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Synthesis of New 2-Substituted 6,7-Dimethoxy-1-(methylcarbamoyl)-4-spirocyclopentane-1,2,3,4-tetrahydroisoquinolines

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Abstract—New 2-(heterylmethyl) derivatives were synthesized from 6,7-dimethoxy-4-spirocyclopentane-1,2,3,4-tetrahydroisoquinoline-1-carboxylic acid N-methylamide and heterylmethyl chlorides. The reactions of 2-chloroacetyl-substituted tetrahydroisoquinoline with versatile secondary amines and heterylthiols afforded the corresponding 2-aminoacetyl and 2-(heterylsulfanylacetyl) derivatives of tetrahydroisoquinoline series.

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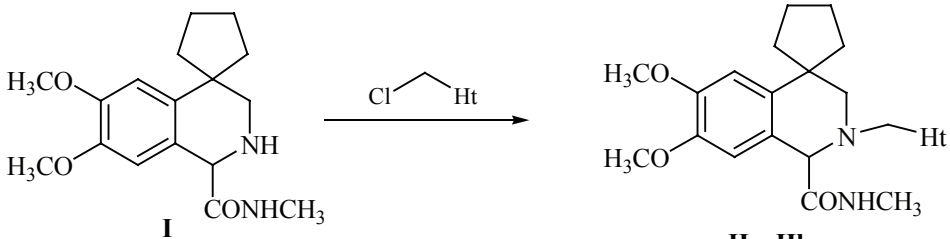
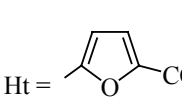
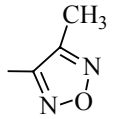
Tetrahydroisoquinoline derivatives possess a wide range of biological actions depending on the nature of substituents and their position in the heterocyclic ring. Therefore the research in this field continues, the attempts to vary the substituents introduced into the structure of new 1,2,3,4-substituted tetrahydroisoquinoline is going on [1]. Compounds containing a spirocyclopentane substituent and a carboxamide group in the positions *4* and *1* of the tetrahydroisoquinoline, respectively, have been the objects of our research in recent years. Here we report on the synthesis of new derivatives of tetrahydroisoquinoline containing in the position *2* heterylmethyl, aminoacetyl, and heterylsulfanylacetyl substituents. To this end we carried out alkylation and acylation of 6,7-dimethoxy-4-spirocyclopentane-1,2,3,4-tetrahydroisoquinoline-1-carboxylic acid *N*-methylamide (**I**).

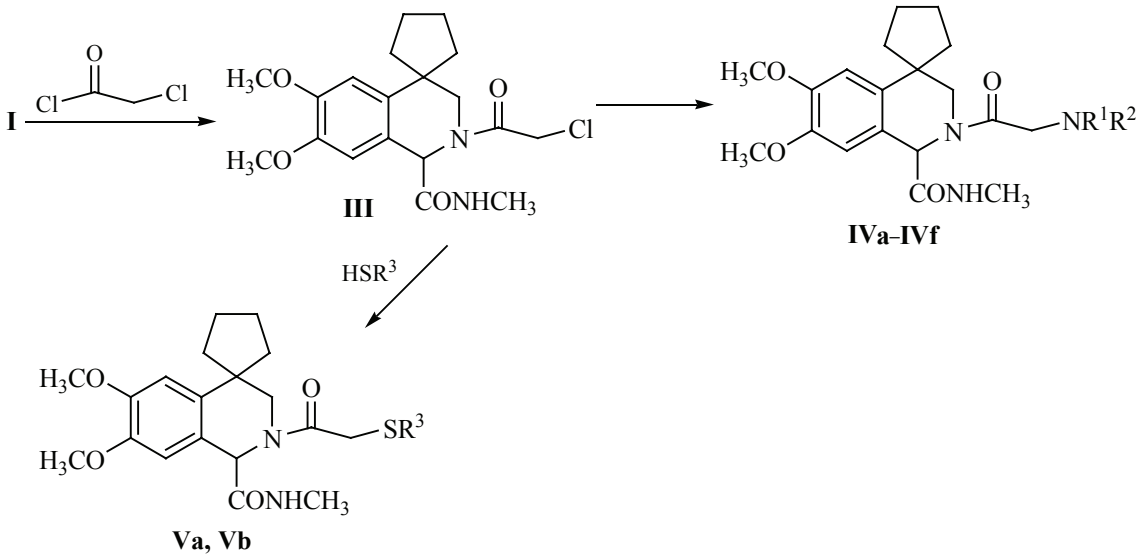
The alkylation of compound **I** with methyl 5-chloromethylfuran-2-carboxylate and with chloromethylfurazan in a mixture dioxane–methanol, 10 : 1, afforded 2-(heterylmethyl)-substituted tetrahydroisoquinolines **IIa, IIb** as crystalline substances.



I **IIa, IIb**

Ht =  (**a**),  (**b**).

The acylation of compound **I** with chloroacetyl chloride gave 2-(chloroacetyl) derivative **III,** which was subjected to condensation with secondary amines and potassium phthalimide, and also with heterocyclic thiols. The reactions with secondary amines (diethylamine, pyrrolidine, piperidine, morpholine, 4-fluorobenzylpi-



IV, $R^1 = R^2 = C_2H_5$ (**a**); $R^1R^2 = (CH_2)_4$ (**b**), $(CH_2)_5$ (**c**), $CH_2CH_2OCH_2CH_2$ (**d**), $(CH_2CH_2)_2NCH_2C_6H_4F$-4 (**e**), 1,2-$(C{=}O)_2C_6H_4$ (**f**); **V**, R^3 = 4,6-dimethylpyrimidin-2-yl (**a**), 5-phenyl-1,3,4-oxadiazol-2-yl (**b**).

perazine) were performed in a mixture dioxane–ethanol, 20 : 1, in the presence of catalytic amounts of KI. We isolated 2-aminoacetyl-substituted compounds **IVa–IVe** in 65–70% yields. The phthalimide derivative **IVf** was obtained by condensation of substance **III** with potassium phthalimide in ethanol. The corresponding 2-(heterylsulfanylacetyl)-substituted tetrahydroisoquinolines **V** were obtained by the reactions of chloroamide **III** with pyrimidine- and oxadiazolethiols in alcohol in the presence of KOH.

The structure of all compounds synthesized was confirmed by the data of IR and ^{1}H NMR spectra, their purity was checked by chromatography.

The ratio of diastereomers in compounds **IV, V** containing two asymmetric sites was established by ^{1}H NMR spectroscopy.

EXPERIMENTAL

IR spectra were recorded on a spectrophotometer Nicolet Avatar 330 FT-IR from mulls in mineral oil. ^{1}H NMR spectra were registered on a spectrometer Varian Mercury-300, operating frequency 300 MHz, solvent DMSO-d_6, internal reference TMS. The melting points were measured on a Boëtius heating microblock. TLC was carried out on Silufol UV-254 plates, development in iodine vapor.

6,7-Dimethoxy-4-spirocyclopentane-1,2,3,4-tetrahydroisoquinoline-1-carboxylic acid *N*-methylamide (I) was obtained by method [2].

Methyl 5-({6',7'-dimethoxy-1'-methylcarbamoyl-1'*H*-spiro[cyclopentane-1,4'-isoquinoline]-2'(3'*H*)-yl}methyl)furan-2-carboxylate (IIa). A mixture of 1.1 g (36 mmol) of tetrahydroisoquinoline **I**, 0.63 g (36 mmol) of methyl 5-chloromethylfuran-2-carboxylate, 0.36 g (36 mmol) of triethylamine, and a crystal of KI in a mixture dioxane–methanol, 10 : 1, was heated at 60–65°C for 15 h. On distilling off the solvent the residue was dissolved in 20 mL of 5% HCl, the impurity were extracted with benzene. The acid solution was alkalinized with 10% solution of NaOH, the reaction products were extracted with benzene. The extract was dried with anhydrous sodium sulfate, the solvent was distilled off, the oily residue was crystallized from ether. Yield 0.8 g (50%), mp 113–115°C (benzene–hexane, 1 : 1), R_f 0.55 (benzene–acetone, 2 : 1). ^{1}H NMR spectrum, δ, ppm: 1.48–2.14 m (8H, C_5H_8), 2.34 d, 2.80 d (1H each, NCH_2, ^2J 11.2 Hz), 2.72 d (3H, NCH_3, ^3J 4.8 Hz), 3.64 d, 3.77 d (1H each, NCH_2 -furyl, ^2J 14.9 Hz), 3.74 s, 3.76 s (3H each, OCH_3), 3.84 s [3H, $C(O)OCH_3$], 4.03 s (1H, NCH), 6.51 d (1H, H^4_{furyl}, ^3J 3.4 Hz), 6.64 s, 6.87 s (1H each, H^5 and $H^8_{isoquinoline}$), 7.11 d (1H, H^3_{furyl}, ^3J 3.4 Hz), 7.22 q (1H, NH, ^3J 4.8 Hz). Found, %: C 65.35; H 6.72; N 6.23. $C_{24}H_{30}N_2O_6$. Calculated, %: C 65.14; H 6.83; N 6.33. Hydrochloride, mp 162–164°C (ethanol).

***N*-Methyl-6',7'-dimethoxy-2'-(4-methyl-1,2,5-oxadiazol-3-ylmethyl)-2',3'-dihydro-1'*H*-spiro-**

cyclopentane-1,4'-isoquinoline-1'-carboxamide (IIb) was obtained similarly to compound **IIa** from tetrahydroisoquinoline **I** and 4-methyl-3-chloromethyl-1,2,5-oxadiazole. Yield 55%, mp 118–120°C (ether), R_f 0.49 (benzene–acetone, 2 : 1). ^{1}H NMR spectrum, δ, ppm: 1.48–1.98 m (8H, C_5H_8), 2.29 d, 2.91 d (1H each, NCH_2, ^2J 11.3 Hz), 2.40 s (3H, CH_3), 2.70 d (3H, NCH_3, ^3J 4.8 Hz), 3.74 s, 3.77 s (3H each, OCH_3), 3.76 d, 3.84 d (1H each, NCH_2-Het, ^2J 14.3 Hz), 4.06 s (1H, CH), 6.66 s, 6.73 s (1H each, H^5 and $H^8{}_{isoquinoline}$), 7.35 q (1H, NH, ^3J 4.8 Hz). Found, %: C 62.70; H 7.20; N 14.12. $C_{21}H_{28}N_4O_4$. Calculated, %: C 62.98; H 7.05; N 13.99.

***N*-Methyl-6',7'-dimethoxy-2'-(2-chloroacetyl)-2',3'-dihydro-1'*H*-spirocyclopentane-1,4'-isoquinoline-1'-carboxamide (III)**. To a benzene solution of 4.5 g (40 mmol) of chloroacetyl chloride cooled to 10°C was added dropwise a mixture of 12.1 g (40 mmol) of tetrahydroisoquinoline **I** and 3.2 g (40 mmol) of pyridine. The reaction mixture was left overnight, then it was filtered, the filtrate was washed in succession with 5% aqueous HCl, with H_2O, 10% solution of NaOH, and again with H_2O. The benzene solution was dried with Na_2SO_4, the solvent was distilled off, the residue was recrystallized from ethanol. Stereoisomers mixture, 60 : 40**.** Yield 10 g (65%), mp 190–192°C, R_f 0.55 (benzene–acetone, 3 : 1). ^{1}H NMR spectrum, δ, ppm: 1.33–1.97 m, 2.08–2.18 m (7H and 1H, C_5H_8), 3.10 d.d (0.4H, ^2J 13.0, ^4J 1.5 Hz), 3.57 d (0.6H, ^2J 13.5 Hz), 3.74 d.d (0.6H, ^2J 13.5, ^4J 1.5 Hz), 4.34 d (0.4H, NCH_2, ^2J 13.0 Hz), 3.78 s, 3.78 s, 3.80 s (6H, OCH_3), 4.14 d, 4.47 d (0.4 H each, ^2J 12.7 Hz), 4.29 d, 4.33 d (0.6 H each, NCH_2Cl, ^2J 13.0 Hz), 5.30 s, 5.54 s (0.4H and 0.6H, CH), 6.68 s, 6.73 s, 6.87 s, 7.06 s (0.6H, 0.4H, 0.4H, 0.6H, H_{arom}), 7.56 m (1H, NH). Found, %: C 59.70; H 6.78; Cl 9.40; N 7.47. $C_{19}H_{25}ClN_2O_4$. Calculated, %: C 59.92; H 6.62; Cl 9.31; N 7.36.

Compounds IVa–IVe. A mixture of 42 mmol of compound **III**, 84 mmol of amine (diethylamine, pyrrolidine, piperidine, morpholine, or 4-fluorobenzylpiperazine) and 2–3 crystals of KI in 50 mL of a mixture ethanol–dioxane, 20 : 1, was boiled for 10–12 h. The solvent was distilled off, to the residue was added 50 mL of benzene and 5% aqueous HCl till acid reaction. The water layer was separated, alkalinized with 10% solution of NaOH, the reaction products were extracted with benzene. The extract was dried with anhydrous Na_2SO_4, the solvent was distilled off, the residue was recrystallized from ether.

***N*-Methyl-6',7'-dimethoxy-2'-[2-(diethylamino)-acetyl]-2',3'-dihydro-1'*H*-spirocyclopentane-1,4'-isoquinoline-1'-carboxamide (IVa)**. Stereoisomers mixture, 70 : 30**.** Yield 67%, mp 155–157°C, R_f 0.52 (benzene–acetone, 1 : 1, ammonia vapor). ^{1}H NMR spectrum, δ, ppm: 0.99 t, 1.04 t (1.8H and 4.2H, $NCH_2\underline{CH_3}$, J 7.1 Hz), 1.31–2.18 m (8H, C_5H_8), 2.55 q, 2.56 q (1.2H and 2.8H, $N\underline{CH_2}CH_3$, J 7.1 Hz), 2.67 d, 2.68 d (0.9H and 2.1H, $NH\underline{CH_3}$, J 4.5 Hz), 2.75 d, 3.74 d, 3.92 d, 4.39 d (0.3H, 0.7H, 0.7H, 0.3H, $CONCH_2$, ^2J 13.0 Hz), 3.22 d, 3.25 d, 3.28 d, 3.40 d (0.3H, 0.7H, 0.7H, 0.3H, $COCH_2N$, ^2J 13.5 Hz), 3.76 s, 3.78 s, 3.79 s, 3.80 s (2.1H, 2.1H, 0.9H, 0.9H, OCH_3), 5.49 s, 5.73 s (0.7H, 0.3H, CH), 6.70 s (1H, $H^5{}_{isoquinoline}$), 6.82 s, 6.88 s (0.3H, 0.7H, $H^8{}_{isoquinoline}$), 7.69 q, 7.92 q (0.3H, 0.7H, NH, J 4.5 Hz). Found, %: C 66.40; H 8.30; N 9.95. $C_{23}H_{35}N_3O_4$. Calculated, %: C 66.16; H 8.45; N 10.06.

***N*-Methyl-6',7'-dimethoxy-2'-[2-(pyrrolidin-1-yl) acetyl]-2',3'-dihydro-1'*H*-spirocyclopentane-1,4'-isoquinoline-1'-carboxamide (IVb)**. Stereoisomers mixture, 60 : 40. Yield 65%, mp 110–112°C, R_f 0.58 (benzene–acetone, 1 : 1, ammonia vapor). ^{1}H NMR spectrum, δ, ppm: 1.30–2.16 m [12H, C_5H_8, β,β'-CH_2, (C_4H_8N)], 2.54 m (4H, α,α'-CH_2, C_4H_8N), 2.67 d, 2.68 d (1.2H, 1.8H, NCH_3), 2.87 d, 3.73 d, 3.86 d, 4.39 d (0.4H, 0.6H, 0.6H, 0.4H, $CONCH_2$, ^2J 13.0 Hz), 3.22 d, 3.28 d, 3.37 d (0.4H, 0.6H, 1H, $COCH_2N$, ^2J 13.0 Hz), 3.76 s, 3.78 s, 3.78 s, 3.79 s (1.8H, 1.8H, 1.2H, 1.2H, OCH_3), 5.49 s, 5.54 s (0.6H, 0.4H, $H^5{}_{isoquinoline}$), 6.85 s, 6.89 s (0.4H, 0.6H, $H^8{}_{isoquinoline}$), 7.95 m (1H, NH). Found, %: C 66.20; H 8.14; N 10.25. $C_{23}H_{33}N_3O_4$. Calculated, %: C 66.48; H 8.00; N 10.11.

***N*-Methyl-6',7'-dimethoxy-2'-[2-(piperidin-1-yl) acetyl]-2',3'-dihydro-1'*H*-spirocyclopentane-1,4'-isoquinoline-1'-carboxamide (IVc)**. Stereoisomers mixture, 63:37. Yield 68%, mp 120–122°C, R_f 0.56 (benzene–acetone, 1 : 1, ammonia vapor). ^{1}H NMR spectrum, δ, ppm: 1.28–1.70 m, 1.73–1.94 m, 1.99–2.16 m [8H, 4.4H, 1.6H, C_5H_8 + $(CH_2)_3$ from $C_5H_{10}N$], 2.35–2.47 m [4H, $N(CH_2)_2$ from $C_5H_{10}N$], 2.67d, 2.69 d (1.8H, 1.2H, NCH_3, J 4.6 Hz), 2.84 d, 4.38 d (0.4 H each, ^2J 13.0 Hz), 3.74 d, 3.88 d (0.6H each, CH_2NCO, ^2J 12.8 Hz), 3.00 d, 3.09 d, 3.22 d, 3.24 d (0.6H, 0.4H, 0.4H, 0.6H, $COCH_2N$, ^2J 12.8 Hz), 3.76 s, 3.78 s, 3.79 s, 3.80 s (1.8H, 1.8H, 1.2H, 1.2 H, OCH_3), 5.46 s, 5.58 s (0.6H, 0.4H, CH), 6.68 s, 6.68 s (0.6H, 0.4H, C_6H_2), 6.86 s, 6.89 s (0.4H, 0.6H, C_6H_2), 7.91–7.96 m (1H, NH). Found, %: C 67.35;

H 8.11; N 9.63. $C_{24}H_{35}N_3O_4$. Calculated, %: C 67.11; H 8.21; N 9.78.

***N*-Methyl-6',7'-dimethoxy-2'-[2-(morpholin-4-yl) acetyl]-2',3'-dihydro-1'*H*-spirocyclopentane-1,4'-isoquinoline-1'-carboxamide (IVd)**. Stereoisomers mixture, 60:40. Yield 70%, mp 132–134°C, R_f 0.53 (benzene–acetone, 1 : 1, ammonia vapor). ^{1}H NMR spectrum, δ, ppm: 1.24–2.17 m (8H, C_5H_8), 2.40–2.52 m [4H, $N(CH_2)_{2\ morpholine}$], 2.67 d, 2.69 d (1.8H, 1.2H, NCH_3, *J* 4.5 Hz), 2.95 d, 4.39 d (0.4 H each, ^2J 13.0 Hz), 3.79 s (1.2H, CH_2NCO), 3.13 d, 3.17 d, 3.23 d, 3.26 d (0.6H, 0.4H, 0.4H, 0.6H, NCH_2CO, ^2J 13.0 Hz), 3.52 m, 3.61 m [1.6H, 2.4H, $O(CH_2)_2$], 3.76 s, 3.78 s, 3.79 s, 3.81 s (1.8H, 1.8H, 1.2H, 1.2H, OCH_3), 5.47 s, 5.53 s (0.6H, 0.4H, CH), 6.68 s, 6.69 s (0.6H, 0.4H, C_6H_2), 6.91 s, 6.93 s (0.6H, 0.4H, C_6H_2), 7.75 br.q, 8.00 br.q (0.4H, 0.6H, NH, *J* 4.5 Hz). Found, %: C 64.31; H 7.55; N 9.61. $C_{23}H_{33}N_3O_5$. Calculated, %: C 64.02; H 7.71; N 9.74.

***N*-Methyl-6',7'-dimethoxy-2'-{2-[(4-fluorobenzyl)piperazin-1-yl]acetyl}-2',3'-dihydro-1'*H*-spirocyclopentane-1,4'-isoquinoline-1'-carboxamide (IVe)**. Stereoisomers mixture, 60:40. Yield 65%, mp 175–177°C, R_f 0.50 (benzene–acetone, 1:1, ammonia vapor). ^{1}H NMR spectrum, δ, ppm: 1.28–2.14 m (8H, C_5H_8), 2.36–2.58 m (8H, $C_4H_8N_2$), 2.61 d, 2.67 d (1.2H, 1.8H, NCH_3, *J* 4.6 Hz), 2.88 d, 4.37 d (0.4 H each, ^2J 13.1 Hz), 3.75 d, 3.82 d (0.6 H each, CH_2NCO, ^2J 12.8 Hz), 3.09 d, 3.26 d (0.6 H each, ^2J 12.9 Hz), 3.12 d, 3.27 d (0.4 H each, NCH_2CO, ^2J 13.1 Hz), 3.52 s, 3.53 s (0.8H, 1.2H, CH_2Ar), 3.76 s, 3.78 s, 3.79 s, 3.80 s (1.8H, 1.8H, 1.2H,1.2H, OCH_3), 5.46 s, 5.52 s (0.6H, 0.4H, CH), 6.68 s, 6.68 s (0.6H, 0.4H, $H^5_{isoquinoline}$), 6.86 s, 6.89 s (0.4H, 0.6H, $H^8_{isoquinoline}$), 6.96–7.03 m, 7.05–7.11 m, 7.18–7.25 m, 7.33–7.40 m (0.8H, 1.2H, 1.2H, 0.8H, C_6H_4), 7.79 br.q, 7.95 br.q (0.4H, 0.6H, NH, *J* 4.6 Hz). Found, %: C 66.65; H 7.48; F 3.40; N 10.60. $C_{30}H_{39}FN_4O_4$. Calculated, %: C 66.89; H 7.30; F 3.53; N 10.40.

2'-[2-(1,3-Dioxoisoindolin-2-yl)acetyl]-*N*-methyl-6-',7'-dimethoxy-2',3'-dihydro-1'*H*-spiro-cyclopentane-1,4'-isoquinoline-1'-carboxamide (IVf). A mixture of 0.6 g (16 mmol) of compound **III** and 0.3 g (16 mmol) of potassium phthalimide in 30 mL of ethanol was boiled for 12 h. The precipitated crystals were filtered off, washed with hot water 2–3 times, with acetone, and recrystallized from ethanol. Stereoisomers mixture, 70 : 30. Yield 0.43 g (56%), mp 238–240°C (ethanol), R_f 0.52 (benzene–acetone, 1 : 1). ^{1}H NMR spectrum, δ, ppm: 1.28–2.23 m (8H, C_5H_8), 2.68 d (2.1H, *J* 4.2 Hz) and 2.76 d (0.9H, NCH_3, *J* 4.2 Hz), 3. 06 d (0.3H, *J* 13.1 Hz), 3.72 d (0.7H, *J* 14.1 Hz), 3.85 d (0.7H, *J* 14.1 Hz), 4.30 d (0.3H, NCH_2, *J* 13.1 Hz), 3.76 s (2.1H), 3.79 s (2.1H), 3.81 s (0.9H), 3.82 s (0.9H, OCH_3), 4.40 d (0.7H, *J* 16.3 Hz), 4.54 d (0.3H, *J* 16.3 Hz), 4.69 d (0.3H, *J* 16.3 Hz), 4.79 d (0.7H, $COCH_2N$, *J* 16.3 Hz), 5.47 s (0.3H), 5.54 s (0.7H, NCH), 6.72 s (0.7H), 6.75 s (0.3H), 6.87 s (0.3H) and 6.94 s (0.7H, C_6H_2), 7.74–7.89 m (4H, C_6H_4), 7.99 m (1H, NH). Found, %: C 65.70; H 6.10; N 8.67. $C_{27}H_{29}N_3O_6$. Calculated, %: C 65.97; H 5.95; N 8.55.

***N*-Methyl-6',7'-dimethoxy-2'-[2-(5-phenyl-1,3,4-oxadiazol-2-ylsulfanyl)acetyl]-2',3'-dihydro-1'*H*-spirocyclopentane-1,4'-isoquinoline-1'-carboxamide (Va)**. To a solution of 0.6 g (34 mmol) of 5-phenyl-1,3,4-oxadiazole-2-thiol and 0.2 g of KOH in 15 mL of anhydrous ethanol was added a solution of 1.2 g (32 mmol) of compound **III** in 20 mL of ethanol, and the mixture was boiled for 3 h. The mixture was left overnight, the precipitated crystals were filtered off, washed with water on the filter, then with 10% water solution of KOH, again with water, dried, and recrystallized from ethanol. Stereoisomers mixture, 60 : 40. Yield 53%, mp 260–262°C, R_f 0.53 (benzene–acetone, 2 : 1). ^{1}H NMR spectrum, δ, ppm: 1.34–2.21 m (8H, C_5H_8), 2.69 d, 2.73 d (1.8H, 1.2H, NCH_3, *J* 4.5 Hz), 3.13 d, 4.38 d (on 0.4H, ^2J 12.9 Hz), 3.74 d, 3.82 d (0.6 H each, CH_2NCO, ^2J 14.2 Hz), 4.40 d, 4.46 d, 4.66 d, 4.69 d (0.6H, 0.4H, 0.4H, 0.6H, SCH_2, ^2J 15.6 Hz), 5.41 s, 5.61 s (0.4H, 0.6H, CH), 3.76 s, 3.78 s, 3.79 s, 3.80 s (1.8H, 1.8H, 1.2H, 1.2H, OCH_3), 6.71 s, 6.73 s (0.6H, 0.4H, $H^5_{isoquinoline}$), 6.92 s, 6.97 s (0.4H, 0.6H, $H^8_{isoquinoline}$), 7.47–7.57 m, 7.98 m (3H, 2H, C_6H_5), 7.93 q, 7.98 q (0.4H, 0.6H, NH, *J* 4.5 Hz). Found, %: C 62.24; H 5.60; N 10.63; S 6.25. $C_{27}H_{30}N_4O_5S$. Calculated, %: C 62.05; H 5.79; N 10.72; S 6.14.

***N*-Methyl-6',7'-dimethoxy-2'-[2-(4,6-dimethylpyrimidin-2-ylsulfanyl)acetyl]-2',3'-dihydro-1'*H*-spirocyclopentane-1,4'-isoquinoline-1'-carboxamide (Vb)** was similarly obtained from compound **III** and 4,6-dimethylpyrimidine-2-thiol. Stereoisomers mixture, 70:30. Yield 51%, mp 222–224°C (ethanol), R_f 0.48 (benzene–acetone, 1 : 1). ^{1}H NMR spectrum, δ, ppm: 1.46–2.00 m (8H, C_5H_8), 2.24 s, 2.36 s (1.8H, 4.2H, CH_3), 2.67 d, 2.71 d (2.1H, 0.9H, NCH_3, *J* 4.6 Hz), 3.76 s, 3.78 s, 3.78 s, 3.79 s (2.1H, 0.9H, 2.1H, 0.9H, OCH_3), 3.00 d, 4.44 d (0.3 H each, ^2J 13.0 Hz), 3.78 d, 3.85 d (0.7 H each, NCH_2, ^2J 13.7 Hz), 3.80 d, 4.16 d, 4.20 d, 4.33 d (0.3H, 0.7H, 0.7H, 0.3H, SCH_2, ^2J 15.4 Hz), 5.60 s

(1H, CH), 6.70 s, 6.72 s, 6.78 s (1H, 0.3H, 0.7H, C_6H_2), 6.90 s ($1H_{pyrimidin}$), 7. 84 br.q, 7.97 br.q (0.3H, 0.7H, NH, *J* 4.6 Hz). Found, %: C 61.80; H 6.50; N 11.67; S 6.74. $C_{25}H_{32}N_4O_4S$. Calculated, %: C 61.96; H 6.66; N 11.56; S 6.62.

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