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Synthesis and Some Reactions of Derivatives of 5-(1,2,3-Thiadiazol-4-yl)furan-2-carboxylic and 3-[5-(1,2,3- Thiadiazol-4-yl)fur-2-yl]acrylic Acids

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Abstract—Alkyl 5-(1,2,3-thiadiazol-4-yl)furan-2-furoate and 3-[5-(1,2,3-thiadiazol-4-yl)fur-2-yl]acrylate were synthesized via cyclization of carbethoxyhydrazones of acetyl derivatives of furan-2-carboxylic and 3-(2-furyl)-acrylic acids under the conditions of the Hurd–Mori reaction. Corresponding acids, acid chlorides, amides, furoyl hydrazide and acryloyl azide were prepared. It was shown that in all above-mentioned substances furylthiadiazole fragment is thermally stable. Treating of methyl 5-(1,2,3-thiadiazol-4-yl)furan-2-furoate with morpholine in the presence of potassium hydroxide leads to the cleavage of thiadiazole ring with the liberation of nitrogen and the formation of [5-(methoxycarbonyl)fur-2-yl]acetic acid morpholide.

Keywords: hydrazones, Hurd–Mori reaction, (1,2,3-thiadiazol-4-yl)furans, acid derivatives
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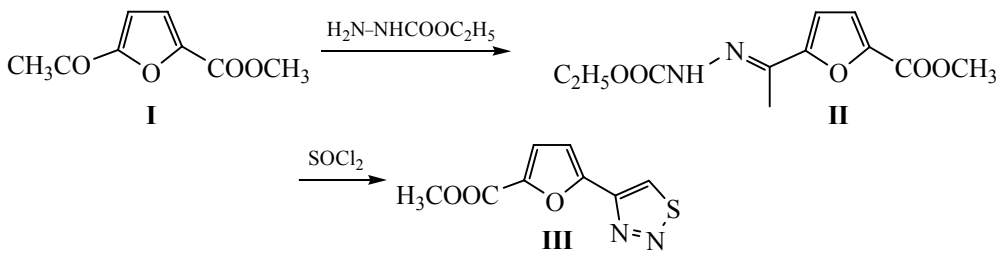
Recently [1] we have shown that unsubstituted 1,2,3-thiadiazol-4-ylfurans and their methyl derivatives may be prepared by cyclization of acetylfuran carbethoxyhydrazones according to the Hurd-Mori reaction, but this process is ambiguous, and the products formed are thermally unstable. At the same time this unusual polar system consisting of π-excessive and π-deficient heterocycles directly bound with one another presents interest due to the possibility of bonding with biomolecules. Therefore the aim of this work was elucidation of factors providing the stability of such systems.

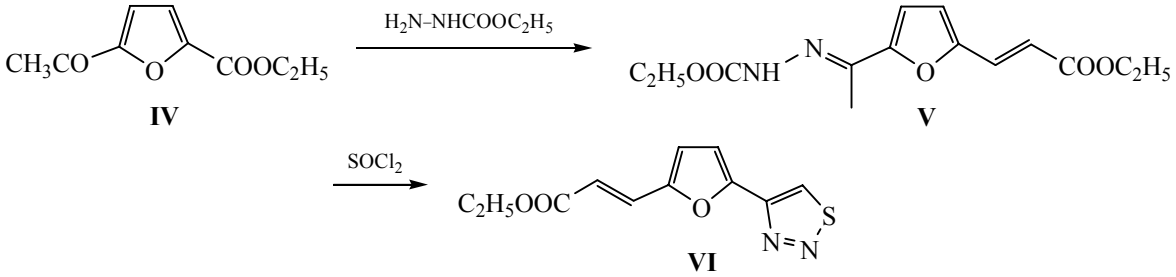
Considering that introduction of electron-donating methyl groups in the furan ring decreases the thermal stability of thiadiazolylfurans compared to the unsubstituted compounds [1] we suggested that the action of electron-acceptor substituents in the furan ring will be the opposite. For checking this hypothesis we turned to the most simple case of 2-(1,2,3-thiadiazol-4-yl)furan containing carboxy group in the position 5 and its vinylog, the derivative of 3-(2-furyl)-acrylic acid.

Hydrazone **II** was synthesized via the reaction of methyl 5-acetyl-2-furoate **I** with carbethoxyhydrazine in ethanol in the presence of catalytic amount of acetic acid. Boiling hydrazone **II** with 3 equivalents of thionyl chloride in chloroform for 1.5 h lead to the formation of 1,2,3-thiadiazole ring. The target product,

Scheme 1.



Scheme 2.



methyl 5-(1,2,3-thiadiazol-4-yl)-2-furoate **III,** was prepared in 93% yield. It proved to be a stable compound of mp 132–133ºC (Scheme 1).

Analogously from ethyl 3-(5-acetylfur-2-yl)acrylate **IV** through the hydrazone **V** furylthiadiazole **VI** was synthesized. The Hurd –Mori reaction was carried out at 65ºC in chloroform with 3 equiv. of thionyl chloride for 1.5 h. The target product **VI** was a stable crystalline compound of mp 103–104ºC obtained in 82% yield (Scheme 2).

Synthetic procedures, physicochemical and spectral characteristics are presented in the Experimental.

Hence, our suggestion that withdrawing electron density from the furan ring should lead to the stabilization of furan-thiadiazole system was confirmed. Next step of our work was the elucidation of the reactions which could be performed with participation of carboxy group without destroying the heterocyclic fragment.

By hydrolysis of methyl ester **III** with potassium hydroxide solution in ethanol free acid **VII** was prepared. Hydrolysis was carried out by gradual addition of potassium hydroxide to the reaction mixture maintaining pH within 8–10. In this way we tried to prevent the cleavage of thiadiazole ring. The acid **VII** was isolated in 69% yield as light brown crystals stable at room temperature and at moderate heating. Its decomposition with gas evolution took place at 165ºC.

Treating acid **VII** with thionyl chloride in benzene in the presence of catalytic amount of DMF yielded crystalline acid chloride **VIII**. This substance was stable at room temperature and slight heating, but decomposed below its melting point. It had no characteristic decomposition temperature. Depending on the rate of heating the gas evolution takes place at 95–112ºC.

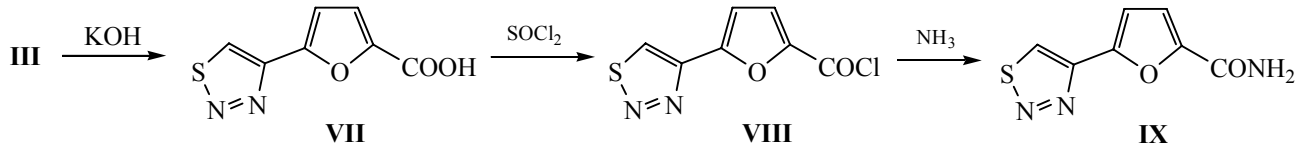
While treating benzene solution of acid chloride **VIII** with ammonia under cooling and intense stirring amide **IX** was formed in a moderate yield (30%). It was light brown crystalline product with a characteristic decomposition temperature of 110ºC. The stability of furylthiadiazole fragment in this compound was preserved at room temperature and moderate heating (Scheme 3).

Synthesis of acid chloride **VIII** opens broad prospects for preparing conjugated systems consisting of heterocycles of different nature. It was shown by an example of compound **XI** where 1,2,3-thiadiazole, furan, 1,3,4-oxadiazole, and pyridine rings are bound with one another (Scheme 4).

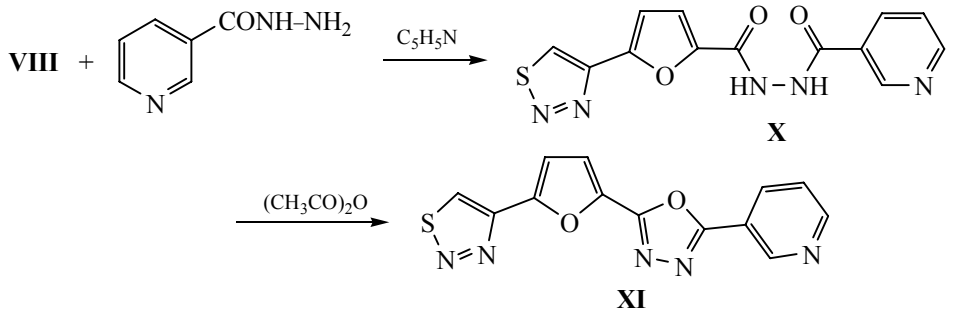
Acylation of the nicotinic acid hydrazide with acid chloride **VIII** in pyridine led to the formation of bishydrazide **X**. The latter under heating in acetic anhydride eliminates water to form 1,3,4-oxadiazole **XI**. It was isolated as light pink crystals after decomposition of the reaction mixture with water and then treating it with ammonia. The product is stable at room temperature. It has no characteristic melting point and decomposes above 138ºC.

Via hydrolysis of ethyl ester **VI** with ethanol solution of potassium hydroxide at the controlled pH

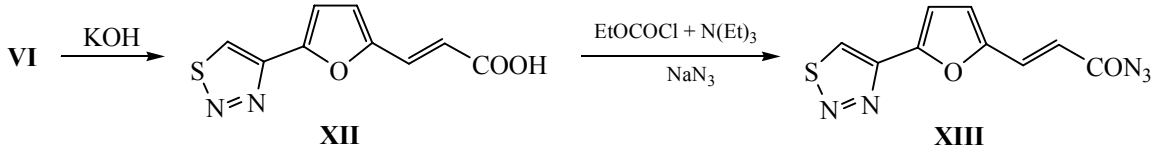
Scheme 3.



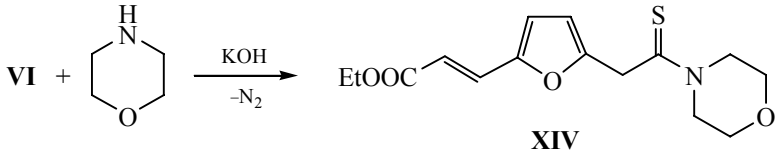
Scheme 4.



Scheme 5.



Scheme 6.



free acid **XII** was prepared. ^{1}H NMR spectrum of the compound obtained showed that it contained no significant admixtures. Despite of this fact the acid had intense violet coloration which did not disappear after boiling with charcoal. The product **XII** has no characteristic melting point. Under heating it quickly becomes black and decomposes at 145–147ºC.

Because of the sensitivity of the acid **XII** towards heating we tried to convert it to acyl azide by means of the standard procedure [2] based on the intermediate formation of mixed anhydride with ethyl chloroformate. All reactions were carried out at 2–4ºC. The conversion of the starting acid along this protocol was 70%, and the crystalline azide **XIII,** stable at room temperature, was prepared in 90% yield. Its structure was established by means of the ^{1}H and ^{13}C NMR spectroscopy. The formation of azide group was proved by the presence of characteristic absorption band at 2137 cm^{-1} in the IR spectrum (Scheme 5).

Compound **XII** may be widely used in the synthetic practice, e.g., for the modification of amino group or in the Curtius reaction.

Hence, the introduction of an acceptor substituent in the position 5 of the furan ring permits to provide thermal stability to the 2-(1,2,3-thiadiazol-4-yl)furan fragment. Nature of substituent may be varied in a considerably broad range.

We tried also to elucidate how linking of the furan and 1,2,3-thiadiazole rings influences chemical properties of the latter. As is known [2], characteristic reaction of monosubstituted 1,2,3-thiadiazoles is the cleavage of the ring under the action of bases with the liberation of nitrogen. In the presence of amines it results in the formation of thioamides of the acetic acid derivatives. Ester **VI** was involved in this reaction under the conditions of previously reported protocol [2]. The process was carried out in dioxane in the presence of excess morpholine and solid potassium hydroxide at 104–105ºC for 3 h. Furylacetic acid thiomorpholide **XIV** was the only reaction product. The ester group, the double bond, and the furan ring were not affected by the process (Scheme 6).

Hence, typical reaction of 1,2,3-thiadiazole ring cleavage with the elimination of nitrogen and intermediate formation of acetylene thiolates proceeds as usual in the presence of linked heteroring.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were taken on a Bruker DPX-400 spectrometer [400.13 (^{1}H), 100.16 MHz (^{13}C)]. IR spectra were registered on a Perkin-Elmer Spectrum 100 spectrophotometer with the help of the disturbed complete internal reflection adapter. Mass spectra were obtained on a Finnigan INCOS MAT 95 spectrometer (direct admission of the sample, ionization chamber temperature 200ºC, ionizing electrons energy 70 eV).

Methyl 5-acetylfuran-2-furoate carbethoxyhydrazone (II). Methyl 5-acetylfuran-2-furoate **I**, 6.3 g, was dissolved in 10 mL of ethanol, and 3.9 g of carbethoxyhydrazine and 8 drops of acetic acid were added to the obtained solution. The reaction mixture was refluxed for 1 h. The reaction progress was monitored by TLC (Silufol plates, eluent acetone : chloroform, 1 : 1, for compound **I** R_f 0.69). After completion of the reaction the mixture obtained was diluted by 2 volumes of water. The crystals formed were filtered off and crystallized from a mixture of 15 mL of ethanol and 15 mL of water. Hydrazone **II**, 6.8 g (72%), mp 110ºC. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.39 t (3H, CH_3, *J* 7.2 Hz), 2.24 s (3H, CH_3-hydrazone), 3.90 s (3H, CH_3O), 4.31 q (2H, CH_2, *J* 7.2 Hz), 6.64 d (1H, H^4-furan, *J* 3.6 Hz), 7.20 d (1H, H^3-furan, *J* 3.6 Hz), 8.16 br.s (1H, NH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 11.76 (CH_3-hydrazone), 14.48 (CH_3-ester), 51.97 (CH_3O), 62.37 (CH_2O), 110.24 (C^4-furan), 119.71 (C^3-furan), 140.21 (C^5-furan), 144.27 (C^2-furan), 153.79 (C=N), 155.50 (C=O-hydrazide), 158.91 (C=O-ester). Mass spectrum, *m/z* (I_{rel}, %): 254(45) $[M + 1]^+$, 223(6) $[M + 1 - OCH_3]^+$, 208 (6), 182(32), 153(16), 121(25.5), 109(5), 93(74), 65 (38), 29(100). Found, %: C 52.32, H 5.01, N 11.32. $C_{11}H_{13}N_2O_5$. Calculated, %: C 52.17, H 5.17, N 11.06. *M* 253.23.

Methyl 5-(1,2,3-thiadiazol-4-yl)furan-2-carboxylate (III). Carbethoxyhydrazone of methyl 5-acetylfuran-2-furoate **II**, 5.7 g, was dissolved in 20 mL of chloroform, and 5.1 mL of thionyl chloride was added. The mixture obtained was gradually heated to 65ºC and kept at this temperature. The reaction progress was monitored by TLC (Silufol plates, eluent acetone : chloroform, 1 : 1, for compound **II** R_f 0.54). After 1.5 h the volatile products were distilled off on a rotary evaporator. The crystalline residue was suspended in 20 mL of hexane, filtered, and dried in air at room temperature. Yield 4.4 g (93%), dark brown crystals, mp 132–133ºC. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.96 s (3H, CH_3), 7.29 d (1H, H^4-furan, *J* 3.2 Hz), 7.34 d (1H, H^3-furan, *J* 3.2 Hz), 8.91 s (1H, H^5-thiadiazole). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 52.16 (CH_3O), 111.04 (C^4-furan), 119.77 (C^3-furan), 131.13 (C^5-thiadiazole), 144.77 (C^4-thiadiazole), 149.75 (C^5-furan), 153.53 (C^2-furan), 158.88 (C=O). Mass spectrum, *m/z* (I_{rel}, %): 210(29) $[M]^+$, 182(80) $[M - N_2]^+$, 168(1), 151 (45), 124(35), 111(6), 95(100), 69(22), 51(19), 45 (23). Found, %: C 45.89, H 3.04, N 13.57. $C_8H_6N_2O_3S$. Calculated, %: C 45.71, H 2.89, N 13.33. *M* 210.21.

Ethyl 3-(5-acetylfur-2-yl)acrylate carbethoxyhydrazone (V). Ethyl 3-(5-acetylfur-2-yl)acrylate **IV**, 3.8 g, and 1.9 g of carbethoxyhydrazine were dissolved with stirring in 10 mL of ethanol and 0.5 mL of acetic acid was added. The mixture obtained was refluxed for 1 h. The reaction progress was monitored by TLC (Silufol plates, eluent acetone : chloroform, 1 : 1, for compound **V** R_f 0.72). After completion of the reaction the mixture obtained was diluted in 2 volumes of water. The obtained bright yellow crystals were filtered off and dried in air at room temperature. Yield 4.4 g (82%), mp 152ºC. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.34 t (3H, CH_3-ethyl, *J* 7.2 Hz), 1.38 t (3H, CH_3-ethyl, *J* 6.8 Hz), 2.20 s (3H, CH_3-hydrazone), 4.26 q (2H, CH_2O, *J* 7.2 Hz), 4.34 q (2H, CH_2O, *J* 6.8 Hz), 6.42 d (1H, CH^2-acrylic, *J* 16.0 Hz), 6.67 d (1H, H^3-furan, *J* 3.6 Hz), 6.91 br.d (1H, H^4-furan, *J* 3.6 Hz), 7.42 d (1H, CH^3-acrylic, *J* 16.0 Hz), 7.93 br.s (1H, NH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 11.73 (CH_3-hydrazone), 14.23 (CH_3-ester), 14.52 (CH_3-ester), 60.52 (CH_2O), 62.34 (CH_2O), 111.69 (=<u>CH</u>–C=O), 116.46, 116.93 (C^3-furan, C^4-furan), 130.33 (furan-CH=), 140.13 (C^5-furan), 146.46 (C^2-furan) 151.46 (C=N), 153.47 (C=O-hydrazide), 166.84 (C=O-ester). Mass spectrum, *m/z* (I_{rel}, %): 294(40) $[M + 1]^+$, 248 (25), 208(6), 221(3), 192(60), 175(7), 147(30), 119 (41), 91(27), 65(21), 29(100). Found, %: C 57.61, H 5.52, N 9.37. $C_{14}H_{17}N_2O_5$. Calculated, %: C 57.33, H 5.84, N 9.55. *M* 293.30.

Ethyl 3-[5-(1,2,3-thiadiazol-4-yl)fur-2-yl]acrylate (VI). Ethyl 3-(5-acetylfur-2-yl)acrylate carbethoxyhydrazone **V**, 3.3 g, was suspended in 14 mL of chloroform, and 2.5 mL of thionyl chloride was added. The mixture obtained was gradually heated to 65ºC. The reaction progress was monitored by TLC (Silufol plates, eluent acetone : chloroform, 1 : 1, for compound **V** R_f 0.73). After 1.5 h the volatile products were removed on a rotary evaporator. The residue was triturated with 30 mL of hexane, the crystals formed

were filtered off and dried in air. Yield 2.3 g (82%), dark brown crystals, mp 103–104ºC. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.35 t (3H, CH_3, *J* 7.2 Hz), 4.28 q (2H, CH_2O, *J* 7.2 Hz), 6.45 d (1H, H^2-acrylic, 15.6 Hz), 6.79 d (1H, H^3-furan, *J* 3.4 Hz), 7.24 d (1H, H^4-furan *J* 3.4 Hz), 7.48 d (1H, H^3-acrylic, *J* 15.6 Hz), 8.71 s (1H, H^5-thiadiazole). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.33 (CH_3), 60.66 (C_2O), 111.92 (C^2-acrylic), 116.58, 117.10 (C^3-furan, C^4-furan), 129.77 (C^5-thiadiazole), 130.25 (C^3-acrylic), 148.24 (C^4-thiadiazole), 151.60, 153.58 (C^2-furan, C^5-furan, 166.71 (C=O). Mass spectrum, *m/z* (I_{rel}, %): 250(100) $[M]^+$, 222(86) $[M - N_2]^+$, 205(26), 177(60), 150(96), 137(85), 109(23), 95(46), 63(42). Found, %: C 52.53, H 3.84, N 11.37. $C_{11}H_{10}N_2O_3S$. Calculated %: C 52.79, H 4.03, N 11.19. *M* 250.27.

5-(1,2,3-Thiadiazol-4-yl)furan-2-carboxylic acid (VII). To the suspension of 2.5 g of 5-(1,2,3-thiadiazol-4-yl)-2-furoate in 15 mL of ethanol 7.3 mL of 10% ethanol solution of potassium hydroxide was added. The reaction mixture was gradually heated to 45ºC under the control of pH value. After 1 h it decreased to 8 units. Then additional 0.2 mL of the same solution was added, and after 30 min pH value again decreased to 8 units. Again 0.2 mL of alkaline solution was added, and after 30 min pH became equal to 9 and did not change further. The reaction mixture was cooled and diluted with 20 mL of water. Solvent was removed on a rotary evaporator, the residue was diluted with water to 15 mL, acidified with conc. hydrochloric acid to pH 2 and cooled on an ice bath for 30 min. The precipitate formed was filtered off and dried in air. Yield of the light brown powder 1.6 g (69%), decomposition temperature 165ºC. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.33 d (1H, H^4-furan, *J* 3.6 Hz), 7.41 d (1H, H^3-furan, *J* 3.6 Hz), 9.53 s (1H, H^5-thiadiazole). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 111.63 (C^4-furan), 119.93 (C^3-furan), 134.84 (C^5-thiadiazole), 148.24 (C^4-thiadiazole), 151.60, 154.00 (C^2-furan, C^5-furan), 159.53 (C=O).

5-(1,2,3-Thiadiazol-4-yl)furan-2-carboxylic acid chloride (VIII). To the suspension of 2.2 g of 5-(1,2,3-thiadiazol-4-yl)furan-2-carboxylic acid in 10 mL of benzene 2 drops of DMF and 1.2 mL of thionyl chloride was added. The reaction mixture was refluxed for 6 h at 80ºC. After the complete evolution of hydrogen chloride the solvent and excess thionyl chloride were distilled off. The residue, dark brown crystals, were suspended in hexane, filtered, and kept for 20 min at room temperature and residual pressure 1 mmHg. Yield 2.2 g (86%). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 7.39 d (1H, H^4-furan, *J* 3.8 Hz), 7.67 d (1H, H^3-furan, *J* 3.8 Hz), 8.99 s (1H, H^5-thiadiazole). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 111.9 (C^4-furan), 126.47 (C^3-furan), 132.81 (C^5-thiadiazole), 145.97 (C^4-thiadiazole), 152.27, 152.68 (C^2-furan, C^5-furan), 155.27 (C=O).

5-(1,2,3-Thiadiazol-4-yl)furan-2-carboxamide (IX). To the solution of 1.1 g of 5-(1,2,3-thiadiazol-4-yl)-furan-2-carboxylic acid chloride in 5 mL of benzene 4 mL of ammonia was added under the intense stirring and cooling on an ice bath. The reaction mixture was stirred for 2 h at 4–5ºC. The precipitate formed was filtered off, washed with 2 mL of water, and dried in air at room temperature. Yield 0.3 g (30%), decomposition temperature 110ºC. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.28 d (1H, H^4-furan, *J* 3.8 Hz), 7.59 d (1H, H^3-furan, *J* 3.8 Hz), 8.06 s (2H, NH_2), 9.52 s (1H, H^5-thiadiazole). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 111.09 (C^4-furan), 115.83 (C^3-furan), 134.12 (C^5-thiadiazole), 147.67 (C^4-thiadiazole), 148.42 (C^2-furan), 153.47 (C^5-furan), 159.47 (C=O).

1-[5-(1,2,3-Thiadiazol-4-yl)fur-2-yl]carbo-2-[(3-pyridyl)carbo]hydrazine (X). To a solution of 0.7 g of nicotinoylhydrazine in 7 mL of pyridine 1.0 g of 5-(1,2,3-thiadiazol-4-yl)furan-2-carboxylic acid chloride **VII** was added in small portions with stirring at 25ºC. After homogenization of the reaction mixture it was left overnight, and then pyridine was removed on a rotary evaporator. The residue was suspended in 15 mL of water, and light brown crystals formed. The reaction mixture was kept for 30 min, the precipitate was filtered off, washed with 3 mL of water, and dried in air at room temperature. Yield of compound **X** 0.7 g (48%), light brown crystals, decomposition temperature 105ºC. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.37 d (1H, H^4-furan, *J* 3.0 Hz), 7.47 d (1H, H^3-furan, *J* 3.0 Hz), 7.60 br.t (1H, H^5-pyridine), 8.28 d (1H, H^4-pyridine, *J* 7.6 Hz), 8.80 br.s (1H, H^6-pyridine), 9.10 s (1H, H^2-pyridine), 9.56 s (1H, H^5-thiadiazole), 10.78 s, 10.82 s (2H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 111.17 (C^4-furan), 117.19 (C^3-furan), 124.24 (C^5-pyridine), 128.52 (C^3-pyridine), 134.68 (C^5-thiadiazole), 135.77 (C^4-pyridine), 146.75 (C^4-thiadiazole), 148.38 (C^2-furan), 148.51 (C^6-pyridine), 153.13, 153.17 (C^5-furan C^2-pyridine), 157.38 (C=O-furan), 165.10 (C=O-pyridine). Attribution of signals of carbon atoms of the pyridine ring was carried out on the basis of data [3, 4].

3-{5[5-(1,2,3-Thiadiazol-4-yl)fur-2-yl][1,3,4-oxadiazol-2-yl]}pyridine (XI). 1-[5-(1,2,3-[(Thiadiazol-4-yl)fur-2-yl]carbo-2-[(3-pyridyl)carbo]hydrazine **X**, 0.6 g, was refluxed with 20 mL of acetic anhydride for 3 h. The reaction mixture was cooled, diluted with 30 mL of water, and stirred for 30 min. Tar-like precipitate was filtered off, and water and acetic acid were distilled from filtrate on a rotary evaporator. Residual light yellow precipitate melting in air was dissolved in 20 mL of ammonia and left standing for 48 h. The precipitate formed was filtered off and dried in air until the constant weight. Yield of compound **XI** 0.1 g (17%), light pink powder. It becomes black at heating and decomposes without melting. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.54 br.s (1H, H^4-furan), 7.73 br.s (2H, H^3-furan and H^5-pyridine), 8.50 br.s (1H, H^4-pyridine), 8.66 br.s (1H, H^{6}pyridine), 9.31 br.s (1H, H^2-pyridine), 9.67 c (1H, H^5-thiadiazole). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 112.34 (C^4-furan), 117.57 (C^3-furan), 124.88 (C^5-pyridine), 134.84 (C^5-thiadiazole), 135.46 (C^3-pyridine), 139.47 (C^4-pyridine), 147.92 (C^4-thiadiazole and C^6-pyridine), 149.58, 152.64, 153.16 (C^2-pyridine, C^2-furan, and C^5-furan), 157.45 (C^5-oxadiazole), 162.31 (C^2-oxadiazole). Attribution of signals of carbon atoms of the oxadiazole ring was carried out on the basis of [5].

3-[5-(1,2,3-Thiadiazol-4-yl)fur-2-yl]acrylic acid (XII). To the suspension of 1 g of ethyl 3-[5-(1,2,3-thiadiazol-4-yl)fur-2-yl]acrylate **VI** in 5 mL of ethanol 2.5 mL of 10% ethanol solution of potassium hydroxide was added. The reaction mixture was heated to 40ºC under the intermittent pH control. After 15 min of keeping at the above-mentioned temperature pH of reaction mixture have decreased to 8 units. Extra 0.2 mL of alkaline solution was added, and the reaction mixture was kept for 1 h. pH of the reaction mixture was 9 units. The reaction mixture was diluted with 5 mL of water, and ethanol was distilled off on a rotary evaporator. The suspension formed was diluted with 6 mL of water and filtered. The filtrate was acidified with conc. hydrochloric acid to pH 2 and left overnight. The precipitate formed was filtered off and dried in air. Yield 0.6 g (67%), claret crystals having decomposition temperature 145–147ºC. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 6.44 d (1H, H^2-acrylic, *J* 16.0 Hz), 7.07 d (1H, H^3-furan, *J* 3.6 Hz), 7.27 d (1H, H^4-furan, *J* 3.6 Hz), 7.45 d (1H, H^3-acrylic, *J* 16.0 Hz), 9.52 br.s (1H, OH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 112.26 (C^2-acrylic), 117.73, 117.96 (C^3-furan, C^4-furan), 130.65 (C^5-thiadiazole), 133.82 (C^3-acrylic), 148.25 (C^4-thiadiazole), 151.56, 153.43 (C^2-furan, C^5-furan), 166.73 (C=O).

3-[5-(1,2,3-Thiadiazol-4-yl)fur-2-yl]acryl azide (XIII). To a suspension of 1 g of 3-[5-(1,2,3-thiadiazol-4-yl)-2-furyl]acrylic acid in 7 mL of acetone 0.7 mL of triethylamine was added, and the reaction mixture was cooled to 0ºC. After that 0.7 mL of ethyl chloroformate dissolved in 2 mL of acetone was added dropwise with stirring. The reaction mixture was kept for 35 min at 0ºC, and then a solution of 0.4 g of sodium azide in 3 mL of water was added. The mixture obtained was stirred for 2 h at 0–2ºC and then poured in 20 mL of ice water. The obtained solution was extracted with chloroform (4 × 20 mL), dried over calcium chloride, and evaporated. The residue was suspended in hexane, and the crystals formed were filtered off and dried in air. Yield 0.7 g (90%), conversion of starting acid 70%, light brown powder. After evaporation of water-acetone layer on a rotary evaporator 0.3 g of starting acid **XII** was isolated. IR spectrum, ν, cm^{-1}: 2137.22 (ν N_3). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 6.39 d (1H, H^2-acrylic, *J* 15.6 Hz), 6.87 d (1H, H^3-furan, *J* 3.2 Hz), 7.24 d (1H, H^4-furan, *J* 3.2 Hz), 7.51 d (1H, H^3-acrylic, *J* 15.6 Hz), 8.77 s (1H, H^5-thiadiazole). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 112.23 (C^2-acrylic), 117.46, 118.70 (C^3-furan, C^4-furan), 130.45 (C^5-thiadiazole), 131.67 (C^3-acrylic), 149.16 (C^4-thiadiazole), 151.06, 153.61 (C^2-furan, C^5-furan), 171.63 (C=O).

[5-(2-Ethoxycarbonylvinyl)fur-2-yl]thioacetylmorpholide (XIV). To a solution of 1.4 g of ethyl 3-[5-(1,2,3-thiadiazol-4-yl)-2-furyl]acrylate **VI** in 8 mL of dioxane 4.4 mL of morpholine was added. After that 0.3 g of freshly pulverized potassium hydroxide was added under the intense stirring. The mixture obtained was refluxed with stirring for 3 h. The reaction progress was monitored by TLC (Silufol plates, eluent acetone : chloroform, 1 : 1, for compound **VI** R_f 0.15). After the complete conversion of the starting substance the reaction mixture was cooled and treated with 0.32 mL of acetic acid. Water, dioxane, and residual morpholine were removed on a rotary evaporator. The residue was treated with 10 mL of water and extracted with methylene chloride (3 × 220 mL). The extract was dried over calcium chloride, methylene chloride was removed, and the residue was kept in a vacuum (1 mmHg) for 1 h at room temperature. Yield of compound **XIV** 1.3 g (75%), it is a syrup. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.32 t (3H, CH_3-ethyl, *J* 7.2 Hz), 3.79 m (4H, CH_2N), 4.24 q (2H, CH_2O-ethyl,

J 7.2 Hz), 4.35 m (4H, CH_2O), 5.31 s (2H, CH_2-furan) 6.20 d (1H, H^2-acrylic, *J* 15.6 Hz), 6.35 d (1H, H^3-furan, *J* 3.2 Hz), 6.57 d (1H, H^4-furan, *J* 3.2 Hz, 7.37 d (1H, H^3-acrylic, *J* 15.6 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.31 (CH_3-ethyl), 43.540 (furan-$\underline{CH_2}$–C=S), 50.27 (N-CH_2-morpholine), 51.11 (N-CH_2-morpholine), 60.48 (CH_2O-ester), 66.35 (O-CH_2-morpholine), 110.54 (C^2-acrylic), 115.50, 115.98 (C^3-furan, C^4-furan), 130.64 (C^3-acrylic), 150.42 (C^5-furan), 152.21 (C^2-furan), 166.86 (C=O), 196.20 (C=S). Mass spectrum, *m/z* (I_{rel}, %): 309(44) $[M]^+$, 264(7), 230(10), 222(30), 177(11), 151(9), 130(100), 86(79), 60(11), 29(37). Found, %: C 58.44, H 6.27, N 4.38. $C_{15}H_{19}NO_4S$. Calculated, %: C 58.23, H 6.19, N 4.53. *M* 309.38.

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