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CHEMISTRY OF 3-HETARYLCOUMARINS.

1. 3-(2-BENZAZOLYL)COUMARINS

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The reaction of substituted salicylaldehydes with 2-benzimidazolyl- and 2-benzothiazolylacetonitriles gives the corresponding 3-hetarylcoumarins. The alkylation, acylation, and aminomethylation reactions of these 7-hydroxy-substituted hetero isoflavonoid analogs has been studied.

Keywords: alkoxycoumarins, 8-aminomethyl-7-hydroxycoumarins, acyloxycoumarins, 3-(2-benzimidazolyl)coumarin, 3-(2-benzothiazolyl)coumarin.

In recent times there have been broad developments in investigations of both the synthesis and the study of the chemical properties of coumarins which have valuable pharmacological activity. Hence, 4-hydroxycoumarin derivatives are anticoagulants (the drugs syncoumar (acenocoumarol) and neodicoumarin) and a series of coumarins find use in laser spectroscopy [1, 2]. Amongst compounds possessing valuable optical properties are the 3-hetarylcoumarins containing 2-benzimidazole, 2-benzothiazole, 2-benzoxazole, 2-thiazole, and 4-thiazole residues, the latter having the greatest interest.

The following methods have been developed for the synthesis of 3-benzazolylcoumarins. Reaction of substituted salicylaldehydes with 2-benzazolylacetonitriles of benzazolylacetic acid esters in the presence of base [3-11] as well as with 2-benzazolylacetonitrile perchlorates [12] and subsequent acid hydrolysis of the 2-iminocoumarins formed; the reaction of 2-iminocoumarin-3-carboxyimides with *o*-aminothiophenol, *o*-aminophenol, and *o*-phenylenediamine [13]; the condensation of methyl coumarin-3-carboxylate with *o*-phenylenediamines in polyphosphoric acid [14]; the cyclodehydrogenation of coumarin-3-thiocarboxamides [15]; the reaction of 4-hydroxy-3-formylcoumarin and *o*-aminothiophenol to form 3-(2-benzothiazolyl)-4-hydroxycoumarin [16]; and the photochemical reaction of 3-iodo-4-methyl-7-diethylaminocoumarin with benzimidazole [17].

However, despite the numerous publications concerning the synthesis and investigation of the spectroscopic properties of 3-benzazolylcoumarins, only their oxidative cyanation [18], acylation of 3-(2-benzazolyl)-7-hydroxycoumarins using carboxylic acid anhydrides and chlorides in dimethylformamide, and also their reaction with chlorosulfonic acid and phosphorus oxychloride in pyridine [19] have been reported.

In order to extend our work on the chemistry of 3-benzazolylbenzopyrones and to add to the previously prepared benzimidazole [20] and benzothiazole [21] isoflavone analogs we have carried out the synthesis of the isomeric 3-(2-benzimidazolyl)- and 3-(2-benzothiazolyl)coumarins **1**, **2**, and **3** respectively. In contrast to the oxadiazolyl coumarin derivatives [22], the condensation of the 5-chloro-, 5-bromo-, 5-nitro-, 3,5-dichloro-, 4-hydroxy-, and 3-methoxysalicylaldehydes with 2-benzimidazolyl(benzothiazolyl)acetonitriles permits the preparation of the substituted 3-hetarylcoumarins **1a-f** to **3a-f** in yields which are sometimes close to

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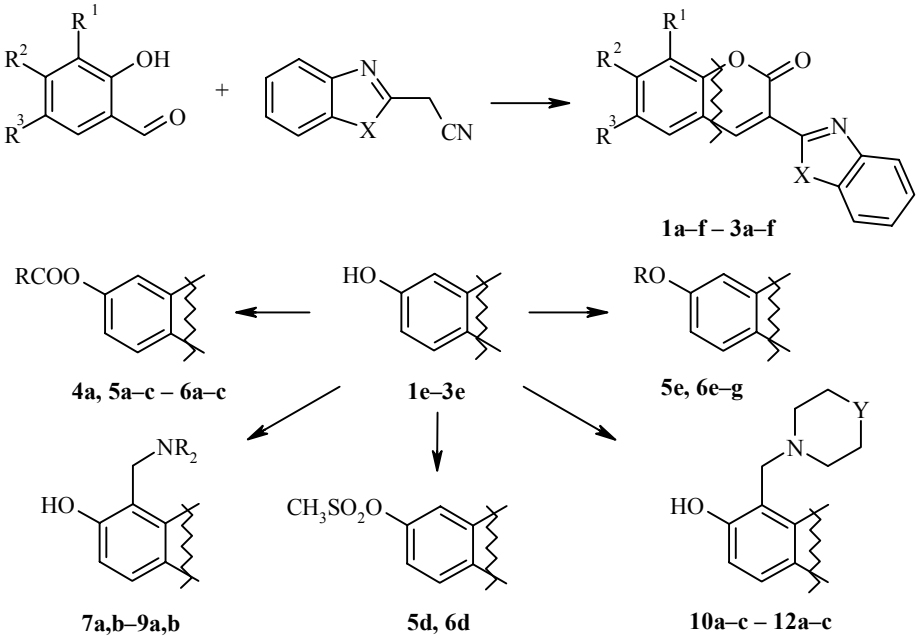
quantitative. We have used piperidine as the base, whereas the authors of [3] employed ammonium acetate. The products obtained were high melting, colored materials which were difficultly soluble in organic solvents, insoluble in water, and poorly soluble upon heating in mineral acids (Table 1).



1, 4, 7, 10 X = NH; **2, 5, 8, 11** X = NCH_3; **3**, **6, 9, 12** X = S. **1-3** $R^1 = R^2 = H$, **a** $R^3 = Cl$; **b** $R^3 = Br$, **c** $R^3 = NO_2$, **d** $R^1 = R^3 = Cl$, $R^2 = H$, **e** $R^1 = R^3 = H$, $R^2 = OH$, **f** $R^1 = OCH_3$, $R^2 = R^3 = H$. **4-6 a,e** R = CH_3, **b** R = 2-furyl, **c** R = $C_6H_4OCH_3$-4, **f** R = $CH_2COOC_2H_5$, **g** R = CH_2COOH; **7-9 a** R = CH_3, **b** R = C_2H_5, **10-12 a** Y = O, **b** Y = CH_2, **c** Y = NCH_3

Conformation of the formation of the α-pyrone ring comes from the ^{1}H NMR spectra of these compounds measured in DMSO-d_6. Hence the lowest field region (8.4-9.3 ppm) shows a singlet signal for the proton in position 4 of the coumarin system and signals for the protons of the benzazole fragment which appear as multiplets in the range 7.2-8.1 ppm. The signals for the protons of ring A of the coumarin in compounds **1a-c,e** to **3a-c, e** are characteristic for a 1,2,4-trisubstituted aromatic system (Table 2).

The signals for the protons in positions 5, 6, and 7 of the 8-methoxycoumarins **1f-3f** appear, in most cases, as multiplets which are found within the region of the signals of the benzazole fragment and hence their exact assignment is impossible (the spectra of these compounds are presented in the Experimental section).

The obtained 7-hydroxy substituted 3-benzazolylcoumarins **1e-3e** are readily acylated using acetic anhydride and also the acid chlorides of 2-furancarboxylic, 4-methoxybenzoic, and methanesulfonic acids. The reactions occur smoothly in pyridine to form the 7-acyloxy derivatives **4a**, **5a-c**, and **6a-c** and the 7-mesyloxycoumarins **5d**, **6d**. In contrast to the results presented in [3], the coumarin **1e** and acetic anhydride gave only the O-acetyl derivative **4a**.

The signal for a 7-OH group is absent in the ^{1}H NMR spectra of the acyl derivatives **4a**, **5a-d**, and **6a-d** and, instead, there are observed the signals for the acyl substituents or the mesyl group. Due to a paramagnetic shift, the signals of the protons in positions 6 and 8 of the coumarin fragment are shifted into the region of the benzazole signals and this markedly complicates the interpretation of the spectra of these compounds (see Experimental section).

TABLE 1. Characteristics of 3-(2-Benzazolyl)coumarins **1-12**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %
		N	Cl or Br	S		
1	2	3	4	5	6	7
1a	$C_{16}H_9ClN_2O_2$	10.17 / 9.44	12.86* / 11.95*		271-272	44
1b	$C_{16}H_9BrN_2O_2$	8.51 / 8.21	23.32*[2] / 23.46*[2]		279-281	46
1c	$C_{16}H_9N_3O_4$	13.88 / 13.68			330-331	81
1d	$C_{16}H_8Cl_2N_2O_2$	8.65 / 8.46	21.04* / 21.41*		318-319	79
1e	$C_{16}H_{10}N_2O_3$	10.40 / 10.07			>360	97
1f	$C_{17}H_{12}N_2O_3$	9.72 / 9.58			280-282	92
2a	$C_{17}H_{11}ClN_2O_2$	8.80 / 9.01	11.22* / 11.41*		272-273	99
2b	$C_{17}H_{11}BrN_2O_2$	8.08 / 7.89	22.94*[2] / 22.54*[2]		262-264	82
2c	$C_{17}H_{11}N_3O_4$	12.67 / 13.08			282-284	73
2d	$C_{17}H_{10}Cl_2N_2O_2$	8.37 / 8.12	20.18* / 20.54*		266-267	69
2e	$C_{17}H_{12}N_2O_3$	9.50 / 9.58			331-333*[5]	97
2f	$C_{18}H_{14}N_2O_3$	9.33 / 9.15			282-284	65
3a	$C_{16}H_8ClNO_2S$	4.32 / 4.46	11.342* / 11.30*	10.10 / 10.22	239-241	96
3b	$C_{16}H_8BrNO_2S$	4.11 / 3.91	22.15 / 22.31*	9.10 / 8.95	266-269*[3]	95
3c	$C_{16}H_8N_2O_4S$	8.55 / 8.64		10.12 / 9.89	303-304*[4]	94
3d	$C_{16}H_7Cl_2NO_2S$	4.29 / 4.02	20.34* / 20.36*	9.38 / 9.21	250-252	97
3e	$C_{16}H_9NO_3S$	4.50 / 4.74		10.83 / 10.86	295	98
3f	$C_{17}H_{11}NO_3S$	4.55 / 4.53		10.50 / 10.57	250-251	95
4a	$C_{18}H_{12}N_2O_4$	8.50 / 8.75			268-270*[6]	65
5a	$C_{19}H_{14}N_2O_4$	8.12 / 8.38			238-240	70
5b	$C_{22}H_{14}N_2O_5$	7.14 / 7.25			252-255	80
5c	$C_{25}H_{18}N_2O_5$	6.80 / 6.57			275-277	65
5d	$C_{18}H_{14}N_2O_5S$	7.45 / 7.56		8.70 / 8.66	217-218	63
5e	$C_{18}H_{14}N_2O_3$	9.23 / 9.15			236-237	55
6a	$C_{18}H_{11}NO_4S$	4.12 / 4.15		9.35 / 9.50	282-284	80
6b	$C_{21}H_{11}NO_5S$	3.44 / 3.60		8.30 / 8.23	253-255	76
6c	$C_{24}H_{15}NO_5S$	3.04 / 3.26		7.78 / 7.47	255-256	70
6d	$C_{17}H_{11}NO_5S_2$	3.62 / 3.75		17.31 / 17.17	249-251	85
6e	$C_{17}H_{11}NO_3S$	4.58 / 4.53		10.55 / 10.37	242-244	76
6f	$C_{20}H_{15}NO_5S$	3.55 / 3.67		8.50 / 8.41	206-208	78
6g	$C_{18}H_{11}NO_5S$	3.80 / 3.96		8.92 / 9.07	>300	74

TABLE 1 (continued)

1	2	3	4	5	6	7
7a	$C_{19}H_{17}N_3O_3$	13.07 / 12.53			284-286	80
7b	$C_{21}H_{21}N_3O_3$	11.43 / 11.56			238-240	45
8a	$C_{20}H_{19}N_3O_3$	11.96 / 12.03			227-228	90
8b	$C_{22}H_{23}N_3O_3$	11.25 / 11.13			186-188	55
9a	$C_{19}H_{16}N_2O_3S$	7.90 / 7.95		8.97 / 9.10	260	95
9b	$C_{21}H_{20}N_2O_3S$	7.52 / 7.36		8.28 / 8.43	175-177	70
10a	$C_{21}H_{19}N_3O_4$	10.95 / 11.13			272-274	88
10b	$C_{22}H_{21}N_3O_3$	11.37 / 11.19			269-270	75
10c	$C_{22}H_{22}N_4O_3$	14.21 / 14.35			254-257	72
11a	$C_{22}H_{21}N_3O_4$	10.68 / 10.74			257-259	78
11b	$C_{23}H_{23}N_3O_3$	10.92 / 10.79			228-229	70
11c	$C_{23}H_{24}N_4O_3$	13.93 / 13.85			184-186	58
12a	$C_{21}H_{18}N_2O_4S$	7.25 / 7.10		8.32 / 8.13	258-260	90
12b	$C_{22}H_{20}N_2O_3S$	7.28 / 7.14		8.07 / 8.17	250-251	82
12c	$C_{22}H_{21}N_3O_3S$	10.36 / 10.31		7.76 / 7.87	228-230	81

* Cl, %.
*[2] Br, %.
*[3] 267-269°C [10].
*[4] 260°C [3]; 305-306°C [10].
*[5] 295°C [3].
*[6] 270-272°C [19].

We have also studied the possible alkylation of the 7-hydroxycoumarins **2e**, **3e**. Prolonged refluxing of the latter with dimethylsulfate in acetone in the presence of excess potassium carbonate gives the 7-methoxycoumarins **5e**, **6e** and coumarin **3e** and ethyl bromoacetate yields the 7-carbethoxymethyl-substituted **6f** under similar conditions. Hydrolysis of the latter in acetic acid in the presence of sulfuric acid then gives the 7-coumaryloxyacetic acid **6g**.

In a continuation of work on the aminomethylation of 3-benzazolylbenzopyrones we have carried out the synthesis of the Mannich bases **7a,b-9a,b and 10a-c** to **12a-c**, which are isomeric to the previously obtained chromone derivatives [23]. As in the case of the 3-benzazolylchromones, the aminomethylation of the coumarin nucleus does not occur when using formalin and a secondary amine in organic solvents or in water. The lowering of the reactivity towards electrophilic substitution of the coumarin system can be explained in terms of the effect of the electron-accepting benzazole substituent in position 3 of the pyrone ring. When carrying out the Mannich reaction with the amine hydrochlorides in alcohol or acetic acid, the formation of the aminomethyl derivatives is again not observed. The presence of acid causes protonation of the nitrogen atom of the benzazole substituent and this hinders even further the electrophilic attack at the coumarin nucleus. In this connection we have attempted to use aminals to carry out the aminomethylation. The reaction with these occurs in neutral or weakly basic medium and so the effect of the benzazole nucleus on the activity of the coumarin system is not so significant. In most cases the aminals can be used as efficient media for carrying out the aminomethylation of the benzopyrone system. Hence the 3-(2-benzazolyl)-7-hydroxycoumarins **1e-3e** have two reactive centers for

TABLE 2. ^{1}H NMR Spectra of 3-(2-Benzazolyl)coumarins **1a-e** to **3a-e, 5e,** and **6e-g,** δ, ppm

Com-pound	Coumarin residue					3-Het*[2]	
	4-H, s	5-H	6-H	7-H / R	8-H	4-and 7-H, m	5- and 6-H, m
1a	9.08	8.09 *[3]	—	7.70 *[4]	7.57 *[5]	7.65	7.21
1b	9.08	8.24 *[3]	—	8.85 *[4]	7.47 *[5]	7.71	7.25
1c	9.19	8.88 *[3]	—	8.38 *[4]	7.46 *[5]	7.64	7.19
1d	9.07	8.08, s	—	7.97, s	—	7.67	7.21
1e	9.02	7.83 *[5]	6.90 *[4]	12.36 (br. s, OH)	6.85 *[3]	7.65	7.20
2a	8.58	8.04 *[3]	—	7.80 *[4]	7.58 *[5]	7.75	7.37
2b	8.51	8.14 *[3]	—	7.88 *[4]	7.48 *[5]	7.67	7.32
2c	8.72	8.90 *[3]	—	8.50 *[4]	7.74 *[5]	7.68	7.34
2d	8.54	8.06, s	—	7.98, s	—	7.66	7.32
2e	8.40	7.65 *[5]	6.87 *[4]	10.74 (br. s, OH)	6.84 *[3]	7.65	7.30
3a	9.07	8.08 *[3]	—	7.67 *[4]	7.50 *[5]	8.08	7.53
3b	9.14	8.28 *[3]	—	7.86 *[4]	7.46 *[5]	8.12	7.51
3c	9.33	9.00 *[3]	—	8.46 *[4]	7.75 *[5]	8.14	7.53
3d	8.98	8.0, c	—	7.82, s	—	8.0	7.46
3e	9.12	8.06 *[5]	6.90 *[4]	11.07 (br. s, OH)	6.85 *[3]	7.88	7.48
5e	8.68	7.89 *[5]	7.10 *[4]	3.94 (3H, s, OCH_3)	7.17 *[3]	7.80	7.49
6e	9.06	7.90 *[5]	6.98 *[4]	3.87 (3H, s, OCH_3)	7.05 *[3]	8.05	7.50
6f	9.18	8.01 *[5]	7.11 *[4]	1.26 (3H, t, CH_3*[6]); 4.29 (2H, q, CH_2O*[6]); 4.99 (2H, s, OCH_2).	7.15 *[3]	8.06	7.52
6g	9.10	7.92 *[5]	6.92 *[4]	4.43 (2H, s, OCH_2)	7.97 *[3]	7.47	8.08

* The exact positions of the 7-OH group of the coumarin cycle and the NH group proton signals cannot be given due to their considerable broadening.
*[2] In compounds **2a-e**, **5e** the signal for the protons of the NCH_3 group appears as a three-proton singlet in the region 3.76-3.92 ppm.
*[3] d, ^4J = 2.5-3.0 Hz.
*[4] dd, ^4J , ^3J =8.5-9.1, 2.5-3.0 Hz.
*[5] d, ^3J = 8.5-9.1 Hz.
*[6] ^3J = 7.2 Hz.

electrophilic substitution and these are positions 6 and 8 of the coumarin nucleus. In the case of compound **3e** (according to TLC and ^{1}H NMR data) it was found that carrying out the aminomethylation with a marked excess of bis(dimethylamino)methane (10-15 times) formed both the 8-dimethylaminomethyl and also the 6,8-bisdimethylaminomethyl derivatives. Attempts to prepare only the latter did not end successfully both with an excess of the aminomethylating agent and with a longer reaction time (20-30 h). On the other hand, the use of a slight excess of the aminal (10-15%) led to the exclusive formation of the 8-aminomethyl derivative. The ^{1}H NMR spectra of the products **7a-b** to **12a-b** were in agreement and showed signals for the protons at positions 5 and 6 which appeared as doublets with ^3J = 8.5-9.0 Hz (Table 3).

TABLE 3. ^{1}H NMR Spectra of the Mannich Bases **7a,b** to **9a,b**, and **10a-c** to **12a-c**, δ, ppm*

Compound	Coumarin residue					Het*^{2}	
	4-H, s	5-H, ^3J = 8.5-9.1 Hz	6-H, ^3J = 8.5-9.1 Hz	8-CH_2, s	NR^2R^3	4- and 7-H, m	5- and 6-H, m
7a	8.96	7.70	6.70	4.08	2.49 (6H, s $2NCH_3$)	7.63	7.17
7b	8.93	7.67	6.70	4.15	2.80 (4H, q, $2NCH_2$*^{3}), 1.15 (6H, t, $2CH_3$*^{3})	7.65	7.17
8a	8.36	7.62	6.72	4.07	2.45 (6H, s $2NCH_3$)	7.65	7.27
8b	8.35	7.62	6.70	4.15	2.75 (4H, q, $2NCH_2$*^{3}), 1.10 (6H, t, $2CH_3$*^{3})	7.65	7.30
9a	8.95	7.67	6.57	4.13	2.59 (6H, s $N(CH_3)_2$)	8.00	7.45
9b	8.94	7.64	6.55	4.17	2.92 (4H, q, $2NCH_2$*^{3}), 1.19 (6H, t, $2CH_3$*^{3})	8.11	7.44
10a	8.99	7.78	6.88	3.90	2.62 (4H, m, $2NCH_2$), 3.65 (4H, m, $2OCH_2$)	7.65	7.20
10b	9.00	7.73	6.87	4.08	2.73 (4H, m, $2NCH_2$), 1.56 (6H, m, $3CH_2$)	7.65	7.20
10c	9.01	7.73	6.88	4.0	2.41 (4H, m, $2NCH_2$), 2.65 (4H, m, $2NCH_2$), 2.18 (3H, s, NCH_3)	7.64	7.16
11a	8.44	7.68	6.88	3.99	2.56 (4H, m, $2NCH_2$), 3.64 (4H, m, $2OCH_2$)	7.64	7.28
11b	8.36	7.62	6.87	4.05	2.66 (4H, m, $2NCH_2$), 1.55 (6H, m, $3CH_2$)	7.65	7.30
11c	8.46	7.63	6.82	4.0	2.40 (4H, m, $2NCH_2$), 2.64 (4H, m, $2NCH_2$), 2.18 (3H, s, NCH_3)	7.60	7.25
12a	9.12	7.86	6.90	3.93	2.60 (4H, m, $2NCH_2$), 3.65 (4H, m, $2OCH_2$)	8.09	7.49
12b	8.99	7.72	6.69	4.09	2.79 (4H, m, $2NCH_2$), 1.58 (6H, m, $3CH_2$)	8.07	7.46
12c	9.02	7.77	6.80	3.98	2.42 (4H, m, $2NCH_2$), 2.68 (4H, m, $2NCH_2$), 2.20 (3H, s, NCH_3)	8.06	7.46

* The exact positions of the 7-OH and NH groups cannot be given due to their considerable broadening.

*^{2} In compounds **8a,b**, **11a-c** the signal for the protons of the NCH_3 groups appears as a three-proton singlet in the region 3.76-3.92 ppm.

*^{3} ^3J = 7.0-7.2 Hz.

In contrast to the 3-(2-benzazolyl)chromones, the preparation of the aminomethyl derivatives of 3-(2-benzazolyl)coumarins needed more prolonged refluxing of the reaction mixture. Hence the reaction with bis(dimethylamino/diethylamino)methane was completed in 4-5 h and in the case of the reaction with 4,4'-methylenebismorpholine, 1,1'-methylenebispiperidine, or -bis(4-methylpiperazinyl)methane needed up to 12 h.

In contrast to the starting compounds **1e-3e**, the ^{1}H NMR spectra of the Mannich bases **7-12** did not show the signals for the 8-H of the coumarin ring and, in their place, showed the signals for the protons of the aminoalkyl substituents. By analogy with 3-(2-benzazolyl)chromones [23], only the monoaminomethyl derivatives at position 8 of the coumarin ring were obtained and aminomethylation of the benzimidazole NH group did not occur.

By contrast with the starting materials **1-3,** the aminomethylated derivatives of the 3-(2-benzazolyl)coumarins **7-12** are high melting, crystalline materials which are readily soluble in organic solvents. They are also soluble in dilute mineral acids and some in water. Solutions of the compounds prepared fluoresce when excited by visible light.

Hence condensation of salicylaldehydes with 2-benzazolylacetonitriles can be used to prepare 3-benzazolylcoumarins. We have shown that secondary amine aminals are efficient reagents for the selective aminomethylation of coumarins which contain azole substituents.

EXPERIMENTAL

Monitoring of the reaction course and the purity of the compounds prepared was carried out by TLC on Silufol UV-254 plates. A mixture of chloroform-methanol (9: 1, 95: 5) or ethyl acetate were used as eluent. ^{1}H NMR spectra were measured on Bruker WP 100SY and Varian VXR 300 instruments at working frequencies of 100 and 300 MHz respectively for solutions in DMSO-d_6 (acetone-d_6 for compound **5a**) and using TMS as internal standard. Parameters for the synthesized compounds are given in Table 1 and ^{1}H NMR spectra in Tables 2 and 3.

3-Hetaryl-7-hydroxycoumarins 1a-f to 3a-f. The corresponding substituted 2-hydroxybenzaldehyde (0.1 mol) and 2-heterylacetonitrile (0.1 mol) were dissolved in the minimum volume of ethanol or 2-propanol at 40-50°C. Piperidine (3-5 drops) was added to the solution and the reaction mixture was held for one day at room temperature. After filtration, the precipitated 2-iminocoumarin was washed with alcohol and refluxed for 2-3 h in water (500 ml) containing conc. H_2SO_4 (5-10 ml) in order to hydrolyze the 2-iminocoumarin. The precipitate formed was filtered off, dried, and recrystallized from DMF or from a mixture of DMF and 2-propanol.

3-(2-Benzimidazolyl)-8-methoxycoumarin (1f). ^{1}H NMR spectrum, δ, ppm: 9.04 (1H, s, 4-H); 7.17-7.77 (7H, m, 3H coumarin (coum) residue and 4H benzimidazole (bzi) residue); 3.91 (3H, s, OCH_3).

3-(1-Methylbenzimidazol-2-yl)-8-methoxycoumarin (2f). ^{1}H NMR spectrum, δ, ppm: 8.75 (1H, s, 4-H); 7.42-7.90 (7H, m, 3H coum and 4H bzi); 3.98 (6H, s, OCH_3 and NCH_3).

3-(2-Benzothiazolyl)-8-methoxycoumarin (3f). ^{1}H NMR spectrum, δ, ppm: 9.15 (1H, s, 4-H); 8.00-8.22 (2H, m, 5- and 8-H benzothiazole (bzt)); 7.32-7.65 (5H, m, 5-, 6-, 7-H coum and 6-, 7-H bzt); 3.94 (3H, s, OCH_3).

7-Acyloxy-3-(2-benzazolyl)coumarins (4a, 5a-c, 6a-c). The appropriate acid anhydride or acid chloride (10 mmol) was added to a solution of the corresponding coumarin **1e-3e** (5 mmol) and the mixture was held for one day at room temperature. The precipitated products **4a, 5a-c, 6a-c** were filtered off, washed with 2-propanol, dried, and crystallized from DMF.

7-Acetoxy-3-(2-benzimidazolyl)coumarin (4a). ^{1}H NMR spectrum, δ, ppm, *J* (Hz): 9.08 (1H, s, 4-H); 8.05 (1H, d, ^3J = 8.8, 5-H); 7.17-7.72 (6H, m, 4H bzi and 6-, 8-H coum); 2.35 (3H, s, 7-$OCOCH_3$).

7-Acetoxy-3-(1-methylbenzimidazol-2-yl)coumarin (5a). ^{1}H NMR spectrum, δ, ppm: 8.44 (1H, s, 4-H); 7.17-8.00 (7H, m, 3H coum and 4H bzi); 3.87 (3H, s, NCH_3); 2.35 (3H, s, 7-$OCOCH_3$).

3-(1-Methylbenzimidazol-2-yl)-7-furoyloxycoumarin (5b). ^{1}H NMR spectrum, δ, ppm, *J* (Hz): 8.62 (1H, s, 4-H); 8.16 (1H, m, 5-H_R); 8.00 (1H, d, ^3J = 8.8, 5-H); 7.20-7.75 (7H, m, 2H coum, 4H bzi, and 3-H_R); 6.86 (1H, m, 4-H_R); 3.81 (3H, s, NCH_3).

3-(1-Methylbenzimidazol-2-yl)-7-(4-methoxybenzoyl)oxycoumarin (5c). ^{1}H NMR spectrum, δ, ppm, *J* (Hz); 8.60 (1H, s, 4-H); 8.0 (1H, d, ^3J = 9.0, 5-H); 7.20-7.60 (6H, m, 2H coum and 4H bzi); 7.16 and 8.15 (2H, 2H, two d, ^3J = 8.4, H_R); 3.89 (3H, s, OCH_3); 3.78 (3H, s, NCH_3).

7-Acetoxy-3-(2-benzothiazolyl)coumarin (6a). ^{1}H NMR spectrum, δ, ppm, *J* (Hz): 9.16 (1H, s, 4-H); 8.07 (1H, d, ^3J = 9.0, 5-H); 7.18-8.20 (6H, m, 2H coum, and 4H bzt); 2.33 (3H, s, 7-$OCOCH_3$).

3-(2-Benzothiazolyl)-7-(2-furoyloxy)coumarin (6b). ^{1}H NMR spectrum, δ, ppm: 9.26 (1H, s, 4-H); 8.00-8.23 and 7.35-7.70 (4H and 5H, two m, 3H coum, 4H bzt, and $2H_R$); 6.85 (1H, m, 4-H_R).

3-(2-Benzothiazolyl)-7-(4-methoxybenzoyl)oxycoumarin (6c). ^{1}H NMR spectrum, δ, ppm, *J* (Hz): 9.23 (1H, s, 4-H); 8.00-8.20 and 7.30-7.65 (5H and 4H, two m, 3H coum, 4H bzt, and $2H_R$); 7.13 (2H, d, ^3J = 8.4, H_R); 3.87 (3H, s, OCH_3).

3-(2-Benzothiazolyl)-7-mesyloxycoumarins 5d, 6d were prepared similarly to **4a**, **5a-c**, and **6a-c** from the coumarin **2e**, **3e** (5 mmol) and methanesulfonyl chloride (0.8 ml, 10 mmol). They were crystallized from a mixture of DMF and 2-propanol.

3-(1-Methylbenzimidazol-2-yl)-7-methylsulfonyloxycoumarin (5d). ^{1}H NMR spectrum, δ, ppm, *J* (Hz); 8.61 (1H, s, 4-H); 8.03 (1H, d, ^3J = 8.7, 5-H); 7.25-7.80 (6H, m, 2H coum and 4H bzi); 3.79 (3H, s, NCH_3); 3.52 (3H, s, 7-OSO_2CH_3).

3-(2-Benzothiazolyl)-7-methylsulfonyloxycoumarin (6d). ^{1}H NMR spectrum, δ, ppm, *J* (Hz): 9.22 (1H, s, 4-H); 8.18 (1H, d, ^3J = 9.0, 5-H); 8.00-8.15 and 7.40-7.65 (4H and 2H, two m, 2H coum and 4H bzt); 3.53 (3H, s, 7-OSO_2CH_3).

7-Alkoxy-3-(2-benzazolyl)coumarins (5e, 6e,f). A mixture of coumarin **2e** or **3e** (5 mmol), freshly ignited potassium carbonate (2.5 g, 18 mmol), and dimethylsulfate (0.7 ml, 7 mmol) or ethyl bromoacetate (0.75 ml, 6.7 mmol) in acetone (30 ml) was refluxed with stirring for 8-10 h. The precipitate was filtered off, washed with acetone poured into water (300 ml), and neutralized with hydrochloric acid. The precipitated product was filtered off and crystallized from dimethylformamide.

3-(2-Benzothiazolyl)-2-oxo-2H-chromen-7-yloxyacetic Acid (6g). A solution of the ethyl ester **6f** (1.9 g, 5 mmol) in acetic acid (20 ml) and sulfuric acid (1 ml) was refluxed for 4-5 h. The solution was poured onto ice and the precipitate was filtered off and crystallized from dimethylformamide.

Aminomethylation of the Coumarins 1e-3e A mixture of the coumarin (5 mmol) and bis(dimethylamino)methane, bis(diethylamino)methane, bis(morpholino)methane, bis(piperidino)methane, or bis(4-methylpiperazinyl)methane (6 mmol) in absolute dioxane (25 ml) was refluxed until a clear solution was obtained. The reaction mixture was cooled and the precipitated crystals were filtered off and recrystallized from dioxane to give the compounds **7a-b** to **9a-b** and **10a-c** to **12a-c**. The diethylaminomethyl derivatives **7-9** were obtained after evaporation of the reaction mixture and crystallization of the residue from toluene.

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