Synthesis of 3-(*N*-arylcarbamoyl)chromones from 2-hydroxyarylaminoenones and isocyanates

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A new method for the synthesis of 2-unsubstituted and 2-substituted 3-(*N*-arylcarbamoyl)-chromones by the reaction of 3-dimethylamino-1-(2-hydroxyaryl)prop-2-en-1-ones with arylisocyanates has been proposed.

Key words: heterocyclic compounds, chromones, enaminones, amides, isocyanates.

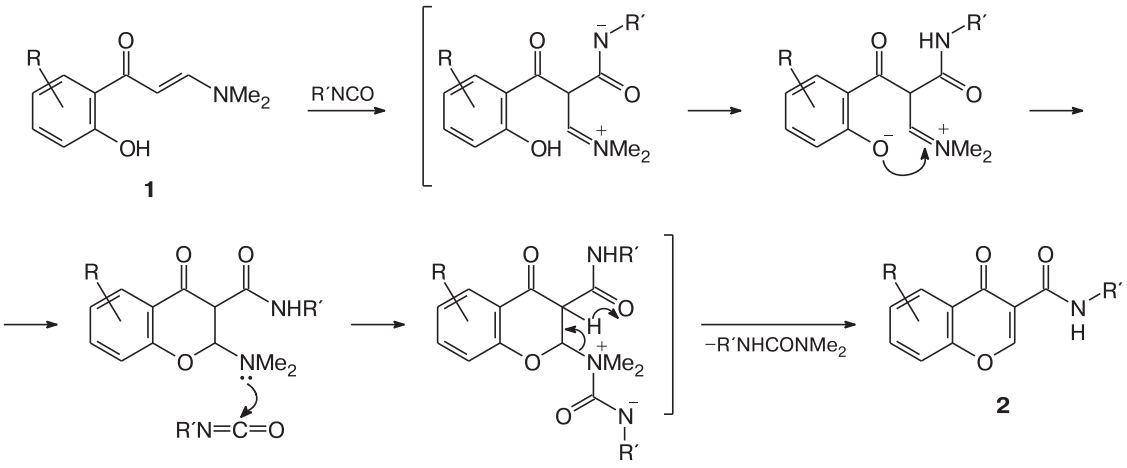
Chromones containing carbamoyl groups are of considerable interest. Much attention is paid, in particular, to the synthesis and study of the biological activity of 3-carbamoylchromones. They are being studied as antioxidants and ligands of adenosine receptor that regulate a number of important biological functions and are useful for treating various diseases, such as cancer and cardiovascular diseases.[1,2] It was also established that they are of interest as promising monoamineoxidase inhibitors, which are used in the treatment of a number of diseases, for example, Alzheimer´s and Parkinson´s diseases.[3—5] Thus, the synthetic and practical potential of these benzopyrans stimulates the development of new convenient methods for their preparation.

The most common approach to the synthesis of 3-carbamoylchromones involves the conversion of hydroxyacetophenones to formylchromones, their oxidation to the corresponding acids, and subsequent reaction with amines.[6—8] The disadvantages of this method include the multistage process, as well as the limitation associated with the difficulties of using substances with substituents that are sensitive to oxidizing agents. We also note that using this method it was not possible to obtain 3-carbamoylchromones containing substituents in position 2.

Earlier,[9] we have shown that thiocarbamoylchromones can be formed by the interaction of β-benzoenaminone compounds with isothiocyanates.

In this work, we investigated the reaction of enaminone **1** with isocyanates. It could be assumed that heterocyclization will occur after the addition of the isocyanate to the enaminone, and subsequent elimination of the amine will lead to the formation of 3-carbamoylchromones **2** (Scheme 1).

Scheme 1



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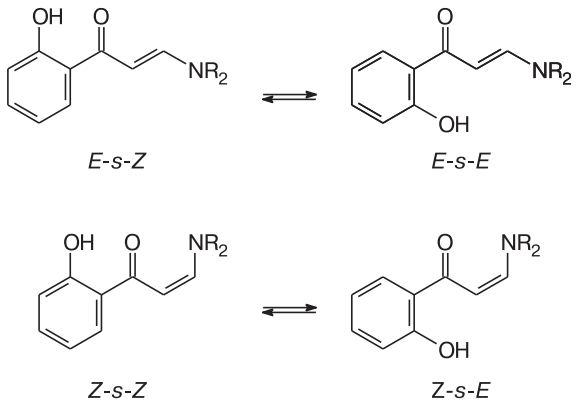
It is known that β-enaminones, combining in their molecule the ambident nucleophilicity of enamines with the ambident electrophilicity of enones, are widely used in the synthesis of various heterocyclic compounds. β-Enaminones, obtained by reacting the corresponding hydroxyacetophenones with dimethylformamide diacetal, have been used, for example, in the synthesis of halogen, mercapto, and acetyl derivatives of chromone with substituents in position 3.[10—12] However, nothing is known on application of β-enaminones in the synthesis of 3-carbamoylchromones and their derivatives substituted in position 2. We investigated the interaction of β-benzoenaminone **1** containing primary, secondary, and tertiary amino groups with isocyanates. It is known[13,14] that, depending on the nature of the amino group, β-enaminones can be in the form of *Z*- or *E*-isomers. The β-enaminones **1** with a tertiary amino group show in ^{1}H NMR spectrum signals of vinyl proton at 9 and 5 ppm with the coupling constants of 12.1 Hz, and the signal of the OH group is shifted to the weak field region (δ 11) due to the formation of a hydrogen bond with the keto group. This is also confirmed by the data of IR spectra, where there is a broad vibration band of the hydroxyl group in the region of 3000 cm^{-1}. On this basis, the β-enaminones can be attributed to the configuration of the *E-s-Z* isomer (Scheme 2).

Scheme 2



Along with the nature of the amino group, we investigated the effect of solvents, temperature, duration of the reaction, as well as substituents in substrates and reagents on the yields of carboxamides. Reactions were carried out in an inert atmosphere with a twofold excess of isocyanate to bind the amine released during the reaction. It turned out that solvents play a significant role in this process. Conducting the reaction in acetonitrile, dichloroethane, *N*-methylpyrrolidone and varying the temperature did not lead to the formation of carboxamides. At the same time, in DMF, nitromethane, and toluene, the carboxamides are obtained at room temperature keeping for a long time, and at 110—120 °C for 8 h. The best yields were observed in DMF and toluene.

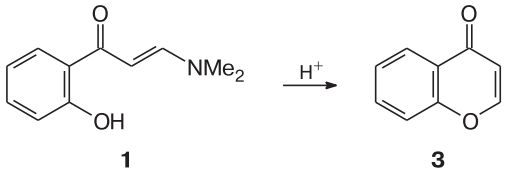
Table 1. Influence of solvents, temperature (*T*), and reaction duration (*t*) on yields of carboxamide **2f**

Solvent	*T*/°C	*t*/h	Yield (%)
DMF	120	8	50
DMF	110	8	65
Toluene	110	8	65
Nitromethane	110	8	32
1,2-Dichloroethane	101	1	—
1,4-Dioxane	84	1	—
Without solvent	120	2	60

With an increase in the process temperature in DMF, the yield of the target product decreased, possibly due to the decomposition of the reactants and reaction products (Table 1).

The effect of basic and acid catalysts on the process was also investigated. It turned out that with the use of acetic or *p*-toluenesulfonic acid, only the cyclization of the starting enaminone into unsubstituted chromone **3** occurs (Scheme 3).

Scheme 3



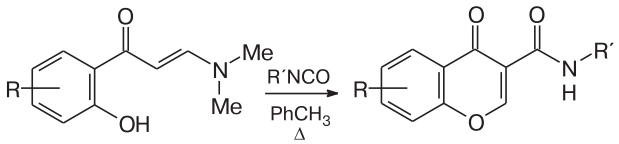
Potassium carbonate, triethylamine or Hünig´s base had no significant effect on the process.

Electron-withdrawing substituents in isocyanates promote the reaction, electron-donating groups reduce the yields of 3-carbamoylchromones, while the influence of substituents in β-enaminones on the process is not detected.

It turned out that the structure of the amine fragment in β-enaminone has virtually no effect on the yields of chromones **2** or on the rate of the process, which makes it possible to use the most accessible enaminones with dimethylamine group in the synthesis of 3-carbamoylchromones. The method allowed to obtain a wide range of 3-carbamoylchromones containing various substituents (Scheme 4).

It is important to emphasize that the proposed approach can be used to obtain 3-carbamoylchromones with substituents in position 2. This requires the presence of a corresponding group in the ketoenamine moiety, which

Scheme 4

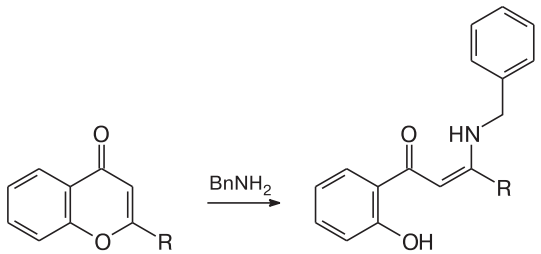


1 **2a—t**

2	R	R′	2	R	R′
a	H	Ph	**k**	H	1-Naphthyl
b	6-Me	Ph	**l**	6-Br	Ph
c	H	4-$MeOC_6H_4$	**m**	6-Br	3-ClC_6H_4
d	H	3-$MeOC_6H_4$	**n**	6-Br	1-Naphthyl
e	6,7-Cl_2	Ph	**o**	6-Me	3-ClC_6H_4
f	H	2,4-$Cl_2C_6H_3$	**p**	6-Me	1-Naphthyl
g	H	4-$CF_3C_6H_4$	**q**	Benzo[*h*]	Ph
h	7-MeO	Ph	**r**	Benzo[*h*]	3-ClC_6H_4
i	H	3-ClC_6H_4	**s**	Benzo[*h*]	1-Naphthyl
j	H	4-ClC_6H_4	**t**	8*H*-[1,3]dioxolo[4,5-*g*]	Ph

can be introduced, for example, by reacting benzylamine with benzopyrans[15] **4** in ethanol (Scheme 5).

Scheme 5

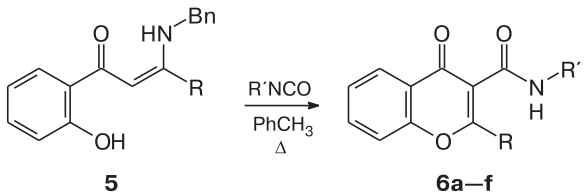


4a—e **5a—e**

R = Ph (**a**), 2-MeC_6H_4 (**b**), 4-MeC_6H_4 (**c**), furan-2-yl (**d**), thiophen-2-yl (**e**)

The reaction of enaminones **5** with isocyanates led to the formation of carbamoylchromones **6a—f** with substituents in position 2 (Scheme 6).

Scheme 6



5 **6a—f**

R = R′ = Ph (**6a**); R = 4-MeC_6H_4, R′ = Ph (**6b**);
R = furan-2-yl, R′ = Ph (**6c**);
R = furan-2-yl, R′ = 2,4-$Cl_2C_6H_3$ (**6d**);
R = furan-2-yl, R′ = 4-$CF_3C_6H_4$ (**6e**);
R = thiophen-2-yl, R′ = 2,4-$Cl_2C_6H_3$ (**6f**)

Thus, the interaction of *o*-hydroxyarylenaminones containing amino groups in the β-enaminone moiety with isocyanates has been investigated. This resulted in a method for producing various 3-carbamoylchromones with and without a substituent in position 2.

Experimental

NMR spectra were recorded in deuterated solvents using a Bruker Avance 300 spectrometer (300.13 (^{1}H) and 75.77 MHz (^{13}C)). High-resolution mass spectra (HRMS) were obtained by spray ionization (ESI) in acetonitrile using a Bruker MicroTOF spectrometer. Elemental analysis was performed on an automatic analyzer Eurovector EA 3000.

Synthesis of chromone-3-carboxamides 2 (general procedure). Mixture of β-enaminone **1** (1 mmol) and corresponding isocyanate (2.2 mmol) was heated in a minimal amount of DMF (1 mL) or toluene (3 mL) at 110 °C. After heating for 1—8 h (TLC control) and subsequent cooling, a white precipitate appeared, which was filtered, washed with ethanol and diethyl ether, and dried in air. If enaminone remained in the precipitate, the mixture was recrystallized from ethanol.

4-Oxo-*N*-phenyl-4*H*-chromen-3-carboxamide (2a). White crystals, yield 0.35 g (65%), m.p. 214—215 °C (see Ref. 16: m.p. 214—216 °C). ^{1}H NMR (DMSO-d_6), δ: 7.13 (t, 1 H, $H_{Ar'}$, J = 7.0 Hz); 7.39 (t, 2 H, $H_{Ar'}$, J = 7.4 Hz); 7.62—7.73 (m, 3 H, H_{Ar}); 7.82 (d, 1 H, H_{Ar}, J = 8.3 Hz); 7.94 (t, 1 H, H_{Ar}, J = 7.4 Hz); 8.25 (d, 1 H, H(4), J = 7.8 Hz); 9.17 (s, 1 H, H(2)); 11.28 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 116.0, 118.5, 120.5 (2 C), 124.1, 124.4, 126.2, 126.5, 129.0 (2 C), 134.8, 138.0, 156.2, 160.7, 162.8, 177.4. Found (%): C, 72.57; H, 4.22; N, 5.18. $C_{16}H_{11}NO_3$. Calculated (%): C, 72.45; H, 4.18; N, 5.28.

6-Methyl-4-oxo-*N*-phenyl-4*H*-chromen-3-carboxamide (2b). White crystals, yield 0.3 g (54%), m.p. 187—189 °C (see Ref. 17). ^{1}H NMR ($CDCl_3$), δ: 2.53 (s, 3 H, CH_3); 7.16 (t, 1 H, $H_{Ar'}$, J = 7.3 Hz); 7.39 (t, 2 H, $H_{Ar'}$, J = 7.7 Hz); 7.49 (d, 1 H, H_{Ar}, J = 8.5 Hz); 7.60 (d, 1 H, H_{Ar}, J = 8.5 Hz); 7.75 (d, 2 H, $H_{Ar'}$, J = 8.0 Hz); 8.12 (s, 1 H, H(5)); 9.06 (s, 1 H, H(2)); 11.46 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 21.0, 115.8, 118.2, 120.5 (2 C), 123.7, 124.4, 125.5, 129.0 (2 C), 136.1, 136.7, 138.0, 154.5, 160.8, 162.6, 177.4. Found (%): C, 73.18; H, 4.73; N, 5.10. $C_{17}H_{13}NO_3$. Calculated (%): C, 73.11; H, 4.69; N, 5.02.

***N*-(4-Methoxyphenyl)-4-oxo-4*H*-chromen-3-carboxamide (2c).** White crystals, yield 0.15 g (50%), m.p. 168—170 °C (see Ref. 18). ^{1}H NMR ($CDCl_3$), δ: 3.81 (s, 3 H, CH_3); 6.92 (d, 2 H, $H_{Ar'}$, J = 8.9 Hz); 7.51—7.71 (m, 4 H, H_{Ar}, $H_{Ar'}$); 7.80 (t, 1 H, H_{Ar}, J = 7.2 Hz); 8.34 (d, 1 H, H(5), J = 8.1 Hz); 9.08 (s, 1 H, H(2)); 11.28 (s, 1 H, NH). Found (%): C, 69.18; H, 4.23; N, 4.60. $C_{17}H_{13}NO_4$. Calculated (%): C, 69.15; H, 4.44; N, 4.74.

***N*-(3-Methoxyphenyl)-4-oxo-4*H*-chromen-3-carboxamide (2d).** White crystals, yield 0.16 g (71%), m.p. 160—161 °C (see Ref. 18). ^{1}H NMR (DMSO-d_6), δ: 3.77 (s, 3 H, CH_3); 7.26 (m, 2 H, H(5′), H(6′)); 6.72 (d, 1 H, H(4′), J = 8.6 Hz); 7.64 (t, 1 H, H(6), J = 7.7 Hz); 7.42 (s, 1 H, H(2′)); 7.81 (d, 1 H, H(8), J = 8.1 Hz); 7.94 (t, 1 H, H(7), J = 7.6 Hz); 8.24 (d, 1 H, H(5), J = 8.2 Hz); 9.17 (s, 1 H, H(2)); 11.28 (s, 1 H, NH). Found (%): C, 69.05; H, 4.52; N, 4.64. $C_{17}H_{13}NO_4$. Calculated (%): C, 69.15; H, 4.44; N, 4.74.

6,7-Dichloro-4-oxo-*N*-phenyl-4*H*-chromen-3-carboxamide (2e). White crystals, yield 0.16 g (71%), m.p. 250—252 °C.

^{1}H NMR (DMSO-d_6), δ: 7.14 (d, 1 H, H_{Ar}, J = 6.7 Hz); 7.33—7.42 (m, 2 H, H_{Ar}); 7.66 (d, 2 H, H_{Ar}, J = 7.4 Hz); 8.19 (s, 1 H, H(8)); 8.31 (s, 1 H, H(5)); 9.08 (s, 1 H, H(2)); 10.90 (s, 1 H, NH). Found (%): C, 57.45; H, 2.65; N, 4.12. $C_{16}H_9Cl_2NO_3$. Calculated (%): C, 57.51; H, 2.71; N, 4.19.

***N*-(2,4-Dichlorophenyl)-4-oxo-4*H*-chromen-3-carboxamide (2f).** White crystals, yield 0.16 g (58%), m.p. 208—209 °C. ^{1}H NMR ($CDCl_3$), δ: 7.26 (d, 1 H, $H_{Ar'}$, J = 9.7 Hz); 7.42 (s, 1 H, $H_{Ar'}$); 7.51—7.61 (m, 2 H, H_{Ar}); 7.79 (t, 1 H, H_{Ar}, J = 7.8 Hz); 8.37 (d, 1 H, J = 7.9 Hz); 8.53 (d, 1 H, H(5), J = 8.9 Hz); 9.05 (s, 1 H, H(2)); 11.84 (s, 1 H, NH). Found (%): C, 57.60; H, 2.68; N, 4.25. $C_{16}H_9Cl_2NO_3$. Calculated (%): C, 57.51; H, 2.71; N, 4.19.

4-Oxo-*N*-(4-trifluoromethylphenyl)-4*H*-chromen-3-carboxamide (2g). White crystals, yield 0.16 g (71%), m.p. 252 °C (see Ref. 3: m.p. 251—254 °C). ^{1}H NMR (DMSO-d_6), δ: 7.66 (d, 1 H, H_{Ar}, J = 7.6 Hz); 7.73 (d, 2 H, $H_{Ar'}$, J = 8.7 Hz); 7.81 (d, 1 H, H_{Ar}, J = 8.1 Hz); 7.93 (m, 3 H, $H_{Ar'}$, H_{Ar}); 8.25 (d, 1 H, H(5), J = 8.1 Hz); 9.17 (s, 1 H, H(2)); 11.50 (s, 1 H, NH). Found (%): C, 61.15; H, 3.08; N, 4.14. $C_{17}H_{10}F_3NO_3$. Calculated (%): C, 61.27; H, 3.02; N, 4.20.

7-Methoxy-4-oxo-*N*-phenyl-4*H*-chromen-3-carboxamide (2h). White crystals, yield 0.16 g (71%), m.p. 167—169 °C. ^{1}H NMR ($CDCl_3$), δ: 3.96 (s, 3 H, CH_3); 6.97 (s, 1 H, H_{Ar}); 7.05—7.21 (m, 2 H, H_{Ar}, $H_{Ar'}$); 7.38 (t, 2 H, $H_{Ar'}$, J = 7.7 Hz); 7.75 (d, 2 H, $H_{Ar'}$, J = 7.7 Hz); 8.24 (d, 1 H, H(5), J = 9.0 Hz); 9.01 (s, 1 H, H(2)); 11.53 (s, 1 H, NH). Found (%): C, 69.22; H, 4.35; N, 4.62. $C_{17}H_{13}NO_4$. Calculated (%): C, 69.15; H, 4.44; N, 4.74.

***N*-(3-Chlorophenyl)-4-oxo-4*H*-chromen-3-carboxamide (2i).** White crystals, yield 0.34 g (69%), m.p. 220—221 °C. ^{1}H NMR ($CDCl_3$), δ: 7.19 (d, 1 H, J = 7.9 Hz); 7.33 (t, 1 H, J = 8.0 Hz); 7.52 (d, 1 H, J = 8.0 Hz); 7.59—7.68 (m, 2 H); 7.74 (s, 1 H, H(2′)); 7.88 (t, 1 H, J = 8.3 Hz); 8.33 (d, 1 H, H(5), J = 8.0 Hz); 9.20 (s, 1 H, H(2)); 11.77 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 114.6, 118.5, 119.5, 121.6, 123.2, 125.7, 126.0, 127.0, 130.0, 134.5, 135.5, 137.4, 156.0, 162.3, 163.9, 177.6. Found (%): C, 64.13; H, 3.38; N, 4.74. $C_{16}H_{10}ClNO_3$. Calculated (%): C, 64.12; H, 3.36; N, 4.67.

***N*-(4-Chlorophenyl)-4-oxo-4*H*-chromen-3-carboxamide (2j).** White crystals, yield 0.36 g (63%), m.p. 254—256 °C (see Ref. 2: m.p. 255—259 °C). ^{1}H NMR ($CDCl_3$), δ: 7.32 (d, 2 H, J = 8.6 Hz); 7.38—7.67 (m, 4 H); 7.86 (t, 1 H, J = 7.6 Hz); 8.34 (d, 1 H, J = 7.9 Hz); 9.18 (s, 1 H, H(2)); 11.75 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 114.7, 118.7, 122.7 (2 C), 123.4, 126.3, 127.1, 129.2 (2 C), 129.9, 130.8, 135.6, 156.9, 162.9, 163.8, 178.1. Found (%): C, 64.16; H, 3.34; N, 4.72. $C_{16}H_{10}ClNO_3$. Calculated (%): C, 64.12; H, 3.36; N, 4.67.

***N*-(1-Naphthyl)-4-oxo-4*H*-chromen-3-carboxamide (2k).** White crystals, yield 0.24 g (76%), m.p. 219—220 °C. ^{1}H NMR ($CDCl_3$), δ: 7.51—7.67 (m, 5 H); 7.77 (d, 1 H, J = 8.1 Hz); 7.83—7.93 (m, 2 H); 8.22 (t, 2 H, J = 8.0 Hz); 8.43 (d, 1 H, H(5), J = 8.0 Hz); 9.22 (s, 1 H, H(2)); 12.22 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 115.3, 118.5, 120.3, 120.9, 123.7, 125.5, 126.1 (2 C), 126.2 (2 C), 126.7 (2 C), 128.59, 131.0, 134.0, 135.1, 156.1, 162.5, 163.5, 177.7. Found (%): C, 76.23; H, 4.24. $C_{20}H_{13}NO_3$. Calculated (%): C, 76.18; H, 4.16.

6-Bromo-4-oxo-*N*-phenyl-4*H*-chromen-3-carboxamide (2l). White crystals, yield 0.34 g (76%), m.p. 211—213 °C. ^{1}H NMR ($CDCl_3$), δ: 7.23 (t, 1 H, J = 7.7 Hz); 7.41 (t, 2 H, J = 7.8 Hz); 7.55 (d, 1 H, J = 8.9 Hz); 7.62 (d, 2 H, J = 7.9 Hz); 7.92 (dd, 1 H, J = 8.9 Hz, J = 2.1 Hz); 8.46 (s, 1 H, H(5)); 9.18 (s, 1 H, H(2)); 11.62 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 115.2, 120.5, 120.7, 121.9 (2 C), 125.0, 126.2, 128.9, 129.3 (2 C), 136.3, 138.5, 155.0, 162.2, 163.9, 176.4. Found (%): C, 55.80; H, 2.90; Br, 23.31. $C_{16}H_{10}BrNO_3$. Calculated (%): C, 55.84; H, 2.93; Br, 23.22.

6-Bromo-*N*-(3-chlorophenyl)-4-oxo-4*H*-chromen-3-carboxamide (2m). White crystals, yield 0.34 g (61%), m.p. 274—275 °C. ^{1}H NMR ($CDCl_3$), δ: 7.26 (t, 1 H, J = 7.9 Hz); 7.36 (t, 1 H, J = 7.9 Hz); 7.50 (d, 1 H, J = 7.9 Hz); 7.58 (d, 1 H, J = 8.9 Hz); 7.70 (s, 1 H); 7.96 (d, 1 H, J = 8.9 Hz); 8.46 (s, 1 H, H(5)); 9.21 (s, 1 H, H(2)); 11.69 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 120.1, 120.5, 120.9, 121.4, 122.2, 124.8, 126.4, 128.8, 130.2, 134.9, 137.0, 138.8, 155.0, 160.2, 164.3, 176.6. Found (%): C, 50.78; H, 2.44; N, 3.78. $C_{16}H_9BrClNO_3$. Calculated (%): C, 50.76; H, 2.40; N, 3.70.

6-Bromo-*N*-(1-naphthyl)-4-oxo-4*H*-chromen-3-carboxamide (2n). White crystals, yield 0.21 g (52%), m.p. 228—229 °C. ^{1}H NMR ($CDCl_3$), δ: 7.28—7.55 (m, 3 H); 7.65 (t, 1 H, J = 7.6 Hz); 7.72 (d, 1 H, J = 8.1 Hz); 7.89 (d, 2 H, J = 8.5 Hz); 8.24 (d, 1 H, J = 8.3 Hz); 8.34 (d, 1 H, J = 7.3 Hz); 8.54 (s, 1 H, H(5)); 9.16 (s, 1 H, H(2)); 11.97 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 116.4, 119.1, 120.3, 120.4, 120.9, 125.3, 125.9, 126.1 (2 C), 126.7, 128.7, 129.0, 131.3, 132.8, 134.1, 138.0, 155.0, 160.9, 163.3, 176.6. Found (%): C, 60.88; H, 3.06; N, 3.58. $C_{20}H_{12}BrNO_3$. Calculated (%): C, 60.94; H, 3.07; N, 3.55.

***N*-(3-Chlorophenyl)-6-methyl-4-oxo-4*H*-chromen-3-carboxamide (2o).** White crystals, yield 0.29 g (92%), m.p. 222—223 °C. ^{1}H NMR ($CDCl_3$), δ: 2.53 (s, 3 H, CH_3); 7.19 (d, 1 H, J = 7.9 Hz); 7.31 (t, 1 H, J = 8.0 Hz); 7.52 (t, 2 H, J = 8.6 Hz); 7.64 (d, 1 H, J = 8.4 Hz); 7.73 (s, 1 H, H(2′)); 8.08 (s, 1 H, H(5)); 9.15 (s, 1 H, H(2)); 11.81 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 21.0, 114.7, 118.4, 119.5, 121.6, 123.2, 125.4, 125.6, 130.1, 134.8, 136.8, 137.5, 137.9, 154.6, 162.4, 163.7, 177.7. Found (%): C, 65.10; H, 3.79; N, 4.49. $C_{17}H_{12}ClNO_3$. Calculated (%): C, 65.08; H, 3.86; N, 4.46.

6-Methyl-*N*-(1-naphthyl)-4-oxo-4*H*-chromen-3-carboxamide (2p). White crystals, yield 0.17 g (51%), m.p. 243—244 °C. ^{1}H NMR ($CDCl_3$), δ: 2.53 (s, 3 H, CH_3); 7.49—7.62 (m, 5 H); 7.68 (t, 1 H, J = 8.5 Hz); 7.89 (d, 1 H, J = 8.1 Hz); 8.20 (s, 1 H, H(5)); 8.33 (d, 1 H, J = 8.5 Hz); 8.47 (d, 1 H, J = 7.6 Hz); 9.13 (s, 1 H, H(2)); 12.09 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 21.0, 116.1, 118.2, 118.7, 120.9, 123.7, 124.9, 125.6, 125.8, 125.9, 126.1, 126.5, 128.6, 133.1, 134.0, 136.1, 136.8, 154.5, 161.9, 162.8, 177.8. Found (%): C, 76.59; H, 4.63; N, 4.33. $C_{21}H_{15}NO_3$. Calculated (%): C, 76.58; H, 4.59; N, 4.25.

4-Oxo-*N*-phenyl-4*H*-benzo[*h*]chromen-3-carboxamide (2q). White crystals, yield 0.22 g (71%), m.p. 241—242 °C. ^{1}H NMR ($CDCl_3$), δ: 7.25—7.27 (m, 1 H); 7.43 (t, 2 H, J = 7.7 Hz); 7.67 (d, 2 H, J = 7.8 Hz); 7.75—7.84 (m, 2 H); 7.93 (d, 1 H, J = 8.7 Hz); 8.00 (d, 1 H, J = 7.8 Hz); 8.17 (d, 1 H, J = 8.8 Hz); 8.58 (d, 1 H, H(5), J = 7.9 Hz); 9.35 (s, 1 H, H(2)); 11.15 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 116.2, 119.9, 120.1, 121.9 (2 C), 122.5, 123.4, 126.2, 127.5, 128.3, 128.3, 129.3 (2 C), 130.8, 136.3, 136.5, 154.4, 162.4, 162.8, 177.6. Found (%): C, 76.24; H, 4.20; N, 4.38. $C_{20}H_{13}NO_3$. Calculated (%): C, 76.18; H, 4.16; N, 4.44.

***N*-(3-Chlorophenyl)-4-oxo-4*H*-benzo[*h*]chromen-3-carboxamide (2r).** White crystals, yield 0.26 g (75%), m.p. 267—269 °C. ^{1}H NMR ($CDCl_3$), δ: 7.24—7.27 (m, 1 H); 7.37 (t, 1 H, J = 7.7 Hz); 7.50 (d, 1 H, J = 7.7 Hz); 7.73 (s, 1 H, H(2′)); 7.80—7.92 (m, 2 H); 7.98—8.07 (m, 2 H); 8.24 (d, 1 H, J = 8.8 Hz); 8.65 (d, 1 H, H(5), J = 7.9 Hz); 9.46 (s, 1 H, H(2)); 11.82 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 105.9, 116.0, 119.4, 119.8, 120.6, 122.7,

122.7, 123.4, 126.9, 128.4, 128.5, 128.8, 130.5, 131.5, 135.2, 137.0, 155.2, 163.4, 163.8, 178.5. Found (%): C, 68.74; H, 3.43; N, 4.07. $C_{20}H_{12}ClNO_3$. Calculated (%): C, 68.68; H, 3.46; N, 4.00.

***N*-(1-Naphthyl)-4-oxo-4*H*-benzo[*h*]chromen-3-carboxamide (2s).** White crystals, yield 0.27 g (75%), m.p. 269—271 °C. ^{1}H NMR ($CDCl_3$), δ: 7.44—7.83 (m, 3 H); 7.50—7.58 (m, 2 H); 7.66 (t, 1 H, J = 8.0 Hz); 7.88—7.94 (m, 2 H); 8.00 (d, 1 H, J = 8.0 Hz); 8.23—8.30 (m, 3 H); 8.58 (d, 1 H, J = 7.3 Hz); 9.34 (s, 1 H, H(2)); 12.34 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 116.7, 120.2, 120.3, 120.5, 121.0, 122.4, 123.5, 125.3, 126.2 (2 C), 126.8 (2 C), 127.0, 128.0, 128.2, 128.6, 130.4, 132.0, 134.1, 136.4, 154.1, 162.3, 162.5, 177.4. Found (%): C, 78.95; H, 4.17; N, 3.90. $C_{24}H_{15}NO_3$. Calculated (%): C, 78.89; H, 4.14; N, 3.83.

8-Oxo-*N*-phenyl-8*H*-[1,3]dioxolo[4,5-*g*]chromen-7-carboxamide (2t). White crystals, yield 0.16 g (71%), m.p. 270–272 °C. ^{1}H NMR (DMSO-d_6), δ: 6.27 (s, 2 H, CH_2); 7.14 (t, 1 H, $H_{Ar'}$, J = 7.4 Hz); 7.32—7.43 (m, 3 H, H_{Ar}, $H_{Ar'}$); 7.51 (s, 1 H, H_{Ar}); 7.70 (d, 2 H, $H_{Ar,}$ J = 8.0 Hz); 9.04 (s, 1 H, H(2)); 11.38 (s, 1 H, NH). Found (%): C, 66.22; H, 3.55; N, 4.54. $C_{17}H_{11}NO_5$. Calculated (%): C, 66.02; H, 3.58; N, 4.53. HRMS (ESI), found: m/z 310.0718. Calculated for $C_{17}H_{11}NO_5$: M + H = 310.0710.

Synthesis of 3,3-disubstituted prop-2-en-1-ones 5 (general procedure). Solution of 4*H*-chromene-4-one **4** (10 mmol) and corresponding amine (30 mmol) in toluene (10 mL) was refluxed for 24 h. Then the reaction mixture was evaporated, the dry residue was dissolved in methylene chloride with the addition of petroleum ether (PE) and the products were isolated by column chromatography with eluent CH_2Cl_2—PE (9 : 1).

(*Z*)-3-Benzylamino-1-(2-hydroxyphenyl)-3-(*o*-tolyl)prop-2-en-1-one (5b). Yellow oil, yield 3.05 g (89%). ^{1}H NMR ($CDCl_3$), δ: 2.36 (s, 3 H, CH_3); 4.20—4.35 (m, 2 H, C$\underline{H}_2$—Ph); 5.75—5.89 (s, 1 H, HC=C); 6.81 (t, 1 H, H_{Ar}, J = 7.6 Hz); 7.00 (d, 1 H, H_{Ar}, J = 8.3 Hz); 7.18—7.31 (m, 4 H, H_{Ar}); 7.31—7.51 (m, 6 H, H_{Ar}); 7.63 (d, 1 H, H_{Ar}, J = 8.0 Hz); 11.40 (s, 1 H, OH); 13.59 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 19.3, 48.4, 92.0, 118.2, 120.6, 126.0, 127.6, 127.1 (2 C), 127.7, 127.9, 128.0, 128.3, 128.8 (2 C), 129.4, 130.4, 134.8, 135.1, 137.6, 162.4, 167.0, 191.4. Found (%): C, 80.28; H, 6.20; N, 4.05. $C_{23}H_{21}NO_2$. Calculated (%): C, 80.44; H, 6.16; N, 4.08.

3-Benzylamino-1-(2-hydroxyphenyl)-3-(thiophen-2-yl)prop-2-en-1-one (5e). Yellow crystals, yield 2.61 g (78%), m.p. 115—116 °C. ^{1}H NMR ($CDCl_3$), δ: 3.93 (s, 2 H, C$\underline{H}_2$—Ph); 6.35 (s, 1 H, HC=C); 6.96 (d, 1 H, H_{Ar}, J = 7.3); 7.23—7.30 (m, 5 H, H_{Ar}); 7.47 (d, 1 H, H_{Ar}, J = 8.2 Hz); 7.51 (m, 1 H, H_{Th}); 7.56 (t, 1 H, H_{Ar}, J = 7.3 Hz); 8.05 (d, 1 H, H_{Ar}, J = 7.9 Hz); 8.08 (d, 1 H, H_{Th}, J = 3.55 Hz); 8.11 (d, 1 H, H_{Th}, J = 4.47 Hz); 12.19 (s, 1 H, OH); 13.45 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 48.4, 99.2, 118.2, 120.8, 126.1, 126.9 (3 C), 128.1, 128.8 (2 C), 129.0, 133.7, 134.7, 135.9, 136.6, 137.8, 163.1, 163.8, 189.4. Found (%): C, 71.43; H, 5.70; N, 4.11. $C_{20}H_{17}NO_2S$. Calculated (%): C, 71.62; H, 5.11; N, 4.18.

Synthesis of chromone-3-carboxamides 6 (general procedure). Mixture of β-enaminone **5** (1 mmol) and corresponding phenylisocyanate derivative (2.2 mmol) was heated in a minimal amount of DMF (1 mL) or toluene (3 mL) at 110 °C. After heating for 1—8 h (TLC control) and subsequent cooling, a white precipitate appeared, which was filtered, washed with ethanol and diethyl ether, and dried in air. If enaminone remained in the precipitate, the mixture was recrystallized from ethanol.

4-Oxo-*N*,2-diphenyl-4*H*-chromen-3-carboxamide (6a). White crystals, yield 0.12 g (35%), m.p. 195—197 °C (see Ref. 19: m.p. 196—197 °C). ^{1}H NMR ($CDCl_3$), δ: 7.10 (t, 1 H, H_{Ar}, J = 7.4 Hz); 7.21—7.34 (m, 4 H, H_{Ar}); 7.48—7.57 (m, 4 H, H_{Ar}); 7.64 (d, 2 H, H_{Ar}, J = 7.8 Hz); 7.71—7.77 (m, 2 H, H_{Ar}); 8.29 (d, 1 H, H(5), J = 6.8 Hz); 10.59 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 116.5, 120.2, 121.3 (2 C), 123.1, 123.9, 124.2, 125.2, 126.9, 127.9 (2 C), 128.0, 128.3 (2 C), 128.6 (2 C), 131.2, 137.3, 156.2, 161.0, 165.9, 177.5. HRMS (ESI), found: m/z 364.1087. Calculated for $C_{22}H_{15}NO_3$: M + Na = 364.1085.

4-Oxo-*N*-phenyl-2-(*p*-tolyl)-4*H*-chromen-3-carboxamide (6b). White crystals, yield 0.11 g (31%), m.p. 197—199 °C. ^{1}H NMR ($CDCl_3$), δ: 2.44 (s, 3 H, CH_3); 6.51—6.60 (m, 2 H); 7.22—7.30 (m, 2 H, $H_{Ar'}$); 7.33 (d, 2 H, $H_{Ar'}$, J = 7.9 Hz); 7.37—7.46 (m, 2 H, $H_{Ar'}$); 7.50 (d, 1 H, H_{Ar}, J = 8.1 Hz); 7.62 (t, 1 H, H_{Ar}, J = 7.9 Hz); 8.21 (d, 2 H, $H_{Ar'}$, J = 8.1 Hz); 8.90 (d, 1 H, H(5), J = 7.8 Hz); 11.1 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 20.02, 114.4, 116.5, 120.2, 121.3 (2 C), 123.9, 124.2, 125.2, 126.6, 127.9 (2 C), 128.0, 128.1 (2 C), 128.6 (2 C), 134.4, 136.7, 155.8, 160.0, 163.9, 177.9. HRMS (ESI), found: m/z 378.1210. Calculated for $C_{23}H_{17}NO_3$: M + Na = 378.1208.

2-(Furan-2-yl)-4-oxo-*N*-phenyl-4*H*-chromen-3-carboxamide (6c). White crystals, yield 0.16 g (52%), m.p. 167—169 °C. ^{1}H NMR (DMSO-d_6), δ: 6.81 (dd, 1 H, H_{Fur}, J = 3.5 Hz, J = 1.7 Hz); 7.12 (t, 1 H, $H_{Ar'}$, J = 7.4 Hz); 7.32—7.44 (m, 3 H, $H_{Ar'}$ + H_{Fur}); 7.56 (t, 1 H, H_{Ar}, J = 7.5 Hz); 7.69 (d, 2 H, $H_{Ar'}$, J = 7.9 Hz); 7 .77 (d, 1 H, H_{Ar}, J = 8.3 Hz); 7.89 (t, 1 H, H_{Ar}, J = 7.8 Hz); 8.06 (s, 1 H, H_{Fur}); 8.11 (d, 1 H, H(5), J = 7.9 Hz); 10.50 (s, 1 H, NH). ^{13}C NMR (DMSO-d_6), δ: 113.5, 116.7, 117.9, 118.7, 119.7 (2 C), 123.2, 124.1 (2 C), 125.5, 126.3, 129.3, 135.4, 139.5, 144.9, 148.3, 151.3, 155.3, 161.8, 174.9. Found (%): C, 72.42; H, 4.30; N, 4.11. $C_{20}H_{13}NO_4$. Calculated (%): C, 72.50; H, 3.95; N, 4.23. HRMS (ESI), found: m/z 354.0737. Calculated for $C_{20}H_{13}NO_4$: M + Na = 354.0732.

***N*-(2,4-Dichlorophenyl)-2-(furan-2-yl)-4-oxo-4*H*-chromen-3-carboxamide (6d).** White crystals, yield 0.28 g (71%), m.p. 168—171 °C. ^{1}H NMR (DMSO-d_6), δ: 6.81 (dd, 1 H, H_{Fur}, J = 3.5 Hz, J = 1.5 Hz); 7.26—7.34 (m, 1 H); 7.41 (d, 1 H, H_{Fur}, J = 3.6 Hz); 7.44—7.58 (m, 1 H); 7.66 (d, 1 H, J = 2.3 Hz); 7.74 (d, 1 H, J = 8.3 Hz); 7.87 (t, 1 H, J = 7.2 Hz); 8.00—8.11 (m, 1 H, H_{Fur}); 8.17 (m, 1 H, H_{Ar}); 8.54 (d, 1 H, H(5), J = 8.9 Hz); 10.17 (s, 1 H, NH). Found (%): C, 60.12; H, 2.83; N, 3.41. $C_{20}H_{11}Cl_2NO_4$. Calculated (%): C, 60.02; H, 2.77; N, 3.50. HRMS (ESI), found: m/z 421.9957. Calculated for $C_{20}H_{11}Cl_2NO_4$: M + Na = 421.9954.

2-(Furan-2-yl)-4-oxo-*N*-[4-(trifluoromethyl)phenyl]-4*H*-chromen-3-carboxamide (6e). White crystals, yield 0.28 g (71%), m.p. 192—195 °C. ^{1}H NMR (DMSO-d_6), δ: 6.76—6.83 (m, 1 H, H_{Fur}); 7.40 (d, 1 H, H_{Ar}, J = 3.6 Hz); 7.55 (t, 1 H, H_{Ar}, J = 7.6 Hz); 7.69—7.81 (m, 3 H, H_{Ar} + $H_{Ar'}$); 7.82—7.94 (m, 3 H, H_{Ar} + H_{Fur}); 8.02 (s, 1 H, H_{Fur}); 8.09 (d, 1 H, H(4), J = 7.9 Hz); 10.86 (s, 1 H, NH). ^{13}C NMR (DMSO-d_6), δ: 113.1, 116.5, 118.3, 119.2 (2 C), 122.7 (2 C), 124.1, 125.0, 126.0, 126.2, 126.3, 126.4, 135.1, 142.4, 144.4, 148.1, 148.1, 150.9, 162.0, 174.5. Found (%): C, 63.12; H, 3.13; N, 3.22. $C_{21}H_{12}F_3NO_4$. Calculated (%): C, 63.16; H, 3.03; N, 3.51. HRMS (ESI), found: m/z 422.0611. Calculated for $C_{21}H_{12}F_3NO_4$: M + Na = 422.0611.

***N*-(2,4-Dichlorophenyl)-4-oxo-2-(thiophen-2-yl)-4*H*-chromen-3-carboxamide (6f).** White crystals, yield 0.33 g (80%), m.p. 155—156 °C. ^{1}H NMR (DMSO-d_6), δ: 7.39 (m, 2 H, H_{Ar}); 7.47—7.52 (m, 2 H, H_{Ar} + H_{Th}); 7.68 (d, 1 H, H_{Th}, J = 2.2 Hz); 7.74—7.81 (m, 1 H, H_{Ar}); 8.03 (d, 1 H, H_{Th}, J = 4.9 Hz); 8.19 (m, 2 H, H_{Ar}); 8.23 (s, 1 H, H_{Ar}); 10.33 (s, 1 H, NH). ^{13}C NMR

(DMSO-d_6), δ: 118.6, 122.1, 123.8, 125.5, 126.3, 126.6, 127.3, 127.7, 127.9, 128.0, 128.1, 128.8, 129.0, 129.1, 129.5, 131.8, 133.4, 135.3, 155.0, 180.2. Found (%): C, 57.58; H, 2.82; N, 3.20. $C_{20}H_{11}Cl_2NO_3S$. Calculated (%): C, 57.71; H, 2.66; N, 3.36. HRMS (ESI), found: *m/z* 437.9729. Calculated for $C_{20}H_{11}Cl_2NO_3S$: M + Na = 437.9729.

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