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Synthesis of 3-(4-Fluorophenyl)-3-(furan-2-yl)propanoic Acid and 5-[2-(4-Fluorophenyl)-2-(furan-2-yl)ethyl]-1,3,4-oxadiazole-2-thiol Derivatives

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Abstract—Synthesis of 3-(4-fluorophenyl)-3-furan-2-ylpropionyl chloride has been performed, and selected transformations of the product have been studied.

Keywords: acylation, hydrolysis, propionamide, acetamide, alcoholysis

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3-(4-Fluorophenyl)-3-furan-2-ylpropionic acid **II** was obtained via hydrolysis of 3-(4-fluorophenyl)-3-(furan-2-yl)propane nitrile **I** synthesized earlier [1]. Reaction of the acid with thionyl chloride resulted in chloride **IIa**. Acylation of various amines with chloride **IIa** afforded the corresponding propanamides **III**–**XIII**. Reaction of the acid chloride with anhydrous ethanol yielded ethyl ester **IIb**. The latter reacted with hydrazine hydrate to give 3-(4-fluorophenyl)-3-(furan-2-yl)propionic acid hydrazide **XIV**. Interaction of **XIV** with carbon disulfide in alkaline medium led to 5-[2-(4-fluorophenyl)-2-(furan-2-yl)-ethyl]-1,3,4-oxadiazole-2-thiol **XV**; reactions of the latter with various chloroacetamides and aryl(alkyl) halides afforded the corresponding amides **XVI**–**XVIII** and oxadiazole derivatives **XIX**–**XXI** (Scheme 1).

Structures of the prepared compounds were confirmed by IR and NMR spectroscopy.

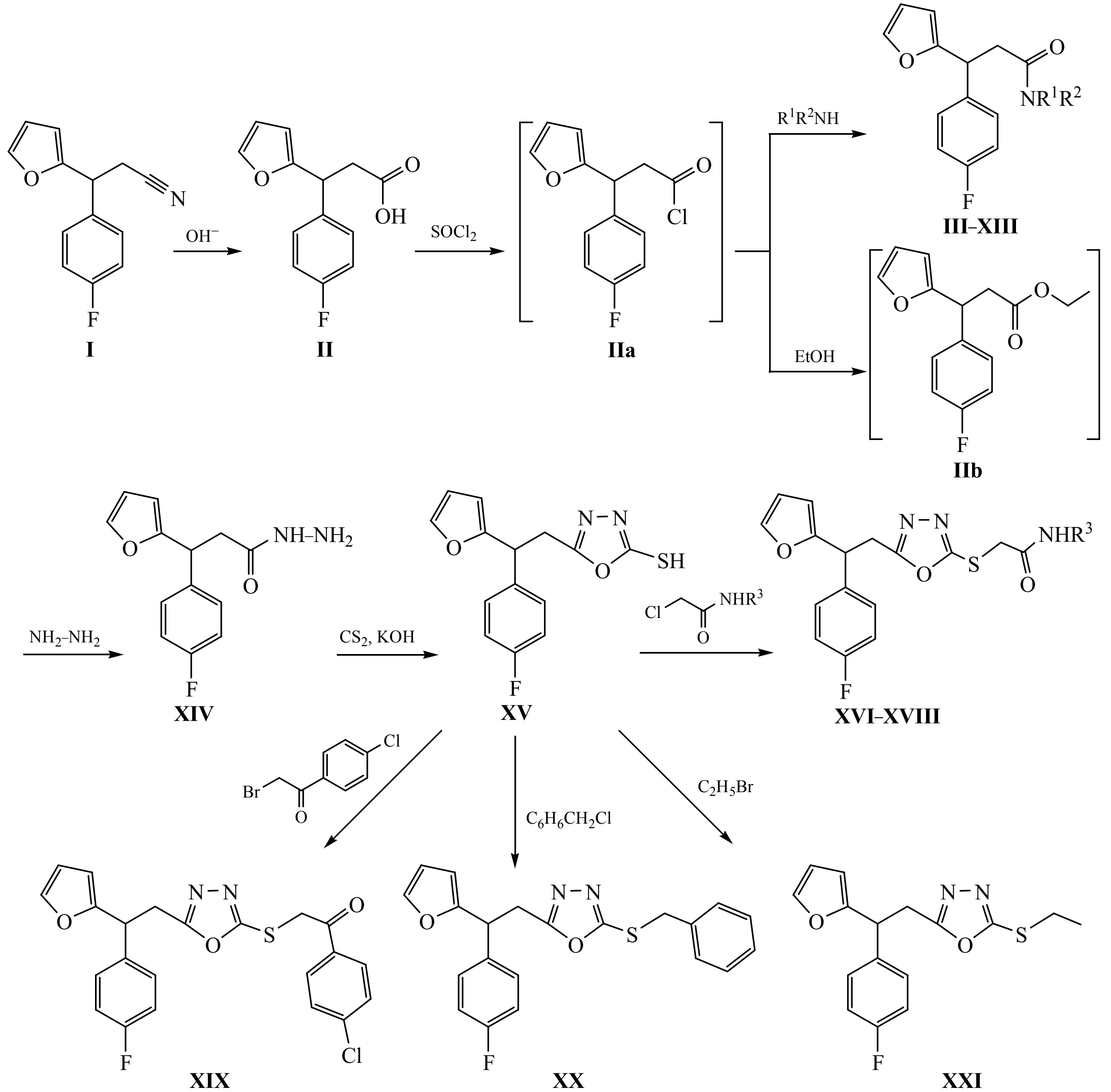
EXPERIMENTAL

IR spectra were recorded using a Nicolet AVATAR 330 FT-IR spectrophotometer. ^{1}H NMR spectra were registered with a Mercury VX-300 spectrometer (300 MHz) in DMSO-d_6–CCl_4 relative to internal TMS as reference.

3-(4-Fluorophenyl)-3-(furan-2-yl)propanoic acid (II). A mixture of 22.4 g (0.4 mol) of KOH, 80 mL of ethylene glycol, and 21 g (0.1 mol) of nitrile **I** was refluxed during 6 h. After cooling, the mixture was diluted with 80 mL of water and extracted with diethyl ether. The aqueous layer was acidified with 40 mL of conc. HCl and acid **II** was extracted with benzene (3 × 100 mL). The benzene layer was washed with water and dried. After removal of benzene the residue was distilled in vacuum. Yield 19 g (83%) bp 175–177°C (2 mmHg). IR spectrum, ν, cm^{-1}: 3400–3200 (OH), 1710 (C=O), 1610–1590 (C=CAr). ^{1}H NMR spectrum, δ, ppm: 2.76 d.d (1H, CH_2, *J* 15.9, 8.1 Hz), 2.95 d.d (1H, CH_2, *J* 15.9, 7.3 Hz), 4.46 d.d (1H, CH, *J* 8.1, 7.3 Hz), 6.07 d.d (1H, H^3_{furan}, *J* 3.2, 0.8 Hz), 6.26 d.d (1H, H^4_{furan}, *J* 3.2, 1.9 Hz), 6.95–7.03 m (2H, C_6H_4F), 7.20–7.27 m (2H, C_6H_4F), 7.33 d.d (1H, H^5_{furan}, *J* 1.9, 0.8 Hz), 11.95 br.s (1H, OH). Found, %: C 67.0; H 5.04. $C_{13}H_{11}O_3$. Calculated, %: C 66.66; H 4.73.

3-(4-Fluorophenyl)-3-(furan-2-yl)propanoyl chloride (IIa). A mixture of 23 g (0.11 mol) of acid **II**, 13.1 g (0.11 mol) of $SOCl_2$, and 50 mL of benzene was refluxed during 2 h. After benzene removal, the resulting acid chloride was used without further purification.

Scheme 1.



R^1 = H, R^2 = 1-phenylethyl (**III**), $(CH_2)_3N(CH_3)_2$ (**IV**), thiazol-2-yl (**V**), 3-MeC_6H_4 (**VI**), 4-$MeOC_6H_4$ (**VII**), Bn (**VIII**), 4-ClC_6H_4 (**IX**), cyclohexyl (**X**), 2-$MeOC_6H_4$ (**XI**), α-naphthyl (**XII**); NR^1R^2 = *N*,*N*-diethyl (**XIII**), R^3 = H (**XVI**), 4-ClC_6H_4 (**XVII**), furan-2-ylmethyl (**XVIII**).

3-(4-Fluorophenyl)-3-(furan-2-yl)propanamides (III–XIII) (*general procedure*). Equimolar amount of the acid chloride **IIa** was added dropwise to a solution of 0.01 mol of the amine and 0.01 mol of triethylamine in anhydrous benzene upon stirring. The mixture was refluxed during 3 h, cooled, and acidified with a solution of HCl until slightly acidic reaction. The reaction products were extracted with benzene; the extract was washed with water, dried, and evaporated. The residue was distilled (**III**, **IV**, **VI**, and **XIII**) or recrystallized from ethanol (**V** and **VII–XII**).

***N*-(1-Phenylethyl)-3-(4-fluorophenyl)-3-(furan-2-yl)propanamide (III).** Yield 61%, bp 225–230°C (4 mmHg). IR spectrum, ν, cm^{-1}: 3270 (NH), 1642 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.24 d and 1.33 d (3H, CH_3, *J* 7.0 Hz), 2.63–2.87 m (2H, CH_2), 4.46–4.53 m (1H, $\underline{CH}CH_2$), 4.80–4.91 m (1H, $\underline{CH}CH_3$), 6.07 d.d and 6.09 d.d (1H, H^3_{furan}, *J* 3.2, 0.8 Hz), 6.25 d.d and 6.27 d.d (1H, H^4_{furan}, *J* 3.2, 1.9 Hz), 6.89–7.01 and 7.10–7.26 m (9H, C_6H_4, C_6H_5), 7.31 d.d and 7.34 d.d (1H, H^5_{furan}, *J* 1.9, 0.8 Hz), 8.00 br.d (1H, NH, *J* 7.9 Hz). Found, %: C 75.02; H 6.45; N 4.67. $C_{21}H_{20}FNO_2$. Calculated, %: C 74.76; H 5.97; N 4.15.

***N*-[3-(Dimethylamino)propyl]-3-(4-fluorophenyl)-3-(furan-2-yl)propanamide (IV).** Yield 64%, bp 210–214°C (4 mmHg). IR spectrum, ν, cm^{-1}: 3280 (NH), 1654 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.37–1.46 m (2H, NCH_2), 2.08 t (2H, NH_2, *J* 7.1 Hz), 2.10 s (6H, CH_3NCH_3), 2.60 d.d (1H, $\underline{CH_2}CH$, *J* 14.2, 8.3 Hz), 2.76 d.d (1H, $CH_2C{=}O$, *J* 14.2, 7.2 Hz), 2.96–3.04 m (2H, $HN\underline{CH_2}$), 4.50 d.d (1H, $\underline{CH}C_6H_4$, *J* 8.3, 7.2 Hz), 6.08 d.d (1H, H^3_{furan}, *J* 3.2, 0.8 Hz), 6.25 d.d (1H, H^4_{furan}, *J* 3.2, 1.8 Hz), 6.91–6.99 m and 7.17–7.24 m (4H, C_6H_4F), 7.32 d.d (1H, H^5_{furan}, *J* 1.8, 0.8 Hz), 7.57 br. t (1H, NH, *J* 5.6 Hz). Found, %: C 68.20; H 7.64; N 9.32. $C_{18}H_{29}FN_2O_2$. Calculated, %: C 67.90; H 7.28; N 8.80.

***N*-(Thiazol-2-yl)-3-(4-fluorophenyl)-3-(furan-2-yl)propanamide (V).** Yield 58%, mp 162–164°C. IR spectrum, ν, cm^{-1}: 3270 (NH), 1685 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.01 d.d and 3.15 d.d (2H, $O{=}CCH_2$, *J* 15.1, 7.5 Hz), 4.67 d.d (1H, $ArC\underline{H}$, *J* 7.9, 7.5 Hz), 6.13 d.d (1H, H^3_{furan}, *J* 3.2, 7.09 Hz), 6.27 d.d (1H, H^4_{furan}, *J* 3.2, 1.8 Hz), 6.93 d (1H, CHS, *J* 3.5 Hz), 6.95–7.03 m and 7.23–7.30 (4H, C_6H_4), 7.33 d (1H, =CHN, *J* 3.5 Hz), 7.35 d.d (1H, H^5_{furan}, *J* 1.8, 0.9 Hz), 12.04 br.s (1H, NH). Found, %: C 61.15; H 4.57; N 9.30. $C_{16}H_{13}FN_2O_2S$. Calculated, %: C 60.75; H 4.14; N 8.86.

***N*-(3-Methylphenyl)-3-(4-fluorophenyl)-3-(furan-2-yl)propanamide (VI).** Yield 64%, bp 225–228°C (2 mmHg). IR spectrum, ν, cm^{-1}: 3292 (NH), 1652 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.30 s (3H, CH_3), 2.85 d.d and 3.02 d.d (1H, $O{=}CCH_2$, *J* 14.8, 7.3 Hz), 4.62 d.d (1H, $Ar\underline{CH}$, *J* 8.1, 7.3 Hz), 6.14 d.d (1H, H^3_{furan}, *J* 3.2, 0.9 Hz), 6.27 d.d (1H, H^4_{furan}, *J* 3.2, 1.8 Hz), 6.75 br.d (1H, $C_6\underline{H}_4CH_3$, *J* 7.6 Hz), 6.94–7.02 m (2H, C_6H_4F), 7.05 t (1H, $C_6\underline{H}_4CH_3$), 7.22–7.29 and 7.33–7.36 m (5H, H_{arom}), 9.55 br.s (1H, NH). Found, %: C 74.92; H 6.11; N 5.82. $C_{20}H_{18}FNO_2$. Calculated, %: C 74.29; H 5.61; N 4.33.

***N*-(4-Methoxyphenyl)-3-(4-fluorophenyl)-3-(furan-2-yl)propanamide (VII).** Yield 62%, mp 148–150°C. IR spectrum, ν, cm^{-1}: 3304 (NH), 1656 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.82 d.d and 2.99 d.d (2H, $O{=}CCH_2$, *J* 14.6, 7.4 Hz), 3.73 s (3H, OCH_3), 4.60 d.d (1H, $Ar\underline{CH}$, *J* 8.0, 7.4 Hz), 6.14 d.d (1H, H^3_{furan}, *J* 3.2, 0.9 Hz), 6.28 d.d (1H, H^4_{furan}, *J* 3.2, 1.9 Hz), 6.71–6.76 m (2H, $C_6\underline{H}_4OMe$), 6.95–7.03 m (2H, C_6H_4F), 7.22–7.29 m (2H, C_6H_4F), 7.35–7.40 m (2H, $C_6\underline{H}_4OMe$), 7.36 d.d (1H, H^5_{furan}, *J* 1.9, 0.9 Hz), 9.55 br.s (1H, NH). Found, %: C 71.25; H 5.90; N 4.68. $C_{20}H_{18}FNO_3$. Calculated, %: C 70.79; H 5.35; N 4.13.

***N*-Benzyl-3-(4-fluorophenyl)-3-(furan-2-yl)propanamide (VIII).** Yield 65%, mp 118–120°C. IR spectrum, ν, cm^{-1}: 3261 (NH), 1640 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.72 d.d and 2.86 d.d (2H, $CH\underline{CH_2}$, *J* 14.2, 7.0 Hz), 4.14 d.d and 4.28 d.d (2H, NCH_2, *J* 15.1, 6.2 Hz), 4.55 d.d (1H, $\underline{CH}Ar$, *J* 8.7, 7.0 Hz), 6.09 d.d (1H, H^3_{furan}, *J* 3.2, 0.9 Hz), 6.26 d.d (1H, H^4_{furan}, *J* 3.2, 1.8 Hz), 6.92–7.00 m and 7.13–7.27 m (9H, C_6H_5, C_6H_4F), 7.33 d.d (1H, H^5_{furan}, *J* 1.8, 0.9 Hz), 8.09 br.d.d (1H, NH, *J* 6.2, 5.5 Hz). Found, %: C 74.83; H 6.00; N 4.82. $C_{20}H_{18}FNO_2$. Calculated, %: C 74.29; H 5.61; N 4.33.

3-(4-Fluorophenyl)-3-(furan-2-yl)-*N*-(4-chlorophenyl)propanamide (IX). Yield 61%, mp 138–140°C. IR spectrum, ν, cm^{-1}: 3296 (NH), 1660 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.86 d.d and 3.03 d.d (2H, CH_2, *J* 14.9, 7.4 Hz), 4.61 d.d (1H, CH, *J* 8.2, 7.4 Hz), 6.12 d.d (1H, H^3_{furan}, *J* 3.2, 0.9 Hz), 6.27 d.d (1H, H^4_{furan}, *J* 3.2, 2.0 Hz), 6.94–7.02 m (2H, C_6H_4F), 7.14–7.19 m (2H, C_6H_4Cl), 7.22–7.29 (2H, C_6H_4F), 7.34 d.d (1H, H^5_{furan}, *J* 2.0, 0.9 Hz), 7.50–7.55 m (2H, C_6H_4Cl), 9.79 br.s (1H, NH). Found, %: C 66.83; H 4.85; N 4.67. $C_{19}H_{15}ClFNO_2$. Calculated, %: C 66.38; H 4.40; N 4.07.

3-(4-Fluorophenyl)-3-(furan-2-yl)-*N*-cyclohexylpropanamide (X). Yield 59%, mp 98°C. IR spectrum, ν, cm^{-1}: 3284 (NH), 1636 (C=O). ^{1}H NMR spectrum, δ, ppm: 0.90–1.36 m and 1.52–1.73 (10H, C_6H_{11}), 2.57 d.d and 2.74 d.d (2H, CH_2, *J* 14.1, 7.2 Hz), 3.39–3.52 m (1H, NCH), 4.49 d.d (1H, $Ar\underline{CH}$, *J* 8.4, 7.2 Hz), 6.08 d.d (1H, H^3_{furan}, *J* 3.2, 0.9 Hz), 6.25 d.d (1H, H^4_{furan}, *J* 3.2, 1.8 Hz), 6.91–6.99 m (2H, C_6H_4F), 7.15–7.23 m (2H, C_6H_4F), 7.29 br.d (1H, NH, *J* 7.7 Hz), 7.31 d.d (1H, H^5_{furan}, *J* 1.8, 0.9 Hz). Found, %: C

71.05; H 7.25; N 5.32. $C_{17}H_{20}FNO_2$. Calculated, %: C 70.57; H 6.97; N 4.84.

***N*-(4-Methoxyphenyl)-3-(4-fluorophenyl)-3-(furan-2-yl)propanamide (XI).** Yield 60%, mp 223–225°C (2 mmHg). IR spectrum, ν, cm^{-1}: 3304 (NH), 1660 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.97 d.d and 3.14 d.d (1H, CH_2, *J* 14.8, 7.2 Hz), 3.84 s (3H, OCH_3), 4.60 d.d (1H, CH, *J* 8.1, 7.2 Hz), 6.15 d.d (1H, H^3_{furan}, *J* 3.2, 0.9 Hz), 6.27 d.d (1H, H^4_{furan}, *J* 3.2, 1.9 Hz), 6.79–6.88 m and 6.92–7.02 m (9H, C_6H_4F, OCH_3), 7.24–7.31 m (2H, C_6H_4F), 7.34 d.d (1H, H^5_{furan}, *J* 1.9, 0.9 Hz), 7.97 br.d (1H, $C_6\underline{H}_4OMe$, *J* 7.9 Hz), 8.62 br.s (1H, NH). Found, %: C 71.13; H 5.84; N 4.62. $C_{20}H_{18}FNO_3$. Calculated, %: C 70.79; H 5.35; N 4.13.

***N*-(Naphthalen-1-yl)-3-(4-fluorophenyl)-3-(furan-2-yl)propanamide (XII).** Yield 58%, mp 178–180°C. IR spectrum, ν, cm^{-1}: 3294 (NH), 1645 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.06 d.d and 3.15 d.d (2H, CH_2, *J* 14.1, 7.0 Hz), 4.63 d.d (1H, $\underline{CH}$Ar, *J* 8.6, 7.0 Hz), 6.17 br.d (1H, H^3_{furan}, *J* 3.1 Hz), 6.51 br.d (1H, H^4_{furan}, *J* 3.1 Hz), 6.99–7.08 (2H, C_6H_4F), 7.27–7.82 m (10 H, H_{arom}), 9.73 br.s (1H, NH). Found, %: C 77.85; H 6.74; N 4.00. $C_{23}H_{18}FNO_2$. Calculated, %: C 77.10; H 6.21; N 3.60.

***N*,*N*-Diethyl-3-(4-fluorophenyl)-3-(furan-2-yl)propanamide (XIII).** Yield 62%, bp 160°C (1 mmHg). IR spectrum, ν, cm^{-1}: 1665 (C=O). ^{1}H NMR spectrum, δ, ppm: 0.98 t (3H, CH_3, *J* 7.1 Hz), 1.08 t (3H, CH_3, *J* 7.1 Hz), 2.80 d.d and 2.96 d.d (1H, CH_2C=O, *J* 15.3, 6.6 Hz), 3.19–3.28 m (4H, CH_2NCH_2), 4.61 d.d (1H, $\underline{CH}$Ar, *J* 7.9, 6.6 Hz), 6.04 d.d (1H, H^3_{furan}, *J* 3.2, 0.8 Hz), 6.26 d.d (1H, H^4_{furan}, *J* 3.2, 1.8 Hz), 6.92–7.00 m and 7.20–7.26 m (4H, C_6H_4F), 7.33 d.d (1H, H^5_{furan}, *J* 1.8, 0.8 Hz). Found, %: C 71.05; H 7.32; N 5.25. $C_{17}H_{20}FNO_2$. Calculated, %: C 70.57; H 6.97; N 4.84.

3-(4-Fluorophenyl)-3-(furan-2-yl)propane hydrazide (XIV). A mixture of 0.015 mol of the chloride **IIa** in 100 mL of anhydrous ethanol was refluxed during 5–6 h. After removal of ethanol, the residue (0.03 mol, ester **IIb**) and 0.045 mol of hydrazine hydrate were refluxed in isobutyl alcohol during 6 h and then cooled. The crystalline hydrazide was filtered off and recrystallized from ethanol. Yield 73%, mp 125–127°C. IR spectrum, ν, cm^{-1}: 3312, 3278 (NH_2). ^{1}H NMR spectrum, δ, ppm: 2.59 d.d and 2.75 d.d (2H, CH_2, *J* 14.5, 7.4 Hz), 3.86 br.s (2H, NH_2), 4.52 d.d (1H, CHAr, *J* 8.2, 7.4 Hz), 6.09 br.d (1H, H^3_{furan}, *J* 3.2 Hz), 6.25 d.d (1H, H^4_{furan}, *J* 3.2, 1.9 Hz), 6.92–7.00 m and 7.17–7.24 m (4H, C_6H_4F), 7.32 br.d (1H, H^5_{furan}, *J* 1.9 Hz), 8.91 br.s (1H, NH). Found, %: C 63.15; H 5.80; N 11.67. $C_{13}H_{13}FN_2O_2$. Calculated, %: C 62.90; H 5.28; N 11.28.

5-[2-(4-Fluorophenyl)-2-(furan-2-yl)ethyl]-1,3,4-oxadiazole-2-thiol (XV). 1.7 g (0.03 mol) of KOH was added to a solution of 6.2 g (0.025 mol) of compound **XIV** in 50 mL of ethanol. The mixture was refluxed during 0.5 h; 6 mL of carbon disulfide was added after cooling, and the mixture was further refluxed during 30–35 h. Ethanol was distilled off; the residue was dissolved in water and acidified with hydrochloric acid (1 : 1). The precipitated crystals were filtered off, washed with water, and recrystallized from ethanol. Yield 6.5 g (78%), mp 95–96°C. IR spectrum, ν, cm^{-1}: 3150 (SH), 1628 (C=N), 1604, 1590 (Ar). ^{1}H NMR spectrum, δ, ppm: 3.29 d.d and 3.46 d.d (2H, CH_2, *J* 15.5, 7.8 Hz), 4.56 d.d (1H, CHAr, *J* 8.1, 7.8 Hz), 6.16 d.d (1H, H^3_{furan}, *J* 3.2, 0.8 Hz), 6.29 d.d (1H, H^4_{furan}, *J* 3.2, 1.9 Hz), 6.98–7.06 m and 7.26–7.33 m (4H, C_6H_4F), 7.38 d.d (1H, H^5_{furan}, *J* 1.9, 0.8), 13.80 br.s (1H, SH). Found, %: C 58.38; H 4.26; N 10.12. $C_{14}H_{11}FN_2O_2S$. Calculated, %: C 57.92; H 3.82; N 9.65.

Compounds XVI–XXI (*general procedure*). A mixture of 50 mL of ethanol, 0.07 mol of compound **XV**, and 0.07 mol of KOH was heated during several minutes and mixed with a solution of chloroacetamide or alkyl(aryl-alkyl)halide in ethanol. The reaction mixture was incubated overnight; the precipitate was filtered off, washed several times with water, dried, and recrystallized from ethanol.

2-{5-[2-(4-Fluorophenyl)-2-(furan-2-yl)ethyl]-1,3,4-oxadiazol-2-ylsulfanyl}acetamide (XVI). Yield 58%, mp 90–92°C. IR spectrum, ν, cm^{-1}: 3328, 3615 (NH_2), 1675 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.41 d.d and 3.57 d.d (2H, $\underline{CH_2}$CH, *J* 15.4, 7.6 Hz), 3.90 s (2H, SCH_2), 4.58 d.d (1H, $\underline{CH}$Ar, *J* 8.2, 7.6 Hz), 6.15 d.d (1H, H^3_{furan}, *J* 3.2, 0.8 Hz), 6.29 d.d (1H, H^4_{furan}, *J* 3.2, 1.9 Hz), 6.97–7.05 m and 7.24–7.31 m (4H, C_6H_4F), 7.07 br.s and 7.51 br.s (2H, NH_2), 7.38 d.d (1H, H^5_{furan}, *J* 1.9, 0.8 Hz). Found, %: C 55.90; H 4.68; N 12.70. $C_{16}H_{14}FN_3O_3S$. Calculated, %: C 55.32; H 4.06; N 12.10.

2-{5-[2-(4-Fluorophenyl)-2-(furan-2-yl)ethyl]-1,3,4-oxadiazol-2-ylsulfanyl}-*N*-(4-chlorophenyl)acetamide (XVII). Yield 54%, mp 136–138°C. IR spectrum, ν, cm^{-1}: 3344 (NH), 1656 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.41 d.d and 3.58 d.d (2H, $\underline{CH_2}$CH, *J* 15.5, 7.6 Hz), 4.14 s (2H, SCH_2), 6.14 d.d (1H, H^3_{furan}, *J* 3.2, 0.8 Hz), 6.28 d.d (1H, H^4_{furan}, *J* 3.2, 1.9 Hz), 6.95–7.03 m and 7.23–7.30 m (4H, C_6H_4F), 7.21–7.25 m and 7.56–7.61 m (4H, C_6H_4Cl), 7.37 d.d (1H, H^5_{furan}, *J* 1.9, 0.8 Hz), 10.30 s (1H, NH). Found, %: C 58.42; H 4.15; N 9.95. $C_{22}H_{17}ClFN_3O_3S$. Calculated, %: C 57.71; H 3.74; N 9.18.

2-{5-[2-(4-Fluorophenyl)-2-(furan-2-yl)ethyl]-1,3,4-oxadiazol-2-ylsulfanyl}-*N*-(furan-2-ylmethyl)acetamide (XVIII). Yield 60%, mp 93–95°C. IR spectrum, ν, cm^{-1}: 3303 (NH), 1650 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.40 d.d and 3.57 d.d (2H, $\underline{CH_2}$CH, *J* 15.5, 7.6 Hz), 3.93 s (2H, SCH_2), 4.31 d (2H, NCH_2, *J* 5.6 Hz), 4.57 d.d (1H, $\underline{CH}$Ar, *J* 8.3, 7.6 Hz), 6.15 d. t and 6.21 d.d (2H, H^3_{furan}, *J* 3.3, 0.9 Hz), 6.28 d.d and 6.30 d.d (1H, H^4_{furan}, *J* 3.3, 1.9 Hz), 6.96–7.04 m and 7.24–7.31 m (4H, C_6H_4F), 7.37 d.d and 7.38 d.d (2H, H^5_{furan}, *J* 1.9, 0.9 Hz), 8.56 br. t (1H, NH, *J* 5.6 Hz). Found, %: C 59.87; H 4.95; N 10.27. $C_{21}H_{18}FN_3O_4S$. Calculated, %: C 59.01; H 4.25; N 9.83.

2-{5-[2-(4-Fluorophenyl)-2-(furan-2-yl)ethyl]-1,3,4-oxadiazol-2-ylsulfanyl}-1-(4-chlorophenyl)ethanone (XIX). Yield 57%, mp 95–96°C. IR spectrum, ν, cm^{-1}: 1685 (C=O), 1600, 1587 (Ar). ^{1}H NMR spectrum, δ, ppm: 3.41 d.d and 3.58 d.d (2H, $\underline{CH_2}$CH, *J* 15.4, 7.6 Hz), 4.56 d.d (1H, $\underline{CH}$Ar, *J* 8.2, 7.6 Hz), 4.89 s (2H, SCH_2), 6.14 d.d (1H, H^3_{furan}, *J* 3.2, 0.8 Hz), 6.28 d.d (1H, H^4_{furan}, *J* 3.2, 1.9 Hz), 6.96–7.04 m and 7.23–7.30 m (4H, C_6H_4F), 7.37 d.d (1H, H^5_{furan}, *J* 1.9, 0.8 Hz), 7.50–7.54 m and 8.01–8.06 m (4H, C_6H_4Cl). Found, %: C 60.15; H 4.17; N 7.00. $C_{22}H_{16}ClFN_2O_3S$. Calculated, %: C 59.66; H 3.64; N 6.32.

2-(Benzylsulfanyl)-5-[2-(4-fluorophenyl)-2-(furan-2-yl)ethyl]-1,3,4-oxadiazole (XX). Yield 55%, mp 48°C. IR spectrum, ν, cm^{-1}: 1580, 1610 (Ar). ^{1}H NMR spectrum, δ, ppm: 3.40 d.d and 3.57 d.d (2H, $\underline{CH_2}$CH, *J* 15.4, 7.6 Hz), 4.38 s (2H, SCH_2), 4.55 d.d (1H, $\underline{CH}$Ar, *J* 8.2, 7.6), 6.13 br.d (1H, H^3_{furan}, *J* 3.2 Hz), 6.28 d.d (1H, H^4_{furan}, *J* 3.2, 1.9 Hz), 6.95–7.03 m and 7.22–7.38 m (4H, C_6H_4F), 7.30–7.38 m (6H, C_6H_5, H^5_{furan}). Found, %: C 66.90; H 5.00; N 7.00 $C_{21}H_{17}FN_2O_2S$. Calculated, %: C 66.30; H 4.50; N 7.36.

2-(Ethylsulfanyl)-5-[2-(4-fluorophenyl)-2-(furan-2-yl)ethyl]-1,3,4-oxadiazole (XXI). Yield 55%, mp 36°C. IR spectrum, ν, cm^{-1}: 1628 (C=N), 1610, 1584 (Ar). ^{1}H NMR spectrum, δ, ppm: 1.40 t (3H, CH_3, *J* 7.3 Hz), 3.15 q (2H, SCH_2, *J* 7.3 Hz), 3.41 d.d and 3.58 d.d (2H, $\underline{CH_2}$CH, *J* 15.4, 7.6 Hz), 4.57 d.d (1H, $\underline{CH}$Ar, *J* 8.3, 7.6 Hz), 6.14 d.d (1H, H^3_{furan}, *J* 3.2, 0.8 Hz), 6.28 d.d (1H, H^4_{furan}, *J* 3.2, 1.9 Hz), 6.96–7.04 m and 7.24–7.31 m (4H, C_6H_4F). Found, %: C 61.00; H 5.27; N 9.38. $C_{16}H_{15}FN_2O_2S$. Calculated, %: C 60.36; H 4.75; N 8.80.

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