3-(2-PYRIDYL)COUMARINS

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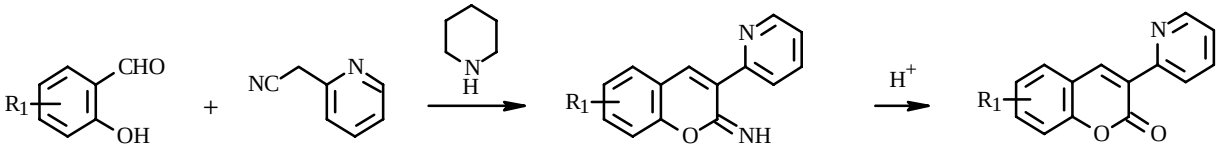
3-(2-Pyridyl)coumarins were prepared by reaction of substituted salicylaldehydes and 2-pyridylacetonitrile. Benzylation, acylation, and aminomethylation of 7-hydroxy-3-(2-pyridyl)coumarin was studied.

Key words: 8-aminomethyl-7-hydroxy-3-(2-pyridyl)coumarins, 7-acyloxy-3-(2-pyridyl)coumarins, 7-benzyloxy-3-(2-pyridyl)coumarins, 3-(2-pyridyl)coumarins.

Compounds with a coumarin ring are widely distributed throughout the plant kingdom and much less in animals. They belong to a large group of so-called phenolic compounds, the formation of which is characteristic of all representatives of the plant kingdom. Therefore, the important role in the life-cycle of plants of these compounds, which contribute to plant protective reactions and in many instances their pigmentation, cannot be disputed.

As a rule, coumarins in nature occur as glycosides (highest contents in plants of the Umbelliferae, Rutaceae, Solanaceae, and Fabaceae families). Natural coumarins have been used in medicine (anticoagulants), foods, and fragrances. Synthetic coumarins and their analogs are used as fluorescent probes and markers for biological research and as antibiotics, antiallergens, and fungicides in medicine.

We studied the synthesis of coumarins with a pyridine substituent via Knoevenagel condensation of substituted salicylaldehydes with 2-pyridylacetonitrile [1-8]. The resulting 2-iminocoumarins were converted to coumarins **1**-**10** by hydrolysis of the imine (Scheme 1).



1 - 10

1: R_1 = H; **2:** R_1 = 7-OH; **3:** R_1 = 8-OH; **4:** R_1 = 7,8-$(OH)_2$; **5:** R_1 = 8-OMe; **6:** R_1 = 8-OEt; **7:** R_1 = 6-NO_2; **8:** R_1 = 6-Cl; **9:** R_1 = 6,8-Cl_2; **10:** R_1 = 6-Br

Scheme 1.

Properties of the synthesized compounds (**1**-**10**) and their IR, UV and PMR spectra are given in the Experimental section.

The most characteristic signal in the PMR spectra of the 3-(2-pyridyl)coumarins is that for the coumarin 4-H, a singlet at 8.70-8.95 ppm. The signals of the other coumarin protons depend on the nature and position of the substituent in the coumarin ring whereas the signals for the pyridine protons are practically the same in all compounds **1**-**10**: (3′-H: 8.2-8.5 ppm, br.d, ^3J = 8 Hz; 4′-H: 7.8-7.9 ppm, br.t, ^3J = 8 Hz; 5′-H: 7.2-7.4 ppm, br.t, ^3J = 4.5-6 Hz; 6′-H: 8.7-8.9 ppm, br.d, ^3J = 4.5-6 Hz).

Two planar conformations (**I** and **II**) are possible for 3-(2-pyridyl)coumarins. In these, the pyridine and coumarin systems are conjugated:

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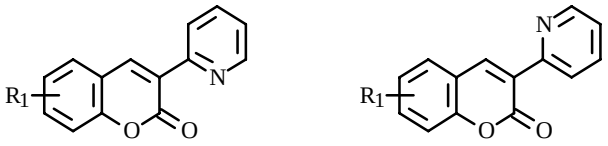
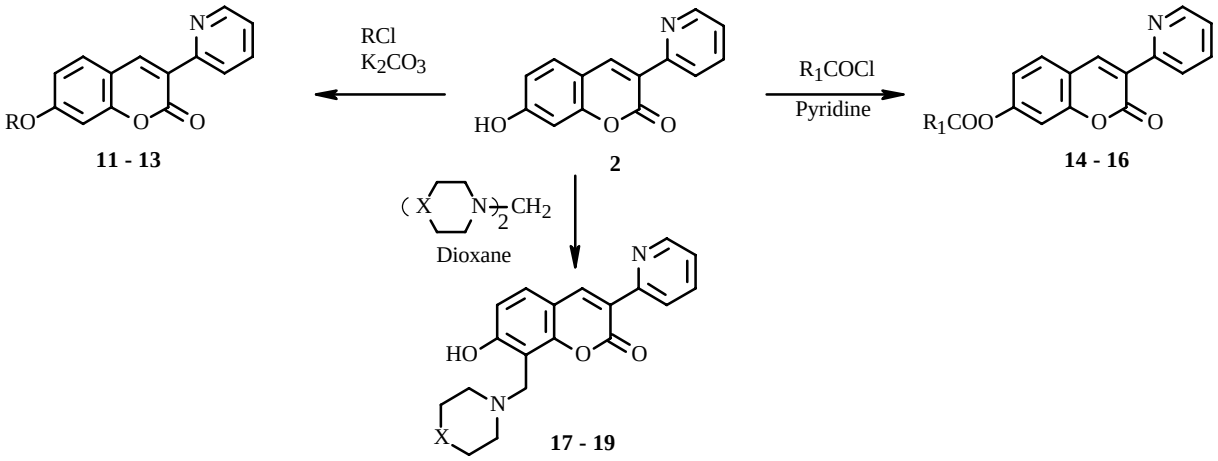


I **II**

Conformation **I**, as was demonstrated previously for 3-pyridylchromones [9], is much less favorable than **II** owing to mutual repulsion of the two electron-rich atoms, the carbonyl oxygen of coumarin and the pyridine nitrogen. An argument in favor of this conformation is the significant difference in the chemical shifts of the pyridine β-protons in the PMR spectra. The signal for 3′-H is located at weaker field than that for 5′-H because of the deshielding effect of the carbonyl O atom. The difference is about 1 ppm. However, the chemical shifts of 3′-H and 5′-H would be practically identical for conformation **I** and for structures in which the coumarin and pyridine rings are not coplanar.

Benzylation, acylation, and aminomethylation of **2** was performed in order to study the effect of the pyridine ring on the chemical behavior of the coumarin system (Scheme 2).



11 - 13 **2** **14 - 16**

17 - 19

11: R = $C_6H_5CH_2$; **12:** R = 2-$FC_6H_4CH_2$; **13:** R = 4-$FC_6H_4CH_2$; **14:** R_1 = Me; **15:** R_1 = Ph; **16:** R_1 = Furyl; **17:** X = CH_2; **18:** X = CH_2CH_2; **19:** X = O

Scheme 2.

Benzylation of 7-hydroxycoumarin in acetone or DMF with potash and a 40% excess of benzylchloride for 8-10 h formed **11-13**.

Compounds **14-16** were synthesized using a two-fold excess of carboxylic acid chlorides and a solution of **2** in pyridine (acetic anhydride was used to prepare acetylcoumarin).

The PMR spectra of the resulting 7-benzyloxy- and 7-acyloxycoumarins exhibited signals for the benzyl and acyl protons. Signals of the coumarin system were shifted to weak field.

The presence of the 7-OH enabled the 8-position of the coumarin to be activated toward electrophilic attack by aminomethylating agents. Such a reaction is atypical of a pyrone ring without electron-donating substituents. It was impossible to carry out the aminomethylation of 7-hydroxy-3-(2-pyridyl)coumarin under classical conditions (in acidic medium) because of protonation of the pyridine N, which significantly deactivates the compound toward electrophilic substitution and removes the pyridylcoumarin from the reaction medium since it precipitates as the salt. Therefore, the coumarin Mannich bases were prepared using formaldehyde aminal [1]. The reaction occurred on boiling **2** with a 20% excess of the aminal in absolute dioxane over 12 h. Compounds **17-19** were synthesized this way. Introducing the aminomethyl substituent in the coumarin 8-position shifted the signals for 5-H and 6-H (d, J = 8.5 Hz) of **17-19** to strong field in the PMR spectra. A characteristic signal for 8-CH_2 (s, 4.1-4.2 ppm) also appeared.

The UV absorption spectra of the 3-(2-pyridyl)coumarins exhibited a long-wavelength maximum at 310-365 nm (except for aminomethyl derivative **18**, for which λ_{max} = 400 nm). Its position depended on the nature of the coumarin substituent as follows. A donor substituent (hydroxyl or O-benzyl) in the coumarin 7-position shifted the absorption maximum to long-

wavelength to 351-357 nm compared with unsubstituted **1** (332 nm). Substituents in the coumarin 8-position decreased λ_{max}: 326 nm, **3**; 322, **5** and **6**; 310, **9**. However, if the molecule contained a 7-OH in addition to an electron-donating substituent in the 8-position, then the effect of the former was intensified. Thus, the highest λ_{max} was seen for aminomethyl derivative **18** (400 nm) and the λ_{max} values were also high for the other aminomethyl derivatives and 7,8-dihydroxy-3-(2-pyridyl)coumarin (359-365 and 362 nm, respectively).

The IR spectrum of **1** had the coumarin C=O absorption at 1722 cm^{-1}. Introducing electron-donating substituents, especially in the coumarin 7-position, decreased the frequency (to 1700 for **2** and **4**). The C=O frequency was correspondingly greater for compounds with electron-accepting substituents [1748 cm^{-1} for 6,8-dichloro-3-(2-pyridyl)coumarin, **9**].

Thus, condensation of salicylaldehydes and 2-pyridylacetonitrile is a convenient preparative method for synthesizing 3-(2-pyridyl)coumarins. The presence of the hydroxyl enabled 7-O-benzyl- and 7-O-acyl derivatives of 7-hydroxy-3-(2-pyridyl)coumarin to be prepared and the 8-position of the coumarin system to be activated for electrophilic attack by aminomethylating agents.

EXPERIMENTAL

The course of reactions and purity of products were monitored by TLC on Silufol UV-254 plates with elution by $CHCl_3$:CH_3OH (9:1 and 19:1). PMR spectra were measured on a Varian Mercury 400 instrument in DMSO-d_6 with TMS internal standard; UV absorption spectra, on a Shimadzu UV-3100; IR spectra, on a Nexus IR-Fourier spectrometer. Elemental analyses agreed with those calculated.

General Method for Synthesizing 3-(2-Pyridyl)coumarins 1-10. Substituted salicylaldehyde (0.1 mol) and 2-pyridylacetonitrile (0.1 mol) were dissolved in the minimal volume of ethanol or isopropanol at 40°C and treated with piperidine (0.1 mL). The reaction mixture was held for 1 d at room temperature, treated with H_2SO_4 (50 mL, 3%) and boiled for 2-12 h to hydrolyze the iminocoumarin. When the reaction was finished, the acidic solution was neutralized with aqueous ammonia until the pH was 7. The solid coumarin was filtered off and washed thoroughly with water.

Crystallization: **1**, **3**, **9**, **10**, ethanol; **2**, reprecipitation from acidic aqueous solution; **4** and **5**, *n*-butanol; **6**, dioxane; **7** and **8**, DMF.

3-(2-Pyridyl)coumarin (1). Yield 87%, $C_{14}H_9NO_2$, mp 139-139.5°C (141-142°C [6]).

IR spectrum (KBr, cm^{-1}): 1723, 1605, 1579, 1462, 1244, 1109, 1089.

UV spectrum (EtOH, λ_{max}, nm, log ε): 332 (4.199).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 7.34-7.42 (3H, m, H-6, H-8, H-5′), 7.63 (1H, br.t, ^3J = 8, H-7), 7.82-7.87 (2H, m, H-5, H-4′), 8.32 (1H, br.d, ^3J = 8, H-3′), 8.66 (1H, br.d, ^3J = 4.5, H-6′), 8.87 (1H, s, H-4).

7-Hydroxy-3-(2-pyridyl)coumarin (2). Yield 66%, $C_{14}H_9NO_3$, mp 255-256°C (254-255°C [2]; 254-260°C [5]).

IR spectrum (KBr, cm^{-1}): 1702, 1603, 1581, 1487, 1462, 1221.

UV spectrum (EtOH, λ_{max}, nm, log ε): 357 (4.286), 251 (3.898).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 6.78 (1H, d, ^4J = 1.5, H-8), 6.85 (1H, dd, ^3J = 8, ^4J = 1.5, H-6), 7.63 (1H, br.t, ^3J = 5, H-5′), 7.68 (1H, d, ^3J = 8, H-5), 8.18 (1H, br.t, ^3J = 8, H-4′), 8.41 (1H, d, ^3J = 8, H-3′), 8.75 (1H, br.d, ^3J = 5, H-6′), 8.86 (1H, s, H-4), 10.79 (1H, br.s, OH-7).

8-Hydroxy-3-(2-pyridyl)coumarin (3). Yield 63%, $C_{14}H_9NO_3$, mp 218-219°C.

IR spectrum (KBr, cm^{-1}): 1714, 1596, 1465, 1243, 1225, 1129, 1080.

UV spectrum (EtOH, λ_{max}, nm, log ε): 326 (4.255), 255 (3.968).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 7.10-7.17 (2H, m, H-6, H-7), 7.24 (1H, dd, ^3J = 7.5, ^4J = 1.5, H-5), 7.37 (1H, br.t, ^3J = 4, H-5′), 7.85 (1H, br.t, ^3J = 8, H-4′), 8.33 (1H, d, ^3J = 8, H-3′), 8.66 (1H, br.d, ^3J = 5, H-6′), 8.80 (1H, s, H-4), 10.12 (1H, br.s, OH-8).

7,8-Dihydroxy-3-(2-pyridyl)coumarin (4). Yield 61%, $C_{14}H_9NO_4$, mp 242-243°C.

IR spectrum (KBr, cm^{-1}): 1698, 1608, 1592, 1510, 1478, 1465, 1303, 1245, 1218, 1177.

UV spectrum (EtOH, λ_{max}, nm, log ε): 362 (4.350), 269 (4.143).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 6.82 (1H, d, J = 8.5, H-6), 7.13 (1H, d, J = 8.5, H-5), 7.28 (1H, br.t, ^3J = 6, H-5′), 7.79 (1H, br.t, ^3J = 8, H-4′), 8.31 (1H, d, ^3J = 8, H-3′), 8.60 (1H, br.d, ^3J = 6, H-6′), 8.74 (1H, s, H-4), 9.51 (1H, br.s, OH-8), 10.34 (1H, br.s, OH-7).

8-Methoxy-3-(2-pyridyl)coumarin (5). Yield 72%, $C_{15}H_{11}NO_3$, mp 164-165°C.

IR spectrum (KBr, cm^{-1}): 1720, 1615, 1590, 1440.

UV spectrum (EtOH, λ_{max}, nm, log ε): 322 (4.322), 253 (4.0).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 4.00 (3H, s, MeO-8), 7.11 (1H, dd, $^3J = 7$, $^4J = 2$, H-6), 7.21-7.32 (3H, m, H-5, H-7, H-5′), 7.79 (1H, br.t, $^3J = 8$, H-4′), 8.44 (1H, d, $^3J = 8$, H-3′), 8.68 (1H, br.d, $^3J = 4.5$, H-6′), 8.76 (1H, s, H-4).

8-Ethoxy-3-(2-pyridyl)coumarin (6). Yield 82%, $C_{16}H_{13}NO_3$, mp 162-163°C.

IR spectrum (KBr, cm^{-1}): 1721, 1608, 1579, 1472, 1278, 1092.

UV spectrum (EtOH, λ_{max}, nm, log ε): 322 (4.303), 253 (4.004).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.53 (3H, t, Me-8β), 4.23 (2H, q, CH_2O-8α), 7.11 (1H, dd, $^3J = 7$, $^4J = 2$, H-6), 7.21-7.23 (2H, m, H-5, H-7), 7.31 (1H, br.t, $^3J = 5$, H-5′), 7.79 (1H, br.t, $^3J = 8$, H-4′), 8.43 (1H, d, $^3J = 8$, H-3′), 8.68 (1H, br.d, $^3J = 5$, H-6′), 8.74 (1H, s, H-4).

6-Nitro-3-(2-pyridyl)coumarin (7). Yield 79%, $C_{14}H_8N_2O_4$, mp 216-217°C.

IR spectrum (KBr, cm^{-1}): 1735, 1610, 1523, 1350, 1111, 1096.

UV spectrum (EtOH, λ_{max}, nm, log ε): 322 (4.204), 269 (4.283), 227 (4.127).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 7.40 (1H, br.t, $^3J = 5$, H-5′), 7.62 (1H, d, J = 8.5, H-8), 7.88 (1H, br.t, $^3J = 8$, H-4′), 8.27 (1H, br.d, J = 8.5, H-7), 8.42 (1H, d, $^3J = 8$, H-3′), 8.68 (1H, br.d, $^3J = 5$, H-6′), 8.84 (1H, br.s, H-5), 9.00 (1H, s, H-4).

6-Chloro-3-(2-pyridyl)coumarin (8). Yield 73%, $C_{14}H_7ClNO_2$, mp 187-188°C.

IR spectrum (KBr, cm^{-1}): 1727, 1584, 1463, 1437, 1240, 1118, 1067.

UV spectrum (EtOH, λ_{max}, nm, log ε): 341 (4.079), 307 (4.137).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 7.35-7.40 (2H, m, H-8, H-5′), 7.71 (1H, dd, $^3J = 8.5$, $^4J = 2$, H-7), 7.87 (1H, br.t, $^3J = 8$, H-4′), 8.07 (1H, d, $^4J = 2$, H-5), 8.33 (1H, d, $^3J = 8$, H-3′), 8.67 (1H, br.d, $^3J = 5$, H-6′), 8.54 (1H, s, H-4).

6,8-Dichloro-3-(2-pyridyl)coumarin (9). Yield 82%, $C_{14}H_7Cl_2NO_2$, mp 151-151.5°C.

IR spectrum (KBr, cm^{-1}): 1748, 1473, 1456, 1439, 1243, 1092, 992.

UV spectrum (EtOH, λ_{max}, nm, log ε): 310 (4.210), 220 (4.465).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 7.41 (1H, br.t, $^3J = 4.5$, H-5′), 7.75 (1H, d, $^4J = 2$, H-7), 7.87 (1H, br.t, $^3J = 8$, H-4′), 7.98 (1H, d, $^4J = 2$, H-5), 8.30 (1H, d, $^3J = 8$, H-3′), 8.68 (1H, br.d, $^3J = 5$, H-6′), 8.89 (1H, s, H-4).

6-Bromo-3-(2-pyridyl)coumarin (10). Yield 80%, $C_{14}H_8BrNO_2$, mp 225°C.

IR spectrum (KBr, cm^{-1}): 1723, 1462, 1240, 1118, 1080.

UV spectrum (EtOH, λ_{max}, nm, log ε): 340 (4.167), 307 (4.207), 220 (4.517).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 7.38 (1H, br.t, $^3J = 4.5$, H-5′), 7.43 (1H, d, J = 8.5, H-8), 7.59 (1H, dd, $^3J = 8.5$, $^4J = 2$, H-7), 7.86 (1H, br.t, $^3J = 8$, H-4′), 7.94 (1H, d, $^4J = 2$, H-5), 8.31 (1H, d, $^3J = 8$, H-3′), 8.67 (1H, br.d, $^3J = 5$, H-6′), 8.86 (1H, s, H-4).

General Method for Synthesizing 7-Benzyloxy-3-(2-pyridyl)coumarins 11-13. A mixture of 7-hydroxy-3-(2-pyridyl)coumarin (5 mmol), benzylchloride (7 mmol), and freshly calcined potash (2 g) was boiled in acetone (30 mL) or DMF (10 mL) with stirring for 8-10 h. The solid was filtered off. If acetone was used as solvent, the product was isolated after adding water to the solid and neutralizing the potash; if DMF, by precipitation with water from the mother liquor.

Crystallization: **11**, DMF; **12**, DMF:isopropanol; **13**, isopropanol.

7-Benzyloxy-3-(2-pyridyl)coumarin (11). Yield 88%, $C_{21}H_{15}NO_3$, mp 160-161°C.

IR spectrum (KBr, cm^{-1}): 1710, 1620, 1585, 1510, 1465, 1440.

UV spectrum (EtOH, λ_{max}, nm, log ε): 352 (4.405), 248 (4.021), 206 (4.585).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 5.13 (2H, s, CH_2O-7), 7.01 (1H, d, $^3J = 8$, H-6), 7.08 (1H, br.s, H-8), 7.33 (1H, br.t, $^3J = 4$, H-5′), 7.31-7.45 (5H, m, Ph-7), 7.76 (1H, d, $^3J = 8$, H-5), 7.82 (1H, br.t, $^3J = 8$, H-4′), 8.29 (1H, d, $^3J = 8$, H-3′), 8.65 (1H, br.d, $^3J = 4$, H-6′), 8.83 (1H, s, H-4).

7-(2-Fluorobenzyloxy)-3-(2-pyridyl)coumarin (12). Yield 93%, $C_{21}H_{14}FNO_3$, mp 168-169°C.

IR spectrum (KBr, cm^{-1}): 1713, 1612, 1582, 1462, 1238, 1196, 1173, 1127.

UV spectrum (EtOH, λ_{max}, nm, log ε): 351 (4.447), 248 (4.076), 207 (4.614).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 5.24 (2H, s, CH_2O-7), 7.00 (1H, dd, J = 8, J = 1.5, H-6), 7.11 (1H, d, J = 1.5, H-8), 7.16-7.24 [2H, m, H-4″, H-6″ (2-FC_6H_4)], 7.41 [1H, m, H-5″ (2-FC_6H_4)], 7.32 (1H, br.t, $^3J = 6$, H-5′), 7.76 (1H,

d, ^{3}J = 8, H-5), 7.56 [1H, br.t, ^{3}J = 8, H-3″ (2-FC$_6$H$_4$)], 7.81 (1H, br.t, ^{3}J = 8, H-4′), 8.30 (1H, d, ^{3}J = 8, H-3′), 8.62 (1H, br.d, ^{3}J = 6, H-6′), 8.83 (1H, s, H-4).

7-(4-Fluorobenzyloxy)-3-(2-pyridyl)coumarin (13). Yield 94%, $C_{21}H_{14}FNO_3$, mp 168-169°C.

IR spectrum (KBr, cm^{-1}): 1715, 1616, 1585, 1520, 1472, 1238.

UV spectrum (EtOH, λ_{max}, nm, log ε): 352 (4.438), 248 (4.061), 212 (4.709).

PMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, J/Hz): 5.20 (2H, s, CH$_2$O-7), 7.00 (1H, dd, J = 8, J = 2, H-6), 7.09 (1H, d, J = 2, H-8), 7.15 [2H, m, H-2″, H-6″ (4-FC$_6$H$_4$)], 7.33 (1H, br.t, ^{3}J = 5, H-5′), 7.51 [2H, m, H-3″, H-5″ (4-FC$_6$H$_4$)], 7.77 (1H, d, ^{3}J = 8, H-5), 7.82 (1H, br.t, ^{3}J = 8, H-4′), 8.30 (1H, d, ^{3}J = 8, H-3′), 8.64 (1H, br.d, ^{3}J = 5, H-6′), 8.84 (1H, s, H-4).

General Method for Synthesizing 7-Acyloxy-3-(2-pyridyl)coumarins 14-16. A solution of 7-hydroxy-3-(2-pyridyl)coumarin (5 mmol) in pyridine (7 mL) was treated with acid chloride (or anhydride) (10 mmol) and heated at ~80°C for 10-15 min. The reaction mixture was left for 1 d at room temperature and poured onto ice. The 7-acyloxycoumarin was filtered off.

Crystallization: DMF.

7-Acetyloxy-3-(2-pyridyl)coumarin (14). Yield 86%, $C_{16}H_{11}NO_4$, mp 172-173°C (177-178°C [2]).

IR spectrum (KBr, cm^{-1}): 1764, 1725, 1606, 1581, 1467, 1366, 1190, 1121.

UV spectrum (EtOH, λ_{max}, nm, log ε): 336 (4.294), 207 (4.461).

PMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, J/Hz): 2.34 (3H, s, CH$_3$COO-7), 7.12 (1H, dd, ^{3}J = 8, ^{4}J = 2, H-6), 7.23 (1H, d, ^{4}J = 2, H-8), 7.36 (1H, br.t, ^{3}J = 4.5, H-5′), 7.83 (1H, br.t, ^{3}J = 8, H-4′), 7.89 (1H, d, ^{3}J = 8, H-5), 8.28 (1H, d, ^{3}J = 8, H-3′), 8.64 (1H, br.d, ^{3}J = 4.5, H-6′), 8.86 (1H, s, H-4).

7-Benzyloxy-3-(2-pyridyl)coumarin (15). Yield 85%, $C_{21}H_{13}NO_4$, mp 168°C.

IR spectrum (KBr, cm^{-1}): 1721, 1614, 1577, 1464, 1435, 1273, 1243, 1152, 1128.

UV spectrum (EtOH, λ_{max}, nm, log ε): 336 (4.352), 234 (4.356).

PMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, J/Hz): 7.29 (1H, dd, ^{3}J = 8.5, ^{4}J = 2, H-6), 7.41 (1H, d, ^{4}J = 2, H-8), 7.38 (1H, br.t, ^{3}J = 4.5, H-5′), 7.60 [2H, t, ^{3}J = 8, H-3″, H-5″ (Ph)], 7.73 [1H, t, ^{3}J = 8, H-4″ (Ph)], 7.86 (1H, br.t, ^{3}J = 8, H-4′), 7.99 (1H, d, ^{3}J = 8.5, H-5), 8.17 [2H, d, ^{3}J = 8, H-2″, H-6″ (Ph)], 8.31 (1H, d, ^{3}J = 8, H-3′), 8.68 (1H, br.d, ^{3}J = 4.5, H-6′), 8.92 (1H, s, H-4).

7-(2-Furylcarboxy)-3-(2-pyridyl)coumarin (16). Yield 96%, $C_{19}H_{11}NO_5$, mp 182-183°C.

IR spectrum (KBr, cm^{-1}): 1736, 1616, 1578, 1562, 1464, 1296, 1242, 1180, 1132, 1085.

UV spectrum (EtOH, λ_{max}, nm, log ε): 336 (4.320), 259 (4.167), 212 (4.367).

PMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, J/Hz): 6.76 [1H, dd, ^{3}J = 4, ^{4}J = 1.5, H-4″ (furyl)], 7.28 (1H, dd, ^{3}J = 8.5, ^{4}J = 2, H-6), 7.38 (1H, br.t, ^{3}J = 4.5, H-5′), 7.40 (1H, d, ^{4}J = 2, H-8), 7.54 [1H, d, ^{3}J = 4, H-5″ (furyl], 7.86 (1H, br.t, ^{3}J = 8, H-4′), 7.98 (1H, d, ^{3}J = 8.5, H-5), 8.04 [1H, d, ^{4}J = 1.5, H-3″ (furyl)], 8.31 (1H, d, ^{3}J = 8, H-3′), 8.67 (1H, br.d, ^{3}J = 4.5, H-6′), 8.91 (1H, s, H-4).

General Method for Synthesizing 8-Aminomethyl-7-hydroxy-3-(2-pyridyl)coumarins 17-19. 7-Hydroxy-3-(2-pyridyl)coumarin (5 mmol) and formaldehyde aminal (6 mmol) were boiled in absolute dioxane (25 mL) for 12 h. The resulting solution was evaporated to dryness in a rotary evaporator. The solid was crystallized from hexane:toluene.

7-Hydroxy-8-(piperidinomethyl)-3-(2-pyridyl)coumarin (17). Yield 66%, $C_{20}H_{20}N_2O_3$, mp 165-165.5°C.

IR spectrum (KBr, cm^{-1}): 1720, 1614, 1565, 1506, 1463, 1306, 1230, 1132, 1063.

UV spectrum (EtOH, λ_{max}, nm, log ε): 365 (4.301), 265 (4.201).

PMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, J/Hz): 1.69 [6H, m, CH$_2$-3″, CH$_2$-4″, CH$_2$-5″ (piperidyl)], 2.26 [2H, m, CH$_2$-2″ (piperidyl)], 3.04 [2H, m, CH$_2$-6″ (piperidyl)], 4.07 (2H, s, CH$_2$-8), 6.77 (1H, d, ^{3}J = 8.5, H-6), 7.24 (1H, br.t, ^{3}J = 5, H-5′), 7.42 (1H, d, ^{3}J = 8.5, H-5), 7.76 (1H, br.t, ^{3}J = 8, H-4′), 8.38 (1H, d, ^{3}J = 8, H-3′), 8.65 (1H, br.d, ^{3}J = 5, H-6′), 8.69 (1H, s, H-4), 9.91 (1H, br.s, OH-7).

7-Hydroxy-8-(azepanomethyl)-3-(2-pyridyl)coumarin (18). Yield 72%, $C_{21}H_{22}N_2O_3$, mp 105-106°C.

IR spectrum (KBr, cm^{-1}): 1719, 1604, 1580, 1478, 1462.

UV spectrum (EtOH, λ_{max}, nm, log ε): 400 (4.393), 266 (4.0), 212 (4.602).

PMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, J/Hz): 1.67 [4H, m, CH$_2$-4″, CH$_2$-5″ (azepinyl)], 1.74 [4H, m, CH$_2$-3″, CH$_2$-6″ (azepinyl)], 2.84 [4H, m, CH$_2$-2″, CH$_2$-7″ (azepinyl)], 4.18 (2H, s, CH$_2$-8), 6.77 (1H, d, ^{3}J = 8.5, H-6), 7.23 (1H, br.t, ^{3}J = 5, H-5′), 7.43 (1H, d, ^{3}J = 8.5, H-5), 7.76 (1H, br.t, ^{3}J = 8, H-4′), 8.36 (1H, d, ^{3}J = 8, H-3′), 8.64 (1H, br.d, ^{3}J = 5, H-6′), 8.68 (1H, s, H-4), 11.83 (1H, br.s, OH-7).

7-Hydroxy-8-(morpholinomethyl)-3-(2-pyridyl)coumarin (19). Yield 71%, $C_{19}H_{18}N_2O_4$, mp 181-182°C.

IR spectrum (KBr, cm^{-1}): 1717, 1604, 1581, 1463, 1267, 1114.

UV spectrum (EtOH, λ_{max}, nm, log ε): 359 (4.344), 252 (3.949).

PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.69 [4H, m, CH_2-3″, CH_2-5″ (morpholyl)], 3.80 [4H, m, CH_2-2″, CH_2-6″ (morpholyl)], 4.12 (2H, s, CH_2-8), 6.81 (1H, d, ^3J = 8.5, H-6), 7.24 (1H, br.t, ^3J = 4.5, H-5′), 7.47 (1H, d, ^3J = 8.5, H-5), 7.78 (1H, br.t, ^3J = 8, H-4′), 8.37 (1H, d, ^3J = 8, H-3′), 8.65 (1H, br.d, ^3J = 4.5, H-6′), 8.70 (1H, s, H-4).

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