By an example of compound **IIIi** we explored the effect of solvent on the tautomeric equilibrium (Table 2). In low-polar $CDCl_3$ even trace amounts of the cyclic form were not detected. In going to basic dipolar solvents (DMSO-d_6 and DMF-d_7) the appearance of the thiadiazine form **B** was favored. Its stabilization is due to the possibility of hydrogen bonds formation between the NH groups of the thiadiazine ring and the polar solvent molecules.

The relative amounts of *E,E'*- and *E,Z'*-isomers of the linear form **A** of aromatic aldehydes **IIIi–IIIn** mercaptoacetylhydrazones was practically independent of the electronic effect of the substituent in the aromatic ring. Going over from $CDCl_3$ to polar solvents as show the data on the benzaldehyde derivative **IIIi** increased the stability of more polar *E,Z'*-stereoisomer (Table 2).

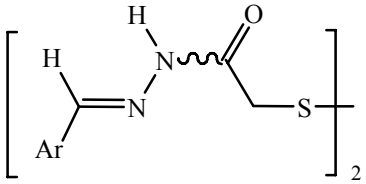
The conformational composition of linear form **A** might significantly change on introduction into the aromatic ring of benzaldehyde of a substituent capable to form an intramolecular hydrogen bond. For salicylaldehyde mercaptoacetylhydrazone (**IIIn**) the prevailing isomer in the solution became *E,Z'*-isomer. The stabilization of this stereoisomer may be due to the formation of an additional intramolecular hydrogen bond between OH and C=O groups alongside the hydrogen bond between OH and C=N possible in both conformers.



E,E'-**A** *E,Z'*-**A**

IIIn

Compounds **IIIi–IIIn** are prone to oxidation giving dimerization products **IV**. In reactions performed directly in the NMR tubes in DMSO-d_6 solution at room temperature these products for the majority of compounds were spectrally detected after 2–3 weeks. The products of compounds **IIIi–IIIn** dimerization were obtained in high yield by treating methanol solutions of aromatic aldehydes mercaptoacetylhydrazones with 5% solution of hydrogen peroxide. In the ^{1}H and ^{13}C NMR spectra of benzaldehyde thiobisacetylhydrazone (**IVa**) appeared three sets of resonances corresponding to conformational isomers *E,E'*, *E,Z'*, and *Z,Z'* (40, 45, and 15% respectively).



IV

Thus unlike the described [11–13] condensation products of aldehydes with hydrazides of glycolic and aminoacetic acids potentially able to undergo cyclization into 1,3,4-oxydiazine or 1,3,4-triazine forms respectively, mercaptoacetylhydrazones of aromatic and aliphatic aldehydes are capcble of cyclization giving six-membered 1,3,4-thiadiazine ring. This is understandable taking into account considerably greater nucleophilicity of sulfur in the SH group involved into the cyclization compared to the nucleophilicity of oxygen and nitrogen from OH and NH groups in the hydrazones obtained by the use of the hydrazides of glycolic and aminoacetic acids. The tendency to intramolecular cyclization is common to the mercaptoacetylhydrazones and to products we have formerly investigated of the carbonyl compounds condensation with hydrazides of thiobenzoic and 2-mercaptobenzoic acids where the intramolecular attack of the sulfur atom on the C=N bond of the hydrazone fragment has given 1,3,4-thiadiazoline [14] and 1,3,4-benzothiadiazepine [10, 15] rings respectively.

The data obtained provide certain possibility for forecasting more complex tautomeric systems [16–18] with the mercaptoacetylhydrazone fragment involving into the equilibrium additional cyclic forms, for instance, resulting from the condensation of the thioglycolic acid hydrazide with 1,3-dioxo compounds and monosaccharides that we plan for our further investigations.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were registered on a spectrometer Bruker AV-400 at operating frequencies 400 and 100 MHz respectively (internal reference HMDS). The quantitative composition of isomeric and tautomeric mixtures was determined from the integration of the corresponding resonances in the ^{1}H NMR spectra. The reaction progress was monitored and the purity of compounds obtained was checked by TLC on Silufol UV-254 plates, eluent benzene–acetone, 4:1.

Aldehydes mercaptoacetylhydrazones IIIa–IIIn. A mixture of 15 mmol of an aliphatic aldehyde **Ia–If** and 1.06 g (10 mmol) of thioglycolic acid hydrazide (**II**) in 50 ml of a mixture methanol–water, 1:4, or 9 mmol of aromatic aldehyde **Ig–In** and 10 mmol of compound **II** in 50 ml of methanol was kept at 25°C for 2 h. The separated crystals were filtered off, washed with ether, dried, and recrystallized from a mixture benzene–petroleum ether, 1:4. Compound **IIIa** was purified by column chromatography, eluent benzene–acetone, 4:1.

Acetic aldehyde mercaptoacetylhydrazone (IIIa). Yield 40%, viscous oily substance. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, form **A**-*E,E'* (4%): 3.42 d (CH_2S, *J* 8.0 Hz), 7.32 br.s (HC=N), 11.02 br.s (NH); form **A**-*E,Z'* (2%): 7.49 br.s (HC=N), 11.05 br.s (NH); form **A**-*Z,E'* (1%): 7.16 br.s (HC=N), 11.12 br.s (NH); form **B** (93%): 3.47, 3.55 (H^6, J_{AB} 15.5 Hz), 4.48 q (H^2, *J* 6.8 Hz,), 5.77 d (H^3, *J* 6.8 Hz), 9.00 br.s (H^4). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm, form **B**: 20.8 (CH_3), 28.4 (C^6), 63.8 (C^2), 172.7 (C^5). Found, %: C 36.29; H 6.05; N 21.23. $C_4H_8N_2OS$. Calculated, %: C 36.35; H 6.10; N 21.19.

Propionic aldehyde mercaptoacetylhydrazone (IIIb). Yield 75%, mp 103–104°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, form **A**-*E,E'* (6%): 1.01 t (CH_3, *J* 7.6 Hz), 2.21 m (CH_2), 2.67 t (SH, *J* 7.1 Hz), 3.43 d (CH_2S, *J* 7.1 Hz), 7.34 t (HC=N, *J* 5.0 Hz), 11.01 br.s (NH); form **A**-*E,Z'* (3%): 2.84 t (SH, *J* 7.8 Hz), 3.32 d (CH_2S, *J* 7.8 Hz), 7.47 t (HC=N, *J* 5.0 Hz), 11.07 br.s

(NH); form **A**-*Z,E*' (1%): 6.72 br.s (HC=N), 3.88 d (CH_2S, *J* 8.8 Hz), 11.14 br.s (NH); form **B** (90%): 0.90 t (CH_3, *J* 7.5 Hz), 1.64 m (CH_2), 3.12, 3.18 (H^6, J_{AB} 14.3 Hz), 4.28 t (H^2, *J* 6.4 Hz), 5.73 d (H^3, *J* 6.4 Hz), 8.97 br.s (H^4). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm, form **B**: 11.0 (CH_3), 27.6 (CH_2), 28.8 (C^6), 66.0 (C^2), 172.8 (C^5). Found, %: C 40.98; H 6.92; N 19.21. $C_5H_{10}N_2OS$. Calculated, %: C 41.07; H 6.89; N 19.16.

Butyric aldehyde mercaptoacetylhydrazone (IIIc). Yield 70%, mp 81–83°C. ^1H NMR spectrum (DMSO-d_6), δ, ppm, form **A**-*E,E*' (6%): 1.02 t (CH_3, *J* 7.5 Hz), 2.16 m ($2CH_2$), 2.67 t (SH, *J* 7.8 Hz), 3.43 d (CH_2S, *J* 7.8 Hz), 7.31 t (HC=N, *J* 4.7 Hz), 10.89 br.s (NH); form **A**-*E,Z*' (4%): 2.73 t (SH, *J* 8.3 Hz), 3.35 d (CH_2S, *J* 8.3 Hz), 7.46 t (HC=N, *J* 6.0 Hz), 10.91 br.s (NH); form **A**-*Z,E*' (1%): 3.89 d (CH_2S, *J* 11.4 Hz), 6.73 t (HC=N, *J* 6.3 Hz), 11.15 br.s (NH); form **B** (88%): 0.91 t (CH_3, *J* 7.5 Hz), 1.34 m (CH_2), 1.61 m (CH_2), 3.12, 3.19 (H^6, J_{AB} 13.5 Hz), 4.34 t (H^2, *J* 6.8 Hz), 5.73 d (H^3, *J* 6.8 Hz), 8.96 br.s (H^4). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm, form **B**: 13.7 (CH_3), 19.3 (CH_2), 27.5 (C^6), 37.7 (CH_2), 64.1 (C^2), 172.4 (C^5). Found, %: C 45.04; H 7.50; N 17.53. $C_6H_{12}N_2OS$. Calculated, %: C 44.98; H 7.55; N 17.48.

Valeric aldehyde mercaptoacetylhydrazone (IIId). Yield 65%, mp 63–65°C. ^1H NMR spectrum (DMSO-d_6), δ, ppm, form **A**-*E,E*' (8%): 0.94 t (CH_3, *J* 7.4 Hz), 1.53 m ($2CH_2$), 2.11 m (CH_2), 2.67 t (SH, *J* 7.1 Hz), 3.40 d (CH_2S, *J* 7.1 Hz), 7.44 t (HC=N, *J* 3.1 Hz), 11.01 br.s (NH); form **A**-*E,Z*' (4%): 0.94 t (CH_3, *J* 7.4 Hz), 1.53 m ($2CH_2$), 2.11 m (CH_2), 2.85 t (SH, *J* 7.6 Hz), 3.32 d (CH_2S, *J* 8.3 Hz), 7.47 t (HC=N, *J* 3.1 Hz), 11.08 br.s (NH); form **A**-*Z,E*' (1%): 3.89 d (CH_2S, *J* 11.4 Hz), 7.30 t (HC=N, *J* 6.0 Hz), 11.13 br.s (NH); form **B** (86%): 0.89 t (CH_3, *J* 7.5 Hz), 1.43 m ($2CH_2$), 1.73 m (CH_2), 3.13, 3.19 (H^6, J_{AB} 14.3 Hz), 4.33 t (H^2, *J* 6.8 Hz), 5.73 d (H^3, *J* 6.8 Hz), 8.97 br.s (H^4). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm, form **B**: 13.8 (CH_3), 22.1 (CH_2), 27.6 (CH_2), 28.3 (C^6), 35.4 (CH_2), 64.4 (C^2), 172.6 (C^5). Found, %: C 48.21; H 8.06; N 16.13. $C_7H_{14}N_2OS$. Calculated, %: C 48.25; H 8.10; N 16.08.

Isobutyric aldehyde mercaptoacetylhydrazone (IIIe). Yield 80%, mp 142–144°C. ^1H NMR spectrum (DMSO-d_6), δ, ppm, form **A**-*E,E*' (10%): 1.12 d ($2CH_3$, *J* 6.7 Hz), 2.34 t (SH, *J* 7.5 Hz), 2.56 m (CH), 3.43 d (CH_2S, *J* 7.5 Hz), 7.26 d (HC=N, *J* 4.0 Hz), 10.98 br.s (NH); form **A**-*E,Z*' (7%): 1.12 d ($2CH_3$, *J* 6.7 Hz), 2.41 t (SH, *J* 8.0 Hz), 2.56 m (CH), 3.34 d (CH_2S, *J* 8.0 Hz), 7.39 d (HC=N, *J* 5.0 Hz), 11.03 br.s (NH); form **B** (83%): 0.97 d (CH_3, *J* 6.5 Hz), 1.01 d (CH_3, *J* 6.6 Hz), 1.93 m (CH), 3.10, 3.17 (H^6, J_{AB} 13.5 Hz), 4.10 br.s (H^2), 5.68 br.s (H^3), 8.96 br.s (H^4). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm, form **B**: 19.0 (CH_3), 19.9 (CH_3), 29.2 (C^6), 33.1 (CH), 71.7 (C^2), 173.6 (C^5). Found, %: C 45.04; H 7.51; N 17.54. $C_6H_{12}N_2OS$. Calculated, %: C 44.97; H 7.55; N 17.48.

Isovaleric aldehyde mercaptoacetylhydrazone (IIIf). Yield 60%, mp 90–91°C. ^1H NMR spectrum (DMSO-d_6), δ, ppm, form **A**-*E,E*' (18%): 0.92 d ($2CH_3$, *J* 6.7 Hz), 1.83 m (CH_2), 2.18 m (CH), 2.65 t (SH, *J* 7.2 Hz), 3.50 d (CH_2S, *J* 7.2 Hz), 7.32 t (HC=N, *J* 4.0 Hz), 11.00 br.s (NH); form **A**-*E,Z*' (15%): 0.92 d ($2CH_3$, *J* 6.7 Hz), 1.83 m (CH_2), 2.18 m (CH), 2.84 t (SH, *J* 7.8 Hz), 3.87 d (CH_2S, *J* 7.8 Hz), 7.47 t (HC=N, *J* 4.7 Hz), 11.10 br.s (NH); form **B** (67%): 0.88 d (CH_3, *J* 6.5 Hz), 0.90 d (CH_3, *J* 6.5 Hz), 1.36 m (CH_2), 1.79 m (CH), 3.13, 3.20 (H^6, J_{AB} 13.6 Hz), 4.41 br.s (H^2), 5.73 br.s (H^3), 8.97 br.s (H^4). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm, form **A**-*E,E*': 22.3 ($2CH_3$), 26.1 (CH_2S), 38.3 (CH), 40.6 (CH_2), 147.1 (C=N), 170.1 (C=O); form **A**-*E,Z*': 22.3 ($2CH_3$), 26.6 (CH_2S), 38.3 (CH), 41.2 (CH_2), 150.8 (C=N), 164.7 (C=O); form **B**: 21.5 ($2CH_3$), 24.9 (CH), 28.1 (C^6), 37.6 (CH_2), 65.3 (C^2), 173.0 (C^5). Found, %: C 48.31; H 8.17; N 15.97. $C_7H_{14}N_2OS$. Calculated, %: C 48.25; H 8.10; N 16.08.

4-Nitrobenzoic aldehyde mercaptoacetylhydrazone (IIIg). Yield 55%, mp 187–190°C. ^1H NMR spectrum (DMSO-d_6), δ, ppm, form **A**-*E,E*' (56%): 2.82 t (SH, *J* 7.7 Hz), 3.65 d (CH_2S, *J* 7.7 Hz), 7.94–8.27 m (Ar), 8.10 s (HC=N), 11.74 br.s (NH); form **A**-*E,Z*' (43%): 2.98 t (SH, *J* 8.6 Hz), 3.25 d (CH_2S, *J* 8.6 Hz), 8.17 s (HC=N), 11.82 br.s (NH); form **B** (2%): 5.78 d (H^2, *J* 8.0 Hz), 6.38 d (H^3, *J* 8.0 Hz), 9.21 br.s (H^5). Found, %: C 45.22; H 3.84; N 17.52. $C_9H_9N_3O_3S$. Calculated, %: C 45.18; H 3.79; N 17.56.

3-Nitrobenzoic aldehyde mercaptoacetylhydrazone (IIIh). Yield 65%, mp 166–168°C. ^1H NMR spectrum (DMSO-d_6), δ, ppm, form **A**-*E,E*' (57%): 2.82 t (SH, *J* 8.0 Hz), 3.64 d (CH_2S, *J* 8.0 Hz), 7.79–8.34 m (Ar), 8.10 s (HC=N), 11.68 br.s (NH); form **A**-*E,Z*' (39%): 2.98 t (SH, *J* 8.4 Hz), 3.25 d (CH_2S, *J* 8.4 Hz), 8.12 s (HC=N), 11.72 br.s (NH); form **B** (2%): 3.31, 3.57 (H^6, J_{AB} 13.3 Hz), 5.79 d (H^2, *J* 7.3 Hz), 6.42 d (H^3, *J* 7.3 Hz), 9.22 br.s (H^5). Found, %: C 45.13; H 3.72; N 17.60. $C_9H_9N_3O_3S$. Calculated, %: C 45.18; H 3.79; N 17.56.

Benzoic aldehyde mercaptoacetylhydrazone (IIIi). Yield 85%, mp 111–113°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, form **A**-*E,E*' (60%): 2.71 t (SH, *J* 7.8 Hz), 3.59 d (CH_2S, *J* 7.8 Hz), 7.42–7.67 m (Ar), 8.10 s (HC=N), 11.44 br.s (NH); form **A**-*E,Z*' (34%): 2.89 t (SH, *J* 8.1 Hz), 3.20 d (CH_2S, *J* 8.1 Hz), 8.18 s (HC=N), 11.52 br.s (NH); form **B** (6%): 3.24, 3.51 (H^6, J_{AB} 14.7 Hz), 5.54 s (H^2), 6.20 br.s (H^3), 9.13 br.s (H^5). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm, form *E,E*': 24.7 (CH_2S), 127.7–134.2 (Ar), 143.7 (C=N), 170.2 (C=O); form *E,Z*': 26.3 (CH_2S), 147.6 (C=N), 164.8 (C=O); form **B**: 27.2 (C^6), 65.6 (C^2), 172.8 (C^5). Found, %: C 55.63; H 5.23; N 14.38. $C_9H_{10}N_2OS$. Calculated, %: C 55.65; H 5.19; N 14.42.

4-Methylbenzoic aldehyde mercaptoacetylhydrazone (IIIj). Yield 60%, mp 143–145°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, form **A**-*E,E*' (60%): 2.32 s (CH_3), 2.75 t (SH, *J* 7.6 Hz), 3.58 d (CH_2S, *J* 7.6 Hz), 7.23–7.56 m (Ar), 7.97 s (HC=N), 11.39 br.s (NH); form **A**-*E,Z*' (35%): 2.30 s (CH_3), 2.93 t (SH, *J* 8.0 Hz), 3.21 d (CH_2S, *J* 8.0 Hz), 8.14 s (HC=N), 11.47 br.s (NH); form **B** (5%): 2.28 s (CH_3), 3.23, 3.54 (H^6, J_{AB} 13.3 Hz), 5.51 d (H^2, *J* 8.4 Hz), 6.14 d (H^3, *J* 8.4 Hz), 9.15 br.s (H^5). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm, form *E,E*': 21.1 (CH_3), 24.7 (CH_2S), 126.8–131.5 (Ar), 143.5 (C=N), 171.2 (C=O); form *E,Z*': 21.0 (CH_3), 26.3 (CH_2S), 146.9 (C=N), 166.1 (C=O). form **B**: 26.9 (C^6), 64.8 (C^2), 173.0 (C^5). Found, %: C 57.71; H 5.77; N 13.49. $C_{10}H_{12}N_2OS$. Calculated, %: C 57.67; H 5.81; N 13.45.

4-Hydroxybenzoic aldehyde mercaptoacetylhydrazone (IIIk). Yield 75%, mp 104–106°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, form **A**-*E,E*' (67%): 2.70 t (SH, *J* 7.5 Hz), 3.56 d (CH_2S, *J* 7.5 Hz), 6.80–7.49 m (Ar), 7.90 s (HC=N), 9.90 br.s (OH), 11.41 br.s (NH); form **A**-*E,Z*' (30%): 2.88 t (SH, *J* 8.2 Hz), 3.18 d (CH_2S, *J* 8.2 Hz), 8.07 s (HC=N), 9.90 br.s (OH), 11.44 br.s (NH); form **B** (3%): 5.42 C (H^2), 9.09 br.s (H^5). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm, form *E,E*': 24.8 (CH_2S), 115.8–159.6 (Ar), 143.9 (C=N), 171.3 (C=O); form *E,Z*': 26.4 (CH_2S), 147.4 (C=N), 166.1 (C=O). Found, %: C 51.46; H 4.73; N 13.38. $C_9H_{10}N_2O_2S$. Calculated, %: C 51.41; H 4.79; N 13.32.

4-Methoxybenzoic aldehyde mercaptoacetylhydrazone (IIIl). Yield 60%, mp 119–121°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, form **A**-*E,E*' (63%): 2.75 t (SH, *J* 7.5 Hz), 3.59 d (CH_2S, *J* 7.5 Hz), 3.83 s (CH_3O), 7.03–7.80 m (Ar), 7.95 s (HC=N), 11.32 br.s (NH); form **A**-*E,Z*' (33%): 2.92 t (SH, *J* 8.2 Hz), 3.20 d (CH_2S, *J* 8.2 Hz), 3.79 s (CH_3O), 8.12 s (HC=N), 11.41 br.s (NH); form **B** (4%): 3.22, 3.52 (H^6, J_{AB} 13.1 Hz), 5.50 d (H^2, *J* 8.5 Hz), 6.11 d (H^3, *J* 8.5 Hz), 9.14 br.s (H^5). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm, form *E,E*': 24.8 (CH_2S), 55.4 (CH_3O), 114.4–160.8 (Ar), 143.4 (C=N), 171.4 (C=O); form *E,Z*': 26.4 (CH_2S), 55.2 (CH_3O), 147.0 (C=N), 166.2 (C=O). Found, %: C 53.53; H 5.39; N 12.49. $C_{10}H_{12}N_2O_2S$. Calculated, %: C 53.55; H 5.39; N 12.49.

4-Dimethylaminobenzoic aldehyde mercaptoacetylhydrazone (IIIm). Yield 65%, mp 112–115°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, form **A**-*E,E*' (68%): 2.71 t (SH, *J* 8.0 Hz), 2.92 s ($2CH_3N$), 3.55 d (CH_2S, *J* 8.0 Hz), 6.68–7.46 m (Ar), 8.09 s (HC=N), 11.28 br.s (NH); form **A**-*E,Z*' (30%): 2.77 t (SH, *J* 8.5 Hz), 2.96 s ($2CH_3N$), 3.16 d (CH_2S, *J* 8.5 Hz), 8.12 s (HC=N), 11.36 br.s (NH); form **B** (2%): 5.50 br.s (H^2), 8.98 br.s (H^5). Found, %: C 55.72; H 6.41; N 17.67. $C_{11}H_{15}N_3OS$. Calculated, %: C 55.67; H 6.37; N 17.71.

2-Hydroxybenzoic aldehyde mercaptoacetylhydrazone (IIIn). Yield 70%, mp 183–184°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, form **A**-*E,E*' (40%): 2.68 t (SH, *J* 7.6 Hz), 3.59 d (CH_2S, *J* 7.6 Hz), 6.85–7.48 m (Ar), 8.30 s (HC=N), 10.07 br.s (OH), 11.07 br.s (NH); form **A**-*E,Z*' (56%): 2.87 t (SH, *J* 8.1 Hz), 3.21 d (CH_2S, *J* 8.1 Hz), 8.37 s (HC=N), 10.07 br.s (OH), 11.38 br.s (NH); form **B** (4%): 3.16, 3.49 (H^6, J_{AB} 13.2 Hz), 5.68 d (H^2, *J* 7.1 Hz), 6.10 d (H^3, *J* 7.1 Hz), 9.13 br.s (H^5). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm, form *E,E*': 24.9 (CH_2S), 116.4–157.5 (Ar), 143.6 (C=N), 171.0 (C=O); form *E,Z*': 26.1 (CH_2S), 147.7 (C=N), 166.1 (C=O). Found, %: C 51.37; H 4.84; N 13.27. $C_9H_{10}N_2O_2S$. Calculated, %: C 51.41; H 4.79; N 13.32.

Benzaldehyde 2,2'-thiobisacetylhydrazone. To a solution of 0.45 g (5 mmol) of compound **IIIa** in 5 ml of methanol was added 0.5 ml of 5% solution of H_2O_2, and the mixture was kept at 25°C for 2 h. The separated crystals were filtered off, washed with ether, and dried. Yield 85%, mp 182–184°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, form *E,E*' (40%): 4.05 s (CH_2S), 7.14–7.46 m (Ar), 7.99 s (HC=N), 11.56 br.s (NH); form *E,Z*' (45%): 3.63 C (CH_2S), 4.08 s (CH_2S), 7.99 s (HC=N), 8.21 s (HC=N), 11.56 br.s (NH), 11.62 br.s (NH); form *Z,Z*' (15%): 3.67 s (CH_2S), 8.22 s (HC=N), 11.64 br.s (NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm, form *E,E*': 40.6 (CH_2), 127.9–134.6 (Ar), 143.9 (C=N), 170.1 (C=O); form *E,Z*': 41.3 (CH_2S), 147.8 (C=N), 164.9 (C=O); form *Z,Z*': 41.5 (CH_2S), 147.3 (C=N), 165.4

(C=O). Found, %: C 56.02; H 4.73; N 14.47; $C_{18}H_{18}N_4O_2S_2$. Calculated, %: C 55.94; H 4.69; N 14.50.

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