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Thioamides from 5-Arylfurfural and Monosubstituted Piperazine Derivatives (Wilgerodt–Kindler Reaction)

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Abstract—Interaction of 5-arylfurfurals or arylaldehydes with secondary amines (monosubstituted piperazines, morpholine, piperidine) and sulfur under conditions of Wilgerodt–Kindler reaction provided N-substituted thioamides of 5-arylfuran-2-carboxylic and benzoic acids.

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Thioamides are reactive compounds successfully used in organic synthesis, in particular, in the preparation of mesoionic betaines [1], thiazole derivatives [2, 3], rhodanine [4], and other heterocycles [5], as thioacylating reagents [6]. Owing to their versatile properties the thioamides are used in medicine, in rubber vulcanization as boosters, as inhibitors of metal corrosion [7].

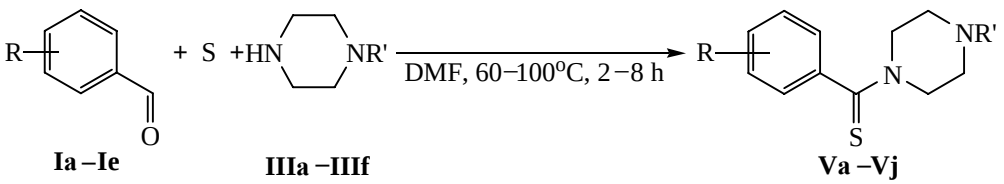
Thioamides are prepared by various known methods [7, 8] based on reactions of nitriles, amidoximes, imino-esters, and imidoyl chlorides with hydrogen sulfide or other sulfur derivatives. Wilgerodt–Kindler reaction is among the most common procedures for thioamides synthesis. The reaction is carried out in various modifications [7, 9].

5-Arylfurfurals were not yet brought into the Wilgerodt–Kindler reaction. On the other hand thio-amides containing a piperazine ring are of interest since many among piperazine derivatives are endowed with a biologic action [10].

In the present study we investigated the interaction of substituted benzaldehydes **Ia–Ie** and 5-arylfurfurals **IIa–IIj** with piperazine derivatives **IIIa–IIIh** and sulfur under the conditions of Wilgerodt–Kindler reaction. We also reacted aldehydes **IIa–IIj** with morpholine (**IVa**) and piperidine (**IVb**). In all events thioamides **V–VII** were obtained in high or moderate yields (Scheme 1).

Sometimes benzene was used as solvent, but the best results were obtained in reactions carried out in DMF. The optimum ratio aldehyde (**I,II**):sulfur:amine was 1:1:1.3. The reaction time and temperature was adjusted depending on the reactivity of the reagents. The process was more vigorous with aromatic aldehydes possessing electron-acceptor substituents. We failed to bring into the reaction aldehydes with alkoxy substituents. In contrast the aldehydes containing *p*-dimethylamino and *p*-diethylamino groups gave thioamides in good yields. With 5-arylfurfurals **IIa–IIj** the character of the substituent in the aromatic ring did not significantly affect

Scheme 1.



Ia–Ie **IIIa–IIIf** **Va–Vj**

I, R = 4-*t*-Bu (**a**), 3-NO_2 (**b**), 4-NMe_2 (**c**), 4-Cl (**d**), 4-OH (**e**); **III**, R' = Ac (**a**), Ph (**b**), 2-MeC_6H_4 (**c**), 3-ClC_6H_4 (**d**), 2-$O_2NC_6H_4$ (**e**), 1-$C_{10}H_7$ (**f**); **V**, R' = Ac, R = 4-*t*-Bu (**a**), 3-NO_2 (**b**), 4-NMe_2 (**c**); R' = Ph, R = 4-Cl (**d**), 4-OH (**e**), 4-NMe_2 (**f**); R = 4-NMe_2, R' = 2-MeC_6H_4 (**g**), 3-ClC_6H_4 (**h**), 1-$C_{10}H_7$ (**j**); R = 4-*t*-Bu, R' = 2-O_2NC_6H (**i**).

the reactivity. The unsubstituted furfural is unstable under the reaction conditions, and the reaction mixture suffers tarring due to the opening of the furan ring in the presence of amine. The amine nature also affected the yield of thioamides **V–VII**: The reaction took less time at the use of more basic amines [piperidine and 4-(2-cyanoethyl)piperazine (**IIIg**)] (Scheme 2).

The reaction progress was monitored by TLC (eluent hexane–acetone, 4:1), and also by qualitative tests for carbonyl group and H_2S.

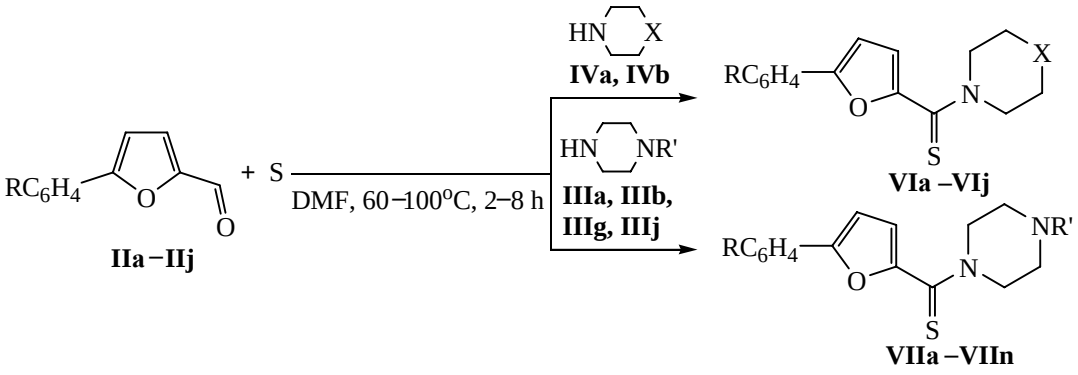
The structure of compounds synthesized was confirmed by ^{1}H NMR spectra. The structure of compound **VIe** was also proved by transforming it into 5-(3-nitrophenyl)-furan-2-carboxylic acid morpholide (**VIII**) by treating with potassium permanganate (Scheme 3). Compound **VIII** was also obtained by an independent synthesis through arylating the furan-2-carboxylic acid with 3- nitrophenyldiazonium chloride [11], converting the acid obtained into the acyl chloride and reacting the latter with morpholine.

Hence the available 5-arylfurfurals are convenient reagents for thioamides synthesis by Wilgerodt–Kindler reaction.

EXPERIMENTAL

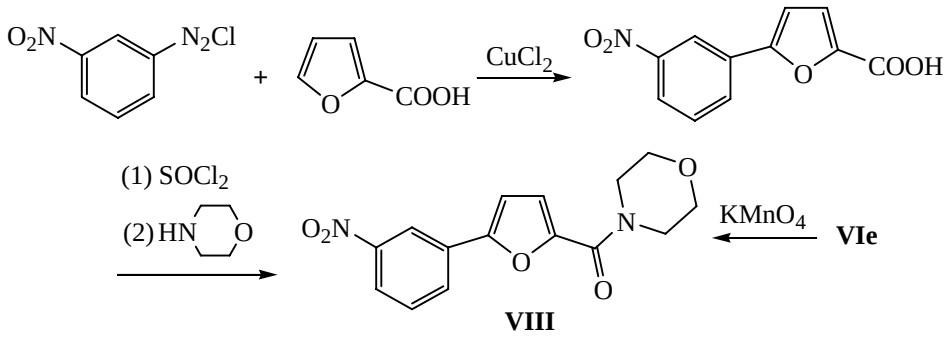
^{1}H NMR spectra were registered on spectrometers Bruker at operating frequencies 500 (**Vd–Vf**), 400 (**Va–Vc, Vi**, and **Vj**), and 300 MHz (**VIa, VIc, VIe, VIh, VIIa–VIIn**). Solvents used were $CDCl_3$ (**VIe** and **VIh**), DMSO-d_6 (**Va–Vc, VId–VIf, VIi, VIj**, and **VIIi**), and DMSO-d_6–CCl_4 (the other compounds). Chemical shifts were measured with respect to the solvent signal (DMSO, 2.50 ppm) or to the internal reference.

Scheme 2.



II, R = 3-CF_3 (**a**), 2-Cl (**b**), 4-Cl (**c**), 2,3-Cl_2 (**d**), 2,4-Cl_2 (**e**), 2,5-Cl_2 (**f**), 3,4-Cl_2 (**g**), 4-Br (**h**), 2-NO_2 (**i**), 3-NO_2 (j); **III**, R' = CH_2CH_2CN (**g**), 4-MeC_6H_4 (**h**); **IV**, X = O (**a**), CH_2 (b); **VI**, X = O, R = 2,3-Cl_2 (**a**), 2,5-Cl_2 (**b**), 3,4-Cl_2 (**c**), 4-Br (**d**), 3-NO_2 (**e**); X = CH_2, R = 4-Cl (**f**), 2,4-Cl_2 (**g**), 2,5-Cl_2 (**h**), 4-Br (**i**), 3-NO_2 (**j**); **VII**, R' = CH_2CH_2CN, R = 2,3-Cl_2 (**a**), 2,5-Cl_2 (**b**), 2-NO_2 (**c**), 3-NO_2 (**d**); R' = Ac, R = 2,5-Cl_2 (**e**), 2-NO_2 (**f**), 3-NO_2 (**g**); R' = Ph, R = 3-CF_3 (**h**), 2-Cl (**i**), 2,5-Cl_2 (**j**), 2-NO_2 (**k**); R' = 4-MeC_6H_4, R = 3-CF_3 (**l**), 2,5-Cl_2 (**m**), 2-NO_2 (**n**).

Scheme 3.



Initial 5-arylfurfurals were obtained by procedure from [12]. Monosubstituted piperazines were prepared as described in [13].

1-(2-Cyanoethyl)piperazine (IIIg). To a mixture of 20.4 ml (0.31 mol) of acrylonitrile and 20 ml of ethanol was added gradually at cooling while stirring 25.8 g (0.3 mol) of anhydrous piperazine. The reaction mixture was boiled for 3 h, the solvent was distilled off, and the residue was subjected to fractional distillation in a vacuum. Yield 24.7 g (59%), bp 106°C (1.5 mm Hg), n_D^{20} 1.4909.

Thioamides V–VII. A mixture of 0.01 mol of aldehyde **I** or **II**, 0.013 mol of secondary amine **III** or **IV**, and 0.32 g (0.01 mol) of fine powder of sulfur in 20 ml of DMF was heated at 60–100°C with stirring till the end of hydrogen sulfide liberation (from 2 to 8 h). The cooled reaction mixture was diluted with water (100 ml), the separated precipitate was filtered off and recrystallized from ethanol with DMF added.

1-Acetyl-4-(4-*tert*-butylbenzothioyl)piperazine (Va). Yield 74%, mp 165–166°C. ^{1}H NMR spectrum, δ, ppm: 1.32 s (9H, Me_3C), 1.99 s + 2.07 s (3H, Me), 3.48 br.s (2H, CH_2NAc), 3.59 br.s + 3.64 br.s (2H, $CH_2NC{=}S$), 3.69 br.s (2H, CH_2NAc), 4.23 br.s + 4.30 br.s (2H, $CH_2NC{=}S$), 7.21 d (2H, C_6H_4), 7.37 d (2H, C_6H_4). Found, %: N 9.34; S 10.45. $C_{17}H_{24}N_2OS$. Calculated, %: N 9.20; S 10.53.

1-Acetyl-4-(3-nitrobenzothioyl)piperazine (Vb). Yield 50%, mp 82–83°C. ^{1}H NMR spectrum, δ, ppm: 2.00 s + 2.07 s (3H, Me), 3.50 br.s (2H, CH_2NAc), 3.57 br.s + 3.62 br.s (2H, $CH_2NC{=}S$), 3.72 br.s (2H, CH_2NAc), 4.24 br.s + 4.31 br.s (2H, $CH_2NC{=}S$), 7.63–7.74 m (2H, C_6H_4), 8.12–8.22 m (2H, C_6H_4). Found, %: N 14.47; S 10.82. $C_{13}H_{15}N_3O_3S$. Calculated, %: N 14.32; S 10.93.

1-Acetyl-4-(4-dimethylaminobenzothioyl)-piperazine (Vc). Yield 65%, mp 118–119°C. ^{1}H NMR spectrum, δ, ppm: 2.04 s (3H, Me), 2.98 C (6H, Me_2N), 3.57 br.s [4H, $(CH_2)_2NAc$], 3.75 br.s (2H, $CH_2NC{=}S$), 4.17 br.s (2H, $CH_2NC{=}S$), 6.62 d (2H, C_6H_4), 7.22 d (2H, C_6H_4). Found, %: N 14.53; S 10.88. $C_{15}H_{21}N_3OS$. Calculated, %: N 14.42; S 11.00.

(4-Chlorophenyl)-(4-phenylpiperazin-1-yl)-methanethione (Vd). Yield 46%, mp 145–146°C. ^{1}H NMR spectrum, δ, ppm: 3.20 t (2H, CH_2NPh), 3.40 t (2H, CH_2NPh), 3.73 t (2H, $CH_2NC{=}S$), 4.44 t (2H, $CH_2NC{=}S$), 6.81 t (1H, Ph), 6.92 d (2H, Ph), 7.22 t (2H, Ph), 7.33 d (2H, C_6H_4), 7.41 d (2H, C_6H_4). Found, %: N 8.95; S 10.01. $C_{17}H_{17}ClN_2S$. Calculated, %: N 8.84; S 10.12.

(4-Hydroxyphenyl)-(4-phenylpiperazin-1-yl)-methanethione (Ve). Yield 56%, mp 217–218°C. ^{1}H NMR spectrum, δ, ppm: 3.19 br.s (2H, CH_2NPh), 3.38 br.s (2H, CH_2NPh), 3.81 br.s (2H, $CH_2NC{=}S$), 4.42 br.s (2H, $CH_2NC{=}S$), 6.74 d (2H, C_6H_4), 6.80 t (1H, Ph), 6.92 d (2H, Ph), 7.21 t (2H, Ph), 7.17 d (2H, C_6H_4), 9.61 C (1H, OH). Found, %: N 9.48; S 10.65. $C_{17}H_{18}N_2OS$. Calculated, %: N 9.39; S 10.74.

(4-Dimethylaminophenyl)-(4-phenylpiperazin-1-yl)methanethione (Vf). Yield 71%, mp 139–140°C. ^{1}H NMR spectrum, δ, ppm: 3.00 s (6H, Me_2N), 3.29 br.s [4H, $(CH_2)_2NPh$], 3.88 br.s (2H, $CH_2NC{=}S$), 4.38 br.s (2H, $CH_2NC{=}S$), 6.65 d (2H, C_6H_4), 6.81 t (1H, Ph), 6.92 d (2H, Ph), 7.21 t (2H, Ph), 7.24 d (2H, C_6H_4). Found, %: N 13.03; S 9.77. $C_{19}H_{23}N_3S$. Calculated, %: N 12.91; S 9.85.

(4-Dimethylaminophenyl)-[4-(2-methylphenyl)-piperazin-1-yl]methanethione (Vg). Yield 64%, mp 145–146°C. Found, %: C 70.61; H 7.59; N 12.24; S 9.36. $C_{20}H_{25}N_3S$. Calculated, %: C 70.76; H 7.42; N 12.38; S 9.44.

(4-Dimethylaminophenyl)-[4-(3-chlorophenyl)-piperazin-1-yl]methanethione (Vh). Yield 68%, mp 153–154°C. Found, %: C 63.62; H 6.04; N 11.52; S 9.03. $C_{19}H_{22}ClN_3S$. Calculated, %: C 63.41; H 6.16; N 11.67; S 8.81.

(4-*tert*-Butylphenyl)-[4-(2-nitrophenyl)-piperazin-1-yl]methanethione (Vi). Yield 65%, mp 122–123°C. ^{1}H NMR spectrum, δ, ppm: 1.32 s (9H, Me_3C), 3.07 t (2H, CH_2NAr), 3.29 t (2H, CH_2NAr), 3.75 t (2H, $CH_2NC{=}S$), 4.44 t (2H, $CH_2NC{=}S$), 7.16 t (1H, C_6H_4N), 7.23 d (2H, C_6H_4), 7.38 d (2H, C_6H_4), 7.34 d (1H, C_6H_4N), 7.59 t (1H, C_6H_4N), 7.80 d (1H, C_6H_4N). Found, %: N 11.17; S 8.28. $C_{21}H_{25}N_3O_2S$. Calculated, %: N 10.96; S 8.36.

(4-Dimethylaminophenyl)-[4-(1-naphthyl)-piperazin-1-yl]methanethione (Vj). Yield 45%, mp 106–107°C. ^{1}H NMR spectrum, δ, ppm: 2.99 s (6H, Me_2N), 3.15 br.s [4H, $(CH_2)_2NAr$], 4.00 br.s [4H, $(CH_2)_2NC{=}S$], 6.64 d (2H, C_6H_4), 7.12 d (1H, $C_{10}H_7$), 7.25 d (2H, C_6H_4), 7.39 t (1H, $C_{10}H_7$), 7.44–7.52 m (2H, $C_{10}H_7$), 7.57 d (1H, $C_{10}H_7$), 7.83 d (1H, $C_{10}H_7$), 8.19 d (1H, $C_{10}H_7$). Found, %: N 11.02; S 8.68. $C_{23}H_{25}N_3S$. Calculated, %: N 11.19; S 8.54.

[5-(2,3-Dichlorophenyl)-2-furyl]-(morpholin-4-yl)methanethione (VIa). Yield 78%, mp 128–129°C.

^{1}H NMR spectrum, δ, ppm: 3.79 t [4H, $(CH_2)_2N$], 4.18 br.s [4H, $(CH_2)_2O$], 7.12 d (1H, furan), 7.20 d (1H, furan), 7.40 t (1H, C_6H_3), 7.52 d (1H, C_6H_3), 7.80 d (1H, C_6H_3). Found, %: N 4.17; S 9.22. $C_{15}H_{13}Cl_2NO_2S$. Calculated, %: N 4.09; S 9.37.

[5-(2,5-Dichlorophenyl)-2-furyl]-(morpholin-4-yl)-methanethione (VIb). Yield 85%, mp 145–146°C. Found, %: C 52.40; H 4.01; N 4.15; S 9.54. $C_{15}H_{13}Cl_2NO_2S$. Calculated, %: C 52.64; H 3.83; N 4.09; S 9.37.

[5-(3,4-Dichlorophenyl)-2-furyl]-(morpholin-4-yl)methanethione (VIc). Yield 75%, mp 134–135°C. ^{1}H NMR spectrum, δ, ppm: 3.80 t [4H, $(CH_2)_2N$], 4.16 br.s [4H, $(CH_2)_2O$], 7.05 d (1H, furan), 7.09 d (1H, furan), 7.55 d (1H, C_6H_3), 7.67 d (1H, C_6H_3), 7.88 s (1H, C_6H_3). Found, %: N 4.26; S 9.18. $C_{15}H_{13}Cl_2NO_2S$. Calculated, %: N 4.09; S 9.37.

[5-(4-Bromophenyl)-2-furyl]-(morpholin-4-yl)-methanethione (VId). Yield 82%, mp 148–149°C. Found, %: C 51.34; H 4.12; N 3.78; S 9.22. $C_{15}H_{14}BrNO_2S$. Calculated, %: C 51.15; H 4.01; N 3.98; S 9.10.

[5-(3-Nitrophenyl)-2-furyl]-(morpholin-4-yl)-methanethione (V²e). Yield 82%, mp 152–153°C. ^{1}H NMR spectrum, δ, ppm: 3.88 br.s [4H, $(CH_2)_2N$], 4.10 br.s (2H, CH_2O), 4.35 br.s (2H, CH_2O), 6.89 d (1H, furan), 7.21 d (1H, furan), 7.61 t (1H, C_6H_4), 7.96 d (1H, C_6H_4), 8.18 d (1H, C_6H_4), 8.48 C (1H, C_6H_4). Found, %: N 8.62; S 10.28. $C_{15}H_{14}N_2O_4S$. Calculated, %: N 8.79; S 10.06.

[5-(4-Chlorophenyl)-2-furyl]-(piperidin-1-yl)-methanethione (VIf). Yield 72%, mp 108–109°C. Found, %: C 62.80; H 5.39; N 4.67; S 10.53. $C_{16}H_{16}ClNOS$. Calculated, %: C 62.84; H 5.27; N 4.58; S 10.48.

[5-(2,4-Dichlorophenyl)-2-furyl]-(piperidin-1-yl)methanethione (VIg). Yield 68%, mp 103–104°C. Found, %: C 56.34; H 4.38; N 4.18; S 9.58. $C_{16}H_{15}Cl_2NOS$. Calculated, %: C 56.48; H 4.44; N 4.12; S 9.42.

[5-(2,5-Dichlorophenyl)-2-furyl]-(piperidin-1-yl)methanethione (VIh). Yield 78%, mp 122–123°C. ^{1}H NMR spectrum, δ, ppm: 1.81 br.s [6H, $(CH_2)_3$], 3.87 br.s (2H, CH_2N), 4.28 br.s (2H, CH_2N), 7.11 d (1H, furan), 7.18 d (1H, furan), 7.23 d.d (1H, C_6H_3), 7.37 d (1H, C_6H_3), 7.77 d (1H, C_6H_3). Found, %: C 56.50; H 4.60; N 4.25. $C_{16}H_{15}Cl_2NOS$. Calculated, %: C 56.48; H 4.44; N 4.12.

[5-(4-Bromophenyl)-2-furyl]-(piperidin-1-yl)-methanethione (VIi). Yield 60%, mp 137–138°C. Found, %: C 54.72; H 4.49; N 4.05; S 9.22. $C_{16}H_{16}BrNOS$. Calculated, %: C 54.86; H 4.60; N 4.00; S 9.15.

[5-(3-Nitrophenyl)-2-furyl]-(piperidin-1-yl)methanethione (VIj). Yield 75%, mp 92–93°C. Found, %: C 60.58; H 5.02; N 8.94; S 10.32. $C_{16}H_{16}N_2O_3S$. Calculated, %: C 60.74; H 5.10; N 8.85; S 10.13.

3-{4-[5-(2,3-Dichlorophenyl)-2-furylcarbothioyl]-piperazin-1-yl}propionitrile (VIIa). Yield 65%, mp 87–88°C. ^{1}H NMR spectrum, δ, ppm: 2.60–2.80 m [4H, $(CH_2)_2CN$], 2.73 s [4H, $(CH_2)_2NAlk$], 4.16 br.s [4H, $(CH_2)_2NC=S$], 7.09 d (1H, furan), 7.20 d (1H, furan), 7.40 t (1H, C_6H_3), 7.53 d (1H, C_6H_3), 7.80 d (1H, C_6H_3). Found, %: C 54.70; H 4.21; N 10.60. $C_{18}H_{17}Cl_2N_3OS$. Calculated, %: C 54.83; H 4.35; N 10.66.

3-{4-[5-(2,5-Dichlorophenyl)-2-furylcarbothioyl]-piperazin-1-yl}propionitrile (VIIb). Yield 62%, mp 140–141°C. ^{1}H NMR spectrum, δ, ppm: 2.63 t (2H, CH_2N), 2.75 t (2H, CH_2CN), 2.70 s [4H, $(CH_2)_2NAlk$], 4.15 br.s [4H, $(CH_2)_2NC=S$], 7.06 d (1H, furan), 7.22 d (1H, furan), 7.31 d.d (1H, C_6H_3), 7.50 d (1H, C_6H_3), 7.81 d (1H, C_6H_3). Found, %: C 54.97; H 4.26; N 10.82. $C_{18}H_{17}Cl_2N_3OS$. Calculated, %: C 54.83; H 4.35; N 10.66.

3-{4-[5-(2-Nitrophenyl)-2-furylcarbothioyl]-piperazin-1-yl}propionitrile (VIIc). Yield 65%, mp 134–135°C. ^{1}H NMR spectrum, δ, ppm: 2.59–2.79 m [8H, $(CH_2)_2CN$ + $(CH_2)_2NAlk$], 4.07 br.s [4H, $(CH_2)_2NC=S$], 6.89 d (1H, furan), 7.12 d (1H, furan), 7.60 t (1H, C_6H_4), 7.71 t (1H, C_6H_4), 7.83 t (2H, C_6H_4). Found, %: C 58.24; H 4.77; N 14.98. $C_{18}H_{18}N_4O_3S$. Calculated, %: C 58.36; H 4.90; N 15.12.

3-{4-[5-(3-Nitrophenyl)-2-furylcarbothioyl]-piperazin-1-yl}propionitrile (VIId). Yield 67%, mp 94–95°C. ^{1}H NMR spectrum, δ, ppm: 2.65 t (2H, CH_2N), 2.76 t (2H, CH_2CN), 2.74 s [4H, $(CH_2)_2NAlk$], 4.18 br.s [4H, $(CH_2)_2NC=S$], 7.09 d (1H, furan), 7.19 d (1H, furan), 7.70 t (1H, C_6H_4), 8.14 d (2H, C_6H_4), 8.51 C (1H, C_6H_4). Found, %: C 58.50; H 4.98; N 15.31. $C_{18}H_{18}N_4O_3S$. Calculated, %: C 58.36; H 4.90; N 15.12.

1-Acetyl-4-{[5-(2,5-dichlorophenyl)-2-furyl]-carbothioyl}piperazine (VIIe). Yield 68%, mp 165–166°C. ^{1}H NMR spectrum, δ, ppm: 2.09 s (3H, Me), 3.70 t [4H, $(CH_2)_2NAC$], 4.13 br.s (2H, $CH_2NC=S$), 4.19 br.s (2H, $CH_2NC=S$), 7.12 d (1H, furan), 7.23 d (1H, furan), 7.33 d.d (1H, C_6H_3), 7.51 d (1H, C_6H_3),

7.84 d (1H, C_6H_3). Found, %: C 53.12; H 4.38; N 7.17. $C_{17}H_{16}Cl_2N_2O_2S$. Calculated, %: C 53.27; H 4.21; N 7.31.

1-Acetyl-4-{[5-(2-nitrophenyl)-2-furyl]carbothioyl}piperazine (VIIf). Yield 68%, mp 153–154°C. ^{1}H NMR spectrum, δ, ppm: 2.09 s (3H, Me), 3.68 br.s [4H, $(CH_2)_2NAC$], 4.07 br.s [4H, $(CH_2)_2NC{=}S$], 6.90 d (1H, furan), 7.19 d (1H, furan), 7.60 t (1H, C_6H_4), 7.72 t (1H, C_6H_4), 7.80–7.90 m (2H, C_6H_4). Found, %: C 56.70; H 4.75; N 11.80. $C_{17}H_{17}N_3O_4S$. Calculated, %: C 56.81; H 4.77; N 11.69.

1-Acetyl-4-{[5-(3-nitrophenyl)-2-furyl]carbothioyl}piperazine (VIIg). Yield 65%, mp 145–146°C. ^{1}H NMR spectrum, δ, ppm: 2.09 s (3H, Me), 3.71 br.s [4H, $(CH_2)_2NAC$], 4.15 br.s (2H, $CH_2NC{=}S$), 4.21 br.s (2H, $CH_2NC{=}S$), 7.15 d (1H, furan), 7.22 d (1H, furan), 7.71 t (1H, C_6H_4), 8.11–8.20 m (2H, C_6H_4), 8.52 C (1H, C_6H_4). Found, %: C 56.94; H 4.60; N 11.54. $C_{17}H_{17}N_3O_4S$. Calculated, %: C 56.81; H 4.77; N 11.69.

{[5-(3-Trifluoromethylphenyl)-2-furyl]-(4-phenylpiperazin-1-yl)}methanethione (VIIh). Yield 76%, mp 158–159°C. ^{1}H NMR spectrum, δ, ppm: 3.41 t [4H, $(CH_2)_2NPh$], 4.30 br.s [4H, $(CH_2)_2NC{=}S$], 7.12 d (1H, furan), 7.15 d (1H, furan), 6.80 t (1H, Ph), 6.92 d (2H, Ph), 7.22 t (2H, Ph), 7.56–7.69 m (2H, C_6H_4), 7.98–8.03 m (2H, C_6H_4). Found, %: C 63. 59; H 4.72; N 6.85. $C_{22}H_{19}F_3N_2OS$. Calculated, %: C 63.45; H 4.60; N 6.73.

{[5-(2-Chlorophenyl)-2-furyl]-(4-phenylpiperazin-1-yl)}methanethione (VIIi). Yield 70%, mp 165–166°C. ^{1}H NMR spectrum, δ, ppm: 3.40 br.s [4H, $(CH_2)_2NPh$], 4.29 br.s [4H, $(CH_2)_2NC{=}S$], 7.17 d (1H, furan), 7.22 d (1H, furan), 6.80 t (1H, Ph), 6.95 d (2H, Ph), 7.20 t (2H, Ph), 7.37–7.48 m (2H, C_6H_4), 7.53 d (1H, C_6H_4), 7.89 d (1H, C_6H_4). Found, %: C 65.59; H 5.17; N 7.21. $C_{21}H_{19}ClN_2OS$. Calculated, %: C 65.87; H 5.00; N 7.32.

{[5-(2,5-Dichlorophenyl)-2-furyl]-(4-phenylpiperazin-1-yl)}methanethione (VIIj). Yield 69%, mp 108–109°C. ^{1}H NMR spectrum, δ, ppm: 3.40 br.s [4H, $(CH_2)_2NPh$], 4.30 br.s [4H, $(CH_2)_2NC{=}S$], 7.12 d (1H, furan), 7.24 d (1H, furan), 6.81 t (1H, Ph), 6.91 d (2H, Ph), 7.22 t (2H, Ph), 7.33 d.d (1H, C_6H_3), 7.50 d (1H, C_6H_3), 7.84 d (1H, C_6H_3). Found, %: C 60.61; H 4.21; N 6.62. $C_{21}H_{18}Cl_2N_2OS$. Calculated, %: C 60.44; H 4.35; N 6.71.

{[5-(2-Nitrophenyl)-2-furyl]-(4-phenylpiperazin-1-yl)}methanethione (VIIk). Yield 60%, mp 110–111°C. ^{1}H NMR spectrum, δ, ppm: 3.37 br.s [4H, $(CH_2)_2NPh$], 4.20 br.s [4H, $(CH_2)_2NC{=}S$], 6.81 t (1H, Ph), 6.90–6.97 m (1H furan + 2H, Ph), 7.17–7.27 m (1H furan + 2H, Ph), 7.60 t (1H, C_6H_4), 7.71 t (1H, C_6H_4), 7.81–7.89 m (2H, C_6H_4). Found, %: C 64.38; H 5.03; N 10.80. $C_{21}H_{19}N_3O_3S$. Calculated, %: C 64.11; H 4.87; N 10.68.

{[5-(2-Trifluoromethylphenyl)-2-furyl]-[(4-methylphenyl)piperazin-1-yl]}methanethione (VIIl). Yield 75%, mp 128–129°C. ^{1}H NMR spectrum, δ, ppm: 2.26 C (3H, Me), 3.33 t [4H, $(CH_2)_2NAr$], 4.30 br.s [4H, $(CH_2)_2NC{=}S$], 7.12 c (2H, furan), 6.82 d (2H, C_6H_4N), 7.02 d (2H, C_6H_4N), 7.57–7.69 m (2H, C_6H_4), 8.01 br.s (2H, C_6H_4). Found, %: C 64.26; H 4.84; N 6.38. $C_{23}H_{21}F_3N_2OS$. Calculated, %: C 64.17; H 4.92; N 6.51.

{[5-(2,5-Dichlorophenyl)-2-furyl]-[(4-methylphenyl)piperazin-1-yl]}methanethione (VIIm). Yield 68%, mp 145–146°C. ^{1}H NMR spectrum, δ, ppm: 2.26 s (3H, Me), 3.31 br.s [4H, $(CH_2)_2NAr$], 4.28 br.s [4H, $(CH_2)_2NC{=}S$], 7.11 d (1H, furan), 7.25 d (1H, furan), 6.81 d (2H, C_6H_4N), 7.02 d (2H, C_6H_4N), 7.33 d.d (1H, C_6H_3), 7.50 d (1H, C_6H_3), 7.83 d (1H, C_6H_3). Found, %: C 61.42; H 4.49; N 6.65. $C_{22}H_{20}Cl_2N_2OS$. Calculated, %: C 61.25; H 4.67; N 6.49.

{[5-(2-Nitrophenyl)-2-furyl]-[(4-methylphenyl)-piperazin-1-yl]}methanethione (VIIn). Yield 78%, mp 146–147°C. ^{1}H NMR spectrum, δ, ppm: 2.28 s (3H, Me), 3.29 br.s [4H, $(CH_2)_2NAr$], 4.20 br.s [4H, $(CH_2)_2NC{=}S$], 6.92 d (1H, furan), 7.17 d (1H, furan), 6.82 d (2H, C_6H_4N), 7.03 d (2H, C_6H_4N), 7.60 t (1H, C_6H_4), 7.71 t (1H, C_6H_4), 7.81–7.88 m (2H, C_6H_4). Found, %: C 64.71; H 5.07; N 10.49. $C_{22}H_{21}N_3O_3S$. Calculated, %: C 64.85; H 5.19; N 10.31.

Morpholin-4-yl-[5-(3-nitrophenyl)furan-2-yl]-methanone (VIII). *a*. To a solution of 1.27 g (4 mmol) of 5-(3-nitrophenyl)-2-furylmorpholinomethanethione (**VIe**) in 25 ml of methanol was added 1.42 g (9 mmol) of $KMnO_4$ dissolved in 25 ml of water. The mixture was boiled for 3 h. On cooling the precipitate of manganese(IV) oxide was filtered off, the filtrate was neutralized with acetic acid, evaporated by half, and extracted with ether. On distilling off the solvent we obtained compound **VIII** as light-yellow crystals. Yield 40%, mp 166–167°C. Found, %: C 59.34; H 4.61; N 9.33. $C_{15}H_{14}N_2O_5$. Calculated, %: C 59.60; H 4.67; N 9.27.

b. To 0.5 g (2 mmol) of 5-(3-nitrophenyl)furan-2-carbonyl chloride dissolved in 5 ml of anhydrous dioxane was added at stirring 1 ml of triethylamine and 0.52 g (6 mmol) of morpholine. The mixture was stirred for 1 h, the precipitate was filtered off, washed with water, and recrystallized from ethanol. Yield 0.30 g (50%), mp 166–167°C.

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