Pavlo E. Shynkarenko,[a] Sergiy V. Vlasov,[a] Sergiy M. Kovalenko,[a]*
Svitlana V. Shishkina,[b] Oleg V. Shishkin,[b] and Valentin P. Chernykh[a]

[a]National University of Pharmacy, Kharkiv, 61002, Ukraine
[b]STC 'Institute for Single Crystals,' NAS of Ukraine, 61001, Kharkiv, Ukraine
*E-mail: kosn@ukrfa.kharkov.ua
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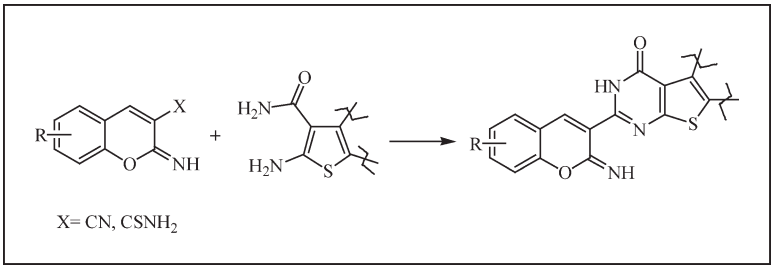

The interaction of both 2-iminocoumarin-3-carbonitriles and 2-iminocoumarin-3-carbothioamides with 2-aminothiophen-3-carboxamides lead to formation of 3-(4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidin-2-yl)-2-iminocoumarins in two steps. The simplicity of the procedure, as well as the high yields of the target products make this method to be a good alternative of Knoevenagel condensation for the synthesis of 3-(4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidin-2-yl)-2-iminocoumarins.

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INTRODUCTION

3-Substituted-2-iminocoumarins are known not only due to their versatile biological activity, such as anti-inflammatory [1,2], antimicrobial, antifungal [3,4], and antitumor [5–9], but also as luminescent indicators [10] and laser dyes [11–13]. They can also be useful as effective reagents for 2-substituted 2*H*-1-benzopyrans syntheses [14]. Therefore, the development of a simple methodology for synthesis 2-iminocoumarins substituted with heterocyclic moiety at position 3 is important problem of benzopyrans chemisrty.

With regard to the pharmacological potential of thieno[2,3-*d*]pyrimidines [15–24] as the part of our research work on the synthesis of 3-heteryl-2-iminocoumarins [25,26], we focused our efforts on the synthesis of 3-(4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidin-2-yl)-2-iminocoumarins.

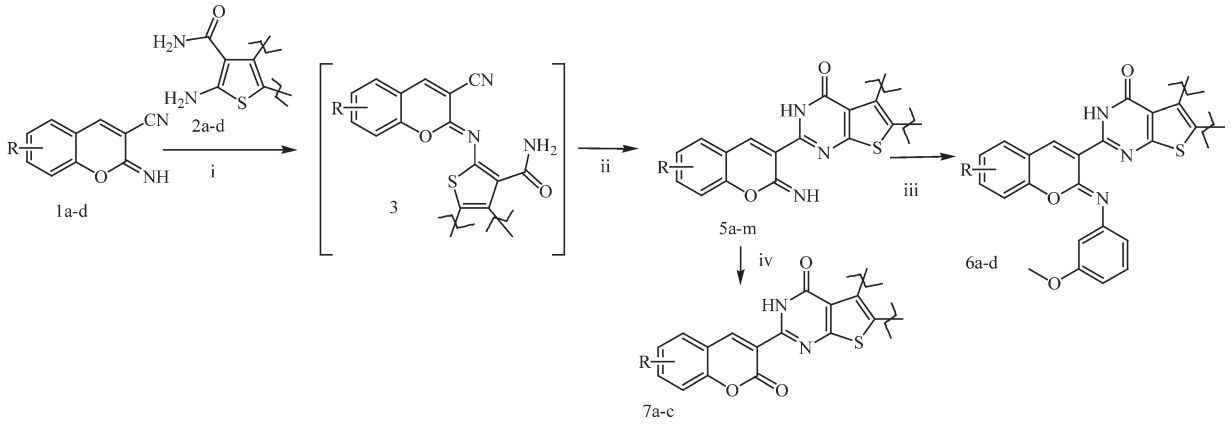
The most commonly used method for synthesis of 3-heteryl-2-iminocoumarins is the Knoevenagel condensation of salicylic aldehydes with nitriles of heterylacetic acids [27–30]. However, for synthesis of 3-(4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidin-2-yl)-2-iminocoumarins this approach is not convenient enough due to the difficulties in the starting building-blocks, the corresponding 2-(4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidin-2-yl)acetonitriles, preparation [31]. With the aim to develop more suitable method, we tested the alternative route for synthesis of 3-(4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidin-2-yl)-2-iminocoumarins based on intramolecular rearrangement of 2-iminocoumarins, so-called ''recyclization'' approach.

Recently it was shown that ''recyclization'' of 2-iminocoumarin-3-carboxamides under the action of binucleophlic reagents results in various 3-heterylcoumarins [25,26,32–37]. According to the proposed mechanism of these reactions the carboxamide group of 2-iminocoumarin-3-carboxamide serves as precursor of lactone C=O group of the resulting 3-heterylcoumarin. Thus, it was worthy to assume that utilization of 2-iminocoumarin-3-carbonitriles in a similar rearrangement would lead to the formation of products with the C=NH moiety in the 2 position of benzopyran ring. Therefore, we studied the interaction between 2-iminocoumarin-3-carbonitriles and 2-aminothiophen-3-carboxamides as the possible convenient approach for synthesis of desired 3-(4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidin-2-yl)-2-iminocoumarins.

RESULTS AND DISCUSSION

It is known that the interaction of 2-iminocoumarin-3-carboxamides with arylamines in the glacial acetic acid leads to formation of 2-*N*-aryliminocoumarin-3-carboxamides [34–38]. We applied a similar reaction to obtain the key-intermediates, which apparently were 2-(3-carbamoyl-2-thienylimino)-coumarin-3-carbonitriles **3** by interaction between 2-iminocoumarin-3-carbonitriles 1

Scheme 1



and 2-aminothiophen-3-carboxamides 2. The compounds **3** were isolated from glacial acetic acid as red solids and used without any additional purification.

The ''recyclization'' of 2-(3-carbamoyl-2-thienylimino)coumarin-3-carbonitriles **3** was performed by heating in DMF. The anhydrous solvent was used to avoid hydrolysis of the imino group of product **5** formed (Scheme 1). The proposed mechanism of ''recyclization'' reaction is depicted on the Scheme 2.

The compounds **5a–m** were obtained in the high yields (65–89%) (Method A).

In the ^{1}H NMR spectra of the compounds **5a–m**, the signal of proton in the position 4 of coumarin resonate in the range δ 8.66–8.83 ppm, as well as the signal of imino group proton (δ 9.31–9.51 ppm) and aromatic protons (δ 7.20–7.94 ppm) are present. All these spectra also contain signal of thieno[2,3-*d*]pyrimidine fragment NH (14.08–14.50 ppm). Though the LC/MS spectra for compound **5** show their high purity, in most cases the ^{1}H NMR spectra of derivatives **5** in DMSO-d_6 contain some additional signals, possibly from the open form of the iminolactone ring.

The IR-spectra (KBr) of the compounds **5a–m** have the strong absorption bands of υ C=O and υ C=N at 1700–1621 cm^{-1}, the broad band of υ N—H (pyrimidine and imino-group) at 3500–3150 cm^{-1}. In the spectra of the products **5**, the signal of υ CN is absent comparatively with the spectra of intermediates 3 (2240–2220 cm^{-1}).

Unfortunately the compounds **5** appeared to be slightly soluble in the suitable solvents to measure ^{13}C NMR spectra. Thus with the aim to prove the presence of imino-group in the molecule of these derivatives we performed their acidic hydrolysis (HCl) in 2-propanol-water mixture. The obtained products appeared to be the same as previously reported 3-(4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidin-2-yl)coumarins **7a–c** [34–36] (Table 1).

Also the presence of the imino group in the structure of **5** allowed us to obtain 2-*N*-aryliminoproducts **6** (using reaction of **5** with *m*-anisidine in glacial acetic acid) as crystalline substances.

In the ^{1}H NMR spectra of the compounds **6a–d** the signals of methoxygroup (3.76–3.78 ppm) and aromatic protons (6.73–7.53 ppm) of 3-methoxyphenyl substituent appear.

The crystals of compound **6a** appeared to be suitable for X-ray diffraction analysis after the crystallization from DMF. In the crystal phase of the compound **6** was observed as hemisolvate with DMF.

According to X-ray diffraction data the 2-minocoumarin fragment and 4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidin fragment are coplanar within 0.04 Å (Fig. 1). Such arrangement of these fragments relatively each other is stabilized by the formation of the N(2)—H(2N)...N(3) intramolecular hydrogen bond (H...N 1.96 Å N—H...N 138°) and the H(19)...N(1) attractive interaction (2.39 Å when compared with the van der Waals radii sum [39] 2.67 Å). The

Scheme 2

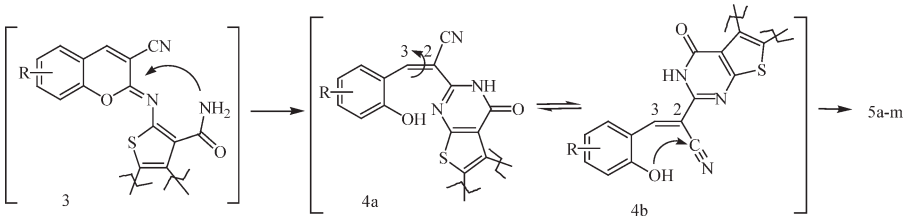
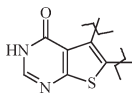
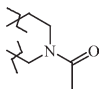
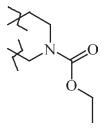


Table 1

Synthesis of compounds **5a–m**, **6a–d**, and **7a–c**.

No.		R	Yield[a] (%)
5a		H	74
5b		6-Cl	65
5c		8-OMe	84
5d		8-OEt	88
6a		6-Cl	83
6b		8-OMe	90
6c		8-OEt	92
7a		H	90
5e		H	66
5f		6-Cl	69
5g		8-OMe	75
5h		8-OEt	78
6d		8-OMe	89
7b		H	88
7c		8-OMe	89
5i		H	68
5j		H	85
5k		6-Cl	65
5l		8-OMe	79
5m		8-OEt	80

[a] Isolated yields of **5** based on **1** used (Method A); Isolated yields of **6** and **7** based on **5** used.

tetrahydrocycle is disordered over two half-chair conformation (A and B) with population 75:25%. Deviations of the C(4) and C(5) atoms from the mean plane of the remaining atoms of the ring are −0.50 and 0.19 Å, respectively for conformer A and 0.31 and −0.47 Å, respectively for B. The methoxyphenyl substituent is located in the cis-conformation relatively the C(12)—O(2) bond [the C(20)—N(3)—C(12)—O(2) torsion angle is 1.7(5)°] and it adopts –sc conformation relatively the C(12)—N(3) bond [the C(12)—N(3)—C(20)—C(25) torsion angle is -43.4(5)°]. The methoxy group is coplanar to the plane of the aromatic ring [the C(26)—O(3)—C(24)—C(25) torsion angle is 2.0(6)°].

The structures of the products 6 have been also confirmed using elemental analyses, IR, and LC/MS-spectra.

Following the mechanism of ''recyclization'' reaction, we tested whether the 2-iminocoumarin-3-carbothioamides were suitable precursors for 2-thiocoumarins synthesis. We obtained the intermediate 2-(3-carbamoyl-2-thienylimino)-coumarin-3-carbothioamides **9** by reaction of 2-iminocoumarin-3-carbothioamides **8** [40] with 2-aminothiophen-3-carboxamides **2** in glacial acetic acid. Further ''recyclization'' have been performed by heating compounds **9** in DMF. Though instead of the desired 2-(2-thiocoumarin-3-yl)thieno[2,3-*d*]pyrimidin-4-ones **10** 3-(4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidin-2-yl)-2-iminocoumarins **5** were isolated (Scheme 3). Thus it can be deduced that in this case the hydrogen sulfide cleavage is preferable way for recyclization the 2-iminocoumarin-3-carbothioamides (Scheme 4) (Method B).

CONCLUSION

It was established that interaction of both 2-iminocoumarin-3-carbonitriles and 2-iminocoumarin-3-carbothioamides with 2-aminothiophen-3-carboxamides after the rearrangement of arylimino intermediates lead to formation of 3-(4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidin-2-yl)-2-iminocoumarins. The simplicity of the proposed procedure as well as the high yields of the target products make this method to be a good alternative of Knoevenagel condensation for the synthesis of derivatives **5**. The further reaction of **5** with *m*-anisidine allowed us to obtain 2-(2-(3-methoxyphenylimino)-coumarin-3-yl)thieno[2,3-*d*]pyrimidin-4-ones **6**.

EXPERIMENTAL

Melting points were measured with a Buchi B-520 melting point apparatus and were not corrected. Elemental analyses were within ± 0.4% of the theoretical value. IR spectra were recorded on Specord M80 spectrometers in KBr. ^{1}H NMR spectra were recorded on Varian Mercury-200 spectrometer in DMSO-d_6 and $CDCl_3$ using TMS as an internal standard. Mass spectral analyses were obtained on a PE SCIEX API 150EX mass spectrometer.

X-ray study. The colourless crystals of 6a ($C_{26}H_{20}N_3O_3SCl$ 0.5 C_3H_7NO) are triclinic. At 293 K, a = 8.760(1), b = 11.321(1), c = 13.895(1) Å, α = 86.85(1)°, β = 83.36(1)°, γ = 85.46(1)°, V = 1363.0(3) Å^3, M_r = 562.0, Z = 2, space

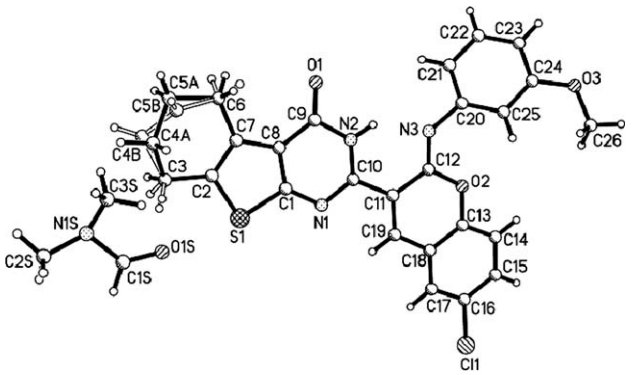
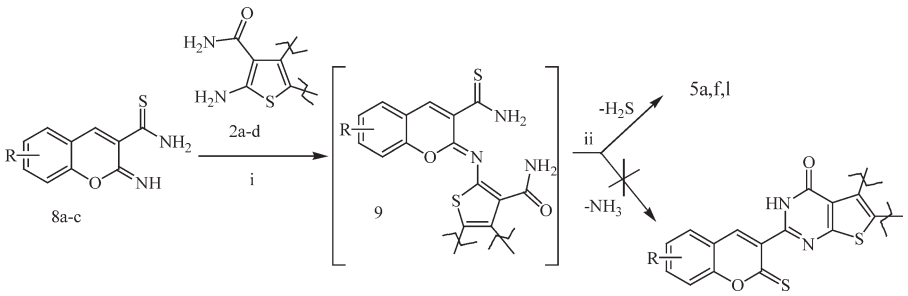


Figure 1. The molecular structure of the compound 6a according to X-ray diffraction data.

Scheme 3



group $P\bar{1}$, d_{calc} = 1.282 g/cm^3, μ(MoK$_\alpha$) = 0.253 mm^{-1}, $F(000)$ = 547. Intensities of 7751 reflections (4600 independent, R_{int} = 0.038) were measured using the ''Xcalibur-3'' diffractometer (graphite monochromated MoK$_\alpha$ radiation, CCD detector, ω-scanning, $2T_{max}$ = 50°). The structure was solved by direct method using SHELXTL package [41]. The restrains for bond lengths in the disordered fragment were applied during refinement (Csp^2—Csp^3 1.51 Å, Csp^3—Csp^3 1.54 Å). Positions of the hydrogen atoms were located from electron density difference maps and refined by ''riding'' model with U_{iso} = nU_{eq} of the carrier atom (n = 1.5 for methyl group and n = 1.2 for other hydrogen atoms). Full-matrix least-squares refinement against F^2 in anisotropic approximation for nonhydrogen atoms using 4517 reflections was converged to wR_2 = 0.191 (R_1 = 0.063 for 2815 reflections with F > 4σ(F), S = 1.156). The final atomic coordinates, and crystallographic data for molecule 6a have been deposited to with the Cambridge Crystallographic Data Centre, 12 Union Road, CB2 1EZ, UK and are available on request quoting the deposition numbers CCDC 705029.

2-Iminocoumarin-3-carbonitriles. 1a–d were obtained starting of malononitrile by interaction with corresponding salicylic aldehydes [42]. 2-Iminocoumarin-3-carbothioamides **8a-c** were synthesized by interaction of salicylic aldehydes of 2-cyanoethanethioamide [40].

2-Iminocoumarin-3-carbonitrile (1a). This compound was obtained in 65% yield as a yellow solid, mp 160–162°C; IR (cm^{-1}): 3293, 3038, 2228, 1651, 1601, 1450; ^{1}H NMR ($CDCl_3$): δ 7.12 (m, 2 H), 7.32 (d, J = 6.41 Hz, 1 H), 7.46 (t, J = 7.63 Hz, 1 H), 7.64 (br.s, 1 H), 7.70 (br.s, 1 H); Anal. calcd. for $C_{10}H_6N_2O$: H, 3.34; C, 55.36; N, 10.33. Found: H, 3.20; C, 55.08; N, 10.14.

6-Chloro-2-Iminocoumarin-3-carbonitrile (1b). This compound was obtained in 72% yield as a yellow solid, mp 172–174°C; IR (cm^{-1}): 3307, 3046, 2233, 1649, 1599, 1478; ^{1}H NMR ($CDCl_3$): δ 7.09 (d, J = 8.85 Hz, 1 H), 7.37 (d, J = 2.14 Hz, 1 H), 7.47 (dd, J = 8.85, 2.44 Hz, 1 H), 7.69 (br.s, 1 H), 7.80 (br.s, 1 H); Anal. calcd. for $C_{10}H_5ClN_2O$: H, 3.15; C, 53.66; N, 10.01. Found: H, 3.22; C, 53.33; N, 9.77.

2-Imino-8-methoxy-coumarin-3-carbonitrile (1c). This compound was obtained in 70% yield as a yellow solid, mp 165–167°C; IR (cm^{-1}): 3287, 3054, 2226, 1651, 1607, 1477; ^{1}H NMR ($CDCl_3$): δ 3.84 (s, 3 H), 6.89 (d, J = 6.71 Hz, 1 H), 7.05 (m, 2 H), 7.67 (br.s, 1 H), 7.78 (br.s, 1 H); Anal. calcd. for $C_{11}H_8N_2O_2$: H, 3.44; C, 54.95; N, 10.05. Found: H, 3.40; C, 54.70; N, 9.82.

8-Ethoxy-2-iminocoumarin-3-carbonitrile (1d). This compound was obtained in 78% yield as a yellow solid, mp 161–163°C; IR (cm^{-1}): 3320, 3036, 2228, 1655, 1604, 1467; ^{1}H NMR ($CDCl_3$): δ 1.36 (t, J = 6.71 Hz, 3 H), 4.03 (q, J = 6.71 Hz, 2 H), 6.84 (m, 1 H), 6.98 (m, 2 H), 7.61 (br.s, 1 H) 7.71 (br.s, 1 H); Anal. calcd. for $C_{12}H_{10}N_2O_2$: H, 3.57; C, 55.33; N, 9.93. Found: H, 3.31; C, 55.25; N, 9.67.

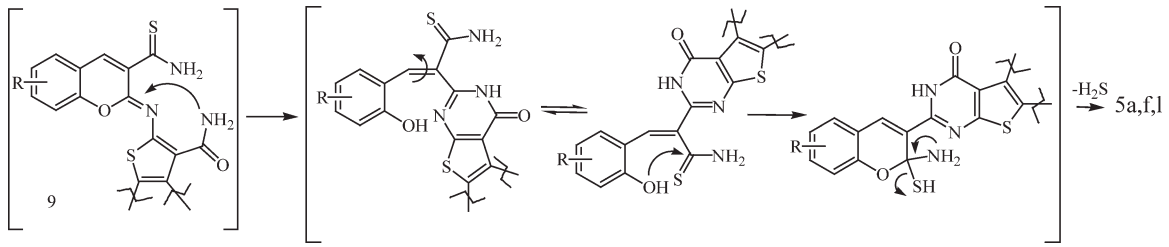
2-Aminothiophene-3-carboxamides. 2a–d were obtained from cyclohexanone, 4-methyl-cyclohexanone, and *N*-substituted piperidin-4-ones according to the Gewald procedure [43–45].

2-Amino-6-methyl-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxamide 2(b). This compound was obtained in 62% yield as a colorless solid, mp 187–189°C; IR (cm^{-1}): 3400, 3259, 3180, 2944, 1632, 1584, 1561, 1499; ^{1}H NMR (DMSO-d_6): δ 0.97 (t, J = 6.22 Hz, 3 H), 1.25 (m, 1 H), 1.74 (m, 2 H), 2.05 (m, 1 H), 2.58 (m, 2 H), 3.31 (br.s, 1 H), 6.49 (br.s, 2 H), 6.87 (s, 2 H).

6-Acetyl-2-amino-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide 2(c). This compound was obtained in 65% yield as a colorless solid, mp 250–252°C; IR (cm^{-1}): 3497, 3394, 3280, 3159, 1651, 1563, 1480; ^{1}H NMR (DMSO-d_6): δ 2.01, 2.05 (s, 3 H), 2.63 (br.s, 2 H), 2.73 (br.s, 2 H), 3.57 (br.s, 2 H), 4.35, 4.39 (s, 2 H), 6.56 (br.s, 2 H), 6.92 (s, 1 H), 6.98 (s, 1 H).

Ethyl 2-amino-3-(aminocarbonyl)-4,7-dihydrothieno[2,3-*c*] pyridine-6(5*H*)-carboxylate 2(d). This compound was obtained in 60% yield as a colorless solid, mp 185–187°C; IR

Scheme 4



(cm^{-1}): 3431, 3365, 3319, 3172, 1690, 1638, 1572, 1427; ^1H NMR (DMSO-d_6): δ 1.18 (t, J = 7.32 Hz, 3 H), 2.68 (t, J = 5.49 Hz, 2 H), 3.55 (t, J = 5.49 Hz, 2 H), 4.06 (q, J = 7.32 Hz, 2 H), 4.29 (s, 2 H), 6.48 (s, 2 H), 6.88 (s, 2 H).

General procedure for the preparation of 2-(2-iminocoumarin-3-yl)thieno[2,3-*d*]pyrimidin-4-ones 5a–m. To the warm (40–50°C) solution of 2-aminothiophene-3-carboxamide 2 (2 mmol) in glacial acetic acid (3 mL) the solution of either 2-iminocoumarine-carbonitrile 1 (Method A) or 2-iminocoumarine-3-carbothioamide 8 (Method B) (2 mmol) in glacial acetic acid (3 mL) was added and the mixture was heated at 70–80°C for 30 min. Then the reaction mixture was cooled. The precipitate that formed was collected by filtration and dried. The product **3** (Method A) or **9** (Method B) was dissolved in DMF (5 mL) at 140–150°C and heated for 3 h. The precipitate of **5** formed after cooling was filtered out, washed with 2-propanol and dried.

2-(2-Iminocoumarin-3-yl)-5,6,7,8-tetrahydro-benzo[4,5]-thieno[2,3-*d*]pyrimidin-4-one (5a). This compound was obtained in 74% yield (Method A) and 72% (Method B) as a red solid, mp 280–282°C; IR (cm^{-1}): 3451, 3156, 2932, 2846, 1654, 1615, 1535, 1473; ^1H NMR (DMSO-d_6): δ 1.72 (br.s, 4 H), 2.63 (br.s, 2 H), 2.79 (br.s, 2 H), 7.21 (m, 2 H), 7.53 (t, J = 6.7 Hz, 1 H), 7.79 (d, J = 6.4 Hz, 1 H), 8.71 (s, 1H, H-4), 9.31 (br.s, 1H, =NH), 14.17 (br.s, 1H, -NHCO); lcms: m/z (MH^+) 350. Anal. calcd. for $C_{19}H_{15}N_3O_2S$: H, 4.33; C, 65.31; N, 12.03. Found: H, 4.12; C, 65.55; N, 11.72.

2-(6-Chloro-2-iminocoumarin-3-yl)-5,6,7,8-tetrahydro-benzo [4,5]thieno[2,3-*d*]pyrimidin-4-one (5b). This compound was obtained in 65% yield as a orange solid, mp 294–296°C; IR (cm^{-1}): 3450, 3232, 2932, 2854, 1679, 1651, 1592, 1554, 1477; ^1H NMR (DMSO-d_6): δ 1.74 (br.s, 4 H), 2.67 (br.s, 2 H), 2.82 (br.s, 2 H), 7.20 (d, J = 8.9 Hz, 1 H), 7.54 (d, J = 8.9 Hz, 1 H), 7.89 (s, 1 H), 8.68 (s, 1H, H-4), 9.45 (br.s, 1H, =NH), 14.10 (br.s, 1H, -NHCO); lcms: *m/z* (MH^+) 384. Anal. calcd. for $C_{19}H_{14}ClN_3O_2S$: H, 3.68; C, 59.45; N, 10.95. Found: H, 3.40; C, 59.28; N, 10.57.

2-(2-Imino-8-methoxycoumarin-3-yl)-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one (5c). This compound was obtained in 84% yield as a yellow solid, mp 275–277; IR (cm^{-1}): 3436, 3326, 2925, 2842, 1679, 1660, 1605, 1574, 1533; ^1H NMR (DMSO-d_6): δ 1.76 (br.s, 4 H), 2.74 (br.s, 2 H), 2.88 (br.s, 2 H), 3.89 (s, 3 H), 7.32 (m, 3 H), 8.81 (s, 1H, H-4), 9.49 (br.s, 1H, =NH), 14.32 (br.s, 1H, -NHCO); lcms: m/z (MH^+) 379. Anal. calcd. for $C_{20}H_{17}N_3O_3S$: H, 4.52; C, 63.31; N, 11.07. Found: H, 4.22; C, 63.65; N, 10.73.

2-(8-Ethoxy-2-iminocoumarin-3-yl)-5,6,7,8-tetrahydro-benzo [4,5]thieno[2,3-*d*]pyrimidin-4-one (5d). This compound was obtained in 88% yield as a yellow solid, mp 278–280°C; IR (cm^{-1}): 3442, 3188, 2985, 2936, 1651, 1603, 1573, 1484; ^1H NMR (DMSO-d_6): δ 1.37 (t, J = 7.0 Hz, 3 H), 1.75 (br.s, 4 H), 2.69 (br.s, 2 H), 2.83 (br.s, 2 H), 4.17 (q, J = 7.0 Hz, 2 H), 7.26 (m, 3 H), 8.74 (s, 1H, H-4), 9.38 (br.s, 1H, =NH), 14.25 (br.s, 1H, —NHCO); lcms: *m/z* (MH^+) 394. Anal. calcd. for $C_{21}H_{19}N_3O_3S$: H, 4.87; C, 64.11; N, 10.68. Found: H, 4.68; C, 64.25; N, 10.30.

2-(2-Iminocoumarin-3-yl)-7-methyl-5,6,7,8-tetrahydro-benzo [4,5]thieno[2,3-*d*]pyrimidin-4-one (5e). This compound was obtained in 66% yield as a yellow solid, mp 282–284°C; IR (cm^{-1}): 3446, 3165, 2944, 2921, 1654, 1613, 1602, 1535, 1475; ^1H NMR (DMSO-d_6): δ 1.02 (d, J = 6.4 Hz, 3 H), 1.36 (m, 1 H), 1.85 (m, 2 H), 2.31 (m, 1 H), 2.78 (m, 2 H), 3.06 (m, 1 H), 7.26 (m, 2 H), 7.57 (t, J = 7.6 Hz, 1 H), 7.85 (d, J = 7.3 Hz, 1 H), 8.80 (s, 1H, H-4), 9.35 (br.s, 1H, =NH), 14.23 (br.s, 1H, —NHCO); lcms: *m/z* (MH^+) 364. Anal. calcd. for $C_{20}H_{17}N_3O_2S$: H, 4.71; C, 66.10; N, 11.56. Found: H, 4.52; C, 65.84; N, 11.32.

2-(6-Chloro-2-iminocoumarin-3-yl)-7-methyl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-one (5f). This compound was obtained in 69% yield (Method A) and 63% (Method B) as a yellow solid, mp 290–292; IR (cm^{-1}): 3440, 3251, 2931, 2823, 1671, 1595, 1552, 1492, 1446; ^1H NMR (DMSO-d_6): δ 1.01 (d, J = 6.1 Hz, 3 H), 1.31 (m, 1 H), 1.82 (m, 2 H), 2.25 (m, 1 H), 2.72 (m, 2 H), 3.00 (m, 1 H), 7.20 (d, J = 8.9 Hz, 1 H), 7.53 (d, J = 8.9 Hz, 1 H), 7.90 (s, 1 H), 8.66 (s, 1H, H-4), 9.42 (br.s, 1H, =NH), 14.08 (br.s, 1H, NHCO); lcms: *m/z* (MH^+) 399. Anal. calcd. for $C_{20}H_{16}ClN_3O_2S$: H, 4.05; C, 60.37; N, 10.56. Found: H, 3.91; C, 60.11; N, 10.22.

2-(2-Imino-8-methoxycoumarin-3-yl)-7-methyl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one (5g). This compound was obtained in 75% yield as a yellow solid, mp 268–270°C; IR (cm^{-1}): 3446, 3328, 2930, 1681, 1658, 1604, 1576, 1479; ^1H NMR (DMSO-d_6): δ 1.03 (d, J = 6.4 Hz, 3 H), 1.38 (m, 1 H), 1.86 (m, 2 H), 2.23 (m, 1 H), 2.79 (m, 2 H), 3.07 (m, 1 H), 3.89 (s, 3 H), 7.25 (m, 2 H), 7.42 (dd, J = 7.3 Hz, 1 H), 8.79 (s, 1H, H-4), 9.43 (br.s, 1H, =NH), 14.31 (br.s, 1H, —NHCO); lcms: *m/z* (MH^+) 394. Anal. calcd. for $C_{21}H_{19}N_3O_3S$: H, 4.87; C, 64.11; N, 10.68. Found: H, 4.68; C, 64.29; N, 10.42.

2-(8-Ethoxy-2-iminocoumarin-3-yl)-7-methyl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one (5h). This compound was obtained in 78% yield as a yellow solid, mp 265–267°C; IR (cm^{-1}): 3445, 3169, 2976, 2950, 1685, 1656,1603, 1573,1467; ^1H NMR (DMSO-d_6): δ 1.01 (d, J = 6.4 Hz, 3 H), 1.37 (t, J = 6.7 Hz, 3 H), 1.81 (m, 2 H), 2.24 (m, 1 H), 2.72 (m, 2 H), 3.02 (m, 1 H), 4.14 (q, J = 7.0 Hz, 2 H), 7.25 (m, 3 H), 8.67 (s, 1H, H-4), 9.36 (br.s, 1H, =NH), 14.24 (br.s, 1H, —NHCO); lcms: *m/z* (MH^+) 408. Anal. calcd. for $C_{22}H_{21}N_3O_3S$: H, 5.19; C, 64.85; N, 10.31. Found: H, 5.00; C, 64.72; N, 10.04.

7-Acetyl-2-(2-iminocoumarin-3-yl)-3,4,5,6,7,8-hexa-hydropyrido[4′,3′:4,5]thieno[2,3-*d*]pyrimidin-4-one (5i). This compound was obtained in 68% yield as a brown solid, mp 284–286°C; IR (cm^{-1}): 3442, 3317, 3050, 2930, 1650, 1599, 1565, 1453, 1427; ^1H NMR (DMSO-d_6): δ 2.11 (s, 3 H), 2.99 (m, 2 H), 3.73 (s, 2 H), 4.71 (m, 2 H), 7.27 (m, 2 H), 7.58 (t, J = 7.3 Hz, 1 H), 7.84 (d, J = 7.3 Hz, 1 H), 8.83 (s, 1H, H-4), 9.32 (br.s, 1H, =NH), 14.31 (br.s, 1H, —NHCO); lcms: *m/z* (M) 392. Anal. calcd. for $C_{20}H_{16}N_4O_3S$: H, 4.11; C, 61.21; N, 14.28. Found: H, 4.04; C, 61.39; N, 14.03.

Ethyl 4-oxo-2-(2-iminocoumarin-3-yl)-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5]thieno[2,3-*d*]pyrimidine-7-carboxylate (5j). This compound was obtained in 85% yield as a yellow solid, mp 274–276°C; IR (cm^{-1}): 3437, 3261, 2979, 2929, 1673, 1653, 1537, 1693, 1429; ^1H NMR (DMSO-d_6): δ 1.21 (t, J = 6.8 Hz, 3 H), 2.88 (s, 2 H), 3.64 (t, J = 5.1 Hz, 2 H), 4.09 (q, J = 6.8 Hz, 2 H), 4.58 (s, 2 H), 7.23 (m, 2 H), 7.55 (td, J = 7.7 Hz, 1 H), 7.81 (d, J = 6.8 Hz, 1 H), 8.78 (s, 1H, H-4), 9.36 (br.s, 1H, =NH), 14.34 (br.s, 1H, —NHCO); lcms: *m/z* (MH^+) 423. Anal. calcd. for $C_{21}H_{18}N_4O_4S$: H, 4.29; C, 59.71; N, 13.26. Found: H, 4.17; C, 59.46; N, 12.96.

Ethyl 4-oxo-2-(6-chloro-2-iminocoumarin-3-yl)-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5]thieno[2,3-*d*]pyrimidine-7-carboxylate (5k). This compound was obtained in 65% yield as a yellow solid, mp 287–289°C; IR (cm^{-1}): 3440, 3322, 2914,

2853, 1675, 1649,1592, 1563, 1698, 1452; ^{1}H NMR (DMSO-d_6): δ 1.22 (t, J = 7.3 Hz, 3 H), 2.96 (m, 2 H), 3.68 (s, 2 H), 4.10 (q, J = 6.8 Hz, 2 H), 4.64 (s, 2 H), 7.25 (d, J = 9.0 Hz, 1 H), 7.57 (dd, J = 8.5, 2.6 Hz, 1 H), 7.94 (s, 1 H), 8.78 (s, 1H, H-4), 9.43 (br.s, 1H, =NH), 14.15 (br.s, 1H, —NHCO); lcms: *m/z* (M) 457. Anal. calcd. for $C_{21}H_{17}ClN_4O_4S$: H, 3.75; C, 55.20; N, 12.26. Found: H, 3.65; C, 55.52; N, 11.88.

Ethyl 4-oxo-2-(2-imino-8-methoxycoumarin-3-yl)-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5]thieno[2,3-*d*]pyrimidine-7-carboxylate (5l). This compound was obtained in 79% yield (Method A) and 70% (Method B) as a yellow solid, mp 280–282°C; IR (cm^{-1}): 3449, 3328, 2974, 2929, 1672, 1653, 1604, 1574,1697, 1472; ^{1}H NMR (DMSO-d_6): δ 1.19 (t, J = 6.8 Hz, 3 H), 2.94 (s, 2 H), 3.66 (t, J = 5.1 Hz, 2 H), 3.89 (s, 3 H), 4.08 (q, J = 7.3 Hz, 2 H), 4.62 (s, 2 H), 7.25 (m, 2 H), 7.40 (d, J = 7.3 Hz, 1 H), 8.81 (s, 1H, H-4), 9.51 (br.s, 1H, =NH), 14.44 (br.s, 1H, —NHCO); lcms: *m/z* (MH^+) 453. Anal. calcd. for $C_{22}H_{20}N_4O_5S$: H, 4.46; C, 58.40; N, 12.38. Found: H, 4.31; C, 58.24; N, 12.17.

Ethyl 4-oxo-2-(2-imino-8-ethoxycoumarin-3-yl)-3,4,5,6,7,8-hexahydropyrido[4′,3′:4,5]thieno[2,3-*d*]pyrimidine-7-carboxylate (5m). This compound was obtained in 80% yield as a yellow solid, mp 273–275°C; IR (cm^{-1}): 3452, 3159, 2979, 2928, 1651, 1603, 1546, 1698, 1425; ^{1}H NMR (DMSO-d_6): δ 1.20 (t, J = 7.3 Hz, 3 H), 1.39 (t, J = 6.8 Hz, 3 H), 2.97 (br.s, 2 H), 3.67 (t, J = 6.4 Hz, 2 H), 4.08 (q, J = 7.3 Hz, 2 H), 4.19 (q, J = 6.4 Hz, 2 H), 4.65 (s, 2 H), 7.25 (m, 2 H), 7.42 (dd, J = 7.7 Hz, 1 H), 8.86 (s, 1H, H-4), 9.50 (br.s, 1H, =NH), 14.50 (br.s, 1H, —NHCO); lcms: *m/z* (MH^+) 467. Anal. calcd. for $C_{23}H_{22}N_4O_5S$: H, 4.75; C, 59.22; N, 12.01. Found: H, 4.61; C, 59.43; N, 11.66.

General procedure for the preparation of 2-(2-(3-methoxyphenylimino)-coumarin-3-yl)thieno[2,3-*d*]pyrimidin-4-ones 6a-d. To a solution of corresponding 2-(2-iminocoumarin-3-yl)thieno[2,3-*d*]pyrimidin-4-ones 5 (2mmol) in glacial acetic acid (10 mL) 3-methoxy-phenylamine (2 mmol) was added at 40–50°C. The reaction mixture was heated at 70–80°C and stirred for 30 min. After cooling down to room temperature the precipitate was filtered out, washed with 2-propanol and recrystallized form DMF.

2-(6-Chloro-2-(3-methoxyphenylimino)-coumarin-3-yl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-*d*]pyrimidin-4-one (6a). This compound was obtained in 83% yield as a yellow solid, mp >300°C; IR (cm^{-1}): 3450, 2935, 2835, 1672, 1645, 1587, 1566; ^{1}H NMR (DMSO-d_6): δ 1.75 (br.s, 4 H), 2.74 (br.s, 2 H), 2.86 (br.s, 2 H), 3.77 (s, 3H, 3-OCH_3), 6.74 (d, J = 7.3 Hz, 1 H), 6.84 (m, 2 H), 7.25 (m, 2 H), 7.53 (dd, J = 8.3 Hz, 1 H), 8.00 (s, 1 H), 8.79 (s, 1H, H-4), 13.50 (br.s, 1H, NHCO). Anal. calcd. for $C_{26}H_{20}ClN_3O_3S$: H, 4.11; C, 63.73; N, 8.58. Found: H, 3.88; C, 63.46; N, 8.33.

2-(2-(3-Methoxyphenylimino)-8-methoxycoumarin-3-yl)-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one (6b). This compound was obtained in 90% yield as a yellow solid, mp >300°C; IR (cm^{-1}): 3442, 2925, 2836, 1672, 1647, 1588, 1572; ^{1}H NMR (DMSO-d_6): δ 1.71 (br.s, 4 H), 2.67 (br.s, 2 H), 2.82 (br.s, 2 H), 3.74 (s, 3 H), 3.76 (s, 3H, 3-OCH_3), 6.75 (dd, J = 7.5 Hz, 1 H), 6.98 (d, J = 7.8 Hz, 1 H), 7.26 (m, 5 H), 8.72 (s, 1H, H-4), 13.88 (br.s, 1H, —NHCO—). Anal. calcd. for $C_{27}H_{23}N_3O_4S$: H, 4.77; C, 66.79; N, 8.65. Found: H, 4.65; C, 66.95 N, 8.33.

2-(8-Ethoxy-2-(3-methoxyphenylimino)-coumarin-3-yl)-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one (6c). This compound was obtained in 92% yield as a yellow solid, mp >300°C; IR (cm^{-1}): 3440, 2931, 2833, 1667, 1642, 1604, 1587; ^{1}H NMR (DMSO-d_6): δ 1.30 (t, J = 7.0 Hz, 3 H), 1.73 (br.s, 4 H), 2.68 (br.s, 2 H), 2.83 (br.s, 2 H), 4.04 (q, J = 7.0 Hz, 2 H), 3.78 (s, 3H, 3-OCH_3), 6.76 (d, J = 7.4 Hz, 1 H), 7.23 (m, 6 H), 8.72 (s, 1H, H-4), 13.82 (br.s, 1H, —NHCO—). Anal. calcd. for $C_{28}H_{25}N_3O_4S$: H, 5.04; C, 67.32; N, 8.41. Found: H, 5.80; C, 67.21; N, 8.22.

2-(2-(3-Methoxyphenylimino)-8-methoxycoumarin-3-yl)-7-methyl-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-*d*]pyrimidin-4-one (6d). This compound was obtained in 89% yield as a yellow solid, mp >300°C; IR (cm^{-1}): 3426, 2931, 2833, 1676, 1640, 1603, 1526; ^{1}H NMR (DMSO-d_6): δ 1.00 (d, J = 6.4 Hz, 3 H), 1.31 (m, 1 H), 1.79 (m, 2 H), 2.20 (m, 1 H), 2.71 (m, 2 H), 3.03 (m, 1 H), 3.77 (s, 3 H), 3.77 (s, 3H, 3-OCH_3), 6.73 (d, J = 7.4 Hz, 1 H), 6.97 (d, J = 7.6 Hz, 1 H), 7.25 (m, 5 H), 8.70 (s, 1H, H-4), 13.83 (br.s, 1H, —NHCO—). Anal. calcd. for $C_{28}H_{25}N_3O_4S$: H, 5.04; C, 67.32; N, 8.41. Found: H, 4.82; C, 67.13; N, 8.09.

General procedure for the preparation of 2-(coumarin-3-yl)thieno[2,3-*d*]pyrimidin-4-ones 7a–c. Corresponding 2-(2-iminocoumarin-3-yl)thieno[2,3-d]pyrimidin-4-ones 5a, e, g (2 mmol) was dissolved at 60–70°C in mixture of 2-propanol (10 mL) and concentrated hydrochloric acid (1 mL). The reaction mixture was heated with reflux for 20 min, then cooled and the precipitate was collected by filtration and dried.

2-(Coumarin-3-yl)-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one (7a). This compound was obtained in 92% yield as a yellow solid, mp >300°C.

2-(Coumarin-3-yl)-7-methyl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one (7b). This compound was obtained in 88% yield as a yellow solid, mp 235–237°C.

2-(8-Methoxy-coumarin-3-yl)-7-methyl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one (7c). This compound was obtained in 89% yield as a yellow solid, mp 277–279°C.

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