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Chemical Transformations of *N*-Morpholinylacetic Acid Hydrazide and Steric Structure of Its Derivatives

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Abstract—The reaction of *N*-morpholinylacetic acid hydrazide with various isothiocyanates and potassium thiocyanate resulted in the corresponding potentially biologically active thiosemicarbazide derivatives. Potassium *N'*-(2-morpholin-4-ylacetyl)hydrazinocarbothioate was synthesized and involved into heterocyclization in acidic environment to yield cyclic 5-(morpholinomethyl)-1,3,4-thiadiazole-2-thione. The structure of the synthesized compounds was established by IR, ^{1}H NMR spectroscopy, mass spectrometry, and XRD analysis.

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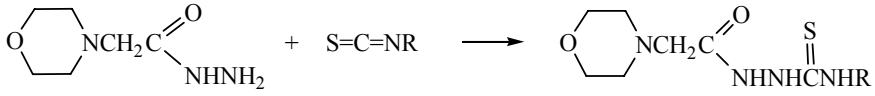
Thiosemicarbazide derivatives are known [1–3] as compounds possessing a wide range of biological action, including anticonvulsant, hypoglycemic, antiphlogistic, and antibacterial. In this regard, we were interested to carry out the synthesis of new thiosemicarbazide derivatives **II–IV** based on the *N*-morpholinylacetic acid hydrazide (**I**). The isothiocyanate method allows introducing a thioamide group into the structure of the initial hydrazide to form the corresponding thiosemicarbazide. This not only expands the possibility of the modification of these com-pounds, but may lead to new types of bioactivity.

We studied the condensation reaction of allyl-, benzoyl-, and 4-bromobenzoyl isothiocyanates with *N*-morpholinylacetic acid hydrazide **I** in the alcohol medium at the equimolar ratio of the reactants. The synthesis of new thiosemicarbazides **II–IV** was performed in two stages, the first of which involves the synthesis of the corresponding isothiocyanate by heating allyl bromide and benzoyl chloride with potassium thiocyanate in acetone medium and further its reaction in situ (without isolation) with *N*-morpholinylacetic acid hydrazide along the following scheme:



I **II–IV**

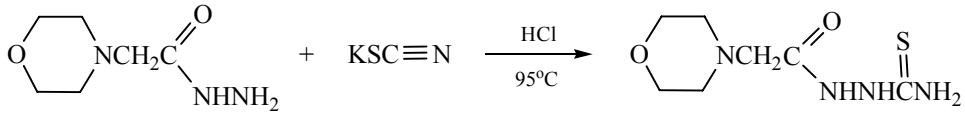
R = CH_2=$CHCH_2$ (**II**), $C_6H_5C(O)$ (**III**), 4-Br-$C_6H_4C(O)$ (**IV**).

The yield of thiosemicarbazides **II–IV** was 59–74%. The synthesized thiosemicarbazide derivatives **II–IV** are white crystals, soluble in polar organic solvents. The composition, structure, homogeneity of the compounds **II–IV** were confirmed by elemental analysis, IR, and ^{1}H NMR spectroscopy.

The IR spectra of compounds **II–IV** contain an absorption band in the region of 1140–1240 cm^{-1} characteristic of the NH–CS group of the thiosemicarbazide fragment. The absorption band of the amide group C(O)NH appears in the region of 1690–1675 cm^{-1} and of NH group, at 3390–3360 cm^{-1}. In the

^{1}H NMR spectrum of the *N*-morpholinylacetic acid *N*-allylthiosemicarbazide **II** the signals of methylene protons of morpholine fragment give rise to two triplets centered at 2.45 and 3.59 ppm. The signal of methylene protons of NCH_2 fragment appears at 3.01 ppm as a narrow singlet. Methylene protons of the allyl fragment give a broad triplet at 4.09 ppm. Methine proton of the vinyl fragment is observed as a complex multiplet at 5.82 ppm. Methylene protons of the same vinyl residue give two doublets at 5.04 and 5.13 ppm with spin-spin coupling constants J^1 = 10.3 Hz, J^2 = 17.3 Hz. The signals of the amide and tioamide N–H protons are three singlets in a weak field, at 9.65, 9.20, and 7.98 ppm. The ratio of integral intensities corresponds to the structure **II**.

In order to expand the number of new biologically active substances with thiosemicarbazide fragment we carried out also the synthesis of monosubstituted thiosemicarbazide derivative **V** by the reaction of the *N*-morpholinylacetic acid hydrazide with potassium thiocyanate along the scheme:

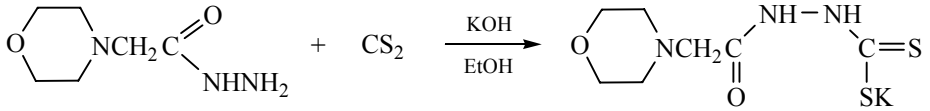


I **V**

The reaction was carried out in an acidic environment (diluted aqueous HCl) at 95°C within 4 h. The reaction product **V** was obtained in 57% yield.

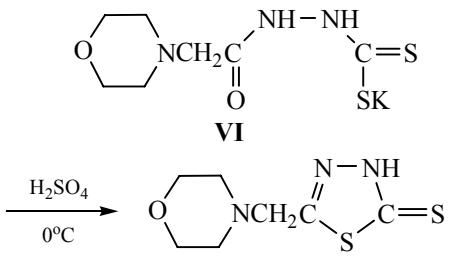
IR spectrum of compound **V** contains absorption bands of stretching vibrations of NH_2 groups at 3305–3240 cm^{-1} and an absorption band at 3210 cm^{-1} characteristic of NH groups. In the regions of 1660 and 1270 cm^{-1} there are absorption bands of carbonyl (C=O) and tiocarbonyl (C=S) groups, respectively.

It is known that derivatives of hydrazides and thiosemicarbazide are important synthons in the synthesis of azaheterocycles [4, 5]. Using a variety of reagents and changing reaction conditions, the cyclization can be directed to the formation of 1,3,4-oxadiazoles, 1,3,4-thiadiazoles, and 1,2,4-triazoles. Among these heterocyclic aza derivatives, a group of 1,3,4-thiadiazoles is interesting in both the chemical and pharmacological respects, being essentially a cyclic analog of thiosemicarbazones. In the literature there are only few data on these cyclic organic compounds [6–8]. In this regard, we studied the possibility of condensation of *N*-morpholinylacetic acid hydrazide **I** to obtain 1,3,4-thiadiazole derivative by the reaction of **I** with carbon disulfide in alkaline medium.



I **VI**

The potassium salt **VI** formed in the first stage further underwent cyclization in 5-(morpholinomethyl)-1,3,4-thiadiazole-2(3*H*)-thione **VII** at low temperature under the action of concentrated sulfuric acid:



VI **VII**

5-(Morpholinomethyl)-1,3,4-thiadiazole-2(3*H*)-thione **VII** belongs to heterocyclic compounds and, moreover, is capable of tautomeric thione-thiol

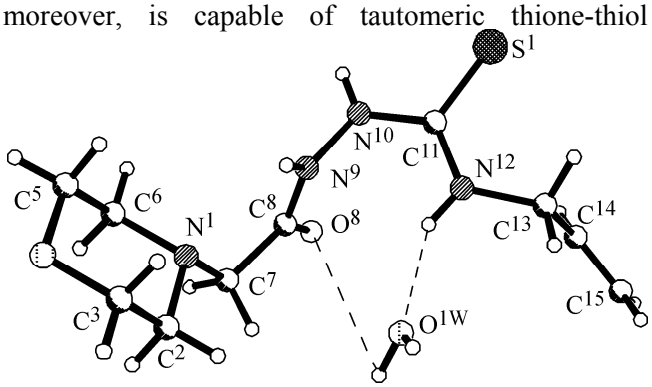


Fig. 1. Spatial arrangement of molecule **II.**

Table 1. Bond lengths (*d*, Å) in structure **II**

Bond	*d*	Bond	*d*
S^1–C^{11}	1.702(3)	C^8–N^9	1.344(4)
N^1–C^7	1.450(4)	N^9–N^{10}	1.383(3)
N^1–C^6	1.453(4)	N^{10}–C^{11}	1.343(4)
N^1–C^2	1.470(3)	C^{11}–N^{12}	1.320(4)
C^2–C^3	1.499(6)	N^{12}–C^{13}	1.446(4)
C^3–O^4	1.416(5)	C^{13}–C^{14}	1.546(6)
O^4–C^5	1.420(4)	C^{14}–C^{15}	1.267(6)
C^5–C^6	1.504(5)	O^{1W}–H^{1W}	0.68(7)
C^7–C^8	1.518(3)	O^{1W}–H^{2W}	0.89(7)
C^8–O^8	1.209(3)		

Table 2. Bond angles (ω, deg) in structure **II**

Angle	ω	Angle	ω
$C^7N^1C^6$	111.9(2)	$O^8C^8C^7$	122.4(3)
$C^7N^1C^2$	111.2(3)	$N^9C^8C^7$	114.3(2)
$C^6N^1C^2$	109.6(2)	$C^8N^9N^{10}$	122.0(2)
$N^1C^2C^3$	109.5(3)	$C^{11}N^{10}N^9$	121.6(2)
$O^4C^3C^2$	111.3(3)	$N^{12}C^{11}N^{10}$	118.8(2)
$C^3O^4C^5$	110.3(3)	$N^{12}C^{11}S^1$	124.1(2)
$O^4C^5C^6$	111.2(3)	$N^{10}C^{11}S^1$	117.1(2)
$N^1C^6C^5$	110.3(3)	$C^{11}N^{12}C^{13}$	124.0(2)
$N^1C^7C^8$	114.2(2)	$N^{12}C^{13}C^{14}$	111.7(3)
$O^8C^8N^9$	123.2(2)	$C^{15}C^{14}C^{13}$	125.7(5)

transformations. This type of compounds in the crystalline state are usually thiones, which is confirmed by IR spectra. A band in the region of 2700–2450 cm^{-1} characteristic of stretching vibrations of SH-group is not observed, but there are distinct bands of the group NH (3300–3100 cm^{-1}) and C=S (1350 cm^{-1}) .

In order to establish the steric structure of compounds **II**, **VII,** and to confirm the cation structure of compound **VII** an X-ray diffraction study of these compounds was performed. The study of compound **II** revealed that the *N*-morpholinylacetic acid *N*-allyl-thiosemicarbazide **II** at recrystallization formed the corresponding monohydrate crystal. Its general view is shown in Fig. 1. It follows from the XRD data that the bond lengths and bond angles in compounds **II** are close to normal (Tables 1 and 2) [9]. The morpholine ring is present in an almost ideal *chair* conformation (ΔC_S^3 = 0.9° and $\Delta C_2^{4,5}$ = 0.6°) (the intracyclic torsion angles are given in Table 3), and C^7 atom is oriented equatorially with respect to the ring. In the crystal, the molecules of **II** are associated with the hydration water molecules by hydrogen bonds N^{12}–H (*x, y, z*)···O^1W (*x, y, z*) (the distances N^{12}···O^1W 2.86 Å, H^{12}···O^1W 2.09 Å, angle NH···O 149.5°), O^1W–H (*x, y, z*)···O^8 (*x, y, z*) (the distances O^1W····O^8 2.78 Å, H^1W···O^8 1.90 Å, the angle OH···O 167.3°).

Table 3. Torsion angles (τ, deg) in structure **II**

Angle	τ	Angle	τ
$C^6N^1C^2C^3$	–56.9(4)	$C^3O^4C^5C^6$	58.0(4)
$N^1C^2C^3O^4$	58.7(4)	$O^4C^5C^6N^1$	–57.3(4)
$C^2C^3O^4C^5$	–59.2(4)	$C^2N^1C^6C^5$	56.3(3)

A general view of the molecule of 5-(morpholinomethyl)-1,3,4-thiadiazolo-2(3*H*)-thione **VII** is shown in Fig. 2. In the independent part of the unit cell of **VII** there are two molecules, **VIIa** and **VIIb**. It follows from the data obtained that the bond lengths and bond angles in both molecules are close to normal (Tables 4 and 5) [9]. The morpholine rings in **VIIa** and **VIIb** are present in an almost perfect chair conformation (ΔC_S^2 = 0.3° and $\Delta C_2^{4,5}$ = 1.6° for **VIIa**, ΔC_S^2 = 1.7° and $\Delta C_2^{5,6}$ = 0.3° for **VIIb**). Thiadiazole rings in both molecules are planar (the atoms S^1, C^2, N^3, N^4 and C^5 in **VIIa** and $S^{1'}$, $C^{2'}$, $N^{3'}$, $N^{4'}$, and $C^{5'}$ in **VIIb** are coplanar with an accuracy of ±0.004 and ±0.003 Å, respectively), the intracyclic torsion angles are shown in Table 6. The C^6 atom is oriented equatorially with respect to the morpholine ring.

In the crystal the molecules are linked into infinite bands along the crystallographic axis 2_1 (0,*y*,0) by the hydrogen bonds O^1–H (*x, y, z*)···O^2 (–*x*, 0.5 + *y*, 1/2 – *z*) (the distances O^1···O^2 2.77 Å, H···O^2 1.99 Å, angle OH···O 158.7°), O^3–H (1 – *x*, 0.5 + *y*, 0.5 – *z*)···O^1 (*x, y, z*) (the distances O^1···O^2 2.76 Å, H···O^1 1.94 Å, angle OH···O 173.8°), O^4–H(*x, y, z*) ···O^5 (–1 + *x, y, z*) (the distances O^4···O^5 2.75 Å, H···O^5 2.03 Å, angle OH···O 170.7°) and O^4–H (*x, y, z*)···O^5 (–0.5 + *x*, 0.5 – *y*, 1 – *z*) (the distances O^4···O^5 2.74 Å, H···O^5 1.91 Å, angle OH···O 177.5°).

Thus, proceeding from the *N*-morpholinylacetic acid hydrazide **I** using one-step isothiocyanate method we synthesized related thiosemicarbazides **II–V** and performed heterocyclization of compound **I** into the corresponding 5-(morpholinomethyl)-1,3,4-thiadiazole-2-thione **VII.**

Table 4. Bond lengths (*d*, Å) in structure **VII**

Bond	*d*	Bond	*d*
S^1–C^5	1.740(3)	$S^{1'}$–$C^{5'}$	1.740(3)
S^1–C^2	1.744(3)	$S^{1'}$–$C^{2'}$	1.745(4)
S^2–C^2	1.659(3)	$S^{2'}$–$C^{2'}$	1.658(4)
C^2–N^3	1.331(4)	$C^{2'}$–$N^{3'}$	1.344(5)
N^3–N^4	1.364(4)	$N^{3'}$–$N^{4'}$	1.352(5)
N^4–C^5	1.283(4)	$N^{4'}$–$C^{5'}$	1.283(5)
C^5–C^6	1.493(4)	$C^{5'}$–$C^{6'}$	1.494(5)
C^6–N^7	1.459(4)	$C^{6'}$–$N^{7'}$	1.456(4)
N^7–C^{12}	1.458(4)	$N^{7'}$–$C^{8'}$	1.454(4)
N^7–C^8	1.468(4)	$N^{7'}$–$C^{12'}$	1.474(4)
C^8–C^9	1.506(5)	$C^{8'}$–$C^{9'}$	1.512(5)
C^9–O^{10}	1.426(5)	$C^{9'}$–$O^{10'}$	1.441(5)
O^{10}–C^{11}	1.432(5)	$O^{10'}$–$C^{11'}$	1.422(4)
C^{11}–C^{12}	1.507(5)	$C^{11'}$–$C^{12'}$	1.507(4)

EXPERIMENTAL

IR spectra were recorded on a NICOLET Fourier transform spectrometer AVATAR-320 from tablets with KBr. ^{1}H NMR spectra were recorded on a Bruker DRX500 spectrometer at a frequency 500 MHz from DMSO-d_6 solution with internal reference TMS. Mass spectra were recorded on a FINNIGAN MAT.INCOS 50 instrument with direct input, ionization energy 70 eV. Melting points were measured on a Boetius heating block. The TLC analysis was performed on Sorbfil plates, development by iodine vapor.

XRD analysis of compounds II and VII. The cell parameters and the intensities of the 2938 and 4063 independent reflections for crystals **II** and **VII**, respectively, were measured on a Xcalibur diffractometer (CuK_α radiation, graphite monochromator, θ/2θ-scanning, 2θ ≤ 151° and 169° for **II** and **VII**, respectively). Crystals of **II** are monoclinic: a = 11.2684(6), b = 9.5490(5), c = 14.0296(9) Å, β = 108.606(6)°, V = 1430.7(9) Å^3, Z = 4 ($C_{10}H_{18}N_4O_2S\cdot H_2O$), space group $P2_1/n$, d_{calc} = 1.283 g cm^{-3}. The crystals of **VII** are triclinic: a = 8.837(6), b = 9.818(5), c = 12.126(13) Å, α = 83.78(6), β = 80.74(7), γ = 80.40(5)°, V = 1020 (2) Å^3, Z = 4 ($C_7H_{11}N_3OS_2$), space group $P1$, d_{calc} = 1.413 g cm^{-3}. The structure was solved by the direct method. The positions of nonhydrogen atoms were refined in the anisotropic full-matrix approximation. Hydrogen atoms were placed in geometrically calculated positions and included in the refinement within the *rider* model, except for the hydrogen atoms of hydration water in compound **II**, which were identified from the difference electron density syn-

Table 5. Bond angles (ω, deg) in structure **VII**

Angle	ω	Angle	ω
$C^5S^1C^2$	89.3(1)	$C^{5'}S^{1'}C^{2'}$	89.7(2)
$N^3C^2S^2$	126.2(2)	$N^{3'}C^{2'}S^{2'}$	126.8(3)
$N^3C^2S^1$	107.0(2)	$N^{3'}C^{2'}S^{1'}$	106.3(3)
$S^2C^2S^1$	126.8(2)	$S^{2'}C^{2'}S^{1'}$	126.9(2)
$C^2N^3N^4$	119.5(3)	$C^{2'}N^{3'}N^{4'}$	119.7(3)
$C^5N^4N^3$	109.5(3)	$C^{5'}N^{4'}N^{3'}$	110.0(3)
$N^4C^5C^6$	122.8(3)	$N^{4'}C^{5'}C^{6'}$	122.5(3)
$N^4C^5S^1$	114.7(2)	$N^{4'}C^{5'}S^{1'}$	114.4(3)
$C^6C^5S^1$	122.4(2)	$C^{6'}C^{5'}S^{1'}$	123.1(2)
$N^7C^6C^5$	112.4(3)	$N^{7'}C^{6'}C^{5'}$	112.3(3)
$C^{12}N^7C^6$	111.6(3)	$C^{8'}N^{7'}C^{6'}$	109.2(3)
$C^{12}N^7C^8$	109.7(2)	$C^{8'}N^{7'}C^{12'}$	108.5(3)
$C^6N^7C^8$	108.9(3)	$C^{6'}N^{7'}C^{12'}$	111.3(3)
$N^7C^8C^9$	110.6(3)	$N^{7'}C^{8'}C^{9'}$	110.9(3)
$O^{10}C^9C^8$	111.2(3)	$O^{10'}C^{9'}C^{8'}$	111.0(3)
$C^9O^{10}C^{11}$	110.6(3)	$C^{11'}O^{10'}C^{9'}$	110.3(3)
$O^{10}C^{11}C^{12}$	110.2(3)	$O^{10'}C^{11'}C^{12'}$	110.2(3)
$N^7C^{12}C^{11}$	109.8(3)	$N^{7'}C^{12'}C^{11'}$	109.4(3)

Table 6. Intracyclic torsion angles (τ, deg) in structure **VII**

Angle	τ	Angle	τ
Thiadiazole cycles			
$C^5S^1C^2N^3$	0.9(2)	$C^{5'}S^{1'}C^{2'}N^{3'}$	0.5(3)
$S^1C^2N^3N^4$	–1.3(4)	$S^{1'}C^{2'}N^{3'}N^{4'}$	–0.9(4)
$C^2N^3N^4C^5$	1.1(5)	$C^{2'}N^{3'}N^{4'}C^{5'}$	0.8(5)
$N^3N^4C^5S^1$	–0.2(4)	$N^{3'}N^{4'}C^{5'}S^{1'}$	–0.3(4)
$C^2S^1C^5N^4$	–0.4(3)	$C^{2'}S^{1'}C^{5'}N^{4'}$	–0.1(3)
Morpholine cycles			
$C^{12}N^7C^8C^9$	55.7(4)	$C^{12'}N^{7'}C^{8'}C^{9'}$	57.1(4)
$N^7C^8C^9O^{10}$	–56.0(4)	$N^{7'}C^{8'}C^{9'}O^{10'}$	–56.4(4)
$C^8C^9O^{10}C^{11}$	57.9(4)	$C^{8'}C^{9'}O^{10'}C^{11'}$	57.0(4)
$C^9O^{10}C^{11}C^{12}$	–59.6(4)	$C^{9'}O^{10'}C^{11'}C^{12'}$	–59.7(4)
$O^{10}C^{11}C^{12}N^7$	59.6(4)	$O^{10'}C^{11'}C^{12'}N^{7'}$	61.4(4)
$C^8N^7C^{12}C^{11}$	–57.5(4)	$C^{8'}N^{7'}C^{12'}C^{11'}$	–59.3(3)

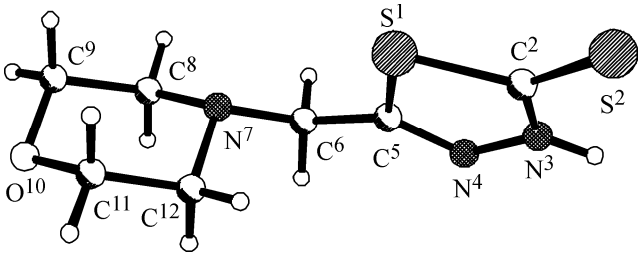


Fig. 2. Spatial arrangement of molecule **VII**.

thesis and refined in the isotropic approximation. In the calculations 2306 and 3447 reflections were used for **II** and **VII**, respectively, with $I \geq 2\sigma(I)$. The final divergence factors $R_1 = 0.0638$, $WR_2 = 0.1999$ for **II** and $R_1 = 0.0731$, $WR_2 = 0.2122$ for **VII**. The structure was solved and refined using the SHELXS-97 and SHELXL-97 software [10]. The CIF-files of the atomic coordinates are deposited at the Cambridge Crystallographic Center Database, (CCCD 853 555) and (CCCD 861 096) for **II** and **VII**, respectively.

***N*-Morpholinylacetic acid *N*-allylthiosemicarbazide (II)**. 1.59 g (0.01 mol) of *N*-morpholinylacetic acid hydrazide was dissolved in ethanol, and then 0.9 g (0.011 mol) of allyl isothiocyanate was added dropwise. The mixture was stirred for 60 min at 50–60°C. The completion of the reaction was controlled by TLC. The solution was cooled, the crystalline precipitate was filtered off and washed with a small amount of cold ethanol. After recrystallization from benzene we isolated 1.91 g (74%) of compound **II**, mp 137–138°C. A crystal of compound **II** for XRD studies was obtained by natural evaporation of a saturated alcoholic solution of the compound. Mass spectrum, *m/z*, (I_{rel}, %): 258 $[M]^+$ (0.2), 115 (26.7), 100 (100), 56 (39.5) 41 (34.3).

***N*-[2-(2-Morpholinoacetyl)hydrazinocarbonothioyl]-benzamide (III).** To a solution of 1.55 g (0.011 mol) of benzoyl chloride in 15 ml of acetone while stirring with a magnetic stirrer was added 1.07 g (0.011 mol) of potassium thiocyanate. The mixture was stirred for 2 h at room temperature and for half an hour under reflux. The solution was filtered from the precipitated KCl through a double paper filter, washed several times with acetone, and then 1.59 g (0.01 mol) of morpholinylacetic acid hydrazide **I** in 10 ml of water-free isopropyl alcohol was added dropwise to the solution. Further stirring was continued at 60°C for 3 h, and the solvent was distilled off. The residue crystallizes upon cooling. 1.91 g (59.5%) of white crystalline substance was isolated, mp 186–187°C (2-propanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.55 t [4H, $N(CH_2)_2$, $J = 4.3$], 3.32 br.s (2H, NCH_2), 3.63 t [4H, $O(CH_2)_2$, $J = 4.6$], 7.66 m (5H, Ar), 10.7 ush.s. (1H, NHNC=O); 11.8 s (1H, NHNC = O); 12.7 br.s [1H, C(O)NNC=S]. Mass spectrum, *m/z*, (I_{rel}, %): 322 $[M]^+$ (2), 105 (76), 100 (100), 77 (66.8) 56 (32.5), 51 (33.9), 42 (28.4).

4-Bromo-*N*-[2-(2-morpholinoacetyl)hydrazinocarbonothioyl]benzamide (IV) was synthesized similarly to compound **III** from 2.41 g (0.011 mol) 4-bromobenzoyl chloride, 1.07 g (0.011 mol) of potassium thiocyanate, and 1.59 g (0.01 mol) of morpholinylacetic acid hydrazide **I**. 9.2 g (52.3%) of white crystalline substance was isolated, mp 229–230°C (2-propanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.55 t [4H, $N(CH_2)_2$, $J = 4.2$], 3.30 br.s (2H, NCH_2), 3.63 t [4H, $O(CH_2)_2$, $J = 4.5$], 7.74 d, 7.89 d (4H, ArBr, $J = 8.55$), 10.65 br.s. (1H, NHNC=O); 11.85 s (1H, NHNC=O); 12.60 br.s [1H, C(O)NHNC=S]. Mass spectrum, *m/z*, (I_{rel},%): 402 $[M]^+$ (4), 400 $[M]^+$ (4), 100 (100), 56 (19), 42 (14.7).

***N*-Morpholinylacetic acid *N*-thiosemicarbazide (V)**. A mixture of 1.59 g (0.01 mol) of *N*-morpholinylacetic acid hydrazide, 1.4 g (0.015 mol) of potassium thiocyanate, and 1.5 ml of conc. hydrochloric acid in 40 ml of water was heated with stirring for 4 h at 95°C. The reaction mixture was left to stand for 24 h at room temperature. The solution was then alkalinized to pH = 6–7, the precipitate formed was filtered off and washed with water. After recrystallization from isopropyl alcohol we isolated 1.24 g (57%) of morpholinylacetic acid *N*-thiosemicarbazide **V,** mp 203–204°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.44 br.s [4H, $N(CH_2)_2$], 3.0 (2H, NCH_2), 3.58 t [4H, $O(CH_2)_2$, $J = 4.5$], 7.37 s, 7.85 s [2H, $H_2NC(S)$], 9.13 s [1H, C(O)NHNH], 9.68 s [1H, C(O)NHNH]. Mass spectrum, *m/z* (I_{rel}, %): 218 $[M]^+$ (12.9), 100 (100), 70 (27.8) 60 (40.45), 56 (50), 43 (42.8), 42 (52.1), 41 (24.6).

Potassium *N*'-(2-morpholin-4-ylacetyl)hydrazinocarbothionate (VI). A mixture of 1.59 g (0.01 mol) of morpholinylacetic acid hydrazide **I** and 0.84 g (0.015 mol) of potassium hydroxide were dissolved in 15 ml of water-free ethanol and 1.52 g (0.02 mol) of carbon disulfide was added dropwise with cooling. The reaction mixture was stirred for 2–3 h. The precipitated powder product was filtered off and washed several times with anhydrous diethyl ether. 2.27 g (83%) was obtained, mp 212–214°C.

5-(Morpholinylmethyl)-1,3,4-thiadiazole-2-thione (VII). 1.36 g (5 mmol) of potassium hydrazinodithiomorpholinylacetate **VI** was dissolved by portions in 3 ml of conc. sulfuric acid cooled to 0°C. The resulting solution was poured into 50 ml of ice-water and neutralized. The reaction product was extracted with ethyl acetate. After drying over calcined potassium carbonate and distilling the solvent off we isolated 0.97 g (45%) of product **VII,** mp 136–137°C (ethanol). Crystals of compound **VII** for X-ray diffraction study were obtained by natural evaporation of a saturated alcoholic solution of the compound. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.46 t [4H, $N(CH_2)_2$, *J* = 4.44], 3.32 s (2H, NCH_2), 3.57 t [4H, $O(CH_2)_2$, *J* = 4.58], 14.37 s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 217 $[M]^+$ (50.3), 132 (20.1), 100 (100), 86 (65.5) 56 (28.8), 55 (24.6), 42 (22.3), 41 (15.7).

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