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SYNTHESIS AND MODIFICATION OF 2-(COUMARIN-3-YL)-3,4,5,6,7,8-HEXAHYDROPYRIDO [4′,3′:4,5]THIENO[2,3-d]PYRIMIDIN-4-ONES

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As the result of interaction of 2-iminocoumarin-3-carboxamides with 2-amino-4,5,6,7-terahydrothieno[2,3-c]pyridin-3-carboxamides the novel 2-(coumarin-3-yl)-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5]thieno[2,3-d]pyrimidin-4-one derivatives were obtained.

СИНТЕЗ ТА МОДИФІКАЦІЯ 2-(КУМАРИН-3-ІЛ)-3,4,5,6,7,8-ГЕКСАГІДРОПІРИДО[4′,3′:4,5]ТІЄНО[2,3-d]ПІРИМІДИН-4-ОНІВ
С.М.Коваленко, С.В.Власов, О.В.Силін, А.І.Федосов, І.О.Журавель, В.П.Черних
В результаті взаємодії 2-імінокумарин-3-карбоксамідів з 2-аміно-4,5,6,7-тетрагідротієно[2,3-c]піридин-3-карбоксамідами були одержані нові похідні 2-(кумарин-3-іл)-3,4,5,6,7,8-гексагідропіридо[4′,3′:4,5]тієно[2,3-d]піримідин-4-онів.

СИНТЕЗ И МОДИФИКАЦИЯ 2-(КУМАРИН-3-ИЛ)-3,4,5,6,7,8-ГЕКСАГИДРОПИРИДО[4′,3′:4,5]ТИЕНО[2,3-d]ПИРИМИДИН-4-ОНОВ
С.Н.Коваленко, С.В.Власов, А.В.Силин, А.И.Федосов, И.А.Журавель, В.П.Черных
В результате взаимодействия 2-иминокумарин-3-карбоксамидов с 2-амино-4,5,6,7-тетрагидротиено[2,3-c]пиридин-3-карбоксамидами были получены новые производные 2-(кумарин-3-ил)-3,4,5,6,7,8-гексагидропиридо[4′,3′:4,5]тиено[2,3-d]пиримидин-4-онов.

Pyrido[4′,3′:4,5]thieno[2,3-d]pyrimidines are known to possess various important biological properties such as anticancer [1], anti-allergic [2], and antimicrobial activity [3]. Some of the similar compounds showed a high affinity to 5-HT1A receptor and can be used for treatment of cerebral ischemia [4]. In view of these facts and in continuation of our work on the synthesis of 3-heterylcoumarins *via* rearrangement of 2-iminocoumarin-3-carboxamides [5-8] it was worthwhile to synthesize novel compounds incorporating pyrido [4′,3′:4,5]thieno[2,3-d]pyrimidine with biogenic coumarin moiety [9].

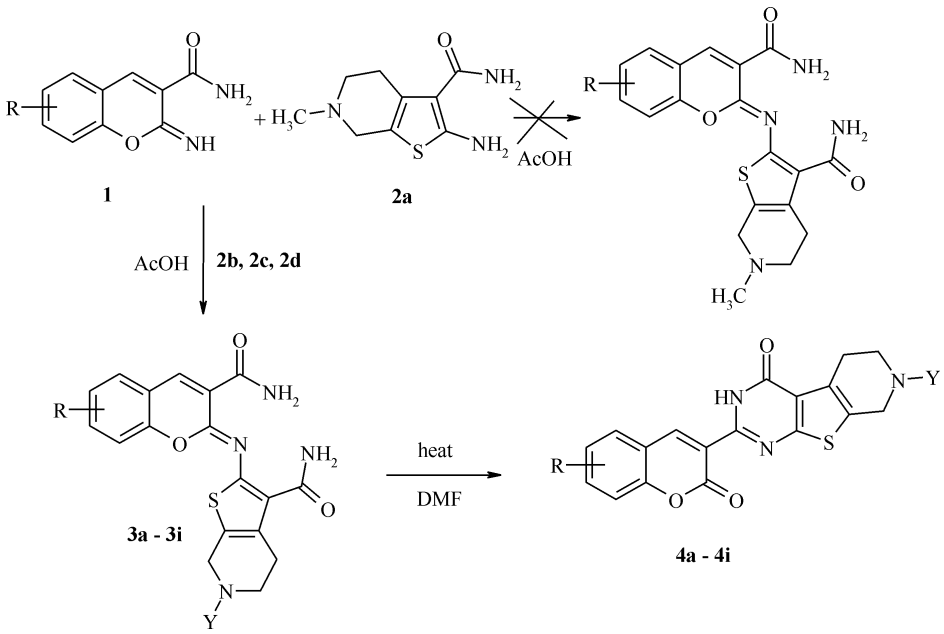
At the firs stage of the synthesis the attempt to obtain 2-(thienylimino)coumarin-3-carboxamides **3** by coupling of 2-iminocoumarin-3-carboxamides with the of corresponding 2-amino-4,5,6,7-terahydrothieno[2,3-c]pyridin-3-carboxamides has been made according to the previously reported procedure (AcOH 70°C), which had been successfully applied for the great number of aromatic amines [5-8]. Though we failed to isolate the desired products **3** in the reaction between 2-iminocoumarin-3-carboxamides and 2-amino-6-methyl-4,5,6,7-tetrahydrothieno[2,3-c]pyridine-3-carboxamide **2a**, either from glacial acetic acid media or even from low alcohols (MeOH, EtOH *i*-PrOH or BuOH), the other compounds **2b-d** readily formed the corresponding products **3a-i** in the common acidic condition (Scheme 1).

Further rearrangement of 2-(thienylimino)coumarin-3-carboxamides 3 has been performed by refluxing in DMF for 1-2 hours. The obtained 2-(coumarin-3-yl)-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5]thieno[2,3-d] pyrimidin-4-one derivatives **4a-i** precipitated at cooling as orange or bright — yellow solids with good or even excellent yield (52-84%).

In order to study the reactivity of compounds **4a-i**, with the aim of their possible functionalization, we have made an attempt to hydrolyze the secondary amide in [4′,3′:4,5]thieno[2,3-d]pyrimidine moiety. In the course of the experiments it was established that the acidic hydrolytic conditions, tenfold molar excess of strong concentrated acid (HCl or H_2SO_4) in 1,4-dioxane-water (1:1) mixture, are too weak for hydrolysis to take place for *N*-acetyl and *N*-ethoxycarbonyl derivatives **4a-h**. At the same time the attempt of basic hydrolysis of **4a** with quintuple molar excess of the strong alkali (NaOH), in propanol-2 — water media, came into collision with the coumarin ring destruction.

The desired result has been obtained only for *N*-Boc derivative 4i, which was converted into the crude product **5** by treatment with trifluoroacetic acid excess in dichloromethane. The product **5** was used in the further transformations to form the corresponding amide **4j** and sulfonamide **4k** (Scheme 2).

The structures of the synthesized compounds **4 a-k** were assigned by elemental analyses, ^{1}H NMR, IR,



1a R = H; **1b** R = 6-Cl; **1c** R = 8- OCH_3; **1d** R = 7-OCH_3; **1e** R = 6-Br; **2a** Y = CH_3; **2b** Y = $COCH_3$; **2c** Y = COOEt; **2d** Y = Boc; **4a** R = H, Y = $COCH_3$; **4b** R = 6-Cl, Y = $COCH_3$; **4c** R = 8-OCH_3, Y = $COCH_3$; **4d** R = 7-OCH_3, Y = $COCH_3$; **4e** R = H, Y = COOEt; **4f** R = 6-Cl, Y = COOEt; **4g** R = 8-OCH_3, Y = COOEt; **4h** R = 6-Br, Y = COOEt; **4i** R = H, Y = Boc.

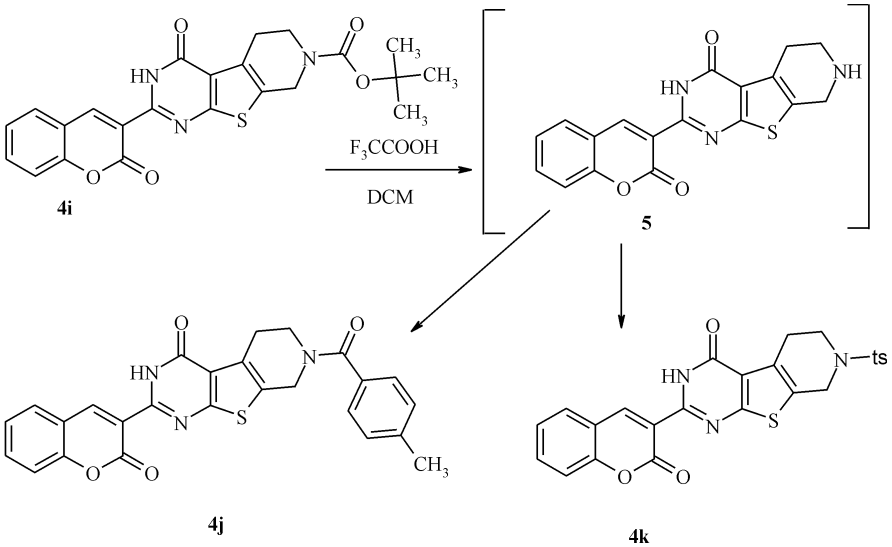
Scheme 1. Synthesis of 2-(coumarin-3-yl)-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5]thieno[2,3-d]pyrimidin-4-one.

UV/Vis spectral data. ^{1}H NMR-spectra of all of the derivatives **4** show the signals of coumarin moiety protons at 9.03-7.0 ppm, and the broad signal corresponding at position 3 of thieno[2,3-d]pyrimidin-4-one ring system at 11.53-12.07 ppm. The spectra of compounds **4a-4d** are characterized with the signal of acetyl group as a strong singlet (3H) 2.05-2.09 ppm.; **4e-4h** possess triplet (3H) and quartet (2H) at 1.15-1.17 ppm. and 4.08-4.14 ppm. respectively, the Boc — substituted derivative **4i** has the singlet (9H) at 1.42 ppm. The signals of AA′BB′ — spin systems of aromatic protons in the range from 7.27 to 7.72 ppm. are present in the spectra of the compounds **4j** and **4k**.

The IR spectra of all compounds **4a-k** exhibit strong absorption bands 1718-1642 cm^{-1} (C=O) and 3251-3208 cm^{-1} (N—H). The strong bands of SO_2 ν_{as} 1123 cm^{-1} and ν_s 1163 cm^{-1} are also present in spectra of compound **4k**.

Experimental

General Information. Melting points (°C) were measured with a Koeffler melting point apparatus and were not corrected. IR-spectra were recorded on FT-IR Bruker Tensor 27 spectrometer in KBr. ^{1}H NMR spectra were recorded on Varian Mercury 200 (200 MHz) spectrometer in DMSO-d_6 using TMS as



Scheme 2. Modification of tert-butyl 4-oxo-2-(coumarin-3-yl)-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5] thieno[2,3-d]pyrimidine-7-carboxylate.

an internal standard (chemical shifts are reported in ppm). UV-VIS absorption spectra were recorded at Specord M-40 spectrophotometer in 1,4-dioxane from 45000 to 20000 cm^{-1}. Elemental analyses were within ± 0.4% of the theoretical values.

2-Amino-4,5,6,7-tetrahydrothieno[2,3-c]pyridin-3-carboxamides (2a-d) [3, 10] and **2-iminocoumarine-3-carboxamides (1a-h)** [11, 12] were prepared according to the reported methods.

General procedure for synthesis of 4a-i

To the suspension of 2-aminothiophene-3-carboxamide **2** (2 mmol) in 8 mL of glacial acetic acid 2-iminocoumarine-3-carboxamide **1** (2 mmol) was added. The mixture was stirred and heated for 2 hours. The solid crystals of **3** was filtered off and thoroughly washed with 2-propanol and dried. The product **3** obtained (1.5 mmol) was heated in DMF (130°C) for 1-2 hours and then cooled. The precipitate formed was filtered off and washed with 2-propanol to give **4** in satisfactory yield.

7-Acetyl-2-(coumarin-3-yl)-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5]thieno[2,3-d]pyrimidin-4-one (4a): Yield 64%.

Mp>300°C.

IR (KBr) 3251 (νN—H), 2992, 2937, 2896, 2836, 1687, 1645, 1609, 1536, 1451 1367 cm^{-1}.

UV/Vis (dioxane): ν_{max} (log ε) = 39260 (4.16), 33380 (4.29), 25100 cm^{-1} (4.30).

^{13}C NMR (DMSO-d_6) δ 212 (CH_3), 25.8, 116.2, 118.0, 118.6, 121.1, 125.4, 130.04, 130.06, 130.3, 134.2, 145.65, 148.4, 153.8, 156.8, 159.9, 163.4, 168.8.

^{1}H NMR (DMSO-d_6) δ 11.75 (br s, 1H, NH), 9.02 (s, 1H, H-4), 8.03 (d, *J* = 7.7 Hz, 1H, H-5); 7.73 (t, *J* = 8.1 Hz, 1H, H-7); 7.48 (m, 2H, H-8+H-6), 4.71 (m, 2H, $CH_2CH_2N(Ac)CH_2$), 3.72 (m, 2H, $CH_2CH_2N(Ac)CH_2$), 2.97 (m, 2H, $CH_2CH_2N(Ac)CH_2$), 2.09 (s, 3H, $COCH_3$).

Anal. Calcd. for $C_{20}H_{15}N_3O_4S$ (393.42): C 61.06; H 3.84; N 10.68. Found: C 61.15; H 3.76; N 10.63.

7-Acetyl-2-(6-chlorocoumarin-3-yl)-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5]thieno[2,3-d]pyrimidin-4-one (4b): Yield 67%.

Mp>300°C.

IR (KBr) 3225 (νN—H), 3108, 2979, 2938, 2850, 1718, 1692, 1642, 1535, 1478, 1441 cm^{-1}.

UV/Vis (dioxane): ν_{max} (log ε) = 39200 (4.33), 34020 (4.39), 24700 cm^{-1} (4.38).

^{1}H NMR (DMSO-d_6) δ 11.95 (br s, 1H, NH), 8.97 (s, 1H, H-4), 8.12 (d, *J* = 2.8 Hz, 1H, H-5), 7.76 (dd, *J* = 10.7, 2.8 Hz, 1H, H-7), 7.53 (d, *J* = 10.7 Hz, 1H, H-8), 4.69 (m, 2H, $CH_2CH_2N(Ac)CH_2$), 3.71 (m, 2H, $CH_2CH_2N(Ac)CH_2$), 2.97 (m, 2H, $CH_2CH_2N(Ac)CH_2$), 2.09 (s, 3H, $COCH_3$).

Anal. Calcd. for $C_{20}H_{14}ClN_3O_4S$ (427.87): C 56.14; H 3.30; N 9.82. Found: C 56.10; H 3.42; N 9.95.

7-Acetyl-2-(8-methoxycoumarin-3-yl)-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5]thieno[2,3-d]pyrimidin-4-one (4c): Yield 78%.

Mp 293-295°C.

IR (KBr) 3208 (νN—H), 2978, 2944, 2893, 2828, 1684, 1644, 1608, 1577, 1539, 1469 cm^{-1}.

UV/Vis (dioxane): ν_{max} (log ε) = 39120 (4.42), 32620 (4.44), 31400 (4.38) 25080 cm^{-1} (4.44).

^{13}C NMR (DMSO-d_6) δ 21.2 (CH_3), 25.9, 56.7 (OCH_3), 117.0, 118.0, 119.3, 121.1, 121.4, 125.4, 130.07, 130.08, 130.10, 145.8, 146.6, 148.4, 156.8, 159.6, 163.4, 168.8.

^{1}H NMR (DMSO-d_6) δ 12.03 (br s, 1H, NH), 8.97 (s, 1H, H-4), 7.45 (m, 3H, H-5+H-6+H-7), 4.68 (m, 2H, $CH_2CH_2N(Ac)CH_2$), 3.92 (s, 3H, OCH_3), 3.69 (m, 2H, $CH_2CH_2N(Ac)CH_2$), 2.93 (m, 2H, $CH_2CH_2N(Ac)CH_2$), 2.05 (s, 3H, $COCH_3$).

Anal. Calcd. for $C_{21}H_{17}N_3O_5S$ (423.45): C 59.57; H 4.05; N 9.92. Found: C 59.61; H 4.01; N 9.79.

7-Acetyl-2-(7-methoxycoumarin-3-yl)-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5]thieno[2,3-d]pyrimidin-4-one (4d): Yield 71%.

Mp 292-294°C.

IR (KBr) 3214 (νN—H), 3009, 2941, 2907, 2858, 1668, 1614, 1534, 1509, 1432 cm^{-1}.

UV/Vis (dioxane): ν_{max} (log ε) = 38820 (4.17), 31980 (4.10), 29140 (4.13), 24680 cm^{-1} (4.43).

^{1}H NMR (DMSO-d_6) δ 11.84 (br s, 1H, NH), 8.96 (s, 1H, H-4), 7.90 (d, *J* = 9.0 Hz, 1H, H-5), 7.0 (m, 2H, H-8+H-6), 4.65 (m, 2H, $CH_2CH_2N(Ac)CH_2$), 3.89 (s, 3H, OCH_3), 3.68 (m, 2H, $CH_2CH_2N(Ac)CH_2$), 2.89 (m, 2H, $CH_2CH_2N(Ac)CH_2$), 2.07 (s, 3H, $COCH_3$).

Anal. Calcd. for $C_{21}H_{17}N_3O_5S$ (423.45): C 59.57; H 4.05; N 9.92. Found: C 59.75; H 4.21; N 9.97.

Ethyl 4-oxo-2-(coumarin-3-yl)-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5]thieno[2,3-d]pyrimidine-7-carboxylate (4e): Yield 52%.

Mp 250-251°C.

IR (KBr) 3238 (νN—H), 3038, 2982, 2937, 2907, 1676, 1608, 1536, 1489, 1467 cm^{-1}.

UV/Vis (dioxane): ν_{max} (log ε) = 39200 (4.30), 33540 (4.42), 25020 cm^{-1} (4.41).

^{13}C NMR (DMSO-d_6) δ 14.6 (OCH_2CH_3), 25.2, 45.1, 61.2 (OCH_2CH_3), 116.33, 188.0, 118.5, 120.96, 125.4, 129.7, 130.3, 134.3, 145.6, 148.5, 153.7, 154.8, 156.8, 159.89, 162.3, 163.3.

^{1}H NMR (DMSO-d_6) δ 12.07 (br s, 1H, NH), 9.01 (s, 1H, H-4), 8.03 (d, *J* = 8.8 Hz, 1H, H-5); 7.73 (t, *J* = 9.4 Hz, 1H, H-7); 7.45 (m, 2H, H-8+H-6), 4.63 (m, 2H, $CH_2CH_2N(COOEt)CH_2$), 4.14 (q, *J* = 7.8 Hz, 2H, $COOCH_2CH_3$), 3.67 (m, 2H, $CH_2CH_2N(COOEt)CH_2$), 2.92 (m, 2H, $CH_2CH_2N(COOEt)CH_2$), 1.17 (t, *J* = 7.8 Hz, 3H, $COOCH_2CH_3$).

Anal. Calcd. for $C_{21}H_{17}N_3O_5S$ (423.45): C 59.57; H 4.05; N 9.92. Found: C 59.83; H 3.89; N 10.02.

Ethyl 2-(6-chlorocoumarin-3-yl)-4-oxo-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5]thieno[2,3-d]pyrimidine-7-carboxylate (4f): Yield 60%.

Mp>300°C.

IR (KBr) 3215 (νN—H), 3103, 2988, 2906, 2873, 1683, 1603, 1562, 1534, 1481 cm^{-1}.

UV/Vis (dioxane): ν_{max} (log ε) = 39120 (4.37), 34000 (4.44), 24540 cm^{-1} (4.42).

^{1}H NMR (DMSO-d_6) δ 11.89 (br s, 1H, NH), 8.94 (s, 1H, H-4), 8.12 (d, *J* = 2.0 Hz, 1H, H-5), 7.76 (dd, *J* = 5.8, 2.0 Hz, 1H, H-7), 7.54 (d, *J* = 5.8 Hz, 1H,

H-8), 4.63 (m, 2H, $CH_2CH_2N(COOEt)C\underline{H}_2$), 4.04 (q, J = 7.9 Hz, 2H, $COOC\underline{H}_2CH_3$), 3.64 (m, 2H, $CH_2C\underline{H}_2N(COOEt)CH_2$), 2.93 (m, 2H, $C\underline{H}_2CH_2N(COOEt)CH_2$), 1.15 (t, J = 7.9 Hz, 3H, $COOCH_2C\underline{H}_3$).

Anal. Calcd. for $C_{21}H_{16}ClN_3O_5S$ (457.90): C 55.09; H 3.52; N 9.18. Found: C 55.07; H 3.34; N 9.26.

Ethyl 2-(8-methoxycoumarin-3-yl)-4-oxo-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5]thieno[2,3-d]pyrimidine-7-carboxylate (4g): Yield 57%.

Mp 241-242°C.

IR (KBr) 3247 (νN—H), 2988, 2939, 1674, 1609, 1576, 1538, 1471 cm^{-1}.

UV/Vis (dioxane): ν_{max} (log ε) = 39180 (4.22), 32540 (4.24), 31340 (4.19) 25280 cm^{-1} (4.18).

^{1}H NMR (DMSO-d_6) δ 11.91 (br s, 1H, NH), 8.93 (s, 1H, H-4), 7.38 (m, 3H, H-5+H-6+H-7), 4.59 (m, 2H, $CH_2CH_2N(COOEt)C\underline{H}_2$), 4.12 (q, J = 7.6 Hz, 2H, $COOC\underline{H}_2CH_3$), 3.92 (m, 2H, $CH_2C\underline{H}_2N(COOEt)CH_2$), 2.89 (m, 2H, $C\underline{H}_2CH_2N(COOEt)CH_2$), 1.17 (t, J = 7.6 Hz, 3H, $COOCH_2C\underline{H}_3$).

Anal. Calcd. for $C_{22}H_{19}N_3O_6S$ (453.48): C 58.27; H 4.22; N 9.27. Found: C 58.42; H 4.38; N 9.32.

Ethyl 2-(6-bromocoumarin-3-yl)-4-oxo-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5]thieno[2,3-d]pyrimidine-7-carboxylate (4h): Yield 84%.

Mp>300°C.

IR (KBr) 3210 (νN—H), 3094, 3048, 2986, 2860, 1677, 1599, 1561, 1536, 1493 cm^{-1}.

UV/Vis (dioxane): ν_{max} (log ε) = 39020 (4.24), 33900 (4.31), 24620 cm^{-1} (4.28).

^{1}H NMR (DMSO-d_6) δ 11.87 (br s, 1H, NH), 8.93 (s, 1H, H-4), 8.21 (s, 1H, H-5), 7.82 (d, J = 10.9 Hz, 1H, H-7), 7.48 (d, J = 10.9 Hz, 1H, H-8), 4.67 (m, 2H, $CH_2CH_2N(COOEt)C\underline{H}_2$), 4.12 (q, J = 8.0 Hz, 2H, $COOC\underline{H}_2CH_3$), 3.68 (m, 2H, $CH_2C\underline{H}_2N(COOEt)CH_2$), 3.10 (m, 2H, $C\underline{H}_2CH_2N(COOEt)CH_2$), 1.17 (t, J = 8.0 Hz, 3H, $COOCH_2C\underline{H}_3$).

Anal. Calcd. for $C_{21}H_{16}BrN_3O_5S$ (502.35): C 50.21; H 3.21; N 8.36. Found: C 50.37; H 3.22; N 8.25.

Tert-butyl 4-oxo-2-(coumarin-3-yl)-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5]thieno[2,3-d]pyrimidine-7-carboxylate (4i): Yield 76%.

Mp 264-265°C.

IR (KBr) 3236 (νN—H), 3041, 3006, 2970, 2905, 2839, 1697, 1679, 1609, 1537, 1490 cm^{-1}.

UV/Vis (dioxane): ν_{max} (log ε) = 39100 (4.21), 33500 (4.33), 25020 cm^{-1} (4.34).

^{13}C NMR (DMSO-d_6) δ 25.4, 28.21 ($C(\underline{C}H_3)_3$), 43.0, 79.6 ($\underline{C}(CH_3)_3$), 116.2, 118.8, 118.6, 121.20, 125.4, 129.7, 129.9, 130.2, 134.2, 145.6, 148.4, 153.8, 154.1, 156.8, 159.9, 163.4.

^{1}H NMR (DMSO-d_6) δ 11.53 (br s, 1H, NH), 9.03 (s, 1H, H-4), 8.02 (d, J = 7.6 Hz, 1H, H-5); 7.76 (t, J = 8.2 Hz, 1H, H-7); 7.48 (m, 2H, H-8+H-6), 4.63 (m, 2H, $CH_2CH_2N(Boc)C\underline{H}_2$), 3.62 (m, 2H, $CH_2C\underline{H}_2N(Boc)CH_2$), 2.91 (m, 2H, $C\underline{H}_2CH_2N(Boc)CH_2$), 1.42 (s, 9H, $COOC(C\underline{H}_3)_3$).

Anal. Calcd. for $C_{23}H_{21}N_3O_5S$ (451.50): C 61.19; H 4.69; N 9.31. Found: C 61.15; H 4.72; N 9.23.

General procedure for synthesis of 4 j and 4k

To the 1 g of *tert*-butyl 4-oxo-2-(coumarin-3-yl)-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5]thieno[2,3-d] pyrimidine-7-carboxylate **4i** in 50 mL of dichloromethane 2 mL of trifluoracetic acid was added. The reaction mixture was stirred and heated during 5 hours. The excess liquid had been removed on rotary evaporator and the residue was treated with 30% sodium carbonate. The precipitate formed was filtered and washed with methanol.

To the suspension of **5** (15 g) in 3 mL of anhydrous 1,4-dioxane with 0.07 mL of triethylamine, 0.07 mL of *p*-methylbenzoylchloride was added. The reaction mixture was stirred at 80°C overnight. The precipitate of **4j** formed was filtered off without cooling and washed with 50% propanol-2.

7-Benzoyl-2-(coumarin-3-yl)-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5]thieno[2,3-d]pyrimidin-4-one (4j): Yield 47%.

Mp 281-282°C.

IR (KBr) 3231 (νN—H), 3053, 2974, 2946, 2895, 1709, 1683, 1631, 1609, 1566, 1537 cm^{-1}.

UV/Vis (dioxane): ν_{max} (log ε) = 33540 (4.42), 25020 cm^{-1} (4.43).

^{13}C NMR (DMSO-d_6) δ 20.8 (CH_3), 25.8, 42.5, 116.2, 117.9, 118.6, 121.1, 125.4, 126.9, 129.0, 129.6, 129.9, 130.3, 133.13, 134.30, 139.5, 145.6, 148.5, 153.8, 156.8, 159.9, 163.5, 169.3.

^{1}H NMR δ (DMSO-d_6) δ 12.09 (br s, 1H, NH), 9.08 (s, 1H, H-4), 8.02 (d, J = 7.6 Hz, 1H, H-5); 7.76 (t, J = 6.8 Hz, 1H, H-7); 7.25-7.65 (m, 6H, H-8+H-6+H-2′ + H-6′ + H-3′ + H-5′), 4.68 (m, 2H, $CH_2CH_2N(COAr)C\underline{H}_2$), 3.67 (m, 2H, $CH_2C\underline{H}_2N(COAr)CH_2$), 3.02 (m, 2H, $C\underline{H}_2CH_2N(COAr)CH_2$), 2.31 (s, 2H, $C\underline{H}_3$).

Anal. Calcd. for $C_{26}H_{19}N_3O_4S$ (469.52): C 66.51; H 4.08; N 8.95. Found: C 66.43; H 4.11; N 8.89.

7-(4-Methylphenylsulfonyl)-2-(coumarin-3-yl)-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5]thieno[2,3-d]pyrimidin-4-one (4k): The compound **4k** was obtained analogously to **4j** starting from tosyl chloride. Yield 64%.

Mp>300°C.

IR (KBr) 3216 (νN—H), 2994, 2941, 2867, 2832, 1698, 1607, 1537, 1491, 1474, 1123 (ν_{as} SO_2), 1163 (ν_s SO_2) cm^{-1}.

UV/Vis (dioxane): ν_{max} (log ε) = 33620 (4.48), 25100 cm^{-1} (4.49).

^{1}H NMR δ (DMSO-d_6) δ 12.09 (br s, 1H, NH), 8.97 (s, 1H, H-4), 7.98 (d, J = 7.9 Hz, 1H, H-5); 7.72 (m, 3H, H-7+H-2′+H-6′); 7.44 (m, 4H, H-8+H-6+H-3′+H-5′), 4.34 (m, 2H, $CH_2CH_2N(COAr)C\underline{H}_2$), 3.43 (m, 2H, $CH_2C\underline{H}_2N(COAr)CH_2$), 2.92 (m, 2H, $C\underline{H}_2CH_2N(COAr)CH_2$), 2.32 (s, 2H, $C\underline{H}_3$).

Anal. Calcd. for $C_{25}H_{19}N_3O_5S_2$ (505.58): C 59.39; H 3.79; N 8.31. Found: C 59.44; H 3.92; N 8.22.

Conclusion

A series of novel 2-(coumarin-3-yl)-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5]thieno[2,3-d]pyrimidin-4-one derivatives were obtained with the application of

2-iminocoumarin-3-carboxamide rearrangement, using 2-amino-4,5,6,7-tetrahydrothieno[2,3-c]pyridin-3-carboxamides as dinucleophiles. The ways of their modification has been studied.

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